

# The Discovery of Quinoxaline-Based Metathesis Catalysts from Synthesis of Grazoprevir (MK-5172)

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## General Information

All reactions were carried out under a nitrogen atmosphere unless otherwise stated. All solvents and reagents were purchased from commercial sources and were used without further purification. <sup>1</sup>H and <sup>13</sup>C NMR chemical shifts were reported relative to residual proton solvent peaks, and were obtained on 400 or 500 MHz spectrometer as noted. High resolution mass spectra (HRMS) were obtained on Accurate-Mass Time-of-Flight (TOF) mass spectrometer and

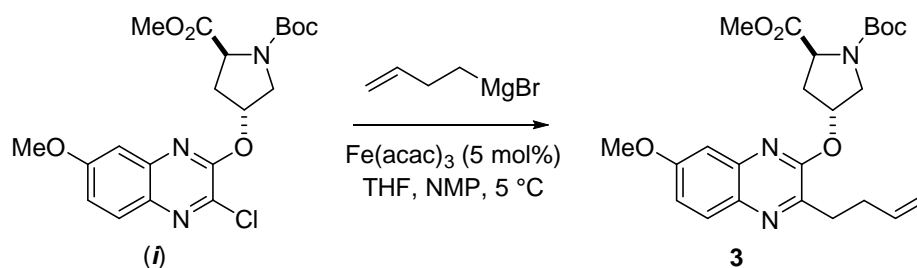
reported as m/z (relative intensity). Accurate masses are reported for the molecular ion as noted. For high through-put experimentation, all reagents were done in a glovebox to a 96 well aluminum-based vial rack designed to hold 96- 8x30 mm vials (Analytical Sales and Services, Inc. P# 84001) containing parylene coated stir dowels (1.98 x 4.80 mm) (V&P Scientific, P# 711D-1) and stirred on a tumble stirrer. Reagents were dosed to 96 well vials as solutions via an Eppendorf® Repeater® Xstream electronic pipettor s in a nitrogen filled glovebox. After sealing the vials using the aluminum vial rack cover equipped with silicone and PFA mats, the reactor was placed stirred via tumble stirring. The temperature of the reaction mixture was monitored using a thermocouple fixing inside of the aluminum vial rack, and the 25-30 °C reaction temperature was controlled by the ambient temperature of the glovebox and tumble stirrer unit.

## Known compounds

The following compounds referred to in this communication have previously been reported in the literature: 13,<sup>1</sup> 14,<sup>2</sup> 15,<sup>3</sup> 16<sup>3</sup>, 17,<sup>1</sup> 18,<sup>4</sup> 19,<sup>9</sup> 20,<sup>4</sup> 21.<sup>4</sup>

## Quinoxaline Preparation

1-(tert-butyl) 2-methyl (2S,4R)-4-((3-(but-3-en-1-yl)-7-methoxyquinoxalin-2-yl)oxy)pyrrolidine-1,2-dicarboxylate (**3**)



To 500 mL 3-neck round bottom flask was charged 1-(tert-butyl) 2-methyl (2S,4R)-4-((3-chloro-7-methoxyquinoxalin-2-yl)oxy)pyrrolidine-1,2-dicarboxylate (**i**)<sup>5</sup> (20.0 g, 44.8 mmol, 1.0 equiv.), ferric acetylacetonate (0.790 g, 2.238 mmol, 0.05 equiv.), NMP (100 ml, 5X, KF = 333 ppm), and then THF (100 ml, 5X, KF = 56 ppm) under N<sub>2</sub>. The reaction mixture was cooled between 0 and 10 °C, and then 3-butenylmagnesium bromide (94 ml, 47.0 mmol, 1.05 equiv.) was charged dropwise to the reaction mixture keeping the internal temperature between 0 and 10 °C [Note: color went from red to brown to black upon addition]. The mixture was allowed to stir, and deemed complete (30 minutes) by HPLC analysis. The reaction was then quenched with 1 M HCl (100 ml, 5X) and MTBE (100 ml, 5X) keeping the internal temp below 25 °C,

<sup>1</sup> Matsugi, M.; Kobayashi, Y.; Suzumura, N.; Tsuchiya, Y.; Shioiri, T. *J. Org. Chem.* **2010**, 75, 7906.

<sup>2</sup> Yao, Q.; Zhang, Y. *J. Am. Chem. Soc.* **2004**, 126, 74.

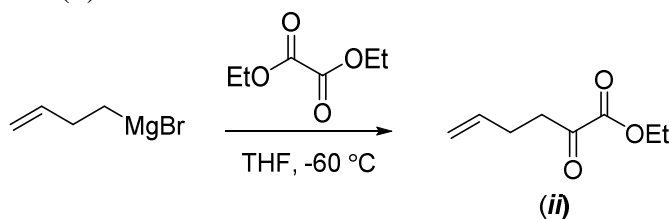
<sup>3</sup> Michalek F.; Mädege D.; Rühle, J.; Bannwarth, W. *J. Organomet. Chem.* **2006**, 691, 5172.

<sup>4</sup> Commercially available.

<sup>5</sup> Please see the following reference for the synthesis of compound **i**: Kuethe, J.; Zhong, Y.-L.; Yasuda, N.; Beutner, G.; Linn, K.; Kim, M.; Marcune, B.; Dreher, S. D.; Humphrey, G.; Pei, T. *Org. Lett.* **2013**, 15, 4174.

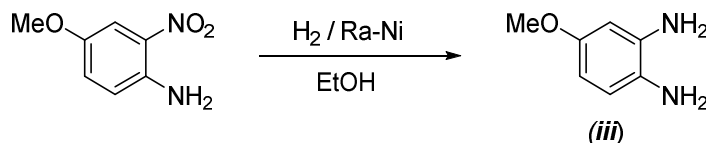
where it was transferred to a separatory funnel, and the layers were separated. The resulting organic layer (dark black-red colored) was extracted with water (100 ml, 5X) and then 10 wt% brine (100 ml, 5X). The organic layer was assayed by HPLC and found to yield the desired product (**3**) (18.0 g, 39.2 mmol, 88% yield). The resulting organic layer was concentrated to yield an orange opaque oil which was suitable for further manipulations or could be further purified via silica gel chromatography (340g Biotage SNAP Si gel column; loaded with 1:1 MTBE:hex; 15% to 50% EtOAc in hexanes over 8 col vol. and then held; detect at 254 & 290 nm). <sup>1</sup>H NMR (500 MHz, CD<sub>2</sub>Cl<sub>2</sub>) δ 7.80 (dd, *J* = 8.7, 3.8 Hz, 1H), 7.21 – 7.13 (m, 2H), 5.93 (ddt, *J* = 16.9, 10.1, 6.7 Hz, 1H), 5.80 – 5.69 (m, 1H), 5.06 (dq, *J* = 17.1, 1.7 Hz, 1H), 4.97 (ddt, *J* = 10.2, 2.2, 1.2 Hz, 1H), 4.49 (dt, *J* = 19.2, 7.9 Hz, 1H), 3.93 (s, 3H), 3.91 – 3.85 (m, 1H), 3.86 – 3.67 (m, 4H), 3.03 – 2.92 (m, 2H), 2.69 – 2.56 (m, 1H), 2.56 – 2.48 (m, 2H), 2.38 (ddd, *J* = 13.4, 8.0, 5.1 Hz, 1H), 1.42 (d, *J* = 13.5 Hz, 9H). <sup>13</sup>C-NMR (125 MHz, CD<sub>2</sub>Cl<sub>2</sub>): δ 173.3, 173.0, 160.3, 155.3, 153.5, 147.3, 141.0, 137.9, 134.3, 129.1, 118.3, 114.8, 105.9, 80.1, 74.2, 73.6, 58.2, 57.9, 55.7, 52.4, 52.14, 52.10, 52.0, 36.6, 35.7, 32.5, 31.5, 31.4, 28.1, 27.9. ESI-HRMS (*m/z*): Calc'd for C<sub>24</sub>H<sub>32</sub>N<sub>3</sub>O<sub>6</sub> (M+H): 458.2286; Found: 458.2303.

#### Ethyl 2-oxohex-5-enoate (*ii*)



To a solution of diethyl oxalate (100 g, 684 mmol) in THF (500 ml) at -65 °C was added 3-butenylmagnesium bromide (0.5 M in THF, 1382 ml, 691 mmol) slowly to keep reaction temperature below -60 °C. The reaction was stirred at -60 °C for 1 h to reach completion monitored by <sup>1</sup>H NMR. The reaction was diluted with MTBE (1500 ml), quenched with 10 wt% citric acid (1100 ml) at -60 °C, maintaining temperature below -20 °C. The reaction was warmed to RT. The organic layer was separated, washed with 10 wt% citric acid (550 ml), followed by water wash (600 ml). The organic layer was washed with saturated NaHCO<sub>3</sub> (500 ml X 2), followed by brine (500 ml), dried over MgSO<sub>4</sub>, filtered, concentrated under vacuum to yield Ethyl 2-oxohex-5-enoate (*ii*) (111.5, 87% yield) as a pale yellow oil. The characterization data matched that of known reports.<sup>6</sup>

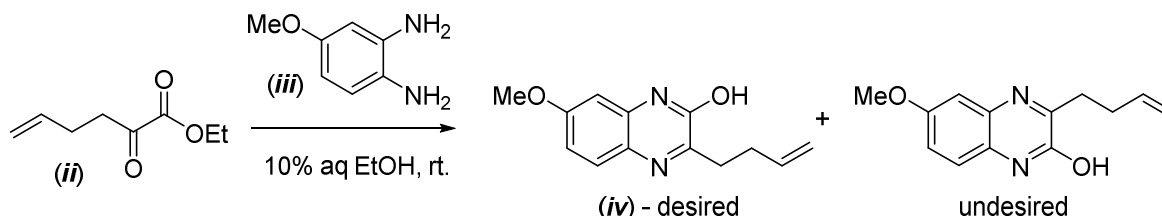
#### 4-Methoxybenzene-1,2-diamine (*iii*)



<sup>6</sup> Macritchie, J. A.; Silcock, A.; Willis, C. L. *Tetrahedron Asymmetry*, **1997**, 8, 3895-3902.

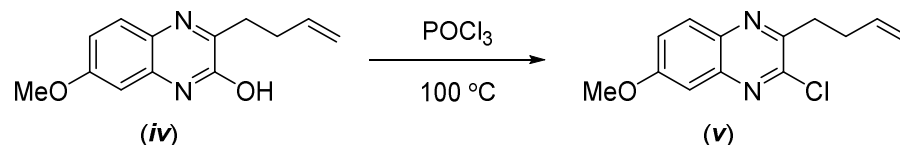
4-Methoxy-2-nitroaniline (27.0 g, 160 mmol) was dissolved in EtOH (300 ml). The reaction was flushed with N<sub>2</sub>, and Raney Ni pre-catalyst (14.0 g) was added. The reaction was hydrogenated under 45 psi H<sub>2</sub> for 10 h, (**NOTE:** The initial time period of this reaction is extremely exothermic. Care should be taken when conducting). The resulting mixture was filtered through a layer of CELITE®, rinsed with EtOH (60 ml), and the filtrate was concentrated to yield desired product (**iii**) as a dark brown solid (20 g), which was used in the next step without purification. Characterization data matched commercially available material.<sup>7</sup>

### 3-(But-3-en-1-yl)-7-methoxyquinoxalin-2-ol (**iv**)



To a solution of ethyl 2-oxohex-5-enoate (**ii**) (7.27 g, 38.6 mmol) in EtOH (65.0 ml, 13X) and water (7.50 ml, 1.5X) at 50 °C was added a solution of 4-methoxybenzene-1, 2-diamine (**iii**) (5 g, 35.1 mmol) in EtOH (10.00 ml, 2X) through syringe pump (30 min) whereupon a slurry formed. The reaction mixture was then stirred and heated at 50 °C for 3 h. The reaction reached completion, at which point the ratio of desired isomer to undesired isomer was 12 to 1 monitored by HPLC. The reaction mixture was cooled to RT. The precipitate was collected by filtration, rinsed with water (2 x 15 ml), dried under vacuum and N<sub>2</sub> sweep overnight to yield desired product (**iv**) (6.82 g, 85% isolated yield) as an off white solid. **<sup>1</sup>H NMR** (400 MHz, CDCl<sub>3</sub>) δ 11.75 (br s, 1H), 7.73 (d, *J* = 8.9 Hz, 1H), 6.93 (dd, *J* = 8.9, 2.7 Hz, 1H), 6.73 (d, *J* = 2.6 Hz, 1H), 5.98 (ddt, *J* = 16.8, 10.2, 6.6 Hz, 1H), 5.13 (dq, *J* = 17.1, 1.7 Hz, 1H), 5.01 (ddt, *J* = 10.2, 2.0, 1.2 Hz, 1H), 3.92 (s, 3H), 3.09 – 2.99 (m, 2H), 2.65 – 2.54 (m, 2H). **<sup>13</sup>C-NMR** (100MHz, CDCl<sub>3</sub>): δ 161.07, 157.38, 156.86, 138.01, 132.62, 130.24, 128.02, 115.36, 113.02, 98.23, 77.55, 77.43, 77.23, 76.91, 56.02, 32.71, 31.07. **ESI-HRMS** (m/z): Calc'd for C<sub>13</sub>H<sub>15</sub>N<sub>2</sub>O<sub>2</sub> (M+H): 231.1128; Found: 231.1131.

### 2-(But-3-en-1-yl)-3-chloro-6-methoxyquinoxaline (**v**)

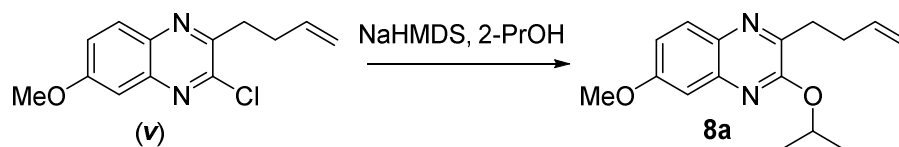


To 3-(but-3-en-1-yl)-7-methoxyquinoxalin-2-ol (**iv**) (4.63 g, 18.50 mmol) was charged POCl<sub>3</sub> (17.24 ml, 185 mmol, 10.0 equiv.) to form a thick slurry. The mixture was heated to 100 °C and

<sup>7</sup> CAS [102-51-2]; commercially available as HCl salt

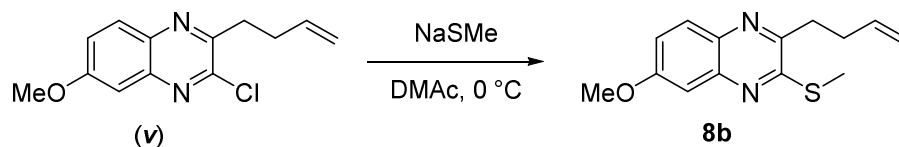
judged complete (1 h) after HPLC analysis. The mixture was cooled to RT, and concentrated on a rotary evaporator to remove most of the POCl<sub>3</sub>. The resulting residue was quenched into a mixture of saturated NaHCO<sub>3</sub> (200 mL), ice (200 mL), and EtOAc (300 mL) with good agitation. The layers were split, and the organic layer was washed with brine (100 mL), dried over MgSO<sub>4</sub>, filtered and concentrated to afford the desired product (**v**) (3.74 g, 75%) as an off-white solid. <sup>1</sup>H NMR (400 MHz, CD<sub>2</sub>Cl<sub>2</sub>) δ 7.90 (d, *J* = 9.2 Hz, 1H), 7.38 (dd, *J* = 9.2, 2.8 Hz, 1H), 7.27 (d, *J* = 2.8 Hz, 1H), 5.98 (ddt, *J* = 16.9, 10.2, 6.6 Hz, 1H), 5.12 (dq, *J* = 17.1, 1.7 Hz, 1H), 5.01 (ddt, *J* = 10.2, 1.9, 1.2 Hz, 1H), 3.95 (s, 3H), 3.25 – 3.07 (m, 2H), 2.62 (tdt, *J* = 7.8, 6.5, 1.4 Hz, 2H). <sup>13</sup>C NMR (100 MHz, CD<sub>2</sub>Cl<sub>2</sub>) δ 161.53, 152.48, 148.41, 143.13, 138.11, 137.60, 130.05, 123.39, 115.66, 106.52, 56.47, 35.25, 32.00. ESI-HRMS (*m/z*): Calc'd for C<sub>13</sub>H<sub>14</sub>ClN<sub>2</sub>O (*M*+*H*): 249.0789; Found: 249.0794.

#### 2-(But-3-en-1-yl)-3-isopropoxyquinoxaline (**8a**)



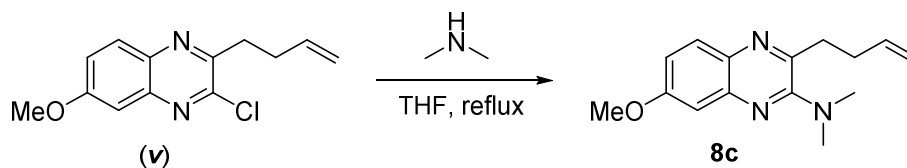
To a 250-mL round-bottom flask was charged 2-(but-3-en-1-yl)-3-chloro-6-methoxyquinoxaline (**v**) (3.50 g, 14.07 mmol), isopropanol (2.16 mL, 28.1 mmol), and dimethylacetamide (35 mL). The system was cooled in an ice/water bath and NaHMDS (8.80 mL, 17.6 mmol) was slowly charged to the reaction mixture via syringe. The mixture was allowed to stir at RT under N<sub>2</sub> and judged complete (72 h) by HPLC analysis. The system was quenched with water (100 mL), 1 M HCl (50 mL), and EtOAc (100 mL). The resulting biphasic system was split, and the aqueous layer extracted with EtOAc (100 mL). The organic layers were combined, washed with water (50 mL), washed with 10 wt% brine (50 mL), dried over MgSO<sub>4</sub>, filtered, and concentrated. The crude blackish oil was purified via silica gel chromatography (loaded with 1:1 DCM:hex; 220 g silica gel column (ISCO, Inc. Lincoln, NE, USA); eluted with 100% hexanes for 1 column volume; then 0 to 30% EtOAc in hexanes over 10 column volumes) to yield the desired product (**8a**) (3.03 g, 79% yield) as light yellow oil. <sup>1</sup>H NMR (500 MHz, CD<sub>2</sub>Cl<sub>2</sub>) δ 7.79 – 7.74 (m, 1H), 7.15 – 7.10 (m, 2H), 5.96 (ddt, *J* = 16.9, 10.2, 6.6 Hz, 1H), 5.51 (hept, *J* = 6.2 Hz, 1H), 5.07 (dq, *J* = 17.1, 1.7 Hz, 1H), 4.97 (ddt, *J* = 10.2, 2.2, 1.2 Hz, 1H), 3.92 (s, 3H), 3.01 – 2.93 (m, 2H), 2.55 (tdt, *J* = 7.8, 6.4, 1.4 Hz, 2H), 1.43 (d, *J* = 6.2 Hz, 6H). <sup>13</sup>C-NMR (125 MHz, CD<sub>2</sub>Cl<sub>2</sub>): δ 160.7, 156.6, 148.5, 142.0, 138.9, 134.4, 129.6, 118.0, 115.1, 106.4, 69.5, 56.2, 33.2, 31.9, 22.2. ESI-HRMS (*m/z*): Calc'd for C<sub>15</sub>H<sub>19</sub>N<sub>2</sub>O<sub>2</sub> (*M*+*H*): 259.1441; Found: 259.1460.

#### 2-(But-3-en-1-yl)-6-methoxy-3-(methylthio)quinoxaline (**8b**)



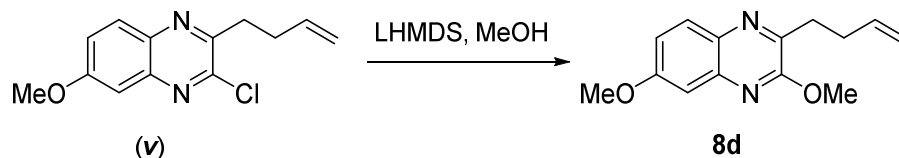
To a 200-mL round-bottom flask were charged 2-(but-3-en-1-yl)-3-chloro-6-methoxyquinoxaline (**v**) (3.00 g, 12.1 mmol, 1.0 equiv.) and N,N-dimethylacetamide (45.0 ml). The reaction mixture was cooled to 0 °C, and sodium thiomethoxide (1.860 g, 26.5 mmol, 2.2 equiv.) was charged as a solid. The reaction mixture was allowed to age at 0 °C and judged complete (45 min) by HPLC analysis. Water (150 mL) was then slowly charged to the reaction mixture, whereupon a white precipitate formed. The resulting slurry was warmed to RT and filtered. The resulting wet cake was washed with water (3 x 50 mL), and dried on the filter with N<sub>2</sub> and vacuum, yielding the desired product (**8b**) (3.01 g, 96% yield) as an off-white solid. **<sup>1</sup>H NMR** (400 MHz, CDCl<sub>3</sub>) δ 7.87 (dd, *J* = 8.7, 0.8 Hz, 1H), 7.27 – 7.22 (m, 2H), 5.99 (ddt, *J* = 16.9, 10.2, 6.6 Hz, 1H), 5.13 (dq, *J* = 17.1, 1.7 Hz, 1H), 5.03 (dq, *J* = 10.2, 1.3 Hz, 1H), 3.96 (s, 3H), 3.17 – 3.00 (m, 2H), 2.69 (s, 3H), 2.67 – 2.60 (m, 2H). **<sup>13</sup>C NMR** (100 MHz, CDCl<sub>3</sub>) δ 160.1, 156.0, 151.6, 142.7, 137.6, 134.9, 129.4, 120.0, 115.2, 105.8, 55.6, 33.9, 31.3, 12.8. **ESI-HRMS** (*m/z*): Calc'd for C<sub>14</sub>H<sub>17</sub>N<sub>2</sub>OS (M+H): 261.1056; Found: 261.1063.

3-(But-3-en-1-yl)-7-methoxy-N,N-dimethylquinoxalin-2-amine (**8c**)



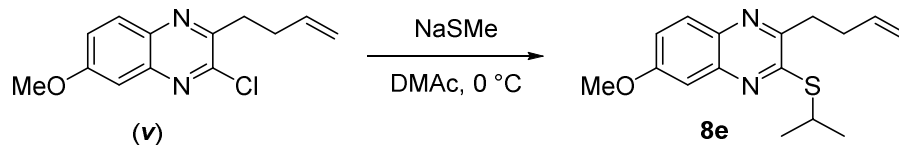
To a 250-mL round-bottom flask were charged 2-(but-3-en-1-yl)-3-chloro-6-methoxyquinoxaline (**v**) (3.00 g, 12.06 mmol), dimethylacetamide (22.5 ml), and dimethylamine (7.64 ml, 15.28 mmol, 1.27 equiv. as a 2.0 M solution in THF). The reaction mixture was heated to 55 °C, and judged incomplete (5 h) by HPLC analysis, and additional dimethylamine (20 ml, 40 mmol, 3.3 equiv.) was charged to the mixture. The reaction was then heated (10 h) at 55 °C and allowed to stir at room temperature over the weekend. The reaction mixture was judged complete (>90% conversion by HPLC analysis), and the reaction was quenched with water (200 mL) and EtOAc (75 mL). The layers were split, and the aqueous layer was extracted again with EtOAc (50 mL). The organic layers were combined, washed with water (100 mL), 10 wt% LiCl (75 mL), dried over MgSO<sub>4</sub>, filtered, and concentrated. The resulting crude product was purified via silica gel chromatography (0 to 50 % EtOAc in hexanes over 10 column volumes) to yield the desired product (**8c**) (2.76 g, 89% yield) as light yellow oil. **<sup>1</sup>H-NMR** (500 MHz, CDCl<sub>3</sub>) δ 7.78 (d, *J* = 9.0 Hz, 1H), 7.19 (d, *J* = 20.8 Hz, 1H), 7.13 (dd, *J* = 9.0, 2.8 Hz, 1H), 5.93 (ddt, *J* = 16.8, 10.2, 6.6, 1H), 5.09 (dq, *J* = 17.2, 1.7 Hz, 1H), 4.98 (dq, *J* = 10.2, 1.4 Hz, 1H), 3.93 (s, 3H), 3.12-2.90 (m, 8H), 2.66 – 2.61 (m, 2H). **<sup>13</sup>C-NMR** (125 MHz, CDCl<sub>3</sub>): δ 160.2, 156.7, 148.4, 138.0, 133.8, 128.8, 118.23, 115.0, 105.3, 55.6, 41.7, 34.4, 32.2. **ESI-HRMS** (*m/z*): Calc'd for C<sub>15</sub>H<sub>20</sub>N<sub>3</sub>O (M+H): 258.1601; Found: 258.1607.

2-(but-3-en-1-yl)-3,6-dimethoxyquinoxaline (**8d**)



To a 250-mL flask were charged 2-(but-3-en-1-yl)-3-chloro-6-methoxyquinoxaline (**v**) (3.00 g, 12.1 mmol), dimethylacetamide (45.0 ml), and then MeOH (2.79 ml, 69.0 mmol, 5.7 equiv.). The mixture was cooled in an ice/water bath below 5 °C, and LiHMDS (13.3 ml, 13.3 mmol, 1.1 equiv.) was charged keeping the internal temperature below 10 °C. The reaction mixture was stirred for 10 min and then allowed to warm to RT. When the reaction mixture was judged complete (23 h) by HPLC analysis, the system was quenched with water (100 mL), EtOAc (100 mL), and 1 M HCl (50 mL). The resulting organic layer was washed with water (2 x 50 mL), dried over MgSO<sub>4</sub>, filtered, and concentrated. The crude material was purified via silica gel chromatography (120 g silica gel column (ISCO, Inc. Lincoln, NE, USA), 0 to 50% EtOAc in hexanes over 10 column volumes) to yield the desired product (**8d**) (2.47 g, 84% yield) as light yellow oil, which crystallized to a white solid upon standing at -20 °C. <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 7.88 – 7.81 (m, 1H), 7.23 – 7.13 (m, 2H), 5.96 (ddt, *J* = 16.9, 10.2, 6.6 Hz, 1H), 5.09 (dq, *J* = 17.1, 1.7 Hz, 1H), 4.99 (ddt, *J* = 10.2, 2.0, 1.2 Hz, 1H), 4.10 (s, 3H), 3.94 (s, 3H), 3.10 – 2.98 (m, 2H), 2.56 (dt, *J* = 9.2, 6.3, 1.4 Hz, 2H). <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>) δ 160.2, 156.8, 147.3, 141.3, 137.9, 134.1, 129.2, 118.1, 115.0, 105.8, 55.6, 53.6, 32.5, 31.4. ESI-HRMS (*m/z*): Calc'd for C<sub>14</sub>H<sub>17</sub>N<sub>2</sub>O<sub>2</sub> (*M*+H): 245.1285; Found: 245.1296.

2-(but-3-en-1-yl)-3-(isopropylthio)-6-methoxyquinoxaline (**8e**)

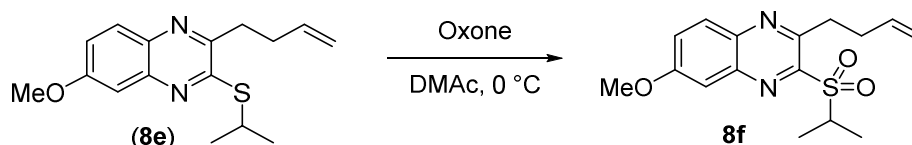


To a 100-mL round-bottom flask were charged 2-(but-3-en-1-yl)-3-chloro-6-methoxyquinoxaline (**v**) (3.99 g, 16.0 mmol, 1.0 equiv.) and dimethylformamide (61.0 ml). After aging the reaction mixture over 5 minutes at room temperature, sodium propane-2-thiolate (7.87g, 80 mmol, 5.0 equiv) was charged to the reaction mixture. The reaction mixture was aged at room temperature over 1 hour. Water (150 mL) was then slowly charged to the reaction mixture, whereupon a white precipitate formed. The resulting slurry was then filtered. The wet cake was washed with water (3 x 50 mL), and the cake was dried on the filter with N<sub>2</sub> and vacuum. The further purification by SiO<sub>2</sub> purification (0 – 50% EtOAc to hexane) yielded the desired product (**8e**) (4.10 g, 89% yield) as an off-white solid. <sup>1</sup>H NMR (400 MHz, CD<sub>2</sub>Cl<sub>2</sub>): δ



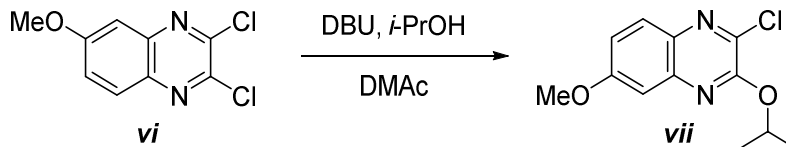
7.88 – 7.76 (m, 1H), 7.25 (d,  $J = 7.7$  Hz, 2H), 6.02 (ddt,  $J = 16.8, 10.2, 6.5$  Hz, 1H), 5.15 (dq,  $J = 17.2, 1.7$  Hz, 1H), 5.03 (ddt,  $J = 10.2, 2.2, 1.3$  Hz, 1H), 4.26 (hept,  $J = 6.8$  Hz, 1H), 3.98 (s, 3H), 3.12 – 2.87 (m, 2H), 2.73 – 2.53 (m, 2H), 1.52 (d,  $J = 6.9$  Hz, 6H).  **$^{13}\text{C-NMR}$**  (100 MHz,  $\text{CD}_2\text{Cl}_2$ ):  $\delta$  160.1, 156.2, 151.7, 142.7, 138.0, 134.9, 129.4, 119.8, 114.8, 105.9, 55.7, 34.9, 33.9, 31.1, 22.7. **ESI-HRMS** ( $m/z$ ): Calc'd for  $\text{C}_{16}\text{H}_{21}\text{N}_2\text{OS}^+$  ( $\text{M}+\text{H}$ ): 289.1369; Found: 289.1371.

2-(but-3-en-1-yl)-3-(isopropylsulfonyl)-6-methoxyquinoxaline (**8f**)



To a 250-mL round-bottom flask were charged 2-(but-3-en-1-yl)-3-(isopropylthio)-6-methoxyquinoxaline (**8e**) (2.76 g, 9.57 mmol) and MeOH (55.2 mL) was charged. Potassium peroxymonosulfate (11.77 g, 19.14 mmol, commercially known as Oxone®) was added to the reaction, and the resulting heterogeneous solution was aged overnight at room temperature. The reaction was deemed complete by HPLC analysis and then quenched with water (50 mL) and EtOAc (75 mL). The layers were split, and the aqueous layer was extracted again with EtOAc (50 mL). The organic layers were combined, washed with water (50 mL), brine (50 mL), dried over  $\text{MgSO}_4$ , filtered, and concentrated to yield yellow oil. The resulting crude product was purified via silica gel chromatography (0 to 50 % EtOAc in hexanes over 20 column volumes) to yield the desired product (**8f**) (2.10 g, 69% yield) as light yellow oil.  **$^1\text{H NMR}$**  (500 MHz,  $\text{CD}_2\text{Cl}_2$ ):  $\delta$  8.00 (d,  $J = 9.2$  Hz, 1H), 7.56 (dd,  $J = 9.2, 2.8$  Hz, 1H), 7.40 (d,  $J = 2.8$  Hz, 1H), 6.04 (ddt,  $J = 16.9, 10.2, 6.6$  Hz, 1H), 5.16 (dq,  $J = 17.1, 1.7$  Hz, 1H), 5.04 (ddt,  $J = 10.2, 2.0, 1.3$  Hz, 1H), 4.36 (hept,  $J = 6.9$  Hz, 1H), 4.02 (s, 3H), 3.56 – 3.49 (m, 2H), 2.75 – 2.68 (m, 2H), 1.49 (d,  $J = 6.9$  Hz, 6H).  **$^{13}\text{C-NMR}$**  (125 MHz,  $\text{CD}_2\text{Cl}_2$ ):  $\delta$  161.3, 151.3, 151.1, 140.4, 139.1, 137.8, 129.6, 126.0, 115.0, 106.3, 56.0, 51.3, 33.8, 32.6, 15.1. **ESI-HRMS** ( $m/z$ ): Calc'd for  $\text{C}_{16}\text{H}_{21}\text{N}_2\text{O}_3\text{S}^+$  ( $\text{M}+\text{H}$ ): 321.1267; Found: 321.1273.

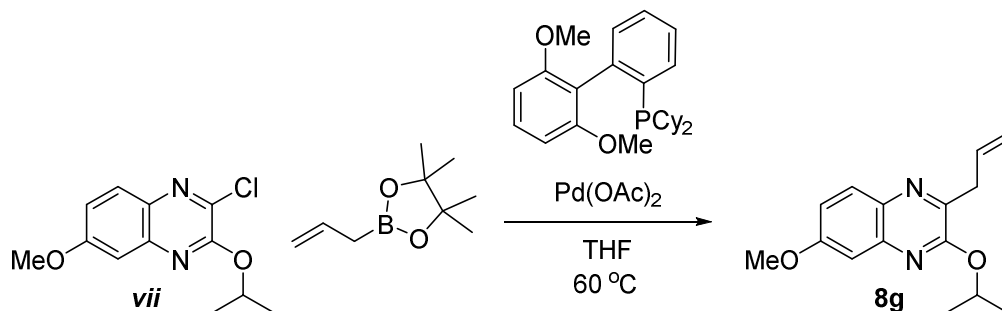
2-Chloro-3-isopropoxy-6-methoxyquinoxaline (**vii**)



To a 100-mL round-bottom flask were charged 2,3-dichloro-6-methoxyquinoxaline (**vi**) (9.00 g, 39.3 mmol), 2-propanol (3.31 mL, 43.2 mmol), N,N-dimethylacetamide (45 mL) and DBU (7.62 mL, 51.1 mmol), and then system was warmed to 40 °C. The reaction was aged at 40 °C for 48 h, and then quenched with water (10 mL), 1M HCl (30 mL), and EtOAc (50 mL). The layers were separated, and the aqueous layer was washed again with EtOAc (50 mL). The organic layers were combined, washed with water (50 mL), 10 wt% brine (50 mL), dried over

MgSO<sub>4</sub>, filtered and concentrated. The resulting material was purified via silica gel chromatography (loaded with toluene) and eluted with EtOAc and Hex (EtOAc:Hexane = 1:5) to yield the desired product (**vii**) (3.5 g, 35% yield). <sup>1</sup>H NMR (400 MHz, CD<sub>2</sub>Cl<sub>2</sub>): δ 7.79 (d, *J* = 8.9 Hz, 1H), 7.28 – 7.16 (m, 2H), 5.54 (hept, *J* = 6.2 Hz, 1H), 3.97 (s, 3H), 1.49 (d, *J* = 6.2 Hz, 6H). <sup>13</sup>C-NMR (100 MHz, CD<sub>2</sub>Cl<sub>2</sub>): δ 161.1, 153.1, 141.4, 136.6, 133.4, 128.7, 118.8, 105.7, 71.0, 55.8, 21.5. ESI-HRMS (m/z): Calc'd for C<sub>12</sub>H<sub>14</sub>ClN<sub>2</sub>O<sub>2</sub>+ (M+H): 253.0738; Found: 253.0738.

#### 2-Allyl-3-isopropoxy-6-methoxyquinoxaline (**8g**)

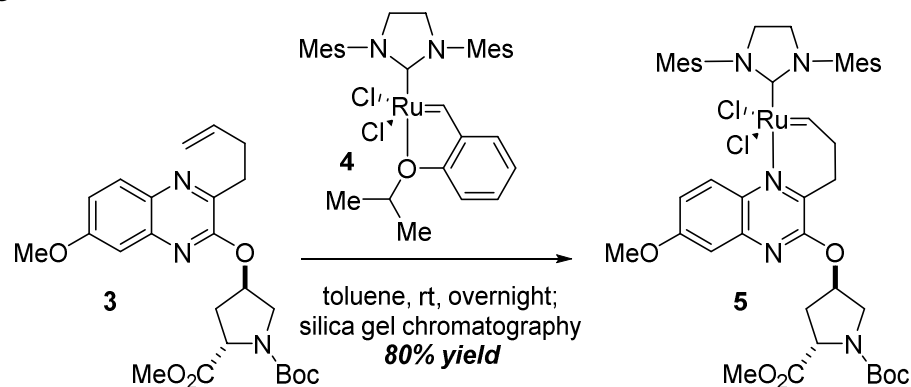


To a round-bottom flask was charged potassium phosphate tribasic (8.82 g, 41.6 mmol), 2-dicyclohexylphosphino-2',6'-dimethoxybiphenyl (0.569 g, 1.385 mmol), 2-chloro-3-isopropoxy-6-methoxy quinoxaline (**vii**) (3.5g, 13.9 mmol) and palladium (II) acetate (0.155 g, 0.693 mmol). After the mixture was degassed, THF (35 mL) was charged followed by the slow addition of allylboronic acid pinacol ester (5.20 mL, 27.7 mmol). Again, the system was again degassed, and then heated to 60 °C and aged overnight. After aging, the reaction was filtered to remove black insoluble particles, and the solids were subsequently washed with MTBE several times. The organic solution was transferred to a separatory funnel where water (50 mL) and EtOAc (50 mL) were then charged. The layers were split, and the aqueous layer was extracted with EtOAc (50 mL). The organic layers were combined, washed with water (50 mL), 10 wt% brined (50 mL), dried over MgSO<sub>4</sub>, filtered and concentrated. The crude material was further purified via silica gel chromatography (loaded with toluene) and eluted with EtOAc:Hex (1:20) to yield the desired product (**8g**) (2.5 g, 70%) as light yellow oil. <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 7.83 (d, *J* = 8.7 Hz, 1H), 7.20 – 7.07 (m, 2H), 6.14 (ddt, *J* = 16.9, 10.1, 6.8 Hz, 1H), 5.52 (hept, *J* = 6.2 Hz, 1H), 5.22 (dq, *J* = 17.1, 1.6 Hz, 1H), 5.14 (dq, *J* = 10.1, 1.5 Hz, 1H), 3.93 (s, 3H), 3.69 (dt, *J* = 6.8, 1.4 Hz, 2H), 1.44 (d, *J* = 6.2 Hz, 6H). <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>): δ 160.32, 155.97, 146.39, 141.69, 134.06, 133.94, 129.33, 117.91, 117.11, 105.93, 69.05, 55.68, 38.21, 22.05. ESI-HRMS (m/z): Calc'd for C<sub>15</sub>H<sub>19</sub>N<sub>2</sub>O<sub>2</sub>+ (M+H): 259.1441; Found: 259.1460.

## Complex Preparation

Note: where specifically stated, precatalysts **4**, **6a** and **6b** can be utilized to obtain similar results.

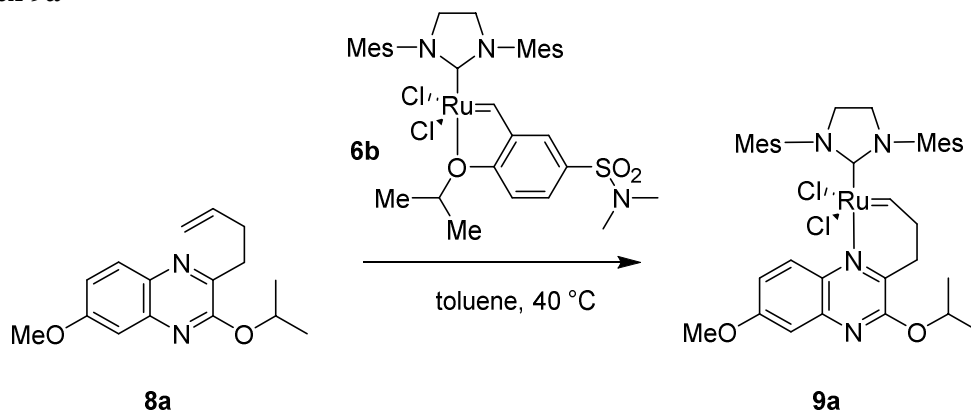
### Complex 5



To a 3-neck flask was charged (2*S*,4*R*)-1-*tert*-butyl 2-methyl 4-((3-(but-3-en-1-yl)-7-methoxyquinoxalin-2-yl)oxy)pyrrolidine-1,2-dicarboxylate (**3**) (1.00 g, 2.12 mmol, 1.18 equiv.) dichloromethane (12.00 ml), and then Hoveyda-Grubbs 2<sup>nd</sup> generation precatalyst (**4**) (1.129 g, 1.802 mmol, 1.00 equiv.) was then charged to the mixture as a solid under a stream of N<sub>2</sub>. <sup>1</sup>H NMR analysis of the crude reaction mixture (16h) indicated a ratio of 10:1 (Complex **5** : **4**). The reaction was then directly loaded to a 120 g silica gel column and eluted with hexanes/EtOAc from 5% to 50% EtOAc in hexanes over 10 column volumes to yield complex **5** (1.34 g, 1.45 mmol, 80% yield) as a red-brown solid. <sup>1</sup>H NMR (400 MHz, CD<sub>2</sub>Cl<sub>2</sub>) δ 18.41 (t, *J* = 4.6 Hz, 1H), 7.28 – 6.94 (m, 6H), 6.74 (dd, *J* = 9.2, 2.8 Hz, 1H), 5.62 (dtt, *J* = 22.6, 5.1, 2.5 Hz, 1H), 4.43 (dt, *J* = 27.5, 7.8 Hz, 1H), 4.19 – 3.97 (m, 4H), 3.95 – 3.62 (m, 8H), 3.28 – 3.18 (m, 2H), 2.83 (ddd, *J* = 11.7, 5.8, 3.3 Hz, 2H), 2.76 – 2.24 (m, 21H), 1.42 (d, *J* = 7.7 Hz, 9H). <sup>13</sup>C NMR (100 MHz, CD<sub>2</sub>Cl<sub>2</sub>)<sup>8</sup>: δ 216.04, 215.95, 173.73, 173.45, 160.80, 155.24, 154.69, 153.97, 149.14, 149.04, 141.58, 140.82 (br), 139.39 (br), 139.00 (br), (138.17 (tol-*d*<sub>8</sub>)), 137.91 (br), 137.71 (br), 135.65 (br), 134.45, 130.18, 130.04, (129.34, 129.11, 128.87, 128.45, 128.21, 127.97 – tol-*d*<sub>8</sub>), 126.72, (125.55, 125.31, 125.06 – tol-*d*<sub>8</sub>) 118.81, 118.75, 107.02, 80.69, 80.63, 75.61, 74.98, 58.62, 58.40, 56.26, 52.86, 52.62, 52.56, 52.53, 52.44, 52.26 (br), 51.44 (br), 37.01, 36.15, 28.63, 28.53, 26.05, 21.73 (br), 21.49 (br), (21.17, 20.99, 20.80, 20.43, 20.23 – tol-*d*<sub>8</sub>), 20.58 (br), 18.59 (br). ESI-HRMS (*m/z*): Calc'd for C<sub>44</sub>H<sub>56</sub>Cl<sub>2</sub>N<sub>5</sub>O<sub>6</sub>Ru (*M*+*H*): 922.2651; Found: 922.2537.

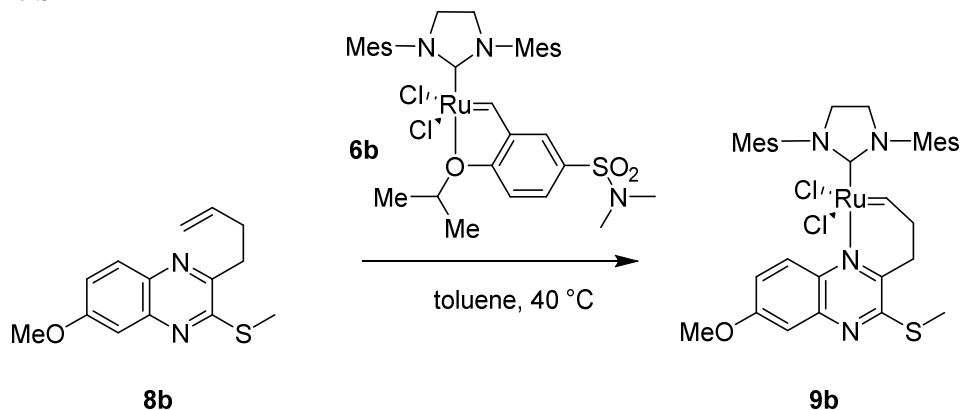
<sup>8</sup> Note: for characterization, the complex was solvent switched with toluene-*d*<sub>8</sub> to remove troublesome residual hexane and ethyl acetate. Subsequently, the toluene-*d*<sub>8</sub> was difficult to remove post solvent switch and can be observed in the <sup>13</sup>C NMR. The solvent peaks in the <sup>13</sup>C NMR are specifically noted in the spectral peak list.

### Complex 9a



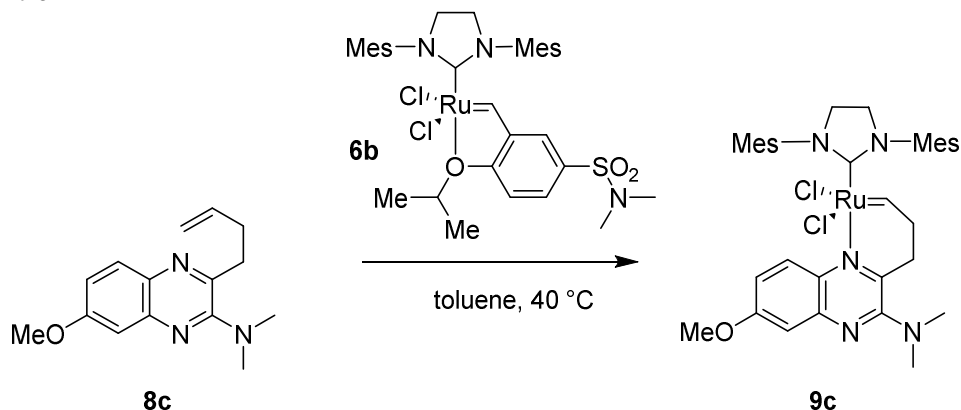
To a round-bottom flask was charged 2-(but-3-en-1-yl)-3-isopropoxy-6-methoxyquinoxaline (**8a**) (0.98 g, 3.60 mmol, 2.64 equiv.). The system was purged with N<sub>2</sub>, and degassed toluene (3.00 ml) was charged to the system under inert handling. Pre-catalyst **6b** (1.00 g, 1.363 mmol, commercially available as Zhan 1B) was charged to the system under a stream of N<sub>2</sub>, and the system was sealed. The walls of the flask were then washed with degassed toluene (2 mL). The system was heated and aged at 40 °C, where it was judged complete by <sup>1</sup>H NMR and TLC analysis (30 min). The mixture was treated with hexanes (10.00 ml) dropwise at 40 °C was then allowed to cool to room temperature and aged (1 h). The red slurry was filtered through a sintered funnel, and the solid was slurry washed with 3:1 hexanes:toluene (20 mL; 2 x 10 mL portions), and then hexanes (40 mL; 4 x 10 mL portions) to yield the desired product (**9a**) (985 mg, 98% yield) as a light red solid after drying in a vacuum oven at RT. <sup>1</sup>H-NMR (500MHz, CD<sub>2</sub>Cl<sub>2</sub>) δ 18.40 (t, *J* = 4.7 Hz, 1H), 7.28 – 7.11 (m, 2H), 7.11 – 6.96 (m, 4H), 6.67 (dd, *J* = 9.1, 2.9 Hz, 1H), 5.39 (hept, *J* = 6.2 Hz, 1H), 4.08 (d, *J* = 26.2 Hz, 4H), 3.88 (s, 3H), 3.32 – 3.11 (m, 2H), 2.96 – 2.78 (m, 2H), 2.73 – 2.29 (m, 18H), 1.40 – 1.33 (d, *J* = 6.2 Hz, 6H). <sup>13</sup>C-NMR (125MHz, CD<sub>2</sub>Cl<sub>2</sub>): δ 216.4, 160.6, 155.9, 149.7, 142.0, 140.8 (br), 139.4 (br), 139.0 (br), 137.9 (br), 137.7 (br), 135.7 (br), 133.8, 130.5 (br), 130.2 (br), 130.0, 129.5, 128.7, 126.5, 125.8, 117.9, 106.9, 70.4, 56.2, 54.5, 54.3, 52.5, 52.2 (br), 51.4 (br), 26.1, 22.1, 21.7 (br), 21.4 (br), 20.5 (br), 18.6 (br). ESI-HRMS (*m/z*): Calc'd for C<sub>36</sub>H<sub>45</sub>Cl<sub>2</sub>N<sub>4</sub>O<sub>2</sub>Ru (*M*+*H*): 737.1963; Found: 737.1932.

### Complex 9b



To a round-bottom flask was charged 2-(but-3-en-1-yl)-6-methoxy-3-(methylthio)quinoxaline (**8b**) (0.797 g, 3.06 mmol, 2.25 equiv.), and purged with N<sub>2</sub>. After toluene (3.00 ml) and pre-catalyst **6b** (1.00 g, 1.361 mmol, commercially available as Zhan 1B) were charged under a stream of N<sub>2</sub>, the system was sealed, and the walls were washed with additional toluene (2 mL). The resulting mixture was aged (3 h) at 40 °C, deemed complete by <sup>1</sup>H NMR, and hexanes (10.00 ml) were charged at 40 °C. The resulting slurry was then allowed to cool to RT, filtered through a sintered funnel, washed in 2 portions with 25% toluene in hexane (20.00 ml; 2 x 10 mL), and then washed with 4 portions of hexanes (40.0 ml; 4 x 10 mL). The resulting wet cake was dried in a vacuum oven to yield the desired product (981 mg, 97% yield) as a deep red solid. <sup>1</sup>H NMR (400 MHz, CD<sub>2</sub>Cl<sub>2</sub>) δ 18.31 (t, *J* = 4.6 Hz, 1H), 7.32 – 6.93 (m, 6H), 6.76 (ddd, *J* = 9.3, 3.0, 1.2 Hz, 1H), 4.08 (br d, *J* = 16.0 Hz, 4H), 3.90 (d, *J* = 1.2 Hz, 3H), 3.26–3.20 (m, 2H), 2.78 (ddt, *J* = 8.2, 4.8, 2.3 Hz, 2H), 2.75 – 2.19 (m, 21H). <sup>13</sup>C NMR (100 MHz, CD<sub>2</sub>Cl<sub>2</sub>) δ 215.7, 160.6, 157.2, 153.3, 143.5, 140.8 (br), 139.4 (br), 139.0 (br), 137.9 (br), 137.7 (br), 135.8 (br), 135.0, 130.5, 130.1, 130.0, 126.9, 120.2, 106.9, 56.3, 54.4, 52.6, 52.3, 51.5, 28.4, 21.7 (br), 21.5 (br), 20.5 (br), 18.6 (br), 13.9. ESI-HRMS (*m/z*): Calc'd for C<sub>14</sub>H<sub>17</sub>N<sub>2</sub>OS (M+H): 725.1422; Found: 725.1411.

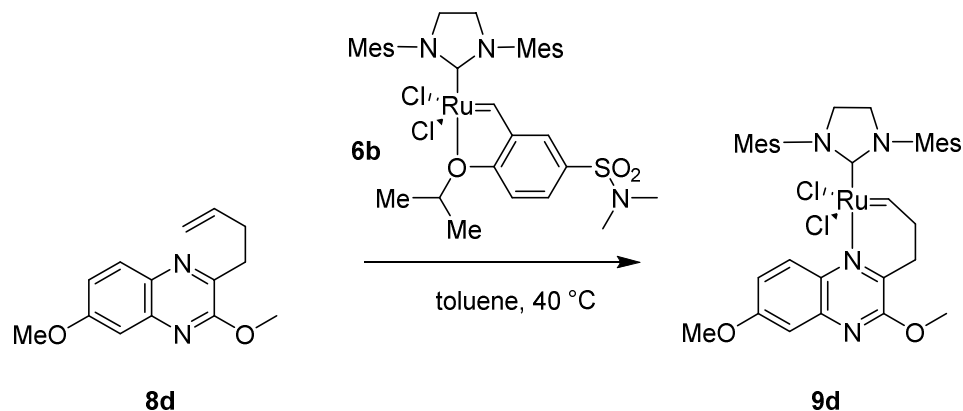
### Complex 9c



To a round-bottom flask was charged 3-(but-3-en-1-yl)-7-methoxy-N,N-dimethylquinoxalin-2-amine (**8c**) (0.788 g, 3.06 mmol, 2.25 equiv.), and the system was purged with N<sub>2</sub>. Toluene (3.00 ml) was charged to the system under inert handling; pre-catalyst **6b** (1.00 g, 1.361 mmol, commercially available as Zhan 1B) was charged under a stream of N<sub>2</sub>; the system was sealed; and toluene (2 mL) was utilized to wash down the walls of the flask. The system was aged at 40 °C until judged complete by <sup>1</sup>H NMR. Addition hexanes (10.00 ml) were changed at 40 °C. The resulting mixture was allowed to age for approximately 1 h at RT, then filtered through a sintered funnel, washed in two portions with 25% toluene in hexanes (20.00 ml; 2 x 10 mL), and in four portions with hexanes (40.0 ml; 4 x 10 mL). The resulting wet cake was dried on the filter with vacuum and N<sub>2</sub> purge to yield the desired product (**9c**) (962 mg, 98% yield) as a red solid. <sup>1</sup>H-NMR (500MHz, CD<sub>2</sub>Cl<sub>2</sub>) δ 18.28 (t, *J* = 4.0 Hz, 1H), 7.29 – 6.96 (m, 5H), 6.91 (d, *J* = 9.1 Hz, 1H), 6.63 (dd, *J* = 9.1, 2.9 Hz, 1H), 4.08 (d, *J* = 21.8 Hz, 4H), 3.87 (s, 3H), 3.51 – 3.28 (m, 2H), 2.88 (s, 6H), 2.77 – 2.26 (m, 18H). <sup>13</sup>C-NMR (125 MHz, CD<sub>2</sub>Cl<sub>2</sub>): δ 215.6, 160.5,

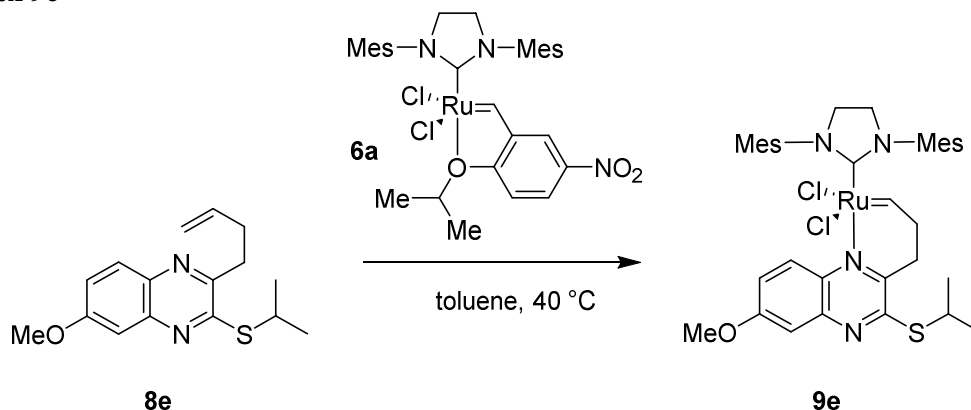
157.6, 151.2, 142.4, 140.8 (br), 139.3 (br), 138.9 (br), 138.0 (br), 137.8 (br), 135.8, 135.7 (br), 134.3, 130.5 (br), 130.1 (br), 129.9, 129.5, 128.7, 126.5, 125.8, 125.4, 117.9, 106.5, 56.2, 54.5, 54.3, 54.1, 52.3 (br), 51.4 (br), 41.3, 21.7 (br), 21.4 (br), 20.6 (br), 19.4 (br), 18.6 (br). **ESI-HRMS** (m/z): Calc'd for C<sub>35</sub>H<sub>44</sub>Cl<sub>2</sub>N<sub>5</sub>ORu (M+H): 722.1966; Found: 722.1967.

### Complex 9d



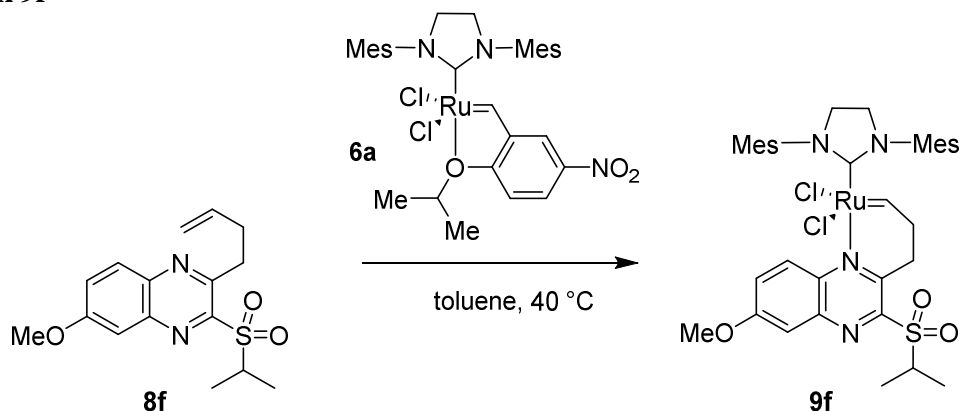
To a round-bottom flask was charged 2-(but-3-en-1-yl)-3,6-dimethoxyquinoxaline (**8d**) (0.916 g, 3.75 mmol, 2.25 equiv.), and then the system was purged with N<sub>2</sub>. Toluene (3.00 ml) was charged to the system under inert handling, pre-catalyst **6b** (1.00 g, 1.363 mmol, commercially available as Zhan 1B) was then charged under a stream of N<sub>2</sub>, and the system was sealed. Toluene (2.0 mL) was utilized to wash the sides of the flask. The system was aged at 40 °C (45 min) until judged complete by <sup>1</sup>H NMR. Hexanes (15.00 ml) were added dropwise at 40 °C, and then the mixture was allowed to cool to RT and to age for 1 h. To the resulting slurry was further added 25% toluene in hexane (20.00 ml). The slurry was filtered through a sintered funnel, and the solid was slurry washed with hexanes (40.0 ml; 4 x 10 mL) to yield the desired product (**9d**) (984 mg, 99% yield) as an orange solid. **<sup>1</sup>H NMR** (400 MHz, CD<sub>2</sub>Cl<sub>2</sub>) δ 18.40 (t, *J* = 4.6 Hz, 1H), 7.36 – 6.91 (m, 6H), 6.70 (dd, *J* = 9.2, 2.9 Hz, 1H), 4.32 – 4.03 (m, 4H), 4.00 (s, 3H), 3.88 (s, 3H), 3.23 (t, *J* = 6.3 Hz, 2H), 2.83 (dt, *J* = 7.1, 5.0 Hz, 2H), 2.76 – 2.23 (m, 18H). **<sup>13</sup>C NMR** (400 MHz, CD<sub>2</sub>Cl<sub>2</sub>) δ 216.2, 160.7, 156.7, 149.3, 141.9, 140.8 (br), 139.4 (br), 139.0 (br), 137.9 (br), 137.7 (br), 135.7 (br), 134.2, 130.1 (br), 130.0 (br), 129.5, 128.7, 126.7, 125.8, 118.3, 107.0, 56.2, 52.5, 52.2 (br), 51.4 (br), 27.3, 26.1, 21.7 (br), 21.5 (br), 20.5 (br), 18.6 (br). **ESI-HRMS** (m/z): Calc'd for C<sub>34</sub>H<sub>41</sub>Cl<sub>2</sub>N<sub>4</sub>O<sub>2</sub>Ru (M+H): 709.1650; Found: 709.1544.

### Complex 9e



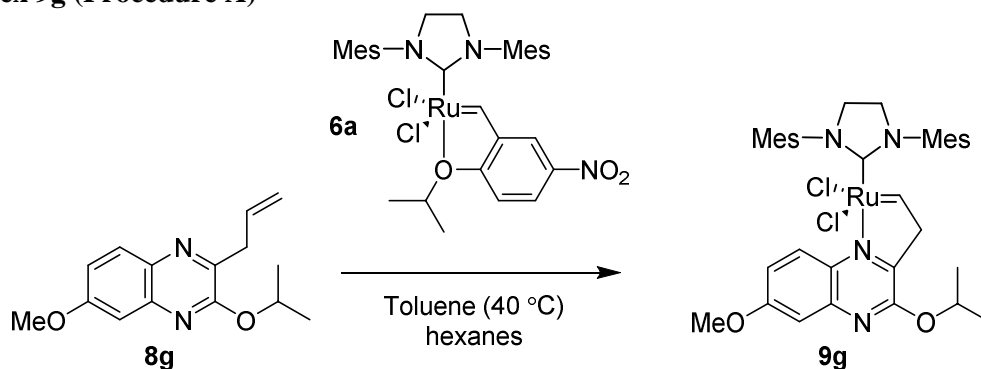
To a round-bottom flask was charged 2-(but-3-en-1-yl)-3-(isopropylthio)-6-methoxyquinoxaline (**8e**) (0.644 g, 2.23 mmol, 1.5 equiv.), and purged with N<sub>2</sub>. After toluene (5.00 ml) and precatalyst **6a** (1.00 g, 1.49 mmol, commercially available as the Nitro-Grela catalyst) were charged under a stream of N<sub>2</sub>, the system was sealed. The resulting mixture was aged (1 h) at 40 °C, deemed complete by <sup>1</sup>H NMR, and hexanes (15.00 ml) was slowly charged at 40 °C over 30 minutes. The resulting slurry was then allowed to cool to RT, filtered through a sintered funnel, washed in 2 portions with 25% toluene in hexane (20.00 ml; 2 x 10 mL), and then washed with 4 portions of hexanes (40.0 ml; 4 x 10 mL). The resulting wet cake was dried in a vacuum oven to yield the desired product **9e** (900 mg, 80% yield) as a reddish solid. <sup>1</sup>H NMR (400 MHz, CD<sub>2</sub>Cl<sub>2</sub>): δ 18.34 (t, *J* = 4.5 Hz, 1H), 7.37 – 6.96 (m, 6H), 6.78 (dd, *J* = 9.2, 2.9 Hz, 1H), 4.13 (ddd, *J* = 14.3, 8.9, 3.5 Hz, 5H), 3.93 (s, 3H), 3.29 – 3.16 (m, 2H), 2.80 (ddd, *J* = 7.9, 6.3, 4.6 Hz, 2H), 2.73 – 2.25 (m, 18H), 1.52 – 1.35 (m, 6H); <sup>13</sup>C-NMR (100 MHz, CD<sub>2</sub>Cl<sub>2</sub>): δ 215.2, 160.0, 156.6, 152.8, 143.0, 140.5, 140.3 (br), 138.8 (br), 138.5 (br), 137.4 (br), 137.2 (br), 135.3 (br), 135.1 (br), 134.4, 130.3, 129.9, 129.6, 129.5, 129.3, 129.0, 128.2, 126.9, 126.2, 125.2, 119.6, 106.4, 55.8, 52.1, 51.7 (br), 50.9 (br), 35.6, 27.9, 22.4, 21.2 (br), 20.9 (br), 20.0 (br), 18.0 (br). ESI-HRMS (*m/z*): Calc'd for C<sub>36</sub>H<sub>45</sub>Cl<sub>2</sub>N<sub>4</sub>ORuS (M+H): 753.1735; Found: 753.1628.

### Complex 9f



To a round-bottom flask was charged 2-(but-3-en-1-yl)-3-(isopropylsulfonyl)-6-methoxyquinoxaline (**8f**) (1.19 g, 3.72 mmol, 1.5 equiv.), and the system was purged with N<sub>2</sub>. Toluene (10.00 ml) was charged to the system under inert handling; precatalyst **6a** (1.00g, 1.49 mmol, commercially available as the Nitro-Grela catalyst) was charged under a stream of N<sub>2</sub>; the system was sealed. The system was aged at 40 °C over 1 hour. Then hexanes (11.70 mL) was slowly added to the reaction at 40 °C over 30 minutes. The resulting mixture was allowed to age for approximately 1 h at RT, then filtered through a sintered funnel, washed in two portions with 25% toluene in hexanes (20.00 ml; 2 x 10 mL), and in four portions with hexanes (40.0 ml; 4 x 10 mL). The resulting wet cake was dried on the filter with vacuum and N<sub>2</sub> purge to yield the desired product (**9f**) (1.00 g, 85% yield). <sup>1</sup>H NMR (400 MHz, CD<sub>2</sub>Cl<sub>2</sub>): δ 18.24 (t, *J* = 4.0 Hz, 1H), 7.26 (d, *J* = 2.8 Hz, 1H), 7.25 – 7.16 (m, 3H), 7.16 – 6.96 (m, 3H), 5.37 (s, 1H), 4.30 (hept, *J* = 6.9 Hz, 1H), 4.14 (d, *J* = 7.7 Hz, 4H), 3.97 (s, 3H), 3.96 – 3.90 (m, 2H), 2.67 – 2.14 (m, 18H), 1.45 (d, *J* = 6.9 Hz, 6H). <sup>13</sup>C-NMR (100MHz, CD<sub>2</sub>Cl<sub>2</sub>): δ 213.5, 161.0, 152.8, 151.1, 140.8, 140.5 (br), 139.1, 138.8 (br), 138.7 (br), 137.3 (br), 136.9 (br), 135.2, 135.0 (br), 129.9, 129.5, 126.6, 125.3, 107.0, 56.1, 53.97, 53.90, 53.1, 51.8, 51.6, 50.9, 28.2, 21.1 (br), 20.9 (br), 20.1 (br), 18.0 (br), 15.3. ESI-HRMS (m/z): Calc'd for C<sub>36</sub>H<sub>45</sub>Cl<sub>2</sub>N<sub>4</sub>O<sub>3</sub>RuS (M+H): 785.1633; Found: 785.1565.

#### Complex **9g** (Procedure A)

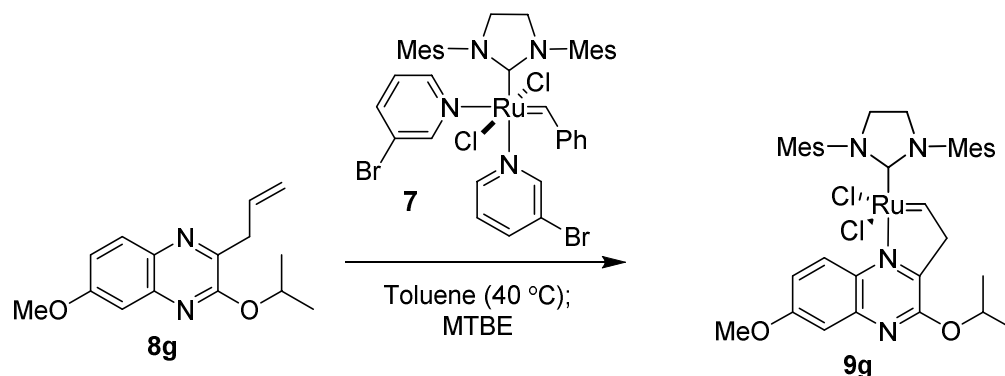


To a Schlenk flask was charged 2-allyl-3-isopropoxy-6-methoxyquinoxaline (**8g**) (0.865 g, 3.35 mmol, 2.25 equiv.) and toluene (5 mL). The system was degassed. Pre-catalyst **6a** (1.00 g, 1.49 mmol, commercially available as the Nitro-Grela catalyst) was charged under a stream of N<sub>2</sub>, and the system was sealed. The mixture was heated and aged (2.5 h) at 40°C. The mixture was deemed complete by <sup>1</sup>H NMR analysis and the mixture allowed to cool to room temperature. MTBE (5 mL) was slowly added, allowed to stir, and then filtered through a sintered funnel at RT. The wet cake was washed with additional MTBE (3 x 5 mL; slurry, slurry, displacement washes), and then dried in a vacuum oven with a slow nitrogen bleed at room temperature to yield the toluene hemi-solvate of the desired product (**9g**) (1.04 g, 91% yield) as a dark orange solid. <sup>1</sup>H NMR (500 MHz, CD<sub>2</sub>Cl<sub>2</sub>) δ 17.06 (t, *J* = 2.7 Hz, 1H), 7.28 – 7.14 (m, 2.5H - toluene), 7.14 – 7.04 (m, 6H), 6.91 (dd, *J* = 9.1, 2.7 Hz, 1H), 5.47 (hept, *J* = 6.2 Hz, 1H), 4.15 (s, 4H), 3.90 (s, 3H), 2.85 (d, *J* = 2.7 Hz, 2H), 2.47-2.48 (m, 18H), 2.35 (d, *J* = 0.7 Hz, 2H), 1.38 (d, *J* = 6.2 Hz, 6H). <sup>13</sup>C-NMR (125 MHz, CD<sub>2</sub>Cl<sub>2</sub>): δ 215.4, 161.3, 155.0, 147.9, 143.5, 139.6 (br),



139.3, 138.5 (toluene), 133.0, 129.8, 129.5 (toluene), 128.7 (toluene), 126.7, 125.8 (toluene), 118.3, 106.8, 70.3, 67.5, 56.3, 52.1, 22.2, 21.6 (toluene), 21.5, 19.8 (br). **ESI-HRMS** (m/z): Calc'd for C<sub>35</sub>H<sub>43</sub>Cl<sub>2</sub>N<sub>4</sub>O<sub>2</sub>Ru (M+H): 723.1801; Found: 723.1768.

### Complex 9g (Procedure B)

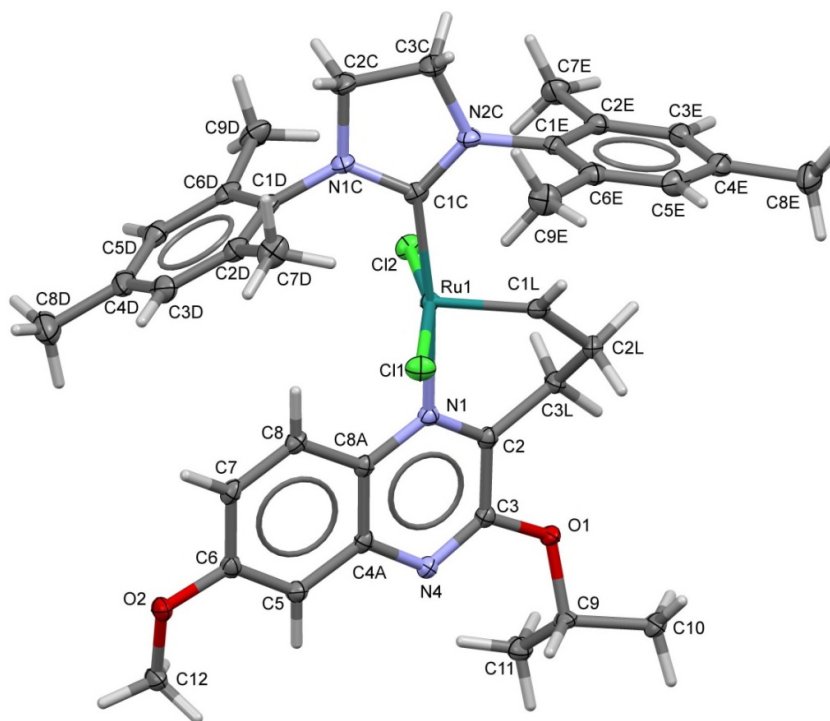


To a 10 mL schlenk flask was charged precatalyst **7** (700 mg, 0.791 mmol, ) and then sealed. A solution of 2-allyl-3-isopropoxy-6-methoxyquinoxaline (**8g**) (460 mg, 1.781 mmol, 2.25 equiv.) in Toluene (2.80 ml, 4 volumes) was then charged under N<sub>2</sub>. The system was stirred and heated to 40 °C whereupon it deemed complete via <sup>1</sup>H NMR analysis (1h). The reaction mixture was allowed to cool to room temperature where it was then treated with MTBE (2.80 mL, 4 volumes), allowed to age at room temperature (~15 minutes) and the system was then filtered to yield an orange solid which was further washed with MTBE (2 x 2.8 mL). The result wet slurry was then dried in a vacuum oven with a slow nitrogen bleed at room temperature to yield the toluene hemi-solvate of the desired product (**9g**) (470 mg, 77% yield) as a dark orange solid. The characterization data matched that of the Procedure A provided above. Note: The material prepared from this procedure (**9g**) was utilized in all the kinetic studies and reactions for this publication.

### Crystal Data and Structure Refinement for Complex 9a (CCDC 1444069)

A single crystal of Complex **9a** grown from dichloromethane and hexane by solvent evaporation was selected for single crystal X-ray data analysis. The crystal was a small red plate with dimensions of 0.20 mm x 0.20 mm x 0.05mm. Data collection was performed on a Bruker Apex II system at 100K. The unit cell was determined to be monoclinic in space group P2<sub>1</sub>/n. The structure contained one molecule in the crystallographic asymmetric unit. Crystallographic data is summarized in Table S1. Figure S1 shows an ORTEP representation of Complex 9a with thermal ellipsoids set at the 50% probability level. Coordinates, refinement details and structure factors have been deposited with the Cambridge Crystallographic Data Centre (CCDC 1444069).

**Figure S1:** ORTEP representation of Complex **9a** with thermal ellipsoids set at the 50% probability level.



**Table S1.** Crystal Data and Structure Refinement for Complex **9a** [CCDC 1444069]

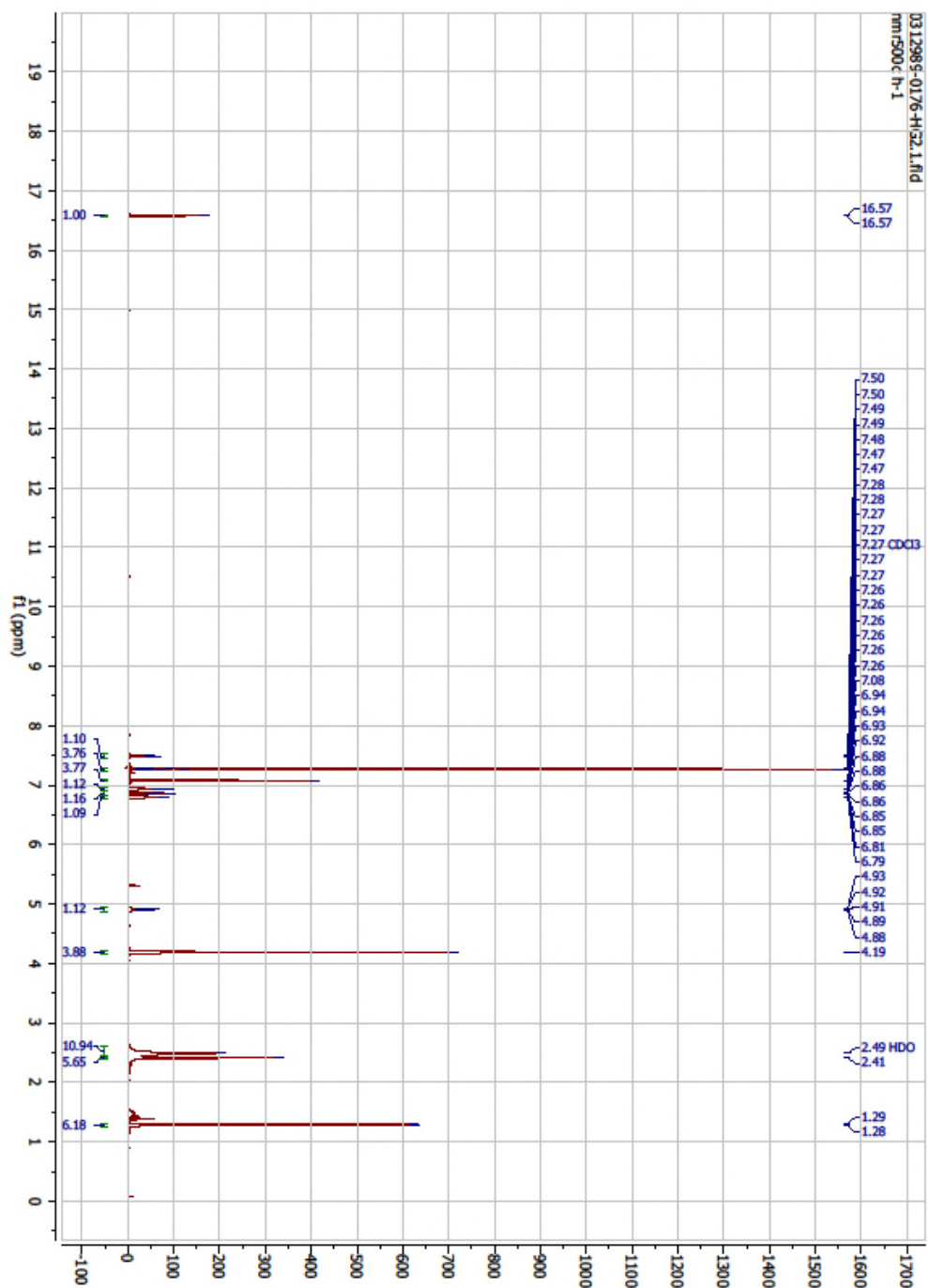
Identification code	mdk001	
Empirical formula	C <sub>36</sub> H <sub>44</sub> Cl <sub>2</sub> N <sub>4</sub> O <sub>2</sub> Ru	
Formula weight	736.72	
Temperature	100(2) K	
Wavelength	1.54178 Å	
Crystal system	Monoclinic	
Space group	P2 <sub>1</sub> /n	
Unit cell dimensions	a = 11.9275(8) Å	α = 90°.
	b = 15.7557(10) Å	β = 97.6486(17)°.
	c = 18.3669(12) Å	γ = 90°.
Volume	3420.9(4) Å <sup>3</sup>	
Z	4	
Density (calculated)	1.430 Mg/m <sup>3</sup>	
Absorption coefficient	5.442 mm <sup>-1</sup>	

F(000)	1528
Crystal size	0.200 x 0.200 x 0.050 mm <sup>3</sup>
Theta range for data collection	3.710 to 66.716°.
Index ranges	-14<=h<=12, -18<=k<=18, -21<=l<=20
Reflections collected	23191
Independent reflections	6031 [R(int) = 0.0255]
Completeness to theta = 66.500°	99.7 %
Absorption correction	Semi-empirical from equivalents
Max. and min. transmission	0.762 and 0.533
Refinement method	Full-matrix least-squares on F <sup>2</sup>
Data / restraints / parameters	6031 / 0 / 415
Goodness-of-fit on F <sup>2</sup>	1.057
Final R indices [I>2sigma(I)]	R1 = 0.0211, wR2 = 0.0534
R indices (all data)	R1 = 0.0216, wR2 = 0.0536
Largest diff. peak and hole	0.359 and -0.396 e.Å <sup>-3</sup>

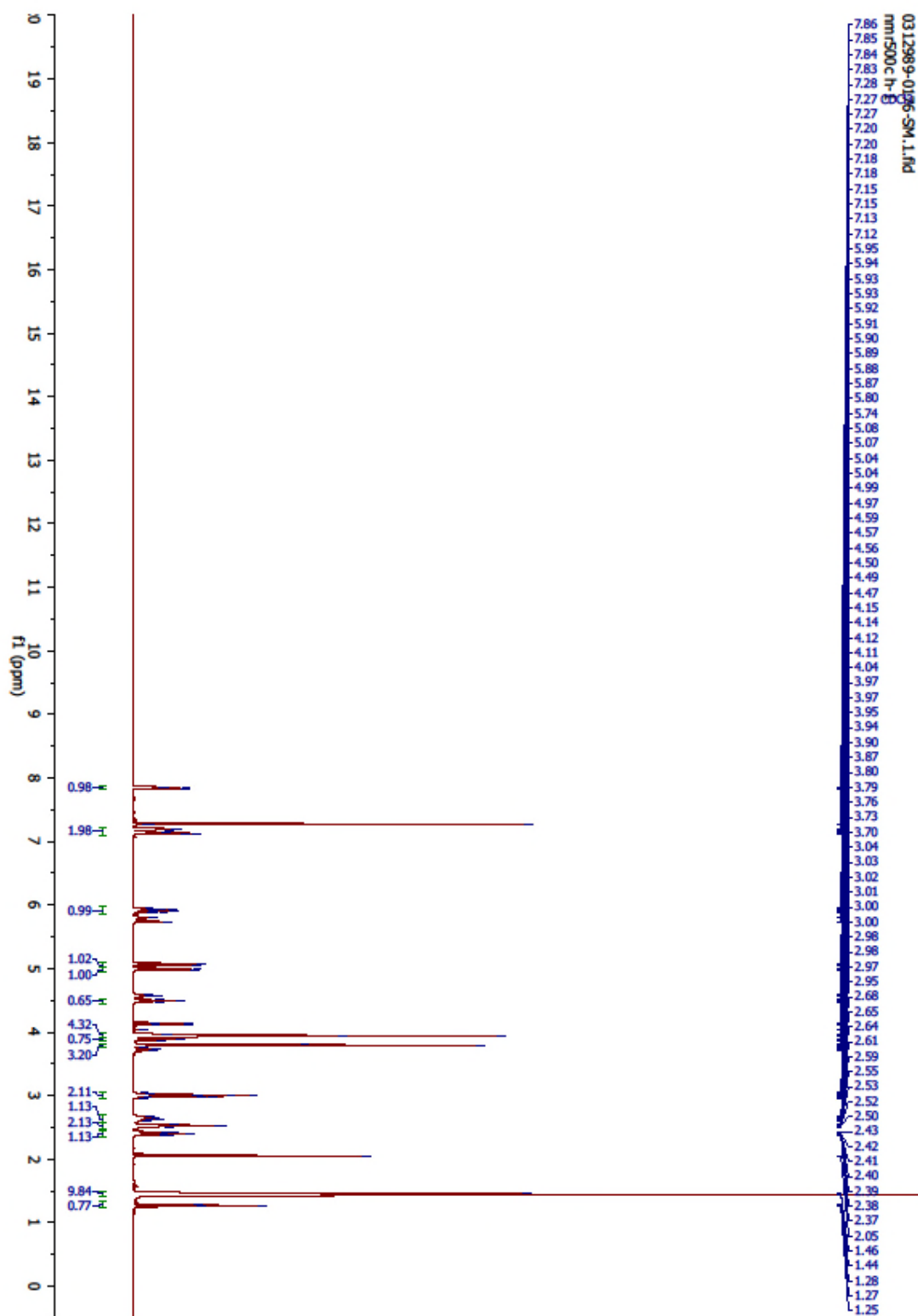
## Experimental Procedure for Discovery of Quinoxaline-Based Complex 5

To a 2 dram vial was charged (2S,4R)-1-tert-butyl 2-methyl 4-((3-(but-3-en-1-yl)-7-methoxyquinoxalin-2-yl)oxy)pyrrolidine-1,2-dicarboxylate (**3**) (133 mg, 0.212 mmol, 1 equiv) dichloromethane (12.00 ml), and then Hoveyda-Grubbs 2<sup>nd</sup> generation precatalyst (**4**) (133 mg, 0.212 mmol, 1 equiv) was then charged to the mixture as a solid under a stream of N<sub>2</sub>. Then charged deuterated chloroform (4 mL). The reaction was monitored by <sup>1</sup>H NMR.

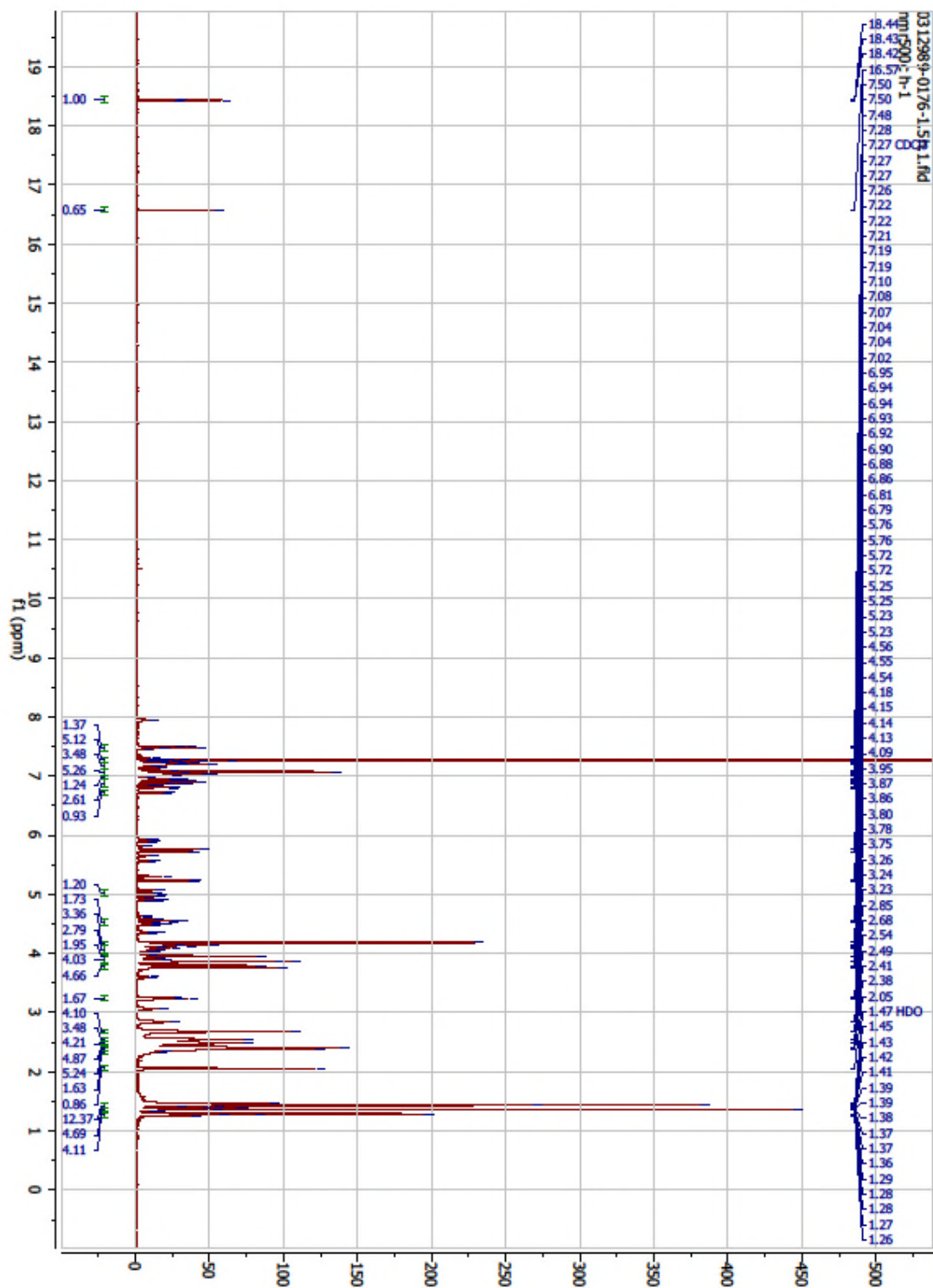
# Reference <sup>1</sup>H-NMR of Hoveyda-Grubbs-2G (4)



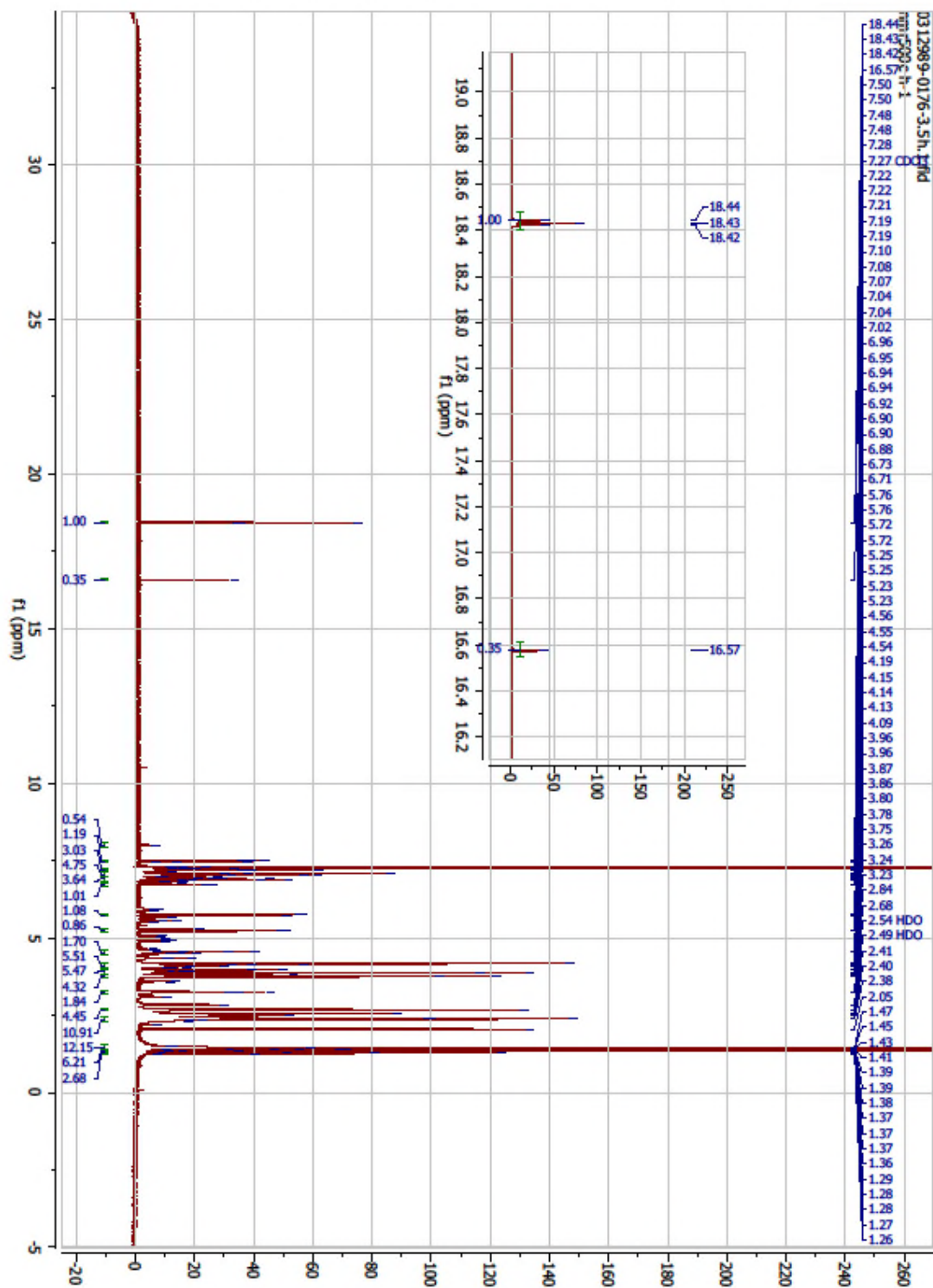
# **<sup>1</sup>H-NMR of compound 3**



### 1H-NMR of the Reaction after 1.5 hour

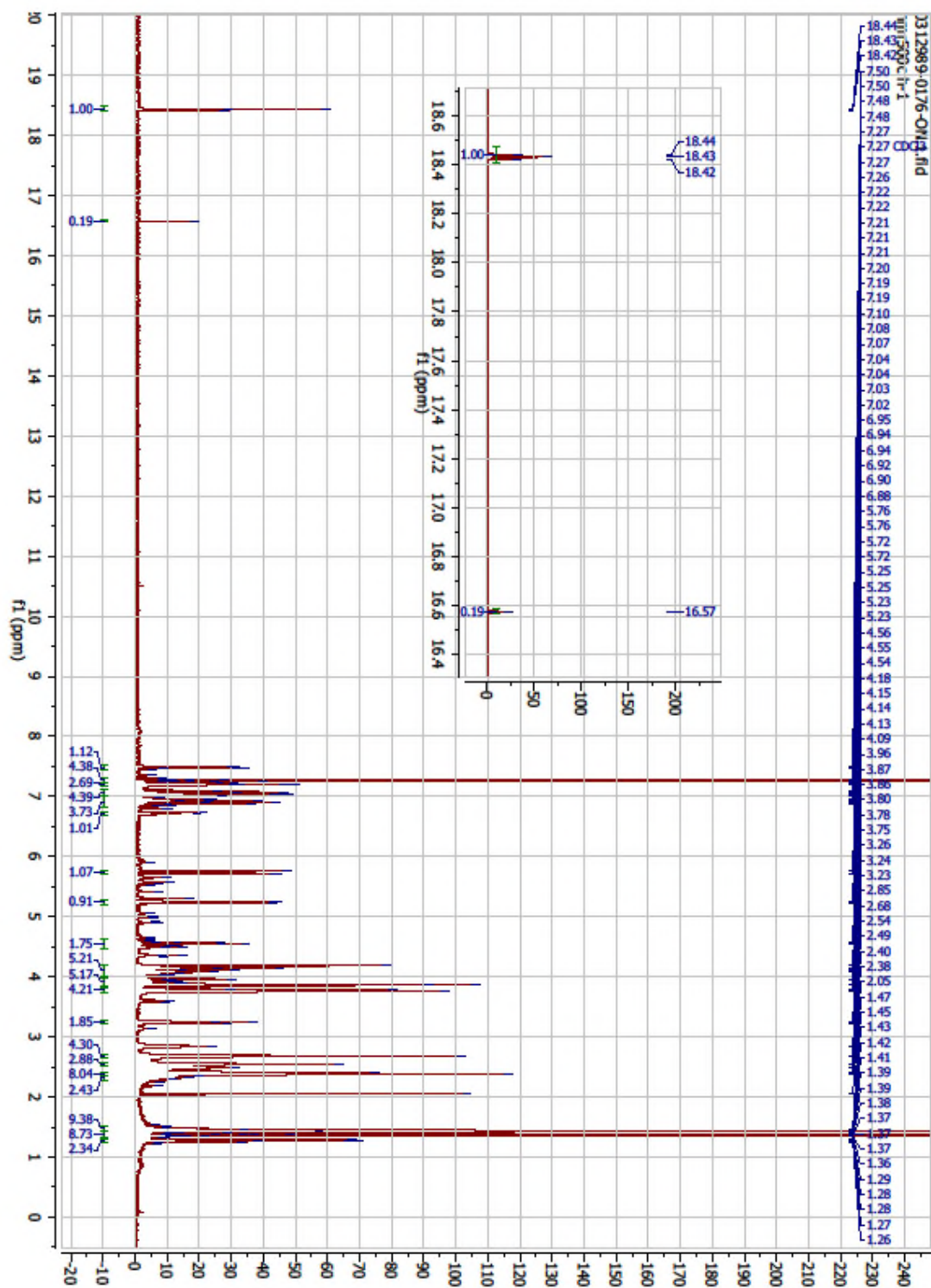


### 1H-NMR of the Reaction after 3.5 hour





# **<sup>1</sup>H-NMR of the Reaction after overnight**





## Experimental Procedures for Solution Stability Study of Complex 9a

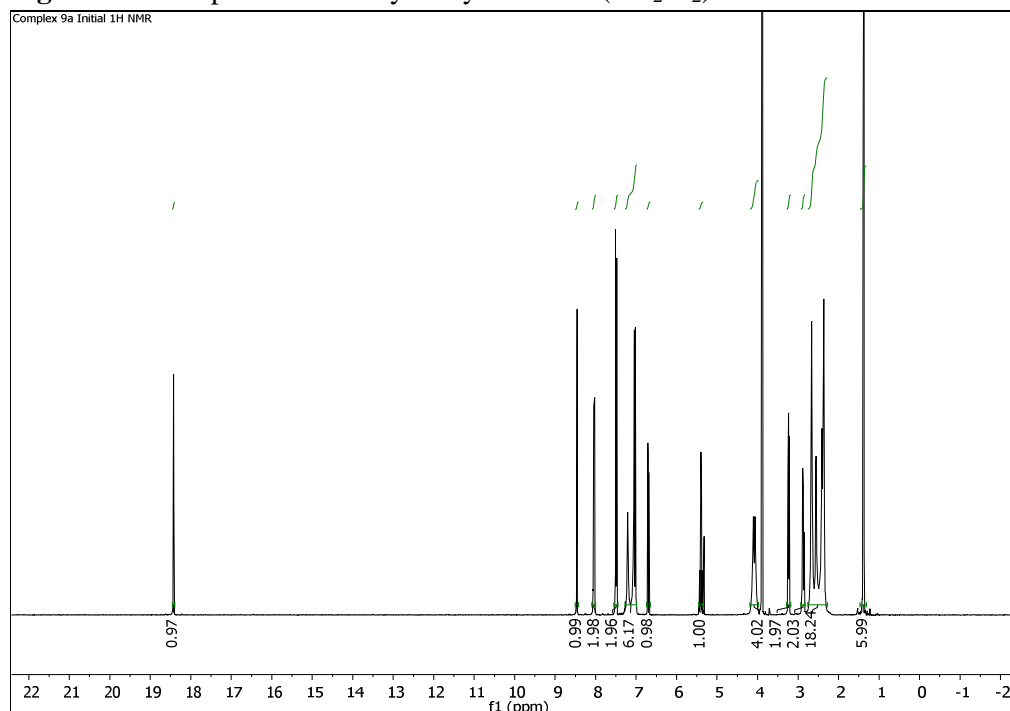
### Solution Stability

In a glovebox, anthracene (27.6 mg, 99.9% purity) was dissolved in CD<sub>2</sub>Cl<sub>2</sub> (3 mL volumetric flask). In a separated 4 mL vial was weighed out complex **9a** (50 mg, 0.068 mmol). To the vial containing the complex **9a** was charged the anthracene solution in CD<sub>2</sub>Cl<sub>2</sub> (650  $\mu$ L, 6.0 mg, 0.034 mmol, 0.05 equiv.) and the mixtures was stirred until the solids dissolved. The resulting dark solution was then placed into a J-young NMR tube and sealed under N<sub>2</sub>. The NMR tube was removed from the glovebox, and aged at room temperature (21-26  $^{\circ}$ C) in the absence of light. An initial <sup>1</sup>H NMR was obtained and then another <sup>1</sup>H NMR was obtained after 30 days. No decomposition was observed (Figure S2 and S3).

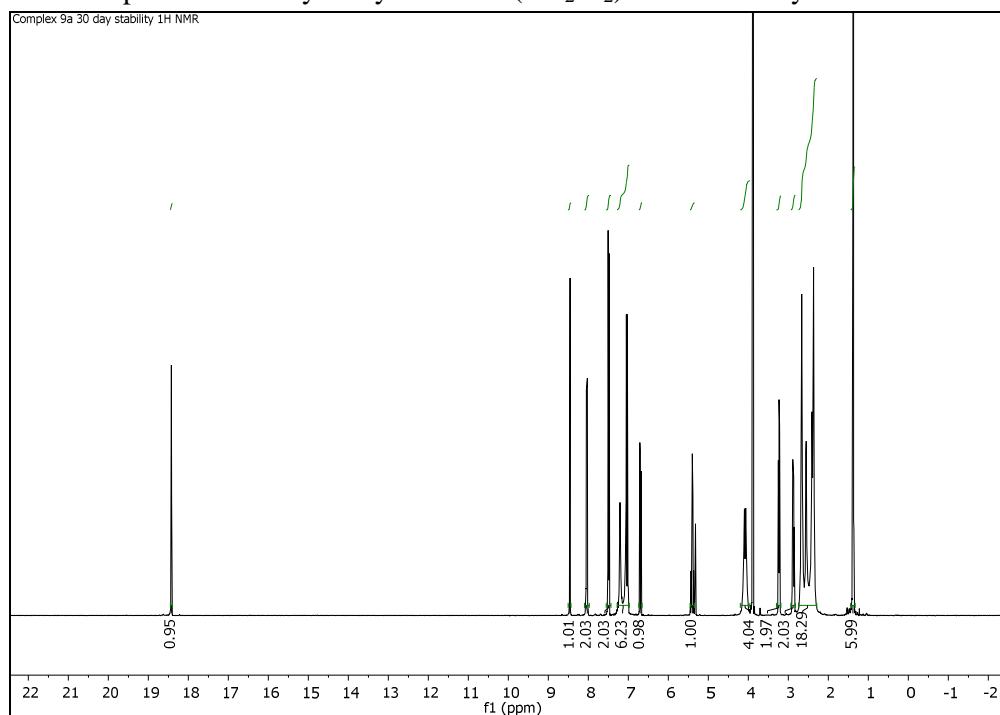
### Solid Stability:

The general purity and stability of solids was obtained by <sup>1</sup>H NMR measurements using high purity 1,3,5-trimethoxybenzene as an external standard. Typically CD<sub>2</sub>Cl<sub>2</sub> was utilized as the <sup>1</sup>H NMR solvent. During the course of production, no decomposition was observed after measuring the wt% purity of the solid complex (**9a**) after being stored in an amber bottle at room temperature in a desiccator for approximately 6 months.

**Figure S2:** Complex **9a** stability study <sup>1</sup>H NMR (CD<sub>2</sub>Cl<sub>2</sub>) – Initial NMR



**Figure S3:** Complex **9a** stability study  $^1\text{H}$  NMR ( $\text{CD}_2\text{Cl}_2$ ) – After 30 days



## Experimental Procedures for Figure 2<sup>9</sup>

### General Procedure

In a glovebox, to a 2-mL volumetric flask with screw-top septum was charged the ruthenium complex described (0.0325 mmol). The system was diluted with  $\text{CD}_2\text{Cl}_2$  (0.016 M) to the appropriate volume marker and then sealed. To an NMR tube with screw cap septum, in a glovebox, was charged  $\text{CD}_2\text{Cl}_2$  (0.75 mL). Subsequently, the ruthenium complex solution (50  $\mu\text{L}$ , 0.8  $\mu\text{mol}$ , 1 mol%) was then charged via 50  $\mu\text{L}$  syringe to the NMR tube, sealed, and taken out of the glovebox. The NMR tube was then placed in the NMR and the system was equilibrated to 303 K for ~10-15 minutes. The NMR sample was locked, tuned, and then shimmed. The sample was ejected, *tert*-butyl diallylcarbamate (**10**) (18  $\mu\text{L}$ , 0.083 mmol, 0.1 M) was charged via 25  $\mu\text{L}$  syringe, and the mixed sample was placed back into the NMR where conversion was measured  $^1\text{H}$  NMR scans approximately every 1 minute.<sup>9</sup> The data can be seen below.

<sup>9</sup> See the following for a catalyst characterization and comparator technique that was utilized to obtain the ruthenium complex kinetic profiles: Ritter, T.; Hejl, A.; Wenzel, A. G.; Funk, T. W.; Grubbs, R. H. *Organometallics* **2006**, 25, 5740-5745.

## Conversion Table for Figure 2

RCM of *tert*-butyl diallylcarbamate **10** with complexes **9a**, **9c**, **9f** and **9g**

Complex <b>9a</b> data				Complex <b>9c</b> data			
Rxn Time (min)	Product Int	SM Int	Conv. (%)	Rxn Time (min)	Product Int	SM Int	Conv. (%)
0.0	0	100	0%	0.0	0	100	0%
1.0	1.68662	98.3134	2%	1.1	1.67069	98.3293	2%
2.2	4.12398	94.9057	4%	2.2	3.0165	96.333	3%
3.3	8.88972	89.9743	9%	3.3	4.53929	94.8626	5%
4.4	15.3762	83.3304	16%	4.5	7.43786	91.8685	7%
5.6	22.7334	78.2245	23%	5.7	10.9828	88.227	11%
6.7	29.5033	71.1775	29%	6.8	15.5549	83.6033	16%
7.8	34.9331	65.8164	35%	7.9	20.0794	79.0801	20%
8.9	39.962	60.4811	40%	9.0	24.6513	74.5479	25%
10.0	44.4192	56.0573	44%	10.1	28.7582	70.3401	29%
11.2	48.4441	51.7929	48%	11.2	32.8975	66.204	33%
12.3	51.846	48.6621	52%	12.3	36.4058	62.5479	37%
13.4	55.2007	45.0258	55%	13.5	39.8392	59.2362	40%
14.6	58.1278	42.0076	58%	14.6	42.8172	56.0528	43%
15.8	60.7823	39.4185	61%	15.7	45.551	53.327	46%
16.9	63.0489	36.9925	63%	16.8	48.079	50.8944	49%
18.0	65.0548	35.0266	65%	17.9	50.4944	48.4187	51%
19.1	67.048	33.0528	67%	19.0	52.5806	46.3028	53%
20.2	68.7674	31.0646	69%	20.1	54.6114	44.3062	55%
21.4	70.3137	29.5925	70%	21.2	56.5528	42.2163	57%
22.5	71.71	28.168	72%	22.4	58.3509	40.2898	59%
23.6	73.0542	26.9145	73%	23.5	59.9926	38.4796	61%
24.7	74.2042	25.775	74%	24.7	61.7442	36.8178	63%
25.8	75.3473	24.4149	76%	25.8	63.21	35.3659	64%
27.0	76.3827	23.42	77%	27.0	64.4834	34.045	65%
28.1	77.4026	22.5217	77%	28.1	65.7236	32.9489	67%
29.3	78.3222	21.4328	79%	29.3	67.0029	31.5431	68%
30.5	79.1463	20.59	79%	30.5	68.0747	30.3419	69%
Complex <b>9f</b> data				Complex <b>9g</b> data			
Rxn Time (min)	Product Int	SM Int	Conv. (%)	Rxn Time (min)	Product Int	SM Int	Conv. (%)
0.00	0	100	0%	0.00	0	100	0.0%
1.13	9.55762	90.4424	10%	1.07	0.209227	99.790773	0.2%
2.30	28.3847	70.7709	29%	2.20	0.373543	98.3786	0.4%
3.40	42.1799	56.5764	43%	3.37	0.491804	97.9064	0.5%
4.48	52.3946	46.2975	53%	4.48	0.511241	97.9493	0.5%

5.60	60.2683	38.4629	61%	5.67	0.55485	97.8993	0.6%
6.77	66.354	32.2157	67%	6.83	0.563846	97.7651	0.6%
7.93	71.0504	27.3864	72%	7.93	0.553172	97.5429	0.6%
9.03	74.4207	23.8536	76%	9.05	0.609036	97.4232	0.6%
10.15	77.2509	21.1605	78%	10.17	0.588657	97.5173	0.6%
11.27	79.4467	19.0182	81%	11.28	0.5623	97.4907	0.6%
12.43	81.2867	16.726	83%	12.47	0.568121	97.6685	0.6%
13.57	82.8365	15.1739	85%	13.57	0.574393	97.823	0.6%
14.65	84.1026	13.8087	86%	14.72	0.587702	98.127	0.6%
15.77	85.0106	12.6222	87%	15.83	0.572307	98.1381	0.6%
16.87	86.126	11.7491	88%	16.95	0.592879	97.9956	0.6%
17.98	87.0635	10.9901	89%	18.13	0.566536	98.1386	0.6%
19.10	87.6842	10.2693	90%	19.28	0.583352	98.1308	0.6%
20.20	88.1294	9.79746	90%	20.45	0.59526	97.8626	0.6%
21.38	88.5557	8.93073	91%	21.62	0.5647	97.6674	0.6%
22.57	89.0256	8.58622	91%	22.78	0.542687	97.8955	0.6%
23.98	89.4474	7.98282	92%	23.90	0.620397	97.5705	0.6%
25.15	89.7599	7.55357	92%	24.98	0.586982	97.8534	0.6%
26.32	90.2424	7.29483	93%	26.08	0.558267	98.1734	0.6%
27.47	90.5705	7.01371	93%	27.18	0.591675	97.5133	0.6%
28.58	90.7569	6.93225	93%	28.30	0.541654	98.1042	0.5%
29.70	91.1992	6.46975	93%	29.47	0.59855	97.494	0.6%
30.85	91.4865	6.23461	94%	30.65	0.625901	96.883	0.6%

## Experimental Procedures for Figure 3

### General procedure without acid co-catalyst:

In a glovebox, to a 2-mL volumetric flask with screw-top septum was charged the ruthenium complex (0.0325 mmol). The system was diluted with CD<sub>2</sub>Cl<sub>2</sub> (0.016 M) to the appropriate volume marker and then sealed. To an NMR tube with screw cap septum, in a glovebox, was charged CD<sub>2</sub>Cl<sub>2</sub> (0.75 mL). Subsequently, the ruthenium complex solution (50  $\mu$ L, 0.8  $\mu$ mol, 1 mol%) was then charged to the NMR tube, sealed, and taken out of the glovebox. The NMR tube was then placed in the NMR and the system was equilibrated to 303 K for ~10-15 minutes. The NMR tube was locked, tuned, and then shimmed. The sample was ejected, 2,2-diallylmalonate (20  $\mu$ L, 83  $\mu$ mol, 0.1 M) was charged via 25  $\mu$ L syringe, and the mixed sample was placed back into the NMR where conversion was measured utilizing a macro to obtain <sup>1</sup>H NMR scans approximately every 1 minute.

### General procedure with acid co-catalyst:

In a glovebox, benzene sulfonic acid (25 mg, 0.16 mmol) was charged to a 2 mL volumetric flask and then diluted with CD<sub>2</sub>Cl<sub>2</sub> (0.08 M). To an NMR tube with a screw top septum was charged CD<sub>2</sub>Cl<sub>2</sub> (0.70 mL) and then the benzene sulfonic acid solution prepared above was charged (50  $\mu$ L, 3.95  $\mu$ mol, 5 mol%). Diethyl 2,2-diallylmalonate (**12**) (20  $\mu$ L, 83  $\mu$ mol, 0.1 M) was charged via 25  $\mu$ L syringe to the NMR tube, the solution was sealed, and then brought outside of the glove box. The NMR tube was then placed in the NMR, and the system was equilibrated to 303 K for approximately 10-15 minutes, and the sample was locked, the probe was tuned, and then shimmed. The sample was then ejected, and the ruthenium pre-catalyst solution (50  $\mu$ L, 0.8  $\mu$ mol, 1 mol%, 0.001M) was charged, under inert handling, and placed back into the NMR where the conversion was measured where conversion was measured to obtain <sup>1</sup>H NMR scans approximately every 1 minute.<sup>9</sup>

### Conversion Table for Figure 3

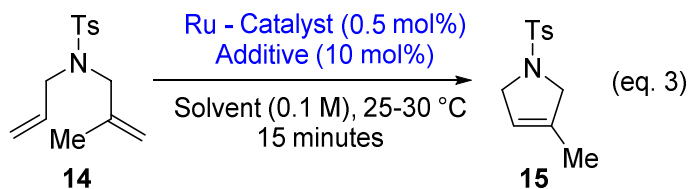
RCM of diene **12** with catalysts **9a** and **9f** in the presence and absence benzenesulfonic acid (5 mol%)

Complex <b>9a</b> w/out BSA				Complex <b>9a</b> w/ BSA (5 mol%)			
Rxn Time (min)	Product Int	SM Int	Conv. (%)	Rxn Time (min)	Product Int	SM Int	Conv. (%)
0.0	0	100	0%	0.0	0	100	0%
1.0	3.25923	96.1501	3%	1.2	61.0817	39.4233	61%
2.1	8.14875	90.9048	8%	2.4	79.1996	20.3788	80%
3.3	13.2346	85.6957	13%	3.5	85.8637	13.5678	86%
4.4	18.2057	80.5365	18%	4.7	89.504	9.92667	90%
5.6	22.8319	75.8501	23%	5.9	91.5772	7.64519	92%
6.8	27.0015	71.5535	27%	7.1	92.9819	6.36688	94%
8.0	30.8594	67.5704	31%	8.3	93.9336	5.44472	95%
9.2	34.4667	63.8662	35%	9.5	94.616	4.7609	95%
10.4	37.6541	60.6798	38%	10.7	95.0335	4.35166	95%
11.5	40.555	57.6842	41%	11.9	95.4822	3.9432	96%
12.6	43.2144	55.0133	44%	13.0	95.8137	3.70256	96%
13.8	45.8111	52.3233	47%	14.2	95.9841	3.51712	96%
15.0	48.1825	49.8499	49%	15.4	96.2242	3.30426	97%
16.2	50.4422	47.5186	51%	16.5	96.4254	3.16491	97%
17.4	52.5144	45.4613	54%	17.7	96.5259	3.04847	97%
18.6	54.4776	43.4369	56%	18.8	96.6475	2.96846	97%
19.8	56.2225	41.5701	57%	20.0	96.8076	2.89998	97%
21.0	57.9756	39.8627	59%	21.1	96.8408	2.84504	97%
22.1	59.5451	38.2478	61%	22.3	97.0248	2.76802	97%

23.3	60.9726	36.7402	62%	23.5	97.0618	2.69251	97%
24.5	62.3687	35.278	64%	24.6	97.1688	2.65447	97%
25.7	63.6742	33.922	65%	25.8	97.1964	2.66535	97%
26.9	64.8684	32.7626	66%	26.9	97.2631	2.57419	97%
28.1	65.9952	31.5634	68%	28.1	97.3121	2.55492	97%
29.2	67.0958	30.4076	69%	29.3	97.3186	2.57517	97%
30.4	68.2991	29.3974	70%	30.5	97.3949	2.49577	98%
Complex 9g w/out BSA				Complex 9g w/ BSA (5 mol%)			
Rxn Time (min)	Product Int	SM Int	Conv. (%)	Rxn Time (min)	Product Int	SM Int	Conv. (%)
0.0	0	100	0%	0.0	0	100	0%
0.9	-0.229122	100	0%	1.0	0.096948	99.9031	0%
2.1	-0.008229	99.3256	0%	2.1	0.255756	99.1703	0%
3.2	-0.034513	99.1347	0%	3.2	0.504588	99.0096	1%
4.4	0.003182	99.1984	0%	4.4	0.829232	98.78	1%
5.6	0.004836	98.8676	0%	5.5	1.09848	98.3559	1%
6.7	0.004288	98.8601	0%	6.7	1.40705	98.2386	1%
7.8	-0.176685	98.6489	0%	7.8	1.77719	97.9462	2%
9.0	-0.03218	98.712	0%	8.9	2.03038	97.5603	2%
10.1	-0.124882	98.5983	0%	10.0	2.47319	97.3211	2%
11.2	0.212538	98.9327	0%	11.1	2.72716	96.987	3%
12.4	-0.114671	98.5422	0%	12.3	3.14518	96.5475	3%
13.5	0.038869	98.5651	0%	13.4	3.51544	96.2494	4%
14.7	0.150147	98.5715	0%	14.5	3.80119	95.854	4%
15.8	-0.201914	98.3515	0%	15.7	4.08377	95.4675	4%
16.9	0.205121	98.6678	0%	16.8	4.57519	95.1153	5%
18.1	0.091723	98.7386	0%	18.0	4.91851	94.8037	5%
19.2	0.245683	98.6951	0%	19.1	5.30226	94.1543	5%
20.3	0.212886	98.6709	0%	20.2	5.64462	93.731	6%
21.5	0.269898	98.8922	0%	21.4	6.04911	93.3396	6%
22.7	0.135889	98.6908	0%	22.5	6.47421	92.8696	7%
23.8	-0.090473	98.8424	0%	23.7	6.85251	92.4625	7%
25.0	0.142239	98.9475	0%	24.9	7.24716	92.1036	7%
26.1	-0.017736	98.496	0%	26.0	7.65542	91.6869	8%
27.2	0.208718	98.7192	0%	27.1	7.99662	91.2518	8%
28.4	0.255848	98.7089	0%	28.2	8.35968	90.842	8%
29.5	0.528361	99.0693	1%	29.4	8.65156	90.4146	9%
30.7	0.229817	98.9674	0%	30.6	9.12685	90.0096	9%

## Experimental Procedure for Table 2

### High-Throughput Experimentation General Procedure:



To each 8 x 30 mm vial in an 8x12 well plate format (Analytical Sales and Services, Inc.), positions A1 to F12, was charged N-allyl-4-methyl-N-(2-methylallyl)benzenesulfonamide (**14**) (10  $\mu\text{mol}$ , 0.2 M) and 4-isopropyl-1,1'-biphenyl (1  $\mu\text{mol}$ , 0.2 M) as a solution in THF (50  $\mu\text{L}$ ). Upon complete addition, the rack was concentrated to remove the THF at room temperature. After concentration, to each row was then charged a Lewis or Brønsted acid co-catalyst solution (1  $\mu\text{mol}$ , 0.02 M) either in 1,2-dichloroethane or toluene (50  $\mu\text{L}$ ) previously prepared. Subsequently, a solution of each catalyst [**9a**, **9c**, or **9g**] (0.05  $\mu\text{mol}$ , 0.001 M) in either in 1,2-dichloroethane or toluene (50  $\mu\text{L}$ ) was quickly charged to the respective vial and then the reaction mixtures were sealed and allowed to stir between 25-30  $^{\circ}\text{C}$  as was monitored by block temperature. After a 15 minutes age time, diisopropylethylamine (2  $\mu\text{mol}$ , 0.02 M) in acetonitrile (200  $\mu\text{L}$ ) was charged to each reaction mixture and subsequently, a solution of ethyl vinyl ether (50  $\mu\text{mol}$ , 0.2 M) in acetonitrile was charged (250  $\mu\text{L}$ ) quickly to each vial. The quenched reactions were then further diluted (25  $\mu\text{L}$  aliquot was diluted into 500  $\mu\text{L}$  of MeCN) for UPLC-MS analysis. The specific reagent, positions, solvents, and solution yields can be seen in the subsequent screen data table.

### Screen Data for Table 2:

Location	Solvent	Complex	Co-catalyst	Solution Yield (%)
2:A:1	DCE	<b>9a</b>	HOAc	9.0
2:A:2	DCE	<b>9a</b>	BSA	79.8
2:A:3	DCE	<b>9a</b>	HCl in dioxane (4 M)	87.4
2:A:4	DCE	<b>9a</b>	HB $\text{F}_4$	86.7
2:A:5	DCE	<b>9a</b>	TFA	86.6
2:A:6	DCE	<b>9a</b>	TFMSA	50.9
2:A:7	DCE	<b>9a</b>	CSA	87.1
2:A:8	DCE	<b>9a</b>	TCA	86.9
2:A:9	DCE	<b>9a</b>	HI	74.8
2:A:10	DCE	<b>9a</b>	ZnCl $_2$ in THF (0.5 M)	6.5
2:A:11	DCE	<b>9a</b>	AlCl $_3$ in THF (0.5 M)	88.0
2:A:12	DCE	<b>9a</b>	Control	17.8
2:B:1	DCE	<b>9g</b>	HOAc	0.2
2:B:2	DCE	<b>9g</b>	BSA	6.1
2:B:3	DCE	<b>9g</b>	HCl in dioxane (4 M)	0.1

2:B:4	DCE	9g	HBF <sub>4</sub>	1.6
2:B:5	DCE	9g	TFA	0.2
2:B:6	DCE	9g	TFMSA	1.0
2:B:7	DCE	9g	CSA	0.1
2:B:8	DCE	9g	TCA	0.1
2:B:9	DCE	9g	HI	0.3
2:B:10	DCE	9g	ZnCl <sub>2</sub> in THF (0.5 M)	0.1
2:B:11	DCE	9g	AlCl <sub>3</sub> in THF (0.5 M)	5.1
2:B:12	DCE	9g	Control	0.2
2:C:1	DCE	9c	HOAc	31.5
2:C:2	DCE	9c	BSA	93.9
2:C:3	DCE	9c	HCl in dioxane (4 M)	83.7
2:C:4	DCE	9c	HBF <sub>4</sub>	96.5
2:C:5	DCE	9c	TFA	75.2
2:C:6	DCE	9c	TFMSA	44.6
2:C:7	DCE	9c	CSA	65.2
2:C:8	DCE	9c	TCA	75.2
2:C:9	DCE	9c	HI	62.0
2:C:10	DCE	9c	ZnCl <sub>2</sub> in THF (0.5 M)	11.2
2:C:11	DCE	9c	AlCl <sub>3</sub> in THF (0.5 M)	96.3
2:C:12	DCE	9c	Control	29.4
2:D:1	toluene	9a	HOAc	58.7
2:D:2	toluene	9a	BSA	85.9
2:D:3	toluene	9a	HCl in dioxane (4 M)	78.4
2:D:4	toluene	9a	HBF <sub>4</sub>	93.5
2:D:5	toluene	9a	TFA	88.7
2:D:6	toluene	9a	TFMSA	44.5
2:D:7	toluene	9a	CSA	86.6
2:D:8	toluene	9a	TCA	86.5
2:D:9	toluene	9a	HI	69.0
2:D:10	toluene	9a	ZnCl <sub>2</sub> in THF (0.5 M)	18.2
2:D:11	toluene	9a	AlCl <sub>3</sub> in THF (0.5 M)	92.5
2:D:12	toluene	9a	Control	59.5
2:E:1	toluene	9g	HOAc	0.3
2:E:2	toluene	9g	BSA	1.6
2:E:3	toluene	9g	HCl in dioxane (4 M)	0.1
2:E:4	toluene	9g	HBF <sub>4</sub>	0.9
2:E:5	toluene	9g	TFA	0.1
2:E:6	toluene	9g	TFMSA	1.0
2:E:7	toluene	9g	CSA	0.1
2:E:8	toluene	9g	TCA	0.1
2:E:9	toluene	9g	HI	0.1
2:E:10	toluene	9g	ZnCl <sub>2</sub> in THF (0.5 M)	0.1
2:E:11	toluene	9g	AlCl <sub>3</sub> in THF (0.5 M)	0.4
2:E:12	toluene	9g	Control	0.0
2:F:1	toluene	9c	HOAc	70.4
2:F:2	toluene	9c	BSA	93.7
2:F:3	toluene	9c	HCl in dioxane (4 M)	76.4
2:F:4	toluene	9c	HBF <sub>4</sub>	96.8
2:F:5	toluene	9c	TFA	83.3
2:F:6	toluene	9c	TFMSA	33.2



2:F:7	toluene	<b>9c</b>	CSA	73.1
2:F:8	toluene	<b>9c</b>	TCA	79.1
2:F:9	toluene	<b>9c</b>	HI	82.3
2:F:10	toluene	<b>9c</b>	ZnCl <sub>2</sub> in THF (0.5 M)	30.7
2:F:11	toluene	<b>9c</b>	AlCl <sub>3</sub> in THF (0.5 M)	95.3
2:F:12	toluene	<b>9c</b>	Control	73.0

## Experimental procedures for Table 3

### Ring-closing Metathesis Procedures (Table 3; Entries 1-8)

In a glove box was prepared reaction mixtures containing diene substrates **14**, or **16** (100 mg) in DCM or toluene (4 ml). To this was added a solution of catalyst **9a** in DCM (0.1 M, 1 mol%). The resulting mixture was stirred at 30 °C in the presence or absence of AlCl<sub>3</sub> (0.2 eq. Added as a 0.5 M THF solution). Aliquots were taken and analyzed with HPLC to monitor the conversion. When the reaction was completed (LC conversion > 99%), the reaction mixture was cooled to room temperature, diluted with aq. acetonitrile, and quantitatively assayed with HPLC.

LC conv (Assay Yield)	0.5 h	1.5 h	3 h	6 h
1	100% (99.8%)			
2	100% (94.5%)			
3	82%	89%	94%	97% (98.6%)
4			98%	100% (98.7%)
5	97% (94.2%)			
6	100% (95.0%)			
7		80%	87%	93% (91.7%)
8			99%	100% (97.0%)

### Representative Procedure for Isolation of RCM (Table 3; Entry 8)

In a glove box was prepared reaction mixtures containing diene substrates **14** (1.0 g, 3.73 mmol) in degassed toluene (40 ml). To this was added catalyst **9a** (27 mg, 0.037 mmol, 1 mol %). The resulting mixture was stirred at 30 °C for 6 hour. The reaction mixture was cooled to

room temperature and concentrated to 10 mL under reduced pressure. The SiO<sub>2</sub> purification (EtOAc/DCM/hexane = 1/2/10) of the crude material afforded a white solid product (0.831g, 95% isolated yield). <sup>1</sup>H NMR of the isolated material was matched with the known compound **15**.<sup>3</sup> <sup>1</sup>H NMR (CDCl<sub>3</sub>, 500 MHz): 7.73 – 7.71 (m, 2H), 7.33 – 7.31 (m, 2H), 5.26 – 5.24 (m, 1H), 4.09 – 4.06 (m, 2H), 3.98 – 3.96 (m, 2H), 2.43 (s, 3H), 1.67 – 1.65 (m, 3H).

### Ring-opening Metathesis Polymerization Procedure (Table 3; Entries 9-10)

In a glove box were prepared reaction mixtures containing cyclooctadiene **18** (0.40 mmol, 43 mg) in CD<sub>2</sub>Cl<sub>2</sub> (0.74 ml). To this was added a solution of catalyst **9a** in CD<sub>2</sub>Cl<sub>2</sub> (0.01 M, 0.1 mol%). The resulting mixture was stirred at 30 °C in the presence or absence of AlCl<sub>3</sub> (0.02 eq. Added as a 0.5 M THF solution). The conversion to **19** was determined by comparing the ratio of the integrals of the methylene protons in the starting material, δ 2.36 (m), with those in the product, δ 2.09 (br m), 2.04 (br m).

### Cross-metathesis Procedures (Table 3; Entries 11-12)

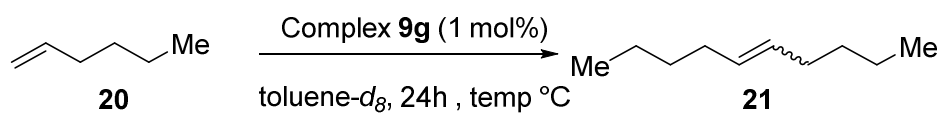
In a glovebox, a catalyst stock solution was prepared by dissolving complex **9a** (36.2 mg) in toluene-d<sub>6</sub> (5 mL). To two separate NMR tubes, in a glovebox, with screw top septa was charged either tetrahydrofuran (157 μL) or AlCl<sub>3</sub>•THF complex 0.5 M in THF (157 μL, 0.078 mmol, 20 mol%) and then toluene-d<sub>6</sub> (158 μL). The solution of complex **9a** prepared above (400 μL, 3.92 μmol, 1 mol%) was then charged each NMR tube. Finally, 1-hexene (50 μL, 0.39 mmol, 0.5 M) was charged to each tube via a 50 μL syringe. The NMR tubes were then sealed and the contents mixed, after which time they were brought out of the glovebox and allowed to age (16 h) at room temperature (23 °C). The conversion to dodecane (**21**) was determined by comparing the ratio of integrals of the methylene protons in the starting material with those of the product which was determined to be 99% (entry 11, table 3) for sample containing AlCl<sub>3</sub> and 97% for the background (entry 12, table 3).<sup>10</sup> The <sup>1</sup>H NMR spectrum of the desired product matched the corresponding <sup>1</sup>H NMR's of *cis*-5-decene and *trans*-5-decene which are commercially available.<sup>4</sup>

### Experimental Procedure for Figure 4

In a glovebox, a catalyst stock solution was prepared by dissolving complex **9g**, from Complex **9g** procedure B, (21.0 mg) in toluene-d<sub>6</sub> (5 mL). To four separate J-Young (sealable) NMR tubes was charged 0.715 mL of the complex **9g** stock solution (3.01 mg, 3.92 μmol, 1 mol%). Subsequently, to each tube was charged 1-hexene (50 μL, 0.39 mmol, 0.5 M) via a 50 μL syringe. The NMR tubes were then sealed and the contents mixed, after which time they were

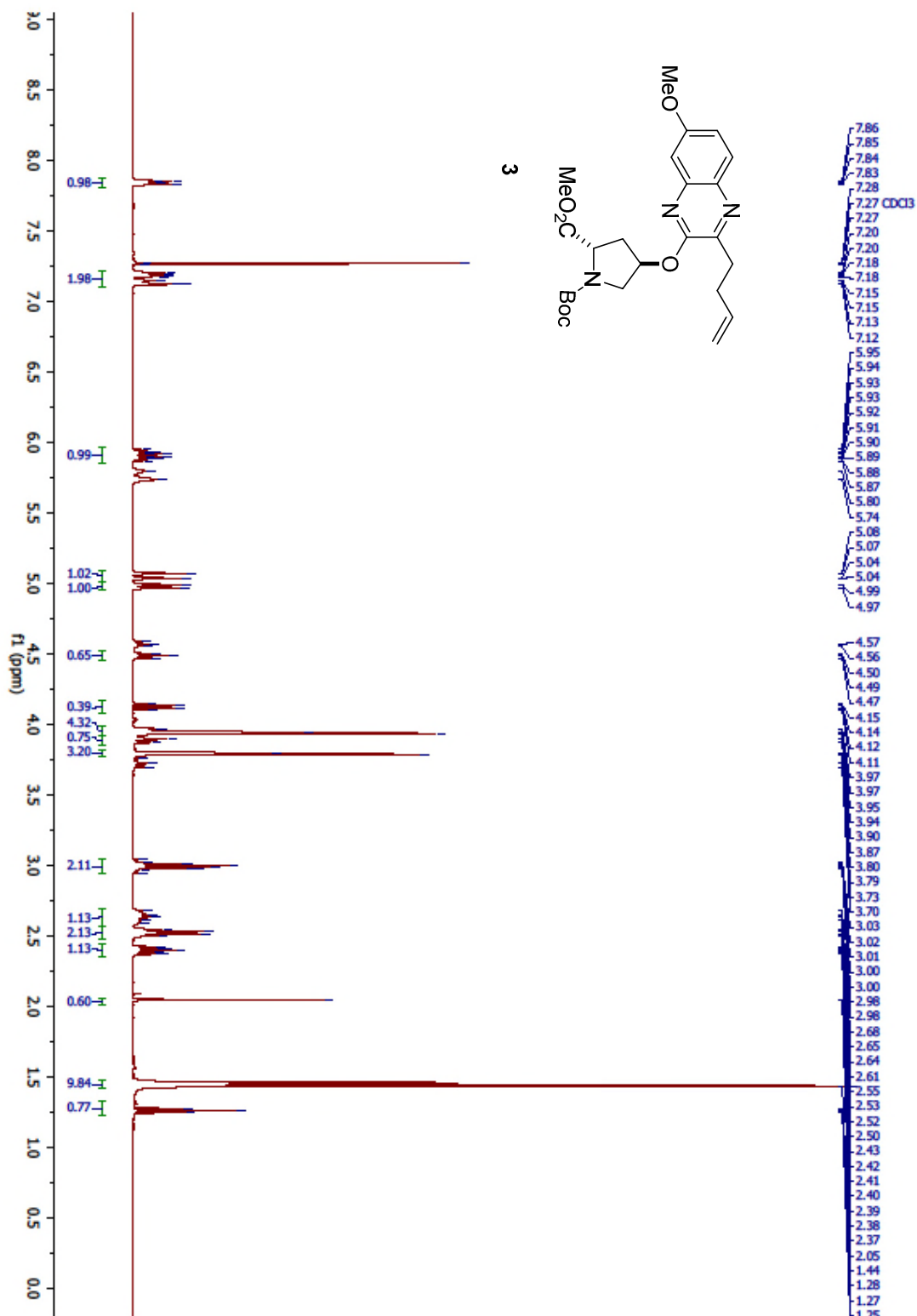
<sup>10</sup> See the following reference for representative example: Thomas, R. M.; Fedorov, A.; Keitz, B. K.; Grubbs, R. H. *Organometallics* **2011**, 30, 6713.

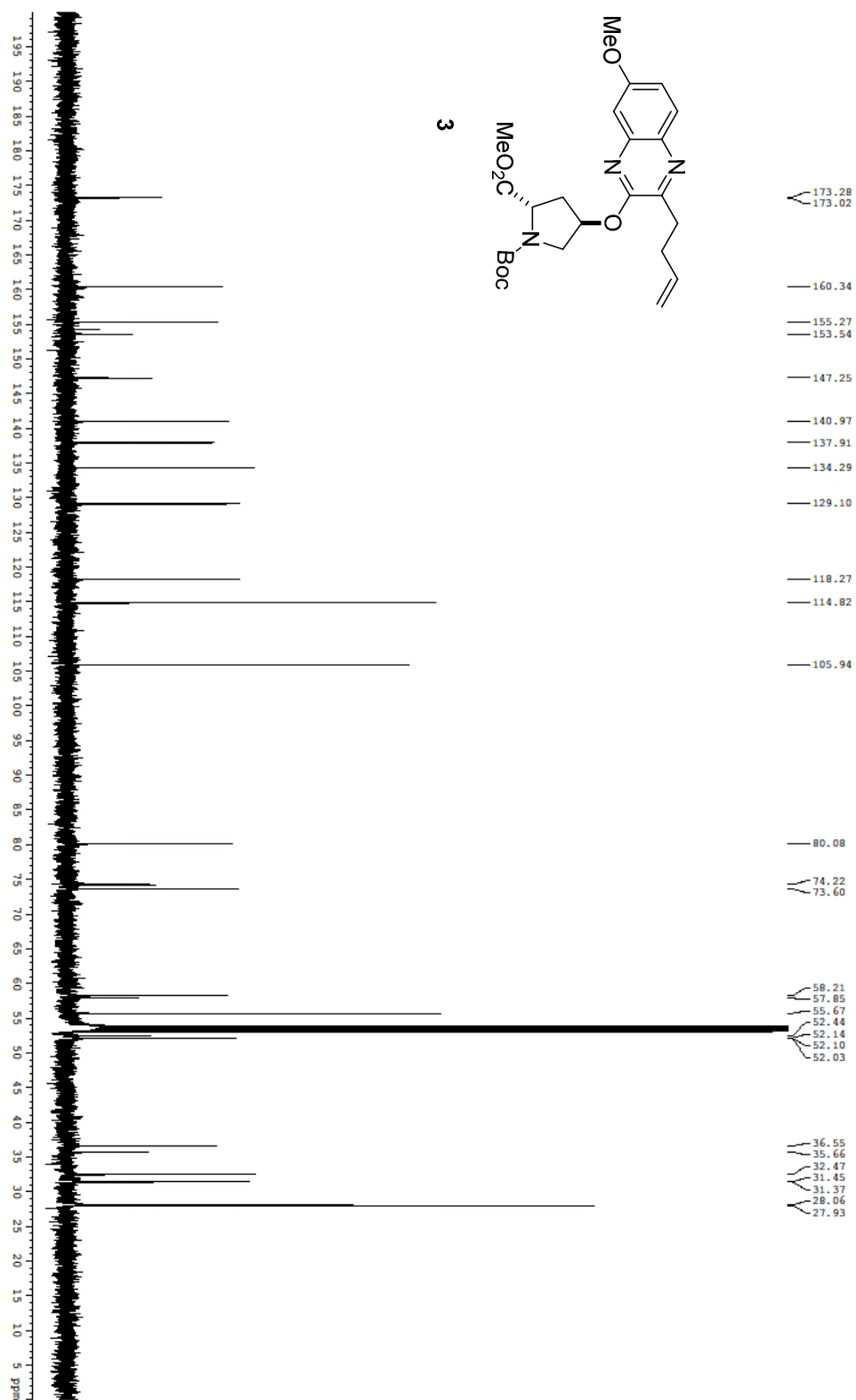
brought out of the glovebox and separately heated to the following temperatures independently sealed at 23, 50, 75, and 95 °C in an oil bath for 24 hours.<sup>10</sup> A <sup>1</sup>H NMR spectrum was taken to determine the percent conversion of 1-hexene (**20**) to 5-decene (**21**) for each sample. All samples were observed to show a clean conversion of starting material to desired product where observed. The <sup>1</sup>H NMR spectrum of the desired product matched the corresponding <sup>1</sup>H NMR's of *cis*-5-decene and *trans*-5-decene which are commercially available.<sup>4</sup>



Entry <sup>a</sup>	Temperature (°C)	Conversion (%) <sup>b</sup>
1	23	<5
2	50	8
3	75	27
4	95	90

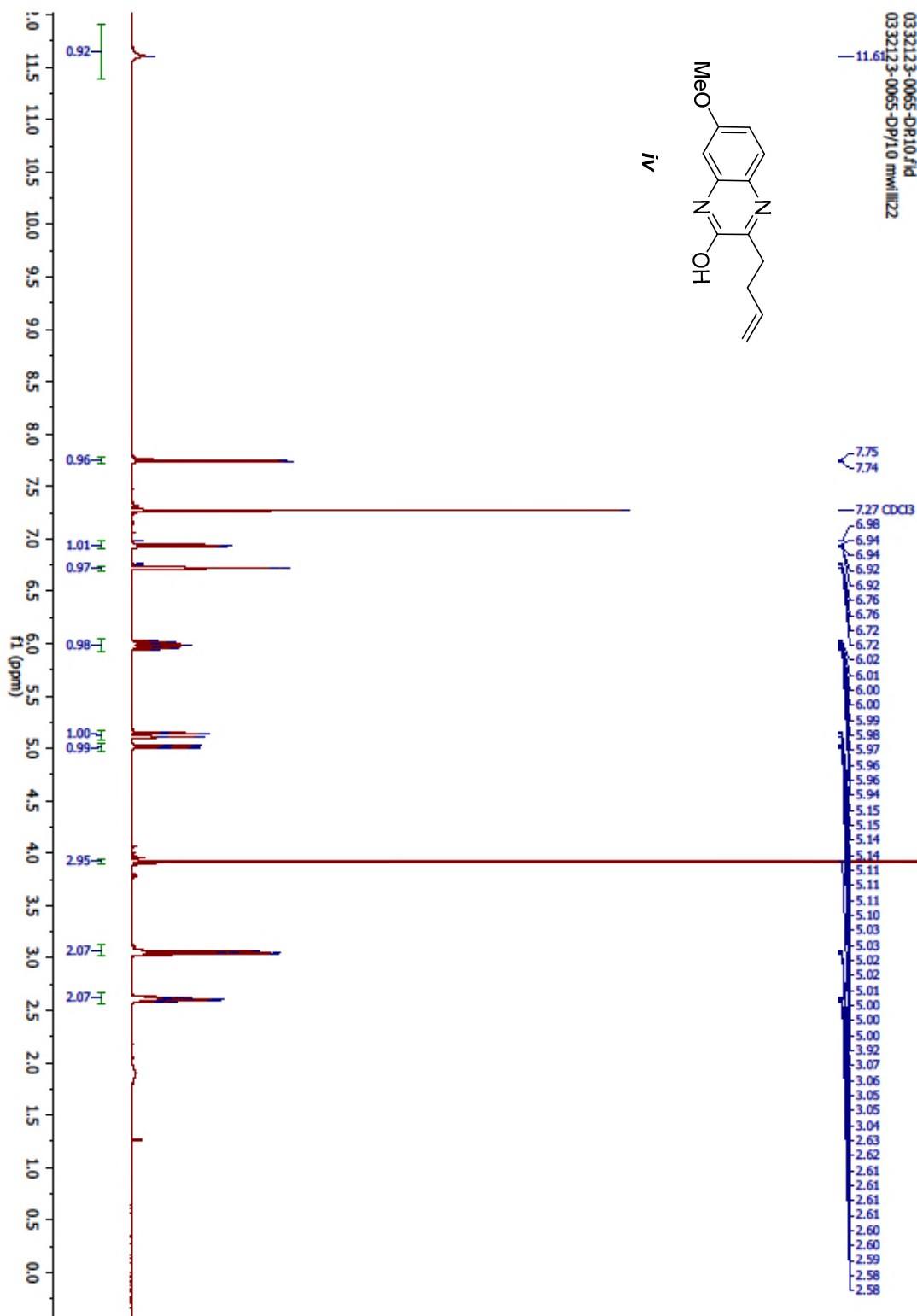
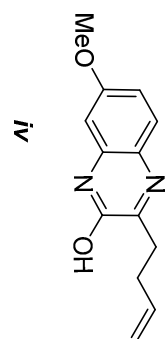
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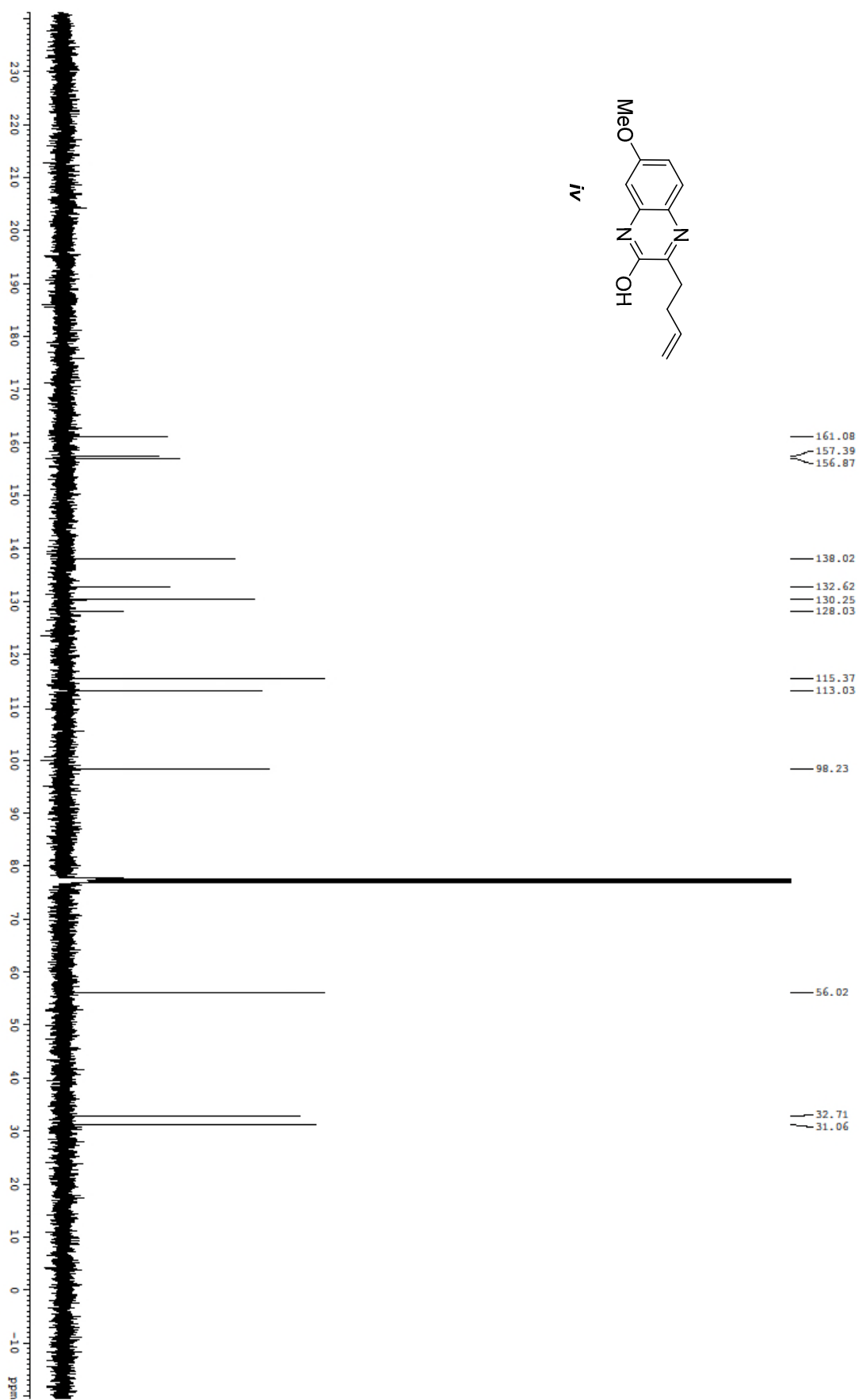
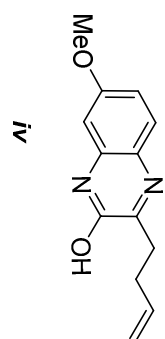


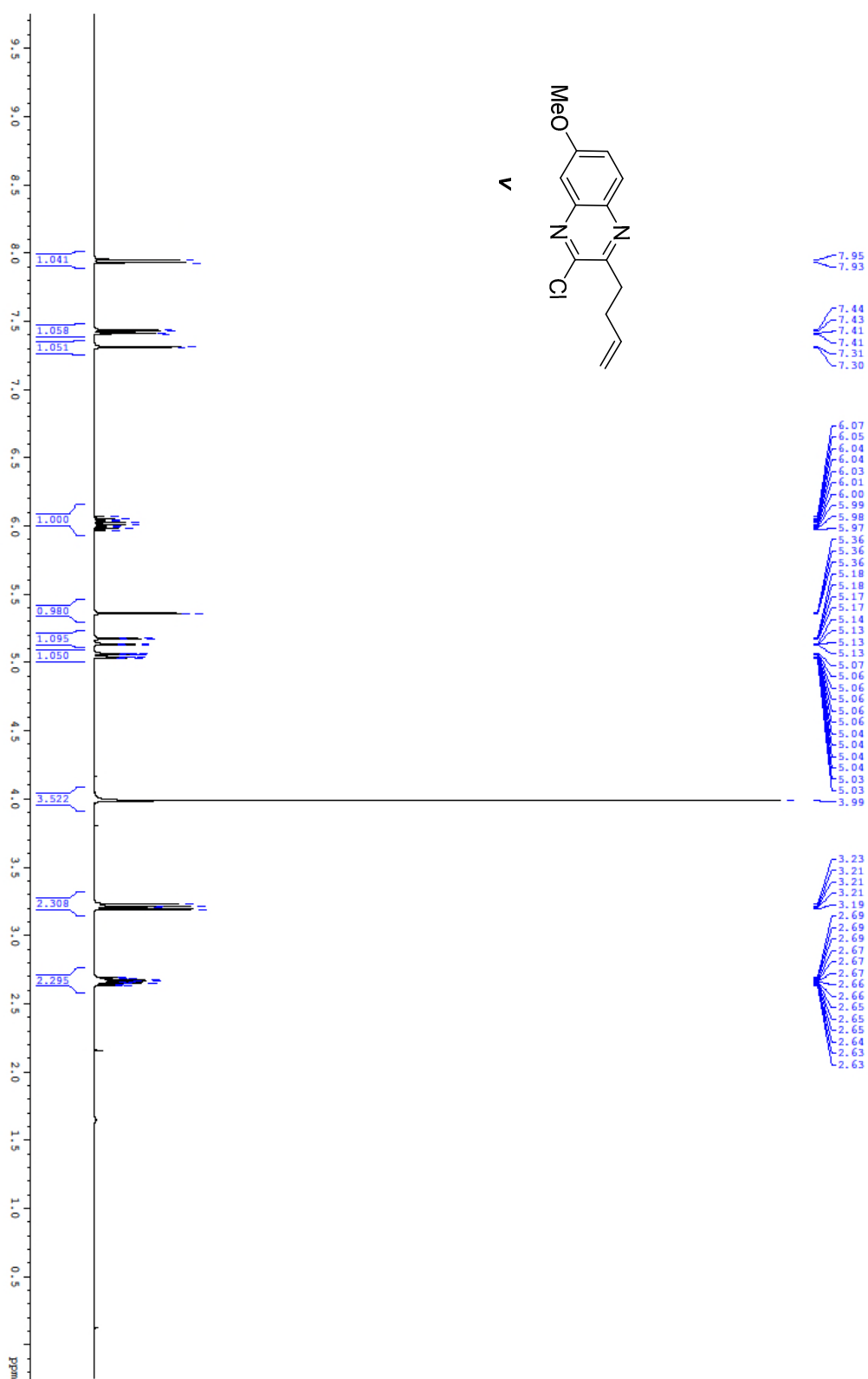


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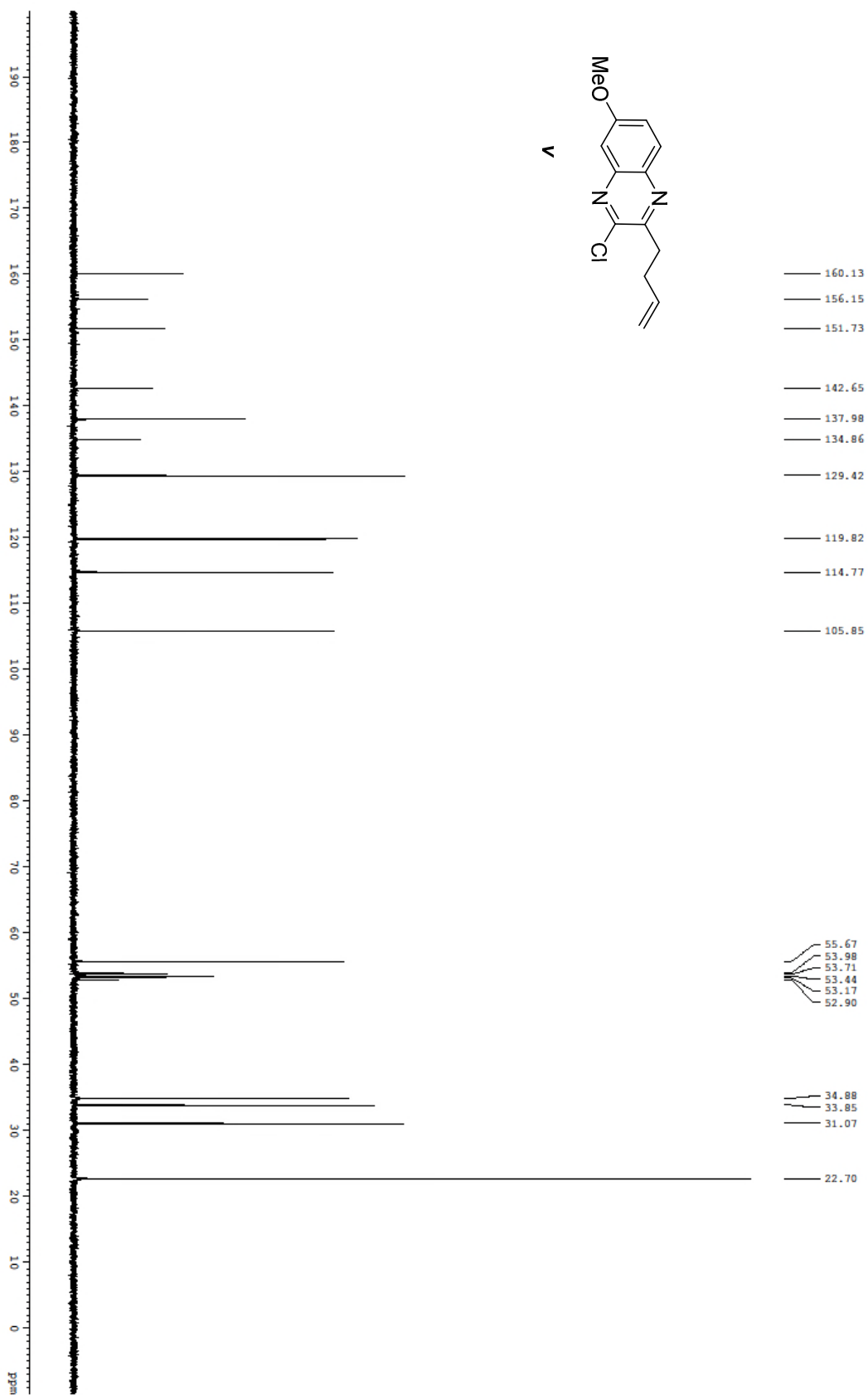
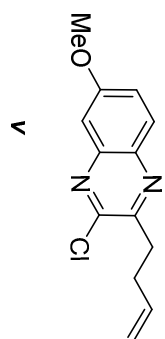
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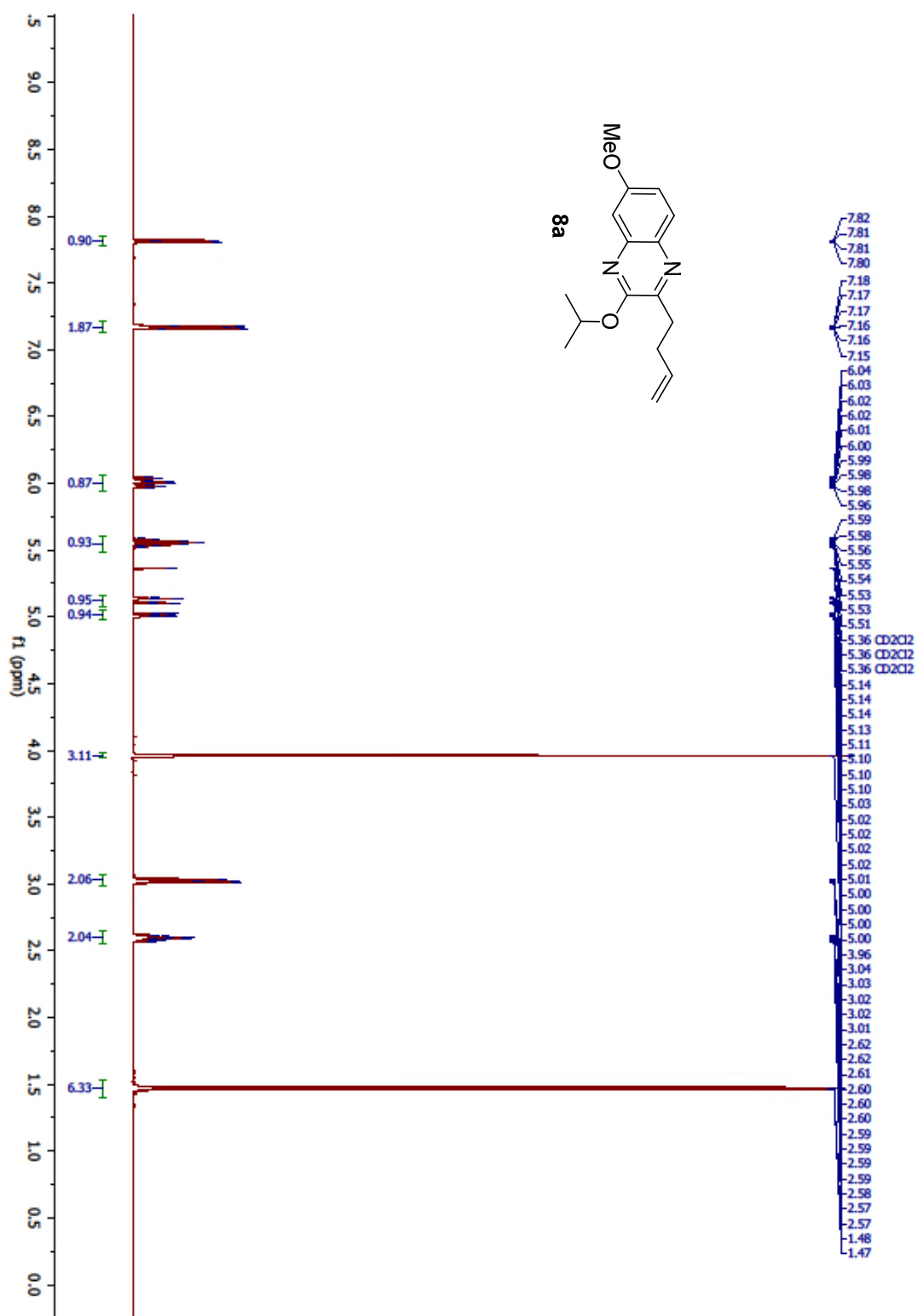


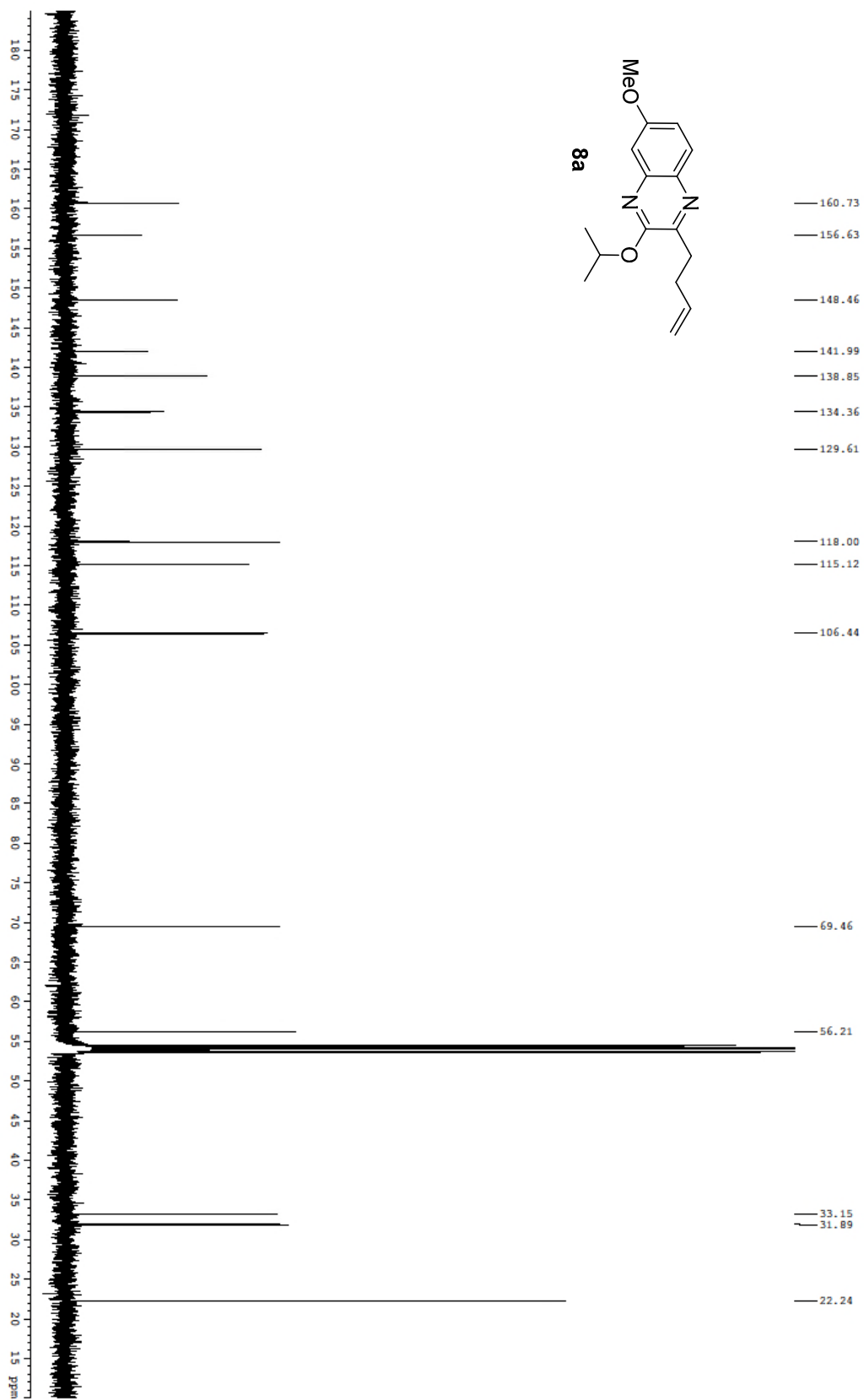
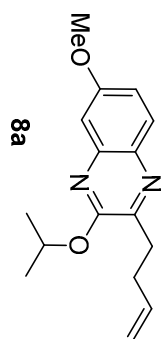


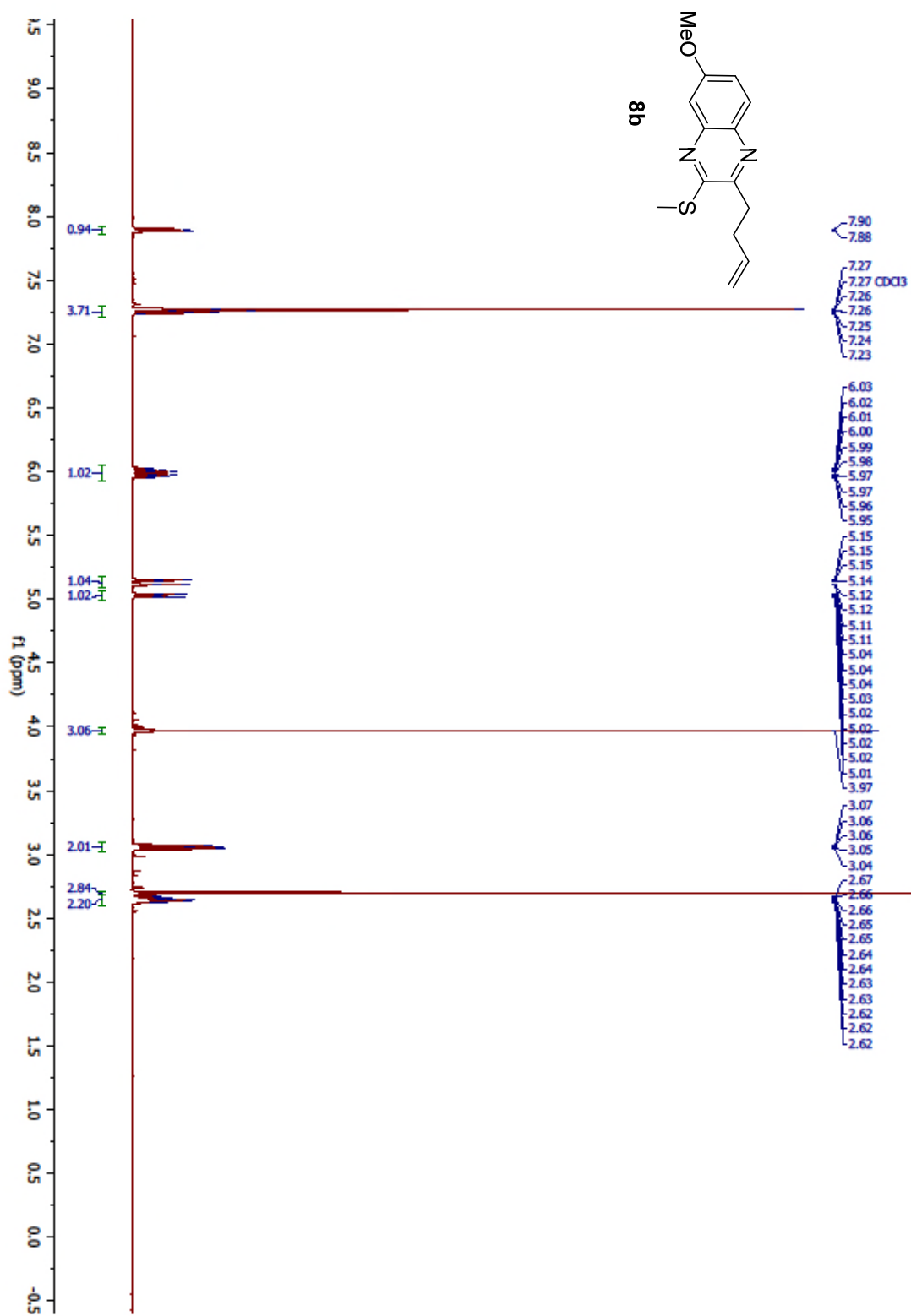


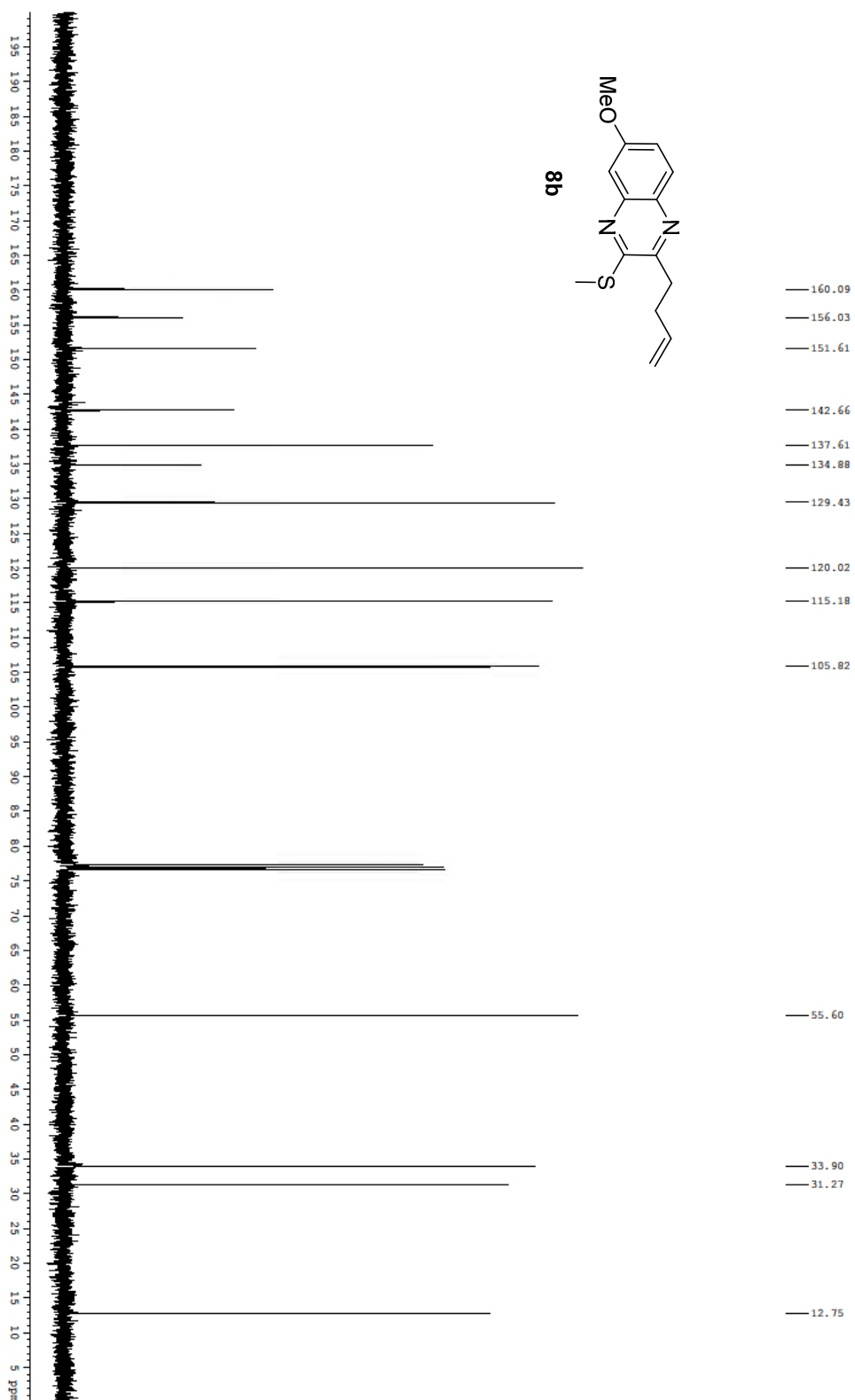


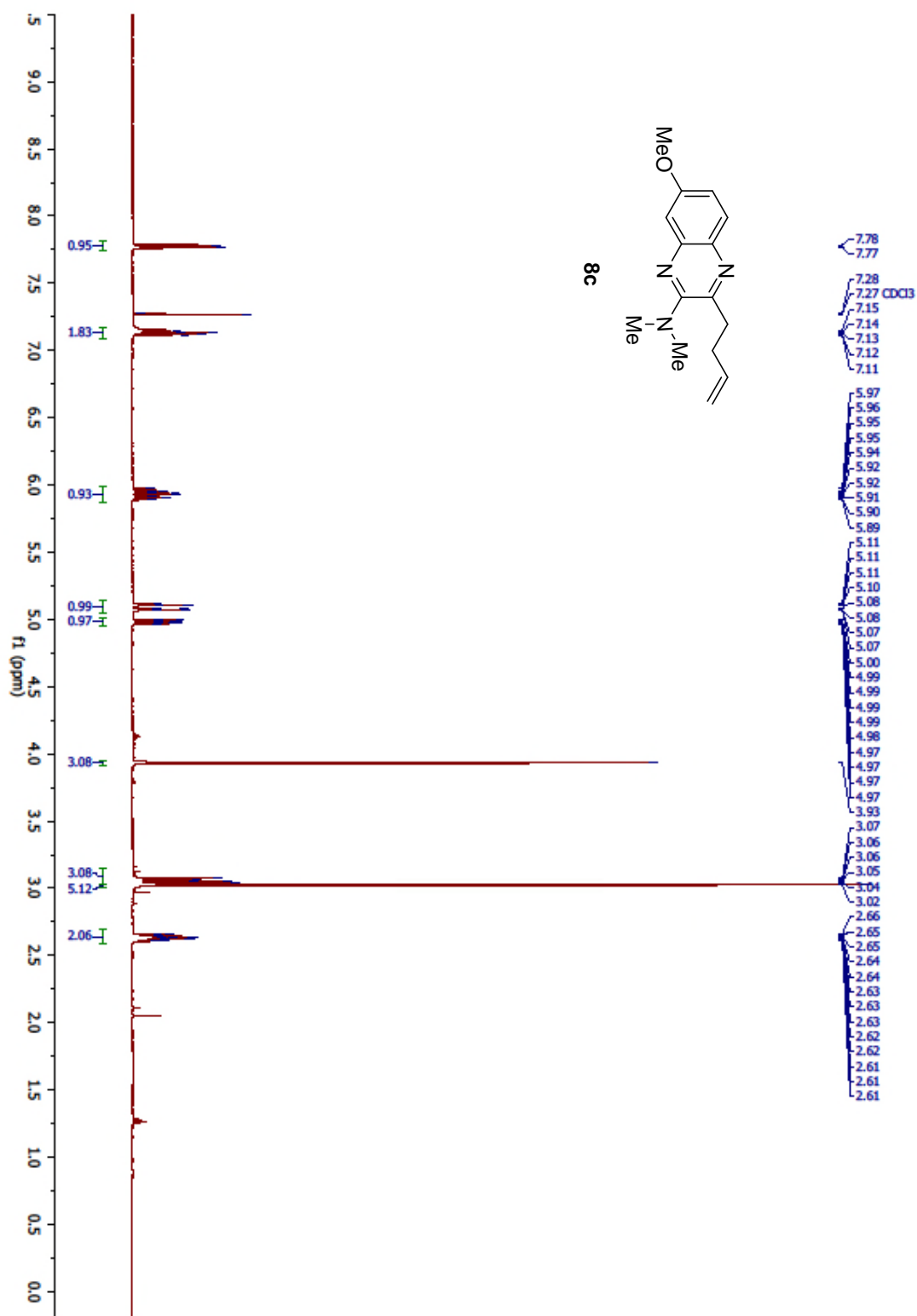


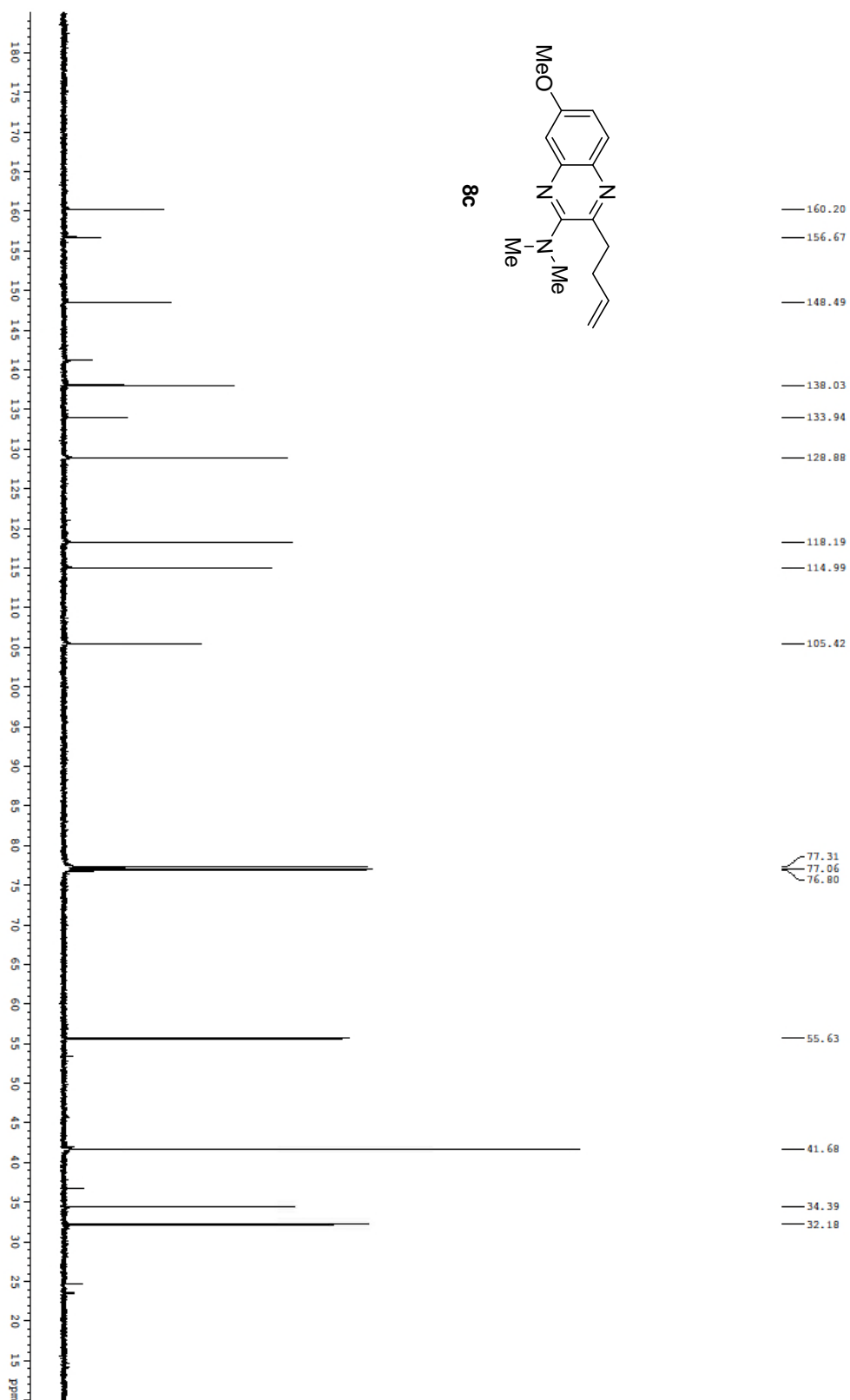


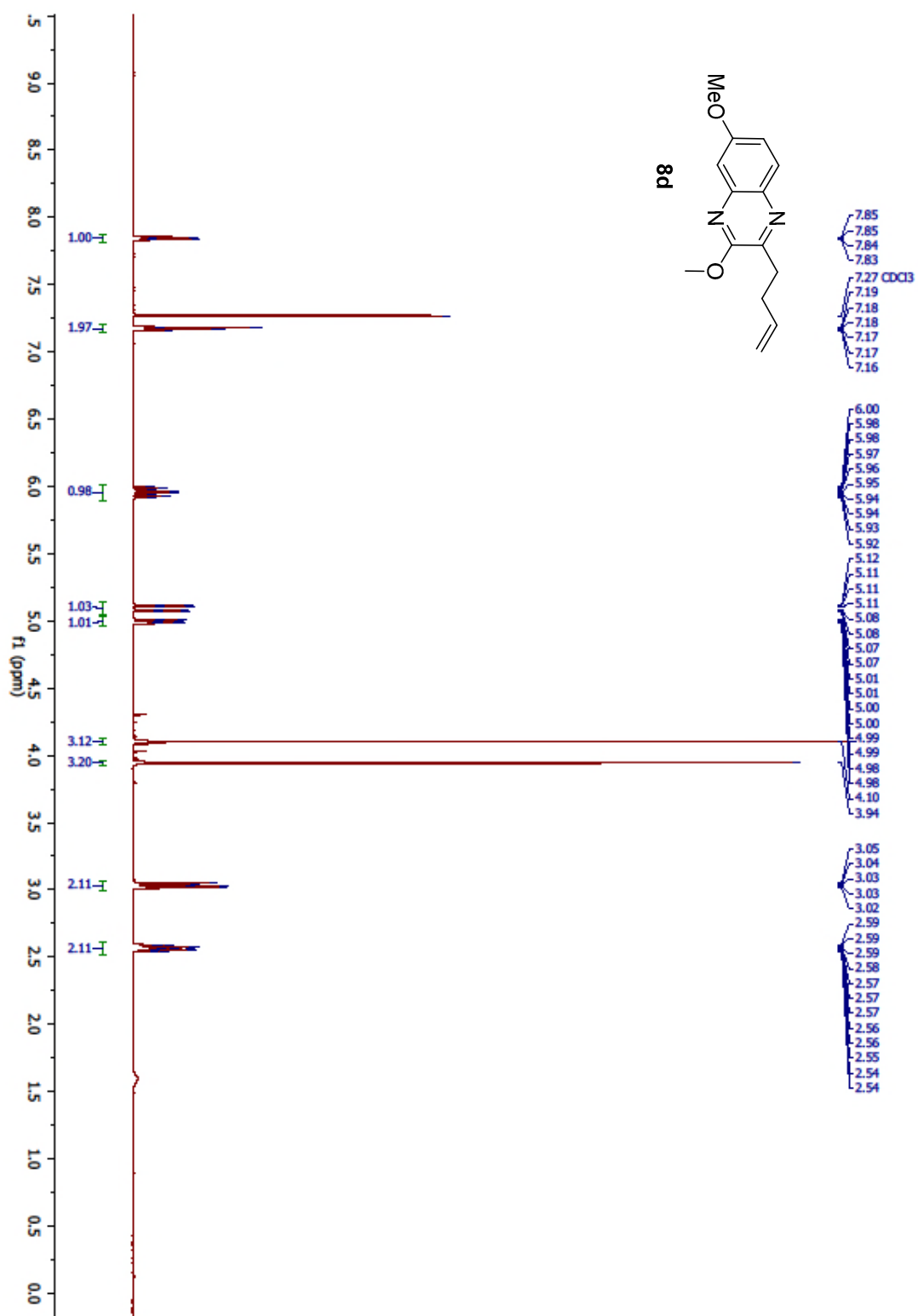




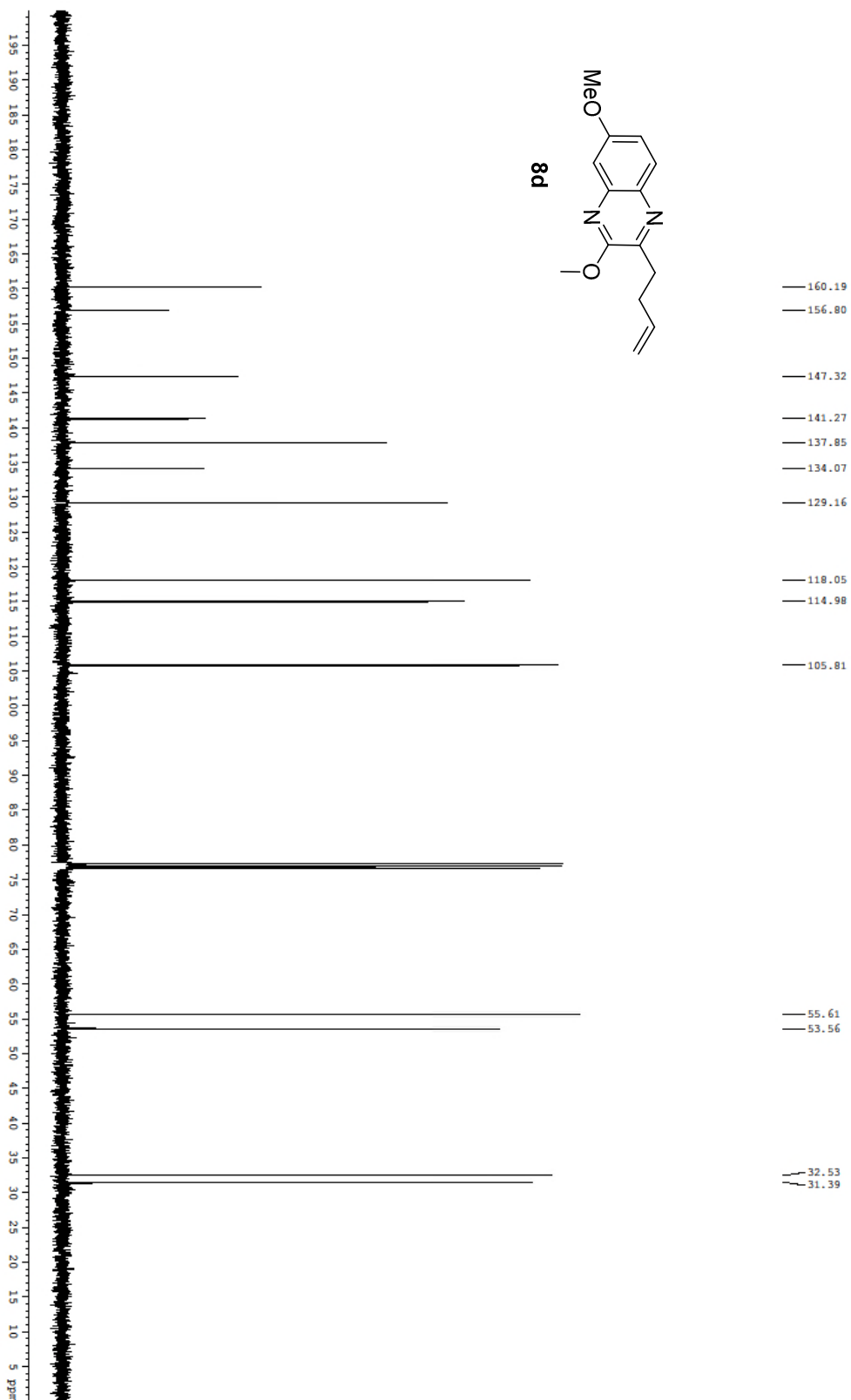
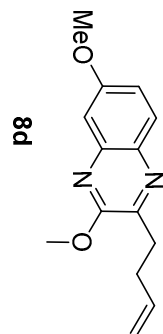


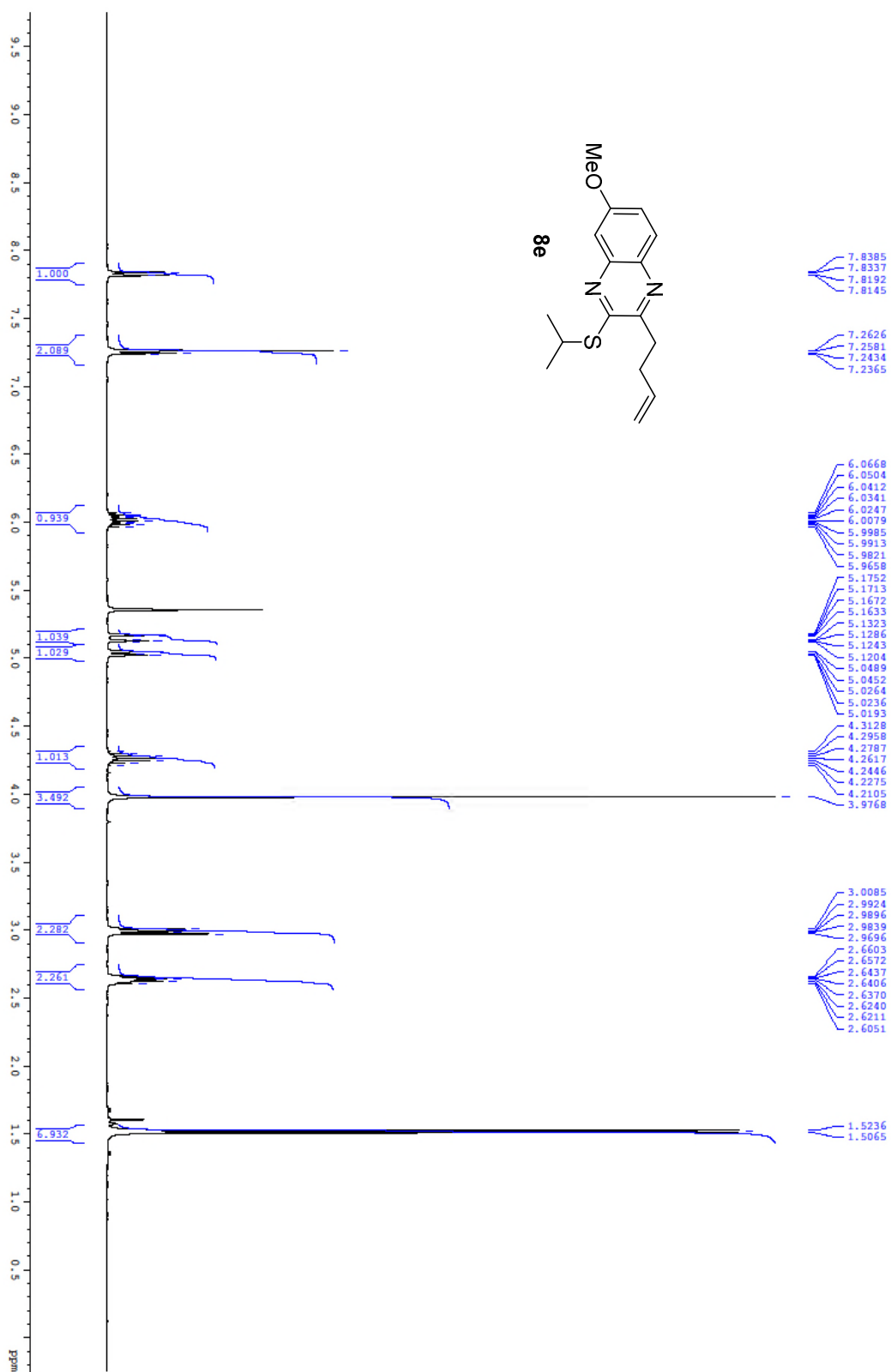


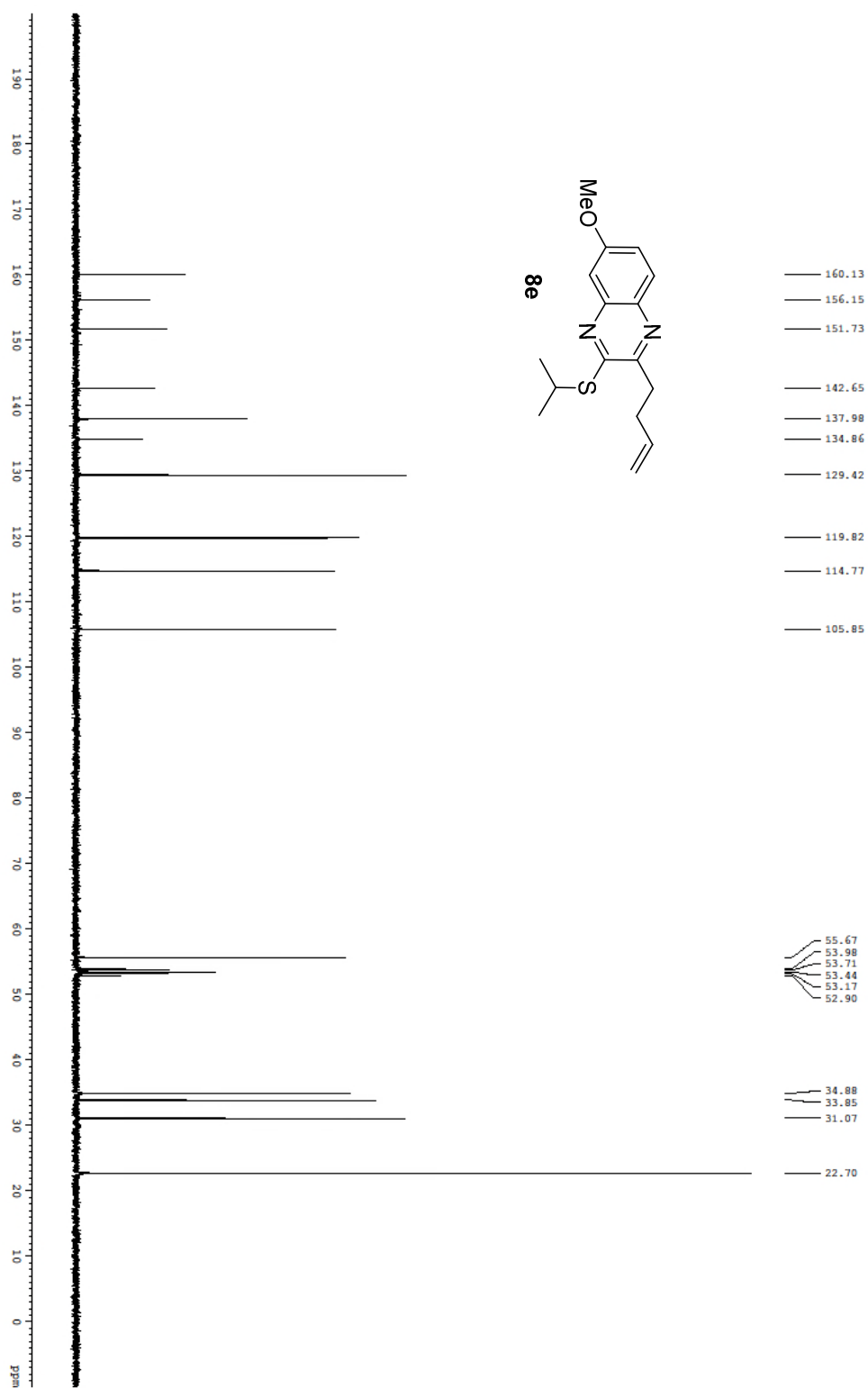


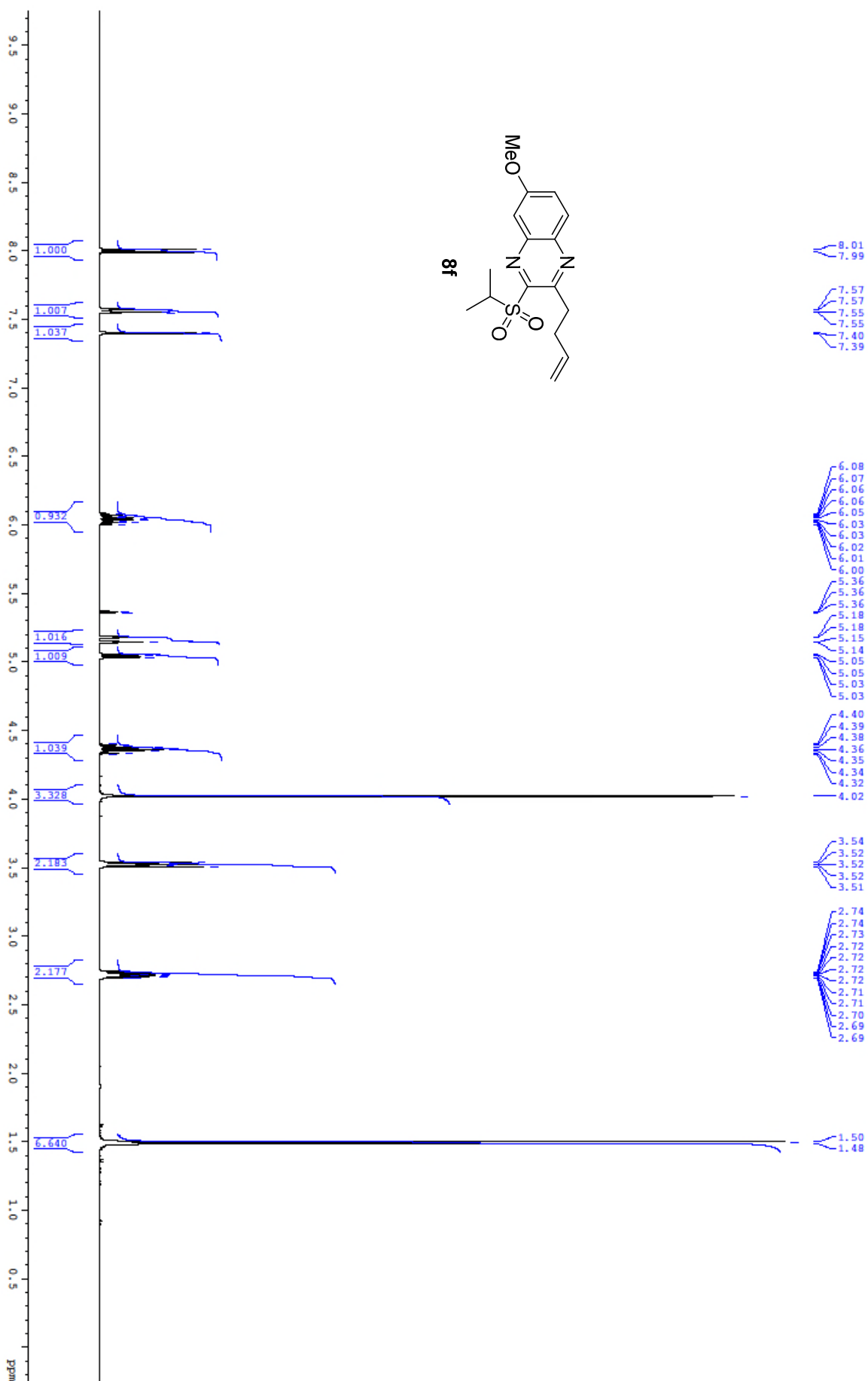


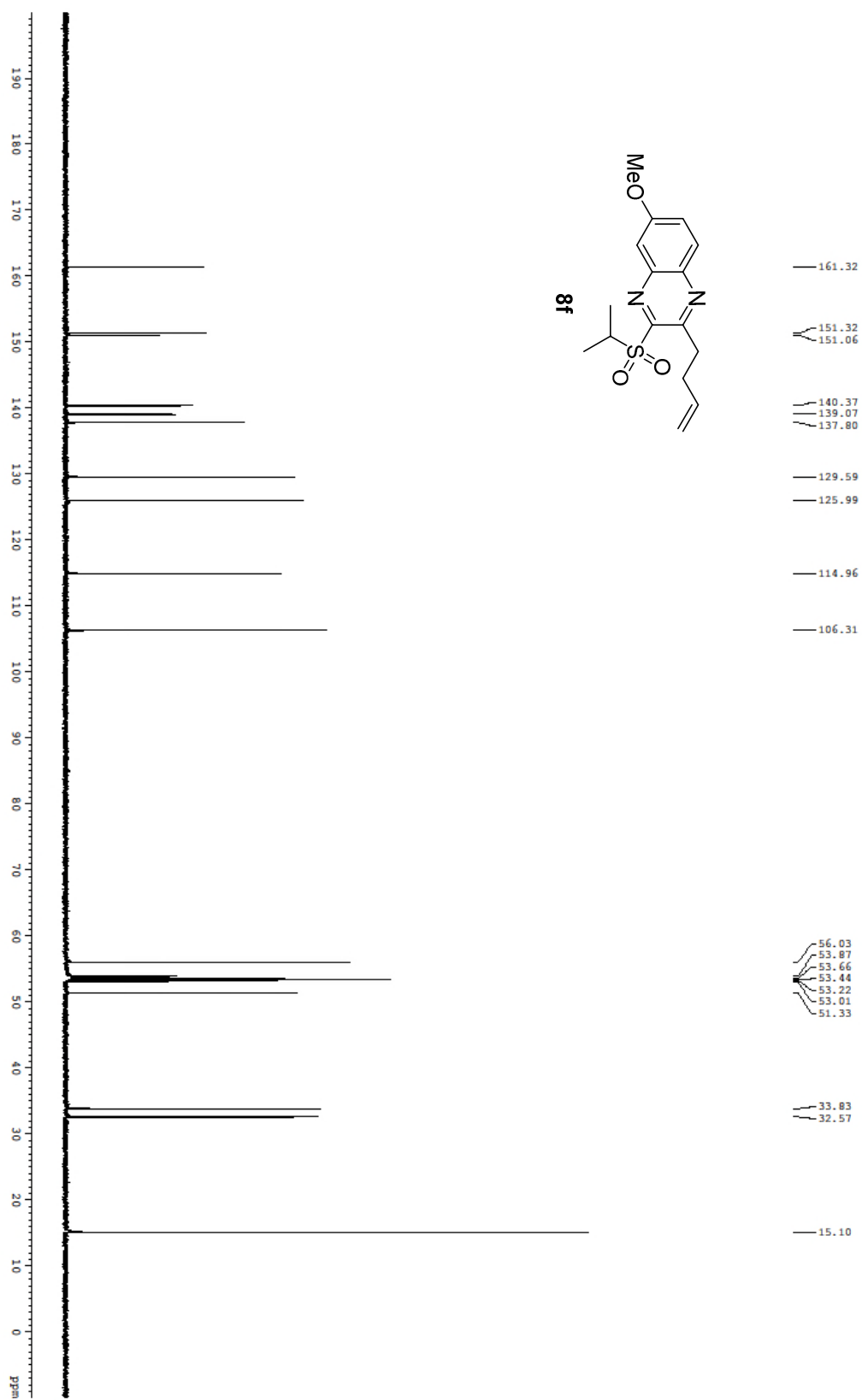


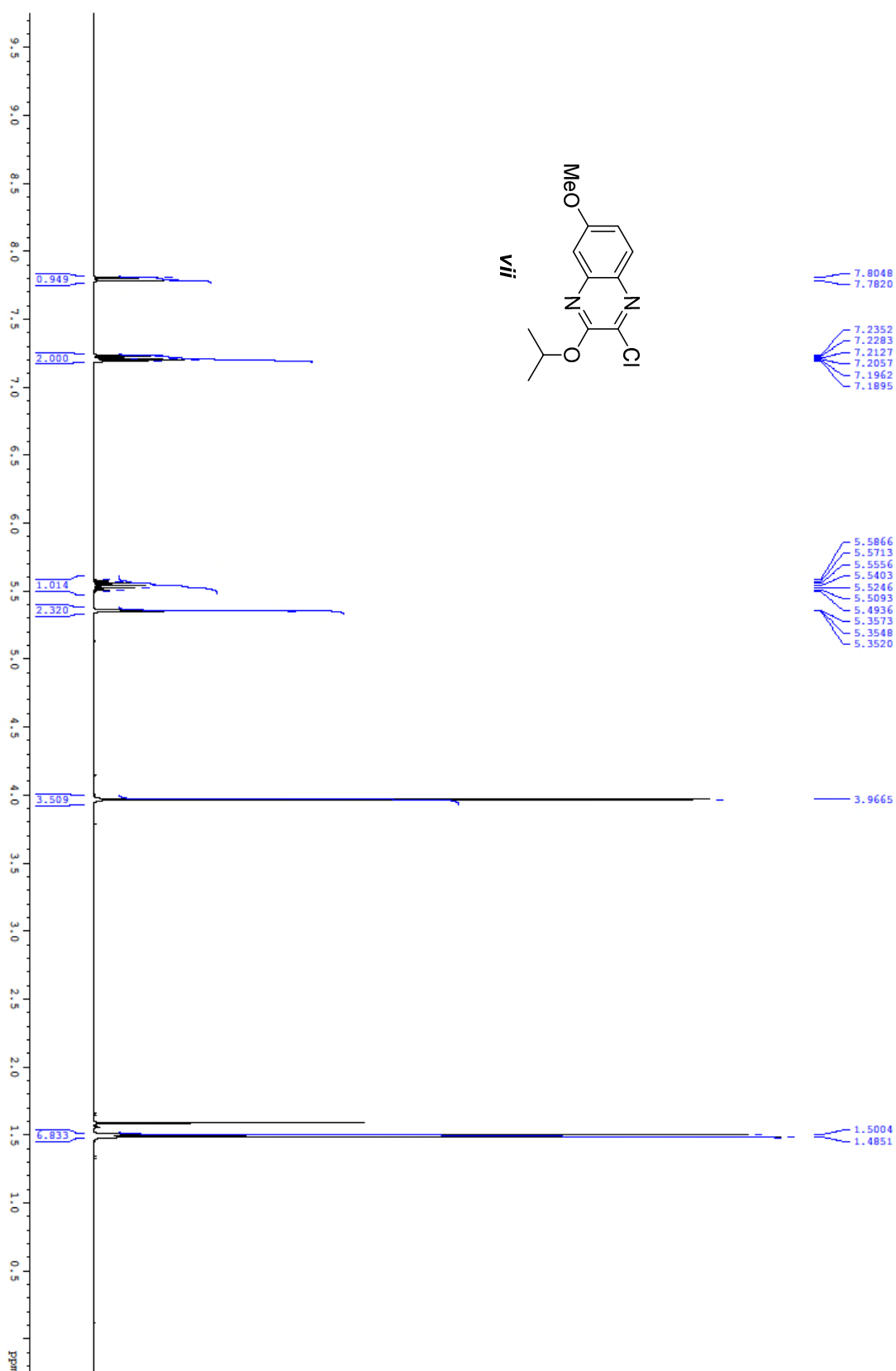
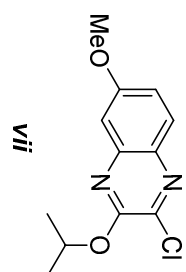


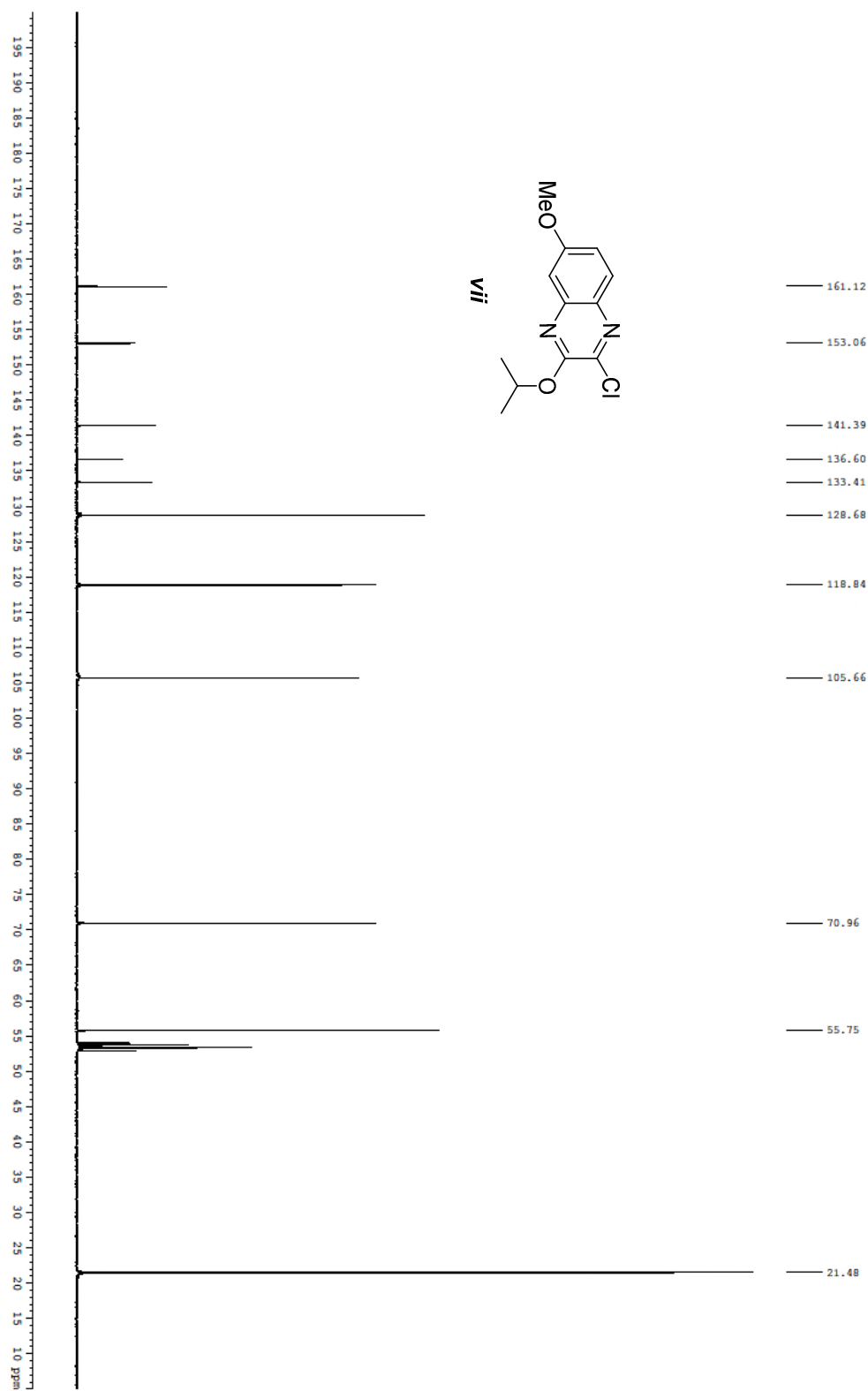


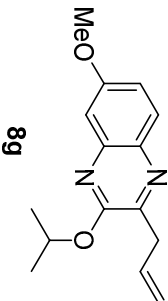




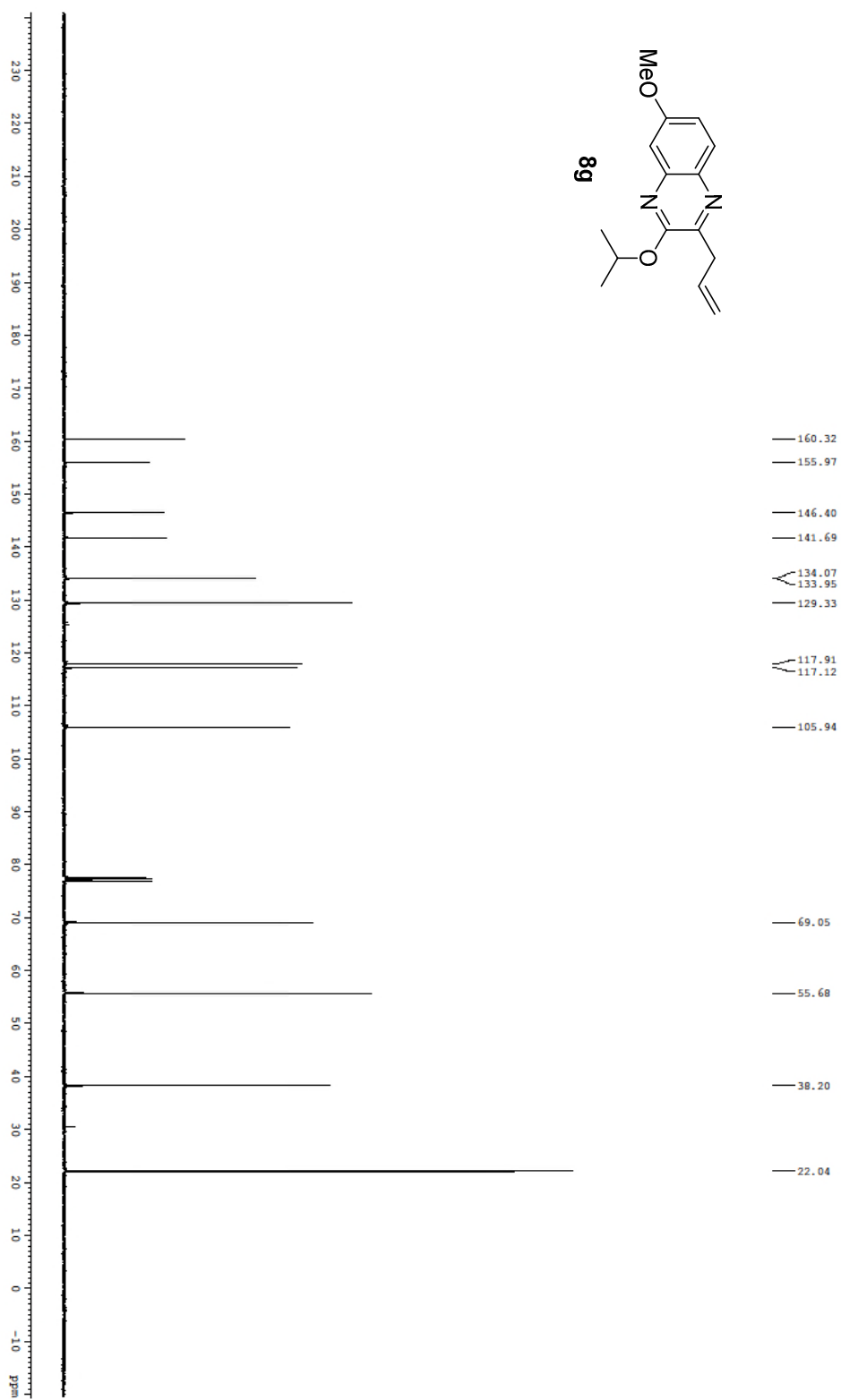
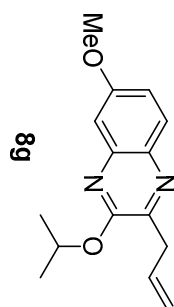


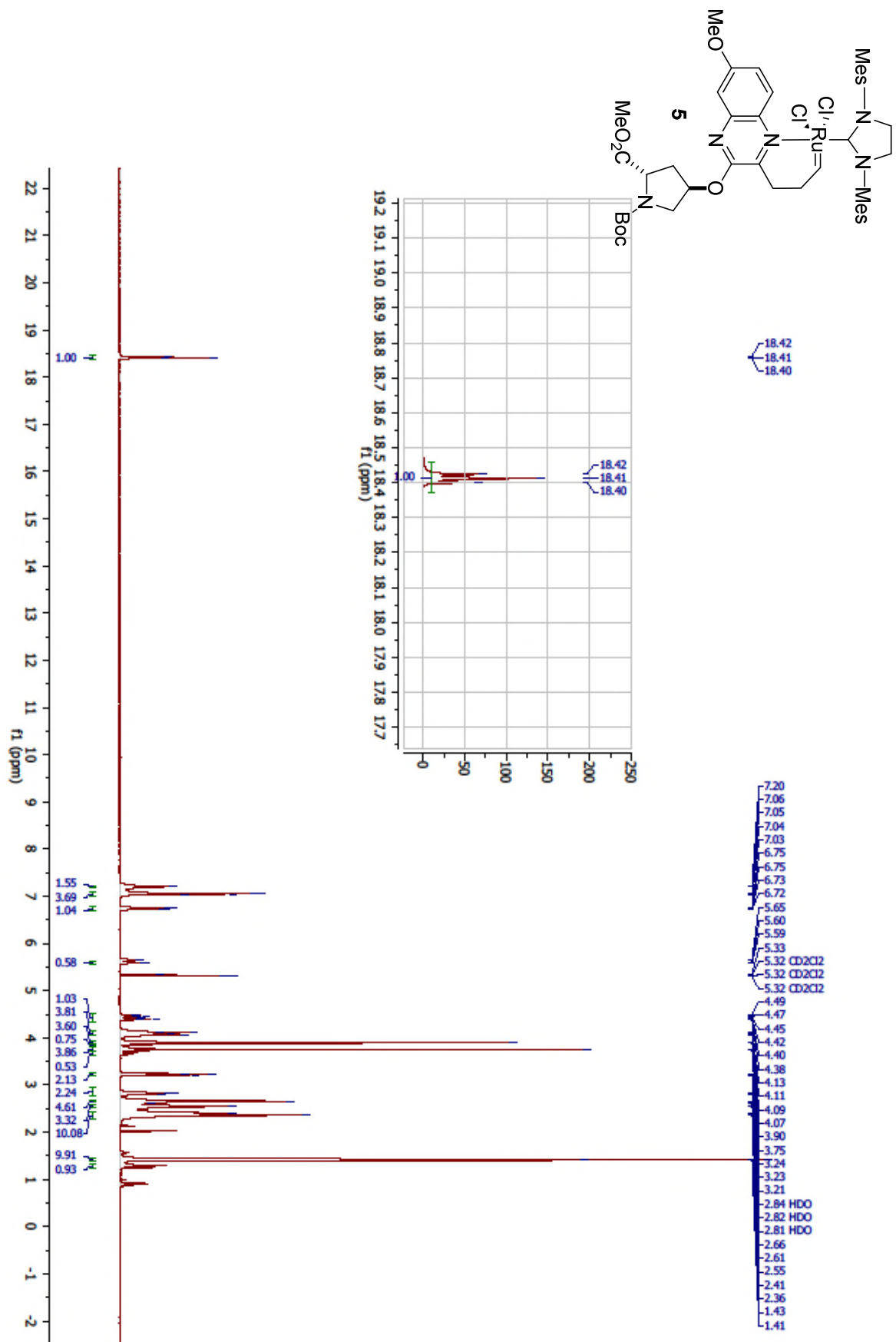


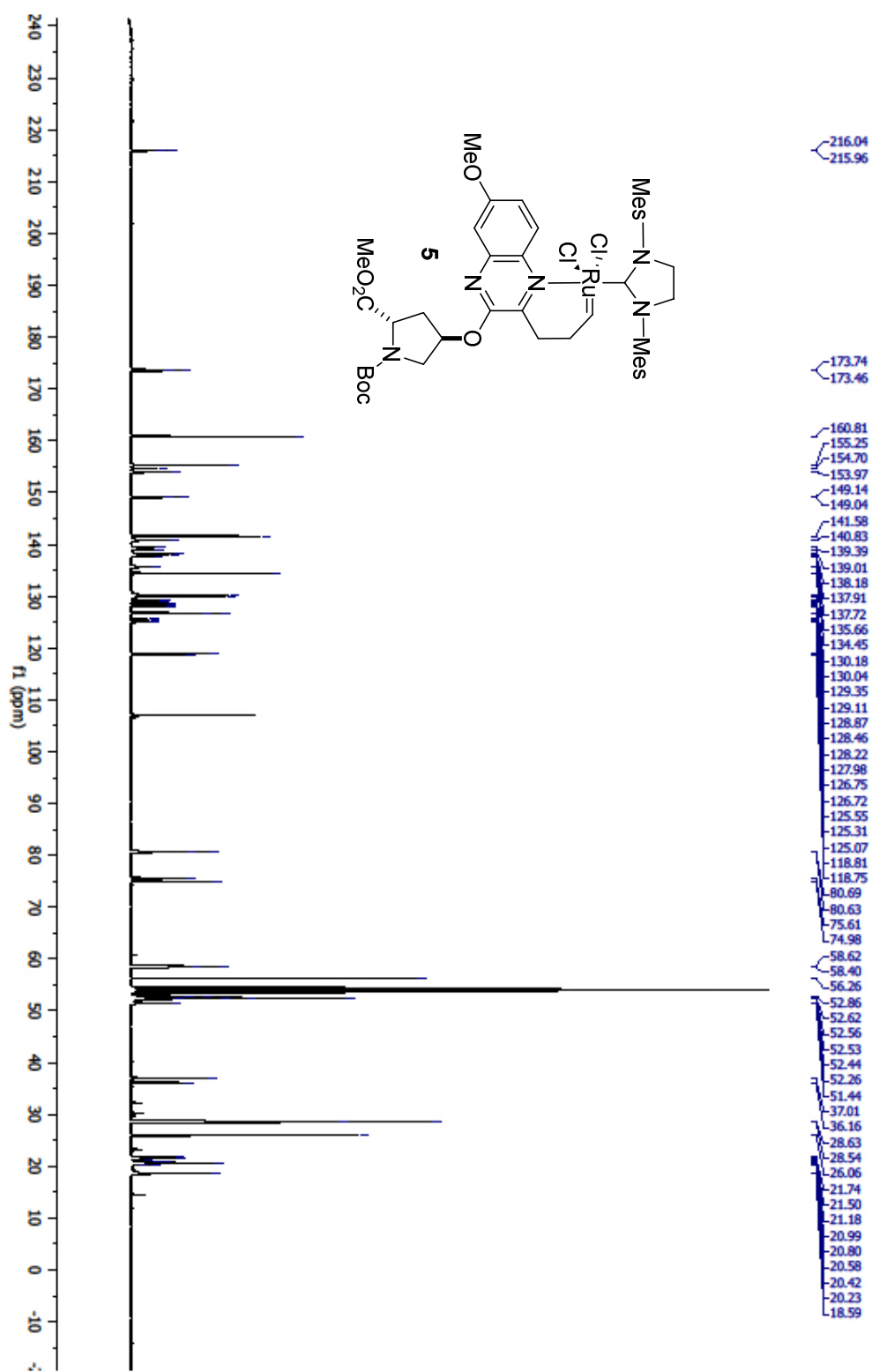


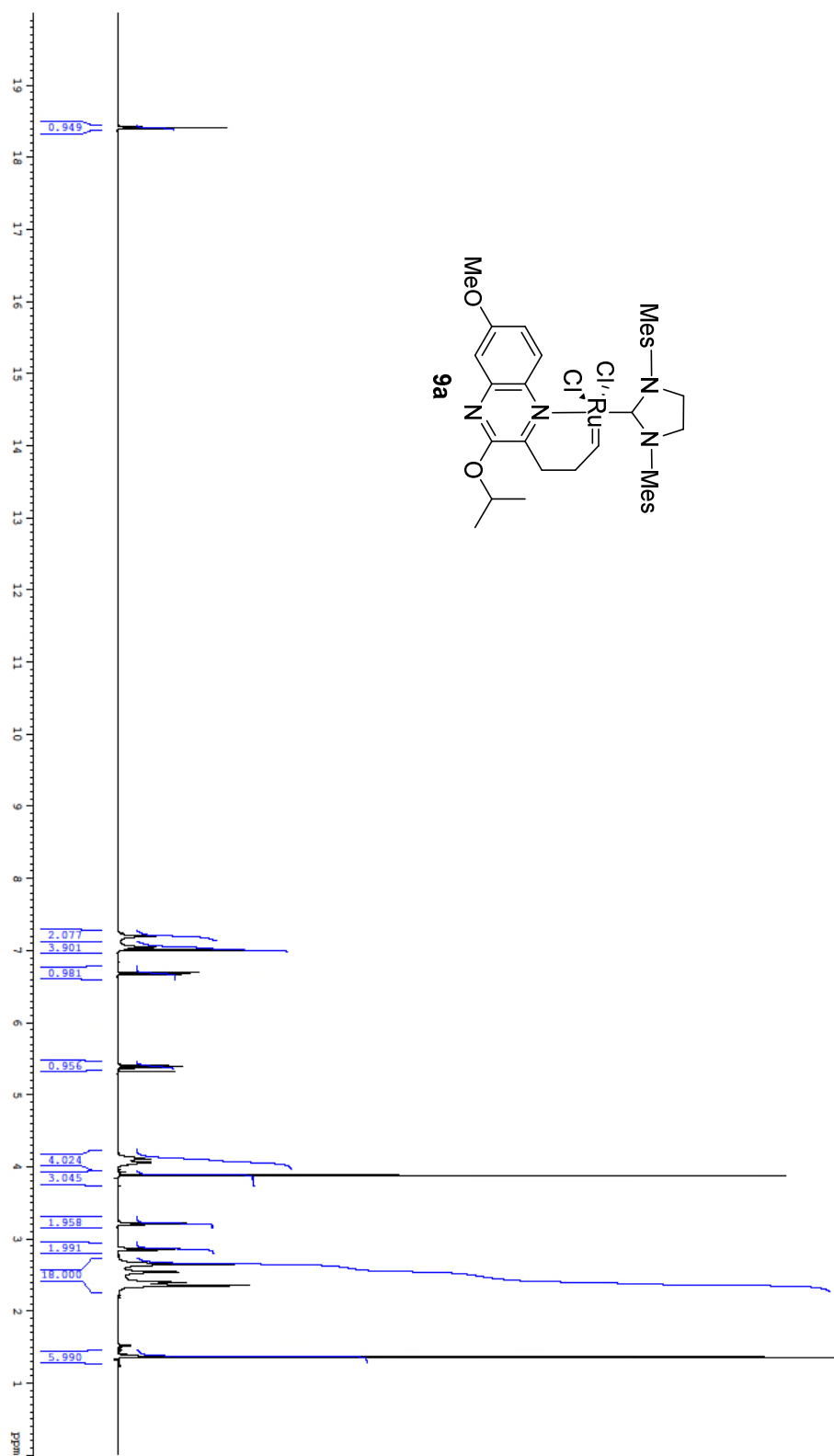


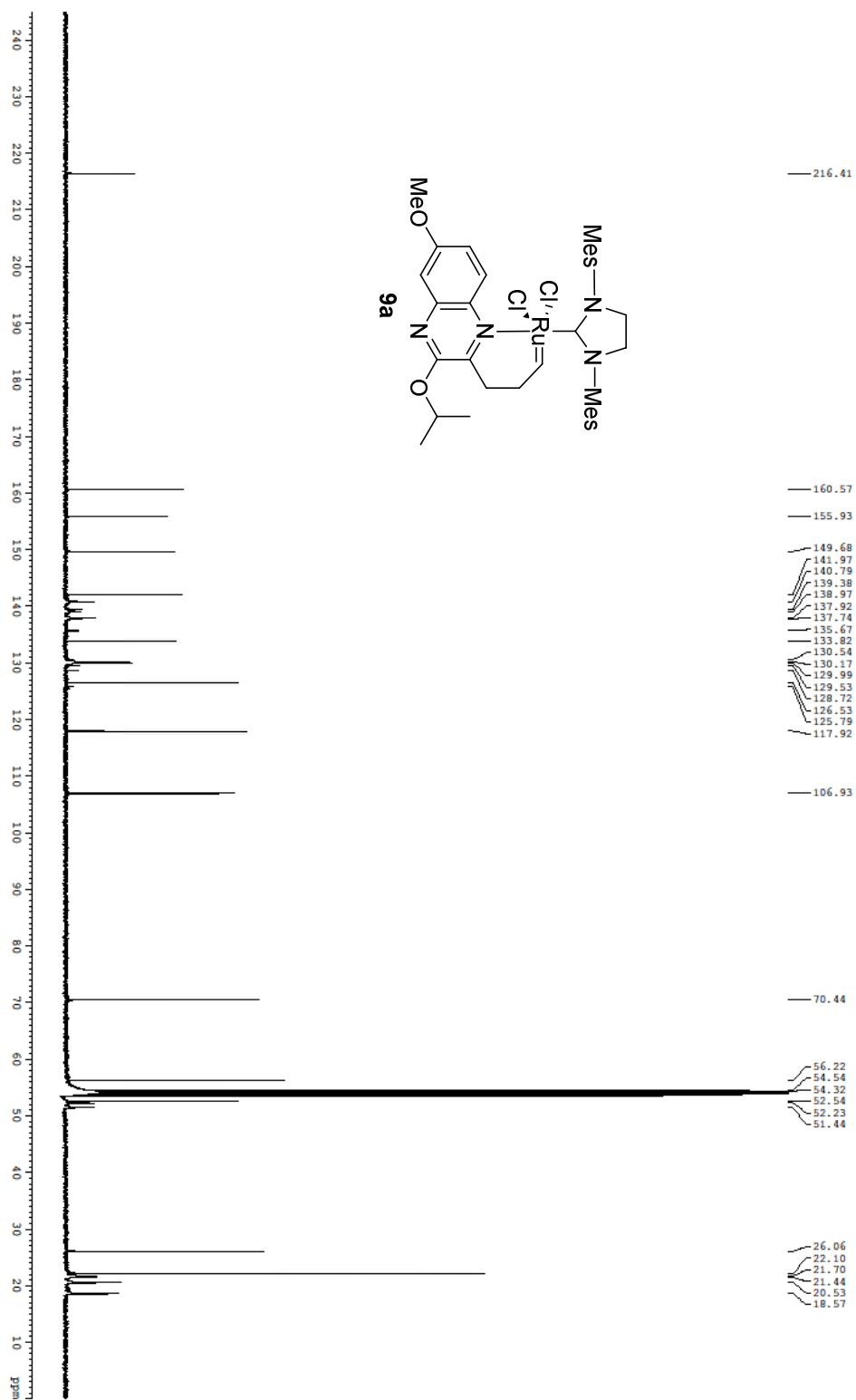


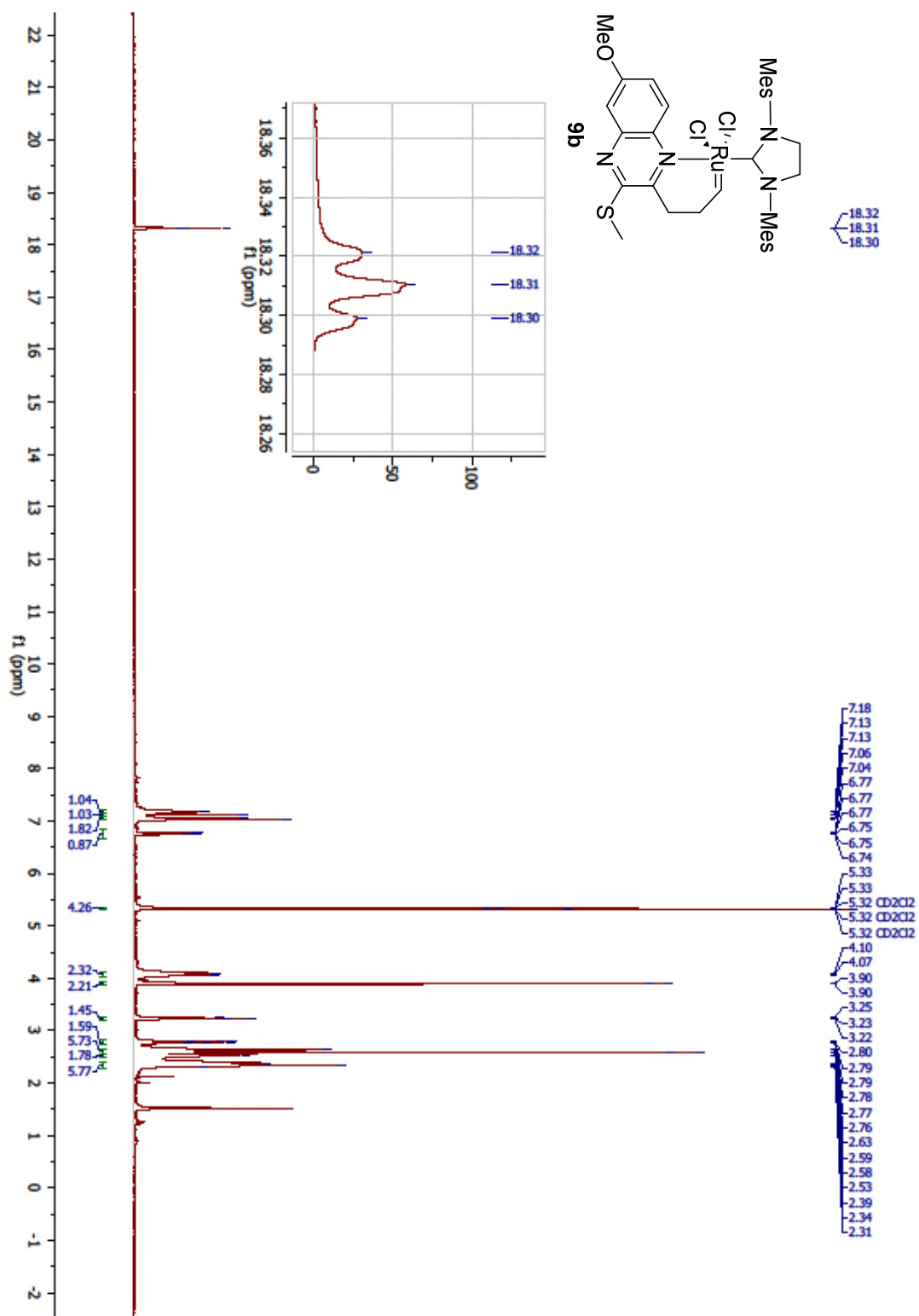


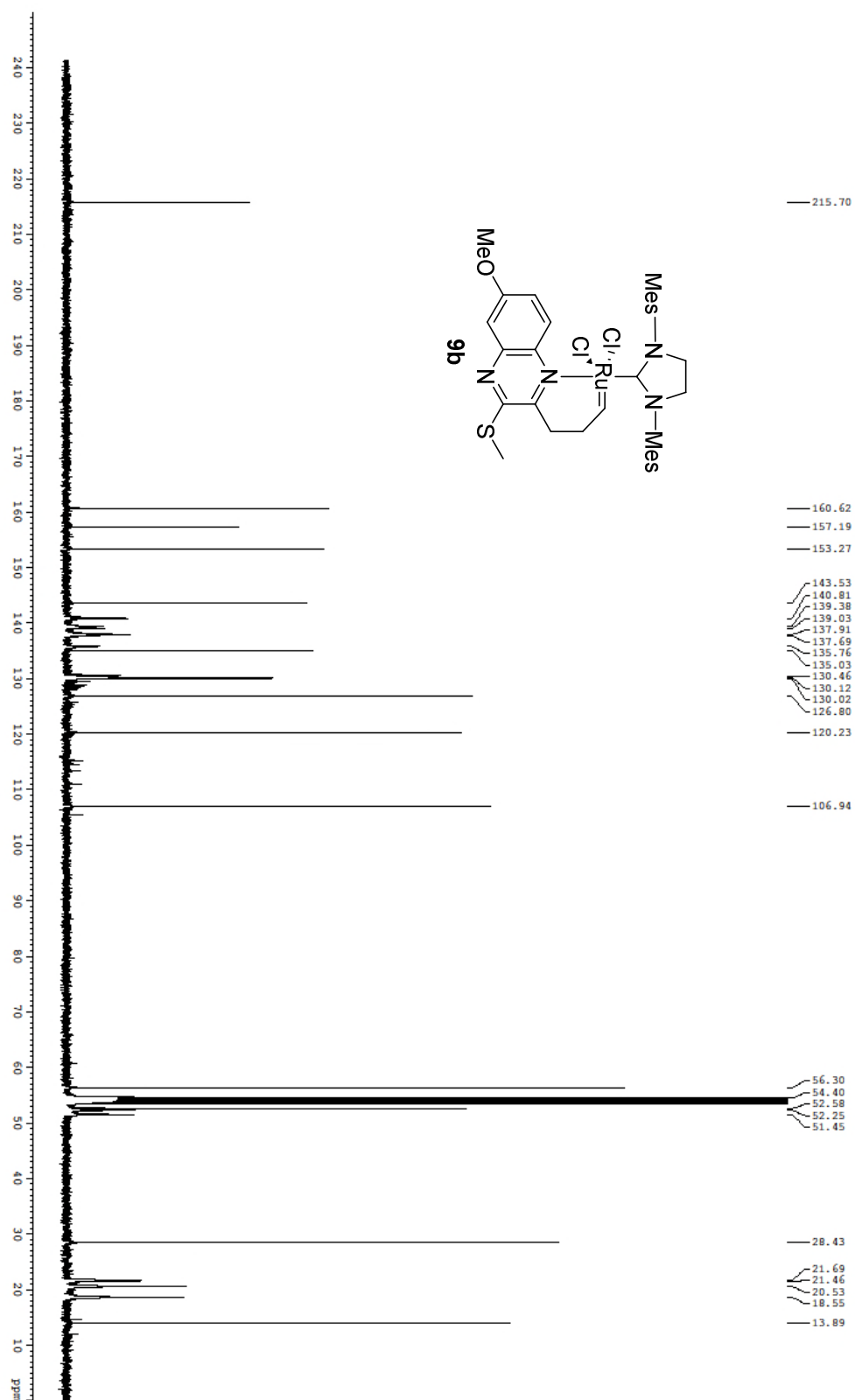


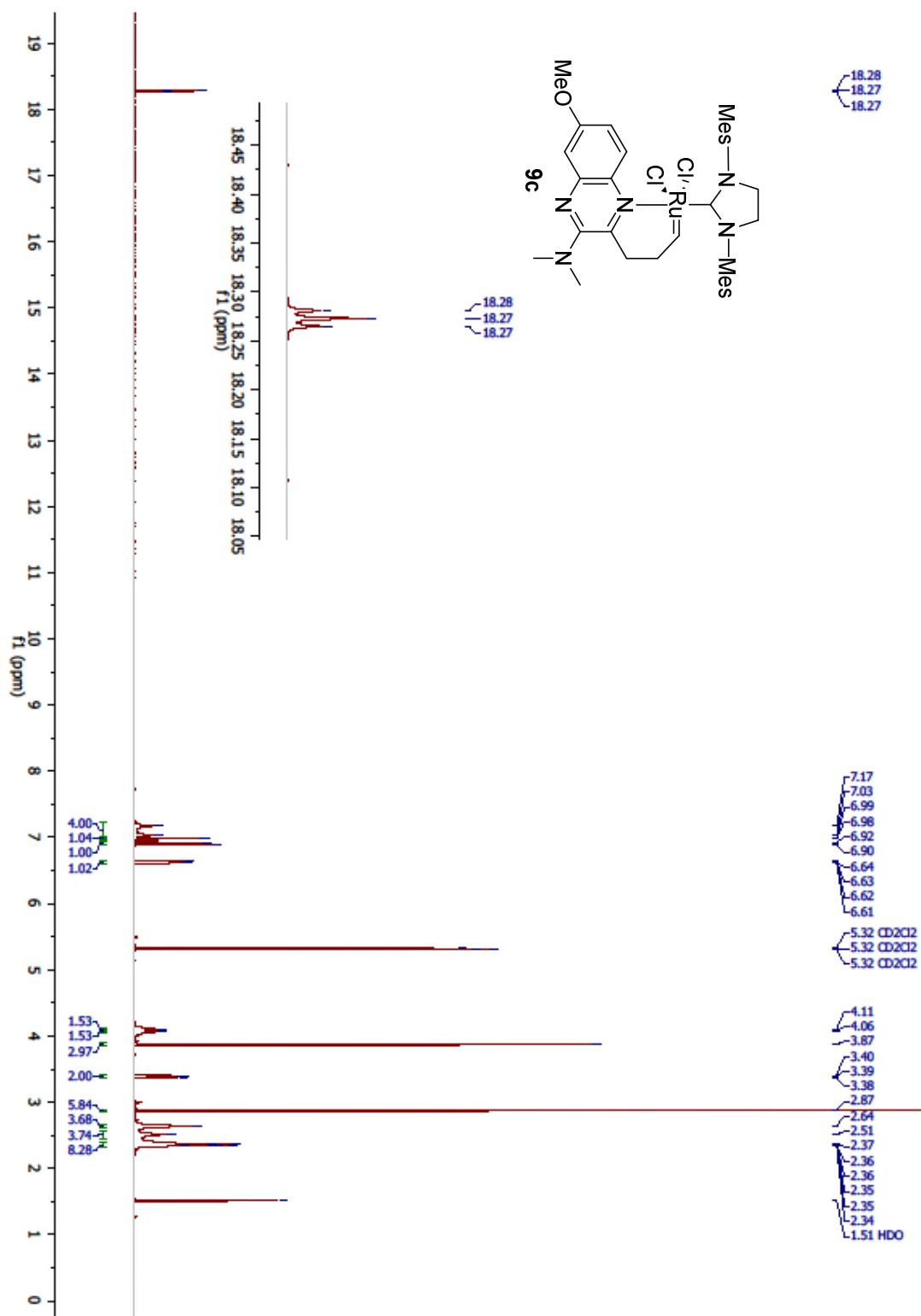




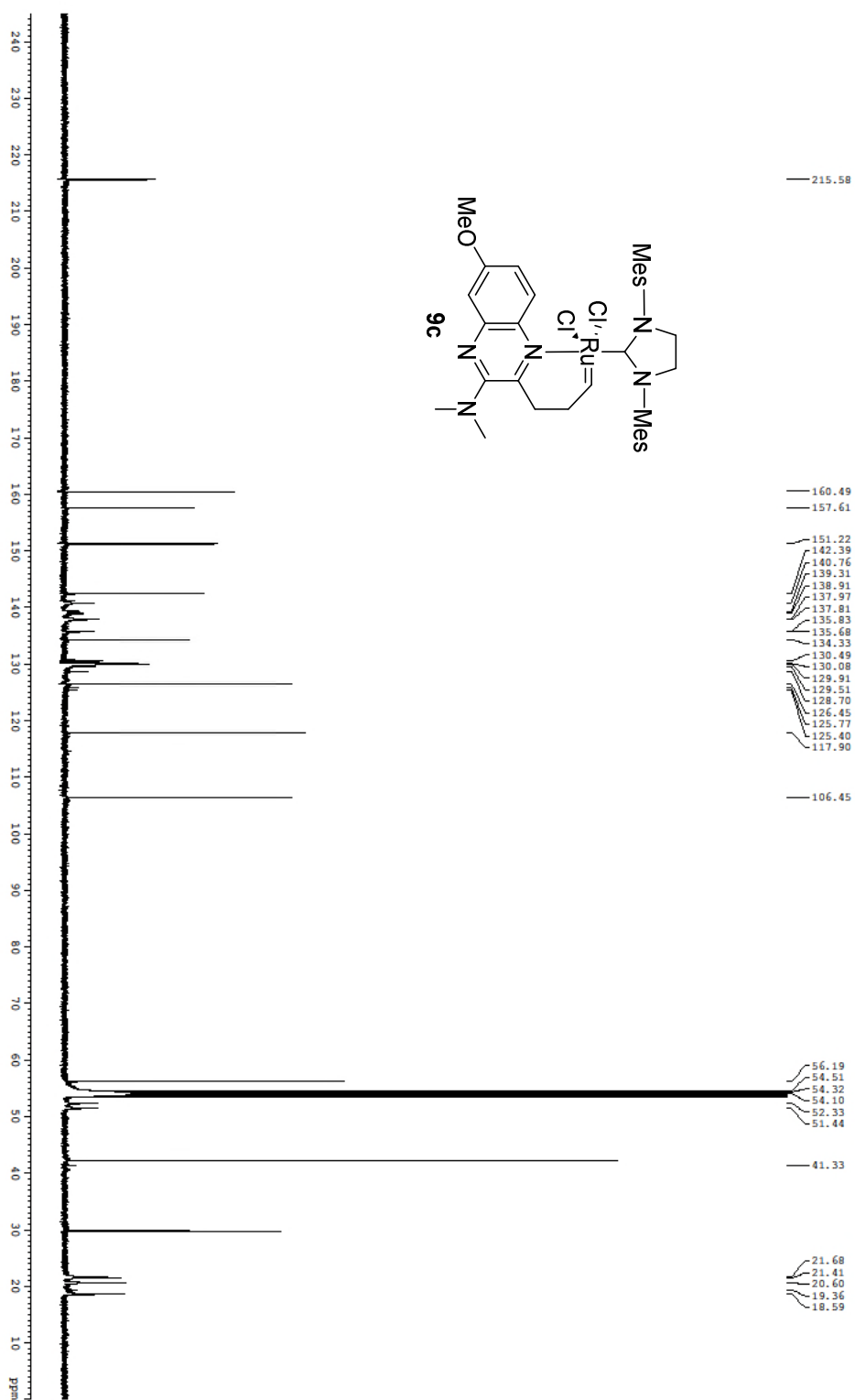


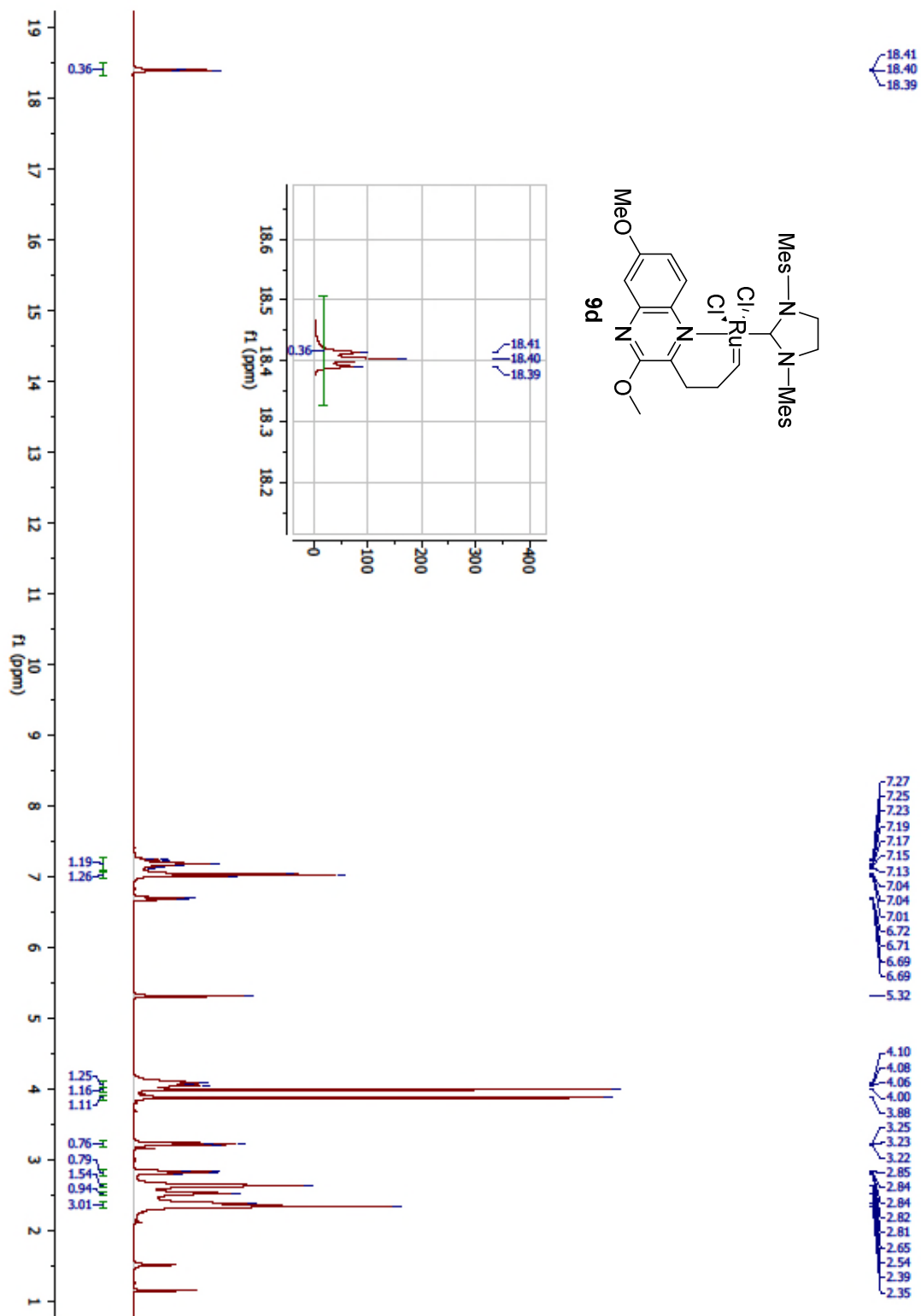


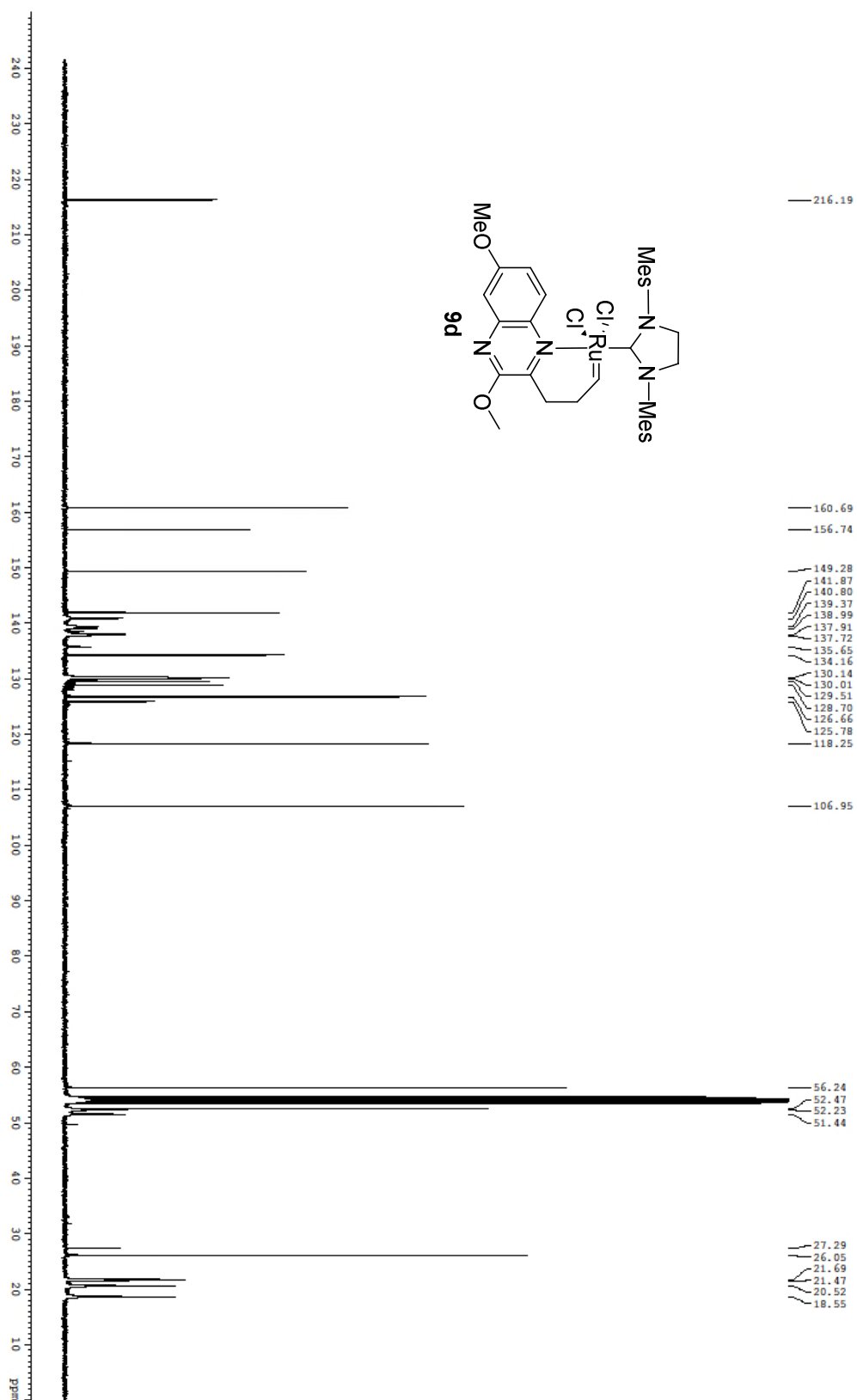












0361051-0015-6/1 kongjo  
nmr400c h-1

NAME 0361051-0015-6  
EXPNO 1  
PROCNO 1  
PROCNAME 20150602  
F2 - 500.132710  
INSTRUM spect  
PROBHD 5 mm QNP1H/BB-  
PULPROG zgpg30  
TD 32768  
SOLVENT CDCl3  
NS 12  
DS 2  
SWH 16025.641 Hz  
F2 F2 F2 0.469064 Hz  
RG 1.024376 sec  
RG 1.024376 sec  
AQ 31.200 usec  
DE 6.50 usec  
TE 298.2 K  
D1 0.10000000 sec  
D10 1

===== CHANNEL f1 =====  
NUC1 1H  
P1 10.40 usec  
PL1 0.00 dB  
SFO1 400.132710 MHz  
SI 32768  
SF 400.130000 MHz  
WDW EM  
SSB 0  
LB 0.30 Hz  
GB 0  
PC 1.00

