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September 2014: The paragraphs above replace the section "Handling and Disposal of Hazardous Chemicals" in the originally published version of this article. The statements above do not supersede any specific hazard caution notes and safety instructions included in the procedure.

Organic Syntheses

Enantioselective Rhodium-Catalyzed [2+2+2] Cycloaddition of Pentenyl Isocyanate and 4-Ethynylanisole: Preparation and Use of Taddol-pyrrolidine Phosphoramidite

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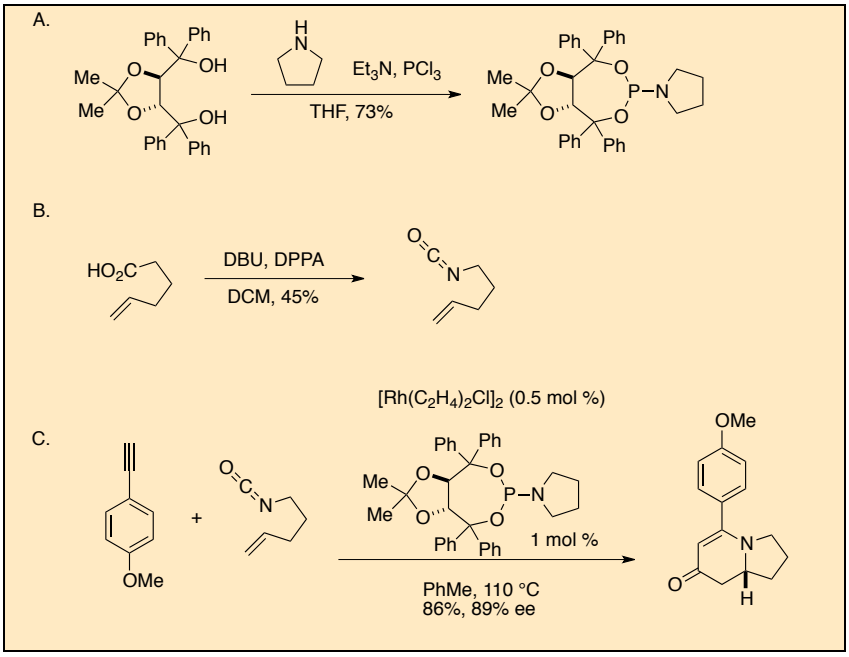
Checked by Yiyang Liu and Brian M. Stoltz



Procedure

Caution! Alkyl acyl azides can rapidly decompose with heat to release large amounts of nitrogen. Care should be taken during handling: do not attempt to convert neat and avoid handling neat.

A. *Taddol-pyrrolidine phosphoramidite.* A 250-mL single-necked, round-bottomed flask equipped with an egg-shaped magnetic stir bar (12.7 x 25.4 mm) is flame-dried under vacuum. After cooling to 23 °C, (*R*,*R*)-Taddol (2.0 g, 4.29 mmol) (Note 1) is added to the round-bottomed flask, a rubber septum is fitted, the reaction flask is put under an atmosphere of N_2, and tetrahydrofuran (75 mL) (Note 2) is added via syringe. To this clear, colorless solution, triethylamine (2.4 mL, 17.2 mmol, 4 equiv) (Note 3) is added via syringe resulting in a clear solution with a slight yellow color. The reaction mixture is cooled to 0 °C with an ice bath and phosphorous trichloride (0.39 mL, 4.5 mmol, 1.05 equiv) (Note 4) is added dropwise over 2 min via syringe resulting in a white suspension. The ice bath is removed, the reaction is allowed to warm to 23 °C and stirred for 1 h. The reaction mixture is cooled to 0 °C with an ice bath, and pyrrolidine (1.8 mL, 21.4 mmol, 5 equiv) (Note 5) is added via syringe. The ice bath is removed, the reaction is allowed to warm to 23 °C and stir for 1 h. Diethyl ether (50 mL) is then added, and the reaction mixture is filtered through a medium-fritted funnel into a 250-mL round-bottomed flask. The solid residue in the reaction flask is washed with diethyl ether (2 x 25 mL) and the filtrates are added into the round-bottomed flask. The ether is transferred to a 500-mL separatory funnel and washed with deionized water (50 mL) (Note 6). The organic layer is dried over $MgSO_4$, vacuum-filtered through a 100 mL course-fritted filter funnel into a 250-mL round-bottomed flask using a water aspirator, and the $MgSO_4$ is rinsed with diethyl ether (2 x 10 mL). The filtrate is concentrated *in vacuo* using a rotovap, and the off-white solid put under high vacuum for 30 min. An egg-shaped magnetic stir bar (12.7 x 25.4 mm) and EtOAc (5 mL) are added to the round-bottomed flask containing the solid and a reflux condenser is attached. Using an oil bath, the mixture is heated to reflux with stirring and EtOAc (~20 mL) is added dropwise until all of the solids dissolve. The stir bar is removed from the clear, slightly yellow solution. The round-bottomed flask is allowed to cool slowly in the oil bath to 23 °C, placed in a –10 °C fridge for 12 h, and then placed in a –24 °C freezer for 12 h. The

solid is collected with a Büchner funnel (5 cm) with medium porosity filter paper to yield 1.78 g of Taddol-pyrrolidine phosphoramidite as white crystals (73% yield) (Notes 7 and 8).

B. *Pentenyl isocyanate.* A 500-mL single-necked round-bottomed flask equipped with an egg-shaped magnetic stir bar (12.7 x 25.4 mm) is flame-dried under vacuum. After cooling to 23 °C, a rubber septum is fitted to the round-bottomed flask and the flask is put under an atmosphere of N_2. Dichloromethane (50 mL) (Note 9) and 5-hexenoic acid (10.4 mL, 87.6 mmol) (Note 10) are added via syringe to the round-bottomed flask and the flask is cooled to 0 °C with an ice bath. 1,8-Diazabicylo[5.4.0]undec-7-ene (14.2 mL, 94.6 mmol, 1.08 equiv) (Note 11) is added to the round-bottomed flask via syringe over 5 min and the clear solution is stirred for 20 min. Diphenyl phosphoryl azide (20.4 mL, 94.6 mmol, 1.08 equiv) (Note 12) is added over 5 min via syringe resulting in a clear, yellow solution. The reaction mixture is stirred for 3 h at 0 °C. The ice bath is removed, the septum is removed, and hexanes (200 mL) (Note 13) is added. The reaction is stirred for 5 min and transferred to a 500-mL separatory funnel. After the layers separate, the lower, yellow dichloromethane layer is collected in a 250 mL Erlenmeyer flask and the upper, cloudy hexane layer is transferred to a 1-L round-bottomed flask. The dichloromethane layer is returned to the separatory flask and the 250 mL Erlenmeyer flask is rinsed with hexanes (200 mL) and transferred to the separatory funnel. The dichloromethane layer is extracted with hexanes. The lower dichloromethane layer is collected in the 250 mL Erlenmeyer flask and the cloudy hexane layer is transferred to the 1-L round-bottomed flask, which (without a septum) is placed into a 23 °C oil bath that is heated to 50 °C for 3 h and then at 55 °C for 3 h. After cooling to ambient temperature, the solvent is removed *in vacuo* using a 23 °C bath. This yellow solution is transferred to a 25-mL round-bottomed flask, and the 1 L flask is rinsed with minimal hexanes, which are transferred to the 25-mL round-bottomed flask. The 25-mL flask is concentrated *in vacuo* using a 23 °C bath (40 mmHg). The resultant yellow oil is purified via vacuum distillation and the first clear fraction distilling at 63 °C (50 mmHg) is collected in a 25 mL round-bottomed flask cooled to 0 °C. Pentenyl isocyanate (4.34 g, 45%) is isolated as a clear liquid (Notes 14 and 15).

C. *(R)-5-(4-Methoxyphenyl)-2,3,8,8a-tetrahydroindolizin-7(1H)-one.* An oven-dried 250-mL round-bottomed flask equipped with a polygon magnetic stir bar (6.4 x 25.4 mm) and an oven-dried reflux condenser with septum attached are loaded into an inert atmosphere (N_2) glove box (Note

16). Chlorobis(ethylene)rhodium(I) dimer (58 mg, 0.15 mmol, 0.005 equiv) (Note 17) and Taddol-pyrrolidine phosphoramidite (170 mg, 0.3 mmol, 0.01 equiv) are added to the round-bottomed flask. The reflux condenser is attached, the apparatus is removed from the glove box, and toluene (110 mL) (Note 18) is added via syringe resulting in a clear, gold solution. Toluene (5 mL) is added to a vial containing pentenyl isocyanate (3.33 g, 30 mmol) and 4-ethynylanisole (6.0 g, 45 mmol, 1.5 equiv) (Note 19) and this solution is added to the reaction mixture via syringe. The vial is rinsed with toluene (5 mL), which is added to the reaction vessel. Additional toluene (50 mL) is added to the reaction mixture resulting in a crimson solution. The reaction mixture is heated to 110 °C in an oil bath for 36 h resulting in a dark brown solution. The reaction mixture is concentrated *in vacuo*, and the crude reaction mixture is purified via flash chromatography (Note 20) resulting in the isolation of 6.26 g (86%) of (*R*)-5-(4-methoxyphenyl)-2,3,8,8a-tetrahydroindolizin-7(1H)-one as a light brown solid (89% ee) (Notes 21, 22, and 23).

Notes

1. (*R*,*R*)-Taddol was purchased from AK Scientific, Inc. and used as received.
2. Tetrahydrofuran (inhibitor-free, Chromasolv®, for HPLC, 99.9%) was purchased from Sigma-Aldrich, degassed with Ar and passed through two columns of neutral alumina.
3. Triethylamine was purchased from Sigma-Aldrich and distilled over KOH before use.
4. Phosphorous trichloride was purchased from Sigma-Aldrich and distilled before use.
5. Pyrrolidine was purchased from Sigma-Aldrich and distilled over KOH before use.
6. Use of deionized water is necessary. If tap water or acidic water is used, degradation of the ligand can be observed by ^{31}P NMR.
7. Physical characteristics of Taddol-pyrrolidine phosphoramidite: $[\alpha]^{25}_{D}$ = –157.8 (conc = 0.0106 g/mL, $CHCl_3$). ^{1}H NMR (500 MHz, $CDCl_3$) δ: 0.29 (s, 3 H), 1.27 (s, 3 H), 1.68–1.94 (m, 4 H), 3.14–3.31 (m, 2 H), 3.32–3.49 (m, 2 H), 4.83 (d, *J* = 8.5 Hz, 1 H), 5.21 (dd, *J* = 8.4, 3.2 Hz, 1 H), 7.16–7.35 (m, 12 H), 7.41 (d, *J* = 7.1 Hz, 2 H), 7.48 (d, *J* = 7.1 Hz, 2 H),

7.60 (d, J = 7.1 Hz, 2 H), 7.75 (d, J = 7.1 Hz, 2 H). ^{13}C NMR (126 MHz, $CDCl_3$) δ: 25.3, 26.0, 26.0, 27.5, 44.9, 45.0, 81.1, 81.2, 81.8, 82.2, 82.4, 82.5, 82.6, 111.7, 127.0, 127.1, 127.1, 127.2, 127.2, 127.4, 127.4, 127.6, 128.1, 128.7, 128.8, 129.0, 142.0, 142.3, 146.6, 146.9. ^{31}P NMR (121 MHz, $CDCl_3$) δ: 137.1. IR (NaCl, Thin Film) 3058, 2967, 2869, 1493, 1446, 1035, 1003, 878, 737, 699 cm^{-1}. Mp = 214–216 °C (EtOAc). HRMS (ESI) m/z $[C_{35}H_{37}NO_4P]^+$ calcd 566.2455, found 566.2445. Anal. calcd for $C_{35}H_{36}NO_4P$: C, 74.32; H, 6.42; N, 2.48; O, 11.31; P, 5.48, found C, 74.33; H, 6.71; N, 2.54; O, 11.09; P, 5.41.

8. On half scale (2.15 mmol Taddol), the yield was 68%.
9. Dichloromethane (methylene chloride, not stabilized, HPLC grade) was purchased from Fisher Scientific, degassed with Ar and passed through two columns of neutral alumina.
10. 5-Hexenoic acid was purchased from TCI and used as received.
11. 1,8-Diazabicyclo[5.4.0]undec-7-ene was purchased from AK Scientific, Inc. and distilled over KOH before use.
12. Diphenylphosphoryl azide was purchased from AK Scientific, Inc. and used as received.
13. Hexanes were distilled at ambient pressure over boiling chips.
14. Physical characteristics of pentenyl isocyanate: ^{1}H NMR (500 MHz, $CDCl_3$) δ: 1.66–1.77 (m, 2 H), 2.12–2.21 (m, 2 H), 3.32 (t, J = 6.7 Hz, 2 H), 5.02 (ddt, J = 10.2, 1.9, 1.2 Hz, 1 H), 5.07 (dq, J = 17.1, 1.7 Hz, 1 H), 5.77 (ddt, J = 17.0, 10.2, 6.7 Hz, 1 H). ^{13}C NMR (126 MHz, $CDCl_3$) δ: 30.2, 30.5, 42.2, 115.9, 136.8. IR (NaCl, Thin Film) 3369, 2932, 2275, 1687, 1641, 1524, 1211, 911 cm^{-1}.
15. On half scale (43.8 mmol of 5-hexenoic acid), the yield of the product was 44%.
16. The use of a glove box is for simplicity of set up due to the air sensitive nature of chlorobis(ethylene)rhodium(I) dimer. Use of standard Schlenk techniques in place of a glove box should provide similar results if the chlorobis(ethylene)rhodium(I) dimer is of high quality. Chlorobis(cyclooctadiene)rhodium(I) dimer may be used as an air stable alternative, but the submitter has observed lower yields (15–25% lower) when this catalyst is used on smaller scales. The phosphoramidite ligand is air stable and can be stored outside the glovebox, but the ligand is stored in the glovebox for ease of reaction setup.

17. Chlorobis(ethylene)rhodium(I) dimer was purchased from Strem, Inc., stored cold in an inert atmosphere glove box (N_2), and used as received.
18. Toluene (Chromasolv®, for HPLC, 99.9%) was purchased from Sigma-Aldrich, degassed with Ar and passed through one column of neutral alumina and one column of Q5 reactant.
19. 4-Ethynylanisole was purchased from AK Scientific, Inc. and used as received.
20. Column diameter: 6 cm, silica: 140 g (Silicycle, Inc. silica 60 (230-400 mesh)), eluant: 2.5 L (20:1 EtOAc:MeOH), fraction size: 50 mL (25 x 150 mm test tubes), product typically found in fractions 16-49. The first three fractions usually contain a small amount of impurity.
21. Physical characteristics of (*R*)-5-(4-methoxyphenyl)-2,3,8,8a-tetrahydroindolizin-7(1H)-one: 89% ee by HPLC: Chiralcel ODH column, 90:10 Hex:iPrOH, 1 mL/min, 330nm, RT_{major} = 35.48 min, RT_{minor} = 41.75 min. $[\alpha]^{25}_D$ = +637.3 (conc = 0.0084 g/mL $CHCl_3$). ^{1}H NMR (500 MHz, $CDCl_3$) δ: 1.71–2.06 (m, 3 H), 2.25– 2.51 (m, 3 H), 3.27 (dt, *J* = 11.0, 7.1 Hz, 1 H), 3.50–3.58 (m, 1 H), 3.83 (s, 3 H), 3.98–4.09 (m, 1 H), 5.07 (s, 1 H), 6.91 (d, *J* = 8.9 Hz, 2 H), 7.33 (d, *J* = 8.8 Hz, 2 H). ^{13}C NMR (126 MHz, $CDCl_3$) δ: 24.6, 31.7, 41.5, 49.5, 55.3, 58.7, 99.8, 113.8, 128.5, 129.2, 160.8, 162.6, 191.9. R_f = 0.16 (20:1 EtOAc:MeOH). IR (NaCl, Thin Film) 2969, 2875, 1623, 1606, 1510, 1472, 1242, 1176, 1030 cm^{-1}. Mp = 129–132 °C. HRMS (ESI) *m/z* $[C_{15}H_{18}NO_2]^+$ calcd 244.1332, found 244.1327. Anal. calcd for $C_{15}H_{17}NO_2$: C, 74.05; H, 7.04; N, 5.76; O, 13.15, found C, 74.08; H, 7.48; N, 5.80; O, 13.55.
22. On half scale (15 mmol of pentenyl isocyanate), the product was obtained as a viscous dark brown oil (86% yield, 88% ee) that slowly solidified after storing in –10 °C fridge for a week.
23. (*R*)-5-(4-Methoxyphenyl)-2,3,8,8a-tetrahydroindolizin-7(1H)-one can be recrystallized from EtOAc to yield light yellow crystals with 41% (98% ee) recovery. mp = 133–135 °C (EtOAc).

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described in references such as "Prudent Practices in the Laboratory" (The National Academies Press, Washington, D.C., 2011 www.nap.edu). All chemical waste should be disposed of in accordance with local regulations. For general guidelines for the management of chemical waste, see Chapter 8 of Prudent Practices.

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Discussion

The use of chiral phosphoramidites is prevalent in organic chemistry.[2] In our lab, we have found phosphoramidites to be excellent ligands for many of our rhodium-catalyzed syntheses of nitrogen-containing heterocycles.[3] This procedure describes an improved synthesis of Taddol-pyrrolidine phosphoramidite, a chromatography free synthesis of pentenyl isocyanate, and use of these compounds in the enantioselective rhodium-catalyzed [2+2+2] cycloaddition of pentenyl isocyanate and 4-ethynylanisole.

Our first synthesis of Taddol-pyrrolidine phosphoramidite used column chromatography for purification of the phosphoramidite.[4] We have observed that the phosphoramidite is oxidized under acidic conditions and purification via column chromatography can result in partially oxidized ligand. Recrystallization avoids use of acidic silica for purification and makes the overall isolation of the ligand more convenient. Additionally, if the phosphoramidite is partially oxidized, recrystallization allows for isolation of the pure ligand without contamination with the oxidized ligand.

We have traditionally synthesized alkenyl isocyanates in one of two ways: conversion of the acyl azide to the isocyanate under reduced pressure[4] and column chromatography of the acyl azide followed by neat conversion.[5] These methods work well for small scale, but on larger scale, these approaches can potentially be dangerous if proper precautions are not observed. In order to make the synthesis more accessible, we developed a method where the acyl azide is not purified via column

chromatography or isolated neat. The choice of 1,8-diazabicyclo[5.4.0]undec-7-ene as the base allows for good conversion to the acyl azide and makes purification by distillation easier due to its high boiling point.

The enantioselective rhodium-catalyzed [2+2+2] cycloaddition of alkenyl isocyanates and alkynes has been extensively investigated in our lab.[6] This procedure demonstrates the scalability of the reaction and the ability to lower catalyst loadings to 1 mol %.

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1. Department of Chemistry, Colorado State University, Fort Collins, CO 80523, rovis@lamar.colostate.edu. We thank NIGMS (GM80442) for support. We thank Johnson Matthey for a loan of rhodium salts. T. R. thanks Roche for an Excellence in Chemistry Award and Amgen for unrestricted support. D. M. D. thanks NSF-LSAMP Bridge to the Doctorate Program and NIH Ruth M. Kirchstein Fellowship for support.
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6. For a discussion of mechanism, see; Dalton, D. M.; Oberg, K. M.; Yu, R. T.; Lee, E. E.; Perreault, S.; Oinen, M. E.; Pease, M. L.; Malik, G.; Rovis, T. *J. Am. Chem. Soc.* **2009**, *131*, 15717–15728.

Appendix
Chemical Abstracts Nomenclature (Registry Number)

(*R*,*R*)-Taddol: 1,3-Dioxolane-4,5-dimethanol, 2,2-dimethyl-a4,a4, a5,aα-tetraphenyl-, (4*R*,5*R*)-; (93379-48-7)

Triethylamine: Ethanamine, *N*,*N*-diethyl-; (121-44-8)
Phosphorous trichloride; (7719-12-2)
Taddol-pyrrolidine phosphoramidite: Pyrrolidine, 1-[(3a*R*,8a*R*)-tetrahydro-2,2-dimethyl-4,4,8,8-tetraphenyl-1,3-dioxolo[4,5-e][1,3,2]dioxaphosphepin-6-yl]-; (913706-72-6)
5-Hexenoic acid; (1577-22-6)
1-8-Diazabicyclo[5.4.0]undec-7-ene: Pyrimido[1,2-*a*]azepine, 2,3,4,6,7,8,9,10-octahydro-; (6674-22-2)
Diphenyl phosphoryl azide: Phosphorazidic acid, diphenyl ester; (26386-88-9)
4-Pentenyl isocyanate: 1-Pentene, 5-isocyanato-; (2487-98-1)
Chlorobis(ethylene)rhodium(I) dimer: Rhodium, di-μ-chlorotetrakis(η2-ethene)di-; (12081-16-2)
4-Ethynylanisole: Benzene, 1-ethynyl-4-methoxy-; (768-60-5)
(*R*)-5-(4-methoxyphenyl)-2,3,8,8a-tetrahydroindolizin-7(1H)-one: 7(1H)-Indolizinone, 2,3,8,8a-tetrahydro-5-(4-methoxyphenyl)-,(8a*R*)-; (913626-94-5)

Tomislav Rovis was born in Zagreb in the former Yugoslavia but was raised in Southern Ontario, Canada. Following his undergraduate studies at the University of Toronto, he earned his Ph. D. degree at the same institute in 1998 under the direction of Professor Mark Lautens. From 1998-2000, he was an NSERC postdoctoral fellow at Harvard University with Professor David A. Evans. In 2000, he began his independent career at Colorado State University and was promoted in 2005 to Associate Professor and in 2008 to Professor. He currently holds the John K. Stille Chair in Chemistry.

Kevin M. Oberg received his B. A. from Gustavus Adolphus College, where he worked under the supervision of Professor Brian A. O'Brien. He is now pursuing his graduate studies at Colorado State University under the guidance of Professor Tomislav Rovis. His graduate research focuses on the development of metal-catalyzed cycloadditions.

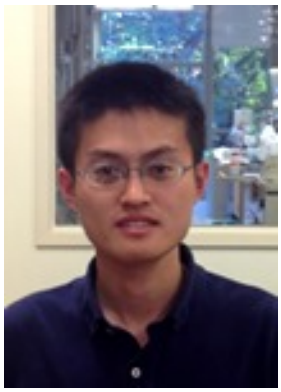
Timothy J. Martin received his B. Sc. in chemistry from University of Delaware. He received his Ph. D. in 2011 from University of North Carolina - Chapel Hill under the direction of Professor Michael Crimmins. His graduate studies were focused on the synthesis of amphidinol 3 and his post-doctoral studies focused on nitrogen heterocycle synthesis using rhodium catalysis.

Mark Emil Oinen graduated with a B.Sc. in chemistry from State University of New York college at Brockport 2005, under the supervision of Professor Margaret Logan. He received his M. Sc. In Chemistry in 2010 from the Colorado State University under the guidance of Professor Tomislav Rovis. Mark is currently an associate research scientist for Crestone Pharmaceuticals in Fort Collins, CO.

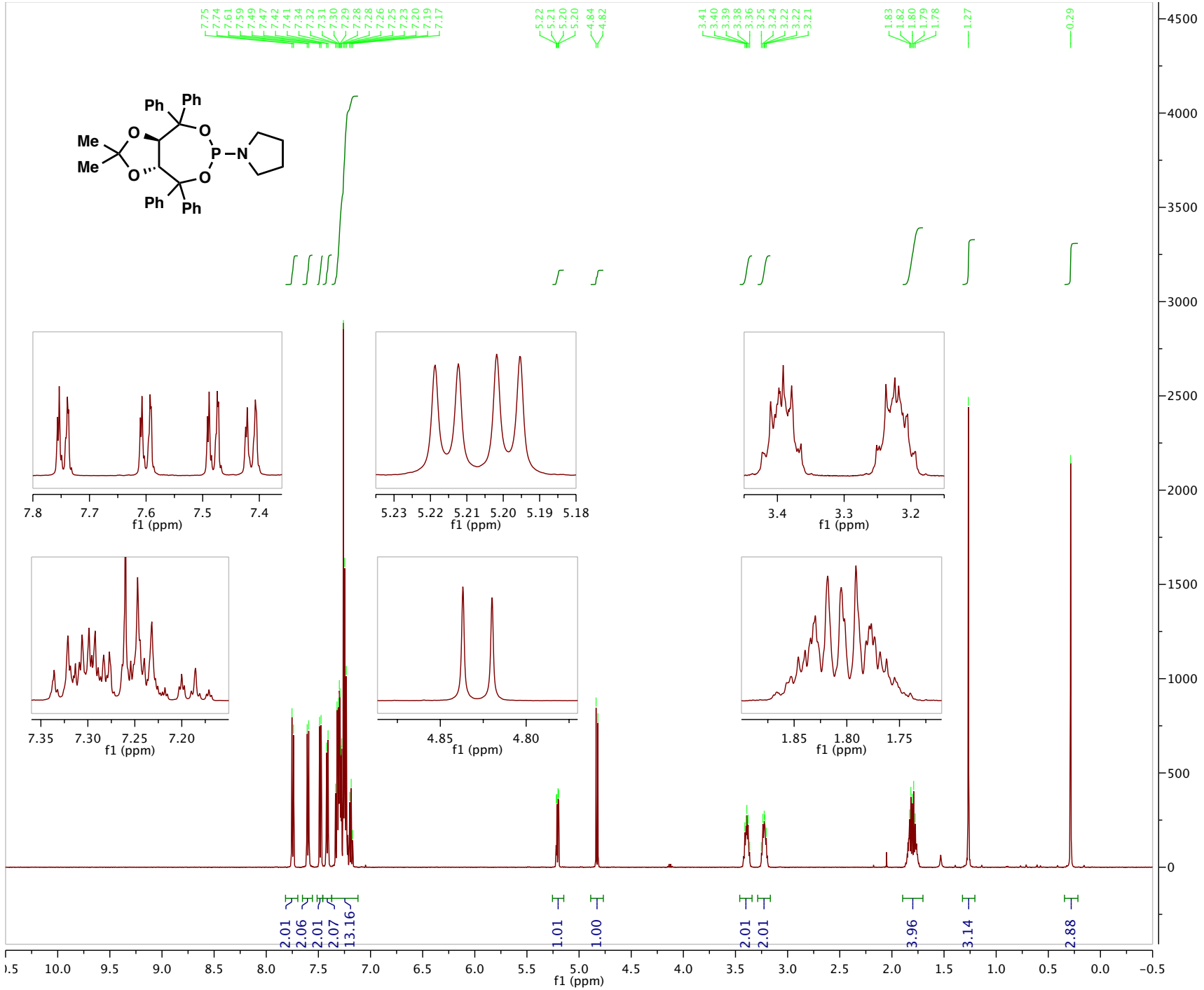
Derek M. Dalton was born in Aurora, Colorado in 1981. After earning a B. A. (Religion) at the Colorado College in 2004 and a B. Sc. (Chemistry) at the University of Colorado Denver in 2007, he entered into his current position as a Ph. D. candidate at Colorado State University where he investigates metal-catalyzed cycloadditions with Tomislav Rovis.

Rebecca Keller Friedman (born 1983) graduated with a B.A. in chemistry from Washington University in St. Louis in 2005. She received her Ph. D. in 2010 from Colorado State University under the guidance of Tomislav Rovis working on the development of rhodium-catalyzed [2+2+2] and [4+2+2] cyclizations. She then joined the labs of Xiang Wang (University of Colorado, Boulder) as a post-doctoral researcher, focusing on the method development of gold-catalyzed [3,3]-rearrangements of indole derivatives. She is currently working as a scientific analyst for Stratfor: Global Intelligence.

Jamie M. Neely received her B. Sc. in chemistry from the University of Missouri in Columbia, where she worked under the supervision of Professor Timothy Glass. She began her graduate studies in 2008 at Colorado State University under the advisement of Professor Tomislav Rovis. Her current research focuses on the synthesis of heterocycles via C-H activation.



Yiyang Liu received his B.S. degree in Chemistry from Peking University in 2010 under the direction of Prof. Jianbo Wang and Prof. Yan Zhang. He then moved to the California Institute of Technology and began his doctoral studies under the guidance of Prof. Brian Stoltz. His graduate research focuses on chemical synthesis using renewable resources.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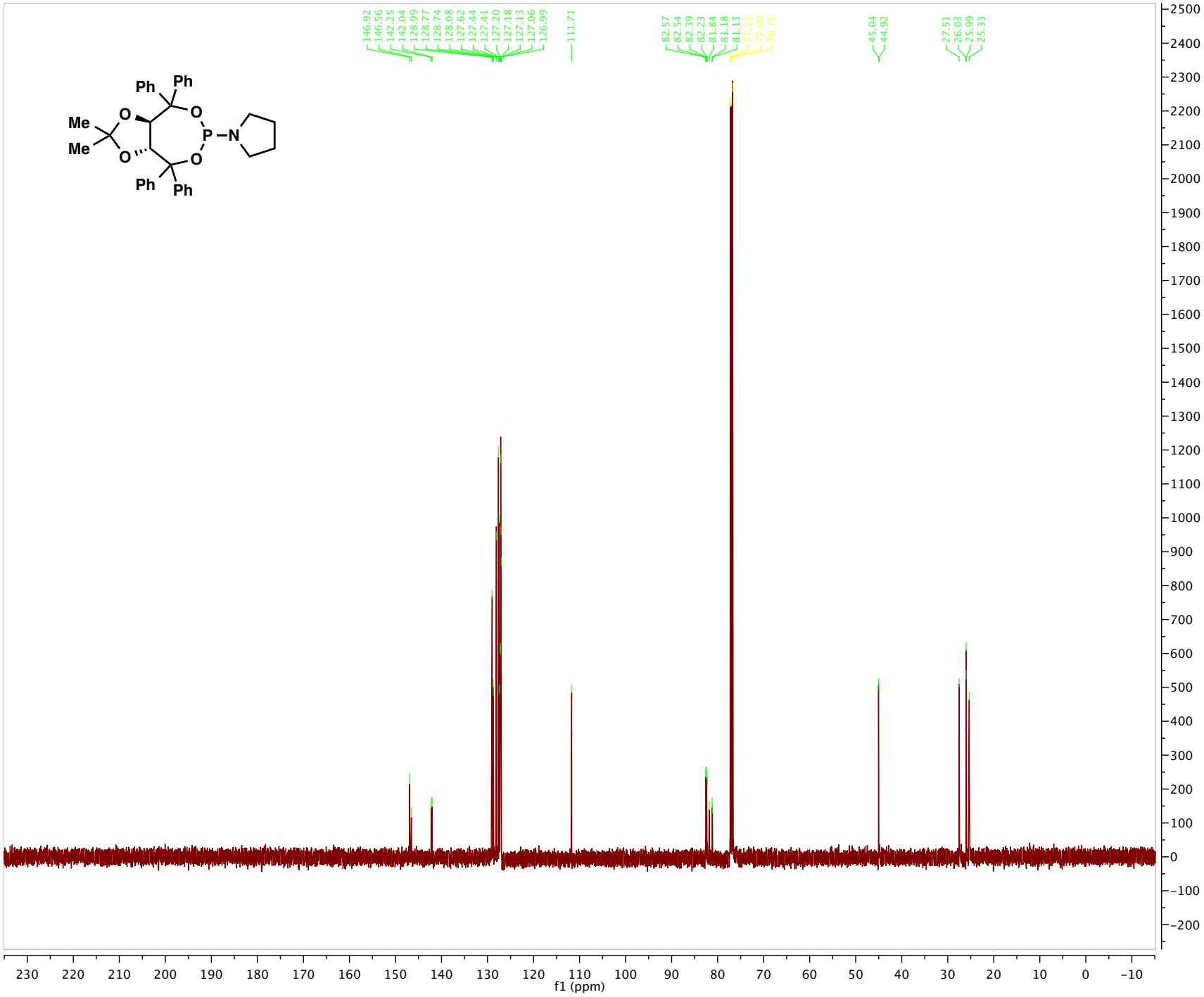
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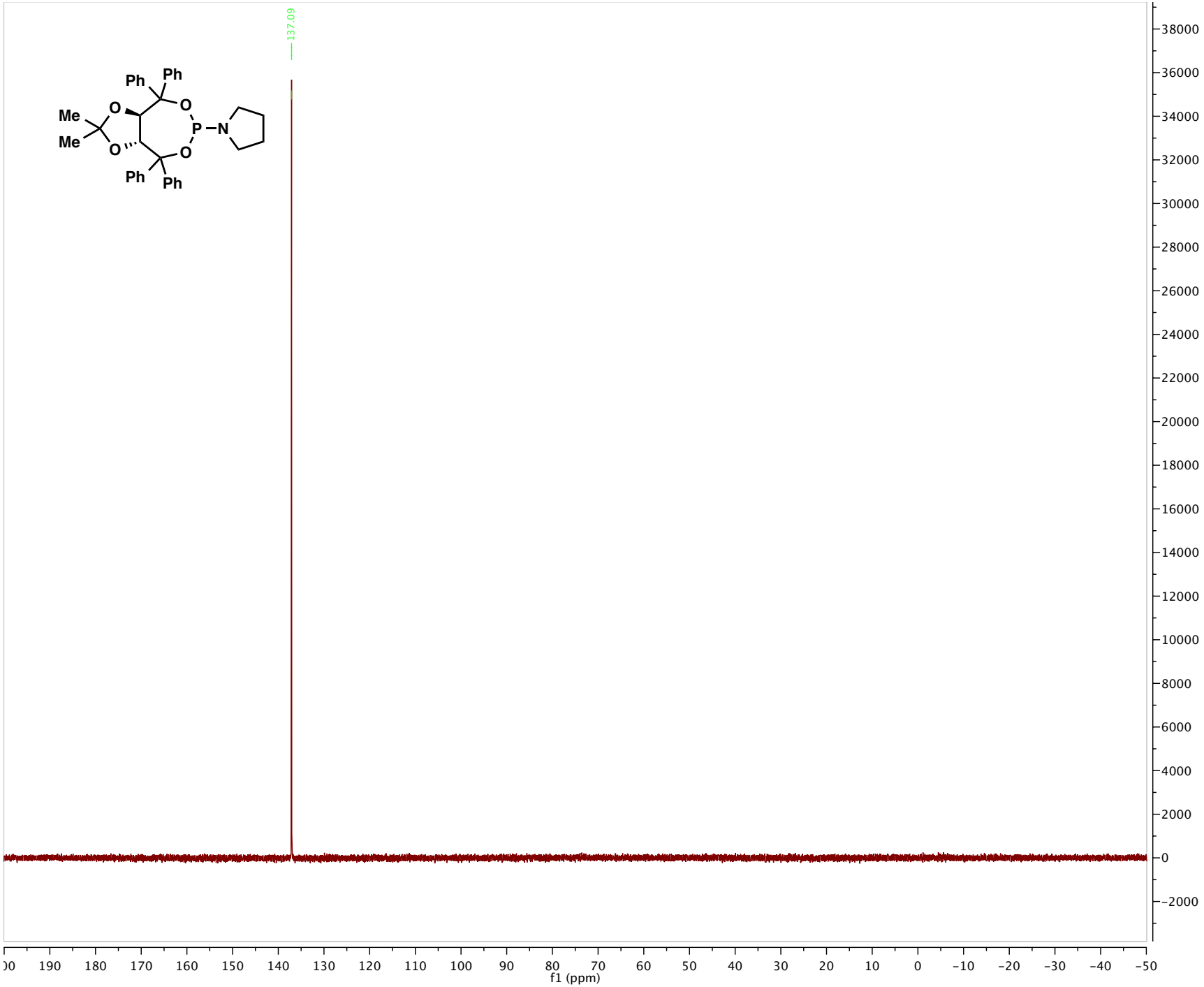
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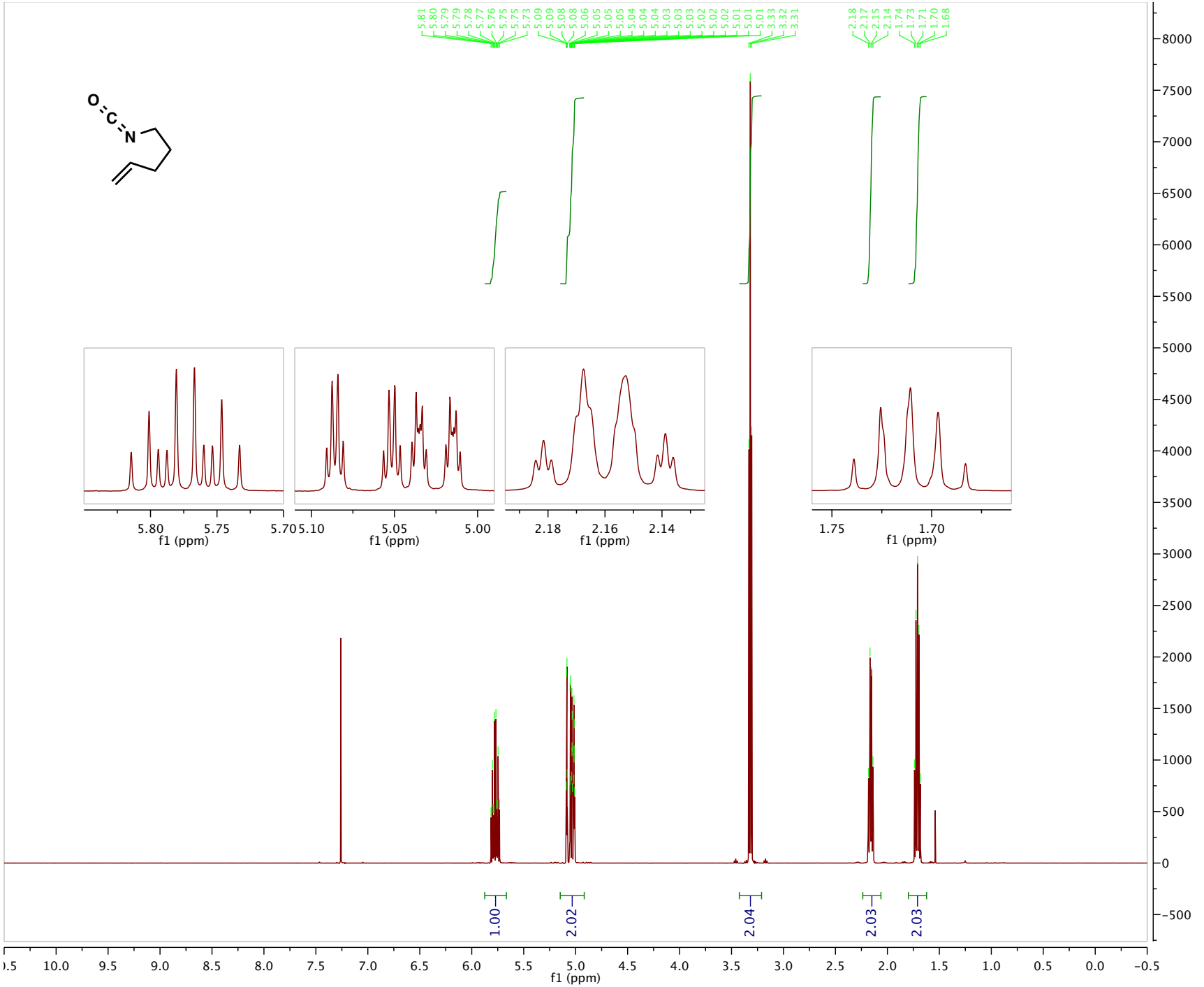
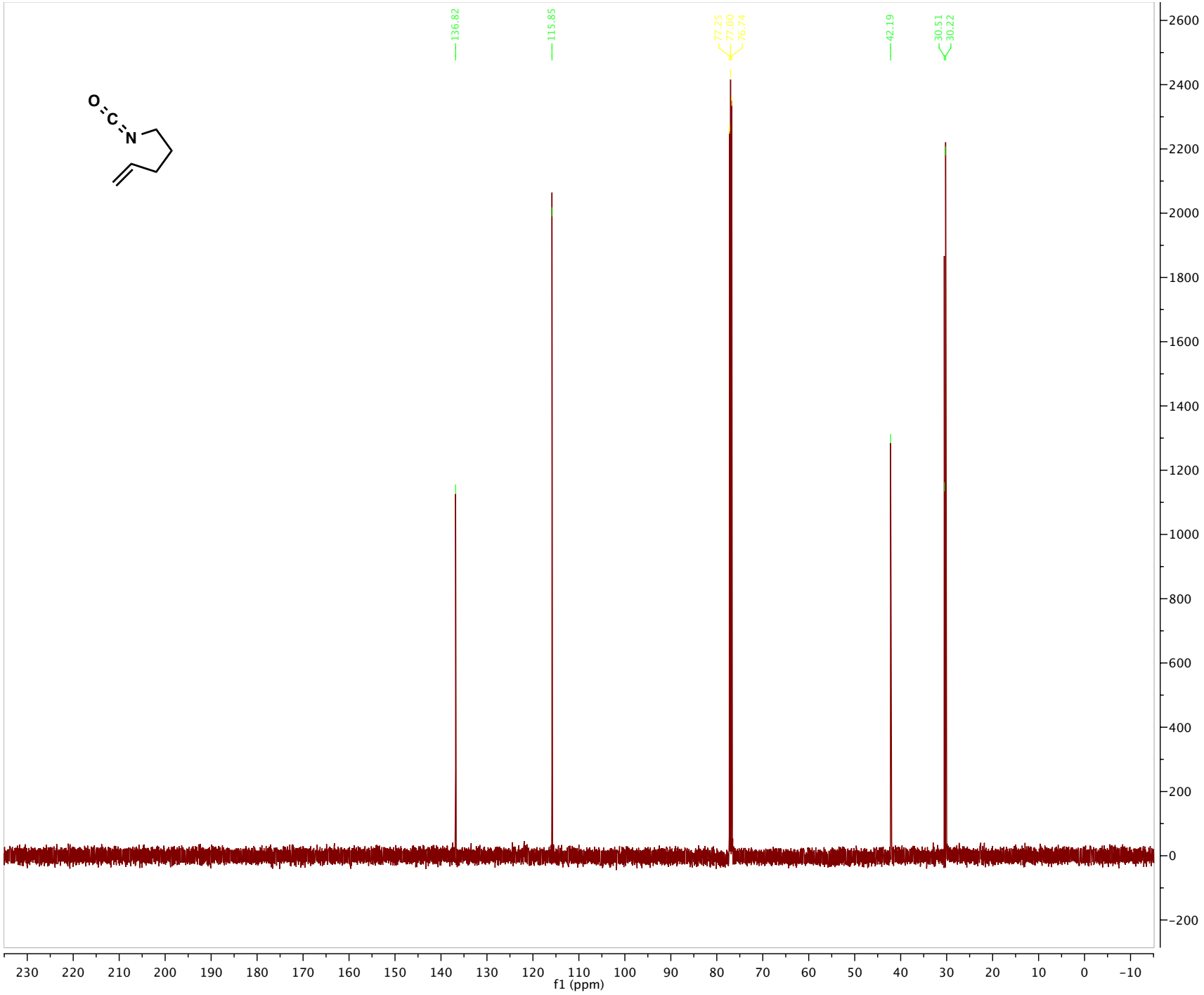
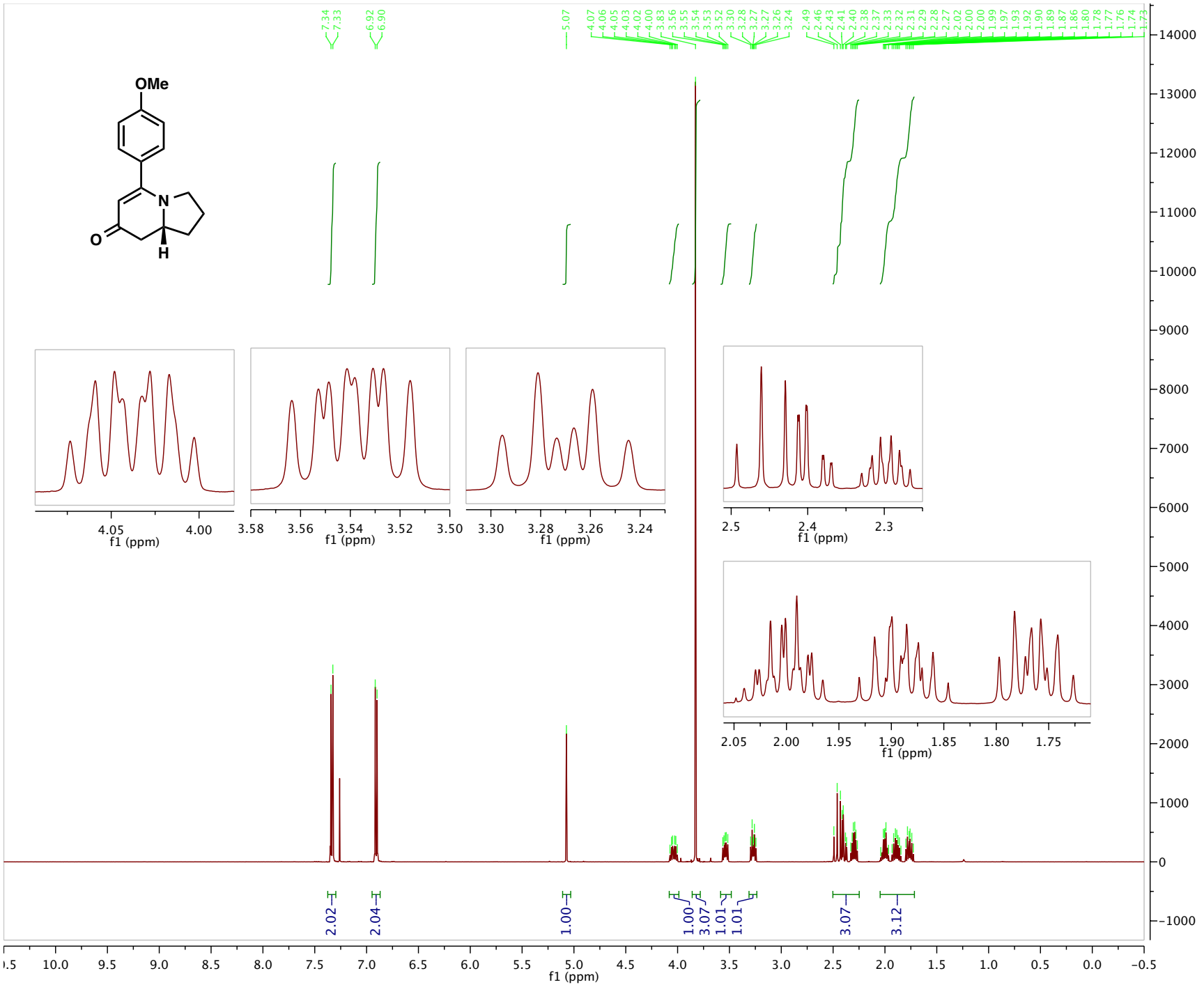
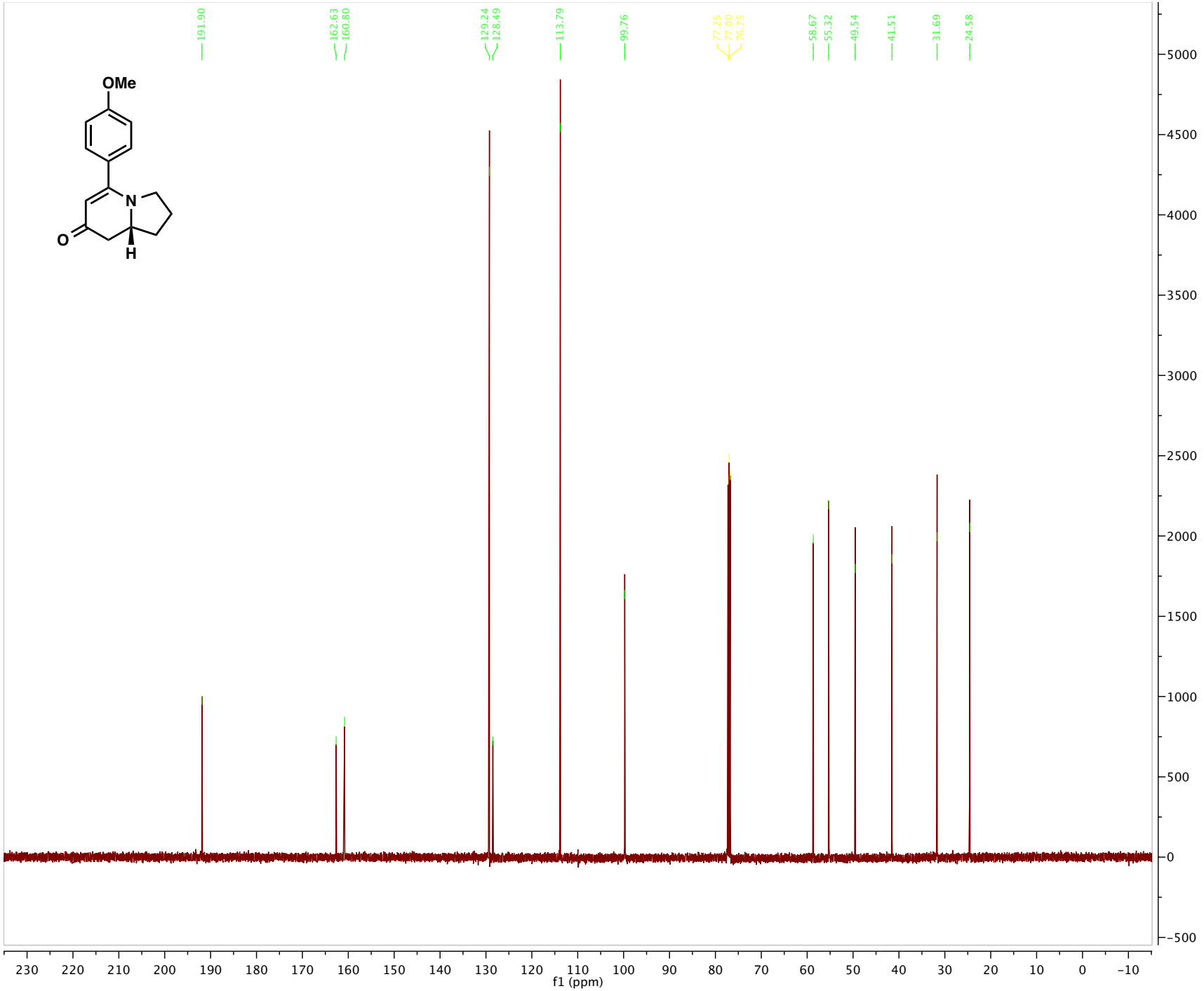
10
0
−10
−20
−30
−40
−50
f1 (ppm)


5.81 5.80 5.79 5.79 5.78 5.77 5.76 5.75 5.75 5.73 5.09 5.09 5.08 5.08 5.06 5.05 5.05 5.05 5.04 5.04 5.03 5.03 5.03 5.02 5.02 5.02 5.01 5.01 5.01 3.33 3.32 3.31 2.18 2.17 2.15 2.14 1.74 1.73 1.71 1.70 1.68
O C N
5.80 5.75 5.70 f1 (ppm)
5.10 5.05 5.00 f1 (ppm)
2.18 2.16 2.14 f1 (ppm)
1.75 1.70 f1 (ppm)
1.00 2.02 2.04 2.03 2.03
f1 (ppm)


136.82
115.85
77.25
77.00
76.74
42.19
30.51
30.22
O
C
N
2600
2400
2200
2000
1800
1600
1400
1200
1000
800
600
400
200
0
-200
230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)


OMe
N
O
H
7.34
7.33
6.92
6.90
5.07
4.07
4.06
4.05
4.03
4.02
4.00
3.83
3.56
3.55
3.54
3.53
3.52
3.30
3.28
3.27
3.27
3.26
3.24
2.49
2.46
2.43
2.41
2.40
2.38
2.37
2.33
2.32
2.31
2.29
2.28
2.27
2.02
2.00
2.00
1.99
1.97
1.93
1.92
1.90
1.89
1.87
1.86
1.80
1.78
1.77
1.76
1.74
1.73
4.05
4.00
f1 (ppm)
3.58
3.56
3.54
3.52
3.50
f1 (ppm)
3.30
3.28
3.26
3.24
f1 (ppm)
2.5
2.4
2.3
f1 (ppm)
2.05
2.00
1.95
1.90
1.85
1.80
1.75
f1 (ppm)
2.02
2.04
1.00
1.00
3.07
1.01
1.01
3.07
3.12
f1 (ppm)


191.90
162.63
160.80
129.24
128.49
113.79
99.76
77.25
77.00
76.75
58.67
55.32
49.54
41.51
31.69
24.58
OMe
N
O
H
f1 (ppm)