

# Rhodium(III)-catalysed C-H Activation/Annulation with Vinyl Esters as an Acetylene Equivalent

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## General Experimental

All experiments were conducted in oven-dried glassware, under a dry nitrogen atmosphere with anhydrous solvents, unless otherwise stated. Hygroscopic cesium acetate (CsOAc) was ground and dried in the oven at 160 °C, then stored in a desiccator. MeOH was distilled from CaH<sub>2</sub> onto 3Å molecular sieves. All other solvents and reagents were obtained from commercial sources and used without further purification. *O*-(Pivaloyl)hydroxylammonium chloride<sup>1</sup> and *O*-(pivaloyl)-hydroxylamine triflic acid<sup>2</sup> were prepared according to literature procedures.

Flash column chromatography was performed using Fischer Matrix silica gel (35-70 µm particles) and thin layer chromatography was carried out using pre-coated silica plates (Merck silica Kieselgel 60F<sub>254</sub>). Spots were visualised using UV fluorescence ( $\lambda_{\text{max}}$  = 254 nm) or chemical staining with potassium permanganate. All chromatography eluents were BDH GPR grade and used without purification. Petrol refers to petroleum ether (b.p. 40-60°C).

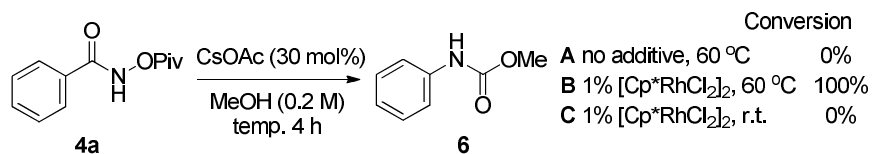
Proton (<sup>1</sup>H) and carbon (<sup>13</sup>C{<sup>1</sup>H}) nuclear magnetic resonance spectra were recorded using a Bruker DPX 300, a Bruker DRX 500 or a Bruker Avance 500 spectrometer using an internal deuterium lock. <sup>1</sup>H NMR chemical shifts ( $\delta$ ) are quoted in ppm downfield of tetramethylsilane or residual solvent peaks and coupling constants (*J*) are quoted in Hz. <sup>13</sup>C{<sup>1</sup>H} NMR spectra were recorded with broadband proton decoupling at 75 MHz and 125 MHz. Assignments were made on the basis of chemical shift and coupling data, using COSY and DEPT where necessary. Infra-red spectra were recorded on a Perkin Elmer Spectrum one FT-IR spectrometer, with absorption reported in wavenumbers (cm<sup>-1</sup>). High resolution electrospray mass spectra (ESI-MS) were measured on a Bruker MicroTOF-Q or Bruker MaXis Impact spectrometer in positive mode.

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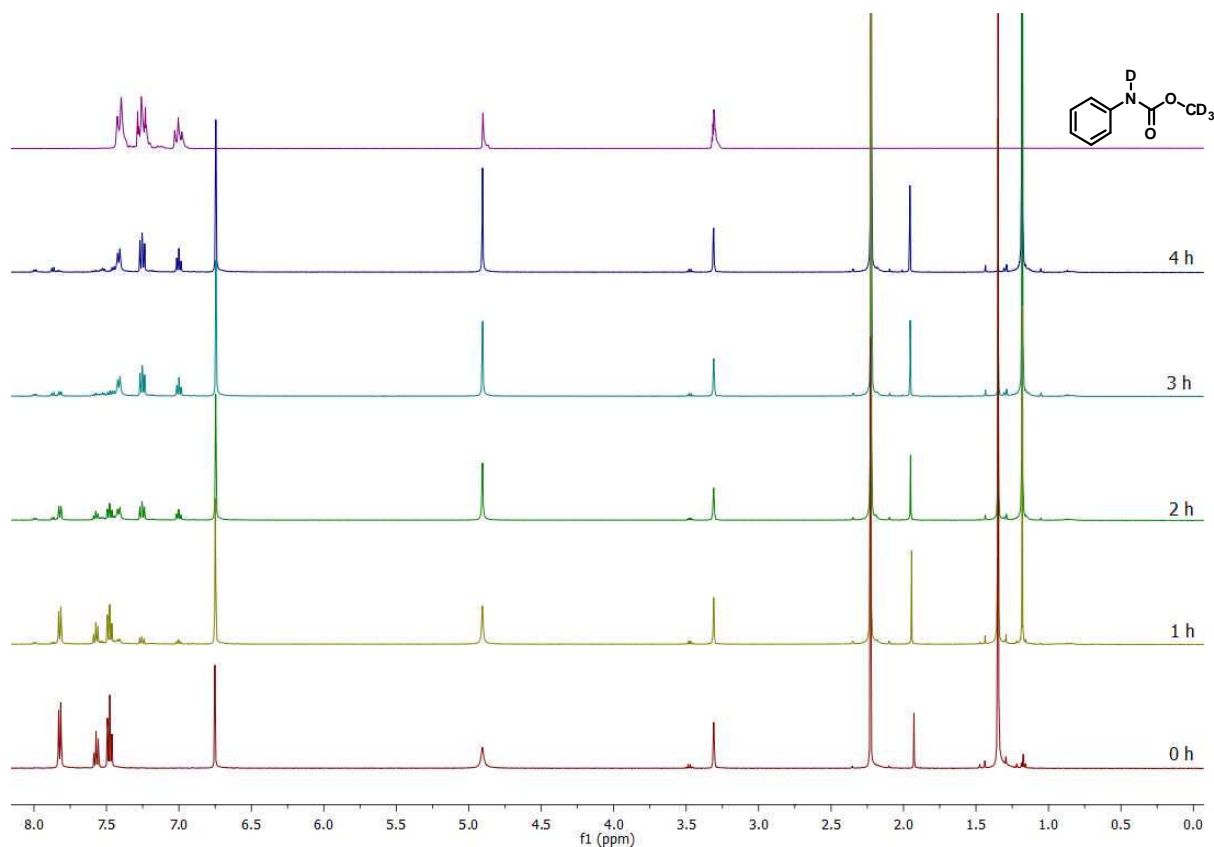
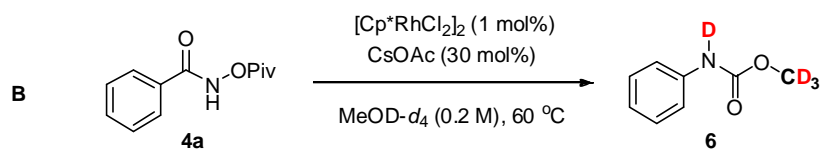
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## Experimental

### $^1\text{H}$ NMR study of the Lossen rearrangement

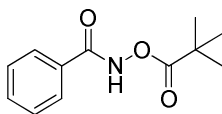


*N*-(Pivaloyloxy)benzamide (22 mg, 0.10 mmol), CsOAc (6.0 mg, 0.3 mmol) and  $[\text{Cp}^*\text{RhCl}_2]_2$  (0.6 mg, 1  $\mu\text{mol}$ ) for **B** and **C**) were weighed into a NMR tube fitted with a Young's tap under an  $\text{N}_2$  atmosphere. To each NMR tube was added mesitylene (14  $\mu\text{L}$ , 0.10 mmol), followed by  $\text{MeOD-}d_4$  (0.5 mL, 0.2 M). The tubes were sealed and shaken and reactions **A** and **B** were heated to 60 °C.  $^1\text{H}$  NMR analysis was taken at the following time points: 0, 1, 2, 3 and 4 hours. After this time the reactions **A** and **C** contained unreacted starting material and reaction **B** showed >95% conversion to the methyl phenyl carbamate.



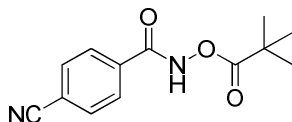
## Preparation of Starting Materials

### *N*-(Pivaloyloxy)benzamide (4a)<sup>3</sup>



A solution of benzhydroxamic acid (1.47 g, 10.7 mmol), NEt<sub>3</sub> (1.30 mL, 11.0 mmol) and pivaloyl chloride (1.30 mL, 11.0 mmol) in THF (60 mL, 0.18 M) was stirred at room temperature for 16 hours. The reaction mixture was diluted with EtOAc (50 mL) and washed with 1 M HCl (50 mL), water (2 x 50 mL) and brine (50 mL). The organic layer was dried over MgSO<sub>4</sub> and concentrated *in vacuo* to give an amorphous cream solid. The material was crystallised from Et<sub>2</sub>O–pentane to give a colourless microcrystalline powder, *N*-(pivaloyloxy)benzamide (2.08 g, 88%). m.p. 170-172 °C (Et<sub>2</sub>O–pentane) (literature value m.p. 169-170 °C);<sup>3</sup> R<sub>F</sub> 0.80 (50% EtOAc in hexane); δ<sub>H</sub> (500 MHz, CDCl<sub>3</sub>) 9.30 (1H, br s, NH), 7.83 (2H, d, *J* 7.9, ArH), 7.58 (1H, t, *J* 7.9, ArH), 7.48 (2H, t, *J* 7.9, ArH), 1.38 (9H, s, (CH<sub>3</sub>)<sub>3</sub>); δ<sub>C</sub> (75 MHz, CDCl<sub>3</sub>) 177.0 (C<sub>q</sub>O), 166.8 (C<sub>q</sub>N), 132.7, 131.0 (C<sub>q</sub>), 128.8, 127.5, 38.5 (C<sub>q</sub>), 27.1 ((CH<sub>3</sub>)<sub>3</sub>); HRMS: *m/z* calculated for formula C<sub>12</sub>H<sub>15</sub>NNaO<sub>3</sub> [MNa<sup>+</sup>]: 244.0944; found 244.0939. IR (ν<sub>max</sub>, solid, cm<sup>-1</sup>): 3240, 2975, 1781, 1650, 1516, 1482, 1369, 1267, 1068, 1025. Spectral data consistent with the literature.<sup>3</sup>

### 4-Cyano-*N*-(pivaloyloxy)benzamide (4b)

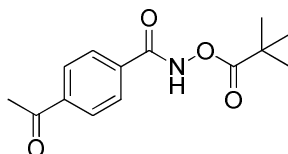


Oxalyl chloride (514 μL, 6.00 mmol) was added to a solution of 4-cyanobenzoic acid (736 mg, 5.00 mmol) in anhydrous DCM (25 mL, 0.2 M) with cat. DMF. The mixture was stirred at room temperature for 3 hours, then concentrated *in vacuo* to afford the crude acid chloride. The crude acid chloride was diluted in THF (5 mL) and transferred to a flask containing *O*-(pivaloyl)hydroxylammonium chloride (845 mg, 5.50 mmol) and NEt<sub>3</sub> (1.39 mL, 10.0 mmol) in THF (25 mL, 0.2 M) at 0 °C. After 2 hours the reaction was concentrated *in vacuo* and the residue was rediluted with sat. NaHCO<sub>3</sub> (50 mL) and EtOAc (50 mL). The two phases were separated and the organic layer was washed with brine (50 mL). The organic layer was dried over MgSO<sub>4</sub> and concentrated *in vacuo*. The final compound was isolated as a colourless solid (459 mg, 37%) by flash column chromatography using 10-20% EtOAc in hexane. A sample was taken and crystallised from CDCl<sub>3</sub>. R<sub>F</sub> 0.33 (9:1 hexane–EtOAc); m.p. 103.4-105.5 °C (CDCl<sub>3</sub>); δ<sub>H</sub> (500 MHz, CDCl<sub>3</sub>) 9.30 (1H, br s, NH), 7.92 (2H, d, *J* 8.5, ArH), 7.78 (2H, d, *J* 8.6, ArH), 1.37 (9H, s, (CH<sub>3</sub>)<sub>3</sub>); δ<sub>C</sub> (75 MHz, CDCl<sub>3</sub>) 176.8 (C<sub>q</sub>O), 165.0 (C<sub>q</sub>O), 134.8 (C<sub>q</sub>), 132.6, 128.2, 117.7 (C<sub>q</sub>), 116.2 (C<sub>q</sub>), 38.5 (C<sub>q</sub>), 27.0



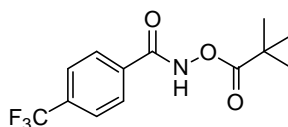
((CH<sub>3</sub>)<sub>3</sub>); HRMS:  $m/z$  calculated for formula C<sub>13</sub>H<sub>14</sub>N<sub>2</sub>NaO<sub>3</sub> [MNa<sup>+</sup>] 269.0897; found 269.0895; IR ( $\nu_{\text{max}}$ , solid, cm<sup>-1</sup>): 3223, 2982, 2234, 1781, 1648, 1519, 1480, 1398, 1366, 1308, 1281, 1064.

#### 4-Acetyl-*N*-(pivaloyloxy)benzamide (4c)



Oxalyl chloride (206  $\mu$ L, 2.40 mmol) was added to a solution of 4-acetylbenzoic acid (329 mg, 2.00 mmol) in anhydrous DCM (10 mL, 0.2 M) with cat. DMF. The mixture was stirred at room temperature for 3 hours, then concentrated *in vacuo* to afford the crude acid chloride. The crude acid chloride was diluted in EtOAc (5 mL) and transferred to a flask containing *O*-(pivaloyl)hydroxylammonium chloride (338 mg, 2.20 mmol) and K<sub>2</sub>CO<sub>3</sub> (552 mg, 4.00 mmol) dissolved in a 2:1 mixture of EtOAc–H<sub>2</sub>O (10 mL, 0.2 M) at 0 °C. After 2 hours the reaction was quenched with sat. NaHCO<sub>3</sub> (50 mL) and diluted with EtOAc (50 mL). The two phases were separated and the organic layer was washed with brine (50 mL). The organic layer was dried over MgSO<sub>4</sub> and concentrated *in vacuo*. The final compound was isolated as a colourless solid (105 mg, 10%) by flash column chromatography using 30% EtOAc in hexane.  $\delta_{\text{H}}$  (300 MHz, CDCl<sub>3</sub>) 9.72 (1H, s, NH), 7.98 (2H, d,  $J$  8.4, ArH), 7.87 (2H, d,  $J$  8.4, ArH), 2.61 (3H, s, CH<sub>3</sub>), 1.34 (9H, s, (CH<sub>3</sub>)<sub>3</sub>);  $\delta_{\text{C}}$  (75 MHz, CDCl<sub>3</sub>) 197.5 (C<sub>q</sub>O), 176.9 (C<sub>q</sub>O), 165.6 (C<sub>q</sub>O), 140.0 (C<sub>q</sub>), 134.8 (C<sub>q</sub>), 128.6, 127.8, 38.5 (C<sub>q</sub>), 27.0 ((CH<sub>3</sub>)<sub>3</sub>), 26.9 (CH<sub>3</sub>); HRMS:  $m/z$  calculated for formula C<sub>14</sub>H<sub>17</sub>NNaO<sub>4</sub> [MNa<sup>+</sup>] 286.1050; found 286.1048; IR ( $\nu_{\text{max}}$ , solid, cm<sup>-1</sup>): 3209, 2975, 1779, 1682, 1514, 1070.

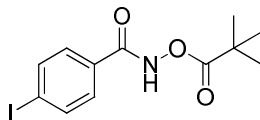
#### 4-(Trifluoromethyl)-*N*-(pivaloyloxy)benzamide (4d)



Oxalyl chloride (483  $\mu$ L, 5.63 mmol) was added to a solution of 4-(trifluoromethyl)benzoic acid (891 mg, 4.69 mmol) in anhydrous DCM (24 mL, 0.20 M) with cat. DMF. The mixture was stirred at room temperature for 3 hours, then concentrated *in vacuo* to afford the crude acid chloride. The crude acid chloride was diluted in THF (5 mL) and transferred to a flask containing *O*-(pivaloyl)hydroxylammonium chloride (794 mg, 5.16 mmol) and NEt<sub>3</sub> (1.31 mL, 9.38 mmol) in THF (24 mL, 0.20 M) at 0 °C. After 2 hours the reaction was concentrated *in vacuo* and the residue was rediluted with sat. NaHCO<sub>3</sub> (50 mL) and EtOAc (50 mL). The two phases were separated and the organic layer was washed with brine (50 mL). The organic layer was dried over MgSO<sub>4</sub> and concentrated *in vacuo* to give the crude *N*-(pivaloyloxy)benzamide derivative. The final compound was isolated as a colourless crystalline solid (813 mg, 60%) by crystallisation from Et<sub>2</sub>O–pentane. M.p. 121.1–123.7 °C (Et<sub>2</sub>O–pentane);  $\delta_{\text{H}}$  (300 MHz, CDCl<sub>3</sub>) 9.53 (1H, br s, NH), 7.91 (2H, d,  $J$  8.1,

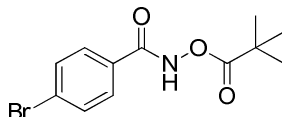
ArH), 7.71(2H, d, *J* 8.2, ArH), 1.36 (9H, s, <sup>t</sup>Bu);  $\delta_C$  (75MHz, CDCl<sub>3</sub>) 177.1 (OC=O), 165.5 (CONH), 134.5 (d, *J* 32.9, C<sub>4</sub>-CF<sub>3</sub>), 134.3 (C<sub>q</sub>), 128.1, 126.0 (q, *J* 3.7, C<sub>3</sub> and C<sub>5</sub>), 123.6 (d, *J* 272.8, CF<sub>3</sub>), 38.64 (C<sub>q</sub>), 27.1 ((CH<sub>3</sub>)<sub>3</sub>); HRMS: *m/z* calculated for formula C<sub>13</sub>H<sub>15</sub>F<sub>3</sub>NO<sub>3</sub> [MH<sup>+</sup>] 290.0999; found 290.0997; IR ( $\nu_{\max}$ , solid, cm<sup>-1</sup>): 2978, 1780, 1663, 1582, 1323, 1128, 1065, 1016.

#### 4-Iodo-*N*-(pivaloyloxy)benzamide (4e)



4-Iodobenzoyl chloride (799 mg, 3.00 mmol) was added to a flask containing *O*-(pivaloyl)hydroxylammonium chloride (508 mg, 3.30 mmol) and NEt<sub>3</sub> (836  $\mu$ L, 6.00 eq) in THF (15 mL, 0.2 M) at 0 °C. After 2 hours the reaction was concentrated *in vacuo* and the residue was rediluted with sat. NaHCO<sub>3</sub> (50 mL) and EtOAc (50 mL). The two phases were separated and the organic layer was washed with brine (50 mL). The organic layer was dried over MgSO<sub>4</sub> and concentrated *in vacuo*. The final compound was isolated by crystallisation from EtOAc–hexane. m.p. 152.5-153.2 °C (EtOAc–hexane);  $\delta_H$  (300 MHz, MeOD-*d*<sub>4</sub>) NH peak missing, 7.78 (2H, d, *J* 8.6, ArH), 7.46 (2H, d, *J* 8.6, ArH), 1.24 (9H, s, (CH<sub>3</sub>)<sub>3</sub>);  $\delta_C$  (75 MHz, MeOD-*d*<sub>4</sub>) 177.5 (C<sub>q</sub>O), 167.2 (C<sub>q</sub>-O), 139.2, 132.3 (C<sub>q</sub>), 130.1, 100.2 (C-I), 39.4 (C<sub>q</sub>), 27.5 ((CH<sub>3</sub>)<sub>3</sub>); HRMS: *m/z* calculated for formula C<sub>12</sub>H<sub>14</sub>INNaO<sub>3</sub> [MNa<sup>+</sup>] 369.9911; found 369.9903; IR ( $\nu_{\max}$ , solid, cm<sup>-1</sup>): 3140, 2971, 1781, 1648, 1584, 1475, 1007, 1004. Spectral data consistent with the literature.<sup>4</sup>

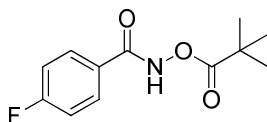
#### 4-Bromo-*N*-(pivaloyloxy)benzamide (4f)



Oxalyl chloride (514  $\mu$ L, 6.00 mmol) was added to a solution of 4-bromobenzoic acid (1.01 mg, 5.00 mmol) in anhydrous DCM (25 mL, 0.2 M) with cat. DMF. The mixture was stirred at room temperature for 3 hours, then concentrated *in vacuo* to afford the crude acid chloride. The crude acid chloride was diluted in THF (5 mL) and transferred to a flask containing *O*-(pivaloyl)hydroxylammonium chloride (845 mg, 5.50 mmol) and NEt<sub>3</sub> (1.39 mL, 10.0 mmol) in THF (25 mL, 0.2 M) at 0 °C. After 2 hours the reaction was concentrated *in vacuo* and the residue was rediluted with sat. NaHCO<sub>3</sub> (50 mL) and EtOAc (50 mL). The two phases were separated and the organic layer was washed with brine (50 mL). The organic layer was dried over MgSO<sub>4</sub> and concentrated *in vacuo*. The desired compound was isolated as a colourless microcrystalline powder (924 mg, 62%) by flash column chromatography using 10-50% EtOAc in hexane followed by crystallisation from EtOAc–hexane. R<sub>F</sub> 0.28 (4:1 EtOAc–hexane); R<sub>F</sub> 0.53 (7:3 EtOAc–hexane); m.p. 141.2-141.7 °C (EtOAc–hexane);  $\delta_H$  (500 MHz, CDCl<sub>3</sub>) 9.24 (1H, br s, NH), 7.69 (2H, d, *J* 8.7, ArH), 7.62 (2H, d, *J* 8.7, ArH), 1.37 (9H, s, (CH<sub>3</sub>)<sub>3</sub>);  $\delta_C$  (75 MHz, CDCl<sub>3</sub>) 177.0 (C<sub>q</sub>O), 165.8 (C<sub>q</sub>O), 132.1,

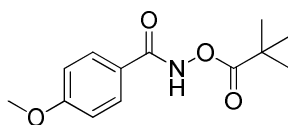
129.7 ( $C_q$ ), 129.0, 127.6 ( $C_q$ ), 38.5 ( $C_q$ ), 27.0 ( $((CH_3)_3)$ ); HRMS:  $m/z$  calculated for formula  $C_{12}H_{14-}^{79}BrNNaO_3 [MNa^+]$  322.0049; found 322.0050; IR ( $\nu_{max}$ , solid,  $cm^{-1}$ ): 3165, 2980, 1779, 1644, 1480, 1069. Spectral data consistent with the literature.<sup>5</sup>

#### 4-Fluoro-*N*-(pivaloyloxy)benzamide (4g)



Oxalyl chloride (309  $\mu$ L, 3.60 mmol) was added to a solution of 4-fluorobenzoic acid (420 mg, 3.00 mmol) in anhydrous DCM (15 mL, 0.2 M) with cat. DMF. The mixture was stirred at room temperature for 3 hours, then concentrated *in vacuo* to afford the crude acid chloride. The crude acid chloride was diluted in THF (5 mL) and transferred to a flask containing *O*-(pivaloyl)hydroxylammonium chloride (508 mg, 3.30 mmol) and  $NEt_3$  (836  $\mu$ L, 6.00 eq) in THF (15 mL, 0.2 M) at 0 °C. After 2 hours the reaction was concentrated *in vacuo* and the residue was rediluted with sat.  $NaHCO_3$  (50 mL) and EtOAc (50 mL). The two phases were separated and the organic layer was washed with brine (50 mL). The organic layer was dried over  $MgSO_4$  and concentrated *in vacuo*. The desired compound was isolated as a colourless microcrystalline powder (317 mg, 44%) by flash column chromatography using 20% EtOAc in hexane.  $\delta_H$  (300 MHz,  $CDCl_3$ ) 9.26 (1H, br s, NH), 7.86 (2H, dd,  $J$  8.7, 5.3, ArH), 7.17 (2H, t,  $J$  8.6, ArH), 1.38 (9H, s,  $(CH_3)_3$ );  $\delta_C$  (75 MHz,  $CDCl_3$ ) 177.1 ( $C_qO$ ), 165.9 ( $C_qO$ ), 165.4 (d,  $J$  252.8, C-F), 130.0 (d,  $J$  9.2,  $C_2$  and  $C_6$ ), 127.0 (d,  $J$  3.3,  $C_1$ ), 116.1 (d,  $J$  22.1,  $C_3$  and  $C_5$ ), 38.5 ( $C_q$ ), 27.2 ( $((CH_3)_3)$ ); HRMS:  $m/z$  calculated for formula  $C_{12}H_{14}FNNaO_3 [MNa^+]$  262.0850; found 262.0847; IR ( $\nu_{max}$ , solid,  $cm^{-1}$ ): 3194, 2976, 1784, 1652, 1602, 1493, 1237, 1075.

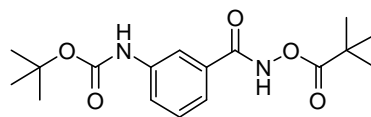
#### 4-Methoxy-*N*-(pivaloyloxy)benzamide (4h)



4-Methoxybenzoyl chloride (510 mg, 3.00 mmol) was diluted in THF (5 mL) and transferred to a flask containing *O*-(pivaloyl)hydroxylammonium chloride (508 mg, 3.30 mmol) and  $NEt_3$  (836  $\mu$ L, 6.00 eq) in THF (15 mL, 0.2 M) at 0 °C. After 2 hours the reaction was concentrated *in vacuo* and the residue was rediluted with sat.  $NaHCO_3$  (50 mL) and EtOAc (50 mL). The two phases were separated and the organic layer was washed with brine (50 mL). The organic layer was dried over  $MgSO_4$  and concentrated *in vacuo*. The desired compound was isolated as a colourless crystalline solid (613 mg, 81%) by crystallisation from  $CHCl_3$ . M.p. 149.0-150.2 °C ( $CHCl_3$ );  $\delta_H$  (300 MHz,  $CDCl_3$ ) 9.27 (1H, br s, NH), 7.81 (2H, d,  $J$  9.0, ArH), 6.96 (2H, d,  $J$  9.0, ArH), 3.88 (3H, s, OMe), 1.38 (9H, s,  $(CH_3)_3$ );  $\delta_C$  (75 MHz,  $CDCl_3$ ) 177.3 ( $C_qO$ ), 166.7 ( $C_qO$ ), 163.2 ( $C_qO$ ), 129.5, 123.0 ( $C_q$ ), 114.1, 55.5, 38.5 ( $C_q$ ), 27.1 ( $((CH_3)_3)$ ); HRMS:  $m/z$  calculated for formula  $C_{13}H_{17}NNaO_4 [MNa^+]$  274.1050; found 274.1045;

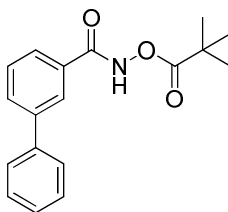
IR ( $\nu_{\max}$ , solid,  $\text{cm}^{-1}$ ): 3259, 2974, 1774, 1605, 1494, 1318, 1260, 1073, 1028, 751, 622. Spectral data consistent with the literature.<sup>2</sup>

***tert*-Butyl (3-((pivaloyloxy)carbamoyl)phenyl) carbamate (4i)**



Oxalyl chloride (309  $\mu\text{L}$ , 3.60 mmol) was added to a solution of 3-((*tert*-butoxycarbonyl)amino)benzoic acid (1.01 g, 3.00 mmol) in anhydrous DCM (15 mL, 0.2 M) with cat. DMF. The mixture was stirred at room temperature for 3 hours, then concentrated *in vacuo* to afford the crude acid chloride. The crude acid chloride was diluted in THF (5 mL) and transferred to a flask containing *O*-(pivaloyl)hydroxylammonium chloride (508 mg, 3.30 mmol) and  $\text{NEt}_3$  (836  $\mu\text{L}$ , 6.00 eq) in THF (15 mL, 0.2 M) at 0  $^{\circ}\text{C}$ . After 2 hours the reaction was concentrated *in vacuo* and the residue was rediluted with sat.  $\text{NaHCO}_3$  (50 mL) and EtOAc (50 mL). The two phases were separated and the organic layer was washed with brine (50 mL). The organic layer was dried over  $\text{MgSO}_4$  and concentrated *in vacuo*. The desired compound was isolated as a colourless dried foam (628 mg, 62%) by flash column chromatography using 20% EtOAc in hexane.  $\delta_{\text{H}}$  (300 MHz,  $\text{CDCl}_3$ ) 9.39 (1H, br s, NH), 7.85 (1H, s, ArH), 7.55 (1H, d,  $J$  7.6, ArH), 7.48 (1H, d,  $J$  7.6, ArH), 7.38 (1H, t,  $J$  7.8, ArH), 6.58 (1H, s, NH), 1.52 (9H, s,  $\text{O}(\text{CH}_3)_3$ ), 1.36 (9H, s,  $(\text{CH}_3)_3$ );  $\delta_{\text{C}}$  (75 MHz,  $\text{CDCl}_3$ ) 177.1 ( $\text{C}_\text{q}\text{O}$ ), 166.4 ( $\text{C}_\text{q}\text{O}$ ), 152.9 ( $\text{C}_\text{q}\text{O}$ ), 139.0 ( $\text{C}_\text{q}$ ), 131.7 ( $\text{C}_\text{q}$ ), 129.5, 122.6, 122.0, 117.4, 81.1 ( $\text{OC}_\text{q}(\text{CH}_3)_3$ ), 38.5 ( $\text{C}_\text{q}(\text{CH}_3)_3$ ), 28.4 ( $\text{O}(\text{CH}_3)_3$ ), 27.1 ( $(\text{CH}_3)_3$ ); HRMS:  $m/z$  calculated for formula  $\text{C}_{17}\text{H}_{24}\text{N}_2\text{NaO}_5$  [ $\text{MNa}^+$ ] 359.1577; found 359.1571; IR ( $\nu_{\max}$ , solid,  $\text{cm}^{-1}$ ): 3288, 2978, 1781, 1727, 1672, 1591, 1543, 1480, 1236, 1159, 1078.

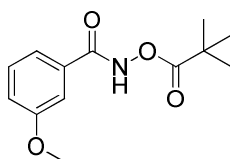
***N*-(Pivaloyloxy)-[1,1'-biphenyl]-3-carboxamide (4j)**



Oxalyl chloride (206  $\mu\text{L}$ , 2.40 mmol) was added to a solution of 3-biphenylcarboxylic acid (490 mg, 2.00 mmol) in anhydrous DCM (10 mL, 0.2 M) with cat. DMF. The mixture was stirred at room temperature for 3 hours, then concentrated *in vacuo* to afford the crude acid chloride. The crude acid chloride was diluted in EtOAc (5 mL) and transferred to a flask containing *O*-(pivaloyl)hydroxylammonium chloride (339 mg, 2.20 mmol) and  $\text{K}_2\text{CO}_3$  (552 mg, 4.00 mmol) dissolved in a 2:1 mixture of EtOAc– $\text{H}_2\text{O}$  (10 mL, 0.2 M) at 0  $^{\circ}\text{C}$ . After 2 hours the reaction was quenched with sat.  $\text{NaHCO}_3$  (50 mL) and diluted with EtOAc (50 mL). The two phases were separated and the organic layer was washed with brine (50 mL). The organic layer was dried over

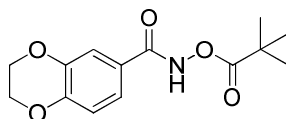
MgSO<sub>4</sub> and concentrated *in vacuo*. The desired compound was isolated as a colourless dried foam (180 mg, 30%) by flash column chromatography using 20% EtOAc in petrol.  $R_F$  0.33 (20% EtOAc in petrol);  $\delta_H$  (300 MHz, CDCl<sub>3</sub>) 9.33 (1H, s, NH), 8.05 (1H, t,  $J$  1.6, ArH), 7.82-7.76 (2H, m, ArH), 7.63-7.58 (2H, m, ArH), 7.55-7.35 (4H, m, ArH), 1.38 (9H, s, (CH<sub>3</sub>)<sub>3</sub>);  $\delta_C$  (75 MHz, CDCl<sub>3</sub>) 177.1 (C<sub>q</sub>O), 166.8 (C<sub>q</sub>O), 142.0 (C<sub>q</sub>), 139.8 (C<sub>q</sub>), 131.5 (C<sub>q</sub>), 131.4, 129.3, 129.0, 128.0, 127.2, 126.3, 126.1, 38.5 (C<sub>q</sub>), 27.1 ((CH<sub>3</sub>)<sub>3</sub>); HRMS:  $m/z$  calculated for formula: C<sub>18</sub>H<sub>20</sub>NO<sub>3</sub> [MH<sup>+</sup>] 298.1438; found 298.1436; IR ( $\nu_{max}$ , solid, cm<sup>-1</sup>): 3038, 2975, 1786, 1652, 1514, 1077.

### 3-Methoxy-*N*-(pivaloyloxy)benzamide (4k)



Oxalyl chloride (514  $\mu$ L, 6.00 mmol) was added to a solution of 3-methoxybenzoic acid (760 mg, 5.00 mmol) in anhydrous DCM (25 mL, 0.2 M) with cat. DMF. The mixture was stirred at room temperature for 3 hours and then concentrated *in vacuo* to afford the crude acid chloride. The crude acid chloride was diluted in EtOAc (5 mL) and transferred to a flask containing *O*-(pivaloyl)hydroxylammonium chloride (845 mg, 5.50 mmol) and K<sub>2</sub>CO<sub>3</sub> (1.38 g, 10.0 mmol) dissolved in a 2:1 mixture of EtOAc–H<sub>2</sub>O (25 mL, 0.2 M) at 0 °C. After 2 hours the reaction was quenched with sat. NaHCO<sub>3</sub> (50 mL) and diluted with EtOAc (50 mL). The two phases were separated and the organic layer was washed with brine (50 mL). The organic layer was dried over MgSO<sub>4</sub> and concentrated *in vacuo*. The desired compound was isolated as an amorphous solid (984 mg, 76%) by flash column chromatography using 20% EtOAc in hexane.  $\delta_H$  (300 MHz, CDCl<sub>3</sub>) 9.41 (1H, s, NH), 7.25 (3H, m, ArH), 6.98 (1H, dt,  $J$  9.8, 3.4, ArH), 3.74 (3H, s, OMe), 1.37 (9H, s, (CH<sub>3</sub>)<sub>3</sub>);  $\delta_C$  (75 MHz, CDCl<sub>3</sub>) 177.0 (C<sub>q</sub>O), 166.6 (C<sub>q</sub>O), 159.8 (C<sub>q</sub>O), 132.1 (C<sub>q</sub>), 129.8, 119.3, 119.2, 112.3, 55.5, 38.5 (C<sub>q</sub>), 27.0 ((CH<sub>3</sub>)<sub>3</sub>); HRMS:  $m/z$  calculated for formula C<sub>13</sub>H<sub>17</sub>NNaO<sub>4</sub> [MNa<sup>+</sup>] 274.1050; found 274.1055; IR ( $\nu_{max}$ , solid, cm<sup>-1</sup>): 3550, 3212, 2970, 1783, 1667, 1067.

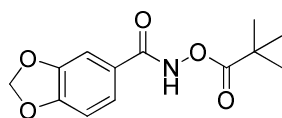
### *N*-(Pivaloyloxy)-2,3-dihydrobenzo[*b*][1,4]dioxine-6-carboxamide (4l)



Oxalyl chloride (285  $\mu$ L, 3.32 mmol) was added to a solution of 2,3-dihydrobenzo[*b*][1,4]dioxine-6-carboxylic acid (500 mg, 2.77 mmol) in anhydrous DCM (14 mL, 0.2 M) with cat. DMF. The mixture was stirred at room temperature for 3 hours, then concentrated *in vacuo* to afford the crude acid chloride. The crude acid chloride was diluted in EtOAc (5 mL) and transferred to a flask containing *O*-(pivaloyl)hydroxylammonium chloride (469 mg, 3.05 mmol) and K<sub>2</sub>CO<sub>3</sub> (765 mg, 5.54 mmol) dissolved in a 2:1 mixture of EtOAc–H<sub>2</sub>O (14 mL, 0.2 M) at 0 °C. After 2 hours the reaction

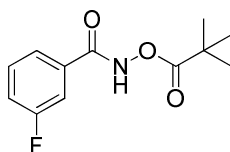
was quenched with sat.  $\text{NaHCO}_3$  (50 mL) and diluted with EtOAc (50 mL). The two phases were separated and the organic layer was washed with brine (50 mL). The organic layer was dried over  $\text{MgSO}_4$  and concentrated *in vacuo*. The desired compound was isolated as a colourless microcrystalline solid (565 mg, 73%) by flash column chromatography using 33% EtOAc in hexane followed by crystallisation from hexane–EtOAc. m.p. 126.1 – 128.6 °C (hexane–EtOAc);  $\delta_{\text{H}}$  (300 MHz,  $\text{CDCl}_3$ ) 9.29 (1H, br s, NH), 7.37–7.29 (2H, m, ArH), 6.89 (1H, d,  $J$  8.4, ArH), 4.34–4.21 (4H, m,  $\text{O}(\text{CH}_2)_2$ ), 1.35 (9H, s,  $(\text{CH}_3)_3$ );  $\delta_{\text{C}}$  (75 MHz,  $\text{CDCl}_3$ ) 177.2 ( $\text{C}_q\text{O}$ ), 166.3 ( $\text{C}_q\text{O}$ ), 147.6 ( $\text{C}_q$ ), 143.6 ( $\text{C}_q$ ), 123.9 ( $\text{C}_q$ ), 121.1, 117.6, 117.0, 64.6 ( $\text{O}(\text{CH}_2)\text{O}$ ), 64.1 ( $\text{CH}_2$ ), 38.5 ( $\text{C}_q$ ), 27.0 ( $(\text{CH}_3)_3$ ); HRMS:  $m/z$  calculated for formula  $\text{C}_{14}\text{H}_{17}\text{NNaO}_5$  [ $\text{MNa}^+$ ] 302.0999; found 302.0998; IR ( $\nu_{\text{max}}$ , solid,  $\text{cm}^{-1}$ ): 3208, 2976, 1777, 1645, 1488, 1288, 1062.

### ***N*-(Pivaloyloxy)benzo[*d*][1,3]dioxole-5-carboxamide (4m)**



Oxalyl chloride (309  $\mu\text{L}$ , 3.60 mmol) was added to a solution of piperonylic acid (498 mg, 3.00 mmol) in anhydrous DCM (15 mL, 0.2 M) with cat. DMF. The mixture was stirred at room temperature for 3 hours, then concentrated *in vacuo* to afford the crude acid chloride. The crude acid chloride was diluted in EtOAc (5 mL) and transferred to a flask containing *O*-(pivaloyl)hydroxylammonium chloride (508 mg, 3.30 mmol) and  $\text{K}_2\text{CO}_3$  (828 mg, 6.00 mmol) dissolved in a 2:1 mixture of EtOAc– $\text{H}_2\text{O}$  (15 mL, 0.2 M) at 0 °C. After 2 hours the reaction was quenched with sat.  $\text{NaHCO}_3$  (50 mL) and diluted with EtOAc (50 mL). The two phases were separated and the organic layer was washed with brine (50 mL). The organic layer was dried over  $\text{MgSO}_4$  and concentrated *in vacuo*. The desired compound was isolated as a colourless crystalline solid (663 mg, 83%) by crystallisation from EtOAc. M.p. 140.6–141.9 °C (EtOAc);  $\delta_{\text{H}}$  (300 MHz,  $\text{CDCl}_3$ ) 9.17 (1H, s, NH), 7.39 (1H, dd,  $J$  8.1, 1.7, ArH), 7.29 (1H, d,  $J$  1.7, ArH), 6.86 (1H, d,  $J$  8.1, ArH), 6.05 (2H, s,  $\text{OCH}_2\text{O}$ ), 1.36 (9H, s,  $(\text{CH}_3)_3$ );  $\delta_{\text{C}}$  (75 MHz,  $\text{CDCl}_3$ ) 177.2 ( $\text{C}_q\text{O}$ ), 166.4 ( $\text{C}_q\text{O}$ ), 151.4 ( $\text{C}_q\text{O}$ ), 148.1 ( $\text{C}_q\text{O}$ ), 124.8 ( $\text{C}_q$ ), 122.6, 108.3, 107.9, 101.9, 38.5 ( $\text{C}_q$ ), 27.0 ( $(\text{CH}_3)_3$ ); HRMS:  $m/z$  calculated for formula  $\text{C}_{13}\text{H}_{15}\text{NNaO}_5$  [ $\text{MNa}^+$ ] 288.0842; found 288.0848; IR ( $\nu_{\text{max}}$ , solid,  $\text{cm}^{-1}$ ): 3215, 2971, 1771, 1645, 1479, 1263, 1094.

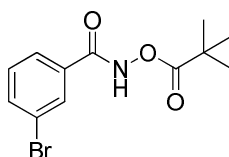
### **3-Fluoro-*N*-(pivaloyloxy)benzamide (4n)**



Oxalyl chloride (309  $\mu\text{L}$ , 3.60 mmol) was added to a solution of 3-fluorobenzoic acid (420 mg, 3.00 mmol) in anhydrous DCM (15 mL, 0.2 M) with cat. DMF. The mixture was stirred at room

temperature for 3 hours, then concentrated *in vacuo* to afford the crude acid chloride. The crude acid chloride was diluted in THF (5 mL) and transferred to a flask containing *O*-(pivaloyl)hydroxylammonium chloride (508 mg, 3.30 mmol) and NEt<sub>3</sub> (836  $\mu$ L, 6.00 eq) in THF (15 mL, 0.2 M) at 0 °C. After 2 hours the reaction was concentrated *in vacuo* and the residue was diluted with sat. NaHCO<sub>3</sub> (50 mL) and EtOAc (50 mL). The two phases were separated and the organic layer was washed with brine (50 mL). The organic layer was dried over MgSO<sub>4</sub> and concentrated *in vacuo*. The desired compound was isolated as a colourless crystalline solid (474 mg, 66%) by flash column chromatography using 20% EtOAc in hexane.  $\delta_{\text{H}}$  (300 MHz, CDCl<sub>3</sub>) 9.30 (1H, s, NH), 7.61-7.56 (1H, m, ArH), 7.55-7.50 (1H, m, ArH), 7.47 (1H, td, *J* 8.0, 5.4, ArH), 7.31-7.29 (1H, m, ArH), 1.39 (9H, s, (CH<sub>3</sub>)<sub>3</sub>);  $\delta_{\text{C}}$  (75 MHz, CDCl<sub>3</sub>) 177.1 (C<sub>q</sub>O), 165.5 (C<sub>q</sub>O), 162.8 (d, *J* 248.7, C-F), 133.1 (d, *J* 7.0, C<sub>1</sub>), 130.7 (d, *J* 7.9, C<sub>5</sub>), 123.1 (d, *J* 3.2, C<sub>6</sub>), 119.9 (d, *J* 21.2, C<sub>2</sub>), 115.0 (d, *J* 23.3, C<sub>4</sub>), 38.6 (C<sub>q</sub>), 27.3 ((CH<sub>3</sub>)<sub>3</sub>); HRMS: *m/z* calculated for formula C<sub>12</sub>H<sub>14</sub>FNNaO<sub>3</sub> [MNa<sup>+</sup>] 262.0850; found 262.0847; IR ( $\nu_{\text{max}}$ , solid, cm<sup>-1</sup>): 3194, 2976, 1784, 1652, 1602, 1493, 1237, 1075.

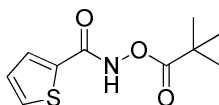
### 3-Bromo-*N*-(pivaloyloxy)benzamide (4o)



Oxalyl chloride (514  $\mu$ L, 6.00 mmol) was added to a solution of 3-bromocarboxylic acid (1.01 g, 5.00 mmol) in anhydrous DCM (25 mL, 0.2 M) with cat. DMF. The mixture was stirred at room temperature for 3 hours and then concentrated *in vacuo* to afford the crude acid chloride. The crude acid chloride was diluted in EtOAc (5 mL) and transferred to a flask containing *O*-(pivaloyl)hydroxylammonium chloride (845 mg, 5.50 mmol) and K<sub>2</sub>CO<sub>3</sub> (1.38 g, 10.0 mmol) dissolved in a 2:1 mixture of EtOAc–H<sub>2</sub>O (25 mL, 0.2 M) at 0 °C. After 2 hours the reaction was quenched with sat. NaHCO<sub>3</sub> (50 mL) and diluted with EtOAc (50 mL). The two phases were separated and the organic layer was washed with brine (50 mL). The organic layer was dried over MgSO<sub>4</sub> and concentrated *in vacuo*. The desired compound was isolated as colourless crystals (850 mg, 57%) by flash column chromatography using 20% EtOAc in hexane. *R*<sub>F</sub> 0.13 (20% EtOAc in hexane);  $\delta_{\text{H}}$  (300 MHz, CDCl<sub>3</sub>) 9.27 (1H, s, NH), 7.96 (1H, t, *J* 1.6, ArH), 7.80-7.63 (2H, m, ArH), 7.35 (1H, t, *J* 7.9, ArH), 1.36 (9H, s, (CH<sub>3</sub>)<sub>3</sub>);  $\delta_{\text{C}}$  (75 MHz, CDCl<sub>3</sub>) 176.7 (C<sub>q</sub>O), 165.1 (C<sub>q</sub>O), 135.5, 132.6 (C<sub>q</sub>), 130.7, 130.3, 126.0, 122.8 (C<sub>q</sub>), 38.5 (C<sub>q</sub>), 27.2 ((CH<sub>3</sub>)<sub>3</sub>); HRMS: *m/z* calculated for formula C<sub>12</sub>H<sub>14</sub><sup>79</sup>BrNNaO<sub>3</sub> [MNa<sup>+</sup>] 322.0049; found 322.0053; IR ( $\nu_{\text{max}}$ , solid, cm<sup>-1</sup>): 3251, 2816, 1784, 1660, 1301, 1068.

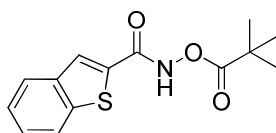
## Heterocyclic pivalate esters

### *N*-(Pivaloyloxy)thiophene-2-carboxamide (8a)



Oxalyl chloride (514  $\mu$ L, 6.00 mmol) was added to a solution of 2-thiophenecarboxylic acid (641 mg, 5.00 mmol) in anhydrous DCM (25 mL, 0.2 M) with cat. DMF. The mixture was stirred at room temperature for 3 hours and then concentrated *in vacuo* to afford the crude acid chloride. The crude acid chloride was diluted in EtOAc (5 mL) and transferred to a flask containing *O*-(pivaloyl)hydroxylammonium chloride (845 mg, 5.50 mmol) and  $K_2CO_3$  (1.38 g, 10.0 mmol) dissolved in a 2:1 mixture of EtOAc–H<sub>2</sub>O (25 mL, 0.2 M) at 0 °C. After 2 hours the reaction was quenched with sat.  $NaHCO_3$  (50 mL) and diluted with EtOAc (50 mL). The two phases were separated and the organic layer was washed with brine (50 mL). The organic layer was dried over  $MgSO_4$  and concentrated *in vacuo*. The desired compound was isolated as a colourless amorphous solid (455 mg, 40%) by flash column chromatography using 10% EtOAc in hexane.  $R_F$  0.22 (10% EtOAc in hexane);  $\delta_H$  (300 MHz,  $CDCl_3$ ) 9.18 (1H, s, NH), 7.67 (1H, dd,  $J$  3.8, 1.2, ArH), 7.59 (1H, dd,  $J$  5.0, 1.2, ArH); 7.13 (1H, dd,  $J$  5.0, 3.8, ArH), 1.38 (9H, s,  $(CH_3)_3$ );  $\delta_C$  (75 MHz,  $CDCl_3$ ) 177.1 ( $C_qO$ ), 161.9 ( $C_qO$ ), 133.6 ( $C_q$ ), 131.7, 130.5, 127.9, 38.5 ( $C_q$ ), 27.0 ( $(CH_3)_3$ ); HRMS:  $m/z$  calculated for formula:  $C_{10}H_{13}NNaO_3S$  [ $MNa^+$ ] 250.0508; found 250.0502; IR ( $\nu_{max}$ , solid,  $cm^{-1}$ ): 3208, 2938, 1784, 1625, 1478, 1245, 1070.

### *N*-(Pivaloyloxy)benzo[*b*]thiophene-2-carboxamide (8b)

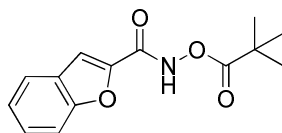


Oxalyl chloride (514  $\mu$ L, 6.00 mmol) was added to a solution of benzo[*b*]thiophene-2-carboxylic acid (891 mg, 5.00 mmol) in anhydrous DCM (25 mL, 0.2 M) with cat. DMF. The mixture was stirred at room temperature for 3 hours and then concentrated *in vacuo* to afford the crude acid chloride. The crude acid chloride was diluted in EtOAc (5 mL) and transferred to a flask containing *O*-(pivaloyl)hydroxylammonium chloride (845 mg, 5.50 mmol) and  $K_2CO_3$  (1.38 g, 10.0 mmol) dissolved in a 2:1 mixture of EtOAc–H<sub>2</sub>O (25 mL, 0.2 M) at 0 °C. After 2 hours the reaction was quenched with sat.  $NaHCO_3$  (50 mL) and diluted with EtOAc (50 mL). The two phases were separated and the organic layer was washed with brine (50 mL). The organic layer was dried over  $MgSO_4$  and concentrated *in vacuo*. The desired compound was isolated as a colourless solid (356 mg, 25%) by flash column chromatography using 30-50% EtOAc in hexane.  $R_F$  0.41 (50% EtOAc in hexane); m.p. 134.0-134.6 °C (EtOAc–hexane);  $\delta_H$  (300 MHz,  $CDCl_3$ ) 9.33 (1H, br s, NH), 7.93 (1H, s, ArH), 7.90-7.87 (2H, m, ArH), 7.51-7.40 (2H, m, ArH), 1.38 (9H, s,  $(CH_3)_3$ );  $\delta_C$  (75 MHz,  $CDCl_3$ )



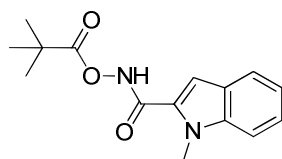
177.0 ( $C_qO$ ), 162.0 ( $C_qO$ ), 138.6 ( $C_q$ ), 133.2 ( $C_q$ ), 127.6, 127.0, 125.5, 125.1, 122.7, 38.5 ( $C_q$ ), 27.0 ( $((CH_3)_3)$ ) (one quaternary peak overlapped in the aromatic region); HRMS:  $m/z$  calculated for formula  $C_{14}H_{15}NNaO_3S$  [ $MNa^+$ ] 300.0665; found 300.0654; IR ( $\nu_{max}$ , solid,  $cm^{-1}$ ): 3170, 2970, 1781, 1632, 1528, 1064.

### ***N*-(Pivaloyloxy)benzofuran-2-carboxamide (8c)**



Oxalyl chloride (206  $\mu$ L, 2.40 mmol) was added to a solution of benzo[*b*]furan-2-carboxylic acid (416 mg, 2.00 mmol) in anhydrous DCM (10 mL, 0.2 M) with cat. DMF. The mixture was stirred at room temperature for 3 hours, then concentrated *in vacuo* to afford the crude acid chloride. The crude acid chloride was diluted in EtOAc (5 mL) and transferred to a flask containing *O*-(pivaloyl)hydroxylammonium chloride (339 mg, 2.20 mmol) and  $K_2CO_3$  (552 mg, 4.00 mmol) dissolved in a 2:1 mixture of EtOAc– $H_2O$  (10 mL, 0.2 M) at 0 °C. After 2 hours the reaction was quenched with sat.  $NaHCO_3$  (50 mL) and diluted with EtOAc (50 mL). The two phases were separated and the organic layer was washed with brine (50 mL). The organic layer was dried over  $MgSO_4$  and concentrated *in vacuo*. The desired compound was isolated as a colourless crystalline solid (258 mg, 49%) by crystallisation from EtOAc. m.p. 111–115 °C (EtOAc);  $\delta_H$  (300 MHz,  $CDCl_3$ ) missing NH peak, 7.70 (1H, d,  $J$  7.8, ArH), 7.59 (1H, s, ArH), 7.53 (1H, d,  $J$  8.2, ArH), 7.50–7.43 (1H, m, ArH), 7.32 (1H, t,  $J$  7.4, ArH), 1.38 (9H, s,  $(CH_3)_3$ );  $\delta_C$  (75 MHz,  $CDCl_3$ ) 176.6 ( $C_qO$ ), 157.2 ( $C_qO$ ), 155.2 ( $C_qO$ ), 146.2 ( $C_qO$ ), 127.8, 127.1 ( $C_q$ ), 124.2, 123.0, 112.8, 112.1, 38.6 ( $C_q$ ), 27.2 ( $((CH_3)_3)$ ); HRMS:  $m/z$  calculated for formula:  $C_{14}H_{15}NNaO_4$  [ $MNa^+$ ] 284.0893; found 284.0889; IR ( $\nu_{max}$ , solid,  $cm^{-1}$ ): 3128, 2971, 1787, 1653, 1072.

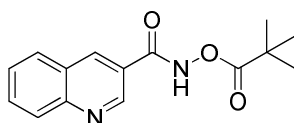
### **1-Methyl-*N*-(pivaloyloxy)-1*H*-indole-2-carboxamide (8d)**



Oxalyl chloride (422  $\mu$ L, 4.92 mmol) was added to a solution of 1-methyl-1*H*-indole-2-carboxylic acid (718 mg, 4.10 mmol) in anhydrous DCM (25 mL, 0.2 M) with cat. DMF. The mixture was stirred at room temperature for 3 hours, then concentrated *in vacuo* to afford the crude acid chloride. The crude acid chloride was diluted in THF (5 mL) and transferred to a flask containing *O*-(pivaloyl)hydroxylammonium chloride (692 mg, 4.51 mmol) and  $NEt_3$  (1.14 mL, 8.20 mmol) in THF (25 mL, 0.2 M) at 0 °C. After 2 hours the reaction was concentrated *in vacuo* and the residue was rediluted with sat.  $NaHCO_3$  (50 mL) and EtOAc (50 mL). The two phases were separated and the

organic layer was washed with brine (50 mL). The organic layer was dried over  $\text{MgSO}_4$  and concentrated *in vacuo*. The desired compound was isolated as a colourless solid (392 mg, 35%) by flash column chromatography using 0-5% EtOAc in hexane.  $R_F$  0.28 (20% EtOAc in hexane); m.p. 132.1-133.4 °C (EtOAc–hexane);  $\delta_H$  (300 MHz,  $\text{CDCl}_3$ ) 9.27 (1H, s, NH), 7.67 (1H, d,  $J$  8.0, ArH), 7.44-7.36 (2H, m, ArH), 7.18 (1H, ddd,  $J$  7.9, 6.3, 1.5, ArH), 7.08 (1H, s, ArH), 4.04 (3H, s,  $\text{NCH}_3$ ), 1.39 (9H, s,  $(\text{CH}_3)_3$ );  $\delta_C$  (75 MHz,  $\text{CDCl}_3$ ) 177.2 ( $\text{C}_q\text{O}$ ), 162.0 ( $\text{C}_q\text{O}$ ), 139.4 ( $\text{NC}_q$ ), 127.2 ( $\text{C}_q$ ), 125.9 ( $\text{C}_q$ ), 125.0, 122.3, 120.8, 110.2, 106.1, 38.5 ( $\text{C}_q$ ), 31.4 ( $\text{NCH}_3$ ), 27.1 ( $(\text{CH}_3)_3$ ); HRMS:  $m/z$  calculated for formula  $\text{C}_{15}\text{H}_{18}\text{N}_2\text{NaO}_3$  [ $\text{MNa}^+$ ] 297.1210; found 297.1211; IR ( $\nu_{\text{max}}$ , solid,  $\text{cm}^{-1}$ ): 3179, 2973, 1783, 1660, 1520, 1464, 1267, 1114, 1073, 1028.

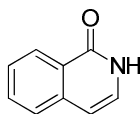
### ***N*-(Pivaloyloxy)isoquinoline-3-carboxamide (8g)**



Oxalyl chloride (309  $\mu\text{L}$ , 3.60 mmol) was added to a solution of quinoline-3-carboxylic acid (520 mg, 3.00 mmol) in anhydrous DCM (15 mL, 0.2 M) with cat. DMF. The mixture was stirred at room temperature for 3 hours, then concentrated *in vacuo* to afford the crude acid chloride. The crude acid chloride was diluted in THF (5 mL) and transferred to a flask containing *O*-(pivaloyl)hydroxylammonium chloride (508 mg, 3.30 mmol) and  $\text{NEt}_3$  (836  $\mu\text{L}$ , 6.00 eq) in THF (15 mL, 0.2 M) at 0 °C. After 2 hours the reaction was concentrated *in vacuo* and the residue was rediluted with sat.  $\text{NaHCO}_3$  (50 mL) and EtOAc (50 mL). The two phases were separated and the organic layer was washed with brine (50 mL). The organic layer was dried over  $\text{MgSO}_4$  and concentrated *in vacuo*. The desired compound was isolated as a colourless crystalline solid (365 mg, 45%) by crystallisation from DCM. M.p. 154.3-155.8 °C (DCM),  $\delta_H$  (300 MHz,  $\text{CDCl}_3$ ) 10.24 (1H, br s, NH), 9.24 (1H, d,  $J$  2.0, ArH), 8.62 (1H, d,  $J$  1.8, ArH), 8.09 (1H, d,  $J$  8.5, ArH), 7.82 (1H, t,  $J$  7.1, ArH), 7.78 (1H, d,  $J$  7.1, ArH), 7.59 (1H, app t,  $J$  7.3, ArH), 1.36 (9H, s,  $(\text{CH}_3)_3$ );  $\delta_C$  (75 MHz,  $\text{CDCl}_3$ ) 176.9 ( $\text{C}_q\text{O}$ ), 164.9 ( $\text{C}_q\text{O}$ ), 149.4 ( $\text{C}_q$ ), 147.8, 136.8, 131.9, 129.2, 128.9, 127.8, 126.7 ( $\text{C}_q$ ), 124.0 ( $\text{C}_q$ ), 38.5 ( $\text{C}_q$ ), 27.0 ( $(\text{CH}_3)_3$ ); HRMS:  $m/z$  calculated for formula  $\text{C}_{15}\text{H}_{16}\text{N}_2\text{O}_3$  [ $\text{MH}^+$ ] 273.1234; found 273.1230; IR ( $\nu_{\text{max}}$ , solid,  $\text{cm}^{-1}$ ): 3096, 1765, 1695, 1523, 1291, 1079.

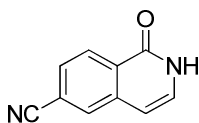
## Isoquinolone Substrate Scope

### Isoquinolin-1(2H)-one (5a)



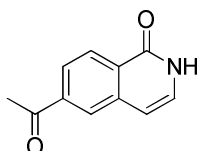
Vinyl acetate (138  $\mu$ L, 1.50 mmol) was added to a solution of  $[\text{Cp}^*\text{RhCl}_2]_2$  (6 mg, 0.01 mmol), CsOAc (58 mg, 0.3 mmol) and *N*-(pivaloyloxy)benzamide (221 mg, 1.00 mmol) in MeOH (5 mL, 0.2 M) in a vial under a nitrogen atmosphere. The reaction was heated to 45  $^\circ\text{C}$  for 16 hours, after which time the solvent was removed *in vacuo*. The product was triturated with a 2:1 mixture of Et<sub>2</sub>O–MeOH (5 mL) and crystallised from MeOH. The desired compound was isolated as a colourless solid (126 mg, 87%).  $\delta_{\text{H}}$  (500 MHz, DMSO-*d*<sub>6</sub>) 11.25 (1H, br s, NH), 8.19 (1H, d, *J* 9.0, ArH), 7.69–7.66 (2H, m, ArH), 7.65–7.47 (1H, m, ArH), 7.20–7.18 (1H, m, ArH), 6.54 (1H, d, *J* 9.0, ArH);  $\delta_{\text{C}}$  (75 MHz, DMSO-*d*<sub>6</sub>) 161.8 (C<sub>q</sub>O), 137.8 (C<sub>q</sub>), 132.3, 128.9, 126.6, 126.3, 126.2 (C<sub>q</sub>), 126.0, 104.6; HRMS: *m/z* calculated for formula C<sub>9</sub>H<sub>8</sub>NO [MH<sup>+</sup>]: 146.0600; found 146.0606; IR ( $\nu_{\text{max}}$ , solid, cm<sup>-1</sup>): 3286, 3158, 2852, 1633, 1548, 1475, 1343, 1228. Spectral data consistent with the literature.<sup>6</sup>

### 6-Cyanoisoquinolin-1(2H)-one (5b)



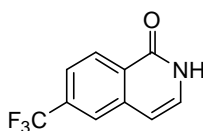
Vinyl acetate (50  $\mu$ L, 0.54 mmol) was added to a solution of  $[\text{Cp}^*\text{RhCl}_2]_2$  (3 mg, 0.005 mmol), CsOAc (28 mg, 0.15 mmol) and 4-cyano-*N*-(pivaloyloxy)benzamide (120 mg, 0.49 mmol) in MeOH (2.5 mL, 0.2 M) in a vial under a nitrogen atmosphere. The reaction was heated to 45  $^\circ\text{C}$  for 16 hours, after which time the solvent was removed *in vacuo*. The product was triturated with a 2:1 mixture of Et<sub>2</sub>O–MeOH (5 mL) and crystallised from MeOH. The desired compound was isolated as a pale yellow solid (68 mg, 81%). m.p. 307–312  $^\circ\text{C}$  (MeOH);  $\delta_{\text{H}}$  (300 MHz, DMSO-*d*<sub>6</sub>) 11.62 (1H, s, NH), 8.28 (1H, d, *J* 8.4, ArH), 8.25 (1H, s, ArH), 7.81 (1H, dd, *J* 8.3, 1.4, ArH), 7.35–7.29 (1H, m, ArH), 6.62 (1H, d, *J* 7.1, ArH);  $\delta_{\text{C}}$  (75 MHz, DMSO-*d*<sub>6</sub>) 106.9 (C<sub>q</sub>O), 137.9 (C<sub>q</sub>), 131.3, 131.0, 128.4 (C<sub>q</sub>), 128.0, 127.9, 118.3 (C<sub>q</sub>), 114.6 (C<sub>q</sub>), 103.6; HRMS: *m/z* calculated for formula C<sub>10</sub>H<sub>7</sub>N<sub>2</sub>O [MH<sup>+</sup>]: 171.0553; found 171.0575; IR ( $\nu_{\text{max}}$ , solid, cm<sup>-1</sup>): 3307, 2227, 1652, 1539, 1498, 1460, 1337, 1235, 951.

### 6-Acetylisquinolin-1(2H)-one (5c)



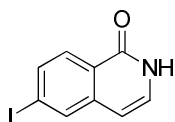
Vinyl acetate (35  $\mu$ L, 0.38 mmol) was added to a solution of [Cp\*RhCl<sub>2</sub>]<sub>2</sub> (2 mg, 0.003 mmol), CsOAc (14 mg, 0.075 mmol) and 4-acetyl-*N*-(pivaloyloxy)-benzamide (68 mg, 0.25 mmol) in MeOH (1.25 mL, 0.2 M) in a vial under a nitrogen atmosphere. The reaction was heated to 45 °C for 16 hours, after which time the solvent was removed *in vacuo*. The product was filtered from the crude reaction mixture and washed with MeOH–Et<sub>2</sub>O (1:4) (5 mL). The desired compound was isolated as a tan amorphous solid (48 mg, 99%).  $\delta_{\text{H}}$  (300 MHz, DMSO-*d*<sub>6</sub>) 11.79 (1H, s, NH), 8.28 (1H, s, ArH), 8.26 (1H, d, obscured by singlet, ArH), 7.93 (1H, dd, *J* 8.3, 1.2, ArH), 7.29 (1H, d, *J* 7.1, ArH), 6.68 (1H, d, *J* 7.1, ArH), 2.67 (3H, s, CH<sub>3</sub>);  $\delta_{\text{C}}$  (75 MHz, DMSO-*d*<sub>6</sub>) 198.0 (C<sub>q</sub>O), 161.4 (C<sub>q</sub>O), 139.3 (C<sub>q</sub>), 138.0 (C<sub>q</sub>), 130.1, 128.6 (C<sub>q</sub>), 127.2, 127.1, 124.5, 104.8, 27.0 (CH<sub>3</sub>); HRMS: *m/z* calculated for formula C<sub>11</sub>H<sub>10</sub>NO<sub>2</sub> [MH<sup>+</sup>] 188.0706; found 188.0699; IR ( $\nu_{\text{max}}$ , solid, cm<sup>-1</sup>): 3299, 2911, 1751, 1692, 1542, 1461, 1347, 1267, 1186, 961, 887, 801.

#### 6-(Trifluoromethyl)isoquinolin-1(2*H*)-one (5d)



Vinyl acetate (138  $\mu$ L, 1.50 mmol) was added to a solution of [Cp\*RhCl<sub>2</sub>]<sub>2</sub> (6 mg, 0.01 mmol), CsOAc (58 mg, 0.3 mmol) and 4-trifluoromethyl-*N*-(pivaloyloxy)benzamide (289 mg, 1.00 mmol) in MeOH (5 mL, 0.2 M) in a vial under a nitrogen atmosphere. The reaction was heated to 45 °C for 16 hours, after which time the solvent was removed *in vacuo*. The product was triturated with a 2:1 mixture of Et<sub>2</sub>O–MeOH (5 mL) and crystallised from CHCl<sub>3</sub>. The desired compound was isolated as a pale yellow crystalline solid (151 mg, 71%). *R*<sub>F</sub> 0.2 (1:1 EtOAc–hexane); M.p. 176–181 °C (chloroform);  $\delta_{\text{H}}$  (300 MHz, CDCl<sub>3</sub>) 11.6 (1H, br s, NH), 8.53 (1H, d, *J* 8.4, ArH), 7.86 (1H, s, ArH), 7.71 (1H, dd, *J* 8.4, 1.4, ArH), 7.29 (1H, d, *J* 7.1, ArH), 6.65 (1H, d, *J* 7.1, ArH);  $\delta_{\text{C}}$  (75 MHz, CDCl<sub>3</sub>) 163.7 (CONH), 138.2 (C<sub>q</sub>), 134.5 (d, *J* = 32.4), 129.3, 128.6, 128.3 (C<sub>q</sub>) 123.8 (d, *J* = 272.9, CF<sub>3</sub>), 123.8 (dd, *J* 8.0, 3.9), 123.0 (q, *J* 3.2), 106.6; HRMS: *m/z* calculated for formula C<sub>10</sub>H<sub>7</sub>F<sub>3</sub>NO [MH<sup>+</sup>] 214.0474; found 214.0475; IR ( $\nu_{\text{max}}$ , solid, cm<sup>-1</sup>): 3299, 2911, 1751, 1692, 1542, 1461, 1347, 1267, 1186, 961, 887, 801.

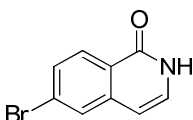
#### 6-Iodoisoquinolin-1(2*H*)-one (5e)



Vinyl acetate (138  $\mu$ L, 1.50 mmol) was added to a solution of [Cp\*RhCl<sub>2</sub>]<sub>2</sub> (6 mg, 0.01 mmol), CsOAc (58 mg, 0.3 mmol) and 4-iodo-*N*-(pivaloyloxy)benzamide (347 mg, 1.00 mmol) in MeOH (5 mL, 0.2 M) in a vial under a nitrogen atmosphere. The reaction was heated to 45 °C for 16 hours, after which time the solvent was removed *in vacuo*. The product was triturated with a 2:1 mixture of

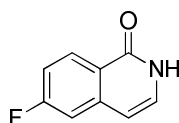
Et<sub>2</sub>O–MeOH (5 mL) and crystallised from MeOH. The desired compound was isolated as a cream amorphous solid (211 mg, 83%). m.p. decomposed at 231 °C (MeOH);  $\delta_{\text{H}}$  (300 MHz, DMSO-*d*<sub>6</sub>) 11.35 (1H, br s, NH), 8.12 (1H, s, ArH), 7.90 (1H, d, *J* 8.4, ArH), 7.78 (1H, d, *J* 8.2, ArH), 7.20–7.18 (1H, m, ArH), 6.49 (1H, d, *J* 7.1, ArH);  $\delta_{\text{C}}$  (75 MHz, DMSO-*d*<sub>6</sub>) 161.6 (C<sub>q</sub>O), 139.5 (C<sub>q</sub>), 134.8, 134.5, 130.2, 128.5, 125.1 (C<sub>q</sub>), 103.3, 100.7 (C<sub>q</sub>); HRMS: *m/z* calculated for formula C<sub>9</sub>H<sub>7</sub>INO [MH<sup>+</sup>] 271.9567; found 271.9571; IR ( $\nu_{\text{max}}$ , solid, cm<sup>-1</sup>): 3012, 2851, 1659, 1633, 1587, 1494, 1237, 813, 784, 677, 556.

### 6-Bromoisquinolin-1(2H)-one (5f)



Vinyl acetate (138  $\mu$ L, 1.50 mmol) was added to a solution of [Cp\*RhCl<sub>2</sub>]<sub>2</sub> (6 mg, 0.01 mmol), CsOAc (58 mg, 0.3 mmol) and 4-bromo-*N*-(pivaloyloxy)benzamide (300 mg, 1.00 mmol) in MeOH (5 mL, 0.2 M) in a vial under a nitrogen atmosphere. The reaction was heated to 45 °C for 16 hours, after which time the solvent was removed *in vacuo*. The product was isolated by flash column chromatography using 50% EtOAc in hexane. The desired compound was isolated as a colourless solid (186 mg, 70%). *R<sub>F</sub>* 0.4 (1:1 hexane–EtOAc).  $\delta_{\text{H}}$  (300 MHz, DMSO-*d*<sub>6</sub>) 11.36 (1H, br s, NH), 8.07 (1H, d, *J* 8.5, ArH), 7.94 (1H, s, ArH), 7.61 (1H, dd, *J* 8.5, 1.4, ArH), 7.28–7.18 (1H, m, ArH), 6.52 (1H, d, *J* 7.1, ArH);  $\delta_{\text{C}}$  (75 MHz, CDCl<sub>3</sub>) 161.4 (C<sub>q</sub>O), 139.6 (C<sub>q</sub>O), 130.5, 129.2, 129.0, 128.4, 126.3 (C<sub>q</sub>), 124.9 (C<sub>q</sub>), 103.6; HRMS: *m/z* calculated for formula C<sub>9</sub>H<sub>6</sub><sup>79</sup>BrNNaO [MNa<sup>+</sup>] 245.9525; found 247.9505; IR ( $\nu_{\text{max}}$ , solid, cm<sup>-1</sup>): 2735, 1665, 1632, 1239, 952. Spectral data consistent with the literature.<sup>7</sup>

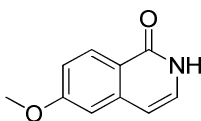
### 6-Fluoroisquinolin-1(2H)-one (5g)



Vinyl acetate (138  $\mu$ L, 1.50 mmol) was added to a solution of [Cp\*RhCl<sub>2</sub>]<sub>2</sub> (6 mg, 0.01 mmol), CsOAc (58 mg, 0.3 mmol) and 4-fluoro-*N*-(pivaloyloxy)-benzamide (239 mg, 1.00 mmol) in MeOH (5 mL, 0.2 M) in a vial under a nitrogen atmosphere. The reaction was heated to 45 °C for 16 hours, after which time the solvent was removed *in vacuo*. The product was triturated with a 4:1 mixture of Et<sub>2</sub>O–MeOH (5 mL) and crystallised from acetone. The desired compound was isolated as pale yellow crystalline needles (40 mg, 71%). m.p. 207–210 °C (acetone);  $\delta_{\text{H}}$  (300 MHz, DMSO-*d*<sub>6</sub>) 11.34 (1H, br s, NH), 8.22 (1H, dd, *J* 8.8, 6.1, ArH), 7.49 (1H, dd, *J* 10.1, 2.5, ArH), 7.32–7.27 (1H, m, ArH), 7.23 (1H, d, *J* 7.1, ArH), 6.54 (1H, d, *J* 7.2, ArH);  $\delta_{\text{C}}$  (75 MHz, DMSO-*d*<sub>6</sub>) 164.3 (d, *J* 249.2, C<sub>q</sub>-F), 161.2 (C<sub>q</sub>O), 140.3 (d, *J* 10.8), 130.5, 130.1 (d, *J* 10.3), 122.9 (d, *J* 1.5), 114.7 (d, *J* 23.7), 110.9 (d, *J* 21.9), 104.1 (d, *J* 3.1); HRMS: *m/z* calculated for formula C<sub>9</sub>H<sub>6</sub>FNNaO [MNa<sup>+</sup>] 186.0326; found

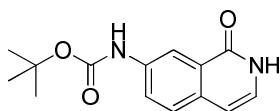
186.0323; IR ( $\nu_{\text{max}}$ , solid,  $\text{cm}^{-1}$ ): 3392, 2968, 1669, 1551, 1408, 1015. Spectral data consistent with the literature.<sup>8</sup>

### 6-Methoxyisoquinolin-1(2H)-one (5h)



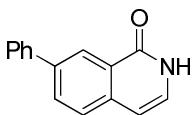
Vinyl acetate (138  $\mu\text{L}$ , 1.50 mmol) was added to a solution of  $[\text{Cp}^*\text{RhCl}_2]_2$  (6 mg, 0.01 mmol), CsOAc (58 mg, 0.3 mmol) and 4-methoxy-*N*-(pivaloyloxy)benzamide (251 mg, 1.00 mmol) in MeOH (2.5 mL, **0.4 M**) in a vial under a nitrogen atmosphere. The reaction was heated to **30 °C** for 16 hours, after which time the solvent was removed *in vacuo*. The product was isolated by flash column chromatography using a solvent gradient of 50% EtOAc in hexane followed by a solvent swap to 5% MeOH in DCM. The product was crystallised from EtOAc to afford colourless crystalline needles (110 mg, 63%). m.p. 179.1–181.3 °C (EtOAc);  $\delta_{\text{H}}$  (300 MHz,  $\text{CDCl}_3$ ) 11.12 (1H, br s, NH), 8.33 (1H, d, *J* 8.9, ArH), 7.15 (1H, d, *J* 7.1, ArH), 7.08 (1H, dd, *J* 8.9, 2.5, ArH), 6.91 (1H, d, *J* 2.5, ArH), 6.48 (1H, d, *J* 7.2, ArH), 3.92 (3H, s, OMe);  $\delta_{\text{C}}$  (75 MHz,  $\text{CDCl}_3$ ) 163.9 ( $\text{C}_q\text{O}$ ), 163.0 ( $\text{C}_q\text{O}$ ), 140.3 ( $\text{C}_q$ ), 129.3, 128.3, 116.5, 107.0, 106.4, 55.5, missing a quaternary carbon; HRMS: *m/z* calculated for formula  $\text{C}_{10}\text{H}_9\text{NNaO}_2$  [ $\text{MNa}^+$ ] 198.0525; found 198.0529; IR ( $\nu_{\text{max}}$ , solid,  $\text{cm}^{-1}$ ): 3162, 1605, 1468, 1231.

### *tert*-Butyl (1-oxo-1,2dihydroisoquinolin-7-yl) carbamate (5i)



Vinyl acetate (138  $\mu\text{L}$ , 1.50 mmol) was added to a solution of  $[\text{Cp}^*\text{RhCl}_2]_2$  (6 mg, 0.01 mmol), CsOAc (58 mg, 0.3 mmol) and *tert*-butyl (3-((pivaloyloxy)carbamoyl)phenyl) carbamate (260 mg, 1.00 mmol) in MeOH (5 mL, 0.2 M) in a vial under a nitrogen atmosphere. The reaction was heated to 45 °C for 16 hours, after which time the solvent was removed *in vacuo*. The product was purified by trituration with a 4:1 mixture of pentane–ethanol (5 mL) to afford a colourless amorphous solid (81 mg, 81%).  $\delta_{\text{H}}$  (300 MHz,  $\text{DMSO}-d_6$ ) 11.10 (1H, br s, NH), 9.61 (1H, s, NH), 8.37 (1H, d, *J* 1.7, ArH), 7.70 (1H, dd, *J* 8.6, 2.2, ArH), 7.54 (1H, d, *J* 8.6, ArH), 7.08–6.97 (1H, m, ArH), 6.45 (1H, d, *J* 7.0, ArH), 1.50 (9H, s,  $\text{O}(\text{CH}_3)_3$ );  $\delta_{\text{C}}$  (75 MHz,  $\text{DMSO}-d_6$ ) 161.6 ( $\text{C}_q\text{O}$ ), 152.7 ( $\text{C}_q\text{O}$ ), 137.9 ( $\text{C}_q$ ), 132.6 ( $\text{C}_q$ ), 126.8, 126.7, 126.6 ( $\text{C}_q$ ), 123.5, 114.2, 104.4, 79.3 ( $\text{C}_q$ ), 28.1 ( $(\text{CH}_3)_3$ ); HRMS: *m/z* calculated for formula  $\text{C}_{14}\text{H}_{16}\text{N}_2\text{NaO}_3$  [ $\text{MNa}^+$ ] 283.1053; found 283.1054; IR ( $\nu_{\text{max}}$ , solid,  $\text{cm}^{-1}$ ): 3355, 2993, 2980, 2932, 2834, 1694, 1663, 1564, 1522, 1250, 1167, 836, 557.

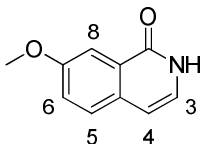
### 7-Phenylisoquinolin-1(2H)-one (5j)



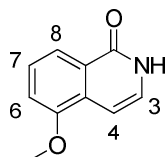
Vinyl acetate (69  $\mu$ L, 0.75 mmol) was added to a solution of  $[\text{Cp}^*\text{RhCl}_2]_2$  (3 mg, 0.005 mmol), CsOAc (28 mg, 0.15 mmol) and *N*-(pivaloyloxy)(1,1'-biphenyl)-3-carboxamide (150 mg, 0.50 mmol) in MeOH (2.5 mL, 0.2 M) in a vial under a nitrogen atmosphere. The reaction was heated to 45  $^\circ\text{C}$  for 16 hours, after which time the solvent was removed *in vacuo*. The product was triturated with a 2:1 mixture of  $\text{Et}_2\text{O}$ –MeOH (5 mL) and crystallised from EtOAc–hexane to afford pale yellow crystals (101 mg, 91%). m.p. 223–226  $^\circ\text{C}$  (EtOAc–hexane);  $\delta_{\text{H}}$  (300 MHz,  $\text{CDCl}_3$ ) 10.29 (1H, s, NH), 8.66 (1H, s, ArH), 7.95 (1H, dd, *J* 8.3, 2.0, ArH), 7.72 (2H, d, *J* 7.1, ArH), 7.65 (1H, d, *J* 8.3, ArH), 7.48 (2H, t, *J* 7.4, ArH), 7.40 (1H, d, *J* 7.3, ArH), 7.11 (1H, br s, ArH), 6.62 (1H, d, *J* 7.4, ArH);  $\delta_{\text{C}}$  (75 MHz,  $\text{CDCl}_3$ ) 164.0 ( $\text{C}_q\text{O}$ ), 140.0 ( $\text{C}_q$ ), 139.9 ( $\text{C}_q$ ), 137.2 ( $\text{C}_q$ ), 131.8, 129.1, 127.9, 127.5, 127.4, 127.0, 126.7 ( $\text{C}_q$ ), 125.5, 106.6; HRMS: *m/z* calculated for formula  $\text{C}_{15}\text{H}_{11}\text{NNaO}$  [ $\text{MNa}^+$ ] 244.0733; found 244.0724; IR ( $\nu_{\text{max}}$ , solid,  $\text{cm}^{-1}$ ): 3159, 2907, 1654, 1449, 1223.

### 5-Methoxyisoquinolin-1(2H)-one (5k(i)) and 7-methoxyisoquinolin-1(2H)-one (5k(ii))

Vinyl acetate (138  $\mu$ L, 1.50 mmol) was added to a solution of  $[\text{Cp}^*\text{RhCl}_2]_2$  (6 mg, 0.01 mmol), CsOAc (58 mg, 0.3 mmol) and 3-methoxy-*N*-(pivaloyloxy)benzamide (251 mg, 1.00 mmol) in MeOH (5 mL, 0.2 M) in a vial under a nitrogen atmosphere. The reaction was heated to 45  $^\circ\text{C}$  for 16 hours, after which time the solvent was removed *in vacuo*. The products were isolated by flash column chromatography using 1% MeOH in EtOAc to afford an amorphous off-white solid containing an inseparable 3:2 mixture of 7-methoxyisoquinolin-1(2H)-one **5k(ii)** and 5-methoxyisoquinolin-1(2H)-one **5k(i)** (172 mg, 98%). IR ( $\nu_{\text{max}}$ , solid,  $\text{cm}^{-1}$ ): 2828, 1653 (CO amide), 1258, 1057; HRMS: *m/z* calculated for formula  $\text{C}_{10}\text{H}_{10}\text{NO}_2$  [ $\text{MH}^+$ ] 176.0706; found 176.0711.  $^{13}\text{C}$  spectral values consistent with the literature in  $\text{CDCl}_3$ <sup>9</sup> however separation of the proton peaks were observed in  $\text{MeOD-}d_4$ .



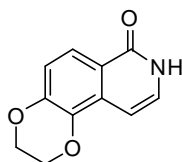
$\delta_{\text{H}}$  (500 MHz,  $\text{MeOD-}d_4$ ) missing NH peak, 7.74 (1H, d, *J* 2.6,  $\text{H}_8$ ), 7.59 (1H, d, *J* 8.7,  $\text{H}_5$ ), 7.34 (1H, dd, *J* 8.7, 2.7,  $\text{H}_6$ ), 7.07 (1H, d, *J* 7.1,  $\text{H}_3$ ), 6.65 (1H, d, *J* 7.1,  $\text{H}_4$ ), 3.91 (s, 3H, OMe);  $\delta_{\text{C}}$  (75 MHz,  $\text{CDCl}_3$ ) 164.3 ( $\text{C}_q\text{O}$ ), 158.7 ( $\text{C}_q\text{O}$ ), 132.4 ( $\text{C}_q$ ), 127.9, 127.2, 125.5, 123.6, 106.7 (2x $\text{C}$ ), 55.7.



$\delta_{\text{H}}$  (500 MHz, MeOD- $d_4$ ) missing NH peak, 7.86 (1H, d,  $J$  8.1, H<sub>6</sub>), 7.46 (1H, t,  $J$  8.1, H<sub>7</sub>), 7.23 (1H, d,  $J$  8.3, H<sub>8</sub>), 7.15 (1H, d,  $J$  7.2, H<sub>3</sub>), 6.96 (1H, d,  $J$  7.3, H<sub>4</sub>), 3.97 (3H, s, MeO);  $\delta_{\text{C}}$  (75 MHz, CDCl<sub>3</sub>); 164.4 (C<sub>q</sub>O), 154.5 (C<sub>q</sub>O), 129.4, 127.0, 127.0, 118.8, 111.6, 101.2, 55.8 (hidden peak at 127.2);  $^{13}\text{C}$  spectral values consistent with the literature.<sup>9</sup>

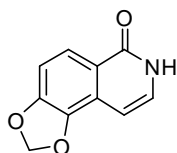
Carbon peaks for the mixture of regioisomers:  $\delta_{\text{C}}$  (75 MHz, MeOD- $d_4$ ) 164.8, 160.3, 156.1, 134.0, 130.8, 129.2, 128.3, 128.2, 128.0, 126.4, 124.3, 119.4, 113.1, 107.9 (2C), 102.2, 56.4, 56.0.

### 2,3-Dihydro-[1,4]dioxino[2,3-f]isoquinolin-7(8H)-one (5l)



Vinyl acetate (138  $\mu\text{L}$ , 1.50 mmol) was added to a solution of [Cp\*RhCl<sub>2</sub>]<sub>2</sub> (6 mg, 0.01 mmol), CsOAc (58 mg, 0.3 mmol) and *N*-(pivaloyloxy)-2,3-dihydrobenzo[*b*][1,4]dioxine-6-carboxamide (279 mg, 1.00 mmol) in MeOH (5 mL, 0.2 M) in a vial under a nitrogen atmosphere. The reaction was heated to 45 °C for 16 hours, after which time the solvent was removed *in vacuo*. The product was triturated with a 9:1 mixture of pentane–ethanol (5 mL), then crystallised from EtOH. The desired compound was isolated as a tan microcrystalline powder (97 mg, 48%). m.p. decomposed at 225 °C (EtOH);  $^1\text{H}$  NMR (300 MHz, DMSO- $d_6$ )  $\delta$  11.08 (1H, br s, NH), 7.67 (1H, d,  $J$  8.8, ArH), 7.12 (1H, dd,  $J$  7.0, 5.6, ArH), 6.99 (1H, d,  $J$  8.8, ArH), 6.54 (1H, d,  $J$  7.3, ArH), 4.42–4.31 (4H, m, 2CH<sub>2</sub>-O);  $\delta_{\text{C}}$  (75 MHz, DMSO- $d_6$ ) 161.2 (C<sub>q</sub>=O), 145.0 (C<sub>q</sub>O), 136.5 (C<sub>q</sub>O), 129.0, 128.9 (C<sub>q</sub>), 120.2 (C<sub>q</sub>), 119.7, 116.5, 97.6, 64.2 (CH<sub>2</sub>), 64.1 (CH<sub>2</sub>); HRMS:  $m/z$  calculated for formula C<sub>11</sub>H<sub>10</sub>NO<sub>3</sub>[MH<sup>+</sup>] 204.0655; found 204.0649; IR ( $\nu_{\text{max}}$ , solid, cm<sup>-1</sup>): 3259, 2980, 1655, 1603, 1462, 1286, 1088.

### [1,3]-Dioxolo[4,5-f]isoquinolin-6(7H)-one (5m)

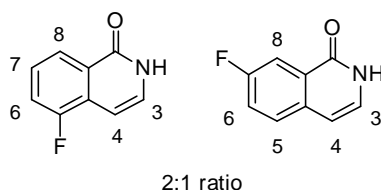


Vinyl acetate (138  $\mu\text{L}$ , 1.50 mmol) was added to a solution of [Cp\*RhCl<sub>2</sub>]<sub>2</sub> (6 mg, 0.01 mmol), CsOAc (58 mg, 0.3 mmol) and *N*-(pivaloyloxy)benzo[*d*][1,3]dioxole-5-carboxamide (265 mg, 1.00 mmol) in MeOH (5 mL, 0.2 M) in a vial under a nitrogen atmosphere. The reaction was heated to 45 °C for 16 hours, after which time the product was filtered from the cooled reaction mixture and subsequently washed with a 3:7 mixture of MeOH–Et<sub>2</sub>O (5 mL). The desired compound was isolated as a cream amorphous solid (101 mg, 53%).  $\delta_{\text{H}}$  (300 MHz, CDCl<sub>3</sub>) 11.04 (1H, s, NH), 7.79 (1H, d,  $J$



8.5, ArH), 7.19 – 7.07 (2H, m, ArH), 6.34 (1H, d,  $J$  7.2, ArH), 6.22 (2H, s, OCH<sub>2</sub>O);  $\delta_C$  (75 MHz, CDCl<sub>3</sub>) 161.0 (C<sub>q</sub>O), 149.1 (C<sub>q</sub>O), 140.9 (C<sub>q</sub>O), 129.7, 121.0, 121.6 (C<sub>q</sub>), 121.1 (C<sub>q</sub>), 108.2, 102.3 (CH<sub>2</sub>), 96.9; HRMS:  $m/z$  calculated for formula C<sub>10</sub>H<sub>8</sub>NO<sub>3</sub> [MH<sup>+</sup>] 190.0499 and C<sub>10</sub>H<sub>7</sub>NNaO<sub>3</sub> [MNa<sup>+</sup>] 212.0318; found 190.0507 and 212.0315; IR ( $\nu_{\max}$ , solid, cm<sup>-1</sup>): 3282, 2844, 1688, 1663, 1633, 1442, 1270, 1236, 1048, 944.

### 5-Fluoroisoquinolin-1(2H)-one (5n(i)) and 7-fluoroisoquinolin-1(2H)-one (5n(ii))



Vinyl acetate (207  $\mu$ L, 2.25 mmol) was added to a solution of [Cp\*RhCl<sub>2</sub>]<sub>2</sub> (9.0 mg, 0.015 mmol), CsOAc (86 mg, 0.45 mmol) and 3-fluoro-*N*-(pivaloyloxy)benzamide (588 mg, 1.50 mmol) in MeOH (7.5 mL, 0.2 M) in a vial under a nitrogen atmosphere. The reaction was heated to 45 °C for 16 hours, after which time the solvent was removed *in vacuo*. The products were isolated by trituration with a 9:1 mixture of pentane–ethanol (5 mL), the material was then recrystallised from acetone. The desired compounds were isolated, as an inseparable mixture of regioisomers, as a colourless crystalline powder (170 mg, 71%). HRMS:  $m/z$  calculated for formula C<sub>9</sub>H<sub>6</sub>FNNaO [MNa<sup>+</sup>] 186.0326; found 186.0318; IR ( $\nu_{\max}$ , solid, cm<sup>-1</sup>): 3162, 2999, 2861, 1633, 1549, 1480, 1352, 1247, 954.

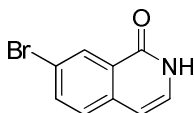
#### 5n(i)

$\delta_H$  (300 MHz, acetone-*d*<sub>6</sub>) 10.35 (1H, br s, NH), 8.12–8.07 (1H, m, ArH), 7.49 (2H, dd,  $J$  8.4, 3.7, ArH), 7.33 (1H, d,  $J$  7.3, H<sub>3</sub>), 6.63 (1H, d,  $J$  7.4, H<sub>4</sub>); <sup>1</sup>H NMR data consistent with the literature.<sup>10</sup>  $\delta_H$  (300 MHz, DMSO-*d*<sub>6</sub>) 11.49 (1H, s, NH), 8.01 (1H, d,  $J$  7.9, H<sub>8</sub>), 7.62–7.53 (1H, m, H<sub>6</sub>), 7.48 (1H, td,  $J$  8.0, 5.5, H<sub>7</sub>), 7.33–7.23 (1H, m, H<sub>3</sub>), 6.58 (1H, d,  $J$  7.2, H<sub>4</sub>);  $\delta_C$  (75 MHz, DMSO-*d*<sub>6</sub>) 160.7 (d,  $J$  2.9, C<sub>q</sub>O), 156.9 (d,  $J$  248.6, C-F), 130.1 (C<sub>3</sub>), 127.8 (d,  $J$  4.0, C<sub>q</sub>), 126.9 (C<sub>q</sub>), 126.7 (d,  $J$  7.9, C<sub>7</sub>), 122.7 (d,  $J$  3.6, C<sub>8</sub>), 117.2 (d,  $J$  19.6, C<sub>6</sub>), 96.4 (d,  $J$  5.7, C<sub>4</sub>).

#### 5n(ii)

$\delta_H$  (300 MHz, acetone-*d*<sub>6</sub>) 10.35 (1H, br s, NH), 7.90 (1H, dd,  $J$  9.6, 2.6, H<sub>8</sub>), 7.74 (1H, dd,  $J$  8.8, 5.2, H<sub>6</sub>), 7.55 (1H, peak obscured, H<sub>5</sub>), 7.23 (1H, d,  $J$  7.4, H<sub>3</sub>), 6.58 (1H, d,  $J$  7.4, H<sub>4</sub>). <sup>1</sup>H NMR data consistent with the literature.<sup>10</sup>

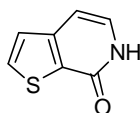
### 7-Bromoisoquinolin-1(2H)-one (5o(ii))



Vinyl acetate (138  $\mu$ L, 1.50 mmol) was added to a solution of [Cp\*RhCl<sub>2</sub>]<sub>2</sub> (6 mg, 0.01 mmol), CsOAc (58 mg, 0.3 mmol) and 3-bromo-*N*-(pivaloyloxy)benzamide (300 mg, 1.00 mmol) in MeOH (5 mL, 0.2 M) in a vial under a nitrogen atmosphere. The reaction was heated to 45 °C for 16 hours, after which time the solvent was removed *in vacuo*. The products were isolated as an inseparable mixture of 7- and 5-bromoisquinolin-1(2*H*)-one (9:1, 215 mg, 95%) as a yellow amorphous solid following purification by flash column chromatography using 30% EtOAc in hexane as an eluent.  $\delta_{\text{H}}$  (500 MHz, DMSO-*d*<sub>6</sub>)  $\delta$  11.42 (1H, s, NH), 8.25 (1H, d, *J* 2.1, ArH), 7.84 (1H, dd, *J* 8.5, 2.2, ArH), 7.64 (1H, d, *J* 8.5, ArH), 7.22 (1H, dd, *J* 6.8, 5.7, ArH), 6.56 (1H, d, *J* 7.1, ArH);  $\delta_{\text{C}}$  (125 MHz, DMSO-*d*<sub>6</sub>) 160.6 (C<sub>q</sub>O), 136.8, 135.1, 129.7, 128.8, 128.6, 127.5, 119.0, 104.1; HRMS: *m/z* calculated for formula C<sub>9</sub>H<sub>7</sub><sup>79</sup>BrNO [MH<sup>+</sup>] 223.9706; found 223.9703; IR ( $\nu_{\text{max}}$ , solid, cm<sup>-1</sup>): 3152, 3002, 2923, 1660, 1223. Spectral data consistent with literature values.<sup>11</sup>

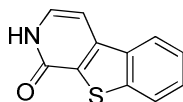
## Heterocyclic Pyridones

### Thieno[2,3-*c*]pyridin-7(6*H*)-one (9a)



Vinyl acetate (138  $\mu$ L, 1.50 mmol) was added to a solution of [Cp\*RhCl<sub>2</sub>]<sub>2</sub> (6 mg, 0.01 mmol), CsOAc (58 mg, 0.3 mmol) and *N*-(pivaloyloxy)thiophene-2-carboxamide (227 mg, 1.00 mmol) in MeOH (5 mL, 0.2 M) in a vial under a nitrogen atmosphere. The reaction was heated to 45 °C for 16 hours, after which time the solvent was removed *in vacuo*. The product was purified by flash column chromatography using a solvent gradient of 10-100% EtOAc in hexane. The desired compound was isolated as a colourless solid (74 mg, 49%). A sample was taken and crystallised from CDCl<sub>3</sub>. m.p. 186-189 °C (CDCl<sub>3</sub>), (literature value 195 °C);<sup>12</sup>  $\delta_{\text{H}}$  (300 MHz, CDCl<sub>3</sub>) 12.68 (1H, s, NH), 7.69 (1H, d, *J* 5.2, ArH), 7.29 (1H, d, *J* 6.9, ArH), 7.21 (1H, d, *J* 5.2, ArH), 6.70 (1H, d, *J* 6.9, ArH);  $\delta_{\text{C}}$  (75 MHz, CDCl<sub>3</sub>) 161.4 (C<sub>q</sub>O), 146.9 (C<sub>q</sub>), 133.6, 129.5 (C<sub>q</sub>), 129.4, 124.6, 104.0; HRMS: *m/z* calculated for formula C<sub>7</sub>H<sub>5</sub>NNaOS [MNa<sup>+</sup>] 173.9984; found 174.0008; IR ( $\nu_{\text{max}}$ , solid, cm<sup>-1</sup>): 3100, 1627, 1526, 1480.

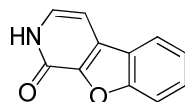
### Benzo[4,5]thieno[2,3-*c*]pyridine-1(2*H*)-one (9b)



Vinyl acetate (25  $\mu$ L, 0.27 mmol) was added to a solution of [Cp\*RhCl<sub>2</sub>]<sub>2</sub> (1 mg, 0.002 mmol), CsOAc (11 mg, 0.06 mmol) and *N*-(pivaloyloxy)-benzo[*b*]thiophene-2-carboxamide (50 mg, 0.18 mmol) in MeOH (0.9 mL, 0.2 M) in a vial under a nitrogen atmosphere. The reaction was heated to 45 °C for 16 hours, after which time the solvent was removed *in vacuo*. The product was isolated by

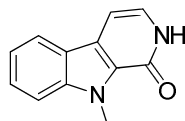
tritulating with MeOH (0.5 mL). The desired compound was isolated as a colourless amorphous solid (23 mg, 64%).  $\delta_{\text{H}}$  (300 MHz, DMSO- $d_6$ ) 11.87 (1H, br s, NH), 8.33 (1H, d,  $J$  7.6, ArH), 8.13 (1H, d,  $J$  7.8, ArH), 7.59 (2H, roofed triplets, H<sub>6</sub> and H<sub>7</sub>), 7.49 (1H, d,  $J$  6.8, ArH), 7.20 (1H, d,  $J$  6.8, ArH);  $\delta_{\text{C}}$  (75 MHz, DMSO- $d_6$ ) 158.8 (C<sub>q</sub>O), 142.1 (SC<sub>q</sub>), 140.9 (SC<sub>q</sub>), 135.0 (C<sub>q</sub>), 131.4, 128.4 (C<sub>q</sub>), 128.2, 125.0, 123.9, 123.6, 100.1; HRMS:  $m/z$  calculated for formula C<sub>11</sub>H<sub>8</sub>NOS [MH<sup>+</sup>] 202.0321; found 202.0314; IR ( $\nu_{\text{max}}$ , solid, cm<sup>-1</sup>): 2949, 1652, 1610, 1464, 1235, 1056.

### Benzofuro[2,3-*c*]pyridine-1(2*H*)-one (9c)



Vinyl acetate (138  $\mu$ L, 1.50 mmol) was added to a solution of [Cp\*RhCl<sub>2</sub>]<sub>2</sub> (6 mg, 0.01 mmol), CsOAc (58 mg, 0.3 mmol) and *N*-(pivaloyloxy)benzo[*b*]furan carboxamide (261 mg, 1.00 mmol) in MeOH (5 mL, 0.2 M) in a vial under a nitrogen atmosphere. The reaction was heated to 45 °C for **48 hours**, after which time the solvent was removed *in vacuo*. The product was triturated with a 1:4 mixture of MeOH–Et<sub>2</sub>O (5 mL) and subsequently crystallised from *sec*-butanol. The desired compound was isolated as a colourless solid (70 mg, 38%). m.p. decomposed above 260 °C (*sec*-butanol), (literature value 276 °C (ethanol));<sup>13</sup>  $\delta_{\text{H}}$  (300 MHz, DMSO- $d_6$ ) 11.90 (1H, br s, NH), 8.14 (1H, d,  $J$  7.8, ArH), 7.80 (1H, d,  $J$  8.5, ArH), 7.62 (1H, t,  $J$  7.4, ArH), 7.45 (1H, t,  $J$  7.5, ArH), 7.36 (1H, appears as a br d (coupling to NH), H<sub>3</sub>), 6.99 (1H, d,  $J$  7.6, H<sub>4</sub>);  $\delta_{\text{C}}$  (75 MHz, DMSO- $d_6$ ) 155.7 (C<sub>q</sub>O), 153.7 (C<sub>q</sub>O), 143.8 (C<sub>q</sub>O), 130.2, 129.5 (C<sub>q</sub>), 129.0, 123.7, 122.9 (C<sub>q</sub>), 122.5, 112.5, 98.4; HRMS:  $m/z$  calculated for formula C<sub>11</sub>H<sub>7</sub>NNaO<sub>2</sub> [MNa<sup>+</sup>] 208.0369; found 208.0363; IR ( $\nu_{\text{max}}$ , solid, cm<sup>-1</sup>): 2876, 1699, 1572, 1473, 1184.

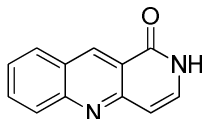
### 9-Methyl-2,9-dihydro-1*H*-pyrido[3,4-*b*]indol-1-one (9d)



Vinyl acetate (108  $\mu$ L, 1.17 mmol) was added to a solution of [Cp\*RhCl<sub>2</sub>]<sub>2</sub> (5 mg, 0.008 mmol), CsOAc (45 mg, 0.23 mmol) and 1-methyl-*N*-(pivaloyloxy)-1*H*-indole-2-carboxamide (214 mg, 0.78 mmol) in MeOH (3.9 mL, 0.2 M) in a vial under a nitrogen atmosphere. The reaction was heated to 45 °C for 16 hours, after which time the solvent was removed *in vacuo*. The product was isolated by flash silica chromatography using an eluent of 0-100% EtOAc in hexane then recrystallised from CDCl<sub>3</sub>–Et<sub>2</sub>O. The desired compound was isolated as a colourless solid (17 mg, 11%). m.p. decomposed above 260 °C (CDCl<sub>3</sub>–Et<sub>2</sub>O);  $\delta_{\text{H}}$  (500 MHz, CDCl<sub>3</sub>) 11.35 (1H, br s, NH), 7.98 (1H, d,  $J$  8.0, ArH), 7.54 (1H, t,  $J$  7.5, ArH), 7.48 (1H, d,  $J$  8.4, ArH), 7.28 (1H, t,  $J$  7.4, ArH), 7.13 (1H, d,  $J$  6.8, ArH), 6.99 (1H, d,  $J$  6.7, ArH), 4.36 (3H, s, NMe);  $\delta_{\text{C}}$  (126 MHz, CDCl<sub>3</sub>) 158.2 (CO), 141.1 (C<sub>q</sub>),

127.3 (C<sub>q</sub>), 127.1, 126.2 (C<sub>q</sub>), 124.2, 121.7 (C<sub>q</sub>), 121.5, 120.2, 110.2, 101.4, 31.5 (NMe); HRMS: *m/z* calculated for formula C<sub>12</sub>H<sub>11</sub>N<sub>2</sub>O [MNa<sup>+</sup>] 199.0866; found 199.0861; IR (ν<sub>max</sub>, solid, cm<sup>-1</sup>): 3140, 2955, 2854, 1642, 1458, 1351, 1329, 1226.

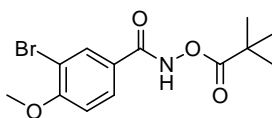
### Benzo[b][1,6]naphthyridin-1(2*H*)-one (9g)



Vinyl acetate (33 μL, 0.36 mmol) was added to a solution of [Cp\*RhCl<sub>2</sub>]<sub>2</sub> (1.5 mg, 0.002 mmol), CsOAc (13 mg, 0.07 mmol) and *N*-(pivaloyloxy)isoquinoline-3-carboxamide (65 mg, 0.24 mmol) in MeOH (1.2 mL, 0.2 M) in a vial under a nitrogen atmosphere. The reaction was heated to 45 °C for 16 hours, after which time the solvent was removed *in vacuo*. After filtration from the reaction solution the solid precipitate was washed with a 1:4 mixture of EtOH–pentane (5 mL) and subsequently crystallised from isopropanol. The desired compound was isolated as a colourless solid (31 mg, 54%). m.p. 288 °C (isopropanol); (literature value - decomposed above 290 °C (DMF));<sup>14</sup> δ<sub>H</sub> (300 MHz, DMSO-*d*<sub>6</sub>) 11.37 (1H, br s, NH), 9.25 (1H, s, ArH), 8.24 (1H, d, *J* 7.9, ArH), 8.06 (1H, d, *J* 8.5, ArH), 7.95–7.87 (1H, m, ArH), 7.63 (1H, t, *J* 7.5, ArH), 7.47 (1H, dd, *J* 7.4, 5.8 (coupling to NH), ArH), 6.68 (1H, d, *J* 7.5 ArH); δ<sub>C</sub> (75 MHz, DMSO-*d*<sub>6</sub>) missing C<sub>q</sub>, 162.5 (C<sub>q</sub>), 153.2 (C<sub>q</sub>), 150.3 (C<sub>q</sub>), 137.5, 133.5, 132.4, 129.6, 128.1, 126.0, 120.8, 106.1; HRMS: *m/z* calculated for formula C<sub>12</sub>H<sub>9</sub>N<sub>2</sub>O [MH<sup>+</sup>] 197.0709; found 197.0704; IR (ν<sub>max</sub>, solid, cm<sup>-1</sup>): 3166, 3029, 2930, 1661, 1614, 1587, 1499, 1202.

## Synthesis of the intermediate isoquinolone for MK-1220<sup>15,16</sup>

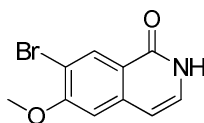
### 3-Bromo-4-methoxy-*N*-(pivaloyloxy)benzamide (4p)



Oxalyl chloride (480 μL, 5.50 mmol) was added to a solution of 3-bromo-4-methoxybenzoic acid (1.16 g, 5.00 mmol) in DCM (25 mL, 0.2 M) with cat. DMF. The mixture was stirred at room temperature for 2 hours, then concentrated *in vacuo* to afford the crude acid chloride. The crude acid chloride was diluted in EtOAc (5 mL) and transferred to a flask containing *O*-(pivaloyl)-hydroxylamine triflic acid<sup>2</sup> (1.47 g, 5.50 mmol) and NaHCO<sub>3</sub> (840 mg, 10.0 mmol) dissolved in a 2:1 mixture of EtOAc–H<sub>2</sub>O (45 mL, 0.1 M) at 0 °C. After 2 hours the reaction was quenched with sat. NaHCO<sub>3</sub> (50 mL) and diluted with EtOAc (50 mL). The two phases were separated and the organic layer was washed with brine (50 mL). The organic layer was dried over MgSO<sub>4</sub> and concentrated *in vacuo* to give 3-bromo-4-methoxy-*N*-(pivaloyloxy)benzamide (1.65g, quant.) (>95% pure by <sup>1</sup>H NMR). A sample of the crude product (1 g) was purified by crystallisation from Et<sub>2</sub>O–pentane,

recovery (0.65 g).  $R_F$  0.7 (33% EtOAc in pentane); m.p. 94-96 °C (Et<sub>2</sub>O–pentane);  $\delta_H$  (500 MHz, CDCl<sub>3</sub>) 9.65 (1H, br s, NH), 7.99 (1H, d,  $J$  2.2, ArH), 7.72 (1H, dd,  $J$  8.6, 2.2, ArH), 6.86 (1H, d,  $J$  8.6, ArH), 3.91 (3H, s, OMe), 1.33 (9H, s, (CH<sub>3</sub>)<sub>3</sub>);  $\delta_C$  NMR (126 MHz, CDCl<sub>3</sub>) 177.2 (C<sub>q</sub>O), 165.3 (C-OMe), 159.3 (C<sub>q</sub>O), 132.9, 128.5, 124.3, 112.0 (C<sub>q</sub>), 111.5, 56.5 (OMe), 38.6 (C<sub>q</sub>(CH<sub>3</sub>)<sub>3</sub>), 27.1 ((CH<sub>3</sub>)<sub>3</sub>); HRMS:  $m/z$  calculated for formula C<sub>13</sub>H<sub>17</sub><sup>79</sup>BrNO<sub>4</sub> [MH<sup>+</sup>] 330.0335; found 330.0335; IR ( $\nu_{max}$ , solid, cm<sup>-1</sup>): 3167, 2976, 1772, 1648, 1597, 1560, 1510, 1481, 1461, 1443, 1397, 1370, 1311, 1268.

### 7-Bromo-6-methoxyisoquinolin-1(2H)-one (5p)

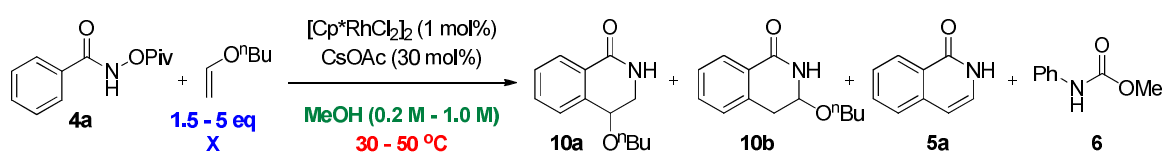


Vinyl acetate (69  $\mu$ L, 0.75 mmol) was added to a solution of [Cp\*RhCl<sub>2</sub>]<sub>2</sub> (3 mg, 0.005 mmol), CsOAc (28 mg, 0.15 mmol) and 3-bromo-4-methoxy-*N*-(pivaloyloxy)benzamide (165 mg, 0.5 mmol) in MeOH (1.25 mL, **0.4 M**) in a vial under a nitrogen atmosphere. The reaction was heated to **30 °C** for 16 hours, after which time the solvent was removed *in vacuo*. The product was triturated with a 1:4 mixture of MeOH–Et<sub>2</sub>O (2 mL) to afford a cream amorphous solid (108 mg, 85%). A sample was crystallised from THF to afford colourless crystals.  $R_F$  0.12 (33% EtOAc in pentane); m.p. decomposed at 250 °C (THF);  $\delta_H$  (500 MHz, DMSO-*d*<sub>6</sub>) 11.23 (1H, br s, NH), 8.26 (1H, s, ArH), 7.29 (1H, s, ArH), 7.18 (1H, dd,  $J$  6.7, 6.6, ArH), 6.51 (1H, d,  $J$  7.1, H<sub>4</sub>), 3.97 (3H, s, OMe);  $\delta_C$  (125 MHz, DMSO) 160.5 (C<sub>q</sub>O), 158.0 (C<sub>q</sub>O), 139.3 (C<sub>q</sub>), 131.1, 130.2, 120.7 (C<sub>q</sub>CONH), 110.2, 107.6, 104.1, 56.6 (OMe); HRMS:  $m/z$  calculated for formula C<sub>10</sub>H<sub>9</sub><sup>79</sup>BrNO<sub>2</sub> [MH<sup>+</sup>] 253.9811; found 253.9812; IR ( $\nu_{max}$ , solid, cm<sup>-1</sup>): 2896, 2834, 1647, 1631, 1594, 1494, 1464, 1449, 1426, 1381, 1346, 1279, 1256, 1246, 1219.

## Alkenyl substrate scope

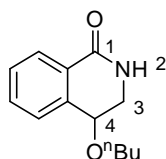
### Optimisation study for vinyl enol ethers

*N*-(Pivaloyloxy)benzamide (221 mg, 1.00 mmol), *n*-butyl vinyl ether (194  $\mu$ L, 1.50 mmol or 647  $\mu$ L, 5.00 mmol), [Cp\*RhCl<sub>2</sub>]<sub>2</sub> (6 mg, 1 mol%) and CsOAc (57.6 mg, 30.0 mol%) were dissolved in MeOH (5.00 mL, 0.20 M or 1.00 mL, 1.00 M) under N<sub>2</sub> in a sealed vessel. After 16 hours the reaction solution was concentrated *in vacuo* (<sup>1</sup>H NMR spectra were taken from the crude samples) and columned on flash silica chromatography using 1:1 EtOAc–hexane with 5% NEt<sub>3</sub>. The desired fractions were concentrated and analysed.



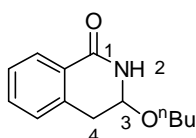
| Entry | Variables |          |            | Yield %<br>(by <sup>1</sup> H NMR) |     |    |    | Ratio<br>(10a & 10b<br>& 5a):6 | Isolated Yield<br>%<br>10a + 10b |
|-------|-----------|----------|------------|------------------------------------|-----|----|----|--------------------------------|----------------------------------|
|       | Temp (°C) | Conc (M) | Equiv<br>X | 10a                                | 10b | 5a | 6  |                                |                                  |
| 1     | 30        | 0.2      | 1.5        | 75                                 | 21  | 0  | 4  | 24 :1                          | 50                               |
| 2     | 30        | 0.2      | 5          | 73                                 | 25  | 0  | 2  | 49:1                           | 76                               |
| 3     | 30        | 1        | 1.5        | 83                                 | 16  | 0  | 1  | 99:1                           | 69                               |
| 4     | 30        | 1        | 5          | 77                                 | 22  | 0  | 1  | 99:1                           | 74                               |
| 5     | 50        | 0.2      | 1.5        | 45                                 | 10  | 5  | 40 | 3:2                            | 33                               |
| 6     | 50        | 0.2      | 5          | 59                                 | 16  | 6  | 19 | 81:9                           | 51                               |
| 7     | 50        | 1        | 1.5        | 66                                 | 11  | 14 | 9  | 91:9                           | 49                               |
| 8     | 50        | 1        | 5          | 62                                 | 19  | 14 | 5  | 19:1                           | 64                               |
| 9     | 40        | 0.6      | 3.25       | 71                                 | 26  | 0  | 3  | 97:3                           | 62                               |
| 10    | 40        | 0.6      | 3.25       | 71                                 | 25  | 0  | 4  | 24:1                           | 68                               |

### 4-Butoxy-3,4-dihydroisoquinolin-1(2H)-one (10a)



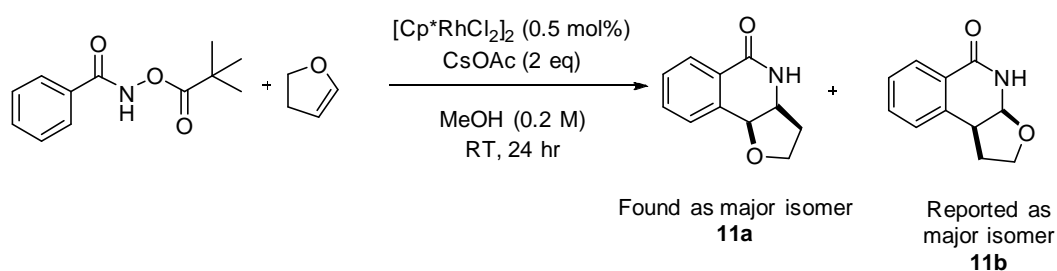
$\delta_{\text{H}}$  (300 MHz,  $\text{CDCl}_3$ ) 8.09 (1H, dd,  $J$  7.6, 1.2, ArH), 7.54 (1H, td,  $J$  7.5, 1.4, ArH), 7.47-7.43 (2H, m, ArH), 7.13 (1H, br s, NH), 4.50-4.48 (1H, m (roofed dd),  $\text{H}_4$ ), 3.70 (1H, ddd,  $J$  12.8, 4.1, 2.6,  $\text{H}_3$ ), 3.62 (1H, ddd,  $J$  12.8, 5.8, 3.4,  $\text{H}_3$ ), 3.56 (1H, dt,  $J$  9.0, 6.5,  $\text{OCH}_2$ ), 3.45 (1H, dt,  $J$  9.0, 6.6,  $\text{OCH}_2$ ), 1.60-1.52 (2H, m), 1.31-1.40 (2H, m), 0.88 (3H, t,  $J$  7.4,  $\text{CH}_3$ );  $\delta_{\text{C}}$  (75 MHz,  $\text{CDCl}_3$ ) 165.9 ( $\text{C}_\text{q}\text{O}$ ), 138.7 ( $\text{C}_\text{q}$ ), 132.1, 128.7, 128.3 ( $\text{C}_\text{q}$ ), 128.0, 126.7, 72.4, 68.9, 44.7, 31.7, 19.3, 13.9; HRMS:  $m/z$  calculated for formula  $\text{C}_{13}\text{H}_{17}\text{NNaO}_2$  [ $\text{MNa}^+$ ]: 242.1151; found 242.1158; IR ( $\nu_{\text{max}}$ , film,  $\text{cm}^{-1}$ ): 3255, 3064, 2870, 1944, 1668, 1473, 1090.

### 3-Butoxy-3,4-dihydroisoquinolin-1(2H)-one (10b)



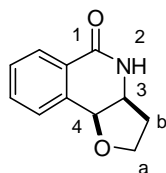
Isolated as an orange oil. Yields from the optimisation study are outlined in Table 5.  $\delta_{\text{H}}$  (500 MHz,  $\text{CDCl}_3$ ) 8.08 (1H, dd,  $J$  7.7, 1.2, ArH), 7.47 (1H td,  $J$  7.5, 1.4, ArH), 7.35 (1H, tt,  $J$  7.5, 1.0, ArH), 7.24 (1H, br d,  $J$  7.5, ArH), 4.88 (1H, td,  $J$  4.5, 2.5,  $\text{H}_3$ ), 3.58 (1H, dt,  $J$  9.2, 6.7,  $\text{OCH}_2$ ), 3.38 (1H, dt,  $J$  9.0, 6.5,  $\text{OCH}_2$ ), 3.29 (1H, dd,  $J$  16.4, 4.5,  $\text{H}_4$ ), 3.10 (1H, br d,  $J$  16.4,  $\text{H}_4$ ), 1.51-1.45 (2H, m,  $\text{OCH}_2\text{CH}_2$ ), 1.31-1.23 (2H, m,  $\text{O}(\text{CH}_2)_2\text{CH}_2$ ), 0.85 (3H, t,  $J$  7.5,  $\text{CH}_3$ ), missing NH peak;  $\delta_{\text{C}}$  (75 MHz,  $\text{CDCl}_3$ ) 167.0 ( $\text{C}_\text{q}\text{O}$ ), 136.5 ( $\text{C}_\text{q}$ ), 132.7, 128.1, 127.8, 127.5 ( $\text{C}_\text{q}$ ), 126.9, 80.3 ( $\text{C}_3$ ), 67.1 ( $\text{C}_4$ ), 33.8 ( $\text{OCH}_2$ ), 31.5, 19.2, 13.7; HRMS:  $m/z$  calculated for formula  $\text{C}_{13}\text{H}_{17}\text{NNaO}_2$  [ $\text{MNa}^+$ ]: 242.1151; found 242.1142; IR ( $\nu_{\text{max}}$ , film,  $\text{cm}^{-1}$ ): 2956, 2889, 1652, 1475, 1343, 1228.

### Verification of Regiochemistry: Repeat of Fagnou experiment.<sup>2</sup>



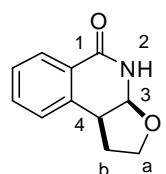
Dihydrofuran (83.0  $\mu\text{L}$ , 1.10 mmol) was added to a solution of *N*-(pivaloyloxy)benzamide (221 mg, 1.00 mmol), CsOAc (384 mg, 2.00 mmol) and  $[\text{Cp}^*\text{RhCl}_2]_2$  (3 mg, 0.5 mol%) in MeOH (5.00 mL, 0.20 M). The solution was left to stir at room temperature for 24 hours. The material was concentrated and purified using flash silica chromatography with 8% isopropanol in toluene to separate a mixture of regioisomers (145 mg, 77%, **11a**) and (5 mg, 3%, **11b**).

### 2,3,3a,4-Tetrahydrofuro[3,2-c]isoquinolin-5(9bH)-one (11a)



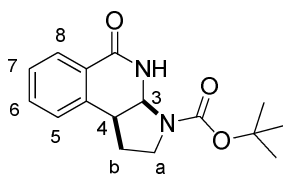
Isolated as a cream solid (145 mg, 77%).  $R_F$  0.08 (8% isopropanol in toluene). M.p. 136-139 °C (isopropanol–toluene);  $\delta_H$  (300 MHz,  $CDCl_3$ ) 8.16 (1H, dd,  $J$  7.3, 1.2, ArH), 7.61-7.45 (3H, m ArH), 6.00 (1H, br s, NH), 4.85 (1H, d,  $J$  4.6,  $H_4$ ), 4.36-4.34 (1H, m,  $H_3$ ), 4.13-3.99 (2H, m,  $H_a$ ), 2.52-2.39 (1H, m,  $H_b$ ), 2.19-2.09 (1H, m,  $H_b$ );  $\delta_C$  (75 MHz,  $CDCl_3$ ) 164.8 ( $C_qO$ ), 135.3 ( $C_q$ ), 132.7, 129.4, 129.1, 128.0, 127.4 ( $C_q$ ), 72.2, 66.7, 54.3, 34.9; HRMS:  $m/z$  calculated for formula:  $C_{11}H_{11}NNaO_2$  [ $MNa^+$ ] 212.0682; found 212.0680; IR ( $\nu_{max}$ , solid,  $cm^{-1}$ ): 3196, 2957, 1668, 1456, 1335, 1040.

### 1,3a,4,9b-Tetrahydrofuro[2,3-c]isoquinolin-5(2H)-one (11b)



Isolated as an orange oil (5 mg, 3%).  $R_F$  0.15 (8% isopropanol in toluene),  $\delta_H$  (300 MHz,  $CDCl_3$ ) 8.07 (1H, dd,  $J$  7.8, 1.3, ArH), 7.45 (1H, td,  $J$  7.5, 1.4, ArH), 7.31 (1H, td,  $J$  7.6, 1.1, ArH), 7.23 (1H, dd,  $J$  7.6, 0.5, ArH), 6.76 (1H, br s, NH), 5.51 (1H, dd,  $J$  6.0, 1.6  $H_3$ ), 3.98-3.99 (2H, m,  $H_a$ ), 3.48 (1H, ddd,  $J$  14.4, 8.3, 6.2,  $H_4$ ), 2.50-2.38 (1H, m,  $H_b$ ), 2.12-2.00 (1H, m,  $H_b$ ). Insufficient material to obtain a  $^{13}C$  spectrum. HRMS:  $m/z$  calculated for formula  $C_{11}H_{11}NNaO_2$  [ $MNa^+$ ] 212.0682; found 212.0689; IR ( $\nu_{max}$ , solid,  $cm^{-1}$ ): 3254, 2935, 1695, 1471, 1190, 1042.

### *tert*-Butyl 5-oxo-3a,4,5,9b-tetrahydro-1*H*-pyrrolo[2,3-*c*]isoquinoline-3(2*H*)-carboxylate (12)

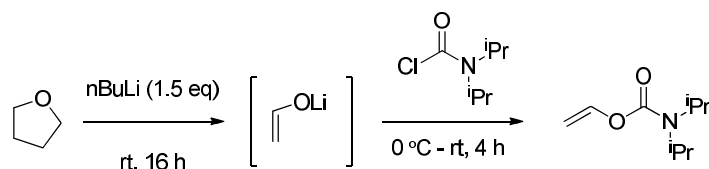


*N*-Boc-2,3-dihydro-1*H*-pyrrole (172  $\mu$ L, 1.50 mmol) was added to a solution of  $[Cp^*RhCl_2]_2$  (6 mg, 0.01 mmol), CsOAc (58 mg, 0.3 mmol) and *N*-(pivaloyloxy)benzamide (221 mg, 1.00 mmol) in MeOH (5 mL, 0.2 M) in a vial under a nitrogen atmosphere. The reaction was heated to 45 °C for 16 hours, after which time the solvent was removed *in vacuo*. The crude material was purified by flash silica chromatography using an eluent of 50% EtOAc in hexane then crystallised from EtOAc–pentane to afford pale yellow crystals (131 mg, 45%). M.p. 161-165 °C (DCM–pentane);  $\delta_H$  (500 MHz, 343K,  $DMSO-d_6$ ) 7.94 (1H, d,  $J$  7.2,  $H_8$ ), 7.53 (1H, td,  $J$  7.3, 1.0,  $H_6$ ), 7.42-7.38 (2H, m,  $H_7$  and  $H_5$ ), 7.27 (1H, br s, NH), 5.51 (1H, d,  $J$  6.4,  $H_3$ ), 3.54 (2H, dt,  $J$  10.8, 6.7,  $H_4$ ), 3.46-3.33 (2H, m,  $2H_a$ ),



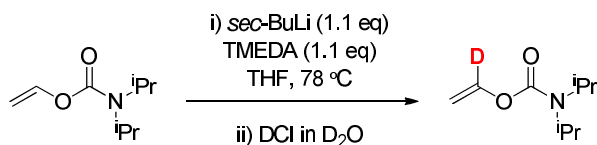
2.38 – 2.26 (1H, m, H<sub>b</sub>), 2.01-1.91 (1H, m, H<sub>b</sub>), 1.47 (9H, s, <sup>t</sup>Bu); δ<sub>C</sub> (126 MHz, 343K, DMSO-*d*<sub>6</sub>) δ 161.9 (CONH), 153.0 (CO<sub>2</sub><sup>t</sup>Bu), 138.3 (C<sub>q</sub>CONH), 131.9, 127.3, 127.0, 126.8, 126.3 (C<sub>q</sub>), 79.3 (O-C<sup>t</sup>Bu), 66.7 (C<sub>3</sub>), 44.4 (C<sub>a</sub>), 31.9 (C<sub>b</sub>), 27.8 (C(CH<sub>3</sub>)<sub>3</sub>). C<sub>4</sub> is obscured by the DMSO signal (identified in the HMQC); IR (ν<sub>max</sub>, solid, cm<sup>-1</sup>): 3585, 3518, 3199, 2955, 2849, 1705, 1650, 1464, 1387, 1284, 1122; HRMS: *m/z* calculated for formula C<sub>16</sub>H<sub>20</sub>N<sub>2</sub>O<sub>3</sub> [MH<sup>+</sup>] 289.1547; found 289.1542.

### Vinyl *N,N*-diisopropylcarbamate (13a)



Following a modified procedure by Clayden *et al.*,<sup>17</sup> *n*-butyllithium (2.5 M in hexanes, 6.0 mL, 15 mmol) was added to THF (11 mL, 1.3 M) at room temperature. After 16 hours *N,N*-diisopropyl carbamoyl chloride (1.6 g, 10 mmol) was dissolved in DMPU (11 mL, 0.91 M) and added dropwise to a cooled solution (0 °C) containing the lithium ethenolate. The reaction was warmed to room temperature over four hours. The reaction was quenched with saturated NH<sub>4</sub>Cl and extracted with Et<sub>2</sub>O (3 x 25 mL). The organic layer was washed with water and dried over Na<sub>2</sub>SO<sub>4</sub>. The solvent was removed *in vacuo* and purified by flash silica chromatography using 33% EtOAc in hexane to afford a clear oil (1.42 g, 83%). R<sub>F</sub> 0.84 (50% EtOAc in hexane); δ<sub>H</sub> (300 MHz, CDCl<sub>3</sub>) 7.26 (1H, dd, *J* 14.7, 5.6, C=CH-O), 4.77 (1H, dd, *J* 14.0, 1.4, OC=CH *trans*), 4.43 (1H, dd, *J* 6.3, 1.4, OC=CH *cis*), 4.07 (1H, br s, CH-(Me)<sub>2</sub>), 3.86 (1H, br s, CH-(Me)<sub>2</sub>), 1.25 (12H, d, *J* 6.7, Me); δ<sub>C</sub> (75 MHz, CDCl<sub>3</sub>) 152.7 (CO), 142.3 (C=CO), 94.5 (C=CO), 46.7 (C(Me)<sub>2</sub>), 45.8 (C(Me)<sub>2</sub>), 20.4 (Me), 19.4 (Me); IR (ν<sub>max</sub>, film, cm<sup>-1</sup>): 3417, 2972, 1713, 1646, 1436, 1371, 1316, 1144, 1048; HRMS: *m/z* calculated for formula C<sub>9</sub>H<sub>18</sub>NO<sub>2</sub> [MH<sup>+</sup>] 172.1332; found 172.1328. The <sup>1</sup>H NMR spectral data corresponds to the literature values.<sup>18</sup>

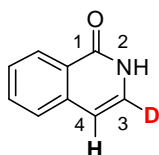
### Vinyl *N,N*-diisopropylcarbamate-*d*<sub>1</sub> (13b)



*sec*-Butyllithium (1.4 M in hexanes, 1.40 mL, 1.90 mmol) was added dropwise to a solution of TMEDA (290 mL, 1.93 mmol) in THF (2 mL) at -78 °C. After ten minutes *O*-vinyl-*N,N*-diisopropylcarbamate (300 mg, 1.75 mmol) was added to the yellow solution. After two hours at -78 °C, the reaction was quenched with DCl in D<sub>2</sub>O (35% wt solution, 100 mL, 2.47 mmol) and the solution was allowed to warm to room temperature. The reaction was diluted with water and the product was extracted with Et<sub>2</sub>O (3 x 20 mL). The organic layers were combined and washed with brine (30 mL) and dried over Na<sub>2</sub>SO<sub>4</sub>. The crude material was passed through a silica plug to remove

base line impurities using 50% EtOAc in hexane. The solvent was concentrated *in vacuo* to afford a colourless oil (288 mg, 96%, 87% D by  $^1\text{H}$  NMR).  $R_F$  0.84 (50% EtOAc in hexane);  $\delta_H$  (500 MHz,  $\text{CD}_3\text{CN}$ ) 7.20 (0.13 H, dd,  $J$  14.1, 6.3 Hz, 1H), 4.75 (1H, s,  $\text{HHC}=\text{CD}$ ), 4.41 (1H, s,  $\text{HHC}=\text{CD}$ ), 3.99 (2H, br s,  $\text{CH}(\text{Me})_2$ ), 1.22 (12H, d,  $J$  6.8,  $\text{CH}(\text{Me})_2$ );  $\delta_C$  (126 MHz,  $\text{CD}_3\text{CN}$ ) 153.47, 143.2 ( $\text{C}=\text{CH}-\text{O}$ ), 142.9 (t,  $J$  16.3,  $\text{C}=\text{CDO}$ ), 94.9 ( $\text{C}=\text{CO}$ ), 47.6 ( $\text{C}(\text{Me})_2$ ), 46.8 ( $\text{C}(\text{Me})_2$ ), 21.7 (Me), 20.7 (Me); IR ( $\nu_{\text{max}}$ , film,  $\text{cm}^{-1}$ ): 2972, 1714, 1622, 1435, 1371, 1314, 1144, 1050. HRMS:  $m/z$  calculated for formula  $\text{C}_9\text{H}_{16}\text{DNO}_2$  [ $\text{M}_2\text{H}^+$ ] 345.2748; found 345.2761.

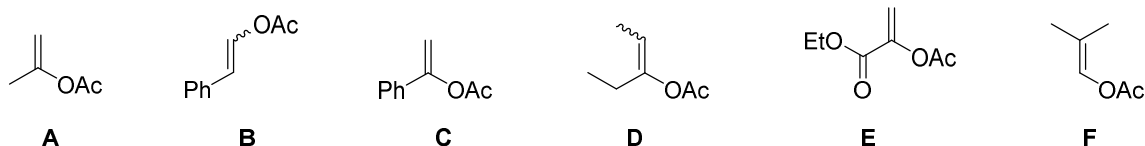
### Isoquinolin-1(2H)-one- $d_1$ (5aD)



Vinyl *N,N*-diisopropylcarbamate- $d_1$  (258 mg, 1.50 mmol) was added to a solution of *N*-(pivaloyloxy)benzamide (221 mg, 1.00 mmol), CsOAc (57 mg, 0.30 mmol) and  $[\text{Cp}^*\text{RhCl}_2]_2$  (6 mg, 0.01 mmol) in MeOH (5.00 mL, 0.20 M) with mesitylene (46  $\mu\text{L}$ , 0.33 mmol), as an internal standard. The reaction was heated to 45  $^\circ\text{C}$  for 16 hours after which time the reaction was concentrated *in vacuo*. The  $^1\text{H}$  NMR of the crude reaction mixture indicated 10% conversion to the isoquinolone (5aD) (see spectrum). The desired compound was isolated as a crude solid (10 mg, 6%, 85% D by  $^1\text{H}$  NMR) containing impurities (<90% pure) by preparative TLC using 50% EtOAc in hexane.  $\delta_H$  (500 MHz,  $\text{CDCl}_3$ ) 10.68 (1H, s, NH), 8.42 (1H, d,  $J$  8.1, ArH), 7.67 (1H, t,  $J$  8.1, ArH), 7.56 (2H, d,  $J$  7.8, ArH), 7.51 (1H, t,  $J$  7.1, ArH), 7.14 (**0.15 H**, d,  $J$  7.1,  $\text{H}_3$ ), 6.55 (1H, s,  $\text{H}_4$ ).

### Substituted vinylic ester substrates

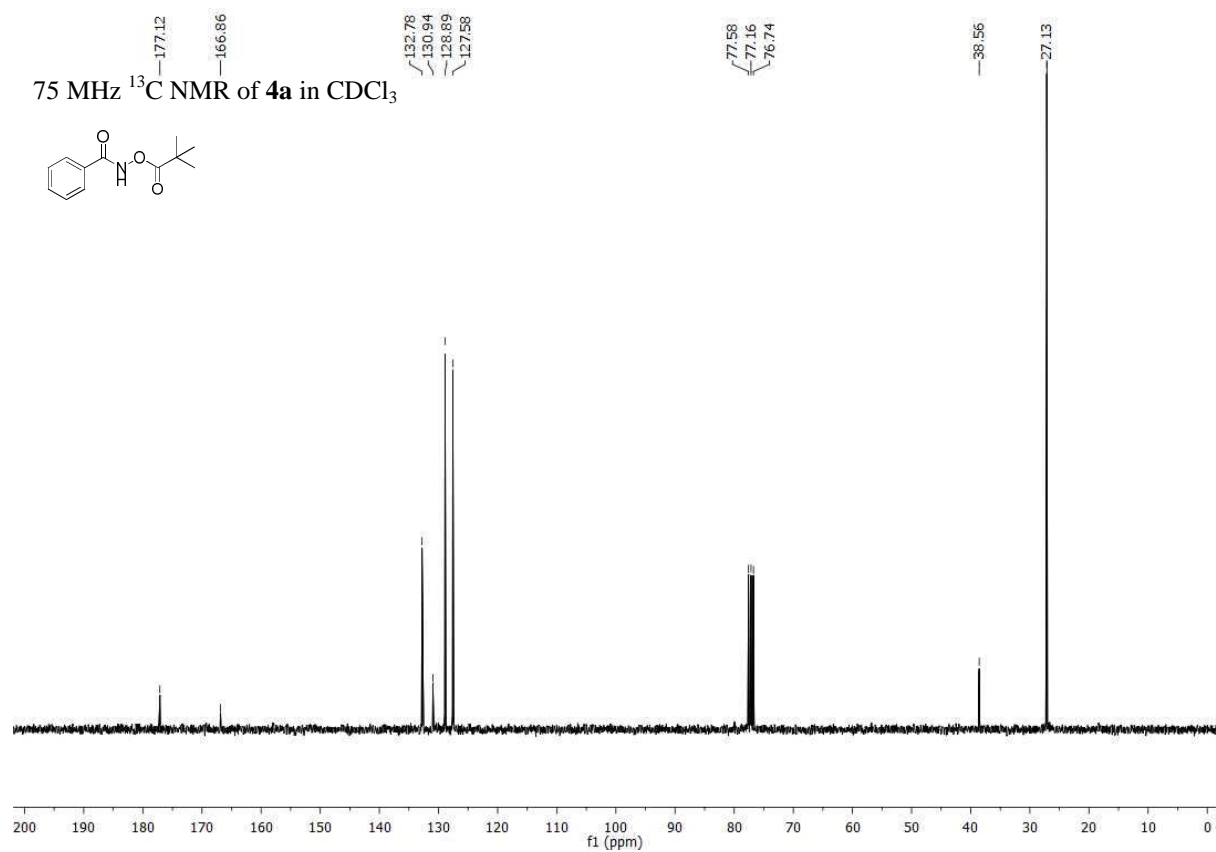
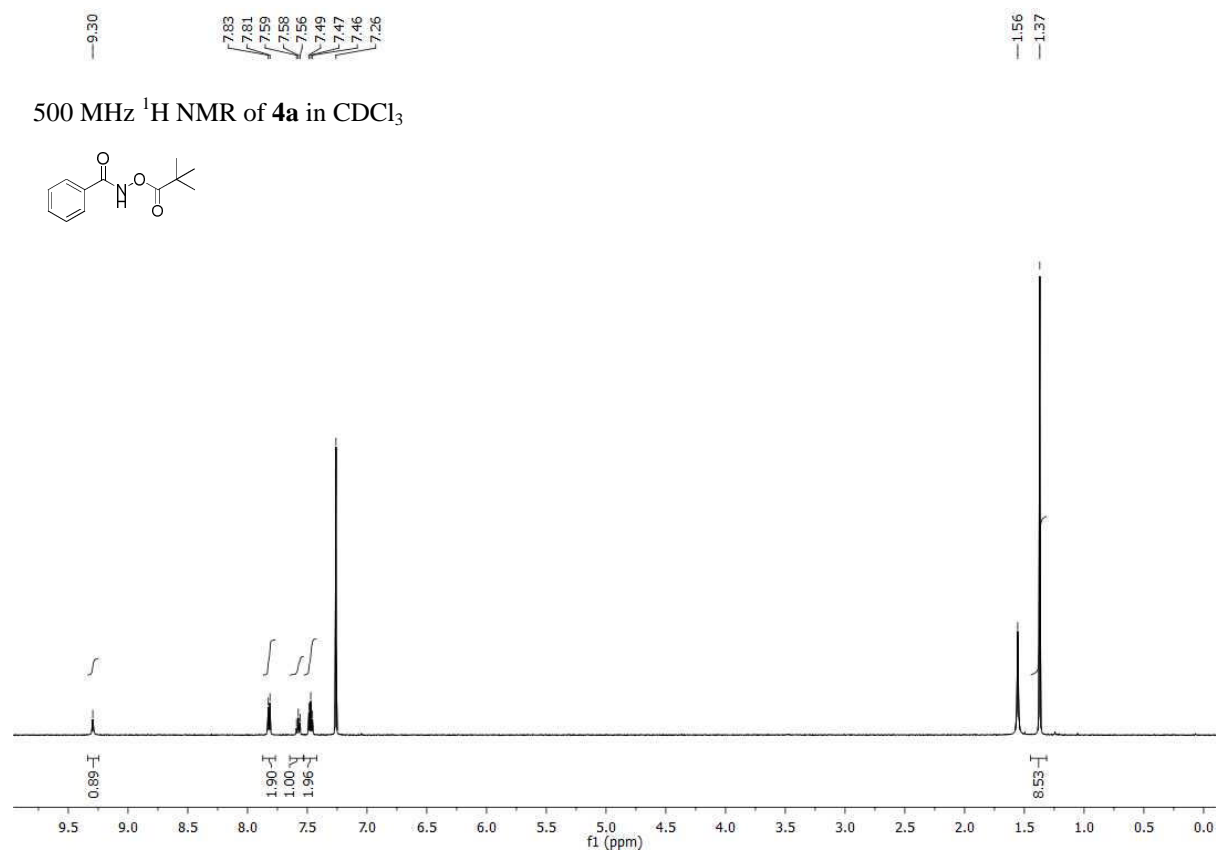
The following substrates were investigated under the standard reaction conditions. The only substrate to return product was propenyl acetate **A**, which gave a 7% yield of 3-methylisoquinoline-1(2H)-one.

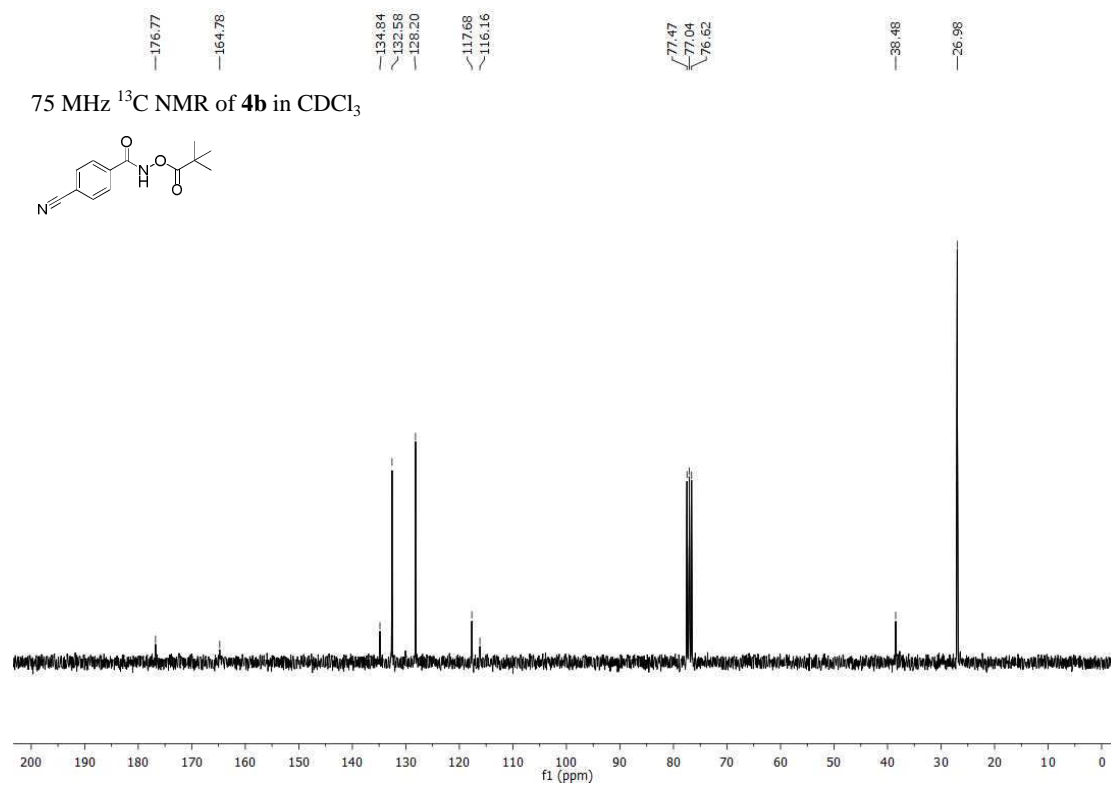
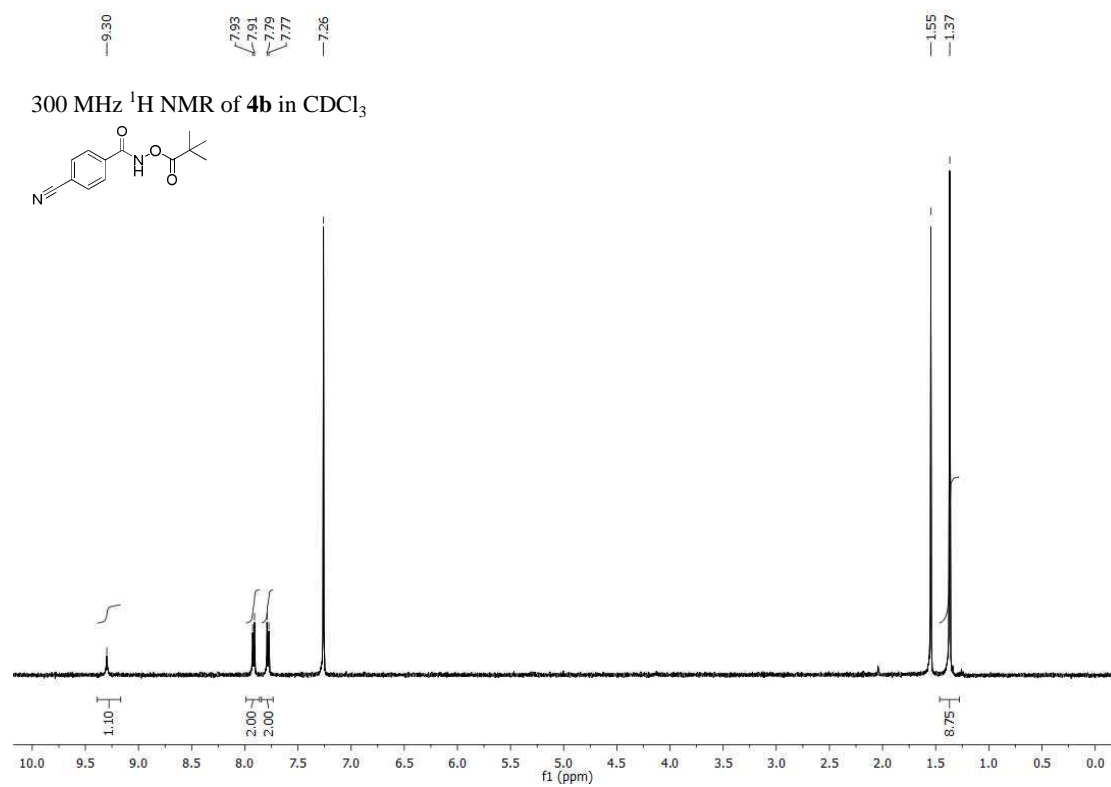


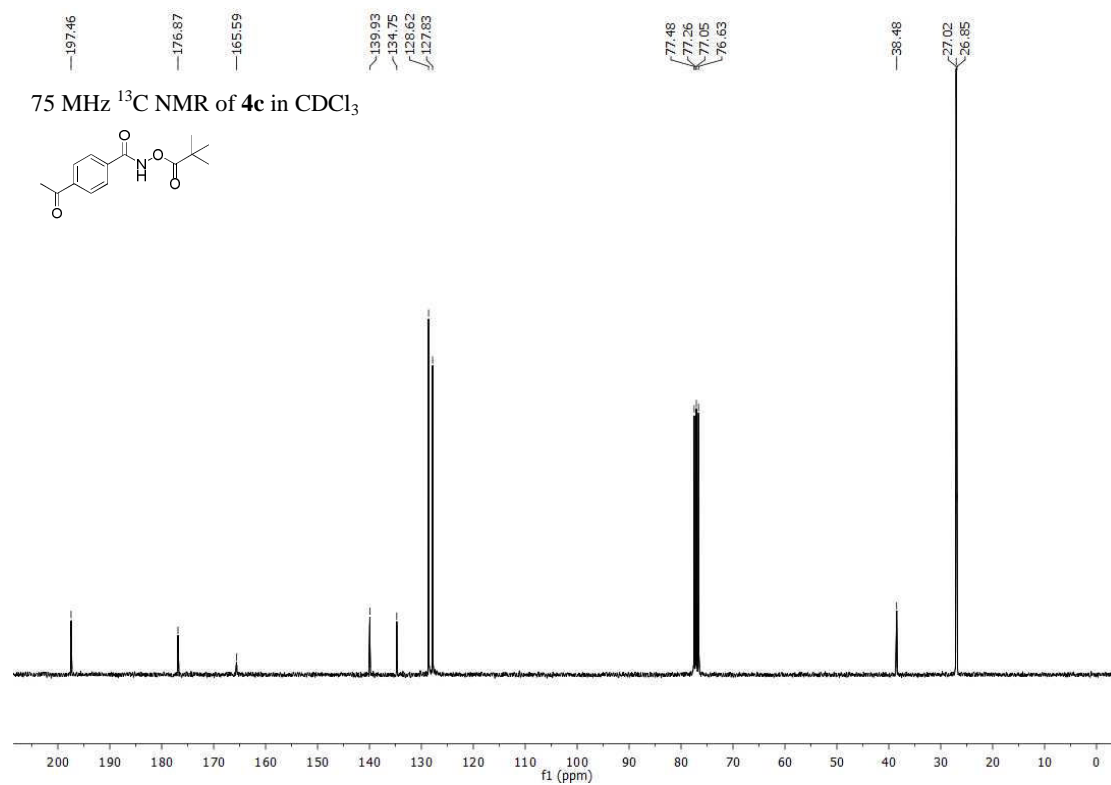
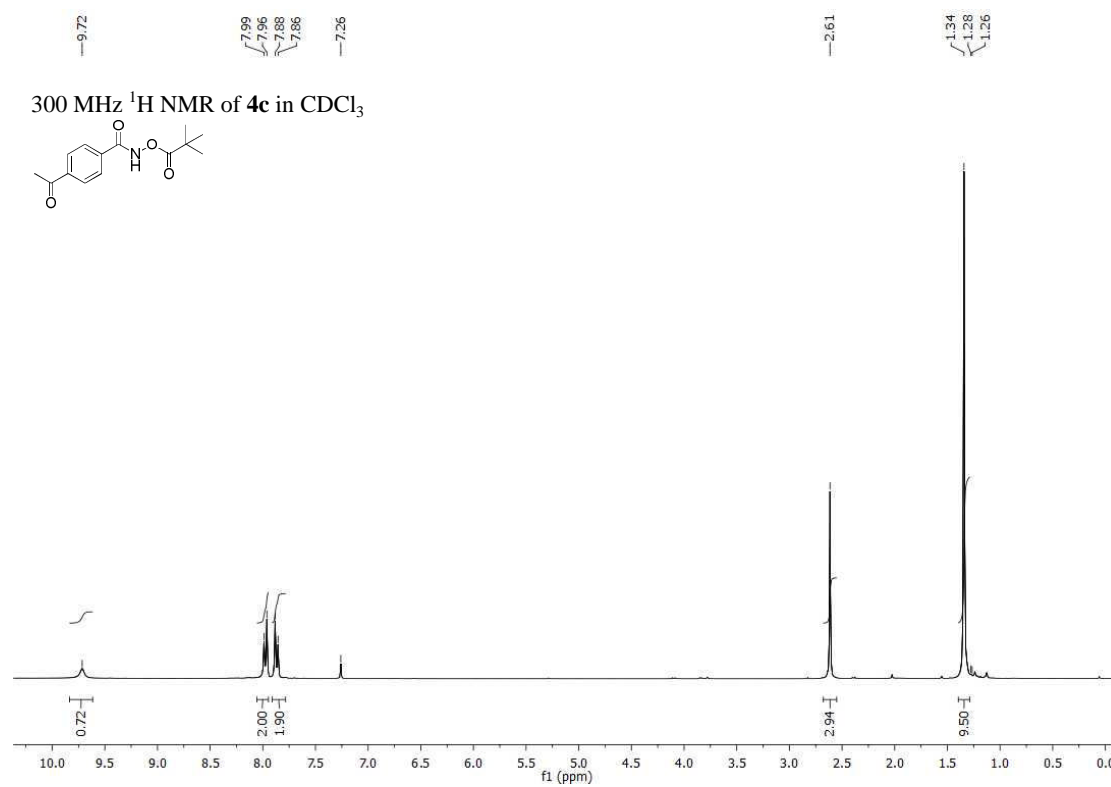
## References

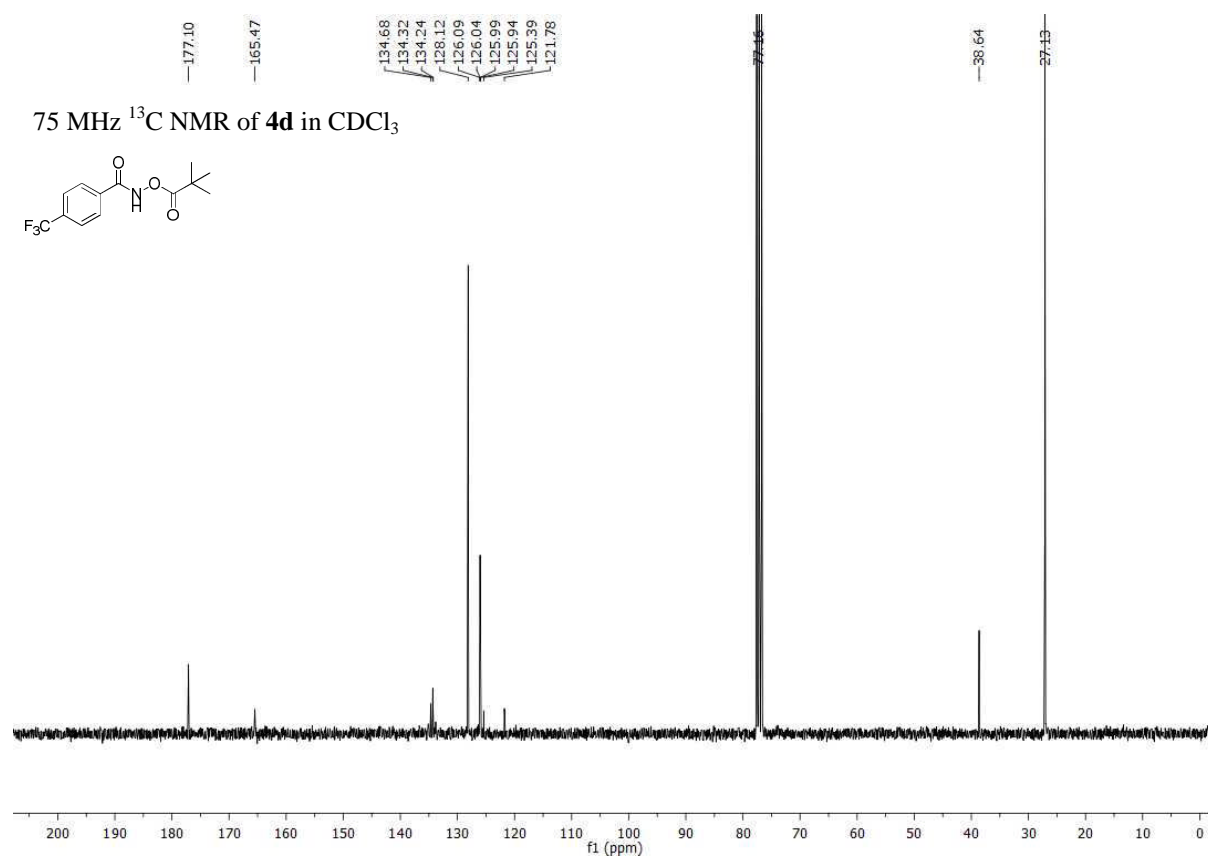
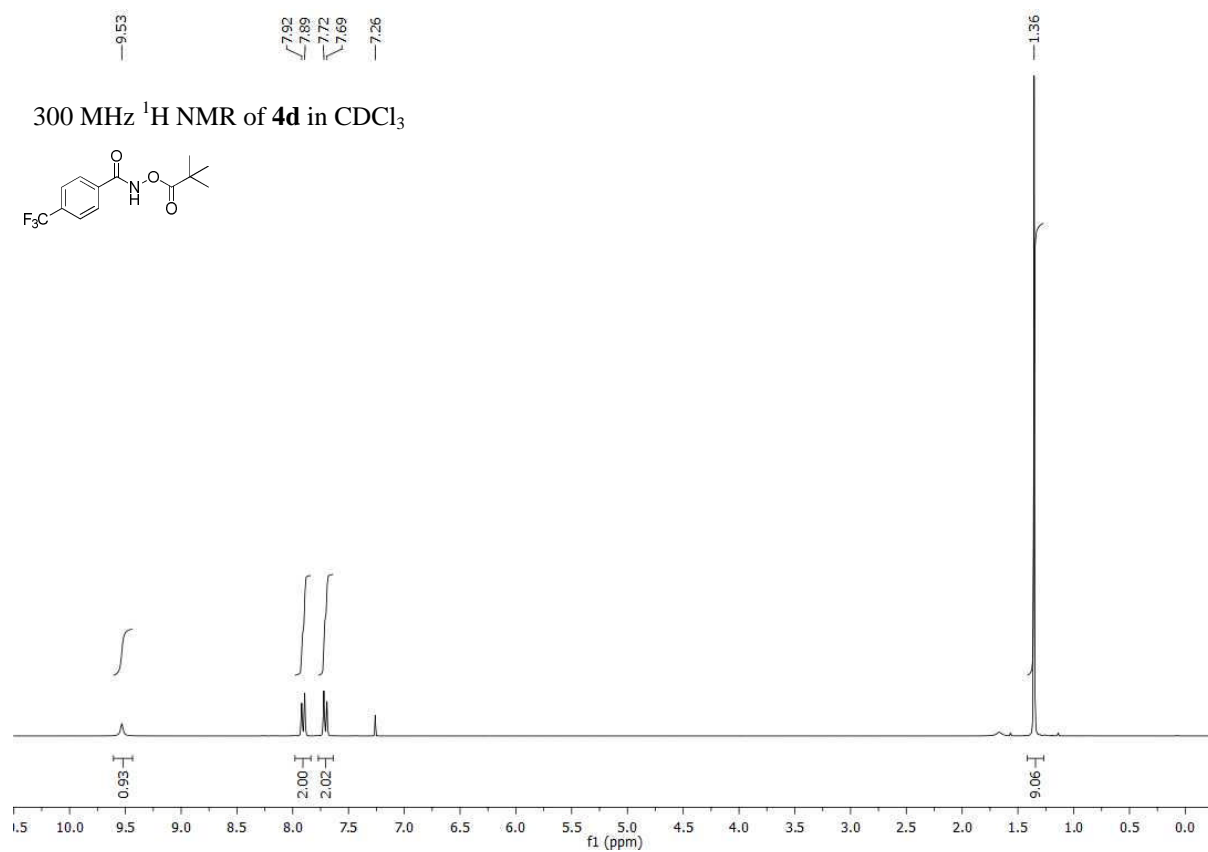
- (1) Geffken, V. D. *Chemiker-Zeitung*. **1986**, *10*, 377.
- (2) Guimond, N.; Gorelsky, S. I.; Fagnou, K. *J. Am. Chem. Soc.* **2011**, *133*, 6449.
- (3) Zhang, Z.; Yu, Y.; Liebeskind, L. S. *Org. Lett.* **2008**, *10*, 3005.
- (4) Rakshit, S.; Grohmann, C.; Besset, T.; Glorius, F. *J. Am. Chem. Soc.* **2011**, *133*, 2350.
- (5) Hesp, K. D.; Bergman, R. G.; Ellman, J. A. *J. Am. Chem. Soc.* **2011**, *133*, 11430.
- (6) Lu, W.-D.; Lin, C.-F.; Wang, C.-J.; Wang, S.-J.; Wu, M.-J. *Tetrahedron* **2002**, *58*, 7315.
- (7) Gfesser, G. A.; Whittern, D.; Cowart, M. A.; Faghih, R. *Heterocycles* **2008**, *75*, 1199.
- (8) Hirao, K.; Suchiya, R.; Yanu, Y.; Tsue, H. *Heterocycles* **1996**, *42*, 415.
- (9) Chuang, T.-H.; Wu, P.-L. *J. Chin. Chem. Soc.* **2006**, *53*, 413.
- (10) Wang, X. A.; Sun, L.-Q.; Sit, S.-Y.; Sin, N.; Scola, P. M.; Hewawasam, P.; Good, A. C.; Chen, Y.; Campbell, J. A. Hepatitis C Virus Inhibitors. WO 03/099274 A1, 2003.
- (11) Shkavrov, S.; Popov, S.; Kravchenko, D.; Krasavin, M. *Synth. Commun.* **2005**, *35*, 725.
- (12) Farnier, M.; Soth, S.; Fournari, P. *Can. J. Chem.* **1976**, *54*, 1066.
- (13) Chatterjea, J. N.; Sahai, R. P.; Swaroopa, B. B.; Bhakta, C.; Jha, H. C.; Zilliken, F. *Chem. Ber.* **1980**, *113*, 3656.
- (14) Rivalle, C.; Bisagni, E. *J. Heterocycl. Chem.* **1980**, *17*, 245.
- (15) Song, Z. J.; Tellers, D. M.; Dormer, P. G.; Zewge, D.; Janey, J. M.; Nolting, A.; Steinhuebel, D.; Oliver, S.; Devine, P. N.; Tschaen, D. M. *Org. Process Res. Dev.* **2014**, *18*, 423.
- (16) Rudd, M. T.; McCauley, J. A.; Butcher, J. W.; Romano, J. J.; McIntyre, C. J.; Nguyen, K. T.; Gilbert, K. F.; Bush, K. J.; Holloway, M. K.; Swestock, J.; Wan, B.-L.; Carroll, S. S.; DiMuzio, J. M.; Graham, D. J.; Ludmerer, S. W.; Stahlhut, M. W.; Fandozzi, C. M.; Trainor, N.; Olsen, D. B.; Vacca, J. P.; Liverton, N. J. *ACS Med. Chem. Lett.* **2011**, *2*, 207.
- (17) Fournier, A. M.; Clayden, J. *Org. Lett.* **2012**, *14*, 142.
- (18) Siemer, M.; Fröhlich, R.; Hoppe, D. *Synthesis* **2008**, *14*, 2264.

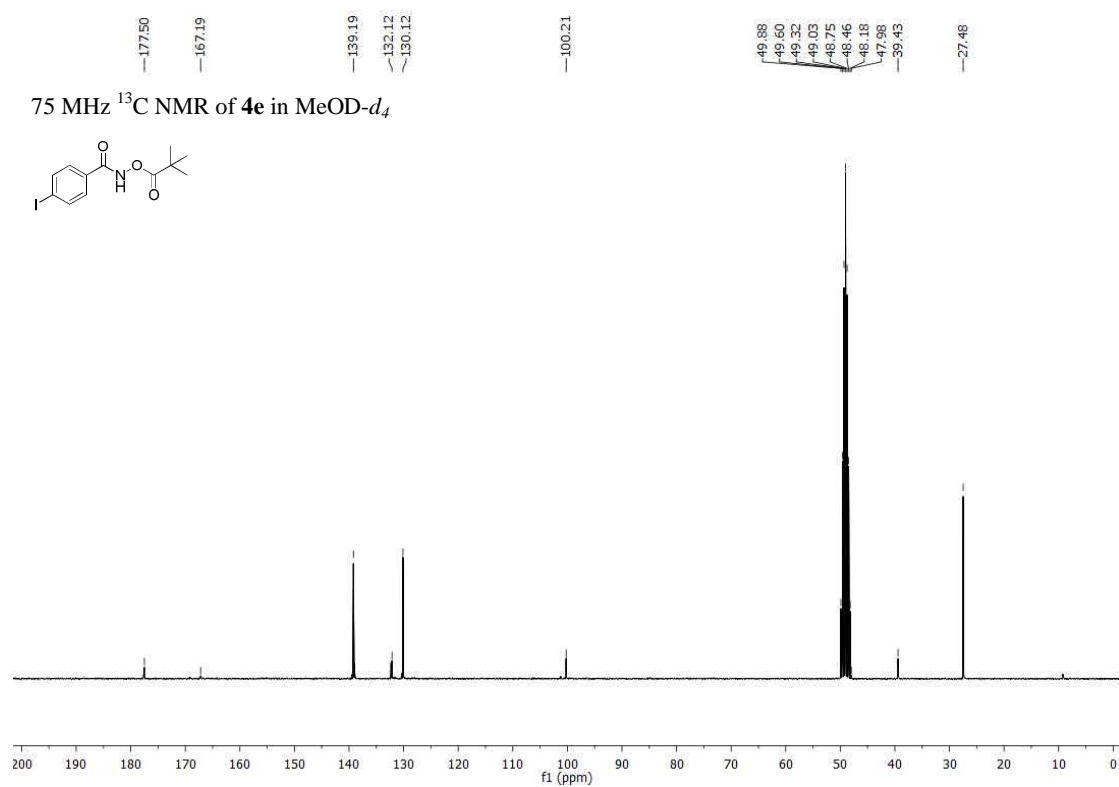
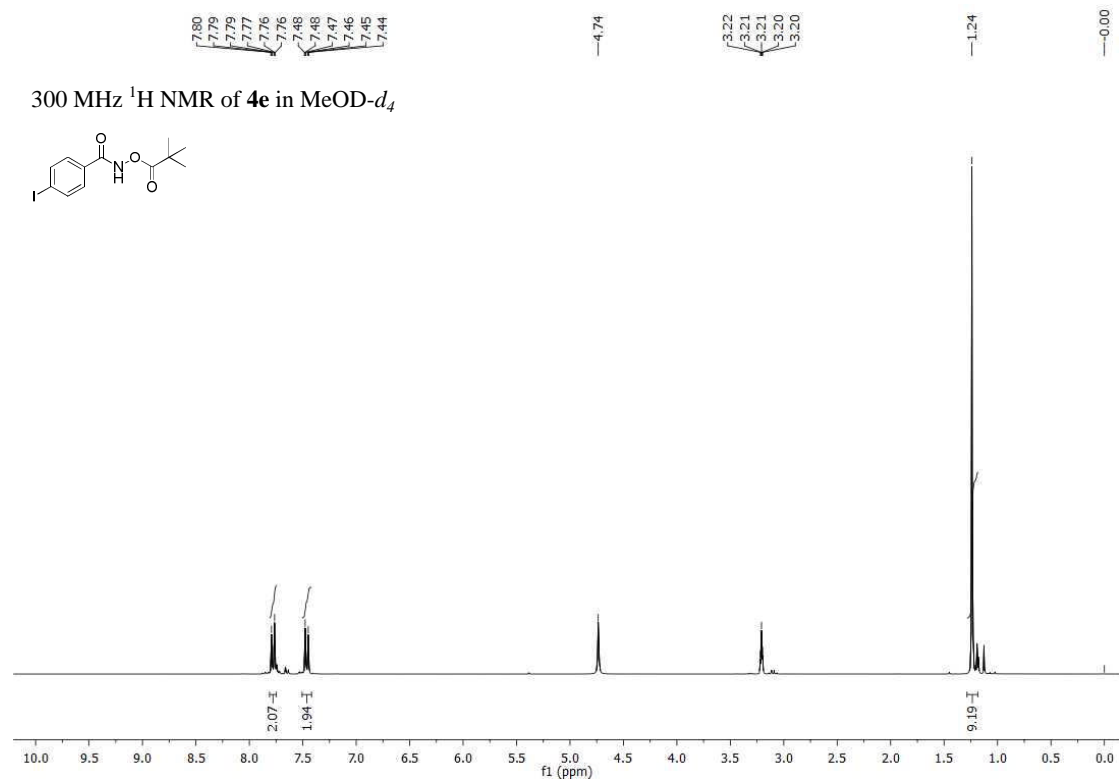
## Spectra for *N*-(pivaloyloxy)benzamide derivatives



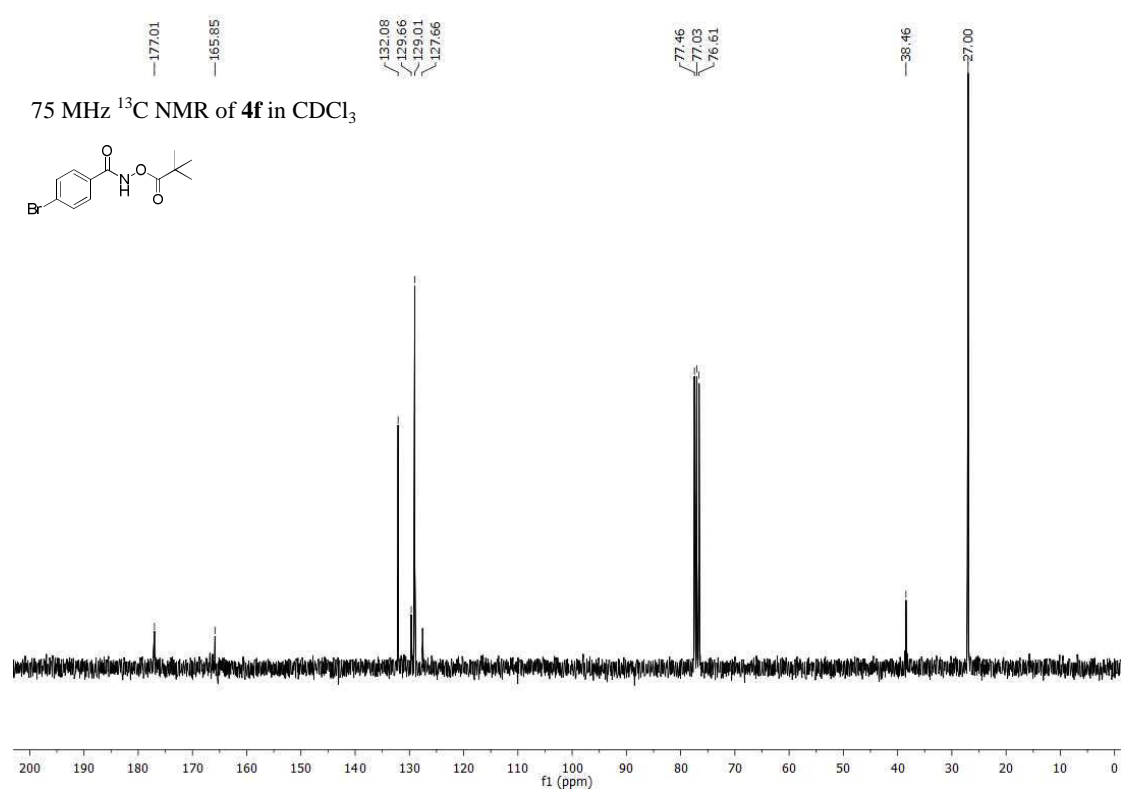
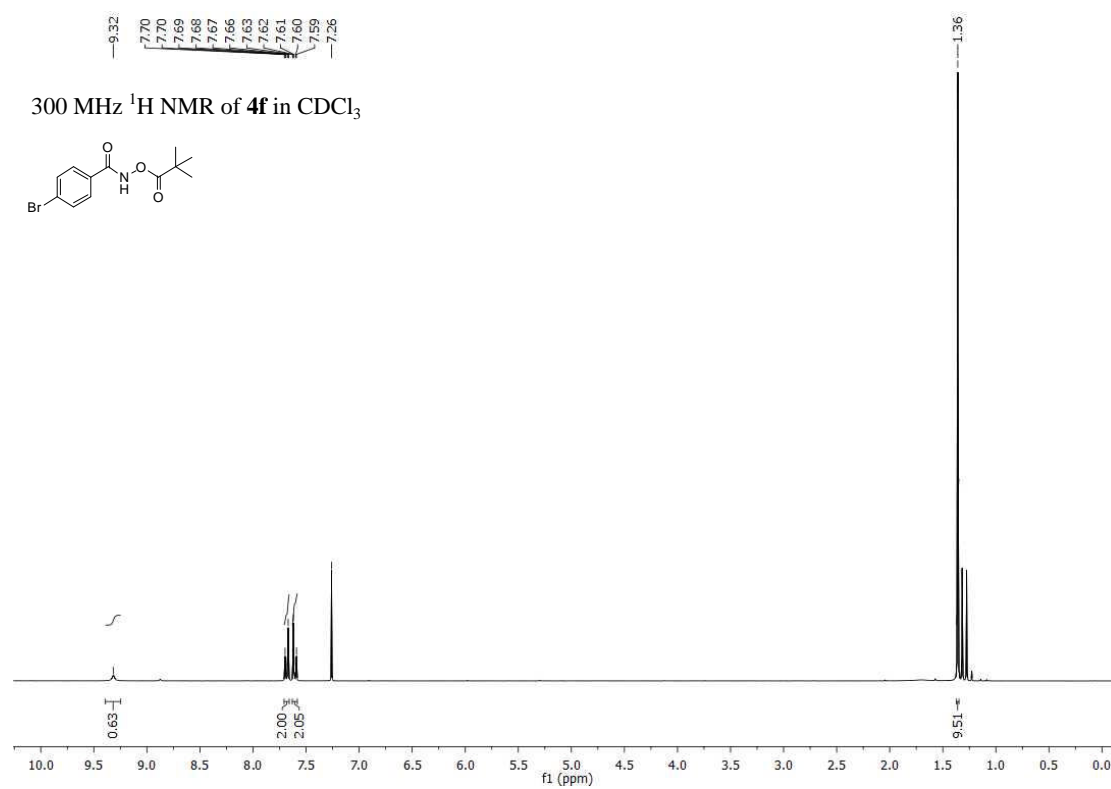


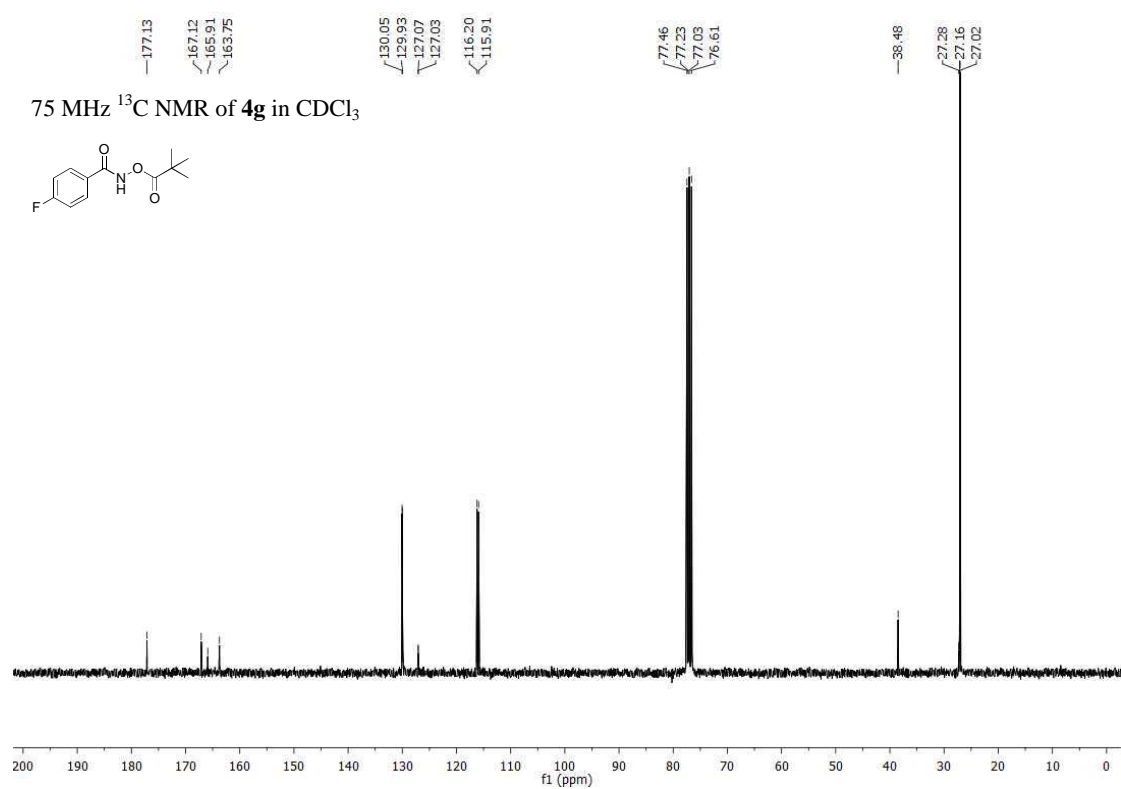
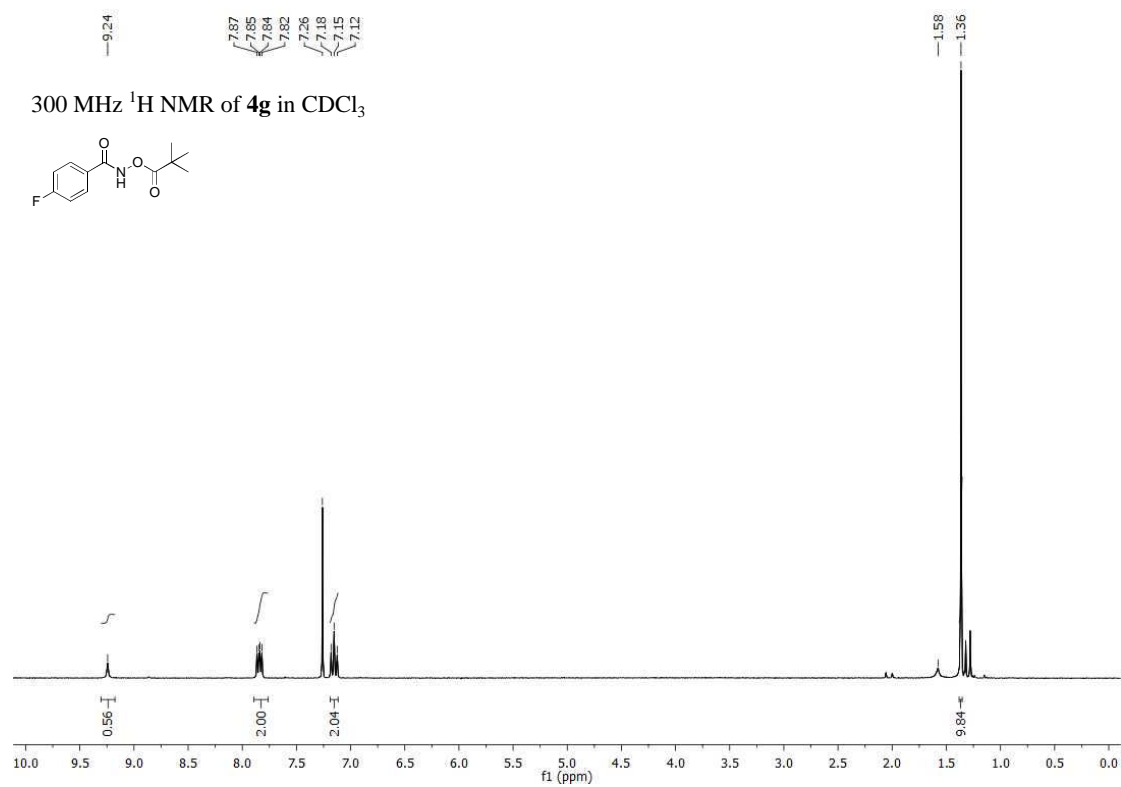


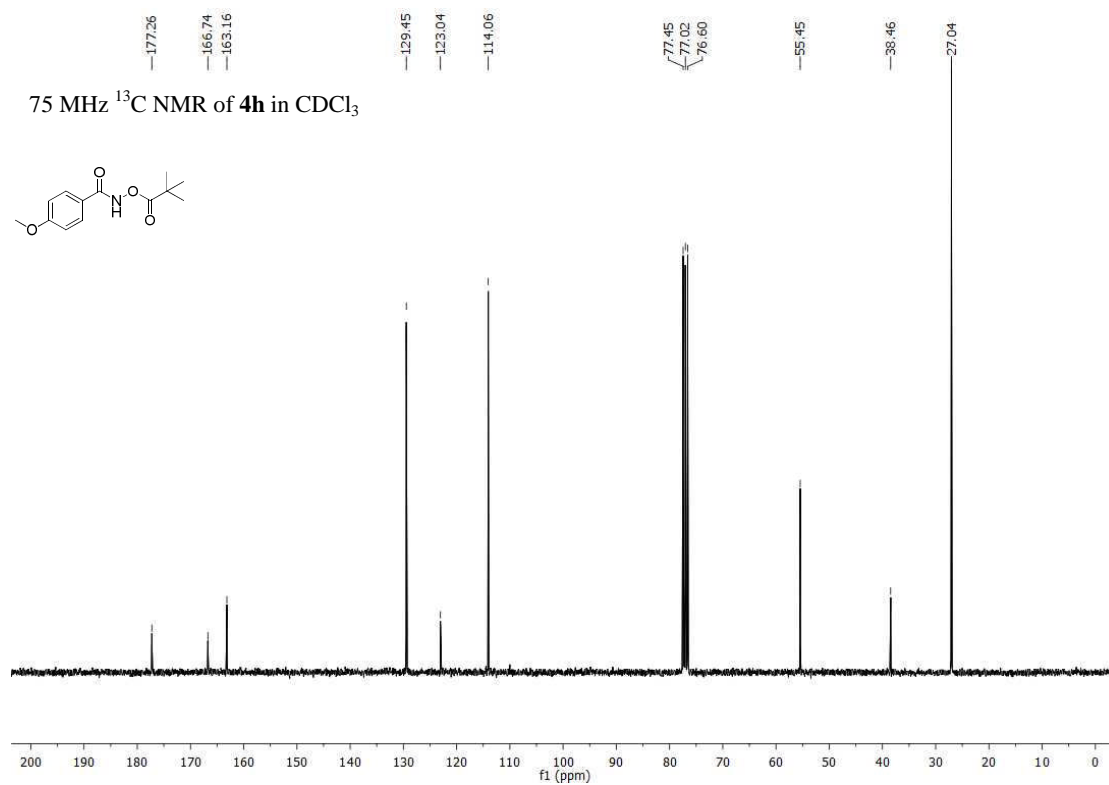
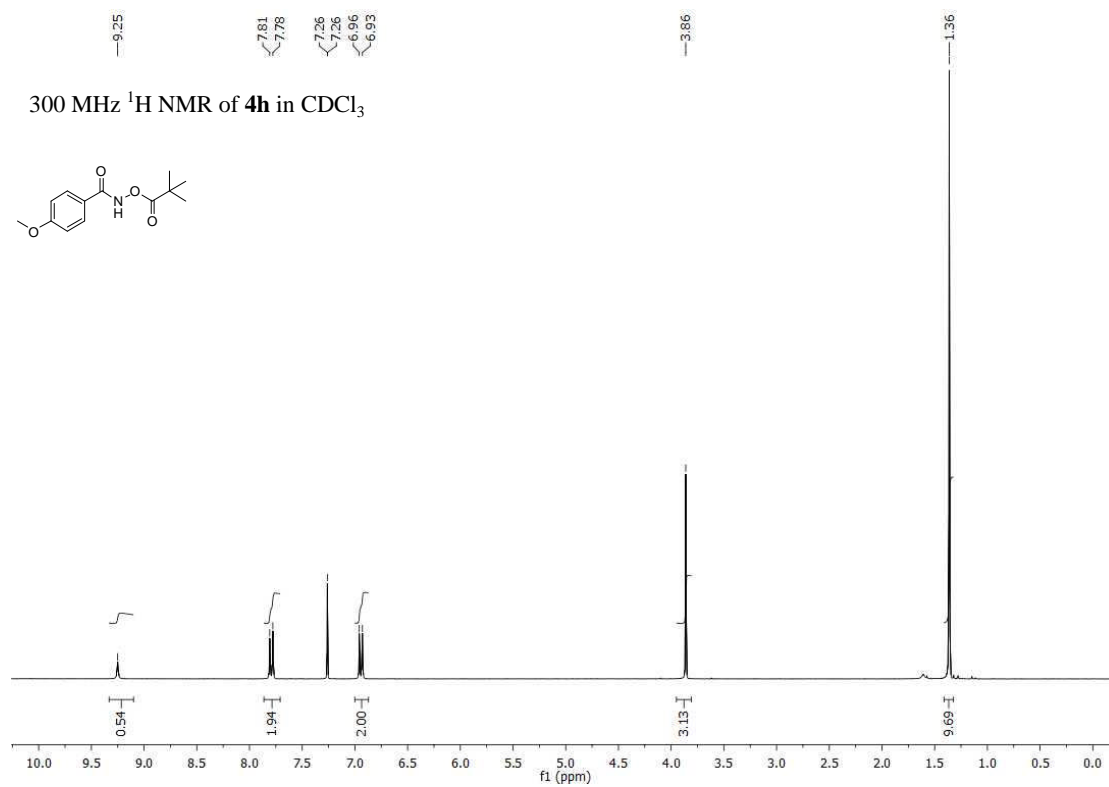


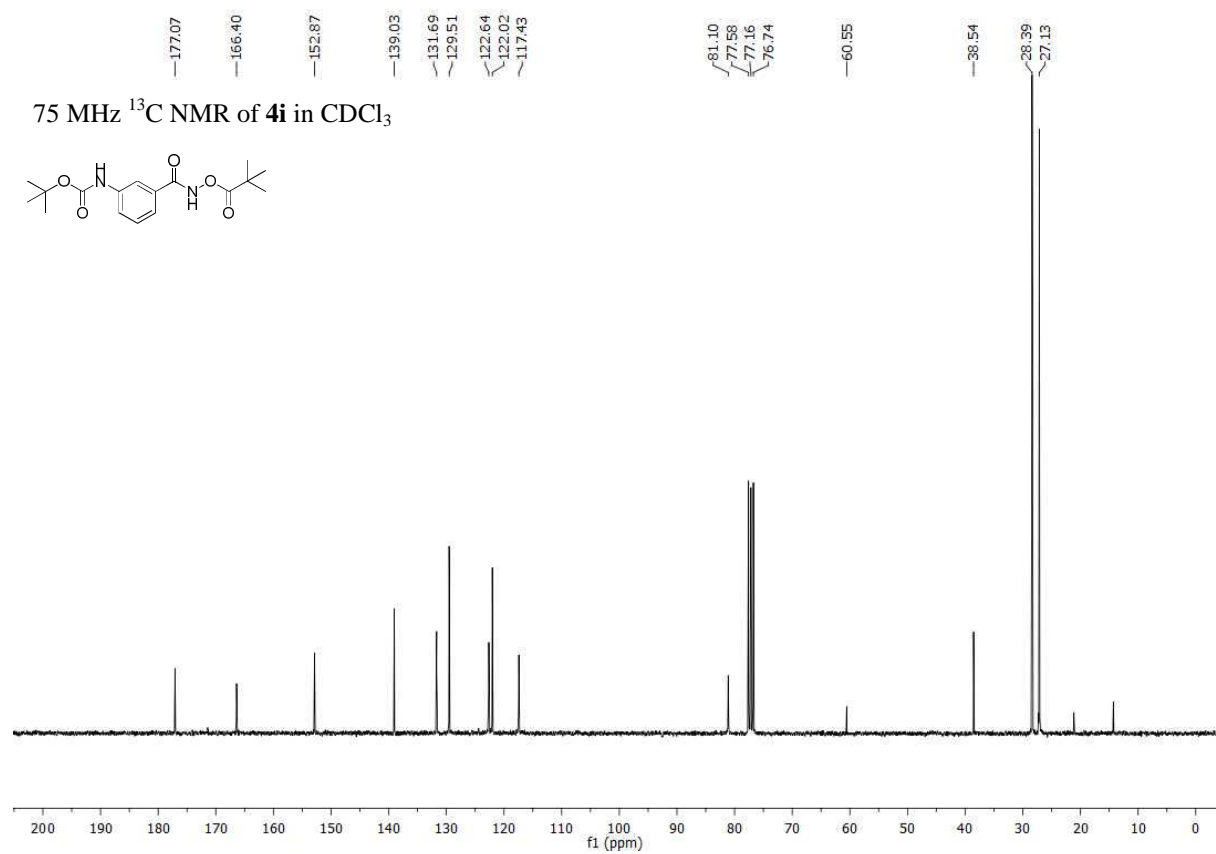
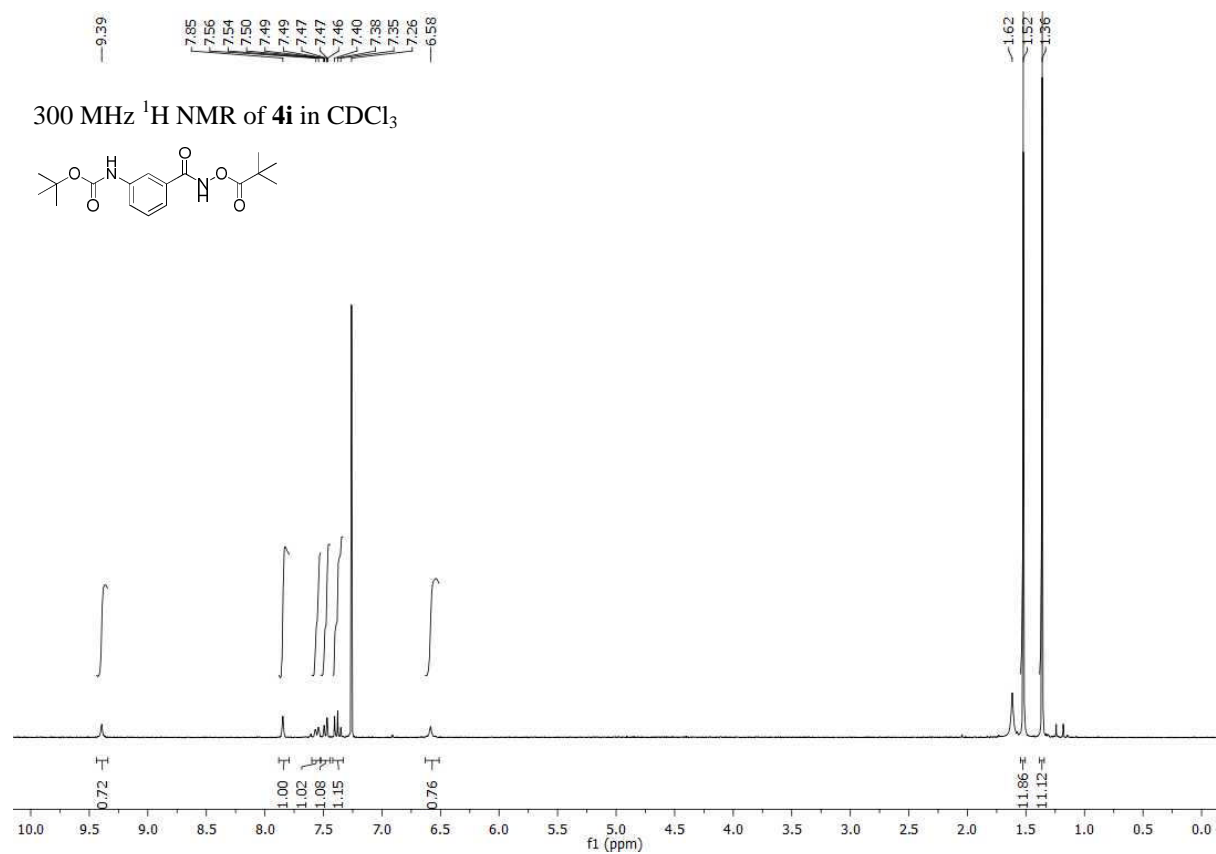


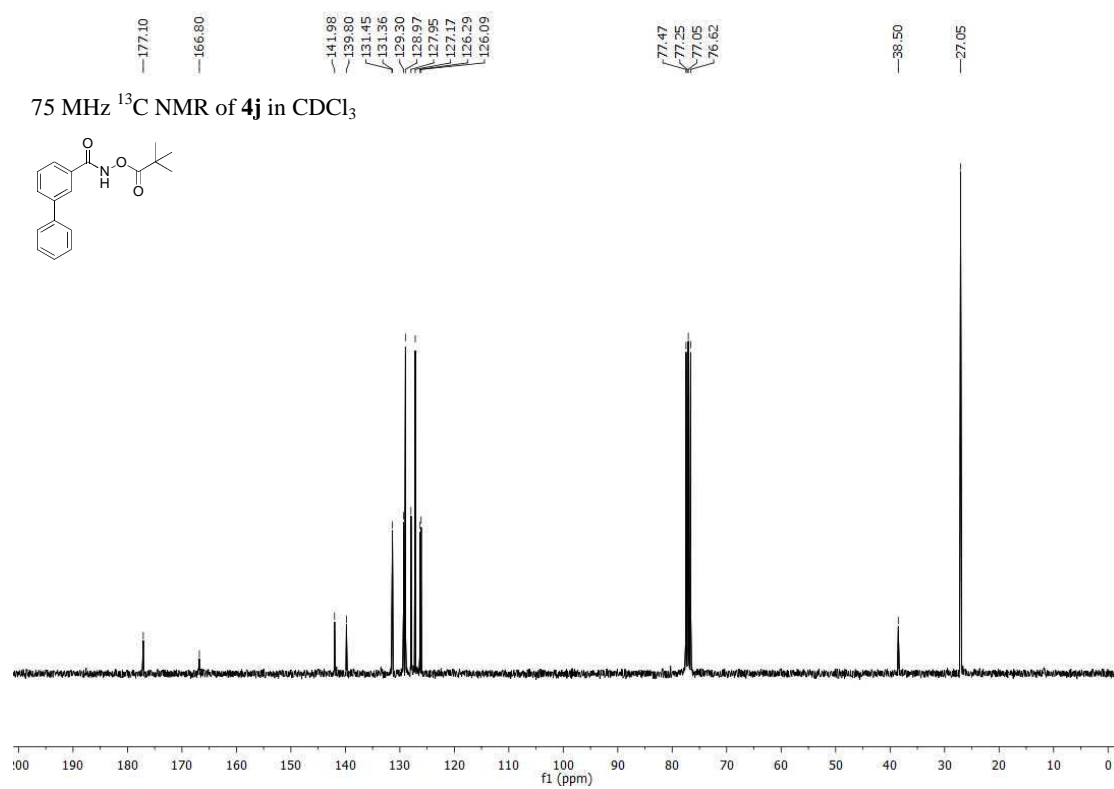
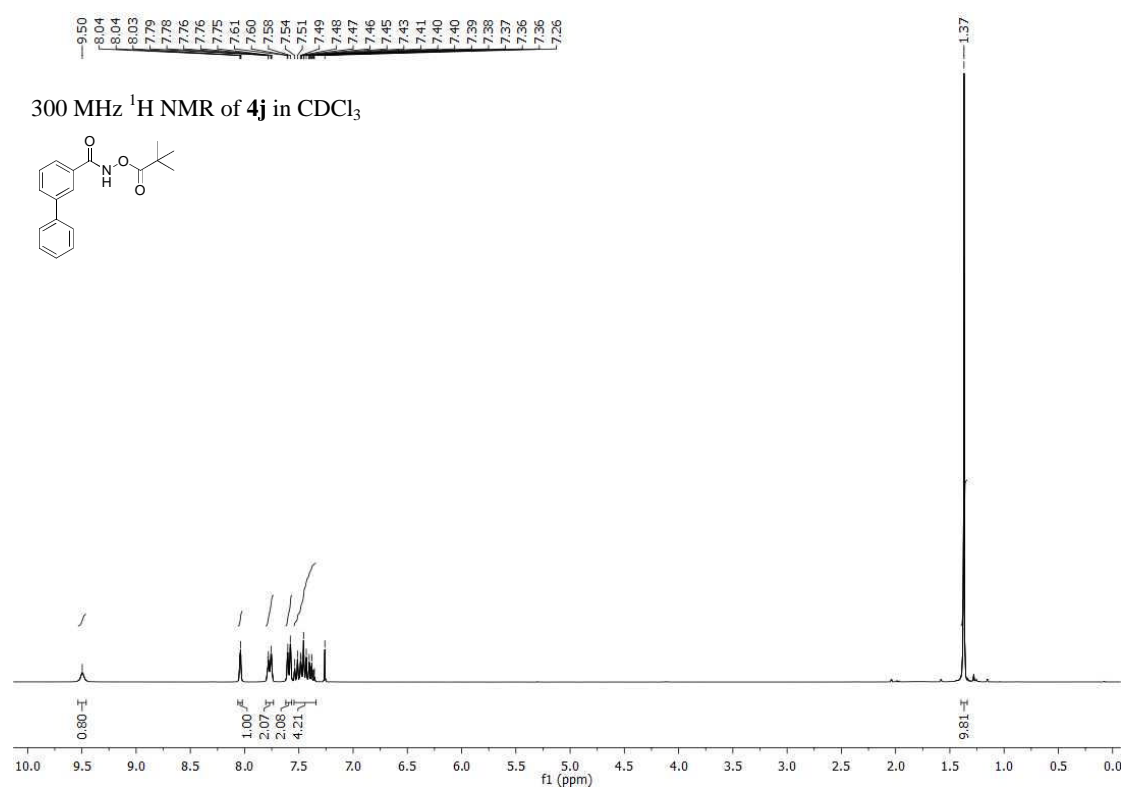


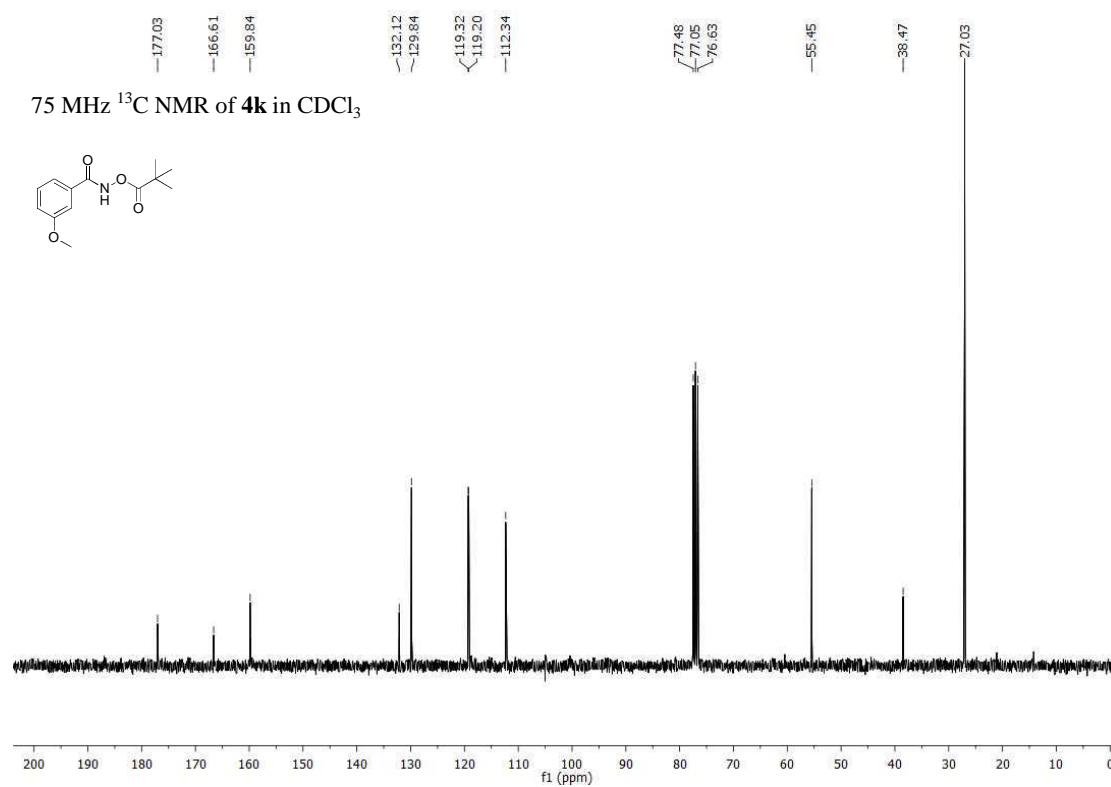
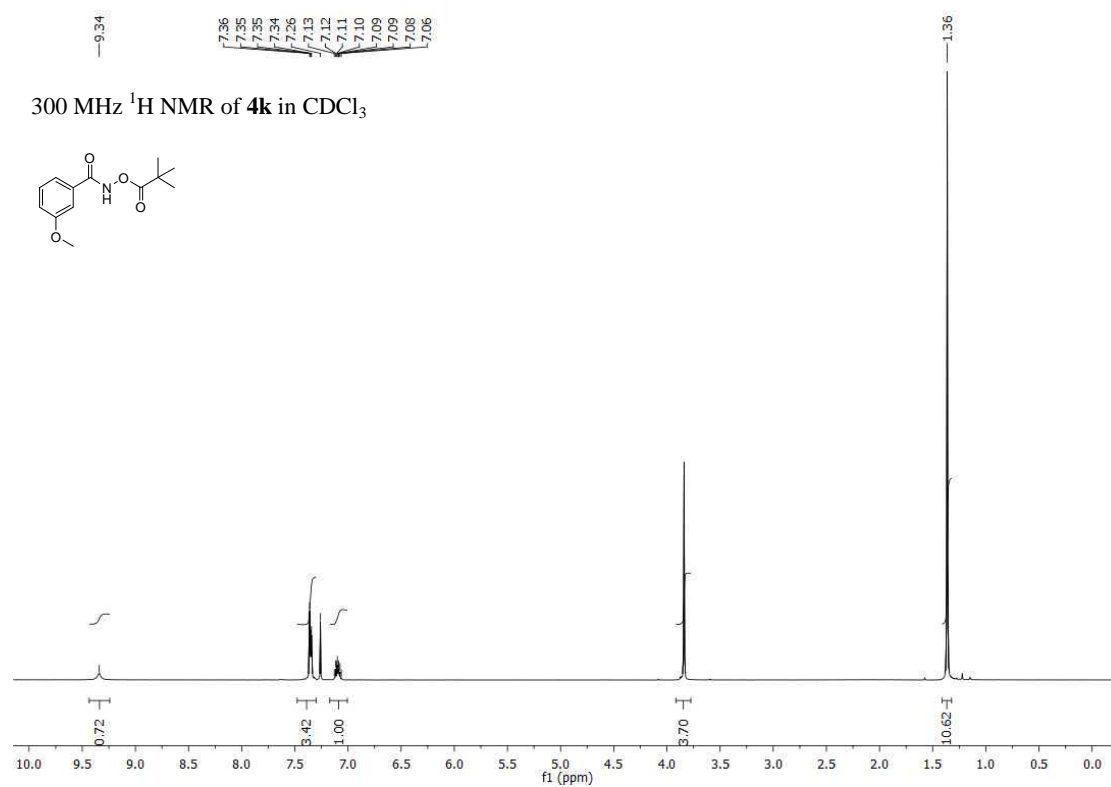


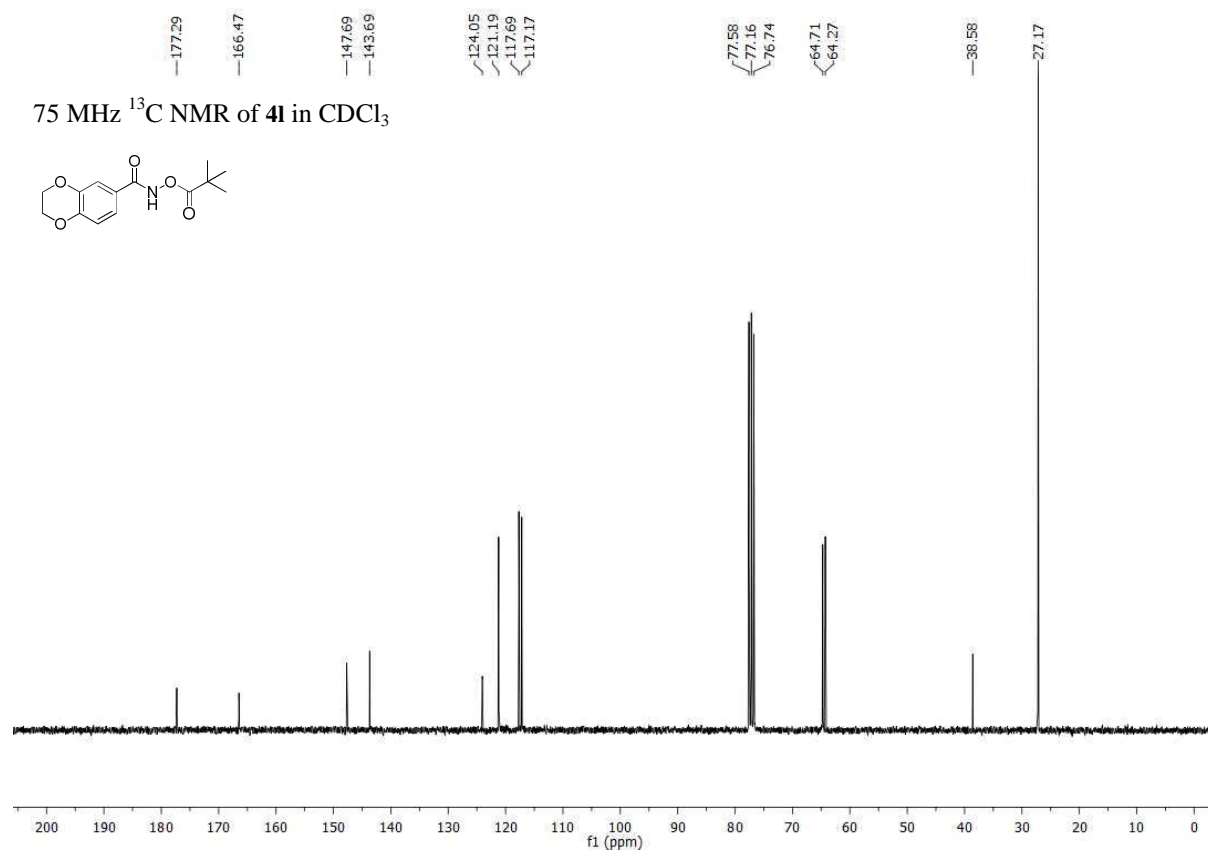
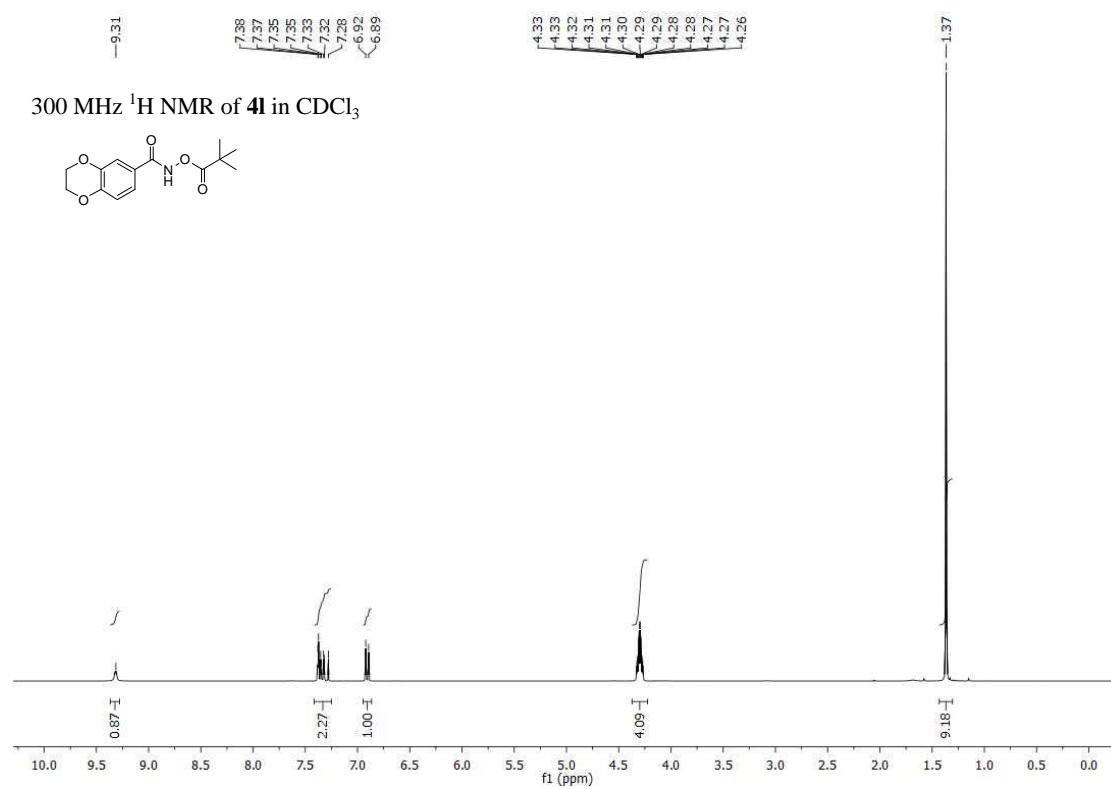


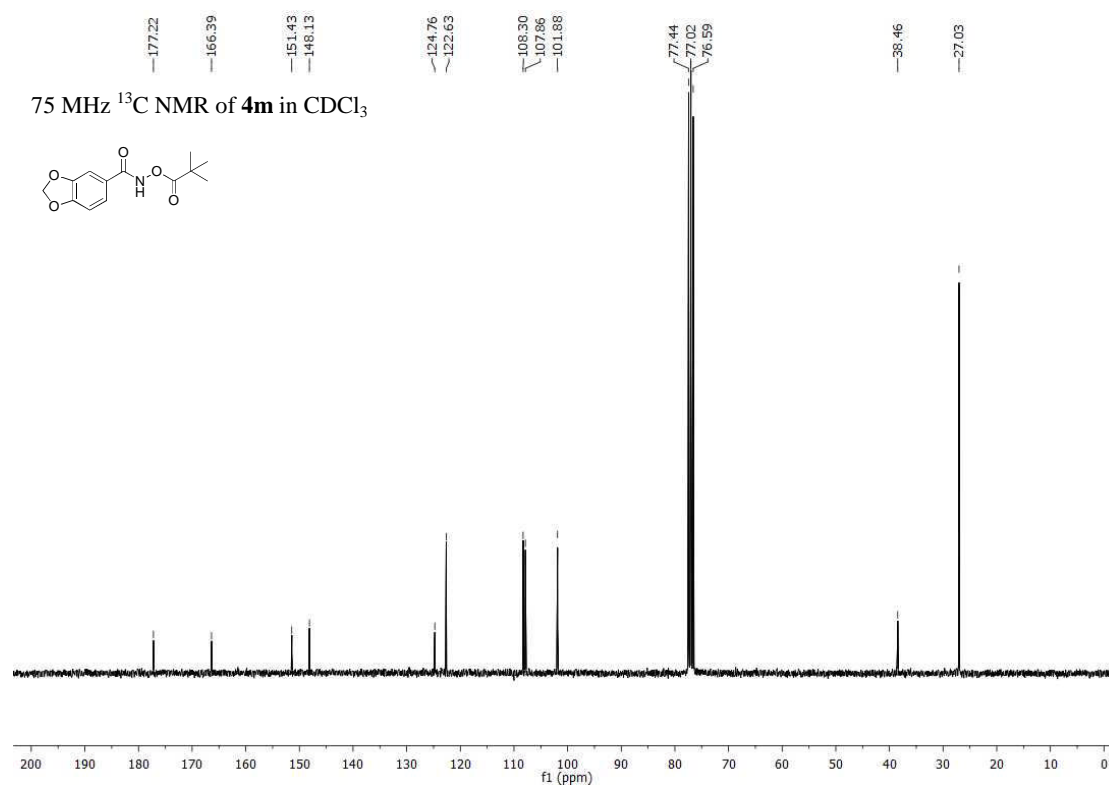
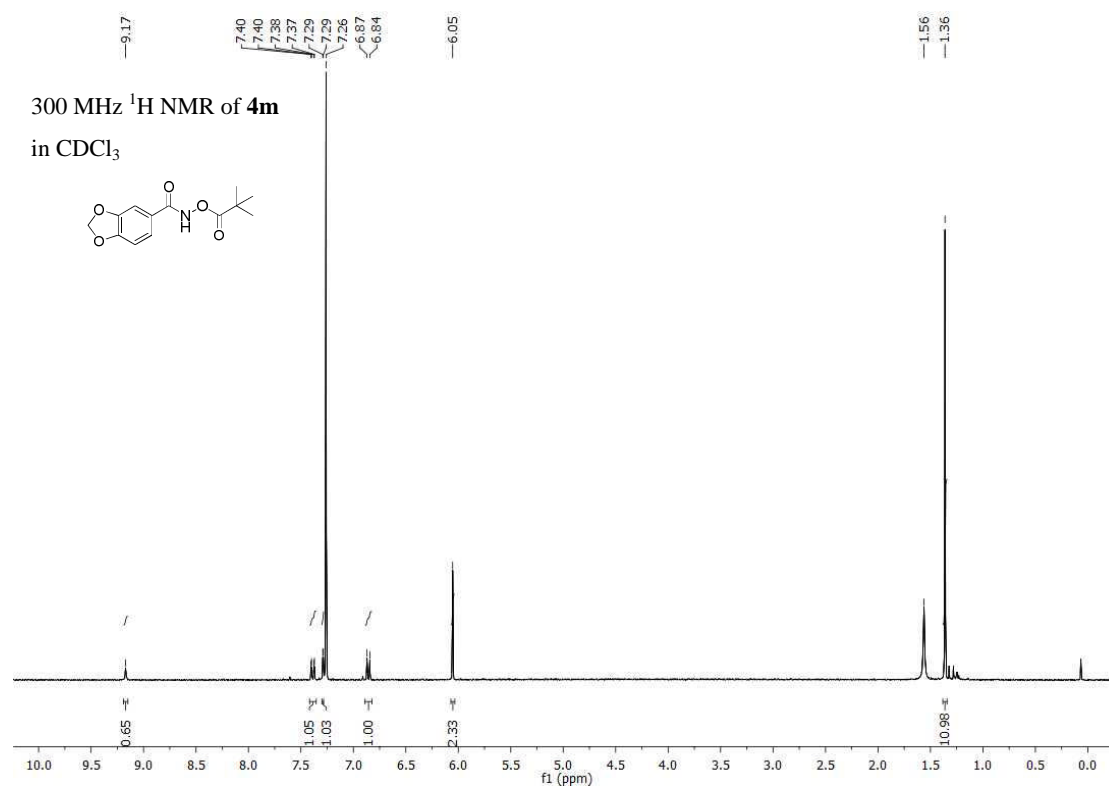




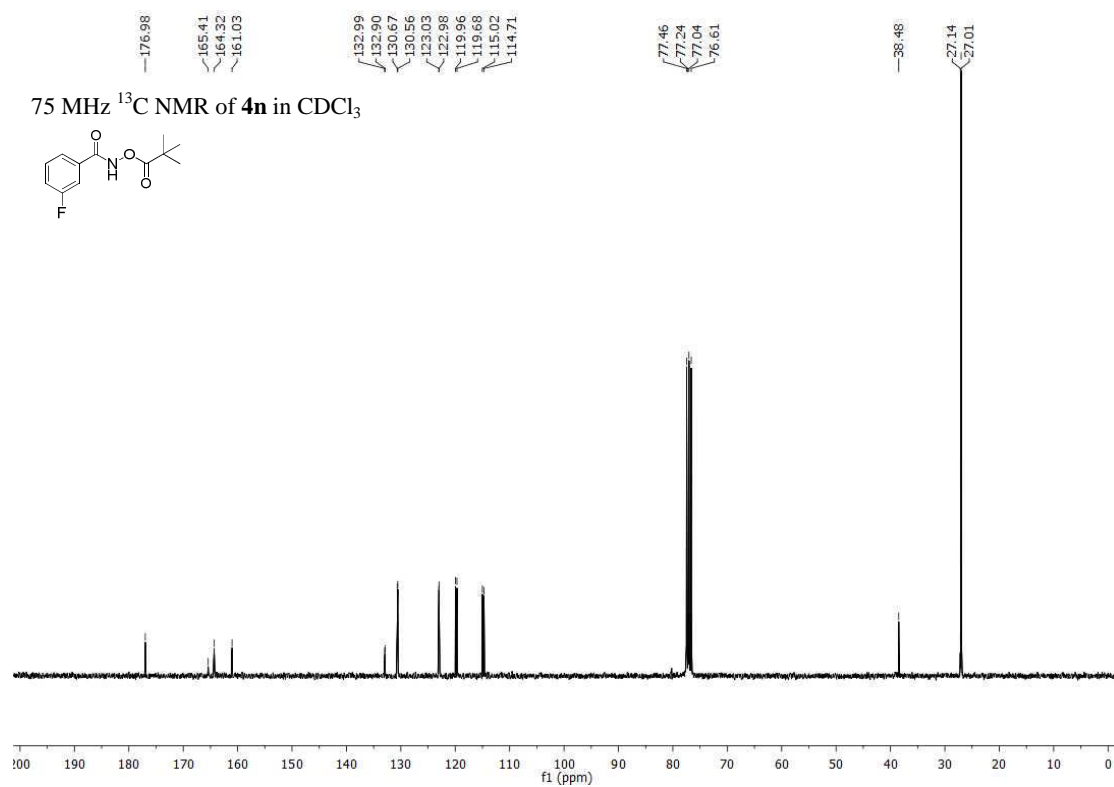
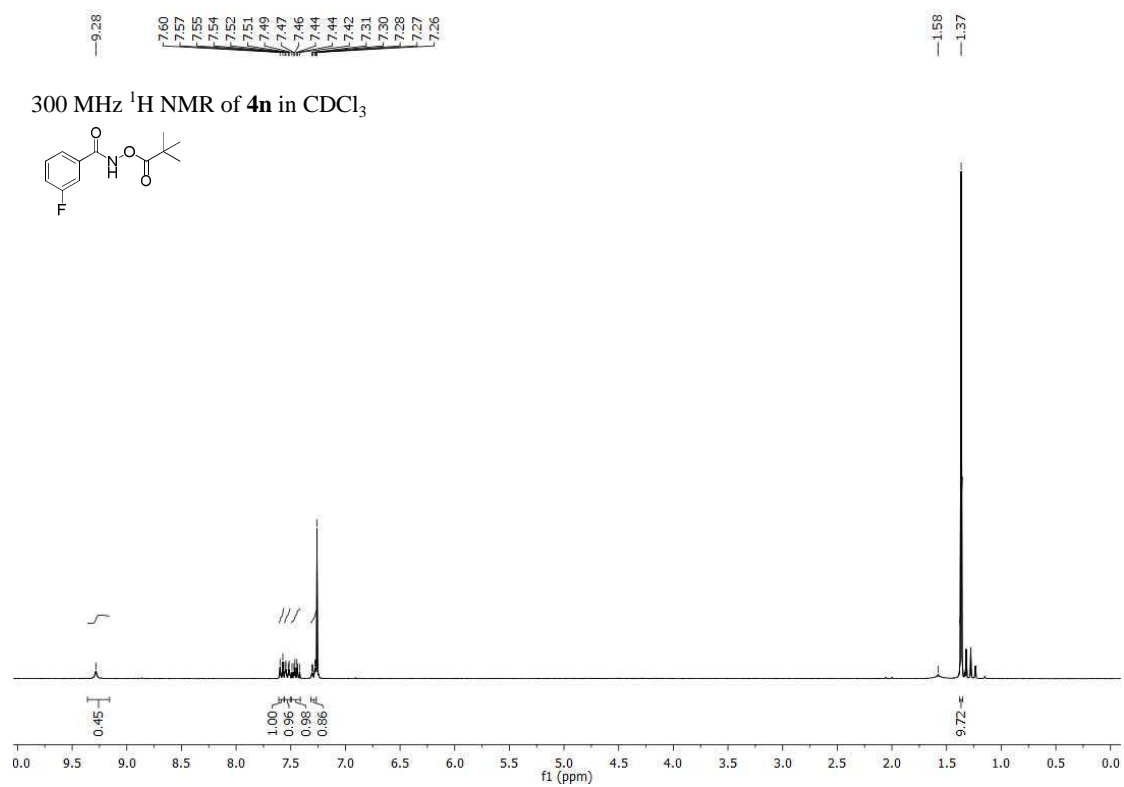


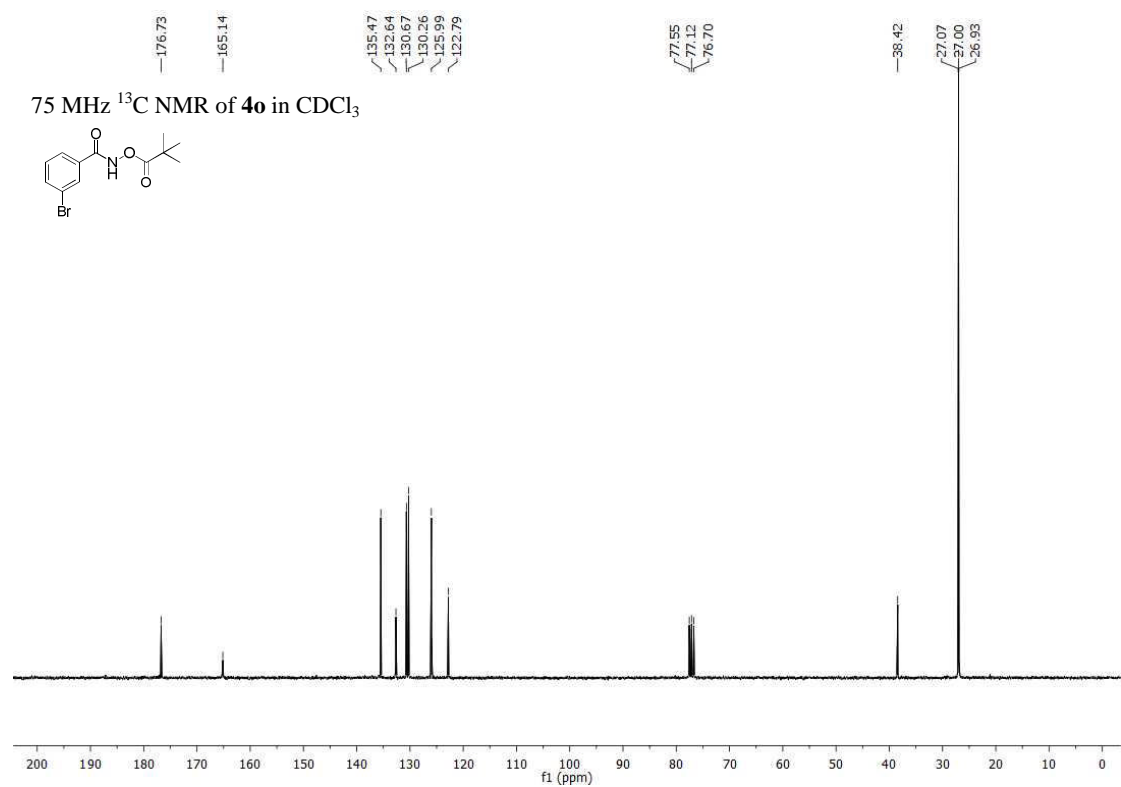
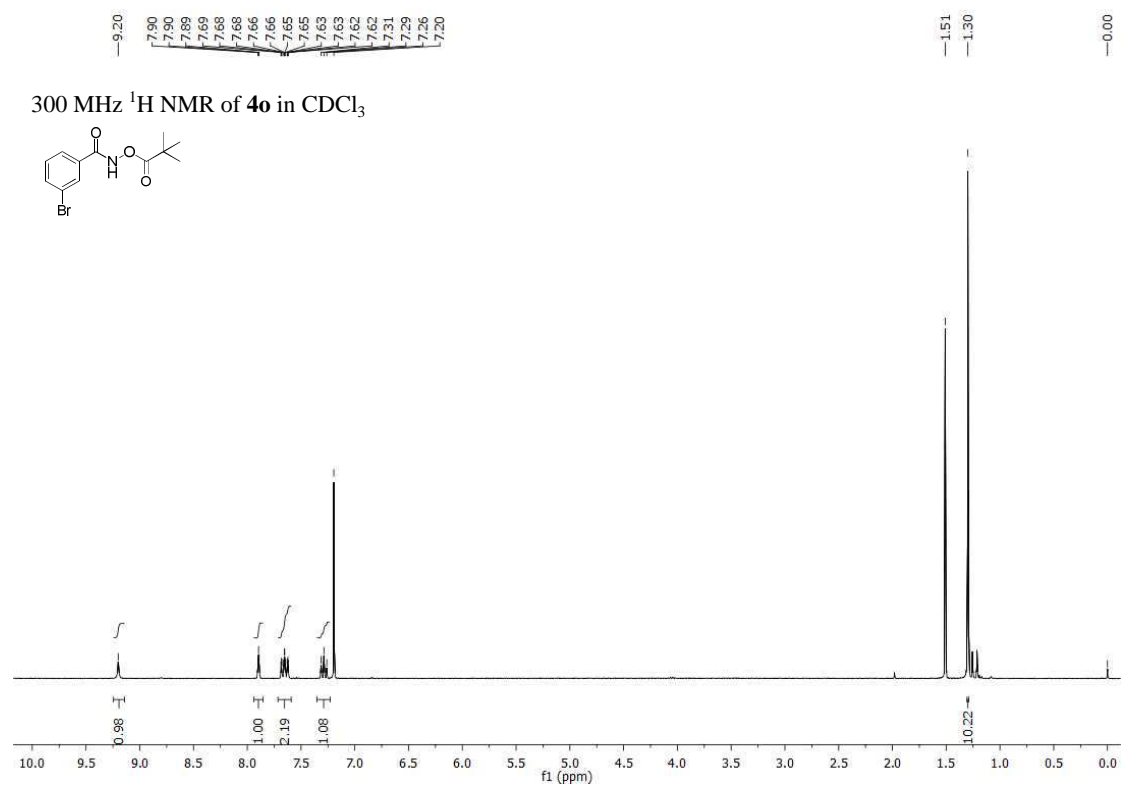


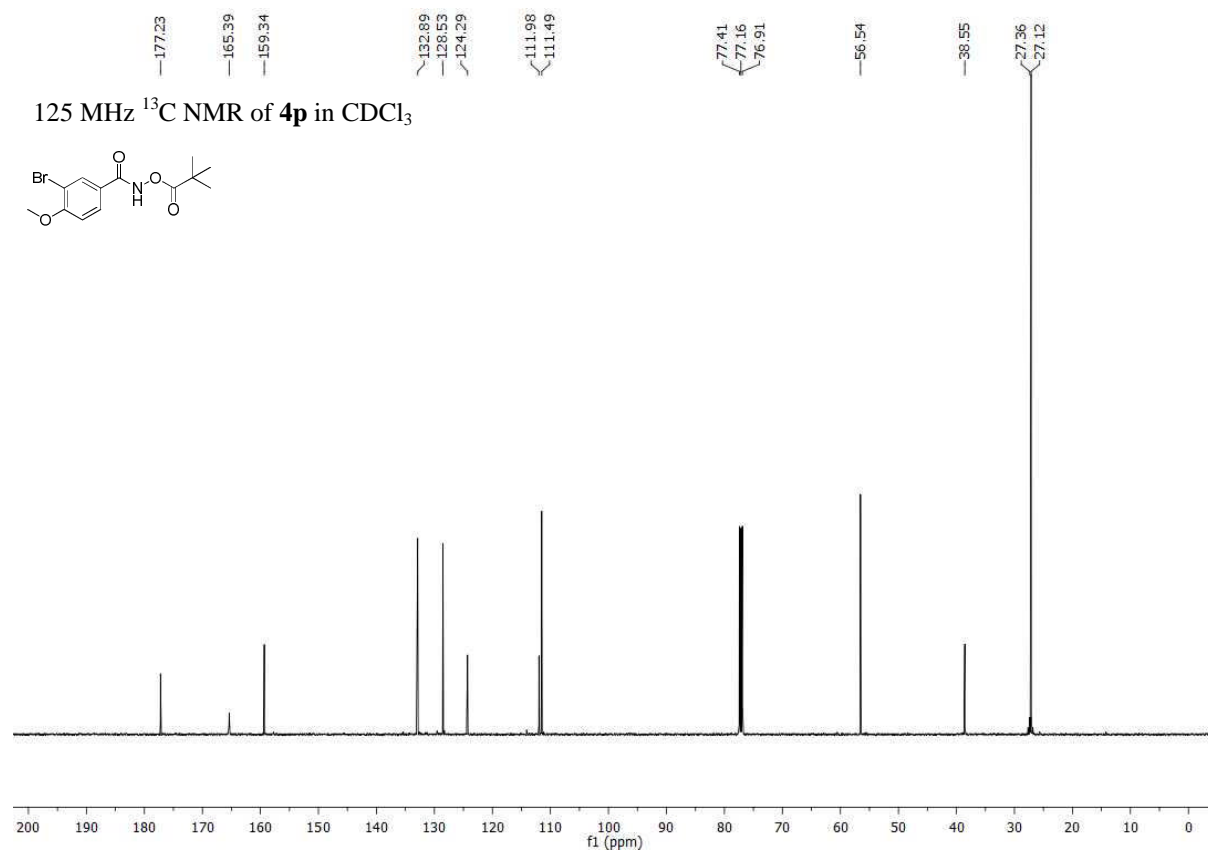
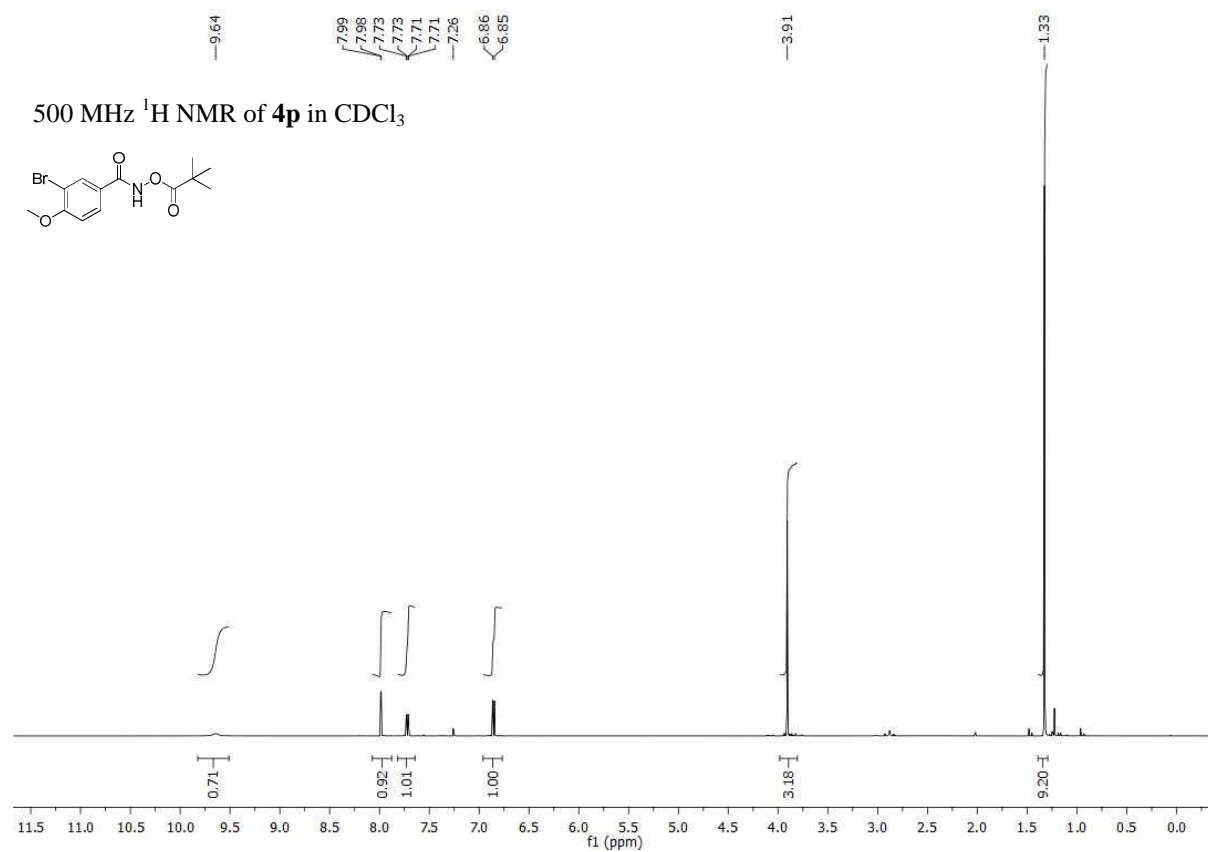




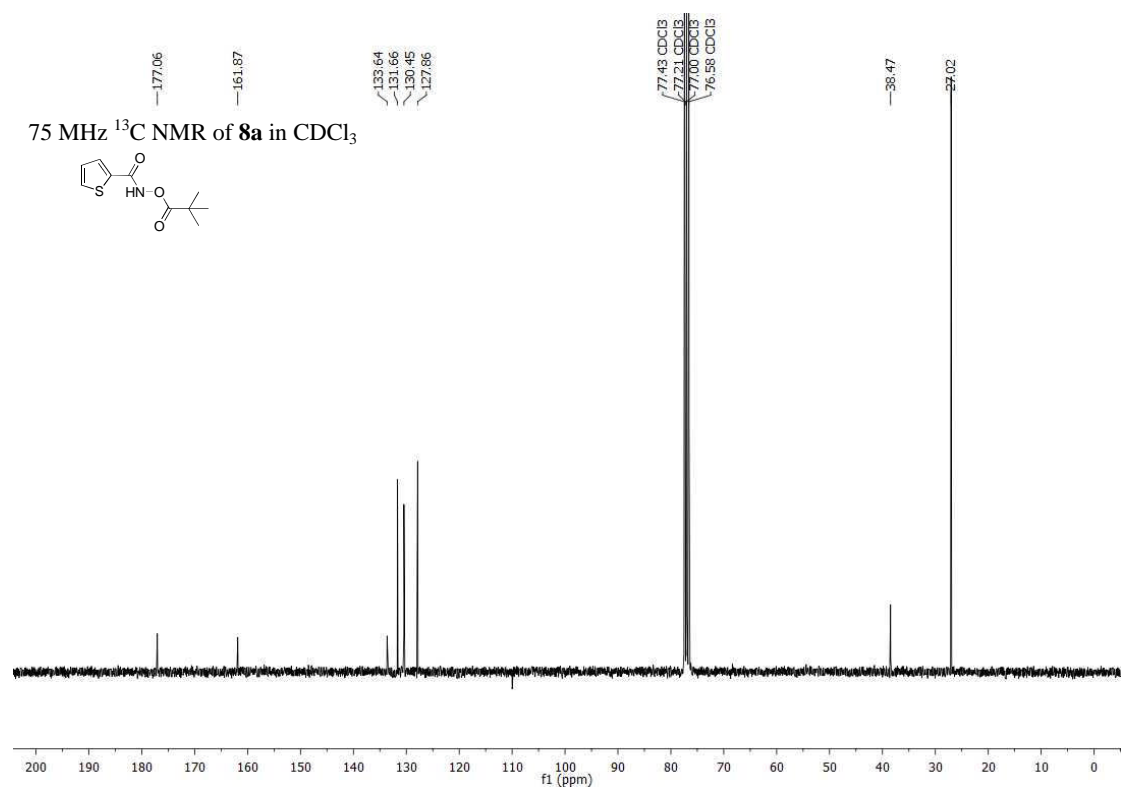
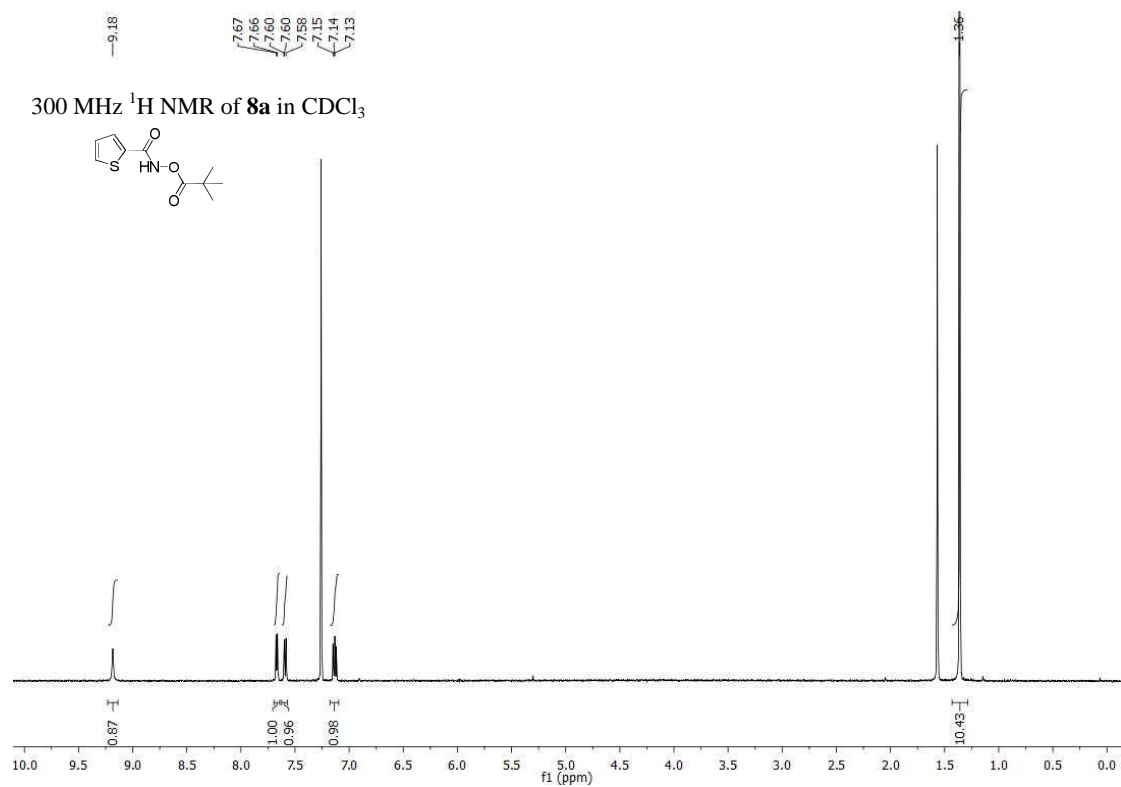


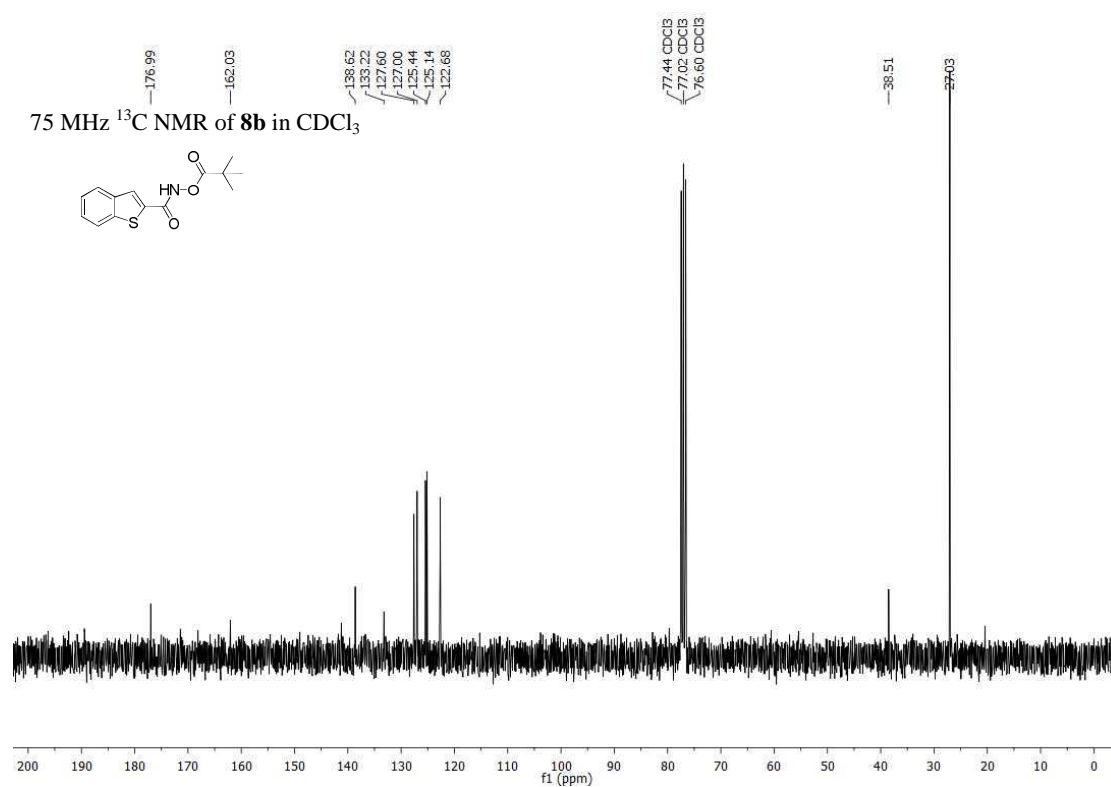
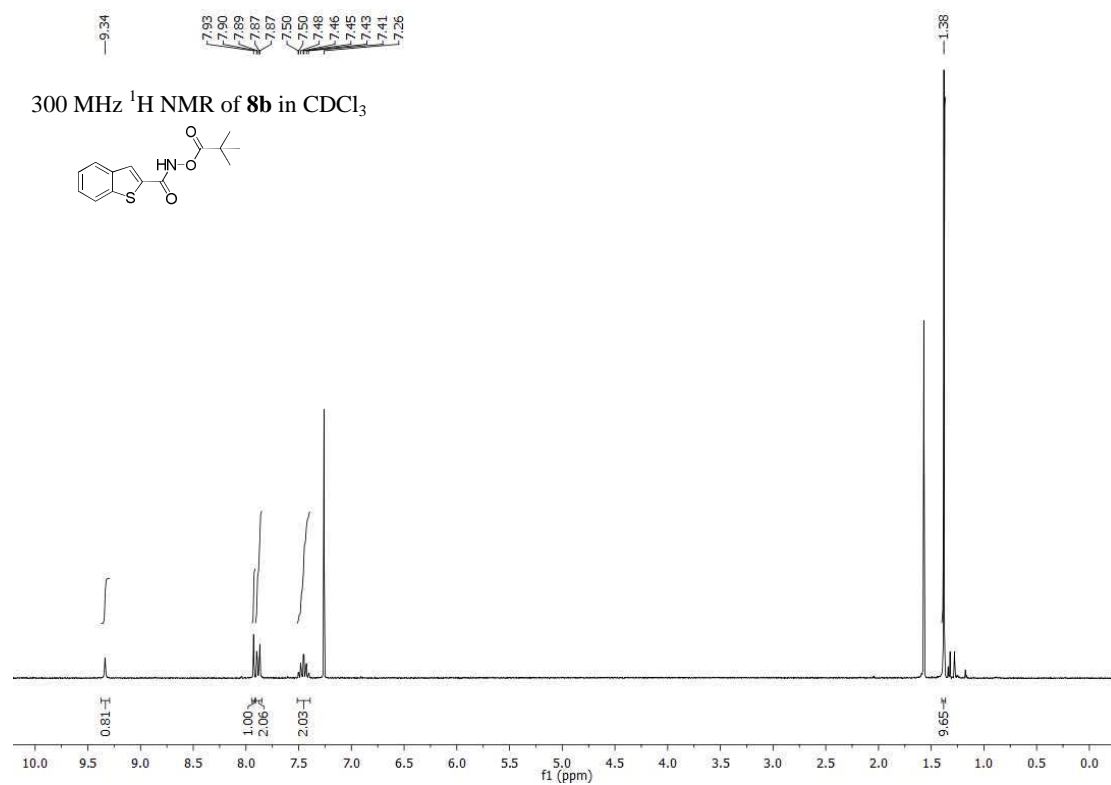


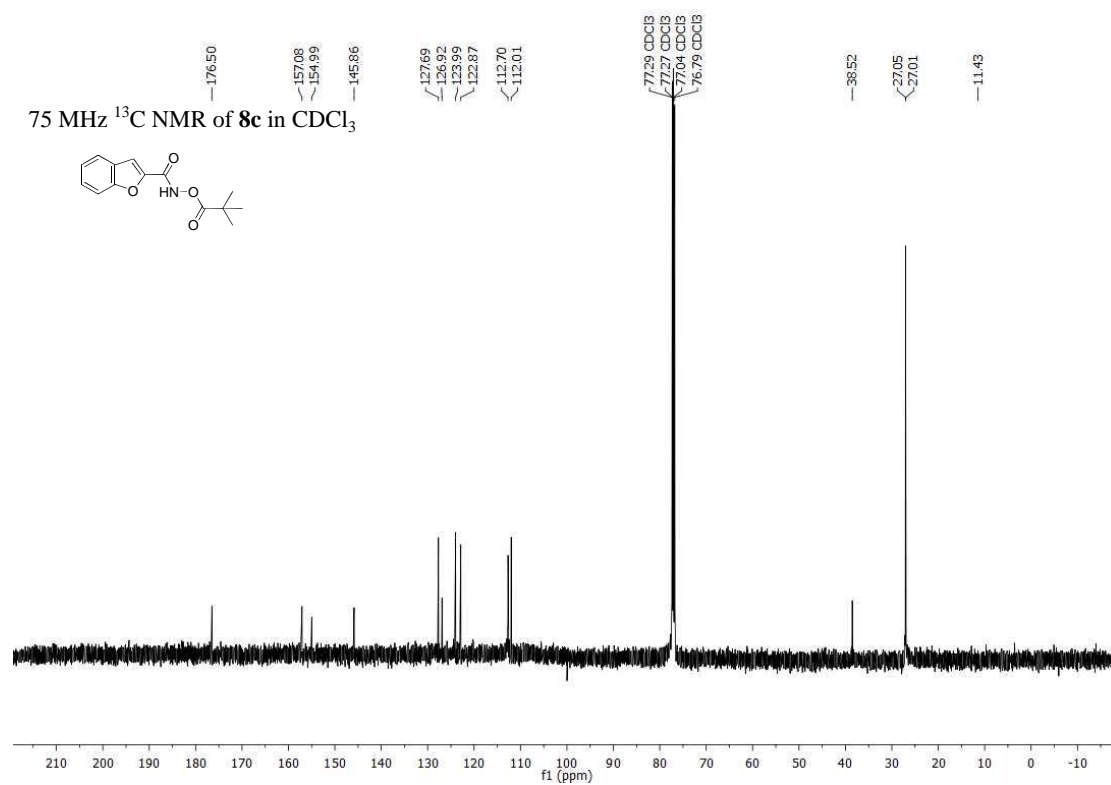
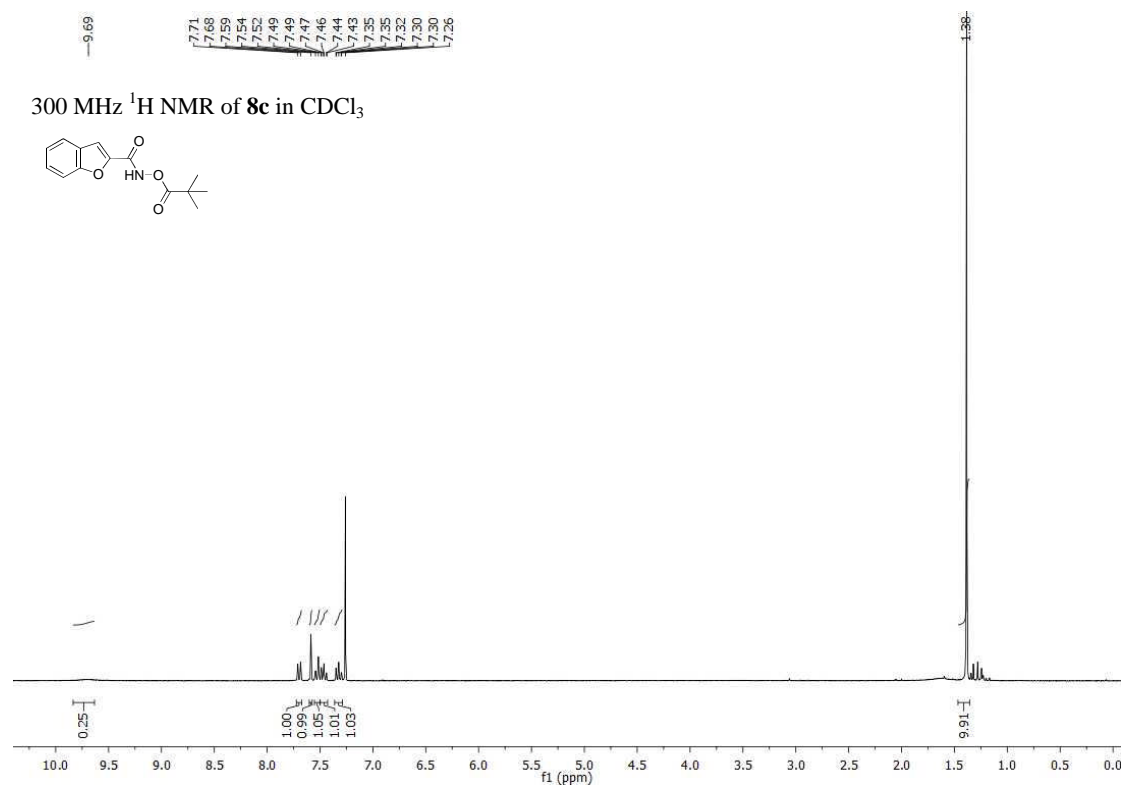


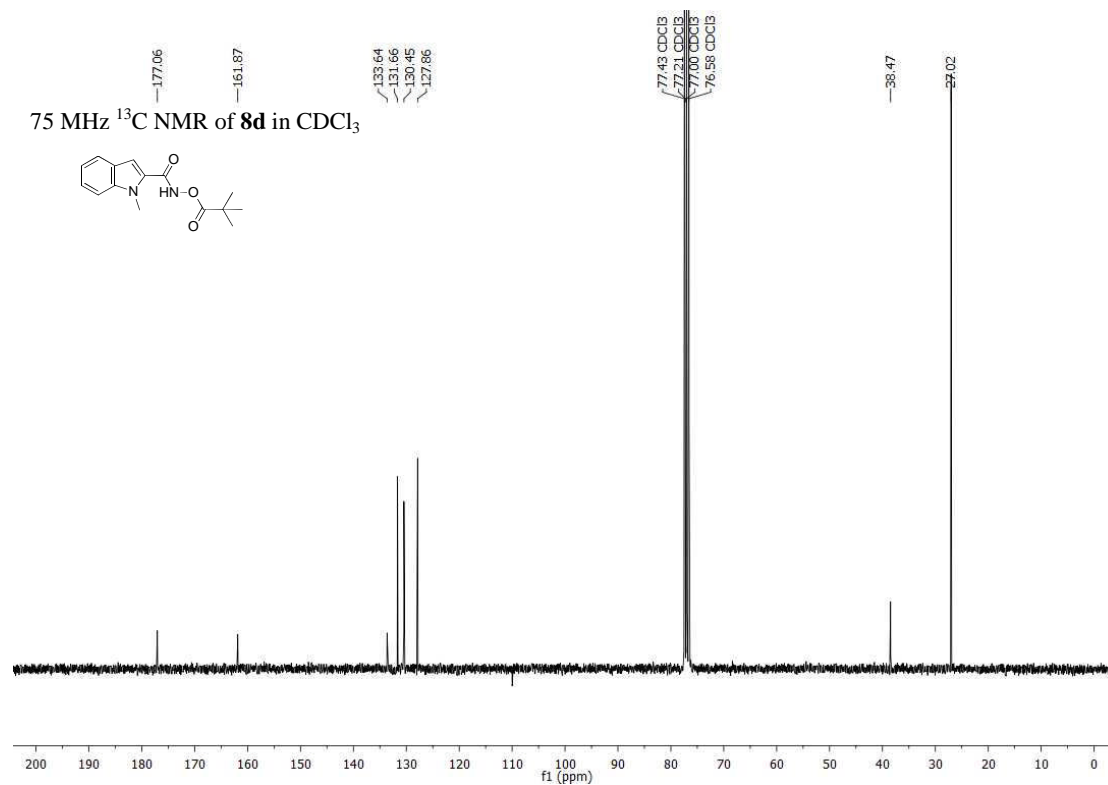
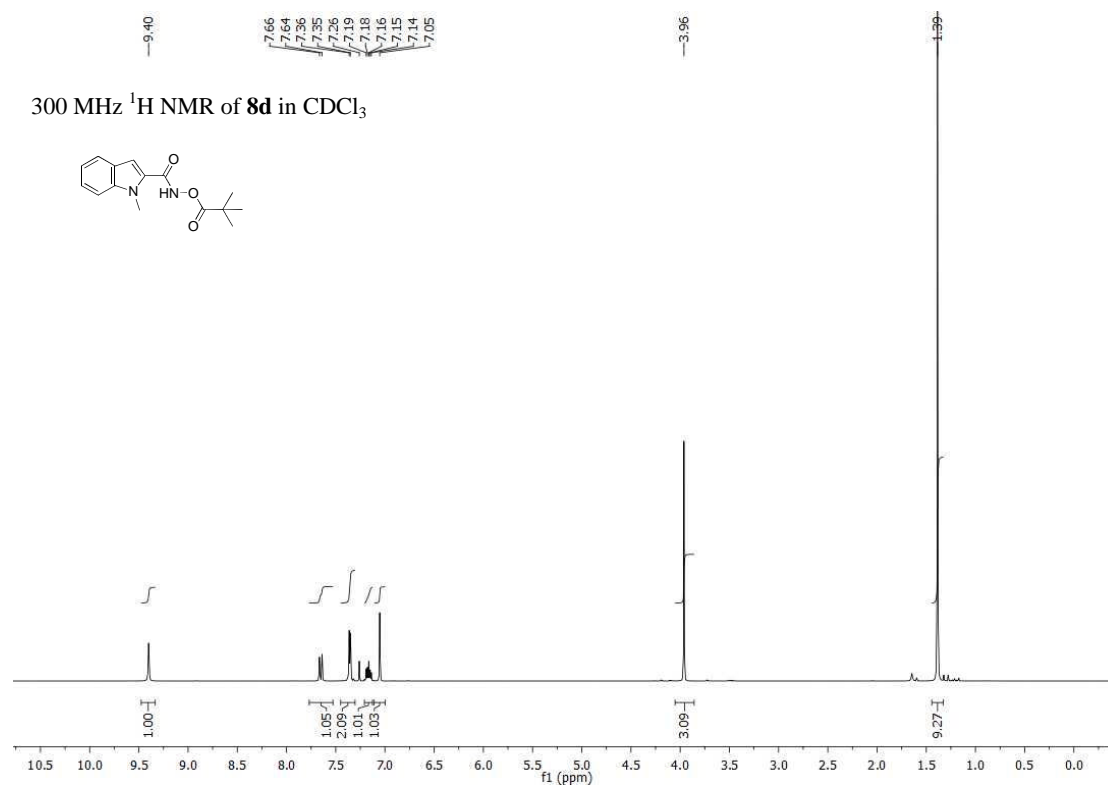


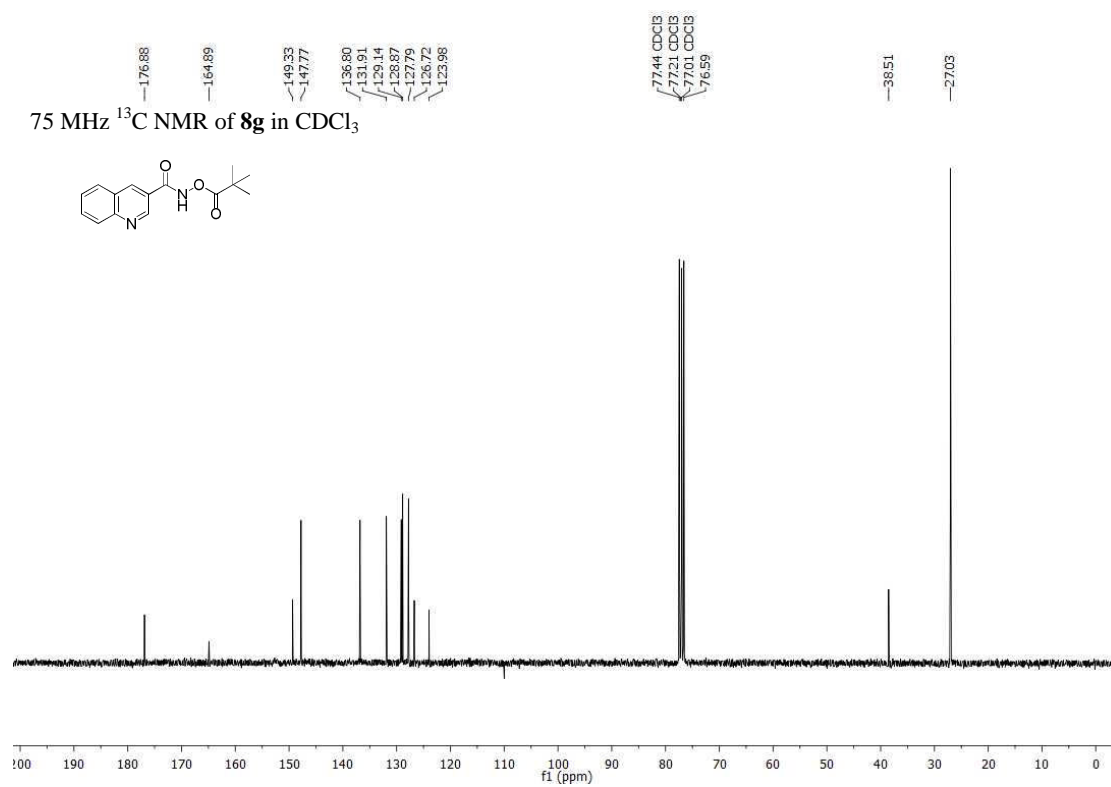
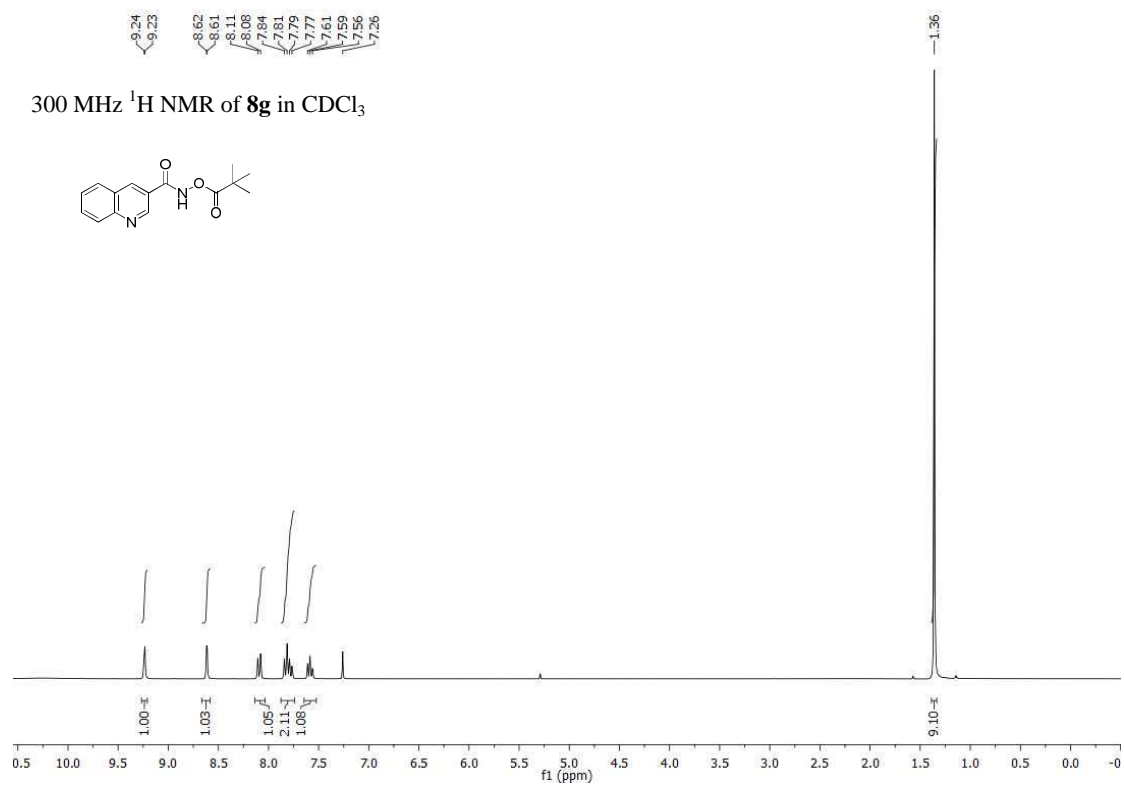
## Heterocyclic hydroxamate esters





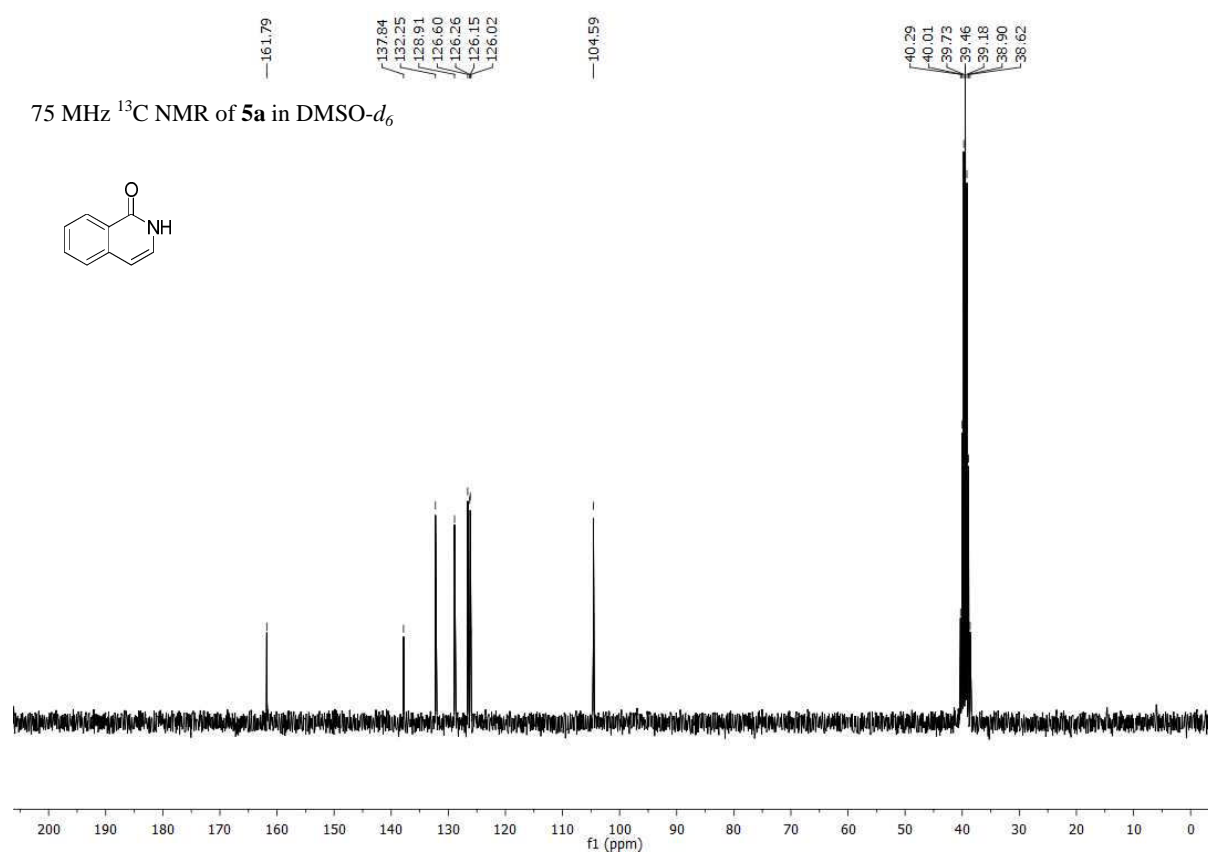
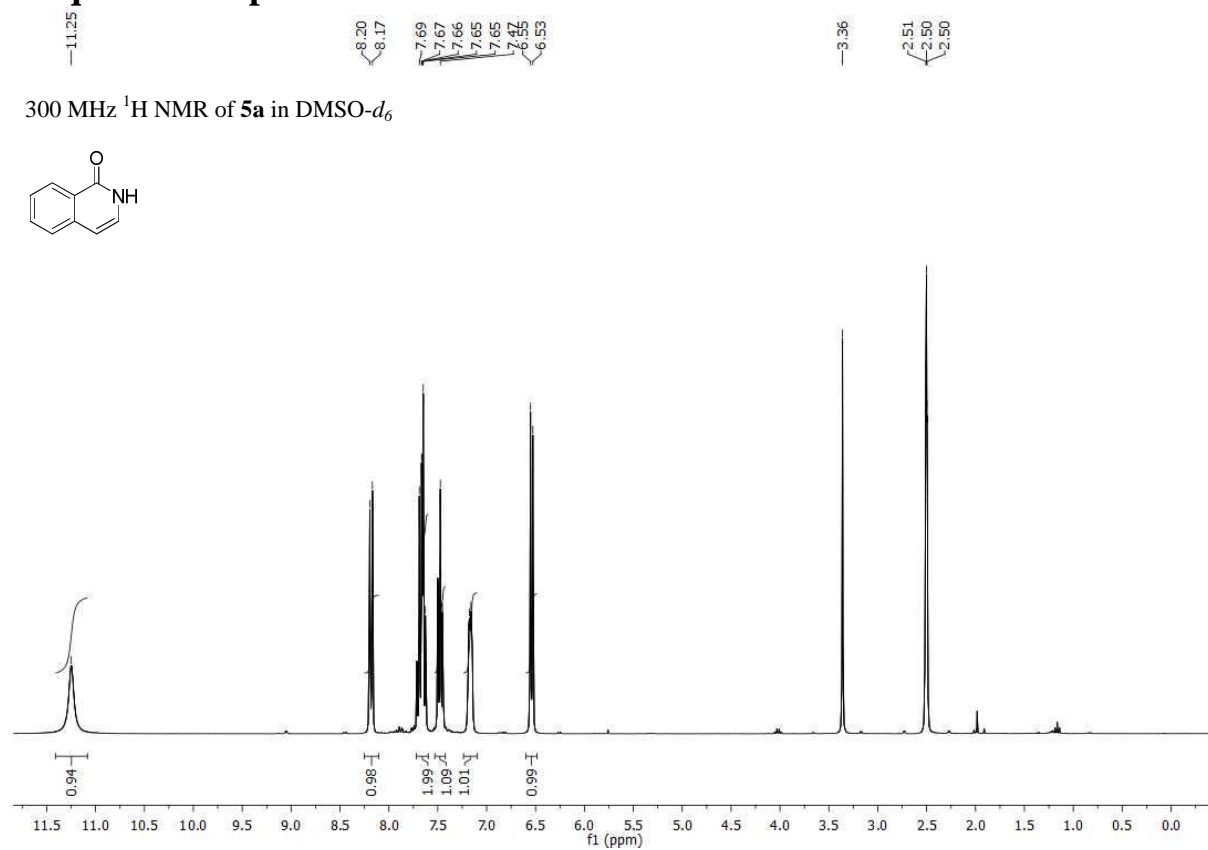


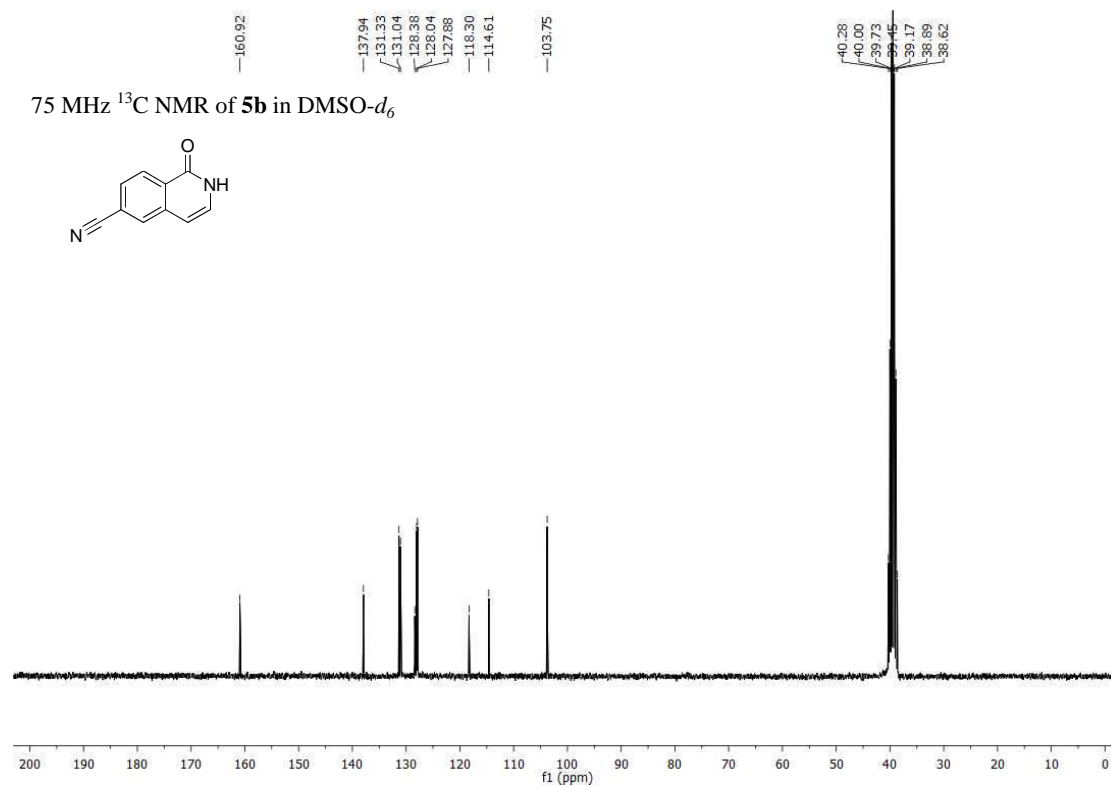
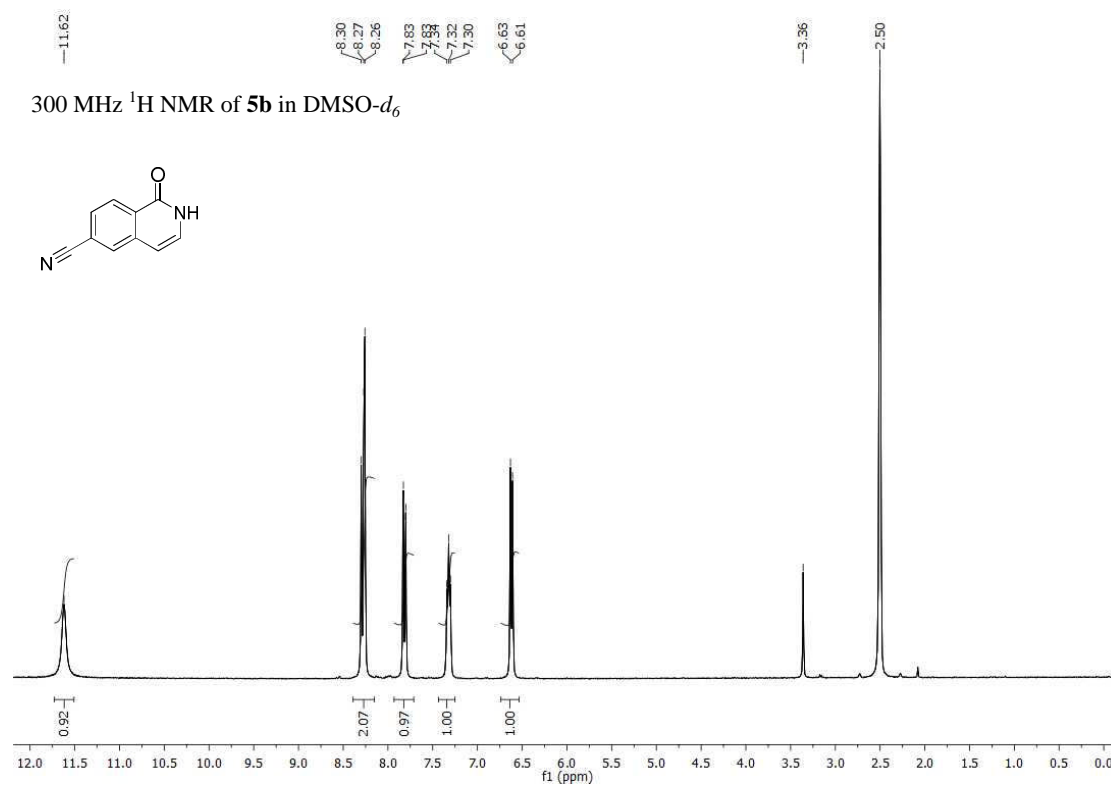


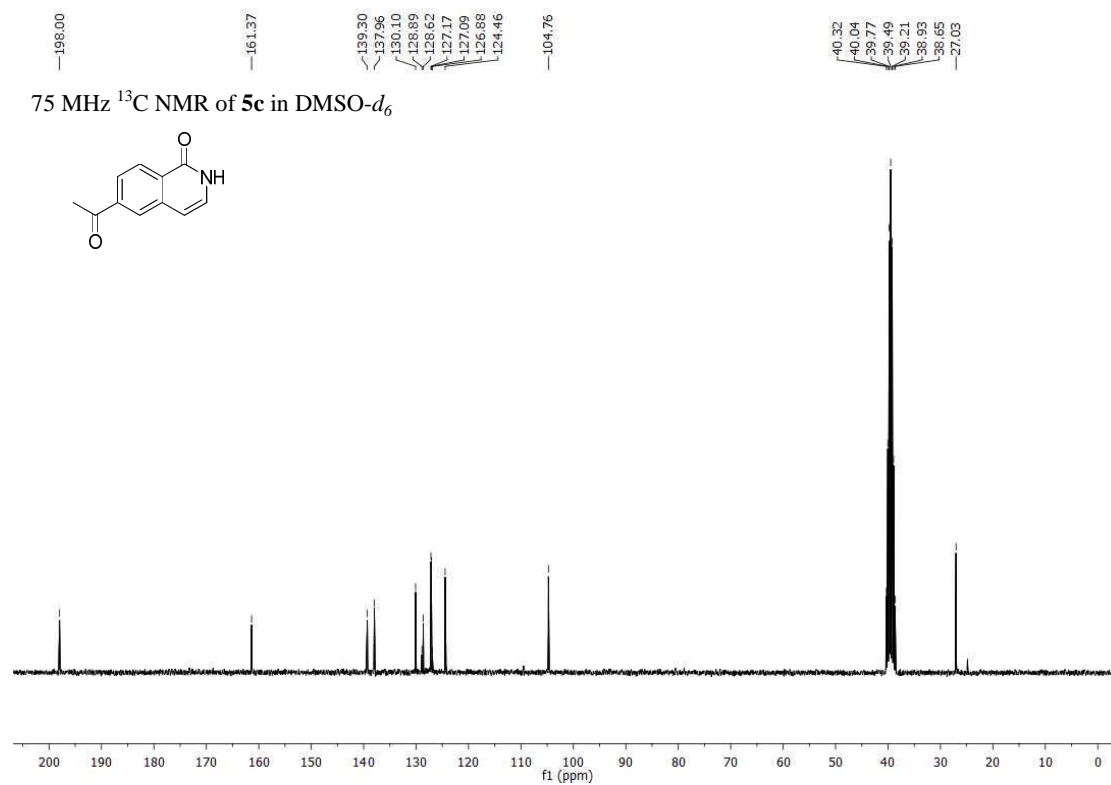
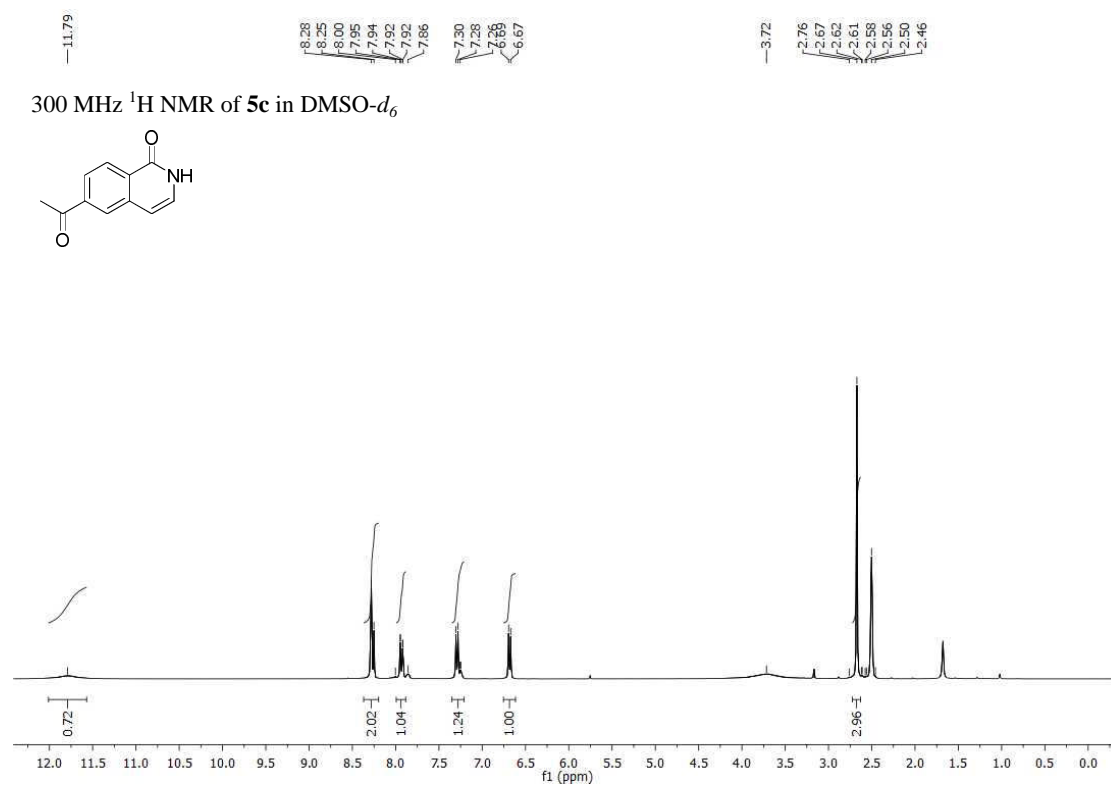




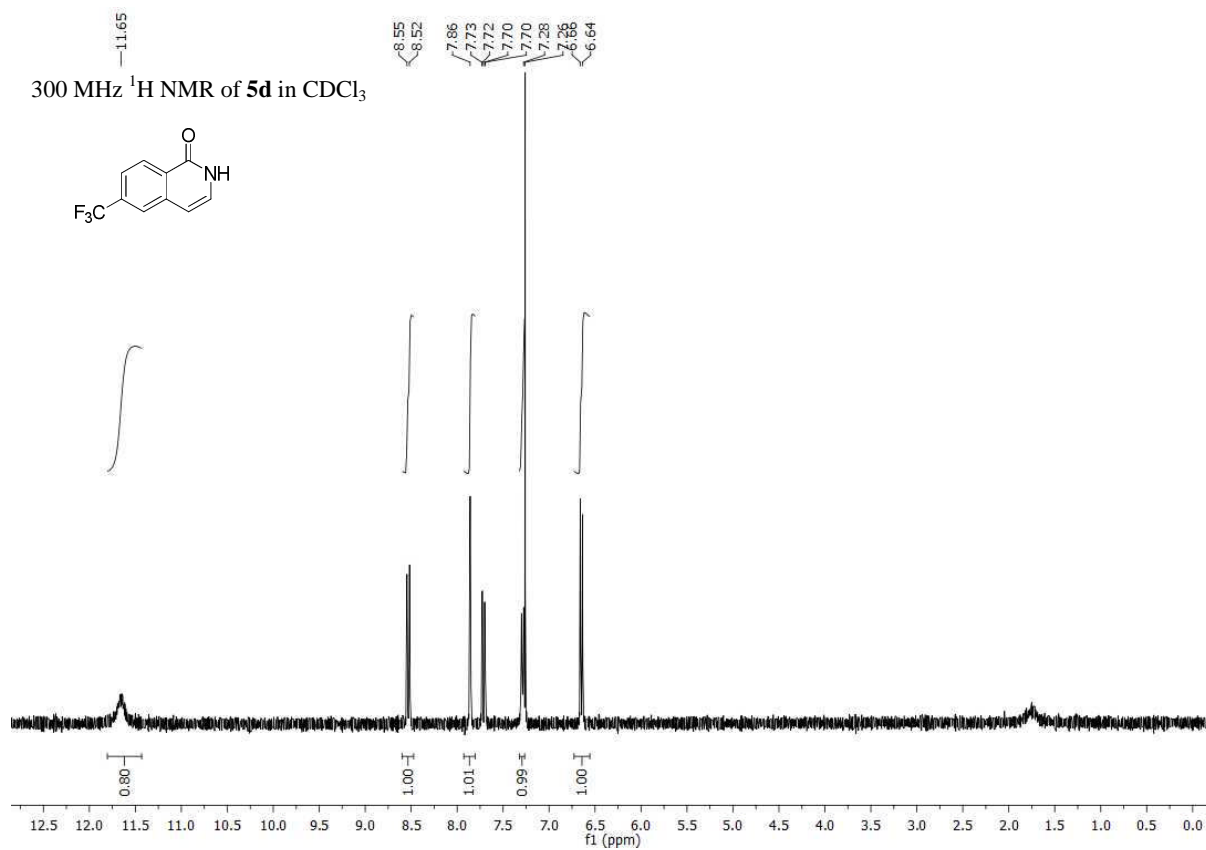
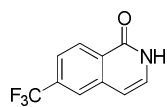
## Isoquinolone Spectra



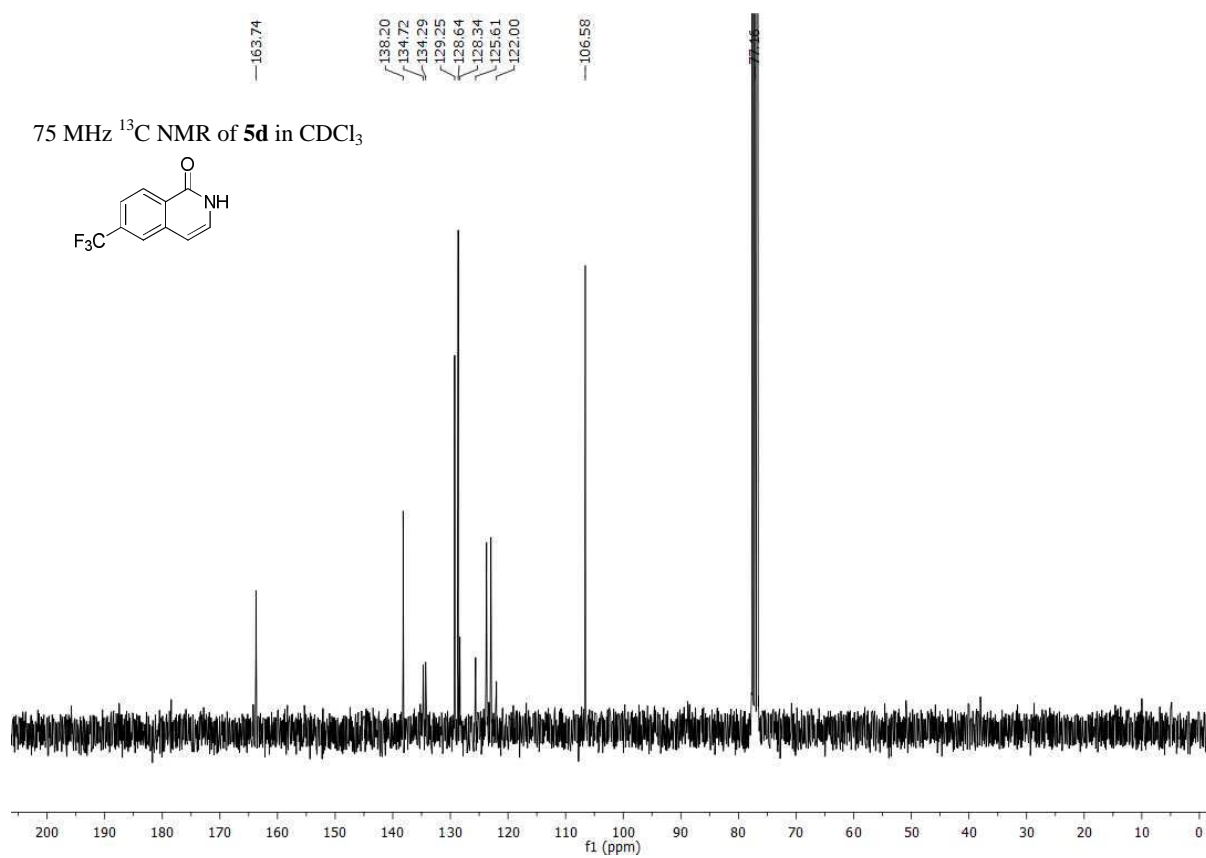
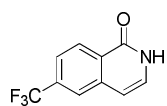


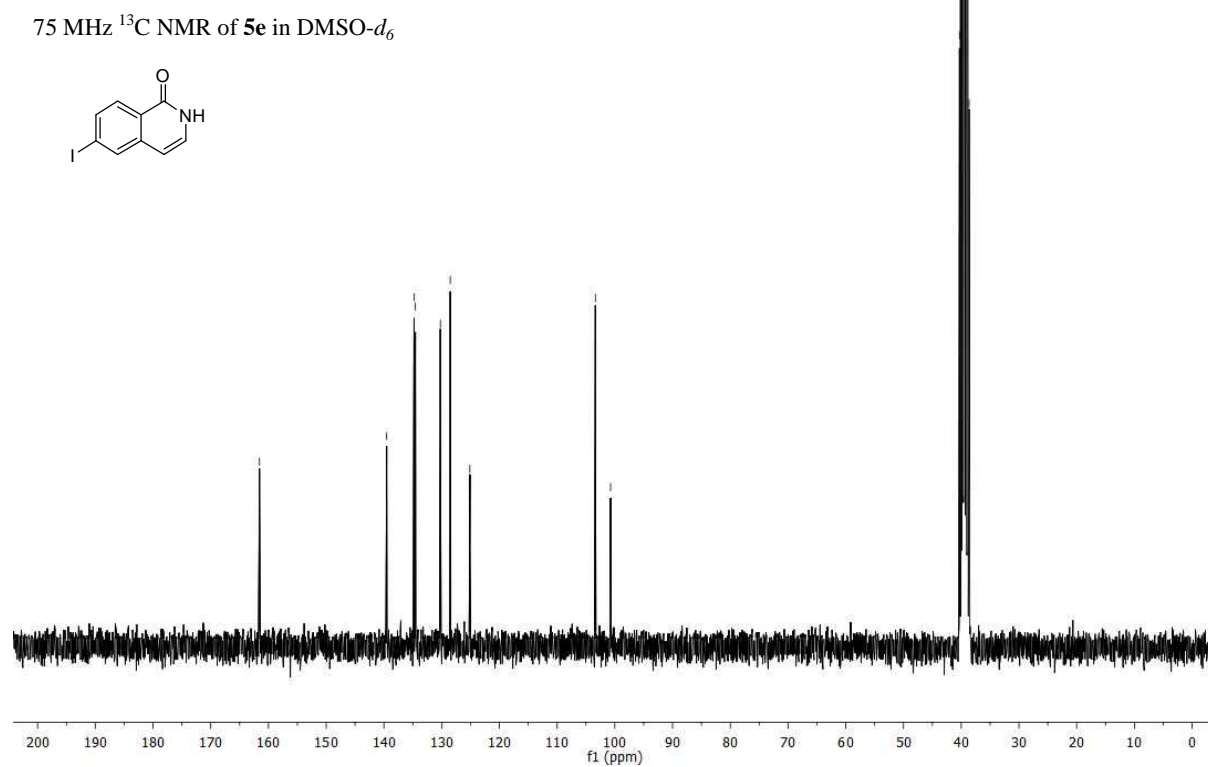
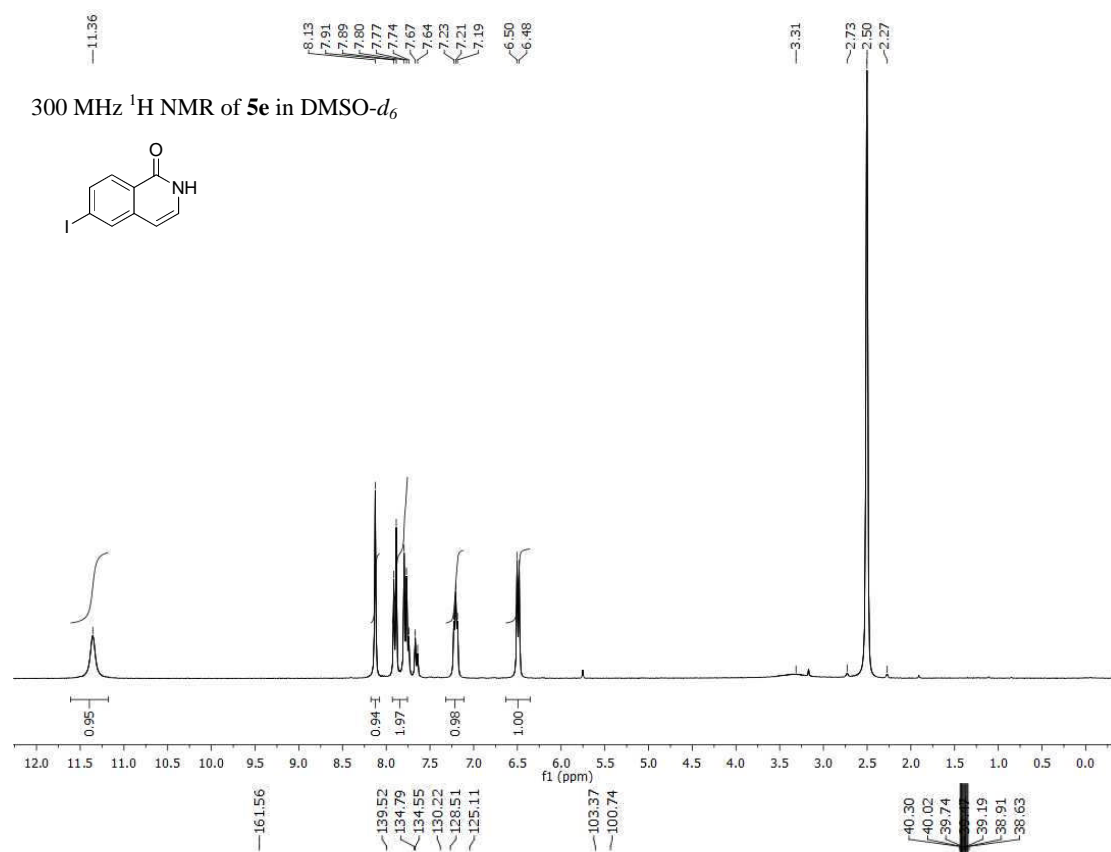


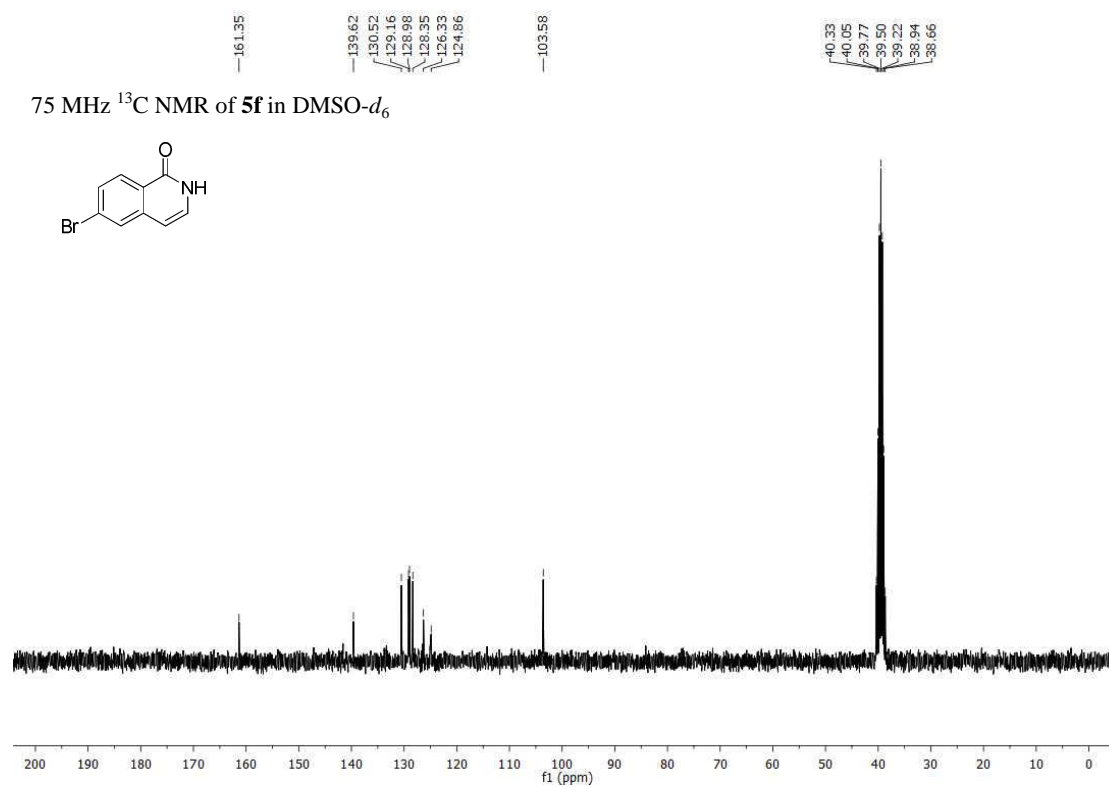
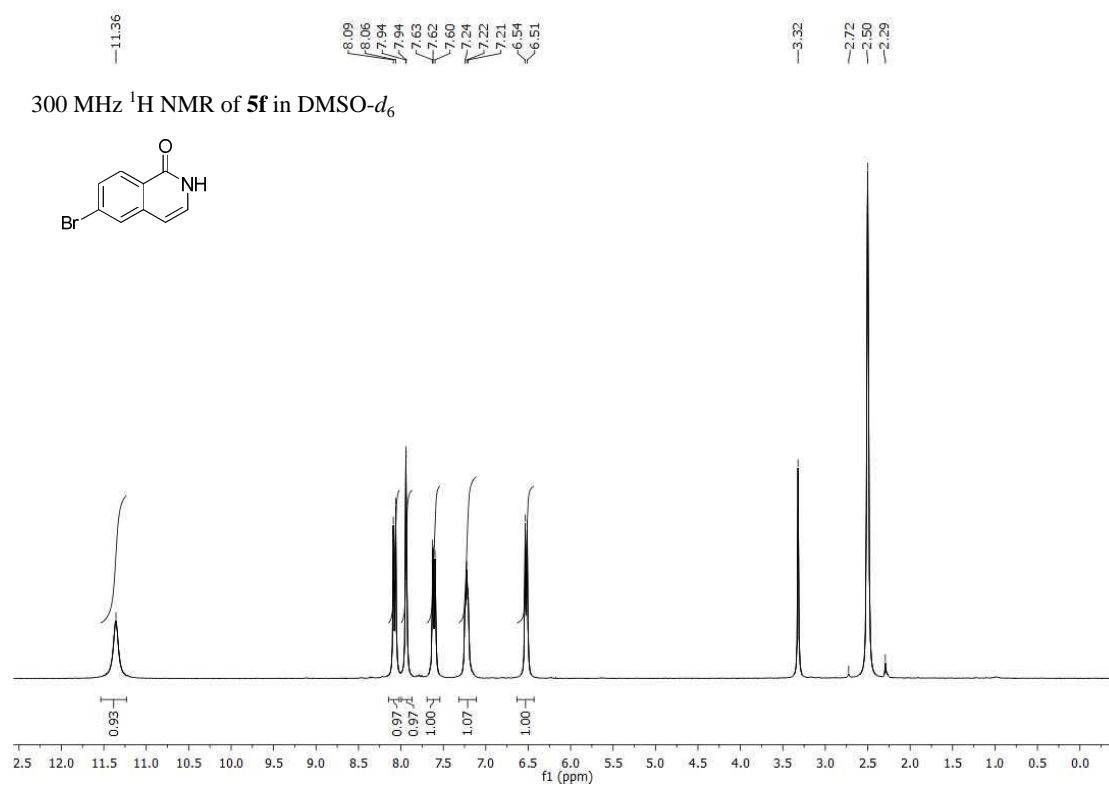
300 MHz  $^1\text{H}$  NMR of **5d** in  $\text{CDCl}_3$

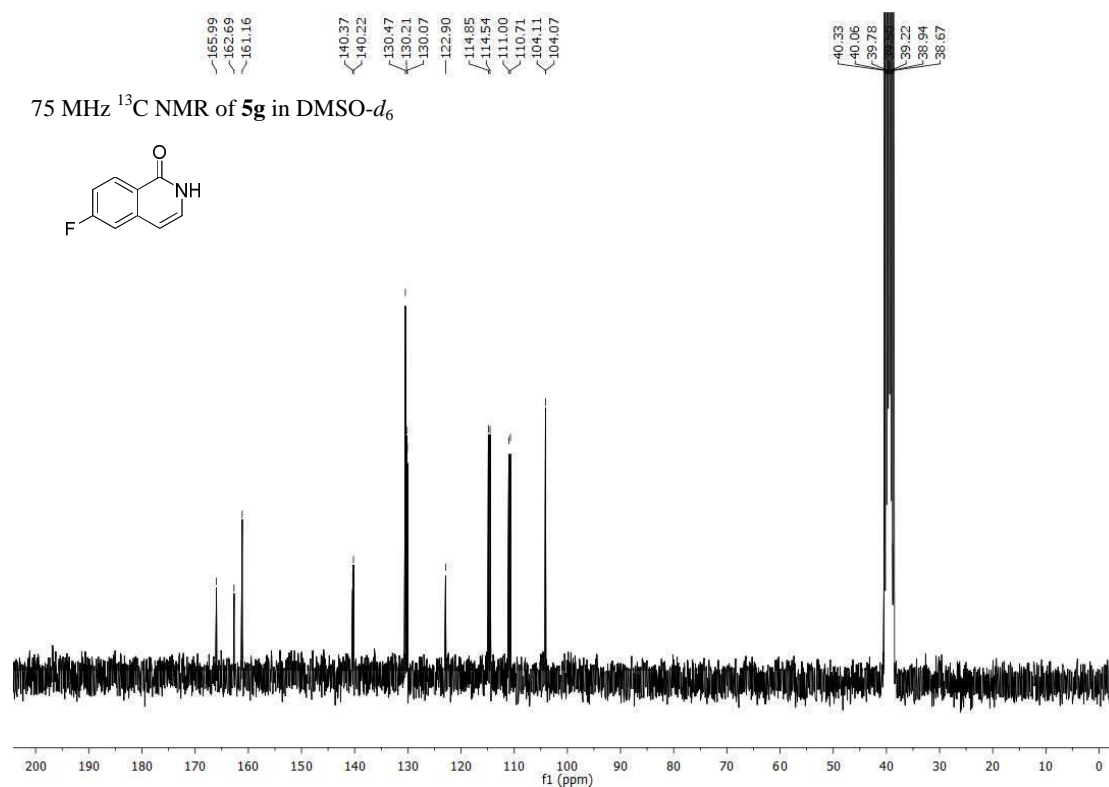
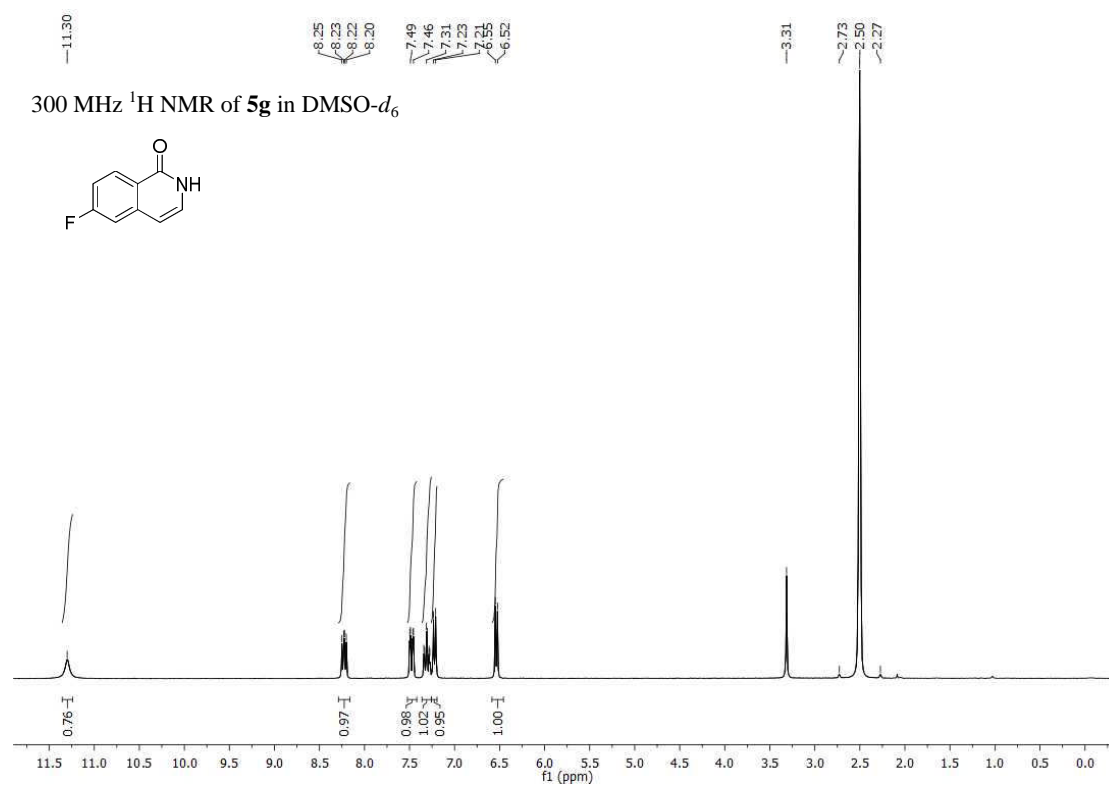


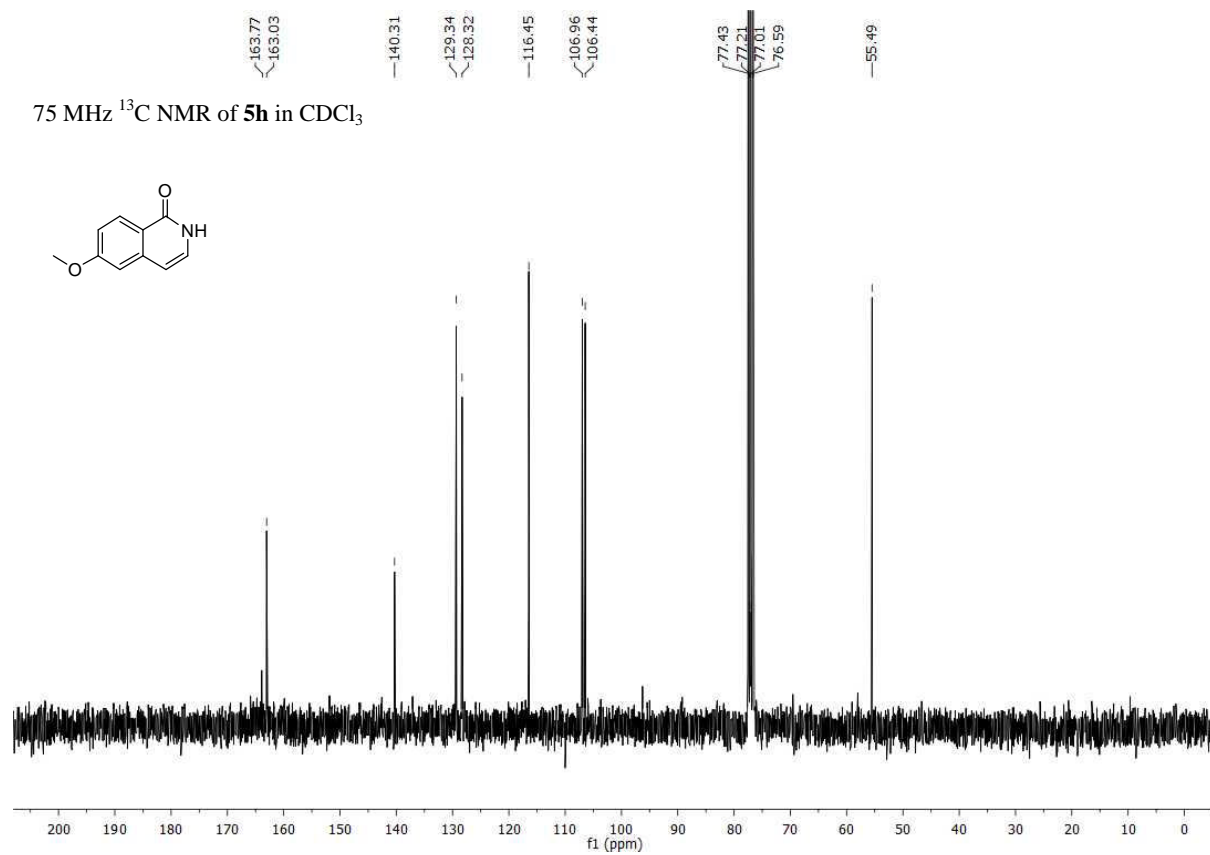
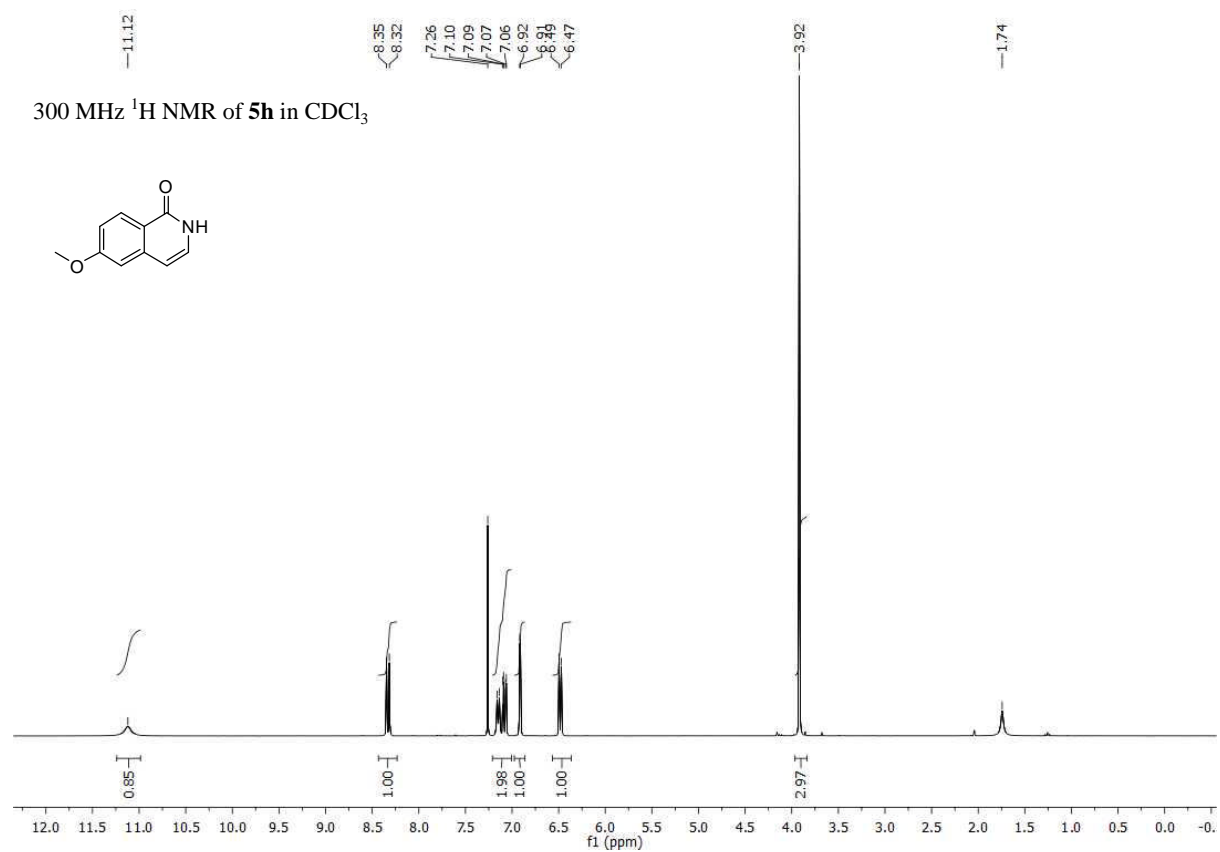
75 MHz  $^{13}\text{C}$  NMR of **5d** in  $\text{CDCl}_3$



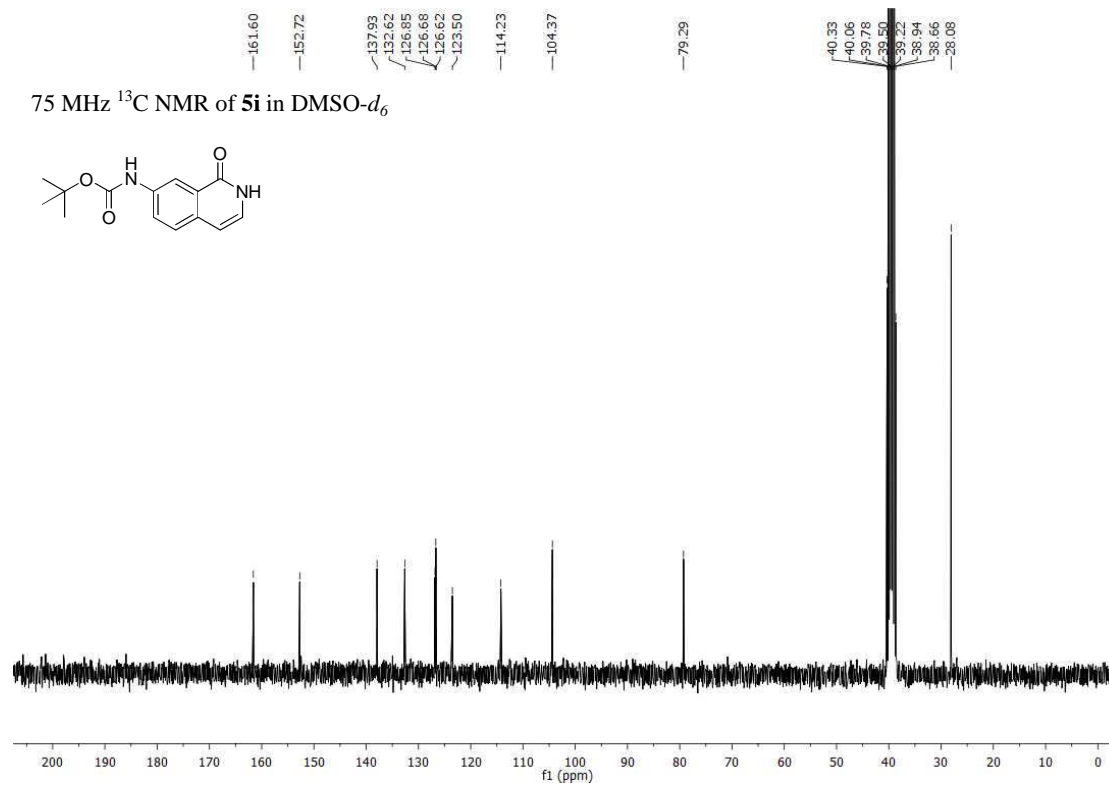
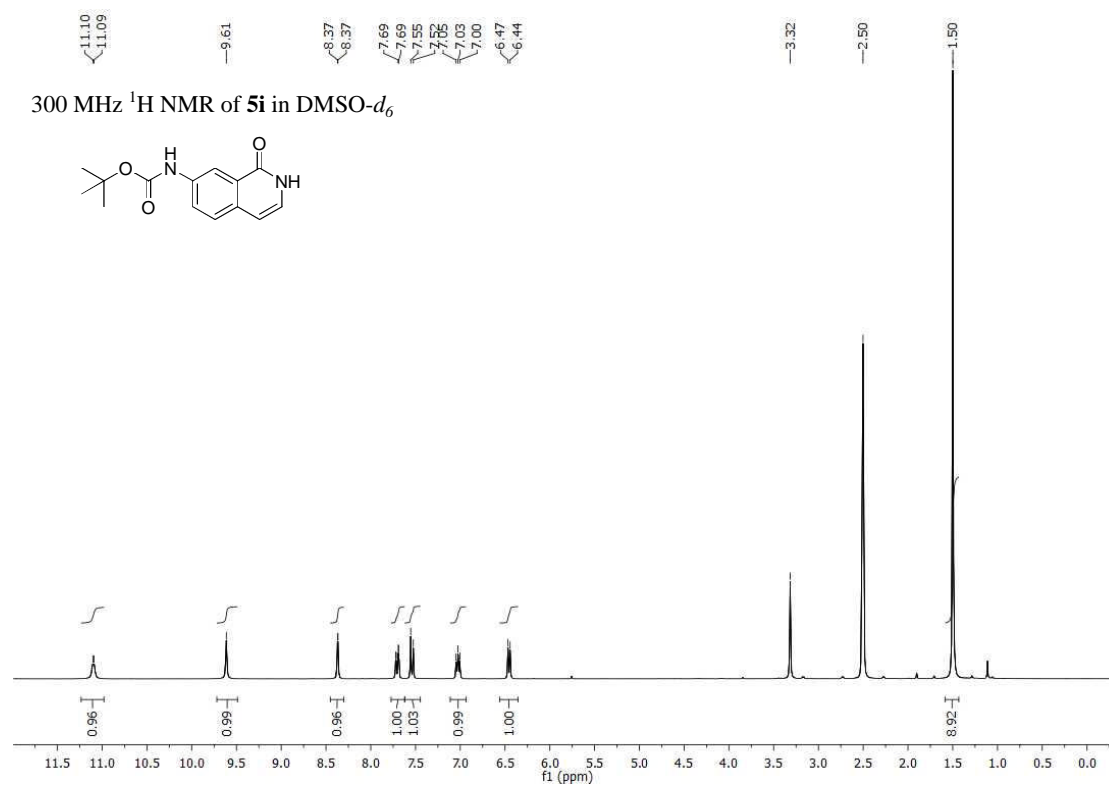


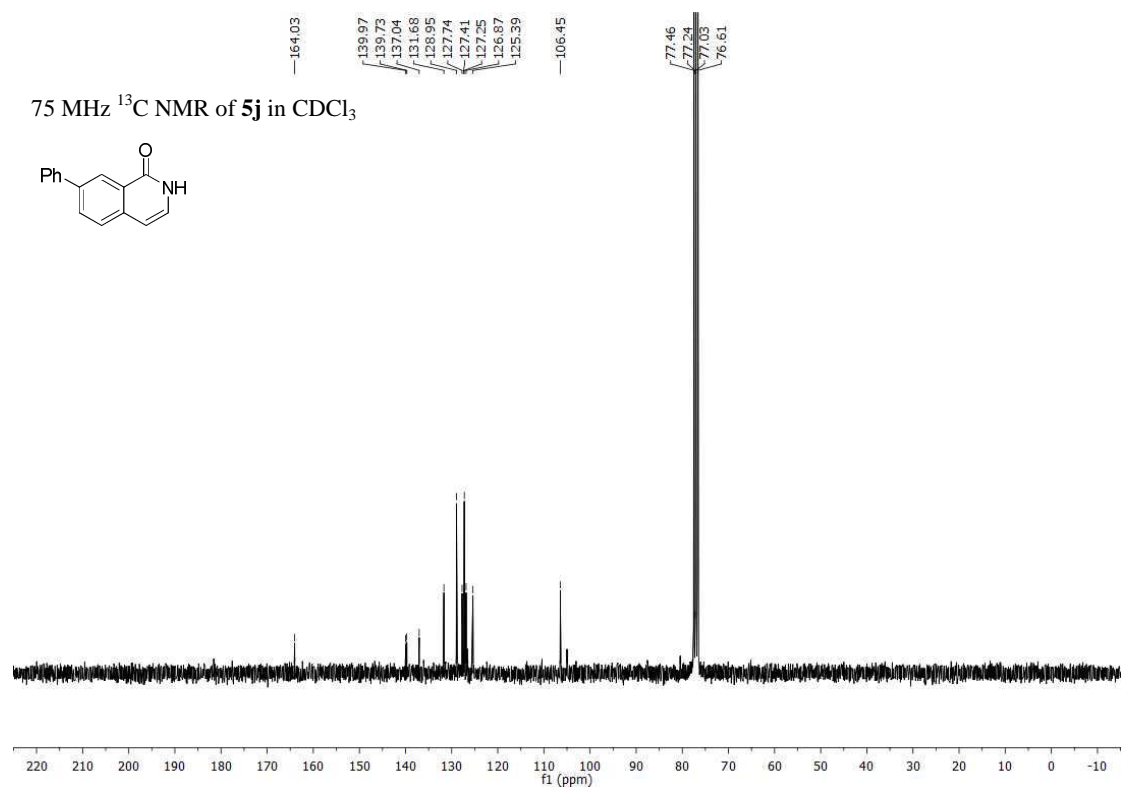
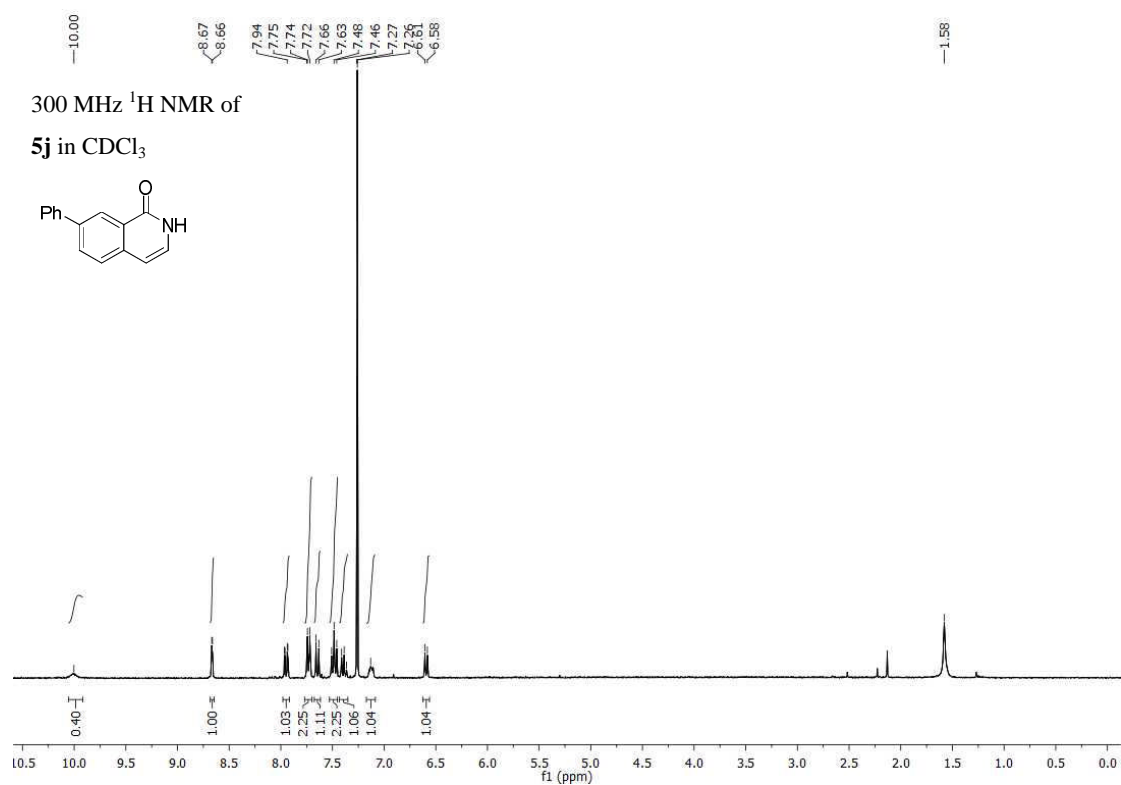


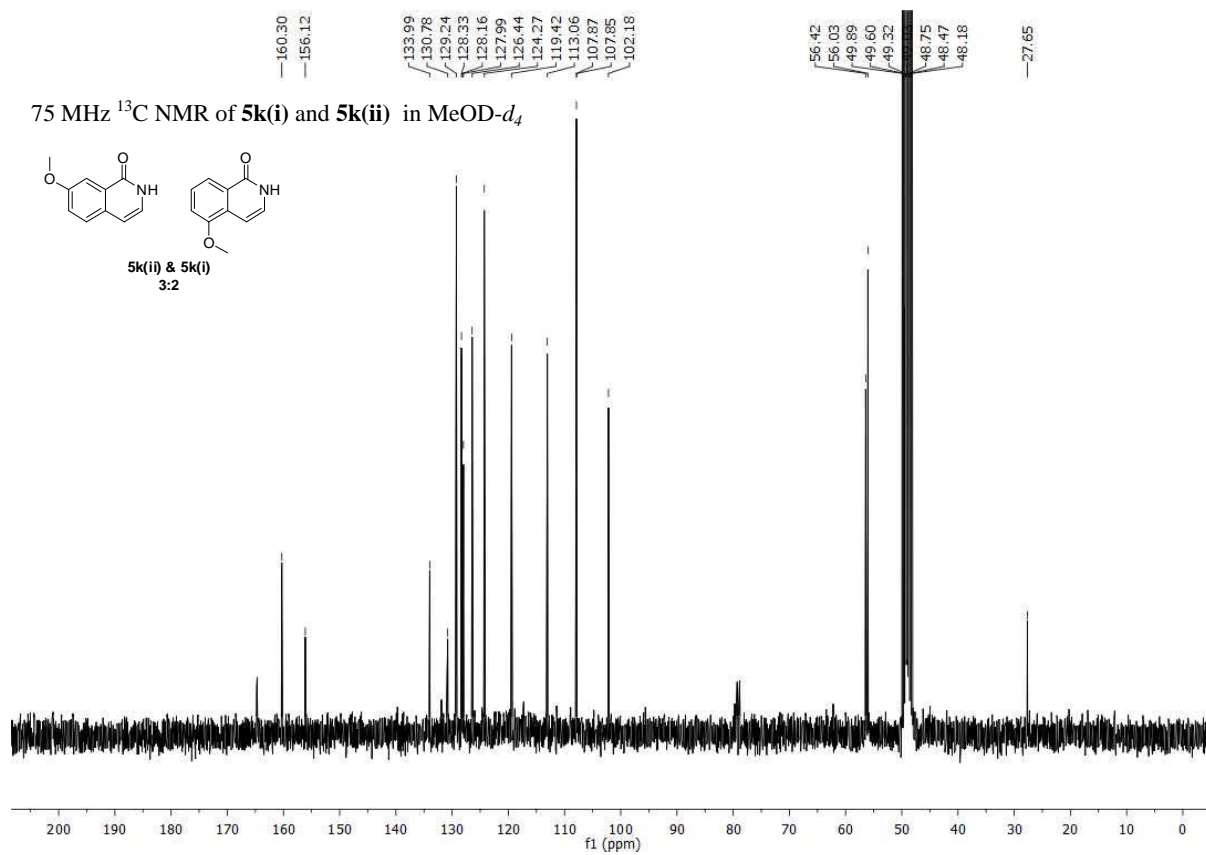
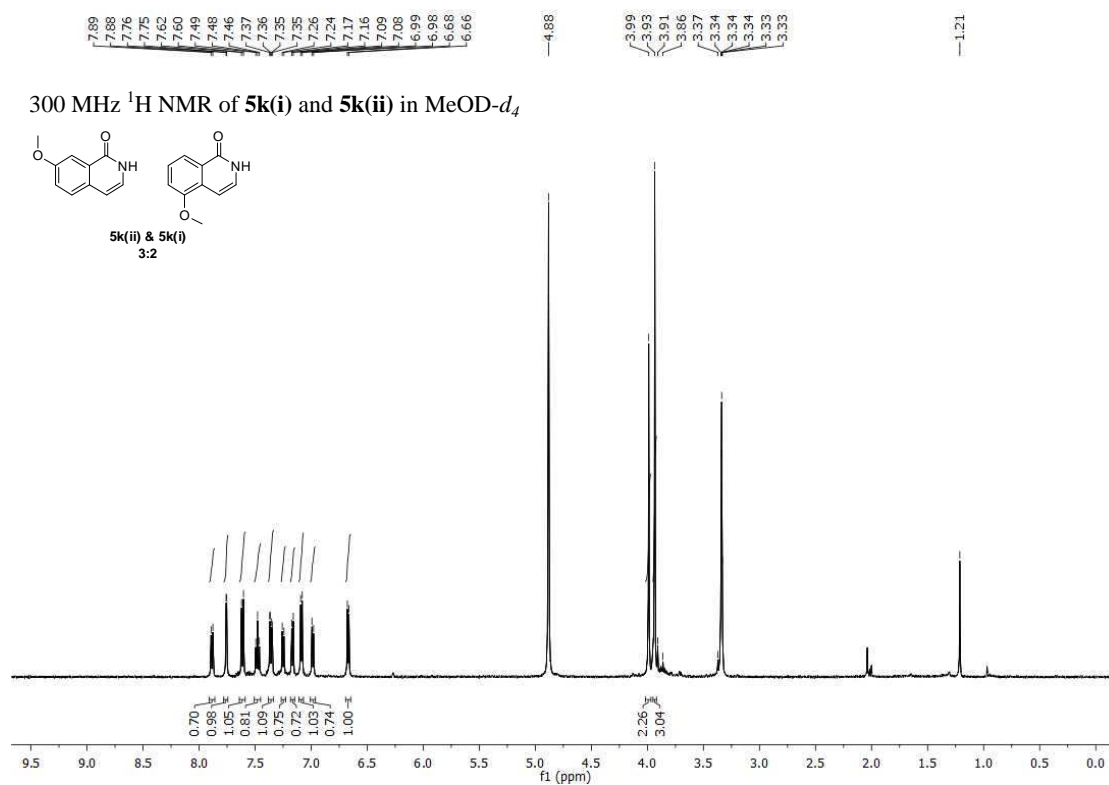


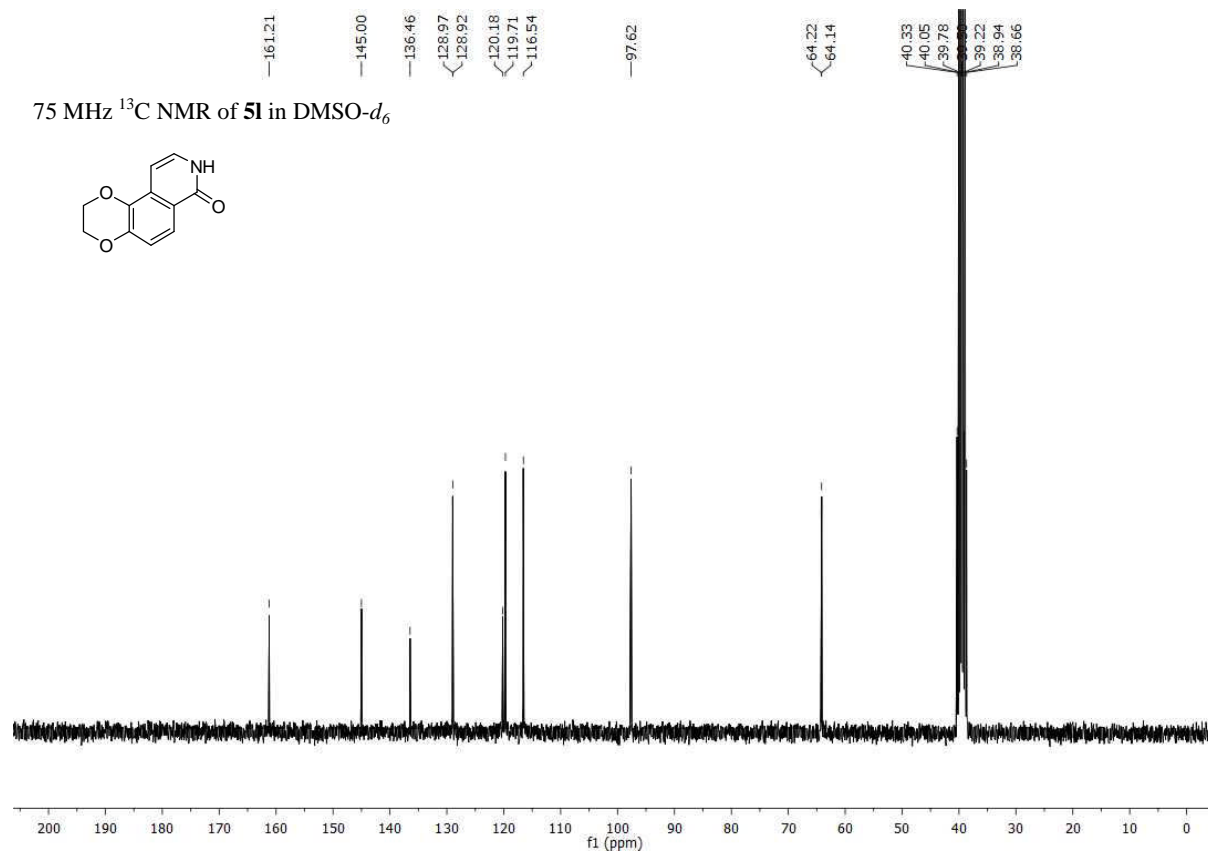
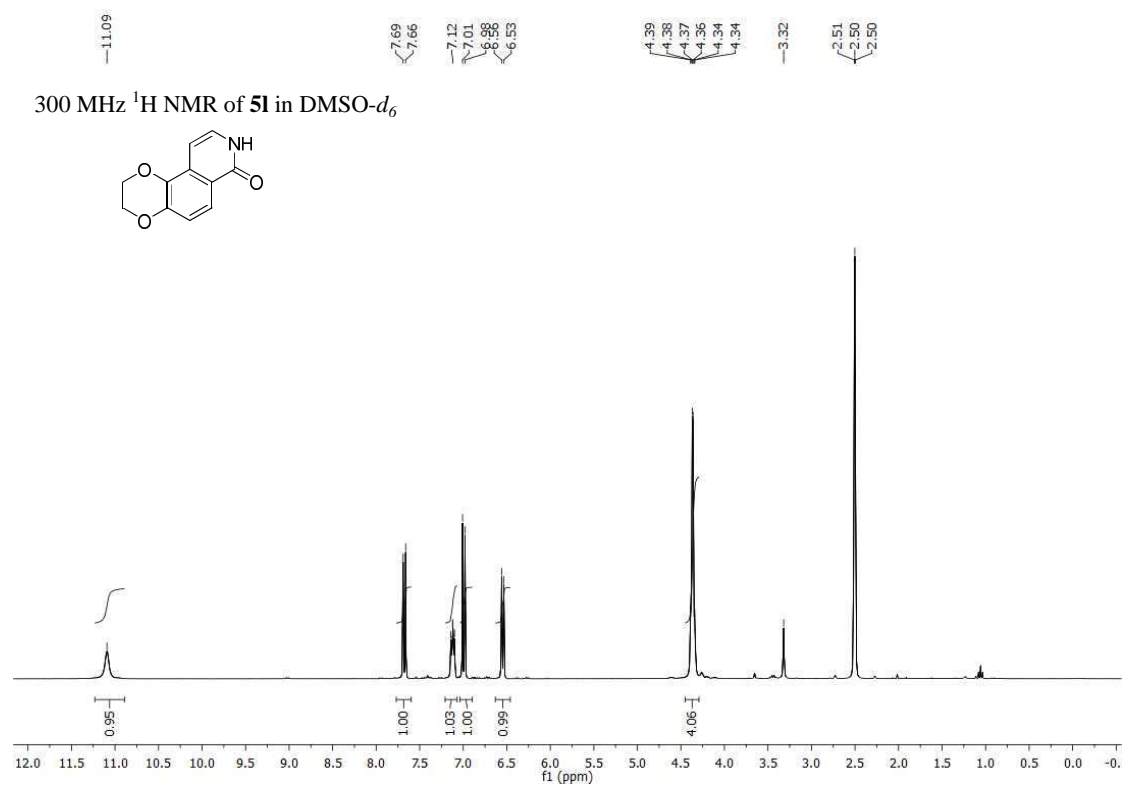


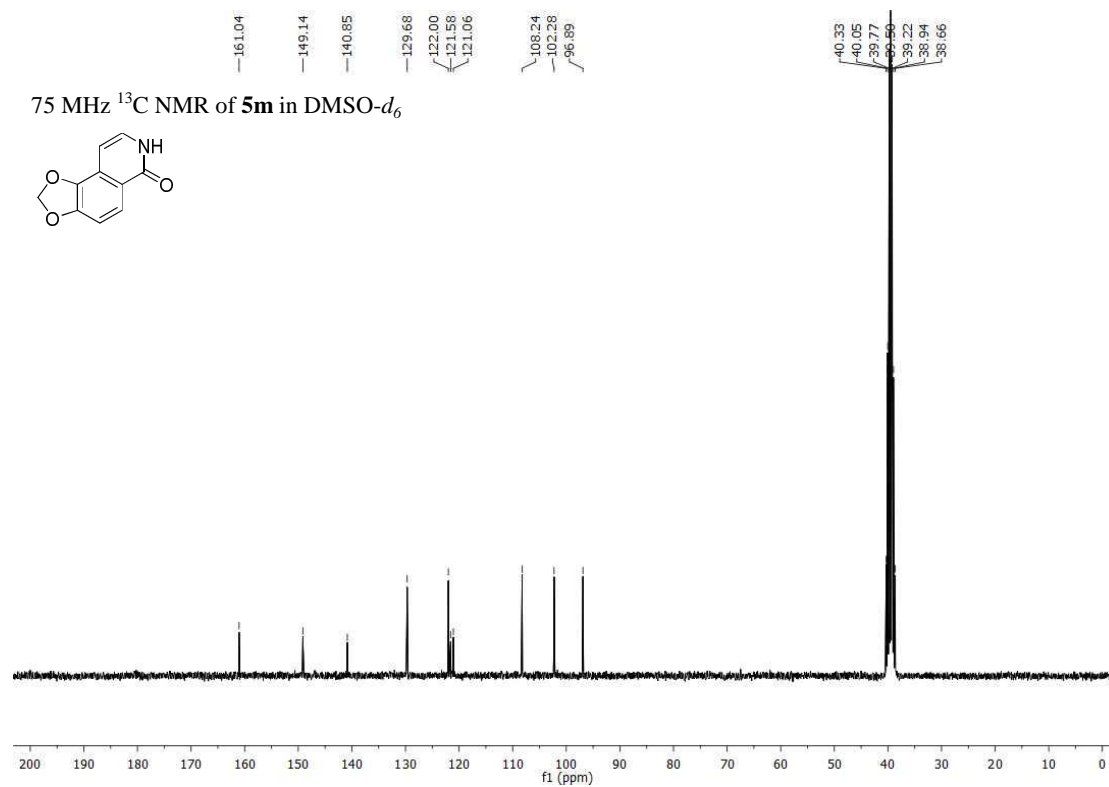
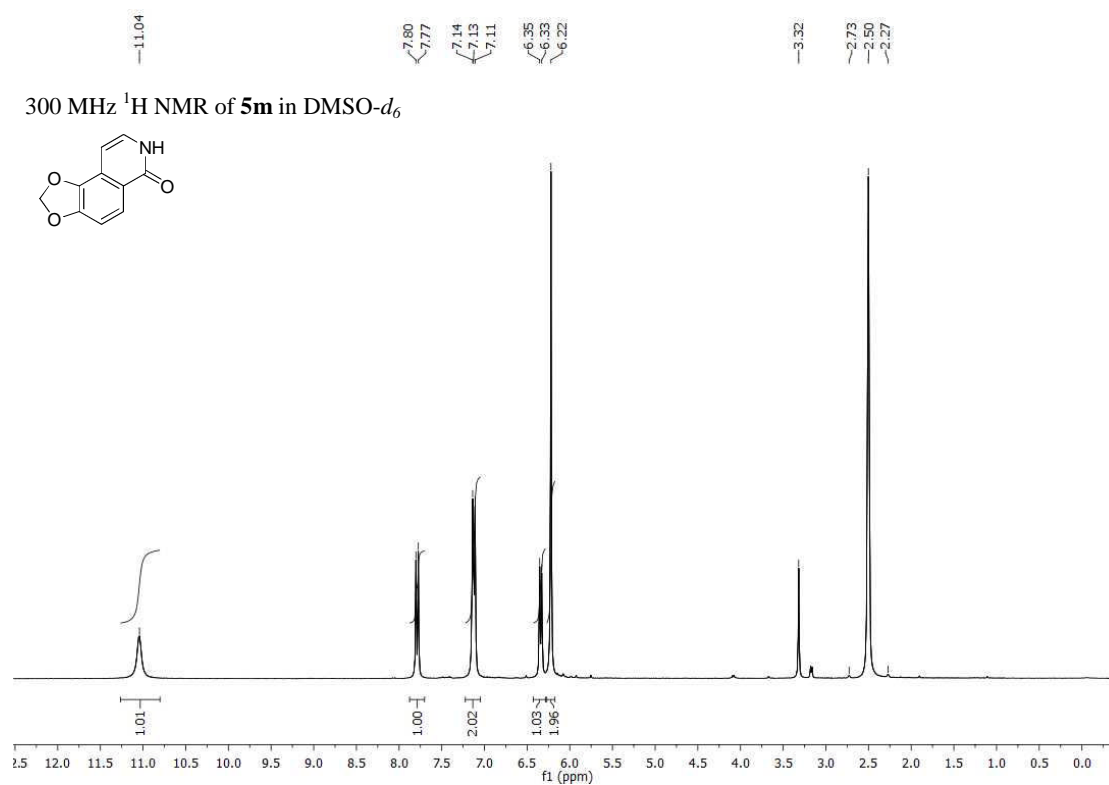


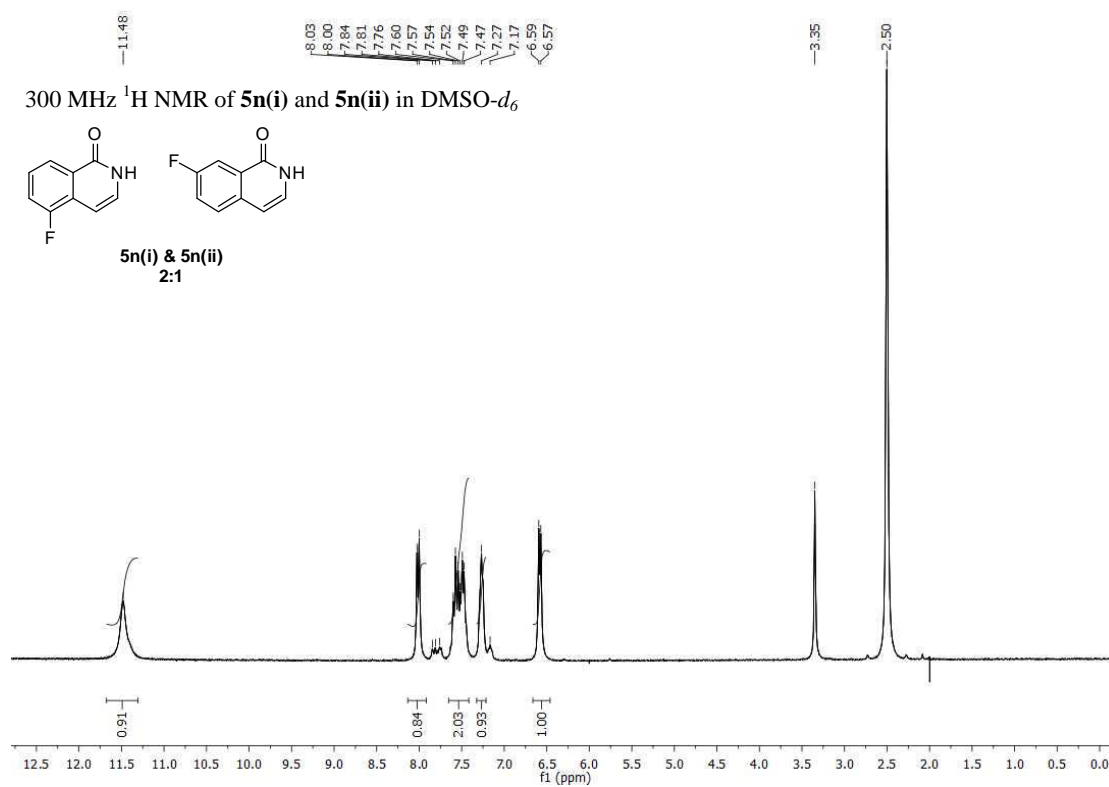
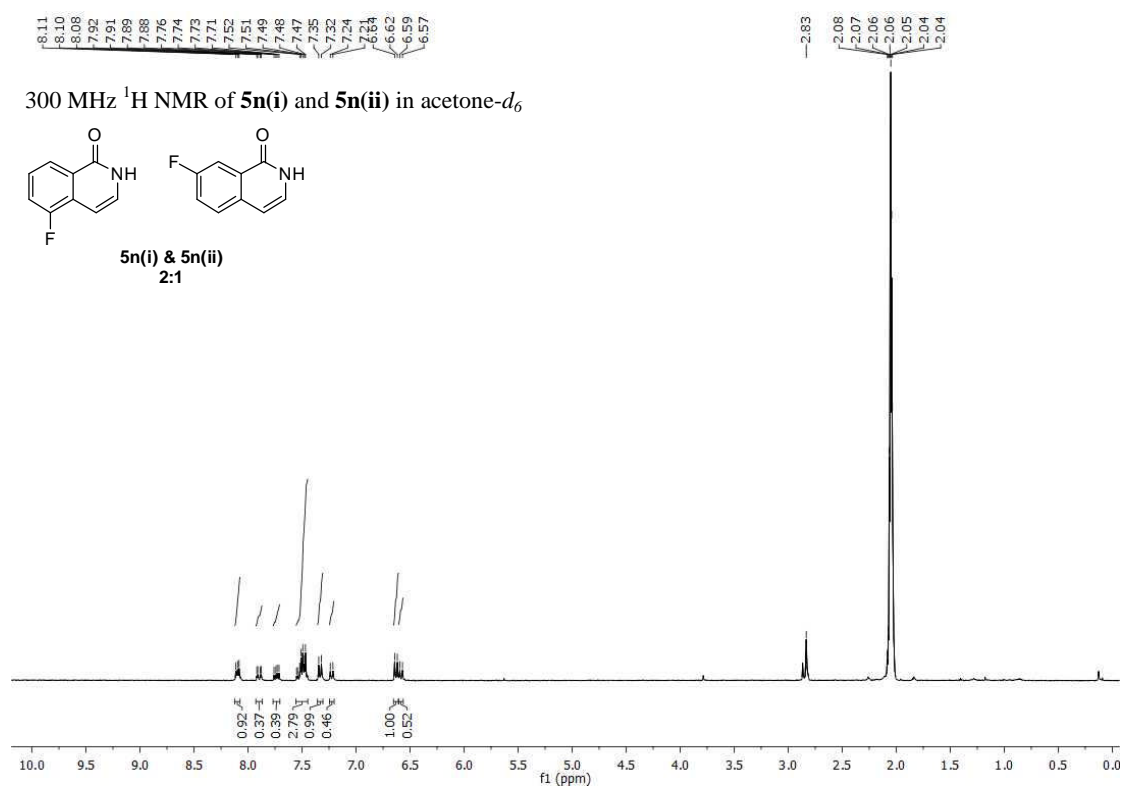


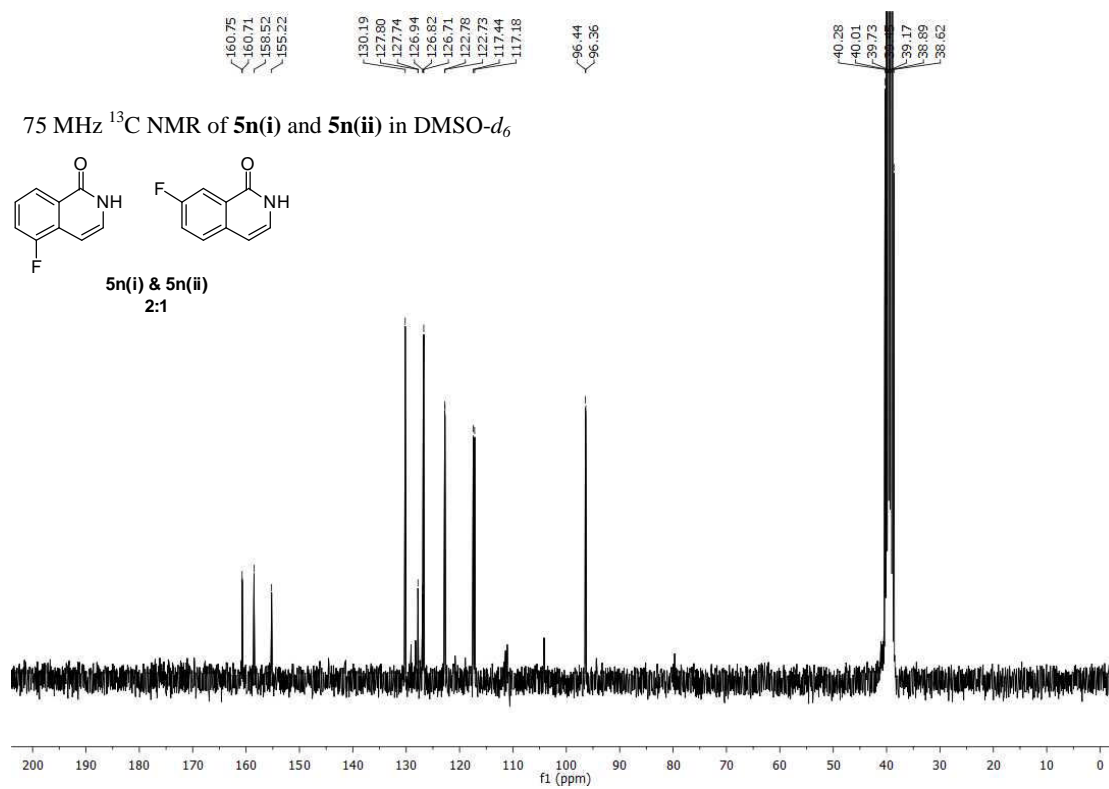


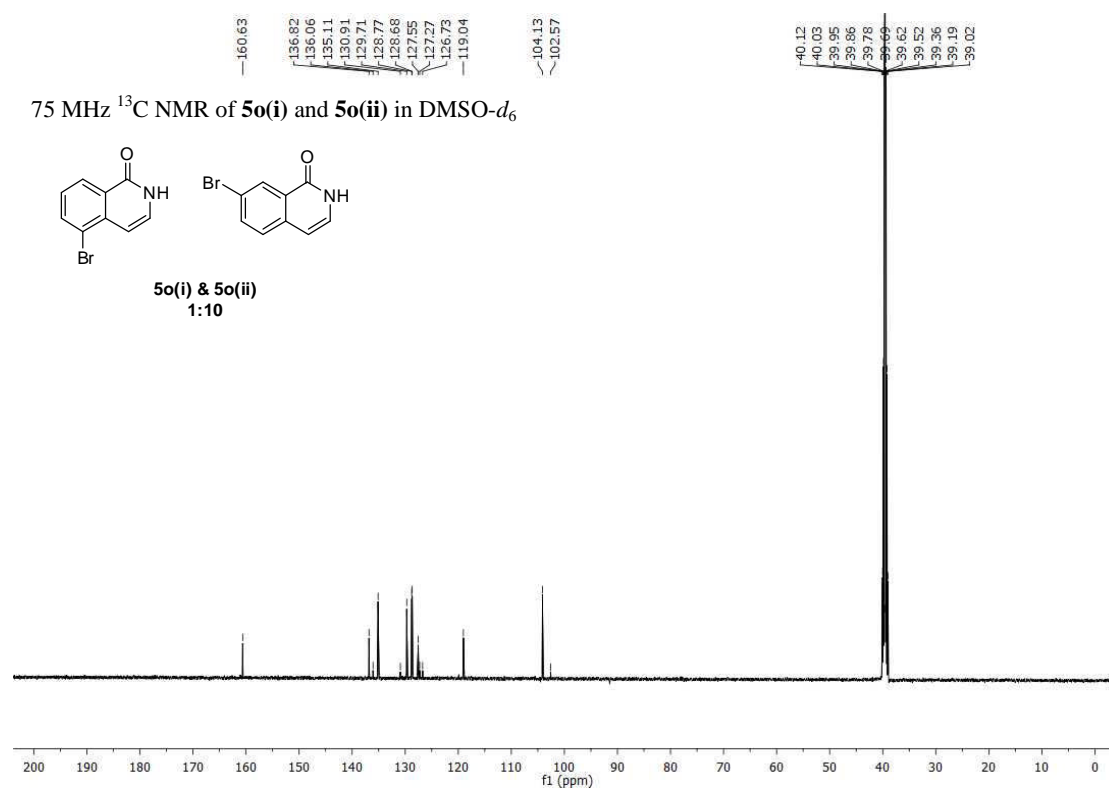
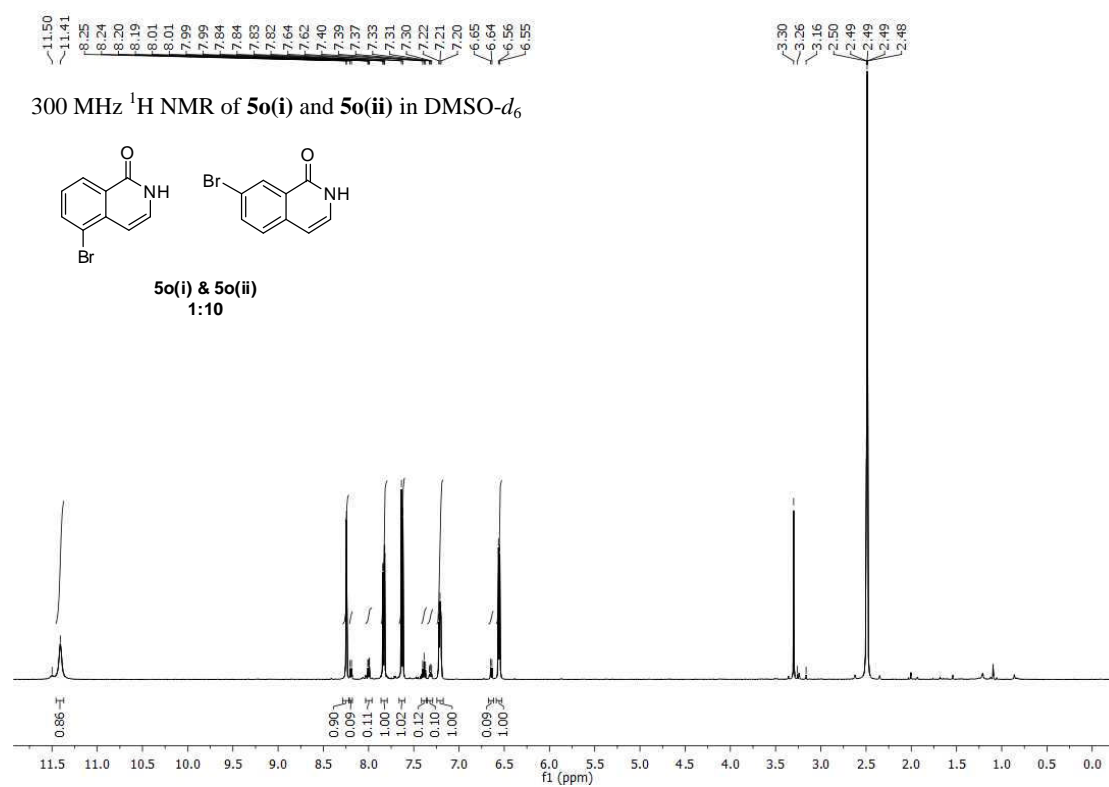




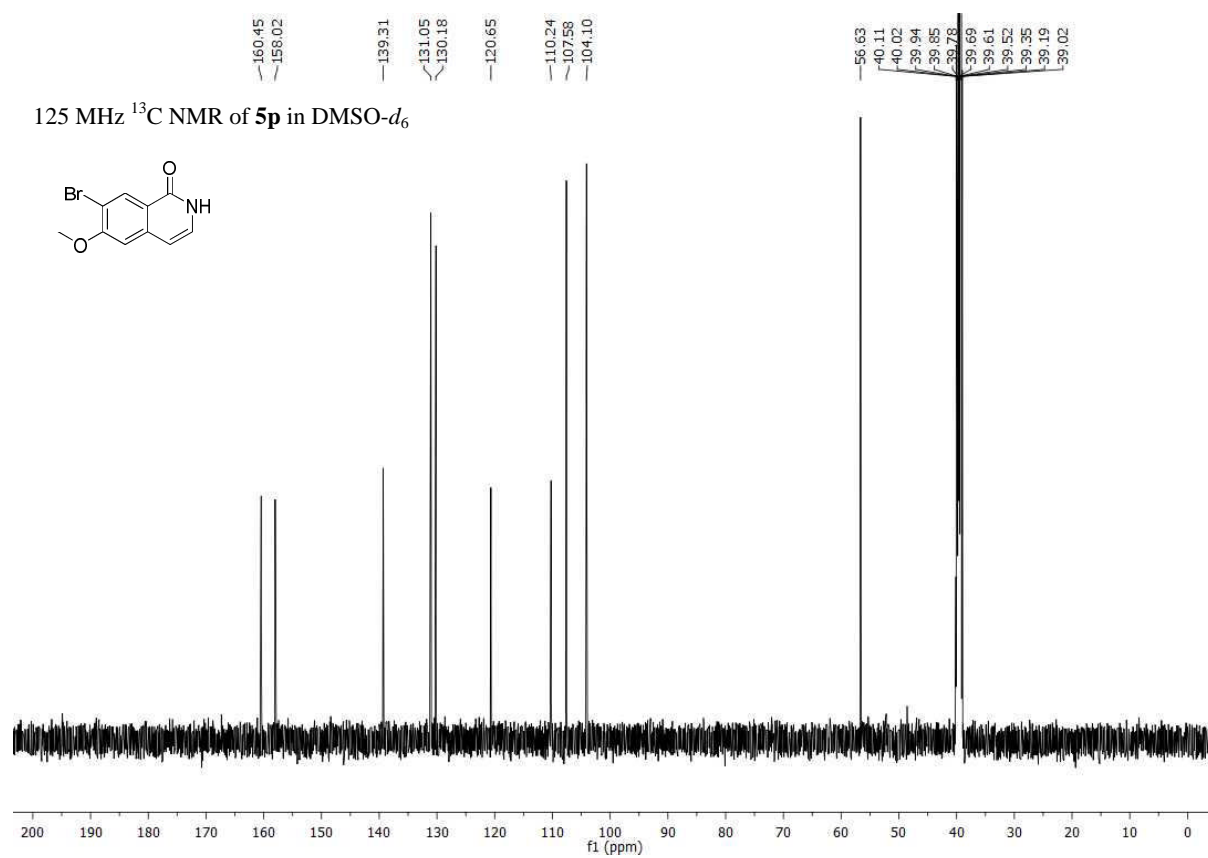
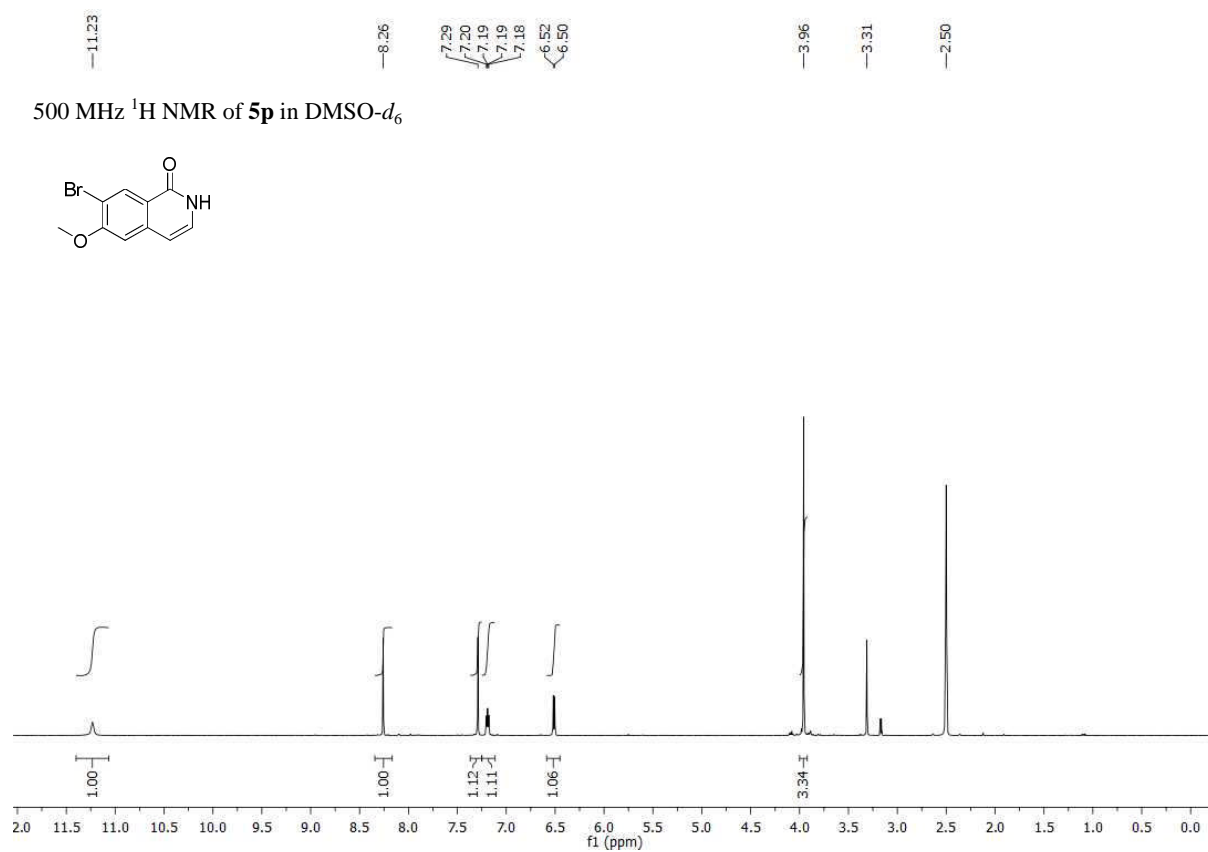




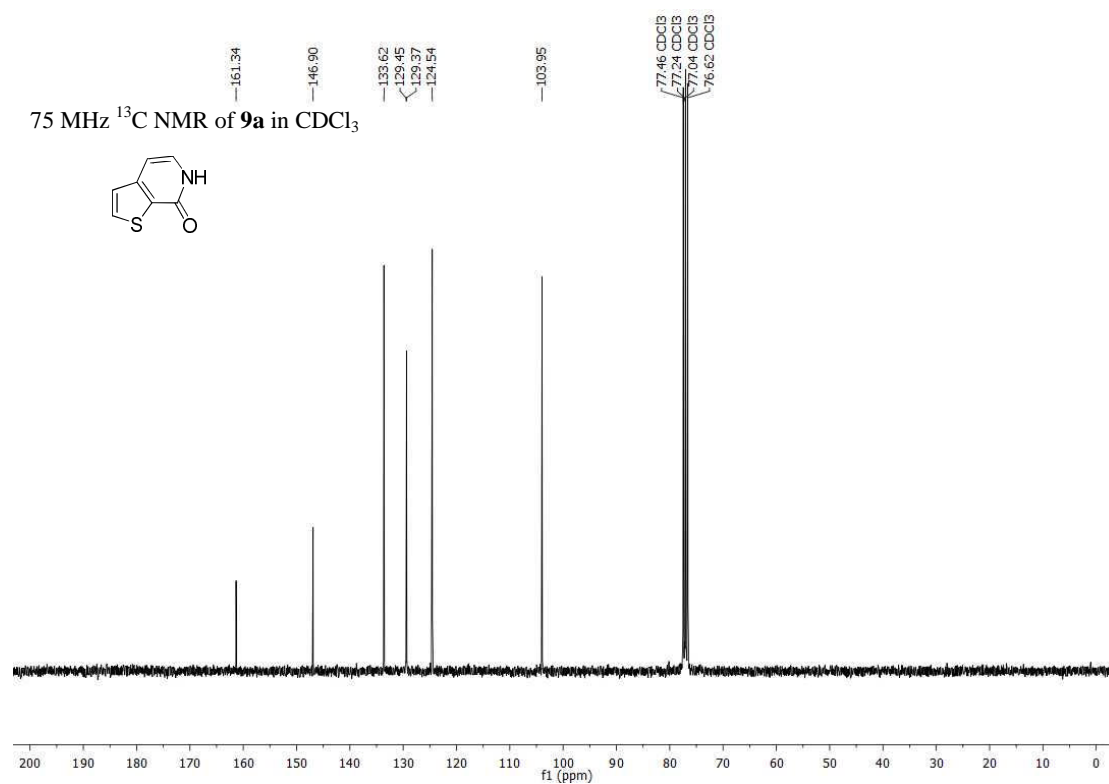
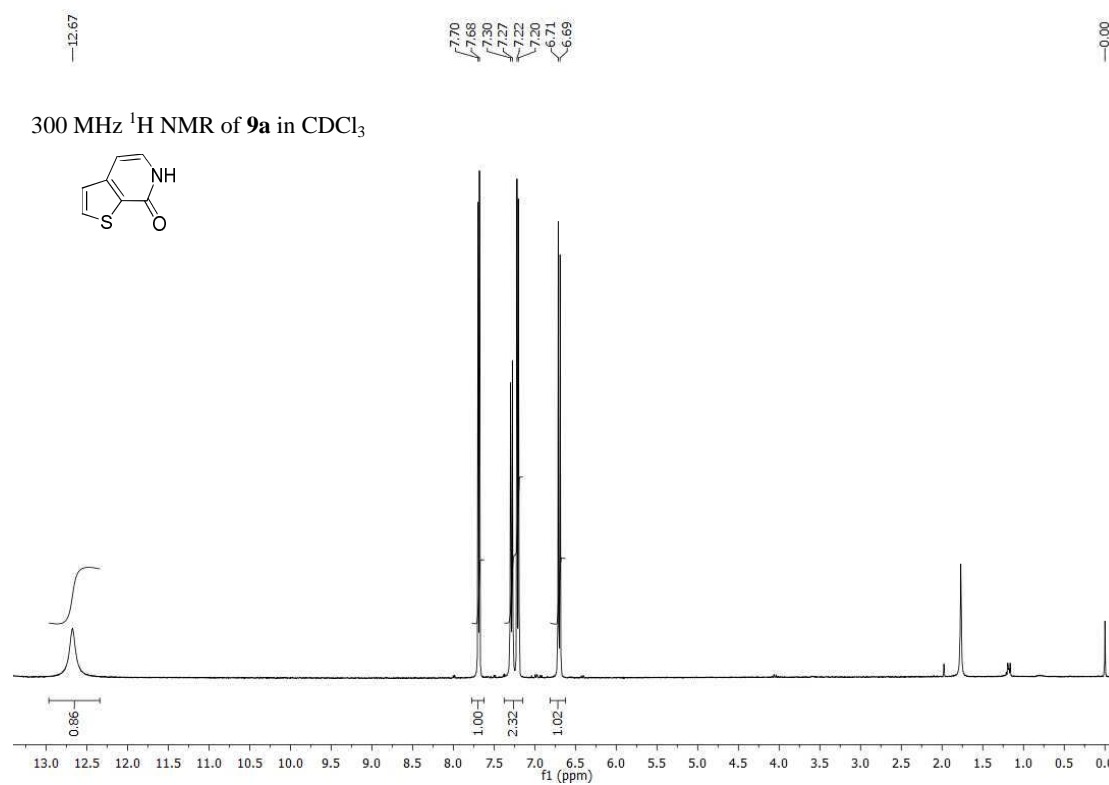


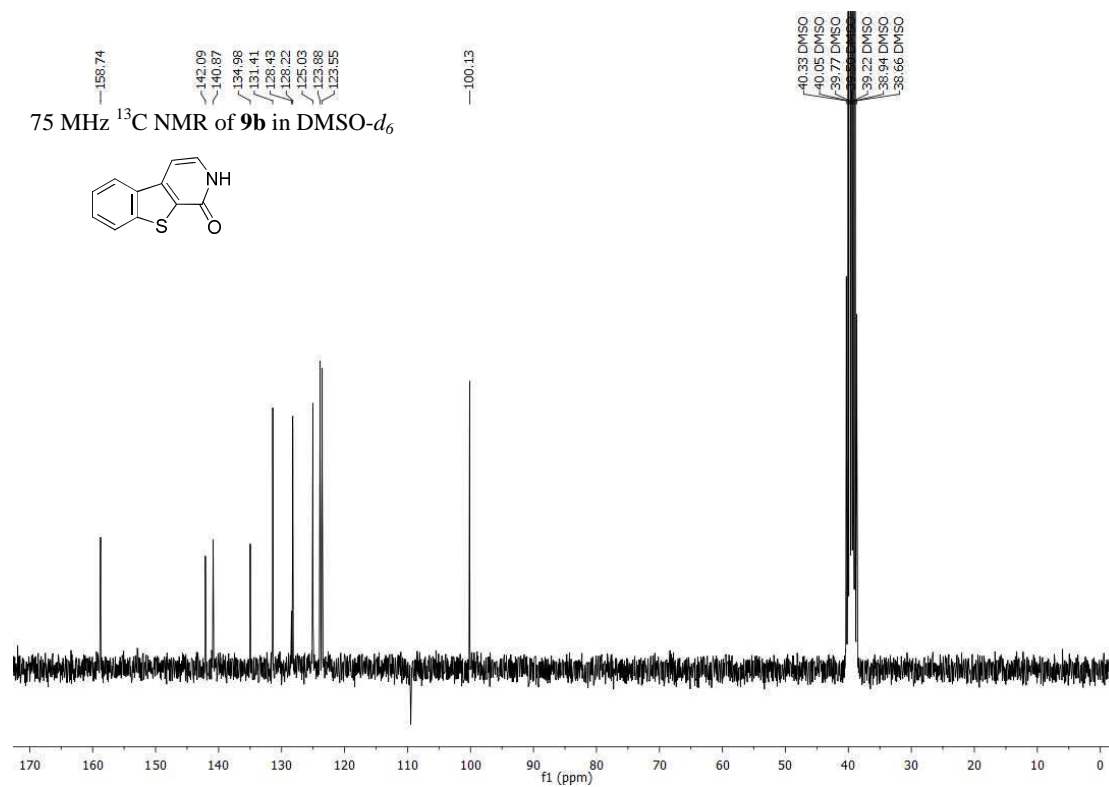
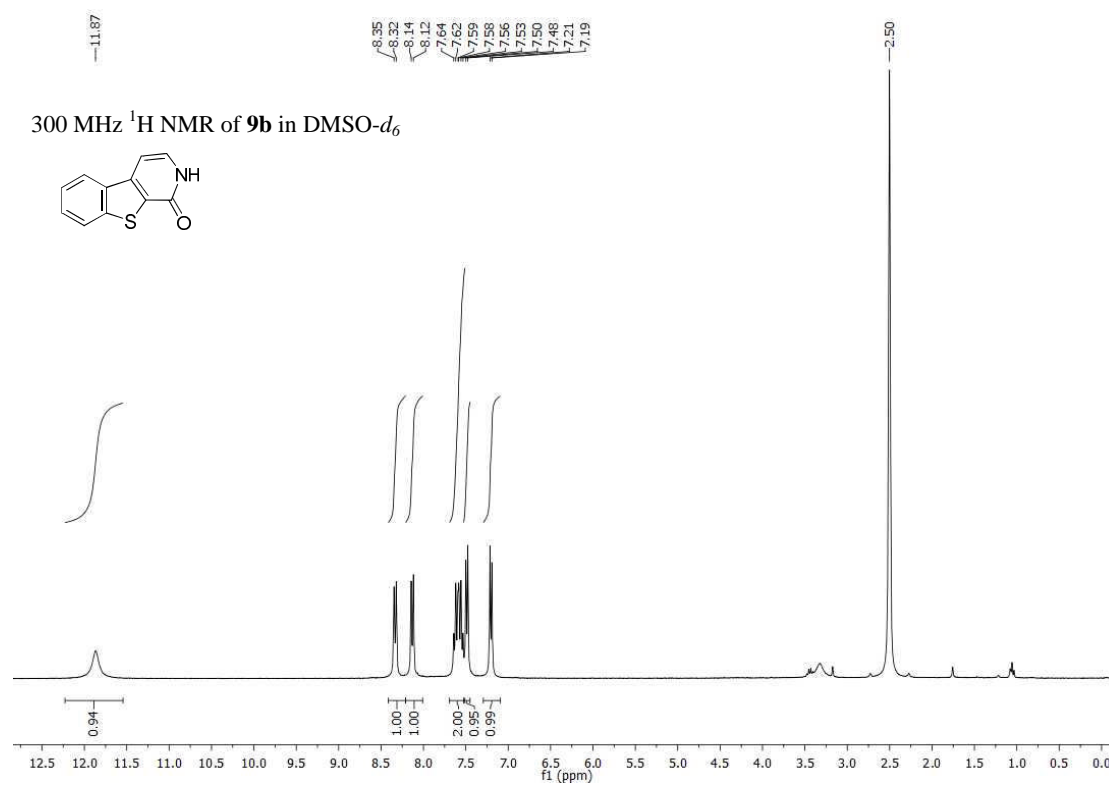


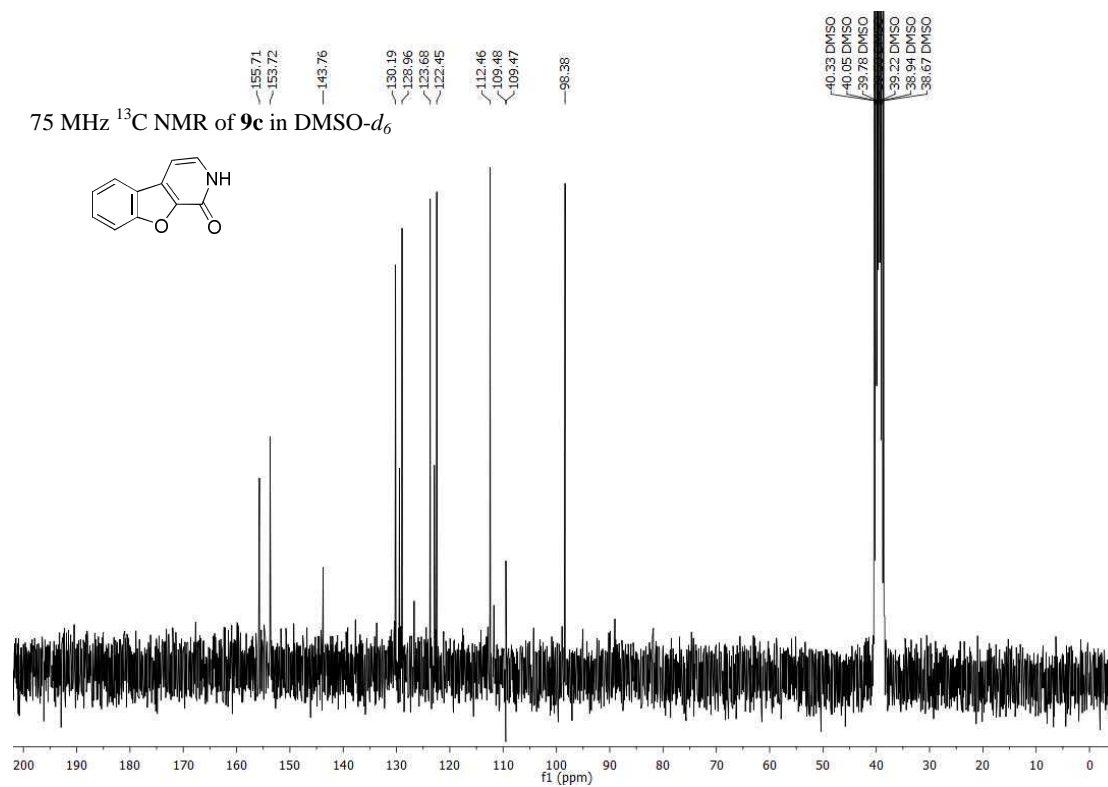
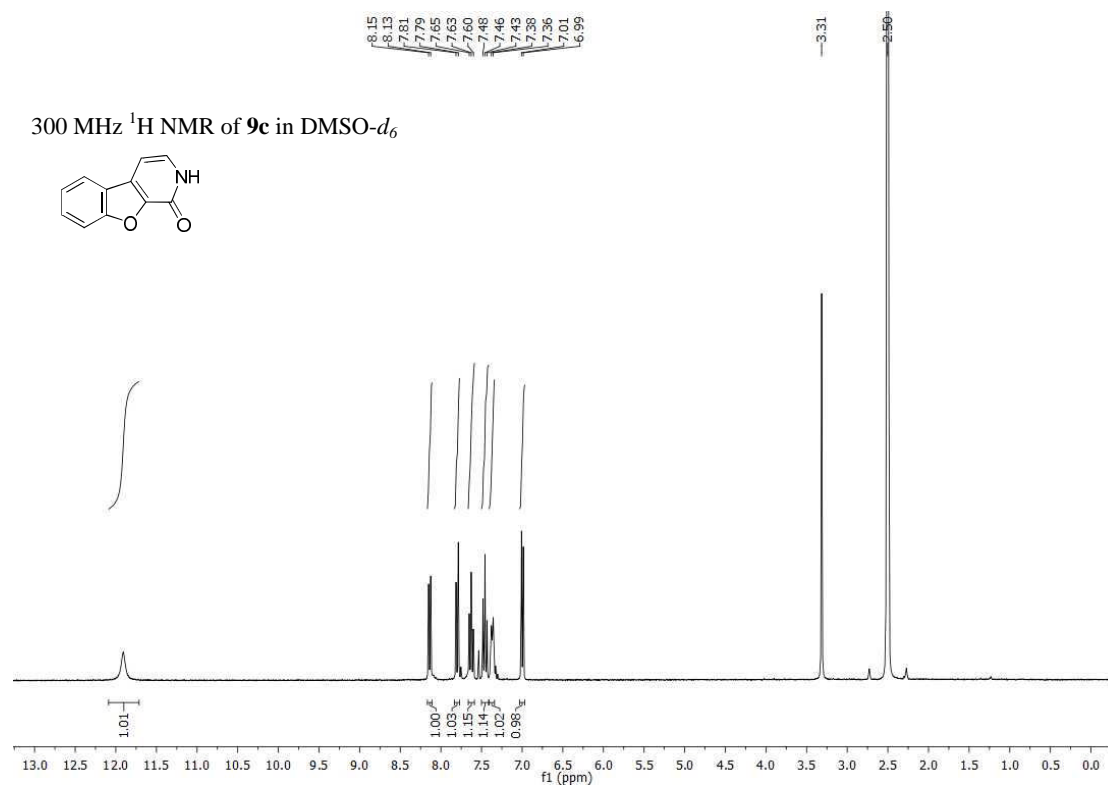


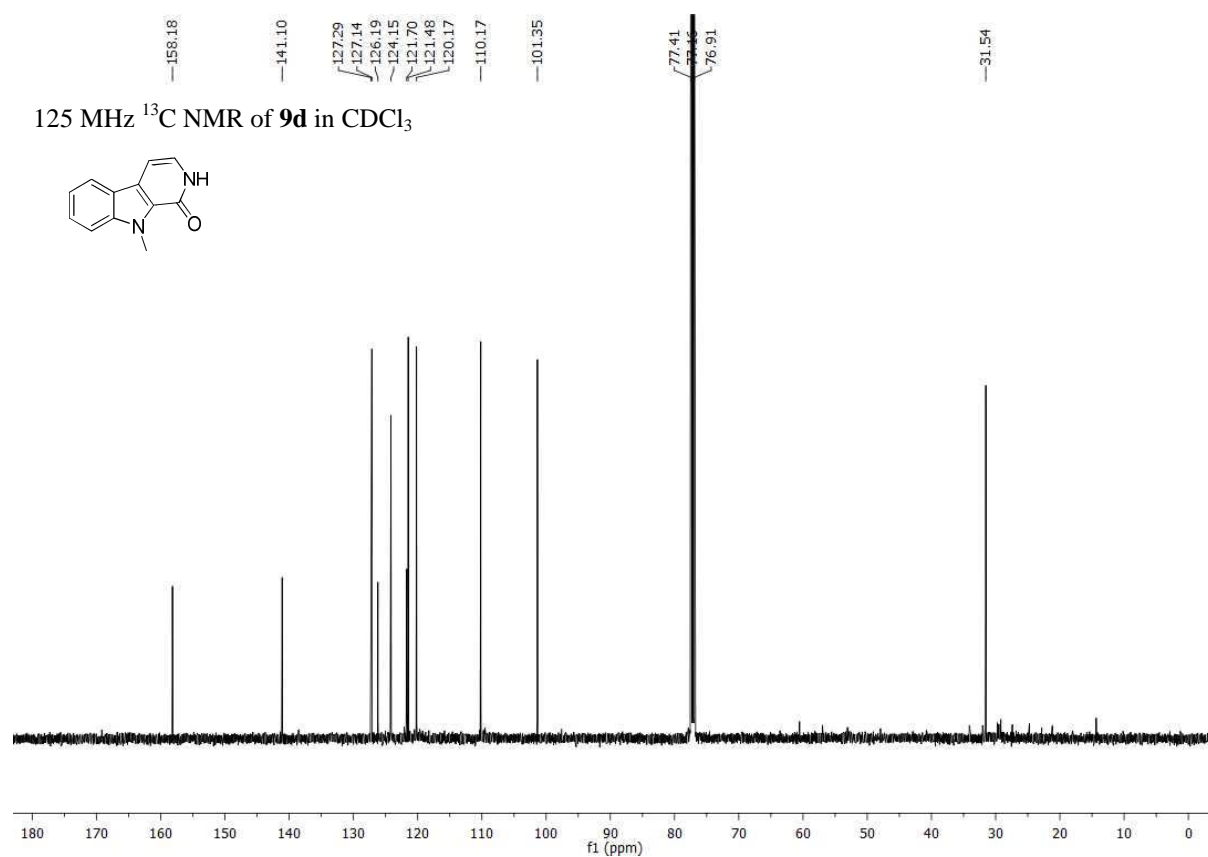
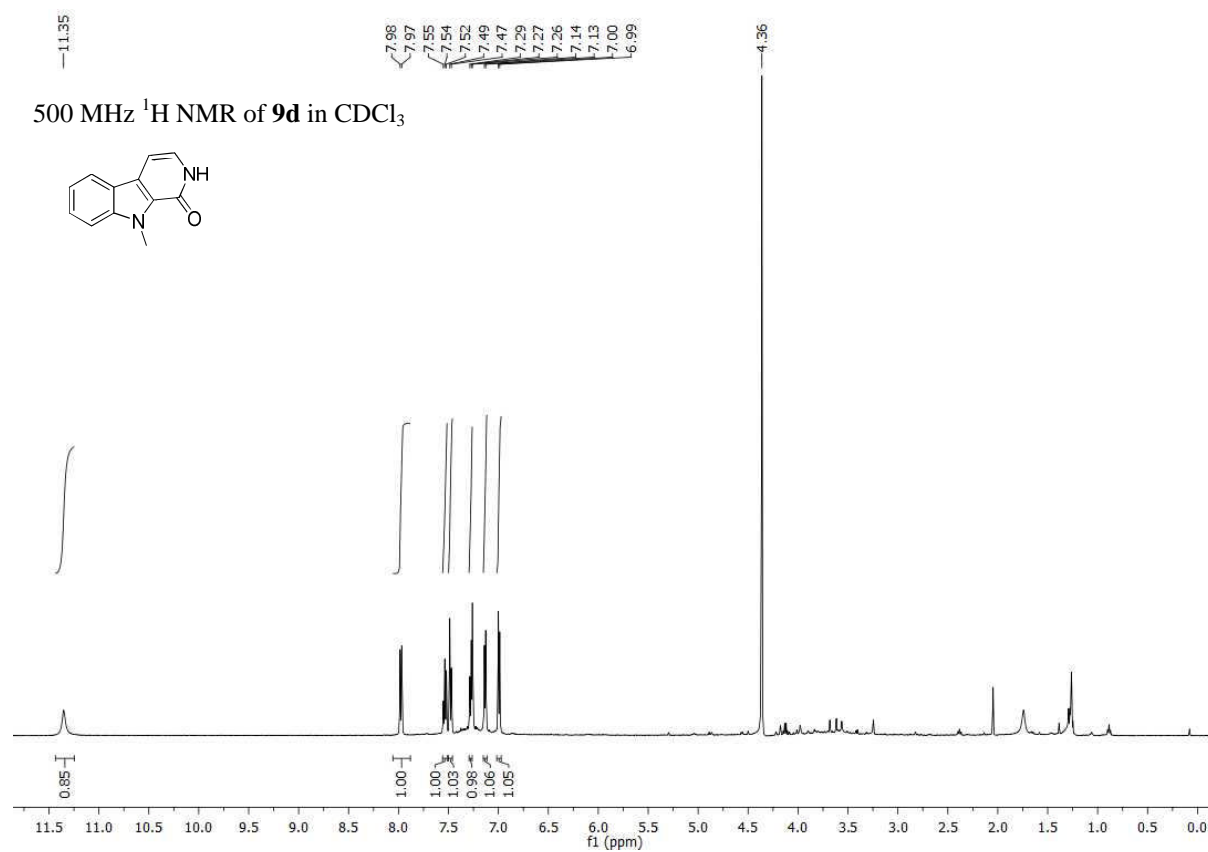


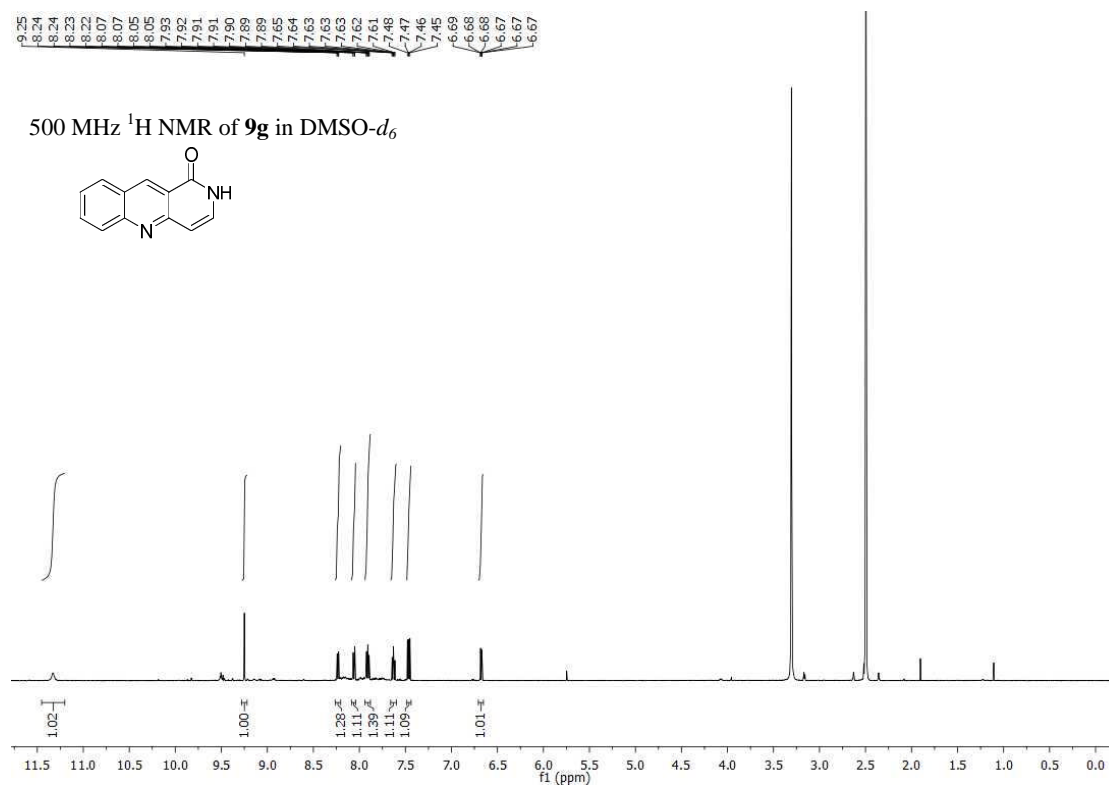
## Heterocyclic pyridones



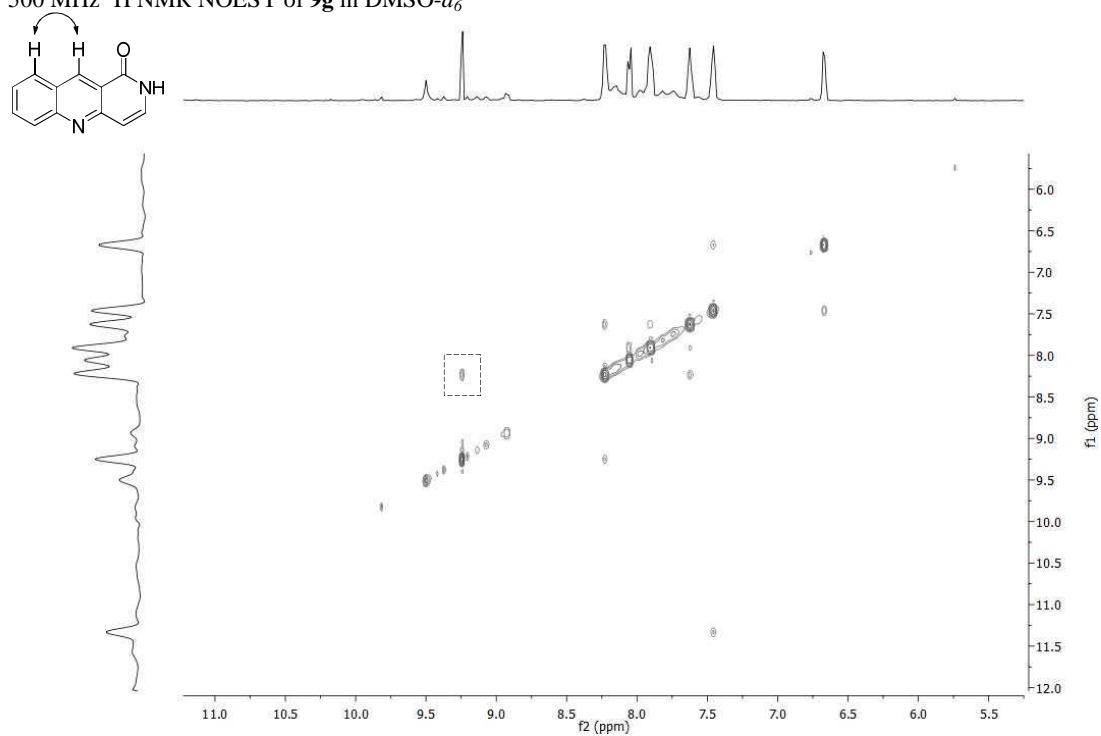


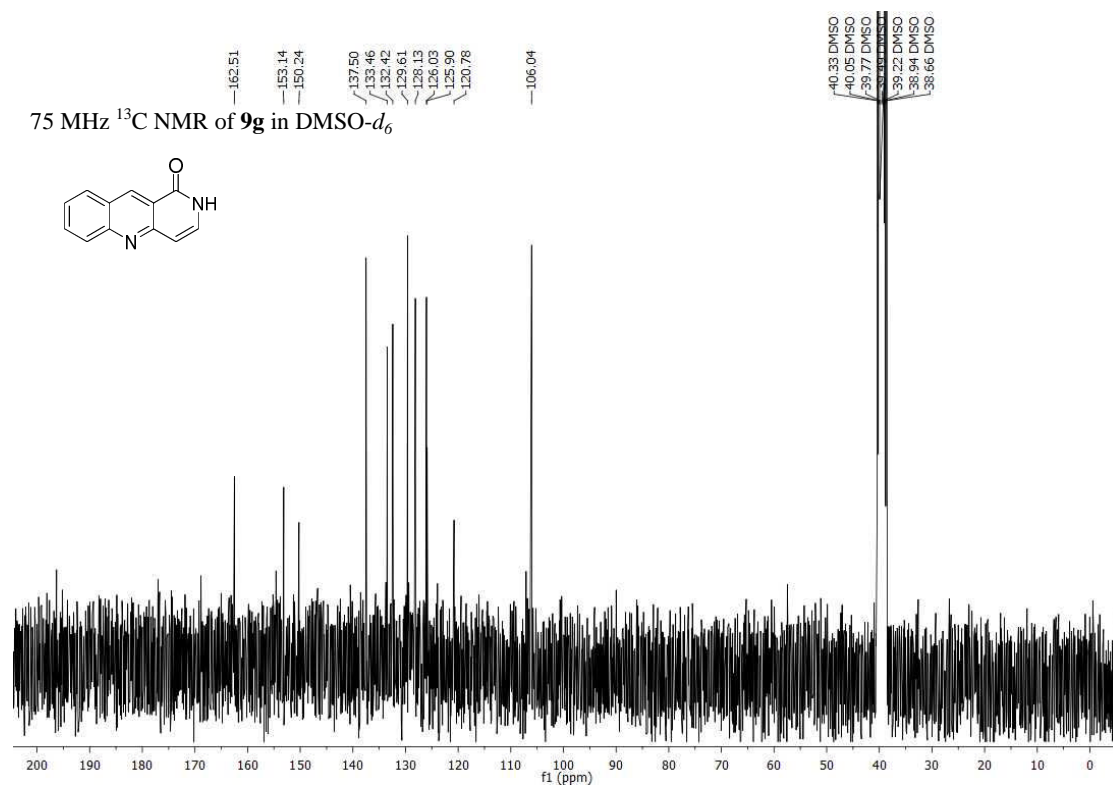




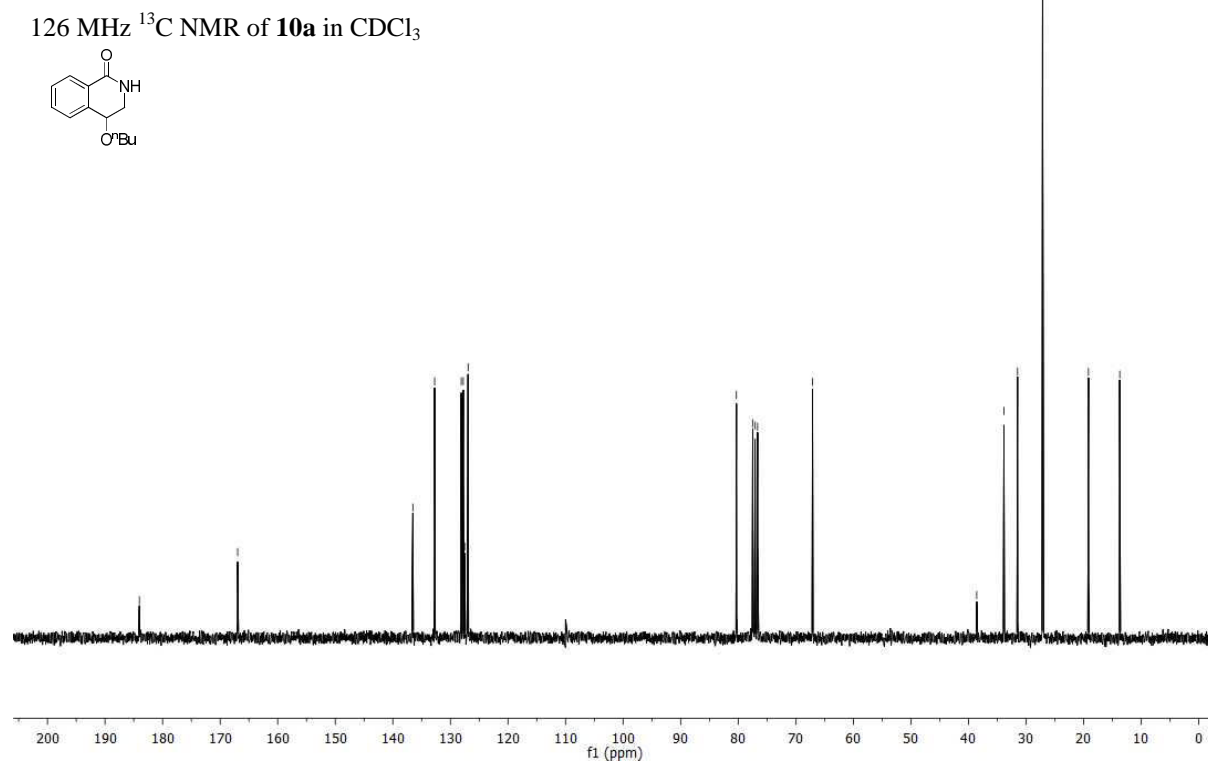
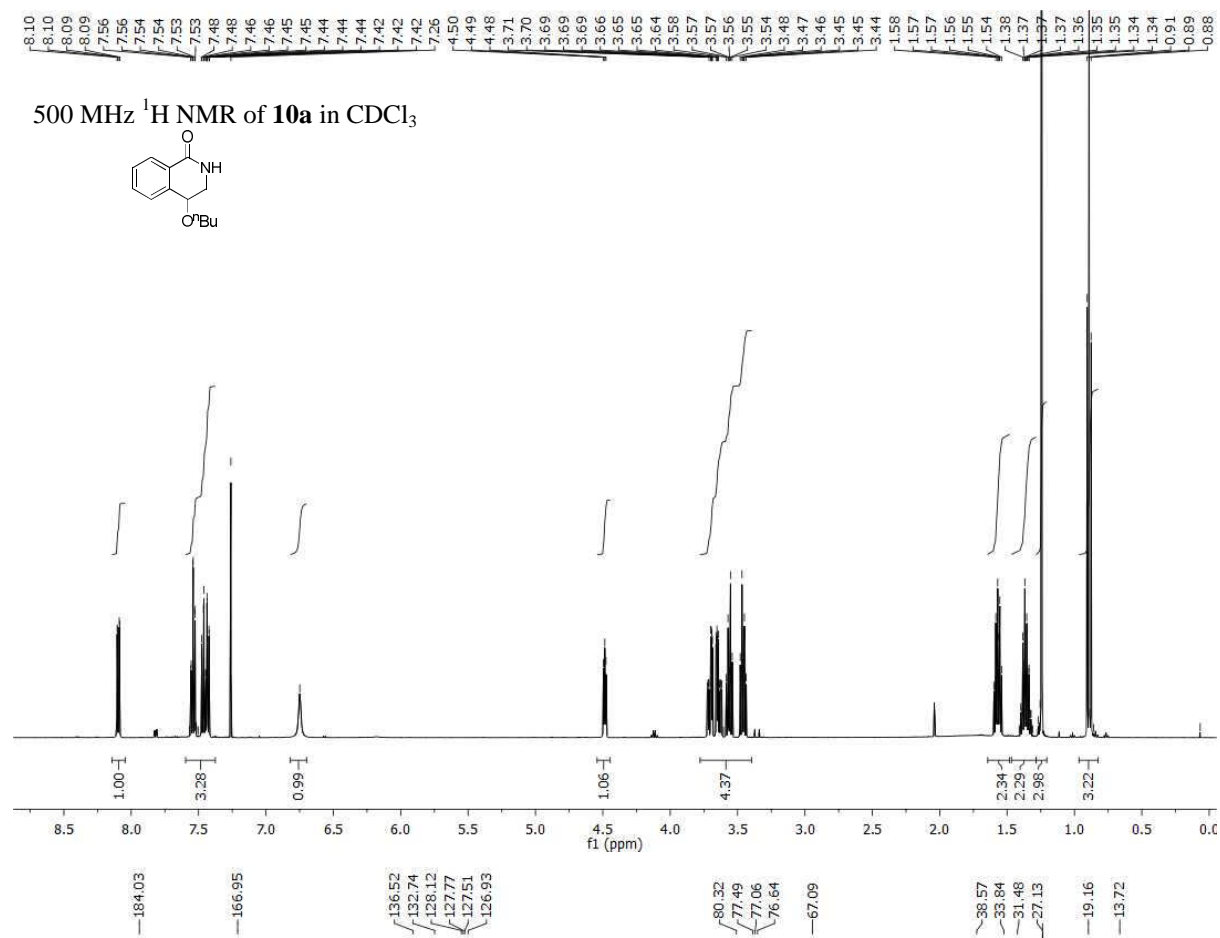


500 MHz  $^1\text{H}$  NMR NOESY of **9g** in  $\text{DMSO-}d_6$



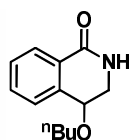


## Regiochemical Assignment

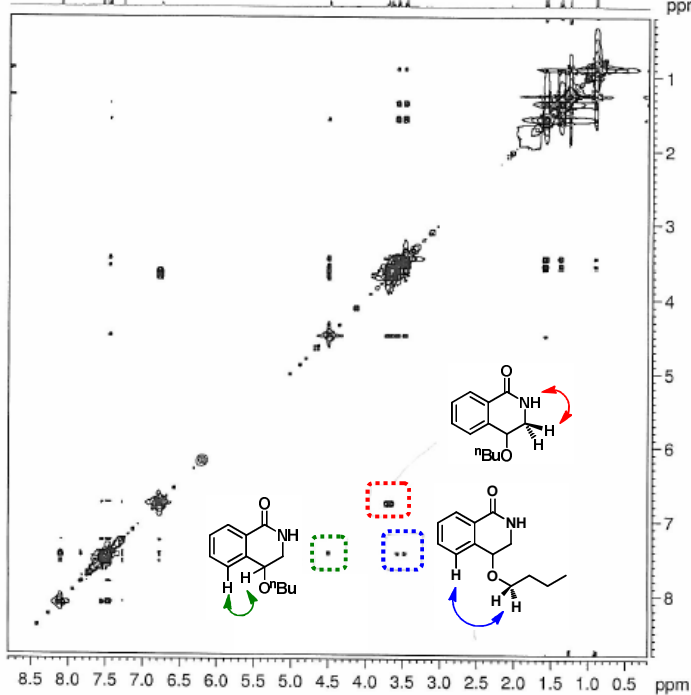




Name njw  
Room No g53b  
Sample NW72 f11-23



2D NOESY



NAME NW72 f11-23  
EXFNO 11  
PROCNO 1  
Date\_ 20110916  
Time 10.46  
INSTRUM av500LC  
PROBHD 5 mm PABBO BBO  
PULPROG noesygpgp\_m  
TD 2048  
SOLVENT CDCl3  
NS 20  
DS 16  
SWH 4310.345 Hz  
FIDRES 2.104661 Hz  
AQ 0.2377340 sec  
RG 114  
DM 116.000 usec  
DE 6.00 usec  
TE 300.0 K  
DO 0.00003300 sec  
D1 2.00573301 sec  
D8 1.20000005 sec  
D16 0.00020000 sec  
D30 0.59880000 sec  
IM0 0.00011600 sec

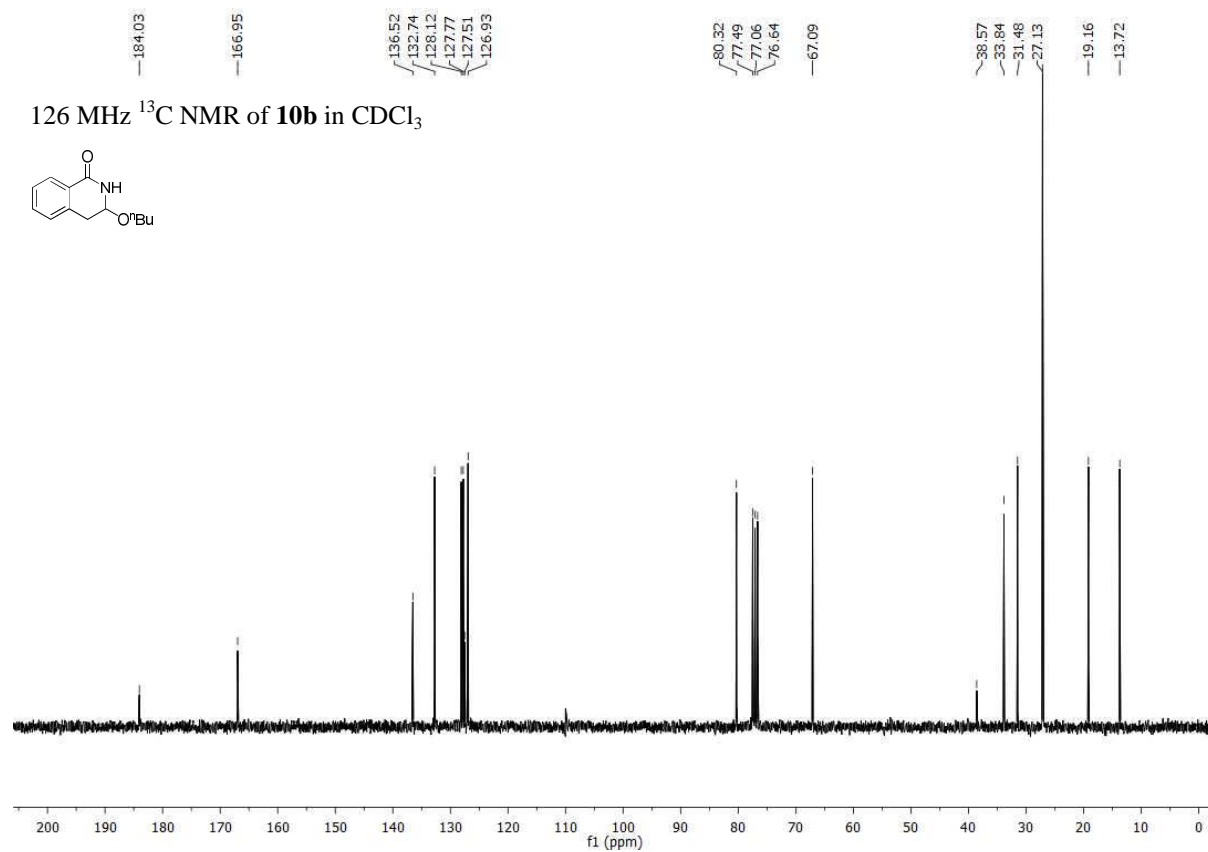
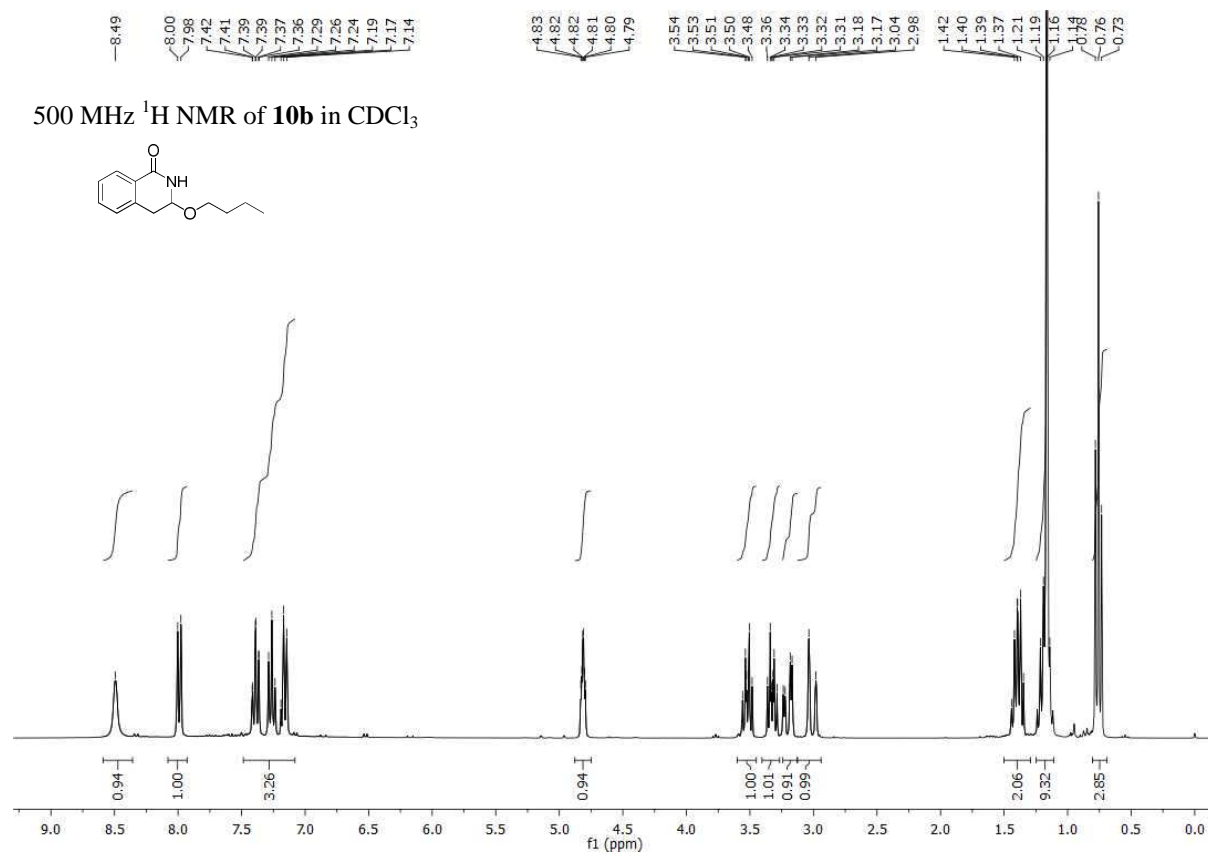
CHANNEL F1

MUCL 1H  
P1 10.00 usec  
P2 20.00 usec  
PL1 -2.40 dB  
SF01 500.5722650 MHz

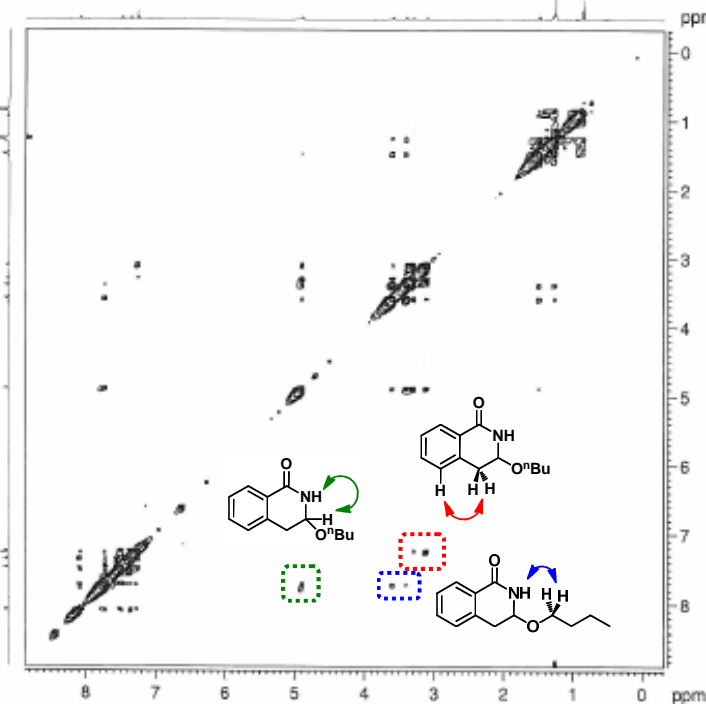
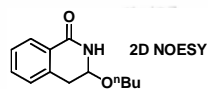
GRADIENT CHANNEL

GPMAM1 SINE.100  
GPMAM2 SINE.100  
GP21 40.00 %  
GP22 -40.00 %  
P16 1000.00 usec  
ND0 2  
TD 180  
SF01 500.5723 MHz  
FIDRES 23.946360 Hz  
SW 8.611 ppm  
F2MODE TPPI  
ST 2048  
SF 500.5700125 MHz  
MDW QSIGN  
SSB 2  
LB 0.00 Hz  
GB 0  
PC 0.40  
ST 1024  
MC2 TPPI  
SF 500.5700125 MHz  
WDM QSIGN  
SSB 2  
LB 0.00 Hz  
GB 0





Name njw  
Room No g53b  
Sample MN72 B F7-11

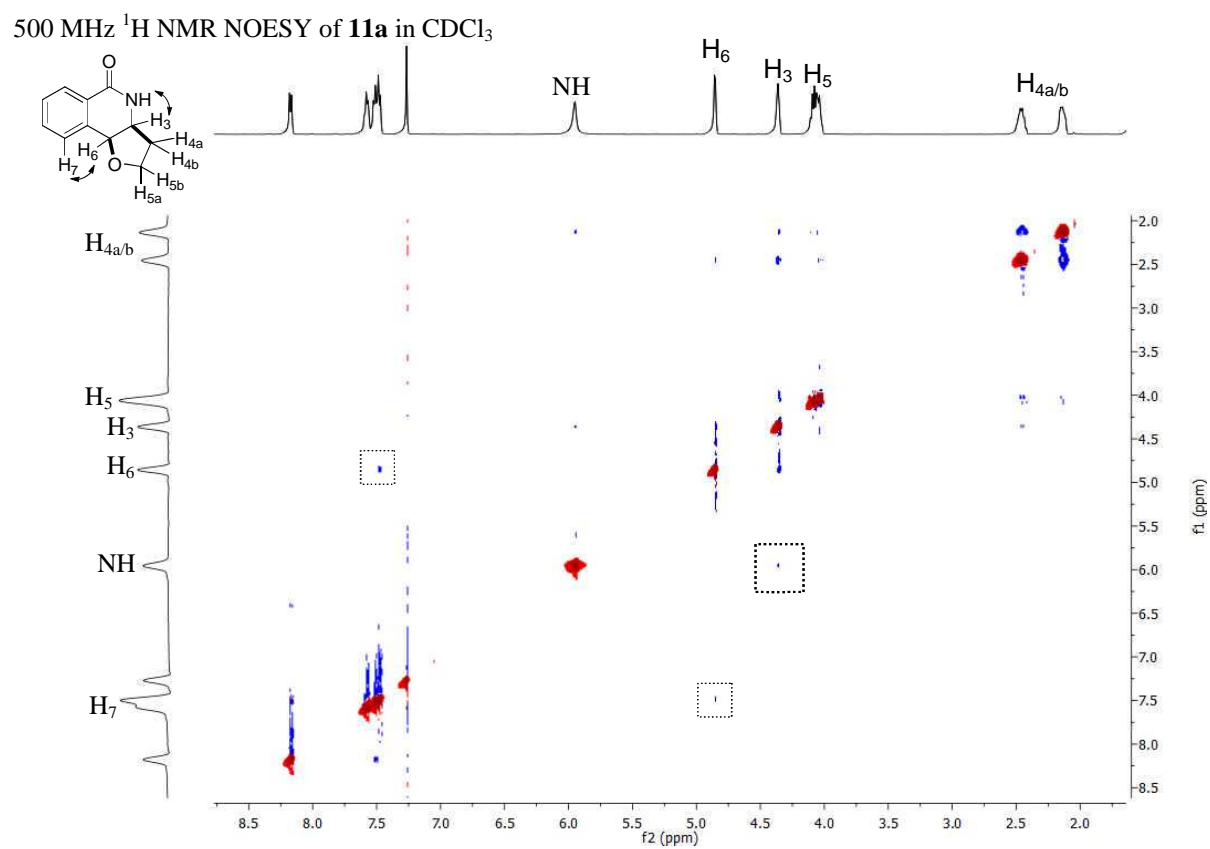
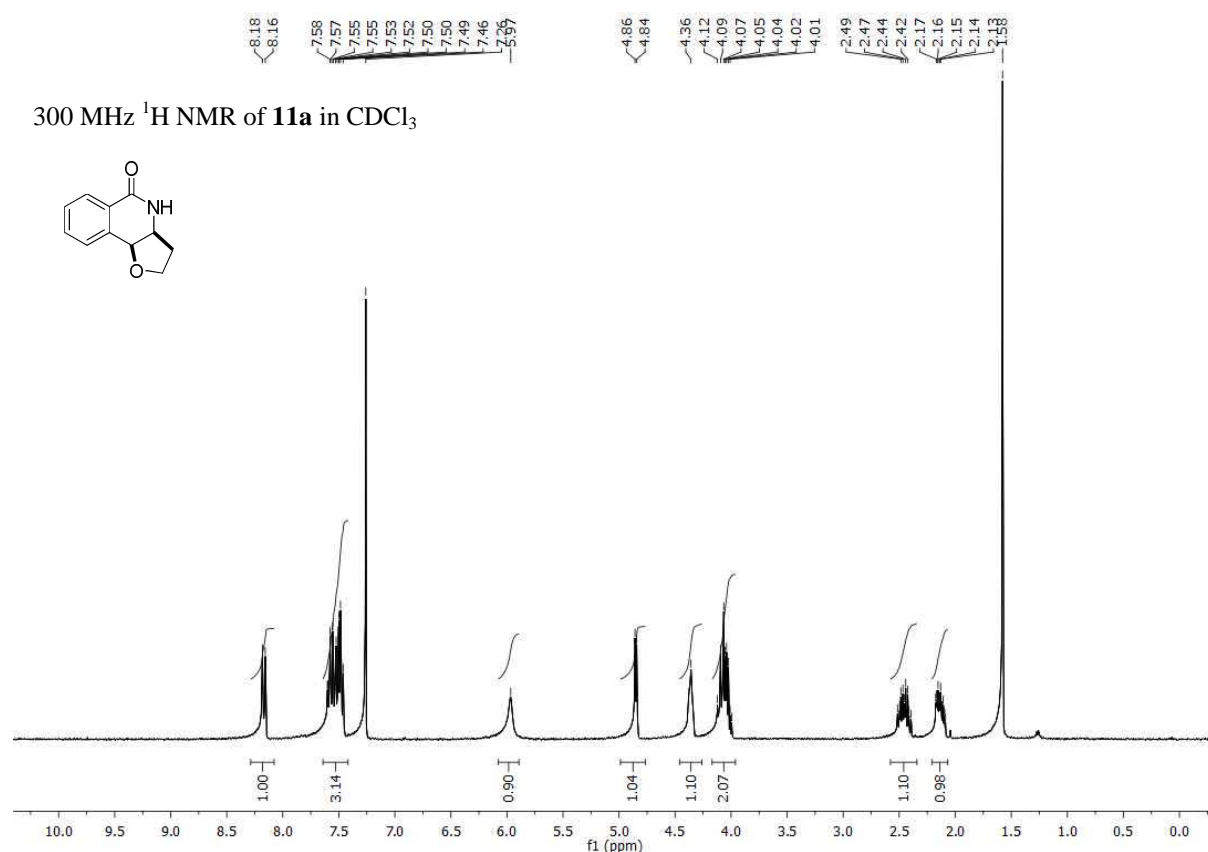


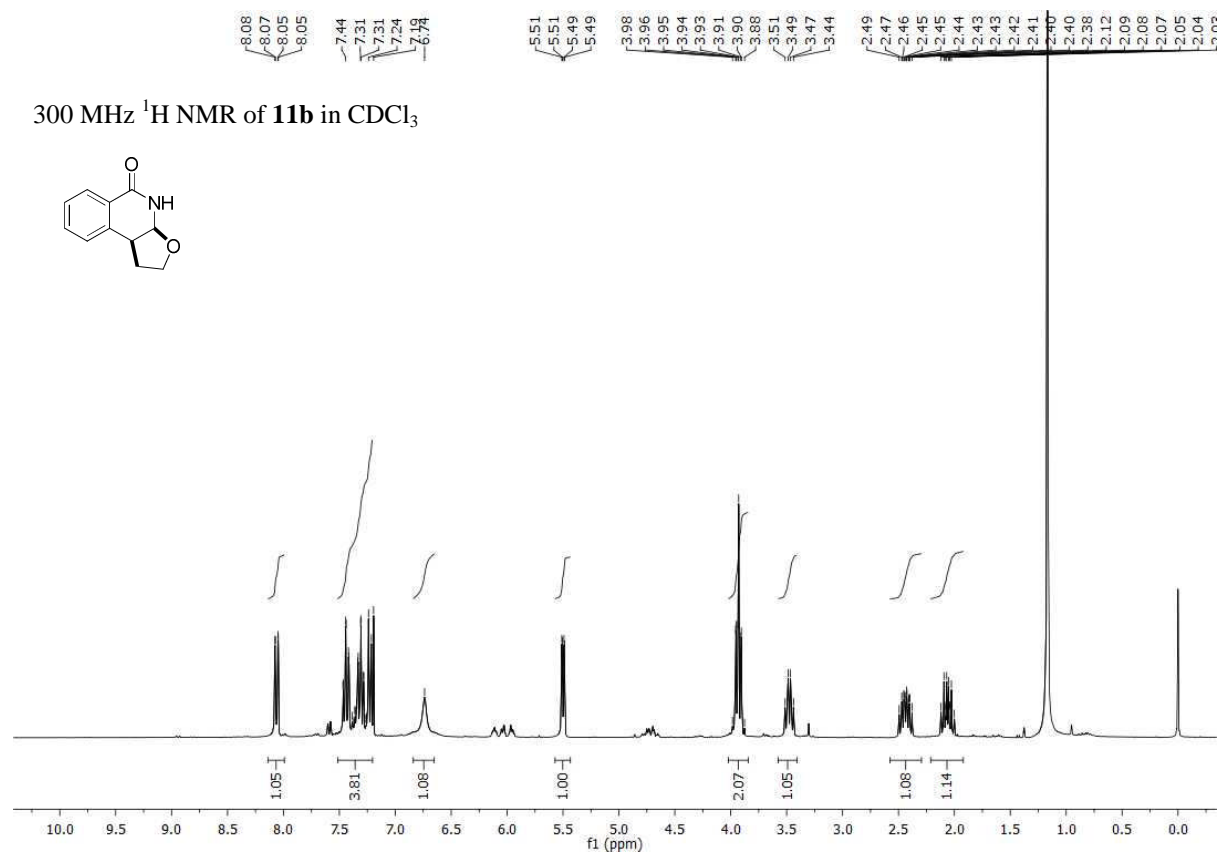
NAME MN72 B F7-11 runny  
EXPNO 11  
PROCNO 1  
Date\_ 28110916  
Time 3.31  
INSTRUM av50016  
PROBHD 5 mm MAREZ  
PULPROG zgpg30  
TD 2648  
F2 2048  
SOLVENT CDCl3  
NS 20  
DS 16  
SWH 4959.566 Hz  
FIDRES 2.243940 Hz  
AQ 0.2225912 sec  
RG 128  
OV 184.800 usad  
DE 6.00 usad  
TE 300.2 K  
D3 8.0000000 sec  
D1 2.0000000 sec  
D8 1.2000000 sec  
D16 8.0000000 sec  
D20 8.5000000 sec  
IN0 8.0000000 sec

===== CHANNEL f1 =====  
NUC1 1H  
PT 10.00 usad  
P2 20.00 usad  
PL1 -2.00 dB  
PC1 500.570125 MHz

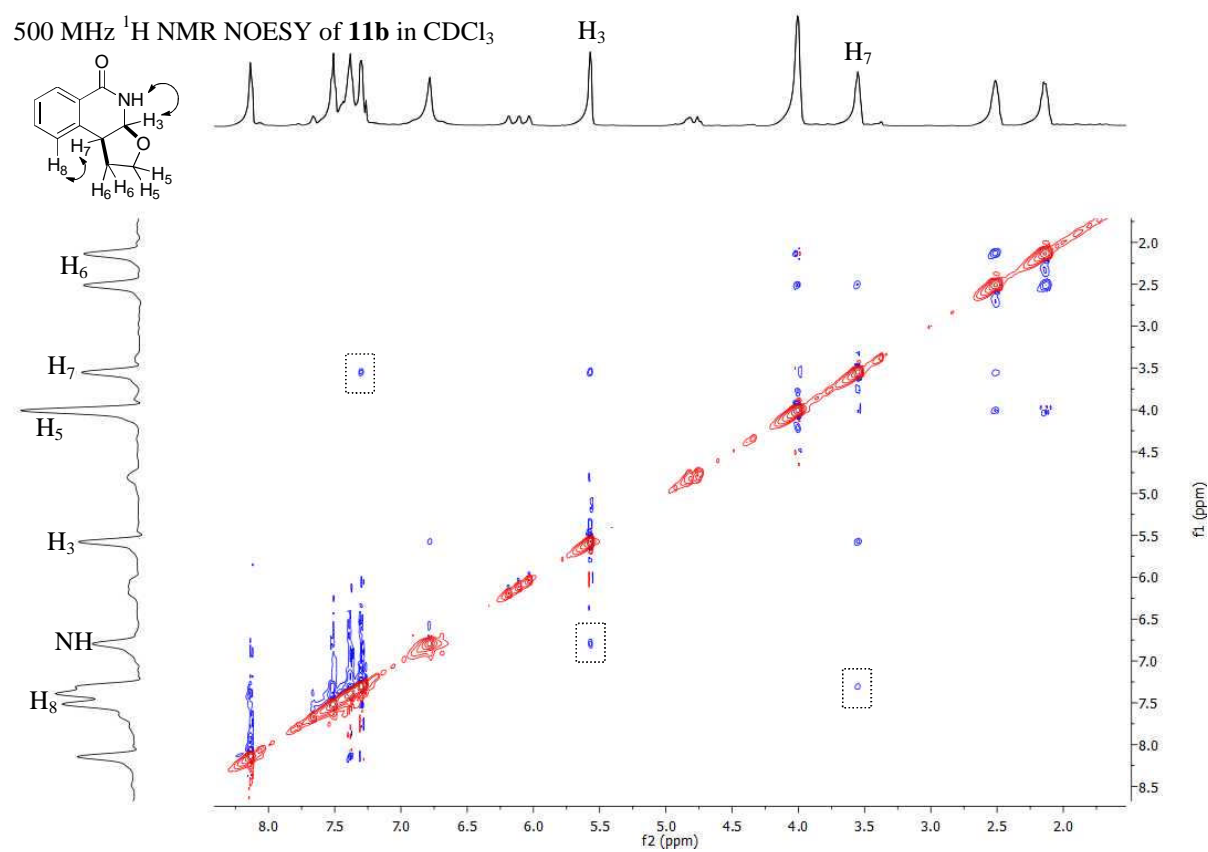
===== CHANNEL CHANNEL =====  
GPRM1 8196.100  
GPRM2 8196.100  
CPD3 48.00 %  
CPD4 48.00 %  
P4 1000.00 usad  
M01 2  
T0 100  
SFO1 500.5722 MHz  
FIDRES 25.330466 Hz  
RM 9.101 ppm  
F2PROG zgpg30  
SI 16384  
SF 500.570125 MHz  
RG 65536  
SOL 2  
DS 8.00 Hz  
GB 0  
PC 2.40  
ST 1624  
MC1 TPPI  
SFO 500.570125 MHz  
SI 16384  
LB 2  
GB 0

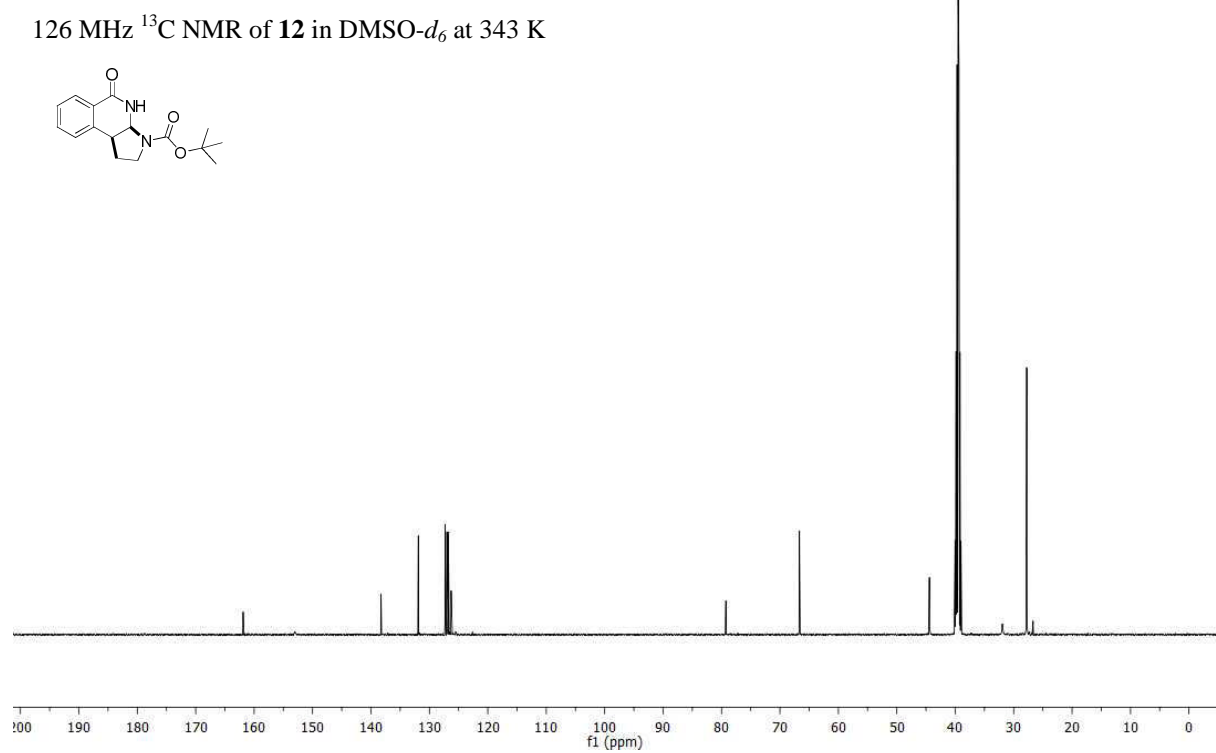
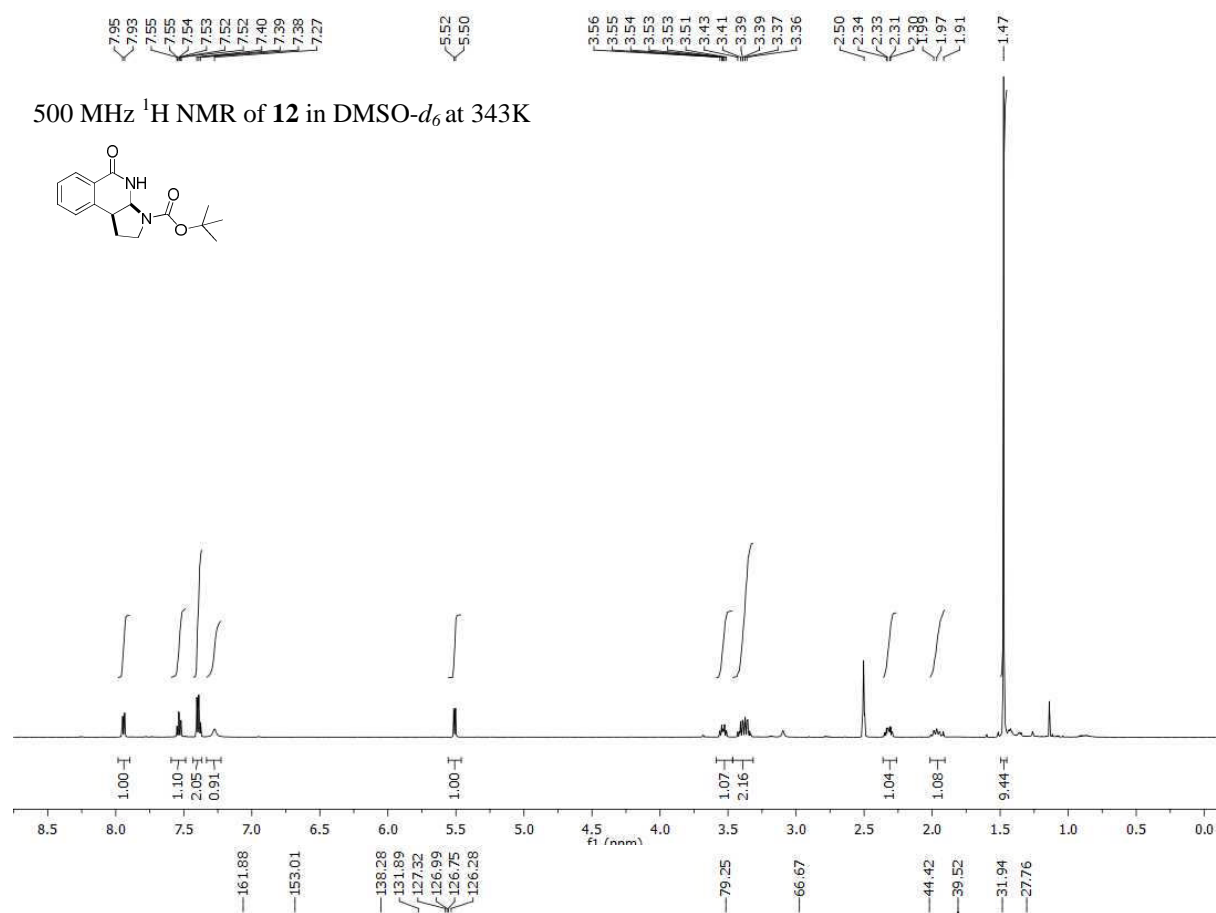


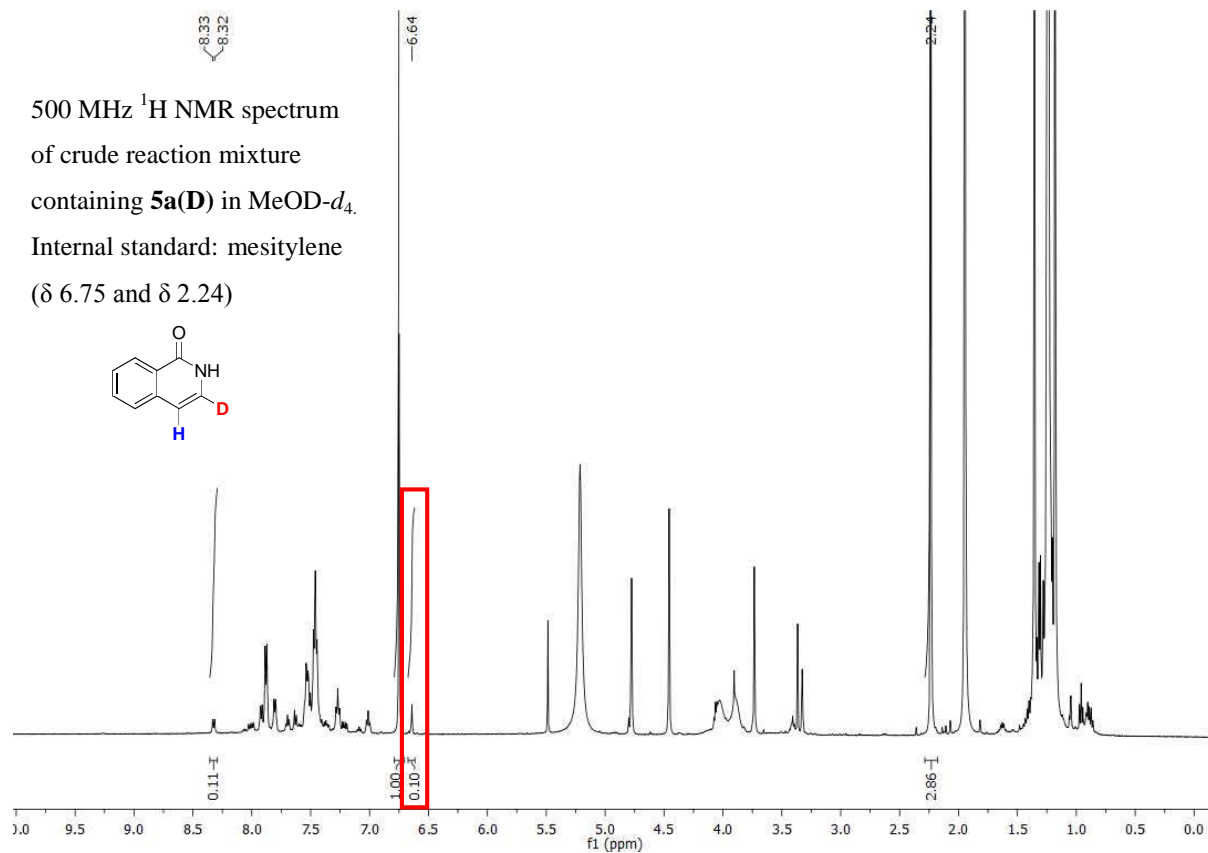
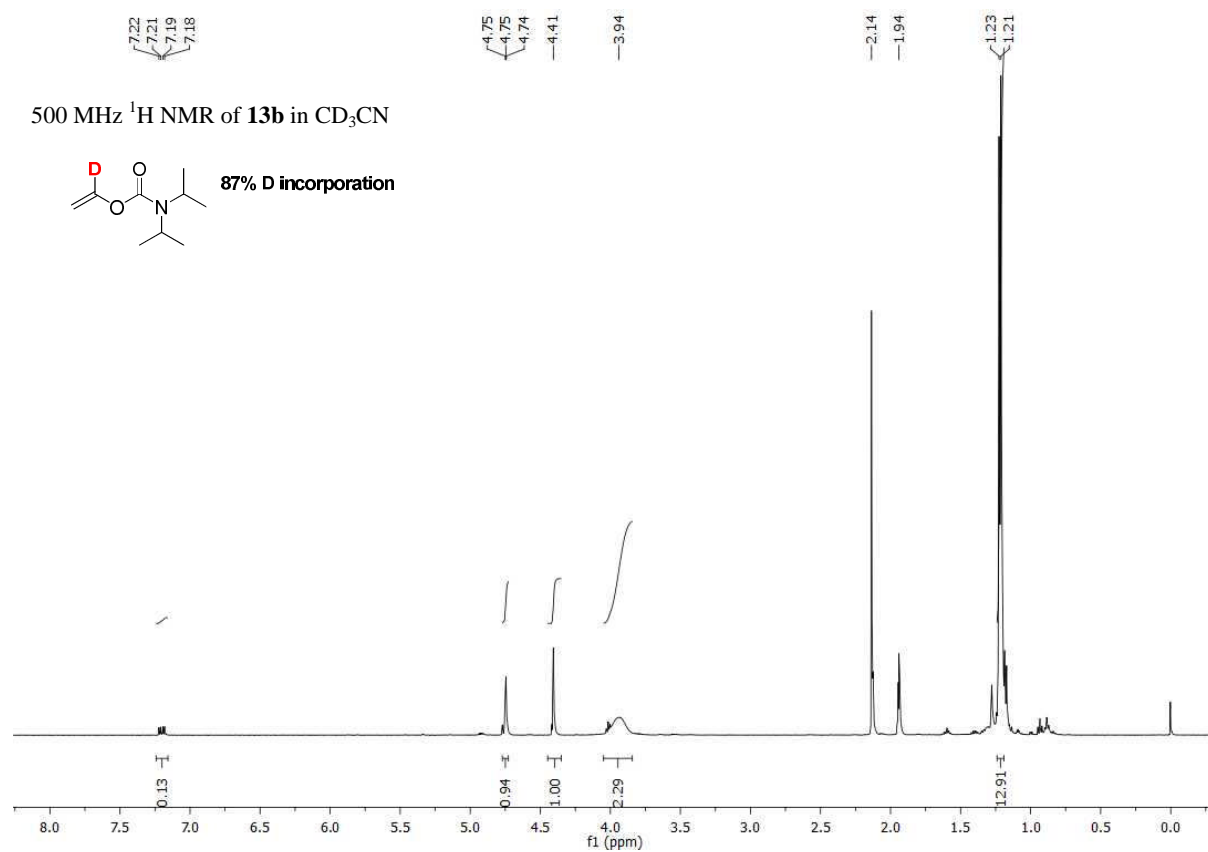


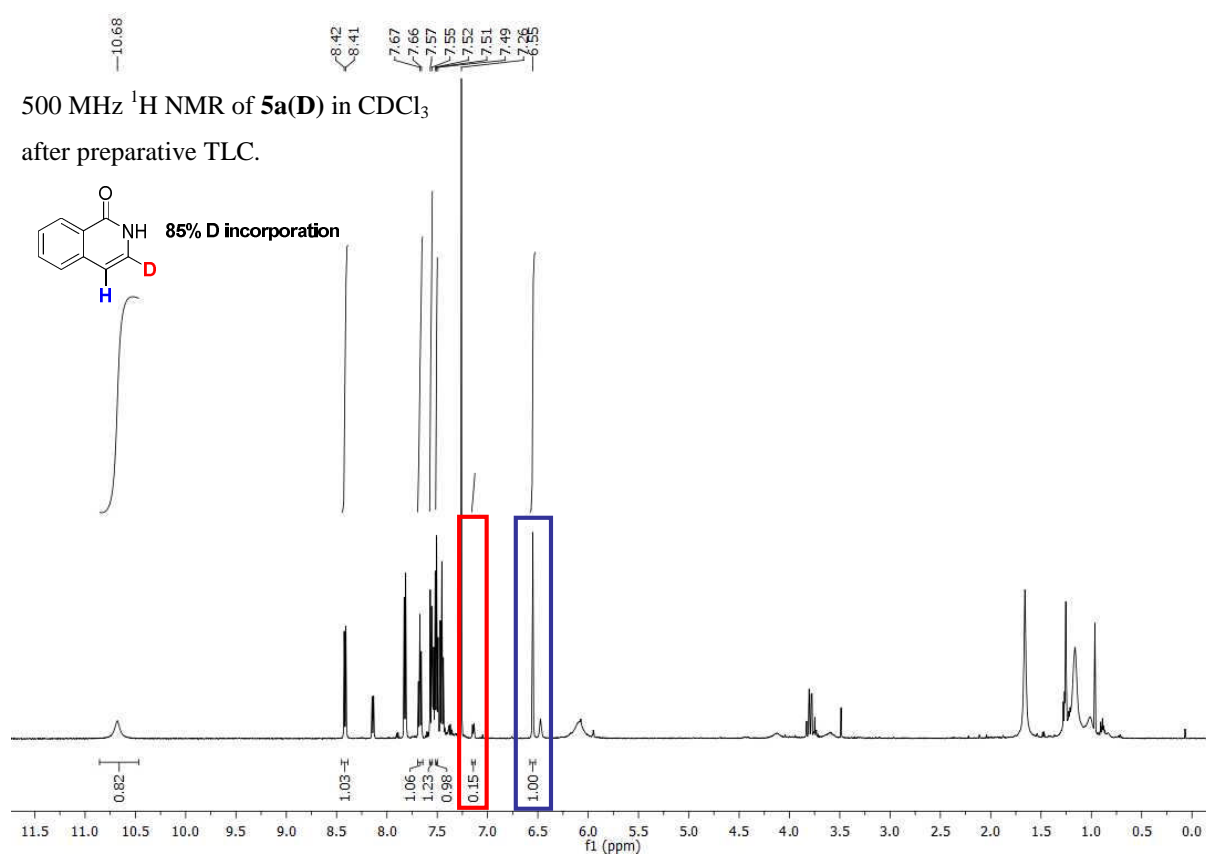


500 MHz  $^1\text{H}$  NMR NOESY of **11b** in  $\text{CDCl}_3$











## Appendix

### Compound 11a

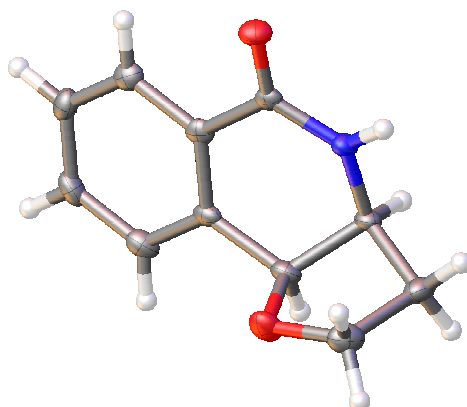


Table 1. Crystal data and structure refinement.

|                            |  |                     |
|----------------------------|--|---------------------|
| Identification code        | Compound 11a   |                     |
| Formula                    | $C_{11}H_{11}NO_2$   |                     |
| Formula weight             | 189.21   |                     |
| Size                       | 0.5284 x 0.2603 x 0.1529 mm                                      |                     |
| Crystal morphology         | Colourless block   |                     |
| Temperature                | 100.00(10) K   |                     |
| Wavelength                 | 0.7107 Å [Mo - $K_\alpha$ ]                                      |                     |
| Crystal system             | Orthorhombic   |                     |
| Space group                | $Pna2_1$   |                     |
| Unit cell dimensions       | $a = 7.2675(4)$ Å  | $\alpha = 90^\circ$ |
|                            | $b = 12.9319(6)$ Å   | $\beta = 90^\circ$  |
|                            | $c = 9.6419(5)$ Å  | $\gamma = 90^\circ$ |
| Volume                     | 906.18(8) Å <sup>3</sup>   |                     |
| Z                          | 4  |                     |
| Density (calculated)       | 1.387 Mg/m <sup>3</sup>  |                     |
| Absorption coefficient     | 0.096 mm <sup>-1</sup>   |                     |
| $F(000)$                   | 400  |                     |
| Data collection range      | $3.15 \leq \theta \leq 26.35^\circ$                              |                     |
| Index ranges               | $-7 \leq h \leq 9$ , $-16 \leq k \leq 15$ , $-12 \leq l \leq 10$ |                     |
| Reflections collected      | 3228   |                     |
| Independent reflections    | 1560 [ $R(\text{int}) = 0.0632$ ]                                |                     |
| Observed reflections       | 1315 [ $I > 2\sigma(I)$ ]  |                     |
| Absorption correction      | multi-scan   |                     |
| Max. and min. transmission | 1 and 0.46407  |                     |

|   |   |
|---|---|
| Refinement method                                   | Full  |
| Data / restraints / parameters                      | 1560 / 1 / 127  |
| Goodness of fit                                     | 1.07  |
| Final <i>R</i> indices [ <i>I</i> > 2σ( <i>I</i> )] | <i>R</i> <sub>1</sub> = 0.0529, <i>wR</i> <sub>2</sub> = 0.1146 |
| <i>R</i> indices (all data)                         | <i>R</i> <sub>1</sub> = 0.0661, <i>wR</i> <sub>2</sub> = 0.1307 |
| Largest diff. peak and hole                         | 0.235 and -0.27 e.Å <sup>-3</sup>                               |
| Absolute structure parameter                        | -1(2)   |

Table 2. Atomic co-ordinates (x 10<sup>4</sup>) and equivalent isotropic displacement parameters (Å<sup>2</sup> x 10<sup>4</sup>) with standard uncertainties (s.u.s) in parentheses. *U*<sub>eq</sub> is defined as <sup>1</sup>/<sub>3</sub> of the trace of the orthogonalized *U*<sub>ij</sub> tensor.

|       | x       | y          | z        | <i>U</i> <sub>eq</sub> |
|-------|---------|------------|----------|------------------------|
| O(2)  | 1974(3) | 3108.8(13) | 2622(2)  | 196(5)                 |
| O(1)  | 4405(3) | 4199.2(15) | -1392(2) | 249(6)                 |
| N(1)  | 4637(3) | 3526.3(17) | 1551(3)  | 165(6)                 |
| C(8)  | -331(4) | 5979.4(19) | 1487(3)  | 199(7)                 |
| C(5)  | 2955(4) | 5262(2)    | 336(3)   | 155(6)                 |
| C(7)  | 542(4)  | 6536(2)    | 441(3)   | 215(7)                 |
| C(10) | 2069(4) | 4704(2)    | 1373(3)  | 157(6)                 |
| C(11) | 2885(4) | 3715(2)    | 1901(3)  | 141(7)                 |
| C(4)  | 4749(5) | 4872(2)    | -231(3)  | 174(7)                 |
| C(9)  | 420(4)  | 5052(2)    | 1941(3)  | 187(7)                 |
| C(6)  | 2166(4) | 6177(2)    | -135(3)  | 205(7)                 |
| C(1)  | 5796(4) | 3404(2)    | -1419(4) | 246(8)                 |
| C(2)  | 7081(4) | 3623(2)    | -207(3)  | 224(7)                 |
| C(3)  | 5846(4) | 4230(2)    | 785(3)   | 159(6)                 |

Table 3. Anisotropic displacement parameters (Å<sup>2</sup> x 10<sup>3</sup>). The anisotropic displacement factor exponent takes the form:

$$-2\pi^2[h^2a^{*2}U_{11} + \dots + 2hk a^* b^* U_{12}]$$

|      | <i>U</i> <sub>11</sub> | <i>U</i> <sub>22</sub> | <i>U</i> <sub>33</sub> | <i>U</i> <sub>23</sub> | <i>U</i> <sub>13</sub> | <i>U</i> <sub>12</sub> |
|------|------------------------|------------------------|------------------------|------------------------|------------------------|------------------------|
| O(2) | 24.1(11)               | 16.4(9)                | 18.4(11)               | 2.1(9)                 | 3.4(11)                | -3.6(8)                |
| O(1) | 30.7(13)               | 28.9(10)               | 15.2(11)               | -4.6(10)               | -4.0(11)               | 4.8(10)                |
| N(1) | 18.3(13)               | 16.8(10)               | 14.4(13)               | 3.6(11)                | 1.6(13)                | 2.1(10)                |
| C(8) | 14.1(15)               | 22.6(13)               | 22.9(17)               | -5.0(14)               | -2.1(15)               | 0.7(12)                |
| C(5) | 18.0(16)               | 18.1(13)               | 10.3(14)               | 0.0(12)                | -2.3(14)               | -5.6(12)               |

|       |          |          |          |          |           |          |
|-------|----------|----------|----------|----------|-----------|----------|
| C(7)  | 25.8(18) | 17.1(13) | 21.8(18) | 0.0(13)  | -10.4(15) | 2.9(12)  |
| C(10) | 18.8(15) | 15.7(12) | 12.6(15) | -4.6(11) | -2.3(13)  | -3.5(12) |
| C(11) | 16.9(16) | 15.5(13) | 10.0(14) | -3.6(12) | -0.5(13)  | -2.8(12) |
| C(4)  | 23.3(17) | 17.4(12) | 11.6(15) | 1.7(12)  | -0.6(13)  | -1.5(12) |
| C(9)  | 18.3(17) | 19.5(13) | 18.4(16) | -3.4(12) | -1.5(14)  | -4.8(12) |
| C(6)  | 29.0(18) | 15.8(13) | 16.6(15) | 0.3(13)  | -3.2(15)  | -2.1(12) |
| C(1)  | 33(2)    | 18.3(13) | 22.3(17) | -1.0(13) | 4.5(16)   | 1.1(13)  |
| C(2)  | 20.8(17) | 25.7(14) | 20.6(16) | 2.9(13)  | 6.4(15)   | 1.4(14)  |
| C(3)  | 16.7(14) | 18.8(12) | 12.1(14) | 3.1(11)  | 1.2(13)   | -1.7(12) |

Table 4. Hydrogen atom co-ordinates ( $\times 10^3$ ) and isotropic displacement parameters ( $\text{\AA}^2 \times 10^2$ ) with s.u.s in parentheses.

|       | x      | y     | z      | $U_{\text{eq}}$ |
|-------|--------|-------|--------|-----------------|
| H(1)  | 5092.  | 2941. | 1798.  | 20.             |
| H(8)  | -1413. | 6227. | 1879.  | 24.             |
| H(7)  | 32.    | 7153. | 128.   | 26.             |
| H(4)  | 5496.  | 5461. | -537.  | 21.             |
| H(9)  | -174.  | 4666. | 2621.  | 22.             |
| H(6)  | 2732.  | 6549. | -842.  | 25.             |
| H(1a) | 6468.  | 3425. | -2288. | 30.             |
| H(1b) | 5238.  | 2727. | -1321. | 30.             |
| H(2a) | 8132.  | 4032. | -497.  | 27.             |
| H(2b) | 7512.  | 2987. | 215.   | 27.             |
| H(3)  | 6569.  | 4666. | 1413.  | 19.             |

Table 5. Interatomic distances ( $\text{\AA}$ ) with s.u.s in parentheses.

|            |          |             |          |
|------------|----------|-------------|----------|
| O(2)-C(11) | 1.240(3) | O(1)-C(4)   | 1.440(3) |
| O(1)-C(1)  | 1.442(4) | N(1)-C(11)  | 1.339(3) |
| N(1)-C(3)  | 1.465(4) | C(8)-C(7)   | 1.392(5) |
| C(8)-C(9)  | 1.389(4) | C(5)-C(10)  | 1.391(4) |
| C(5)-C(4)  | 1.501(4) | C(5)-C(6)   | 1.391(4) |
| C(7)-C(6)  | 1.385(5) | C(10)-C(11) | 1.498(4) |
| C(10)-C(9) | 1.392(4) | C(4)-C(3)   | 1.511(4) |
| C(1)-C(2)  | 1.523(5) | C(2)-C(3)   | 1.528(4) |

Table 6. Angles between interatomic vectors ( $^\circ$ ) with s.u.s in parentheses.

|                 |          |                 |          |
|-----------------|----------|-----------------|----------|
| C(4)-O(1)-C(1)  | 108.8(2) | C(11)-N(1)-C(3) | 125.7(2) |
| C(9)-C(8)-C(7)  | 119.8(3) | C(10)-C(5)-C(4) | 119.4(2) |
| C(10)-C(5)-C(6) | 119.0(3) | C(6)-C(5)-C(4)  | 121.6(3) |

|                  |          |                  |          |
|------------------|----------|------------------|----------|
| C(6)-C(7)-C(8)   | 120.3(3) | C(5)-C(10)-C(11) | 120.2(3) |
| C(5)-C(10)-C(9)  | 120.9(3) | C(9)-C(10)-C(11) | 118.9(3) |
| O(2)-C(11)-N(1)  | 122.3(2) | O(2)-C(11)-C(10) | 121.2(3) |
| N(1)-C(11)-C(10) | 116.5(2) | O(1)-C(4)-C(5)   | 109.6(2) |
| O(1)-C(4)-C(3)   | 105.3(2) | C(5)-C(4)-C(3)   | 114.0(2) |
| C(8)-C(9)-C(10)  | 119.6(3) | C(7)-C(6)-C(5)   | 120.4(3) |
| O(1)-C(1)-C(2)   | 106.5(2) | C(1)-C(2)-C(3)   | 102.4(2) |
| N(1)-C(3)-C(4)   | 110.6(2) | N(1)-C(3)-C(2)   | 110.4(2) |
| C(4)-C(3)-C(2)   | 100.8(2) |                  |          |

Table 7. Torsion angles (°) with s.u.s in parentheses.

|                       |           |                       |           |
|-----------------------|-----------|-----------------------|-----------|
| O(1)-C(4)-C(3)-N(1)   | -78.5(3)  | O(1)-C(4)-C(3)-C(2)   | 38.3(3)   |
| O(1)-C(1)-C(2)-C(3)   | 24.8(3)   | C(8)-C(7)-C(6)-C(5)   | -0.8(5)   |
| C(5)-C(10)-C(11)-O(2) | -166.2(2) | C(5)-C(10)-C(11)-N(1) | 13.7(4)   |
| C(5)-C(10)-C(9)-C(8)  | -1.3(4)   | C(5)-C(4)-C(3)-N(1)   | 41.6(3)   |
| C(5)-C(4)-C(3)-C(2)   | 158.4(2)  | C(7)-C(8)-C(9)-C(10)  | 1.8(4)    |
| C(10)-C(5)-C(4)-O(1)  | 90.0(3)   | C(10)-C(5)-C(4)-C(3)  | -27.6(3)  |
| C(10)-C(5)-C(6)-C(7)  | 1.4(4)    | C(11)-N(1)-C(3)-C(4)  | -32.1(4)  |
| C(11)-N(1)-C(3)-C(2)  | -142.7(3) | C(11)-C(10)-C(9)-C(8) | 178.5(3)  |
| C(4)-O(1)-C(1)-C(2)   | -1.0(3)   | C(4)-C(5)-C(10)-C(11) | -0.9(4)   |
| C(4)-C(5)-C(10)-C(9)  | 178.8(3)  | C(4)-C(5)-C(6)-C(7)   | -177.7(3) |
| C(9)-C(8)-C(7)-C(6)   | -0.8(5)   | C(9)-C(10)-C(11)-O(2) | 14.0(4)   |
| C(9)-C(10)-C(11)-N(1) | -166.0(2) | C(6)-C(5)-C(10)-C(11) | 179.9(3)  |
| C(6)-C(5)-C(10)-C(9)  | -0.3(4)   | C(6)-C(5)-C(4)-O(1)   | -90.9(3)  |
| C(6)-C(5)-C(4)-C(3)   | 151.5(3)  | C(1)-O(1)-C(4)-C(5)   | -146.8(2) |
| C(1)-O(1)-C(4)-C(3)   | -23.8(3)  | C(1)-C(2)-C(3)-N(1)   | 79.2(3)   |
| C(1)-C(2)-C(3)-C(4)   | -37.7(3)  | C(3)-N(1)-C(11)-O(2)  | -175.7(3) |
| C(3)-N(1)-C(11)-C(10) | 4.4(4)    |                       |           |

## Compound 12

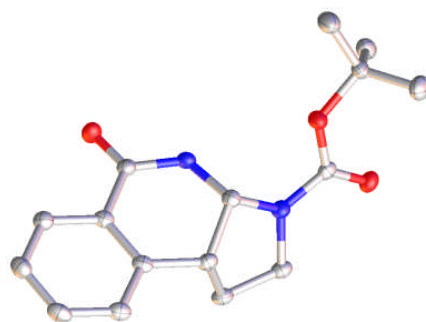


Table 1. Crystal data and structure refinement.

|                                |  |                           |
|--------------------------------|--|---------------------------|
| Identification code            | Compound 12  |                           |
| Formula                        | $C_{32}H_{41}N_4O_{6.50}$  |                           |
| Formula weight                 | 585.69   |                           |
| Size                           | 0.3092 x 0.2031 x 0.1568 mm  |                           |
| Crystal morphology             | Colourless block   |                           |
| Temperature                    | 100.00(10) K   |                           |
| Wavelength                     | 0.7107 Å [Mo - $K_{\alpha}$ ]                                      |                           |
| Crystal system                 | Monoclinic   |                           |
| Space group                    | $P2_1/n$   |                           |
| Unit cell dimensions           | $a = 10.1273(5)$ Å   | $\alpha = 90^\circ$       |
|                                | $b = 12.4095(5)$ Å   | $\beta = 91.343(4)^\circ$ |
|                                | $c = 24.1328(9)$ Å   | $\gamma = 90^\circ$       |
| Volume                         | $3032.0(2)$ Å <sup>3</sup>   |                           |
| $Z$                            | 4  |                           |
| Density (calculated)           | $1.283$ Mg/m <sup>3</sup>  |                           |
| Absorption coefficient         | $0.09$ mm <sup>-1</sup>  |                           |
| $F(000)$                       | 1252   |                           |
| Data collection range          | $1.85 \leq \theta \leq 29.88^\circ$                                |                           |
| Index ranges                   | $-10 \leq h \leq 14$ , $-16 \leq k \leq 14$ , $-32 \leq l \leq 32$ |                           |
| Reflections collected          | 18513  |                           |
| Independent reflections        | 7396 [ $R(\text{int}) = 0.034$ ]                                   |                           |
| Observed reflections           | 6032 [ $I > 2\sigma(I)$ ]  |                           |
| Absorption correction          | multi-scan   |                           |
| Max. and min. transmission     | 1 and 0.87787  |                           |
| Refinement method              | Full   |                           |
| Data / restraints / parameters | 7396 / 0 / 551   |                           |

|  |                                    |
|--|------------------------------------|
| Goodness of fit                        | 1.016                              |
| Final $R$ indices [ $I > 2\sigma(I)$ ] | $R_1 = 0.0461$ , $wR_2 = 0.1063$   |
| $R$ indices (all data)                 | $R_1 = 0.0594$ , $wR_2 = 0.1149$   |
| Largest diff. peak and hole            | 0.295 and -0.275 e.Å <sup>-3</sup> |

Table 2. Atomic co-ordinates ( $\times 10^4$ ) and equivalent isotropic displacement parameters ( $\text{\AA}^2 \times 10^4$ ) with standard uncertainties (s.u.s) in parentheses.  $U_{\text{eq}}$  is defined as  $1/3$  of the trace of the orthogonalized  $U_{ij}$  tensor.

|        | x          | y          | z         | $U_{\text{eq}}$ |
|--------|------------|------------|-----------|-----------------|
| O(1)   | 591.3(9)   | 4073.8(8)  | 2066.7(4) | 210(2)          |
| O(3b)  | -158.1(9)  | 2244.0(8)  | 8436.2(4) | 231(2)          |
| O(2)   | 1307.6(9)  | 2620.5(8)  | 4088.2(4) | 214(2)          |
| O(2b)  | 1098.6(9)  | 3768.1(8)  | 8526.2(4) | 228(2)          |
| O(1b)  | 1162.6(9)  | 5936.2(8)  | 6727.6(4) | 255(2)          |
| O(3)   | -48.8(10)  | 1184.6(9)  | 4244.5(4) | 291(2)          |
| N(2)   | 896.2(11)  | 1451.1(9)  | 3415.6(4) | 184(2)          |
| N(2b)  | 1132.2(11) | 2837.3(9)  | 7745.8(4) | 194(2)          |
| N(1)   | 974.4(11)  | 2907.3(9)  | 2770.3(4) | 170(2)          |
| N(1b)  | 1466.5(11) | 4564.1(9)  | 7330.7(5) | 190(2)          |
| C(1)   | 1180.5(12) | 3272.8(10) | 2257.1(5) | 159(2)          |
| C(12)  | 658.8(13)  | 1717.1(12) | 3948.3(5) | 207(3)          |
| C(7b)  | 3292.6(12) | 3608.2(11) | 6614.1(5) | 180(3)          |
| C(9b)  | 2106.9(12) | 3574.7(11) | 7531.0(5) | 178(3)          |
| C(12b) | 622.8(12)  | 2892.7(11) | 8260.4(5) | 186(3)          |
| C(2)   | 2123.3(12) | 2649.4(11) | 1915.6(5) | 167(3)          |
| C(2b)  | 2806.8(12) | 4638.9(11) | 6515.5(5) | 177(3)          |
| C(7)   | 2603.9(12) | 1654.0(11) | 2098.0(5) | 177(3)          |
| C(8b)  | 2725.5(12) | 2924.0(11) | 7063.8(5) | 188(3)          |
| C(1b)  | 1743.8(12) | 5099.7(11) | 6863.7(5) | 182(3)          |
| C(9)   | 1743.1(12) | 2059.7(11) | 3051.1(5) | 166(3)          |
| C(8)   | 2190.3(13) | 1204.0(11) | 2642.6(5) | 180(3)          |
| C(5b)  | 4801.7(13) | 3849.3(13) | 5865.9(6) | 246(3)          |
| C(11b) | 837.5(13)  | 1923.1(11) | 7379.8(6) | 203(3)          |
| C(3b)  | 3314.8(13) | 5278.1(12) | 6097.0(5) | 209(3)          |
| C(6b)  | 4286.0(13) | 3211.0(12) | 6278.7(6) | 214(3)          |
| C(3)   | 2473.5(13) | 3046.5(12) | 1399.2(6) | 207(3)          |
| C(5)   | 3782.6(13) | 1472.5(13) | 1246.1(6) | 251(3)          |
| C(13b) | 670.8(14)  | 4039.5(12) | 9088.8(5) | 228(3)          |
| C(10b) | 1590.1(13) | 2188.6(12) | 6858.8(6) | 212(3)          |
| C(6)   | 3433.7(13) | 1065.0(12) | 1757.4(6) | 223(3)          |
| C(4b)  | 4324.1(13) | 4881.1(13) | 5775.0(6) | 243(3)          |
| C(13)  | 1180.6(14) | 3122.4(12) | 4637.1(5) | 229(3)          |
| C(11)  | 471.7(13)  | 413.6(11)  | 3184.7(6) | 204(3)          |

|       |            |            |           |        |
|-------|------------|------------|-----------|--------|
| C(16) | 2164.0(16) | 4042.2(14) | 4602.2(7) | 290(3) |
| C(4)  | 3308.6(13) | 2461.4(13) | 1065.6(6) | 247(3) |
| C(15) | 1591.2(18) | 2356.4(15) | 5099.4(6) | 333(4) |

Table 2. (continued)

|                    |            |            |            |        |
|--------------------|------------|------------|------------|--------|
| C(14)              | -224.0(15) | 3536.1(15) | 4688.6(6)  | 301(3) |
| C(10)              | 992.6(13)  | 443.1(11)  | 2596.6(6)  | 202(3) |
| C(15b)             | -817.5(15) | 4187.1(14) | 9087.9(6)  | 274(3) |
| C(14b)             | 1148.0(18) | 3182.2(14) | 9493.7(7)  | 318(3) |
| C(16b)             | 1373.1(18) | 5102.9(14) | 9188.1(7)  | 338(4) |
| O(4) <sup>pg</sup> | 8693(3)    | 540(2)     | 5241.5(10) | 411(6) |

Key to superscripts on atoms with refinement constraints/restraints:

*g* - rigid group refinement of site

*p* - partial occupancy constraint

Table 3. Anisotropic displacement parameters ( $\text{\AA}^2 \times 10^3$ ). The anisotropic displacement factor exponent takes the form:

$$-2\pi^2[h^2a^{*2}U_{11} + \dots + 2hk a^* b^* U_{12}]$$

|        | $U_{11}$ | $U_{22}$ | $U_{33}$ | $U_{23}$ | $U_{13}$ | $U_{12}$ |
|--------|----------|----------|----------|----------|----------|----------|
| O(1)   | 241(5)   | 167(5)   | 223(5)   | 26(4)    | 34(4)    | 28(4)    |
| O(3b)  | 231(5)   | 183(5)   | 280(5)   | 34(4)    | 33(4)    | -25(4)   |
| O(2)   | 246(5)   | 231(5)   | 166(4)   | -22(4)   | 32(4)    | -18(4)   |
| O(2b)  | 279(5)   | 204(5)   | 203(5)   | -27(4)   | 49(4)    | -50(4)   |
| O(1b)  | 270(5)   | 221(5)   | 278(5)   | 38(4)    | 86(4)    | 67(4)    |
| O(3)   | 329(6)   | 309(6)   | 236(5)   | 69(5)    | 53(4)    | -70(4)   |
| N(2)   | 197(5)   | 166(6)   | 188(5)   | 14(5)    | 6(4)     | -25(4)   |
| N(2b)  | 201(5)   | 167(6)   | 215(5)   | -12(5)   | 15(4)    | -35(4)   |
| N(1)   | 176(5)   | 147(6)   | 186(5)   | -4(4)    | 27(4)    | 26(4)    |
| N(1b)  | 190(5)   | 179(6)   | 205(5)   | -24(5)   | 52(4)    | 6(4)     |
| C(1)   | 157(6)   | 135(6)   | 184(6)   | -16(5)   | 4(4)     | -27(5)   |
| C(12)  | 202(6)   | 217(7)   | 203(6)   | 42(6)    | -1(5)    | 18(5)    |
| C(7b)  | 132(6)   | 217(7)   | 191(6)   | -46(5)   | -22(4)   | -10(5)   |
| C(9b)  | 160(6)   | 185(7)   | 190(6)   | -16(5)   | -1(5)    | -22(5)   |
| C(12b) | 183(6)   | 153(7)   | 222(6)   | 16(5)    | -14(5)   | 22(5)    |
| C(2)   | 138(6)   | 178(7)   | 184(6)   | -40(5)   | 2(4)     | -29(5)   |
| C(2b)  | 127(6)   | 211(7)   | 191(6)   | -39(5)   | -9(4)    | -12(5)   |
| C(7)   | 139(6)   | 196(7)   | 194(6)   | -43(5)   | -3(5)    | -23(5)   |
| C(8b)  | 166(6)   | 171(7)   | 227(6)   | -10(5)   | -6(5)    | 15(5)    |
| C(1b)  | 173(6)   | 172(7)   | 202(6)   | -27(5)   | 13(5)    | -17(5)   |

|        |         |         |         |         |        |        |
|--------|---------|---------|---------|---------|--------|--------|
| C(9)   | 157(6)  | 167(7)  | 175(6)  | 10(5)   | -4(5)  | -5(5)  |
| C(8)   | 173(6)  | 166(7)  | 201(6)  | -8(5)   | -16(5) | 26(5)  |
| C(5b)  | 168(6)  | 332(8)  | 239(7)  | -76(6)  | 33(5)  | 10(5)  |
| C(11b) | 181(7)  | 168(7)  | 260(7)  | -28(6)  | -16(5) | -15(5) |
| C(3b)  | 189(6)  | 210(7)  | 227(6)  | -15(6)  | 9(5)   | -9(5)  |
| C(6b)  | 161(6)  | 243(8)  | 237(6)  | -51(6)  | -22(5) | 25(5)  |
| C(3)   | 190(6)  | 221(7)  | 212(6)  | -8(6)   | 15(5)  | -39(5) |
| C(5)   | 199(7)  | 286(8)  | 271(7)  | -101(6) | 55(5)  | -15(6) |
| C(13b) | 309(7)  | 204(7)  | 172(6)  | 0(5)    | 29(5)  | -12(6) |
| C(10b) | 211(7)  | 174(7)  | 251(7)  | -45(6)  | -1(5)  | 1(5)   |
| C(6)   | 186(6)  | 208(7)  | 274(7)  | -62(6)  | 8(5)   | 0(5)   |
| C(4b)  | 206(7)  | 313(8)  | 213(6)  | -21(6)  | 44(5)  | -47(6) |
| C(13)  | 259(7)  | 276(8)  | 153(6)  | -28(6)  | 6(5)   | 36(6)  |
| C(11)  | 205(7)  | 154(7)  | 252(7)  | 19(6)   | -16(5) | -11(5) |
| C(16)  | 294(8)  | 312(9)  | 263(7)  | -57(7)  | -14(6) | 4(6)   |
| C(4)   | 222(7)  | 308(8)  | 213(7)  | -37(6)  | 59(5)  | -62(6) |
| C(15)  | 420(10) | 369(10) | 208(7)  | 25(7)   | -31(6) | 63(8)  |
| C(14)  | 272(8)  | 400(10) | 232(7)  | -39(7)  | 41(6)  | 54(7)  |
| C(10)  | 223(7)  | 146(7)  | 237(7)  | 7(6)    | -4(5)  | -10(5) |
| C(15b) | 326(8)  | 279(9)  | 217(7)  | 17(7)   | 34(6)  | 53(6)  |
| C(14b) | 392(9)  | 294(9)  | 267(8)  | 51(7)   | -47(6) | 19(7)  |
| C(16b) | 462(10) | 300(9)  | 254(8)  | -53(7)  | 64(7)  | -96(7) |
| O(4)   | 524(15) | 381(15) | 332(12) | 64(11)  | 92(10) | 49(11) |

Table 4. Hydrogen atom co-ordinates ( $\times 10^3$ ) and isotropic displacement parameters ( $\text{\AA}^2 \times 10^2$ ) with s.u.s in parentheses.

|        | x         | y         | z        | $U_{\text{eq}}$ |
|--------|-----------|-----------|----------|-----------------|
| H(4a)  | 902.1     | 71.4      | 493.3    | 62.             |
| H(4c)  | 919.8     | 9.        | 540.6    | 62.             |
| H(8)   | 292.9(14) | 81.3(12)  | 282.4(6) | 13.(3)          |
| H(9)   | 246.0(14) | 235.6(12) | 325.8(6) | 14.(3)          |
| H(10a) | 126.5(15) | -28.2(14) | 246.6(6) | 26.(4)          |
| H(10b) | 32.3(15)  | 75.2(13)  | 233.3(6) | 23.(4)          |
| H(8b)  | 341.0(15) | 245.0(13) | 723.8(6) | 21.(4)          |
| H(11a) | -48.1(16) | 34.5(13)  | 319.8(6) | 21.(4)          |
| H(11c) | -10.9(15) | 186.0(12) | 731.7(6) | 17.(4)          |
| H(10c) | 101.1(15) | 256.8(13) | 658.7(6) | 23.(4)          |
| H(9b)  | 277.1(14) | 374.8(12) | 783.8(6) | 13.(3)          |
| H(1)   | 36.9(17)  | 327.3(15) | 296.1(7) | 32.(4)          |
| H(6b)  | 460.7(15) | 248.3(14) | 633.5(6) | 24.(4)          |
| H(1b)  | 88.2(17)  | 485.8(15) | 754.8(7) | 31.(4)          |
| H(4b)  | 469.9(16) | 533.3(14) | 549.0(7) | 27.(4)          |
| H(3b)  | 298.4(15) | 597.4(14) | 604.2(6) | 21.(4)          |
| H(3)   | 212.5(15) | 371.4(14) | 127.6(6) | 23.(4)          |
| H(11b) | 88.1(16)  | -20.5(14) | 340.4(7) | 30.(4)          |



|        |            |           |          |        |
|--------|------------|-----------|----------|--------|
| H(10d) | 191.6(17)  | 153.5(15) | 666.8(7) | 33.(4) |
| H(14d) | 211.(2)    | 307.3(16) | 945.1(7) | 42.(5) |
| H(14a) | -84.1(19)  | 290.7(16) | 470.9(7) | 41.(5) |
| H(4)   | 354.2(16)  | 273.8(15) | 71.7(7)  | 33.(4) |
| H(11d) | 113.9(16)  | 123.0(14) | 756.4(7) | 28.(4) |
| H(15d) | -108.9(17) | 460.5(15) | 877.1(7) | 34.(5) |
| H(14b) | -27.9(17)  | 395.3(15) | 502.7(8) | 34.(5) |
| H(6)   | 375.4(16)  | 35.8(15)  | 188.0(7) | 32.(4) |
| H(15e) | -127.3(17) | 348.3(16) | 907.5(7) | 37.(5) |
| H(14e) | 70.1(17)   | 247.8(16) | 943.5(7) | 33.(5) |
| H(16a) | 195.3(17)  | 450.2(15) | 429.0(7) | 34.(5) |
| H(16d) | 110.6(17)  | 564.0(16) | 889.6(7) | 37.(5) |
| H(14c) | -44.5(18)  | 398.6(15) | 436.8(8) | 38.(5) |
| H(5)   | 439.0(17)  | 105.6(14) | 101.5(7) | 33.(4) |
| H(5b)  | 551.8(18)  | 358.5(15) | 564.6(7) | 35.(5) |
| H(16e) | 114.2(18)  | 539.6(15) | 955.9(8) | 40.(5) |
| H(16f) | 232.(2)    | 502.6(16) | 916.8(7) | 41.(5) |
| H(16b) | 306.8(19)  | 376.5(15) | 454.2(7) | 40.(5) |
| H(15a) | 94.(2)     | 178.2(17) | 513.3(8) | 47.(6) |
| H(14f) | 95.9(18)   | 342.5(16) | 988.3(8) | 47.(5) |
| H(15b) | 164.4(18)  | 275.6(16) | 544.3(8) | 40.(5) |
| H(15c) | 248.(2)    | 204.3(17) | 503.1(8) | 48.(5) |
| H(15f) | -106.3(17) | 455.5(15) | 942.9(8) | 37.(5) |
| H(16c) | 216.0(17)  | 449.5(15) | 495.2(7) | 38.(5) |

Table 5. Interatomic distances (Å) with s.u.s in parentheses.

|               |            |               |            |
|---------------|------------|---------------|------------|
| O(1)-C(1)     | 1.2421(16) | O(3b)-C(12b)  | 1.2121(16) |
| O(2)-C(12)    | 1.3388(17) | O(2)-C(13)    | 1.4720(15) |
| O(2b)-C(12b)  | 1.3450(16) | O(2b)-C(13b)  | 1.4739(16) |
| O(1b)-C(1b)   | 1.2341(16) | O(3)-C(12)    | 1.2187(16) |
| N(2)-C(12)    | 1.3541(17) | N(2)-C(9)     | 1.4543(16) |
| N(2)-C(11)    | 1.4636(17) | N(2b)-C(9b)   | 1.4507(17) |
| N(2b)-C(12b)  | 1.3577(17) | N(2b)-C(11b)  | 1.4641(18) |
| N(1)-C(1)     | 1.3399(16) | N(1)-C(9)     | 1.4653(16) |
| N(1b)-C(9b)   | 1.4652(17) | N(1b)-C(1b)   | 1.3436(17) |
| C(1)-C(2)     | 1.4920(17) | C(7b)-C(2b)   | 1.3890(19) |
| C(7b)-C(8b)   | 1.5026(19) | C(7b)-C(6b)   | 1.3959(18) |
| C(9b)-C(8b)   | 1.5325(18) | C(2)-C(7)     | 1.3950(19) |
| C(2)-C(3)     | 1.3937(18) | C(2b)-C(1b)   | 1.4948(17) |
| C(2b)-C(3b)   | 1.3922(19) | C(7)-C(8)     | 1.4970(18) |
| C(7)-C(6)     | 1.3958(18) | C(8b)-C(10b)  | 1.5405(18) |
| C(9)-C(8)     | 1.5250(18) | C(8)-C(10)    | 1.5391(19) |
| C(5b)-C(6b)   | 1.384(2)   | C(5b)-C(4b)   | 1.384(2)   |
| C(11b)-C(10b) | 1.5218(19) | C(3b)-C(4b)   | 1.3887(19) |
| C(3)-C(4)     | 1.3866(19) | C(5)-C(6)     | 1.387(2)   |
| C(5)-C(4)     | 1.384(2)   | C(13b)-C(15b) | 1.518(2)   |
| C(13b)-C(14b) | 1.516(2)   | C(13b)-C(16b) | 1.516(2)   |

|             |          |             |            |
|-------------|----------|-------------|------------|
| C(13)-C(16) | 1.518(2) | C(13)-C(15) | 1.516(2)   |
| C(13)-C(14) | 1.520(2) | C(11)-C(10) | 1.5261(19) |

Table 6. Angles between interatomic vectors (°) with s.u.s in parentheses.

|                      |            |                      |            |
|----------------------|------------|----------------------|------------|
| C(12)-O(2)-C(13)     | 121.91(10) | C(12b)-O(2b)-C(13b)  | 120.94(10) |
| C(12)-N(2)-C(9)      | 124.61(11) | C(12)-N(2)-C(11)     | 121.25(11) |
| C(9)-N(2)-C(11)      | 113.50(10) | C(9b)-N(2b)-C(11b)   | 113.83(10) |
| C(12b)-N(2b)-C(9b)   | 124.84(11) | C(12b)-N(2b)-C(11b)  | 120.97(11) |
| C(1)-N(1)-C(9)       | 125.30(11) | C(1b)-N(1b)-C(9b)    | 126.27(11) |
| O(1)-C(1)-N(1)       | 121.93(11) | O(1)-C(1)-C(2)       | 121.25(11) |
| N(1)-C(1)-C(2)       | 116.79(11) | O(2)-C(12)-N(2)      | 110.28(11) |
| O(3)-C(12)-O(2)      | 126.72(12) | O(3)-C(12)-N(2)      | 123.00(13) |
| C(2b)-C(7b)-C(8b)    | 120.28(11) | C(2b)-C(7b)-C(6b)    | 118.88(12) |
| C(6b)-C(7b)-C(8b)    | 120.81(12) | N(2b)-C(9b)-N(1b)    | 110.29(10) |
| N(2b)-C(9b)-C(8b)    | 102.93(10) | N(1b)-C(9b)-C(8b)    | 112.60(10) |
| O(3b)-C(12b)-O(2b)   | 126.79(12) | O(3b)-C(12b)-N(2b)   | 123.47(13) |
| O(2b)-C(12b)-N(2b)   | 109.73(11) | C(7)-C(2)-C(1)       | 120.52(11) |
| C(3)-C(2)-C(1)       | 119.35(12) | C(3)-C(2)-C(7)       | 120.06(12) |
| C(7b)-C(2b)-C(1b)    | 120.85(12) | C(7b)-C(2b)-C(3b)    | 120.90(12) |
| C(3b)-C(2b)-C(1b)    | 118.24(12) | C(2)-C(7)-C(8)       | 120.30(11) |
| C(2)-C(7)-C(6)       | 119.23(12) | C(6)-C(7)-C(8)       | 120.42(12) |
| C(7b)-C(8b)-C(9b)    | 113.79(11) | C(7b)-C(8b)-C(10b)   | 113.44(11) |
| C(9b)-C(8b)-C(10b)   | 103.51(10) | O(1b)-C(1b)-N(1b)    | 122.12(12) |
| O(1b)-C(1b)-C(2b)    | 121.16(12) | N(1b)-C(1b)-C(2b)    | 116.72(12) |
| N(2)-C(9)-N(1)       | 109.76(10) | N(2)-C(9)-C(8)       | 102.57(11) |
| N(1)-C(9)-C(8)       | 111.31(10) | C(7)-C(8)-C(9)       | 113.66(11) |
| C(7)-C(8)-C(10)      | 113.68(11) | C(9)-C(8)-C(10)      | 103.20(10) |
| C(4b)-C(5b)-C(6b)    | 120.45(12) | N(2b)-C(11b)-C(10b)  | 103.40(11) |
| C(4b)-C(3b)-C(2b)    | 119.55(14) | C(5b)-C(6b)-C(7b)    | 120.29(13) |
| C(4)-C(3)-C(2)       | 120.37(14) | C(4)-C(5)-C(6)       | 120.63(13) |
| O(2b)-C(13b)-C(15b)  | 109.85(11) | O(2b)-C(13b)-C(14b)  | 109.71(12) |
| O(2b)-C(13b)-C(16b)  | 101.40(11) | C(14b)-C(13b)-C(15b) | 112.77(13) |
| C(16b)-C(13b)-C(15b) | 110.94(13) | C(16b)-C(13b)-C(14b) | 111.59(13) |
| C(11b)-C(10b)-C(8b)  | 104.32(11) | C(5)-C(6)-C(7)       | 120.16(14) |
| C(5b)-C(4b)-C(3b)    | 119.90(13) | O(2)-C(13)-C(16)     | 101.36(11) |
| O(2)-C(13)-C(15)     | 111.63(12) | O(2)-C(13)-C(14)     | 108.55(11) |
| C(16)-C(13)-C(14)    | 111.52(13) | C(15)-C(13)-C(16)    | 110.07(13) |
| C(15)-C(13)-C(14)    | 113.12(13) | N(2)-C(11)-C(10)     | 103.18(11) |
| C(5)-C(4)-C(3)       | 119.55(13) | C(11)-C(10)-C(8)     | 103.69(11) |