

*Supporting Information*

**Titanium Alkoxide-Based Regioselective Alkyne-Alkyne Reductive Coupling Mediated by In Situ Generated Arylamidate**

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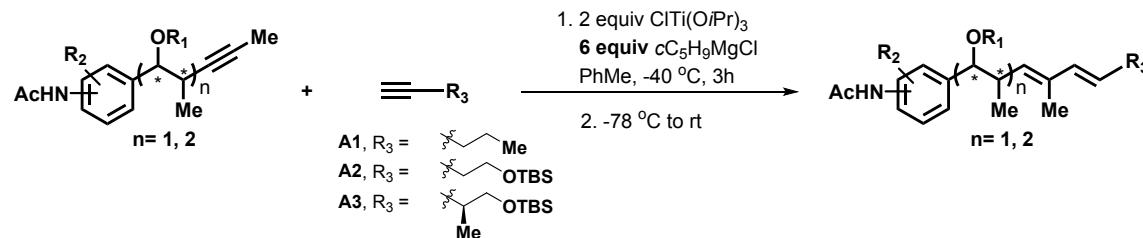
**Part I: General Information:**

All reactions were carried out in oven or flame-dried glassware under argon atmosphere unless otherwise specified. Triethylamine was distilled over calcium hydride and stored over potassium hydroxide. Dichloromethane, tetrahydrofuran, and toluene were obtained from a dry solvent system (alumina) and used without further drying. Propionitrile was distilled over calcium hydride and stored over 4 Å molecular sieves. Sureseal™ anhydrous MeOH and *N,N*-dimethylformamide (DMF) were purchased from Sigma Aldrich. Cyclopentylmagnesium chloride solution was purchased from Sigma-Aldrich, and was titrated by the Watson–Eastham method<sup>1</sup> using 1,10-phenanthroline and *sec*-butanol every three month. Commercially available aldehydes were freshly distilled before use and stored under nitrogen at 4 °C. All other reagents were used as supplied. Unless otherwise noted, reactions were magnetically stirred and monitored by thin layer chromatography with Macherey Nagel Polygram 0.20 mm silica gel 60 Å plates. Flash chromatography was performed on ZEOPrep 60 ECO 40-63µm ZEOCHEM silica gel. Yields referred to chromatographically and spectroscopically pure compounds, unless otherwise noted. <sup>1</sup>H and <sup>13</sup>C NMR spectra were taken in CDCl<sub>3</sub>, C<sub>6</sub>D<sub>6</sub>, and CD<sub>3</sub>OD at 400 or 500 MHz (as indicated), respectively. Chemical shifts are reported as major diastereomer and/or regioisomer in parts per million using the solvent internal standard (chloroform, 7.24 and 77.0 ppm, benzene, 7.16 and 128.06 ppm, and methanol, 3.30 and 47.58 ppm respectively). Data are reported as follows: chemical shift, multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, br = broad), coupling constant, integration. Infrared resonance spectra were recorded on a Nexus 670 FT-IR spectrometer. Optical rotations were recorded on a Rudolph Autopol II digital polarimeter at 589 nm and reported as follows: [α]<sub>D</sub><sup>23.8</sup>(concentration in g/100 mL solvent). High resolution mass spectra were obtained on a Waters Q-TOF Mass Spectrometer at Boston University Chemical Instrumentation Center (CIC).

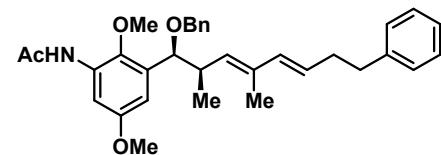
## Part II: Experimental Procedures:

### 1. Table 1.

#### 1.1 General Procedure A for Alkyne-Alkyne Reductive Coupling Using Acetamide<sup>2</sup>



To a solution of internal alkyne (0.2 mmol, 1 equiv) in toluene (2.5 mL) at  $-78^\circ\text{C}$  was added sequentially  $\text{ClTi}(\text{O}i\text{Pr})_3$  (1.0 M in hexanes, 0.4 mL, 0.4 mmol, 2 equiv) and  $c\text{C}_5\text{H}_9\text{MgCl}$  (2.0 M in diethyl ether, 0.6 mL, 1.2 mmol, 6 equiv) in a dropwise manner. The resulting yellow solution turned brown while slowly warming to  $-40^\circ\text{C}$  over 45 minutes. The reaction mixture was placed in  $-40^\circ\text{C}$  chiller and stirred for 3 hours, while solution turned to be black and heterogeneous. It was then cooled to  $-78^\circ\text{C}$ , to which terminal alkyne was added in dropwise. The resulting mixture was gradually warmed to room temperature over 1 hour and 30 minutes and stirred for the specific time for each substrate. The reaction was quenched with saturated aqueous  $\text{NH}_4\text{Cl}$  solution (3 mL). It was then extracted with ethyl acetate (3 x 10 mL). The combined organic layers were dried over  $\text{MgSO}_4$ , filtered, and concentrated. Purification over silica gel chromatography afforded coupled product.



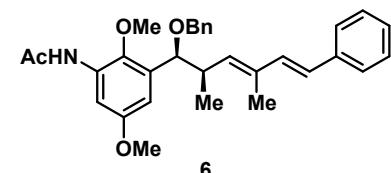
**dimethoxyphenyl)acetamide (5):** Prepared by the *general procedure A* using acetamide **1** (76 mg), 4-phenyl-1-butyne (84  $\mu\text{L}$ , 0.6 mmol, 3 equiv), and stirred for 3h at room temperature. The crude material was purified with Preparative Thin Layer Chromatography using 10%  $\text{Et}_2\text{O}$  in DCM as eluent. **5** (58mg, 57% yield, r.r.>20:1, d.r.>20:1) was obtained as a pale yellow, viscous oil.  $[\alpha]_D^{23.8} = -12.3$  ( $c = 0.13$ ,  $\text{CH}_2\text{Cl}_2$ ).

<sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>): δ7.88 (d, *J* = 2.5 Hz, 1H), δ7.58 (s, 1H), δ7.32-7.17 (m, 10H), δ6.74 (d, *J* = 2.8 Hz, 1H), δ6.01 (d, *J* = 15.6 Hz, 1H), δ5.54 (dt, *J* = 15.5, 7 Hz, 1H), δ5.30 (d, *J* = 9.7 Hz, 1H), δ4.49 (d, *J* = 11.6 Hz, 1H), δ4.49 (d, *J* = 6.55 Hz, 1H), δ4.29 (d, *J* = 11.9 Hz, 1H), δ3.78 (s, 3H), δ3.61 (s, 3H), δ2.92-2.84 (m, 1H), δ2.70-2.67 (m, 2H), δ2.40-2.36 (m, 2H), δ2.21 (s, 3H), δ1.56 (s, 3H), δ1.07 (d, *J* = 6.7 Hz, 3H);

<sup>13</sup>C NMR (125 MHz, CDCl<sub>3</sub>): δ168.2, δ156.2, δ142.0, δ140.9, δ138.5, δ135.2, δ134.3, δ133.2, δ133.1, δ131.7, δ128.4, δ128.3, δ127.5, δ127.4, δ127.1, δ125.8, δ108.1, δ105.5, δ79.0, δ70.9, δ61.3, δ55.6, δ39.0, δ36.2, δ34.8, δ29.3, δ24.9, δ16.3, δ12.5;

IR (neat/cm<sup>-1</sup>)  $\nu_{\text{max}}$ : 3415, 3292, 3026, 2935, 2870, 1674, 1602, 1524, 1497, 1418, 1392, 1368, 1347, 1245, 1206, 1194, 1052, 1028;

HRMS (ESI) *m/z* calcd for C<sub>33</sub>H<sub>39</sub>NO<sub>4</sub> [M+H]<sup>+</sup>: 514.2957, found: 514.2962.



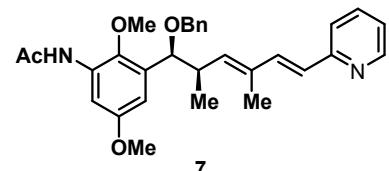
**N-(3-((1*S*,2*R*,3*E*,5*E*)-1-(benzyloxy)-2,4-dimethyl-6-phenylhexa-3,5-dien-1-yl)-2,5-dimethoxyphenyl)acetamide (6):** Prepared by the *general procedure A* using acetamide **1** (76 mg), phenylacetylene (66 μL, 0.6 mmol, 3 equiv), and stirred for 3h at room temperature. The crude material was purified with Preparative Thin Layer Chromatography using 26% Et<sub>2</sub>O in DCM as eluent. **6** (48mg, 50% yield, r.r.>20:1, d.r.>20:1) was obtained as a pale yellow, viscous oil.  $[\alpha]_D^{23.8} = +54.3$  (*c* = 0.6, CH<sub>2</sub>Cl<sub>2</sub>).

<sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>): δ7.88 (d, *J* = 2.9 Hz, 1H), δ7.56 (s, 1H), δ7.39-7.17 (m, 10), δ6.77 (d, *J* = 2.9 Hz, 1H), δ6.70 (d, *J* = 16.1 Hz, 1H), δ6.38 (d, *J* = 16.1 Hz, 1H), δ5.54 (d, *J* = 9.8 Hz, 1H), δ4.53 (d, *J* = 11.8 Hz, 1H), δ4.53 (d, *J* = 6.5 Hz, 1H), δ3.79 (s, 3H), δ3.63 (s, 3H), δ2.98-2.91 (m, 1H), δ2.18 (s, 3H), δ1.68 (d, *J* = 1.2 Hz, 2H), δ1.12 (d, *J* = 6.7 Hz, 2H);

<sup>13</sup>C NMR (125 MHz, CDCl<sub>3</sub>): δ168.2, δ156.2, δ138.4, δ138.2, δ137.9, δ136.3, δ134.2, δ134.0, δ133.4, δ131.8, δ128.5, δ128.3, δ127.6, δ127.5, δ126.9, δ126.2, δ126.1, δ108.1, δ105.5, δ79.0, δ70.9, δ61.2, δ55.6, δ39.5, δ24.9, δ16.3, δ12.4;

IR (neat/cm<sup>-1</sup>)  $\nu_{\text{max}}$ : 3416, 3304, 3028, 2935, 2868, 1675, 1596, 1523, 1461, 1418, 1392, 1348, 1245, 1206, 1170, 1148, 1052, 1028;

HRMS (ESI)  $m/z$  calcd for  $C_{31}H_{35}NO_4$  [M+H] $^+$ : 486.2644, found: 486.2658.



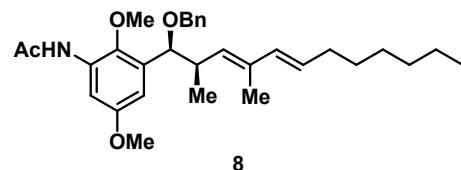
***N*-(3-((1*S*,2*R*,3*E*,5*E*)-1-(benzyloxy)-2,4-dimethyl-6-(pyridin-2-yl)hexa-3,5-dien-1-yl)-2,5-dimethoxyphenyl)acetamide (7):** Prepared by the *general procedure A* using acetamide 1 (76 mg), 3-ethynylpyridine (62 mg, 0.6 mmol, 3 equiv), and stirred for 3h at room temperature. The crude material was purified with Preparative Thin Layer Chromatography using 30% acetone in DCM as eluent. 7 (59mg, 61% yield, r.r.>20:1, d.r.>20:1) was obtained as a pale yellow, viscous oil.  $[\alpha]_D^{23.8} = -49.4$  ( $c = 0.53$ ,  $CH_2Cl_2$ ).

$^1H$  NMR (500 MHz,  $CDCl_3$ ):  $\delta$  8.54-8.52 (m, 1H), 7.85 (d,  $J = 2.8$  Hz, 1H), 7.62-7.59 (m, 2H), 7.33-7.27 (m, 5H), 7.18 (d,  $J = 15.7$  Hz, 1H), 7.09-7.07 (m, 2H), 6.75 (d,  $J = 2.9$  Hz, 1H), 6.45 (d,  $J = 15.8$  Hz, 1H), 5.69 (d,  $J = 9.9$  Hz, 1H), 4.53 (d,  $J = 6.7$  Hz, 1H), 4.51 (d,  $J = 11.8$  Hz, 1H), 4.31 (d,  $J = 11.8$  Hz, 1H), 3.78 (s, 3H), 3.63 (s, 3H), 2.99-2.92 (m, 1H), 2.18 (s, 3H), 1.69 (d,  $J = 1.2$  Hz, 3H), 1.13 (d,  $J = 6.7$  Hz, 2H);

$^{13}C$  NMR (125 MHz,  $CDCl_3$ ):  $\delta$  156.3, 138.3, 134.1, 133.2, 131.8, 128.3, 127.6, 127.5, 121.7, 121.5, 108.0, 105.7, 879.0, 871.0, 861.2, 855.6, 839.8, 835.6, 824.9, 823.3, 816.4, 812.4.

IR (neat/ $cm^{-1}$ )  $\nu_{max}$ : 3280, 2961, 2935, 2870, 1675, 2586, 1561, 1527, 1465, 1419, 1392, 1369, 1347, 1249, 1209, 1195, 1170, 1149, 1052, 1028;

HRMS (ESI)  $m/z$  calcd for  $C_{30}H_{34}N_2O_4$  [M+H] $^+$ : 487.2597, found: 487.2604.

*N*-(3-((1*S*,2*R*,3*E*,5*E*)-1-(benzyloxy)-2,4-dimethyldodeca-3,5-dien-1-yl)-2,5-

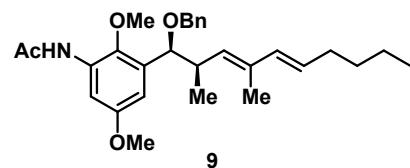
**dimethoxyphenyl)acetamide (8):** Prepared by the *general procedure A* using acetamide **1** (76 mg), 1-octyne (88  $\mu$ L, 0.6 mmol, 3 equiv), and stirred for 3h at room temperature. The crude material was purified with Preparative Thin Layer Chromatography using 27% ethyl acetate in Hexanes as eluent. **8** (61mg, 62% yield, r.r.>20:1, d.r.>20:1) was obtained as a pale yellow, viscous oil.  $[\alpha]_D^{23.8} = +6.4$  ( $c = 0.47$ ,  $\text{CH}_2\text{Cl}_2$ ).

$^1\text{H}$  NMR (500 MHz,  $\text{CDCl}_3$ ):  $\delta$  7.87 (d,  $J = 2.8$  Hz, 1H), 7.58 (s, 1H), 7.34-7.29 (m, 5H), 7.74 (d,  $J = 2.8$  Hz, 1H), 7.59 (d,  $J = 15.6$  Hz, 1H), 7.49 (dt,  $J = 14.8, 7.2$  Hz, 1H), 7.28 (d,  $J = 9.8$  Hz, 1H), 7.49 (d,  $J = 11.6$  Hz, 1H), 7.49 (d,  $J = 6.5$  Hz, 1H), 7.48 (d,  $J = 11.9$  Hz, 1H), 7.78 (s, 3H), 7.61 (s, 3H), 7.91-7.83 (m, 1H), 7.21 (s, 3H), 7.05 (dt,  $J = 7.2$  Hz, 2H), 7.56 (s, 3H), 7.38-7.17 (m, 8H), 7.06 (d,  $J = 6.7$  Hz, 3H), 7.08 (t,  $J = 6.7$  Hz, 3H);

$^{13}\text{C}$  NMR (125 MHz,  $\text{CDCl}_3$ ):  $\delta$  168.2, 156.2, 140.9, 138.5, 134.6, 134.3, 133.2, 132.7, 131.7, 128.3, 128.3, 127.5, 127.4, 108.1, 105.4, 79.0, 70.9, 61.3, 55.6, 39.0, 32.9, 31.8, 29.7, 29.0, 24.9, 22.6, 16.3, 14.1, 12.5;

IR (neat/ $\text{cm}^{-1}$ )  $\nu_{\text{max}}$ : 2955, 2926, 2855, 1672, 1596, 1524, 1498, 1454, 1418, 1391, 1348, 1245, 1207, 1195, 1170, 1053, 1028;

HRMS (ESI)  $m/z$  calcd for  $\text{C}_{31}\text{H}_{43}\text{NO}_4$  [ $\text{M}+\text{Na}]^+$ : 516.3090, found: 516.3096.

*N*-(3-((1*S*,2*R*,3*E*,5*E*)-1-(benzyloxy)-2,4-dimethyldeca-3,5-dien-1-yl)-2,5-

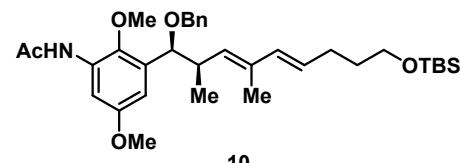
**dimethoxyphenyl)acetamide (9):** Prepared by the *general procedure A* using acetamide **1** (76 mg), 1-hexyne (69  $\mu$ L, 0.6 mmol, 3 equiv), and stirred for 3h at room temperature. The crude material was purified with Preparative Thin Layer Chromatography using 30% ethyl acetate in Hexanes as eluent. **5e** (56mg, 61% yield, r.r.>20:1, d.r.>20:1) was obtained as a pale yellow, viscous oil.  $[\alpha]_D^{23.8} = -1.8$  ( $c = 0.67$ ,  $\text{CH}_2\text{Cl}_2$ ).

<sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>): δ7.87 (d, *J* = 2.7 Hz, 1H), δ7.58 (s, 1H), δ7.34-7.28 (m, 5H), δ6.74 (d, *J* = 2.7 Hz, 1H), δ5.95 (d, *J* = 15.5 Hz, 1H), δ5.49 (dt, *J* = 14.9, 6.8 Hz, 1H), δ5.28 (d, *J* = 9.8 Hz, 1H), δ4.49 (d, *J* = 11.6 Hz, 1H), δ4.49 (d, *J* = 6.8 Hz, 1H), δ4.29 (d, *J* = 11.9 Hz, 1H), δ3.78 (s, 3H), δ3.61 (s, 3H), δ2.90-2.83 (m, 1H), δ2.21 (s, 3H), δ2.06 (dt, *J* = 6.9 Hz, 2H), δ1.56 (s, 3H), δ1.38-1.27 (m, 4H), δ1.06 (d, *J* = 6.7 Hz, 3H), δ0.89 (t, *J* = 7.0 Hz, 3H);

<sup>13</sup>C NMR (125 MHz, CDCl<sub>3</sub>): δ168.2, δ156.2, δ140.9, δ138.5, δ134.6, δ134.3, δ133.2, δ132.7, δ131.7, δ128.3, δ128.2, δ127.5, δ127.4, δ108.1, δ105.4, δ79.0, δ70.9, δ61.3, δ55.6, δ39.0, δ32.5, δ31.8, δ25.0, δ22.3, δ16.3, δ14.0, δ12.5;

IR (neat/cm<sup>-1</sup>)  $\nu_{\text{max}}$ : 3304, 2956, 2930, 2871, 1673, 1596, 1498, 1462, 1418, 1346, 1246, 1221, 1194, 1053, 1028;

HRMS (ESI) *m/z* calcd for C<sub>29</sub>H<sub>39</sub>NO<sub>4</sub> [M+Na]<sup>+</sup>: 488.2777, found: 488.2758.



**N-(3-((1*S*,2*R*,3*E*,5*E*)-1-(benzyloxy)-9-((tert-butyldimethylsilyl)oxy)-2,4-dimethylnona-3,5-dien-1-yl)-2,5-dimethoxyphenylacetamide (10):**

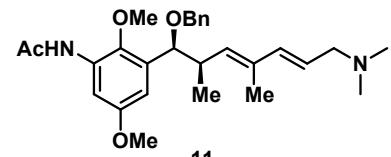
Prepared by the *general procedure A* using acetamide 1 (76 mg), *tert*-butyldimethyl(pent-4-yn-1-yloxy)silane<sup>3</sup> (119 mg, 0.6 mmol, 3 equiv), and stirred for 3h at room temperature. The crude material was purified with Preparative Thin Layer Chromatography using 30% ethyl acetate in Hexanes as eluent. **10** (70 mg, 60% yield, r.r.>20:1, d.r.>20:1) was obtained as a pale yellow, viscous oil.  $[\alpha]_D^{23.8} = -1.6$  (*c* = 1, CH<sub>2</sub>Cl<sub>2</sub>).

<sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>): δ7.87 (d, *J* = 2.9 Hz, 1H), δ7.58 (s, 1H), δ7.34-7.24 (m, 5H), δ6.74 (d, *J* = 2.9 Hz, 1H), δ5.97 (d, *J* = 15.6 Hz, 1H), δ5.49 (dt, *J* = 15.6, 6.9 Hz, 1H), δ5.29 (d, *J* = 9.7 Hz, 1H), δ4.49 (d, *J* = 11.9 Hz, 1H), δ4.49 (d, *J* = 6.3 Hz, 1H), δ4.29 (d, *J* = 11.9 Hz, 1H), δ3.78 (s, 3H), δ3.62 (s, 3H), δ3.61 (t, *J* = 6.5 Hz, 2H), δ2.91-2.84 (m, 1H), δ2.21 (s, 3H), δ2.11 (dt, *J* = 7.3 Hz, 2H), δ1.62-1.56 (m, 2H), δ1.56 (s, 3H), δ1.06 (d, *J* = 6.7 Hz, 3H), δ0.89 (s, 9H), δ0.04 (s, 6H);

<sup>13</sup>C NMR (125 MHz, CDCl<sub>3</sub>): δ168.2, δ156.2, δ141.0, δ138.5, δ135.0, δ134.3, δ133.1, δ132.9, δ131.7, δ128.3, δ127.5, δ127.4, δ108.1, δ105.5, δ79.1, δ70.9, δ62.7, δ61.3, δ55.6, δ39.0, δ32.7, δ29.1, δ26.0, δ24.9, δ18.3, δ16.3, δ12.5, δ-5.3;

IR (neat/cm<sup>-1</sup>)  $\nu_{\text{max}}$ : 3293, 2951, 2930, 2856, 1672, 1596, 1525, 1497, 1462, 1419, 1389, 1369, 1348, 1250, 1207, 1170, 1095, 1053, 1029;

HRMS (ESI)  $m/z$  calcd for C<sub>34</sub>H<sub>51</sub>NO<sub>5</sub>Si [M+Na]<sup>+</sup>: 604.3434, found: 604.3420.



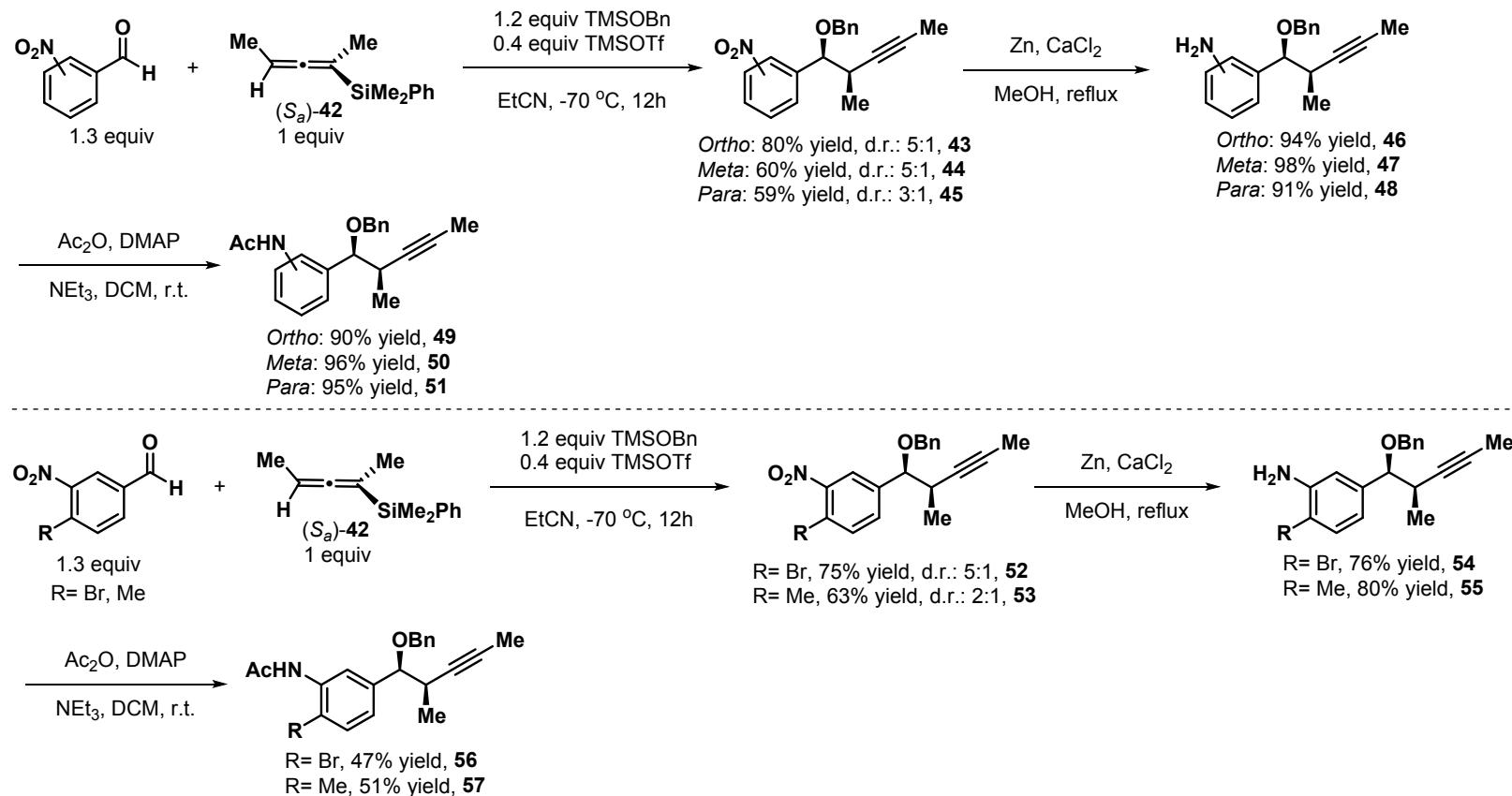
**N-(3-((1S,2R,3E,5E)-1-(benzyloxy)-7-(dimethylamino)-2,4-dimethylhepta-3,5-dien-1-yl)-2,5-dimethoxyphenyl)acetamide (11):** Prepared by the *general procedure A* using acetamide 1 (76 mg), 3-dimethylamino-1-propyne (65  $\mu$ L, 0.6 mmol, 3 equiv), and stirred for 3h at room temperature. The crude material was purified with Preparative Thin Layer Chromatography using 90% MeOH in DCM as eluent. **11** (61 mg, 65% yield, r.r.>20:1, d.r.>20:1) was obtained as a pale yellow, viscous oil.  $[\alpha]_D^{23.8} = -3.1$  ( $c = 0.13$ , CH<sub>2</sub>Cl<sub>2</sub>).

<sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>):  $\delta$  7.86 (d,  $J$  = 2.8 Hz, 1H), 7.60 (s, 1H), 7.32-7.26 (m, 5H), 7.32 (d,  $J$  = 2.8 Hz, 1H), 7.07 (d,  $J$  = 15.7 Hz, 1H), 7.53 (dt,  $J$  = 15.6, 6.8 Hz, 1H), 7.37 (d,  $J$  = 9.5 Hz, 1H), 7.45 (d,  $J$  = 12.0 Hz, 1H), 7.45 (d,  $J$  = 6.1 Hz, 1H), 7.29 (d,  $J$  = 11.9 Hz, 1H), 7.78 (s, 3H), 7.61 (s, 3H), 7.99-7.85 (m, 3H), 7.23 (s, 6H), 7.21 (s, 3H), 7.58 (s, 3H), 7.07 (d,  $J$  = 6.7 Hz, 3H);

<sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>):  $\delta$  168.2, 156.2, 140.9, 138.4, 134.6, 134.2, 132.8, 131.8, 128.3, 127.5, 127.5, 108.1, 105.5, 79.0, 70.9, 62.0, 61.2, 55.6, 45.1, 39.1, 25.0, 16.2, 12.5;

IR (neat/cm<sup>-1</sup>)  $\nu_{\text{max}}$ : 3278, 2937, 2865, 2826, 2774, 1674, 1597, 1528, 1455, 1419, 1392, 1368, 1348, 1248, 1209, 1195, 1149, 1092, 1052, 1028, 1000;

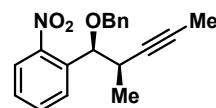
HRMS (ESI)  $m/z$  calcd for C<sub>28</sub>H<sub>38</sub>N<sub>2</sub>O<sub>4</sub> [M+H]<sup>+</sup>: 467.2910, found: 467.2911.

Supplementary Scheme S1. Synthesis of *Syn*-Substrates

**1.2. General Procedure B for the Asymmetric Three-Component Propargylation for the Synthesis of Propargylic Ethers **43**, **44**, **45**, **52** and **53****

A solution of allenylsilane ( $S_a$ )-42 (5 g, 24.7 mmol, 1 equiv), (benzyloxy)trimethylsilane (5.8 mL, 29.64 mmol, 1.2 equiv), and aldehyde (4.85 g, 32.11 mmol, 1.3 equiv) in 123.5 mL propionitrile (EtCN) was stirred at room temperature for 5 minutes and cooled

to -78 °C. Trimethylsilyl trifluoromethanesulfonate (TMSOTf) (1.8 mL, 9.88 mmol, 0.4 equiv) was added to above mixture dropwise. The resulting mixture was placed into -70 °C chiller and stirred for 12 hours. The reaction was quenched by adding 50 mL saturated NaHCO<sub>3</sub> (aq) solution at -78 °C. After the mixture was warmed to room temperature, it was then extracted with ethyl acetate (3 x 50 mL), and the combined organic layers were dried over MgSO<sub>4</sub>, filtered, and concentrated. Purification over silica gel chromatography (CH<sub>2</sub>Cl<sub>2</sub>/Hexanes) afforded product **43**, **44**, **45**, **52** and **53** as an oil.



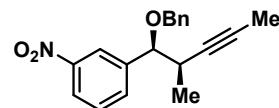
**43 1-((1S,2R)-1-(benzyloxy)-2-methylpent-3-yn-1-yl)-2-nitrobenzene (43):** Prepared by the *general procedure B* using 2-nitrobenzaldehyde. The crude material was purified with silica gel column Chromatography using 48% DCM in Hexanes. **43** (6.11 g, 80% yield, d.r.: 5:1) was obtained as a pale yellow oil.  $[\alpha]_D^{23.8} = +6.4$  (*c* = 0.47, CH<sub>2</sub>Cl<sub>2</sub>).  $[\alpha]_D^{23.8} = -248.6$  (*c* = 3.33, CH<sub>2</sub>Cl<sub>2</sub>).

<sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>): δ7.86 (d, *J* = 8.1 Hz, 1H), δ7.81(d, *J* = 7.8 Hz, 2H), δ7.62 (t, *J* = 7.4 Hz, 2H), δ7.47-7.40 (m, 3H), δ7.34-7.27 (m, 5H), δ5.14 (d, *J* = 8.2 Hz, 1H), δ4.51 (d, *J* = 11.6 Hz, 1H), δ4.44 (d, *J* = 11.7 Hz, 1H), δ2.67-2.60 (m, 1H), δ1.63 (dd, *J* = 2.4, 1.0 Hz, 3H), δ1.27(dd, *J* = 6.8, 0.8 Hz, 3H);

<sup>13</sup>C NMR (125 MHz, CDCl<sub>3</sub>): δ150.3, δ137.8, δ136.4, δ132.8, δ128.5, δ128.4, δ128.3, δ127.9, δ127.8, δ123.9, δ79.3, δ79.0, δ78.5, δ71.9, δ34.6, δ18.1, δ3.4;

IR (neat/cm<sup>-1</sup>)  $\nu_{\text{max}}$ : 3064, 3033, 2975, 2934, 2919, 2872, 1608, 1578, 1527, 1497, 1454, 1397, 1354, 1304, 1112, 1062, 1028;

HRMS (ESI) *m/z* calcd for C<sub>19</sub>H<sub>19</sub>NO<sub>3</sub> [M+H]<sup>+</sup>: 310.1443, found: 310.1443.

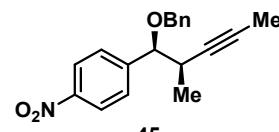


**44 1-((1S,2R)-1-(benzyloxy)-2-methylpent-3-yn-1-yl)-3-nitrobenzene (44):** Prepared by the *general procedure B* using 3-nitrobenzaldehyde. The crude material was purified with silica gel column Chromatography using 48% DCM in Hexanes. **44** (4.58 g, 60% yield, d.r.: 5:1) was obtained as a pale yellow oil.

<sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>): δ8.30-8.29 (m, 1H), δ8.19-8.17, (m, 1H), δ7.73-7.69 (m, 1H), δ7.54 (t, *J* = 7.9 Hz, 1H), δ7.35-7.28 (m, 5H), δ4.52 (d, *J* = 11.9 Hz, 1H), δ4.30 (d, *J* = 11.9 Hz, 1H), δ4.24 (d, *J* = 7.6 Hz, 1H), δ2.81-2.74 (m, 1H), δ1.68 (d, *J* = 2.4 Hz, 3H), δ1.24 (d, *J* = 6.9 Hz, 3H);

<sup>13</sup>C NMR (125 MHz, CDCl<sub>3</sub>): δ147.8, δ142.4, δ137.3, δ133.4, δ128.6, δ128.2, δ127.6, δ122.6, δ122.6, δ83.2, δ79.4, δ78.9, δ71.0, δ33.6, δ17.8, δ3.1;

LCMS (ES+) *m/z* calcd for C<sub>19</sub>H<sub>19</sub>NO<sub>3</sub> [M+H]<sup>+</sup>: 310.14, found: 310.16.



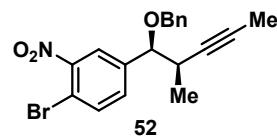
**45 1-((1*S*,2*R*)-1-(benzyloxy)-2-methylpent-3-yn-1-yl)-4-nitrobenzene (45):** Prepared by the *general procedure B* using 4-nitrobenzaldehyde. The crude material was purified with silica gel column chromatography using 40% DCM in Hexanes. **45** (4.51 g, 59% yield, d.r.: 3:1) was obtained as a pale yellow oil.  $[\alpha]_D^{23.8} = -18.2$  (*c* = 5.2, CH<sub>2</sub>Cl<sub>2</sub>).

<sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>): δ8.24-8.21 (m, 2H), δ7.56-7.53 (m, 2H), δ7.36-7.27 (m, 5H), δ4.49 (d, *J* = 11.9 Hz, 1H), δ4.28 (d, *J* = 11.9 Hz, 1H), δ4.24 (d, *J* = 7.6 Hz, 1H), δ2.80-2.73 (m, 1H), δ1.67 (d, *J* = 2.4 Hz, 3H), δ1.24 (d, *J* = 6.9 Hz, 2H);

<sup>13</sup>C NMR (125 MHz, CDCl<sub>3</sub>): δ148.0, δ137.6, δ128.6, δ128.4, δ127.8, δ123.2, δ83.5, δ79.7, δ78.9, δ71.3, δ33.8, δ18.1, δ3.4;

IR (neat/cm<sup>-1</sup>)  $\nu_{\text{max}}$ : 3065, 3031, 2918, 2872, 1606, 1519, 1496, 1454, 1393, 1343, 1108, 1085, 1073, 1028, 1014;

LCMS (ES+) *m/z* calcd for C<sub>19</sub>H<sub>19</sub>NO<sub>3</sub> [M+H]<sup>+</sup>: 310.14, found: 310.16.



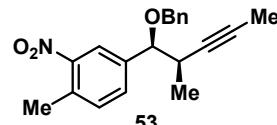
**4-((1S,2R)-1-(benzyloxy)-2-methylpent-3-yn-1-yl)-1-bromo-2-nitrobenzene (52):** Prepared by the *general procedure B* using 4-bromo-3-nitrobenzaldehyde. The crude material was purified with silica gel column chromatography using 40% DCM in Hexanes. **52** (7.19 g, 75% yield, d.r.: 5:1) was obtained as a pale yellow oil.  $[\alpha]_D^{23.8} = -24.5$  ( $c = 3.2$ ,  $\text{CH}_2\text{Cl}_2$ ).

$^1\text{H}$  NMR (500 MHz,  $\text{CDCl}_3$ ):  $\delta$  7.89 (d,  $J = 1.8$  Hz, 1H), 7.72 (d,  $J = 8.2$  Hz, 1H), 7.44 (dd,  $J = 8.2, 1.7$  Hz, 1H), 7.37-7.27 (m, 5H), 84.52 (d,  $J = 11.9$  Hz, 1H), 84.30 (d,  $J = 11.9$  Hz, 1H), 84.16 (d,  $J = 7.6$  Hz, 1H), 82.76-2.70 (m, 1H), 81.70 (d,  $J = 2.3$  Hz, 2H), 81.22 (d,  $J = 6.9$  Hz, 2H);

$^{13}\text{C}$  NMR (125 MHz,  $\text{CDCl}_3$ ):  $\delta$  149.5, 141.8, 137.3, 134.5, 132.2, 128.5, 128.0, 127.9, 125.0, 82.9, 82.9, 879.5, 879.4, 871.4, 833.8, 818.1, 83.4;

IR (neat/ $\text{cm}^{-1}$ )  $\nu_{\text{max}}$ : 3064, 3030, 2974, 2918, 2872, 1738, 1601, 1533, 1496, 1454, 1346, 1206, 1112, 1085, 1075, 1031;

HRMS (ESI)  $m/z$  calcd for  $\text{C}_{19}\text{H}_{18}\text{BrNO}_3$  [ $\text{M}+\text{H}]^+$ : 388.0548, found: 388.0547.



**4-((1S,2R)-1-(benzyloxy)-2-methylpent-3-yn-1-yl)-1-methyl-2-nitrobenzene (53):** Prepared by the *general procedure B* using 4-methyl-3-nitrobenzaldehyde. The crude material was purified with silica gel column Chromatography using 40% DCM in Hexanes. **53** (4.07 g, 51% yield, d.r.: 2:1) was obtained as a pale yellow oil.  $[\alpha]_D^{23.8} = -27.4$  ( $c = 5.3$ ,  $\text{CH}_2\text{Cl}_2$ ).

$^1\text{H}$  NMR (500 MHz,  $\text{CDCl}_3$ ):  $\delta$  8.02 (d,  $J = 1.3$  Hz, 1H), 7.52 (dd,  $J = 7.8, 1.6$  Hz, 1H), 7.36-7.28 (m, 5H), 84.51 (d,  $J = 11.9$  Hz, 1H), 84.27 (d,  $J = 11.9$  Hz, 1H), 84.18 (d,  $J = 7.5$  Hz, 1H), 82.79-2.72 (m, 1H), 82.62 (s, 3H), 81.70 (d,  $J = 2.3$  Hz, 3H), 81.22 (d,  $J = 6.9$  Hz, 3H);

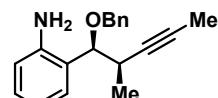
$^{13}\text{C}$  NMR (125 MHz,  $\text{CDCl}_3$ ):  $\delta$  148.9, 139.9, 137.7, 132.9, 132.4, 132.0, 128.4, 127.9, 124.1, 83.1, 879.8, 879.0, 871.1, 833.8, 820.3, 818.0, 83.4;

IR (neat/cm<sup>-1</sup>)  $\nu_{\text{max}}$ : 3064, 3032, 2974, 2932, 2919, 2872, 1738, 1623, 1526, 1496, 1453, 1345, 1203, 1074, 1028;

HRMS (ESI) *m/z* calcd for C<sub>20</sub>H<sub>21</sub>NO<sub>3</sub> [M+H]<sup>+</sup>: 324.1600, found: 324.1600.

### 1.3. General Procedure C for the Arylnitro Reduction<sup>4</sup>

Arylnitro alkyne **43**, **44**, **45**, **52** or **53** (16.16 mmol, 1 equiv) was dissolved in 323.2 mL anhydrous MeOH at room temperature. Zinc powder (57.7g, 888.8 mmol, 55 equiv) and calcium chloride (26.9g, 242.4 mmol, 15 equiv) were added in to the above solution sequentially. The resulting mixture was refluxed for 1 hour. It was then cooled down to room temperature and MeOH was evaporated off before 100 mL saturated NaHCO<sub>3</sub> (aq) solution and 100 mL ethyl acetate were added in. The resulting biphasic mixture was vigorously stirred for 1 hour at room temperature before extractive isolation. The combined organic layers were dried over MgSO<sub>4</sub>, filtered, and concentrated. Purification over silica gel chromatography afforded aniline **46**, **47**, **48**, **54** and **55**.



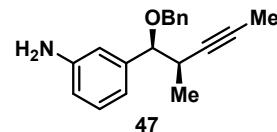
**2-((1*S*,2*R*)-1-(benzyloxy)-2-methylpent-3-yn-1-yl)aniline (46):** Prepared by the *general procedure C* using **43**. The crude material was purified with silica gel column chromatography using 10 % ethyl acetate in Hexanes. **46** (4.24 g, 15.19 mmol, 94% yield) was obtained as a pale yellow, viscous oil.  $[\alpha]_D^{23.8} = -18$  (*c* = 0.6, CH<sub>2</sub>Cl<sub>2</sub>).

<sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>): δ7.35-7.27 (m, 5H), δ7.12 (ddd, *J* = 7.9, 7.4, 1.6 Hz, 1H), δ7.09 (dd, *J* = 7.6, 1.6 Hz, 1H), δ4.54 (d, *J* = 11.8 Hz, 1H), δ4.31 (d, *J* = 11.8 Hz, 1H), δ4.22 (d, *J* = 9.0 Hz, 1H), δ3.09 (dqq, *J* = 9.0, 6.7, 2.3 Hz, 1H), δ1.65 (d, *J* = 2.4 Hz, 3H), δ1.32 (d, *J* = 6.8 Hz, 2H);

<sup>13</sup>C NMR (125 MHz, CDCl<sub>3</sub>): δ144.6, δ138.1, δ130.4, δ128.5, δ128.3, δ127.9, δ127.6, δ123.8, δ118.0, δ116.8, δ85.1, δ80.9, δ77.7, δ70.8, δ30.7, δ18.4, δ3.5;

IR (neat/cm<sup>-1</sup>)  $\nu_{\text{max}}$ : 3456, 3368, 3065, 3028, 2968, 2917, 2859, 1615, 1585, 1496, 1455, 1368, 1304, 1264, 1205, 1157, 1113, 1085, 1068, 1028;

LCMS (ES+)  $m/z$  calcd for C<sub>19</sub>H<sub>21</sub>NO [M+H]<sup>+</sup>: 280.17, found: 280.18.



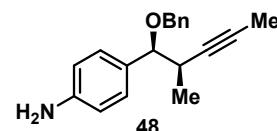
**3-((1S,2R)-1-(benzyloxy)-2-methylpent-3-yn-1-yl)aniline (47):** Prepared by the *general procedure C* using **44**. The crude material was purified with silica gel column Chromatography using 23% ethyl acetate in Hexanes. **47** (4.42 g, 15.84 mmol, 98% yield) was obtained as a pale yellow, viscous oil.

<sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>): δ7.38-7.27 (m, 5H), δ7.15 (t,  $J$  = 7.7 Hz, 1H), δ6.79-6.76 (m, 2H), δ6.68 (ddd,  $J$  = 7.9, 2.4, 0.9 Hz, 1H), δ4.54 (d,  $J$  = 12.0 Hz, 1H), δ4.28 (d,  $J$  = 12.0 Hz, 1H), δ4.11 (d,  $J$  = 7.1 Hz, 1H), δ2.78-2.72 (m, 1H), δ1.71 (d,  $J$  = 2.4 Hz, 3H), δ1.21 (d,  $J$  = 6.9 Hz, 3H);

<sup>13</sup>C NMR (125 MHz, CDCl<sub>3</sub>): δ146.0, δ141.5, δ138.6, δ128.8, δ128.3, δ127.8, δ127.4, δ118.5, δ114.7, δ114.3, δ84.1, δ81.0, δ77.6, δ70.6, δ33.6, δ17.7, δ3.6;

IR (neat/cm<sup>-1</sup>)  $\nu_{\text{max}}$ : 3457, 3369, 3063, 3030, 2971, 2917, 2871, 1618, 1607, 1592, 1494, 1453, 1309, 1296, 1205, 1167, 1113, 1086, 1061, 1028;

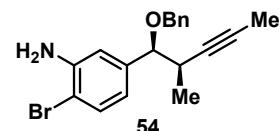
HRMS (ESI)  $m/z$  calcd for C<sub>19</sub>H<sub>21</sub>NO [M+H]<sup>+</sup>: 280.1701, found: 280.1696.



**4-((1S,2R)-1-(benzyloxy)-2-methylpent-3-yn-1-yl)aniline (48):** Prepared by the *general procedure C* using **45**. The crude material was purified with silica gel column Chromatography using 22 % ethyl acetate in Hexanes. **48** (4.11 g, 14.71 mmol, 91% yield) was obtained as a pale yellow, viscous oil.  $[\alpha]_D^{23.8} = -7.8$  ( $c$  = 3.2, CH<sub>2</sub>Cl<sub>2</sub>).

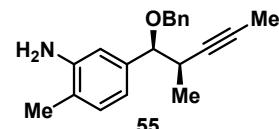
<sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>): δ7.38-7.25 (m, 5H), δ7.19-7.16 (m, 2H), δ6.73 (d,  $J$  = 7.8 Hz, 1H), δ4.49 (d,  $J$  = 12.1 Hz, 1H), δ4.23 (d,  $J$  = 12.1 Hz, 1H), δ4.06 (d,  $J$  = 7.3 Hz, 1H), δ2.78-2.71 (m, 1H), δ1.70 (d,  $J$  = 2.4 Hz, 1H), δ1.19 (d,  $J$  = 6.9 Hz, 1H);

<sup>13</sup>C NMR (125 MHz, CDCl<sub>3</sub>): δ138.6, δ128.8, δ128.2, δ127.8, δ127.4, δ115.1, δ83.8, δ80.9, δ77.6, δ70.2, δ33.8, δ18.0, δ3.6;  
 IR (neat/cm<sup>-1</sup>) ν<sub>max</sub>: 3452, 3363, 3030, 2971, 2872, 1621, 1516, 1496, 1453, 1368, 1280, 1205, 1175, 1113, 1086, 1065, 1028;  
 LCMS (ESI) *m/z* calcd for C<sub>19</sub>H<sub>21</sub>NO [M+H]<sup>+</sup>: 280.17, found: 280.18.



**5-((1S,2R)-1-(benzyloxy)-2-methylpent-3-yn-1-yl)-2-bromoaniline (54):** Prepared by the *general procedure C* using **52**. The crude material was purified with silica gel column Chromatography using 22 % ethyl acetate in Hexanes. **54** (4.40 g, 12.28 mmol, 76% yield) was obtained as a pale yellow, viscous oil. (We preferred to use as crude, so we did not fully characterize it. Proton NMR can be used as reference for reaction reproduction.)

<sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>): δ7.38 (d, *J* = 8.1 Hz, 1H), δ7.35-7.28 (m, 5H), δ6.80 (s, 1H), δ6.62 (d, *J* = 8.0 Hz, 1H), δ4.51 (d, *J* = 12.0 Hz, 1H), δ4.25 (d, *J* = 12.0 Hz, 1H), δ4.04 (d, *J* = 7.3 Hz, 1H), δ2.75-2.69 (m, 1H), δ1.71 (d, *J* = 2.4 Hz, 3H), δ1.20 (d, *J* = 6.9 Hz, 3H);



**5-((1S,2R)-1-(benzyloxy)-2-methylpent-3-yn-1-yl)-2-methylaniline (55):** Prepared by the *general procedure C* using **53**. The crude material was purified with silica gel column Chromatography using 16 % ethyl acetate in Hexanes. **55** (3.79 g, 12.93 mmol, 80% yield) was obtained as a pale yellow, viscous oil.

<sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>): δ7.38-7.27 (m, 5H), δ7.04 (d, *J* = 7.5 Hz, 1H), δ6.73 (s, 1H), δ6.69 (d, *J* = 15.1 Hz, 1H), δ4.54 (d, *J* = 12.1 Hz, 1H), δ4.27 (d, *J* = 12.1 Hz, 1H), δ4.10 (d, *J* = 7.0 Hz, 1H), δ3.66 (brs, 2H), δ2.78-2.72 (m, 1H), δ2.19 (s, 3H), δ1.72 (d, *J* = 2.4 Hz, 3H), δ1.21 (d, *J* = 6.9 Hz, 3H);

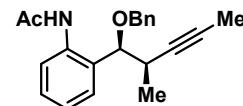
<sup>13</sup>C NMR (125 MHz, CDCl<sub>3</sub>): δ144.1, δ139.0, δ138.6, δ130.0, δ128.2, δ127.8, δ127.4, δ121.9, δ118.5, δ114.1, δ83.9, δ81.1, δ77.5, δ70.5, δ33.7, δ17.7, δ17.2, δ3.6;

IR (neat/cm<sup>-1</sup>)  $\nu_{\text{max}}$ : 3469, 3374, 3061, 3029, 2971, 2930, 2917, 2858, 1623, 1581, 1511, 1496, 1453, 1427, 1368, 1344, 1310, 1299, 1287, 1206, 1146, 1086, 1064, 1028;

HRMS (ESI)  $m/z$  calcd for C<sub>20</sub>H<sub>23</sub>NO [M+H]<sup>+</sup>: 294.1858, found: 294.1854.

#### 1.4. General Procedure D for the Synthesis of **49**, **50**, **51**, **56**, and **57** by *N*-Acylation

Alkynyl aniline **46**, **47**, **48**, **54**, or **55** (14.32 mmol, 1 equiv) was dissolved in 71.6 mL dichloromethane (DCM) at room temperature. Acetic anhydride (2.7 mL, 28.64 mmol, 2 equiv), triethyl amine (6 mL, 42.96 mmol, 3 equiv) (dropwise), and 4-dimethylaminopyridine (DMAP) (525 mg, 4.3 mmol, 30% equiv) was added in sequentially. The resulting mixture was stirred at room temperature for 12 hours before it was quenched with 10 mL saturated NH<sub>4</sub>Cl(aq) solution. It was then extracted with ethyl acetate (50 mL x 3). The combined organic layers were dried over MgSO<sub>4</sub>, filtered, and concentrated. Purification over silica gel chromatography afforded acetamide **49**, **50**, **51**, **56**, and **57**.

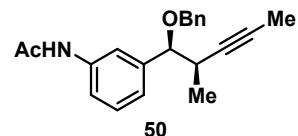


**49**      **N**-(2-((1*S*,2*R*)-1-(benzyloxy)-2-methylpent-3-yn-1-yl)phenyl)acetamide (**49**): Prepared by the *general procedure D* using **46**. The crude material was purified with silica gel column chromatography using 23% ethyl acetate in Hexanes. **49** (4.14 g, 12.89 mmol, 90% yield) was obtained as a pale yellow, viscous oil.

<sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>): δ9.03 (s, 1H), δ8.26 (d,  $J$  = 8.4 Hz, 1H), δ7.37-7.28 (m, 5H), δ7.14 (d,  $J$  = 7.3 Hz, 1H), δ7.09-7.05 (m, 2H), δ4.52 (d,  $J$  = 11.4 Hz, 1H), δ4.37 (d,  $J$  = 11.4 Hz, 1H), δ4.27 (d,  $J$  = 8.2 Hz, 1H), δ2.95-2.87 (m, 1H), δ2.00 (s, 3H), δ1.65 (d,  $J$  = 2.1 Hz, 3H), δ1.28 (d,  $J$  = 6.8 Hz, 3H);

<sup>13</sup>C NMR (125 MHz, CDCl<sub>3</sub>): δ168.2, δ137.1, δ130.0, δ128.7, δ128.5, δ128.2, δ128.1, δ123.4, δ122.1, δ85.4, δ80.3, δ78.6, δ71.3, δ32.5, δ24.8, δ18.5, δ3.4;

HRMS (ESI)  $m/z$  calcd for C<sub>21</sub>H<sub>23</sub>NO<sub>2</sub> [M+Na]<sup>+</sup>: 344.1626, found: 344.1627.



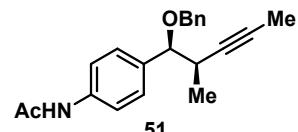
**N-(3-((1S,2R)-1-(benzyloxy)-2-methylpent-3-yn-1-yl)phenyl)acetamide (50):** Prepared by the *general procedure D* using **47**. The crude material was purified with silica gel column Chromatography using 40 % ethyl acetate in Hexanes. **50** (4.42 g, 13.75 mmol, 96% yield) was obtained as a pale yellow, viscous oil.  $[\alpha]_D^{23.8} = -18$  ( $c = 3.7$ ,  $\text{CH}_2\text{Cl}_2$ ).

$^1\text{H}$  NMR (500 MHz,  $\text{CDCl}_3$ ):  $\delta$  7.59 (d,  $J = 8.0$  Hz, 1H), 7.39 (s, 1H), 7.35-7.27 (m, 5H), 7.19 (s, 1H), 7.12 (d,  $J = 7.7$  Hz, 1H), 84.51 (d,  $J = 12.0$  Hz, 1H), 84.27 (d,  $J = 12.0$  Hz, 1H), 84.16 (d,  $J = 7.2$  Hz, 1H), 82.79-2.72 (m, 1H), 82.18 (s, 3H), 81.69 (d,  $J = 2.4$  Hz, 3H), 81.21 (d,  $J = 6.9$  Hz, 3H);

$^{13}\text{C}$  NMR (125 MHz,  $\text{CDCl}_3$ ):  $\delta$  168.4, 141.2, 138.3, 137.8, 128.6, 128.3, 127.7, 127.5, 123.8, 119.4, 118.8, 83.9, 80.6, 78.0, 70.7, 33.7, 324.6, 17.7, 3.5;

IR (neat/ $\text{cm}^{-1}$ )  $\nu_{\text{max}}$ : 3299, 3149, 3088, 3030, 2973, 2917, 2871, 1664, 1611, 1594, 1554, 1488, 1440, 1370, 1317, 1304, 1264, 1065, 1028;

HRMS (ESI)  $m/z$  calcd for  $\text{C}_{21}\text{H}_{23}\text{NO}_2$  [ $\text{M}+\text{Na}]^+$ : 344.1626, found: 344.1632.



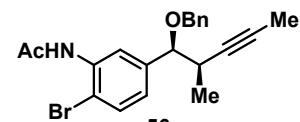
**N-(4-((1S,2R)-1-(benzyloxy)-2-methylpent-3-yn-1-yl)phenyl)acetamide (51):** Prepared by the *general procedure D* using **48**. The crude material was purified with silica gel column Chromatography using 50 % ethyl acetate in Hexanes. **51** (4.37 g, 13.60 mmol, 95% yield) was obtained as a pale yellow, viscous oil.  $[\alpha]_D^{23.8} = -18.2$  ( $c = 0.87$ ,  $\text{CH}_2\text{Cl}_2$ ).

$^1\text{H}$  NMR (500 MHz,  $\text{CDCl}_3$ ):  $\delta$  7.49 (d,  $J = 8.4$  Hz, 1H), 7.34-7.27 (m, 5H), 7.17 (brs, 1H), 84.49 (d,  $J = 12.0$  Hz, 1H), 84.24 (d,  $J = 12.0$  Hz, 1H), 84.12 (d,  $J = 7.3$  Hz, 1H), 82.75 (dddq,  $J = 9.3, 6.9, 4.5, 2.3$  Hz, 1H), 82.19 (s, 3H), 81.68 (d,  $J = 2.4$  Hz, 3H), 81.20 (d,  $J = 6.9$  Hz, 3H);

<sup>13</sup>C NMR (125 MHz, CDCl<sub>3</sub>): δ168.4, δ138.3, δ137.4, δ136.1, δ128.4, δ128.2, δ127.8, δ127.5, δ119.4, δ83.6, δ80.6, δ78.0, δ70.5, δ33.7, δ24.6, δ17.9, δ3.5;

IR (neat/cm<sup>-1</sup>)  $\nu_{\text{max}}$ : 3303, 3193, 3125, 3063, 3032, 2974, 2918, 2817, 1664, 1603, 1537, 1513, 1497, 1453, 1411, 1370, 1315, 1288, 1265, 1204, 1177, 1110, 1085, 1065, 1028;

HRMS (ESI) *m/z* calcd for C<sub>21</sub>H<sub>23</sub>NO<sub>2</sub> [M+H]<sup>+</sup>: 322.1807, found: 322.1814.



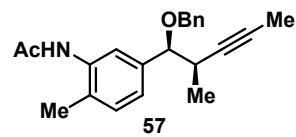
**N-(5-((1S,2R)-1-(benzyloxy)-2-methylpent-3-yn-1-yl)-2-bromophenyl)acetamide (56):** Prepared by the general procedure D using 54. The crude material was purified with silica gel column Chromatography using 34% ethyl acetate in Hexanes. 56 (2.69 g, 6.73 mmol, 47% yield) was obtained as a pale yellow, viscous oil.  $[\alpha]_D^{23.8} = -13.8$  (*c* = 2.6, CH<sub>2</sub>Cl<sub>2</sub>).

<sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>): δ8.36 (s, 1H), δ7.60 (s, 1H), δ7.52 (d, *J* = 8.3 Hz, 1H), δ7.34-7.27 (m, 5H), δ7.07 (dd, *J* = 8.2, 1.8 Hz, 2H), δ4.51 (d, *J* = 12.0 Hz, 1H), δ4.26 (d, *J* = 11.9 Hz, 1H), δ4.15 (d, *J* = 7.3 Hz, 1H), δ2.79-2.72 (m, 1H), δ2.24 (s, 3H), δ1.70 (d, *J* = 2.4 Hz, 3H), δ1.20 (d, *J* = 6.9 Hz, 3H);

<sup>13</sup>C NMR (125 MHz, CDCl<sub>3</sub>): δ168.0, δ141.1, δ140.5, δ138.1, δ135.2, δ131.7, δ128.3, δ127.8, δ127.5, δ124.1, δ121.6, δ112.1, δ83.6, δ80.3, δ78.3, δ70.8, δ33.6, δ24.9, δ17.8, δ3.5;

IR (neat/cm<sup>-1</sup>)  $\nu_{\text{max}}$ : 3063, 3031, 2973, 2934, 2919, 2874, 1712, 1474, 1454, 1415, 1366, 1300, 1263, 1237, 1213, 1113, 1074, 1045, 1020;

HRMS (ESI) *m/z* calcd for C<sub>21</sub>H<sub>22</sub>BrNO<sub>2</sub> [M+H]<sup>+</sup>: 400.0912, found: 400.0912.



**N-(5-((1S,2R)-1-(benzyloxy)-2-methylpent-3-yn-1-yl)-2-methylphenyl)acetamide (57):** Prepared by the general procedure D using **55**. The crude material was purified with silica gel column Chromatography using 37 % ethyl acetate in Hexanes. **57** (2.45 g, 7.30 mmol, 51% yield) was obtained as a pale yellow, viscous oil.  $[\alpha]_D^{23.8} = -18.9$  ( $c = 5.3$ ,  $\text{CH}_2\text{Cl}_2$ ).

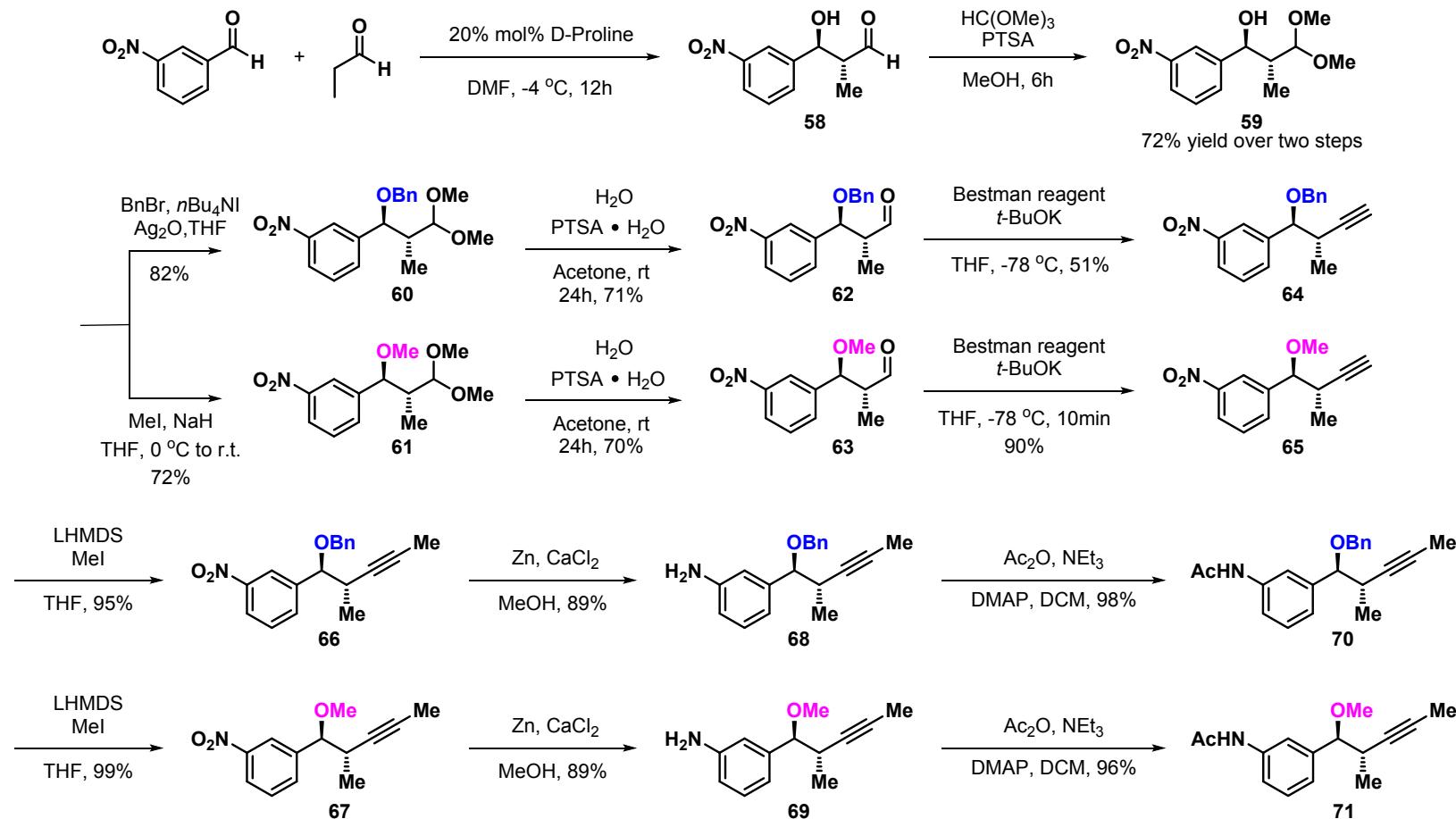
$^1\text{H}$  NMR (500 MHz,  $\text{CDCl}_3$ ):  $\delta$  7.74 (s, 1H), 7.34-7.25 (m, 5H), 7.19-7.13 (m, 2H), 7.06 (brs, 1H), 7.45 (d,  $J = 12.1$  Hz, 1H), 7.26 (d,  $J = 12.0$  Hz, 1H), 7.17 (d,  $J = 6.9$  Hz, 1H), 7.00-6.92 (m, 1H), 6.27 (s, 3H), 6.19 (s, 3H), 6.10 (d,  $J = 6.8$  Hz, 3H);

$^{13}\text{C}$  NMR (125 MHz,  $\text{CDCl}_3$ ):  $\delta$  168.2, 138.8, 138.4, 135.3, 130.2, 129.0, 128.3, 127.8, 127.4, 124.5, 123.1, 83.7, 80.8, 77.9, 70.6, 33.7, 24.3, 17.7, 3.6;

IR (neat/ $\text{cm}^{-1}$ )  $\nu_{\text{max}}$ : 3266, 3029, 2972, 2930, 2918, 2874, 1660, 1581, 1535, 1497, 1453, 1424, 1369, 1335, 1283, 1204, 1114, 1072, 1028;

HRMS (ESI)  $m/z$  calcd for  $\text{C}_{22}\text{H}_{25}\text{NO}_2$  [ $\text{M}+\text{Na}]^+$ : 358.1783, found: 358.1770.

**Supplementary Scheme S2. Synthesis of *Anti*-Substrates**



**1.5. General Procedure E for Enantioselective Cross Aldol Reaction Catalyzed by D- or L-Proline for the Synthesis of *Anti*- $\beta$ -Hydroxyl Aldehyde **58** and Related<sup>5</sup>**

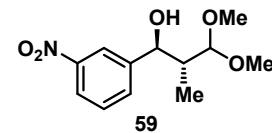
Nitrobenzaldehyde (10g, 66.2 mmol, 1 equiv) and D- or L-proline (1.52g, 13.2 mmol, 0.2 equiv) were dissolved in 662 mL anhydrous *N,N*-dimethylformamide (DMF) at room temperature. Freshly distilled propionaldehyde (6.2 mL, 86.06 mmol, 1.3 equiv) was added into the above mixture, which was subsequently placed into -4 °C chiller and stirred for 6h. The reaction was quenched by adding 200 mL DI water and warmed to room temperature. DMF was removed by washing the mixture with 5% LiCl (50g LiCl and 1 liter DI water) solution. Accordingly, 500 mL 5% LiCl solution and 700 mL ethyl acetate were added into the quenched reaction mixture. After extractive workup, the aqueous layer was back extracted with 250 mL ethyl acetate twice. The combined organic layer was washed with 5% LiCl solution (250 mL x 4). The organic layer was then dried over MgSO<sub>4</sub>, filtered, and concentrated. The afforded *anti*-β-hydroxyl aldehyde was unstable on silica gel column or if stored overnight, and was used immediately in the next reaction.

**58** (dr: 10:1) was synthesized according to *general procedure E* using 2-nitrobenzaldehyde and D-proline. It was used without purification.

<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>): δ9.80 (s, 1H), δ8.23 (d, *J* = 8.7 Hz, 1H), δ7.54 (d, *J* = 8.4 Hz, 1H), δ4.96 (d, *J* = 7.8 Hz, 1H), δ2.80-2.73 (m, 1H), δ0.99 (d, *J* = 7.5 Hz, 3H).

### 1.6. General procedure F for Synthesis of *Anti*-β-Hydroxyl Dimethyl Acetal **59** and Related

To a solution of *anti*-β-hydroxyl aldehyde (10g, 47.8 mmol, 1 equiv, treated as 75% pure from previous step) in 240 mL anhydrous MeOH at room temperature was added trimethyl orthoformate (11 mL, 95.6 mmol, 2 equiv) and *p*-toluenesulfonic acid monohydrate (700mg, 3.83 mmol, 0.08 equiv) sequentially. The resulting solution was stirred at room temperature for 6 hours before it was quenched with saturated NaHCO<sub>3</sub> (aq). It was then extracted with ethyl acetate (400 mL x 3). The combined organic layers were dried over MgSO<sub>4</sub>, filtered, and concentrated. Purification over silica gel chromatography afforded *anti*-β-hydroxyl dimethyl acetal as a pale yellow viscous oil.



**(1*S*,2*R*)-3,3-dimethoxy-2-methyl-1-(3-nitrophenyl)propan-1-ol (59):** Prepared by *general procedure F* using **58**. The crude material was purified with silica gel column Chromatography using 30% ethyl acetate in hexanes. **59** (12.17g, 47.66 mmol, 72% over two steps, dr: 10:1) was afforded as a pale yellow, viscous oil.

<sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>): δ8.23 (t, *J* = 1.9 Hz, 1H), δ8.14 (ddd, *J* = 8.2, 2.3, 1.0 Hz, 1H), δ7.67 (d, *J* = 7.7 Hz, 1H), δ7.51 (t, *J* = 7.9 Hz, 1H), δ4.72 (dd, *J* = 8.5, 1.6 Hz, 1H), δ4.41 (d, *J* = 1.8 Hz, 1H), δ4.34 (d, *J* = 5.5 Hz, 1H), δ3.51 (s, 3H), δ3.43 (s, 3H), δ2.17-2.10 (m, 1H), δ1.55 (s, 3H), δ0.69 (d, *J* = 7.0 Hz, 3H);

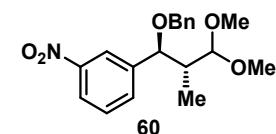
<sup>13</sup>C NMR (125 MHz, CDCl<sub>3</sub>): δ148.3, δ145.2, δ133.3, δ129.1, δ122.6, δ122.1, δ108.6, δ75.6, δ56.2, δ53.7, δ42.5, δ12.4;

IR (neat/cm<sup>-1</sup>)  $\nu_{\text{max}}$ : 3439, 2973, 2938, 2913, 2835, 1527, 1458, 1348, 1206, 1190, 1145, 1096, 1043, 1002;

LCMS (ESI) *m/z* calcd for C<sub>12</sub>H<sub>17</sub>NO<sub>5</sub> [M+H]<sup>+</sup>: 256.11, found: 256.16.

### 1.7. General procedure G for the Hydroxyl Protection of Anti-β-Hydroxyl Dimethyl Acetal 59 and Related as Benzyl Ether<sup>6</sup>

To a solution of *anti*-β-hydroxyl dimethyl acetal (10g, 39.17 mmol, 1 equiv) in a solvent mixture of 50 mL THF and 50 mL DMF was added in benzyl bromide (13.96 mL, 117.51 mmol, 3 equiv) at room temperature. Tetrabutylammonium iodide (2.89g, 7.82 mmol, 0.2 equiv) was added into above mixture and stirred for 5 minutes, followed by silver (I) oxide (27g, 116.5 mmol, 3 equiv). The reaction mixture was stirred at room temperature for 4 hours. It was quenched by filtering through a pad of Celite. 500 mL 5% LiCl (aq) solution and 700 mL ethyl acetate were added in before extractive workup. The aqueous layer was back extracted with 250 mL ethyl acetate for three times. The combined organic layers were washed with 5% LiCl (aq) solution (250 mL x 4), dried over MgSO<sub>4</sub>, filtered, and concentrated. Purification over silica gel chromatography afforded the benzyl protected dimethyl acetal.



**1-((1*S*,2*R*)-1-(benzyloxy)-3,3-dimethoxy-2-methylpropyl)-3-nitrobenzene (60):** Prepared by general procedure G using **59**. The crude material was purified with silica gel column Chromatography using 12.8% ethyl acetate in hexanes. **60** (11.1 g, 32.12 mmol, 82% yield) was afforded as a pale yellow, viscous oil.  $[\alpha]_D^{23.8} = -30.5$  (*c* = 1.9, CH<sub>2</sub>Cl<sub>2</sub>).

<sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>): δ8.22-8.21 (m, 1H), δ8.18-8.16 (m, 1H), δ7.67 (d, *J* = 7.6 Hz, 1H), δ7.54 (t, *J* = 7.9 Hz, 1H), δ7.36-7.27 (m, 5H), δ4.48 (d, *J* = 7.9 Hz, 1H), δ4.40 (d, *J* = 11.6 Hz, 1H), δ4.37 (d, *J* = 4.7 Hz, 1H), δ4.26 (d, *J* = 11.7 Hz, 1H), δ3.40 (s, 3H), δ3.38 (s, 3H), δ2.29-2.23 (m, 1H), δ0.69 (d, *J* = 7.0 Hz, 2H);

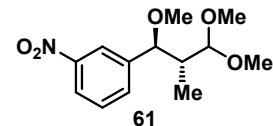
<sup>13</sup>C NMR (125 MHz, CDCl<sub>3</sub>): δ148.4, δ142.7, δ137.8, δ133.9, δ129.2, δ128.4, δ127.8, δ122.8, δ122.7, δ105.8, δ81.3, δ70.9, δ55.6, δ55.0, δ42.3, δ8.8;

IR (neat/cm<sup>-1</sup>) ν<sub>max</sub>: 3089, 3066, 3031, 2981, 2938, 2915, 2832, 1527, 1497, 1454, 1347, 1312, 1207, 1134, 1064, 1047, 1028, 1001;

LCMS (ESI) *m/z* calcd for C<sub>19</sub>H<sub>23</sub>NO<sub>5</sub> [M+Na]<sup>+</sup>: 368.16, found: 368.17.

### 1.8. General procedure H for Hydroxyl Protection of *Anti*-β-Hydroxyl Dimethyl Acetal **59** and Related as Methyl Ether

Sodium hydride (3.1 g, 78 mmol, 60% dispersed in mineral oil, 2 equiv) was washed with Hexanes (~4 mL) twice and suspended in 480 mL THF. Iodomethane (9.7 mL, 156 mmol, 4 equiv) was added into above solution and cooled to 0 °C. *Anti*-β-hydroxyl dimethyl acetal (10 g, 39 mmol, 1 equiv) in 20 mL THF was added into above solution slowly. The resulting mixture was slowly warmed to room temperature and stirred for 4 hours. After the completion of the reaction, it was then quenched with 100 mL saturated NH<sub>4</sub>Cl aqueous solution. The mixture was then partitioned between 480 mL THF and 500 mL DI water, and extracted with ethyl acetate (300 mL x 3). The combined organic layers were dried over MgSO<sub>4</sub>, filtered, and concentrated. Purification over silica gel chromatography afforded methyl ether.



**1-nitro-3-((1*S*,2*R*)-1,3,3-trimethoxy-2-methylpropyl)benzene (61):** Prepared by *general procedure H* using **59**. The crude material was purified with silica gel column Chromatography using 14% ethyl acetate in hexanes. **61** (7.56 g, 28.08 mmol, 72% yield) was afforded as a pale yellow, viscous oil. [α]<sub>D</sub><sup>23.8</sup> = -45.3 (*c* = 1.6, CH<sub>2</sub>Cl<sub>2</sub>).

<sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>): δ8.16-8.14 (m, 1H), δ7.62 (d, *J* = 7.6 Hz, 1H), δ7.53 (td, *J* = 7.6, 1.8 Hz, 1H), δ4.30 (d, *J* = 5.0 Hz, 1H), δ4.26 (d, *J* = 7.7 Hz, 1H), δ3.45 (s, 3H), δ3.42 (s, 3H), δ3.20 (s, 3H), δ2.25-2.18 (m, 1H), δ0.68 (d, *J* = 7.0 Hz, 3H);

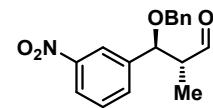
<sup>13</sup>C NMR (125 MHz, CDCl<sub>3</sub>): δ148.3, δ142.5, δ133.8, δ129.1, δ122.7, δ122.5, δ105.8, δ83.6, δ56.8, δ55.5, δ54.9, δ42.1, δ8.7;

IR (neat/cm<sup>-1</sup>) ν<sub>max</sub>: 2978, 2935, 2828, 1528, 1463, 1347, 1313, 1210, 1189, 1134, 1091, 1068, 1047;

HRMS (ESI)  $m/z$  calcd for  $C_{13}H_{19}NO_5 [M+Na]^+$ : 292.1161, found: 292.1150.

### 1.9. General procedure I for the Synthesis of Aldehyde from Dimethyl Acetal

To a solution of dimethyl acetal (25 mmol, 1 equiv) in 250 mL acetone (reagent grade from Sigma Aldrich) at room temperature was added in DI water (13.8 mL, 750 mmol, 30 equiv) followed by *p*-toluenesulfonic acid monohydrate (951 mg, 5 mmol, 0.2 equiv). The resulting reaction mixture was stirred at room temperature until completion (6-12 hours), after which it was quenched with saturated  $NaHCO_3$  (aq) solution. Acetone was evaporated in vacuo before the mixture was then partitioned between 500 mL DI water and 500 mL ethyl acetate. The aqueous layer was extracted with ethyl acetate (200 mL x 3). The combined organic layers were dried over  $MgSO_4$ , filtered, and concentrated. Purification over silica gel chromatography afforded aldehyde.



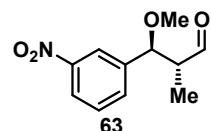
**(2*R*,3*S*)-3-(benzyloxy)-2-methyl-3-(3-nitrophenyl)propanal (62):** Prepared by *general procedure H* using **60**. The crude material was purified with silica gel column Chromatography using 17% ethyl acetate in hexanes. **62** (5.31 g, 17.75 mmol, 71% yield) was afforded as a pale yellow, viscous oil.  $[\alpha]_D^{23.8} = -39.5$  ( $c = 2.1, CH_2Cl_2$ ).

$^1H$  NMR (500 MHz,  $CDCl_3$ ):  $\delta$  9.80 (d,  $J = 2.5$  Hz, 1H), 8.24-8.21 (m, 2H), 8.19 (d,  $J = 7.6$  Hz, 1H), 8.10 (dd,  $J = 8.7, 7.7$  Hz, 1H), 8.00-7.30 (m, 2H), 7.23 (d,  $J = 7.0$  Hz, 2H), 84.61 (d,  $J = 8.8$  Hz, 1H), 84.46 (d,  $J = 11.7$  Hz, 1H), 84.27 (d,  $J = 11.7$  Hz, 1H), 82.85-2.78 (m, 1H), 80.86 (d,  $J = 7.2$  Hz, 3H);

$^{13}C$  NMR (125 MHz,  $CDCl_3$ ):  $\delta$  202.7, 148.5, 141.5, 136.9, 133.4, 129.8, 128.5, 128.1, 128.0, 123.5, 122.5, 881.1, 871.2, 852.4, 810.9;

IR (neat/ $cm^{-1}$ )  $\nu_{max}$ : 3065, 3032, 2980, 2936, 2870, 2719, 1726, 1688, 1526, 1478, 1348, 1311, 1207, 1092, 1066, 1028;

LCMS (ESI)  $m/z$  calcd for  $C_{17}H_{17}NO_4 [M+Na]^+$ : 322.12, found: 322.13.



**(2*R*,3*S*)-3-methoxy-2-methyl-3-(3-nitrophenyl)propanal (63):** Prepared by *general procedure I* using **61**. The crude material was purified with silica gel column Chromatography using 17% ethyl acetate in hexanes. **63** (3.91 g, 17.5 mmol, 70% yield) was afforded as a pale yellow, viscous oil.  $[\alpha]_D^{23.8} = -37.6$  ( $c = 0.93$ ,  $\text{CH}_2\text{Cl}_2$ ).

$^1\text{H}$  NMR (500 MHz,  $\text{CDCl}_3$ ):  $\delta$  9.81 (d,  $J = 2.5$  Hz, 1H), 8.22-8.19 (m, 2H), 87.66 (d,  $J = 7.7$  Hz, 1H), 87.59 (t,  $J = 7.8$  Hz, 1H), 84.43 (d,  $J = 8.7$  Hz, 1H), 83.23 (s, 3H), 82.78-2.72 (m, 1H), 80.88 (d,  $J = 7.2$  Hz, 3H);

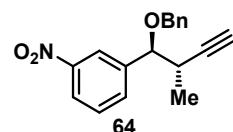
$^{13}\text{C}$  NMR (125 MHz,  $\text{CDCl}_3$ ):  $\delta$  202.8, 148.5, 141.4, 133.3, 129.7, 123.4, 122.3, 83.8, 57.3, 52.4, 10.8;

IR (neat/ $\text{cm}^{-1}$ )  $\nu_{\text{max}}$ : 3088, 2984, 2936, 2830, 2720, 1726, 1688, 1633, 1527, 1479, 1452, 1351, 1312, 1288, 1189, 1096, 1019;

HRMS (ESI)  $m/z$  calcd for  $\text{C}_{11}\text{H}_{13}\text{NO}_4$  [ $\text{M}+\text{Na}]^+$ : 246.0742, found: 246.0746.

### 1.10. General procedure J for Seydel-Gilbert Homologation for the Synthesis of Terminal Alkyne from Aldehyde<sup>7</sup>

Potassium *tert*-butoxide (5.68 g, 50.6 mmol, 2.2 equiv) was suspended in 220 mL THF and cooled to -78 °C. Dimethyl diazomethylphosphonate<sup>8</sup> (6.90 g, 46 mmol, 2 equiv) in 4 mL THF was added into above solution dropwise and stirred for 20 minutes, followed by the dropwise addition of aldehyde (23 mmol, 1 equiv) in 6 mL THF. The resulting mixture was stirred at -78 °C for 10 minutes, before it was quenched with 250 mL saturated  $\text{NH}_4\text{Cl}$  (aq) solution. 500 mL DI water was added into the quenched mixture and the organic layer was collected. The aqueous layer was extracted with ethyl acetate (200 mL x3). The combined organic layers were dried over  $\text{MgSO}_4$ , filtered, and concentrated. Purification over silica gel chromatography afforded aldehyde as a pale yellow oil.



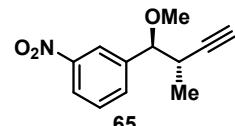
**1-((1*S*,2*S*)-1-(benzyloxy)-2-methylbut-3-yn-1-yl)-3-nitrobenzene (64):** Prepared by *general procedure J* using **62**. The crude material was purified with silica gel column Chromatography using 11% ethyl acetate in hexanes. **64** (3.46 g, 11.73 mmol, 51% yield) was afforded as a pale yellow, viscous oil.  $[\alpha]_D^{23.8} = -67.2$  ( $c = 2.9$ ,  $\text{CH}_2\text{Cl}_2$ ).

<sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>): δ8.25 (s, 1H), δ8.19 (d, *J* = 8.1 Hz, 1H), δ7.74 (d, *J* = 7.6 Hz, 1H), δ7.55 (t, *J* = 7.9 Hz, 1H), δ7.36-7.29 (m, 5H), δ4.59 (d, *J* = 12.1 Hz, 1H), δ4.46 (d, *J* = 5.3 Hz, 1H), δ4.34 (d, *J* = 12.0 Hz, 1H), δ2.92-2.87 (m, 1H), δ2.14 (d, *J* = 2.4 Hz, 1H), δ1.12 (d, *J* = 7.0 Hz, 3H);

<sup>13</sup>C NMR (125 MHz, CDCl<sub>3</sub>): δ148.2, δ141.5, δ137.4, δ133.6, δ129.1, δ128.4, δ127.9, δ127.8, δ123.0, δ122.6, δ84.8, δ81.9, δ71.3, δ71.1, δ33.0, δ16.6;

IR (neat/cm<sup>-1</sup>)  $\nu_{\text{max}}$ : 3295, 3089, 3065, 3030, 2979, 2935, 2873, 1528, 1454, 1349, 1093, 1071, 1028;

HRMS (ESI) *m/z* calcd for C<sub>18</sub>H<sub>17</sub>NO<sub>3</sub> [M+H]<sup>+</sup>: 296.1287, found: 296.1273.



**1-((1*S*,2*S*)-1-methoxy-2-methylbut-3-yn-1-yl)-3-nitrobenzene (65):** Prepared by *general procedure J* using **63**. The crude material was purified with silica gel column Chromatography using 8.7% ethyl acetate in hexanes. **65** (4.54 g, 20.7 mmol, 90% yield) was afforded as a white solid.  $[\alpha]_D^{23.8} = -70.9$  (*c* = 2, CH<sub>2</sub>Cl<sub>2</sub>).

<sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>): δ8.24-8.22 (m, 1H), δ8.19-8.17 (m, 1H), δ7.71 (d, *J* = 7.6 Hz, 1H), δ7.55 (t, *J* = 7.9 Hz, 1H), δ4.26 (d, *J* = 5.3 Hz, 1H), δ3.32 (s, 3H), δ2.89-2.82 (m, 1H), δ2.14 (d, *J* = 2.5 Hz, 1H), δ1.14 (d, *J* = 7.1 Hz, 3H);

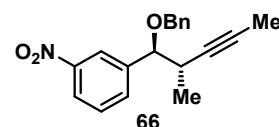
<sup>13</sup>C NMR (125 MHz, CDCl<sub>3</sub>): δ148.2, δ141.4, δ133.4, δ129.1, δ123.0, δ122.4, δ84.9, δ84.6, δ71.0, δ57.7, δ33.0, δ16.6;

IR (neat/cm<sup>-1</sup>)  $\nu_{\text{max}}$ : 3296, 2983, 2936, 2877, 2828, 1526, 1454, 1349, 1203, 1136, 1094;

LCMS (ESI) *m/z* calcd for C<sub>12</sub>H<sub>13</sub>NO<sub>3</sub> [M+Na]<sup>+</sup>: 242.079, found: 242.084.

### 1.11. General Procedure K for Methylation of Terminal Alkyne

To a solution of terminal alkyne (10 mmol, 1 equiv) in 200 mL THF at -78 °C was added in lithium bis(trimethylsilyl)amide solution (20 mL, 20 mmol, 2 equiv, 1M in THF) dropwise. The resulting reaction mixture was stirred at -78 °C for 1 hour (check HNMR for completion of deprotonation). Iodomethane (6.2 mL, 100 mmol, 10 equiv) was added into the above mixture dropwise, which was slowly warmed to room temperature and stirred for 5 hours. The reaction was quenched with 200 mL saturated NH<sub>4</sub>Cl (aq) solution. 200 mL DI water added into the mixture for extractive isolation. The aqueous layer was extracted with ethyl acetate (100 mL x3). The combined organic layers were dried over MgSO<sub>4</sub>, filtered, and concentrated. Purification over silica gel chromatography afforded internal alkyne.



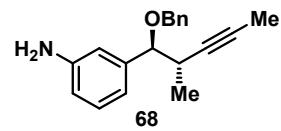
**1-((1S,2S)-1-(benzyloxy)-2-methylpent-3-yn-1-yl)-3-nitrobenzene (66):** Prepared by *general procedure K* using **64**. The crude material was purified with silica gel column Chromatography using 6.3% ethyl acetate in hexanes. **66** (2.94 g, 9.5 mmol, 95% yield) was afforded as a pale yellow oil.  $[\alpha]_D^{23.8} = -68.2$  ( $c = 2.5$ , CH<sub>2</sub>Cl<sub>2</sub>).

<sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>): δ8.27 (s, 1H), δ8.18 (ddd,  $J = 8.2, 2.2, 1.0$  Hz, 1H), δ7.71 (d,  $J = 7.6$  Hz, 1H), δ7.53 (t,  $J = 7.9$  Hz, 1H), δ7.36-7.82 (m, 5H), δ4.60 (d,  $J = 12.2$  Hz, 1H), δ4.42 (d,  $J = 5.2$  Hz, 1H), δ4.33 (d,  $J = 12.2$  Hz, 1H), δ2.88-2.81 (m, 1H), δ1.79 (d,  $J = 2.4$  Hz, 3H), δ1.06 (d,  $J = 7.0$  Hz, 3H);

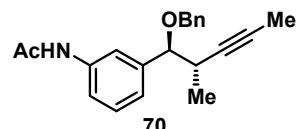
<sup>13</sup>C NMR (125 MHz, CDCl<sub>3</sub>): δ148.1, δ141.9, δ137.6, δ133.6, δ128.9, δ128.4, δ127.8, δ122.8, δ122.7, δ82.3, δ79.8, δ78.8, δ71.9, δ33.0, δ16.7, δ3.5;

IR (neat/cm<sup>-1</sup>)  $\nu_{\max}$ : 3089, 3064, 3032, 2977, 2935, 2918, 2871, 1526, 1497, 1454, 1347, 1312, 1204, 1166, 1094, 1071, 1028;

HRMS (ESI) *m/z* calcd for C<sub>19</sub>H<sub>19</sub>NO<sub>3</sub> [M+H]<sup>+</sup>: 310.1443, found: 310.1458.



**3-((1S,2S)-1-(benzyloxy)-2-methylpent-3-yn-1-yl)aniline (68):** Prepared by *general procedure C* using **66** (2.94g, 9.5 mmol). The crude material was purified with silica gel column Chromatography using 21% ethyl acetate in hexanes. **68** (2.36g, 8.46 mmol, 89% yield) was afforded as a pale yellow, viscous oil. (Use without purification)



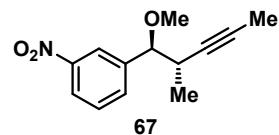
**N-(3-((1S,2S)-1-(benzyloxy)-2-methylpent-3-yn-1-yl)phenyl)acetamide (70):** Prepared by *general procedure D* using **68** (2.36g, 8.46 mmol). The crude material was purified with silica gel column Chromatography using 38% ethyl acetate in hexanes. **70** (2.66g, 8.29 mmol, 98% yield) was afforded as a colorless, viscous oil.  $[\alpha]_D^{23.8} = -52.5$  ( $c = 2$ ,  $\text{CH}_2\text{Cl}_2$ ).

$^1\text{H}$  NMR (500 MHz,  $\text{CDCl}_3$ ):  $\delta$  7.58 (d,  $J = 7.9$  Hz, 1H), 7.37-2.27 (m, 6H), 7.17 (brs, 1H), 7.10 (d,  $J = 7.7$  Hz, 1H), 7.05 (d,  $J = 12.3$  Hz, 1H), 7.02 (d,  $J = 12.3$  Hz, 1H), 7.01 (d,  $J = 6.7$  Hz, 1H), 7.00-6.98 (m, 1H), 6.95 (s, 3H), 6.92 (d,  $J = 2.2$  Hz, 3H), 6.88 (s, 3H), 6.85 (d,  $J = 7.0$  Hz, 3H);

$^{13}\text{C}$  NMR (125 MHz,  $\text{CDCl}_3$ ):  $\delta$  168.4, 140.8, 138.3, 137.9, 128.8, 128.3, 127.8, 127.5, 123.6, 119.4, 118.7, 83.7, 81.0, 77.4, 70.6, 33.3, 24.6, 17.4, 3.7;

IR (neat/cm<sup>-1</sup>)  $\nu_{\text{max}}$ : 3302, 3147, 3088, 3063, 3030, 2976, 2917, 2933, 2874, 1665, 1611, 1594, 1554, 1453, 1440, 1392, 1371, 1346, 1317, 1305, 1264, 1097, 1071, 1028;

HRMS (ESI)  $m/z$  calcd for  $\text{C}_{21}\text{H}_{23}\text{NO}_2$  [M+Na]<sup>+</sup>: 344.1627, found: 344.1628.



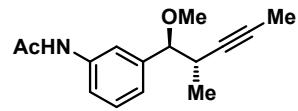
**1-((1S,2S)-1-methoxy-2-methylpent-3-yn-1-yl)-3-nitrobenzene (67):** Prepared by *general procedure K* using 66. The crude material was purified with silica gel column Chromatography using 7.3% ethyl acetate in hexanes. **67** (2.31 g, 9.9 mmol, 99% yield) was afforded as a pale yellow oil.  $[\alpha]_D^{23.8} = -70.2$  ( $c = 2.1$ ,  $\text{CH}_2\text{Cl}_2$ ).

$^1\text{H}$  NMR (500 MHz,  $\text{CDCl}_3$ ):  $\delta$  8.24 (s, 1H), 8.17-8.15 (m, 1H), 87.68 (d,  $J = 7.7$  Hz, 1H), 87.53 (t,  $J = 7.9$  Hz, 1H), 84.23 (d,  $J = 5.0$  Hz, 1H), 83.31 (s, 3H), 82.83-2.76 (m, 1H), 81.79 (d,  $J = 2.3$  Hz, 3H), 81.08 (d,  $J = 7.0$  Hz, 3H);

$^{13}\text{C}$  NMR (125 MHz,  $\text{CDCl}_3$ ):  $\delta$  148.1, 141.8, 133.3, 128.9, 122.7, 122.5, 85.3, 879.5, 878.8, 857.6, 833.0, 816.8, 83.5;

IR (neat/ $\text{cm}^{-1}$ )  $\nu_{\text{max}}$ : 2980, 2935, 2877, 2827, 1526, 1452, 1347, 1203, 1192, 1156, 1108, 1093, 1067;

HRMS (ESI)  $m/z$  calcd for  $\text{C}_{13}\text{H}_{15}\text{NO}_3$  [ $\text{M}+\text{Na}]^+$ : 256.0950, found: 256.0976.



***N*-(3-((1S,2S)-1-methoxy-2-methylpent-3-yn-1-yl)phenyl)acetamide (71):** Prepared by *general procedure D* using **69** (1.79 g, 8.81 mmol). The crude material was purified with silica gel column Chromatography using 46% ethyl acetate in hexanes. **71** (2.08 g, 8.46 mmol, 96% yield) was afforded as a brown solid.  $[\alpha]_D^{23.8} = -45$  ( $c = 2.2$ ,  $\text{CH}_2\text{Cl}_2$ ).

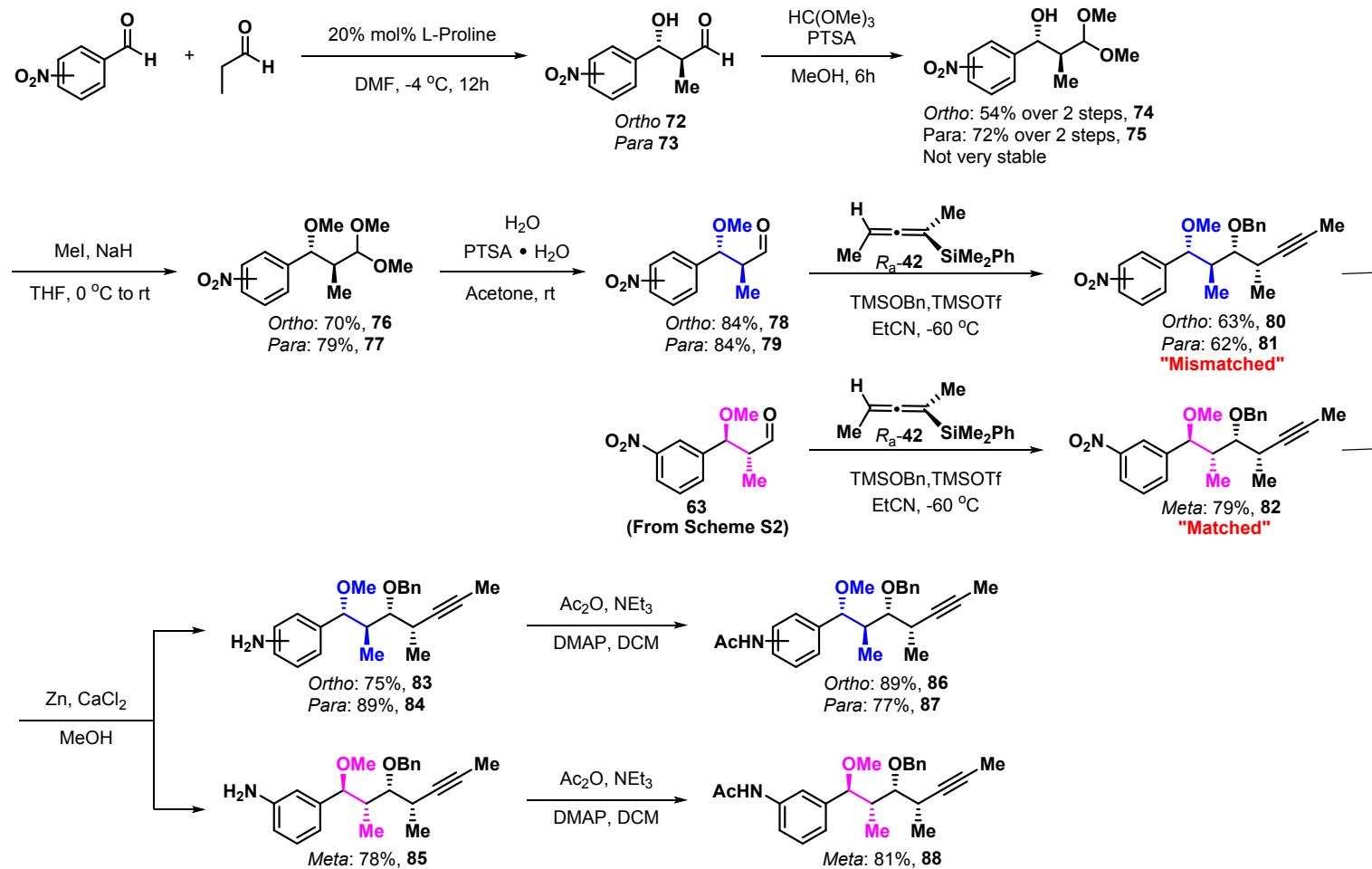
$^1\text{H}$  NMR (500 MHz,  $\text{CDCl}_3$ ):  $\delta$  7.54 (d,  $J = 8.2$  Hz, 1H), 87.37 (s, 1H), 87.31-7.27 (m, 2H), 87.07 (d,  $J = 7.6$  Hz, 1H), 84.01 (d,  $J = 6.5$  Hz, 1H), 83.25 (s, 3H), 82.77-2.69 (m, 1H), 82.18 (s, 3H), 81.80 (d,  $J = 2.2$  Hz, 3H), 81.01 (d,  $J = 7.0$  Hz, 3H);

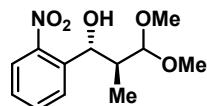
$^{13}\text{C}$  NMR (125 MHz,  $\text{CDCl}_3$ ):  $\delta$  168.6, 140.7, 138.1, 128.7, 123.3, 119.4, 118.5, 86.9, 80.8, 877.4, 857.2, 833.4, 824.5, 817.7, 83.7;

IR (neat/ $\text{cm}^{-1}$ )  $\nu_{\text{max}}$ : 3302, 3149, 3092, 2978, 2933, 2883, 2823, 1665, 1610, 1594, 1551, 1487, 1435, 1371, 1337, 1317, 1305, 1266, 1195, 1169, 1109, 1095, 1068;

HRMS (ESI) *m/z* calcd for C<sub>15</sub>H<sub>19</sub>NO<sub>2</sub> [M+Na]<sup>+</sup>: 268.1313, found: 268.1317.

### Supplementary Scheme S3. Synthesis of *Anti*, *Anti*, *Syn*- and *Anti*, *Syn*, *Syn*-Substrates





74

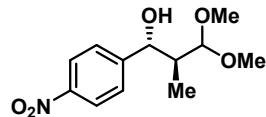
**(1*R*,2*S*)-3,3-dimethoxy-2-methyl-1-(2-nitrophenyl)propan-1-ol (74):** Prepared by *general procedure E* and *F* using 2-nitrobenzaldehyde (10g, 66.2 mmol). The crude material was purified with silica gel column Chromatography using 28% ethyl acetate in hexanes. **74** (9.13 g, 35.75 mmol, 54% yield over two steps, dr>20:1) was afforded as yellow oil.  $[\alpha]_D^{23.8} = +28.7$  ( $c = 1.5$ ,  $\text{CH}_2\text{Cl}_2$ ).

$^1\text{H}$  NMR (500 MHz,  $\text{CDCl}_3$ ):  $\delta$  7.81 (dd,  $J = 8.2, 1.2$  Hz, 1H), 7.72 (dd,  $J = 7.9, 1.4$  Hz, 1H), 7.62 (td,  $J = 7.8, 1.2$  Hz, 1H), 7.41 (ddd,  $J = 8.7, 7.4, 1.4$  Hz, 1H), 7.24 (dd,  $J = 7.8, 2.9$  Hz, 1H), 7.35 (d,  $J = 5.5$  Hz, 1H), 7.31 (d,  $J = 2.9$  Hz, 1H), 7.46 (s, 3H), 7.41 (s, 3H), 7.29-7.21 (m, 1H), 7.09 (d,  $J = 7.1$  Hz, 3H);

$^{13}\text{C}$  NMR (125 MHz,  $\text{CDCl}_3$ ):  $\delta$  149.1, 137.6, 132.8, 129.2, 128.1, 124.0, 108.5, 71.0, 56.2, 53.7, 42.4, 11.9;

IR (neat/ $\text{cm}^{-1}$ )  $\nu_{\text{max}}$ : 3031, 2978, 2937, 2912, 2833, 1606, 1599, 1519, 1497, 1454, 1382, 1343, 1318, 1206, 1133, 1064, 1047;

LCMS (ESI)  $m/z$  calcd for  $\text{C}_{12}\text{H}_{17}\text{NO}_5$  [ $\text{M}+\text{H}]^+$ : 256.11, found: 256.16.



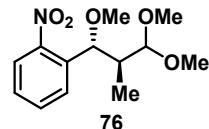
75

**(1*R*,2*S*)-3,3-dimethoxy-2-methyl-1-(4-nitrophenyl)propan-1-ol (75):**<sup>5a</sup> Prepared by *general procedure E* and *F* using 4-nitrobenzaldehyde (10g, 66.2 mmol). The crude material was purified with silica gel column Chromatography using 31% ethyl acetate in hexanes. **75** (12.17 g, 47.66 mmol, 72% yield over two steps, dr>20:1) was afforded as yellow oil.  $[\alpha]_D^{23.8} = -10.8$  ( $c = 1.5$ ,  $\text{CH}_2\text{Cl}_2$ ).

$^1\text{H}$  NMR (500 MHz,  $\text{CDCl}_3$ ):  $\delta$  8.22-8.19 (m, 2H), 7.53-7.50 (m, 2H), 7.42 (dd,  $J = 8.3, 2.0$  Hz, 1H), 7.37 (d,  $J = 2.0$  Hz, 1H), 7.31 (d,  $J = 5.4$  Hz, 1H), 7.30 (s, 3H), 7.42 (s, 3H), 7.15-7.08 (m, 1H), 7.09 (d,  $J = 7.0$  Hz, 3H);

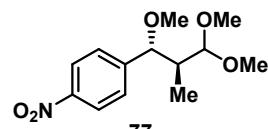
$^{13}\text{C}$  NMR (125 MHz,  $\text{CDCl}_3$ ):  $\delta$  150.4, 147.4, 127.8, 123.4, 108.6, 75.5, 56.1, 53.9, 42.6, 12.2.

IR (neat/cm<sup>-1</sup>)  $\nu_{\text{max}}$ : 3440, 2972, 2939, 2914, 2835, 1606, 1516, 1458, 1343, 1314, 1195, 1144, 1098, 1045, 1014;



**1-nitro-2-((1R,2S)-1,3,3-trimethoxy-2-methylpropyl)benzene (76):** Prepared by *general procedure H* using **74** (9.13 g, 35.75 mmol). The crude material was purified with silica gel column Chromatography using 17% ethyl acetate in hexanes. **76** (6.74 g, 25.03 mmol, 70% yield) was afforded as a pale yellow crystal. (We preferred to use as crude for the next step, so we did not fully characterize it.)

<sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>): δ7.80-7.76 (m, 1H), δ7.64-7.59 (m, 2H), δ7.43-7.40 (m, 1H), δ4.76 (d, *J* = 8.0 Hz, 1H), δ4.50 (d, *J* = 4.0 Hz, 1H), δ3.45 (s, 3H), δ3.33 (s, 3H), δ3.21 (s, 3H), δ2.18 (ddq, *J* = 11.2, 7.2, 4.1, 3.6 Hz, 1H), δ0.73 (d, *J* = 7.1 Hz, 3H);



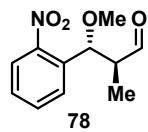
**1-nitro-4-((1R,2S)-1,3,3-trimethoxy-2-methylpropyl)benzene (77):** Prepared by *general procedure H* using **75** (12.17 g, 47.66 mmol). The crude material was purified with silica gel column Chromatography using 18% ethyl acetate in hexanes. **77** (10.14, 37.65 mmol, 79% yield) was afforded as a pale yellow oil.

<sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>): δ8.21 (d, *J* = 8.7 Hz, 2H), δ7.46 (d, *J* = 8.7 Hz, 2H), δ4.30 (d, *J* = 5.0 Hz, 1H), δ4.25 (d, *J* = 7.7 Hz, 1H), δ3.44 (s, 3H), δ3.41 (s, 3H), δ3.19 (s, 3H), δ2.23-2.17 (m, 1H), δ0.67 (d, *J* = 7.0 Hz, 3H);

<sup>13</sup>C NMR (125 MHz, CDCl<sub>3</sub>): δ147.8, δ128.5, δ123.4, δ105.7, δ83.7, δ56.9, δ55.6, δ54.8, δ42.2, δ8.8;

IR (neat/cm<sup>-1</sup>)  $\nu_{\text{max}}$ : 2982, 2936, 2828, 1606, 1599, 1520, 1462, 1382, 1343, 1319, 1244, 1210, 1188, 1133, 1087, 1067, 1047, 1015;

LCMS (ESI) *m/z* calcd for C<sub>13</sub>H<sub>19</sub>NO<sub>5</sub> [M+H]<sup>+</sup>: 270.13, found: 270.16;



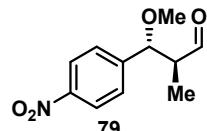
**(2S,3R)-3-methoxy-2-methyl-3-(2-nitrophenyl)propanal (78):** Prepared by *general procedure I* using **76** (6.74 g, 25.03 mmol) (12 hours reaction time). The crude material was purified with silica gel column Chromatography using 17% ethyl acetate in hexanes. **78** (4.69 g, 21.03 mmol, 84% yield, dr: 7:1) was afforded as a pale yellow oil.  $[\alpha]_D^{23.8} = +26$  ( $c = 0.47$ ,  $\text{CH}_2\text{Cl}_2$ ).

$^1\text{H}$  NMR (500 MHz,  $\text{CDCl}_3$ ):  $\delta$  9.76 (d,  $J = 2.6$  Hz, 1H), 8.99-8.97 (m, 1H), 8.72-8.67 (m, 2H), 8.50 (ddd,  $J = 8.5, 6.2, 2.6$  Hz, 1H), 8.06 (d,  $J = 6.5$  Hz, 1H), 8.23 (s, 3H), 8.75 (dq,  $J = 7.1, 2.6$  Hz, 1H), 8.08 (d,  $J = 7.2$  Hz, 3H);

$^{13}\text{C}$  NMR (125 MHz,  $\text{CDCl}_3$ ):  $\delta$  202.5, 135.1, 133.4, 128.9, 128.5, 124.5, 79.8, 57.7, 52.6, 11.2;

IR (neat/ $\text{cm}^{-1}$ )  $\nu_{\text{max}}$ : 2984, 2937, 2829, 2731, 1727, 1690, 1609, 1578, 1526, 1355, 1342, 1298, 1189, 1122, 1093, 1076;

LCMS (ESI)  $m/z$  calcd for  $\text{C}_{11}\text{H}_{13}\text{NO}_4$  [ $\text{M}+\text{Na}]^+$ : 246.07, found: 246.07.



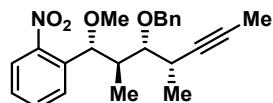
**(2S,3R)-3-methoxy-2-methyl-3-(4-nitrophenyl)propanal (79):** Prepared by *general procedure I* using **77** (10.14, 37.65 mmol) (12 hours reaction time). The crude material was purified with silica gel column Chromatography using 18% ethyl acetate in hexanes. **79** (4.69 g, 21.03 mmol, 84% yield, dr: 10:1) was afforded as a pale yellow oil.  $[\alpha]_D^{23.8} = +74$  ( $c = 1.8$ ,  $\text{CH}_2\text{Cl}_2$ ).

$^1\text{H}$  NMR (500 MHz,  $\text{CDCl}_3$ ):  $\delta$  9.80 (d,  $J = 2.5$  Hz, 1H), 8.27-8.24 (m, 2H), 8.51-8.48 (m, 2H), 8.43 (d,  $J = 8.5$  Hz, 1H), 8.22 (s, 3H), 8.73 (dq,  $J = 8.5, 7.2, 2.5$  Hz, 1H), 8.08 (d,  $J = 7.2$  Hz, 3H);

$^{13}\text{C}$  NMR (125 MHz,  $\text{CDCl}_3$ ):  $\delta$  202.6, 146.5, 128.2, 123.9, 83.8, 57.3, 52.4, 10.8;

IR (neat/ $\text{cm}^{-1}$ )  $\nu_{\text{max}}$ : 2982, 2937, 2827, 2728, 1725, 1607, 1600, 1519, 1492, 1457, 1342, 1316, 1125, 1104, 1085, 1014;

LCMS (ESI)  $m/z$  calcd for  $\text{C}_{11}\text{H}_{13}\text{NO}_4$  [ $\text{M}+\text{H}]^+$ : 224.09, found: 224.11.



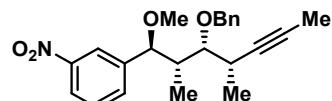
**1-((1R,2R,3R,4S)-3-(benzyloxy)-1-methoxy-2,4-dimethylhept-5-yn-1-yl)-2-nitrobenzene (80):** Prepared by general procedure B using **78** (4.69 g, 21.03 mmol, 1.05 equiv), **R<sub>a</sub>-42** (4.05g, 20.03 mmol, 1 equiv), (benzyloxy)trimethylsilane (4.1 mL, 21.03 mmol, 1.05 equiv), and TMSOTf (1.5 mL, 8 mmol, 0.4 equiv). The reaction was stirred at -60 °C for 12 hours. The crude material (dr: 2:1, double stereodifferentiation, “mismatched”) was purified with silica gel column Chromatography using 61% DCM in Hexanes. **80** (3.21g, 8.41 mmol, 42% major isomer yield) was afforded as a pale yellow oil.  $[\alpha]_D^{23.8} = +120$  ( $c = 2.4$ , CH<sub>2</sub>Cl<sub>2</sub>).

<sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>): δ7.71 (dd,  $J = 8.1, 1.2$  Hz, 1H), δ7.67 (dd,  $J = 7.9, 1.4$  Hz, 1H), δ7.62-7.58 (m, 1H), δ7.42-7.39 (m, 1H), δ7.35-7.27 (m, 5H), δ5.23 (d,  $J = 10.1$  Hz, 1H), δ4.65 (d,  $J = 11.4$  Hz, 1H), δ4.54 (d,  $J = 11.4$  Hz, 1H), δ3.70 (dd,  $J = 9.6, 2.0$  Hz, 1H), δ3.20 (s, 3H), δ2.71-2.65 (m, 1H), δ2.3 (dq,  $J = 9.3, 7.3, 1.9$  Hz, 1H), δ1.87 (d,  $J = 2.4$  Hz, 3H), δ1.26 (d,  $J = 6.7$  Hz, 3H), δ0.72 (d,  $J = 7.3$  Hz, 3H);

<sup>13</sup>C NMR (125 MHz, CDCl<sub>3</sub>): δ151.0, δ138.8, δ136.8, δ132.5, δ128.6, δ128.2, δ128.1, δ127.8, δ127.4, δ123.0, δ82.8, δ81.7, δ79.3, δ77.8, δ72.8, δ56.7, δ43.6, δ28.2, δ19.4, δ11.3, δ3.6;

IR (neat/cm<sup>-1</sup>)  $\nu_{\max}$ : 3065, 3031, 2971, 2932, 2878, 2825, 1607, 1527, 1497, 1454, 1357, 1296, 1206, 1091, 1067, 1028;

HRMS (ESI) *m/z* calcd for C<sub>23</sub>H<sub>27</sub>NO<sub>4</sub> [M+Na]<sup>+</sup>: 404.1838, found: 404.1840.



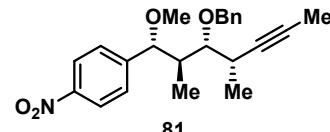
**1-((1S,2S,3R,4S)-3-(benzyloxy)-1-methoxy-2,4-dimethylhept-5-yn-1-yl)-3-nitrobenzene (82):** Prepared by general procedure B using **63** (4.69 g, 21.03 mmol, 1.05 equiv), **R<sub>a</sub>-42** (4.05g, 20.03 mmol, 1 equiv), (benzyloxy)trimethylsilane (4.1 mL, 21.03 mmol, 1.05 equiv), and TMSOTf (1.5 mL, 8 mmol, 0.4 equiv). The reaction was stirred at -60 °C for 12 hours. The crude material (dr> 20:1, double stereodifferentiation, “matched”) was purified with silica gel column Chromatography using 10% ethyl acetate in Hexanes. **82** was (6.34 g, 16.61 mmol, 79% yield) was afforded as a pale yellow oil.  $[\alpha]_D^{23.8} = -30$  ( $c = 1.5$ , CH<sub>2</sub>Cl<sub>2</sub>).

<sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>): δ8.17-8.13 (m, 2H), δ7.63 (d, *J* = 7.6 Hz, 1H), δ7.55-7.52 (m, 1H), δ7.42-7.30 (m, 5H), δ4.77 (d, *J* = 11.6 Hz, 1H), δ4.64 (d, *J* = 11.6 Hz, 1H), δ4.01 (d, *J* = 10.0 Hz, 1H), δ3.92 (dd, *J* = 9.5, 1.6 Hz, 1H), δ3.07 (s, 3H), δ2.69-2.63 (m, 1H), δ2.39-2.33 (m, 1H), δ1.80 (d, *J* = 2.4 Hz, 3H), δ1.31 (d, *J* = 6.8 Hz, 3H), δ0.66 (d, *J* = 7.0 Hz, 3H);

<sup>13</sup>C NMR (125 MHz, CDCl<sub>3</sub>): δ148.4, δ144.0, δ139.0, δ133.9, δ129.2, δ128.4, δ127.5, δ127.3, δ122.8, δ122.7, δ84.9, δ81.8, δ80.8, δ77.8, δ74.9, δ56.3, δ42.8, δ30.1, δ19.0, δ9.8, δ3.7;

IR (neat/cm<sup>-1</sup>)  $\nu_{\text{max}}$ : 3089, 3066, 3031, 2975, 2920, 2876, 2823, 1530, 1453, 1347, 1309, 1210, 1127, 1096, 1072, 1061, 1028;

HRMS (ESI) *m/z* calcd for C<sub>23</sub>H<sub>27</sub>NO<sub>4</sub> [M+H]<sup>+</sup>: 382.2018, found: 382.2029.



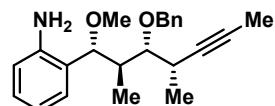
**1-((1*R*,2*R*,3*R*,4*S*)-3-(benzyloxy)-1-methoxy-2,4-dimethylhept-5-yn-1-yl)-4-nitrobenzene (81):** Prepared by *general procedure B* using **79** (4.69 g, 21.03 mmol, 1.05 equiv), **R<sub>a</sub>-42** (4.05g, 20.03 mmol, 1 equiv), (benzyloxy)trimethylsilane (4.1 mL, 21.03 mmol, 1.05 equiv), and TMSOTf (1.5 mL, 8 mmol, 0.4 equiv). The reaction was stirred at -60 °C for 12 hours. The crude material (dr: 3:1, double stereodifferentiation, “mismatched”) was purified with silica gel column Chromatography using 61% DCM in Hexanes. **81** (3.21 g, 8.41 mmol, 42 % major isomer yield) was afforded as a pale yellow oil.  $[\alpha]_D^{23.8} = -6.4$  (*c* = 2.1, CH<sub>2</sub>Cl<sub>2</sub>).

<sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>): δ8.20-8.17 (m, 2H), δ7.43-7.41 (m, 2H), δ7.35-7.28 (m, 5H), δ4.70 (d, *J* = 11.5 Hz, 1H), δ4.64 (d, *J* = 8.3 Hz, 1H), δ4.60 (d, *J* = 11.5 Hz, 1H), δ3.51 (dd, *J* = 7.8, 3.8 Hz, 1H), δ3.18 (s, 3H), δ2.76-2.69 (m, 1H), δ2.32 (ddq, *J* = 11.1, 7.2, 3.6 Hz, 1H), δ1.85 (d, *J* = 2.4 Hz, 3H), δ1.26 (d, *J* = 6.8 Hz, 3H), δ0.72 (d, *J* = 7.2 Hz, 3H);

<sup>13</sup>C NMR (125 MHz, CDCl<sub>3</sub>): δ149.0, δ147.4, δ138.6, δ128.5, δ128.3, δ127.7, δ127.6, δ123.4, δ84.2, δ82.9, δ82.3, δ77.5, δ72.8, δ56.9, δ42.4, δ28.1, δ18.4, δ12.0, δ3.7;

IR (neat/cm<sup>-1</sup>)  $\nu_{\text{max}}$ : 3031, 2973, 2932, 2878, 2822, 1606, 1599, 1521, 1497, 1454, 1344, 1209, 1103, 1087, 1069, 1028, 1014;

HRMS (ESI) *m/z* calcd for C<sub>23</sub>H<sub>27</sub>NO<sub>4</sub> [M+H]<sup>+</sup>: 382.2018, found: 382.2005.



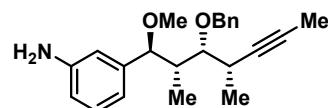
**2-((1*R*,2*R*,3*R*,4*S*)-3-(benzyloxy)-1-methoxy-2,4-dimethylhept-5-yn-1-yl)aniline (83):** Prepared by *general procedure C* using **80** (3.21 g, 8.41 mmol). The crude material was purified with silica gel column Chromatography using 10% ethyl acetate in hexanes. **83** (2.22 g, 6.31 mmol, 75% yield) was afforded as a pale yellow, viscous oil.  $[\alpha]_D^{23.8} = +5.7$  ( $c = 1.2$ ,  $\text{CH}_2\text{Cl}_2$ ).

$^1\text{H}$  NMR (500 MHz,  $\text{CDCl}_3$ ):  $\delta$  7.38-7.28 (m, 5H), 7.08 (td,  $J = 7.6$ , 1.6 Hz, 1H), 6.94 (dd,  $J = 7.5$ , 1.4 Hz, 1H), 6.67 (td,  $J = 7.4$ , 0.7 Hz, 1H), 6.62 (dd,  $J = 8.8$ , 0.8 Hz, 1H), 6.66 (d,  $J = 11.4$  Hz, 1H), 6.57 (d,  $J = 11.4$  Hz, 1H), 6.54 (d,  $J = 10.1$  Hz, 1H), 6.31 (brs, 2H), 6.62 (dd,  $J = 9.5$ , 1.9 Hz, 1H), 6.24 (s, 3H), 6.85-6.71 (m, 2H), 6.86 (d,  $J = 2.4$  Hz, 3H), 6.28 (d,  $J = 6.7$  Hz, 3H), 6.76 (d,  $J = 7.2$  Hz, 3H);

$^{13}\text{C}$  NMR (125 MHz,  $\text{CDCl}_3$ ):  $\delta$  145.5, 138.9, 130.6, 128.3, 128.3, 127.9, 127.4, 123.7, 117.3, 116.1, 86.9, 83.7, 82.5, 73.1, 56.4, 38.4, 28.6, 19.5, 13.2, 8.8;

IR (neat/ $\text{cm}^{-1}$ )  $\nu_{\text{max}}$ : 3456, 3365, 3029, 2971, 2932, 2918, 2876, 2821, 1614, 1584, 1495, 1455, 1377, 1368, 1298, 1270, 1212, 1082, 1028;

HRMS (ESI)  $m/z$  calcd for  $\text{C}_{23}\text{H}_{29}\text{NO}_2$  [ $\text{M}+\text{H}]^+$ : 352.2277, found: 352.2277.



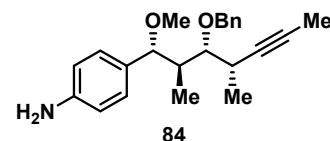
**3-((1*S*,2*S*,3*R*,4*S*)-3-(benzyloxy)-1-methoxy-2,4-dimethylhept-5-yn-1-yl)aniline (85):** Prepared by *general procedure C* using **82** (6.34 g, 16.61 mmol). The crude material was purified with silica gel column Chromatography using 20% ethyl acetate in hexanes. **85** (4.55 g, 12.96 mmol, 78% yield) was afforded as a pale yellow, viscous oil.  $[\alpha]_D^{23.8} = -42.4$  ( $c = 0.33$ ,  $\text{CH}_2\text{Cl}_2$ ).

<sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>): δ7.42-7.28 (m, 5H), δ7.12 (t, *J* = 7.6 Hz, 1H), δ6.68 (d, *J* = 7.5 Hz, 1H), δ6.64-6.61 (m, 2H), δ4.73 (d, *J* = 11.5 Hz, 1H), δ4.66 (d, *J* = 11.6 Hz, 1H), δ3.91 (d, *J* = 9.5 Hz, 1H), δ3.83 (d, *J* = 10.1 Hz, 1H), δ3.65 (brs, 2H), δ3.08 (s, 3H), δ2.68-2.60 (m, 1H), δ2.38-2.32 (m, 1H), δ1.79 (d, *J* = 2.3 Hz, 3H), δ1.29 (d, *J* = 6.8 Hz, 3H), δ0.66 (d, *J* = 7.0 Hz, 3H);

<sup>13</sup>C NMR (125 MHz, CDCl<sub>3</sub>): δ146.3, δ142.6, δ139.3, δ129.0, δ128.3, δ127.4, δ118.7, δ114.5, δ114.3, δ85.6, δ82.1, δ81.1, δ77.4, δ74.9, δ55.9, δ42.5, δ30.1, δ19.0, δ9.9, δ3.7;

IR (neat/cm<sup>-1</sup>)  $\nu_{\text{max}}$ : 3452, 3365, 3066, 3032, 2974, 2932, 2919, 2875, 2819, 1620, 1607, 1492, 1454, 1376, 1350, 1307, 1206, 1167, 1127, 1095, 1062, 1028;

HRMS (ESI) *m/z* calcd for C<sub>23</sub>H<sub>29</sub>NO<sub>2</sub> [M+H]<sup>+</sup>: 352.2277, found: 352.2277.



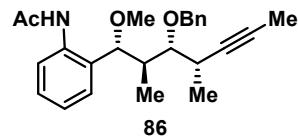
**4-((1*R*,2*R*,3*R*,4*S*)-3-(benzyloxy)-1-methoxy-2,4-dimethylhept-5-yn-1-yl)aniline (84):** Prepared by *general procedure C* using **81** (3.21 g, 8.41 mmol). The crude material was purified with silica gel column Chromatography using 24% ethyl acetate in hexanes. **84** (2.63 g, 7.49 mmol, 89%) was afforded as a pale yellow, viscous oil.  $[\alpha]_D^{23.8} = +22.3$  (*c* = 2.5, CH<sub>2</sub>Cl<sub>2</sub>).

<sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>): δ7.40-7.26 (m, 5H), δ7.07-7.04 (m, 2H), δ6.68-6.65 (m, 2H), δ4.69 (d, *J* = 11.5 Hz, 1H), δ4.64 (d, *J* = 11.5 Hz, 1H), δ4.40 (d, *J* = 8.7 Hz, 1H), δ3.64 (brs, 2H), δ3.58 (dd, *J* = 7.7, 3.9 Hz, 1H), δ3.14 (s, 3H), δ2.73-2.66 (m, 1H), δ2.30 (ddq, *J* = 14.4, 7.2, 3.9 Hz, 1H), δ1.83 (d, *J* = 2.4 Hz, 3H), δ1.25 (d, *J* = 6.8 Hz, 3H), δ0.72 (d, *J* = 7.2 Hz, 3H);

<sup>13</sup>C NMR (125 MHz, CDCl<sub>3</sub>): δ145.7, δ139.1, δ130.8, δ128.8, δ128.3, δ127.7, δ127.3, δ114.8, δ84.8, δ83.0, δ82.8, δ77.0, δ72.5, δ56.1, δ42.4, δ27.8, δ18.4, δ11.7, δ3.7;

IR (neat/cm<sup>-1</sup>)  $\nu_{\text{max}}$ : 3461, 3367, 3030, 2972, 2917, 2876, 2818, 1621, 1516, 1497, 1454, 1377, 1368, 1283, 1212, 1175, 1085, 1068, 1028;

HRMS (ESI) *m/z* calcd for C<sub>23</sub>H<sub>29</sub>NO<sub>2</sub> [M+H]<sup>+</sup>: 352.2277, found: 352.2281.



**N-(2-((1*R*,2*R*,3*R*,4*S*)-3-(benzyloxy)-1-methoxy-2,4-dimethylhept-5-yn-1-yl)phenyl)acetamide (86):**

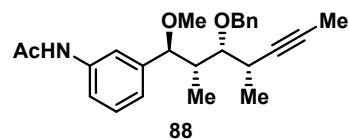
Prepared by *general procedure D* using **83** (2.22 g, 6.31 mmol) and 0.5 equiv of DMAP (386 mg). The crude material was purified with silica gel column chromatography using 21% ethyl acetate in hexanes. **86** (2.21 g, 5.62 mmol, 89% yield) was afforded as a brown solid.  $[\alpha]_D^{23.8} = +14.2$  ( $c = 1.2$ ,  $\text{CH}_2\text{Cl}_2$ ).

$^1\text{H}$  NMR (500 MHz,  $\text{CDCl}_3$ ):  $\delta$  9.24 (brs, 1H), 88.26 (d,  $J = 8.1$  Hz, 1H), 87.46-7.28 (m, 6H), 87.04-7.01 (m, 2H), 84.63 (s, 2H), 84.54 (d,  $J = 10.0$  Hz, 1H), 83.49 (dd,  $J = 9.7, 1.5$  Hz, 1H), 83.28 (s, 3H), 82.94-2.87 (m, 1H), 82.73-2.66 (m, 1H), 82.13 (s, 3H), 81.83 (d,  $J = 2.4$  Hz, 3H), 81.29 (d,  $J = 6.8$  Hz, 3H), 80.70 (d,  $J = 7.2$  Hz, 3H);

$^{13}\text{C}$  NMR (125 MHz,  $\text{CDCl}_3$ ):  $\delta$  168.1, 138.5, 137.0, 130.4, 128.5, 128.4, 127.7, 127.6, 123.1, 121.8, 87.6, 85.4, 82.3, 87.4, 87.2, 85.9, 83.3, 82.9, 82.4, 81.4, 81.2, 83.8;

IR (neat/ $\text{cm}^{-1}$ )  $\nu_{\text{max}}$ : 3346, 3031, 2970, 2933, 2877, 2826, 1695, 1608, 1539, 1524, 1498, 1478, 1447, 1367, 1303, 1290, 1255, 1223, 1208, 1140, 1076, 1028;

HRMS (ESI)  $m/z$  calcd for  $\text{C}_{25}\text{H}_{31}\text{NO}_3$  [ $\text{M}+\text{H}]^+$ : 394.2382, found: 394.2384.



**N-(3-((1*S*,2*S*,3*R*,4*S*)-3-(benzyloxy)-1-methoxy-2,4-dimethylhept-5-yn-1-yl)phenyl)acetamide (88):**

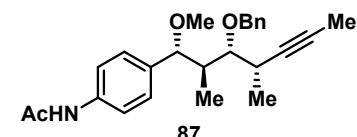
Prepared by *general procedure D* using **85** (4.55 g, 12.96 mmol). The crude material was purified with silica gel column Chromatography using 41% ethyl acetate in hexanes. **88** (4.13 g, 10.50 mmol, 81% yield) was afforded as a brown solid.  $[\alpha]_D^{23.8} = -22.8$  ( $c = 1.3$ ,  $\text{CH}_2\text{Cl}_2$ ).

$^1\text{H}$  NMR (500 MHz,  $\text{CDCl}_3$ ):  $\delta$  7.60 (d,  $J = 8.0$  Hz, 1H), 87.41-7.28 (m, 7H), 87.21 (brs, 1H), 87.04 (d,  $J = 7.5$  Hz, 1H), 84.73 (d,  $J = 11.6$  Hz, 1H), 84.65 (d,  $J = 11.6$  Hz, 1H), 83.95-3.82 (m, 2H), 83.07 (s, 3H), 82.67-2.61 (m, 1H), 82.37-2.31 (m, 1H), 82.18 (s, 3H), 81.79 (d,  $J = 2.4$  Hz, 3H), 81.29 (d,  $J = 6.8$  Hz, 3H), 80.65 (d,  $J = 7.0$  Hz, 3H);

<sup>13</sup>C NMR (125 MHz, CDCl<sub>3</sub>): δ168.2, δ142.5, δ139.2, δ137.9, δ129.0, δ128.4, δ127.4, δ123.8, δ119.2, δ118.9, δ85.5, δ81.9, δ81.0, δ77.5, δ74.9, δ56.0, δ42.6, δ30.1, δ24.7, δ19.0, δ9.9, δ3.7;

IR (neat/cm<sup>-1</sup>)  $\nu_{\text{max}}$ : 3300, 2974, 2920, 2874, 1665, 1612, 1595, 1557, 1489, 1452, 1436, 1372, 1347, 1318, 1305, 1268, 1127, 1097, 1062, 1028;

HRMS (ESI) *m/z* calcd for C<sub>25</sub>H<sub>31</sub>NO<sub>3</sub> [M+H]<sup>+</sup>: 394.2382, found: 394.2361.



**N-(4-((1*R*,2*R*,3*R*,4*S*)-3-(benzyloxy)-1-methoxy-2,4-dimethylhept-5-yn-1-yl)phenyl)acetamide (87):**

Prepared by *general procedure D* using **84** (2.63 g, 7.49 mmol). The crude material was purified with silica gel column chromatography using 19% ethyl acetate in DCM. **87** (2.27 g, 5.77 mmol, 77% yield) was afforded as a brown solid.  $[\alpha]_D^{23.8} = +11.1$  (*c* = 1.1, CH<sub>2</sub>Cl<sub>2</sub>).

<sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>): δ7.48-7.46 (m, 2H), δ7.39-7.26 (m, 5H), δ7.23-7.19 (m, 3H), δ4.69 (d, *J* = 11.5 Hz, 1H), δ4.63 (d, *J* = 11.5 Hz, 1H), δ4.48 (d, *J* = 8.6 Hz, 1H), δ3.55 (dd, *J* = 7.7, 3.9 Hz, 1H), δ3.14 (s, 3H), δ2.73-2.66 (m, 1H), δ2.30 (ddq, *J* = 14.6, 7.3, 3.7 Hz, 1H), δ2.18 (d, *J* = 4.0 Hz, 3H), δ1.83 (d, *J* = 2.4 Hz, 3H), δ1.25 (d, *J* = 6.8 Hz, 3H), δ0.70 (d, *J* = 7.2 Hz, 3H);

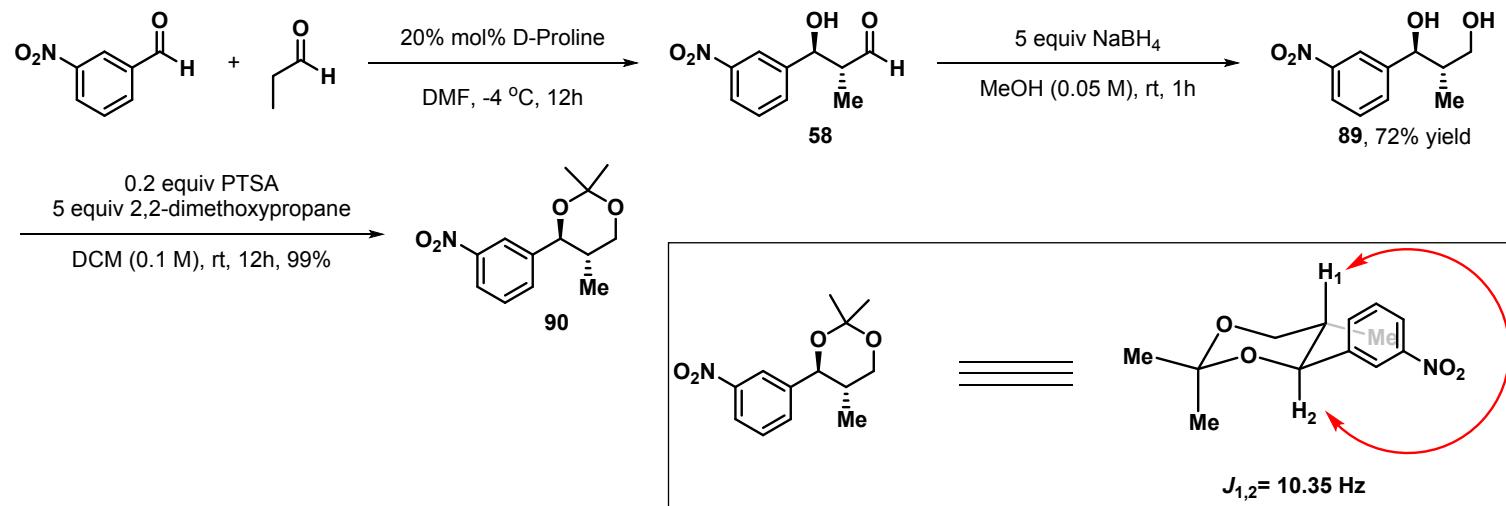
<sup>13</sup>C NMR (125 MHz, CDCl<sub>3</sub>): δ168.2, δ138.9, δ137.1, δ136.9, δ128.3, δ128.3, δ127.7, δ127.4, δ119.5, δ84.6, δ82.9, δ82.6, δ77.2, δ72.6, δ56.4, δ42.4, δ27.9, δ24.6, δ18.4, δ11.7, δ3.7;

IR (neat/cm<sup>-1</sup>)  $\nu_{\text{max}}$ : 3301, 3196, 3127, 3064, 3032, 2972, 2918, 2877, 2819, 1665, 1604, 1538, 1512, 1454, 1411, 1370, 1315, 1268, 1210, 1177, 1150, 1087, 1070, 1028;

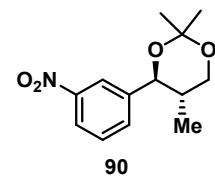
HRMS (ESI) *m/z* calcd for C<sub>25</sub>H<sub>31</sub>NO<sub>3</sub> [M+Na]<sup>+</sup>: 416.2202, found: 416.2195.

## 1.12. Relative and Absolute Stereochemistry Confirmation of Product Obtained from Enantioselective Cross-Aldol Reaction

### 1.12.1 Confirmation of Relative Stereochemistry



$\beta$ -hydroxyl aldehyde **58** was reduced to diol **89** using sodium borohydride, which was under acid-catalyzed ketalization to form acetonide **90**. Three-bond coupling constant between H<sub>1</sub> and H<sub>2</sub> is 10.35 Hz, indicating the *anti* relationship between C1 methyl and C2 oxygen.



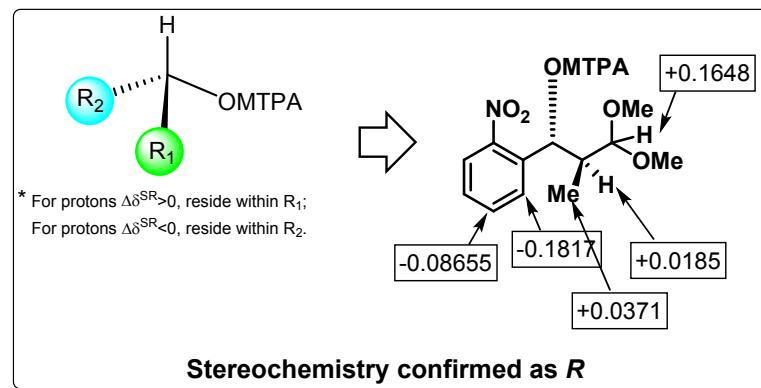
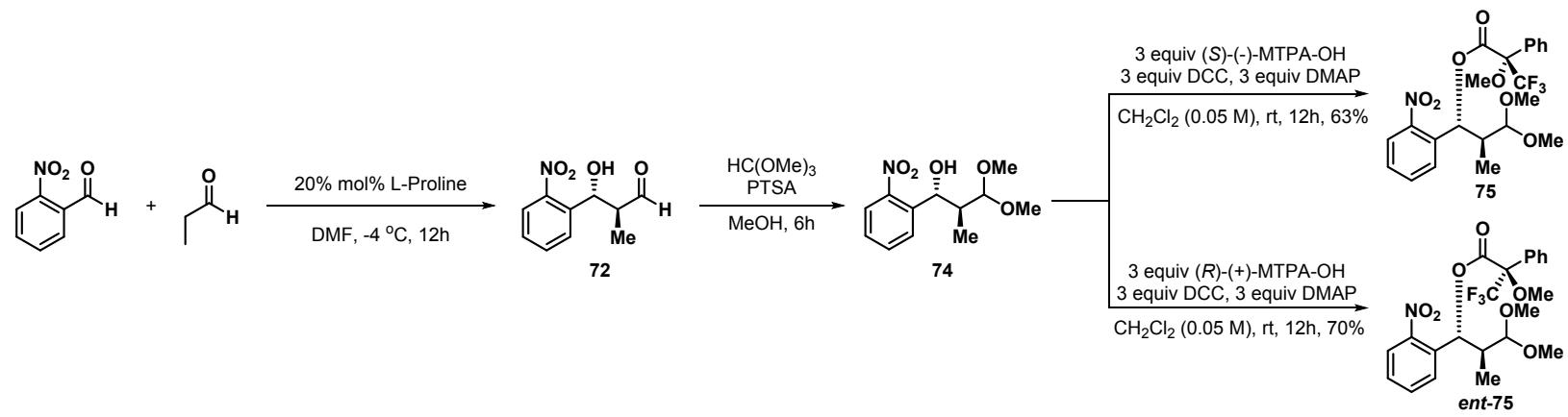
**90** was afforded as a pale yellow, viscous oil.

<sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>): δ8.25 (s, 1H), δ8.17 (d,  $J = 7.2$  Hz, 1H), δ7.71 (d,  $J = 7.6$  Hz, 1H), δ7.53 (t,  $J = 8.0$  Hz, 1H), δ4.54 (d,  $J = 10.3$  Hz, 1H), δ3.85 (dd,  $J = 11.8, 5.0$  Hz, 1H), δ3.71 (dd,  $J = 23, 11.5$  Hz, 1H), δ1.92(ddq,  $J = 17.8, 11.9, 6.5$  Hz, 1H), δ1.56 (s, 3H), δ1.50 (s, 3H), δ0.65 (d,  $J = 6.7$  Hz, 3H);

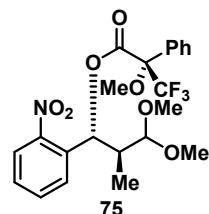
<sup>13</sup>C NMR (125 MHz, CDCl<sub>3</sub>): δ148.2, δ142.6, δ133.6, δ129.3, δ122.9, δ122.4, δ98.9, δ78.0, δ66.0, δ36.2, δ29.8, δ19.0, δ12.3;

HRMS (ESI) *m/z* calcd for C<sub>13</sub>H<sub>17</sub>NO<sub>4</sub> [M+H]<sup>+</sup>: 252.1236, found: 252.1238.

### 1.12.2 Confirmation of Absolute Stereochemistry



The absolute stereochemistry of the secondary alcohol in **20** and **22** was determined by converting the alcohol to Mosher's esters **75** and *ent*-**75**. Using Hoye's protocol, the absolute stereochemistry of the secondary alcohol was determined to be *R*. If the cross aldol reaction is catalyzed by D-proline, the absolute stereochemistry of the secondary alcohol should be *S*.



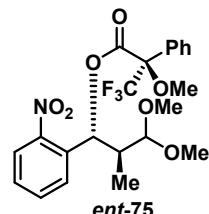
**(1*R*,2*S*)-3,3-dimethoxy-2-methyl-1-(2-nitrophenyl)propyl (S)-3,3,3-trifluoro-2-methoxy-2-phenylpropanoate (75):** **75** was afforded as a pale yellow solid.  $[\alpha]_D^{23.8} = -94.5$  ( $c = 2.7$ , CH<sub>2</sub>Cl<sub>2</sub>).

<sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>): δ7.96 (dd,  $J = 8.0, 1.5$  Hz, 1H), δ7.51-7.33 (m, 6H), δ7.28 (dd,  $J = 7.7, 1.5$  Hz, 1H), δ6.55 (d,  $J = 7.7$  Hz, 1H), δ4.35 (d,  $J = 4.5$  Hz, 1H), δ3.46 (d,  $J = 1.0$  Hz, 3H), δ3.35 (s, 3H), δ3.29 (s, 3H), δ2.50-2.43 (m, 1H), δ0.89 (d,  $J = 7.2$  Hz, 3H);

<sup>13</sup>C NMR (125 MHz, CDCl<sub>3</sub>): δ165.4, δ148.9, δ133.9, δ132.9, δ131.6, δ129.7, δ128.9, δ128.4, δ128.3, δ127.4, δ124.5, δ105.3, δ74.3, δ55.55, δ55.45, δ54.85, δ41.49, δ10.09;

IR (neat/cm<sup>-1</sup>)  $\nu_{\text{max}}$ : 2986, 2945, 2838, 1746, 1611, 1581, 1529, 1451, 1384, 1357, 1270, 1248, 1167, 1122, 1080, 1065, 1014;

HRMS (ESI) *m/z* calcd for C<sub>22</sub>H<sub>24</sub>F<sub>3</sub>NO<sub>7</sub> [M+Na]<sup>+</sup>: 494.1403, found: 494.1390.



**(1*R*,2*S*)-3,3-dimethoxy-2-methyl-1-(2-nitrophenyl)propyl (R)-3,3,3-trifluoro-2-methoxy-2-phenylpropanoate (*ent*-**75**):** *Ent*-**75** was afforded as a pale yellow solid.  $[\alpha]_D^{23.8} = -73$  ( $c = 2.7$ , CH<sub>2</sub>Cl<sub>2</sub>).

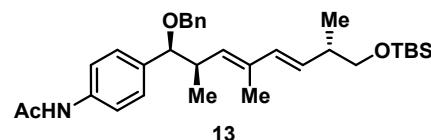
<sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>): δ7.96 (dd, *J* = 8.1, 1.2 Hz, 1H), δ7.58 (td, *J* = 7.6, 1.2 Hz, 1H), δ7.49-7.45 (m, 2H), δ7.42-7.32 (m, 4H), δ6.57 (d, *J* = 8.2 Hz, 1H), δ4.19 (d, *J* = 4.1 Hz, 1H), δ3.42 (d, *J* = 1.0 Hz, 3H), δ3.31 (s, 3H), δ3.23 (s, 3H), δ2.48-2.41 (m, 1H), δ0.85 (d, *J* = 7.1 Hz, 3H);

<sup>13</sup>C NMR (125 MHz, CDCl<sub>3</sub>): δ165.5, δ149.2, δ133.5, δ132.8, δ131.8, δ129.7, δ129.1, δ128.6, δ128.4, δ127.4, δ124.6, δ105.1, δ73.9, δ55.5, δ55.5, δ55.4, δ41.6, δ9.4;

IR (neat/cm<sup>-1</sup>)  $\nu_{\text{max}}$ : 2986, 2946, 2841, 1748, 1611, 1581, 1530, 1497, 1451, 1385, 1354, 1271, 1251, 1169, 1122, 1080, 1065, 1014;

HRMS (ESI) *m/z* calcd for C<sub>22</sub>H<sub>24</sub>F<sub>3</sub>NO<sub>7</sub> [M+Na]<sup>+</sup>: 494.1403, found: 494.1411;

### 1.13. Alkyne-Alkyne Reductive Coupling to Generate 13-22 Prepared by General Procedure A



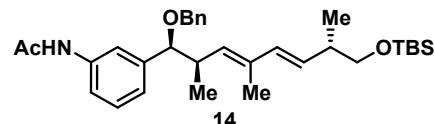
**N-((1*S*,2*R*,3*E*,5*E*,7*S*)-1-(benzyloxy)-8-((tert-butyldimethylsilyl)oxy)-2,4,7-trimethylocta-3,5-dien-1-yl)acetamide (13):** Prepared by *general procedure A* using **51** and **A3<sup>9</sup>** (1.1 equiv) and stirred for 3h. The crude material was purified with Preparative Thin Layer Chromatography using 30% ethyl acetate in Hexanes. **13** (49 mg, 0.094 mmol, 47% yield) was afforded as a pale yellow, viscous oil.  $[\alpha]_D^{23.8} = -17.7$  (*c* = 1.4, CH<sub>2</sub>Cl<sub>2</sub>).

<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>): δ7.46-7.18 (m, 10H), δ5.94 (d, *J* = 15.8 Hz, 1H), δ5.36 (dd, *J* = 15.8, 7.4 Hz, 1H), δ5.17 (d, *J* = 9.9 Hz, 1H), δ4.44 (d, *J* = 11.9 Hz, 1H), δ4.22 (d, *J* = 11.9 Hz, 1H), δ4.09 (d, *J* = 6.9 Hz, 1H), δ3.47 (dd, *J* = 9.7, 6.0 Hz, 1H), δ3.36 (dd, *J* = 9.7, 7.3 Hz, 1H), δ2.89-2.79 (m, 1H), δ2.37-2.27 (m, 1H), δ2.18 (s, 3H), δ1.48 (s, 3H), δ1.06 (d, *J* = 6.6 Hz, 3H), δ0.98 (d, *J* = 6.7 Hz, 3H), δ0.88 (s, 9H), δ0.01 (s, 6H);

<sup>13</sup>C NMR (125 MHz, CDCl<sub>3</sub>): δ168.3, δ138.6, δ137.0, δ136.8, δ136.1, δ133.8, δ133.1, δ129.3, δ128.3, δ128.1, δ127.6, δ127.4, δ119.5, δ84.8, δ70.5, δ67.5, δ39.9, δ25.9, δ25.7, δ24.6, δ17.0, δ16.6, δ12.6, δ-3.6, δ-5.3;

IR (neat/cm<sup>-1</sup>)  $\nu_{\text{max}}$ : 3301, 2956, 2928, 2857, 1668, 1604, 1540, 1513, 1497, 1471, 1454, 1412, 1371, 1256, 1085, 1070, 1028;

HRMS (ESI)  $m/z$  calcd for  $C_{32}H_{47}NO_3Si$  [M+H] $^+$ : 522.3403, found: 522.3397.



*N*-(3-((1*S*,2*R*,3*E*,5*E*,7*S*)-1-(benzyloxy)-8-((*tert*-butyldimethylsilyl)oxy)-2,4,7-trimethylocta-3,5-

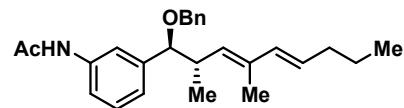
**dien-1-yl)phenyl)acetamide (14):** Prepared by *general procedure A* using **50** and **A3** (1.1 equiv) and stirred for 3h. The crude material was purified with Preparative Thin Layer Chromatography using 30% ethyl acetate in Hexanes. **14** (50 mg, 0.096 mmol, 48% yield) was afforded as a pale yellow, viscous oil.  $[\alpha]_D^{23.8} = -13.4$  ( $c = 0.67$ ,  $CH_2Cl_2$ ).

$^1H$  NMR (500 MHz,  $CDCl_3$ ):  $\delta$  7.57 (d,  $J = 7.6$  Hz, 1H), 7.35-7.27 (m, 7H), 7.17 (s, 1H), 7.03 (d,  $J = 7.4$  Hz, 1H), 85.97 (d,  $J = 15.8$  Hz, 1H), 85.37 (dd,  $J = 15.7, 7.4$  Hz, 1H), 85.22 (d,  $J = 9.5$  Hz, 1H), 84.48 (d,  $J = 12.0$  Hz, 1H), 84.25 (d,  $J = 12.0$  Hz, 1H), 84.14 (d,  $J = 6.5$  Hz, 1H), 83.48 (dd,  $J = 9.7, 5.9$  Hz, 1H), 83.37 (dd,  $J = 9.7, 7.3$  Hz, 1H), 82.84 (dq,  $J = 9.5, 6.6$  Hz, 1H), 82.34-2.29 (m, 1H), 82.17 (s, 3H), 81.50 (s, 3H), 81.06 (d,  $J = 6.6$  Hz, 3H), 80.99 (d,  $J = 6.8$  Hz, 3H), 80.88 (s, 9H), 80.02 (d,  $J = 1.2$  Hz, 6H);

$^{13}C$  NMR (125 MHz,  $CDCl_3$ ):  $\delta$  168.1, 142.0, 138.7, 137.7, 134.4, 133.5, 132.9, 130.2, 128.7, 128.2, 127.5, 127.4, 123.4, 118.9, 118.4, 85.0, 80.8, 68.2, 39.5, 25.9, 25.9, 25.6, 24.7, 18.3, 16.8, 12.5, 3.6, 5.3;

IR (neat/cm $^{-1}$ )  $\nu_{max}$ : 3299, 3278, 2956, 2928, 2857, 1669, 1612, 1557, 1471, 1453, 1441, 1389, 1371, 1318, 1305, 1257, 1094, 1070, 1028;

HRMS (ESI)  $m/z$  calcd for  $C_{32}H_{47}NO_3Si$  [M+H] $^+$ : 522.3403, found: 522.3395.



*N*-(3-((1*S*,2*S*,3*E*,5*E*)-1-(benzyloxy)-2,4-dimethylnona-3,5-dien-1-yl)phenyl)acetamide (16):

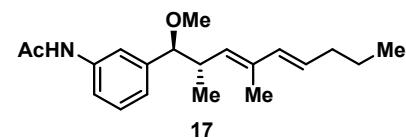
Prepared by *general procedure A* using **70** and **A1** (1.1 equiv) and stirred for 3h. The crude material was purified with Preparative Thin Layer Chromatography using 11% diethyl ether in DCM. **16** (48 mg, 0.124 mmol, 62% yield) was afforded as a pale yellow, viscous oil.  $[\alpha]_D^{23.8} = -39.7$  ( $c = 1.3$ ,  $CH_2Cl_2$ ).

<sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>): δ7.62 (d, *J* = 8.3 Hz, 1H), δ7.33-7.25 (m, 8H), δ7.03 (d, *J* = 7.6 Hz, 1H), δ6.06 (d, *J* = 15.6 Hz, 1H), δ5.54 (td, *J* = 15.6, 7.0 Hz, 1H), δ5.25 (d, *J* = 9.5 Hz, 1H), δ4.48 (d, *J* = 12.2 Hz, 1H), δ4.22 (d, *J* = 12.2 Hz, 1H), δ4.13 (d, *J* = 6.3 Hz, 1H), δ2.85 (dq, *J* = 9.5, 6.8 Hz, 1H), δ2.17 (s, 3H), δ2.07 (dt, *J* = 7.1 Hz, 2H), δ1.59 (s, 3H), δ1.46-1.39 (m, 2H), δ0.92 (t, *J* = 7.4 Hz, 3H), δ0.87 (d, *J* = 6.8 Hz, 3H);

<sup>13</sup>C NMR (125 MHz, CDCl<sub>3</sub>): δ168.3, δ141.9, δ138.7, δ137.8, δ135.0, δ134.0, δ132.7, δ128.8, δ128.2, δ127.8, δ127.6, δ127.3, δ123.6, δ119.0, δ118.6, δ85.3, δ70.5, δ39.5, δ35.0, δ24.7, δ22.8, δ17.4, δ13.8, δ12.8;

IR (neat/cm<sup>-1</sup>)  $\nu_{\text{max}}$ : 3298, 3205, 3149, 3088, 3064, 3028, 2958, 2928, 2869, 1665, 1611, 1594, 1556, 1488, 1453, 1441, 1371, 1317, 1304, 1265, 1095, 1070, 1028;

HRMS (ESI) *m/z* calcd for C<sub>26</sub>H<sub>33</sub>NO<sub>2</sub> [M+Na]<sup>+</sup>: 414.2409, found: 414.2396.



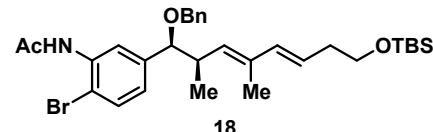
*N*-(3-((1*S*,2*S*,3*E*,5*E*)-1-methoxy-2,4-dimethylnona-3,5-dien-1-yl)phenyl)acetamide (**17**): Prepared by *general procedure A* using **71** and **A1** (1.1 equiv) and stirred for 3h. The crude material was purified with Preparative Thin Layer Chromatography using 16% diethyl ether in DCM. **17** (34 mg, 0.108 mmol, 54% yield) was afforded as a pale yellow, viscous oil.  $[\alpha]_D^{23.8} = -55$  (*c* = 0.6, CH<sub>2</sub>Cl<sub>2</sub>).

<sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>): δ7.62 (d, *J* = 8.1 Hz, 1H), δ7.35 (brs, 1H), δ7.30-7.26 (m, 2H), δ6.99 (d, *J* = 7.3 Hz, 1H), δ6.06 (d, *J* = 15.6 Hz, 1H), δ5.53 (td, *J* = 19.4, 8.7 Hz, 1H), δ5.26 (d, *J* = 9.3 Hz, 1H), δ3.94 (d, *J* = 6.7 Hz, 1H), δ3.18 (s, 3H), δ2.85-2.76 (m, 1H), δ2.16 (s, 3H), δ2.05 (dt, *J* = 7.3 Hz, 2H), δ1.58 (s, 3H), δ1.43-1.38 (m, 2H), δ0.90 (t, *J* = 7.4 Hz, 3H), δ0.84 (d, *J* = 6.8 Hz, 3H);

<sup>13</sup>C NMR (125 MHz, CDCl<sub>3</sub>): δ168.2, δ141.7, δ137.9, δ134.9, δ134.0, δ132.6, δ128.7, δ127.9, δ123.6, δ118.9, δ118.3, δ88.3, δ57.0, δ39.5, δ35.0, δ24.6, δ22.8, δ17.4, δ13.8, δ12.7;

IR (neat/cm<sup>-1</sup>)  $\nu_{\text{max}}$ : 3307, 3151, 3092, 3023, 2958, 2928, 2871, 2821, 1666, 1611, 1555, 1488, 1436, 1371, 1338, 1317, 1305, 1267, 1102;

HRMS (ESI)  $m/z$  calcd for  $C_{20}H_{29}NO_2$  [M+Na] $^+$ : 338.2096, found: 338.2087.



*N*-(5-((1*S*,2*R*,3*E*,5*E*)-1-(benzyloxy)-8-((*tert*-butyldimethylsilyl)oxy)-2,4-dimethylocta-3,5-dien-1-yl)-2-bromophenylacetamide (**18**):

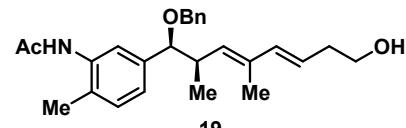
Prepared by *general procedure A* using **56** and **A2**<sup>10</sup> (1.3 equiv) and stirred for 1h. The crude material was purified with Preparative Thin Layer Chromatography using 20% ethyl acetate in Hexanes. **18** (23 mg, 0.04 mmol, 20% yield) was afforded as a pale yellow, viscous oil.  $[\alpha]_D^{23.8} = -4.5$  ( $c = 0.4$ ,  $\text{CH}_2\text{Cl}_2$ ).

$^1\text{H}$  NMR (500 MHz,  $\text{CDCl}_3$ ):  $\delta$  88.28 (s, 1H), 87.57 (s, 1H), 87.47 (d,  $J = 8.3$  Hz, 1H), 87.35-7.28 (m, 5H), 86.95 (d,  $J = 7.0$  Hz, 1H), 85.97 (d,  $J = 15.6$  Hz, 1H), 85.46 (td,  $J = 15.6, 7$  Hz, 1H), 85.17 (d,  $J = 9.8$  Hz, 1H), 84.46 (d,  $J = 11.8$  Hz, 1H), 84.24 (d,  $J = 11.8$  Hz, 1H), 84.11 (d,  $J = 6.9$  Hz, 1H), 83.61 (t,  $J = 6.9$  Hz, 2H), 82.89-2.82 (m, 1H), 82.28-2.24 (m, 5H), 81.56 (s, 3H), 81.06 (d,  $J = 6.6$  Hz, 3H), 80.88 (s, 9H), 80.03 (s, 6H);

$^{13}\text{C}$  NMR (125 MHz,  $\text{CDCl}_3$ ):  $\delta$  168.0, 141.9, 138.5, 136.6, 135.3, 133.5, 132.6, 131.7, 128.3, 127.6, 127.4, 124.0, 123.9, 121.1, 84.8, 80.8, 63.2, 59.6, 56.4, 52.9, 49.9, 48.4, 46.9, 42.6, 5.3;

IR (neat/ $\text{cm}^{-1}$ )  $\nu_{\text{max}}$ : 3307, 2954, 2927, 2856, 1683, 1583, 1523, 1498, 1471, 1461, 1454, 1420, 1389, 1369, 1256, 1093, 1028;

HRMS (ESI)  $m/z$  calcd for  $C_{31}H_{44}BrNO_3Si$  [M+Na] $^+$ : 608.2172, found: 608.2176.



*N*-(5-((1*S*,2*R*,3*E*,5*E*)-1-(benzyloxy)-8-hydroxy-2,4-dimethylocta-3,5-dien-1-yl)-2-

*methylphenylacetamide (**19**):* Prepared by *general procedure A* using **57** and **A2** (1.1 equiv) and stirred for 3h. The crude material was subject to TBS deprotection using TBAF (1M in THF, Sigma Aldrich). It was then purified with Preparative Thin Layer

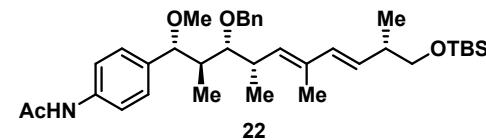
Chromatography using 70% ethyl acetate in DCM. **19** (33 mg, 0.08 mmol, 40% yield) was afforded as a colorless viscous oil.  $[\alpha]_D^{23.8} = -45.5$  ( $c = 0.4$ ,  $\text{CH}_2\text{Cl}_2$ ).

$^1\text{H}$  NMR (500 MHz,  $\text{CDCl}_3$ ):  $\delta$  7.56 (s, 1H), 7.34-7.27 (m, 5H), 7.15 (d,  $J = 7.8$  Hz, 1H), 7.08 (d,  $J = 7.7$  Hz, 1H), 6.96 (brs, 1H), 6.06 (d,  $J = 15.7$  Hz, 1H), 5.41 (dt,  $J = 15.2, 7.2$  Hz, 1H), 5.21 (d,  $J = 9.6$  Hz, 1H), 4.48 (d,  $J = 11.9$  Hz, 1H), 4.23 (d,  $J = 11.9$  Hz, 1H), 4.08 (d,  $J = 7.0$  Hz, 1H), 3.69-3.60 (m, 2H), 2.84 (dq,  $J = 9.6, 6.6$  Hz, 1H), 2.33-2.28 (m, 2H), 2.25 (s, 3H), 2.19 (s, 3H), 1.45 (s, 3H), 1.08 (d,  $J = 6.6$  Hz, 3H);

$^{13}\text{C}$  NMR (125 MHz,  $\text{CDCl}_3$ ):  $\delta$  139.5, 138.7, 138.0, 135.0, 133.4, 133.4, 130.2, 128.2, 127.6, 127.3, 124.1, 123.4, 123.1, 84.9, 70.7, 61.9, 39.9, 36.2, 24.2, 17.6, 17.1, 12.6;

IR (neat/ $\text{cm}^{-1}$ )  $\nu_{\text{max}}$ : 3268, 3028, 2962, 2926, 2869, 1665, 1581, 1538, 1497, 1453, 1424, 1389, 1370, 1340, 1285, 1205, 1112, 1062, 1028;

HRMS (ESI)  $m/z$  calcd for  $\text{C}_{26}\text{H}_{33}\text{NO}_3$  [ $\text{M}+\text{Na}]^+$ : 430.2358, found: 430.2361.



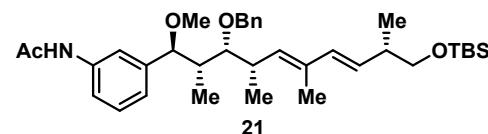
**N-(4-((1R,2R,3R,4S,5E,7E,9S)-3-(benzyloxy)-10-((tert-butyldimethylsilyl)oxy)-1-methoxy-2,4,6,9-tetramethyldeca-5,7-dien-1-yl)phenyl)acetamide (22):** Prepared by *general procedure A* using **87** and **A3** (2 equiv) and stirred for 8 hours. The crude material was purified with Preparative Thin Layer Chromatography using 15% diethyl ether in DCM. **22** (58 mg, 0.098 mmol, 49% yield) was afforded as a pale yellow, viscous oil.  $[\alpha]_D^{23.8} = +5.2$  ( $c = 1.3$ ,  $\text{CH}_2\text{Cl}_2$ ).

$^1\text{H}$  NMR (500 MHz,  $\text{CDCl}_3$ ):  $\delta$  7.44 (d,  $J = 8.4$  Hz, 2H), 7.38-7.27 (m, 5H), 7.20 (brs, 1H), 7.15 (d,  $J = 8.4$  Hz, 2H), 6.09 (d,  $J = 15.7$  Hz, 1H), 5.53 (dd,  $J = 15.7, 7.4$  Hz, 1H), 5.35 (d,  $J = 10.1$  Hz, 1H), 4.62 (d,  $J = 11.4$  Hz, 1H), 4.54 (d,  $J = 11.4$  Hz, 1H), 3.98 (d,  $J = 9.4$  Hz, 1H), 3.62 (dd,  $J = 8.1, 3.5$  Hz, 1H), 3.53 (dd,  $J = 9.7, 6.2$  Hz, 1H), 3.43 (dd,  $J = 9.7, 7.1$  Hz, 1H), 3.07 (s, 3H), 2.91-2.83 (m, 1H), 2.42-2.36 (m, 1H), 2.26-2.19 (m, 1H), 2.17 (s, 3H), 1.77 (s, 3H), 1.08 (d,  $J = 6.6$  Hz, 3H), 1.03 (d,  $J = 6.7$  Hz, 3H), 0.89 (s, 9H), 0.63 (d,  $J = 7.1$  Hz, 3H), 0.04 (d,  $J = 2.5$  Hz, 6H);

<sup>13</sup>C NMR (125 MHz, CDCl<sub>3</sub>): δ168.2, δ139.2, δ137.2, δ137.2, δ135.0, δ134.5, δ131.7, δ130.5, δ128.3, δ128.2, δ127.6, δ127.3, δ119.5, δ85.0, δ83.6, δ72.8, δ68.4, δ56.0, δ42.4, δ39.7, δ35.1, δ26.0, δ24.6, δ18.4, δ18.1, δ16.8, δ12.7, δ11.8, δ-5.2;

IR (neat/cm<sup>-1</sup>)  $\nu_{\text{max}}$ : 3303, 2956, 2928, 2856, 2820, 1669, 1605, 1542, 1513, 1497, 1471, 1462, 1454, 1412, 1371, 1317, 1256, 1086, 1028;

HRMS (ESI) *m/z* calcd for C<sub>36</sub>H<sub>55</sub>NO<sub>4</sub>Si [M+Na]<sup>+</sup>: 616.3798, found: 616.3792.



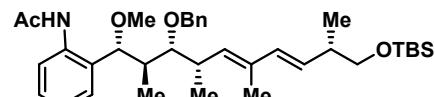
**N-(3-((1S,2S,3R,4S,5E,7E,9S)-3-(benzyloxy)-10-((tert-butyldimethylsilyl)oxy)-1-methoxy-2,4,6,9-tetramethyldeca-5,7-dien-1-yl)phenyl)acetamide (21):** Prepared by *general procedure A* using **88** and **A3** (2 equiv) and stirred for 8 hours. The crude material was purified with Preparative Thin Layer Chromatography using 70% diethyl ether in Hexanes. **21** (70 mg, 0.116 mmol, 59% yield) was afforded as a pale yellow, viscous oil.  $[\alpha]_D^{23.8} = -28.8$  (*c* = 1.9, CH<sub>2</sub>Cl<sub>2</sub>).

<sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>): δ7.65 (d, *J* = 7.2 Hz, 1H), δ7.44-7.27 (m, 6H), δ7.15 (brs, 2H), δ6.99 (d, *J* = 7.8 Hz, 2H), δ6.08 (d, *J* = 15.8 Hz, 1H), δ5.45 (dd, *J* = 15.7, 7.4 Hz, 1H), δ5.21 (d, *J* = 10.0 Hz, 1H), δ4.75 (d, *J* = 11.6 Hz, 1H), δ4.67 (d, *J* = 11.5 Hz, 1H), δ3.90 (d, *J* = 9.9 Hz, 1H), δ3.85 (d, *J* = 9.6 Hz, 1H), δ3.51 (dd, *J* = 9.7, 6.4 Hz, 1H), δ3.42 (dd, *J* = 9.7, 7.1 Hz, 1H), δ3.07 (s, 3H), δ2.82-2.74 (m, 1H), δ2.42-2.33 (m, 1H), δ2.17 (s, 3H), δ1.87-1.81 (m, 1H), δ1.12 (d, *J* = 6.5 Hz, 3H), δ1.02 (d, *J* = 6.7 Hz, 3H), δ0.88 (s, 9H), δ0.56 (d, *J* = 6.9 Hz, 3H), δ0.035 (s, 3H), δ0.028 (s, 3H);

<sup>13</sup>C NMR (125 MHz, CDCl<sub>3</sub>): δ168.2, δ142.4, δ139.4, δ137.9, δ134.6, δ133.6, δ132.6, δ130.2, δ129.0, δ128.4, δ127.4, δ127.4, δ123.7, δ119.3, δ118.8, δ85.6, δ82.8, δ75.3, δ68.3, δ56.0, δ43.0, δ39.6, δ37.0, δ25.9, δ24.6, δ18.6, δ18.4, δ16.7, δ12.5, δ9.9, δ-5.3;

IR (neat/cm<sup>-1</sup>)  $\nu_{\text{max}}$ : 3304, 3030, 2955, 2928, 2901, 2856, 2819, 1666, 1611, 1595, 1557, 1489, 1471, 1462, 1453, 1372, 1344, 1318, 1305, 1256, 1204, 1094, 1028;

HRMS (ESI) *m/z* calcd for C<sub>36</sub>H<sub>55</sub>NO<sub>4</sub>Si [M+Na]<sup>+</sup>: 616.3798, found: 616.3773.

**20*****N*-(2-((1*R*,2*R*,3*R*,4*S*,5*E*,7*E*,9*S*)-3-(benzyloxy)-10-((*tert*-butyldimethylsilyl)oxy)-1-methoxy-2,4,6,9-tetramethyldeca-5,7-dien-1-yl)phenyl)acetamide (20):**

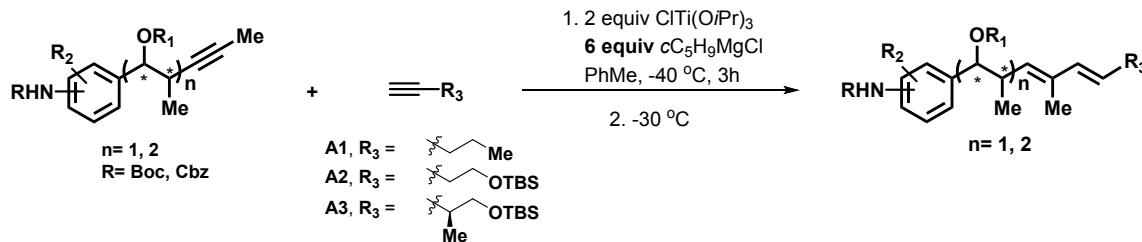
Prepared by *general procedure A* using **86** and **A3** (2 equiv) and stirred for 8 hours. The crude material was purified with Preparative Thin Layer Chromatography using 18% ethyl acetate in Hexanes. **20** (59 mg, 0.099 mmol, 49% yield) was afforded as a pale yellow, viscous oil.

<sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>): δ9.05 (s, 1H), 88.21 (d, *J* = 8.1 Hz, 1H), δ7.36-7.26 (m, 5H), δ6.99 (t, *J* = 7.4 Hz, 1H), δ6.92 (d, *J* = 7.3 Hz, 1H), δ6.09 (d, *J* = 15.8 Hz, 1H), δ5.56 (dd, *J* = 15.8, 7.3 Hz, 1H), δ5.29 (d, *J* = 10.1 Hz, 1H), δ4.61 (d, *J* = 11.0 Hz, 1H), δ4.56 (d, *J* = 11.0 Hz, 1H), δ4.22 (d, *J* = 9.8 Hz, 1H), δ3.56-3.51 (m, 2H), δ3.41 (dd, *J* = 9.7, 7.2 Hz, 1H), δ3.22 (s, 3H), δ3.01-2.93 (m, 1H), δ2.50-2.44 (m, 1H), δ2.41-2.36 (m, 1H), δ2.03 (s, 3H), δ1.80 (s, 3H), δ1.10 (d, *J* = 6.6 Hz, 3H), δ1.03 (d, *J* = 6.7 Hz, 3H), δ0.89 (s, 9H), δ0.65 (d, *J* = 7.2 Hz, 3H), δ0.045 (s, 3H), δ0.042 (s, 3H);

<sup>13</sup>C NMR (125 MHz, CDCl<sub>3</sub>): δ168.1, δ138.6, δ136.8, δ134.2, δ134.2, δ132.3, δ130.8, δ130.4, δ128.5, δ128.4, δ127.7, δ127.6, δ123.2, δ121.9, δ87.0, δ85.3, δ74.0, δ68.3, δ56.6, δ39.6, δ36.1, δ25.9, δ24.9, δ18.8, δ18.4, δ16.8, δ14.3, δ12.8, δ-5.3, δ-5.3;

IR (neat/cm<sup>-1</sup>)  $\nu_{\text{max}}$ : 3346, 2955, 2928, 2884, 2856, 1699, 1608, 1590, 1526, 1472, 1447, 1366, 1304, 1252, 1076, 1028;

HRMS (ESI) *m/z* calcd for C<sub>36</sub>H<sub>55</sub>NO<sub>4</sub>Si [M+Na]<sup>+</sup>: 616.3798, found: 616.3787.

**2. Table 2.**

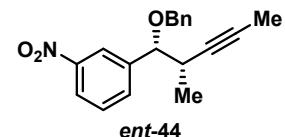
## 2.1 General Procedure L for the Synthesis of Carbamates by *Tert*-butyloxycarbonyl (Boc) Protection

Alkynyl aniline (1 mmol, 1 equiv) was dissolved in 5 mL anhydrous THF at room temperature. Di-*tert*-butyl dicarbonate ((Boc)<sub>2</sub>O) (437 mg, 2 mmol, 2 equiv) and sodium bicarbonate (101 mg, 1.2 mmol, 1.2 equiv) were added sequentially. The resulting solution was stirred at room temperature for 12 hours. The reaction was quenched with 10 mL DI water. It was then extracted with ethyl acetate (10 mL x 3). The combined organic layers were dried over MgSO<sub>4</sub>, filtered, and concentrated. Purification over silica gel chromatography afforded Boc carbamate.

## 2.2 General Procedure M for the Synthesis of Carbamates by Carboxybenzyl (Cbz) Protection

Alkynyl aniline (1 mmol, 1 equiv) was dissolved in 2.5 mL anhydrous THF at room temperature and cooled to 0 °C. Benzyl chloroformate (188 mg, 1.1 mmol, 1.1 equiv) and sodium bicarbonate (92 mg, 1.1 mmol, 1.1 equiv) were added sequentially. The resulting solution was stirred at room temperature until reaction completed (usually less than 30 minutes). The reaction was quenched with 10 mL DI water. It was then extracted with ethyl acetate (10 mL x 3). The combined organic layers were dried over MgSO<sub>4</sub>, filtered, and concentrated. Purification over silica gel chromatography afforded Cbz carbamate.

The synthesis of the substrates was achieved following a sequence of propargylation (*general procedure B*), arylnitro reduction (*general procedure C*), and Boc (*general procedure L*) or Cbz protection (*general procedure M*).

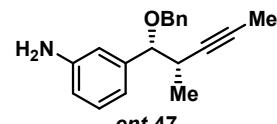


**1-((1*R*,2*S*)-1-(benzyloxy)-2-methylpent-3-yn-1-yl)-3-nitrobenzene (*ent*-44):** Prepared by the same way as for 44 but used (*R<sub>a</sub>*)-42.  $[\alpha]_D^{23.8} = +33$  ( $c = 0.8$ , CH<sub>2</sub>Cl<sub>2</sub>).

<sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>): δ8.30-8.29 (m, 1H), δ8.19-8.17, (m, 1H), δ7.73-7.69 (m, 1H), δ7.54 (t,  $J = 7.9$  Hz, 1H), δ7.35-7.28 (m, 5H), δ4.52 (d,  $J = 11.9$  Hz, 1H), δ4.30 (d,  $J = 11.9$  Hz, 1H), δ4.24 (d,  $J = 7.6$  Hz, 1H), δ2.81-2.74 (m, 1H), δ1.68 (d,  $J = 2.4$  Hz, 3H), δ1.24 (d,  $J = 6.9$  Hz, 3H);

<sup>13</sup>C NMR (125 MHz, CDCl<sub>3</sub>): δ147.8, δ142.4, δ137.3, δ133.4, δ128.6, δ128.2, δ127.6, δ122.6, δ122.6, δ83.2, δ79.4, δ78.9, δ71.0, δ33.6, δ17.8, δ3.1;

LCMS (ES+) *m/z* calcd for C<sub>19</sub>H<sub>19</sub>NO<sub>3</sub> [M+H]<sup>+</sup>: 310.14, found: 310.16.

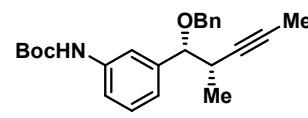


**3-((1*R*,2*S*)-1-(benzyloxy)-2-methylpent-3-yn-1-yl)aniline (*ent*-47):** Prepared by the same way as for **47** using *ent*-**44**. [α]<sub>D</sub><sup>23.8</sup>= +25.2 (*c* = 2.5, CH<sub>2</sub>Cl<sub>2</sub>).

<sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>): δ7.38-7.27 (m, 5H), δ7.15 (t, *J* = 7.7 Hz, 1H), δ6.79-6.76 (m, 2H), δ6.68 (ddd, *J* = 7.9, 2.4, 0.9 Hz, 1H), δ4.54 (d, *J* = 12.0 Hz, 1H), δ4.28 (d, *J* = 12.0 Hz, 1H), δ4.11 (d, *J* = 7.1 Hz, 1H), δ2.78-2.72 (m, 1H), δ1.71 (d, *J* = 2.4 Hz, 3H), δ1.21 (d, *J* = 6.9 Hz, 3H);

<sup>13</sup>C NMR (125 MHz, CDCl<sub>3</sub>): δ146.0, δ141.5, δ138.6, δ128.8, δ128.3, δ127.8, δ127.4, δ118.5, δ114.7, δ114.3, δ84.1, δ81.0, δ77.6, δ70.6, δ33.6, δ17.7, δ3.6;

HRMS (ESI) *m/z* calcd for C<sub>19</sub>H<sub>21</sub>NO [M+H]<sup>+</sup>: 280.1701, found: 280.1696.



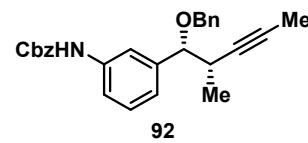
**Tert-butyl (3-((1*R*,2*S*)-1-(benzyloxy)-2-methylpent-3-yn-1-yl)phenyl)carbamate (91):** Prepared by *general procedure L* using *ent*-**47** (170 mg, 0.608 mmol). The crude material was purified with silica gel column chromatography using 11% ethyl acetate in Hexanes. **91** was afforded (229 mg, 0.602 mmol, 99% yield) as a pale yellow, viscous oil. [α]<sub>D</sub><sup>23.8</sup>= +20.3 (*c* = 2.3, CH<sub>2</sub>Cl<sub>2</sub>).

<sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>): δ7.40 (d, *J* = 7.8 Hz, 1H), δ7.34-7.26 (m, 7H), δ7.06-7.04 (m, 1H), δ6.47 (s, 1H), δ4.52 (d, *J* = 12.1 Hz, 1H), δ4.27 (d, *J* = 12.1 Hz, 1H), δ4.15 (d, *J* = 7.2 Hz, 1H), δ2.78-2.72 (m, 1H), δ1.70 (d, *J* = 2.4 Hz, 3H), δ1.52 (s, 9H), δ1.20 (d, *J* = 6.9 Hz, 3H);

<sup>13</sup>C NMR (125 MHz, CDCl<sub>3</sub>): δ152.7, δ141.2, δ138.4, δ138.1, δ128.6, δ128.3, δ127.8, δ127.5, δ122.5, δ117.9, δ117.7, δ84.0, δ80.7, δ80.4, δ77.9, δ70.7, δ33.7, δ28.4, δ17.7, δ3.5;

IR (neat/cm<sup>-1</sup>)  $\nu_{\text{max}}$ : 3333, 2976, 2932, 2873, 1728, 1701, 1610, 1594, 1528, 1491, 1453, 1440, 1392, 1366, 1231, 1154, 1059, 1028;

HRMS (ESI) *m/z* calcd for C<sub>24</sub>H<sub>29</sub>NO<sub>3</sub> [M+Na]<sup>+</sup>: 402.2045, found: 402.2061.



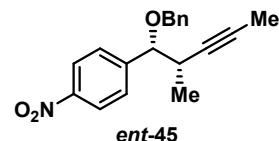
**Benzyl (3-((1*R*,2*S*)-1-(benzyloxy)-2-methylpent-3-yn-1-yl)phenyl)carbamate (92):** Prepared by general procedure *M* using *ent-47* (200 mg, 0.716 mmol). The crude material was purified with silica gel column chromatography using 13% ethyl acetate in Hexanes. **92** was afforded (275 mg, 0.67 mmol, 93% yield) as a viscous, pale yellow oil.  $[\alpha]_D^{23.8} = +15.1$  (*c* = 15.1, CH<sub>2</sub>Cl<sub>2</sub>).

<sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>): δ7.43-7.27 (m, 14H), δ7.09-7.07 (m, 1H), δ6.67 (s, 1H), δ5.21 (s, 2H), δ4.51 (d, *J* = 12.1 Hz, 1H), δ4.26 (d, *J* = 12.0 Hz, 1H), δ4.15 (d, *J* = 7.2 Hz, 1H), δ2.79-2.72 (m, 1H), δ1.69 (d, *J* = 2.4 Hz, 3H), δ1.20 (d, *J* = 6.9 Hz, 3H);

<sup>13</sup>C NMR (125 MHz, CDCl<sub>3</sub>): δ153.3, δ141.4, δ138.3, δ137.6, δ136.1, δ128.7, δ128.6, δ128.4, δ128.3, δ128.3, δ127.8, δ127.5, δ123.0, δ118.0, δ117.8, δ83.9, δ80.6, δ78.0, δ70.7, δ67.0, δ33.7, δ17.8, δ3.5;

IR (neat/cm<sup>-1</sup>)  $\nu_{\text{max}}$ : 3320, 3064, 3031, 2972, 2917, 2874, 1734, 1705, 1610, 1597, 1537, 1493, 1453, 1444, 1338, 1305, 1214, 1171, 1058, 1028;

HRMS (ESI)  $m/z$  calcd for  $C_{27}H_{27}NO_3$  [M+Na] $^+$ : 436.1889, found: 436.1883.



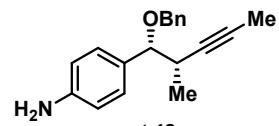
**ent-45** 1-((1*R*,2*S*)-1-(benzylloxy)-2-methylpent-3-yn-1-yl)-4-nitrobenzene (**ent-45**): Prepared by the same way as for **45** but used (*R<sub>a</sub>*)-**42**.  $[\alpha]_D^{23.8} = +21.3$  ( $c = 1.5$ ,  $\text{CH}_2\text{Cl}_2$ ).

<sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>): δ 88.24-8.21 (m, 2H), δ 7.56-7.53 (m, 2H), δ 7.36-7.27 (m, 5H), δ 4.49 (d, *J* = 11.9 Hz, 1H), δ 4.28 (d, *J* = 11.9 Hz, 1H), δ 4.24 (d, *J* = 7.6 Hz, 1H), δ 2.80-2.73 (m, 1H), δ 1.67 (d, *J* = 2.4 Hz, 3H), δ 1.24 (d, *J* = 6.9 Hz, 2H);

<sup>13</sup>C NMR (125 MHz, CDCl<sub>3</sub>): δ 148.0, 137.6, 128.6, 128.4, 127.8, 123.2, 83.5, 83.7, 78.9, 71.3, 63.8, 63.4.

IR (neat/cm<sup>-1</sup>)  $\nu_{\text{max}}$ : 3030, 2975, 2933, 2918, 2873, 1606, 1600, 1519, 1496, 1454, 1393, 1343, 1205, 1108, 1085, 1073, 1028, 1014;

HRMS (ES+)  $m/z$  calcd for  $C_{19}H_{19}NO_3 [M+Na]^+$ : 332.1263, found: 332.1260.



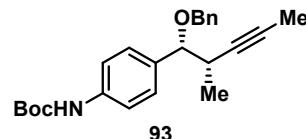
**ent-48** 4-((1*R*,2*S*)-1-(benzylloxy)-2-methylpent-3-yn-1-yl)aniline (**ent-48**): Prepared by the same way as for **48** using **ent-45**.  $[\alpha]_D^{23.8} = +16.9$  ( $c = 3.3$ ,  $\text{CH}_2\text{Cl}_2$ ).

<sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>): δ 7.38-7.25 (m, 5H), δ 7.19-7.16 (m, 2H), δ 6.73 (d, *J* = 7.8 Hz, 1H), δ 4.49 (d, *J* = 12.1 Hz, 1H), δ 4.23 (d, *J* = 12.1 Hz, 1H), δ 4.06 (d, *J* = 7.3 Hz, 1H), δ 2.78-2.71 (m, 1H), δ 1.70 (d, *J* = 2.4 Hz, 1H), δ 1.19 (d, *J* = 6.9 Hz, 1H);

<sup>13</sup>C NMR (125 MHz, CDCl<sub>3</sub>): δ 138.6, 128.8, 128.2, 127.8, 127.4, 115.1, 83.8, 80.9, 77.6, 70.2, 33.8, 18.0, 13.6.

IR (neat/cm<sup>-1</sup>)  $\nu_{\text{max}}$ : 3458, 3368, 3224, 3061, 3029, 2970, 2931, 2917, 2872, 1621, 1516, 1453, 1280, 1113, 1086, 1065, 1028;

HRMS (ESI) *m/z* calcd for C<sub>19</sub>H<sub>21</sub>NO [M+H]<sup>+</sup>: 280.1701, found: 280.1698.



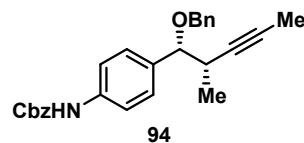
**Tert-butyl (4-((1*R*,2*S*)-1-(benzyloxy)-2-methylpent-3-yn-1-yl)phenyl)carbamate (93):** Prepared by general procedure *L* using *ent*-31 (240 mg, 0.86 mmol). The crude material was purified with silica gel column chromatography using 11% ethyl acetate in Hexanes. **93** was afforded (313 mg, 0.826 mmol, 96% yield) as a pale yellow, viscous oil.  $[\alpha]_D^{23.8} = +8.3$  (*c* = 5.3, CH<sub>2</sub>Cl<sub>2</sub>).

<sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>):  $\delta$  7.36-7.25 (m, 9H), 6.48 (s, 1H), 4.48 (d, *J* = 12.1 Hz, 1H), 4.23 (d, *J* = 12.0 Hz, 1H), 4.10 (d, *J* = 7.3 Hz, 1H), 2.78-2.72 (m, 1H), 1.68 (d, *J* = 2.4 Hz, 3H), 1.53 (s, 9H), 1.20 (d, *J* = 6.9 Hz, 3H);

<sup>13</sup>C NMR (125 MHz, CDCl<sub>3</sub>):  $\delta$  152.8, 146.7, 138.4, 137.8, 134.7, 128.4, 128.3, 127.8, 127.5, 83.6, 80.7, 77.9, 70.4, 33.7, 28.3, 27.4, 17.9, 3.5;

IR (neat/cm<sup>-1</sup>)  $\nu_{\text{max}}$ : 3337, 2977, 2932, 2873, 1810, 1727, 1702, 1614, 1596, 1521, 1454, 1413, 1392, 1367, 1313, 1230, 1155, 1117, 1052, 1028, 1016;

HRMS (ESI) *m/z* calcd for C<sub>24</sub>H<sub>29</sub>NO<sub>3</sub> [M+Na]<sup>+</sup>: 402.2045, found: 402.2063.



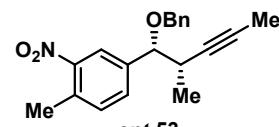
**Benzyl (4-((1*R*,2*S*)-1-(benzyloxy)-2-methylpent-3-yn-1-yl)phenyl)carbamate (94):** Prepared by *general procedure M* using *ent*-31 (240 mg, 0.86 mmol). The crude material was purified with silica gel column chromatography using 15% ethyl acetate in Hexanes. **94** was afforded (249 mg, 0.60 mmol, 70% yield) as a viscous, pale yellow oil.  $[\alpha]_D^{23.8} = +17.8$  ( $c = 1.5$ ,  $\text{CH}_2\text{Cl}_2$ ).

$^1\text{H}$  NMR (500 MHz,  $\text{CDCl}_3$ ):  $\delta$  7.43-7.27 (m, 14H), 86.67 (s, 1H), 85.22 (s, 2H), 84.49 (d,  $J = 12.0$  Hz, 1H), 84.23 (d,  $J = 12.0$  Hz, 1H), 84.11 (d,  $J = 7.4$  Hz, 1H), 82.78-2.72 (m, 1H), 81.68 (d,  $J = 2.4$  Hz, 3H), 81.20 (d,  $J = 6.9$  Hz, 3H);

$^{13}\text{C}$  NMR (125 MHz,  $\text{CDCl}_3$ ):  $\delta$  153.3, 138.3, 137.2, 136.1, 135.3, 128.6, 128.5, 128.4, 128.3, 128.3, 127.8, 127.5, 118.2, 83.64, 80.6, 80.6, 87.9, 87.0, 86.0, 83.8, 81.8, 81.5;

IR (neat/ $\text{cm}^{-1}$ )  $\nu_{\text{max}}$ : 3320, 3063, 3032, 2971, 2932, 2917, 2873, 1733, 1704, 1613, 1599, 1525, 1497, 1454, 1415, 1313, 1214, 1083, 1053, 1028, 1017;

HRMS (ESI)  $m/z$  calcd for  $\text{C}_{27}\text{H}_{27}\text{NO}_3$  [ $\text{M}+\text{Na}]^+$ : 436.1889, found: 436.1909.



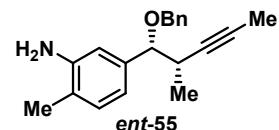
**4-((1*R*,2*S*)-1-(benzyloxy)-2-methylpent-3-yn-1-yl)-1-methyl-2-nitrobenzene (*ent*-53):** Prepared by the same way as for **53** but used (*R<sub>a</sub>*)-42.  $[\alpha]_D^{23.8} = +29.2$  ( $c = 1$ ,  $\text{CH}_2\text{Cl}_2$ ).

$^1\text{H}$  NMR (500 MHz,  $\text{CDCl}_3$ ):  $\delta$  88.02 (d,  $J = 1.3$  Hz, 1H), 87.52 (dd,  $J = 7.8, 1.6$  Hz, 1H), 87.36-7.28 (m, 5H), 84.51 (d,  $J = 11.9$  Hz, 1H), 84.27 (d,  $J = 11.9$  Hz, 1H), 84.18 (d,  $J = 7.5$  Hz, 1H), 82.79-2.72 (m, 1H), 82.62 (s, 3H), 81.70 (d,  $J = 2.3$  Hz, 3H), 81.22 (d,  $J = 6.9$  Hz, 3H);

<sup>13</sup>C NMR (125 MHz, CDCl<sub>3</sub>): δ148.9, δ139.9, δ137.7, δ132.9, δ132.4, δ132.0, δ128.4, δ127.8, δ124.1, δ83.1, δ79.8, δ79.0, δ71.1, δ33.8, δ20.3, δ18.0, δ3.4;

IR (neat/cm<sup>-1</sup>) ν<sub>max</sub>: 3065, 3032, 2974, 2932, 2919, 2873, 1738, 1623, 1526, 1496, 1454, 1346, 1203, 1154, 1074, 1028;

HRMS (ESI) *m/z* calcd for C<sub>20</sub>H<sub>21</sub>NO<sub>3</sub> [M+Na]<sup>+</sup>: 346.1419, found: 346.1408.



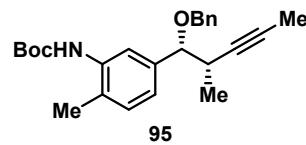
**5-((1*R*,2*S*)-1-(benzyloxy)-2-methylpent-3-yn-1-yl)-2-methylaniline (*ent*-55):** Prepared by the same way as for 55 using *ent*-53. [α]<sub>D</sub><sup>23.8</sup> = +24.5 (*c* = 1.5, CH<sub>2</sub>Cl<sub>2</sub>).

<sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>): δ7.38-7.27 (m, 5H), δ7.04 (d, *J* = 7.5 Hz, 1H), δ6.73 (s, 1H), δ6.69 (d, *J* = 15.1 Hz, 1H), δ4.54 (d, *J* = 12.1 Hz, 1H), δ4.27 (d, *J* = 12.1 Hz, 1H), δ4.10 (d, *J* = 7.0 Hz, 1H), δ3.66 (brs, 2H), δ2.78-2.72 (m, 1H), δ2.19 (s, 3H), δ1.72 (d, *J* = 2.4 Hz, 3H), δ1.21 (d, *J* = 6.9 Hz, 3H);

<sup>13</sup>C NMR (125 MHz, CDCl<sub>3</sub>): δ144.1, δ139.0, δ138.6, δ130.0, δ128.2, δ127.8, δ127.4, δ121.9, δ118.5, δ114.1, δ83.9, δ81.1, δ77.5, δ70.5, δ33.7, δ17.7, δ17.2, δ3.6;

IR (neat/cm<sup>-1</sup>) ν<sub>max</sub>: 3469, 3374, 3061, 3029, 2971, 2930, 2917, 2858, 1623, 1581, 1511, 1496, 1453, 1427, 1344, 1310, 1299, 1287, 1206, 1113, 1086, 1064, 1028;

HRMS (ESI) *m/z* calcd for C<sub>20</sub>H<sub>23</sub>NO [M+H]<sup>+</sup>: 294.1858, found: 294.1854.

**Tert-butyl (5-((1*R*,2*S*)-1-(benzyloxy)-2-methylpent-3-yn-1-yl)-2-methylphenyl)carbamate (95): Ent-55**

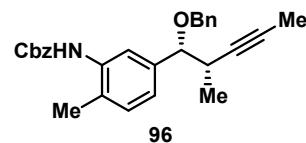
(235 mg, 0.8 mmol, 1 equiv) was dissolved in 4 mL anhydrous THF at room temperature. Di-*tert*-butyl dicarbonate ((Boc)<sub>2</sub>O) (349 mg, 1.6 mmol, 2 equiv) and sodium bicarbonate (81 mg, 0.96 mmol, 1.2 equiv) were added sequentially. The resulting solution was refluxed for 24 hours. The reaction was quenched with 10 mL DI water. It was then extracted with ethyl acetate (10 mL x 3). The combined organic layers were dried over MgSO<sub>4</sub>, filtered, and concentrated. Purification over silica gel chromatography using 10% ethyl acetate in Hexanes afforded **95** (264 mg, 0.672 mmol, 84% yield) as a colorless, viscous oil.  $[\alpha]_D^{23.8} = +21.3$  ( $c = 1.7$ , CH<sub>2</sub>Cl<sub>2</sub>).

<sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>):  $\delta$  7.83 (brs, 1H), 7.37-7.25 (m, 5H), 7.14 (d,  $J$  = 7.8 Hz, 1H), 7.05 (dd,  $J$  = 7.8, 1.5 Hz, 1H), 6.25 (s, 1H), 84.54 (d,  $J$  = 12.1 Hz, 1H), 84.27 (d,  $J$  = 12.1 Hz, 1H), 84.18 (d,  $J$  = 7.1 Hz, 1H), 82.80-2.73 (m, 1H), 82.26 (s, 3H), 81.72 (d,  $J$  = 2.4 Hz, 3H), 81.53 (s, 9H), 81.21 (d,  $J$  = 6.9 Hz, 3H);

<sup>13</sup>C NMR (125 MHz, CDCl<sub>3</sub>):  $\delta$  152.9, 138.9, 138.6, 135.9, 129.9, 128.2, 127.8, 127.4, 122.7, 120.5, 83.9, 80.9, 80.3, 77.8, 70.6, 33.8, 28.4, 27.4, 17.7, 3.6;

IR (neat/cm<sup>-1</sup>)  $\nu_{\max}$ : 3351, 2976, 2931, 2872, 1730, 1698, 1583, 1526, 1496, 1480, 1448, 1391, 1366, 1229, 1153, 1115, 1086, 1065, 1049, 1028;

HRMS (ESI) *m/z* calcd for C<sub>25</sub>H<sub>31</sub>NO<sub>3</sub> [M+Na]<sup>+</sup>: 416.2202, found: 416.2196.

**Benzyl (5-((1*R*,2*S*)-1-(benzyloxy)-2-methylpent-3-yn-1-yl)-2-methylphenyl)carbamate (96): Ent-55**

Ent-55 (235 mg, 0.8 mmol, 1 equiv) was dissolved in 4 mL anhydrous THF at room temperature. Benzyl chloroformate (0.23 mL, 1.6 mmol, 2 equiv) and sodium bicarbonate (81 mg, 0.96 mmol, 1.2 equiv) were added sequentially. The resulting solution was refluxed for 24h. The reaction was quenched with 10 mL DI water. It was then extracted with ethyl acetate (10 mL x 3). The combined organic layers

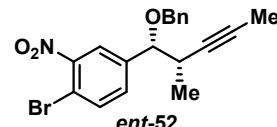
were dried over MgSO<sub>4</sub>, filtered, and concentrated. Purification over silica gel chromatography using 15% ethyl acetate in Hexanes afforded **96** (308 mg, 0.72 mmol, 90% yield) as a colorless, viscous oil.  $[\alpha]_D^{23.8} = +15.8$  ( $c = 1$ , CH<sub>2</sub>Cl<sub>2</sub>).

<sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>):  $\delta$  7.84 (s, 1H), 7.43-7.27 (m, 10H), 7.16 (d,  $J = 7.8$  Hz, 1H), 7.09 (dd,  $J = 7.8, 1.6$  Hz, 1H), 6.47 (s, 1H), 5.22 (s, 2H), 4.53 (d,  $J = 12.0$  Hz, 1H), 4.27 (d,  $J = 12.0$  Hz, 1H), 4.18 (d,  $J = 7.1$  Hz, 1H), 2.80-2.74 (m, 1H), 2.26 (s, 3H), 1.71 (d,  $J = 2.3$  Hz, 3H), 1.21 (d,  $J = 6.9$  Hz, 2H);

<sup>13</sup>C NMR (125 MHz, CDCl<sub>3</sub>):  $\delta$  153.5, 139.1, 138.5, 136.1, 135.4, 130.1, 128.6, 128.4, 128.2, 127.8, 127.4, 123.4, 120.8, 83.8, 80.8, 77.9, 70.6, 67.1, 33.7, 17.8, 3.6;

IR (neat/cm<sup>-1</sup>)  $\nu_{\text{max}}$ : 3335, 3064, 3031, 2970, 2931, 2918, 2873, 1735, 1713, 1584, 1530, 1497, 1453, 1393, 1333, 1216, 1194, 1164, 1126, 1083, 1048, 1028;

HRMS (ESI) *m/z* calcd for C<sub>28</sub>H<sub>29</sub>NO<sub>3</sub> [M+Na]<sup>+</sup>: 450.2045, found: 450.2034.



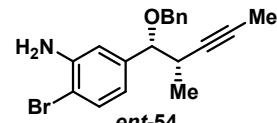
**4-((1*R*,2*S*)-1-(benzyloxy)-2-methylpent-3-yn-1-yl)-1-bromo-2-nitrobenzene (*ent*-52):** Prepared by the same way as for **52** but used (*R<sub>a</sub>*)-**42**.  $[\alpha]_D^{23.8} = +26.2$  ( $c = 2.1$ , CH<sub>2</sub>Cl<sub>2</sub>).

<sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>):  $\delta$  7.89 (d,  $J = 1.8$  Hz, 1H), 7.72 (d,  $J = 8.2$  Hz, 1H), 7.44 (dd,  $J = 8.2, 1.7$  Hz, 1H), 7.37-7.27 (m, 5H), 6.52 (d,  $J = 11.9$  Hz, 1H), 4.30 (d,  $J = 11.9$  Hz, 1H), 4.16 (d,  $J = 7.6$  Hz, 1H), 2.76-2.70 (m, 1H), 1.70 (d,  $J = 2.3$  Hz, 2H), 1.22 (d,  $J = 6.9$  Hz, 2H);

<sup>13</sup>C NMR (125 MHz, CDCl<sub>3</sub>):  $\delta$  149.5, 141.8, 137.3, 134.5, 132.2, 128.5, 128.0, 127.9, 125.0, 82.9, 82.9, 879.5, 879.4, 871.4, 83.8, 81.8, 3.4;

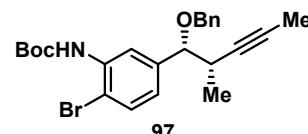
IR (neat/cm<sup>-1</sup>)  $\nu_{\text{max}}$ : 3089, 3065, 3031, 2973, 2932, 2918, 2872, 1601, 1567, 1533, 1496, 1206, 1086, 1075, 1031;

HRMS (ESI)  $m/z$  calcd for  $C_{19}H_{18}BrNO_3$  [M+Na]<sup>+</sup>: 410.0368, found: 410.0372.



**5-((1*R*,2*S*)-1-(benzyloxy)-2-methylpent-3-yn-1-yl)-2-bromoaniline (*ent*-54):** Prepared by the same way as for **54** using *ent*-**52**. (<sup>1</sup>H and <sup>13</sup>C NMR data are identical to that of **54**)

<sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>):  $\delta$  7.38 (d,  $J$  = 8.1 Hz, 1H), 7.35-7.28 (m, 5H), 86.80 (s, 1H), 86.62 (d,  $J$  = 8.0 Hz, 1H), 84.51 (d,  $J$  = 12.0 Hz, 1H), 84.25 (d,  $J$  = 12.0 Hz, 1H), 84.04 (d,  $J$  = 7.3 Hz, 1H), 82.75-2.69 (m, 1H), 81.71 (d,  $J$  = 2.4 Hz, 3H), 81.20 (d,  $J$  = 6.9 Hz, 3H);



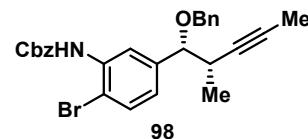
**Tert-butyl (5-((1*R*,2*S*)-1-(benzyloxy)-2-methylpent-3-yn-1-yl)-2-bromophenyl)carbamate (97):** *Ent*-**54** (417 mg, 1.16 mmol, 1 equiv) was dissolved in 3 mL anhydrous THF at room temperature. Di-*tert*-butyl dicarbonate ((Boc)<sub>2</sub>O) (253 mg, 1.16 mmol, 1 equiv) and 4-dimethylaminopyridine (DMAP) (156 mg, 1.28 mmol, 1.1 equiv) were added sequentially. The resulting solution was stirred at room temperature for 36 hours. The reaction was quenched with 10 mL DI water. It was then extracted with ethyl acetate (10 mL x 3). The combined organic layers were dried over MgSO<sub>4</sub>, filtered, and concentrated. Purification over silica gel chromatography using 6.4% ethyl acetate in Hexanes afforded **97** (111 mg, 0.24 mmol, 21% yield) as a pale yellow oil.

<sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>):  $\delta$  88.19 (s, 1H), 87.49 (d,  $J$  = 8.2 Hz, 1H), 87.33-7.27 (m, 5H), 87.00 (s, 1H), 86.98 (dd,  $J$  = 8.3, 2.0 Hz, 1H), 84.52 (d,  $J$  = 12.0 Hz, 1H), 84.27 (d,  $J$  = 12.0 Hz, 1H), 84.16 (d,  $J$  = 7.3 Hz, 1H), 82.78-2.72 (m, 1H), 81.71 (d,  $J$  = 2.4 Hz, 3H), 81.54 (s, 9H), 81.21 (d,  $J$  = 6.9 Hz, 3H);

<sup>13</sup>C NMR (125 MHz, CDCl<sub>3</sub>):  $\delta$  152.2, 141.0, 138.2, 135.8, 131.7, 128.3, 127.8, 127.5, 122.8, 119.7, 111.4, 83.8, 81.0, 80.4, 78.3, 70.8, 33.7, 28.3, 17.8, 3.5;

IR (neat/cm<sup>-1</sup>)  $\nu_{\text{max}}$ : 3413, 2977, 2931, 2918, 2872, 1733, 1582, 1516, 1446, 1426, 1392, 1367, 1248, 1226, 1151, 1087, 1058, 1018;

HRMS (ESI) *m/z* calcd for C<sub>24</sub>H<sub>28</sub>BrNO<sub>3</sub> [M+Na]<sup>+</sup>: 480.1150, found: 480.1168.



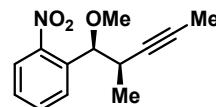
**Benzyl (5-((1*R*,2*S*)-1-(benzyloxy)-2-methylpent-3-yn-1-yl)-2-bromophenyl)carbamate (98): *Ent-54*** (263 mg, 0.74 mmol, 1 equiv) was dissolved in 3.7 mL anhydrous THF at room temperature. Benzyl chloroformate (0.15 mL, 1.03 mmol, 1.4 equiv) and sodium bicarbonate (75 mg, 0.89 mmol, 1.2 equiv) were added sequentially. The resulting solution was stirred at room temperature for 12 hours. The reaction was quenched with 10 mL DI water. It was then extracted with ethyl acetate (10 mL x 3). The combined organic layers were dried over MgSO<sub>4</sub>, filtered, and concentrated. Purification over silica gel chromatography using 7.7% ethyl acetate in Hexanes afforded **98** (291 mg, 0.59 mmol, 80% yield) as a pale yellow oil.  $[\alpha]_D^{23.8} = +25.6$  (*c* = 1.7, CH<sub>2</sub>Cl<sub>2</sub>).

<sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>): δ8.21 (s, 1H), δ7.50 (d, *J* = 8.2 Hz, 1H), δ7.45-7.27 (m, 10H), δ7.21 (s, 1H), δ7.02 (dd, *J* = 8.2, 2.1 Hz, 1H), δ5.23 (s, 2H), δ4.52 (d, *J* = 12.0 Hz, 1H), δ4.27 (d, *J* = 12.0 Hz, 1H), δ4.15 (d, *J* = 7.3 Hz, 1H), δ2.79-2.73 (m, 1H), δ1.70 (d, *J* = 2.4 Hz, 3H), δ1.21 (d, *J* = 6.9 Hz, 3H);

<sup>13</sup>C NMR (125 MHz, CDCl<sub>3</sub>): δ152.9, δ141.1, δ138.2, δ135.8, δ135.3, δ131.8, δ128.6, δ128.5, δ128.4, δ128.3, δ127.8, δ127.5, δ123.4, δ119.9, δ111.6, δ83.7, δ80.3, δ78.4, δ70.8, δ67.3, δ33.6, δ17.9, δ3.5;

IR (neat/cm<sup>-1</sup>)  $\nu_{\text{max}}$ : 3405, 3064, 3032, 2971, 2932, 2917, 2872, 1738, 1583, 1519, 1452, 1426, 1203, 1083, 1058, 1021;

HRMS (ESI) *m/z* calcd for C<sub>27</sub>H<sub>26</sub>BrNO<sub>3</sub> [M+Na]<sup>+</sup>: 514.0994, found: 514.0995.



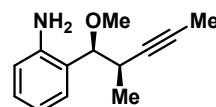
**1-((1*S*,2*R*)-1-methoxy-2-methylpent-3-yn-1-yl)-2-nitrobenzene (99):** A solution of allenylsilane (*S<sub>a</sub>*-**42** (600 mg, 2.96 mmol, 1 equiv), methoxytrimethylsilane (0.45 mL, 3.26 mmol, 1.1 equiv), and 2-nitrobenzaldehyde (582 mg, 3.85 mmol, 1.3 equiv) in 15 mL propionitrile (EtCN) was stirred at room temperature for 5 minutes and cooled to -78 °C. Trimethylsilyl trifluoromethanesulfonate (TMSOTf) (0.54 mL, 2.96 mmol, 1 equiv) was added to above mixture dropwise. The resulting mixture was warmed to -30 °C gradually and placed into -30 °C chiller and stirred for 12 hours. The reaction was quenched by adding 10 mL saturated NaHCO<sub>3</sub> (aq) solution at -30 °C. After the mixture was warmed to room temperature, it was then extracted with ethyl acetate (3 x 10 mL), and the combined organic layers were dried over MgSO<sub>4</sub>, filtered, and concentrated. Purification over silica gel chromatography (64% CH<sub>2</sub>Cl<sub>2</sub>/Hexanes) afforded product **99** (448 mg, 65% yield, dr: 12.5:1). [α]<sub>D</sub><sup>23.8</sup> = -155 (c = 1.4, CH<sub>2</sub>Cl<sub>2</sub>).

<sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>): δ7.85 (d, *J* = 8.1 Hz, 1H), δ7.72 (dd, *J* = 7.9, 1.2 Hz, 1H), δ7.62 (dd, *J* = 15.2, 7.9 Hz, 1H), δ7.44-7.41 (m, 1H), δ4.92 (d, *J* = 7.7 Hz, 1H), δ3.32 (s, 3H), δ2.65-2.58 (m, 1H), δ1.65 (d, *J* = 2.4 Hz, 3H), δ1.22 (d, *J* = 6.9 Hz, 3H);

<sup>13</sup>C NMR (125 MHz, CDCl<sub>3</sub>): δ150.3, δ136.0, δ132.7, δ128.3, δ128.2, δ123.9, δ81.0, δ79.4, δ78.3, δ57.8, δ34.2, δ17.6, δ3.4;

IR (neat/cm<sup>-1</sup>)  $\nu_{\max}$ : 2979, 2934, 2879, 2828, 1609, 1578, 1527, 1453, 1354, 1302, 1196, 1113, 1092, 1077;

HRMS (ESI) *m/z* calcd for C<sub>13</sub>H<sub>15</sub>NO<sub>3</sub> [M+H]<sup>+</sup>: 234.1130, found: 234.1168.



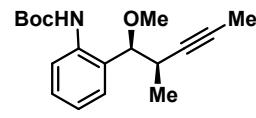
**2-((1*S*,2*R*)-1-methoxy-2-methylpent-3-yn-1-yl)aniline (100):** Prepared by the *general procedure C* using **99**. The crude material was purified with silica gel column chromatography using 11% ethyl acetate in Hexanes. **100** (368 mg, 1.81 mmol, 94% yield) was obtained as a pale yellow, viscous oil. [α]<sub>D</sub><sup>23.8</sup> = -11.3 (c = 3.8, CH<sub>2</sub>Cl<sub>2</sub>).

<sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>): δ7.10-7.05 (m, 2H), δ6.71 (dd, *J* = 15.6, 7.4 Hz, 1H), δ6.63 (d, *J* = 7.9 Hz, 1H), δ4.19 (brs, 2H), δ4.03 (d, *J* = 8.6 Hz, 1H), δ3.27 (s, 3H), δ3.04-2.97 (m, 1H), δ1.66 (d, *J* = 2.4 Hz, 3H), δ1.28 (d, *J* = 6.8 Hz, 3H);

<sup>13</sup>C NMR (125 MHz, CDCl<sub>3</sub>): δ145.1, δ130.3, δ128.4, δ123.4, δ117.5, δ116.4, δ87.7, δ81.0, δ77.5, δ57.0, δ30.8, δ18.1, δ3.5;

IR (neat/cm<sup>-1</sup>) ν<sub>max</sub>: 3455, 3366, 2972, 2932, 2918, 2823, 1614, 1584, 1494, 1458, 1300, 1265, 1201, 1157, 1110, 1080;

LCMS (ESI) *m/z* calcd for C<sub>13</sub>H<sub>17</sub>NO [M+H]<sup>+</sup>: 204.13, found: 204.11.



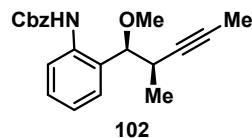
**Tert-butyl (2-((1*S*,2*R*)-1-methoxy-2-methylpent-3-yn-1-yl)phenyl)carbamate (101):** **100** (580 mg, 2.08 mmol, 1 equiv) was dissolved in 7 mL anhydrous THF at room temperature. Di-*tert*-butyl dicarbonate ((Boc)<sub>2</sub>O) (906 mg, 4.15 mmol, 2 equiv) and sodium bicarbonate (210 mg, 2.5 mmol, 1.2 equiv) were added sequentially. The resulting solution was refluxed for 24 hours. The reaction was quenched with 10 mL DI water. It was then extracted with ethyl acetate (10 mL x 3). The combined organic layers were dried over MgSO<sub>4</sub>, filtered, and concentrated. Purification over silica gel chromatography using 6.5% ethyl acetate in Hexanes afforded **101** (315 mg, 1.04 mmol, 50% yield) as a colorless oil. [α]<sub>D</sub><sup>23.8</sup> = -3.9 (*c* = 4.3, CH<sub>2</sub>Cl<sub>2</sub>).

<sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>): δ8.06 (s, 1H), δ8.03 (d, *J* = 7.6 Hz, 1H), δ7.29-7.25 (m, 1H), δ7.11 (dd, *J* = 7.6, 1.4 Hz, 1H), δ7.01-6.97 (m, 1H), δ4.07 (d, *J* = 8.2 Hz, 1H), δ3.29 (s, 3H), δ2.88-2.82 (m, 1H), δ1.67 (d, *J* = 2.4 Hz, 3H), δ1.51 (s, 9H), δ1.26 (d, *J* = 6.9 Hz, 3H);

<sup>13</sup>C NMR (125 MHz, CDCl<sub>3</sub>): δ153.1, δ137.3, δ129.9, δ128.4, δ122.2, δ120.6, δ88.0, δ80.4, δ79.9, δ78.4, δ57.3, δ32.2, δ28.4, δ18.1, δ3.4;

IR (neat/cm<sup>-1</sup>) ν<sub>max</sub>: 3364, 2978, 2933, 2827, 1728, 1590, 1521, 1446, 1392, 1366, 1302, 1229, 1154, 1108, 1079, 1068, 1044, 1023;

HRMS (ESI) *m/z* calcd for C<sub>18</sub>H<sub>25</sub>NO<sub>3</sub> [M+Na]<sup>+</sup>: 326.1732, found: 326.1747.



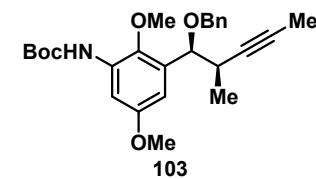
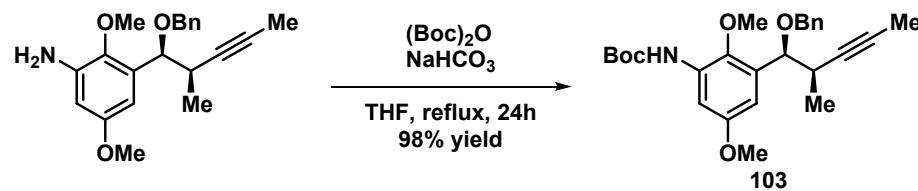
**Benzyl (2-((1*S*,2*R*)-1-methoxy-2-methylpent-3-yn-1-yl)phenyl)carbamate (102):** Prepared by general procedure *M* using **100** (200 mg, 0.716 mmol). The crude material was purified with silica gel column chromatography using 8.6% ethyl acetate in Hexanes. **102** (239 mg, 0.71 mmol, 99% yield) was obtained as a pale yellow oil.  $[\alpha]_D^{23.8} = -3.3$  ( $c = 2.7$ ,  $\text{CH}_2\text{Cl}_2$ ).

$^1\text{H}$  NMR (500 MHz,  $\text{CDCl}_3$ ):  $\delta$  8.42 (s, 1H), 8.08 (s, 1H), 8.43-7.28 (m, 5H), 8.11 (d,  $J = 7.6$  Hz, 1H), 8.02 (dd,  $J = 14.9, 7.45$  Hz, 1H), 8.23 (d,  $J = 12.3$  Hz, 1H), 8.18 (d,  $J = 12.3$  Hz, 1H), 8.06 (d,  $J = 8.3$  Hz, 1H), 8.29 (s, 3H), 8.90-2.83 (m, 1H), 8.61 (d,  $J = 2.4$  Hz, 3H), 8.25 (d,  $J = 6.9$  Hz, 3H);

$^{13}\text{C}$  NMR (125 MHz,  $\text{CDCl}_3$ ):  $\delta$  153.6, 136.9, 136.4, 130.1, 128.6, 128.5, 128.2, 128.2, 122.6, 120.5, 88.3, 88.2, 87.5, 66.7, 57.4, 32.1, 18.3, 33.3;

IR (neat/ $\text{cm}^{-1}$ )  $\nu_{\text{max}}$ : 3347, 2973, 2934, 2919, 2892, 2827, 1732, 1591, 1524, 1447, 1303, 1208, 1108, 1078, 1050, 1039, 1028;

HRMS (ESI)  $m/z$  calcd for  $\text{C}_{21}\text{H}_{23}\text{NO}_3$  [ $\text{M}+\text{Na}]^+$ : 360.1576, found: 360.1587.



**Tert-butyl (3-((1*S*,2*R*)-1-(benzyloxy)-2-methylpent-3-yn-1-yl)-2,5-dimethoxyphenyl)carbamate (103):** Arylamine<sup>11</sup> (800 mg, 2.36 mmol, 1 equiv) was dissolved in 12 mL anhydrous THF (0.2 M). Di-*tert*-butyl dicarbonate ((Boc)<sub>2</sub>O) (1.55

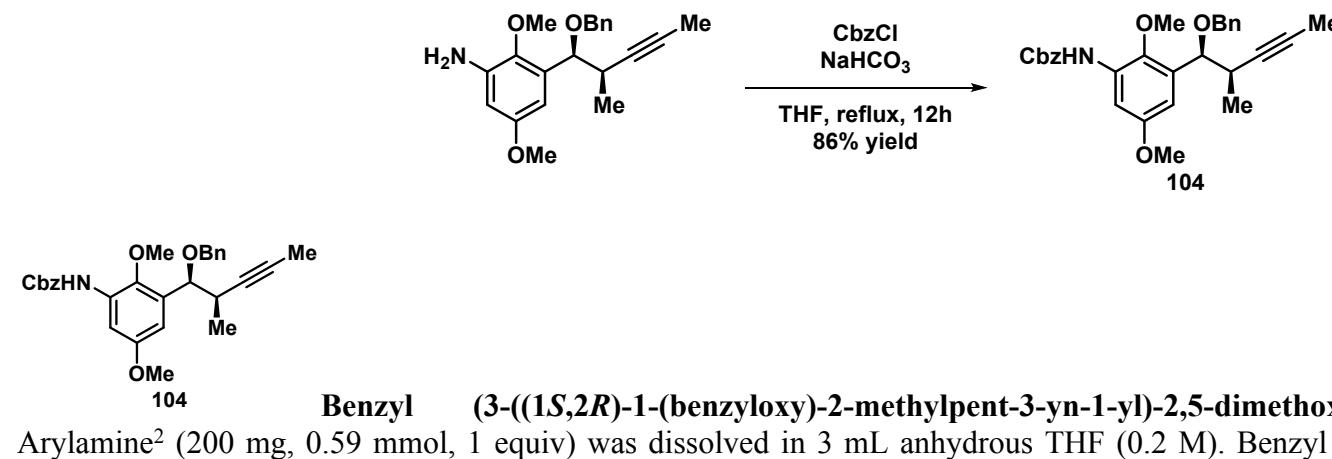
g, 7.08 mmol, 3 equiv) and sodium bicarbonate (198 mg, 2.36 mmol, 1 equiv) were added into the mixture sequentially. The reaction mixture was then heated to reflux for 24 hours. It was then cooled down to room temperature and quenched with DI water. It was then extracted with ethyl acetate (10 mL x 3). The combined organic layers were dried over  $\text{MgSO}_4$ , filtered, and concentrated. Purification over silica gel chromatography using 30% ethyl acetate in Hexanes afforded **103** (1 g, 2.3 mmol, 98% yield) as a pale yellow viscous oil.  $[\alpha]_D^{23.8} = -16.2$  ( $c = 3.5$ ,  $\text{CH}_2\text{Cl}_2$ ).

$^1\text{H}$  NMR (500 MHz,  $\text{CDCl}_3$ ):  $\delta$  7.69 (s, 1H), 7.38-7.25 (m, 5H), 86.95 (s, 1H), 86.69 (d,  $J = 3.1$  Hz, 1H), 84.56 (d,  $J = 7.4$  Hz, 1H), 84.45 (d,  $J = 12.0$  Hz, 1H), 84.29 (d,  $J = 12.0$  Hz, 1H), 83.80 (s, 3H), 83.67 (s, 3H), 82.94-2.84 (m, 1H), 81.67 (d,  $J = 2.4$  Hz, 3H), 81.54 (s, 9H), 81.23 (d,  $J = 6.9$  Hz, 3H);

$^{13}\text{C}$  NMR (125 MHz,  $\text{CDCl}_3$ ):  $\delta$  156.4, 152.7, 141.0, 138.4, 133.6, 132.2, 128.2, 127.7, 127.5, 106.8, 104.1, 88.1, 87.8, 87.4, 870.6, 867.1, 861.5, 855.6, 832.5, 828.4, 817.7, 83.6.

IR (neat/ $\text{cm}^{-1}$ )  $\nu_{\text{max}}$ : 3432, 2977, 2919, 2935, 2874, 2837, 1727, 1600, 1517, 1454, 1420, 1392, 1367, 1348, 1236, 1220, 1204, 1146, 1091, 1064, 1051, 1028;

HRMS (ESI)  $m/z$  calcd for  $\text{C}_{26}\text{H}_{33}\text{NO}_5$  [ $\text{M}+\text{Na}]^+$ : 462.2256, found: 462.2257.



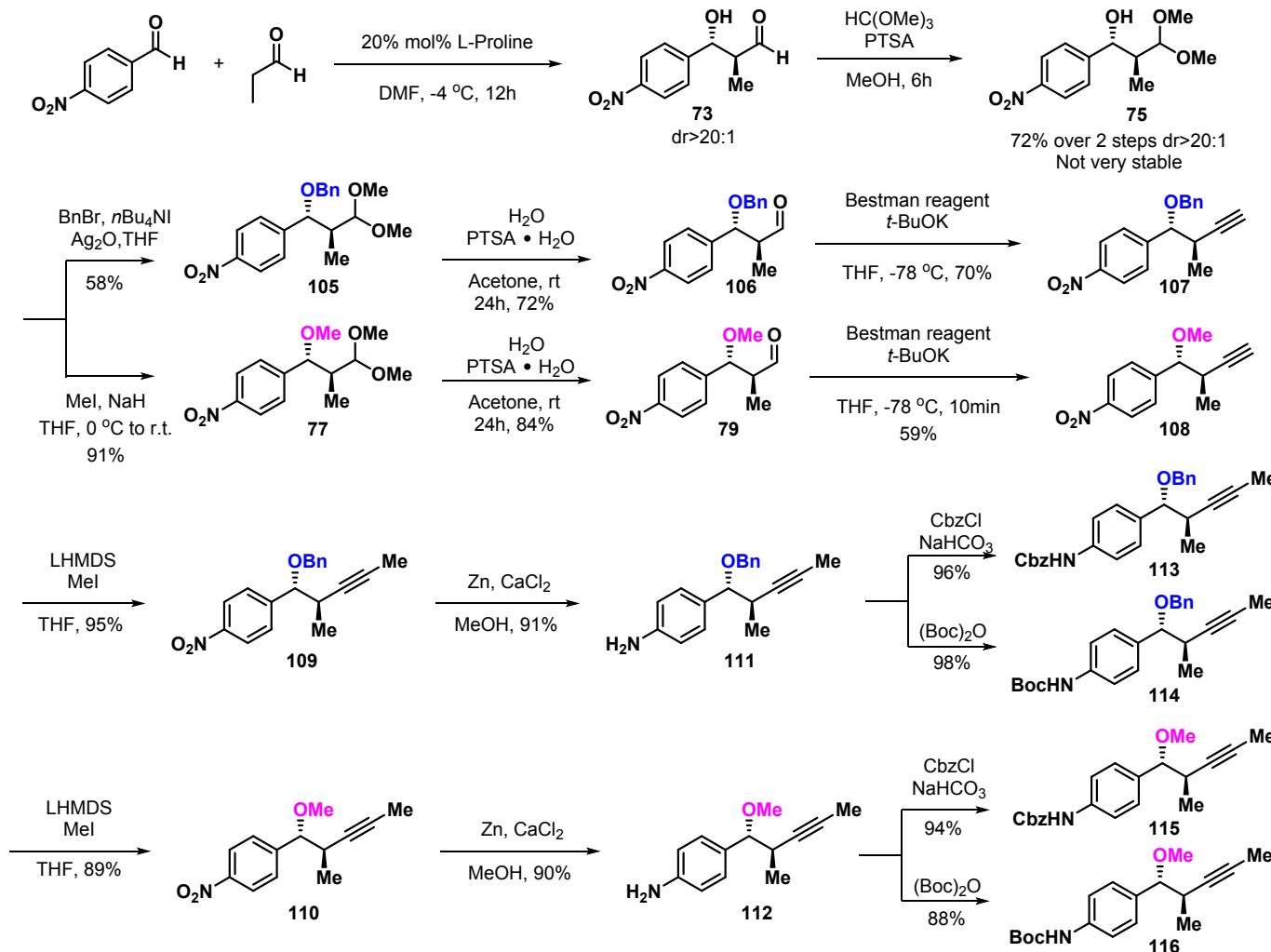
mmol, d=1.2, 1.4 equiv) and sodium bicarbonate (60 mg, 0.71 mmol, 1.2 equiv) were added into the mixture sequentially. The reaction mixture was then heated to reflux for 12 hours. It was then cooled down to room temperature and quenched with DI water. It was then extracted with ethyl acetate (10 mL x 3). The combined organic layers were dried over MgSO<sub>4</sub>, filtered, and concentrated. Purification over silica gel chromatography using 14% ethyl acetate in Hexanes afforded **104** (210 mg, 0.51 mmol, 86% yield) as a pale yellow viscous oil. [α]<sub>D</sub><sup>23.8</sup>= -23.8 (c = 1, CH<sub>2</sub>Cl<sub>2</sub>).

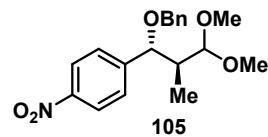
<sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>): δ7.73 (s, 1H), δ7.44-7.25 (m, 10H), δ7.19 (s, 1H), δ6.73 (d, J = 3.1 Hz, 1H), δ5.24 (s, 2H), δ4.56 (d, J = 7.4 Hz, 1H), δ4.46 (d, J = 11.9 Hz, 1H), δ4.30 (d, J = 11.9 Hz, 1H), δ3.80 (s, 3H), δ3.65 (s, 3H), δ2.92-2.86 (m, 1H), δ1.67 (d, J = 2.4 Hz, 3H), δ1.24 (d, J = 6.9 Hz, 3H);

<sup>13</sup>C NMR (125 MHz, CDCl<sub>3</sub>): δ156.4, δ153.2, δ141.1, δ138.3, δ136.0, δ133.8, δ131.6, δ128.6, δ128.4, δ128.4, δ128.3, δ127.7, δ127.5, δ107.2, δ104.4, δ81.0, δ77.5, δ70.7, δ67.1, δ61.7, δ55.6, δ32.5, δ17.7, δ3.6.

IR (neat/cm<sup>-1</sup>) ν<sub>max</sub>: 3427, 3332, 3031, 2936, 2917, 2874, 2856, 2837, 1733, 1598, 1521, 1497, 1464, 1454, 1423, 1346, 1234, 1194, 1087, 1065, 1051, 1028;

HRMS (ESI) *m/z* calcd for C<sub>29</sub>H<sub>31</sub>NO<sub>5</sub> [M+Na]<sup>+</sup>: 496.2100, found: 496.2106.

Supplementary Scheme S4. Synthesis of *Anti*-Substrates



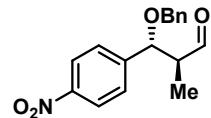
**1-((1R,2S)-1-(benzyloxy)-3,3-dimethoxy-2-methylpropyl)-4-nitrobenzene (105):** Prepared by *general procedure G* using **75** (10.4 g, 40.74 mmol). The crude material was purified with silica gel column chromatography using 12% ethyl acetate in Hexanes. **105** (8.12 g, 23.63 mmol, 58% yield) was obtained as a yellow, viscous oil.  $[\alpha]_D^{23.8} = +35.4$  ( $c = 2.7$ ,  $\text{CH}_2\text{Cl}_2$ ).

$^1\text{H}$  NMR (500 MHz,  $\text{CDCl}_3$ ):  $\delta$  8.23 (d,  $J = 8.6$  Hz, 2H), 7.52 (d,  $J = 8.7$  Hz, 2H), 7.36-7.27 (m, 5H), 7.44 (d,  $J = 7.9$  Hz, 1H), 7.40-7.37 (m, 2H), 7.25 (d,  $J = 11.7$  Hz, 1H), 7.18 (s, 3H), 7.17 (s, 3H), 7.12-7.05 (m, 1H), 7.02 (d,  $J = 7.0$  Hz, 3H);

$^{13}\text{C}$  NMR (125 MHz,  $\text{CDCl}_3$ ):  $\delta$  148.1, 137.8, 128.6, 128.4, 127.8, 127.8, 123.5, 105.7, 88.1, 81.0, 842.3, 88.9;

IR (neat/ $\text{cm}^{-1}$ )  $\nu_{\text{max}}$ : 2978, 2937, 2833, 1606, 1599, 1519, 1454, 1343, 1206, 1188, 1133, 1064, 1047, 1028;

LCMS (ESI)  $m/z$  calcd for  $\text{C}_{19}\text{H}_{23}\text{NO}_5$  [ $\text{M}+\text{H}]^+$ : 346.16, found: 346.18.



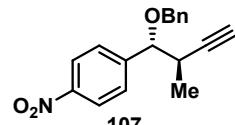
**(2S,3R)-3-(benzyloxy)-2-methyl-3-(4-nitrophenyl)propanal (106):** Prepared by *general procedure I* using **105** (8 g, 23.16 mmol) and stirred for 24 hours. The crude material was purified with silica gel column chromatography using 20% ethyl acetate in Hexanes. **106** (5 g, 16.68 mmol) was obtained as a yellow, viscous oil.  $[\alpha]_D^{23.8} = +70.3$  ( $c = 3.1$ ,  $\text{CH}_2\text{Cl}_2$ ).

$^1\text{H}$  NMR (500 MHz,  $\text{CDCl}_3$ ):  $\delta$  7.79 (d,  $J = 2.5$  Hz, 1H), 7.27 (d,  $J = 8.5$  Hz, 2H), 7.53 (d,  $J = 8.7$  Hz, 2H), 7.36-7.22 (m, 5H), 7.42 (d,  $J = 8.7$  Hz, 1H), 7.45 (d,  $J = 11.6$  Hz, 1H), 7.26 (d,  $J = 11.6$  Hz, 1H), 7.23-7.16 (m, 1H), 7.06 (d,  $J = 7.2$  Hz, 3H);

$^{13}\text{C}$  NMR (125 MHz,  $\text{CDCl}_3$ ):  $\delta$  202.6, 148.0, 146.6, 137.0, 128.5, 128.4, 128.1, 127.9, 123.9, 88.1, 81.2, 852.3, 80.9;

IR (neat/ $\text{cm}^{-1}$ )  $\nu_{\text{max}}$ : 3031, 2979, 2937, 2863, 2863, 2721, 1725, 1607, 1599, 1519, 1497, 1454, 1344, 1315, 1205, 1104, 1088, 1065, 1028, 1014;

LCMS (ESI)  $m/z$  calcd for  $C_{17}H_{17}NO_4 [M+H]^+$ : 300.12, found: 300.17.



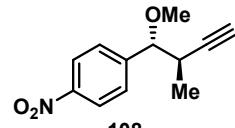
**1-((1R,2R)-1-(benzyloxy)-2-methylbut-3-yn-1-yl)-4-nitrobenzene (107):** Prepared by *general procedure J* using **106** (1 g, 3.25 mmol). The crude material was purified with silica gel column chromatography using 10% ethyl acetate in Hexanes. **107** (680 mg, 2.34 mmol, 70% yield) was obtained as a yellow oil.  $[\alpha]_D^{23.8} = +61.5$  ( $c = 1.3$ ,  $CH_2Cl_2$ ).

$^1H$  NMR (500 MHz,  $CDCl_3$ ):  $\delta$  8.25-8.22 (m, 2H), 87.58-7.55 (m, 2H), 87.37-7.28 (m, 5H), 84.59 (d,  $J = 12.0$  Hz, 1H), 84.46 (d,  $J = 5.4$  Hz, 1H), 84.34 (d,  $J = 12.0$  Hz, 1H), 82.92-2.86 (m, 1H), 82.14 (d,  $J = 2.5$  Hz, 1H), 81.12 (d,  $J = 7.1$  Hz, 3H);

$^{13}C$  NMR (125 MHz,  $CDCl_3$ ):  $\delta$  147.8, 146.7, 137.4, 128.4, 128.4, 127.9, 127.8, 123.4, 84.8, 81.9, 71.3, 71.0, 33.0, 16.7;

IR (neat/cm $^{-1}$ )  $\nu_{max}$ : 3295, 3064, 3032, 2980, 2937, 2873, 1606, 1600, 1518, 1496, 1454, 1343, 1108, 1071, 1028, 1014;

LCMS (ESI)  $m/z$  calcd for  $C_{18}H_{17}NO_3 [M+H]^+$ : 296.12, found: 296.17.



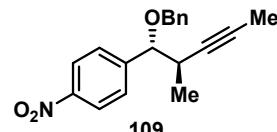
**1-((1R,2R)-1-methoxy-2-methylbut-3-yn-1-yl)-4-nitrobenzene (108):** Prepared by *general procedure J* using **79** (5.08 g, 22.8 mmol). The crude material was purified with silica gel column chromatography using 10% ethyl acetate in Hexanes. **108** (2.94 g, 13.45 mmol, 59% yield) was obtained as a yellow oil.  $[\alpha]_D^{23.8} = +73.4$  ( $c = 3.2$ ,  $CH_2Cl_2$ ).

$^1H$  NMR (500 MHz,  $CDCl_3$ ):  $\delta$  8.23 (d,  $J = 8.5$  Hz, 1H), 87.53 (d,  $J = 8.7$  Hz, 1H), 84.26 (d,  $J = 5.3$  Hz, 1H), 83.31 (s, 3H), 82.88-2.82 (m, 1H), 82.13 (d,  $J = 2.3$  Hz, 1H), 81.13 (d,  $J = 7.0$  Hz, 3H);

$^{13}C$  NMR (125 MHz,  $CDCl_3$ ):  $\delta$  147.7, 146.6, 128.2, 123.3, 885.0, 884.6, 870.9, 857.7, 832.9, 816.7;

IR (neat/cm<sup>-1</sup>)  $\nu_{\text{max}}$ : 3294, 2983, 2937, 2896, 2927, 1606, 1600, 1518, 1454, 1343, 1294, 1200, 1135, 1092, 1014;

LCMS (ESI) *m/z* calcd for C<sub>12</sub>H<sub>13</sub>NO<sub>3</sub> [M+H]<sup>+</sup>: 220.09, found: 220.11.



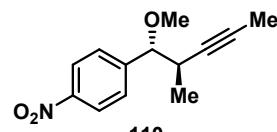
**1-((1*R*,2*R*)-1-(benzyloxy)-2-methylpent-3-yn-1-yl)-4-nitrobenzene (109):** Prepared by *general procedure K* using **107** (689 mg, 2.33 mmol) and stirred for 12 hours. The crude material was purified with silica gel column chromatography using 53% dichloromethane in Hexanes. **109** (685 mg, 2.21 mmol, 95% yield) was obtained as a yellow solid.  $[\alpha]_D^{23.8} = +57$  (*c* = 2.1, CH<sub>2</sub>Cl<sub>2</sub>).

<sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>):  $\delta$  8.24-8.21 (m, 2H), 7.55-7.53 (m, 2H), 7.36-7.28 (m, 5H), 4.58 (d, *J* = 12.2 Hz, 1H), 4.41 (d, *J* = 5.4 Hz, 1H), 4.31 (d, *J* = 12.1 Hz, 1H), 2.87-2.80 (m, 1H), 1.79 (d, *J* = 2.4 Hz, 3H), 1.05 (d, *J* = 7.0 Hz, 3H);

<sup>13</sup>C NMR (125 MHz, CDCl<sub>3</sub>):  $\delta$  147.6, 147.2, 137.6, 128.4, 128.4, 127.8, 127.8, 123.2, 82.4, 79.7, 78.5, 71.2, 33.1, 16.8, 3.5;

IR (neat/cm<sup>-1</sup>)  $\nu_{\text{max}}$ : 3065, 3031, 2977, 2935, 2918, 2874, 1606, 1600, 1519, 1454, 1343, 1198, 1108, 1090, 1074, 1028, 1014;

LCMS (ESI) *m/z* calcd for C<sub>19</sub>H<sub>19</sub>NO<sub>3</sub> [M+H]<sup>+</sup>: 310.14, found: 310.16.



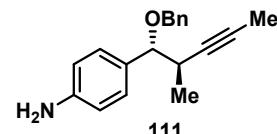
**1-((1*R*,2*R*)-1-methoxy-2-methylpent-3-yn-1-yl)-4-nitrobenzene (110):** Prepared by *general procedure K* using **108** (2.96 g, 13.5 mmol). The crude material was purified with silica gel column chromatography using 8% ethyl acetate in Hexanes. **110** (2.8 g, 12.015 mmol, 89% yield) was obtained as a yellow oil.  $[\alpha]_D^{23.8} = +65.5$  (*c* = 2.6, CH<sub>2</sub>Cl<sub>2</sub>).

<sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>): δ8.21 (d, *J* = 8.5 Hz, 2H), δ7.51 (d, *J* = 8.7 Hz, 1H), δ4.21 (d, *J* = 5.2 Hz, 1H), δ3.29 (s, 3H), δ2.82-2.75 (m, 1H), δ1.77 (d, *J* = 2.0 Hz, 3H), δ1.07 (d, *J* = 7.0 Hz, 3H);

<sup>13</sup>C NMR (125 MHz, CDCl<sub>3</sub>): δ147.6, δ147.2, δ128.2, δ123.1, δ85.5, δ79.4, δ78.5, δ57.6, δ33.1, δ16.9, δ3.5;

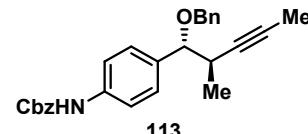
IR (neat/cm<sup>-1</sup>)  $\nu_{\text{max}}$ : 2980, 2935, 2880, 2857, 2825, 1607, 1599, 1518, 1452, 1342, 1294, 1120, 1107, 1100, 1087, 1067, 1014;

LCMS (ESI) *m/z* calcd for C<sub>13</sub>H<sub>15</sub>NO<sub>3</sub> [M+H]<sup>+</sup>: 234.11, found: 234.13.



**4-((1*R*,2*R*)-1-(benzyloxy)-2-methylpent-3-yn-1-yl)aniline (111):** Prepared by *general procedure C* using **109** (2 g, 6.465 mmol). The crude material was purified with silica gel column chromatography using 20% ethyl acetate in Hexanes. **111** (1.64 g, 5.88 mmol, 91% yield) was obtained as a yellow, viscous oil. (We preferred to use as crude, so we did not fully characterize it.)

<sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>): δ7.36-7.24 (m, 5H), δ7.13-7.24 (m, 2H), δ6.69-6.67 (m, 2H), δ4.55 (d, *J* = 12.4 Hz, 1H), δ4.25 (d, *J* = 12.4 Hz, 1H), δ4.09 (d, *J* = 7.2 Hz, 1H), δ3.72 (brs, 2H), δ2.77-2.70 (m, 1H), δ1.83 (d, *J* = 2.4 Hz, 3H), δ0.95 (d, *J* = 7.0 Hz, 3H).



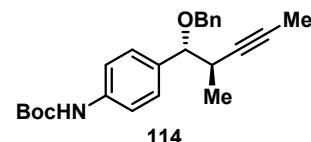
**Benzyl (4-((1*R*,2*R*)-1-(benzyloxy)-2-methylpent-3-yn-1-yl)phenyl)carbamate (10b):** Prepared by *general procedure M* using **111** (220 mg, 0.787 mmol). The crude material was purified with silica gel column chromatography using 20% ethyl acetate in Hexanes. **113** (279 mg, 0.677 mmol, 86% yield) was obtained as a white solid.  $[\alpha]_D^{23.8} = +4.5$  (*c* = 0.67, CH<sub>2</sub>Cl<sub>2</sub>).  $[\alpha]_D^{23.8} = +59.4$  (*c* = 3.4, CH<sub>2</sub>Cl<sub>2</sub>).

<sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>): δ7.43-7.27 (m, 14H), δ6.67 (brs, 1H), δ5.21 (s, 2H), δ4.55 (d, *J* = 12.3 Hz, 1H), δ4.25 (d, *J* = 12.3 Hz, 1H), δ4.18 (d, *J* = 6.7 Hz, 1H), δ2.79-2.72 (m, 1H), δ1.81 (d, *J* = 2.4 Hz, 3H), δ0.97 (d, *J* = 7.0 Hz, 3H);

<sup>13</sup>C NMR (125 MHz, CDCl<sub>3</sub>): δ153.3, δ138.4, δ137.4, δ136.0, δ134.8, δ128.6, δ128.4, δ128.4, δ128.3, δ128.3, δ127.8, δ127.5, δ118.4, δ83.3, δ81.1, δ77.4, δ70.4, δ67.1, δ33.3, δ17.3, δ3.7;

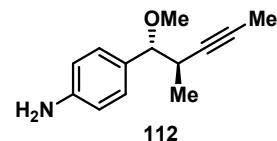
IR (neat/cm<sup>-1</sup>) ν<sub>max</sub>: 3323, 3063, 3032, 2974, 2933, 2917, 2873, 1733, 1705, 1612, 1598, 1525, 1497, 1454, 1415, 1312, 1214, 1082, 1050, 1028;

HRMS (ESI) *m/z* calcd for C<sub>27</sub>H<sub>27</sub>NO<sub>3</sub> [M+H]<sup>+</sup>: 414.2069, found: 414.2080.



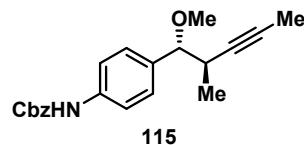
**Tert-butyl (4-((1*R*,2*R*)-1-(benzyloxy)-2-methylpent-3-yn-1-yl)phenyl)carbamate (114):** Prepared by *general procedure L* using **111** (220 mg, 0.787 mmol). The crude material was purified with silica gel column chromatography using 10% ethyl acetate in Hexanes. **114** (269 mg, 0.708 mmol, 90% yield) was obtained as a viscous oil.

<sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>): δ7.36-7.25 (m, 9H), δ6.49 (brs, 1H), δ4.55 (d, *J* = 12.4 Hz, 1H), δ4.24 (d, *J* = 12.4 Hz, 1H), δ4.17 (d, *J* = 6.8 Hz, 1H), δ2.78-2.72 (m, 1H), δ1.81 (d, *J* = 2.4 Hz, 3H), δ1.53 (s, 9H), 0.96 (d, *J* = 7.0 Hz, 3H).



**4-((1*R*,2*R*)-1-methoxy-2-methylpent-3-yn-1-yl)aniline (112):** Prepared by *general procedure C* using **110** (2.8 g, 12 mmol). The crude material was purified with silica gel column chromatography using 30% ethyl acetate in Hexanes. **112** (2.2 g, 10.8 mmol, 90% yield) was obtained as a white solid. (We preferred to use as crude, so we did not fully characterize it.)

<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>): δ7.09-7.07 (m, 2H), δ6.67-6.65 (m, 2H), δ3.90 (d, *J* = 7.0 Hz, 1H), δ3.21 (s, 3H), δ2.72-2.63 (m, 1H), δ1.81 (d, *J* = 2.2 Hz, 3H), δ0.97 (d, *J* = 7.0 Hz, 3H).



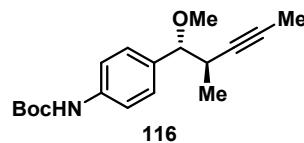
**Benzyl (4-((1*R*,2*R*)-1-methoxy-2-methylpent-3-yn-1-yl)phenyl)carbamate (115):** Prepared by general procedure *M* using **112** (1.05 g, 5.165 mmol). The crude material was purified with silica gel column chromatography using 17% ethyl acetate in Hexanes. **115** (1.64 g, 4.86 mmol, 94% yield) was obtained as a pale yellow solid.  $[\alpha]_D^{23.8} = +55.4$  ( $c = 3.3$ ,  $\text{CH}_2\text{Cl}_2$ ).

$^1\text{H}$  NMR (500 MHz,  $\text{CDCl}_3$ ):  $\delta$  7.42-7.24 (m, 9H), 6.68 (brs, 1H), 5.21 (s, 2H), 4.00 (d,  $J = 6.5$  Hz, 1H), 3.23 (s, 3H), 2.73-2.67 (m, 1H), 1.80 (d,  $J = 2.4$  Hz, 3H), 1.00 (d,  $J = 7.0$  Hz, 3H);

$^{13}\text{C}$  NMR (125 MHz,  $\text{CDCl}_3$ ):  $\delta$  153.4, 137.4, 136.0, 134.8, 128.6, 128.3, 128.3, 128.1, 118.4, 86.5, 80.8, 77.4, 67.0, 57.1, 33.4, 17.5, 3.7;

IR (neat/ $\text{cm}^{-1}$ )  $\nu_{\text{max}}$ : 3315, 3034, 2980, 2934, 2918, 2885, 2822, 1733, 1704, 1613, 1599, 1527, 1455, 1414, 1313, 1214, 1103, 1085, 1049, 1028, 1018;

HRMS (ESI)  $m/z$  calcd for  $\text{C}_{21}\text{H}_{23}\text{NO}_3$  [ $\text{M}+\text{Na}]^+$ : 360.1576, found: 360.1582.



**Tert-butyl (4-((1*R*,2*R*)-1-methoxy-2-methylpent-3-yn-1-yl)phenyl)carbamate (116):** Prepared by general procedure *L* (without sodium bicarbonate) using **112** (1.05 g, 5.165 mmol). The crude material was purified with silica gel column chromatography using 13% ethyl acetate in Hexanes. **116** (1.38 g, 4.54 mmol, 88% yield) was obtained as a white solid.  $[\alpha]_D^{23.8} = +58.7$  ( $c = 3.3$ ,  $\text{CH}_2\text{Cl}_2$ ).

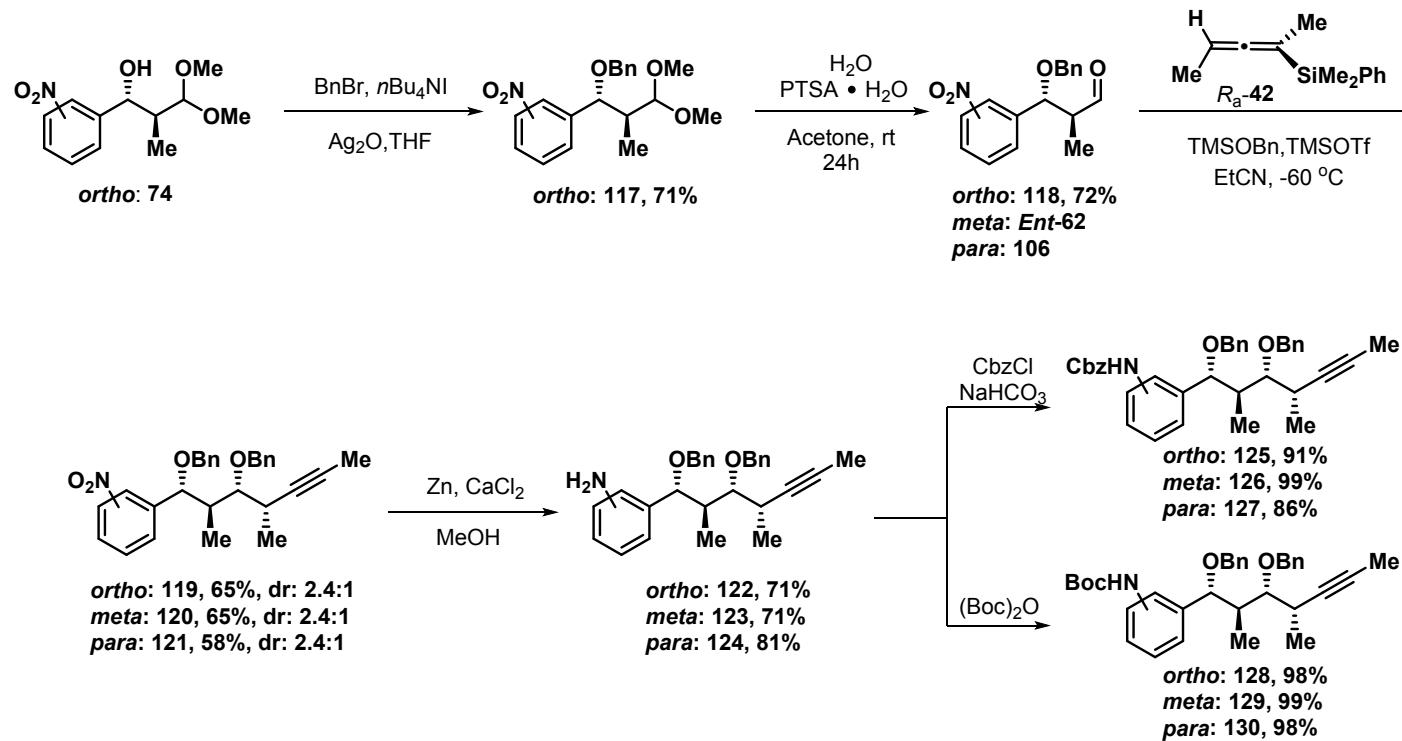
$^1\text{H}$  NMR (500 MHz,  $\text{CDCl}_3$ ):  $\delta$  7.34-7.33 (m, 2H), 7.24-7.21 (m, 2H), 6.48 (brs, 1H), 3.98 (d,  $J = 6.5$  Hz, 1H), 3.23 (s, 3H), 2.73-2.67 (m, 1H), 1.80 (d,  $J = 2.4$  Hz, 3H), 1.52 (s, 9H), 0.99 (d,  $J = 7.0$  Hz, 3H);

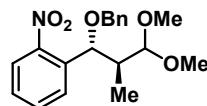
$^{13}\text{C}$  NMR (125 MHz,  $\text{CDCl}_3$ ):  $\delta$  152.8, 137.9, 134.2, 128.0, 118.2, 86.5, 80.9, 57.0, 33.4, 28.3, 17.5, 3.7;

IR (neat/cm<sup>-1</sup>)  $\nu_{\text{max}}$ : 3331, 2978, 2933, 2887, 2823, 1727, 1702, 1614, 1597, 1522, 1454, 1411, 1366, 1313, 1231, 1155, 1104, 1089, 1051, 1028;

HRMS (ESI) *m/z* calcd for C<sub>18</sub>H<sub>25</sub>NO<sub>3</sub> [M+Na]<sup>+</sup>: 326.1732, found: 326.1747.

### Supplementary Scheme S5. Synthesis of Substrates with Extended Tether Length

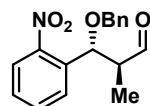




**1-((1R,2S)-1-(benzyloxy)-3,3-dimethoxy-2-methylpropyl)-2-nitrobenzene (117):** Prepared by *general procedure G* using **74** (7g, 27.42 mmol). The crude material was purified with silica gel column chromatography using 14% ethyl acetate in Hexanes. **117** (6.7g, 19.47 mmol, 71% yield) was obtained as pale yellow viscous oil.

<sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>): δ7.80 (dd, *J* = 8.1, 1.1 Hz, 1H), δ7.74 (dd, *J* = 7.9, 1.2 Hz, 1H), δ7.65 – 7.59 (m, 1H), δ7.43 (td, *J* = 8.1, 1.3 Hz, 1H), δ7.37 – 7.26 (m, 5H), δ5.03 (d, *J* = 8.1 Hz, 1H), δ4.54 (d, *J* = 3.9 Hz, 1H), δ4.39 (d, *J* = 11.5 Hz, 1H), δ4.32 (d, *J* = 11.6 Hz, 1H), δ3.36 (s, 3H), δ3.32 (s, 3H), δ2.24 (ddq, *J* = 11.1, 7.2, 3.6 Hz, 1H), δ0.74 (d, *J* = 7.1 Hz, 3H);

<sup>13</sup>C NMR (125 MHz, CDCl<sub>3</sub>): δ150.4, δ137.9, δ136.1, δ132.6, δ129.3, δ128.4, δ128.3, δ127.9, δ127.8, δ123.7, δ105.9, δ71.4, δ56.0, δ55.3, δ43.5, δ9.3;

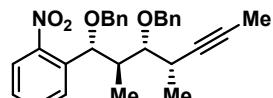


**(2S,3R)-3-(benzyloxy)-2-methyl-3-(2-nitrophenyl)propanal (118):** Prepared by *general procedure I* using **117** (5.8g, 16.8 mmol). The crude material was purified with silica gel column chromatography using 13% ethyl acetate in Hexanes. **118** (4.38g, 14.6 mmol, 87%) was obtained as pale yellow viscous oil. [α]<sub>D</sub><sup>23.8</sup> = +5.2 (*c* = 2.9, CH<sub>2</sub>Cl<sub>2</sub>).

<sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>): δ9.77 (d, *J* = 2.6 Hz, 1H), δ7.98 (dd, *J* = 8.2, 1.2 Hz, 1H), δ7.79 (dd, *J* = 7.9, 1.4 Hz, 1H), δ7.69 (td, *J* = 7.8, 1.2 Hz, 1H), δ7.50 (ddd, *J* = 8.6, 7.4, 1.5 Hz, 1H), δ7.35-7.20 (m, 5H), δ5.28 (d, *J* = 6.8 Hz, 1H), δ4.44 (d, *J* = 11.6 Hz, 1H), δ4.30 (d, *J* = 11.6 Hz, 1H), δ2.80 (ddq, *J* = 11.6, 7.1, 2.6 Hz, 1H), δ1.05 (d, *J* = 7.2 Hz, 3H);

<sup>13</sup>C NMR (125 MHz, CDCl<sub>3</sub>): δ202.7, δ149.5, δ137.0, δ135.2, δ133.6, δ129.0, δ128.9, δ128.5, δ128.0, δ127.9, δ124.6, δ71.8, δ52.7, δ11.3;

IR (neat/cm<sup>-1</sup>)  $\nu_{\max}$ : 3065, 3032, 2979, 2937, 2868, 2733, 1725, 1608, 1578, 1524, 1454, 1393, 1349, 1298, 1088, 1059, 1028;



**((((1*R*,2*R*,3*R*,4*S*)-2,4-dimethyl-1-(2-nitrophenyl)hept-5-yne-1,3-diyl)bis(oxy))dibenzene (119):**

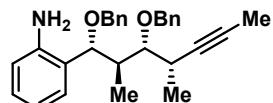
Prepared by *general procedure B* using **118** (2 g, 6.68 mmol, 1.0 equiv), *R<sub>a</sub>-42* (1.08 g, 5.35 mmol, 0.8 equiv), (benzyloxy)trimethylsilane (1 mL, 5.35 mmol, 0.8 equiv), and TMSOTf (0.47 mL, 2.67 mmol, 0.4 equiv). The reaction was stirred at –60 °C for 12 hours. The crude material (dr: 2.4:1, double stereodifferentiation, “mismatched”) was purified with silica gel column Chromatography using 70% DCM in Hexanes. **119** (1.59 g, 3.48 mmol, 65% yield) was afforded as a pale yellow oil.  $[\alpha]_D^{23.8} = +63.9$  (*c* = 3.3, CH<sub>2</sub>Cl<sub>2</sub>).

<sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>): δ7.76–7.72 (m, 2H), δ7.60 (t, *J* = 7.1 Hz, 1H), δ7.44 – 7.39 (m, 1H), δ7.32–7.25 (m, 10H), δ5.49 (d, *J* = 10.1 Hz, 1H), δ4.64 (d, *J* = 11.5 Hz, 1H), δ4.53 (d, *J* = 11.5 Hz, 1H), δ4.40 (d, *J* = 11.4 Hz, 1H), δ4.32 (d, *J* = 11.4 Hz, 1H), δ3.79 (dd, *J* = 9.5, 1.8 Hz, 1H), δ2.71–2.63 (m, 1H), δ2.41–2.34 (m, 1H), δ1.82 (d, *J* = 2.4 Hz, 3H), δ1.22 (d, *J* = 6.7 Hz, 3H), δ0.75 (d, *J* = 7.3 Hz, 3H);

<sup>13</sup>C NMR (125 MHz, CDCl<sub>3</sub>): δ150.8, δ138.6, δ138.4, δ137.0, δ132.7, δ128.8, δ128.3, δ128.1, δ127.7, δ127.5, δ123.2, δ82.1, δ81.5, δ78.0, δ77.6, δ72.5, δ71.1, δ43.8, δ28.1, δ19.6, δ11.1, δ3.7;

IR (neat/cm<sup>−1</sup>)  $\nu_{\max}$ : 3065, 3031, 2970, 2931, 2917, 2873, 1527, 1497, 1454, 1355, 1296, 1207, 1087, 1060, 1028;

HRMS (ESI) *m/z* calcd for C<sub>29</sub>H<sub>31</sub>NO<sub>4</sub> [M+H]<sup>+</sup>: 458.2331, found: 458.2324.



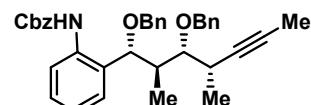
**2-((1*R*,2*R*,3*R*,4*S*)-1,3-bis(benzyloxy)-2,4-dimethylhept-5-yn-1-yl)aniline (122):** Prepared by *general procedure C* using **119** (1.5 g, 3.28 mmol). The crude material was purified with silica gel column chromatography using 9% ethyl acetate in Hexanes. **122** (0.994 g, 2.33 mmol, 71% yield) obtained as pale yellow viscous oil.  $[\alpha]_D^{23.8} = +24.6$  (*c* = 3.8, CH<sub>2</sub>Cl<sub>2</sub>).

<sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>): δ7.34-7.27 (m, 10H), δ7.10 (td, *J* = 7.7, 1.5 Hz, 1H), δ6.97 (dd, *J* = 7.5, 1.4 Hz, 1H), δ6.70 (td, *J* = 7.4, 1.0 Hz, 1H), δ6.64 (d, *J* = 7.8 Hz, 1H), δ4.79 (d, *J* = 10.2 Hz, 1H), δ4.65 (d, *J* = 11.5 Hz, 1H), δ4.55 (d, *J* = 11.5 Hz, 1H), δ4.44 (d, *J* = 11.5 Hz, 1H), δ4.32 (d, *J* = 11.5 Hz, 1H), δ3.71 (dd, *J* = 9.4, 1.8 Hz, 1H), δ2.91-2.85 (m, 1H), δ2.80-2.73 (m, 1H), δ1.78 (d, *J* = 2.4 Hz, 3H), δ1.25 (d, *J* = 6.8 Hz, 3H), δ0.78 (d, *J* = 7.3 Hz, 3H);

<sup>13</sup>C NMR (125 MHz, CDCl<sub>3</sub>): δ145.5, δ138.8, δ138.7, δ130.6, δ128.5, δ128.3, δ128.0, δ127.9, δ127.5, δ127.4, δ123.7, δ117.5, δ116.3, δ84.9, δ83.2 δ82.5, δ72.8, δ70.6, δ38.5, δ28.5, δ19.6, δ12.9, δ3.8;

IR (neat/cm<sup>-1</sup>)  $\nu_{\text{max}}$ : 3459, 3364, 3063, 3029, 2969, 2931, 2916, 2874, 1614, 1585, 1495, 1454, 1390, 1377, 1368, 1298, 1268, 1124, 1085, 1058, 1027;

HRMS (ESI) *m/z* calcd for C<sub>29</sub>H<sub>33</sub>NO<sub>2</sub> [M+H]<sup>+</sup>: 428.2590, found: 428.2582.



125

**Benzyl (2-((1*R*,2*R*,3*R*,4*S*)-1,3-bis(benzyloxy)-2,4-dimethylhept-5-yn-1-yl)phenyl)carbamate (125):**

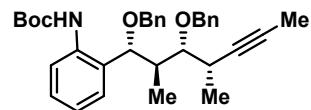
Prepared by *general procedure M* using **122** (385 mg, 0.9 mmol). The crude material was purified with silica gel column chromatography using 11% ethyl acetate in Hexanes. **125** (460 mg, 0.82 mmol, 91% yield) was obtained as colorless viscous oil.  $[\alpha]_D^{23.8} = +41.7$  (*c* = 1.3, CH<sub>2</sub>Cl<sub>2</sub>).

<sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>): δ8.83 (s, 1H), δ8.15 (d, *J* = 7.5 Hz, 1H), δ7.35-7.24 (m, 13H), δ7.02-7.01 (m, 2H), δ5.20 (d, *J* = 12.4 Hz, 1H), δ5.10 (d, *J* = 12.4 Hz, 1H), δ4.85 (d, *J* = 10.2 Hz, 1H), δ4.57 (d, *J* = 11.5 Hz, 1H), δ4.46 (d, *J* = 10.9 Hz, 1H), δ4.33 (d, *J* = 11.5 Hz, 1H), δ3.63 (dd, *J* = 9.5, 1.7 Hz, 1H), δ2.74-2.65 (m, 2H), δ1.70 (d, *J* = 2.4 Hz, 3H), δ1.18 (d, *J* = 6.7 Hz, 3H), δ0.72 (d, *J* = 7.2 Hz, 3H);

<sup>13</sup>C NMR (125 MHz, CDCl<sub>3</sub>): δ153.5, δ138.4, δ137.6, δ137.1, δ136.4, δ130.3, δ128.7, δ128.5, δ128.4, δ128.2, δ128.1, δ128.0, δ127.9, δ127.9, δ127.6, δ127.5, δ122.5, δ120.2, δ85.2, δ82.3, δ82.0, δ77.5, δ72.5, δ71.0, δ66.6, δ39.3, δ28.4, δ19.5, δ12.9, δ3.6;

IR (neat/cm<sup>-1</sup>)  $\nu_{\text{max}}$ : 3340, 3063, 3031, 3005, 2970, 2932, 2918, 2872, 1737, 1591, 1526, 1451, 1369, 1304, 1215, 1116, 1083, 1058, 1042, 1028;

HRMS (ESI)  $m/z$  calcd for  $C_{37}H_{39}NO_4$  [M+Na] $^+$ : 584.2777, found: 584.2767.



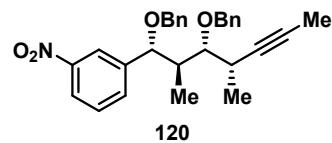
**Tert-butyl (2-((1*R*,2*R*,3*R*,4*S*)-1,3-bis(benzyloxy)-2,4-dimethylhept-5-yn-1-yl)phenyl)carbamate (128):** 122 (220 mg, 0.51 mmol, 1 equiv.) was dissolved in 1.7 mL THF at room temperature. Di-*tert*-butyl dicarbonate (168 mg, 0.77 mmol, 1.5 equiv.), sodium bicarbonate (47 mg, 0.561 mmol, 1.1 equiv.), and 4-dimethylaminopyridine (DMAP) (50 mg, 0.4 mmol, 0.8 equiv.) were added to the reaction mixture. The reaction was stirred for 24 hours at room temperature. It was then quenched with DI water. The mixture was extracted with diethyl ether, and the combined organic layers were dried over  $MgSO_4$ , filtered, and concentrated. Purification over silica gel chromatography (12% ethyl acetate/Hexanes) afforded **128** (264 mg, 0.5 mmol, 98% yield) as a pale yellow viscous oil.  $[\alpha]_D^{23.8} = +28.1$  ( $c = 2.2$ ,  $CH_2Cl_2$ ).

$^1H$  NMR (500 MHz,  $CDCl_3$ ):  $\delta$  8.58 (s, 1H), 8.12 (d,  $J = 8.2$  Hz, 1H), 7.37-7.27 (m, 10H), 7.03-6.98 (m, 2H), 84.85 (d,  $J = 10.3$  Hz, 1H), 84.65 (d,  $J = 11.5$  Hz, 1H), 84.51 (d,  $J = 11.6$  Hz, 1H), 84.48 (d,  $J = 11.5$  Hz, 1H), 84.33 (d,  $J = 11.4$  Hz, 1H), 83.71 (dd,  $J = 9.6$ , 1.7 Hz, 1H), 82.75-2.69 (m, 1H), 82.68-2.62 (m, 1H), 81.78 (d,  $J = 2.4$  Hz, 3H), 81.44 (s, 9H), 81.18 (d,  $J = 6.7$  Hz, 3H), 80.76 (d,  $J = 7.2$  Hz, 3H);

$^{13}C$  NMR (125 MHz,  $CDCl_3$ ):  $\delta$  153.0, 138.3, 137.8, 137.6, 130.3, 128.6, 128.4, 128.3, 128.3, 127.8, 127.6, 122.1, 120.1, 85.4, 82.0, 81.5, 79.9, 72.0, 70.9, 39.3, 28.4, 28.0, 19.5, 12.4, 8.7;

IR (neat/cm $^{-1}$ )  $\nu_{max}$ : 3355, 3031, 2974, 2932, 2918, 2873, 2143, 1729, 1606, 1590, 1521, 1446, 1366, 1304, 1230, 1155, 1084, 1049, 1027;

HRMS (ESI)  $m/z$  calcd for  $C_{34}H_{41}NO_4$  [M+Na] $^+$ : 550.2933, found: 550.2944.



**(((1*R*,2*R*,3*R*,4*S*)-2,4-dimethyl-1-(3-nitrophenyl)hept-5-yne-1,3-diyl)bis(ether))dibenzene**

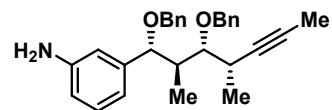
**(120):** Prepared by *general procedure B* using *ent*-**62** (2 g, 6.68 mmol, 1.0 equiv), *R*<sub>a</sub>-**42** (1.08 g, 5.35 mmol, 0.8 equiv), (benzyloxy)trimethylsilane (1 mL, 5.35 mmol, 0.8 equiv), and TMSOTf (0.47 mL, 2.67 mmol, 0.4 equiv). The reaction was stirred at –60 °C for 12 hours. The crude material (dr: 2.4:1, double stereodifferentiation, “mismatched”) was purified with silica gel column Chromatography using 70% DCM in Hexanes. **120** (1.59 g, 3.48 mmol, 65% yield) was afforded as a pale yellow oil.  $[\alpha]_D^{23.8} = +4.8$  (*c* = 1.5, CH<sub>2</sub>Cl<sub>2</sub>).

<sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>): δ8.17–8.14 (m, 2H), δ7.63 (d, *J* = 7.7 Hz, 1H), δ7.51 (t, *J* = 7.8 Hz, 1H), δ7.34–7.27 (m, 10H), δ4.89 (d, *J* = 8.3 Hz, 1H), δ4.68 (d, *J* = 11.5 Hz, 1H), δ4.60 (d, *J* = 11.6 Hz, 1H), δ4.35 (d, *J* = 11.6 Hz, 1H), δ4.29 (d, *J* = 11.5 Hz, 1H), δ3.58 (dd, *J* = 7.9, 3.6 Hz, 1H), δ2.74–2.67 (m, 1H), δ2.39 (ddq, *J* = 10.9, 7.4, 3.6 Hz, 1H), δ1.80 (d, *J* = 2.3 Hz, 3H), δ1.23 (d, *J* = 6.8 Hz, 3H), δ0.75 (d, *J* = 7.2 Hz, 3H);

<sup>13</sup>C NMR (125 MHz, CDCl<sub>3</sub>): δ148.3, δ143.7, δ138.6, δ138.1, δ133.8, δ129.2, δ128.4, δ128.3, δ127.9, δ127.7, δ127.6, δ127.5, δ122.7, δ122.7, δ82.6, δ82.3, δ82.1, δ77.6, δ72.6, δ70.9, δ42.5, δ28.1, δ18.5, δ11.9, δ3.7;

IR (neat/cm<sup>−1</sup>)  $\nu_{\max}$ : 3065, 3030, 2971, 2932, 2917, 2872, 1528, 1497, 1454, 1394, 1347, 1206, 1088, 1064, 1028;

HRMS (ESI) *m/z* calcd for C<sub>29</sub>H<sub>31</sub>NO<sub>4</sub> [M+Na]<sup>+</sup>: 480.2151, found: 480.2154.



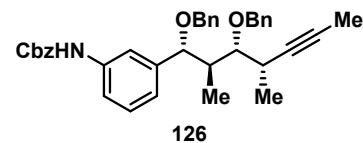
**3-((1*R*,2*R*,3*R*,4*S*)-1,3-bis(benzyloxy)-2,4-dimethylhept-5-yn-1-yl)aniline (123):** Prepared by *general procedure C* using **120** (1.5 g, 3.28 mmol). The crude material was purified with silica gel column chromatography using 17% ethyl acetate in Hexanes. **123** (0.994 g, 2.33 mmol, 71% yield) obtained as pale yellow viscous oil.  $[\alpha]_D^{23.8} = +17.8$  (*c* = 2.1, CH<sub>2</sub>Cl<sub>2</sub>).

<sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>): δ7.35-7.26 (m, 10H), δ7.14 (t, *J* = 7.7 Hz, 1H), δ6.72 (d, *J* = 7.6 Hz, 1H), δ6.67 (s, 1H), δ6.64 (dd, *J* = 7.9, 2.3 Hz, 1H), δ4.64 (s, 3H), δ4.39 (d, *J* = 11.7 Hz, 1H), δ4.24 (d, *J* = 11.7 Hz, 1H), δ3.83 (brs, 2H), δ3.69 (dd, *J* = 8.0, 3.4 Hz, 1H), δ2.72-2.65 (m, 1H), δ2.39-2.32 (m, 1H), δ1.76 (d, *J* = 2.4 Hz, 3H), δ1.22 (d, *J* = 6.8 Hz, 3H), δ0.75 (d, *J* = 7.2 Hz, 3H);

<sup>13</sup>C NMR (125 MHz, CDCl<sub>3</sub>): δ146.0, δ142.6, δ139.1, δ139.0, δ129.0, δ128.3, δ128.2, δ127.9, δ127.7, δ127.4, δ127.2, δ118.8, δ114.7, δ114.3, δ83.2, δ82.7, δ82.5, δ72.3, δ70.3, δ42.6, δ27.8, δ18.7, δ11.7, δ3.7.

IR (neat/cm<sup>-1</sup>)  $\nu_{\text{max}}$ : 3464, 3372, 3088, 3063, 3030, 2970, 2932, 2916, 2874, 1618, 1606, 1493, 1453, 1309, 1296, 1207, 1087, 1061, 1028;

HRMS (ESI) *m/z* calcd for C<sub>29</sub>H<sub>33</sub>NO<sub>2</sub> [M+Na]<sup>+</sup>: 450.2409, found: 450.2419.



**Benzyl (3-((1*R*,2*R*,3*R*,4*S*)-1,3-bis(benzyloxy)-2,4-dimethylhept-5-yn-1-yl)phenyl)carbamate (126):**

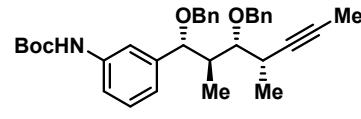
Prepared by *general procedure M* using **123** (385 mg, 0.9 mmol). The crude material was purified with silica gel column chromatography using 13% ethyl acetate in Hexanes. **126** (500 mg, 0.89 mmol, 99% yield) was obtained as colorless viscous oil.  $[\alpha]_D^{23.8} = +7.8$  (*c* = 2, CH<sub>2</sub>Cl<sub>2</sub>).

<sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>): δ7.43-7.25 (m, 16H), δ7.20 (s, 1H), δ7.03 (d, *J* = 7.6 Hz, 1H), δ6.62 (s, 1H), δ5.21 (s, 2H), δ4.72 (d, *J* = 8.7 Hz, 1H), δ4.64 (s, 2H), δ4.36 (d, *J* = 11.6 Hz, 1H), δ4.24 (d, *J* = 11.6 Hz, 1H), δ3.65 (dd, *J* = 7.9, 3.5 Hz, 1H), δ2.71-2.65 (m, 1H), δ2.39-2.33 (m, 1H), δ1.77 (d, *J* = 2.4 Hz, 3H), δ1.21 (d, *J* = 6.8 Hz, 3H), δ0.74 (d, *J* = 7.2 Hz, 3H);

<sup>13</sup>C NMR (125 MHz, CDCl<sub>3</sub>): δ153.3, δ142.4, δ138.92, δ138.9, δ137.8, δ136.1, δ129.0, δ128.6, δ128.4, δ128.3, δ128.3, δ128.2, δ128.0, δ127.7, δ127.4, δ127.3, δ123.0, δ117.8, δ82.9, δ82.9, δ82.6, δ82.4, δ77.3, δ72.3, δ70.4, δ67.0, δ42.6, δ27.9, δ18.5, δ11.7, δ3.7.

IR (neat/cm<sup>-1</sup>)  $\nu_{\text{max}}$ : 3392, 3317, 3063, 3031, 2968, 2932, 2916, 2875, 1735, 1707, 1610, 1597, 1534, 1493, 1453, 1445, 1393, 1376, 1339, 1306, 1213, 1177, 1084, 1058, 1028;

HRMS (ESI)  $m/z$  calcd for  $C_{37}H_{39}NO_4$  [M+Na]<sup>+</sup>: 584.2777, found: 584.2806.



**Tert-butyl (3-((1R,2R,3R,4S)-1,3-bis(benzyloxy)-2,4-dimethylhept-5-yn-1-yl)phenyl)carbamate (129):**

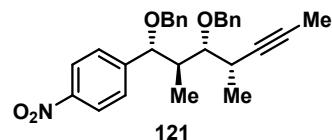
Prepared by *general procedure L* using **123** (385 mg, 0.9 mmol). The crude material was purified with silica gel column chromatography using 12% ethyl acetate in Hexanes. **129** (470 mg, 0.89 mmol, 99% yield) was obtained as colorless viscous oil.  $[\alpha]_D^{23.8}=+13.5$  ( $c = 1.5$ ,  $\text{CH}_2\text{Cl}_2$ ).

<sup>1</sup>H NMR (500 MHz,  $\text{CDCl}_3$ ):  $\delta$  7.46 (d,  $J = 9.3$  Hz, 1H), 7.35-7.27 (m, 10H), 7.13 (m, 1H), 6.99 (d,  $J = 7.6$  Hz, 1H), 6.43 (s, 1H), 6.71 (d,  $J = 8.7$  Hz, 1H), 6.65 (s, 3H), 6.36 (d,  $J = 11.6$  Hz, 1H), 6.24 (d,  $J = 11.6$  Hz, 1H), 6.66 (dd,  $J = 7.8, 3.5$  Hz, 1H), 6.73-6.66 (m, 1H), 6.40-6.32 (m, 1H), 6.77 (d,  $J = 2.5$  Hz, 3H), 6.53 (s, 9H), 6.21 (d,  $J = 6.8$  Hz, 3H), 6.75 (d,  $J = 7.2$  Hz, 3H);

<sup>13</sup>C NMR (125 MHz,  $\text{CDCl}_3$ ):  $\delta$  152.7, 142.2, 139.0, 138.4, 128.9, 128.3, 128.2, 128.0, 127.7, 127.4, 127.3, 122.5, 117.7, 83.0, 82.6, 82.4, 80.4, 77.2, 72.3, 70.4, 42.6, 28.4, 27.8, 18.5, 11.7, 3.7;

IR (neat/cm<sup>-1</sup>)  $\nu_{\text{max}}$ : 3396, 3331, 3088, 3064, 3030, 2974, 2931, 2917, 2874, 1729, 1704, 1609, 1593, 1527, 1492, 1453, 1440, 1392, 1366, 1306, 1229, 1155, 1098, 1061, 1028;

HRMS (ESI)  $m/z$  calcd for  $C_{34}H_{41}NO_4$  [M+Na]<sup>+</sup>: 550.2933, found: 550.2944.



**(((1R,2R,3R,4S)-2,4-dimethyl-1-(4-nitrophenyl)hept-5-yne-1,3-diy)bis(oxo))bis(methylene))dibenzene**

**(121):** Prepared by *general procedure B* using **106** (2 g, 6.68 mmol, 1.0 equiv), *R<sub>a</sub>-42* (1.08 g, 5.35 mmol, 0.8 equiv), (benzyloxy)trimethylsilane (1 mL, 5.35 mmol, 0.8 equiv), and TMSOTf (0.47 mL, 2.67 mmol, 0.4 equiv). The reaction was stirred at -60 °C for 12 hours. The crude material (dr: 2.4:1, double stereodifferentiation, “mismatched”) was purified with silica gel column

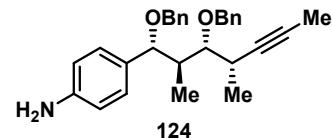
Chromatography using 6% ethyl acetate in Hexanes. **121** (1.77 g, 3.87 mmol, 58% yield) was afforded as a pale yellow oil.  $[\alpha]_D^{23.8} = -0.94$  ( $c = 3.6$ ,  $\text{CH}_2\text{Cl}_2$ ).

$^1\text{H}$  NMR (500 MHz,  $\text{CDCl}_3$ ):  $\delta$  8.19 (d,  $J = 8.7$  Hz, 2H), 7.45 (d,  $J = 8.7$  Hz, 2H), 7.37-7.28 (m, 10H), 84.88 (d,  $J = 8.3$  Hz, 1H), 84.67 (d,  $J = 11.6$  Hz, 1H), 84.60 (d,  $J = 11.6$  Hz, 1H), 84.34 (d,  $J = 11.5$  Hz, 1H), 84.28 (d,  $J = 11.6$  Hz, 1H), 83.58 (dd,  $J = 7.9, 3.6$  Hz, 1H), 82.75-2.68 (m, 1H), 82.42-2.36 (m, 1H), 81.78 (d,  $J = 2.4$  Hz, 3H), 81.23 (d,  $J = 6.8$  Hz, 3H), 80.74 (d,  $J = 7.2$  Hz, 3H);

$^{13}\text{C}$  NMR (125 MHz,  $\text{CDCl}_3$ ):  $\delta$  149.1, 147.5, 138.6, 138.1, 133.0, 129.3, 128.5, 128.4, 128.3, 127.9, 127.8, 127.7, 127.6, 123.5, 88.2.6, 88.2.3, 88.2.1, 87.6, 87.2.6, 87.1.0, 84.2.6, 82.8.1, 81.8.5, 81.1.9, 83.7;

IR (neat/ $\text{cm}^{-1}$ )  $\nu_{\text{max}}$ : 3088, 3065, 3030, 2971, 2933, 2917, 2874, 1606, 1598, 1520, 1497, 1454, 1345, 1255, 1206, 1107, 1086, 1062, 1028, 1014;

LCMS (ESI)  $m/z$  calcd for  $\text{C}_{29}\text{H}_{31}\text{NO}_4$  [ $\text{M}+\text{Na}]^+$ : 480.22, found: 480.23.



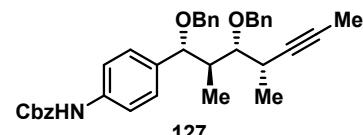
**4-((1*R*,2*R*,3*R*,4*S*)-1,3-bis(benzyloxy)-2,4-dimethylhept-5-yn-1-yl)aniline (124):** Prepared by *general procedure C* using **121** (1.5 g, 3.28 mmol). The crude material was purified with silica gel column chromatography using 20% ethyl acetate in Hexanes. **124** (346 mg, 2.66 mmol, 81% yield) obtained as pale yellow viscous oil.  $[\alpha]_D^{23.8} = -2.1$  ( $c = 2.7$ ,  $\text{CH}_2\text{Cl}_2$ ).

$^1\text{H}$  NMR (500 MHz,  $\text{CDCl}_3$ ):  $\delta$  7.35-7.25 (m, 10H), 7.10 (d,  $J = 8.3$  Hz, 2H), 86.72-6.65 (m, 2H), 84.65 (d,  $J = 1.6$  Hz, 2H), 84.35 (d,  $J = 11.7$  Hz, 1H), 84.21 (d,  $J = 11.6$  Hz, 1H), 83.82 (brs, 2H), 83.67 (dd,  $J = 7.8, 3.6$  Hz, 1H), 82.71-2.65 (m, 1H), 82.39-2.32 (m, 1H), 81.75 (d,  $J = 2.4$  Hz, 3H), 81.21 (d,  $J = 6.8$  Hz, 3H), 80.74 (d,  $J = 7.2$  Hz, 3H);

$^{13}\text{C}$  NMR (125 MHz,  $\text{CDCl}_3$ ):  $\delta$  145.6, 139.2, 139.0, 131.1, 128.9, 128.3, 128.2, 127.9, 127.7, 127.4, 127.2, 127.0, 115.0, 88.2.8, 88.2.7, 88.2.6, 87.2.3, 87.0.0, 84.2.7, 82.7.8, 81.8.5, 81.1.7, 83.7;

IR (neat/cm<sup>-1</sup>)  $\nu_{\text{max}}$ : 3376, 3087, 3062, 3029, 2971, 2932, 2916, 2873, 1612, 1586, 1515, 1496, 1453, 1377, 1367, 1348, 1312, 1276, 1207, 1175, 1087, 1062, 1027;

HRMS (ESI) *m/z* calcd for C<sub>29</sub>H<sub>33</sub>NO<sub>2</sub> [M+H]<sup>+</sup>: 428.2590, found: 428.2608.



**Benzyl (4-((1*R*,2*R*,3*R*,4*S*)-1,3-bis(benzyloxy)-2,4-dimethylhept-5-yn-1-yl)phenyl)carbamate (127):**

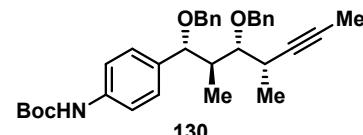
Prepared by *general procedure M* using **124** (530 mg, 1.24 mmol). The crude material was purified with silica gel column chromatography using 21% ethyl acetate in Hexanes. **127** (483 mg, 1.07 mmol, 86% yield) was obtained as colorless viscous oil.  $[\alpha]_D^{23.8} = +7.1$  (*c* = 3, CH<sub>2</sub>Cl<sub>2</sub>).

<sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>):  $\delta$  7.44-7.26 (m, 18H), 6.72 (s, 1H), 5.23 (s, 2H), 4.73 (d, *J* = 8.7 Hz, 1H), 4.68 (ABq, *J* = 11.6 Hz, 1H), 4.64 (ABq, *J* = 11.6 Hz, 1H), 4.36 (d, *J* = 11.6 Hz, 1H), 4.24 (d, *J* = 11.6 Hz, 1H), 3.66 (dd, *J* = 7.8, 3.6 Hz, 1H), 2.73-2.67 (m, 1H), 2.38 (ddq, *J* = 14.5, 7.2, 3.6 Hz, 1H), 1.77 (d, *J* = 2.4 Hz, 3H), 1.23 (d, *J* = 6.8 Hz, 3H), 0.75 (d, *J* = 7.2 Hz, 3H);

<sup>13</sup>C NMR (125 MHz, CDCl<sub>3</sub>):  $\delta$  153.4, 138.9, 137.1, 136.3, 136.1, 128.7, 128.5, 128.4, 128.4, 128.3, 128.3, 128.2, 127.9, 127.7, 127.4, 127.3, 118.5, 82.6, 82.5, 77.2, 72.4, 70.3, 67.1, 42.6, 27.9, 18.5, 11.7, 8.7;

IR (neat/cm<sup>-1</sup>)  $\nu_{\text{max}}$ : 3324, 3088, 3064, 3031, 2970, 2934, 2916, 2875, 1734, 1706, 1612, 1598, 1524, 1497, 1454, 1415, 1311, 1265, 1214, 1180, 1110, 1084, 1052, 1028, 1017;

HRMS (ESI) *m/z* calcd for C<sub>37</sub>H<sub>39</sub>NO<sub>4</sub> [M+Na]<sup>+</sup>: 584.2777, found: 584.2780.



**Tert-butyl (4-((1*R*,2*R*,3*R*,4*S*)-1,3-bis(benzyloxy)-2,4-dimethylhept-5-yn-1-yl)phenyl)carbamate (130):**

Prepared by *general procedure L* using **124** (530 mg, 1.24 mmol). The crude material was purified with silica gel column

chromatography using 18% ethyl acetate in Hexanes. **130** (641 mg, 1.22 mmol, 98% yield) was obtained as colorless viscous oil.  $[\alpha]_D^{23.8} = +16.2$  ( $c = 2.5$ ,  $\text{CH}_2\text{Cl}_2$ ).

$^1\text{H}$  NMR (500 MHz,  $\text{CDCl}_3$ ):  $\delta$  7.36-7.22 (m, 13H), 86.48 (s, 1H), 84.70 (d,  $J = 8.7$  Hz, 1H), 84.67 (ABq,  $J = 11.6$  Hz, 1H), 84.63 (d,  $J = 11.6$  Hz, 1H), 83.65 (dd,  $J = 7.7, 3.7$  Hz, 1H), 82.71-2.65 (m, 1H), 82.39-2.33 (m, 1H), 81.76 (d,  $J = 2.4$  Hz, 3H), 81.53 (s, 9H), 81.21 (d,  $J = 6.8$  Hz, 3H), 80.73 (d,  $J = 7.2$  Hz, 3H);

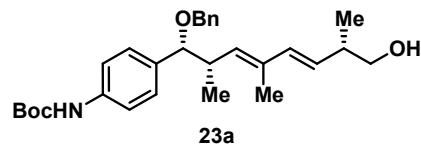
$^{13}\text{C}$  NMR (125 MHz,  $\text{CDCl}_3$ ):  $\delta$  152.8, 139.0, 137.7, 135.7, 128.5, 128.3, 128.2, 127.9, 127.7, 127.4, 127.3, 118.3, 882.7, 882.6, 880.5, 877.1, 872.4, 870.2, 842.6, 828.4, 827.8, 818.4, 811.7, 83.7;

IR (neat/ $\text{cm}^{-1}$ )  $\nu_{\text{max}}$ : 3331, 3063, 3031, 2975, 2931, 2917, 2876, 1728, 1705, 1613, 1596, 1521, 1497, 1454, 1413, 1392, 1367, 1311, 1229, 1155, 1087, 1052, 1027, 1016;

HRMS (ESI)  $m/z$  calcd for  $\text{C}_{34}\text{H}_{41}\text{NO}_4$  [ $\text{M}+\text{Na}]^+$ : 550.2933, found: 550.2934.

### 2.3. General Procedure O for Alkyne-Alkyne Reductive Coupling Using Carbamates

To a solution of internal alkyne (0.2 mmol, 1 equiv) in toluene (2.5 mL) at -78 °C was added sequentially  $\text{ClTi(OiPr)}_3$  (1.0 M in hexanes, 0.4 mL, 0.4 mmol, 2 equiv) and  $c\text{C}_5\text{H}_9\text{MgCl}$  (2.0 M in diethyl ether, 0.6 mL, 1.2 mmol, 6 equiv) in a dropwise manner. The resulting yellow solution turned brown while slowly warming to -40 °C over 45 minutes. The reaction mixture was placed in -40 °C chiller and stirred for 3 hours, while solution turned to be black and heterogenous. It was then cooled to -78 °C, to which terminal alkyne was added in dropwise. The resulting mixture was gradually warmed to -30 °C over 1 hour and 30 minutes and stirred for 12 hours at -30 °C. The reaction was quenched with saturated aqueous  $\text{NH}_4\text{Cl}$  solution (3 mL). It was then extract with ethyl acetate (3 x 10 mL). The combined organic layers were dried over  $\text{MgSO}_4$ , filtered, and concentrated. Purification over silica gel chromatography afforded coupled product **23-33**.



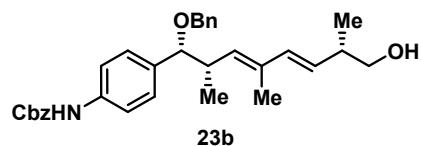
**Tert-butyl (4-((1R,2S,3E,5E,7S)-1-(benzyloxy)-8-hydroxy-2,4,7-trimethylocta-3,5-dien-1-yl)phenyl)carbamate (23a):** Prepared by *general procedure O* using **93** and **A3** (1.5 equiv). The crude material was purified with Preparative Thin Layer Chromatography using 10% ethyl acetate in Hexanes. The obtained TBS ether was treated with TBAF (1 M in THF, 2 equiv) in 1 mL THF at room temperature for 2 hours to afford alcohol **23a**. **23a** (60 mg, 0.13 mmol, 65% yield) was afforded as a pale yellow, viscous oil.  $[\alpha]_D^{23.8} = +4.5$  ( $c = 0.67$ ,  $\text{CH}_2\text{Cl}_2$ ).

$^1\text{H}$  NMR (500 MHz,  $\text{CDCl}_3$ ):  $\delta$  7.34-7.18 (m, 9H), 86.48 (s, 1H), 86.02 (d,  $J = 15.7$  Hz, 1H), 85.27 (dd,  $J = 15.7, 8.0$  Hz, 1H), 85.20 (d,  $J = 9.7$  Hz, 1H), 84.44 (d,  $J = 11.9$  Hz, 1H), 84.21 (d,  $J = 11.9$  Hz, 1H), 84.07 (d,  $J = 7.2$  Hz, 1H), 83.55-3.48 (m, 1H), 83.39-3.35 (m, 1H), 82.88-2.81 (m, 1H), 82.38-2.32 (m, 1H), 81.52 (s, 9H), 81.07 (dd,  $J = 6.6, 3.0$  Hz, 3H), 80.99 (dd,  $J = 6.8, 3.6$  Hz, 3H);

$^{13}\text{C}$  NMR (125 MHz,  $\text{CDCl}_3$ ):  $\delta$  152.8, 138.7, 137.5, 136.2, 135.5, 133.0, 129.2, 128.3, 128.1, 127.7, 127.4, 118.2, 84.8, 80.5, 80.5, 80.2, 87.5, 84.0, 83.9, 82.3, 81.7, 81.6, 81.2;

IR (neat/ $\text{cm}^{-1}$ )  $\nu_{\text{max}}$ : 3315, 2974, 2928, 2869, 1725, 1702, 1613, 1598, 1523, 1454, 1413, 1392, 1367, 1313, 1236, 1159, 1111, 1085, 1053, 1028, 1017;

HRMS (ESI)  $m/z$  calcd for  $\text{C}_{29}\text{H}_{39}\text{NO}_4$  [ $\text{M}+\text{Na}]^+$ : 488.2777, found: 488.2762.



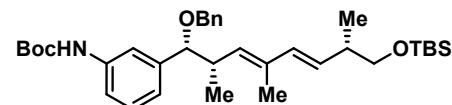
**Benzyl (4-((1R,2S,3E,5E,7S)-1-(benzyloxy)-8-hydroxy-2,4,7-trimethylocta-3,5-dien-1-yl)phenyl)carbamate (23b):** Prepared by *general procedure O* using **94** and **A3** (1.5 equiv). The crude material was purified with Preparative Thin Layer Chromatography using 10% ethyl acetate in Hexanes. The obtained TBS ether was treated with TBAF (1 M in THF, 2 equiv) in 1 mL THF at room temperature for 2 hours to afford alcohol **23b**. **23b** (61 mg, 0.122 mmol, 61% yield) was afforded as a pale yellow, viscous oil.  $[\alpha]_D^{23.8} = +3.6$  ( $c = 1.3$ ,  $\text{CH}_2\text{Cl}_2$ ).

<sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>): δ7.42-7.20 (m, 14H), δ6.73 (s, 1H), δ6.02 (d, *J* = 15.7 Hz, 1H), δ5.28 (dd, *J* = 15.7, 8.0 Hz, 1H), δ5.21 (s, 3H), δ4.45 (d, *J* = 11.9 Hz, 1H), δ4.22 (d, *J* = 11.9 Hz, 1H), δ4.08 (d, *J* = 7.1 Hz, 1H), δ3.51-3.47 (m, 1H), δ3.39-3.36 (m, 1H), δ2.88-2.81 (m, 1H), δ2.38-2.32 (m, 1H), δ1.49 (d, *J* = 1.1 Hz, 3H), δ1.08 (d, *J* = 6.7 Hz, 3H), δ0.99 (d, *J* = 6.8 Hz, 3H);

<sup>13</sup>C NMR (125 MHz, CDCl<sub>3</sub>): δ153.4, δ138.6, δ136.9, δ136.2, δ136.1, δ133.9, δ133.8, δ133.4, δ133.1, δ129.3, δ128.6, δ128.4, δ128.3, δ128.3, δ128.2, δ127.7, δ127.4, δ118.4, δ84.8, δ70.6, δ67.5, δ67.0, δ40.0, δ39.9, δ17.0, δ16.7, δ12.6;

IR (neat/cm<sup>-1</sup>)  $\nu_{\text{max}}$ : 3305, 3063, 3031, 2959, 2926, 2869, 1732, 1706, 1602, 1534, 1497, 1454, 1415, 1391, 1370, 1313, 1219, 1109, 1083, 1053, 1028, 1018;

HRMS (ESI) *m/z* calcd for C<sub>32</sub>H<sub>37</sub>NO<sub>4</sub> [M+Na]<sup>+</sup>: 522.2620, found: 522.2603.

**24a****Tert-butyl (3-((1*R*,2*S*,3*E*,5*E*,7*S*)-1-(benzyloxy)-8-((tert-butyldimethylsilyl)oxy)-2,4,7-**

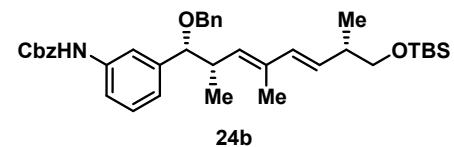
**trimethylocta-3,5-dien-1-ylphenyl)carbamate (24a):** Prepared by *general procedure O* using **91** and **A3** (1.5 equiv). The crude material was purified with Preparative Thin Layer Chromatography using 9.7% ethyl acetate in Hexanes. **24a** (72 mg, 0.124 mmol, 62% yield) was afforded as a pale yellow, viscous oil.  $[\alpha]_D^{23.8} = +0.67$  (*c* = 2.7, CH<sub>2</sub>Cl<sub>2</sub>).

<sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>): δ7.40 (d, *J* = 6.8 Hz, 1H), δ7.35-7.22 (m, 6H), δ7.16 -7.12 (m, 1H), δ6.96 (dd, *J* = 7.5, 4.1 Hz, 1H), δ6.44 (s, 1H), δ5.97 (d, *J* = 15.8 Hz, 1H), δ5.37 (ddd, *J* = 15.7, 7.3, 4.0 Hz, 1H), δ5.22 (d, *J* = 9.7 Hz, 1H), δ4.47 (d, *J* = 12.0 Hz, 1H), δ4.24 (d, *J* = 12.0 Hz, 1H), δ4.11 (d, *J* = 6.6 Hz, 1H), δ3.47 (dd, *J* = 9.7, 6.2 Hz, 1H), δ3.38 (dd, *J* = 9.7, 7.1 Hz, 1H), δ2.89-2.79 (m, 1H), δ2.35-2.29 (m, 1H), δ1.52 (s, 9H), δ1.51 (d, *J* = 1.2 Hz, 3H), δ1.06 (d, *J* = 6.7 Hz, 3H), δ0.98 (d, *J* = 6.7 Hz, 3H), δ0.88 (s, 9H), δ0.02 (d, *J* = 2.2 Hz, 5H);

<sup>13</sup>C NMR (125 MHz, CDCl<sub>3</sub>): δ152.7, δ142.0, δ138.8, δ138.1, δ134.4, δ133.4, δ133.0, δ130.2, δ128.7, δ128.2, δ127.5, δ127.3, δ122.2, δ117.4, δ85.1, δ70.7, δ68.3, δ39.8, δ39.5, δ28.4, δ25.9, δ18.4, δ16.8, δ16.7, δ12.5, δ-5.3, -5.3;

IR (neat/cm<sup>-1</sup>)  $\nu_{\text{max}}$ : 3332, 2956, 2928, 2856, 1731, 1702, 1610, 1594, 1528, 1491, 1472, 1454, 1440, 1391, 1367, 1249, 1231, 1157, 1085, 1068, 1028;

HRMS (ESI) *m/z* calcd for C<sub>35</sub>H<sub>53</sub>NO<sub>4</sub>Si [M+Na]<sup>+</sup>: 602.3642, found: 602.3641.



Benzyl

**(3-((1*R*,2*S*,3*E*,5*E*,7*S*)-1-(benzyloxy)-8-((tert-butyldimethylsilyl)oxy)-2,4,7-**

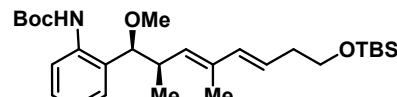
**trimethylocta-3,5-dien-1-ylphenyl)carbamate (24b):** Prepared by *general procedure O* using **92** and **A3** (1.5 equiv). The crude material was purified with Preparative Thin Layer Chromatography using 10% ethyl acetate in Hexanes. **24b** (64 mg, 0.104 mmol, 52% yield) was afforded as a pale yellow, viscous oil.  $[\alpha]_D^{23.8} = -0.95$  (*c* = 2.1, CH<sub>2</sub>Cl<sub>2</sub>).

<sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>): δ7.42-7.21 (m, 12H), δ6.99 (d, *J* = 7.6 Hz, 1H), δ6.65 (s, 1H), δ5.96 (d, *J* = 15.8 Hz, 1H), δ5.37 (ddd, *J* = 15.5, 7.3, 4.5 Hz, 1H), δ5.21 (s, 3H), δ4.47 (d, *J* = 11.9 Hz, 1H), δ4.24 (d, *J* = 11.9 Hz, 1H), δ4.11 (d, *J* = 6.7 Hz, 1H), δ3.48-3.45 (m, 1H), δ3.39-3.36 (m, 1H), δ2.88-2.80 (m, 1H), δ2.35-2.29 (m, 1H), δ1.49 (d, *J* = 1.1 Hz, 3H), δ1.06 (d, *J* = 6.7 Hz, 3H), δ0.98 (d, *J* = 6.7 Hz, 3H), δ0.88 (s, 9H), δ0.01 (d, *J* = 2.5 Hz, 6H);

<sup>13</sup>C NMR (125 MHz, CDCl<sub>3</sub>): δ153.3, δ142.2, δ138.7, δ137.6, δ136.1, δ134.4, δ133.5, δ132.9, δ130.2, δ128.6, δ128.3, δ128.3, δ127.6, δ122.7, δ117.6, δ85.1, δ70.8, δ68.3, δ67.0, δ39.8, δ39.5, δ25.9, δ18.4, δ16.8, δ16.7, δ12.5, δ-5.3;

IR (neat/cm<sup>-1</sup>)  $\nu_{\text{max}}$ : 3328, 3064, 3031, 2955, 2927, 2856, 1737, 1707, 1611, 1597, 1537, 1494, 1471, 1454, 1444, 1389, 1250, 1215, 1170, 1083, 1064, 1028;

HRMS (ESI) *m/z* calcd for C<sub>38</sub>H<sub>51</sub>NO<sub>4</sub>Si [M+Na]<sup>+</sup>: 636.3485, found: 636.3475.



**Tert-butyl (2-((1S,2R,3E,5E)-8-((tert-butyldimethylsilyl)oxy)-1-methoxy-2,4-dimethylocta-3,5-dien-1-yl)phenyl)carbamate (25a):**

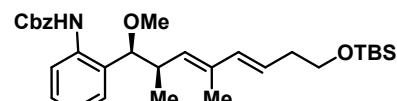
Prepared by *general procedure O* using **101** and **A2** (2 equiv). The crude material was purified with Preparative Thin Layer Chromatography using 100% dichloromethane. **25a** (45 mg, 0.092 mmol, 46% yield) was afforded as a pale yellow, viscous oil.  $[\alpha]_D^{23.8} = +38.5$  ( $c = 0.4$ ,  $\text{CH}_2\text{Cl}_2$ ).

$^1\text{H}$  NMR (500 MHz,  $\text{CDCl}_3$ ):  $\delta$  8.14 (s, 1H), 87.97 (d,  $J = 7.8$  Hz, 1H), 87.20 (dd,  $J = 8.5, 4.4$  Hz, 1H), 86.90 (d,  $J = 4.1$  Hz, 2H), 85.92 (d,  $J = 15.6$  Hz, 1H), 85.45-5.33 (m, 1H), 85.04 (d,  $J = 9.7$  Hz, 1H), 83.89 (d,  $J = 8.3$  Hz, 1H), 83.59 (t,  $J = 6.9$  Hz, 2H), 83.31-3.23 (m, 1H), 83.28 (s, 3H), 83.06-2.98 (m, 1H), 82.23 (dt,  $J = 6.9$  Hz, 2H), 81.51 (s, 9H), 81.36 (d,  $J = 1.1$  Hz, 3H), 81.11 (d,  $J = 6.6$  Hz, 3H), 80.87 (s, 9H), 80.02 (s, 6H);

$^{13}\text{C}$  NMR (125 MHz,  $\text{CDCl}_3$ ):  $\delta$  153.1, 137.3, 136.4, 134.2, 132.0, 130.1, 128.2, 124.3, 121.9, 120.4, 90.2, 879.9, 863.2, 857.2, 837.5, 836.5, 828.4, 825.9, 818.3, 817.8, 812.2, 85.2, 85.3;

IR (neat/ $\text{cm}^{-1}$ )  $\nu_{\text{max}}$ : 3361, 2955, 2929, 2857, 1731, 1590, 1519, 1446, 1391, 1366, 1303, 1250, 1231, 1158, 1094, 1076, 1045, 1024;

HRMS (ESI)  $m/z$  calcd for  $\text{C}_{28}\text{H}_{47}\text{NO}_4\text{Si}$  [ $\text{M}+\text{Na}]^+$ : 512.3172, found: 512.3182.



**Benzyl (2-((1S,2R,3E,5E)-8-((tert-butyldimethylsilyl)oxy)-1-methoxy-2,4-dimethylocta-3,5-dien-1-yl)phenyl)carbamate (25b):**

Prepared by *general procedure O* using **102** and **A2** (2 equiv). The crude material was purified with Preparative Thin Layer Chromatography using 72% dichloromethane in Hexanes. **25b** (50 mg, 0.096 mmol, 48% yield) was afforded as a pale yellow, viscous oil.  $[\alpha]_D^{23.8} = +66.2$  ( $c = 0.87$ ,  $\text{CH}_2\text{Cl}_2$ ).

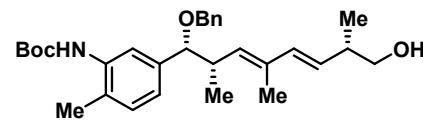
$^1\text{H}$  NMR (500 MHz,  $\text{CDCl}_3$ ):  $\delta$  88.54 (s, 1H), 88.02 (d,  $J = 7.0$  Hz, 1H), 87.43-7.31 (m, 5H), 87.25-7.21 (m, 1H), 86.95-6.89 (m, 2H), 85.91 (d,  $J = 15.6$  Hz, 1H), 85.43-5.33 (m, 1H), 85.23 (d,  $J = 12.4$  Hz, 1H), 85.17 (d,  $J = 12.4$  Hz, 1H), 85.02 (d,  $J = 9.9$  Hz, 1H),

$\delta$ 3.88 (d,  $J$  = 8.4 Hz, 1H),  $\delta$ 3.58 (t,  $J$  = 6.9 Hz, 2H),  $\delta$ 3.28 (s, 3H),  $\delta$ 3.04-2.96 (m, 1H),  $\delta$ 2.23 (dt,  $J$  = 6.9 Hz, 2H),  $\delta$ 1.28 (d,  $J$  = 1.1 Hz, 3H),  $\delta$ 1.10 (d,  $J$  = 6.6 Hz, 3H),  $\delta$ 0.88 (s, 9H),  $\delta$ 0.02 (s, 6H);

$^{13}\text{C}$  NMR (125 MHz,  $\text{CDCl}_3$ ):  $\delta$ 171.1,  $\delta$ 153.6,  $\delta$ 136.9,  $\delta$ 136.6,  $\delta$ 136.3,  $\delta$ 134.4,  $\delta$ 131.8,  $\delta$ 130.2,  $\delta$ 128.5,  $\delta$ 128.3,  $\delta$ 128.1,  $\delta$ 124.4,  $\delta$ 122.3,  $\delta$ 120.3,  $\delta$ 90.4,  $\delta$ 66.6,  $\delta$ 63.1,  $\delta$ 60.4,  $\delta$ 57.3,  $\delta$ 37.6,  $\delta$ 36.4,  $\delta$ 31.6,  $\delta$ 25.9,  $\delta$ 22.6,  $\delta$ 21.0,  $\delta$ 18.3,  $\delta$ 17.9,  $\delta$ 14.2,  $\delta$ 14.1,  $\delta$ 12.2,  $\delta$  -5.3;

IR (neat/ $\text{cm}^{-1}$ )  $\nu_{\text{max}}$ : 3342, 2953, 2928, 2856, 1736, 1591, 1523, 1449, 1303, 1255, 1213, 1187, 1096, 1076, 1050, 1041, 1029;

HRMS (ESI)  $m/z$  calcd for  $\text{C}_{31}\text{H}_{45}\text{NO}_4\text{Si} [\text{M}+\text{H}]^+$ : 524.3196, found: 524.3170.

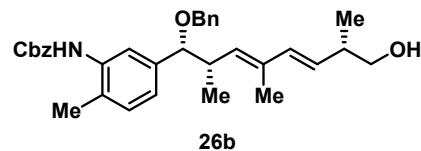


**Tert-butyl ((1R,2S,3E,5E,7S)-1-(benzyloxy)-8-hydroxy-2,4,7-trimethylocta-3,5-dien-1-yl)-2-methylphenyl)carbamate (26a):** Prepared by *general procedure O* using **95** and **A3** (1.5 equiv). The crude material was purified with Preparative Thin Layer Chromatography using 10% ethyl acetate in Hexanes. The obtained TBS ether was treated with TBAF (1 M in THF, 2 equiv) in 1 mL THF at room temperature for 2 hours to afford alcohol **26a**. **26a** (56 mg, 0.116 mmol, 58% yield) was afforded as a pale yellow, viscous oil.

$^1\text{H}$  NMR (500 MHz,  $\text{CDCl}_3$ ):  $\delta$ 7.66 (s, 1H),  $\delta$ 7.33-7.25 (m, 4H),  $\delta$ 7.10 (d,  $J$  = 7.8 Hz, 1H),  $\delta$ 6.97 (dd,  $J$  = 7.7, 1.3 Hz, 1H),  $\delta$ 6.25 (s, 1H),  $\delta$ 6.06 (d,  $J$  = 15.7 Hz, 1H),  $\delta$ 5.29 (d,  $J$  = 8.3 Hz, 1H),  $\delta$ 4.48 (d,  $J$  = 11.9 Hz, 1H),  $\delta$ 4.24 (d,  $J$  = 11.9 Hz, 1H),  $\delta$ 4.14 (d,  $J$  = 6.7 Hz, 1H),  $\delta$ 3.52-3.47 (m, 1H),  $\delta$ 3.38-3.35 (m, 1H),  $\delta$ 2.93-2.80 (m, 1H),  $\delta$ 2.38-2.33 (m, 1H),  $\delta$ 2.24 (s, 3H),  $\delta$ 1.54 (d,  $J$  = 5 Hz, 3H),  $\delta$ 1.52 (s, 9H),  $\delta$ 1.07 (d,  $J$  = 6.7 Hz, 3H),  $\delta$ 0.99 (d,  $J$  = 6.8 Hz, 3H);

$^{13}\text{C}$  NMR (125 MHz,  $\text{CDCl}_3$ ):  $\delta$ 153.0,  $\delta$ 139.6,  $\delta$ 138.9,  $\delta$ 136.4,  $\delta$ 135.9,  $\delta$ 134.3,  $\delta$ 134.2,  $\delta$ 133.3,  $\delta$ 132.8,  $\delta$ 130.1,  $\delta$ 129.0,  $\delta$ 128.2,  $\delta$ 127.6,  $\delta$ 127.3,  $\delta$ 122.5,  $\delta$ 85.0,  $\delta$ 80.3,  $\delta$ 70.6,  $\delta$ 67.5,  $\delta$ 40.0,  $\delta$ 39.8,  $\delta$ 28.4,  $\delta$ 17.6,  $\delta$ 17.5,  $\delta$ 16.8,  $\delta$ 16.7,  $\delta$ 12.6;

HRMS (ESI)  $m/z$  calcd for  $\text{C}_{30}\text{H}_{41}\text{NO}_4 [\text{M}+\text{Na}]^+$ : 502.2933, found: 502.2928.



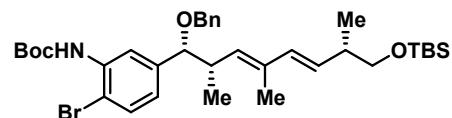
**Benzyl (5-((1*R*,2*S*,3*E*,5*E*,7*S*)-1-(benzyloxy)-8-hydroxy-2,4,7-trimethylocta-3,5-dien-1-yl)-2-methylphenyl)carbamate (26b):**

Prepared by *general procedure O* using **96** and **A3** (1.5 equiv). The crude material was purified with Preparative Thin Layer Chromatography using 10% ethyl acetate in Hexanes. The obtained TBS ether was treated with TBAF (1 M in THF, 2 equiv) in 1 mL THF at room temperature for 2 hours to afford alcohol **26b**. **26b** (51 mg, 0.1 mmol, 50% yield) was afforded as a pale yellow, viscous oil.

<sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>): δ7.65 (s, 1H), δ7.43-7.26 (m, 8H), δ7.11 (d, *J* = 7.6 Hz, 1H), δ7.02 (dd, *J* = 7.8, 1.5 Hz, 1H), δ6.45 (s, 1H), δ6.06 (d, *J* = 15.7 Hz, 1H), δ5.22-5.21 (m, 2H), δ4.48 (d, *J* = 11.9 Hz, 1H), δ4.23 (d, *J* = 11.9 Hz, 1H), δ4.10 (d, *J* = 6.9 Hz, 1H), δ3.52-3.47 (m, 1H), δ3.36-3.31 (m, 1H), δ2.88-2.81 (m, 1H), δ2.38-2.32 (m, 1H), δ2.23 (s, 3H), δ1.57 (s, 3H), δ1.08 (d, *J* = 6.7 Hz, 3H), δ0.98 (d, *J* = 6.8 Hz, 3H);

<sup>13</sup>C NMR (125 MHz, CDCl<sub>3</sub>): δ139.8, δ138.8, δ136.5, δ136.1, δ135.3, δ133.1, δ130.1, δ128.6, δ128.4, δ128.4, δ128.2, δ127.6, δ127.3, δ85.0, δ70.6, δ67.4, δ67.1, δ40.1, δ39.9, δ17.5, δ17.0, δ16.7, δ12.6;

HRMS (ESI) *m/z* calcd for C<sub>33</sub>H<sub>39</sub>NO<sub>4</sub> [M+Na]<sup>+</sup>: 536.2777, found: 536.2766.



**Tert-butyl (5-((1*R*,2*S*,3*E*,5*E*,7*S*)-1-(benzyloxy)-8-((tert-butyldimethylsilyl)oxy)-2,4,7-trimethylocta-3,5-dien-1-yl)-2-bromophenyl)carbamate (27a):**

Prepared by *general procedure O* using **97** and **A3** (1.5 equiv). The crude material was purified with Preparative Thin Layer Chromatography using 40% dichloromethane in Hexanes. **27a** (76 mg, 0.116 mmol, 58% yield) was afforded as a pale yellow, viscous oil. [α]<sub>D</sub><sup>23.8</sup> = +2.8 (*c* = 2, CH<sub>2</sub>Cl<sub>2</sub>).

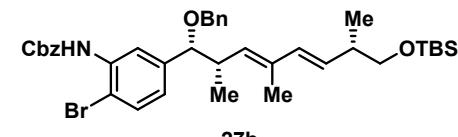
<sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>): δ8.07 (s, 1H), δ7.43 (d, *J* = 8.2 Hz, 1H), δ7.33-7.31 (m, 4H), δ6.97 (s, 1H), δ6.88 (dd, *J* = 8.2, 2.0 Hz, 1H), δ5.97 (d, *J* = 15.8 Hz, 1H), δ5.38 (dd, *J* = 15.7, 7.4 Hz, 1H), δ5.21 (d, *J* = 9.4 Hz, 1H), δ4.46 (d, *J* = 11.8 Hz, 1H), δ3.47 (dd, *J* =

9.7, 6.3 Hz, 1H), δ3.38 (dd,  $J$  = 9.7, 7.0 Hz, 1H), δ2.90-2.83 (m, 1H), δ2.35-2.29 (m, 1H), δ1.55 (d,  $J$  = 15 Hz, 3H), δ1.54 (s, 9H), δ1.07 (d,  $J$  = 6.7 Hz, 3H), δ0.98 (d,  $J$  = 6.7 Hz, 3H), δ0.88 (s, 9H), δ0.01 (d,  $J$  = 3.4 Hz, 6H);

$^{13}\text{C}$  NMR (125 MHz,  $\text{CDCl}_3$ ): δ152.2, δ141.8, δ138.6, δ135.8, δ134.4, δ133.5, δ132.7, δ131.8, δ130.3, δ128.2, δ127.7, δ127.4, δ122.6, δ119.4, δ110.9, δ85.0, δ81.0, δ70.8, δ68.3, δ39.6, δ39.5, δ28.3, δ25.9, δ18.3, δ17.0, δ16.7, δ12.6, δ -5.3, δ -5.4;

IR (neat/ $\text{cm}^{-1}$ )  $\nu_{\text{max}}$ : 3417, 2956, 2928, 2856, 1737, 1583, 1517, 1472, 1447, 1426, 1392, 1368, 1341, 1248, 1223, 1154, 1086, 1072, 1059, 1028, 1018, 1006;

HRMS (ESI)  $m/z$  calcd for  $\text{C}_{35}\text{H}_{52}\text{BrNO}_4\text{Si} [\text{M}+\text{Na}]^+$ : 680.2747, found: 680.2750.

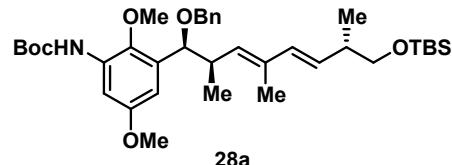


**Benzyl (5-((1*R*,2*S*,3*E*,5*E*,7*S*)-1-(benzyloxy)-8-((*tert*-butyldimethylsilyl)oxy)-2,4,7-trimethylocta-3,5-dien-1-yl)-2-bromophenyl)carbamate (27b):** Prepared by *general procedure O* using **98** and **A3** (1.5 equiv). The crude material was purified with Preparative Thin Layer Chromatography using 40% dichloromethane in Hexanes. **27b** (76 mg, 0.116 mmol, 58% yield) was afforded as a pale yellow, viscous oil.

$^1\text{H}$  NMR (500 MHz,  $\text{CDCl}_3$ ): δ8.11 (s, 1H), δ7.45-7.27 (m, 10H), δ7.18 (s, 1H), δ6.90 (dd,  $J$  = 8.2, 1.9 Hz, 1H), δ5.96 (d,  $J$  = 15.7 Hz, 1H), δ5.38 (dd,  $J$  = 15.8, 7.3 Hz, 1H), δ5.23 (d,  $J$  = 1.7 Hz, 2H), δ5.19 (d,  $J$  = 9.6 Hz, 1H), δ4.46 (d,  $J$  = 11.9 Hz, 1H), δ4.23 (d,  $J$  = 11.8 Hz, 1H), δ4.11 (d,  $J$  = 6.9 Hz, 1H), δ3.47 (dd,  $J$  = 9.7, 6.3 Hz, 1H), δ3.38 (dd,  $J$  = 9.7, 7.0 Hz, 1H), δ2.91-2.82 (m, 1H), δ2.36-2.29 (m, 1H), δ1.53 (s, 3H), δ1.07 (d,  $J$  = 6.6 Hz, 3H), δ0.98 (d,  $J$  = 6.7 Hz, 3H), δ0.89 (d,  $J$  = 7.4 Hz, 3H), δ0.87 (s, 9H), δ0.00 (d,  $J$  = 2.9 Hz, 6H);

$^{13}\text{C}$  NMR (125 MHz,  $\text{CDCl}_3$ ): δ153.0, δ142.0, δ138.5, δ135.8, δ135.4, δ134.4, δ134.1, δ133.6, δ132.7, δ132.6, δ131.9, δ131.9, δ130.4, δ128.7, δ128.5, δ128.3, δ127.7, δ127.4, δ123.3, δ119.6, δ111.2, δ84.9, δ70.8, δ68.3, δ67.3, δ39.7, δ25.9, δ18.4, δ16.9, δ16.9, δ16.7, δ12.6, δ -5.3;

HRMS (ESI)  $m/z$  calcd for  $\text{C}_{38}\text{H}_{50}\text{BrNO}_4\text{Si} [\text{M}+\text{Na}]^+$ : 714.2590, found: 714.2613.



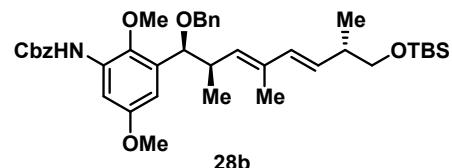
**Tert-butyl (3-((1S,2R,3E,5E,7S)-1-(benzyloxy)-8-((tert-butyldimethylsilyl)oxy)-2,4,7-trimethylocta-3,5-dien-1-yl)-2,5-dimethoxyphenyl)carbamate (28a):** Prepared by *general procedure O* using **103** and **A3** (1.5 equiv). The crude material was purified with Preparative Thin Layer Chromatography using 10% ethyl acetate in Hexanes. **28a** (84 mg, 0.132 mmol, 66% yield) was afforded as a pale yellow, viscous oil.  $[\alpha]_D^{23.8} = +2.5$  ( $c = 4.3$ ,  $\text{CH}_2\text{Cl}_2$ ).

$^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ ):  $\delta$  7.64 (s, 1H), 7.32-7.24 (m, 5H), 6.92 (s, 1H), 6.66 (d,  $J = 3.0$  Hz, 1H), 5.99 (d,  $J = 15.7$  Hz, 1H), 5.42-5.32 (m, 2H), 4.51-4.46 (m, 2H), 4.28 (d,  $J = 11.9$  Hz, 1H), 3.78 (s, 3H), 3.61 (s, 3H), 3.49 (dd,  $J = 9.7, 6.0$  Hz, 1H), 3.37 (dd,  $J = 9.7, 7.4$  Hz, 1H), 2.92-2.82 (m, 1H), 2.39-2.30 (m, 1H), 1.55 (d,  $J = 7.8$  Hz, 3H), 1.53 (s, 9H), 1.04 (d,  $J = 6.6$  Hz, 3H), 1.00 (d,  $J = 6.7$  Hz, 3H), 0.88 (s, 9H), 0.02 (s, 6H);

$^{13}\text{C}$  NMR (125 MHz,  $\text{CDCl}_3$ ):  $\delta$  156.3, 152.7, 140.5, 138.6, 134.5, 134.3, 133.1, 132.3, 130.2, 128.3, 127.6, 127.4, 106.9, 103.6, 80.6, 79.1, 70.8, 68.3, 61.2, 61.1, 55.6, 55.6, 39.6, 38.9, 28.3, 25.9, 25.9, 18.3, 16.9, 16.8, 16.1, 16.1, 12.4, 5.3, 5.3;

IR (neat/ $\text{cm}^{-1}$ )  $\nu_{\text{max}}$ : 3435, 2955, 2930, 2856, 1731, 1601, 1517, 1455, 1419, 1392, 1367, 1349, 1279, 1249, 1236, 1222, 1203, 1147, 1086, 1068, 1052, 1028;

HRMS (ESI)  $m/z$  calcd for  $\text{C}_{37}\text{H}_{57}\text{NO}_6\text{Si} [\text{M}+\text{Na}]^+$ : 662.3853, found: 662.3867.



**Benzyl (3-((1S,2R,3E,5E,7S)-1-(benzyloxy)-8-((tert-butyldimethylsilyl)oxy)-2,4,7-trimethylocta-3,5-dien-1-yl)-2,5-dimethoxyphenyl)carbamate (28b):** Prepared by *general procedure O* using **104** and **A3** (1.5

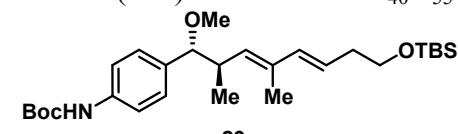
equiv). The crude material was purified with Preparative Thin Layer Chromatography using 12% ethyl acetate in Hexanes. **28b** (85 mg, 0.126 mmol, 63% yield) was afforded as a pale yellow, viscous oil.  $[\alpha]_D^{23.8} = +2.1$  ( $c = 2.1$ ,  $\text{CH}_2\text{Cl}_2$ ).

$^1\text{H}$  NMR (500 MHz,  $\text{CDCl}_3$ ):  $\delta$  7.67 (s, 1H), 7.43-7.24 (m, 10H), 7.14 (s, 1H), 6.69 (d,  $J = 3.1$  Hz, 1H), 5.98 (d,  $J = 15.7$  Hz, 1H), 5.39 (dd,  $J = 15.7$ , 7.5 Hz, 1H), 5.32 (d,  $J = 9.6$  Hz, 1H), 5.22 (s, 3H), 4.51-4.49 (m, 2H), 4.28 (d,  $J = 11.9$  Hz, 1H), 3.78 (s, 3H), 3.76 (d,  $J = 9.5$  Hz, 1H), 3.61 (d,  $J = 9.0$  Hz, 1H), 3.59 (s, 3H), 3.49 (dd,  $J = 9.7$ , 6.1 Hz, 1H), 3.37 (dd,  $J = 9.7$ , 7.3 Hz, 1H), 2.90-2.83 (m, 1H), 2.37-2.30 (m, 1H), 1.54 (s, 3H), 1.04 (d,  $J = 6.7$  Hz, 3H), 1.00 (d,  $J = 6.7$  Hz, 3H), 0.88 (s, 9H), 0.02 (d,  $J = 0.9$  Hz, 6H);

$^{13}\text{C}$  NMR (125 MHz,  $\text{CDCl}_3$ ):  $\delta$  156.3, 153.2, 140.7, 138.5, 136.0, 134.5, 133.5, 133.1, 131.8, 130.2, 128.7, 128.4, 128.3, 127.6, 127.4, 107.3, 103.8, 879.1, 868.3, 867.1, 861.2, 855.6, 839.6, 838.9, 826.0, 818.3, 812.4, 8-5.3.

IR (neat/ $\text{cm}^{-1}$ )  $\nu_{\text{max}}$ : 3429, 2955, 2928, 2856, 1737, 1599, 1521, 1498, 1462, 1454, 1422, 1389, 1348, 1250, 1233, 1213, 1192, 1084, 1068, 1052, 1028;

HRMS (ESI)  $m/z$  calcd for  $\text{C}_{40}\text{H}_{55}\text{NO}_6\text{Si} [\text{M}+\text{Na}]^+$ : 696.3696, found: 696.3708.



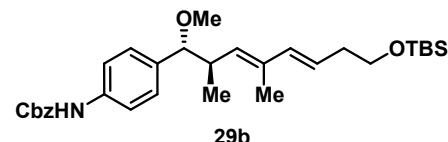
**Tert-butyl (4-((1*R*,2*R*,3*E*,5*E*)-8-((*tert*-butyldimethylsilyl)oxy)-1-methoxy-2,4-dimethylocta-3,5-dien-1-yl)phenyl)carbamate (29a):** Prepared by *general procedure O* using **116** and **A2** (2.5 equiv). The crude material was purified with Preparative Thin Layer Chromatography using 100% dichloromethane. **29a** (47 mg, 0.096 mmol, 48% yield) was afforded as a pale yellow, viscous oil.  $[\alpha]_D^{23.8} = +37.4$  ( $c = 0.53$ ,  $\text{CH}_2\text{Cl}_2$ ).

$^1\text{H}$  NMR (500 MHz,  $\text{CDCl}_3$ ):  $\delta$  7.31 (d,  $J = 8.3$  Hz, 2H), 7.16 (d,  $J = 8.5$  Hz, 2H), 6.46 (s, 1H), 6.10 (d,  $J = 15.6$  Hz, 1H), 5.57-5.47 (m, 1H), 5.25 (d,  $J = 9.4$  Hz, 1H), 3.91 (d,  $J = 6.5$  Hz, 1H), 3.64 (t,  $J = 7.0$  Hz, 2H), 3.16 (s, 3H), 2.80 (dq,  $J = 9.3$ , 6.7, 6.0 Hz, 1H), 2.31 (dt,  $J = 7.1$  Hz, 2H), 1.62 (d,  $J = 1.1$  Hz, 3H), 1.52 (d,  $J = 2.6$  Hz, 9H), 0.90 (s, 9H), 0.82 (d,  $J = 6.8$  Hz, 3H), 0.05 (s, 6H);

<sup>13</sup>C NMR (125 MHz, CDCl<sub>3</sub>): δ152.8, δ137.5, δ136.8, δ135.2, δ133.7, δ133.5, δ128.1, δ123.7, δ118.1, δ87.9, δ63.3, δ56.9, δ39.3, δ36.5, δ28.3, δ26.0, δ18.4, δ17.1, δ12.6, δ-5.2;

IR (neat/cm<sup>-1</sup>)  $\nu_{\text{max}}$ : 3324, 2955, 2928, 2856, 2821, 1730, 1705, 1614, 1597, 1523, 1472, 1463, 1411, 1391, 1367, 1313, 1250, 1231, 1158, 1093, 1051, 1027;

HRMS (ESI) *m/z* calcd for C<sub>28</sub>H<sub>47</sub>NO<sub>4</sub>Si [M+Na]<sup>+</sup>: 512.3172, found: 512.3167.



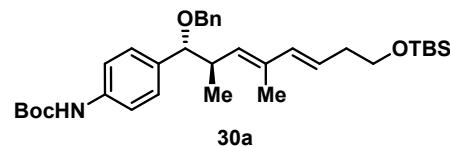
**Benzyl ((4-((1*R*,2*R*,3*E*,5*E*)-8-((tert-butyldimethylsilyl)oxy)-1-methoxy-2,4-dimethylocta-3,5-dien-1-yl)phenyl)carbamate (29b):** Prepared by *general procedure O* using **115** and **A2** (2.0 equiv). The crude material was purified with Preparative Thin Layer Chromatography using 80% dichloromethane in Hexanes. **29b** (49 mg, 0.094 mmol, 47% yield) was afforded as a pale yellow, viscous oil.  $[\alpha]_D^{23.8} = +34.2$  (*c* = 1.3, CH<sub>2</sub>Cl<sub>2</sub>).

<sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>): δ7.42-7.32 (m, 7H), δ7.18 (d, *J* = 8.5 Hz, 2H), δ6.68 (s, 1H), δ6.10 (d, *J* = 15.7 Hz, 1H), δ5.52 (dt, *J* = 14.5 Hz, 1H), δ5.25 (d, *J* = 9.4 Hz, 1H), δ5.21 (s, 3H), δ3.92 (d, *J* = 6.5 Hz, 1H), δ3.64 (t, *J* = 6.9 Hz, 2H), δ3.16 (s, 3H), δ2.80 (dq, *J* = 9.3 Hz, 2.5 Hz, 1H), δ2.31 (q, *J* = 6.9 Hz, 2H), δ1.61 (d, *J* = 1.1 Hz, 3H), δ0.90 (s, 9H), δ0.83 (d, *J* = 6.8 Hz, 3H), δ0.05 (s, 6H);

<sup>13</sup>C NMR (125 MHz, CDCl<sub>3</sub>): δ153.3, δ137.0, δ136.7, δ136.1, δ135.8, δ133.7, δ133.4, δ128.6, δ128.4, δ128.3, δ128.2, δ123.7, δ118.3, δ87.9, δ67.0, δ63.3, δ56.9, δ39.3, δ36.5, δ26.0, δ18.4, δ17.1, δ12.6, δ-5.2;

IR (neat/cm<sup>-1</sup>)  $\nu_{\text{max}}$ : 3311, 2954, 2927, 2895, 2856, 2821, 1736, 1707, 1613, 1600, 1532, 1471, 1462, 1455, 1414, 1389, 1373, 1312, 1251, 1215, 1083, 1050, 1029;

HRMS (ESI) *m/z* calcd for C<sub>31</sub>H<sub>45</sub>NO<sub>4</sub>Si [M+Na]<sup>+</sup>: 546.3016, found: 546.3004.



**Tert-butyl (4-((1R,2R,3E,5E)-1-(benzyloxy)-8-((tert-butyldimethylsilyl)oxy)-2,4-dimethylocta-3,5-dien-1-yl)phenyl)carbamate (30a):**

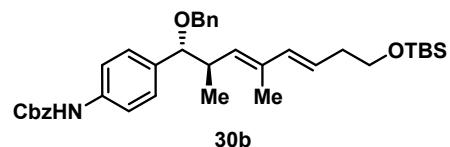
Prepared by *general procedure O* using **114** and **A2** (1.0 equiv) and stirred for 4 hours. The crude material was purified with Preparative Thin Layer Chromatography using 12% ethyl acetate in Hexanes. **30a** (63 mg, 0.112 mmol, 56% yield) was afforded as a pale yellow, viscous oil.  $[\alpha]_D^{23.8} = +33.1$  ( $c = 1.3$ ,  $\text{CH}_2\text{Cl}_2$ ).

$^1\text{H}$  NMR (500 MHz,  $\text{CDCl}_3$ ):  $\delta$  7.34-7.20 (m, 9H), 86.48 (s, 1H), 86.10 (dd,  $J = 15.7, 0.6$  Hz, 1H), 85.57-5.49 (m, 1H), 85.25 (d,  $J = 9.5$  Hz, 1H), 84.45 (d,  $J = 12.2$  Hz, 1H), 84.19 (d,  $J = 12.2$  Hz, 1H), 84.09 (d,  $J = 6.4$  Hz, 1H), 83.66 (t,  $J = 6.9$  Hz, 2H), 82.88-2.81 (m, 1H), 82.32 (td,  $J = 6.95, 6.8$  Hz, 2H), 81.61 (d,  $J = 1.1$  Hz, 3H), 81.53 (s, 9H), 80.90 (s, 9H), 80.84 (d,  $J = 6.8$  Hz, 3H), 80.06 (s, 6H);

$^{13}\text{C}$  NMR (125 MHz,  $\text{CDCl}_3$ ):  $\delta$  152.8, 138.8, 137.6, 136.8, 135.3, 133.7, 133.6, 128.3, 128.3, 128.2, 127.6, 127.5, 127.3, 123.6, 118.2, 84.9, 80.5, 70.2, 63.4, 39.4, 38.2, 36.5, 28.4, 26.0, 17.2, 12.7, 8 -5.2;

IR (neat/ $\text{cm}^{-1}$ )  $\nu_{\text{max}}$ : 3325, 2956, 2928, 2856, 1730, 1703, 1614, 1596, 1522, 1472, 1454, 1413, 1391, 1367, 1312, 1249, 1231, 1157, 1089, 1070, 1052, 1028, 1016;

HRMS (ESI)  $m/z$  calcd for  $\text{C}_{34}\text{H}_{51}\text{NO}_4\text{Si}$  [ $\text{M}+\text{Na}]^+$ : 588.3458, found: 588.3469.



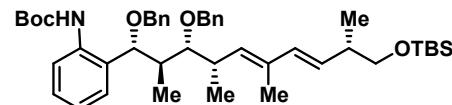
**Benzyl (4-((1R,2R,3E,5E)-1-(benzyloxy)-8-((tert-butyldimethylsilyl)oxy)-2,4-dimethylocta-3,5-dien-1-yl)phenyl)carbamate (30b):** Prepared by *general procedure O* using **113** and **A2** (1.0 equiv) and stirred for 12 hours. The crude material was purified with Preparative Thin Layer Chromatography using 15% ethyl acetate in Hexanes. **30b** (61 mg, 0.102 mmol, 51% yield) was afforded as a pale yellow, viscous oil.  $[\alpha]_D^{23.8} = +25.5$  ( $c = 0.4$ ,  $\text{CH}_2\text{Cl}_2$ ).

<sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>): δ7.43-7.21 (m, 14H), δ6.67 (s, 1H), δ6.10 (d, *J* = 15.7 Hz, 1H), δ5.57-5.48 (m, 1H), δ5.24 (d, *J* = 9.5 Hz, 1H), δ5.21 (s, 2H), δ4.45 (d, *J* = 12.2 Hz, 1H), δ4.19 (d, *J* = 12.2 Hz, 1H), δ4.10 (d, *J* = 6.3 Hz, 1H), δ3.65 (t, *J* = 6.9 Hz, 2H), δ2.87-2.80 (m, 1H), δ2.32 (td, *J* = 6.9 Hz, 2H), δ1.56 (s, 3H), δ0.90 (s, 9H), δ0.84 (d, *J* = 6.8 Hz, 3H), δ0.06 (s, 6H);

<sup>13</sup>C NMR (125 MHz, CDCl<sub>3</sub>): δ153.3, δ138.8, δ136.8, δ133.7, δ133.5, δ128.6, δ128.4, δ128.3, δ128.3, δ128.2, δ127.6, δ127.3, δ123.7, δ118.3, δ84.8, δ70.3, δ67.0, δ63.3, δ39.4, δ36.5, δ26.0, δ18.4, δ17.2, δ12.7, δ -5.2;

IR (neat/cm<sup>-1</sup>)  $\nu_{\text{max}}$ : 3322, 3064, 3031, 2955, 2927, 2856, 1737, 1707, 1613, 1600, 1528, 1497, 1471, 1462, 1454, 1415, 1389, 1313, 1251, 1216, 1087, 1066, 1056, 1028;

HRMS (ESI) *m/z* calcd for C<sub>37</sub>H<sub>49</sub>NO<sub>4</sub>Si [M+Na]<sup>+</sup>: 622.3329, found: 622.3333.



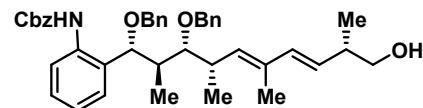
**Tert-butyl (2-((1*R*,2*R*,3*R*,4*S*,5*E*,7*E*,9*S*)-1,3-bis(benzyloxy)-10-((tert-butyldimethylsilyl)oxy)-2,4,6,9-tetramethyldeca-5,7-dien-1-yl)phenyl)carbamate (31a):** Prepared by *general procedure O* using **128** and **A3** (2 equiv). The crude material was purified with Preparative Thin Layer Chromatography using 100% dichloromethane. **31a** (74 mg, 0.102 mmol, 51% yield) was afforded as a pale yellow, viscous oil.  $[\alpha]_D^{23.8} = +37.6$  (*c* = 0.33, CH<sub>2</sub>Cl<sub>2</sub>).

<sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>): δ8.56 (s, 1H), δ8.09 (d, *J* = 8.0 Hz, 1H), δ7.39-7.26 (m, 10H), δ6.93 (td, *J* = 7.4, 1.1 Hz, 1H), δ6.83 (d, *J* = 7.6 Hz, 1H), δ5.85 (d, *J* = 15.7 Hz, 1H), δ5.51 (dd, *J* = 15.7, 7.4 Hz, 1H), δ4.92 (d, *J* = 10.4 Hz, 1H), δ4.65 (d, *J* = 11.4 Hz, 1H), δ4.48 (d, *J* = 11.5 Hz, 1H), δ4.46 (d, *J* = 11.8 Hz, 1H), δ4.26 (d, *J* = 10.4 Hz, 1H), δ4.19 (d, *J* = 11.5 Hz, 1H), δ3.68 (dd, *J* = 9.5, 1.9 Hz, 1H), δ3.54 (dd, *J* = 9.7, 6.0 Hz, 1H), δ3.41 (dd, *J* = 9.7, 7.3 Hz, 1H), δ2.80-2.74 (m, 1H), δ2.65-2.58 (m, 1H), δ2.40-2.34 (m, 1H), δ1.70 (d, *J* = 0.9 Hz, 3H), δ1.44 (s, 9H), δ1.02 (d, *J* = 6.7 Hz, 3H), δ0.94 (d, *J* = 6.5 Hz, 3H), δ0.90 (s, 9H), δ0.61 (d, *J* = 7.1 Hz, 3H), δ0.05 (s, 6H);

<sup>13</sup>C NMR (125 MHz, CDCl<sub>3</sub>): δ152.9, δ138.5, δ137.6, δ137.5, δ134.2, δ133.9, δ131.9, δ130.7, δ130.5, δ128.7, δ128.5, δ128.4, δ128.3, δ128.0, δ127.8, δ127.6, δ122.0, δ85.1, δ81.7, δ79.9, δ71.9, δ70.4, δ68.4, δ39.6, δ38.7, δ35.2, δ28.4, δ26.0, δ18.8, δ18.4, δ16.8, δ12.7, δ12.3, δ-5.3;

IR (neat/cm<sup>-1</sup>)  $\nu_{\text{max}}$ : 3355, 3064, 3031, 2956, 2928, 2857, 1732, 1590, 1524, 1447, 1391, 1366, 1305, 1250, 1231, 1158, 1085, 1067, 1049, 1027;

HRMS (ESI)  $m/z$  calcd for C<sub>45</sub>H<sub>65</sub>NO<sub>5</sub>Si [M+Na]<sup>+</sup>: 750.4530, found: 750.4495.

**31b****Benzyl (2-((1*R*,2*R*,3*R*,4*S*,5*E*,7*E*,9*S*)-1,3-bis(benzyloxy)-10-hydroxy-2,4,6,9-tetramethyldeca-5,7-dien-1-yl)phenyl)carbamate (31b):**

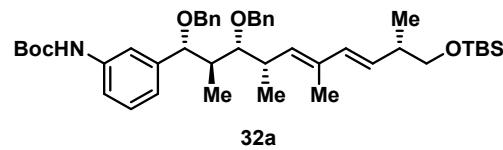
Prepared by *general procedure O* using **125** and **A3** (2 equiv). The crude material was purified with Preparative Thin Layer Chromatography using 10% ethyl acetate in Hexanes. The obtained TBS ether was treated with TBAF (1 M in THF, 2 equiv) in 1 mL THF at room temperature for 2 hours to afford alcohol **31b** (it was purified using 10% ethyl acetate in Hexanes). **31b** (58 mg, 0.09 mmol, 45% yield) was afforded as a pale yellow, viscous oil.  $[\alpha]_D^{23.8} = +31.7$  ( $c = 2.1$ , CH<sub>2</sub>Cl<sub>2</sub>).

<sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>):  $\delta$  8.74 (s, 1H), 8.10 (s, 1H), 7.36-7.25 (m, 15H), 6.99 (t,  $J = 7.0$  Hz, 1H), 6.85 (d,  $J = 7.2$  Hz, 1H), 5.89 (d,  $J = 15.7$  Hz, 1H), 5.39 (dd,  $J = 15.7, 7.9$  Hz, 1H), 5.21 (d,  $J = 12.4$  Hz, 1H), 5.11 (d,  $J = 12.4$  Hz, 1H), 4.91 (d,  $J = 10.5$  Hz, 1H), 4.59 (d,  $J = 11.5$  Hz, 1H), 4.46 (d,  $J = 11.7$  Hz, 1H), 4.44 (d,  $J = 11.6$  Hz, 1H), 4.31 (d,  $J = 10.3$  Hz, 1H), 4.19 (d,  $J = 11.6$  Hz, 1H), 3.61 (dd,  $J = 9.3, 1.8$  Hz, 1H), 3.56-3.49 (m, 1H), 3.46-3.42 (m, 1H), 2.85-2.76 (m, 1H), 2.61-2.54 (m, 1H), 2.42-2.37 (m, 1H), 1.67 (d,  $J = 0.9$  Hz, 3H), 1.03 (d,  $J = 6.8$  Hz, 3H), 0.96 (d,  $J = 6.5$  Hz, 3H), 0.59 (d,  $J = 7.2$  Hz, 3H);

<sup>13</sup>C NMR (125 MHz, CDCl<sub>3</sub>):  $\delta$  153.5, 138.6, 137.4, 137.0, 136.3, 135.9, 134.8, 131.7, 130.4, 129.8, 128.8, 128.5, 128.3, 128.3, 128.2, 128.1, 128.0, 128.0, 127.5, 122.7, 120.4, 84.5, 82.3, 72.3, 70.5, 67.5, 66.7, 39.9, 39.0, 35.5, 18.7, 16.7, 12.7;

IR (neat/cm<sup>-1</sup>)  $\nu_{\text{max}}$ : 3336, 3030, 2960, 2926, 2868, 1735, 1591, 1526, 1449, 1390, 1368, 1305, 1214, 1082, 1039, 1027;

HRMS (ESI)  $m/z$  calcd for C<sub>42</sub>H<sub>49</sub>NO<sub>5</sub> [M+Na]<sup>+</sup>: 670.3508, found: 670.3494.

**Tert-butyl****(3-((1R,2R,3R,4S,5E,7E,9S)-1,3-bis(benzyloxy)-10-((tert-**

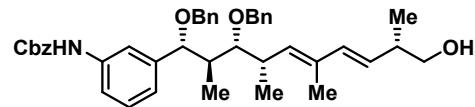
**butyldimethylsilyl)oxy)-2,4,6,9-tetramethyldeca-5,7-dien-1-yl)phenyl)carbamate (32a):** Prepared by *general procedure O* using **129** and **A3** (2 equiv). The crude material was purified with Preparative Thin Layer Chromatography using 100% dichloromethane. **32a** (87 mg, 0.12 mmol, 60% yield) was afforded as a pale yellow, viscous oil.  $[\alpha]_D^{23.8} = +13.6$  ( $c = 0.87$ ,  $\text{CH}_2\text{Cl}_2$ ).

$^1\text{H}$  NMR (500 MHz,  $\text{CDCl}_3$ ):  $\delta$  7.50 (s, 1H), 7.38-7.23 (m, 10H), 7.03 (s, 1H), 86.89 (d,  $J = 7.6$  Hz, 1H), 86.45 (s, 1H), 85.90 (d,  $J = 15.8$  Hz, 1H), 85.49 (dd,  $J = 15.7, 7.4$  Hz, 1H), 85.10 (d,  $J = 10.3$  Hz, 1H), 84.65 (d,  $J = 11.5$  Hz, 1H), 84.54 (d,  $J = 11.6$  Hz, 1H), 84.32 (d,  $J = 11.7$  Hz, 1H), 84.19 (d,  $J = 9.3$  Hz, 1H), 84.13 (d,  $J = 11.8$  Hz, 1H), 83.66 (dd,  $J = 8.3, 3.1$  Hz, 1H), 83.53 (dd,  $J = 9.7, 6.1$  Hz, 1H), 83.41 (dd,  $J = 9.7, 7.2$  Hz, 1H), 82.89-2.79 (m, 1H), 82.37 (dq,  $J = 13.5, 6.6$  Hz, 1H), 82.33-2.26 (m, 1H), 81.70 (d,  $J = 1.0$  Hz, 3H), 81.52 (s, 9H), 81.02 (d,  $J = 2.0$  Hz, 3H), 81.01 (d,  $J = 1.9$  Hz, 3H), 80.90 (s, 9H), 80.64 (d,  $J = 7.2$  Hz, 3H), 80.05 (s, 6H);

$^{13}\text{C}$  NMR (125 MHz,  $\text{CDCl}_3$ ):  $\delta$  152.6, 142.3, 139.1, 138.8, 138.4, 134.8, 134.4, 131.7, 130.4, 128.9, 128.3, 128.2, 127.9, 127.7, 127.4, 127.3, 122.6, 117.8, 117.5, 83.1, 82.9, 80.4, 72.5, 70.0, 68.4, 42.4, 39.6, 35.2, 28.4, 26.0, 18.4, 18.2, 16.8, 12.7, 11.9, -5.2, -5.3;

IR (neat/ $\text{cm}^{-1}$ )  $\nu_{\text{max}}$ : 3326, 2956, 2928, 2856, 1731, 1714, 1703, 1609, 1594, 1528, 1491, 1453, 1441, 1391, 1366, 1249, 1228, 1158, 1085, 1066, 1028;

HRMS (ESI)  $m/z$  calcd for  $\text{C}_{45}\text{H}_{65}\text{NO}_5\text{Si}$  [ $\text{M}+\text{Na}]^+$ : 750.4530, found: 750.4504.

**Benzyl (3-((1R,2R,3R,4S,5E,7E,9S)-1,3-bis(benzyloxy)-10-hydroxy-2,4,6,9-tetramethyldeca-**

**5,7-dien-1-yl)phenyl)carbamate (32b):** Prepared by *general procedure O* using **126** and **A3** (2 equiv). The crude material was purified with Preparative Thin Layer Chromatography using 20% ethyl acetate in Hexanes. The obtained TBS ether was treated with TBAF (1 M in THF, 2 equiv) in 1 mL THF at room temperature for 2 hours to afford alcohol **32b** (it was purified using 30% ethyl

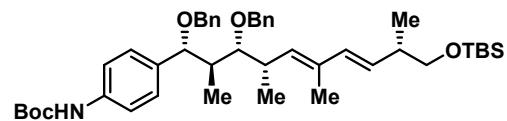
acetate in Hexanes). **32b** (70 mg, 0.108 mmol, 54% yield) was afforded as a pale yellow, viscous oil.  $[\alpha]_D^{23.8} = +4.5$  ( $c = 0.67$ ,  $\text{CH}_2\text{Cl}_2$ ).  $[\alpha]_D^{23.8} = +19.7$  ( $c = 0.6$ ,  $\text{CH}_2\text{Cl}_2$ ).

$^1\text{H}$  NMR (500 MHz,  $\text{CDCl}_3$ ):  $\delta$  7.49 (d,  $J = 6.6$  Hz, 1H), 7.43-7.27 (m, 15H), 7.07 (s, 1H), 86.99 (d,  $J = 7.8$  Hz, 1H), 86.97 (s, 1H), 85.87 (d,  $J = 15.6$  Hz, 1H), 85.36 (dd,  $J = 15.6, 8.3$  Hz, 1H), 85.21 (s, 2H), 84.90 (d,  $J = 10.4$  Hz, 1H), 84.68 (d,  $J = 11.5$  Hz, 1H), 84.53 (d,  $J = 11.5$  Hz, 1H), 84.39 (d,  $J = 11.9$  Hz, 1H), 84.15 (d,  $J = 9.6$  Hz, 1H), 84.08 (d,  $J = 11.9$  Hz, 1H), 83.62 (dd,  $J = 8.7, 2.4$  Hz, 1H), 83.59-3.55 (m, 1H), 83.42-3.37 (m, 1H), 82.79-2.74 (m, 1H), 82.41-2.36 (m, 1H), 82.32-2.28 (m, 1H), 81.69 (d,  $J = 0.9$  Hz, 3H), 81.02 (d,  $J = 6.8$  Hz, 3H), 80.99 (d,  $J = 6.5$  Hz, 3H), 80.56 (d,  $J = 7.3$  Hz, 3H);

$^{13}\text{C}$  NMR (125 MHz,  $\text{CDCl}_3$ ):  $\delta$  153.4, 142.1, 139.0, 138.7, 137.9, 136.3, 136.2, 135.4, 131.2, 129.9, 129.3, 128.6, 128.4, 128.3, 128.3, 128.2, 128.1, 127.6, 127.4, 122.1, 118.3, 117.6, 82.9, 82.1, 72.2, 69.8, 67.5, 66.9, 42.1, 40.4, 35.5, 18.4, 16.9, 12.8, 8.6;

IR (neat/cm<sup>-1</sup>)  $\nu_{\text{max}}$ : 3396, 3305, 3088, 3064, 3031, 2960, 2928, 2869, 1733, 1708, 1611, 1597, 1549, 1495, 1453, 1446, 1217, 1178, 1084, 1063, 1028;

HRMS (ESI)  $m/z$  calcd for  $\text{C}_{42}\text{H}_{49}\text{NO}_5$  [M+H]<sup>+</sup>: 648.3689, found: 648.3695.



**Tert-butyl (4-((1*R*,2*R*,3*R*,4*S*,5*E*,7*E*,9*S*)-1,3-bis(benzyloxy)-10-((tert-butyldimethylsilyl)oxy)-2,4,6,9-tetramethyldeca-5,7-dien-1-yl)phenyl)carbamate (33a):** Prepared by *general procedure O* using **130** and **A3** (2 equiv). The crude material was purified with Preparative Thin Layer Chromatography using 100% dichloromethane. **33a** (68 mg, 0.094 mmol, 47% yield) was afforded as a pale yellow, viscous oil.  $[\alpha]_D^{23.8} = +14.6$  ( $c = 1.3$ ,  $\text{CH}_2\text{Cl}_2$ ).

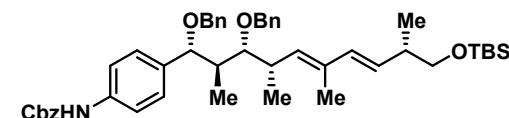
$^1\text{H}$  NMR (500 MHz,  $\text{CDCl}_3$ ):  $\delta$  7.38-7.25 (m, 11H), 7.16 (d,  $J = 8.5$  Hz, 2H), 86.47 (s, 1H), 85.89 (d,  $J = 15.8$  Hz, 1H), 85.49 (dd,  $J = 15.7, 7.4$  Hz, 1H), 85.09 (d,  $J = 10.2$  Hz, 1H), 84.64 (d,  $J = 11.5$  Hz, 1H), 84.55 (d,  $J = 11.5$  Hz, 1H), 84.30 (d,  $J = 11.8$  Hz, 1H), 84.19 (d,  $J = 9.4$  Hz, 1H), 84.11 (d,  $J = 11.8$  Hz, 1H), 83.66 (dd,  $J = 8.3, 3.2$  Hz, 1H), 83.53 (dd,  $J = 9.7, 6.0$  Hz, 1H), 83.41 (dd,  $J = 9.7, 7.3$  Hz, 1H);

Hz, 1H), δ2.87-2.80 (m, 1H), δ2.39-2.34 (m, 1H), δ2.32-2.25 (m, 1H), δ1.70 (d,  $J = 1.0$  Hz, 3H), δ1.53 (s, 9H), δ1.02 (d,  $J = 3.1$  Hz, 3H), δ1.01 (d,  $J = 2.9$  Hz, 3H), δ0.90 (s, 9H), δ0.62 (d,  $J = 7.2$  Hz, 3H), δ0.05 (d,  $J = 1.0$  Hz, 6H);

$^{13}\text{C}$  NMR (125 MHz,  $\text{CDCl}_3$ ): δ152.8, δ139.1, δ138.9, δ137.7, δ135.9, δ134.8, δ134.4, δ131.7, δ130.3, δ128.4, δ128.3, δ128.2, δ127.9, δ127.8, δ127.4, δ127.3, δ118.3, δ83.2, δ82.5, δ72.5, δ69.8, δ68.4, δ42.5, δ39.6, δ35.2, δ28.3, δ26.0, δ18.4, δ18.2, δ16.8, δ12.6, δ11.7, δ-5.2, δ-5.3;

IR (neat/ $\text{cm}^{-1}$ )  $\nu_{\text{max}}$ : 3337, 2956, 2928, 2856, 1731, 1705, 1613, 1596, 1521, 1471, 1454, 1413, 1391, 1367, 1311, 1249, 1229, 1157, 1086, 1067, 1052, 1028;

HRMS (ESI)  $m/z$  calcd for  $\text{C}_{45}\text{H}_{65}\text{NO}_5\text{Si} [\text{M}+\text{Na}]^+$ : 750.4530, found: 750.4520.



**Benzyl (4-((1*R*,2*R*,3*R*,4*S*,5*E*,7*E*,9*S*)-1,3-bis(benzyloxy)-10-((*tert*-butyldimethylsilyl)oxy)-2,4,6,9-tetramethyldeca-5,7-dien-1-yl)phenyl)carbamate (33b):** Prepared by *general procedure O* using **127** and **A3** (2 equiv). The crude material was purified with Preparative Thin Layer Chromatography using 12% ethyl acetate in Hexanes. **33b** (76 mg, 0.1 mmol, 50% yield) was afforded as a pale yellow, viscous oil.  $[\alpha]_D^{23.8} = +11$  ( $c = 1.8$ ,  $\text{CH}_2\text{Cl}_2$ ).

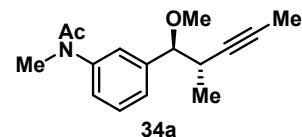
$^1\text{H}$  NMR (500 MHz,  $\text{CDCl}_3$ ): δ7.43-7.27 (m, 16H), δ7.19 (d,  $J = 8.5$  Hz, 2H), δ6.69 (s, 1H), δ5.90 (d,  $J = 15.8$  Hz, 1H), δ5.50 (dd,  $J = 15.7$ , 7.4 Hz, 1H), δ5.22 (s, 2H), δ5.10 (d,  $J = 10.2$  Hz, 1H), δ4.65 (d,  $J = 11.6$  Hz, 1H), δ4.56 (d,  $J = 11.5$  Hz, 1H), δ4.31 (d,  $J = 11.8$  Hz, 1H), δ4.21 (d,  $J = 9.4$  Hz, 1H), δ4.12 (d,  $J = 11.8$  Hz, 1H), δ3.67 (dd,  $J = 8.3$ , 3.1 Hz, 1H), δ3.54 (dd,  $J = 9.7$ , 6.0 Hz, 1H), δ3.42 (dd,  $J = 9.7$ , 7.3 Hz, 1H), δ2.89-2.81 (m, 1H), δ2.41-2.35 (m, 1H), δ2.33-2.26 (m, 1H), δ1.71 (s, 3H), δ1.03 (d,  $J = 2.3$  Hz, 3H), δ1.02 (d,  $J = 2.1$  Hz, 3H), δ0.91 (s, 9H), δ0.63 (d,  $J = 7.2$  Hz, 3H), δ0.06 (d,  $J = 0.9$  Hz, 6H);

$^{13}\text{C}$  NMR (125 MHz,  $\text{CDCl}_3$ ): δ153.3, δ139.1, δ138.8, δ137.1, δ136.5, δ136.1, δ134.8, δ134.4, δ131.7, δ130.4, δ128.6, δ128.5, δ128.4, δ128.3, δ128.3, δ128.2, δ127.9, δ127.8, δ127.4, δ127.3, δ118.5, δ83.2, δ82.5, δ72.5, δ69.8, δ68.4, δ67.1, δ42.5, δ39.6, δ35.3, δ26.0, δ18.2, δ16.8, δ12.6, δ11.8, δ-5.2, δ-5.3;

IR (neat/cm<sup>-1</sup>)  $\nu_{\text{max}}$ : 3321, 3065, 3031, 2955, 2928, 2855, 1737, 1708, 1613, 1599, 1525, 1471, 1454, 1416, 1312, 1250, 1214, 1083, 1057, 1028;

HRMS (ESI)  $m/z$  calcd for C<sub>48</sub>H<sub>63</sub>NO<sub>5</sub>Si [M+Na]<sup>+</sup>: 784.4373, found: 784.4385.

### 3.1. Synthesis of 34a-34e in Scheme 3.

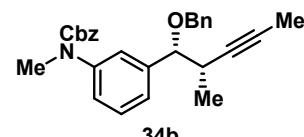


**N-(3-((1S,2S)-1-methoxy-2-methylpent-3-yn-1-yl)phenyl)-N-methylacetamide (34a):** Sodium hydride (60% dispersion in mineral oil, 65 mg, 1.63 mmol, 2 equiv) was washed with Hexanes once and suspended in 7.2 mL THF (0.1 M). **104** (200 mg, 0.815 mmol, 1 equiv) in 1 mL THF was added in followed by iodomethane (0.5 mL, 8.15 mmol, 10 equiv). The mixture was stirred at room temperature overnight and then quenched by saturated ammonium chloride solution. The mixture was partitioned between 20 mL DI water and 10 mL diethyl ether, and extracted with diethyl ether. The combined organic layers were dried over MgSO<sub>4</sub>, filtered, and concentrated. Purification over silica gel chromatography (54% ethyl acetate in dichloromethane) afforded **34a** (179 mg, 0.69 mmol, 85% yield) as a pale yellow, viscous oil.

<sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>): δ7.38 (t,  $J$  = 7.7 Hz, 1H), δ7.26 (d,  $J$  = 5.0 Hz, 1H), δ7.18 (s, 1H), δ7.11 (d,  $J$  = 7.6 Hz, 1H), δ4.10 (d,  $J$  = 5.3 Hz, 1H), δ3.28 (s, 3H), δ3.26 (s, 3H), δ2.78-2.72 (m, 1H), δ1.87 (s, 3H), δ1.77 (d,  $J$  = 2.4 Hz, 3H), δ1.05 (d,  $J$  = 7.0 Hz, 3H).

<sup>13</sup>C NMR (125 MHz, CDCl<sub>3</sub>): δ170.5, δ144.3, δ141.7, δ129.3, δ126.6, δ126.2, δ126.0, δ85.9, δ80.0, δ77.9, δ77.3, δ77.0, δ76.8, δ57.4, δ37.1, δ33.3, δ22.4, δ17.2, δ3.7.

HRMS (ESI)  $m/z$  calcd for C<sub>16</sub>H<sub>21</sub>NO<sub>2</sub> [M+H]<sup>+</sup>: 260.1651, found: 260.1651.



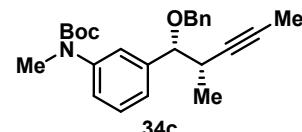
**Benzyl (3-((1R,2S)-1-(benzyloxy)-2-methylpent-3-yn-1-yl)phenyl)(methyl)carbamate (34b):** Sodium hydride (60% dispersion in mineral oil, 49 mg, 1.22 mmol, 2 equiv) was washed with Hexanes once and suspended in 11 mL THF

(0.05 M). **92** (250 mg, 0.61 mmol, 1 equiv) in 1 mL THF was added in followed by iodomethane (0.75 mL, 12.1 mmol, 20 equiv). The mixture was stirred at room temperature for 24 hours and then quenched by saturated ammonium chloride solution. The mixture was partitioned between 20 mL DI water and 10 mL diethyl ether, and extracted with diethyl ether. The combined organic layers were dried over  $\text{MgSO}_4$ , filtered, and concentrated. Purification over silica gel chromatography (15% ethyl acetate in Hexanes) afforded **34b** (201 mg, 0.47 mmol, 77% yield) as a pale yellow, viscous oil.

$^1\text{H}$  NMR (500 MHz,  $\text{CDCl}_3$ ):  $\delta$  7.35-7.18 (m, 14H),  $\delta$  5.19 (ABq,  $J = 12.0$  Hz, 1H),  $\delta$  5.15 (ABq,  $J = 12.0$  Hz, 1H),  $\delta$  4.50 (d,  $J = 12.0$  Hz, 1H),  $\delta$  4.25 (d,  $J = 12.0$  Hz, 1H),  $\delta$  4.15 (d,  $J = 7.1$  Hz, 1H),  $\delta$  3.34 (s, 3H),  $\delta$  2.71-2.71 (m, 1H),  $\delta$  1.68 (d,  $J = 2.3$  Hz, 3H),  $\delta$  1.18 (d,  $J = 6.9$  Hz, 3H).

$^{13}\text{C}$  NMR (125 MHz,  $\text{CDCl}_3$ ):  $\delta$  155.47,  $\delta$  141.13,  $\delta$  138.23,  $\delta$  136.59,  $\delta$  128.35,  $\delta$  128.30,  $\delta$  128.26,  $\delta$  127.89,  $\delta$  127.79,  $\delta$  127.54,  $\delta$  83.73,  $\delta$  80.57,  $\delta$  77.98,  $\delta$  70.74,  $\delta$  67.27,  $\delta$  33.74,  $\delta$  17.73,  $\delta$  3.50.

HRMS (ESI)  $m/z$  calcd for  $\text{C}_{28}\text{H}_{29}\text{NO}_3$  [ $\text{M}+\text{H}]^+$ : 428.2226, found: 428.2230.

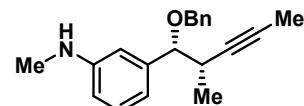


**Tert-butyl (3-((1*R*,2*S*)-1-(benzyloxy)-2-methylpent-3-yn-1-yl)phenyl)(methyl)carbamate (34c):** Sodium hydride (60% dispersion in mineral oil, 43 mg, 1.06 mmol, 2 equiv) was washed with Hexanes once and suspended in 4.3 mL THF (0.1 M). **91** (200 mg, 0.53 mmol, 1 equiv) in 1 mL THF was added in followed by iodomethane (0.65 mL, 10.54 mmol, 20 equiv). The mixture was stirred at room temperature for 12 hours and then quenched by saturated ammonium chloride solution. The mixture was partitioned between 20 mL DI water and 10 mL diethyl ether, and extracted with diethyl ether. The combined organic layers were dried over  $\text{MgSO}_4$ , filtered, and concentrated. Purification over silica gel chromatography (10% ethyl acetate in Hexanes) afforded **34c** (171 mg, 0.435 mmol, 82% yield) as a pale yellow, viscous oil.

$^1\text{H}$  NMR (500 MHz,  $\text{CDCl}_3$ ):  $\delta$  7.35-7.12 (m, 9H),  $\delta$  4.54 (d,  $J = 12.1$  Hz, 1H),  $\delta$  4.29 (d,  $J = 12.0$  Hz, 1H),  $\delta$  4.17 (d,  $J = 7.1$  Hz, 1H),  $\delta$  3.27 (s, 3H),  $\delta$  2.79-2.74 (m, 1H),  $\delta$  1.70 (d,  $J = 2.4$  Hz, 3H),  $\delta$  1.45 (s, 9H),  $\delta$  1.21 (d,  $J = 6.9$  Hz, 3H).

$^{13}\text{C}$  NMR (125 MHz,  $\text{CDCl}_3$ ):  $\delta$  154.80,  $\delta$  143.60,  $\delta$  140.79,  $\delta$  138.29,  $\delta$  128.30,  $\delta$  128.26,  $\delta$  128.07,  $\delta$  127.82,  $\delta$  127.80,  $\delta$  127.54,  $\delta$  124.97,  $\delta$  124.80,  $\delta$  83.82,  $\delta$  80.65,  $\delta$  80.14,  $\delta$  77.88,  $\delta$  70.73,  $\delta$  37.43,  $\delta$  33.72,  $\delta$  28.36,  $\delta$  17.77,  $\delta$  3.52.

HRMS (ESI)  $m/z$  calcd for  $C_{25}H_{31}NO_3$  [M+H] $^+$ : 394.2382, found: 394.2388;

**34d**

**3-((1*R*,2*S*)-1-(benzyloxy)-2-methylpent-3-yn-1-yl)-N-methylaniline (34d):** *Ent-47* (332 mg, 1.19 mmol, 1 equiv) was dissolved in 8 mL anhydrous methanol at room temperature. Sodium methoxide (385 mg, 7.13 mmol, 6 equiv) was added in followed by paraformaldehyde (72 mg, 2.38 mmol, 2 equiv). The mixture was stirred at room temperature for 4 hours. Sodium borohydride (904 mg, 23.8 mmol, 20 equiv) was added in and the reaction was heated to reflux for 24 hours. Methanol was then evaporated. The mixture was partitioned between saturated ammonium chloride (aq) and ethyl acetate, and extracted with diethyl ether. The combined organic layers were dried over  $MgSO_4$ , filtered, and concentrated. Purification over silica gel chromatography (20% ethyl acetate in Hexanes) afforded **34d** (105 mg, 0.36 mmol, 30% yield) as a pale yellow, viscous oil.  $[\alpha]_D^{23.8} = +11.9$  ( $c = 2.5$ ,  $CH_2Cl_2$ ).

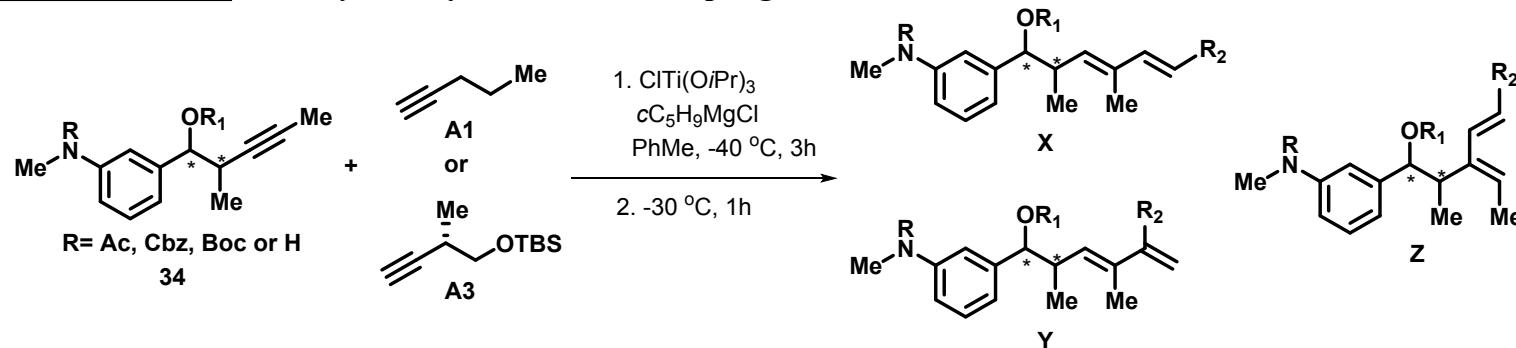
$^1H$  NMR (500 MHz,  $CDCl_3$ ):  $\delta$  7.38-7.25 (m, 5H), 87.18 (t,  $J = 7.7$  Hz, 1H), 86.74 (d,  $J = 7.5$  Hz, 1H), 86.71 (d,  $J = 2.0$  Hz, 2H), 86.61 (d,  $J = 7.9$  Hz, 1H), 84.55 (d,  $J = 12.1$  Hz, 1H), 84.28 (d,  $J = 12.0$  Hz, 1H), 84.13 (d,  $J = 7.0$  Hz, 1H), 82.86 (s, 3H), 82.79-2.73 (m, 1H), 81.71 (d,  $J = 2.4$  Hz, 3H), 81.21 (d,  $J = 6.9$  Hz, 3H);

$^{13}C$  NMR (125 MHz,  $CDCl_3$ ):  $\delta$  149.1, 141.2, 138.6, 128.7, 128.3, 127.8, 127.4, 117.2, 112.0, 111.6, 84.2, 81.1, 77.5, 870.6, 833.7, 830.9, 817.7, 83.6;

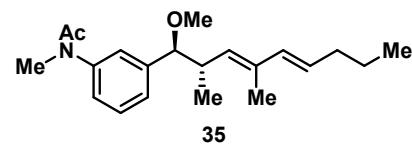
IR (neat/cm $^{-1}$ )  $\nu_{max}$ : 3411, 3030, 2973, 2931, 2916, 2872, 2812, 1607, 1590, 1511, 1494, 1475, 1453, 1328, 1296, 1271, 1167, 1157, 1092, 1063, 1028;

HRMS (ESI)  $m/z$  calcd for  $C_{20}H_{23}NO$  [M+H] $^+$ : 294.1858, found: 294.1852.

### 3.2 General Procedure P for Alkyne-Alkyne Reductive Coupling in Scheme 3



To a solution of internal alkyne (0.2 mmol, 1 equiv) in toluene (3.1 mL) at  $-78^\circ\text{C}$  was added sequentially  $\text{ClTi}(\text{O}i\text{Pr})_3$  (1.0 M in hexanes, 0.4 mL, 0.4 mmol, 2 equiv) and  $c\text{C}_5\text{H}_9\text{MgCl}$  (2.0 M in diethyl ether, 0.4 mL, 0.8 mmol, 4 equiv) in a dropwise manner. The resulting yellow solution turned brown while slowly warming to  $-30^\circ\text{C}$  over an hour. The reaction mixture was placed in  $-30^\circ\text{C}$  chiller and stirred for 1 hours, while solution turned to be black and heterogenous. It was then cooled to  $-78^\circ\text{C}$ , to which terminal alkyne **A1** or **A3** (0.2 mmol, 1 equiv) was added in dropwise. The resulting mixture was gradually warmed to  $-30^\circ\text{C}$  over 1 hour and stirred for an hour. The reaction was quenched with saturated aqueous  $\text{NH}_4\text{Cl}$  solution (3 mL). It was then extract with ethyl acetate (3 x 10 mL). The combined organic layers were dried over  $\text{MgSO}_4$ , filtered, and concentrated. Purification over silica gel chromatography afforded coupled product **35-38**.



***N*-(3-((1*S*,2*S*,3*E*,5*E*)-1-methoxy-2,4-dimethylnona-3,5-dien-1-yl)phenyl)-*N*-methylacetamide (35):**

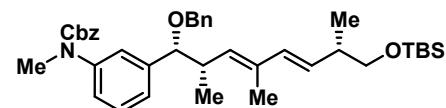
Prepared by *general procedure P* using **34a** and **A1**. The crude material was purified with Preparative Thin Layer Chromatography using 34% dichloromethane in Hexanes. **35** (27 mg, 0.082 mmol, 41% yield) was afforded as a pale yellow oil.  $[\alpha]_D^{23.8} = -23.3$  ( $c = 2.3$ ,  $\text{CH}_2\text{Cl}_2$ ).

<sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>): δ7.35 (dd, *J* = 7.7 Hz, 1H), δ7.19 (d, *J* = 7.5 Hz, 1H), δ7.07 (d, *J* = 7.8 Hz, 1H), δ7.04 (s, 1H), δ6.01 (d, *J* = 15.6 Hz, 1H), δ5.49 (dt, *J* = 15.4, 6.9 Hz, 1H), δ5.18 (d, *J* = 9.6 Hz, 1H), δ4.06 (d, *J* = 5.2 Hz, 1H), δ3.233 (s, 3H), δ3.229 (s, 3H), δ2.83-2.76 (m, 1H), δ2.05-2.00 (m, 2H), δ1.83 (s, 3H), δ1.47 (d, *J* = 1.0 Hz, 3H), δ1.41-1.35 (m, 2H), δ0.95 (d, *J* = 6.8 Hz, 3H), δ0.89 (t, *J* = 7.4 Hz, 3H);

<sup>13</sup>C NMR (125 MHz, CDCl<sub>3</sub>): δ170.5, δ144.4, δ143.0, δ134.7, δ134.2, δ131.3, δ129.3, δ128.2, δ126.7, δ125.8, δ125.8, δ87.6, δ57.3, δ39.4, δ37.2, δ35.0, δ22.8, δ22.4, δ17.3, δ13.8, δ12.6;

IR (neat/cm<sup>-1</sup>)  $\nu_{\text{max}}$ : 2958, 2928, 2871, 2822, 1663, 1602, 1588, 1487, 1447, 1437, 1419, 1375, 1349, 1300, 1185, 1138, 1100, 1086;

HRMS (ESI) *m/z* calcd for C<sub>20</sub>H<sub>29</sub>NO<sub>2</sub> [M+H]<sup>+</sup>: 316.2277, found: 316.2267.

**36**

**Benzyl (3-((1*R*,2*S*,3*E*,5*E*,7*S*)-1-(benzyloxy)-8-((*tert*-butyldimethylsilyl)oxy)-2,4,7-**

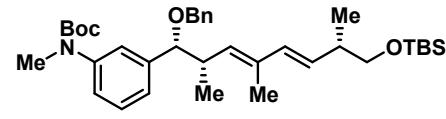
**trimethylocta-3,5-dien-1-yl)phenyl)(methyl)carbamate (36):** Prepared by *general procedure P* using **34b** and **A3**. The crude material was purified with Preparative Thin Layer Chromatography using 12% ethyl acetate in Hexanes. **36** (58 mg, 0.092 mmol, 46% yield) was afforded as a pale yellow oil.  $[\alpha]_D^{23.8} = -0.36$  (*c* = 2.8, CH<sub>2</sub>Cl<sub>2</sub>).

<sup>1</sup>H NMR (500 MHz, C<sub>6</sub>D<sub>6</sub>): δ7.28-6.96 (m, 14H), δ6.07 (d, *J* = 15.8 Hz, 1H), δ5.42 (dd, *J* = 15.8, 7.4 Hz, 1H), δ5.22 (d, *J* = 9.8 Hz, 1H), δ5.08 (d, *J* = 2.4 Hz, 2H), δ4.41 (d, *J* = 12.0 Hz, 1H), δ4.10 (d, *J* = 12.1 Hz, 1H), δ3.99 (d, *J* = 6.9 Hz, 1H), δ3.43 (dd, *J* = 9.6, 5.8 Hz, 1H), δ3.30 (dd, *J* = 9.6, 7.2 Hz, 1H), δ3.04 (s, 3H), δ2.88-2.82 (m, 1H), δ2.36-2.31 (m, 1H), δ1.42 (s, 3H), δ1.15 (d, *J* = 6.6 Hz, 3H), δ1.01 (d, *J* = 6.7 Hz, 3H), δ0.94 (s, 9H), δ0.00 (s, 6H);

<sup>13</sup>C NMR (125 MHz, C<sub>6</sub>D<sub>6</sub>): δ154.9, δ143.5, δ142.0, δ139.0, δ137.1, δ134.7, δ133.8, δ133.2, δ130.1, δ128.3, δ128.3, δ127.4, δ124.8, δ84.9, δ70.7, δ68.2, δ67.1, δ40.3, δ39.7, δ25.9, δ18.3, δ16.9, δ16.8, δ12.5, δ-5.4, δ -5.5;

IR (neat/cm<sup>-1</sup>)  $\nu_{\text{max}}$ : 3032, 2955, 2928, 2855, 1707, 1604, 1589, 1489, 1471, 1454, 1387, 1347, 1302, 1251, 1148, 1084, 1071, 1027.

HRMS (ESI)  $m/z$  calcd for C<sub>39</sub>H<sub>53</sub>NO<sub>4</sub>Si [M+H]<sup>+</sup>: 628.3822, found: 628.3821.



37

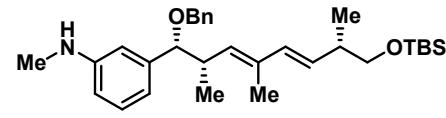
**Tert-butyl (3-((1R,2S,3E,5E,7S)-1-(benzyloxy)-8-((tert-butyldimethylsilyl)oxy)-2,4,7-trimethylocta-3,5-dien-1-yl)phenyl)(methyl)carbamate (37):** Prepared by *general procedure P* using **34c** and **A3**. The crude material was purified with Preparative Thin Layer Chromatography using 10% ethyl acetate in Hexanes. **37** (57 mg, 0.096 mmol, 48% yield) was afforded as a pale yellow oil.  $[\alpha]_D^{23.8} = +2.5$  ( $c = 4.5$ , CH<sub>2</sub>Cl<sub>2</sub>).

<sup>1</sup>H NMR (500 MHz, C<sub>6</sub>D<sub>6</sub>): δ7.27-6.98 (m, 9H), 86.08 (d,  $J = 15.7$  Hz, 1H), 85.43 (dd,  $J = 15.7, 7.4$  Hz, 1H), 85.25 (d,  $J = 9.6$  Hz, 1H), 84.45 (d,  $J = 12.0$  Hz, 1H), 84.13 (d,  $J = 12.0$  Hz, 1H), 84.02 (d,  $J = 6.9$  Hz, 1H), 83.43 (dd,  $J = 9.6, 5.8$  Hz, 1H), 83.30 (dd,  $J = 9.5, 7.2$  Hz, 1H), 83.08 (s, 3H), 82.92-8.86 (m, 1H), 82.37-8.32 (m, 1H), 81.46 (s, 3H), 81.38 (d,  $J = 0.8$  Hz, 9H), 81.18 (d,  $J = 6.6$  Hz, 3H), 81.02 (d,  $J = 6.8$  Hz, 3H), 80.94 (s, 3H), 80.01 (s, 6H);

<sup>13</sup>C NMR (125 MHz, CDCl<sub>3</sub>): δ154.8, 143.6, 141.7, 138.6, 134.2, 133.6, 132.9, 130.3, 128.3, 128.3, 128.2, 128.2, 127.8, 127.6, 127.4, 124.7, 124.6, 85.0, 80.1, 876.8, 870.8, 868.2, 840.0, 839.5, 837.5, 828.4, 825.9, 818.4, 816.9, 816.7, 812.5, 8-5.3;

IR (neat/cm<sup>-1</sup>)  $\nu_{\text{max}}$ : 2956, 2928, 2856, 1701, 1604, 1589, 1488, 1472, 1454, 1435, 1390, 1364, 1308, 1251, 1149, 1088, 1072, 1028;

HRMS (ESI)  $m/z$  calcd for C<sub>36</sub>H<sub>55</sub>NO<sub>4</sub>Si [M+Na]<sup>+</sup>: 616.3798, found: 616.3770.



38

**3-((1R,2S,3E,5E,7S)-1-(benzyloxy)-8-((tert-butyldimethylsilyl)oxy)-2,4,7-trimethylocta-3,5-dien-1-yl)-N-methylaniline (38):** Prepared by *general procedure P* using **34d** and **A3**. The crude material was purified with

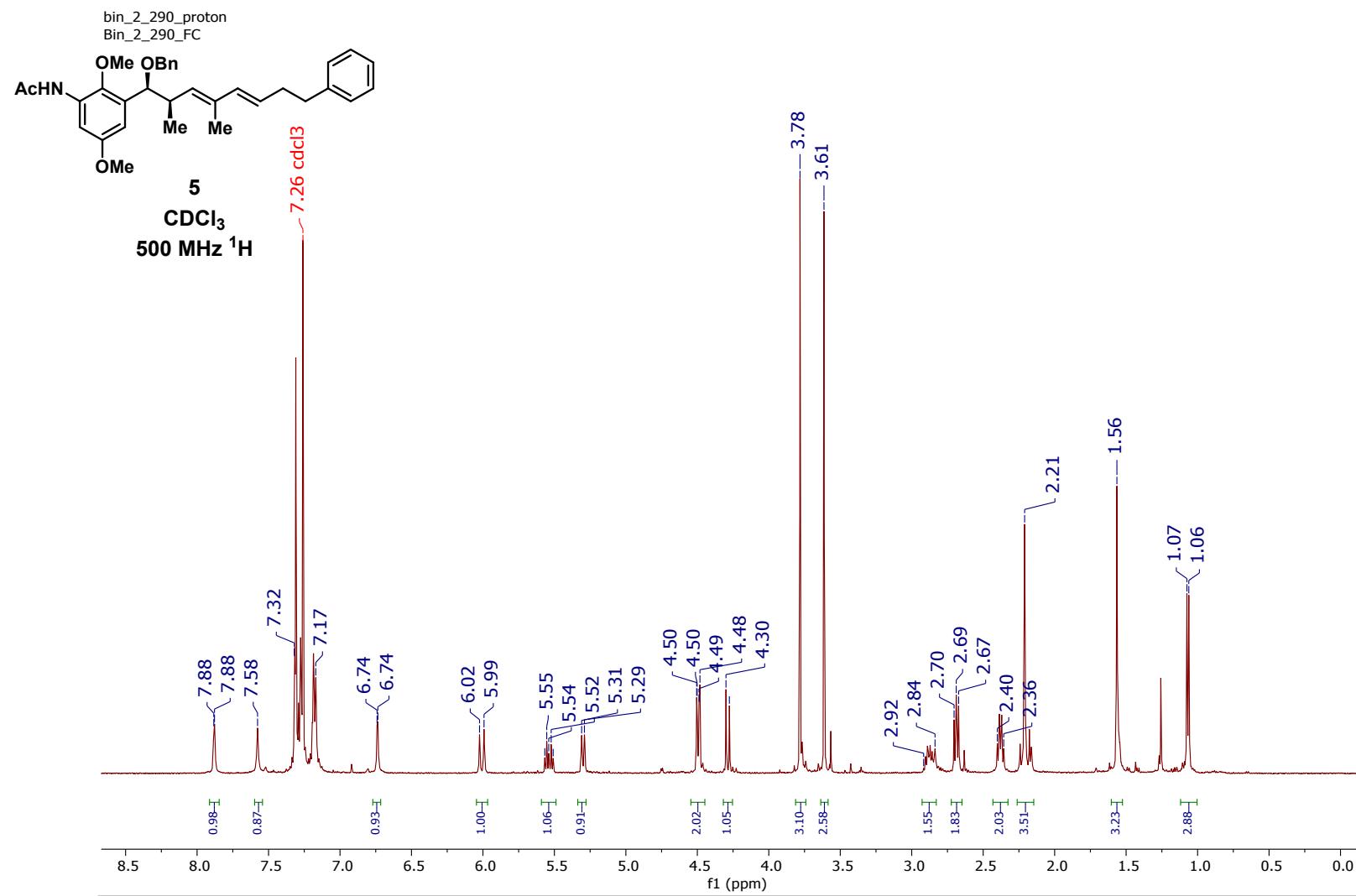
Preparative Thin Layer Chromatography using 12% ethyl acetate in Hexanes. **38** (39 mg, 0.08 mmol, 40% yield) was afforded as a pale yellow oil.  $[\alpha]_D^{23.8} = -2.8$  ( $c = 0.87$ ,  $\text{CH}_2\text{Cl}_2$ ).

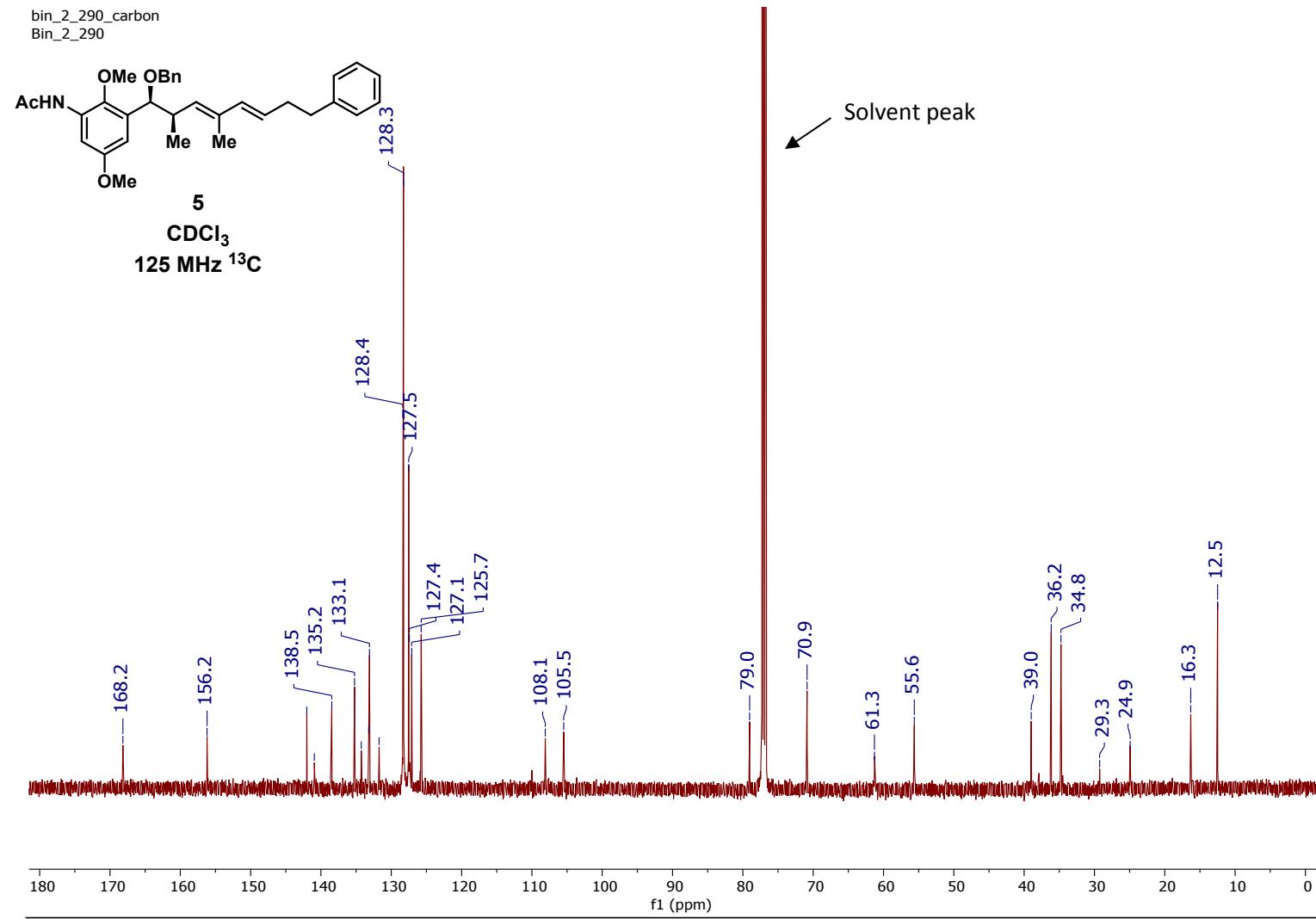
$^1\text{H}$  NMR (500 MHz,  $\text{CDCl}_3$ ):  $\delta$  7.34-7.27 (m, 5H),  $\delta$  6.66-6.52 (m, 4H),  $\delta$  5.99 (d,  $J = 15.8$  Hz, 1H),  $\delta$  5.38 (dd,  $J = 15.7, 7.3$  Hz, 1H),  $\delta$  5.32-5.25 (m, 1H),  $\delta$  4.51 (d,  $J = 11.9$  Hz, 1H),  $\delta$  4.26 (d,  $J = 11.9$  Hz, 1H),  $\delta$  4.09 (d,  $J = 6.5$  Hz, 1H),  $\delta$  3.48 (dd,  $J = 9.7, 6.1$  Hz, 1H),  $\delta$  3.37 (dd,  $J = 9.7, 7.2$  Hz, 1H),  $\delta$  3.13-3.06 (m, 1H),  $\delta$  2.83 (s, 3H),  $\delta$  2.35-2.29 (m, 1H),  $\delta$  1.53 (d,  $J = 1.2$  Hz, 3H),  $\delta$  1.07 (d,  $J = 6.7$  Hz, 3H),  $\delta$  0.99 (d,  $J = 6.7$  Hz, 3H),  $\delta$  0.88 (s, 9H),  $\delta$  0.0236 (s, 3H),  $\delta$  0.02 (s, 3H);

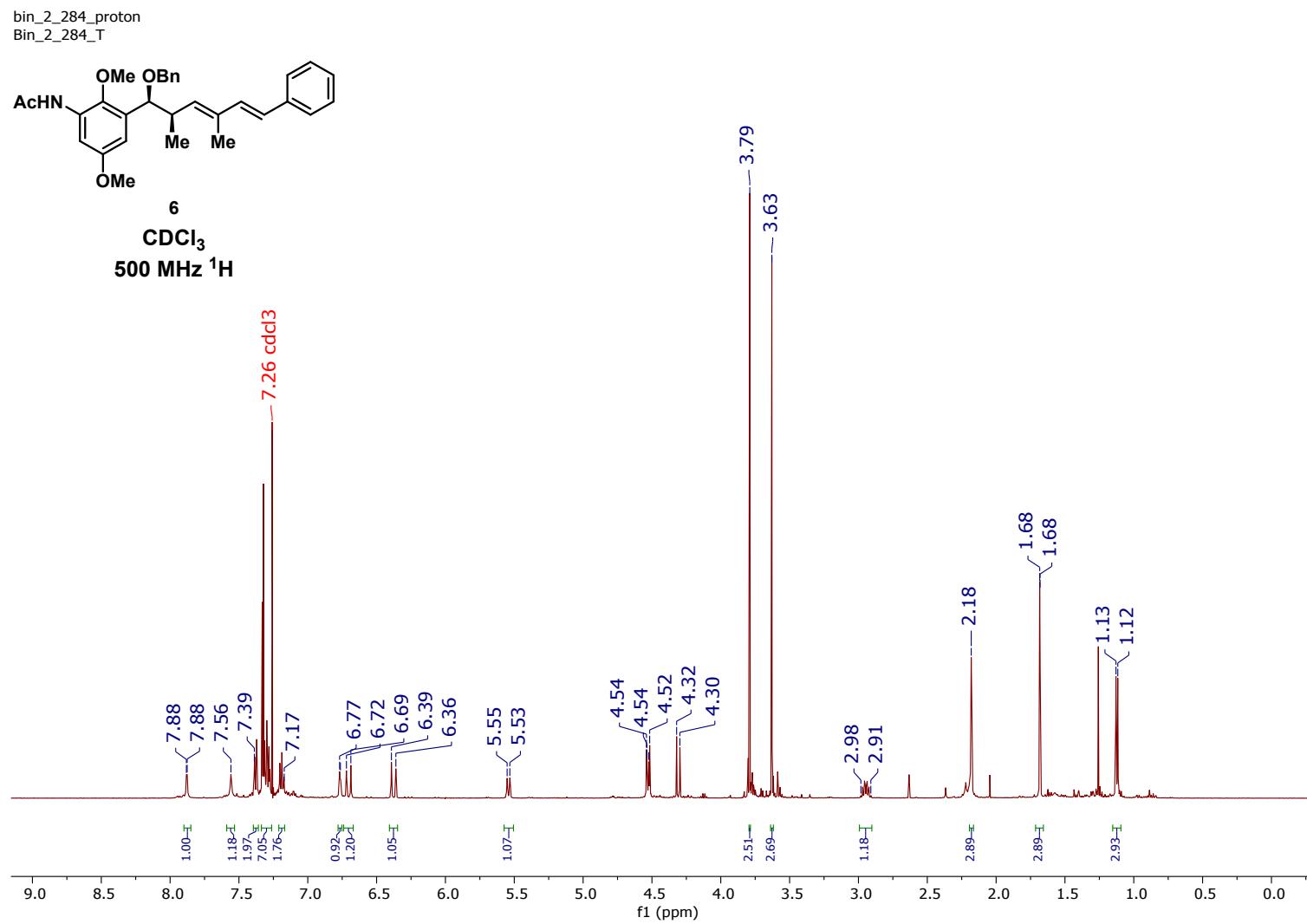
$^{13}\text{C}$  NMR (125 MHz,  $\text{CDCl}_3$ ):  $\delta$  148.9,  $\delta$  148.8,  $\delta$  142.0,  $\delta$  139.0,  $\delta$  134.5,  $\delta$  133.5,  $\delta$  130.0,  $\delta$  128.8,  $\delta$  128.2,  $\delta$  127.6,  $\delta$  127.3,  $\delta$  117.2,  $\delta$  111.6,  $\delta$  85.4,  $\delta$  70.6,  $\delta$  68.3,  $\delta$  48.8,  $\delta$  39.7,  $\delta$  39.5,  $\delta$  31.1,  $\delta$  25.9,  $\delta$  18.4,  $\delta$  17.4,  $\delta$  16.8,  $\delta$  12.5,  $\delta$ -5.3,  $\delta$ -5.3;

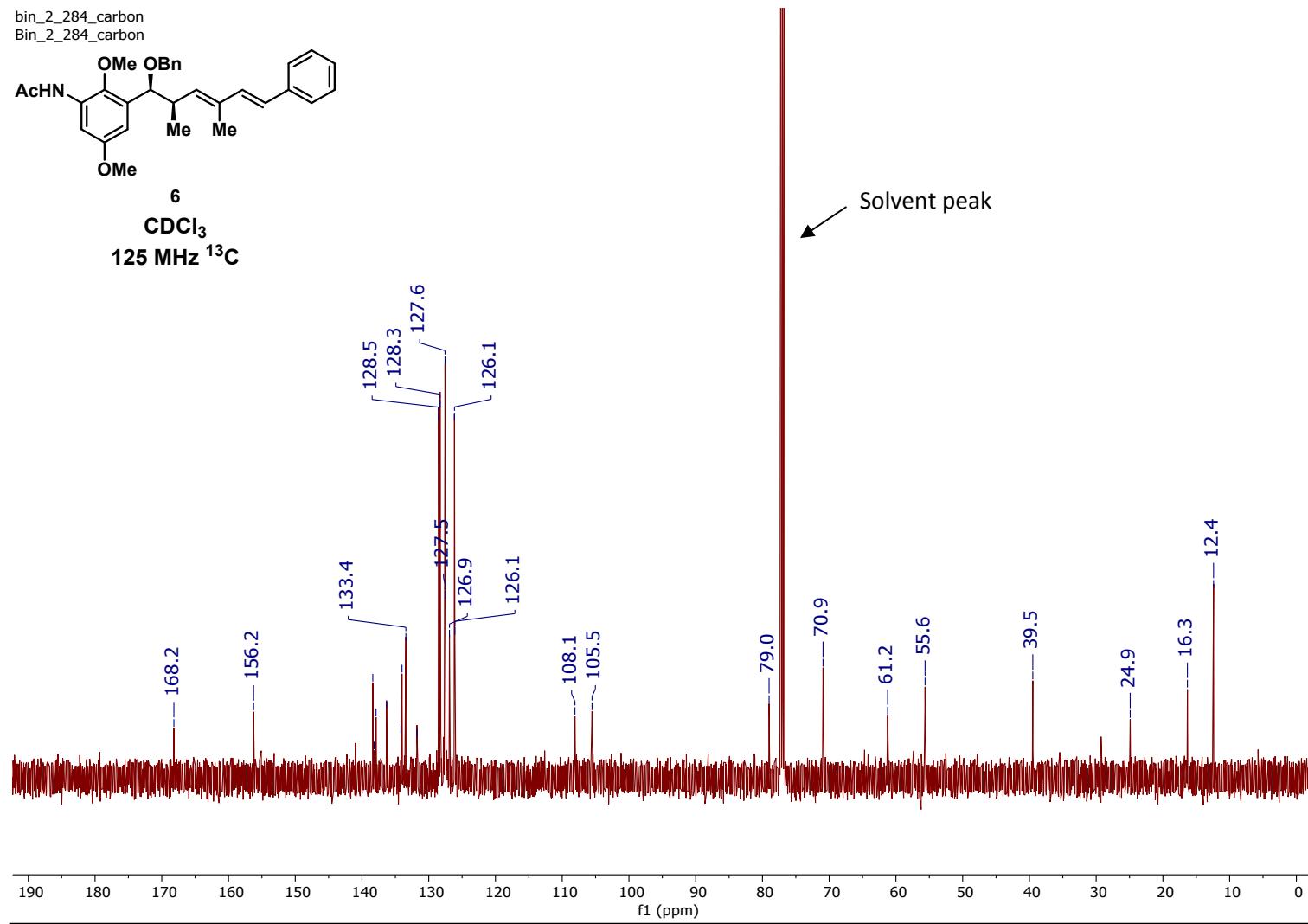
IR (neat/ $\text{cm}^{-1}$ )  $\nu_{\text{max}}$ : 3416, 2955, 2928, 2856, 1607, 1591, 1510, 1495, 1471, 1462, 1453, 1388, 1361, 1328, 1256, 1251, 1088, 1071, 1028;

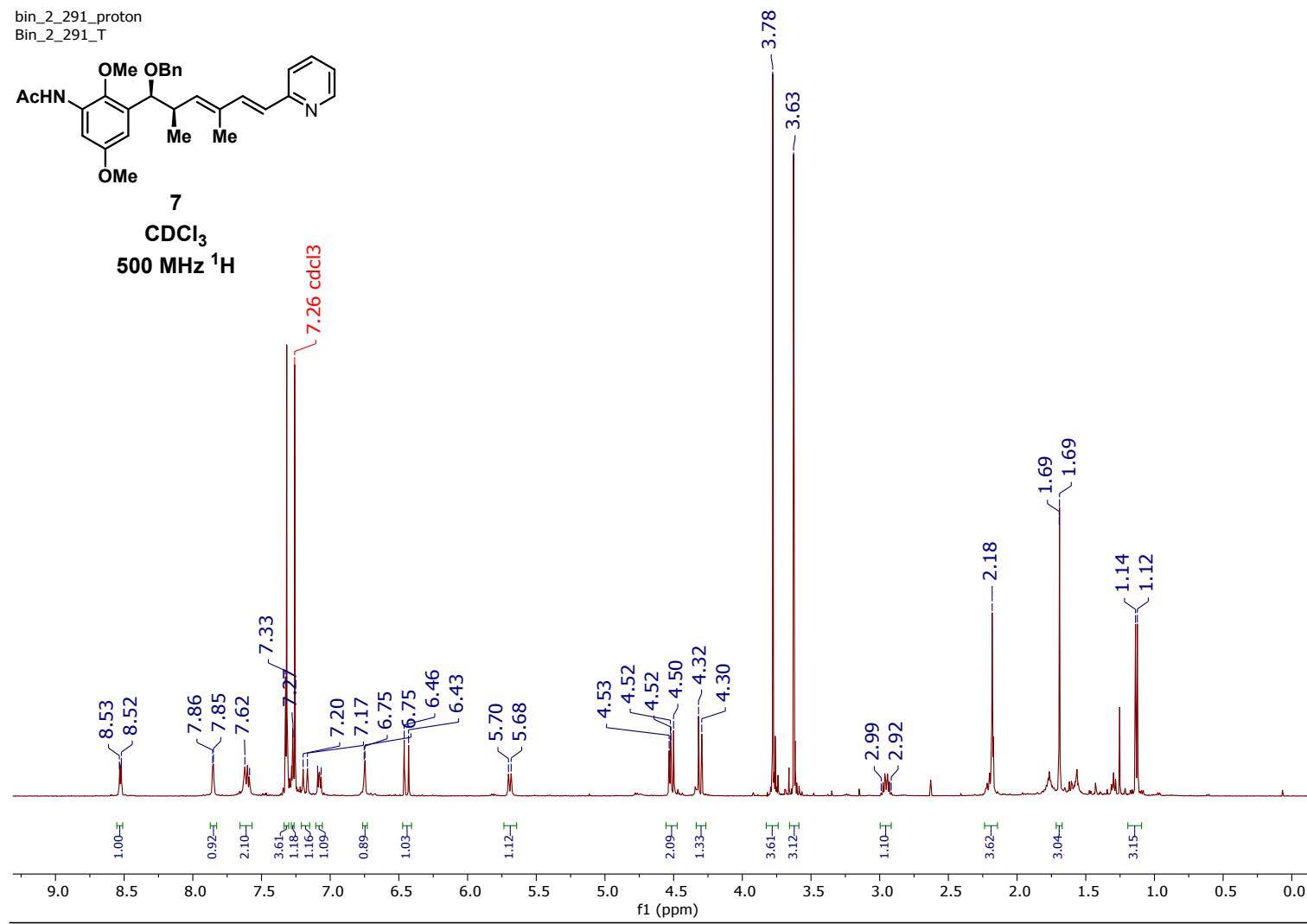
HRMS (ESI)  $m/z$  calcd for  $\text{C}_{31}\text{H}_{47}\text{NO}_2\text{Si} [\text{M}+\text{H}]^+$ : 494.3454, found: 494.3444.

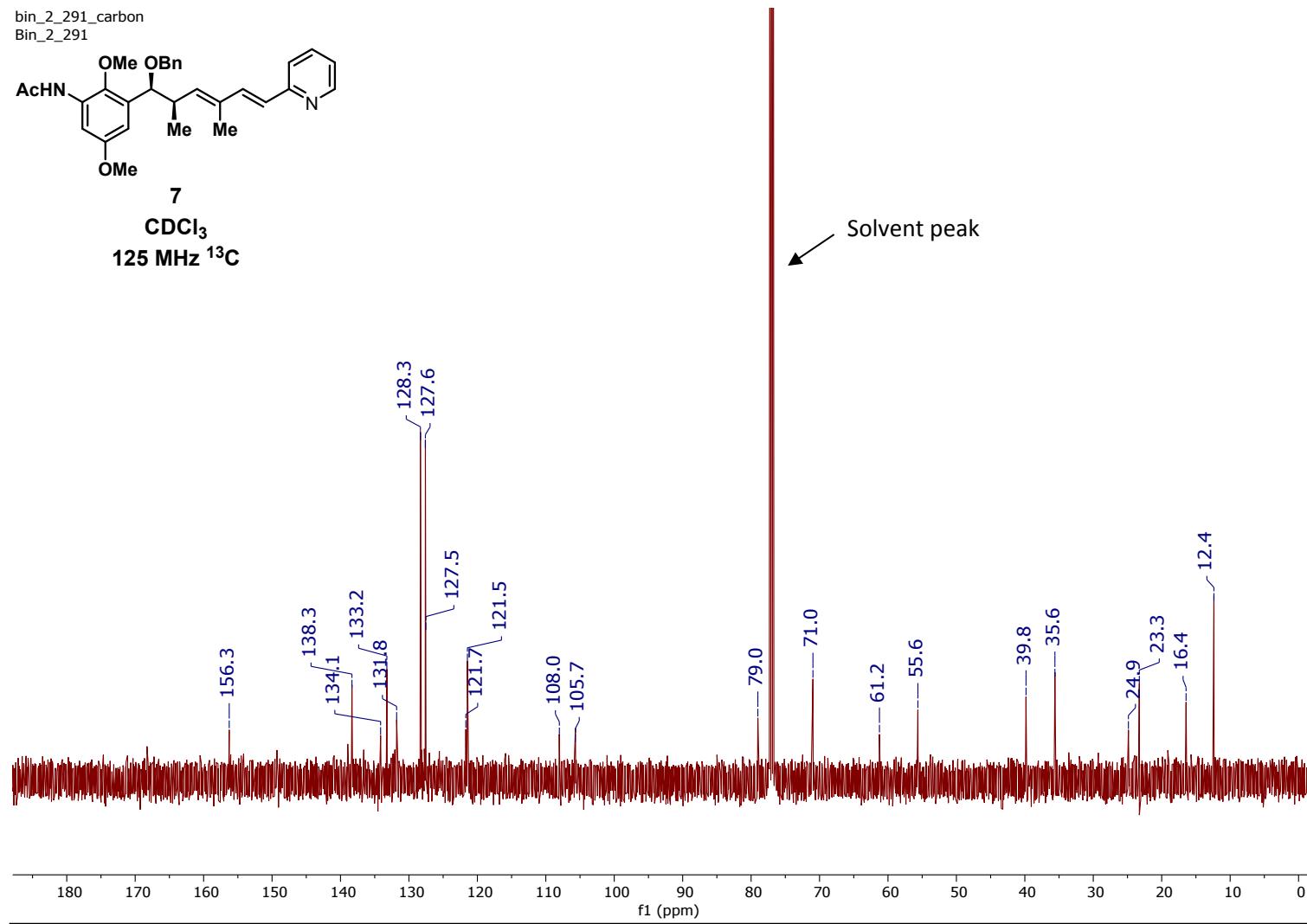
Part III:  $^1\text{H}$ - and  $^{13}\text{C}$ -NMR Spectra:

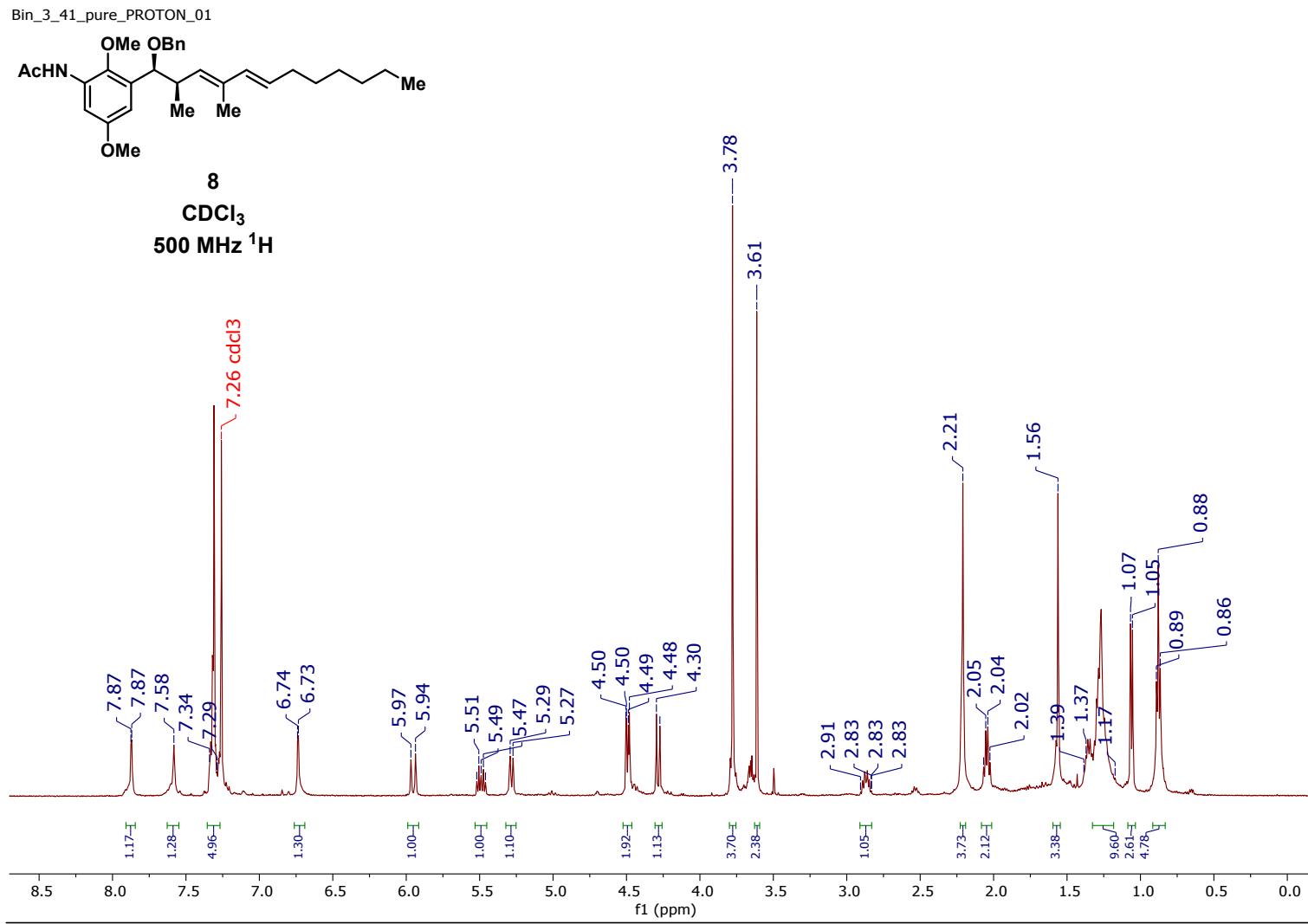


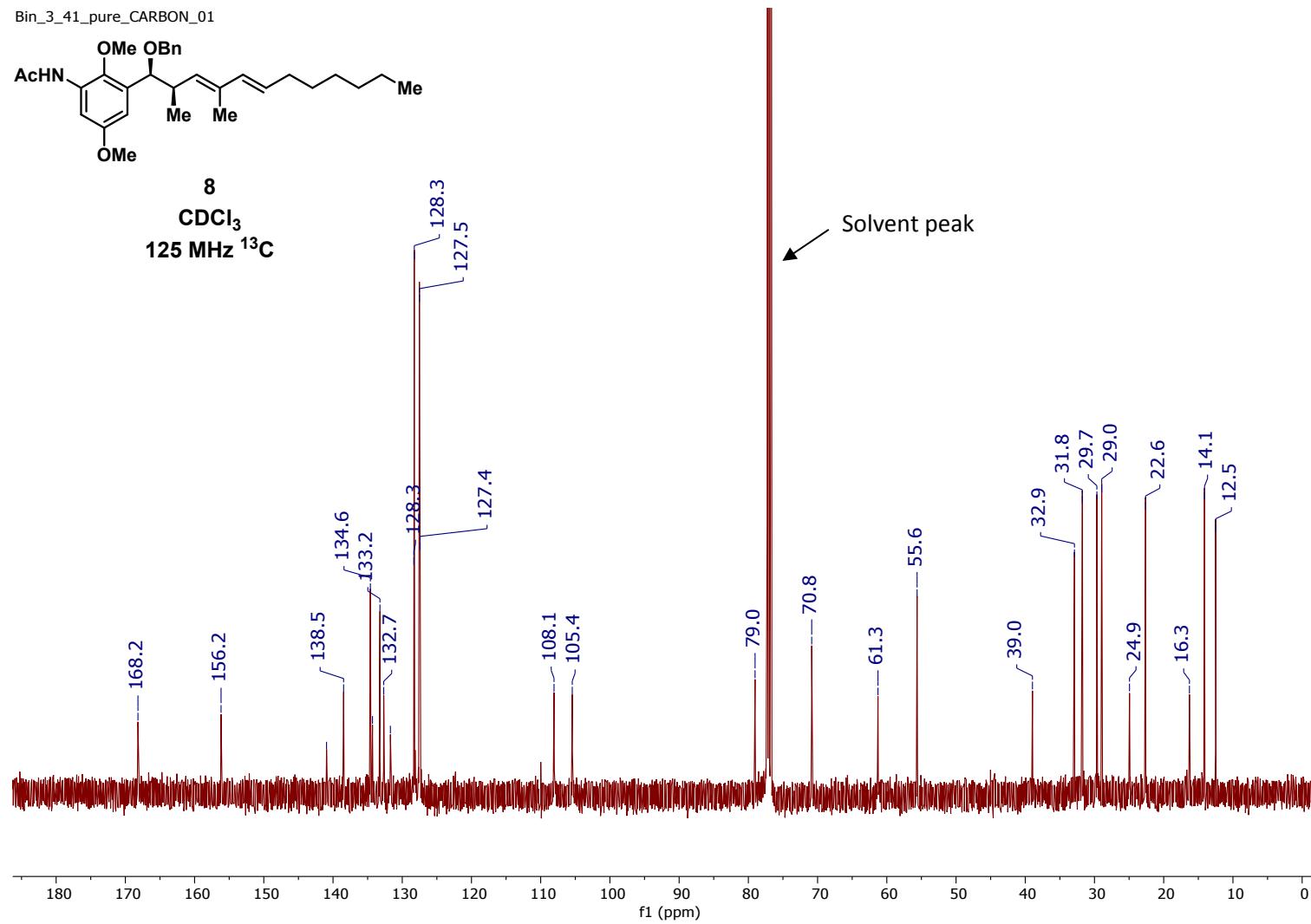




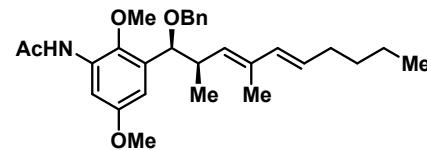
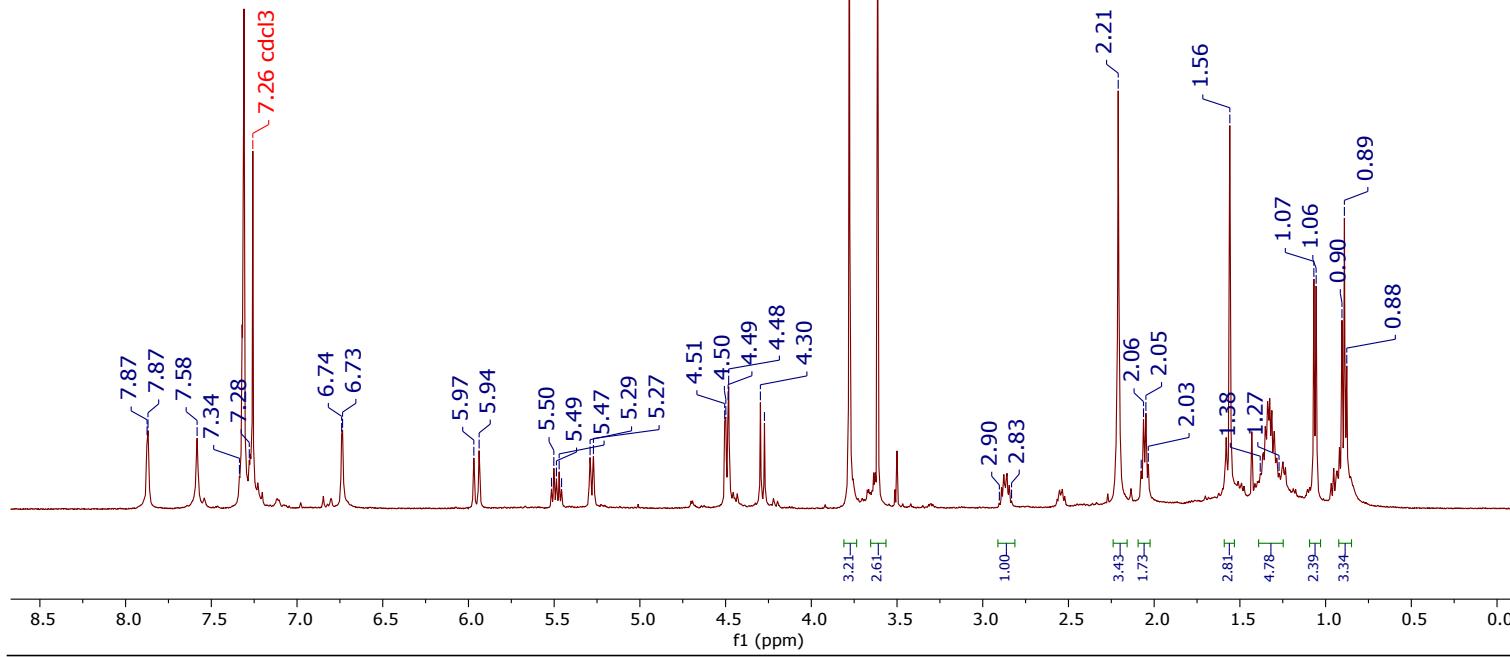


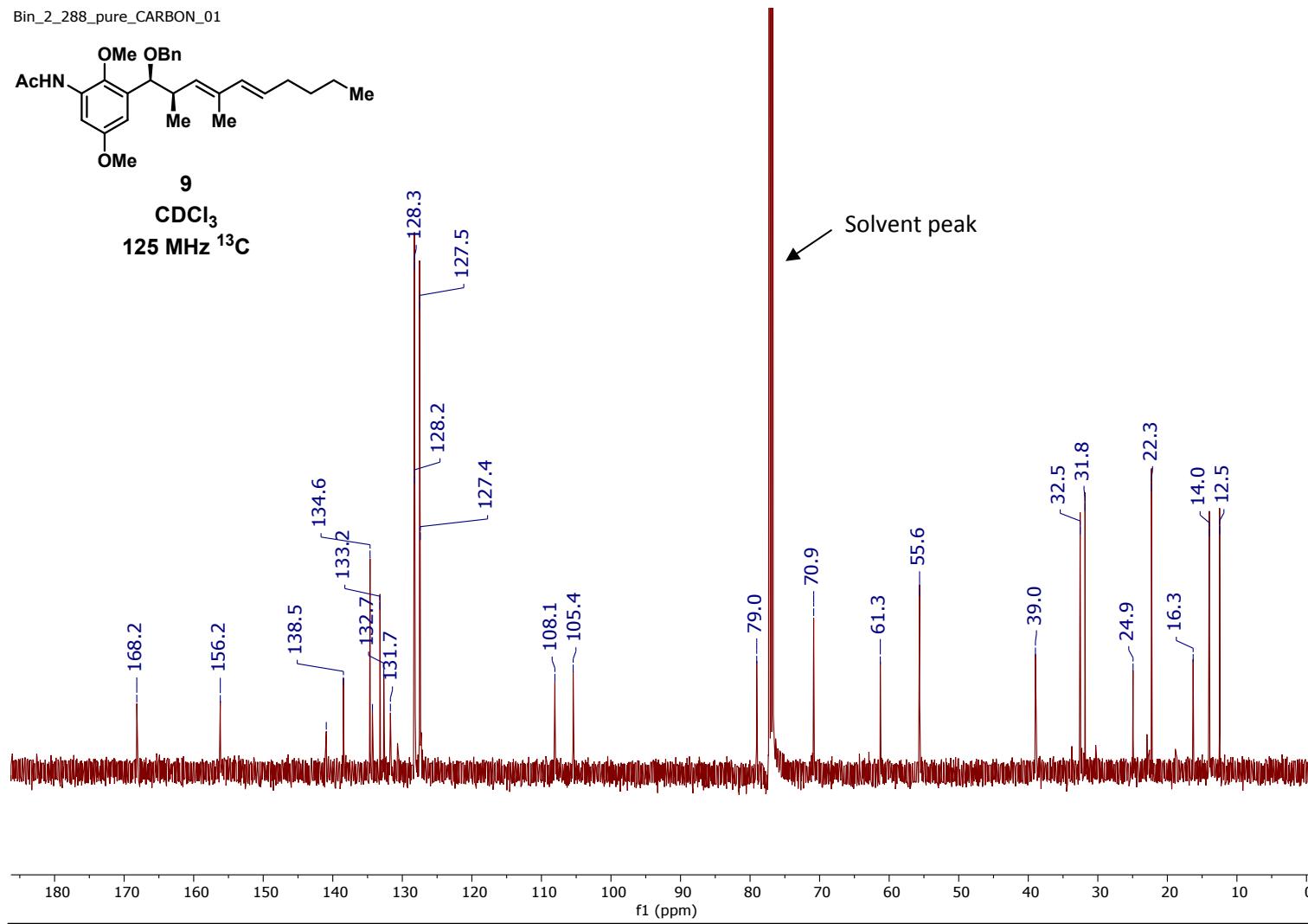


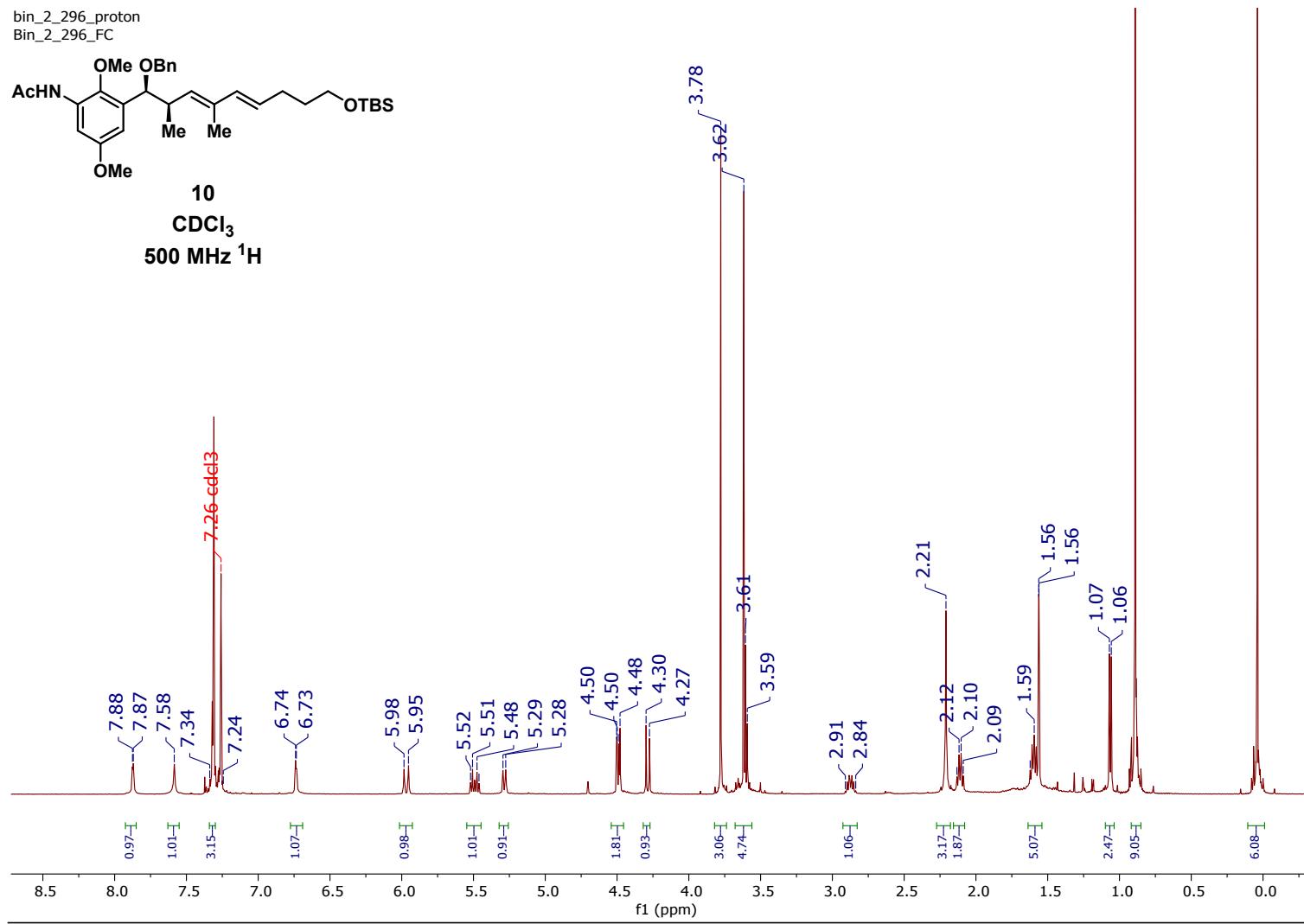


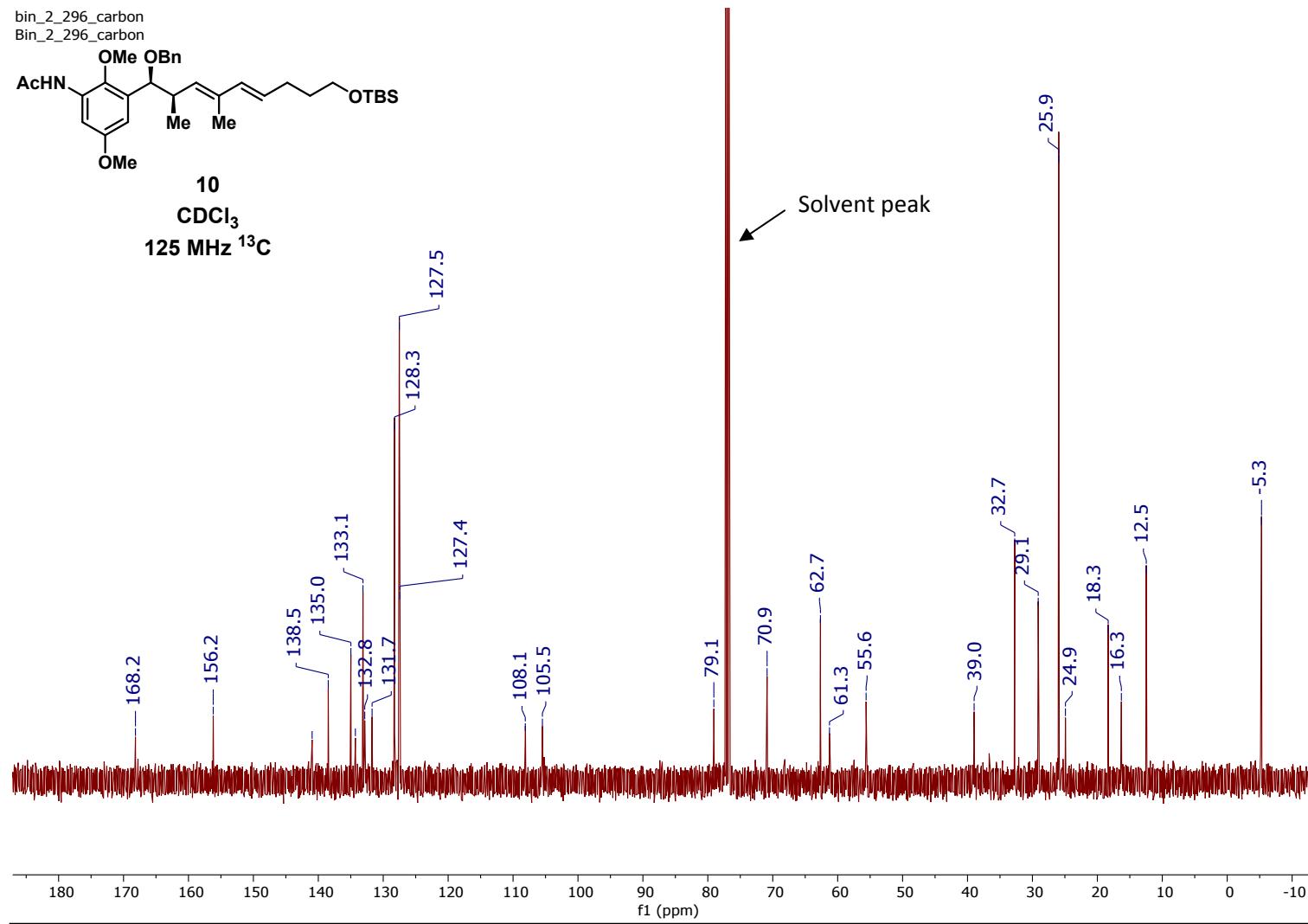


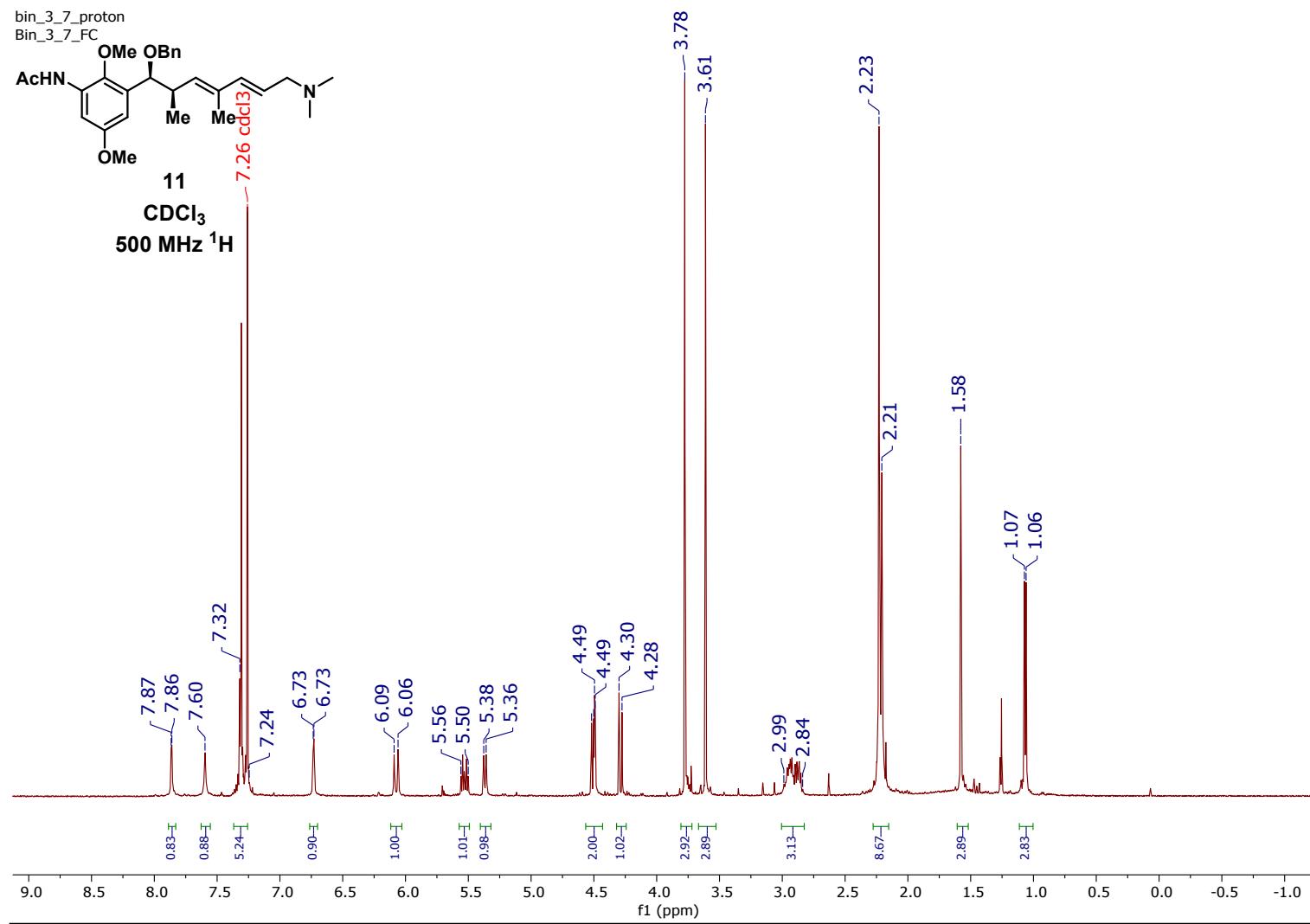
Bin\_2\_288\_pure\_PROTON\_01

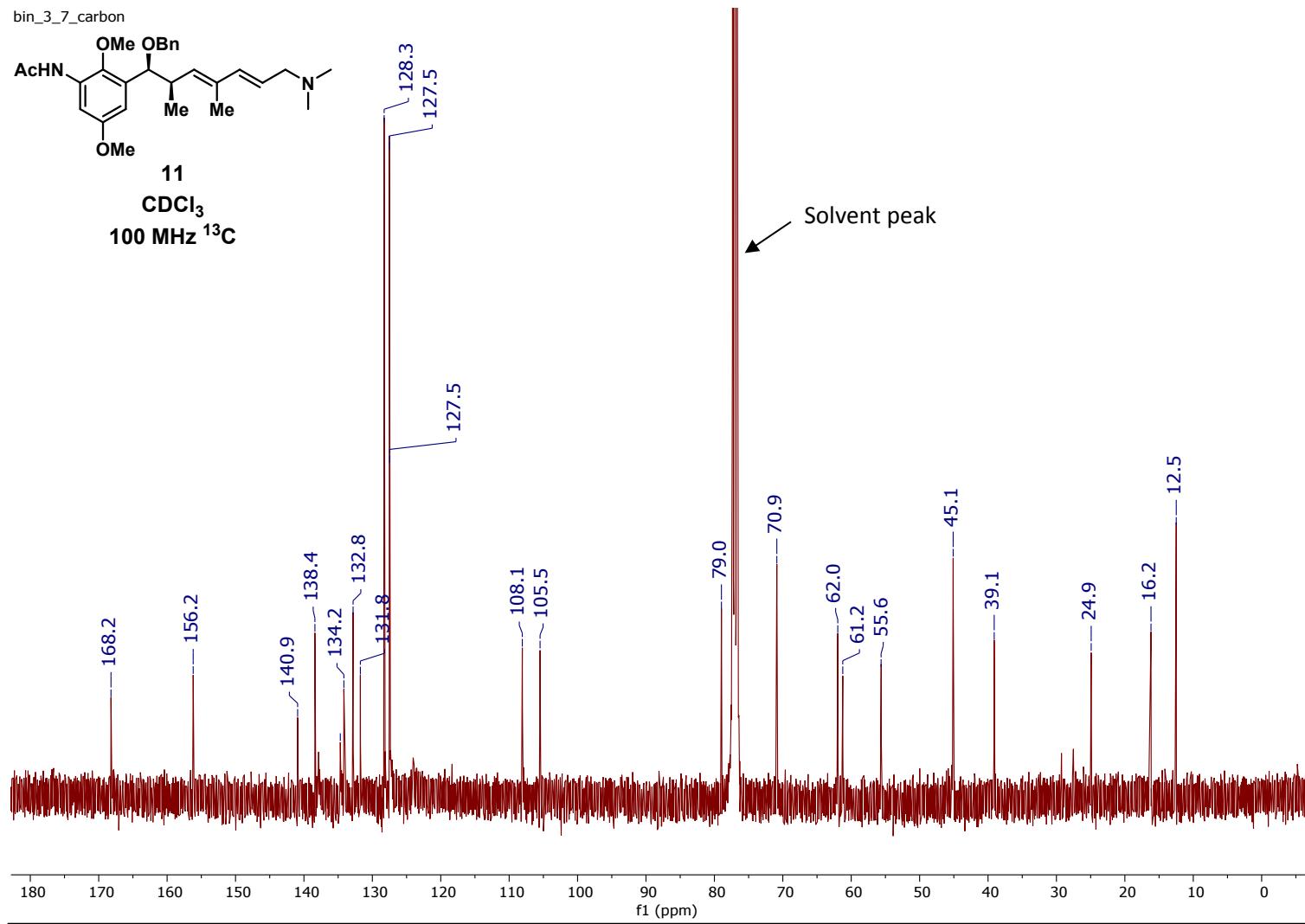
**9** $\text{CDCl}_3$   
500 MHz  $^1\text{H}$ 

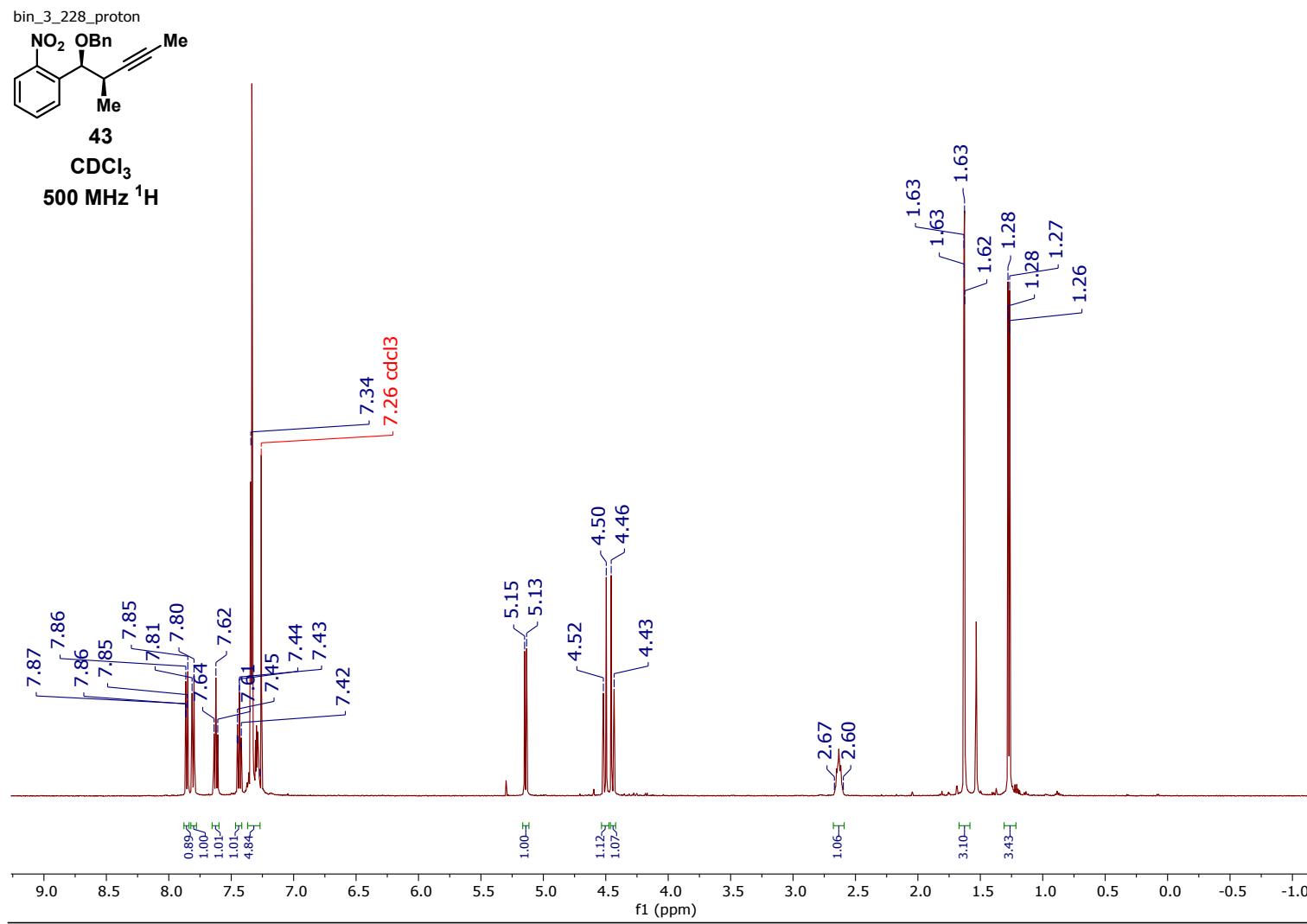


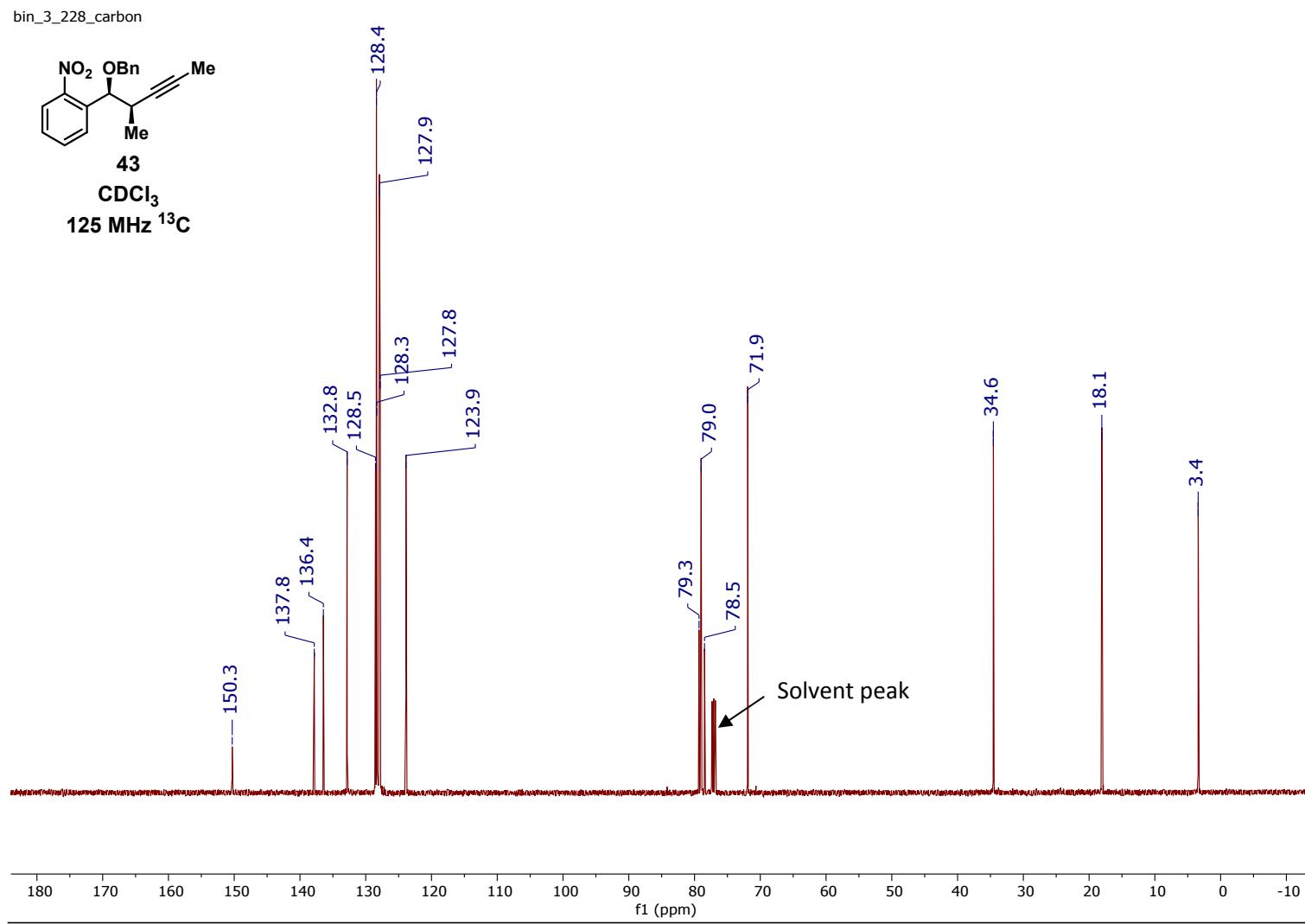


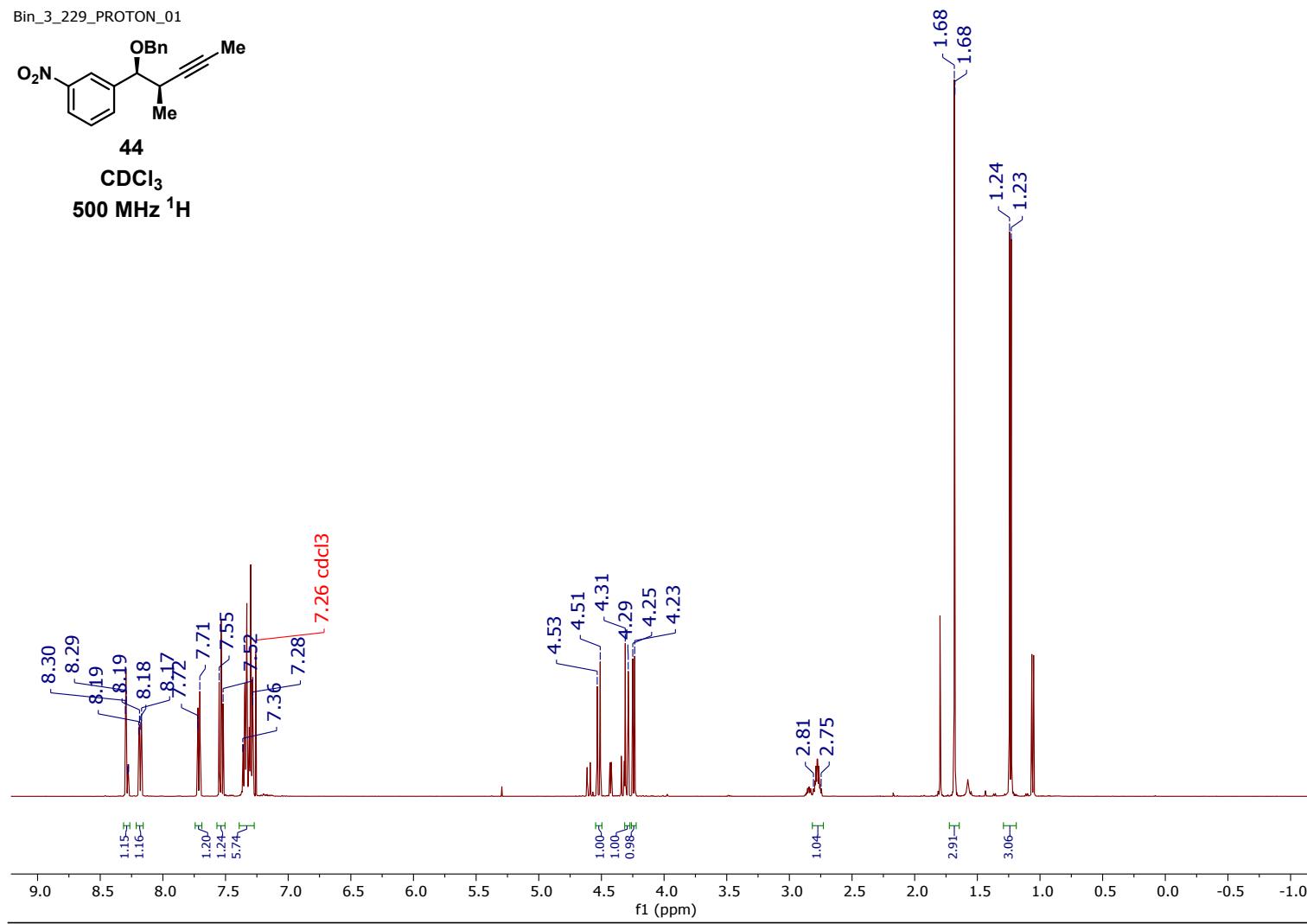


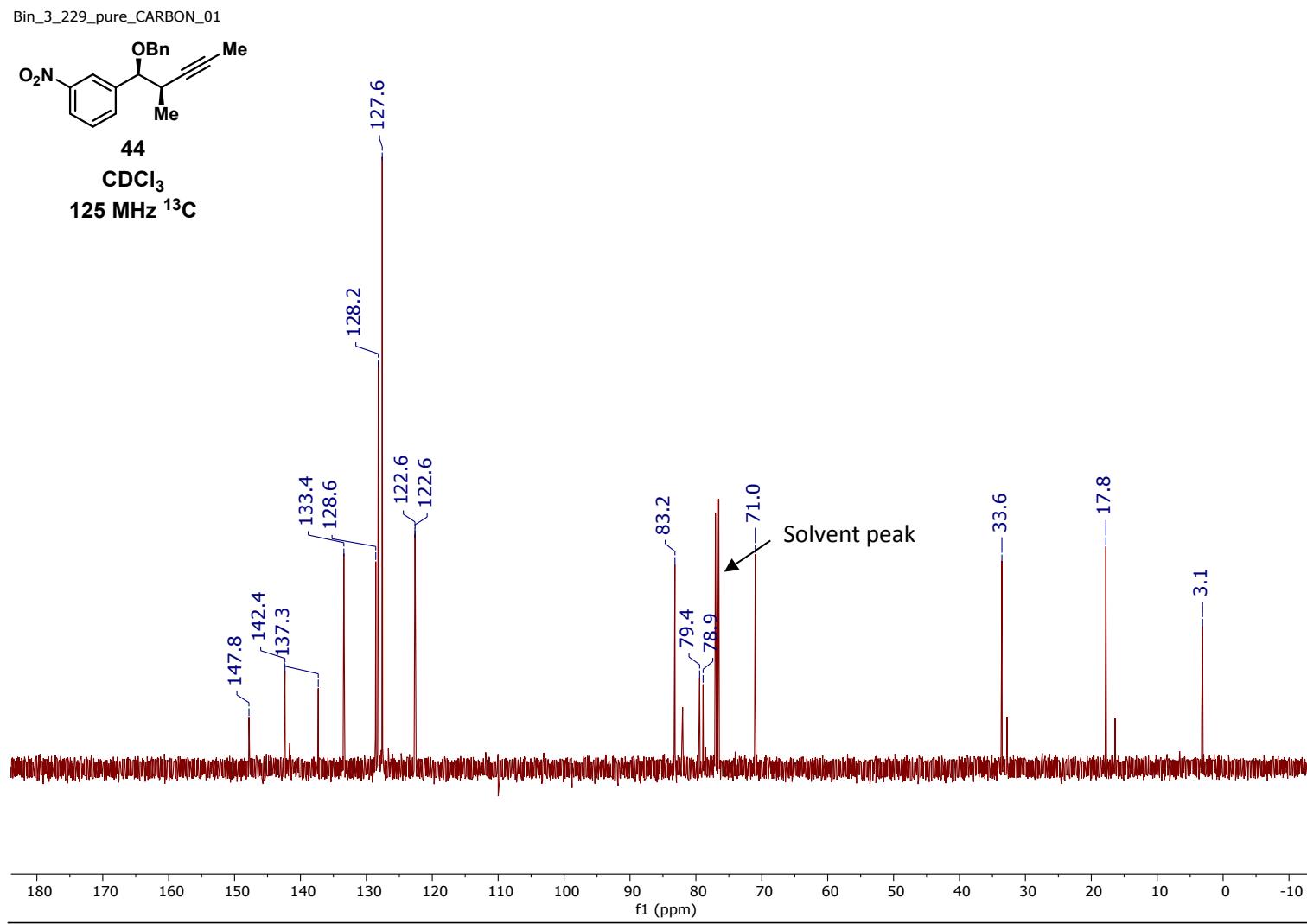


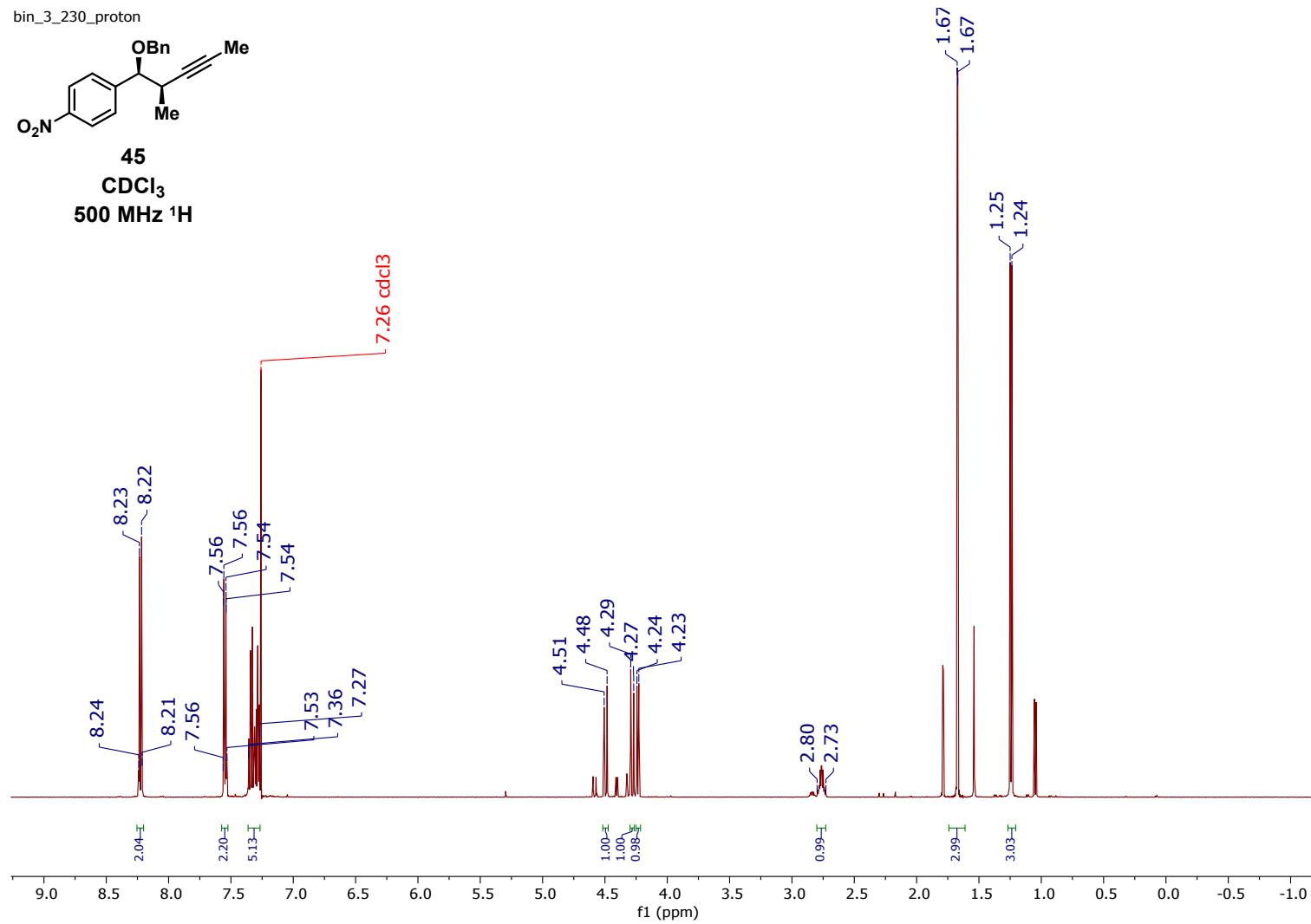


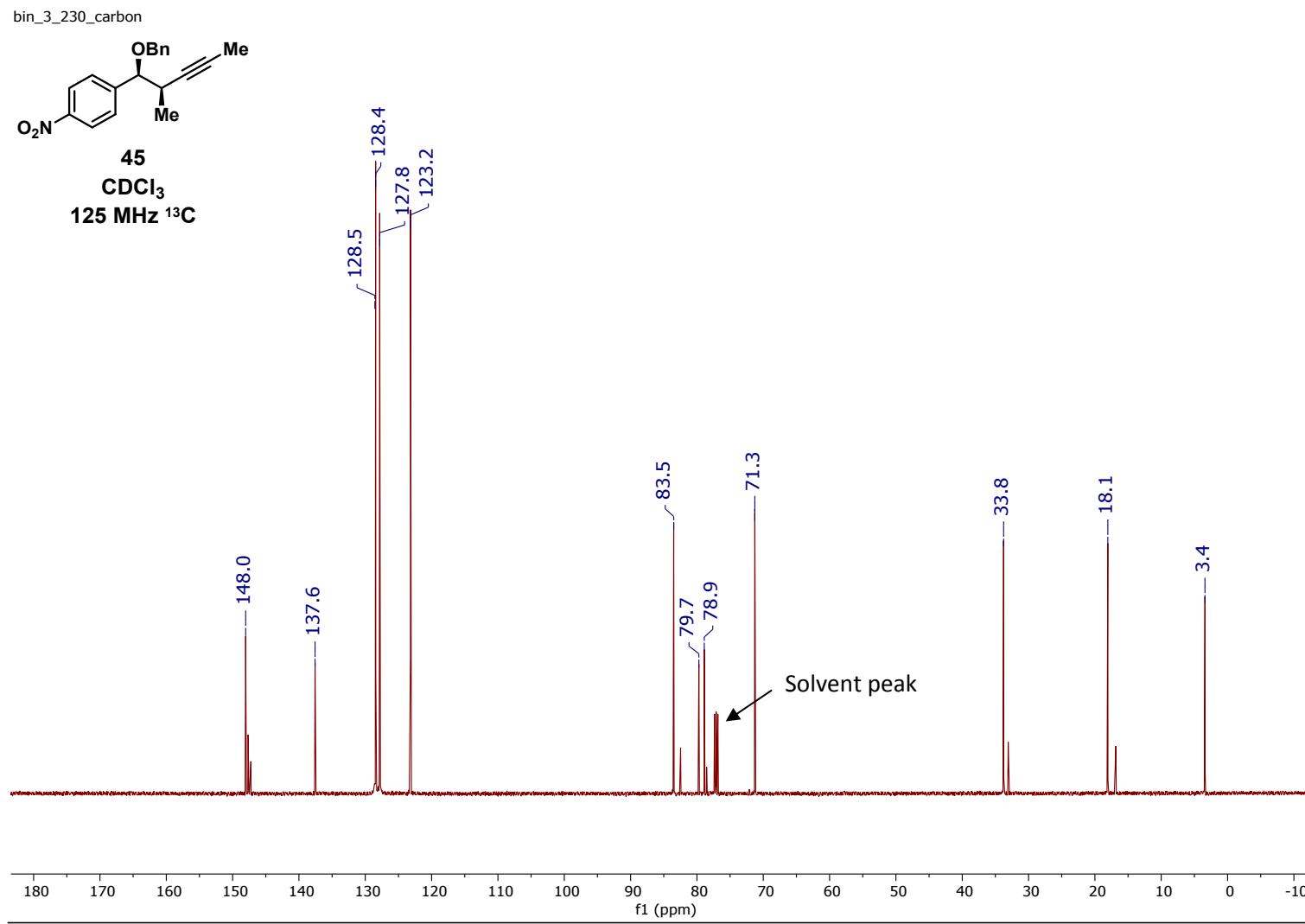


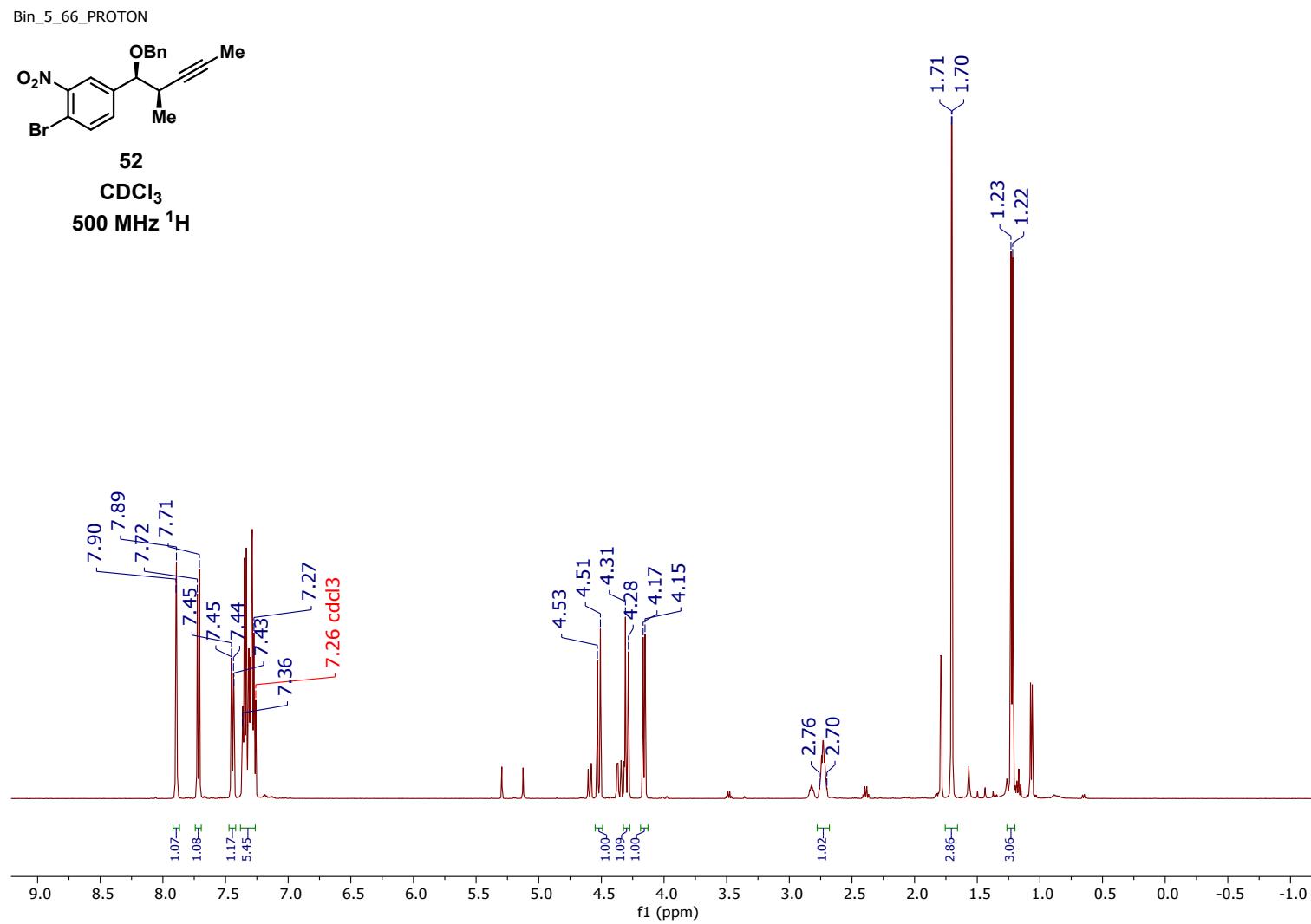


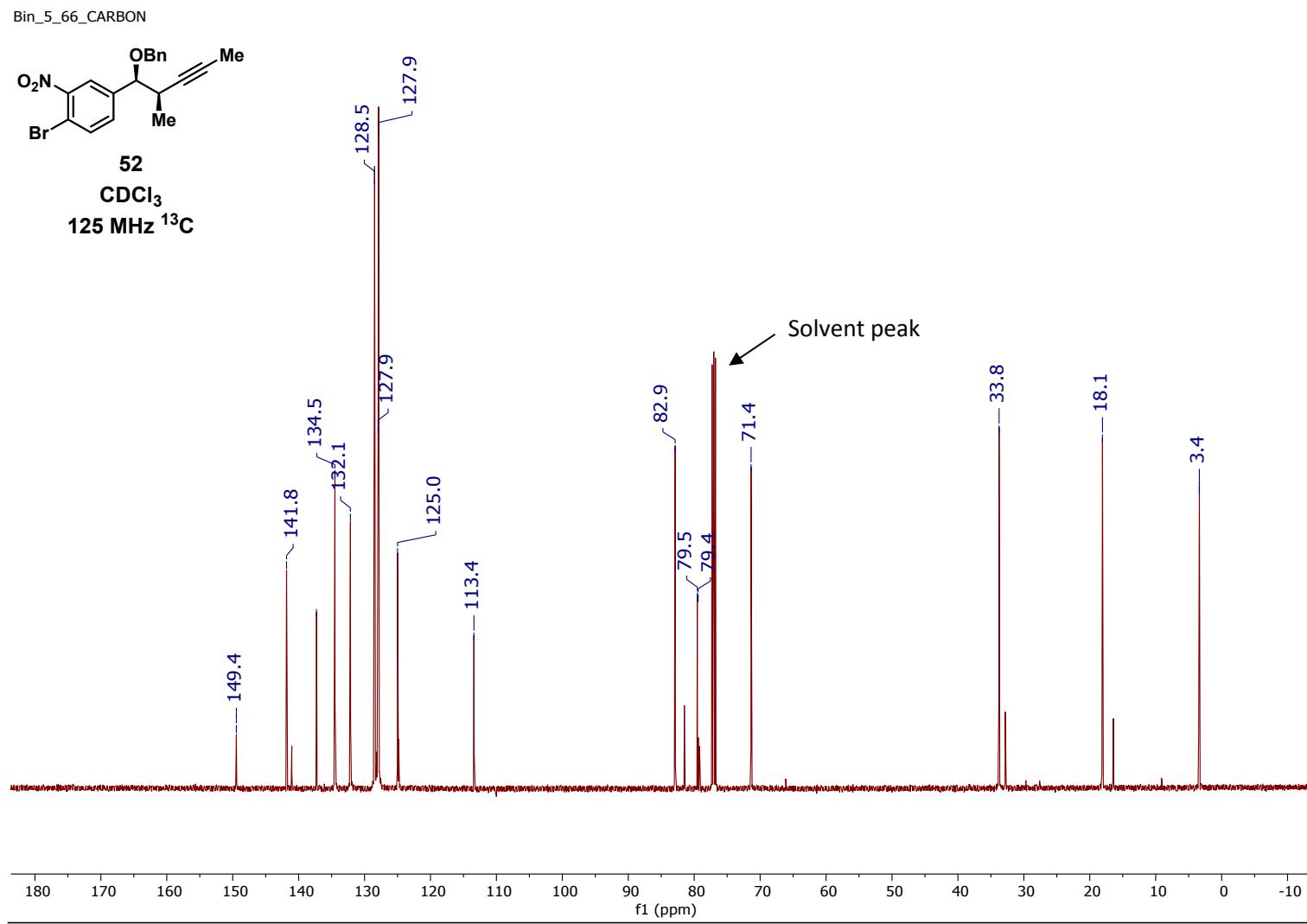


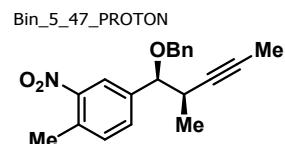








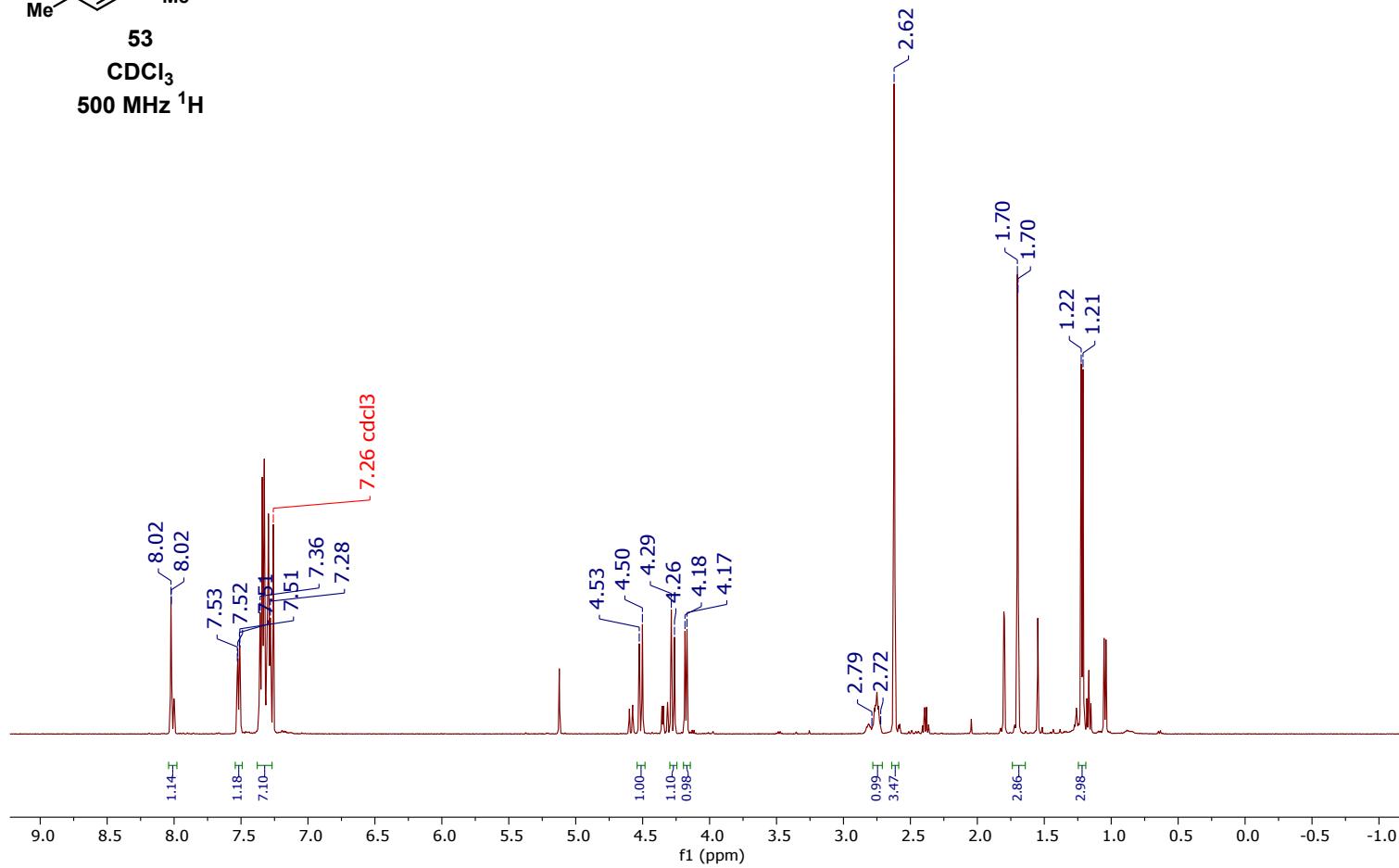


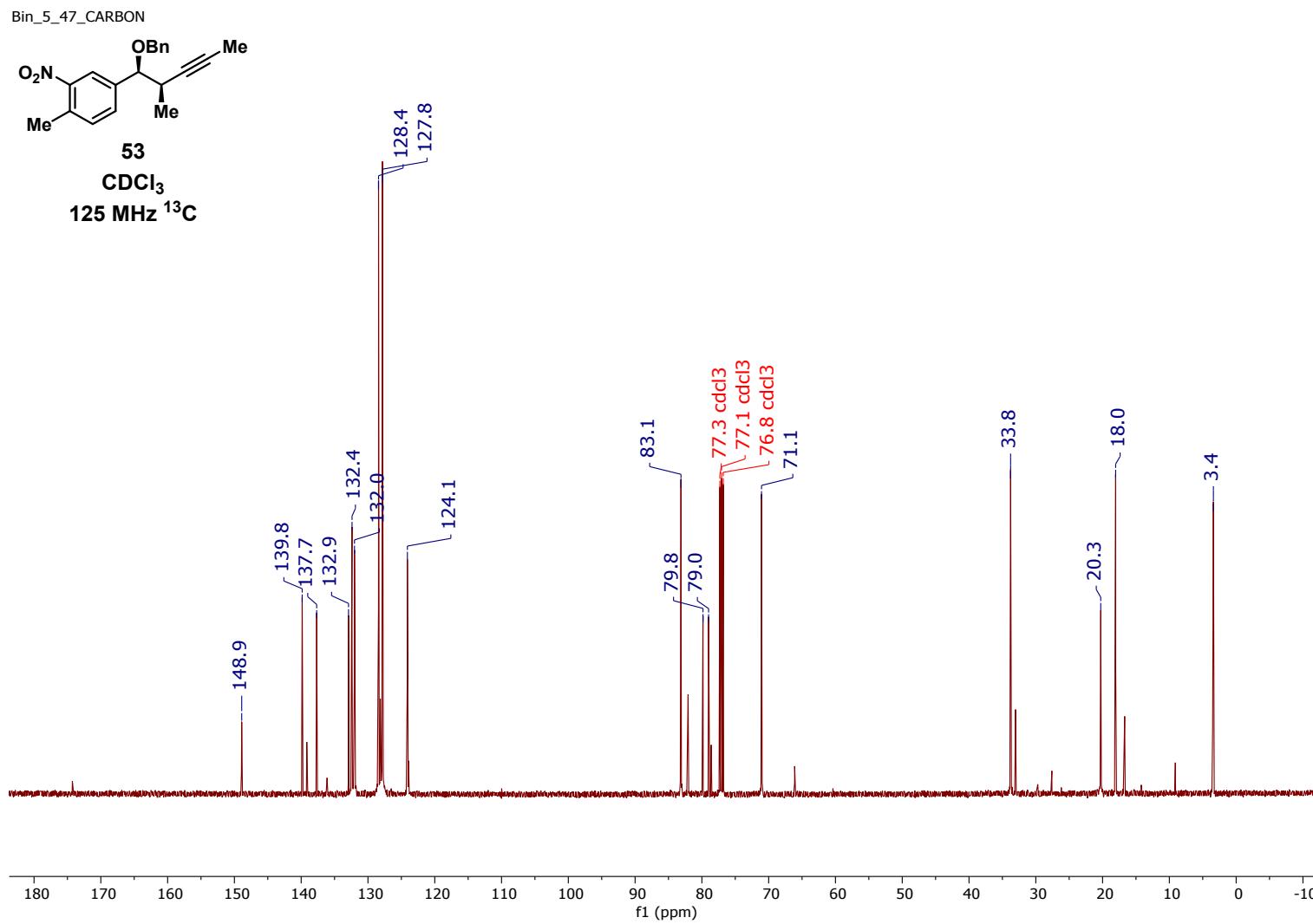


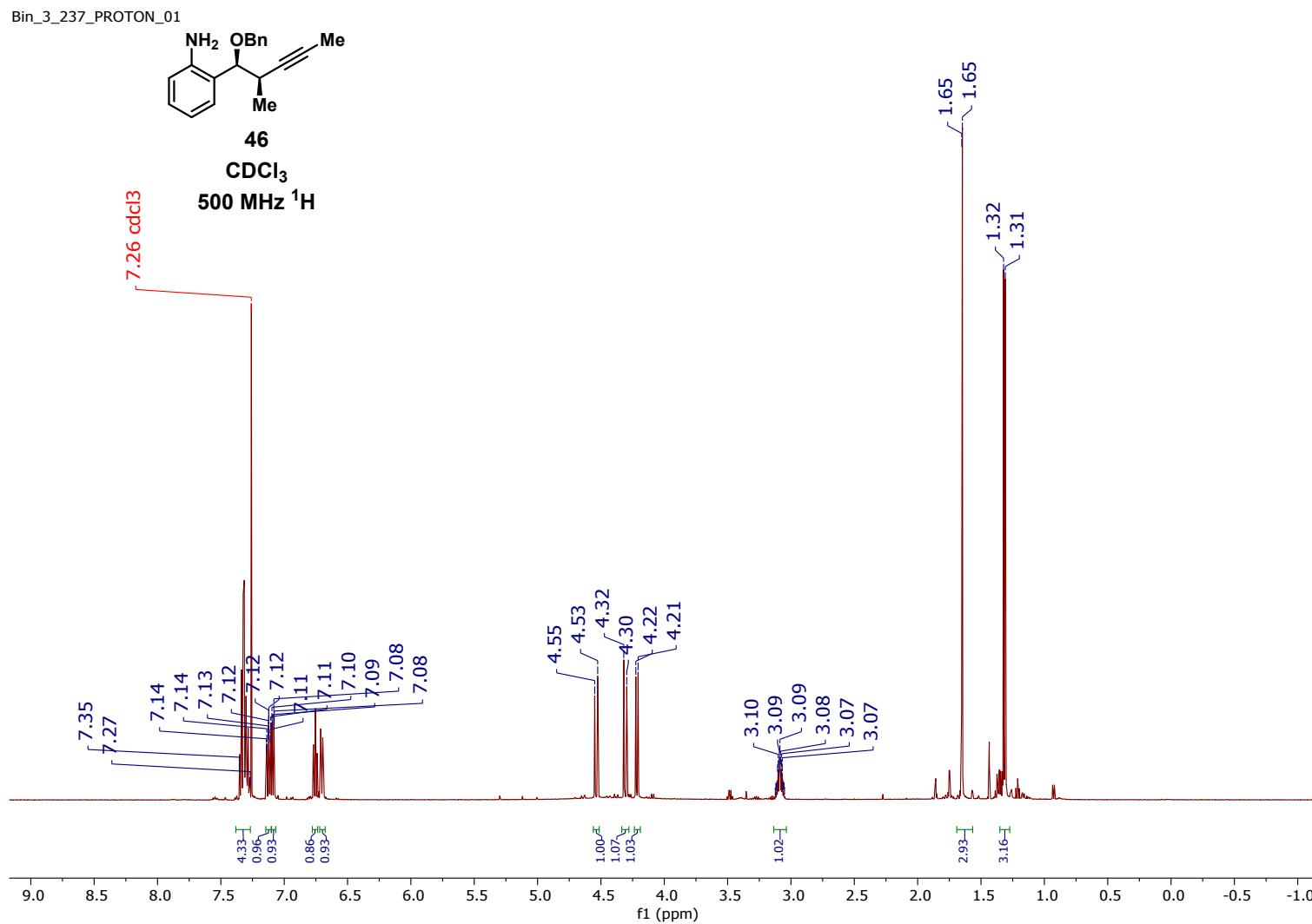
53

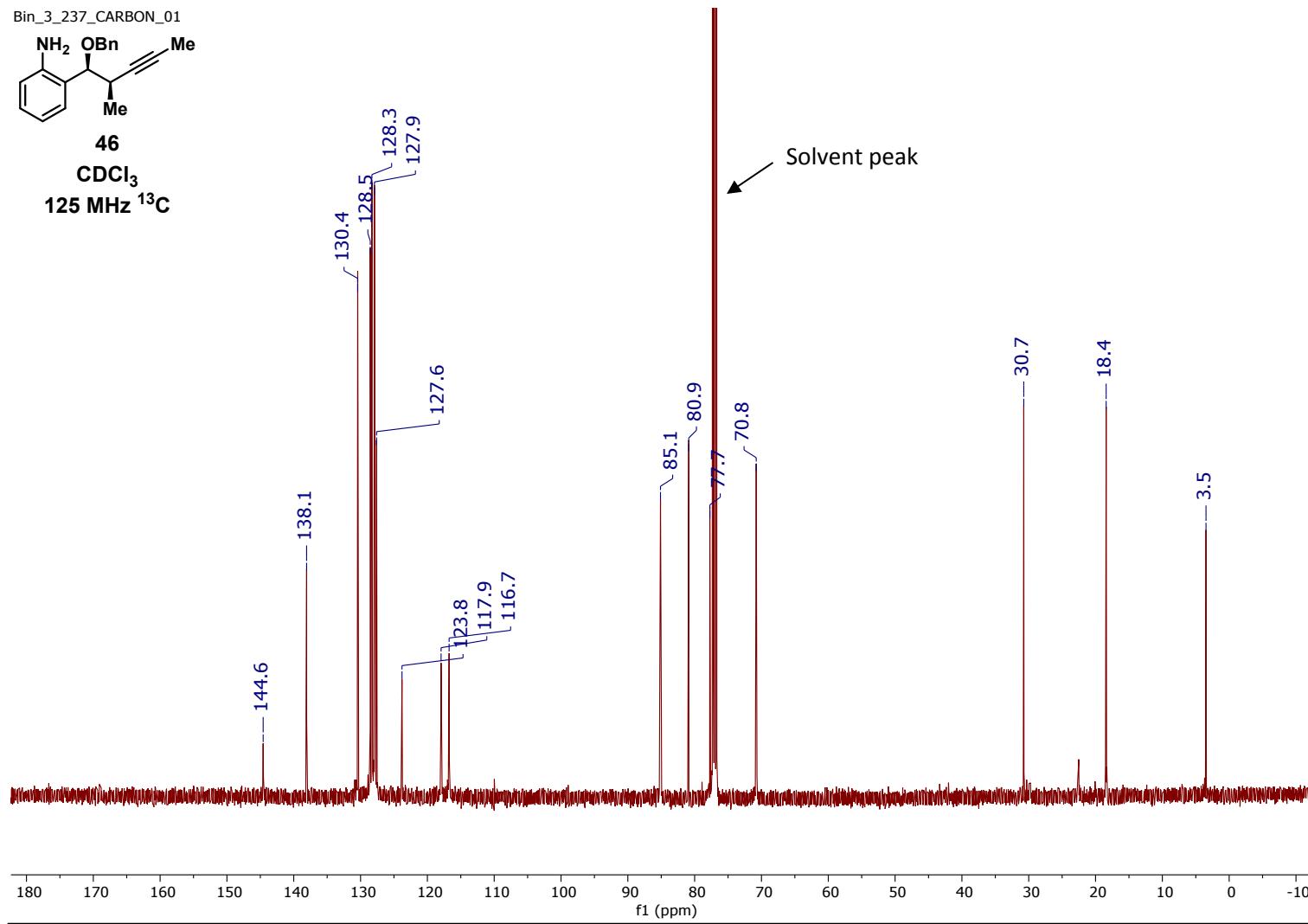
$\text{CDCl}_3$

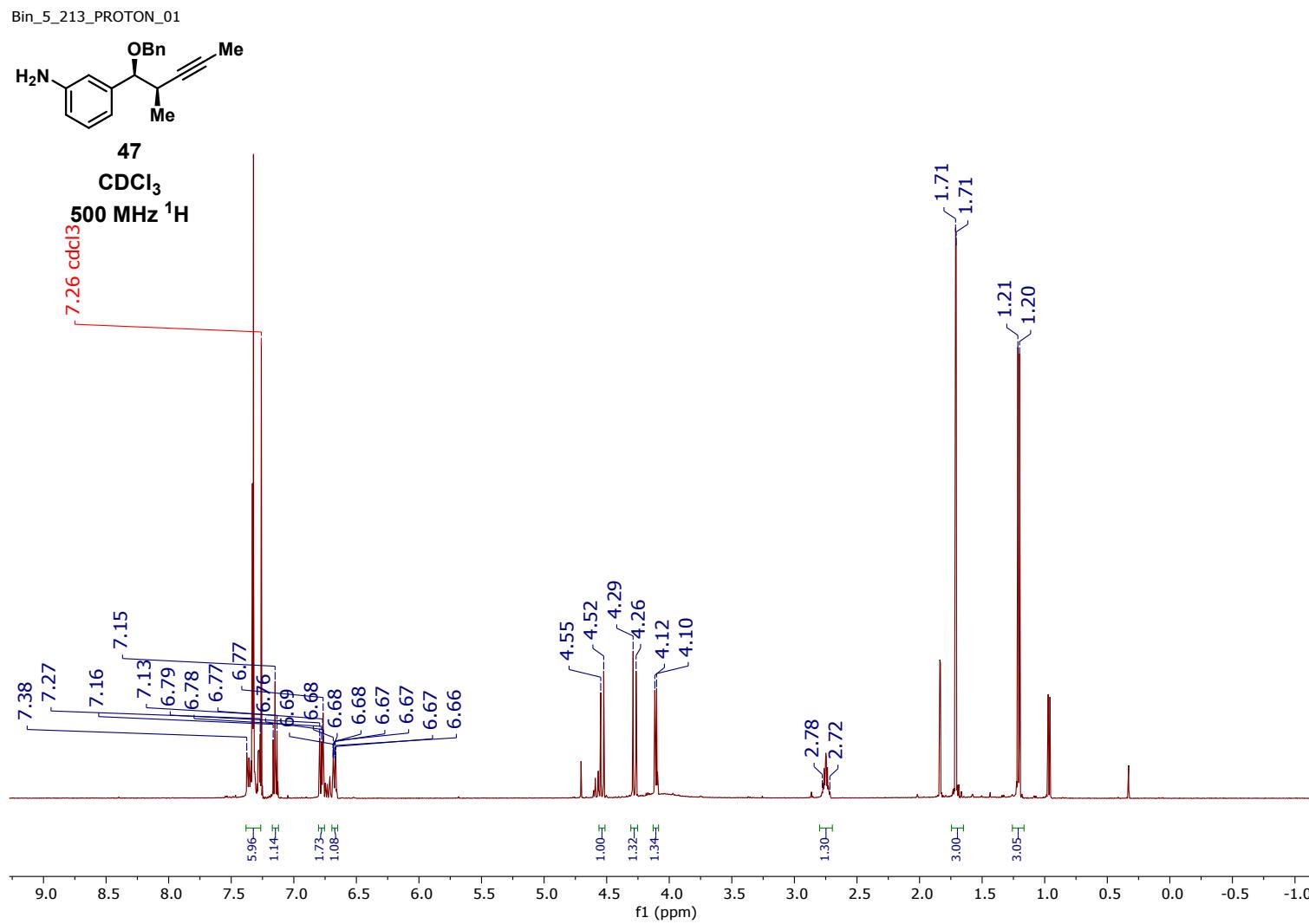
500 MHz  $^1\text{H}$



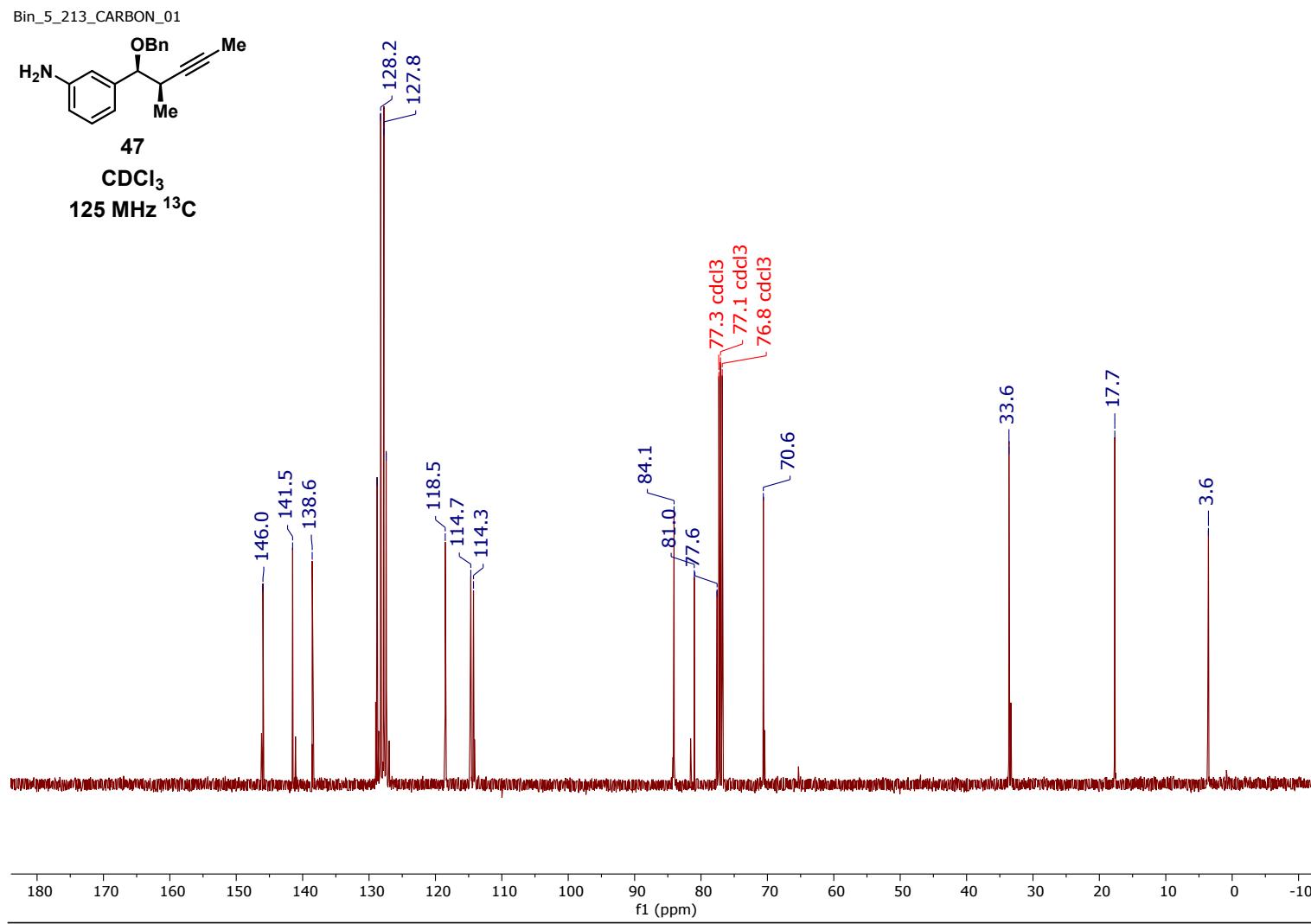


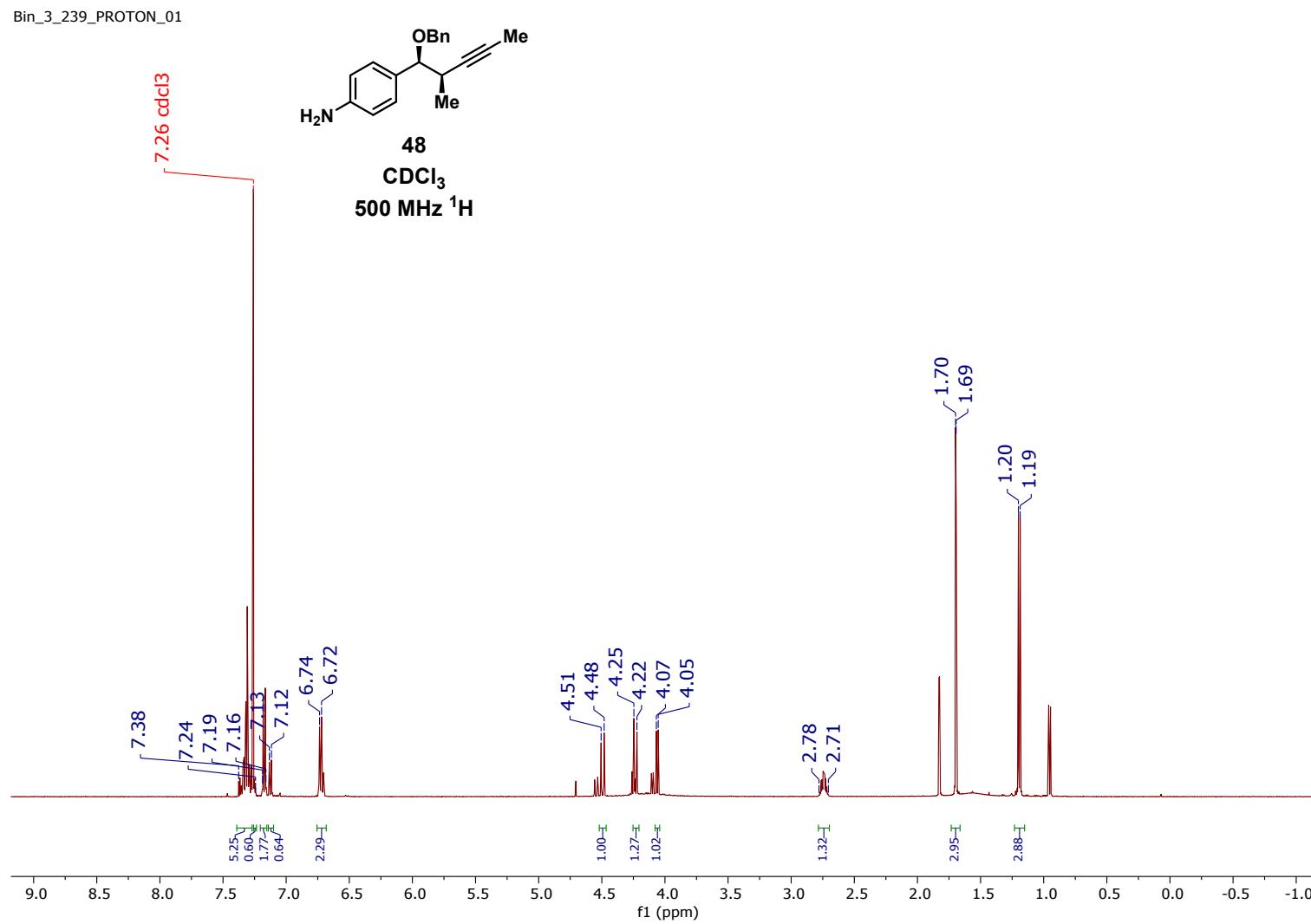


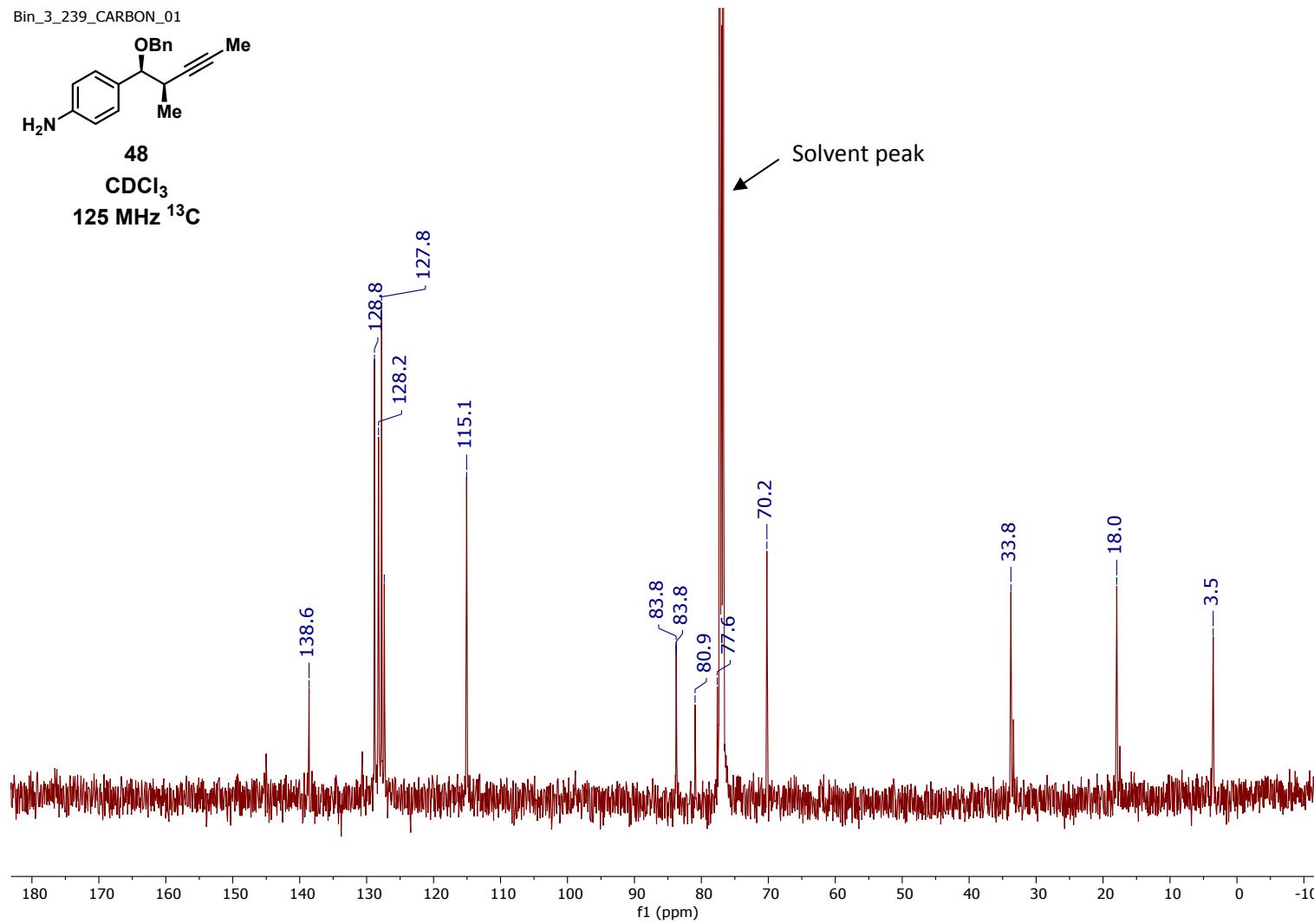


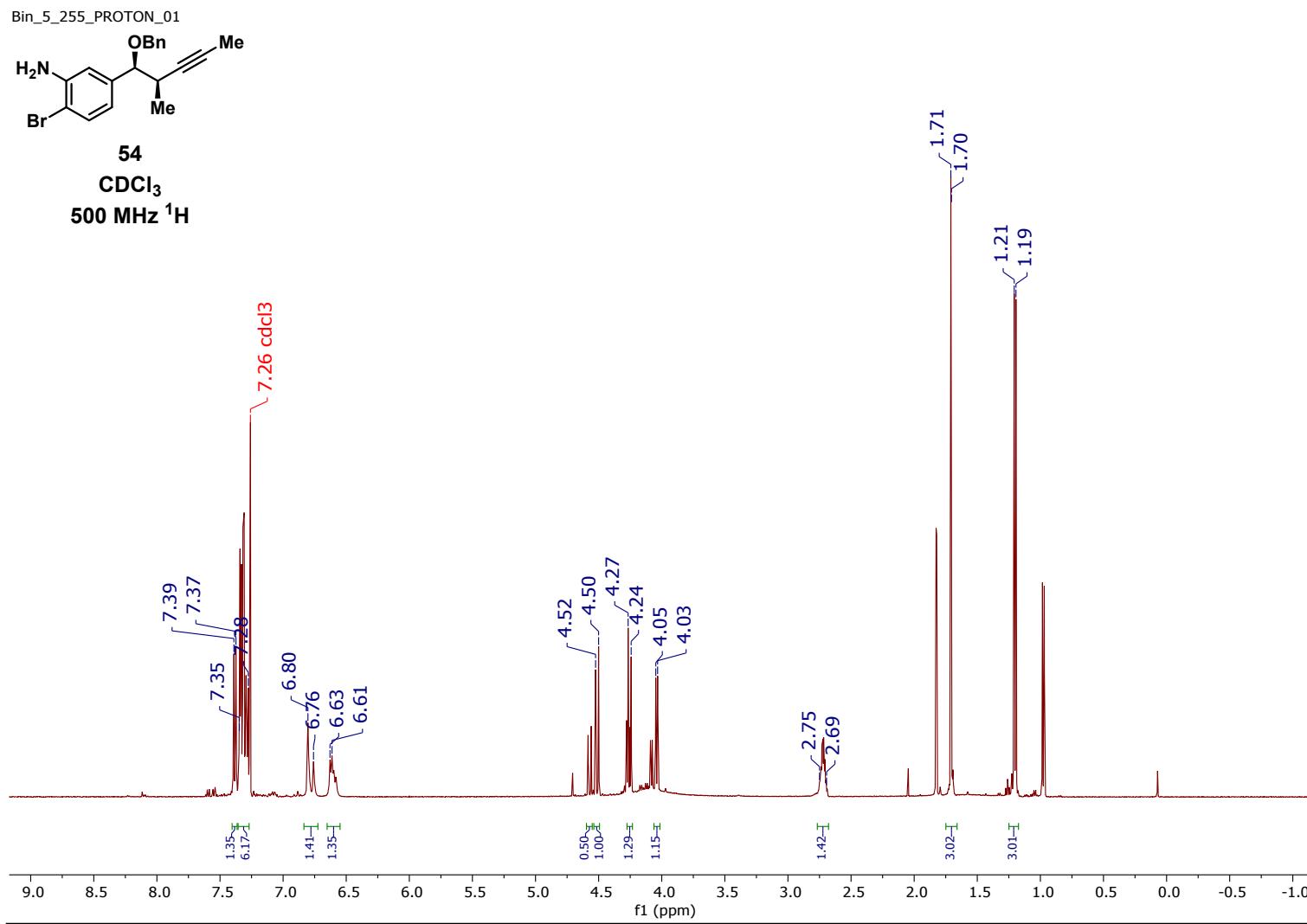


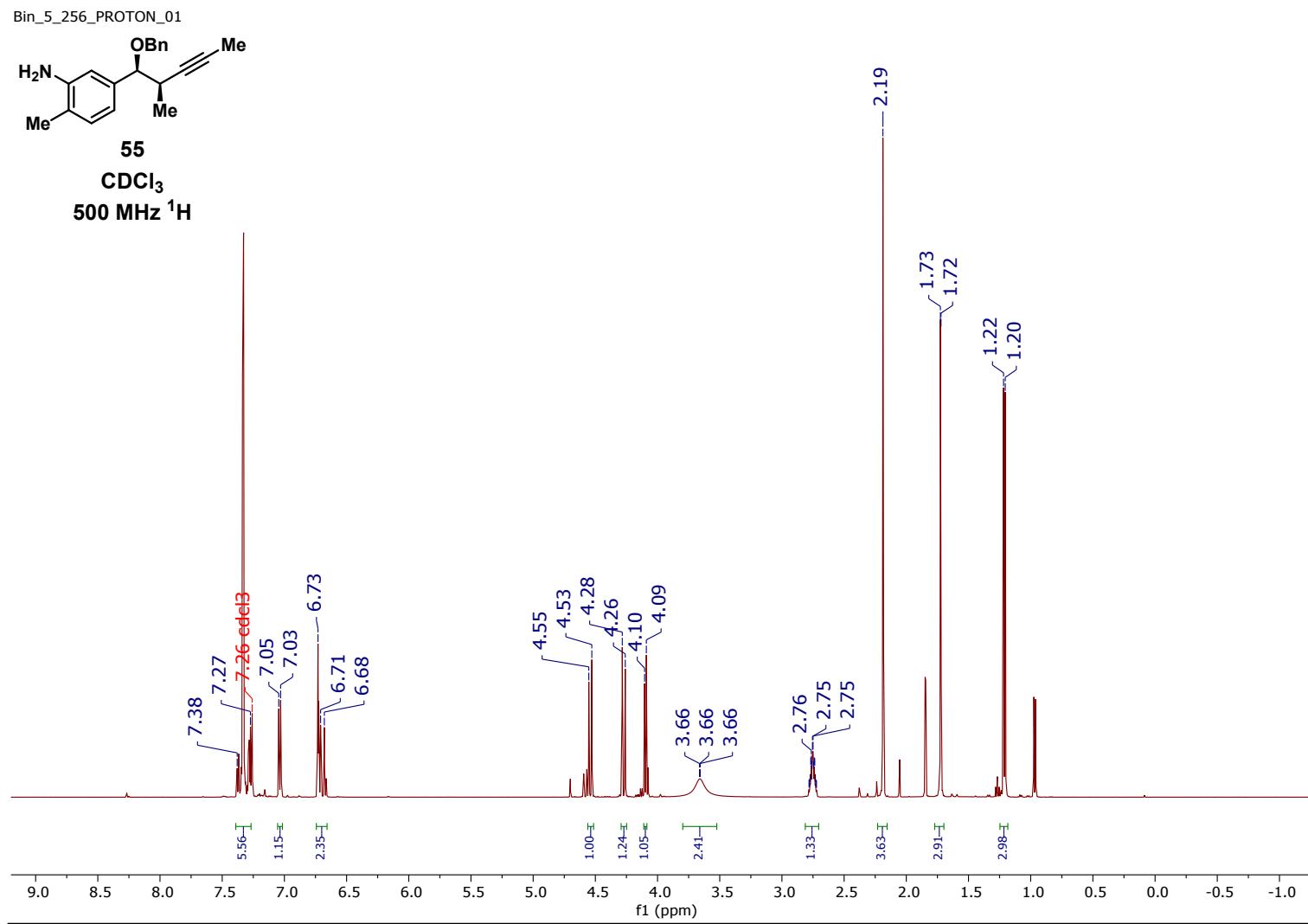
SI-133

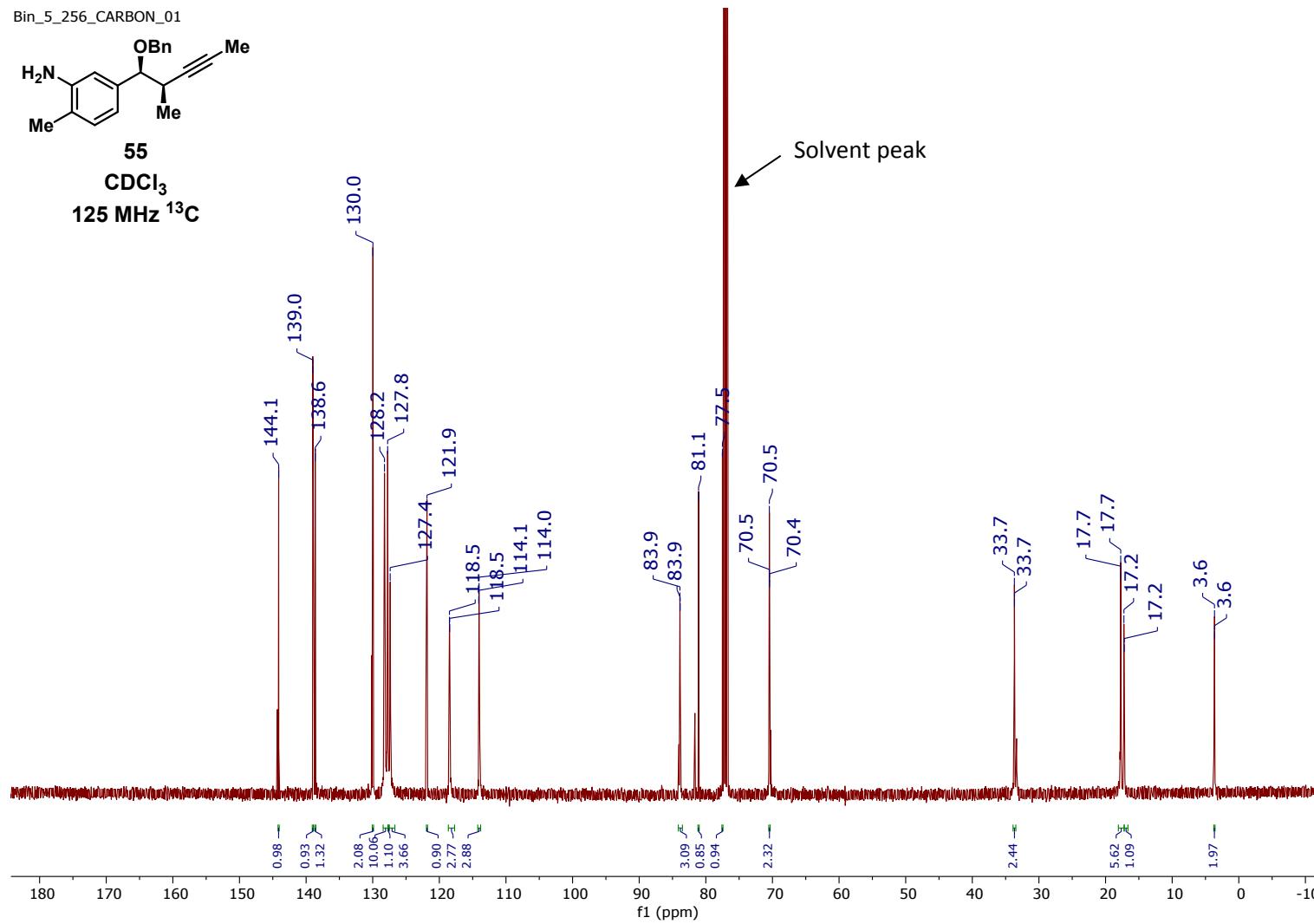




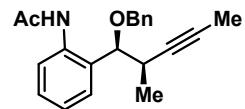
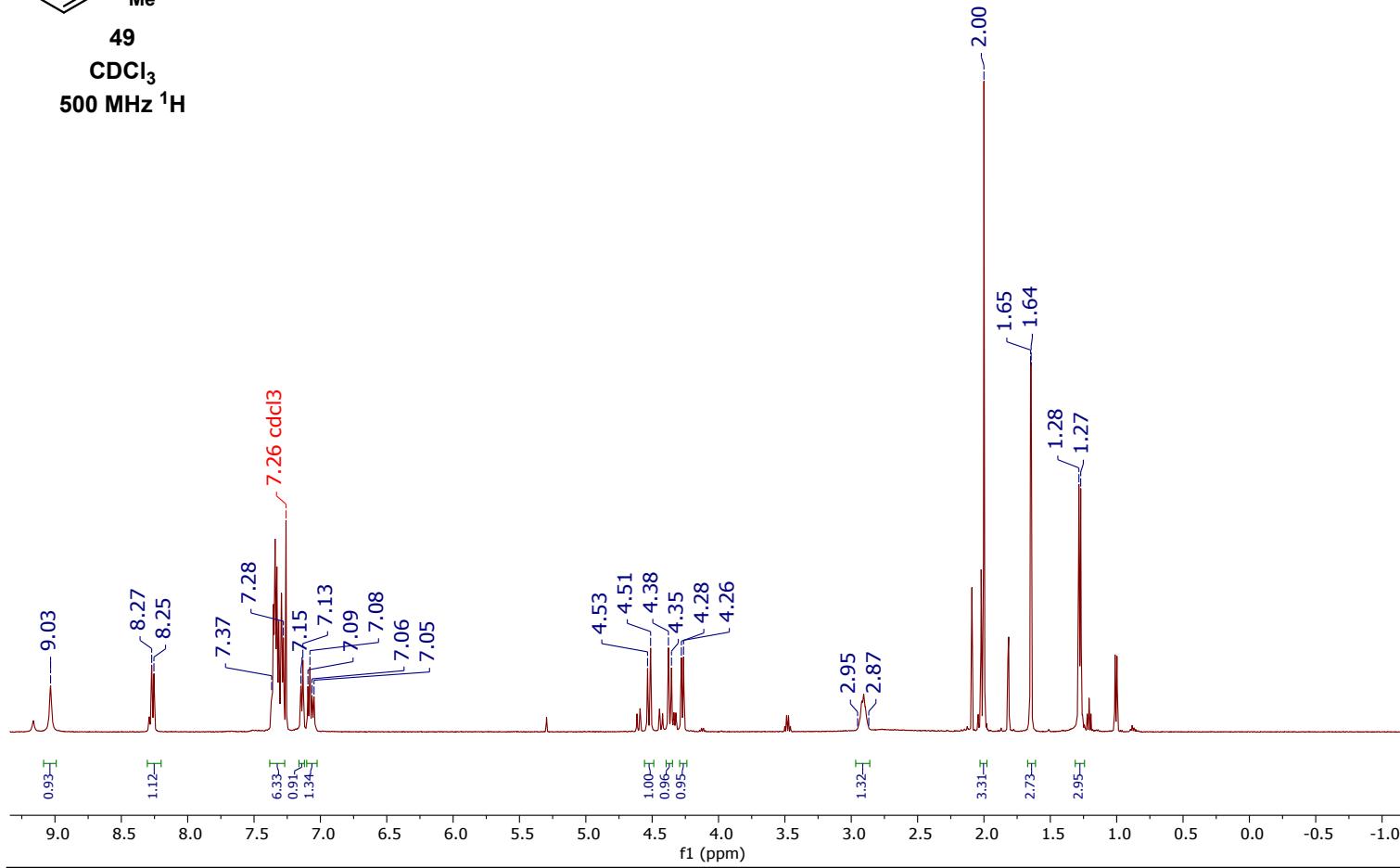


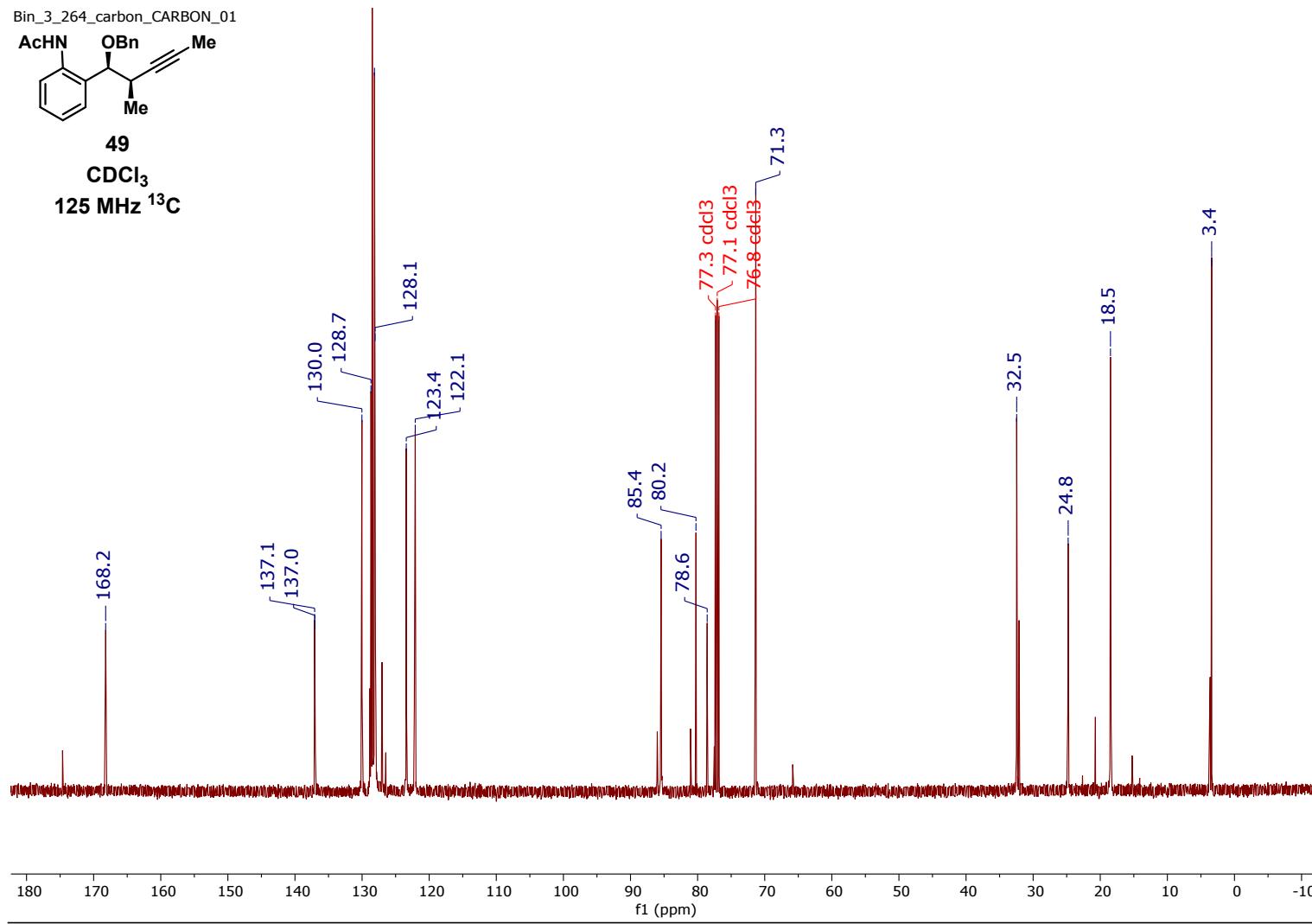


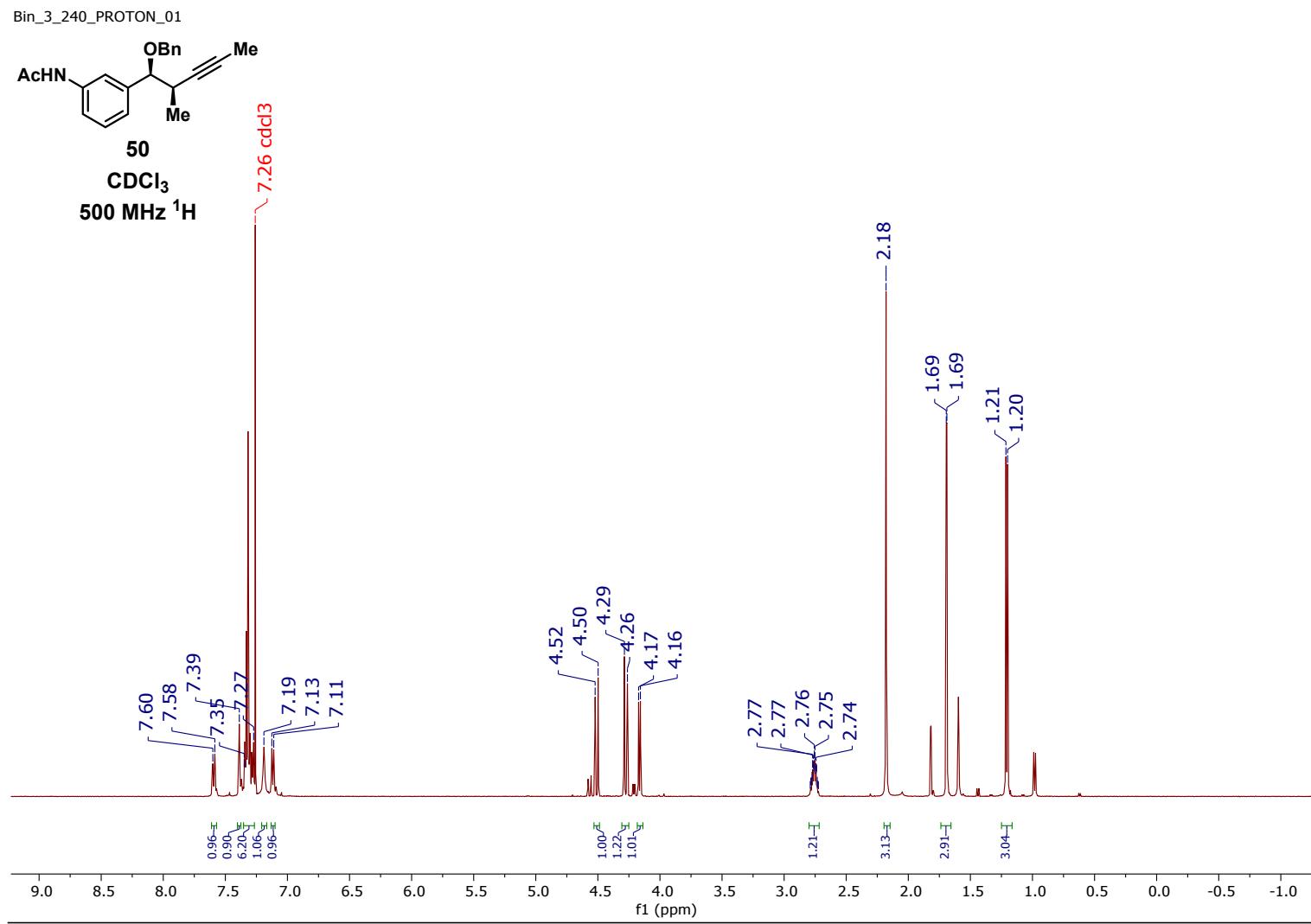


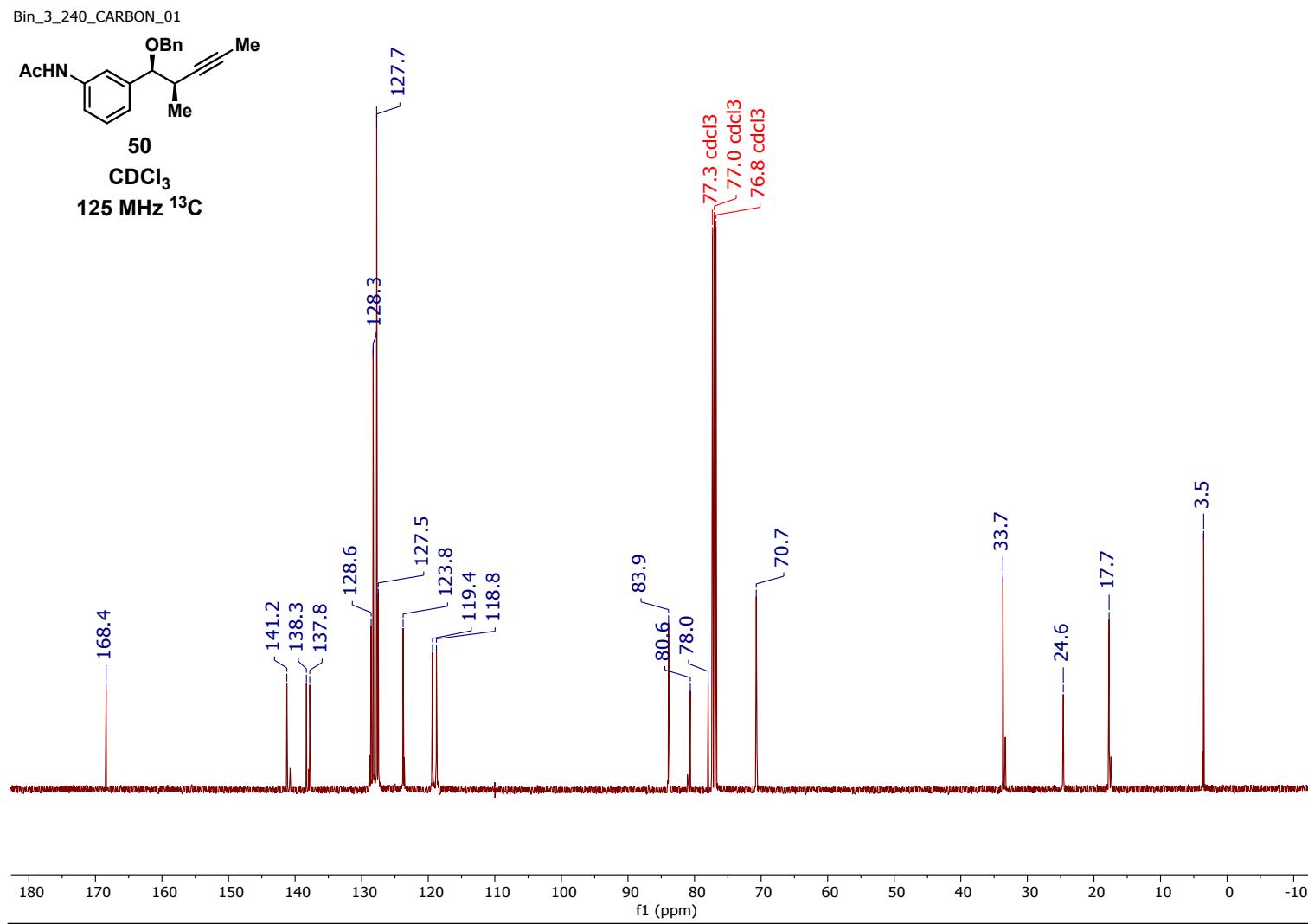


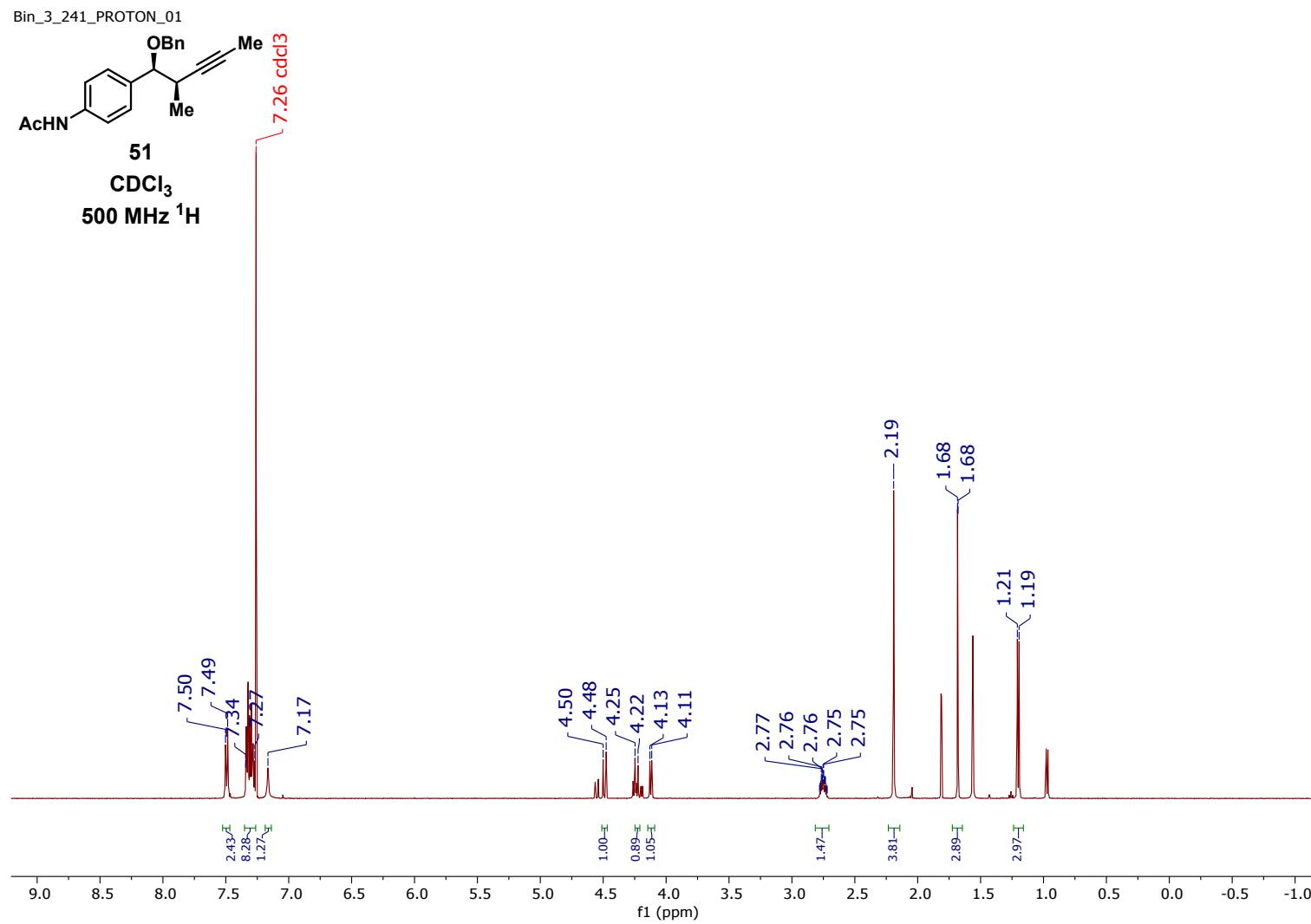
Bin\_3\_264\_proton\_PROTON\_01

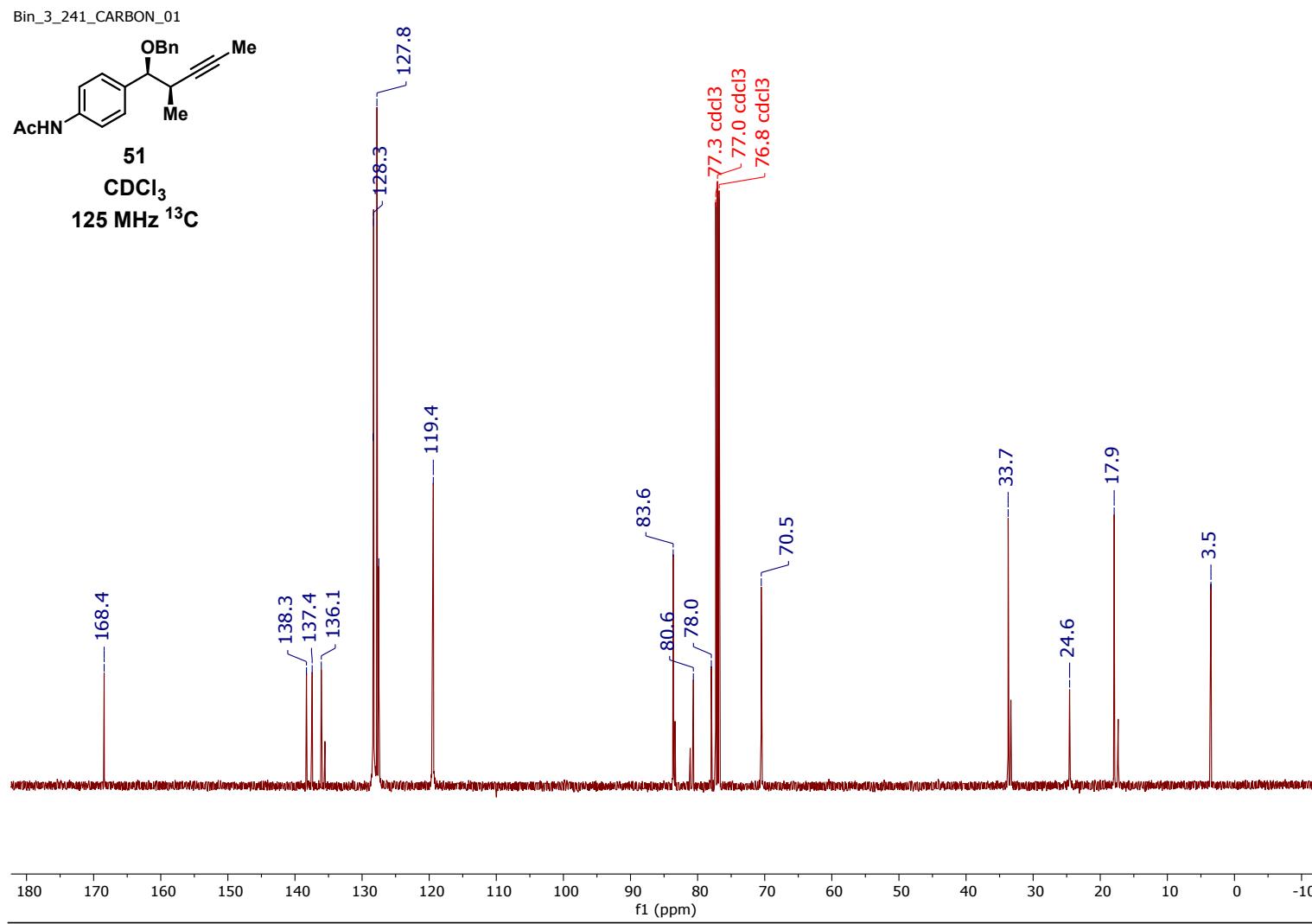
**49**CDCl<sub>3</sub>500 MHz <sup>1</sup>H

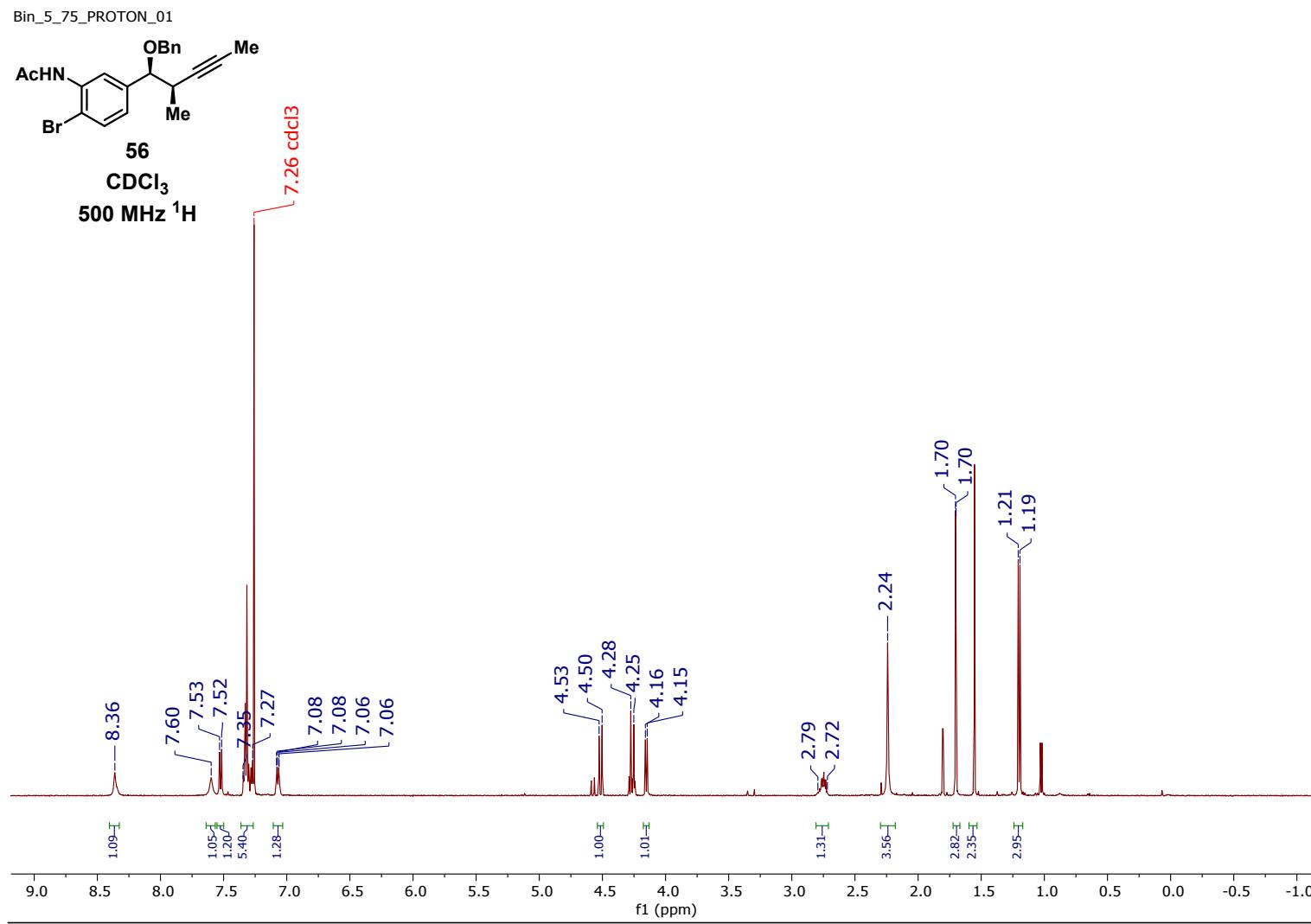


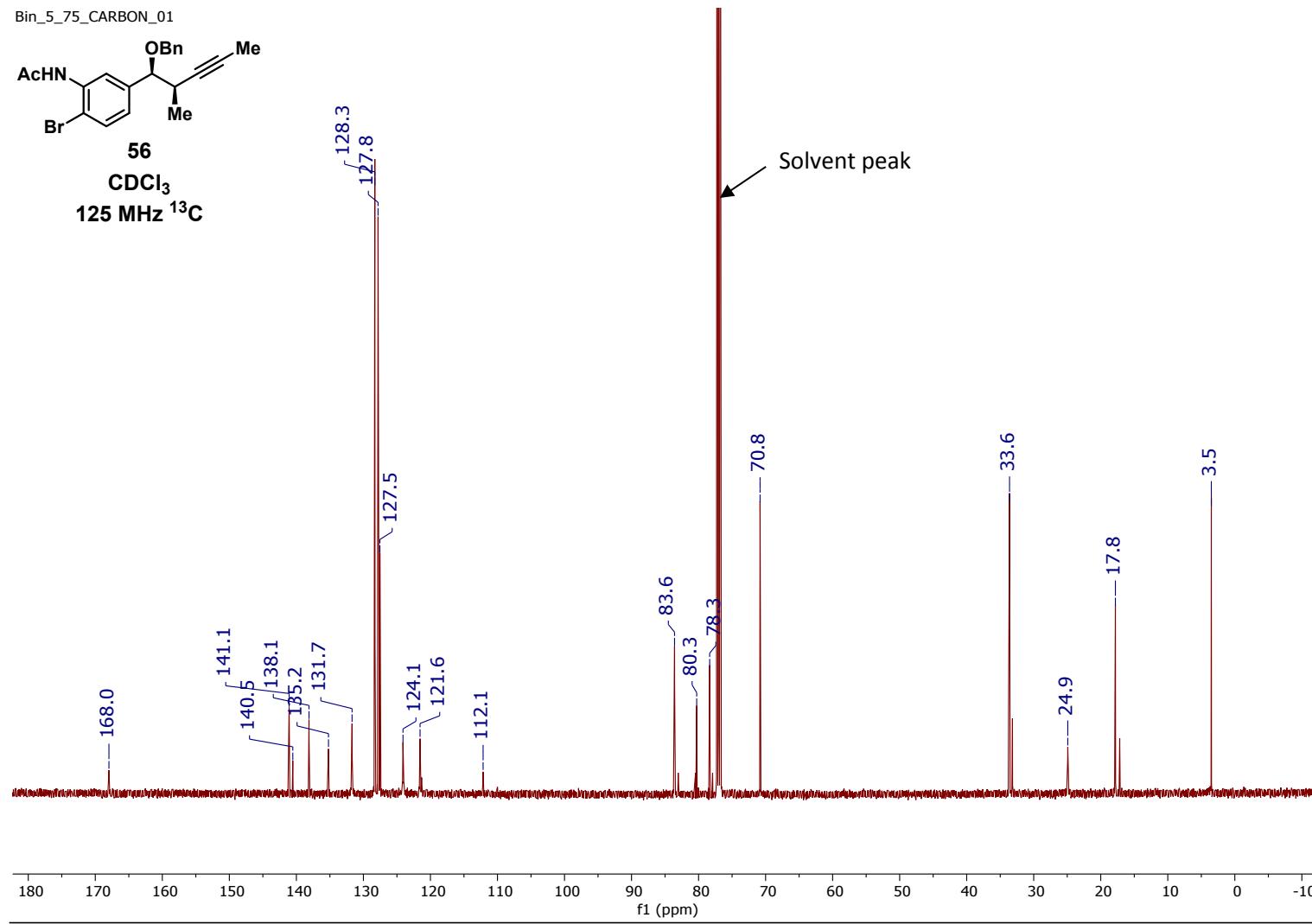


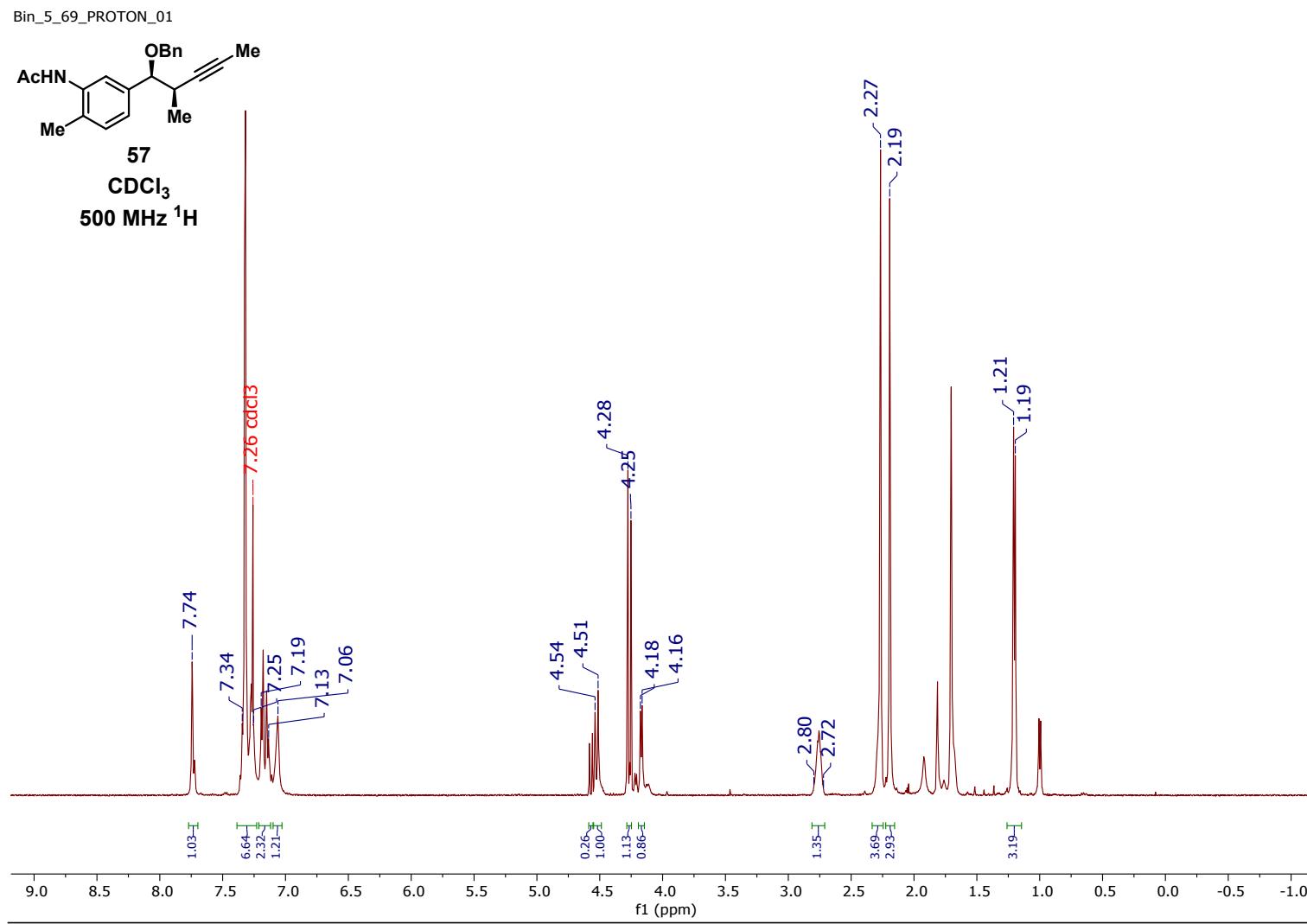


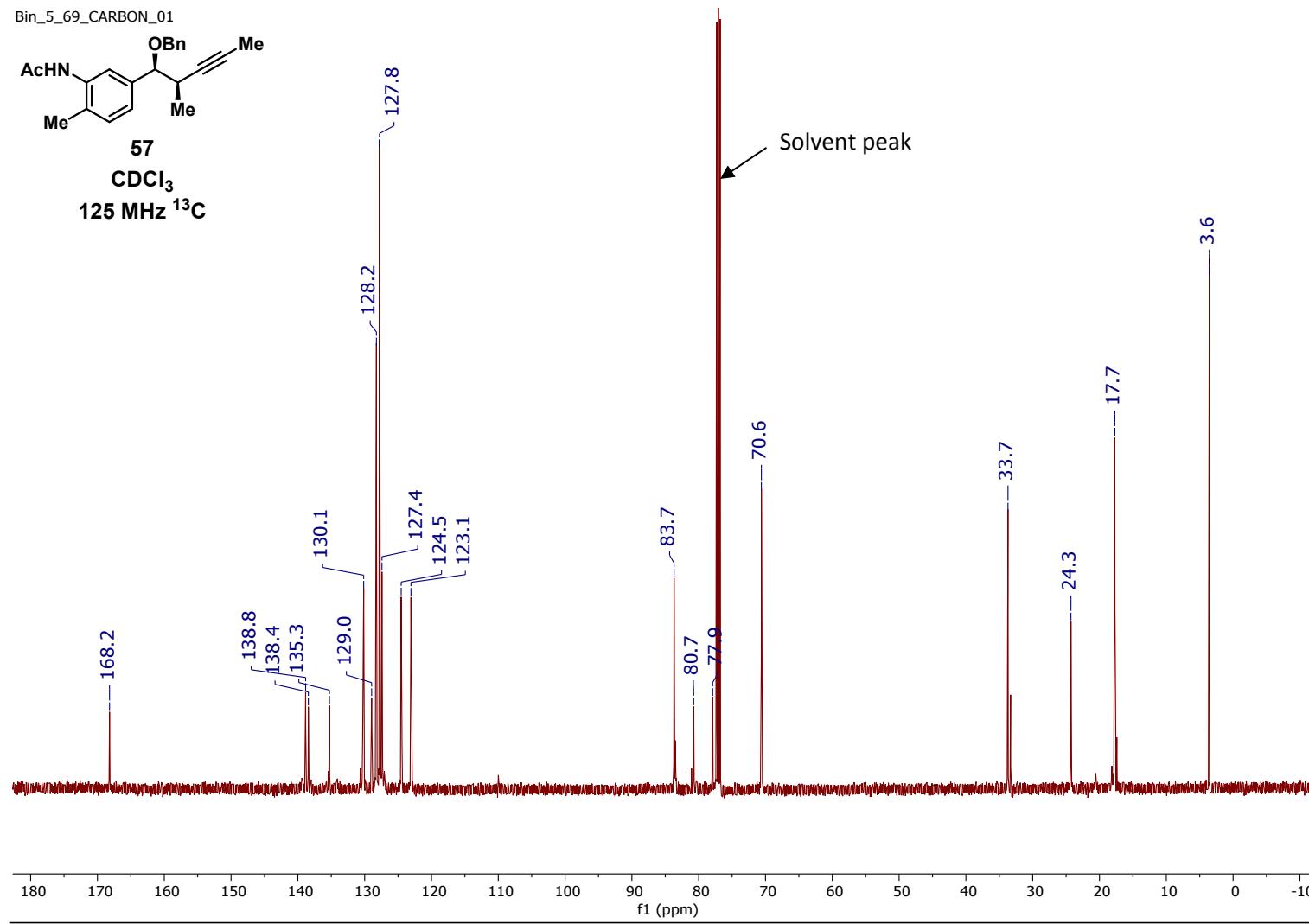




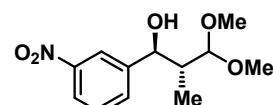




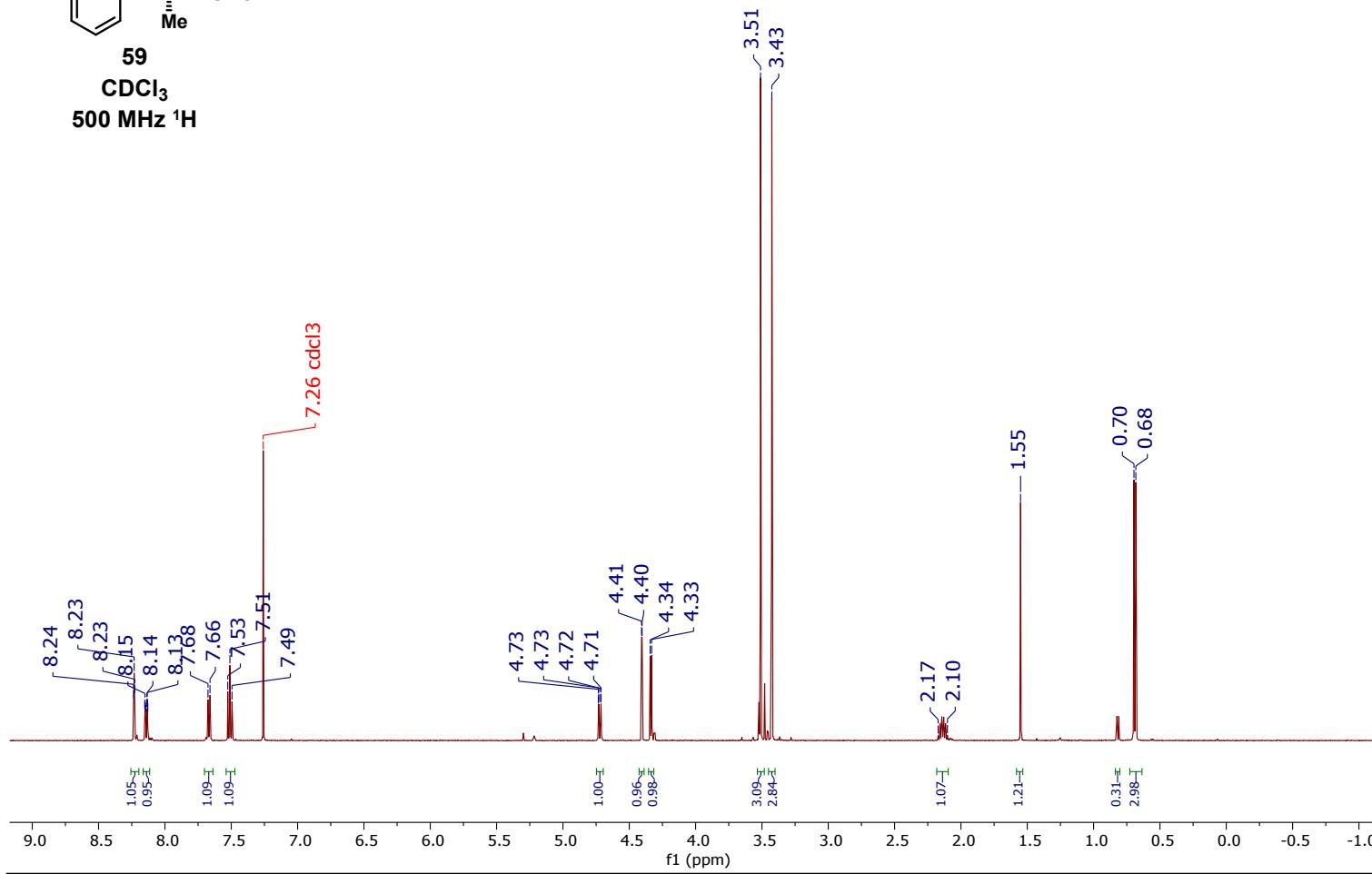


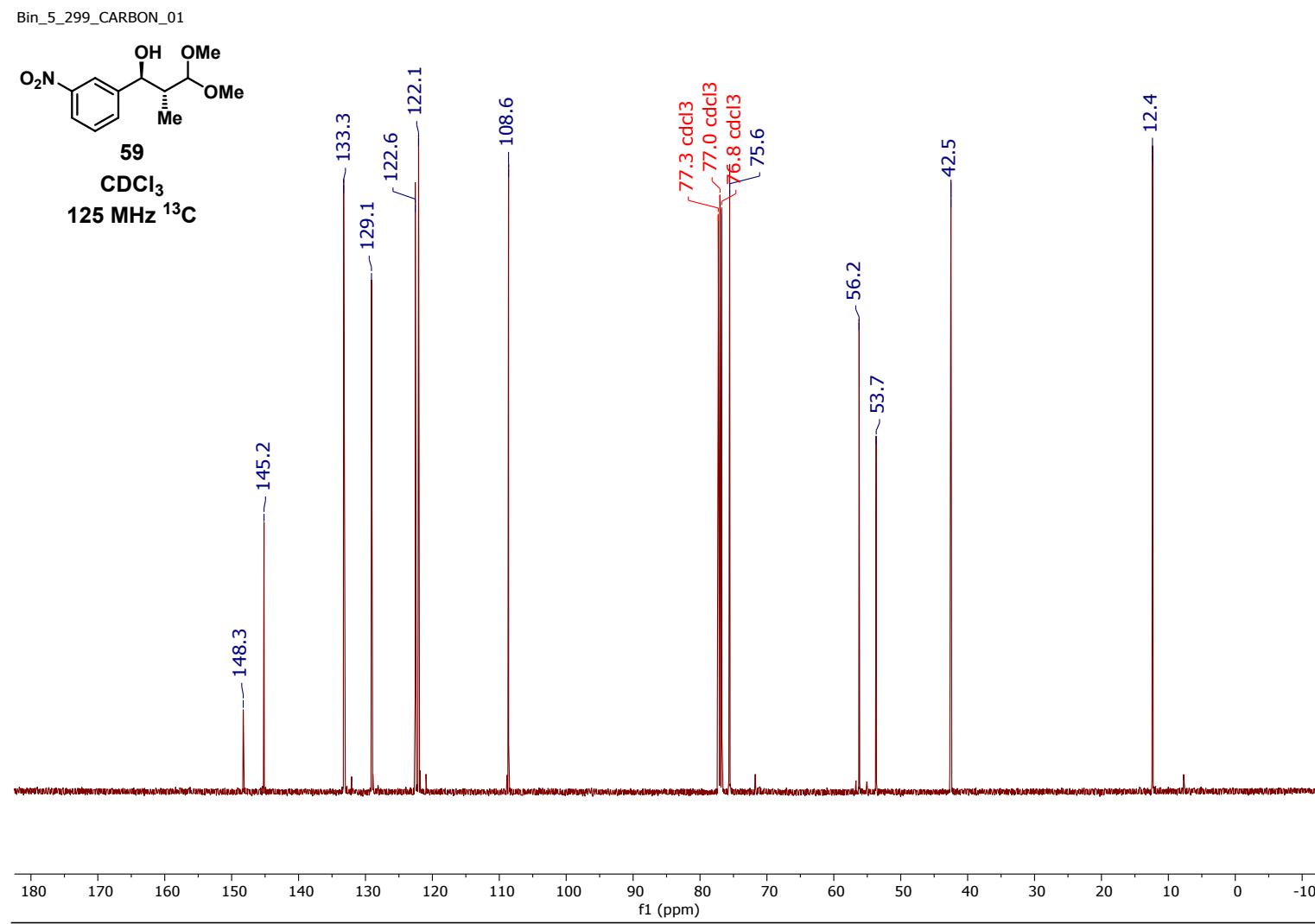


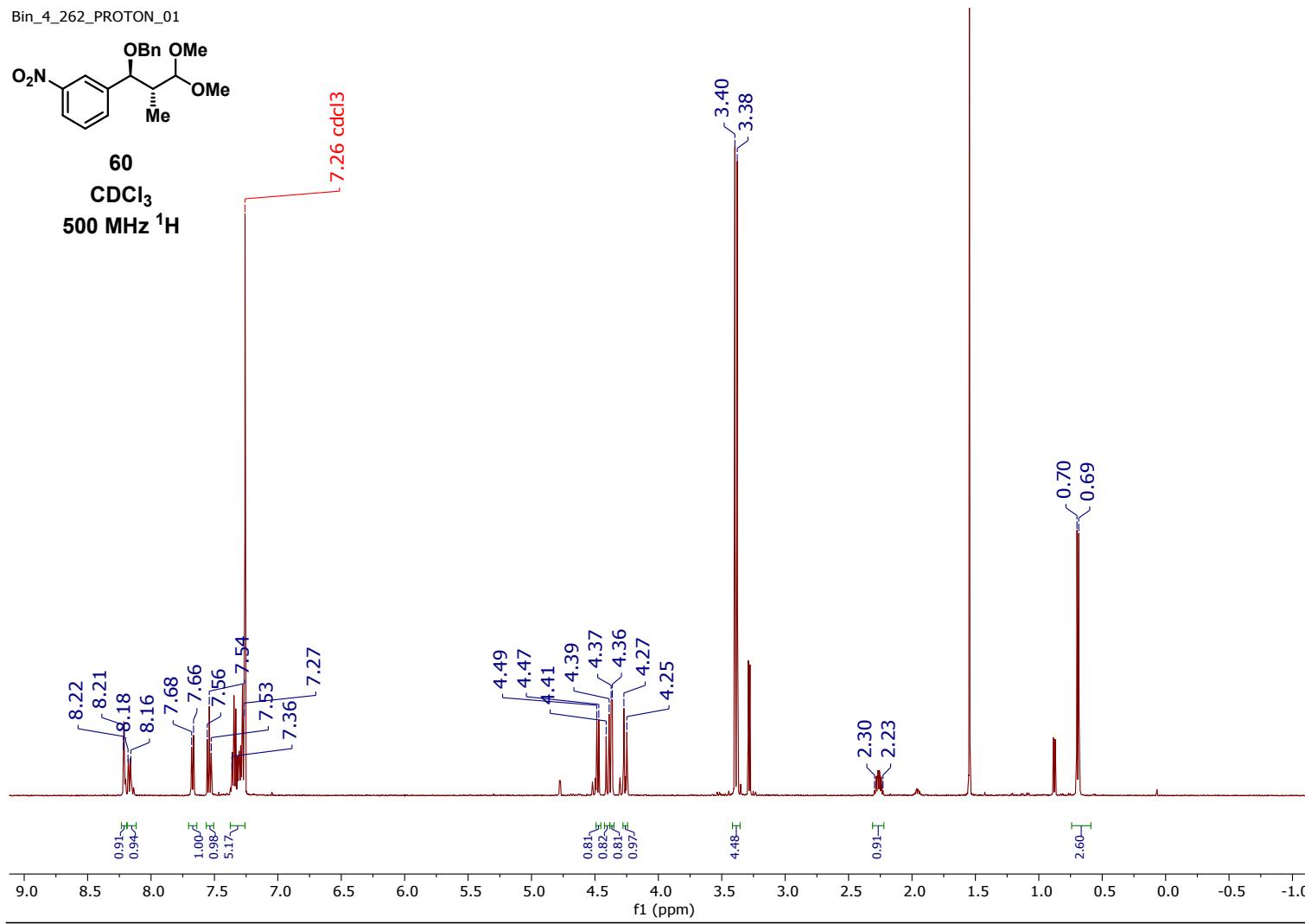
Bin\_5\_299\_PROTON\_01

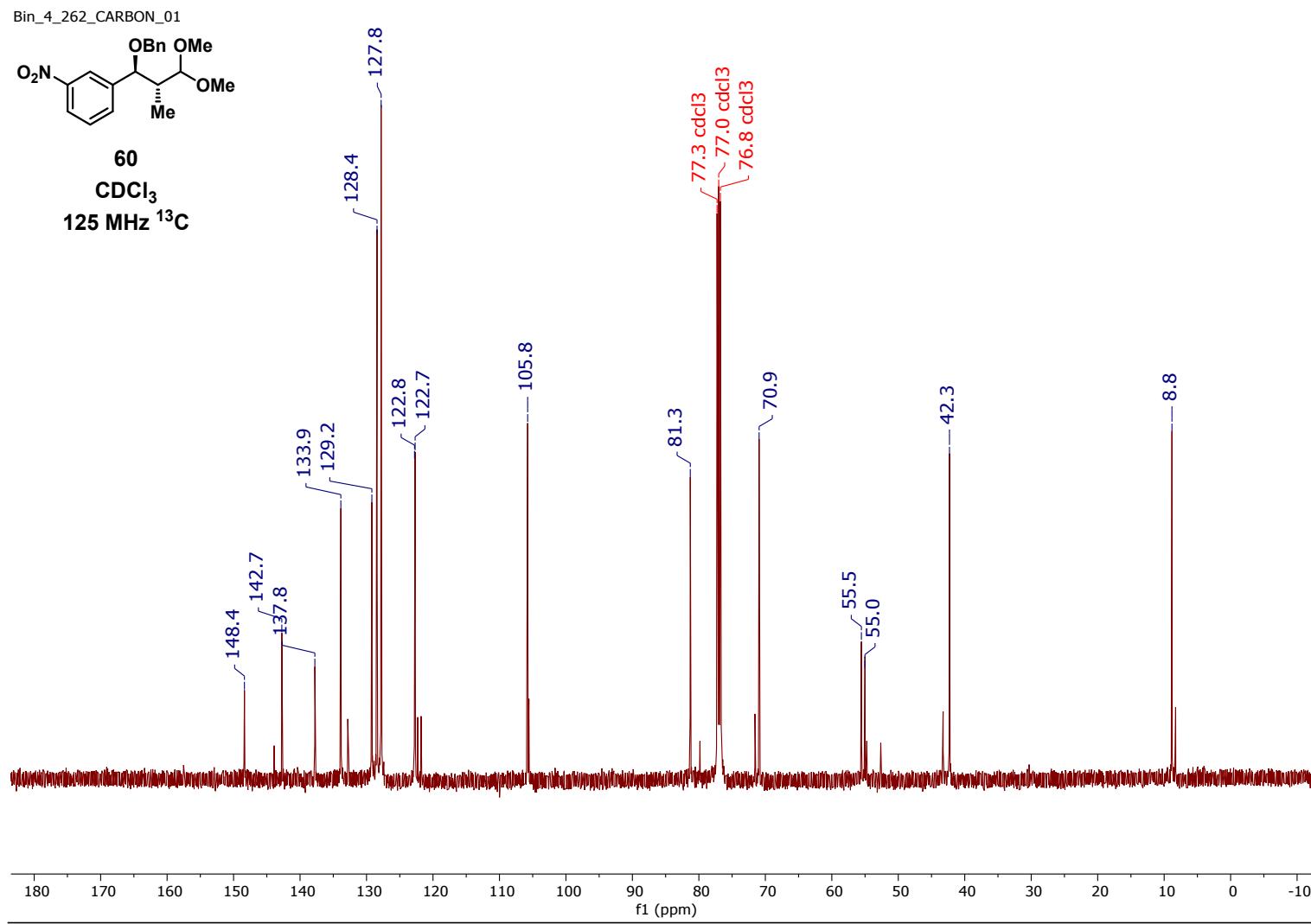


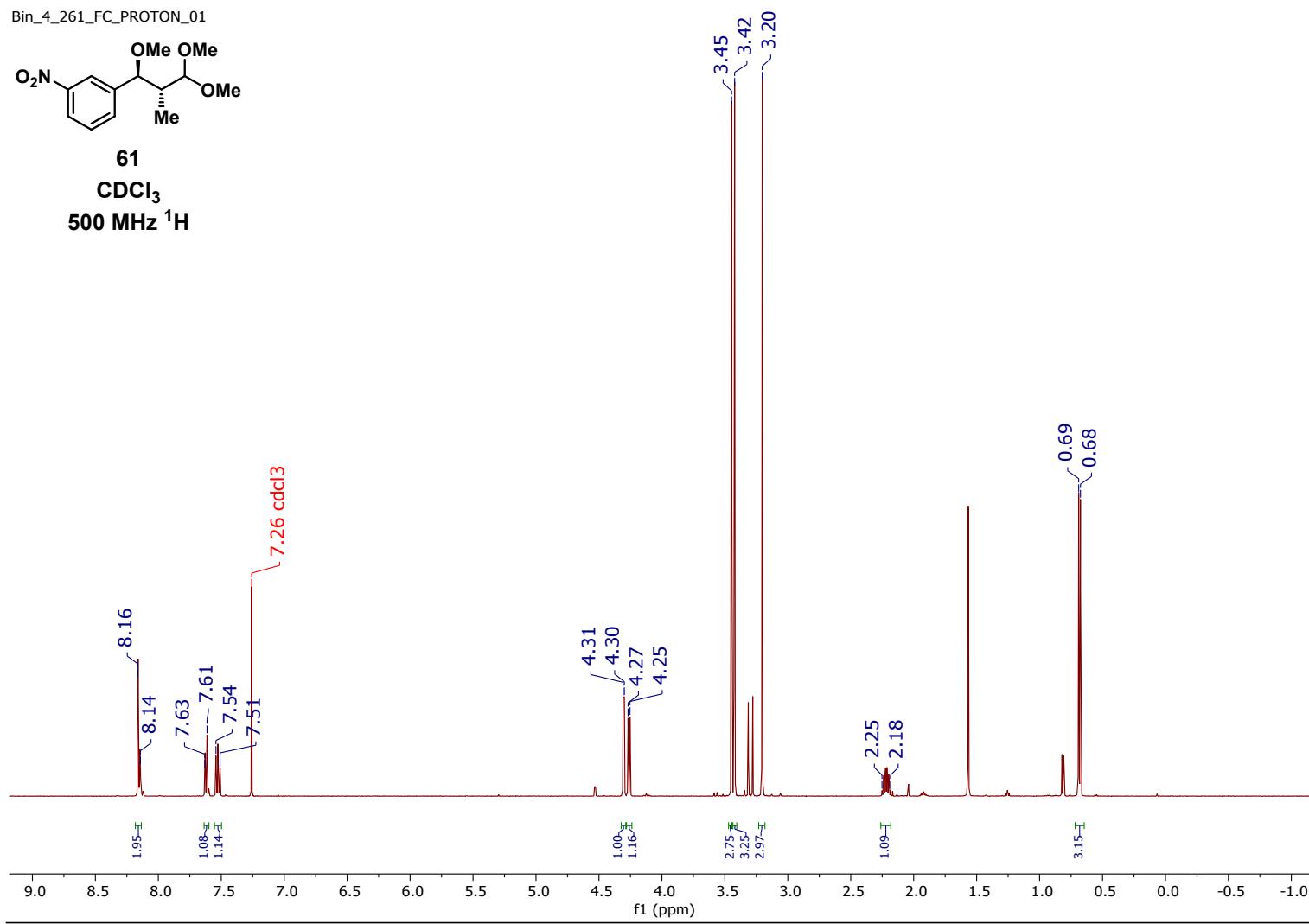
**59**  
 $\text{CDCl}_3$   
500 MHz  $^1\text{H}$

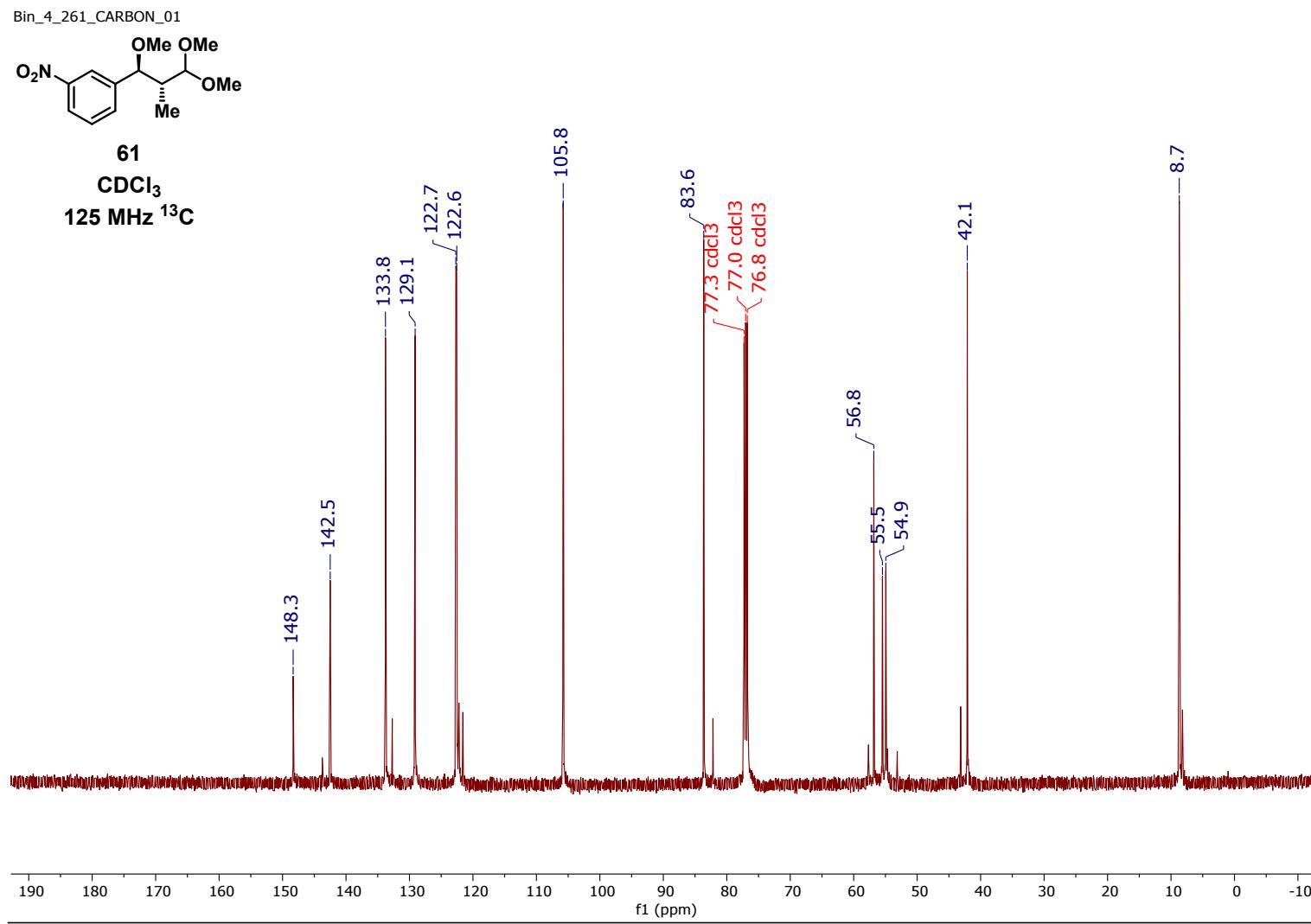


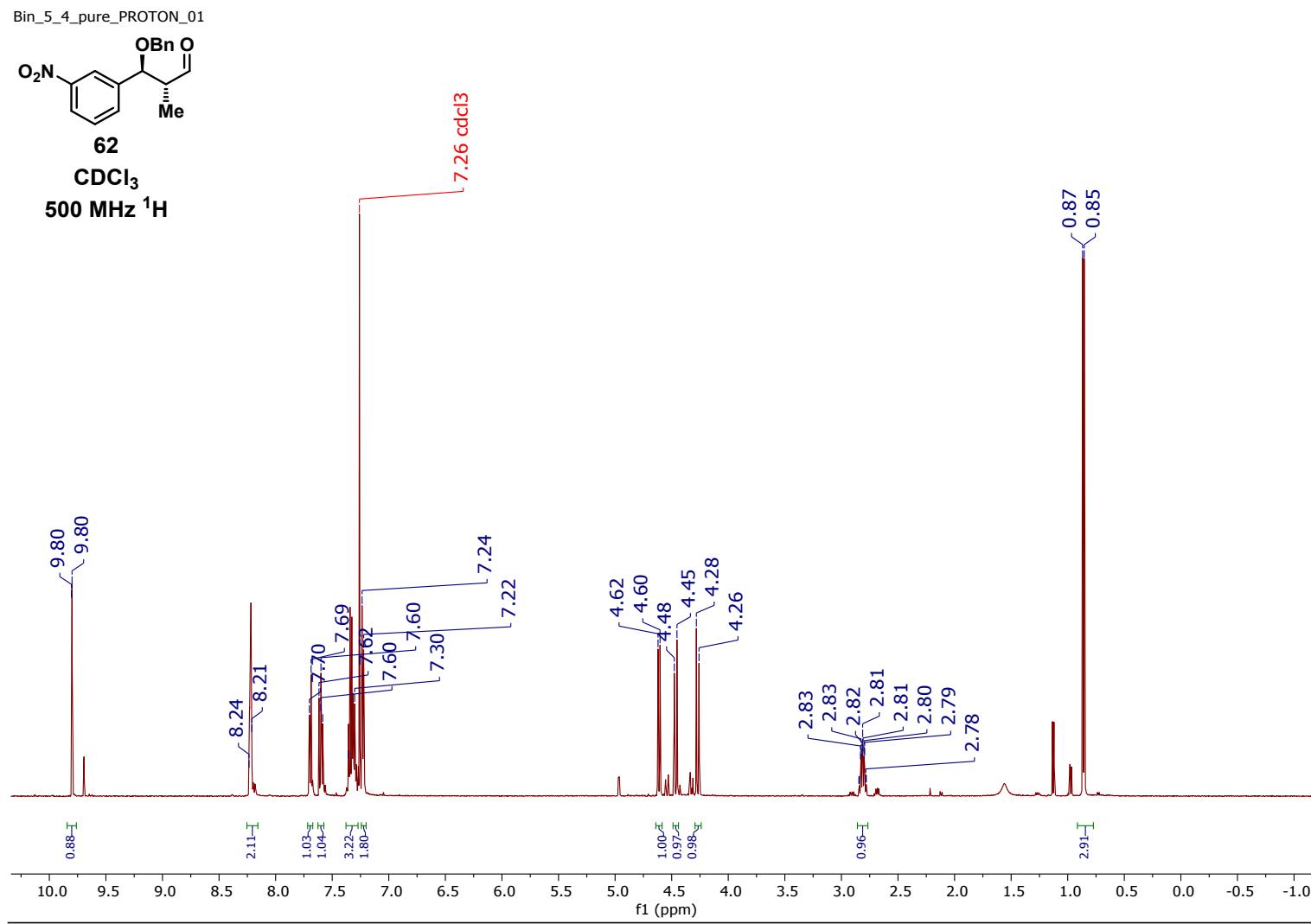




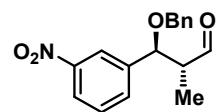
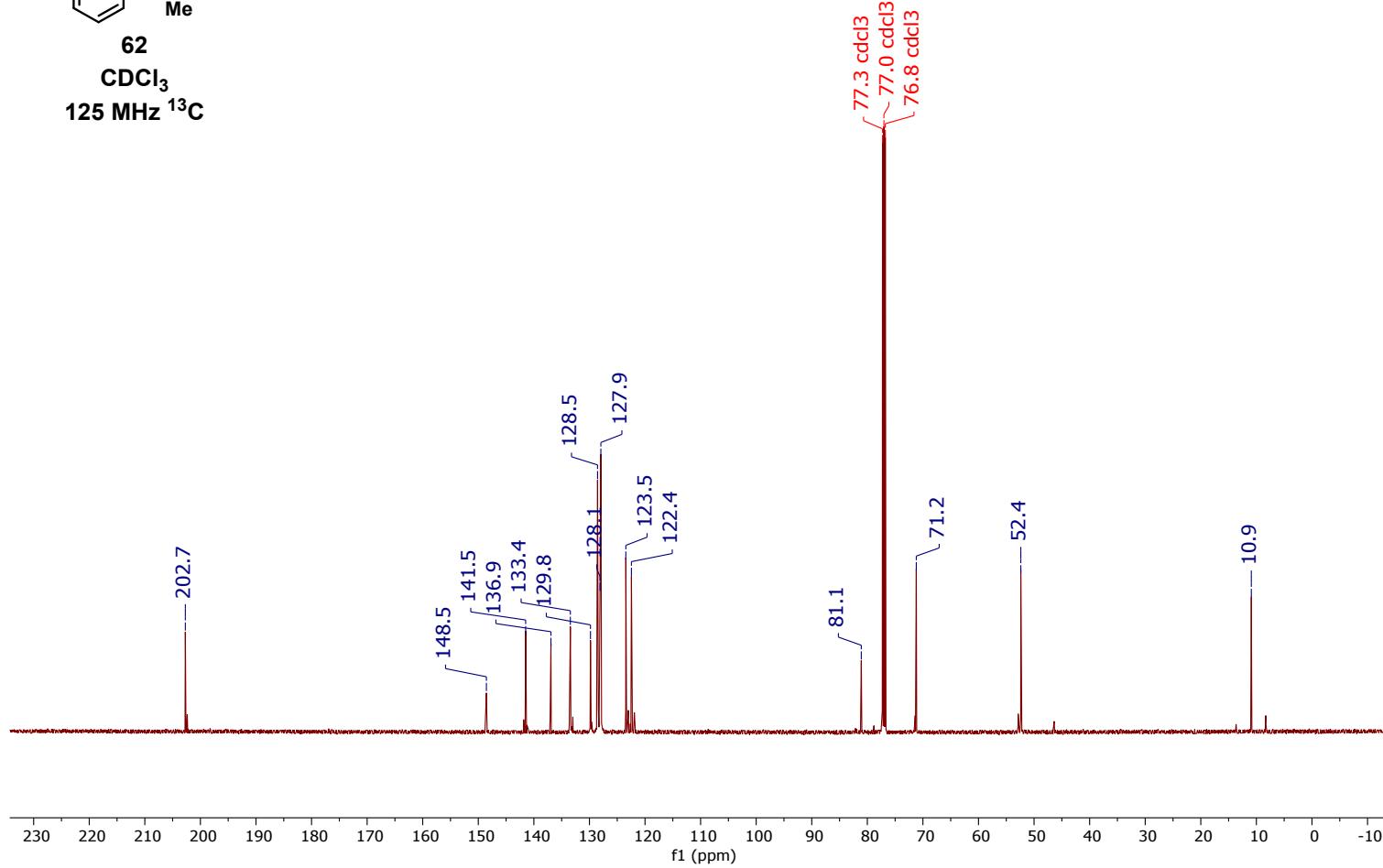


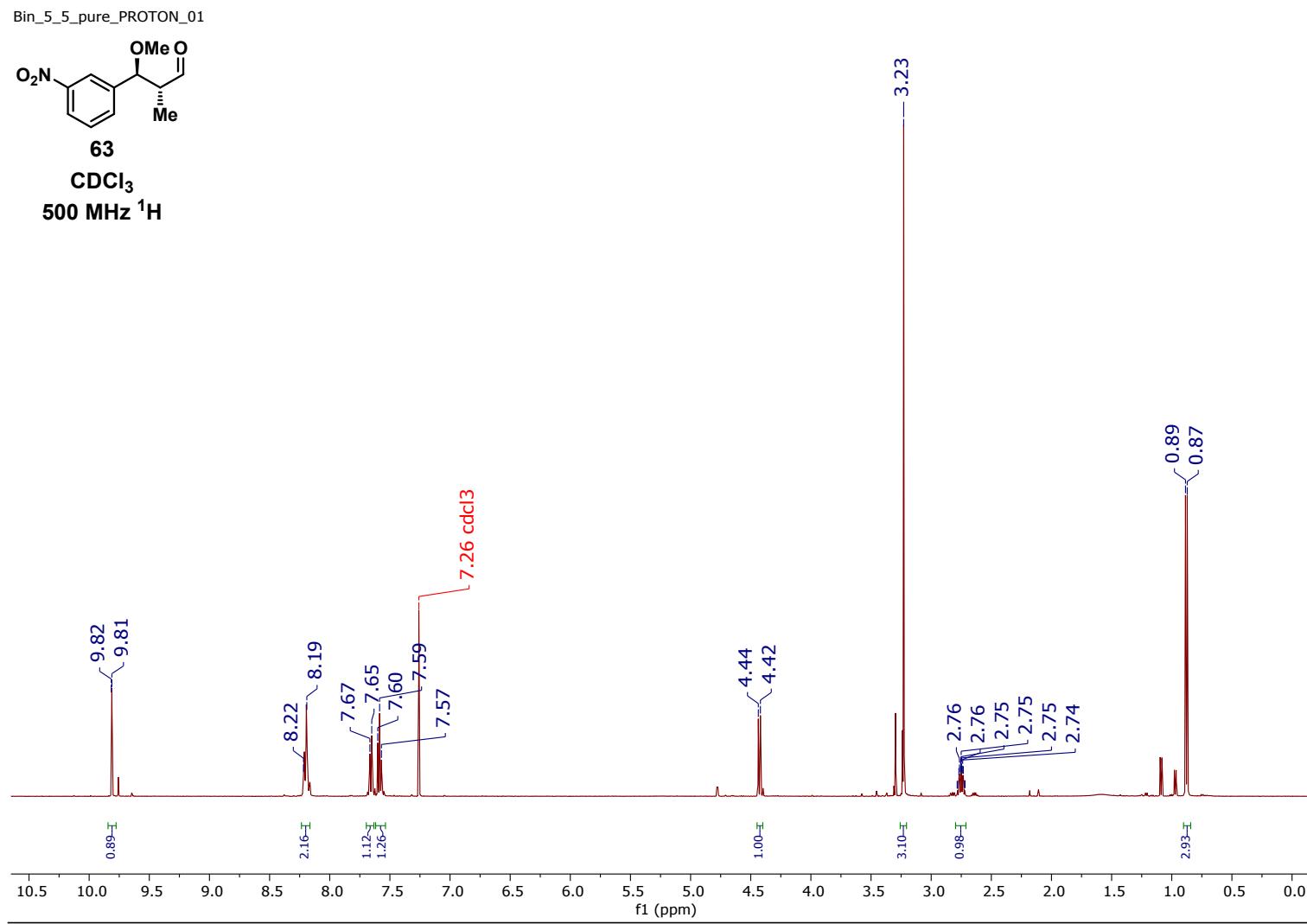


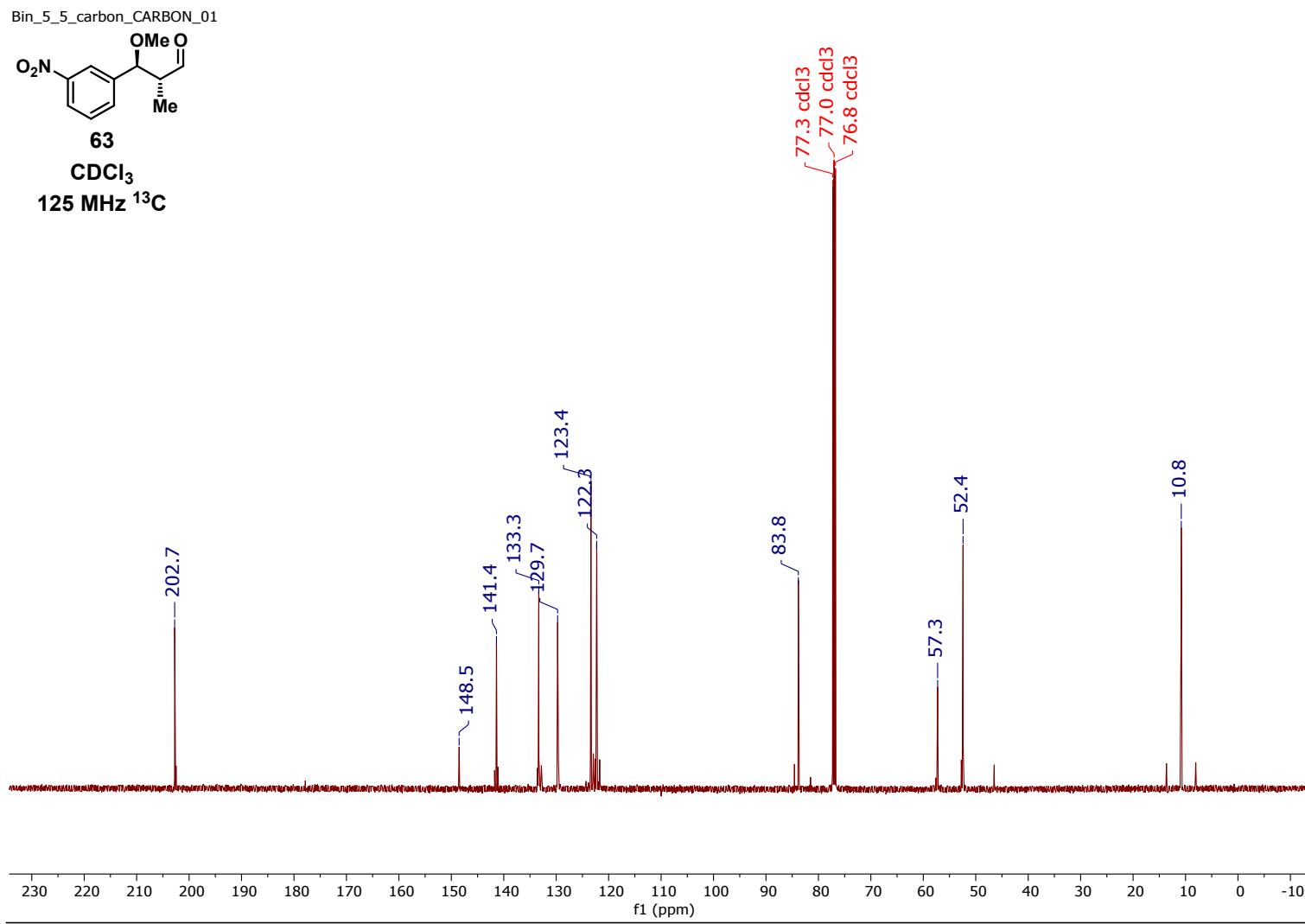


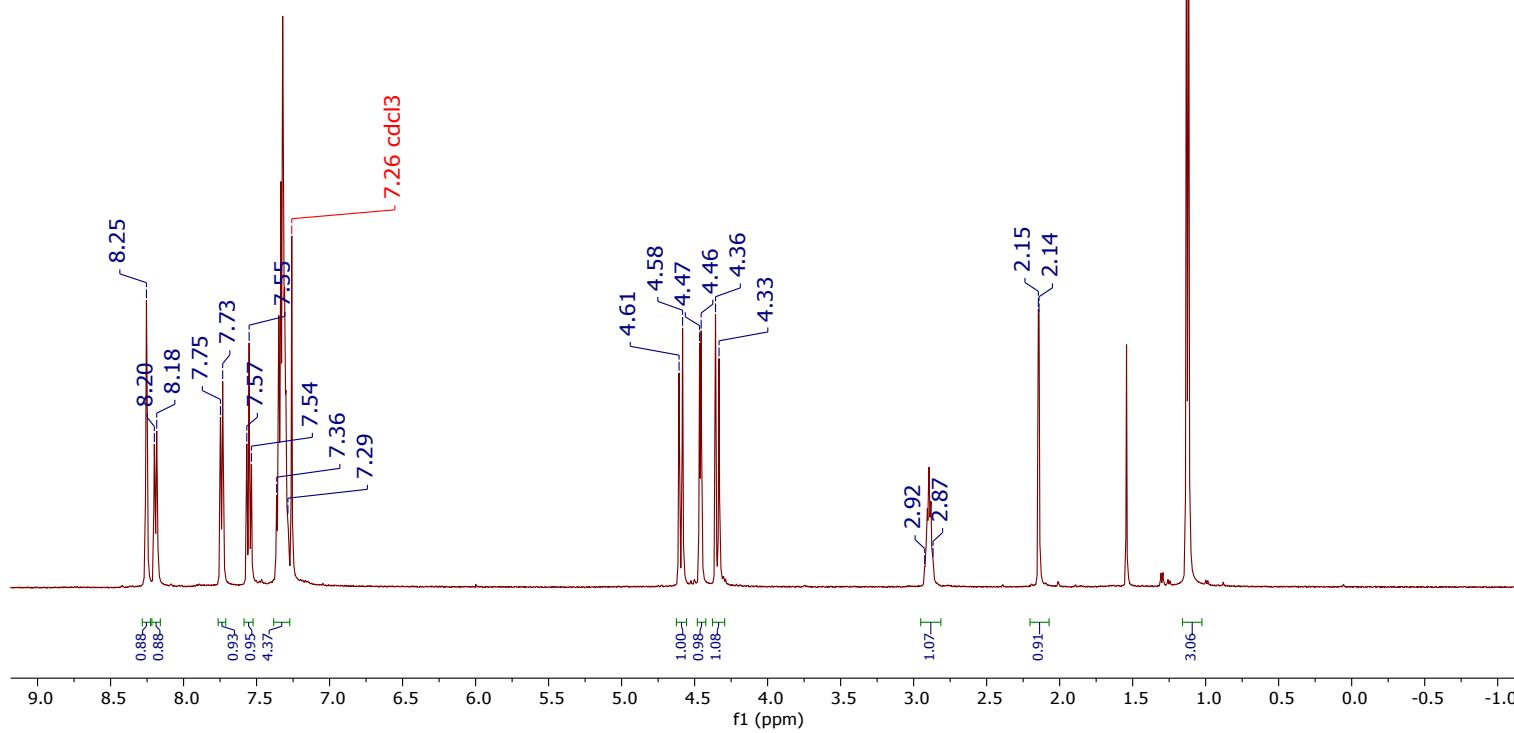
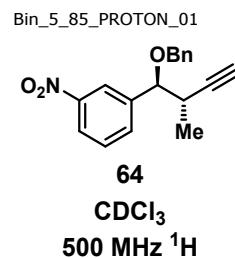


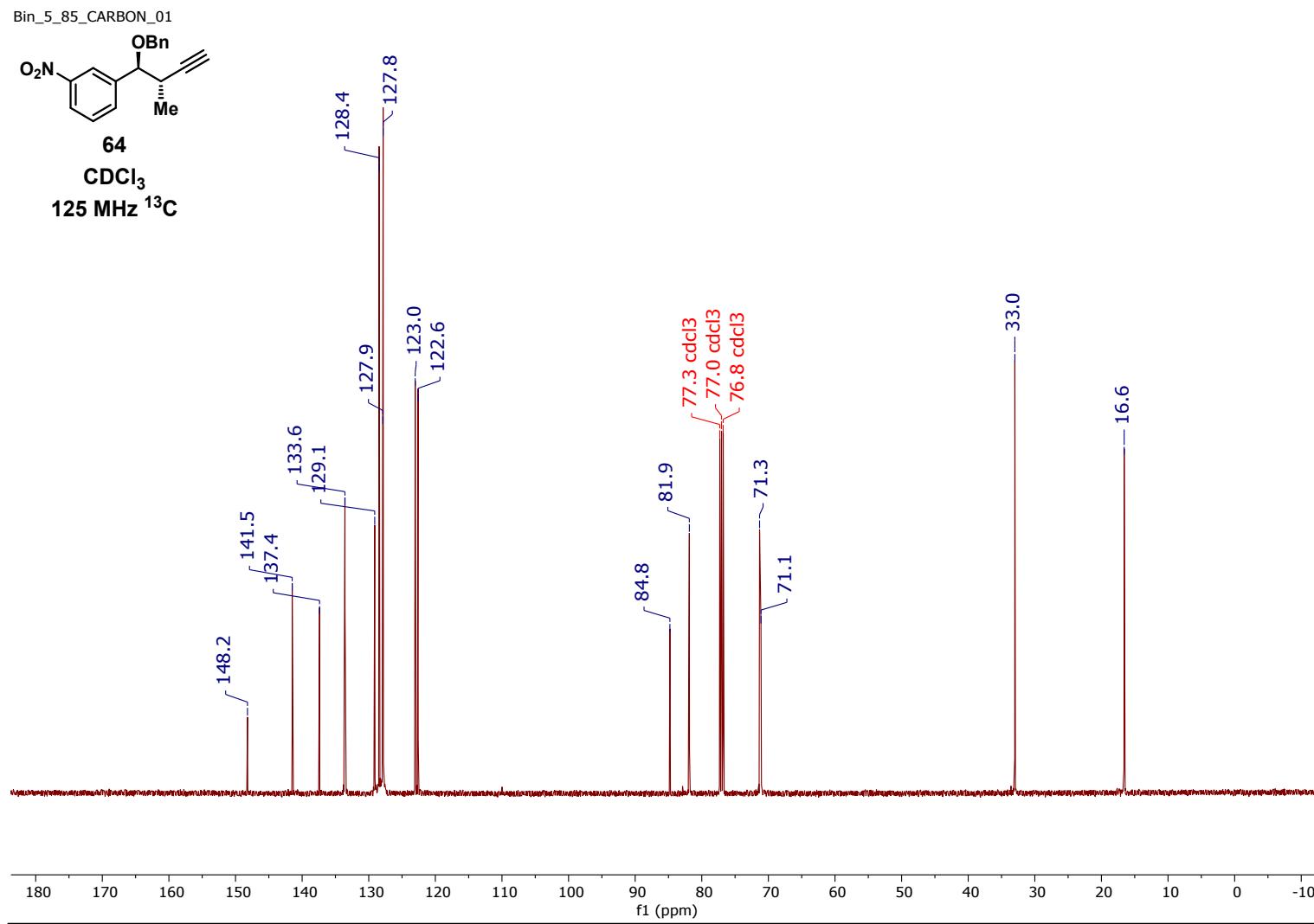
Bin\_5\_4\_carbon\_CARBON\_01

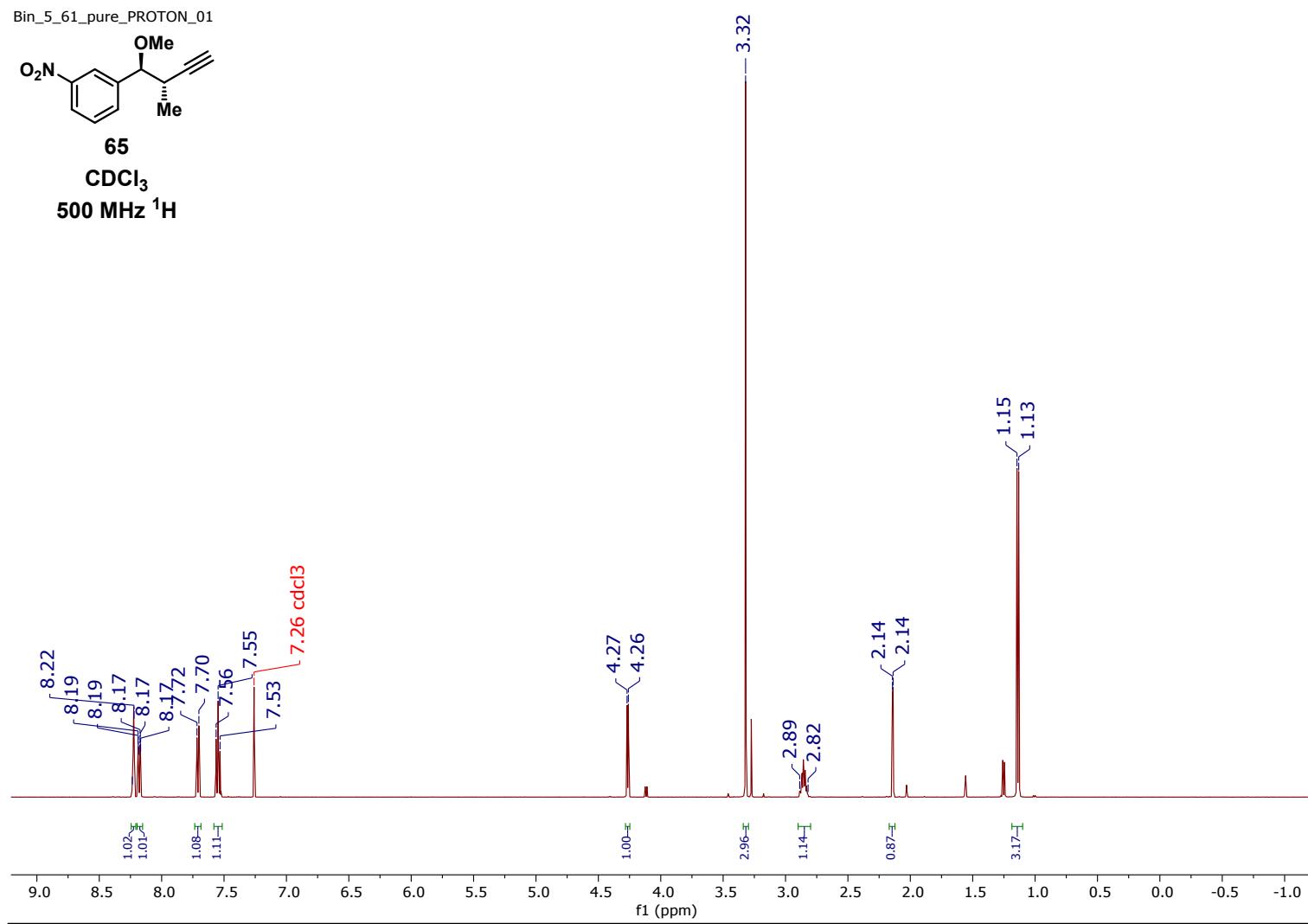
**62** $\text{CDCl}_3$ 125 MHz  $^{13}\text{C}$ 

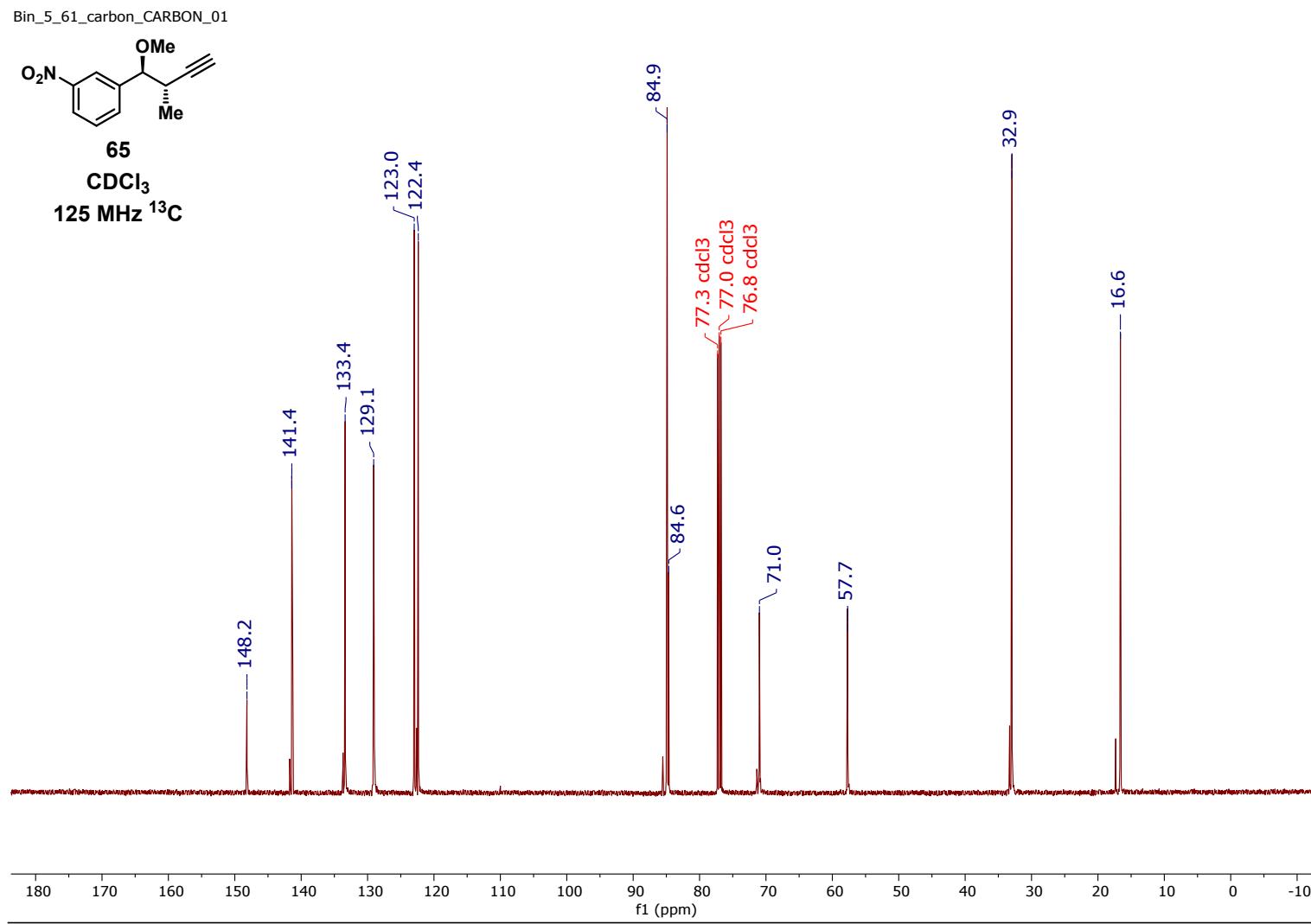


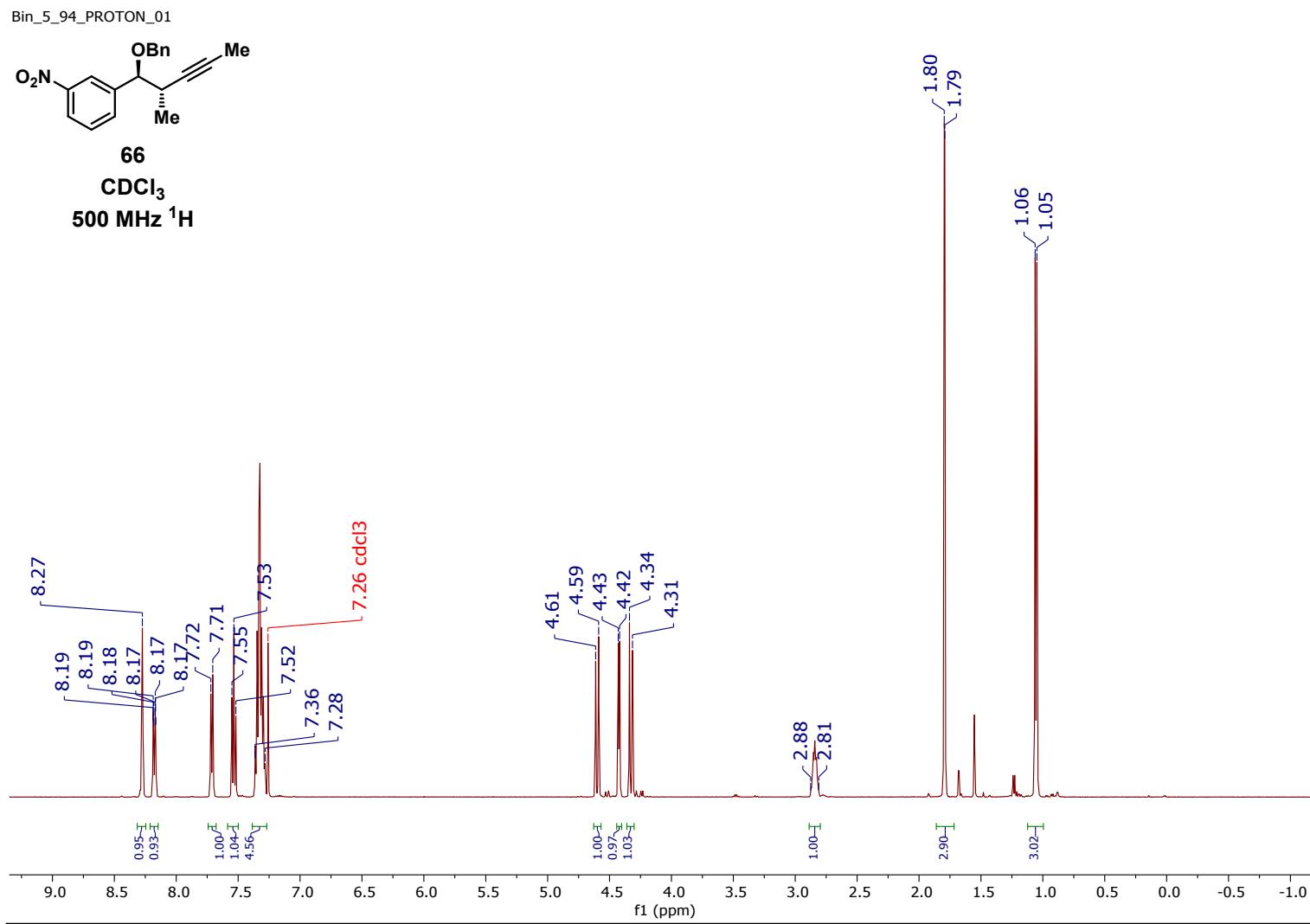


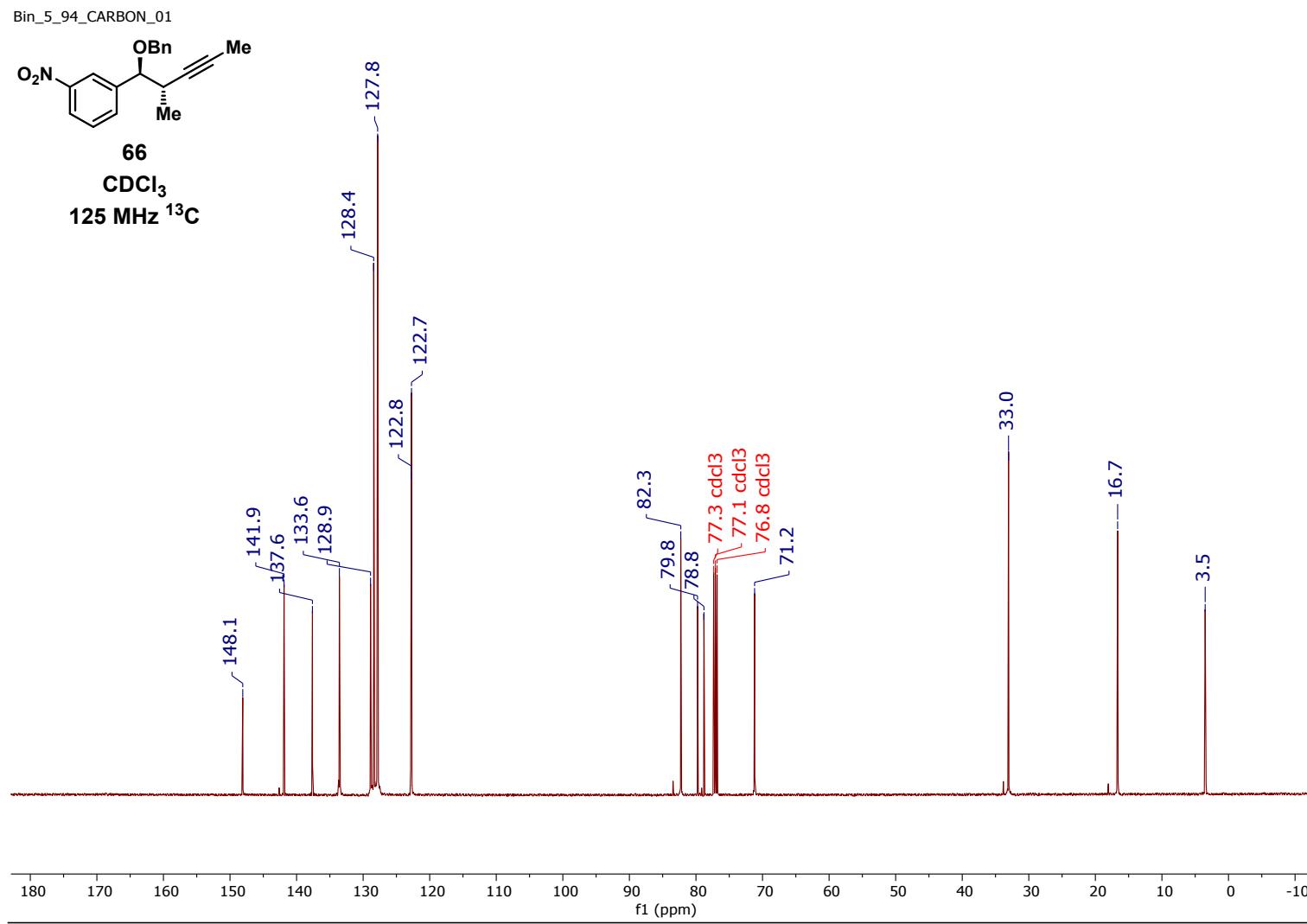


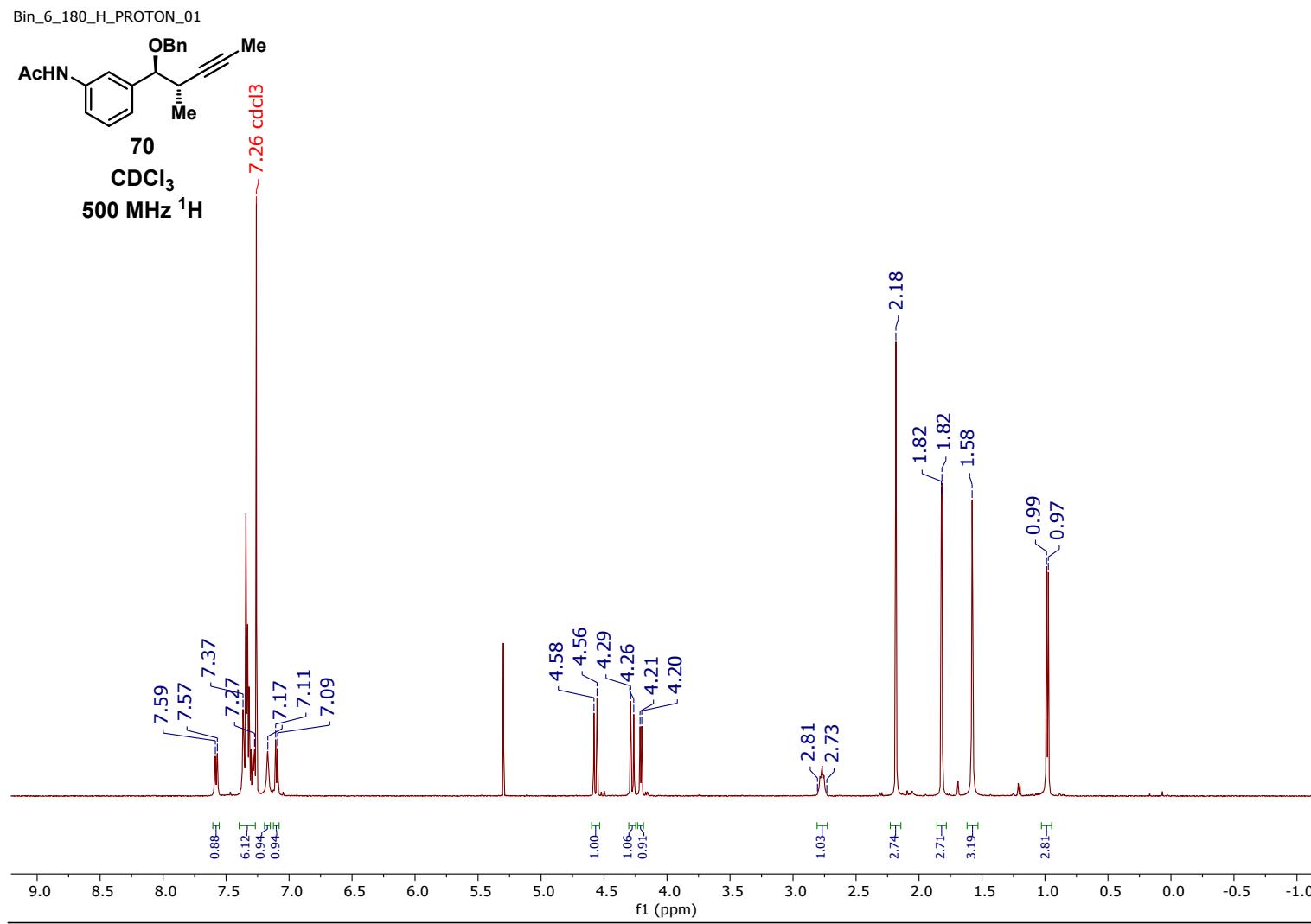


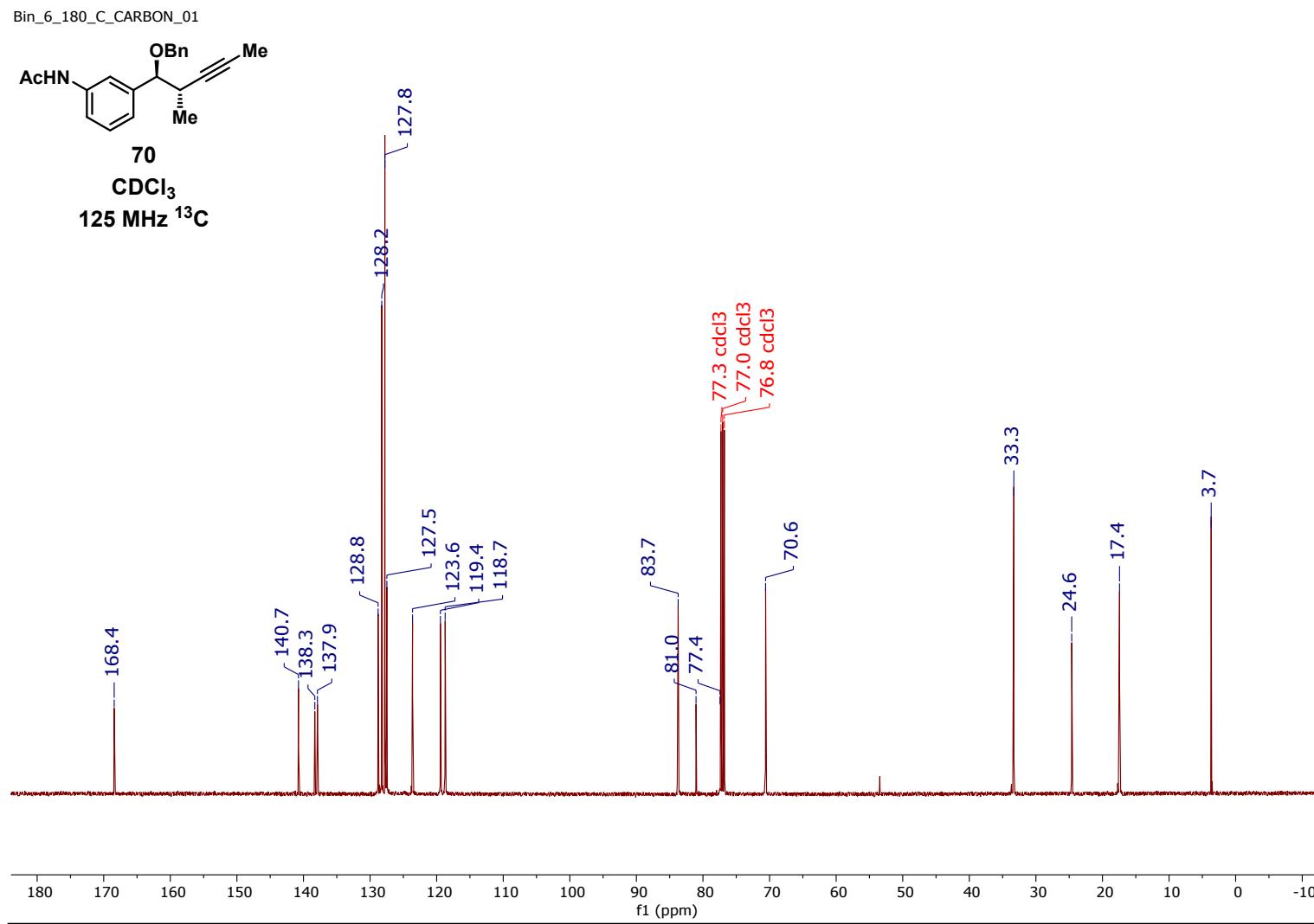


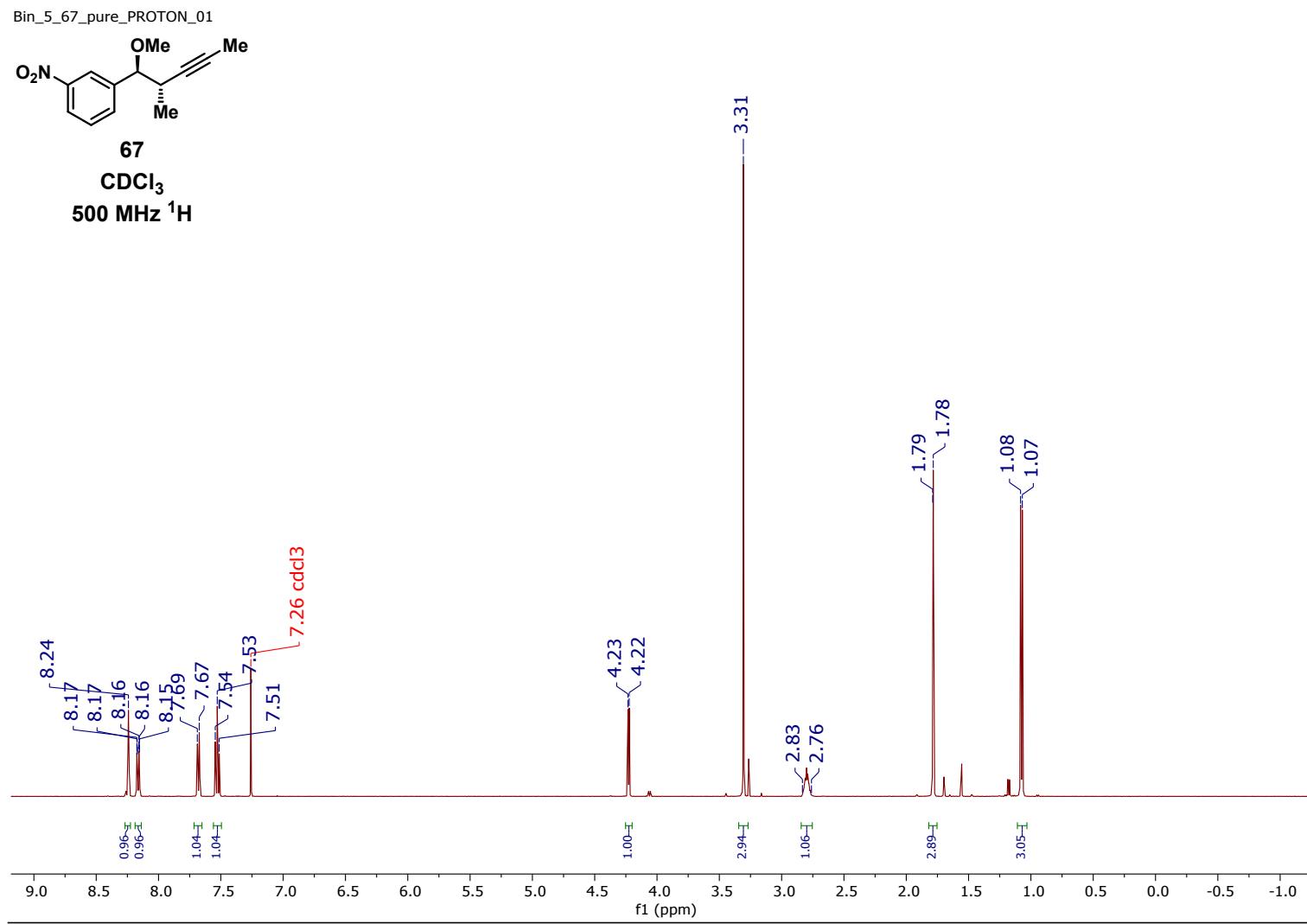


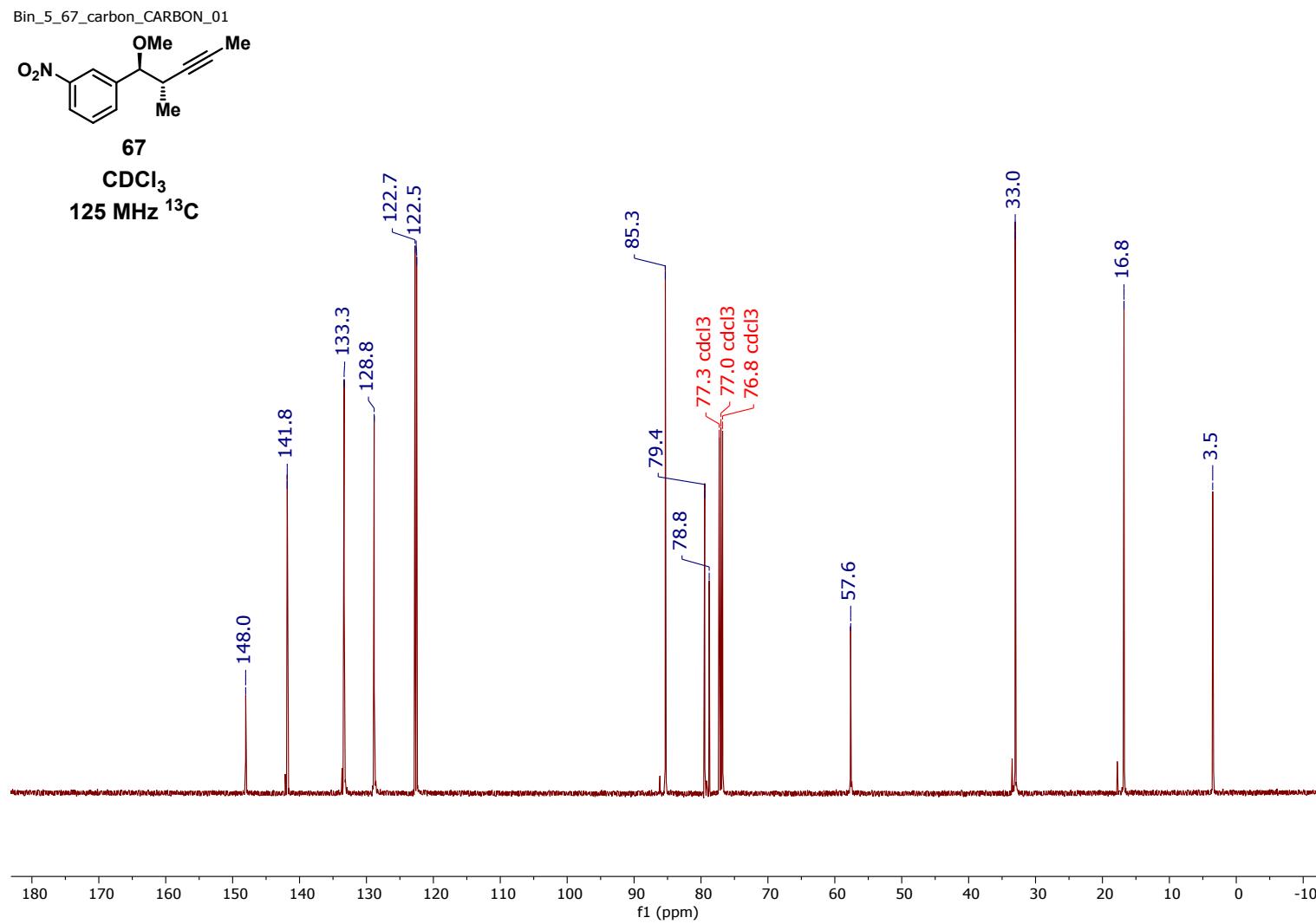


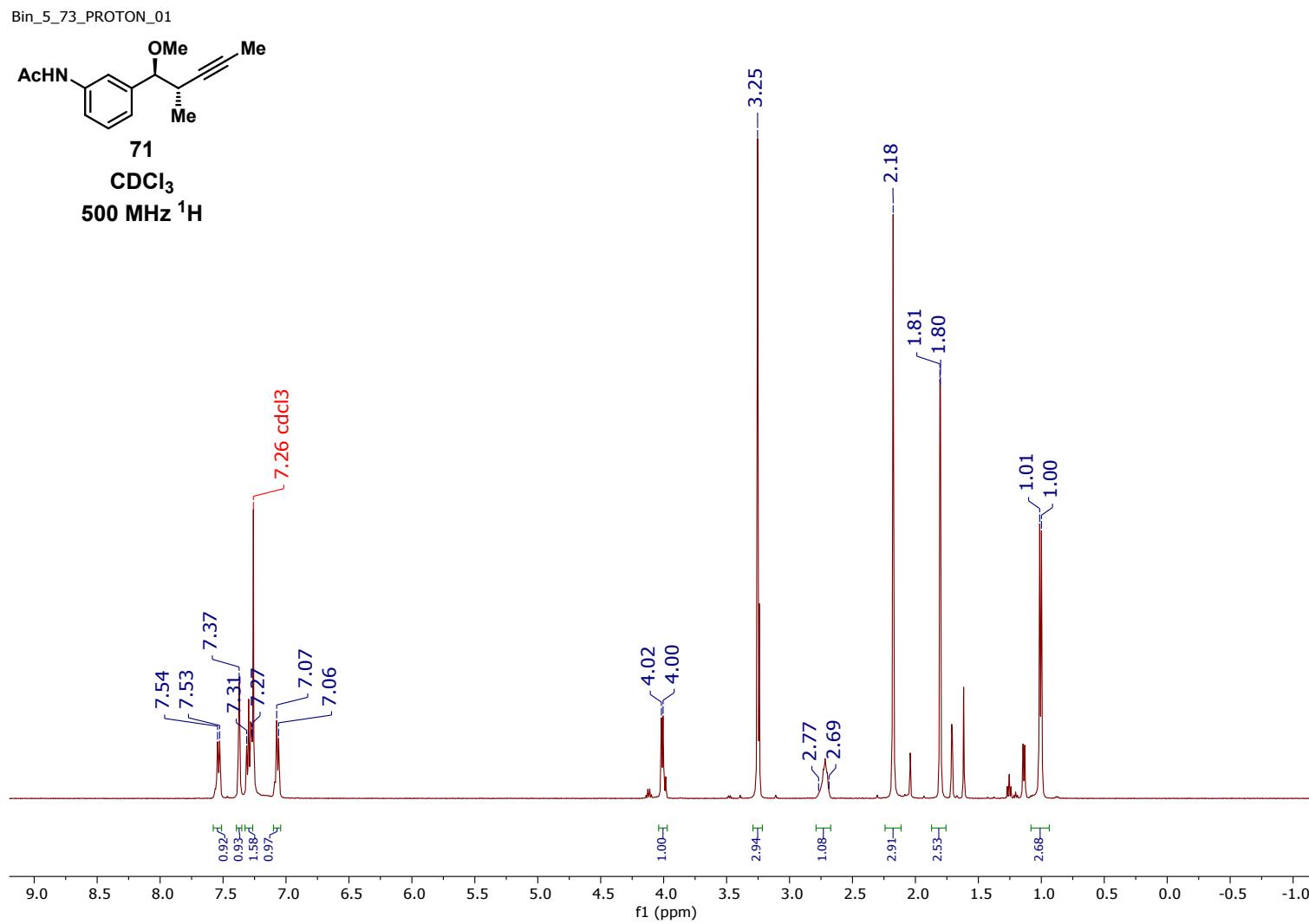


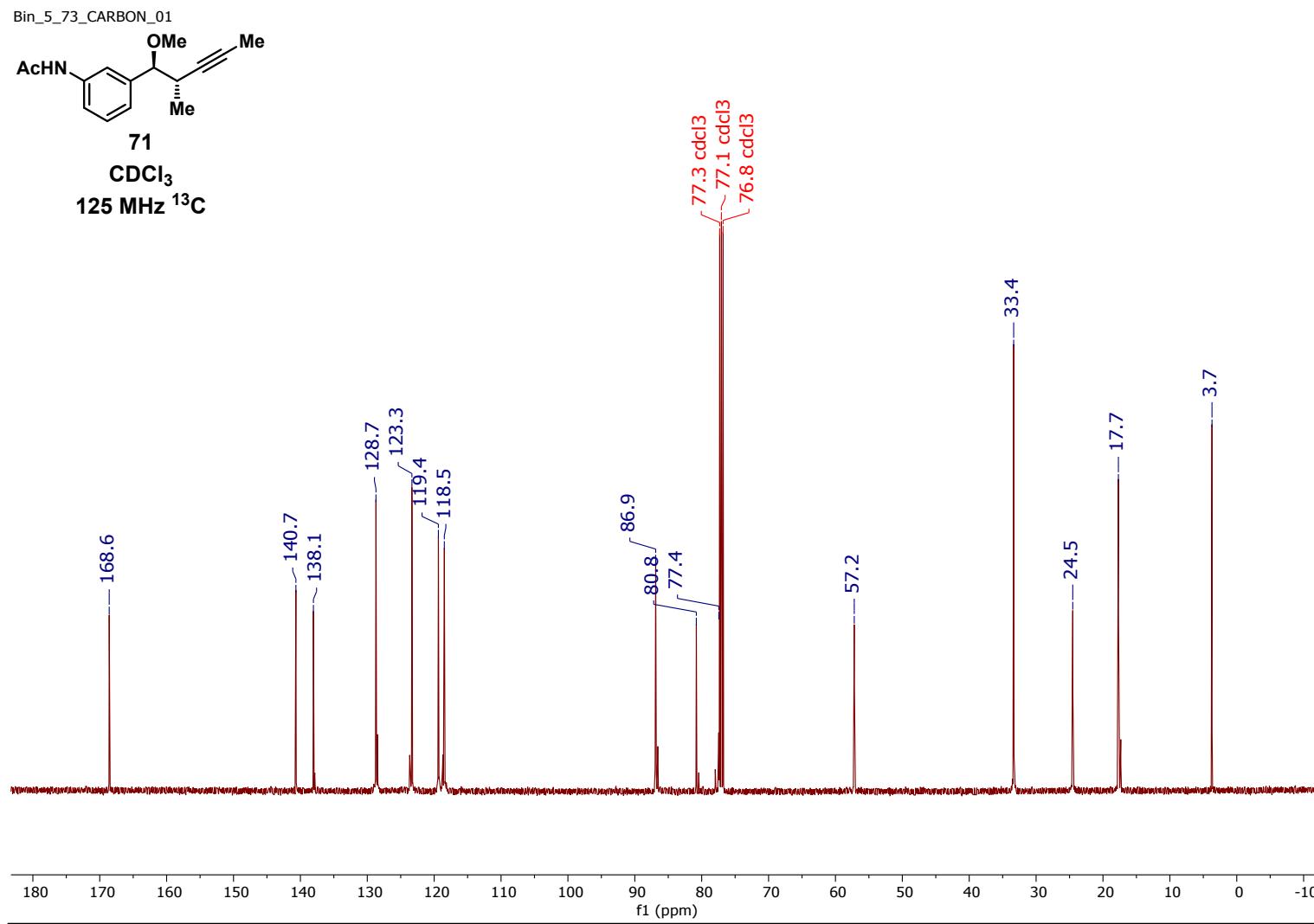




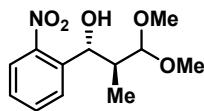
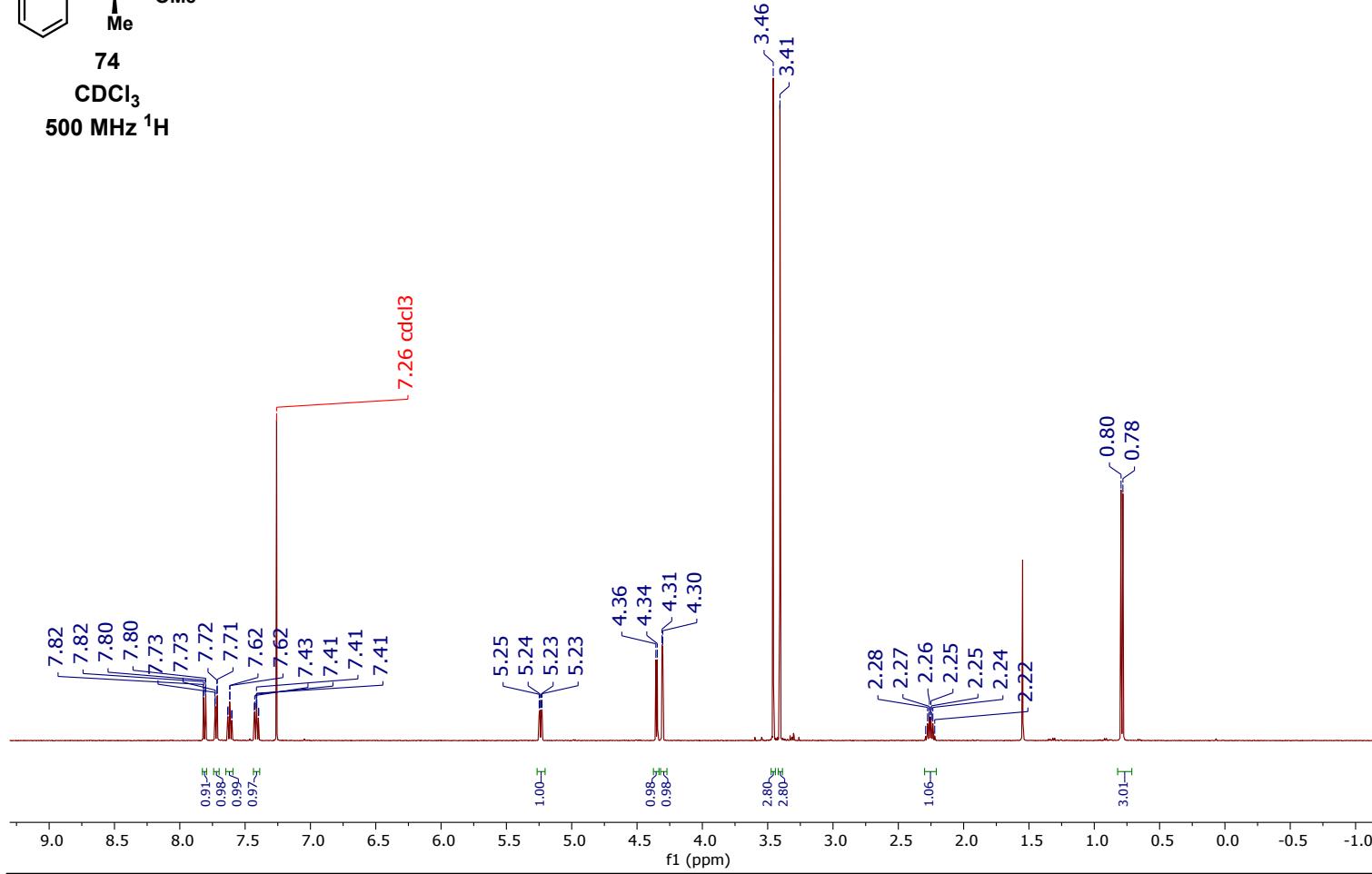


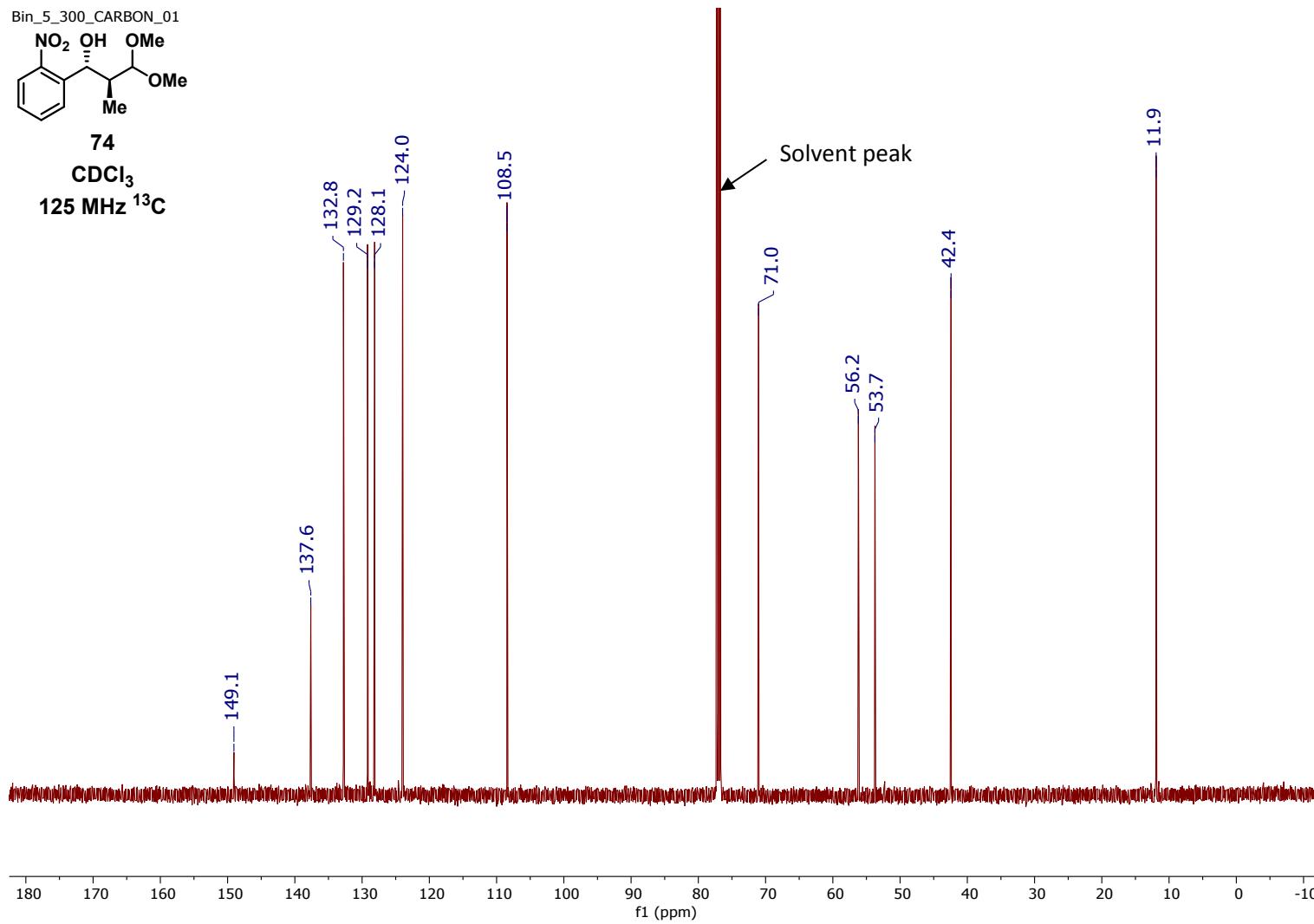


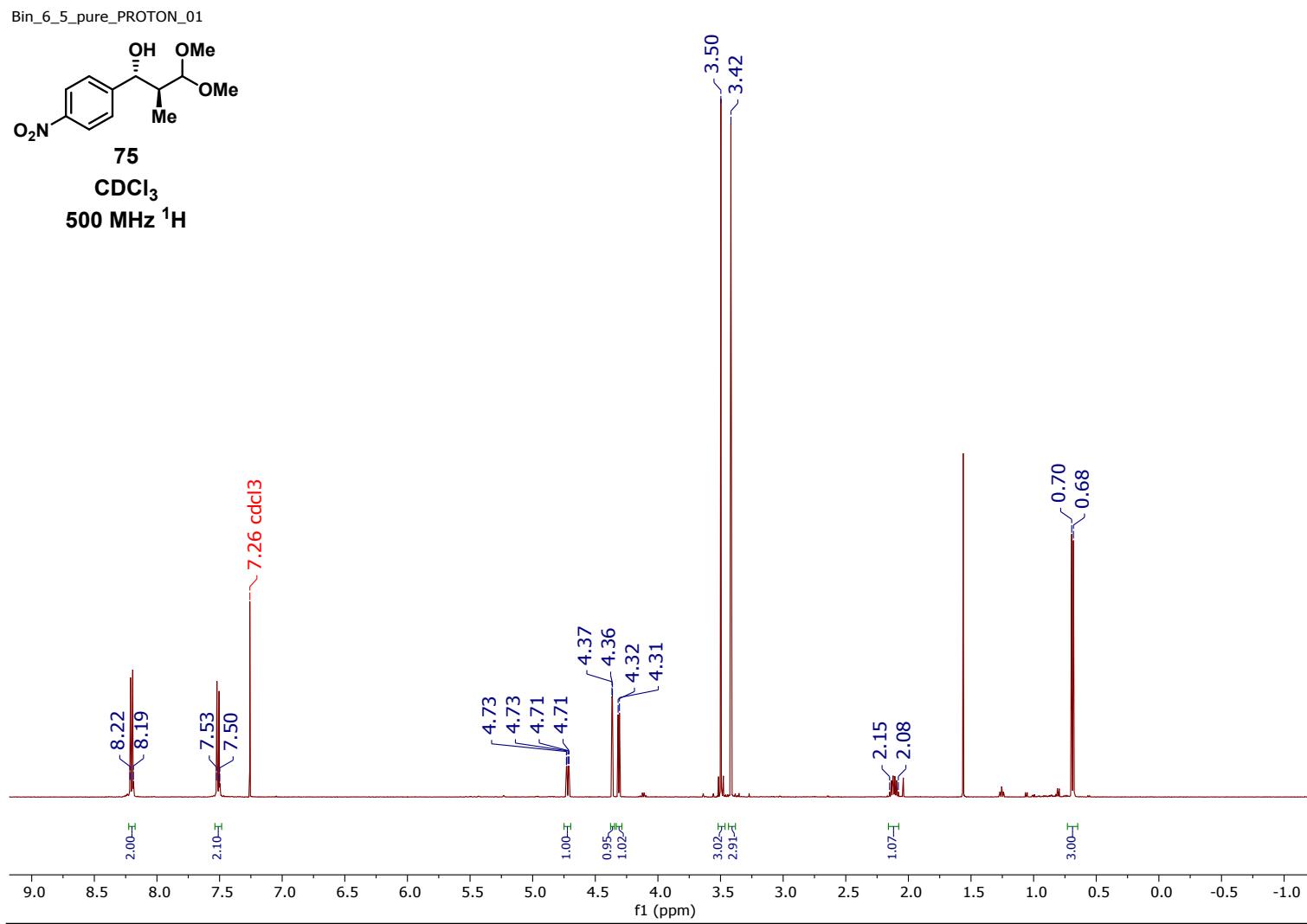


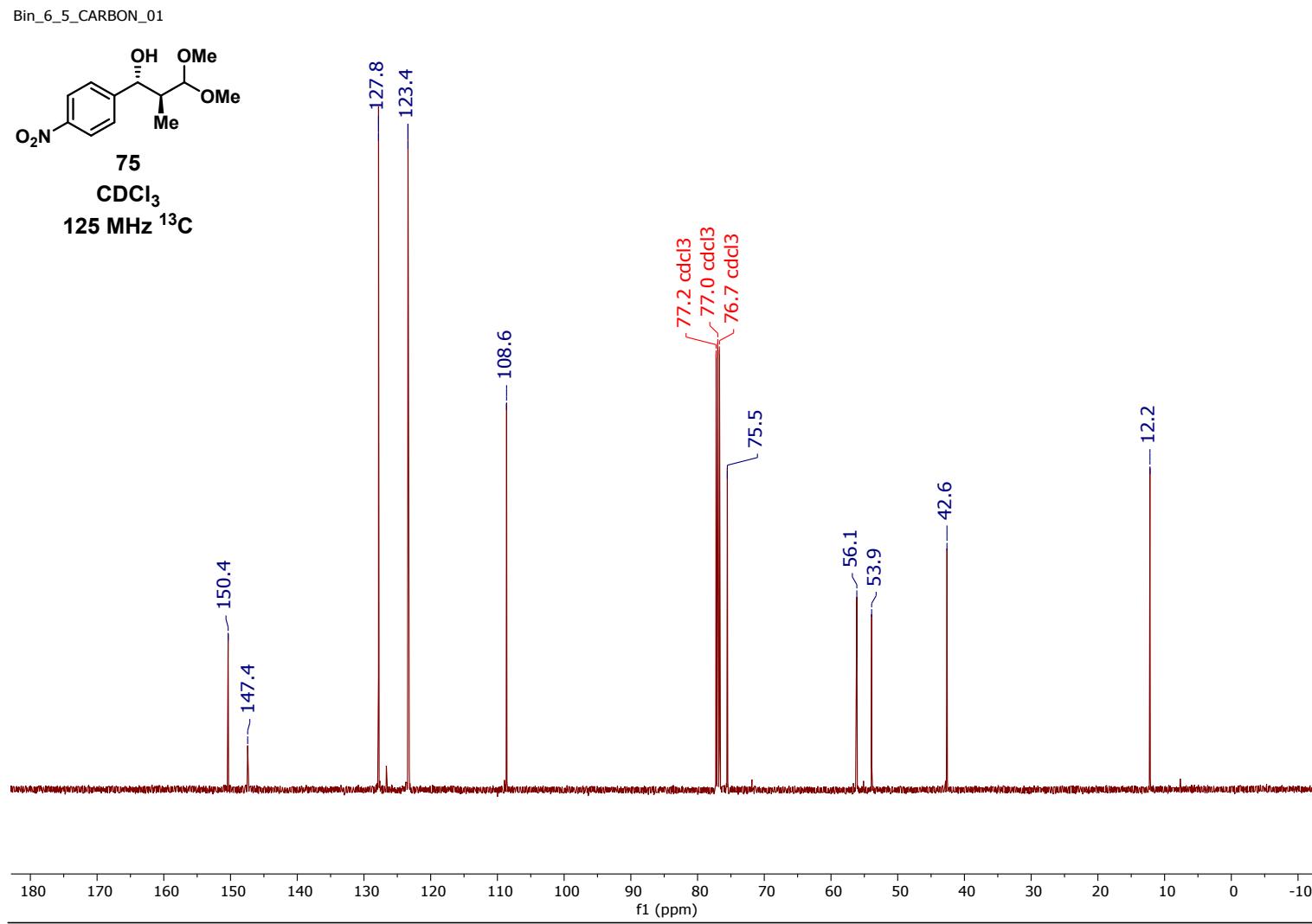


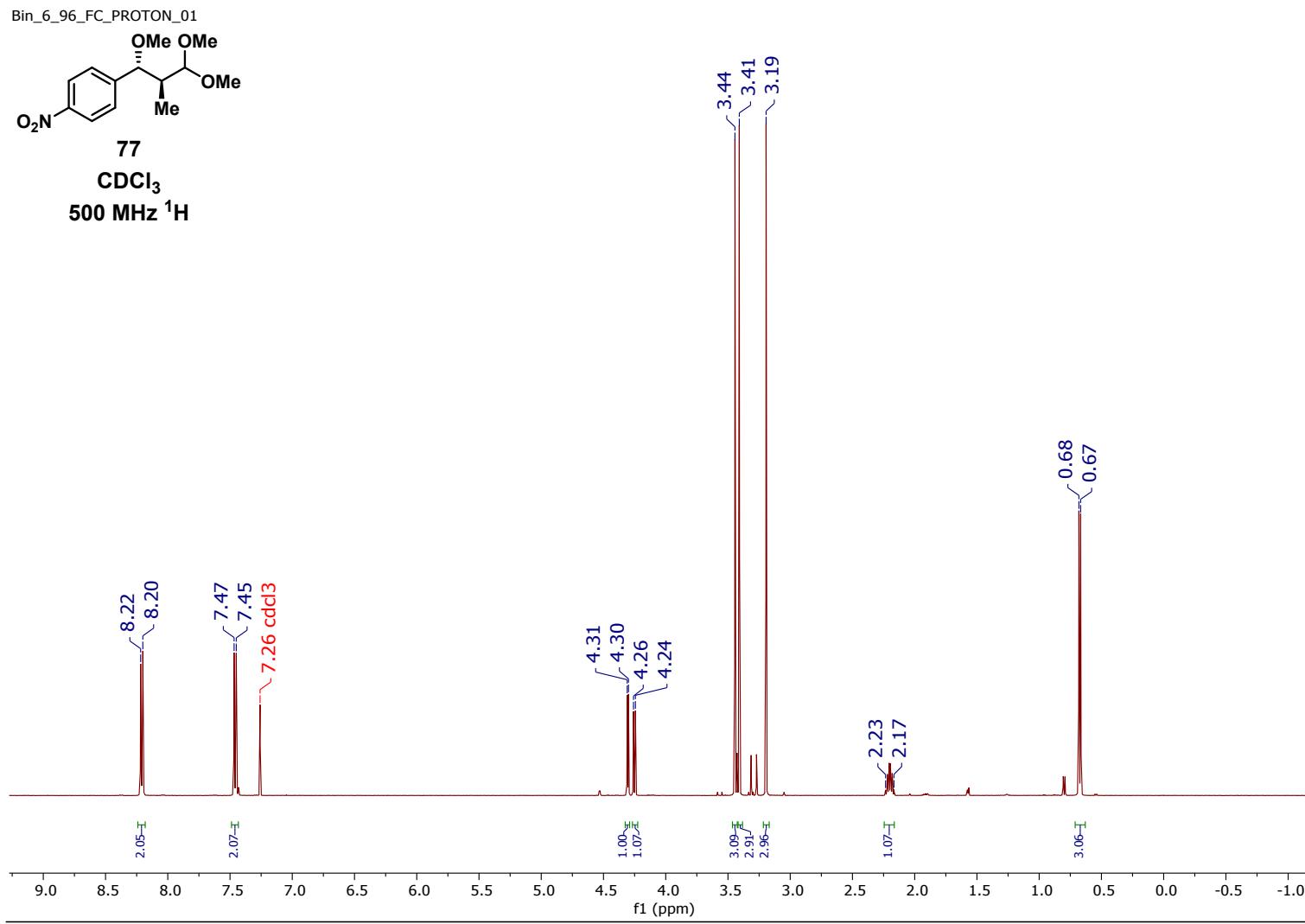
Bin\_5\_300\_PROTON\_01

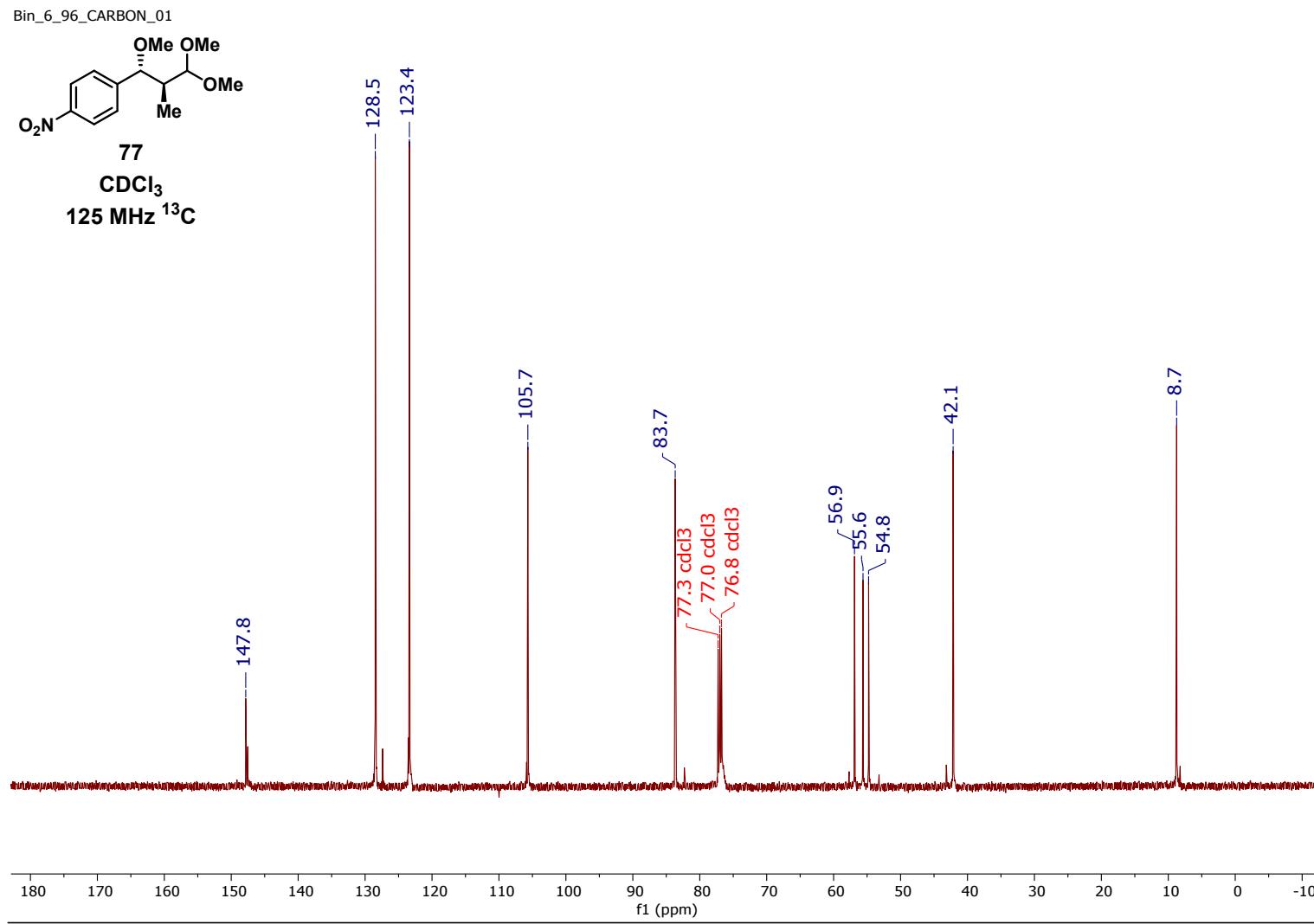
**74** $\text{CDCl}_3$ 500 MHz  $^1\text{H}$ 



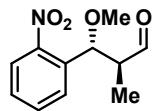




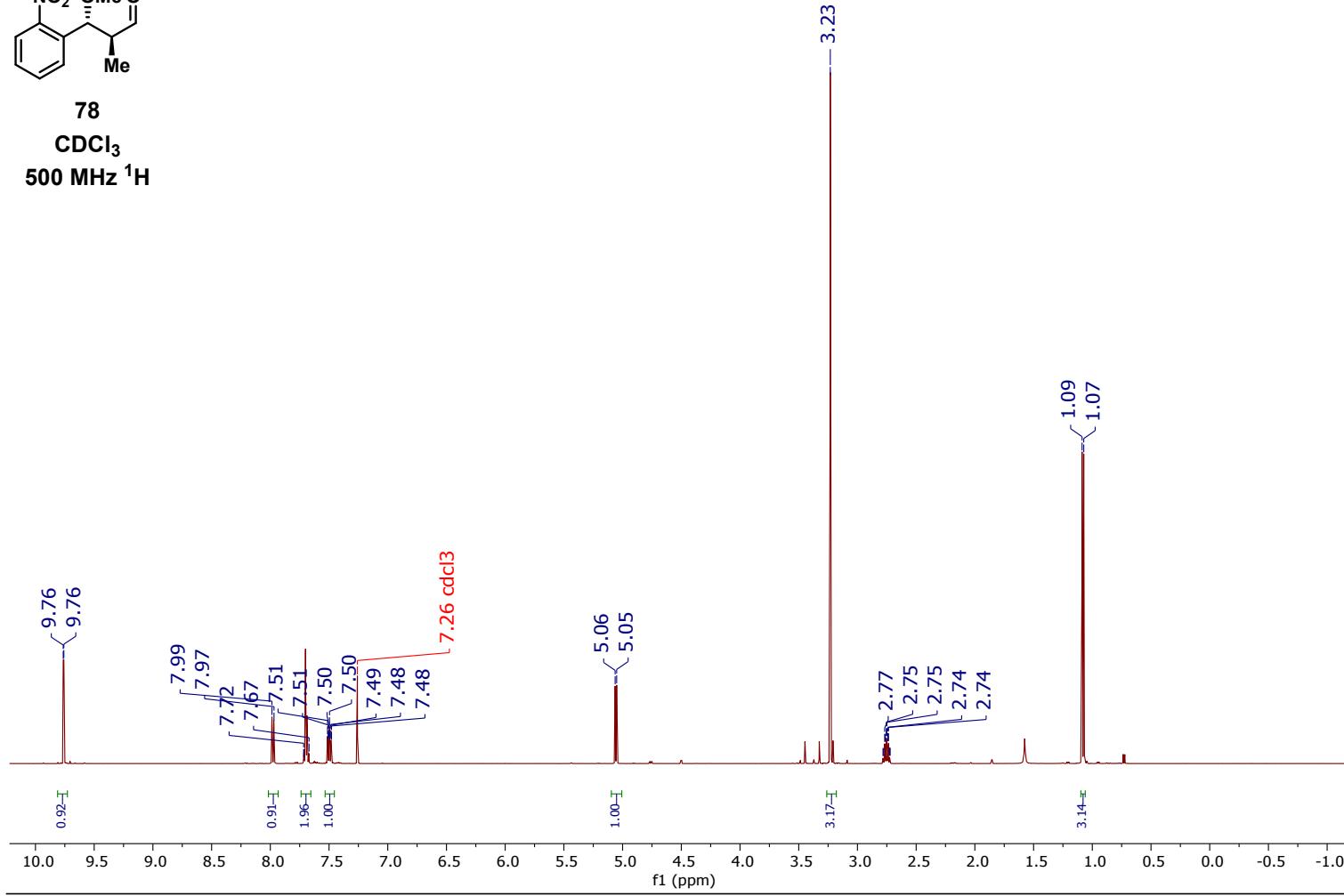




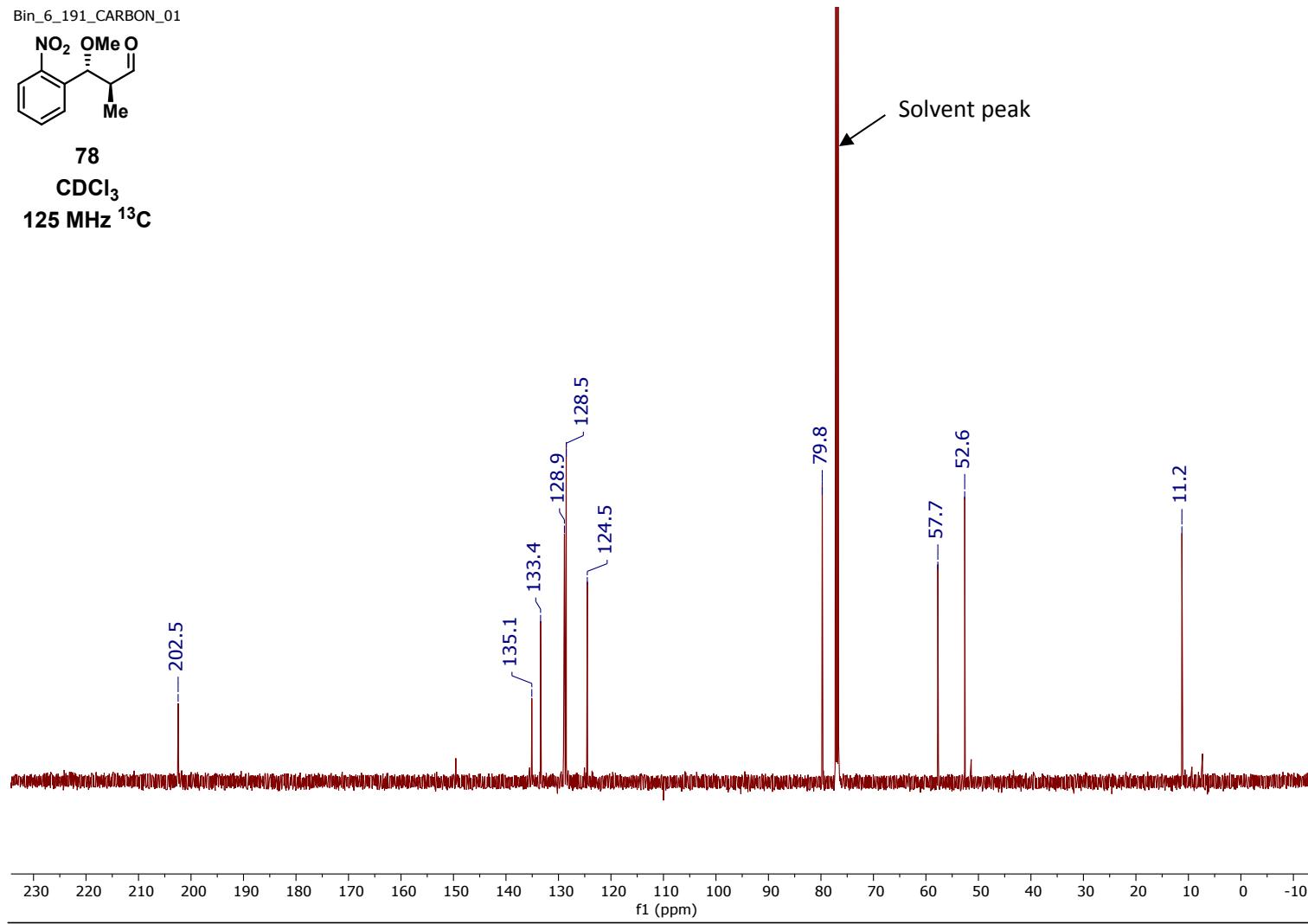
Bin\_6\_191S\_FC\_PROTON\_01

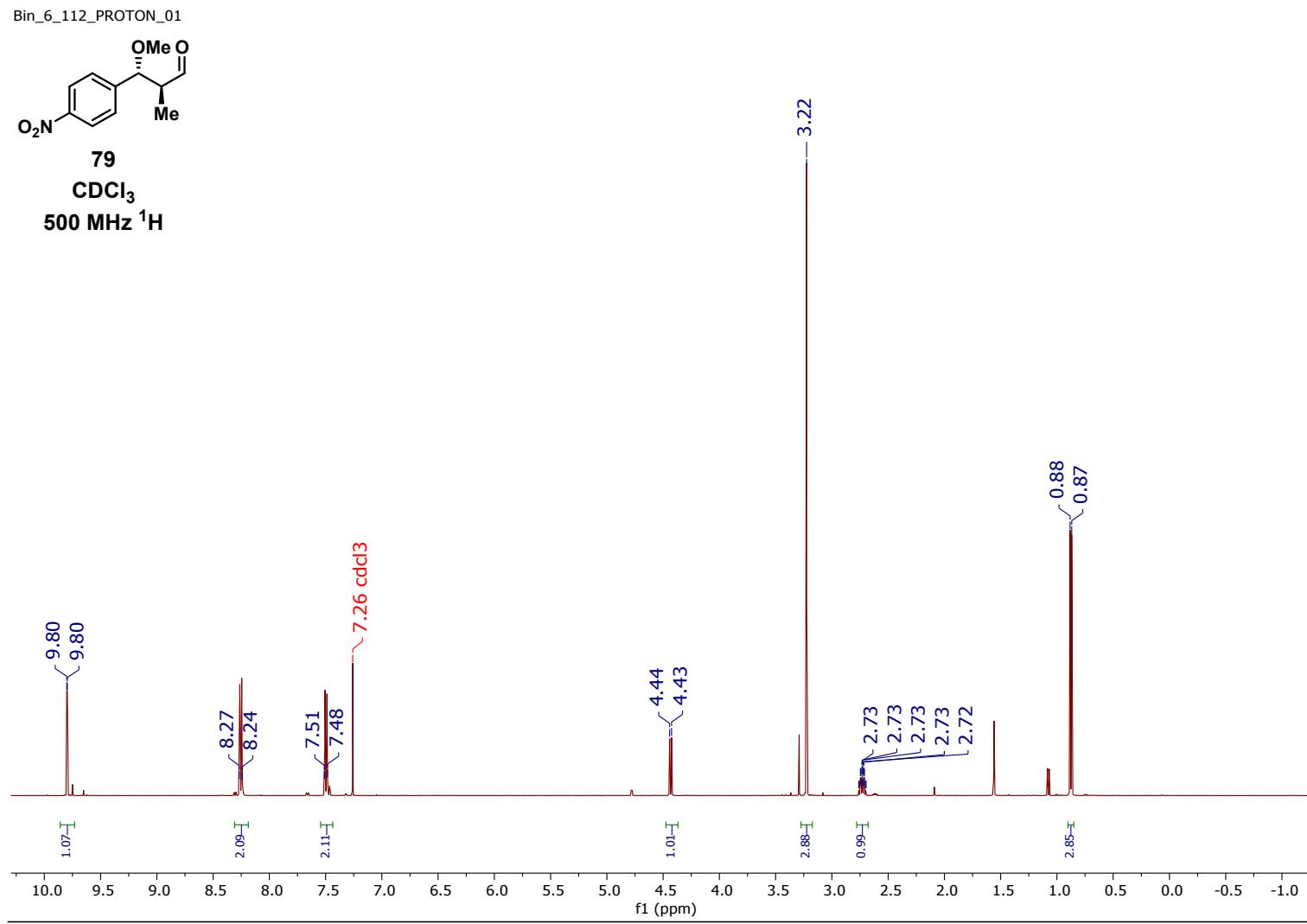


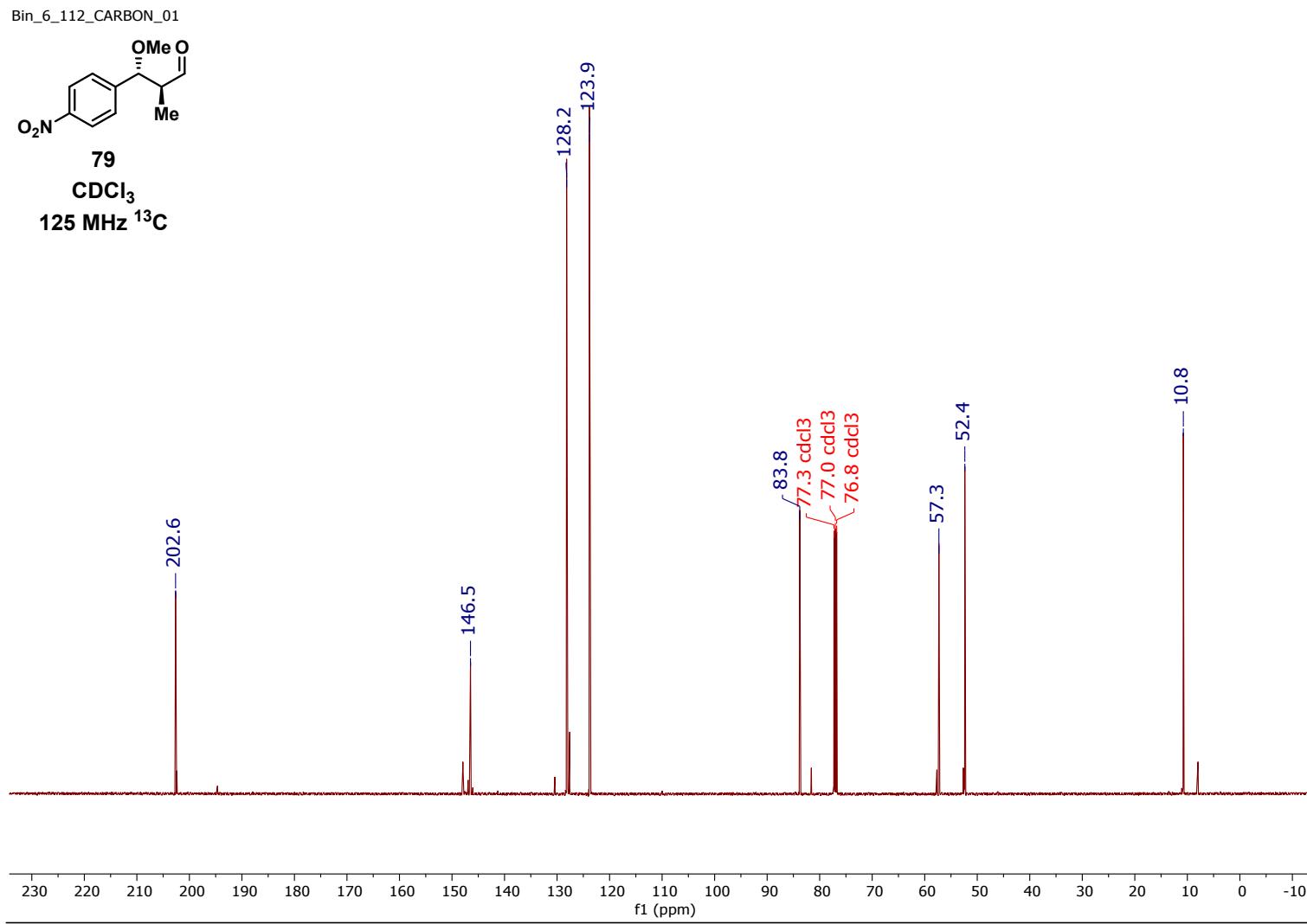
78  
 $\text{CDCl}_3$   
500 MHz  $^1\text{H}$

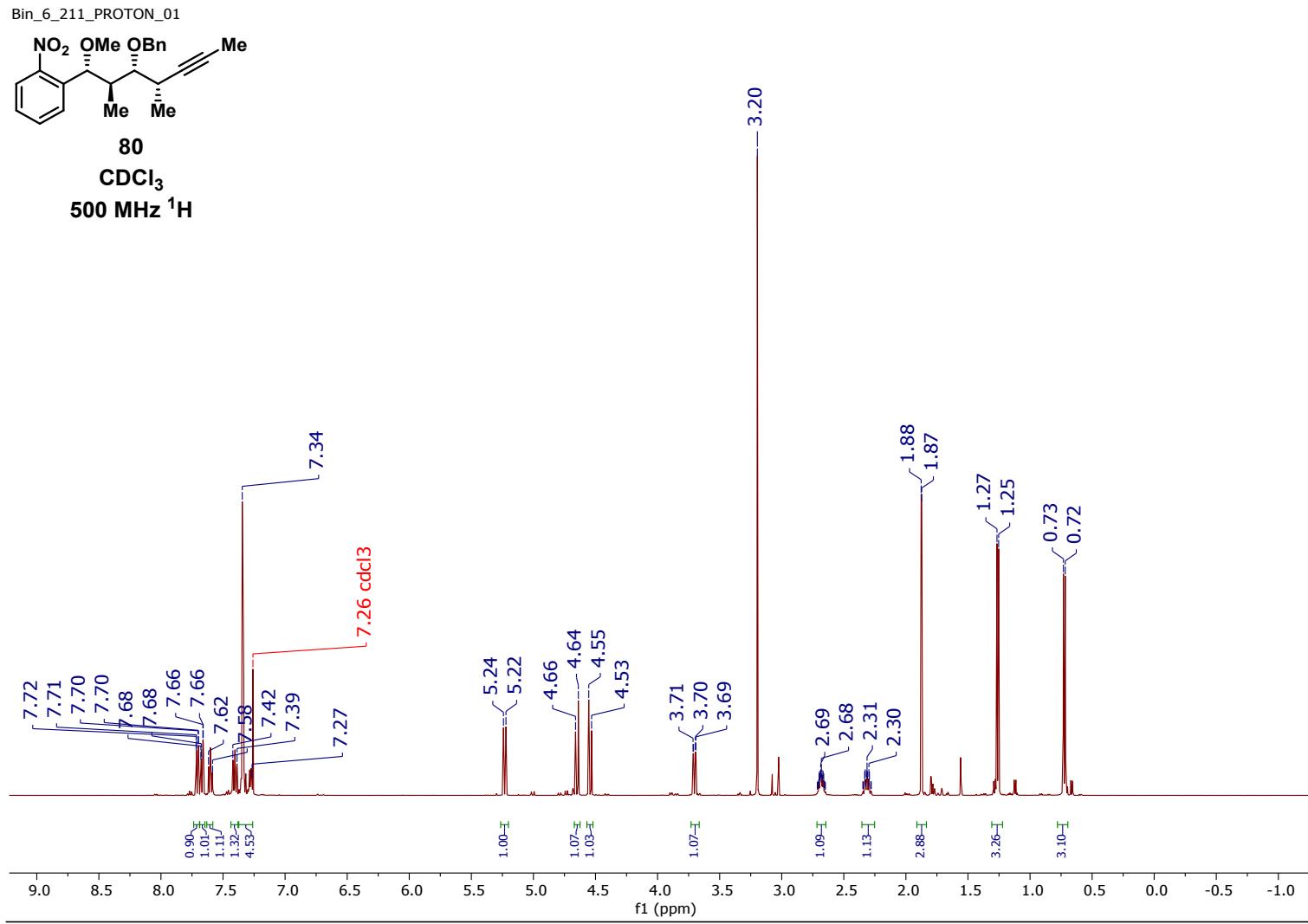


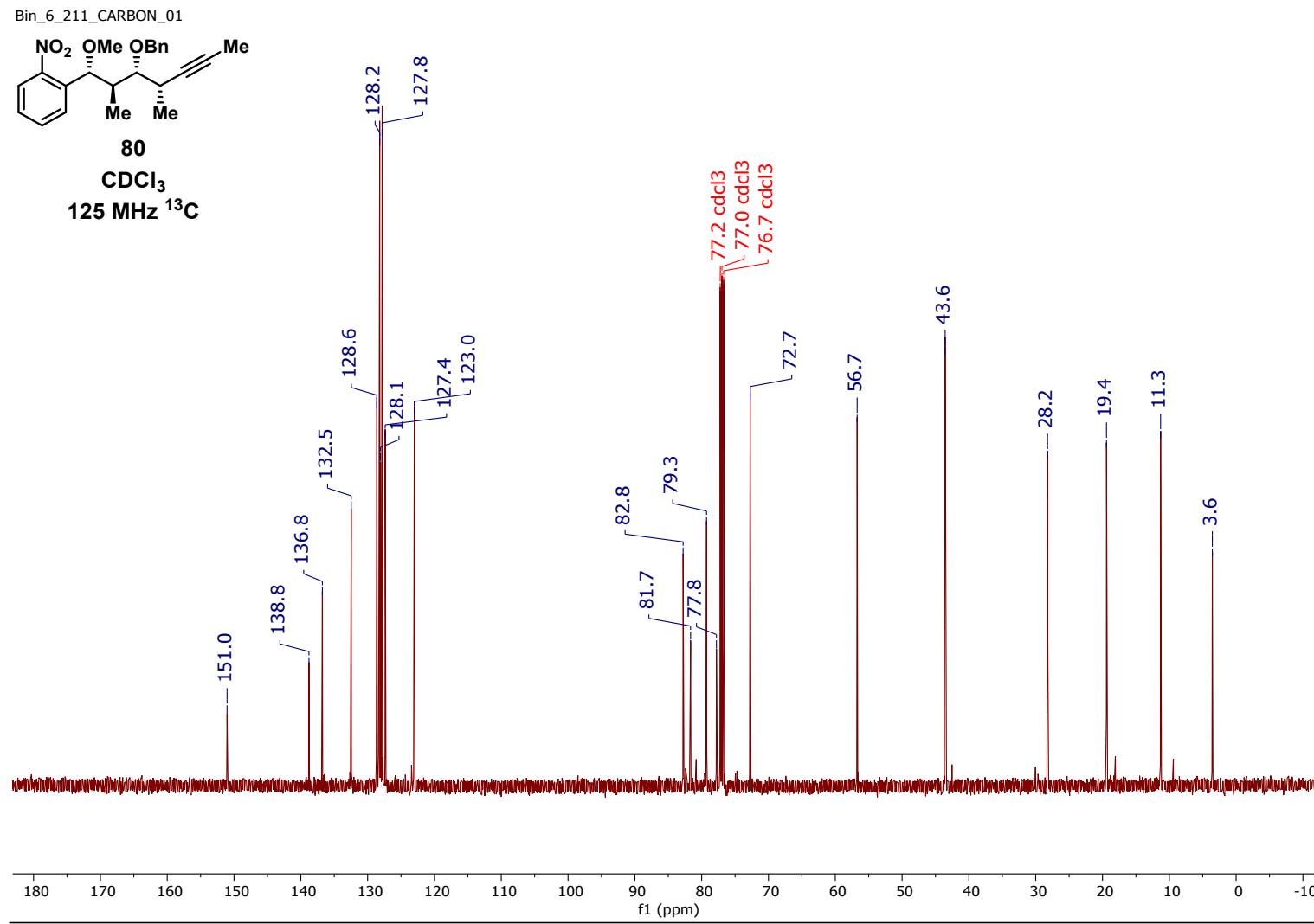
SI-178

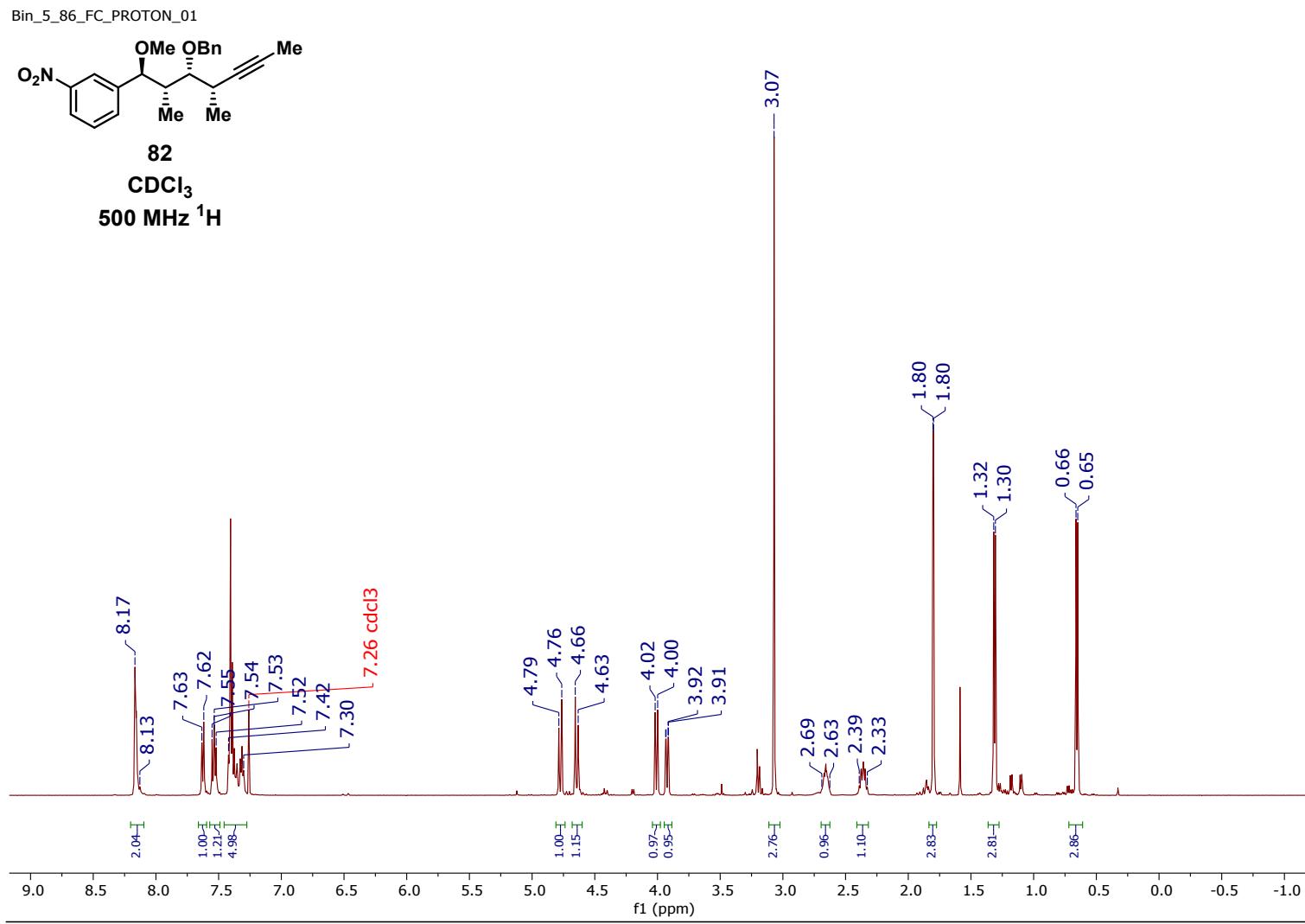


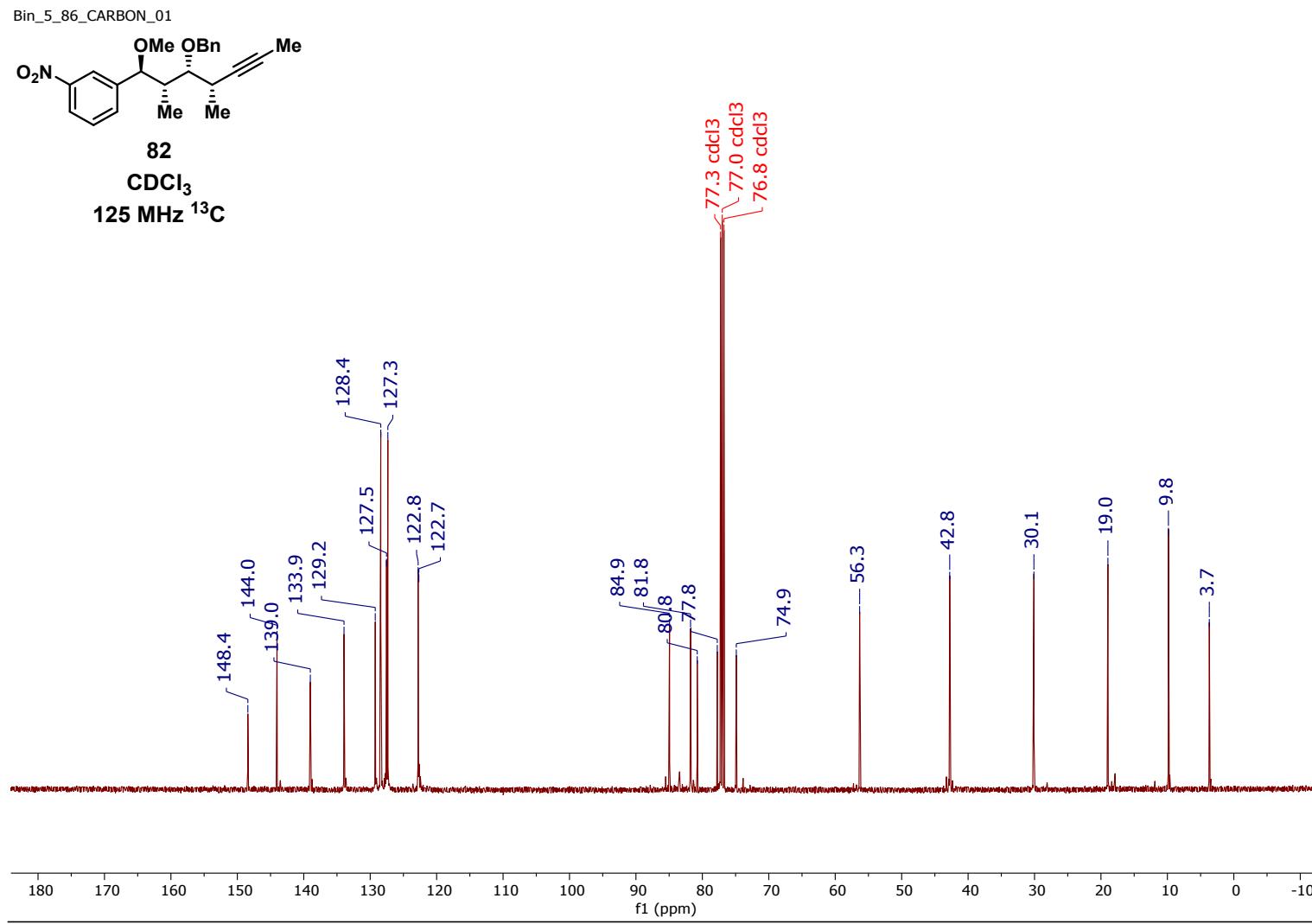


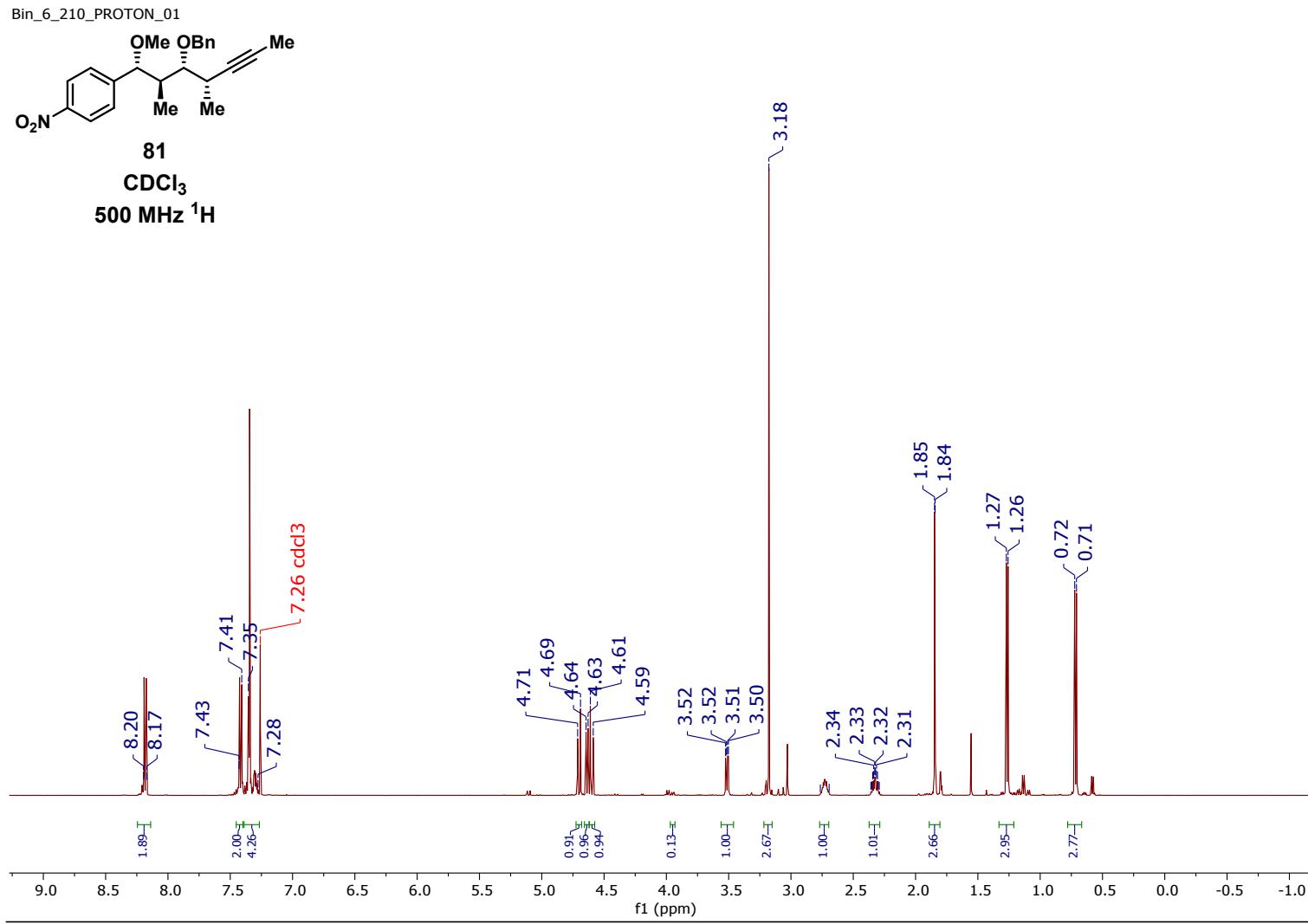


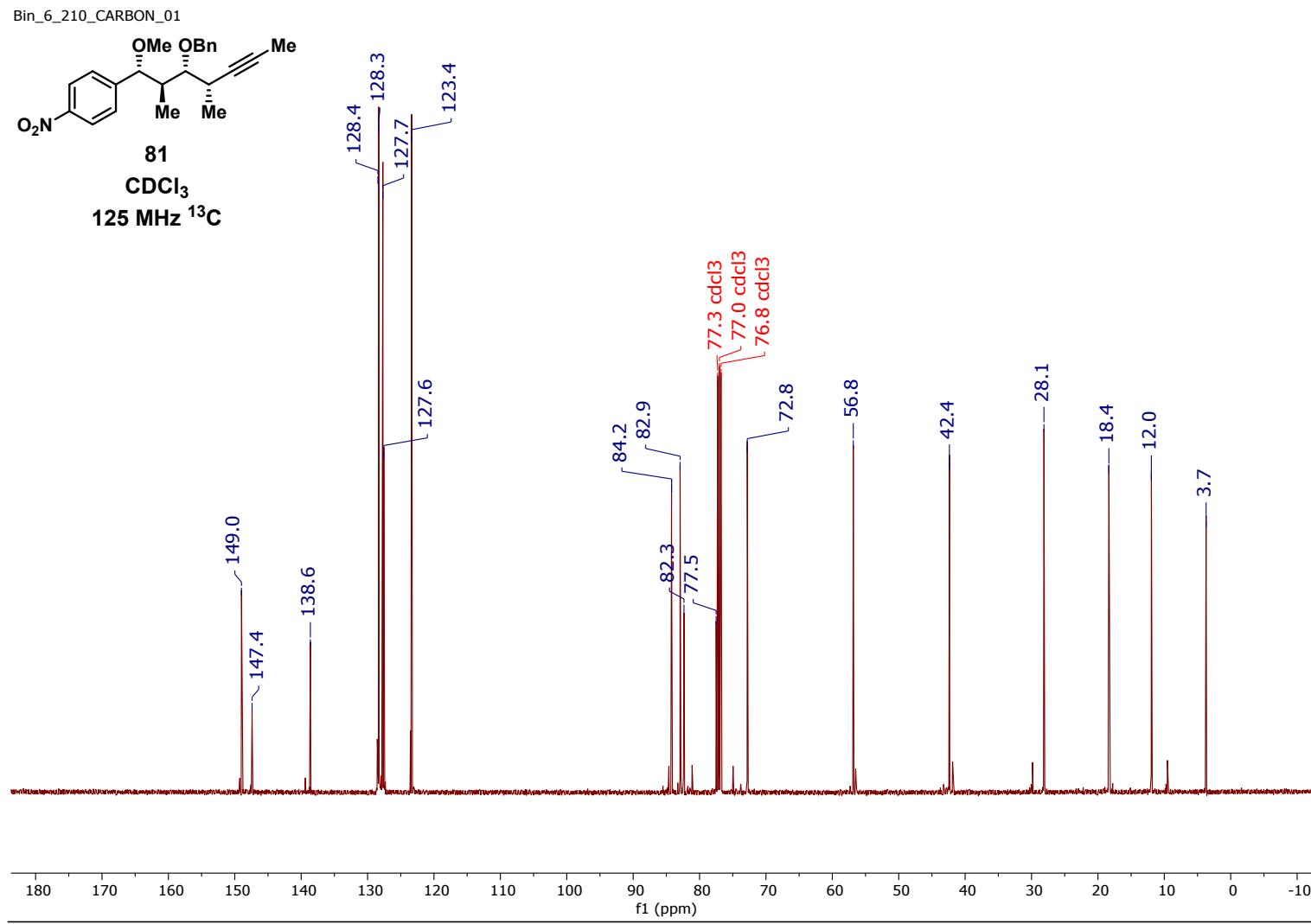


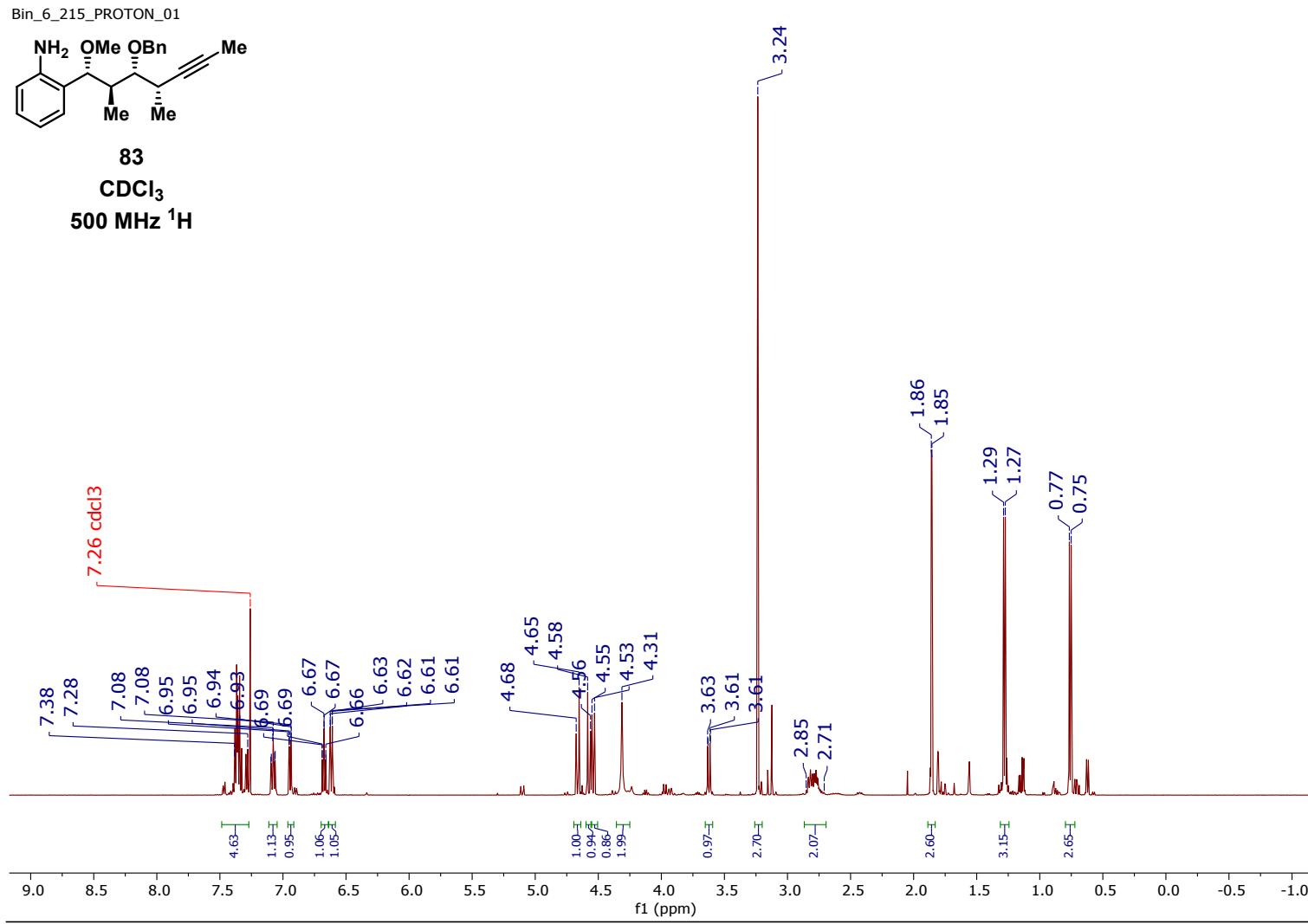


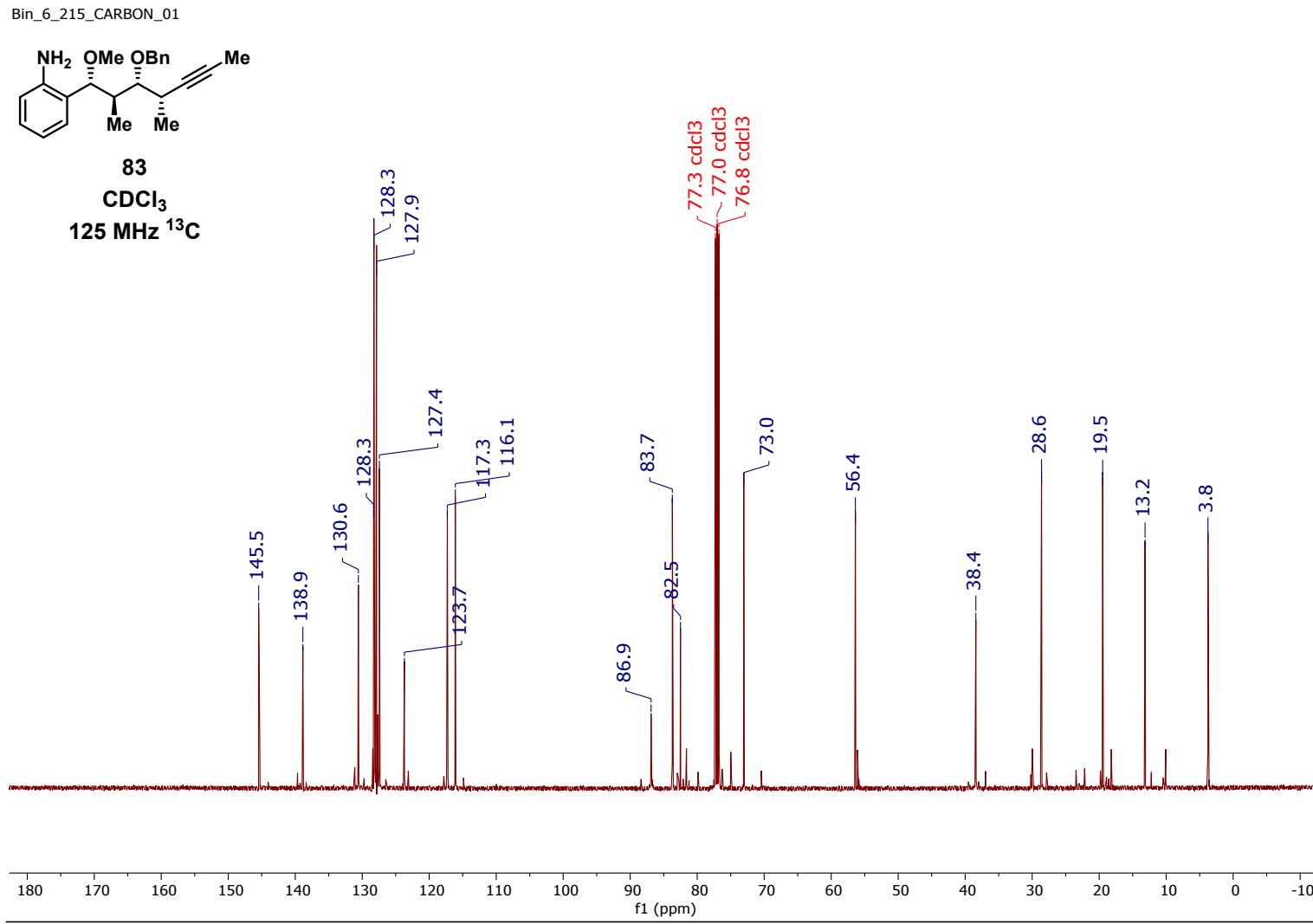


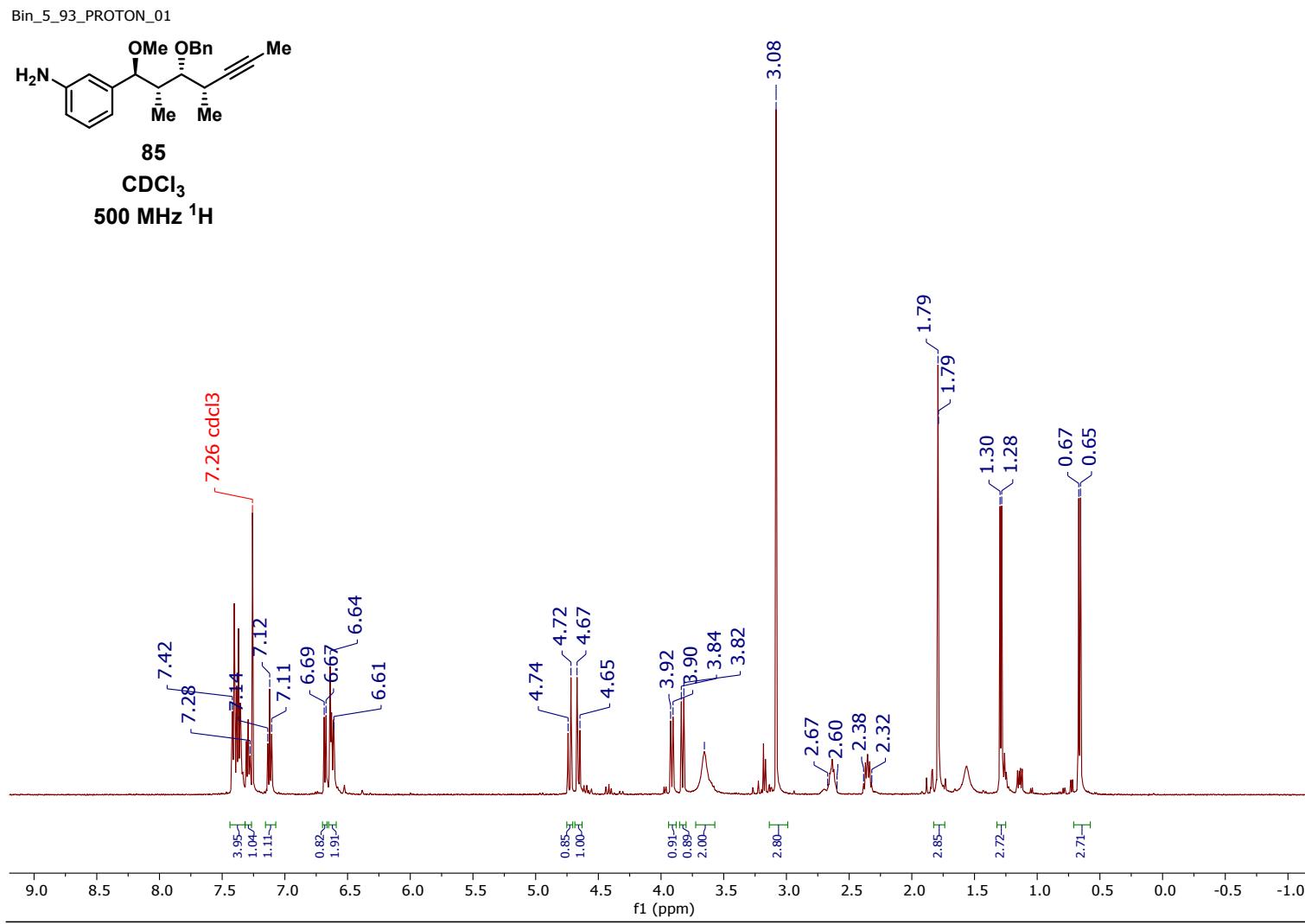




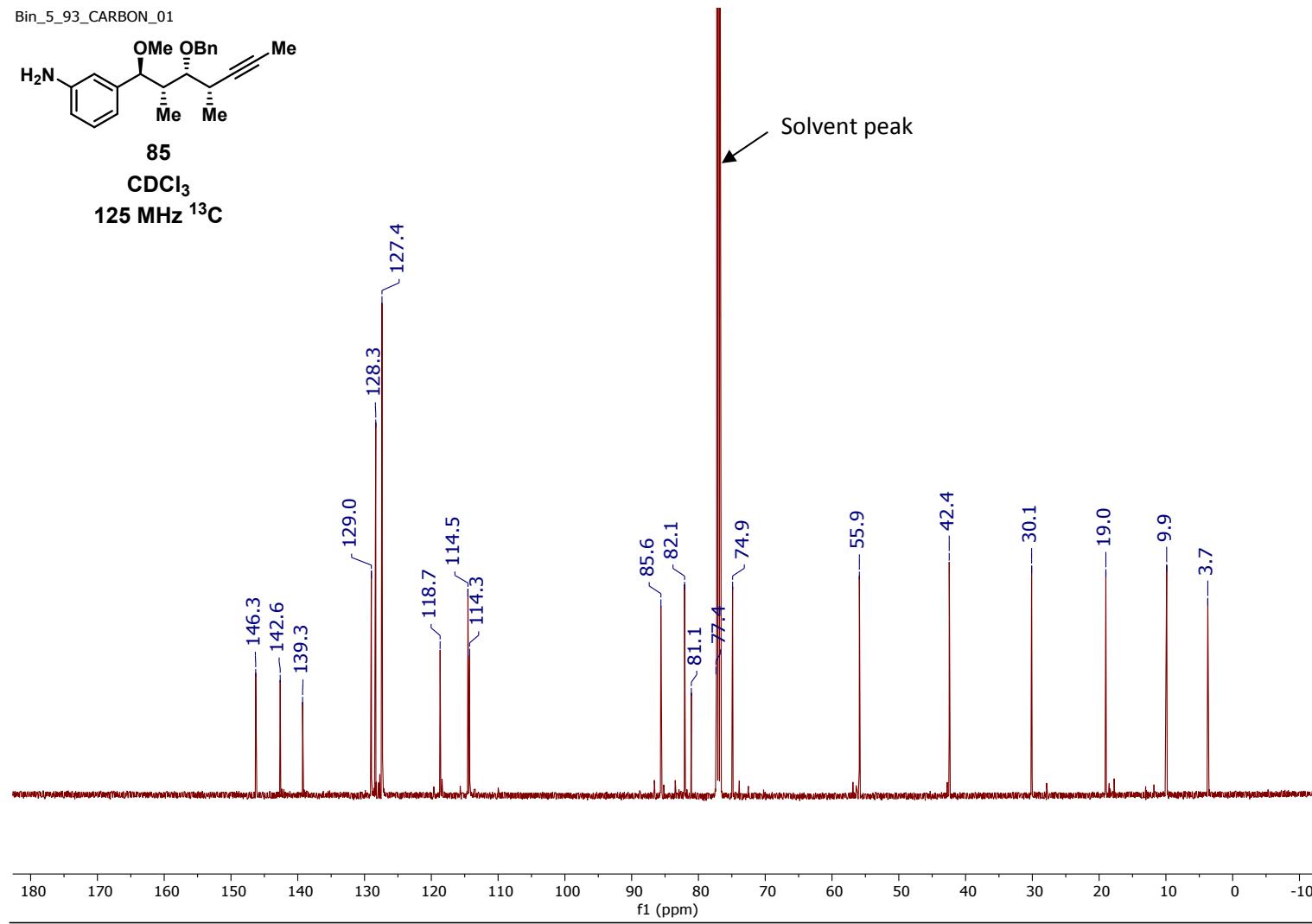


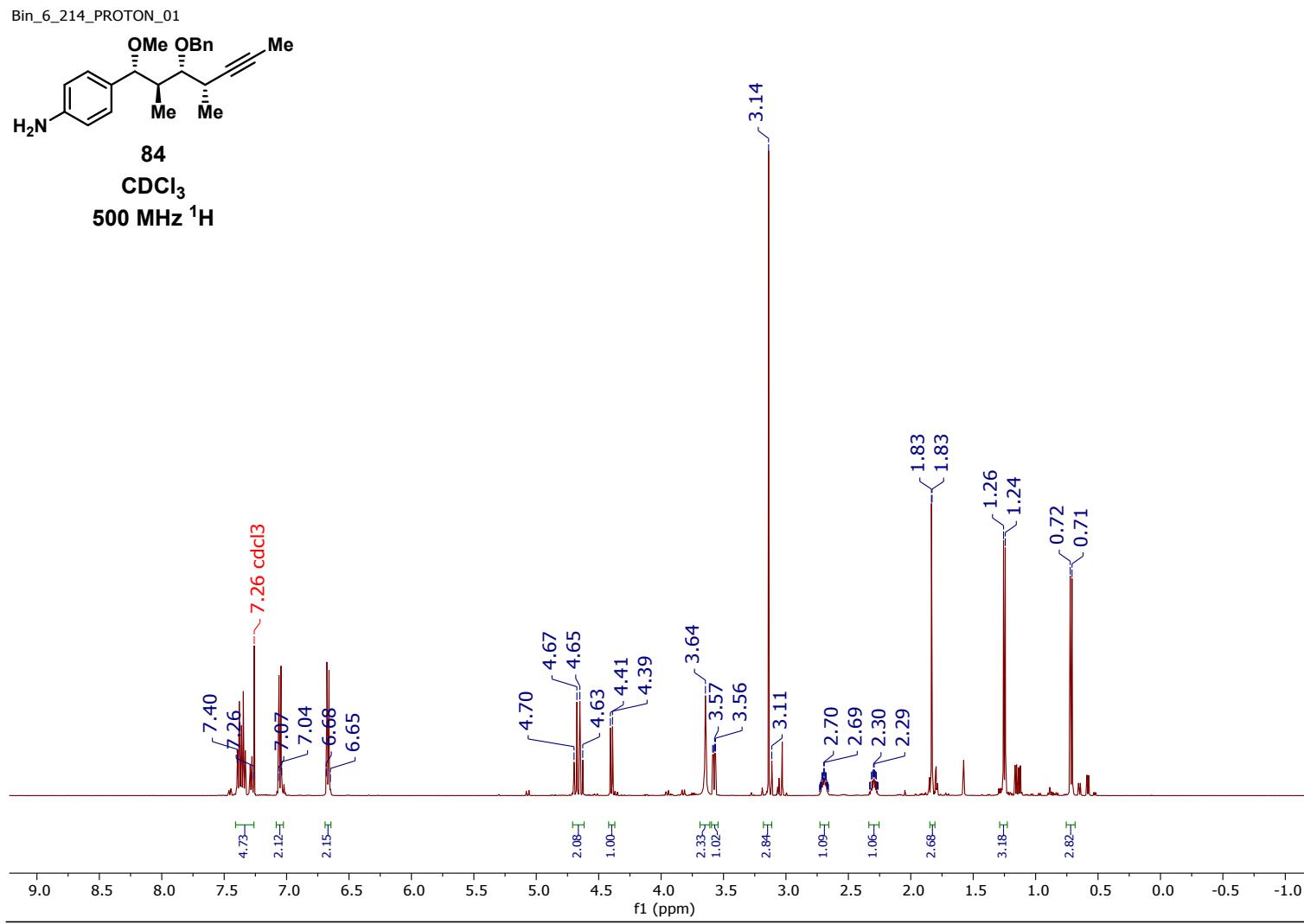


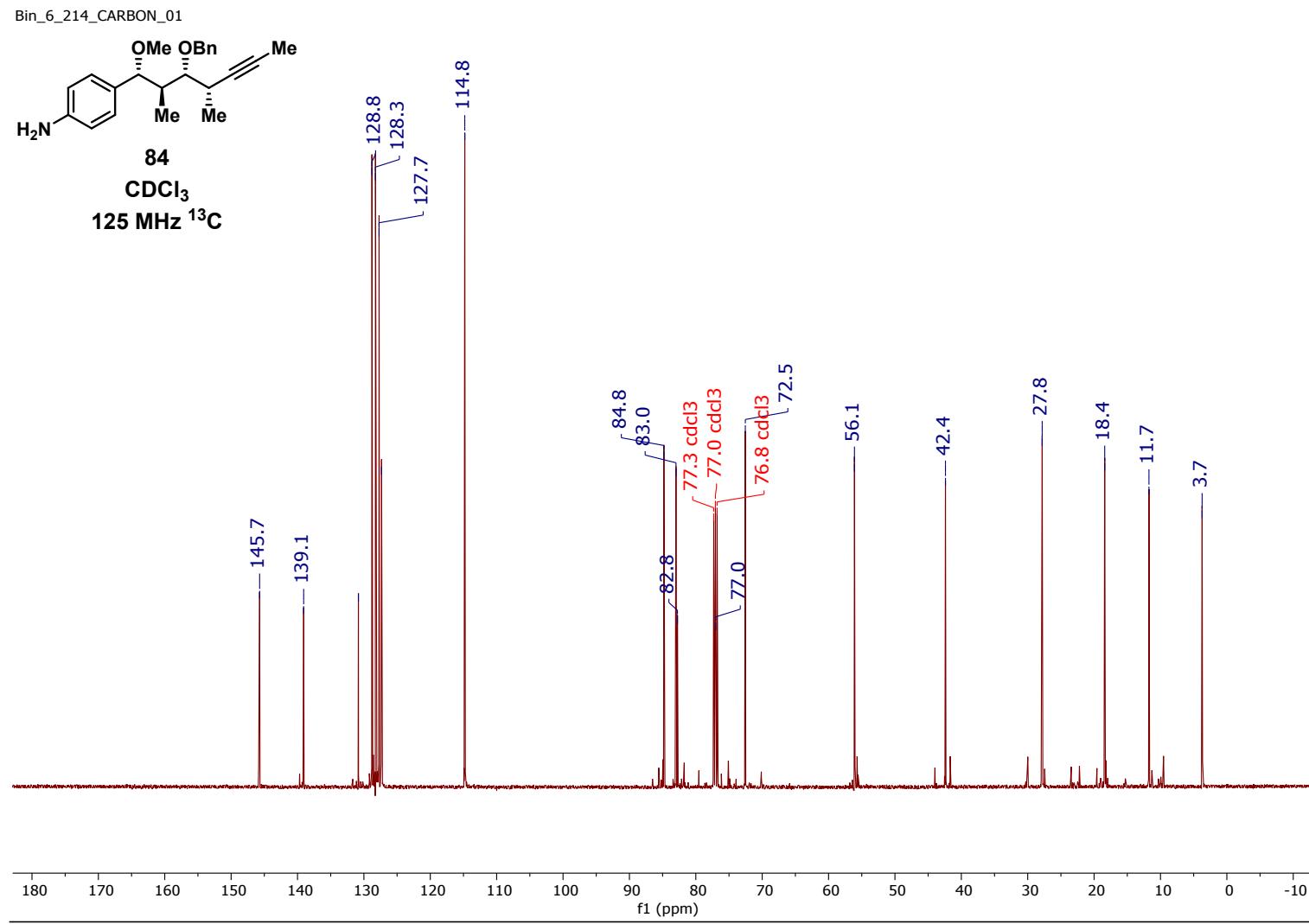


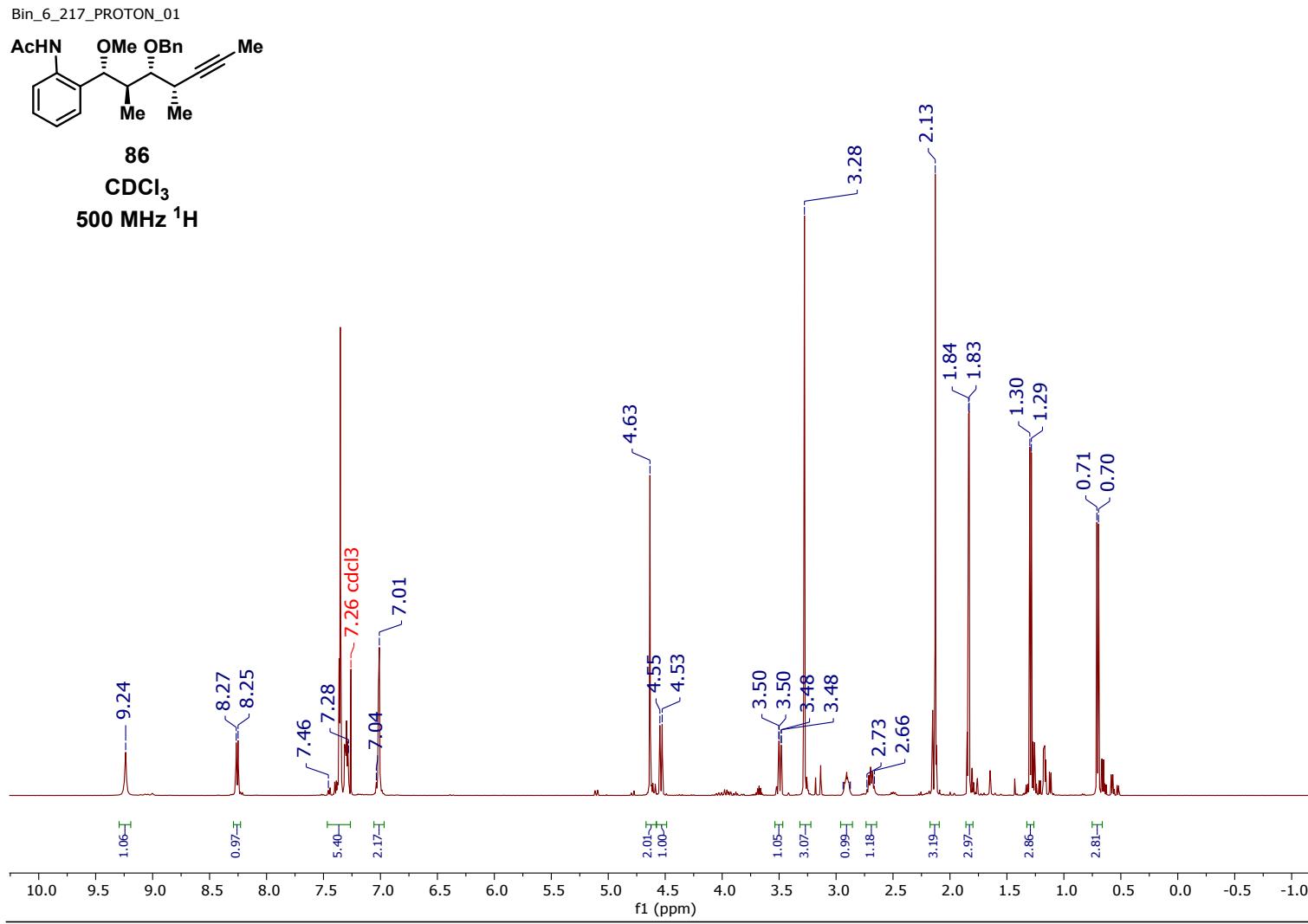


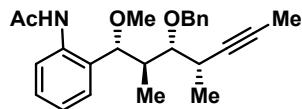
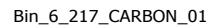
SI-190



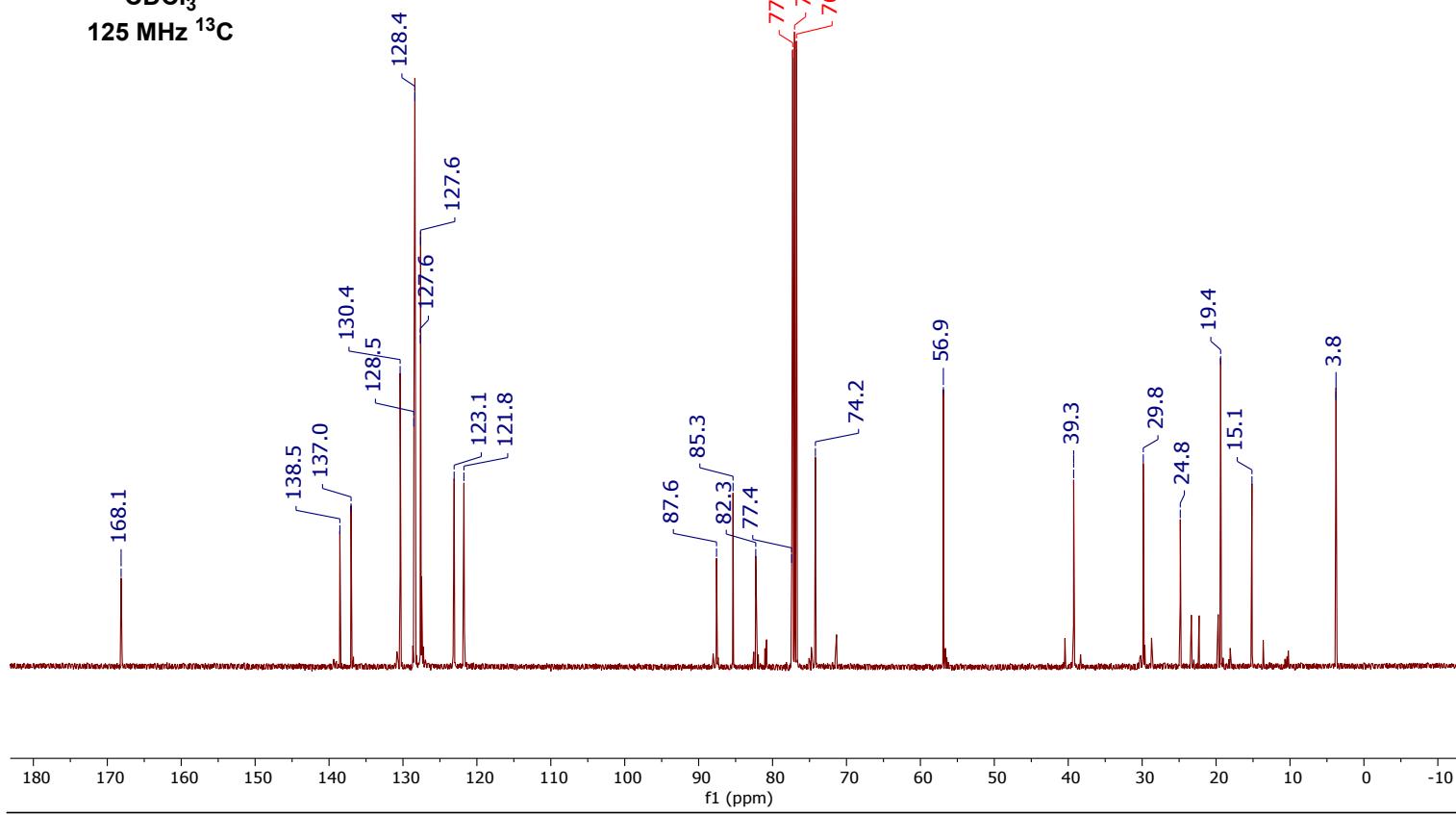


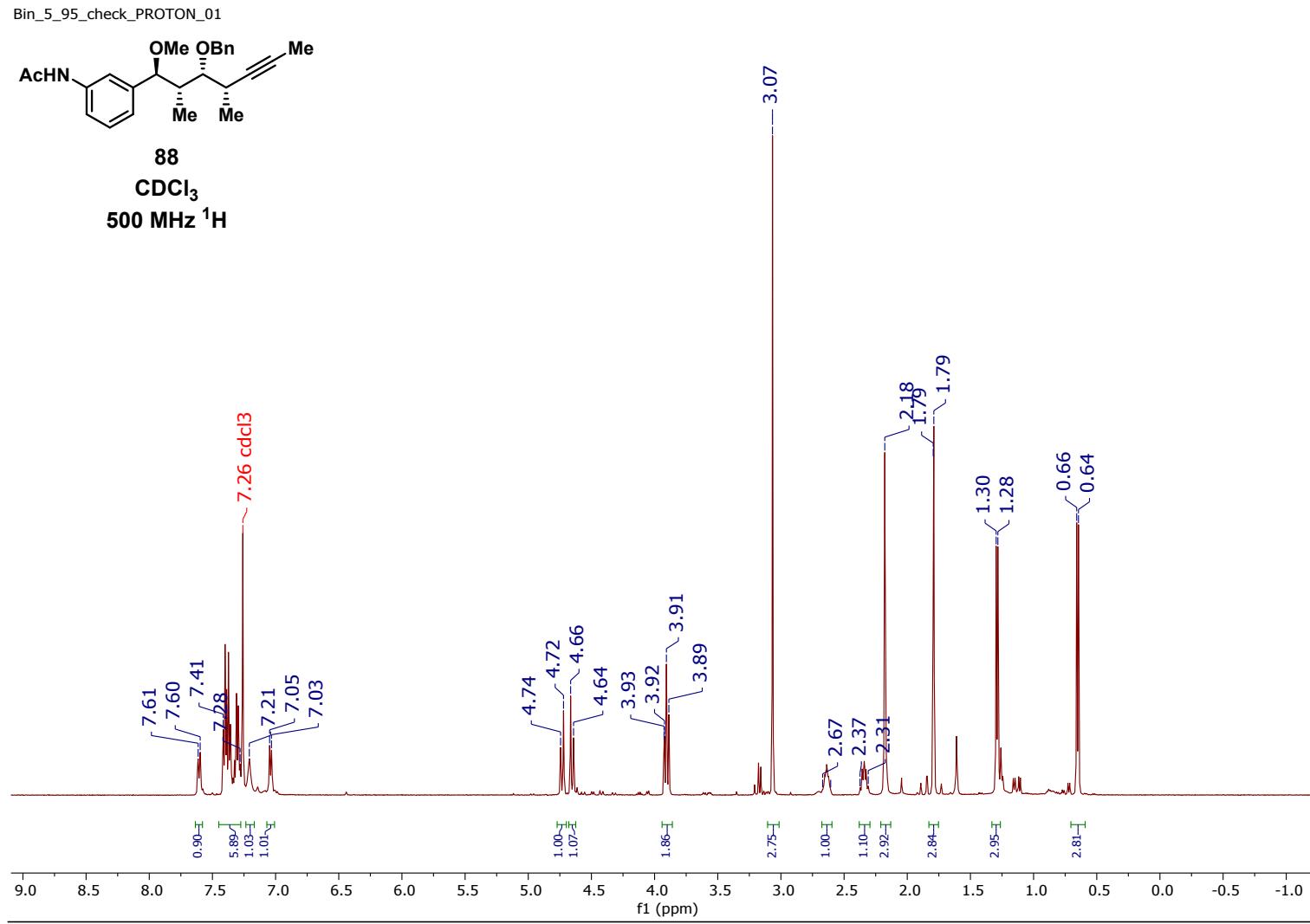


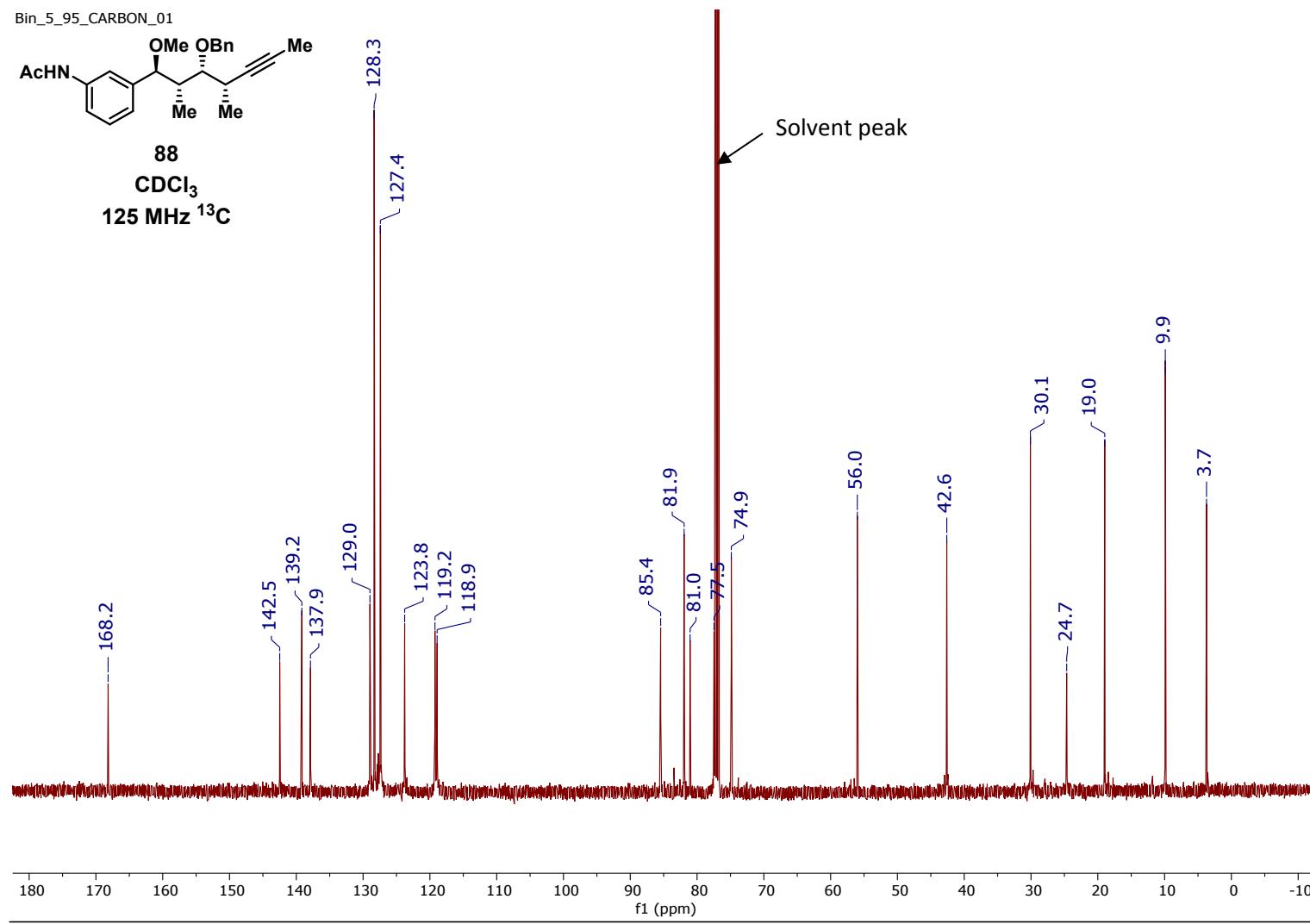


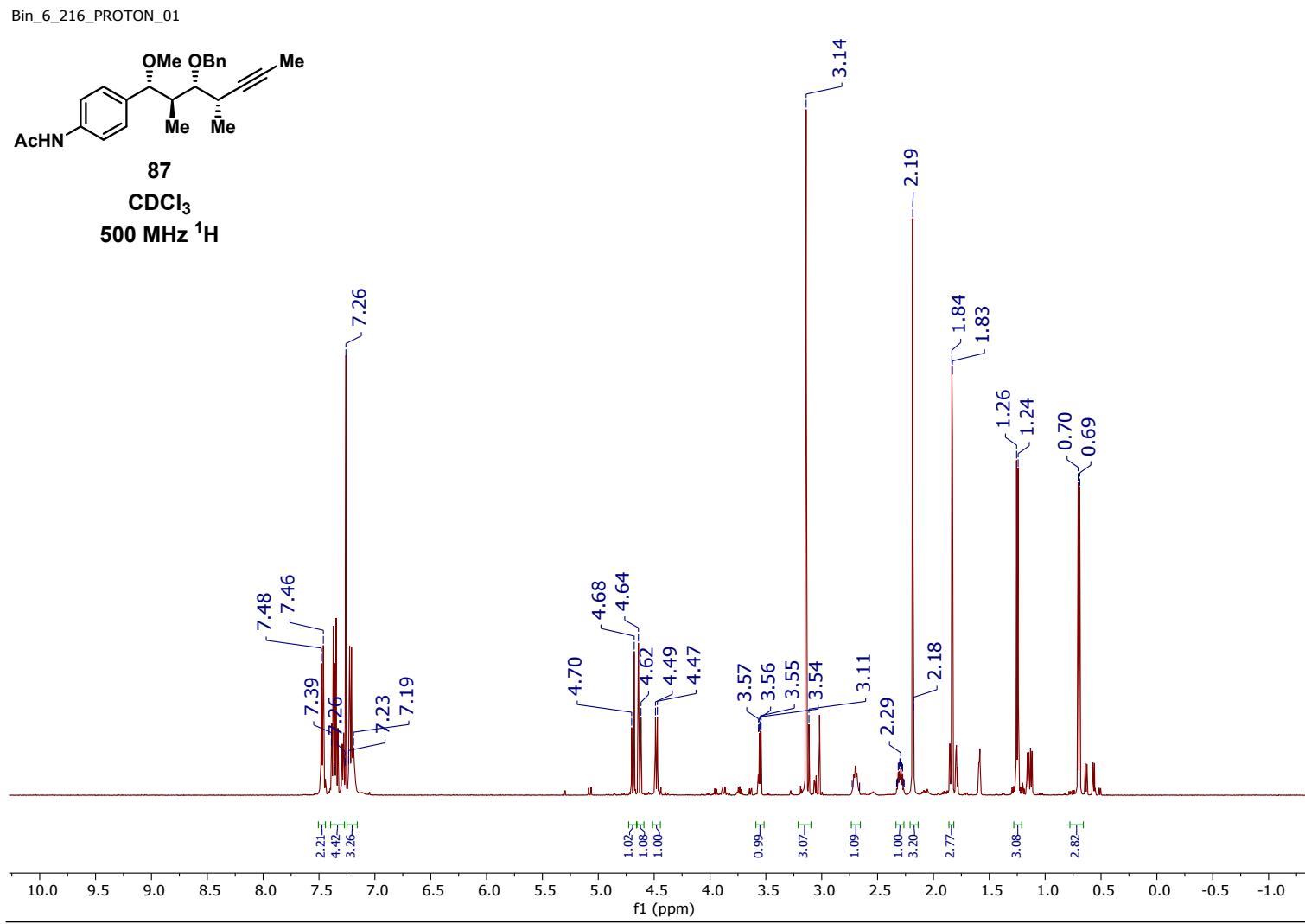


86  
 $\text{CDCl}_3$   
 25 MHz  $^{13}\text{C}$

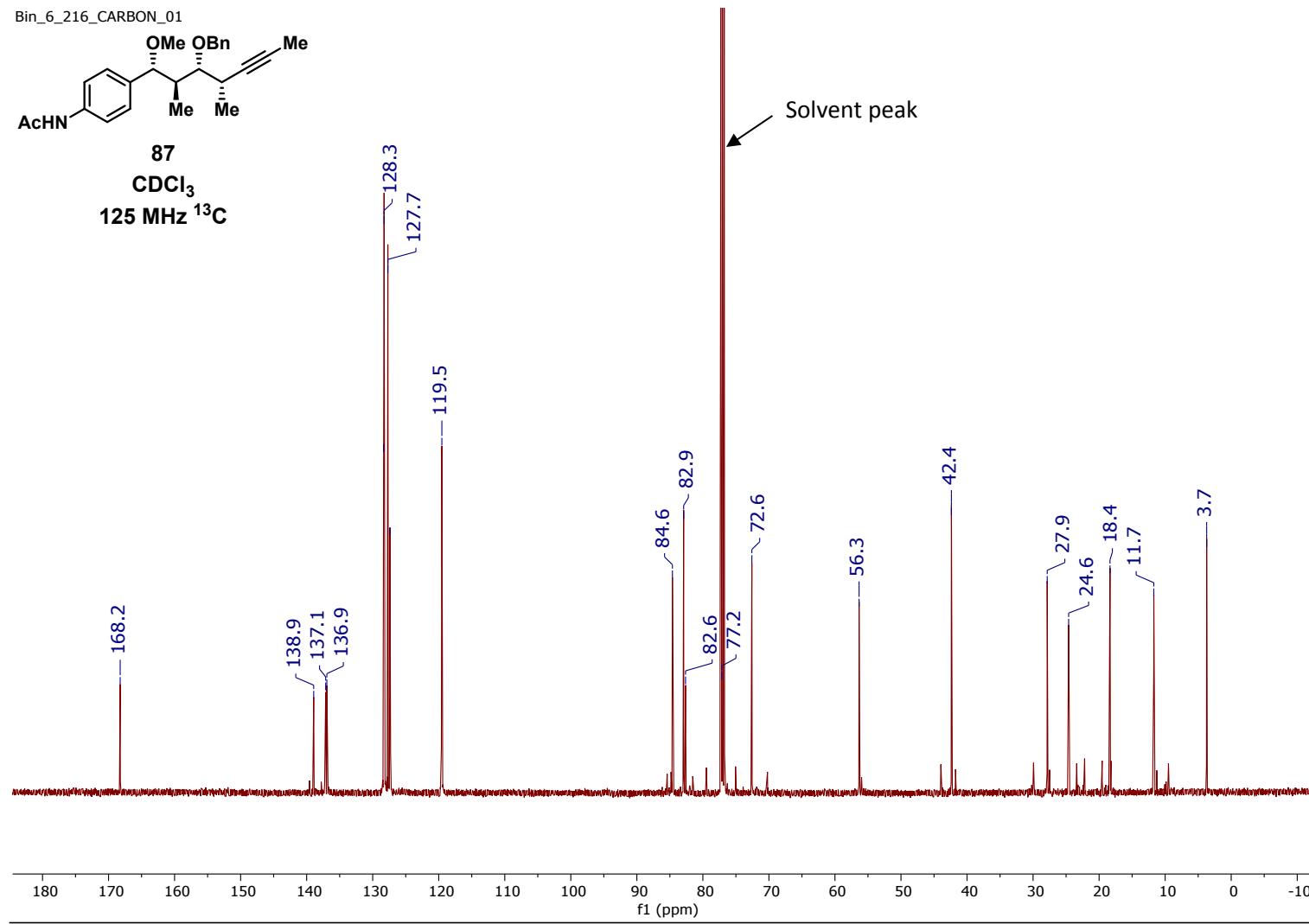


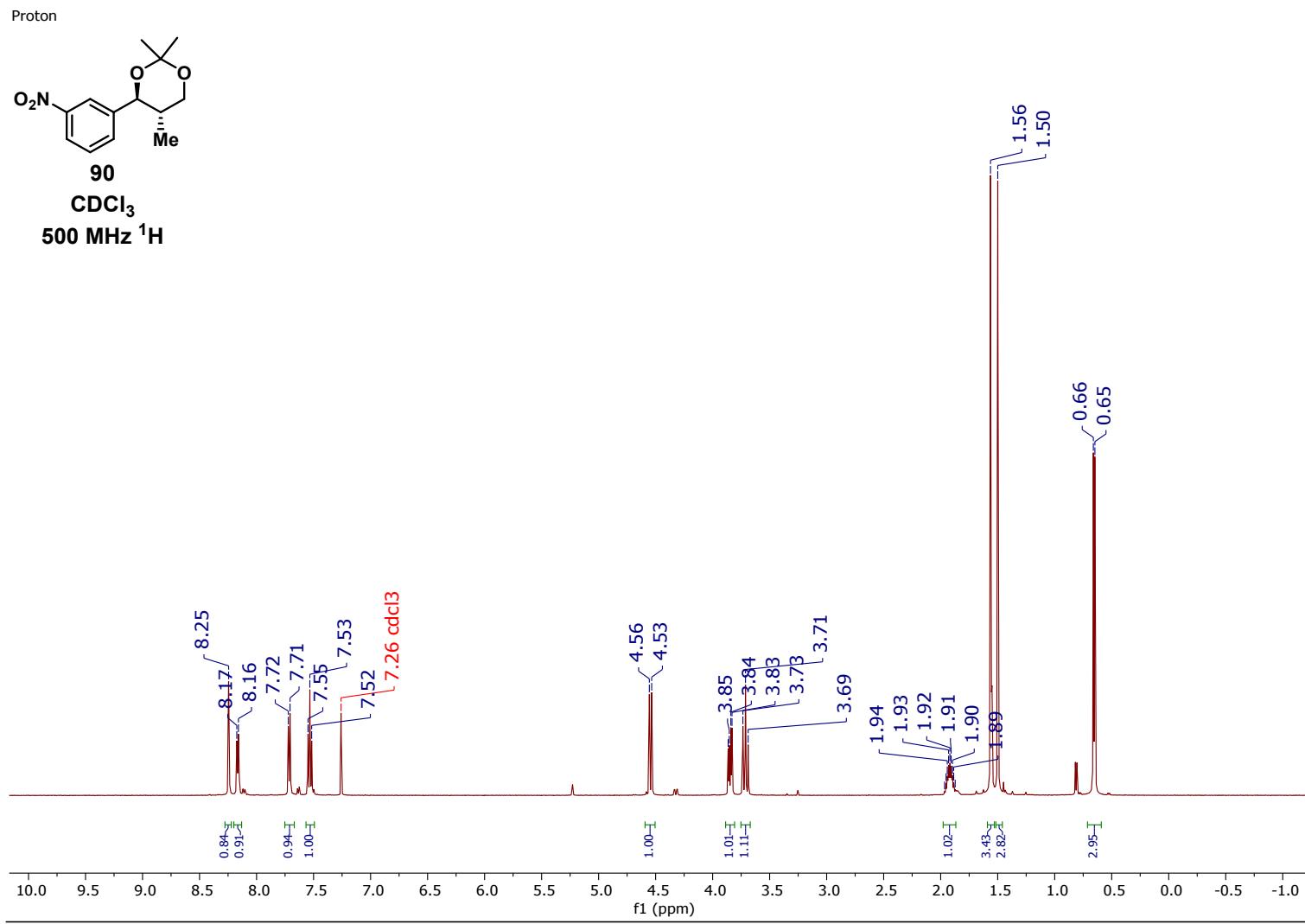




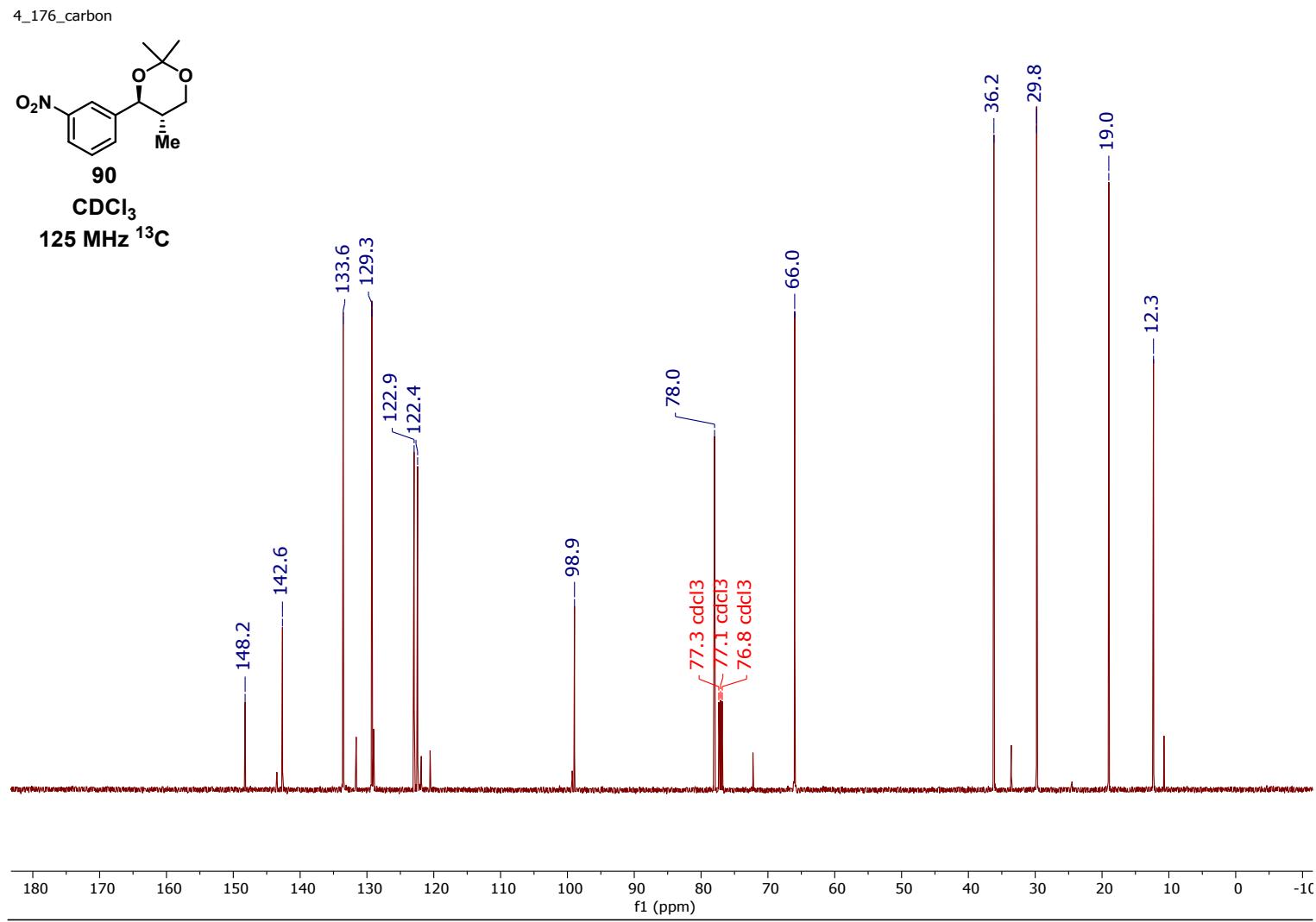


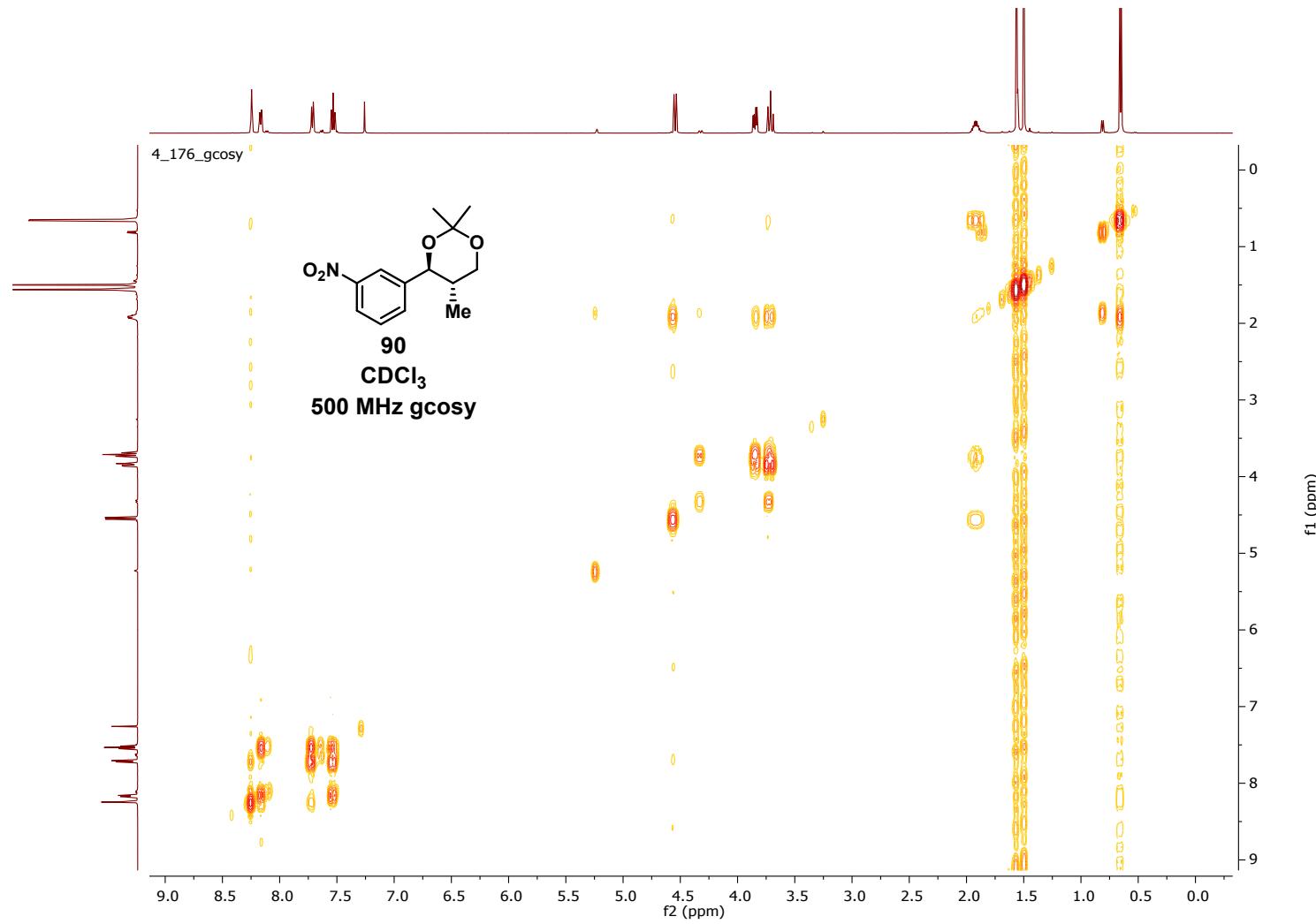
SI-198



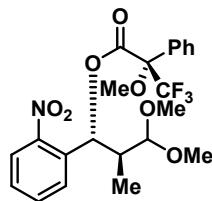


SI-200

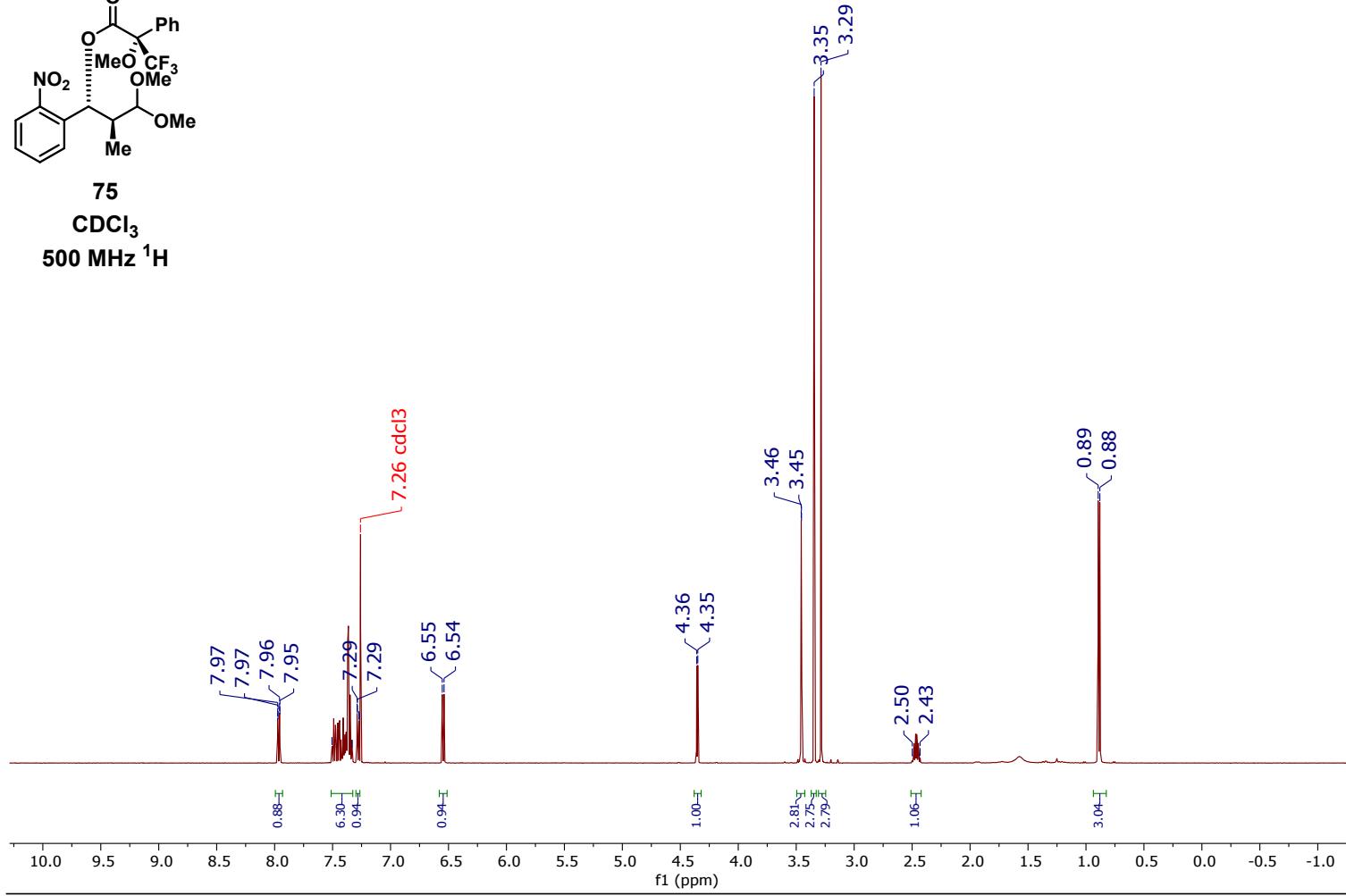




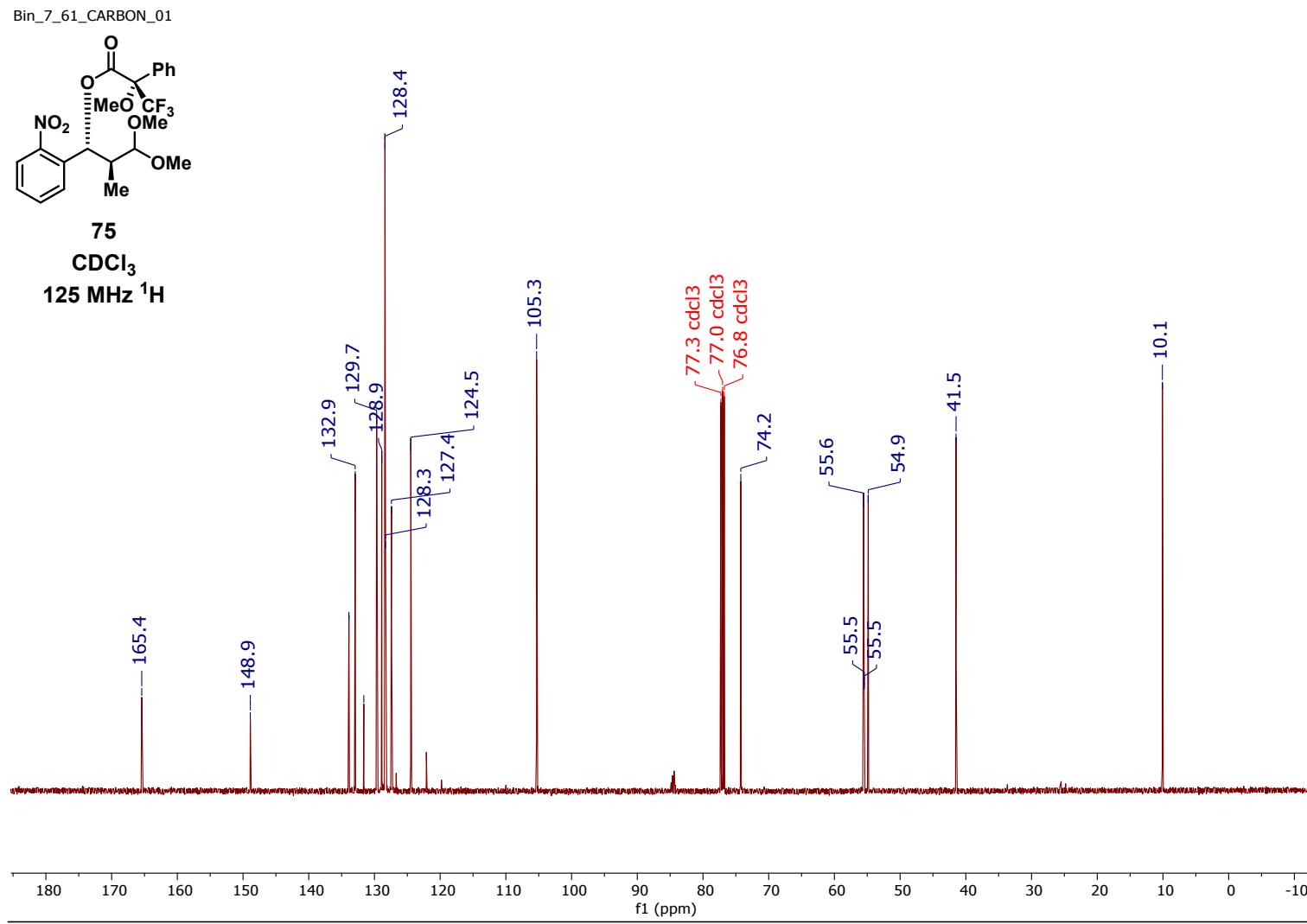
Bin\_7\_61\_PROTON\_01

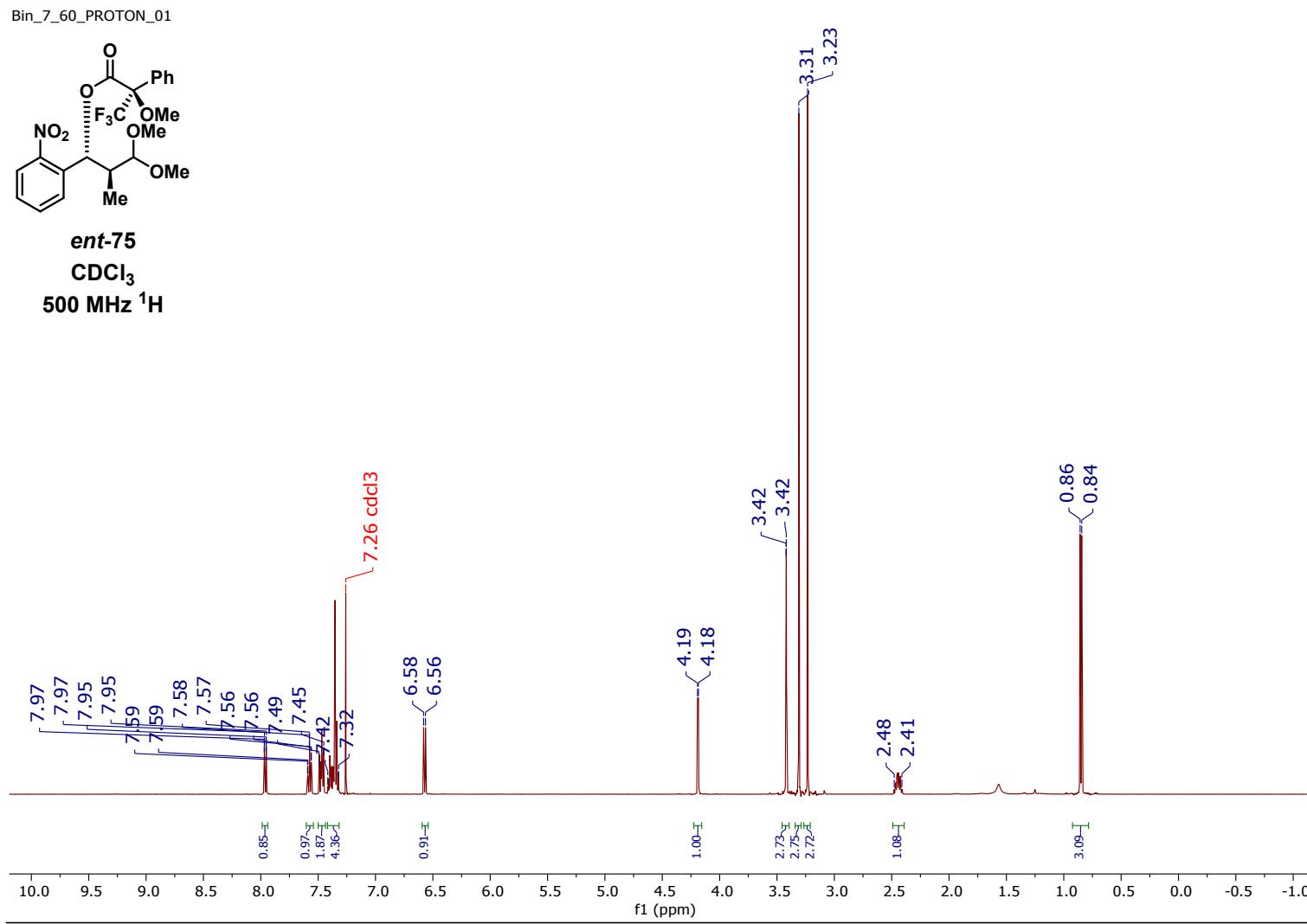


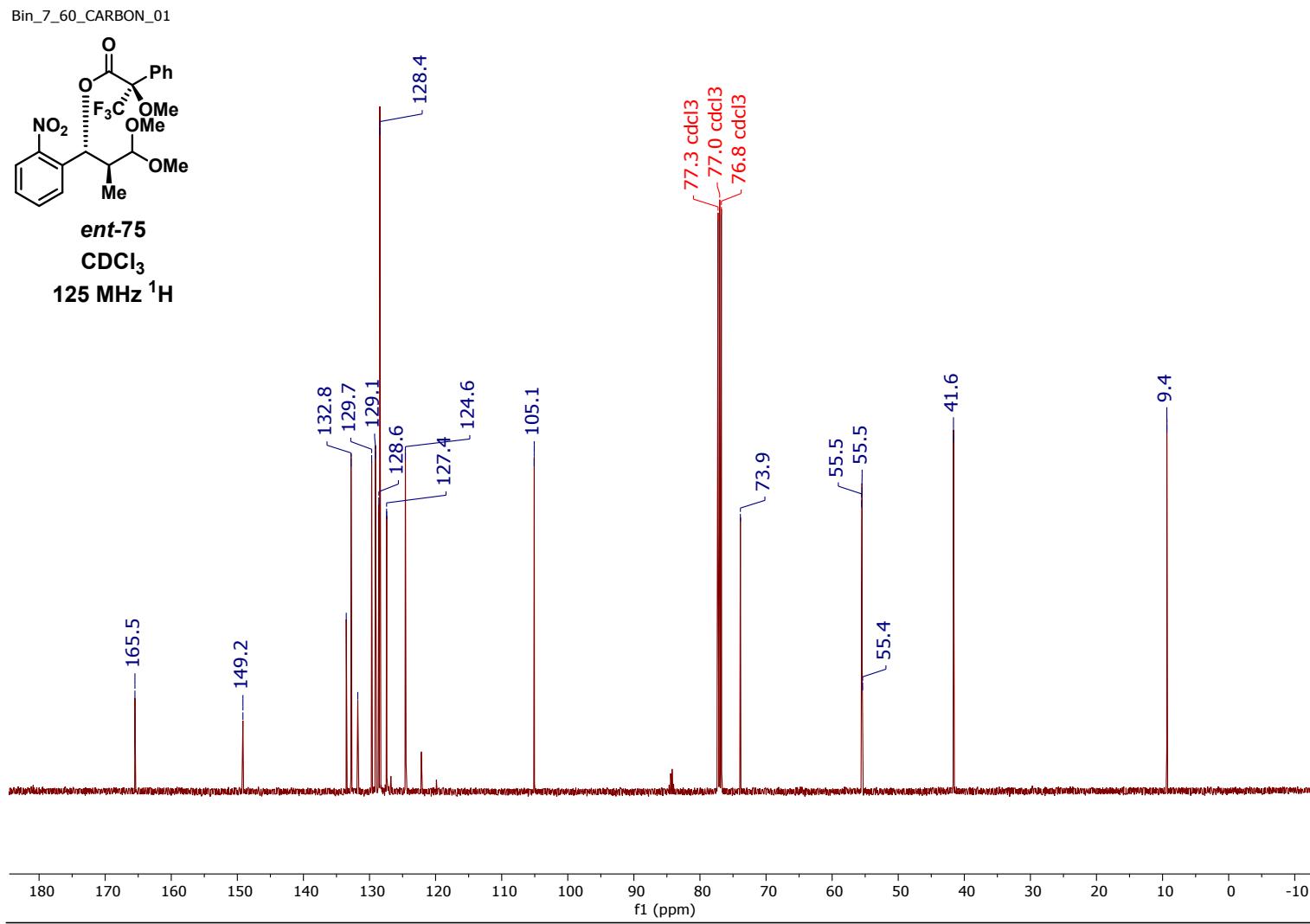
75  
 $\text{CDCl}_3$   
500 MHz  $^1\text{H}$

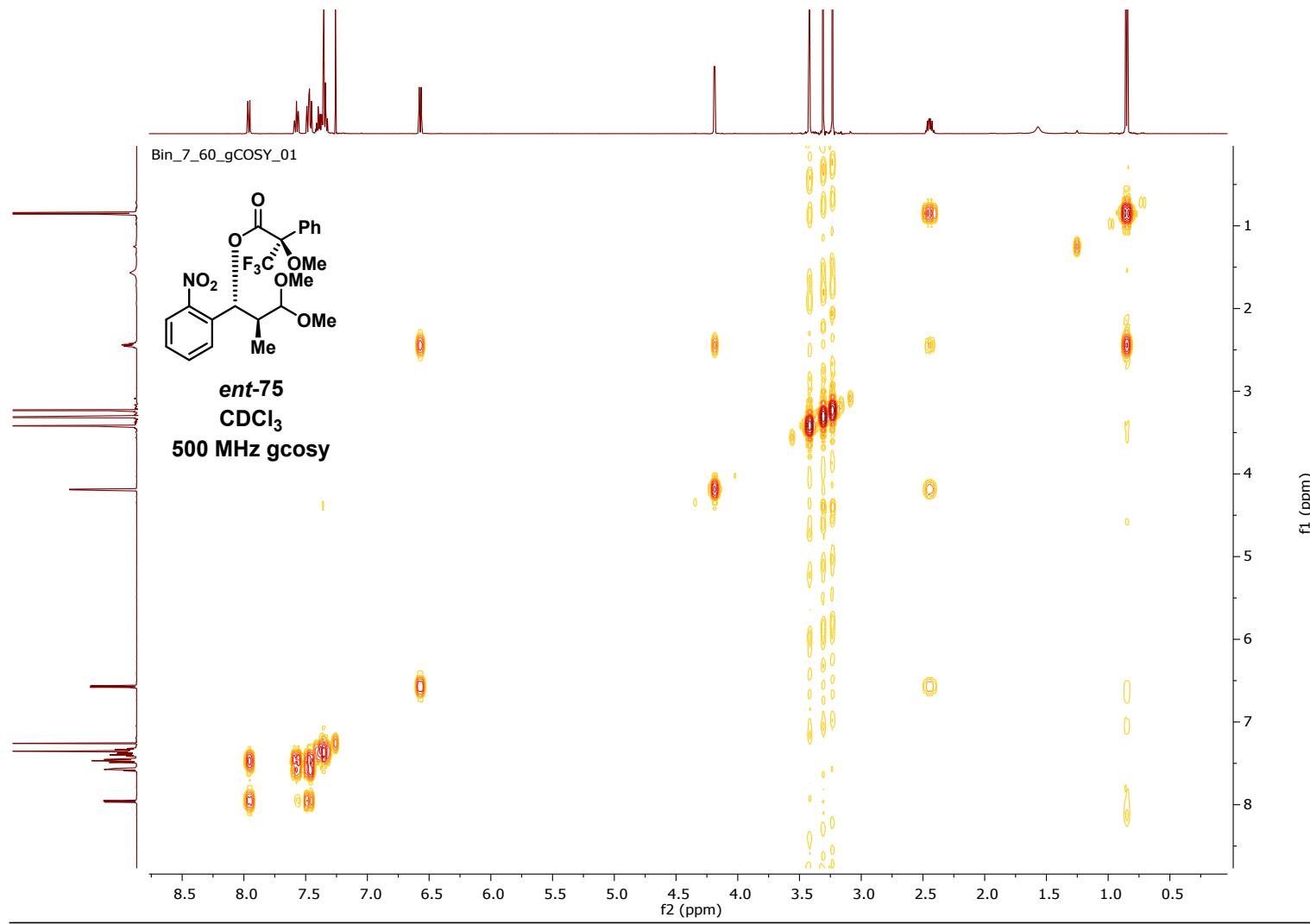


SI-203

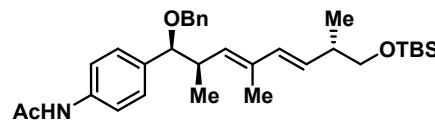




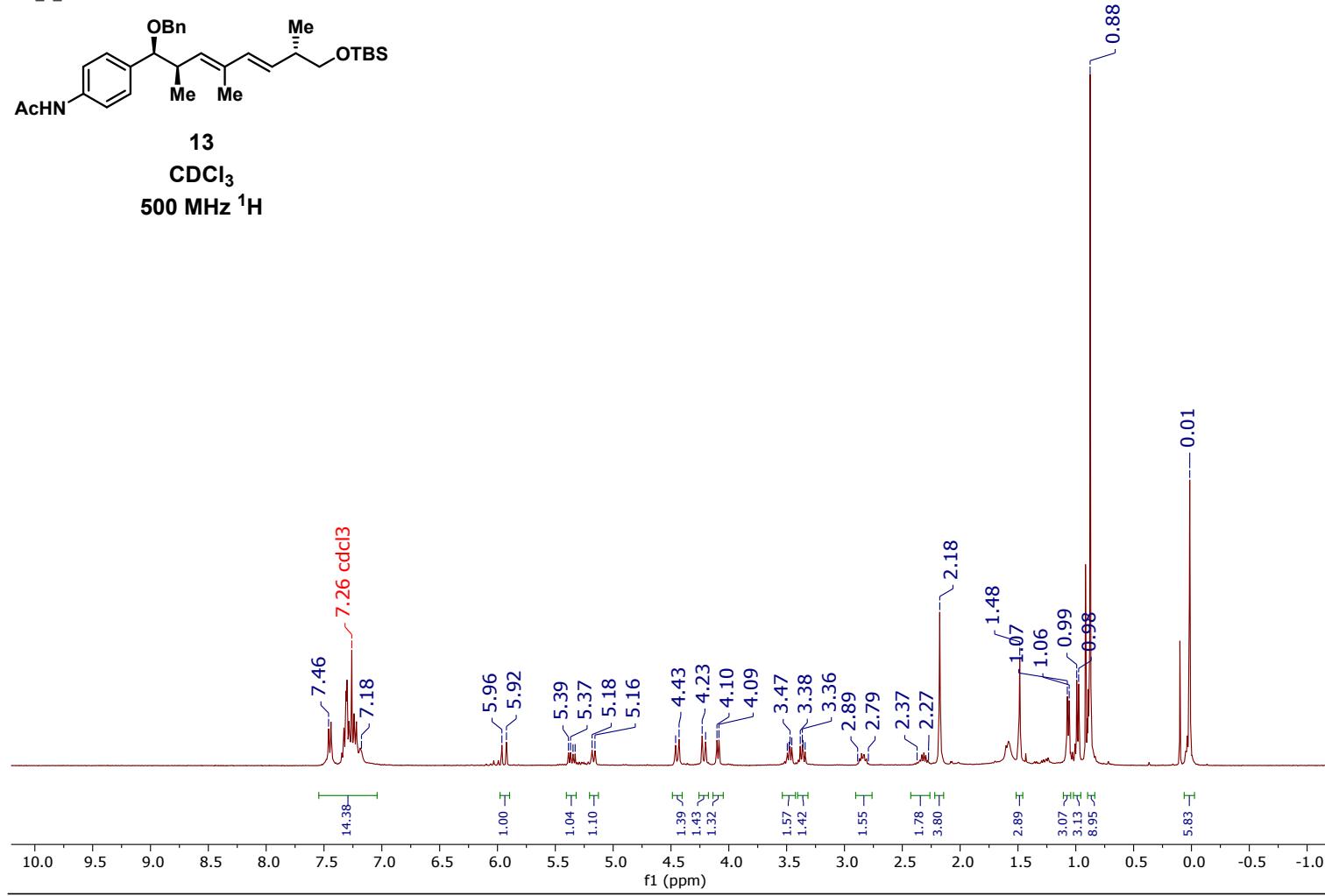


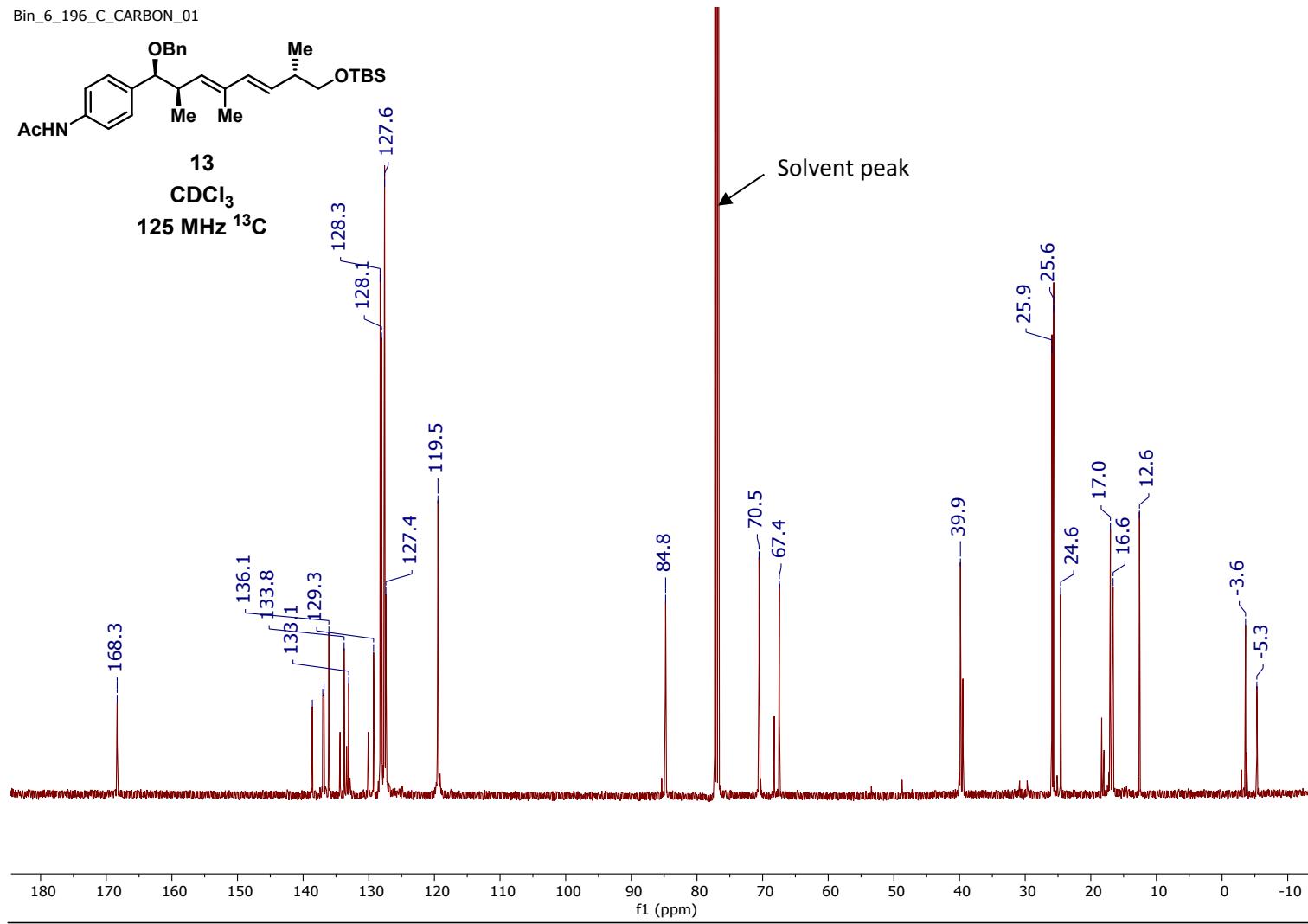


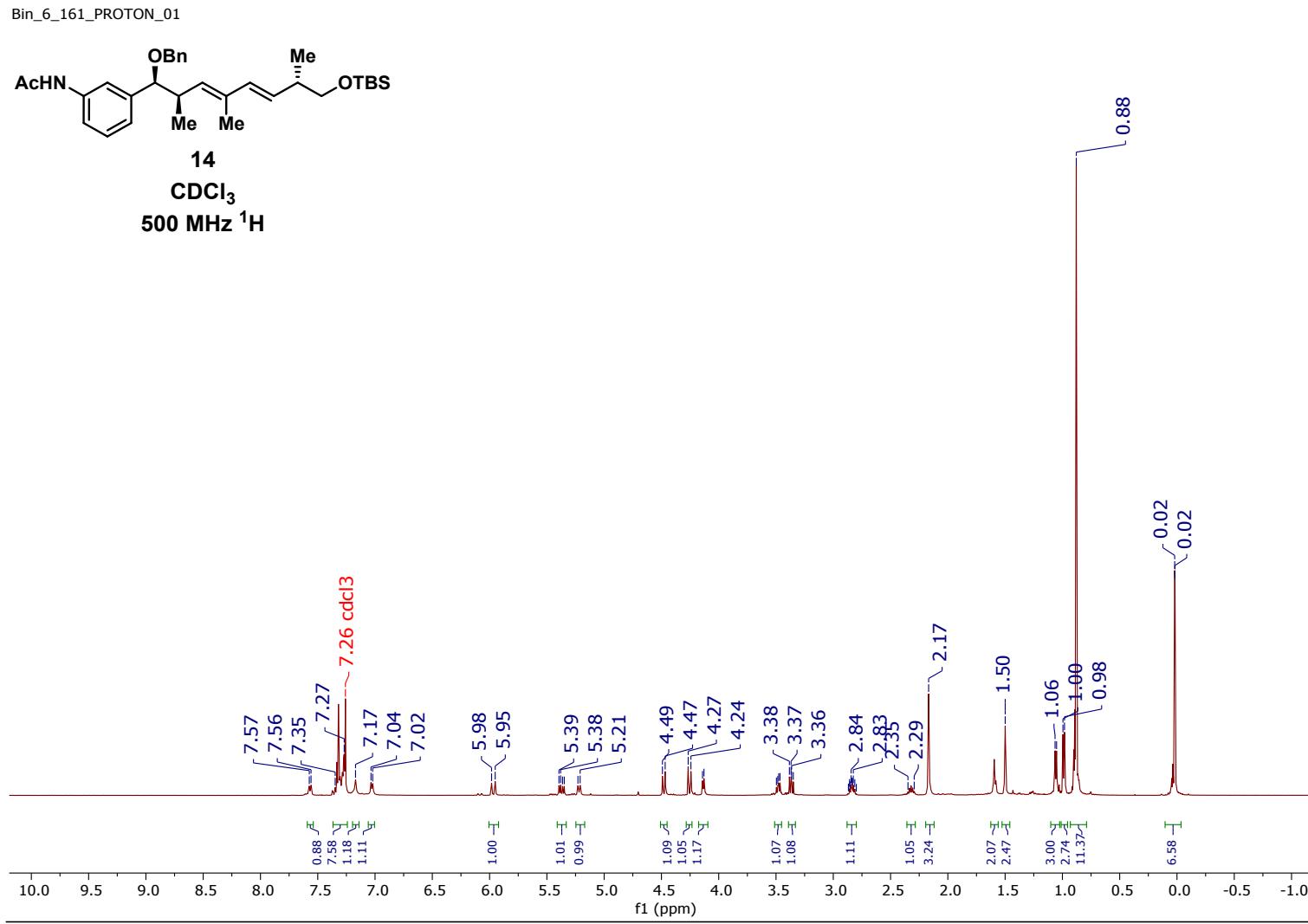
Bin\_6\_196\_PROTON\_01  
Bin\_6\_196

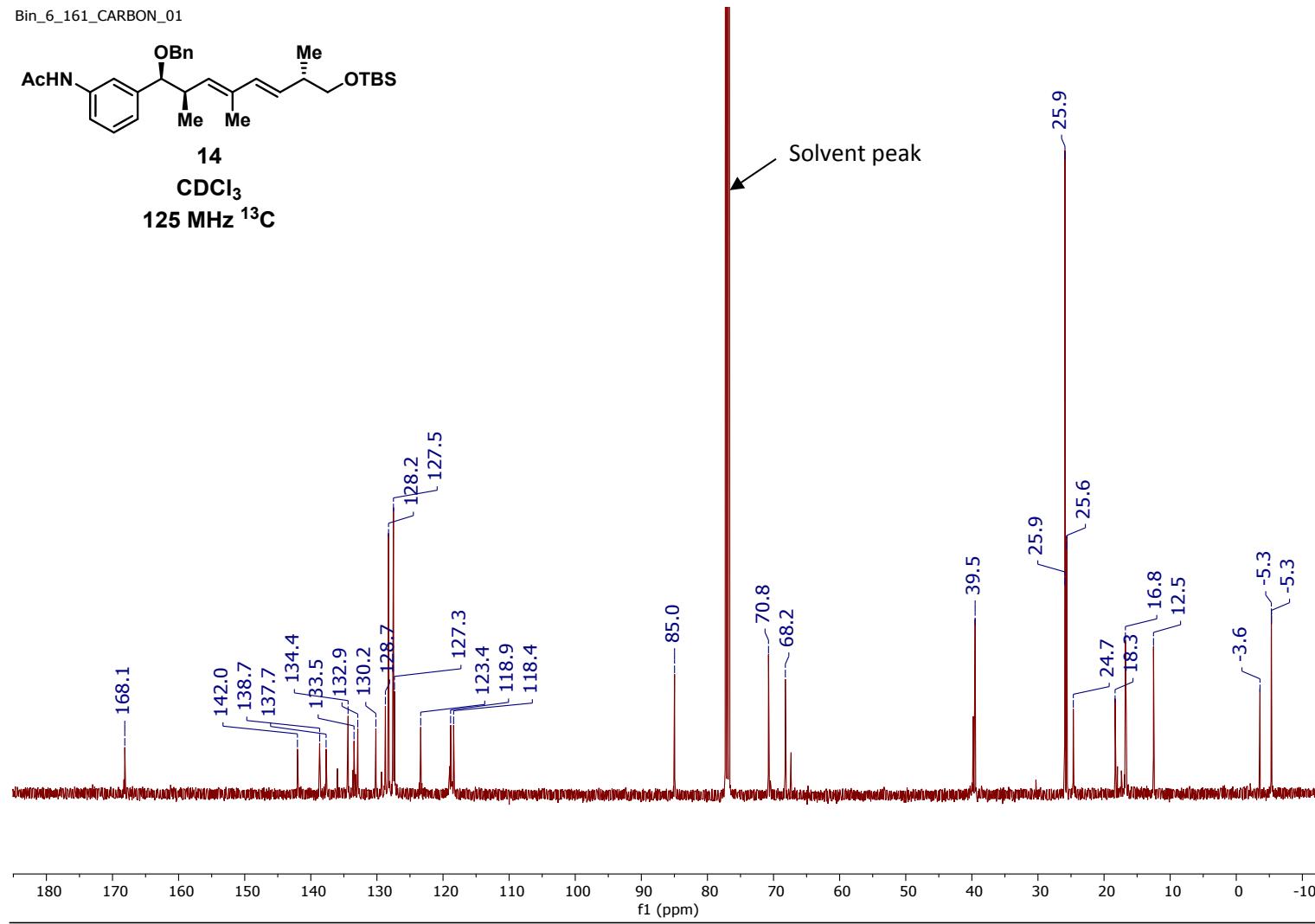


**13**  
 $\text{CDCl}_3$   
500 MHz  $^1\text{H}$

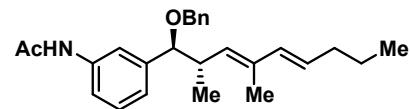




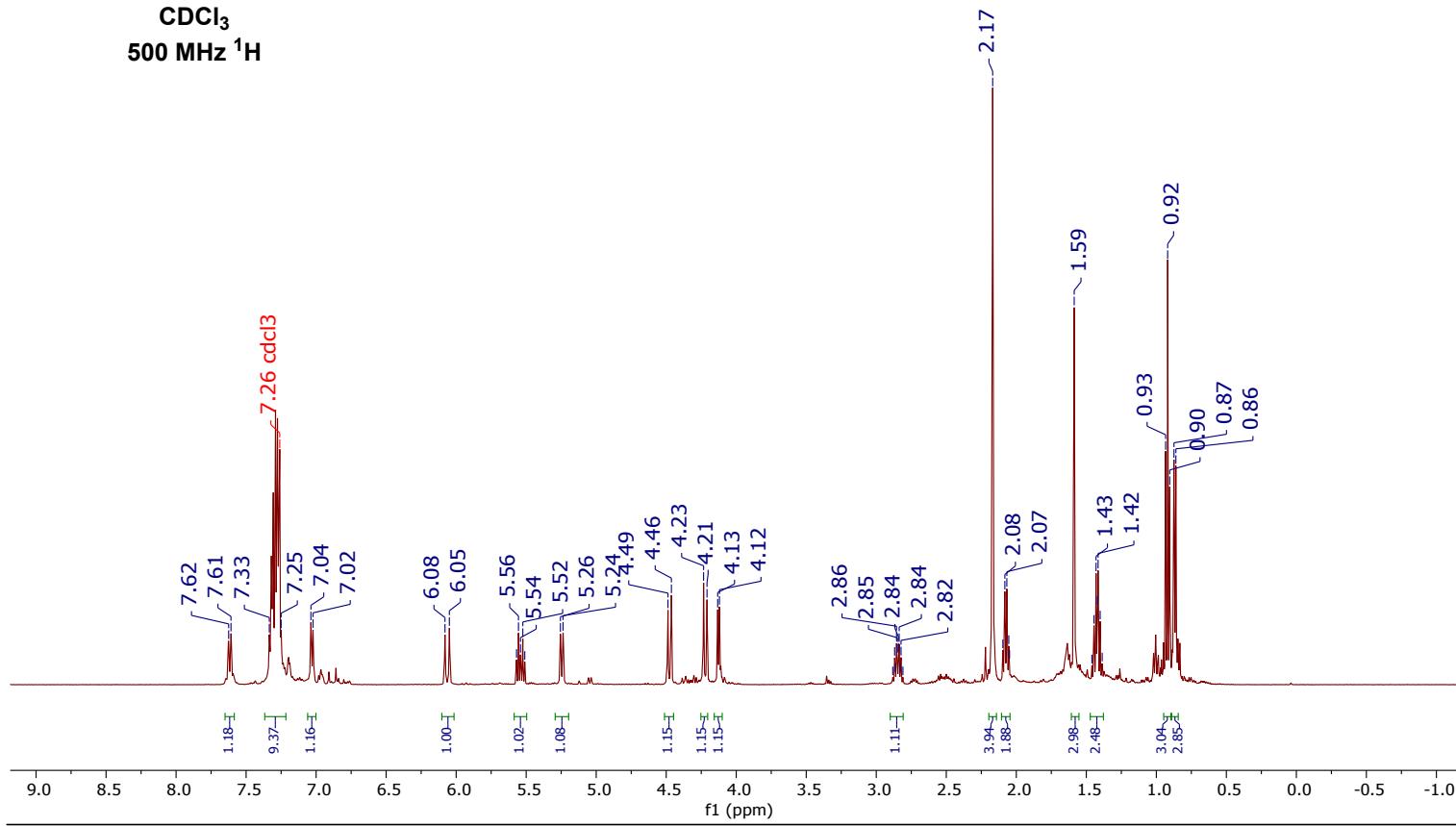


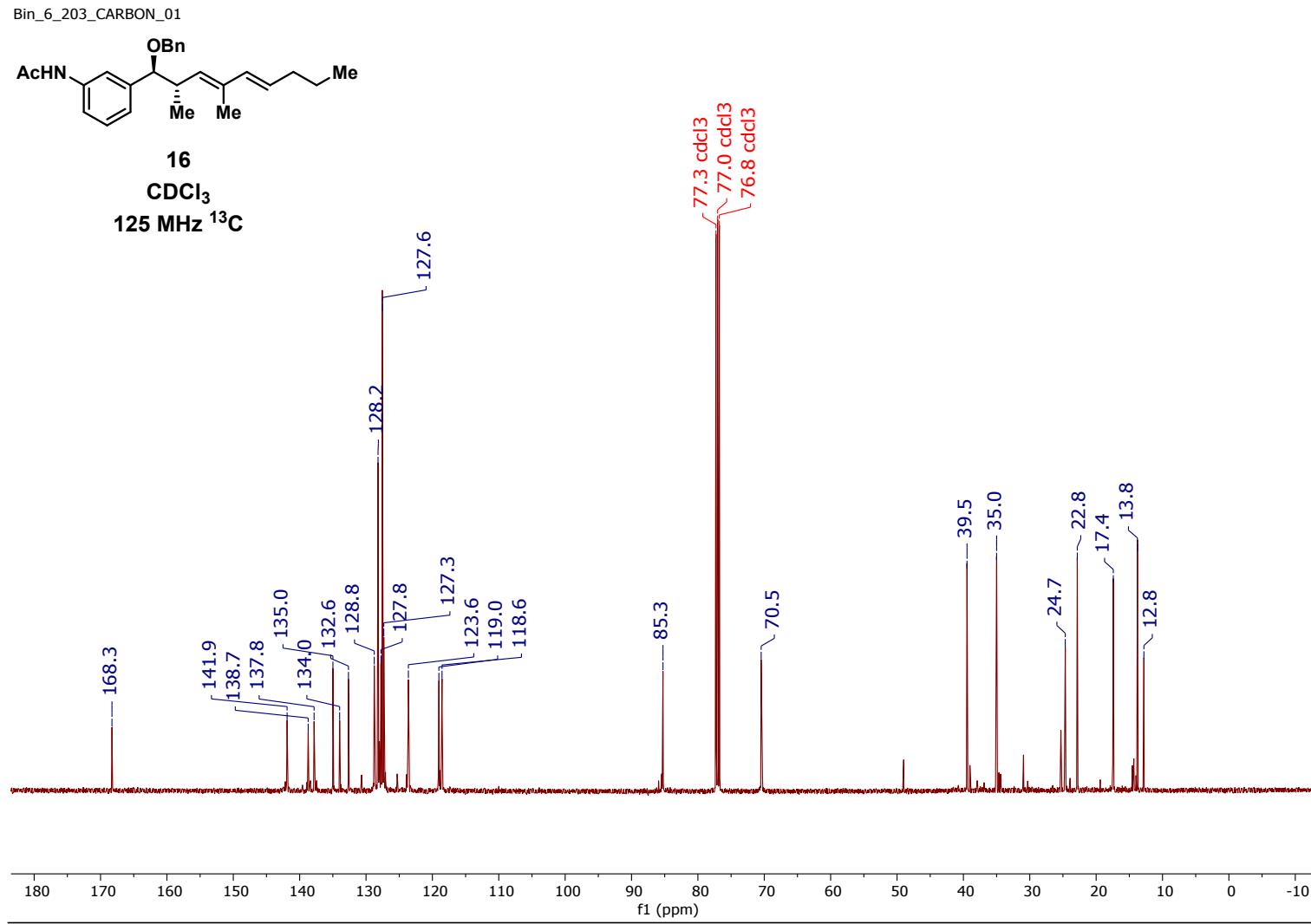


Bin\_6\_203\_FC\_PROTON\_01

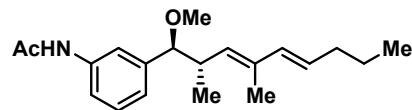


$\text{CDCl}_3$   
500 MHz  $^1\text{H}$

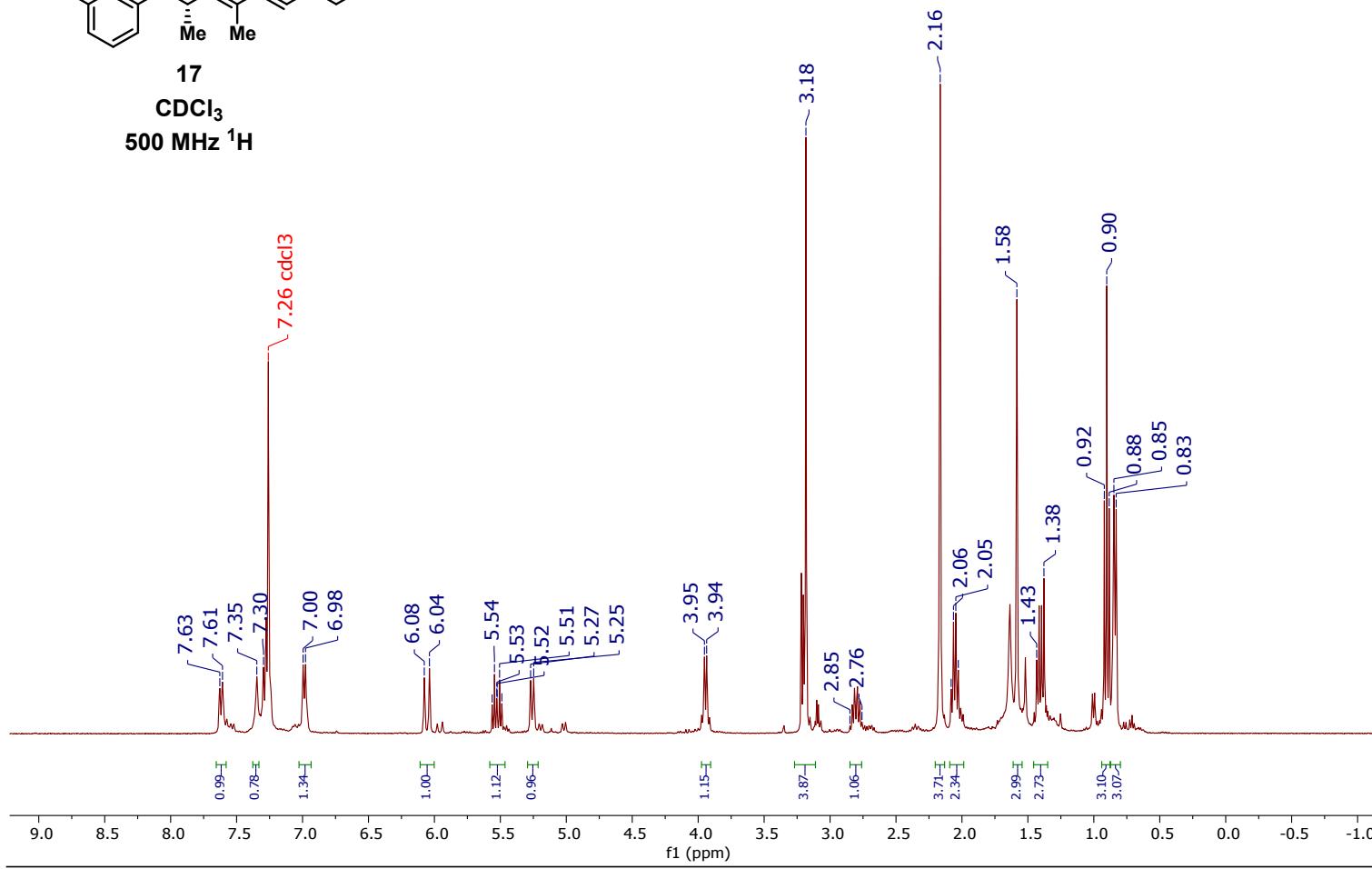


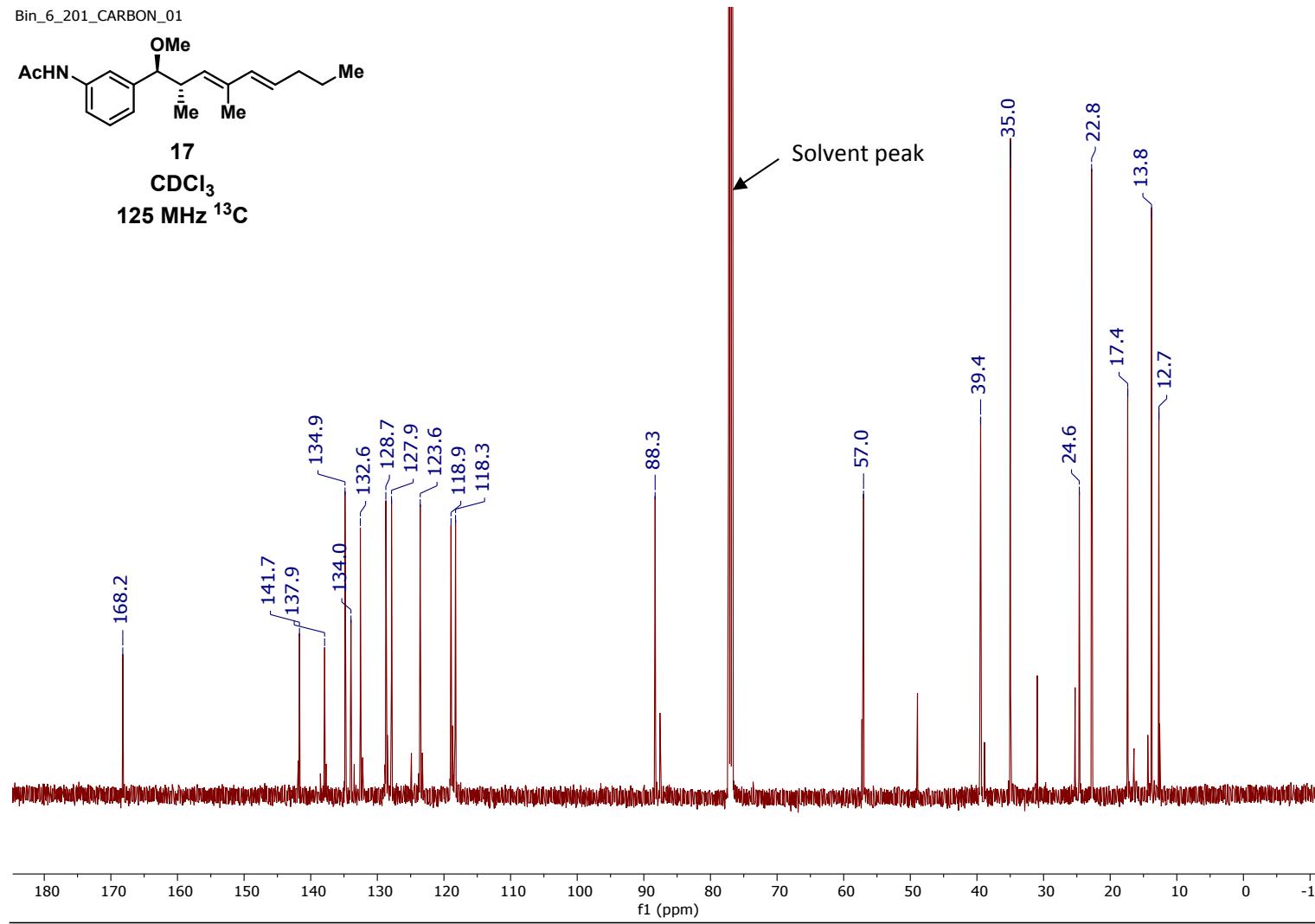


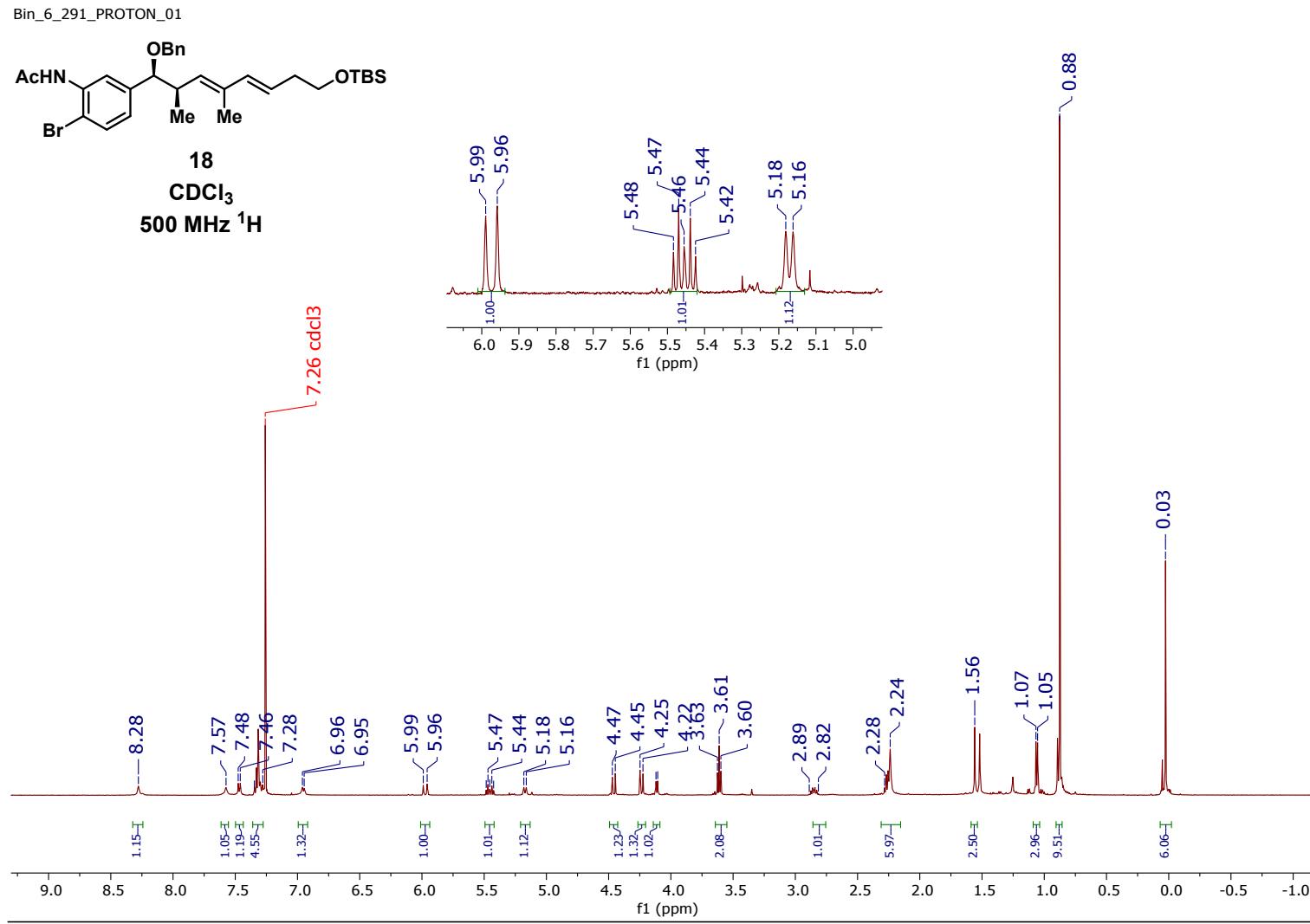
Bin\_6\_201\_FC\_PROTON\_01  
Bin\_6\_201\_FC

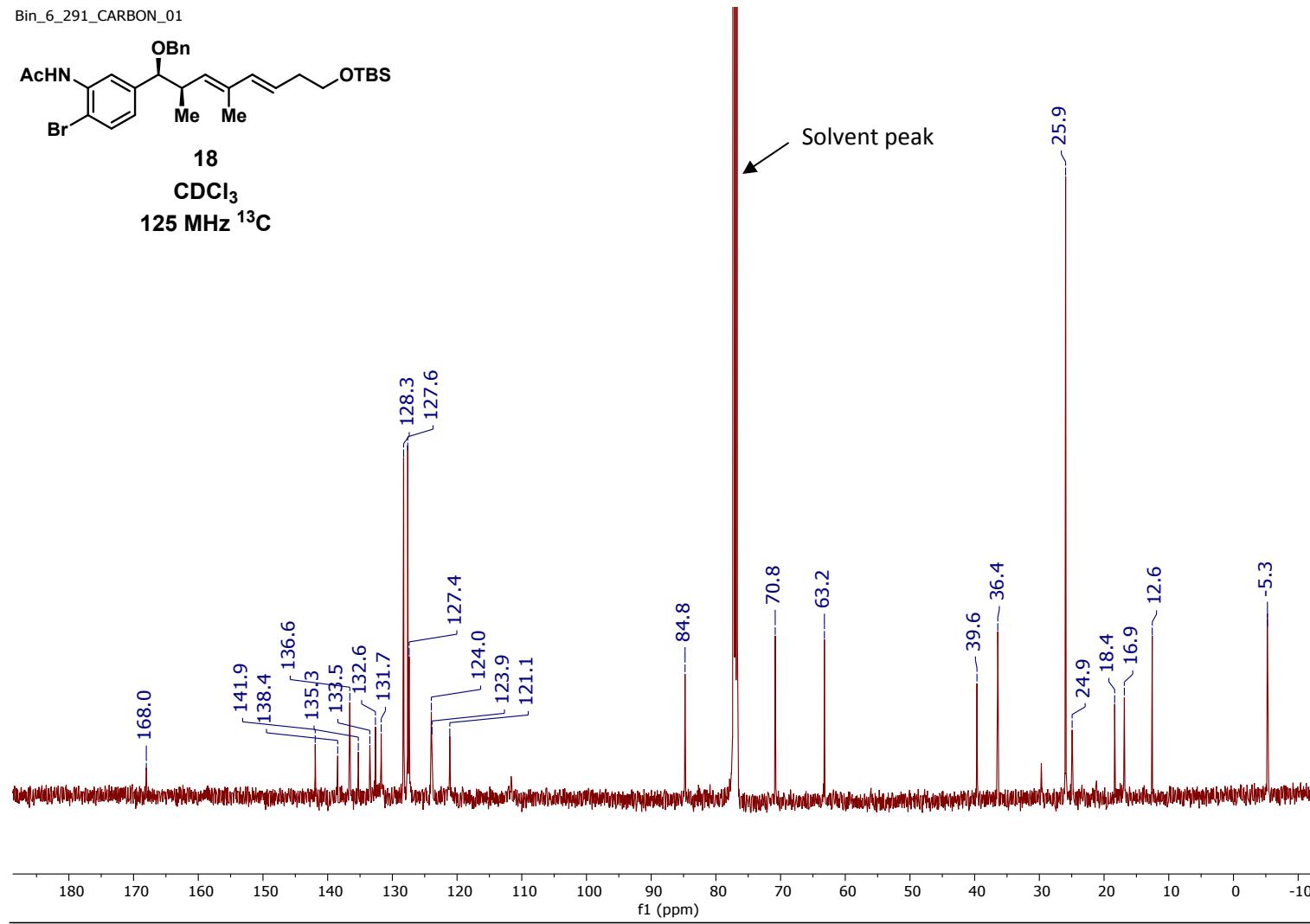


17

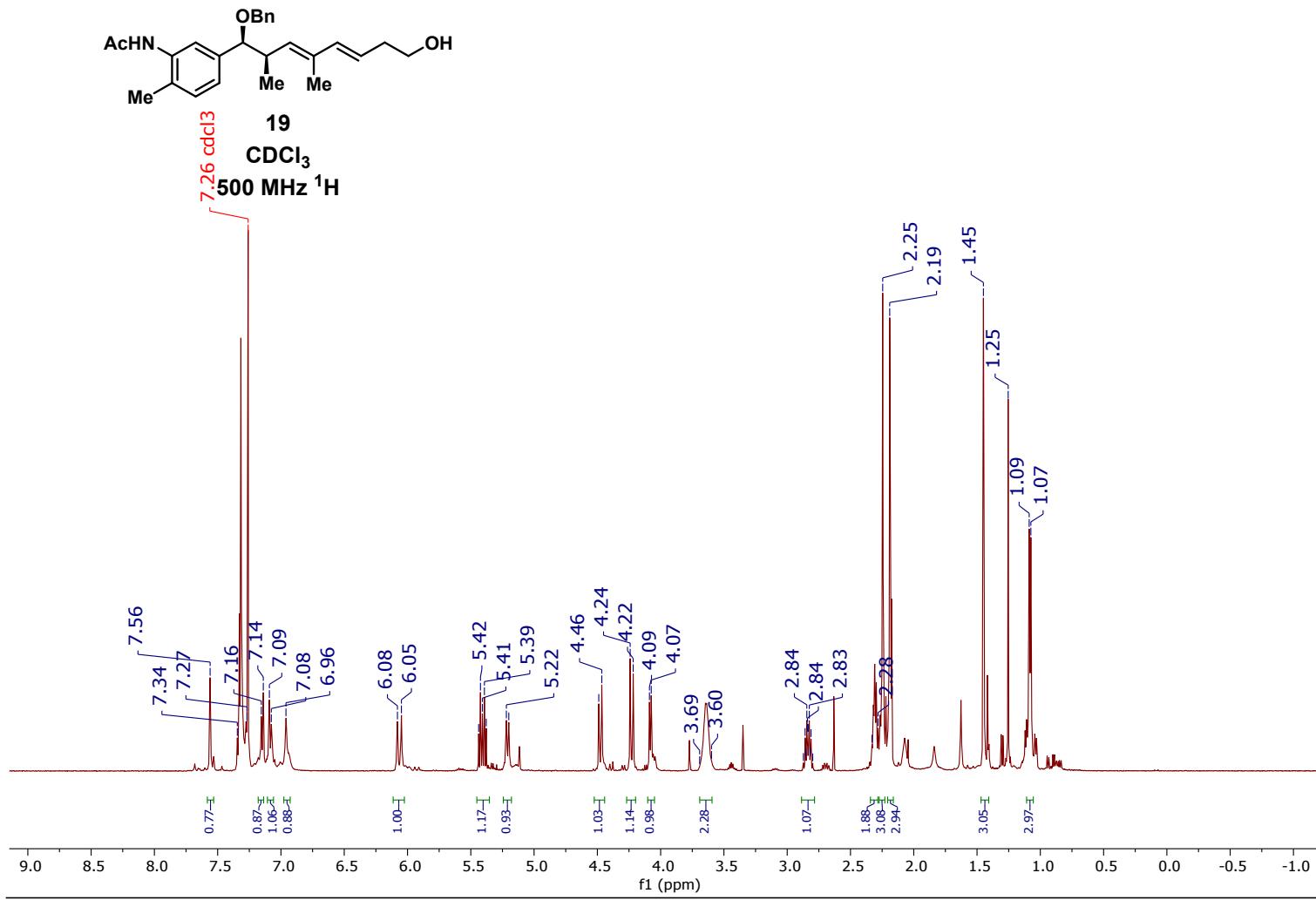
 $\text{CDCl}_3$ 500 MHz  $^1\text{H}$ 

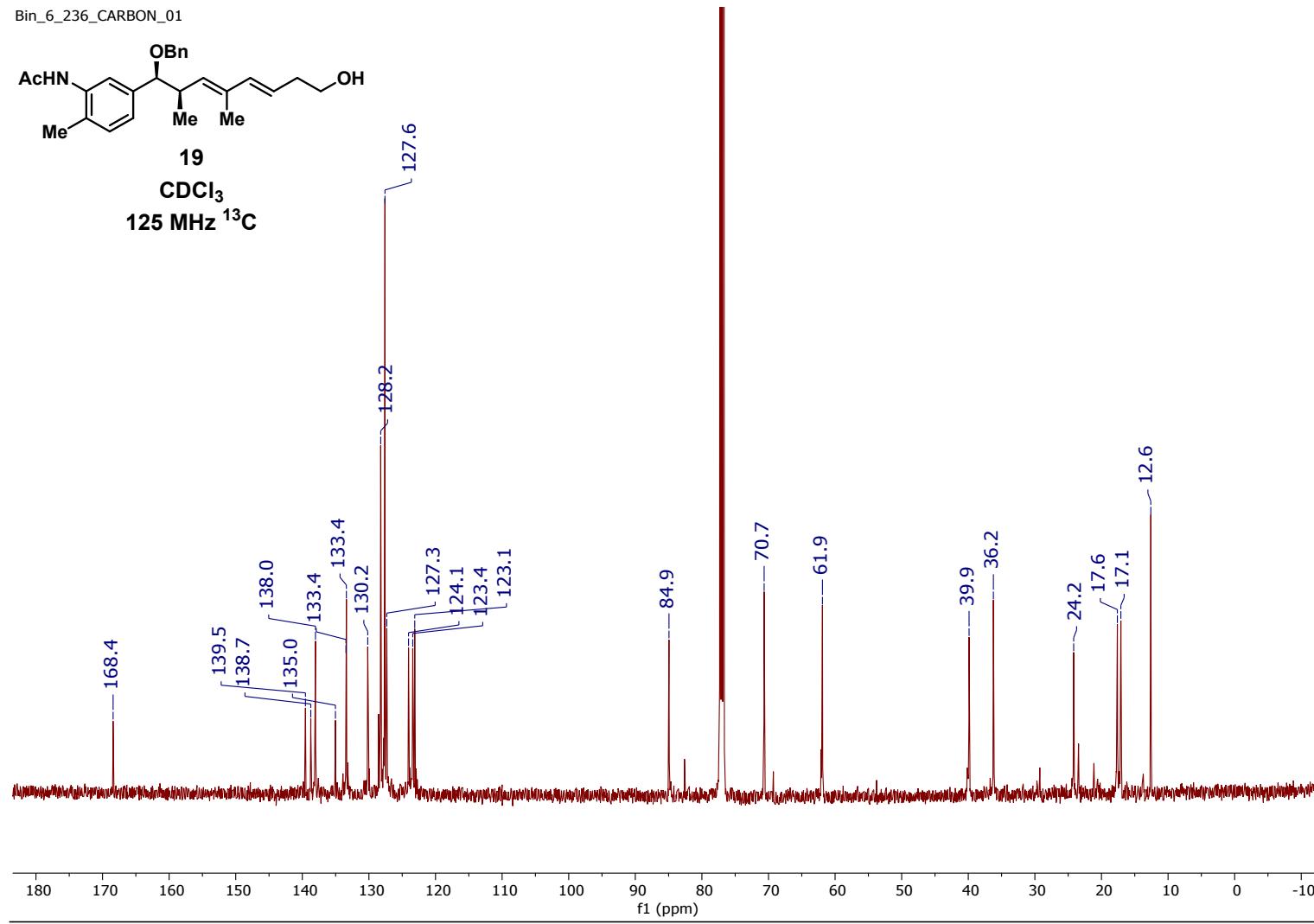


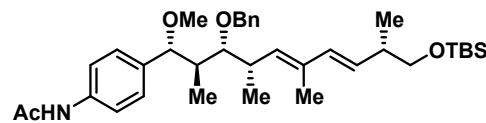




Bin\_6\_236\_PROTON\_01



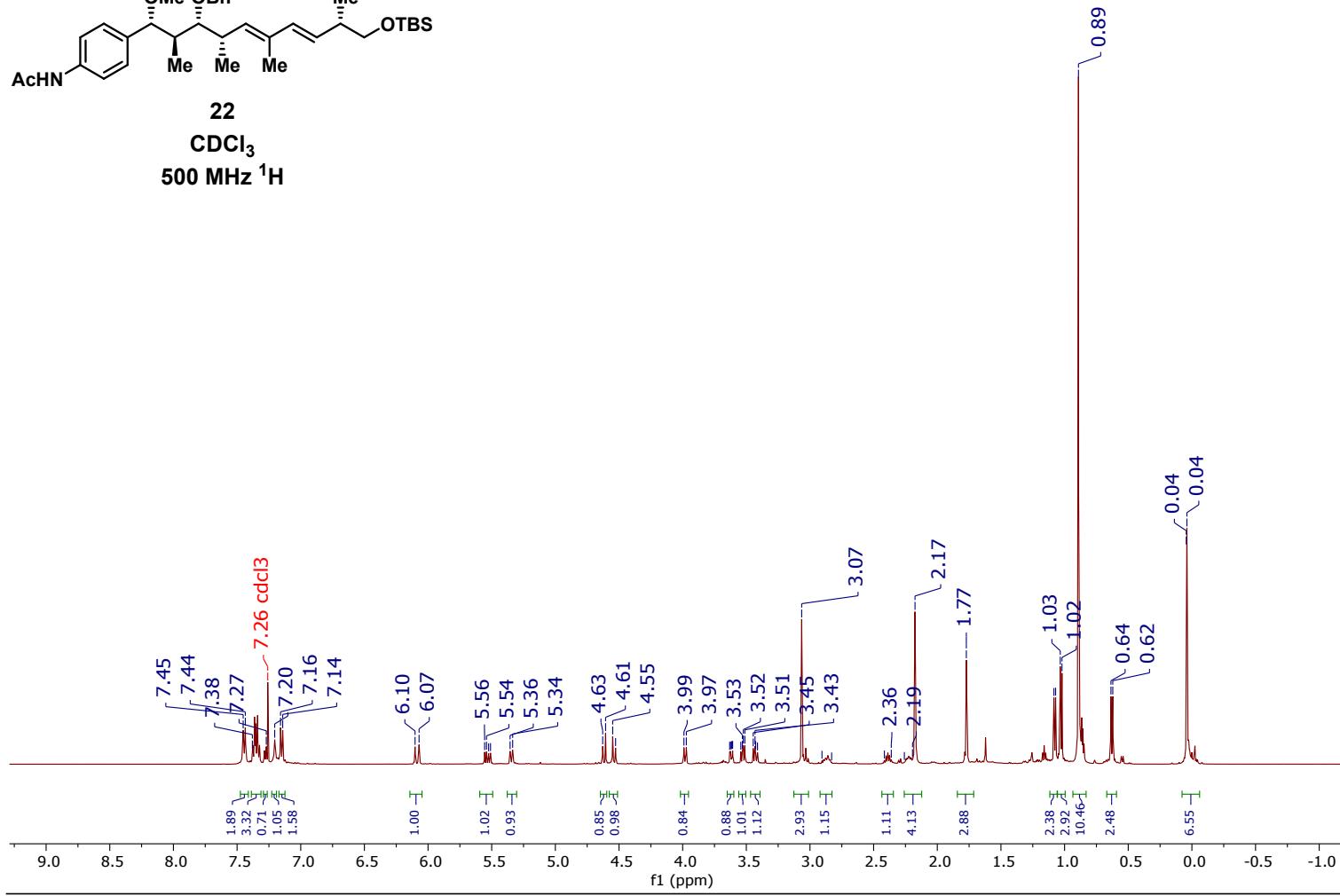


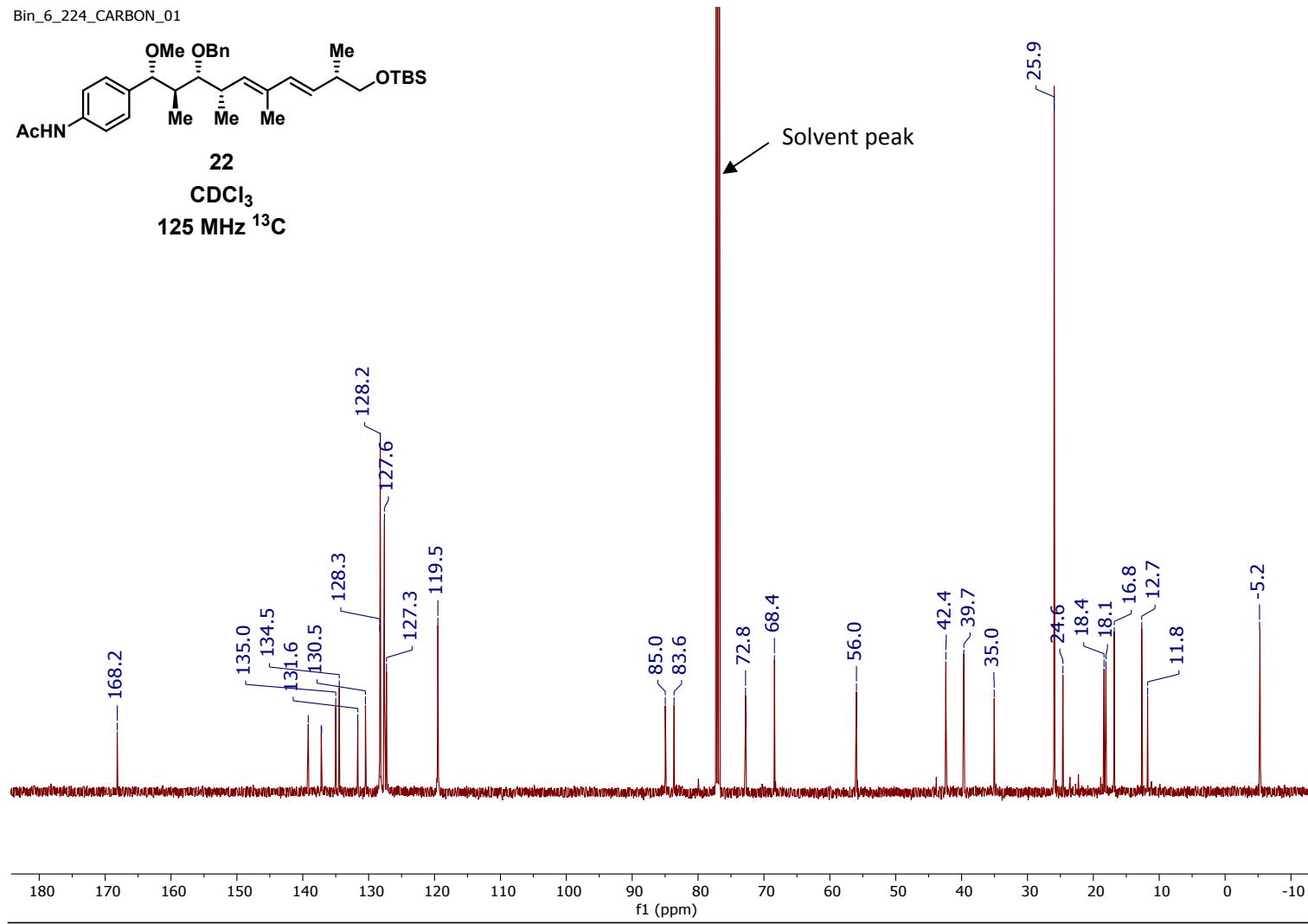


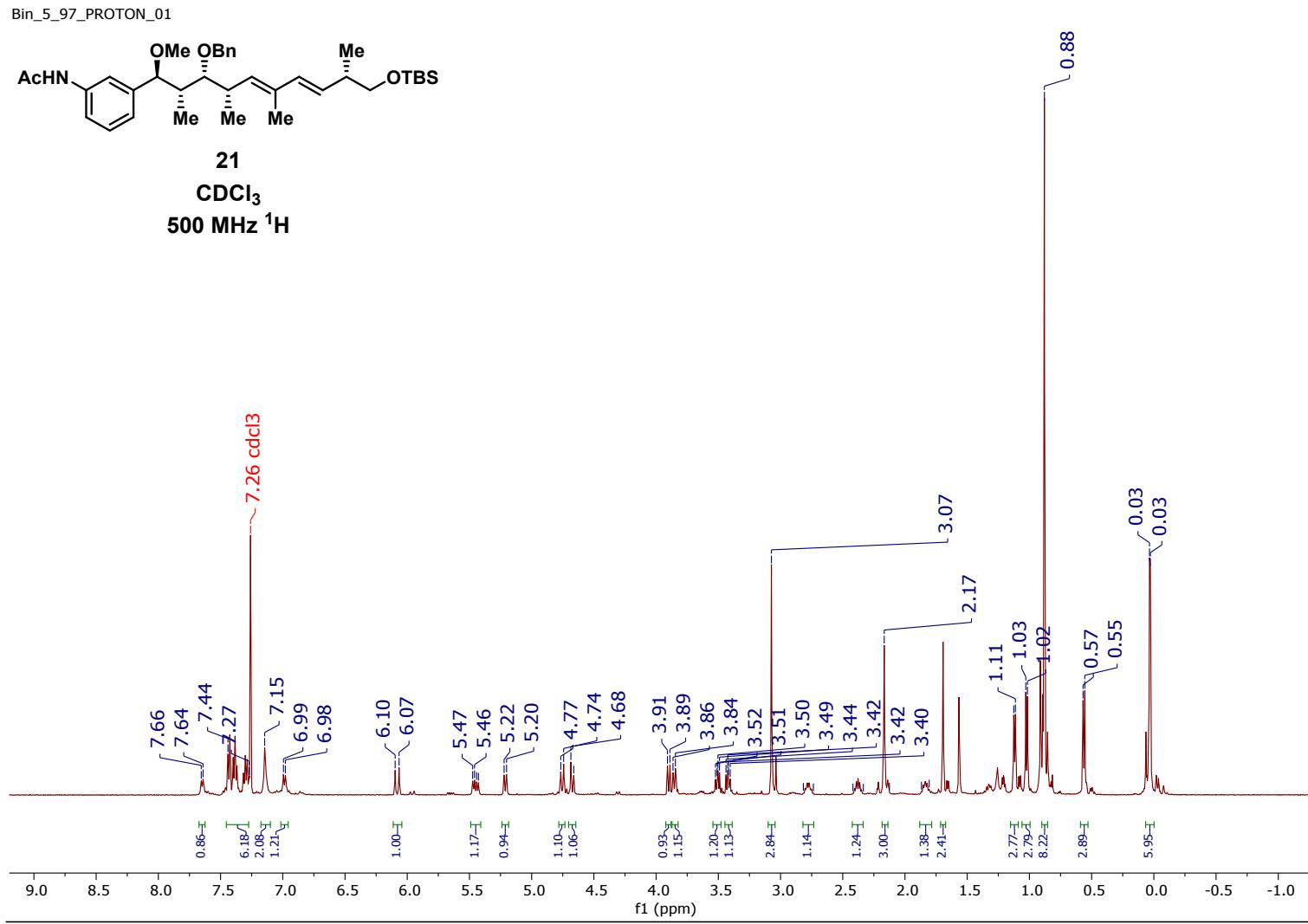
22

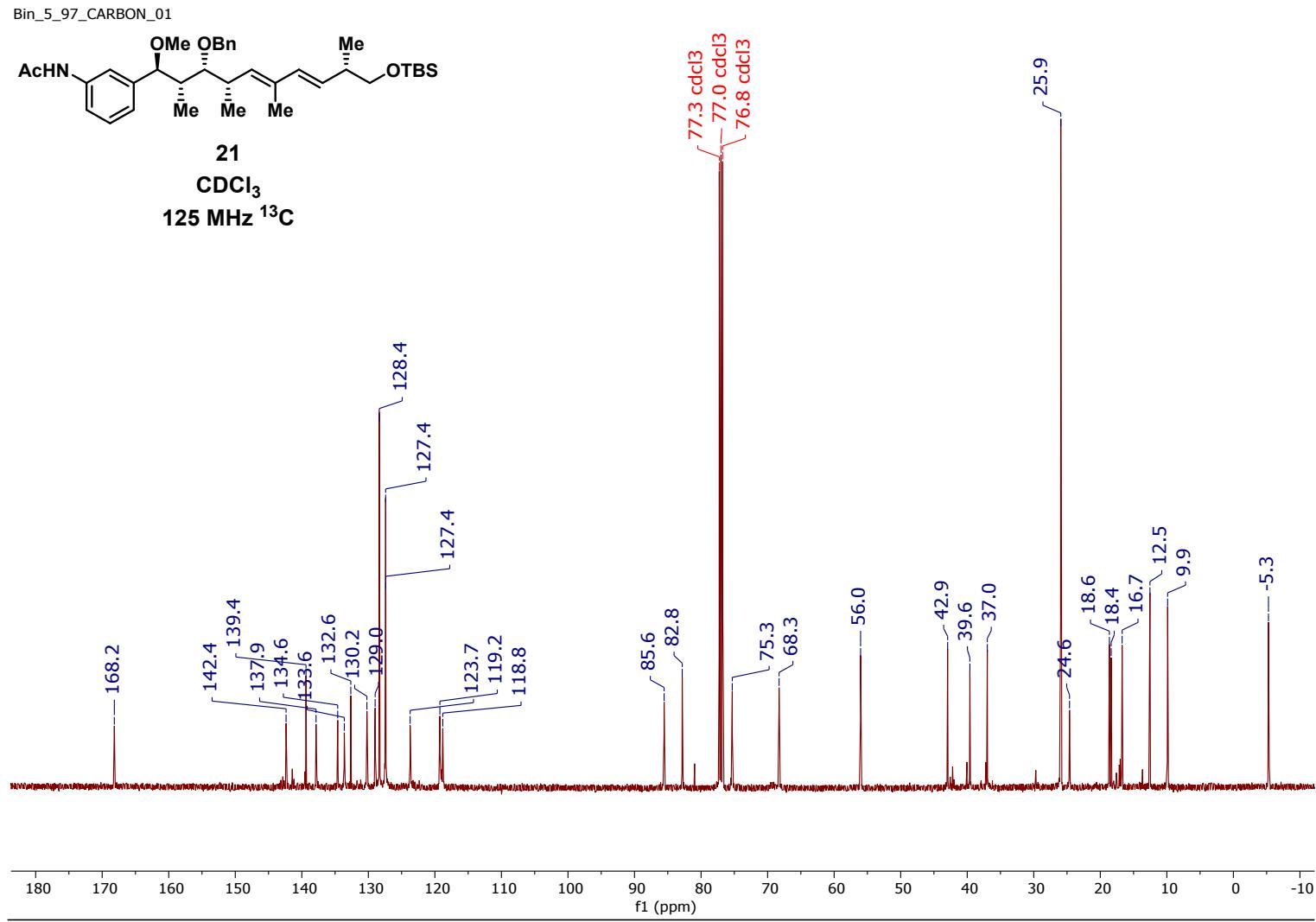
$\text{CDCl}_3$

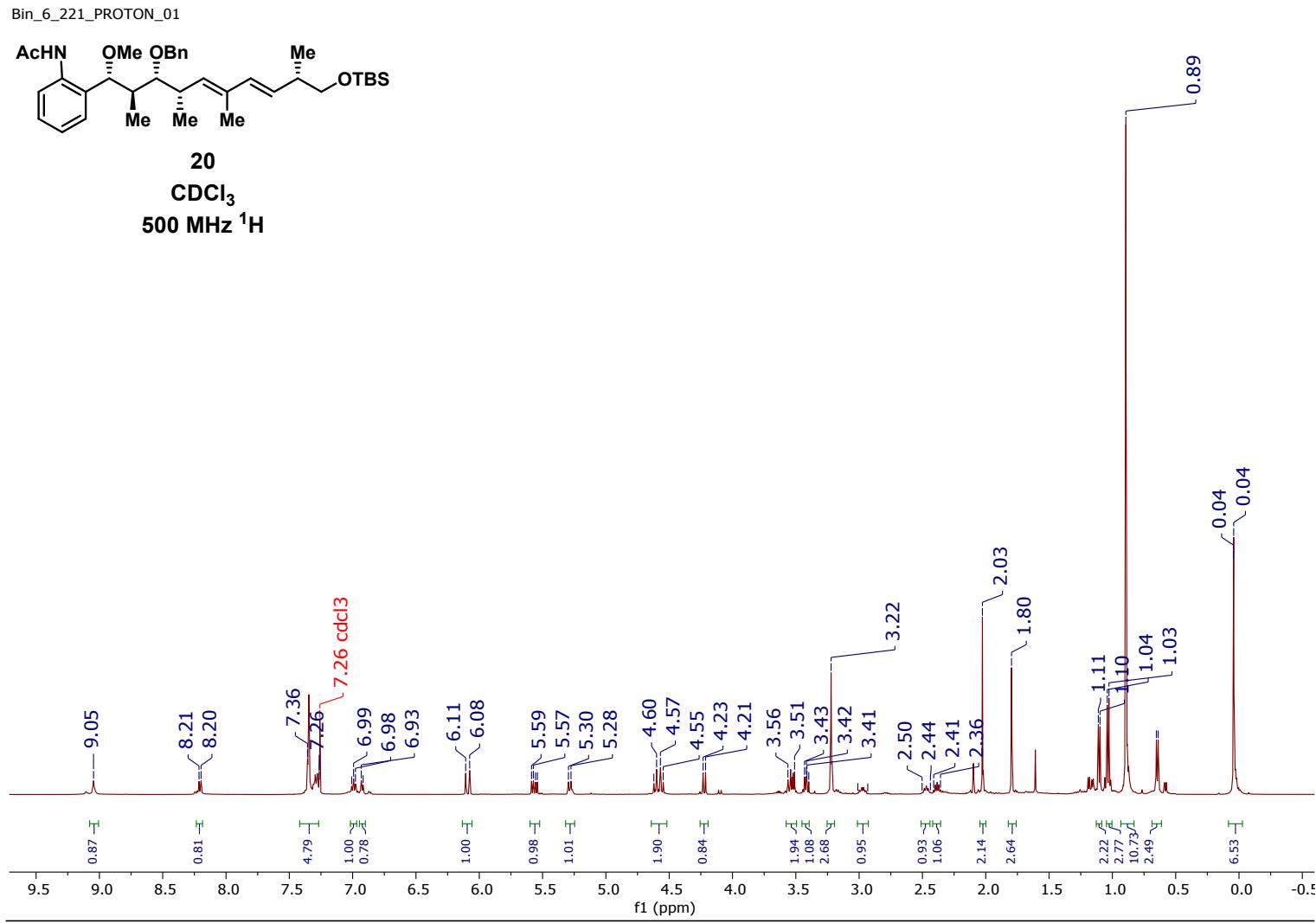
500 MHz  $^1\text{H}$

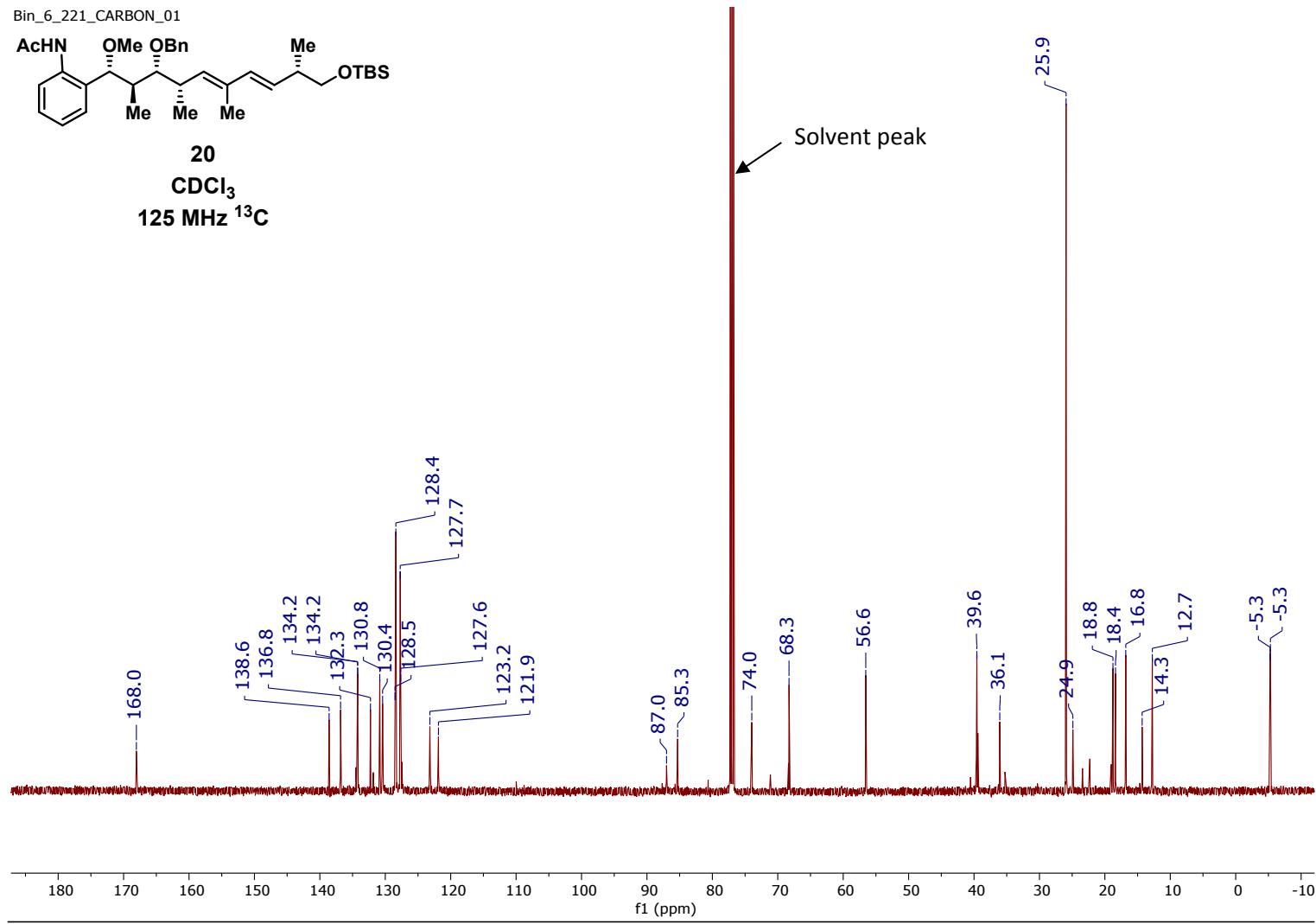


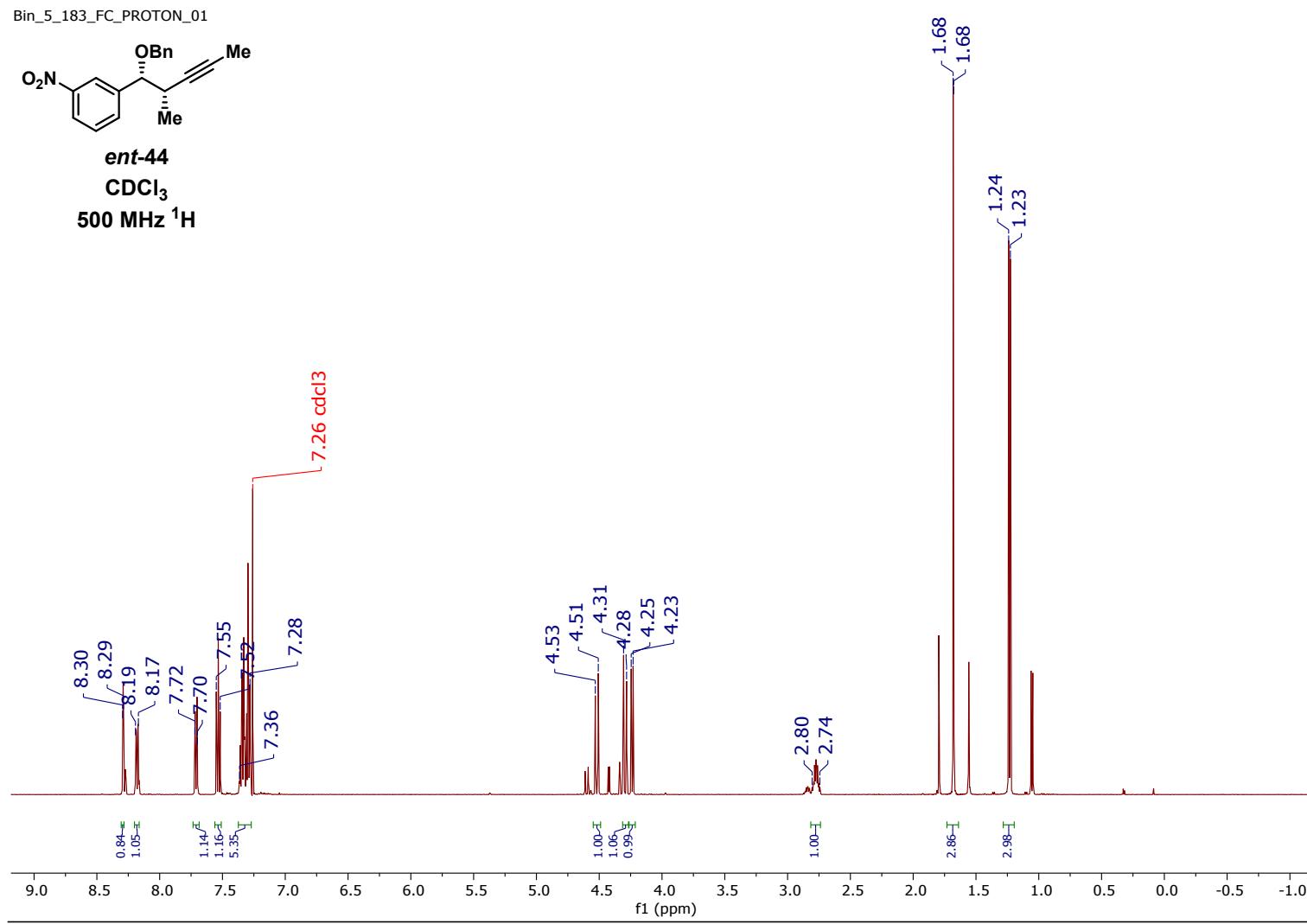


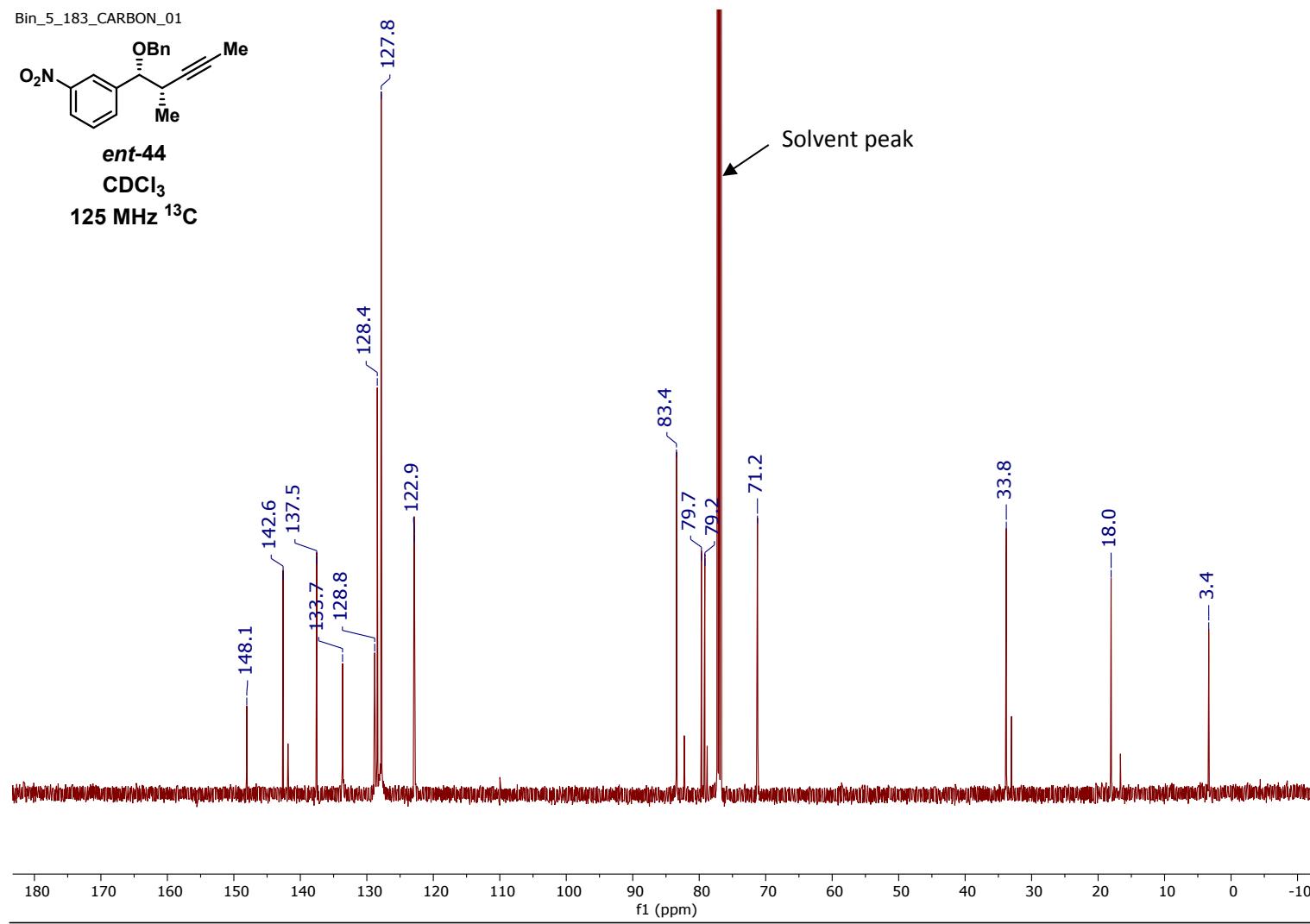


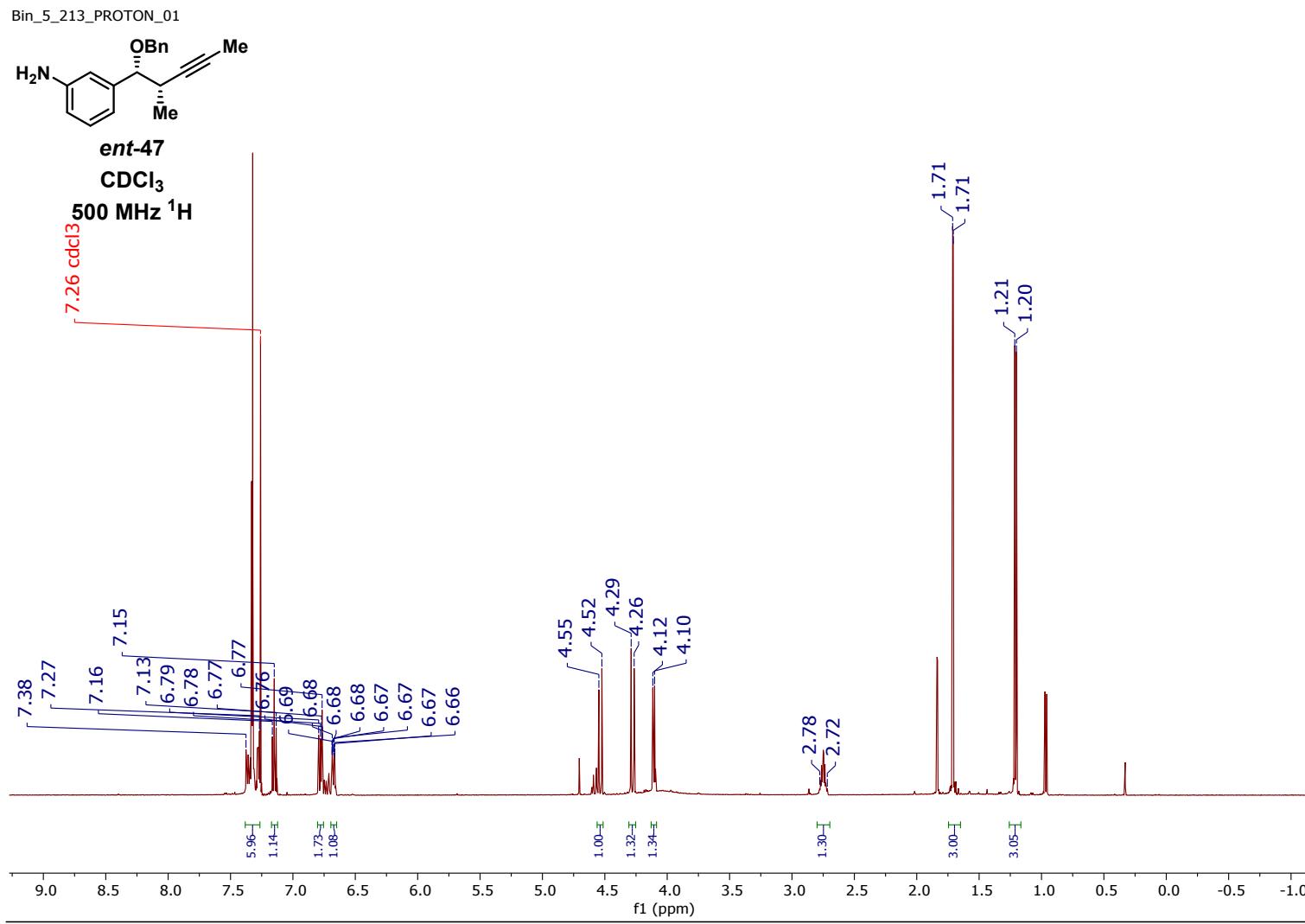


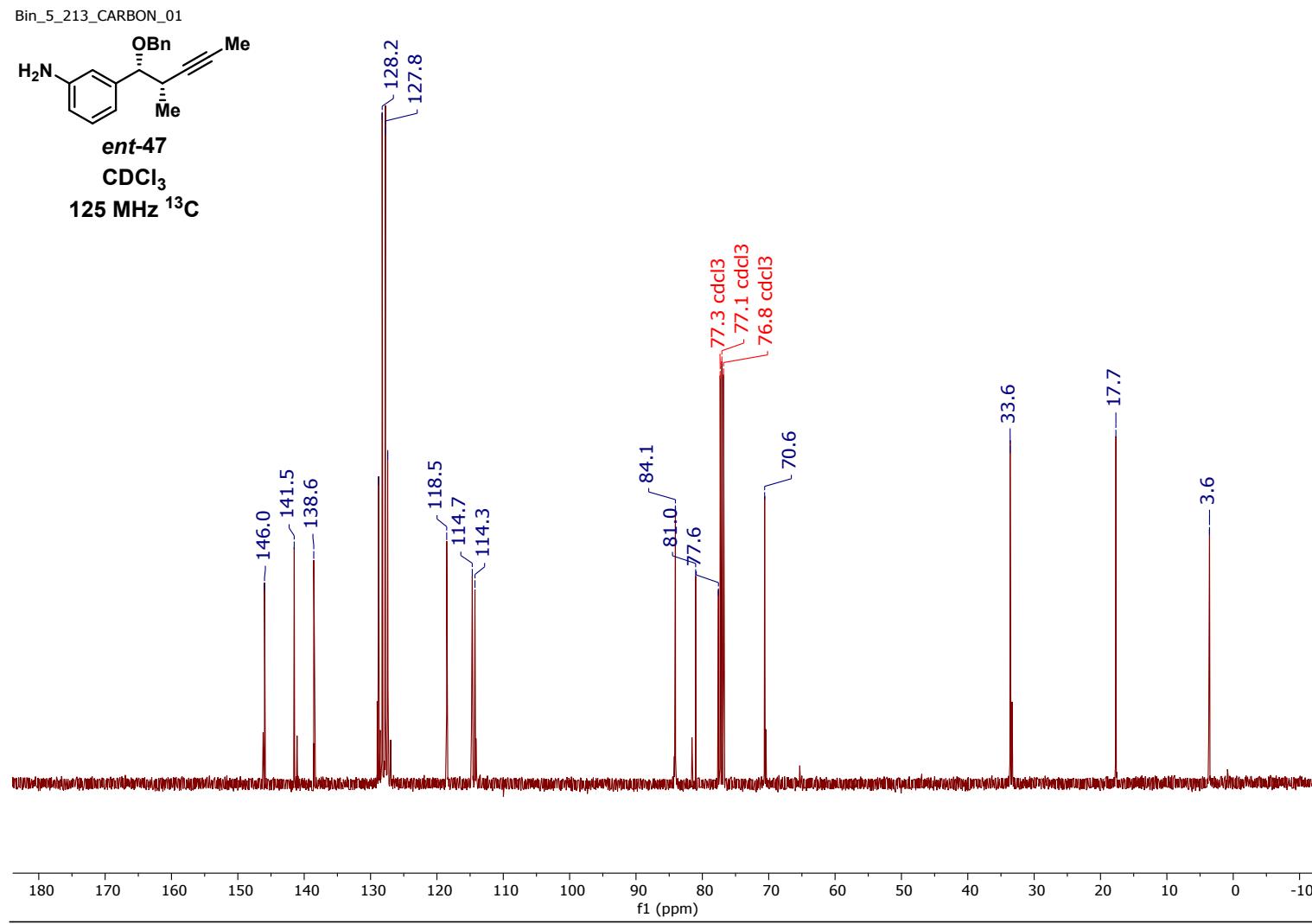


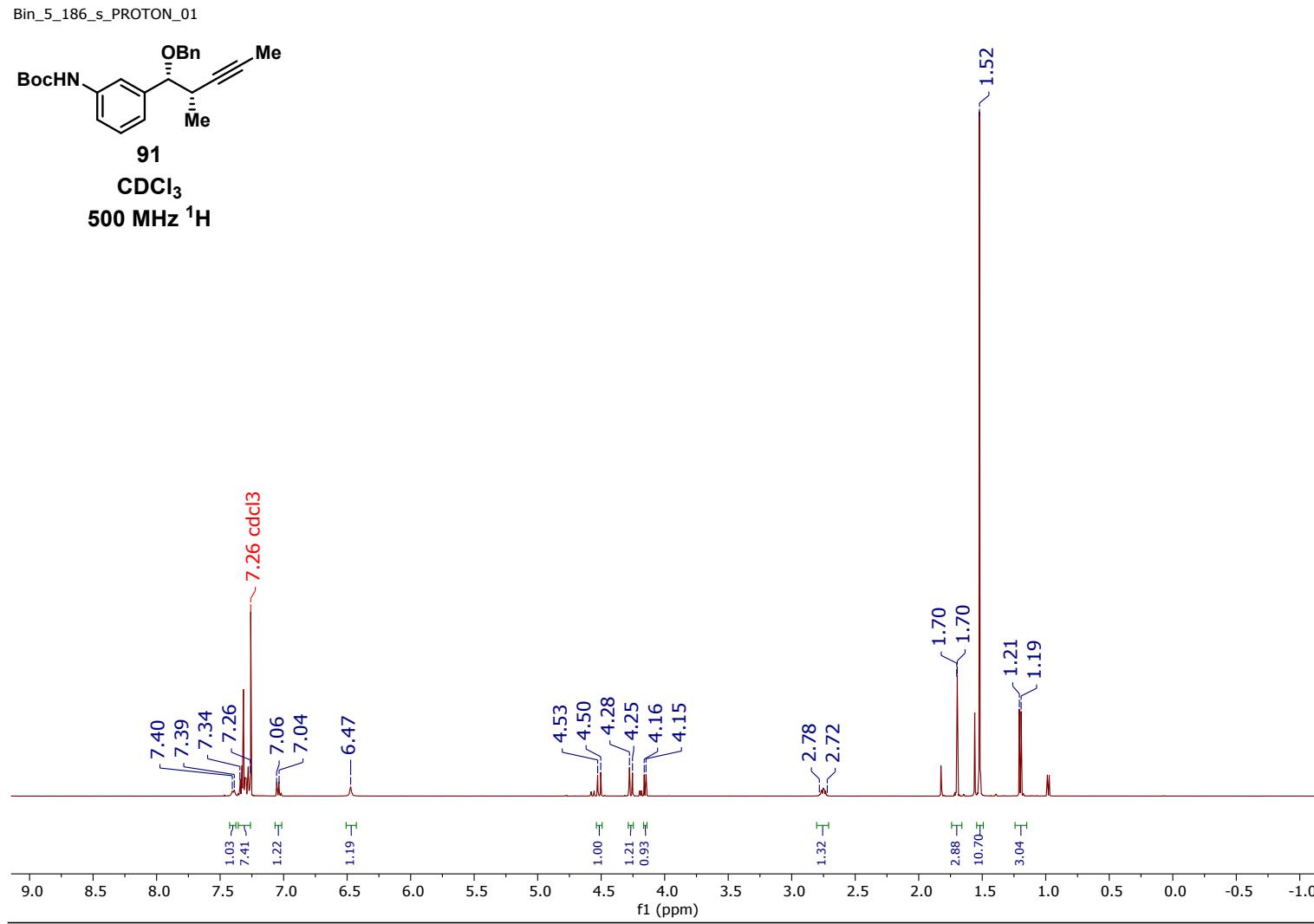


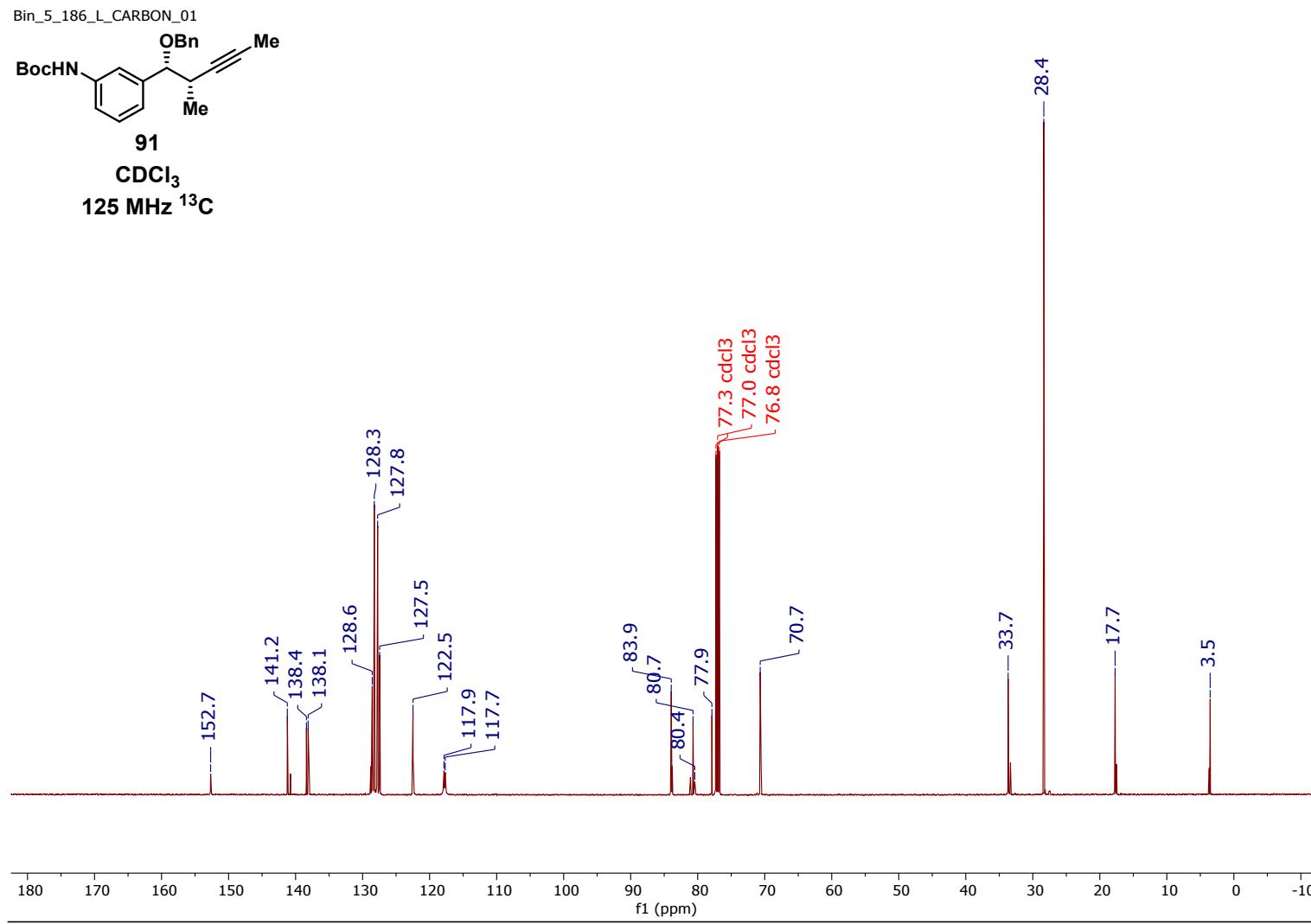


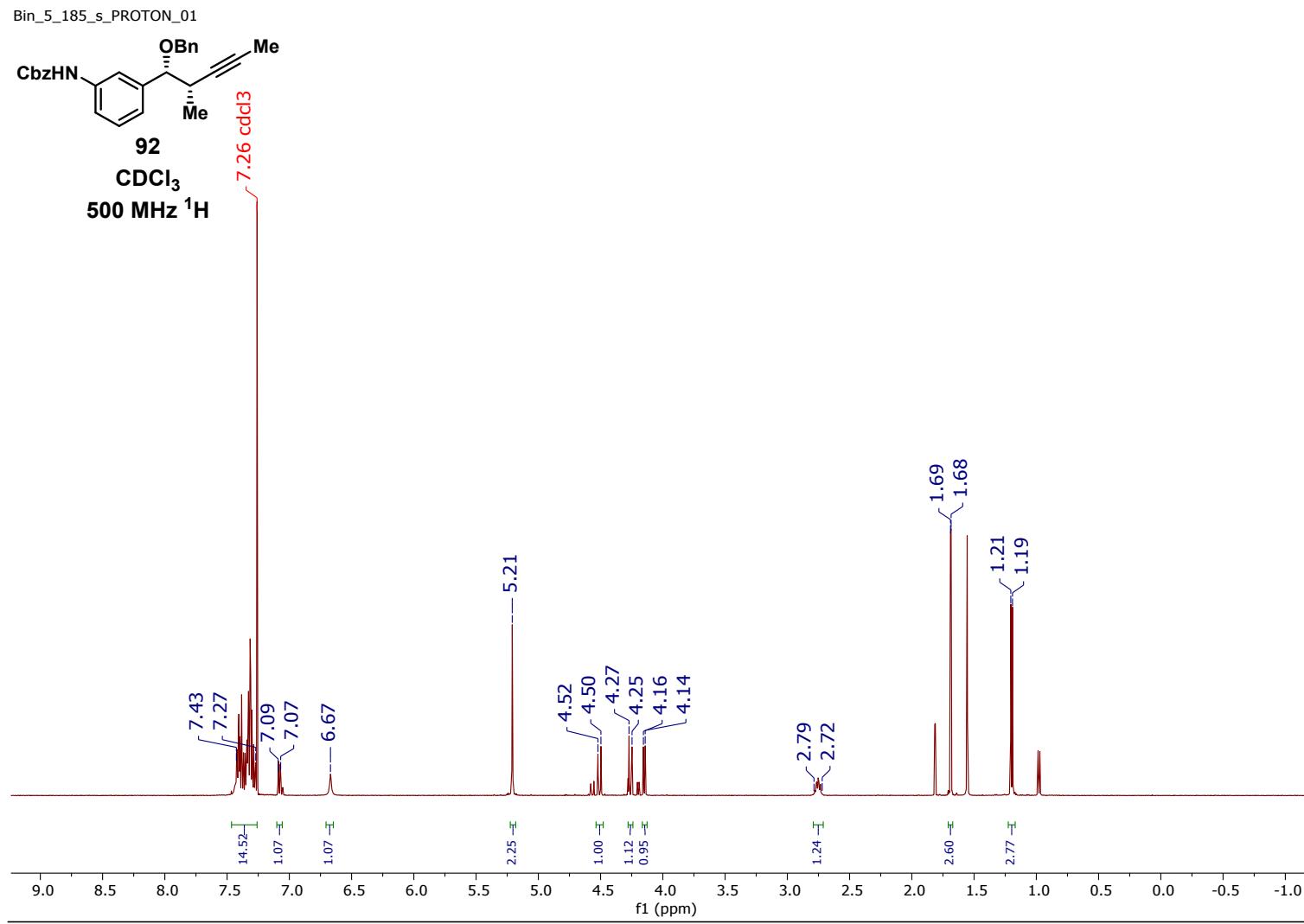


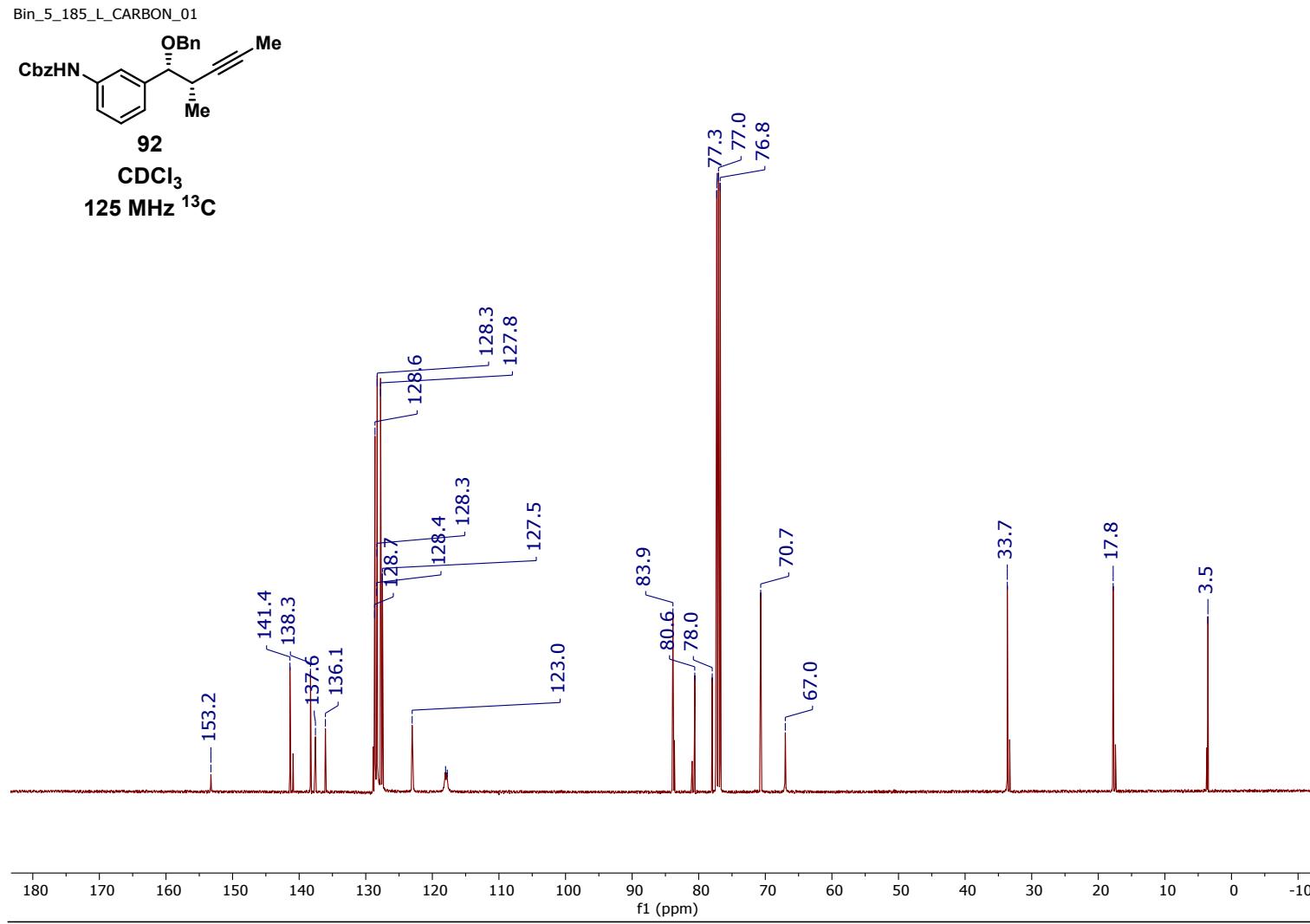


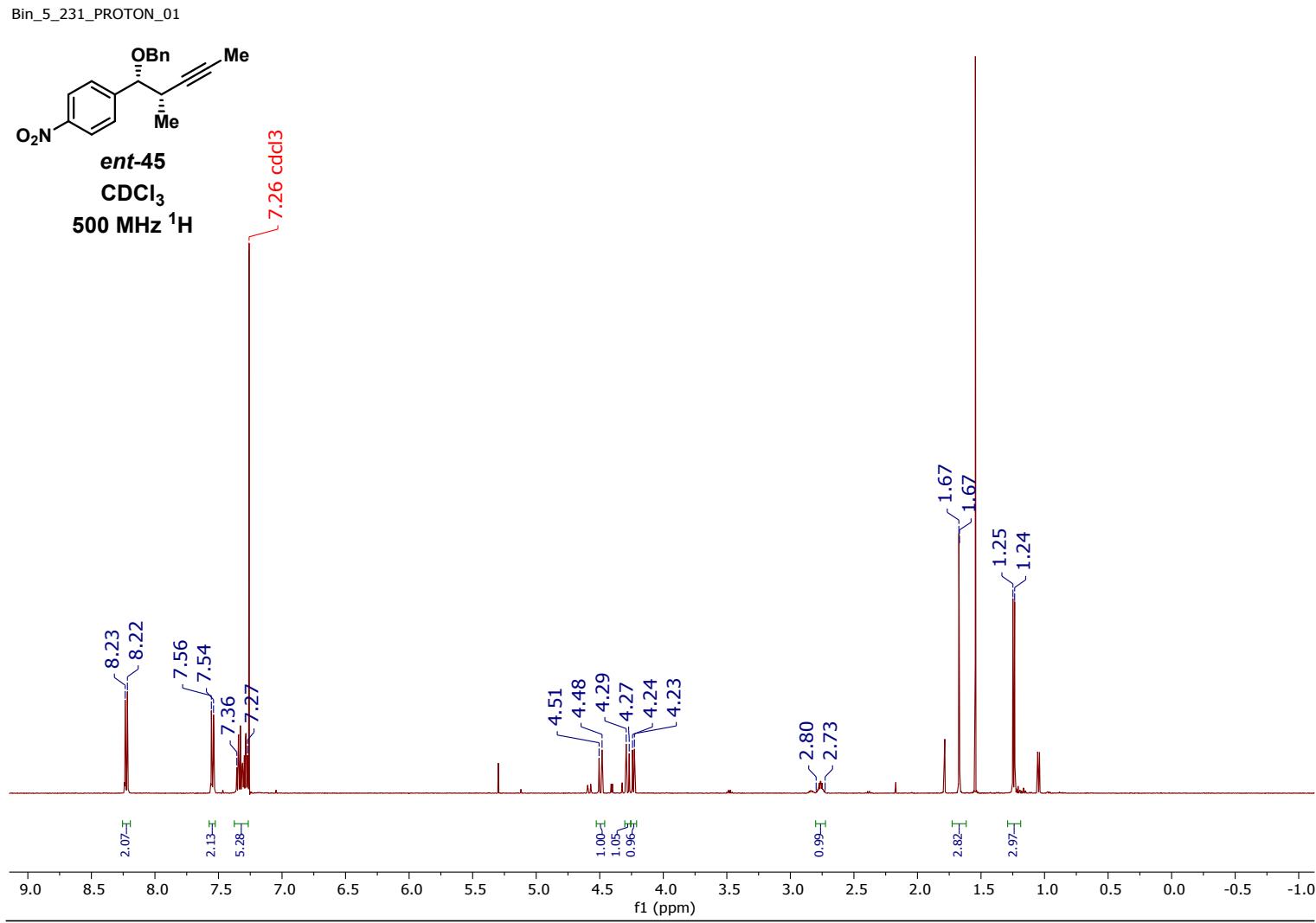


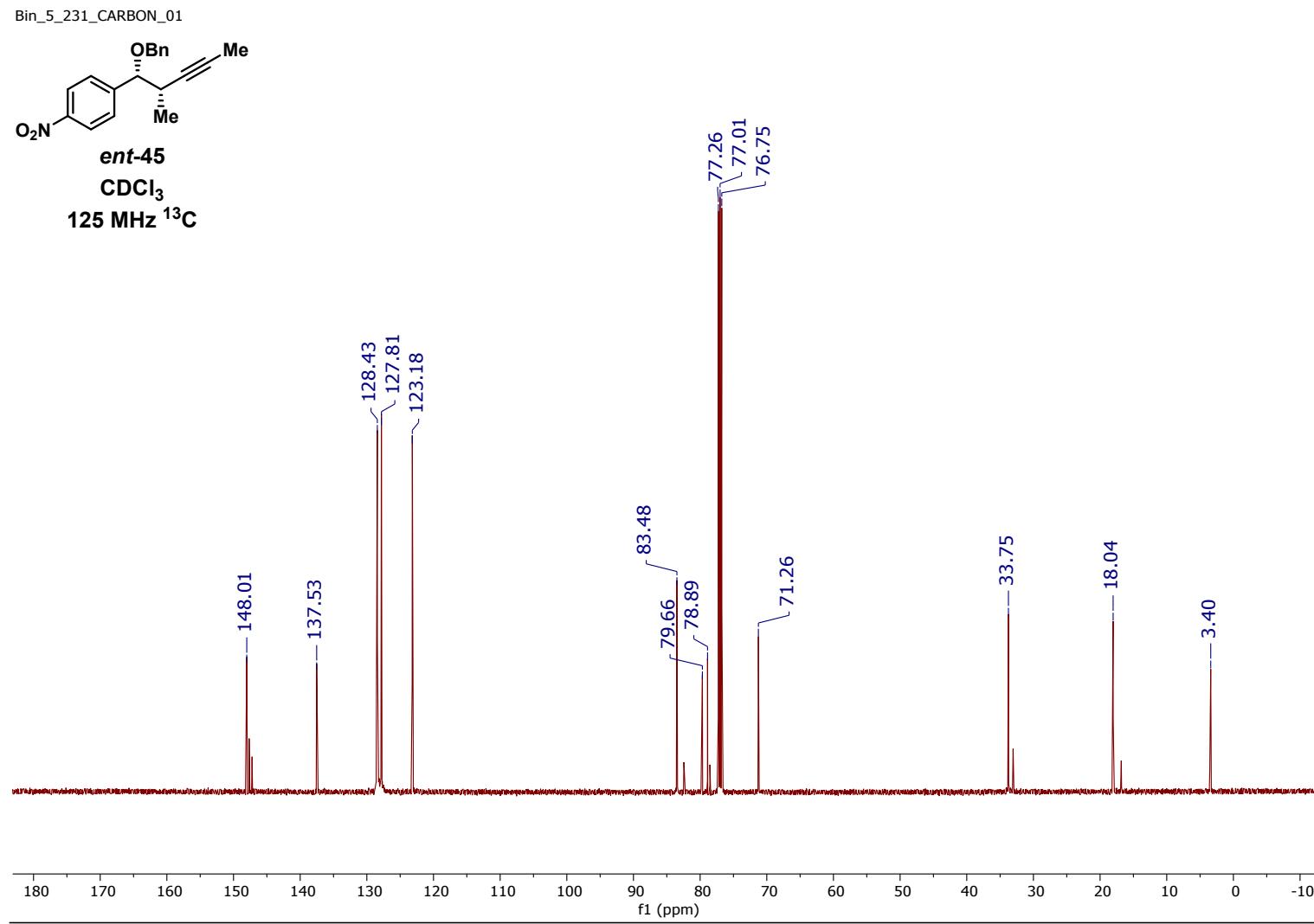


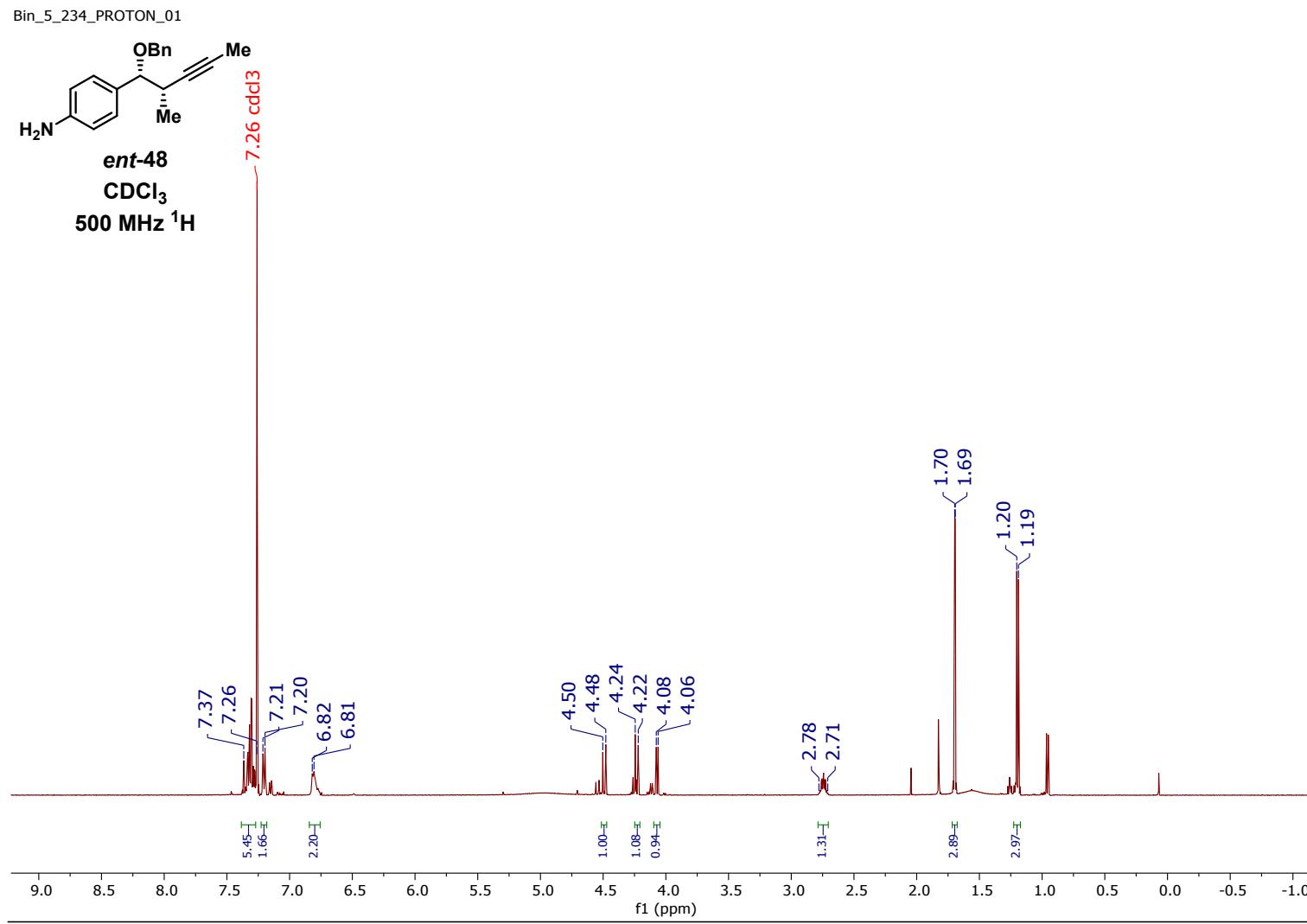


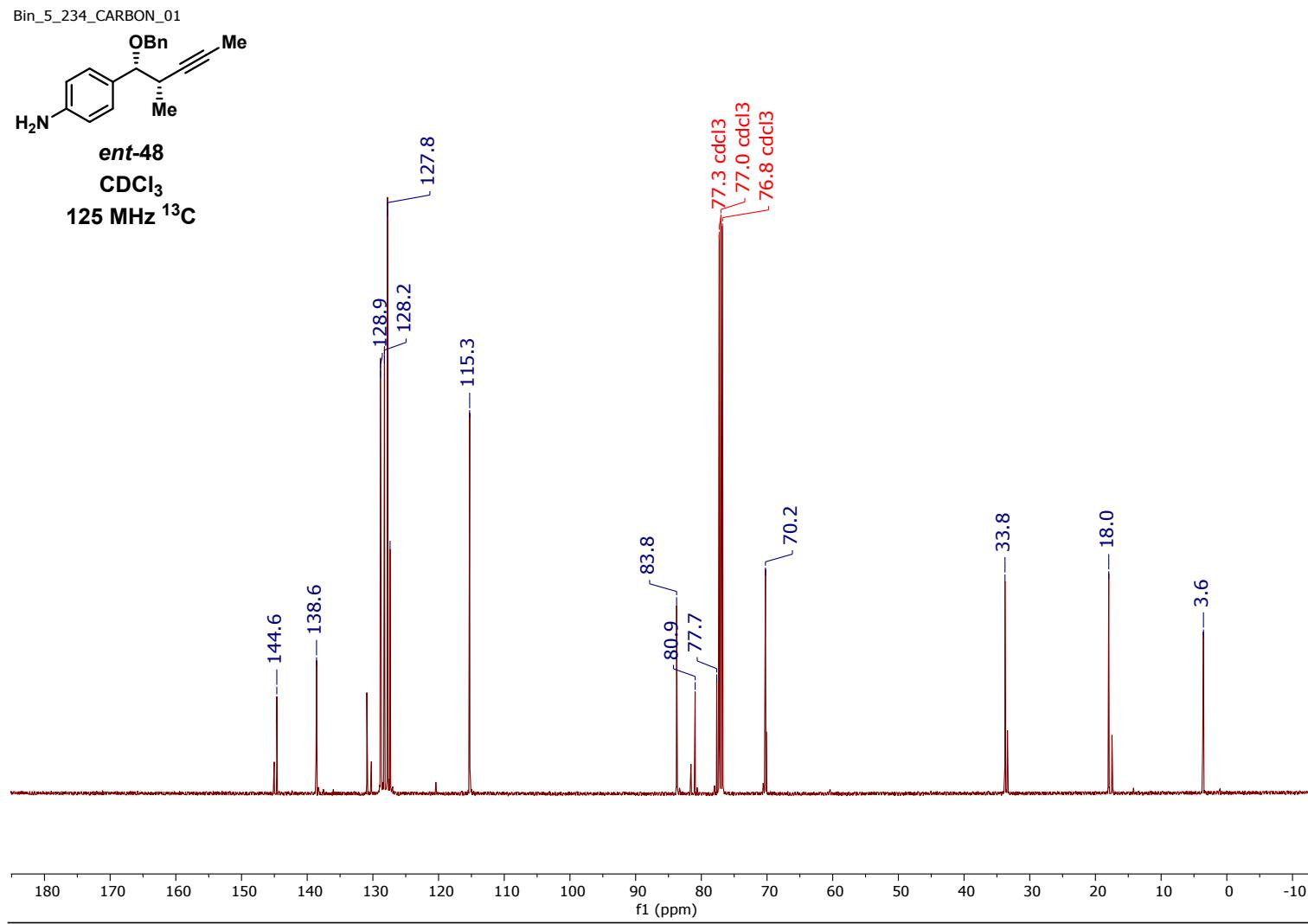


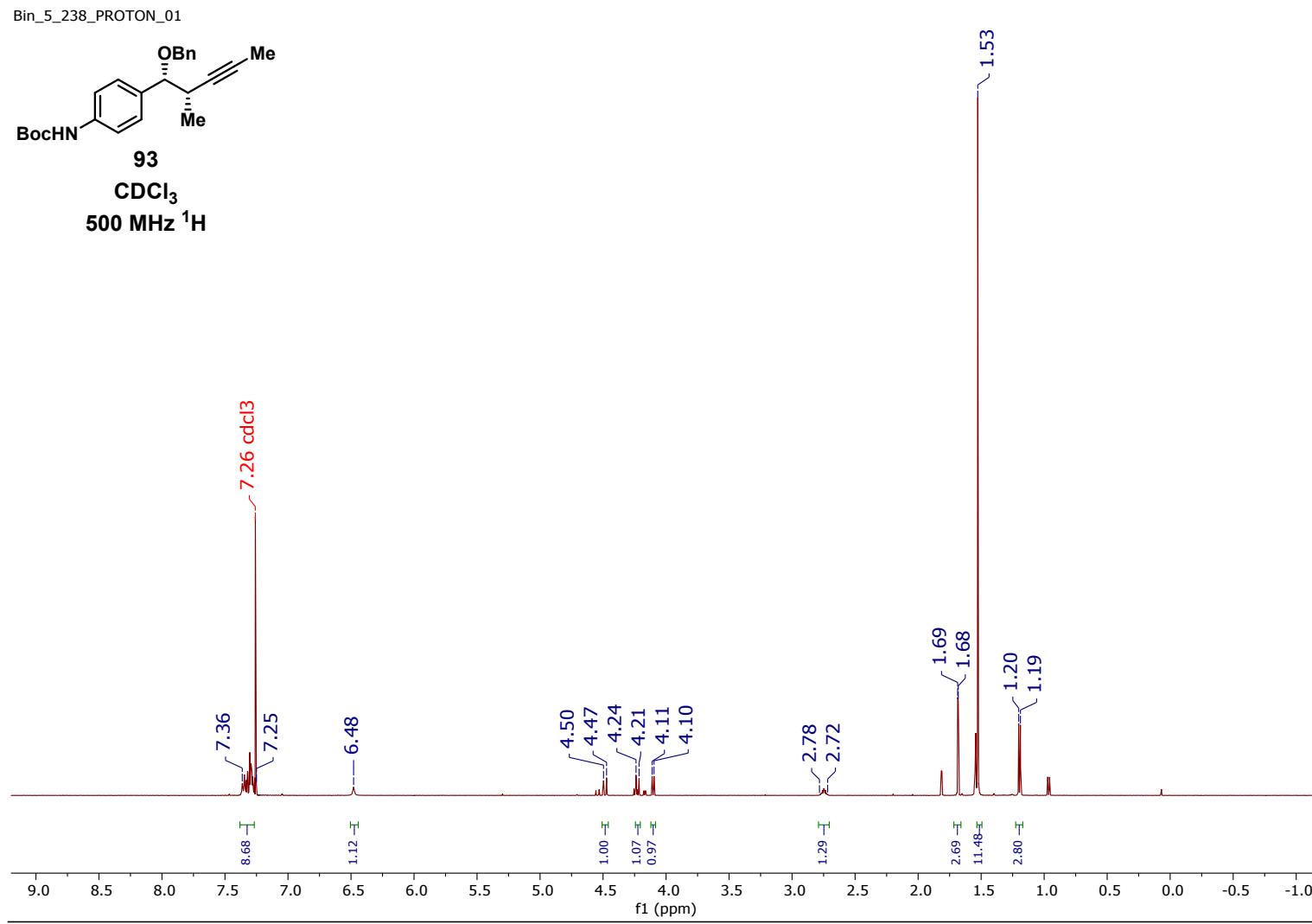


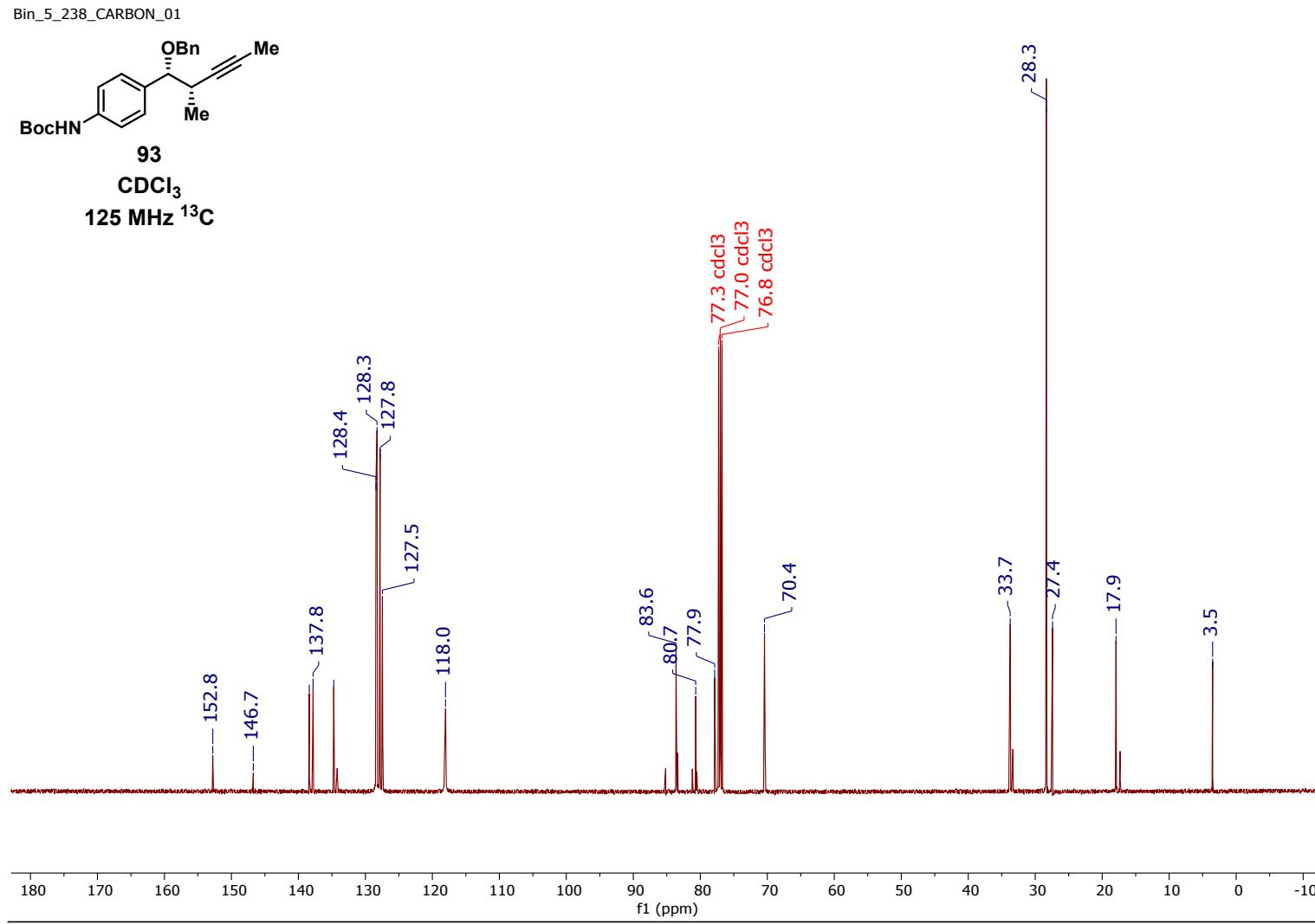


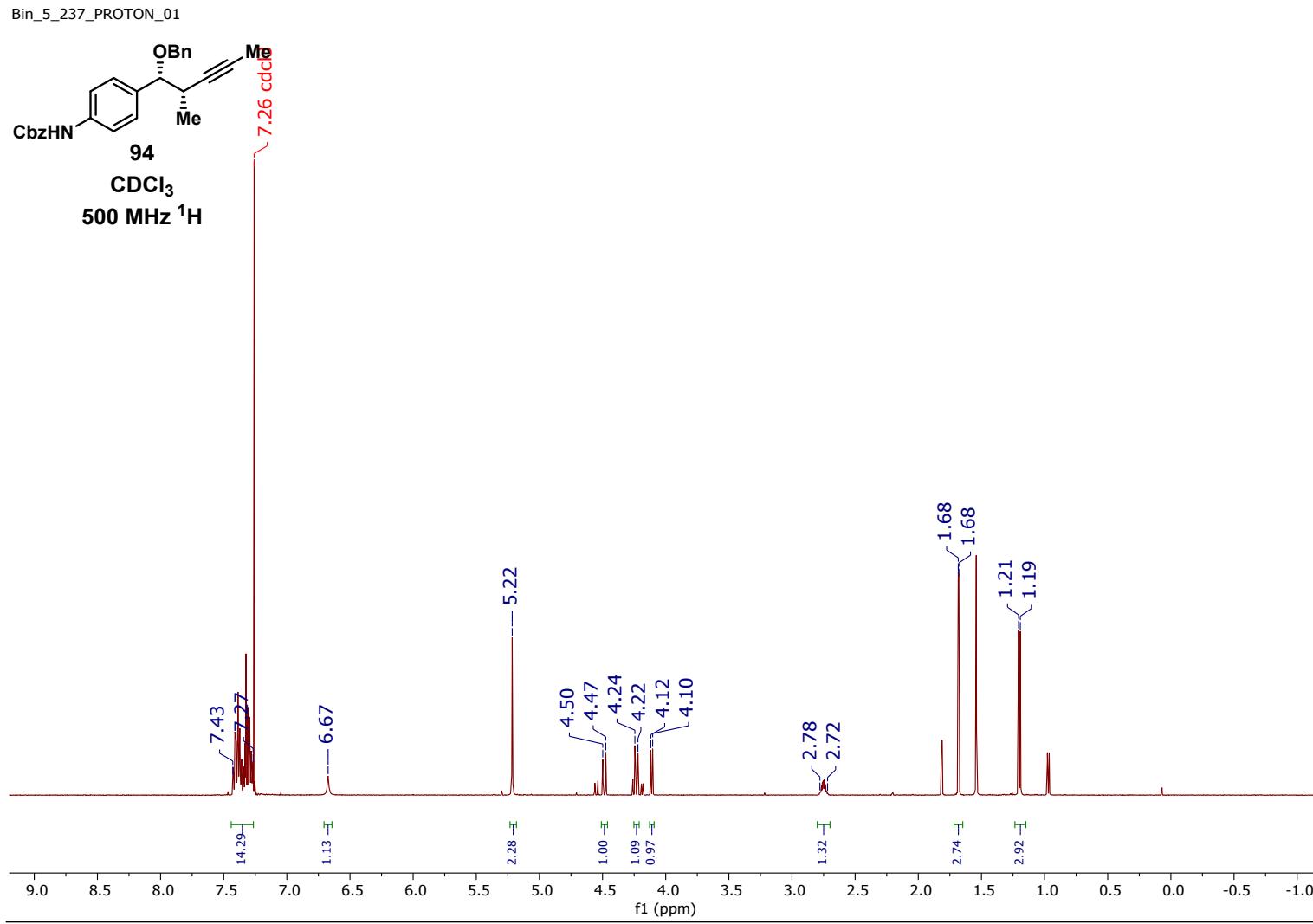


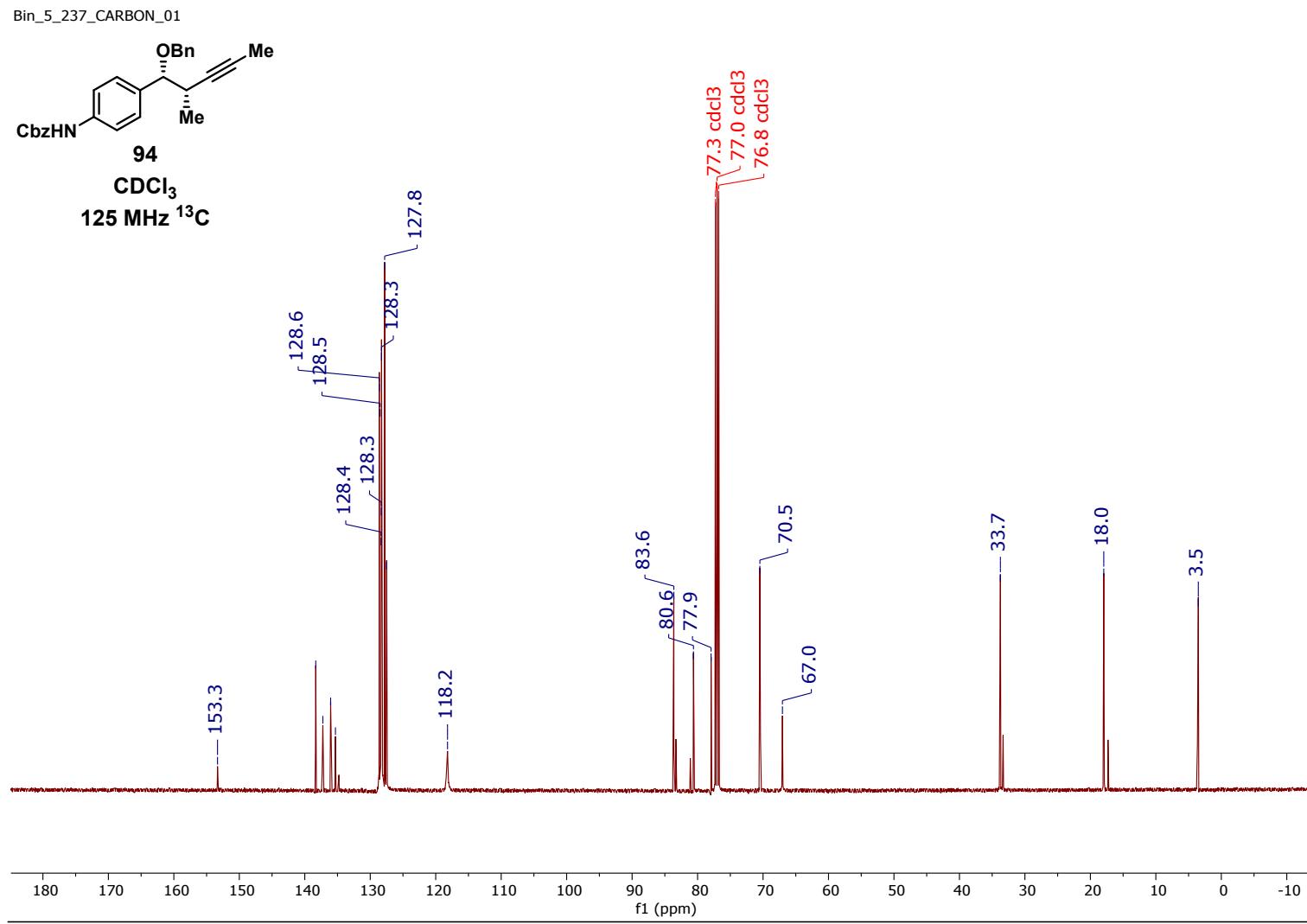


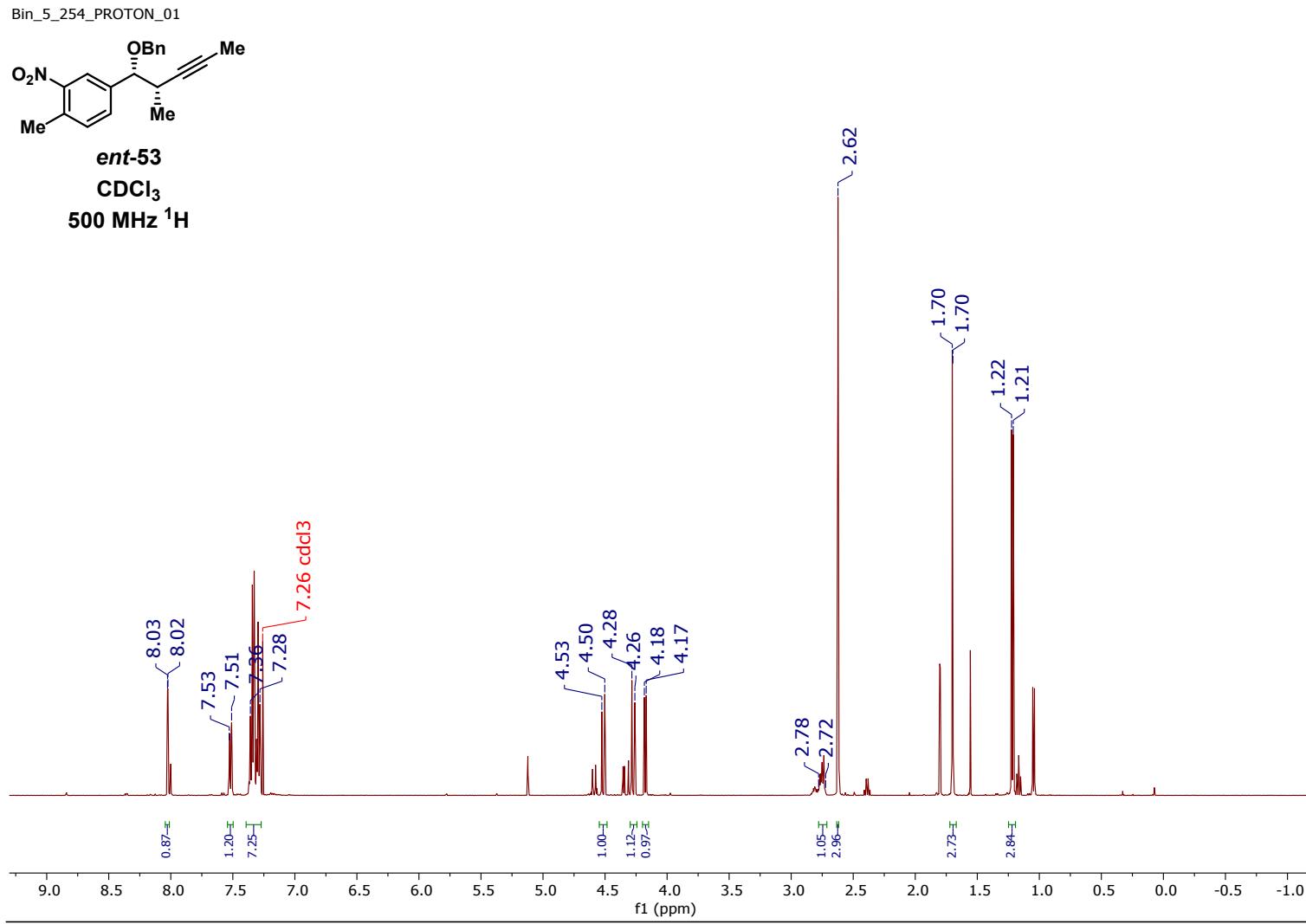


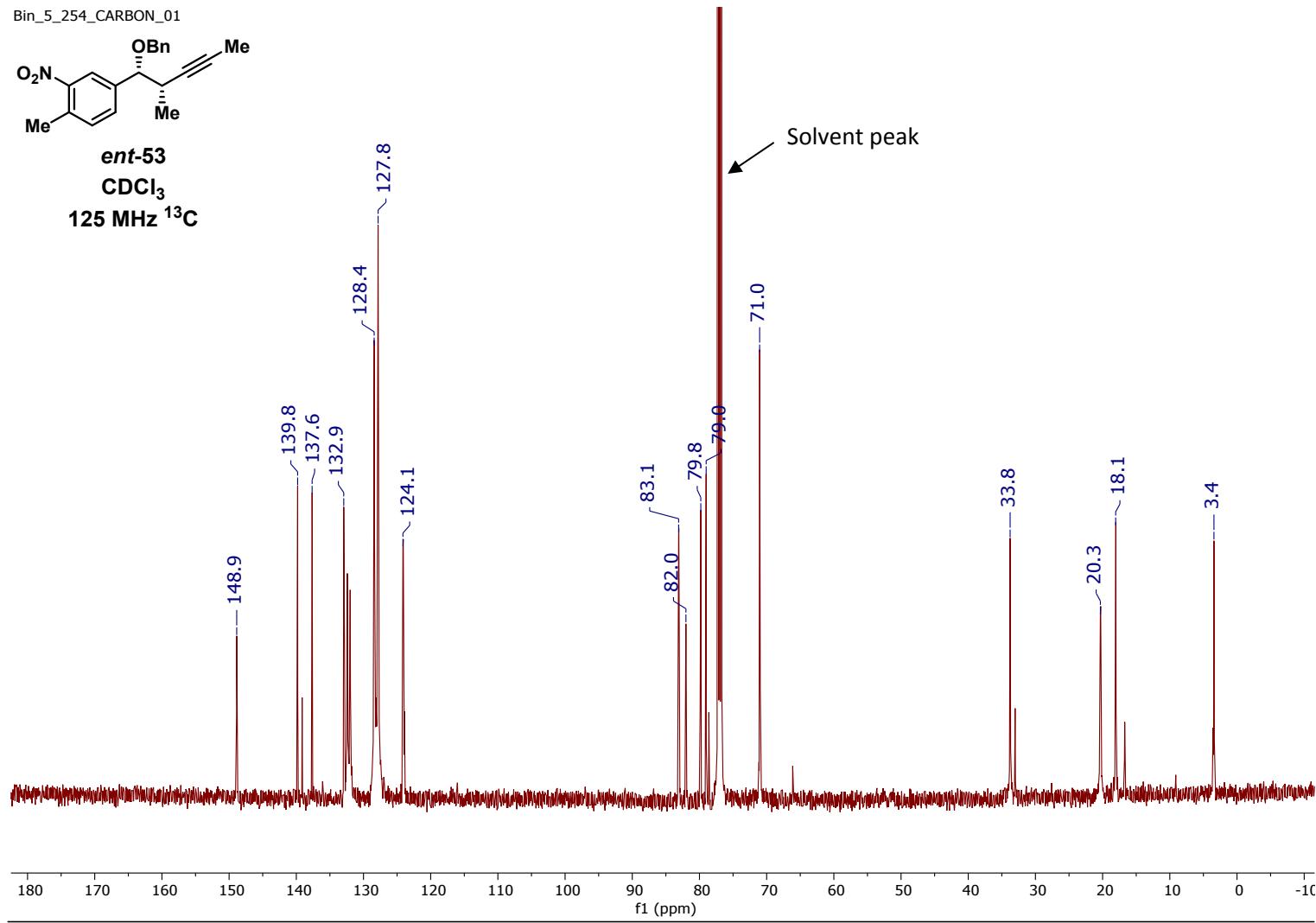


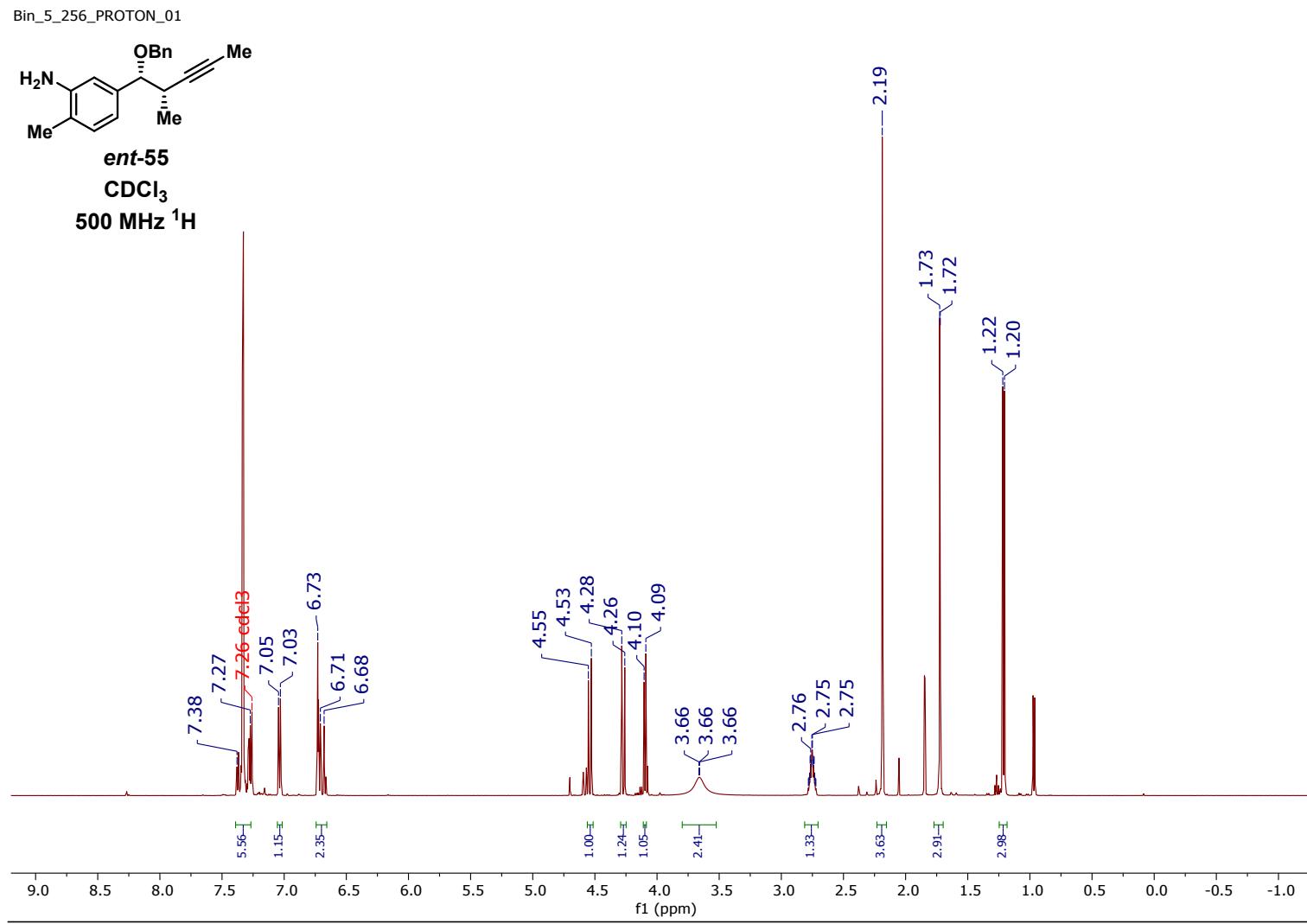


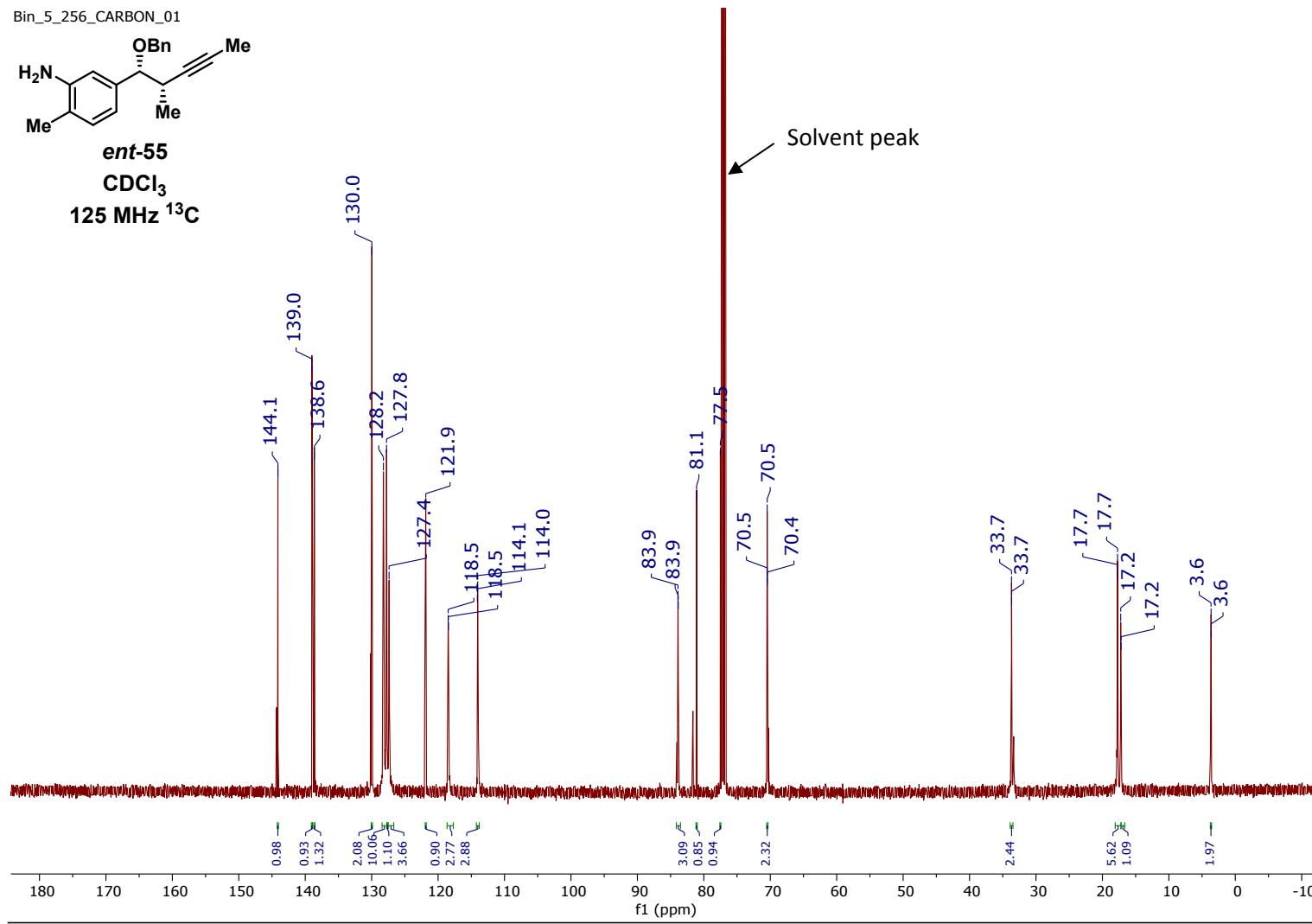


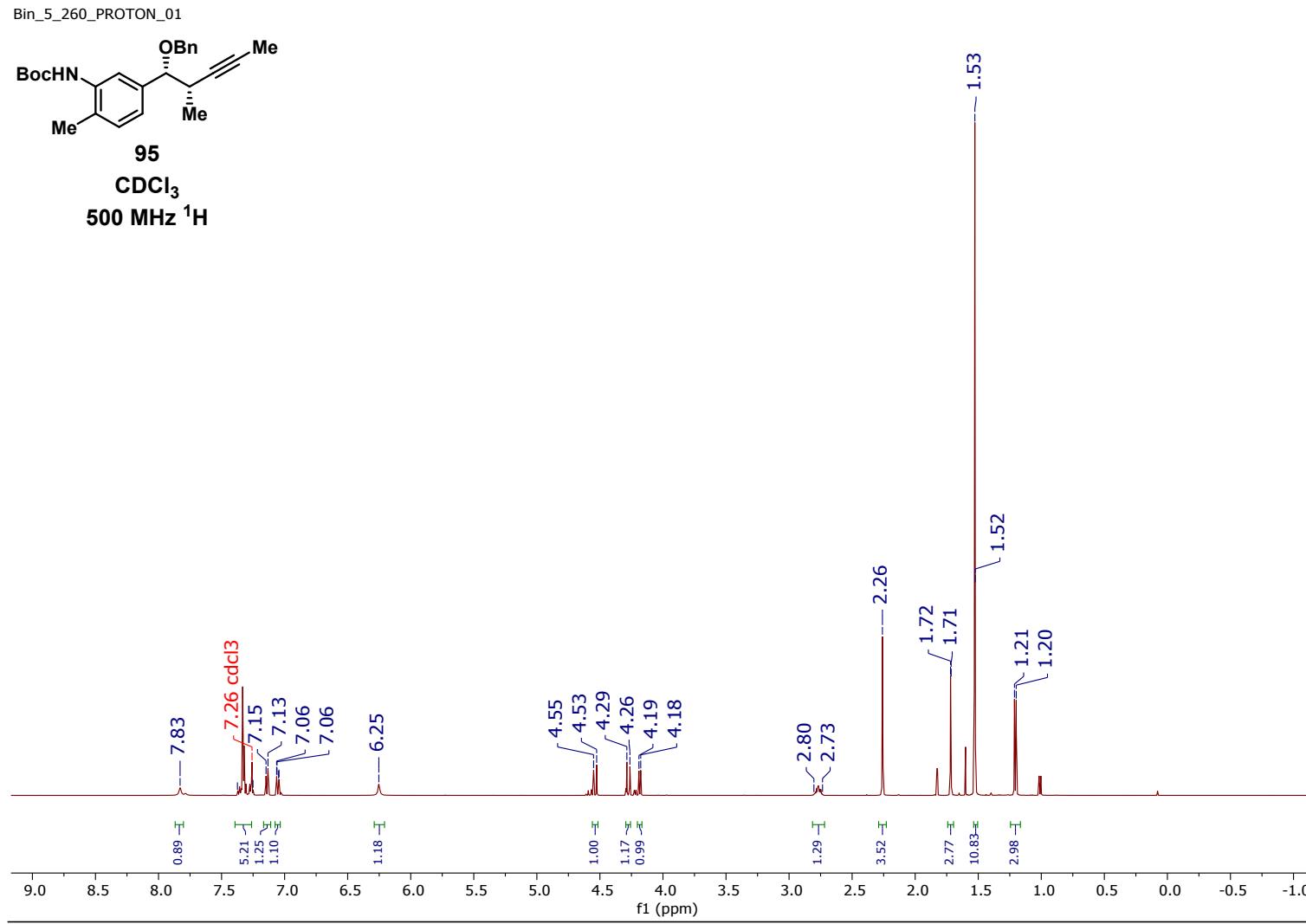


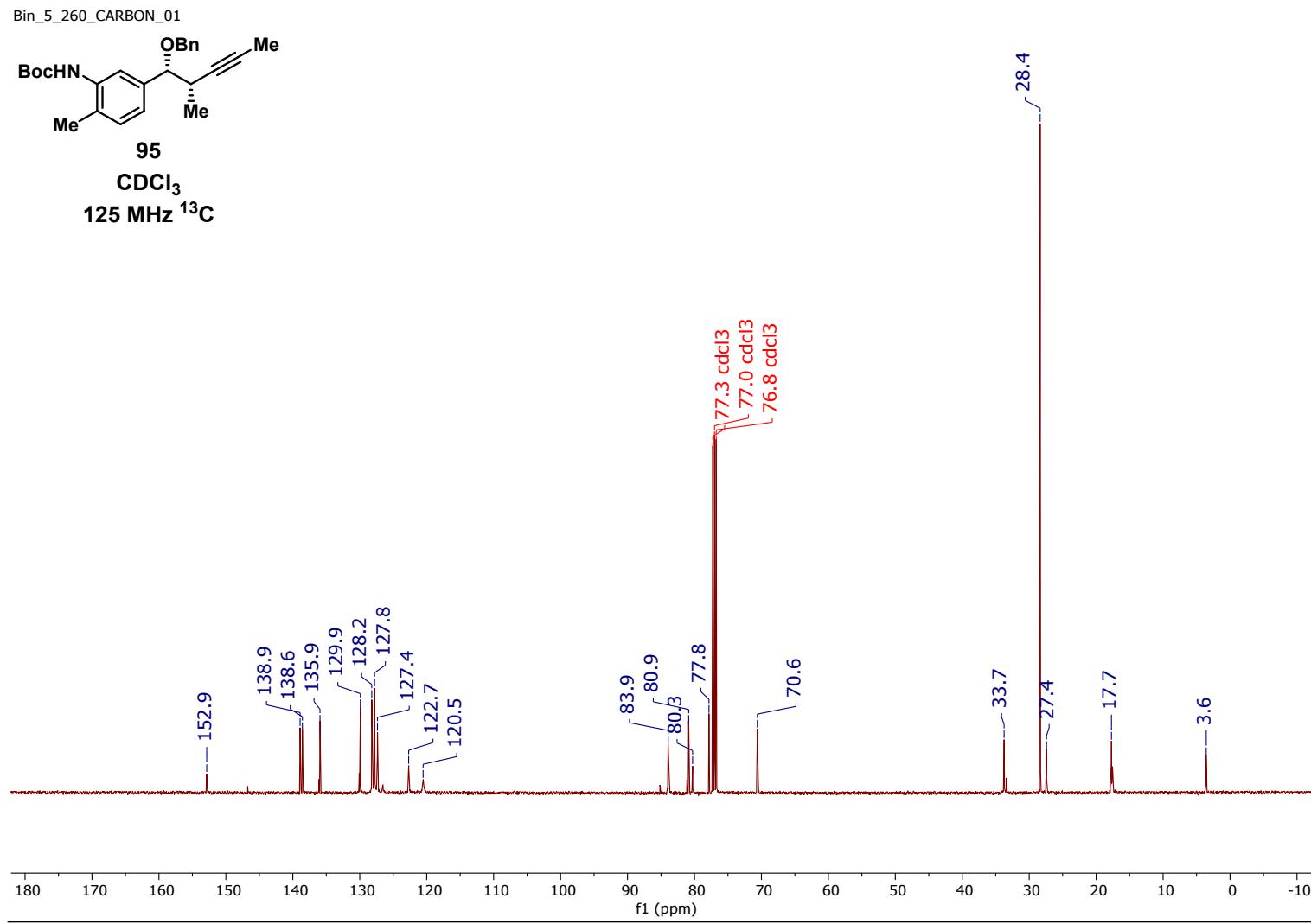


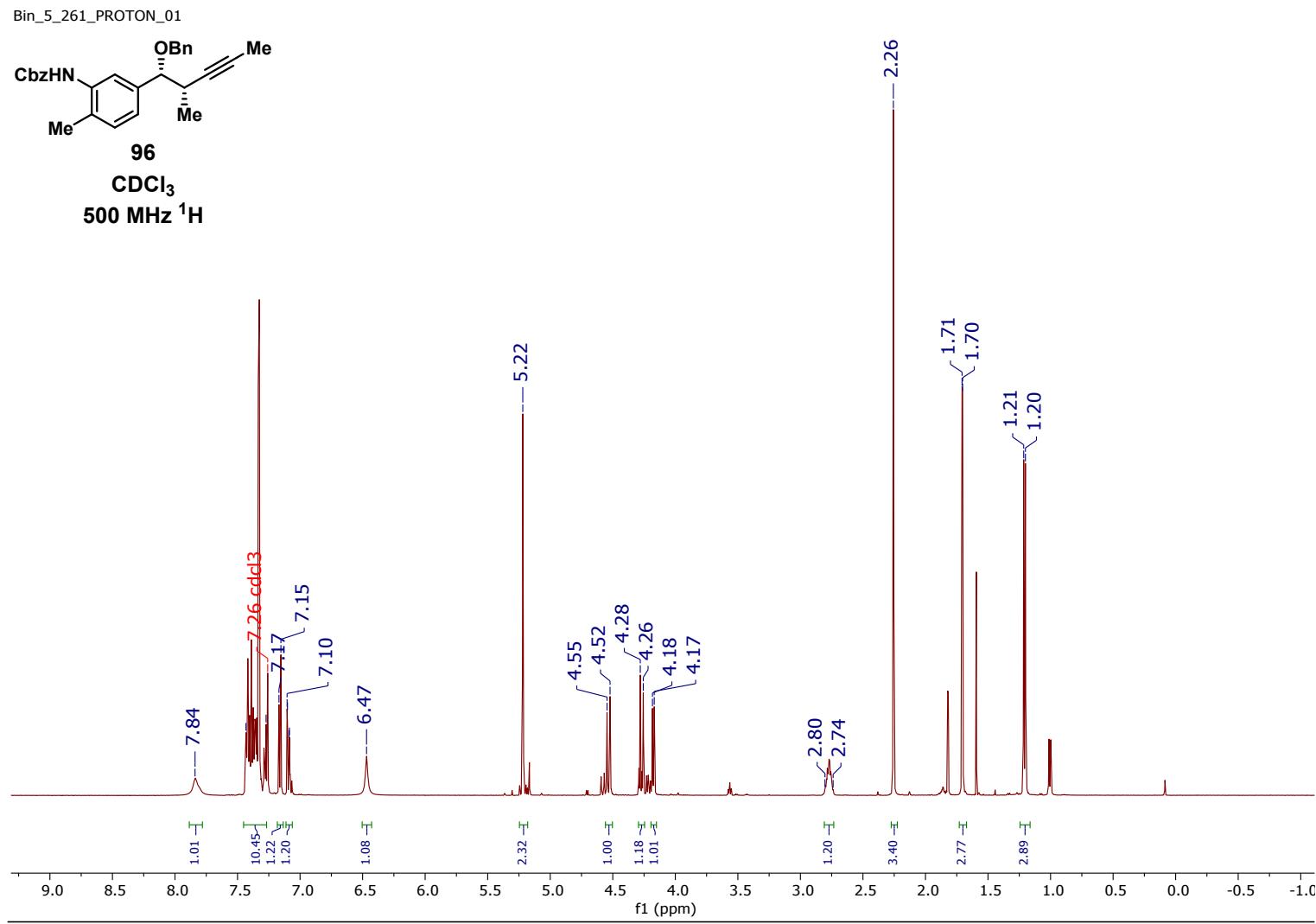


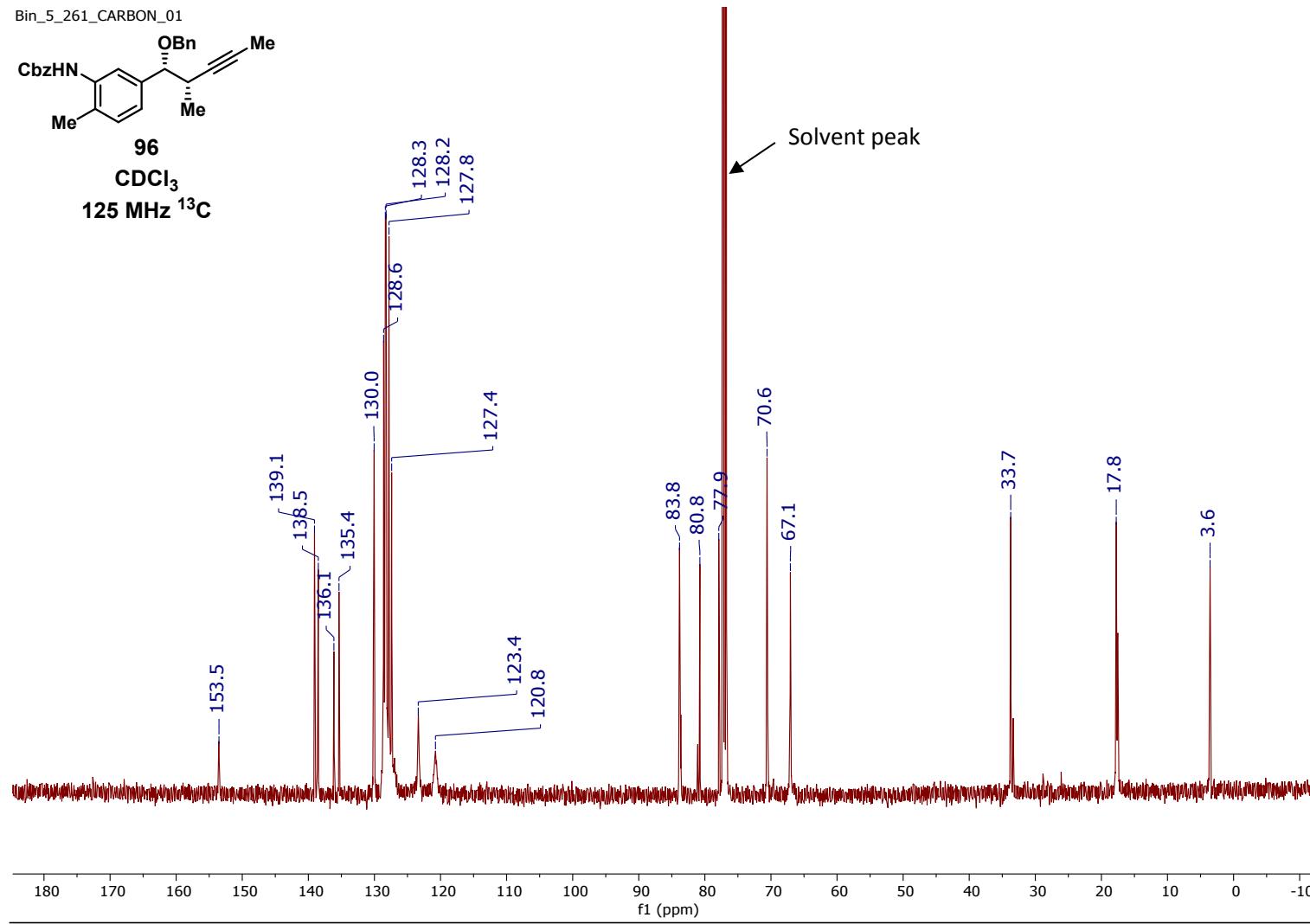


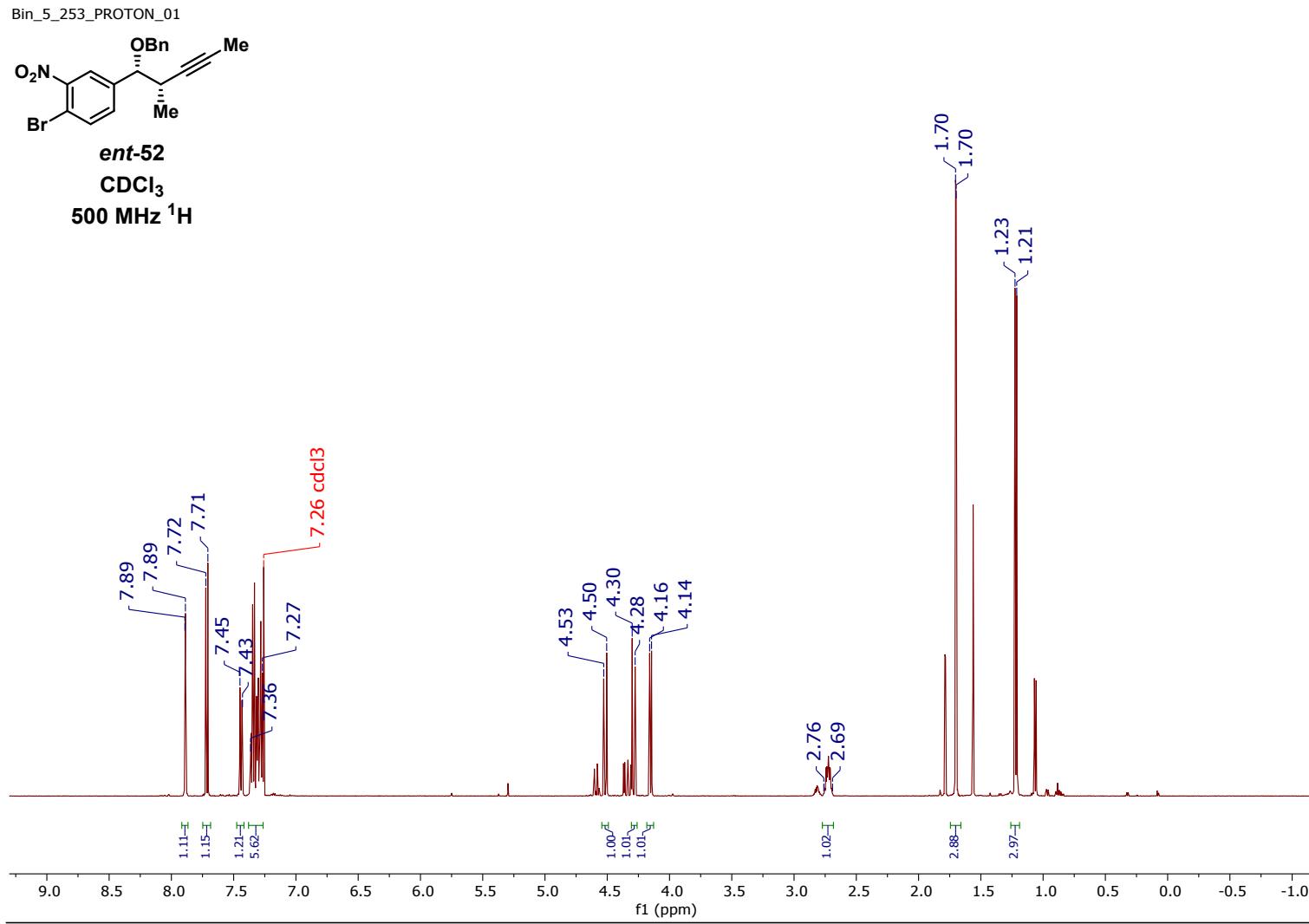


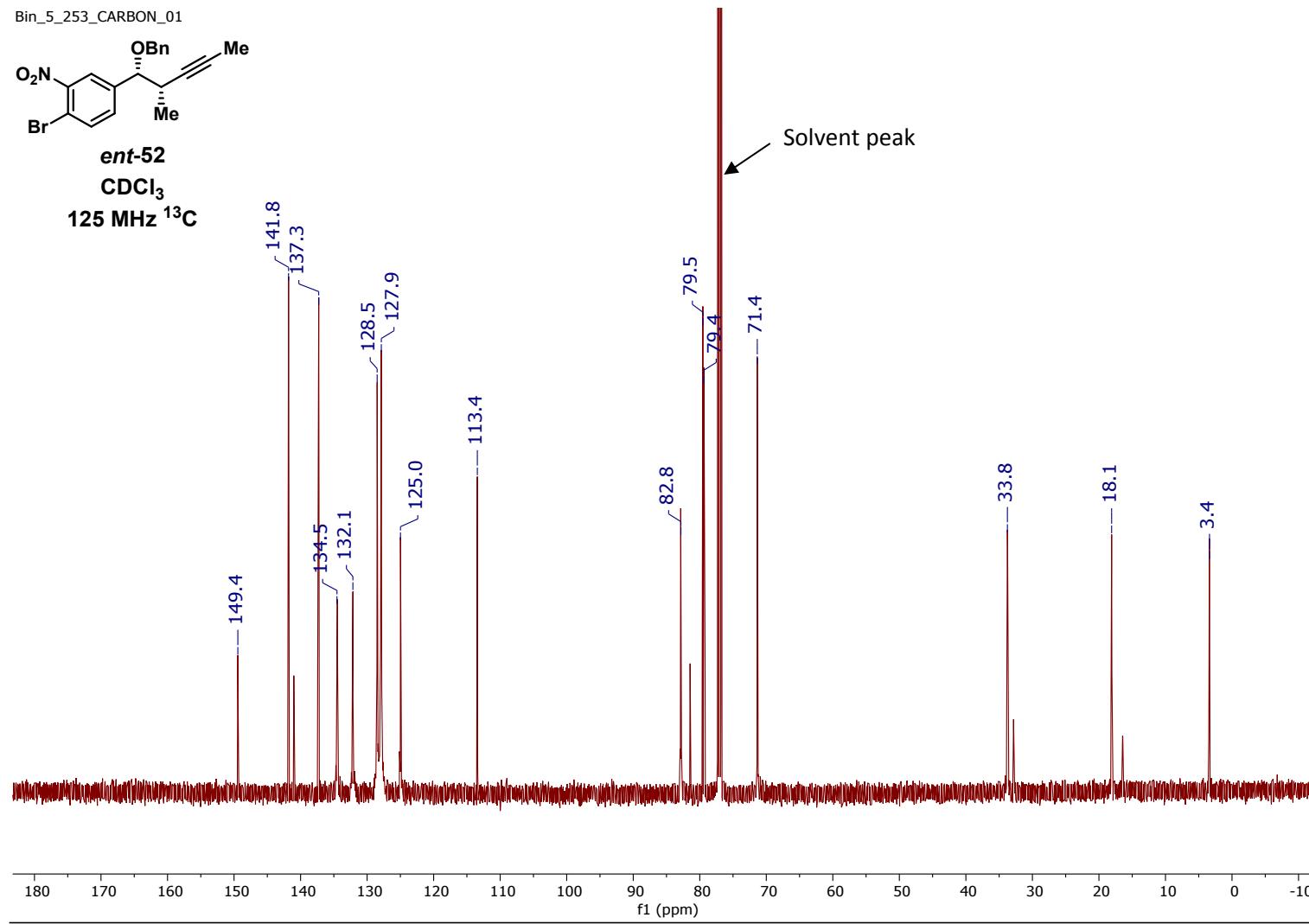


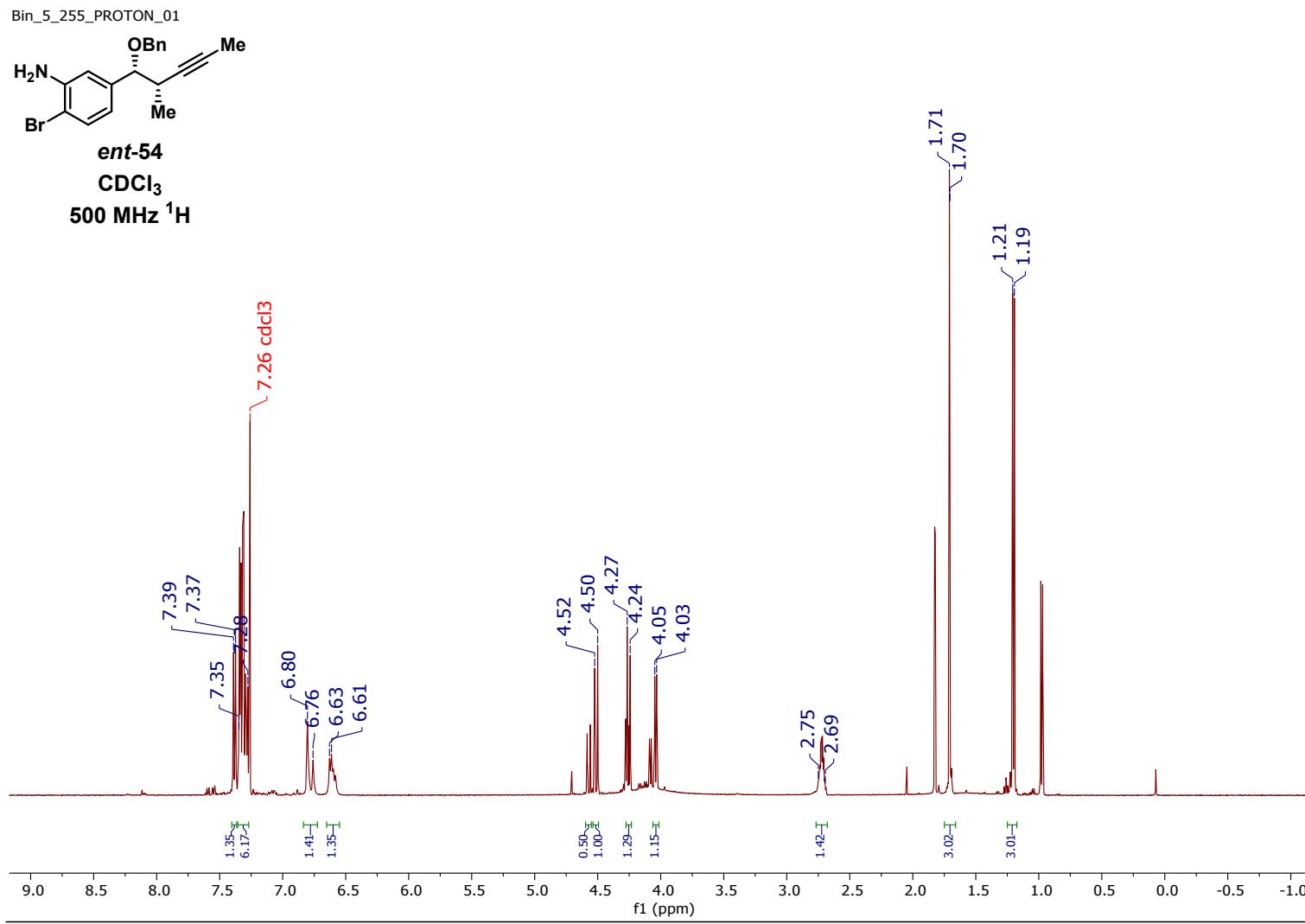


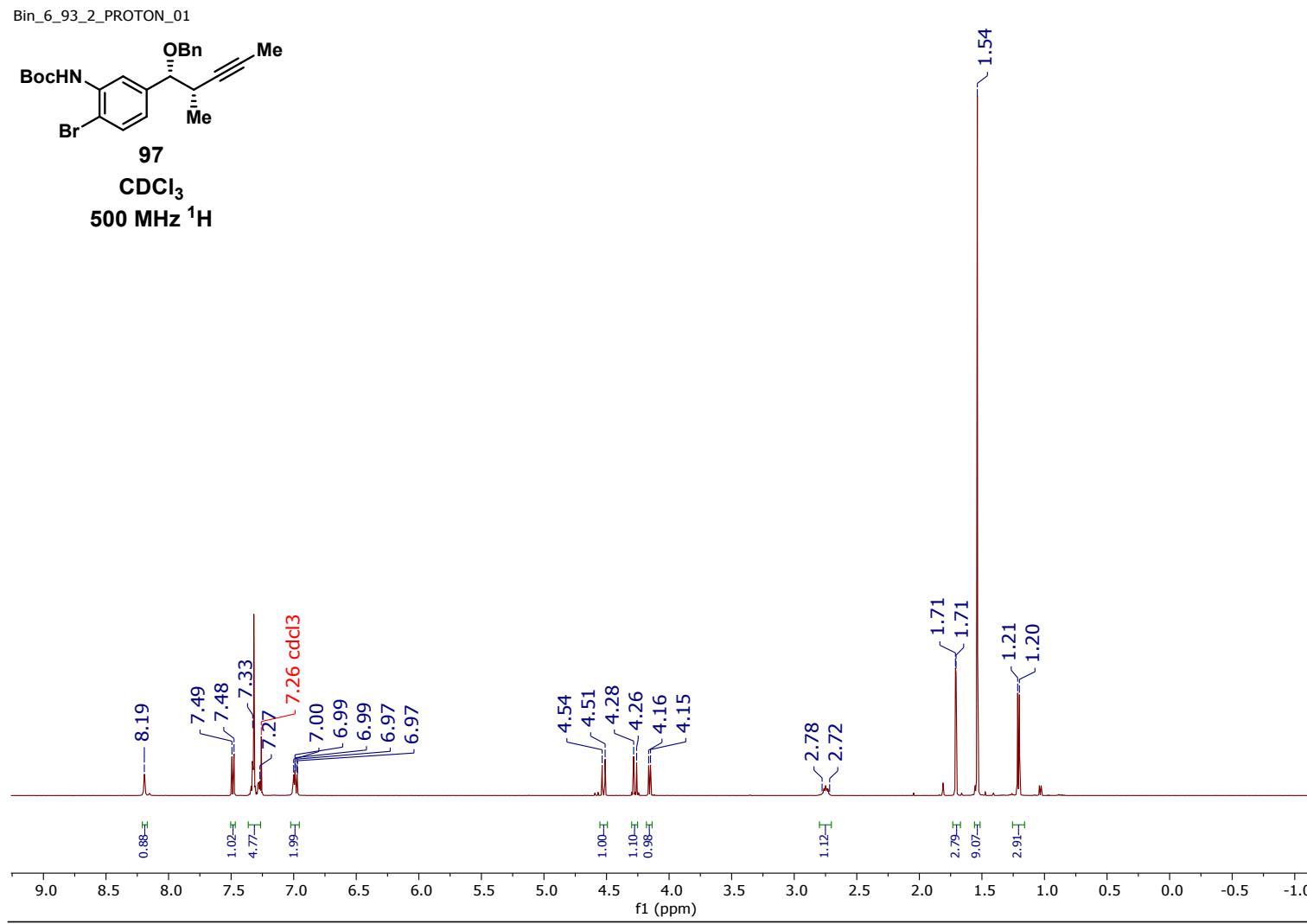


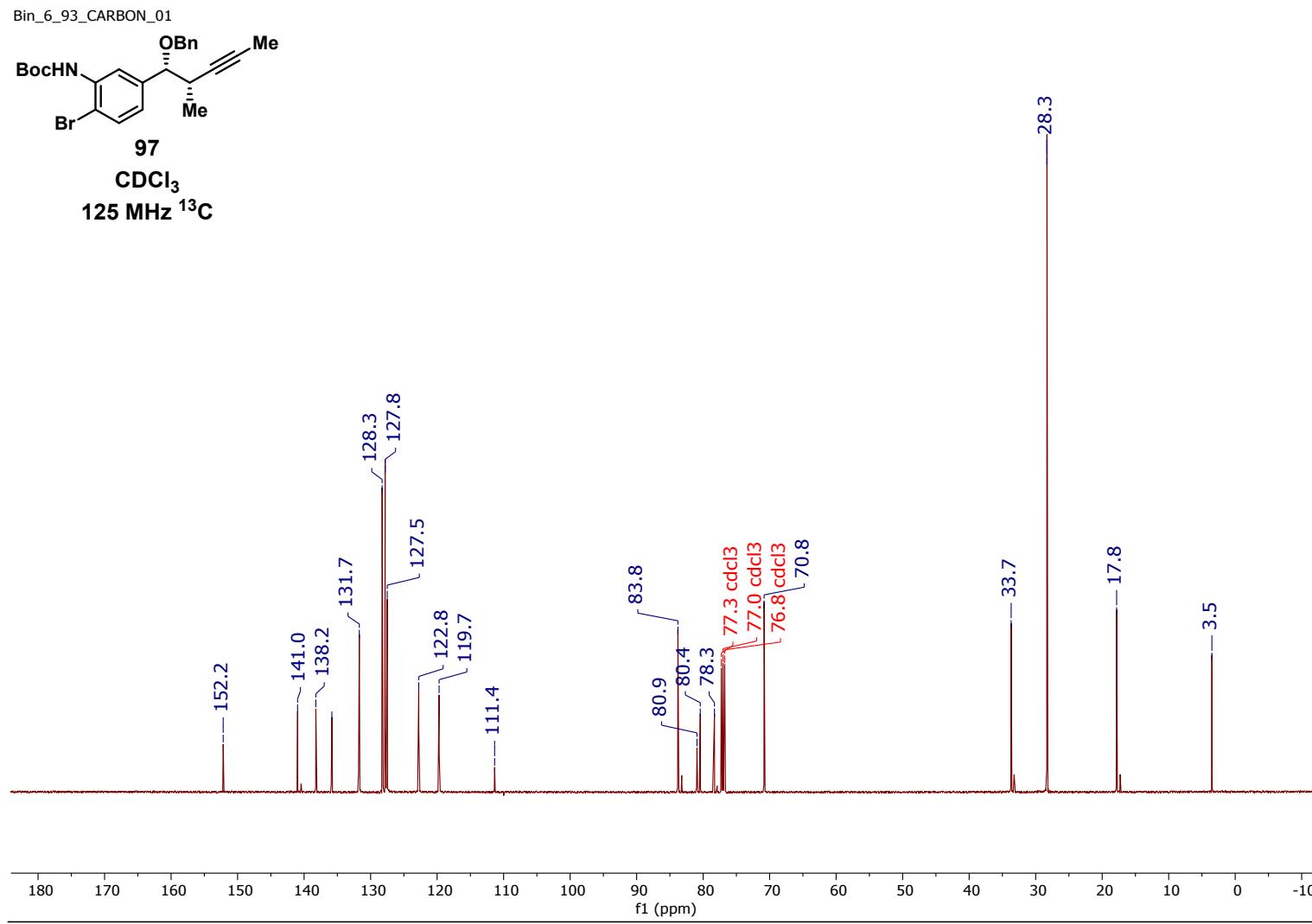


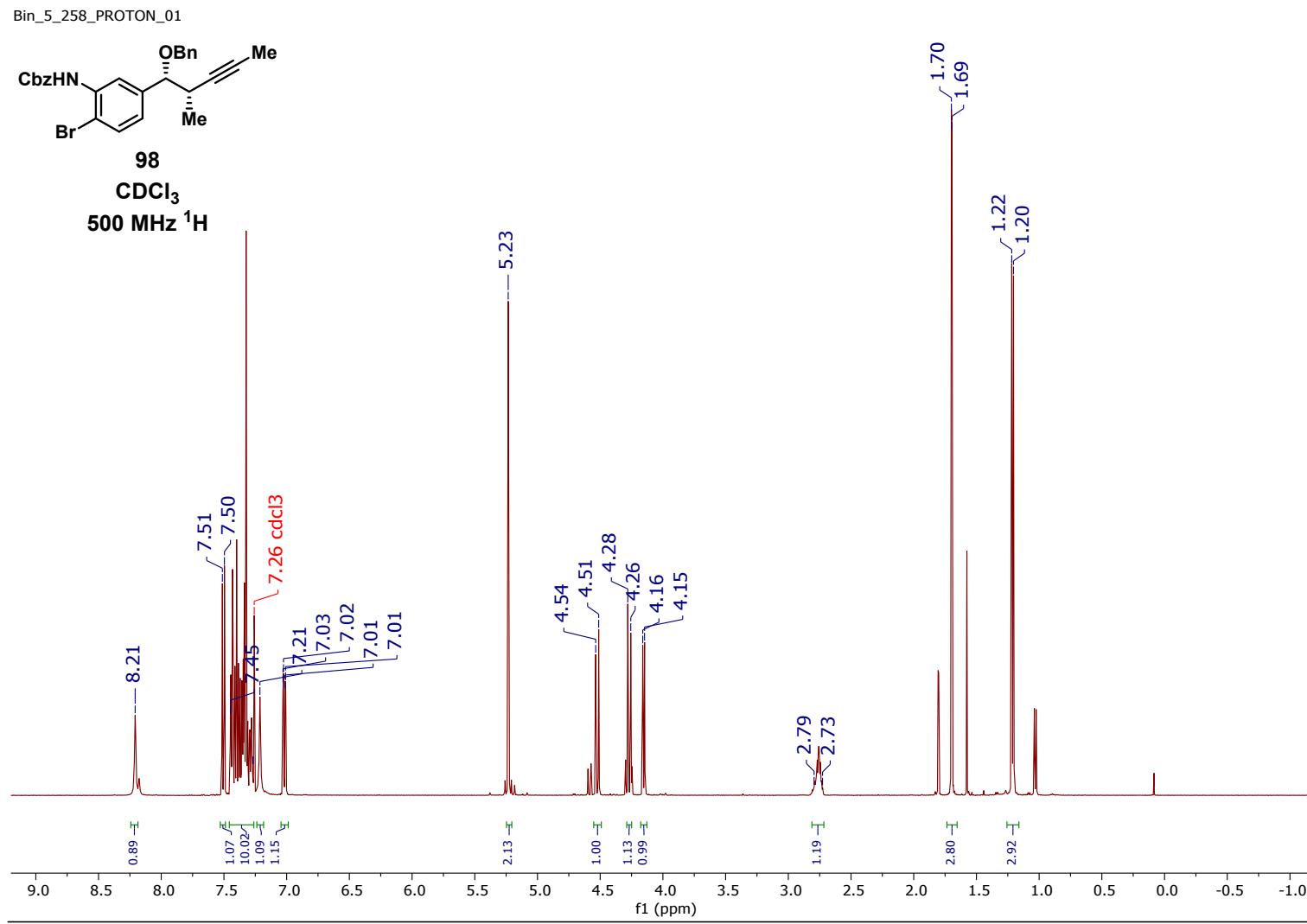


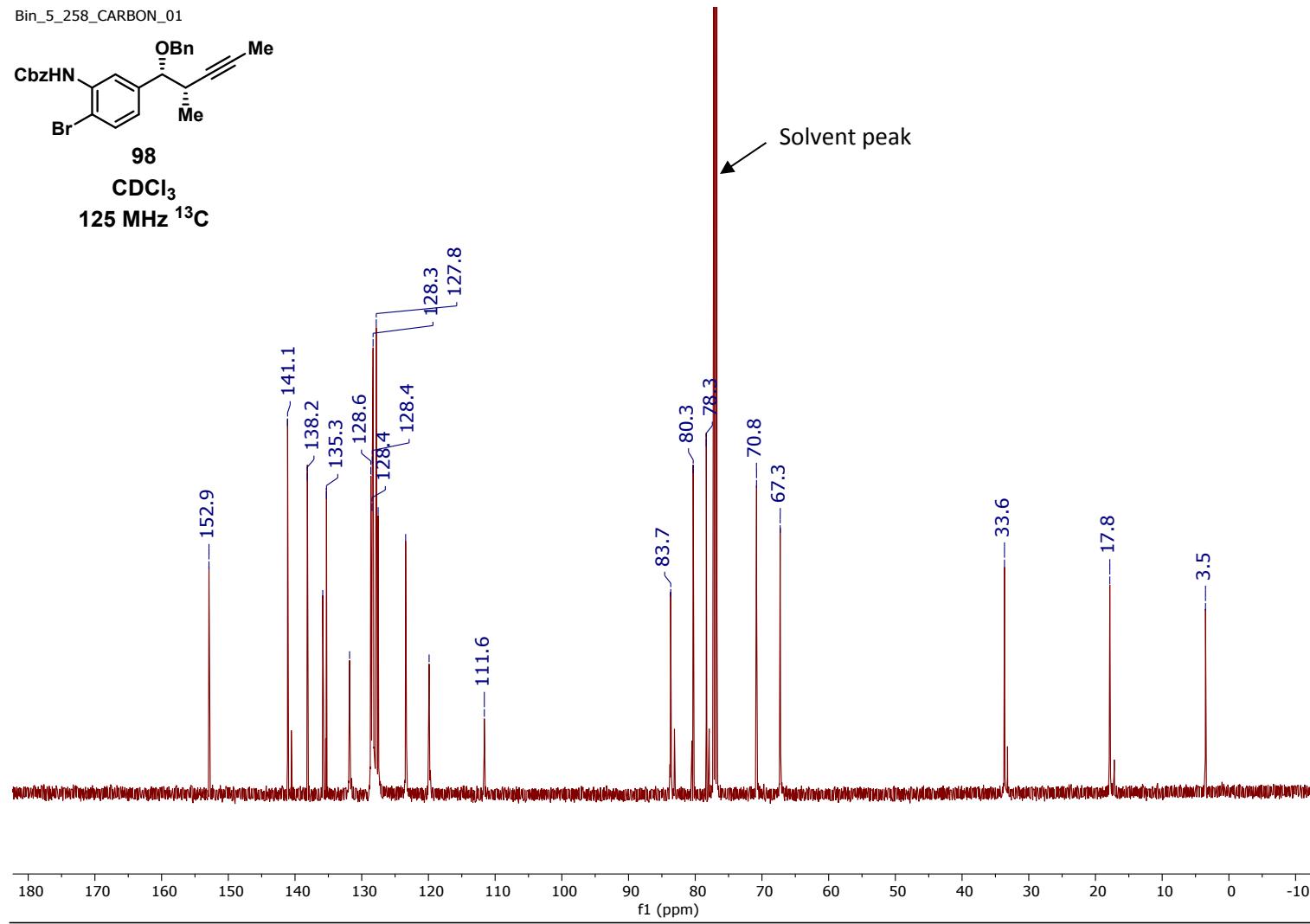


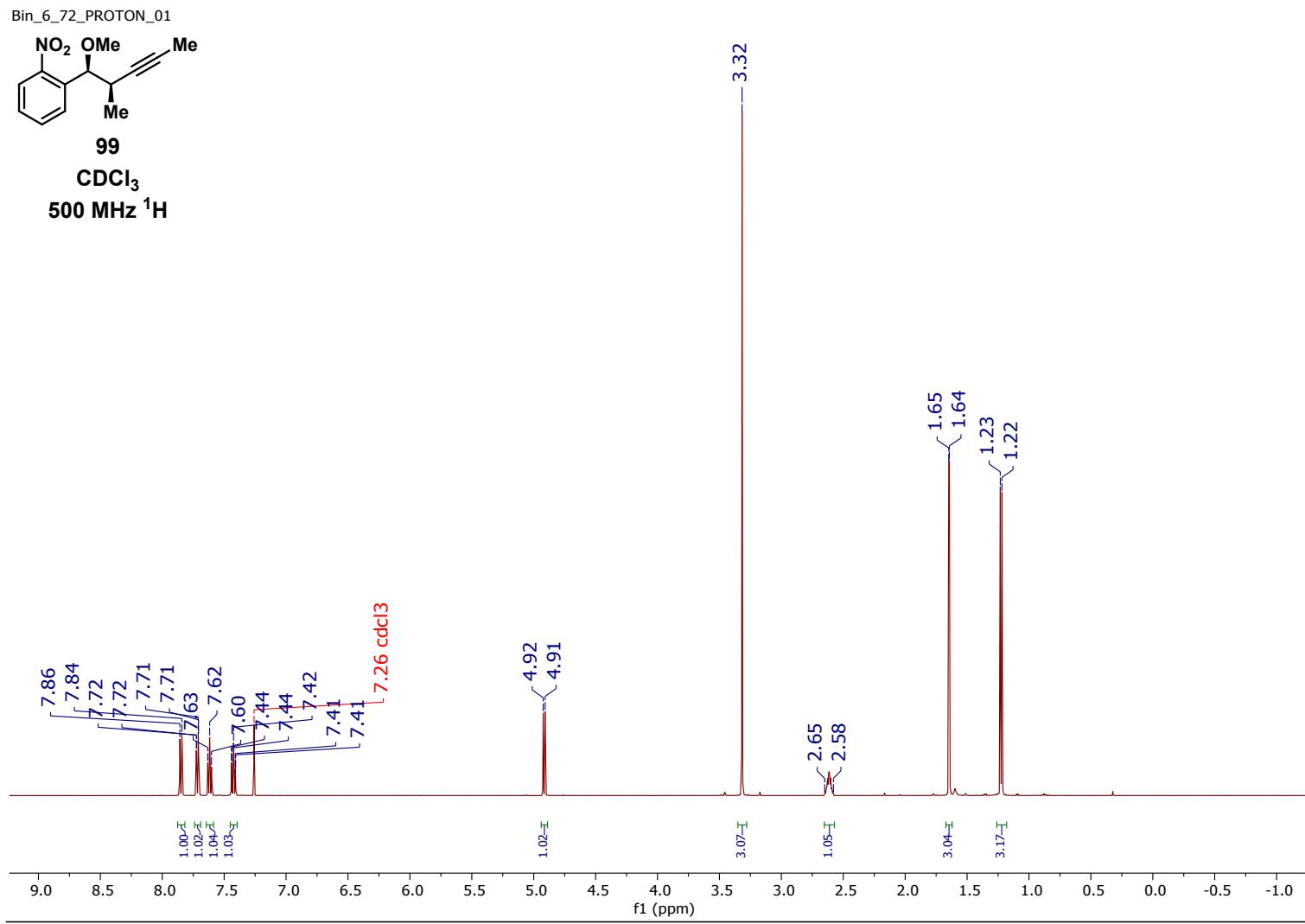


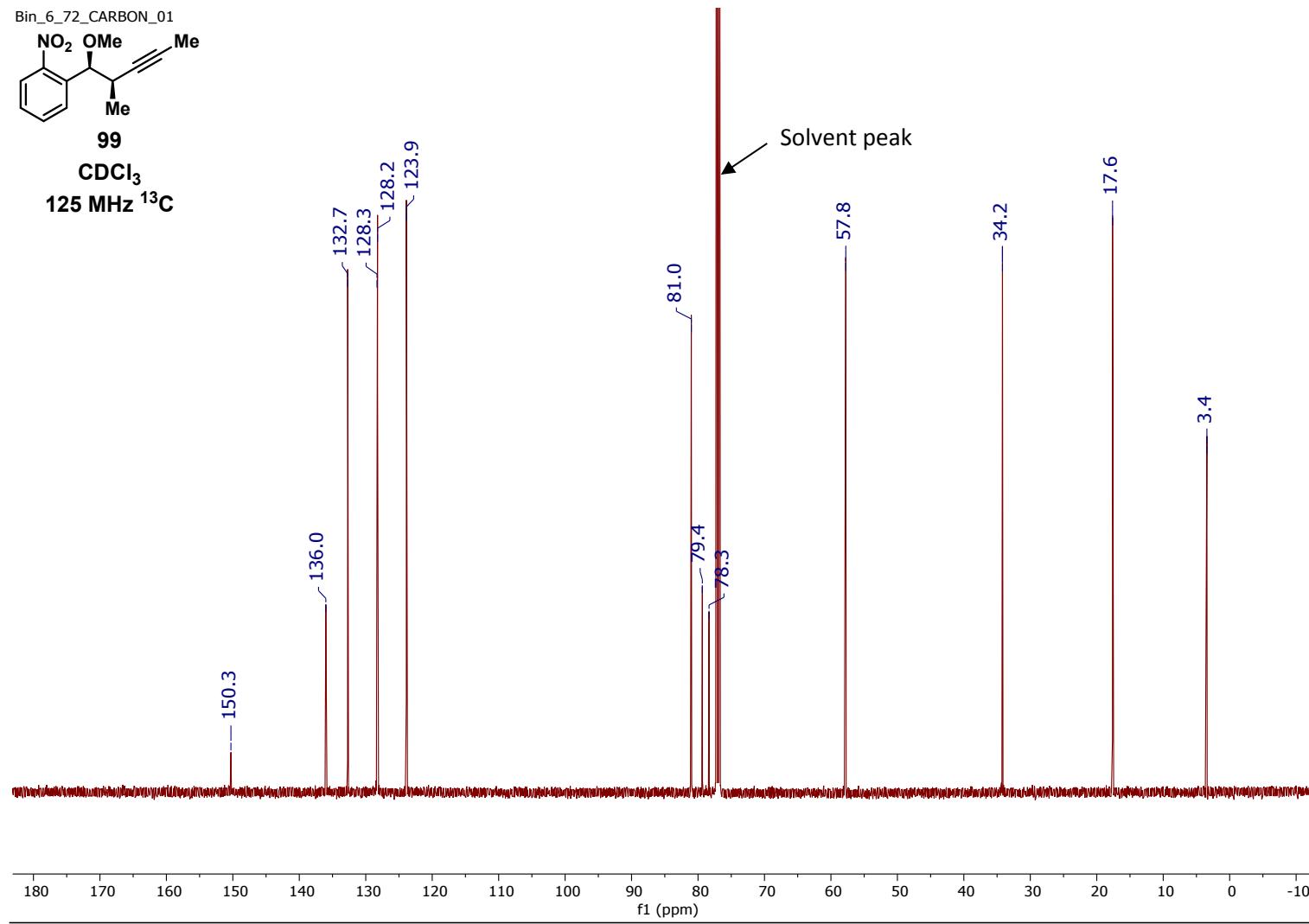


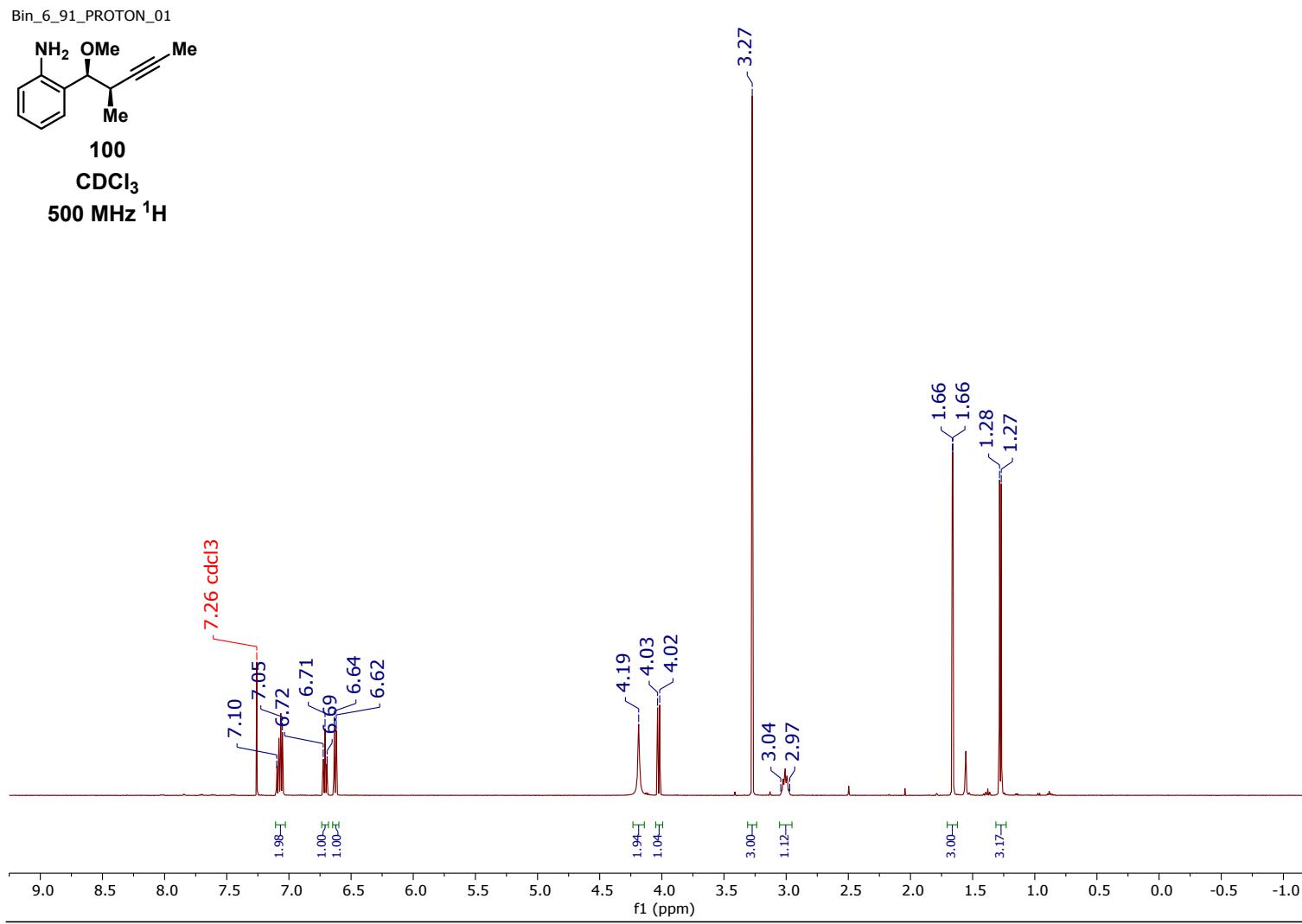




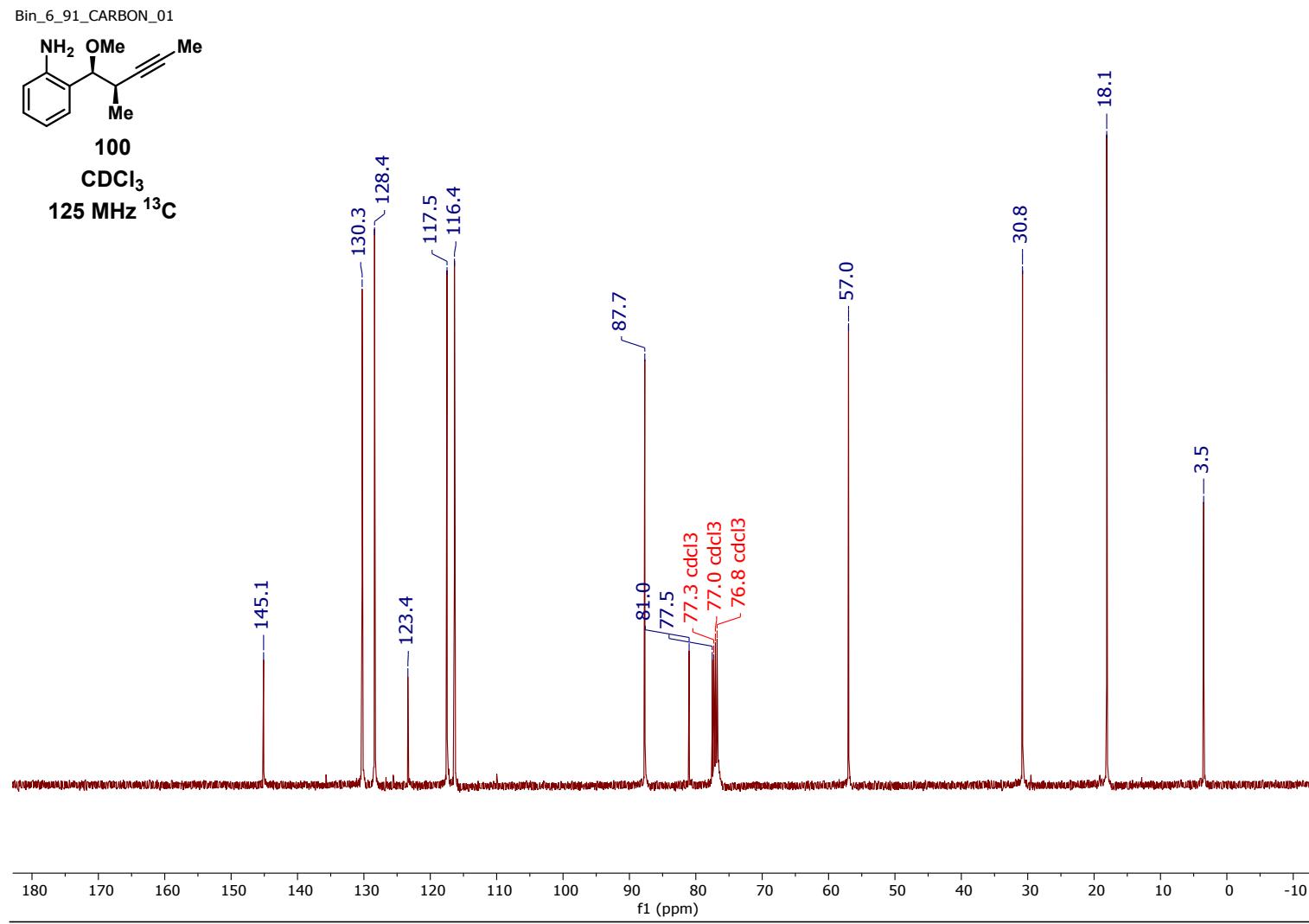


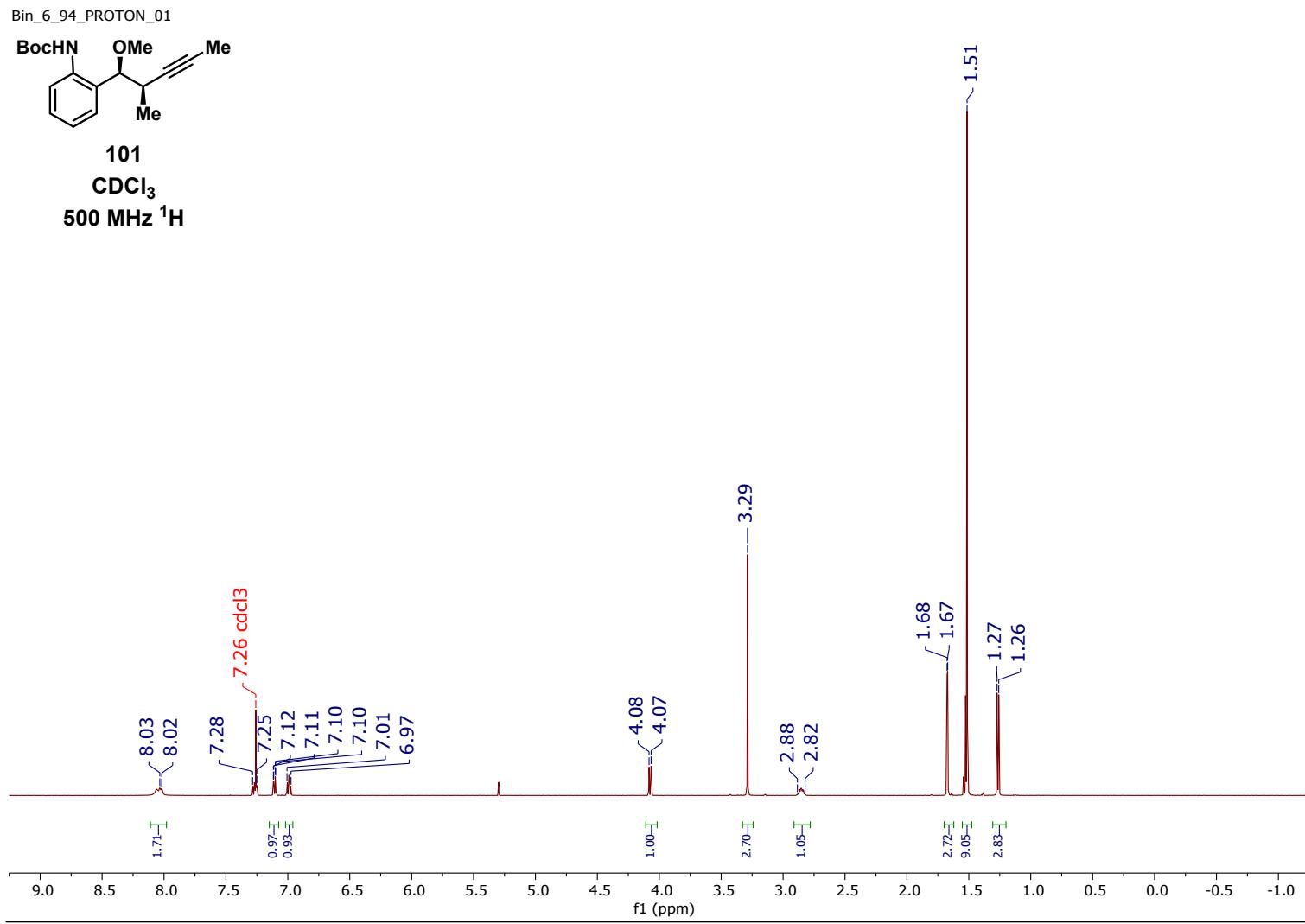




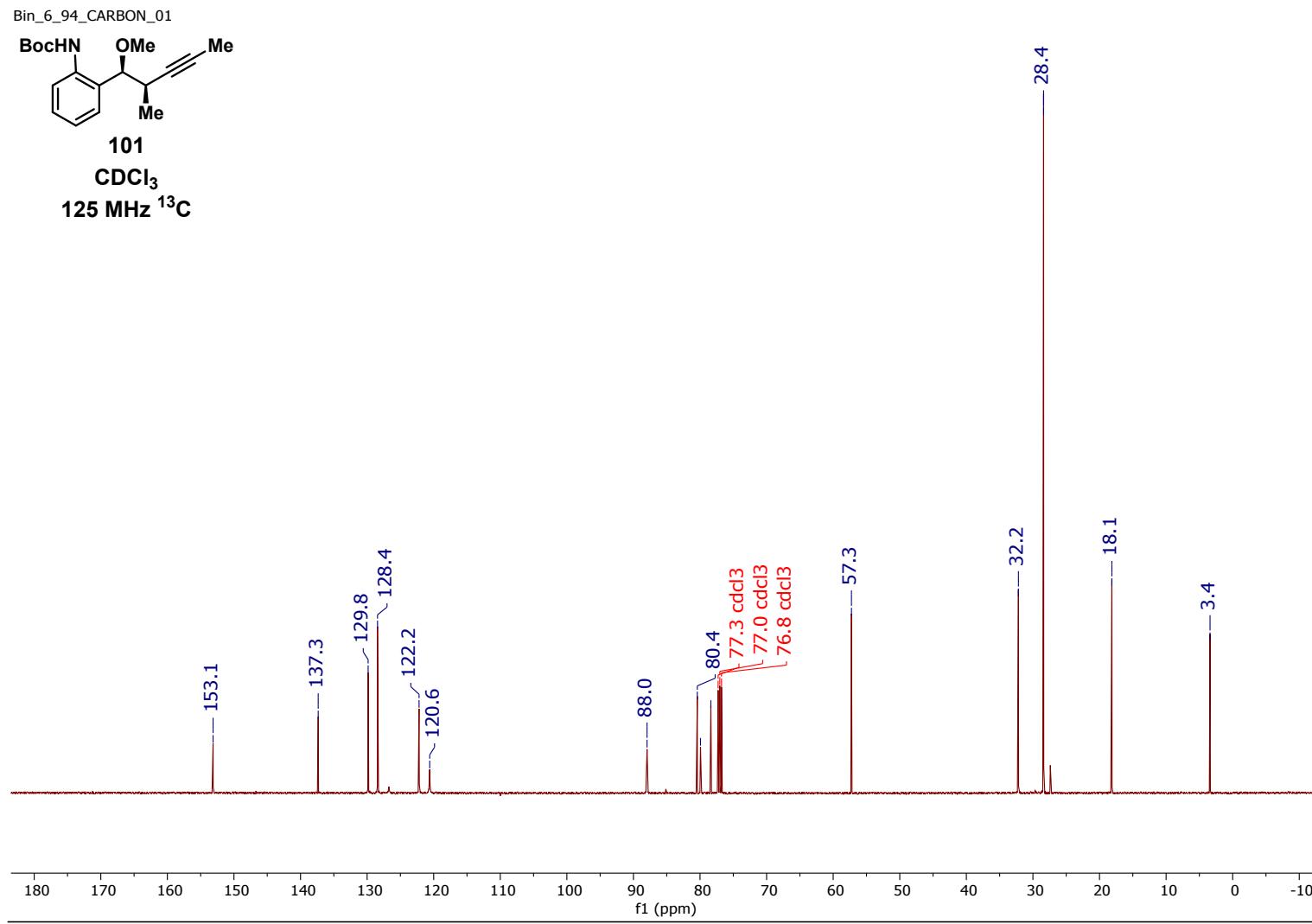


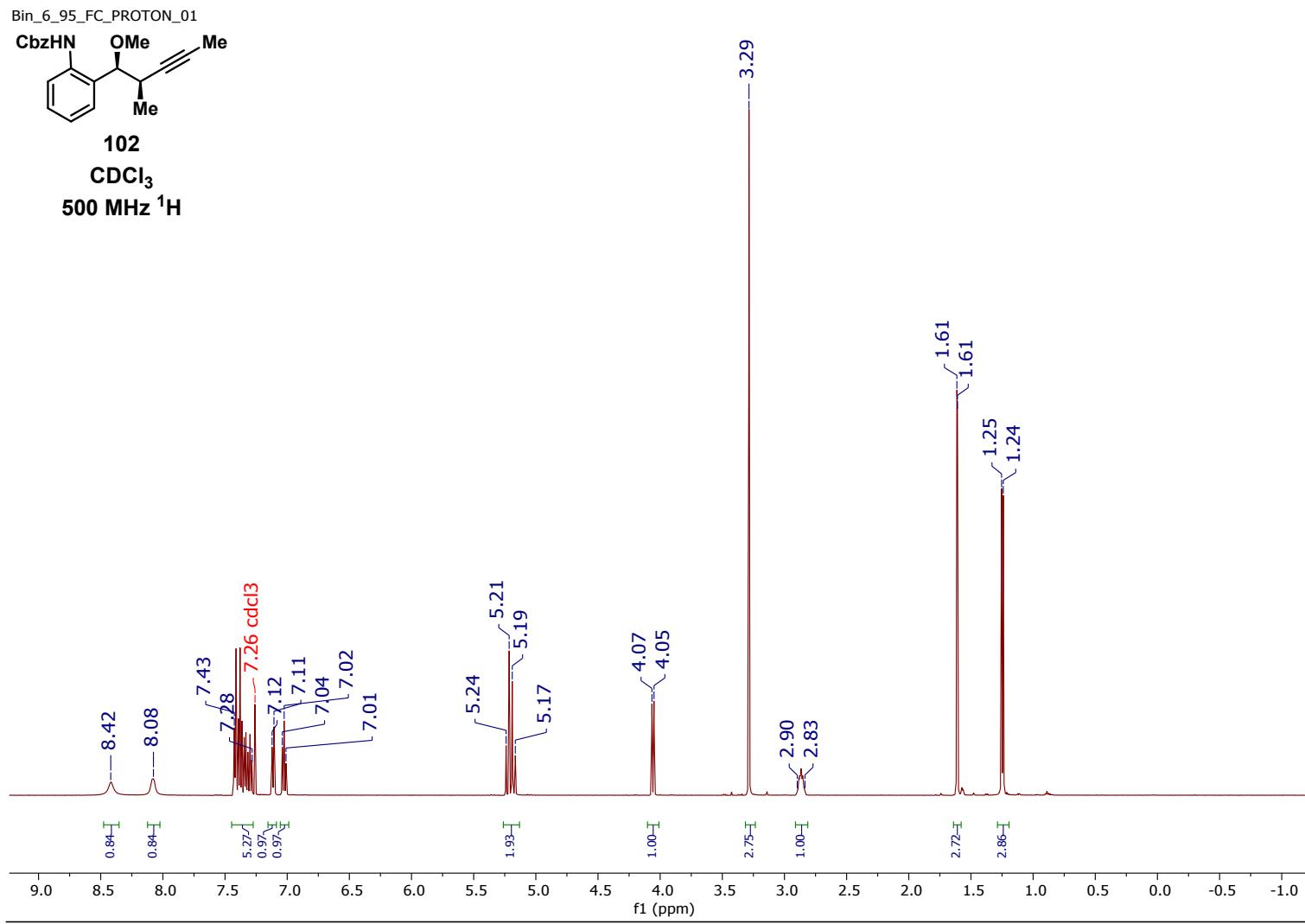
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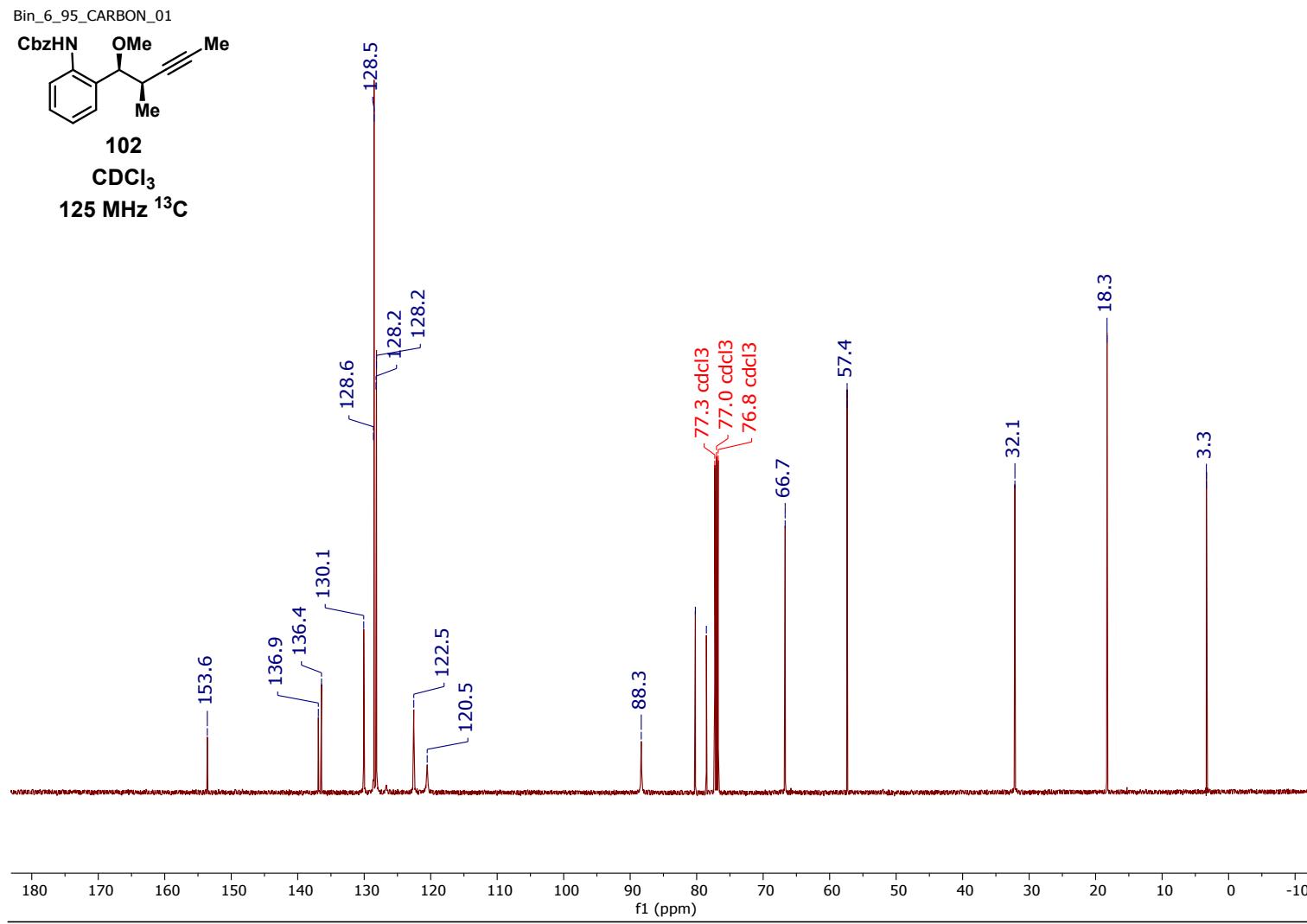


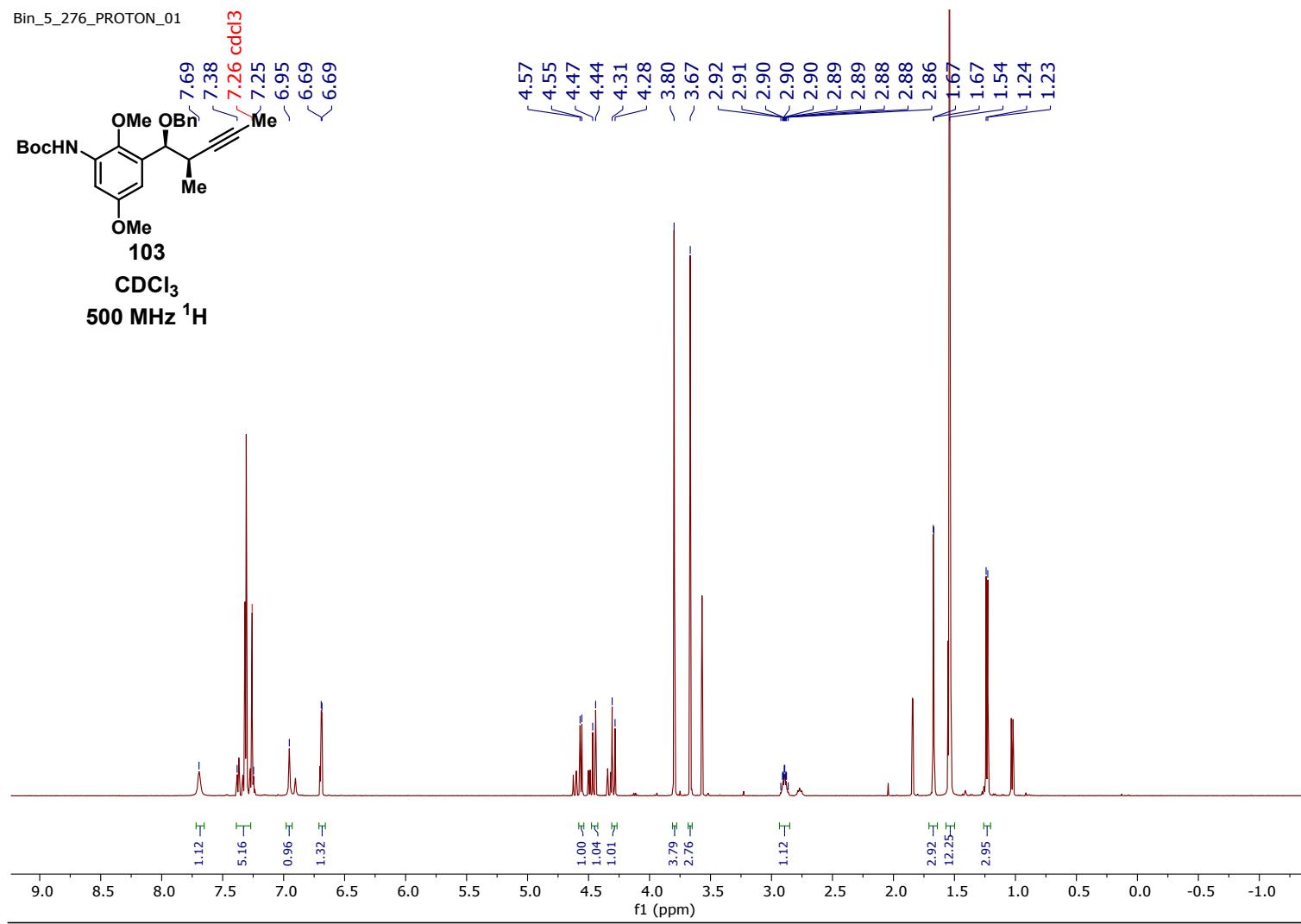


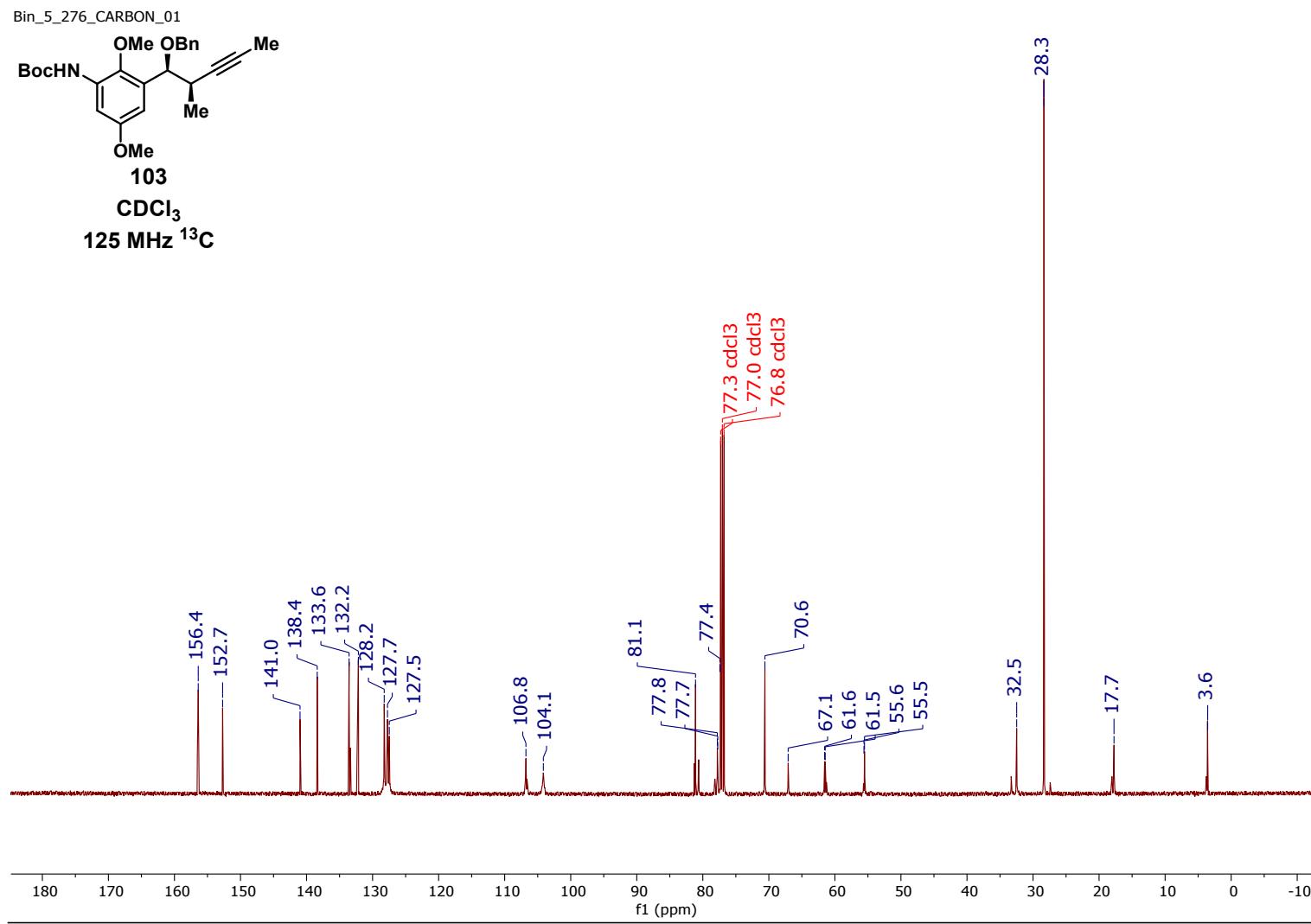
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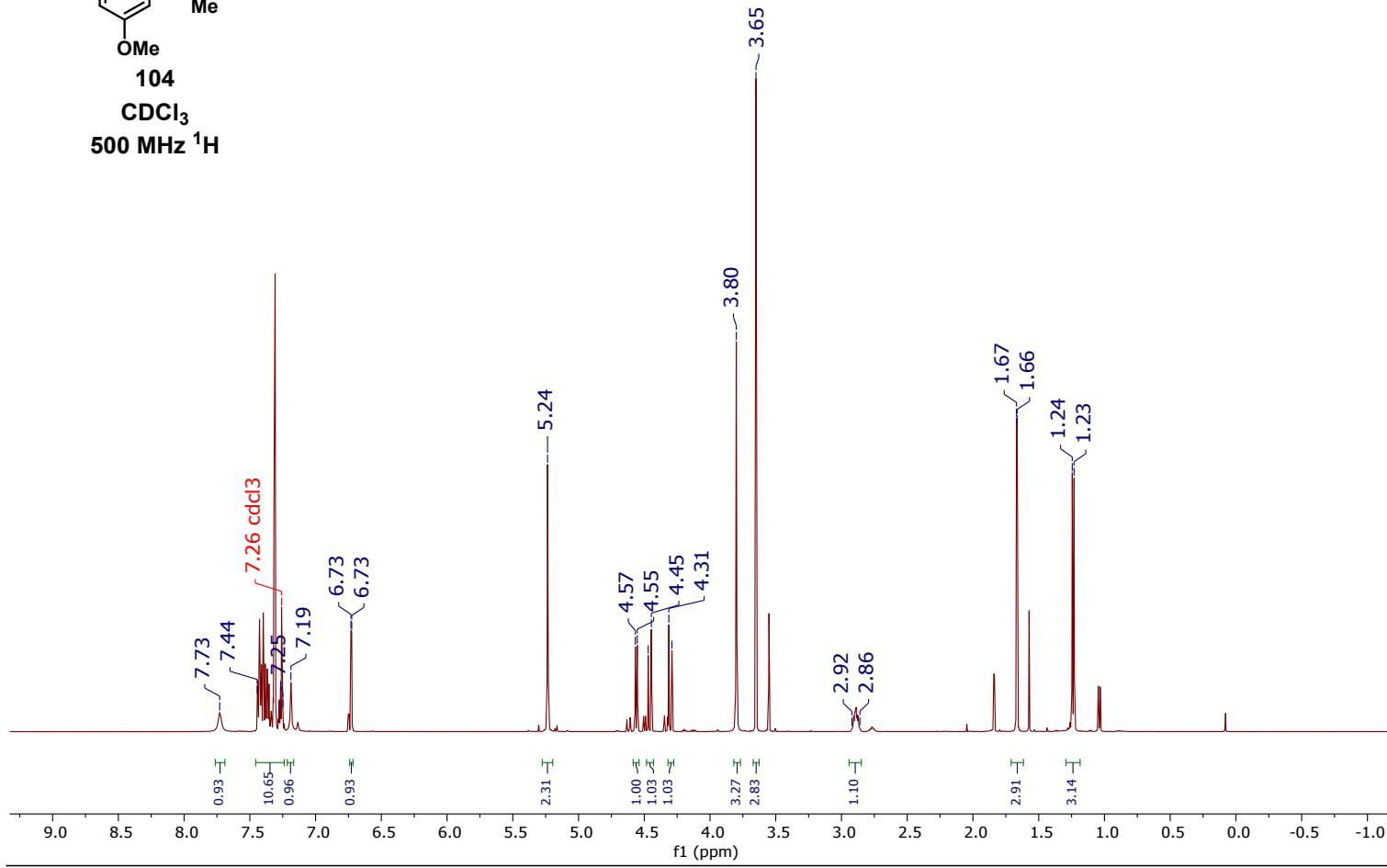
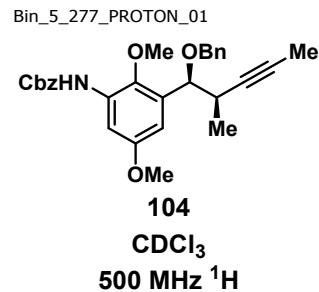


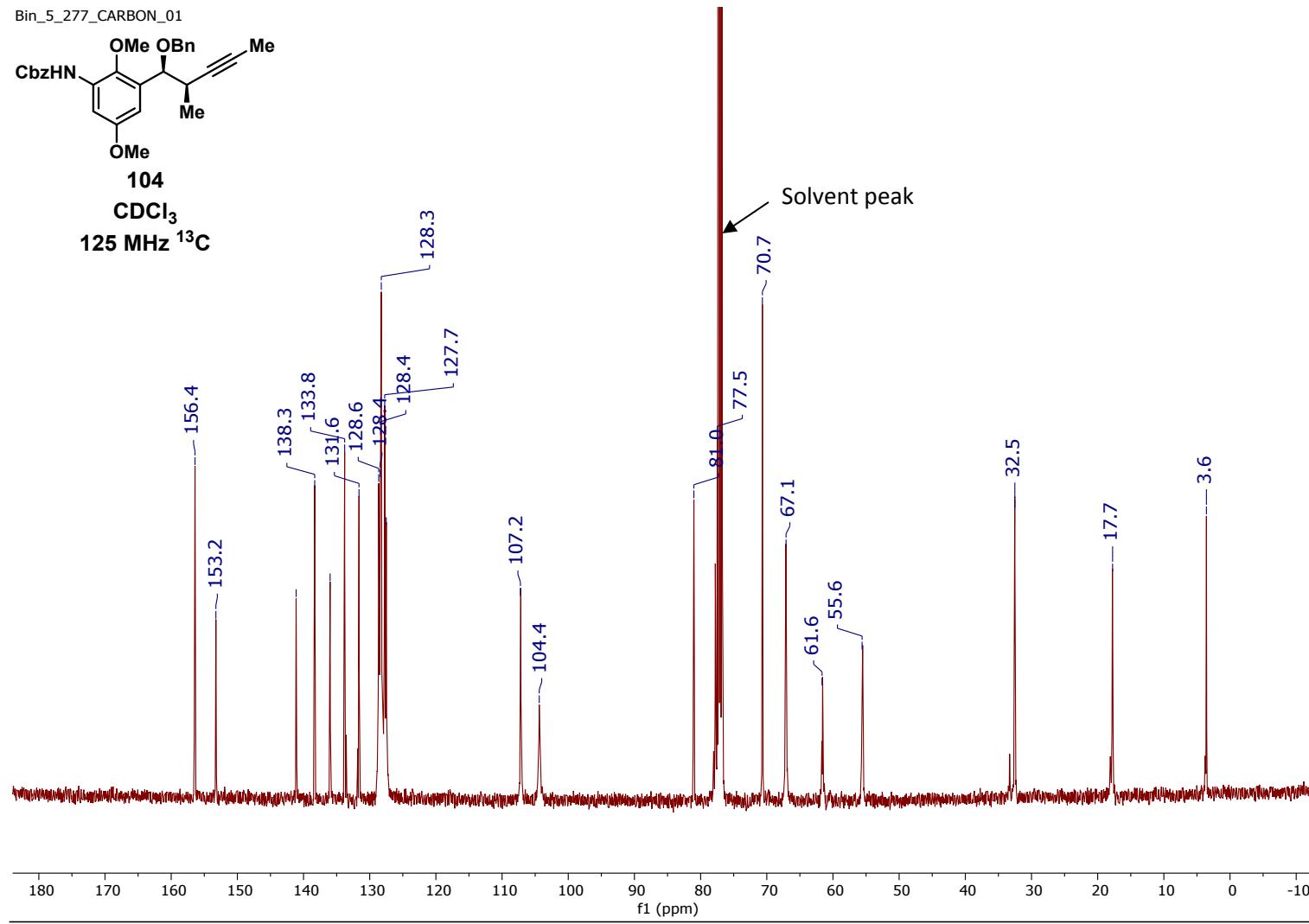


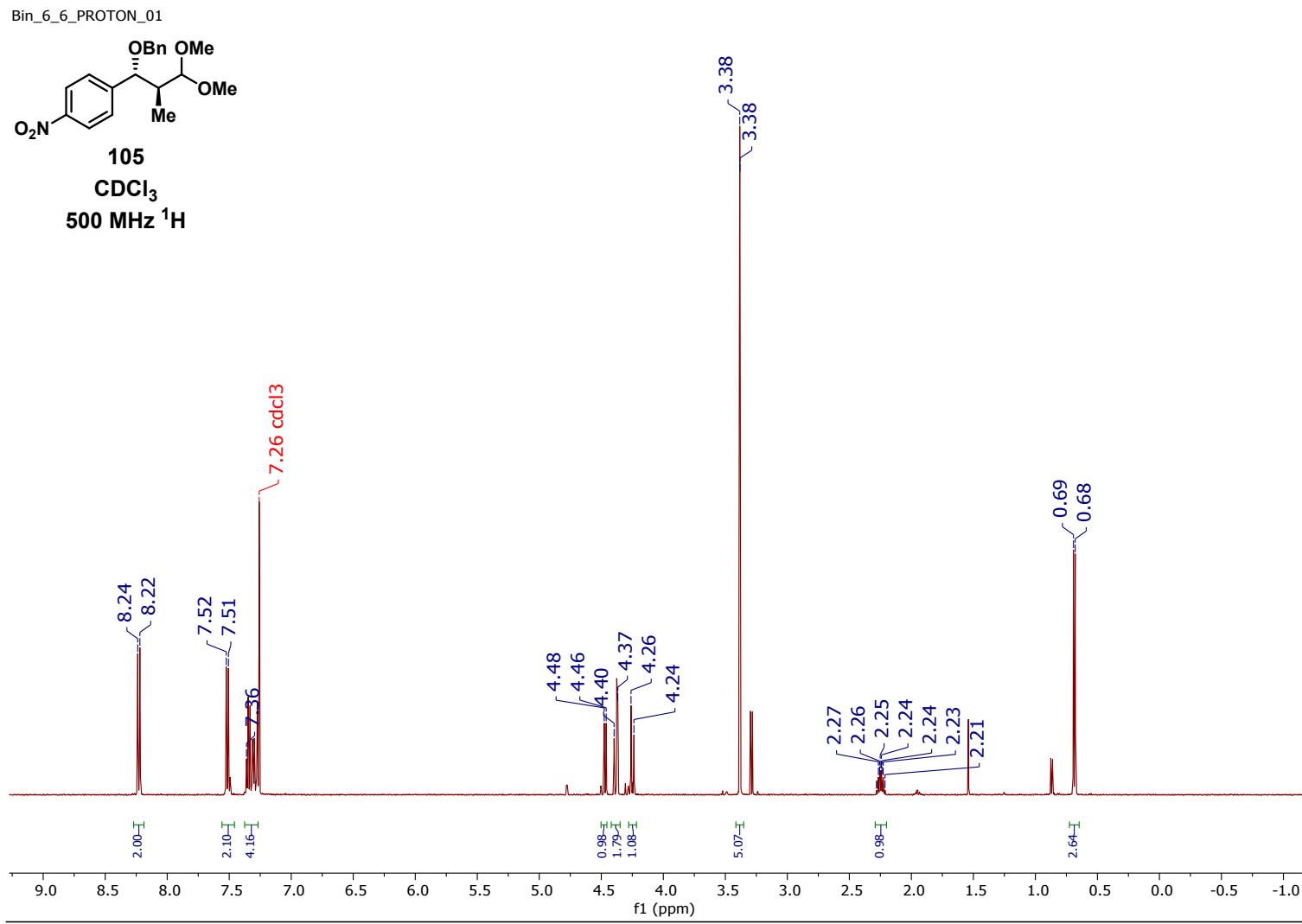


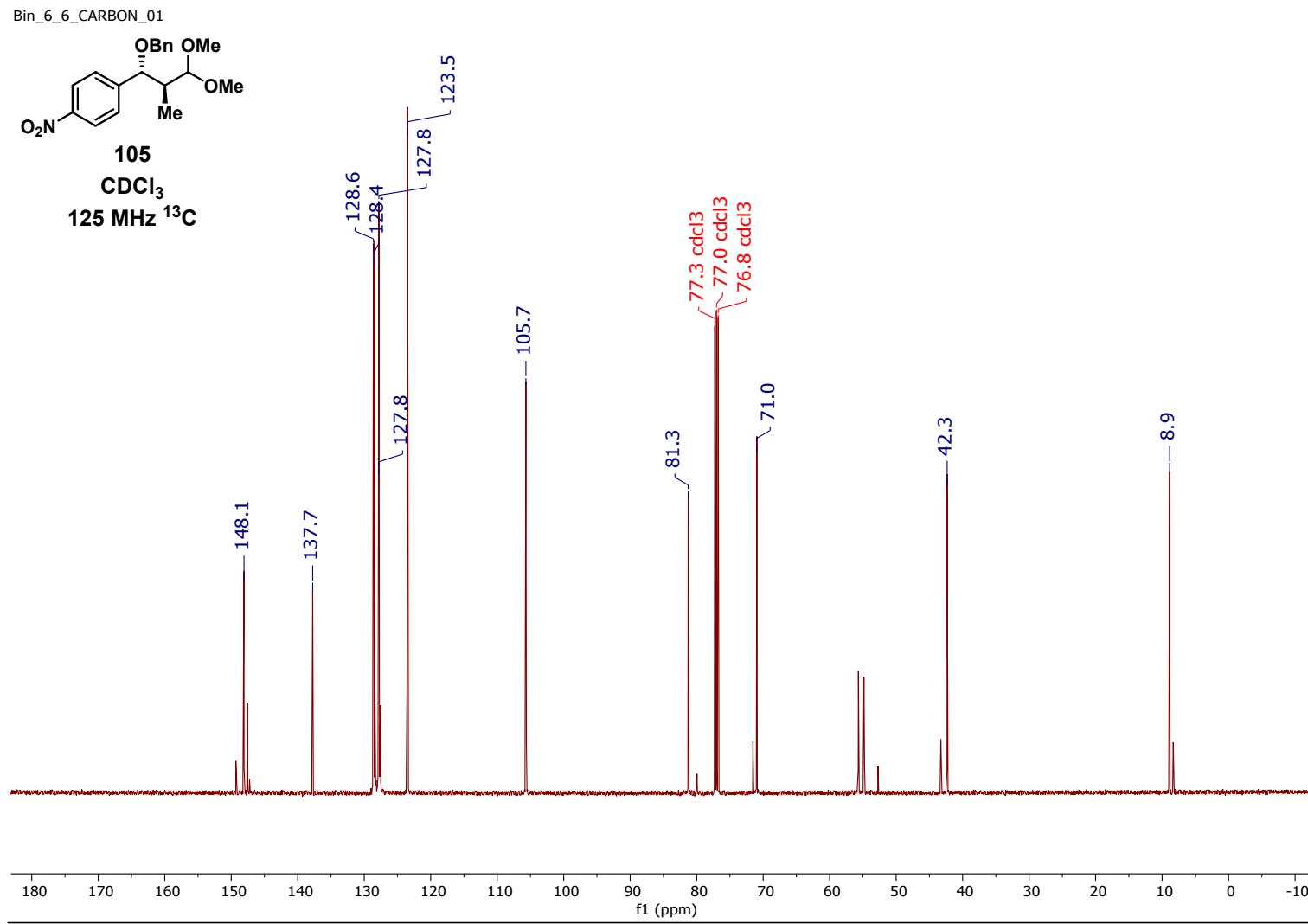


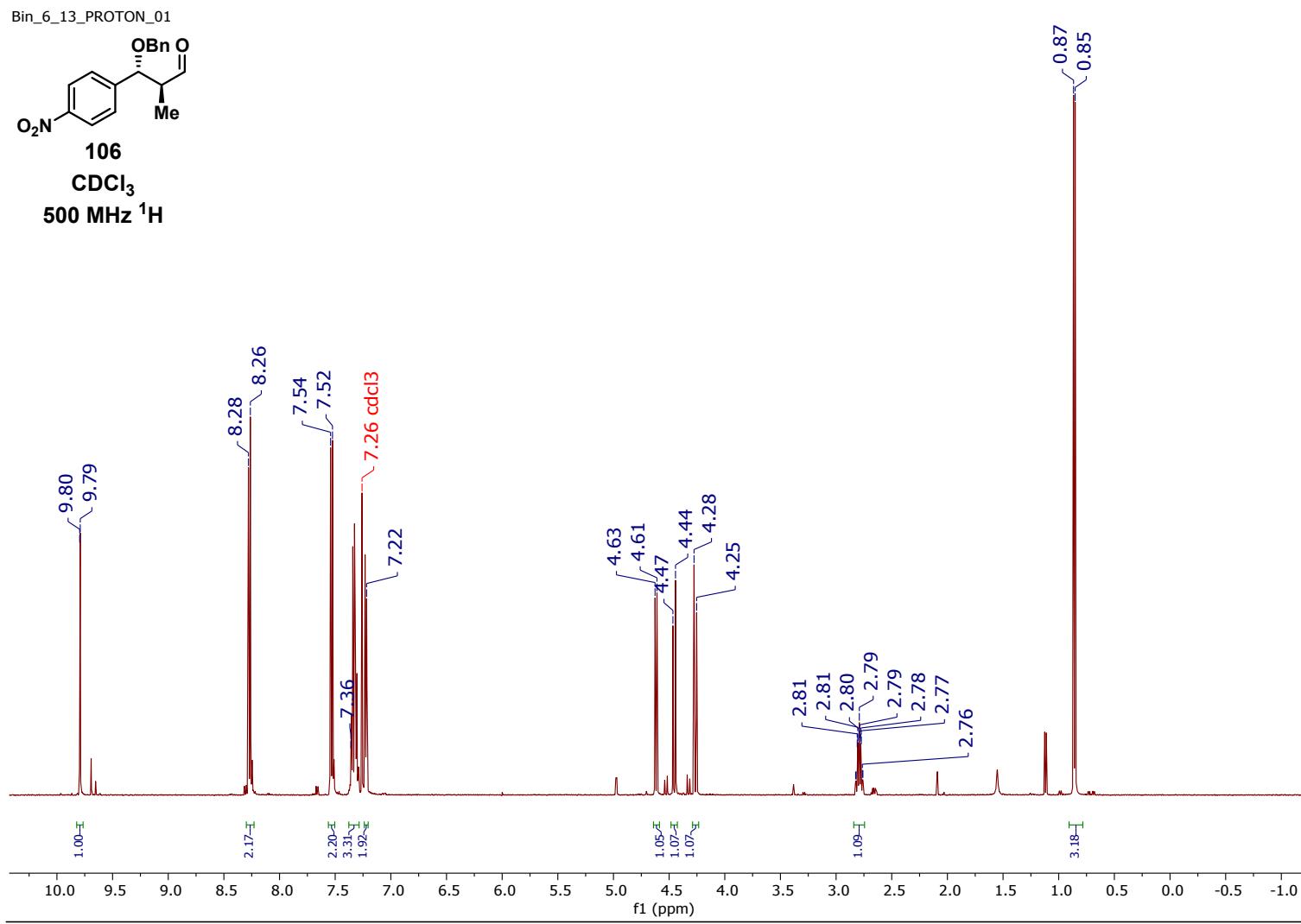


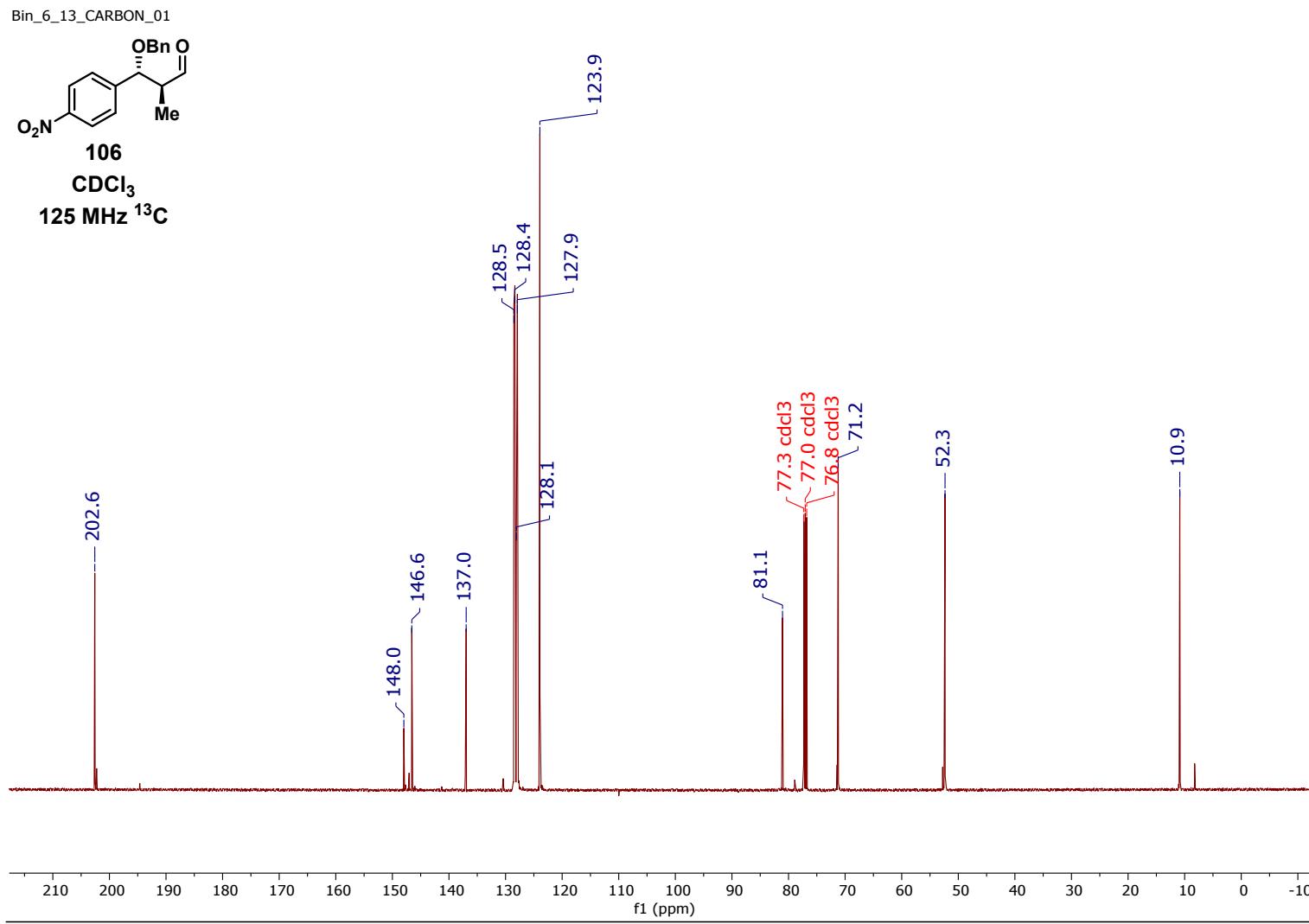


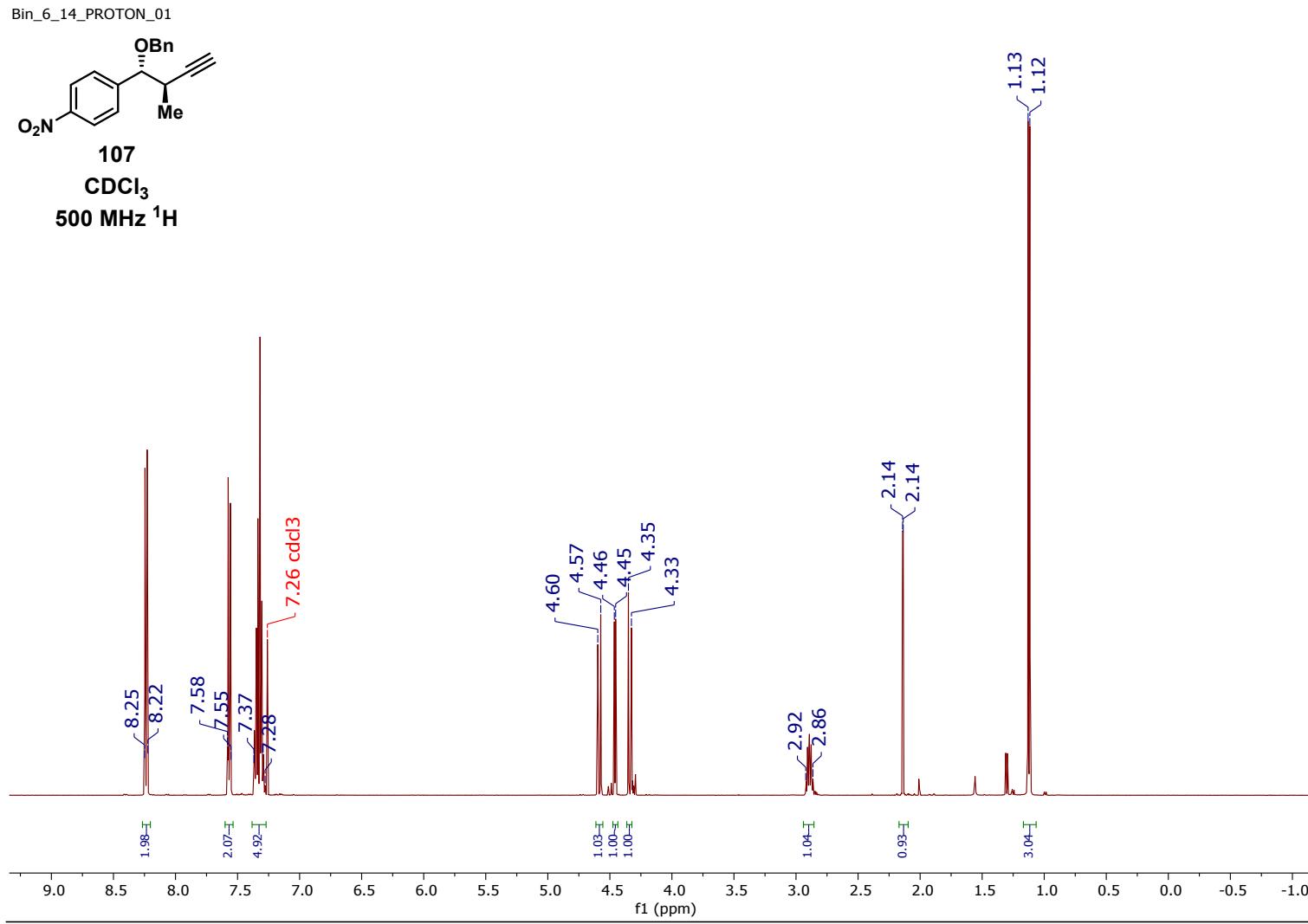


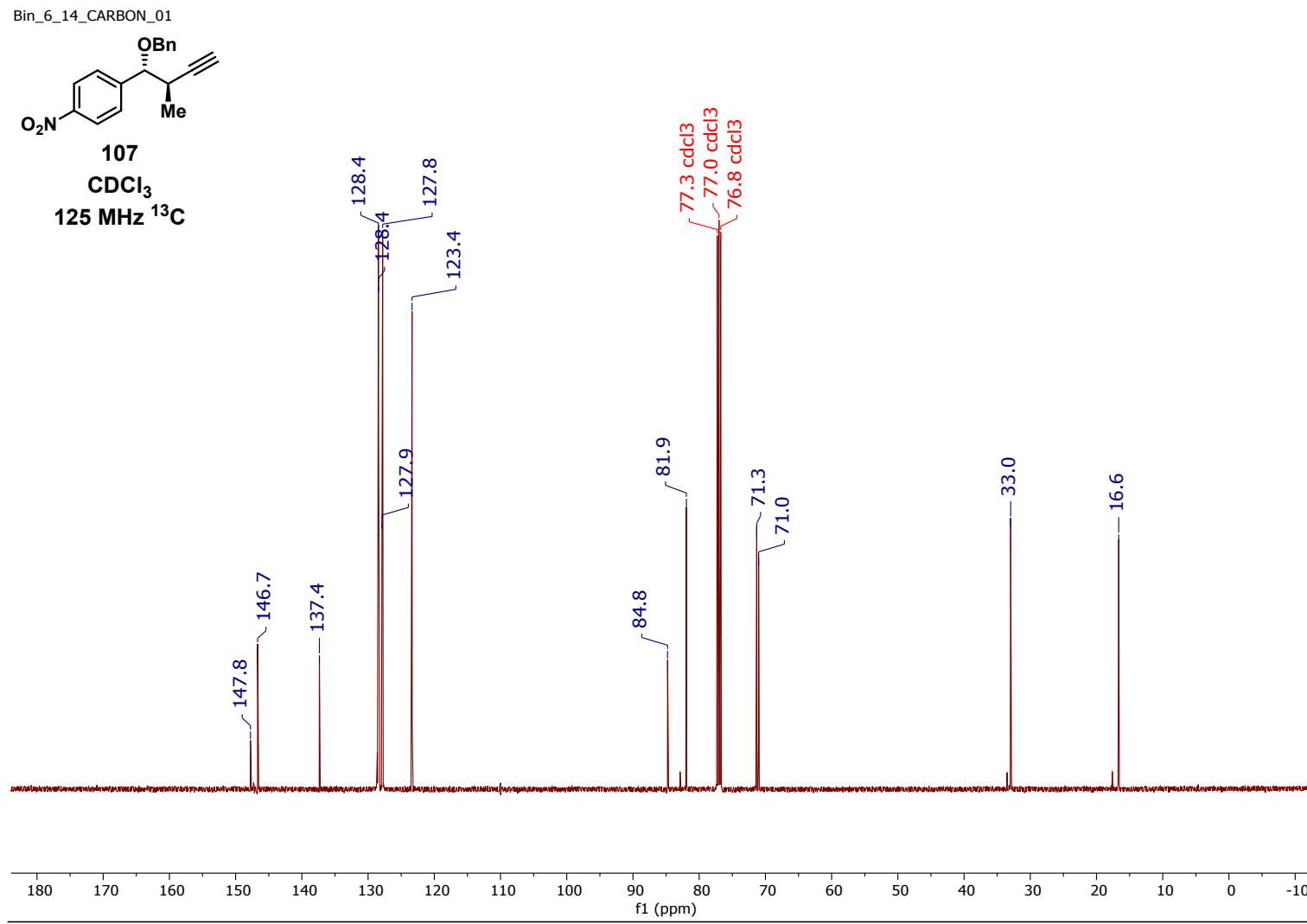


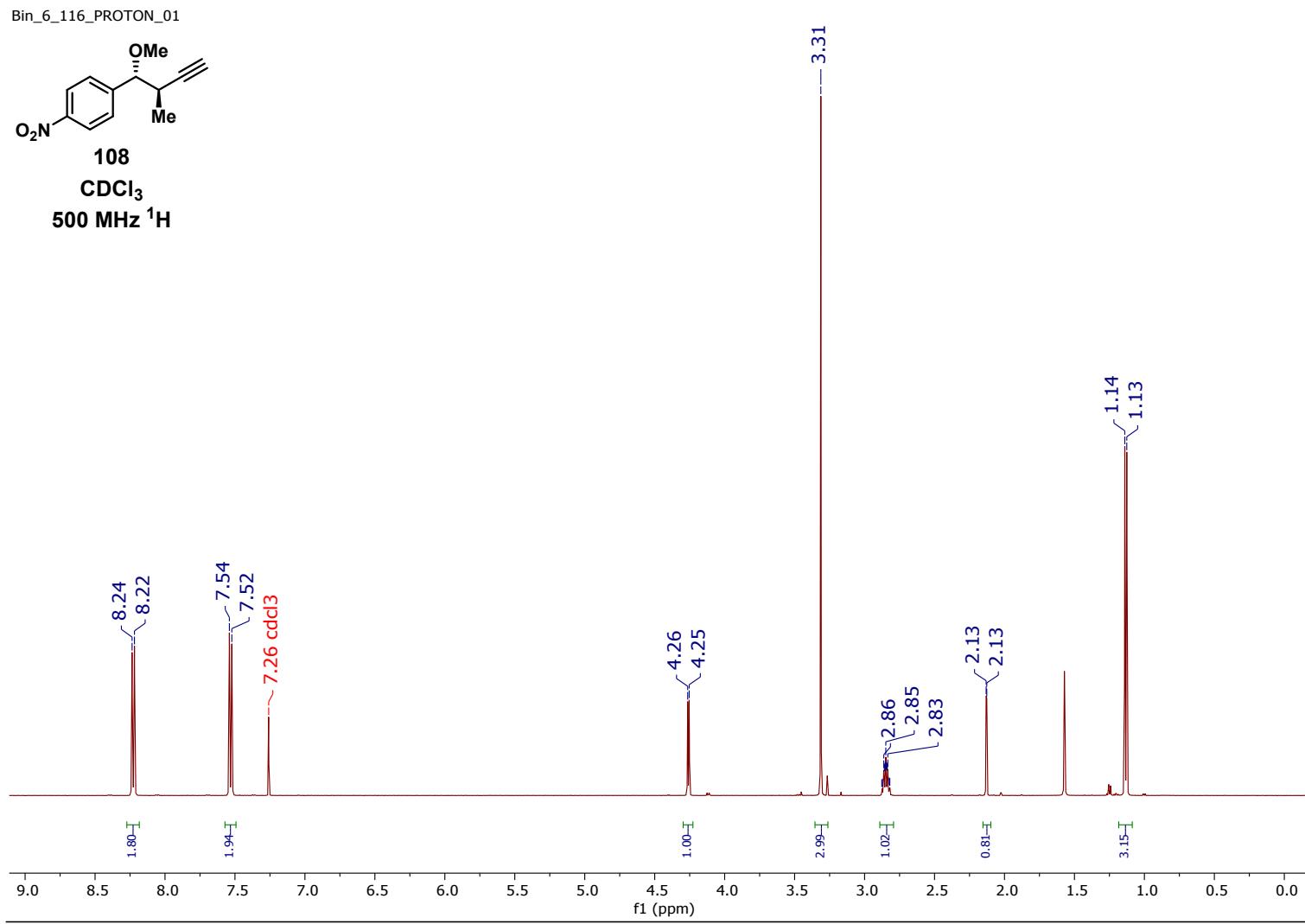


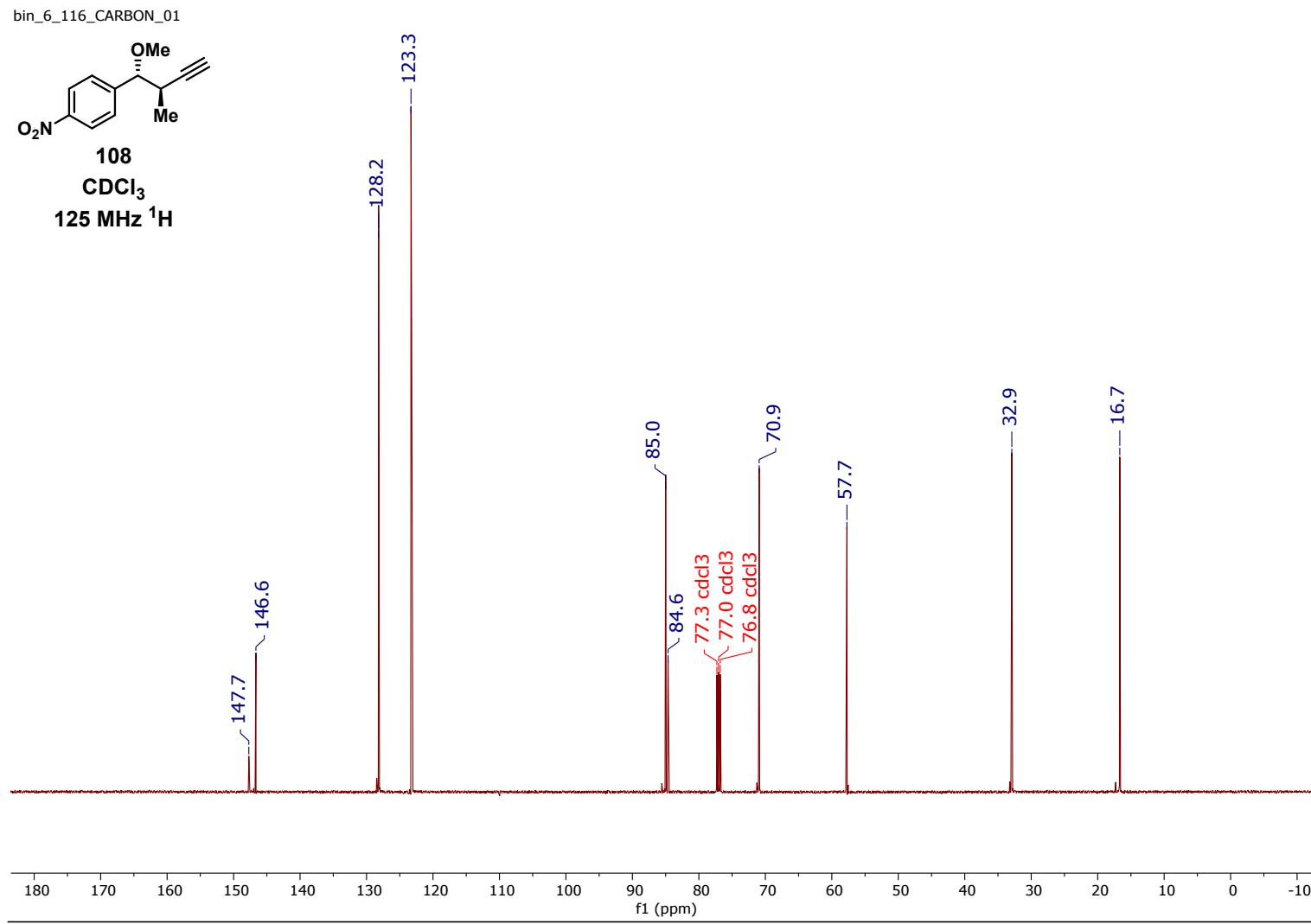


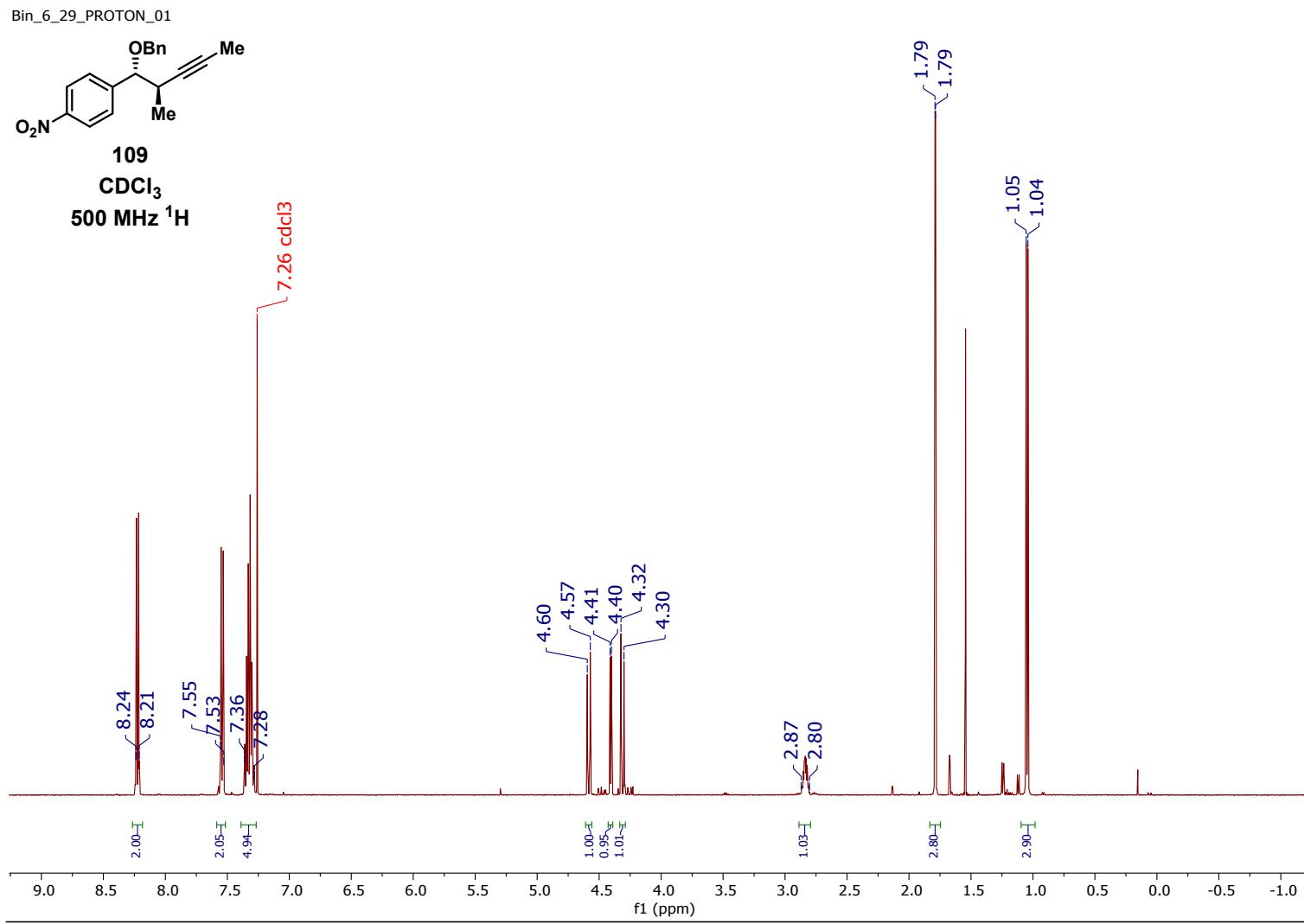


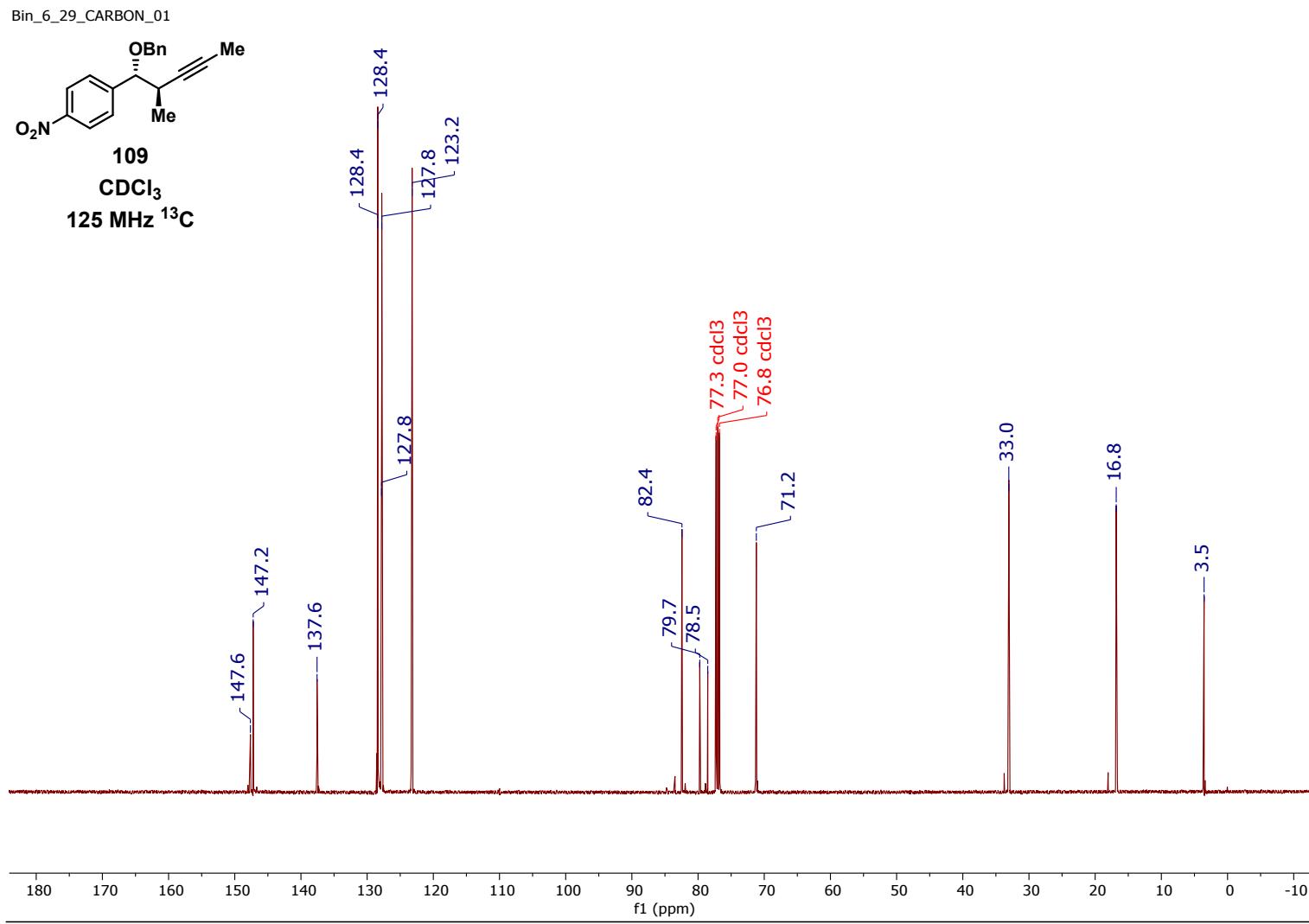


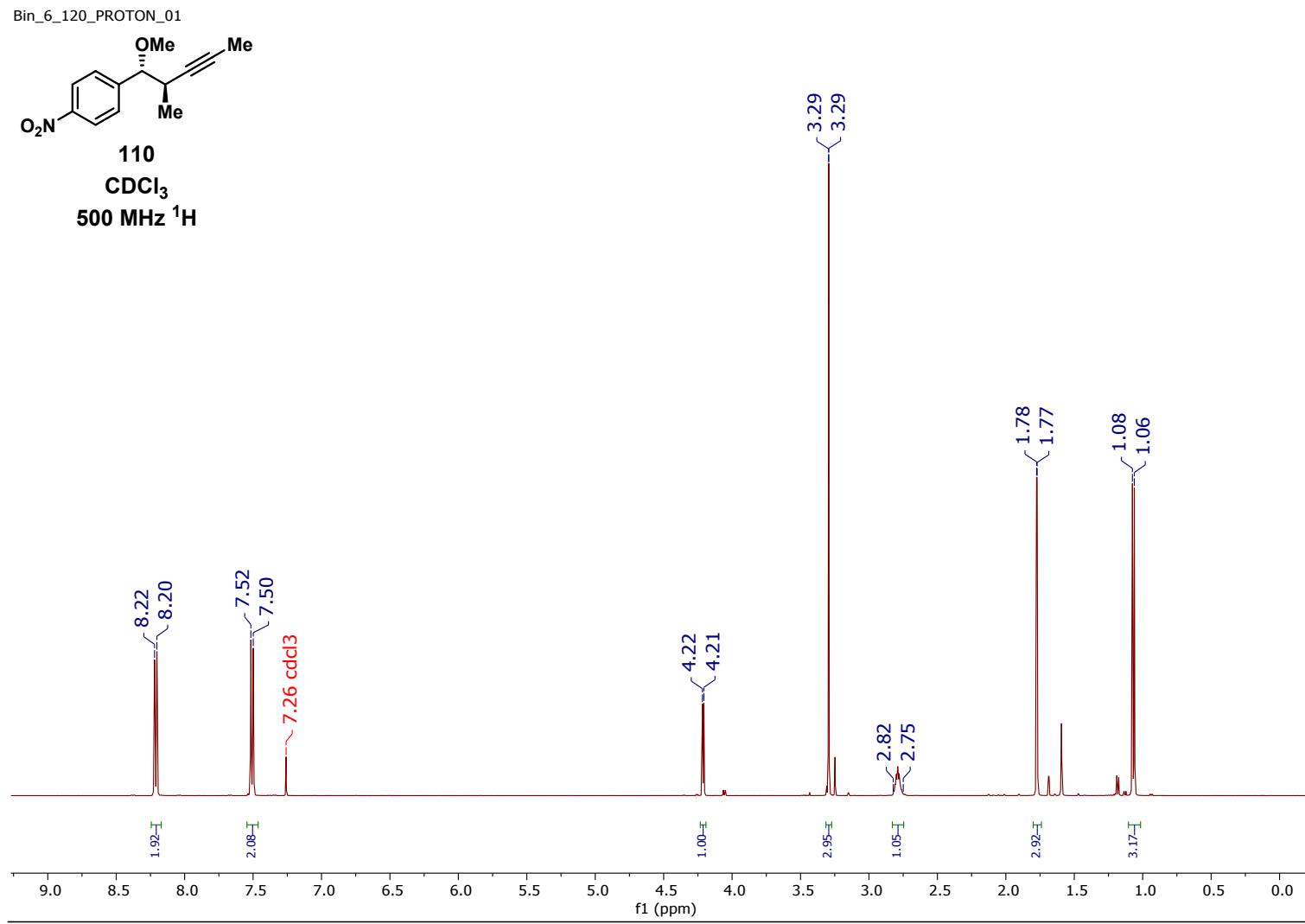


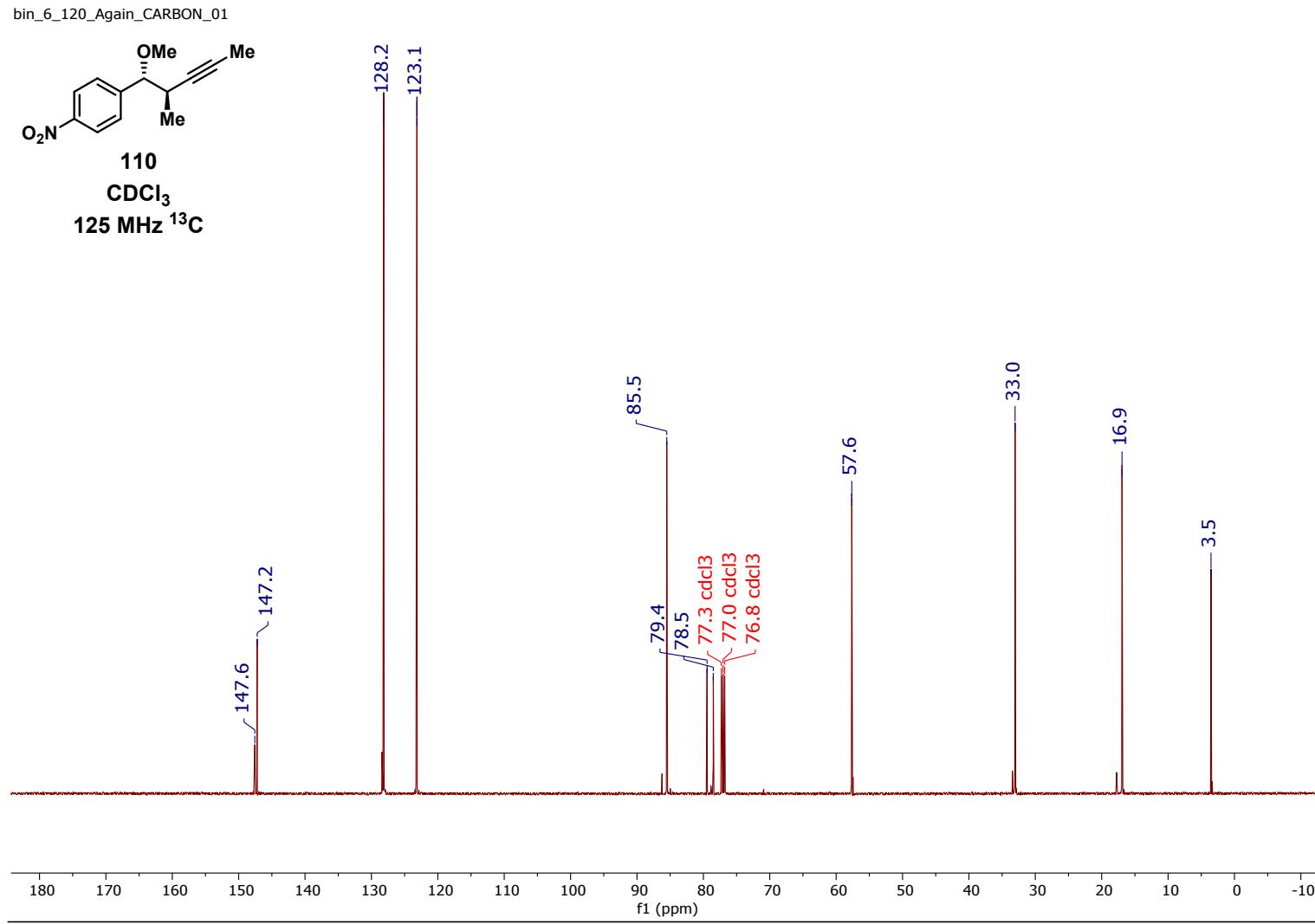


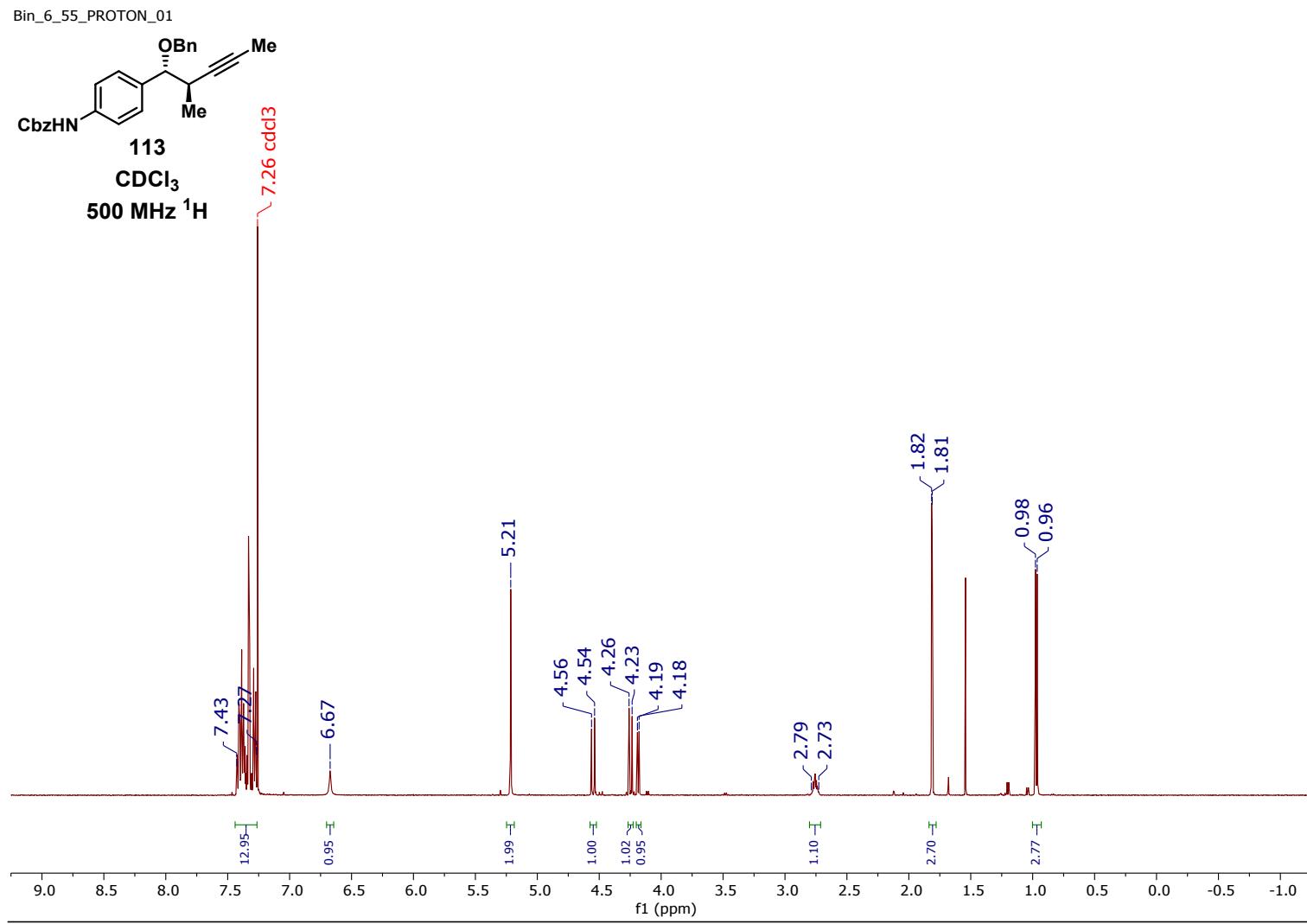


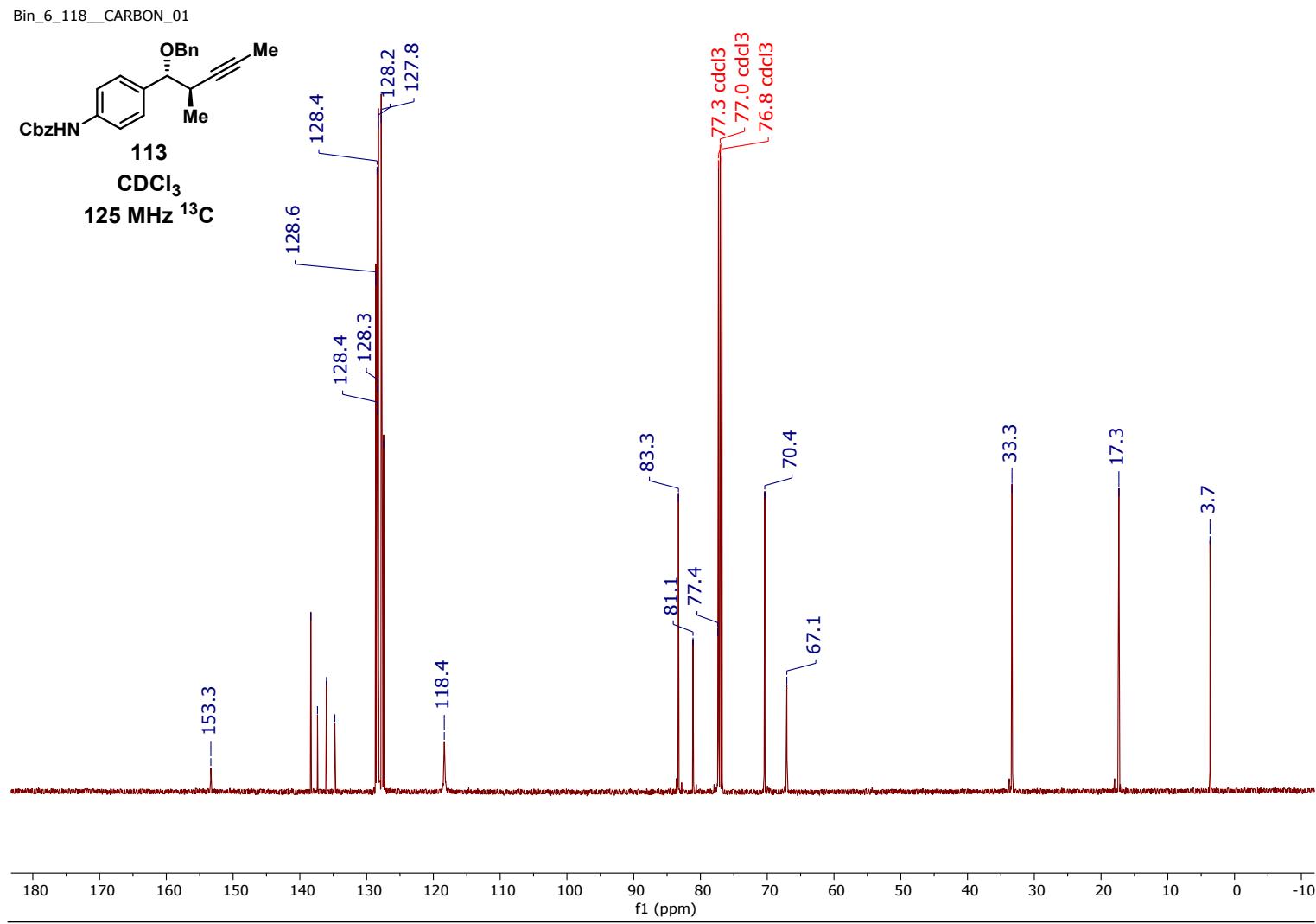


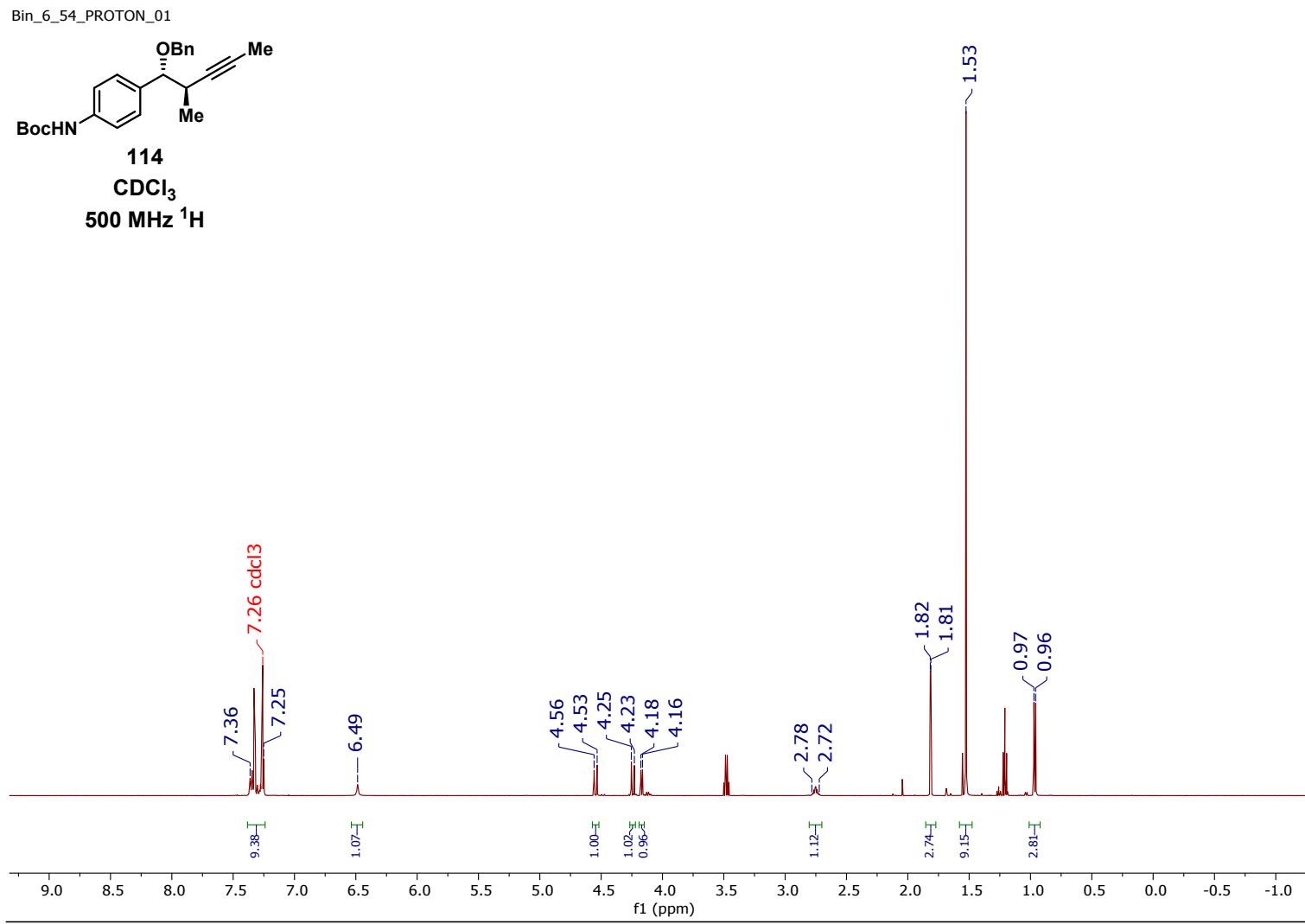


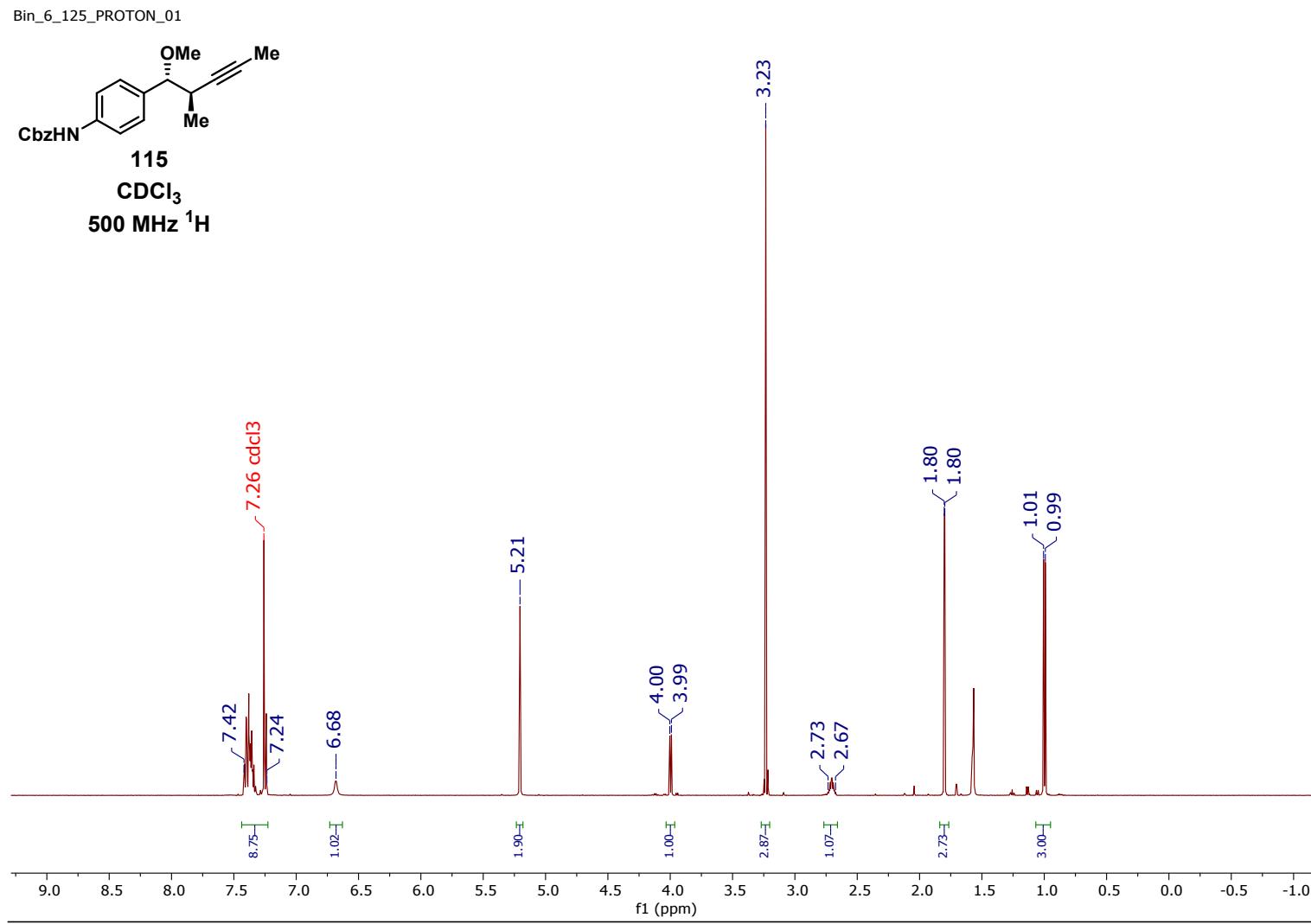


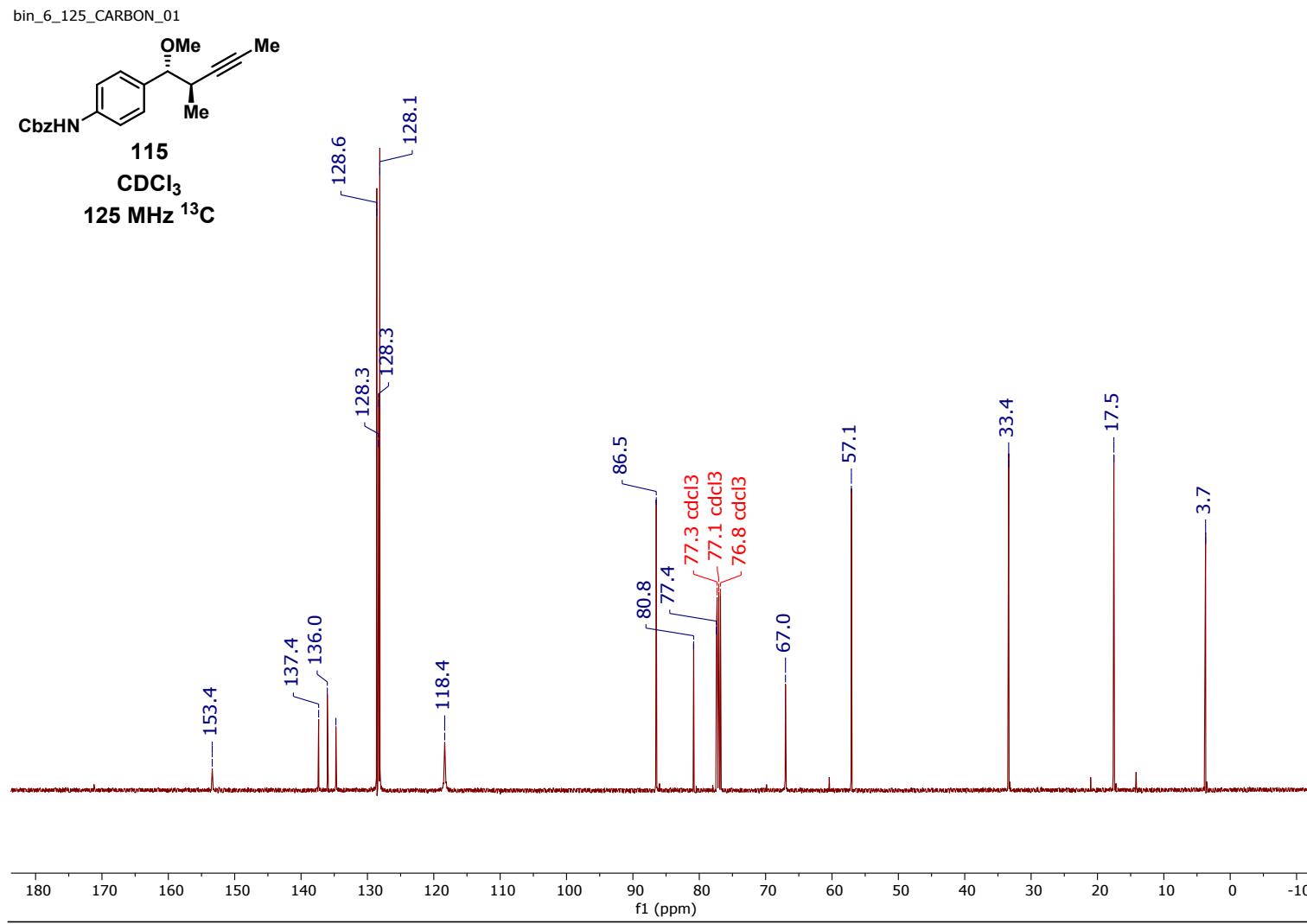


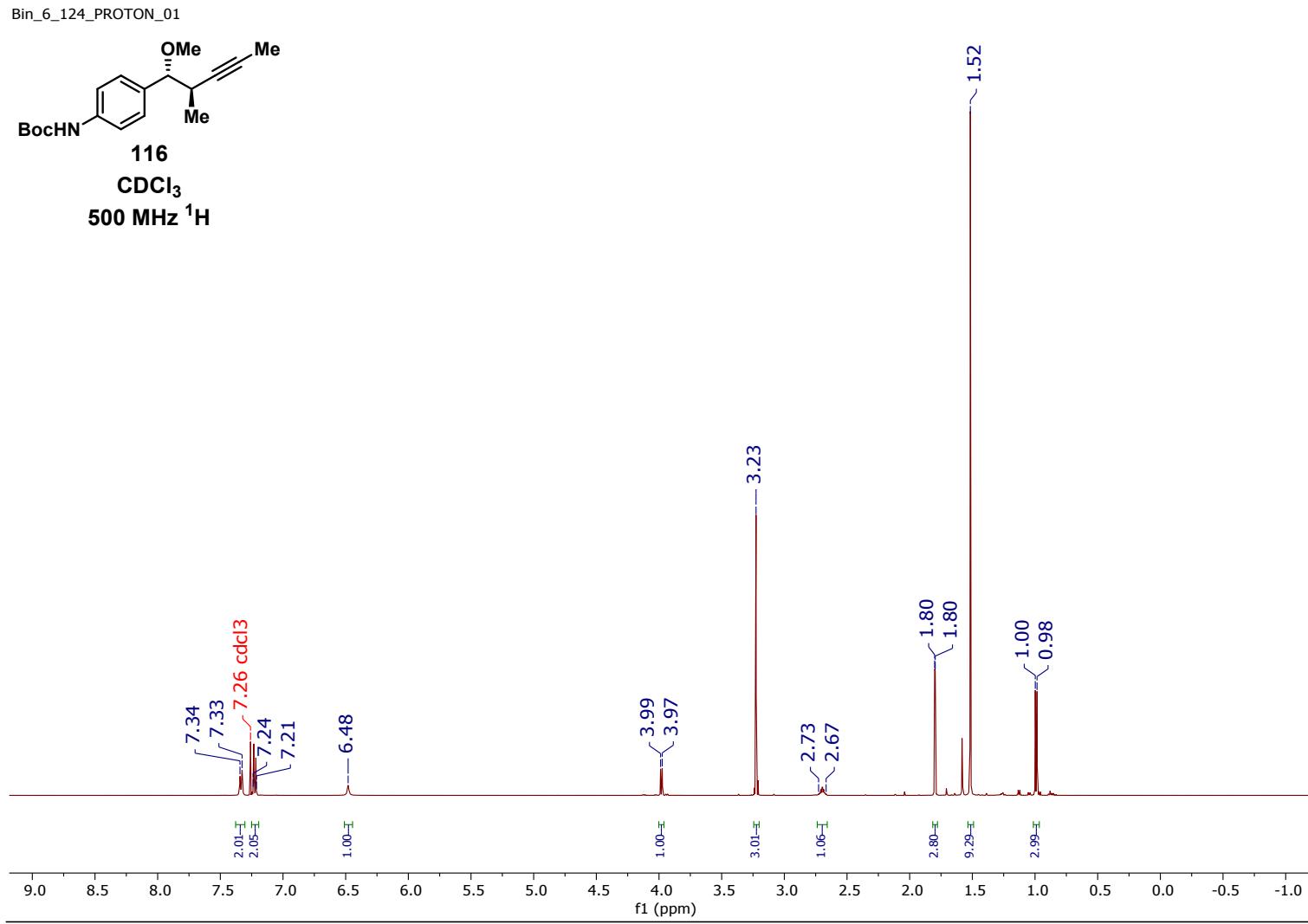


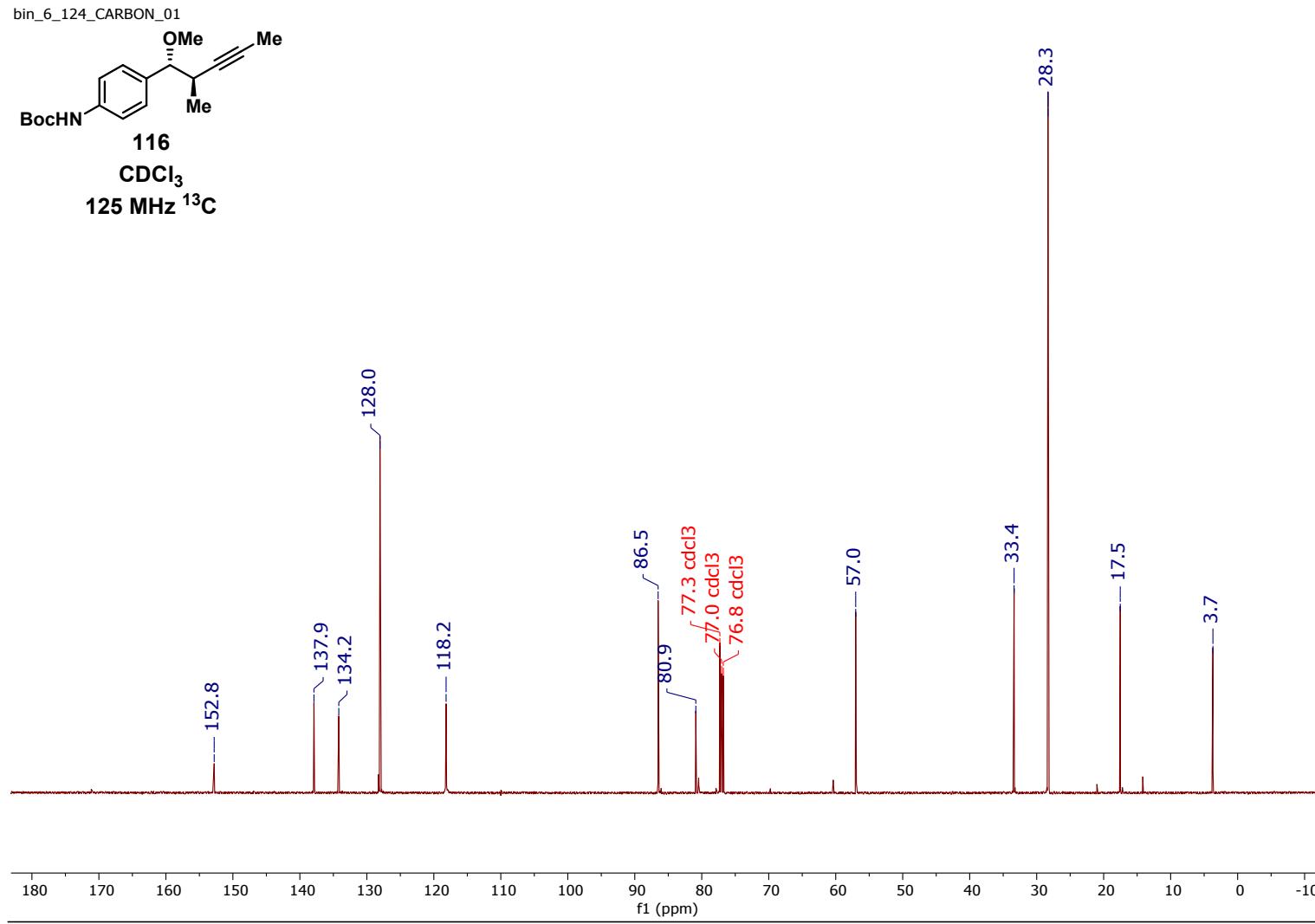


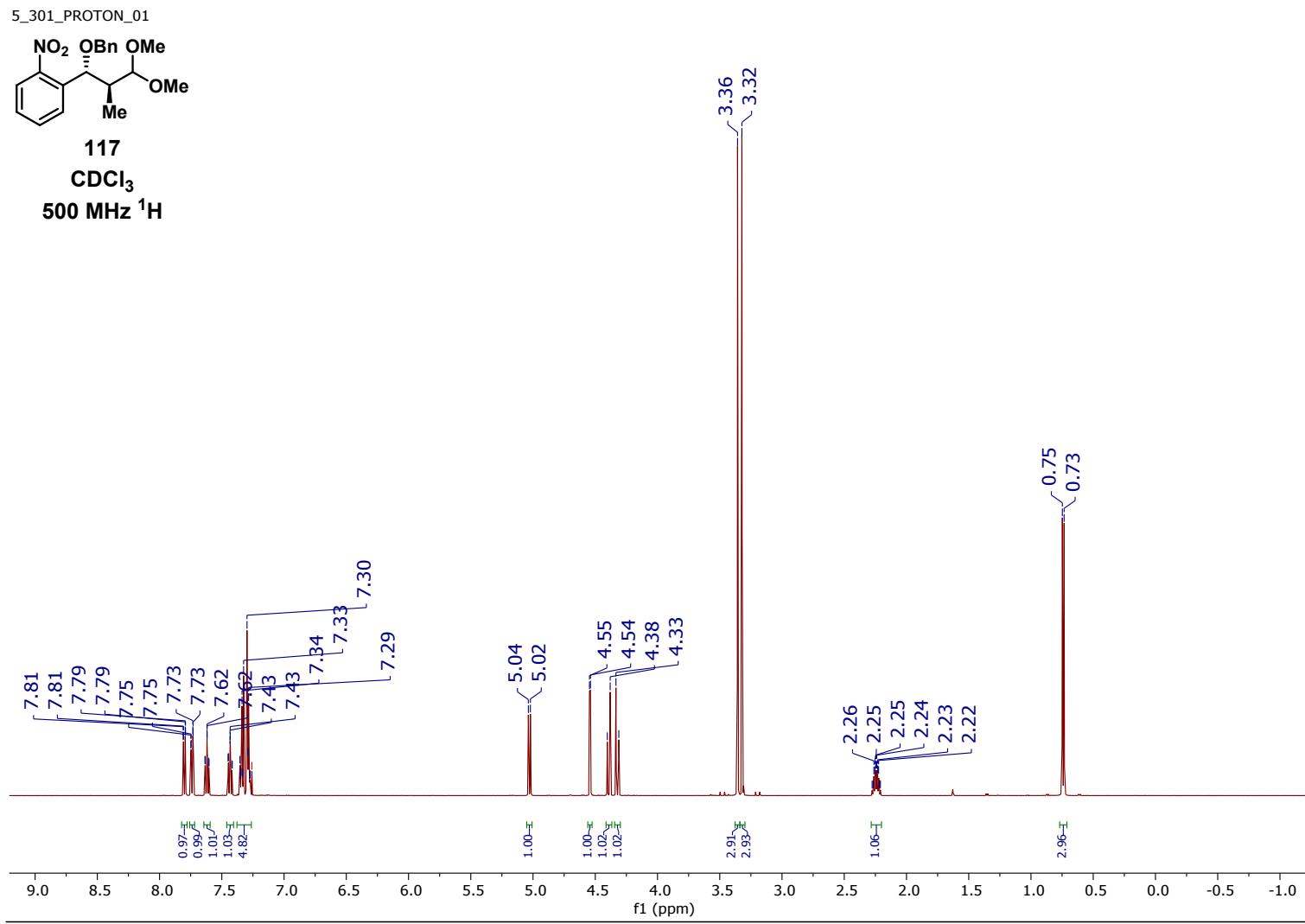


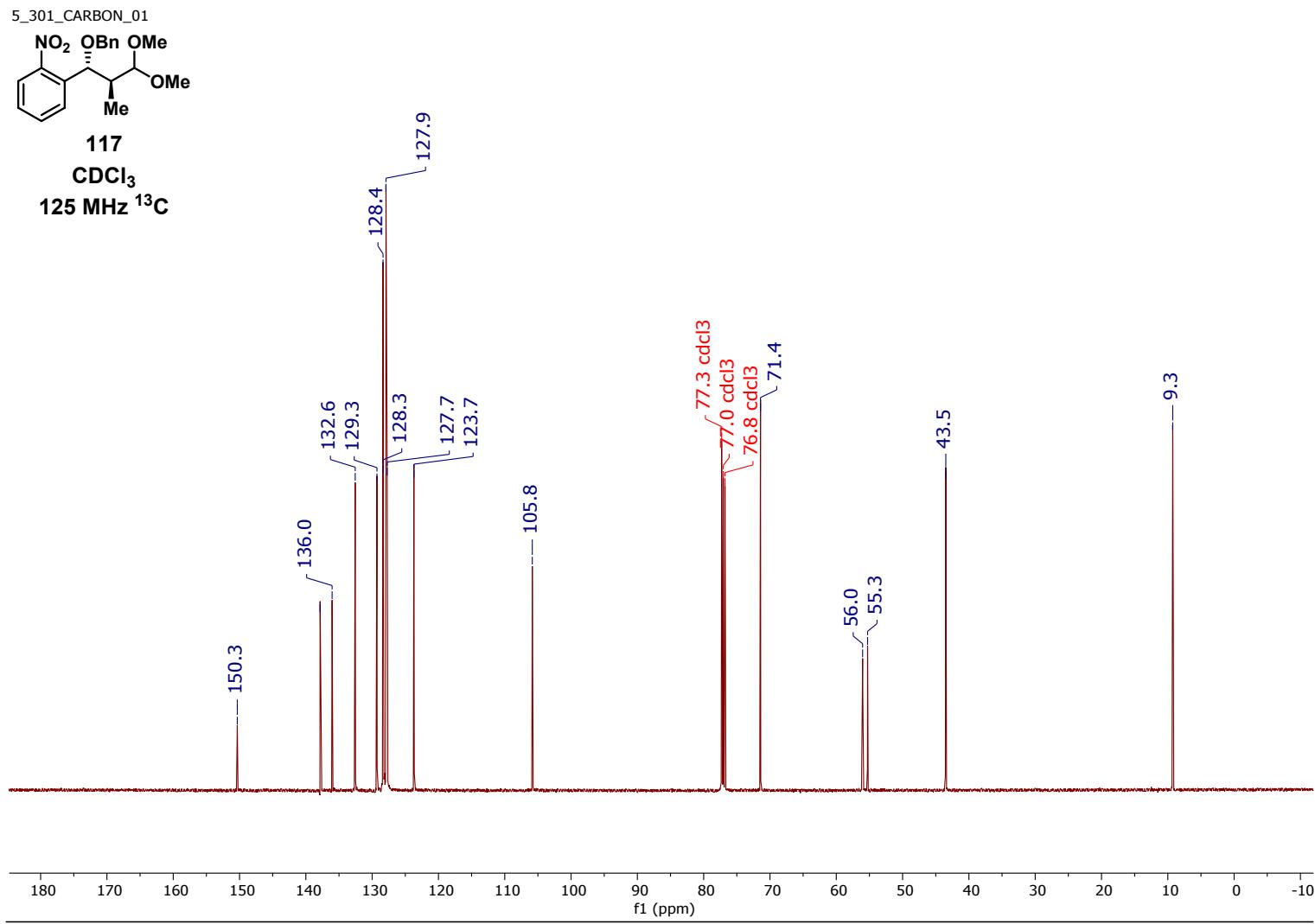


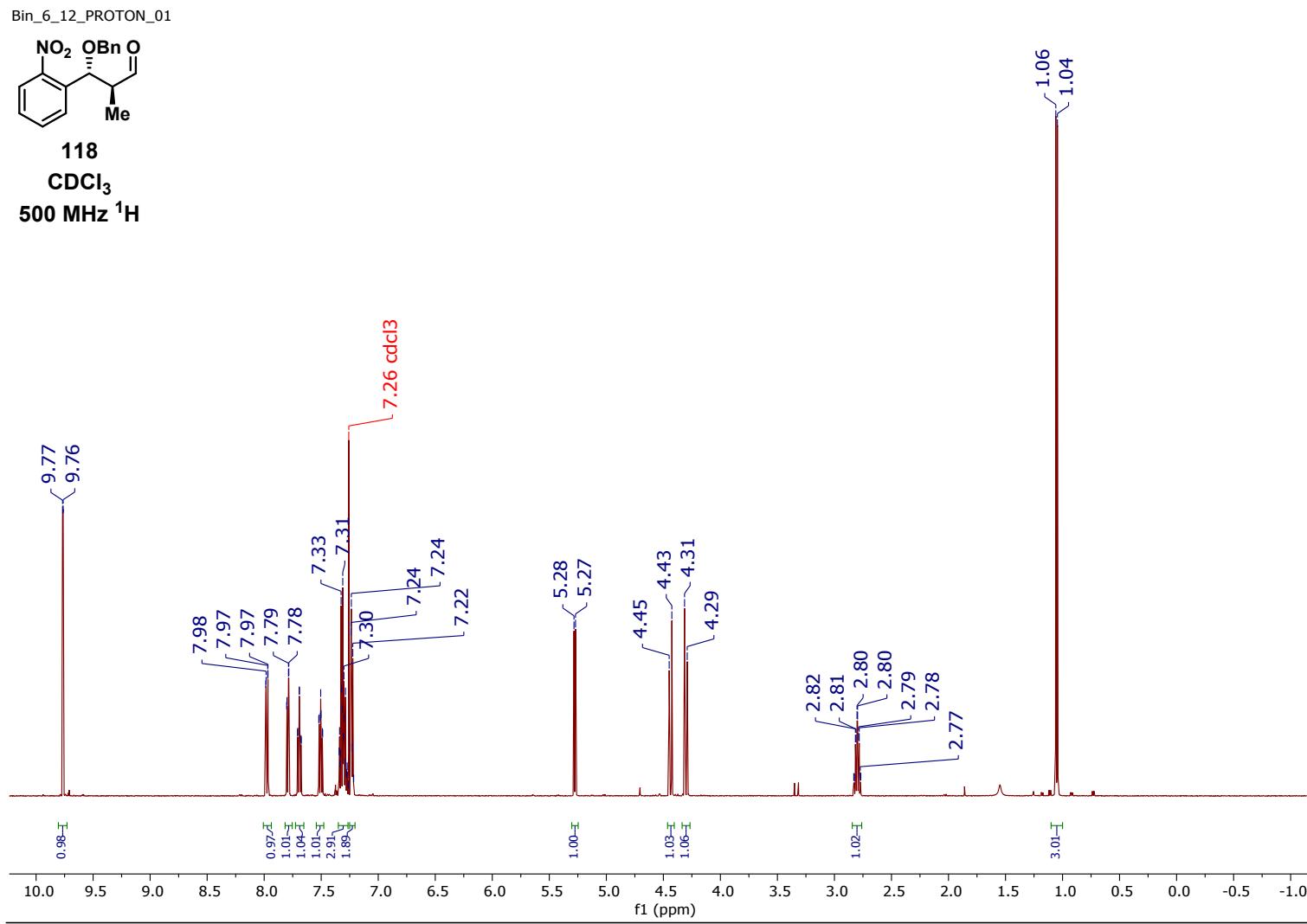


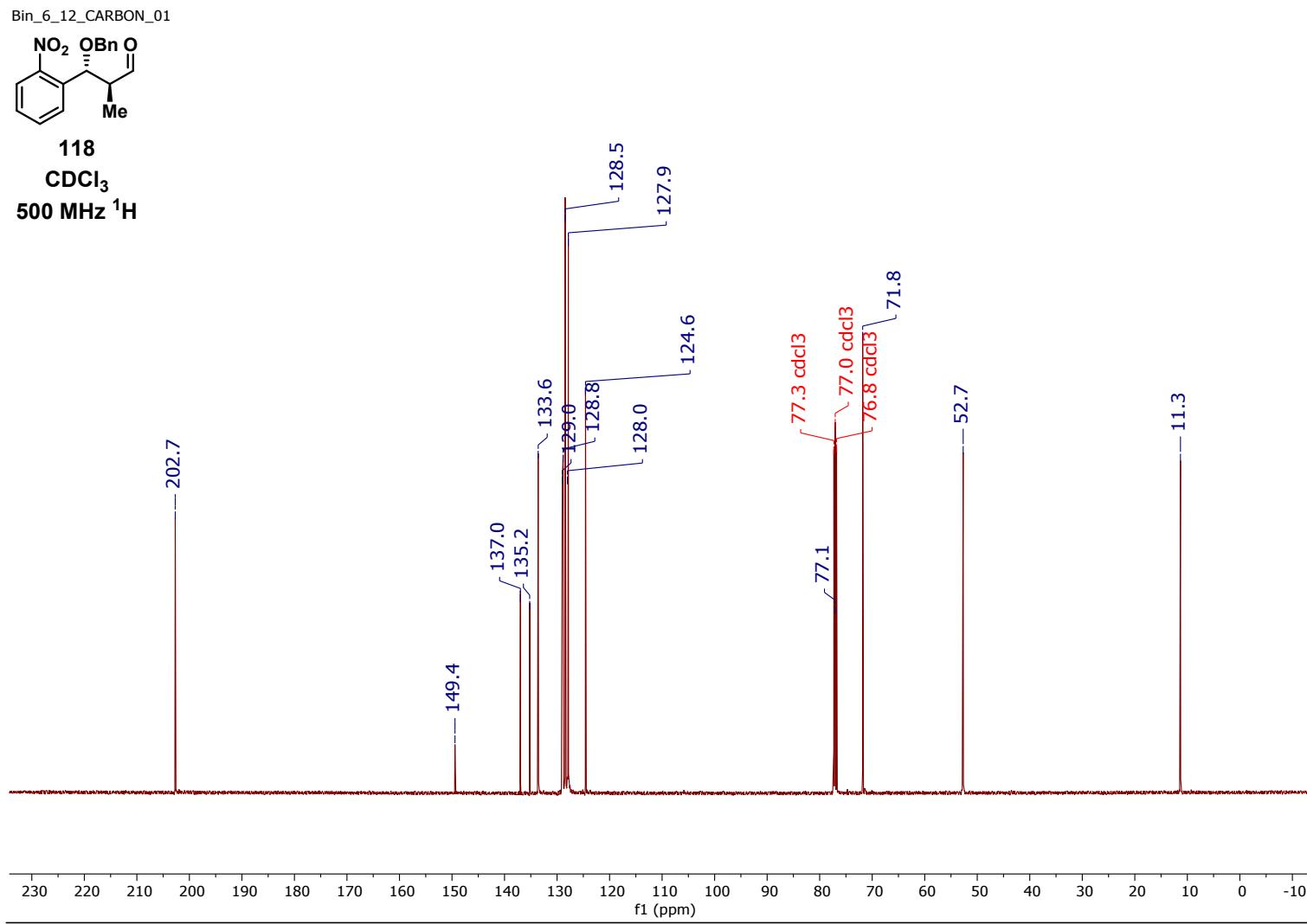


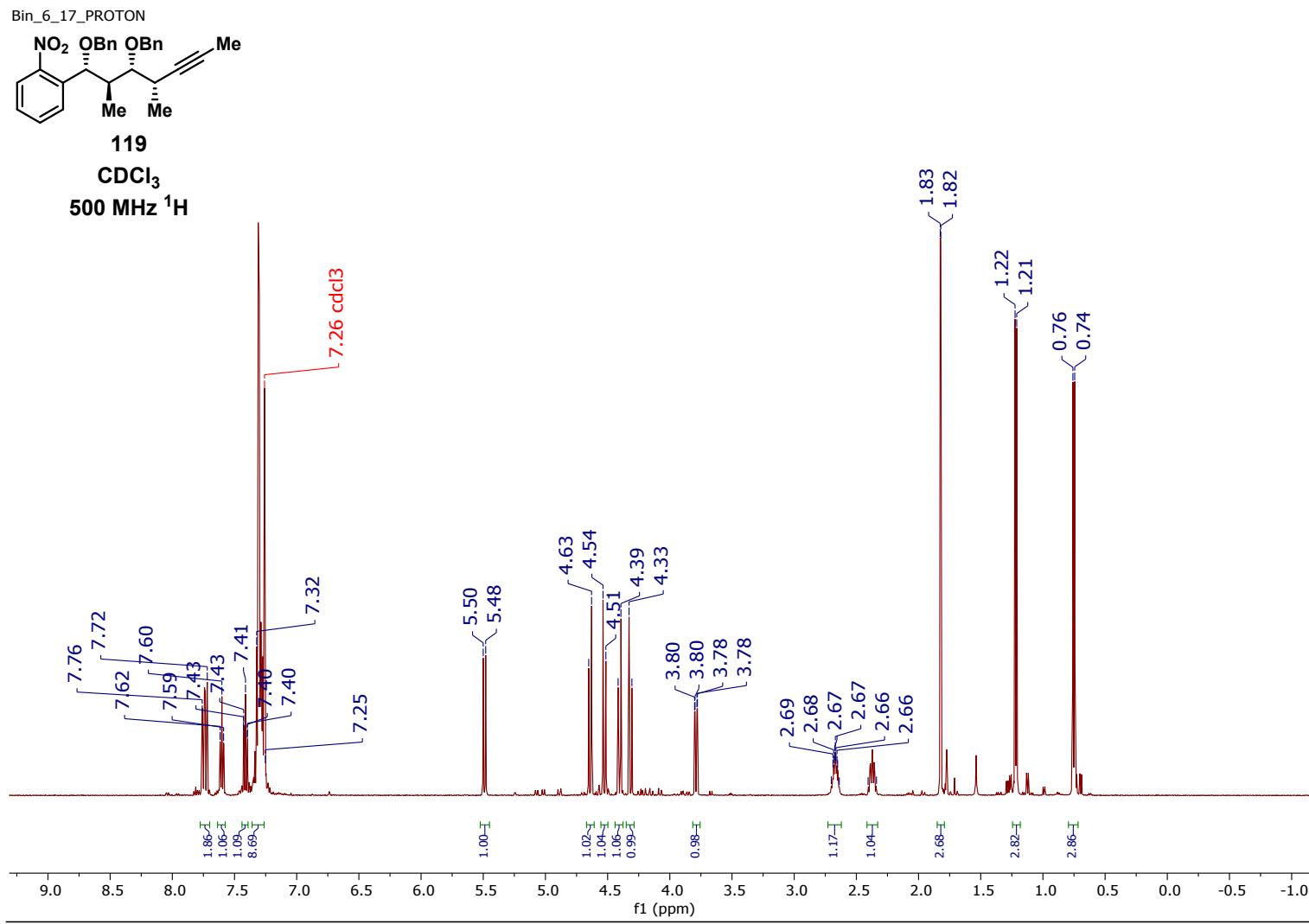


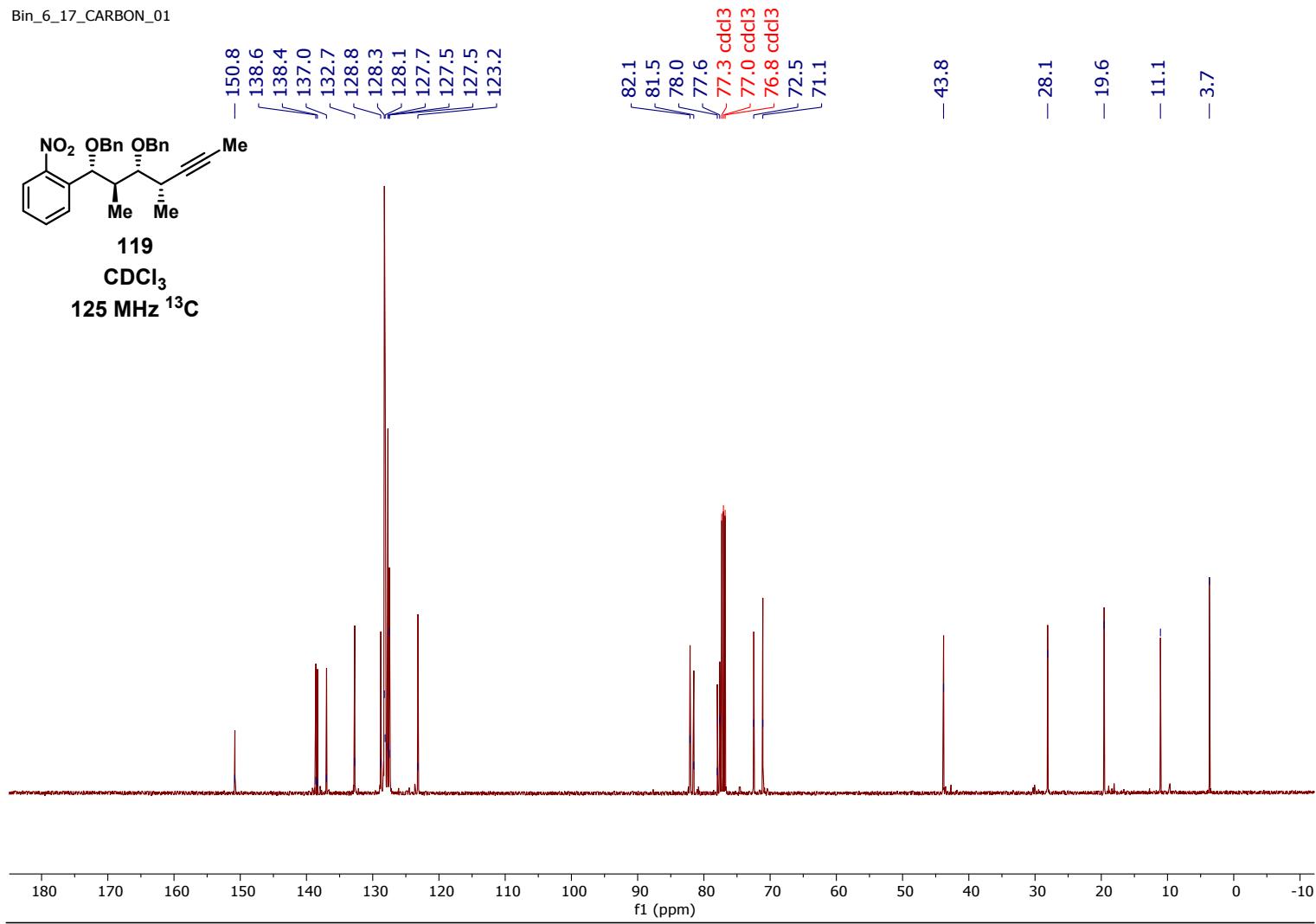


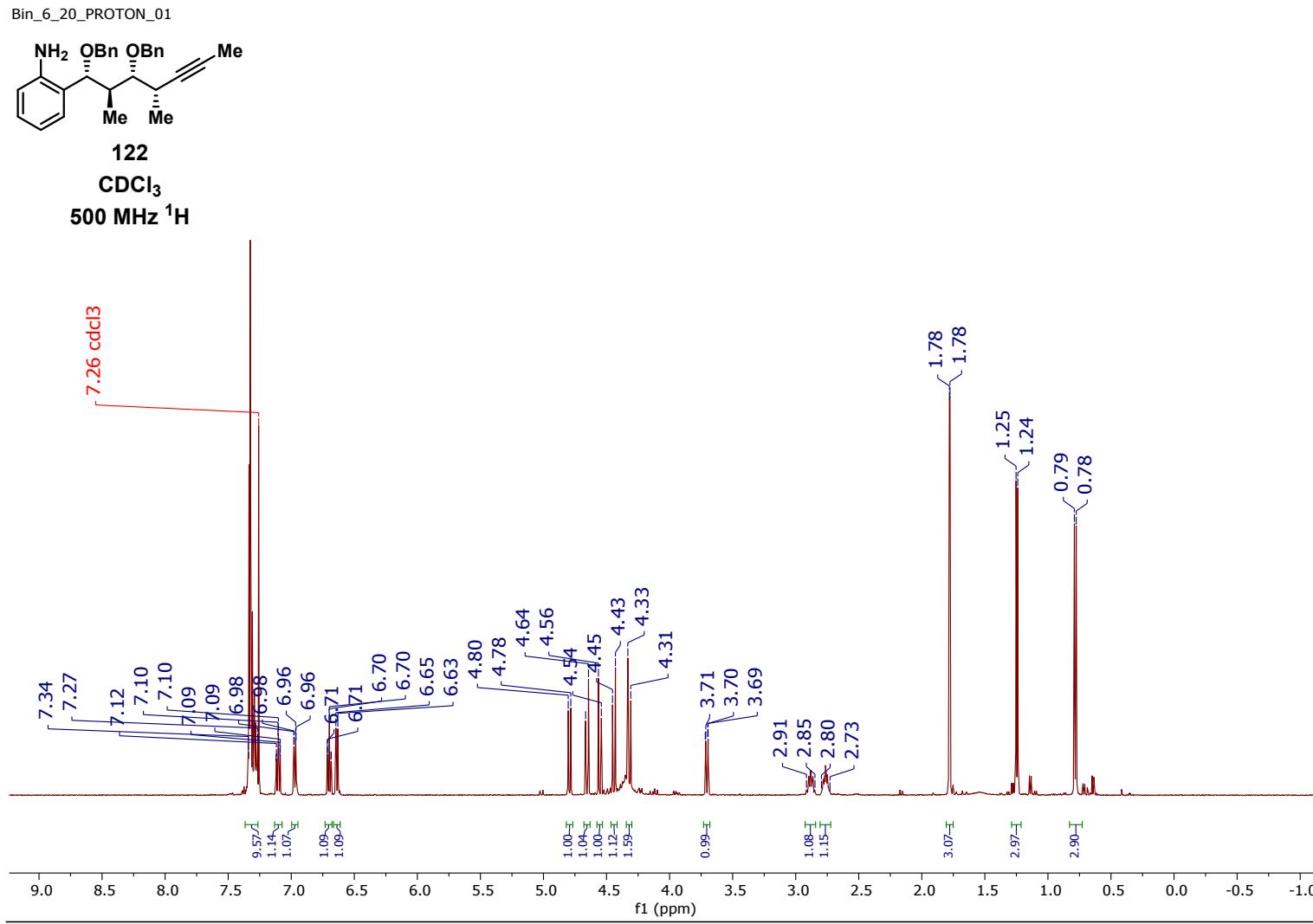


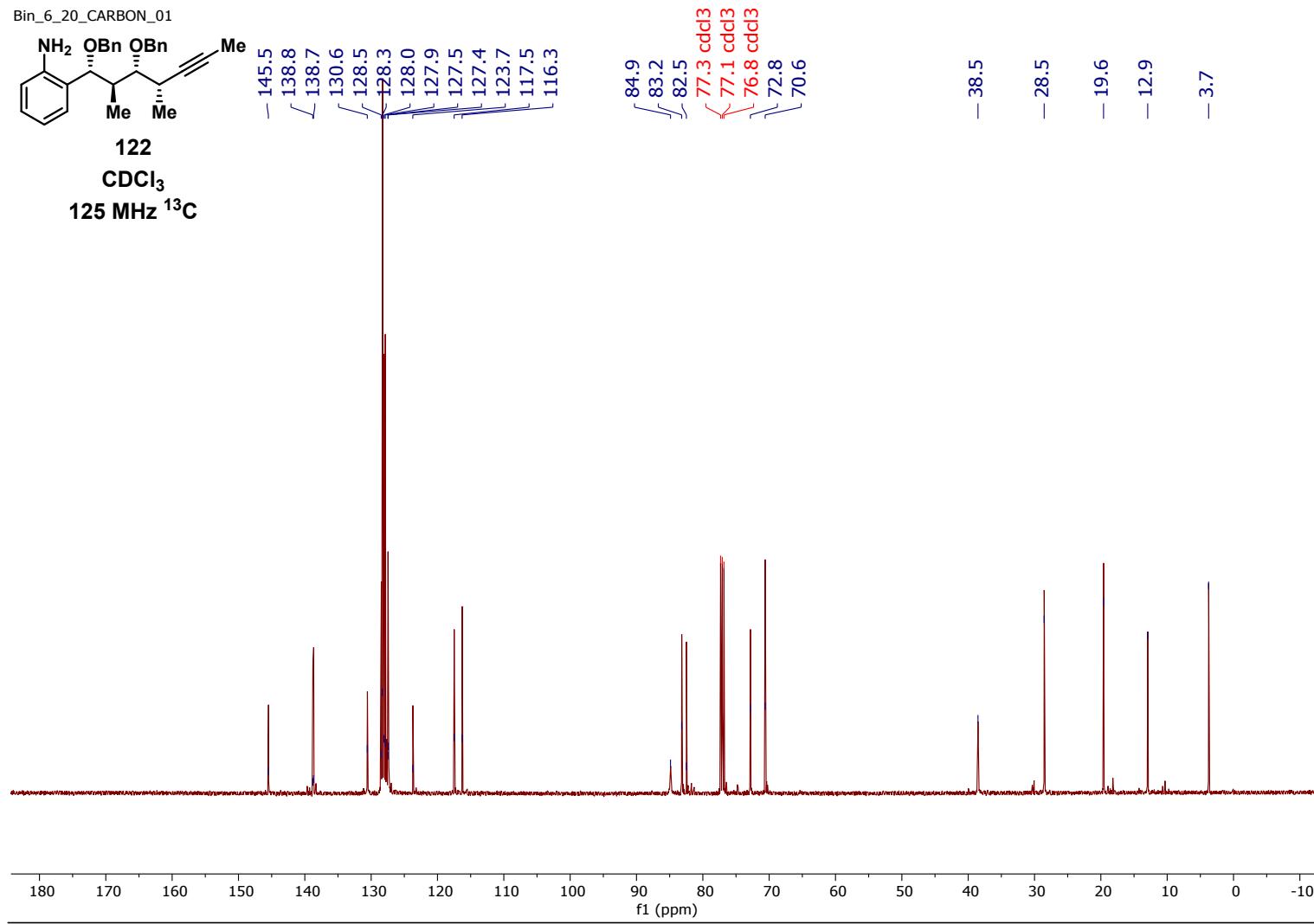


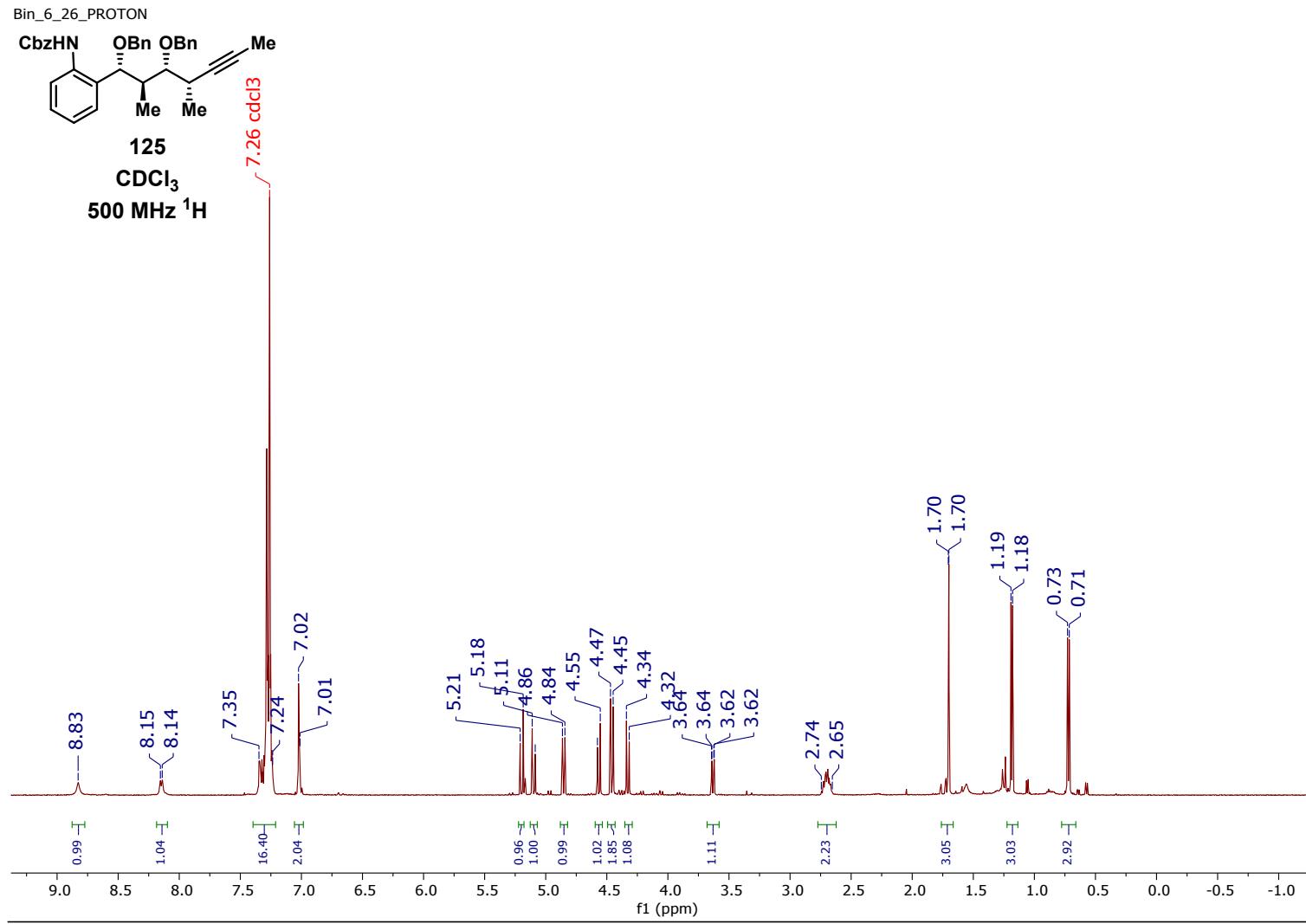


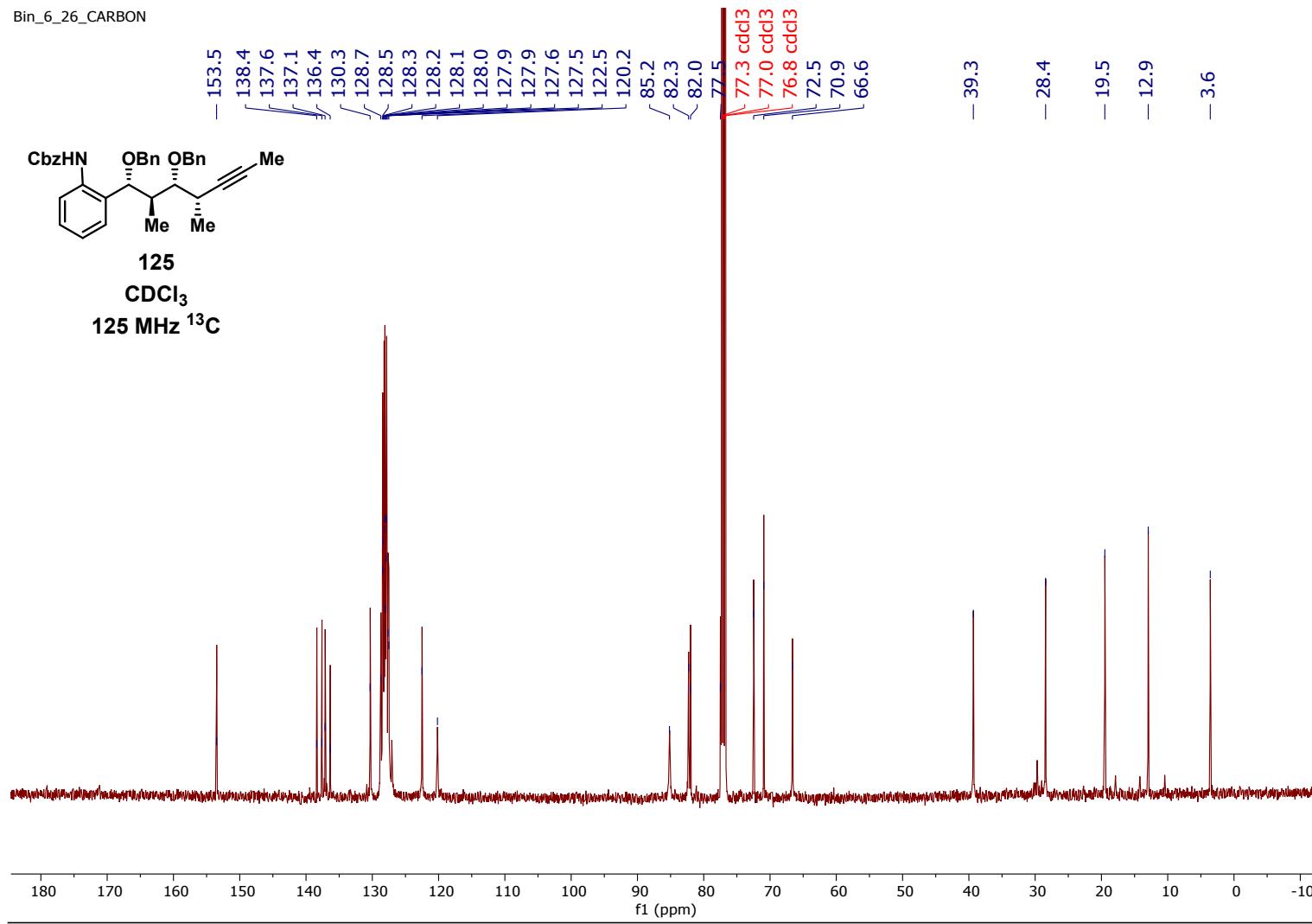


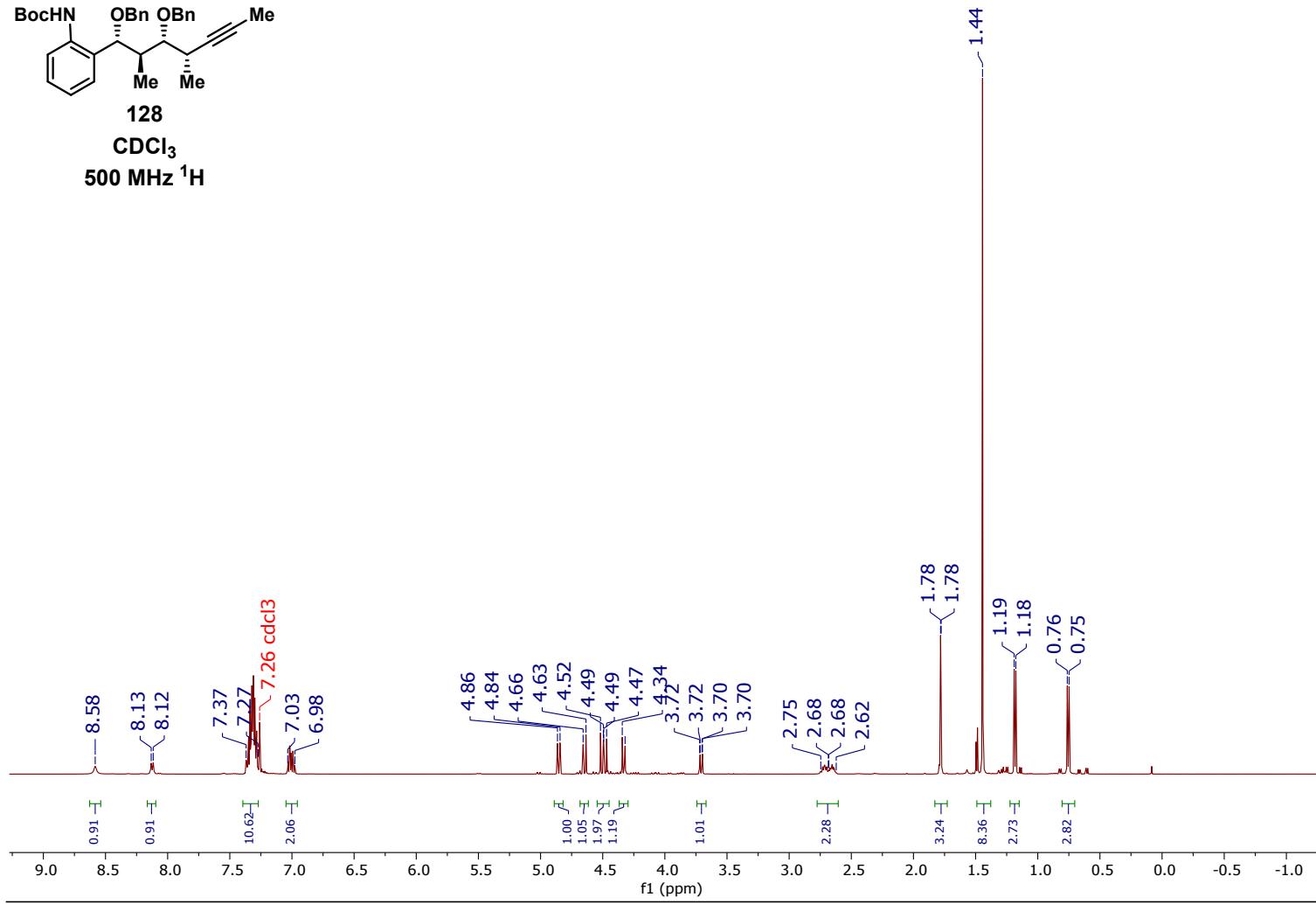
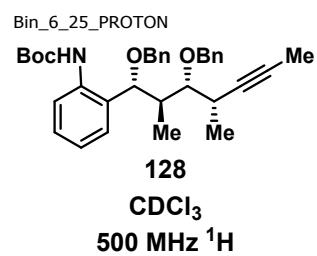




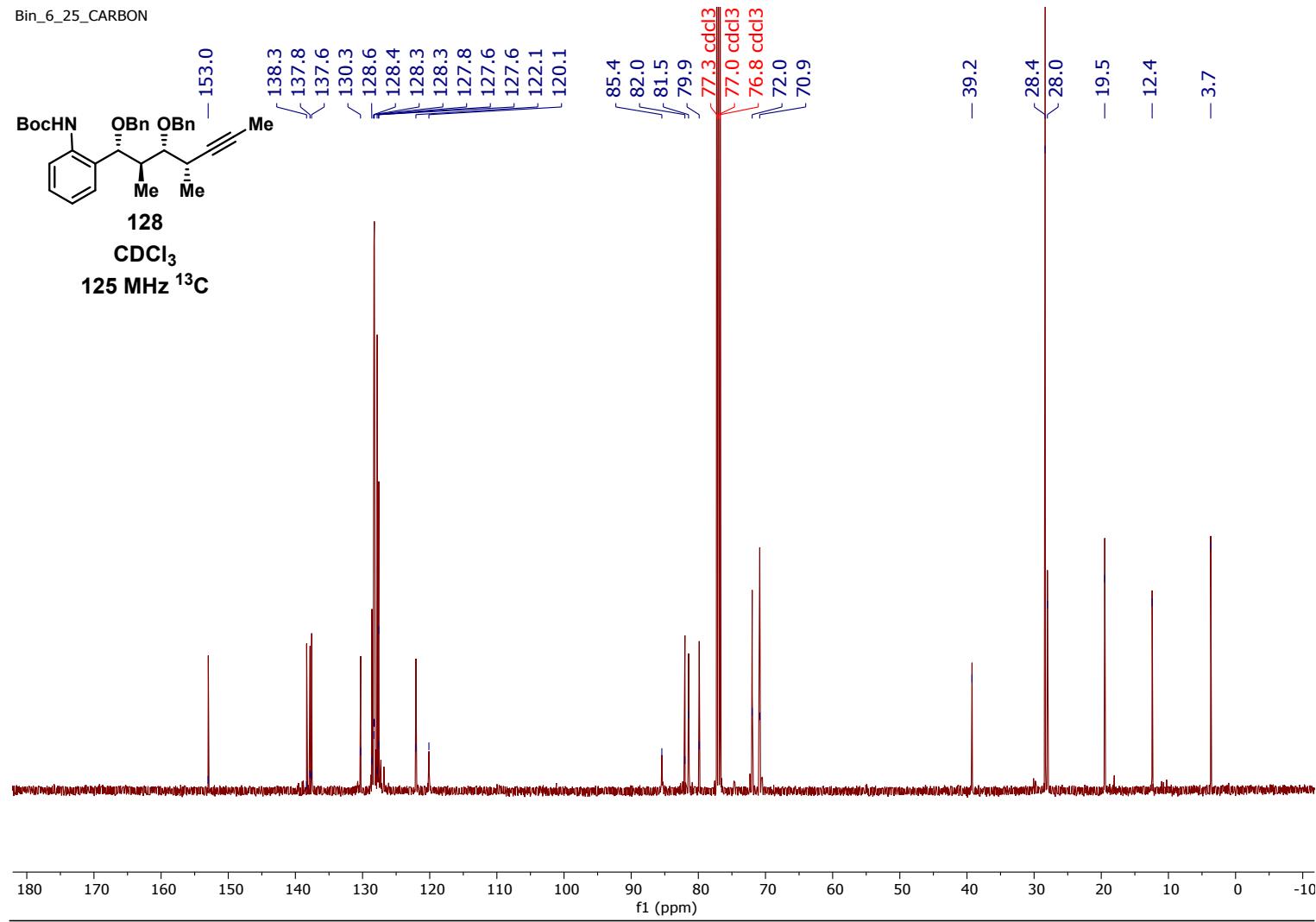


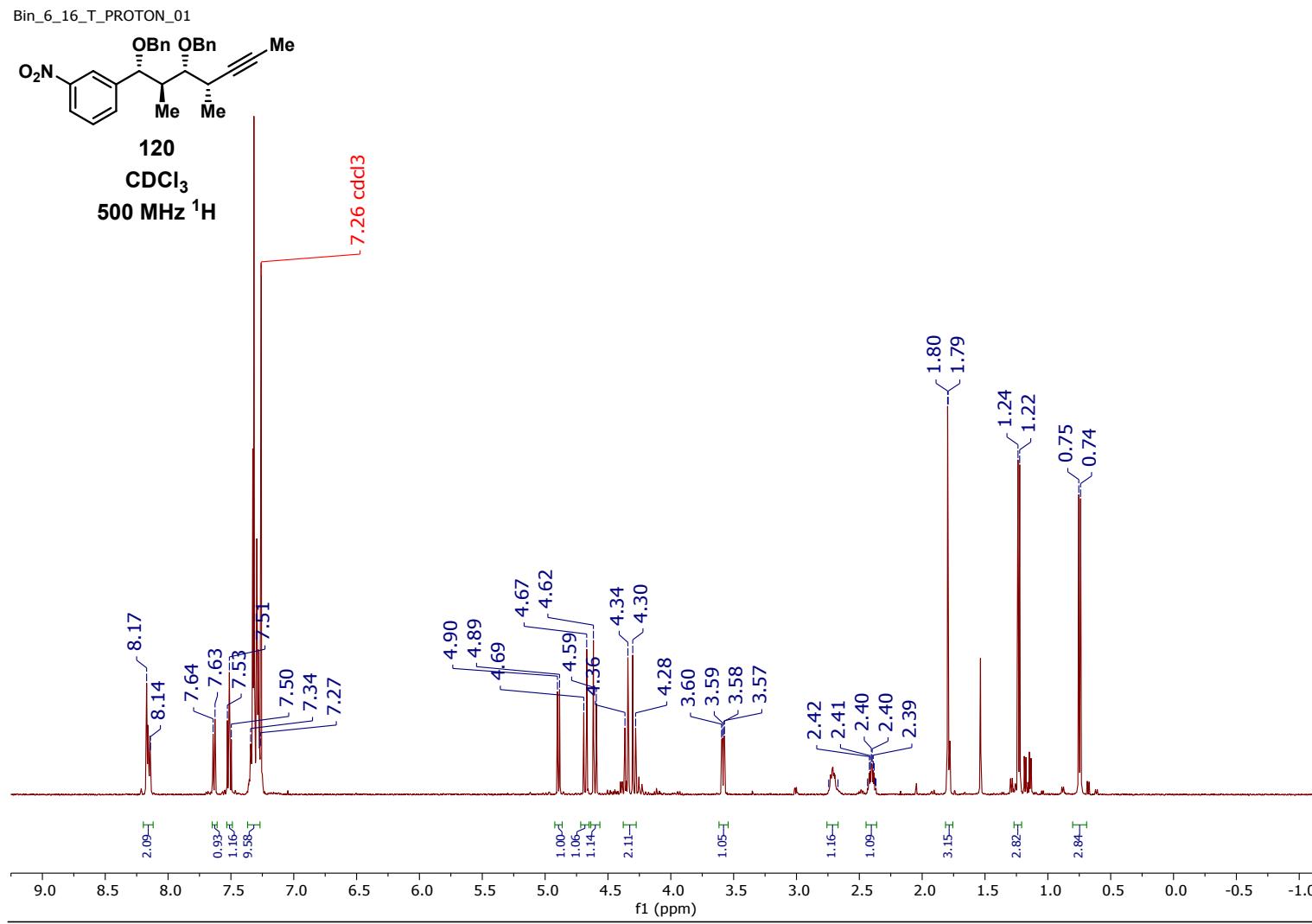


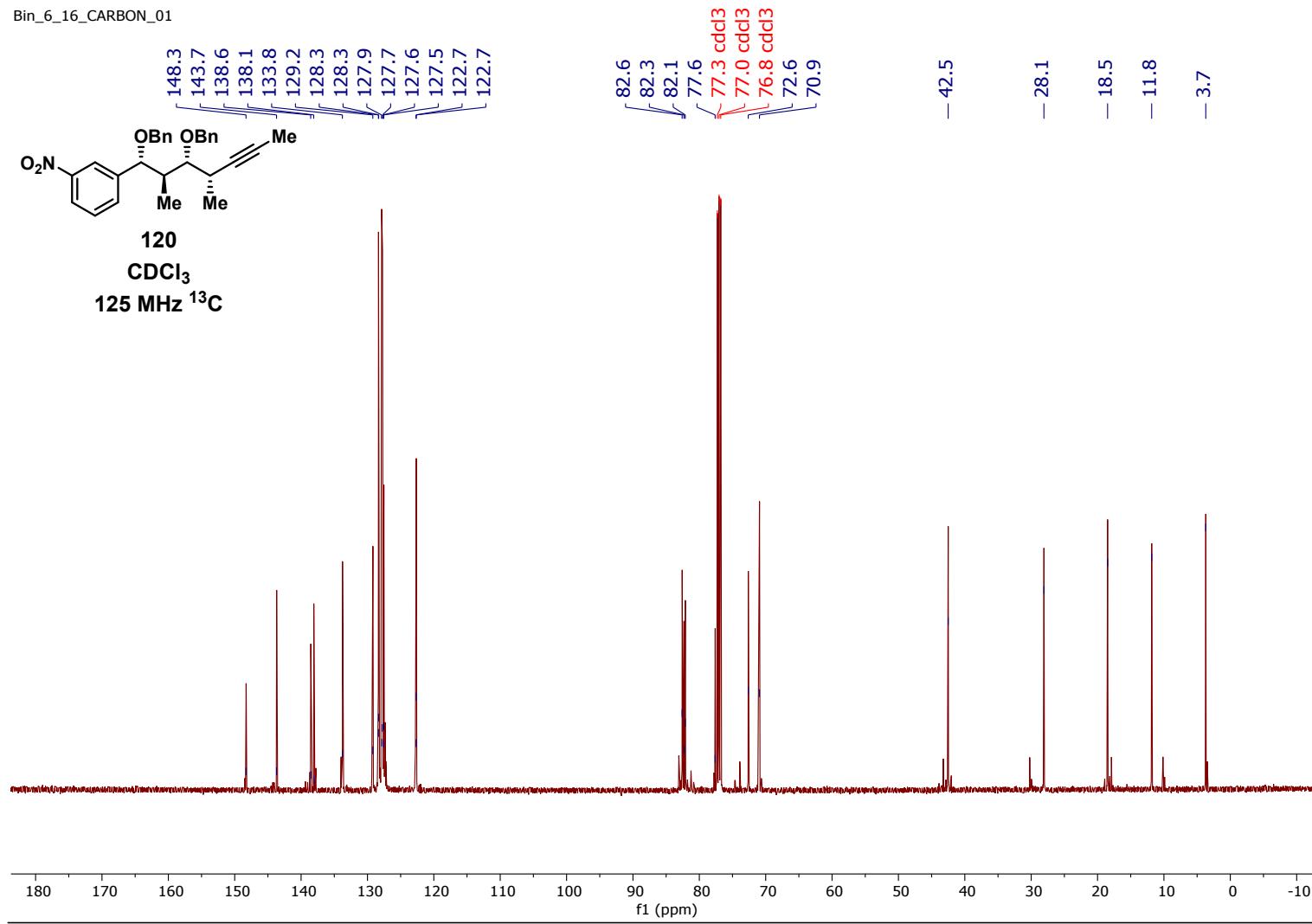


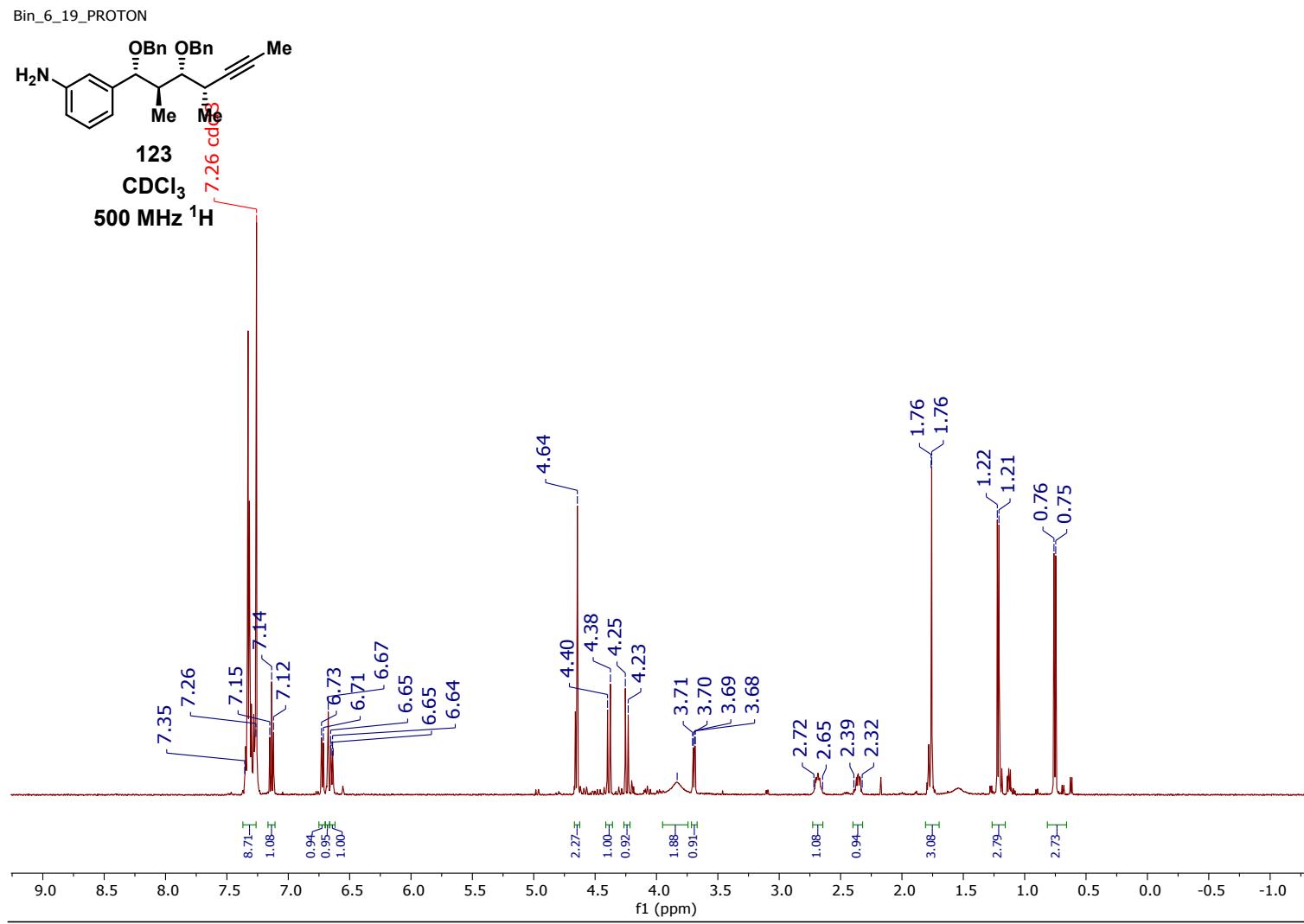


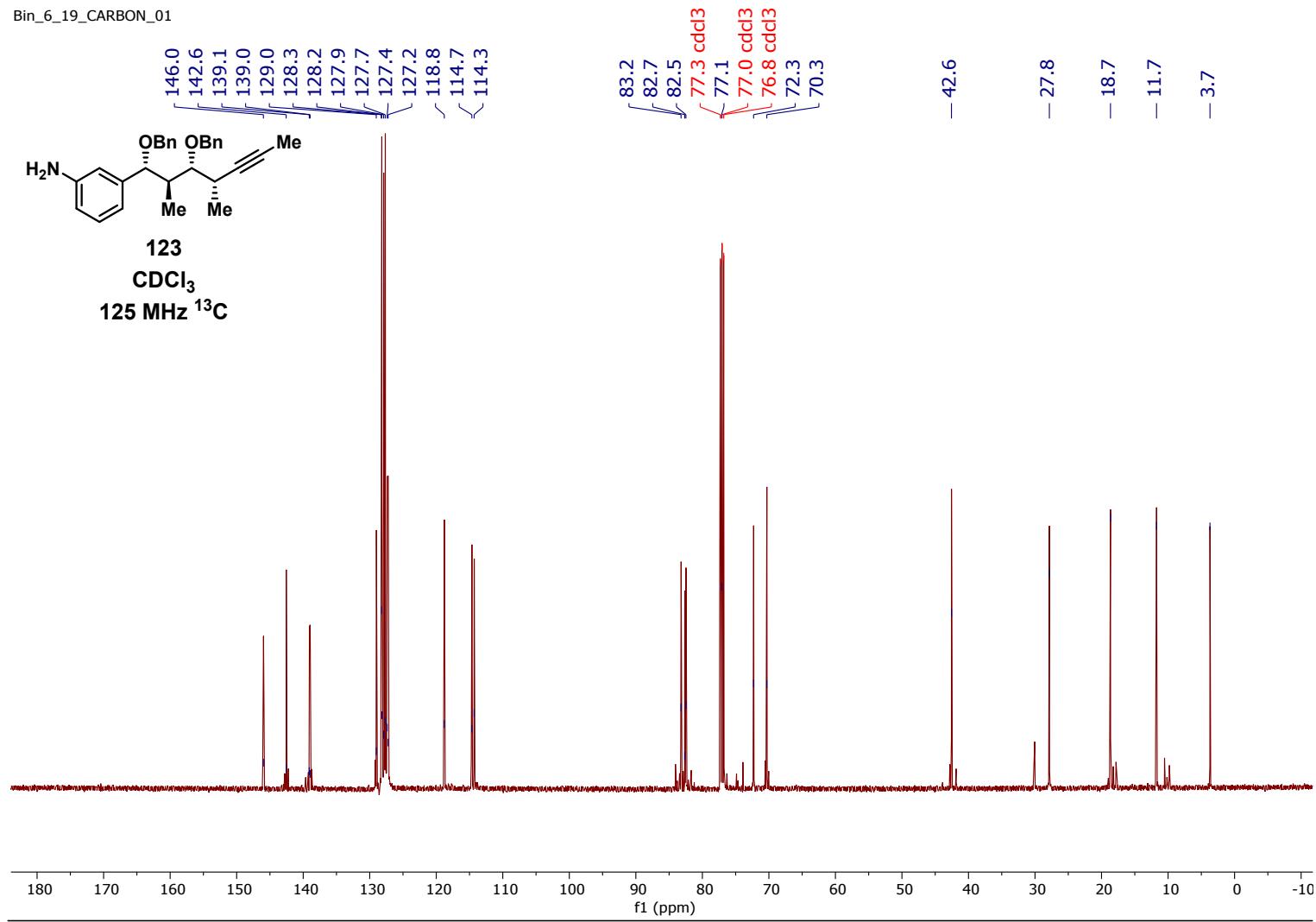
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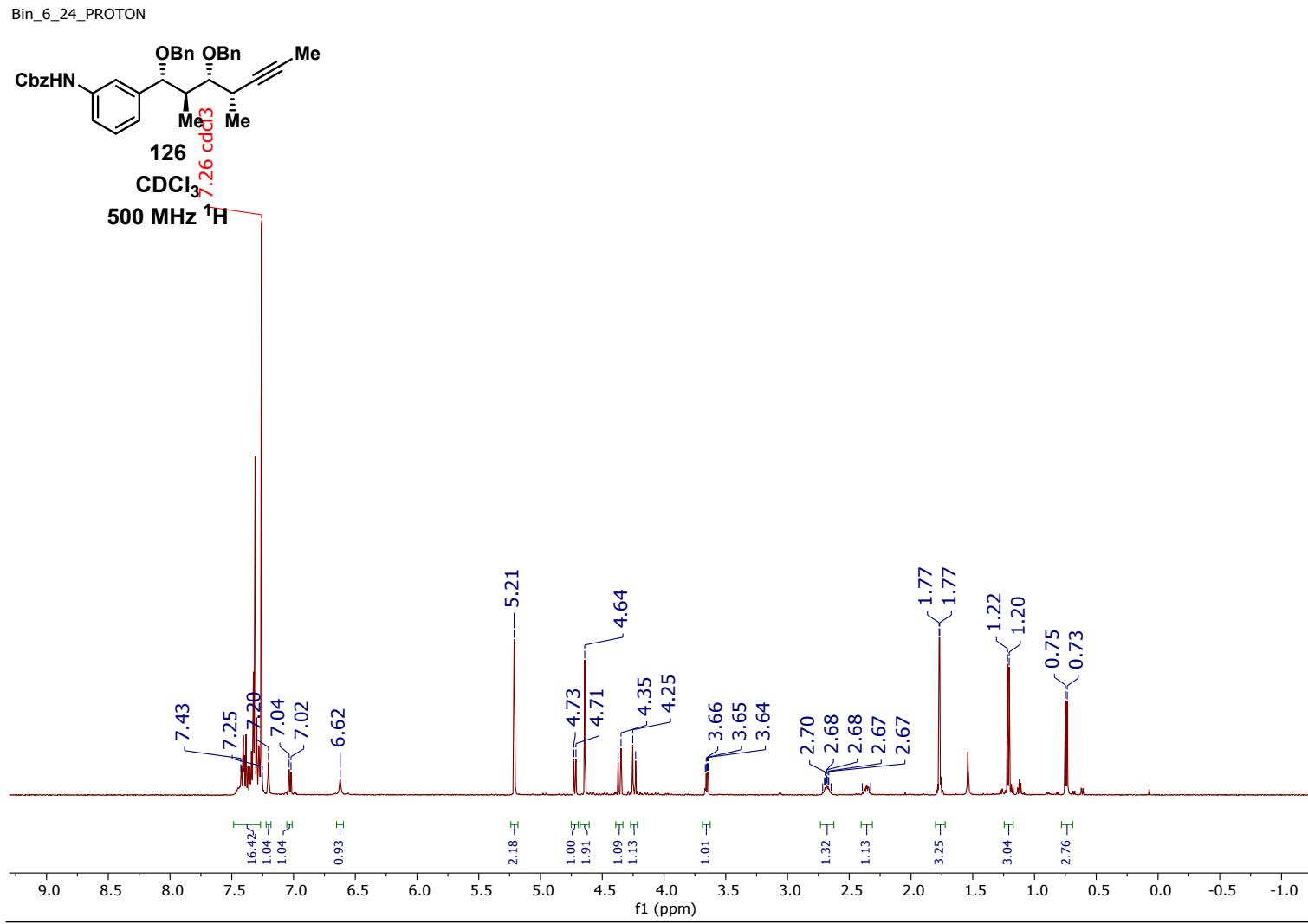


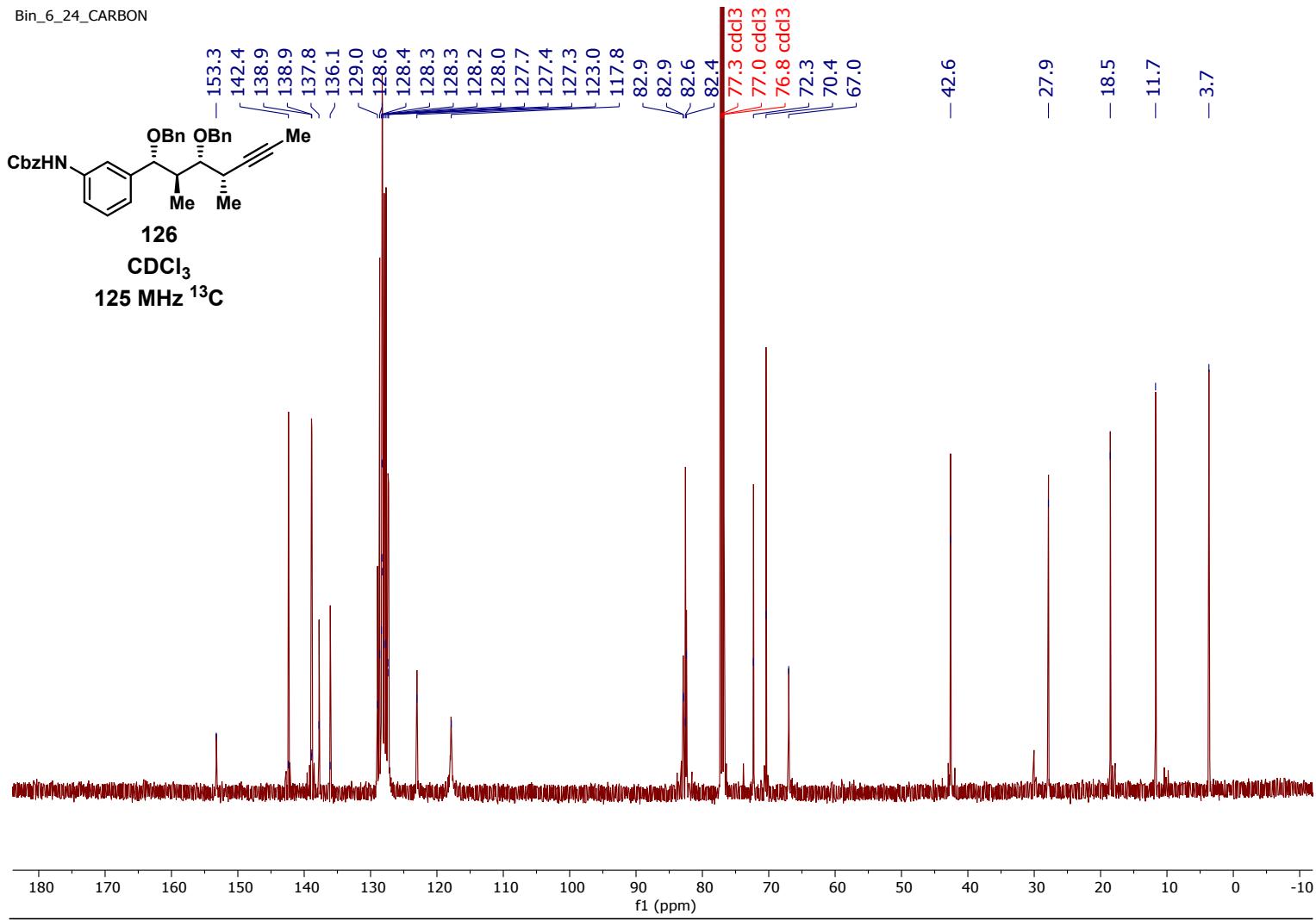


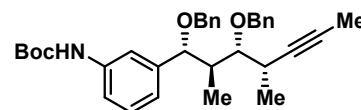
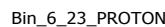




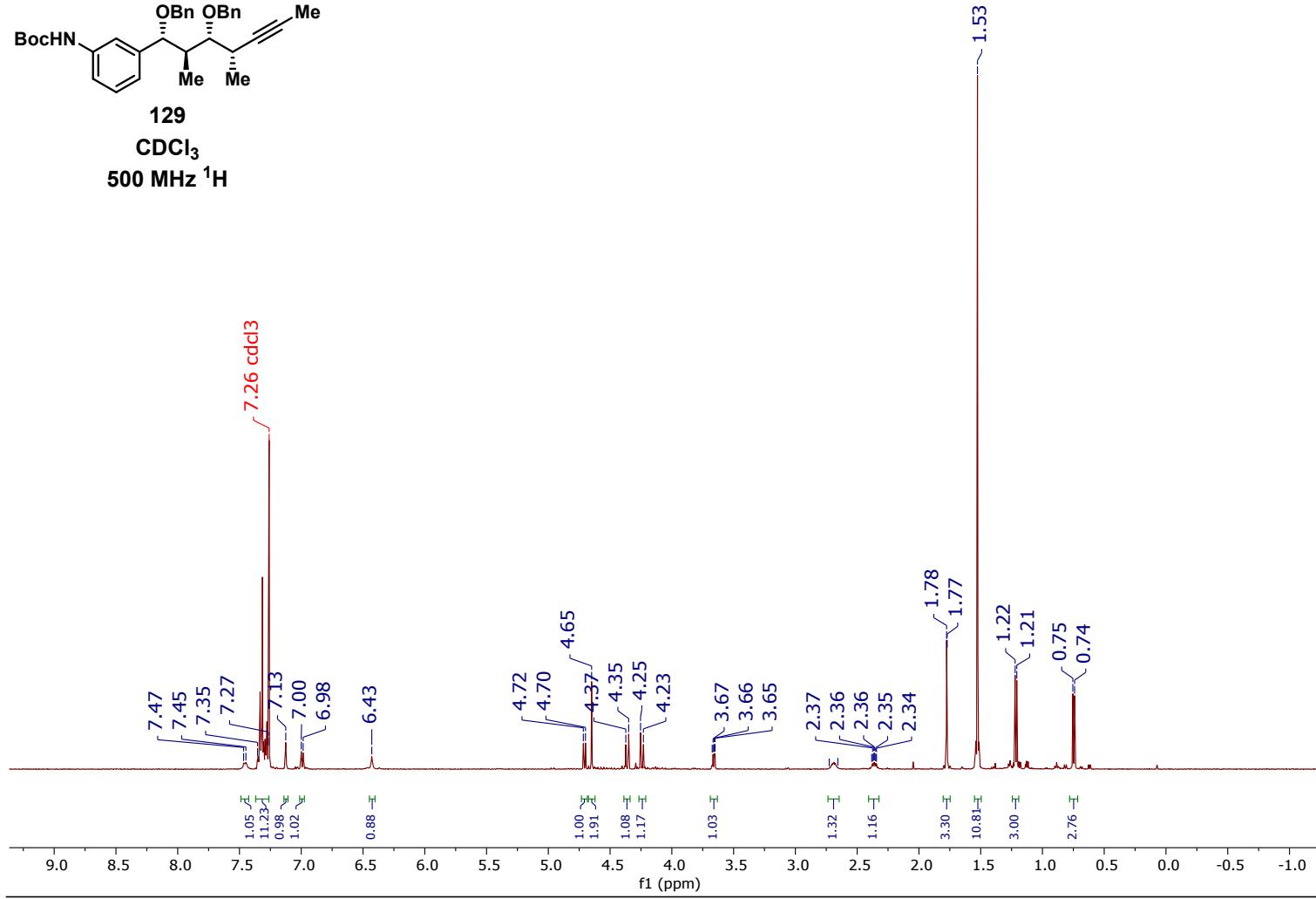


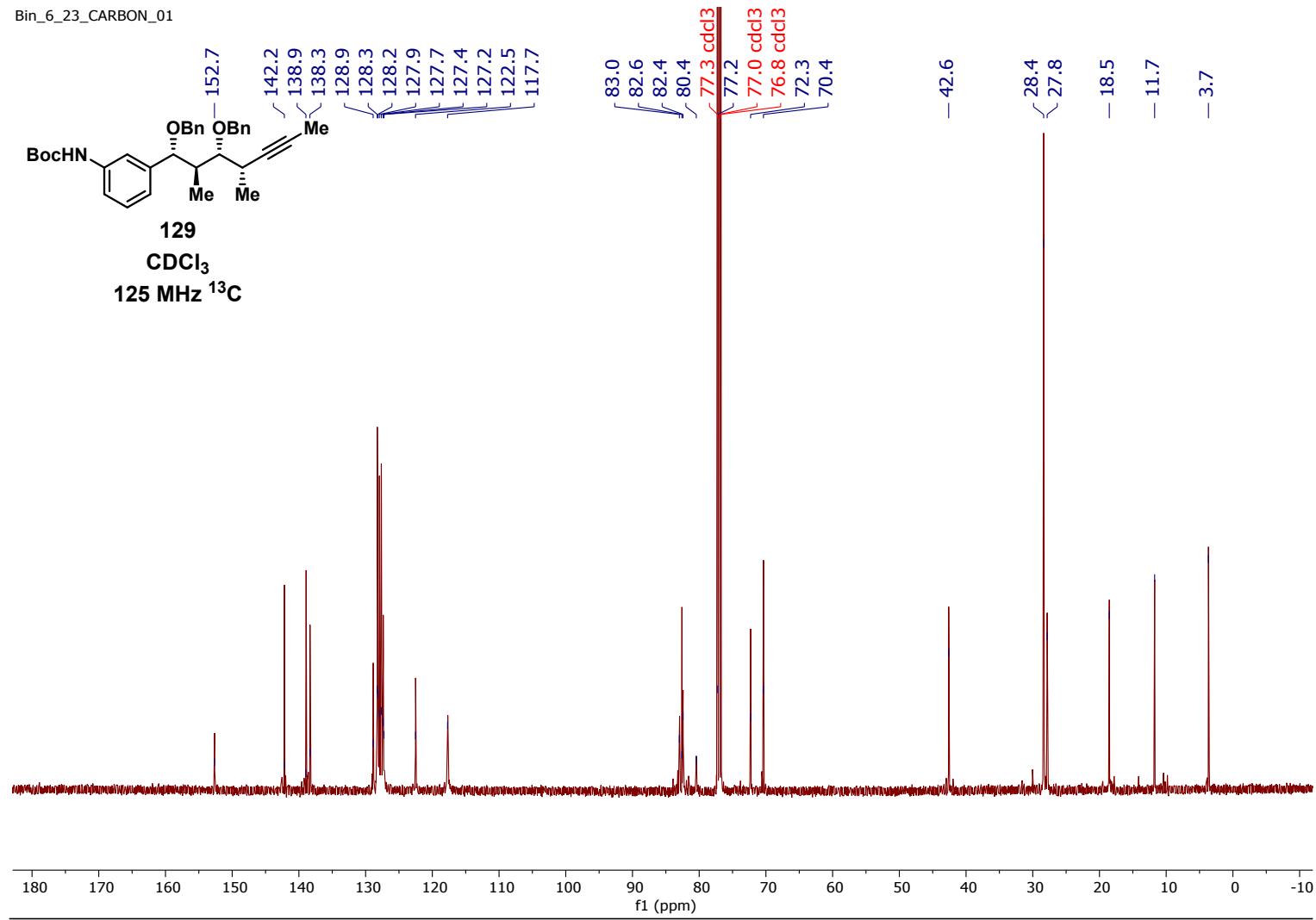


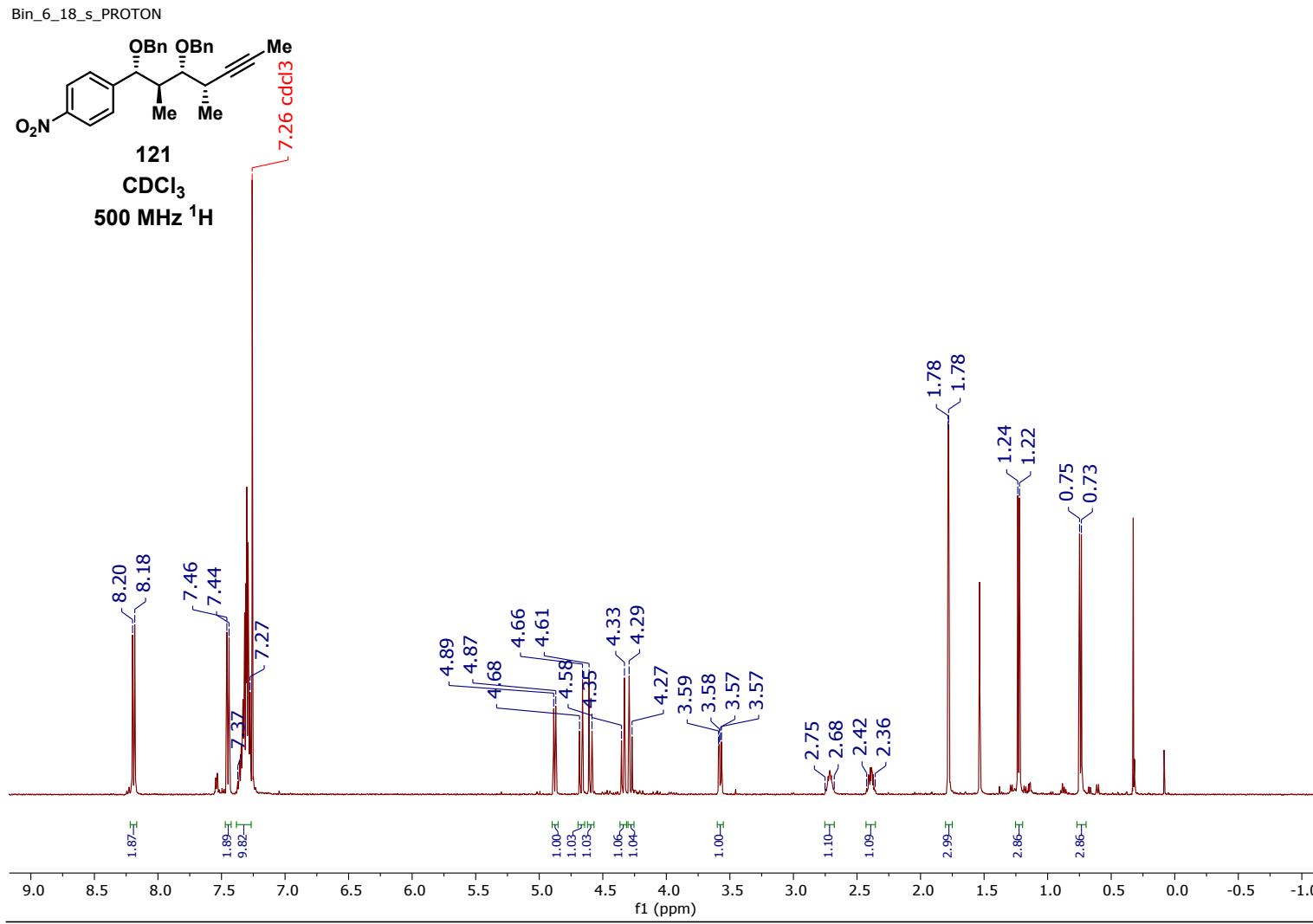


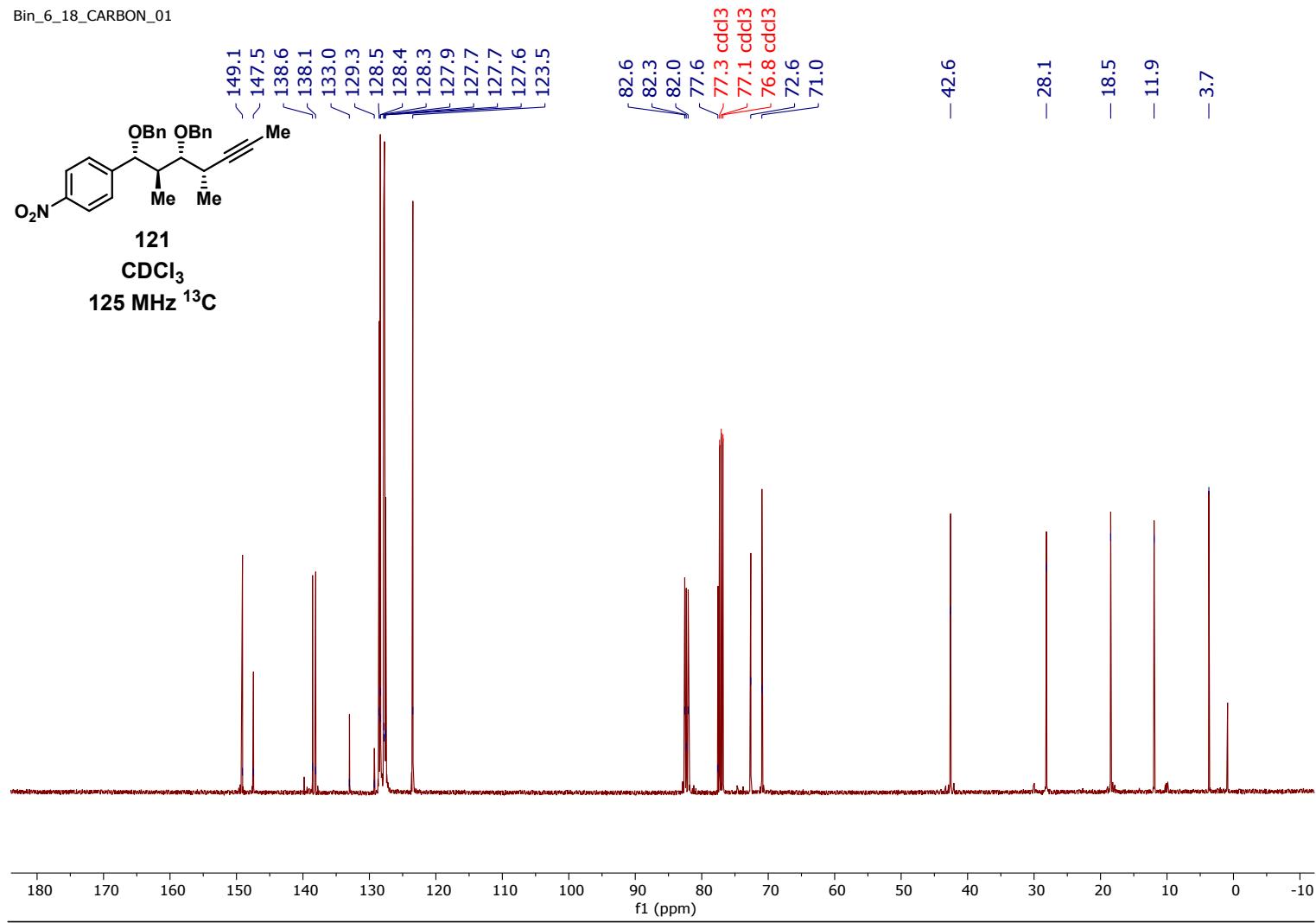


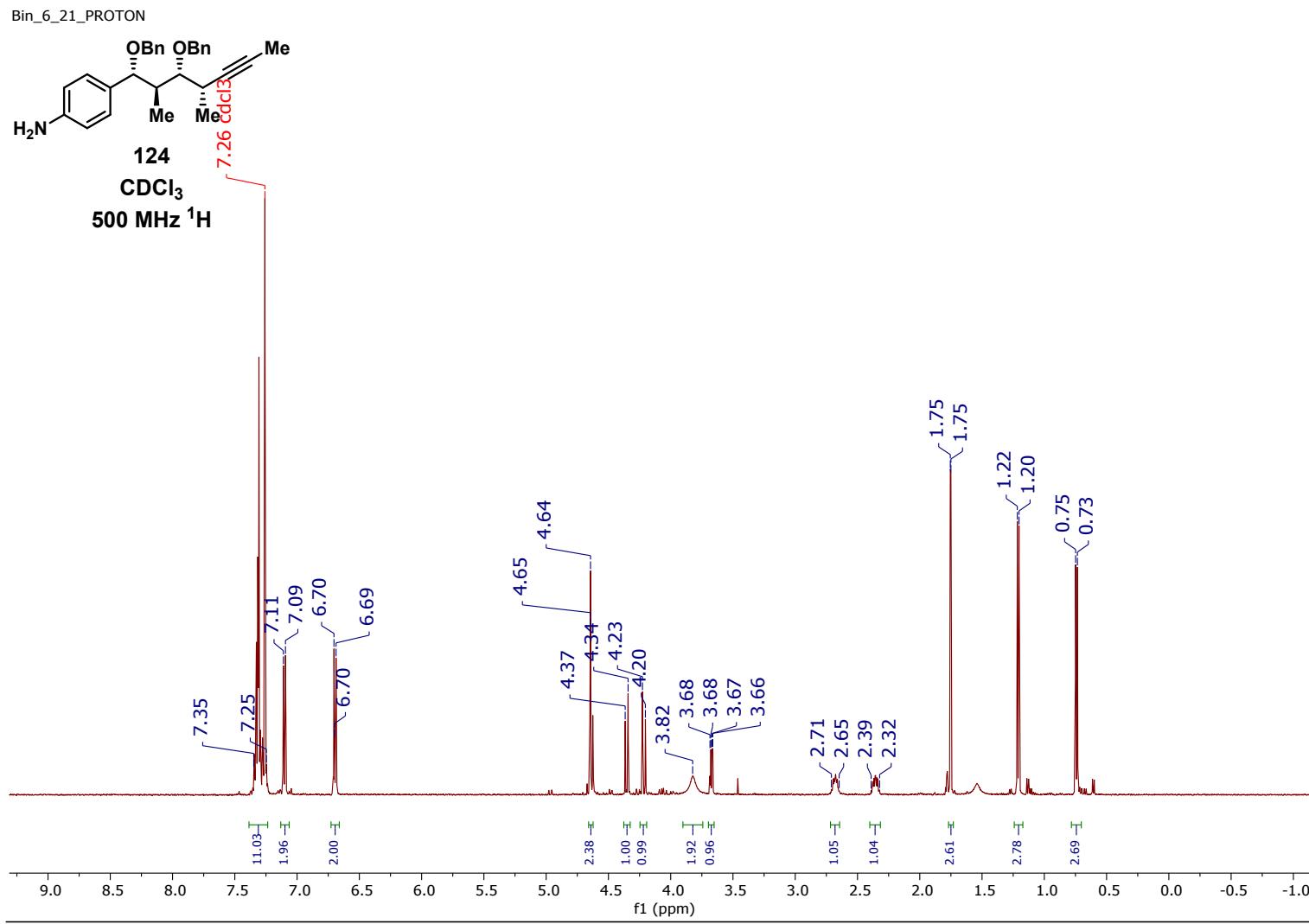
129  
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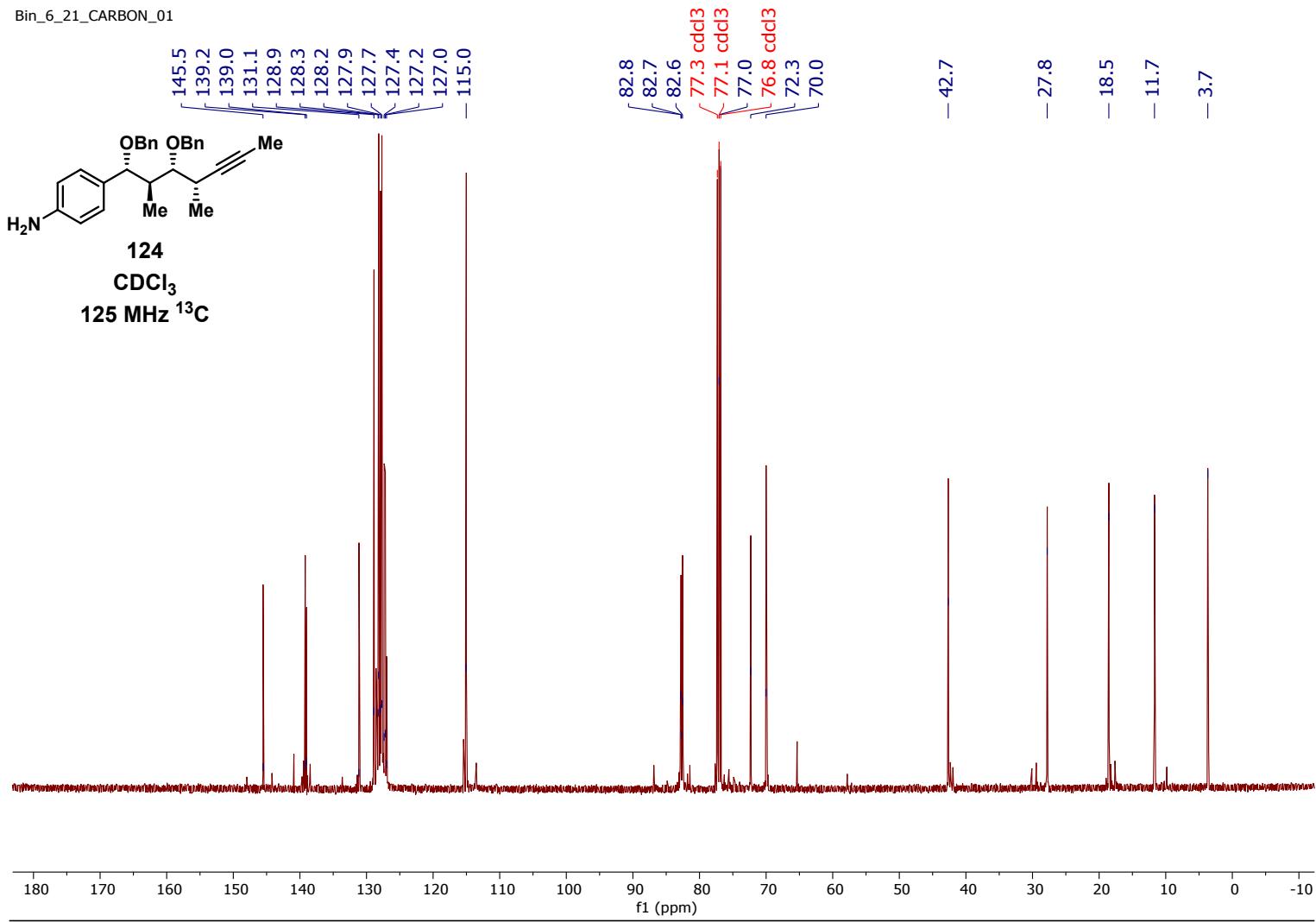


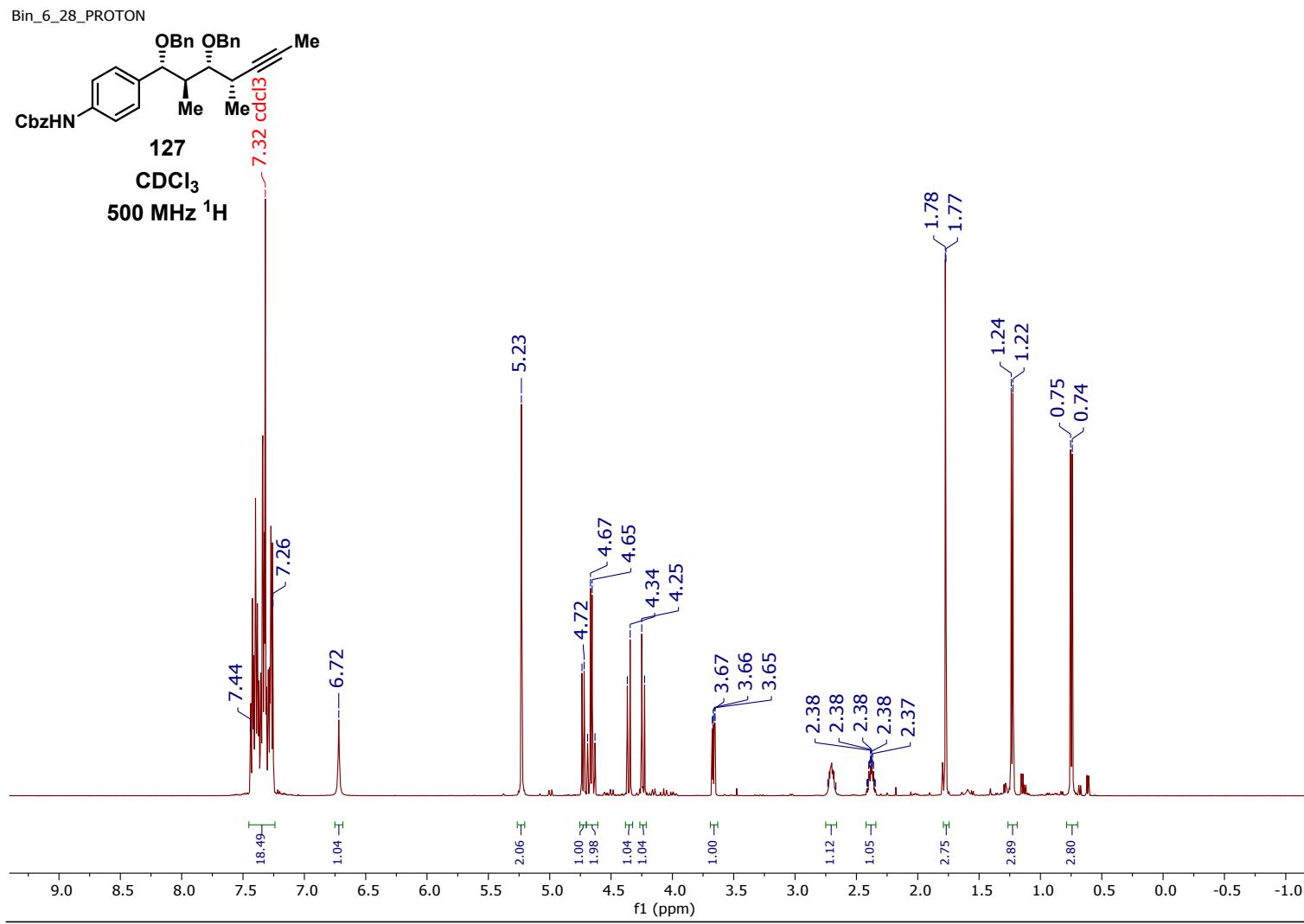


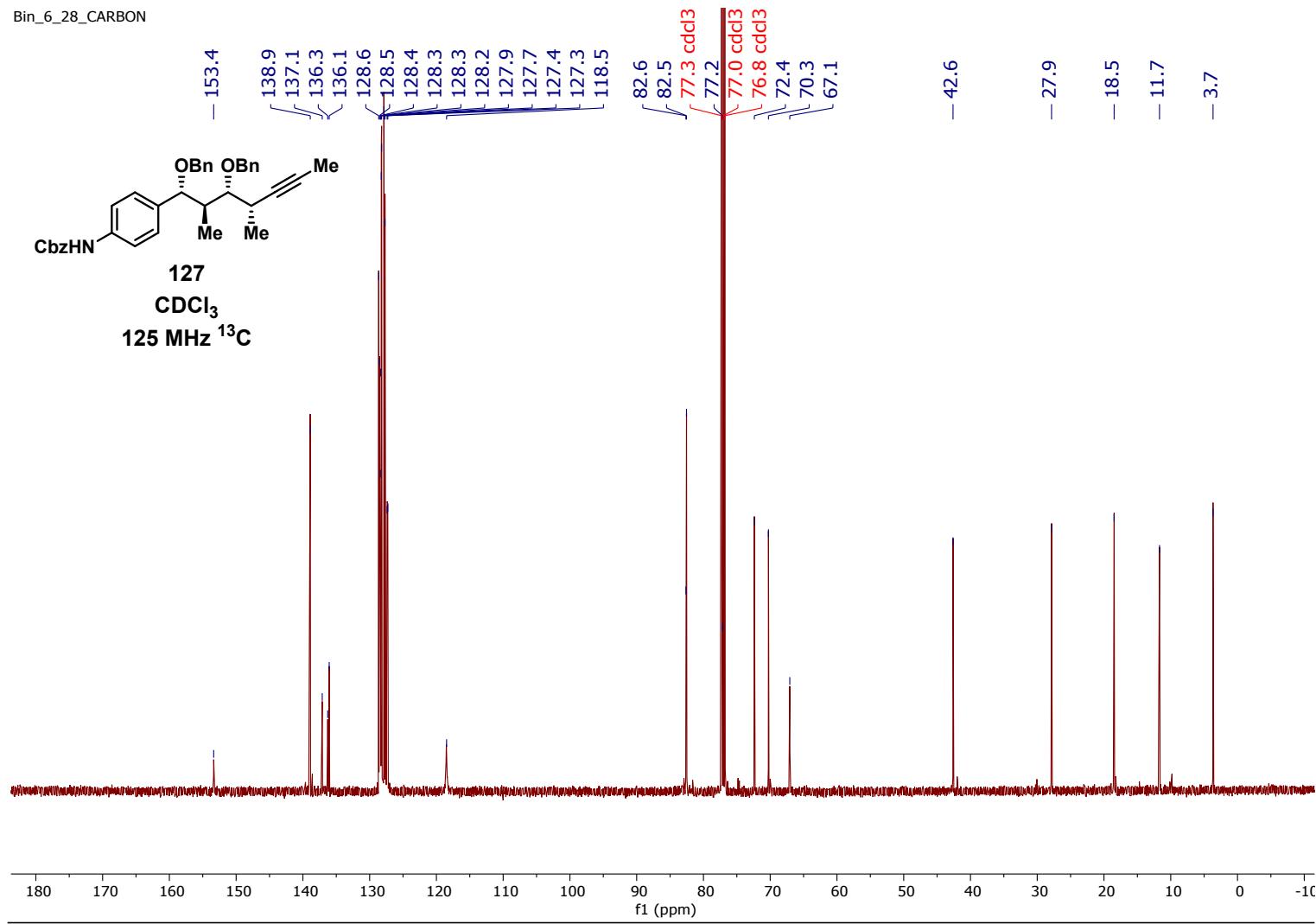


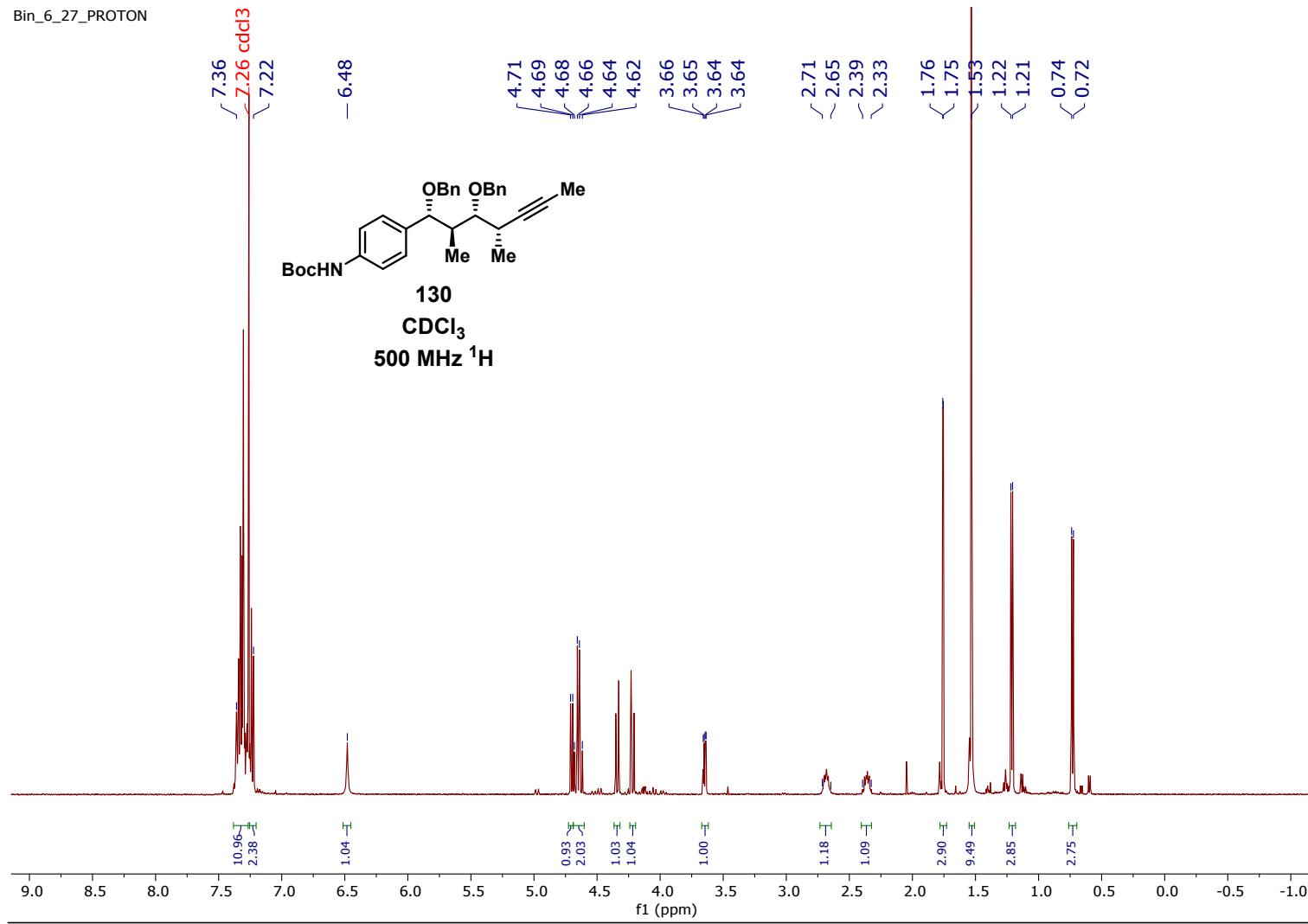


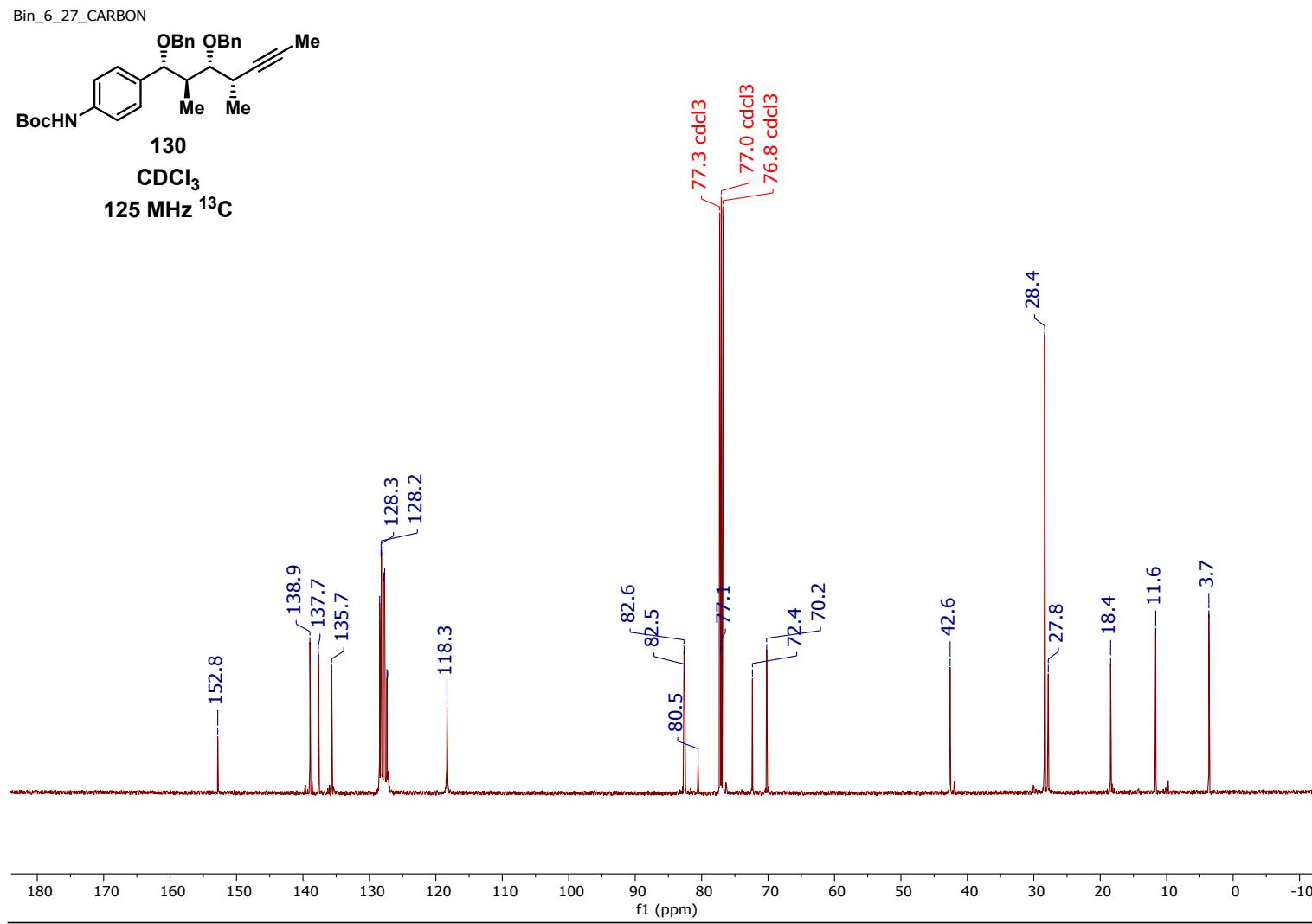




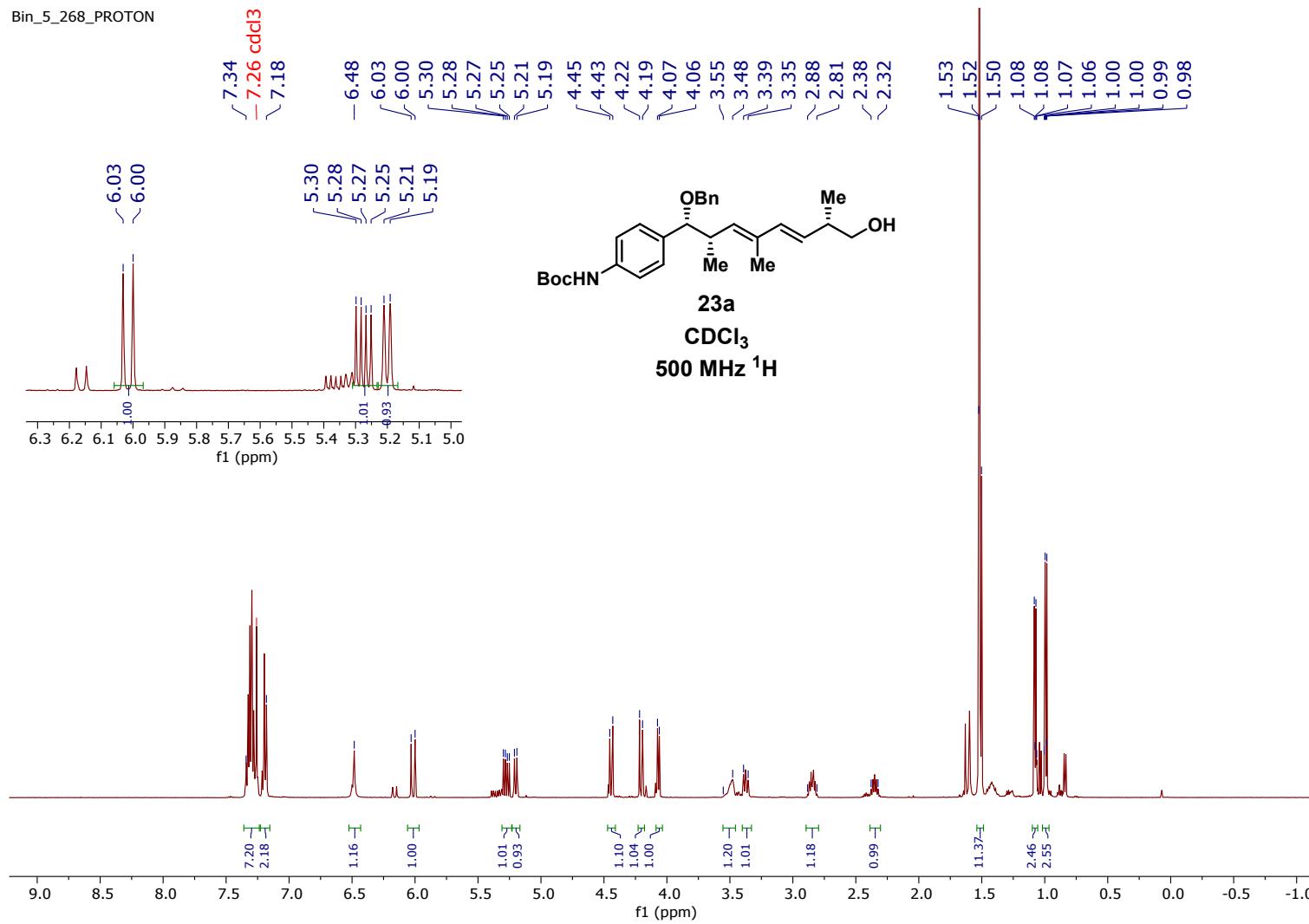


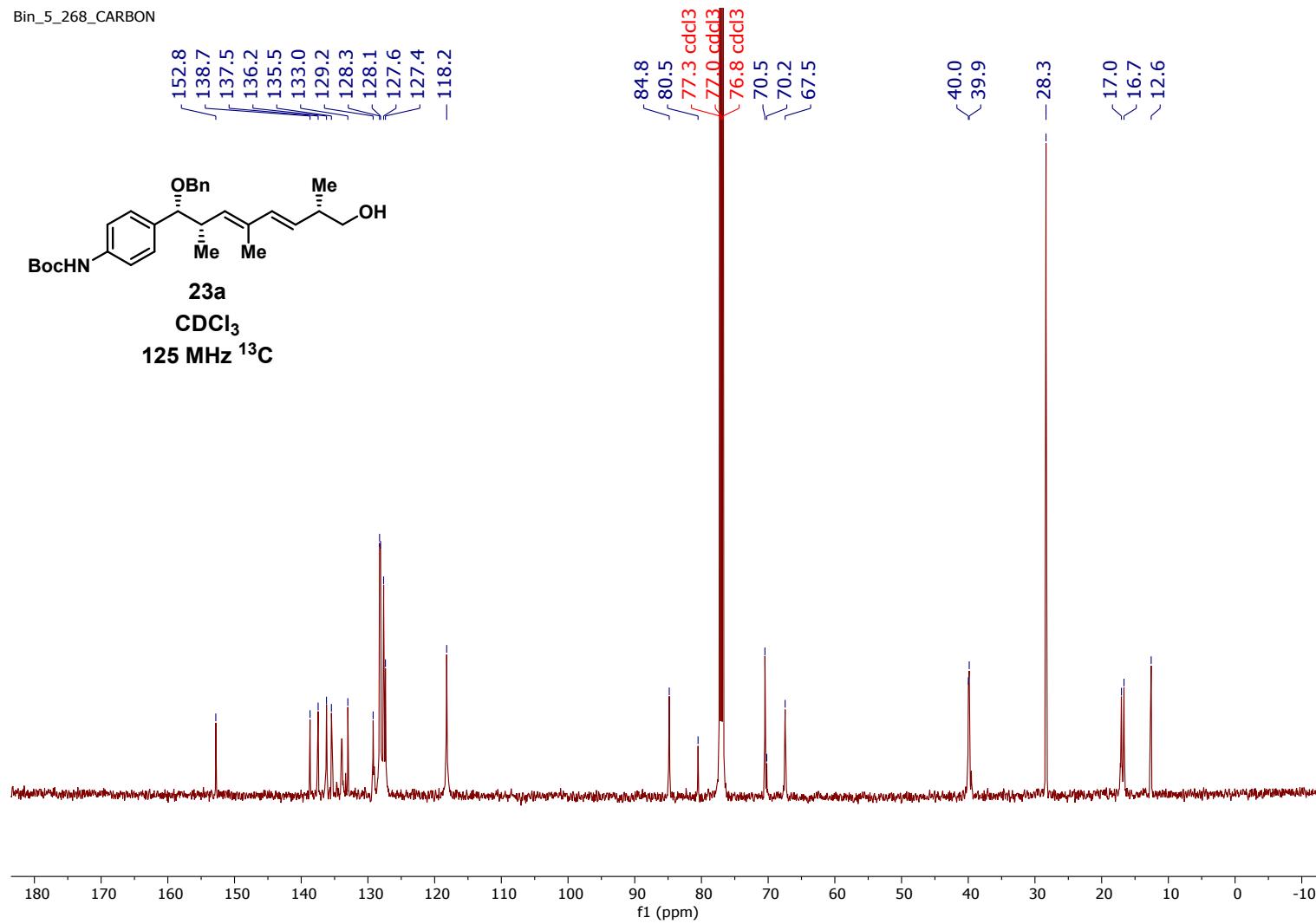




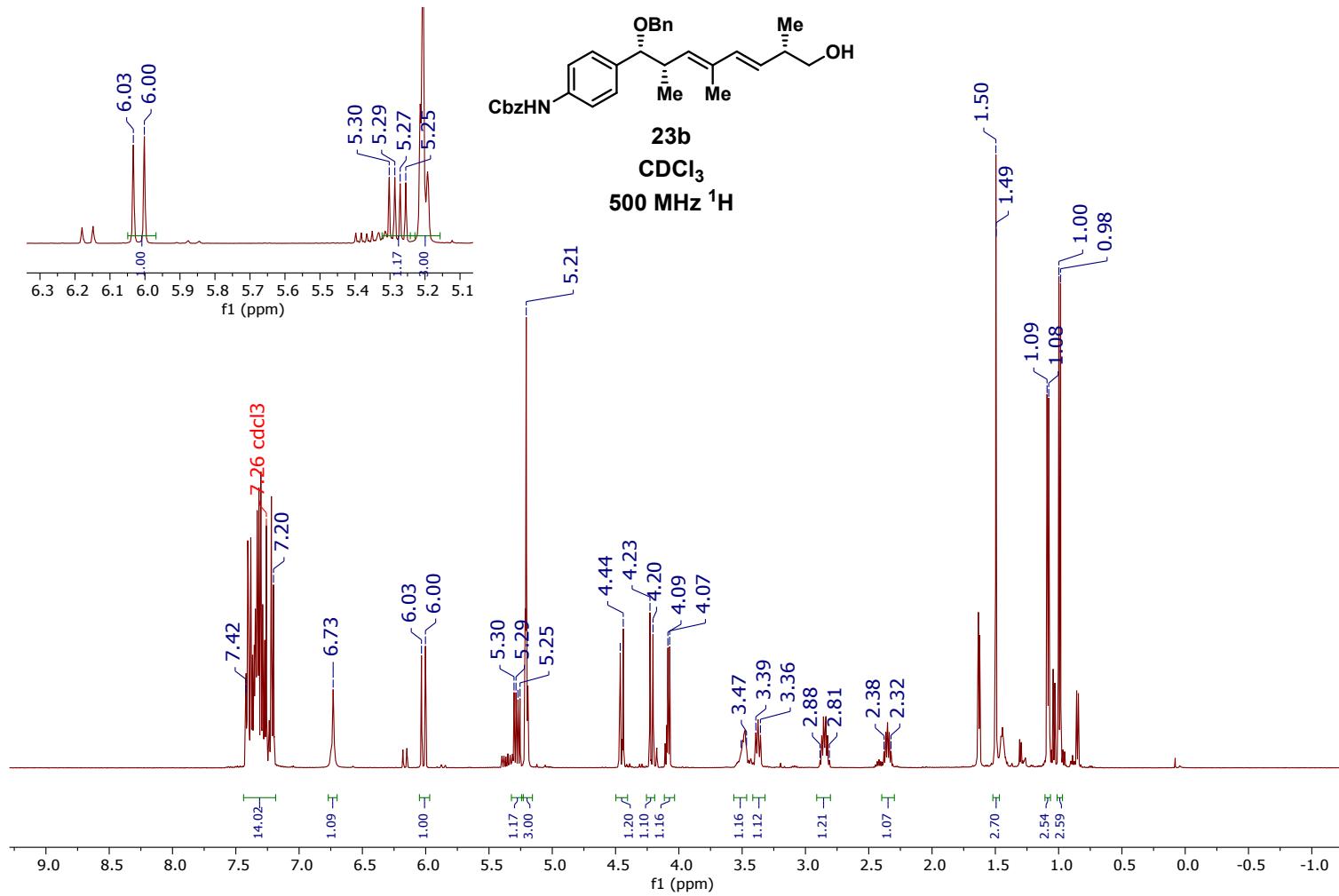


Bin\_5\_268\_PROTON

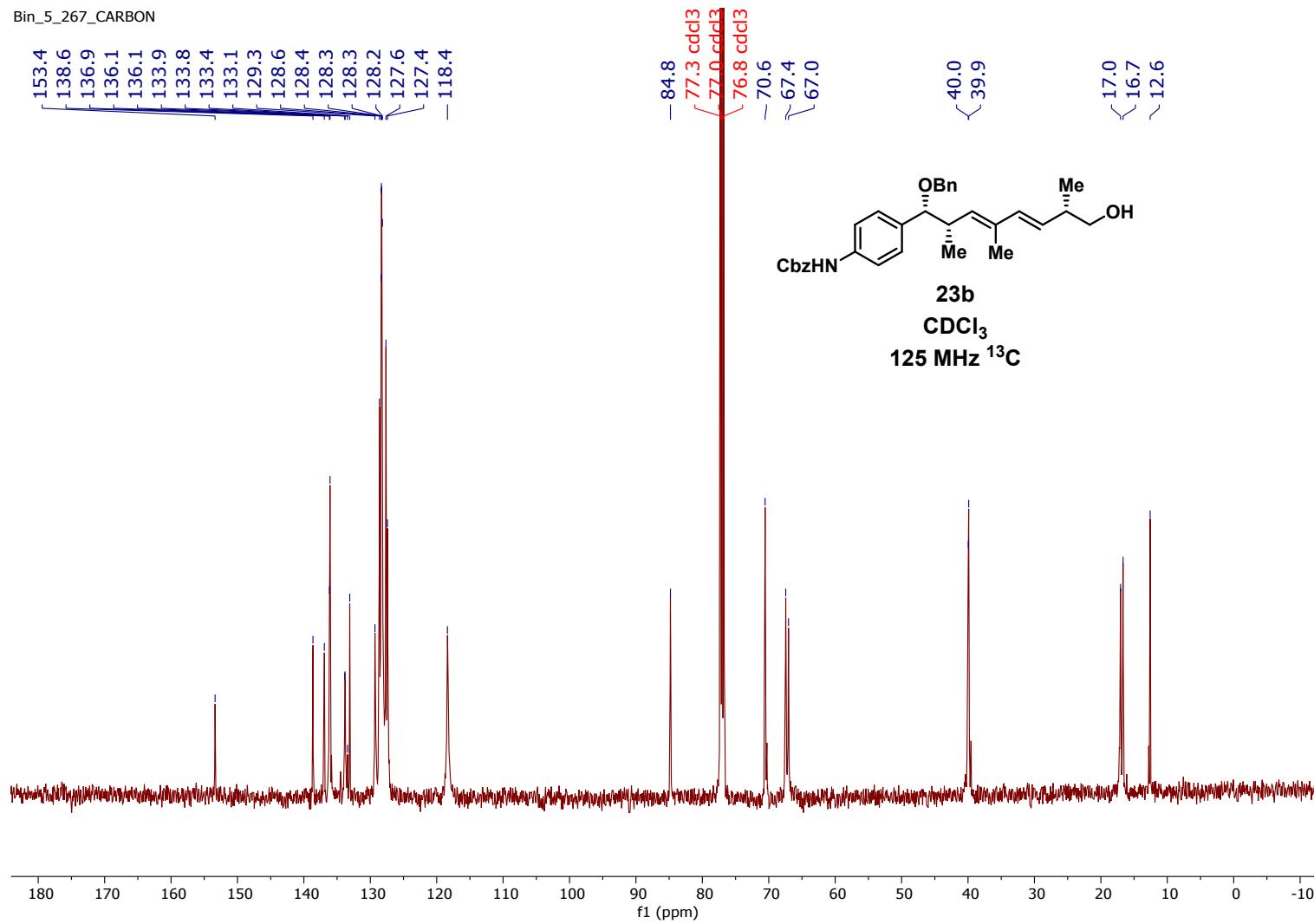


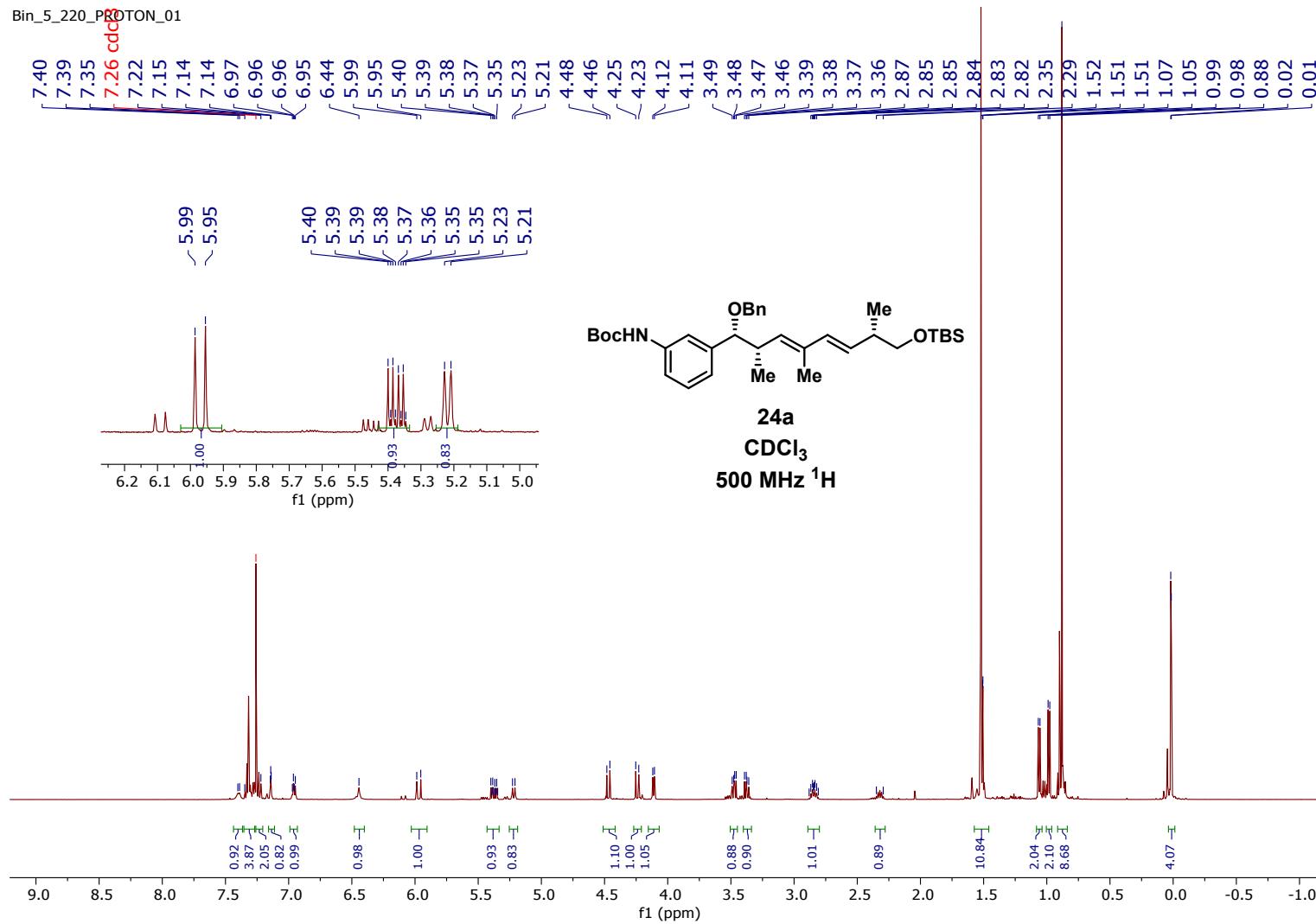


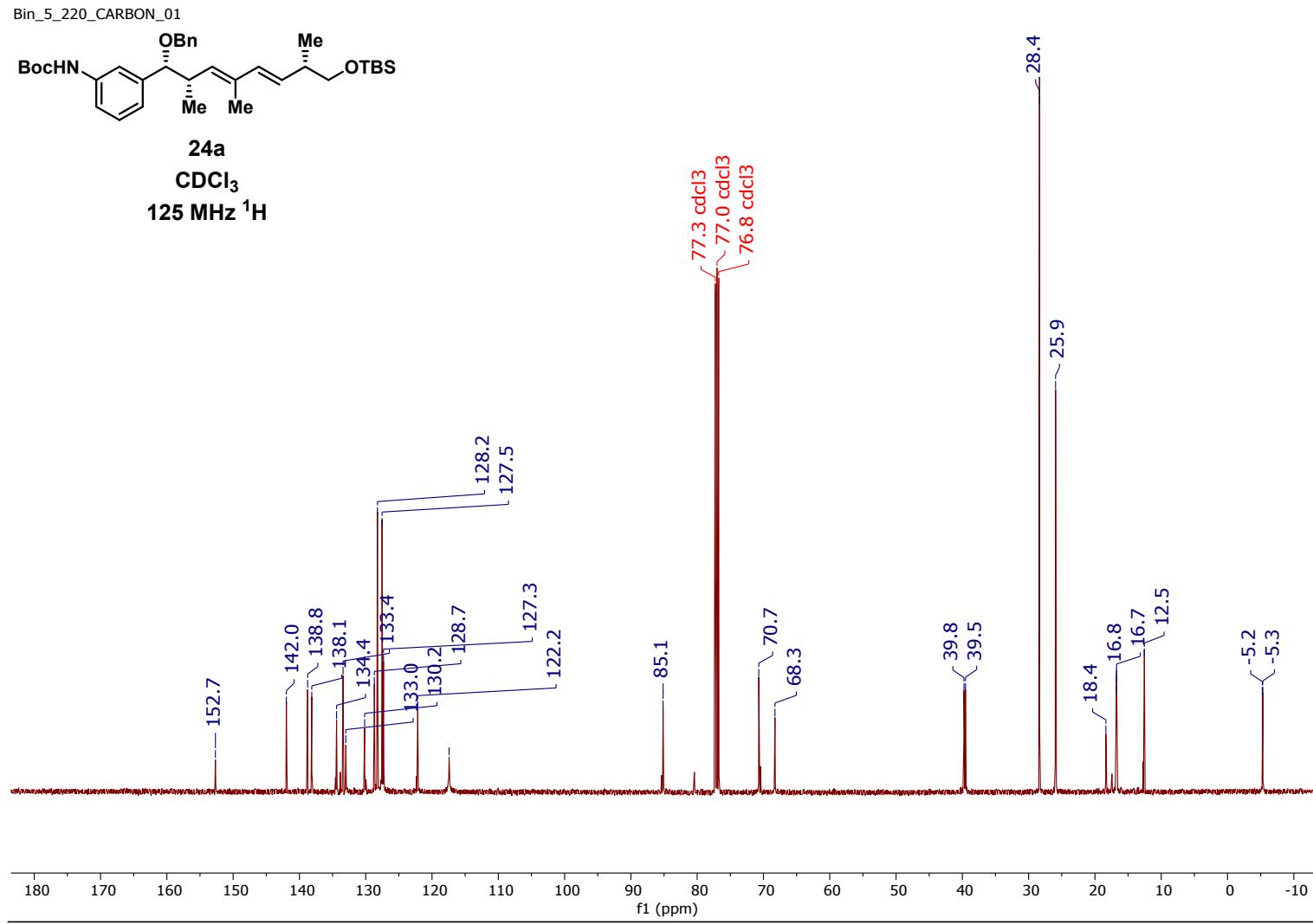
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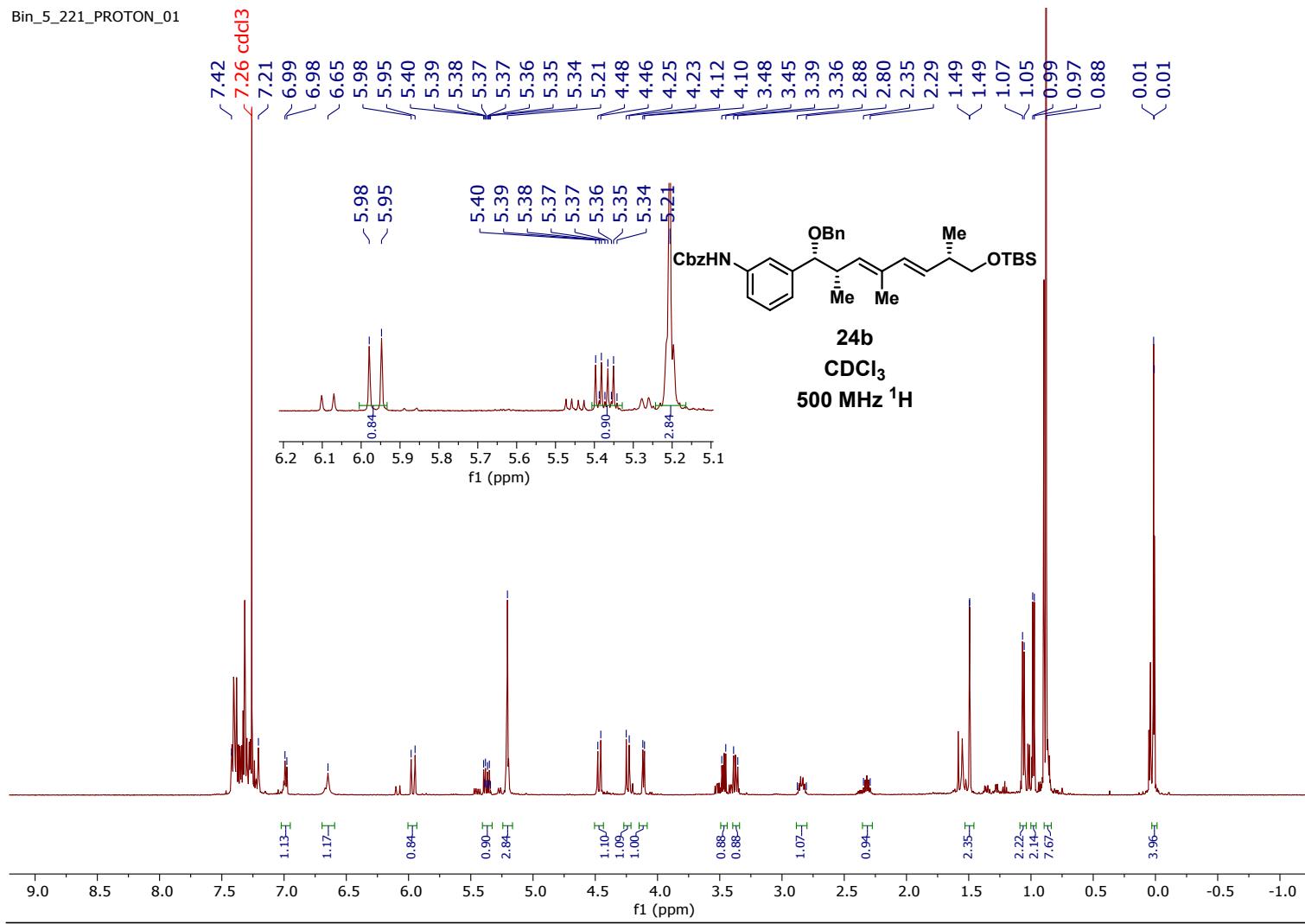


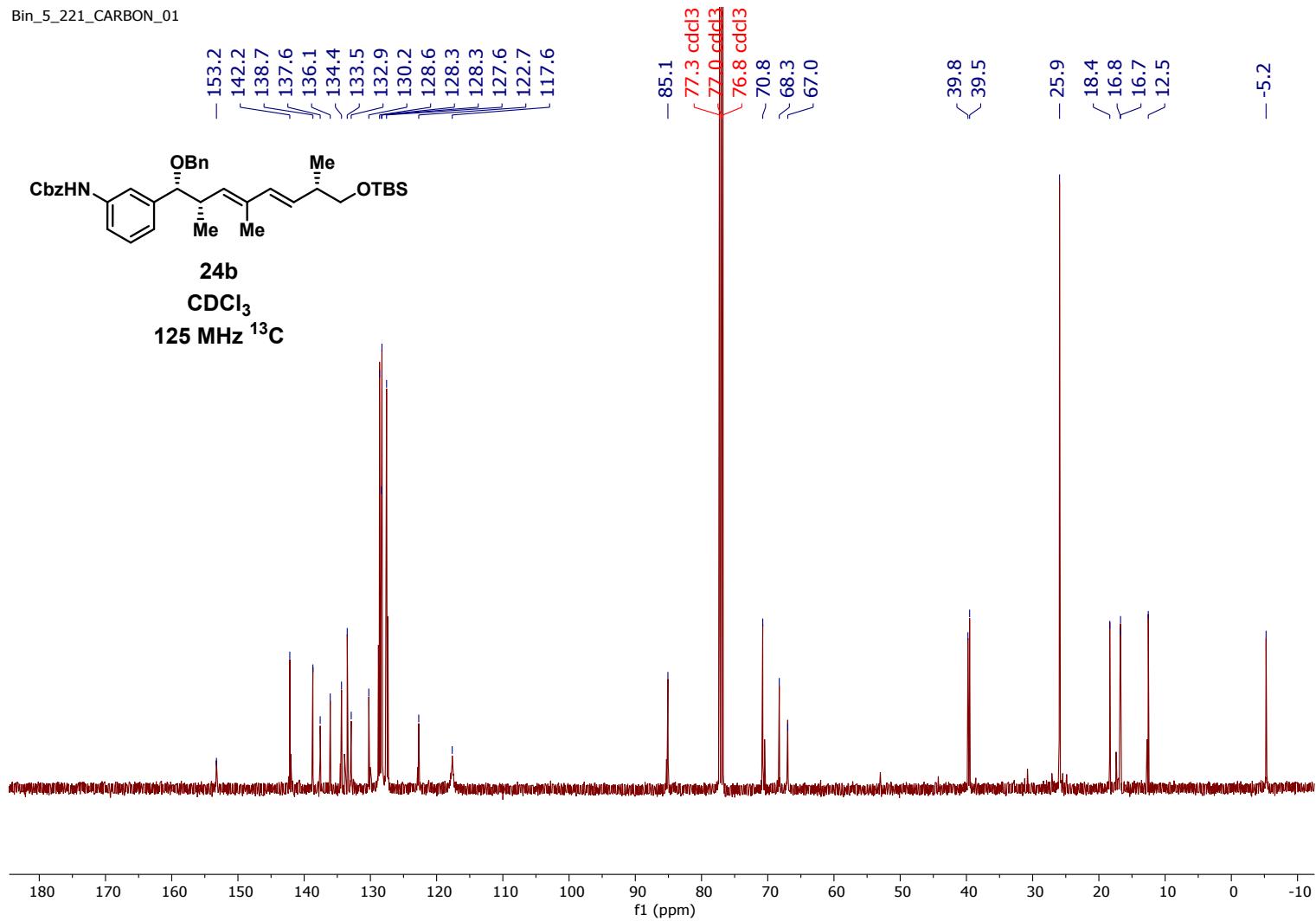
SI-318

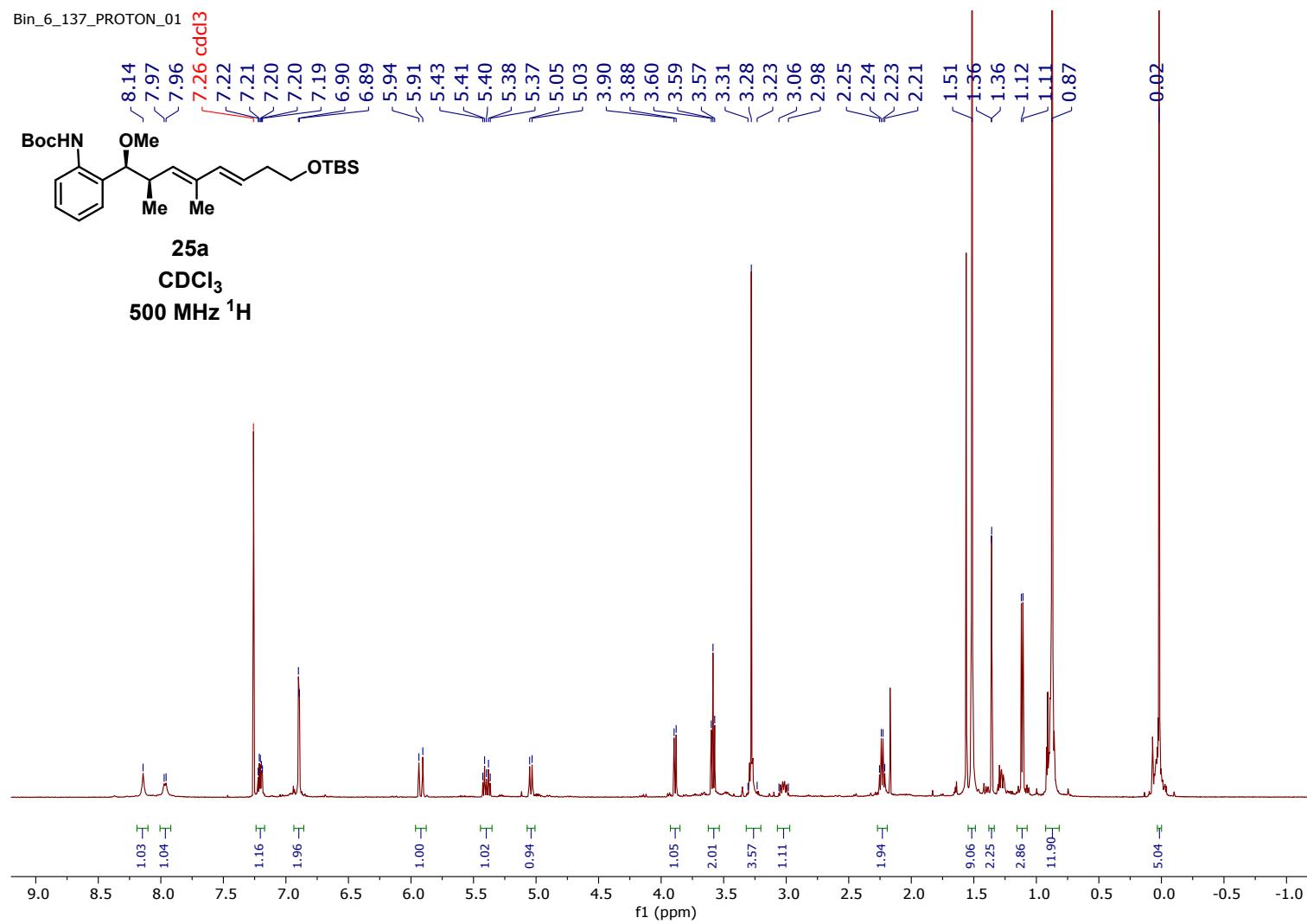


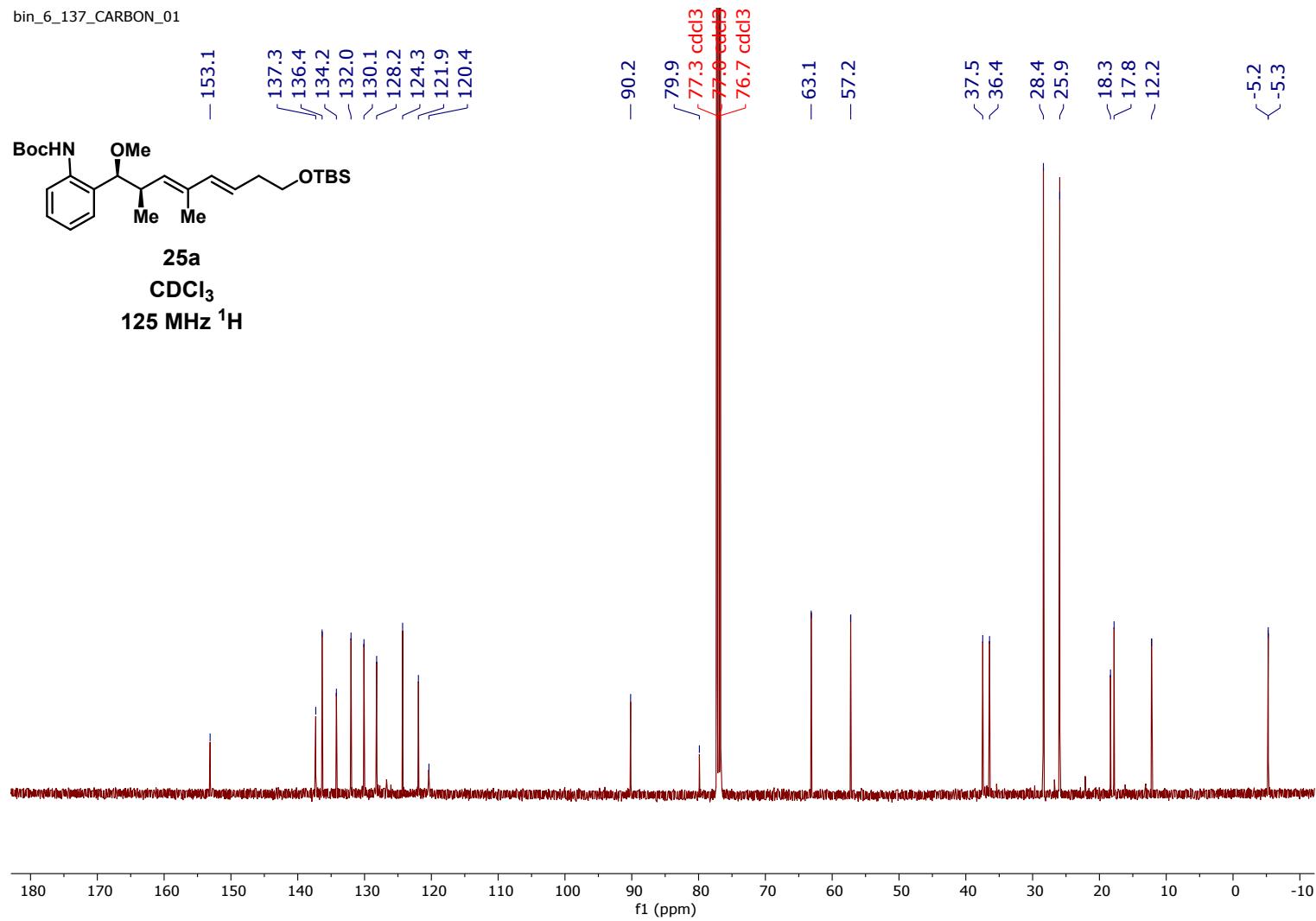


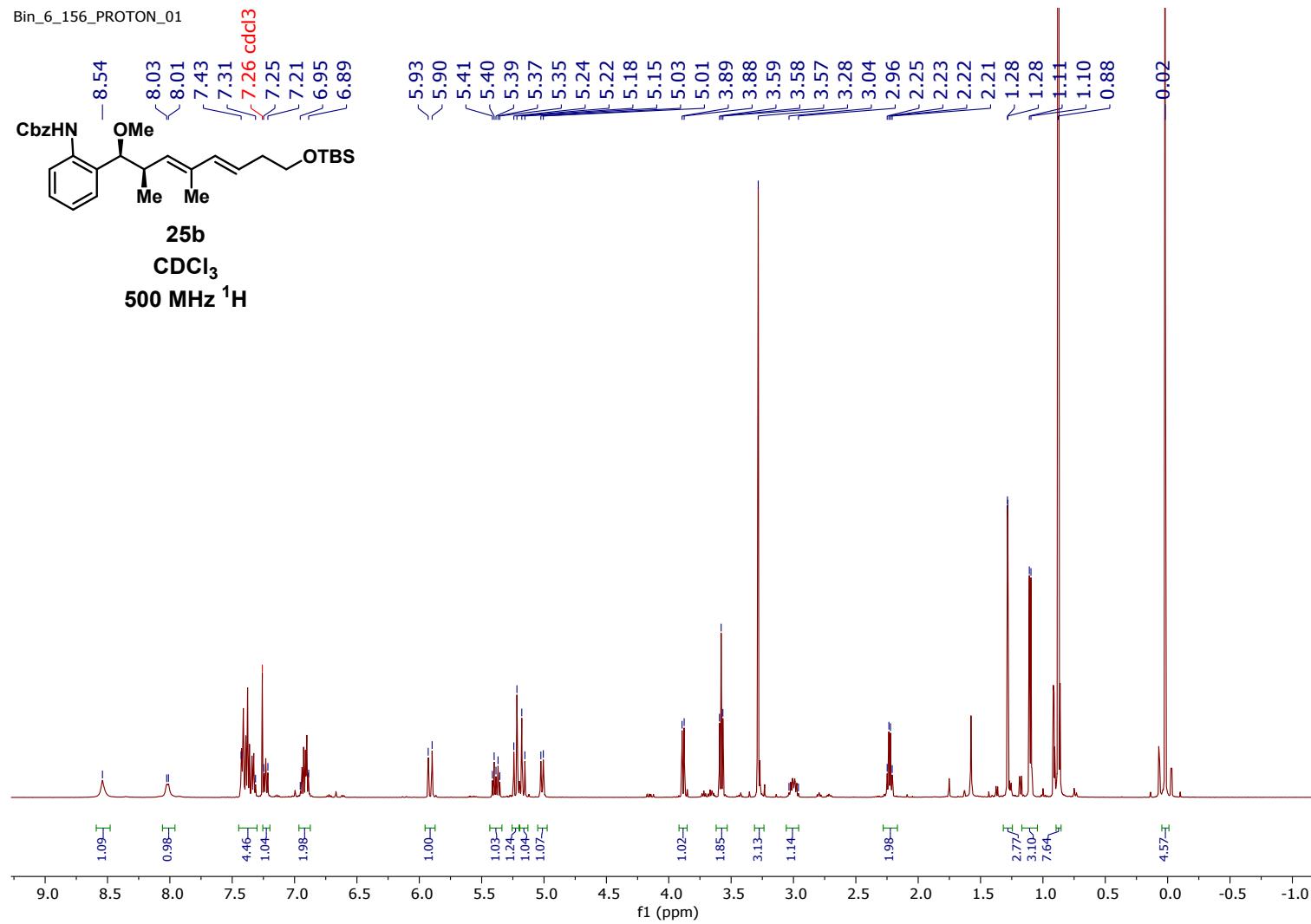


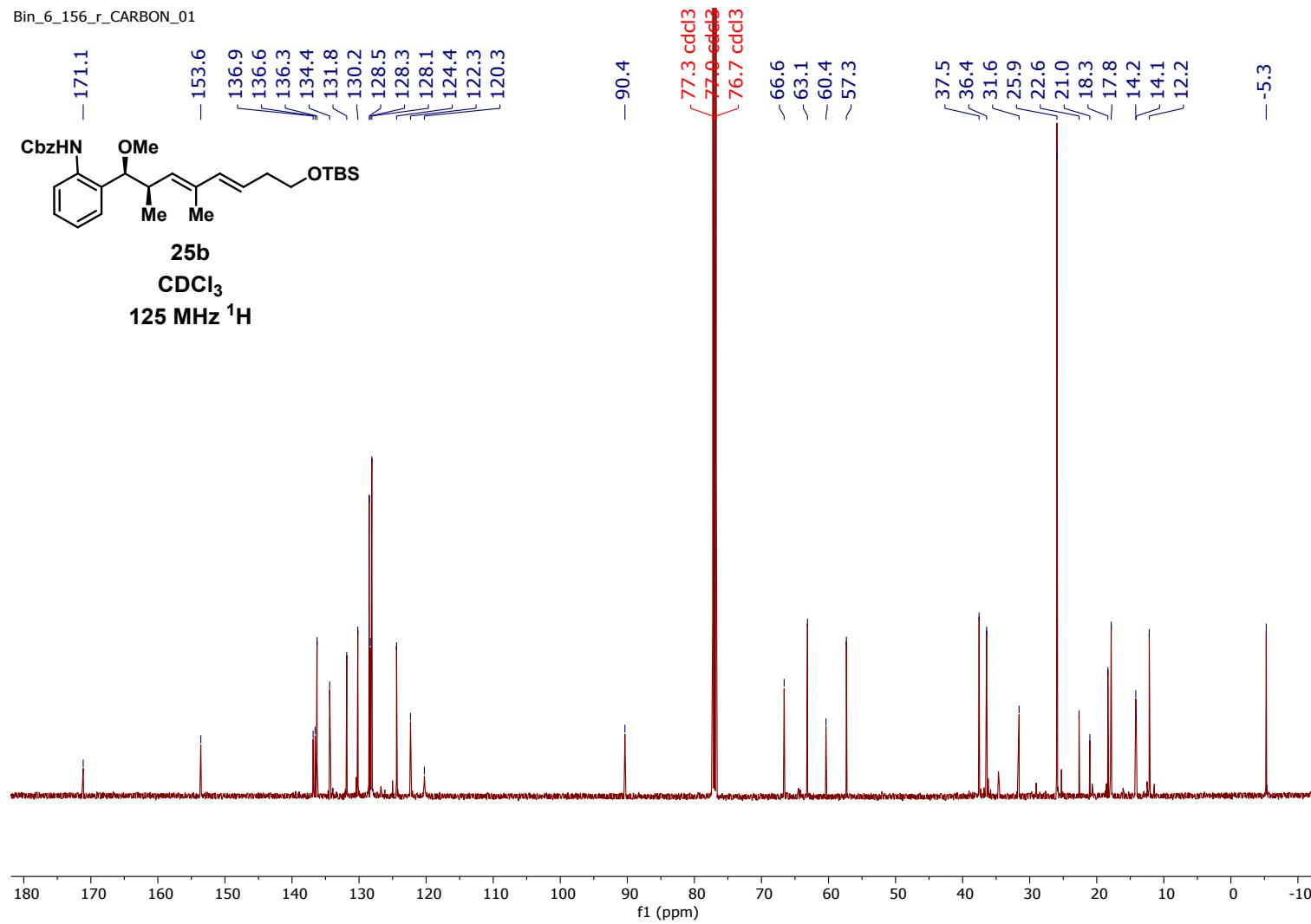


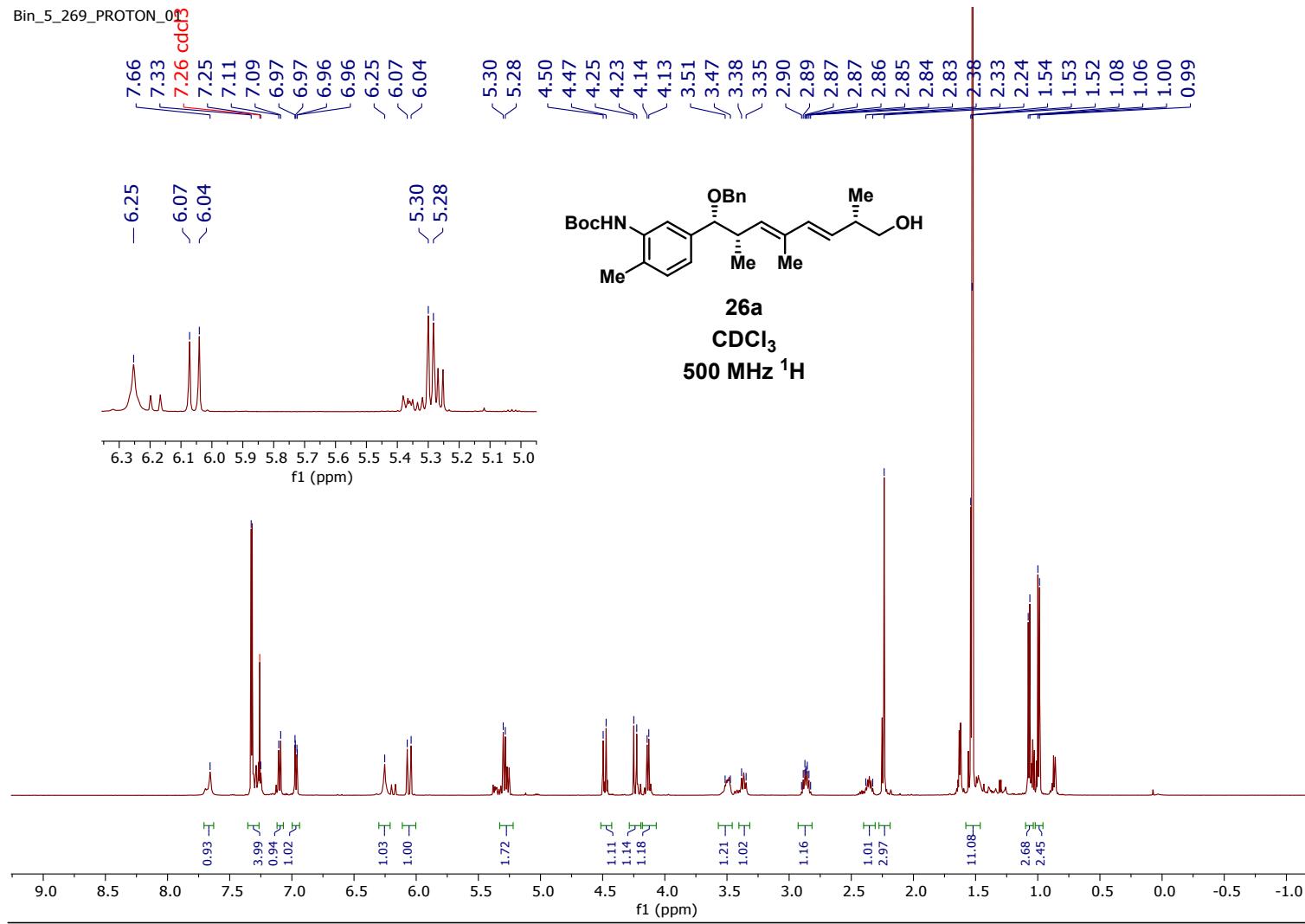


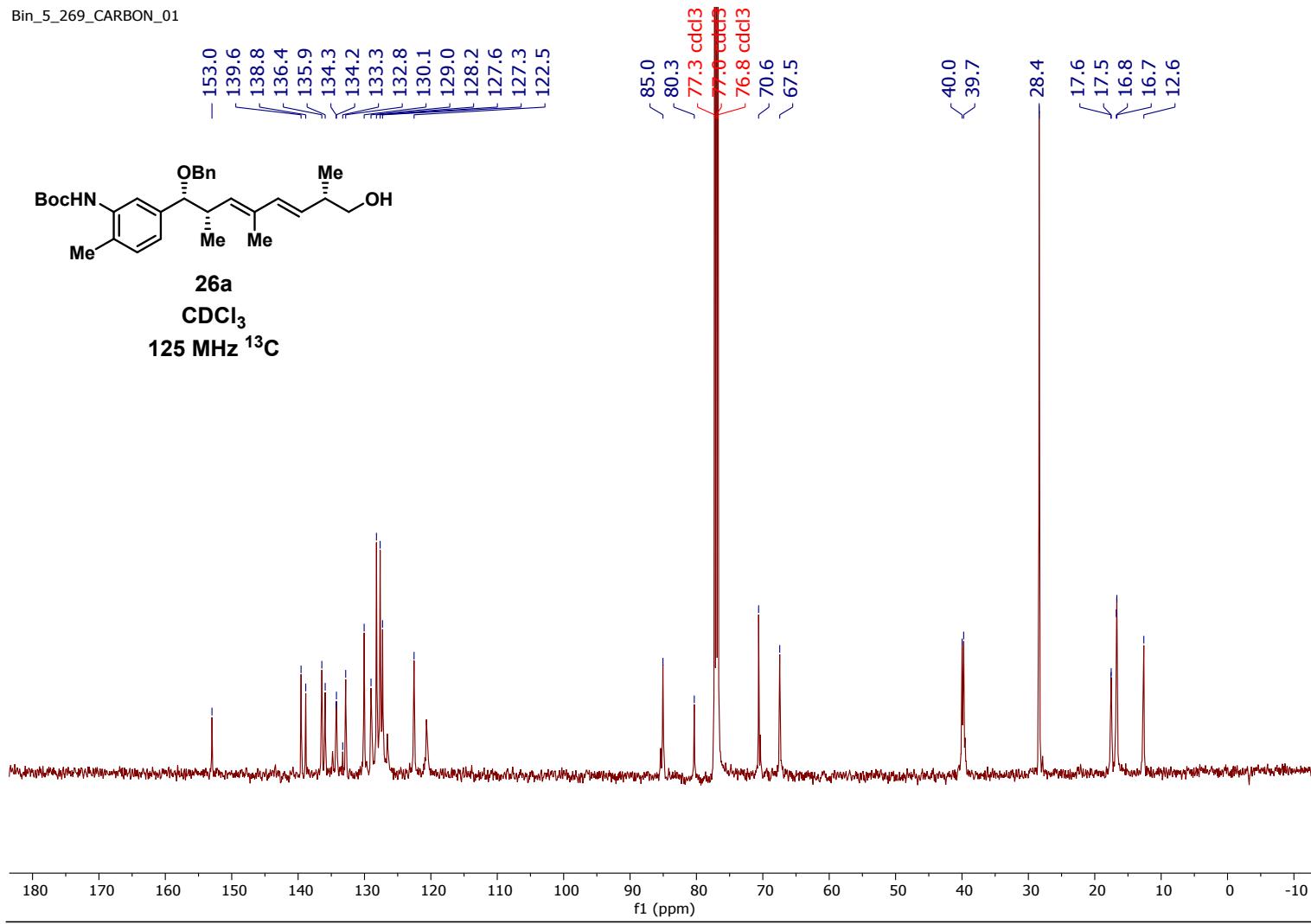


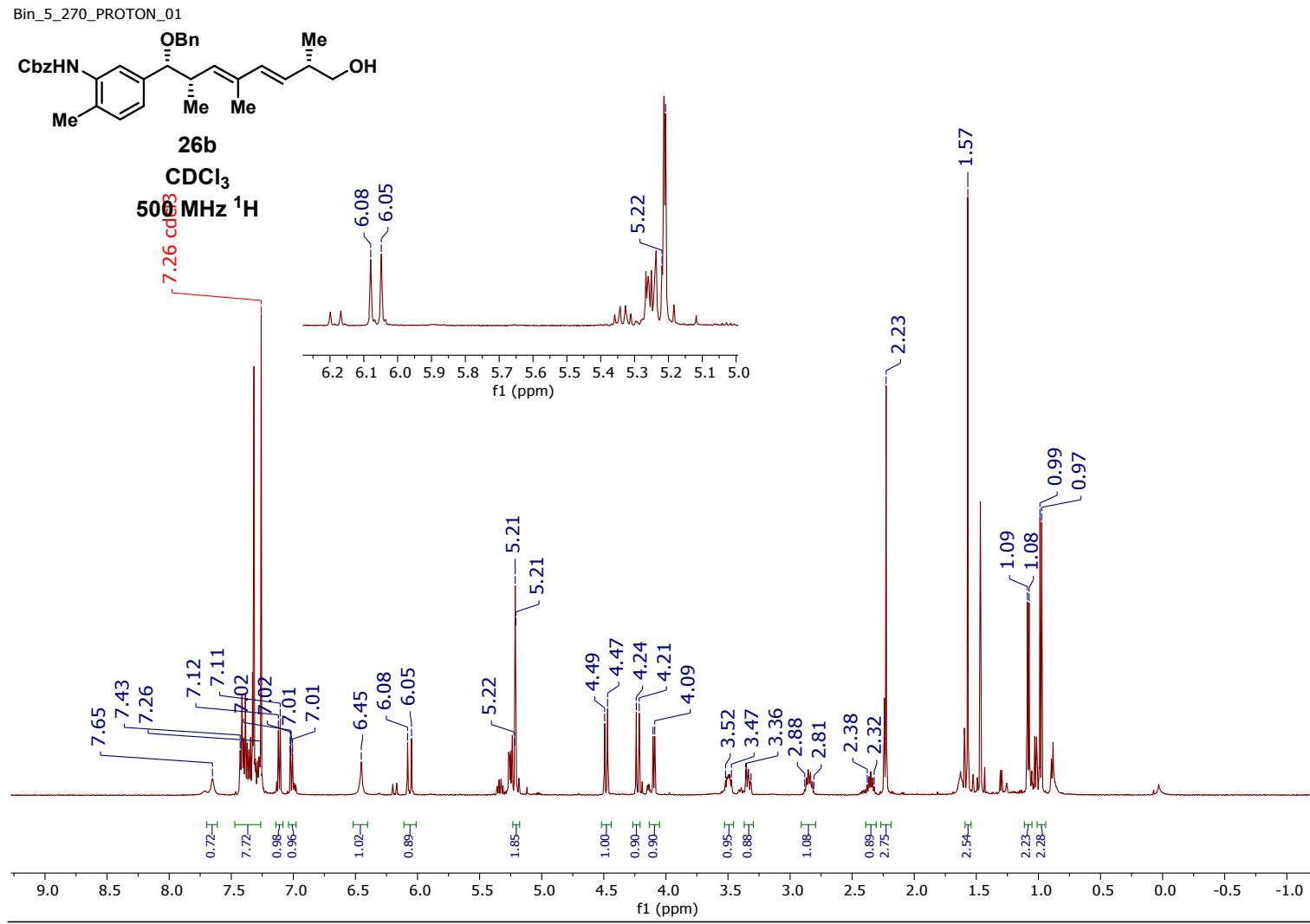


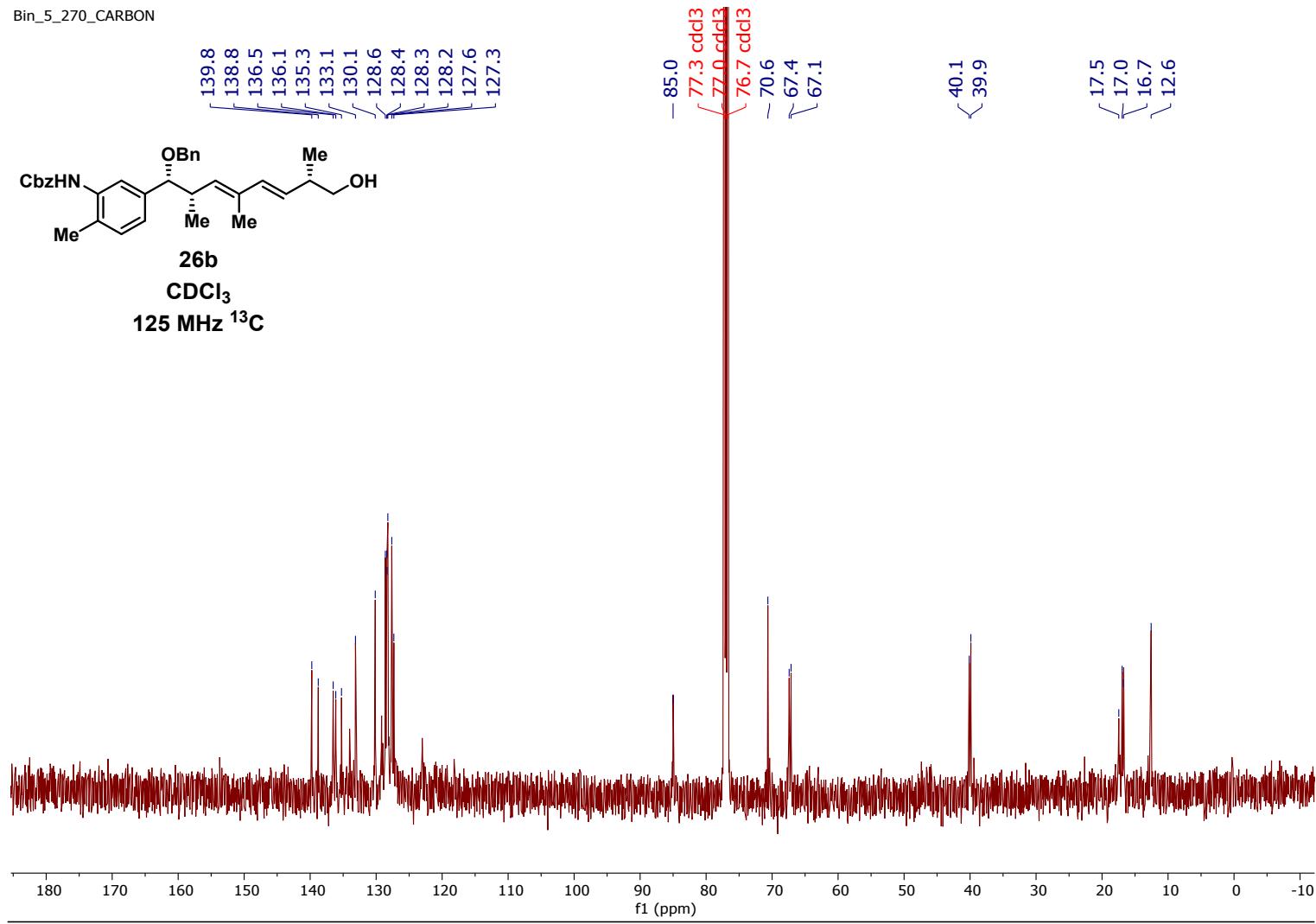


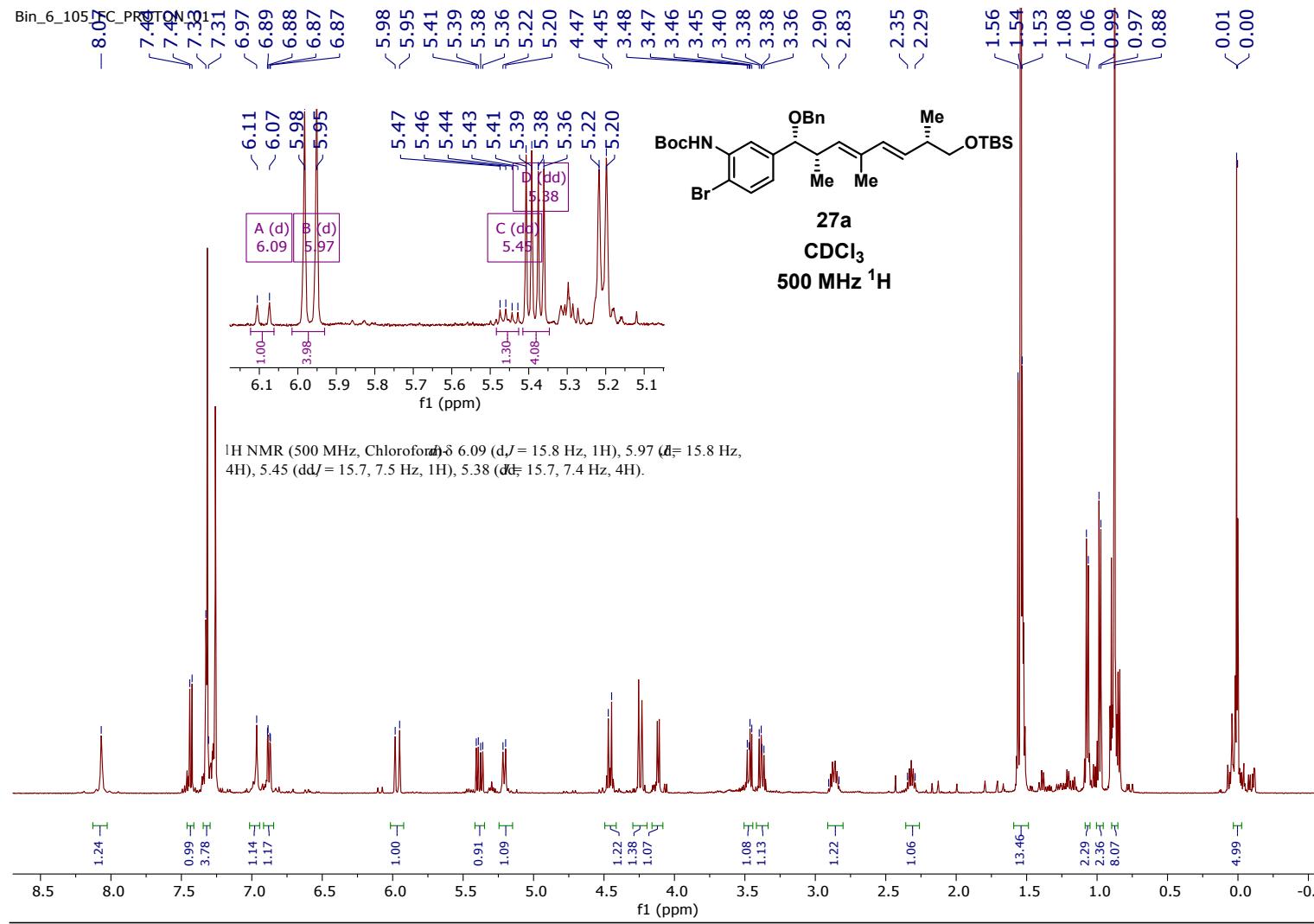


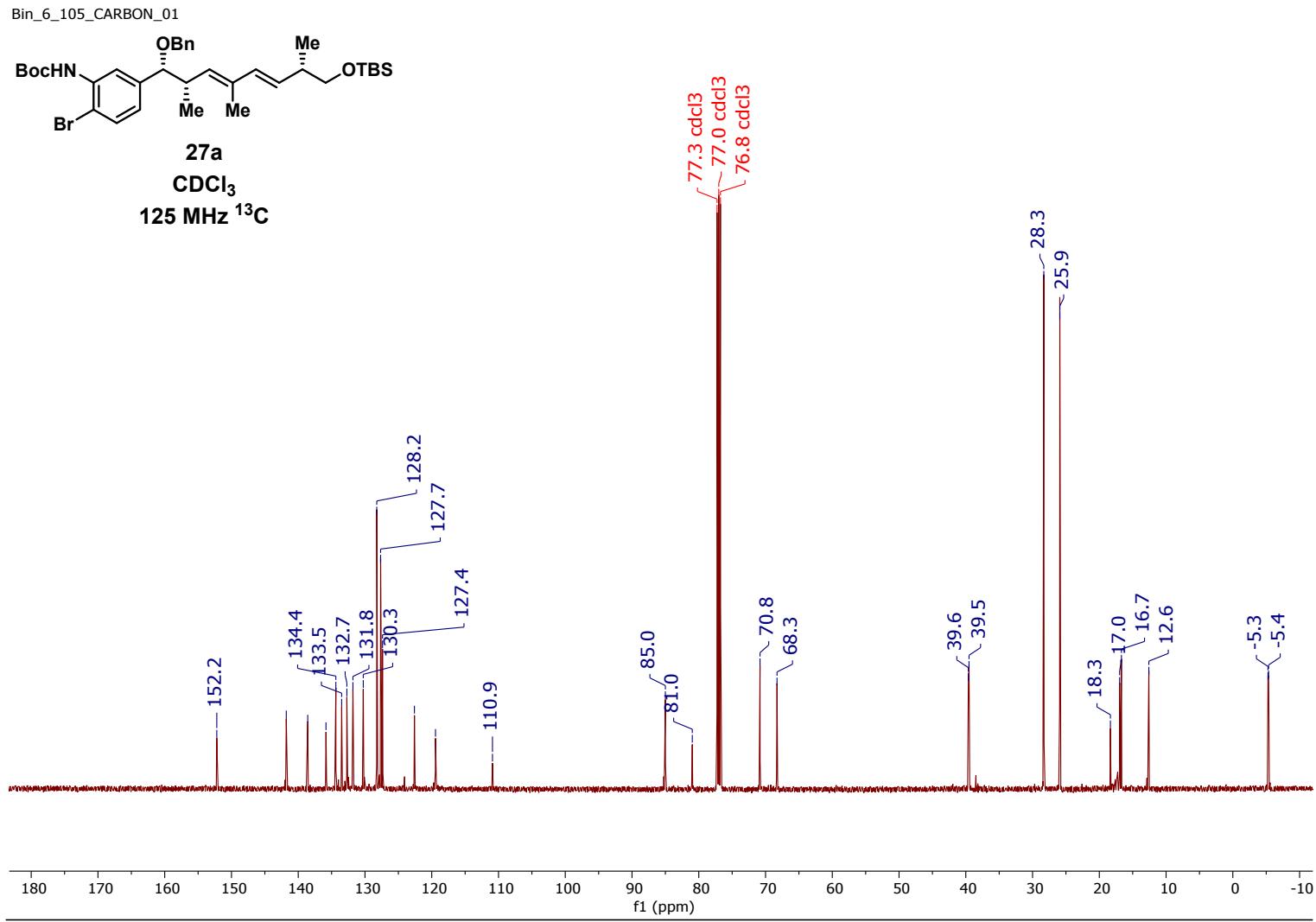


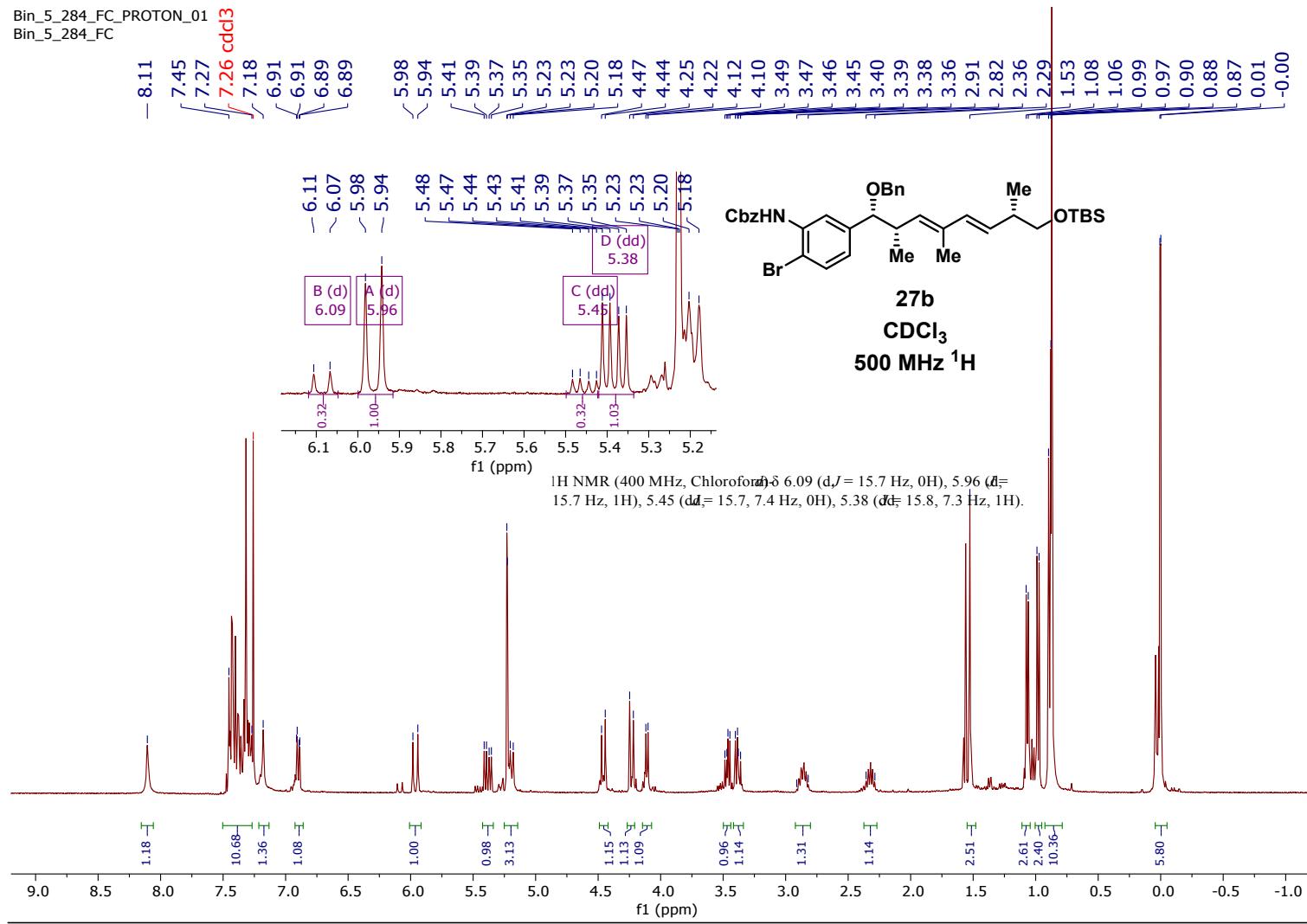


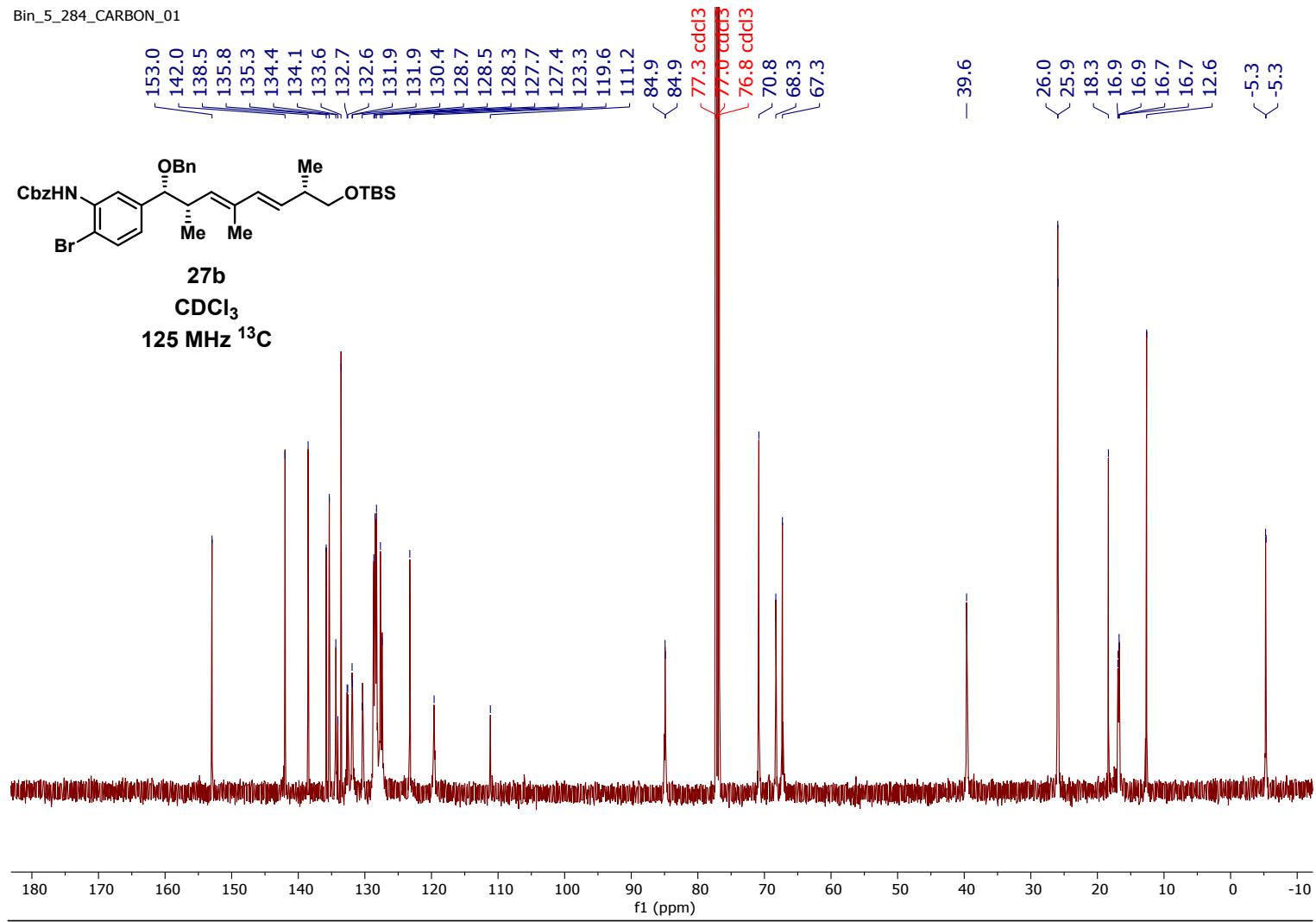


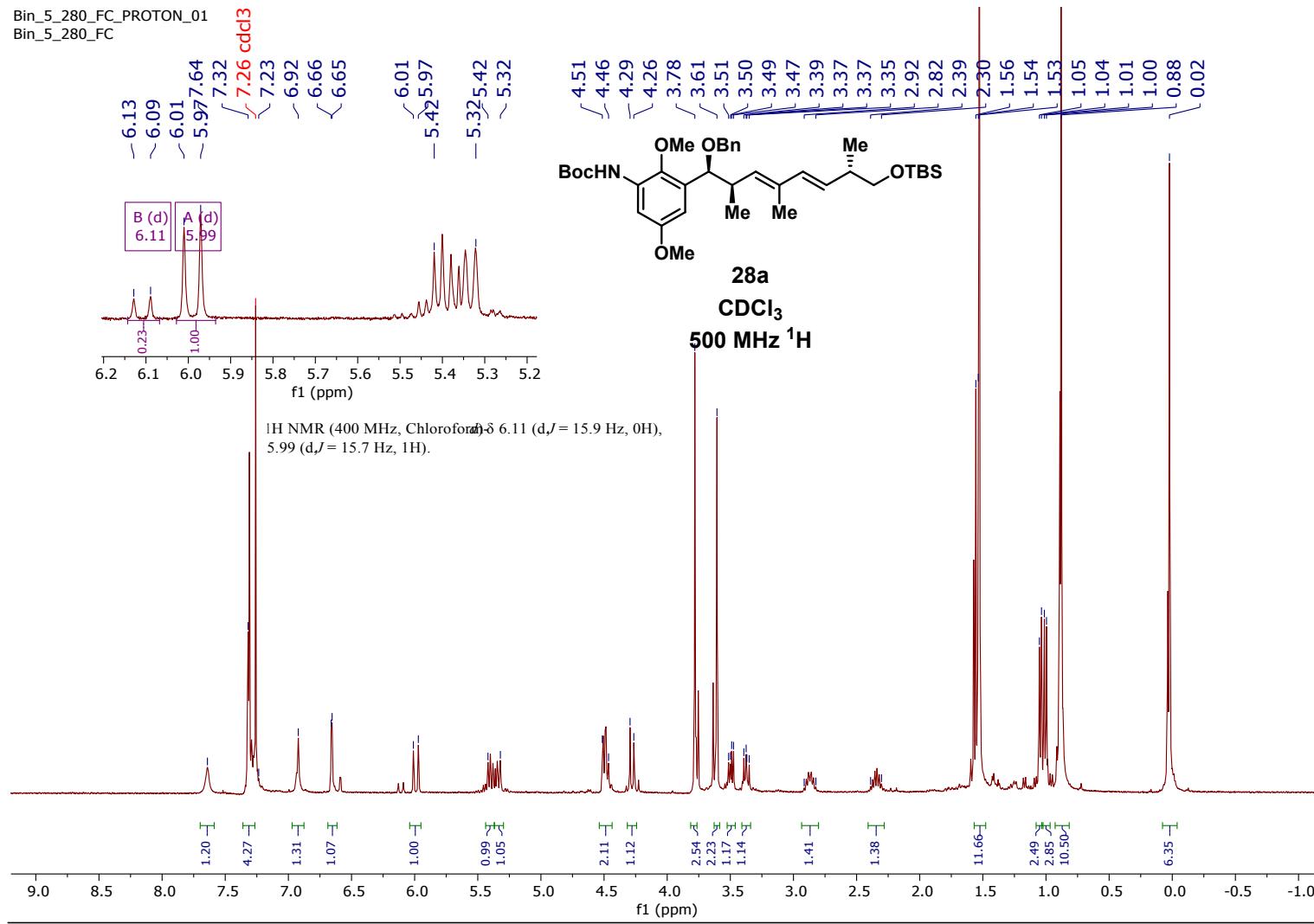


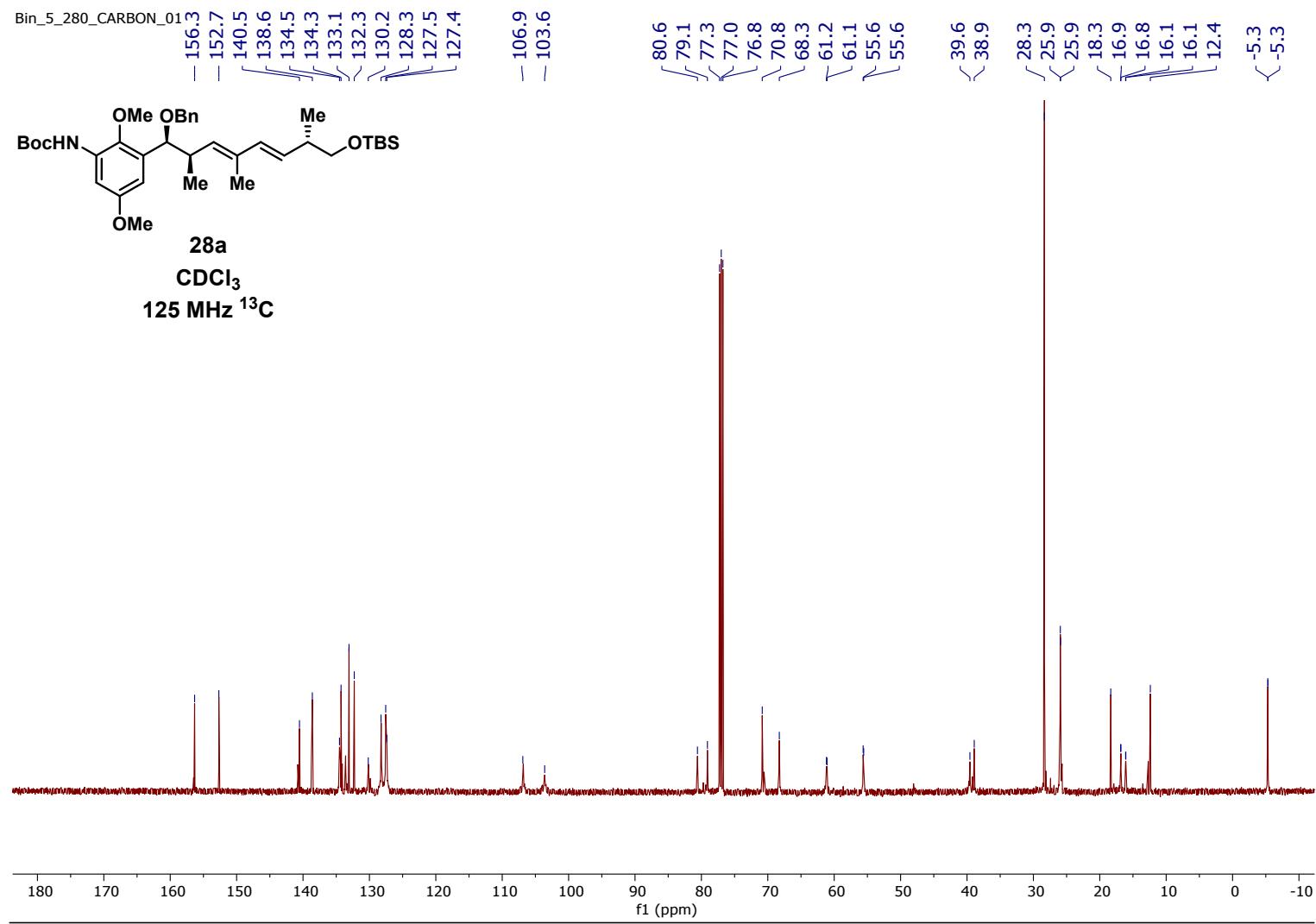


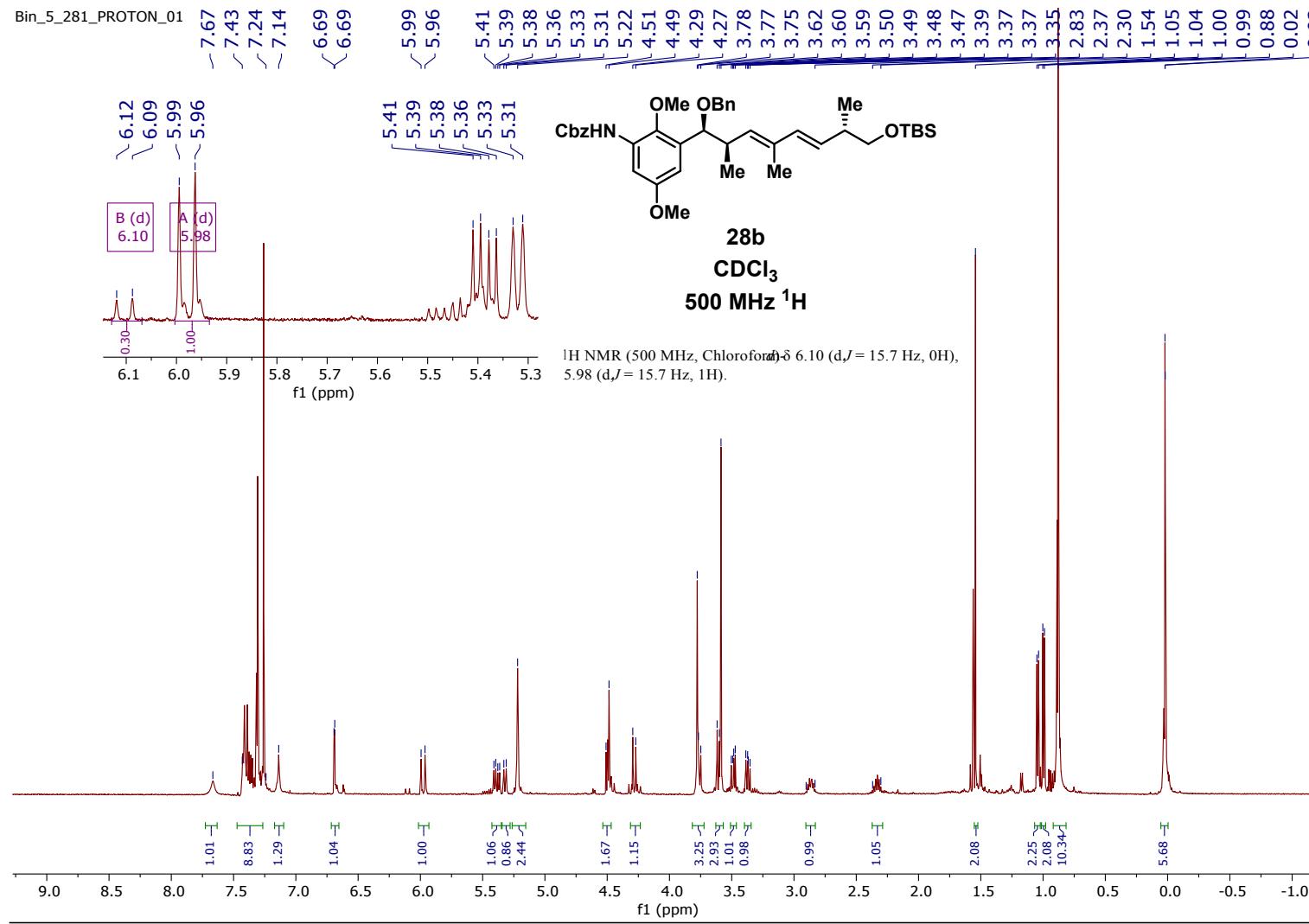


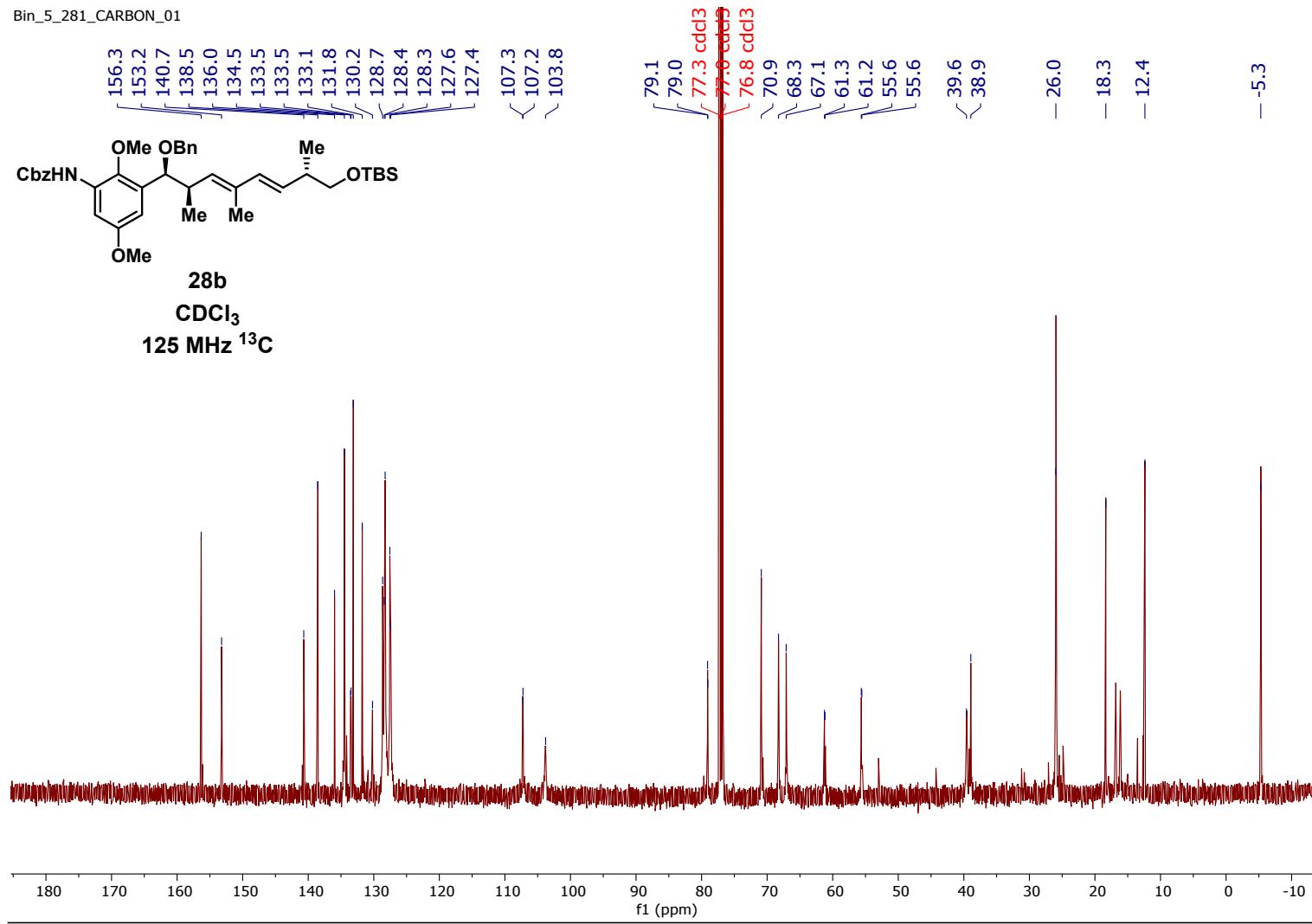


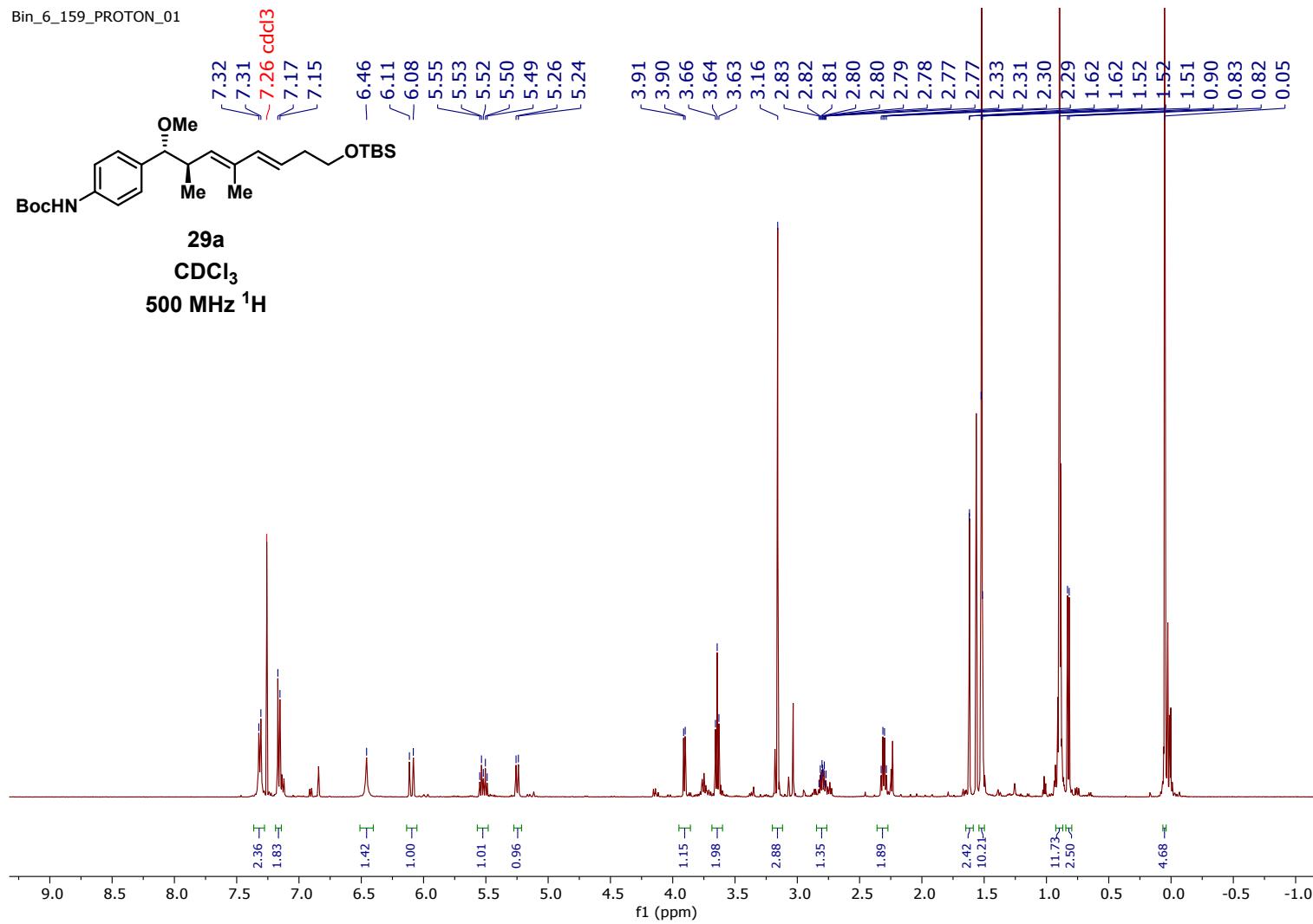


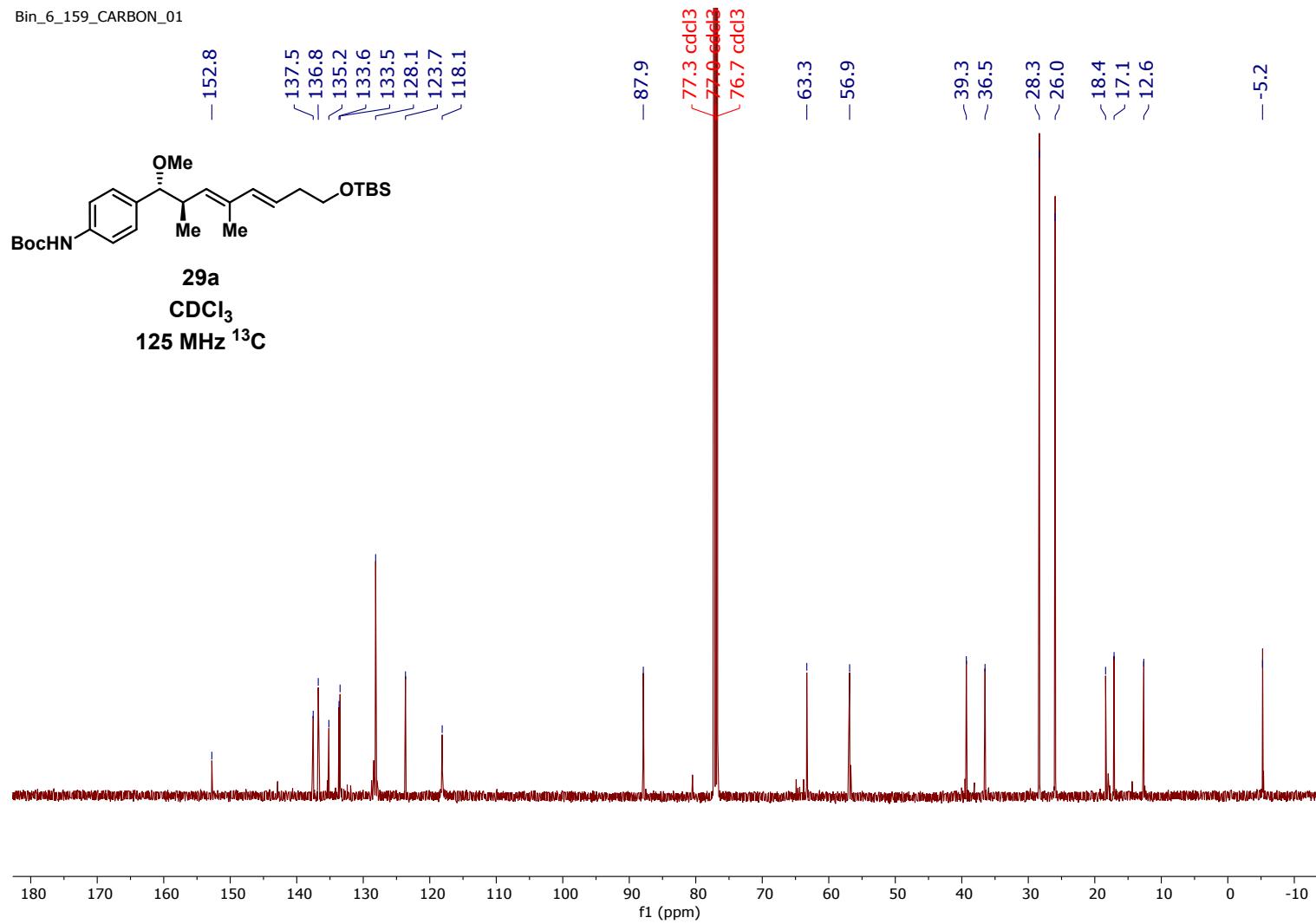


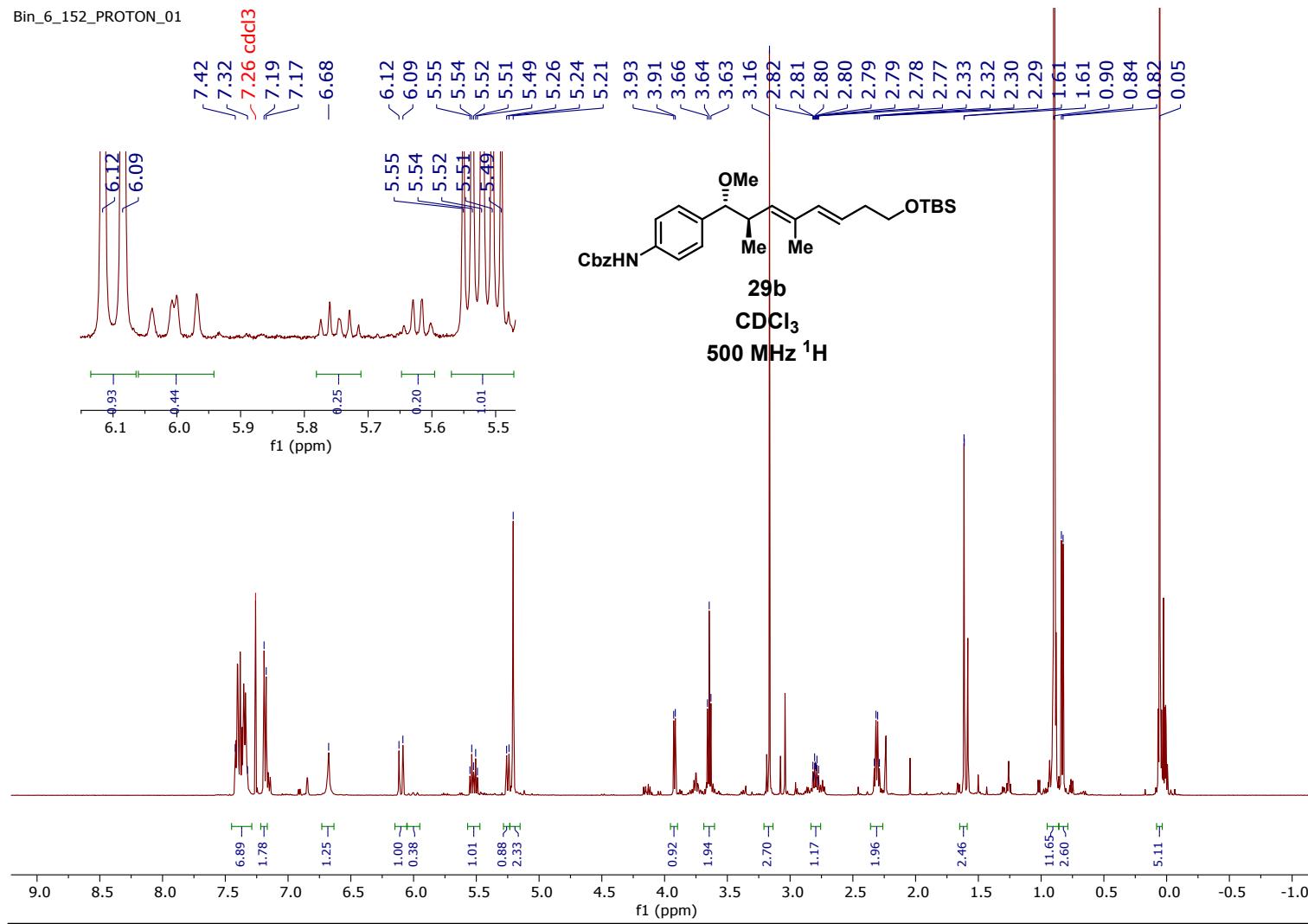


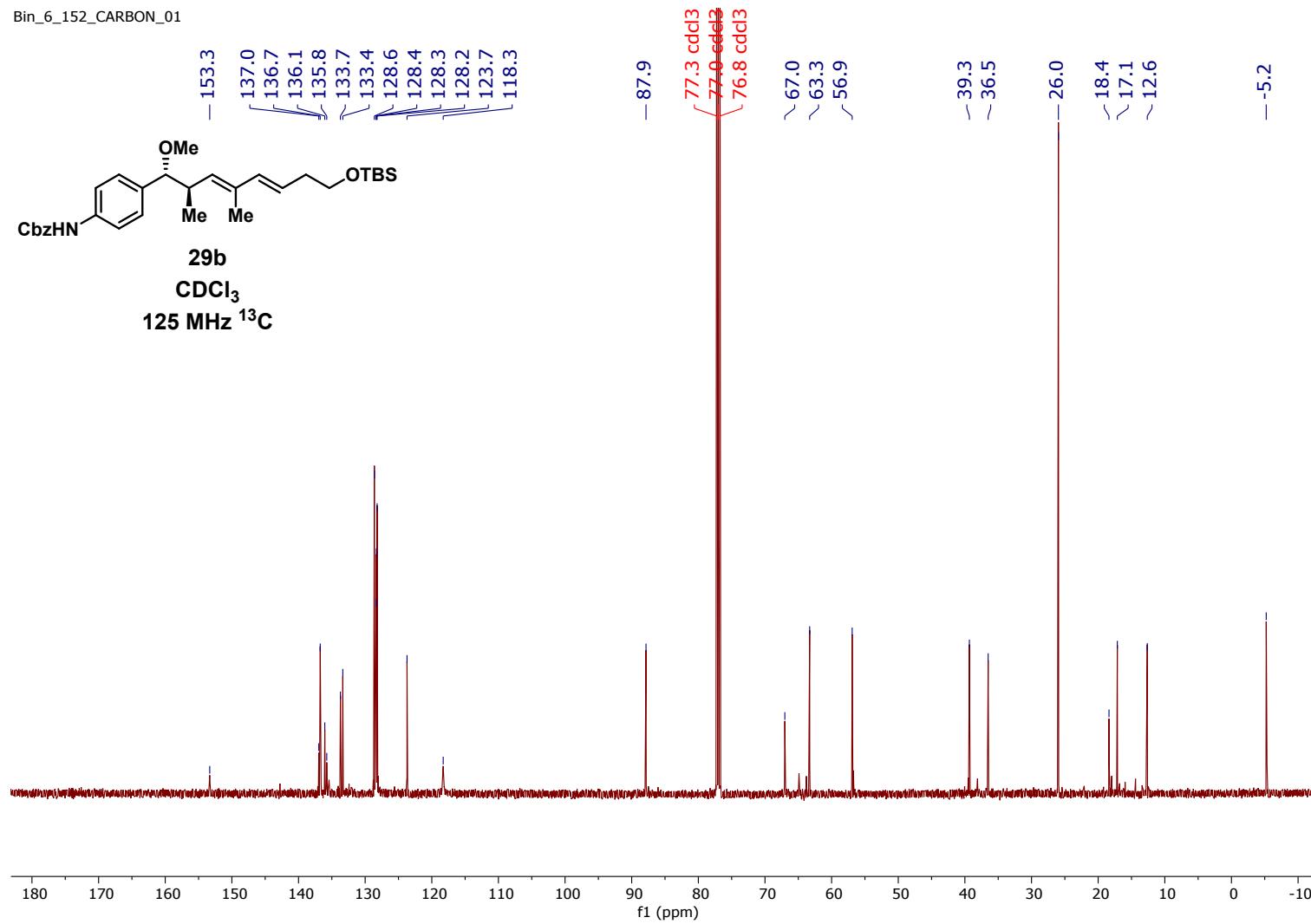


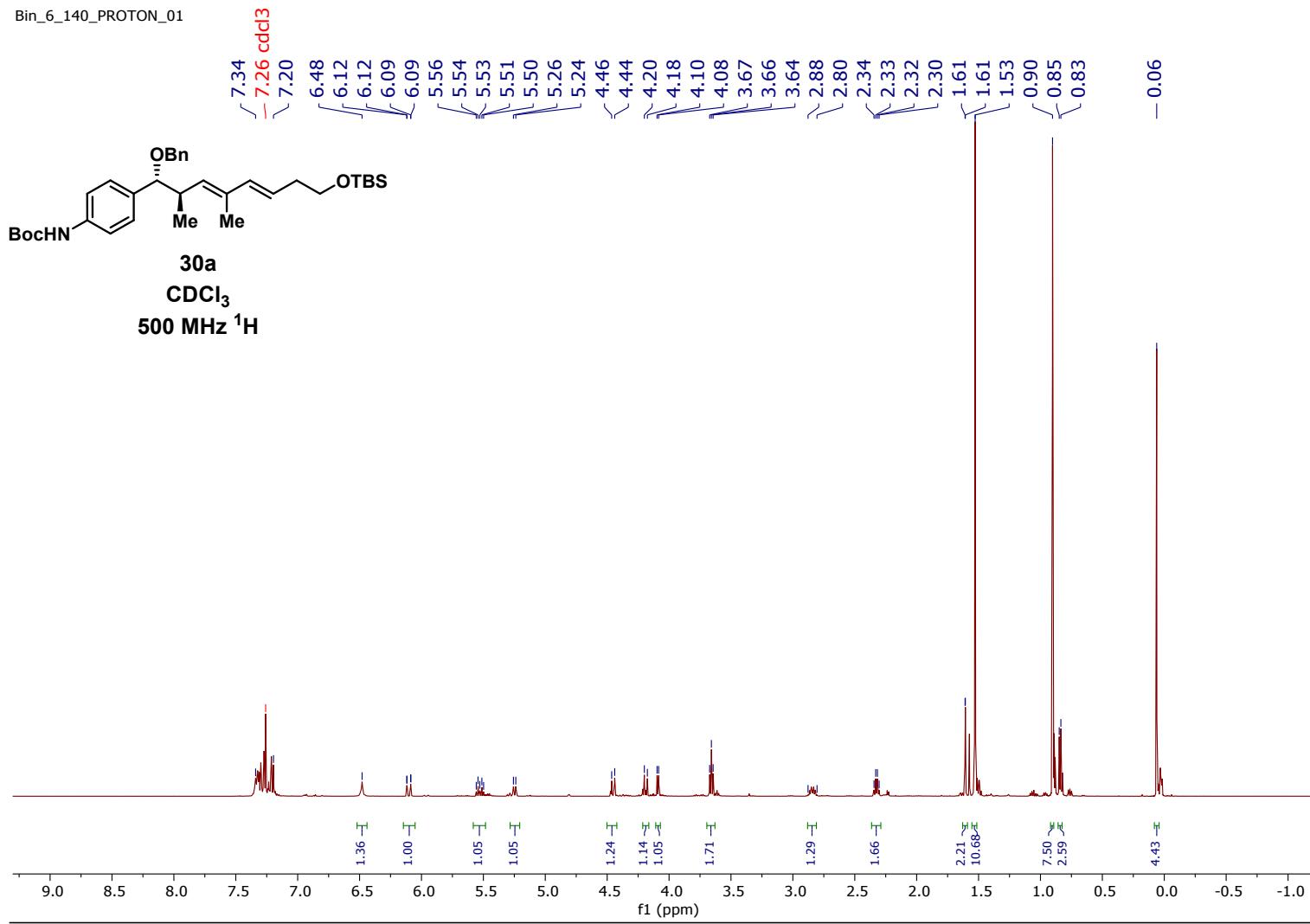


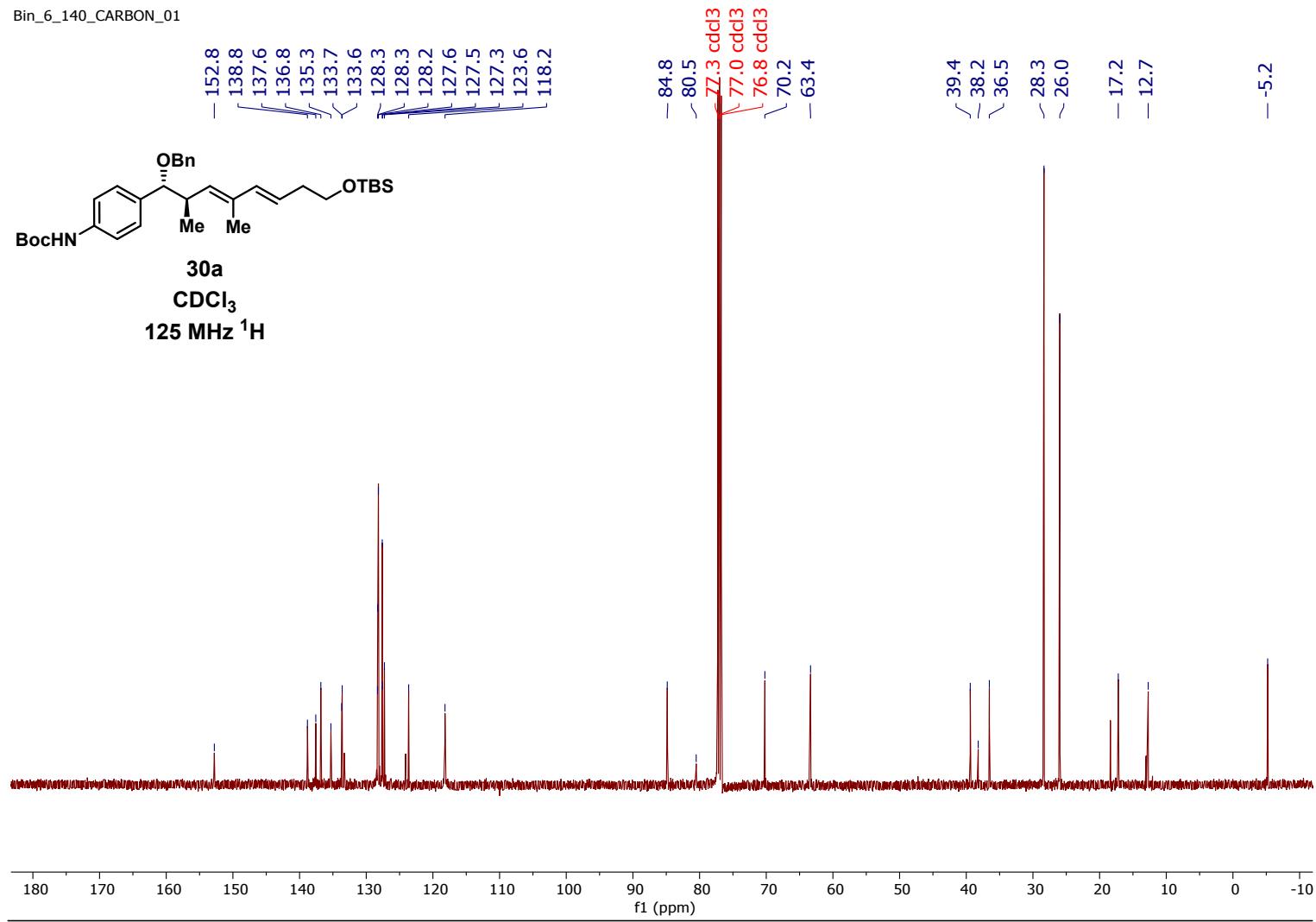


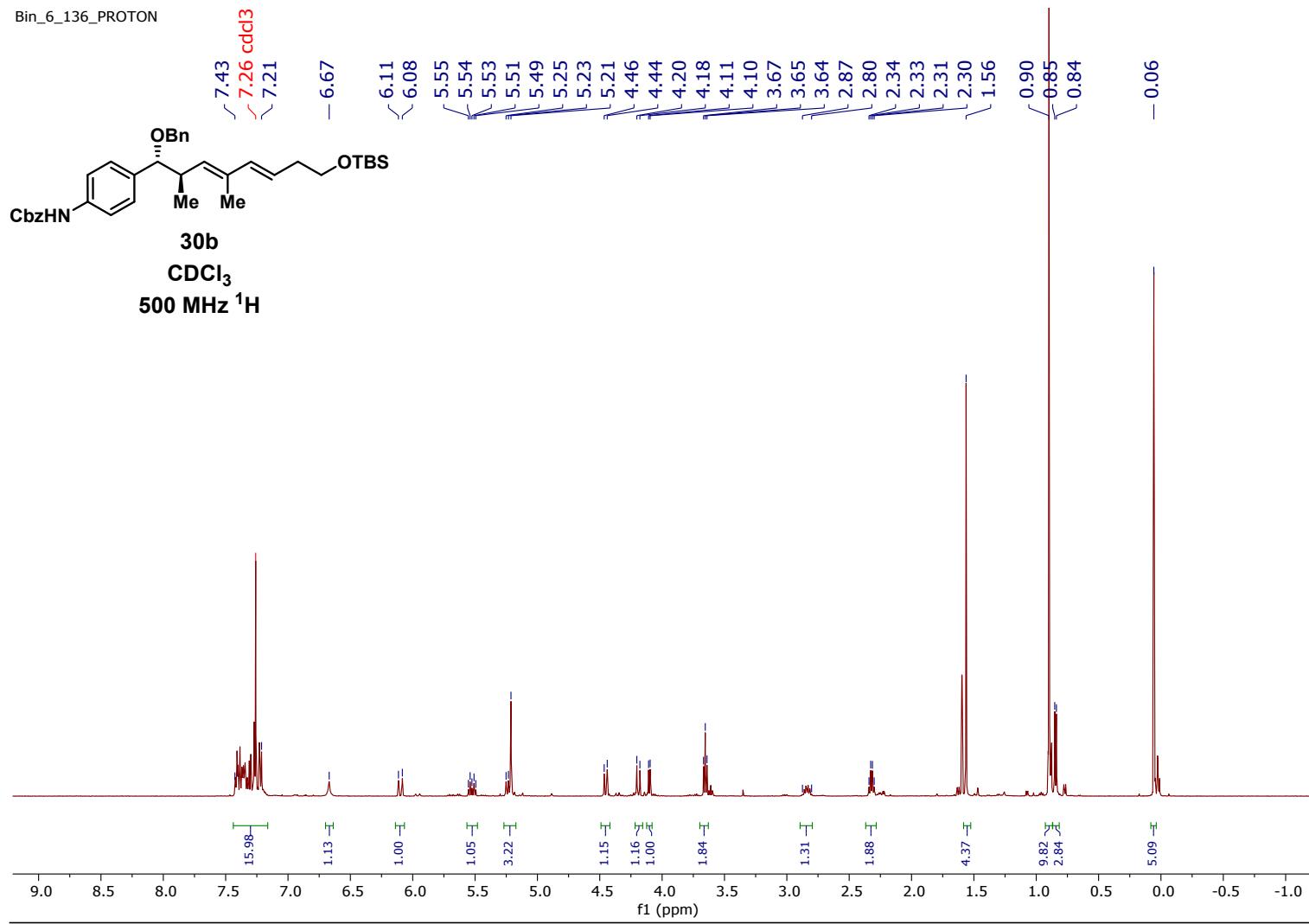


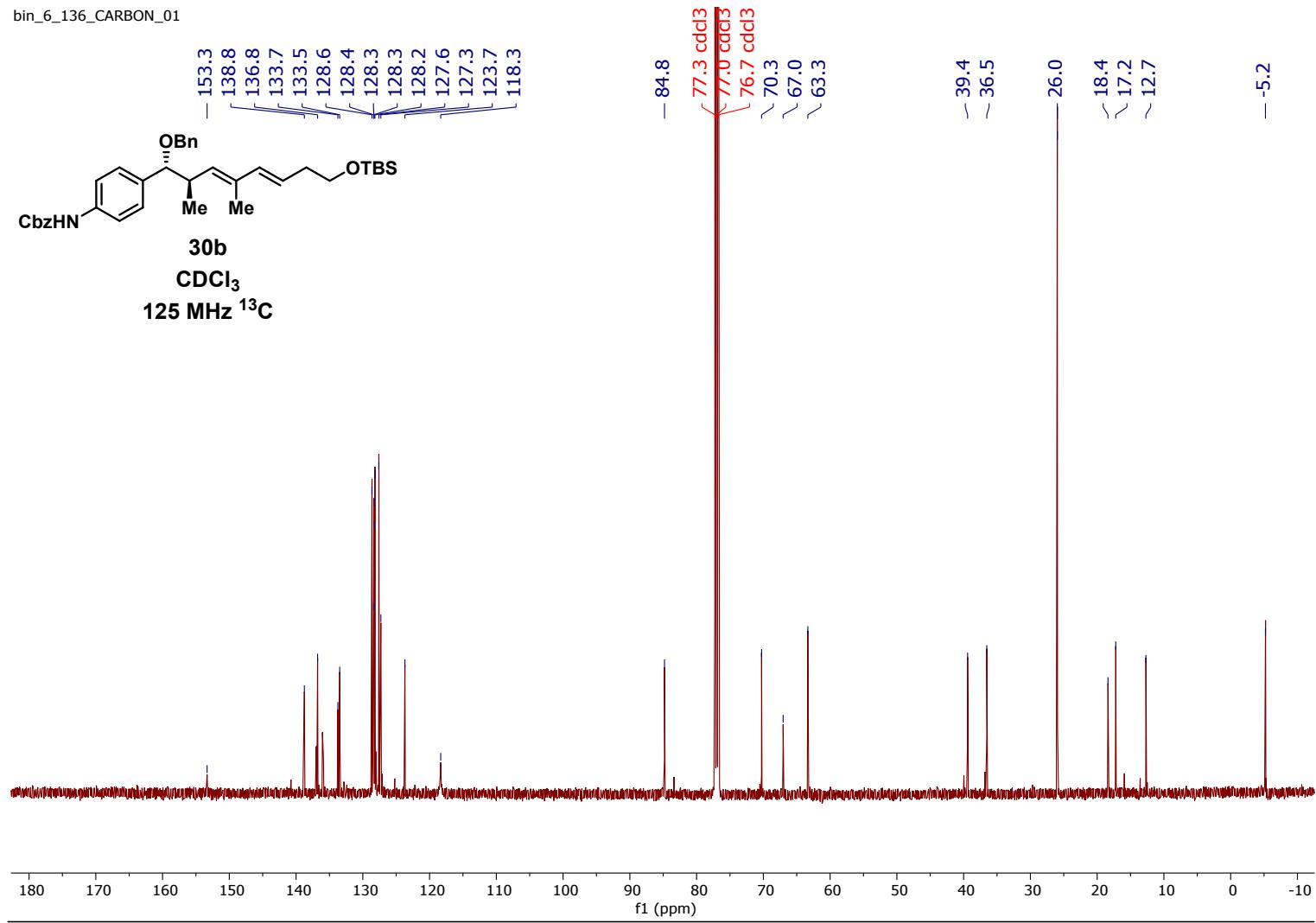


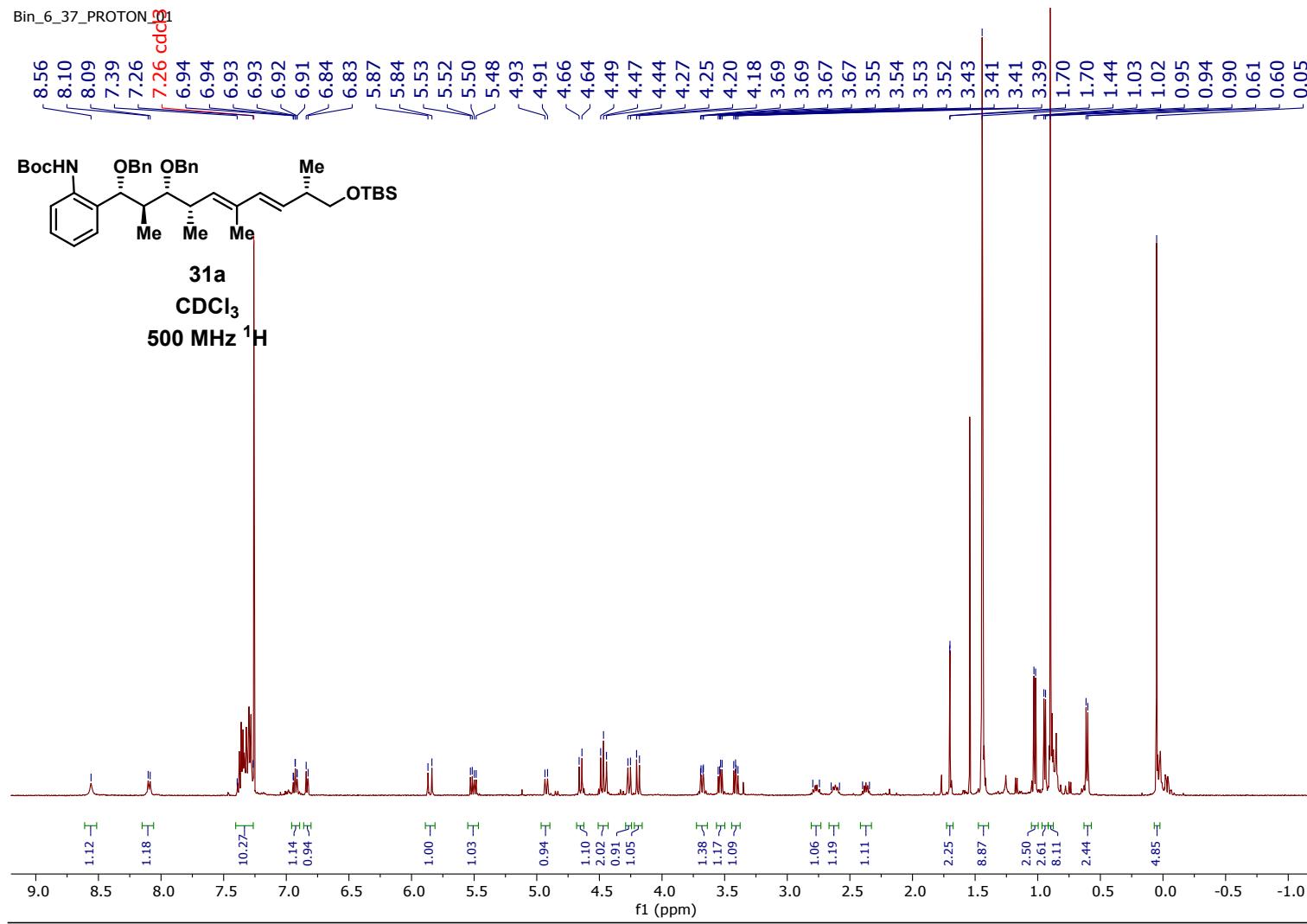


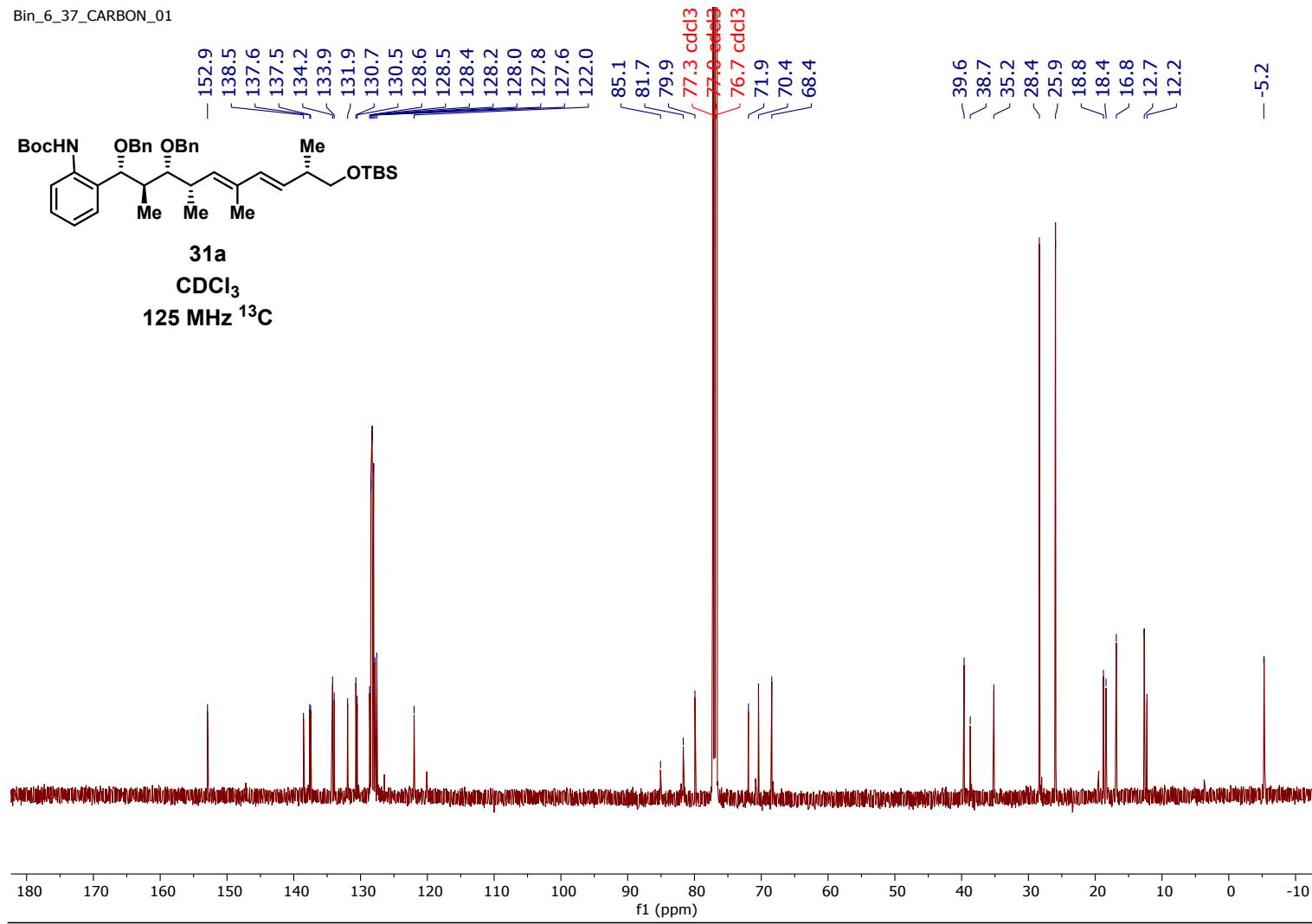


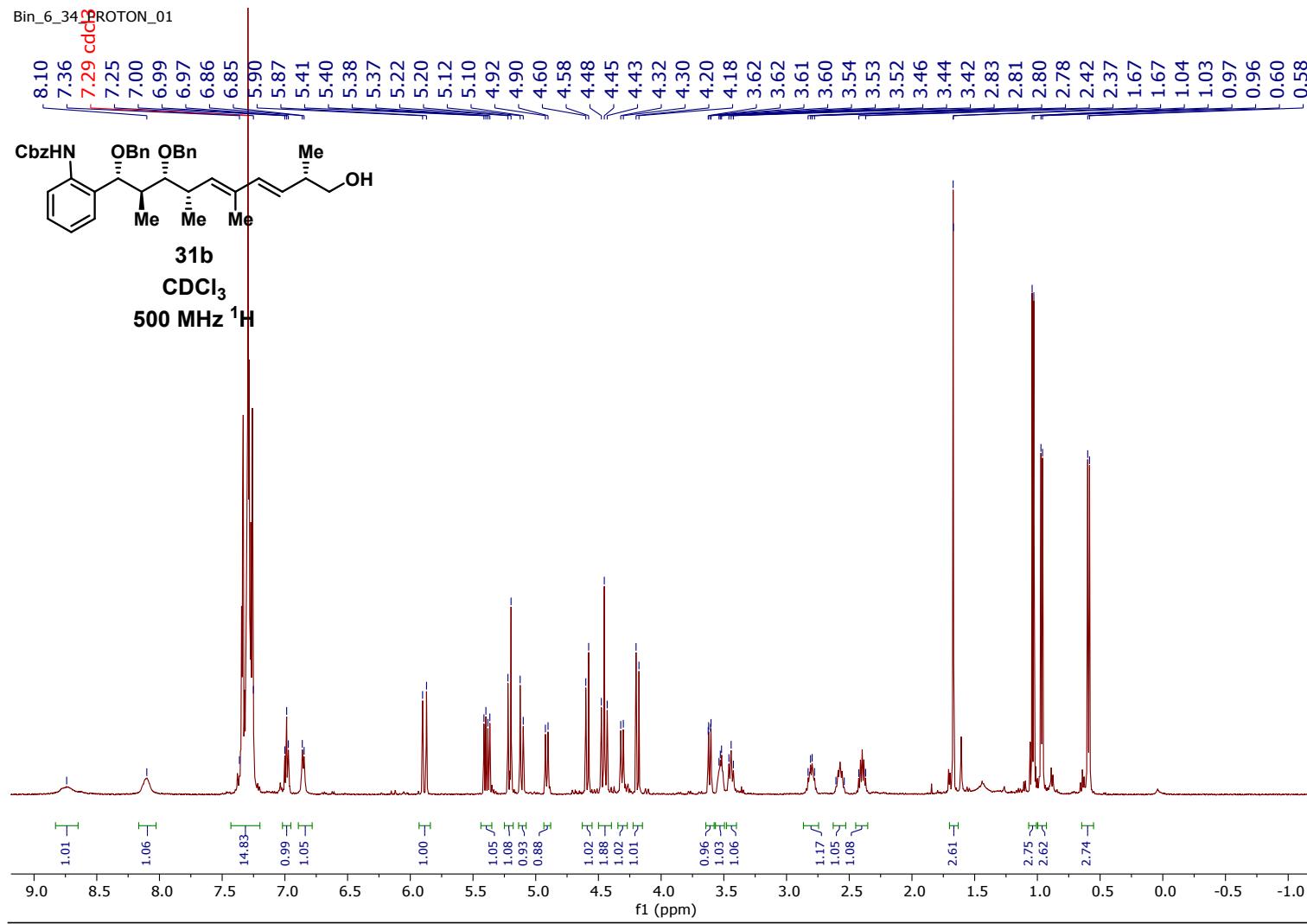


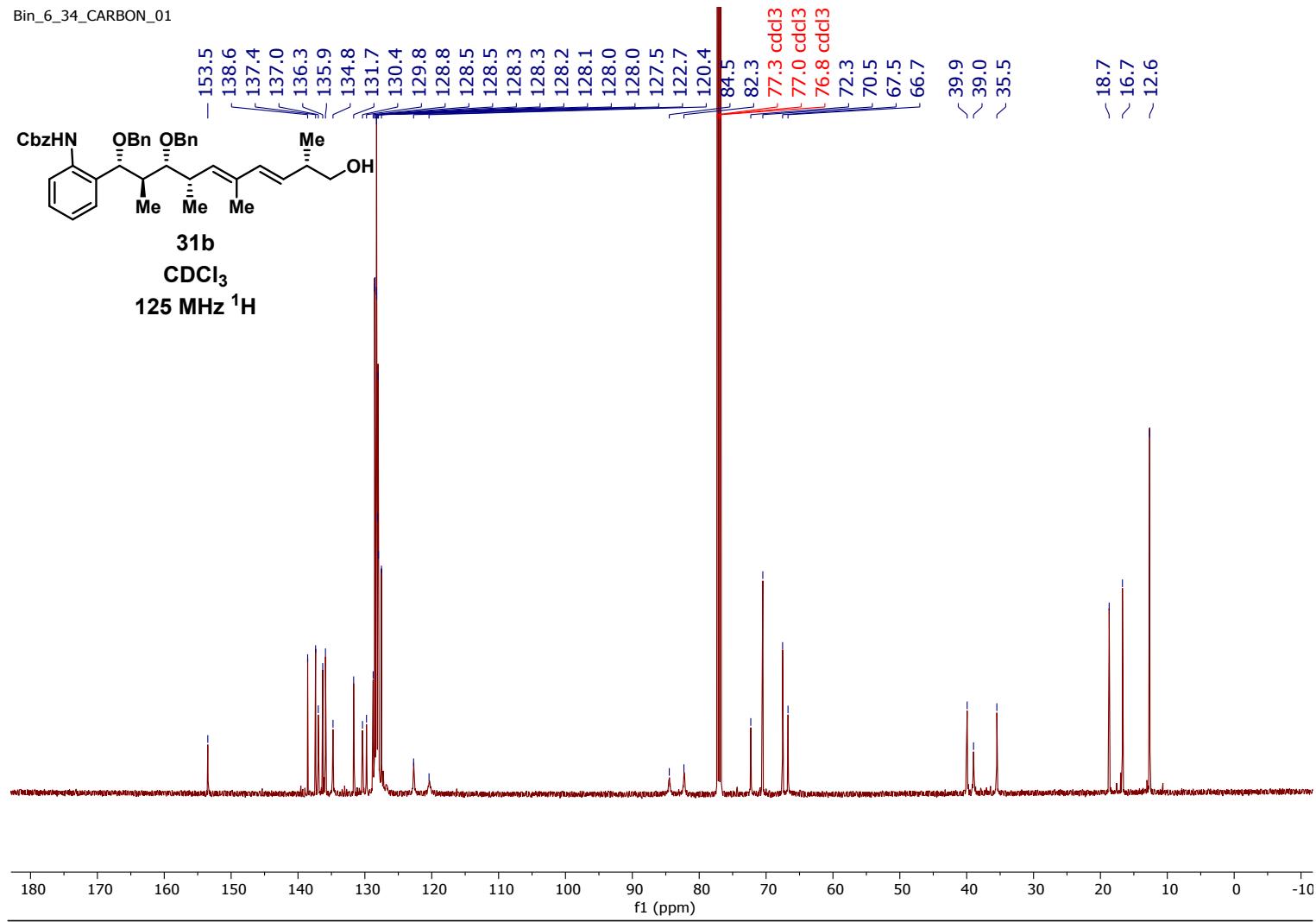


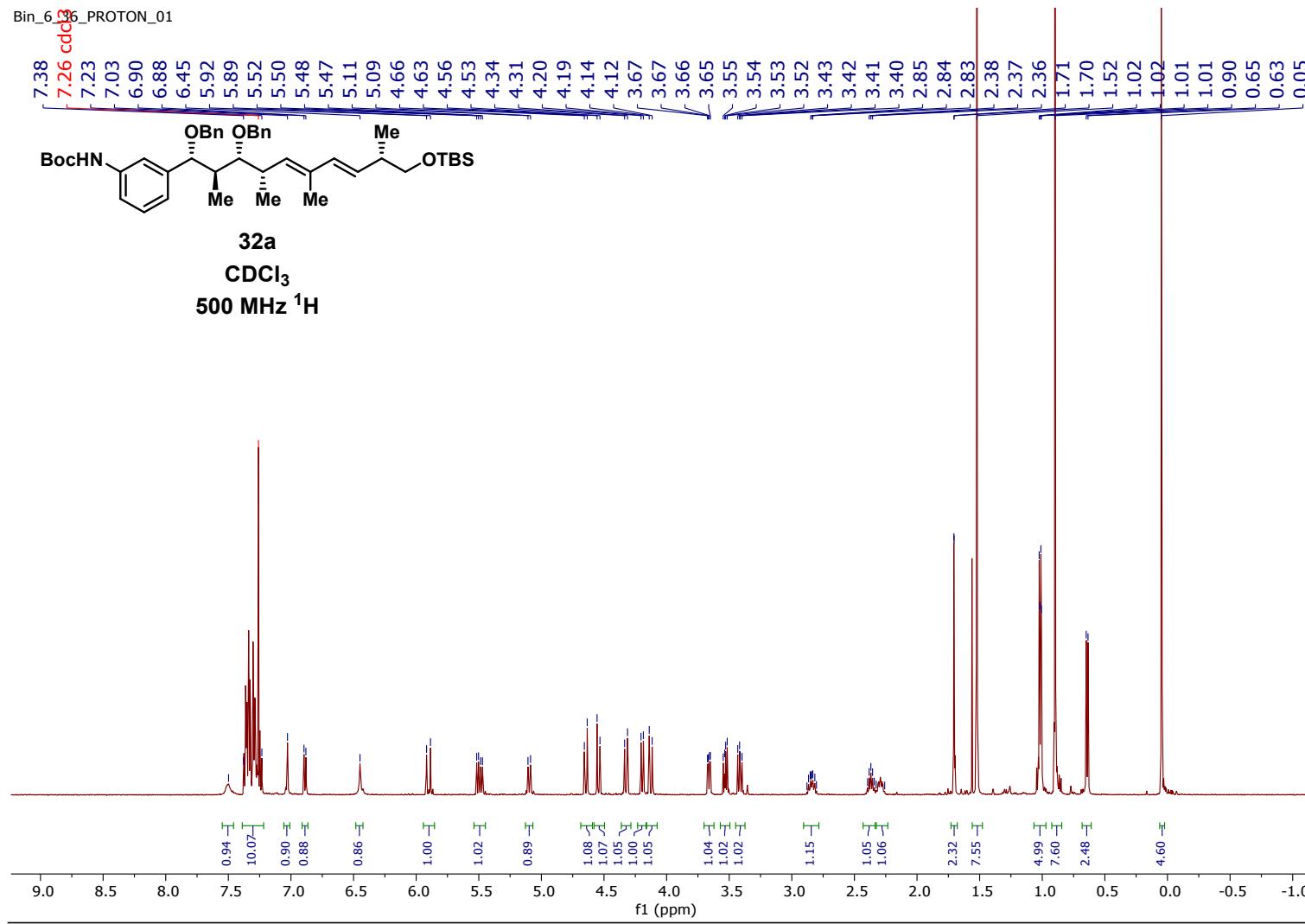


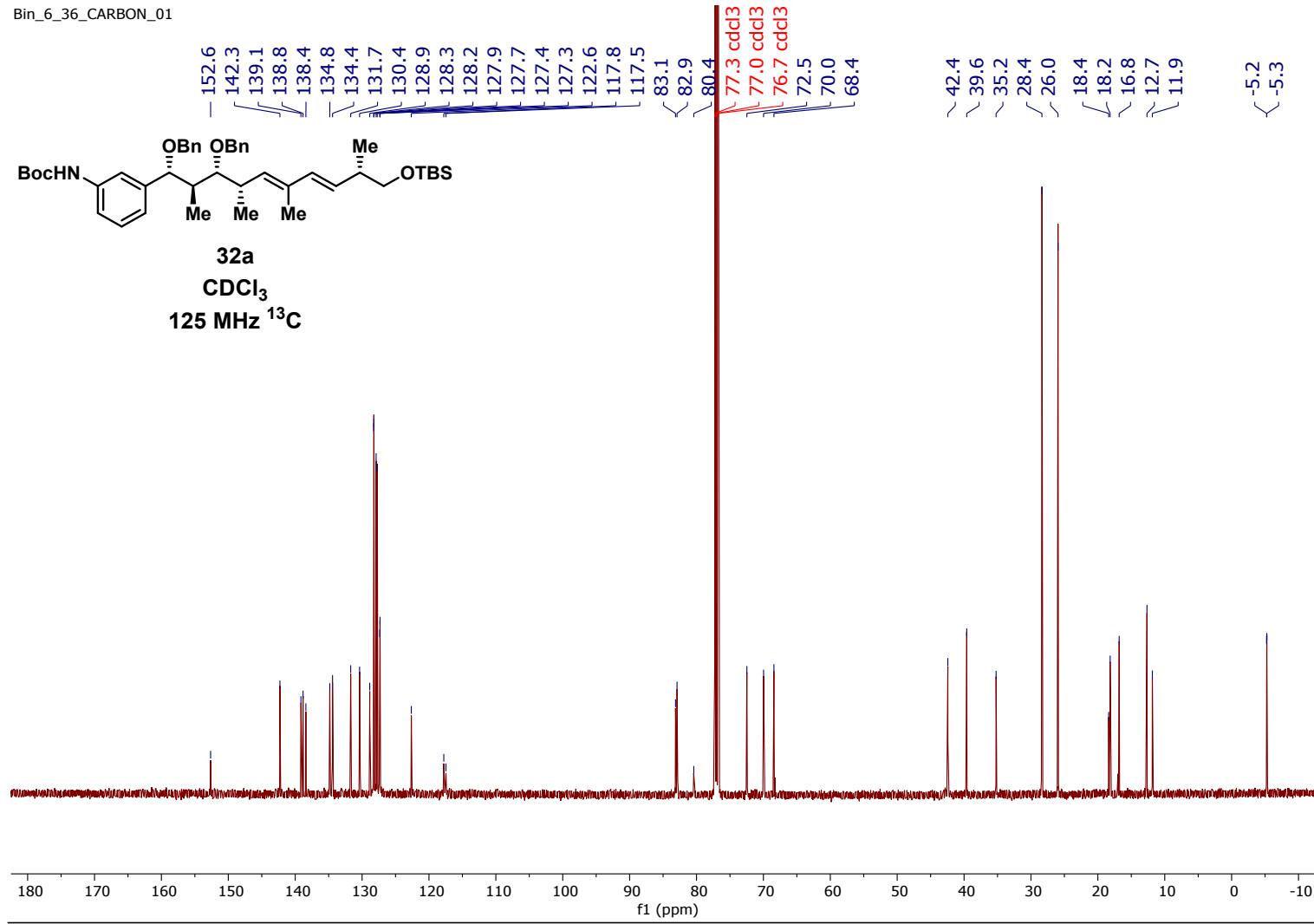


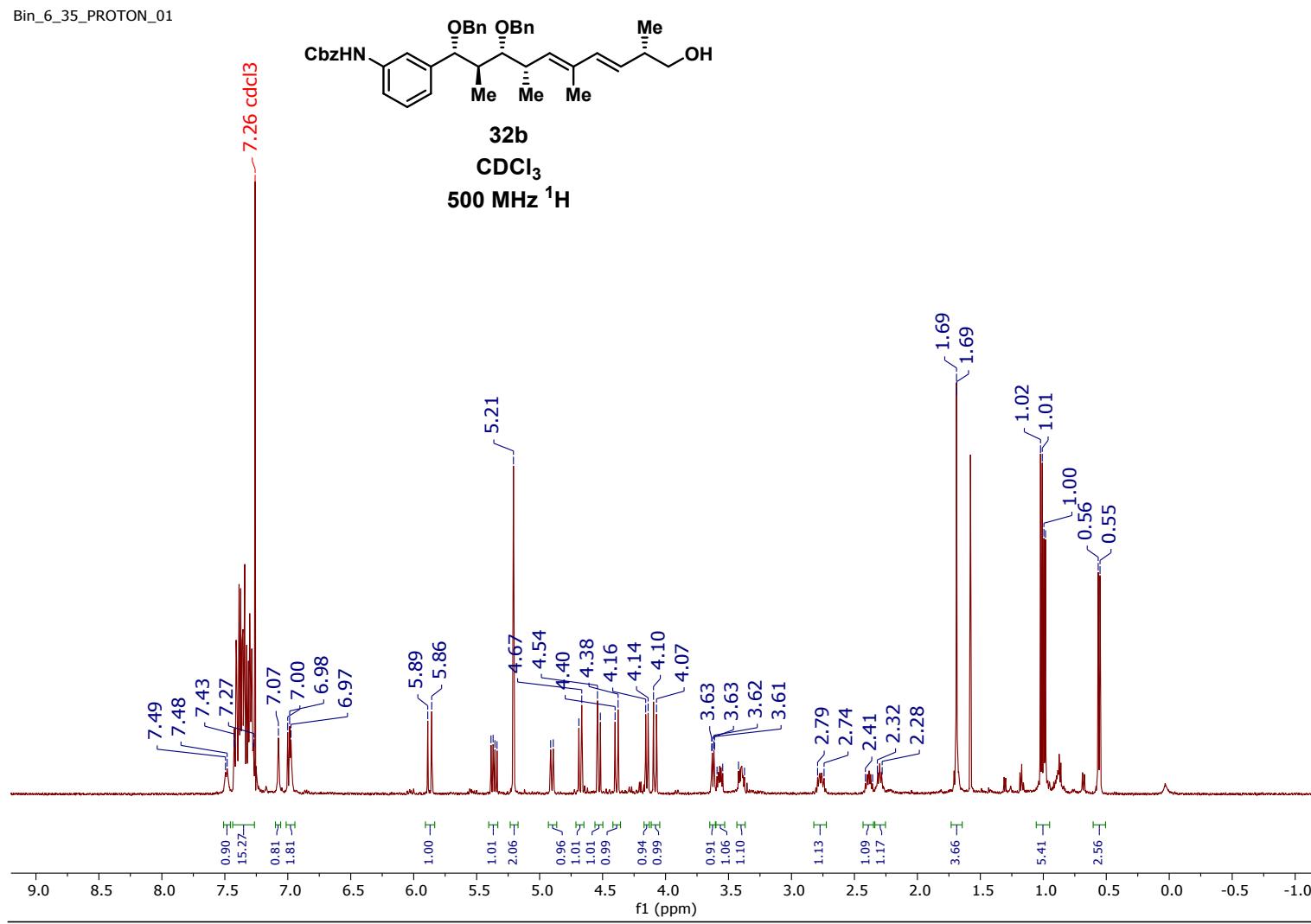


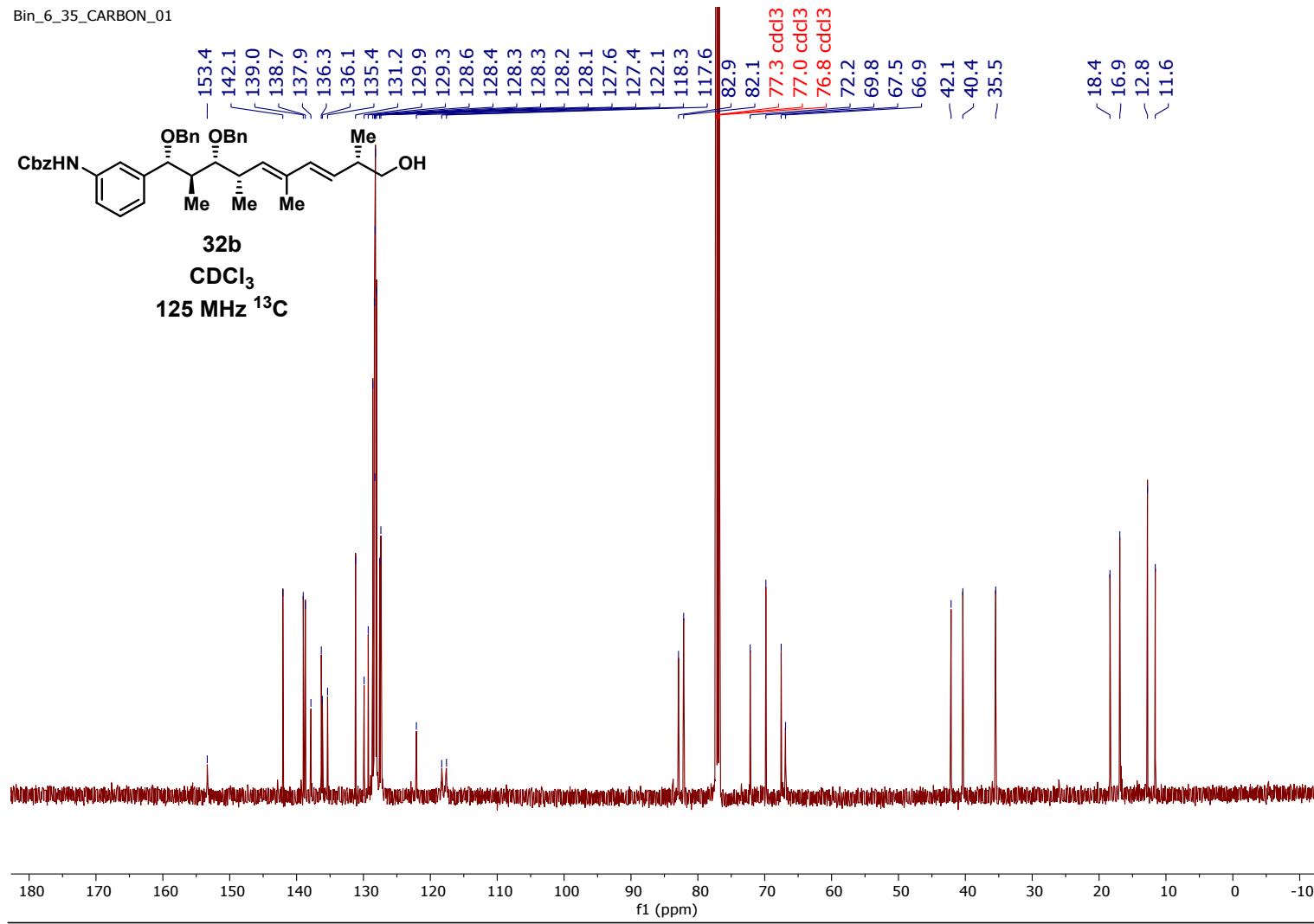


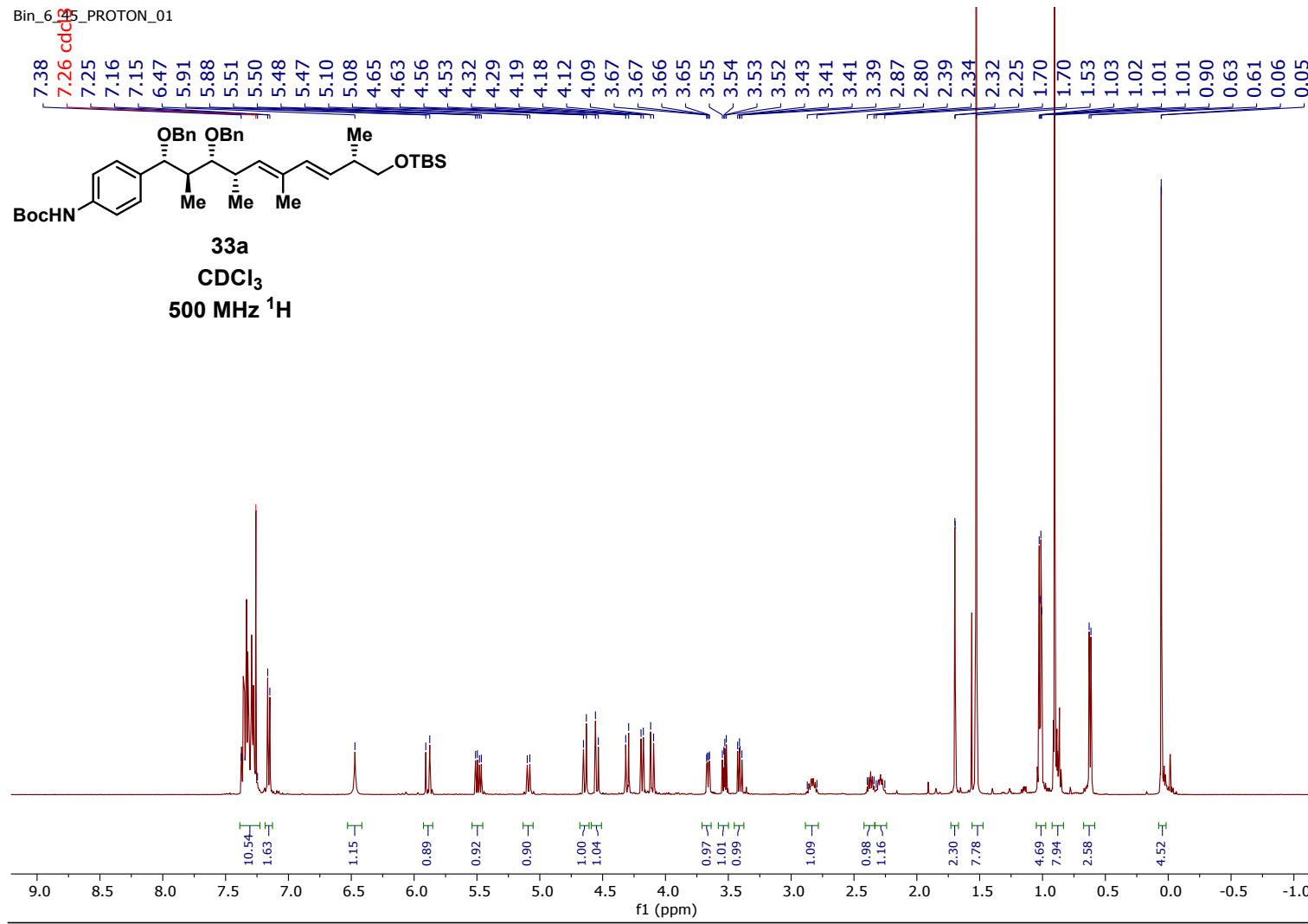


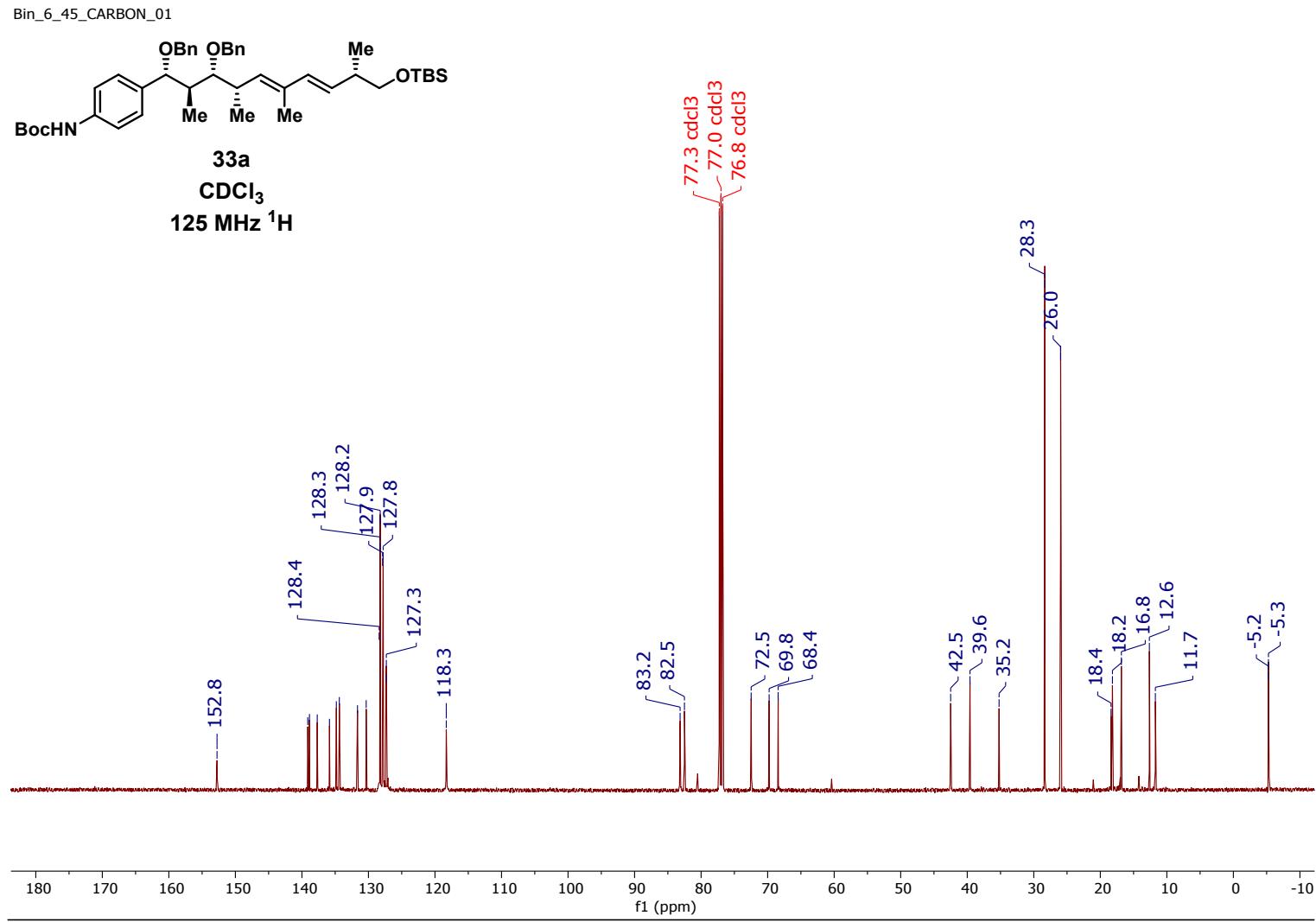


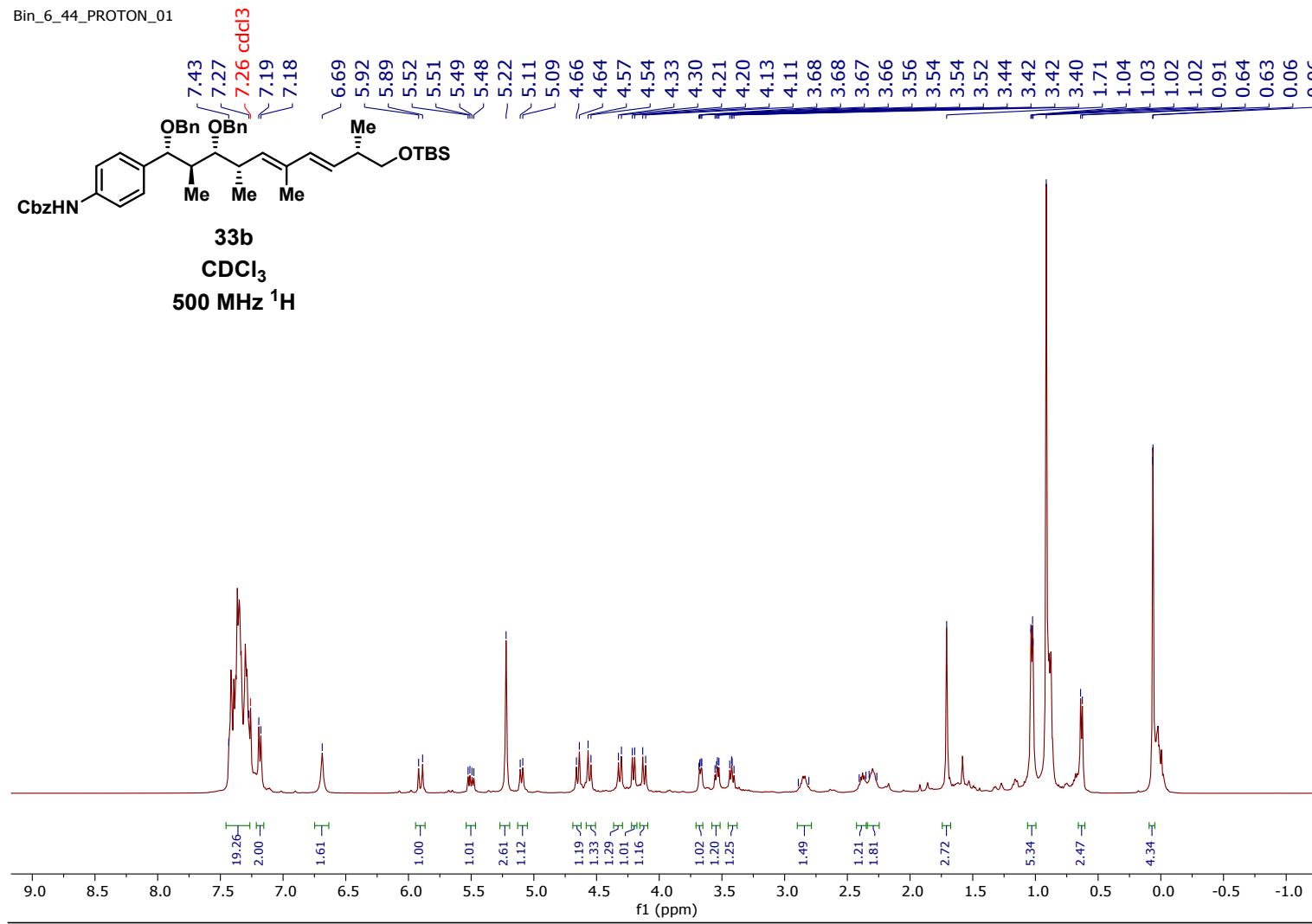


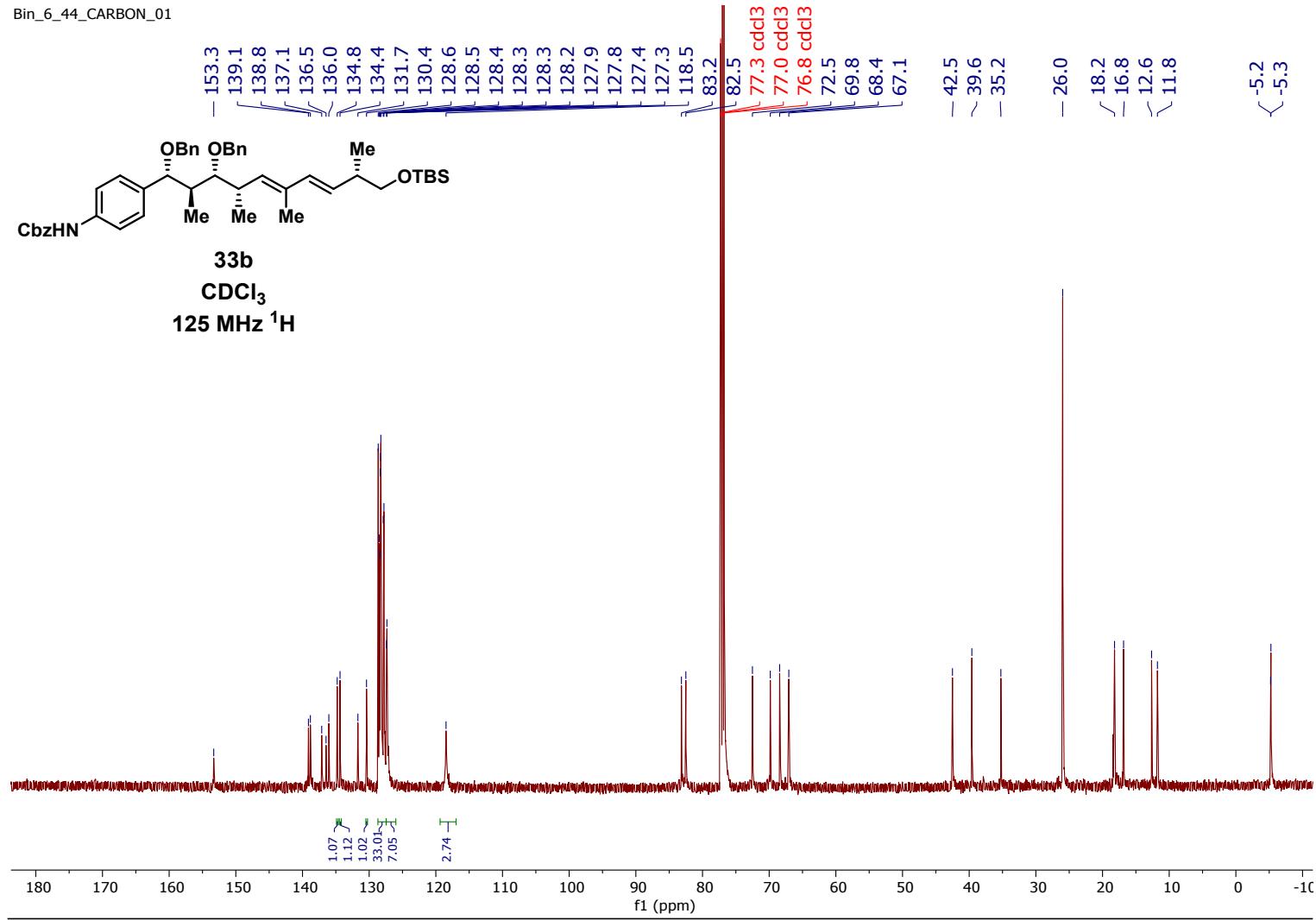




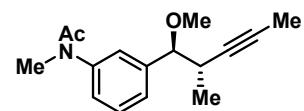




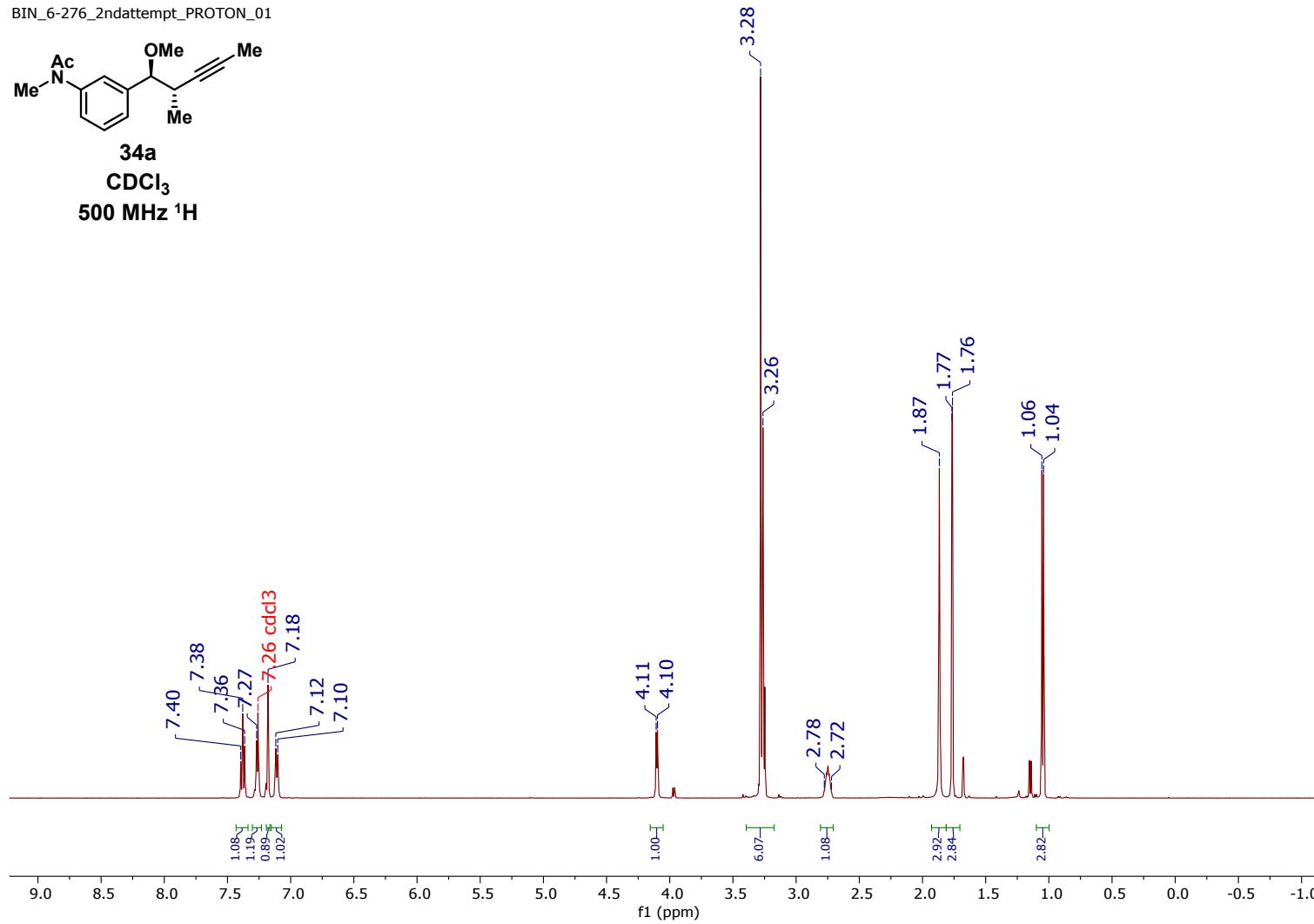




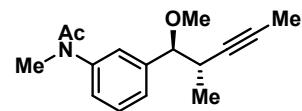
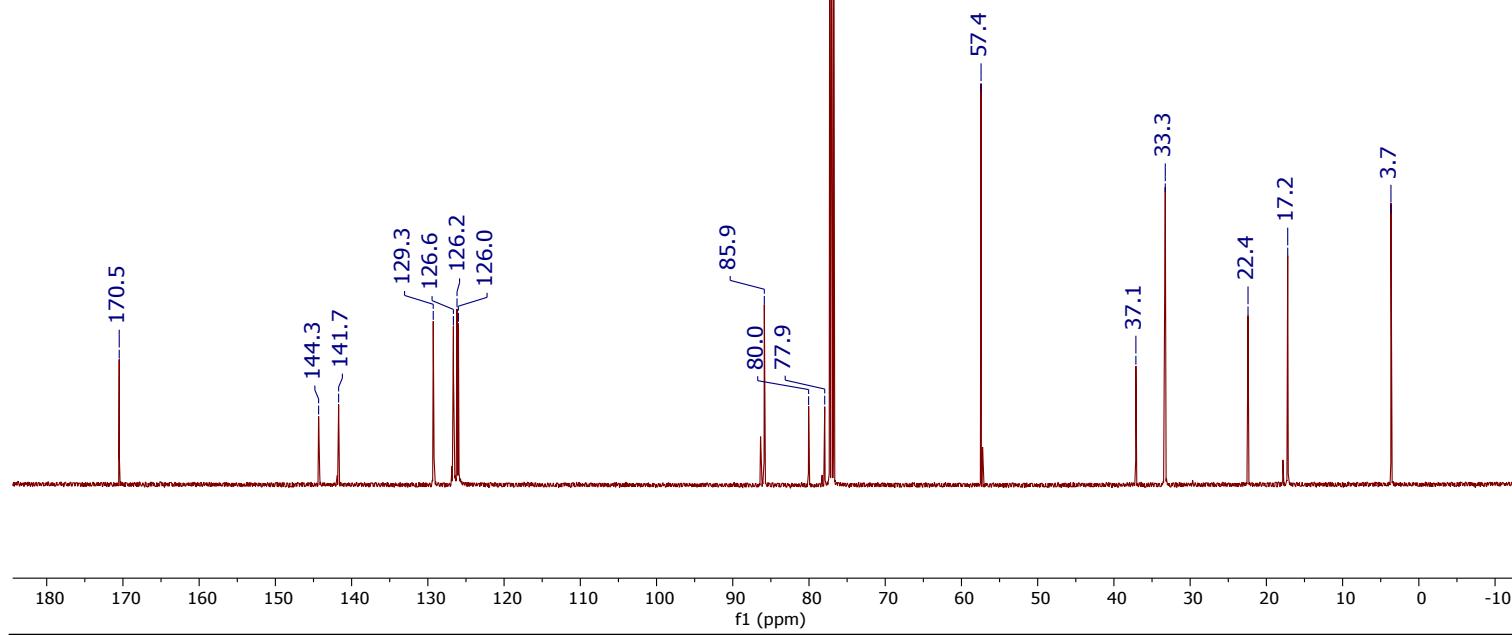
BIN\_6-276\_2ndattempt\_PROTON\_01

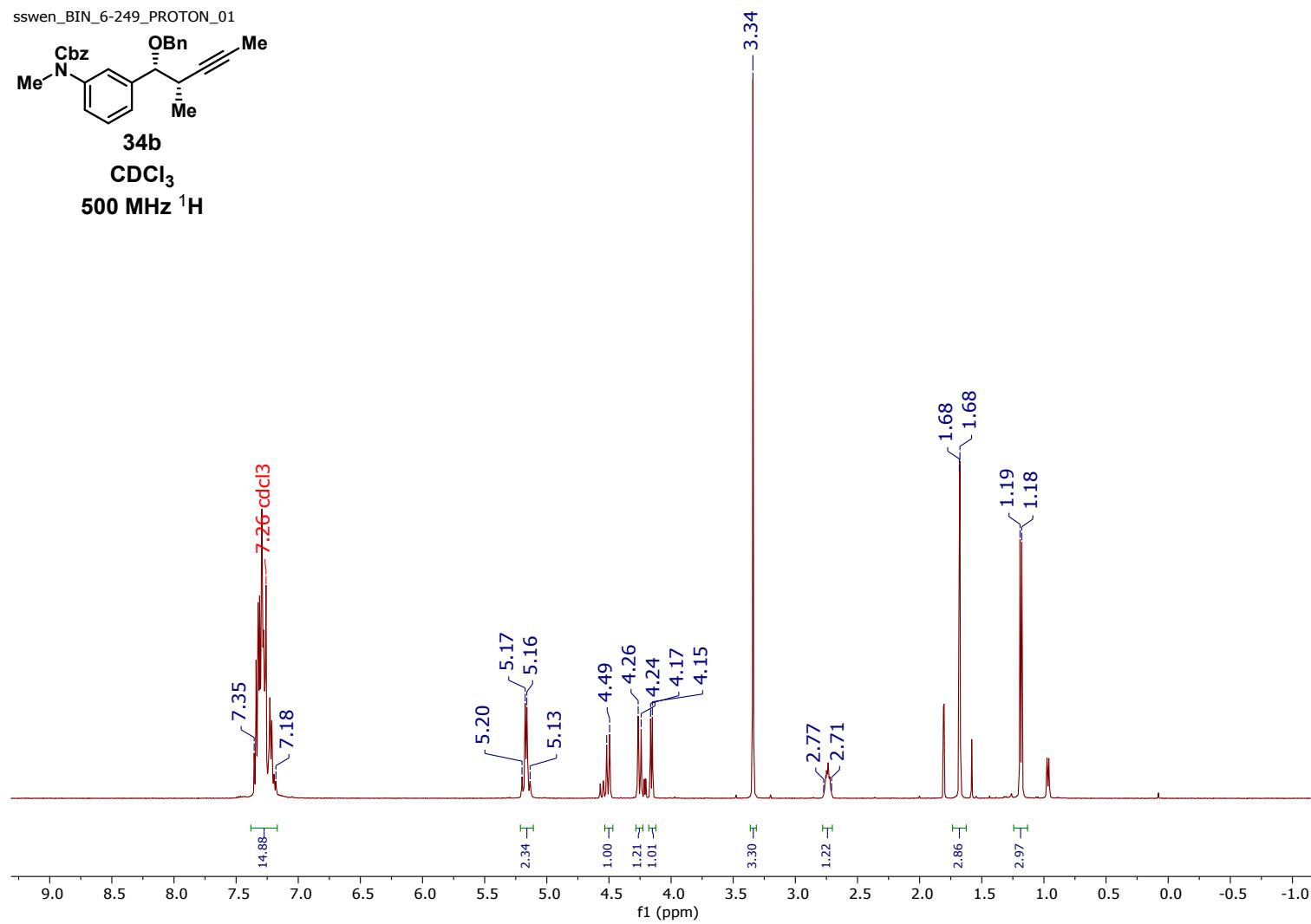


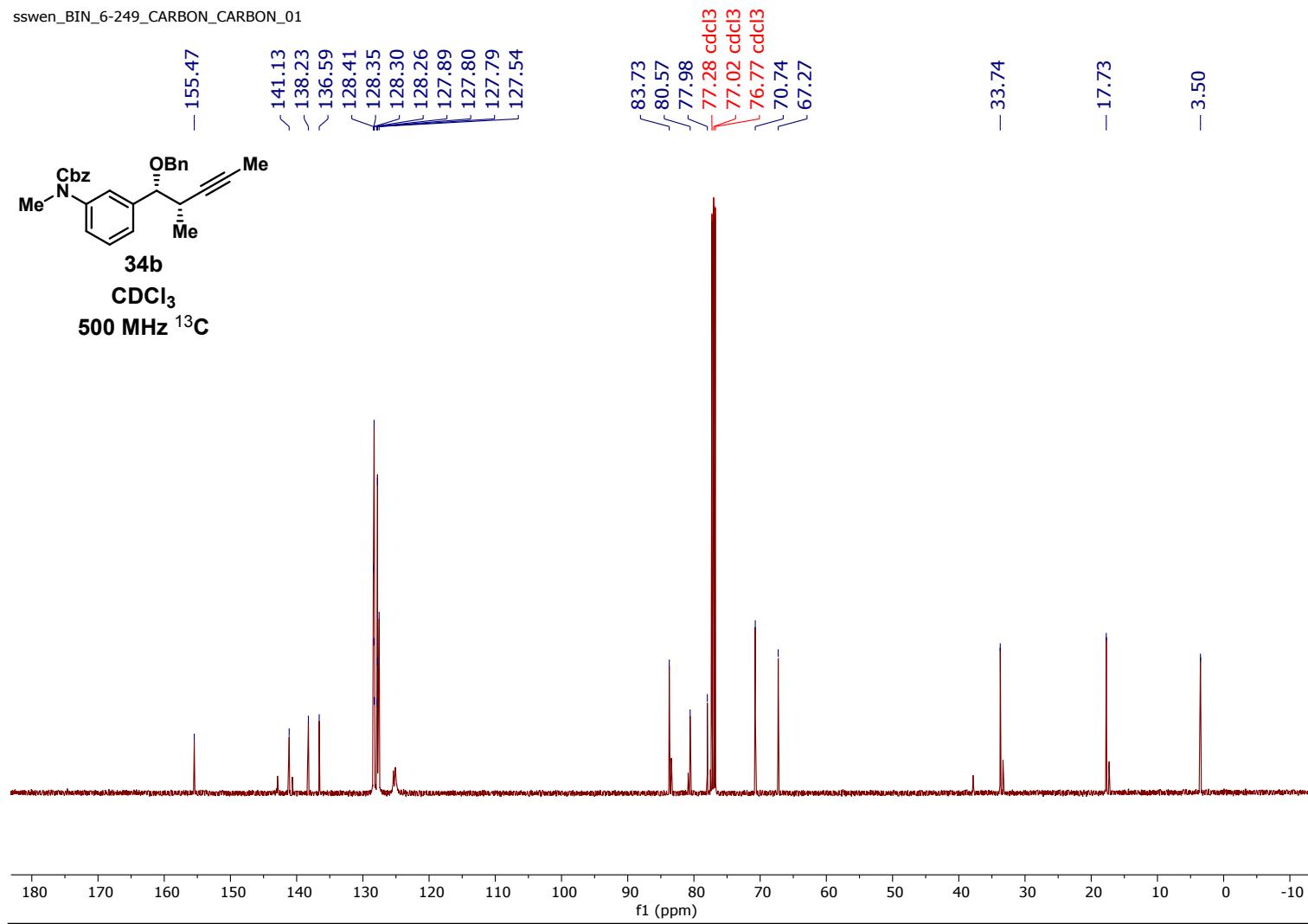
34a

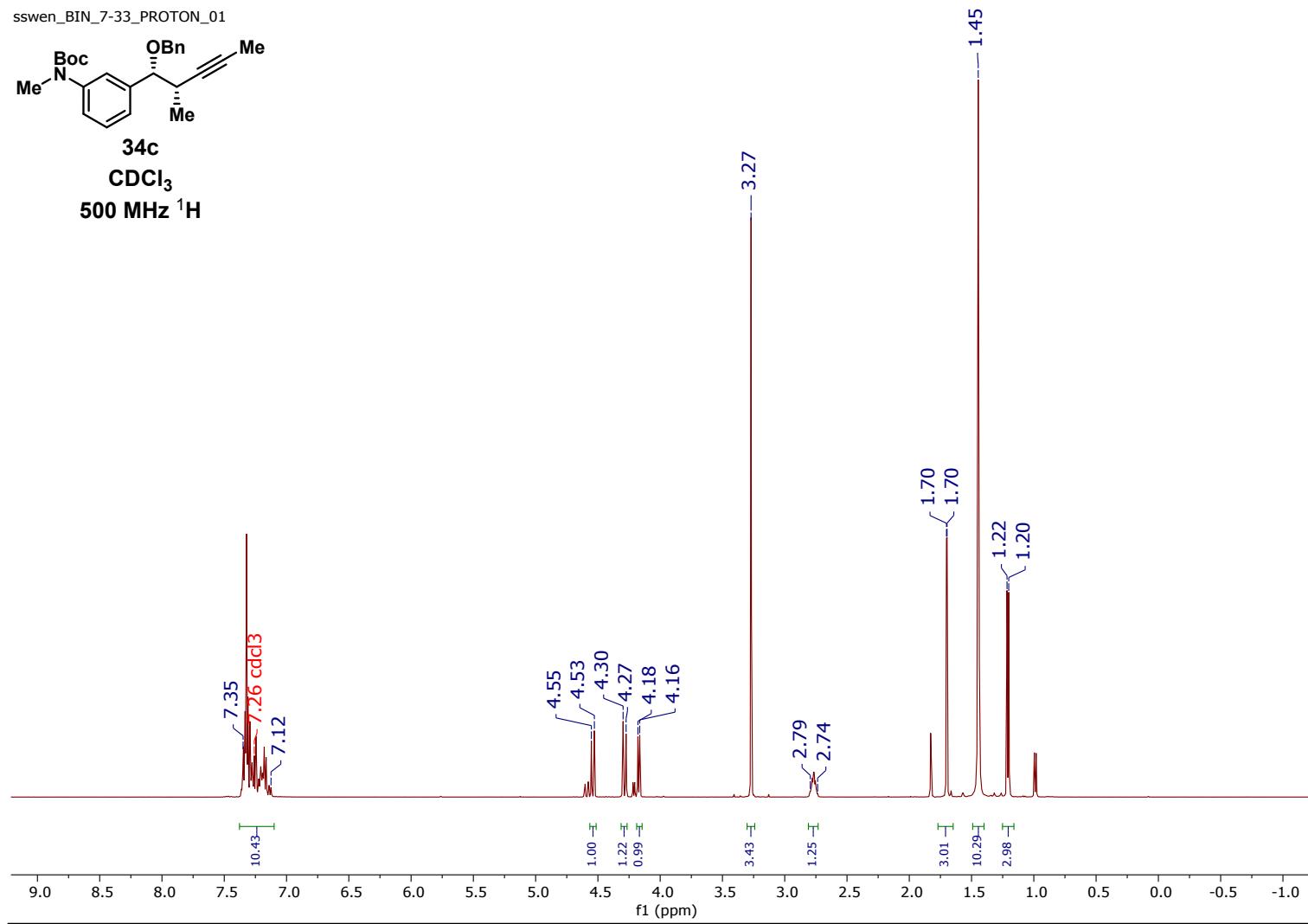
 $\text{CDCl}_3$ 500 MHz  $^1\text{H}$ 

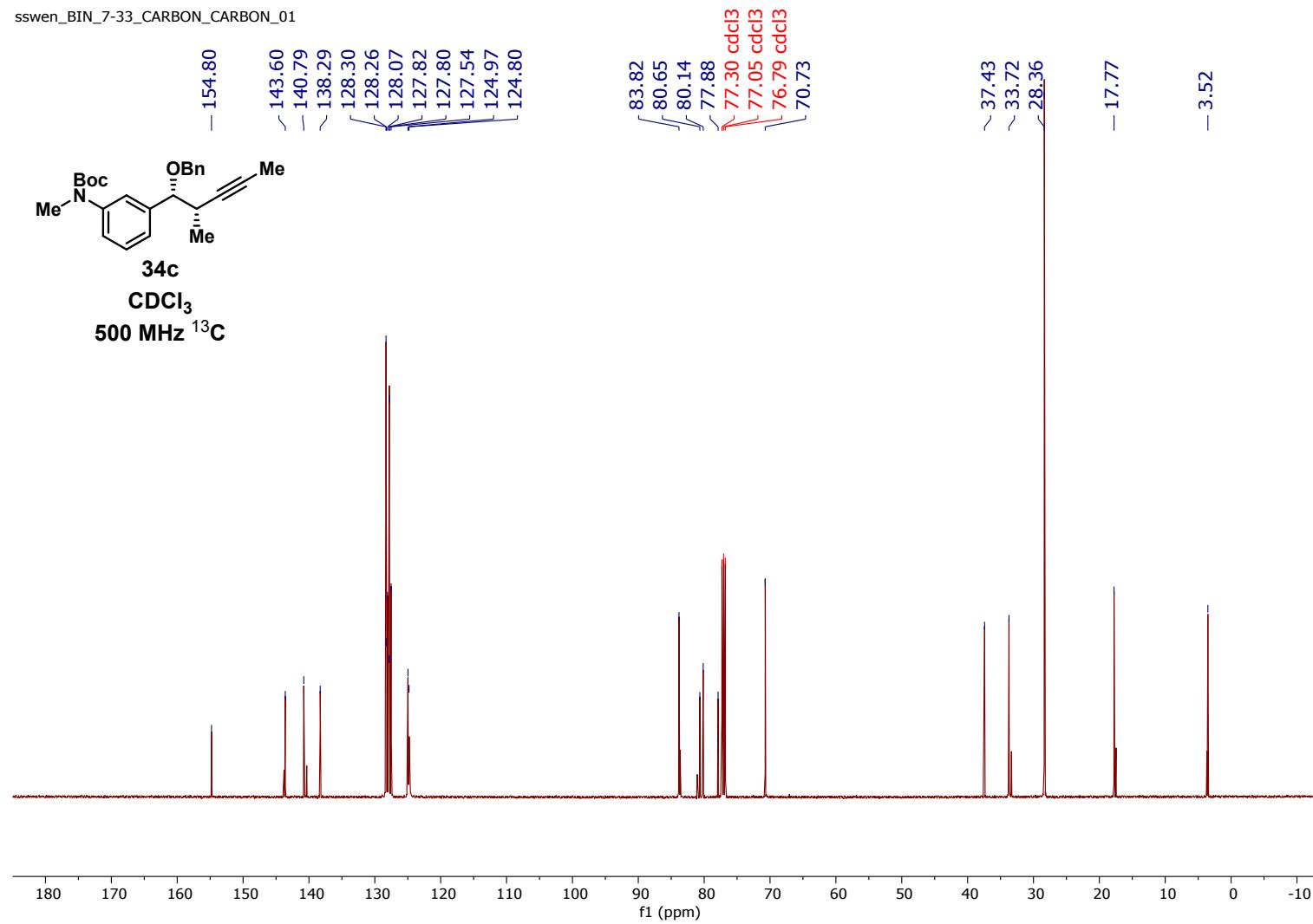
BIN\_6-276\_2ndattempt\_CARBON\_01

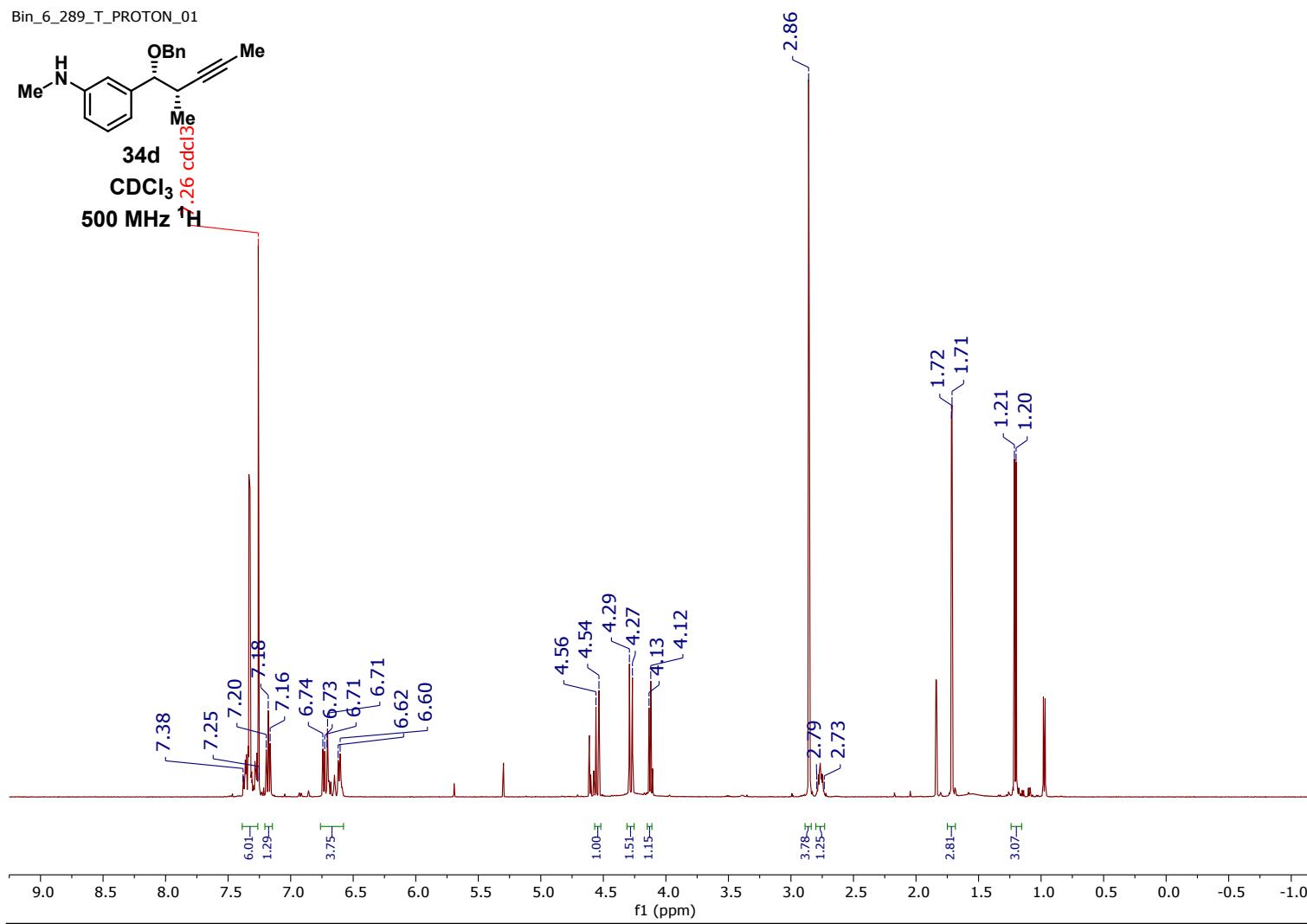
**34a** $\text{CDCl}_3$ 500 MHz  $^{13}\text{C}$ 

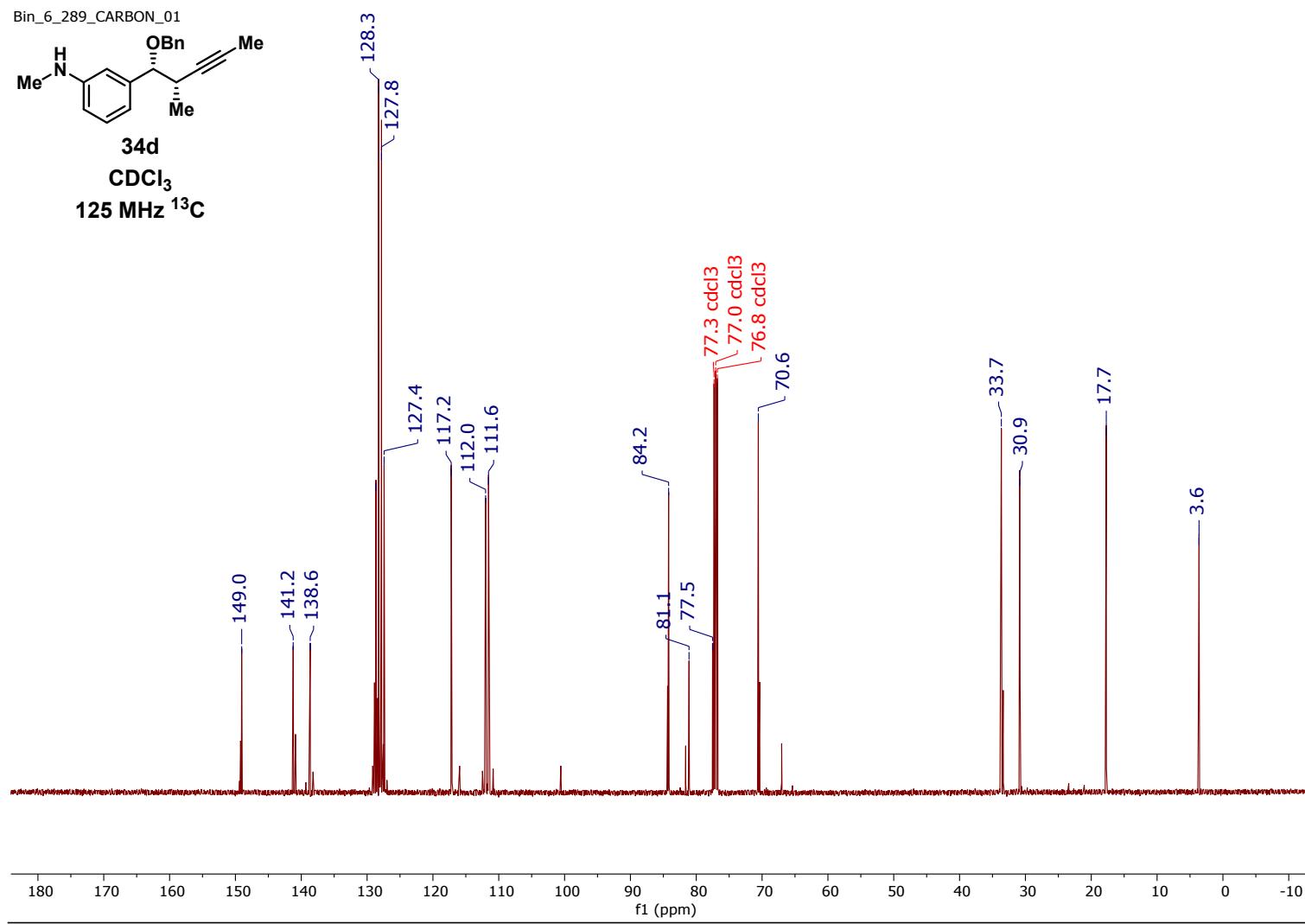




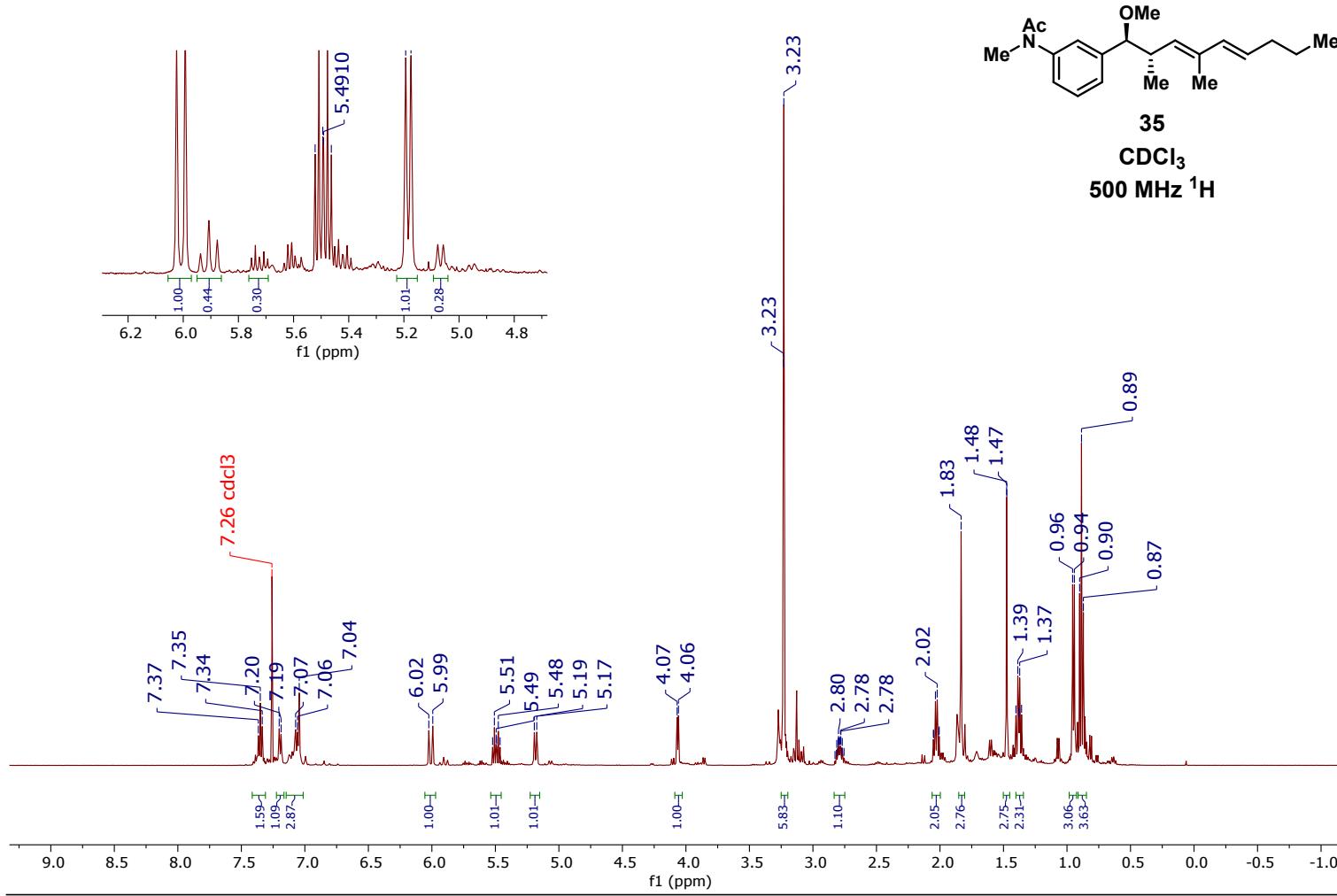


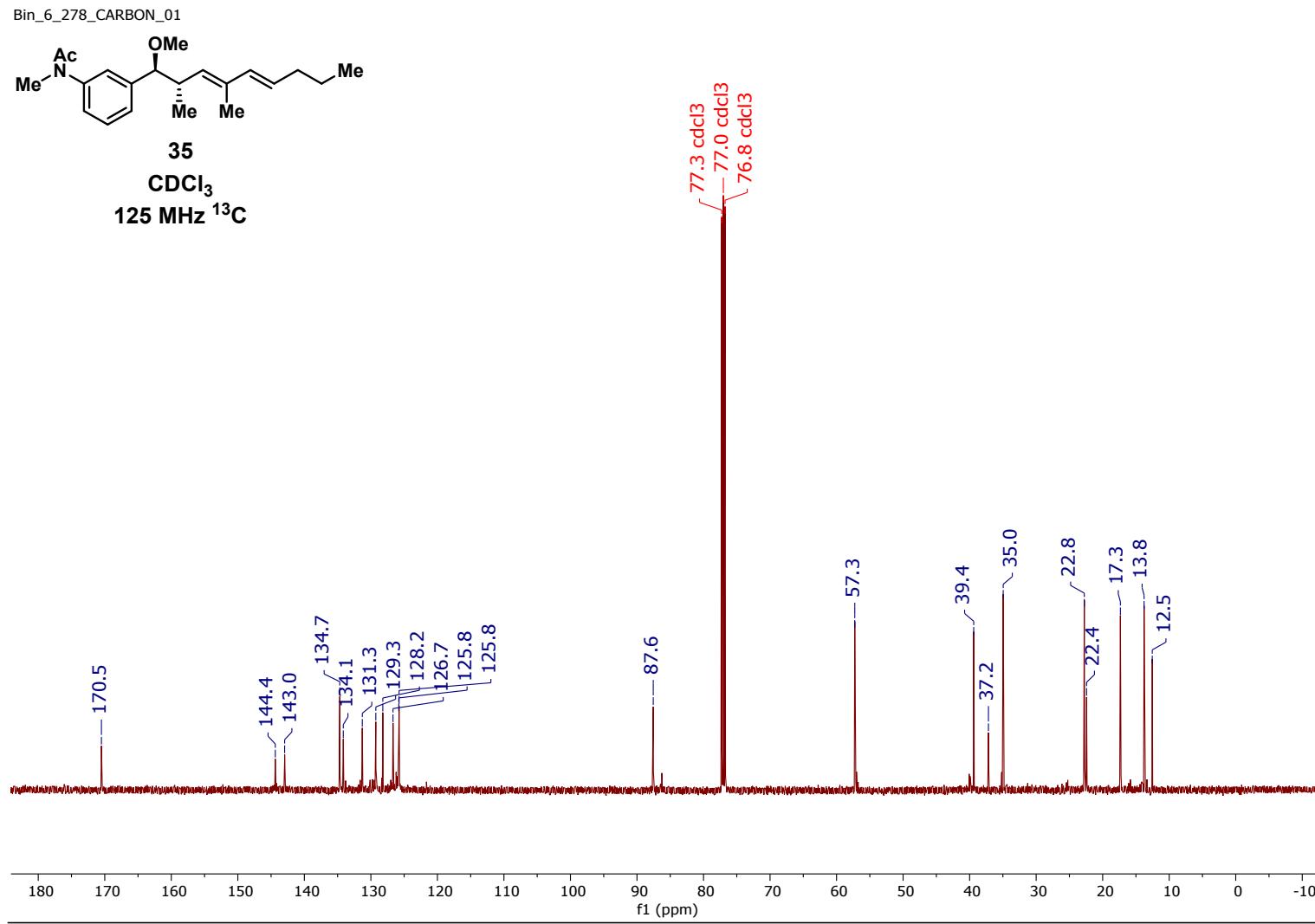




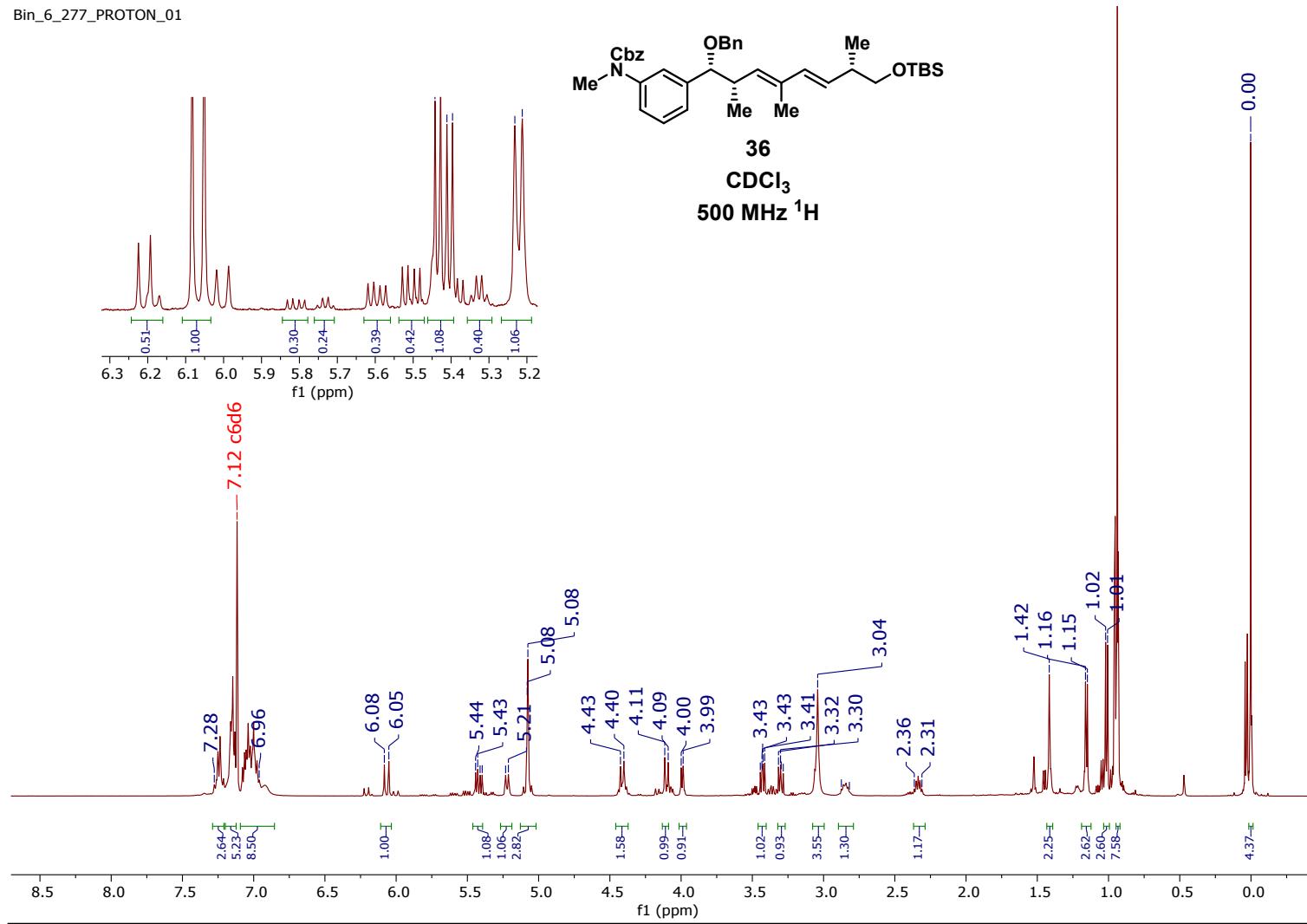


Bin\_6\_278\_PROTON\_01

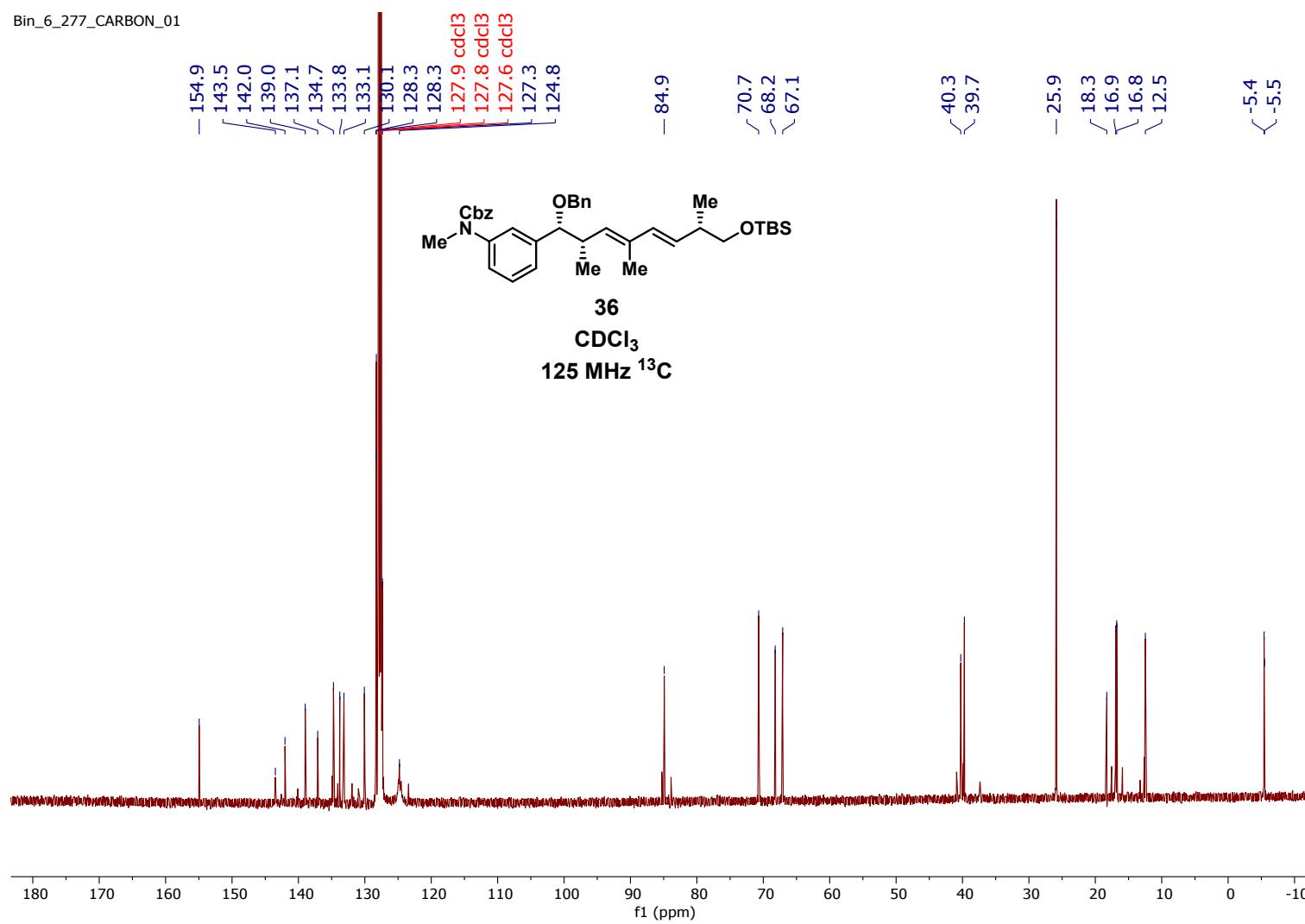




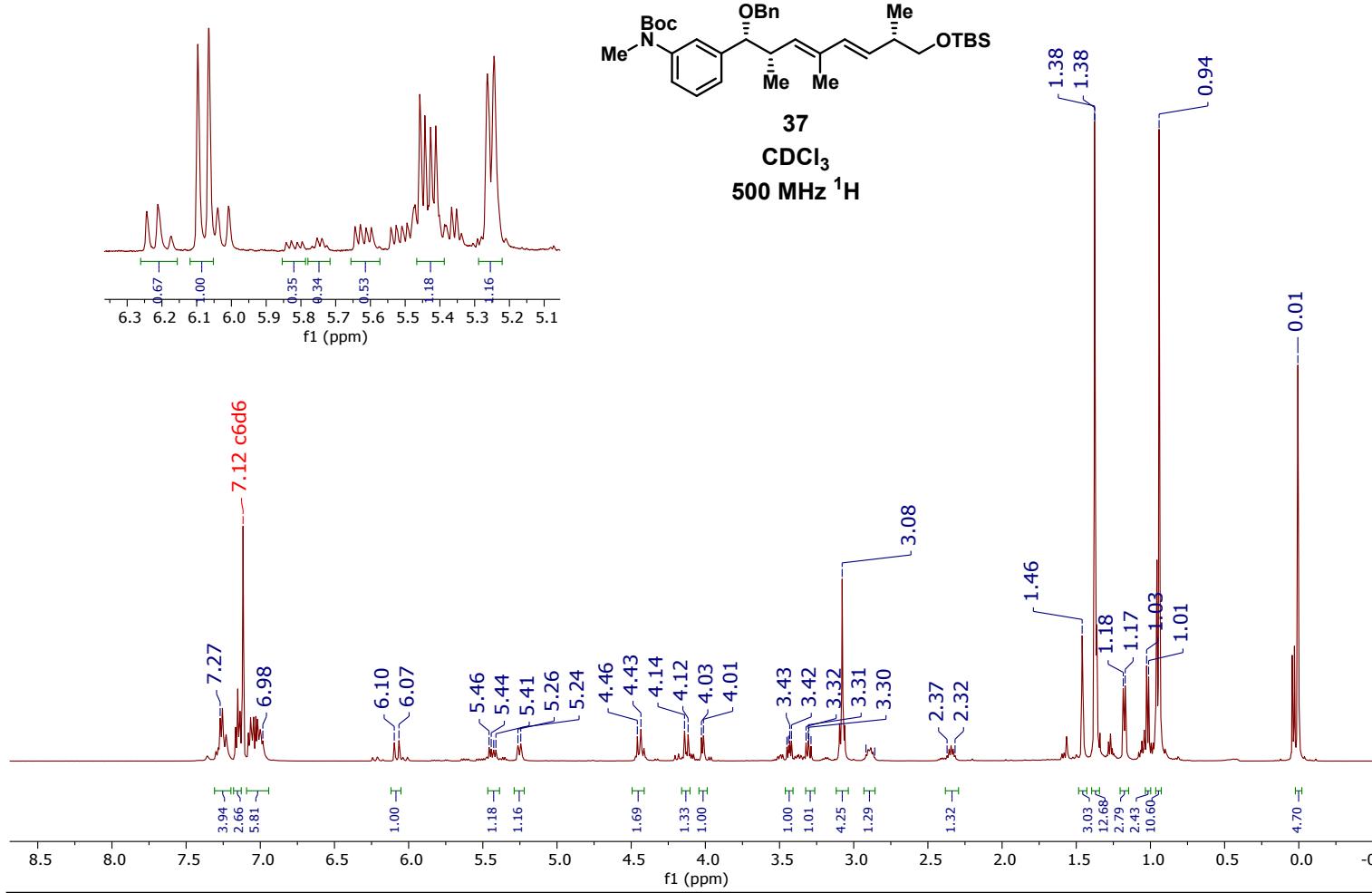
Bin\_6\_277\_PROTON\_01



Bin\_6\_277\_CARBON\_01

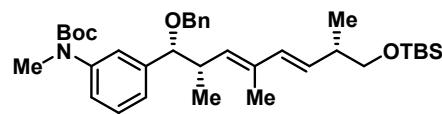


Bin\_7\_35\_PROTON\_01

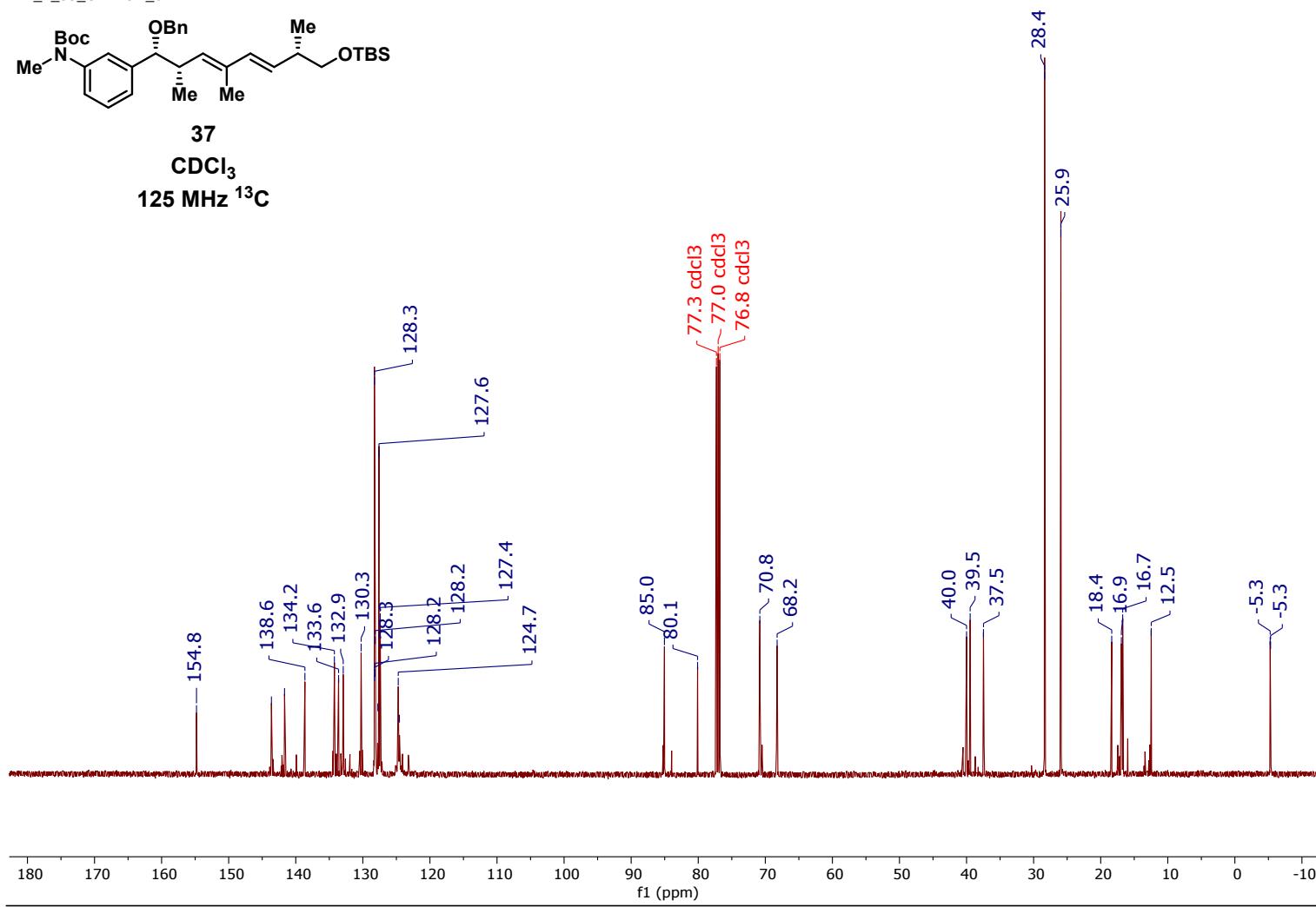


SI-372

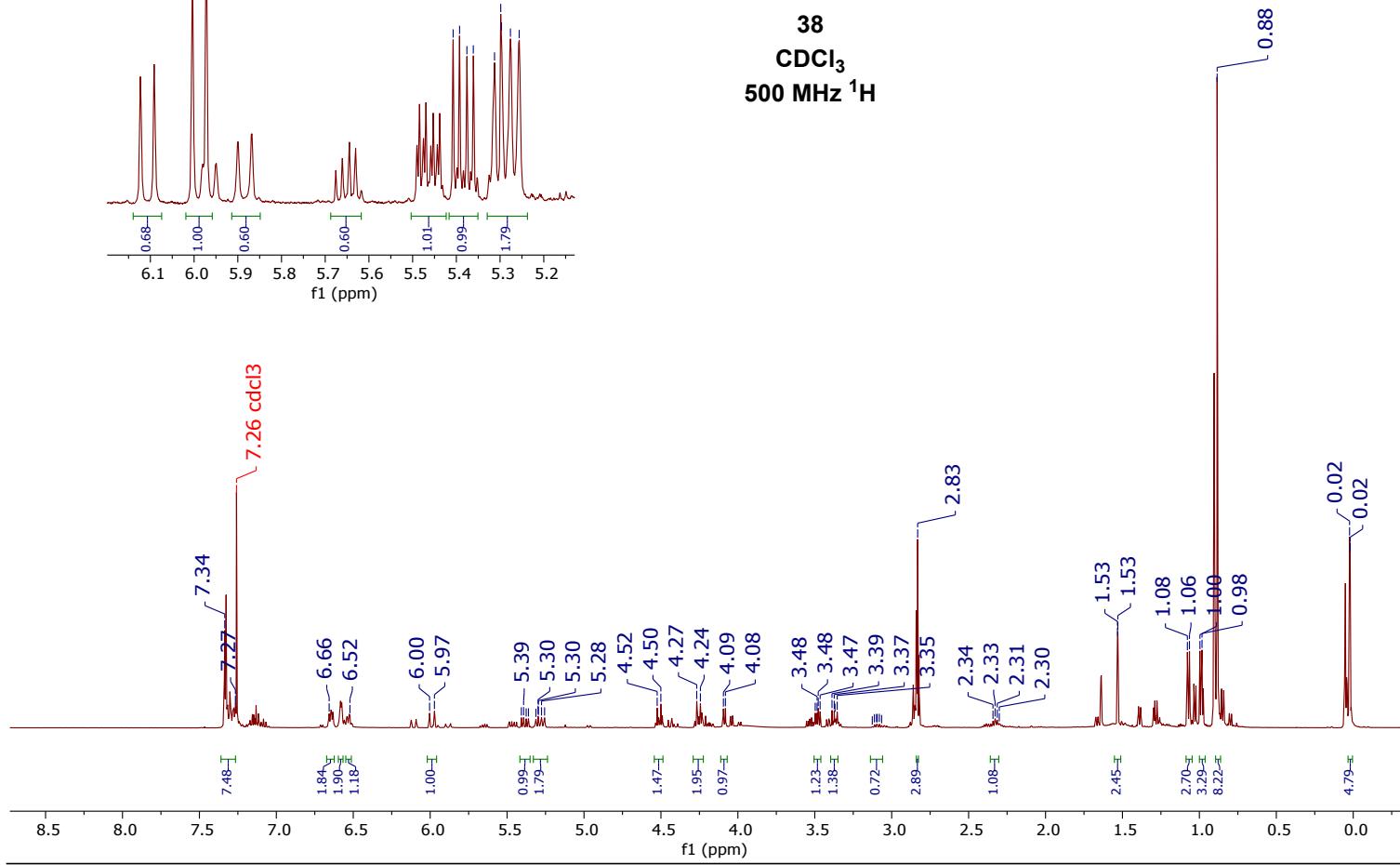
Bin\_7\_35\_CARBON\_01

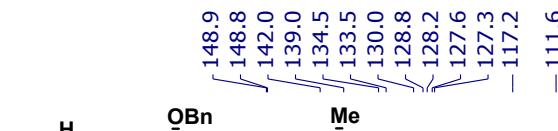
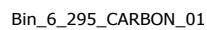


**37**  
 $\text{CDCl}_3$   
 125 MHz  $^{13}\text{C}$



Bin\_6\_295\_PROTON\_01

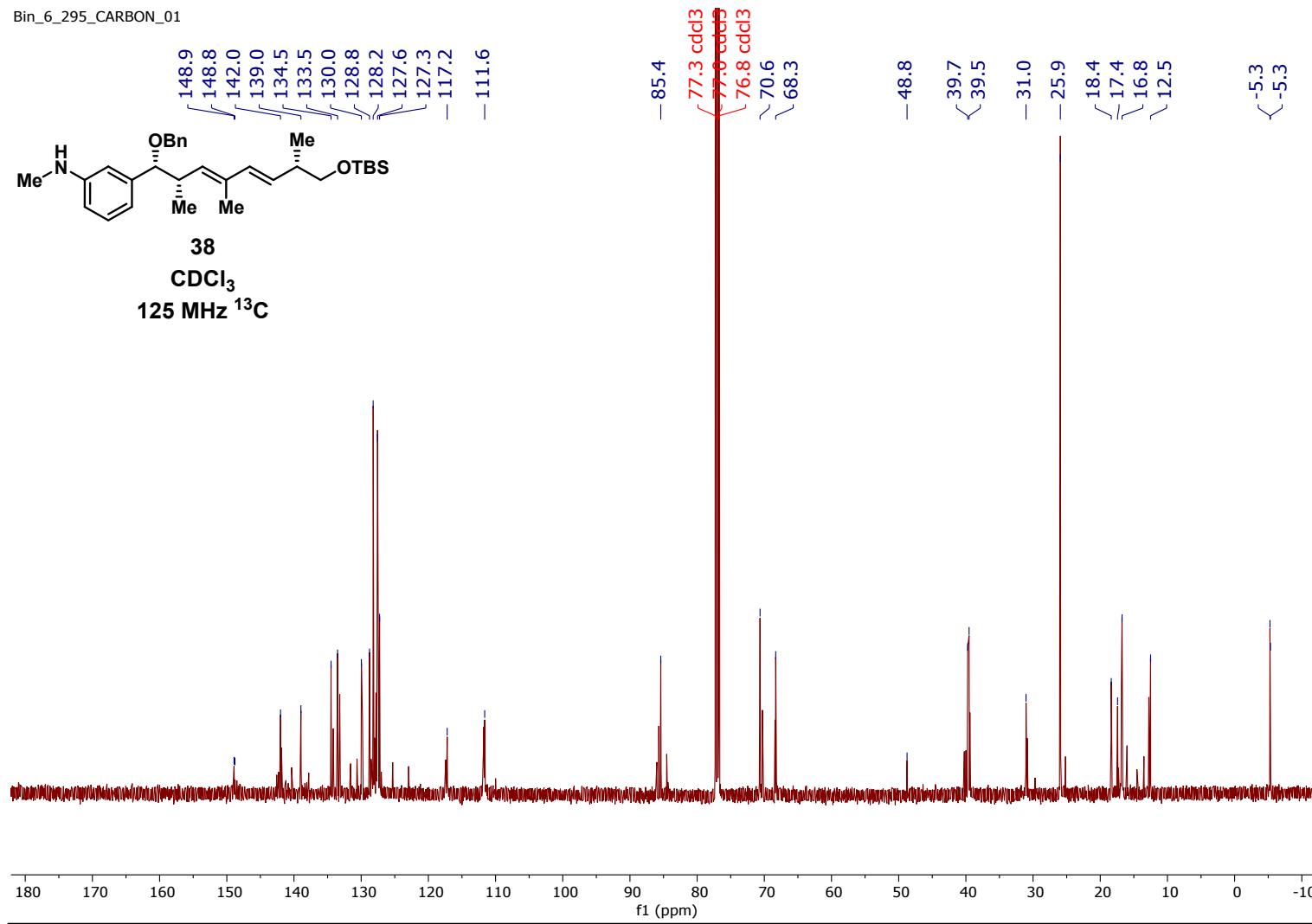




38

$\text{CDCl}_3$

125 MHz  $^{13}\text{C}$



**Part IV: References:**

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