# Electronic Supplemental Information

## Gold(I)-Catalysed Approach towards Harmalidine an Elusive Alkaloid from Peganum harmala

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## General Information

Proton ($^{1}$H NMR) and carbon ($^{13}$C NMR) nuclear magnetic resonance spectra were recorded on 300, 400 or 500 MHz instruments. The chemical shifts are given in parts-per-million (ppm) on the delta scale. The solvent peak was used as reference value. For $^{1}$H NMR: $CDCl_3$ = 7.26 ppm, Acetone-$d_6$ = 2.05 ppm, Benzene-$d_6$ = 7.16 ppm. For $^{13}$C NMR: $CDCl_3$= 77.16 ppm, Acetone-$d_6$ = 29.84 ppm, Benzene-$d_6$ = 128.06 ppm. Data are presented as follows; chemical shift, multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, b = broad), coupling constants (*J* in Hz) and integration and carbons with same chemical shift as follows: chemical shift (x carbons). Infrared spectra were recorded neat. Wavelengths of maximum absorbance ($\nu_{max}$) are quoted in wave numbers ($cm^{-1}$). High resolution mass spectra (HRMS) data were recorded on a microTOF spectrometer equipped with orthogonal electrospray interface (ESI). The parent ions $[M]^+$, $[M+H]^+$, $[M+Li]^+$, $[M+K]^+$ or $[M+Na]^+$ are quoted. Analytical thin layer chromatography (TLC) was carried out on silica gel 60 $F_{254}$ plates with visualization by ultraviolet light, cerium-ammonium-molybdate or potassium permanganate dip. Flash column chromatography was carried out using silica gel 60 (40−63 μm) and the procedure included the subsequent evaporation of solvents *in vacuo*. Reagents and solvents were purified using standard means. Dichloroethane (DCE) was distilled from $CaH_2$, triethylamine ($Et_3N$) and pyridine were distilled from KOH; tetrahydrofuran (THF), diethyl ether ($Et_2O$), acetonitrile (MeCN), toluene (PhMe) and dichloromethane (DCM) were dried by passing through activated alumina under argon pressure using GlassTechnology GTS100 devices. Anhydrous reactions were carried out in flame-dried glassware and under an argon atmosphere. $K_2CO_3$ was dried overnight in an oven at 110 °C. All other chemicals were used as received, all extractive procedures were performed using non-distilled solvents and all aqueous solutions were saturated unless details are given. AuCl (Premion grade, 99.99%), $AuCl_3$ (99.9%) and $NaAuCl_4{\cdot}2H_2O$ (Premion grade, 99.99%) were purchased from Alfa Aesar whereas $AgSbF_6$ (98%), AgOTf (99%), $AgBF_4$ (99%), $Ag_2CO_3$ (99%+) and AgCl (99.9%) were purchased from STREM Chemicals. $AgNTf_2$ was prepared from commercially available $HNTf_2$ (Aldrich) and $Ag_2CO_3$. Triphenylphosphine ($PPh_3$) was recrystallized from MeOH and dried under vacuum. All other phosphine or phosphite ligands were purchased from STREM Chemicals. All phosphinegold(I) chloride precatalysts were prepared by reduction of $NaAuCl_4$ with thiodiethanol followed by subsequent addition of the appropriate phosphine.[1] IPrAuCl was prepared following the procedure described by Nolan *et al.*[2] Silver-free preactivated catalysts were prepared either from the corresponding phosphine gold chloride and $AgSbF_6$ in acetonitrile or $AgNTf_2$ in $CH_2Cl_2$ followed by filtration over a short pad of celite. Silylated propargylic alcohols **1a**[3] and **1b**[4] and $\alpha,\beta$-acetylenic aldehydes **2a**[5], **2b**[6] and **2c**[7] are known compounds and have been prepared according to reported procedures.

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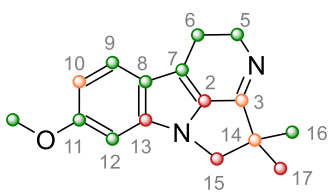
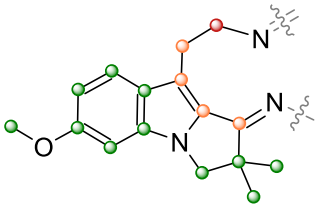
[1] A. K. Al'Sa-Ady, C. A. McAuliffe, R. V. Parish and J. A. Sandeank, *Inorg. Synth*., **1985**, 191.
[2] P. De Frémont, N. M. Scott, E. D. Stevens and S. P. Nolan, *Organometallics,* **2005**, *24*, 2411.
[3] S. F. Kirsch, P. Klahn and H. Menz, *Synthesis,* 2011, **22**, 3592.
[4] K. Nacro, M. Baltas and L. Gorrichon, *Tetrahedron*, 1999, **55**, 14013.
[5] N. Kern, M. Hoffmann, A. Blanc, J.-M. Weibel and P. Pale, *Org. Lett.*, 2013, **15**, 836.
[6] T. Luu and R. R. Tykwinski, *J. Org. Chem.*, 2006, **71**, 8982.
[7] Z.-L. Liu, C. Yang, Q.-Y. Xue, M. Zhao, C.-C. Shan, Y.-H. Xu and T.-P. Loh, *Angew. Chem., Int. Ed.*, 2019, **58**, 16538.

## Experimental and predicted $^{13}$C NMR data of harmalidine & compound 13

**Table S1.** Comparison of experimental and predicted $^{13}$C NMR data of harmalidine and experimental $^{13}$C NMR data pyrrolo[1,2-*a*]indole **13**.




**harmalidine**

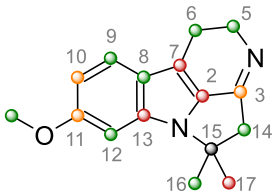



**13**

| Position | harmalidine | | harmalidine | harmalidine | | **13** |
|---|---|---|---|---|---|---|
| Carbon | $^{13}$C[a] | Difference (Exp-Pred/ppm)[b] | $^{13}$C Neural Network Prediction[c] | $^{13}$C HOSE-Code Prediction[c] | $^{13}C_{exp}$ | Difference (Exp-Harmalidine Pred/ppm)[b] |
| 2 | 126.3 | 7.8 | 144.0 | 134.1 | 129.5 | 4.6 |
| 3 | 161.3/144.5[d] | 4.4/12.4 | 172.8 | 156.9 | 168.4 | 4.4 |
| 5 | 42.8 | 2.7 | 46.7 | 45.5 | 56.1 | 9.1 |
| 6 | 19.0 | 0.2 | 22.9 | 19.2 | 28.2 | 5.3 |
| 7 | 119.1 | 3.6 | 115.5 | 133.8 | 109.7 | 5.8 |
| 8 | 126.7/124.4[e] | 0.1/2.4 | 118 | 126.8 | 126.8 | 0.0 |
| 9 | 122.1 | 1.2 | 120.9 | 119.2 | 122.0 | 1.1 |
| 10 | 115.0 | 5.4 | 109.8 | 109.6 | 111.3 | 1.5 |
| 11 | 144.5/161.3[d] | 11.4/1.3 | 155.9 | 160.0 | 158.0 | 2.0 |
| 12 | 94.0 | 0.2 | 92.2 | 94.2 | 91.6 | 0.6 |
| 13 | 124.4/126.7[e] | 10.9/9.1 | 136.6 | 135.3 | 134.2 | 1.1 |
| 14 | 39.7 | 4.6 | 44.3 | 46.4 | 48.6 | 2.2 |
| 15 | 43.0 | 9.7 | 57.6 | 52.7 | 53.9 | 1.2 |
| 16 | 27.0 | 1.4 | 25.6 | 26.5 | 27.2 | 0.7 |
| 17 | 14.0 | 11.6 | 25.6 | 26.5 | 27.2 | 0.7 |
| OMe | 55.2 | 0.3 | 56.0 | 55.5 | 55.6 | 0.1 |

[a]NMR data from reference 1; [b]Difference of experimental and the closest predicted value in ppm (green < 4 ppm; orange = 4-6 ppm; red > 6 ppm); [c]Neural Network or HOSE-Code NMR predictions obtained from CSEARCH Robot-Referee at https://nmrpredict.orc.univie.ac.at/c13robot/robot.php; [d]Values may be reversed. [e]Values may be reversed.

**Table S2.** Comparison of experimental $^{13}C$ NMR data of harmalidine and predicted $^{13}C$ NMR data of dimethyl isomer of harmaline.

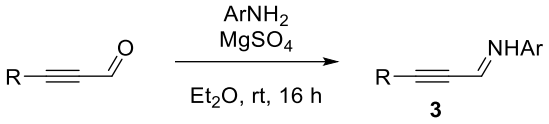



**Dimethyl isomer of harmalidine**

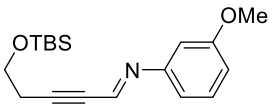
| Position | harmalidine | **dimethyl isomer of harmaline** | | |
|---|---|---|---|---|
| Carbon | $^{13}C$ | Difference (Exp-Pred/ppm)[b] | $^{13}C$ Neural Network Prediction | $^{13}C$ HOSE-Code Prediction |
| 2 | 126.3 | 7.8 | 156.1 | 134.1 |
| 3 | 161.3/144.5[d] | 4.4/12.4 | 157.2 | 156.9 |
| 5 | 42.8 | 0.2 | 47.5 | 42.6 |
| 6 | 19.0 | 0.2 | 22.9 | 19.2 |
| 7 | 119.1 | 14.7 | 98.7 | 133.8 |
| 8 | 126.7/124.4[e] | 0.1/2.4 | 119.3 | 126.8 |
| 9 | 122.1 | 1.8 | 120.3 | 119.2 |
| 10 | 115.0 | 5.4 | 107.5 | 109.6 |
| 11 | 144.5/161.3[d] | 9.6/5.5 | 154.1 | 155.8 |
| 12 | 94.0 | 2.7 | 98.0 | 96.7 |
| 13 | 124.4/126.7[e] | 10.9/9.1 | 140.7 | 135.3 |
| 14 | 39.7 | 3.5 | 43.2 | 33.7 |
| 15 | 43.0 | 19.6 | 77.4 | 62.6 |
| 16 | 27.0 | 0.2 | 27.2 | 26.2 |
| 17 | 14.0 | 12.2 | 27.2 | 26.2 |
| OMe | 55.2 | 0.3 | 56.0 | 55.5 |

[a]NMR data from reference 1; [b]Difference of experimental and the closest predicted value in ppm (green < 4 ppm; orange = 4-6 ppm; red > 6 ppm, black > 15 ppm); [c]Neural Network or HOSE-Code predictions obtained from CSEARCH Robot-Referee at https://nmrpredict.orc.univie.ac.at/c13robot/robot.php; [d]Values may be reversed. [e]Values may be reversed.

## General Procedure 1 for preparation of alkynyl aldimines (GP1)

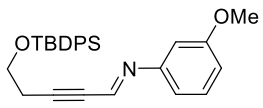



The appropriate $\alpha,\beta$-acetylenic aldehyde (5 mmol, 1 equiv) was dissolved in dry $Et_2O$ (10 mL) with $MgSO_4$ (15 mmol, 3 equiv) and the appropriate aniline derivative (5 mmol, 1 equiv) and vigorously stirred at room temperature for 16 hours. The mixture was then filtered through a pad of celite before being concentrated under vacuum. The crude imine **3** was used in the next step without purification (yields were assumed quantitative).



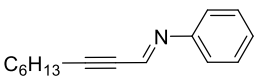

$C_{18}H_{27}NO_2Si$ MW: 317.50

**(*E*)-5-((*tert*-Butyldimethylsilyl)oxy)-*N*-(3-methoxyphenyl)pent-2-yn-1-imine (3a):** Prepared following the **GP1** from 5-((*tert*-butyldimethylsilyl)oxy)pent-2-ynal[5] **2a** (2.33 g, 11 mmol) and 3-methoxyaniline (1.24 mL, 11 mmol, *E*/*Z* ratio 92/8).Yellowish oil; **$^1$H NMR (500 MHz, $CDCl_3$) $\delta$** 0.09 (s, 6 H), 0.91 (s, 9 H), 2.66 (td, *J* = 1.7, 7.2 Hz, 2 H), 3.81 (s, 3 H), 3.83 (t, *J* = 7.2 Hz, 2 H), 6.69 (dd, *J* = 1.7, 2.4 Hz, 1 H), 6.71 (dd, *J* = 1.7, 7.8 Hz, 1 H), 7.00 (dd, *J* = 2.4, 8.3 Hz, 1 H), 7.25 (dd, *J* = 7.8, 8.3 Hz, 1 H), 7.69 (t, *J* = 1.7 Hz, 1 H); **$^{13}$C NMR (126 MHz, $CDCl_3$) $\delta$** -5.2 (x2), 18.5, 24.0, 26.0 (x3), 55.4, 61.4, 80.5, 94.5, 106.8, 112.7, 112.8, 130.0, 144.3, 152.4, 160.4.




$C_{28}H_{31}NO_2Si$ MW: 441.65

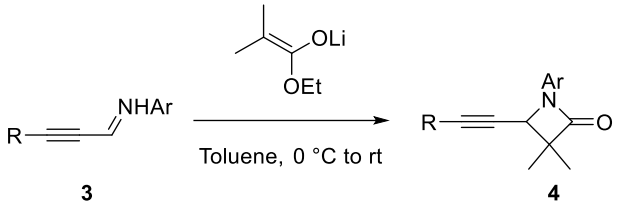
**(*E*)-5-((*tert*-Butyldiphenylsilyl)oxy)-*N*-(3-methoxyphenyl)pent-2-yn-1-imine (3b):** Prepared following the **GP1** from 5-((*tert*-butyldiphenylsilyl)oxy)pent-2-ynal[6] **2b** (4.16 g, 12.36 mmol) and 3-methoxyaniline (1.4 mL, 12.36 mmol, *E*/*Z* ratio 92/8). Yellow oil; **$^1$H NMR (500 MHz, $C_6D_6$) $\delta$** 1.17 (s, 9 H), 2.34 (td, *J* = 1.6, 6.6 Hz, 2 H), 3.24 (s, 3 H), 3.66 (t, *J* = 6.6 Hz, 2 H), 6.62–6.70 (m, 2 H), 6.71–6.74 (m, 1 H), 7.00 (dd, *J* = 8.0, 8.0 Hz, 1 H), 7.19–7.28 (m, 6 H), 7.49 (dd, *J* = 1.3, 1.8 Hz, 1 H), 7.74–7.81 (m, 4 H).




$C_{15}H_{19}N$ MW: 213.32

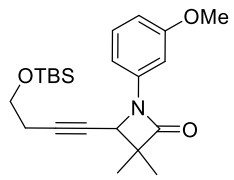
**(*E*)-*N*-Phenylnon-2-yn-1-imine (3c):** Prepared following the **GP1** from non-2-ynal[7] **2c** (2.0 g, 14.5 mmol) and aniline (1.35 g, 14.5 mmol, *E*/*Z* ratio 89/11). Yellowish oil; **$^1$H NMR (500 MHz, $CDCl_3$) $\delta$** 0.90 (t, *J* = 7.0 Hz, 3 H), 1.26–1.35 (m, 4 H), 1.41–1.47 (m, 2 H), 1.58–1.65 (m, 2 H), 2.44 (td, *J* = 1.7, 7.2 Hz, 2 H), 7.14 (d, *J* = 7.6 Hz, 2 H), 7.24 (dd, *J* = 7.6, 7.6 Hz, 1 H), 7.36 (dd, *J* = 7.6, 7.6 Hz, 2 H), 7.69 (t, *J* = 1.7 Hz, 1 H); **$^{13}$C NMR (126 MHz, $CDCl_3$) $\delta$** 14.2, 19.7, 22.7, 28.2, 28.8, 31.4, 79.7, 98.0, 120.9 (x2), 127.0, 129.3 (x2), 144.5, 151.2.

## General Procedure 2 for enolate-imine condensation (GP2)



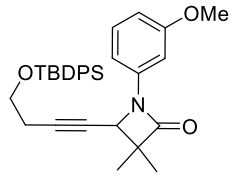

3 4

To a cooled solution of DIPA (4.4 mmol, 2.2 equiv) in toluene (8 mL) at -78 °C under argon was added *n*-BuLi dropwise (1.6 M in hexanes, 4.4 mmol, 2.2 equiv). After 10 min of stirring, ethyl *iso*butyrate (4 mmol, 2 equiv) previously dissolved in 2 mL of toluene was added dropwise and the mixture was warmed to 0 °C. After 30 min of stirring, the imine **3** (2 mmol, 2 equiv) previously dissolved in 2 mL of toluene was added dropwise. The mixture was then warmed to room temperature and stirred overnight. The reaction was quenched with 1N HCl (10 mL) and extracted with EtOAc (3 x 15 mL). The combined organic layers were washed with water, $NaHCO_3$, brine, and dried over $MgSO_4$. After filtration and evaporation, the crude product was purified by flash chromatography ($SiO_2$, Cyclohexane/EtOAc) to afford the title azetidinone **4**.



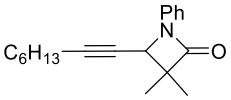

$C_{22}H_{33}NO_3Si$ MW: 387.60

**4-(4-((*tert*-Butyldimethylsilyl)oxy)but-1-yn-1-yl)-1-(3-methoxyphenyl)-3,3-dimethylazetidin-2-one (4a) :** Prepared following the **GP2** in 71 % yield over two steps (3.01 g, 7.77 mmol) from 2.33 g of the crude imine **3a**. Yellow oil; **TLC** $R_f$ 0.48 (Cyclohexane/EtOAc 20 %); **IR (neat)** $\nu_{max}$ 663, 686, 734, 773, 809, 834, 915, 991, 1006, 1041, 1103, 1158, 1185, 1219, 1246, 1279, 1335, 1368, 1389, 1461, 1495, 1600, 1754, 2857, 2929, 2956; **$^1$H NMR (500 MHz, $CDCl_3$)** $\delta$ 0.04 (s, 6 H), 0.88 (s, 9 H), 1.40 (s, 6 H), 2.46 (td, *J* = 2.0, 7.0 Hz, 2 H), 3.70 (t, *J* = 7.0 Hz, 2 H), 3.81 (s, 3 H), 4.29 (t, *J* = 2.0 Hz, 1 H), 6.65 (dd, *J* = 2.4, 8.2 Hz, 1 H), 7.04 (dd, *J* = 1.7, 8.2 Hz, 1 H), 7.16 (dd, *J* = 1.7, 2.5 Hz, 1 H), 7.23 (dd, *J* = 8.2, 8.2 Hz, 1 H); **$^{13}$C NMR (126 MHz, $CDCl_3$)** $\delta$ -5.2 (x2), 18.4, 19.1, 21.8, 23.4, 26.0 (x3), 54.3, 54.6, 55.5, 61.8, 75.1, 87.2, 102.9, 109.2, 110.1, 130.0, 139.0, 160.3, 170.7; **HR-MS** 388.2306 ($C_{22}H_{33}NO_3Si+H^+$) calcd 388.2302.




$C_{32}H_{37}NO_3Si$ MW: 511.74

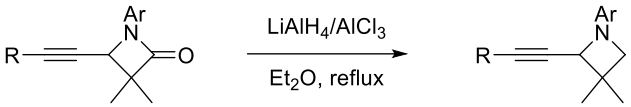
**4-(4-((*tert*-Butyldiphenylsilyl)oxy)but-1-yn-1-yl)-1-(3-methoxyphenyl)-3,3-dimethylazetidin-2-one (4b):** Prepared following the **GP2** in 90 % yield (5.70 g, 11.14 mmol) from 4.16 g of the crude imine **3b**. Yellow oil; **TLC** $R_f$ 0.42 (Cyclohexane/EtOAc 20 %); **IR (neat)** $\nu_{max}$ 488, 503, 613, 686, 701, 735, 772, 822, 851, 938, 997, 1040, 1107, 1157, 1185, 1219, 1246, 1279, 1335, 1368, 1389, 1428, 1460, 1495, 1600, 1754, 2857, 2930, 2960; **$^1$H NMR (500 MHz, $CDCl_3$)** $\delta$ 1.03 (s, 9 H), 1.37 (s, 3 H), 1.39 (s, 3 H), 2.50 (td, *J* = 1.9, 6.8 Hz, 2 H), 3.75 (t, *J* = 6.8 Hz, 2 H), 3.78 (s, 3 H), 4.27 (t, *J* = 1.9 Hz, 1 H), 6.64 (dd, *J* = 2.0, 8.1 Hz, 1 H), 7.02 (dd, *J* = 1.5, 8.1 Hz, 1 H), 7.16 (dd, *J* = 2.0, 2.0 Hz, 1 H), 7.20 (dd, *J* = 8.1, 8.1 Hz, 1 H), 7.34–7.40 (m, 4 H), 7.42–7.46 (m, 2 H), 7.63–7.68 (m, 4 H); **$^{13}$C NMR (126 MHz, $CDCl_3$)** $\delta$ 19.1, 19.3, 21.8, 23.2, 26.8 (x3), 54.3, 54.6, 55.4, 62.3, 75.1, 87.3, 102.8, 109.1, 110.1, 127.8 (x4), 129.9 (x2), 130.0, 133.6 (x2), 135.7 (x4), 138.9, 160.2, 170.7; **HR-MS** 550.2170 ($C_{32}H_{37}NO_3Si+K^+$) calcd 550.2174.




$C_{19}H_{25}NO$ MW: 283.42

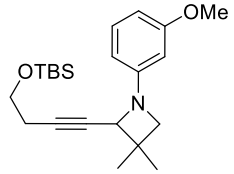
**3,3-Dimethyl-4-(oct-1-yn-1-yl)-1-phenylazetidin-2-one (4c):** Prepared following the **GP2** in 85 % yield (3.51 g, 12.38 mmol) from the crude imine **3c**. Colorless oil; **TLC** $R_f$ 0.42 (Cyclohexane/EtOAc 10 %); **IR (neat)** $\nu_{max}$ 476, 513, 652, 690, 751, 896, 985, 1049, 1082, 1118, 1179, 1278, 1332, 1367, 1388, 1459, 1501, 1598, 1753, 2869, 2927, 2959; **$^1$H NMR (500 MHz, $CDCl_3$)** $\delta$ 0.87 (t, *J* = 6.8 Hz, 3 H), 1.21–1.31 (m, 4 H), 1.32–1.39 (m, 2 H), 1.40 (s, 3 H), 1.41 (s, 3 H), 1.46–1.52 (m, 2 H), 2.24 (td, *J* = 2.0, 7.0 Hz, 2 H), 4.31 (t, *J* = 2.0 Hz, 1 H), 7.09 (dd, *J* = 7.4, 7.4 Hz, 1 H), 7.34 (dd, *J* = 7.4, 8.5 Hz, 2 H), 7.53 (d, *J* = 8.5 Hz, 2 H); **$^{13}$C NMR (126 MHz, $CDCl_3$)** $\delta$ 14.2, 18.9, 19.1, 21.8, 22.7, 28.6 (x2), 31.4, 54.2, 54.6, 74.1, 90.3, 117.1 (x2), 123.9, 129.1 (x2), 137.8, 170.7; **HR-MS** 284.1997 ($C_{19}H_{25}NO+H^+$) calcd 284.2009.

## General Procedure 3 for azetidinone reduction (GP3)




**4** **5**

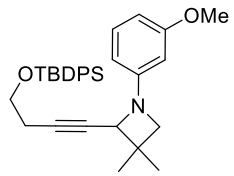
To a stirred solution of $AlCl_3$ (6 mmol, 3 equiv) in $Et_2O$ (5 mL) at room temperature under argon was added a solution of $LiAlH_4$ (6 mmol, 3 equiv) previously dissolved in $Et_2O$ (10 mL). The resulting mixture was refluxed for 30 min and the azetidinone **4** (2 mmol, 1 equiv) was added dropwise as a solution in $Et_2O$ (2 mL). After completion of the reaction (within a few minutes as monitored by TLC), the mixture was cooled to 0 °C, diluted with $Et_2O$ (at least 50 mL) and an aqueous sodium potassium tartrate solution (12 mmol, 6 equiv in 50 mL $H_2O$) was added very carefully and dropwise until bubbling stopped. The mixture was then stirred vigorously for several hours until decantation was clean. After separation of the two layers, the aqueous layer was extracted with $Et_2O$ (3 x 10 mL), the combined organic layers were washed with water and brine, concentrated and the residue was stirred for 30 min in a 3:1 THF/water mixture (30 mL) in the presence of EDTA (4 mmol, 2 equiv). After partitioning the mixture between $Et_2O$ and brine (30 + 30 mL), layers were separated, and the aqueous layer was extracted again with $Et_2O$ (30 mL). The combined organic layers were dried over $MgSO_4$, filtered and concentrated, and the residue was purified by flash chromatography ($SiO_2$, Cyclohexane/EtOAc) to afford the title compound **5.**




$C_{22}H_{35}NO_2Si$ MW: 373.61

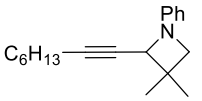
**2-(4-((*tert*-Butyldimethylsilyl)oxy)but-1-yn-1-yl)-1-(3-methoxyphenyl)-3,3-dimethylazetidine (5a):** Prepared following the **GP3** in 77 % yield (1.10 g, 2.94 mmol) from azetidinone **4a** (1.49 g, 3.84 mmol). Colorless oil; **TLC** $R_f$ 0.44 (Cyclohexane/EtOAc 10 %); **IR (neat)** $\nu_{max}$ 546, 584, 665, 687, 775, 832, 915, 1048, 1099, 1163, 1214, 1238, 1252, 1290, 1338, 1460, 1494, 1598, 1611, 2854, 2927, 2954; **$^1$H NMR (500 MHz, $CDCl_3$)** $\delta$ 0.07 (s, 6 H), 0.90 (s, 9 H), 1.20 (s, 3 H), 1.42 (s, 3 H), 2.49 (td, *J* = 2.1, 7.2 Hz, 2 H), 3.35 (d, *J* = 6.5 Hz, 1 H), 3.58 (d, *J* = 6.5 Hz, 1 H), 3.74 (td, *J* = 0.9, 7.2 Hz, 2 H), 3.78 (s, 3 H), 4.16 (t, *J* = 2.1 Hz, 1 H), 6.22 (dd, *J* = 2.5, 2.5 Hz, 1 H), 6.29 (dd, *J* = 2.5, 8.0 Hz, 1 H), 6.35 (dd, *J* = 2.5, 8.0 Hz, 1 H), 7.12 (dd, *J* = 8.0, 8.0 Hz, 1 H); **$^{13}$C NMR (126 MHz, $CDCl_3$)** $\delta$ -5.1 (x2),

18.5, 23.5, 24.7, 26.0 (x3), 26.9, 36.0, 55.2, 62.1, 63.1, 63.7, 78.6, 85.1, 98.8, 103.8, 105.6, 129.8, 153.2, 160.5; **HR-MS** 374.2496 ($C_{22}H_{35}NO_2Si+H^+$) calcd 374.2510.



$C_{32}H_{39}NO_2Si$ MW: 497.75

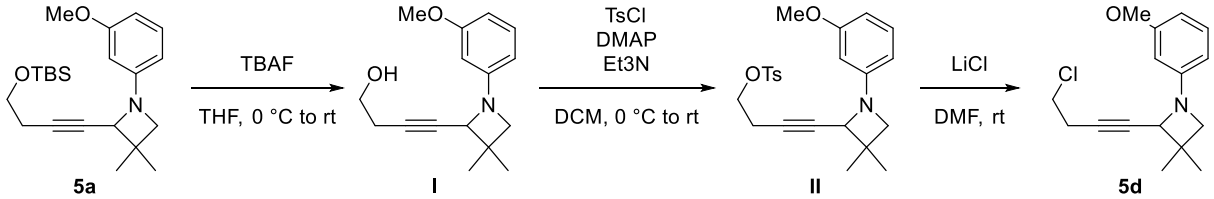
**2-(4-((*tert*-Butyldiphenylsilyl)oxy)but-1-yn-1-yl)-1-(3-methoxyphenyl)-3,3-dimethylazetidine (5b):** Prepared following the **GP3** in 79 % yield (4.09 g, 8.22 mmol) from azetidinone **4b** (5.31 g, 10.38 mmol). Pale yellow oil; **TLC** $R_f$ 0.52 (Cyclohexane/EtOAc 20 %); **IR (neat)** $\nu_{max}$ 487, 504, 613, 687, 700, 736, 757, 821, 916, 1047, 1103, 1264, 1289, 1338, 1427, 1460, 1493, 1598, 1611, 2856, 2929, 2956; **$^1$H NMR (500 MHz, $CDCl_3$)** $\delta$ 1.08 (s, 9 H), 1.09 (s, 3 H), 1.41 (s, 3 H), 2.57 (td, *J* = 2.1, 7.0 Hz, 2 H), 3.36 (d, *J* = 6.4 Hz, 1 H), 3.58 (d, *J* = 6.4 Hz, 1 H), 3.76 (s, 3 H), 3.82 (t, *J* = 7.2 Hz, 2 H), 4.17 (dd, *J* = 1.4, 2.1 Hz, 1 H), 6.22 (dd, *J* = 1.5, 2.3 Hz, 1 H), 6.30 (dd, *J* = 1.5, 8.0 Hz, 1 H), 6.35 (dd, *J* = 2.3, 8.0 Hz, 1 H), 7.12 (dd, *J* = 8.0, 8.0 Hz, 1 H), 7.37–7.47 (m, 6 H), 7.69–7.72 (m, 4 H); **$^{13}$C NMR (126 MHz, $CDCl_3$)** $\delta$ 19.3, 23.3, 24.7, 26.8, 26.9 (x3), 36.0, 55.2, 62.7, 63.1, 63.7, 78.6, 85.1, 98.7, 103.8, 105.5, 127.8 (x4), 129.7, 129.8 (x2), 133.7 (x2), 135.7 (x4), 153.2, 160.5; **HR-MS** 498.2855 ($C_{32}H_{39}NO_2Si+H^+$) calcd 498.2823.



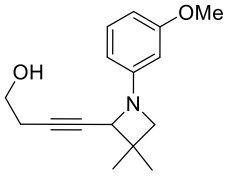
$C_{19}H_{27}N$ MW: 269.43

**3,3-Dimethyl-2-(oct-1-yn-1-yl)-1-phenylazetidine (5c):** Prepared following the **GP3** in 85 % yield (822 mg, 3.05 mmol) from azetidinone **4c** (1.02 g, 3.6 mmol). Colorless oil; **TLC** $R_f$ 0.49 (Pentane/$Et_2O$ 5 %); **IR (neat)** $\nu_{max}$ 516, 692, 746, 786, 872, 989, 1032, 1096, 1112, 1156, 1177, 1294, 1336, 1461, 1473, 1500, 1598, 1857, 2927, 2955; **$^1$H NMR (500 MHz, $CDCl_3$)** $\delta$ 0.89 (t, *J* = 6.8 Hz, 3 H), 1.21 (s, 3 H), 1.25–1.35 (m, 4 H), 1.38–1.45 (m, 2 H), 1.43 (s, 3 H), 1.51–1.57 (m, 2 H), 2.27 (td, *J* = 2.0, 7.0 Hz, 2 H), 3.35 (d, *J* = 6.9 Hz, 1 H), 3.60 (d, *J* = 6.9 Hz, 1 H), 4.16 (t, *J* = 2.0 Hz, 1 H), 6.66 (d, *J* = 8.8 Hz, 2 H), 6.77 (dd, *J* = 7.4, 7.4 Hz, 1 H), 7.21 (dd, *J* = 7.4, 8.8 Hz, 2 H); **$^{13}$C NMR (126 MHz, $CDCl_3$)** $\delta$ 14.2, 19.1, 22.7, 24.7, 26.9, 28.7, 28.9, 31.5, 36.2, 63.1, 63.8, 77.6, 88.4, 112.7 (x2), 118.4, 128.9 (x2), 151.9; **HR-MS** 270.2199 ($C_{19}H_{27}N+H^+$) calcd 270.2216.

## Synthesis of the chloroethyl 2,3-dihydropyrrolo[1,2-*a*]indole derivative 6d



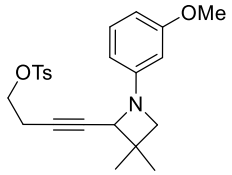
**5a** **I** **II** **5d**



$C_{16}H_{21}NO_2$ MW: 259.35

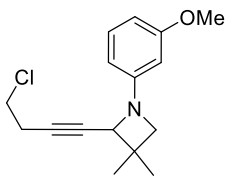
**4-(1-(3-Methoxyphenyl)-3,3-dimethylazetidin-2-yl)but-3-yn-1-ol (I):** To a stirred solution of azetidine **5a** (20 mmol, 1 equiv) in THF (100 mL) at 0 °C was added a solution of TBAF (1.0 M in THF, 30 mmol, 1.5 equiv). After 30 minutes, the reaction was quenched by addition of satd aqueous $NH_4Cl$ (100 mL) and diluted with EtOAc (100 mL). The aqueous layer was extracted with EtOAc (2 x 100 mL) and the combined organic layers were washed with $H_2O$ (100 mL) then brine (100 mL). The solution was dried over $MgSO_4$, filtered and concentrated to yield the compound **I** in 92 % yield (4.69 g) from 7.33 g of **5a**.

Yellow oil; **TLC** $R_f$ 0.21 (Cyclohexane/EtOAc 30 %); **IR (neat)** $\nu_{max}$ 457, 560, 584, 688, 759, 823, 987, 1041, 1100, 1161, 1211, 1236, 1289, 1336, 1438, 1457, 1493, 1598, 2837, 2866, 2924, 2956, 3371; **$^1$H NMR (500 MHz, $CDCl_3$)** $\delta$ 1.23 (s, 3 H), 1.42 (s, 3 H), 2.55 (td, *J* = 2.0, 6.3 Hz, 2 H), 3.37 (d, *J* = 6.5 Hz, 1 H), 3.59 (d, *J* = 6.5 Hz, 1 H), 3.73 (td, *J* = 2.1, 6.3 Hz, 2 H), 3.78 (s, 3 H), 4.19 (t, *J* = 2.1 Hz, 1 H), 6.21 (dd, *J* = 1.5, 2.2 Hz, 1 H), 6.27 (dd, *J* = 2.2, 8.0 Hz, 1 H), 6.35 (dd, *J* = 2.2, 8.0 Hz, 1 H), 7.13 (dd, *J* = 8.0, 8.0 Hz, 1 H); **$^{13}$C NMR (126 MHz, $CDCl_3$)** $\delta$ 23.5, 24.7, 26.9, 36.0, 55.3, 61.3, 63.1, 63.5, 79.6, 84.8, 98.8, 103.8, 105.5, 129.9, 152.9, 160.6; **HR-MS** 260.1666 ($C_{16}H_{21}NO_2$+$H^+$) calcd 260.1645.



$C_{23}H_{27}NO_4S$ MW: 413.53

**4-(1-(3-Methoxyphenyl)-3,3-dimethylazetidin-2-yl)but-3-yn-1-yl 4-methylbenzenesulfonate (II):** Deprotected alcohol **I** was dissolved in $CH_2Cl_2$ (30 mL) and cooled to 0 °C. $Et_3N$ (6.7 mmol, 1.2 equiv), DMAP (0.6 mmol, 0.1 equiv) and finally *para*-toluene sulfonyl chloride (6.7 mmol, 1.2 equiv) were then successively added to the stirring mixture before removal of the cooling bath. The mixture was stirred overnight at room temperature, quenched by addition of satd aqueous $NH_4Cl$ and diluted with EtOAc. The aqueous layer was extracted with EtOAc and the combined organic layers were washed with $H_2O$ then brine. The solution was dried over $MgSO_4$, filtered and concentrated to yield tosylated azetidine derivative **II** in 87 % yield (2.00 g) from 1.44 g of alcohol **I**. Orange/brown oil; **TLC** $R_f$ 0.46 (Cyclohexane/EtOAc 30 %); **IR (neat)** $\nu_{max}$ 458, 499, 552, 662, 688, 728, 760, 815, 838, 903, 973, 1020, 1043, 1071, 1097, 1174, 1188, 1213, 1238, 1264, 1289, 1340, 1359 1458, 1494, 1598, 2839, 2925, 2958; **$^1$H NMR (500 MHz, $CDCl_3$)** $\delta$ 1.19 (s, 3 H), 1.36 (s, 3 H), 2.44 (s, 3 H), 2.65 (td, *J* = 2.0, 7.1 Hz, 2 H), 3.34 (d, *J* = 6.6 Hz, 1 H), 3.56 (d, *J* = 6.6 Hz, 1 H), 3.77 (s, 3 H), 4.08–4.14 (m, 3 H), 6.16 (dd, *J* = 2.1, 2.1 Hz, 1 H), 6.23 (dd, *J* = 2.1, 8.0 Hz, 1 H), 6.35 (dd, *J* = 2.1, 8.0 Hz, 1 H), 7.11 (dd, *J* = 8.0, 8.0 Hz, 1 H), 7.32 (d, *J* = 8.2 Hz, 2 H), 7.79 (d, *J* = 8.2 Hz, 2 H); **$^{13}$C NMR (126 MHz, $CDCl_3$)** $\delta$ 20.1, 21.8, 24.6, 26.9, 36.0, 55.3, 63.1, 63.3, 67.8, 80.0, 82.0, 98.7, 103.8, 105.5, 128.1 (x2), 129.9, 130.1 (x2), 132.9, 145.1, 152.9, 160.5; **HR-MS** 414.1761 ($C_{23}H_{27}NO_4S$+$H^+$) calcd 414.1734.

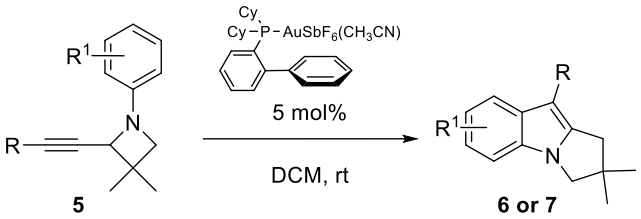


$C_{16}H_{20}ClNO$ MW: 277.79

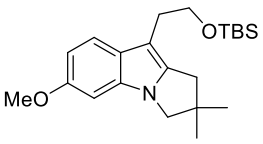
**2-(4-Chlorobut-1-yn-1-yl)-1-(3-methoxyphenyl)-3,3-dimethylazetidine (5d):** Tosyl derivative **II** (5 mmol, 1 equiv) was dissolved in DMF (25 mL) at room temperature with LiCl (15 mmol, 3 equiv) and stirred for 16 hours. The mixture was then dissolved in EtOAc (200 mL) and washed with $H_2O$ then brine. Finally, the crude mixture was dried over MgSO4, filtered and concentrated. After purification on column chromatography ($SiO_2$, Cyclohexane/EtOAc), chloride azetidine derivative **5d** was obtained in 55 % yield (90 mg) from 245 mg of **II**. Colorless oil; **TLC** $R_f$ 0.60 (Cyclohexane/EtOAc 30 %); **IR (neat)** $\nu_{max}$ 458, 661, 688, 739, 758, 798, 821, 833, 987, 1044, 1072, 1101, 1123, 1162, 1212, 1237, 1264, 1297, 1337, 1370, 1457, 1493, 1597, 2837, 2924, 2957; **$^1$H NMR (500 MHz, $CDCl_3$)** $\delta$ 1.22 (s, 3 H), 1.43 (s, 3 H), 2.75 (td, *J* = 2.0, 7.2 Hz, 2 H), 3.36 (d, *J* = 6.5 Hz, 1 H), 3.59 (d, *J* = 6.5 Hz, 1 H), 3.61 (t, *J* = 7.2 Hz, 2 H), 3.78 (s, 3 H), 4.17 (t, *J* = 2.0 Hz, 1 H), 6.21 (dd, *J* = 2.0, 2.5 Hz, 1 H), 6.27 (dd, *J* = 2.0, 8.3 Hz, 1 H), 6.35 (dd, *J* = 2.5, 7.8 Hz, 1 H), 7.13 (dd, *J* = 7.8, 8.3 Hz, 1 H); **$^{13}$C NMR (126**

**MHz, $CDCl_3$) $\delta$** 23.5, 24.7, 27.1, 36.1, 42.4, 55.3, 63.1, 63.4, 79.8, 84.0, 98.7, 103.9, 105.5, 129.9, 153.0, 160.6; **HR-MS** 278.1293 ($C_{16}H_{20}NOCl+H^+$) calcd 278.1306.

## General Procedure 4 for the gold-catalyzed conversion of *N*-aryl alkynylazetidines 3 to pyrrolo[1,2-*a*]indoles 4 (GP4)

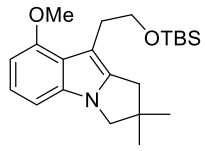



To a solution of *N*-aryl 2-alkynylazetidine **5** (0.2 mmol, 1 equiv) in $CH_2Cl_2$ (1 mL) was added ($Cy_2$)JohnPhosAuSbF$_6$ (0.01 mmol, 5 mol %) at room temperature or at 60 °C (specified for each compound). The solution was stirred until completion of the reaction (as monitored by TLC), solvent was removed *in vacuo*, and the crude residue was purified by flash chromatography ($SiO_2$, cyclohexane/EtOAc) to yield the title compound **6** or **7**.



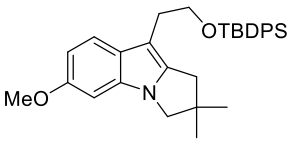
$C_{22}H_{35}NO_2Si$ MW: 373.61

**9-(2-((*tert*-Butyldimethylsilyl)oxy)ethyl)-6-methoxy-2,2-dimethyl-2,3-dihydro-1*H*-pyrrolo[1,2-*a*]indole (6a):** Prepared following the **GP4** in 47 % yield (93 mg, 0.249 mmol) from **5a** (197 mg, 0.527 mmol) after 2 minutes at 60 °C. White solid; **mp** 107 °C; **TLC** $R_f$ 0.37 (Pentane/$Et_2O$ 20 %); **IR (neat) $\nu_{max}$** 512, 570, 596, 628, 679, 740, 774, 800, 813, 834, 938, 969, 1004, 1039, 1084, 1118, 1148, 1177, 1340, 1378, 1435, 1449, 1624, 2855, 2886, 2927, 2953; **$^1$H NMR (500 MHz, $CDCl_3$) $\delta$** 0.05 (s, 6 H), 0.90 (s, 9 H), 1.28 (s, 6 H), 2.73 (s, 2 H), 2.89 (t, *J* = 7.9 Hz, 2 H), 3.71 (s, 2 H), 3.80 (t, *J* = 7.9 Hz, 2 H), 3.85 (s, 3 H), 6.67 (d, *J* = 2.3 Hz, 1 H), 6.72 (dd, *J* = 2.3, 8.5 Hz, 1 H), 7.36 (d, *J* = 8.5 Hz, 1 H); **$^{13}$C NMR (126 MHz, $CDCl_3$) $\delta$** -5.1 (x2), 18.6, 26.2 (x3), 28.2 (x2), 29.0, 39.0, 44.1, 56.0, 56.9, 64.1, 93.4, 102.8, 108.0, 119.0, 126.6, 133.4, 140.2, 155.3; **HR-MS** 374.2531 ($C_{22}H_{35}NO_2Si+H^+$) calcd 374.2510.



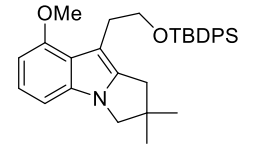
$C_{22}H_{35}NO_2Si$ MW: 373.61

**9-(2-((*tert*-Butyldimethylsilyl)oxy)ethyl)-8-methoxy-2,2-dimethyl-2,3-dihydro-1*H*-pyrrolo[1,2-*a*]indole (7a):** Prepared following the **GP4** in 43 % yield (85 mg, 0.227 mmol) from **5a** (197 mg, 0.527 mmol) of after 2 minutes at 60 °C. White solid; **mp** 86 °C; **TLC** $R_f$ 0.54 (Pentane/$Et_2O$ 20 %); **IR (neat) $\nu_{max}$** 558, 730, 773, 839, 1008, 1042, 1054, 1072, 1088, 1109, 1184, 1198, 1254, 1264, 1337, 1362, 1413, 1443, 1461, 1498, 1562, 1614, 2854, 2897, 2927, 2949; **$^1$H NMR (500 MHz, $CDCl_3$) $\delta$** 0.11 (s, 6 H), 0.96 (s, 9 H), 1.30 (s, 6 H), 2.77 (s, 2 H), 3.07 (t, *J* = 7.7 Hz, 2 H), 3.75 (s, 2 H), 3.86 (t, *J* = 7.7 Hz, 2 H), 3.94 (s, 3 H), 6.49 (d, *J* = 7.8 Hz, 1 H), 6.81 (d, *J* = 8.1 Hz, 1 H), 7.03 (dd, *J* = 7.8, 8.1 Hz, 1 H); **$^{13}$C NMR (126 MHz, $CDCl_3$) $\delta$** -5.0 (x2), 18.6, 26.2 (x3), 28.1 (x2), 30.4, 38.8, 44.0, 55.1, 57.2, 65.4, 98.9, 102.9 (x2), 120.8, 121.2, 134.4, 140.3, 154.3; **HR-MS** 374.2530 ($C_{22}H_{35}NO_2Si+H^+$) calcd 374.2510.



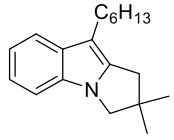

$C_{32}H_{39}NO_2Si$ MW: 497.75

**9-(2-((*tert*-Butyldiphenylsilyl)oxy)ethyl)-6-methoxy-2,2-dimethyl-2,3-dihydro-1*H*-pyrrolo[1,2-*a*]indole (6b):** Prepared following the **GP4** in 54 % yield (1.40 g, 2.812 mmol) from **5b** (2.55 g, 5.946 mmol) after 2 minutes at 60 °C. White solid; **mp** 95 °C; TLC $R_f$ 0.38 (Pentane/$Et_2O$ 20 %); **IR (neat) $\nu_{max}$** 491, 503, 608, 699, 739, 796, 820, 967, 1005, 1042, 1065, 1080, 1110, 1149, 1176, 1220, 1243, 1360, 1382, 1405, 1461, 1568, 1588, 1625, 2855, 2896, 2930, 2953; **$^1$H NMR (500 MHz, $CDCl_3$) $\delta$** 1.08 (s, 9 H), 1.23 (s, 6 H), 2.60 (s, 2 H), 2.93 (t, *J* = 7.7 Hz, 2 H), 3.67 (s, 2 H), 3.85 (s, 3 H), 3.86 (t, *J* = 7.7 Hz, 2 H), 6.62–6.68 (m, 2 H), 7.11 (d, *J* = 9.3 Hz, 1 H), 7.32–7.48 (m, 6 H), 7.63–7.70 (m, 4 H); **$^{13}$C NMR (126 MHz, $CDCl_3$) $\delta$** 19.3, 27.1 (x3), 28.1 (x2), 28.6, 38.8, 44.0, 55.9, 56.9, 64.7, 93.3, 102.6, 107.8, 119.1, 126.5, 127.7 (x4), 129.6 (x2), 133.4, 134.1 (x2), 135.8 (x4), 140.3, 155.3; **HR-MS** 497.2711 ($C_{32}H_{39}NO_2Si^+$) calcd 497.2745.



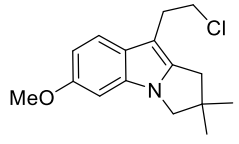

$C_{32}H_{39}NO_2Si$ MW: 497.75

**9-(2-((*tert*-Butyldiphenylsilyl)oxy)ethyl)-8-methoxy-2,2-dimethyl-2,3-dihydro-1*H*-pyrrolo[1,2-*a*]indole (7b):** Prepared following the **GP4** in 37 % yield (945 mg, 1.90 mmol) from **5b** (2.55 g, 5.946 mmol) after 2 minutes at 60 °C. White solid; **mp** 116 °C; **TLC** $R_f$ 0.63 (Pentane/$Et_2O$ 20 %); **IR (neat) $\nu_{max}$** 476, 484, 505, 558, 602, 682, 700, 729, 739, 762, 773, 997, 1005, 1031, 1058, 1112, 1132, 1196, 1281, 1303, 1364, 1375, 1426, 1446, 1567, 1587, 1617, 2861, 2927, 2956; **$^1$H NMR (500 MHz, $CDCl_3$) $\delta$** 1.06 (s, 9 H), 1.22 (s, 6 H), 2.64 (s, 2 H), 3.12 (t, *J* = 7.5 Hz, 2 H), 3.70 (s, 2 H), 3.75 (s, 3 H), 3.94 (t, *J* = 7.5 Hz, 2 H), 6.41 (d, *J* = 7.7 Hz, 1 H), 6.77 (d, *J* = 8.1 Hz, 1 H), 6.99 (dd, *J* = 7.7, 8.1 Hz, 1 H), 7.29–7.43 (m, 6 H), 7.62–7.69 (m, 4 H); **$^{13}$C NMR (126 MHz, $CDCl_3$) $\delta$** 19.4, 27.1 (x3), 28.1 (x2), 30.1, 38.7, 43.9, 55.0, 57.2, 65.9, 99.0, 102.8, 103.1, 120.7, 121.3, 127.6 (x4), 129.4 (x2), 134.4, 134.5 (x2), 135.7 (x4), 140.5, 154.4; **HR-MS** 497.2740 ($C_{32}H_{39}NO_2Si^+$) calcd 497.2745.




$C_{19}H_{27}N$ MW: 269.43

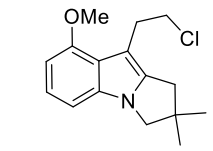
**9-Hexyl-2,2-dimethyl-2,3-dihydro-1*H*-pyrrolo[1,2-*a*]indole (6c):** Prepared following the **GP4** in 97 % yield (568 mg, 2.108 mmol) from **5c** (588 mg, 2.182mmol) in 2 h at room temperature. Colorless oil; **TLC** $R_f$ 0.55 (Pentane/$Et_2O$ 5 %); **IR (neat) $\nu_{max}$** 453, 553, 733, 1010, 1166, 1242, 1336, 1368, 1378, 1410, 1458, 1479, 1619, 2853, 2923, 2955, 3050; **$^1$H NMR (500 MHz, $CDCl_3$) $\delta$** 0.94 (t, *J* = 7.0 Hz, 3 H), 1.34–1.45 (m, 6 H), 1.32 (s, 6 H), 1.71 (tt, *J* = 7.5, 7.5 Hz, 2 H), 2.74 (t, *J* = 7.5 Hz, 2 H), 2.80 (s, 2 H), 3.80 (s, 2 H), 7.09 (dd, *J* = 7.8, 7.8 Hz, 1 H), 7.15 (dd, *J* = 7.8, 7.8 Hz, 1 H), 7.21 (d, *J* = 7.8 Hz, 1 H), 7.57 (d, *J* = 7.8 Hz, 1 H); **$^{13}$C NMR (126 MHz, $CDCl_3$) $\delta$** 14.3, 22.9, 24.8, 28.1 (x2), 29.4, 30.6, 31.9, 39.2, 44.2, 56.8, 107.0, 109.1, 118.2, 118.6, 120.0, 132.1, 132.9, 140.6; **HR-MS** 269.2125 ($C_{19}H_{27}N^+$) calcd 269.2138.




$C_{16}H_{20}ClNO$ MW: 277.79

**9-(2-Chloroethyl)-6-methoxy-2,2-dimethyl-2,3-dihydro-1*H*-pyrrolo[1,2-*a*]indole (6d):** Prepared following the **GP4** in 30 % yield (36 mg) from 171 mg of **5d** after 1 h at 60 °C. Colorless oil; **TLC** $R_f$ 0.37 (Cyclohexane/EtOAc 10 %); **IR (neat) $\nu_{max}$** 436, 628, 646, 730, 810, 908, 1043, 1144, 1176, 1217, 1237, 1319, 1369, 1405, 1460, 1567, 1595, 1625, 2868, 2933, 2956; **$^1$H NMR (500 MHz, $CDCl_3$) $\delta$** 1.29 (s, 6 H), 2.77 (s, 2 H), 3.13 (t, *J* = 7.4

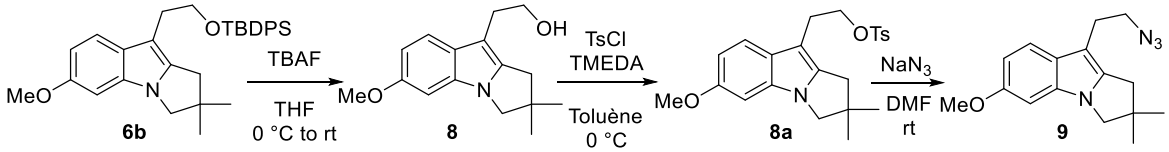
Hz, 2 H), 3.71 (t, *J* = 7.4 Hz, 2 H), 3.74 (s, 2 H), 3.86 (s, 3 H), 6.69 (d, *J* = 2.4 Hz, 1 H), 6.75 (dd, *J* = 2.4, 8.5 Hz, 1 H), 7.36 (d, *J* = 8.5 Hz, 1 H); **$^{13}$C NMR (126 MHz, $CDCl_3$) *δ*** 28.0 (x2), 28.9, 39.0, 44.2, 45.1, 55.9, 56.9, 93.5, 102.5, 108.3, 118.7, 125.9, 133.5, 140.7, 155.5; **HR-MS** 278.1275 ($C_{16}H_{20}ClNO+H^+$) calcd 278.1261.

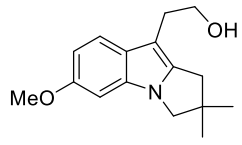


$C_{16}H_{20}ClNO$ MW: 277.79

**9-(2-Chloroethyl)-8-methoxy-2,2-dimethyl-2,3-dihydro-1*H*-pyrrolo[1,2-*a*]indole (7d):** Prepared following the **GP4** in 21 % yield (36 mg) from 171 mg of **5d** after 1 h at 60 °C. Colorless oil; **TLC** $R_f$ 0.51 (Cyclohexane/EtOAc 10 %); **IR (neat) $\nu_{max}$** 555, 605, 627, 653, 729, 770, 800, 905, 941, 1041, 1064, 1108, 1124, 1151, 1200, 1251, 1264 1288, 1306, 1343, 1445, 1496, 1563, 1618, 2872, 2934, 2989; **$^1$H NMR (300 MHz, $CDCl_3$) *δ*** 1.28 (s, 6 H), 2.77 (s, 2 H), 3.23 (t, *J* = 7.4 Hz, 2 H), 3.75 (s, 2 H), 3.79 (t, *J* = 7.4 Hz, 2 H), 3.92 (s, 3 H), 6.47 (d, *J* = 8.0 Hz, 1 H), 6.79 (d, *J* = 8.0 Hz, 1 H), 7.00 (dd, *J* = 8.0, 8.0 Hz, 1 H); **$^{13}$C NMR (126 MHz, $CDCl_3$) *δ*** 28.0 (x2), 30.5, 38.8, 44.2, 46.5, 55.2, 57.3, 99.1, 102.9, 103.0, 120.8, 121.1, 134.5, 140.8, 154.1; **HR-MS** 277.1264 ($C_{16}H_{20}ClNO$) calcd 277.1228.

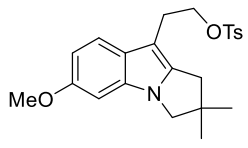
## Derivatization of pyrrolo[1,2-*a*]indoles 6b



$C_{16}H_{21}NO_2$ MW: 259.35

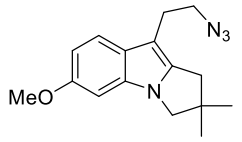
**2-(6-Methoxy-2,2-dimethyl-2,3-dihydro-1*H*-pyrrolo[1,2-*a*]indol-9-yl)ethan-1-ol (8):** To a stirred solution of pyrroloindole **6b** (1.00 g, 2 mmol, 1 equiv) in THF (10 mL) at 0 °C was added a solution of TBAF (4 mL 1.0 M in THF, 4 mmol, 1.5 equiv). After 3 h, the reaction was quenched by addition of satd aqueous $NH_4Cl$ (10 mL) and diluted with EtOAc (10 mL). The aqueous layer was extracted with EtOAc (2 x 10 mL) and the combined organic layers were washed with $H_2O$ (10 mL) then brine (10 mL). The solution was dried over $MgSO_4$, filtered, and concentrated to yield the alcohol **8** in 87 % yield (449 mg, 1.731 mmol) after flash chromatography. White solid; **mp** 98 °C; **TLC** $R_f$ 0.16 (Cyclohexane/EtOAc 30 %); **IR (neat) $\nu_{max}$** 437, 512, 596, 627, 675, 740, 807, 823, 880, 968, 1002, 1036, 1147, 1174, 1222, 1241, 1337, 1379, 1410, 1455, 1488, 1563, 1592, 1623, 2867, 2927, 2954, 3299; **$^1$H NMR (500 MHz, $CDCl_3$) *δ*** 1.26 (s, 6 H), 2.74 (s, 2 H), 2.91 (t, *J* = 6.3 Hz, 2 H), 3.72 (s, 2 H), 3.82 (t, *J* = 6.3 Hz, 2 H), 3.83 (s, 3 H), 6.66 (d, *J* = 2.1 Hz, 1 H), 6.71 (dd, *J* = 2.1, 8.7 Hz, 1 H), 7.37 (d, *J* = 8.7 Hz, 1 H); **$^{13}$C NMR (126 MHz, $CDCl_3$) *δ*** 28.1 (x2), 28.5, 39.0, 44.2, 55.9, 57.0, 62.9, 93.4, 101.9, 108.2, 119.1, 126.3, 133.7, 140.9, 155.6; **HR-MS** 282.1442 ($C_{16}H_{21}NO_2+Na^+$) calcd 282.1465.



$C_{23}H_{27}NO_4S$ MW: 413.53

**2-(6-Methoxy-2,2-dimethyl-2,3-dihydro-1*H*-pyrrolo[1,2-*a*]indol-9-yl)ethyl 4-methylbenzenesulfonate (8a):** *Para*-toluene sulfonylchloride (495 mg, 2.6 mmol, 1.5 equiv) was dissolved in toluene (5 mL) and added to a stirring mixture of TMEDA (0.4 mL, 2.6 mmol, 1.5 equiv) and alcohol

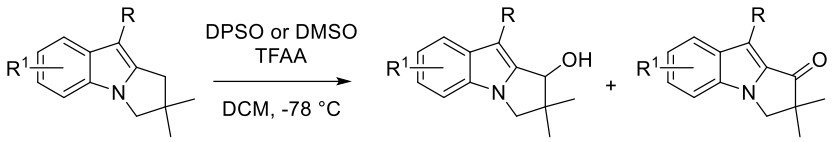
**8** (449 mg, 1.7 mmol, 1 equiv) in 1 mL of toluene.[8] The mixture was stirred at 0 °C for 5 hours, quenched by addition of $H_2O$ and diluted with EtOAc. The aqueous layer was extracted with EtOAc and the combined organic layers were washed with $H_2O$. The solution was dried over $MgSO_4$, filtered, and concentrated to yield tosylated azetidine derivative **8a** used in the following step without purification. **TLC** $R_f$ 0.48 (Cyclohexane/EtOAc 40 %); **$^1$H NMR (500 MHz, $CDCl_3$) $\delta$** 1.25 (s, 6 H), 2.40 (s, 3 H), 2.67 (s, 2 H), 2.99 (t, *J* = 7.2 Hz, 2 H), 3.68 (s, 2 H), 3.84 (s, 3 H), 4.19 (t, *J* = 7.2 Hz, 2 H), 6.63 (d, *J* = 2.2 Hz, 1 H), 6.67 (dd, *J* = 2.2, 8.6 Hz, 1 H), 7.17 (d, *J* = 8.5 Hz, 2 H), 7.21 (d, *J* = 8.5 Hz, 2 H), 7.66 (d, *J* = 8.6 Hz, 1 H).



$C_{16}H_{20}N_4O$ MW: 284.36

**9-(2-Azidoethyl)-6-methoxy-2,2-dimethyl-2,3-dihydro-1*H*-pyrrolo[1,2-*a*]indole (4d):** Crude tosyl derivative **8a** (1.7 mmol, 1 equiv) was dissolved in DMF (9 mL) at room temperature. $NaN_3$ (338 mg, 5.2 mmol, 3 equiv) was then added as a solid in one portion to the mixture which was then stirred for 16 h. The reaction mixture was partitioned between $H_2O$ (5 mL) and $Et_2O$ (10 mL) and layers were separated. The organic layer was washed with $H_2O$ (5 mL) then brine (5 mL). The solution was dried over $MgSO_4$, filtered, and concentrated to yield azide derivative **9** in 87 % yield (428 mg, 1.505 mmol) after flash chromatography over 2 steps from alcohol **8** (449 mg, 1.731 mmol). Orange solid; **mp** 49 °C; **TLC** $R_f$ 0.58 (Cyclohexane/EtOAc 30 %); **IR (neat) $\nu_{max}$** 434, 511, 557, 592, 625, 643, 738, 792, 805, 815, 897, 968, 1063, 1169, 1197, 1238, 1274, 1336, 1355, 1368, 1379, 1405, 1434, 1456, 1488, 1566, 1594, 1622, 2077, 2837, 2873, 2940; **$^1$H NMR (500 MHz, $CDCl_3$) $\delta$** 1.29 (s, 6 H), 2.76 (s, 2 H), 2.95 (t, *J* = 7.2 Hz, 2 H), 3.48 (t, *J* = 7.2 Hz, 2 H), 3.73 (s, 2 H), 3.85 (s, 3 H), 6.68 (d, *J* = 2.2 Hz, 1 H), 6.74 (dd, *J* = 2.2, 8.6 Hz, 1 H), 7.35 (d, *J* = 8.7 Hz, 1 H); **$^{13}$C NMR (126 MHz, $CDCl_3$) $\delta$** 25.0, 28.1 (x2), 39.0, 44.2, 51.9, 56.0, 57.0, 93.6, 102.2, 108.3, 118.7, 126.0, 133.6, 140.6, 155.6; **HR-MS** 307.1565 ($C_{16}H_{20}N_4O$+$Na^+$) calcd 307.1529.

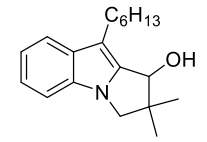
## General Procedure 5 for the oxidation of pyrrolo[1,2-*a*]indoles using TFAA and DPSO or DMSO (GP5)




Anhydrous DMSO or DPSO was dissolved in dry DCM and cooled to -78 °C. Freshly distilled trifluoroacetic anhydride was then carefully added via syringe to the solution, which was then stirred for 15 min at -78 °C. Pyrroloindole **6** (1 equiv) was dissolved in DCM in a second flask, cooled to -78 °C and finally added to the first flask via cannula. In each case, a strong coloration was immediately observed and the reaction reached full conversion within minutes. (All the pyrroloindol-1-ones synthesized in this section strongly revealed under the UV lamp). In some cases, the reaction mixture was quenched via classical workup conditions, or filtered through alumina to yield the crude product. Purification of the product by column chromatography

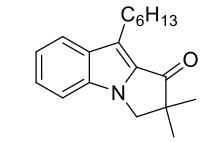
[8] Y. Yoshida, *Synthesis,* **1999**, 1633.

($SiO_2$, cyclohexane/EtOAc) must be done immediately thereafter or the crude mixture has to be stored directly in the freezer to avoid degradation of the product.



$C_{19}H_{27}NO$ MW: 285.43

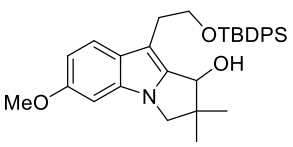
**9-Hexyl-2,2-dimethyl-2,3-dihydro-1*H*-pyrrolo[1,2-*a*]indol-1-ol (10a):** Product obtained following the **GP5** with TFAA (3 equiv) and diphenylsulfoxide (DPSO, 3 equiv). The reaction was quenched after 45 min with $NaHCO_3$, extracted with DCM. The combined organic layers were washed with $H_2O$ then brine, dried over $MgSO_4$ and concentrated under vacuum. After purification, **10a** was obtained in 27 % yield (13.8 mg, 0.048 mmol) from pyrroloindole **6c** (47.8 mg, 0.177 mmol). Colorless oil; **TLC** $R_f$ 0.15 (Cyclohexane/EtOAc 5 %); **IR (neat)** $\nu_{max}$ 434, 734, 809, 1004, 1043, 1170, 1233, 1306, 1335, 1377, 1456, 2853, 2923, 2955, 3312; **$^1$H NMR (500 MHz, $CDCl_3$)** $\delta$ 0.89 (t, *J* = 7.0 Hz, 3 H), 1.12 (s, 3 H), 1.26–1.33 (m, 2 H), 1.32 (s, 3 H), 1.34–1.42 (m, 4 H), 1.58 (s, 1 H), 1.69–1.76 (m, 2 H), 2.82 (dd, *J* = 7.0, 8.1 Hz, 2 H), 3.73 (d, *J* = 9.8 Hz, 1 H), 3.90 (d, *J* = 9.8 Hz, 1 H), 4.67 (s, 1 H), 7.08 (ddd, *J* = 1.5, 6.6, 8.0 Hz, 1 H), 7.16–7.22 (m, 2 H), 7.59 (d, *J* = 8.0 Hz, 1 H); **$^{13}$C NMR (126 MHz, $CDCl_3$)** $\delta$ 14.3, 20.9, 22.9, 24.6, 26.6, 29.5, 31.0, 31.9, 48.3, 54.7, 75.2, 109.7, 110.0, 118.6, 119.9, 121.5, 131.5, 132.9, 141.3; **HR-MS** 308.1985 ($C_{19}H_{27}NO+Na^+$) calcd 308.1985.



$C_{19}H_{25}NO$ MW: 283.42

**9-Hexyl-2,2-dimethyl-2,3-dihydro-1*H*-pyrrolo[1,2-*a*]indol-1-one (11a):** Product obtained following the **GP5** with TFAA (3 equiv) and dimethylsulfoxide (DMSO, 3 equiv). The reaction was quenched after 1 min with $NaHCO_3$, extracted with DCM. The combined organic layers were washed with $H_2O$ then brine, dried over $MgSO_4$ and concentrated under vacuum. After purification, **11a** was obtained in 88 % yield (48.0 mg, 0.17 mmol) from pyrroloindole **6c** (52.0 mg, 0.193 mmol).

Colorless oil with blue reflection; **TLC** $R_f$ 0.25 (Cyclohexane/EtOAc 2.5 %); **IR (neat)** $\nu_{max}$ 434, 484, 737, 944, 1004, 1044, 1109, 1131, 1147, 1184, 1245, 1311, 1342, 1374, 1399, 1463, 1562, 1701, 2855, 2925, 2957; **$^1$H NMR (500 MHz, $CDCl_3$)** $\delta$ 0.87 (t, *J* = 7.0 Hz, 3 H), 1.26–1.34 (m, 4 H), 1.36–1.43 (m, 2 H), 1.39 (s, 6 H), 1.72–1.79 (m, 2 H), 3.03 (dd, *J* = 7.7, 7.7 Hz, 2 H), 4.16 (s, 2 H), 7.13–7.19 (m, 1 H), 7.33–7.38 (m, 2 H), 7.76 (d, *J* = 8.2 Hz, 1 H); **$^{13}$C NMR (126 MHz, $CDCl_3$)** $\delta$ 14.3, 22.8, 24.3, 24.9 (x2), 29.3, 31.0, 31.8, 50.2, 54.5, 110.6, 118.9, 120.4, 122.5, 125.2, 131.1, 132.0, 135.1, 199.0; **HR-MS** 306.1823 ($C_{19}H_{25}NO+Na^+$) calcd 306.1828.

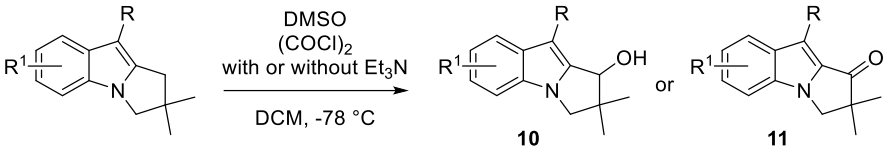


$C_{32}H_{39}NO_3Si$ MW: 513.75

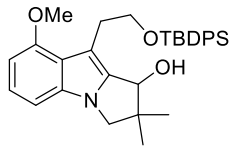
**9-(2-((*tert*-Butyldiphenylsilyl)oxy)ethyl)-6-methoxy-2,2-dimethyl-2,3-dihydro-1*H*-pyrrolo[1,2-*a*]indol-1-ol (10b):** Product obtained following the **GP5** with TFAA (3 equiv), dimethylsulfoxide (3 equiv) and triethylamine (3 equiv). After 1 h, was added to the reaction mixture which was then stirred for a few minutes before being filtered through a small pad of alumina. After purification, **10b** was obtained in 64 % yield (34.4 mg, 0.067 mmol) from pyrroloindole **6b** (51.6 mg, 0.104 mmol). Colorless oil; **TLC** $R_f$ 0.20 (Cyclohexane/EtOAc 10 %); **IR (neat)** $\nu_{max}$ 434, 610, 637, 880, 1045, 1087, 1377, 2879, 2971, 3300; **$^1$H NMR (500 MHz, $CDCl_3$)** $\delta$ 1.03 (s, 9 H), 1.14 (s, 3 H), 1.18 (s, 3 H), 2.53 (d, *J* = 4.4 Hz, 1 H), 2.95–3.08 (m, 2 H), 3.66 (d, *J* = 9.8 Hz, 1 H), 3.82 (d, *J* = 9.8 Hz, 1 H), 3.84–3.88 (m, 1 H),

3.87 (s, 3 H), 3.90–3.96 (m, 1 H), 4.65 (d, *J* = 4.4 Hz, 1 H), 6.66–6.70 (m, 2 H), 7.20 (d, *J* = 9.3 Hz, 1 H), 7.24 (dd, *J* = 7.2, 8.0 Hz, 2 H), 7.30 (dd, *J* = 7.2, 8.0 Hz, 2 H), 7.37 (dd, *J* = 7.0, 8.0 Hz, 1 H), 7.40 (dd, *J* = 7.0, 8.0 Hz, 1 H), 7.48 (d, *J* = 7.9 Hz, 2 H), 7.57 (d, *J* = 7.9 Hz, 2 H); **$^{13}$C NMR (126 MHz, $CDCl_3$) *δ*** 19.2, 21.1, 26.5, 27.1 (x3), 27.7, 48.1, 55.0, 55.9, 64.8, 74.9, 93.2, 105.1, 108.7, 120.1, 126.0, 127.7 (x2), 127.8 (x2), 129.7, 129.8, 133.5 (x2), 133.6, 135.6 (x2), 135.7 (x2), 141.9, 156.2; **HR-MS** 536.2585 ($C_{32}H_{39}NO_3Si$+$Na^+$) calcd 536.2591.

## General Procedure 6 for the oxidation of indoles using oxalyl chloride and DMSO (GP6)

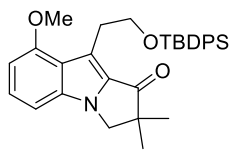



Anhydrous DMSO (1.0 mmol, 6 equiv) was dissolved in dry DCM (0.6 mL) and cooled to -78 °C. Freshly distilled oxalyl chloride (0.5 mmol, 3 equiv) was then carefully added via syringe to the solution, which was then stirred for 15 min at -78 °C. Indole derivatives (0.17 mmol, 1 equiv) were dissolved in DCM (1 mL) in a second flask, cooled to -78 °C and finally added to the first flask via cannula. In each case, a strong coloration was immediately observed, and the reaction reached full conversion within minutes. (All the pyrroloindol-1-ones synthesized in this section strongly revealed under the UV lamp). The flask was then removed from the cooling bath but the mixture was directly filtered through a small pad of celite and finally evaporated without letting it reach room temperature. The delicious smell of $Me_2S$ will tell you if the reaction is successful or not! Purification of the product by column chromatography ($SiO_2$, cyclohexane/EtOAc) must be done immediately thereafter or the crude mixture must be stored directly in the freezer to avoid degradation of the product.



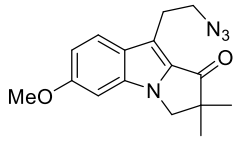

$C_{32}H_{39}NO_3Si$ MW: 513.75

**9-(2-((*tert*-Butyldiphenylsilyl)oxy)ethyl)-8-methoxy-2,2-dimethyl-2,3-dihydro-1*H*-pyrrolo[1,2-*a*]indol-1-ol (10c):** Side-product obtained following the **GP6** but with DMSO (6 equiv), $(COCl)_2$ (3 equiv) and $Et_3N$ (6 equiv) in 60 % yield (17.3 mg, 0.034 mmol) from pyrroloindole **7b** (28.2 mg, 0.057 mmol). White solid; **mp** 128 °C; **TLC** $R_f$ 0.15 (Cyclohexane/EtOAc 10 %); **IR (neat) $\nu_{max}$** 485, 503, 523, 645, 693, 965, 1008, 1064, 107, 1109, 1190, 1219, 1251, 1293, 1362, 1401, 1427, 1445, 1461, 1497, 1562, 2861, 2926, 2959, 3483; **$^1$H NMR (500 MHz, $CDCl_3$) *δ*** 0.99 (s, 9 H), 1.12 (s, 3 H), 1.14 (s, 3 H), 2.86 (d, *J* = 4.6 Hz, 1 H), 3.13 (ddd, *J* = 5.7, 8.9, 14.1 Hz, 1 H), 3.28 (ddd, *J* = 4.3, 4.9, 14.1 Hz, 1 H), 3.69 (d, *J* = 9.6 Hz, 1 H), 3.71 (s, 3 H), 3.83 (d, *J* = 9.6 Hz, 1 H), 3.87–3.99 (m, 2 H), 4.70 (d, *J* = 4.6 Hz, 1 H), 6.42 (d, *J* = 7.8 Hz, 1 H), 6.83 (d, *J* = 7.8 Hz, 1 H), 7.07 (dd, *J* = 7.8, 8.3 Hz, 1 H), 7.17 (dd, *J* = 6.8, 8.3 Hz, 2 H), 7.27 (dd, *J* = 6.8, 8.3 Hz, 2 H), 7.32 (dd, *J* = 6.8, 8.3 Hz, 1 H), 7.37 (dd, *J* = 6.8, 8.3 Hz, 1 H), 7.40 (d, *J* = 7.9 Hz, 2 H), 7.55 (d, *J* = 7.9 Hz, 2 H); **$^{13}$C NMR (126 MHz, $CDCl_3$) *δ*** 19.3, 21.1, 26.5, 27.1 (x3), 29.0, 48.1, 55.1, 55.5, 65.8, 74.8, 99.2, 103.1, 105.5, 121.1, 122.1, 127.6 (x2), 127.7 (x2), 129.5, 129.6, 133.5, 133.6, 134.6, 135.6 (x2), 135.7 (x2), 142.3, 155.2; **HR-MS** 552.2337 ($C_{32}H_{39}NO_3Si$+$K^+$) calcd 552.2331.




$C_{32}H_{37}NO_3Si$ MW: 511.74

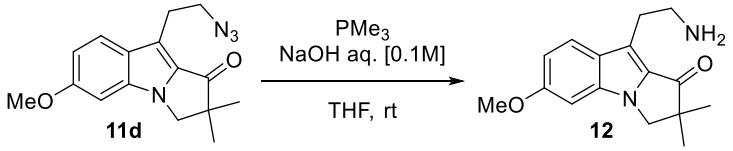
**9-(2-((*tert*-Butyldiphenylsilyl)oxy)ethyl)-8-methoxy-2,2-dimethyl-2,3-dihydro-1*H*-pyrrolo[1,2-*a*]indol-1-one (11c):** Prepared following the **GP6** in 27 % yield (7.6 mg, 0.015 mmol) from pyrroloindole **7b** (28.2 mg, 0.056 mmol). White solid; **mp** 127 °C; **TLC** $R_f$ 0.33 (Cyclohexane/EtOAc 10 %); **IR (neat)** $\nu_{max}$ 501, 616, 641, 655, 683, 781, 827, 857, 912, 926, 996, 1042, 1100, 1141, 1164, 1186, 1213, 1254, 1304, 1373, 1428, 1459, 1502, 1561, 1697, 2855, 2885, 2928; **$^1$H NMR (400 MHz, $C_6D_6$)** $\delta$ 1.01 (s, 6 H), 1.15 (s, 9 H), 3.29 (s, 2 H), 3.30 (s, 3 H), 3.95 (t, *J* = 7.0 Hz, 2 H), 4.34 (t, *J* = 7.0 Hz, 2 H), 6.22 (d, *J* = 7.8 Hz, 1 H), 6.75 (d, *J* = 8.3 Hz, 1 H), 7.16–7.21 (m, 7 H), 7.74–7.79 (m, 4 H); **$^{13}$C NMR (126 MHz, $C_6D_6$)** $\delta$ 19.5, 24.5 (x2), 27.1 (x3), 29.3, 49.5, 53.9, 54.7, 65.5, 99.9, 103.6, 114.9, 123.4, 125.8, 128.3 (x4), 129.6 (x2), 131.4, 134.6 (x2), 136.0 (x4), 136.9, 157.5, 197.3; **HR-MS** 550.2203 ($C_{32}H_{37}NO_3Si+K^+$) calcd 550.2174.



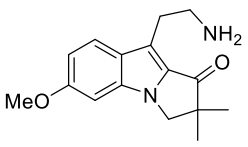

$C_{16}H_{18}N_4O_2$ MW: 298.35

**9-(2-Azidoethyl)-6-methoxy-2,2-dimethyl-2,3-dihydro-1*H*-pyrrolo[1,2-*a*]indol-1-one (11d):** Prepared following the **GP6** in 87 % yield (122 mg, 0.408 mmol) from pyrroloindole **9** (133 mg, 0.467 mmol). Orange solid; **mp** 76 °C; **TLC** $R_f$ 0.20 (Cyclohexane/EtOAc 20 %); **IR (neat)** $\nu_{max}$ 462, 642, 681, 734, 805, 1007, 1039, 1067, 1123, 1164, 1181, 1207, 1258, 1301, 1338, 1380, 1456, 1472, 1504, 1562, 1625, 1689, 2092, 2869, 2889, 2936; **$^1$H NMR (500 MHz, $CDCl_3$)** $\delta$ 1.39 (s, 6 H), 3.26 (t, *J* = 7.2 Hz, 2 H), 3.69 (t, *J* = 7.2 Hz, 2 H), 3.89 (s, 3 H), 4.13 (s, 2 H), 6.70 (d, *J* = 2.3 Hz, 1 H), 6.87 (dd, *J* = 2.3, 9.0 Hz, 1 H), 7.62 (d, *J* = 9.0 Hz, 1 H); **$^{13}$C NMR (126 MHz, $CDCl_3$)** $\delta$ 24.5, 24.9 (x2), 50.2, 51.6, 54.6, 55.7, 91.8, 113.5, 114.1, 122.9, 126.7, 130.8, 136.0, 159.2, 198.0; **HR-MS** 321.1316 ($C_{16}H_{18}N_4O_2+Na^+$) calcd 321.1322.

## General Procedure 7 for the Staudinger Reaction (GP7)



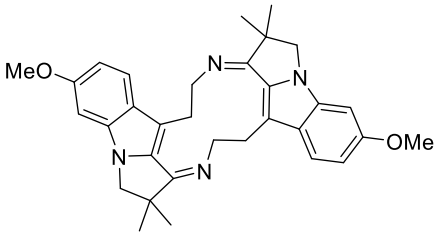

Azide derivative (1.30 mmol, 1 equiv) was dissolved in THF (8 mL) with an aqueous solution of NaOH [0.1M] (1 mL) at room temperature. A solution of trimethylphosphine [1M in THF] (3.9 mmol, 3 equiv) was then carefully and slowly added dropwise to the stirring mixture. The reaction was then stirred for 30 minutes even if the bubbling observed after $PMe_3$ addition seems to indicate an immediate reaction. The mixture was then filtered through a small pad of celite and concentrated. Purification on reversed-phase flash column chromatography ($H_2O$/MeCN) leads to protonated amine due to the presence of TFA in water during the purification process. A deprotonation of the ammonium species using Amberlyst-A resin yield the title amine compound.




$C_{16}H_{20}N_2O_2$ MW: 272.35

**9-(2-Aminoethyl)-6-methoxy-2,2-dimethyl-2,3-dihydro-1*H*-pyrrolo[1,2-*a*]indol-1-one (12):** Prepared following the **GP7** in 63 % yield (222 mg, 0.815 mmol) from azide **11d** (388 mg, 1.3 mmol). Yellow solid; **TLC** $R_f$ 0.10 (EtOAc/MeOH 5 %); **IR (neat)** $\nu_{max}$ 437, 527, 627, 741, 767, 810, 855, 939, 1039, 1164, 1210, 1250, 1339, 1377, 1462, 1503, 1558, 1622, 1687, 2868,

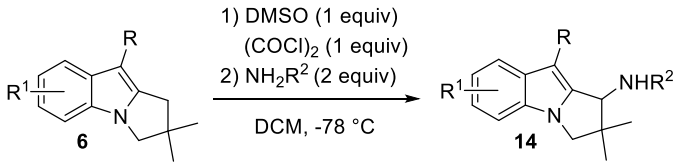
2925, 2959, 3366; **$^1$H NMR (500 MHz, $CDCl_3$) $\delta$** 1.36 (s, 6 H), 3.01 (t, *J* = 6.7 Hz, 2 H), 3.09 (t, *J* = 6.7 Hz, 2 H), 3.86 (s, 3 H), 4.09 (s, 2 H), 6.67 (d, *J* = 2.0 Hz, 1 H), 6.81 (dd, *J* = 2.0, 9.0 Hz, 1 H), 7.59 (d, *J* = 9.0 Hz, 1 H); **$^{13}$C NMR (126 MHz, $CDCl_3$) $\delta$** 24.9 (x2), 28.9, 43.2, 50.1, 54.4, 55.6, 91.7, 113.0, 116.1, 123.1, 126.7, 130.8, 136.1, 159.0, 198.1; HR-MS 273.1586 ($C_{16}H_{20}N_2O_2$+$H^+$) calcd 273.1598.



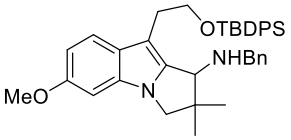
$C_{32}H_{36}N_4O_2$ MW: 508.67

**Harmalidine dimer** (**13**)**:** Pyridinium *para*-toluenesulfonic acid (PPTS, 3 mg, 0.012 mmol) was added to a benzene solution (12 mL) of amine **12** (21.5 mg, 0.079 mmol) in round bottom flask equipped with a Dean-Stark apparatus. The reaction was stirred at 120°C for 6 days. Solvent was removed in vacuo and purification by flash chromatography afforded the harmalidine dimer **13** in 55 % yield (11 mg, 0.022 mmol). White solid; **TLC** $R_f$ 0.41 (EtOAc/MeOH 5 %); **$^1$H NMR (500 MHz, $CDCl_3$) $\delta$** 1.42 (s, 12 H), 3.41 (dd, *J* = 7.7, 10.2 Hz, 4 H), 3.89 (s, 6 H), 3.95 (s, 4 H), 4.26 (dd, *J* = 7.7, 8.7 Hz, 4 H), 6.69 (d, *J* = 2.1 Hz, 2 H), 6.84 (dd, *J* = 2.1, 9.0 Hz, 2 H), 7.78 (d, *J* = 9.0 Hz, 2 H); **$^{13}$C NMR (126 MHz, $CDCl_3$) $\delta$** 27.2 (x4), 28.2 (x2), 48.6 (x2), 53.9 (x2), 55.6 (x2), 56.1 (2x), 91.6 (x2), 109.7 (x2), 111.3 (x2), 122.0 (x2), 126.8 (x2), 129.5 (x2), 134.2 (x2), 158.0 (x2), 168.4 (x2); **HR-MS** 509.2920 ($C_{32}H_{36}N_4O_2$+$H^+$) calcd 509.2911.

## General Procedure 8 for the Amination of 2,3-dihydropyrrolo[1,2-*a*]indole at the 2α position (GP8)

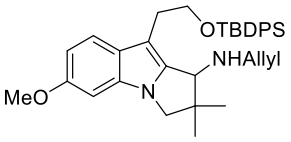



Anhydrous DMSO (1.0 mmol, 1 equiv) was dissolved in dry DCM (3 mL) and cooled to -78 °C. Freshly distilled oxalyl chloride (1.0 mmol, 1 equiv) was then carefully added via syringe to the solution, which was then stirred for 15 min at -78 °C. Pyrroloindole derivative **6** (1.0 mmol, 1 equiv) was dissolved in DCM (6 mL) in a second flask, cooled to -78 °C too and added to the first flask via cannula. In each case, a strong coloration was immediately observed. The amine was finally rapidly added to the reaction mixture via syringe, leading to a strong change of the coloration of the solution and the reaction reached full conversion within minutes. (All the pyrroloindol-1-ones synthesized in this section strongly revealed under the UV lamp). The flask was then removed from the cooling bath but the mixture was directly evaporated without letting it reach room temperature. Purification of the product by column chromatography ($SiO_2$, cyclohexane/EtOAc) has to be done immediately thereafter or the crude mixture has to be stored directly in the freezer to avoid degradation of the product.



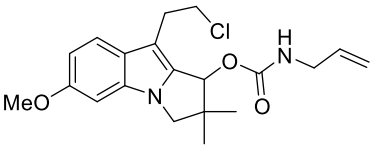

$C_{39}H_{46}N_2O_2Si$ MW: 602.89

***N*-Benzyl-9-(2-((*tert*-butyldiphenylsilyl)oxy)ethyl)-6-methoxy-2,2-dimethyl-2,3-dihydro-1*H*-pyrrolo[1,2-*a*]indol-1-amine (14a):** Prepared following the **GP8** in 78 % yield (25.0 mg) from 27.4 mg of **6b** and 12 µL of benzylamine. It has to be noticed that 18 % of the starting material has also been recovered in this case. Colorless oil; **TLC** $R_f$ 0.42 (Cyclohexane/EtOAc 30 %); **$^1$H NMR (500 MHz, $CDCl_3$) $\delta$** 1.03 (s, 3 H), 1.05 (s, 9 H), 1.22 (s, 3 H), 1.48 (bs, 1 H), 3.00–3.11 (m, 2 H), 3.56 (d, *J* = 9.6 Hz, 1 H), 3.70 (s, 1 H), 3.77–3.92 (m, 5 H), 3.82 (s, 3 H), 6.60–6.64 (m, 2 H), 7.08 (d, *J* = 9.2 Hz, 1 H), 7.22–7.27 (m, 1 H), 7.27–7.36 (m, 8 H), 7.36–7.42 (m, 2 H), 7.59–7.65 (m, 4 H); **$^{13}$C NMR (126 MHz, $CDCl_3$) $\delta$** 19.3, 21.7, 27.1 (x3), 27.7, 28.6, 48.2, 52.7, 55.3, 55.9, 64.0, 65.0, 93.1, 104.6, 108.2, 119.9, 126.0, 127.1, 127.7 (x4), 128.3 (x2), 128.5 (x2), 129.6 (x2), 133.5, 134.0 (x2), 135.7 (x4), 140.7, 141.9, 155.8. **HR-MS** 602.3273 ($C_{39}H_{46}N_2O_2Si$) calcd 602.3223.



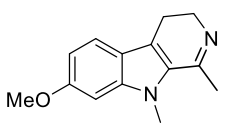

$C_{35}H_{44}N_2O_2Si$ MW: 552.83

***N*-Allyl-9-(2-((*tert*-butyldiphenylsilyl)oxy)ethyl)-6-methoxy-2,2-dimethyl-2,3-dihydro-1*H*-pyrrolo[1,2-*a*]indol-1-amine (14b):** Prepared following the **GP8** in 25 % yield (18 mg) from 68.4 mg of **6b** and 20 µL of allylamine. Yellow oil; **TLC** $R_f$ 0.30 (Cyclohexane/EtOAc 30 %); **IR (neat) $\nu_{max}$** 488, 504, 611, 700, 729, 807, 821, 908, 1088, 1105, 1145, 1215, 1243, 1461, 1490, 1625, 2857, 2929, 2956; **$^1$H NMR (500 MHz, $CDCl_3$) $\delta$** 1.02 (s, 3 H), 1.06 (s, 9 H), 1.21 (s, 3 H), 2.98–3.10 (m, 2 H), 3.24 (ddt, *J* = 1.7, 5.7, 13.8 Hz, 1 H), 3.31 (ddt, *J* = 1.7, 5.7, 13.8 Hz, 1 H), 3.56 (d, *J* = 9.7 Hz, 1 H), 3.64 (s, 1 H), 3.80 (d, *J* = 9.7 Hz, 1 H), 3.83 (s, 3 H), 3.82–3.89 (m, 2 H), 5.08 (dq, *J* = 1.7, 10.2 Hz, 1 H), 5.19 (dq, *J* = 1.7, 17.2 Hz, 1 H), 5.88 (ddt, *J* = 5.9, 10.2, 17.2 Hz, 1 H), 6.61–6.65 (m, 2 H), 7.09 (d, *J* = 9.3 Hz, 1 H), 7.31–7.37 (m, 4 H), 7.39–7.44 (m, 2 H), 7.62–7.68 (m, 4 H); **$^{13}$C NMR (126 MHz, $CDCl_3$) $\delta$** 19.3, 21.6, 27.1 (x3), 27.7, 28.7, 48.2, 51.1, 55.2, 55.9, 63.7, 64.9, 93.1, 104.8, 108.2, 115.9, 119.9, 125.9, 127.7 (x4), 129.7 (x2), 133.5, 134.0, 134.1, 135.7 (x4), 137.2, 141.8, 155.8. **HR-MS** 575.3074 ($C_{35}H_{44}N_2O_2Si+Na^+$) calcd 575.3064.




$C_{20}H_{25}ClN_2O_3$ MW: 376.88

**9-(2-Chloroethyl)-6-methoxy-2,2-dimethyl-2,3-dihydro-1H-pyrrolo[1,2-a]indol-1-yl allylcarbamate (15):** Prepared following the **GP8** in 20 % yield (4.3 mg) from 13.0 mg of **6d** and 7 µL of allylamine. It has to be noticed that 33 % of the starting material has also been recovered in this case. Colorless oil; **TLC** $R_f$ 0.10 (Cyclohexane/EtOAc 10 %); **IR (neat) $\nu_{max}$** 533, 627, 731, 799, 917, 1017, 1092, 1144, 1167, 1258, 1300, 1379, 1458, 1492, 1530, 1626, 1650, 1724, 2853, 2923, 2958, 3296; **$^1$H NMR (500 MHz, $CDCl_3$) $\delta$** 1.14 (s, 3 H), 1.30 (s, 3 H), 3.16–3.35 (m, 2 H), 3.70 (d, *J* = 9.6 Hz, 1 H), 3.75–3.87 (m, 3 H), 3.86 (s, 3 H), 3.90 (d, *J* = 9.6 Hz, 1 H), 3.95 (dddd, *J* = 1.3, 1.3, 5.4, 6.7 Hz, 1 H), 5.18 (ddd, *J* = 1.3, 2.7, 10.1 Hz, 1 H), 5.22 (ddd, *J* = 1.3, 2.7, 17.2 Hz, 2 H), 5.82 (ddt, *J* = 5.4, 10.1, 17.2 Hz, 1 H), 6.67 (d, *J* = 2.3 Hz, 1 H), 6.74 (dd, *J* = 2.6, 8.4 Hz, 1 H), 7.38 (d, *J* = 8.5 Hz, 1 H), 7.53 (bs, 1 H); **$^{13}$C NMR (126 MHz, $CDCl_3$) $\delta$** 20.7, 26.2, 28.2, 42.0, 45.4, 48.2, 54.7, 55.7, 74.7, 93.2, 104.7, 109.1, 117.3, 119.6, 125.1, 132.6, 133.5, 141.7, 156.3, 159.5.



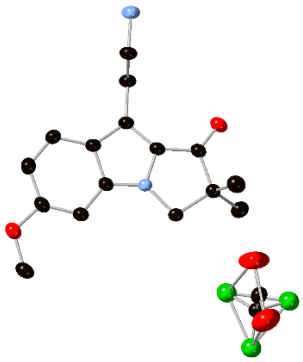

$C_{14}H_{16}N_2O$ MW: 228.13

**7-Methoxy-1,9-dimethyl-4,9-dihydro-3H-pyrido[3,4-b]indole (*N*-methylharmaline):** To a solution of commercially available harmaline (500 mg, 2.33 mmol) in anhydrous DMF (5 mL), NaH (60%, 233 mg, 5.83 mmol) was added under inert atmosphere at room temperature and heated at 55 °C for 3 h. Iodomethane (174 μL, 2.8 mmol) was then added at room temperature and the reaction was stirring for 24 h. The mixture was acidified with 1% HCl and washed with toluene (3x15 mL). The aqueous phase was basified to pH 8.5 and the product extracted with $CH_2Cl_2$ (3x30 mL). The organic phase was collected, dried over $MgSO_4$, filtered, and concentrated. Purification by flash chromatography afforded the *N*-methylharmaline in 47% (249 mg, 1.09 mmol). Pale yellow solid; **TLC** $R_f$ 0.50 (EtOAc/MeOH 5 %); **$^1$H NMR (500 MHz, $CDCl_3$) *δ*** 3.01 (t, *J* = 7.0 Hz, 2 H), 3.11 (s, 3 H), 3.64 (t, *J* = 7.0 Hz, 2 H), 3.89 (s, 3 H), 4.07 (s, 3 H), 6.75 (d, *J* = 2.2 Hz, 1 H), 6.81 (dd, *J* = 8.7, 2.2 Hz, 1 H), 7.43 (dd, *J* = 8.7, 0.6 Hz, 1 H); **$^{13}$C NMR (126 MHz, $CDCl_3$) *δ*** 20.7, 31.2, 34.1, 49.8, 55.5, 92.4, 111.0, 118.2, 118.9, 120.9, 125.6, 140.1, 158.4, 162.3.

## Analytical Data

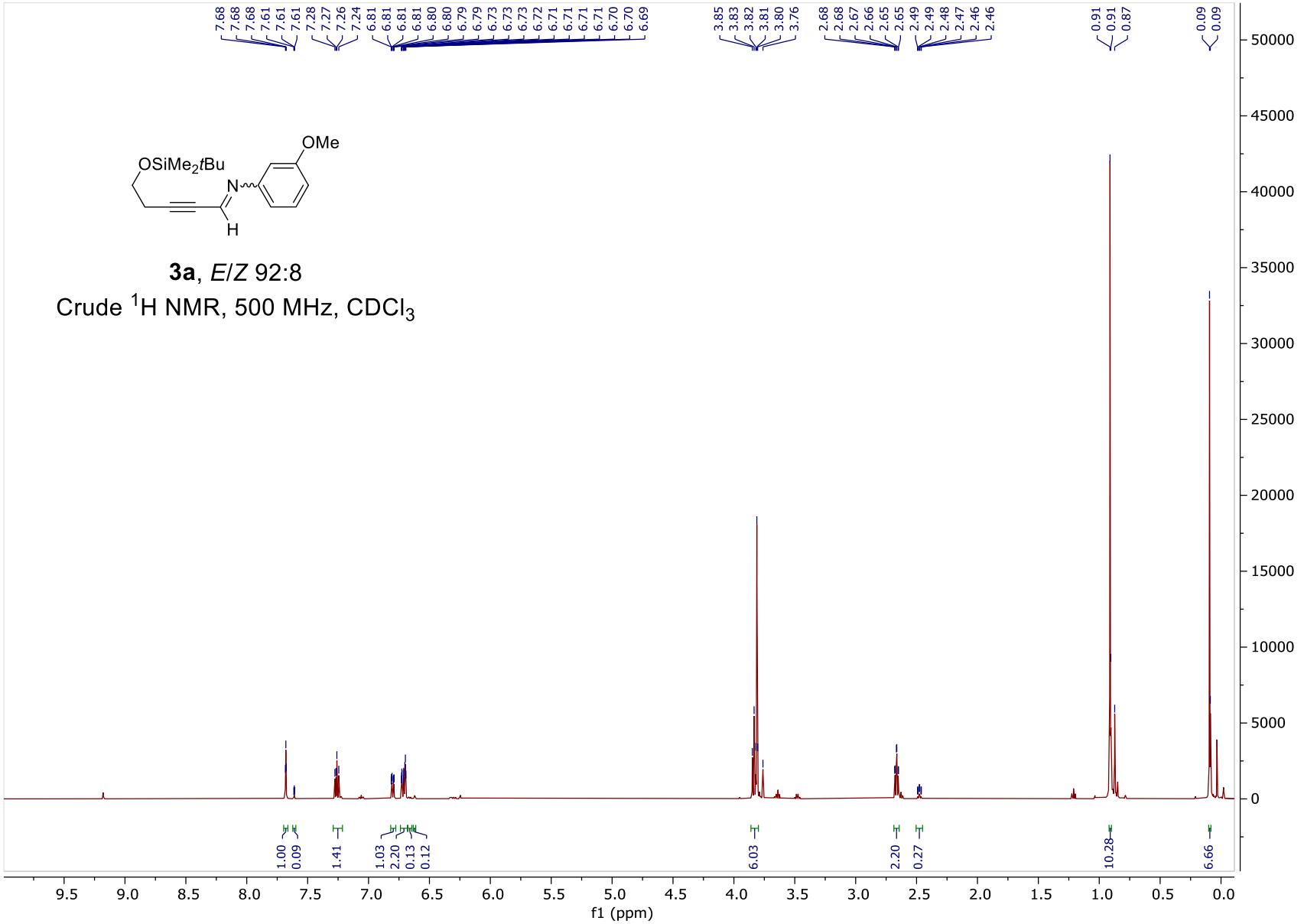
### X-Ray Structure

**Table S1. XRD image of amine 12 (trifluoracetic salt, hydrogens atoms have been omitted for clarity) and table of crystal data and refinement details:**



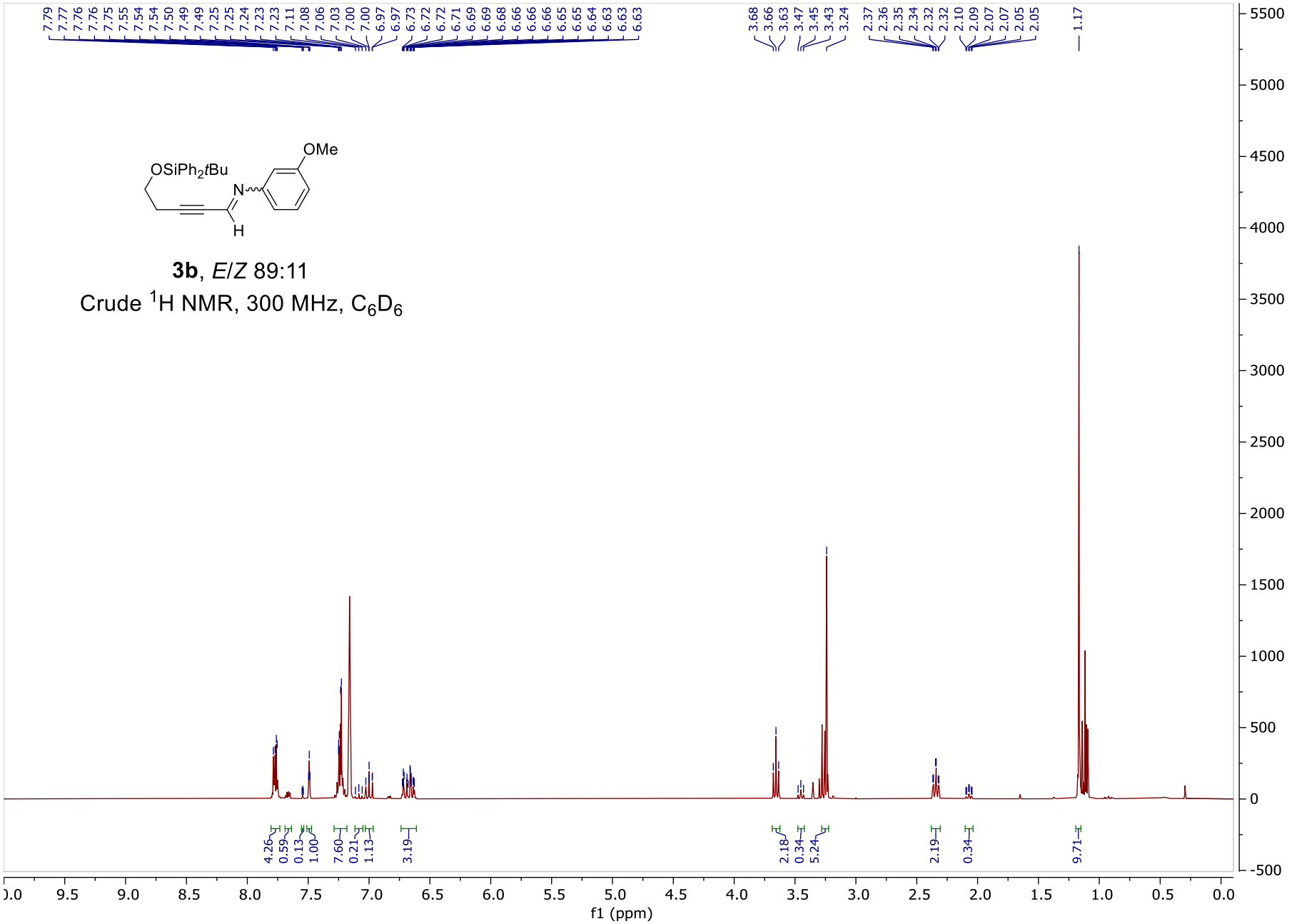
| **Identification Code** | Compound **12** (CCDC 2111055) |
|---|---|
| Formula | $C_{16}H_{21}N_2O_2$, $C_2F_3O_2$ |
| Formula weight | 386.37 |
| Crystal system | triclinic |
| Space group | *P* -1 |
| a (Å) | 8.790(5) |
| b (Å) | 9.963(5) |
| c (Å) | 10.845(5) |
| α (°) | 88.953(5) |
| β (°) | 89.952(5) |
| γ (°) | 73.603(5) |
| V (Å$^3$) | 911.0(8) |
| Z | 2 |
| Density (g cm$^{-3}$) | 1.409 |
| mu (mm$^{-1}$) | 0.119 |
| F(000) | 404 |
| **Data collection** | |
| Temperature (K) | 173 (2) |
| Radiation (Å) | MoK\a – 0.71069 |
| Theta min - max | 0.9362 – 1.0225 |
| Dataset [h, k, l] | -10/10, -12/12, -11/13 |
| Tot., sigmaI/netI, R(int) | 8477, 0.0489, 0.0445 |
| **Refinement** | |
| Nreflections, Nparameters, Nrestrains | 3574, 257, 18 |
| R2, R1, wR2, wR1, Goof | 0.0961, 0.0704, 0.2326, 0.2019, 1.117 |
| Max. and Av. Shift/Error | 0.000, 0.000 |
| Min, Max. Resd Dens. (e-/Å$^3$) | -0.700, 0.845 |

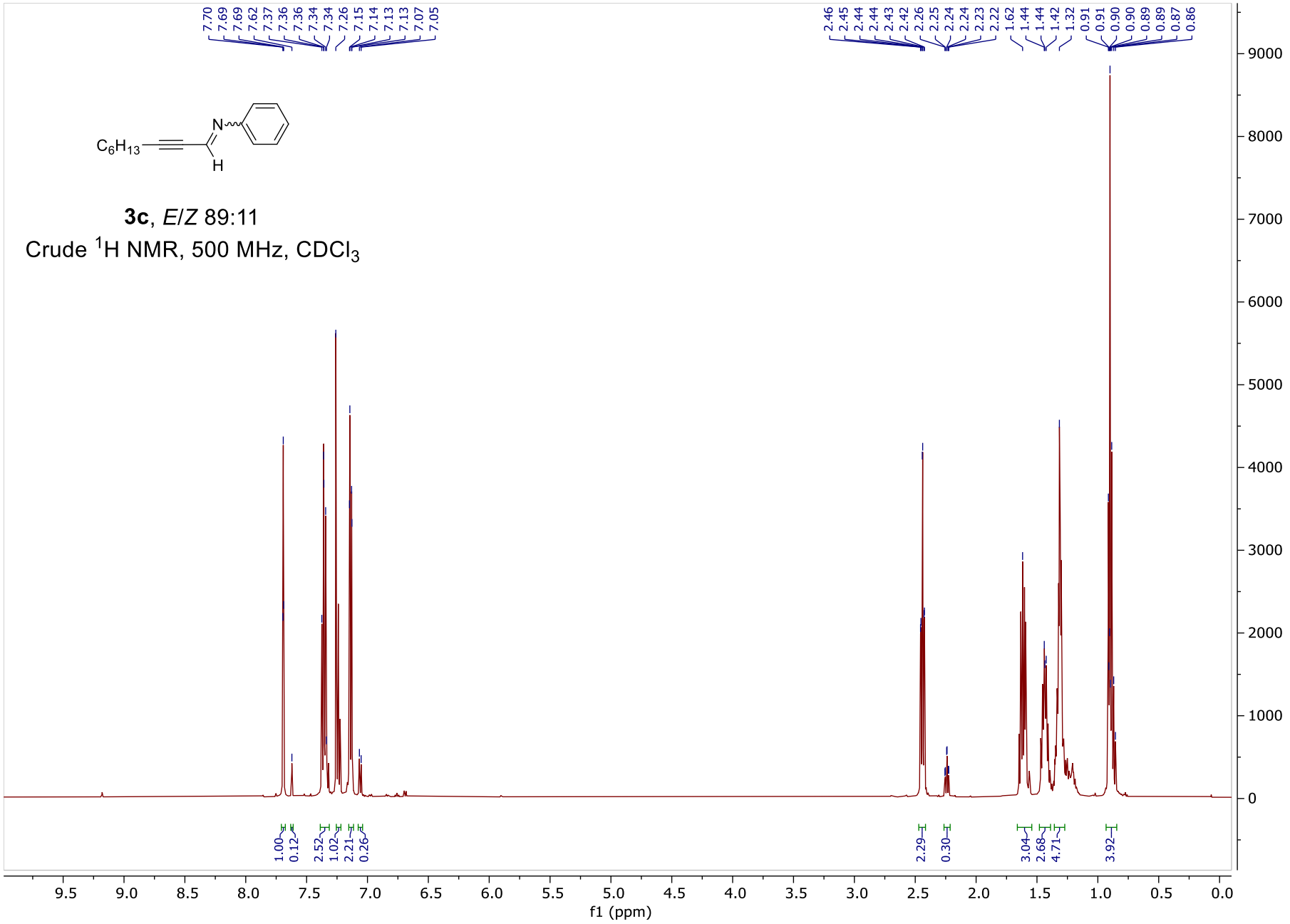
## NMR Spectra

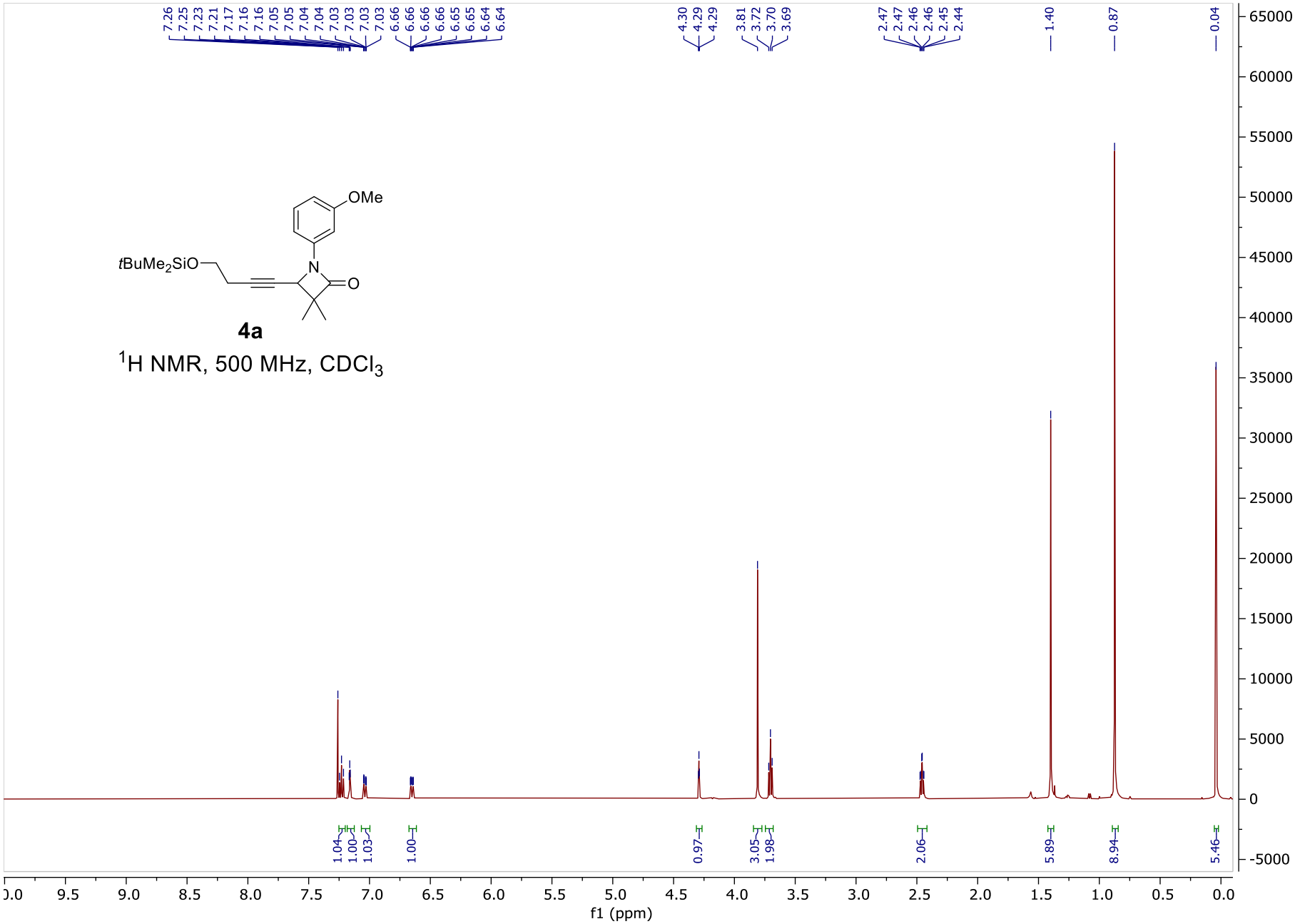


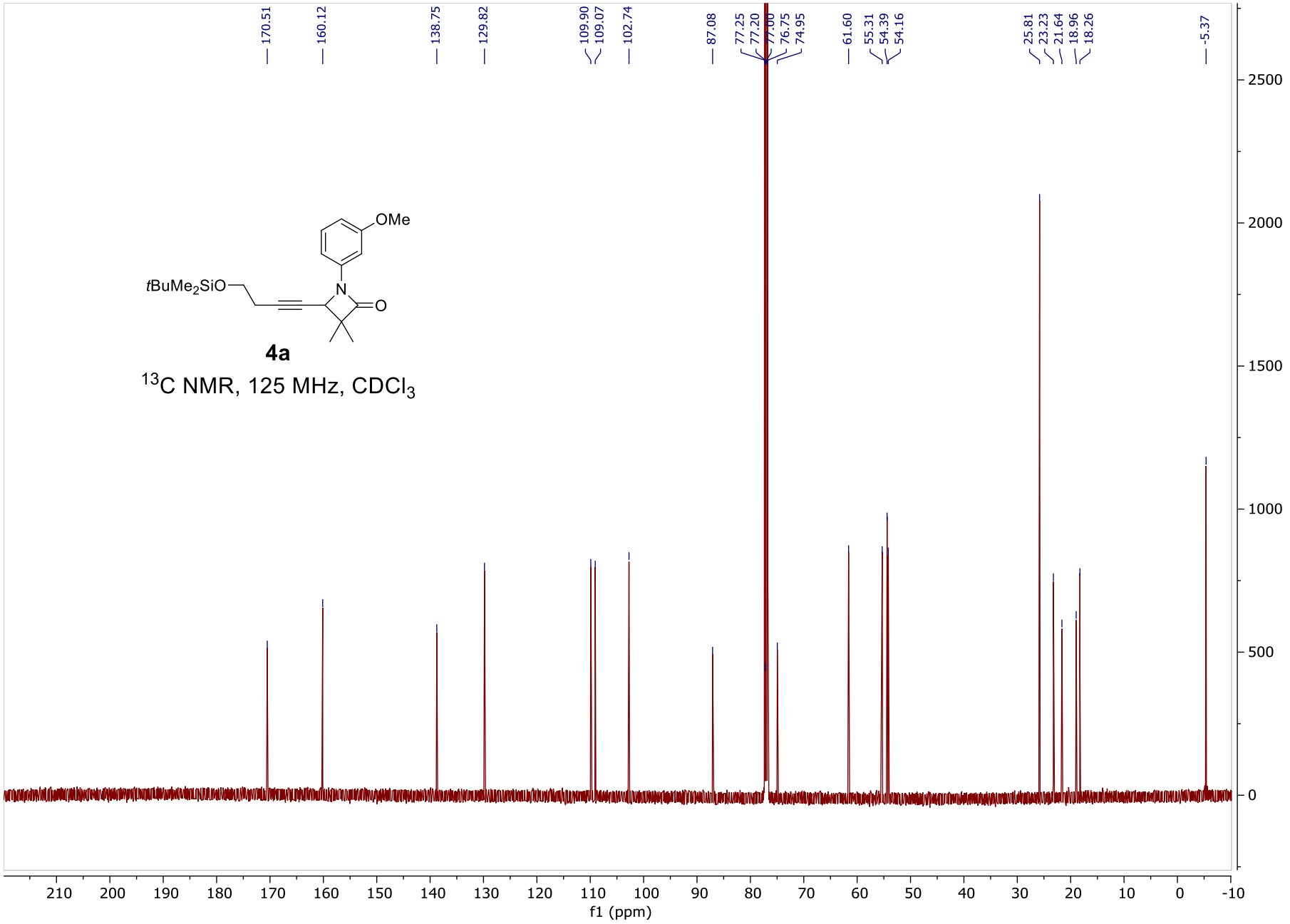

**3a**, *E*/*Z* 92:8

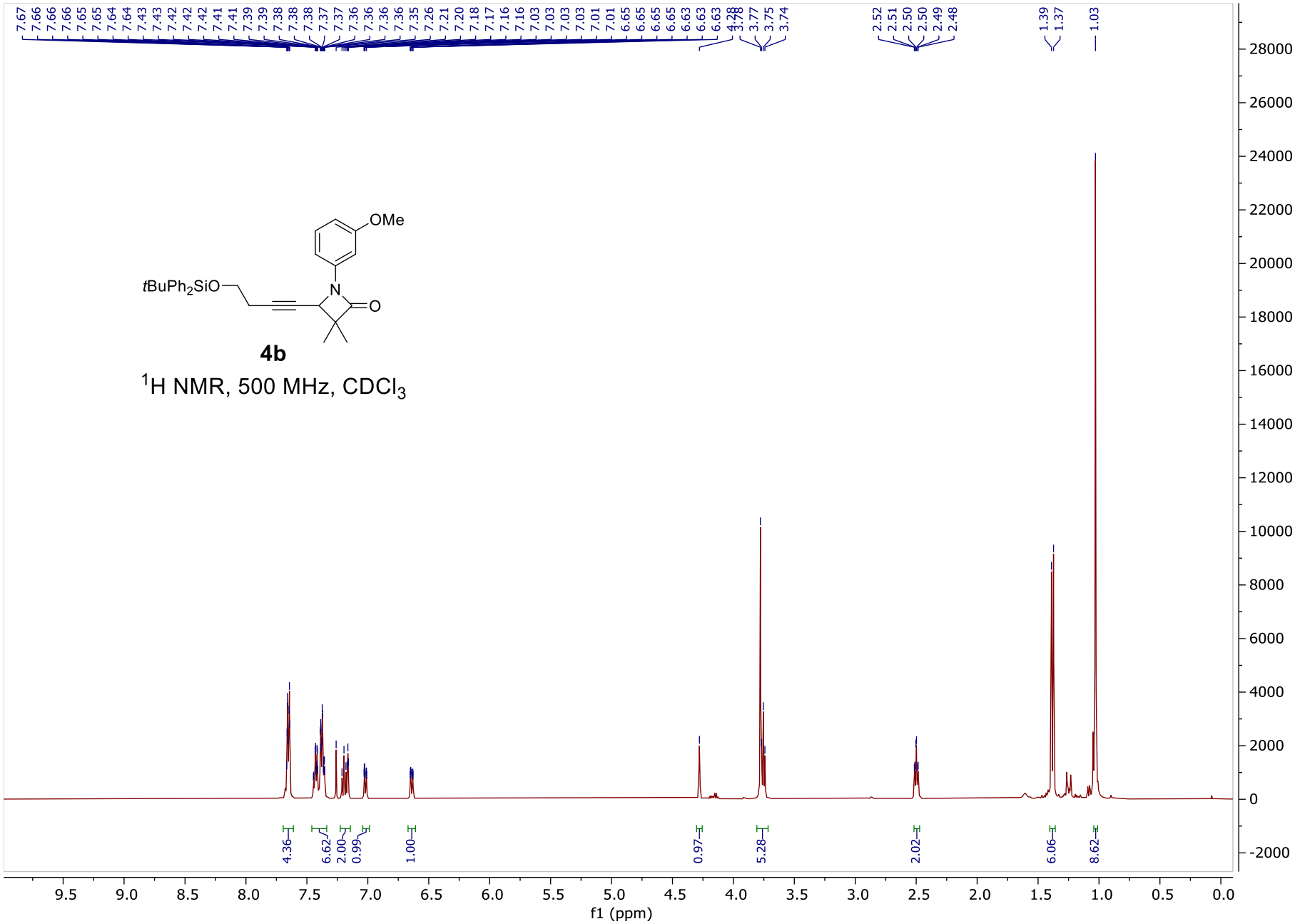
Crude $^{1}$H NMR, 500 MHz, $CDCl_3$

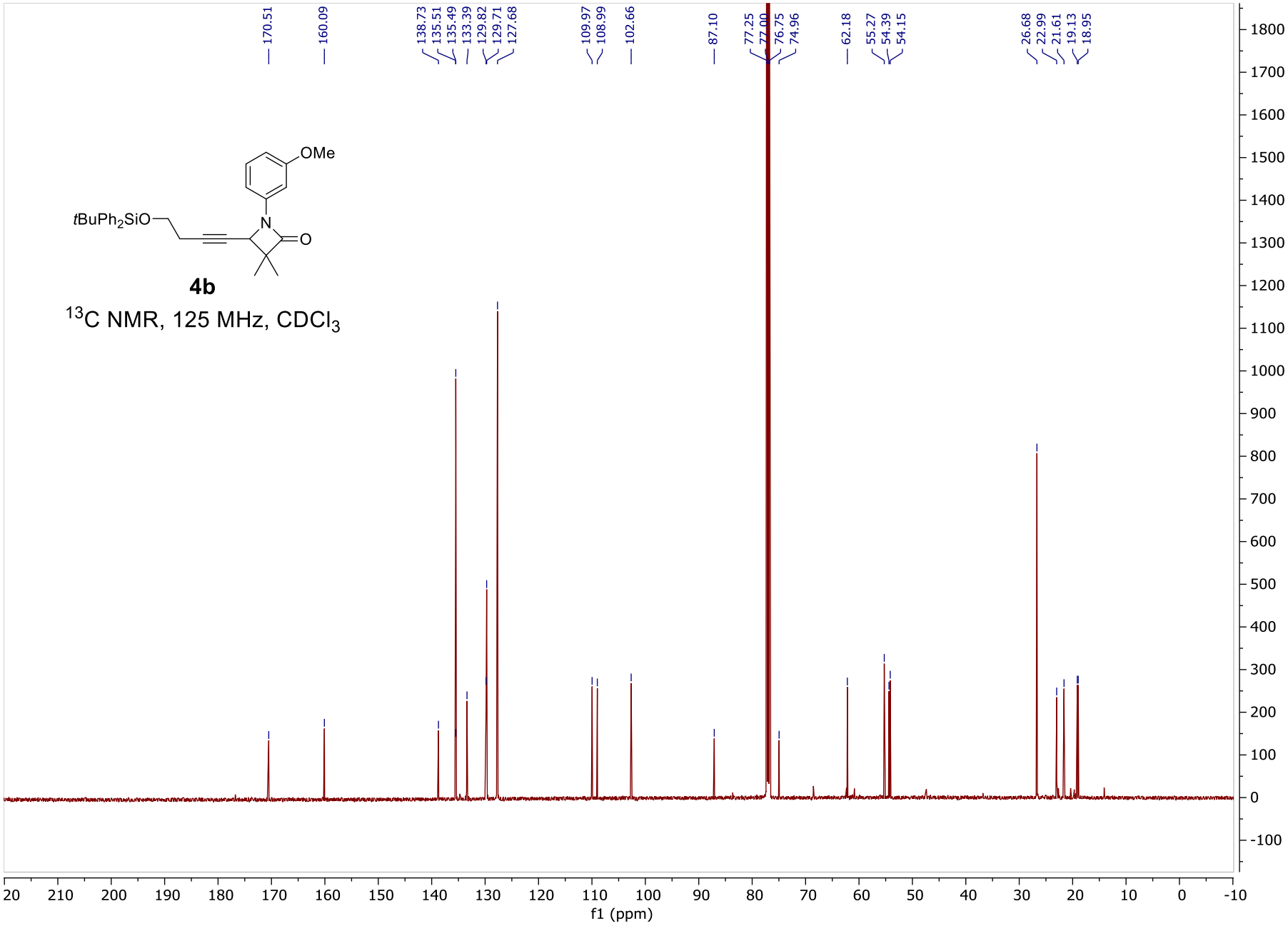

7.79 7.77 7.76 7.76 7.75 7.55 7.54 7.54 7.50 7.49 7.49 7.25 7.25 7.24 7.23 7.23 7.11 7.08 7.06 7.03 7.00 7.00 6.97 6.73 6.72 6.72 6.71 6.69 6.69 6.68 6.66 6.66 6.65 6.65 6.64 6.63 6.63 6.63
3.68 3.66 3.63 3.47 3.45 3.43 3.24 2.37 2.36 2.35 2.34 2.32 2.32 2.10 2.09 2.07 2.07 2.05 2.05 1.17
OMe
OSiPh2tBu
N
H
3b, E/Z 89:11
Crude 1H NMR, 300 MHz, C6D6
4.26 0.59 0.13 1.00 7.60 0.21 1.13 3.19 2.18 0.34 5.24 2.19 0.34 9.71
f1 (ppm)

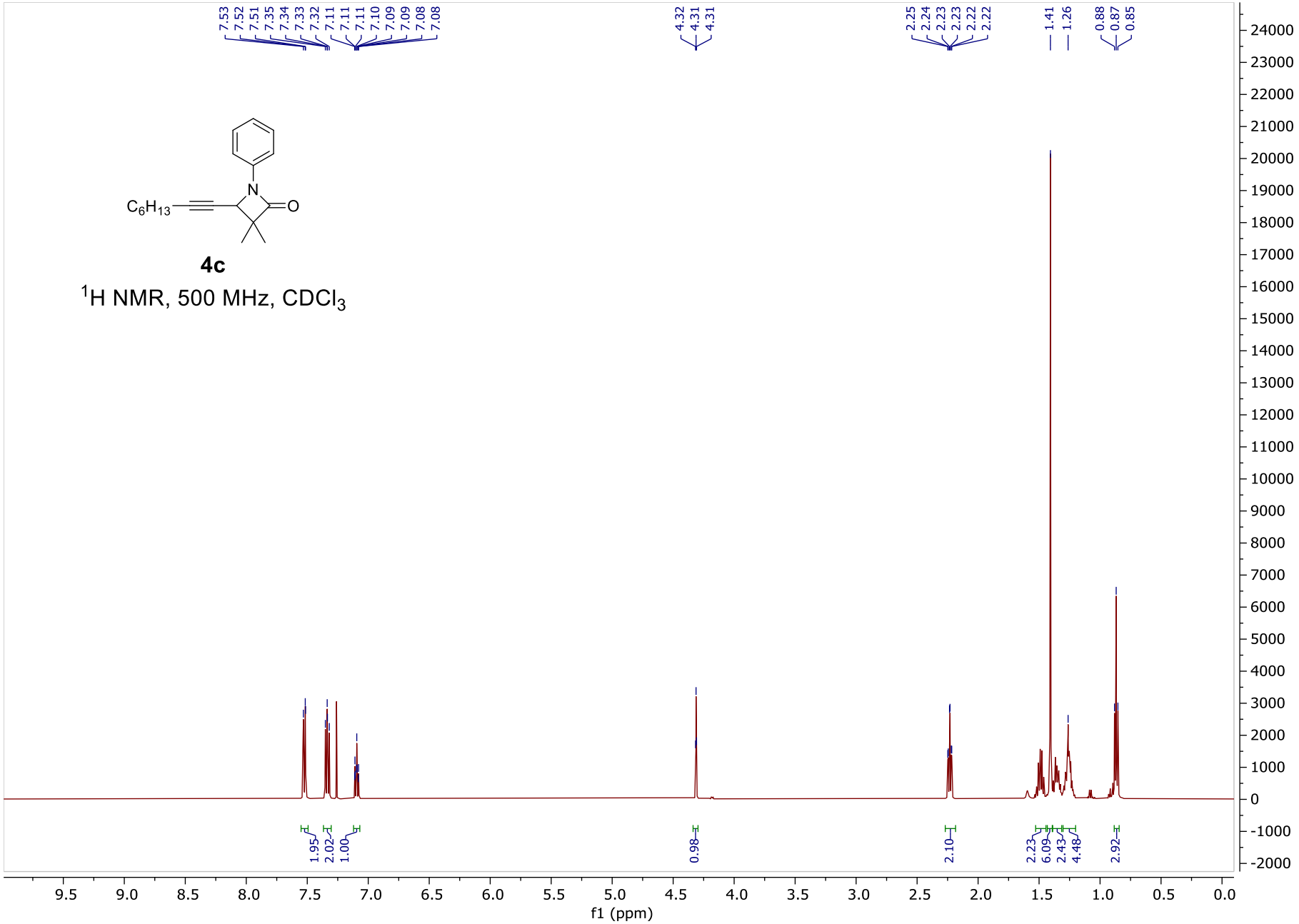

7.70
7.69
7.69
7.62
7.37
7.36
7.36
7.34
7.34
7.26
7.15
7.14
7.13
7.13
7.07
7.05
2.46
2.45
2.44
2.44
2.43
2.42
2.26
2.25
2.24
2.24
2.23
2.22
1.62
1.44
1.44
1.42
1.32
0.91
0.91
0.90
0.90
0.89
0.89
0.87
0.86
N
H
C6H13
3c, E/Z 89:11
Crude 1H NMR, 500 MHz, CDCl3
1.00
0.12
2.52
1.02
2.21
0.26
2.29
0.30
3.04
2.68
4.71
3.92
f1 (ppm)

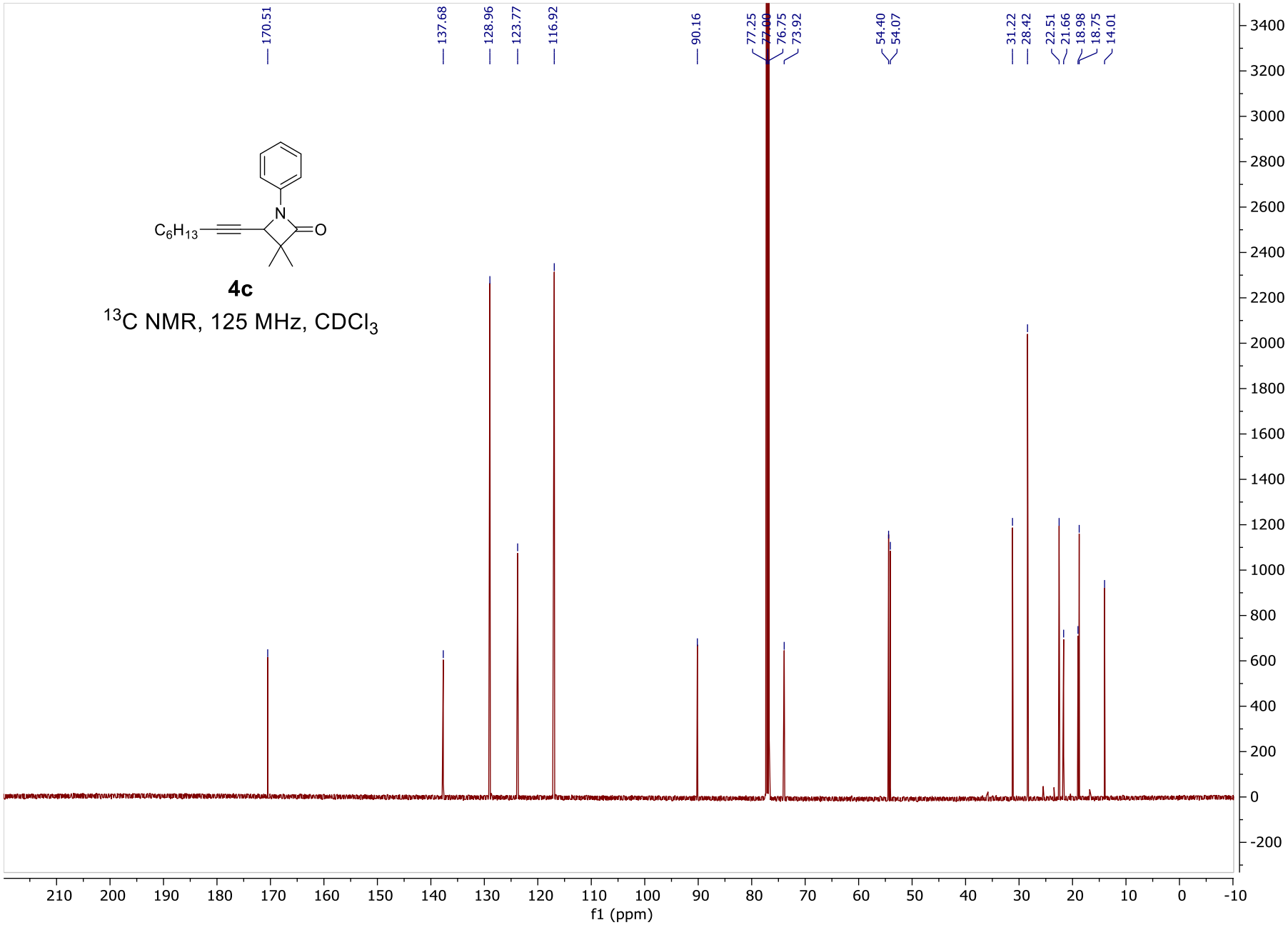

OMe
tBuMe2SiO
N
O
4a
1H NMR, 500 MHz, CDCl3
f1 (ppm)

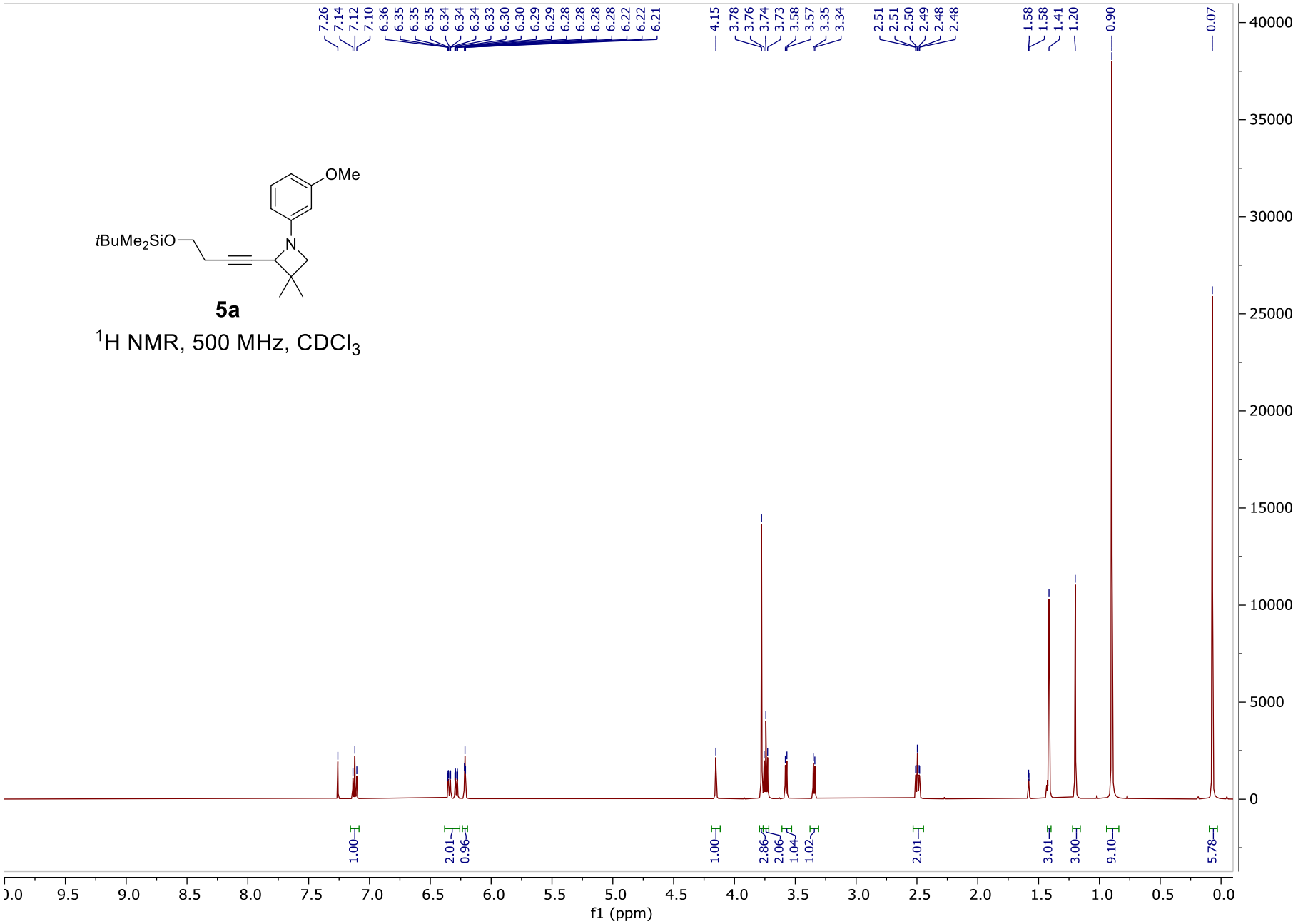

170.51
160.12
138.75
129.82
109.90
109.07
102.74
87.08
77.25
77.20
77.00
76.75
74.95
61.60
55.31
54.39
54.16
25.81
23.23
21.64
18.96
18.26
-5.37
OMe
tBuMe2SiO
N
O
4a
13C NMR, 125 MHz, CDCl3
2500
2000
1500
1000
500
0
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

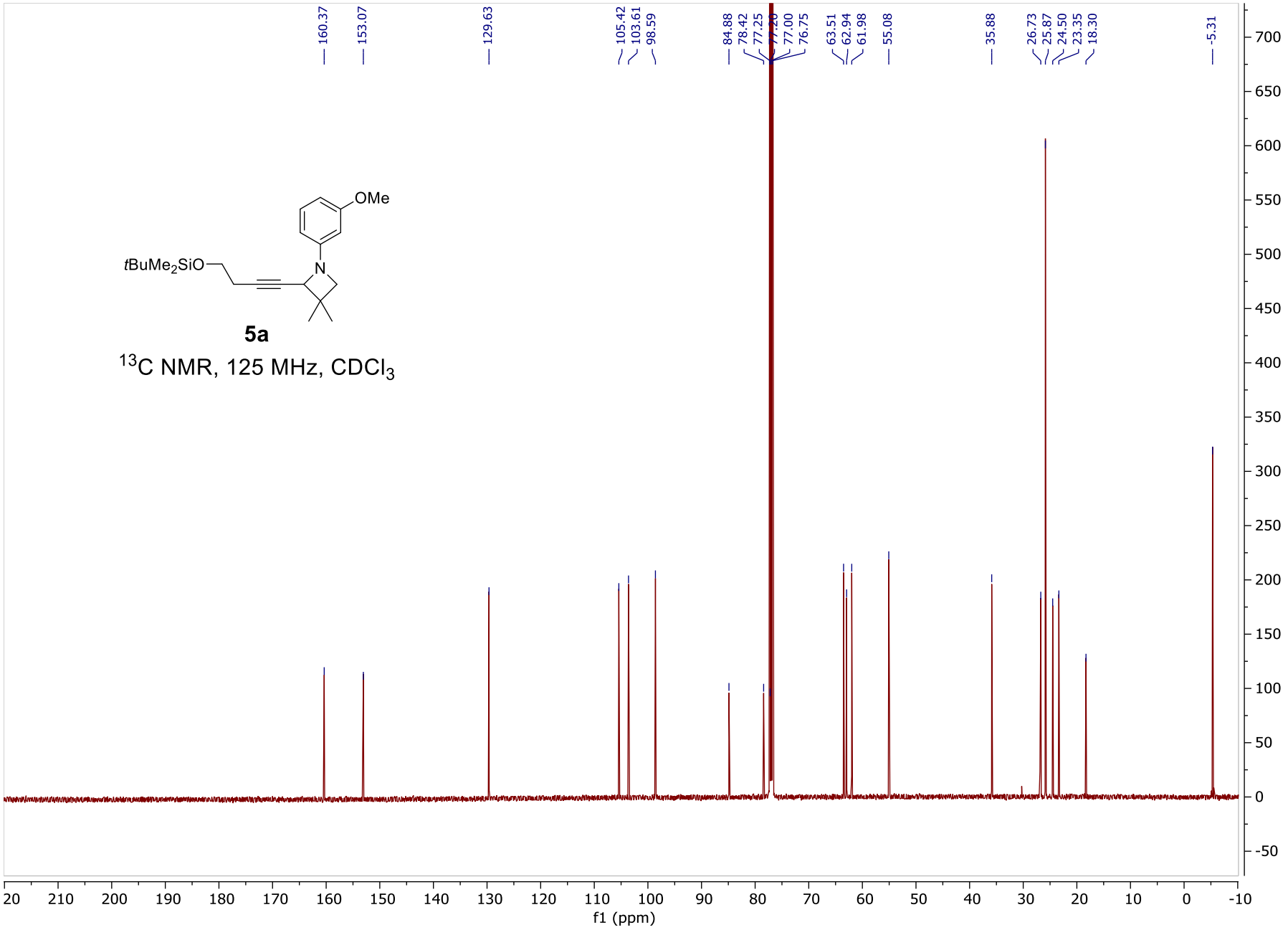

OMe
tBuPh2SiO
N
O
4b
1H NMR, 500 MHz, CDCl3
f1 (ppm)

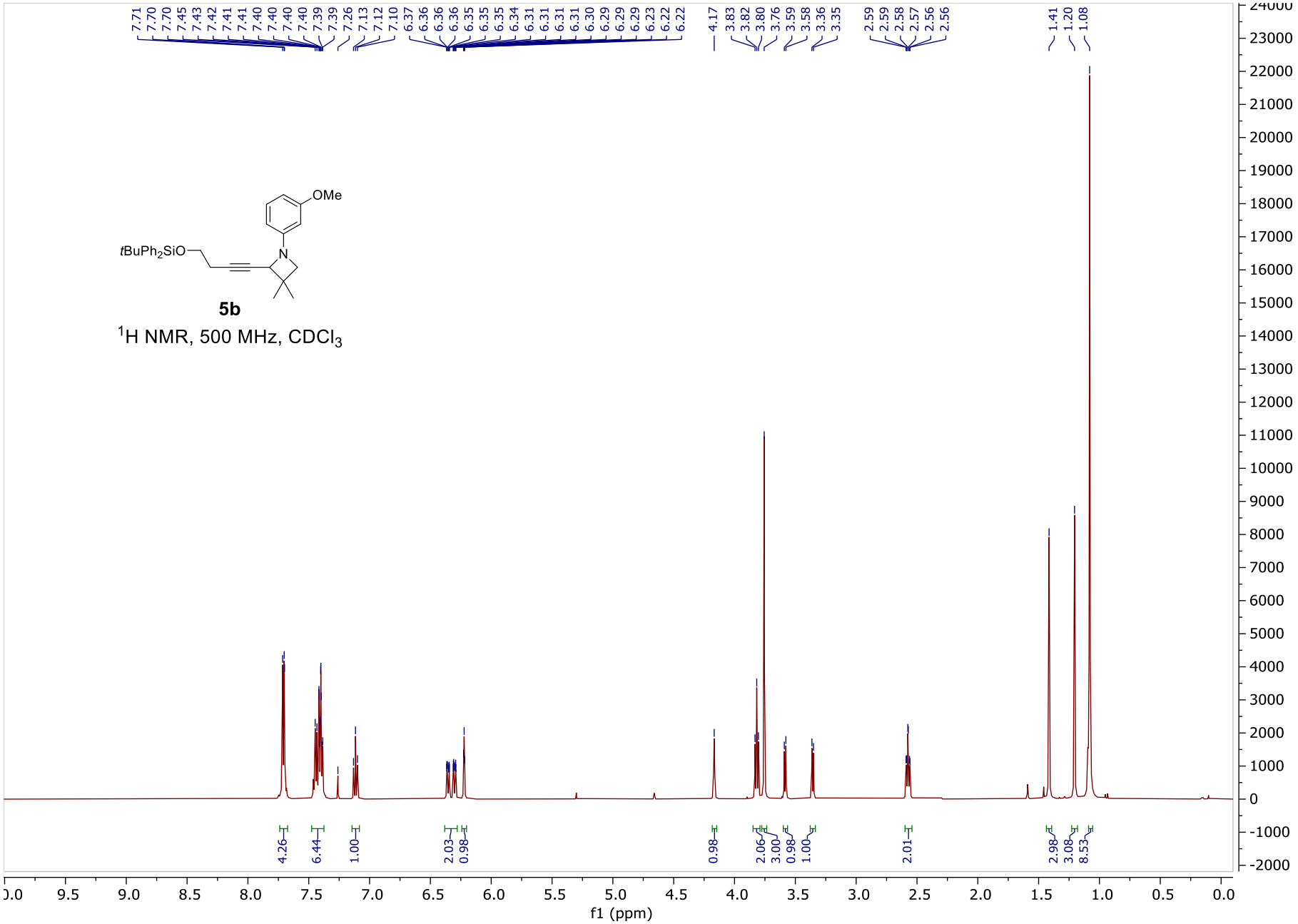

170.51
160.09
138.73
135.51
135.49
133.39
129.82
129.71
127.68
109.97
108.99
102.66
87.10
77.25
77.00
76.75
74.96
62.18
55.27
54.39
54.15
26.68
22.99
21.61
19.13
18.95
OMe
tBuPh2SiO
N
O
4b
13C NMR, 125 MHz, CDCl3
f1 (ppm)

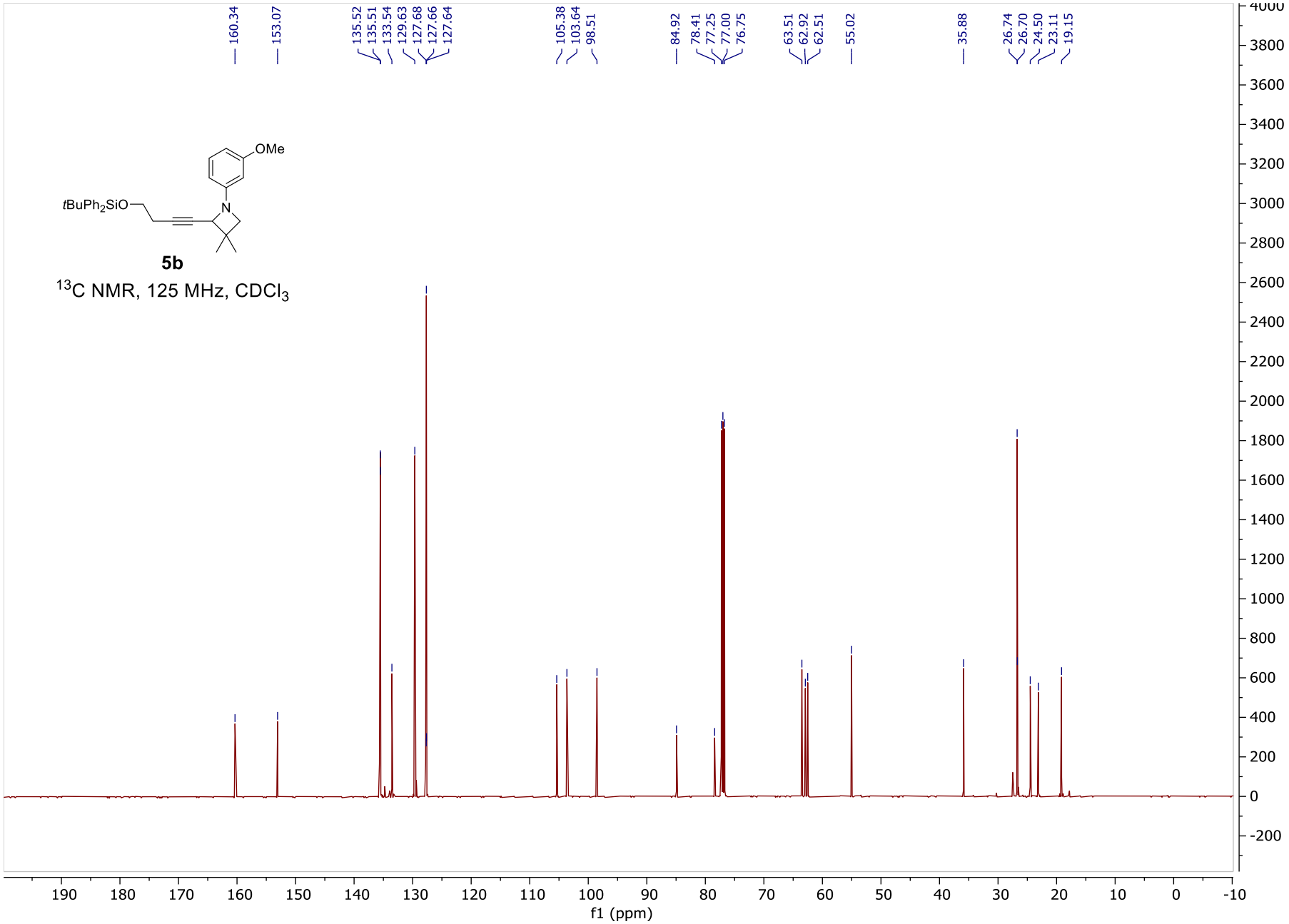

7.53
7.52
7.51
7.35
7.34
7.33
7.32
7.11
7.11
7.11
7.10
7.09
7.09
7.08
7.08
4.32
4.31
4.31
2.25
2.24
2.23
2.23
2.22
2.22
1.41
1.26
0.88
0.87
0.85
N
O
C6H13
4c
1H NMR, 500 MHz, CDCl3
1.95
2.02
1.00
0.98
2.10
2.23
6.09
2.43
4.48
2.92
f1 (ppm)

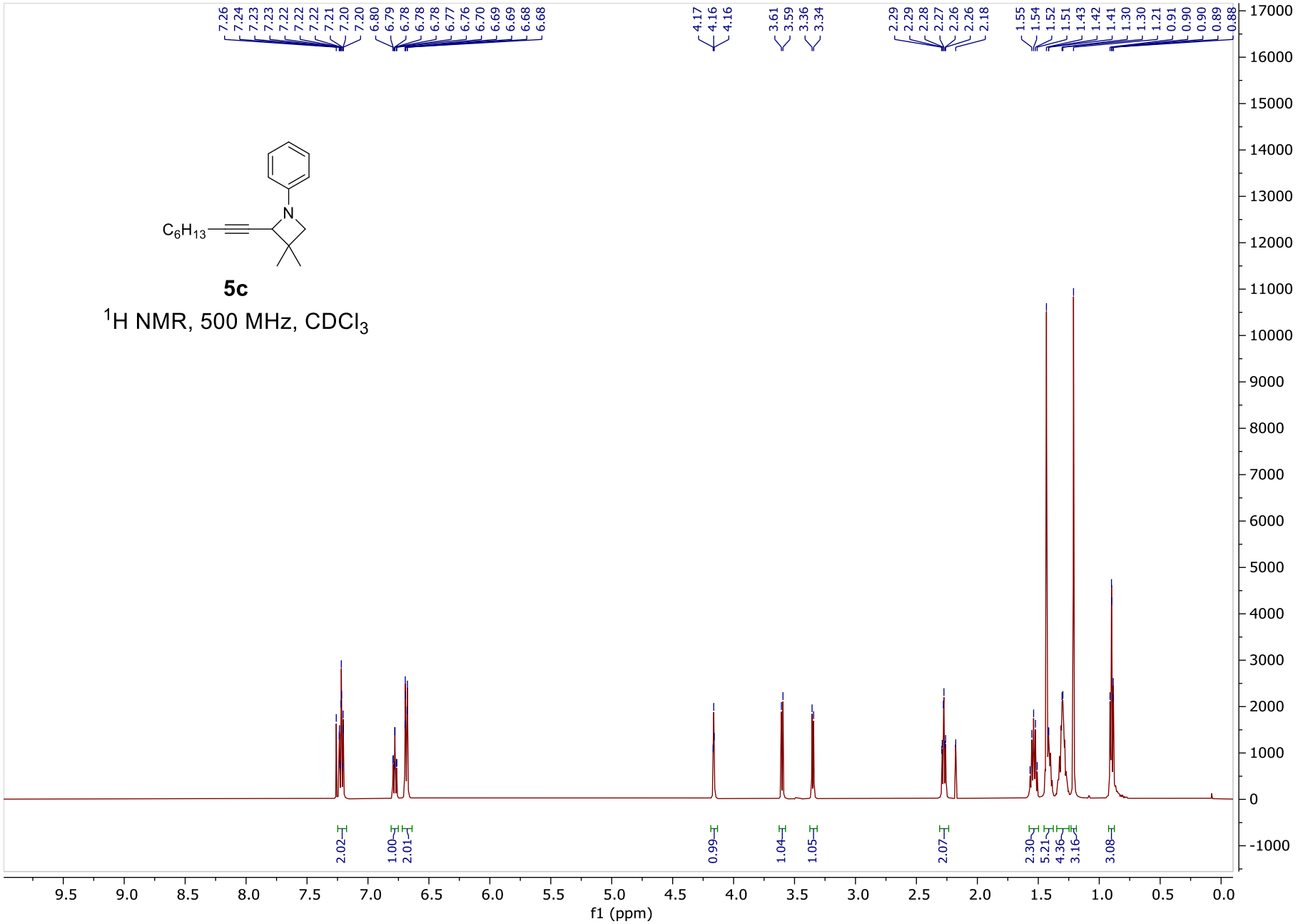

170.51
137.68
128.96
123.77
116.92
90.16
77.25
77.00
76.75
73.92
54.40
54.07
31.22
28.42
22.51
21.66
18.98
18.75
14.01
N
O
$C_6H_{13}$
4c
$^{13}C$ NMR, 125 MHz, $CDCl_3$
f1 (ppm)

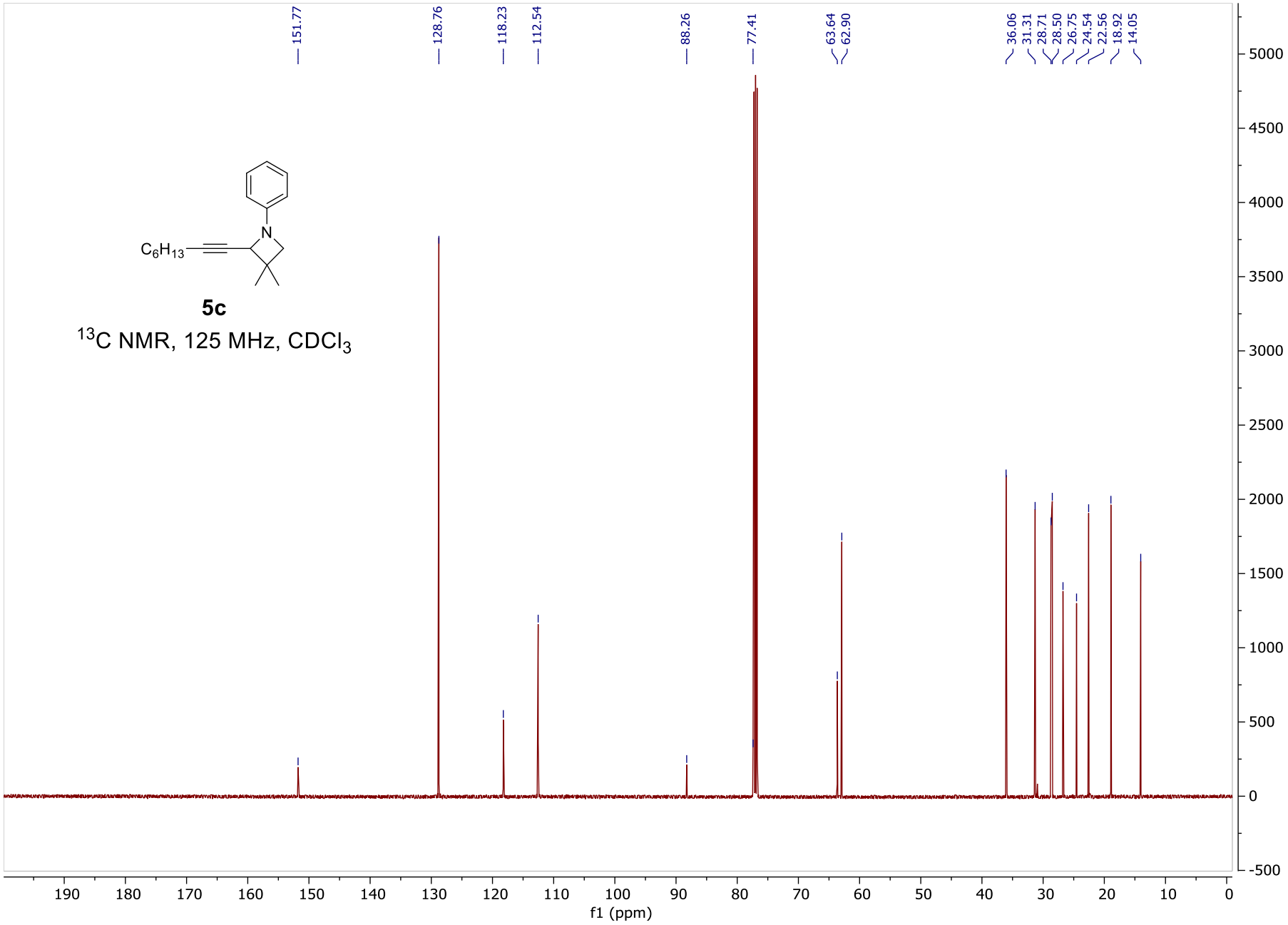

OMe
tBuMe2SiO
N
5a
1H NMR, 500 MHz, CDCl3
f1 (ppm)

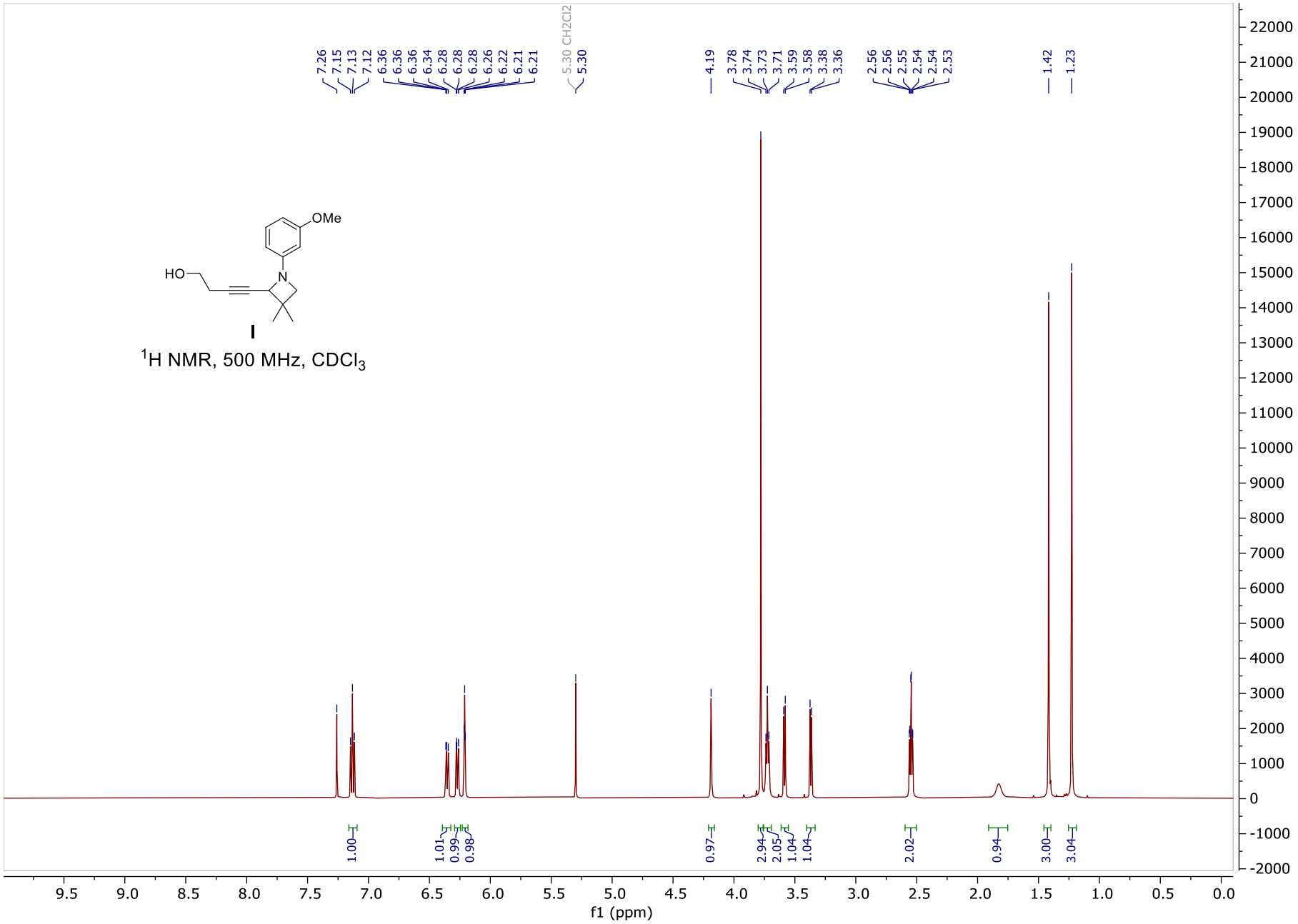

160.37
153.07
129.63
105.42
103.61
98.59
84.88
78.42
77.25
77.00
76.75
63.51
62.94
61.98
55.08
35.88
26.73
25.87
24.50
23.35
18.30
-5.31
OMe
tBuMe2SiO
N
5a
13C NMR, 125 MHz, CDCl3
f1 (ppm)

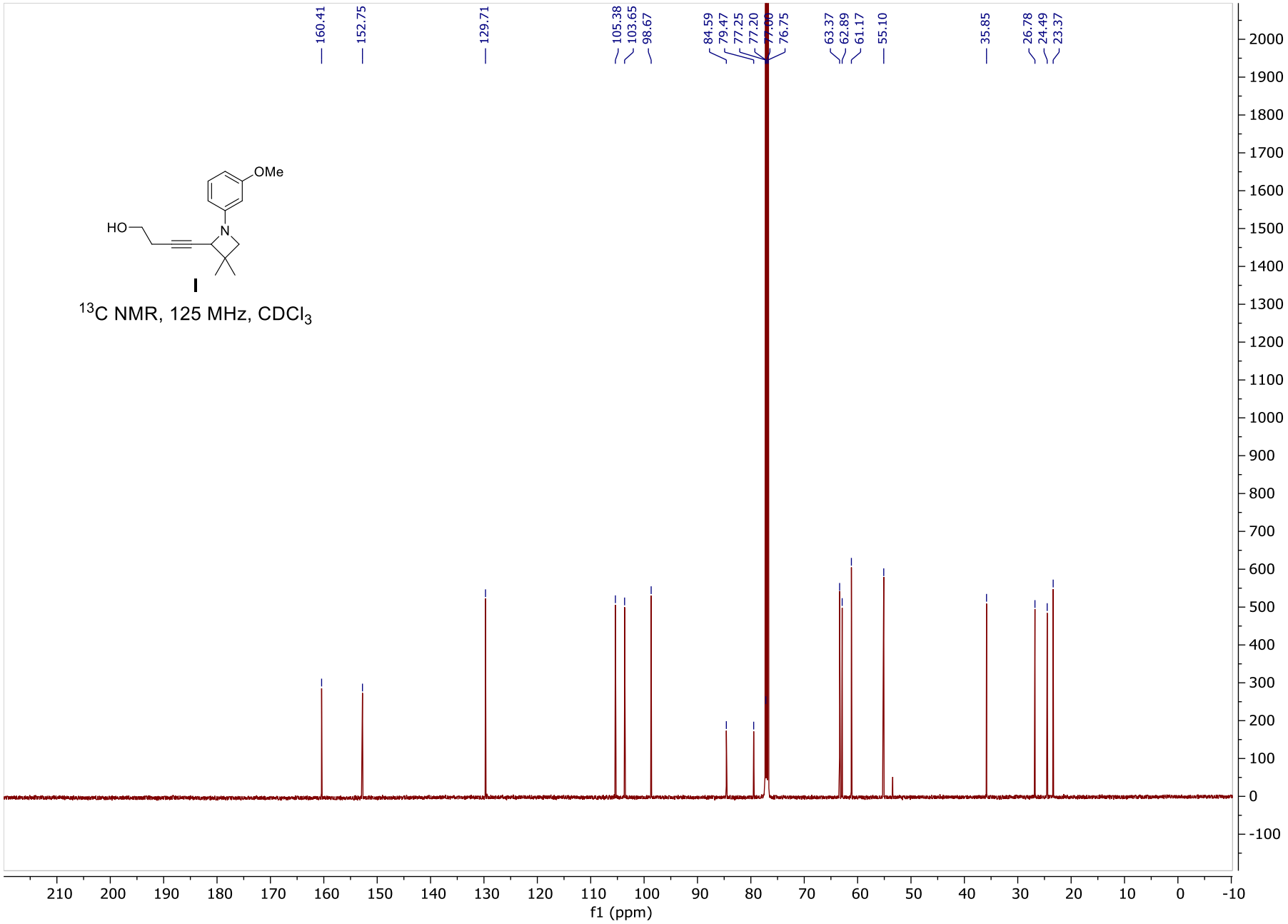

OMe
tBuPh2SiO
N
5b
1H NMR, 500 MHz, CDCl3
f1 (ppm)

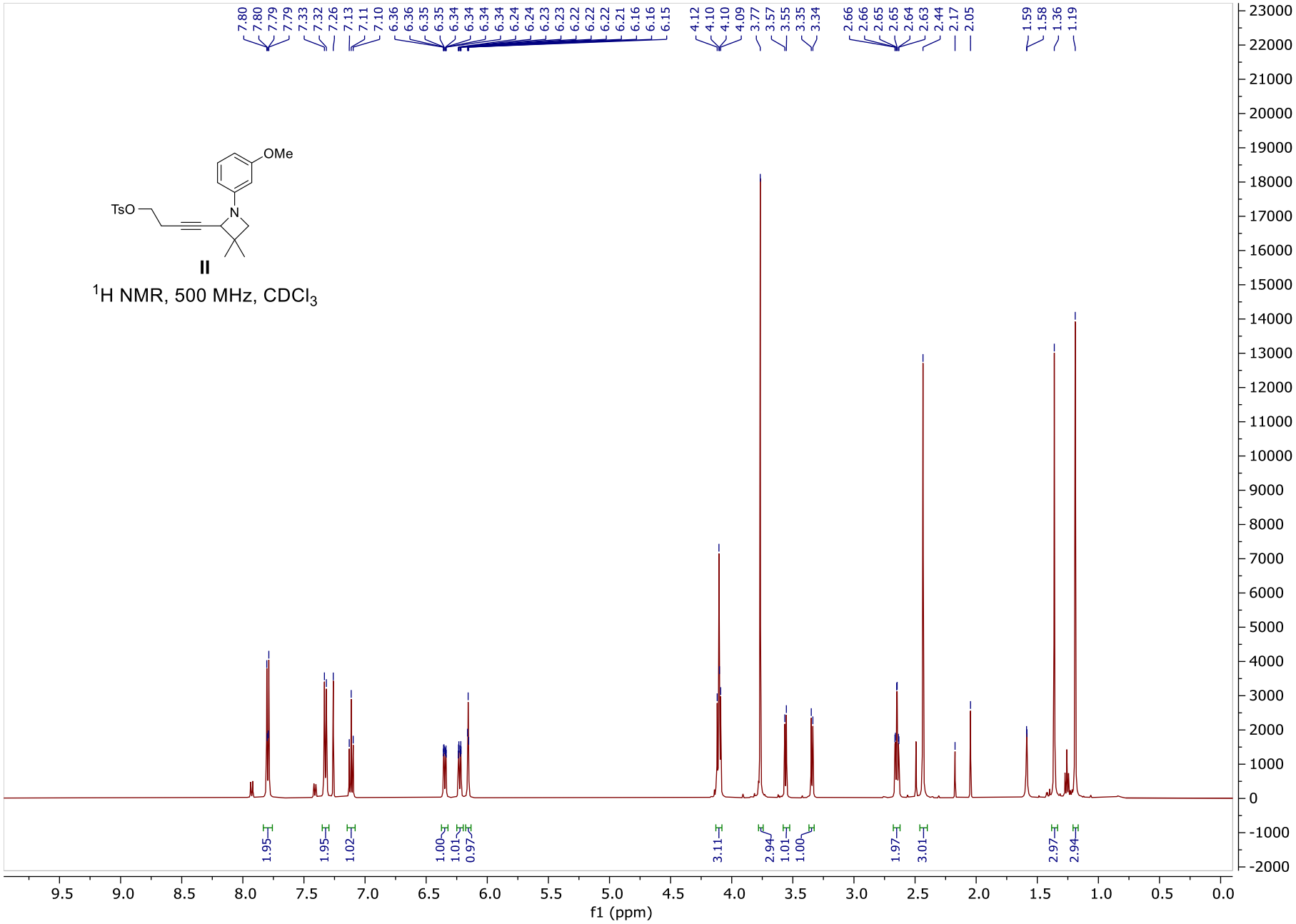

160.34
153.07
135.52
135.51
133.54
129.63
127.68
127.66
127.64
105.38
103.64
98.51
84.92
78.41
77.25
77.00
76.75
63.51
62.92
62.51
55.02
35.88
26.74
26.70
24.50
23.11
19.15
OMe
tBuPh2SiO
N
5b
13C NMR, 125 MHz, CDCl3
f1 (ppm)

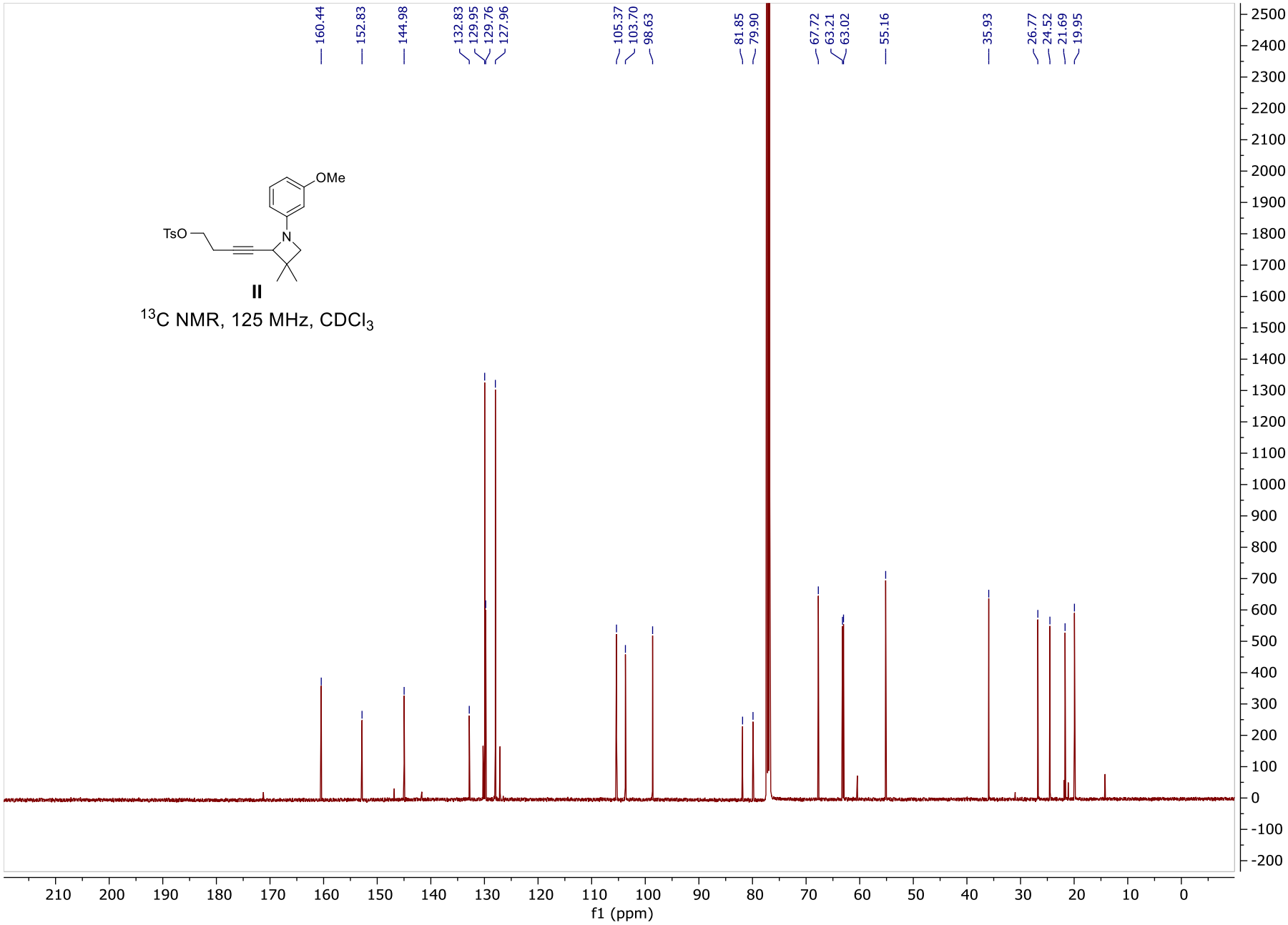

7.26 7.24 7.23 7.23 7.22 7.22 7.22 7.21 7.20 7.20 6.80 6.79 6.78 6.78 6.78 6.77 6.76 6.70 6.69 6.69 6.68 6.68
4.17 4.16 4.16
3.61 3.59 3.36 3.34
2.29 2.29 2.28 2.27 2.26 2.26 2.18
1.55 1.54 1.52 1.51 1.43 1.42 1.41 1.30 1.30 1.21 0.91 0.90 0.90 0.89 0.88
N
C6H13
5c
1H NMR, 500 MHz, CDCl3
2.02 1.00 2.01 0.99 1.04 1.05 2.07 2.30 5.21 4.36 3.16 3.08
f1 (ppm)


151.77
128.76
118.23
112.54
88.26
77.41
63.64
62.90
36.06
31.31
28.71
28.50
26.75
24.54
22.56
18.92
14.05
N
C6H13
5c
13C NMR, 125 MHz, CDCl3
f1 (ppm)


7.26
7.15
7.13
7.12
6.36
6.36
6.36
6.34
6.28
6.28
6.28
6.26
6.22
6.21
6.21
5.30 CH2Cl2
5.30
4.19
3.78
3.74
3.73
3.71
3.59
3.58
3.38
3.36
2.56
2.56
2.55
2.54
2.54
2.53
1.42
1.23
OMe
HO
N
I
1H NMR, 500 MHz, CDCl3
1.00
1.01
0.99
0.98
0.97
2.94
2.05
1.04
1.04
2.02
0.94
3.00
3.04
f1 (ppm)


160.41
152.75
129.71
105.38
103.65
98.67
84.59
79.47
77.25
77.20
77.00
76.75
63.37
62.89
61.17
55.10
35.85
26.78
24.49
23.37
OMe
HO
N
I
$^{13}$C NMR, 125 MHz, CDCl$_3$
f1 (ppm)


OMe
TsO
N
II
$^1$H NMR, 500 MHz, $CDCl_3$
f1 (ppm)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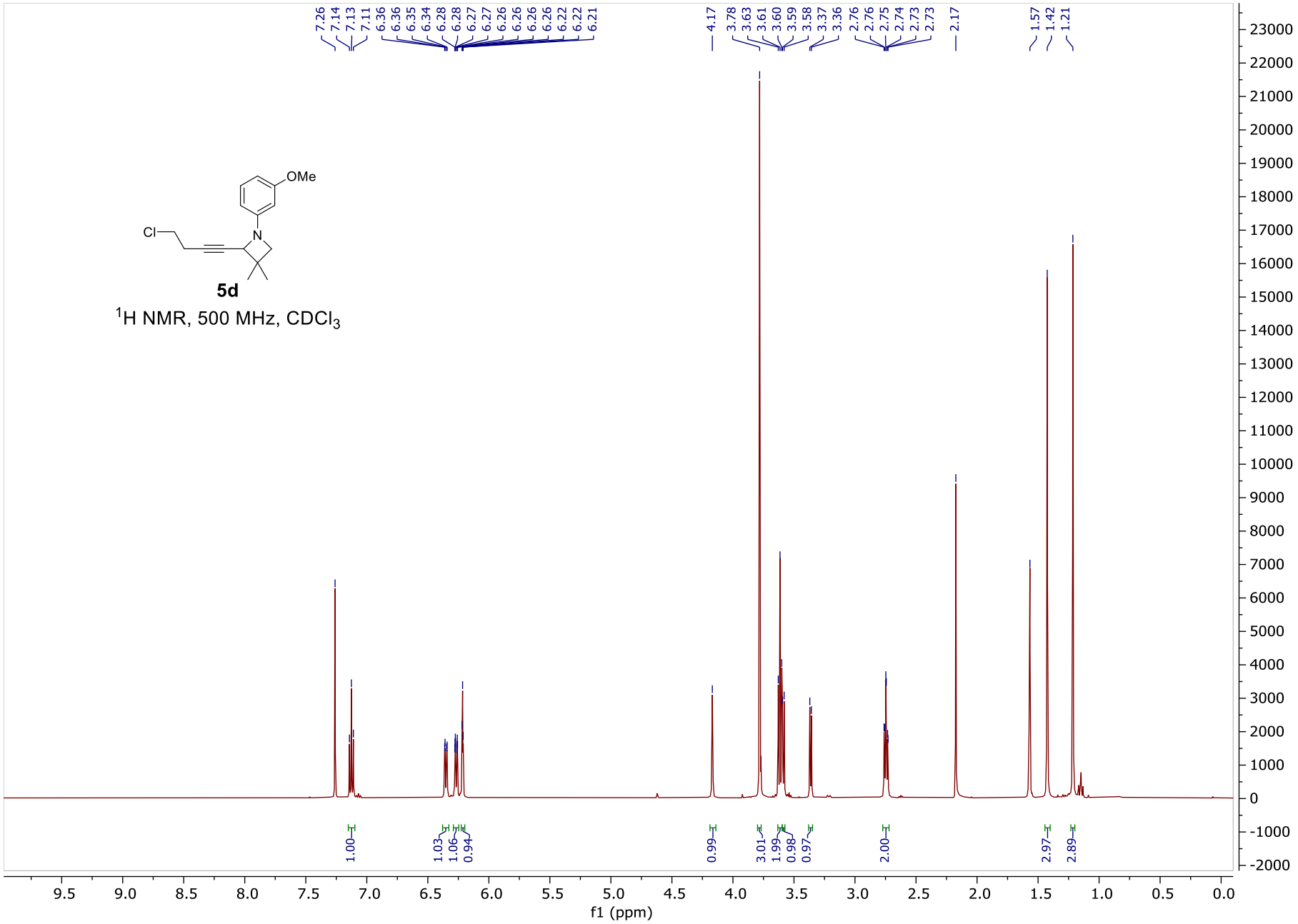
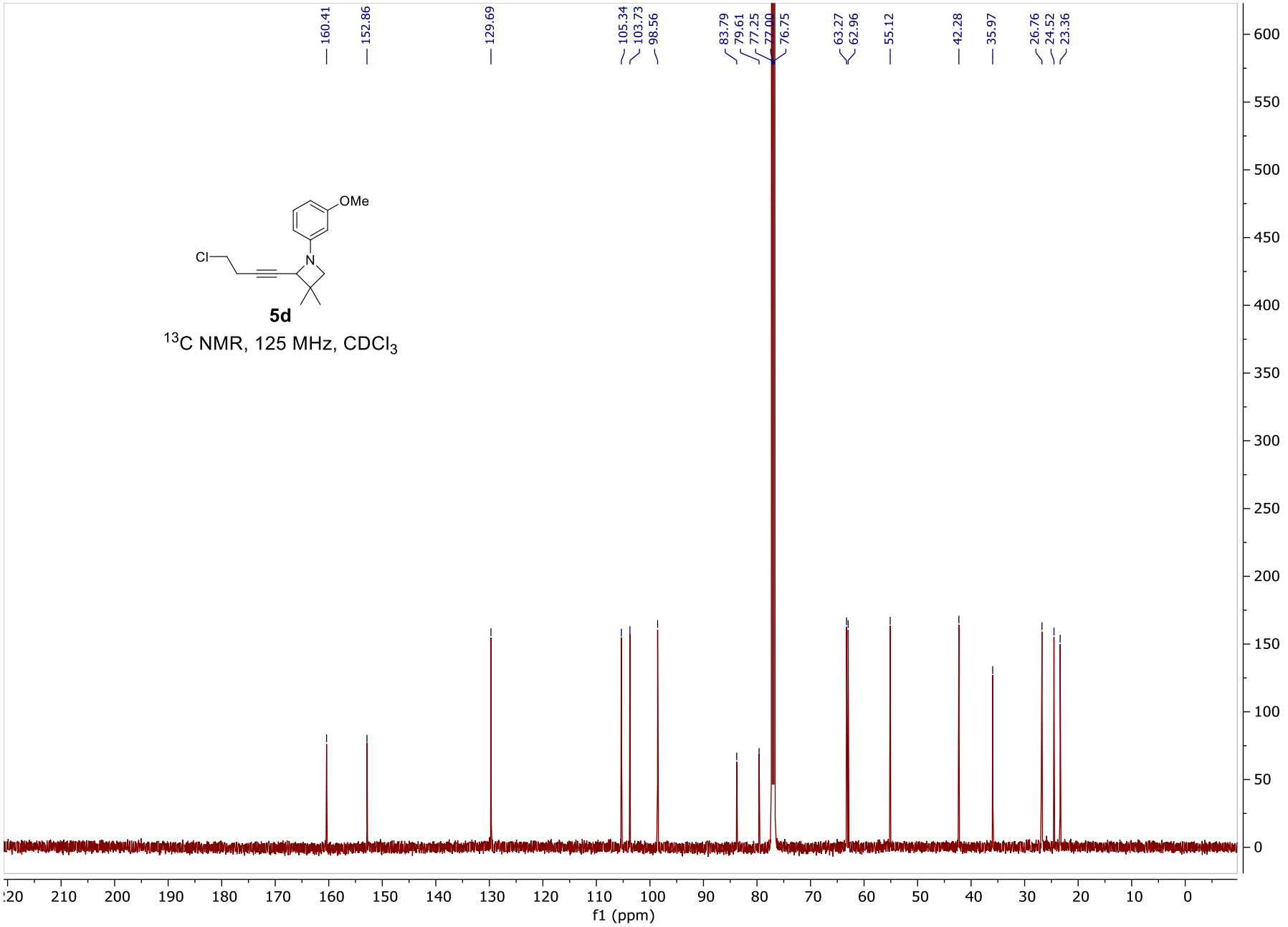
144.98
132.83
129.95
129.76
127.96
105.37
103.70
98.63
81.85
79.90
67.72
63.21
63.02
55.16
35.93
26.77
24.52
21.69
19.95
OMe
TsO
N
II
13C NMR, 125 MHz, CDCl3
f1 (ppm)


OMe
Cl
N
5d
$^1$H NMR, 500 MHz, $CDCl_3$
7.26 7.14 7.13 7.11 6.36 6.36 6.35 6.34 6.28 6.28 6.27 6.27 6.26 6.26 6.26 6.26 6.22 6.22 6.21
4.17 3.78 3.63 3.61 3.60 3.59 3.58 3.37 3.36 2.76 2.76 2.75 2.74 2.73 2.73 2.17 1.57 1.42 1.21
1.00 1.03 1.06 0.94 0.99 3.01 1.99 0.98 0.97 2.00 2.97 2.89
f1 (ppm)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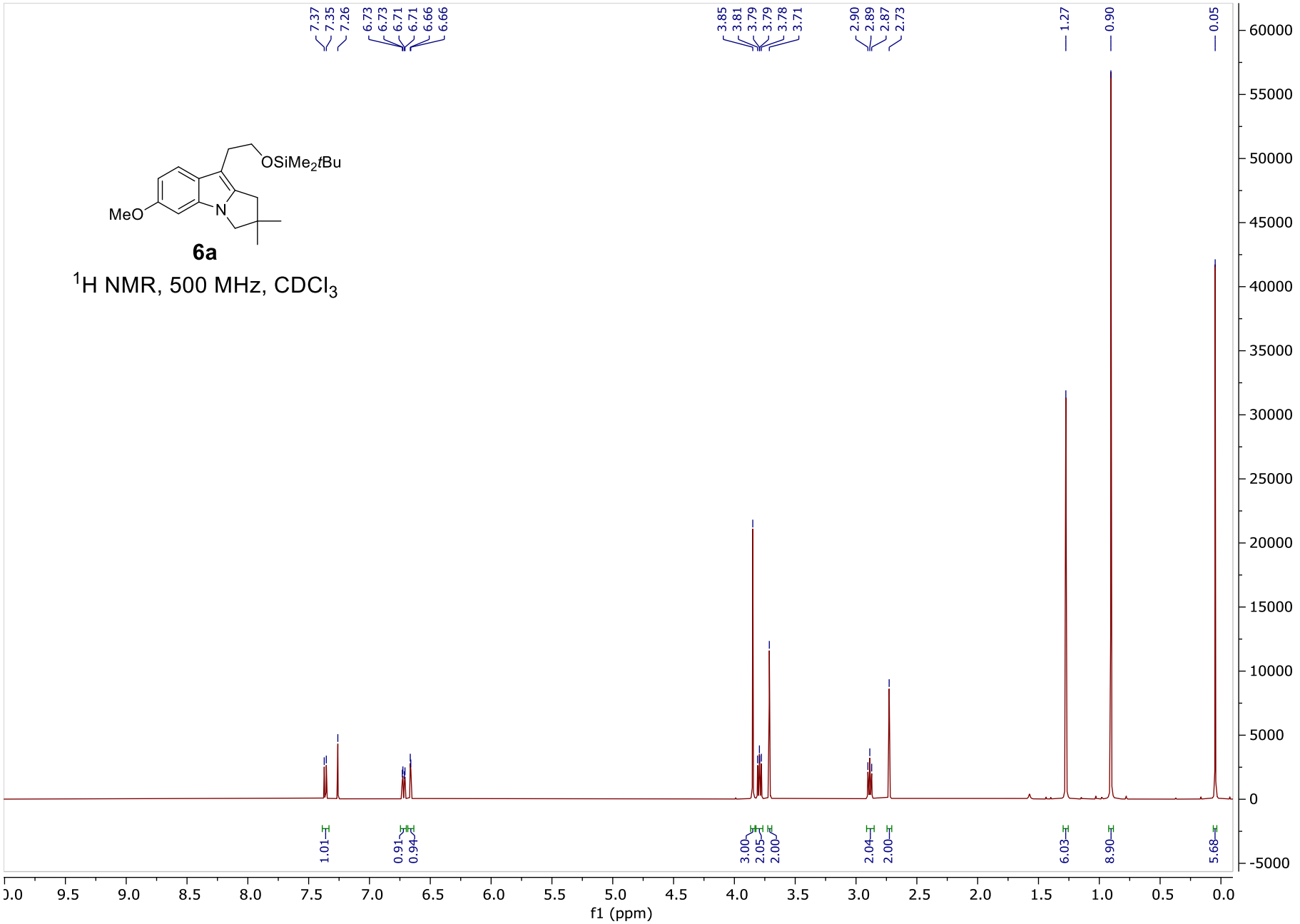
98.56
83.79
79.61
77.25
77.00
76.75
63.27
62.96
55.12
42.28
35.97
26.76
24.52
23.36
OMe
Cl
N
5d
13C NMR, 125 MHz, CDCl3
f1 (ppm)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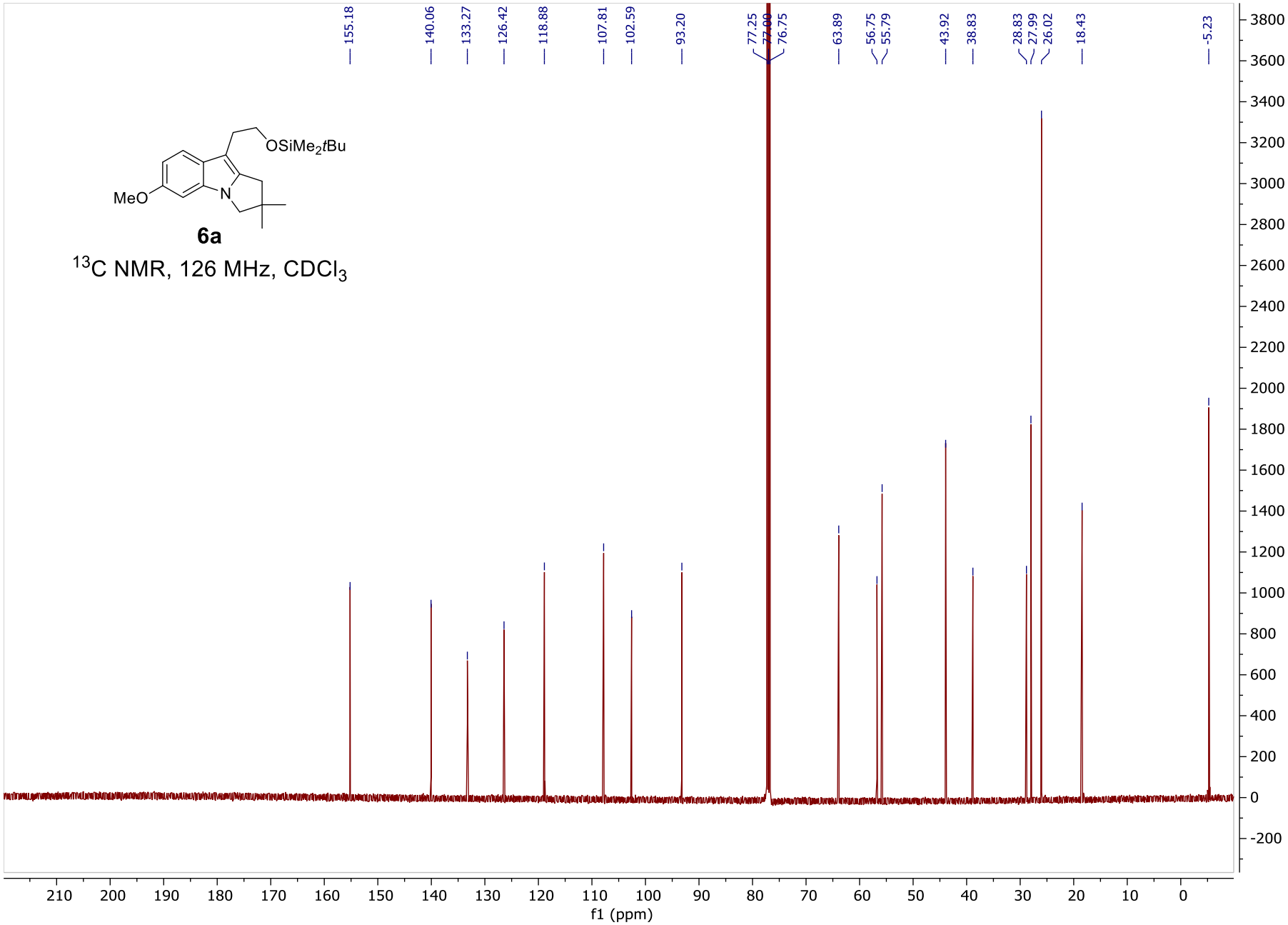
7.35
7.26
6.73
6.73
6.71
6.71
6.66
6.66
3.85
3.81
3.79
3.79
3.78
3.71
2.90
2.89
2.87
2.73
1.27
0.90
0.05
OSiMe2tBu
MeO
N
6a
1H NMR, 500 MHz, CDCl3
1.01
0.91
0.94
3.00
2.05
2.00
2.04
2.00
6.03
8.90
5.68
f1 (ppm)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140.06
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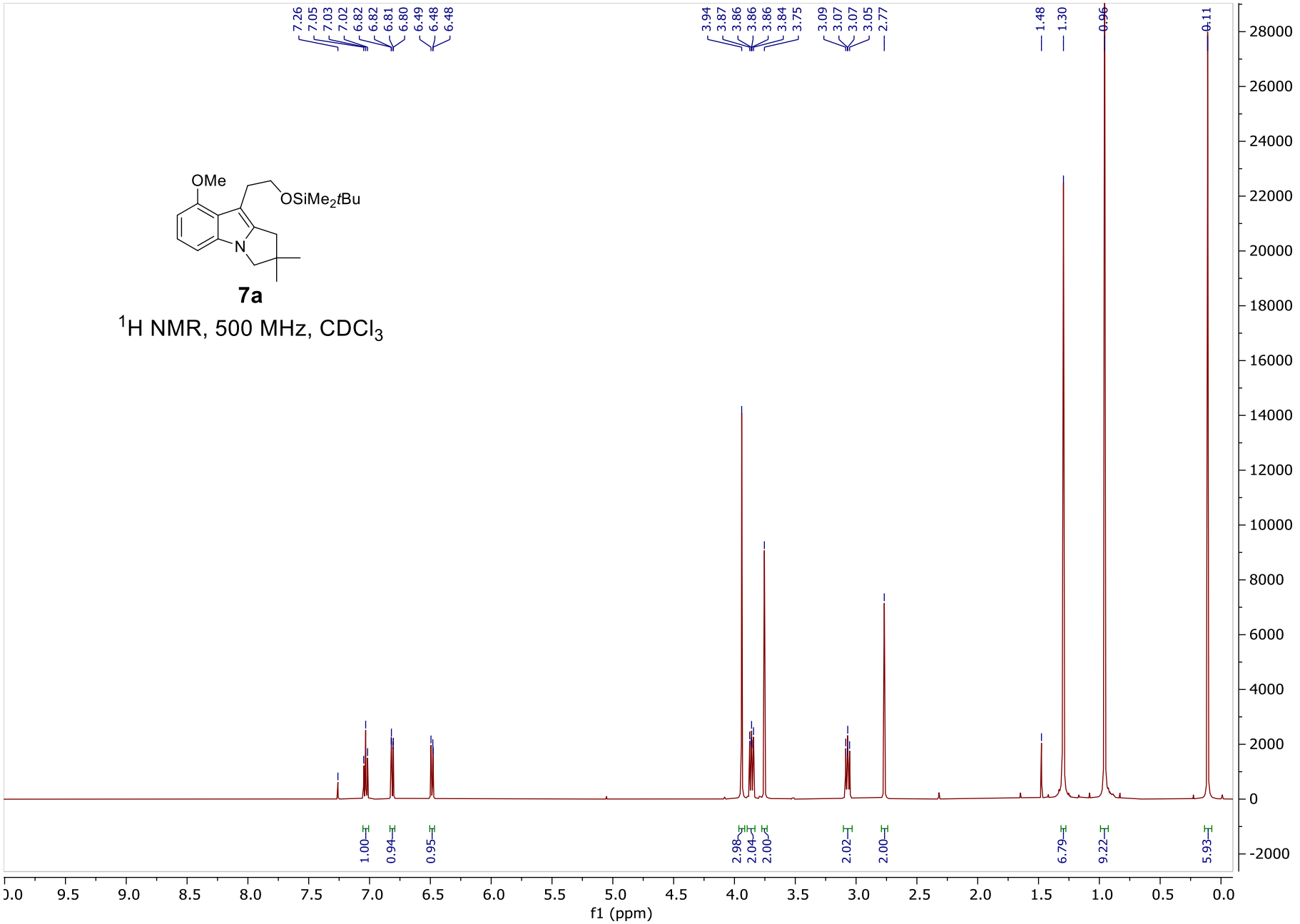
126.42
118.88
107.81
102.59
93.20
77.25
77.00
76.75
63.89
56.75
55.79
43.92
38.83
28.83
27.99
26.02
18.43
-5.23
OSiMe2tBu
MeO
N
6a
13C NMR, 126 MHz, CDCl3
f1 (ppm)


OMe
OSiMe2tBu
N
7a
1H NMR, 500 MHz, CDCl3
7.26
7.05
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7.02
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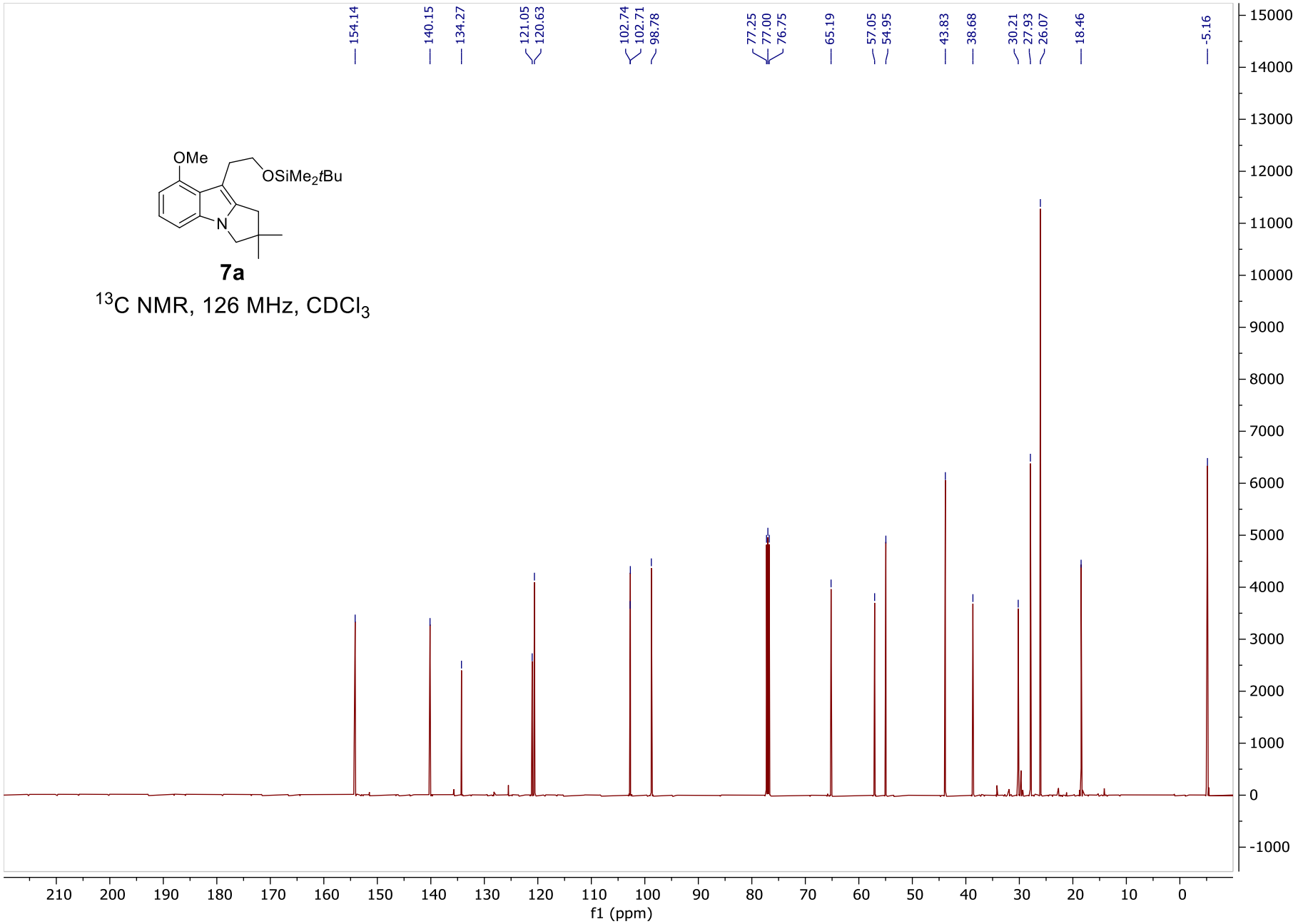
6.82
6.81
6.80
6.49
6.48
6.48
3.94
3.87
3.86
3.86
3.86
3.84
3.75
3.09
3.07
3.07
3.05
2.77
1.48
1.30
0.96
0.11
1.00
0.94
0.95
2.98
2.04
2.00
2.02
2.00
6.79
9.22
5.93
f1 (ppm)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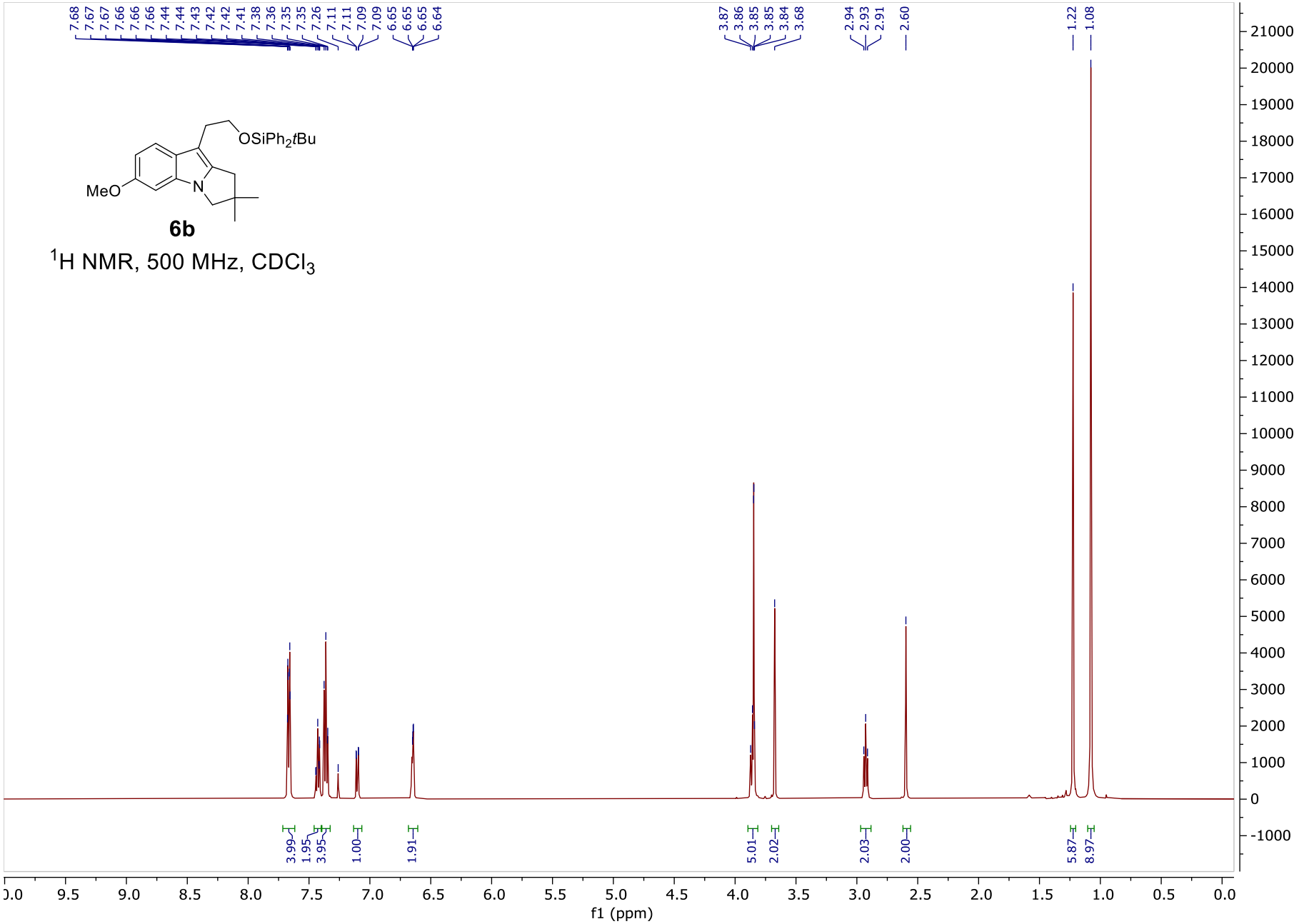
140.15
134.27
121.05
120.63
102.74
102.71
98.78
77.25
77.00
76.75
65.19
57.05
54.95
43.83
38.68
30.21
27.93
26.07
18.46
-5.16
OMe
OSiMe2tBu
N
7a
13C NMR, 126 MHz, CDCl3
f1 (ppm)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7.67
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7.66
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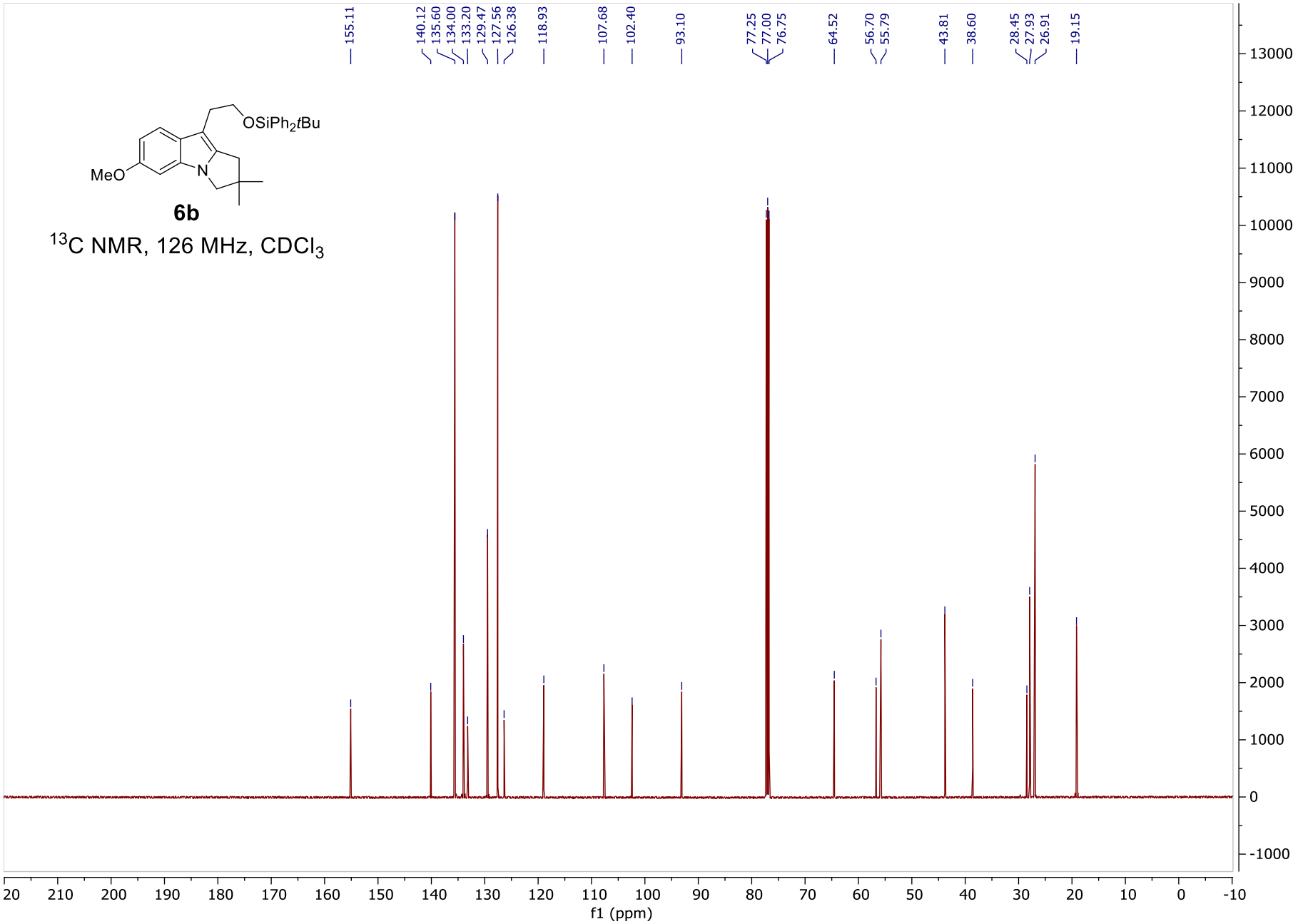
7.44
7.43
7.42
7.42
7.41
7.38
7.36
7.35
7.35
7.26
7.11
7.11
7.09
7.09
6.65
6.65
6.65
6.64
3.87
3.86
3.85
3.85
3.84
3.68
2.94
2.93
2.91
2.60
1.22
1.08
OSiPh2tBu
MeO
N
6b
1H NMR, 500 MHz, CDCl3
3.99
1.95
3.95
1.00
1.91
5.01
2.02
2.03
2.00
5.87
8.97
f1 (ppm)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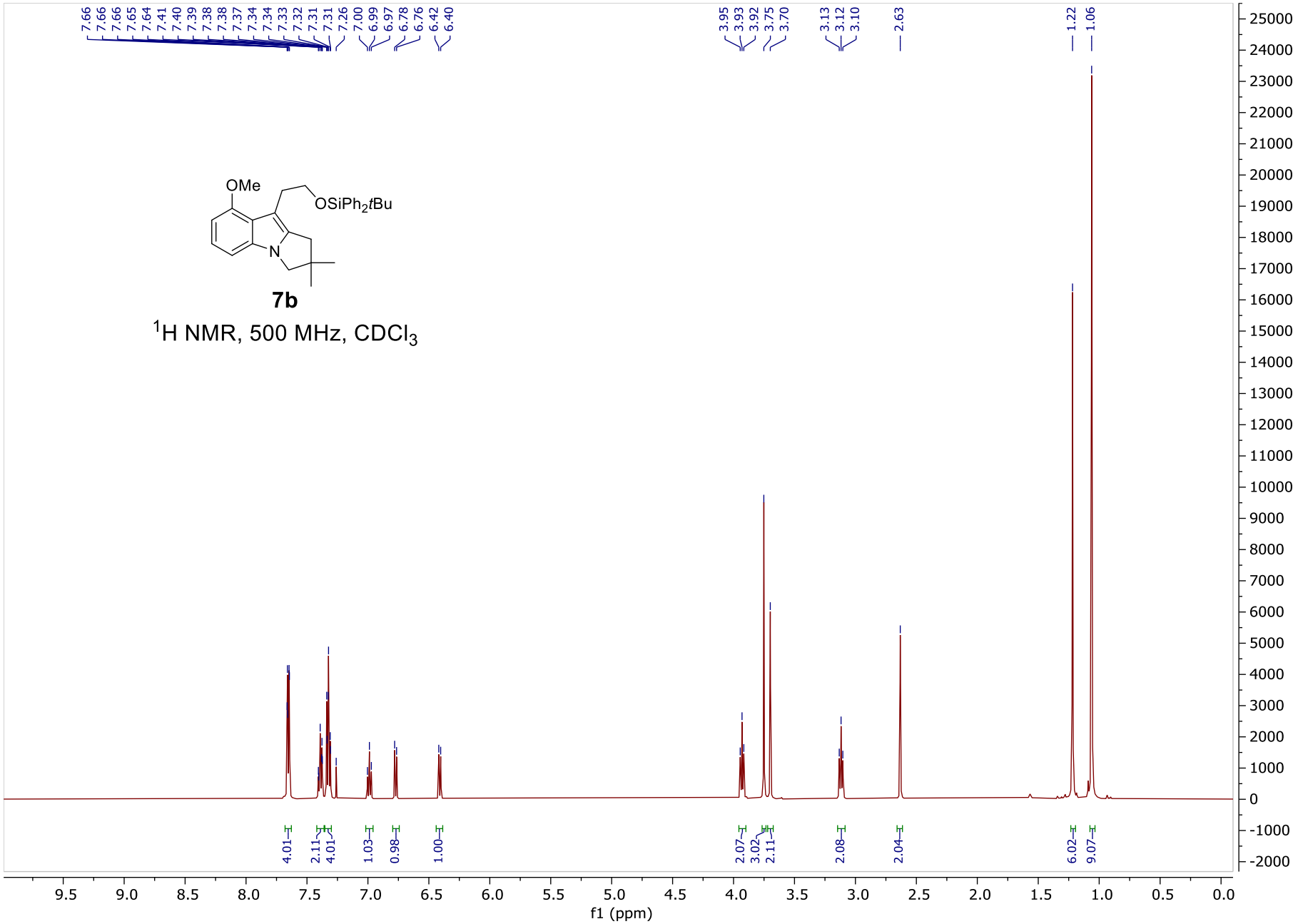
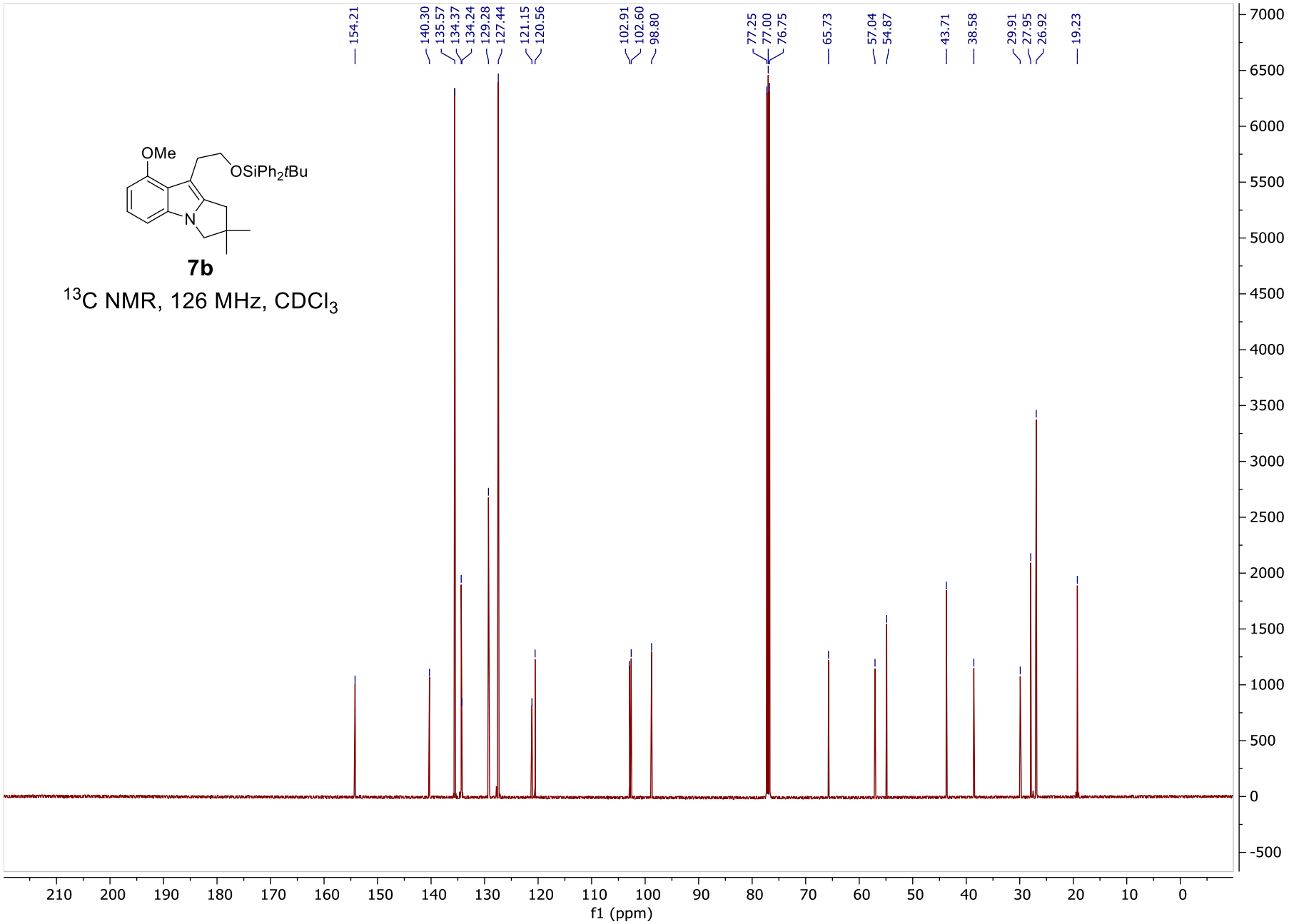
140.12
135.60
134.00
133.20
129.47
127.56
126.38
118.93
107.68
102.40
93.10
77.25
77.00
76.75
64.52
56.70
55.79
43.81
38.60
28.45
27.93
26.91
19.15
OSiPh2tBu
MeO
N
6b
13C NMR, 126 MHz, CDCl3
f1 (ppm)


7.66
7.66
7.66
7.65
7.64
7.41
7.40
7.39
7.38
7.38
7.37
7.34
7.34
7.33
7.32
7.31
7.31
7.26
7.00
6.99
6.97
6.78
6.76
6.42
6.40
3.95
3.93
3.92
3.75
3.70
3.13
3.12
3.10
2.63
1.22
1.06
OMe
OSiPh2tBu
N
7b
1H NMR, 500 MHz, CDCl3
4.01
2.11
4.01
1.03
0.98
1.00
2.07
3.02
2.11
2.08
2.04
6.02
9.07
f1 (ppm)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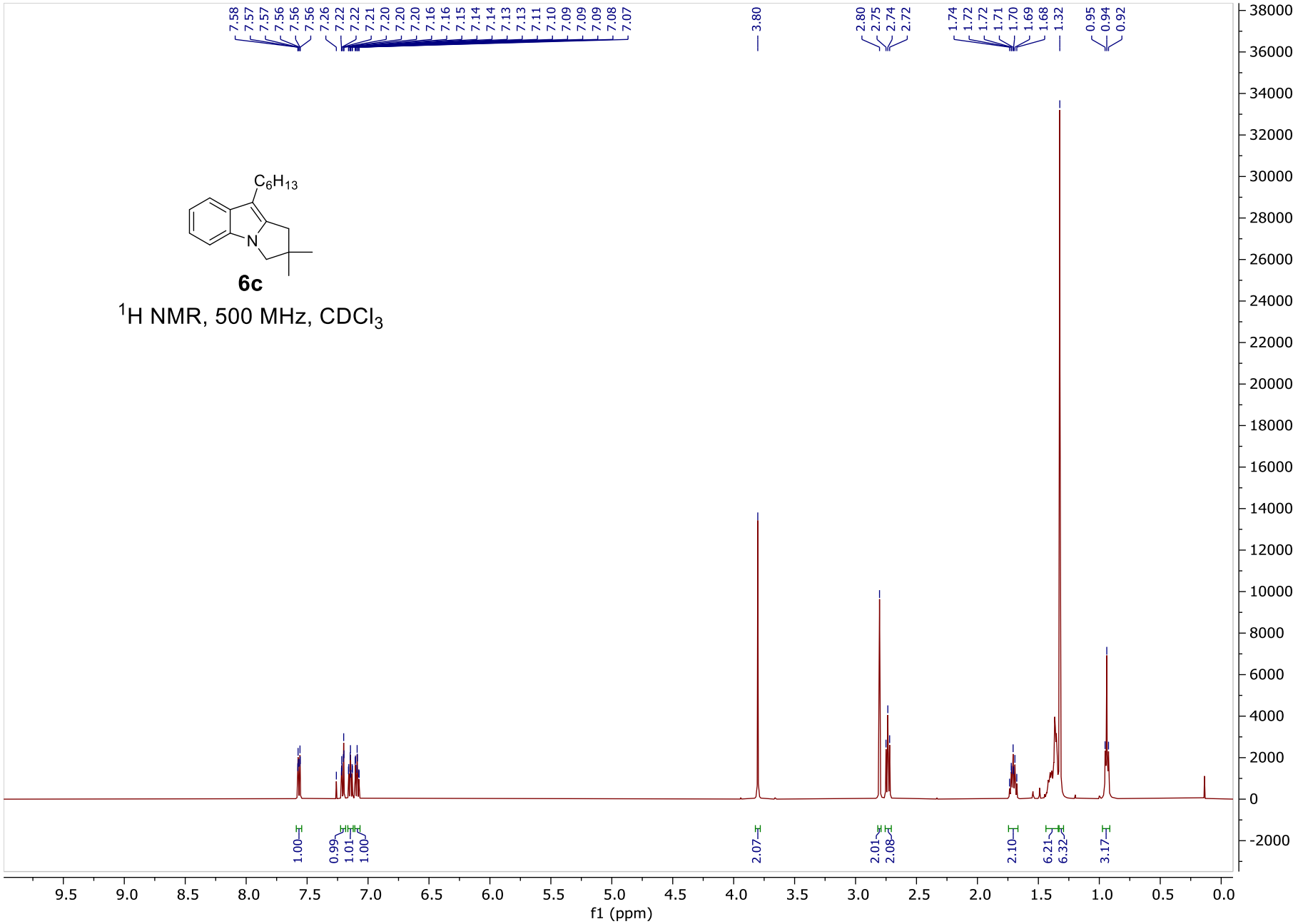
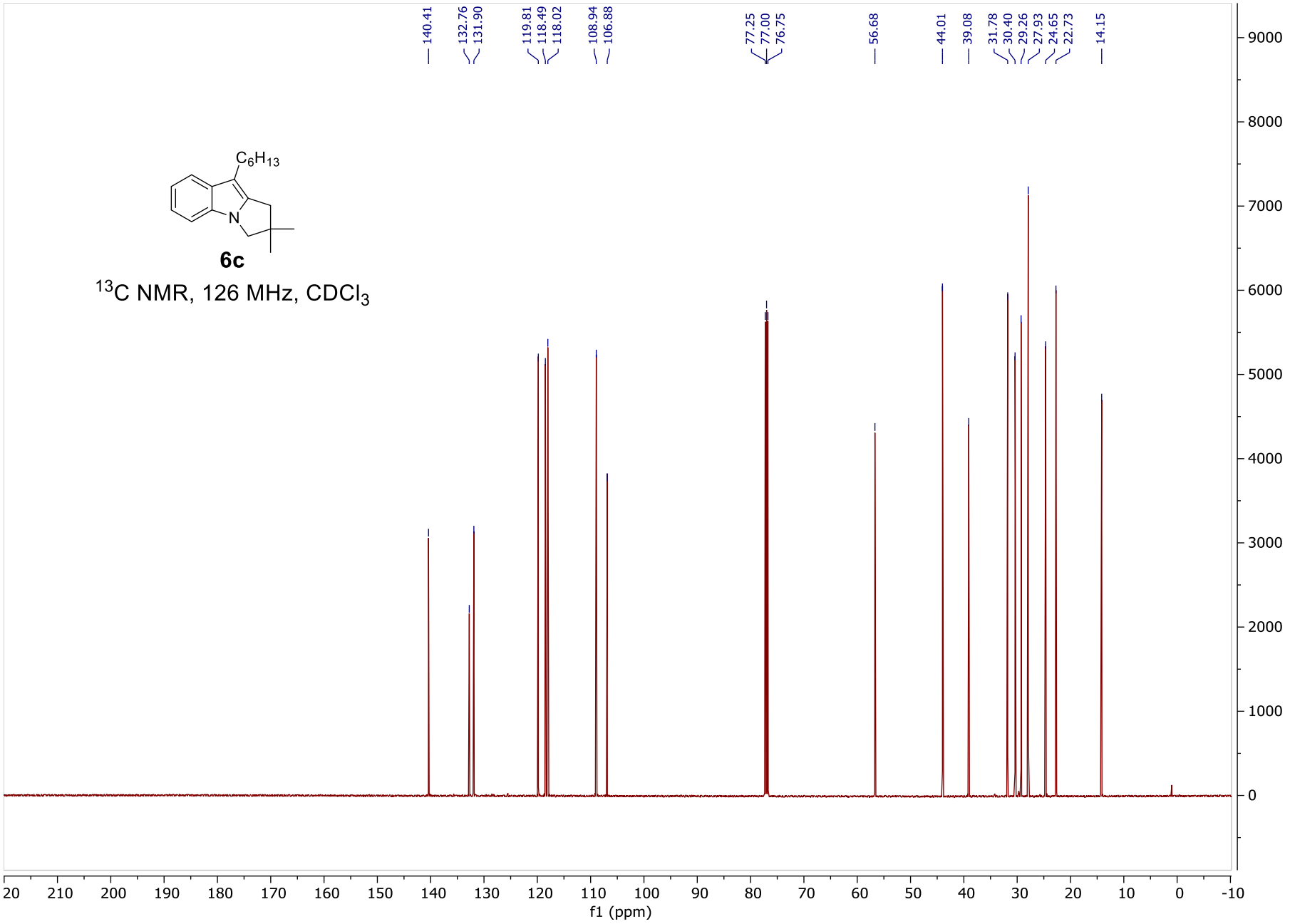
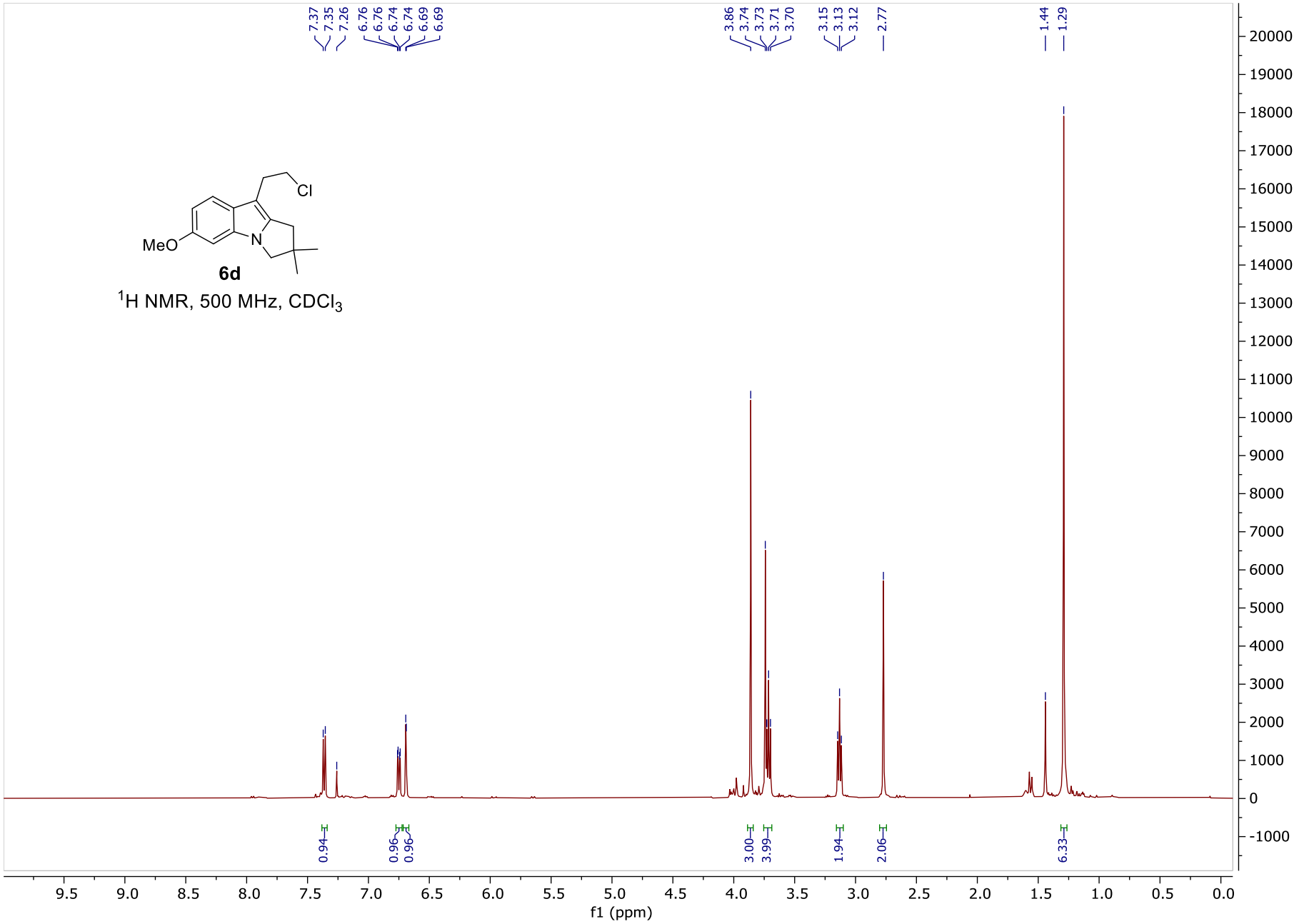
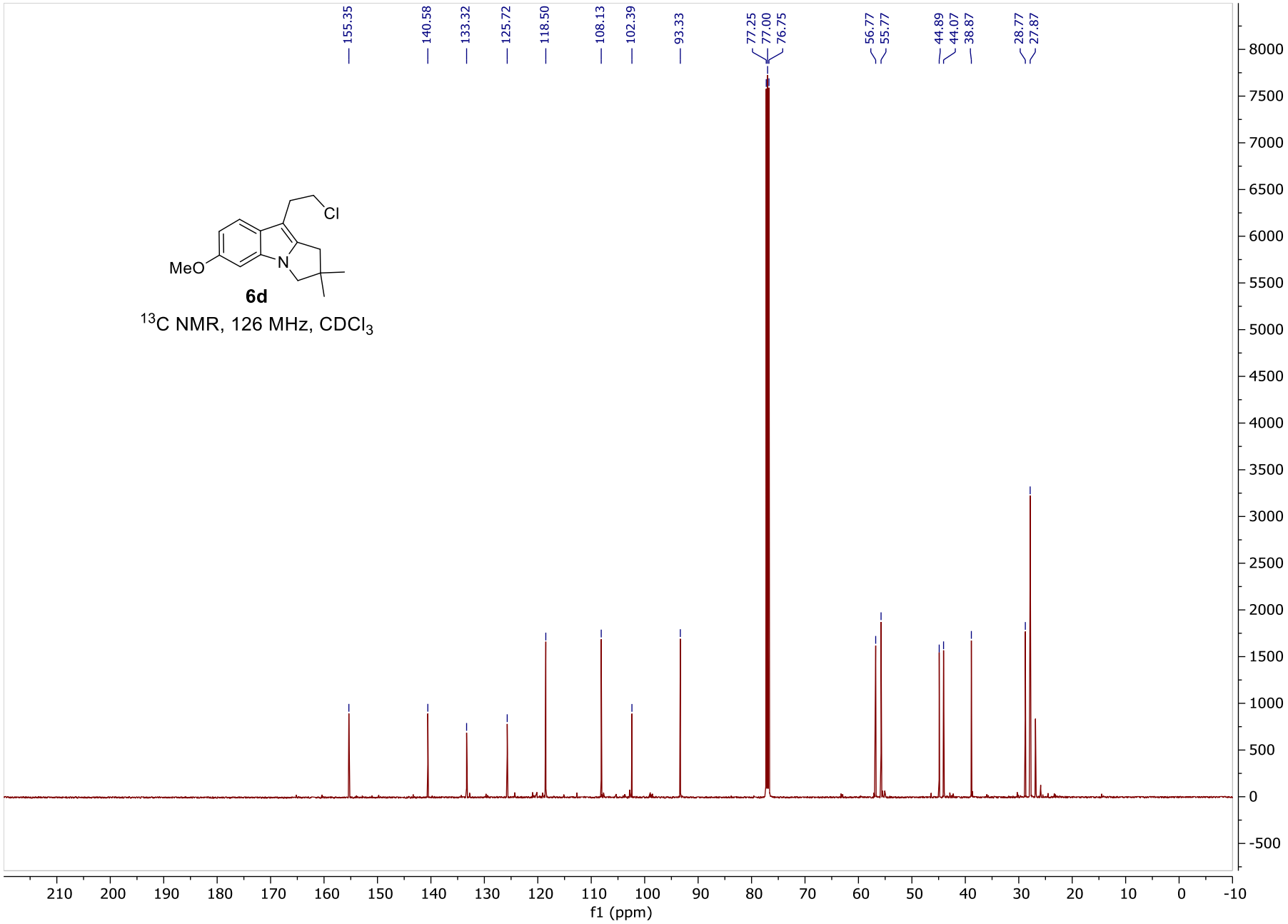
140.30
135.57
134.37
134.24
129.28
127.44
121.15
120.56
102.91
102.60
98.80
77.25
77.00
76.75
65.73
57.04
54.87
43.71
38.58
29.91
27.95
26.92
19.23
OMe
OSiPh2tBu
N
7b
13C NMR, 126 MHz, CDCl3
f1 (ppm)


7.58 7.57 7.57 7.56 7.56 7.56 7.26 7.22 7.22 7.21 7.20 7.20 7.20 7.16 7.15 7.14 7.14 7.13 7.13 7.11 7.10 7.09 7.09 7.09 7.08 7.07
3.80
2.80 2.75 2.74 2.72
1.74 1.72 1.72 1.71 1.70 1.69 1.68 1.32
0.95 0.94 0.92
C6H13
N
6c
1H NMR, 500 MHz, CDCl3
1.00 0.99 1.01 1.00 2.07 2.01 2.08 2.10 6.21 6.32 3.17
f1 (ppm)


140.41
132.76
131.90
119.81
118.49
118.02
108.94
106.88
77.25
77.00
76.75
56.68
44.01
39.08
31.78
30.40
29.26
27.93
24.65
22.73
14.15
C6H13
N
6c
13C NMR, 126 MHz, CDCl3
9000
8000
7000
6000
5000
4000
3000
2000
1000
0
20 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)


7.37
7.35
7.26
6.76
6.76
6.74
6.74
6.69
6.69
3.86
3.74
3.73
3.71
3.70
3.15
3.13
3.12
2.77
1.44
1.29
Cl
MeO
N
6d
$^1$H NMR, 500 MHz, $CDCl_3$
0.94
0.96
0.96
3.00
3.99
1.94
2.06
6.33
f1 (ppm)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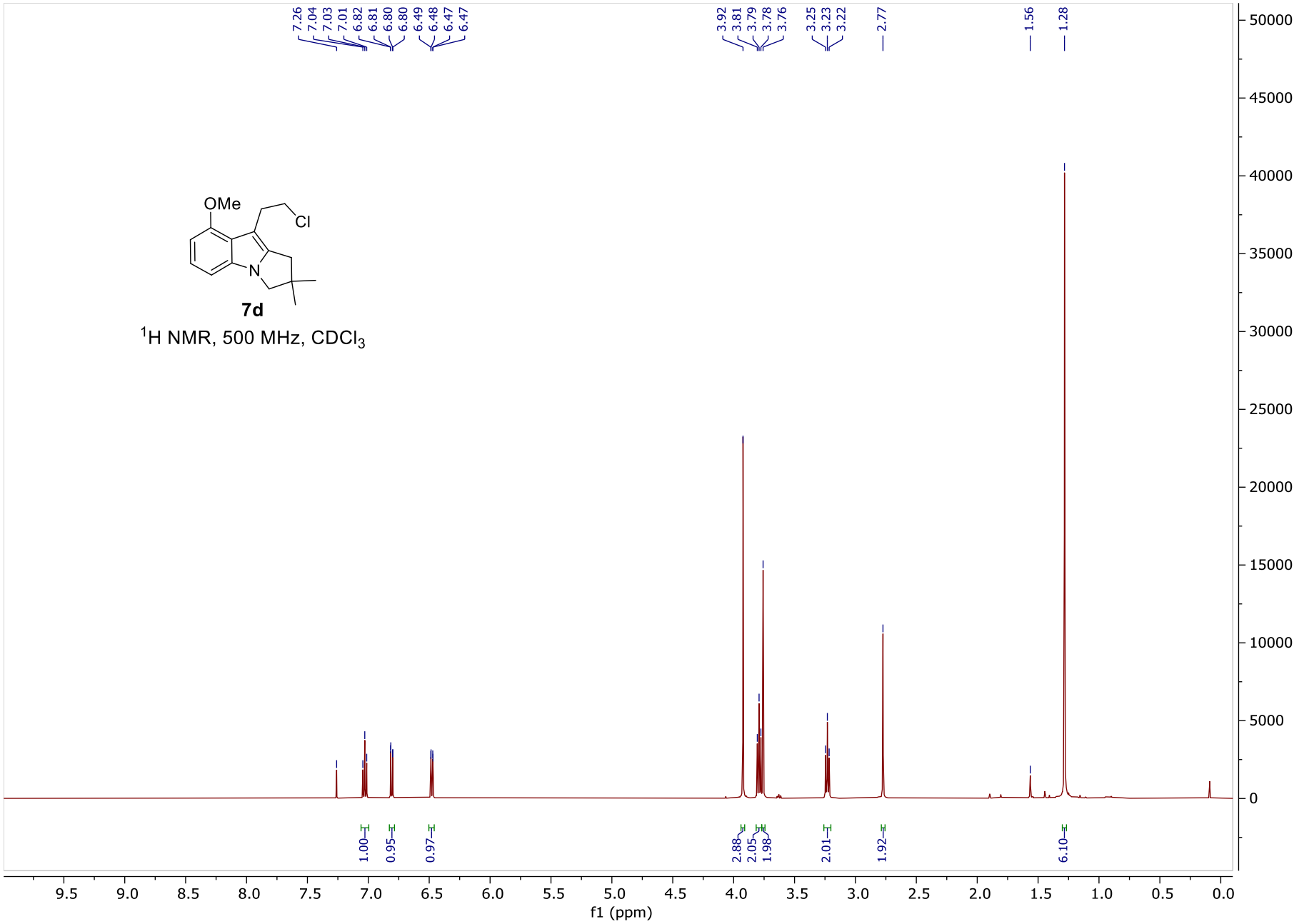
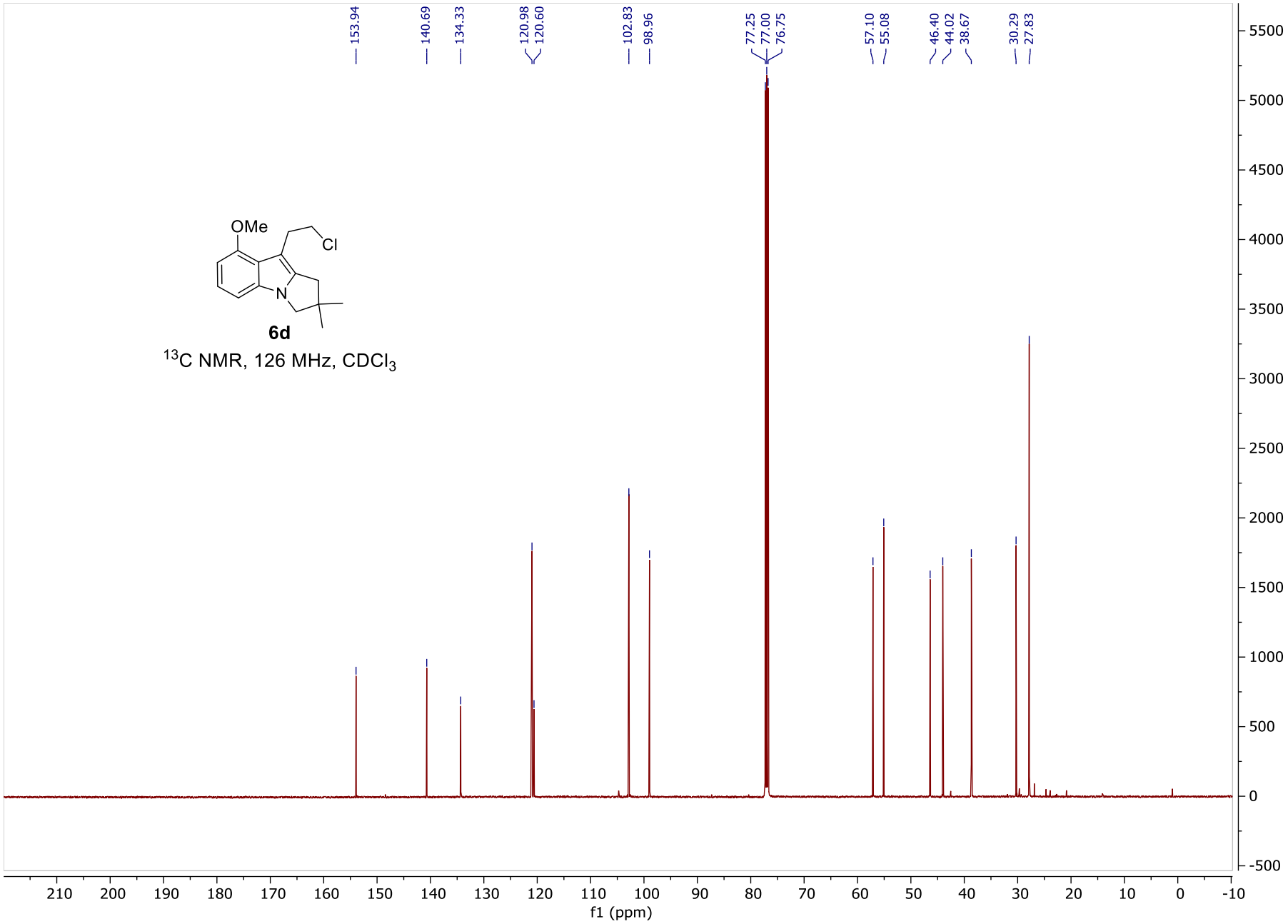
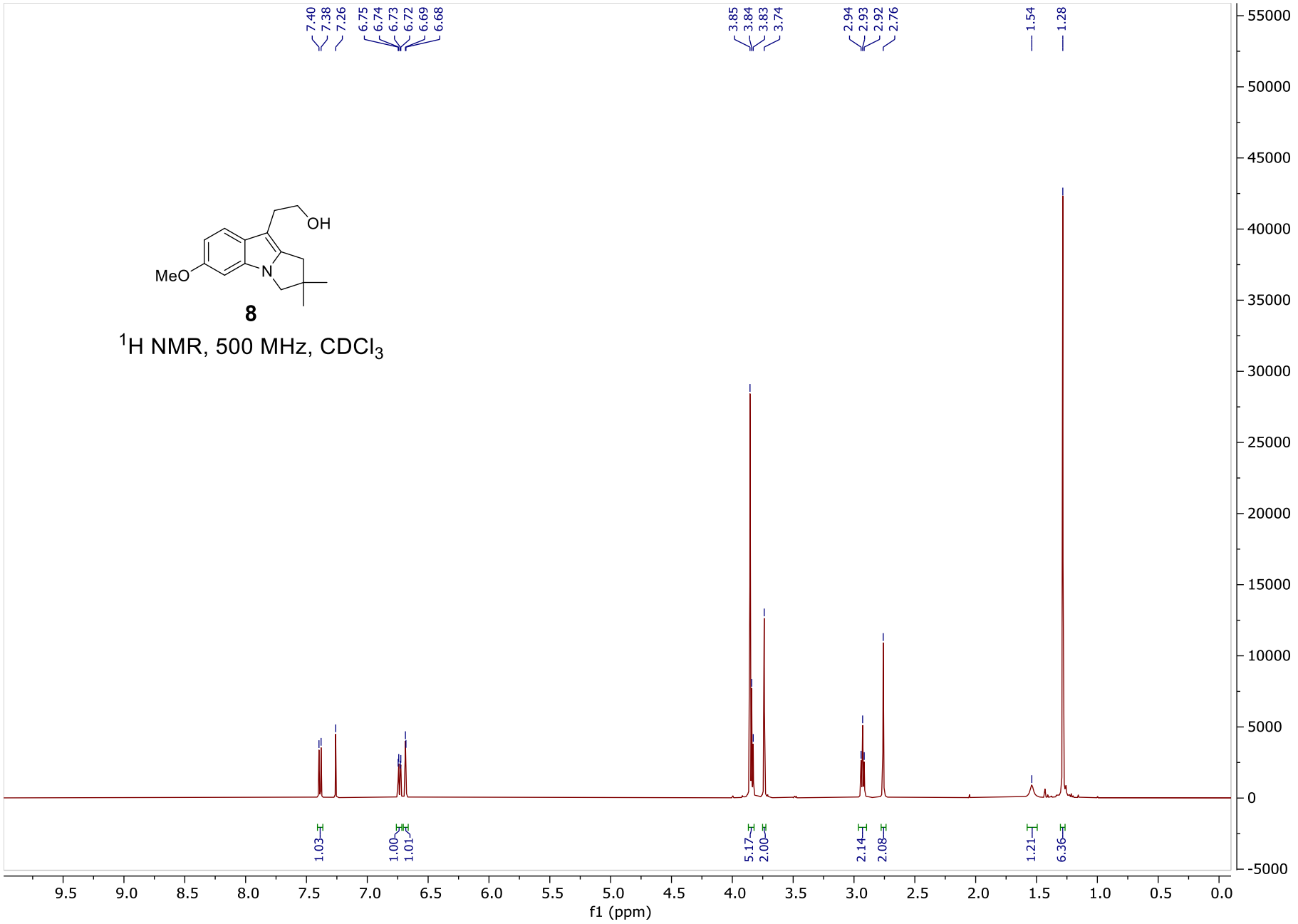
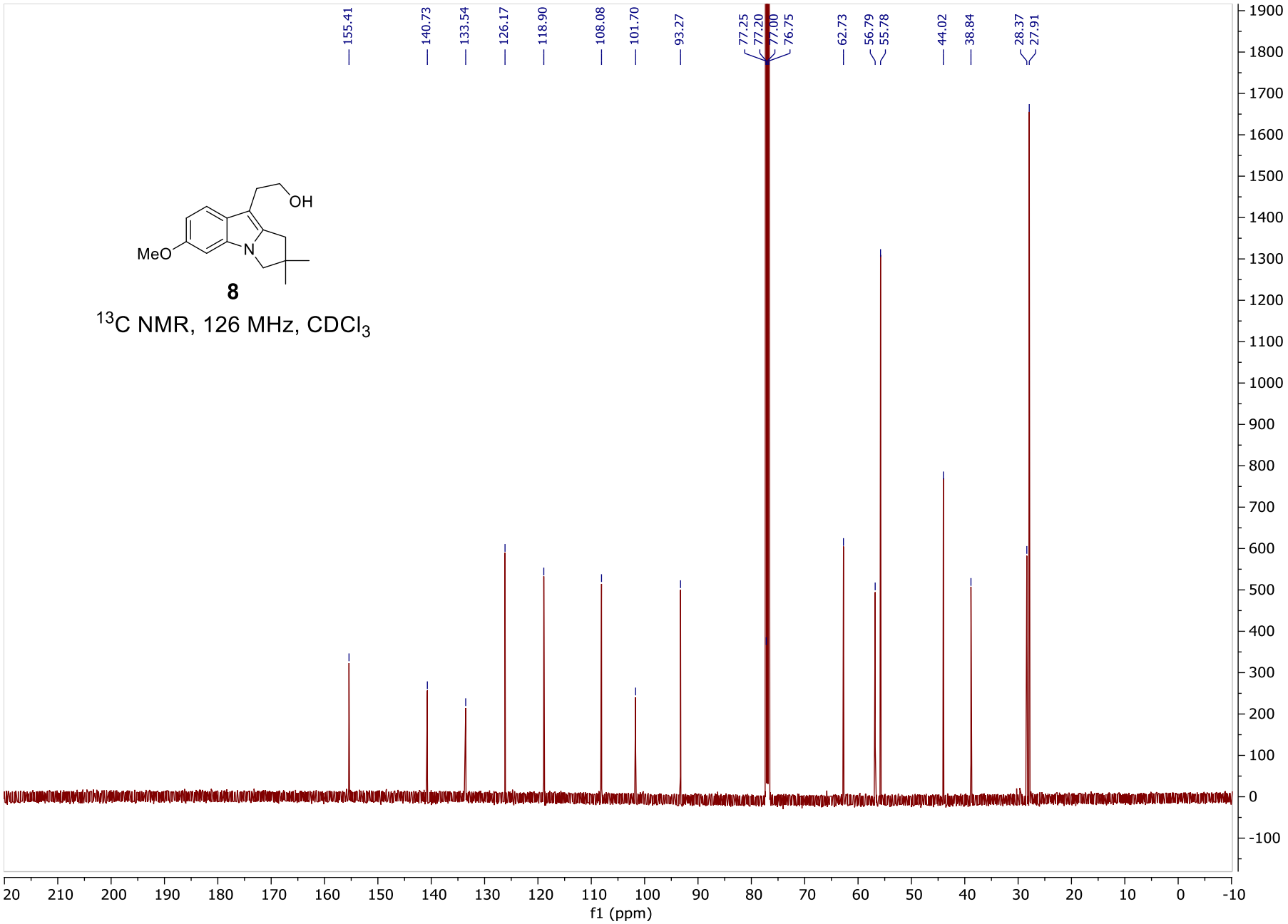
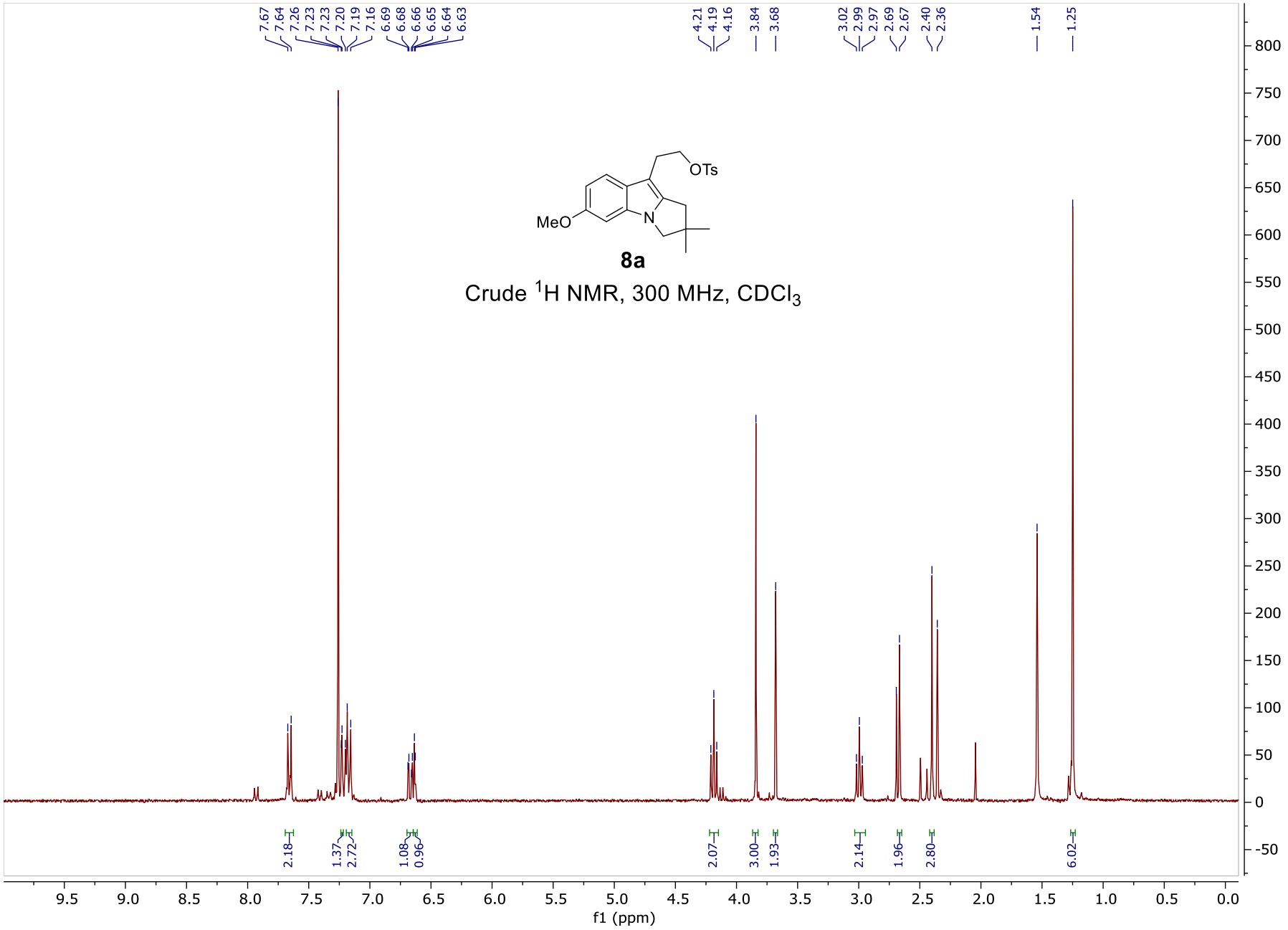
140.58
133.32
125.72
118.50
108.13
102.39
93.33
77.25
77.00
76.75
56.77
55.77
44.89
44.07
38.87
28.77
27.87
Cl
MeO
N
6d
13C NMR, 126 MHz, CDCl3
f1 (ppm)

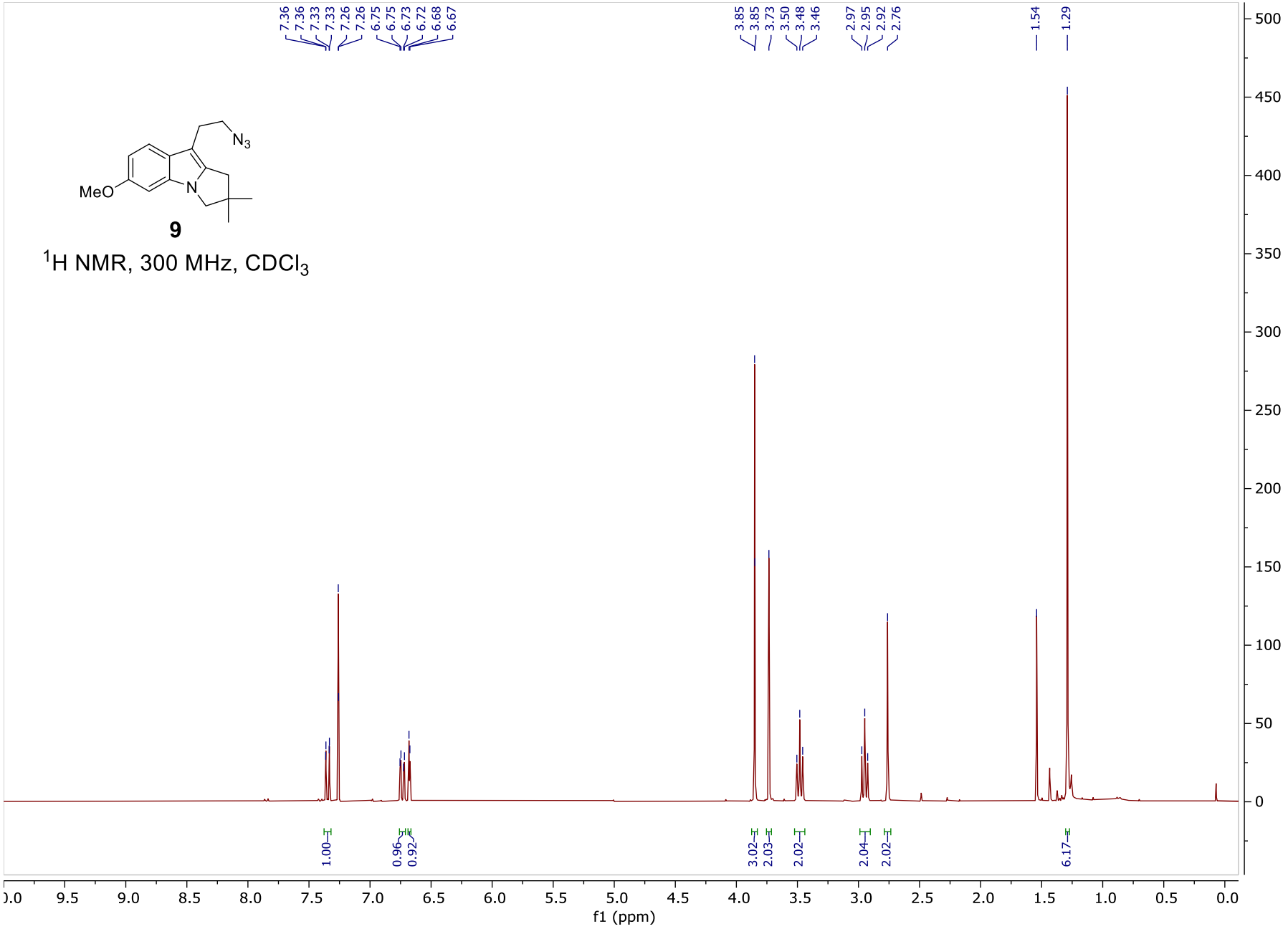

7.26
7.04
7.03
7.01
6.82
6.81
6.80
6.80
6.49
6.48
6.47
6.47
3.92
3.81
3.79
3.78
3.76
3.25
3.23
3.22
2.77
1.56
1.28
OMe
Cl
N
7d
1H NMR, 500 MHz, CDCl3
1.00
0.95
0.97
2.88
2.05
1.98
2.01
1.92
6.10
f1 (ppm)

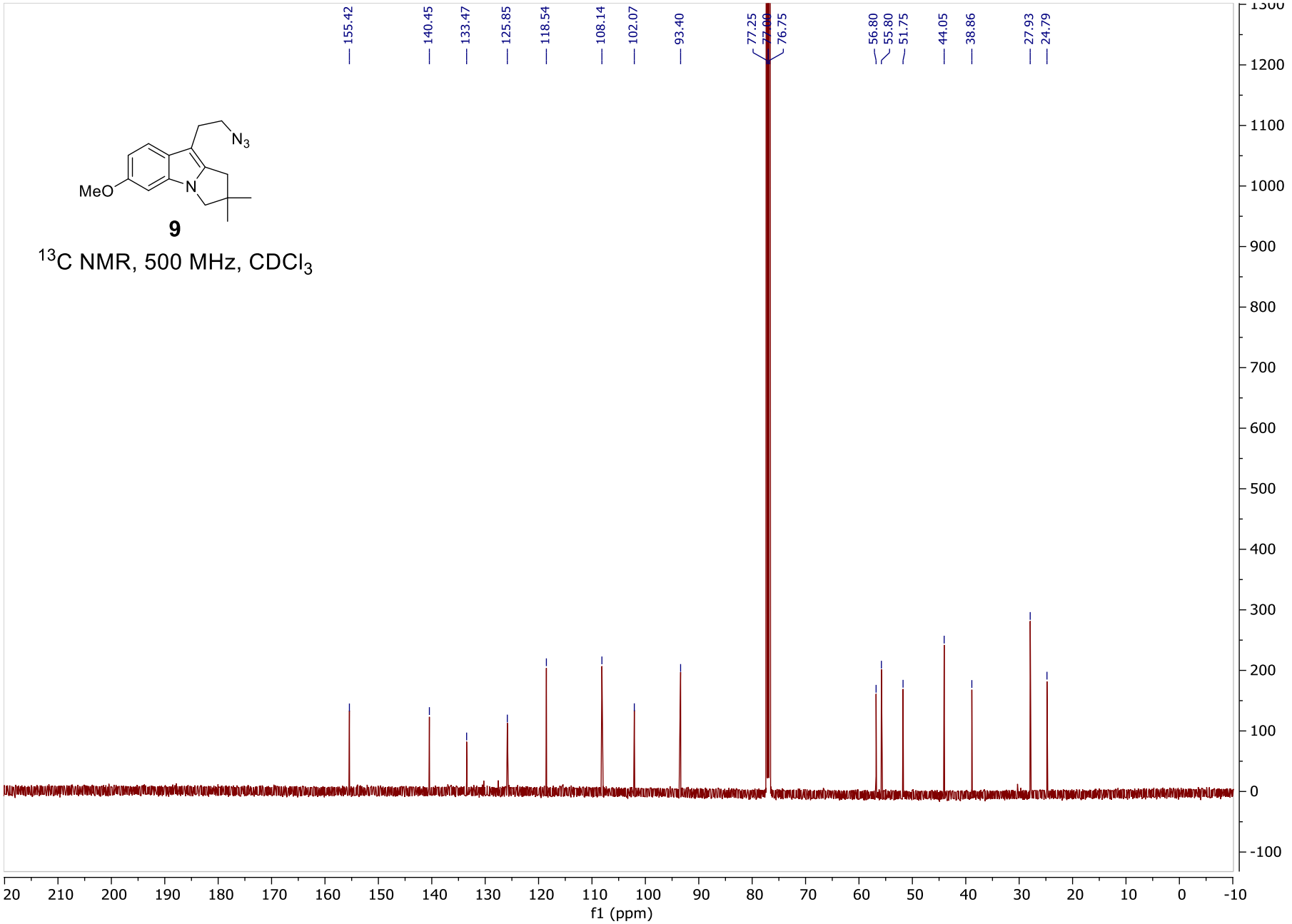

153.94
140.69
134.33
120.98
120.60
102.83
98.96
77.25
77.00
76.75
57.10
55.08
46.40
44.02
38.67
30.29
27.83
OMe
Cl
N
6d
13C NMR, 126 MHz, CDCl3
f1 (ppm)


7.40
7.38
7.26
6.75
6.74
6.73
6.72
6.69
6.68
3.85
3.84
3.83
3.74
2.94
2.93
2.92
2.76
1.54
1.28
OH
MeO
N
8
1H NMR, 500 MHz, CDCl3
1.03
1.00
1.01
5.17
2.00
2.14
2.08
1.21
6.36
f1 (ppm)


155.41
140.73
133.54
126.17
118.90
108.08
101.70
93.27
77.25
77.20
77.00
76.75
62.73
56.79
55.78
44.02
38.84
28.37
27.91
OH
MeO
N
8
13C NMR, 126 MHz, CDCl3
f1 (ppm)


7.67
7.64
7.26
7.23
7.23
7.20
7.19
7.16
6.69
6.68
6.66
6.65
6.64
6.63
4.21
4.19
4.16
3.84
3.68
3.02
2.99
2.97
2.69
2.67
2.40
2.36
1.54
1.25
OTs
MeO
N
8a
Crude $^{1}$H NMR, 300 MHz, $CDCl_3$
2.18
1.37
2.72
1.08
0.96
2.07
3.00
1.93
2.14
1.96
2.80
6.02
f1 (ppm)


7.36
7.36
7.33
7.33
7.26
7.26
6.75
6.73
6.72
6.68
6.67
3.85
3.85
3.73
3.50
3.48
3.46
2.97
2.95
2.92
2.76
1.54
1.29
N3
MeO
N
9
1H NMR, 300 MHz, CDCl3
1.00
0.96
0.92
3.02
2.03
2.02
2.04
2.02
6.17
f1 (ppm)


155.42
140.45
133.47
125.85
118.54
108.14
102.07
93.40
77.25
77.00
76.75
56.80
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27.93
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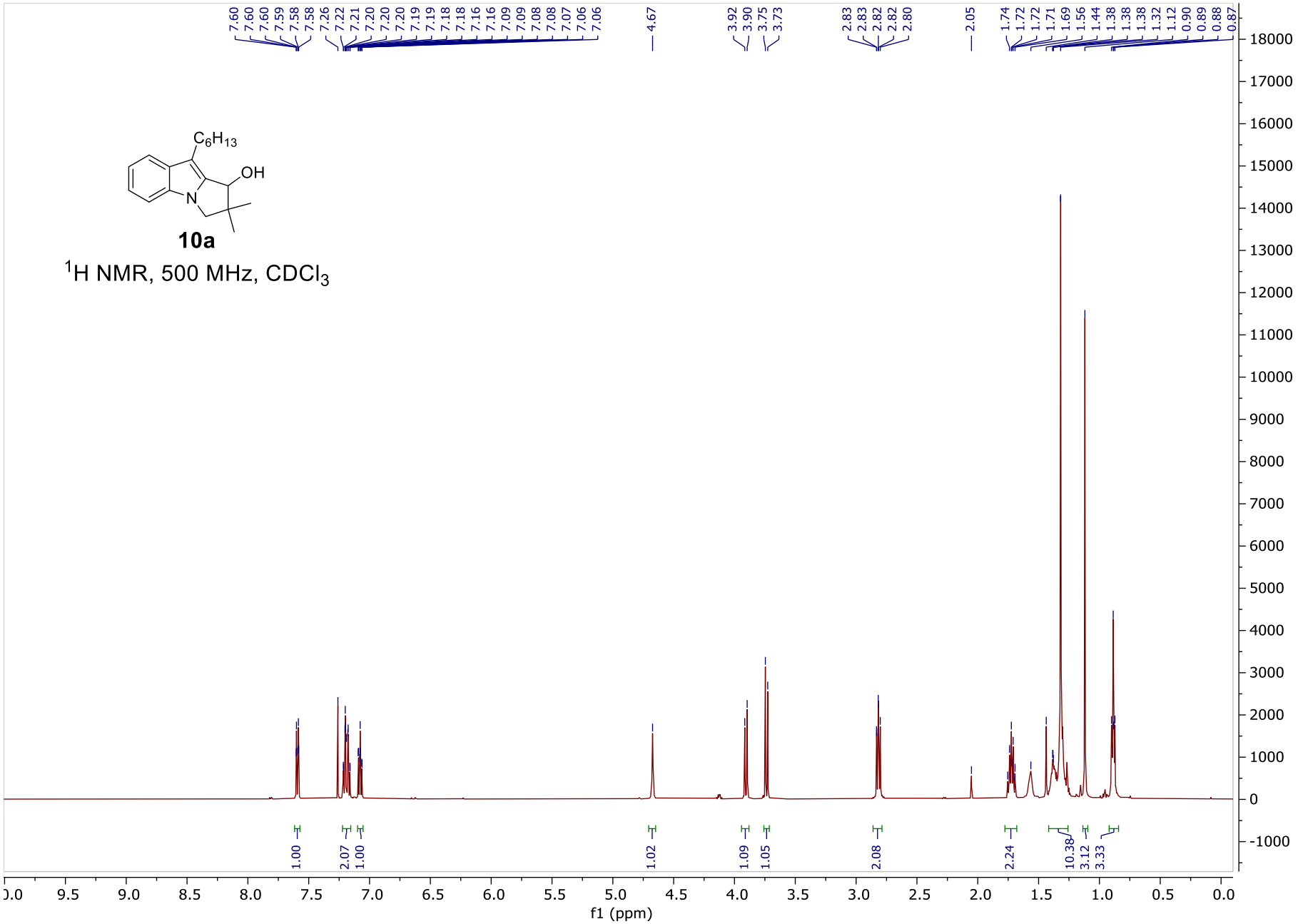
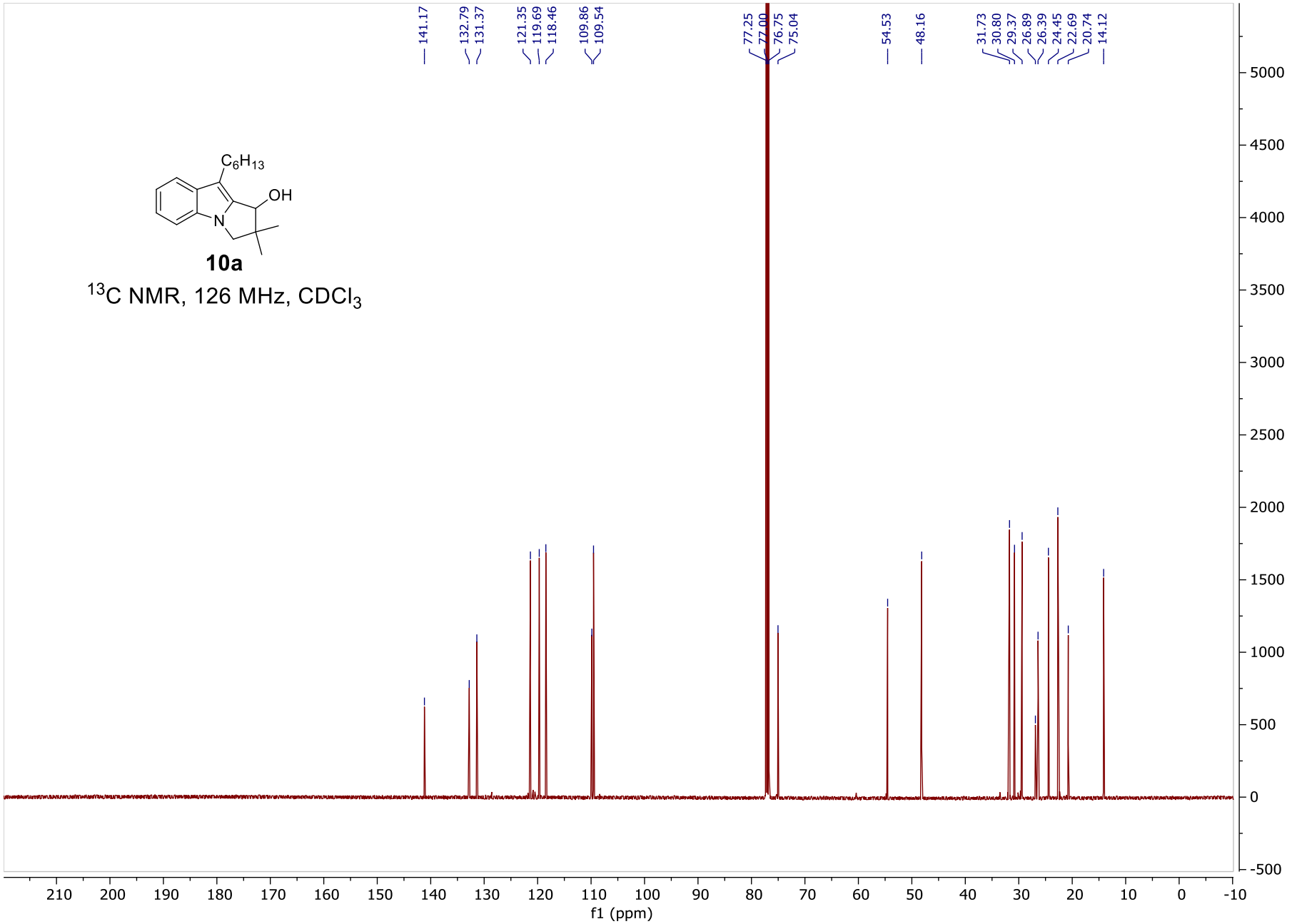
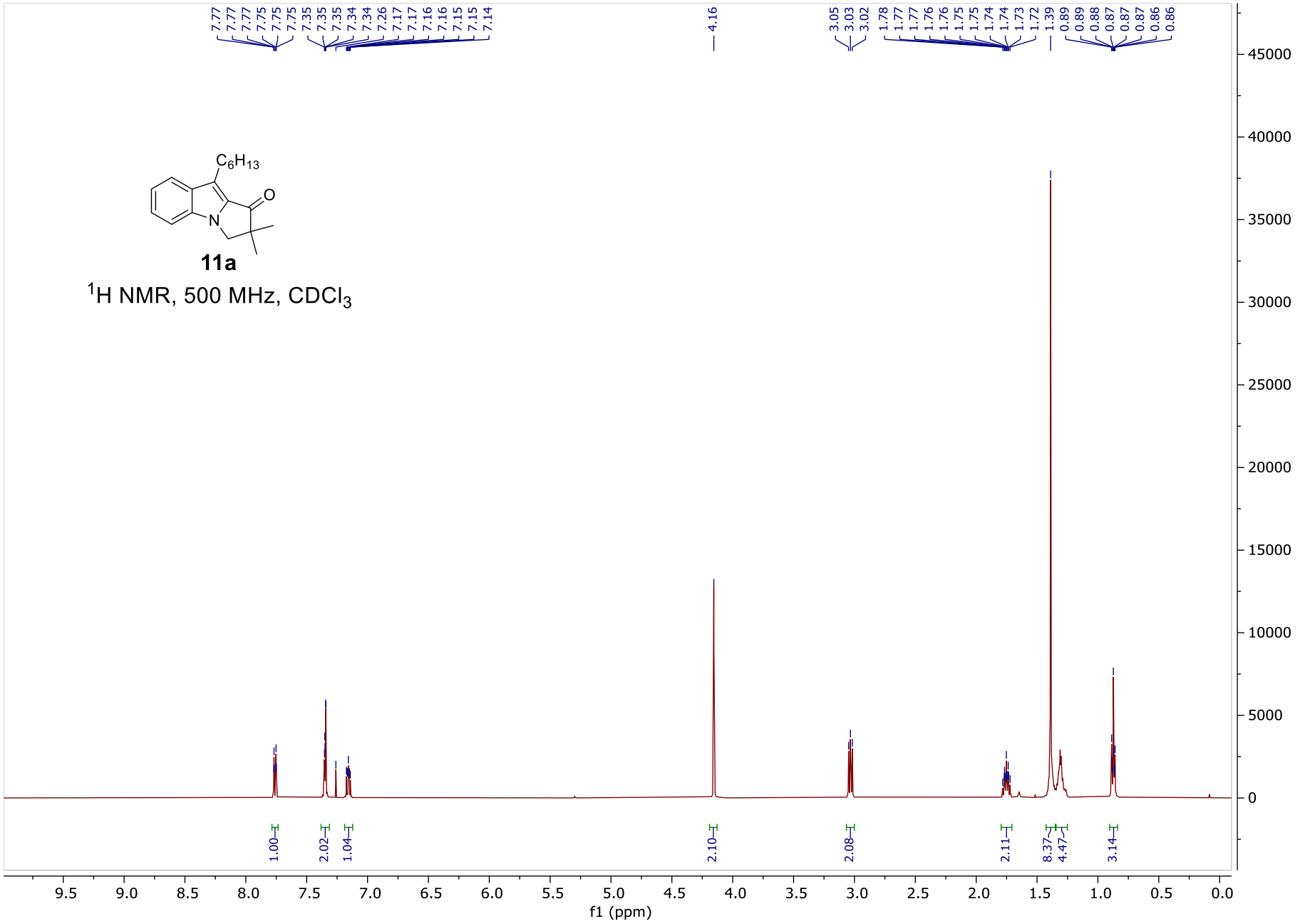
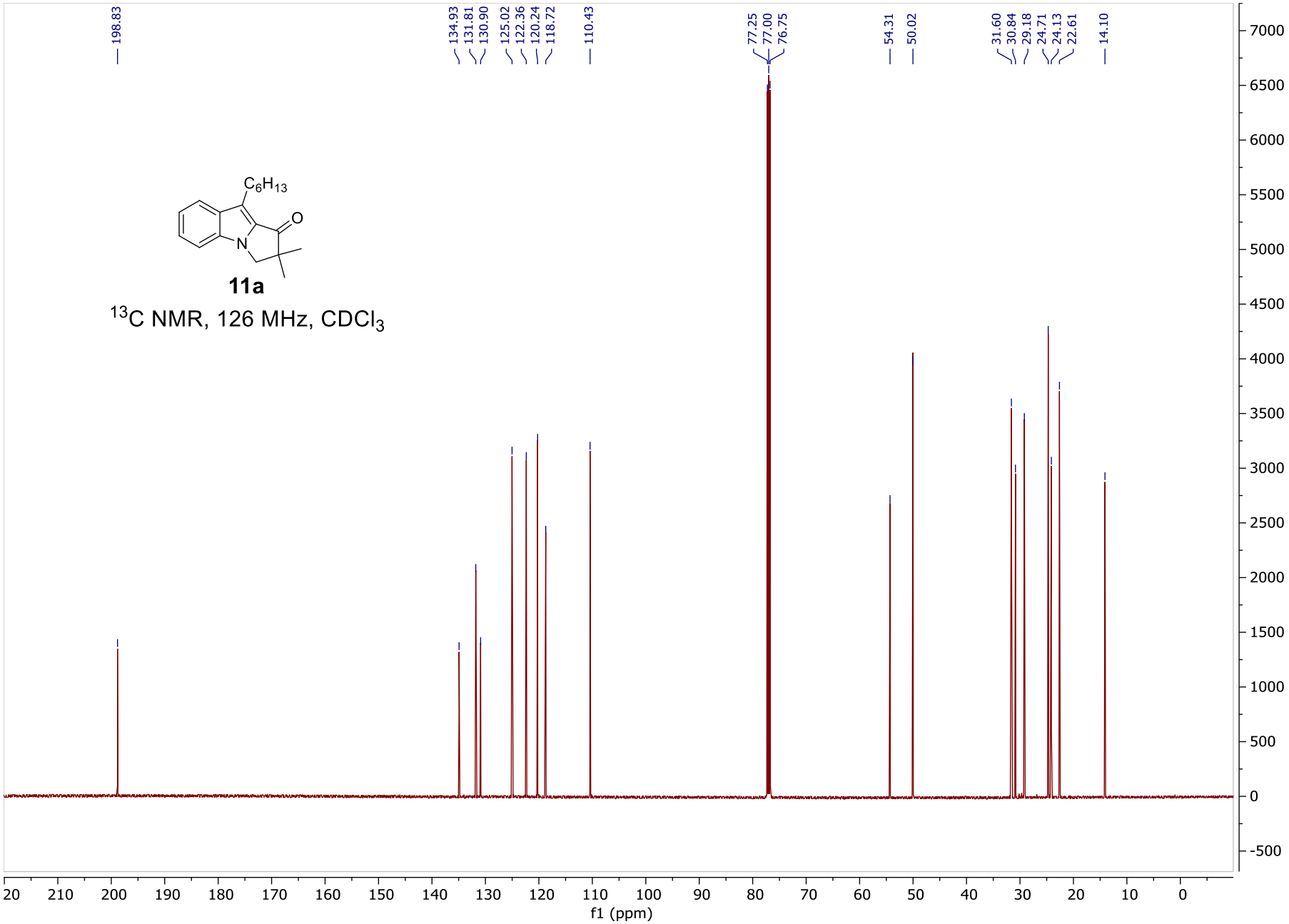
N3
MeO
N
9
13C NMR, 500 MHz, CDCl3
f1 (ppm)


C6H13
OH
N
10a
1H NMR, 500 MHz, CDCl3
f1 (ppm)


141.17
132.79
131.37
121.35
119.69
118.46
109.86
109.54
77.25
77.00
76.75
75.04
54.53
48.16
31.73
30.80
29.37
26.89
26.39
24.45
22.69
20.74
14.12
C6H13
OH
N
10a
13C NMR, 126 MHz, CDCl3
f1 (ppm)


7.77
7.77
7.77
7.75
7.75
7.75
7.35
7.35
7.35
7.34
7.34
7.26
7.17
7.17
7.16
7.16
7.15
7.15
7.14
4.16
3.05
3.03
3.02
1.78
1.77
1.77
1.76
1.76
1.75
1.75
1.74
1.74
1.73
1.72
1.39
0.89
0.89
0.88
0.87
0.87
0.87
0.86
0.86
C6H13
O
N
11a
1H NMR, 500 MHz, CDCl3
45000
40000
35000
30000
25000
20000
15000
10000
5000
0
1.00
2.02
1.04
2.10
2.08
2.11
8.37
4.47
3.14
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)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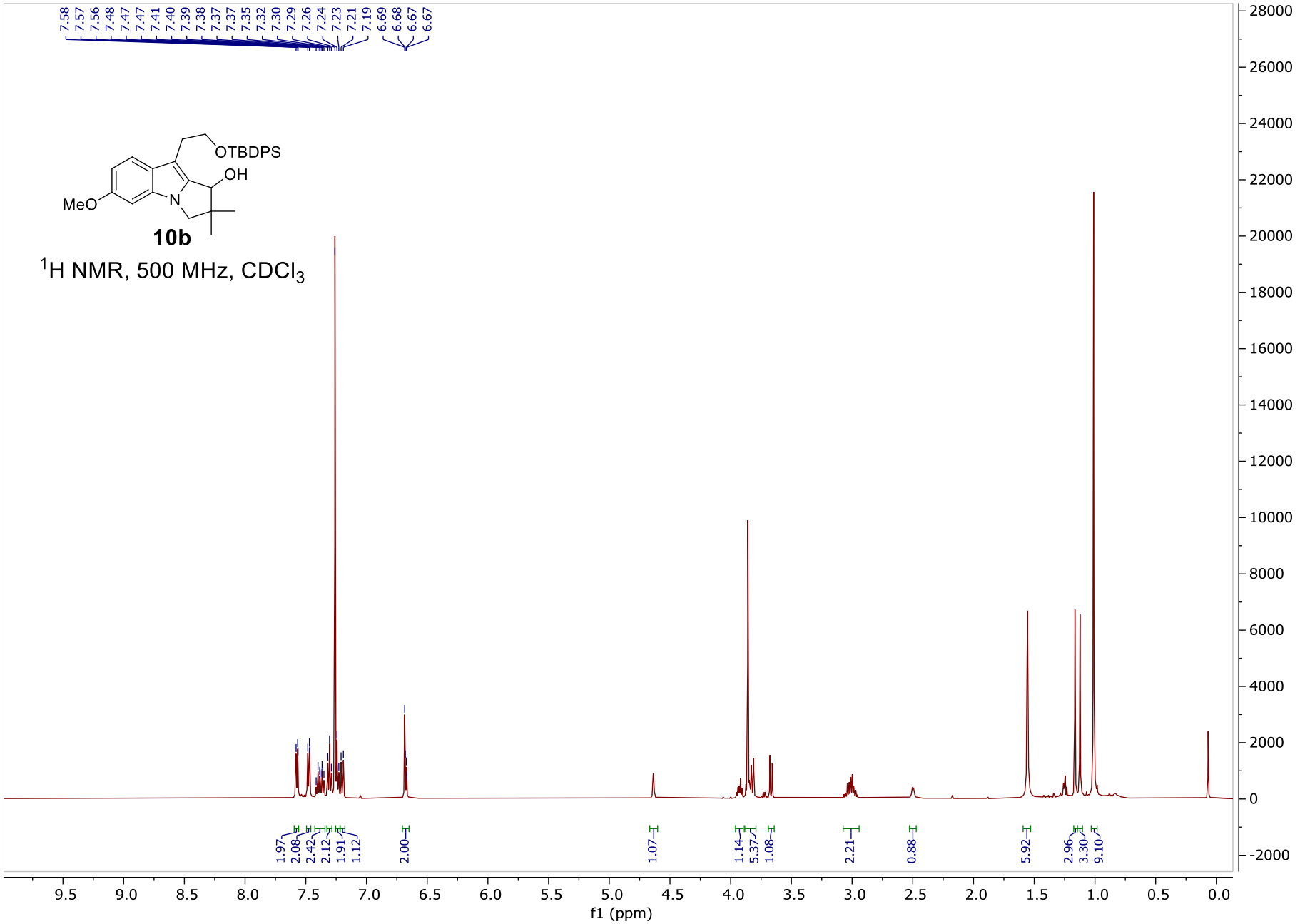
131.81
130.90
125.02
122.36
120.24
118.72
110.43
77.25
77.00
76.75
54.31
50.02
31.60
30.84
29.18
24.71
24.13
22.61
14.10
C6H13
O
N
11a
13C NMR, 126 MHz, CDCl3
f1 (ppm)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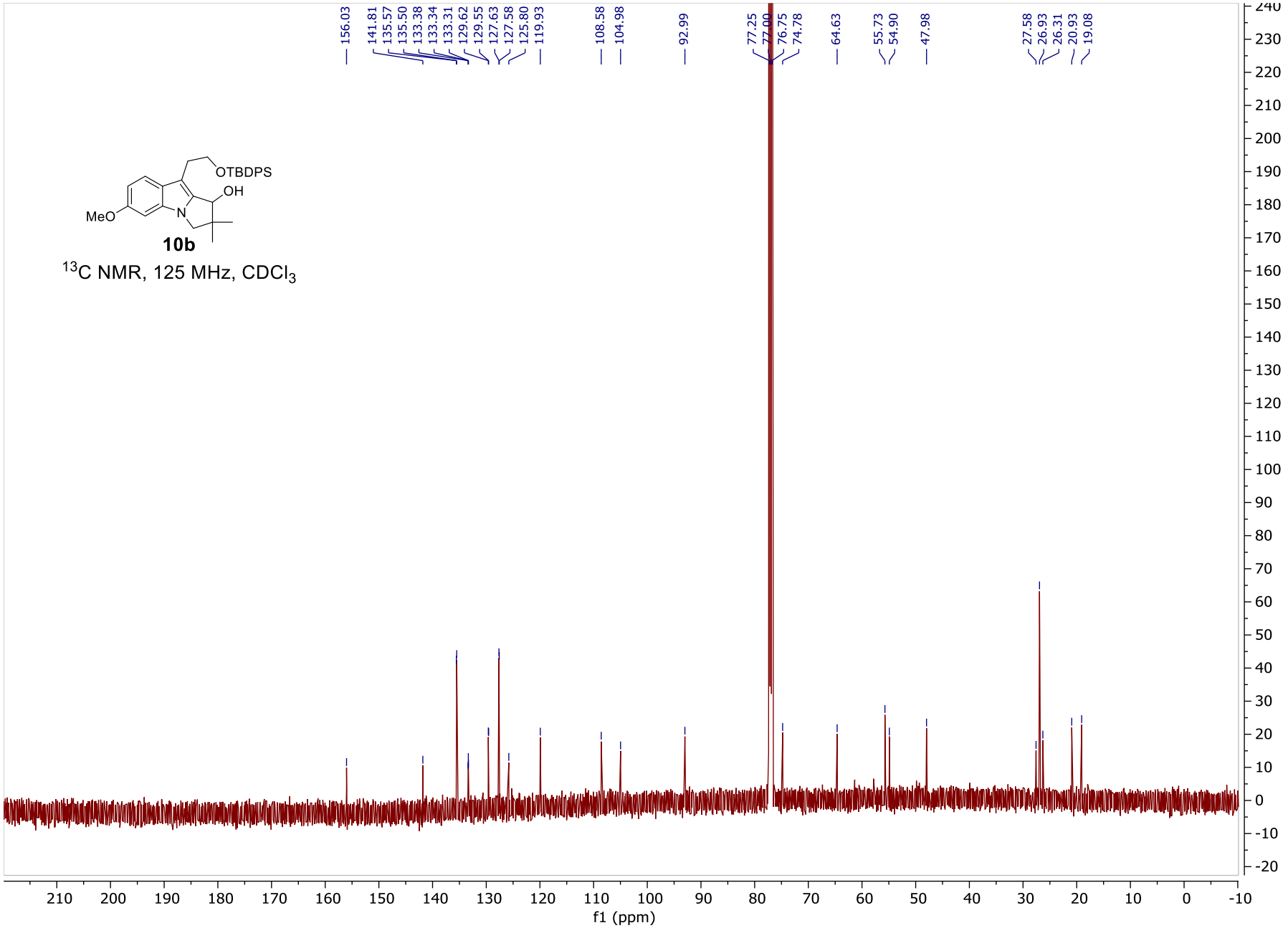
7.57
7.56
7.48
7.47
7.47
7.41
7.40
7.39
7.38
7.37
7.37
7.35
7.32
7.30
7.29
7.26
7.24
7.23
7.21
7.19
6.69
6.68
6.67
6.67
OTBDPS
OH
MeO
N
10b
1H NMR, 500 MHz, CDCl3
28000
26000
24000
22000
20000
18000
16000
14000
12000
10000
8000
6000
4000
2000
0
-2000
1.97
2.08
2.42
2.12
1.91
1.12
2.00
1.07
1.14
5.37
1.08
2.21
0.88
5.92
2.96
3.30
9.10
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)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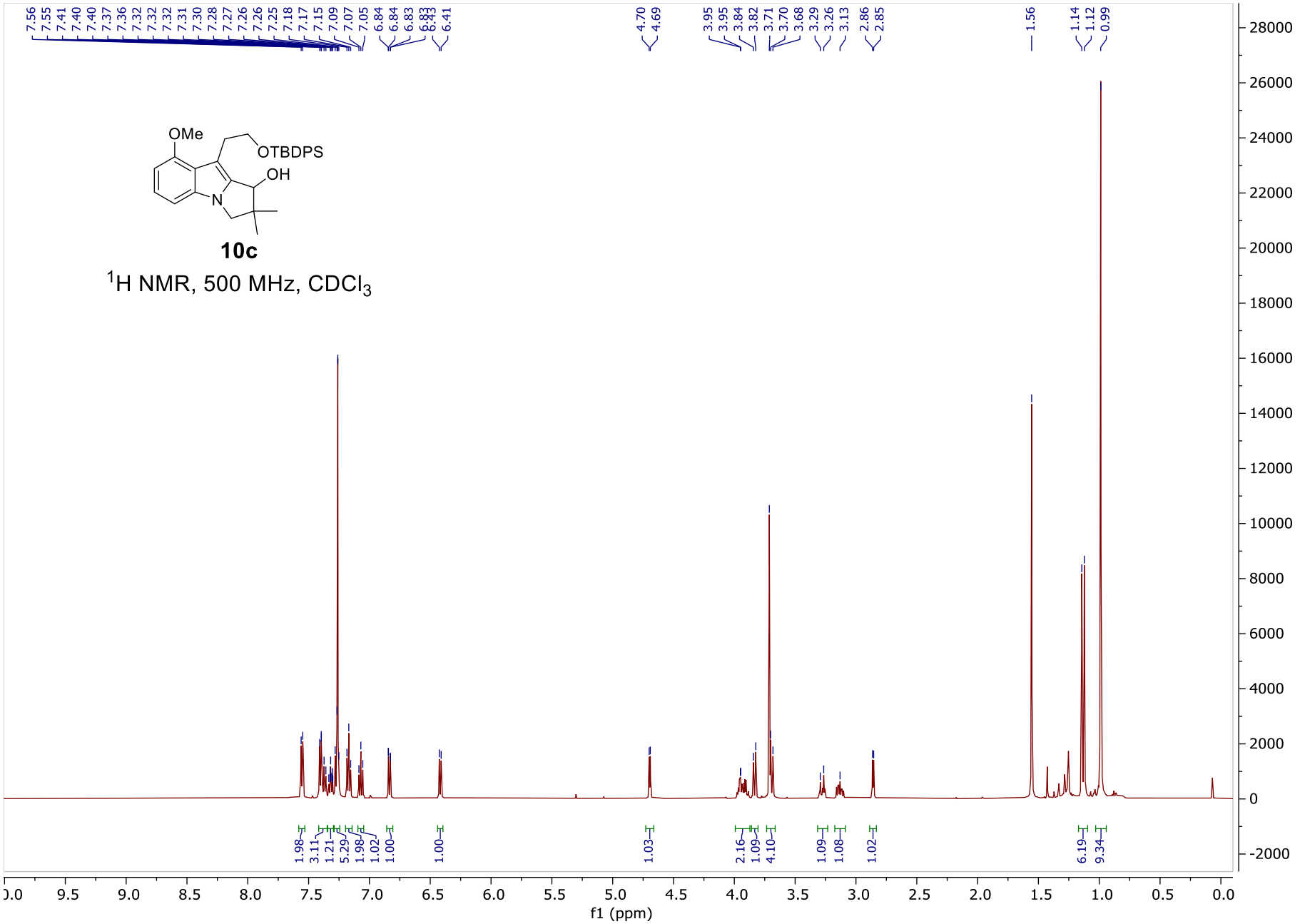
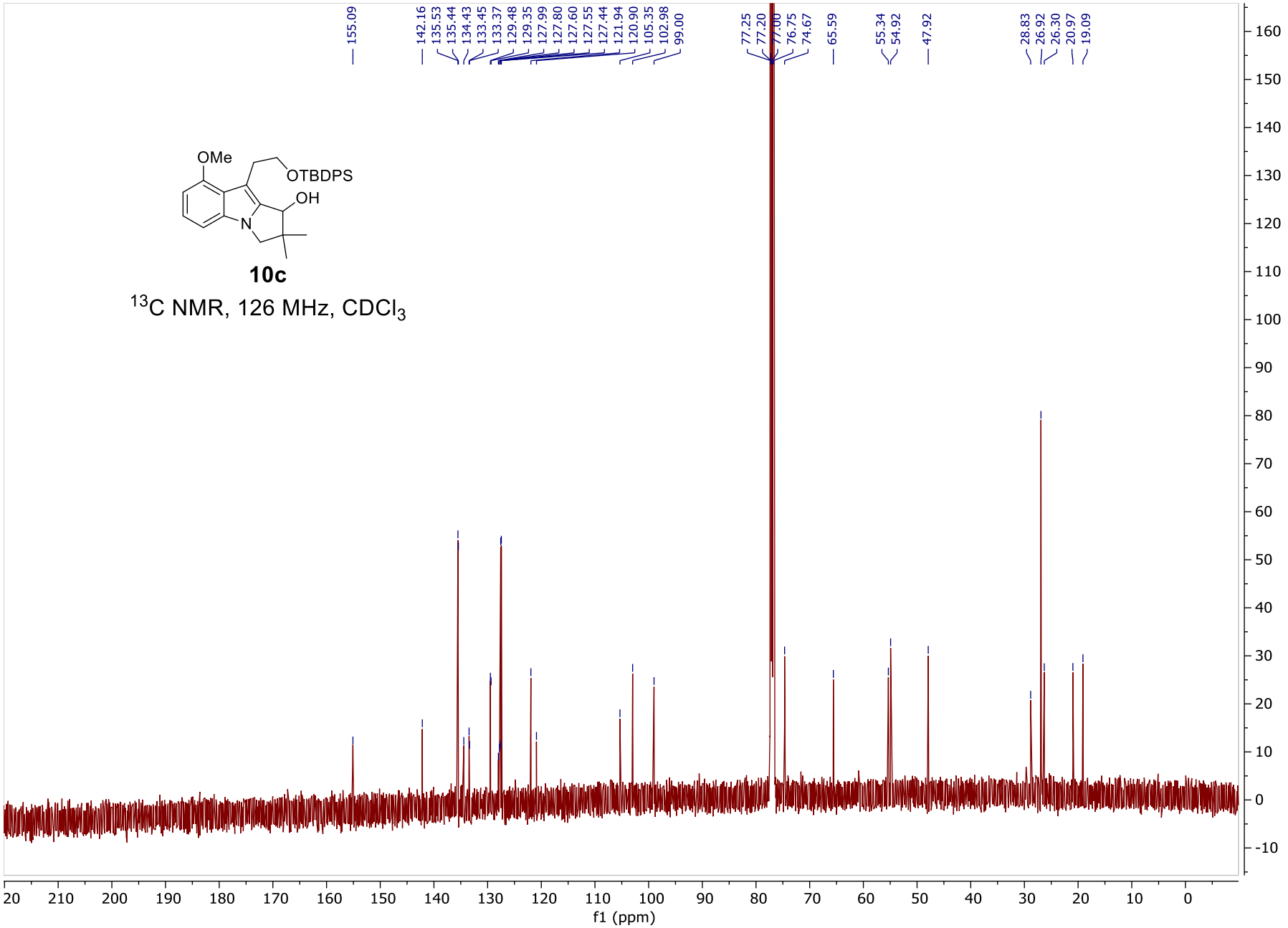
135.57
135.50
133.38
133.34
133.31
129.62
129.55
127.63
127.58
125.80
119.93
108.58
104.98
92.99
77.25
77.00
76.75
74.78
64.63
55.73
54.90
47.98
27.58
26.93
26.31
20.93
19.08
OTBDPS
OH
MeO
N
10b
13C NMR, 125 MHz, CDCl3
f1 (ppm)


OMe
OTBDPS
OH
N
10c
1H NMR, 500 MHz, CDCl3
f1 (ppm)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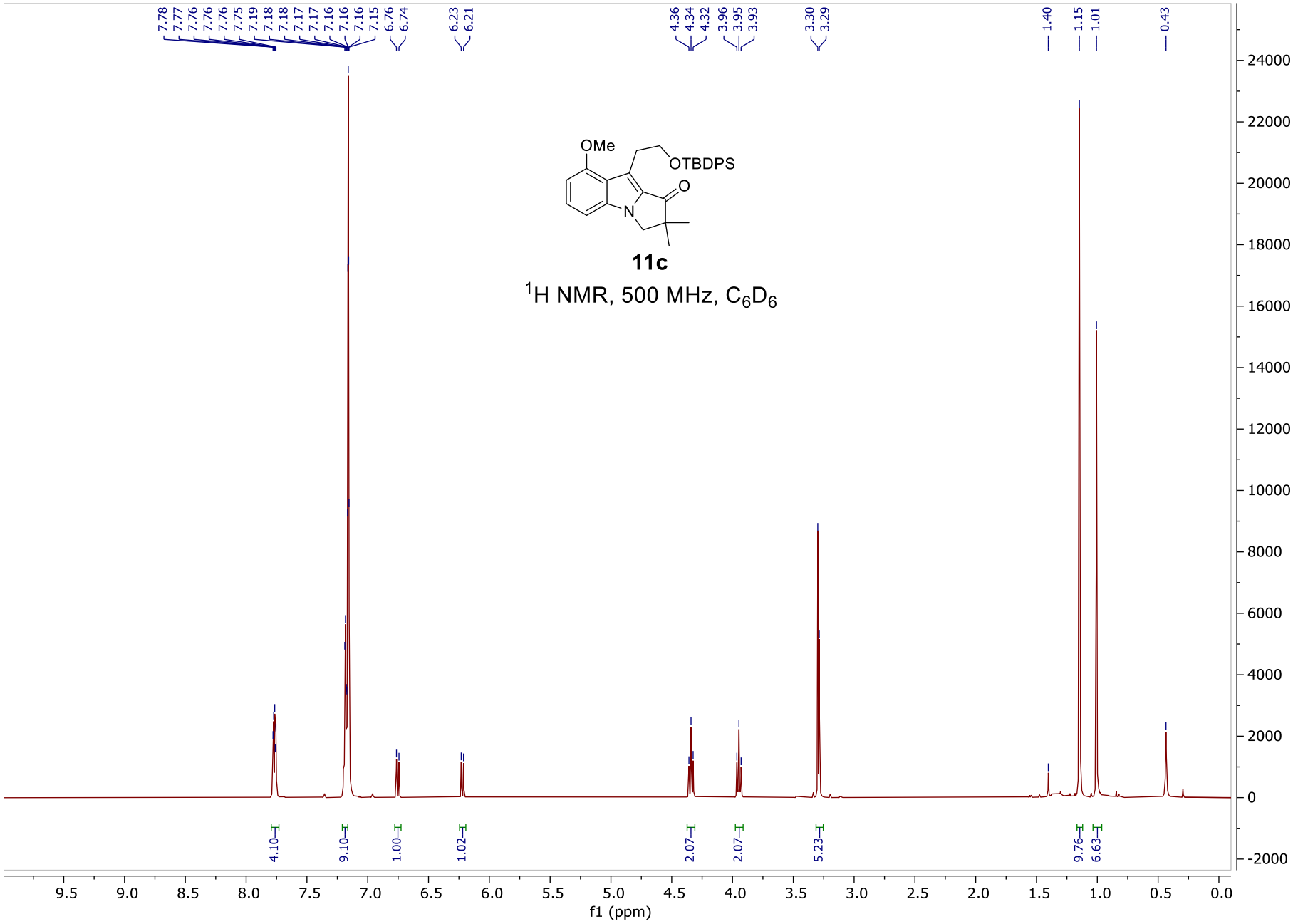
135.44
134.43
133.45
133.37
129.48
129.35
127.99
127.80
127.60
127.55
127.44
121.94
120.90
105.35
102.98
99.00
77.25
77.20
77.00
76.75
74.67
65.59
55.34
54.92
47.92
28.83
26.92
26.30
20.97
19.09
OMe
OTBDPS
OH
N
10c
13C NMR, 126 MHz, CDCl3
f1 (ppm)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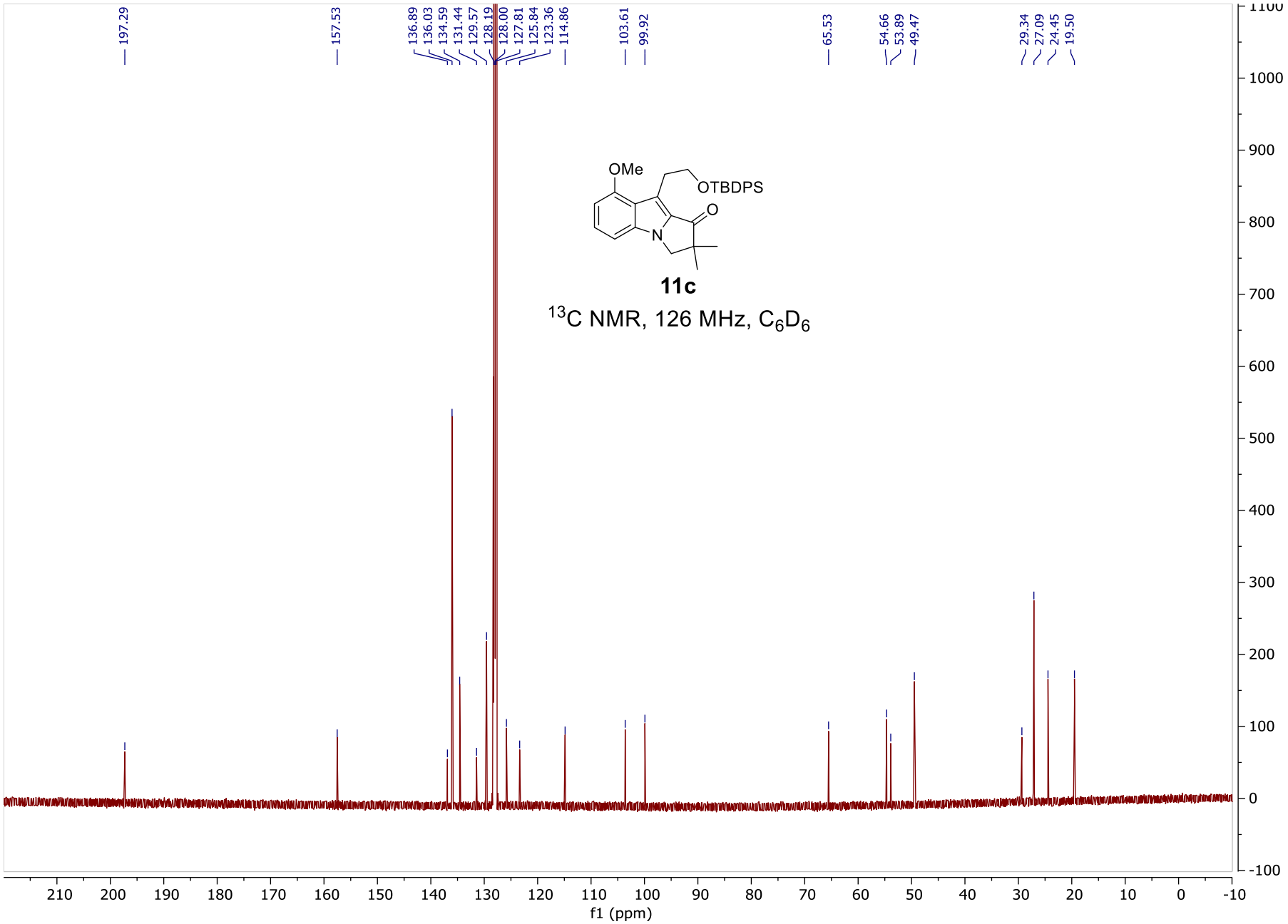
7.76
7.76
7.75
7.19
7.18
7.18
7.17
7.17
7.16
7.16
7.16
7.15
6.76
6.74
6.23
6.21
4.36
4.34
4.32
3.96
3.95
3.93
3.30
3.29
1.40
1.15
1.01
0.43
OMe
OTBDPS
O
N
11c
1H NMR, 500 MHz, C6D6
4.10
9.10
1.00
1.02
2.07
2.07
5.23
9.76
6.63
f1 (ppm)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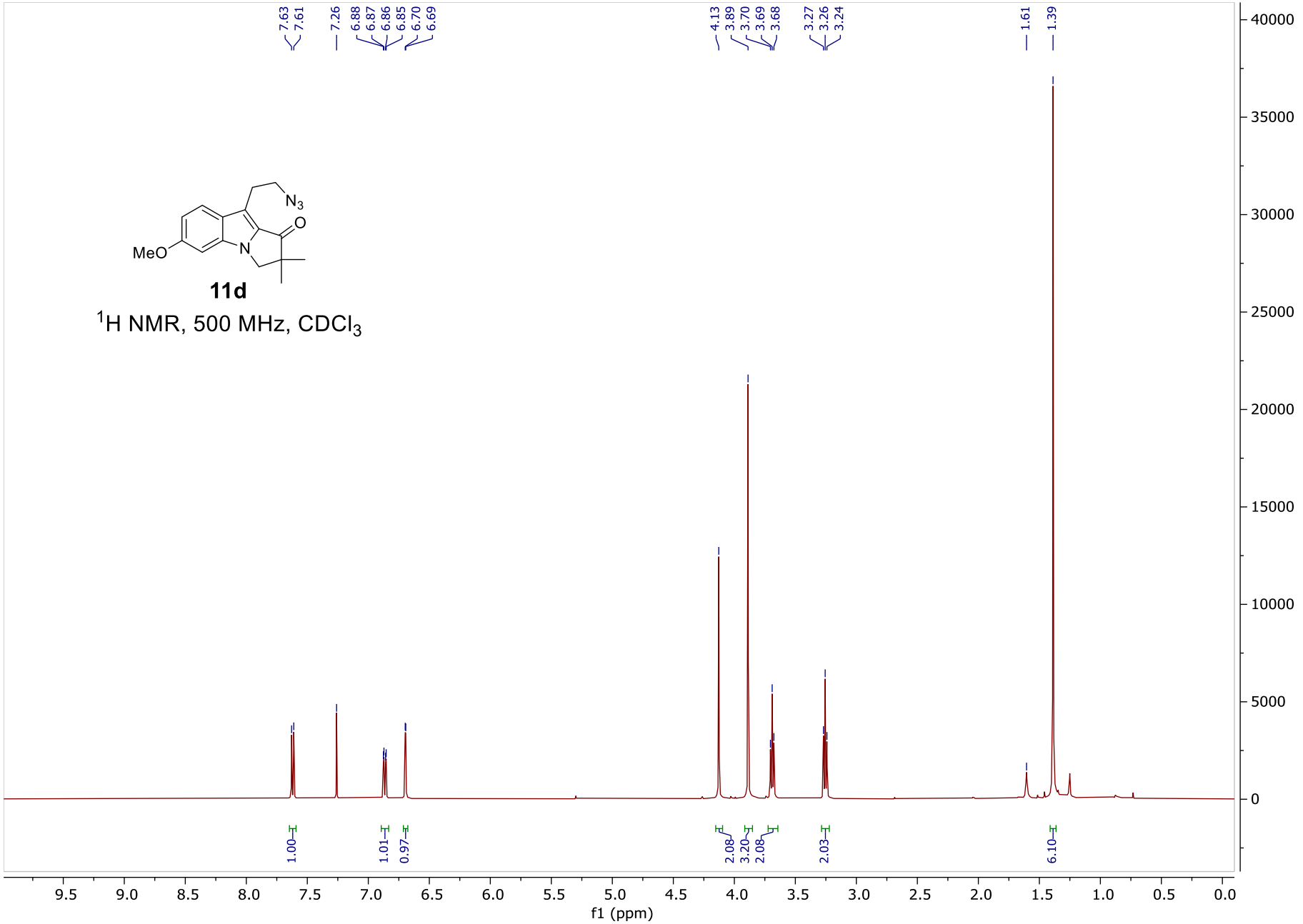
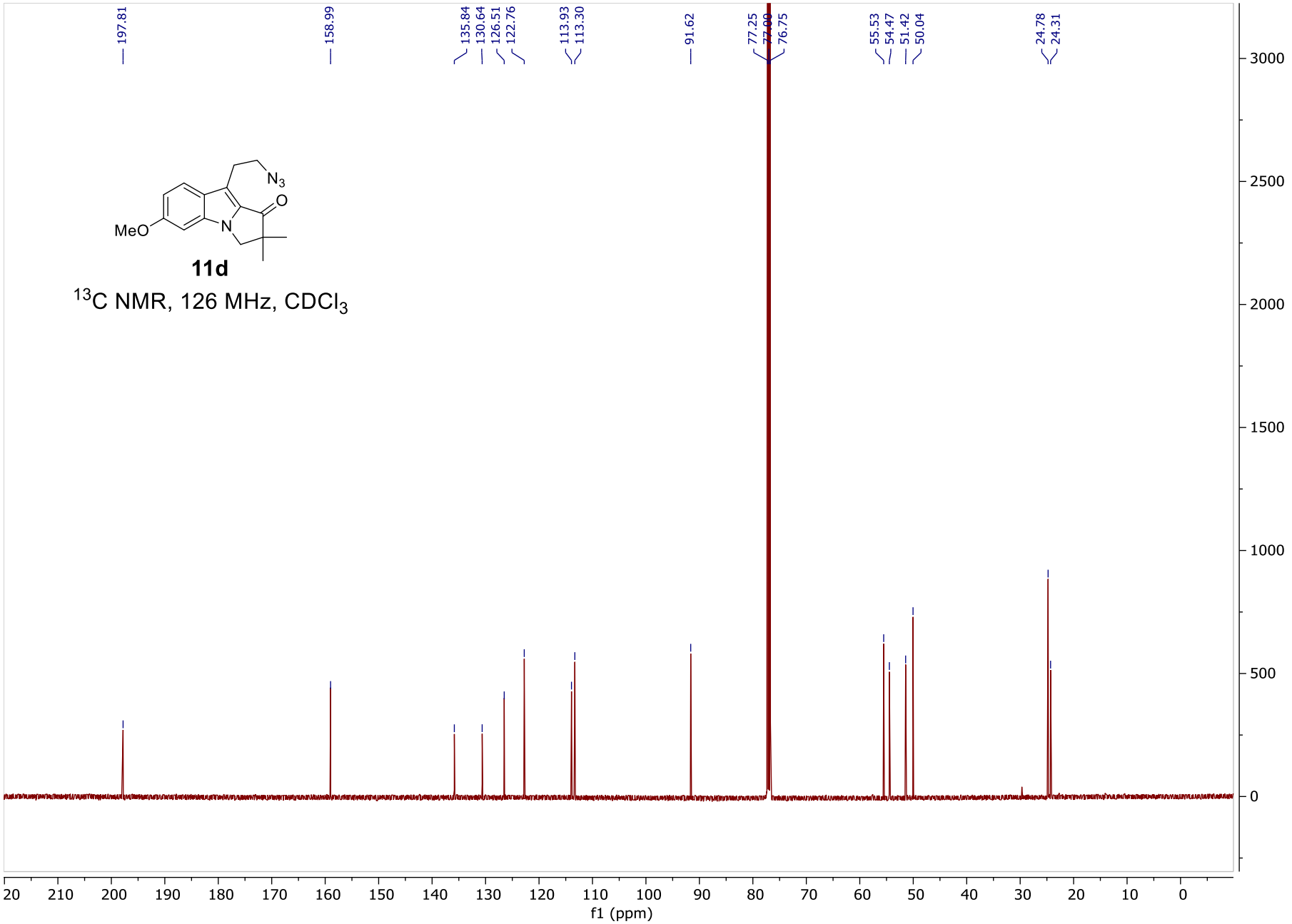
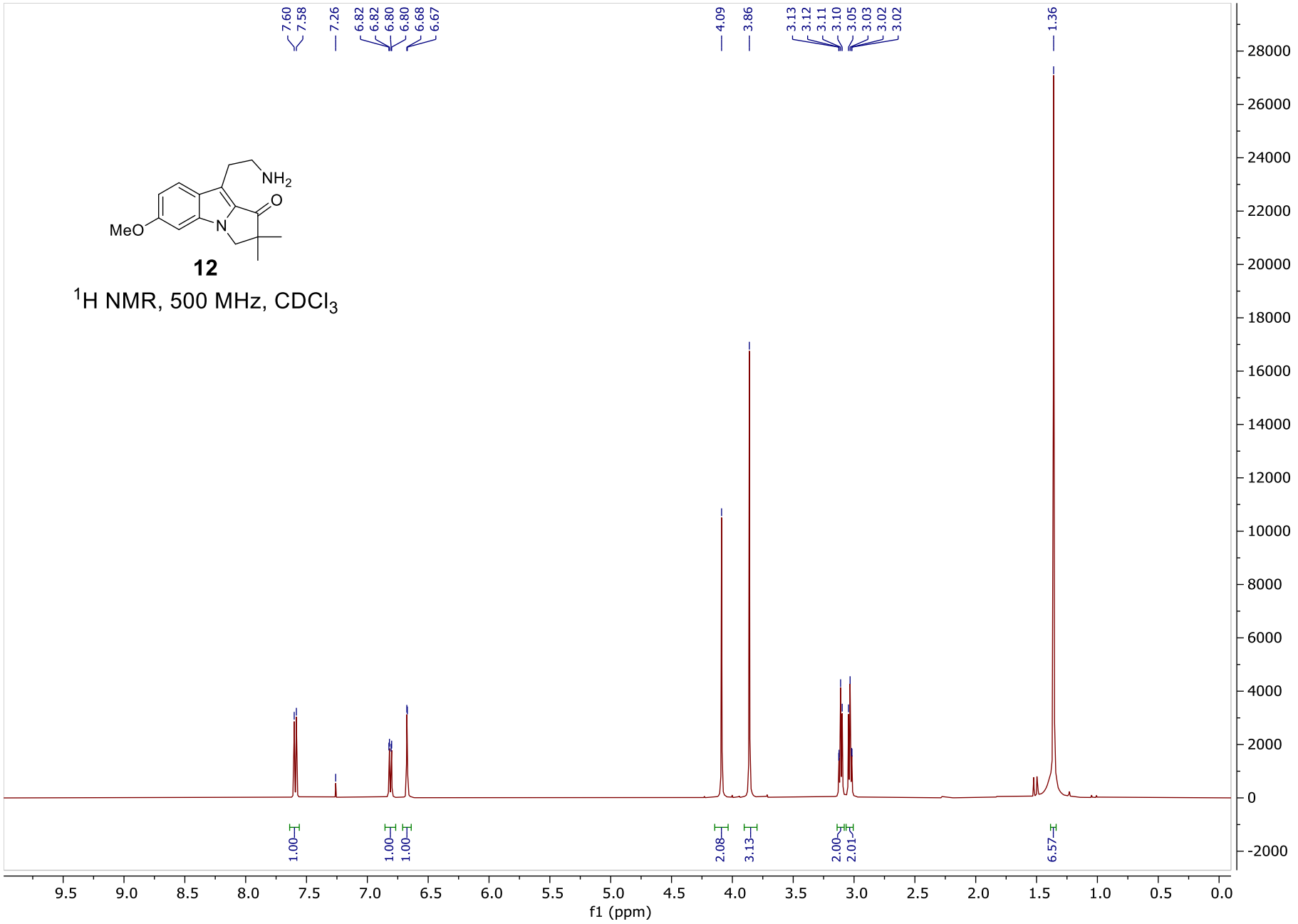
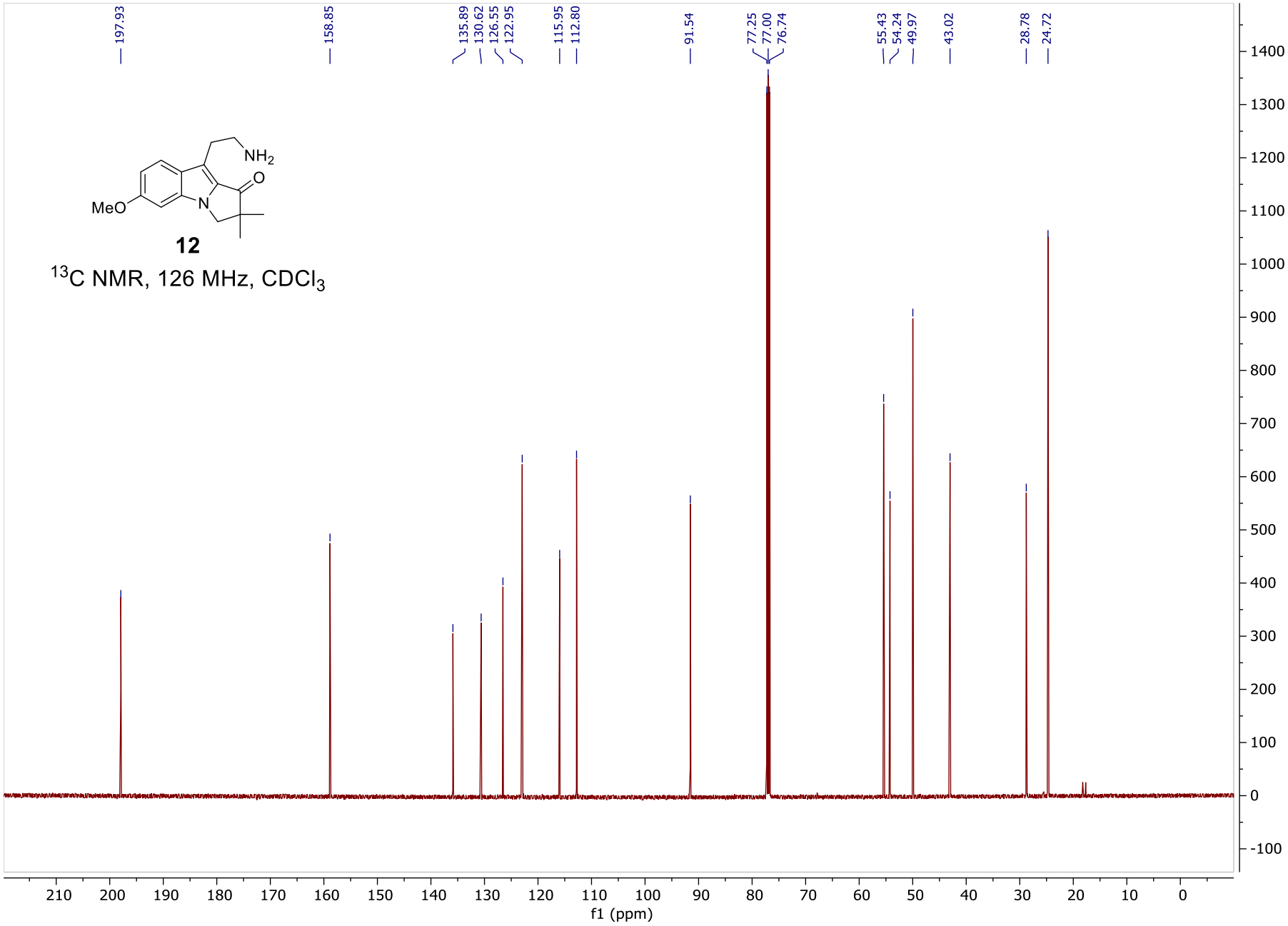
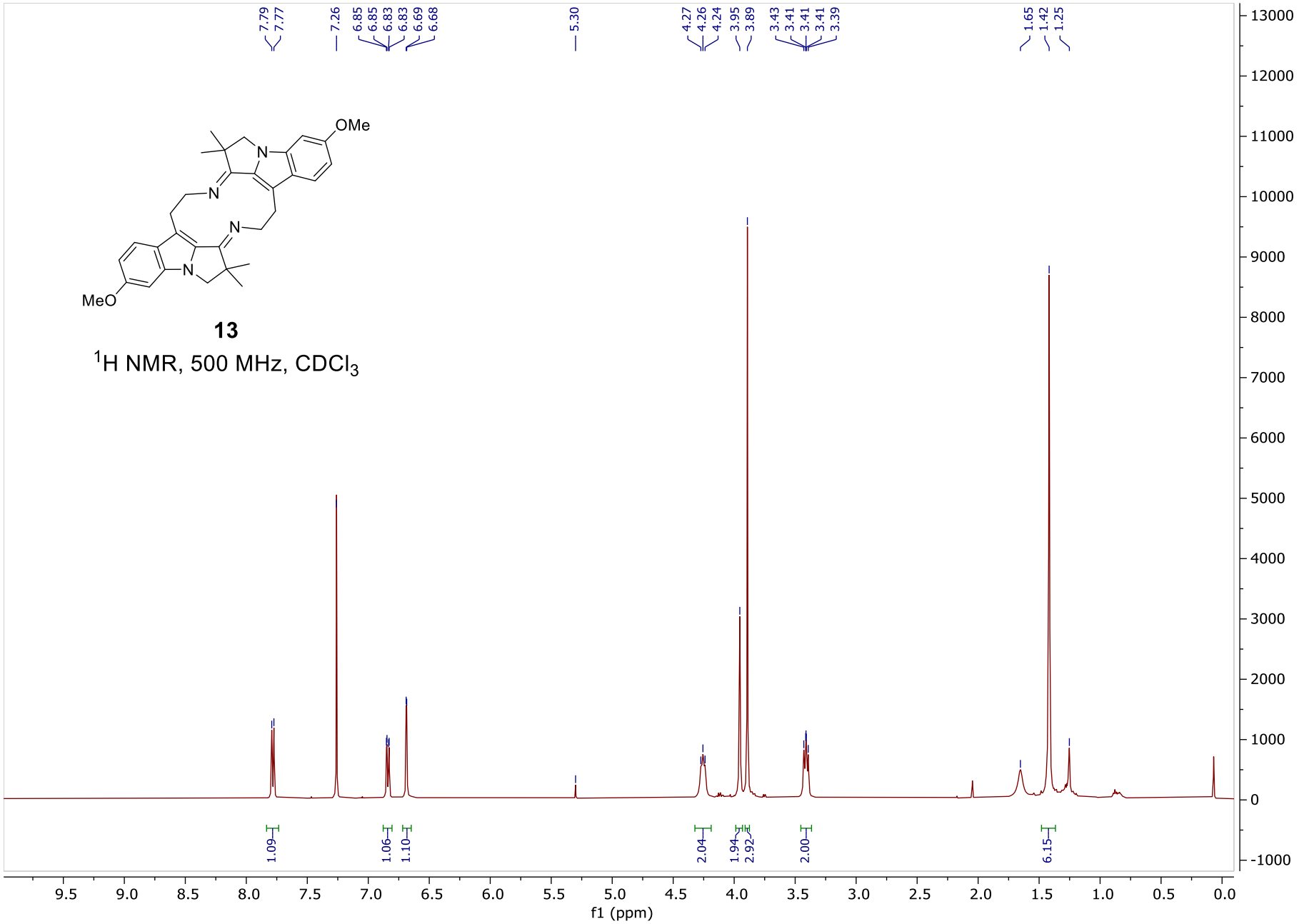
157.53
136.89
136.03
134.59
131.44
129.57
128.19
128.00
127.81
125.84
123.36
114.86
103.61
99.92
65.53
54.66
53.89
49.47
29.34
27.09
24.45
19.50
OMe
OTBDPS
O
N
11c
13C NMR, 126 MHz, C6D6
f1 (ppm)

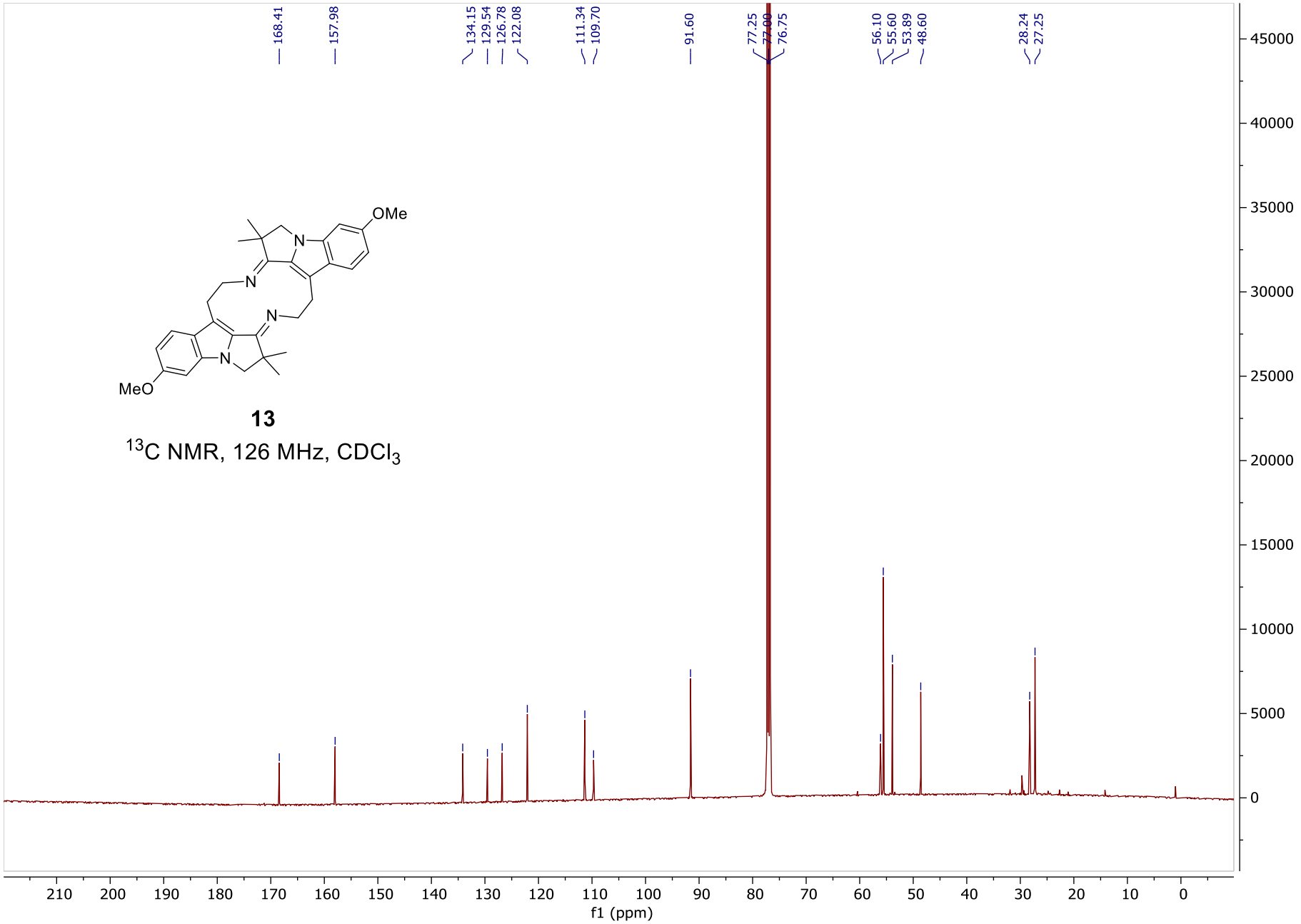

7.63
7.61
7.26
6.88
6.87
6.86
6.85
6.70
6.69
4.13
3.89
3.70
3.69
3.68
3.27
3.26
3.24
1.61
1.39
N3
O
MeO
N
11d
1H NMR, 500 MHz, CDCl3
1.00
1.01
0.97
2.08
3.20
2.08
2.03
6.10
f1 (ppm)


197.81
158.99
135.84
130.64
126.51
122.76
113.93
113.30
91.62
77.25
77.00
76.75
55.53
54.47
51.42
50.04
24.78
24.31
N3
O
MeO
N
11d
13C NMR, 126 MHz, CDCl3
3000
2500
2000
1500
1000
500
0
20 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)


7.60
7.58
7.26
6.82
6.82
6.80
6.80
6.68
6.67
4.09
3.86
3.13
3.12
3.11
3.10
3.05
3.03
3.02
3.02
1.36
NH2
O
MeO
N
12
1H NMR, 500 MHz, CDCl3
1.00
1.00
1.00
2.08
3.13
2.00
2.01
6.57
f1 (ppm)

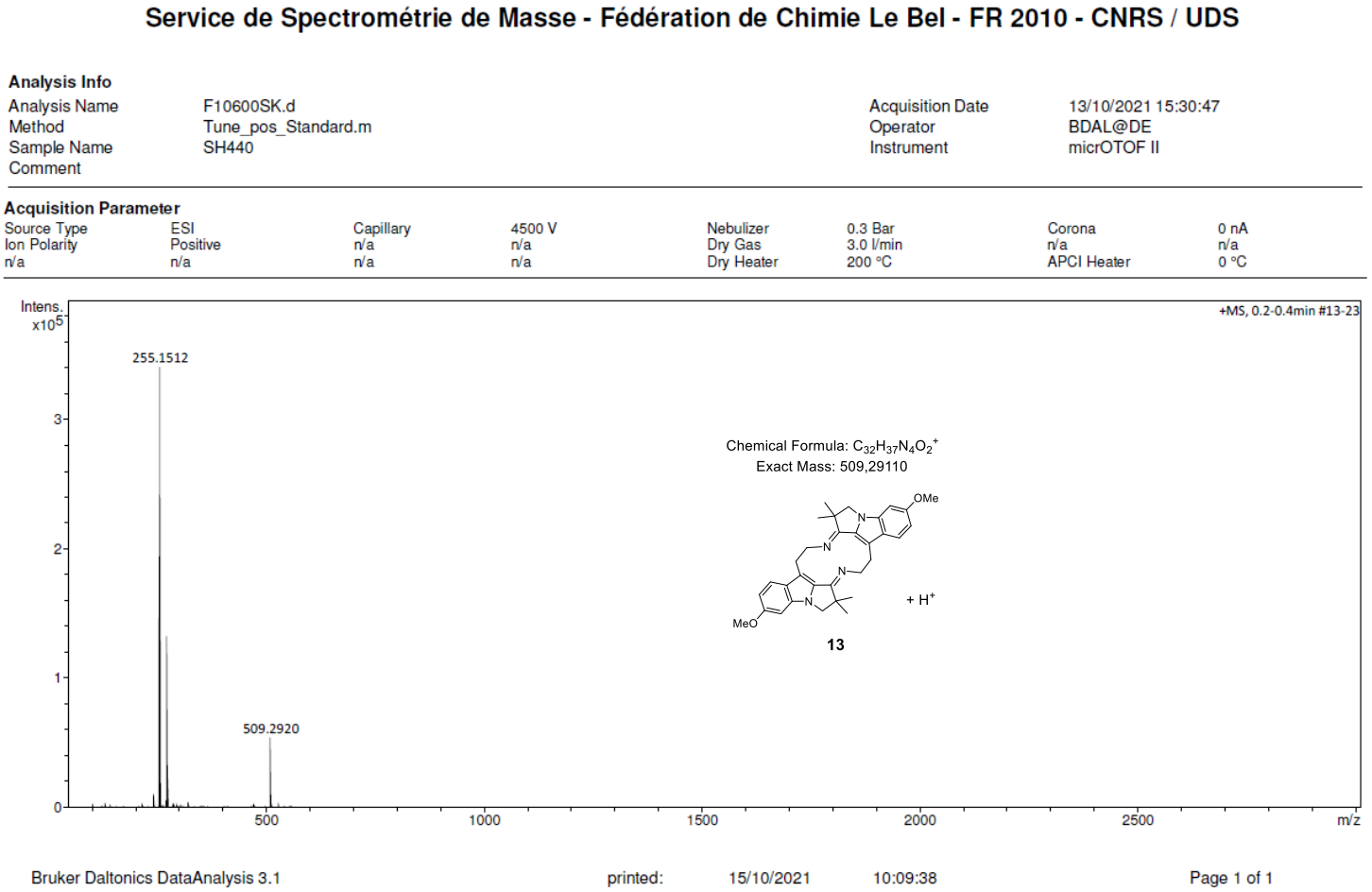

197.93
158.85
135.89
130.62
126.55
122.95
115.95
112.80
91.54
77.25
77.00
76.74
55.43
54.24
49.97
43.02
28.78
24.72
NH2
O
MeO
N
12
13C NMR, 126 MHz, CDCl3
f1 (ppm)


7.79
7.77
7.26
6.85
6.85
6.83
6.83
6.69
6.68
5.30
4.27
4.26
4.24
3.95
3.89
3.43
3.41
3.41
3.41
3.39
1.65
1.42
1.25
OMe
MeO
N
N
N
13
1H NMR, 500 MHz, CDCl3
1.09
1.06
1.10
2.04
1.94
2.92
2.00
6.15
f1 (ppm)


168.41
157.98
134.15
129.54
126.78
122.08
111.34
109.70
91.60
77.25
77.00
76.75
56.10
55.60
53.89
48.60
28.24
27.25
OMe
MeO
N
N
N
N
13
13C NMR, 126 MHz, CDCl3
45000
40000
35000
30000
25000
20000
15000
10000
5000
0
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

# HR-MS Spectra

**Figure S1.** Low- and high-resolution mass spectra for compound **13**.



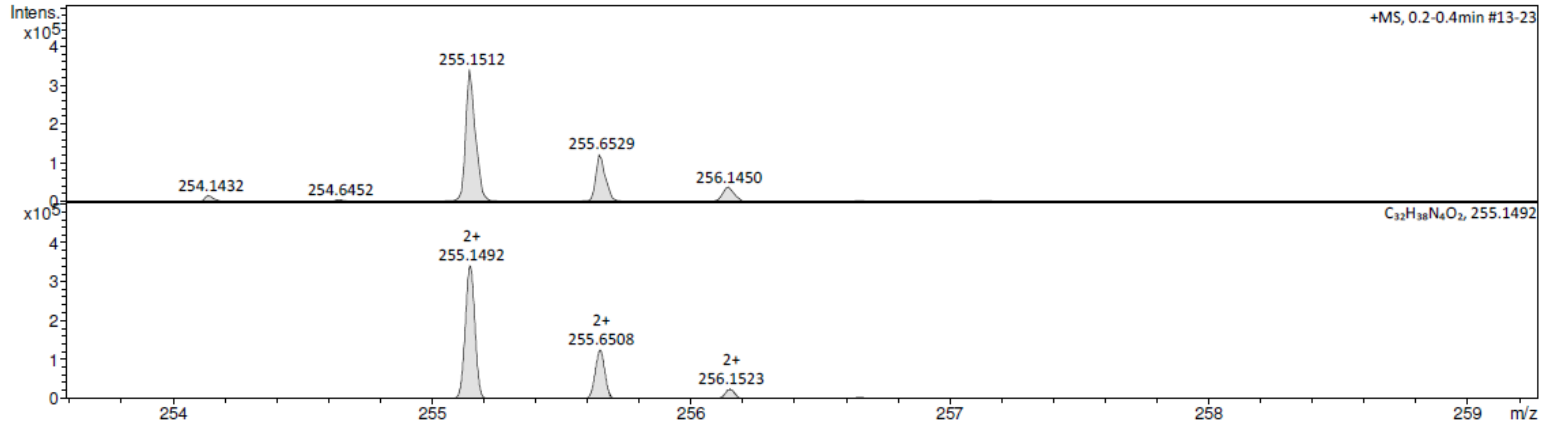
# Mass Spectrum HR Report

**Analysis Info**

| | | | |
|---|---|---|---|
| Analysis Name | Y:\2021\10_Octobre 2021\F10600SK.d | Acquisition Date | 13/10/2021 15:30:47 |
| Method | Tune_pos_Standard.m | Operator | BDAL@DE |
| Sample Name | SH440 | Instrument | micrOTOF II 8213750.10451 |
| Comment | | | |

**Acquisition Parameter**

| | | | | | |
|---|---|---|---|---|---|
| Source Type | ESI | Ion Polarity | Positive | Set Corrector Fill | 50.9 V |
| n/a | n/a | n/a | n/a | n/a | n/a |
| Scan Begin | 50 m/z | n/a | n/a | n/a | n/a |
| Scan End | 3000 m/z | n/a | n/a | Set Reflector | 1800.0 V |
| | | n/a | n/a | Set Flight Tube | 8600.0 V |
| | | n/a | n/a | Set Detector TOF | 2008.9 V |




| Meas. m/z | # | Ion Formula | m/z | err [ppm] | Mean err [ppm] | rdb | N-Rule | e⁻ Conf | mSigma | Std I | Std Mean m/z | Std I VarNorm | Std m/z Diff | Std Comb Dev |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 255.1512 | 1 | C32H38N4O2 | 255.1492 | -8.1 | -1.7 | 16.0 | ok | even | 20.9 | 32.7 | n.a. | n.a. | n.a. | n.a. |
| 509.2920 | 1 | C32H37N4O2 | 509.2911 | -1.8 | 951.2 | 16.5 | ok | even | 14.3 | 22.5 | n.a. | n.a. | n.a. | n.a. |

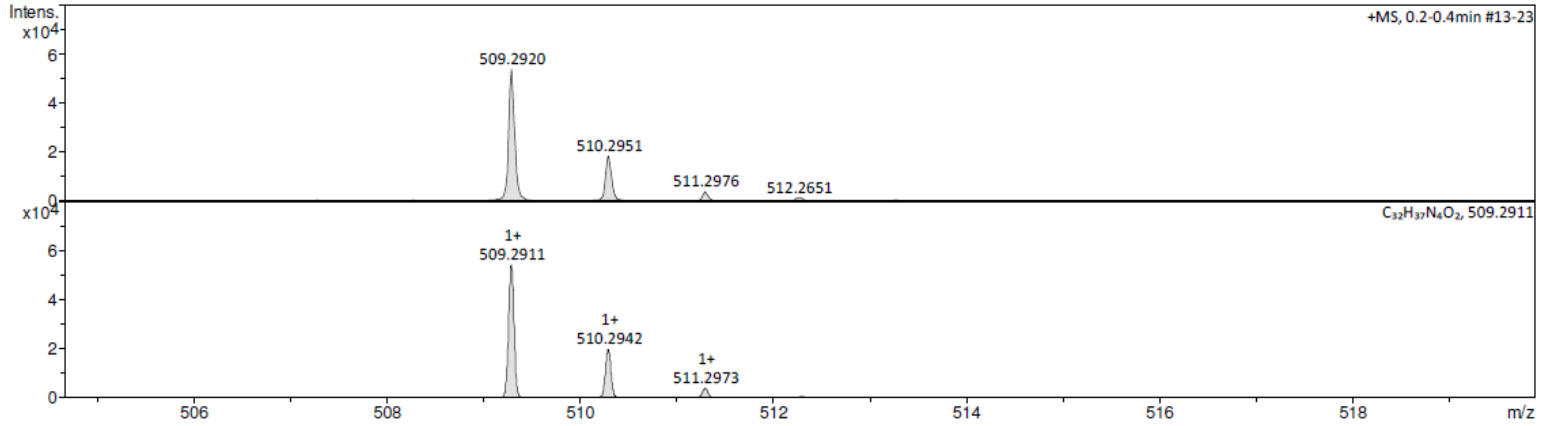
# Mass Spectrum HR Report

**Analysis Info**

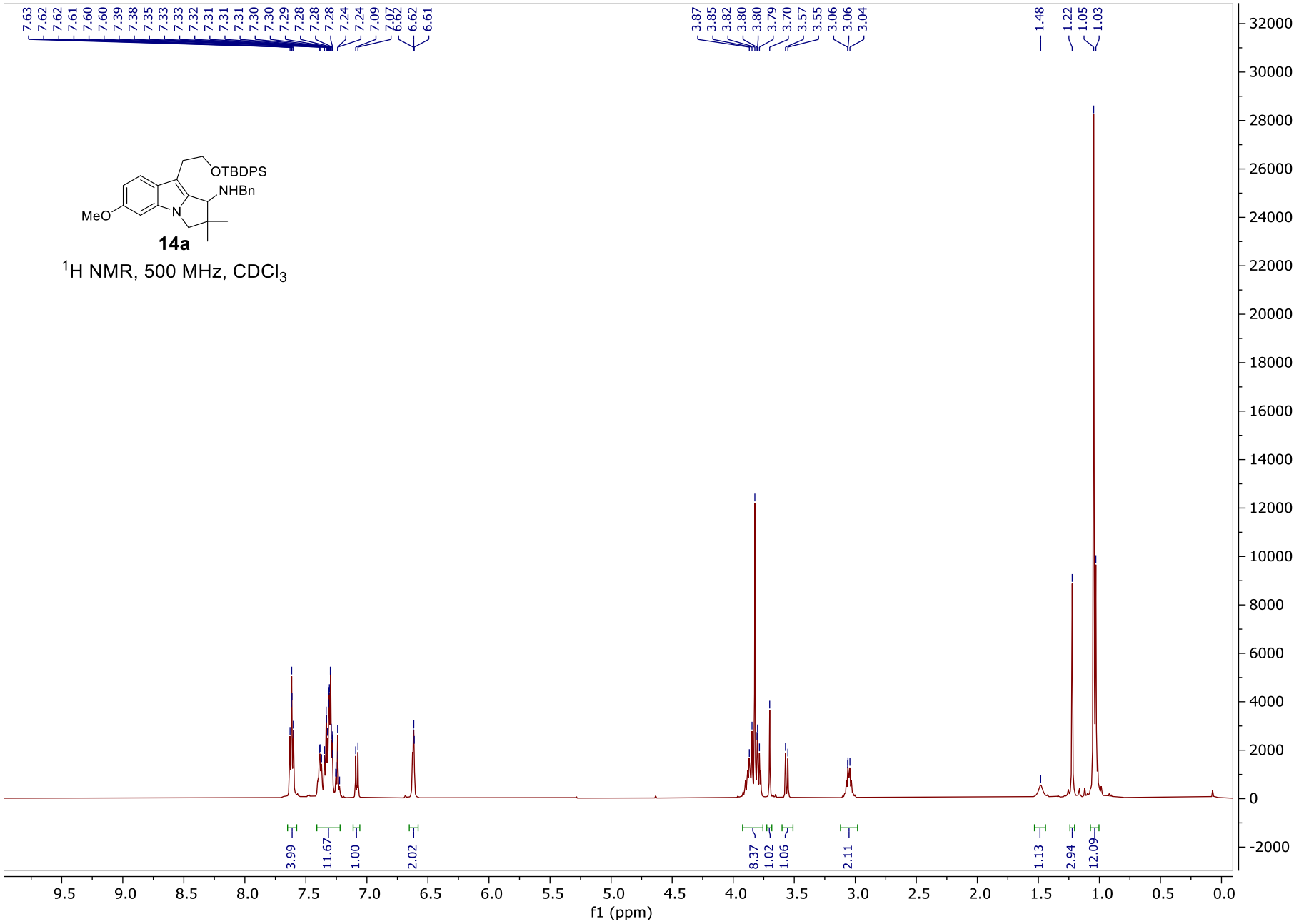
| | | | |
|---|---|---|---|
| Analysis Name | Y:\2021\10_Octobre 2021\F10600SK.d | Acquisition Date | 13/10/2021 15:30:47 |
| Method | Tune_pos_Standard.m | Operator | BDAL@DE |
| Sample Name | SH440 | Instrument | micrOTOF II 8213750.10451 |
| Comment | | | |

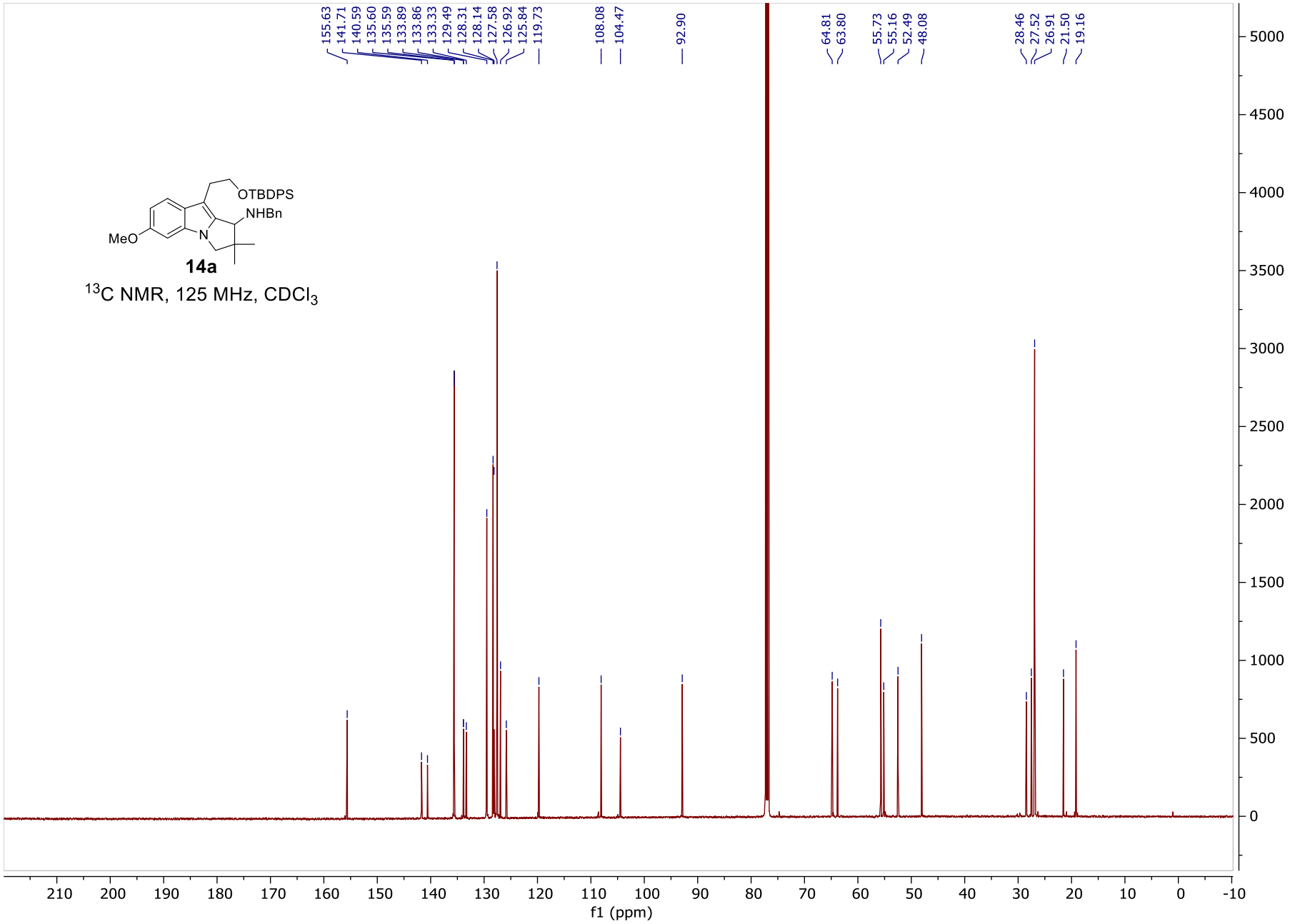
**Acquisition Parameter**

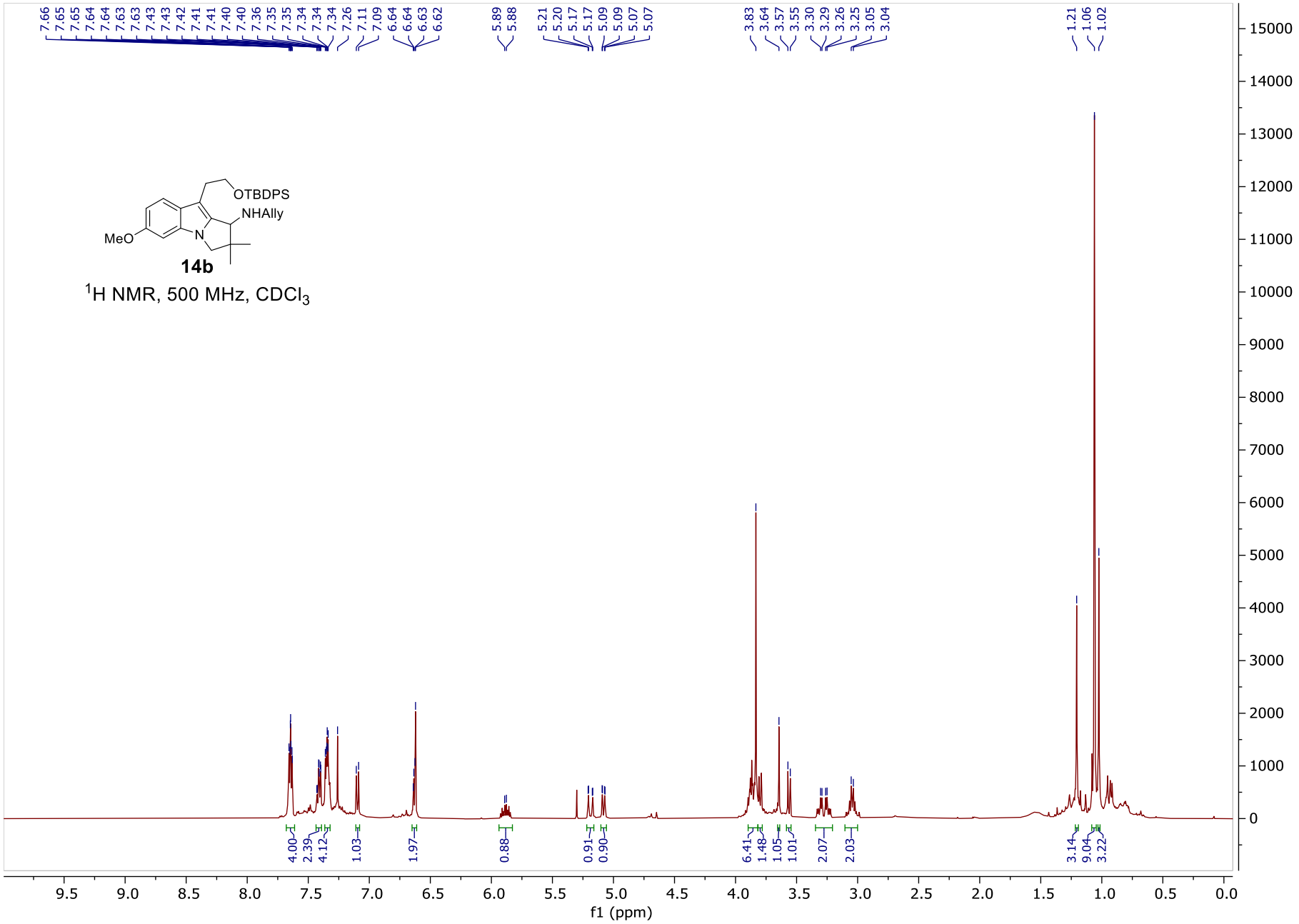
| | | | | | |
|---|---|---|---|---|---|
| Source Type | ESI | Ion Polarity | Positive | Set Corrector Fill | 50.9 V |
| n/a | n/a | n/a | n/a | n/a | n/a |
| Scan Begin | 50 m/z | n/a | n/a | n/a | n/a |
| Scan End | 3000 m/z | n/a | n/a | Set Reflector | 1800.0 V |
| | | n/a | n/a | Set Flight Tube | 8600.0 V |
| | | n/a | n/a | Set Detector TOF | 2008.9 V |

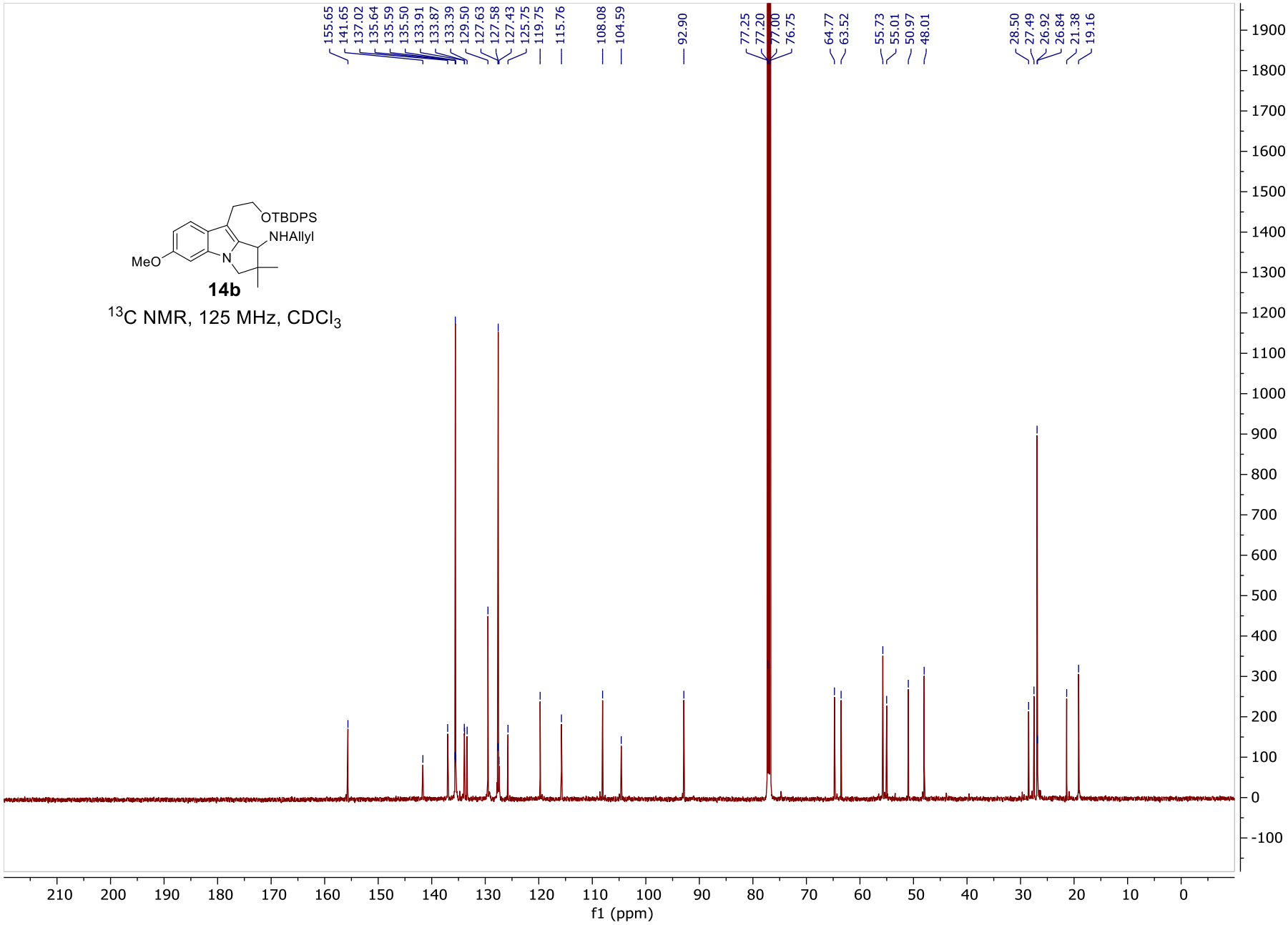


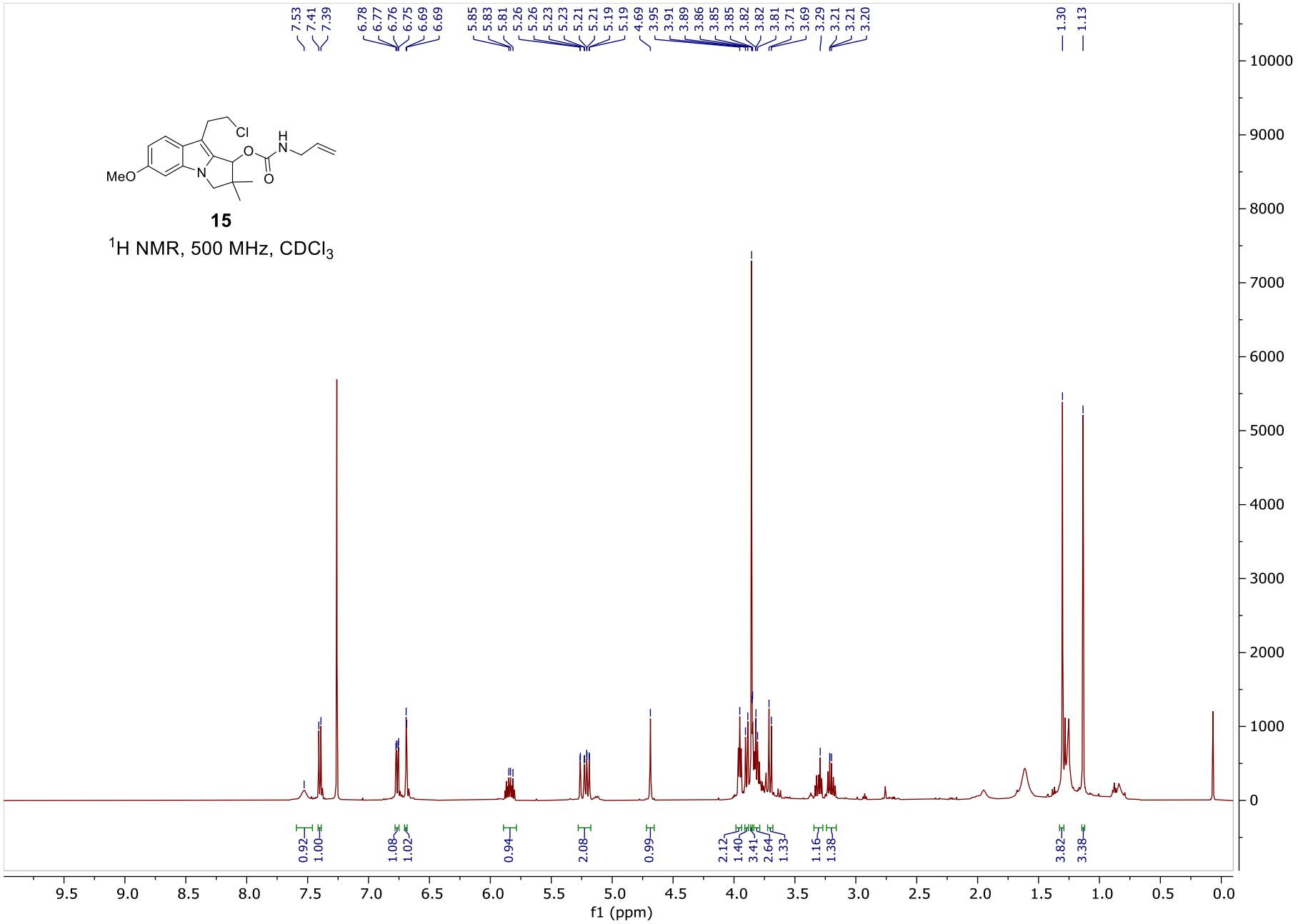

| Meas. m/z | # | Ion Formula | m/z | err [ppm] | Mean err [ppm] | rdb | N-Rule | e⁻ Conf | mSigma | Std I | Std Mean m/z | Std I VarNorm | Std m/z Diff | Std Comb Dev |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 509.2920 | 1 | C32H37N4O2 | 509.2911 | -1.8 | 951.2 | 16.5 | ok | even | 14.3 | 22.5 | n.a. | n.a. | n.a. | n.a. |

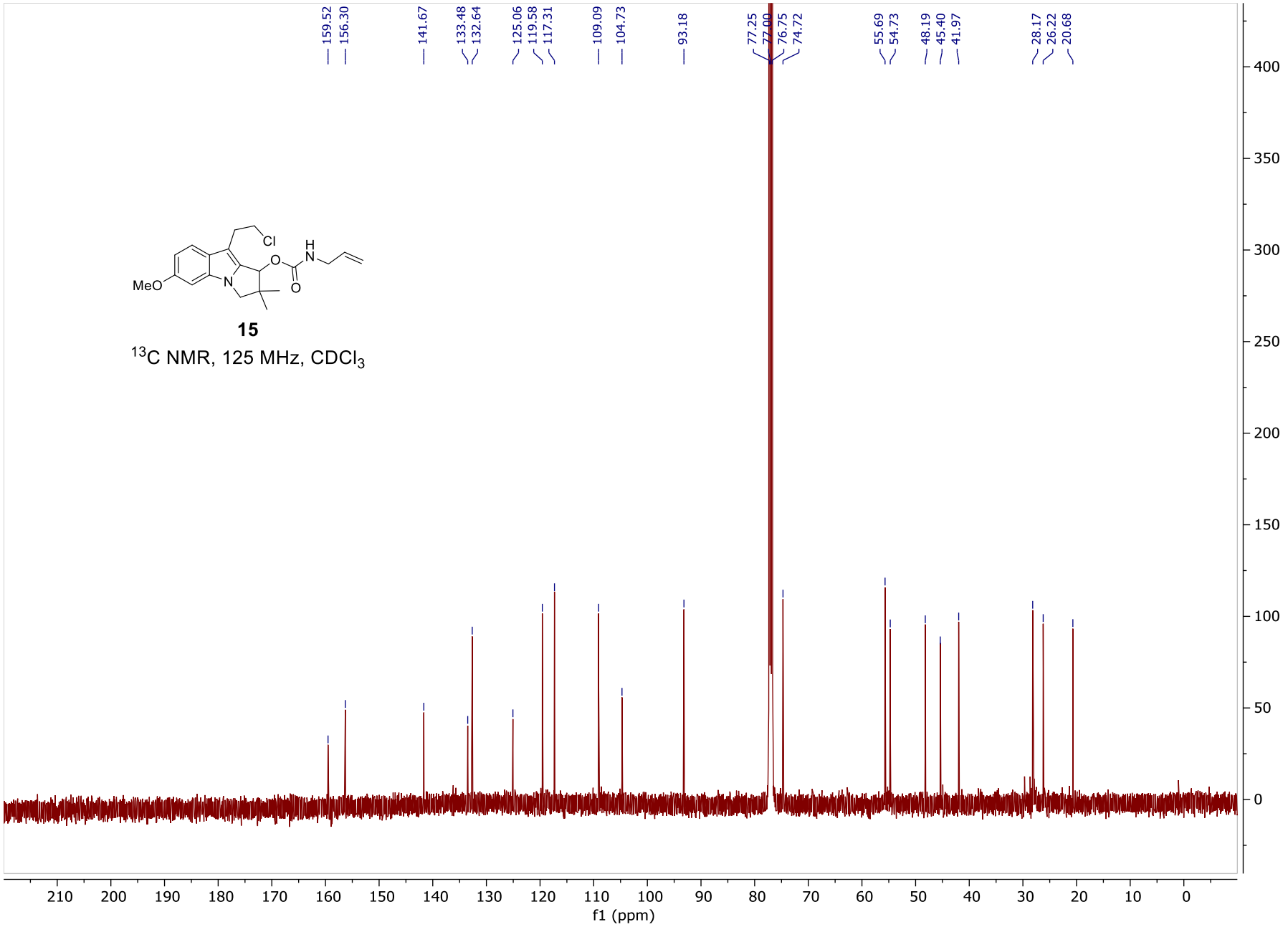

OTBDPS
NHBn
MeO
N
14a
1H NMR, 500 MHz, CDCl3
f1 (ppm)


155.63
141.71
140.59
135.60
135.59
133.89
133.86
133.33
129.49
128.31
128.14
127.58
126.92
125.84
119.73
108.08
104.47
92.90
64.81
63.80
55.73
55.16
52.49
48.08
28.46
27.52
26.91
21.50
19.16
OTBDPS
NHBn
MeO
N
14a
13C NMR, 125 MHz, CDCl3
f1 (ppm)


OTBDPS
NHAlly
MeO
N
14b
$^1$H NMR, 500 MHz, $CDCl_3$
f1 (ppm)


155.65
141.65
137.02
135.64
135.59
135.50
133.91
133.87
133.39
129.50
127.63
127.58
127.43
125.75
119.75
115.76
108.08
104.59
92.90
77.25
77.20
77.00
76.75
64.77
63.52
55.73
55.01
50.97
48.01
28.50
27.49
26.92
26.84
21.38
19.16
OTBDPS
NHAllyl
MeO
N
14b
13C NMR, 125 MHz, CDCl3
f1 (ppm)

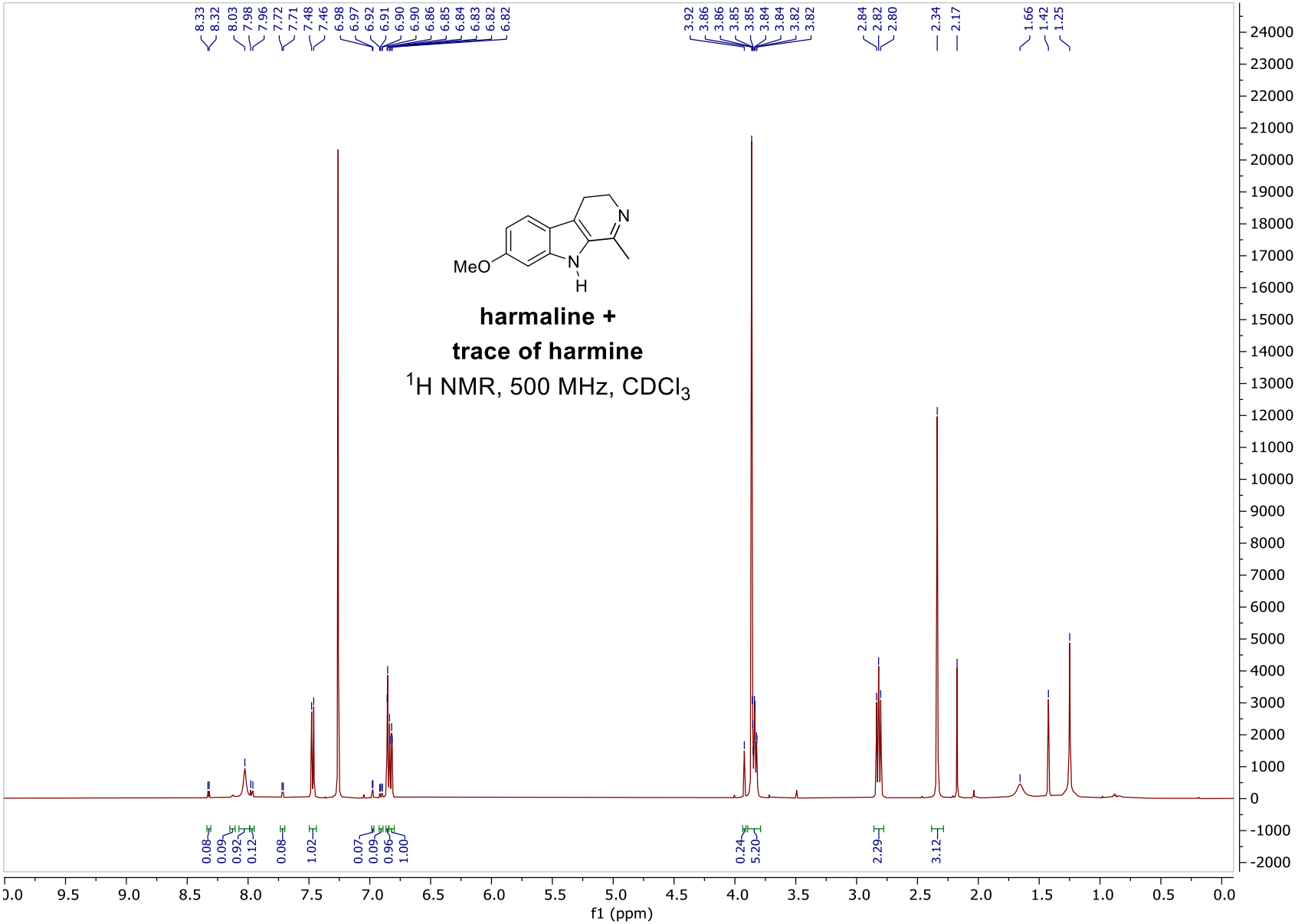

7.53
7.41
7.39
6.78
6.77
6.76
6.75
6.69
6.69
5.85
5.83
5.81
5.26
5.23
5.23
5.21
5.21
5.19
5.19
4.69
3.95
3.91
3.89
3.86
3.85
3.85
3.82
3.82
3.81
3.71
3.69
3.29
3.21
3.21
3.20
1.30
1.13
Cl
H
N
O
O
MeO
N
O
15
1H NMR, 500 MHz, CDCl3
0.92
1.00
1.08
1.02
0.94
2.08
0.99
2.12
1.40
3.41
2.64
1.33
1.16
1.38
3.82
3.38
10000
9000
8000
7000
6000
5000
4000
3000
2000
1000
0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

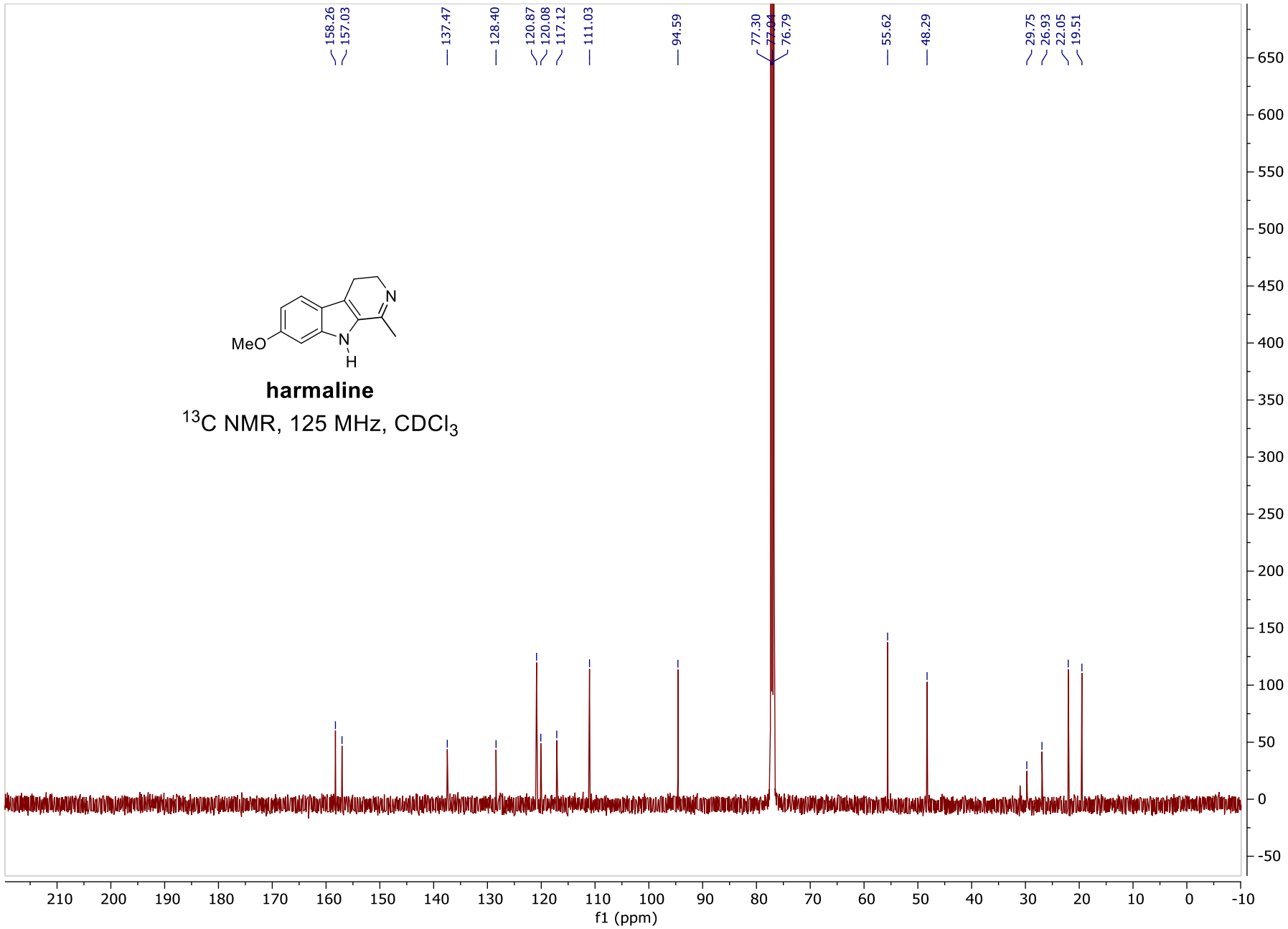


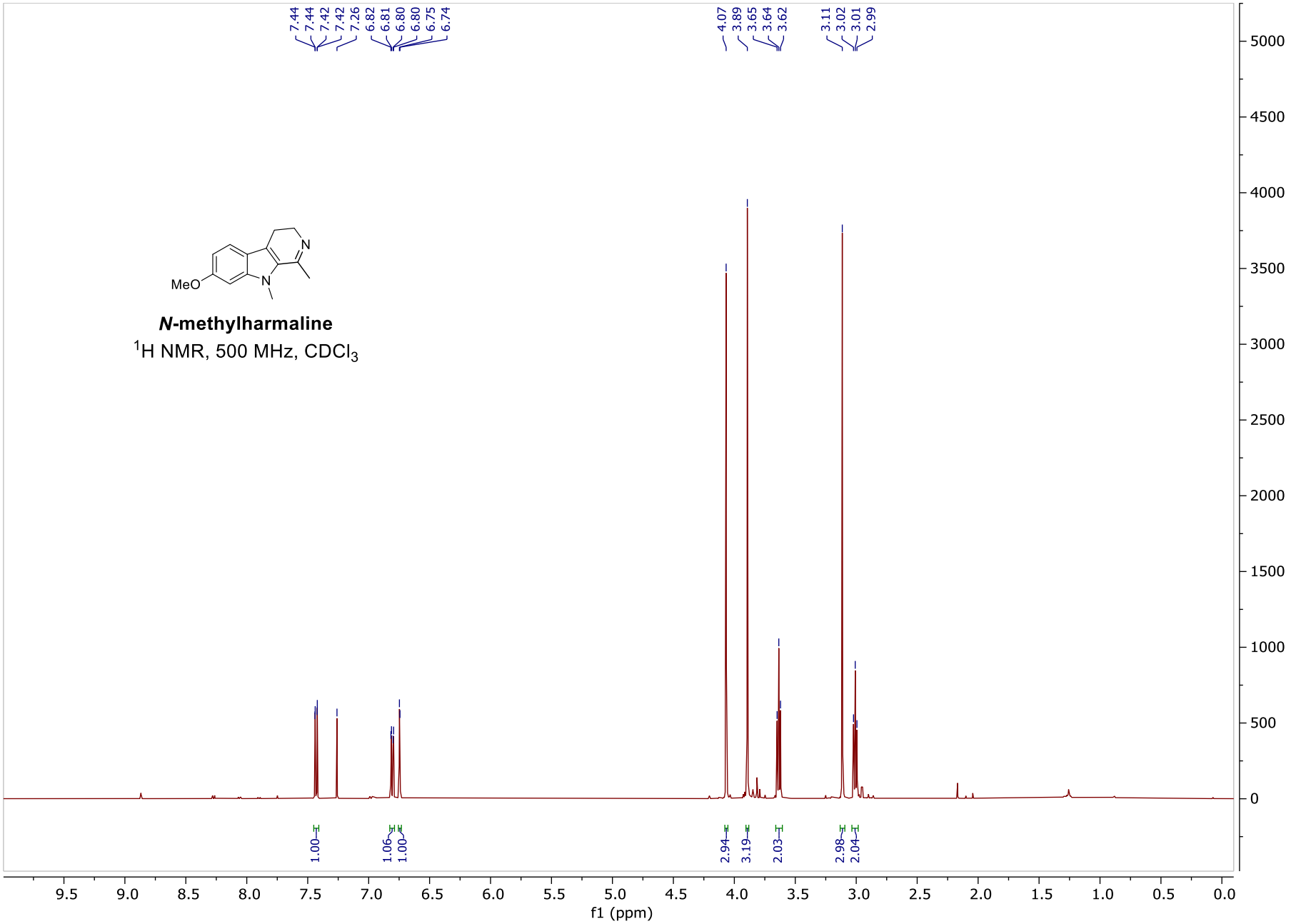

**15**

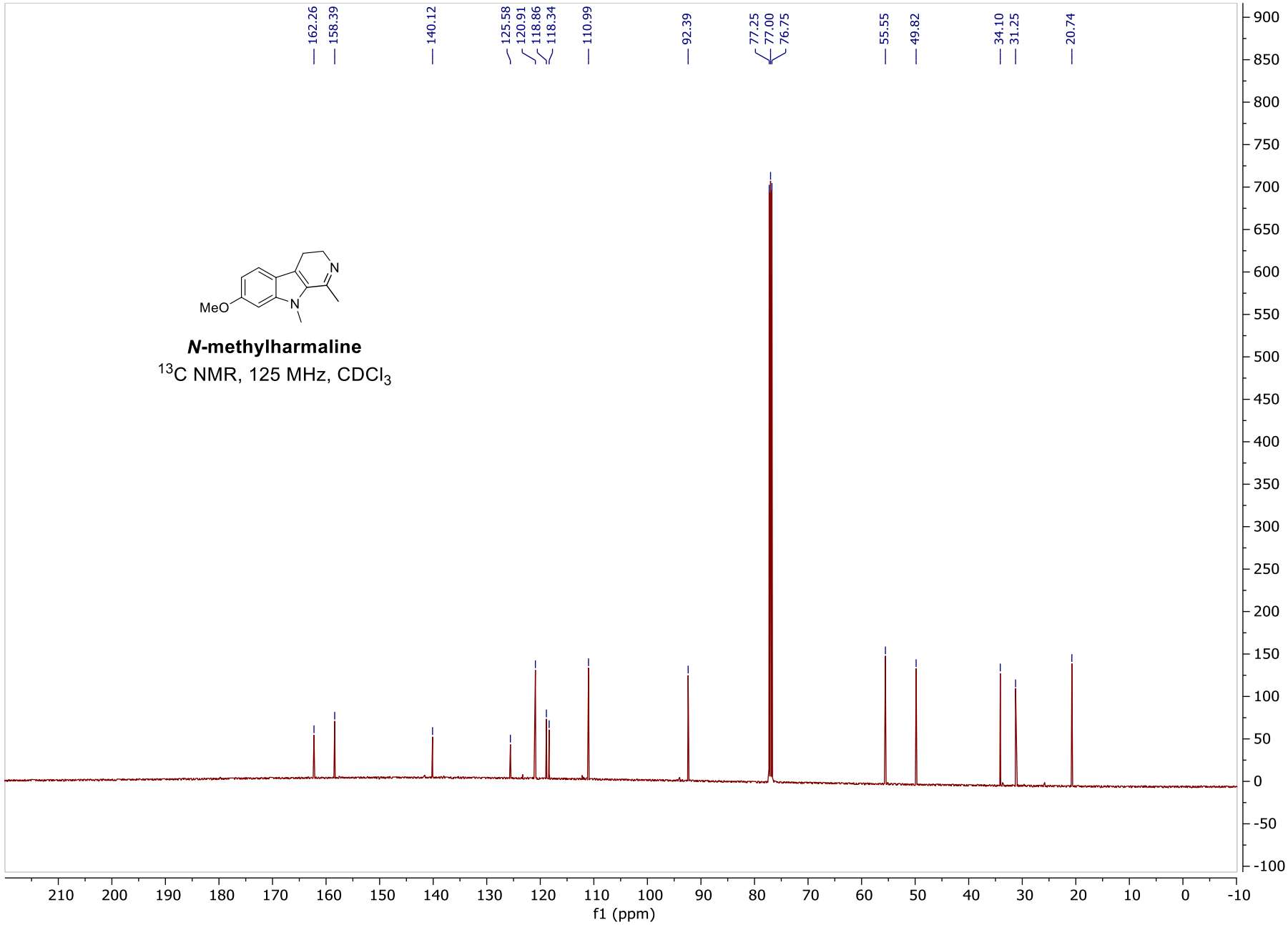
$^{13}C$ NMR, 125 MHz, $CDCl_3$

# $^{1}H$ & $^{13}C$ NMR Spectra of harmaline and *N*-methylharmaline




158.26
157.03
137.47
128.40
120.87
120.08
117.12
111.03
94.59
77.30
77.04
76.79
55.62
48.29
29.75
26.93
22.05
19.51
MeO
N
H
N
harmaline
13C NMR, 125 MHz, CDCl3
650
600
550
500
450
400
350
300
250
200
150
100
50
0
-50
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)


7.44
7.44
7.42
7.42
7.26
6.82
6.81
6.80
6.80
6.75
6.74
4.07
3.89
3.65
3.64
3.62
3.11
3.02
3.01
2.99
MeO
N
N
***N*-methylharmaline**
$^1$H NMR, 500 MHz, $CDCl_3$
1.00
1.06
1.00
2.94
3.19
2.03
2.98
2.04
5000
4500
4000
3500
3000
2500
2000
1500
1000
500
0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)




***N*-methylharmaline**

$^{13}C$ NMR, 125 MHz, $CDCl_3$