Supporting Information for:

Platinum-Catalyzed Terminal-Selective C(sp^3)–H Oxidation of Aliphatic Amines

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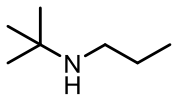
I. Materials and Methods

HPLC grade water, ethyl acetate (EtOAc), hexanes, methanol, and dichloromethane for column chromatography were purchased from VWR. Silica gel for flash column chromatography was purchased from Dynamic Adsorbents. $CDCl_3$ was purchased from Cambridge Isotope Laboratories, Inc. K_2PtCl_4, K_2PtCl_6 (Acros), and copper(II) chloride dihydrate (J.T. Baker Chemicals) were used as purchased without further purification. Amine substrates were purchased from commercial sources (Alfa Aeser, Sigma Aldrich, TCI, and ACROS, Astatech) and used without further purification, unless otherwise noted. Thin layer chromatography (TLC) was performed on Merck TLC plates pre-coated with silica gel 60 F_{254}. NMR spectra were recorded on a Varian vnmrs 700 (700 MHz for ^1H; 176 MHz for ^{13}C), Varian vnmrs 500 (500 MHz for ^1H; 126 MHz for ^{13}C), Varian Inova 500 (500 MHz for ^1H), or Varian MR400 (400 MHz for ^1H; 100 MHz for ^{13}C) with the residual solvent peak ($CDCl_3$; ^1H: δ = 7.26 ppm, ^{13}C: δ = 77.16 ppm) as the internal reference unless otherwise noted. Chemical shifts are reported in parts per million (ppm) (δ) relative to tetramethylsilane. Multiplicities are reported as follows: br (broad signal), s (singlet), d (doublet), t (triplet), q (quartet), quin (quintet), sex (sextet), m (multiplet), dd (doublet of doublets), ddd (doublet of doublet of doublets), qd (quartet of doublets). Coupling constants (*J*) are reported in Hz. Infrared (IR) spectroscopy was performed on a Perkin-Elmer Spectrum BX Ft-IR spectrometer and peaks are reported in cm^{-1}. Melting points were determined with a Thomas Hoover Uni-Melt 6427-H10 Capillary Melting-Point Apparatus and are uncorrected. High-resolution mass spectra were recorded on a Micromass AutoSpec Ultima Magnetic Sector mass spectrometer. Stock solutions were made using volumetric glassware. Liquid reagents were dispensed by difference from syringes. All reagents were weighed out under ambient conditions.

II. Synthesis of Amine Substrates

***N*-(tert-butyl)propan-1-amine**:



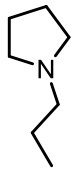
N-(tert-butyl)propan-1-amine was synthesized from *tert*-butylamine and 1-iodopropane using a literature procedure[1] and was purified via distillation.

HRMS: ESI$^+$ (m/z): $[M+H]^+$ calcd for $C_7H_{18}N$: 116.1434; found: 116.1434

^{1}H NMR ($CDCl_3$, 500 MHz): δ 2.50 (t, *J* = 7.5 Hz, 2H), 1.46 (sex, *J* = 7.5 Hz, 2H), 1.08 (s, 9H), 0.91 (t, *J* = 7.5 Hz, 3H), 0.61 (s, 1H, N-H)

^{13}C NMR ($CDCl_3$, 126 MHz): δ 50.2, 44.7, 29.2, 24.4, 12.1

1-propylpyrrolidine:



1-propylpyrrolidine was synthesized from pyrrolidine and 1-iodopropane using a literature procedure[1] and was purified via distillation.

HRMS: ESI$^+$ (m/z): $[M+H]^+$ calcd for $C_7H_{16}N$: 114.1277; found: 114.1279

^{1}H NMR ($CDCl_3$, 500 MHz): δ 2.47 (m, 4H), 2.37 (t, *J* = 7.5 Hz, 2H), 1.76 (m, 4H), 1.52 (sex, *J* = 7.5 Hz, 2H), 0.91 (t, *J* = 7.5 Hz, 3H)

^{13}C NMR ($CDCl_3$, 126 MHz): δ 58.8, 54.4, 23.5, 22.5, 12.3

1-butylpyrrolidine:

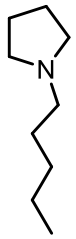
1-butylpyrrolidine was synthesized from pyrrolidine and 1-iodobutane using a literature procedure[1] and was purified via distillation.

HRMS: ESI$^+$ (m/z): $[M+H]^+$ calcd for $C_8H_{18}N$: 128.1434; found: 128.1433

^{1}H NMR ($CDCl_3$, 500 MHz): δ 2.48 (m, 4H), 2.42 (t, *J* = 7.5 Hz, 2H), 1.77 (m, 4H), 1.50 (sex, *J* = 7.5 Hz, 2H), 1.34 (sex, *J* = 7.5 Hz, 2H), 0.92 (t, *J* = 7.5 Hz, 3H)

^{13}C NMR ($CDCl_3$, 126 MHz): δ 56.6, 54.4, 31.4, 23.6, 21.1, 14.2

1-pentylpyrrolidine:



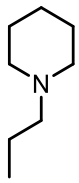
1-pentylpyrrolidine was synthesized from pyrrolidine and 1-iodopentane using a literature procedure[1] and was purified via distillation.

HRMS: ESI$^+$ (m/z): $[M+H]^+$ calcd for $C_8H_{20}N$: 143.1590; found: 143.1590

^{1}H NMR ($CDCl_3$, 500 MHz): δ 2.48 (m, 4H), 2.40 (t, *J* = 7.5 Hz, 2H), 1.77 (m, 4H), 1.51 (quin, *J* = 7.5 Hz, 2H), 1.36-1.28 (multiple peaks, 4H), 0.91 (t, *J* = 7.5 Hz, 3H)

^{13}C NMR ($CDCl_3$, 126 MHz): δ 56.9, 54.4, 30.1, 29.0, 23.6, 22.8, 14.2

1-propylpiperidine:



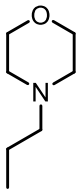
1-Propylpiperidine was synthesized from piperidine and 1-iodopropane using a literature procedure[1] and was purified via distillation.

HRMS: ESI$^+$ (m/z): $[M+H]^+$ calcd for $C_8H_{18}N$: 128.1434; found: 128.1435

^{1}H NMR ($CDCl_3$, 500 MHz): δ 2.35 (br s, 4H), 2.23 (t, *J* = 7.5 Hz, 2H), 1.57 (m, 4H), 1.52 (m, 2H), 1.42 (sex, *J* = 7.5 Hz, 2H), 0.88 (t, *J* = 7.5 Hz, 3H)

^{13}C NMR ($CDCl_3$, 126 MHz): δ 61.8, 54.8, 26.2, 24.7, 20.3, 12.3

4-propylmorpholine:



4-Propylmorpholine was synthesized from morpholine and 1-iodopropane using a literature procedure[1] and was purified via distillation.

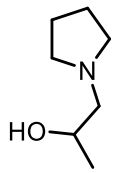
HRMS: ESI$^+$ (m/z): $[M+H]^+$ calcd for $C_7H_{16}N$: 130.1226; found: 130.1227

^{1}H NMR ($CDCl_3$, 500 MHz): δ 3.71 (t, *J* = 4.5 Hz, 4H), 2.42 (m, 4H), 2.29 (t, *J* = 7.5 Hz, 2H), 1.50 (sex, *J* = 7.5 Hz, 2H), 0.90 (t, *J* = 7.5 Hz, 3H)

^{13}C NMR ($CDCl_3$, 126 MHz): δ 67.2, 61.3, 53.9, 19.9, 12.0

III. Synthesis of Authentic Samples of Minor Isomers

1-(pyrrolidin-1-yl)propan-2-ol:



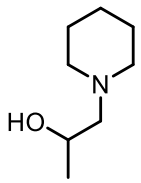
An authentic sample of 1-(pyrrolidin-1-yl)propan-2-ol (for comparison with samples produced from Pt catalysis) was synthesized from pyrrolidine and propylene oxide using a literature procedure.[2]

HRMS: ESI$^+$ (m/z): $[M+H]^+$ calcd for $C_7H_{16}NO$: 130.1226; found: 130.1226

^{1}H NMR ($CDCl_3$, 500 MHz): δ 3.78 (m, 1H), 3.50 (br s, 1H, O-H) 2.66 (m, 2H), 2.52 (app t, *J* = 12.0 Hz, 1H), 2.43 (m, 2H), 2.23 (dd, *J* = 12.0 Hz, *J* = 2.5 Hz, 1H), 1.75 (m, 4H), 1.12 (d, *J* = 6.0 Hz, 3H)

^{13}C NMR ($CDCl_3$, 126 MHz): δ 64.5, 63.7, 54.1, 23.7, 20.4

1-(piperidin-1-yl)propan-2-ol:



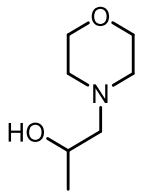
An authentic sample of 1-(piperidin-1-yl)propan-2-ol (for comparison with samples produced from Pt catalysis) was synthesized from piperidine and propylene oxide using a literature procedure.[2]

HRMS: ESI$^+$ (m/z): $[M+H]^+$ calcd for $C_8H_{18}NO$: 144.1383; found: 144.1383

^{1}H NMR ($CDCl_3$, 500 MHz): δ 3.79 (m, 1H), 3.69 (br s, 1H, O-H), 2.57 (m, 2H), 2.27 (m, 2H), 2.24 (dd, *J* = 12.5 Hz, *J* = 3.0 Hz, 1H), 2.13 (t, *J* = 10.5 Hz, 1H), 1.55 (m, 4H), 1.42 (m, 2H), 1.10 (d, *J* = 6.0 Hz, 3H)

^{13}C NMR ($CDCl_3$, 175.95 MHz): δ 66.5, 62.3, 54.8, 26.3, 24.5, 20.2

1-morpholinopropan-2-ol:



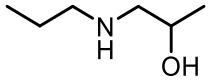
An authentic sample of 1-morpholinopropan-2-ol (for comparison with samples produced from Pt catalysis) was synthesized from morpholine and propylene oxide using a literature procedure.[2]

HRMS: ESI$^+$ (m/z): $[M+H]^+$ calcd for $C_7H_{16}NO_2$: 146.1175; found: 146.1176

^{1}H NMR ($CDCl_3$, 700 MHz): δ 3.84 (m, 1H), 3.70 (m, 4H), 3.40 (br s, 1H, O-H), 2.64 (m, 2H), 2.38 (m, 2H), 2.31 (dd, *J* = 12.5 Hz, *J* = 3.0 Hz, 1H), 2.21 (dd, *J* = 12.5 Hz, *J* = 10.5 Hz, 1H), 1.12 (d, *J* = 6.0 Hz)

^{13}C NMR ($CDCl_3$, 176 MHz): δ 67.2, 66.3, 62.2, 53.8, 20.1

1-(propylamino)propan-2-ol:



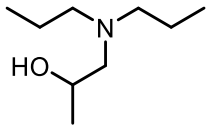
An authentic sample of 1-(propylamino)propan-2-ol (for comparison with samples produced from Pt catalysis) was synthesized from *n*-propylamine and propylene oxide using a literature procedure.[2]

HRMS: ESI$^+$ (m/z): $[M+H]^+$ calcd for $C_6H_{16}NO$: 118.1226; found: 118.1228

^{1}H NMR ($CDCl_3$, 500 MHz): δ 3.76 (m, 1H), 2.70 (dd, *J* = 12.0 Hz, *J* = 3.5 Hz, 1H), 2.61 (m, 1H), 2.56 (m, 1H), 2.39 (dd, *J* = 12.0 Hz, *J* = 9.0 Hz, 1H), 2.16 (br s, 2H, O-H and N-H), 1.50 (sex, *J* = 7.5 Hz, 2H), 1.14 (d, *J* = 6.0 Hz, 3H), 0.92 (t, *J* = 7.5 Hz, 3H)

^{13}C NMR ($CDCl_3$, 126 MHz): δ 65.6, 56.9, 51.6, 23.4, 20.6, 11.8

1-(dipropylamino)propan-2-ol:



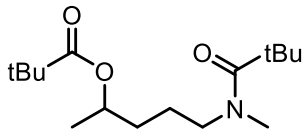
An authentic sample of 1-(dipropylamino)propan-2-ol (for comparison with samples produced from Pt catalysis) was synthesized from dipropylamine and propylene oxide using a literature procedure.[2]

HRMS: ESI$^+$ (m/z): $[M+H]^+$ calcd for $C_9H_{22}NO$: 160.1696; found: 160.1693

^{1}H NMR ($CDCl_3$, 500 MHz): δ 3.70 (multiple peaks, 2H, where 1H from O-H), 2.47 (m, 2H), 2.38-2.33 (multiple peaks, 3H), 2.21 (dd, *J* = 10.5 Hz, *J* = 12.5 Hz, 1H), 1.45 (m, 4H), 1.11 (d, *J* = 6.0 Hz, 3H), 0.88 (t, *J* = 7.0 Hz, 6H)

^{13}C NMR ($CDCl_3$, 126 MHz): δ 63.1, 62.6, 56.4, 20.5, 19.9, 11.9

5-(N-methylpivalamido)pentan-2-yl pivalate:



An authentic sample of 5-(N-methylpivalamido)pentan-2-yl pivalate (for comparison with samples produced from Pt catalysis) was synthesized from 5-chloro-2-pentanone using a literature procedure.[3]

HRMS: ESI^{+} (m/z): $[M+H]^{+}$ calcd for $C_{16}H_{32}NO_3$: 286.2377; found: 286.2376

^{1}H NMR ($CDCl_3$, 400 MHz): δ 4.88 (sex, *J* = 6.8 Hz, 1H), 3.36 (m, 2H), 3.01 (s, 3H), 1.65-1.45 (multiple peaks, 4H), 1.27 (s, 9H), 1.20 (d, *J* = 6.8 Hz, 3H), 1.18 (s, 9H)

^{13}C NMR ($CDCl_3$, 126 MHz): 178.3, 177.4, 70.2, 49.9, 38.9, 38.9, 33.2, 28.5, 27.3, 27.2, 23.5, 20.0

IV. General Procedures

A. General procedure for optimization reactions in Table 1:

120 °C Conditions

To a 4 mL scintillation vial containing K_2PtCl_4 (10 mol %, 2.1 mg), $CuCl_2 \cdot 2H_2O$ (1 equiv, 0.1 mmol, 17 mg) were added aqueous H_2SO_4 (2.2 equiv, 0.11 mmol) from a stock solution and dipropylamine (2.0 equiv, 0.1 mmol, 14 µL). The reaction vial was equipped with a micro stir bar, sealed with a Teflon-lined cap, and placed in an aluminum block preheated to 120 °C. The reaction mixture was stirred for 48 h at 120 ºC. The reaction mixture was then quenched with NH_4OH (28% aqueous solution, 0.5 mL) and saturated with NaCl. The product was extracted into $CDCl_3$ (2.0 mL) containing mesitylene as an internal standard (0.025 mmol). The organic extracts were filtered through a Celite plug and the yield was determined via ^1H NMR spectroscopic analysis.

150 °C Conditions

To a 10 mL scintillation vial (10 cm tall) containing K_2PtCl_4 (10 mol %, 2.1 mg), $CuCl_2 \cdot 2H_2O$ (1 equiv, 0.1 mmol, 17 mg) were added aqueous H_2SO_4 (2.2 or 5.5 equiv, 0.11 mmol or 0.55 mmol) from a stock solution, and dipropylamine (2.0 or 5.0 equiv, 0.1 mmol or 0.25 mmol, 14 µL or 34 µL). The reaction vial was equipped with a micro stir bar, sealed with a Teflon-lined cap and placed in an aluminum block preheated to 150 °C. The reaction mixture was stirred for 30-48 h at 120 ºC. The reaction mixture was then cooled to room temperature and quenched with NH_4OH (28% aqueous solution, 0.5 mL) and saturated with NaCl. The product was extracted into $CDCl_3$ (2.0 mL) containing mesitylene as an internal standard (0.025 mmol). The organic extracts were filtered through a Celite plug and the yield was determined via ^1H NMR spectroscopic analysis. Notably, when 1 mol % of Pt was used, the K_2PtCl_4 was added from a stock solution (0.0124 M aqueous stock solution) and was the last reagent added.

B. General procedure for isolation reactions (Table 2 and 3):

To a 10 mL scintillation vial (10 cm tall) containing $CuCl_2 \cdot 2H_2O$ (1 equiv) were added aqueous H_2SO_4 (5.5 equiv) from a stock solution, the appropriate amine substrate (5 equiv), and K_2PtCl_4 (0.5-1 mol % from a 0.0124 M aqueous stock solution and 5-10 mol % as a solid). The reaction vial was equipped with a micro stir bar, sealed with a Teflon-lined cap, and placed in an aluminum block preheated to 150 °C. The reaction mixture was stirred for 24 to 48 h at 150 ºC. Unless otherwise noted, all reactions were run until all C–H chlorination products transformed into C–H hydroxylation products for accurate determination of selectivity and for ease of isolation. The reaction was cooled to room temperature and quenched with NH_4OH (28% aqueous solution, 0.5 mL) and saturated with NaCl. The product was extracted into $CHCl_3$ (3 x 3 mL), the organic extracts were filtered through a Celite plug, and the resulting mixture was concentrated by rotary evaporation.

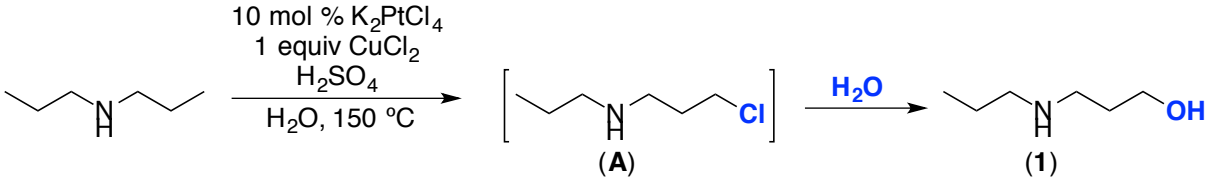
C. General procedure for protection of the amine and alcohol products

Two reactions conducted and worked on the scale of procedure B were combined. To the crude reaction mixture from part B was added dichloromethane (3 mL), and then triethylamine (0.7 mL) and pivaloyl chloride (1 equiv, 61 µL for products **3-5, 11, 14, 15, 19** or 3 equiv, 184 µL for products **6-10, 12, 13**) were added. The resulting mixture was stirred at room temperature for 3 h. The reaction was diluted with dichloromethane (50 mL), and the organic layer was washed three times with NaOH (1M aqueous solution, 50 mL). The organic extracts were collected, and

the volatiles were removed by rotary evaporation. The resulting residue was purified by column chromatography. In all cases, the yield is calculated based on $CuCl_2 \cdot 2H_2O$ as the limiting reagent. Since the copper acts as a 1-electron oxidant, 100% yield = 0.5*(mmol $CuCl_2 \cdot 2H_2O$ added to the reaction).

D. General procedure for the time study in Figure 1

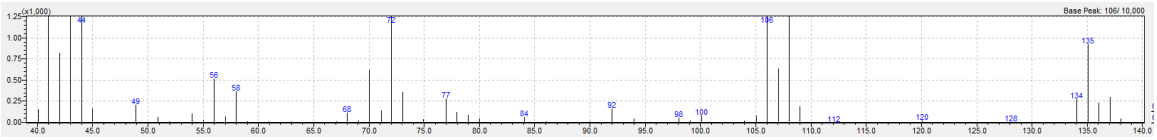
Reactions were set up using general procedure A at 150 °C, and were individually quenched at the appropriate time points. The reactions were worked up using general procedure A, and the product yields and ratios were determined via ^{1}H NMR spectroscopic analysis.



(**A**) (**1**)

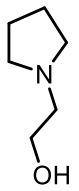
$[M]^+ = 135.05$

GC-MS of **A**: EI^+ (m/z): $[M]^+$ found: 135.05



V. Synthesis and Isolation of Products from Pt-Catalyzed C–H Functionalization

2-(pyrrolidin-1-yl)ethan-1-ol (2-OH):

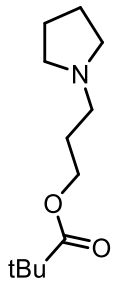


2-OH

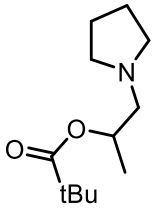
General procedure **A** was followed using 1-ethylpyrrolidine (0.25 mmol, 30.6 µL, 5 equiv), $CuCl_2 \cdot 2H_2O$ (0.1 mmol, 17 mg, 1 equiv), 0.25 mL of aqueous H_2SO_4 (0.28 mmol, 5.5 equiv, 1.1 M stock solution), and K_2PtCl_4 (0.0025, 1.0 mg, 5 mol %). The reaction was stirred at 150 °C for 48 h. The reaction was performed side-by-side in duplicate, and the reaction was quenched and analyzed by ^1H NMR as outlined in general procedure **A**. The identity of the product was confirmed by a commerically available authentic sample of 2-(pyrrolidin-1-yl)ethan-1-ol.

^1H NMR Yield: 25%

3-(pyrrolidin-1-yl)propyl pivalate (3):



3



3a

General procedure **B** was followed using 1-propylpyrrolidine (0.25 mmol, 28.3 mg, 5 equiv), $CuCl_2 \cdot 2H_2O$ (0.1 mmol, 17 mg, 1 equiv), 0.25 mL of aqueous H_2SO_4 (0.28 mmol, 5.5 equiv, 1.1 M stock solution), and K_2PtCl_4 (0.0025, 1.0 mg, 5 mol %). The reaction was stirred at 150 °C for 24 h. The reaction was performed side-by-side in duplicate, the two duplicate runs were combined, and the hydroxylated product was protected via general procedure **C**. The product was then purified by silica column chromatography (gradient of 1% to 10%, MeOH in DCM).

Isolated Yield: 85% (18.2 mg, crude ratio of **3-OH** : **3a-OH** = 10 : 1; isolated ratio of **3** : **3a** = >20 : 1; light yellow oil)

R_f: 0.30 (10% MeOH/90% DCM)

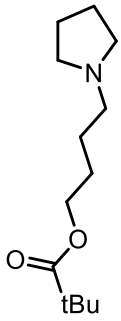
IR (υ, cm^{-1}): 2958, 2791, 1727, 1480, 1459, 1284, 1151, 732

HRMS: APCI$^+$ (m/z): $[M+H]^+$ calcd for $C_{12}H_{24}NO_2$: 214.1807 ; found: 214.1802

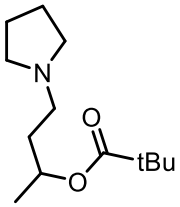
^{1}H NMR ($CDCl_3$, 700 MHz): δ 4.11 (t, *J* = 6.3 Hz, 2H), 2.50 (overlapping m, 6H), 1.85 (quin, *J* = 7.0 Hz, 2H), 1.78 (m, 4H), 1.19 (s, 9H)

^{13}C NMR ($CDCl_3$, 176 MHz): δ 178.7, 63.0, 54.4, 53.2, 38.9, 28.5, 27.3, 23.6

4-(pyrrolidin-1-yl)butyl pivalate (4):



4



4a

General procedure **B** was followed using 1-butylpyrrolidine (0.25 mmol, 31.8 mg, 5 equiv), $CuCl_2$•$2H_2O$ (0.1 mmol, 17 mg, 1 equiv), 0.25 mL of aqueous H_2SO_4 (0.28 mmol, 5.5 equiv, 1.1 M stock solution), and K_2PtCl_4 (0.0025, 1.0 mg, 5 mol %). The reaction was stirred at 150 °C for 24 h. The reaction was performed side-by-side in duplicate, the two duplicate runs were combined, and the hydroxylated product was protected via general procedure **C**. The product was then purified by silica column chromatography (gradient of 1% to 10%, MeOH in DCM).

Isolated Yield: 126% (28.7 mg as a mixture of isomers; crude ratio of **4-OH : 4a-OH** = 4 : 1; isolated ratio of **4 : 4a** = 4 : 1; yellow oil)

R_f: 0.48 (**4**), 0.55 (**4a**) (10% MeOH/90% DCM)

IR (υ, cm^{-1}) (mixture of isomers): 2966, 1719, 1479, 1459, 1284, 1161, 908, 724

HRMS:
4: ESI$^+$ (m/z): $[M+H]^+$ calcd for $C_{13}H_{26}NO_2$: 228.1958; found: 228.1959
4a: ESI$^+$ (m/z): $[M+H]^+$ calcd for $C_{13}H_{26}NO_2$: 228.1958; found: 228.1959

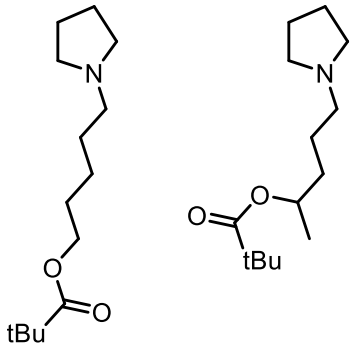
4: ^{1}H NMR ($CDCl_3$, 700 MHz): δ 4.07 (t, *J* = 6.3 Hz, 2H), 2.50 (br s, 4H), 2.47 (t, *J* = 7.0 Hz, 2H), 1.78 (br s, 4H), 1.67 (sex, *J* = 7.0 Hz, 2H), 1.59 (br s, 2H, overlaps with water peak), 1.92 (s, 9H)

4: ^{13}C NMR ($CDCl_3$, 176 MHz): δ 178.8, 64.4, 56.3, 54.3, 38.9, 27.4, 27.0, 25.6, 23.6

4a: ^{1}H NMR ($CDCl_3$, 700 MHz): δ 4.92 (sex, *J* = 6.3 Hz, 1H), 2.50 (overlapping peaks, 6H), 1.78 (overlapping peaks, 6H), 1.22 (d, *J* = 5.6 Hz, 3H), 1.18 (s, 9H)

4a: ^{13}C NMR ($CDCl_3$, 176 MHz): δ 178.2, 69.4, 54.4, 52.7, 38.9, 35.5, 27.3, 23.6, 20.2

5-(pyrrolidin-1-yl)pentyl pivalate (5):



5 **5a**

General procedure **B** was followed using 1-pentylpyrrolidine (0.25 mmol, 35.3 mg, 5 equiv), $CuCl_2 \cdot 2H_2O$ (0.1 mmol, 17 mg, 1 equiv), 0.25 mL of aqueous H_2SO_4 (0.28 mmol, 5.5 equiv, 1.1 M stock solution), and K_2PtCl_4 (0.0025, 1.0 mg, 5 mol %). The reaction was stirred at 150 °C for 24 h. The reaction was performed side-by-side in duplicate, the two duplicate runs were combined, and the hydroxylated product was protected via general procedure **C**. The product was then purified by silica column chromatography (gradient of 1% to 10%, MeOH in DCM).

Isolated Yield: 73% (17.7 mg, crude ratio of **5-OH : 5a-OH** = 2 : 1; isolated ratio of **5 : 5a** = 3 : 1; light yellow oil)

Major R_f (**5**): 0.52 (10% MeOH/90% DCM)

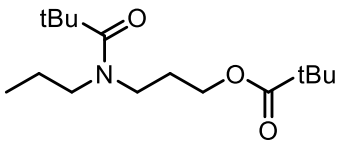
IR (υ, cm^{-1}) (mixture of **5** and **5a**): 2958, 2934, 2872, 2783, 1727, 1480, 1459, 1396, 1284, 1159

HRMS (mixture of **5** and **5a**): ESI^+ (m/z): $[M+H]^+$ calcd for $C_{14}H_{28}NO_2$: 242.2115; found: 242.2116

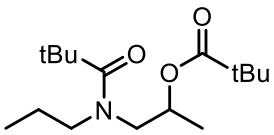
5: ^{1}H NMR ($CDCl_3$, 700 MHz): δ 4.04 (t, *J* = 6.3 Hz, 2H), 3.16 (br s, 4H), 2.94 (t, *J* = 7.7 Hz, 2H), 2.11 (br s, 4H), 1.90 (quin, *J* = 7.7 Hz, 2H), 1.67 (quin, *J* = 7.7 Hz, 2H), 1.41 (quin, *J* = 7.7 Hz, 2H), 1.18 (s, 9H)

5: ^{13}C NMR ($CDCl_3$, 176 MHz): δ 178.7, 63.8, 55.6, 53.7, 38.9, 28.3, 27.3, 23.6, 23.5, 20.1

3-(N-propylpivalamido)propyl pivalate (6):



6



6a

General procedure **B** was followed using dipropylamine (0.50 mmol, 68.5 µL, 5 equiv), $CuCl_2 \cdot 2H_2O$ (0.2 mmol, 34.1 mg, 1 equiv), 0.50 mL of aqueous H_2SO_4 (0.55 mmol, 5.5 equiv, 1.1 M stock solution), and K_2PtCl_4 (0.001 mmol, 80 µL of a 0.0124 M aqueous stock solution, 1 mol %). The reaction was stirred at 150 °C for 24 h. The reaction was performed side-by-side in triplicate, the three triplicate runs were combined, and the hydroxylated product was protected via general procedure **C**. The product was then purified by silica column chromatography (gradient of 0 to 20%, EtOAc in Hex).

Isolated Yield: 87% (74.4 mg, crude ratio of **6-OH** : **6a-OH** = 10 : 1; isolated ratio of **6** : **6a** = >20 : 1; light yellow oil)

R_f: 0.41 (20% EtOAc/ 80% Hex)

IR (υ, cm^{-1}): 2964, 1728, 1625, 1481, 1413, 1365, 1283, 1150, 1124

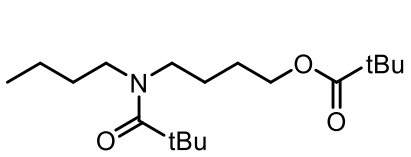
HRMS: ESI^+ (m/z): $[M+H]^+$ calcd for $C_{16}H_{32}NO_3$: 286.2377; found: 286.2377

^1H NMR ($CDCl_3$, 400 MHz): 4.07 (t, J = 6.0 Hz, 2H), 3.39 (poorly resolved triplet, 2H), 3.29 (t, J = 8.0 Hz, 2H), 1.90 (quin, J = 6.4 Hz, 2H), 1.58 (sex, J = 7.6 Hz, 2H), 1.26 (s, 9H), 1.20 (s, 9H), 0.89 (t, J = 7.2 Hz, 3H)

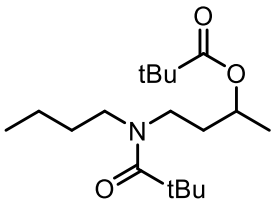
^{13}C NMR ($CDCl_3$, 176 MHz, 50 °C): δ 178.4, 177.3, 62.3, 49.9, 44.9, 41.7, 39.2, 38.9, 28.7, 27.3. 21.7, 11.2

Scale-up of the reaction: The same reaction was carried out on a larger scale using dipropylamine (1.0 mmol, 137 µL, 5 equiv), $CuCl_2 \cdot 2H_2O$ (0.4 mmol, 68.2 mg, 1 equiv), 1.0 mL of aqueous H_2SO_4 (1.1 mmol, 5.5 equiv, 1.1 M stock solution), and K_2PtCl_4 (0.002 mmol, 160 µL of a 0.0124 M aqueous stock solution, 1 mol %). The reaction was stirred at 150 °C for 24 h. The reaction was performed side-by-side in duplicate, the two duplicate runs were combined, and the hydroxylated product was protected via general procedure **C**. The product was then purified as above and a 70% yield was obtained (79.9 mg).

4-(N-butylpivalamido)butyl pivalate (7):



7



7a

General procedure **B** was followed using dibutylamine (0.25 mmol, 42 µL, 5 equiv), $CuCl_2 \cdot 2H_2O$ (0.1 mmol, 17 mg, 1 equiv), 0.25 mL of aqueous H_2SO_4 (0.28 mmol, 5.5 equiv, 1.1 M stock solution), and K_2PtCl_4 (0.0005 mmol, 40 µL of a 0.0124 M aqueous stock solution, 1 mol %). The reaction was stirred at 150 °C for 24 h. The reaction was performed side-by-side in duplicate, the two duplicate runs were combined, and the hydroxylated product was protected via general procedure **C**. The product was then purified by silica column chromatography (gradient of 0 to 30%, EtOAc in Hex).

Isolated Yield: 76% (23.9 mg, crude ratio of **7-OH : 7a-OH** = 5 : 1; isolated ratio of **7 : 7a** = 7 : 1; light yellow oil)

R_f: 0.42 (**7**), 0.52 (**7a**) (20% EtOAc/80% Hex)

IR (υ, cm^{-1}) (mixture of **7** and **7a**): 2958, 1726, 1625, 1480, 1458, 1414, 1364, 1283, 1155, 1126

HRMS:
7: ESI$^+$ (m/z): $[M+H]^+$ calcd for $C_{19}H_{36}NO_3$: 314.2690; found: 314.2690
7a: ESI$^+$ (m/z): $[M+H]^+$ calcd for $C_{19}H_{36}NO_3$: 314.2690; found: 314.2690

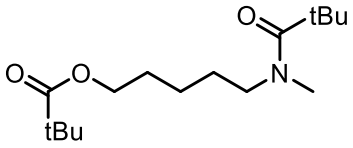
7: ^{1}H NMR ($CDCl_3$, 700 MHz, 50 °C): δ 4.08 (t, *J* = 5.6 Hz, 2H), 3.33 (m, 4H), 1.63 (m, 4H), 1.55 (quin, *J* = 7.0 Hz, 2H), 1.32 (sex, *J* = 7.7 Hz, 2H), 1.27 (s, 9H), 1.20 (s, 9H), 0.95 (t, *J* = 7.7 Hz, 3H)

7: ^{13}C NMR ($CDCl_3$, 176 MHz, 50 °C): δ 178.8, 177.4, 64.2, 48.0, 47.6, 39.4, 39.1, 30.9, 29.0, 27.6, 26.7, 25.1, 20.6, 14.2

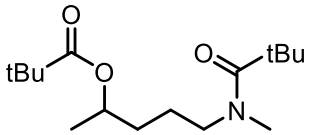
7a: ^{1}H NMR ($CDCl_3$, 700 MHz, 50 °C): δ 4.90 (sex, *J* = 6.3 Hz, 1H), 3.35 (m, 4H), 1.83 (m, 2H), 1.54 (m, 2H), 1.32 (sex, *J* = 7.7 Hz, 2H), 1.27 (s, 9H), 1.24 (d, *J* = 6.3 Hz, 3H), 1.21 (s, 9H), 0.95 (t, *J* = 7.7 Hz, 3H)

7a: ^{13}C NMR ($CDCl_3$, 176 MHz, 50 °C): δ 178.1, 177.3, 69.1, 48.1, 44.5, 39.2, 39.0, 34.5, 30.7, 28.8, 27.4, 20.4, 20.2, 14.0

5-(N-methylpivalamido)pentyl pivalate (8):



8



8a

General procedure **B** was followed using *N*-methylpentylamine (0.25 mmol, 34 µL, 5 equiv), $CuCl_2$•$2H_2O$ (0.1 mmol, 17 mg, 1 equiv), 0.25 mL of aqueous H_2SO_4 (0.28 mmol, 5.5 equiv, 1.1 M stock solution), and K_2PtCl_4 (0.0025 mmol, 1.0 mg, 5 mol %). The reaction was stirred at 150 °C for 24 h. The 2º C-H chlorination product (~14%) was observed at the end of the reaction (24 h). This compound still remained after 48 h. The reaction was performed side-by-side in duplicate, the two duplicate runs were combined, and the hydroxylated product was protected via general procedure **C**. The product was then purified by silica column chromatography (gradient of 0 to 30%, EtOAc in Hex).

Isolated Yield: 47% (13.5 mg, crude ratio of **8-OH : 8a-OH** = 3 : 1; isolated ratio **8** : **8a** = 17 : 1; light yellow oil)

R_f (**8**): 0.50 (30% EtOAc/70% Hex)

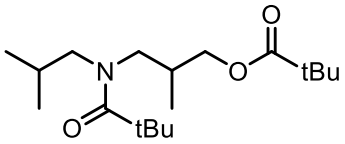
IR (υ, cm^{-1}) (isolated mixture of **8** and **8a**): 2936, 2871, 1725, 1626, 1480, 1401, 1364, 1283, 1152, 1077, 1030

HRMS (isolated mixture of **8** and **8a**): EI^+ (m/z): M^+ calcd for $C_{16}H_{31}NO_3$: 285.2304; found: 285.2308

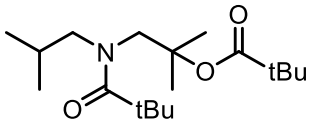
8: ^{1}H NMR ($CDCl_3$, 401 MHz): δ 4.04 (t, *J* = 6.8 Hz, 2H), 3.35 (dd, *J* = 7.6 Hz, 2H), 3.03 (s, 3H), 1.66 (m, 2H), 1.57 (m, 2H), 1.34 (m, 2H), 1.27 (s, 9H), 1.19 (s, 9H)

8: ^{13}C NMR ($CDCl_3$, 176 MHz, 50 °C): δ 178.7, 177.4, 64.3, 50.2, 39.0, 38.9, 36.4, 28.8, 28.6, 27.4, 27.3, 23.6

3-(N-isobutylpivalamido)-2-methylpropyl pivalate (9):



9



9a

General procedure **B** was followed using diisobutylamine (0.25 mmol, 43 µL, 5 equiv), $CuCl_2$•$2H_2O$ (0.1 mmol, 17 mg, 1 equiv), 0.25 mL of aqueous H_2SO_4 (0.28 mmol, 5.5 equiv, 1.1 M stock solution), and K_2PtCl_4 (0.0005 mmol, 40 µL of a 0.0124 M aqueous stock solution, 1 mol %). The reaction was stirred at 150 °C for 48 h. Trace amounts of the aldehyde product were observed at the end of the reaction (see spectra for more detail). The reaction was

performed side-by-side in duplicate, the two duplicate runs were combined, and the hydroxylated product was protected via general procedure **C**. The product was then purified by silica column chromatography (gradient of 0 to 30%, EtOAc in Hex).

Isolated Yield: 54% (16.8 mg, crude ratio of **9-OH** : **9a-OH** = 8 : 1; isolated ratio of **9** : **9a** = >20 : 1, light orange oil)

R_f: 0.54 (20% EtOAc/80% Hex)

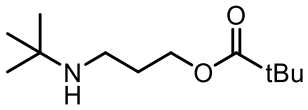
IR (υ, cm^{-1}): 2963, 2872, 1729, 1628, 1479, 1411, 1364, 1283, 1200, 1152, 1126

HRMS: ESI^+ (m/z): $[M+H]^+$ calcd for $C_{19}H_{36}NO_3$: 314.2690; found: 314.2689

^1H NMR ($CDCl_3$, 700 MHz, 50 °C): δ 3.99 (dd, *J* = 11.2 Hz, 4.9 Hz, 1H), 3.89 (dd, *J* = 10.5 Hz, 5.6 Hz, 1H), 3.40 (multiplet, 2H), 3.29 (dd, *J* = 14.0 Hz, 7.7 Hz, 1H), 3.10 (m, 1H), 2.23 (m, 1H), 1.98 (m, 1H), 1.28 (s, 9H), 1.20 (s, 9H), 0.90 (m, 9H)

^{13}C NMR ($CDCl_3$, 175.95 MHz, 50 °C): δ 178.4, 178.4, 67.0, 54.2, 48.9, 39.8, 39.1, 31.4, 29.3, 27.4, 26.8, 20.2, 19.9, 14.9

3-(tert-butylamino)propyl pivalate (10):



10

General procedure **B** was followed using *N*-(tert-butyl)propan-1-amine (0.25 mmol, 28.6 mg, 5 equiv), $CuCl_2 \cdot 2H_2O$ (0.1 mmol, 17 mg, 1 equiv), 0.25 mL of aqueous H_2SO_4 (0.28 mmol, 5.5 equiv, 1.1 M stock solution), and K_2PtCl_4 (0.0005 mmol, 40 µL of a 0.0124 M aqueous stock solution, 1 mol %). The reaction was stirred at 150 °C for 24 h. Trace amounts of the terminal $C(sp^3)$–H chlorination product were present at the end of the reaction. The reaction was performed side-by-side in duplicate, the two duplicate runs were combined, and the hydroxylated product was protected via general procedure **C**. The product was then purified by silica column chromatography (gradient of 1 to 8%, MeOH in DCM).

Isolated Yield: 46% (9.9 mg, >20 : 1 selectivity, yellow oil)

R_f: 0.40 (10% MeOH/90% DCM)

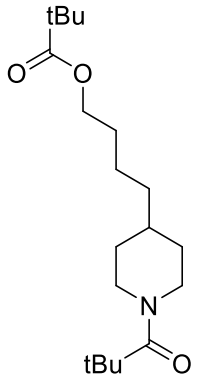
IR (υ, cm^{-1}): 2958, 2924, 2871, 1725, 1480, 1459, 1395, 1363, 1283, 1157

HRMS: ESI^+ (m/z): $[M+H]^+$ calcd for $C_{12}H_{26}NO_2$: 216.1958; found: 216.1956

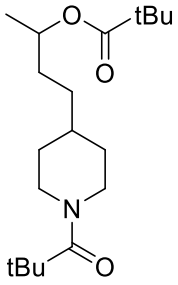
^1H NMR ($CDCl_3$, 500 MHz): δ 4.14 (t, *J* = 6.5 Hz, 2H), 2.63 (t, *J* = 7.0 Hz, 2H), 1.80 (quin, *J* = 7.0 Hz, 2H), 1.19 (s, 9H), 1.10 (s, 9H)

^{13}C NMR ($CDCl_3$, 126 MHz): δ 178.7, 62.8, 39.3, 38.9, 30.3, 29.9, 29.1, 27.4

4-(1-pivaloylpiperidin-4-yl)butyl pivalate (11):



11



11a

General procedure **B** was followed, using commerically available 4-butylpiperidine hydrochloride as the substrate (0.25 mmol, 44.4 mg, 5 equiv), $CuCl_2 \cdot 2H_2O$ (0.1 mmol, 17 mg, 1 equiv), H_2O (0.25 mL), and K_2PtCl_4 (0.005 mmol, 2.1 mg, 10 mol %). The reaction stirred at 150 °C for 24 h. The reaction was performed side-by-side in duplicate, the two duplicate runs were combined, and the hydroxylated product was protected via general procedure **C**. The product was then purified by silica column chromatography (gradient of 0 to 30%, EtOAc in DCM).

Isolated Yield: 65% (21.1 mg, crude ratio of **11-OH : 11a-OH** = 5 : 1; isolated ratio of **11** : **11a** = 17 : 1; yellow oil)

R_f (**11**): 0.24 (20% EtOAc/80% Hex)

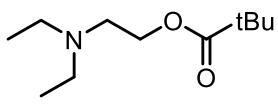
IR (υ, cm^{-1}) (isolated mixture of **11** and **11a**): 2924, 2864, 1725, 1695, 1627, 1480, 1419, 1364, 1283, 1152

HRMS (isolated mixture of **11** and **11a**): ESI^+ (m/z): $[M+H]^+$ calcd for $C_{19}H_{36}NO_3$: 326.2690; found: 326.2693

11: ^{1}H NMR ($CDCl_3$, 700 MHz): δ 4.40 (m, 2H), 4.05 (t, *J* = 6.3 Hz, 2H), 2.73 (m, 2H), 1.70 (m, 2H), 1.61 (quin, *J* = 7.0 Hz, 2H), 1.48 (m, 1H), 1.37 (quin, *J* = 7.0 Hz, 2H), 1.26 (overlapping s and m, 11 H), 1.89 (s, 9H), 1.08 (qd, *J* = 3.5 Hz, *J* = 12.6 Hz, 2H)

11: ^{13}C NMR ($CDCl_3$, 176 MHz): δ 178.8, 176.2, 64.4, 45.7, 38.9, 38.8, 36.3, 36.2, 32.7, 28.9, 28.6, 27.4, 23.1

2-(diethylamino)ethyl pivalate (12):



12

General procedure **B** was followed using triethylamine (0.75 mmol, 104 µL, 15 equiv), $CuCl_2 \cdot 2H_2O$ (0.1 mmol, 17 mg, 1 equiv), 0.25 mL of aqueous H_2SO_4 (0.83 mmol, 16.5 equiv, 3.3 M stock solution), and K_2PtCl_4 (0.0005 mmol, 40 µL of a 0.0124 M aqueous stock solution, 1 mol %). The reaction was stirred at 150 °C for 48 h. The reaction stirred at 150 °C for 24 h. The reaction was performed side-by-side in duplicate, the two duplicate runs were combined, and the hydroxylated product was protected via general procedure **C**. The product was then purified by silica column chromatography (gradient of 1% to 10%, MeOH in DCM).

Isolated Yield: 88% (17.8 mg, single isomer, orange oil)

R_f: 0.31 (10% MeOH/ 90% DCM)

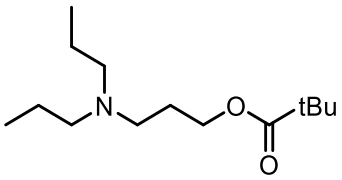
IR (υ, cm^{-1}): 2970, 2818, 1727, 1480, 1460, 1396, 1364, 1282, 1151, 1066, 1036

HRMS: ESI^+ (m/z): $[M+H]^+$ calcd for $C_{11}H_{24}NO_2$: 202.1802; found: 202.1801

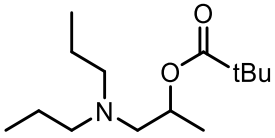
^1H NMR ($CDCl_3$, 700 MHz): δ 4.13 (t, *J* = 6.3 Hz, 2H), 2.70 (t, *J* = 6.3 Hz, 2H), 2.57 (q, *J* = 7.0 Hz, 4H), 1.19 (s, 9H), 1.03 (t, *J* = 7.0 Hz, 6H)

^{13}C NMR ($CDCl_3$, 176 MHz): δ 178.7, 63.1, 51.1, 47.9, 38.8, 27.4, 12.3

3-(dipropylamino)propyl pivalate (13):



13



13a

General procedure **B** was followed using tripropylamine (0.75 mmol, 142 µL, 15 equiv), $CuCl_2 \cdot 2H_2O$ (0.1 mmol, 17 mg, 1 equiv), 0.25 mL of aqueous H_2SO_4 (0.83 mmol, 16.5 equiv, 3.3 M stock solution), and K_2PtCl_4 (0.00025 mmol, 20 µL of a 0.0124 M aqueous stock solution, 0.5 mol %). The reaction was stirred at 150 °C for 24 h. Trace amounts of the dihydroxylated product were observed at the end of the reaction. The reaction was performed side-by-side in duplicate, the two duplicate runs were combined, and the hydroxylated product was protected via general procedure **C**. The product was then purified by silica column chromatography (gradient of 1% to 10%, MeOH in DCM).

Isolated Yield: 102% (24.9 mg, crude ratio of **13-OH** to **13a-OH** = 7 : 1; isolated ratio of **13** : **13a** = >20 : 1; yellow oil)

R_f: 0.50 (10% MeOH/90% DCM)

IR (υ, cm^{-1}): 2958, 2803, 1728, 1480, 1459, 1283, 1079

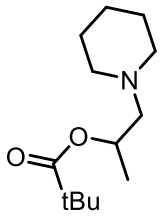
HRMS: ESI^+ (m/z): $[M+H]^+$ calcd for $C_{14}H_{30}NO_2$: 244.2272; found: 244.2271

^{1}H NMR ($CDCl_3$, 400 MHz): δ 4.09 (t, *J* = 6.4 Hz, 2H), 2.47 (t, *J* = 7.2 Hz, 2H), 2.34 (t, *J* = 7.2 Hz, 4H), 1.73 (quin, *J* = 6.4 Hz, 2H), 1.42 (sex, *J* = 7.2 Hz, 4H), 1.19 (s, 9H), 0.86 (t, *J* = 7.2 Hz, 6H)

^{13}C NMR ($CDCl_3$, 176 MHz): δ 178.7, 62.9, 56.3, 50.5, 38.8, 27.3, 26.6, 20.5, 12.1

3-(piperidin-1-yl)propyl pivalate (14):

14



14a

General procedure **B** was followed using 1-propylpiperidine (0.25 mmol, 31.8 mg, 5 equiv), $CuCl_2$•$2H_2O$ (0.1 mmol, 17 mg, 1 equiv), 0.25 mL of aqueous H_2SO_4 (0.28 mmol, 5.5 equiv, 1.1 M stock solution), and K_2PtCl_4 (0.0025, 1.0 mg, 5 mol %). The reaction was stirred at 150 °C for 24 h. The reaction was performed side-by-side in duplicate, the two duplicate runs were combined, and the hydroxylated product was protected via general procedure **C**. The product was then purified by silica column chromatography (gradient 1% to 10%, MeOH in DCM).

Isolated Yield: 90% (20.5 mg, crude ratio of **14-OH** : **14a-OH** = 14 : 1; isolated ratio of **14** : **14a** = >20 : 1; light yellow oil)

R_f: 0.33 (10% MeOH/90% DCM)

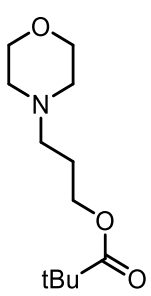
IR (υ, cm^{-1}): 2935, 2769, 1728, 1672, 1480, 1283, 1152, 1126, 1037

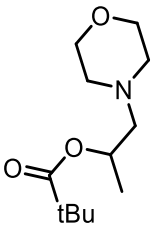
HRMS: ESI$^+$ (m/z): $[M+H]^+$ calcd for $C_{13}H_{26}NO_2$: 228.1958; found: 228.1956

^{1}H NMR ($CDCl_3$, 700 MHz): δ 4.09 (t, *J* = 6.3 Hz, 2H), 2.36 (t, *J* = 7.7 Hz, 6H), 1.82 (quin, *J* = 6.3 Hz, 2H), 1.58 (quin, *J* = 5.6 Hz, 4H), 1.43 (br m, 2H), 1.19 (s, 9H)

^{13}C NMR ($CDCl_3$, 176 MHz): δ 178.5, 62.2, 55.4, 54.1, 39.0, 27.4, 24.9, 24.2, 23.3

3-morpholinopropyl pivalate (15):





15 **15a**

General procedure **B** was followed using 1-propylmorpholine (0.25 mmol, 32.3 mg, 5 equiv), $CuCl_2 \cdot 2H_2O$ (0.1 mmol, 17 mg, 1 equiv), 0.25 mL of aqueous H_2SO_4 (0.28 mmol, 5.5 equiv, 1.1 M stock solution), and K_2PtCl_4 (0.0025, 1.0 mg, 5 mol %). The reaction was stirred at 150 °C for 24 h. The reaction was performed side-by-side in duplicate, the two duplicate runs were combined, and the hydroxylated product was protected via general procedure **C**. The product was then purified by silica column chromatography (gradient of 1% to 10%, MeOH in DCM).

Isolated Yield: 122% (27.9 mg, crude ratio of **15-OH** : **15a-OH** = 10 : 1; isolated ratio of **15** : **15a** = >20 : 1; light yellow oil)

R_f: 0.61 (10% MeOH/90% DCM)

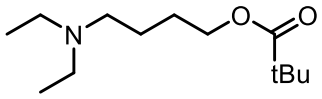
IR (υ, cm^{-1}): 2964, 2906, 1725, 1485, 1284, 1152, 1117, 1036, 862

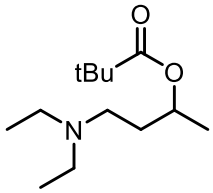
HRMS: ESI$^+$ (m/z): $[M+H]^+$ calcd for $C_{12}H_{24}NO_3$: 230.1752; found: 230.1751

^{1}H NMR ($CDCl_3$, 400 MHz): δ 4.11 (t, *J* = 6.4 Hz, 2H), 3.71 (t, *J* = 4.4 Hz, 4H), 2.43 (multiple peaks, 6H), 1.82 (quin, *J* = 6.4 Hz, 2H), 1.19 (s, 9H)

^{13}C NMR ($CDCl_3$, 176 MHz): δ 178.7, 67.1, 62.8, 55.6, 53.9, 38.9, 27.3, 26.0

4-(diethylamino)butyl pivalate (19):





19-OPiv **19a-OPiv**

General procedure **B** was followed using diethylbutylamine (0.25 mmol, 43 µL, 5 equiv), $CuCl_2 \cdot 2H_2O$ (0.1 mmol, 17 mg, 1 equiv), 0.25 mL of aqueous H_2SO_4 (0.28 mmol, 5.5 equiv, 1.1 M stock solution) and K_2PtCl_4 (0.0005 mmol, 40 µL of a 0.0124 M aqueous stock solution, 1 mol %). The reaction was stirred at 150 °C for 24 h. The reaction was performed side-by-side in duplicate, the two duplicate runs were combined, and the hydroxylated product was protected

via general procedure **C**. The product was then purified by silica column chromatography (gradient of 1% to 10%, MeOH in DCM).

Isolated Yield: 52% (11.9 mg, crude ratio of **19-OH : 19a-OH** = 3 : 1; isolated ratio **19-OPiv : 19a-OPiv** = 6 : 1; yellow oil)

R_f (mixture of isomers): 0.39 (10% MeOH/90% DCM)

IR (υ, cm^{-1}) (mixture of isomers): 2970, 2804, 1728, 1480, 1368, 1284, 1154, 1072, 910, 731

19-OPiv: HRMS: ESI$^+$ (m/z): $[M+H]^+$ calcd for $C_{13}H_{28}NO_2$: 230.2115; found: 230.2112
19a-OPiv: HRMS: ESI$^+$ (m/z): $[M+H]^+$ calcd for $C_{13}H_{28}NO_2$: 230.2115; found: 230.2114

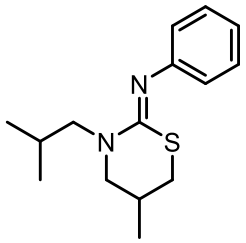
19-OPiv: ^{1}H NMR ($CDCl_3$, 500 MHz): δ 4.07 (t, *J* = 6.5 Hz, 2H), 2.52 (q, *J* = 7.5 Hz, 4H), 2.44 (t, *J* = 7.5 Hz, 2H), 1.64 (quin, *J* = 7.0 Hz, 2H), 1.51 (quin, *J* = 7.5 Hz, 2H), 1.19 (s, 9H), 1.01 (t, *J* = 7.0 Hz, 6H)

19-OPiv: ^{13}C NMR ($CDCl_3$, 100 MHz): δ 178.8, 64.5, 52.6, 47.0, 38.9, 27.4, 27.0, 23.7, 11.8

19a-OPiv: ^{1}H NMR ($CDCl_3$, 500 MHz): δ 4.90 (sex, *J* = 6.5 Hz, 1H), 2.50 (m, 6H), 1.74 (m, 1H), 1.67 (m, 1H), 1.21 (d, *J* = 6.5 Hz, 3H), 1.19 (s, 9H), 1.02 (t, *J* = 7.0 Hz, 6H)

19a-OPiv: ^{13}C NMR ($CDCl_3$, 126 MHz): δ 178.2, 69.5, 48.9, 47.1, 38.9, 29.9, 27.3, 20.3, 11.9

1-isobutyl-5-methyl-3-phenyltetrahydropyrimidine-2(1H)-thione (22)



General procedure **B** was followed using diisobutylamine (0.25 mmol, 43 µL, 5 equiv), $CuCl_2$•$2H_2O$ (0.1 mmol, 17 mg, 1 equiv), 0.25 mL of aqueous H_2SO_4 (0.28 mmol, 5.5 equiv, 1.1 M stock solution), and K_2PtCl_4 (0.005 mmol, 2.1 mg, 10 mol %), and the reaction was stirred at 150 °C for 2 h. The reaction was allowed to cool to room temperature, and the water layer was saturated with NaCl. The reaction mixture was then cooled to room temperature and quenched with NH_4OH (28% aqueous solution, 0.5 mL) and saturated with NaCl. The product was extracted into $CHCl_3$ and filtered through a plug of celite. To the $CHCl_3$ extracts were added triethylamine (0.7 mL) and phenyl isothiocyanate (1.25 mmol, 150 µL, 2.5 equiv). The reaction was allowed to stir overnight at room temperature. The reaction was washed with 1 M NaOH (50 mL), extracted into DCM (2 x 50 mL), and then purified by silica column chromatography (gradient of 1 to 6% MeOH in DCM) and repurified via preparative TLC (5% MeOH in DCM). The product assignment was based on the ^{13}C shift of the imine carbonyl carbon.

Isolated Yield: 73% (19.3 mg, yellow oil)

R_f: 0.53 (10% MeOH/ 90% DCM)

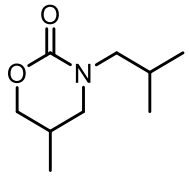
IR (υ, cm^{-1}): 2959, 1575, 1492, 1463, 1358, 1221, 1154

HRMS: ESI^+ (m/z): $[M+H]^+$ calcd for $C_{15}H_{23}N_2S$: 263.1576; found: 263.1578

^1H NMR ($CDCl_3$, 400 MHz): δ 7.24 (t, *J* = 7.6 Hz, 2 H), 6.98 (t, *J* = 7.2 Hz, 1H), 6.81 (d, *J* = 7.6 Hz, 2H), 3.43 (dd, *J* = 7.6 Hz, *J* = 2.4 Hz, 2H), 3.28 (ddd, *J* = 6.0 Hz, *J* = 4.0 Hz, *J* = 1.2 Hz, 1H), 3.11 (dd, *J* = 12.8 Hz, *J* = 9.6 Hz, 1H), 2.86 (ddd, *J* = 11.6 Hz, *J* = 4.4 Hz, *J* = 1.2 Hz, 1H), 2.62 (dd, *J* = 12.0 Hz, *J* = 9.6 Hz, 1H), 2.30 (m, 1H), 2.13 (sep, *J* = 6.8 Hz, 1H), 1.08 (d, *J* = 6.8 Hz, 3H), .98 (d, *J* = 1.2 Hz, 3H), .08 (d, *J* = 1.6 Hz, 3H)

^{13}C NMR ($CDCl_3$, 176 MHz): δ 151.5, 150.8, 128.8, 122.7, 122.4, 58.7, 56.2, 34.7, 30.2, 27.2, 20.4, 20.3, 18.8

3-isobutyl-5-methyl-1,3-oxazinan-2-one (23):



23

General procedure **B** was followed using diisobutylamine (0.25 mmol, 43 µL, 5 equiv), $CuCl_2 \cdot 2H_2O$ (0.1 mmol, 17 mg, 1 equiv), 0.25 mL of aqueous H_2SO_4 (0.28 mmol, 5.5 equiv, 1.1 M stock solution), and K_2PtCl_4 (0.005 mmol, 2.1 mg, 10 mol %), and the reaction was stirred at 150 °C for 2 h. The reaction was allowed to cool to room temperature, and then $KHCO_3$ (1 mL of a saturated aqueous solution) was added. The resulting mixture was stirred for 4 h at 50 °C. The reaction was allowed to cool to room temperature, and NH_4OH (0.5 mL of a 28% aqueous solution) was added. The product was extracted into $CHCl_3$ and purified by silica column chromatography (gradient of 1 to 6%, MeOH in DCM).

Isolated Yield: 65% (11.2 mg, single isomer, yellow oil)

R_f: 0.77 (10% MeOH/ 90% DCM)

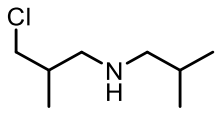
IR (υ, cm^{-1}): 2959, 2925, 2871, 1681, 1488, 1431, 1251, 1204, 1158, 1112, 1073, 758

HRMS: ESI^+ (m/z): $[M+H]^+$ calcd for $C_9H_{18}NO_2$: 172.1332; found: 172.1330

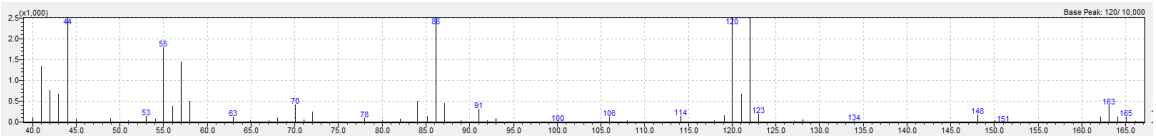
^1H NMR ($CDCl_3$, 700 MHz): δ 4.18 (d, *J* = 10.5 Hz, 1H), 3.85 (t, *J* = 10.5 Hz, 1H), 3.25 (ddd, *J* = 11.9 Hz, *J* = 5.6 Hz, *J* = 1.4 Hz, 1H), 3.21 (dd, *J* = 13.3 Hz, *J* = 7.7 Hz, 1H), 3.06 (dd, *J* = 13.3 Hz, *J* = 7.0 Hz, 1H), 2.97 (dd, *J* = 11.2 Hz, *J* = 9.1 Hz, 1H), 2.25 (m, 1H), 2.00 (sep, *J* = 6.3 Hz, 1H), 1.01 (d, *J* = 7.0 Hz, 3H), 0.91 (d, *J* = 3.5 Hz, 3H), 0.90 (d, *J* = 3.5 Hz, 3H).

^{13}C NMR ($CDCl_3$, 176 MHz): δ 57.0, 52.9, 27.2, 26.5, 20.1, 19.9, 14.1

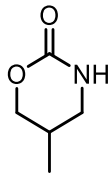
Cl - product **(21)** before derivitization to form **22** and **23**; GC-MS: EI^+ (m/z): $[M]^+$ found: 165.10



21



5-methyl-1,3-oxazinan-2-one (26)



26

General procedure **B** was followed using isobutylamine (0.75 mmol, 74 µL, 15 equiv), $CuCl_2 \cdot 2H_2O$ (0.1 mmol, 17 mg, 1 equiv), 0.25 mL of aqueous H_2SO_4 (0.83 mmol, 16.5 equiv, 3.3 M stock solution), and K_2PtCl_4 (0.005 mmol, 2.1 mg, 10 mol %). The reaction was heated at 150 °C for 2 h. The resulting mixture was allowed to cool to room temperature, after which a solution of saturated aqueous $KHCO_3$ (1 mL) was added. The resulting mixture was stirred at for 1 h at 100 °C, and then allowed to cool to room temperature. NH_4OH (28% aqueous solution, 1 mL) was added. The product was extracted into $CHCl_3$ and purified by silica column chromatography (gradient of 1 to 5%, MeOH in DCM).

Isolated Yield: 59% (6.8 mg, singel isomer, white solid)

R_f: 0.61 (10% MeOH/ 90% DCM)

IR (υ, cm^{-1}): 1688, 1488, 1272, 1112

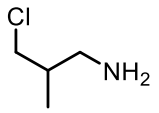
MP: 47-48 °C

HRMS: ESI^+ (m/z): $[M+H]^+$ calcd for $C_5H_{10}NO_2$: 116.0706; found: 116.0707

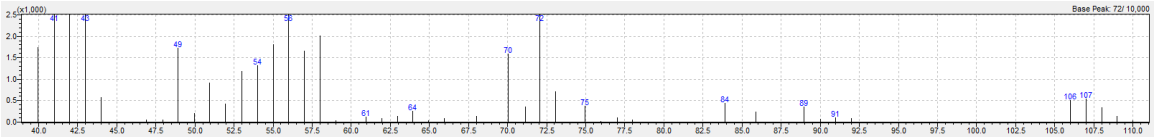
^1H NMR ($CDCl_3$, 500 MHz): δ 5.32 (br s, 1H), 4.24 (ddd, *J* = 11.0 Hz, 3.5 Hz, 2.0 Hz, 1H), 3.92 (dd, *J* = 11.0 Hz, *J* = 10.0 Hz, 1H), 3.39 (m, 1H), 3.01 (t, *J* = 10.0 Hz, 1H), 2.22 (m, 1H), 1.03 (d, *J* = 7.0 Hz, 3H)

^{13}C NMR ($CDCl_3$, 126 MHz): δ 153.9, 72.2, 47.0, 26.3, 13.9

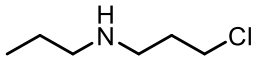
Cl - product **(25)** before derivatization to form **26**; GC-MS: EI^+ (m/z): $[M]^+$ found: 107.00



23



3-chloro-N-propylpropan-1-amine (A):



A

3-(propylamino)propan-1-ol was formed from dipropylamine (General procedure **B**). The volatiles were removed via rotary evaporation. The HCl salt of 3-(propylamino)propan-1-ol was generated using 4M HCl in THF, and dried to obtain a yellow solid. The salt was redissolved in DCM, subjected to excess $SOCl_2$ and allowed to stir at room temperature overnight. The volatiles were removed via rotary evaporation, and the HCl salt of the chlorinated amine was dissolved in $CDCl_3$ and free-based with 1M aqueous NaOH. The ^1H and ^{13}C NMR spectra of the authentic product match the ^1H and ^{13}C NMR shifts of the intermediate formed in the time study, thereby further confirming the identity of terminal chlorinated product as an intermediate en route to the hydroxylated product (see NMR spectra for more detail).

HRMS: ESI^+ (m/z): $[M+H]^+$ calcd for $C_6H_{15}ClN$: 136.0888; found: 136.0888

^1H NMR ($CDCl_3$, 700 MHz): δ 3.59 (t, *J* = 7.0 Hz, 2H), 2.73 (t, *J* = 7.0 Hz, 2H), 2.54 (t, *J* = 7.0 Hz, 2H), 1.92 (quin, *J* = 7.0 Hz, 2H), 1.47 (sex, *J* = 7.0 Hz, 2H), 0.89 (t, *J* = 7.0 Hz, 3H)

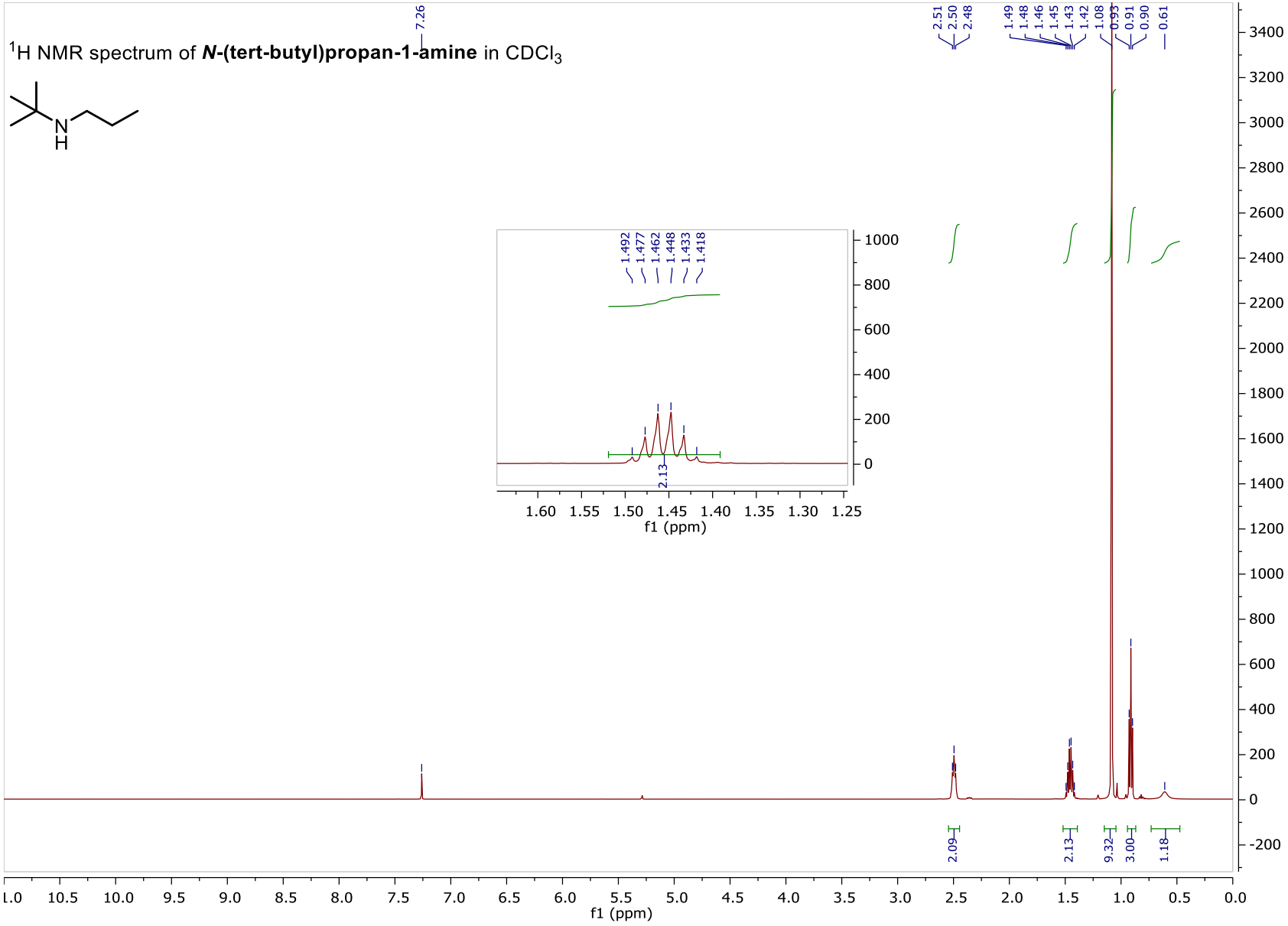
^{13}C NMR ($CDCl_3$, 176 MHz): δ 51.9, 46.9, 43.3, 33.0, 23.3, 11.8

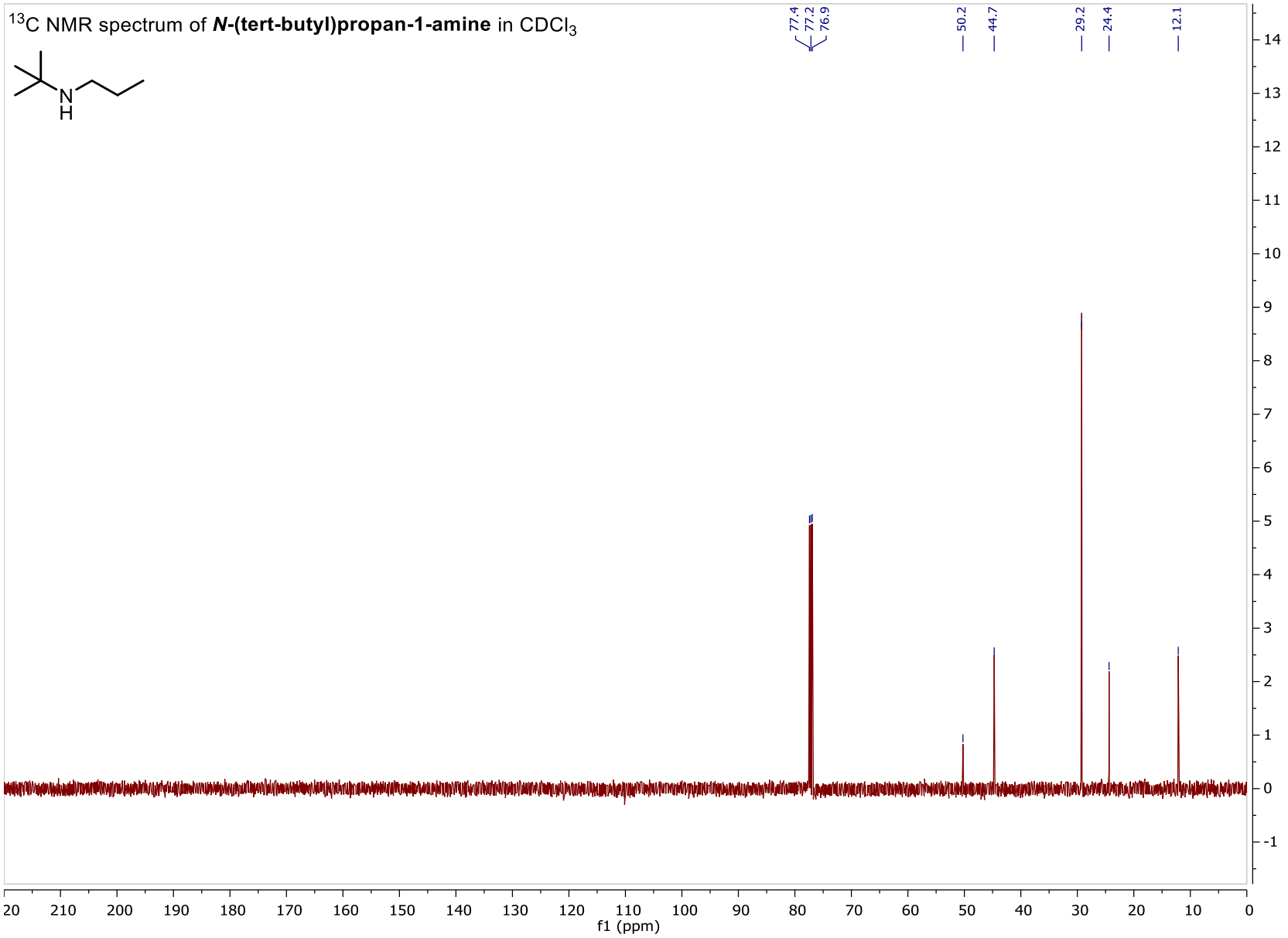
VI. References

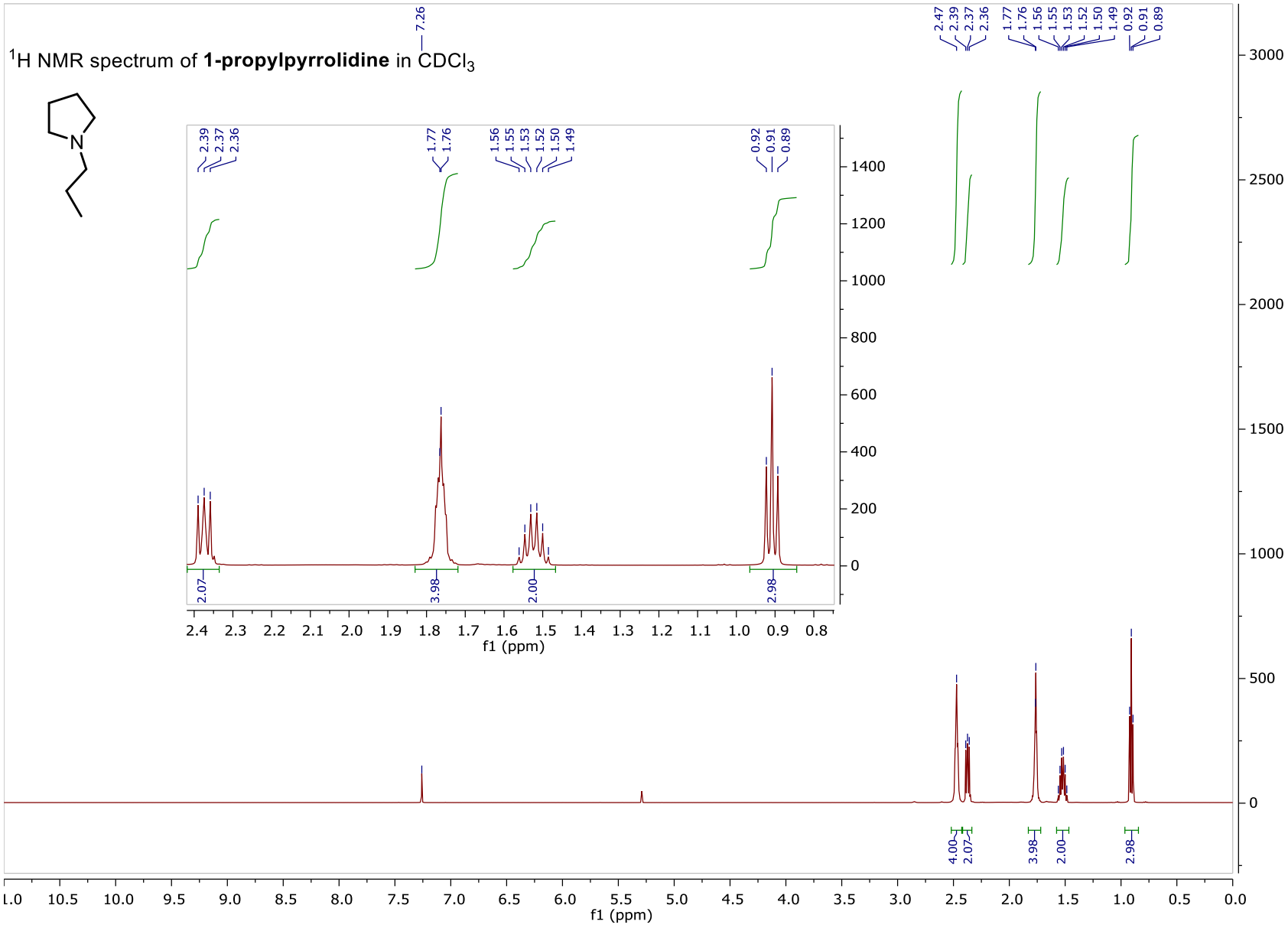
1. Brown, H. C.; Kanth, J. V. B.; Dalvi, P. V.; Zaidlewicz, M. *J. Org. Chem.* **1999**, 64, 6263-6274.

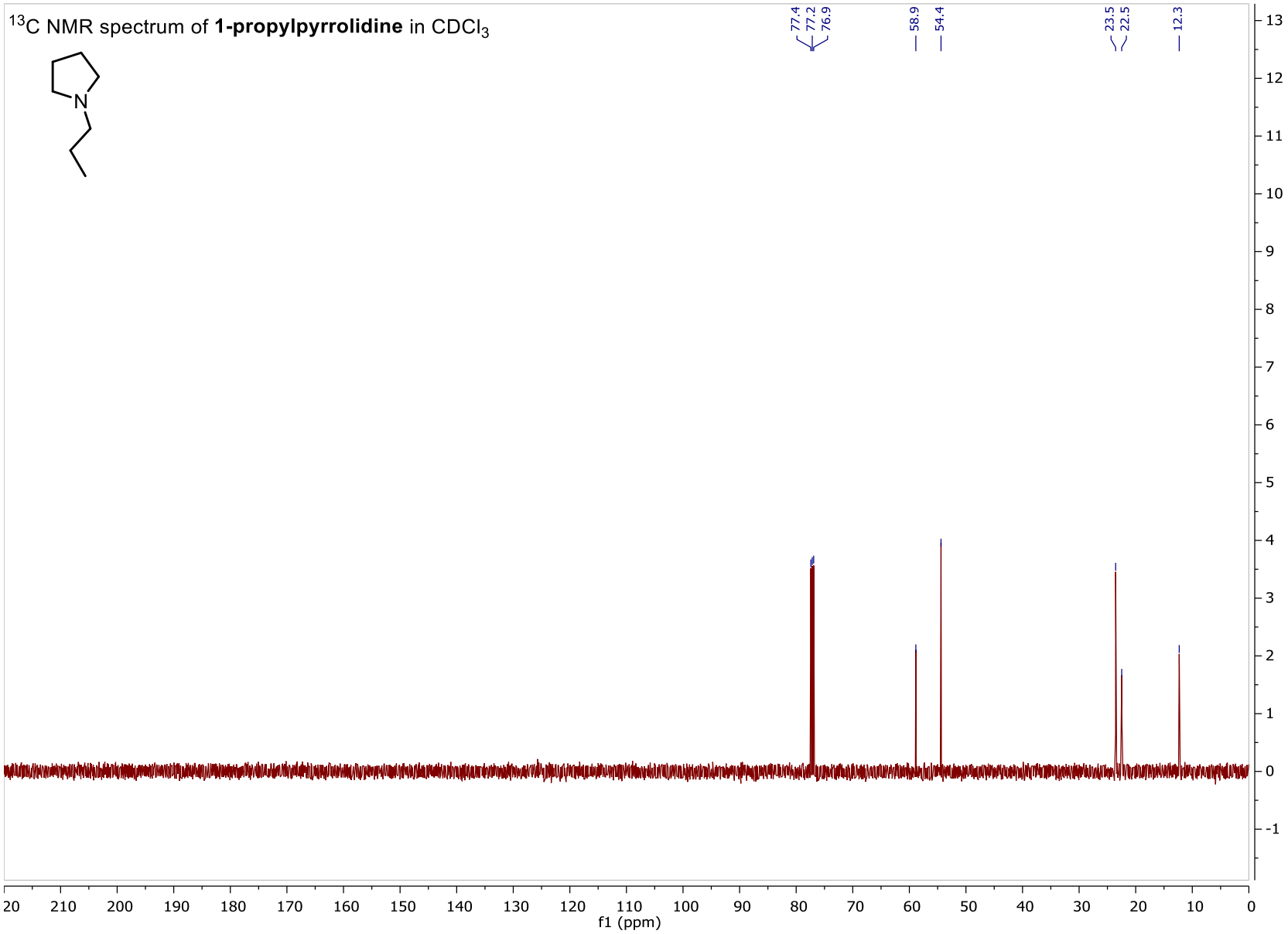
2. Azizi, N.; Saidi, M. R. *Org. Lett.* **2005**, 7, 3649-3651.

3. Velingkar, V. S.; Dandekar, V. D. *Chin. J. Chem.* **2011**, 29, 504-510.

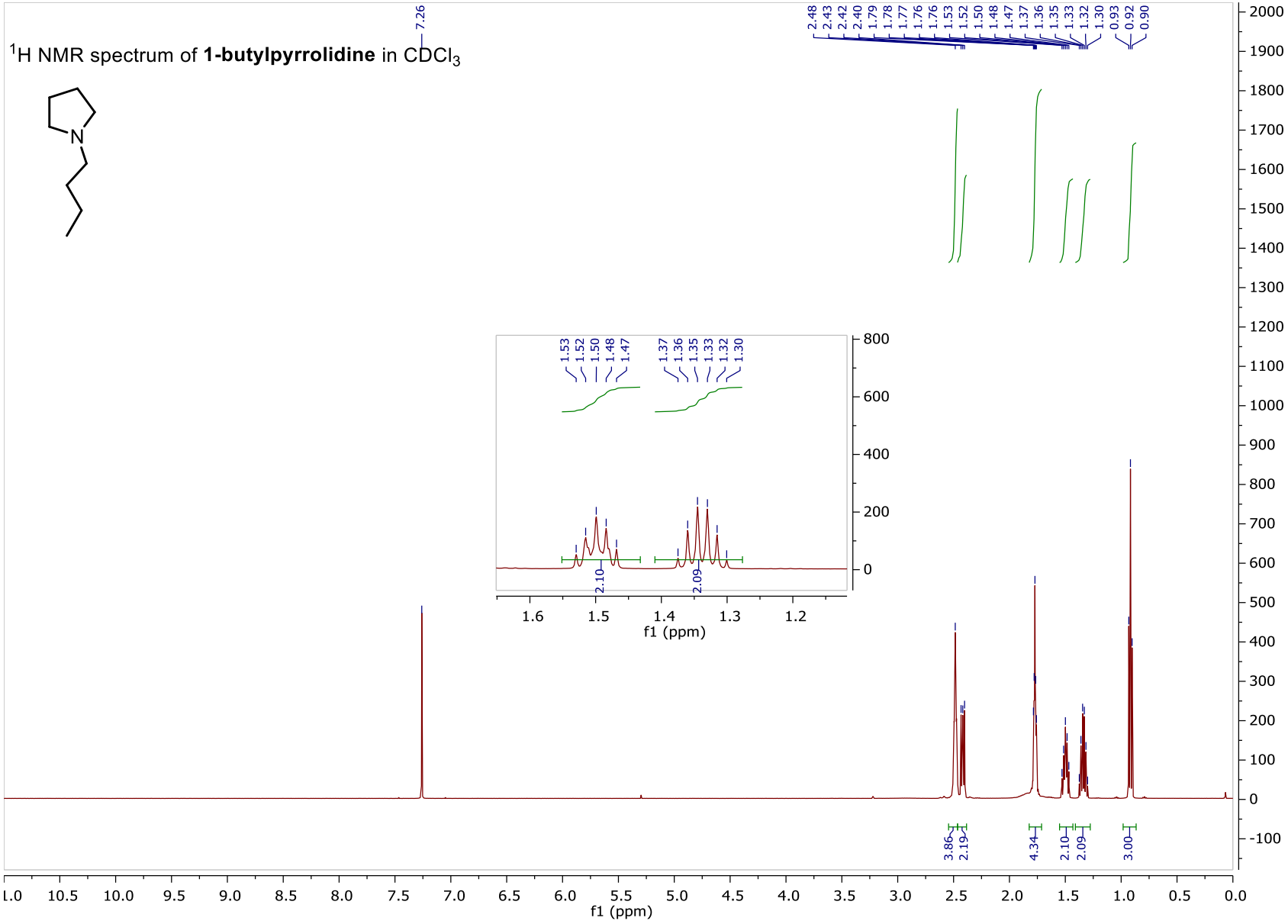

^{1}H NMR spectrum of ***N*-(tert-butyl)propan-1-amine** in $CDCl_3$
7.26
2.51
2.50
2.48
1.49
1.48
1.46
1.45
1.43
1.42
1.08
0.93
0.91
0.90
0.61
1.492
1.477
1.462
1.448
1.433
1.418
2.13
f1 (ppm)
2.09
2.13
9.32
3.00
1.18
f1 (ppm)

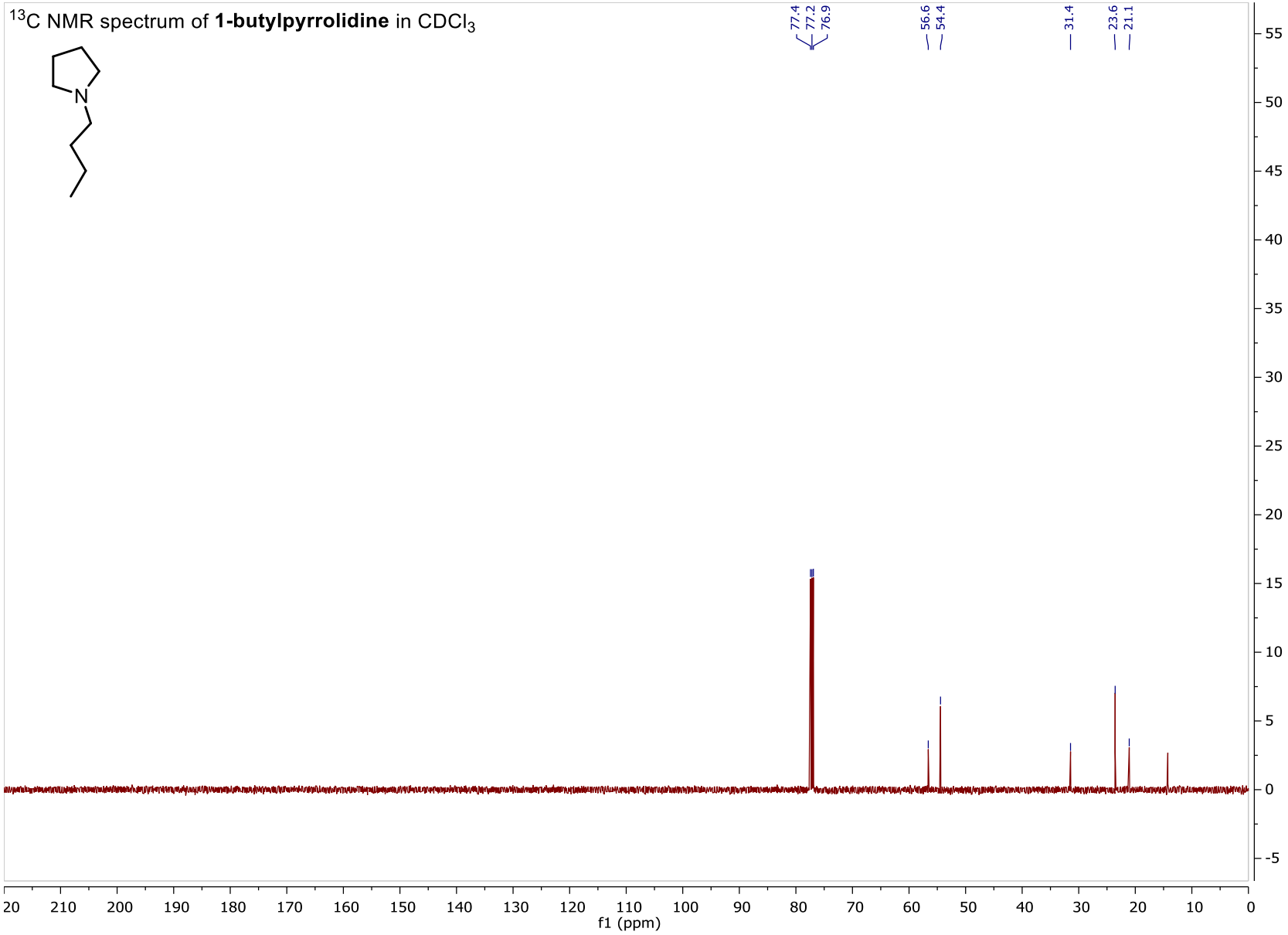

13C NMR spectrum of N-(tert-butyl)propan-1-amine in CDCl3
77.4
77.2
76.9
50.2
44.7
29.2
24.4
12.1
f1 (ppm)

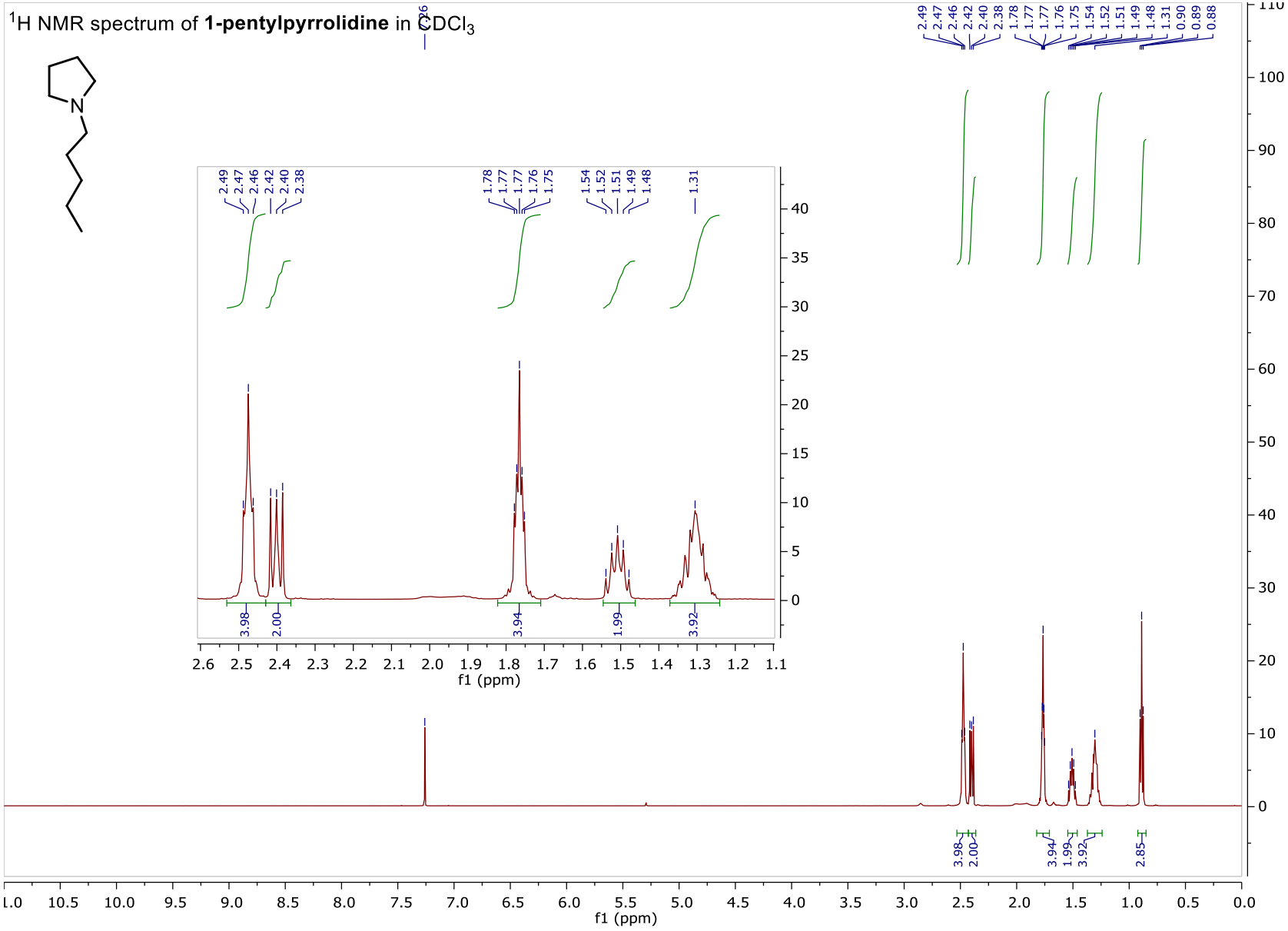

^{1}H NMR spectrum of **1-propylpyrrolidine** in $CDCl_3$
7.26
2.47
2.39
2.37
2.36
1.77
1.76
1.56
1.55
1.53
1.52
1.50
1.49
0.92
0.91
0.89
4.00
2.07
3.98
2.00
2.98
f1 (ppm)

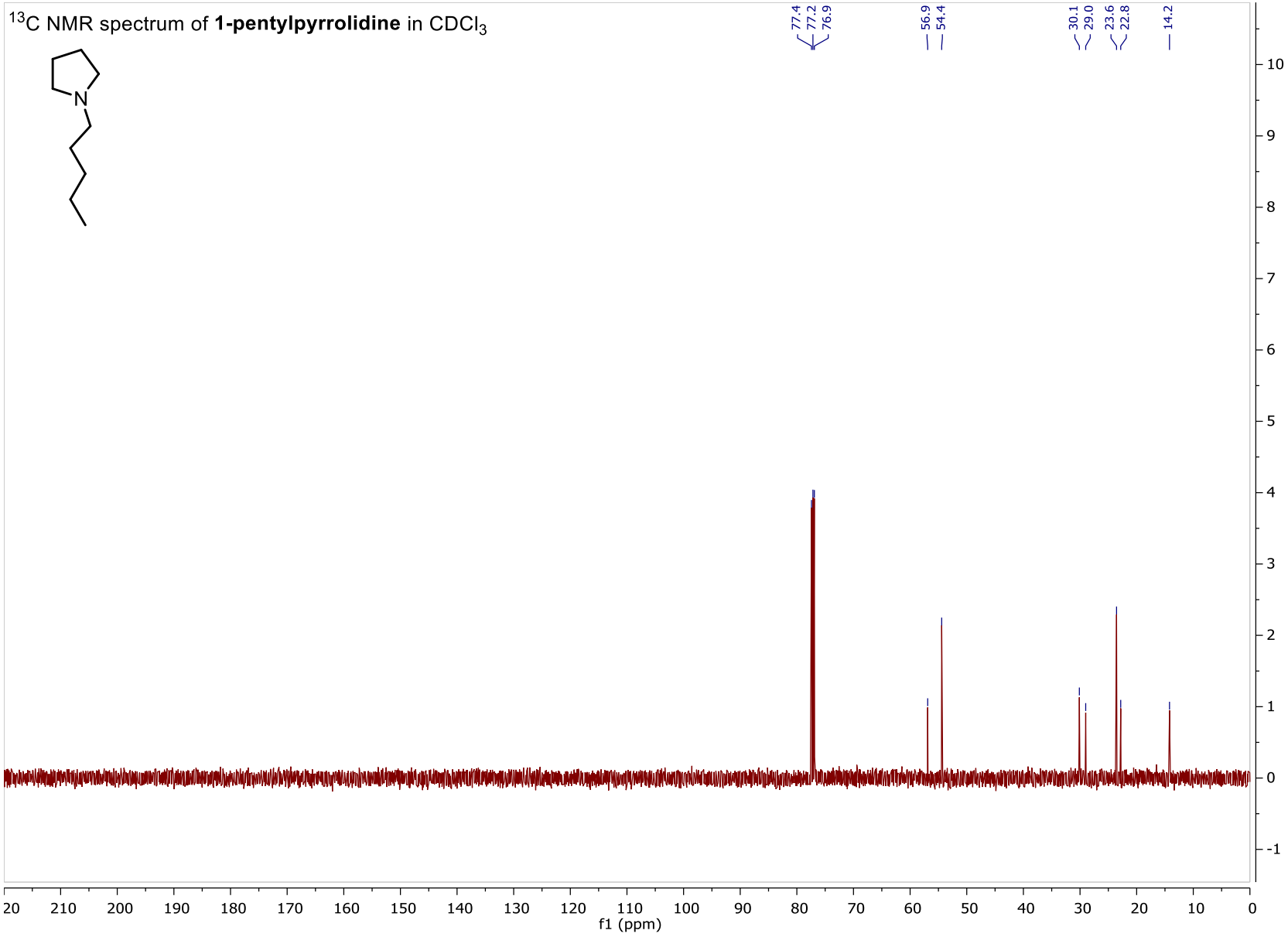

^{13}C NMR spectrum of **1-propylpyrrolidine** in $CDCl_3$
N
77.4
77.2
76.9
58.9
54.4
23.5
22.5
12.3
f1 (ppm)

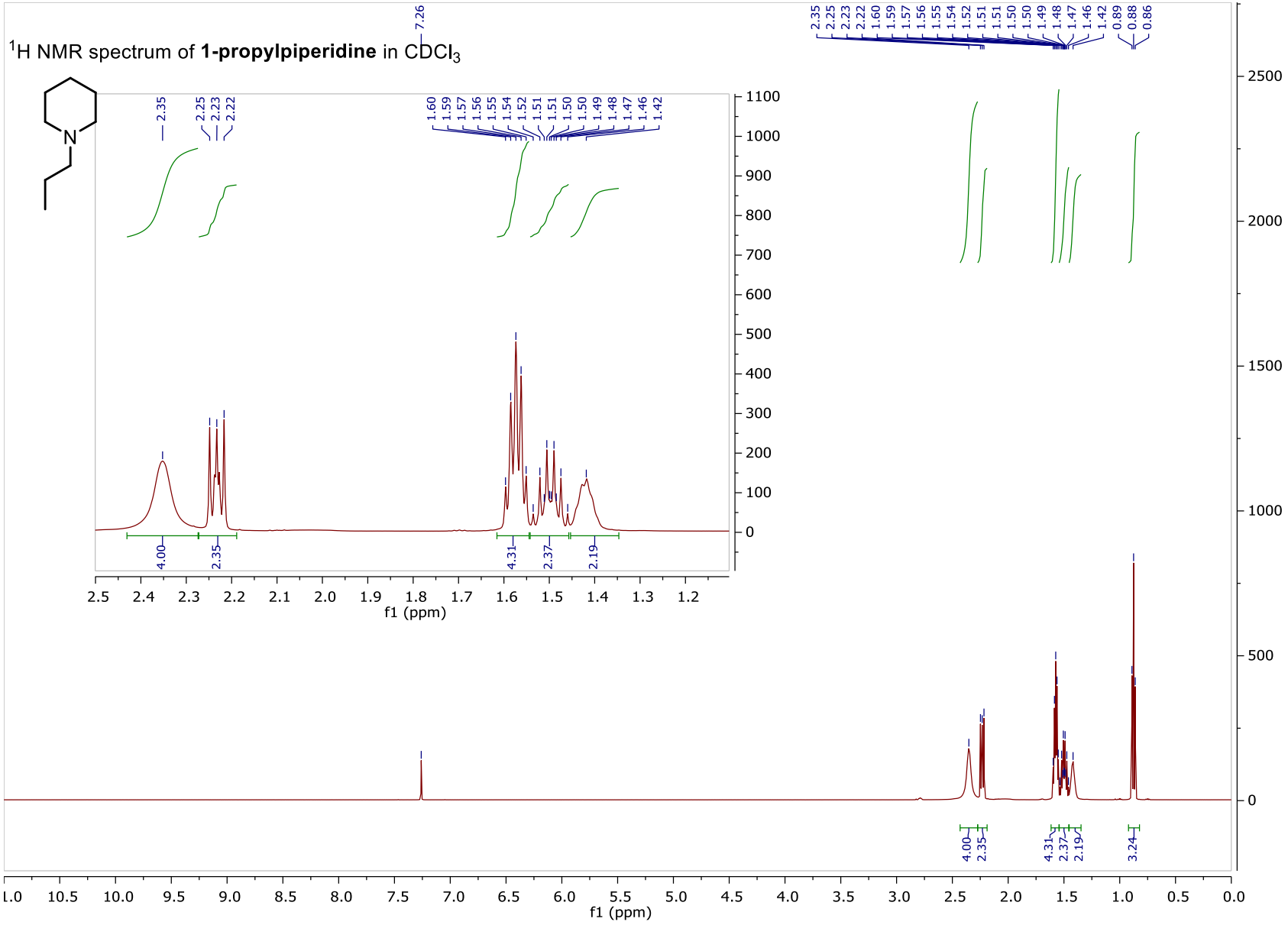
^{1}H NMR spectrum of **1-butylpyrrolidine** in $CDCl_3$



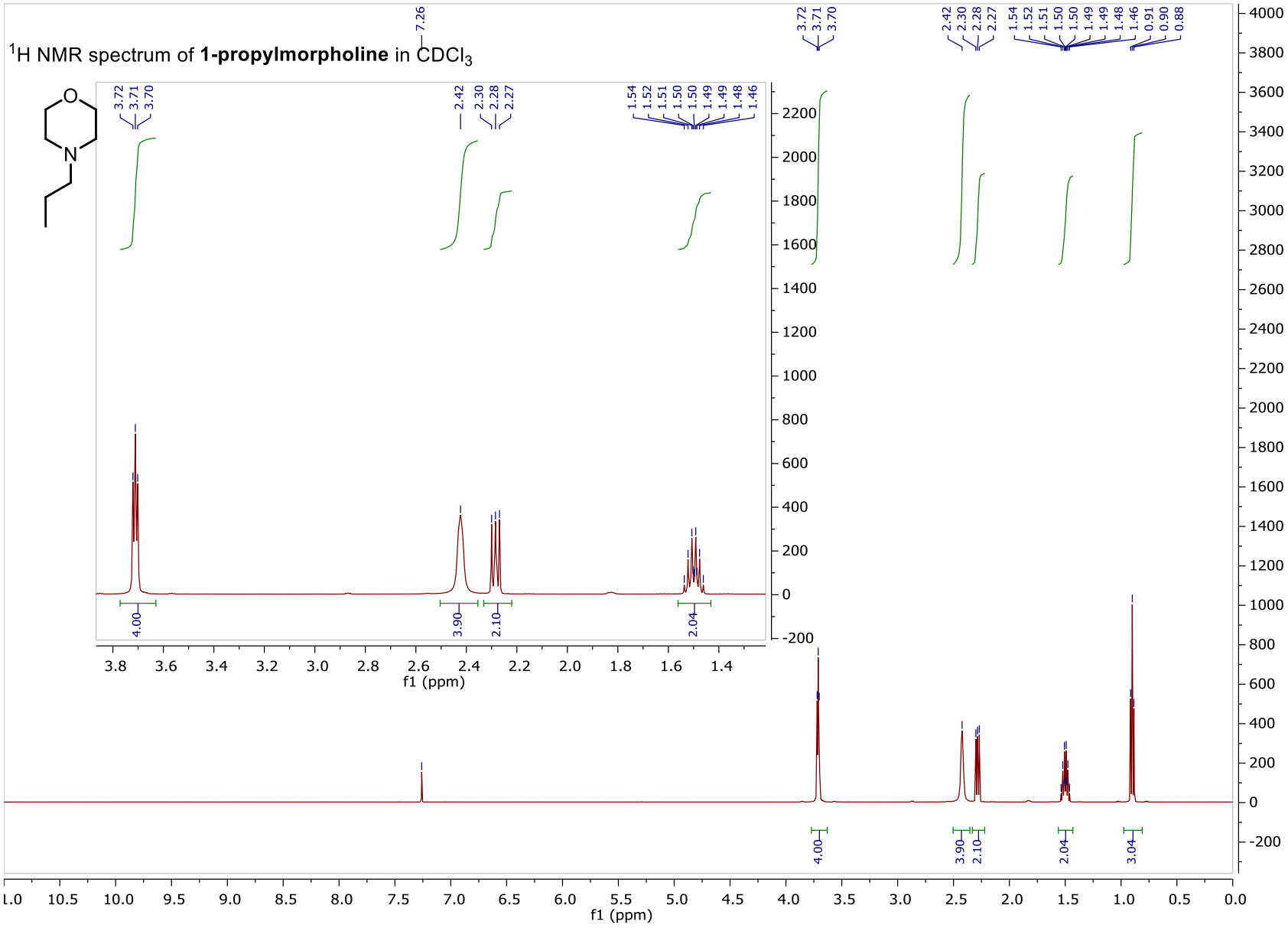

^{13}C NMR spectrum of **1-butylpyrrolidine** in $CDCl_3$
77.4
77.2
76.9
56.6
54.4
31.4
23.6
21.1
f1 (ppm)

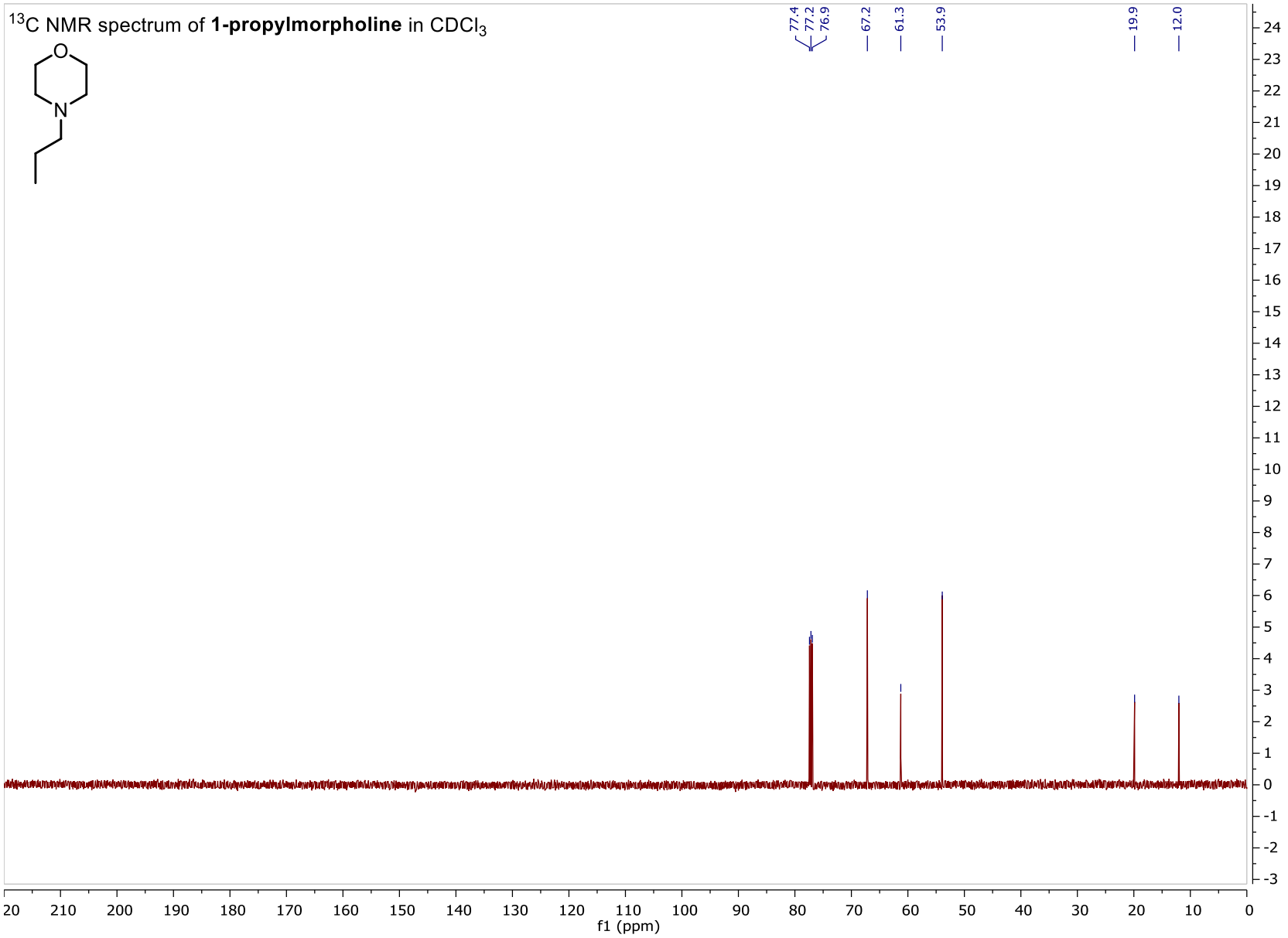

^{1}H NMR spectrum of **1-pentylpyrrolidine** in $CDCl_3$
2.49 2.47 2.46 2.42 2.40 2.38 1.78 1.77 1.77 1.76 1.75 1.54 1.52 1.51 1.49 1.48 1.31 0.90 0.89 0.88
3.98 2.00 3.94 1.99 3.92 2.85
f1 (ppm)

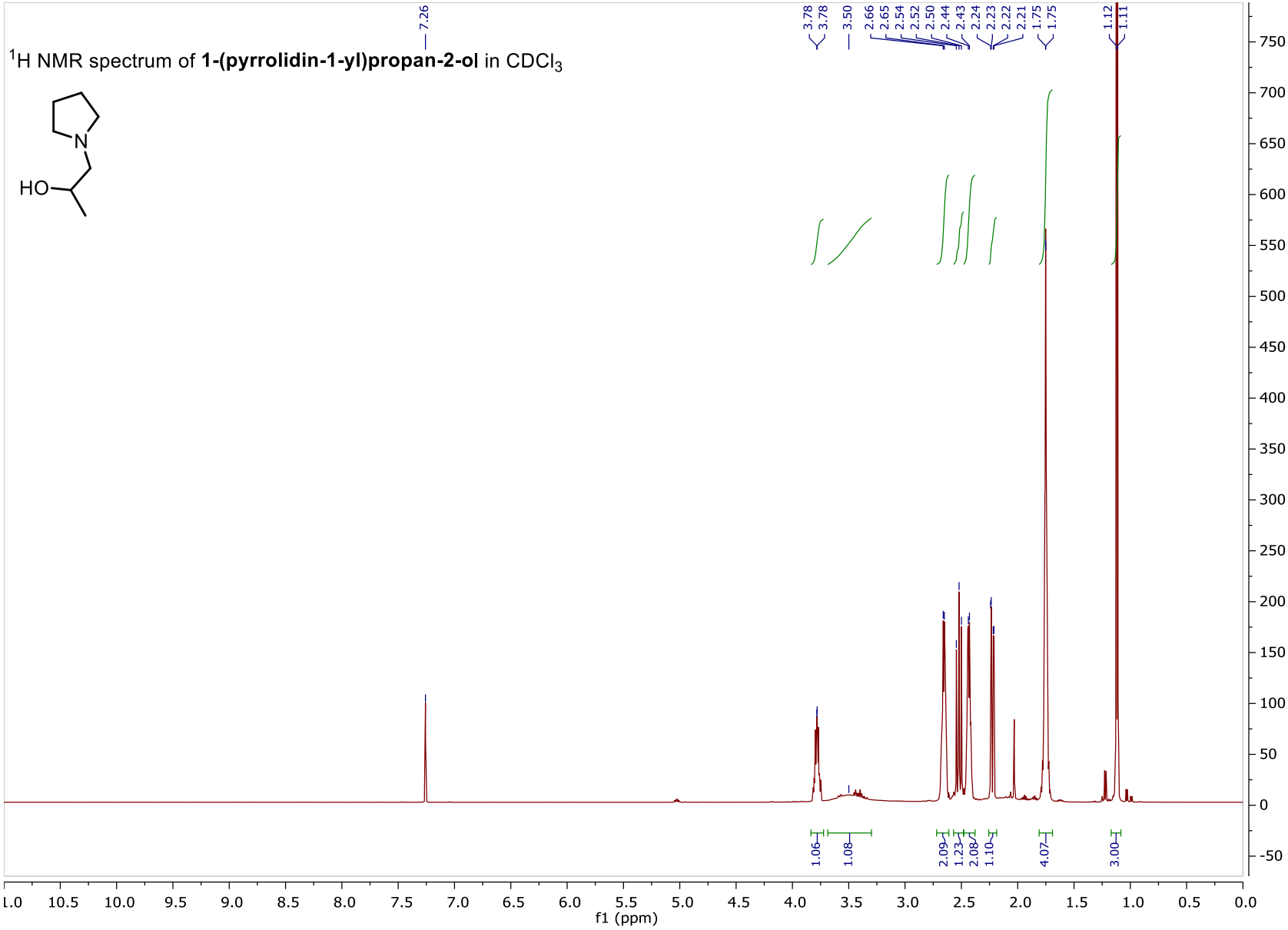

^{13}C NMR spectrum of **1-pentylpyrrolidine** in $CDCl_3$
77.4
77.2
76.9
56.9
54.4
30.1
29.0
23.6
22.8
14.2
f1 (ppm)

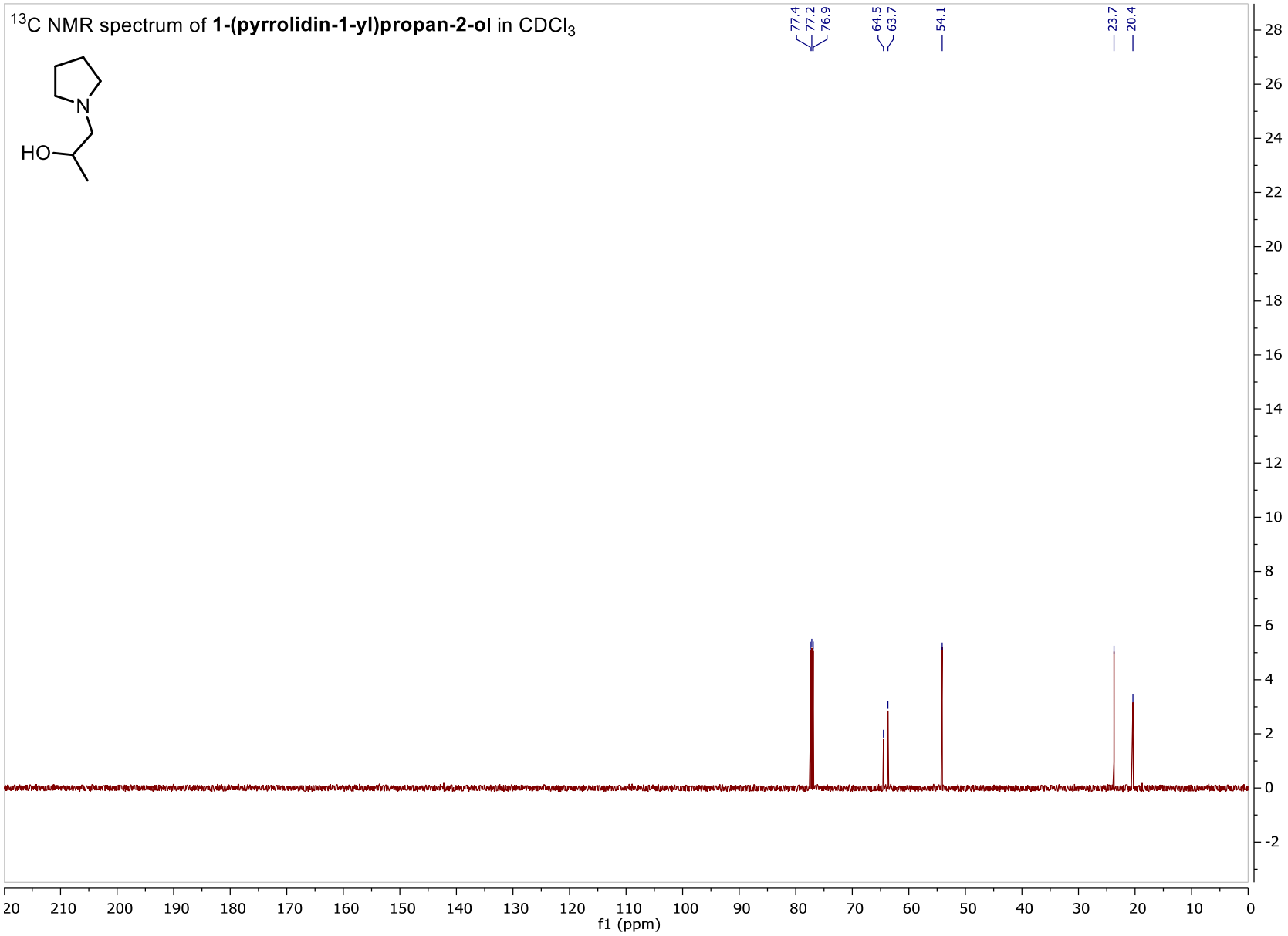

^{1}H NMR spectrum of **1-propylpiperidine** in $CDCl_3$
7.26
2.35
2.25
2.23
2.22
1.60
1.59
1.57
1.56
1.55
1.54
1.52
1.51
1.51
1.50
1.50
1.49
1.48
1.47
1.46
1.42
0.89
0.88
0.86
4.00
2.35
4.31
2.37
2.19
3.24
f1 (ppm)

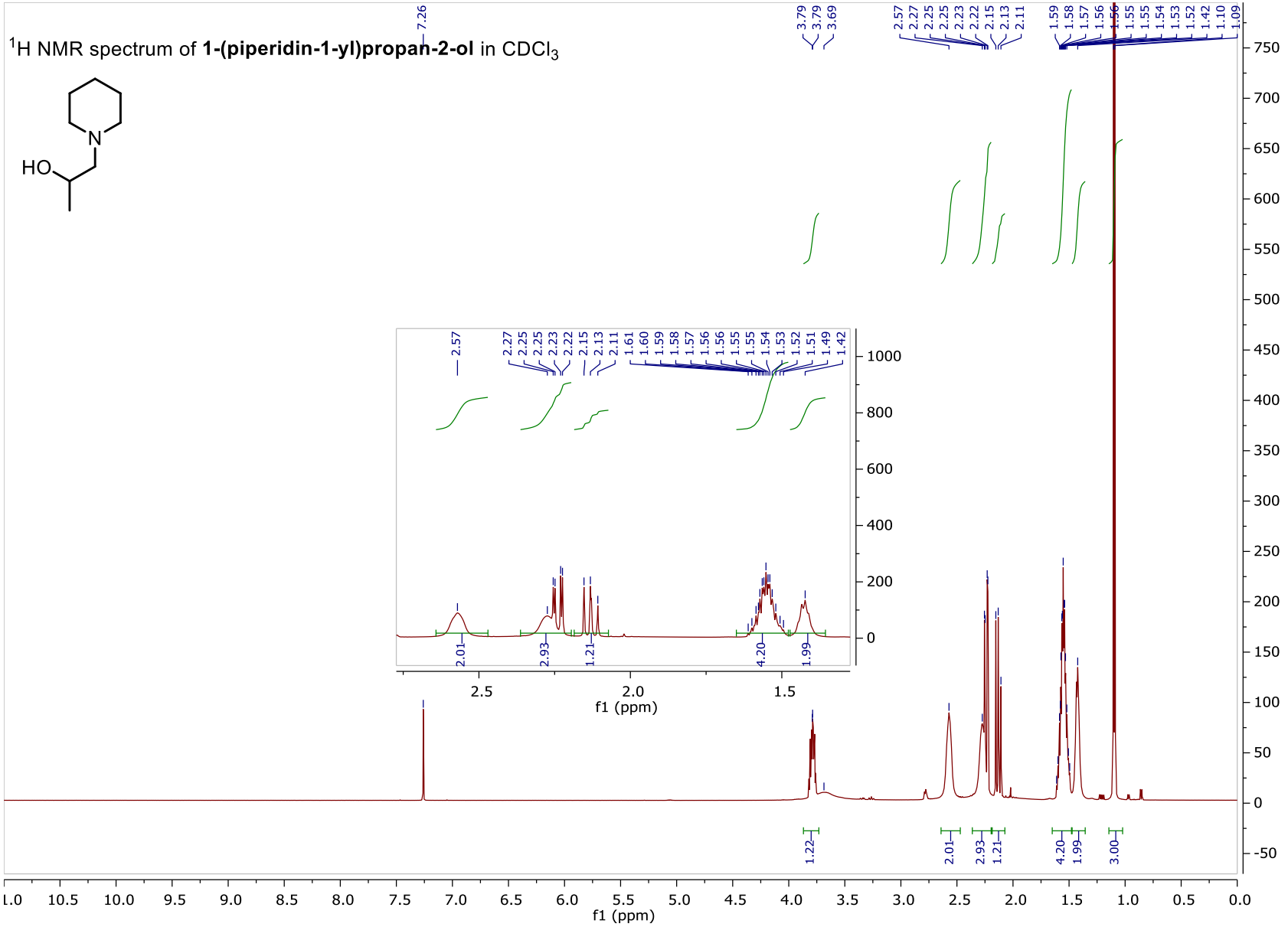
^{13}C NMR spectrum of **1-propylpiperidine** in $CDCl_3$

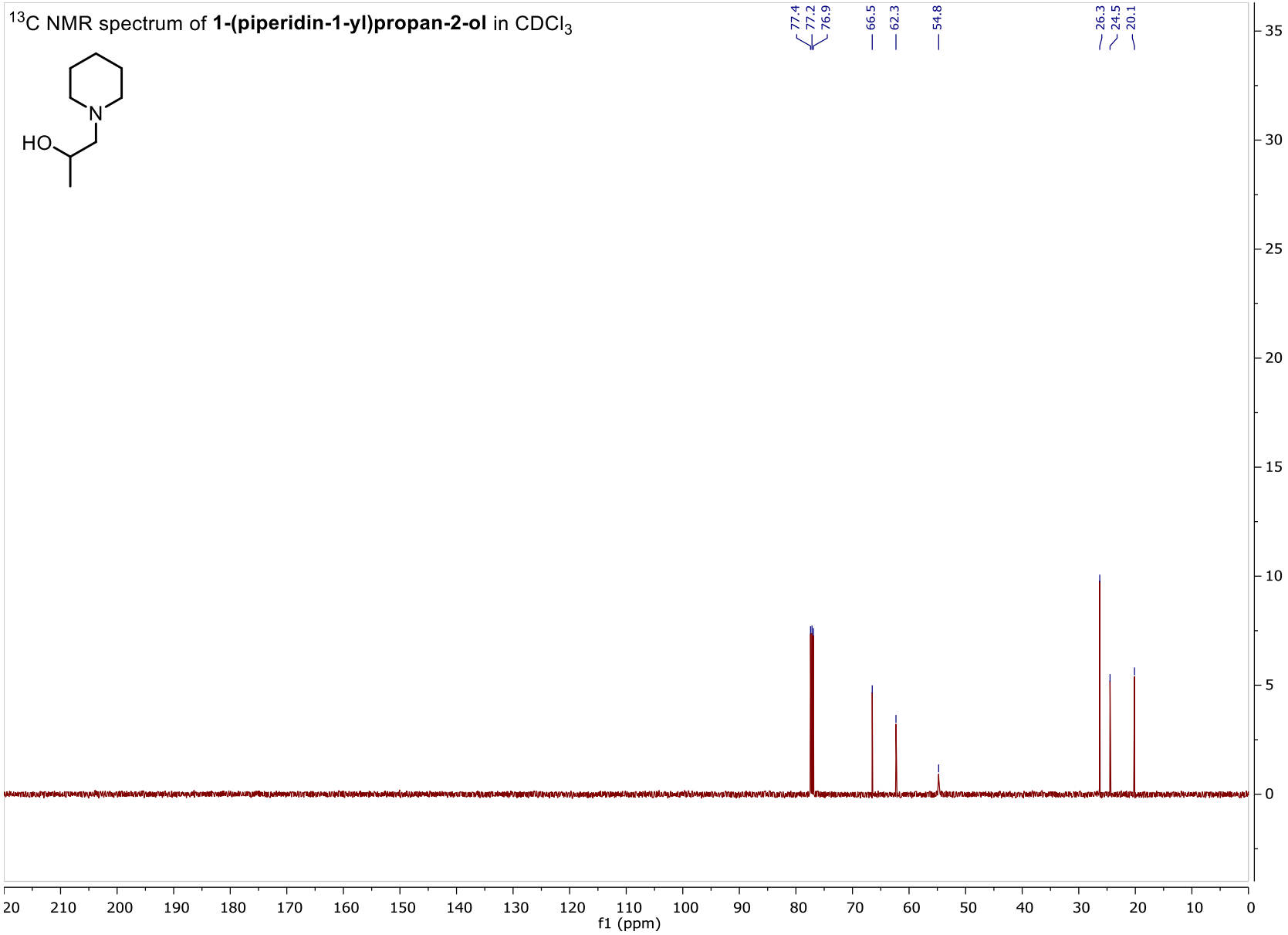

^{1}H NMR spectrum of **1-propylmorpholine** in $CDCl_3$
7.26
3.72
3.71
3.70
2.42
2.30
2.28
2.27
1.54
1.52
1.51
1.50
1.50
1.49
1.49
1.48
1.46
0.91
0.90
0.88
4.00
3.90
2.10
2.04
3.04
f1 (ppm)

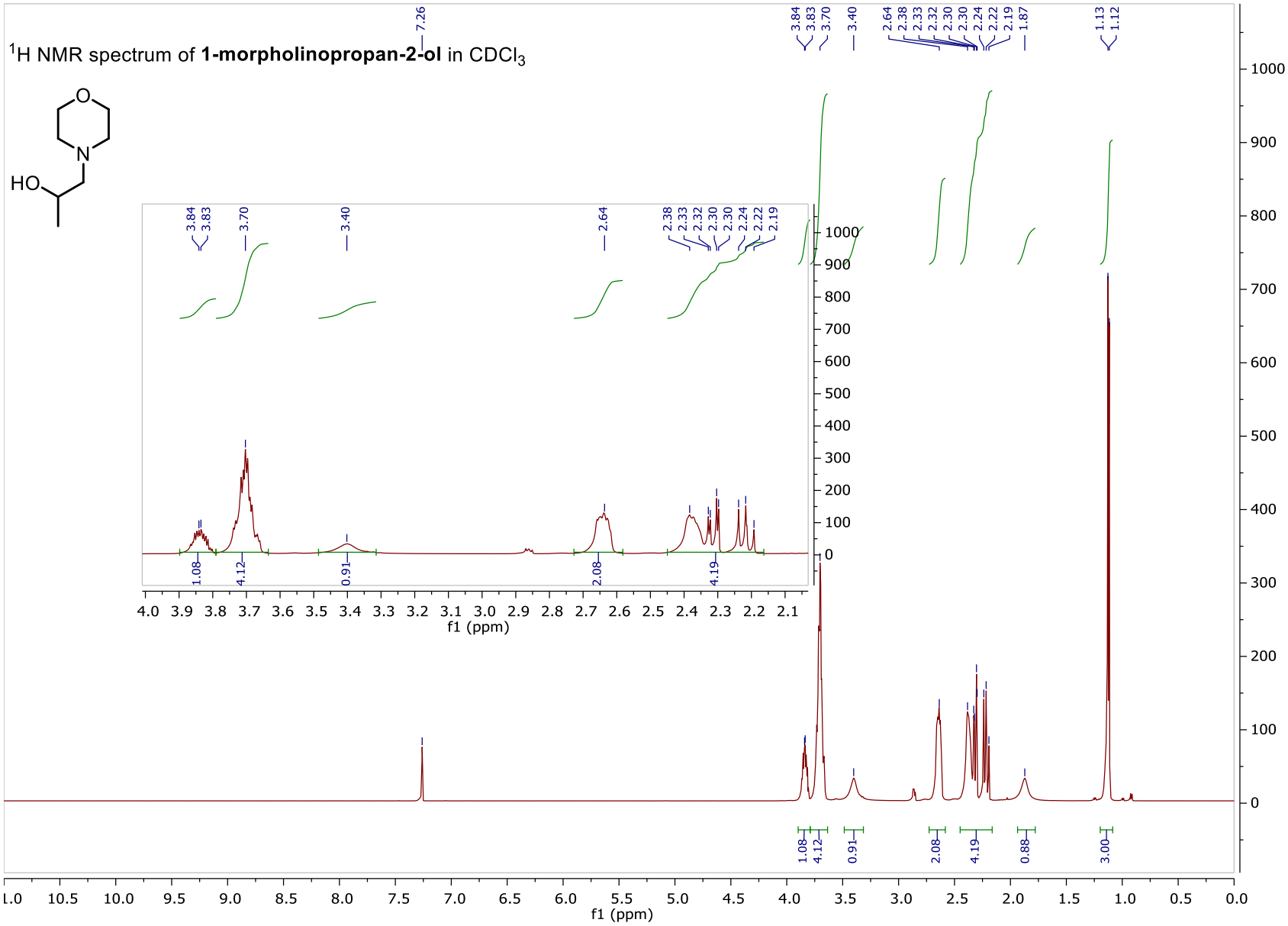

^{13}C NMR spectrum of **1-propylmorpholine** in $CDCl_3$
O
N
77.4
77.2
76.9
67.2
61.3
53.9
19.9
12.0
f1 (ppm)

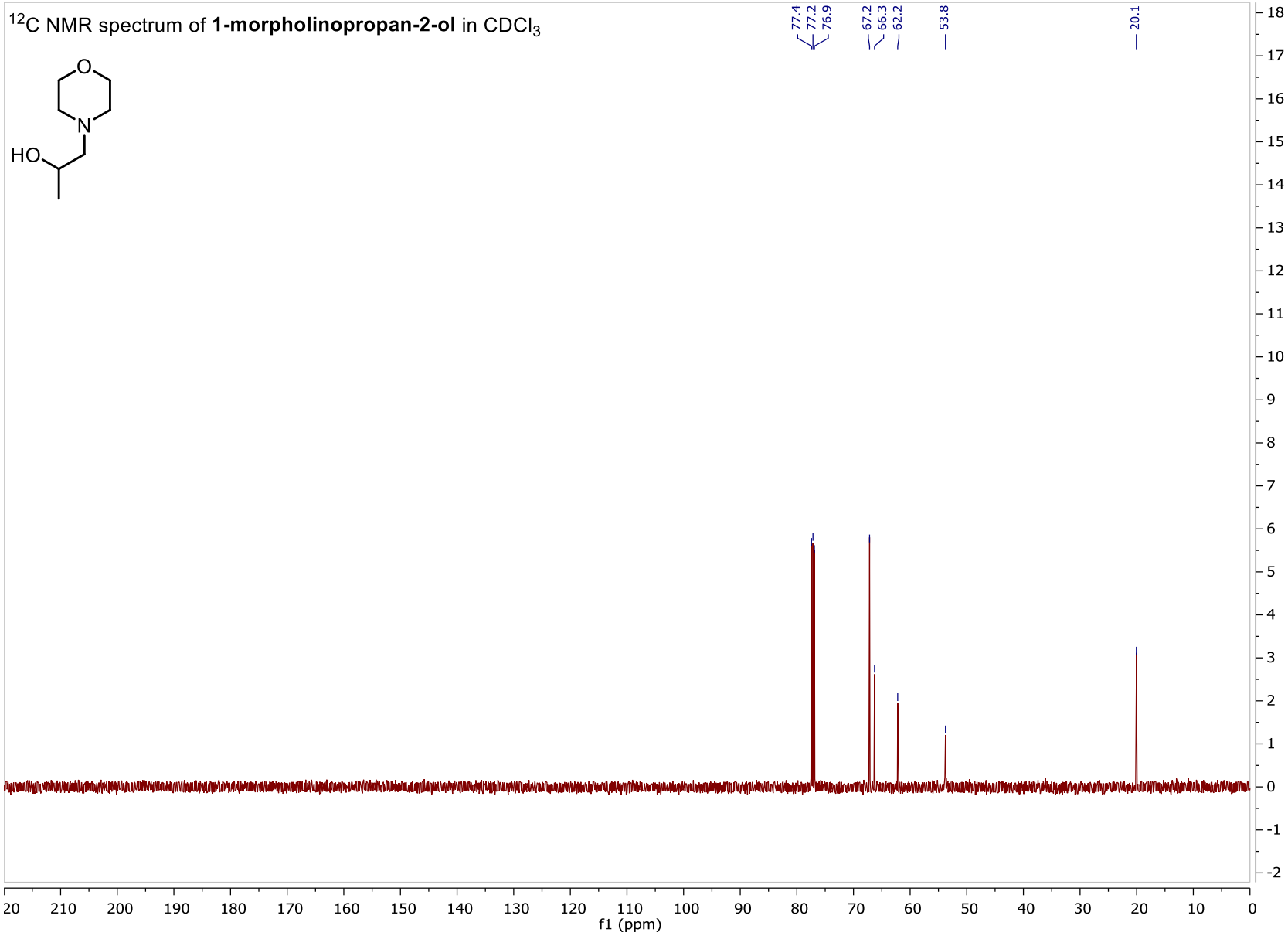

^{1}H NMR spectrum of **1-(pyrrolidin-1-yl)propan-2-ol** in $CDCl_3$
HO
N
7.26
3.78
3.78
3.50
2.66
2.65
2.54
2.52
2.50
2.44
2.43
2.24
2.23
2.22
2.21
1.75
1.75
1.12
1.11
1.06
1.08
2.09
1.23
2.08
1.10
4.07
3.00
f1 (ppm)

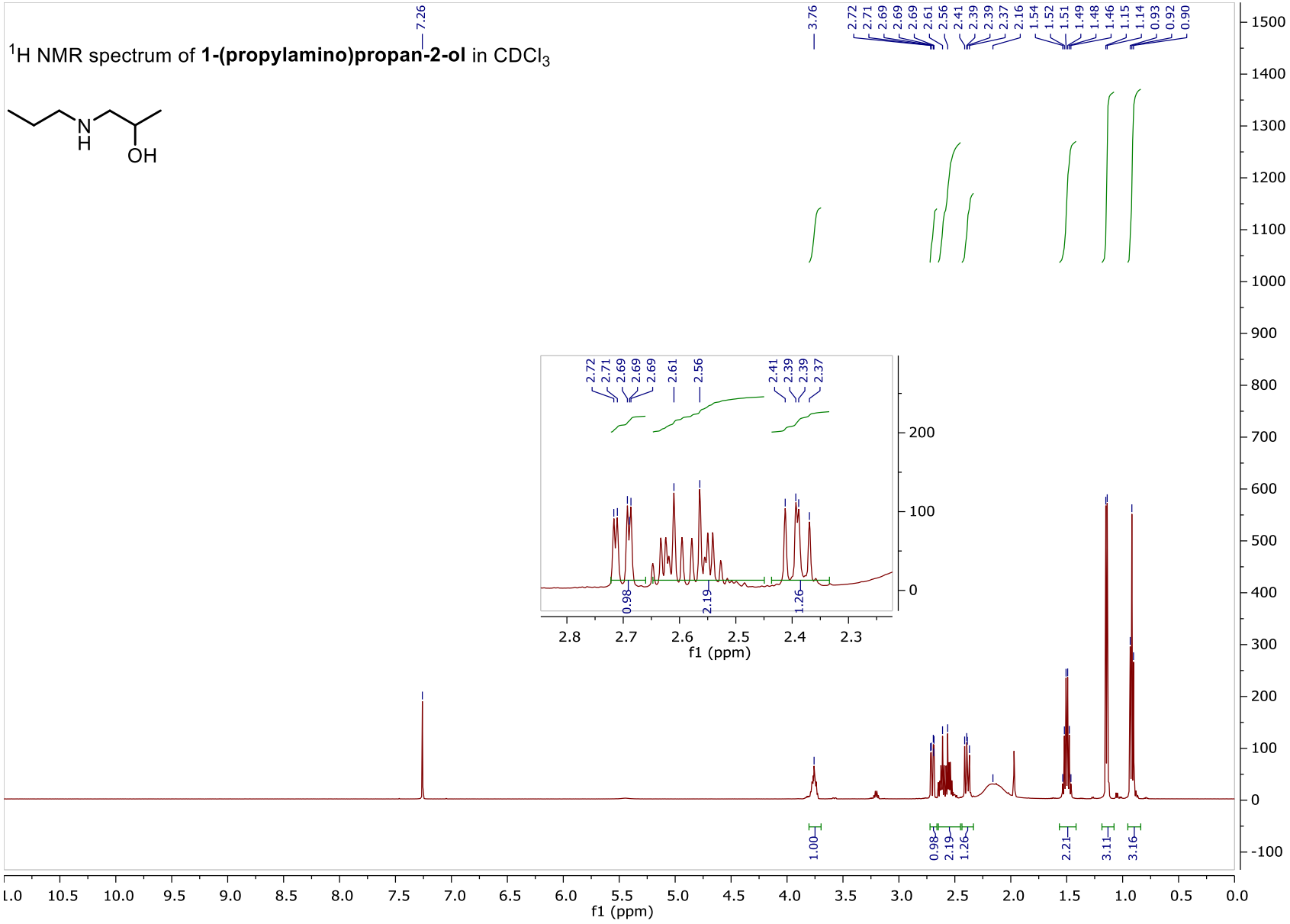

^{13}C NMR spectrum of **1-(pyrrolidin-1-yl)propan-2-ol** in $CDCl_3$
77.4
77.2
76.9
64.5
63.7
54.1
23.7
20.4
N
HO
f1 (ppm)

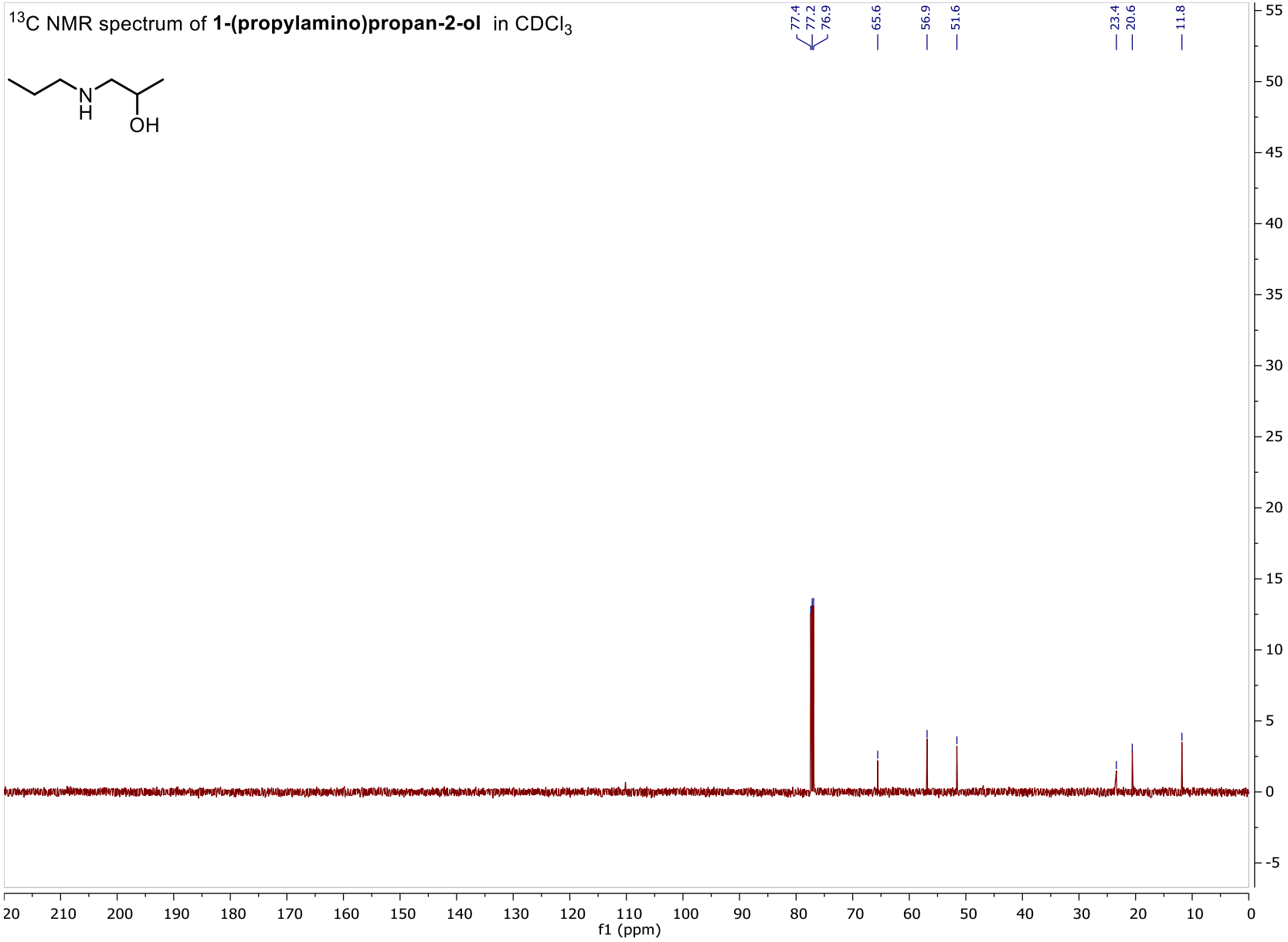

^{1}H NMR spectrum of **1-(piperidin-1-yl)propan-2-ol** in $CDCl_3$
HO
N
f1 (ppm)

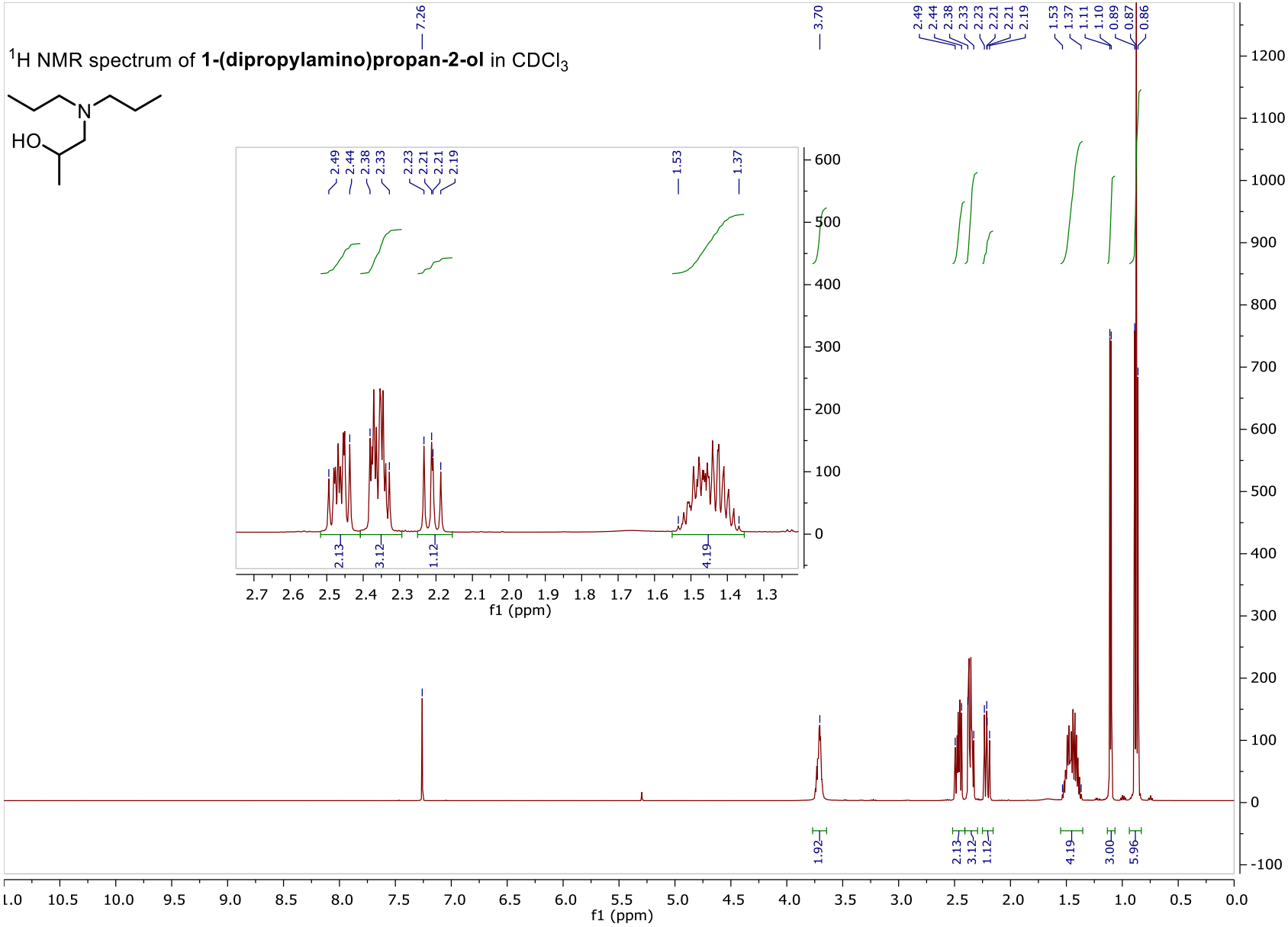

^{13}C NMR spectrum of **1-(piperidin-1-yl)propan-2-ol** in $CDCl_3$
77.4
77.2
76.9
66.5
62.3
54.8
26.3
24.5
20.1
HO
N
f1 (ppm)

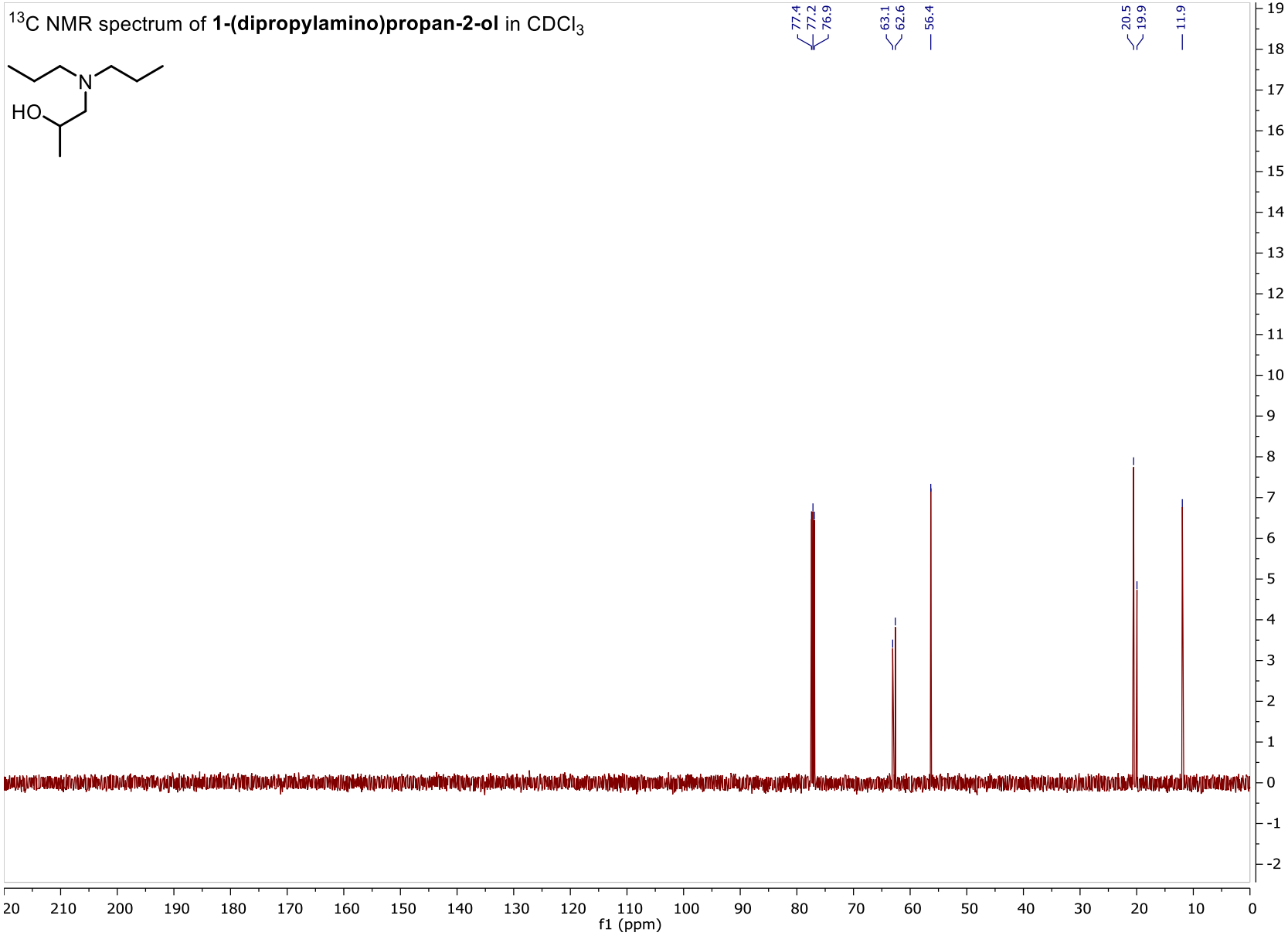

1H NMR spectrum of 1-morpholinopropan-2-ol in CDCl3
HO
O
N
7.26
3.84
3.83
3.70
3.40
2.64
2.38
2.33
2.32
2.30
2.30
2.24
2.22
2.19
1.87
1.13
1.12
1.08
4.12
0.91
2.08
4.19
0.88
3.00
f1 (ppm)

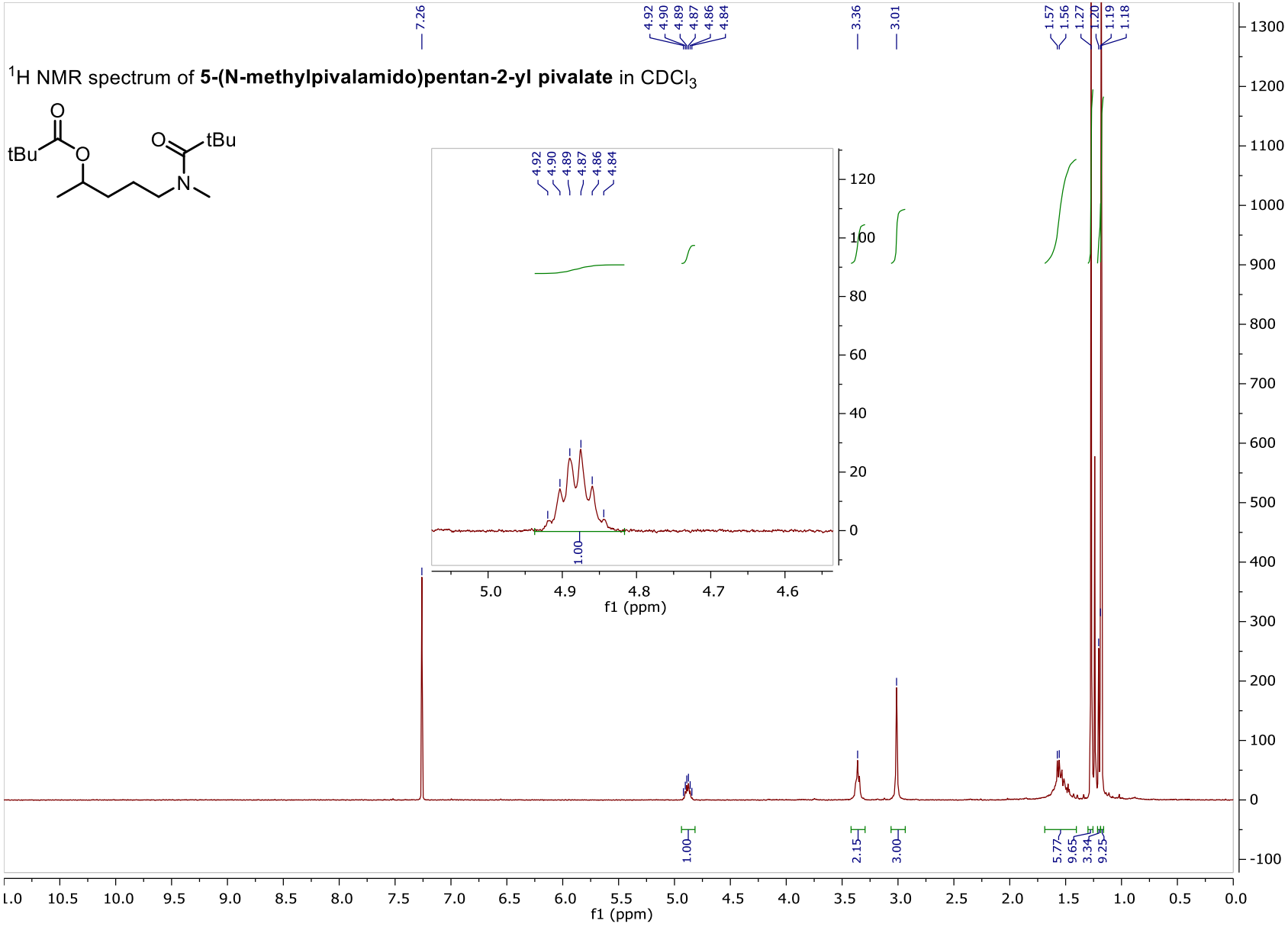

^{12}C NMR spectrum of **1-morpholinopropan-2-ol** in $CDCl_3$
O
N
HO
77.4
77.2
76.9
67.2
66.3
62.2
53.8
20.1
f1 (ppm)

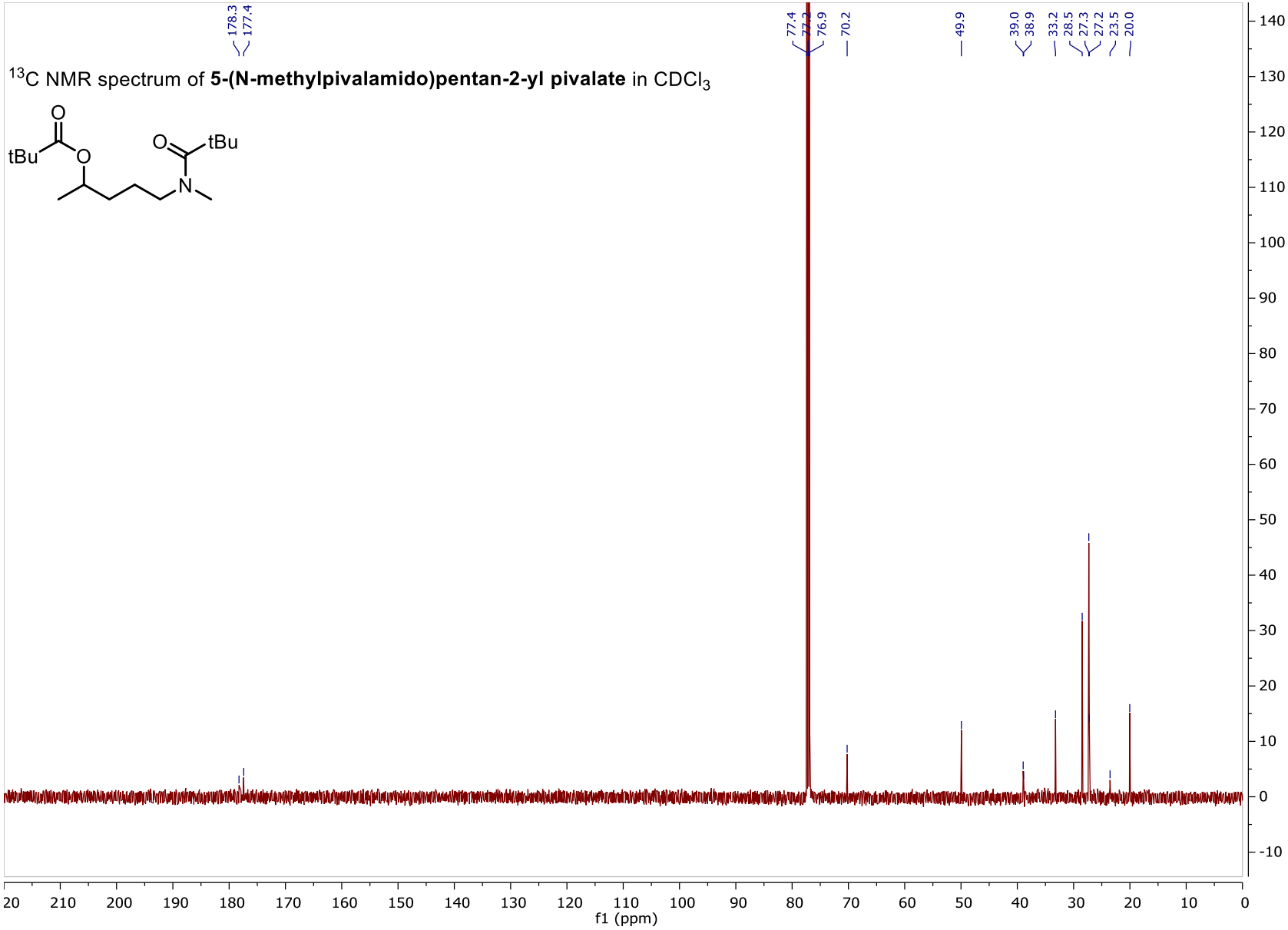

^{1}H NMR spectrum of **1-(propylamino)propan-2-ol** in $CDCl_3$
7.26
3.76
2.72
2.71
2.69
2.69
2.69
2.61
2.56
2.41
2.39
2.39
2.37
2.16
1.54
1.52
1.51
1.49
1.48
1.46
1.15
1.14
0.93
0.92
0.90
N
H
OH
1.00
0.98
2.19
1.26
2.21
3.11
3.16
f1 (ppm)

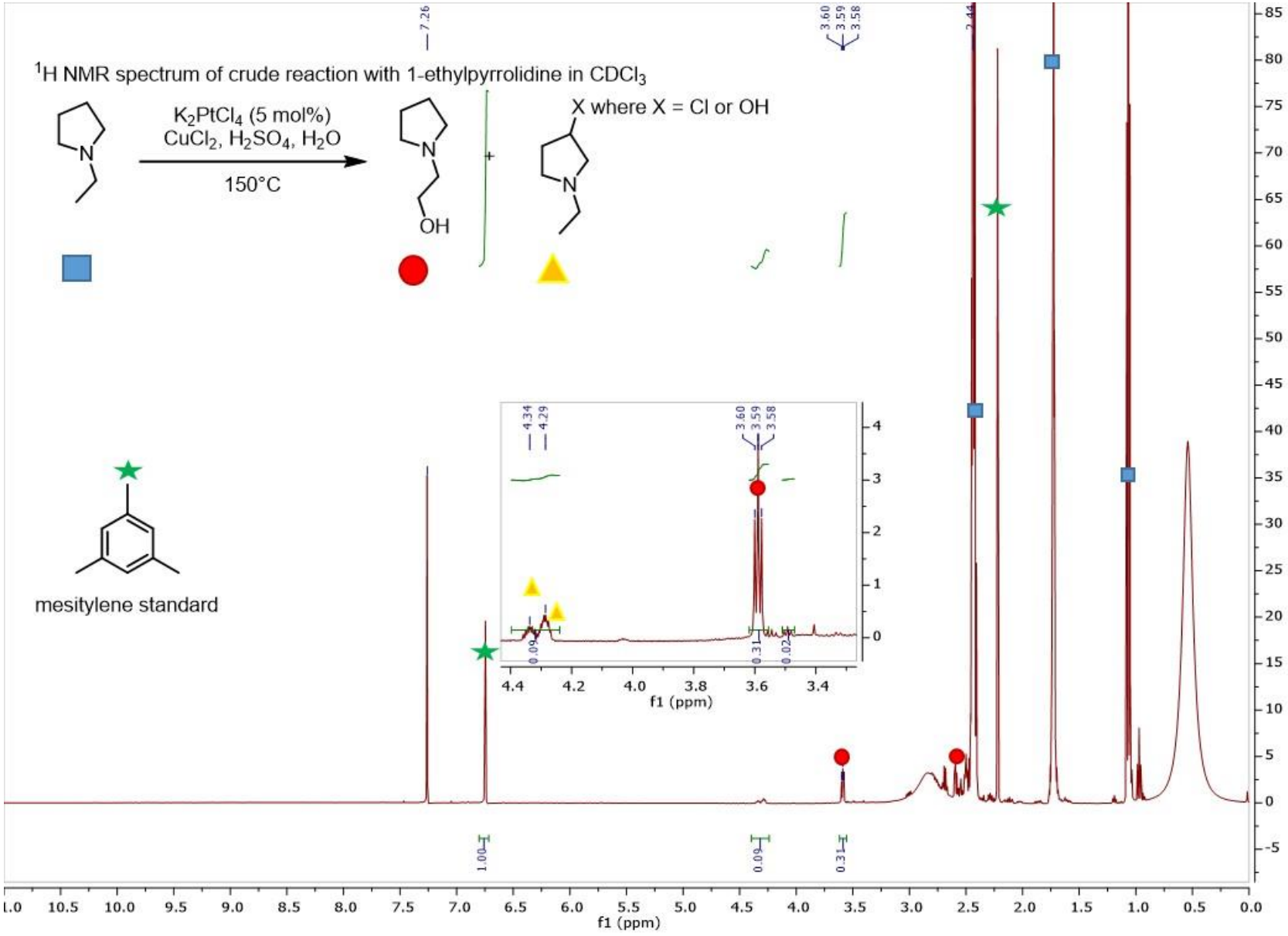

^{13}C NMR spectrum of **1-(propylamino)propan-2-ol** in $CDCl_3$
77.4
77.2
76.9
65.6
56.9
51.6
23.4
20.6
11.8
N
H
OH
f1 (ppm)

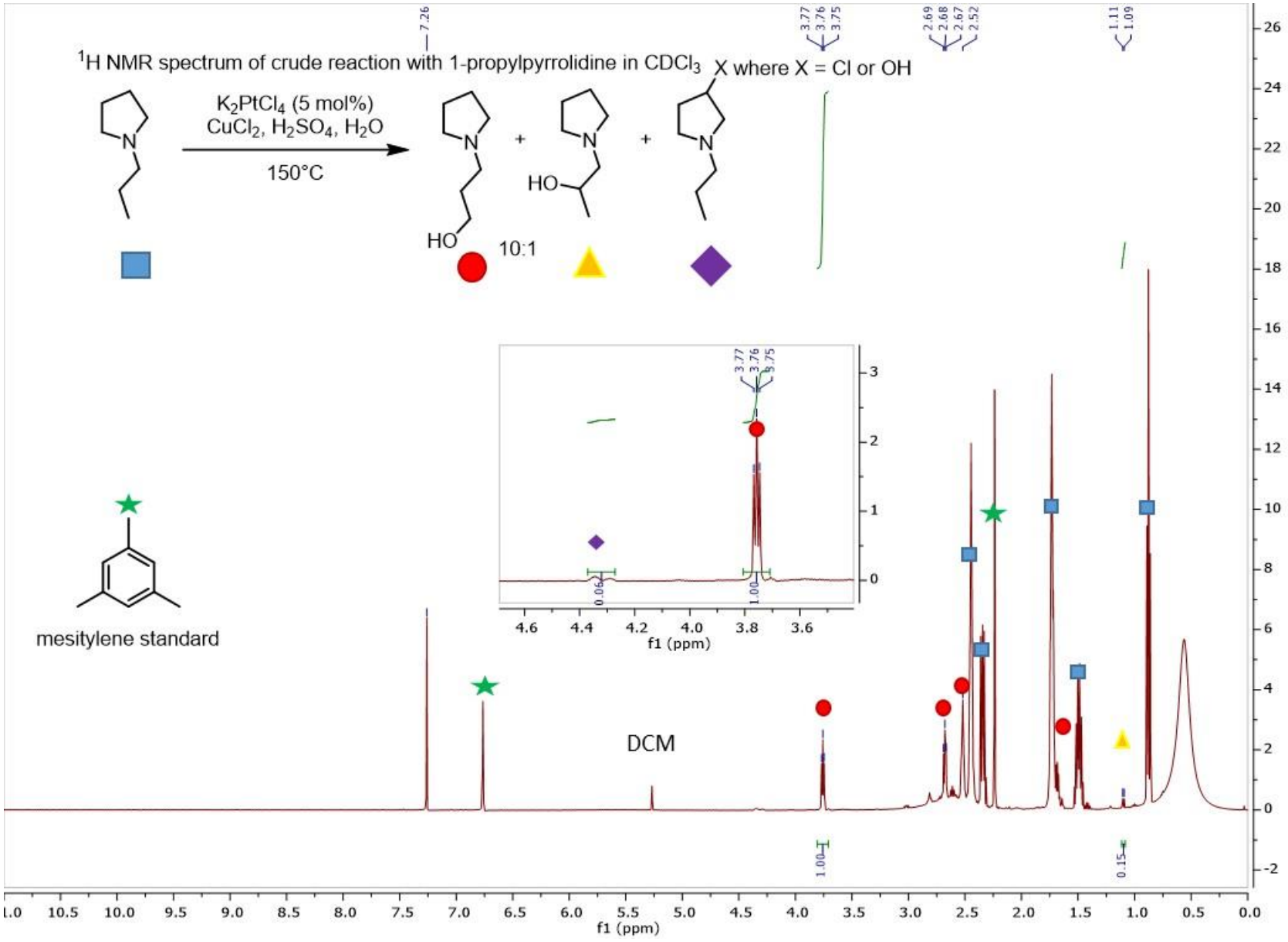

1H NMR spectrum of 1-(dipropylamino)propan-2-ol in CDCl3
HO
N
7.26
3.70
2.49
2.44
2.38
2.33
2.23
2.21
2.21
2.19
1.53
1.37
1.11
1.10
0.89
0.87
0.86
1.92
2.13
3.12
1.12
4.19
3.00
5.96
f1 (ppm)

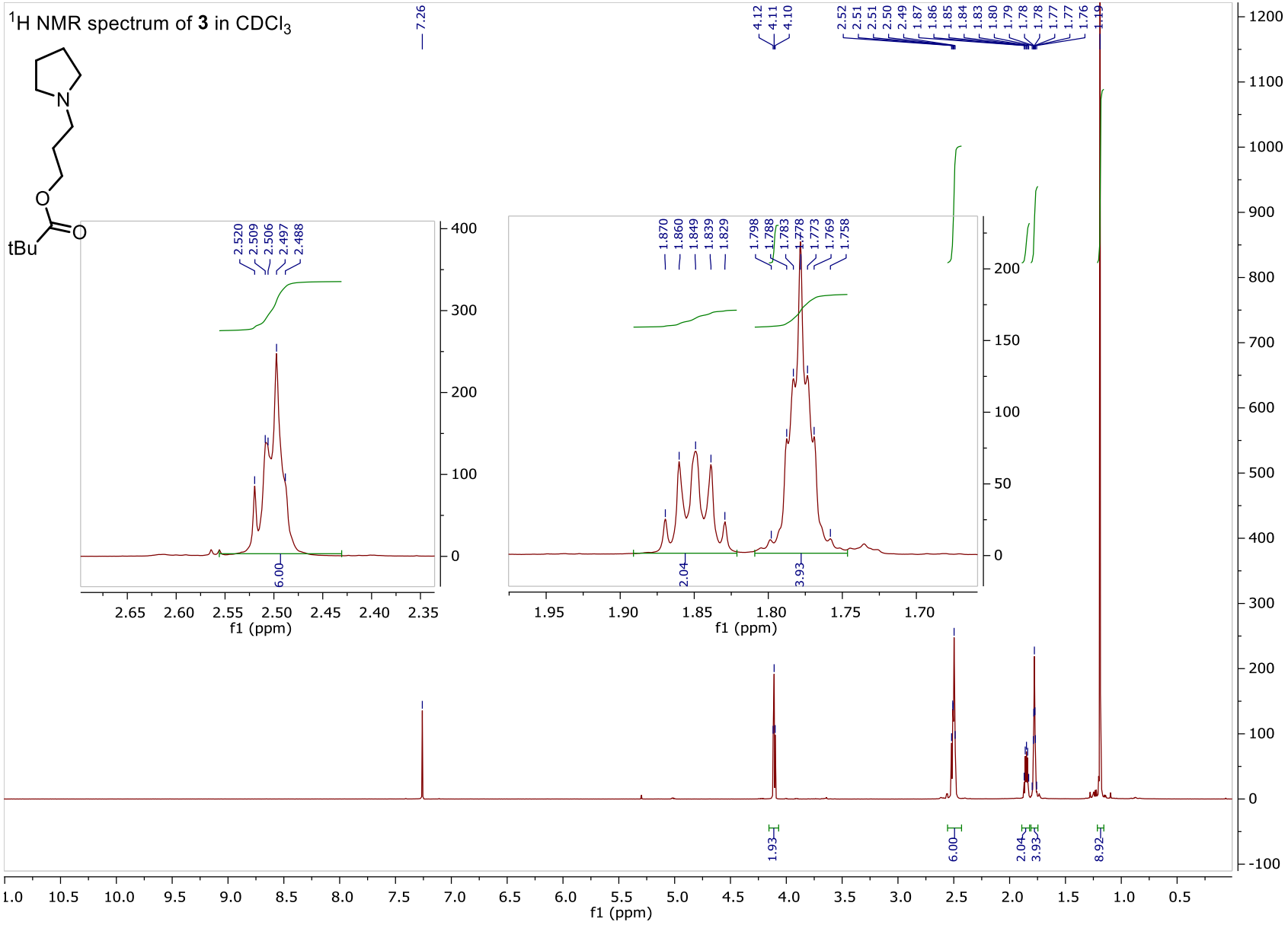

^{13}C NMR spectrum of **1-(dipropylamino)propan-2-ol** in $CDCl_3$
77.4
77.2
76.9
63.1
62.6
56.4
20.5
19.9
11.9
HO
N
f1 (ppm)

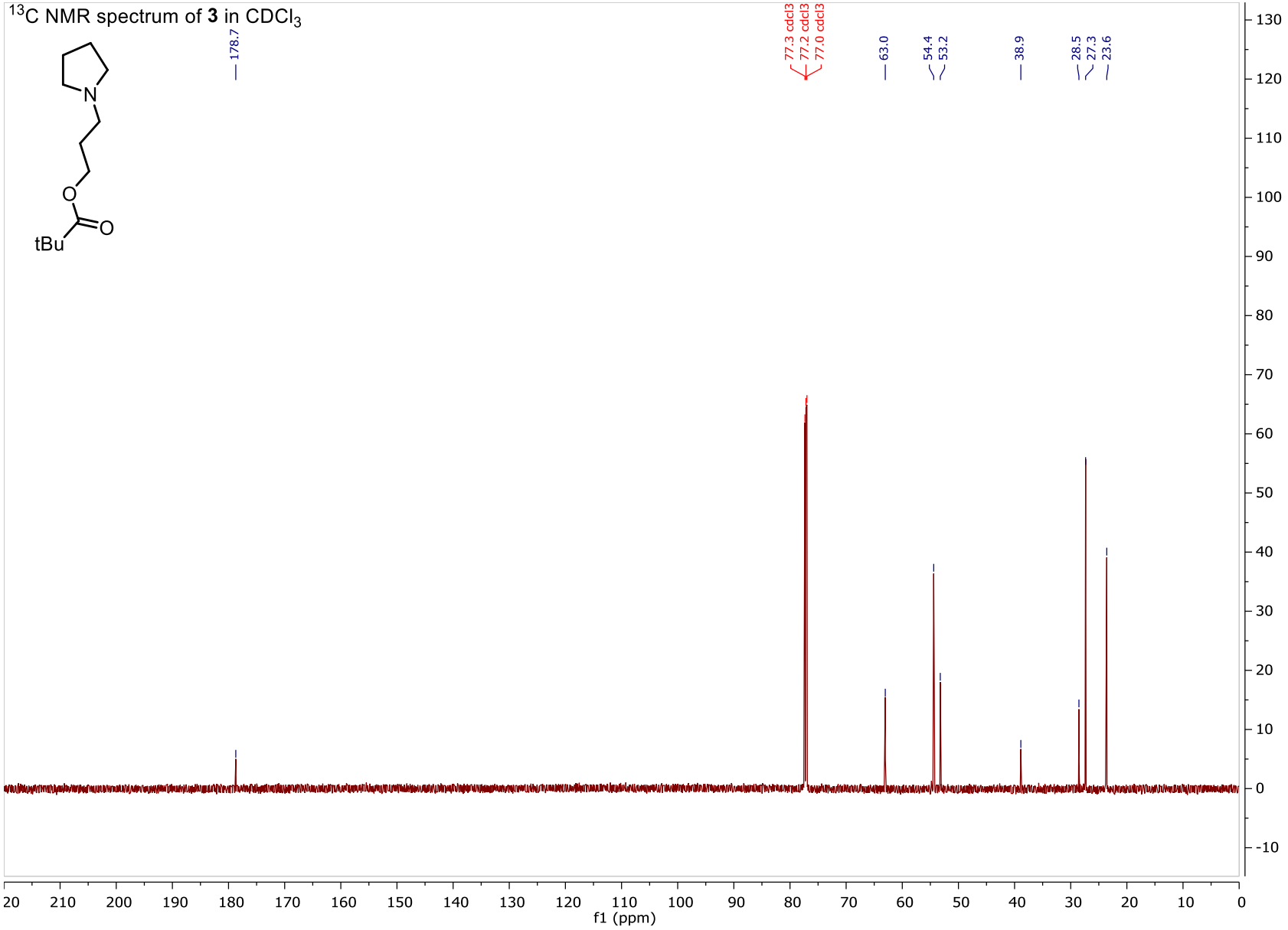

^{1}H NMR spectrum of **5-(N-methylpivalamido)pentan-2-yl pivalate** in $CDCl_3$
tBu
O
O
O
tBu
N
7.26
4.92
4.90
4.89
4.87
4.86
4.84
3.36
3.01
1.57
1.56
1.27
1.20
1.19
1.18
1.00
2.15
3.00
5.77
9.65
3.34
9.25
f1 (ppm)

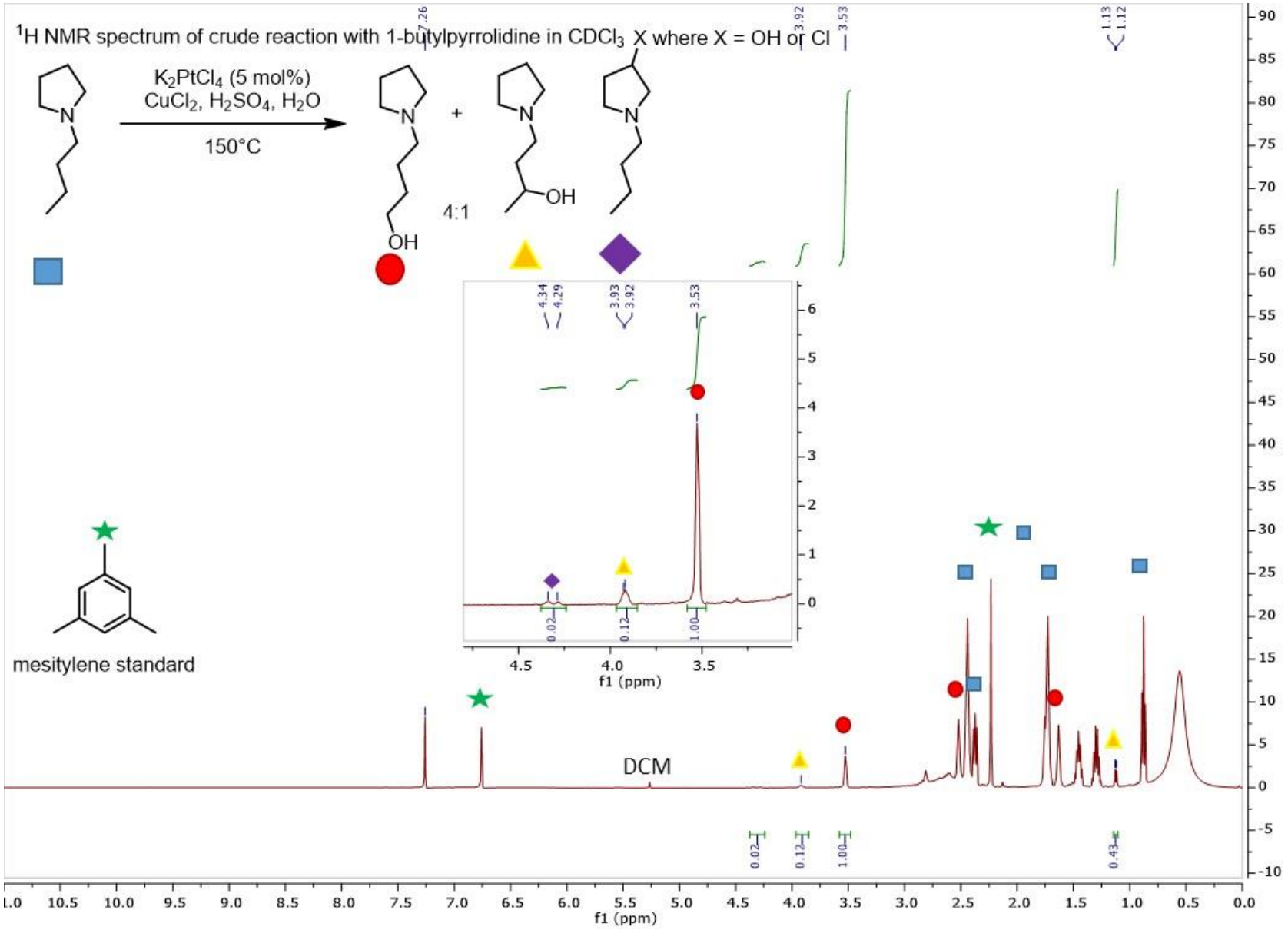

178.3
177.4
77.4
77.2
76.9
70.2
49.9
39.0
38.9
33.2
28.5
27.3
27.2
23.5
20.0
^{13}C NMR spectrum of **5-(N-methylpivalamido)pentan-2-yl pivalate** in $CDCl_3$
O
tBu
O
O
tBu
N
f1 (ppm)

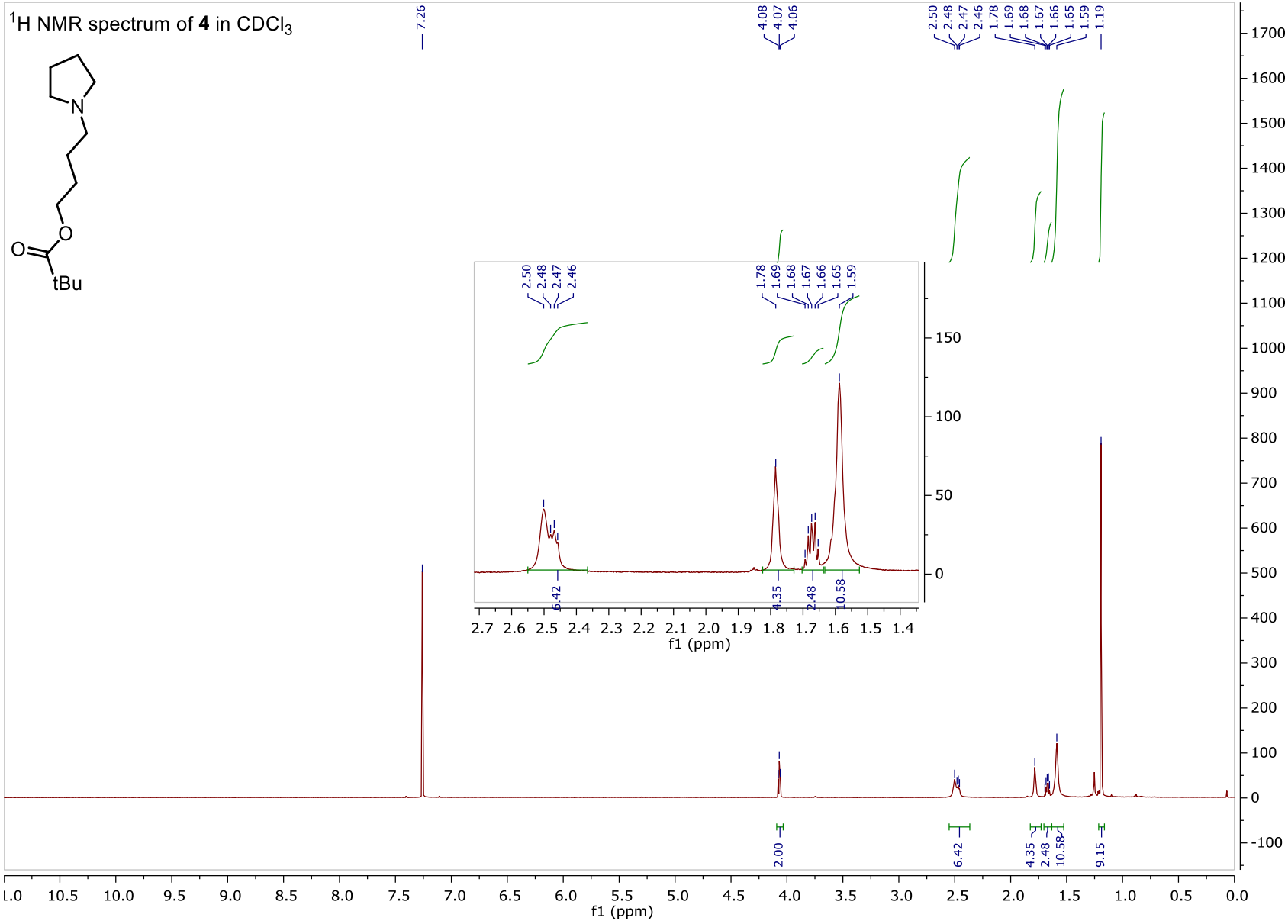

^{1}H NMR spectrum of crude reaction with 1-ethylpyrrolidine in $CDCl_3$
K_2PtCl_4 (5 mol%)
$CuCl_2$, H_2SO_4, H_2O
150°C
OH
X where X = Cl or OH
mesitylene standard
7.26
3.60
3.59
3.58
4.34
4.29
1.00
0.09
0.31
f1 (ppm)

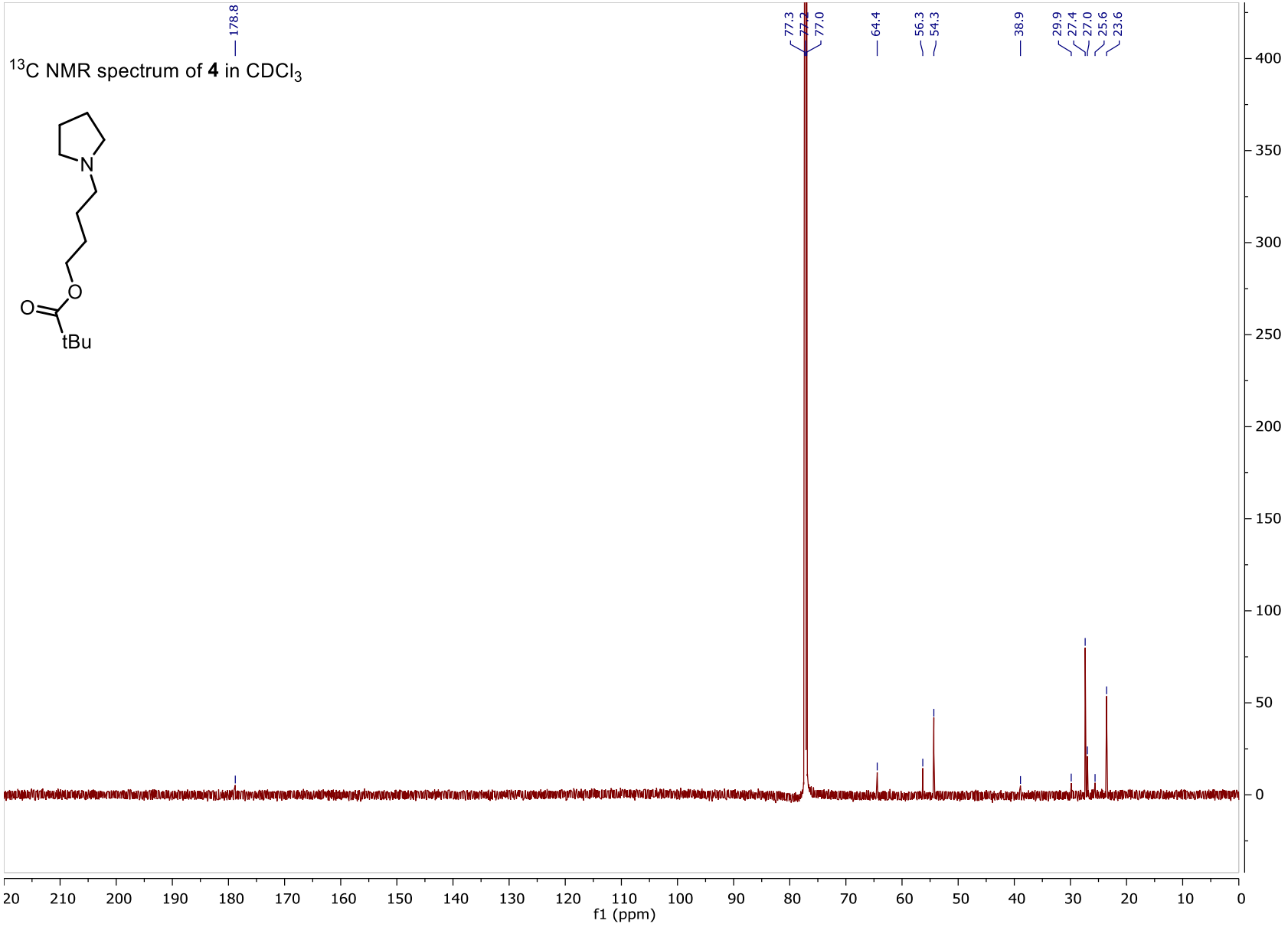

1H NMR spectrum of crude reaction with 1-propylpyrrolidine in CDCl3
X where X = Cl or OH
K2PtCl4 (5 mol%)
CuCl2, H2SO4, H2O
150°C
HO
10:1
mesitylene standard
DCM
f1 (ppm)

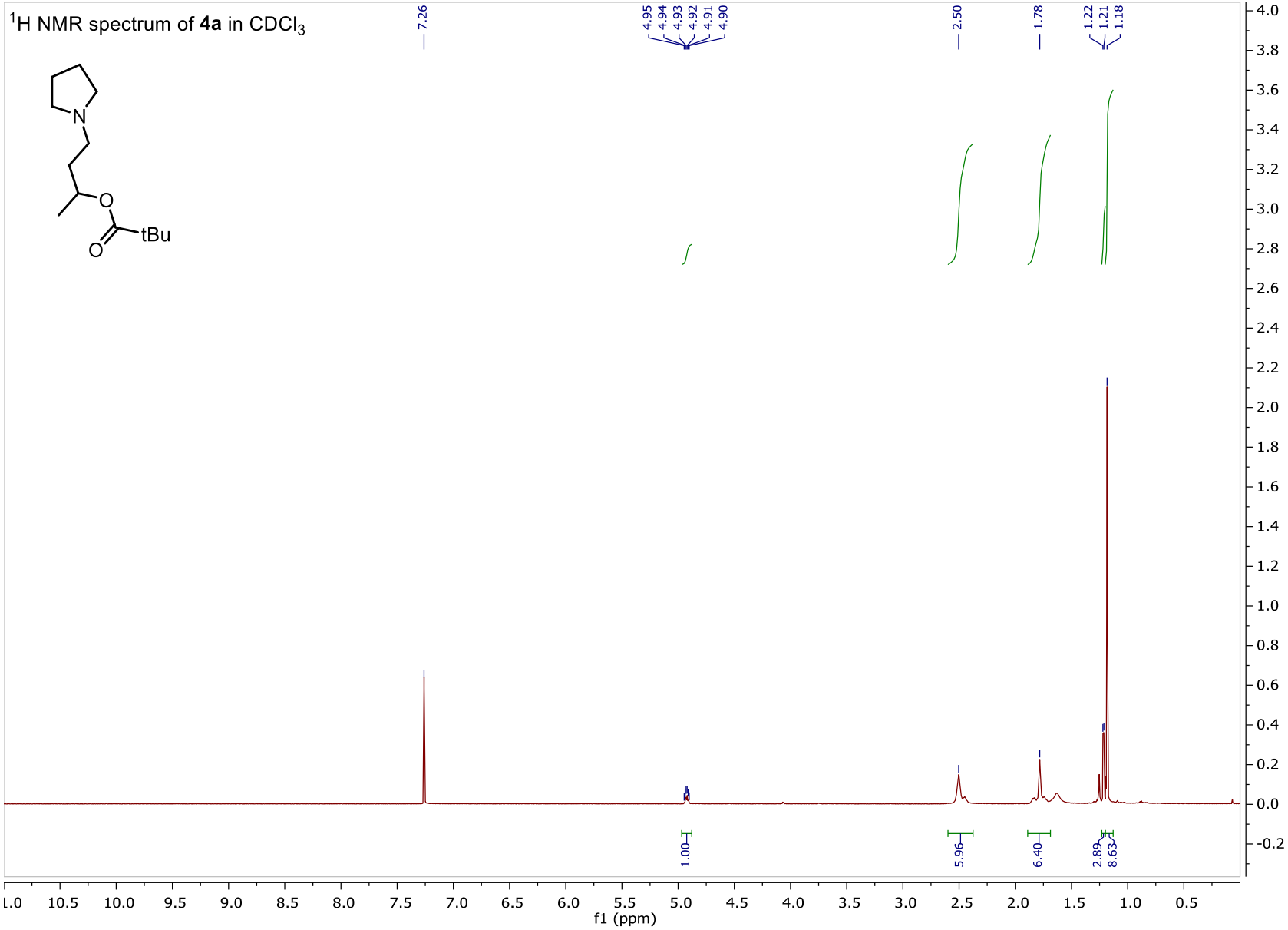

^{1}H NMR spectrum of **3** in $CDCl_3$
tBu
f1 (ppm)

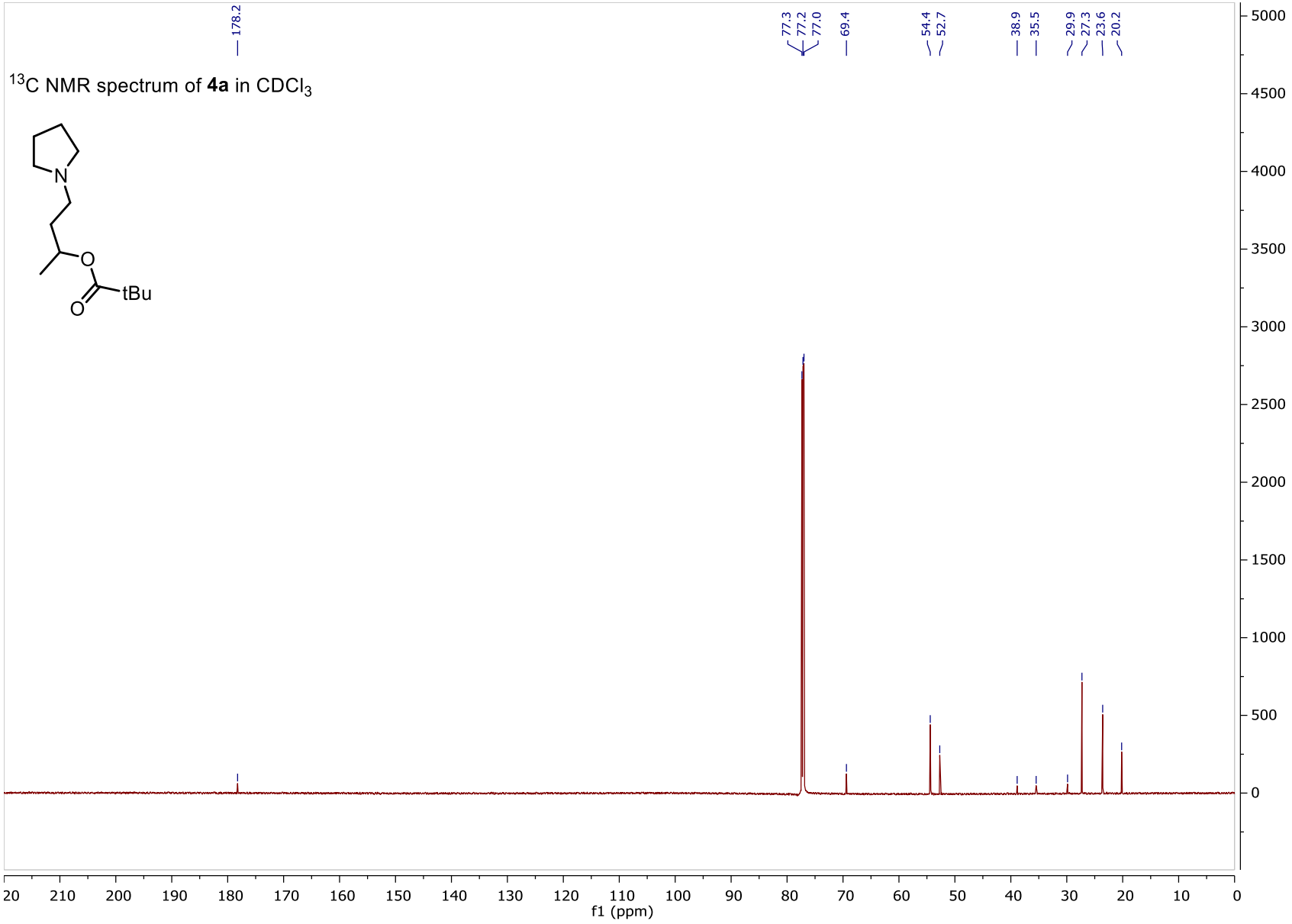

^{13}C NMR spectrum of **3** in $CDCl_3$
178.7
77.3 cdcl3
77.2 cdcl3
77.0 cdcl3
63.0
54.4
53.2
38.9
28.5
27.3
23.6
N
O
O
tBu
f1 (ppm)

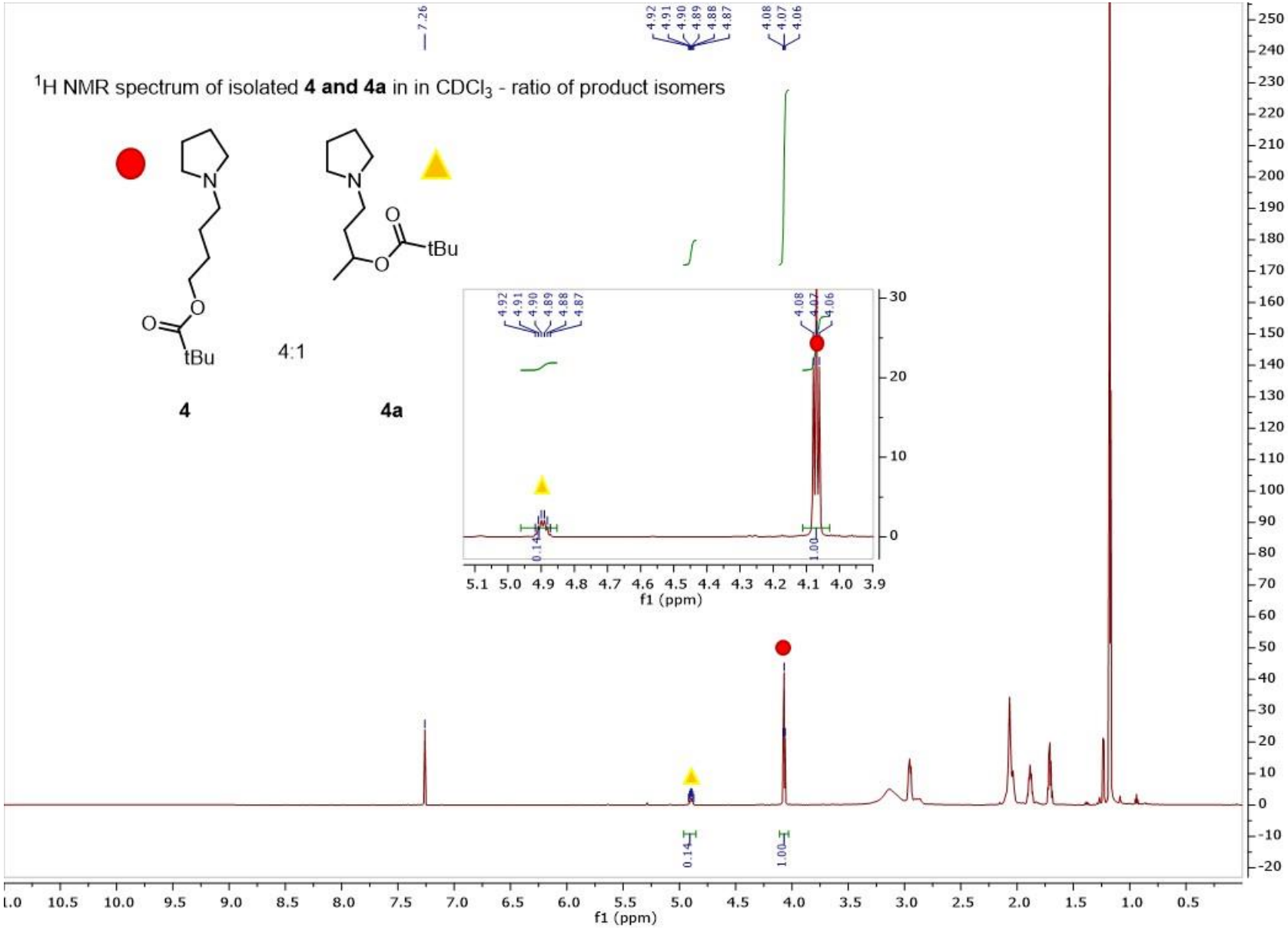

^{1}H NMR spectrum of crude reaction with 1-butylpyrrolidine in $CDCl_3$ X where X = OH or Cl
K_2PtCl_4 (5 mol%)
$CuCl_2$, H_2SO_4, H_2O
150°C
OH
4:1
OH
mesitylene standard
DCM
f1 (ppm)

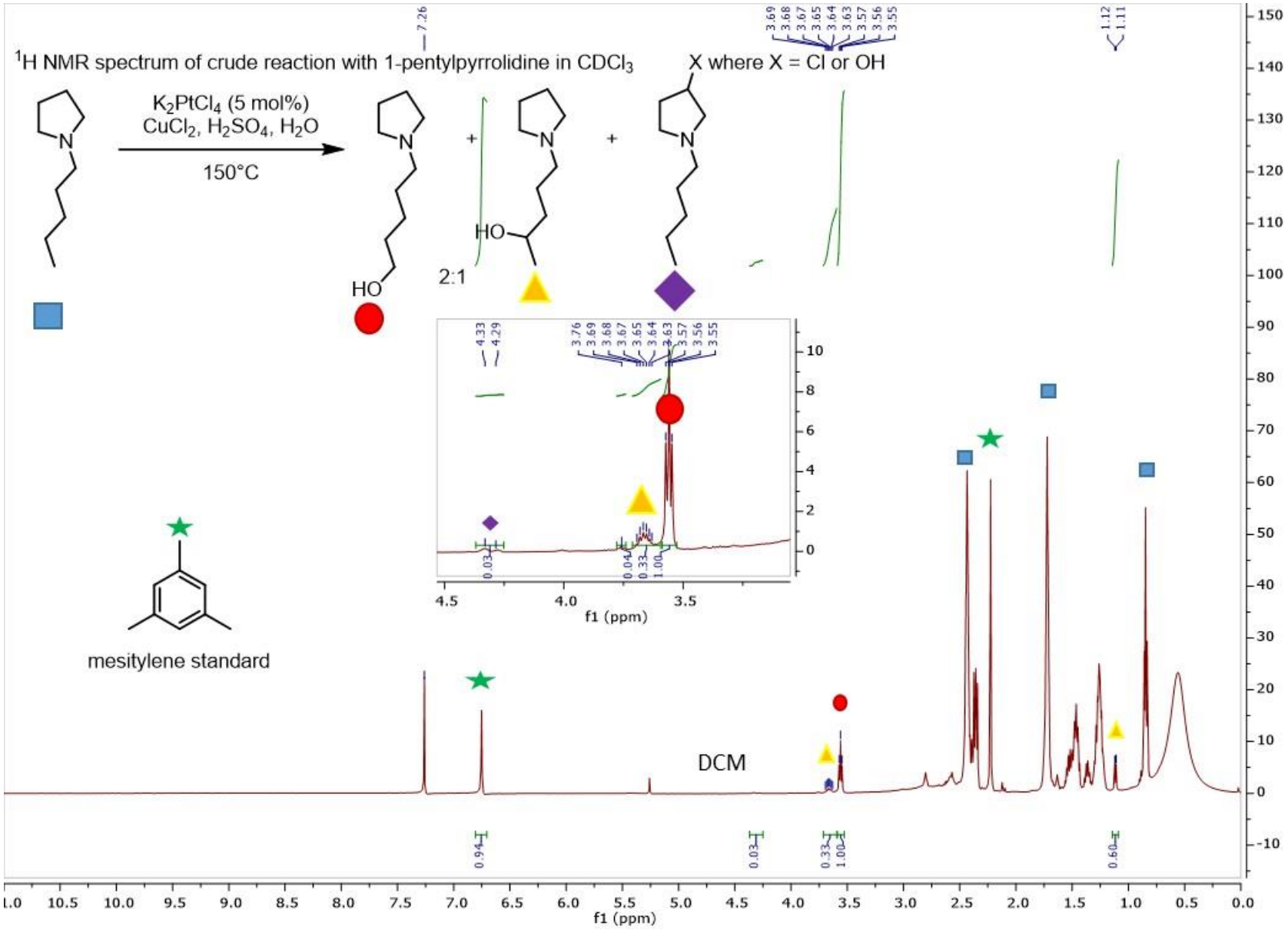

^{1}H NMR spectrum of **4** in $CDCl_3$
7.26
4.08
4.07
4.06
2.50
2.48
2.47
2.46
1.78
1.69
1.68
1.67
1.66
1.65
1.59
1.19
N
O
O
tBu
f1 (ppm)
2.00
6.42
4.35
2.48
10.58
9.15

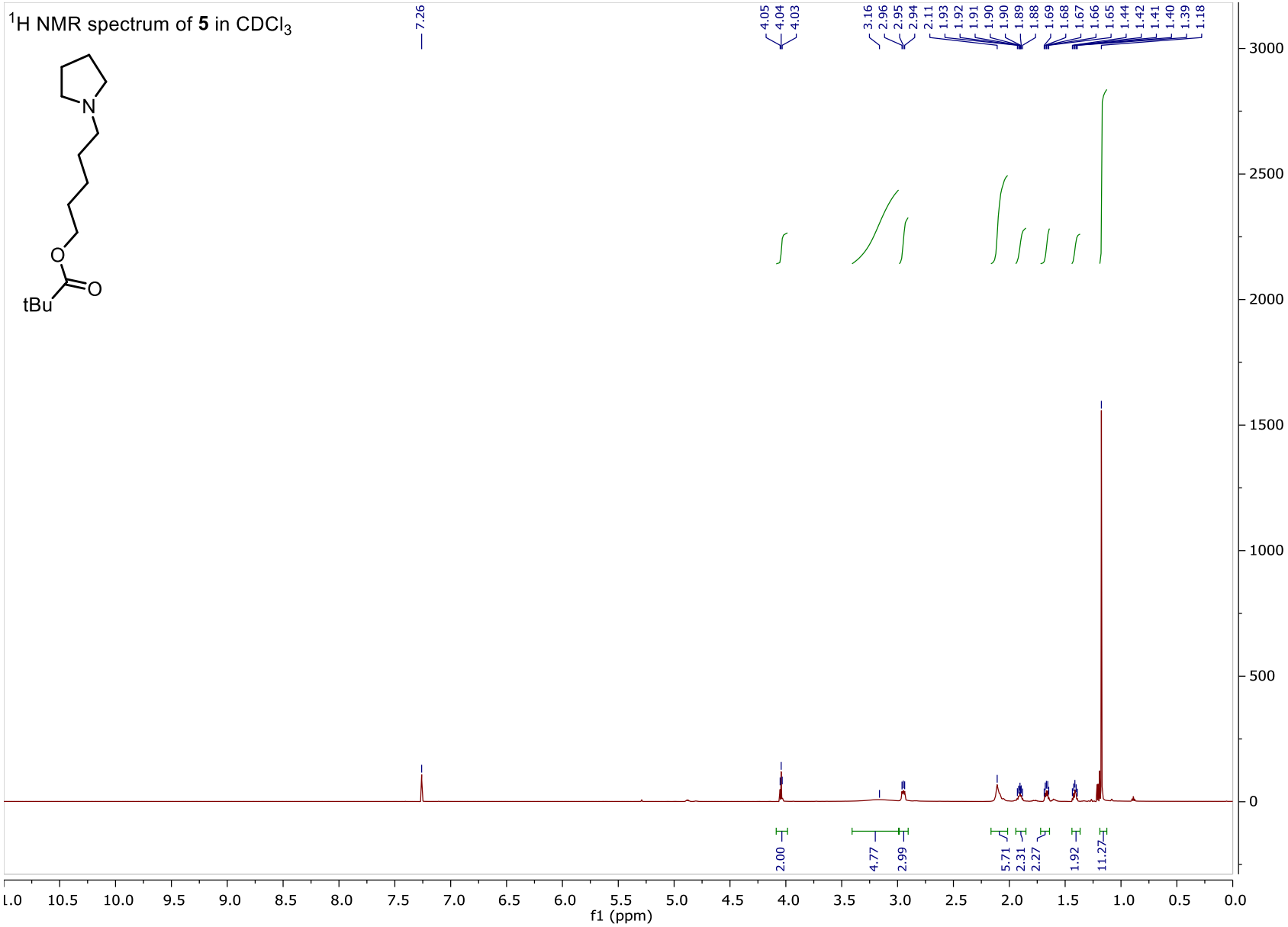

^{13}C NMR spectrum of **4** in $CDCl_3$
178.8
77.3
77.2
77.0
64.4
56.3
54.3
38.9
29.9
27.4
27.0
25.6
23.6
N
O
O
tBu
400
350
300
250
200
150
100
50
0
f1 (ppm)

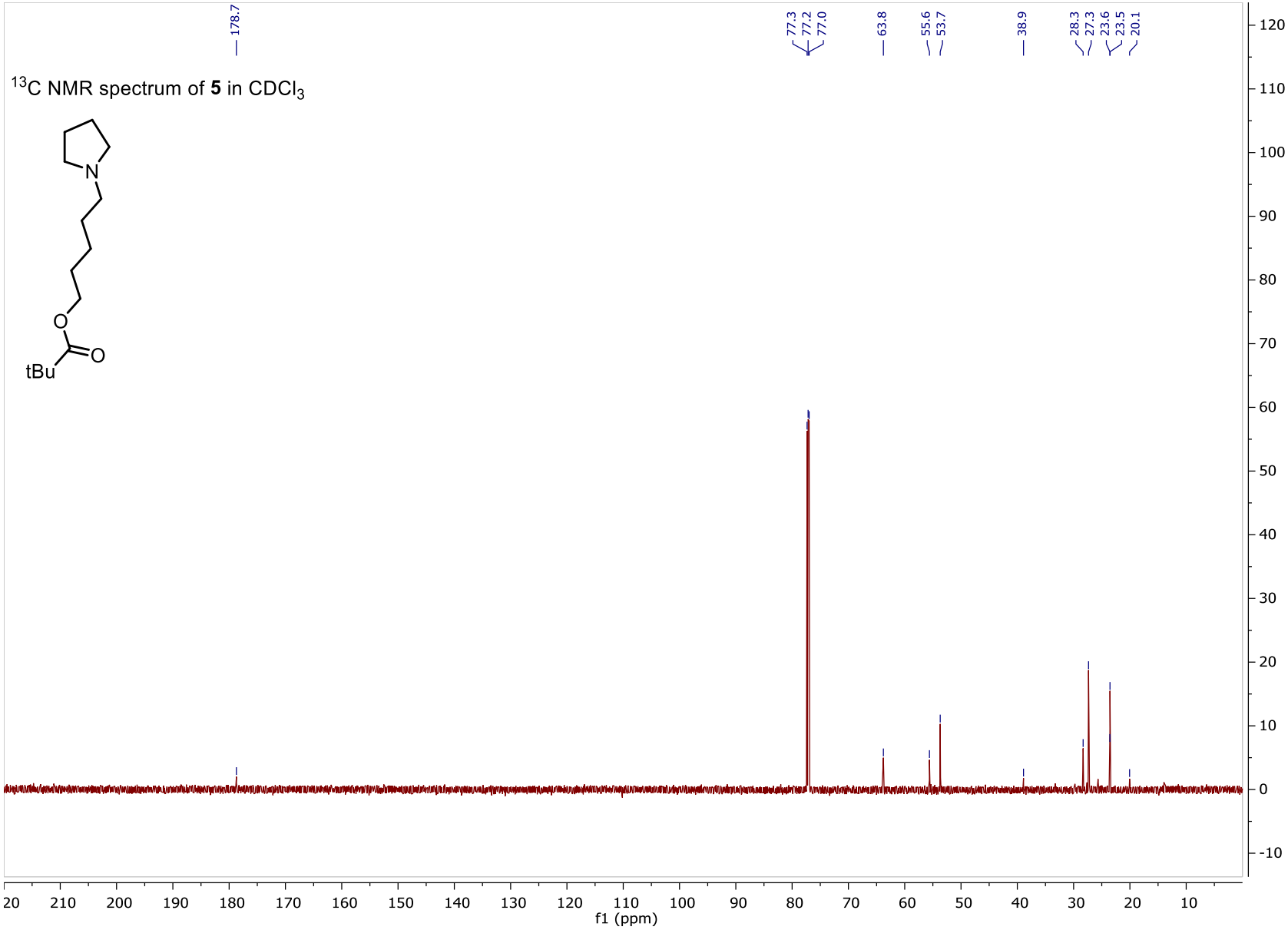

^{1}H NMR spectrum of **4a** in $CDCl_3$
7.26
4.95
4.94
4.93
4.92
4.91
4.90
2.50
1.78
1.22
1.21
1.18
N
O
O
tBu
1.00
5.96
6.40
2.89
8.63
f1 (ppm)

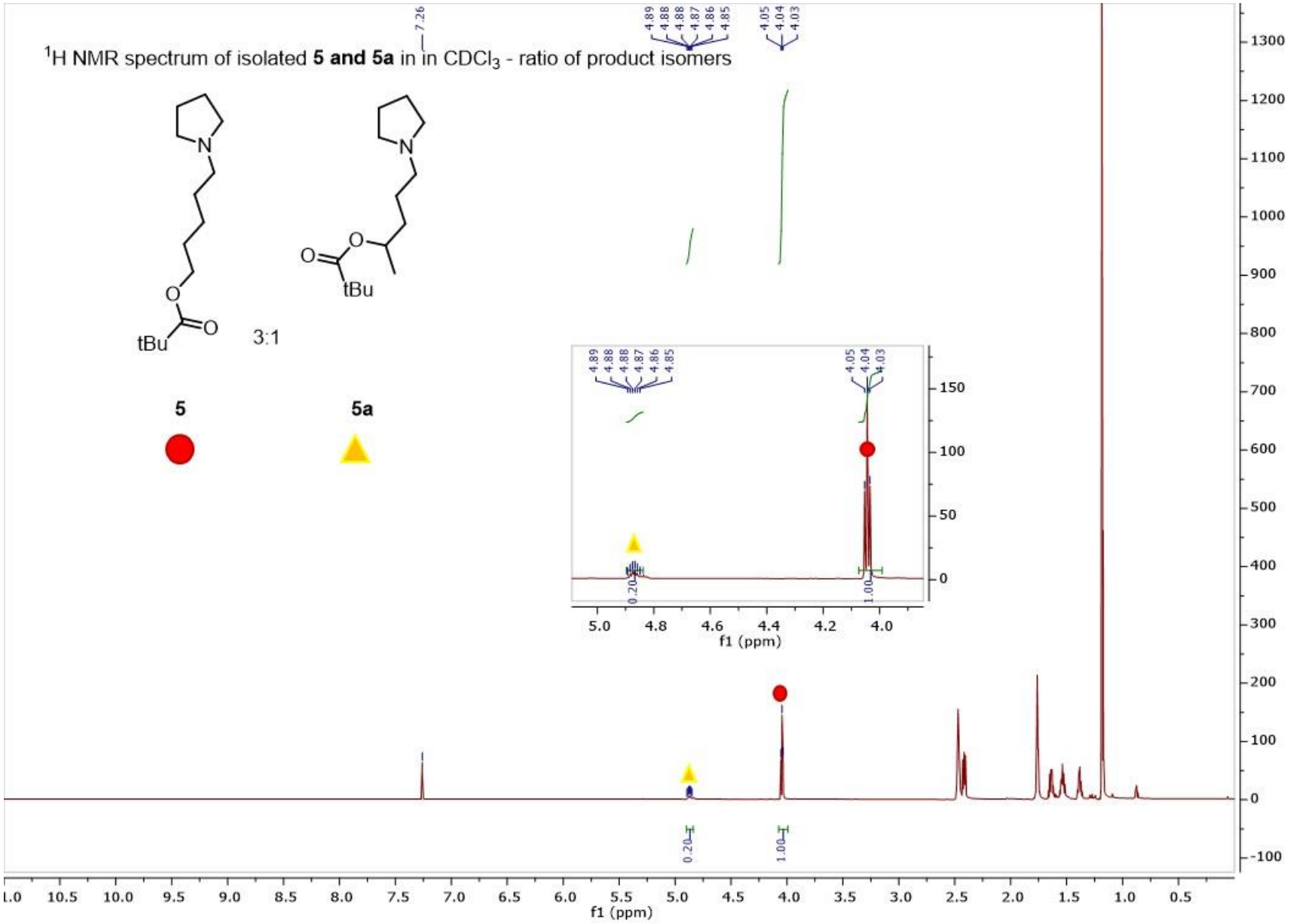

^{13}C NMR spectrum of **4a** in $CDCl_3$
178.2
77.3
77.2
77.0
69.4
54.4
52.7
38.9
35.5
29.9
27.3
23.6
20.2
N
O
O
tBu
5000
4500
4000
3500
3000
2500
2000
1500
1000
500
0
20 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

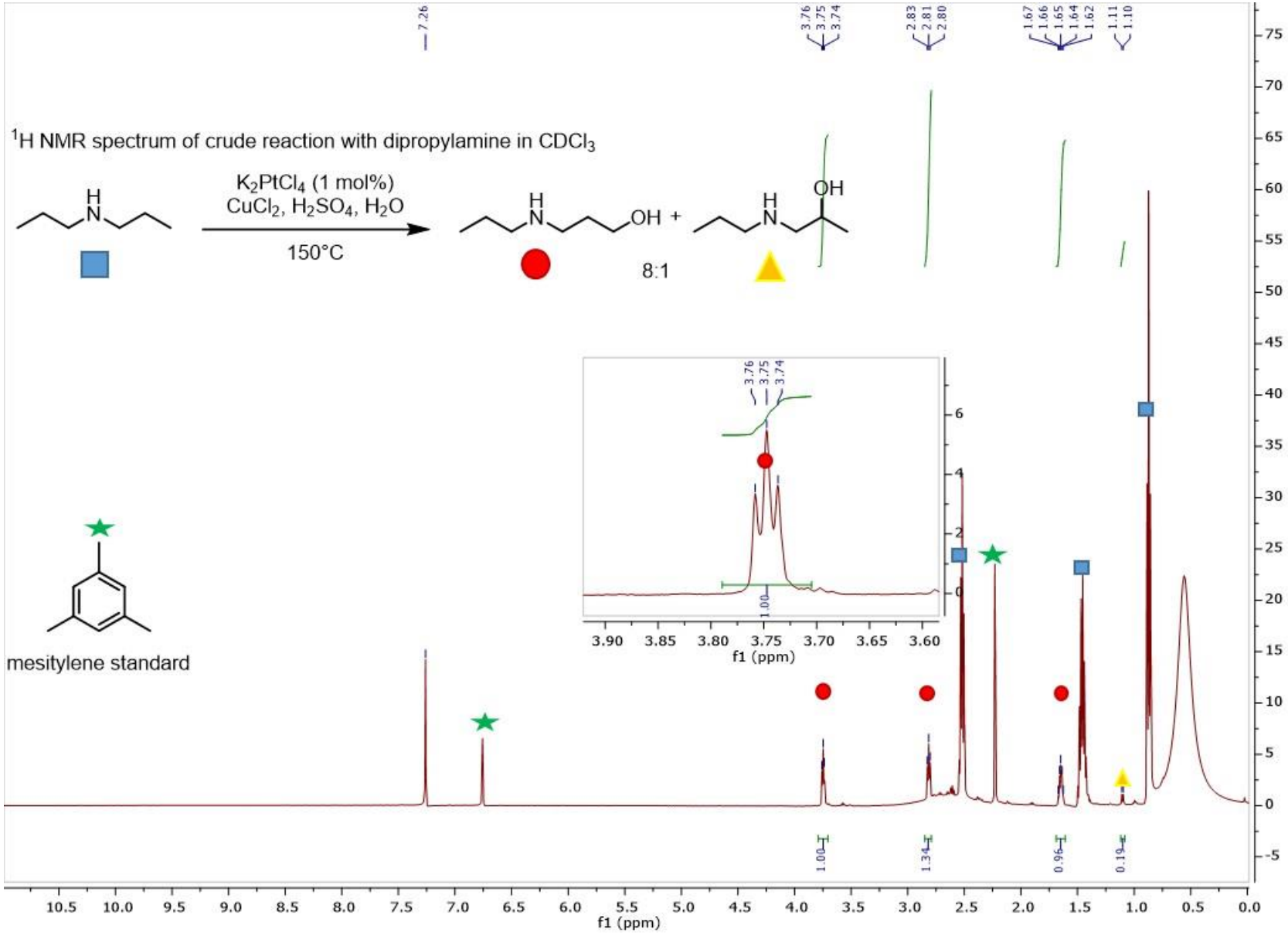

^{1}H NMR spectrum of isolated **4 and 4a** in in $CDCl_3$ - ratio of product isomers
4:1
4
4a
f1 (ppm)

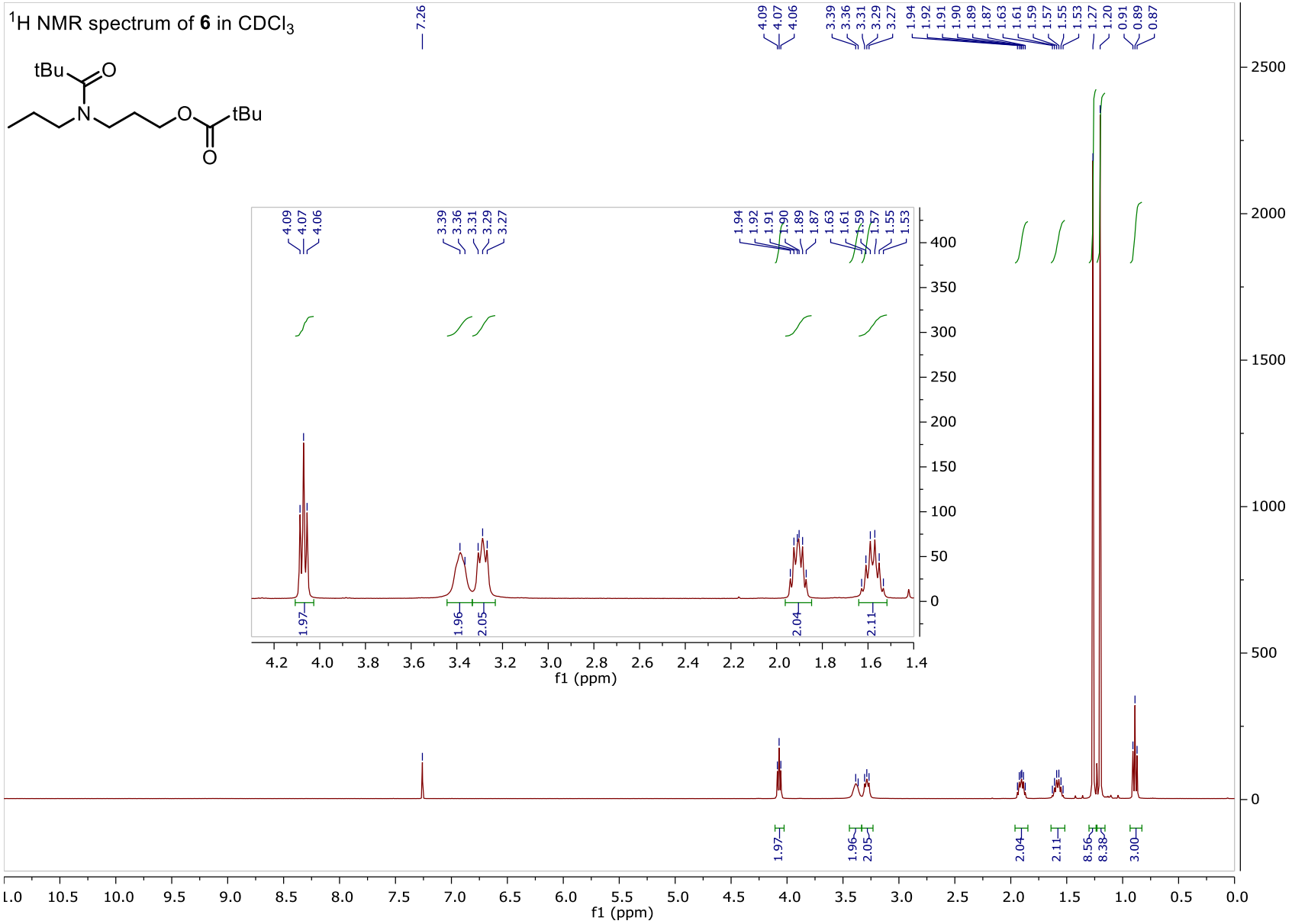

^{1}H NMR spectrum of crude reaction with 1-pentylpyrrolidine in $CDCl_3$
X where X = Cl or OH
K_2PtCl_4 (5 mol%)
$CuCl_2$, H_2SO_4, H_2O
150°C
HO
2:1
mesitylene standard
DCM
f1 (ppm)

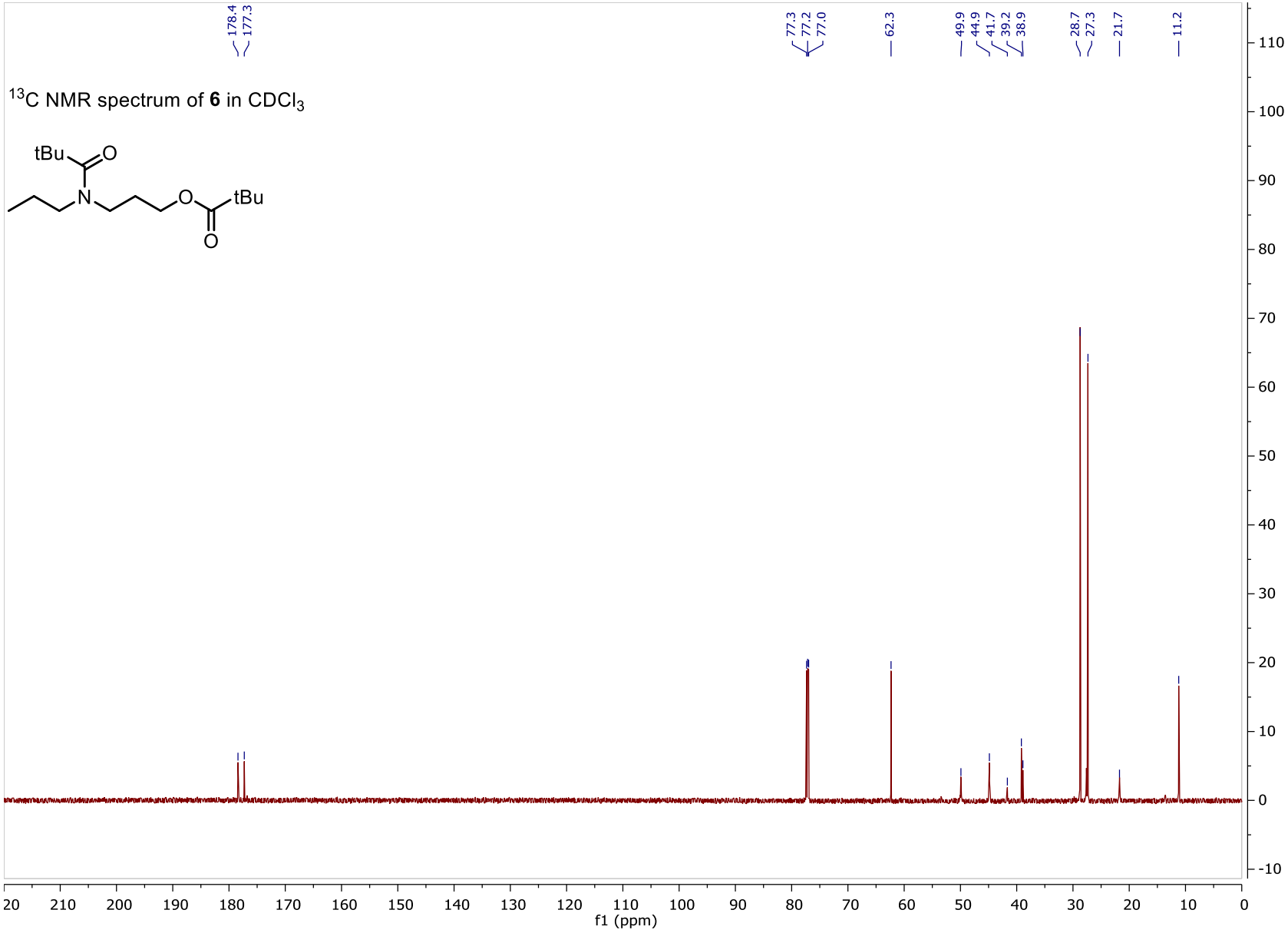

^{1}H NMR spectrum of **5** in $CDCl_3$
7.26
4.05
4.04
4.03
3.16
2.96
2.95
2.94
2.11
1.93
1.92
1.91
1.90
1.90
1.89
1.88
1.69
1.68
1.67
1.66
1.65
1.44
1.42
1.41
1.40
1.39
1.18
N
O
O
tBu
3000
2500
2000
1500
1000
500
0
2.00
4.77
2.99
5.71
2.31
2.27
1.92
11.27
f1 (ppm)

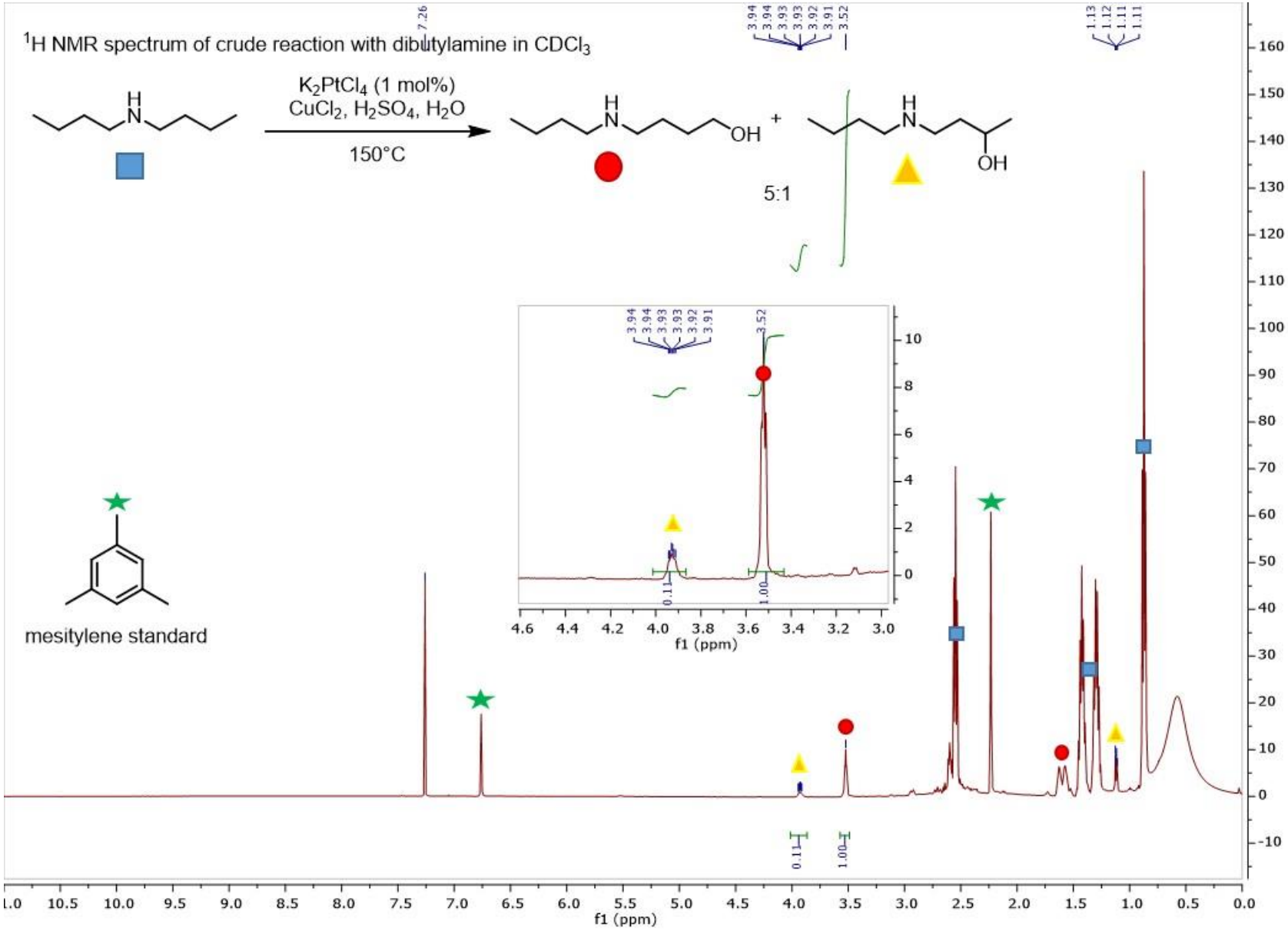

^{13}C NMR spectrum of **5** in $CDCl_3$
178.7
77.3
77.2
77.0
63.8
55.6
53.7
38.9
28.3
27.3
23.6
23.5
20.1
N
O
O
tBu
f1 (ppm)

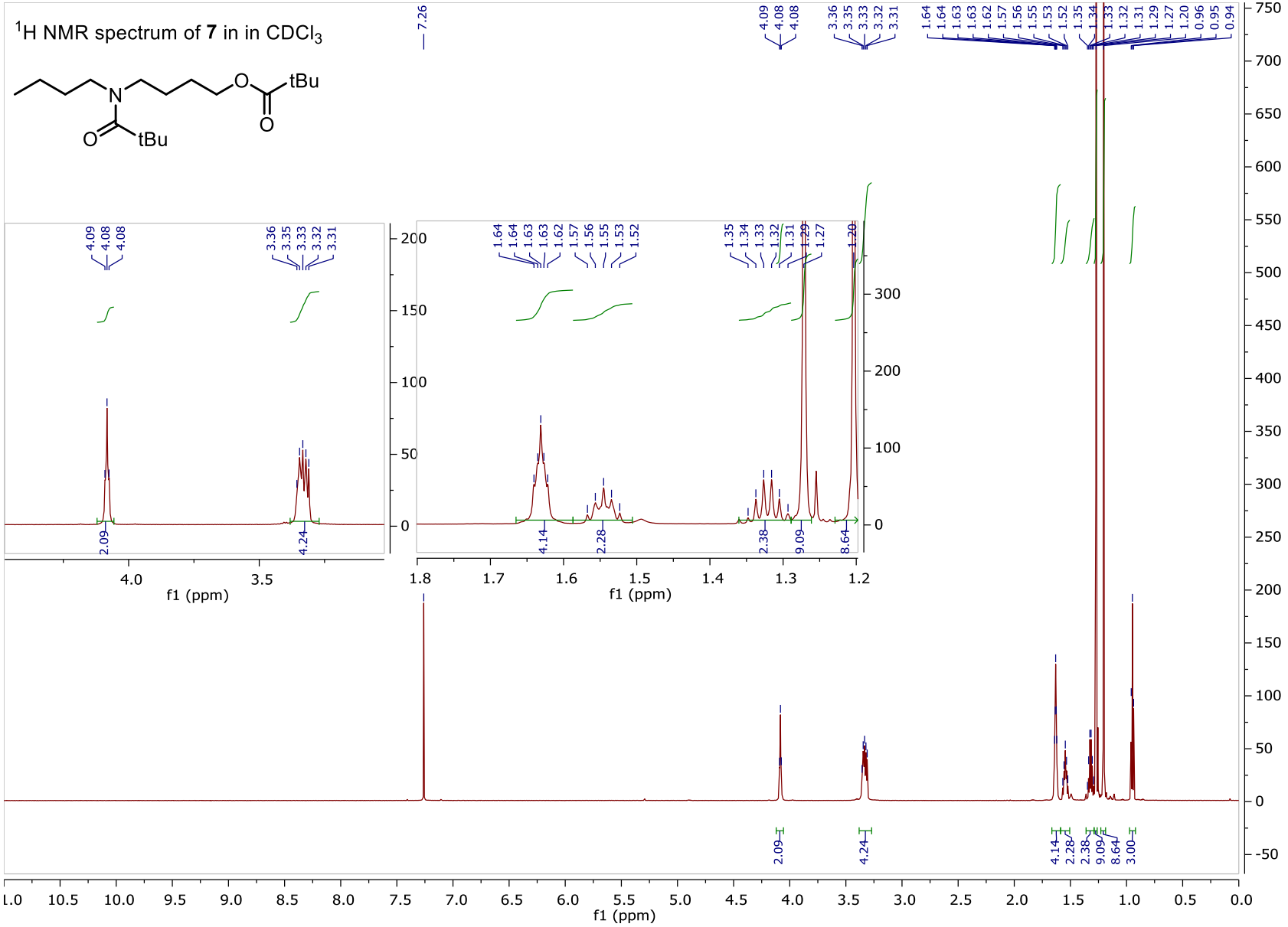

^{1}H NMR spectrum of isolated **5 and 5a** in in $CDCl_3$ - ratio of product isomers
7.26
4.89
4.88
4.88
4.87
4.86
4.85
4.05
4.04
4.03
tBu
3:1
5
5a
0.20
1.00
f1 (ppm)

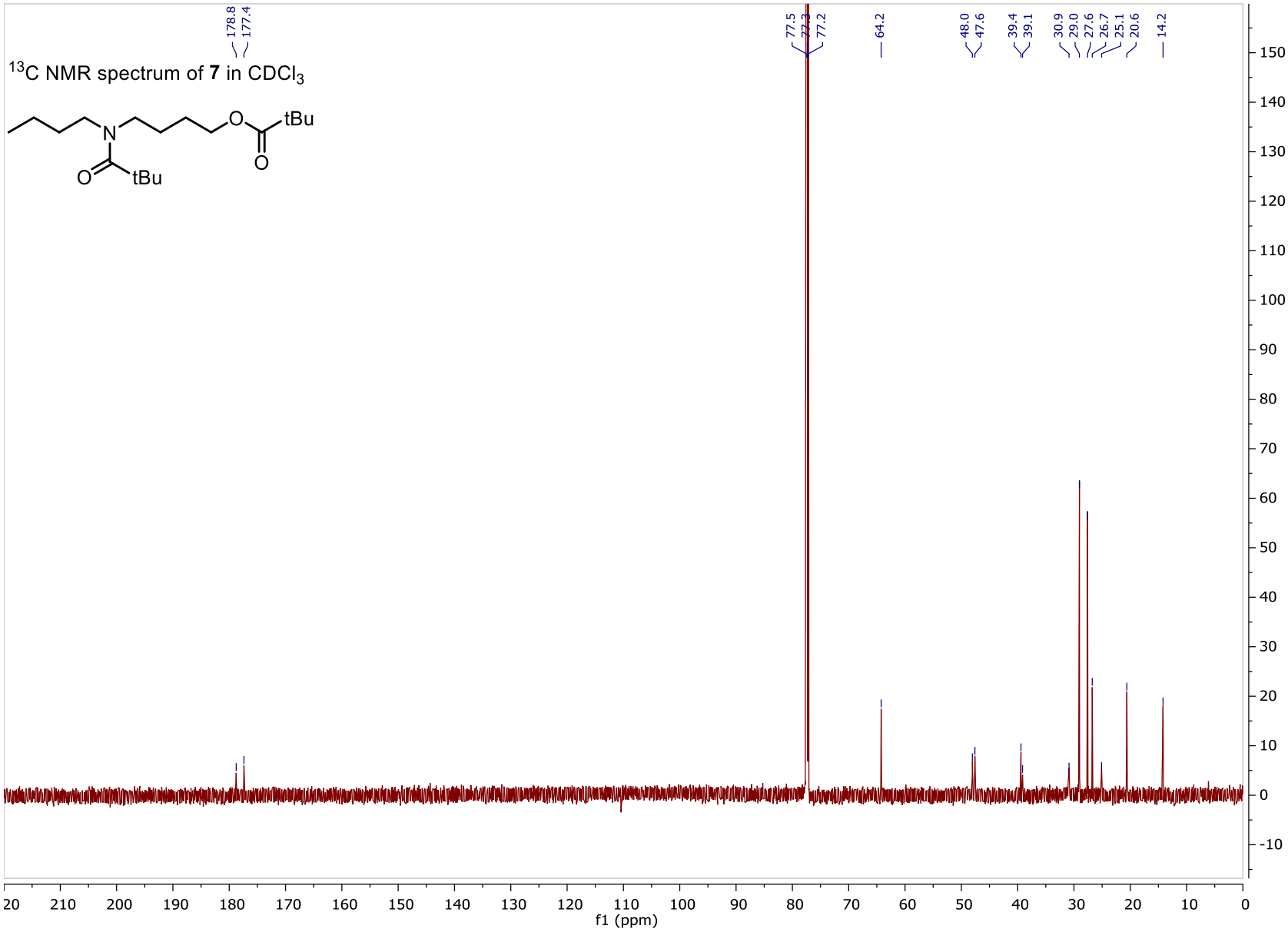

^{1}H NMR spectrum of crude reaction with dipropylamine in $CDCl_3$
K_2PtCl_4 (1 mol%)
$CuCl_2$, H_2SO_4, H_2O
150°C
OH +
8:1
mesitylene standard
7.26
3.76
3.75
3.74
2.83
2.81
2.80
1.67
1.66
1.65
1.64
1.62
1.11
1.10
1.00
1.34
0.96
0.19
f1 (ppm)

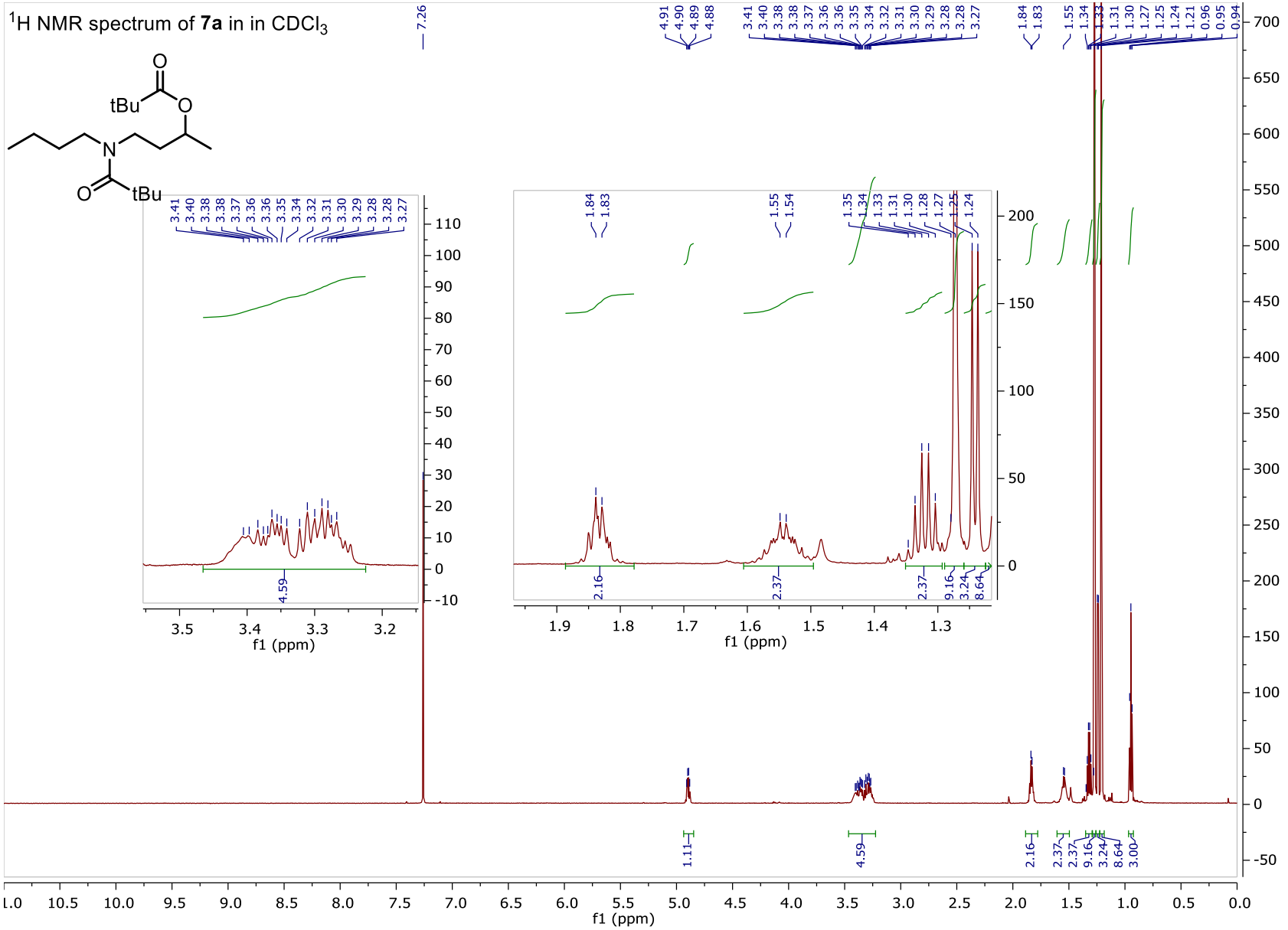

^{1}H NMR spectrum of **6** in $CDCl_3$
tBu
O
N
O
tBu
O
7.26
4.09
4.07
4.06
3.39
3.36
3.31
3.29
3.27
1.94
1.92
1.91
1.90
1.89
1.87
1.63
1.61
1.59
1.57
1.55
1.53
1.27
1.20
0.91
0.89
0.87
1.97
1.96
2.05
2.04
2.11
8.56
8.38
3.00
f1 (ppm)

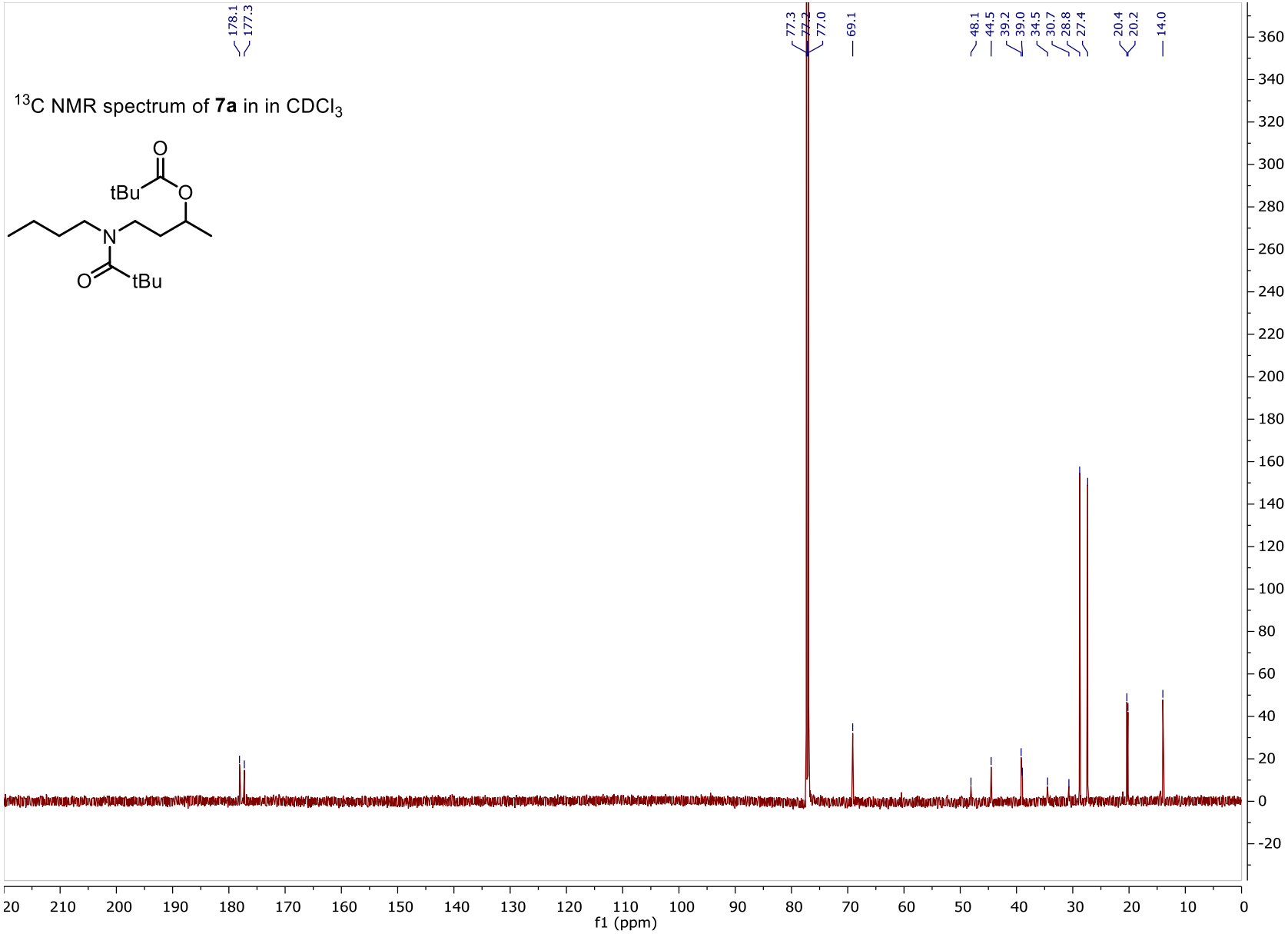

178.4
177.3
77.3
77.2
77.0
62.3
49.9
44.9
41.7
39.2
38.9
28.7
27.3
21.7
11.2
^{13}C NMR spectrum of **6** in $CDCl_3$
tBu
O
N
O
tBu
O
f1 (ppm)

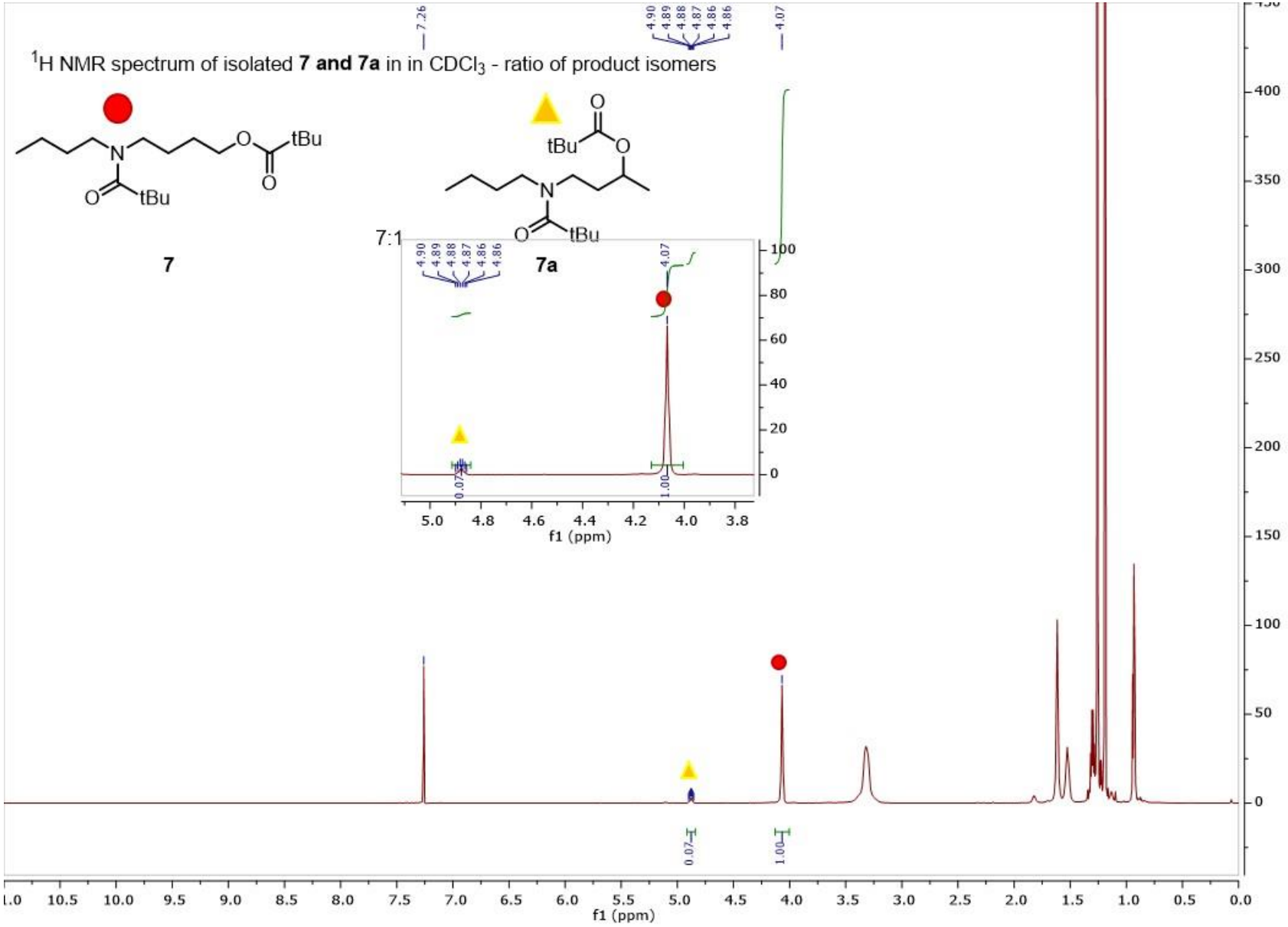

^{1}H NMR spectrum of crude reaction with dibutylamine in $CDCl_3$
K_2PtCl_4 (1 mol%)
$CuCl_2$, H_2SO_4, H_2O
150°C
OH
OH
5:1
mesitylene standard
f1 (ppm)

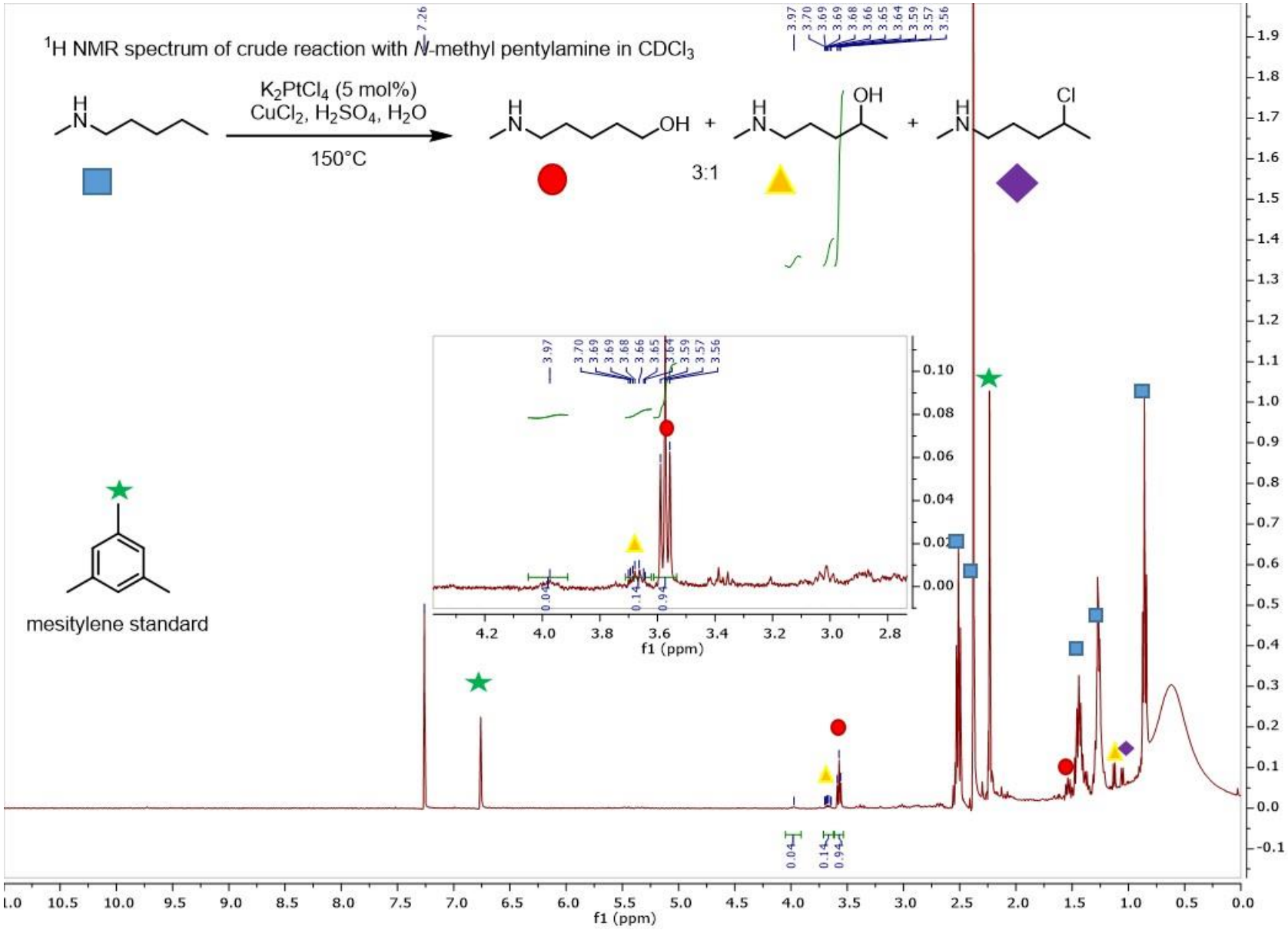

^{1}H NMR spectrum of **7** in in $CDCl_3$
tBu
tBu
f1 (ppm)

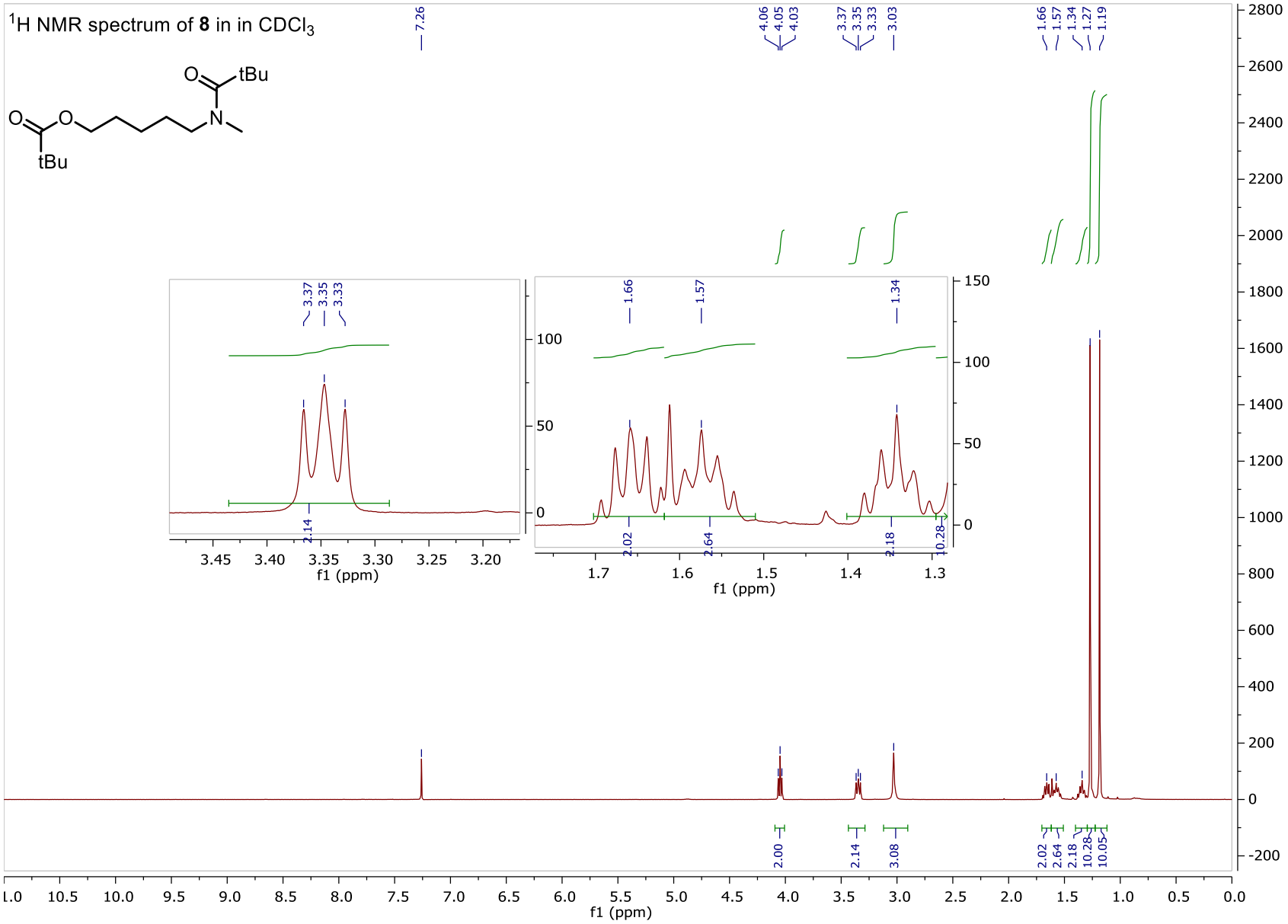

^{13}C NMR spectrum of **7** in $CDCl_3$
178.8
177.4
77.5
77.3
77.2
64.2
48.0
47.6
39.4
39.1
30.9
29.0
27.6
26.7
25.1
20.6
14.2
tBu
tBu
f1 (ppm)

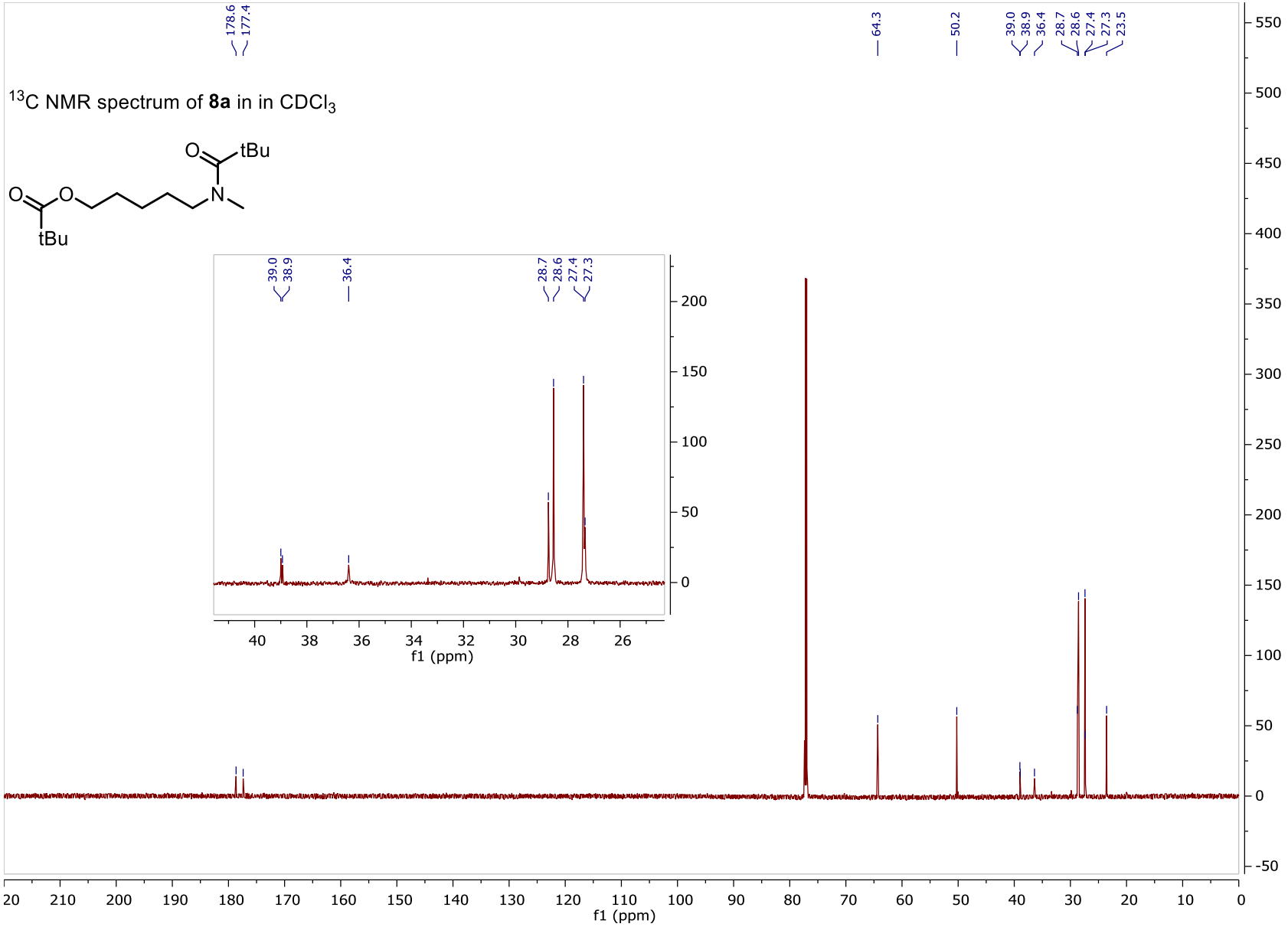

^{1}H NMR spectrum of **7a** in in $CDCl_3$
tBu
O
O
N
O
tBu
f1 (ppm)

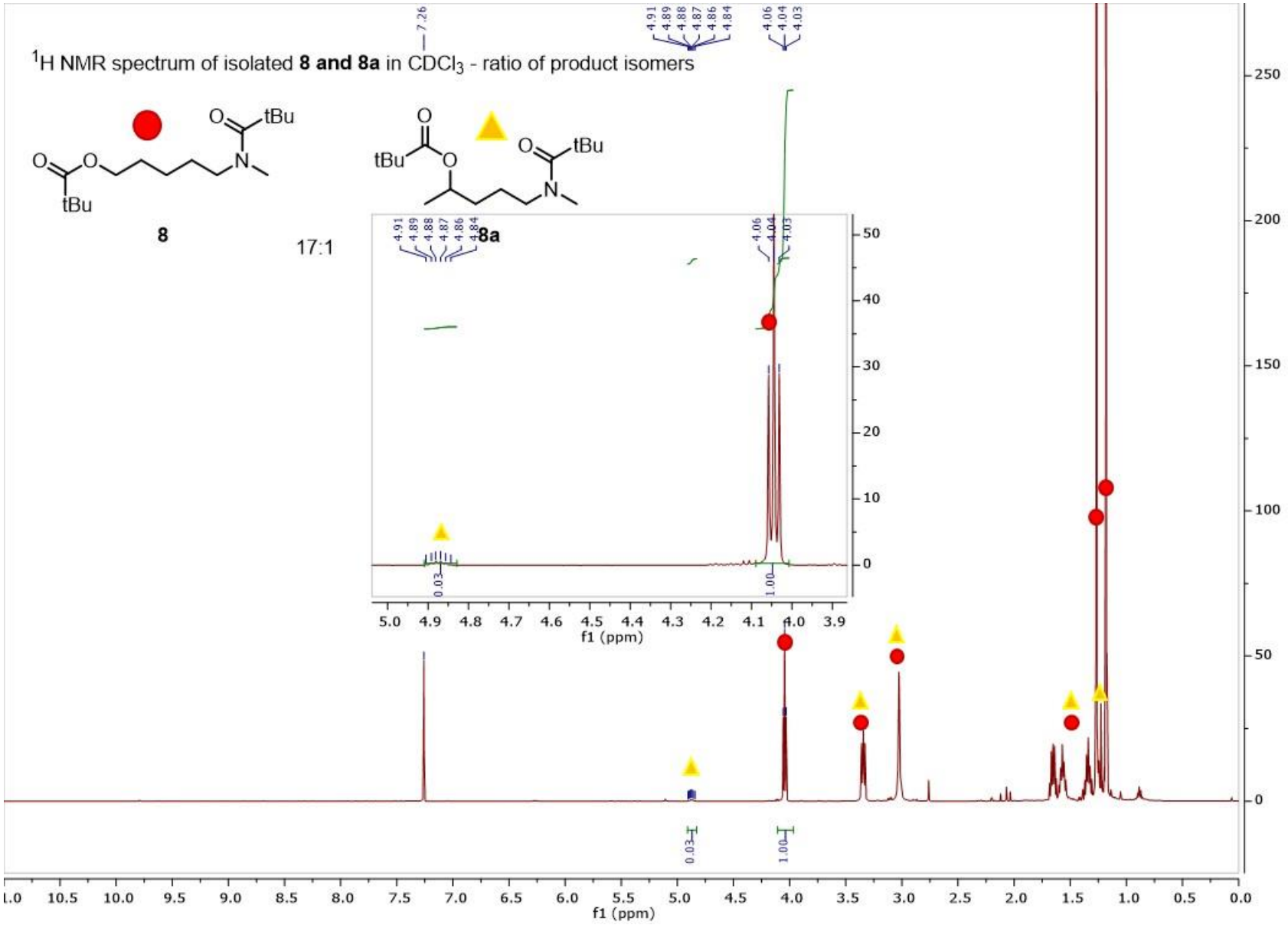

^{13}C NMR spectrum of **7a** in in $CDCl_3$
178.1
177.3
77.3
77.2
77.0
69.1
48.1
44.5
39.2
39.0
34.5
30.7
28.8
27.4
20.4
20.2
14.0
tBu
O
O
N
O
tBu
f1 (ppm)

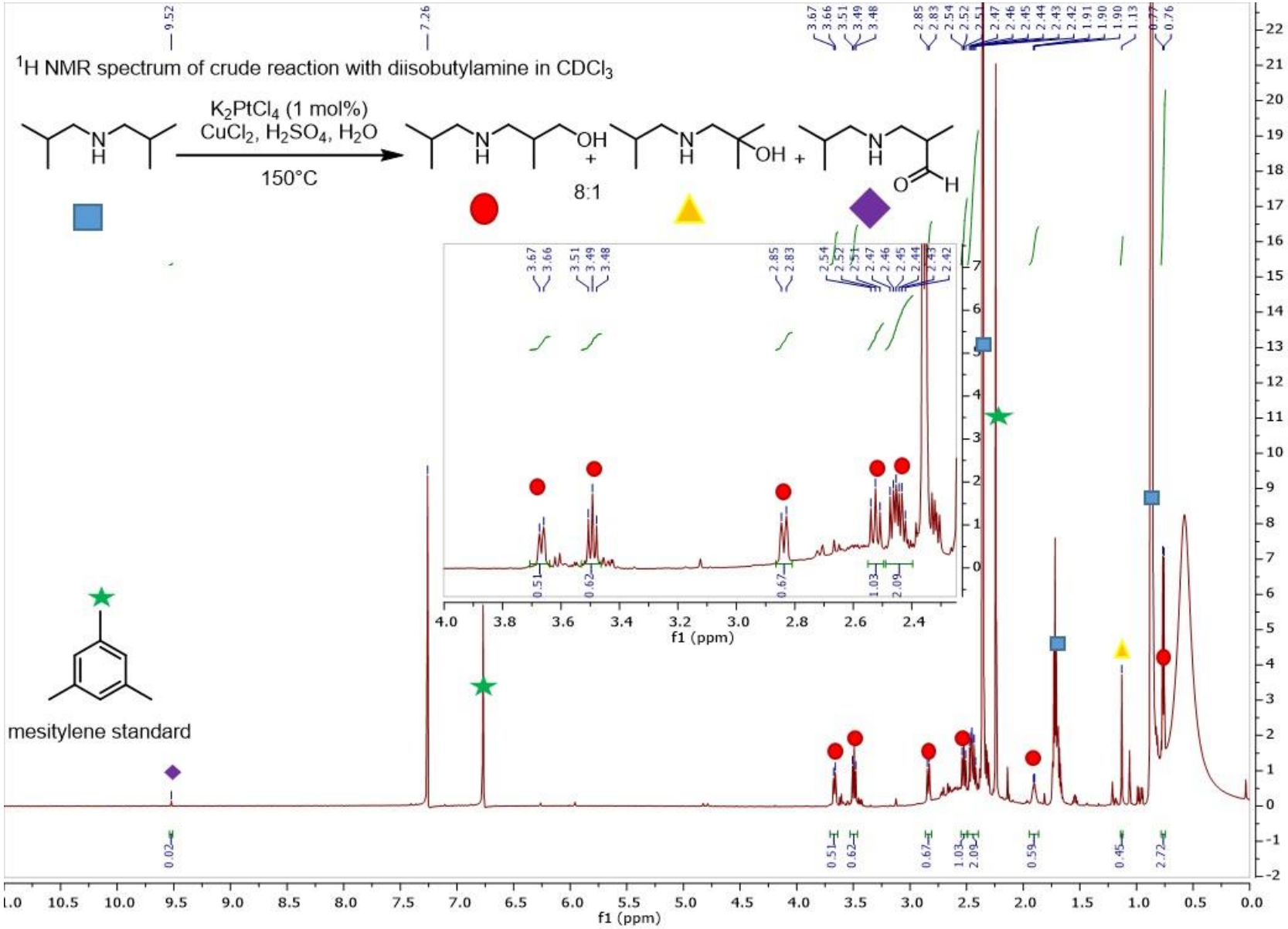

^{1}H NMR spectrum of isolated **7 and 7a** in in $CDCl_3$ - ratio of product isomers
7
7a
7:1
f1 (ppm)

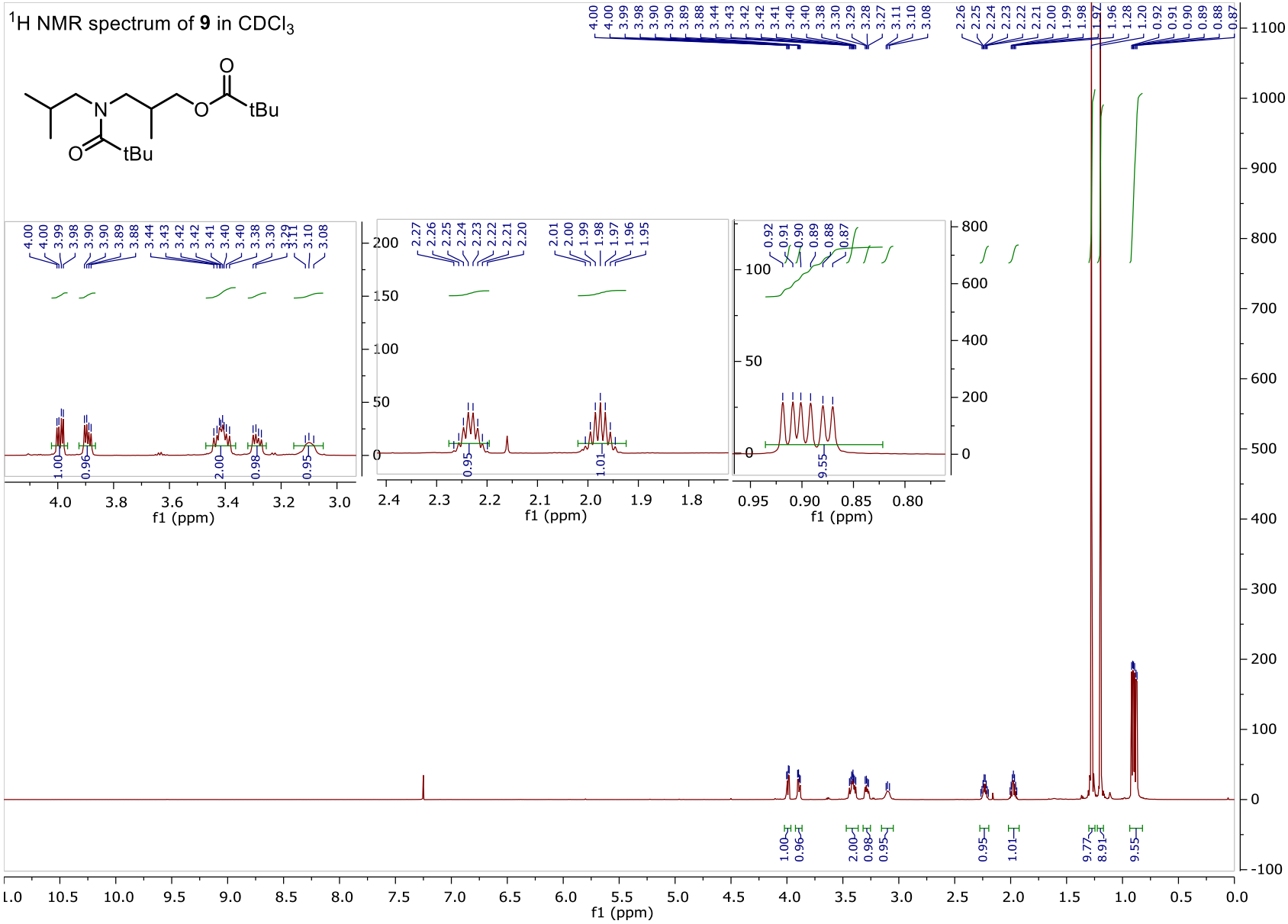

1H NMR spectrum of crude reaction with N-methyl pentylamine in CDCl3
K2PtCl4 (5 mol%)
CuCl2, H2SO4, H2O
150°C
OH
Cl
3:1
mesitylene standard
f1 (ppm)


^{1}H NMR spectrum of **8** in in $CDCl_3$
tBu
tBu
7.26
4.06
4.05
4.03
3.37
3.35
3.33
3.03
1.66
1.57
1.34
1.27
1.19
2.00
2.14
3.08
2.02
2.64
2.18
10.28
10.05
f1 (ppm)

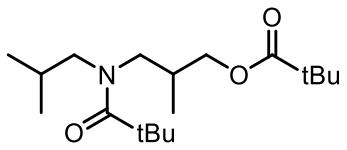

^{13}C NMR spectrum of **8a** in in $CDCl_3$
178.6
177.4
64.3
50.2
39.0
38.9
36.4
28.7
28.6
27.4
27.3
23.5
tBu
tBu
f1 (ppm)

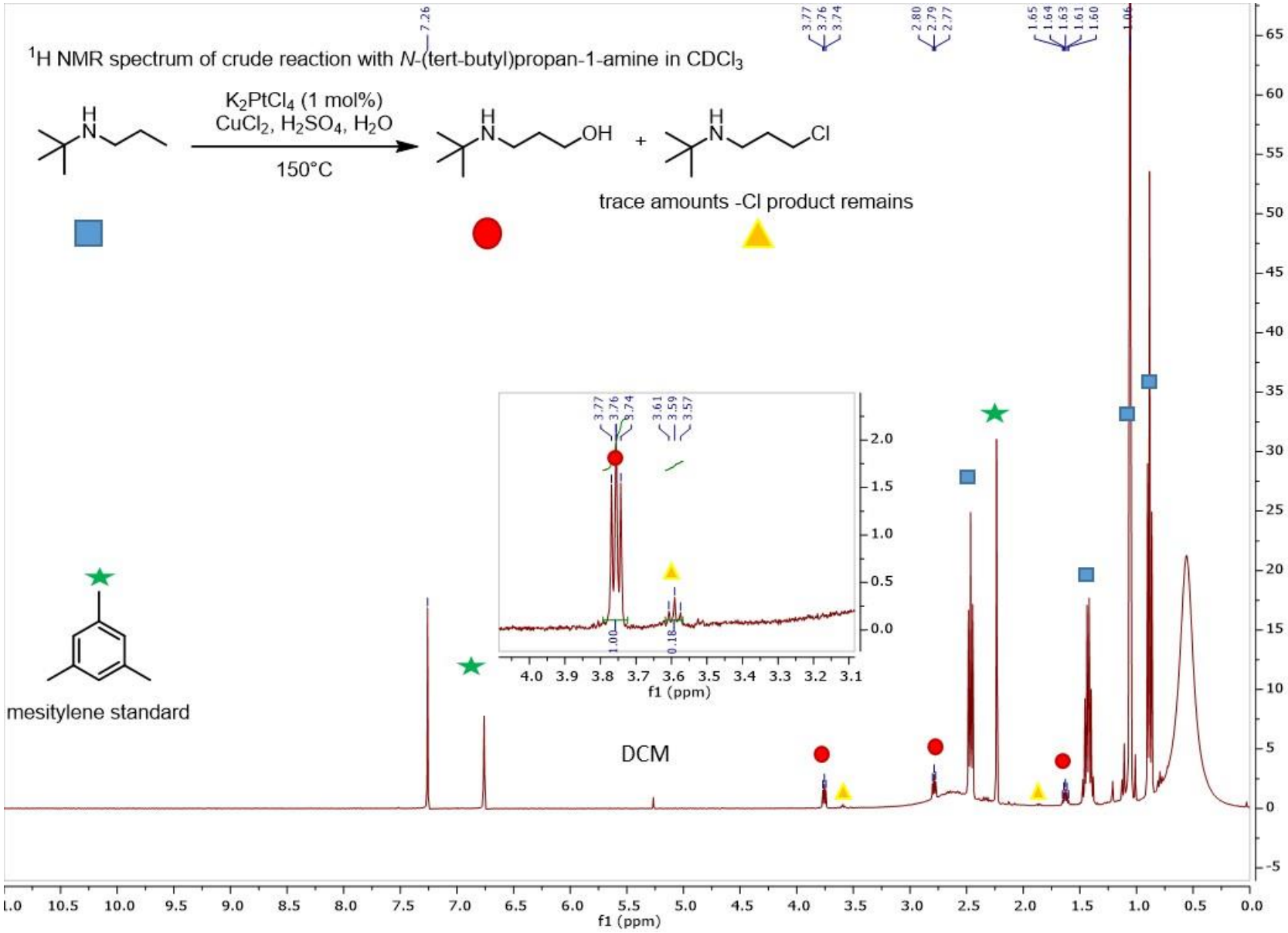

^{1}H NMR spectrum of isolated **8 and 8a** in $CDCl_3$ - ratio of product isomers
8
17:1
8a
f1 (ppm)

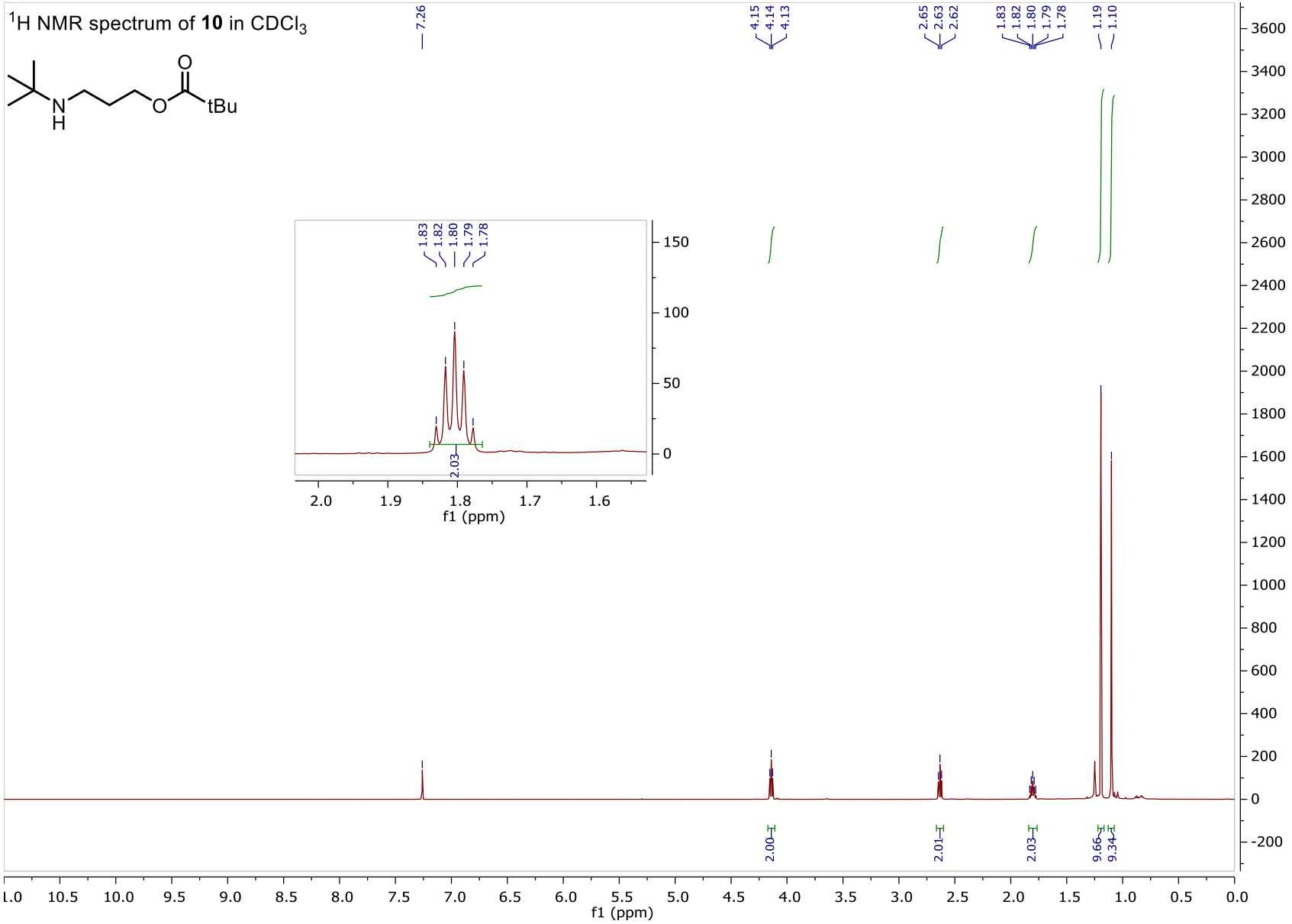

^{1}H NMR spectrum of crude reaction with diisobutylamine in $CDCl_3$
K_2PtCl_4 (1 mol%)
$CuCl_2$, H_2SO_4, H_2O
150°C
8:1
mesitylene standard
f1 (ppm)

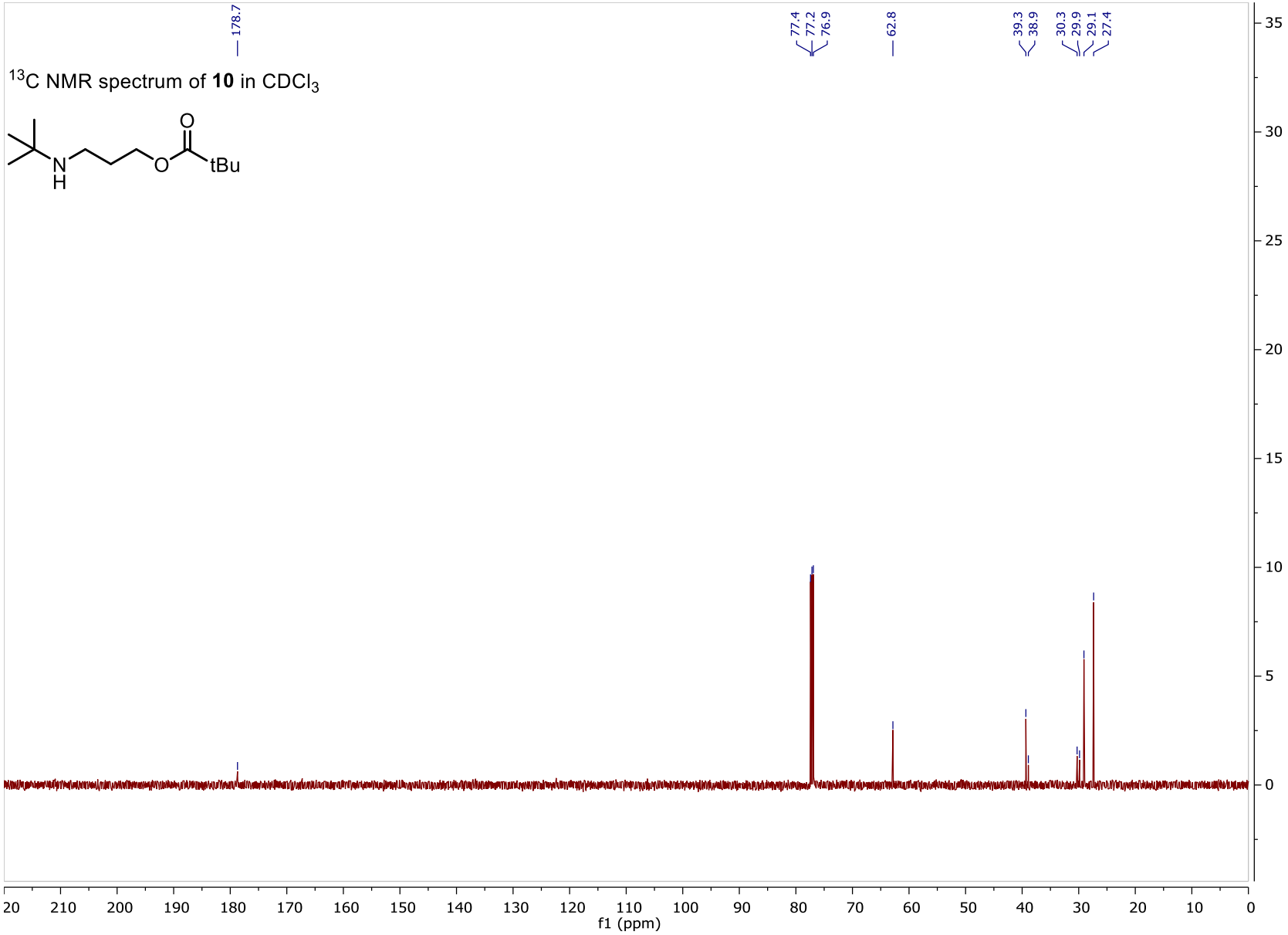

^{1}H NMR spectrum of **9** in $CDCl_3$
O
N
O
tBu
O
tBu
f1 (ppm)

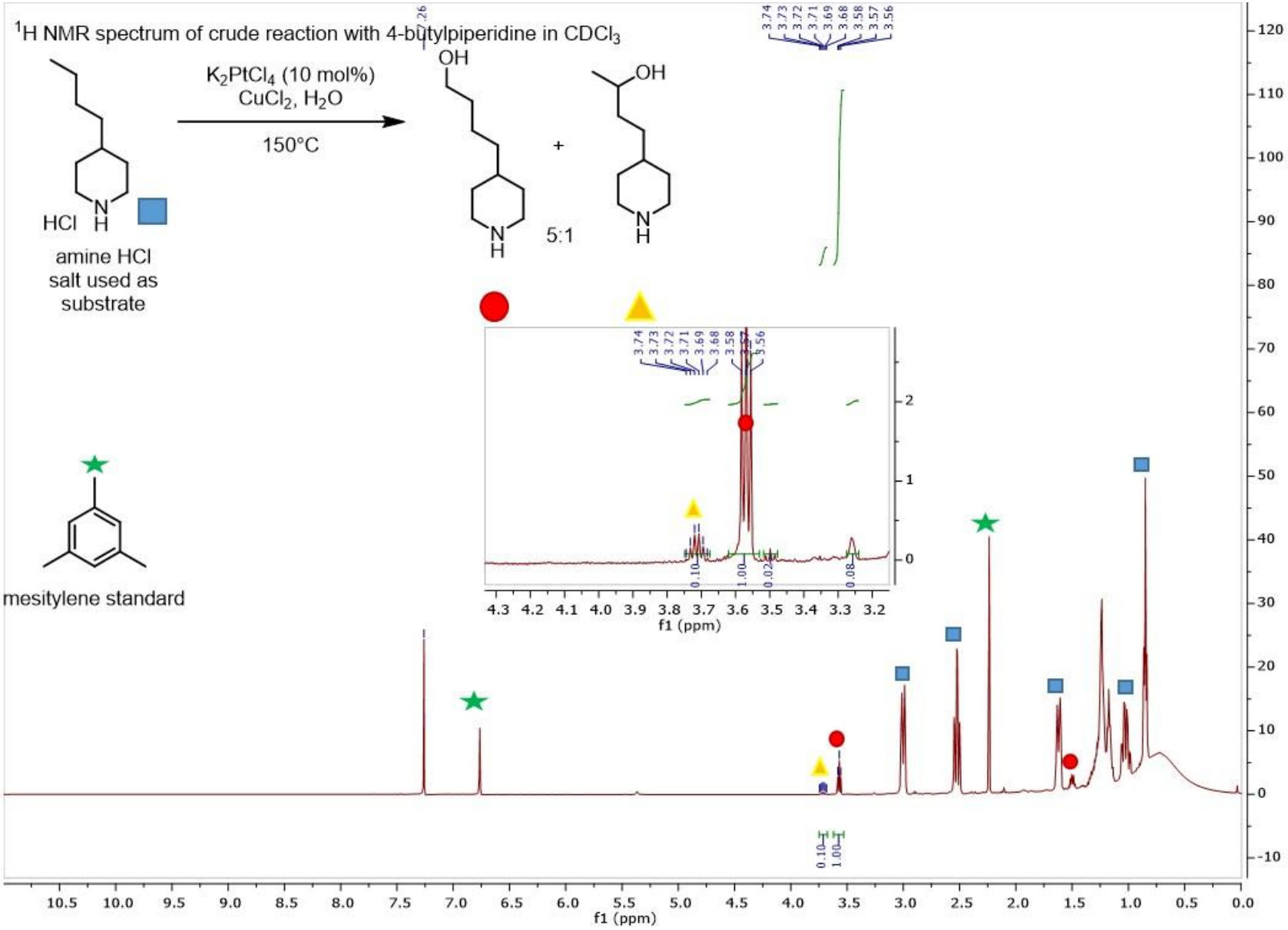
^{13}C NMR spectrum of **9** in $CDCl_3$

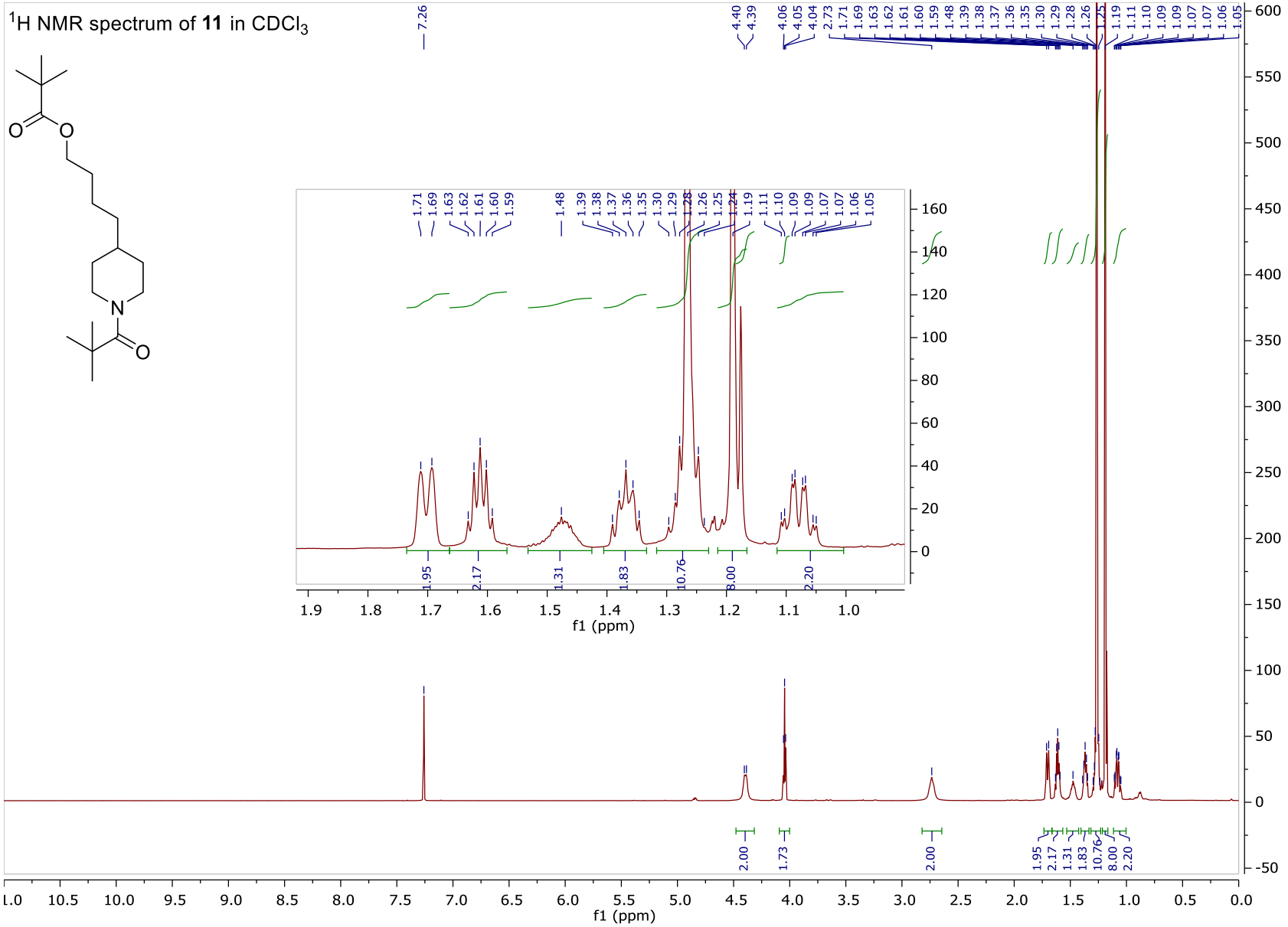


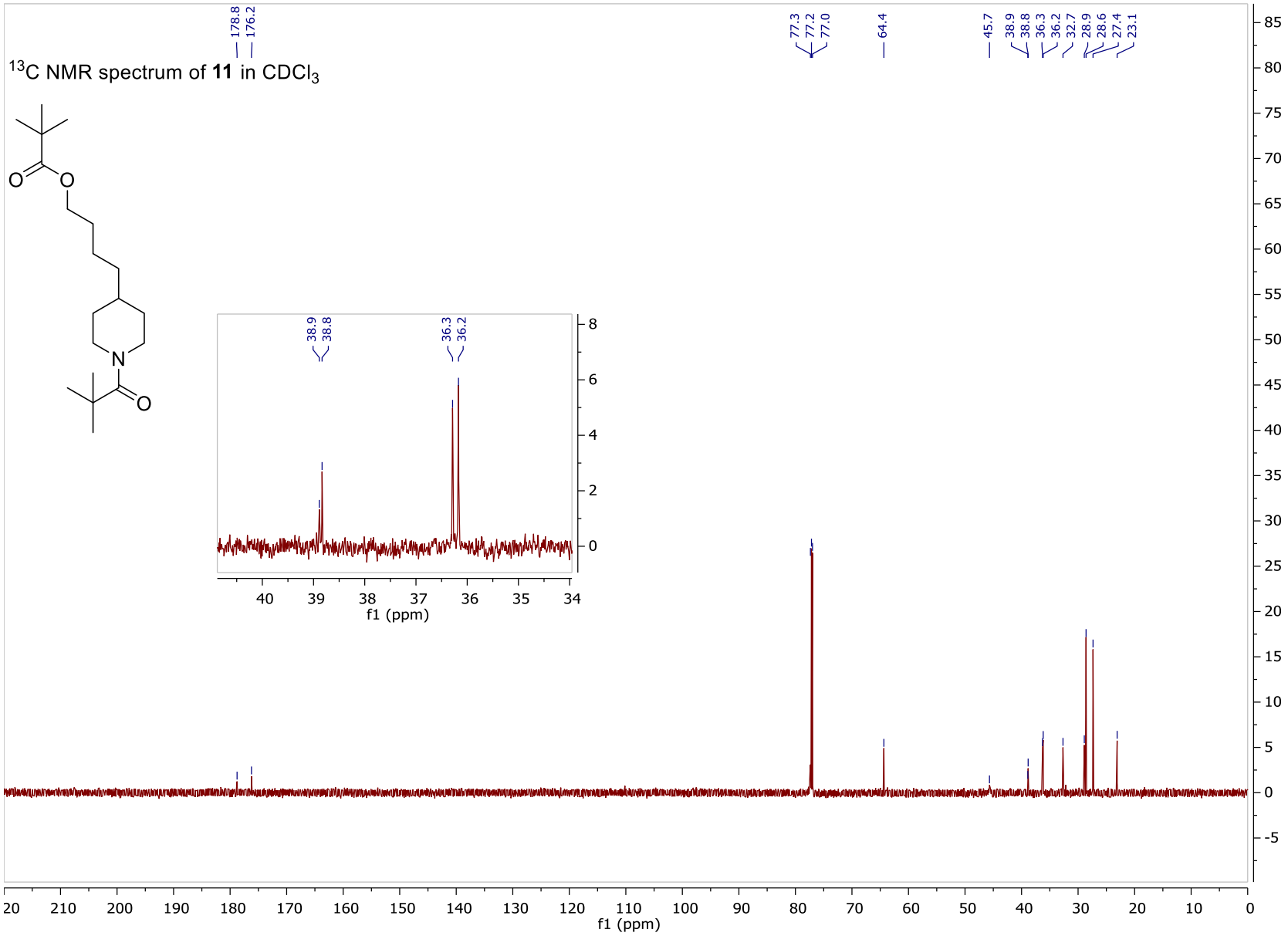

^{1}H NMR spectrum of crude reaction with *N*-(tert-butyl)propan-1-amine in $CDCl_3$
K_2PtCl_4 (1 mol%)
$CuCl_2$, H_2SO_4, H_2O
150°C
OH
Cl
+
trace amounts -Cl product remains
mesitylene standard
DCM
f1 (ppm)

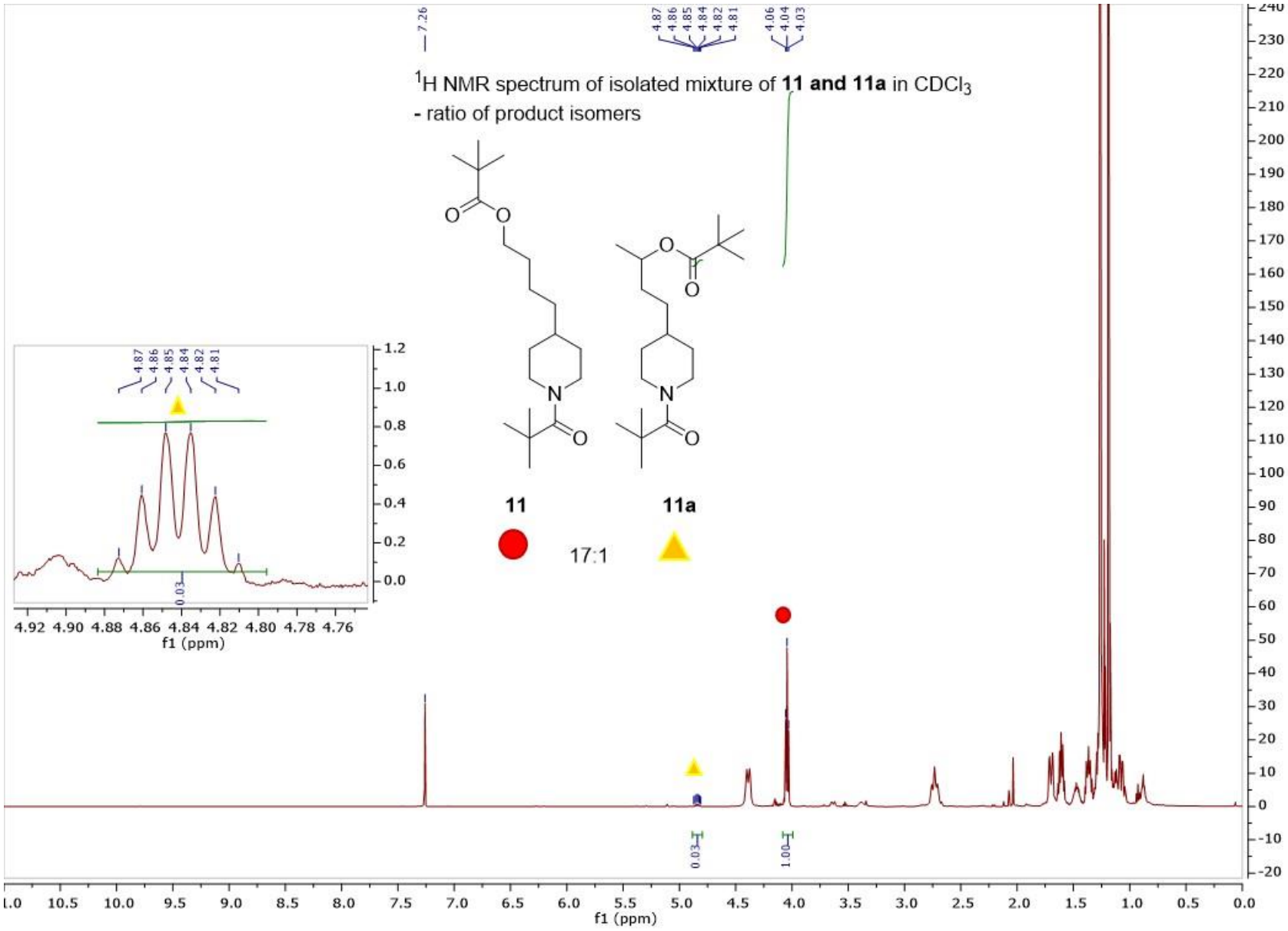

^{1}H NMR spectrum of **10** in $CDCl_3$
7.26
4.15
4.14
4.13
2.65
2.63
2.62
1.83
1.82
1.80
1.79
1.78
1.19
1.10
2.00
2.01
2.03
9.66
9.34
f1 (ppm)

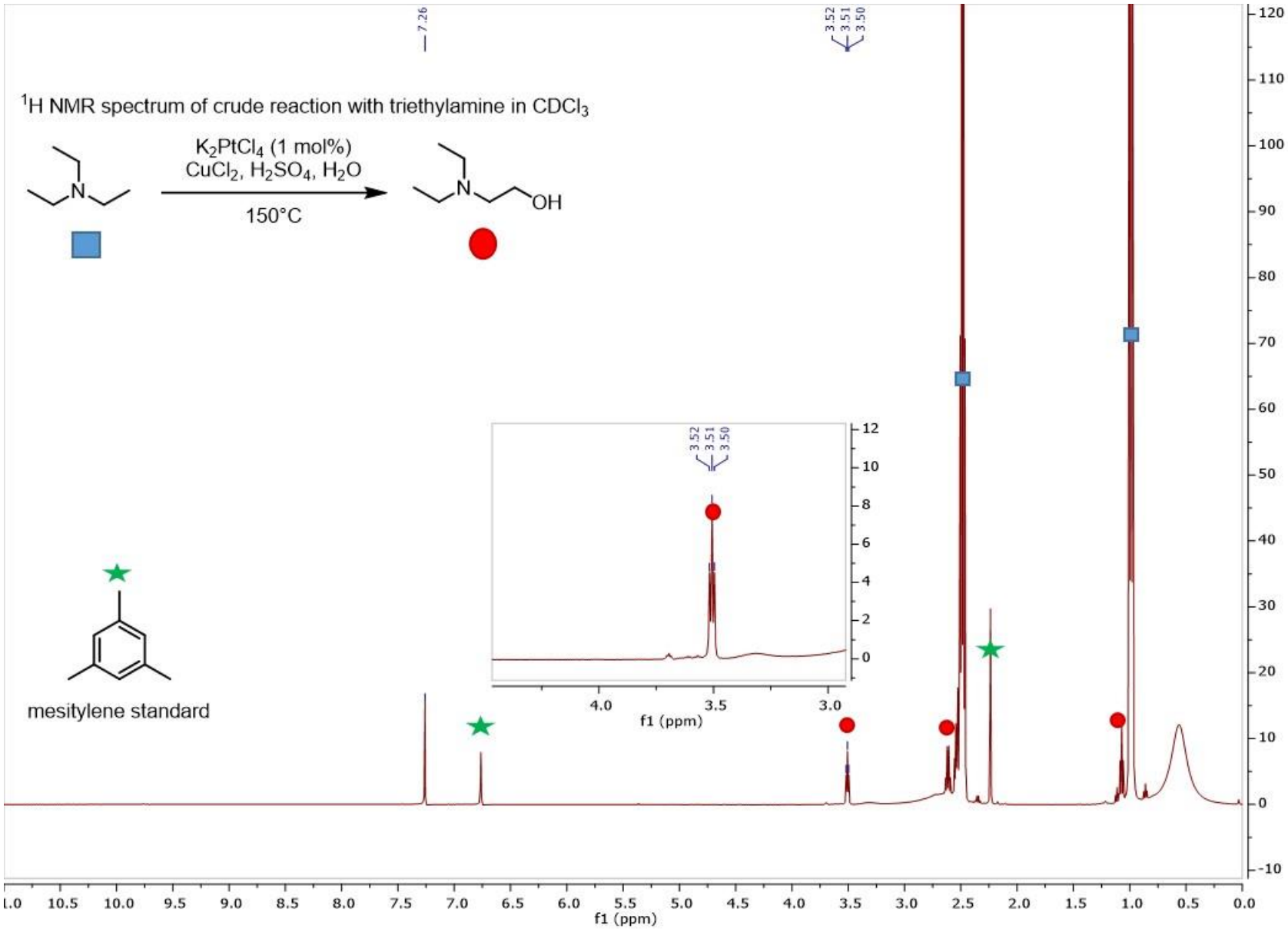

178.7
77.4
77.2
76.9
62.8
39.3
38.9
30.3
29.9
29.1
27.4
13C NMR spectrum of 10 in CDCl3
O
N
H
O
tBu
35
30
25
20
15
10
5
0
20 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

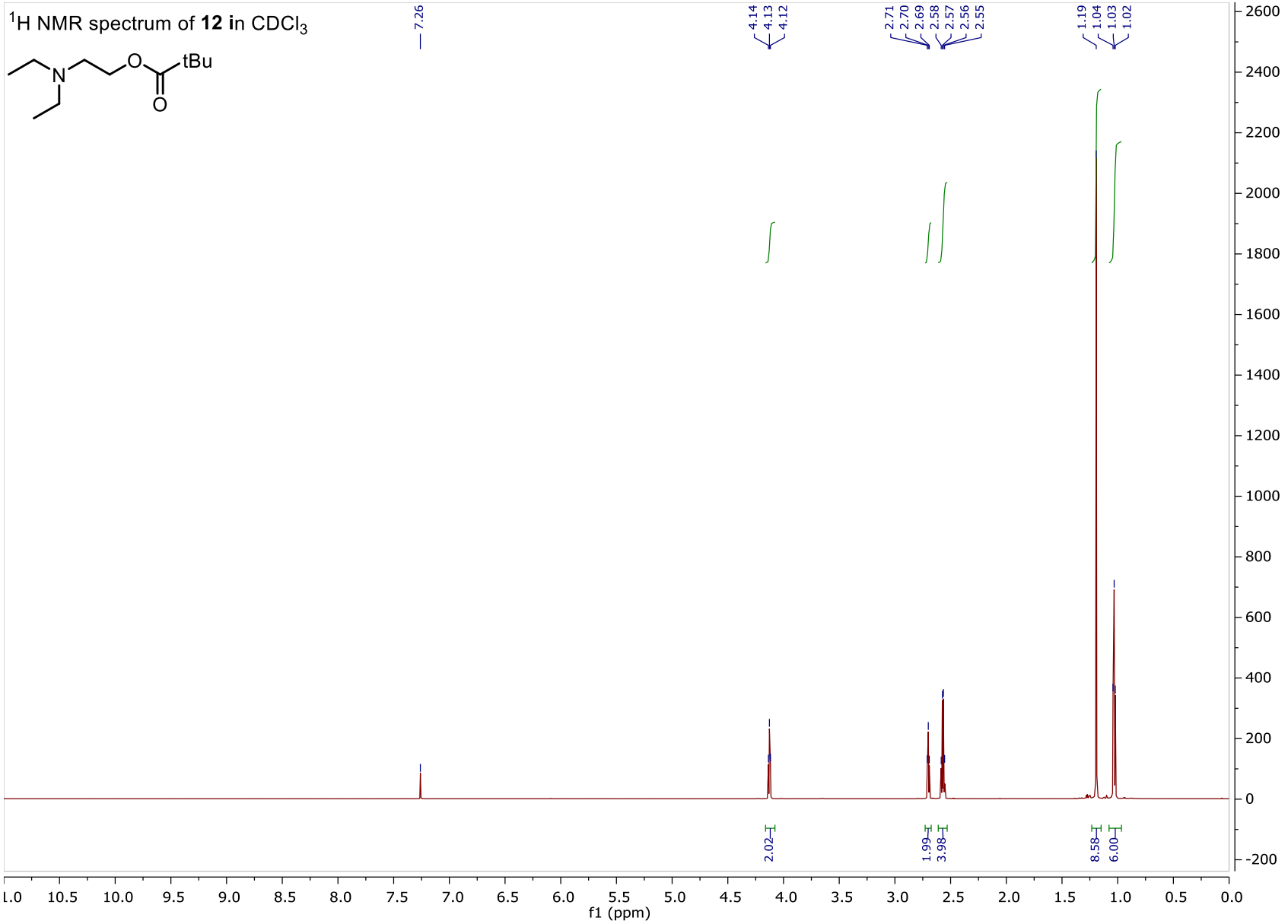

1H NMR spectrum of crude reaction with 4-butylpiperidine in CDCl3
K2PtCl4 (10 mol%)
CuCl2, H2O
150°C
OH
OH
+
5:1
HCl
N
H
amine HCl
salt used as
substrate
mesitylene standard
3.74
3.73
3.72
3.71
3.69
3.68
3.58
3.57
3.56
0.10
1.00
0.02
0.08
4.3 4.2 4.1 4.0 3.9 3.8 3.7 3.6 3.5 3.4 3.3 3.2
f1 (ppm)
10.5 10.0 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)

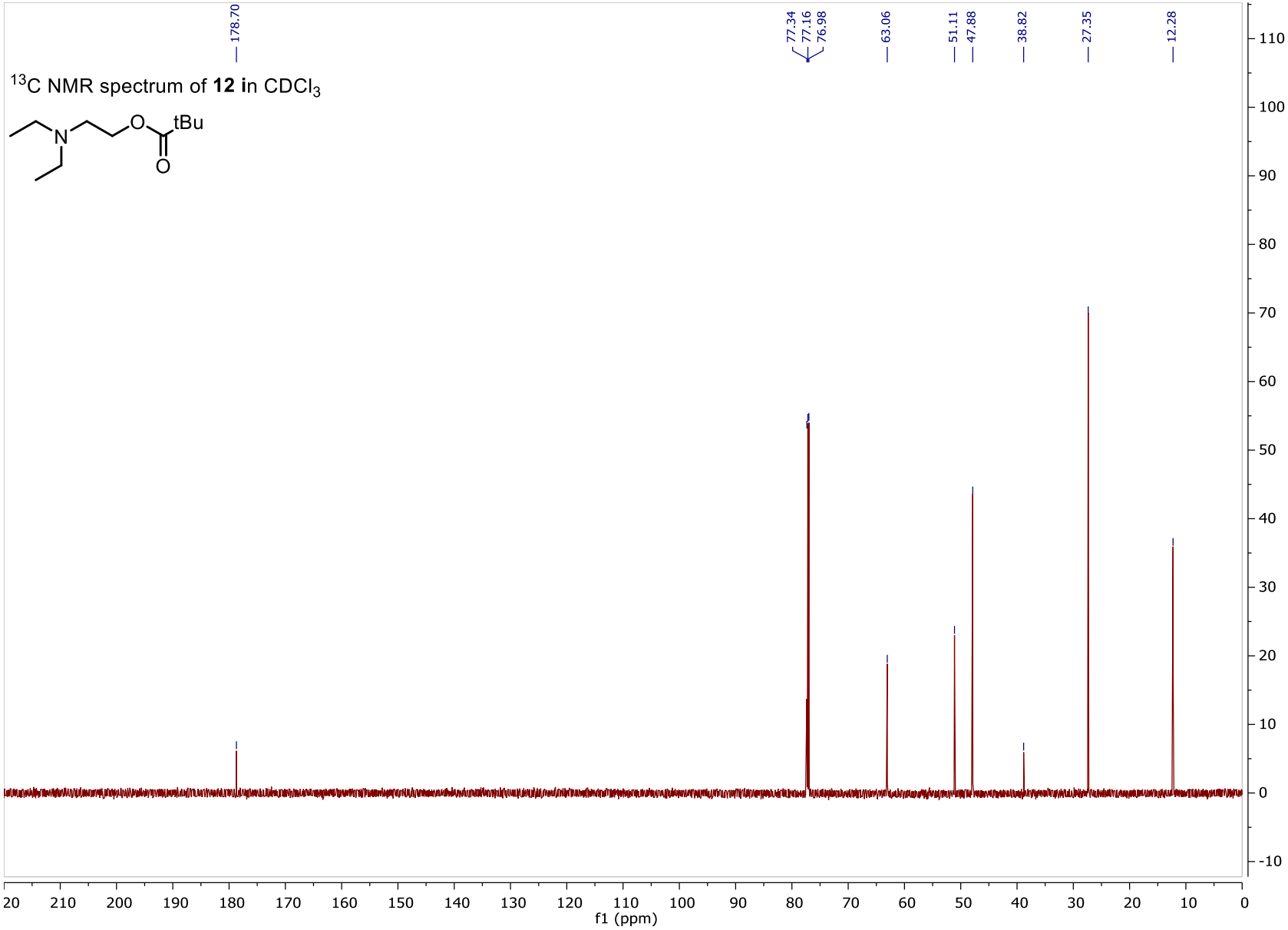

^{1}H NMR spectrum of **11** in $CDCl_3$
f1 (ppm)

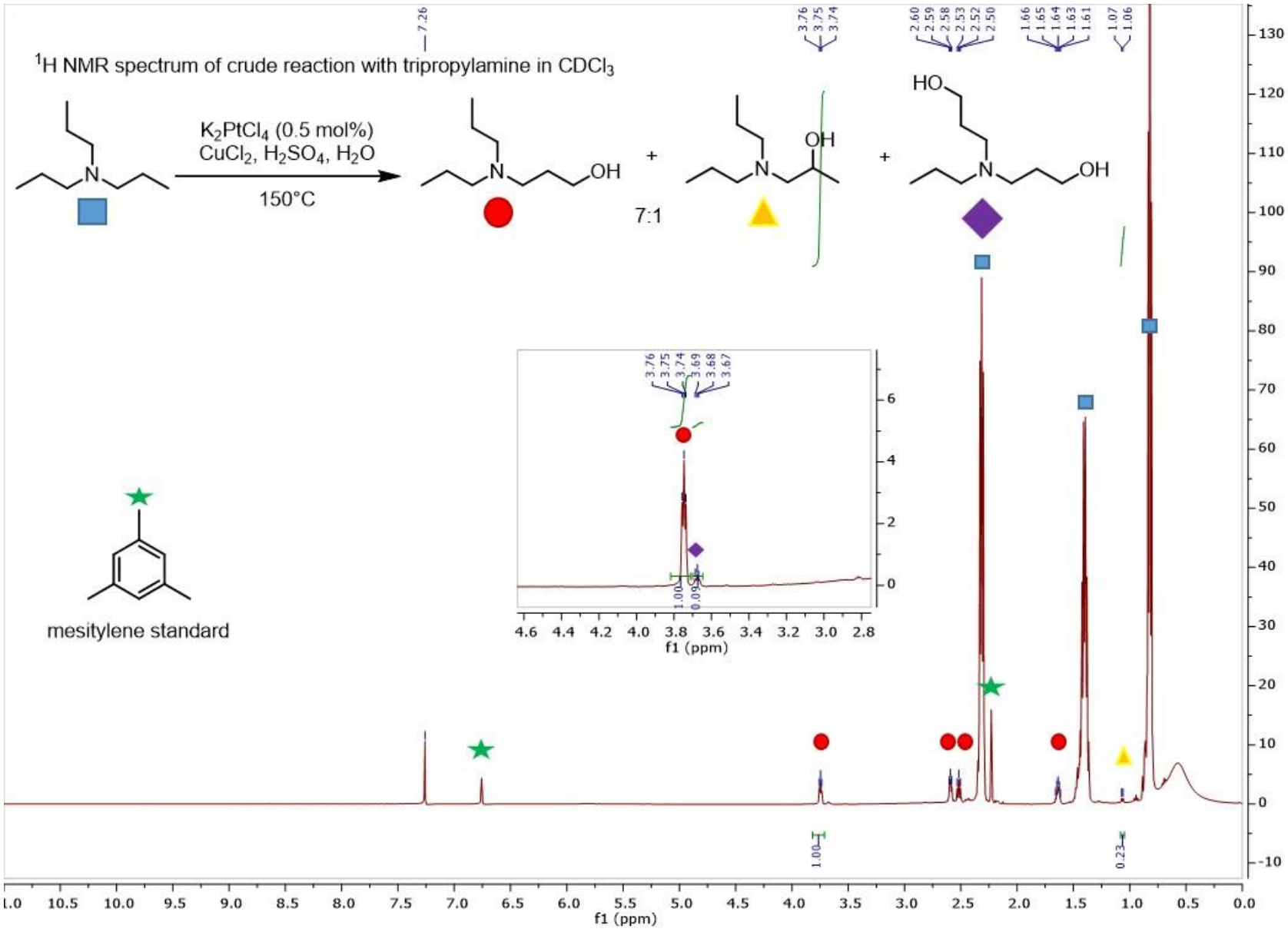

13C NMR spectrum of 11 in CDCl3
178.8
176.2
77.3
77.2
77.0
64.4
45.7
38.9
38.8
36.3
36.2
32.7
28.9
28.6
27.4
23.1
O
O
N
O
38.9
38.8
36.3
36.2
f1 (ppm)
f1 (ppm)

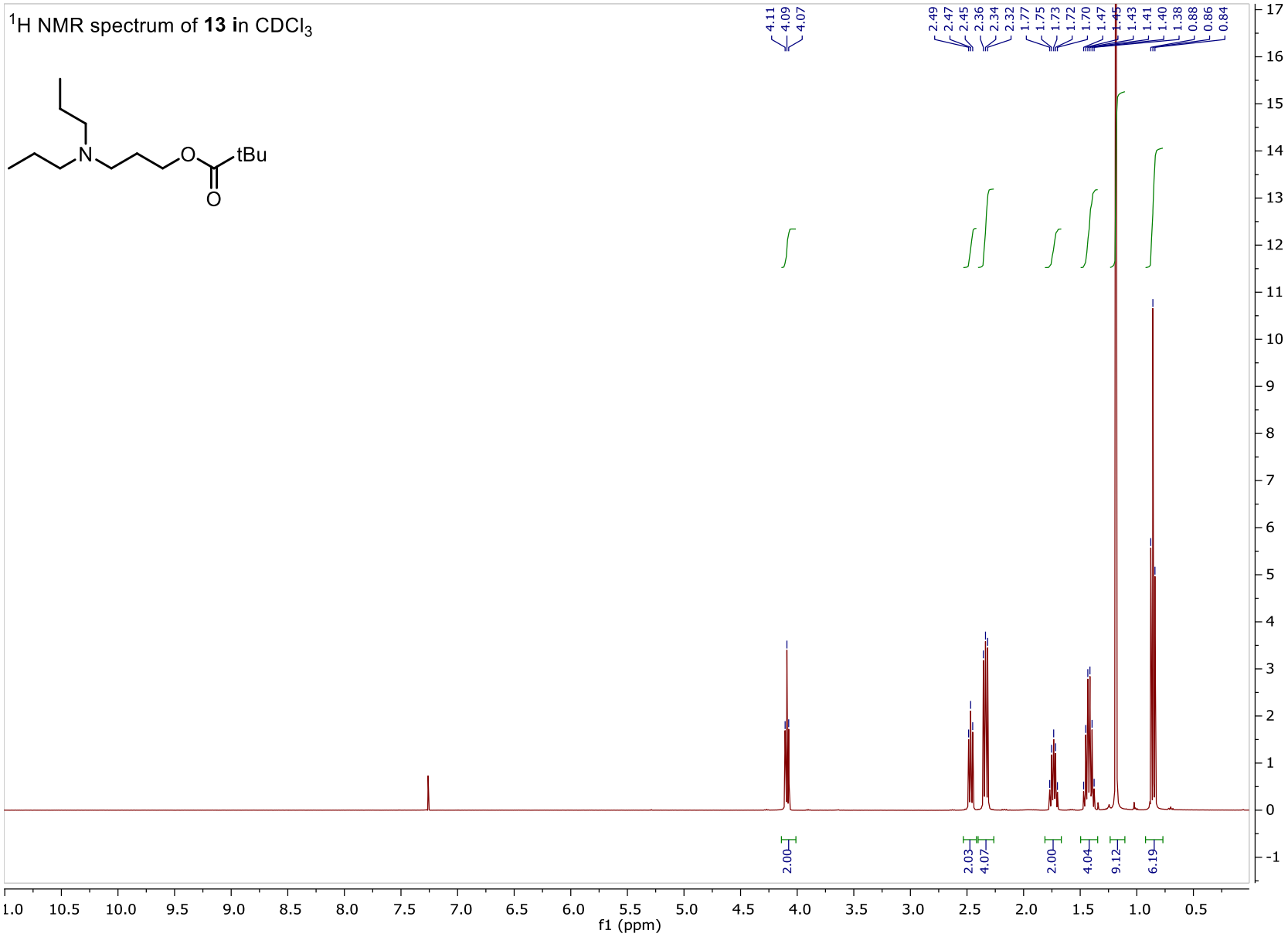

^{1}H NMR spectrum of isolated mixture of **11 and 11a** in $CDCl_3$
- ratio of product isomers
11
11a
17:1
f1 (ppm)

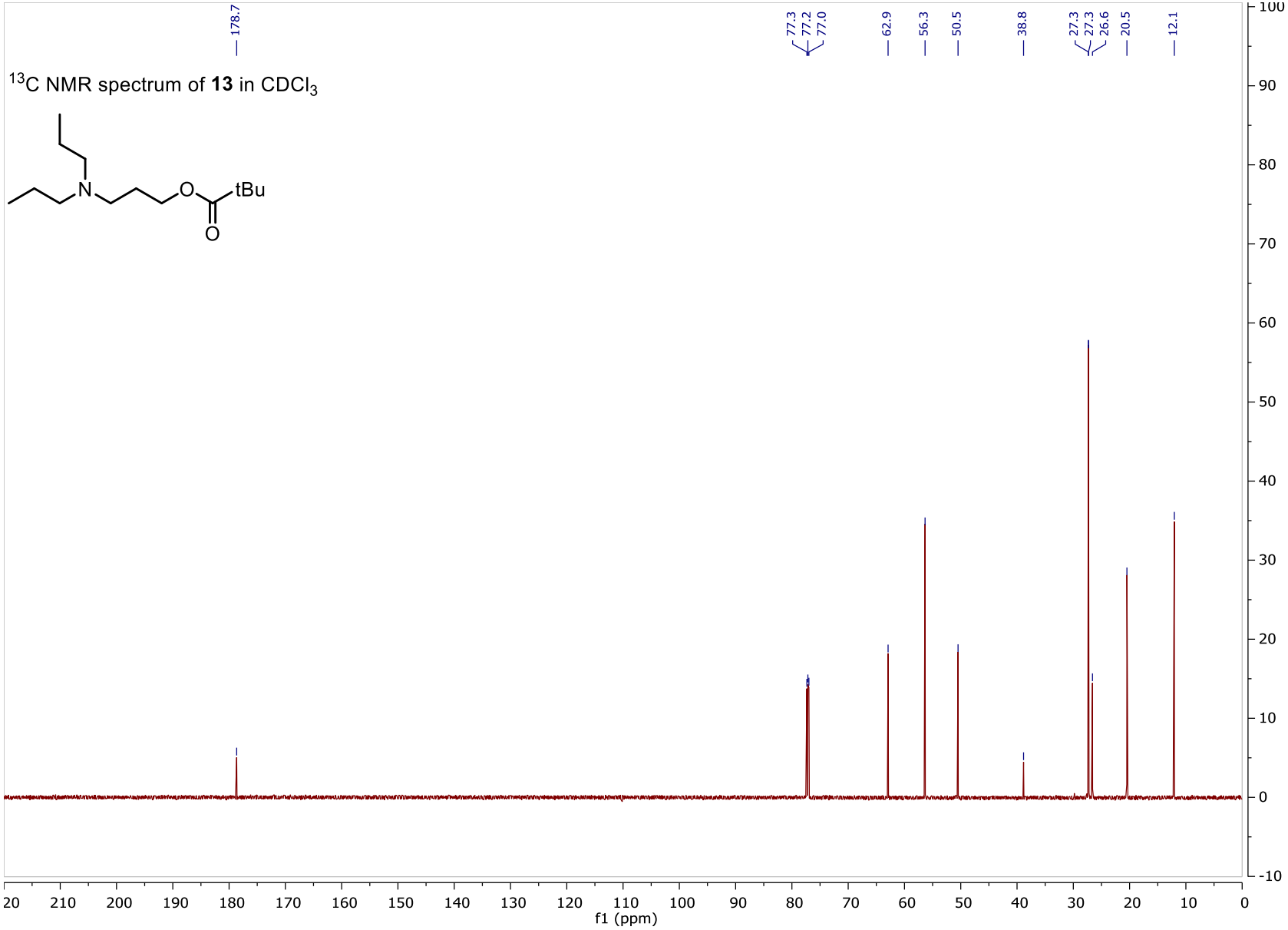

^{1}H NMR spectrum of crude reaction with triethylamine in $CDCl_3$
K_2PtCl_4 (1 mol%)
$CuCl_2$, H_2SO_4, H_2O
150°C
N
OH
mesitylene standard
7.26
3.52
3.51
3.50
f1 (ppm)

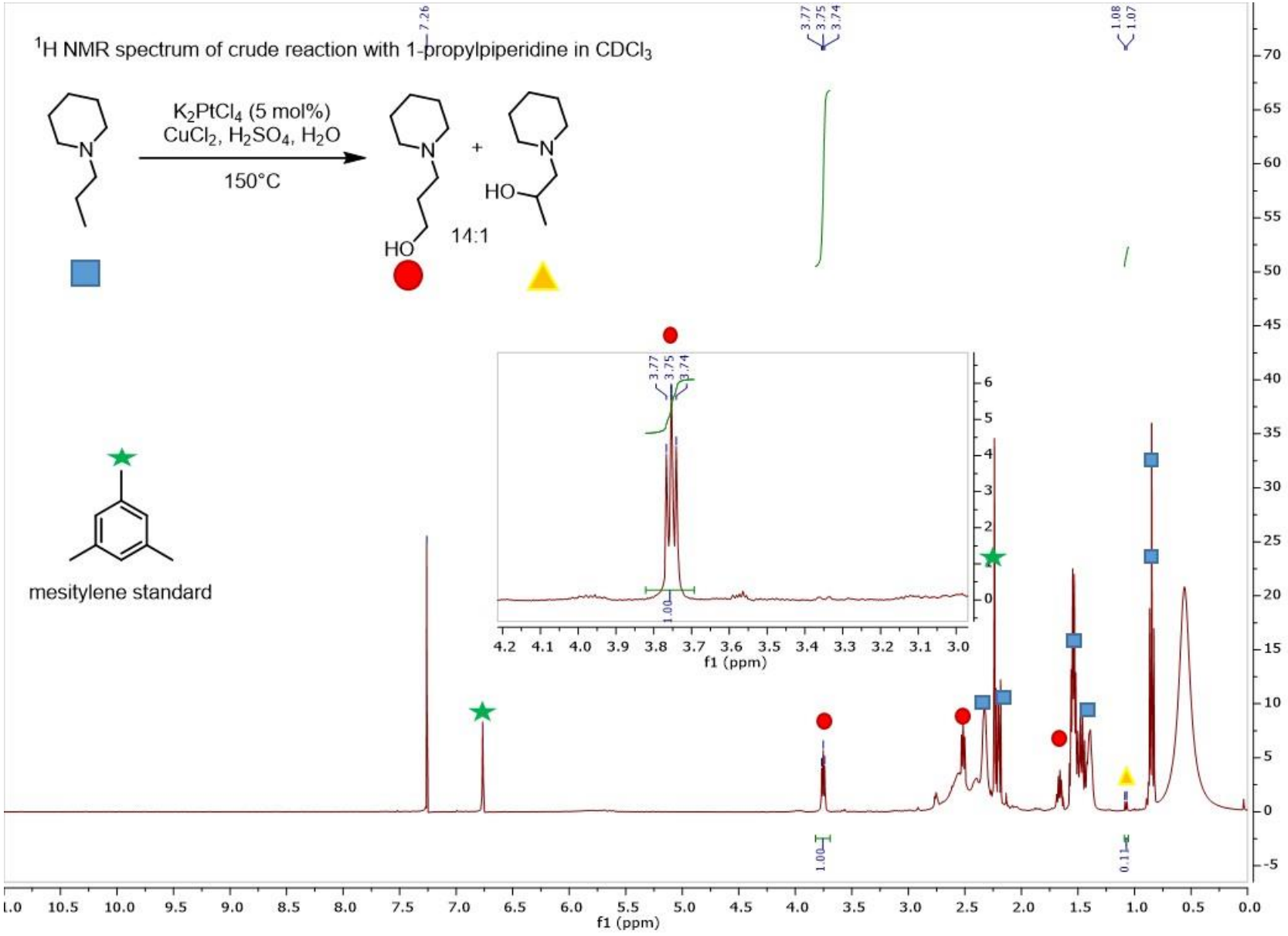

^{1}H NMR spectrum of **12** in $CDCl_3$
N
O
O
tBu
7.26
4.14
4.13
4.12
2.71
2.70
2.69
2.58
2.57
2.56
2.55
1.19
1.04
1.03
1.02
2.02
1.99
3.98
8.58
6.00
f1 (ppm)

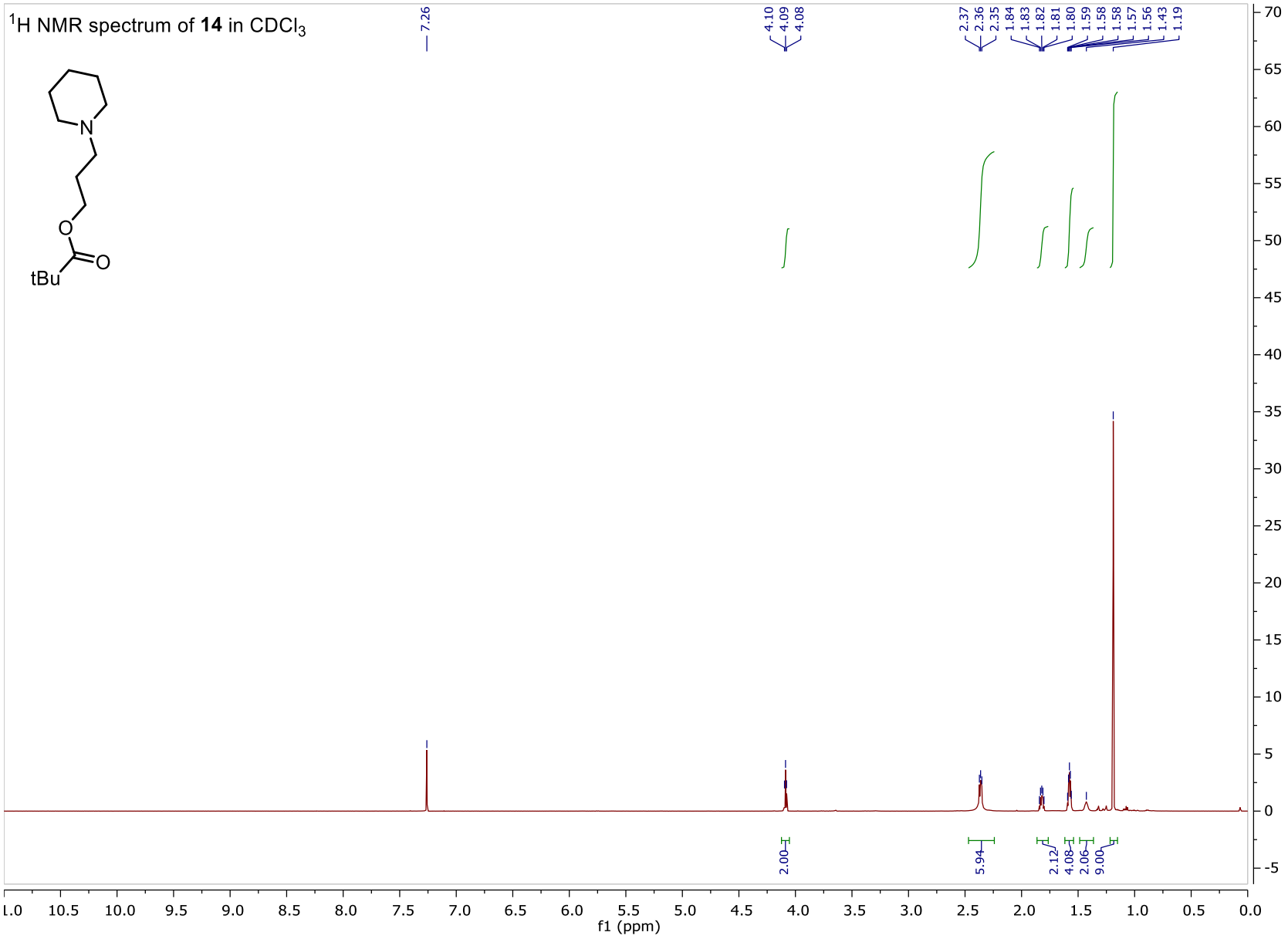

178.70
77.34
77.16
76.98
63.06
51.11
47.88
38.82
27.35
12.28
13C NMR spectrum of 12 in CDCl3
N
O
O
tBu
f1 (ppm)

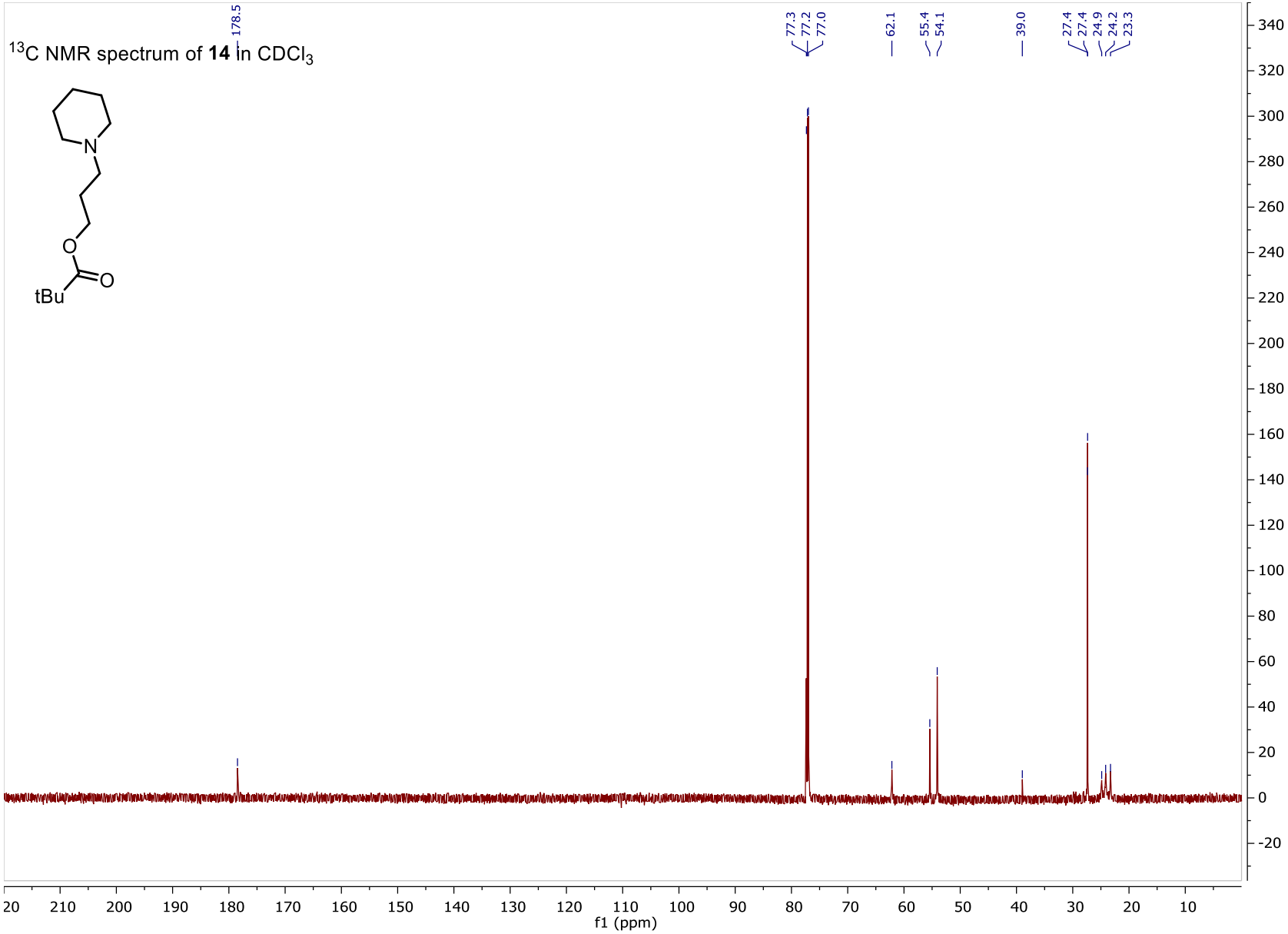

^{1}H NMR spectrum of crude reaction with tripropylamine in $CDCl_3$
K_2PtCl_4 (0.5 mol%)
$CuCl_2$, H_2SO_4, H_2O
150°C
7:1
mesitylene standard
f1 (ppm)

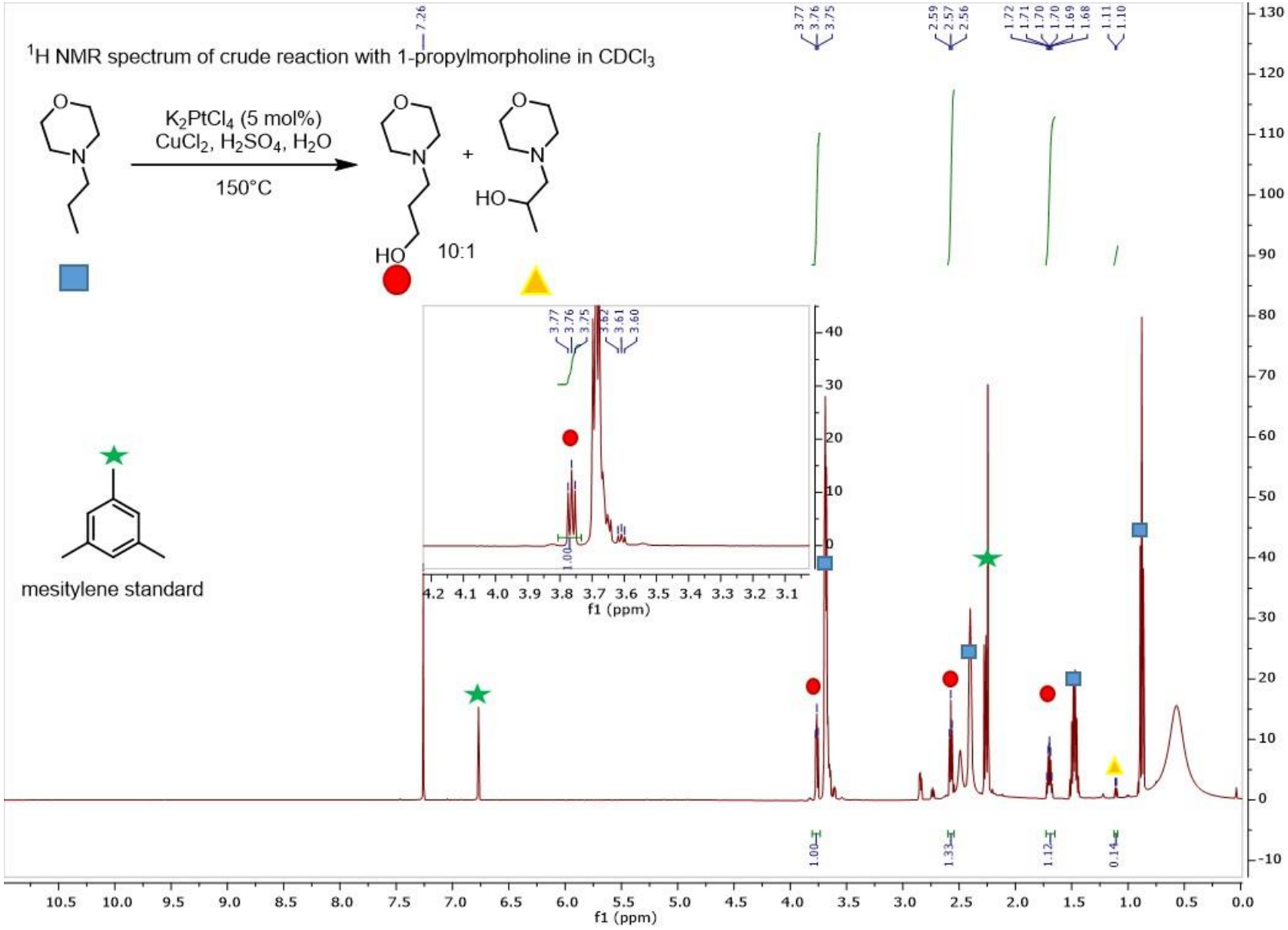

^{1}H NMR spectrum of **13** in $CDCl_3$
N
O
O
tBu
4.11
4.09
4.07
2.49
2.47
2.45
2.36
2.34
2.32
1.77
1.75
1.73
1.72
1.70
1.47
1.45
1.43
1.41
1.40
1.38
0.88
0.86
0.84
2.00
2.03
4.07
2.00
4.04
9.12
6.19
f1 (ppm)

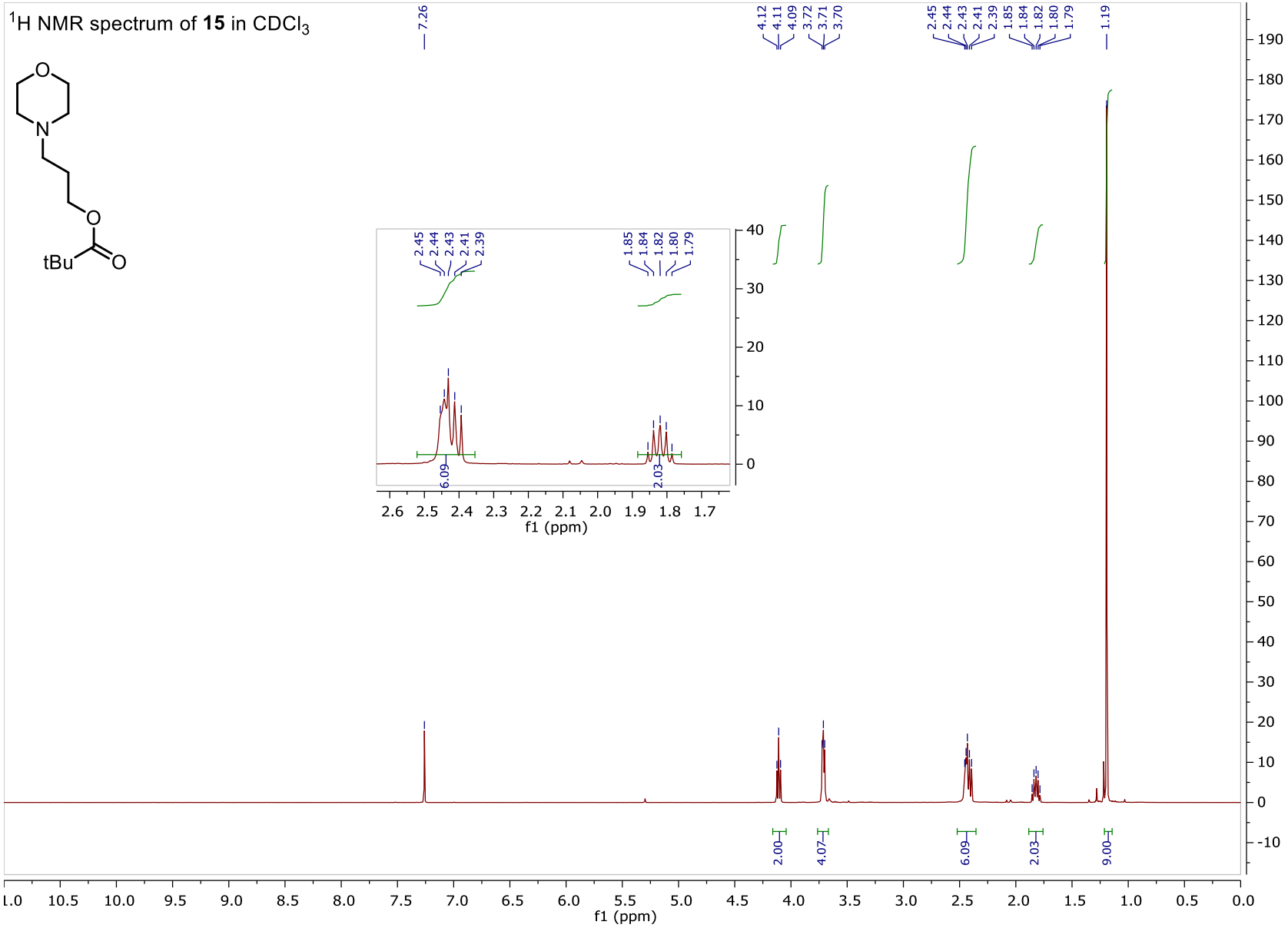

178.7
77.3
77.2
77.0
62.9
56.3
50.5
38.8
27.3
27.3
26.6
20.5
12.1
13C NMR spectrum of 13 in CDCl3
N
O
O
tBu
f1 (ppm)

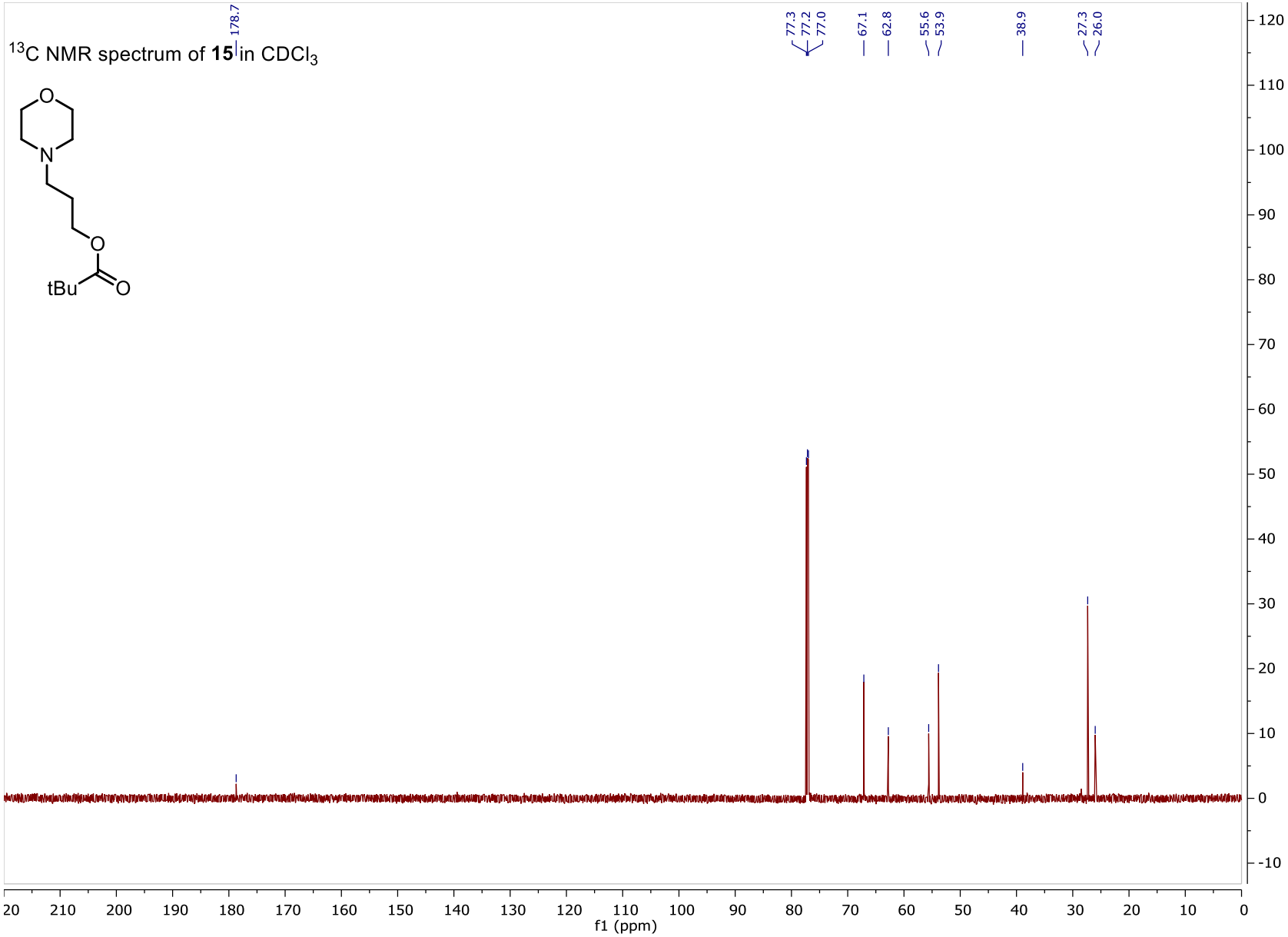

^{1}H NMR spectrum of crude reaction with 1-propylpiperidine in $CDCl_3$
K_2PtCl_4 (5 mol%)
$CuCl_2$, H_2SO_4, H_2O
150°C
14:1
mesitylene standard
f1 (ppm)

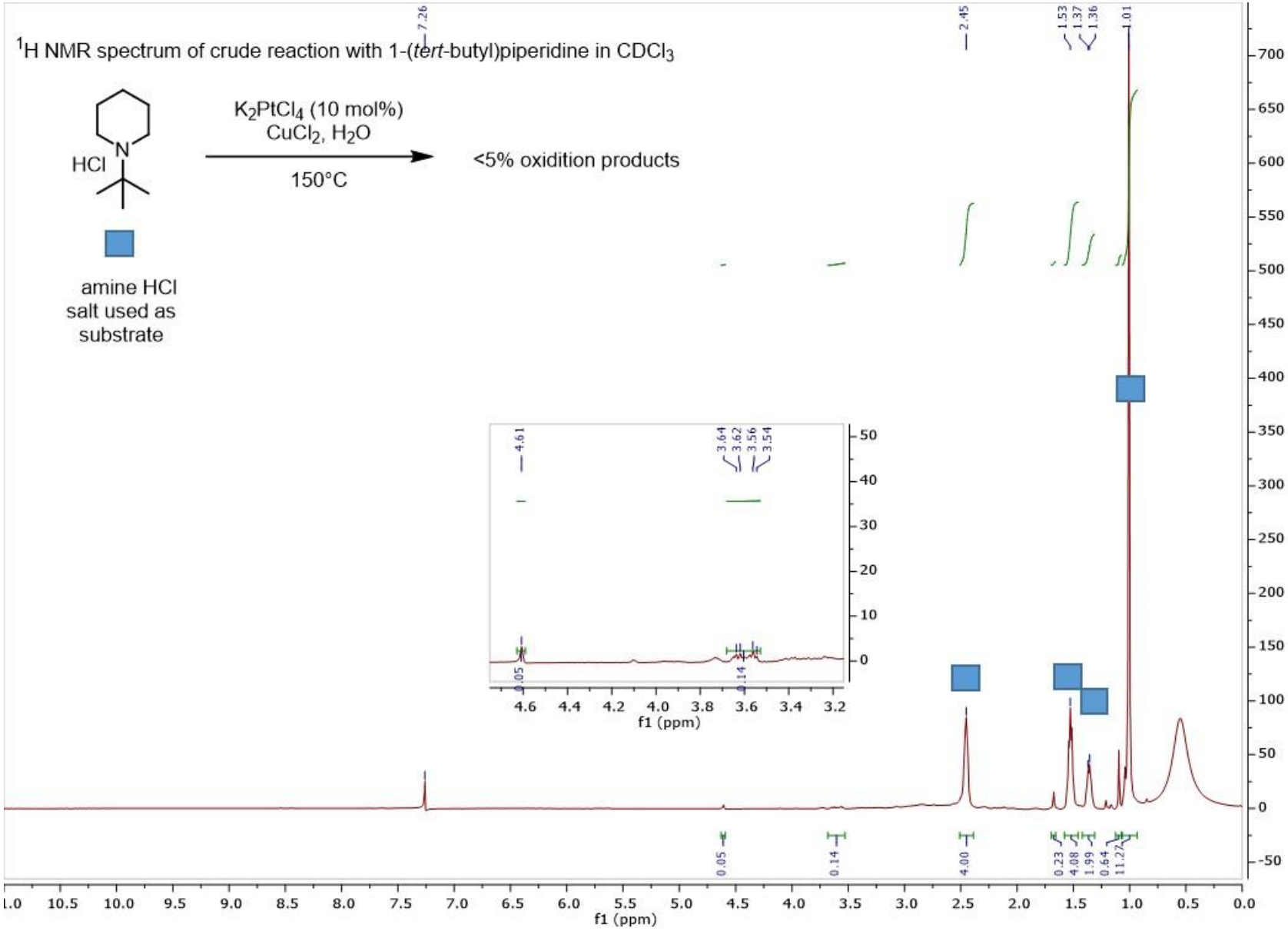

^{1}H NMR spectrum of **14** in $CDCl_3$
7.26
4.10
4.09
4.08
2.37
2.36
2.35
1.84
1.83
1.82
1.81
1.80
1.59
1.58
1.58
1.57
1.56
1.43
1.19
N
O
O
tBu
2.00
5.94
2.12
4.08
2.06
9.00
f1 (ppm)

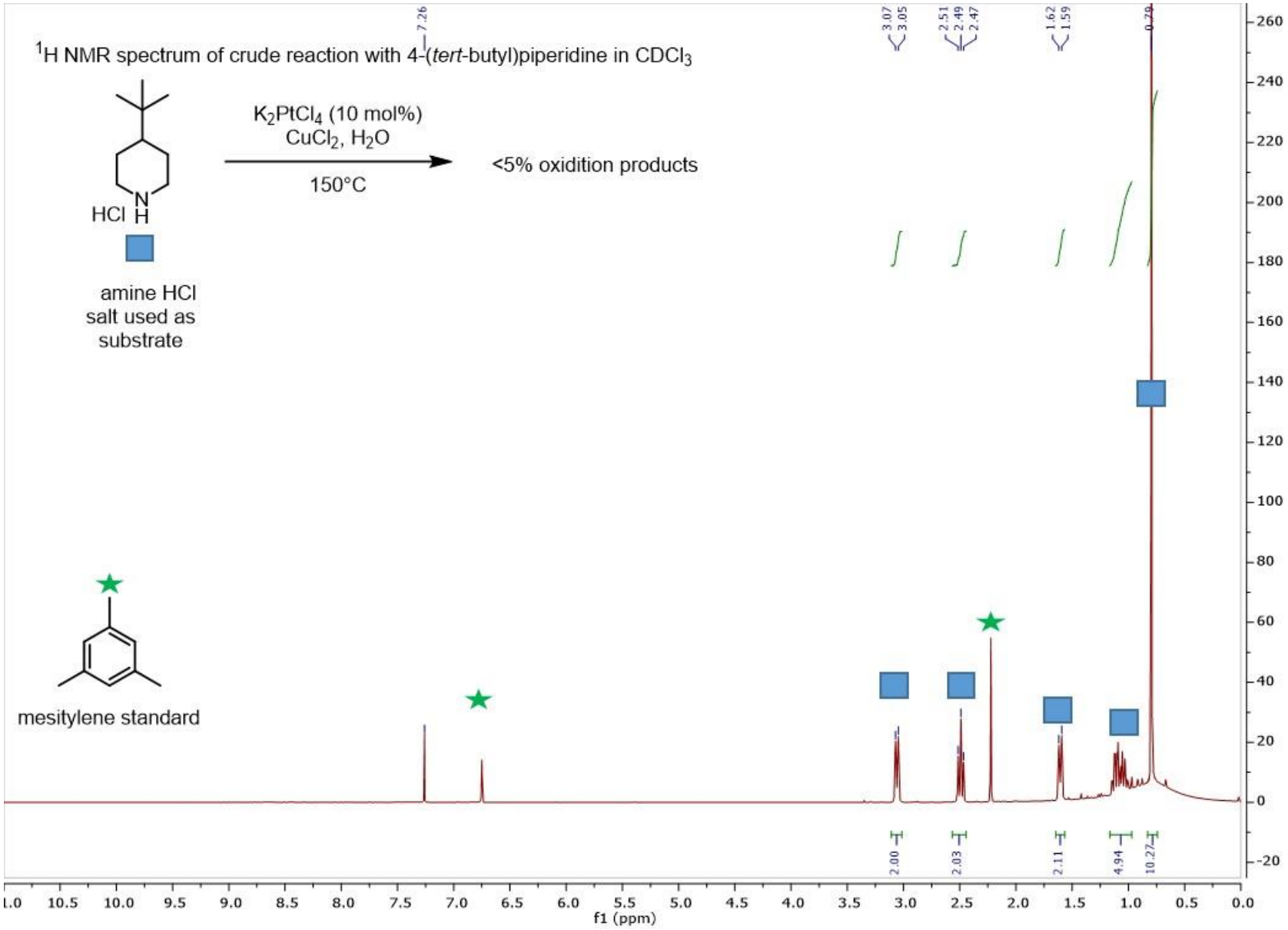

^{13}C NMR spectrum of **14** in $CDCl_3$
178.5
77.3
77.2
77.0
62.1
55.4
54.1
39.0
27.4
27.4
24.9
24.2
23.3
N
O
O
tBu
f1 (ppm)

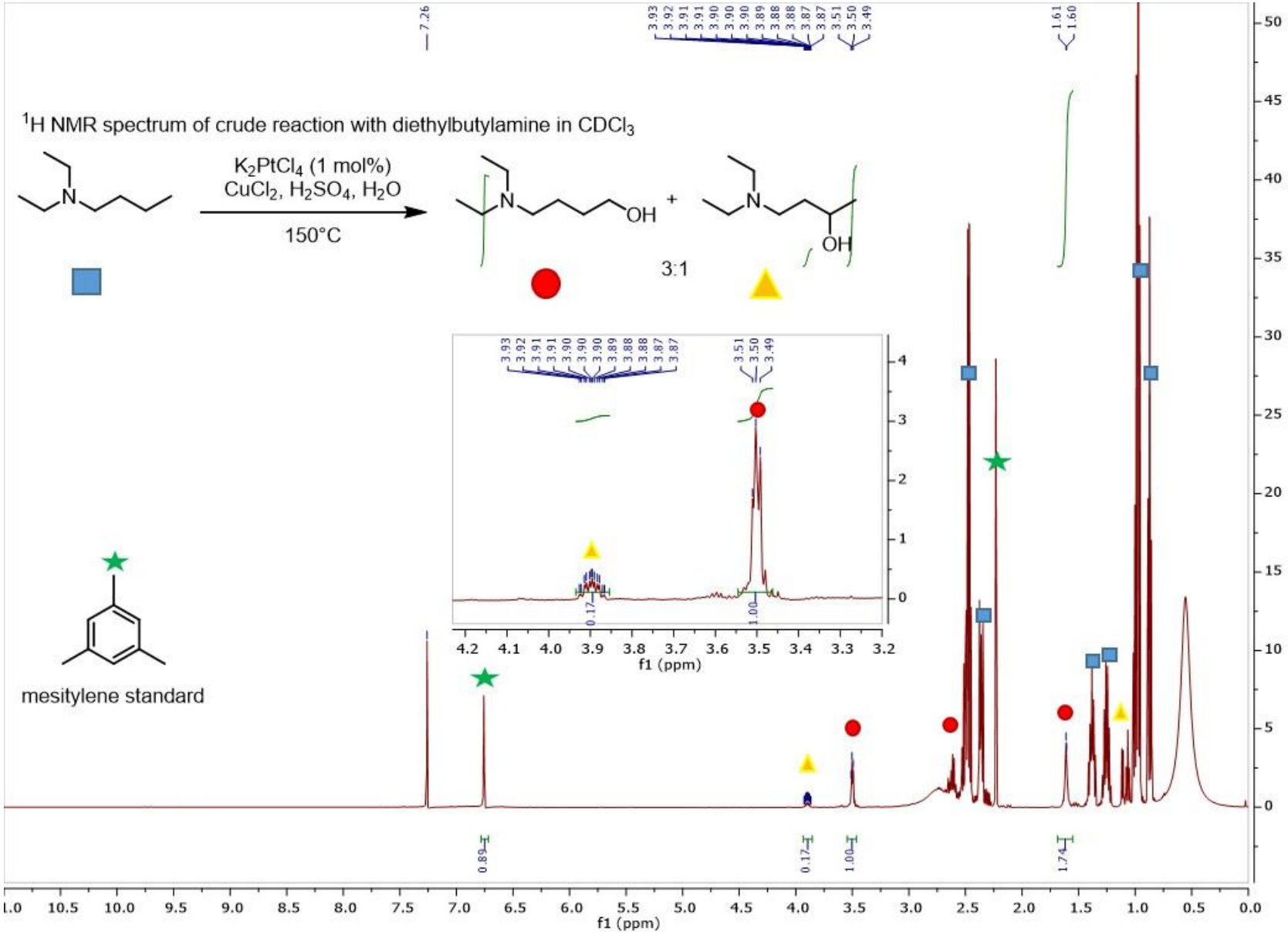

^{1}H NMR spectrum of crude reaction with 1-propylmorpholine in $CDCl_3$
K_2PtCl_4 (5 mol%)
$CuCl_2$, H_2SO_4, H_2O
150°C
10:1
mesitylene standard
f1 (ppm)

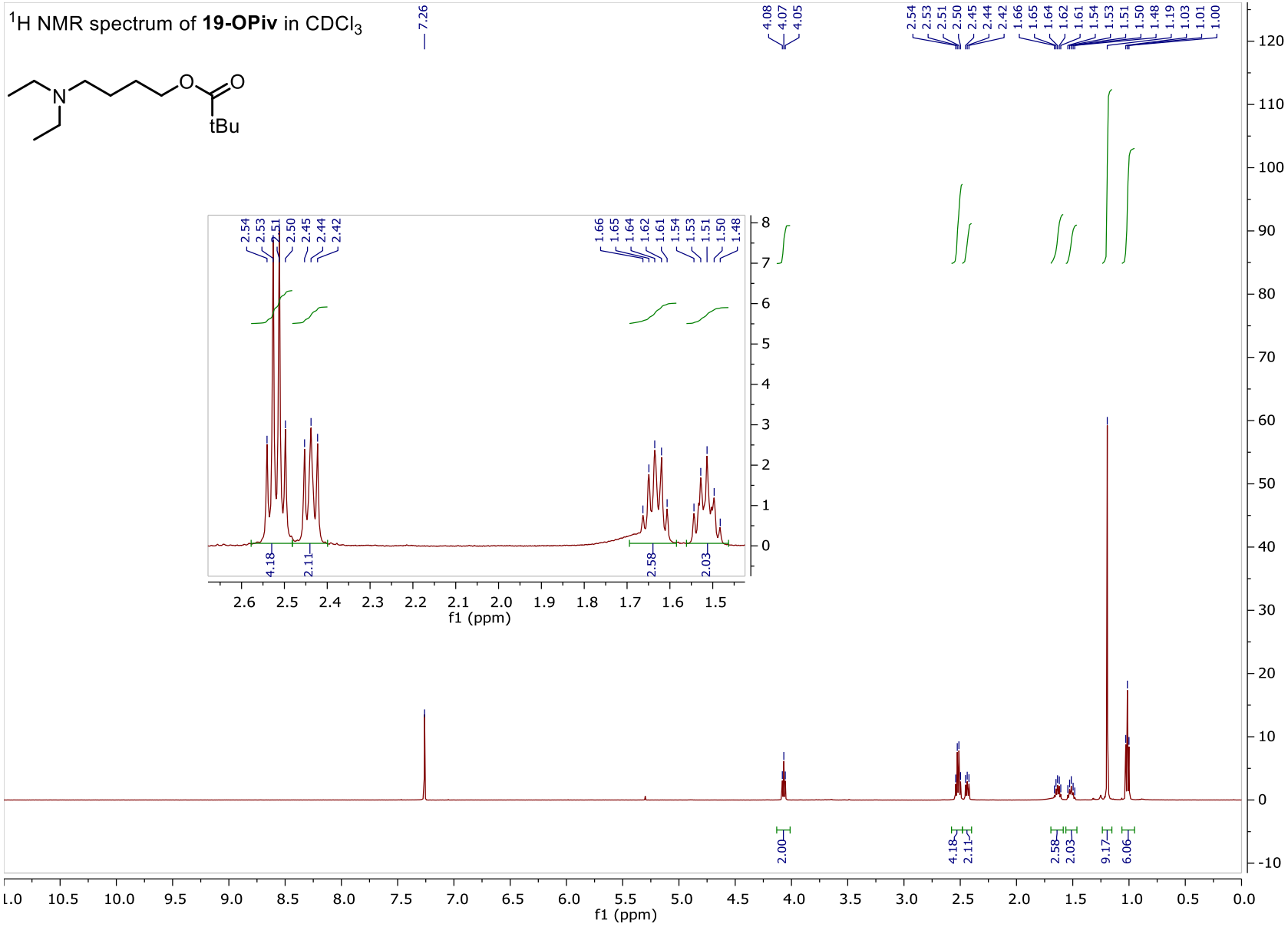

^{1}H NMR spectrum of **15** in $CDCl_3$
O
N
O
tBu
O
7.26
4.12
4.11
4.09
3.72
3.71
3.70
2.45
2.44
2.43
2.41
2.39
1.85
1.84
1.82
1.80
1.79
1.19
6.09
2.03
f1 (ppm)
2.00
4.07
6.09
2.03
9.00
f1 (ppm)

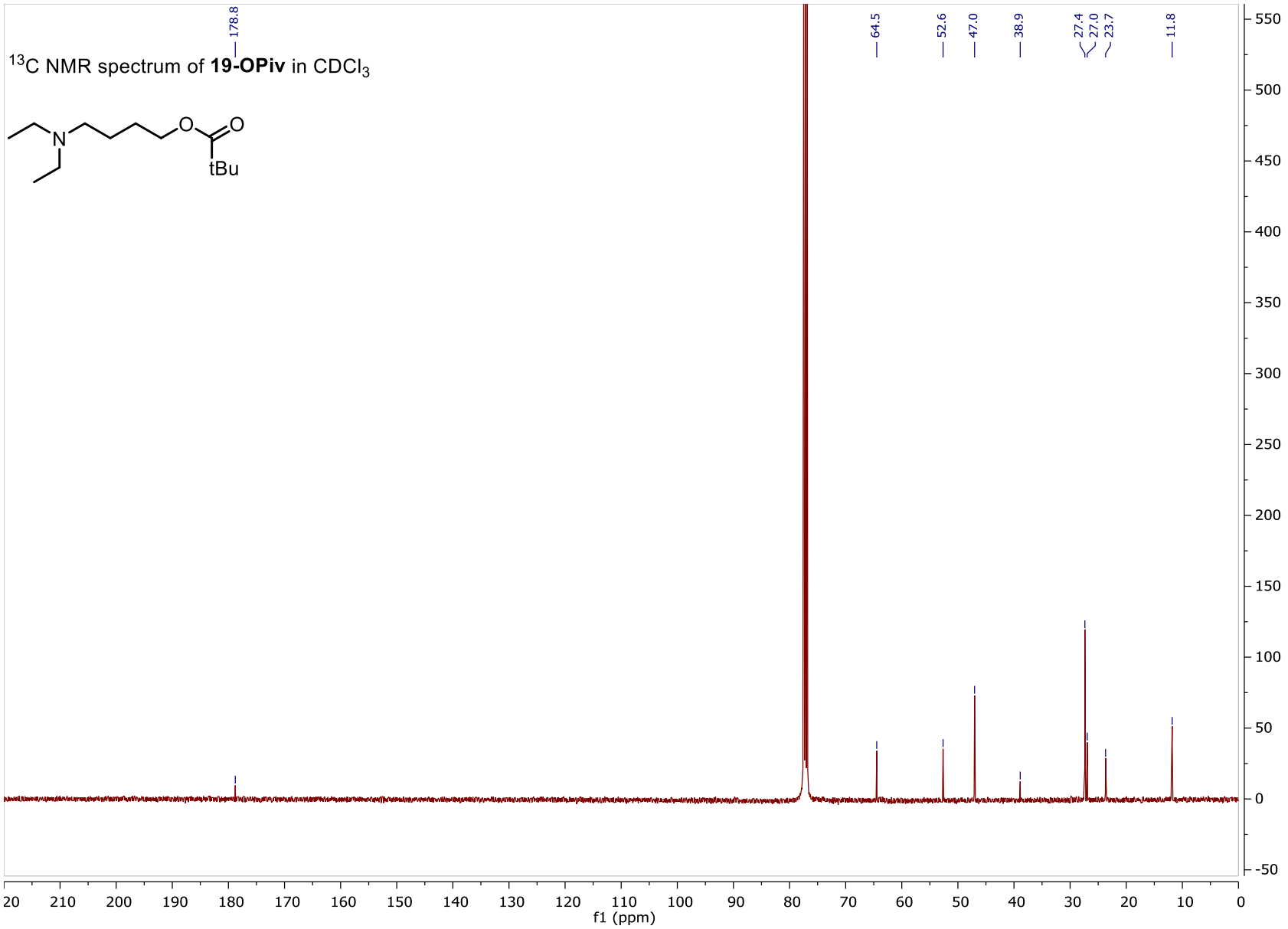

^{13}C NMR spectrum of **15** in $CDCl_3$
178.7
77.3
77.2
77.0
67.1
62.8
55.6
53.9
38.9
27.3
26.0
O
N
O
tBu
O
f1 (ppm)

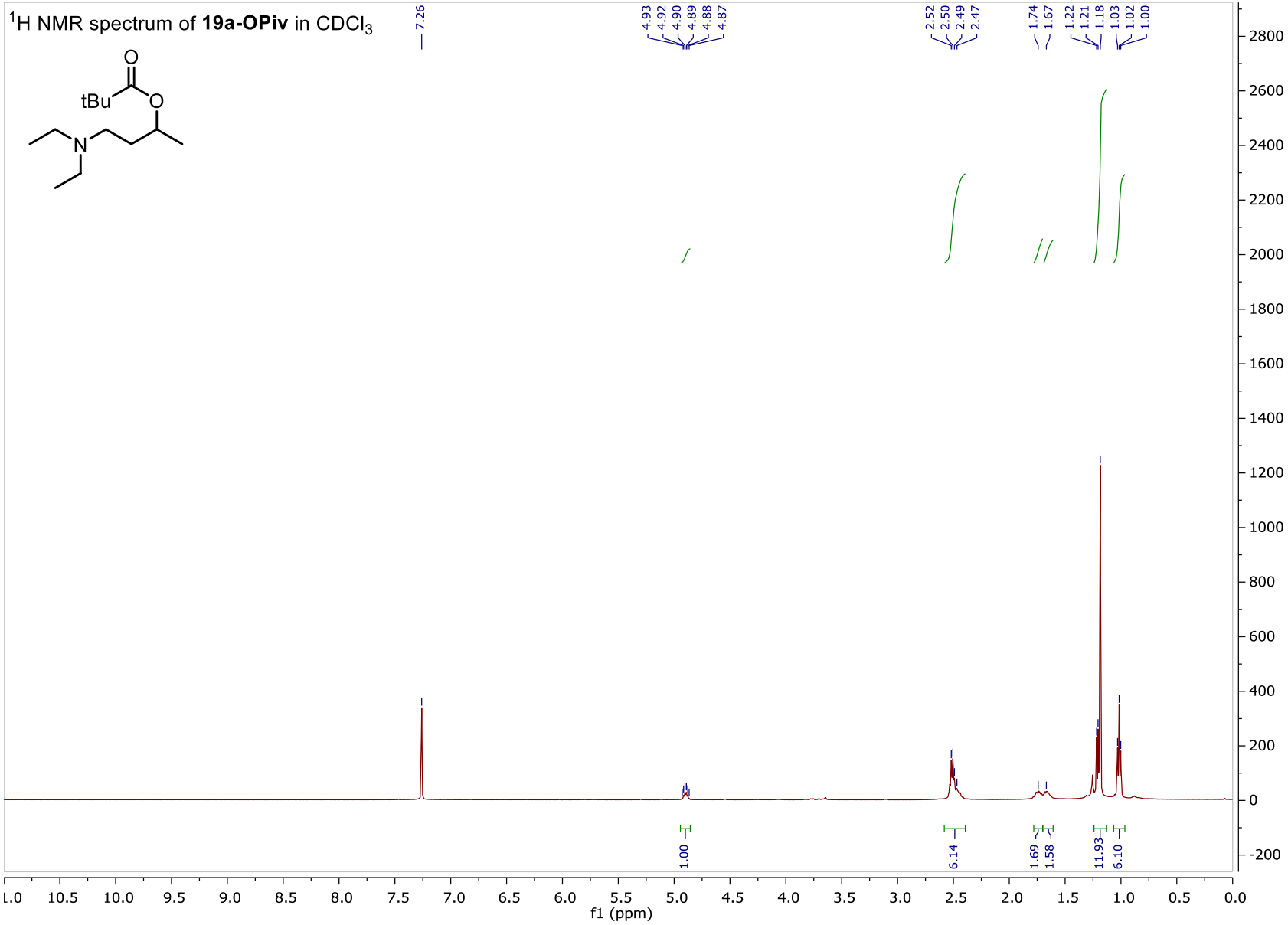

^{1}H NMR spectrum of crude reaction with 1-(*tert*-butyl)piperidine in $CDCl_3$
HCl
K_2PtCl_4 (10 mol%)
$CuCl_2$, H_2O
150°C
<5% oxidition products
amine HCl salt used as substrate
7.26
2.45
1.53
1.37
1.36
1.01
4.61
3.64
3.62
3.56
3.54
0.05
0.14
4.00
0.23
4.08
1.99
0.64
11.22
f1 (ppm)


^{1}H NMR spectrum of crude reaction with 4-(*tert*-butyl)piperidine in $CDCl_3$
K_2PtCl_4 (10 mol%)
$CuCl_2$, H_2O
150°C
<5% oxidition products
HCl
amine HCl salt used as substrate
mesitylene standard
7.26
3.07
3.05
2.51
2.49
2.47
1.62
1.59
0.79
2.00
2.03
2.11
4.94
10.27
f1 (ppm)

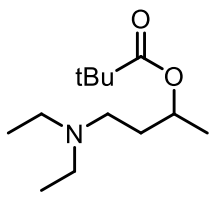

1H NMR spectrum of crude reaction with diethylbutylamine in CDCl3
K2PtCl4 (1 mol%)
CuCl2, H2SO4, H2O
150°C
OH
OH
3:1
mesitylene standard
f1 (ppm)

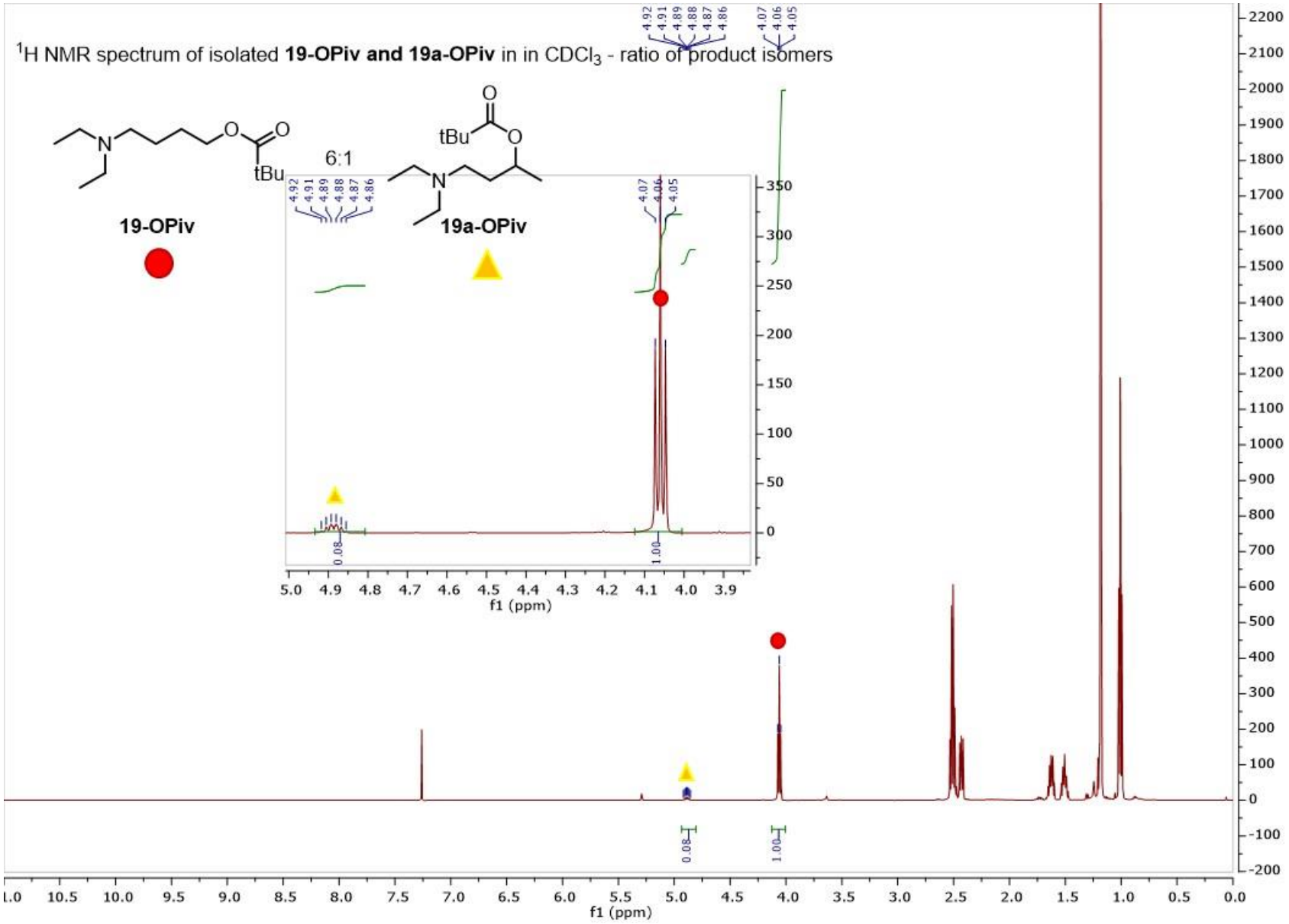

^{1}H NMR spectrum of **19-OPiv** in $CDCl_3$
tBu
f1 (ppm)

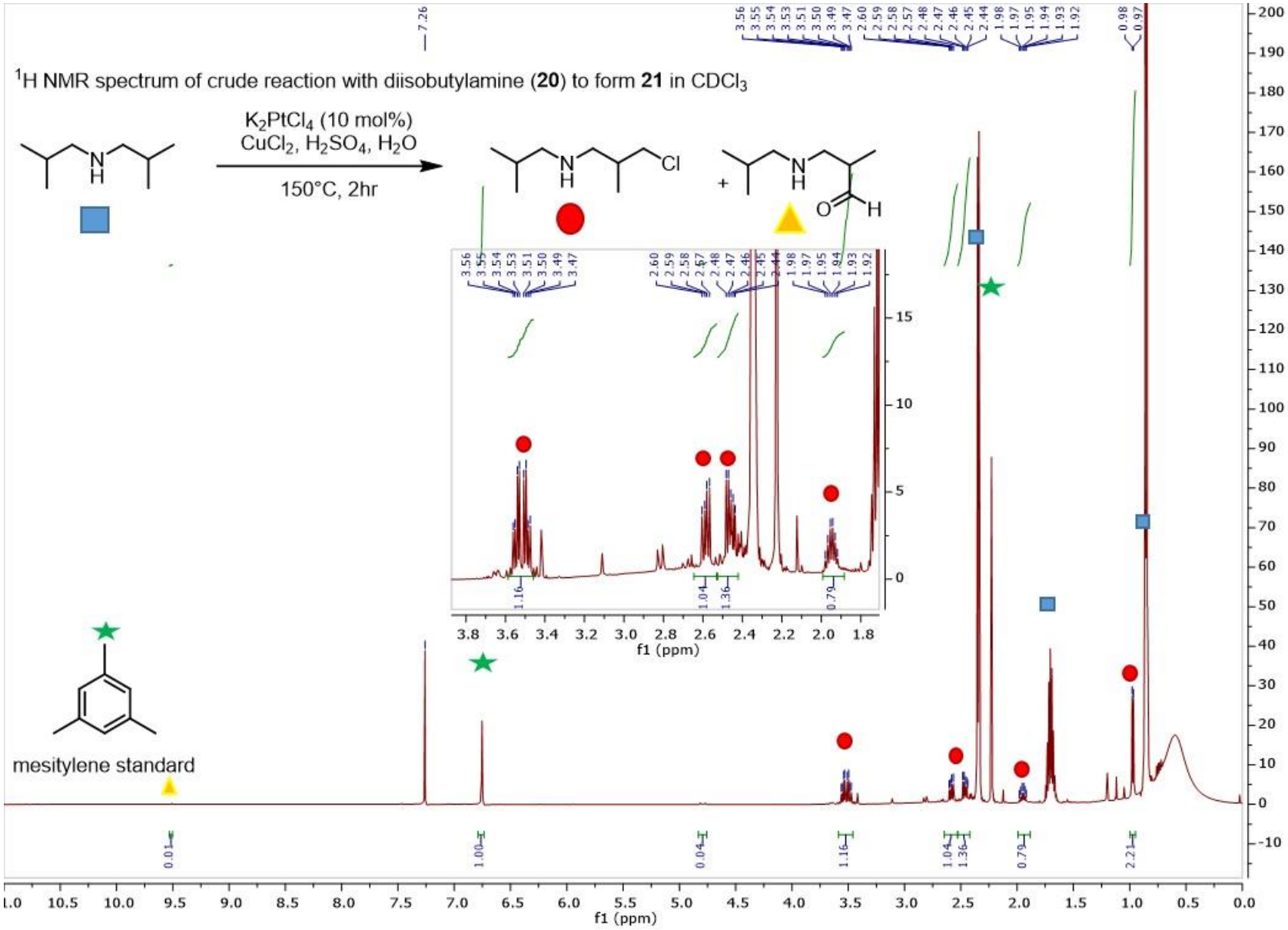

^{13}C NMR spectrum of **19-OPiv** in $CDCl_3$
178.8
64.5
52.6
47.0
38.9
27.4
27.0
23.7
11.8
N
O
O
tBu
f1 (ppm)

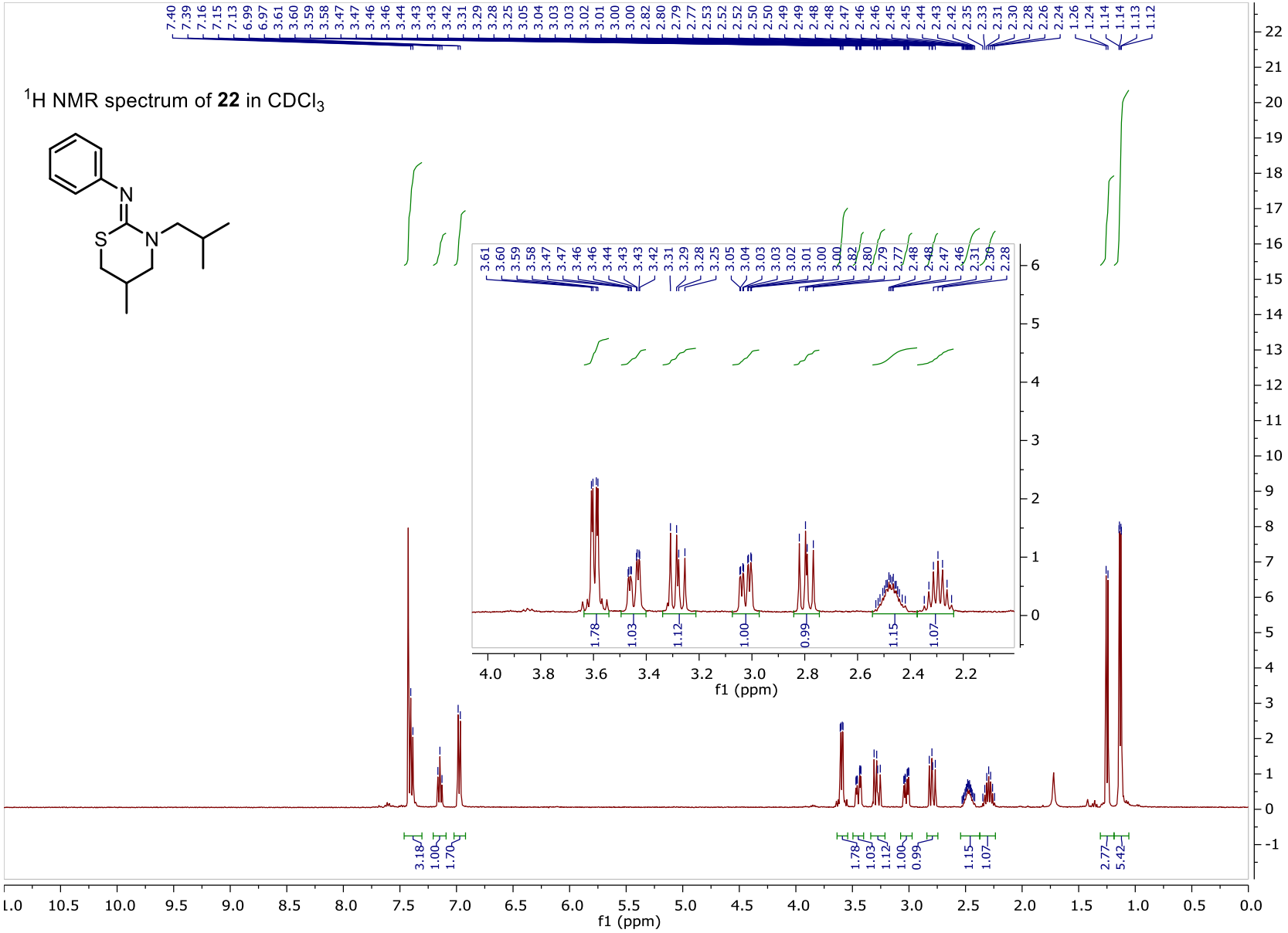

^{1}H NMR spectrum of **19a-OPiv** in $CDCl_3$
tBu
O
O
N
7.26
4.93
4.92
4.90
4.89
4.88
4.87
2.52
2.50
2.49
2.47
1.74
1.67
1.22
1.21
1.18
1.03
1.02
1.00
1.00
6.14
1.69
1.58
11.93
6.10
f1 (ppm)

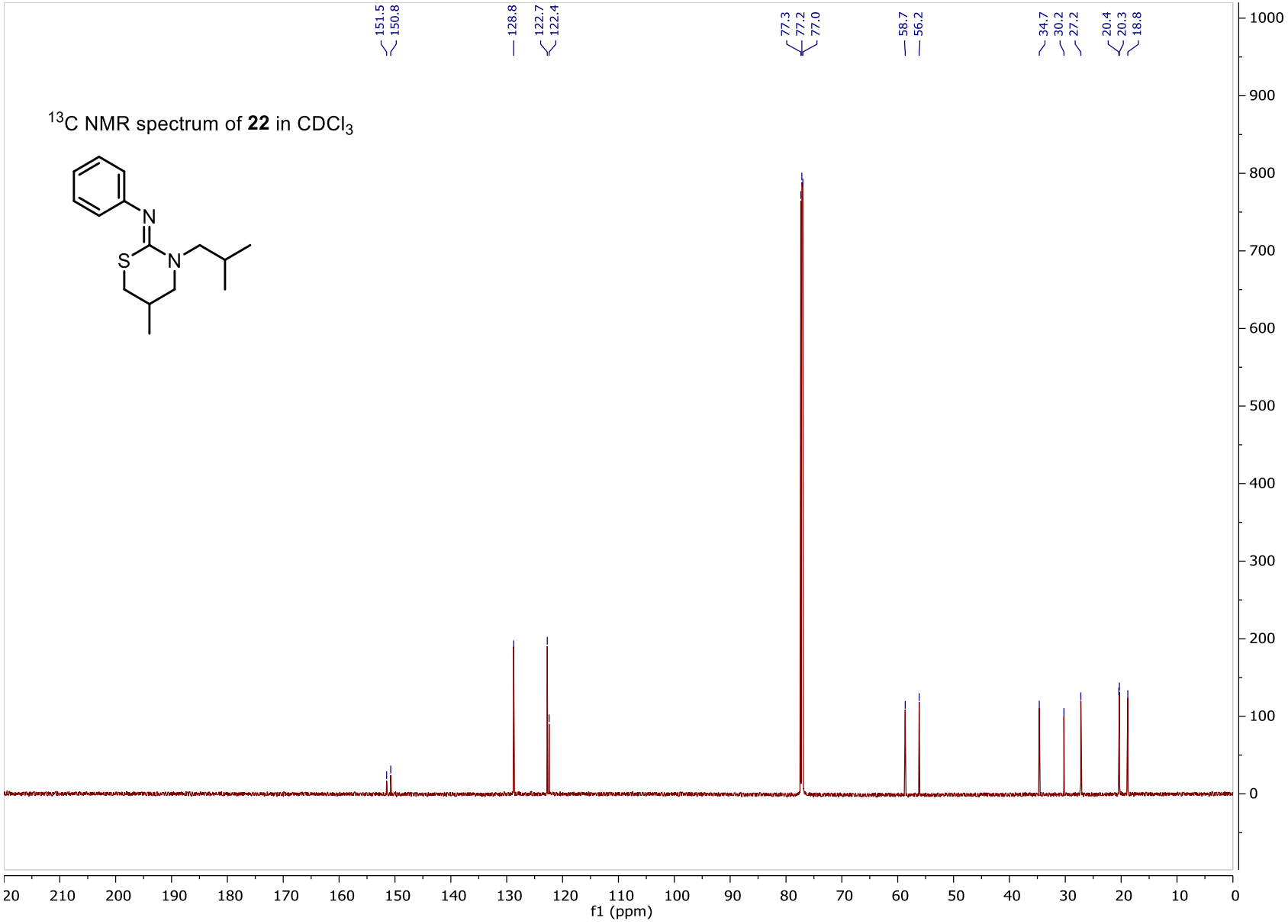
^{13}C NMR spectrum of **19a-OPiv** in $CDCl_3$

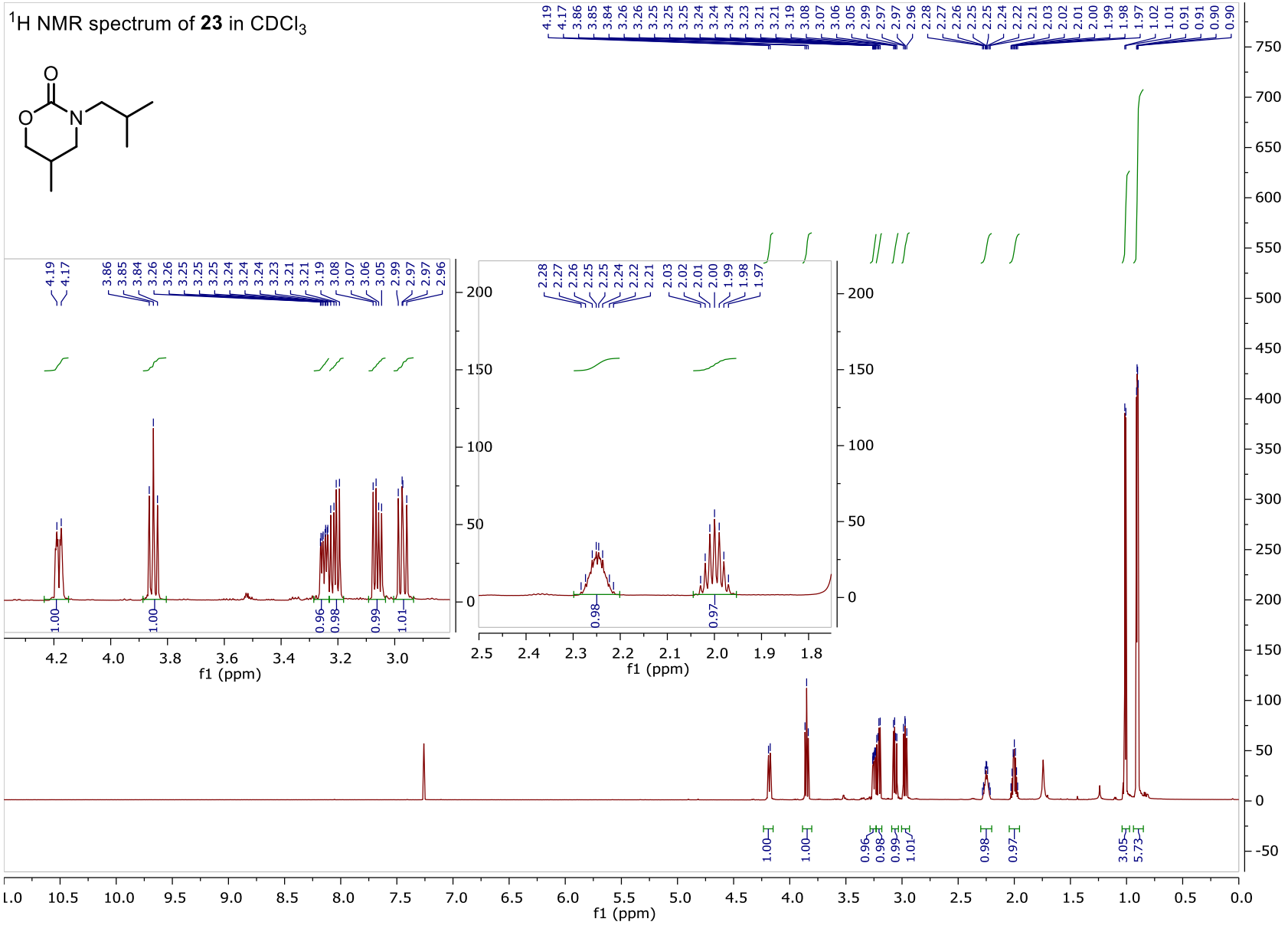


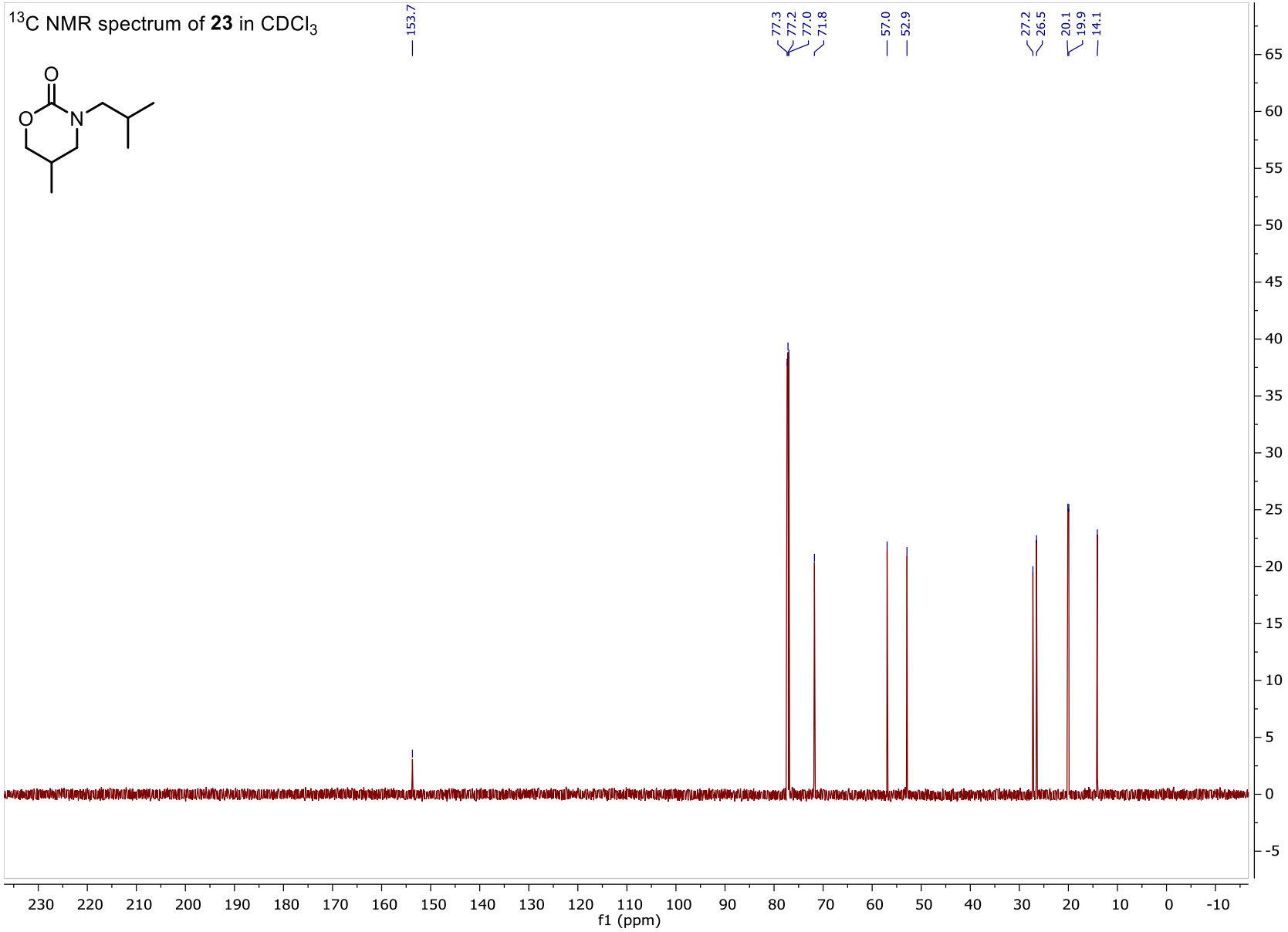

^{1}H NMR spectrum of isolated **19-OPiv and 19a-OPiv** in in $CDCl_3$ - ratio of product isomers
19-OPiv
19a-OPiv
6:1
f1 (ppm)

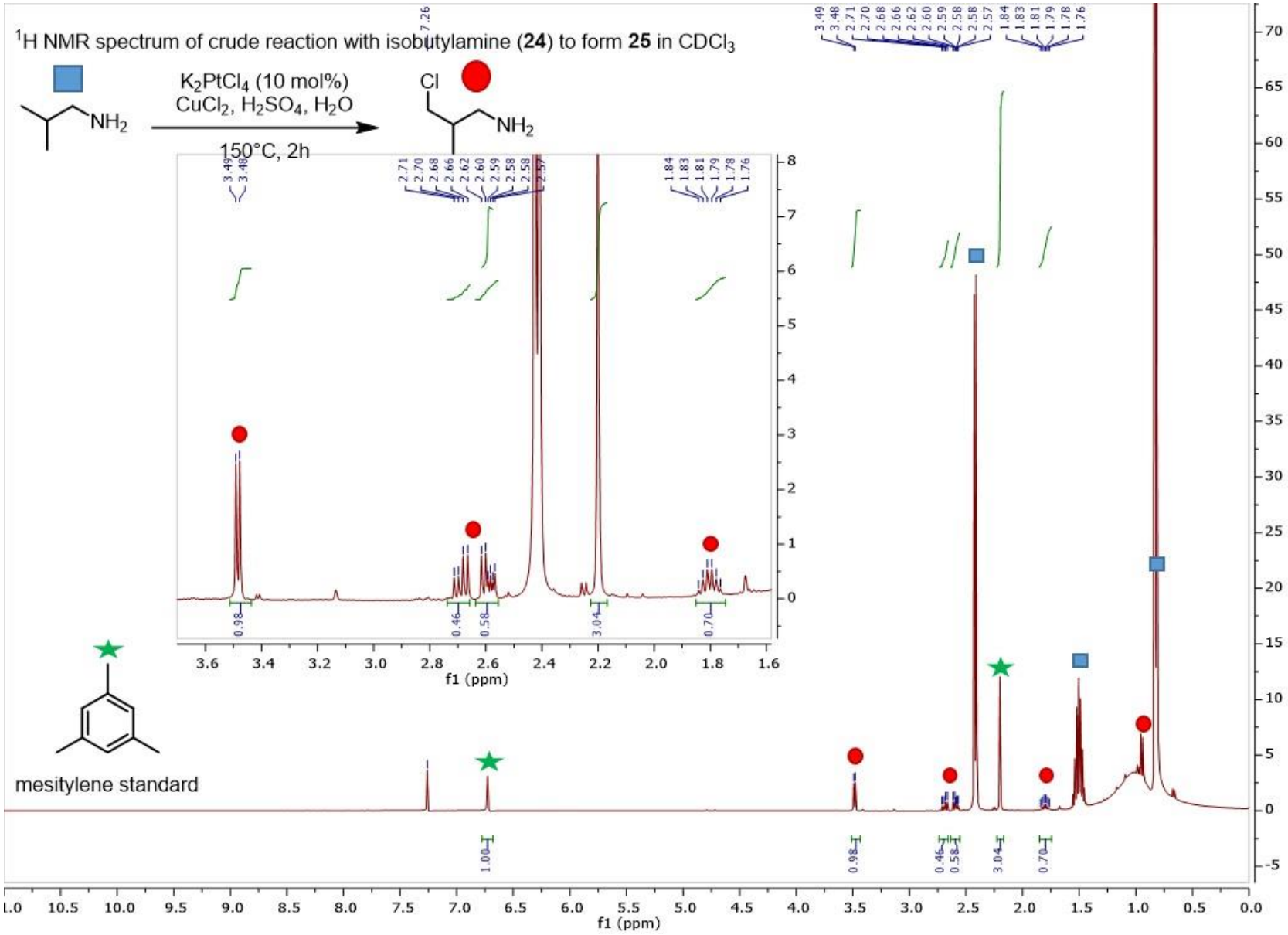

1H NMR spectrum of crude reaction with diisobutylamine (20) to form 21 in CDCl3
K2PtCl4 (10 mol%)
CuCl2, H2SO4, H2O
150°C, 2hr
Cl
O
H
mesitylene standard
f1 (ppm)

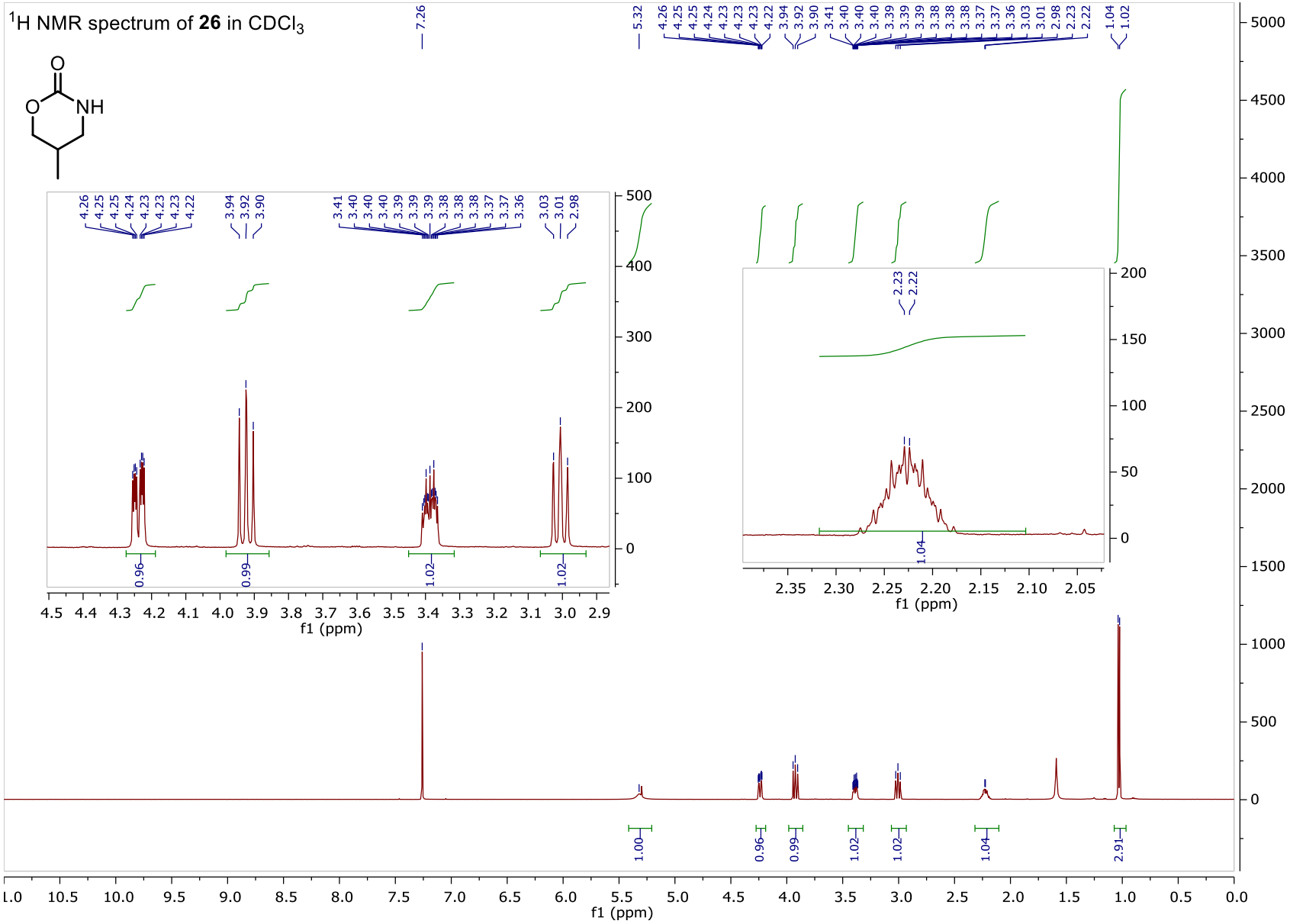

^{1}H NMR spectrum of **22** in $CDCl_3$
f1 (ppm)

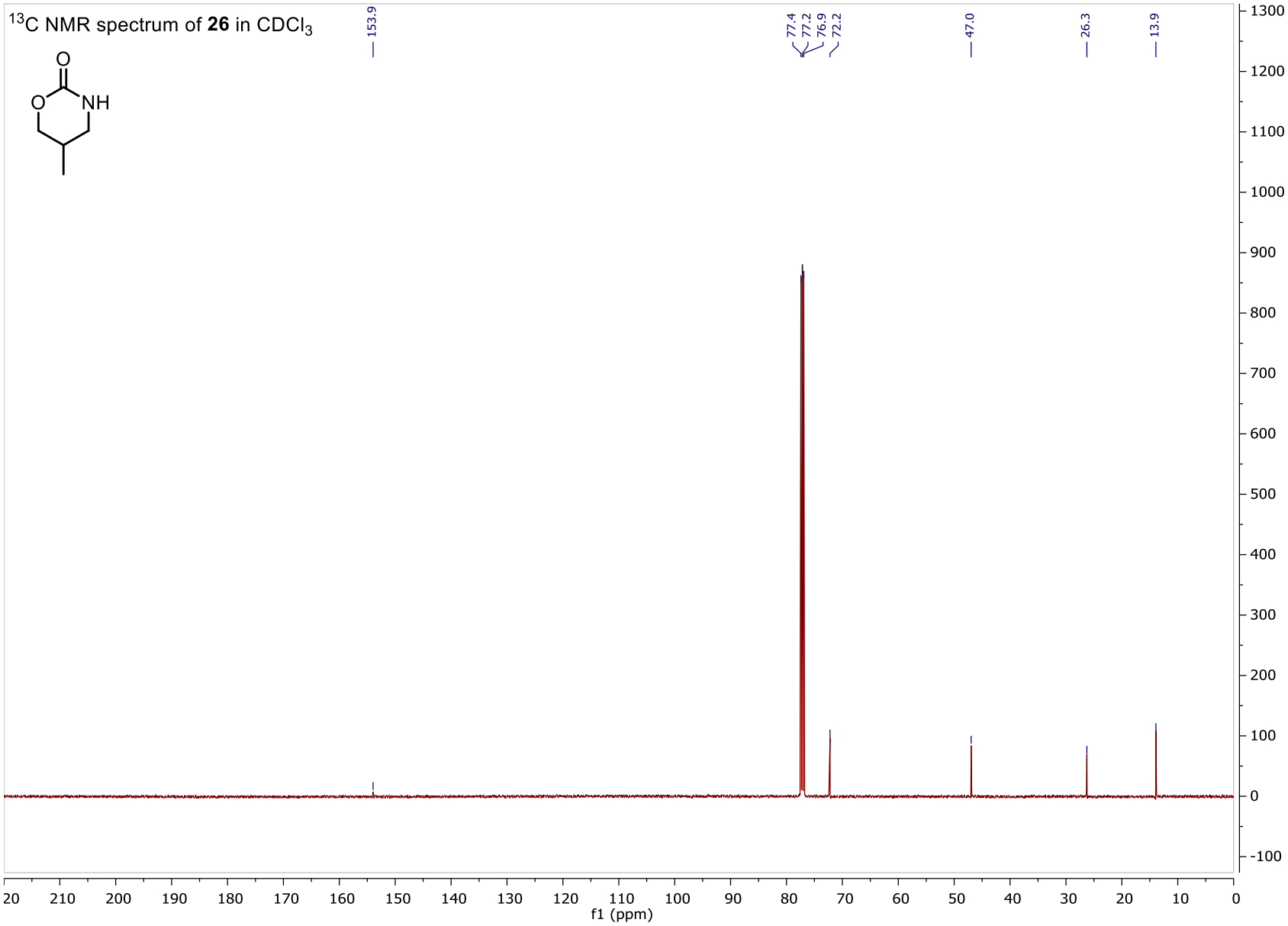

151.5
150.8
128.8
122.7
122.4
77.3
77.2
77.0
58.7
56.2
34.7
30.2
27.2
20.4
20.3
18.8
^{13}C NMR spectrum of **22** in $CDCl_3$
N
S
N
f1 (ppm)

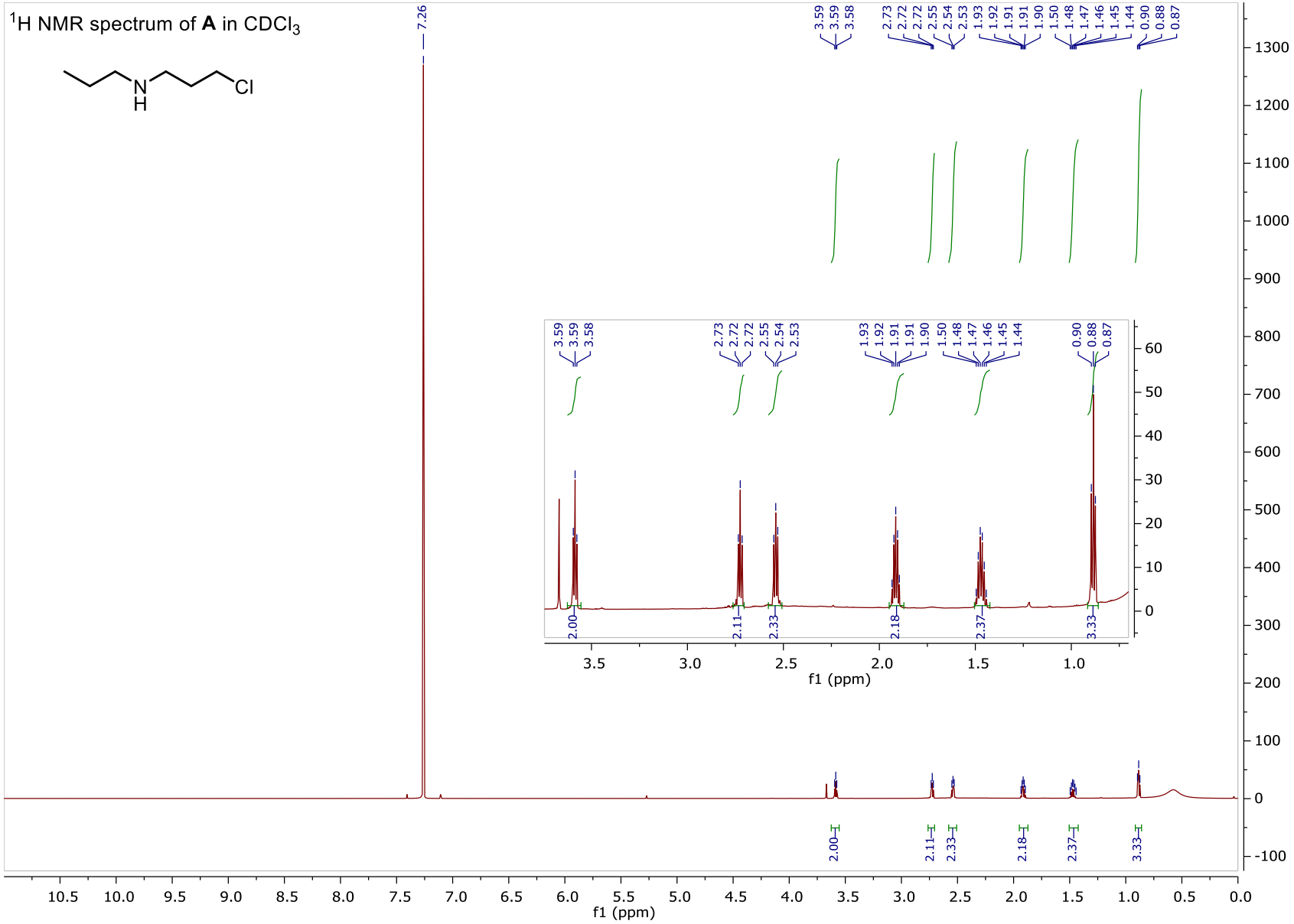

1H NMR spectrum of 23 in CDCl3
f1 (ppm)

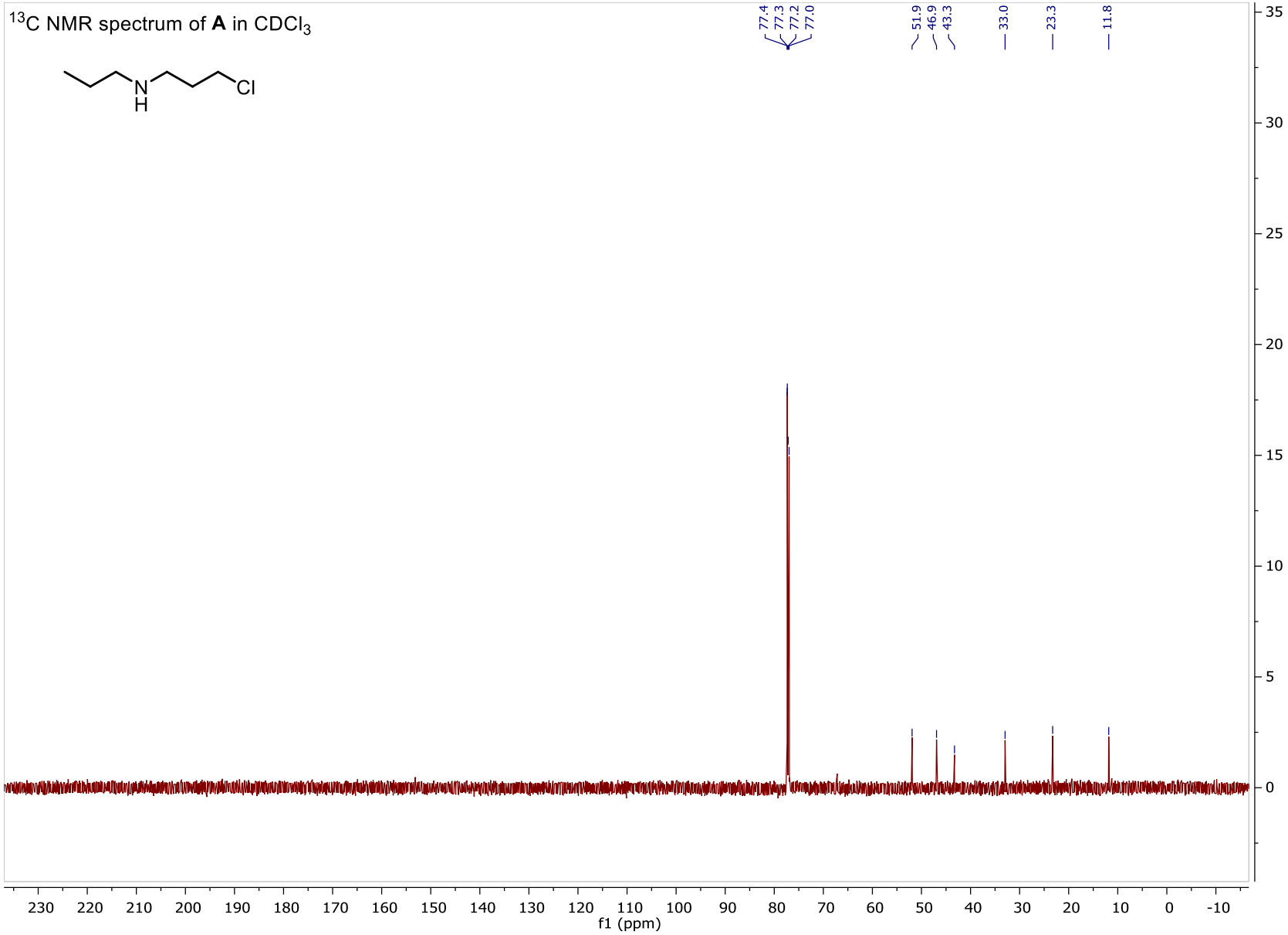

^{13}C NMR spectrum of **23** in $CDCl_3$
153.7
77.3
77.2
77.0
71.8
57.0
52.9
27.2
26.5
20.1
19.9
14.1
f1 (ppm)

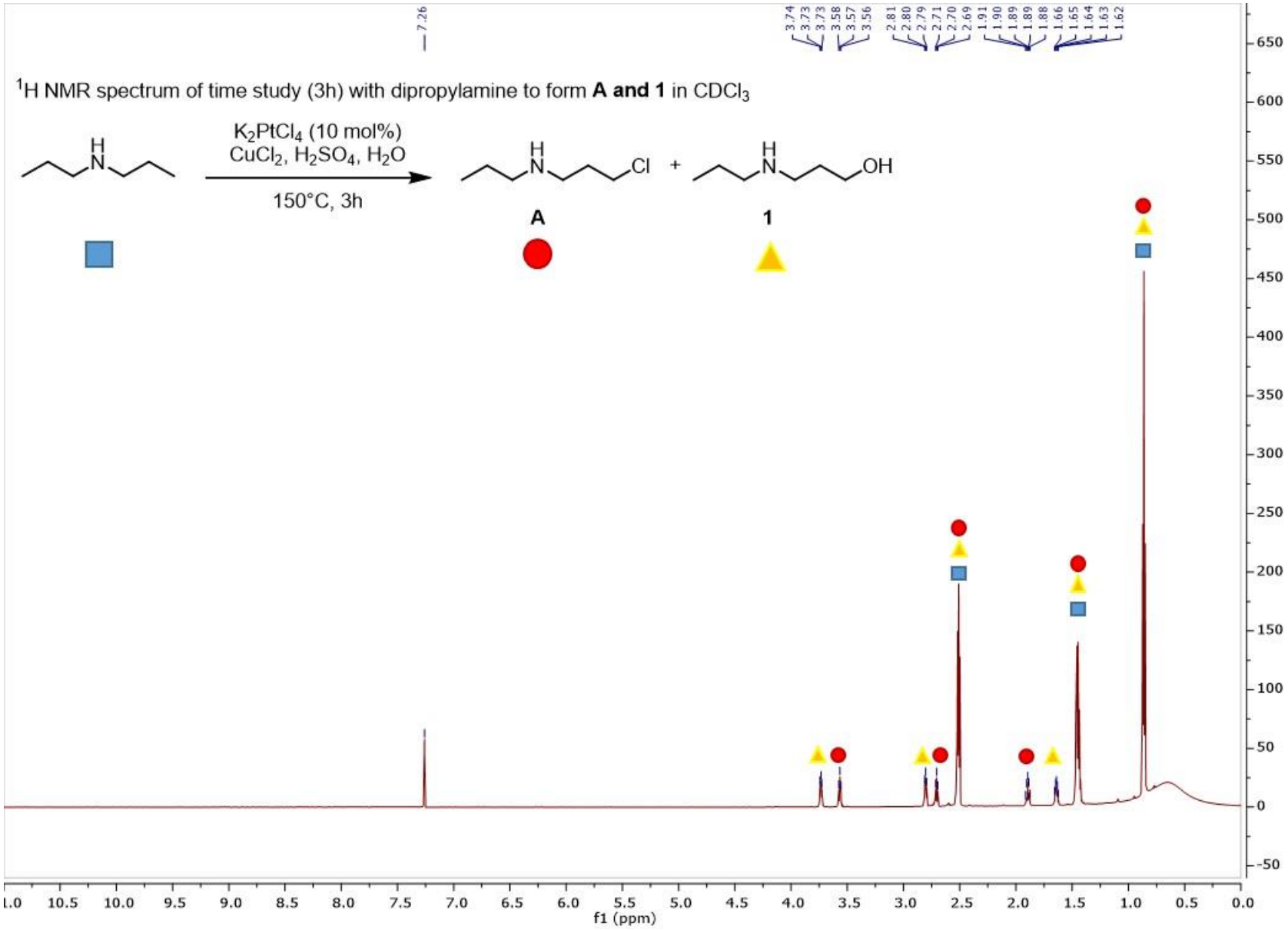

^{1}H NMR spectrum of crude reaction with isobutylamine (**24**) to form **25** in $CDCl_3$
K_2PtCl_4 (10 mol%)
$CuCl_2$, H_2SO_4, H_2O
150°C, 2h
NH2
Cl
NH2
mesitylene standard
f1 (ppm)
f1 (ppm)

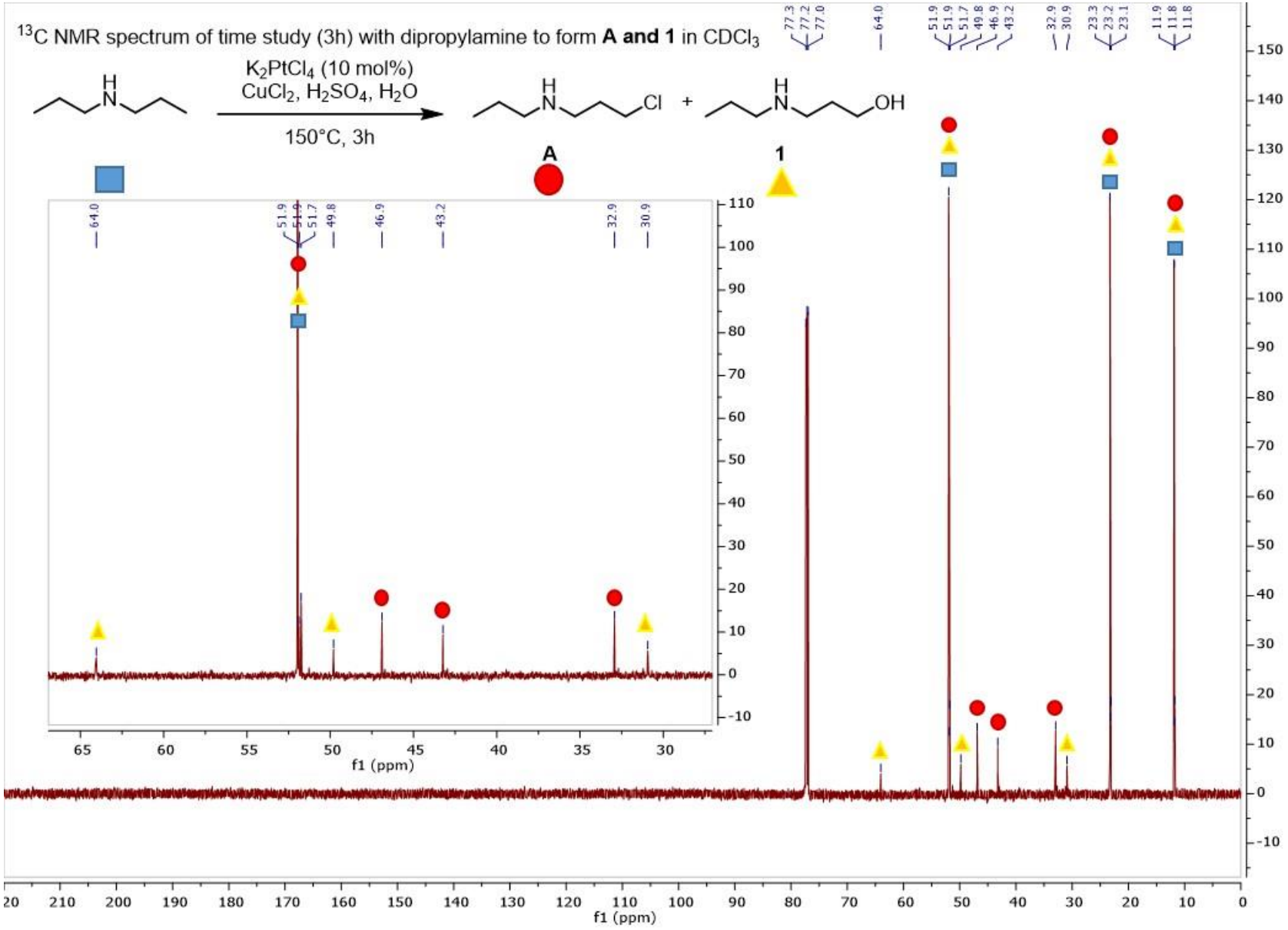

^{1}H NMR spectrum of **26** in $CDCl_3$
O
O
NH
f1 (ppm)

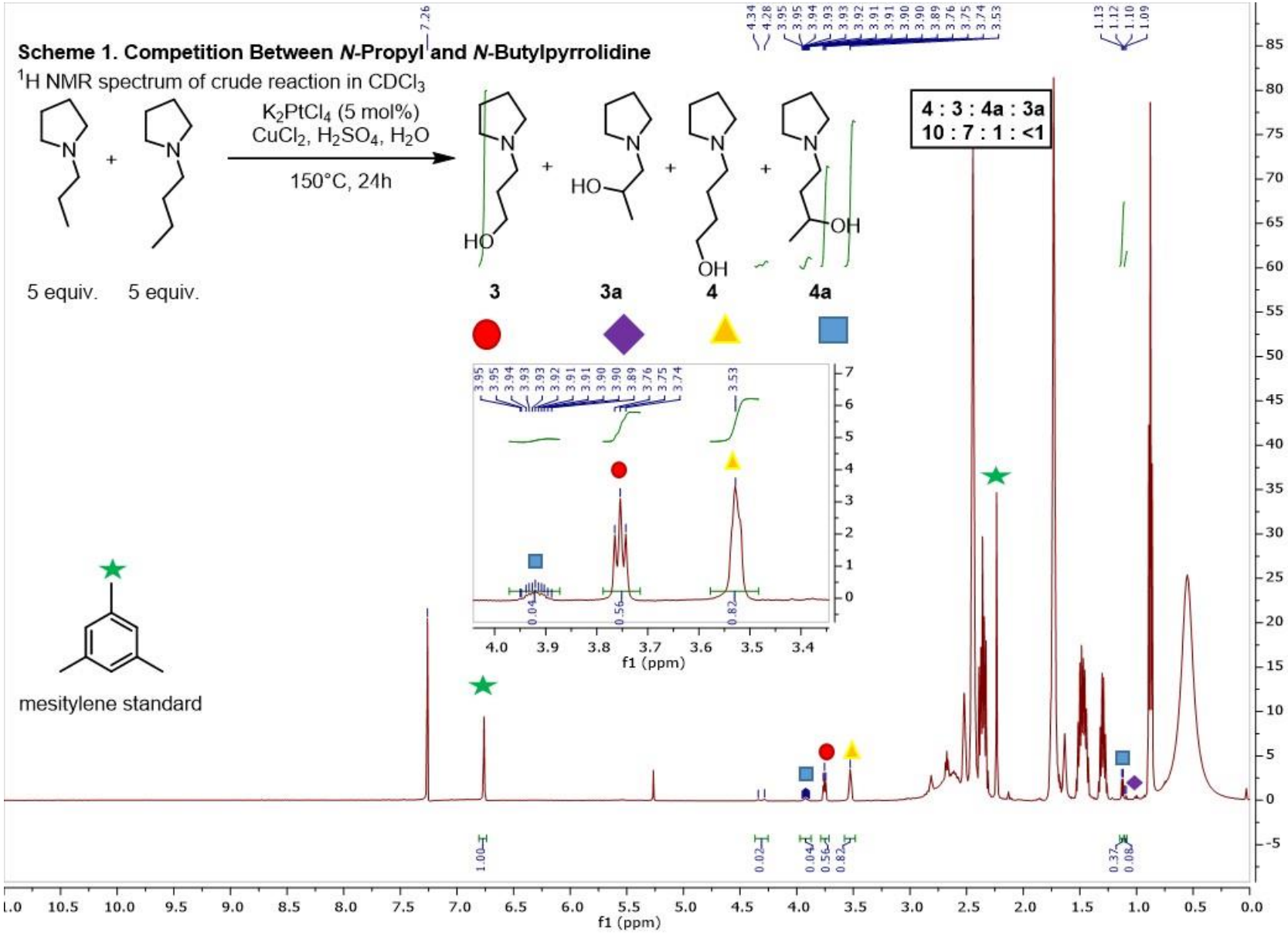

^{13}C NMR spectrum of **26** in $CDCl_3$
O
O
NH
153.9
77.4
77.2
76.9
72.2
47.0
26.3
13.9
1300
1200
1100
1000
900
800
700
600
500
400
300
200
100
0
-100
20 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)


^{1}H NMR spectrum of **A** in $CDCl_3$
N
H
Cl
7.26
3.59 3.59 3.58
2.73 2.72 2.72 2.55 2.54 2.53
1.93 1.92 1.91 1.91 1.90
1.50 1.48 1.47 1.46 1.45 1.44
0.90 0.88 0.87
2.00 2.11 2.33 2.18 2.37 3.33
f1 (ppm)


^{13}C NMR spectrum of **A** in $CDCl_3$
N
H
Cl
77.4
77.3
77.2
77.0
51.9
46.9
43.3
33.0
23.3
11.8
35
30
25
20
15
10
5
0
230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)


7.26
3.74
3.73
3.73
3.58
3.57
3.56
2.81
2.80
2.79
2.71
2.70
2.69
1.91
1.90
1.89
1.89
1.88
1.66
1.65
1.64
1.63
1.62
[1]H NMR spectrum of time study (3h) with dipropylamine to form **A and 1** in $CDCl_3$
K_2PtCl_4 (10 mol%)
$CuCl_2$, H_2SO_4, H_2O
150°C, 3h
Cl
OH
A
1
650
600
550
500
450
400
350
300
250
200
150
100
50
0
-50
10.5
10.0
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)


13C NMR spectrum of time study (3h) with dipropylamine to form A and 1 in CDCl3
K2PtCl4 (10 mol%)
CuCl2, H2SO4, H2O
150°C, 3h
Cl
OH
A
1
77.3
77.2
77.0
64.0
51.9
51.9
51.7
49.8
46.9
43.2
32.9
30.9
23.3
23.2
23.1
11.9
11.8
11.8
f1 (ppm)


Scheme 1. Competition Between N-Propyl and N-Butylpyrrolidine
1H NMR spectrum of crude reaction in CDCl3
K2PtCl4 (5 mol%)
CuCl2, H2SO4, H2O
150°C, 24h
5 equiv.
5 equiv.
3
3a
4
4a
4 : 3 : 4a : 3a
10 : 7 : 1 : <1
mesitylene standard
f1 (ppm)