

Supporting Information for:

Palladium-Catalyzed Ullmann Cross-Coupling of β -Iodoenones and β -Iodoacrylates with *o*-Halonitroarenes or *o*-Iodobenzonitriles and the Reductive Cyclization of the Resulting Products to Give Diverse Heterocyclic Systems

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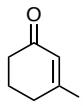
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General Experimental Protocols

Unless otherwise specified, proton (^1H) and carbon (^{13}C) NMR spectra were recorded at room temperature in base-filtered CDCl_3 on a spectrometer operating at 400 MHz for proton and 100 MHz for carbon nuclei. For ^1H NMR spectra, signals arising from the residual protioforms of the solvent were used as internal standards. ^1H NMR data are recorded as follows: chemical shift (δ) [multiplicity, coupling constant(s) J (Hz), relative integral] where multiplicity is defined as: s = singlet; d = doublet; t = triplet; q = quartet; m = multiplet or combinations of the above. The signal due to residual CHCl_3 appearing at δ_{H} 7.26 and the central resonance of the CDCl_3 “triplet” appearing at δ_{C} 77.0 were used to reference ^1H and ^{13}C NMR spectra, respectively. IR spectra were recorded, using neat samples, on an attenuated total reflectance (ATR) infra-red spectrometer. Low-resolution ESI mass spectra were recorded on a single quadrupole liquid chromatograph-mass spectrometer, while high-resolution measurements were conducted on a time-of-flight instrument. Low- and high-resolution EI mass spectra were recorded on a magnetic-sector machine. Melting points were measured on an automated melting point system and are uncorrected. Analytical thin layer chromatography (TLC) was performed on aluminum-backed 0.2 mm thick silica gel 60 F₂₅₄ plates. Eluted plates were visualized using a 254 nm UV lamp and/or by treatment with a suitable dip followed by heating. These dips included phosphomolybdic acid : ceric sulfate : sulfuric acid (conc.) : water (37.5 g : 7.5 g : 37.5 g : 720 mL) or potassium permanganate : potassium carbonate : 5% sodium hydroxide aqueous solution : water (3 g : 20 g : 5 mL : 300 mL). Flash chromatographic separations were carried out following protocols defined by Still et al.¹ with silica gel 60 (40– 63 μm) as the stationary phase and using the AR- or HPLC-grade solvents indicated. Starting materials, reagents and drying agents as well as other inorganic salts were generally available from commercial sources and used as supplied. Tetrahydrofuran (THF), diethyl ether, methanol, acetonitrile and dichloromethane were dried using a solvent purification system that is based upon a technology originally described by Grubbs et al.² Where necessary, reactions were performed under a nitrogen atmosphere.

Specific Chemical Transformations

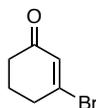
Compound **5** (X = I)



5 (X = I)

A magnetically stirred solution of triphenylphosphine (2.89 g, 11.0 mmol) in dry acetonitrile (50 mL) maintained at 22 °C was treated, in portions, with powdered molecular iodine (2.79 g, 11.0 mmol). After 0.5 h the reaction mixture was treated with triethylamine (1.53 mL, 11.0 mmol) then cyclohexane-1,3-dione (1.12 g, 10.0 mmol) and the resulting mixture heated under reflux for 16 h. The cooled reaction mixture was then concentrated under reduced pressure and the residue thus obtained stirred vigorously with diethyl ether (30 mL) and the supernatant liquid decanted. This process was repeated twice more and the combined organic phases then diluted with 40-60 petroleum ether (50 mL) to precipitate triphenylphosphine oxide. The ensuing mixture was filtered through a plug of TLC-grade silica gel topped with diatomaceous earth and the filtrate concentrated under reduced pressure to afford compound **5** (X = I) (1.84 g, 83%) as a light-yellow oil. The spectral data obtained on this material matched those published in the literature.³

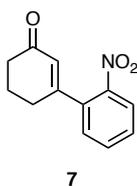
Compound **5** (X = Br)



5 (X = Br)

A magnetically stirred solution of triphenylphosphine (4.33 g, 16.5 mmol) in dry acetonitrile (75 mL) maintained at 0 °C was treated, dropwise *via* addition funnel, with a solution of molecular bromine (851 μ L, 16.5 mmol) in dry acetonitrile (8.25 mL). The resulting mixture was then warmed to 22 °C and after 0.5 h it was treated with triethylamine (2.30 mL, 16.5 mmol) then cyclohexane-1,3-dione (1.68 g, 15.0 mmol) before being stirred at 22 °C for 16 h then concentrated under reduced pressure. The residue thus obtained was stirred vigorously with diethyl ether (30 mL) and the supernatant liquid decanted. This process was repeated twice more and the combined organic phases then diluted with 40-60 petroleum ether (50 mL) to precipitate triphenylphosphine oxide. The ensuing mixture was filtered through a plug of TLC-grade silica gel topped with diatomaceous earth and the filtrate concentrated under reduced pressure to afford compound **5** (X = Br) (2.05 g, 78%) as a light-yellow oil. The spectral data obtained on this material matched those published in the literature.³

Compound 7



A magnetically stirred suspension of compound **5** (X = I) (222 mg, 1.00 mmol), *o*-iodonitrobenzene (**2**) (498 mg, 2.00 mmol) and copper powder (318 mg, 5.00 mmol) in dry DMSO (5 mL) maintained at 50 °C was treated with Pd(dppf)Cl₂•CH₂Cl₂ (41 mg, 0.05 mmol). After 18 h the reaction mixture was cooled to 22 °C, diluted with ethyl acetate (5 mL) and the ensuing mixture filtered through a plug of TLC-grade silica gel topped with diatomaceous earth and the solids so retained were washed with ethyl acetate (20 mL). The combined filtrates were washed with ammonia (2 x 25 mL of a 5% v/v aqueous solution), water (2 x 25 mL) and brine (1 x 25 mL) before being dried (Na₂SO₄), filtered, then concentrated under reduced pressure. The residue so obtained was subjected to flash column chromatography (, 1:9 v/v diethyl ether/toluene elution) and thus affording, after concentration of the appropriate fractions (*R*_f = 0.2), compound **7**⁴ (198 mg, 91%) as a pale-yellow, crystalline solid, m.p. = 74 °C.

¹H NMR (400 MHz, CDCl₃) δ 8.10 (d, *J* = 7.8 Hz, 1H), 7.67 (t, *J* = 7.8 Hz, 1H), 7.55 (t, *J* = 7.8 Hz, 1H), 7.30 (d, *J* = 7.8 Hz, 1H), 5.98 (s, 1H), 2.58–2.48 (complex m, 4H), 2.25–2.17 (complex m, 2H).

¹³C NMR (100 MHz, CDCl₃) δ 199.0, 160.8, 146.8, 136.7, 134.0, 129.8, 129.7, 127.7, 125.1, 37.4, 31.0, 23.4.

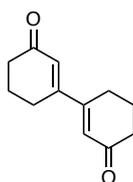
IR (ATR) *v*_{max} 2938, 2870, 1659, 1521, 1345, 1257, 1190, 959, 895, 856, 788, 742, 703 cm⁻¹.

MS (ESI, +ve) *m/z* 240 [(M+Na)⁺, 100%].

HRMS *m/z* 218.0813 [M+H]⁺ (calcd for C₁₂H₁₁NO₃, 218.08112).

Cross-coupling reactions of compound **5** (X = I) such as the one detailed immediately above sometimes delivered small quantities of the corresponding homo-coupling product, viz. [1,1'-bi(cyclohexane)]-1,1'-diene-3,3'-dione and so an authentic sample of this material was produced by the method detailed immediately below.

[1,1'-Bi(cyclohexane)]-1,1'-diene-3,3'-dione



A magnetically stirred mixture of compound **5** (X = I) (222 mg, 1.00 mmol) and copper powder (318 mg, 5.00 mmol) in dry DMSO (5 mL) was heated at 80 °C (41 mg, 0.05 mmol) for 22 h then cooled to 22 °C, diluted with ethyl acetate (5 mL) then filtered through a plug of

TLC-grade silica gel topped with diatomaceous earth and the solids so retained were washed with ethyl acetate (20 mL). The combined filtrates were washed with ammonia (1 x 25 mL of a 5% v/v aqueous solution), water (1 x 25 mL) and brine (1 x 25 mL) before being dried (Na₂SO₄), filtered, then concentrated under reduced pressure. The residue thus obtained was subjected to flash column chromatography (silica, 2:3 v/v ethyl acetate/40-60 petroleum ether elution) and thus affording, after concentration of the appropriate fractions ($R_f = 0.2$), the title compound⁵ (46 mg, 48%) as a brown powder, m.p. = 104 °C.

¹H NMR (400 MHz, CDCl₃) δ 6.29 (s, 2H), 2.52 (td, $J = 6.2$ and 1.2 Hz, 4H), 2.44 (t, $J = 6.2$ Hz, 4H), 2.12–2.02 (complex m, 4H).

¹³C NMR (100 MHz, CDCl₃) δ 199.8, 156.7, 128.1, 37.6, 26.0, 22.4.

IR (ATR) ν_{\max} 2951, 2881, 1661, 1637, 1575, 1415, 1328, 1263, 1186, 1144, 899, 770 cm⁻¹.

MS (ESI, +ve) m/z 213 [(M+Na)⁺, 100%].

HRMS m/z 191.1062 [M+H]⁺ (calcd for C₁₂H₁₄O₂, 191.1067).

Compound 8



8

A magnetically stirred solution of triphenylphosphine (2.89 g, 11.0 mmol) in dry acetonitrile (50 mL) maintained at 22 °C was treated, in portions, with powdered molecular iodine (2.92 g, 11.5 mmol). After 0.5 h the reaction mixture was treated with triethylamine (1.67 mL, 12.0 mmol) and cyclopentene-1,3-dione (981 mg, 10.0 mmol) then it was heated under reflux 16 h before being cooled and concentrated under reduced pressure. The residue thus obtained was stirred vigorously with diethyl ether (30 mL) and the supernatant liquid decanted. This process was repeated twice more and the combined organic phases then diluted with 40-60 petroleum ether (50 mL) to precipitate triphenylphosphine oxide. The ensuing mixture was filtered through a plug of TLC-grade silica gel topped with diatomaceous earth and the filtrate concentrated under reduced pressure to afford compound **8** (1.37 g, 66%) as a white, crystalline solid. The spectral data obtained on this material matched those published in the literature.³

Compound 9

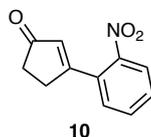


9

A magnetically stirred solution of triphenylphosphine (2.89 g, 11.0 mmol) in dry acetonitrile (50 mL) maintained at 22 °C was treated, in portions, with powdered molecular iodine (2.92 g, 11.5 mmol). After 0.5 h the reaction mixture was treated with triethylamine (1.67 mL, 12.0 mmol) and 2-methylcyclopentane-1,3-dione (1.12 g, 10.0 mmol) before being heated under reflux for 18 h. The cooled reaction mixture was concentrated under reduced pressure and the residue thus obtained stirred vigorously with diethyl ether (30 mL) and the supernatant liquid decanted. This process was repeated twice more and the combined organic phases then diluted with 40-60 petroleum ether (50 mL) to precipitate triphenylphosphine oxide. The ensuing mixture was filtered through a plug of TLC-grade silica gel topped with diatomaceous earth and the filtrate concentrated under reduced pressure to afford **9** (1.80 g,

81%) as a pale-yellow, crystalline solid. The spectral data obtained on this material matched those published in the literature.³

Compound 10



A magnetically stirred suspension of compound **8** (728 mg, 3.50 mmol), *o*-iodonitrobenzene (**2**) (1.74 g, 7.00 mmol) and copper powder (1.11 g, 17.5 mmol) in dry DMSO (15 mL) maintained at 50 °C was treated with Pd(dppf)Cl₂•CH₂Cl₂ (143 mg, 0.18 mmol). The ensuing mixture was stirred at 50 °C for 17 h then cooled to 22 °C and diluted with ethyl acetate (15 mL) before being filtered through a plug of TLC-grade silica gel topped with diatomaceous earth. The solids so retained were washed with ethyl acetate (60 mL) and the combined filtrates washed with ammonia (2 x 75 mL of a 5% v/v aqueous solution), water (2 x 75 mL) and brine (1 x 75 mL) before being dried (Na₂SO₄), filtered, then concentrated under reduced pressure. The ensuing residue was subjected to flash column chromatography (silica, 1:9 v/v diethyl ether/toluene elution) and thus affording, after concentration of the appropriate fractions (*R*_f = 0.2), compound **10** (663 mg, 93%) as a pale-yellow powder, m.p. = 89 °C.

¹H NMR (400 MHz, CDCl₃) δ 8.06 (dd, *J* = 7.8 and 1.0 Hz, 1H), 7.69 (td, *J* = 7.8 and 1.0 Hz, 1H), 7.57 (td, *J* = 7.8 and 1.0 Hz, 1H), 7.38 (dd, *J* = 7.8 and 1.0 Hz, 1H), 6.17 (t, *J* = 1.9 Hz, 1H), 2.95–2.86 (complex m, 2H), 2.64–2.57 (complex m, 2H).

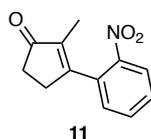
¹³C NMR (100 MHz, CDCl₃) δ 208.5, 173.9, 147.1 133.7, 132.6, 132.0, 130.2, 129.4, 124.9, 35.7, 31.9.

IR (ATR) ν_{max} 3065, 2929, 2850, 1702, 1686, 1592, 1509, 1437, 1345, 1321, 1287, 1254, 1184, 1083, 876, 849, 788, 746 cm⁻¹.

MS (ESI, +ve) *m/z* 226 [(M+Na)⁺, 100%].

HRMS *m/z* 226.0482 [M+Na]⁺ (calcd for C₁₁H₉NO₃, 226.0480).

Compound 11



A magnetically stirred suspension of compound **9** (516 mg, 2.32 mmol), *o*-iodonitrobenzene (**2**) (1.16 g, 4.65 mmol), copper(I) iodide (221 mg, 1.16 mmol) and copper powder (738 mg, 11.6 mmol) in dry DMSO (10 mL) maintained at 50 °C was treated with Pd(dppf)Cl₂•CH₂Cl₂ (190 mg, 0.23 mmol). After 23 h the reaction mixture was cooled to 22 °C then diluted with ethyl acetate (10 mL) before being filtered through a plug of TLC-grade silica gel topped with diatomaceous earth and the solids so retained were washed with ethyl acetate (30 mL). The combined filtrates were washed with ammonia (2 x 40 mL of a 5% v/v aqueous solution), water (2 x 40 mL) and brine (1 x 40 mL) before being dried (Na₂SO₄), filtered, then concentrated under reduced pressure. The residue so obtained was subjected to flash column

chromatography (silica, 1:9 v/v diethyl ether/toluene elution) and thus affording, after concentration of the appropriate fractions ($R_f = 0.2$), compound **11** (247 mg, 49%) as a pale-yellow oil.

$^1\text{H NMR}$ (400 MHz, CDCl_3) δ 8.02 (dd, $J = 8.2$ and 1.2 Hz, 1H), 7.6 (td, $J = 7.5$ and 1.2 Hz, 1H), 7.50 (m, 1H), 7.22 (dd, $J = 7.5$ and 1.2 Hz, 1H), 2.69 (m, 2H), 2.45 (m, 2H), 1.44 (t, $J = 2.2$ Hz, 3H).

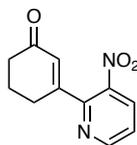
$^{13}\text{C NMR}$ (100 MHz, CDCl_3) δ 208.3, 166.2, 146.8, 138.0, 133.8, 132.8, 129.4, 129.1, 124.7, 34.2, 30.6, 8.4.

IR (ATR) ν_{max} 2919, 1698, 1644, 1515, 1438, 1382, 1353, 1337, 1219, 1102, 1056, 857, 787, 753, 707, 698 cm^{-1} .

MS (ESI, +ve) m/z 240 [(M+Na) $^+$, 100%].

HRMS m/z 218.0822 [M+H] $^+$ (calcd for $\text{C}_{12}\text{H}_{11}\text{NO}_3$, 218.0817).

Compound 15



15

A magnetically stirred suspension of compound **5** ($X = \text{I}$) (1.32 g, 5.91 mmol), copper(I) iodide (845 mg, 4.44 mmol) and copper powder (600 mg, 2.96 mmol) in dry DMSO (40 mL) maintained at $50\text{ }^\circ\text{C}$ was treated with $\text{Pd}(\text{dppf})\text{Cl}_2 \cdot \text{CH}_2\text{Cl}_2$ (241 mg, 0.30 mmol). After 0.75 h the reaction mixture was treated, dropwise over 1 h, with a solution of 2-bromo-3-nitropyridine (**12**) (600 mg, 2.96 mmol) in dry DMSO (10 mL). After a further 4 h the reaction mixture was cooled to $22\text{ }^\circ\text{C}$ before being diluted with ethyl acetate (20 mL). The ensuing mixture was filtered through a plug of TLC-grade silica gel topped with diatomaceous earth and the solids thus retained were washed with ethyl acetate (40 mL). The combined filtrates were washed with ammonia (2 x 60 mL of a 5% v/v aqueous solution), water (2 x 60 mL) and brine (1 x 60 mL) before being dried (Na_2SO_4), filtered and then concentrated under reduced pressure. The residue thus obtained was subjected to flash column chromatography (silica, 4:6 v/v ethyl acetate/40-60 petroleum ether elution) and so affording, after concentration of the appropriate fractions ($R_f = 0.2$ in 1:1 v/v ethyl acetate/40-60 petroleum ether), compound **15** (650 mg, 69%) as an oily, brown solid.

$^1\text{H NMR}$ (400 MHz, CDCl_3) δ 8.80 (d, $J = 4.6$ Hz, 1H), 8.27 (d, $J = 8.2$ Hz, 1H), 7.50 (m, 1H), 5.96 (s, 1H), 2.68 (t, $J = 6.3$ Hz, 2H), 2.48 (t, $J = 6.3$ Hz, 2H), 2.19 (p, $J = 6.3$ Hz, 2H).

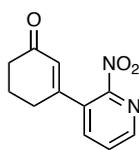
$^{13}\text{C NMR}$ (100 MHz, CDCl_3) δ 198.5, 158.0, 152.8(4), 152.8(2), 144.3, 132.6, 128.1, 123.9, 37.2, 28.7, 22.8.

IR (ATR) ν_{max} 2980, 1669, 1593, 1524, 1346, 1325, 1251, 959, 818, 762, 725 cm^{-1} .

MS (ESI, +ve) m/z 241 [(M+Na) $^+$, 100%].

HRMS m/z 219.0769 [M+H] $^+$ (calcd for $\text{C}_{11}\text{H}_{10}\text{N}_2\text{O}_3$, 219.0770).

Compound 16



16

A magnetically stirred suspension of compound **5** (X = I) (1.96 g, 8.83 mmol), 3-bromo-2-nitropyridine (**13**) (900 mg, 4.41 mmol), copper(I) iodide (1.26 g, 6.62 mmol) and copper powder (1.15 g, 18.1 mmol) in dry DMSO (44 mL) maintained at 50 °C was treated with Pd(dppf)Cl₂•CH₂Cl₂ (241 mg, 0.30 mmol). After 5 h the reaction mixture was cooled to 22 °C then diluted with ethyl acetate (20 mL). The ensuing mixture was filtered through a plug of TLC-grade silica gel topped with diatomaceous earth and the solids so retained were washed with ethyl acetate (40 mL). The combined filtrates were washed with ammonia (2 x 60 mL of a 5% v/v aqueous solution), water (2 x 60 mL) and brine (1 x 60 mL) before being dried (Na₂SO₄), filtered, then concentrated under reduced pressure. The residue thus obtained was subjected to flash column chromatography (silica, 1:4 v/v ethyl acetate/40-60 petroleum ether elution) and so affording, after concentration of the appropriate fractions (*R_f* = 0.2), compound **16** (894 mg, 91%) as a yellow, crystalline solid, m.p. = 90-93 °C.

¹H NMR (400 MHz, CDCl₃) δ 8.59 (dd, *J* = 4.7 and 1.7 Hz, 1H), 7.81 (dd, *J* = 7.7 and 1.7 Hz, 1H), 7.67 (dd, *J* = 7.7 and 4.7 Hz, 1H), 6.00 (s, 1H), 2.56-2.51 (complex m, 4H), 2.20 (m, 2H).

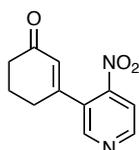
¹³C NMR (100 MHz, CDCl₃) δ 198.3, 156.7, 155.1, 148.8, 139.7, 130.8, 128.8, 128.3, 37.3, 30.3, 23.2.

IR (ATR) *v*_{max} 3061, 2950, 2886, 1668, 1537, 1346, 1238, 1188, 982, 958, 807, 703 cm⁻¹.

MS (ESI, +ve) *m/z* 241 [(M+Na)⁺, 100%], 219 [(M+H)⁺, 10%].

HRMS *m/z* 219.0755 [M+H]⁺ (calcd for C₁₁H₁₀N₂O₃ 219.0764).

Compound 17



17

A magnetically stirred suspension of compound **5** (X = I) (80.0 mg, 0.36 mmol), 3-bromo-4-nitropyridine (**14**) (102 mg, 0.50 mmol) and copper powder (160 mg, 2.52 mmol) in dry DMSO (4 mL) maintained at 80 °C was treated with Pd₂(dba)₃•CHCl₃ (37.3 mg, 0.036 mmol). After 16 h the reaction mixture was cooled to 22 °C, diluted with ethyl acetate (4 mL), filtered through a plug of TLC-grade silica gel topped with diatomaceous earth and the solids so retained washed with ethyl acetate (10 mL). The combined filtrates were washed with ammonia (2 x 20 mL of a 5% v/v aqueous solution), water (2 x 20 mL) and brine (1 x 20 mL) before being dried (Na₂SO₄), filtered, then concentrated under reduced pressure. The residue thus obtained was subjected to flash column chromatography (silica, 1:9 to 4:6 v/v diethyl ether/40-60 petroleum ether elution) and so affording, after concentration of the

appropriate fractions ($R_f = 0.2$ in 1:1 v/v ethyl acetate/40-60 petroleum ether), compound **17** (70 mg, 89%) as a clear, colorless oil.

$^1\text{H NMR}$ (400 MHz, CDCl_3) δ 8.87 (d, $J = 5.3$ Hz, 1H), 8.66 (s, 1H), 7.85 (d, $J = 5.3$ Hz, 1H), 6.01 (s, 1H), 2.51 (m, 4H), 2.19 (m, 2H).

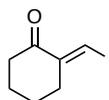
$^{13}\text{C NMR}$ (100 MHz, CDCl_3) δ 198.1, 155.9, 152.2, 151.0, 129.6, 129.1, 117.0, 37.2, 30.6, 23.2 (signal due to one carbon obscured or overlapping).

IR (ATR) ν_{max} 2925, 1669, 1554, 1530, 1348, 1246, 728, 689, 672 cm^{-1} .

MS (ESI, +ve) m/z 241 [(M+Na) $^+$, 100%], 219 [(M+H) $^+$, 18%].

HRMS m/z 219.0766 [(M+H) $^+$] (calcd for $\text{C}_{11}\text{H}_{10}\text{N}_2\text{O}_3$, 219.0764).

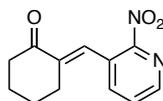
Compound 18



18

Compound **18** was prepared using a procedure reported earlier.³ Thus, a magnetically stirred solution of triphenylphosphine (2.16 g, 8.25 mmol) in dry acetonitrile/HMPA (55 mL of a 10:1 v/v mixture) maintained at 22 °C was treated, in portions, with powdered molecular iodine (2.10 g, 8.25 mmol). After 0.5 h the reaction mixture was treated with triethylamine (1.20 mL, 8.25 mmol) and a solution of (*E*)-2-(hydroxymethylene)cyclohexan-1-one³ (800 mg, 6.35 mmol) in dry acetonitrile (10 mL). The resulting mixture was stirred at 22 °C for 15 h then concentrated under reduced pressure. The residue thus obtained was dissolved in ethyl acetate (50 mL) and the resulting solution washed with water (3 x 30 mL) before being dried (Na_2SO_4), filtered then concentrated under reduced pressure. The residue so obtained was subjected to flash column chromatography (silica, 1:20 v/v ethyl acetate/40-60 petroleum ether elution) and thus affording, after concentration of the appropriate fractions ($R_f = 0.5$), compound **18** (1.18 g, 79%) as a light-yellow oil. The spectral data acquired on this material were identical, in all respects, with those reported in the literature.³

Compound 19



19

A magnetically stirred suspension of compound **18** (472 g, 2.00 mmol), 3-bromo-2-nitropyridine (**13**) (808 mg, 4.00 mmol), copper(I) iodide (570 g, 3.00 mmol) and copper powder (512 mg, 8.00 mmol) in dry DMSO (20 mL) maintained at 50 °C was treated with $\text{Pd}(\text{dppf})\text{Cl}_2 \cdot \text{CH}_2\text{Cl}_2$ (16 mg, 0.02 mmol). After 5 h the reaction mixture was cooled to 22 °C then diluted with ethyl acetate (20 mL) and the ensuing mixture filtered through a plug of TLC-grade silica gel topped with diatomaceous earth. The solids so retained were washed with ethyl acetate (40 mL) and the combined filtrates were washed with ammonia (2 x 60 mL of a 5% v/v aqueous solution), water (2 x 60 mL) and brine (1 x 60 mL) before being dried (Na_2SO_4), filtered and then concentrated under reduced pressure. The residue thus obtained

was subjected to flash column chromatography (silica, 1:4 v/v ethyl acetate/40-60 petroleum ether elution) and thus affording, after concentration of the appropriate fractions ($R_f = 0.2$), compound **19** (402 mg, 87%) as a yellow, crystalline solid, m.p. = 95-98 °C.

$^1\text{H NMR}$ (400 MHz, $[(\text{CD}_3)_2\text{CO}]$) δ 8.56 (dd, $J = 4.6$ and 1.5 Hz, 1H), 8.12 (dd, $J = 7.7$ and 1.5 Hz, 1H), 7.85 (dd, $J = 7.7$ and 4.6 Hz, 1H), 7.32 (t, $J = 4.6$ Hz, 1H), 2.64 (m, 2H), 2.51 (m, 2H), 1.93 (m, 2H), 1.76 (m, 2H).

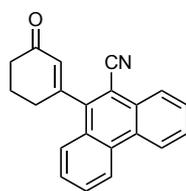
$^{13}\text{C NMR}$ (100 MHz, $[(\text{CD}_3)_2\text{CO}]$) δ 200.0, 148.8, 142.3, 142.2, 128.7, 126.8, 125.9, 41.0, 29.2, 24.4, 24.1. (resonance due to one carbon obscured or overlapping).

IR (ATR) ν_{max} 2941, 2868, 1690, 1595, 1540, 1405, 1360, 1142, 862, 813 cm^{-1} .

MS (ESI, +ve) m/z 255 $[(\text{M}+\text{Na})^+]$, 100%.

HRMS m/z 233.0912 $[(\text{M}+\text{H})^+]$ (calcd for $\text{C}_{12}\text{H}_{12}\text{N}_2\text{O}_3$, 233.0921).

Compound 24



24

A magnetically stirred suspension of compound **5** ($X = \text{I}$) (84.4 mg, 0.38 mmol), compound **20**⁶ (126 mg, 0.38 mmol) and copper powder (170 mg, 2.68 mmol) in dry DMSO (5 mL) maintained at 80 °C was treated with $\text{Pd}_2(\text{dba})_3 \cdot \text{CHCl}_3$ (39.3 mg, 0.038 mmol). After 16 h the reaction mixture was cooled to 22 °C, diluted with ethyl acetate (5 mL), filtered through a plug of TLC-grade silica gel topped with diatomaceous earth and the solids so retained were washed with ethyl acetate (20 mL). The filtrate was washed with ammonia (2 x 25 mL of a 5% v/v aqueous solution), water (2 x 25 mL) and brine (1 x 25 mL) before being dried (Na_2SO_4), filtered, then concentrated under reduced pressure. The residue thus obtained was subjected to flash column chromatography (silica, 1:9 to 4:6 v/v diethyl ether/40-60 petroleum ether elution) and so affording, after concentration of the appropriate fractions ($R_f = 0.2$ in 2:3 v/v diethyl ether/40-60 petroleum ether elution), compound **24** (45 mg, 40%) as a white, crystalline solid, m.p. = 163 °C.

$^1\text{H NMR}$ (400 MHz, CDCl_3) δ 8.75 (m, 2H), 8.36 (d, $J = 9.3$ Hz, 1H), 7.94–7.74 (complex m, 4H), 7.70 (m, 1H), 6.26 (s, 1H), 2.89 (m, 1H), 2.71 (m, 3H), 2.41 (m, 2H).

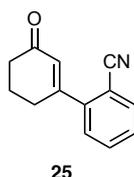
$^{13}\text{C NMR}$ (100 MHz, CDCl_3) δ 198.6, 158.6, 145.9, 132.0, 131.6, 130.2, 129.8, 128.7(0), 127.6(9), 128.4, 128.1, 127.6, 127.1, 126.6, 123.5, 123.1, 116.6, 107.1, 37.6, 31.3, 23.4.

IR (ATR) ν_{max} 3340, 3067, 2949, 2220, 1678, 1450, 907, 757, 725 cm^{-1} .

MS (ESI, +ve) m/z 320 $[(\text{M}+\text{Na})^+]$, 100 %.

HRMS m/z 320.1049 $[(\text{M}+\text{Na})^+]$ (calcd for $\text{C}_{21}\text{H}_{15}\text{NO}$, 320.1051).

Compound 25



A magnetically stirred suspension of compound **5** (X = I) (222 mg, 1.00 mmol), compound **21**⁶ (458 mg, 2.00 mmol), triphenylarsine (61.0 mg, 0.20 mmol) and copper powder (318 mg, 5.00 mmol) in dry DMSO (5 mL) maintained at 80 °C was treated with Pd₂(dba)₃•CHCl₃ (52 mg, 0.05 mmol). After 20 h the reaction mixture was cooled to 22 °C, diluted with ethyl acetate (5 mL) and the resulting mixture filtered through a plug of TLC-grade silica gel topped with diatomaceous earth and the solids so retained were washed with ethyl acetate (20 mL). The combined filtrates were washed with ammonia (2 x 25 mL of a 5% v/v aqueous solution), water (2 x 25 mL) and brine (1 x 25 mL) before being dried (Na₂SO₄), filtered then concentrated under reduced pressure. The residue thus obtained was subjected to flash column chromatography (silica, 1:9 v/v ethyl acetate/40-60 petroleum ether elution) and so affording, after concentration of the appropriate fractions (*R*_f = 0.3), compound **25**⁷ (120 mg, 61%) as a white, crystalline solid, m.p. = 86 °C.

¹H NMR (400 MHz, CDCl₃) δ 7.73 (dd, *J* = 7.7 and 1.4 Hz, 1H), 7.63 (td, *J* = 7.7 and 1.4 Hz, 1H), 7.48 (m, 1H), 7.39 (dd, *J* = 7.8 and 1.4 Hz, 1H), 6.20 (s, 1H), 2.80 (m, 2H), 2.54 (m, 2H), 2.21 (m, 2H).

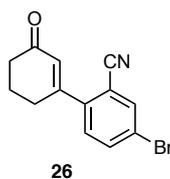
¹³C NMR (100 MHz, CDCl₃) δ 198.9, 158.6, 144.5, 133.9, 133.2, 130.1, 129.2, 128.1, 117.9, 110.2, 37.4, 30.2, 23.3.

IR (ATR) ν_{max} 2949, 2870, 2226, 1669, 1615, 1346, 1326, 1248, 1189, 957, 894, 764 cm⁻¹.

MS (ESI, +ve) *m/z* 220 [(M+Na)⁺, 100%].

HRMS *m/z* 220.0733 [M+Na]⁺ (calcd for C₁₃H₁₁NO, 220.0738).

Compound 26



A magnetically stirred suspension of compound **5** (X = I) (84.4 mg, 0.38 mmol), compound **22**⁶ (176 mg, 0.57 mmol) and copper powder (160 mg, 2.52 mmol) in dry DMSO (5 mL) maintained at 80 °C was treated with Pd₂(dba)₃•CHCl₃ (39.3 mg, 0.038 mmol). After 16 h the reaction mixture was cooled to 22 °C, diluted with ethyl acetate (5 mL) and the resulting mixture filtered through a plug of TLC-grade silica gel topped with diatomaceous earth. The solids so retained were washed with ethyl acetate (20 mL) and the filtrate was washed with ammonia (2 x 25 mL of a 5% v/v aqueous solution), water (2 x 25 mL) and brine (1 x 25 mL) before being dried (Na₂SO₄), filtered then concentrated under reduced pressure. The residue thus obtained was subjected to flash column chromatography (silica, 2:8 to 1:1 v/v ethyl acetate/40-60 petroleum ether elution) and so affording, after concentration of the appropriate

fractions ($R_f = 0.6$ in 2:3 v/v ethyl acetate/40-60 petroleum ether elution), compound **26** (36 mg, 34%) as a white, crystalline solid, m.p. = 123 °C.

$^1\text{H NMR}$ (400 MHz, CDCl_3) δ 7.85 (d, $J = 2.0$ Hz, 1H), 7.75 (dd, $J = 8.4$ and 2.0 Hz, 1H), 7.26 (d, $J = 8.4$ Hz, 1H), 6.18 (m, 1H), 2.80–2.73 (complex m, 2H), 2.56–2.49 (complex m, 2H), 2.24–2.15 (complex m, 2H).

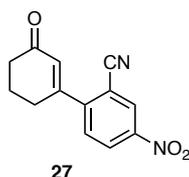
$^{13}\text{C NMR}$ (100 MHz, CDCl_3) δ 198.5, 157.3, 143.3, 136.4, 136.3, 130.3, 129.6, 123.0, 116.5, 112.0, 37.3, 30.1, 23.2.

IR (ATR) ν_{max} 3062, 2951, 2869, 2227, 1669, 1547, 1346, 1252, 822 cm^{-1} .

MS (ESI, +ve) m/z 300 and 298 [(M+Na) $^+$, 98 and 100 %].

HRMS m/z 297.9843 [(M+Na) $^+$ (calcd for $\text{C}_{13}\text{H}_{10}^{79}\text{BrNO}$, 297.9843)].

Compound 27



A magnetically stirred suspension of compound **5** ($\text{X} = \text{I}$) (84.4 mg, 0.38 mmol), compound **23**⁶ (176 mg, 0.57 mmol) and copper powder (160 mg, 2.52 mmol) in dry DMSO (5 mL) maintained at 80 °C was treated with $\text{Pd}_2(\text{dba})_3 \cdot \text{CHCl}_3$ (39.3 mg, 0.038 mmol). After 16 h the reaction mixture was cooled to 22 °C, diluted with ethyl acetate (5 mL) and the resulting mixture filtered through a plug of TLC-grade silica gel topped with diatomaceous earth and the solids so retained were washed with ethyl acetate (20 mL). The combined filtrates were washed with ammonia (2 x 25 mL of a 5% v/v aqueous solution), water (2 x 25 mL) and brine (1 x 25 mL) before being dried (Na_2SO_4), filtered then concentrated under reduced pressure. The residue thus obtained was subjected to flash column chromatography (silica, 2:8 to 1:1 v/v ethyl acetate/40-60 petroleum ether elution) and so affording, after concentration of the appropriate fractions ($R_f = 0.6$ in 2:3 v/v ethyl acetate/40-60 petroleum ether elution), compound **27** (73 mg, 79%) as a red, crystalline solid, m.p. = 152 °C.

$^1\text{H NMR}$ (400 MHz, CDCl_3) δ 8.60 (d, $J = 2.2$ Hz, 1H), 8.47 (dd, $J = 8.6$ and 2.2 Hz, 1H), 7.61 (d, $J = 8.6$ Hz, 1H), 6.24 (t, $J = 1.7$ Hz, 1H), 2.80 (td, $J = 5.9$ and 1.7 Hz, 2H), 2.58 (dd, $J = 7.6$ and 5.9 Hz, 2H), 2.26 (m, 2H).

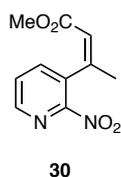
$^{13}\text{C NMR}$ (100 MHz, CDCl_3) δ 198.9, 155.9, 150.1, 147.6, 131.1, 129.6, 128.9, 127.8, 115.8, 111.8, 37.2, 29.8, 23.1.

IR (ATR) ν_{max} 3081, 2953, 2233, 1673, 1526, 1353, 1324, 1247, 744 cm^{-1} .

MS (ESI, +ve) m/z 265 [(M+Na) $^+$, 100 %].

HRMS m/z 265.0591 [(M+Na) $^+$ (calcd for $\text{C}_{13}\text{H}_{10}\text{N}_2\text{O}_3$, 265.0589)].

Compound 30



A magnetically stirred suspension of compound **28**⁸ (79.1 mg, 0.35 mmol), 3-bromo-2-nitropyridine (**12**) (102 mg, 0.50 mmol) and copper powder (160 mg, 2.52 mmol) in dry DMSO (5 mL) maintained at 80 °C was treated with Pd₂(dba)₃•CHCl₃ (29.0 mg, 0.028 mmol). After 16 h the reaction mixture was cooled to 22 °C then diluted with ethyl acetate (5 mL) before being filtered through a plug of TLC-grade silica gel topped with diatomaceous earth and the solids so retained were washed with ethyl acetate (20 mL). The combined filtrates were washed with ammonia (2 x 25 mL of a 5% v/v aqueous solution), water (2 x 25 mL) and brine (1 x 25 mL) before being dried (Na₂SO₄), filtered then concentrated under reduced pressure. The residue thus obtained was subjected to flash column chromatography (silica, 4:6 to 1:1 v/v ethyl acetate/40-60 petroleum ether elution) and so affording, after concentration of the appropriate fractions (*R*_f = 0.3 in 3:7 v/v ethyl acetate/40-60 petroleum ether elution), compound **30** (66 mg, 84%) as a yellow, crystalline solid, m.p. = 68 °C.

¹H NMR (400 MHz, CDCl₃) δ 8.56 (dd, *J* = 4.5 and 1.8 Hz, 1H), 7.68 (dd, *J* = 7.6 and 1.8 Hz, 1H), 7.62 (dd, *J* = 7.6 and 4.5 Hz, 1H), 6.00 (q, *J* = 1.5 Hz, 1H), 3.52 (s, 3H), 2.29 (d, *J* = 1.5 Hz, 3H).

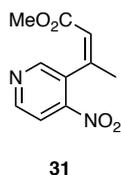
¹³C NMR (100 MHz, CDCl₃) δ 165.4, 154.8, 150.5, 147.5, 139.0, 132.0, 128.0, 118.9, 51.5, 26.1.

IR (ATR) *v*_{max} 2953, 1714, 1650, 1539, 1359, 1249, 1172, 1042, 859, 814, 659 cm⁻¹.

MS (ESI, +ve) *m/z* 245 [(M+Na)⁺, 100 %].

HRMS *m/z* 245.0536 [M+Na]⁺ (calcd for C₁₀H₁₀N₂O₄ 245.0538).

Compound 31



A magnetically stirred suspension of compound **28** (22.6 mg, 0.10 mmol), 3-bromo-4-nitropyridine (**14**) (40.6 mg, 0.20 mmol) and copper powder (31.8 mg, 0.50 mmol) in dry DMSO (1 mL) maintained at 55 °C was treated with Pd(dppf)Cl₂•CH₂Cl₂ (8.2 mg, 0.010 mmol). After 18 h the reaction mixture was cooled to 22 °C, diluted with ethyl acetate (5 mL), filtered through a plug of TLC-grade silica gel topped with diatomaceous earth and the solids so retained were washed with ethyl acetate (10 mL). The filtrate was washed with ammonia (2 x 15 mL of a 5% v/v aqueous solution), water (2 x 15 mL) and brine (1 x 15 mL) before being dried (Na₂SO₄), filtered, then concentrated under reduced pressure. The residue obtained was subjected to flash chromatography (silica, 1:9 v/v diethyl ether/toluene elution) and thus affording, after concentration of the appropriate fractions (*R*_f = 0.12 in 1:9 v/v diethyl ether/toluene), compound **31** (15.3 mg, 69%) as a clear, colorless oil.

¹H NMR (400 MHz, CDCl₃) δ 8.82 (d, *J* = 5.4 Hz, 1H), 8.55 (s, 1H), 7.91 (d, *J* = 5.4 Hz, 1H), 6.08 (d, *J* = 1.5 Hz, 1H), 3.53 (s, 3H), 2.29 (d, *J* = 1.5 Hz, 3H). Irradiation of the

resonance at δ 2.29 led to a significant enhancement of the one at δ 6.08 and so establishing the illustrated *Z*-configuration about the acrylate double-bond.

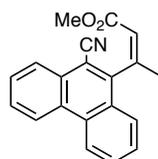
^{13}C NMR (100 MHz, CDCl_3) δ 165.4, 152.3, 150.8, 150.6, 149.7, 130.8, 119.9, 116.5, 51.5, 26.3.

IR (ATR) ν_{max} 2953, 1716, 1650, 1532, 1442, 1354, 1243, 1163, 1047, 858, 676 cm^{-1} .

MS (ESI, +ve) m/z 245 [(M+Na) $^+$, 100 %].

HRMS m/z 245.0539 [M+Na] $^+$ (calcd for $\text{C}_{10}\text{H}_{10}\text{N}_2\text{O}_4$ 245.0538).

Compound 32



32

A magnetically stirred suspension of compound **28** (84.4 mg, 0.38 mmol), compound **20** (160 mg, 0.49 mmol) and copper powder (160 mg, 2.52 mmol) in dry DMSO (5 mL) maintained at 80 °C was treated with $\text{Pd}_2(\text{dba})_3 \cdot \text{CHCl}_3$ (39.3 mg, 0.030 mmol). After 16 h the reaction mixture was cooled to 22 °C, diluted with ethyl acetate (5 mL), filtered through a plug of TLC-grade silica gel topped with diatomaceous earth and the solids so retained were washed with ethyl acetate (20 mL). The combined filtrates were washed with ammonia (2 x 25 mL of a 5% v/v aqueous solution), water (2 x 25 mL) and brine (1 x 25 mL) before being dried (Na_2SO_4), filtered, then concentrated under reduced pressure. The residue thus obtained was subjected to flash column chromatography (silica, 1:4 to 1:1 v/v ethyl acetate/40-60 petroleum ether elution) and so affording, after concentration of the appropriate fractions ($R_f = 0.2$), compound **32** (62 mg, 55%) as a pink, crystalline solid, m.p. = 153-155 °C.

^1H NMR (400 MHz, CDCl_3) δ 8.75 (d, $J = 8.4$ Hz, 1H), 8.72 (m, 1H), 8.31 (m, 1H), 7.86 (dd, $J = 8.4$ and 1.6 Hz, 1H), 7.80 (m, 1H), 7.77–7.73 (complex m, 2H), 7.65 (m, 1H), 6.46 (q, $J = 1.6$ Hz, 1H), 3.48 (s, 3H), 2.40 (d, $J = 1.6$ Hz, 3H). Irradiation of the resonance at δ 2.40 led to a significant enhancement of the one at δ 6.46 and so establishing the illustrated *Z*-configuration about the acrylate double-bond.

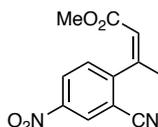
^{13}C NMR (100 MHz, CDCl_3) δ 164.9, 152.2, 147.8, 131.8, 129.7, 129.6, 128.8, 128.2, 128.0, 127.9, 127.6, 126.5, 126.3, 123.5, 123.1, 122.4, 116.9, 106.0, 51.4, 26.0.

IR (ATR) ν_{max} 2950, 2220, 1723, 1651, 1438, 1450, 1208, 1158, 1133, 1044, 759, 725 cm^{-1} .

MS (ESI, +ve) m/z 340 [(M+K) $^+$, 100%], 324 [(M+Na) $^+$, 90%].

HRMS m/z 324.1003 [M+Na] $^+$ (calcd for $\text{C}_{20}\text{H}_{15}\text{NO}_2$, 324.1000).

Compound 33



33

A magnetically stirred suspension of compound **28** (84.4 mg, 0.38 mmol), compound **23** (155 mg, 0.56 mmol) and copper powder (160 mg, 2.52 mmol) in dry DMSO (5 mL) maintained at 80 °C was treated with $\text{Pd}_2(\text{dba})_3 \cdot \text{CHCl}_3$ (31.1 mg, 0.030 mmol). After 16 h the reaction mixture was cooled to 22 °C, diluted with ethyl acetate (5 mL) and the resulting mixture

filtered through a plug of TLC-grade silica gel topped with diatomaceous earth and the solids so retained were washed with ethyl acetate (20 mL). The combined filtrates were washed with ammonia (2 x 25 mL of a 5% v/v aqueous solution), water (2 x 25 mL) and brine (1 x 25 mL) before being dried (Na₂SO₄), filtered then concentrated under reduced pressure. The residue so obtained was subjected to flash column chromatography (silica, 1:4 to 1:1 v/v diethyl ether/40-60 petroleum ether elution) and thus affording, after concentration of the appropriate fractions (*R_f* = 0.3), compound **33** (36 mg, 43%) as a white, crystalline solid, m.p. = 106-107 °C.

¹H NMR (400 MHz, CDCl₃) δ 8.54 (d, *J* = 2.3 Hz, 1H), 8.43 (dd, *J* = 8.6 and 2.3 Hz, 1H), 7.43 (d, *J* = 8.6 Hz, 1H), 6.19 (q, *J* = 1.6 Hz, 1H), 3.60 (s, 3H), 2.26 (d, *J* = 1.6 Hz, 3H).

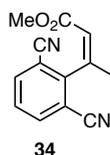
¹³C NMR (100 MHz, CDCl₃) δ 165.1, 152.2, 150.6, 146.9, 128.7, 127.8, 127.5, 121.5, 115.6, 112.3, 51.7, 26.0.

IR (ATR) *v*_{max} 2954, 2236, 1721, 1606, 1529, 1439, 1353, 1241, 1166, 1042, 797 cm⁻¹.

MS (ESI, +ve) *m/z* 269 [(M+Na)⁺, 100 %].

HRMS *m/z* 269.0539 [M+Na]⁺ (calcd for C₁₂H₁₀N₂O₄, 269.0538).

Compound 34



A magnetically stirred suspension of compound **28** (84.4 mg, 0.38 mmol), compound **29**⁹ (134 mg, 0.53 mmol) and copper powder (160 mg, 2.52 mmol) in dry DMSO (5 mL) maintained at 80 °C was treated with Pd₂(dba)₃•CHCl₃ (31.1 mg, 0.030 mmol). After 16 h the reaction mixture was cooled to 22 °C, diluted with ethyl acetate (5 mL) then filtered through a plug of TLC-grade silica gel topped with diatomaceous earth and the solids so retained were washed with ethyl acetate (20 mL). The combined filtrates were washed with ammonia (2 x 25 mL of a 5% v/v aqueous solution), water (2 x 25 mL) and brine (1 x 25 mL) before being dried (Na₂SO₄), filtered then concentrated under reduced pressure. The residue thus obtained was subjected to flash column chromatography (silica, 1:4 to 1:1 v/v diethyl ether/40-60 petroleum ether elution) and so affording, after concentration of the appropriate fractions (*R_f* = 0.2), compound **34** (50 mg, 59%) as a clear, colorless oil.

¹H NMR (400 MHz, CDCl₃) δ 7.90 (d, *J* = 7.8 Hz, 2H), 7.54 (t, *J* = 7.8 Hz, 1H), 6.28 (d, *J* = 1.6 Hz, 1H), 3.61 (s, 3H), 2.30 (d, *J* = 1.6 Hz, 3H).

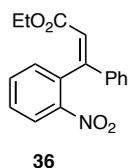
¹³C NMR (100 MHz, CDCl₃) δ 164.9, 149.9, 149.1, 136.5, 128.5, 123.0, 115.9, 112.2, 51.8, 25.1.

IR (ATR) *v*_{max} 2954, 2236, 1719, 1654, 1455, 1434, 1352, 1244, 1166, 1041, 808, 760 cm⁻¹.

MS (ESI, +ve) *m/z* 249 [(M+Na)⁺, 100 %].

HRMS *m/z* 249.0647 [M+Na]⁺ (calcd for C₁₃H₁₀N₂O₂, 249.0640).

Compound 36



A magnetically stirred suspension of compound **35**⁸ (100 mg, 0.33 mmol), compound **5** (X = I) (124 mg, 0.50 mmol) and copper powder (160 mg, 2.52 mmol) in dry DMSO (5 mL) maintained at 80 °C was treated with Pd₂(dba)₃•CHCl₃ (31.1 mg, 0.030 mmol). After 16 h the reaction mixture was cooled to 22 °C, diluted with ethyl acetate (5 mL) and the ensuing mixture filtered through a plug of TLC-grade silica gel topped with diatomaceous earth and the solids so retained were washed with ethyl acetate (20 mL). The combined filtrates were washed with ammonia (2 x 25 mL of a 5% v/v aqueous solution), water (2 x 25 mL) and brine (1 x 25 mL) before being dried (Na₂SO₄), filtered and then concentrated under reduced pressure. The residue so obtained was subjected to flash column chromatography (silica, 1:9 to 1:1 v/v diethyl ether/40-60 petroleum ether elution) and thus affording, after concentration of the appropriate fractions (*R*_f = 0.3 in 1:4 v/v diethyl ether/40-60 petroleum ether elution), compound **36**¹⁰ (60 mg, 61%) as a clear, yellow oil.

¹H NMR (400 MHz, CDCl₃) δ 8.12 (dd, *J* = 8.3 and 1.4 Hz, 1H), 7.60 (td, *J* = 7.5 and 1.3 Hz, 1H), 7.49 (m, 1H), 7.29–7.18 (complex m, 6H), 6.41 (s, 1H), 3.92 (m, 2H), 1.03 (t, *J* = 7.2 Hz, 3H).

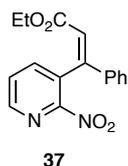
¹³C NMR (100 MHz, CDCl₃) δ 165.5, 153.5, 138.3, 135.2, 133.3, 131.2, 129.9, 128.9, 128.7, 127.6, 127.2, 124.7, 117.2, 60.4, 14.1.

IR (ATR) ν_{\max} 3036, 1712, 1625, 1523, 1346, 1168, 1032, 771, 69 cm⁻¹.

MS (ESI, +ve) *m/z* 320 [(M+Na)⁺, 100 %].

HRMS *m/z* 320.0899 [M+Na]⁺ (calcd for C₁₇H₁₅NO₄, 320.0899).

Compound 37



A magnetically stirred suspension of compound **35**⁸ (130 mg, 0.43 mmol), 3-bromo-2-nitropyridine (**13**) (122 mg, 0.60 mmol) and copper powder (160 mg, 2.52 mmol) in dry DMSO (5 mL) maintained at 80 °C was treated with Pd₂(dba)₃•CHCl₃ (31.1 mg, 0.030 mmol). After 16 h the reaction mixture was cooled to 22 °C, diluted with ethyl acetate (5 mL), filtered through a plug of TLC-grade silica gel topped with diatomaceous earth and the solids so retained were washed with ethyl acetate (20 mL). The combined filtrates were washed with ammonia (2 x 25 mL of a 5% v/v aqueous solution), water (2 x 25 mL) and brine (1 x 25 mL) before being dried (Na₂SO₄), filtered and then concentrated under reduced pressure. The residue thus obtained was subjected to flash column chromatography (silica, 3:7 v/v ethyl acetate/40-60 petroleum ether elution) and so affording, after concentration of the appropriate fractions (*R*_f = 0.5), compound **37** (65 mg, 50%) as a white, crystalline solid, m.p. = 102-103 °C.

¹H NMR (400 MHz, CDCl₃) δ 8.64 (dd, *J* = 4.6 and 1.8 Hz, 1H), 7.76 (dd, *J* = 7.7 and 1.7 Hz, 1H), 7.67 (dd, *J* = 7.7 and 4.6 Hz, 1H), 7.47–7.29 (complex m, 5H), 6.52 (s, 1H), 4.00 (m, 2H), 1.14 (t, *J* = 7.2 Hz, 3H).

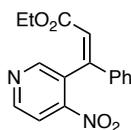
¹³C NMR (100 MHz, CDCl₃) δ 165.2, 155.9, 150.5, 148.0, 141.2, 137.6, 130.4, 129.9, 129.0, 127.7(3), 127.7(0), 118.3, 60.7, 14.1.

IR (ATR) ν_{\max} 3061, 2983, 1709, 1624, 1540, 1367, 1349, 1270, 1175, 1093, 1027, 771, 692 cm⁻¹.

MS (ESI, +ve) *m/z* 321 [(M+Na)⁺, 100 %].

HRMS *m/z* 321.0851 [M+Na]⁺ (calcd for C₁₆H₁₄N₂O₄, 321.0851).

Compound 38



A magnetically stirred suspension of compound **35**⁸ (380 mg, 1.26 mmol), 3-bromo-4-nitropyridine (**14**) (510 mg, 2.52 mmol) and copper powder (400 mg, 6.29 mmol) in dry DMSO (5 mL) maintained at 55 °C was treated with PdCl₂(dppf)•CH₂Cl₂ (103 mg, 0.13 mmol). After 16 h the reaction mixture was cooled to 22 °C, diluted with ethyl acetate (5 mL) and the resulting mixture filtered through a plug of TLC-grade silica gel topped with diatomaceous earth and the solids so retained washed with ethyl acetate (20 mL). The combined filtrates were washed with ammonia (2 x 25 mL of a 5% v/v aqueous solution), water (2 x 25 mL) and brine (1 x 25 mL) before being dried (Na₂SO₄), filtered and then concentrated under reduced pressure. The residue thus obtained was subjected to flash column chromatography (silica, 1:9 to 1:1 v/v diethyl ether/40-60 petroleum ether elution) and so affording, after concentration of the appropriate fractions (*R*_f = 0.3 in 3:7 v/v ethyl acetate/40-60 petroleum ether elution), compound **38** (303 mg, 81%) as a clear, yellow oil.

¹H NMR (400 MHz, CDCl₃) δ 8.91 (broad s, 1H), 8.64 (broad s, 1H), 7.99 (d, *J* = 5.4 Hz, 1H), 7.42–7.29 (complex m, 5H), 6.59 (s, 1H), 4.03 (m, 2H), 1.15 (t, *J* = 7.2 Hz, 3H).

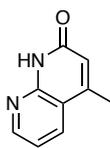
¹³C NMR (100 MHz, CDCl₃) δ 165.3, 153.3, 152.5, 151.3, 149.7, 137.7, 130.4, 129.0, 127.5, 119.2, 60.8, 14.1 (two resonances obscured or overlapping).

IR (ATR) ν_{\max} 2982, 1711, 1624, 1533, 1352, 1268, 1177, 1028, 847, 770, 676 cm⁻¹.

MS (ESI, +ve) *m/z* 321 [(M+Na)⁺, 100 %].

HRMS *m/z* 321.0844 [M+Na]⁺ (calcd for C₁₆H₁₄N₂O₄, 321.0851).

Compound 39



39

A magnetically stirred mixture of compound **30** (55.4 mg, 0.25 mmol), glacial acetic acid (1 mL) and iron powder (30.0 mg, 0.54 mmol) in ethanol (5 mL) maintained at 22 °C was treated with hydrochloric acid (2 drops of a 37% aqueous solution). After 1 h the reaction mixture was quenched with sodium bicarbonate (10 mL of a saturated aqueous solution) and extracted with ethyl acetate (2 x 5 mL). The combined organic phases were dried (Na₂SO₄), filtered and then concentrated under reduced pressure to give compound **39**¹¹ (30.4 mg, 76%) as a brown solid, no m.p., decomposition above 200 °C.

¹H NMR (400 MHz, CDCl₃) δ 9.78 (broad s, 1H), 8.57 (d, *J* = 4.1 Hz, 1H), 7.99 (d, *J* = 7.8 Hz, 1H), 7.22 (m, 1H), 6.57 (s, 1H), 2.48 (s, 3H).

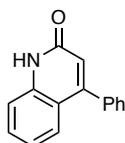
¹³C NMR (100 MHz, CDCl₃) δ 163.7, 150.4, 149.8, 147.2, 133.4, 122.4, 118.4, 115.9, 18.5.

IR (ATR) ν_{\max} 2874, 1664, 1612, 1564, 1423, 1388, 1086, 966, 862, 779, 672, 510 cm⁻¹.

MS (ESI, +ve) *m/z* 183 [(M+Na)⁺, 100%].

HRMS *m/z* 183.0536 [(M+Na)⁺ (calcd for C₉H₈N₂O, 183.0534)].

Compound 40



40

A magnetically stirred mixture of compound **36** (20.3 mg, 0.068 mmol), glacial acetic acid (1 mL) and iron powder (50.0 mg, 0.94 mmol) in ethanol (5 mL) maintained at 60 °C was treated with hydrochloric acid (2 drops of a 37% aqueous solution). After 16 h the reaction mixture was cooled to 22 °C then quenched with sodium bicarbonate (10 mL of a saturated aqueous solution) and extracted with ethyl acetate (2 x 5 mL). The combined organic phases were dried (Na₂SO₄), filtered then concentrated under reduced pressure. The residue thus obtained was subjected to flash column chromatography (silica, 1:1 v/v ethyl acetate/40-60 petroleum ether elution) and so affording, after concentration of the appropriate fractions (*R_f* = 0.2), compound **40**¹² (10.1 mg, 67%) as a white, crystalline solid, m.p. = 189-191 °C

¹H NMR (400 MHz, CDCl₃) δ 12.64 (broad s, 1H), 7.57–7.46 (complex m, 8H), 7.17 (m, 1H), 6.71 (s, 1H).

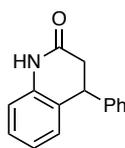
¹³C NMR (100 MHz, CDCl₃) δ 164.6, 153.9, 139.4, 137.6, 131.2, 129.3(3), 129.3(0), 129.1, 127.2, 123.0, 121.3, 120.1, 117.1.

IR (ATR) ν_{\max} 2957, 2920, 2851, 1661, 1610, 1563, 1432, 1386, 876, 751, 700 cm⁻¹.

MS (ESI, +ve) *m/z* 465 [(2M+Na)⁺, 100%], 244 [(M+Na)⁺, 78%].

HRMS *m/z* 244.0744 [(M+Na)⁺ (calcd for C₁₅H₁₁NO, 244.0738)].

Compound 41



41

A magnetically stirred mixture of compound **36** (27.4 mg, 0.092 mmol) and 10% palladium on carbon (27 mg) in dry ethanol (5 mL) maintained at 22 °C was placed under a hydrogen atmosphere. After 16 h the reaction mixture was filtered through a pad of diatomaceous earth and the filtrate concentrated under reduced pressure. The residue thus obtained was subjected to flash column chromatography (silica, 4.6 to 1:1 v/v diethyl ether/40-60 petroleum ether elution) and thus affording, after concentration of the appropriate fractions ($R_f = 0.4$), compound **41**¹³ (17.5 mg, 85%) as a white, crystalline solid, m.p. = 177-179 °C.

¹H NMR (400 MHz, CDCl₃) δ 7.96 (broad s, 1H), 7.39–7.30 (complex m, 2H), 7.30–7.27 (complex m, 1H), 7.23–7.17 (complex m, 3H), 7.02–6.89 (complex m, 2H), 6.82 (d, $J = 7.9$ Hz, 1H), 4.30 (t, $J = 7.5$ Hz, 1H), 2.93 (m, 2H).

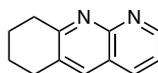
¹³C NMR (100 MHz, CDCl₃) δ 170.3, 141.5, 137.1, 129.1, 128.6, 128.2, 128.0, 127.4, 126.9, 123.5, 115.6, 42.2, 38.6.

IR (ATR) ν_{\max} 3212, 2911, 1679, 1593, 1486, 1376, 1245, 1159, 754, 700 cm⁻¹.

MS (ESI, +ve) m/z 246 [(M+Na)⁺, 100%].

HRMS m/z 246.0894 [M+Na]⁺ (calcd for C₁₅H₁₃NO, 246.0895).

Compound 42



42

A magnetically stirred mixture of compound **19** (232 mg, 1.00 mmol) and iron powder (168 mg, 3.00 mmol) in a mixture of ethanol and water (10 mL of a 7:3 v/v mixture) maintained at 22 °C was treated with calcium chloride (333 mg, 3.00 mmol). The resulting mixture was heated under reflux and after 2 h the reaction mixture was cooled to 22 °C then treated with sodium hydroxide (200 mg, 5.00 mmol) then heated under reflux again. After 1 h the reaction mixture was cooled to 22 °C before diluted with ethyl acetate (20 mL) then filtered through a plug of TLC-grade silica gel topped with diatomaceous earth. The solids so retained were washed with ethyl acetate (2 x 20 mL) and the separated organic phase associated with the combined filtrates dried (MgSO₄) before being concentrated under reduced pressure. The residue thus obtained was subjected to flash column chromatography (silica, 1:99 v/v methanol/ethyl acetate elution) and so affording, after concentration of the appropriate fractions ($R_f = 0.2$), compound **42**¹⁴ (136 mg, 74%) as a yellow solid, no m.p., decomposition above 118 °C.

¹H NMR (400 MHz, CDCl₃) δ 9.01 (dd, $J = 4.3$ and 2.0 Hz, 1H), 8.07 (dd, $J = 8.1$ and 2.0 Hz, 1H), 7.83 (s, 1H), 7.39 (dd, $J = 8.1$ and 4.3 Hz, 1H), 3.23 (t, $J = 6.6$ Hz, 2H), 3.00 (t, $J = 6.0$ Hz, 2H), 2.01 (m, 2H), 1.91 (m, 2H).

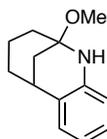
¹³C NMR (100 MHz, CDCl₃) δ 163.3, 154.8, 152.6, 136.1, 135.6, 132.4, 121.5, 121.3, 33.9, 29.2, 23.0, 22.8.

IR (ATR) ν_{\max} 3048, 2936, 2921, 1607, 1597, 1548, 1474, 1446, 1411, 1301, 1245, 1227, 1148, 824, 797, 718, 608 cm^{-1} .

MS (ESI, +ve) m/z 391 [(M+Na)⁺, 37%], 207 [(M+Na)⁺, 100], 185 [(M+H)⁺, 30].

HRMS m/z 185.1068 [(M+H)⁺ (calcd for C₁₂H₁₂N₂, 185.1073)].

Compound 43



43

A magnetically stirred suspension of compound **7** (1.00 g, 4.56 mmol) and 10% palladium on carbon (460 mg) in dry methanol (50 mL) maintained at 50 °C was placed under a hydrogen atmosphere. After 2 h the reaction mixture was cooled to 22 °C then filtered through a pad of diatomaceous earth and the filtrate concentrated under reduced pressure. The residue thus obtained was subjected to flash column chromatography (silica, 5:95 v/v ethyl acetate/40-60 petroleum ether elution) and so affording, after concentration of the appropriate fractions (R_f = 0.11 in 1:9 v/v ethyl acetate/40-60 petroleum ether elution), compound **43** (684 mg, 73%) as white crystals, m.p. = 108 °C.

¹H NMR (400 MHz, CDCl₃) δ 7.02 (m, 1H), 6.94 (dd, J = 7.3 and 1.3 Hz, 1H), 6.63 (m, 1H), 6.55 (dd, J = 8.0 and 1.3 Hz, 1H), 3.82 (s, 1H), 3.32 (s, 3H), 3.14 (m, 1H), 2.26 (m, 1H), 1.79 (m, 2H), 1.72–1.64 (complex m, 3H), 1.65–1.46 (complex m, 2H).

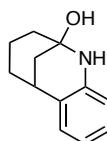
¹³C NMR (100 MHz, CDCl₃) δ 145.8, 128.0, 127.2, 125.7, 117.3, 113.3, 83.9, 48.4, 41.5, 36.3, 34.0, 32.0, 19.5.

IR (KBr) ν_{\max} 3315, 2943, 1606, 1487, 1274, 1114, 1067, 1059, 753 cm^{-1} .

MS (ESI, +ve) m/z 226 [(M+Na)⁺, 45%], 204 [(M+H)⁺, 100].

HRMS m/z 204.1389 [(M+H)⁺ (calcd for C₁₃H₁₇NO, 204.1388)].

Compound 44



44

A magnetically stirred suspension of compound **7** (100 mg, 0.46 mmol) and 10% palladium on carbon (46 mg) in dry toluene (5 mL) maintained at 50 °C was placed under a hydrogen atmosphere. After 1 h the reaction mixture was cooled to 22 °C then filtered through a pad of diatomaceous earth and the filtrate concentrated under reduced pressure. The residue thus obtained was subjected to flash column chromatography (silica, 1:4 v/v ethyl acetate/40-60 petroleum ether elution) and so affording, after concentration of the appropriate fractions (R_f = 0.4), compound **44**¹⁵ (55.2 mg, 64%) as a clear, yellow oil.

¹H NMR (400 MHz, CDCl₃) δ 7.01 (m, 1H), 6.94 (dd, *J* = 7.5 and 1.6 Hz, 1H), 6.65 (m, 1H), 6.50 (dd, *J* = 7.5 and 1.6 Hz, 1H), 4.17 (broad s, 1H), 3.12 (t, *J* = 3.3 Hz, 1H), 2.24 (broad s, 1H), 2.03–1.90 (complex m, 2H), 1.90–1.82 (complex m, 2H), 1.70–1.59 (complex m, 2H), 1.61–1.44 (complex m, 2H).

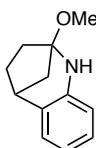
¹³C NMR (100 MHz, CDCl₃) δ 144.9, 128.1, 127.3, 125.7, 117.8, 113.2, 80.5, 40.9, 38.8, 36.7, 33.5, 19.5.

IR (KBr) ν_{\max} 3361, 2930, 2847, 1608, 1493, 1478, 1300, 1267, 1127, 1080, 1063, 979, 910, 744 cm⁻¹.

MS (ESI, +ve) *m/z* 212 [(M+Na)⁺, 100%], 190 [(M+H)⁺, 70].

HRMS *m/z* 190.1236 [M+H]⁺ (calcd for C₁₂H₁₅NO, 190.1232).

Compound 45



45

A magnetically stirred suspension of compound **10** (52.4 mg, 0.26 mmol) and 10% palladium on carbon (26 mg) in dry, degassed methanol (20 mL) maintained at 65 °C was treated with glacial acetic acid (0.2 mL) then placed under a hydrogen atmosphere. After 20 h the reaction mixture was cooled to 22 °C, filtered through a pad of diatomaceous earth and the filtrate concentrated under reduced pressure. The ensuing residue was portioned between diethyl ether (10 mL) and sodium bicarbonate (10 mL of a saturated aqueous solution) then the separated aqueous phase was extracted with diethyl ether (2 x 10 mL) and the combined organic phases washed with brine (1 x 20 mL) before being dried (Na₂SO₄), filtered and concentrated under reduced pressure to give compound **45** (22 mg, 43%) as a white, crystalline solid, m.p. = 77 °C (*R_f* = 0.1 in 1:9 v/v diethyl ether/*n*-hexane).

¹H NMR (400 MHz, CDCl₃) δ 7.00 (m, 1H), 6.90 (m, 1H), 6.64 (m, 1H), 6.58 (m, 1H), 3.83 (broad s, 1H), 3.46 (s, 3H), 3.03 (m, 1H), 2.21–2.05 (complex m, 4H), 1.99–1.89 (complex m, 2H).

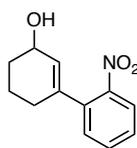
¹³C NMR (100 MHz, CDCl₃) δ 143.9, 131.6, 127.2, 126.6, 118.5, 115.5, 94.3, 52.3, 40.7, 40.0, 35.6, 34.4.

IR (ATR) ν_{\max} 3339, 2941, 2855, 1606, 1493, 1470, 1318, 1298, 1245, 1217, 1199, 1150, 1112, 1070, 1034, 1001, 942, 747 cm⁻¹.

MS (ESI, +ve) *m/z* 190 [(M+H)⁺, 69%], 158 (62), 153 (100), 102 (93).

HRMS *m/z* 190.1233 [M+H]⁺ (calcd for C₁₂H₁₅NO, 190.1232).

Compound 46



46

A magnetically stirred solution of compound **7** (652 mg, 3.0 mmol) and cerium(III) chloride heptahydrate (1.23 g, 3.3 mmol) in dry methanol/dichloromethane (6 mL of a 1:1 v/v mixture) maintained at 0 °C was treated, in portions, with sodium borohydride (125 mg, 3.30 mmol). After 2 h the reaction mixture was concentrated under reduced pressure and the residue dissolved in diethyl ether (10 mL) and the resulting mixture treated hydrochloric acid (10 mL of a 1 M aqueous solution). The separated aqueous phase was extracted with diethyl ether (2 x 10 mL) and the combined organic phases washed with brine (1 x 30 mL) before being dried (Na₂SO₄), filtered, then concentrated under reduced pressure. The residue so obtained was subjected to flash column chromatography (silica, 1:9 v/v diethyl ether/dichloromethane elution) and thus affording, after concentration of the appropriate fractions (*R_f* = 0.3), compound **46** (631 mg, 96%) as a clear, yellow oil.

¹H NMR (400 MHz, CDCl₃) δ 7.88 (dd, *J* = 8.1 and 1.3 Hz, 1H), 7.55 (td, *J* = 7.6 and 1.3 Hz, 1H), 7.40 (td, *J* = 8.1 and 1.4 Hz, 1H), 7.29 (dd, *J* = 7.6 and 1.3 Hz, 1H), 5.67 (m, 1H), 4.30 (m, 1H), 2.31–2.14 (complex m, 2H), 1.99–1.86 (complex m, 2H), 1.80–1.66 (complex m, 3H).

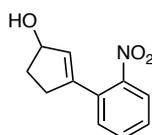
¹³C NMR (100 MHz, CDCl₃) δ 148.3, 139.9, 138.5, 133.0, 130.8, 128.5, 128.1, 124.3, 65.7, 31.4, 29.7, 19.5.

IR (ATR) ν_{\max} 3342, 2937, 2863, 1521, 1346, 1049, 972, 912, 859, 785, 746 cm⁻¹.

MS (ESI, +ve) *m/z* 242 [(M+Na)⁺, 100%].

HRMS *m/z* 242.0794 [M+Na]⁺ (calcd for C₁₂H₁₃NO₃, 242.0793).

Compound 47



47

A magnetically stirred solution of compound **10** (609 mg, 3.0 mmol) and cerium(III) chloride heptahydrate (1.23 g, 3.3 mmol) in methanol/dichloromethane (12 mL of a 1:1 v/v mixture) maintained at 0 °C was treated, in portions, with sodium borohydride (125 mg, 3.30 mmol). After 0.5 h the reaction mixture was concentrated under reduced pressure and the ensuing residue dissolved in diethyl ether (10 mL). The resulting solution was treated with hydrochloric acid (10 mL of a 1 M aqueous solution) and the separated aqueous phase extracted with diethyl ether (2 x 10 mL). The combined organic phases were washed with brine (1 x 30 mL) before being dried (Na₂SO₄), filtered and then concentrated under reduced pressure. The residue thus obtained was subjected to flash column chromatography (silica, 1:9 v/v diethyl ether/dichloromethane elution) and so affording, after concentration of the appropriate fractions (*R_f* = 0.3), compound **47** (414 mg, 67%) as a clear, yellow oil.

¹H NMR (400 MHz, CDCl₃) δ 7.80 (dd, *J* = 8.1 and 1.3 Hz, 1H), 7.51 (td, *J* = 7.5 and 1.3 Hz, 1H), 7.41–7.30 (complex m, 2H), 5.82 (q, *J* = 2.0 Hz, 1H), 4.94 (broad s, 1H), 2.71 (m, 1H), 2.57 (s, 1H), 2.54–2.46 (complex m, 1H), 2.45–2.36 (complex m, 1H), 1.86 (m, 1H).

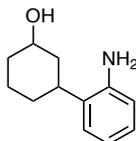
¹³C NMR (100 MHz, CDCl₃) δ 148.4, 144.1, 133.0, 132.7, 132.1, 130.6, 128.4, 124.0, 77.6, 34.3, 34.0.

IR (ATR) ν_{\max} 3338, 2937, 2854, 1520, 1345, 1274, 1239, 1048, 966, 854, 784, 744 cm⁻¹.

MS (ESI, +ve) *m/z* 228 [(M+Na)⁺, 100%].

HRMS *m/z* 228.0638 [M+Na]⁺ (calcd for C₁₁H₁₁NO₃, 228.0637).

Compound 48



48

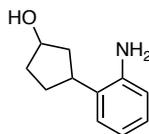
A magnetically stirred mixture of compound **46** (798 mg, 3.64 mmol) and 10% palladium on carbon (80 mg) in dry methanol (8 mL) maintained at 22 °C was placed under a hydrogen atmosphere. After 2.5 h the reaction mixture was filtered through a pad of diatomaceous earth and the filtrate concentrated under reduced pressure. The residue so obtained was subjected to flash column chromatography (silica, 2.5:47.5:50 v/v/v methanol/ethyl acetate/40-60 petroleum ether elution) and thus affording, after concentration of the appropriate fractions (*R_f* = 0.6 in 5:95 v/v methanol/ethyl acetate elution), compound **48** (524 mg, 75%) as a clear, light-brown oil. The product decomposes rapidly at ambient temperatures and so it was used immediately in the next step of the reaction sequence.

IR (ATR) ν_{\max} 3349, 2927, 2855, 1621, 1496, 1453, 1293, 1251, 1051, 976, 959, 748 cm⁻¹.

MS (ESI, +ve) *m/z* 405 [(2M+Na)⁺, 48%], 214 [(M+Na)⁺, 100], 192 [(M+H)⁺, 34].

HRMS *m/z* 192.1381 [M+H]⁺ (calcd for C₁₂H₁₇NO, 192.1383).

Compound 49



49

A magnetically stirred mixture of compound **47** (235 mg, 1.14 mmol) and 10% palladium on carbon (24 mg) in dry methanol (5 mL) maintained at 22 °C was placed under a hydrogen atmosphere. After 2 h the reaction mixture was filtered through a pad of diatomaceous earth and the filtrate concentrated under reduced pressure. The residue so obtained was subjected to flash column chromatography (silica, 1:4 to 1:1 v/v diethyl ether/dichloromethane elution) and thus affording, after concentration of the appropriate fractions (*R_f* = 0.2), compound **49** (102 mg, 51%) as a clear, light-brown oil.

¹H NMR (400 MHz, CDCl₃) δ 7.19 (dd, *J* = 7.6 and 1.5 Hz, 1H), 7.05 (m, 1H), 6.76 (m, 1H), 6.67 (dd, *J* = 7.8 and 1.2 Hz, 1H), 4.46 (m, 1H), 3.33 (broad s, 2H), 3.07 (m, 1H), 2.45–2.31

(complex m, 1H), 2.12–1.94 (complex m, 2H), 1.93–1.80 (complex m, 2H), 1.80–1.73 (complex m, 1H) (resonance due to one proton not observed).

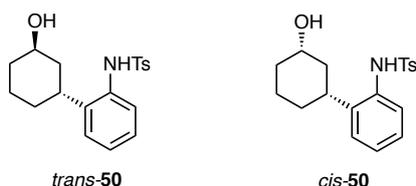
^{13}C NMR (100 MHz, CDCl_3) δ 144.2, 129.0, 127.8, 127.1, 118.7, 116.2, 73.8, 40.9, 40.0, 36.0, 29.5.

IR (ATR) ν_{max} 3350, 3244, 2951, 2865, 1620, 1495, 1454, 1295, 1078, 983, 748 cm^{-1} .

MS (ESI, +ve) m/z 200 [(M+Na) $^+$, 50%], 178 [(M+H) $^+$, 100], 160 (100).

HRMS m/z 178.1232 [(M+H) $^+$] (calcd for $\text{C}_{11}\text{H}_{15}\text{NO}$, 178.1232).

cis- and *trans*- Forms of Compound 50



A magnetically stirred solution of compound **48** (524 mg, 2.74 mmol) and pyridine (665 μL , 8.22 mmol) in dry dichloromethane (5.5 mL) maintained at 0 $^{\circ}\text{C}$ was treated, in portions, with *p*-toluenesulfonyl chloride (575 mg, 3.01 mmol) then warmed to 22 $^{\circ}\text{C}$. After 16 h the reaction mixture was treated with heptane (20 mL) then concentrated under reduced pressure. This dilution/concentration process was repeated twice more in order to remove pyridine. The residue thus obtained was subjected to flash column chromatography (silica, 2:3 v/v ethyl acetate/40-60 petroleum ether elution) and so affording, two fractions, A and B.

Concentration of fraction A (R_f = 0.2) gave compound *trans*-**50** (304 mg, 32%) as a white crystalline solid, m.p. =145 $^{\circ}\text{C}$.

^1H NMR (400 MHz, CDCl_3) δ 7.71 (s, 1H), 7.65 (d, J = 8.3 Hz, 2H), 7.36 (m, 1H), 7.24 (d, J = 8.3 Hz, 2H), 7.20–7.11 (complex m, 3H), 4.20 (t, J = 2.9 Hz, 1H), 3.01 (s, 1H), 2.91 (m, 1H), 2.37 (s, 3H), 1.84 (m, 1H), 1.74 (m, 1H), 1.68–1.55 (complex m, 1H), 1.43 (m, 3H), 1.32–1.20 (complex m, 1H), 1.01 (d, J = 12.5 Hz, 1H).

^{13}C NMR (100 MHz, CDCl_3) δ 143.7, 141.9, 136.9, 133.1, 129.7, 127.4, 127.3, 127.2, 126.9, 126.6, 66.7, 40.4, 32.8, 32.0, 31.1, 21.6, 20.4.

IR (ATR) ν_{max} 3521, 3345, 3284, 2928, 1491, 1406, 1327, 1163, 1091, 976, 808, 756, 664 cm^{-1} .

MS (ESI, +ve) m/z 368 [(M+Na) $^+$, 100%].

HRMS m/z 368.1292 [(M+Na) $^+$] (calcd for $\text{C}_{19}\text{H}_{23}\text{NO}_3\text{S}$, 368.1291).

Concentration of fraction B (R_f = 0.1) gave compound *cis*-**50** (469 mg, 50%) as a white powder, m.p. =152 $^{\circ}\text{C}$.

^1H NMR (400 MHz, CDCl_3) δ 7.57 (d, J = 8.3 Hz, 2H), 7.25–7.22 (complex m, 3H), 7.21–7.11 (complex m, 3H), 6.38 (s, 1H), 3.51 (m, 1H), 2.48 (m, 1H), 2.40 (s, 3H), 1.99 (d, J = 11.2 Hz, 1H), 1.75 (m, 1H), 1.54 (m, 2H), 1.33–1.09 (complex m, 4H) (resonance due to OH group proton not observed).

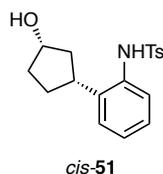
^{13}C NMR (100 MHz, CDCl_3) δ 143.9, 141.7, 136.7, 132.7, 129.7, 127.5, 127.4, 127.3, 127.0, 126.7, 70.7, 42.8, 36.1, 35.1, 32.5, 24.4, 21.6.

IR (ATR) ν_{max} 3249, 2925, 1492, 1401, 1330, 1161, 1092, 915, 809, 756, 706, 671 cm^{-1} .

MS (ESI, +ve) m/z 368 [(M+Na) $^+$, 100%].

HRMS m/z 368.1288 [(M+Na) $^+$] (calcd for $\text{C}_{19}\text{H}_{23}\text{NO}_3\text{S}$, 368.1291).

Compound *cis*-51



A magnetically stirred solution of compound **49** (165 mg, 0.93 mmol) and pyridine (226 μ L, 2.79 mmol) in dry dichloromethane (5 mL) maintained at 0 °C was treated, in portions, with *p*-toluenesulfonyl chloride (186 mg, 0.98 mmol) then warmed to 22 °C. After 19 h the reaction mixture was treated with heptane (20 mL) then concentrated under reduced pressure. This dilution/concentration process was repeated twice more in order to remove pyridine. The residue so obtained was subjected to flash column chromatography (silica, 1:9 v/v diethyl ether/dichloromethane elution) and thus affording, after concentration of the appropriate fractions ($R_f = 0.2$), compound *cis*-**51** (262 mg, 85%) as a clear, colorless oil

^1H NMR (400 MHz, CDCl_3) δ 8.49 (broad s, 1H), 7.78–7.66 (m, 2H), 7.37 (dd, $J = 8.1$ and 1.3 Hz, 1H), 7.24–7.17 (complex m, 3H), 7.09 (m, 1H), 7.02 (m, 1H), 4.46 (m, 1H), 3.15 (m, 1H), 2.65 (broad s, 1H), 2.37 (s, 3H), 2.17 (m, 1H), 1.91–1.76 (complex m, 3H), 1.76–1.65 (complex m, 1H), 1.57 (dd, $J = 14.6$ and 7.0 Hz, 1H).

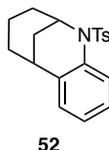
^{13}C NMR (100 MHz, CDCl_3) δ 143.7, 137.2, 136.8, 134.5, 130.0, 129.6, 127.4, 127.1, 125.2, 122.6, 74.0, 41.6, 40.7, 36.4, 30.9, 21.6.

IR (ATR) ν_{max} 3503, 3270, 2955, 2870, 1492, 1326, 1154, 1090, 814, 756, 661 cm^{-1} .

MS (ESI, +ve) m/z 354 [(M+Na) $^+$, 100%].

HRMS m/z 354.1141 [(M+Na) $^+$ (calcd for $\text{C}_{18}\text{H}_{21}\text{NO}_3\text{S}$, 354.1140)].

Compound **52**



A magnetically stirred solution of compound *trans*-**50** (81.4 mg, 0.24 mmol) and triphenylphosphine (148 mg, 0.57 mmol) in dry tetrahydrofuran (5 mL) maintained at 0 °C was treated, dropwise, with DEAD (92 μ L, 0.59 mmol). After 16 h the reaction mixture was concentrated under reduced pressure and the residue so obtained subjected to flash column chromatography (silica, 1:9 v/v ethyl acetate/40-60 petroleum ether elution) and thus affording, after concentration of the appropriate fractions ($R_f = 0.3$), compound **52** (69 mg, 89%) as a clear, colorless oil.

^1H NMR (400 MHz, CDCl_3) δ 7.87 (m, 1H), 7.62 (m, 2H), 7.21 (d, $J = 8.1$ Hz, 2H), 7.09 (m, 1H), 6.99 (m, 1H), 6.94 (m, 1H), 4.80 (m, 1H), 2.93 (t, $J = 3.4$ Hz, 1H), 2.36 (s, 3H), 2.18 (m, 1H), 1.78 (dt, $J = 12.9$ and 2.6 Hz, 1H), 1.74–1.62 (complex m, 3H), 1.54–1.47 (complex m, 1H), 1.47–1.40 (complex m, 1H), 1.31–1.20 (complex m, 1H).

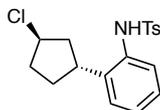
^{13}C NMR (100 MHz, CDCl_3) δ 143.6, 138.5, 137.2, 130.7, 129.8, 129.0, 127.1, 126.7, 122.9, 119.5, 52.3, 33.9, 33.7(2), 33.6(9), 28.4, 21.6, 17.3.

IR (ATR) ν_{max} 2931, 2853, 1489, 1453, 1341, 1158, 1089, 871, 814, 674 cm^{-1} .

MS (ESI, +ve) m/z 677 [(2M+Na) $^+$, 78%], 350 [(M+Na) $^+$, 100], 328 [(M+H) $^+$, 5].

HRMS m/z 328.1361 $[M+H]^+$ (calcd for $C_{19}H_{21}NO_2S$, 328.1366).

***trans*-N-(2-(3-Chlorocyclopentyl)phenyl)-4-methylbenzenesulfonamide**



A magnetically stirred solution of compound *cis*-**51** (61 mg, 0.18 mmol) and triphenylphosphine (97 mg, 0.37 mmol) in dry dichloromethane (2 mL) maintained at 0 °C was treated, dropwise, with carbon tetrachloride (107 μ L, 1.10 mmol) then warmed to 22 °C. After 15 h the reaction mixture was concentrated under reduced pressure and the residue so obtained subjected to flash column chromatography (silica, dichloromethane elution). After concentration of the appropriate fractions ($R_f = 0.4$), the title halide (55.7 mg, 87%) was obtained as a clear, colorless oil.

1H NMR (400 MHz, $CDCl_3$) δ 7.61 (d, $J = 8.2$ Hz, 2H), 7.34 (dd, $J = 7.6$ and 1.6 Hz, 1H), 7.23 (d, $J = 8.2$ Hz, 2H), 7.20–7.10 (complex m, 3H), 6.73 (s, 1H), 4.49 (m, 1H), 3.38 (m, 1H), 2.39 (s, 3H), 2.28 (m, 1H), 2.07–1.95 (complex m, 2H), 1.87 (dd, $J = 9.0$ and 4.2 Hz, 2H), 1.51–1.37 (complex m, 1H).

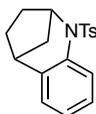
^{13}C NMR (100 MHz, $CDCl_3$) δ 143.9, 139.9, 136.6, 133.7, 129.8, 127.5, 127.4, 127.0, 126.9, 126.7, 61.4, 45.0, 37.2, 36.4, 32.3, 21.6.

IR (ATR) ν_{max} 3267, 2972, 1492, 1399, 1328, 1156, 1091, 904, 813, 757, 732, 662 cm^{-1} .

MS (ESI, +ve) m/z 374 and 372 $[(M+Na)^+]$, 38 and 100%.

HRMS m/z 350.0962 $[M+H]^+$ (calcd for $C_{18}H_{20}^{35}ClNO_2S$, 350.0976).

Compound 53



53

A magnetically stirred solution of the above-mentioned *trans*-N-(2-(3-chlorocyclopentyl)-phenyl)-4-methylbenzenesulfonamide (55.7 mg, 0.16 mmol) in dry methanol (16 mL) maintained at 55 °C was treated with potassium carbonate (110 mg, 0.80 mmol). After 18 h the reaction mixture was cooled to 22 °C then concentrated under reduced pressure. The residue so obtained was subjected to flash column chromatography (silica, dichloromethane elution) and thus affording, after concentration of the appropriate fractions ($R_f = 0.6$), compound **53** (49.6 mg, 99%) as a white, crystalline solid, m.p. =111 °C.

1H NMR (400 MHz, $CDCl_3$) δ 7.85 (m, 1H), 7.65 (d, $J = 8.0$ Hz, 2H), 7.21 (d, $J = 8.0$ Hz, 2H), 7.11 (m, 1H), 6.94 (m, 2H), 5.08 (m, 1H), 2.99 (s, 1H), 2.37 (s, 3H), 2.17–2.04 (complex m, 1H), 1.99–1.89 (complex m, 1H), 1.87–1.74 (complex m, 2H), 1.48 (m, 2H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 143.7, 137.1, 135.2, 134.8, 129.7, 127.9, 127.2, 127.1, 123.7, 121.1, 58.5, 41.4 35.9, 31.9, 31.4, 21.6.

IR (ATR) ν_{\max} 2947, 2866, 1600, 1483, 1455, 1342, 1226, 1165, 1155, 1090, 812, 757, 680 cm^{-1} .

MS (ESI, +ve) m/z 336 $[(M+Na)^+]$, 100%].

HRMS m/z 314.1196 $[M+H]^+$ (calcd for $\text{C}_{18}\text{H}_{19}\text{NO}_2\text{S}$, 314.1209).

X-ray Crystallographic Studies

Crystallographic Data

Crystallographic Data for Compound 7

$C_{12}H_{11}NO_3$, $M = 217.22$, $T = 150$ K, monoclinic, space group $P2_1/c$, $Z = 4$, $a = 9.3274(2)$, $b = 14.6679(2)$, $c = 7.9674(1)$ Å; $\beta = 107.026(2)^\circ$; $V = 1042.27(3)$ Å³, $D_x = 1.384$ g cm⁻³, 2088 unique data ($2\theta_{\max} = 147.2^\circ$), $R = 0.042$ [for 1953 reflections with $I > 2.0\sigma(I)$]; $R_w = 0.111$ (all data), $S = 1.02$.

Crystallographic Data for Compound 19

$C_{12}H_{12}N_2O_3$, $M = 232.24$, $T = 150$ K, monoclinic, space group $C2/c$, $Z = 8$, $a = 7.87923(6)$, $b = 19.95864(19)$, $c = 13.93593(11)$ Å; $\beta = 92.3804(7)^\circ$; $V = 2189.66(3)$ Å³, $D_x = 1.409$ g cm⁻³, 2224 unique data ($2\theta_{\max} = 147.2^\circ$), $R = 0.035$ [for 2127 reflections with $I > 2.0\sigma(I)$]; $R_w = 0.035$ (all data), $S = 1.01$.

Crystallographic Data for Compound 39

$C_{18}H_{22}N_4O_5$, $M = 374.40$, $T = 150$ K, triclinic, space group $P\bar{1}$, $Z = 2$, $a = 7.0058(2)$, $b = 9.5456(3)$, $c = 13.6950(46)$ Å; $\alpha = 79.998(3)^\circ$, $\beta = 83.227(3)^\circ$, $\gamma = 85.094(2)^\circ$; $V = 893.65(5)$ Å³, $D_x = 1.391$ g cm⁻³, 3597 unique data ($2\theta_{\max} = 147.8^\circ$), $R = 0.035$ [for 3346 reflections with $I > 2.0\sigma(I)$]; $R_w = 0.102$ (all data), $S = 0.97$.

Crystallographic Data for Compound 43

$C_{13}H_{17}NO$, $M = 203.28$, $T = 150$ K, monoclinic, space group $P2_1/c$, $Z = 4$, $a = 8.5291(3)$, $b = 18.2560(5)$, $c = 7.6050(3)$ Å; $\beta = 112.547(4)^\circ$; $V = 1093.63(6)$ Å³, $D_x = 1.235$ g cm⁻³, 2919 unique data ($2\theta_{\max} = 60^\circ$), $R = 0.044$ [for 2299 reflections with $I > 2.0\sigma(I)$]; $R_w = 0.117$ (all data), $S = 1.06$.

Crystallographic Data for Compound 45

$C_{12}H_{25}NO$, $M = 189.25$, $T = 150$ K, orthorhombic, space group $Pccn$, $Z = 8$, $a = 19.6584(2)$, $b = 13.0353(1)$, $c = 7.9633(1)$ Å; $V = 2040.62(4)$ Å³, $D_x = 1.232$ g cm⁻³, 2048 unique data ($2\theta_{\max} = 147.4^\circ$), $R = 0.038$ [for 1926 reflections with $I > 2.0\sigma(I)$]; $R_w = 0.105$ (all data), $S = 1.06$.

Crystallographic Data for Compound trans-50

$C_{19}H_{23}NO_3S$, $M = 345.44$, $T = 150$ K, triclinic, space group $P\bar{1}$, $Z = 4$, $a = 9.4185(4)$, $b = 12.9752(7)$, $c = 16.0422(8)$ Å; $\alpha = 70.958(5)^\circ$, $\beta = 77.623(4)^\circ$, $\gamma = 78.202(4)^\circ$; $V = 1790.80(16)$ Å³, $D_x = 1.281$ g cm⁻³, 7108 unique data ($2\theta_{\max} = 147.6^\circ$), $R = 0.048$ [for 6495 reflections with $I > 2.0\sigma(I)$]; $R_w = 0.048$ (all data), $S = 1.05$.

Structure Determinations

The image for compound **43** was measured on a diffractometer (Mo $K\alpha$, graphite monochromator, $\lambda = 0.71073$ Å) fitted with an area detector and the data extracted using the DENZO/Scalepack package.¹⁶ Images for compounds **7**, **19**, **39**, **45**, and *trans*-**50** were measured on a diffractometer (Cu $K\alpha$, mirror monochromator, $\lambda = 1.54184$ Å) fitted with an area detector and the data extracted using the CrysAlis package.¹⁷ The structure solutions for all six compounds were either solved by direct methods (SIR92) and refined using the CRYSTALS program package, or solved with ShelXT¹⁸ and refined using ShelXL¹⁹ in OLEX2.²⁰ Atomic coordinates, bond lengths and angles, and displacement parameters have been deposited at the Cambridge Crystallographic Data Centre (CCDC nos. 1832167, 1832168, 1832169, 1832170, 1832171 and 1832172). These data can be obtained free-of-charge via www.ccdc.cam.ac.uk/data_request/cif, by emailing data_request@ccdc.cam.ac.uk, or by contacting The Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge CB2 1EZ, UK; fax: +44 1223 336033.

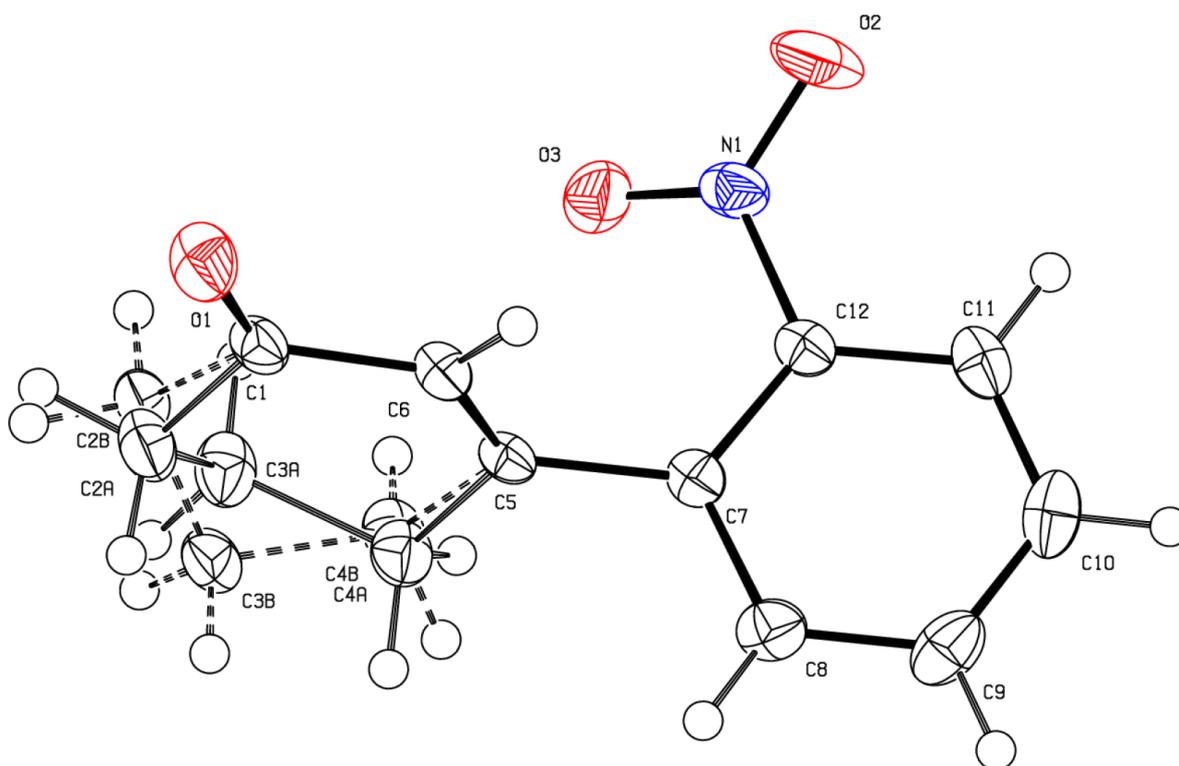


Figure S1: Structure of compound **7** (CCDC 1832167). Anisotropic displacement ellipsoids show 30% probability levels. Hydrogen atoms are drawn as circles with small radii.

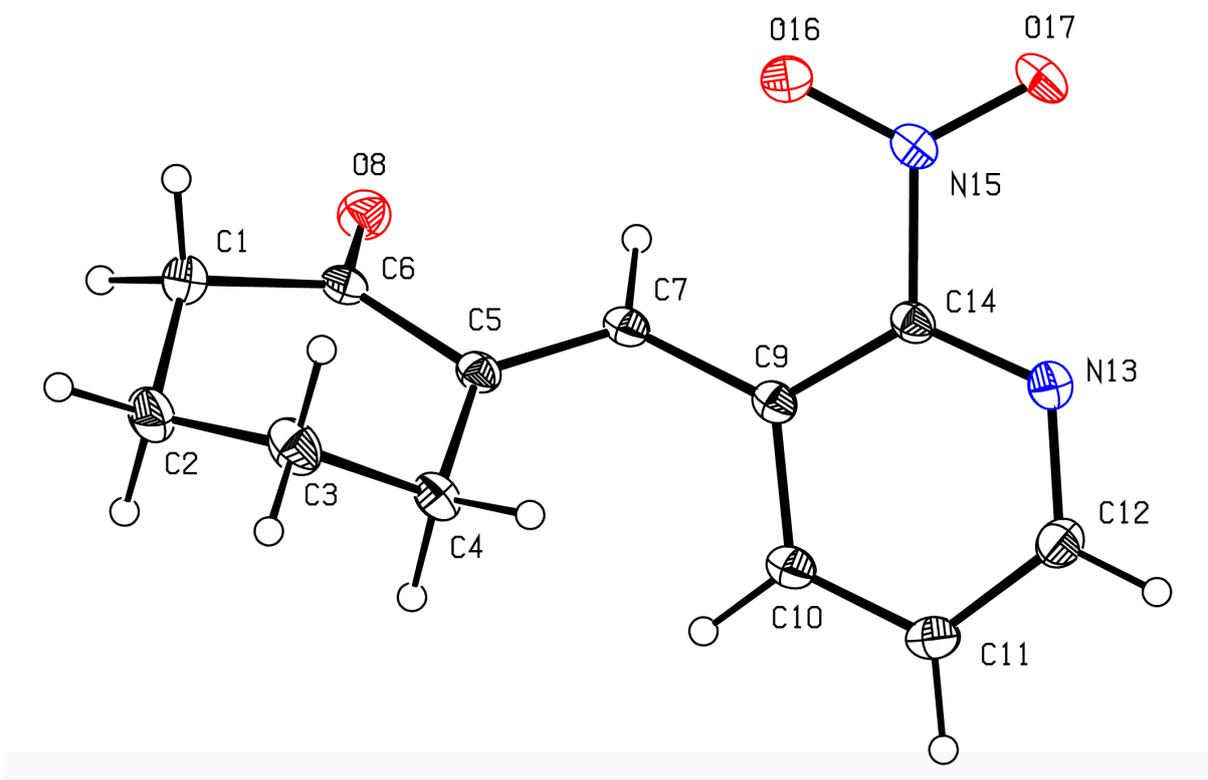


Figure S2: Structure of compound **19** (CCDC 1832168). Anisotropic displacement ellipsoids show 30% probability levels. Hydrogen atoms are drawn as circles with small radii.

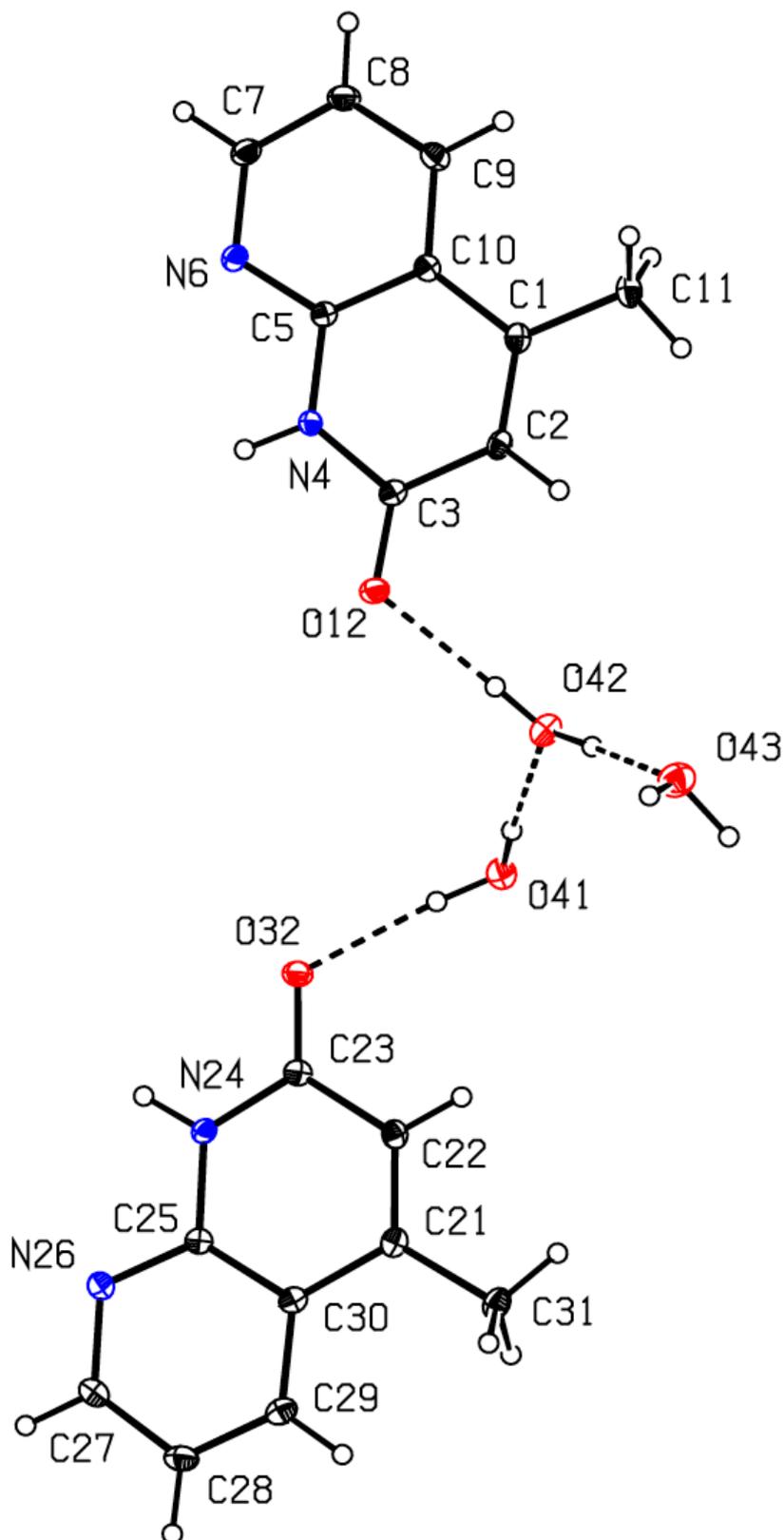


Figure S3: Structure of compound **39** (CCDC 1832169) and associated water molecules. Anisotropic displacement ellipsoids show 30% probability levels. Hydrogen atoms are drawn as circles with small radii.

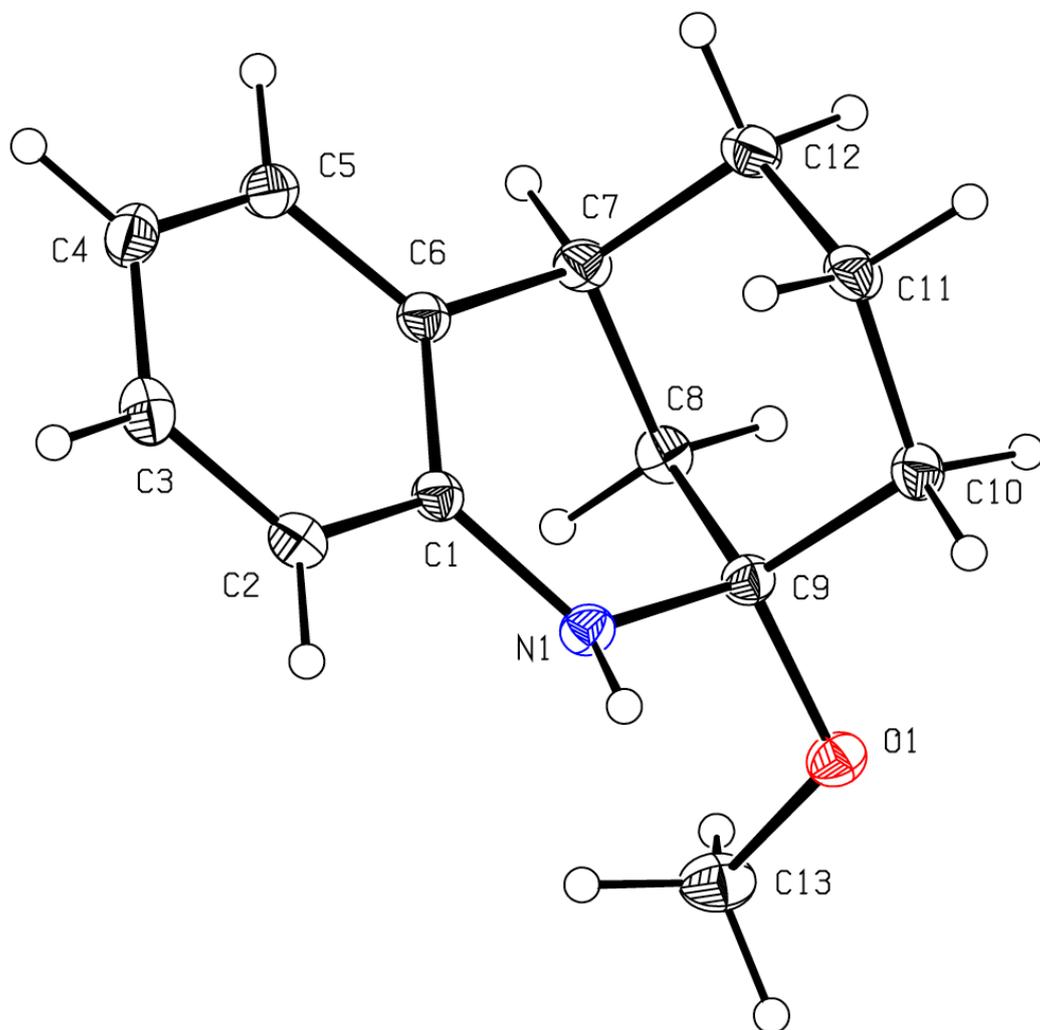


Figure S4: Structure of compound **43** (CCDC 1832170). Anisotropic displacement ellipsoids show 30% probability levels. Hydrogen atoms are drawn as circles with small radii.

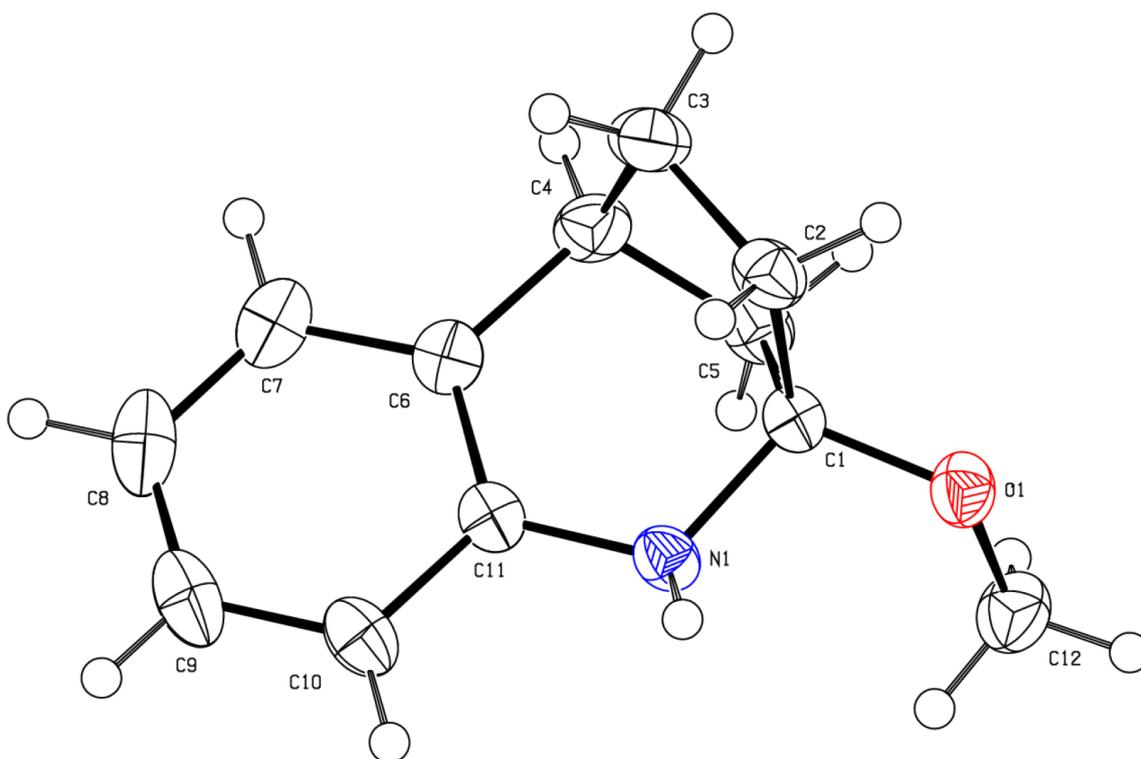


Figure S5: Structure of compound **45** (CCDC 1832171). Anisotropic displacement ellipsoids show 30% probability levels. Hydrogen atoms are drawn as circles with small radii.

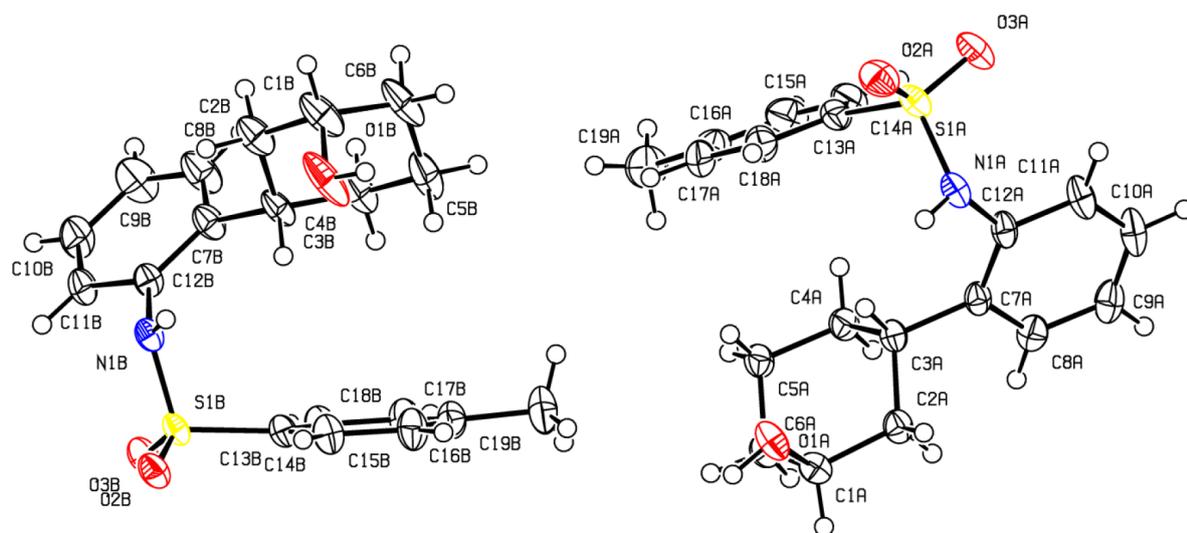
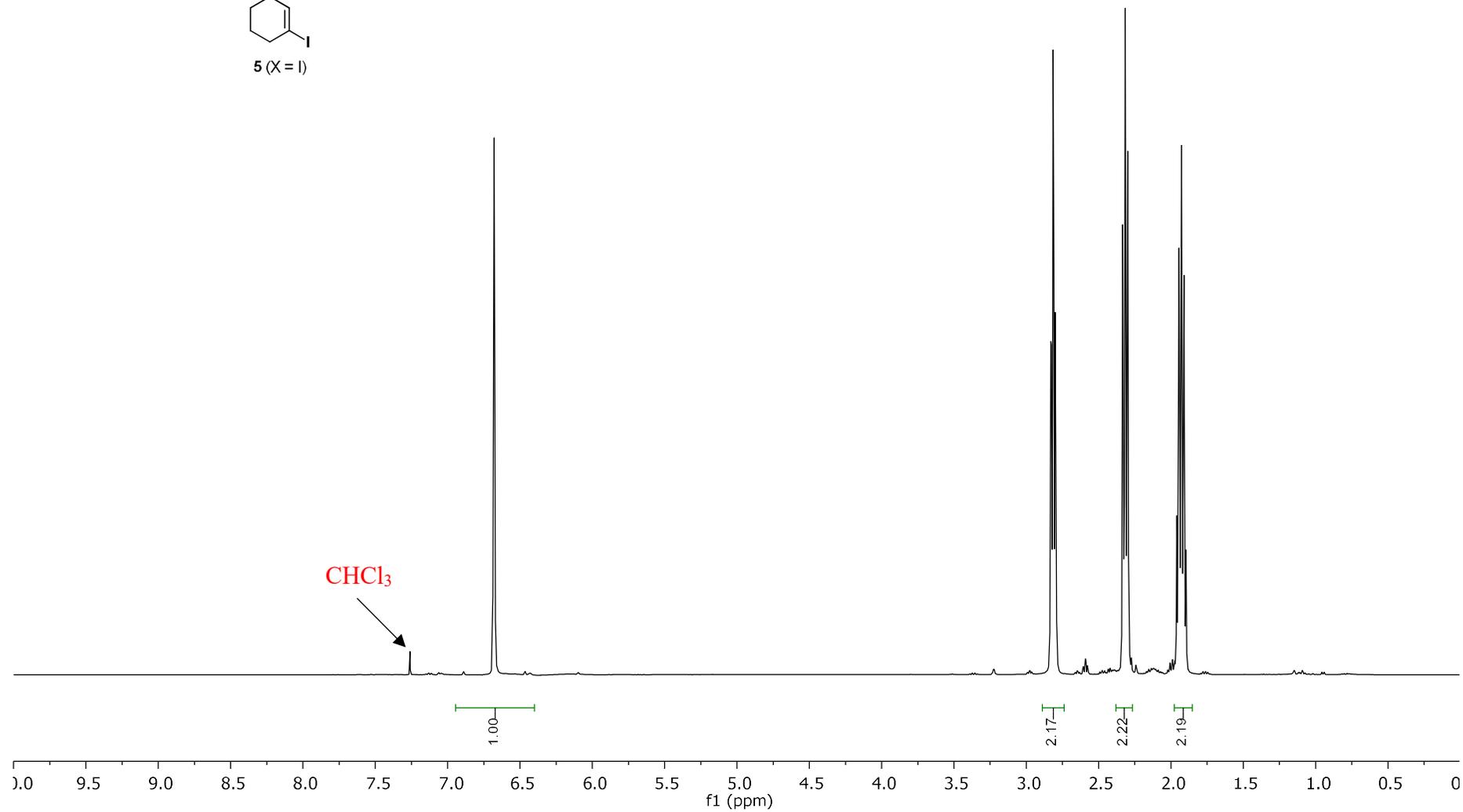
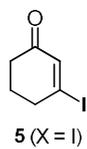


Figure S6: Structure of compound *trans*-**50** (CCDC 1832171). Anisotropic displacement ellipsoids show 30% probability levels. Hydrogen atoms are drawn as circles with small radii.

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400 MHz ^1H NMR Spectrum of Compound **5** (X = I)
(recorded in CDCl_3)



— 194.9

— 140.4

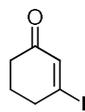
— 127.0

— 40.4

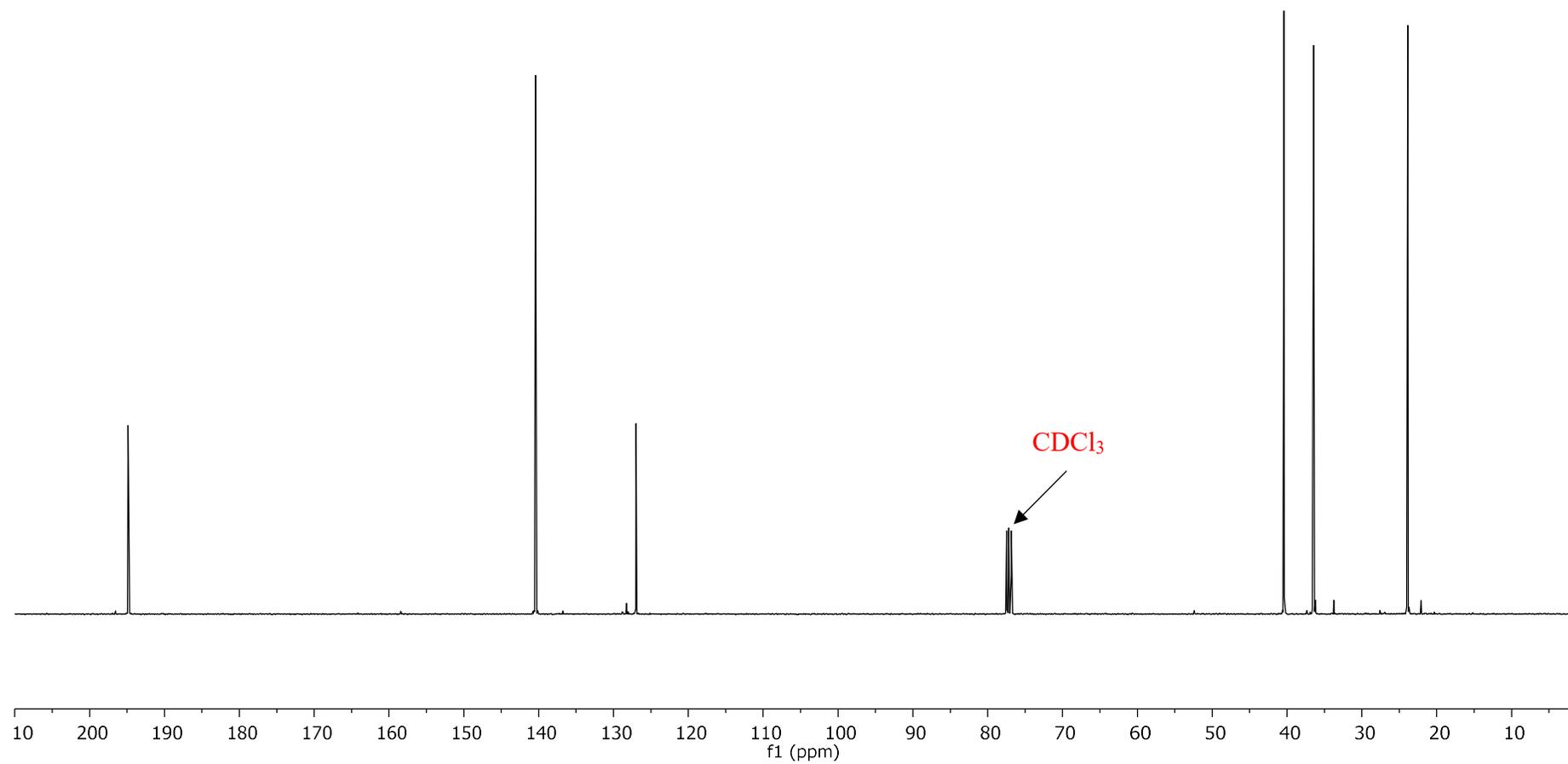
— 36.4

— 23.9

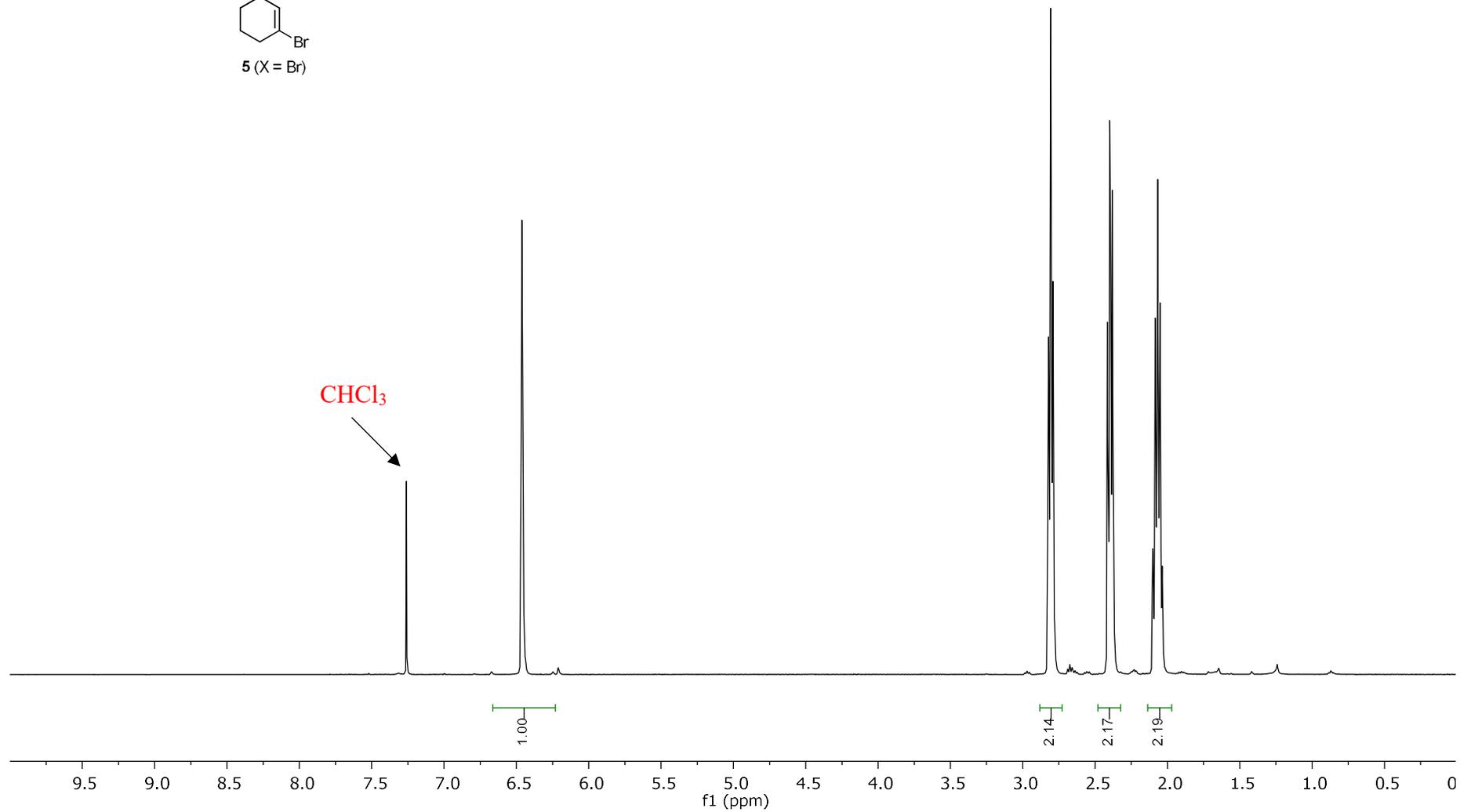
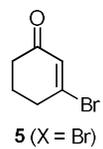
100 MHz ^{13}C NMR Spectrum of Compound **5** (X = I)
(recorded in CDCl_3)

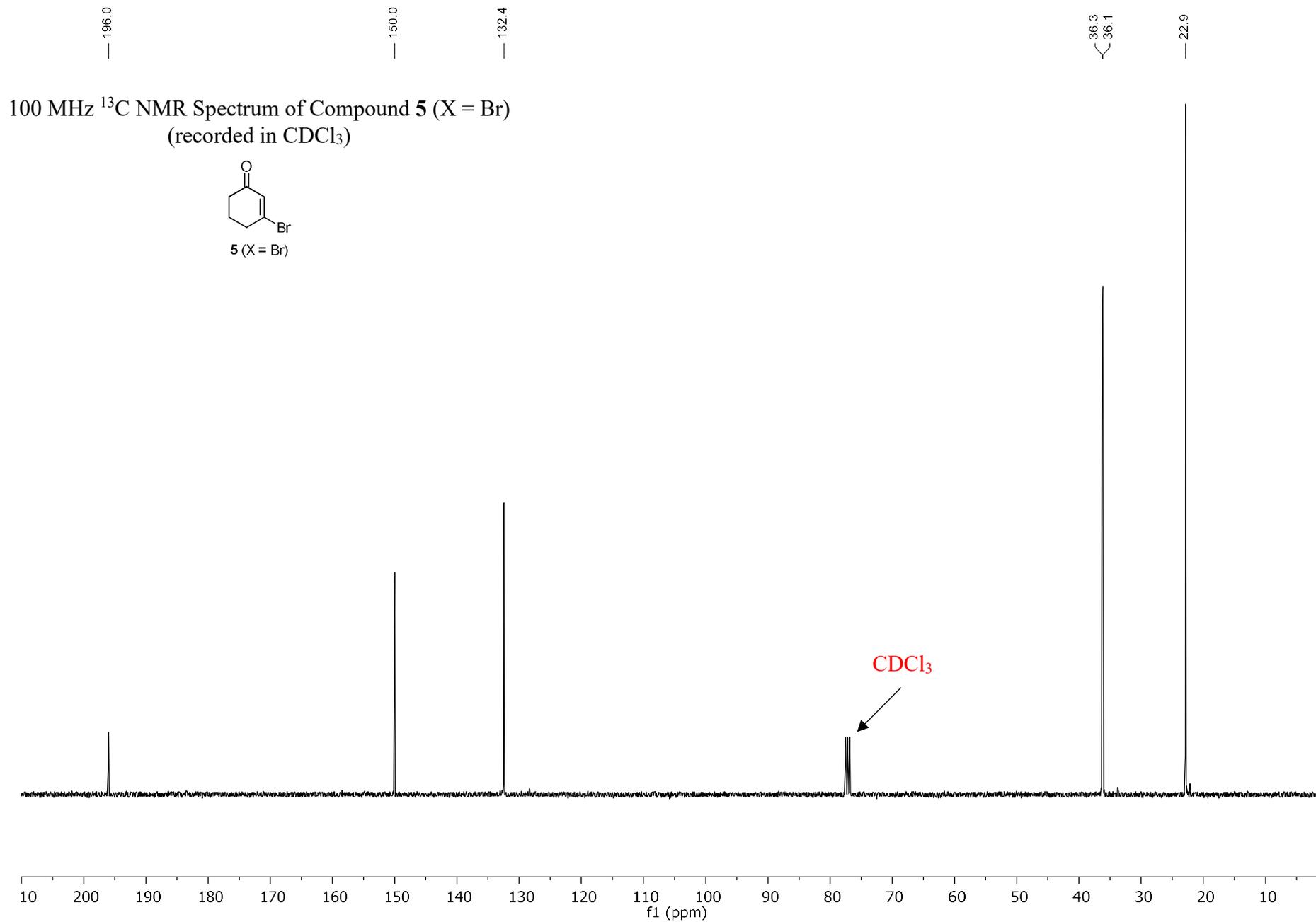


5 (X = I)

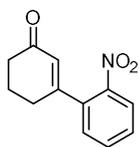


400 MHz ^1H NMR Spectrum of Compound **5** (X = Br)
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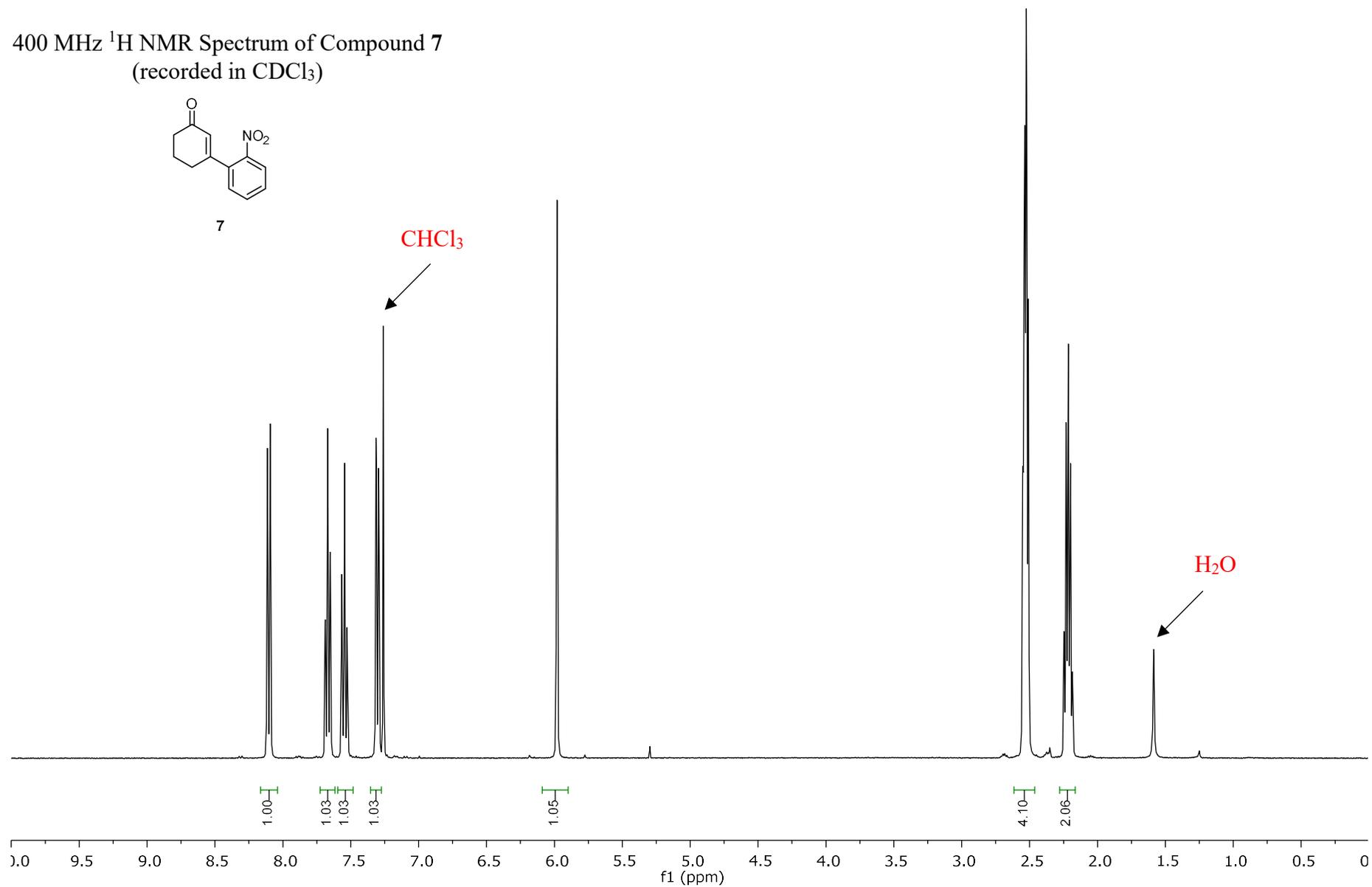


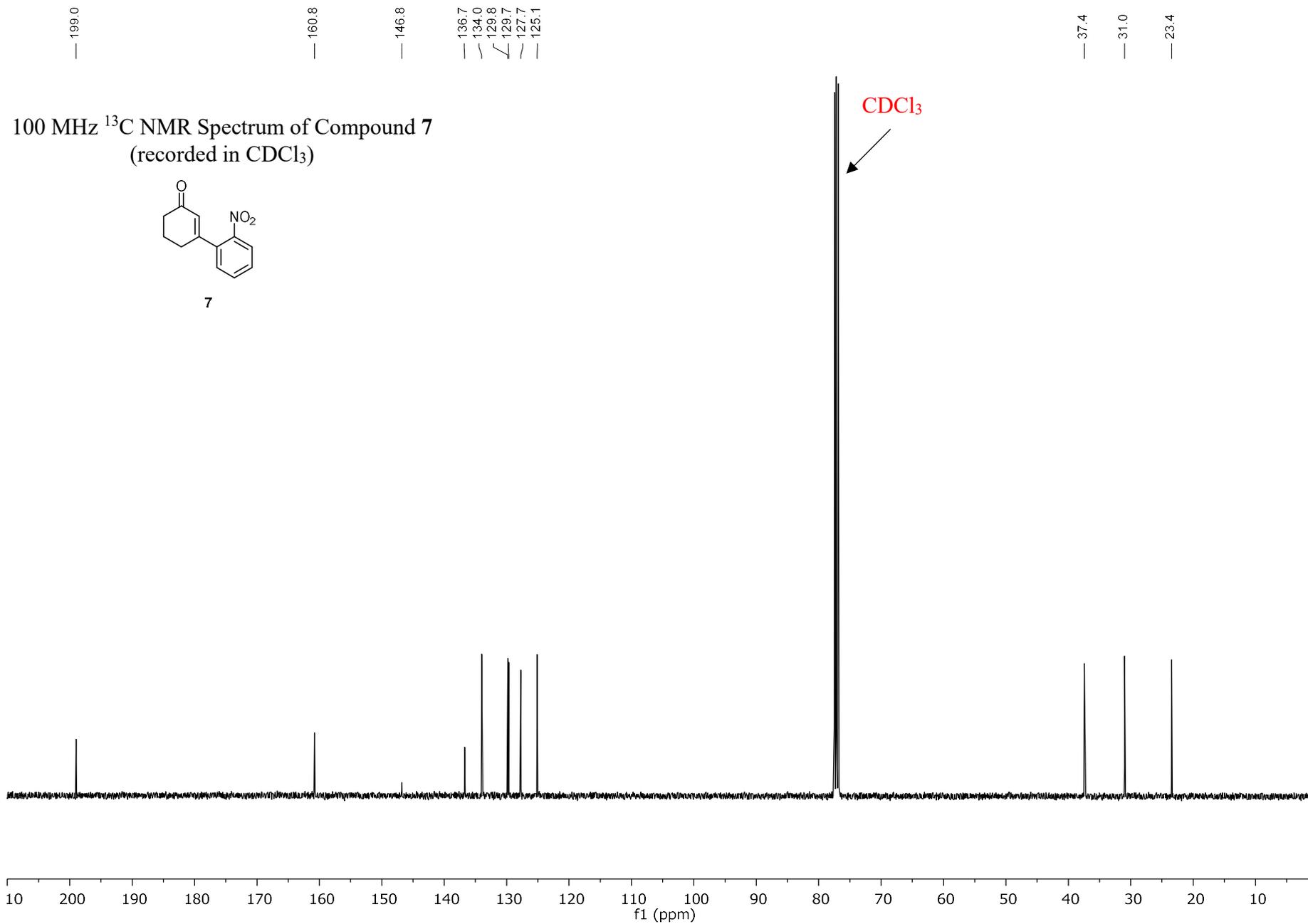


400 MHz ^1H NMR Spectrum of Compound 7
(recorded in CDCl_3)

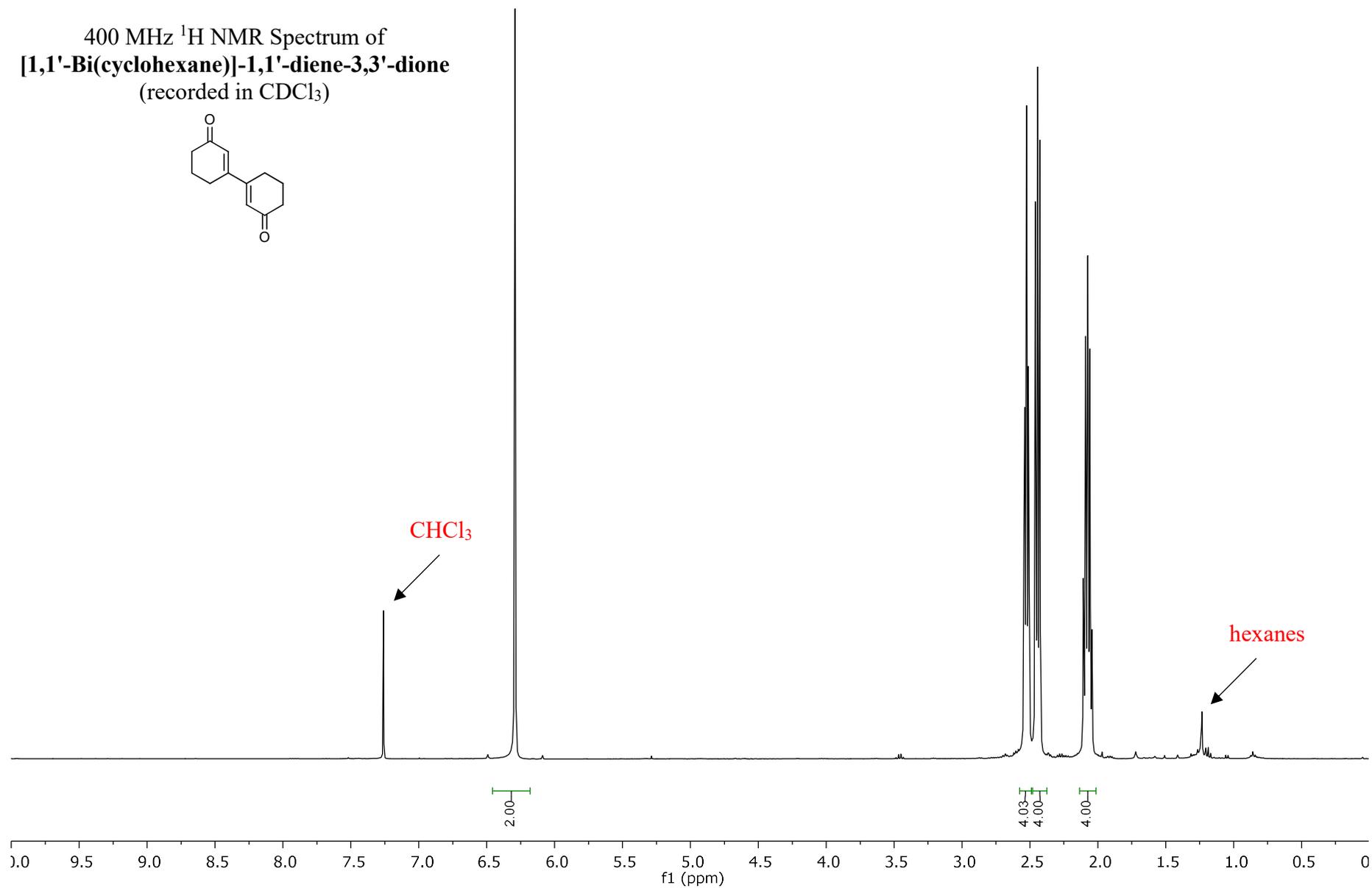
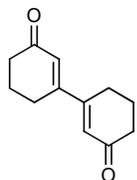


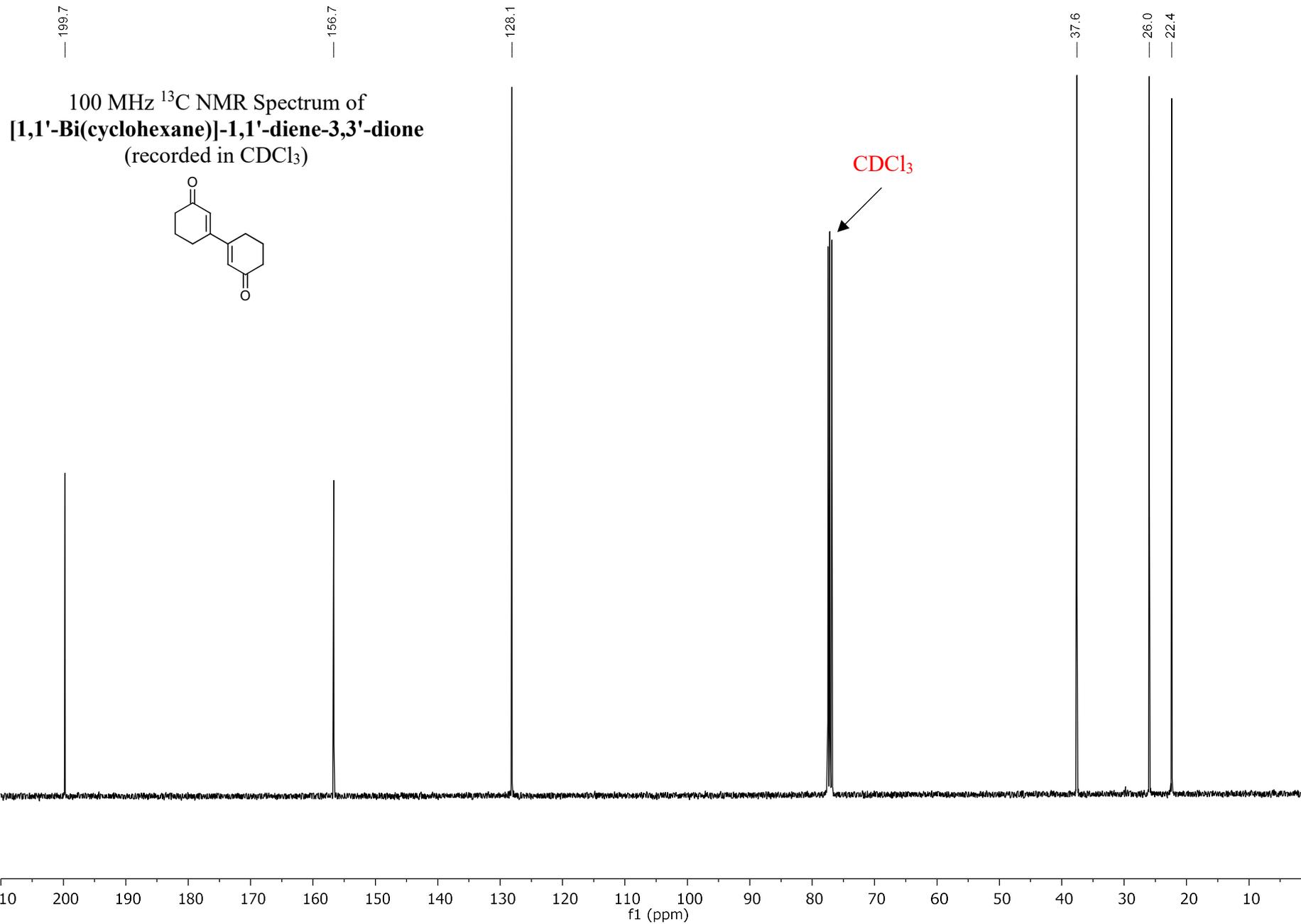
7



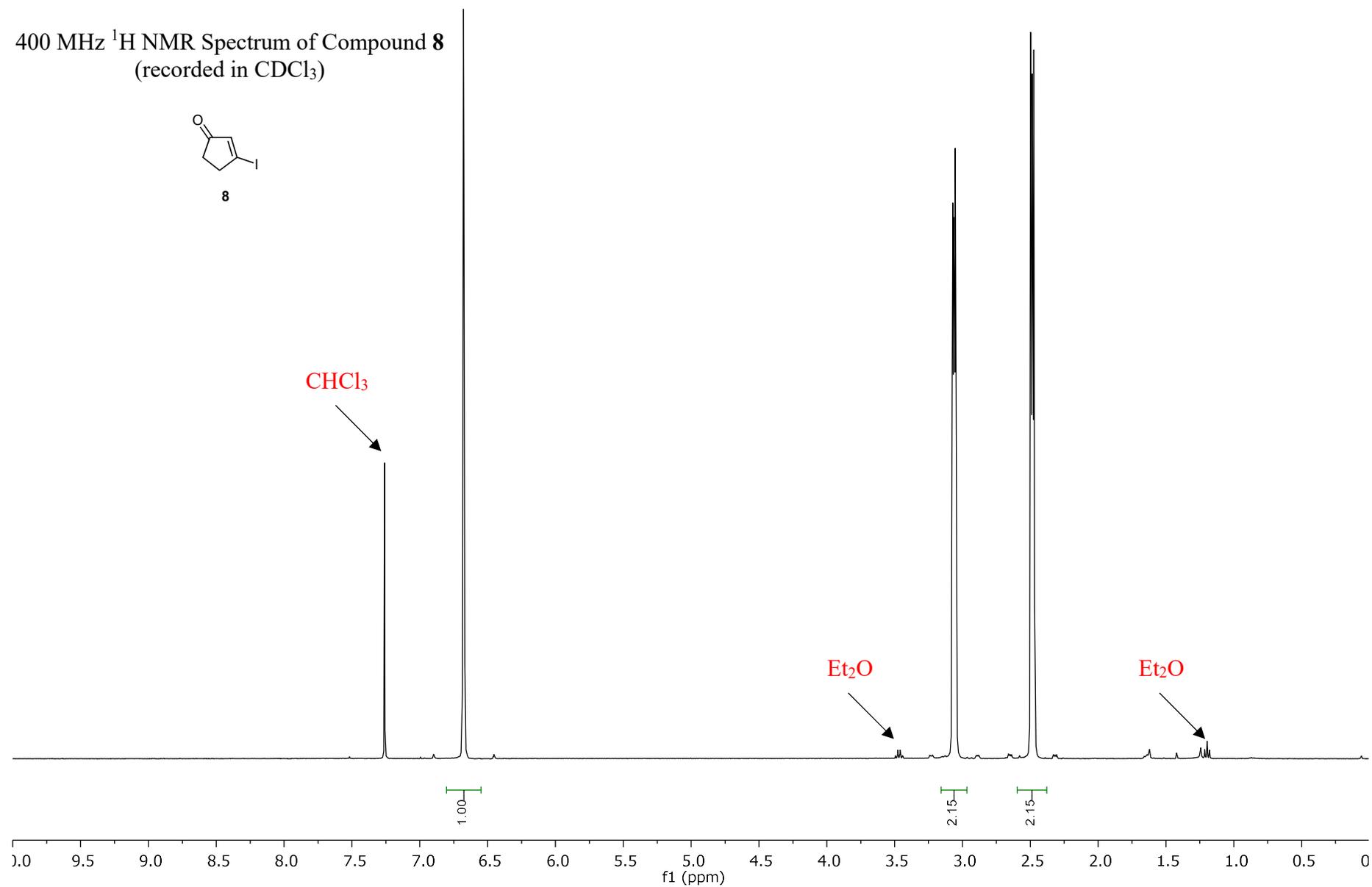
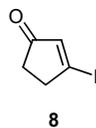


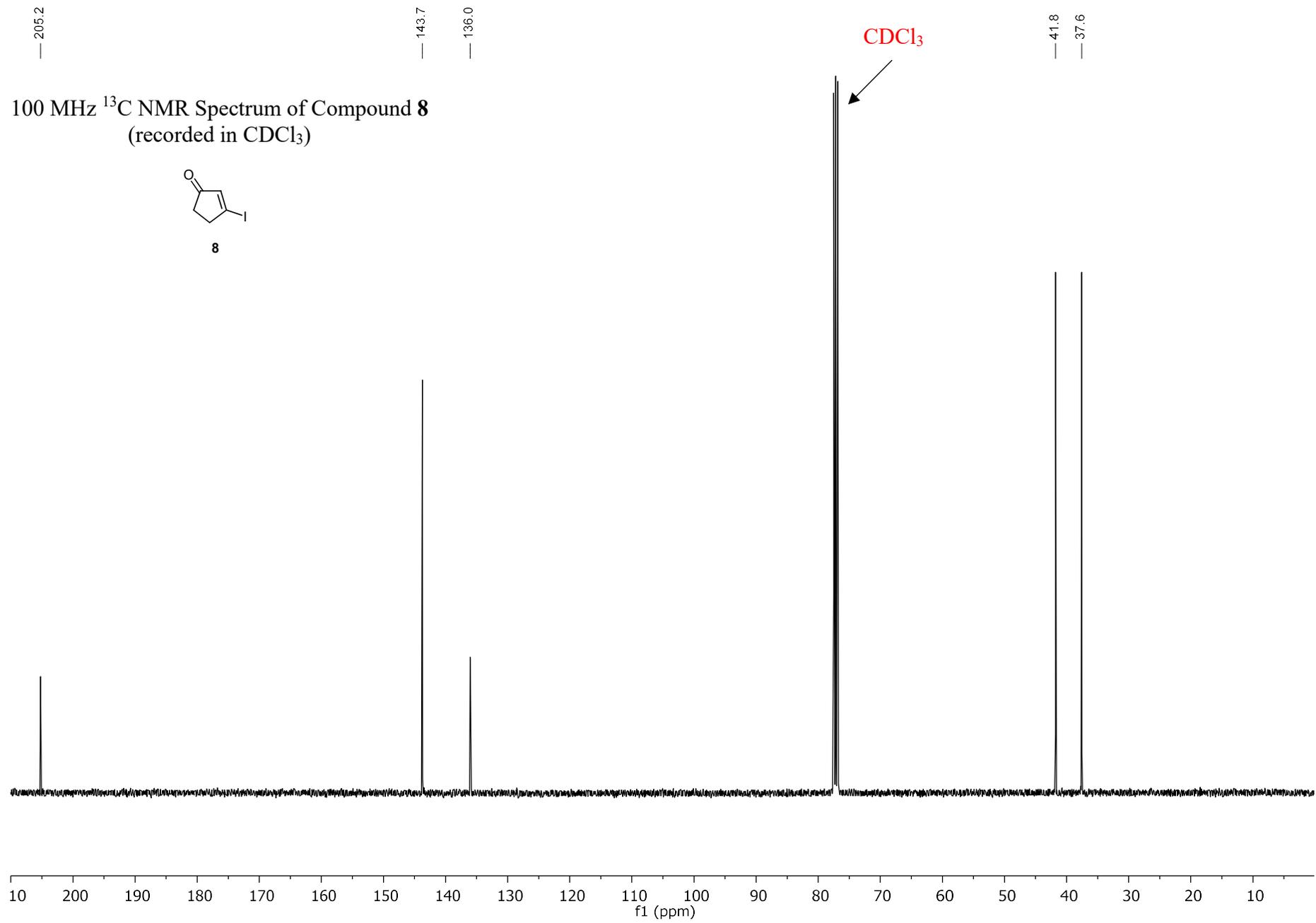
400 MHz ^1H NMR Spectrum of
[1,1'-Bi(cyclohexane)]-1,1'-diene-3,3'-dione
(recorded in CDCl_3)





400 MHz ^1H NMR Spectrum of Compound **8**
(recorded in CDCl_3)

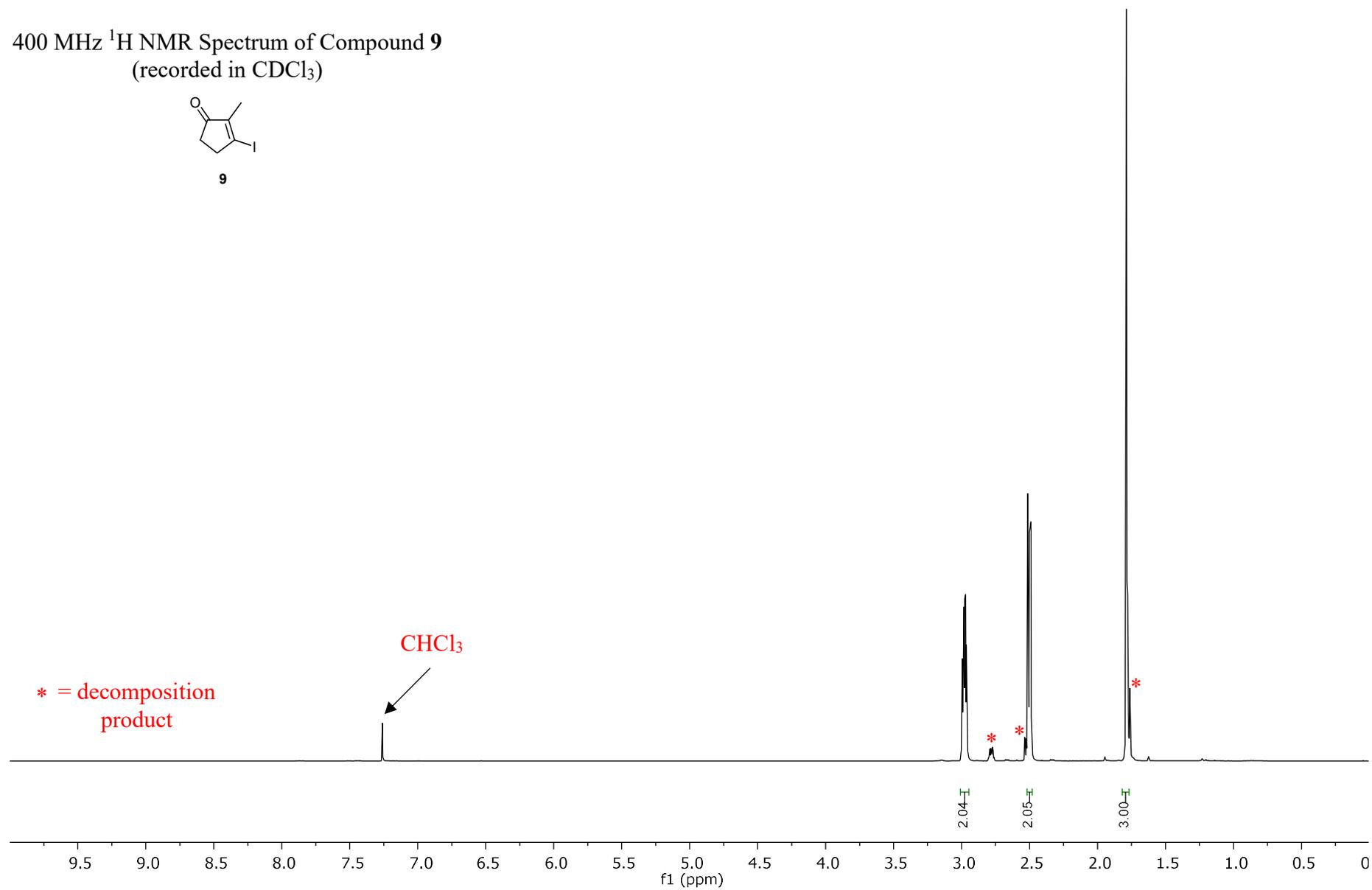


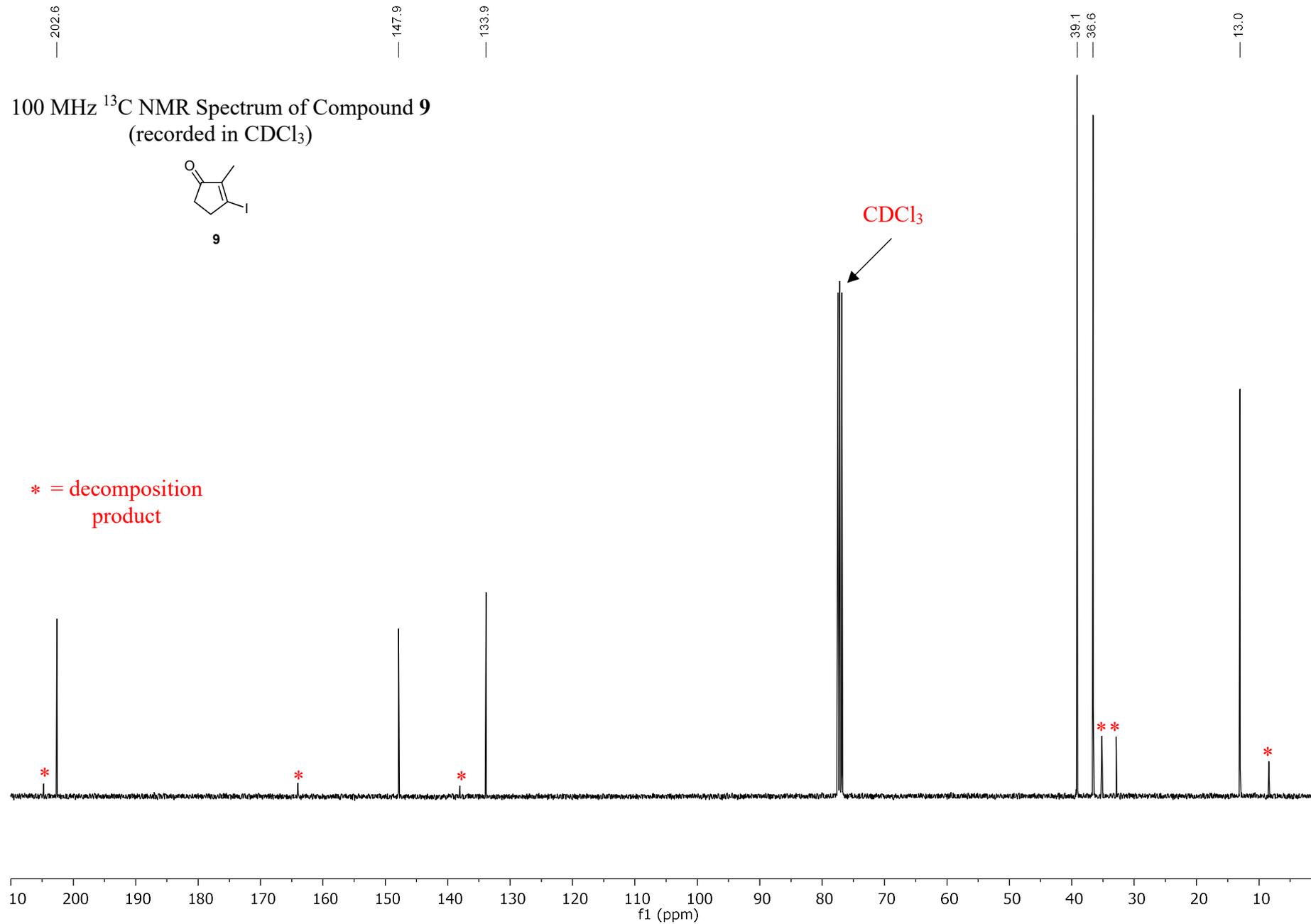


400 MHz ^1H NMR Spectrum of Compound **9**
(recorded in CDCl_3)

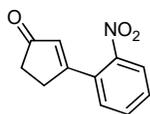


9

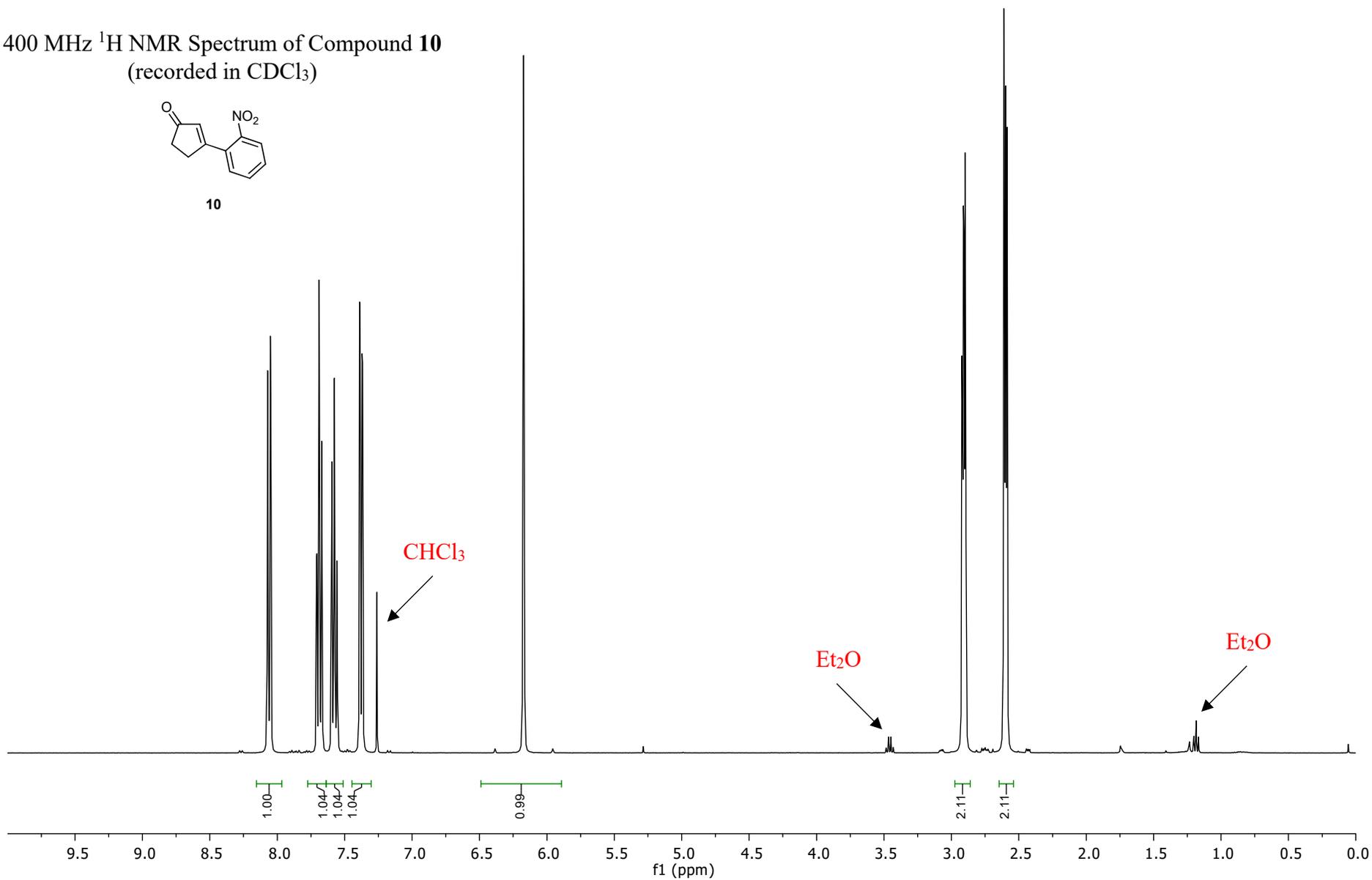


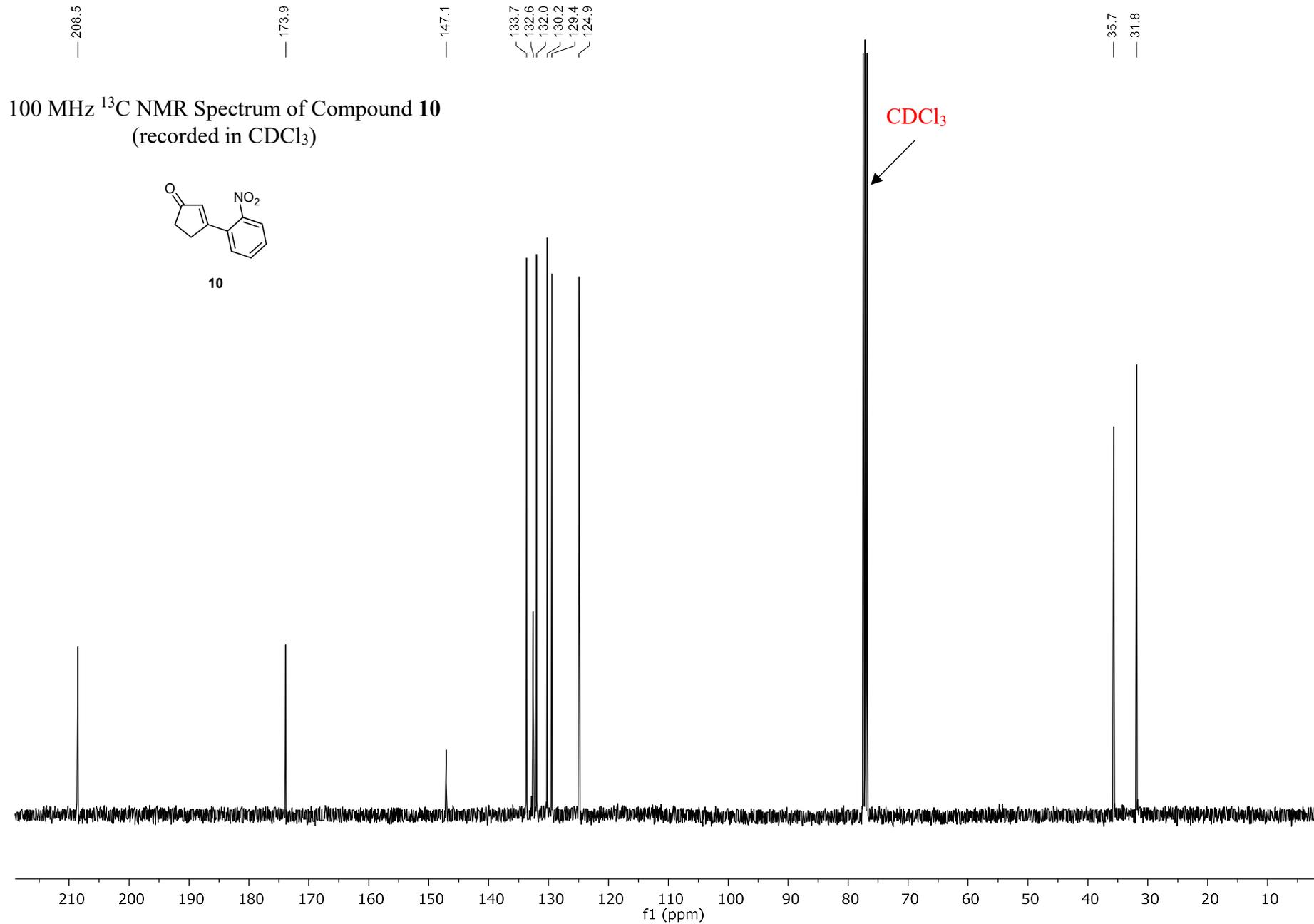


400 MHz ^1H NMR Spectrum of Compound **10**
(recorded in CDCl_3)

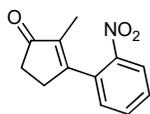


10

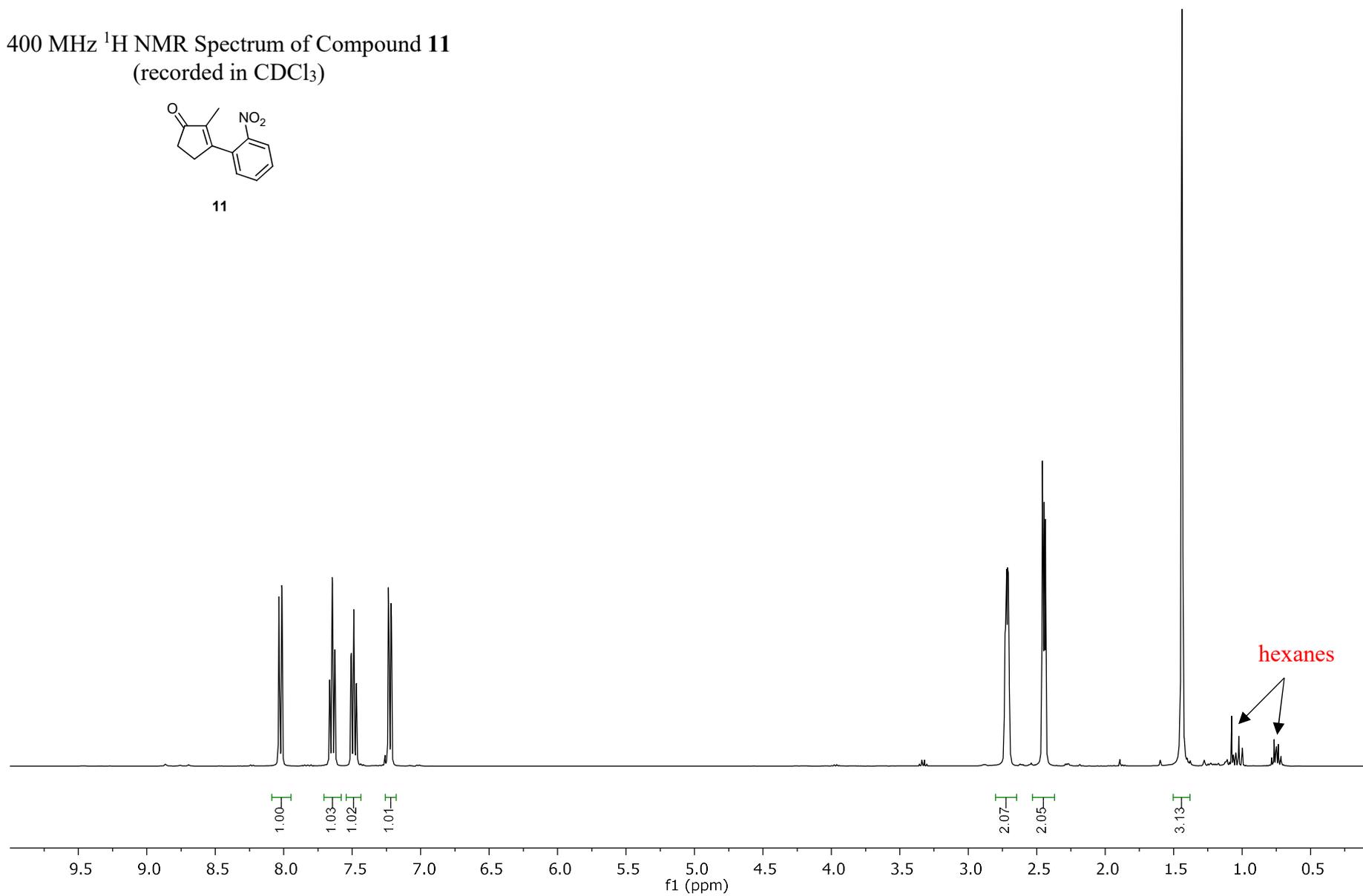


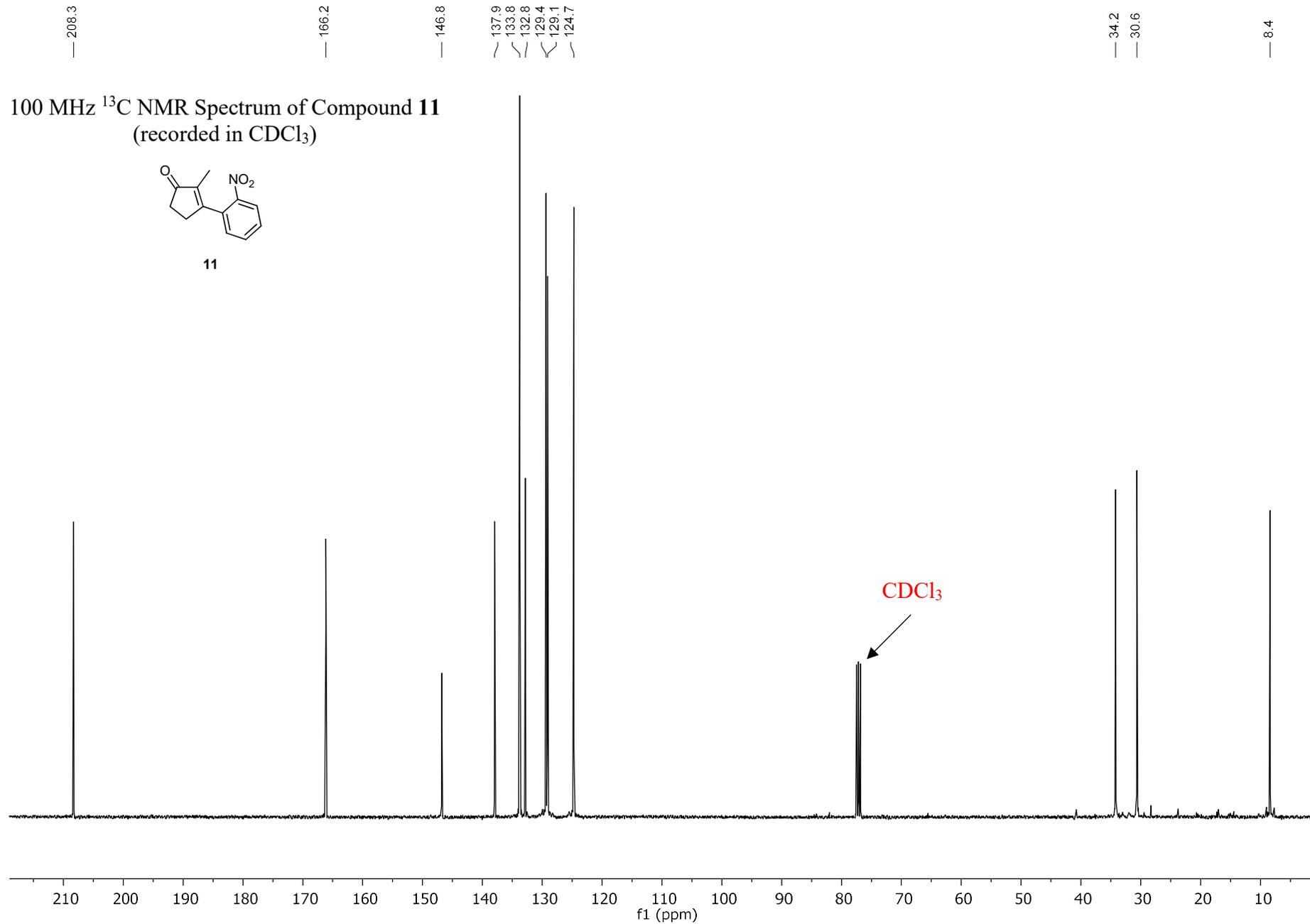


400 MHz ^1H NMR Spectrum of Compound **11**
(recorded in CDCl_3)

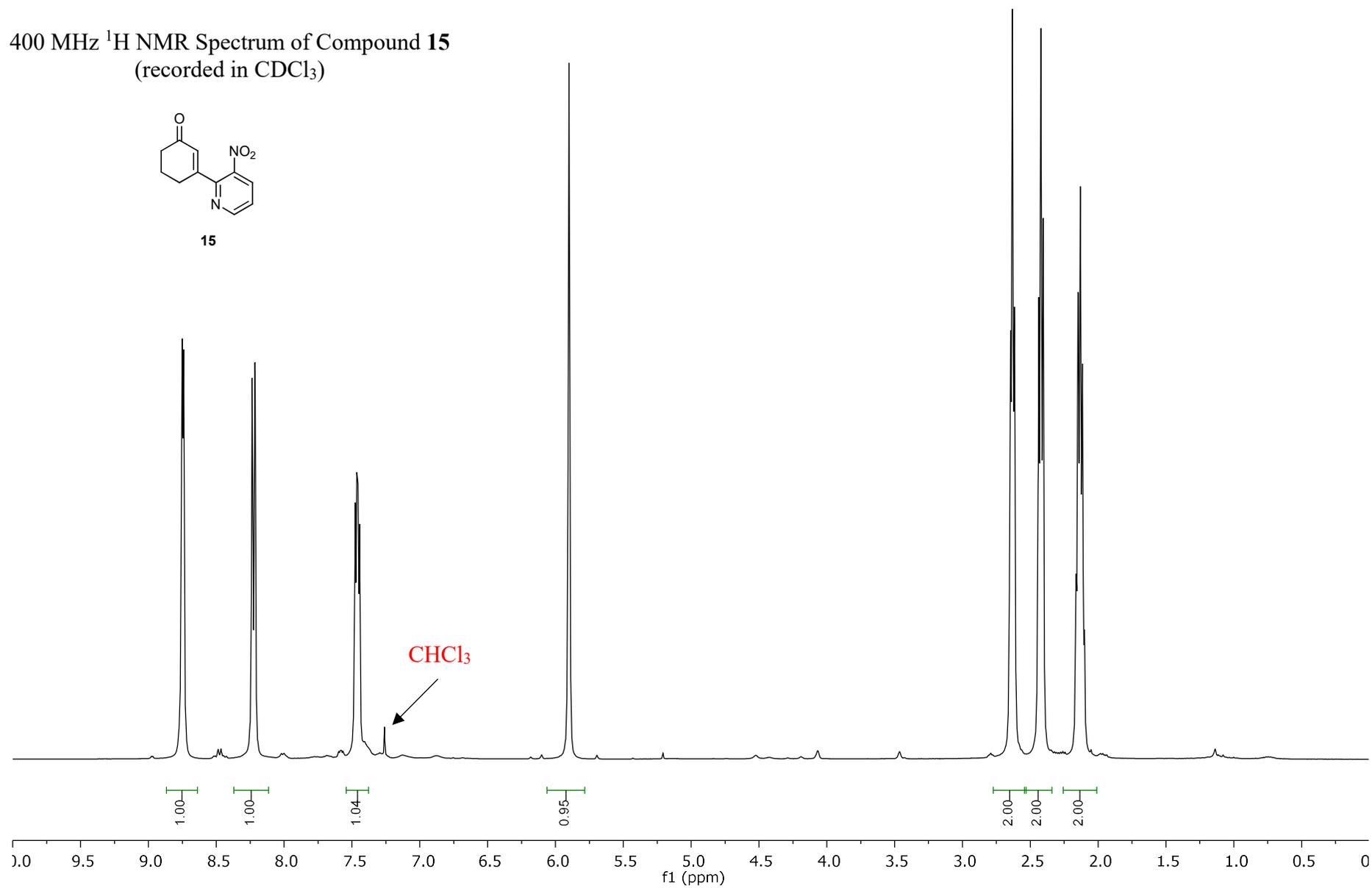
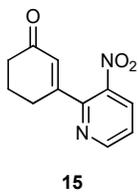


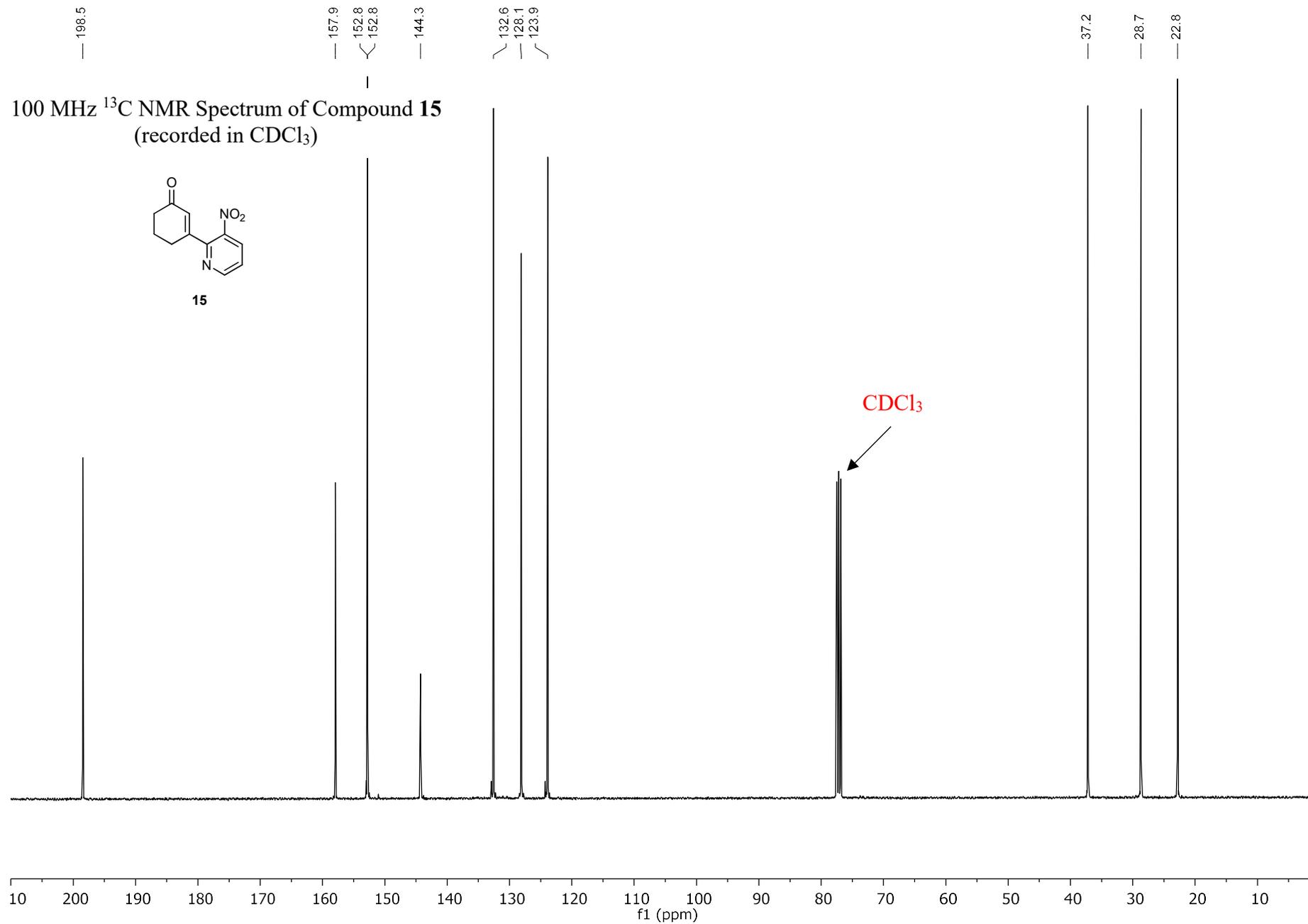
11



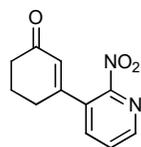


400 MHz ^1H NMR Spectrum of Compound **15**
(recorded in CDCl_3)

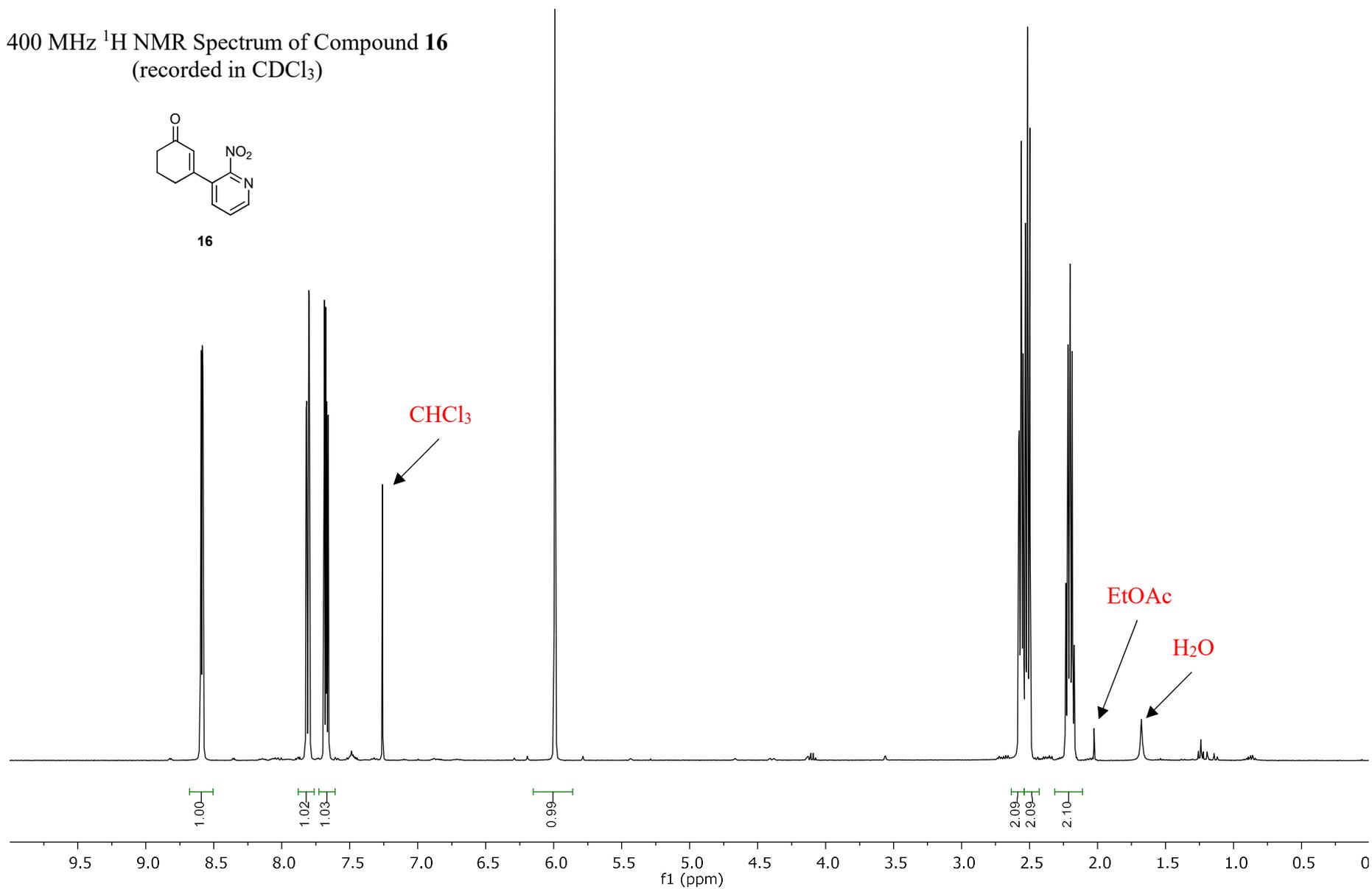


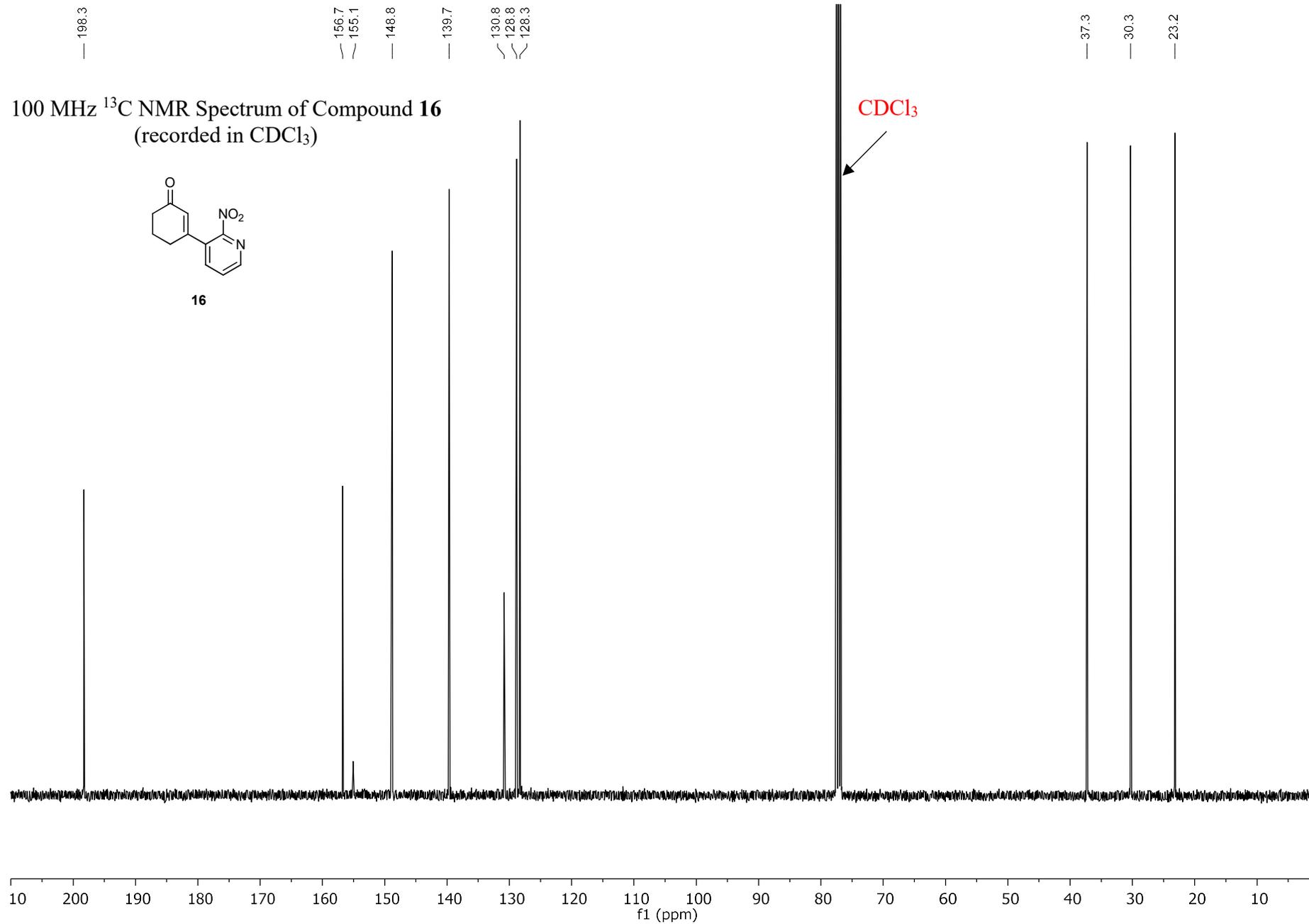


400 MHz ^1H NMR Spectrum of Compound **16**
(recorded in CDCl_3)

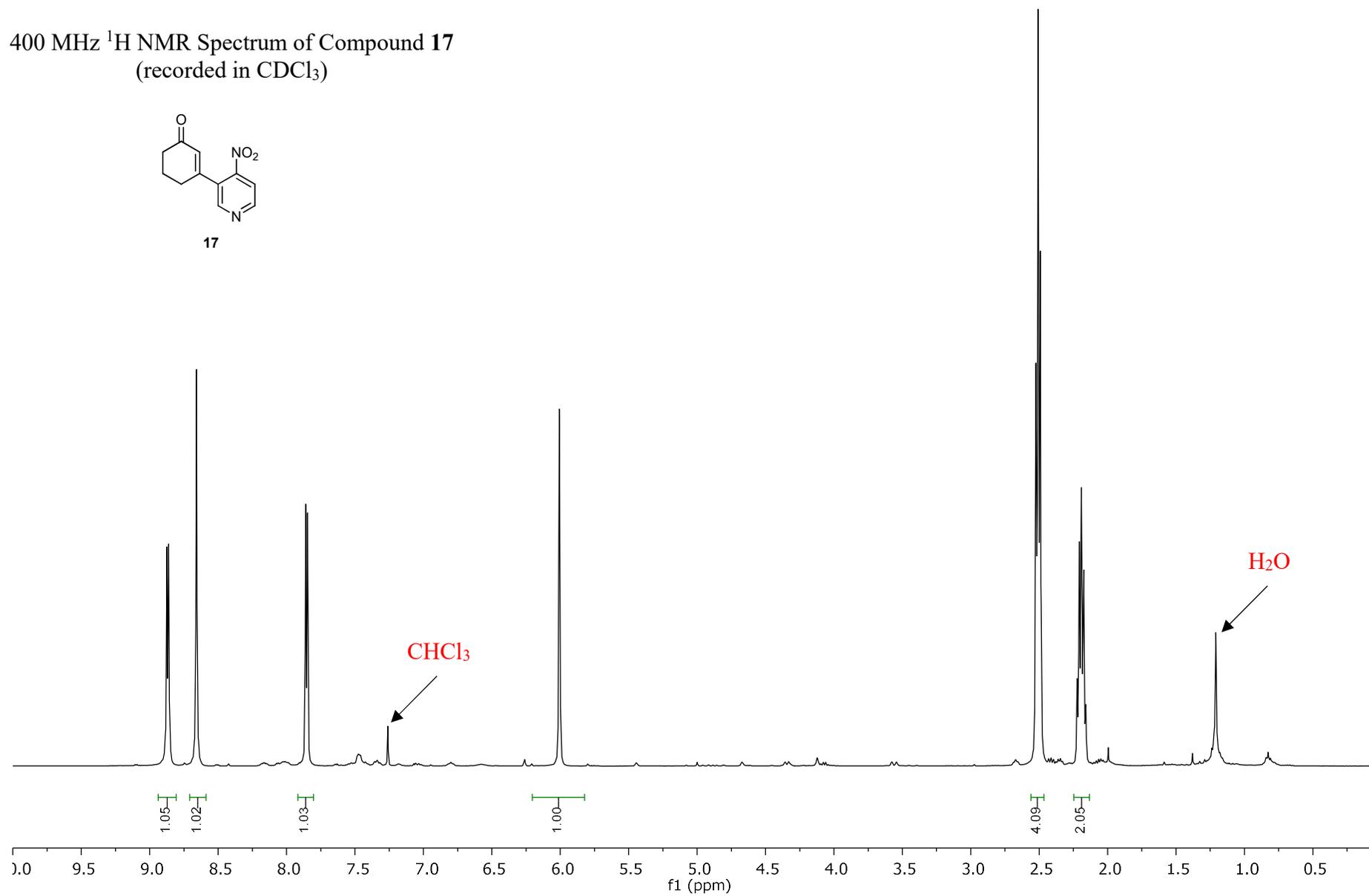
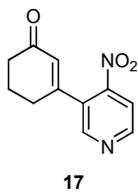


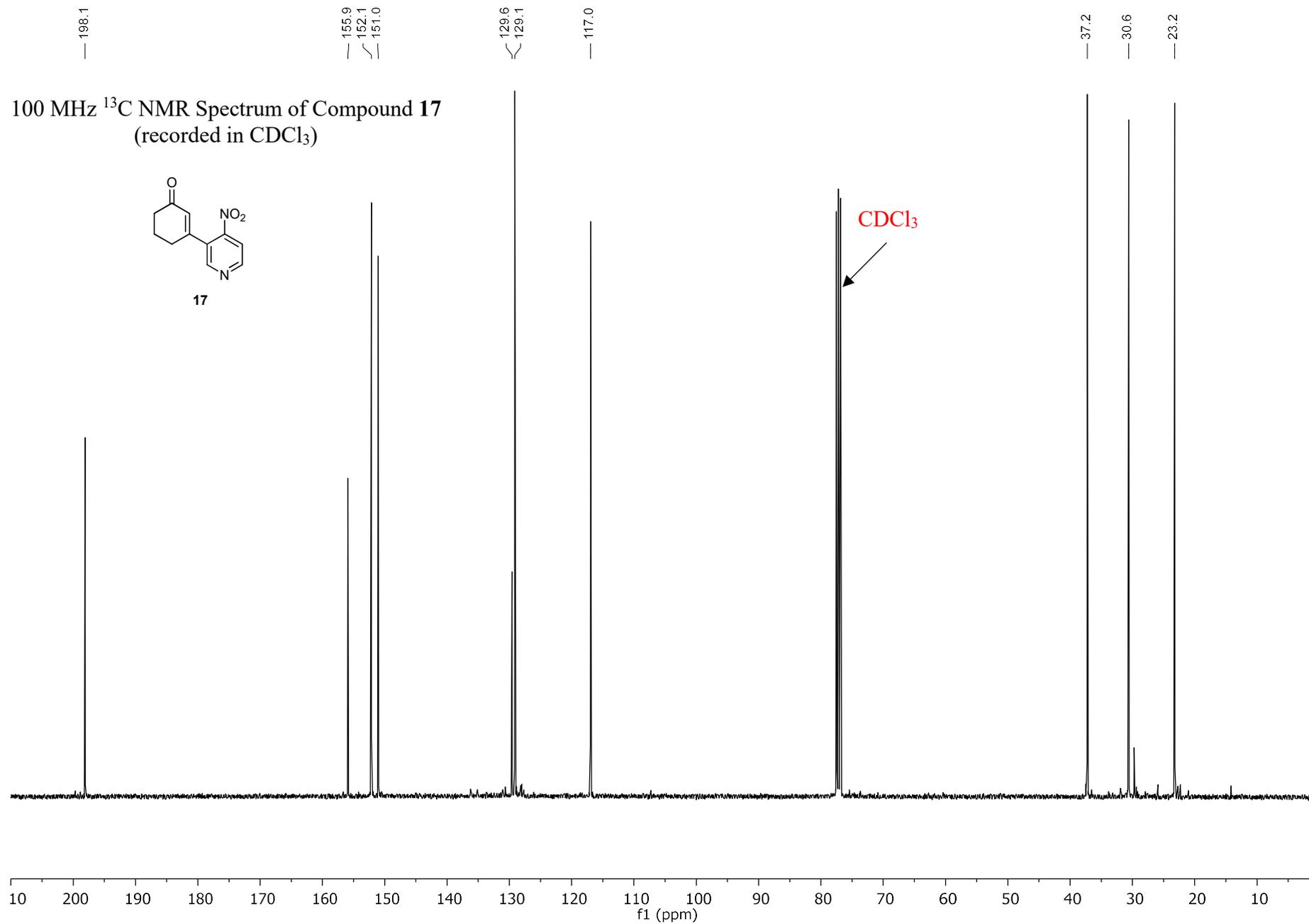
16



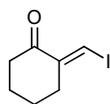


400 MHz ^1H NMR Spectrum of Compound **17**
(recorded in CDCl_3)

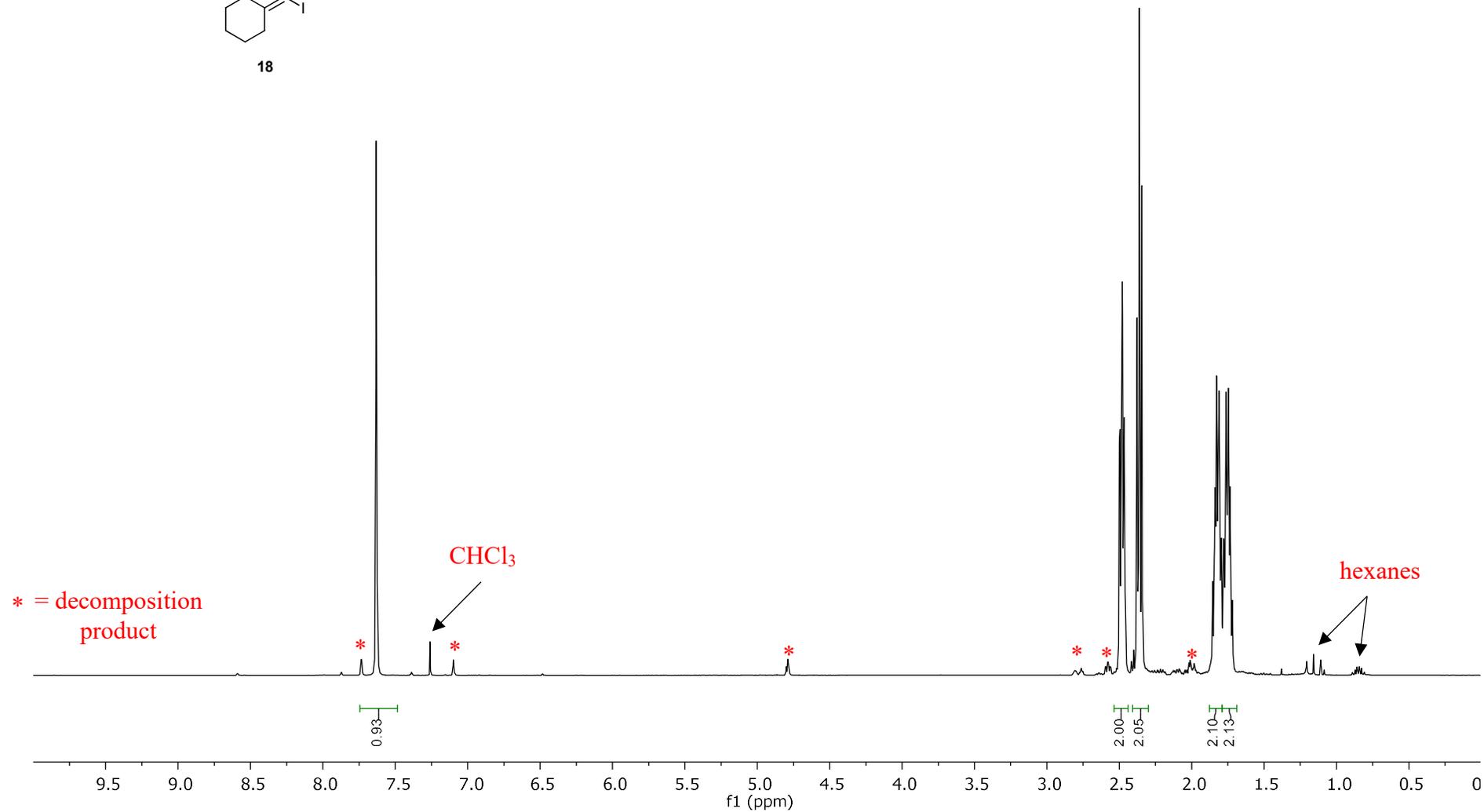


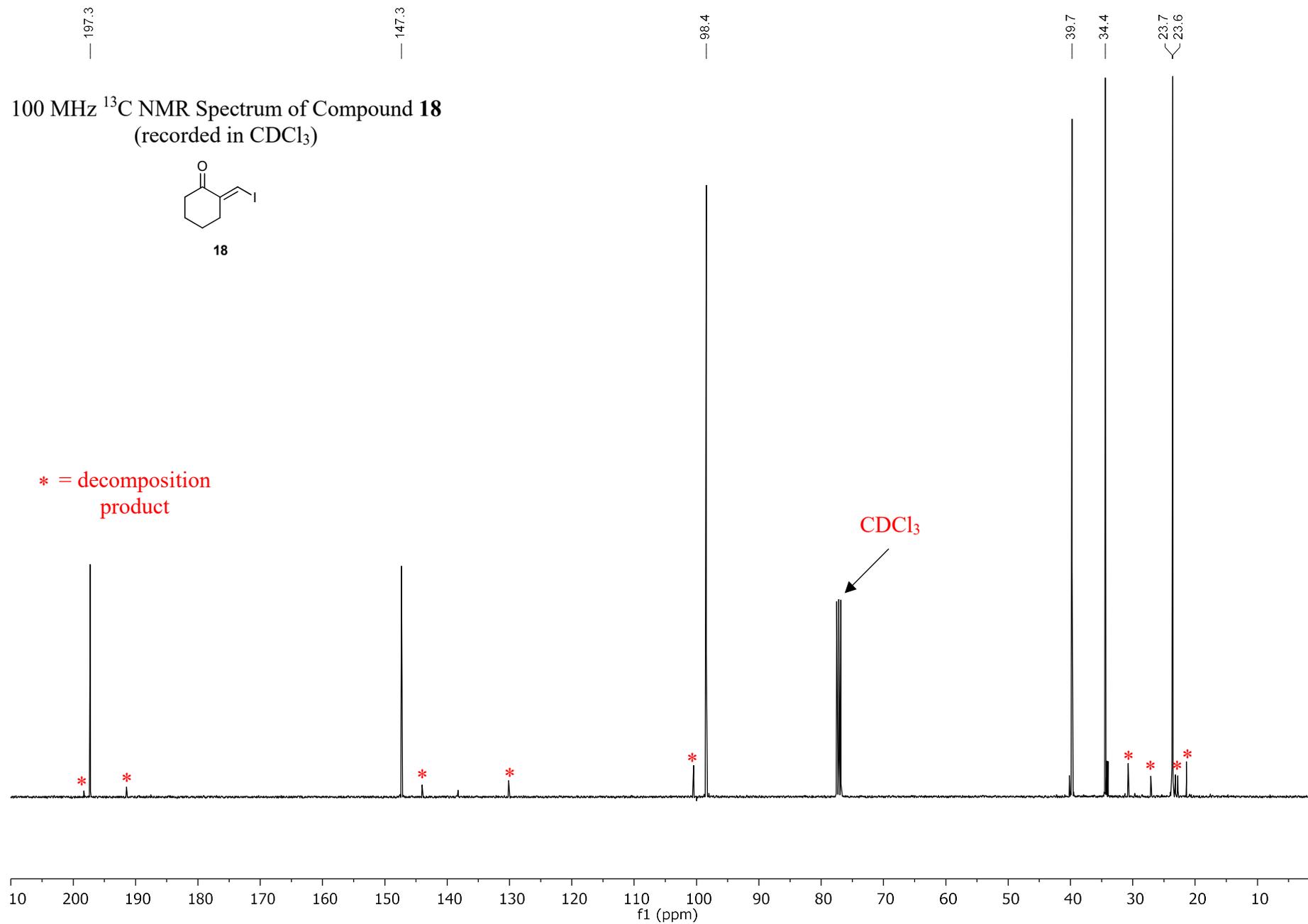


400 MHz ^1H NMR Spectrum of Compound **18**
(recorded in CDCl_3)

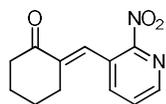


18

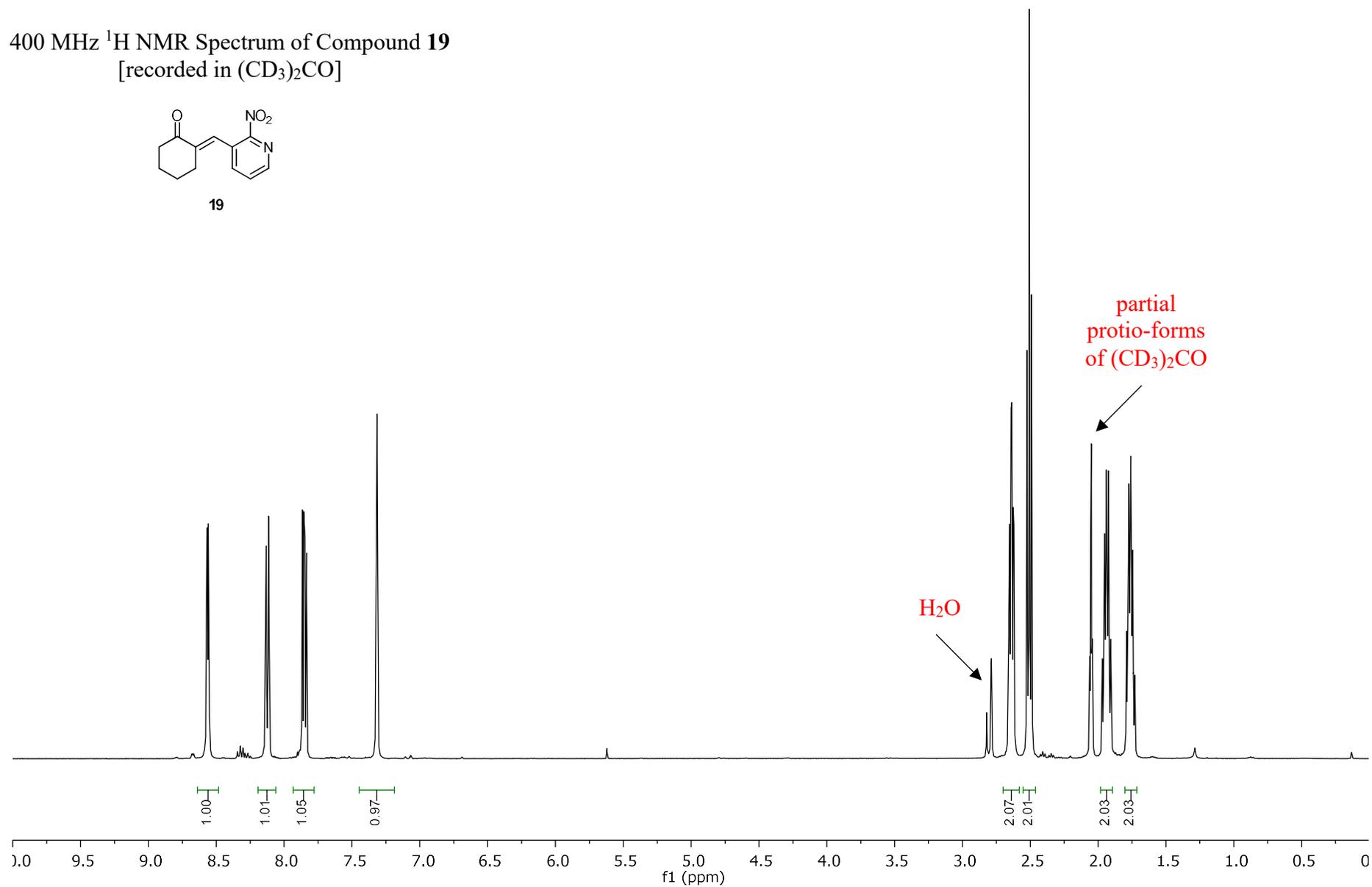


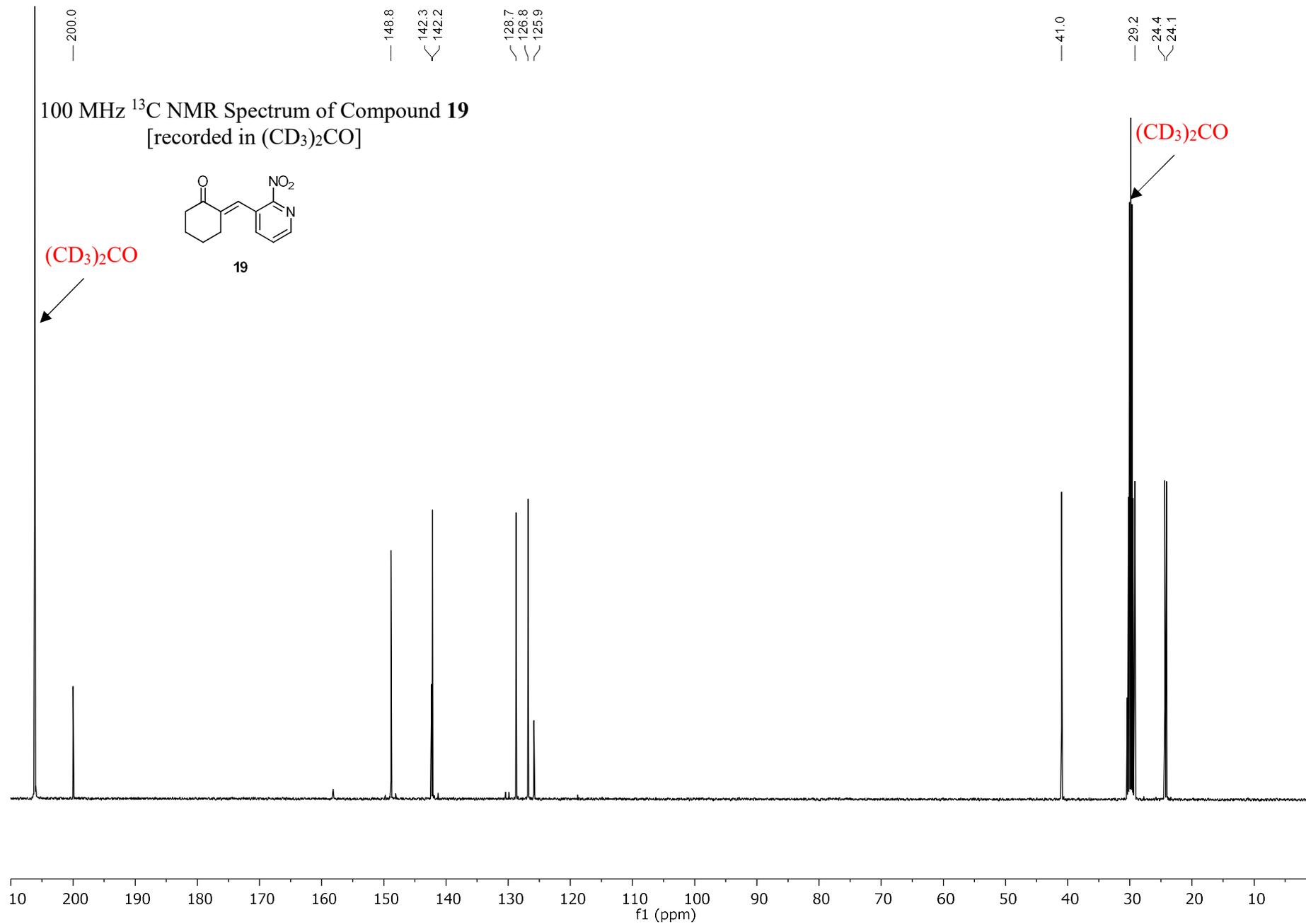


400 MHz ^1H NMR Spectrum of Compound **19**
[recorded in $(\text{CD}_3)_2\text{CO}$]

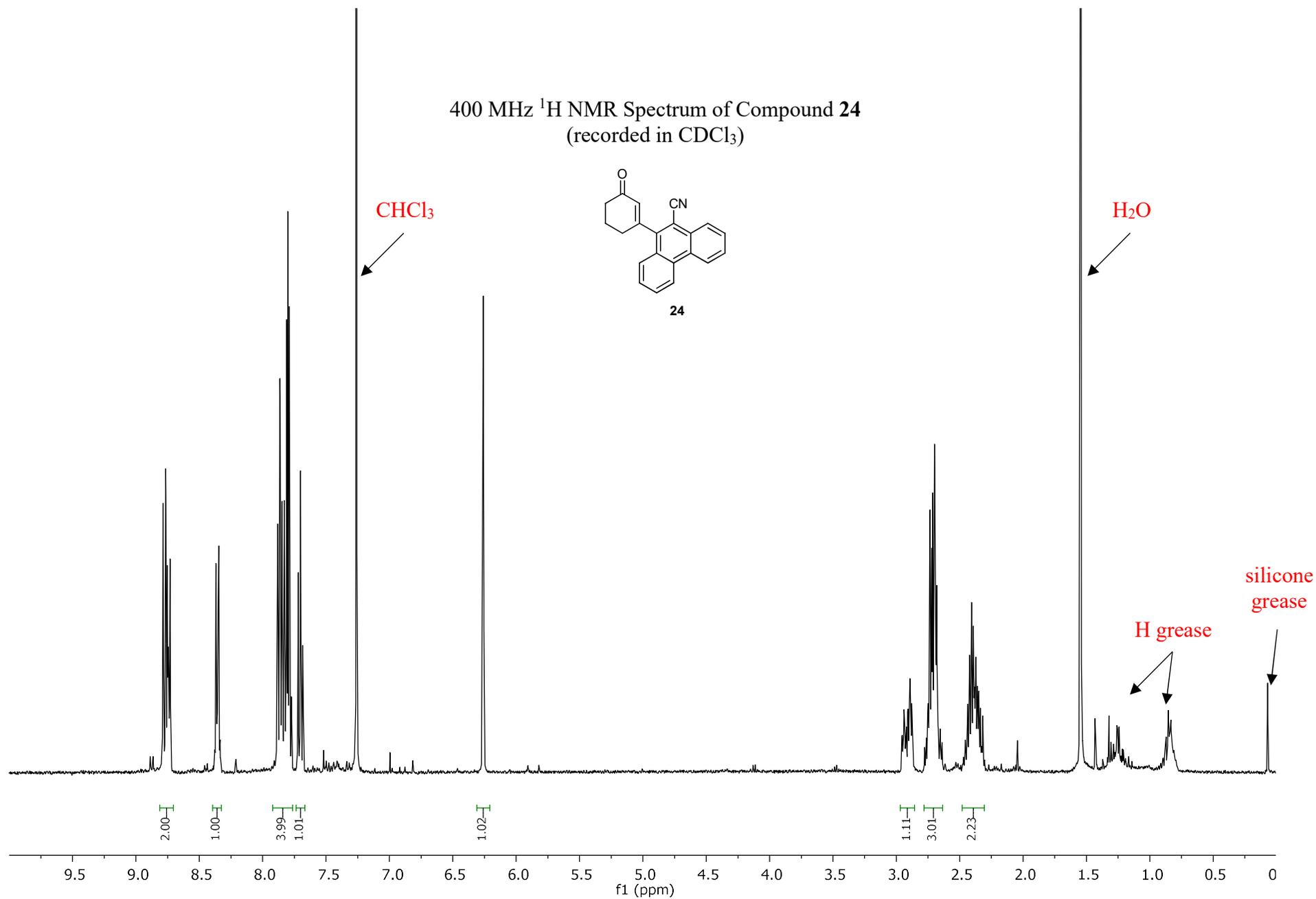
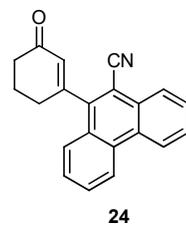


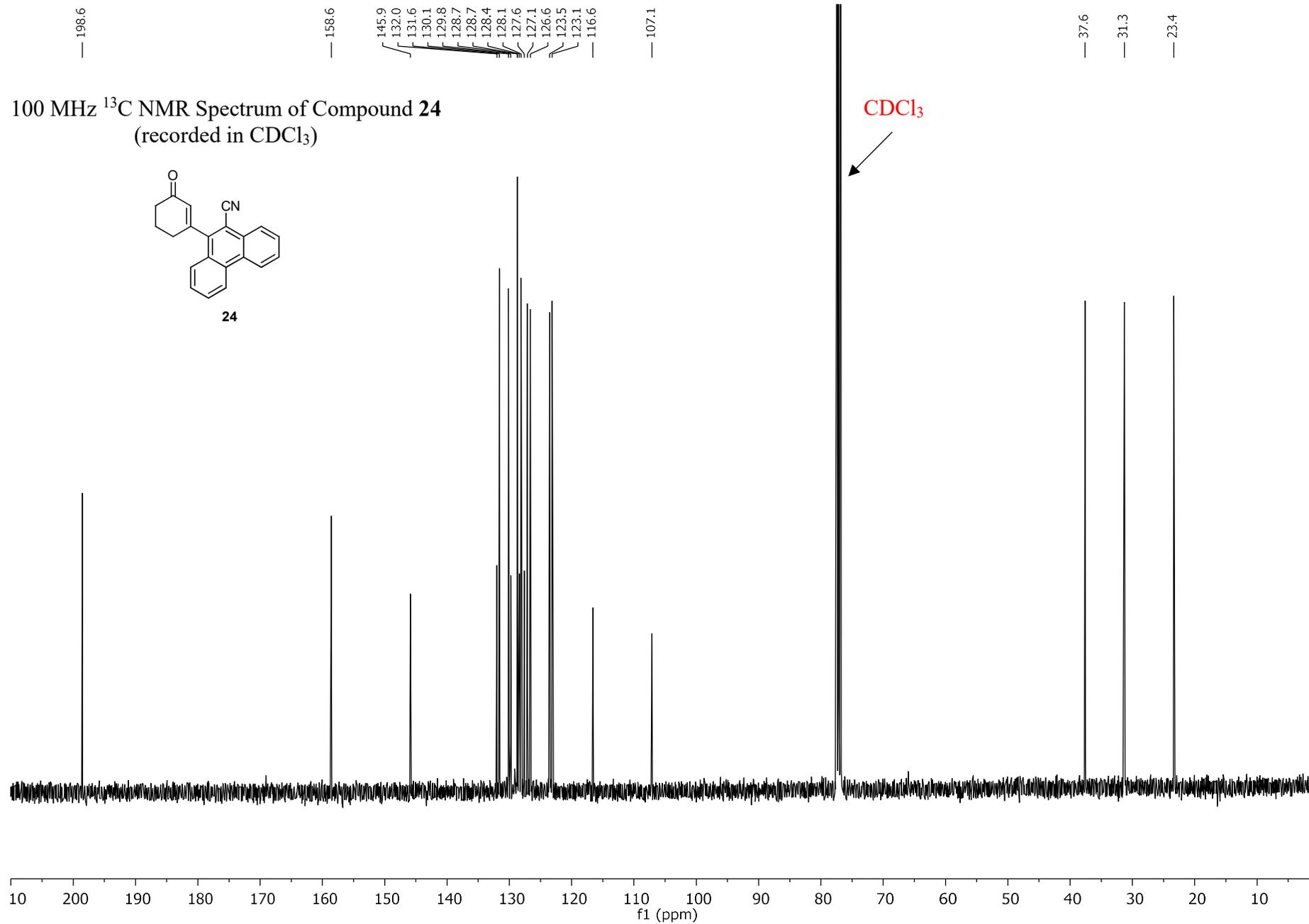
19



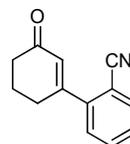


400 MHz ^1H NMR Spectrum of Compound **24**
(recorded in CDCl_3)

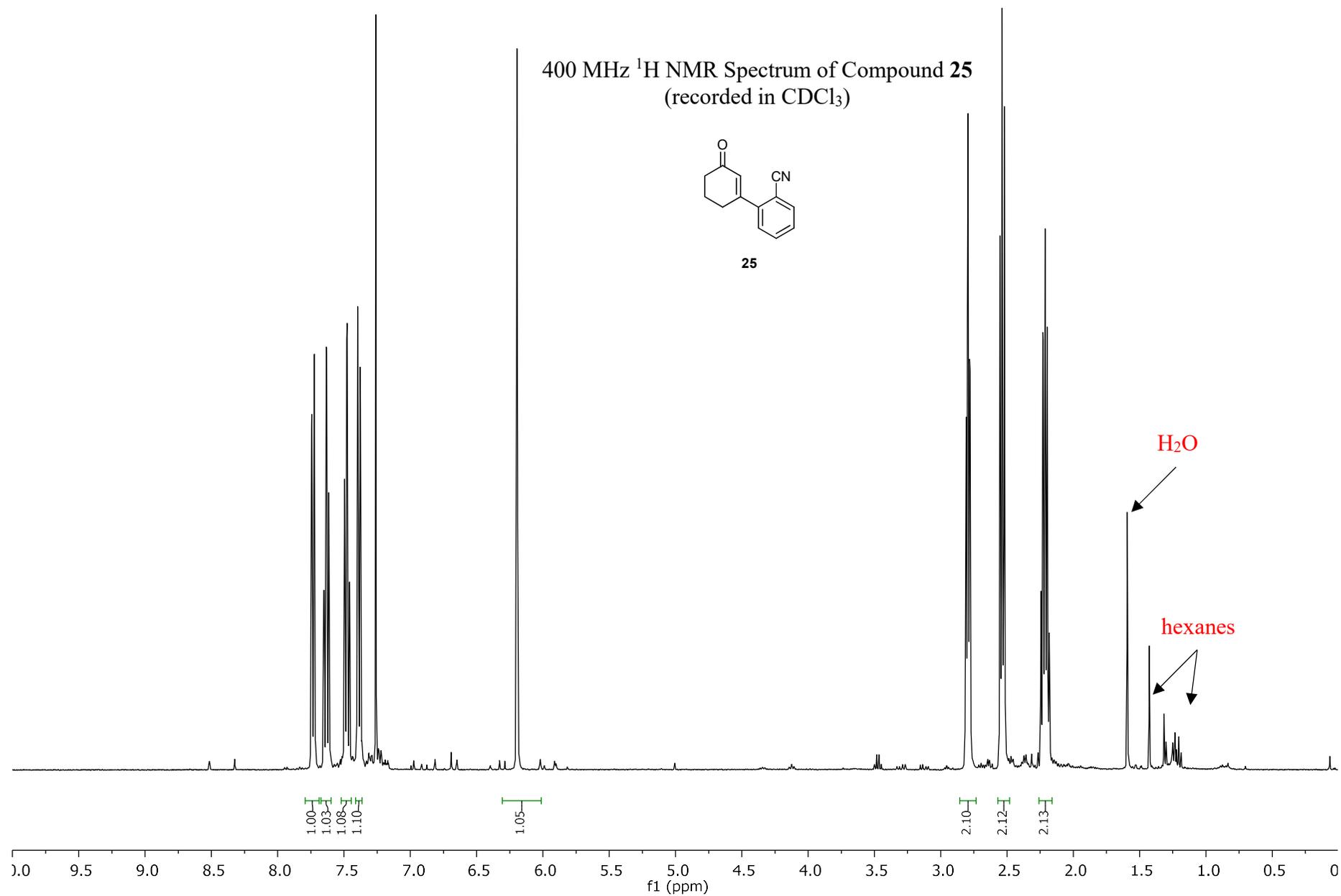


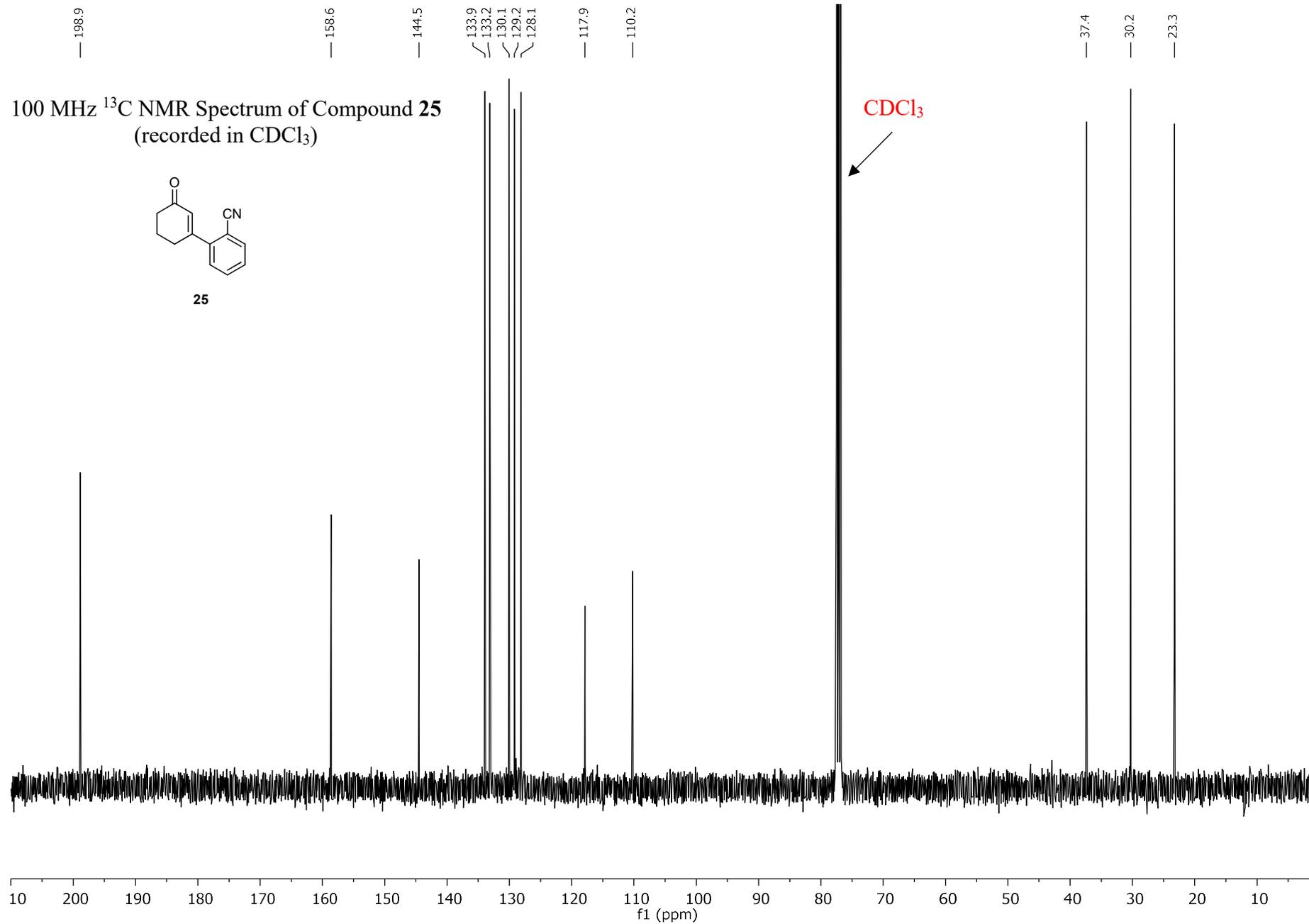


400 MHz ^1H NMR Spectrum of Compound **25**
(recorded in CDCl_3)

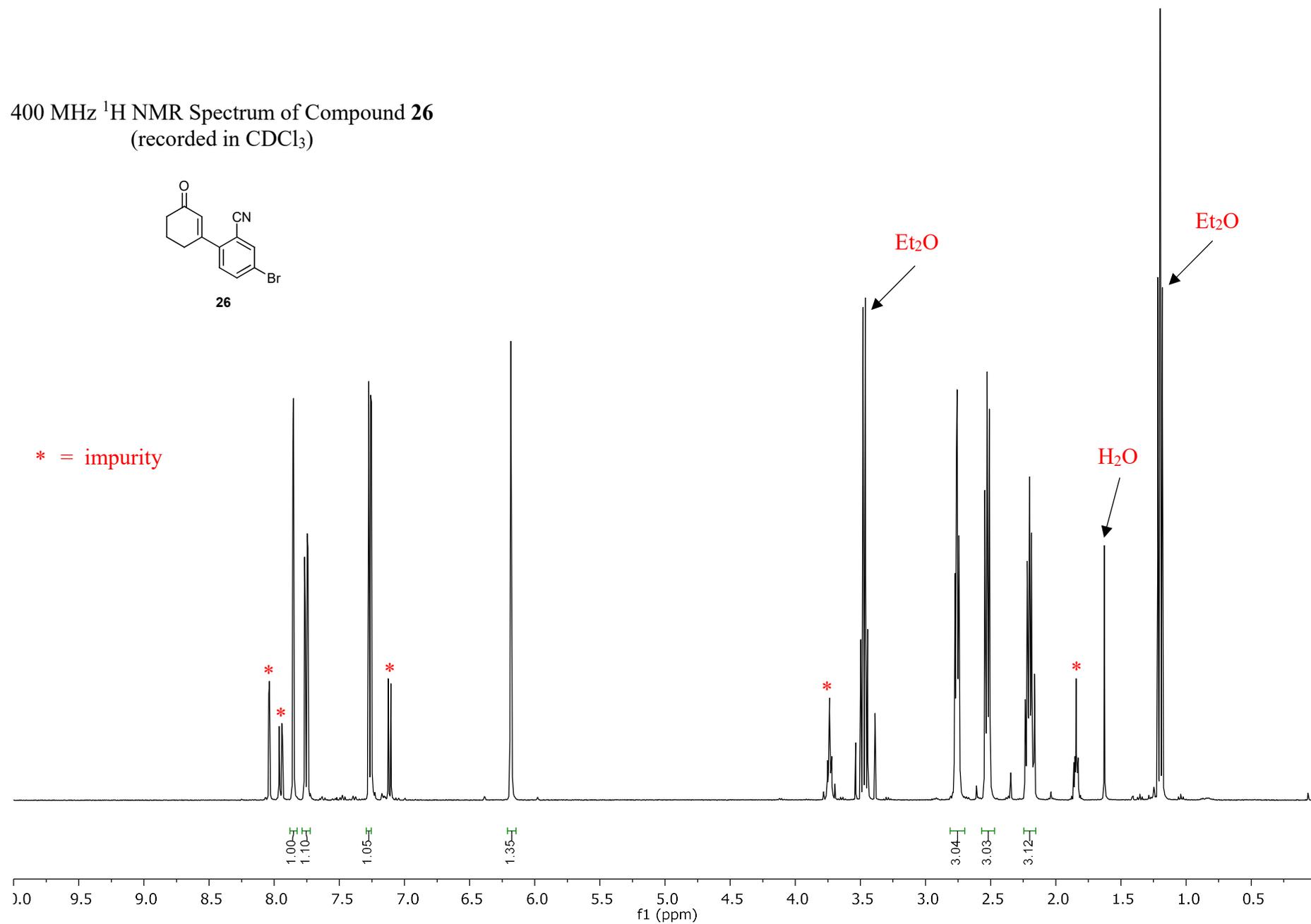
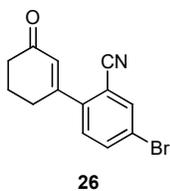


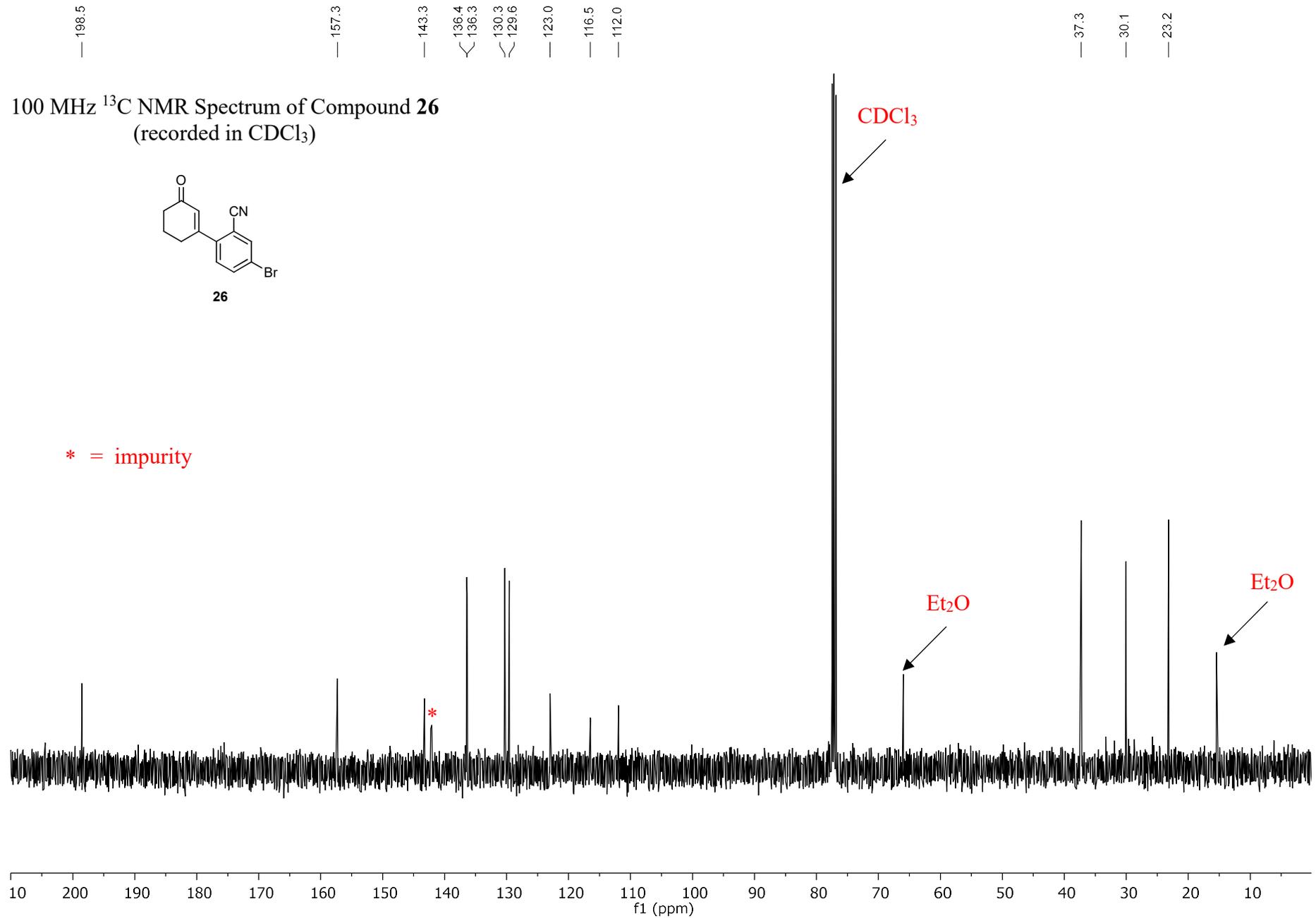
25



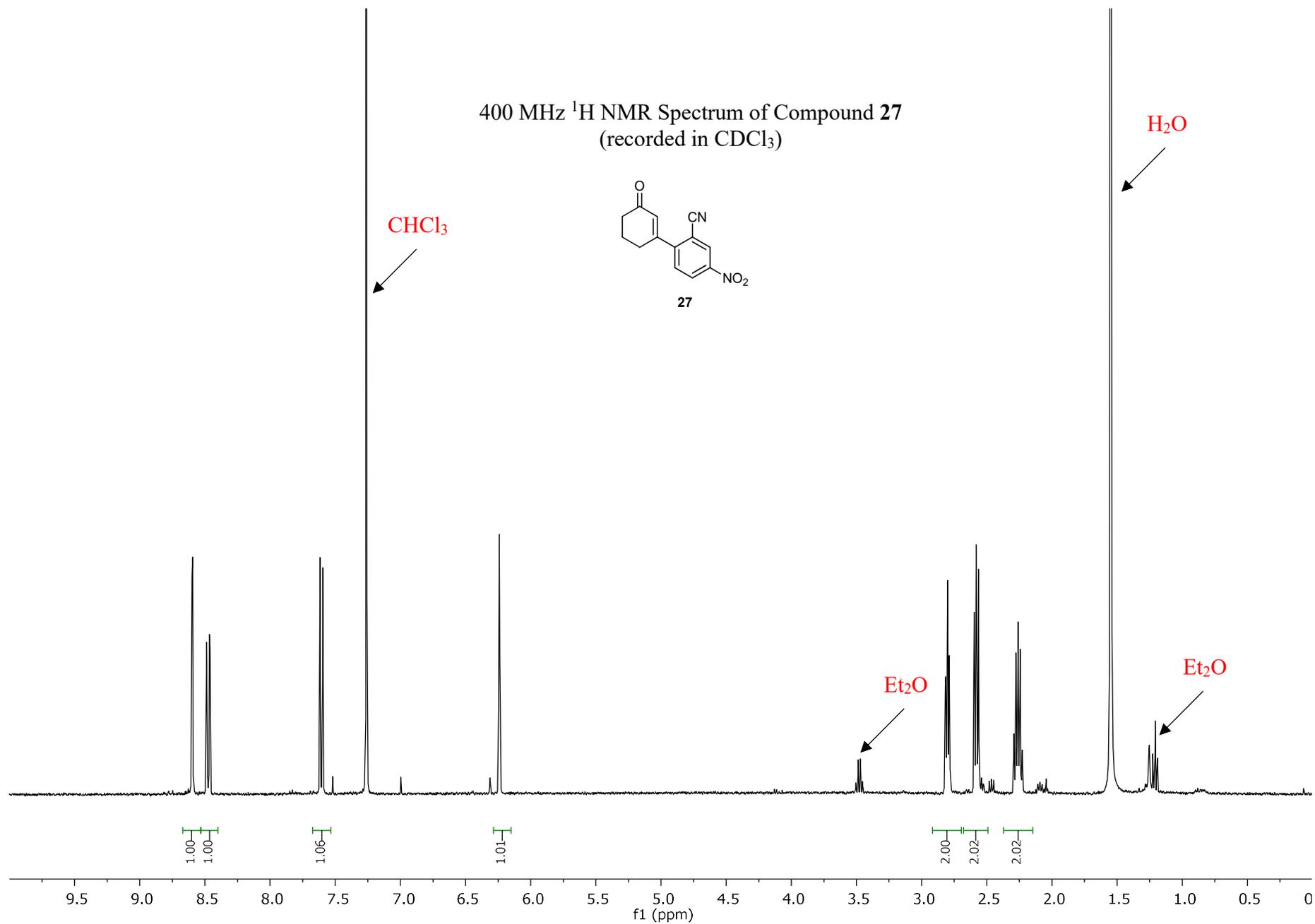
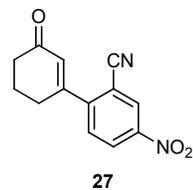


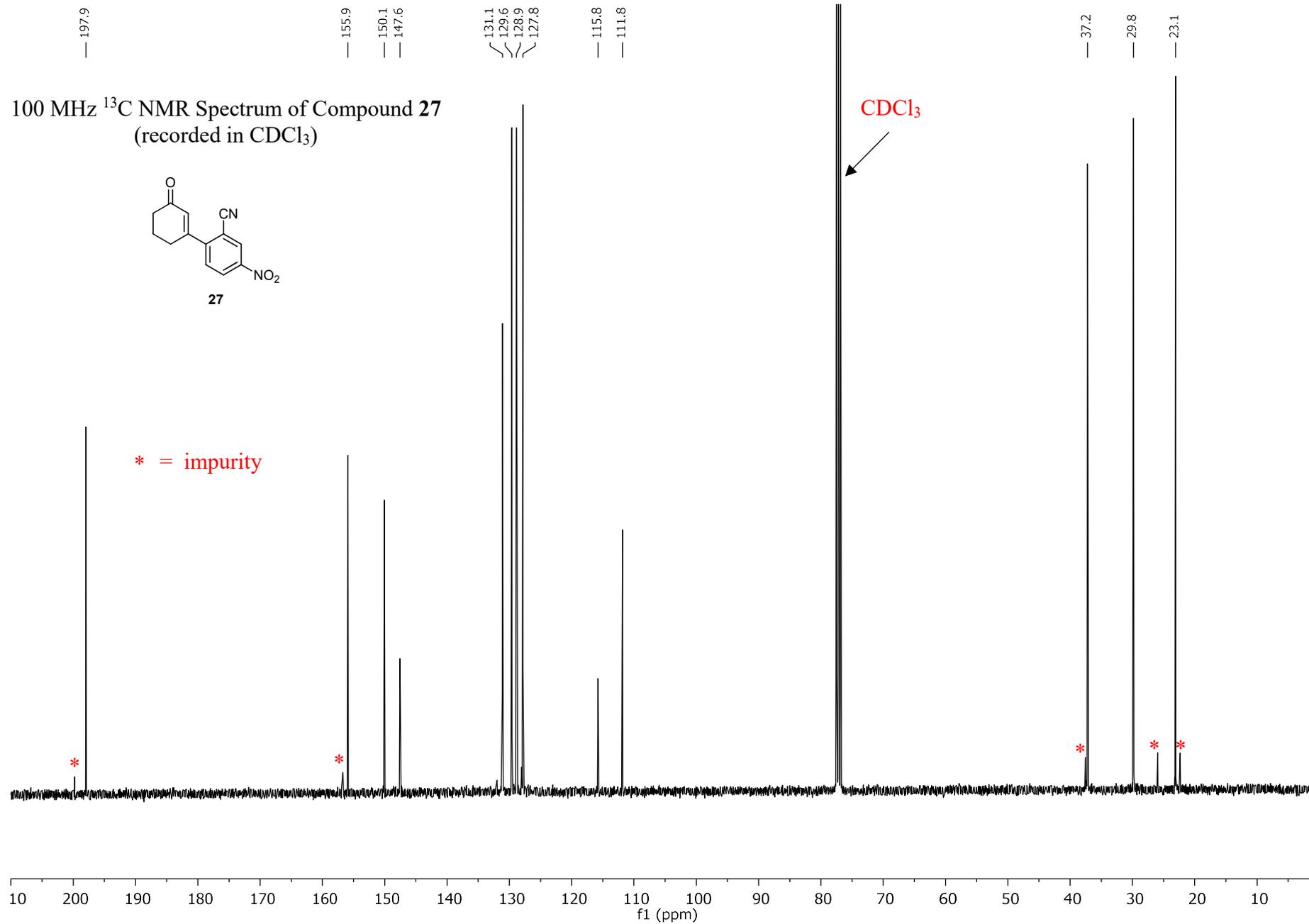
400 MHz ^1H NMR Spectrum of Compound **26**
(recorded in CDCl_3)



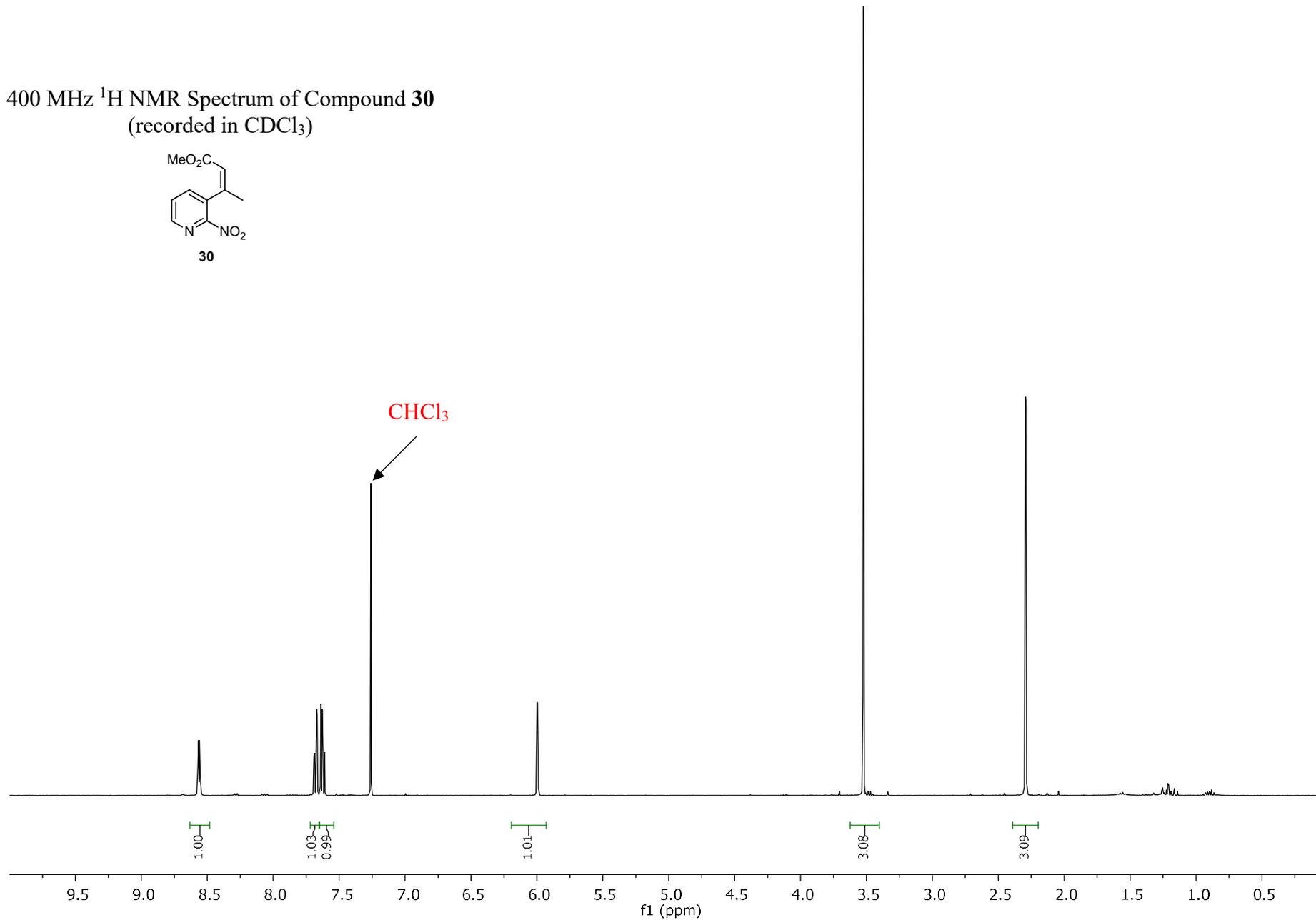
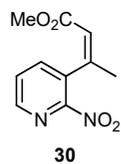


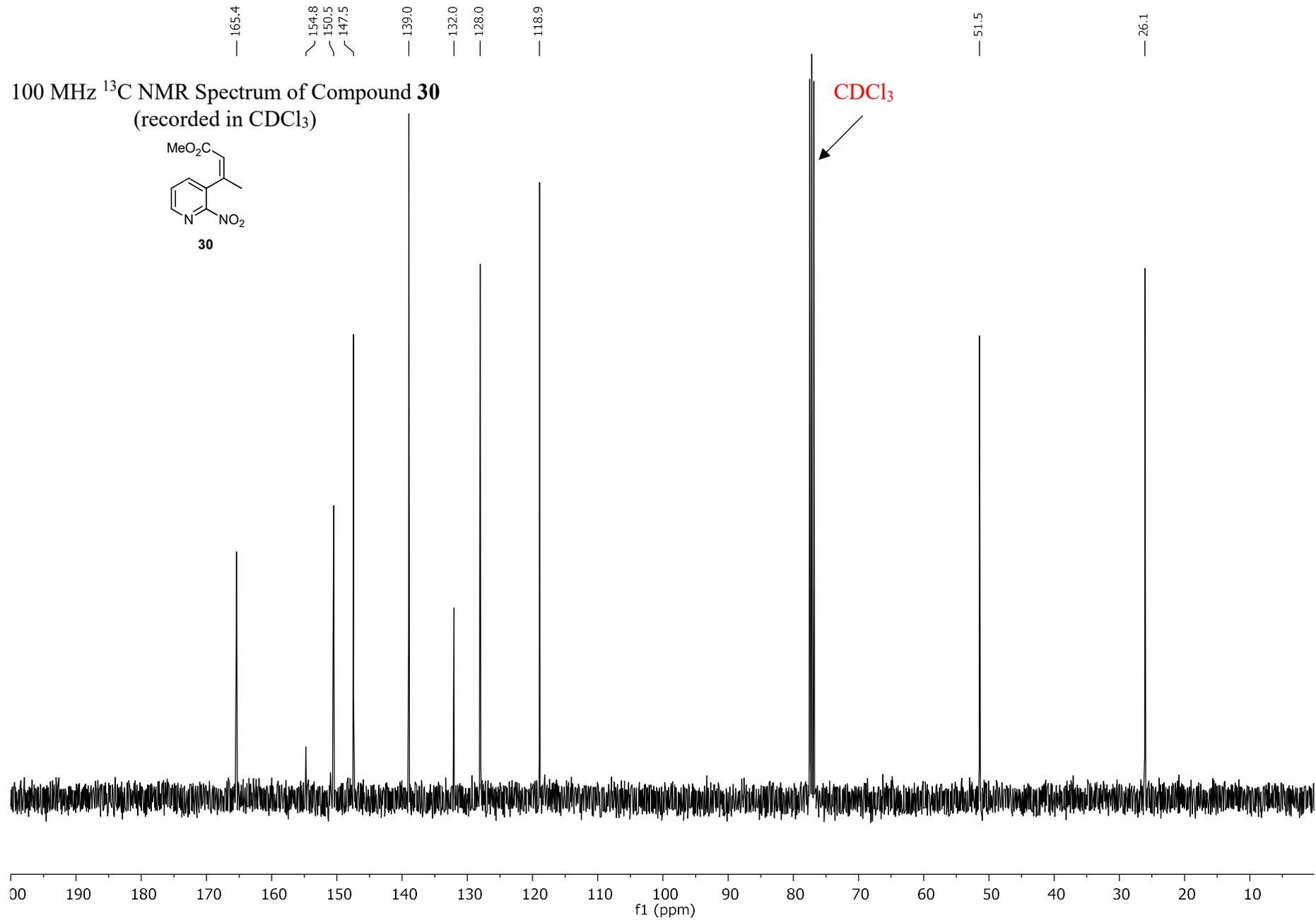
400 MHz ^1H NMR Spectrum of Compound **27**
(recorded in CDCl_3)



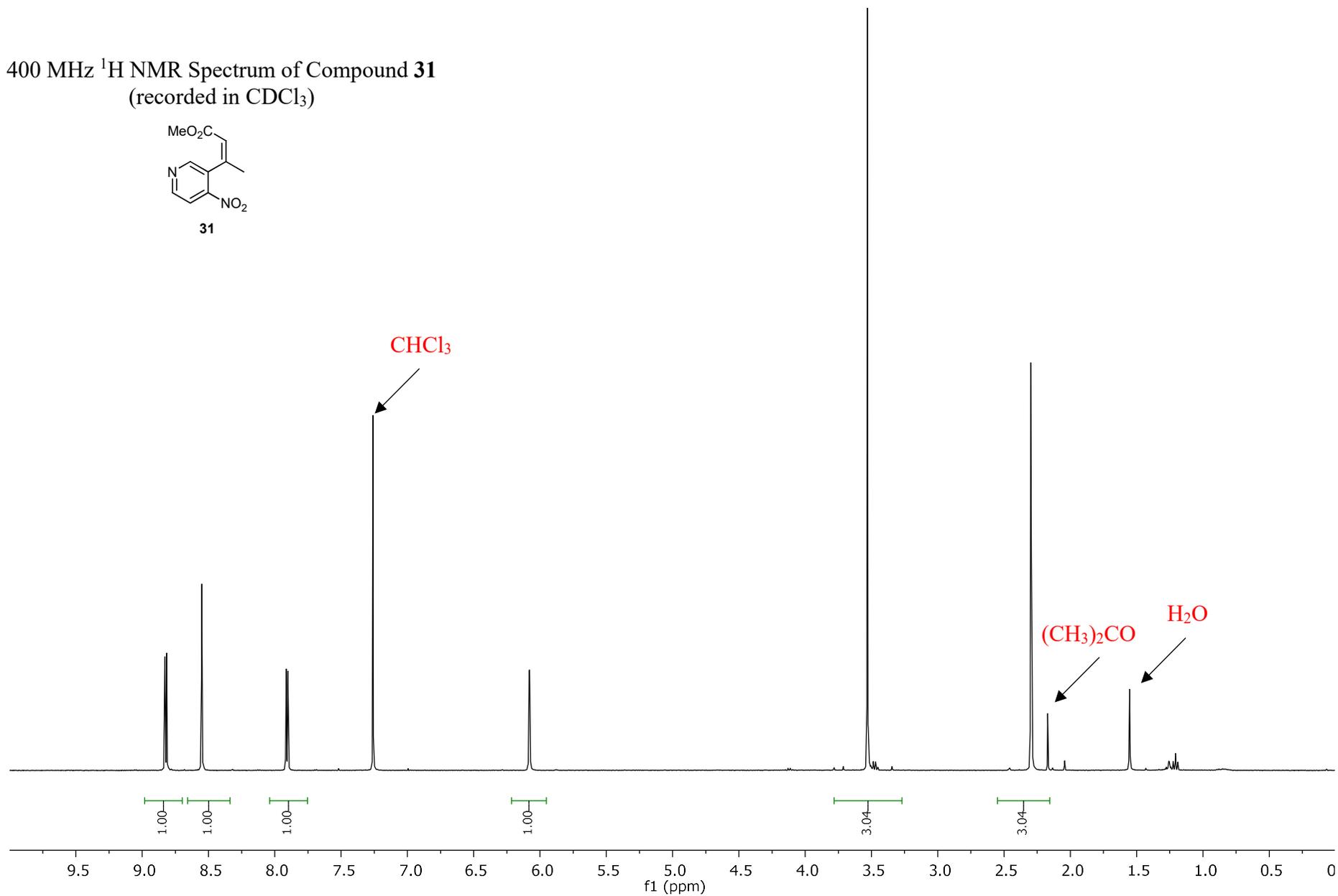
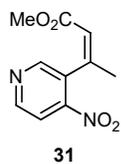


400 MHz ^1H NMR Spectrum of Compound **30**
(recorded in CDCl_3)

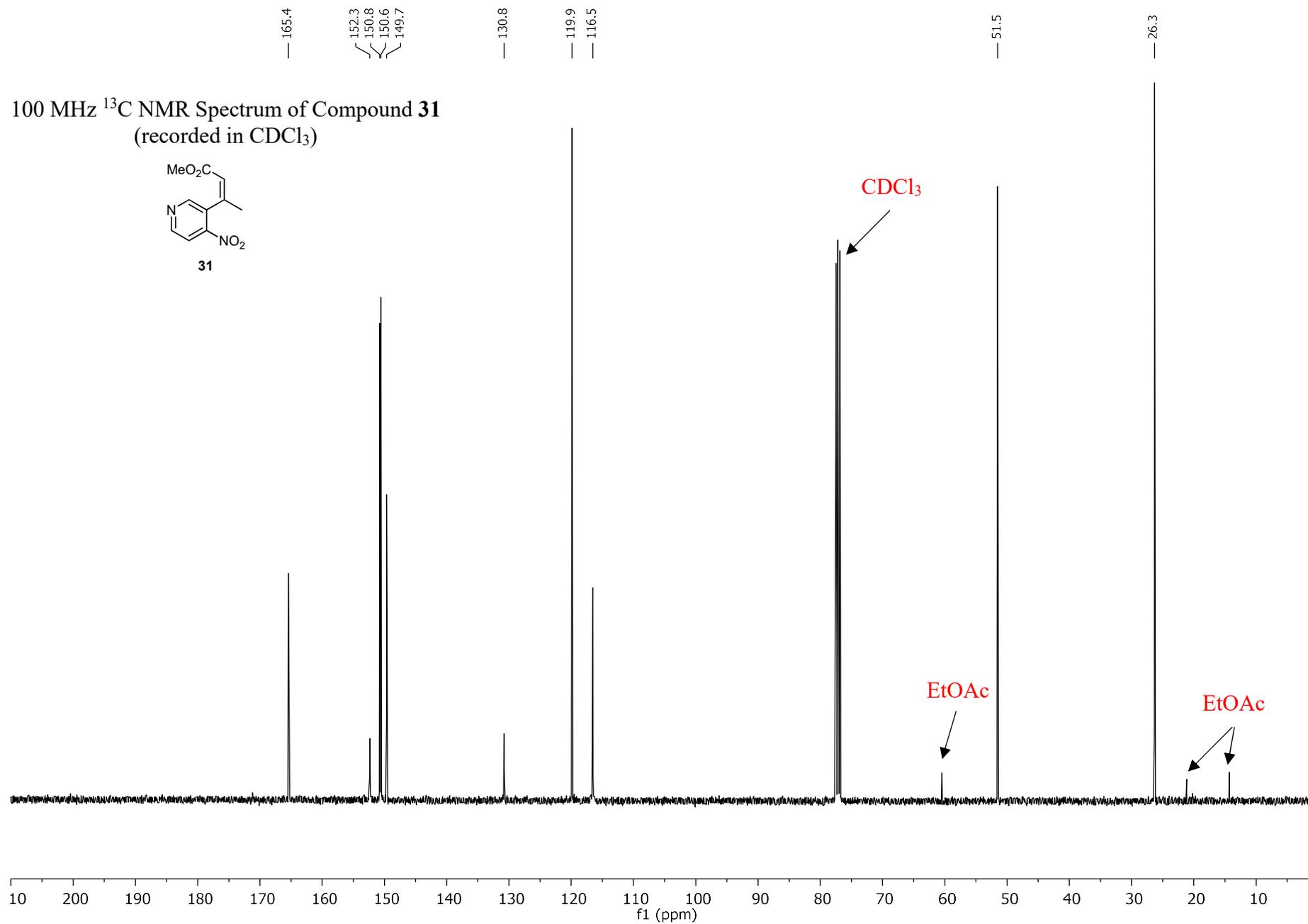
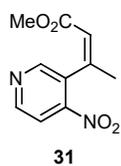


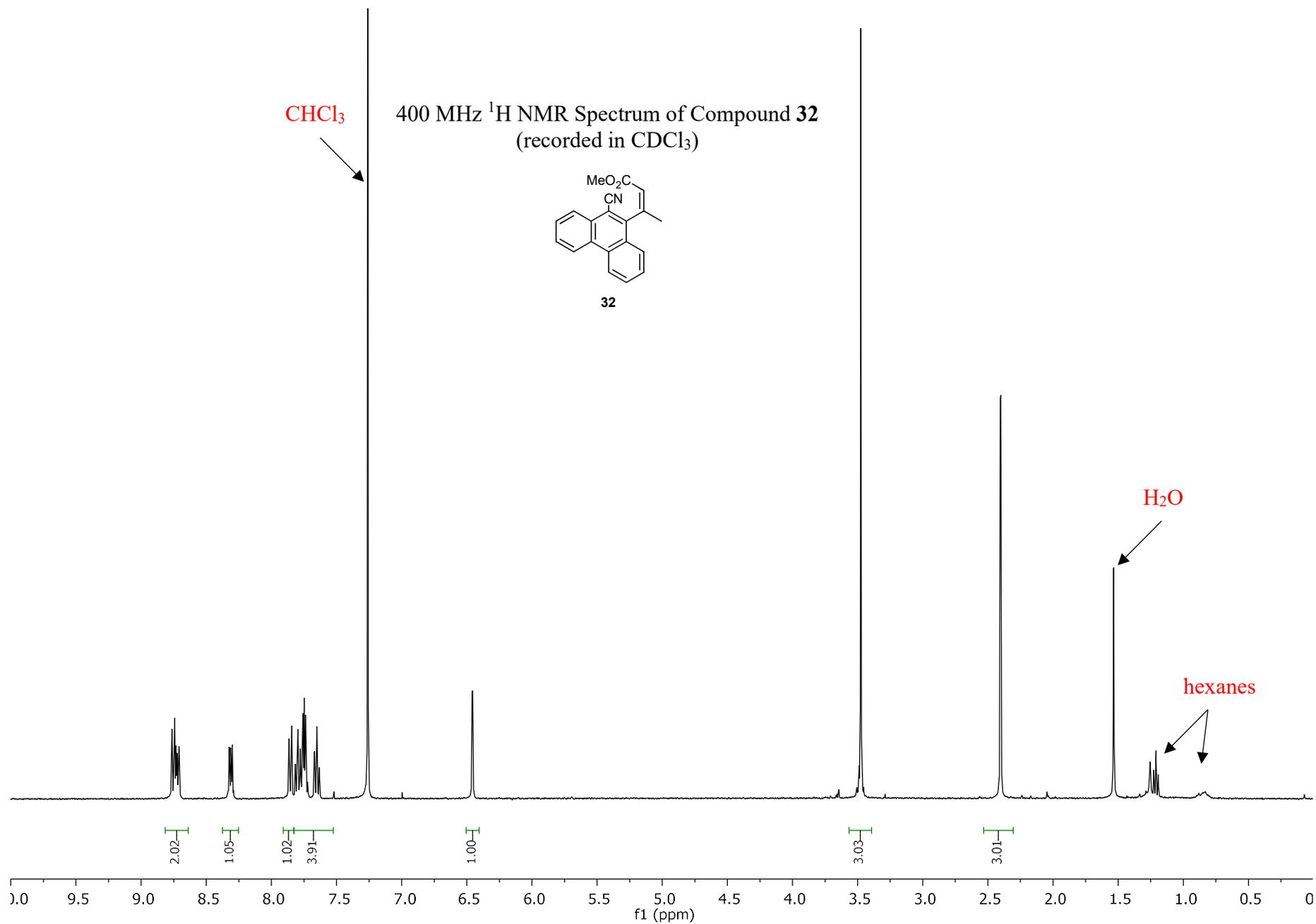


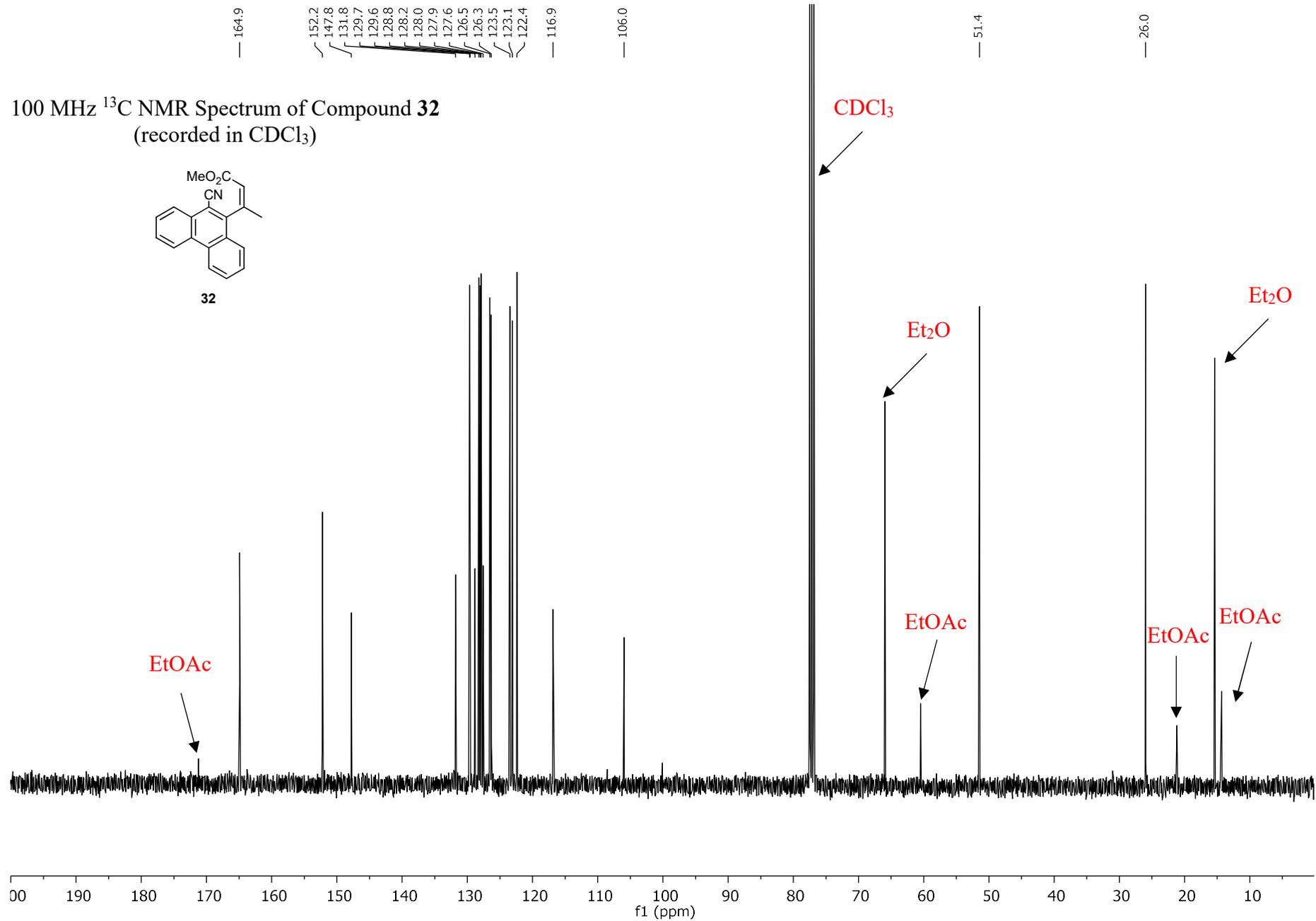
400 MHz ^1H NMR Spectrum of Compound **31**
(recorded in CDCl_3)



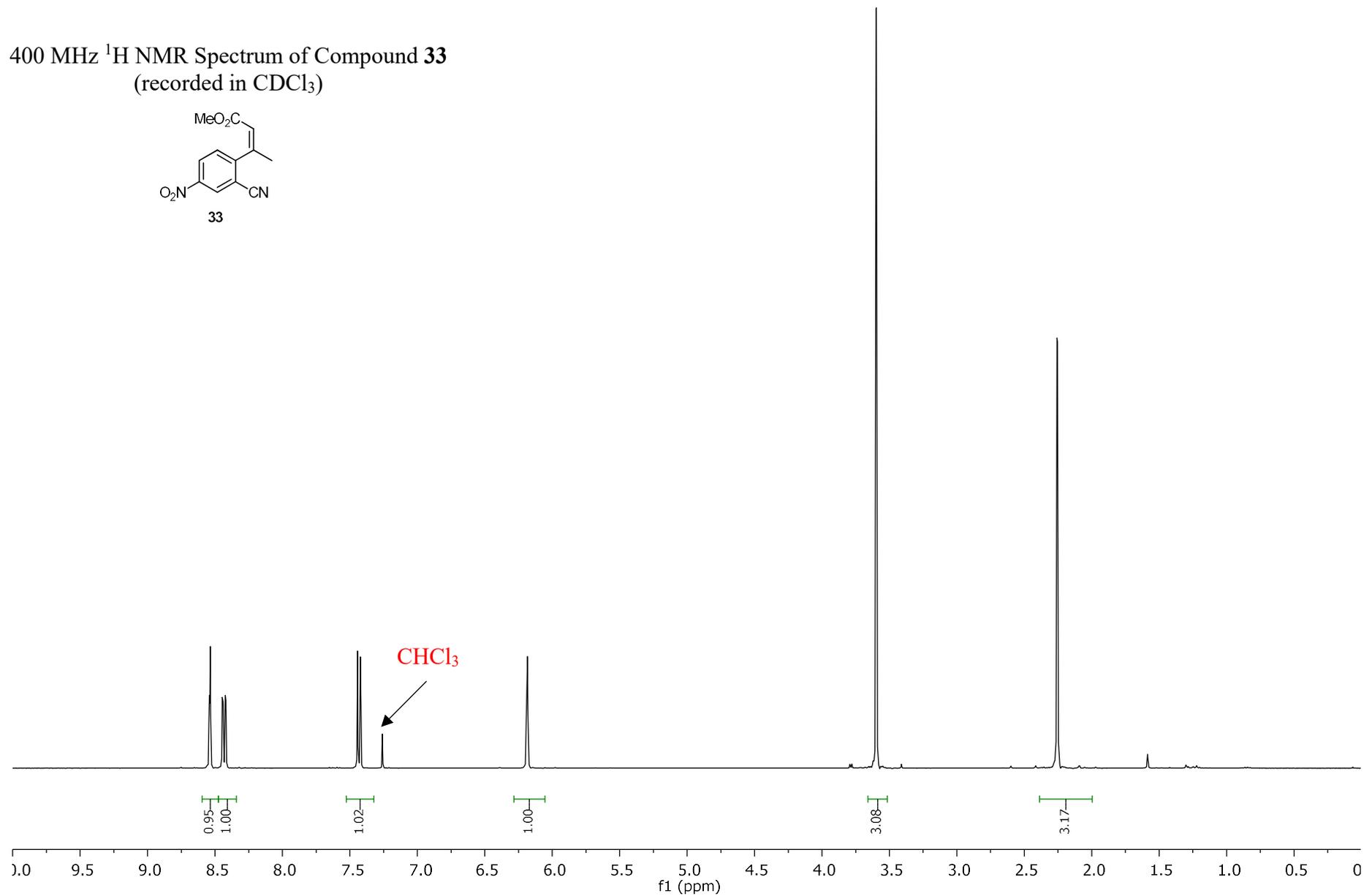
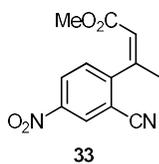
100 MHz ^{13}C NMR Spectrum of Compound **31**
(recorded in CDCl_3)



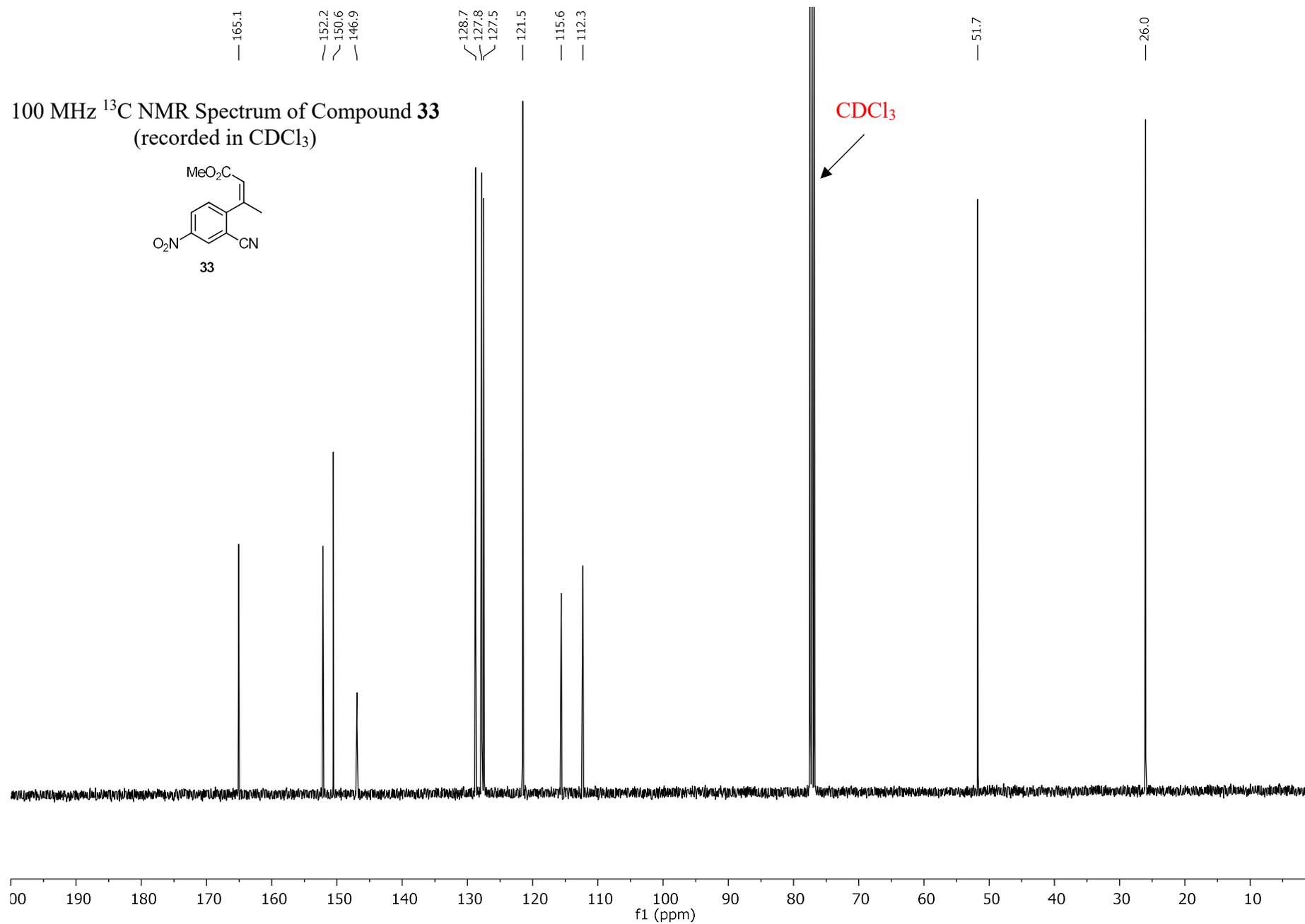
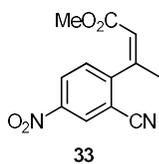




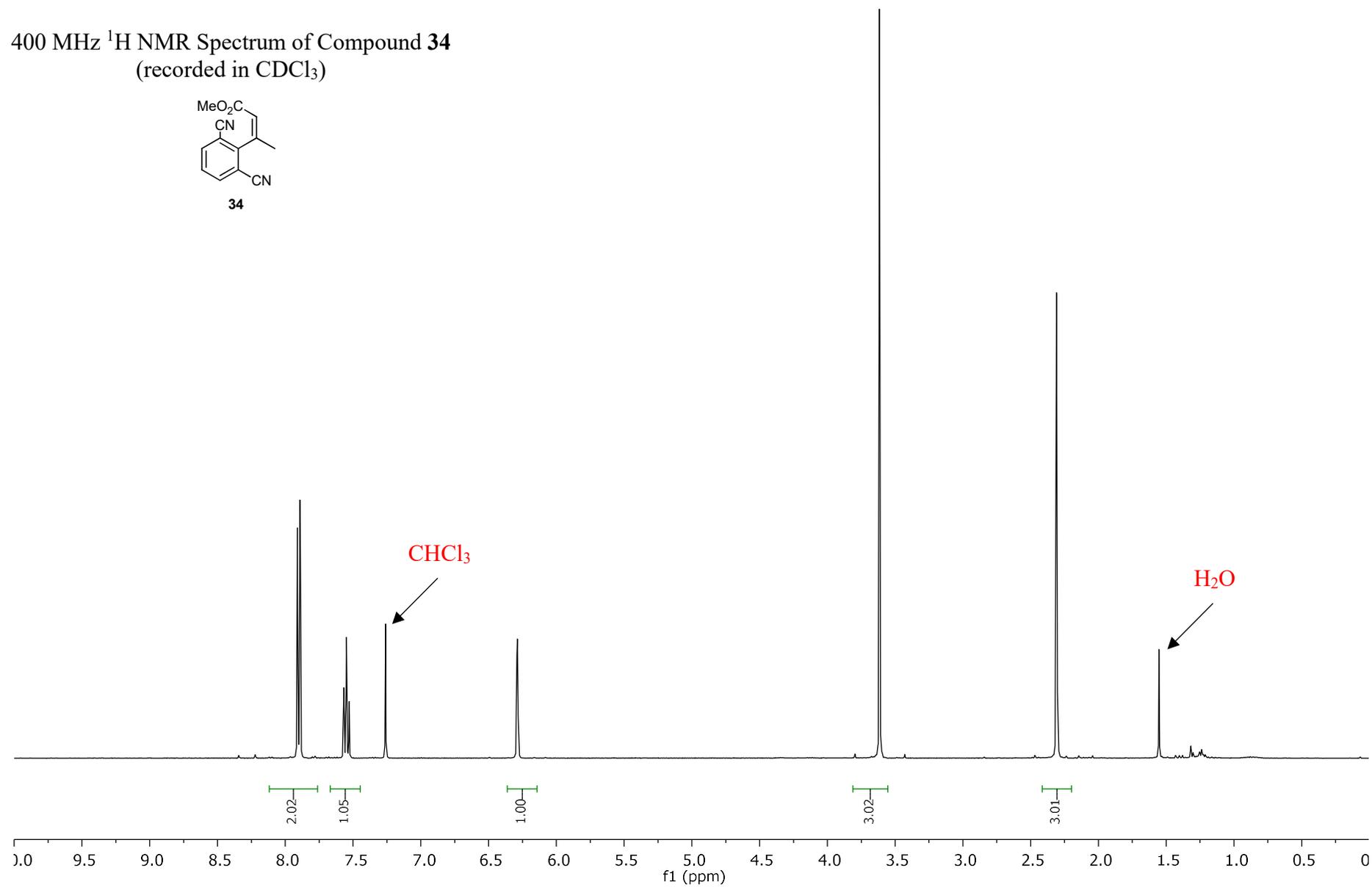
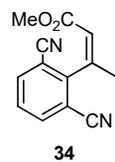
400 MHz ^1H NMR Spectrum of Compound **33**
(recorded in CDCl_3)



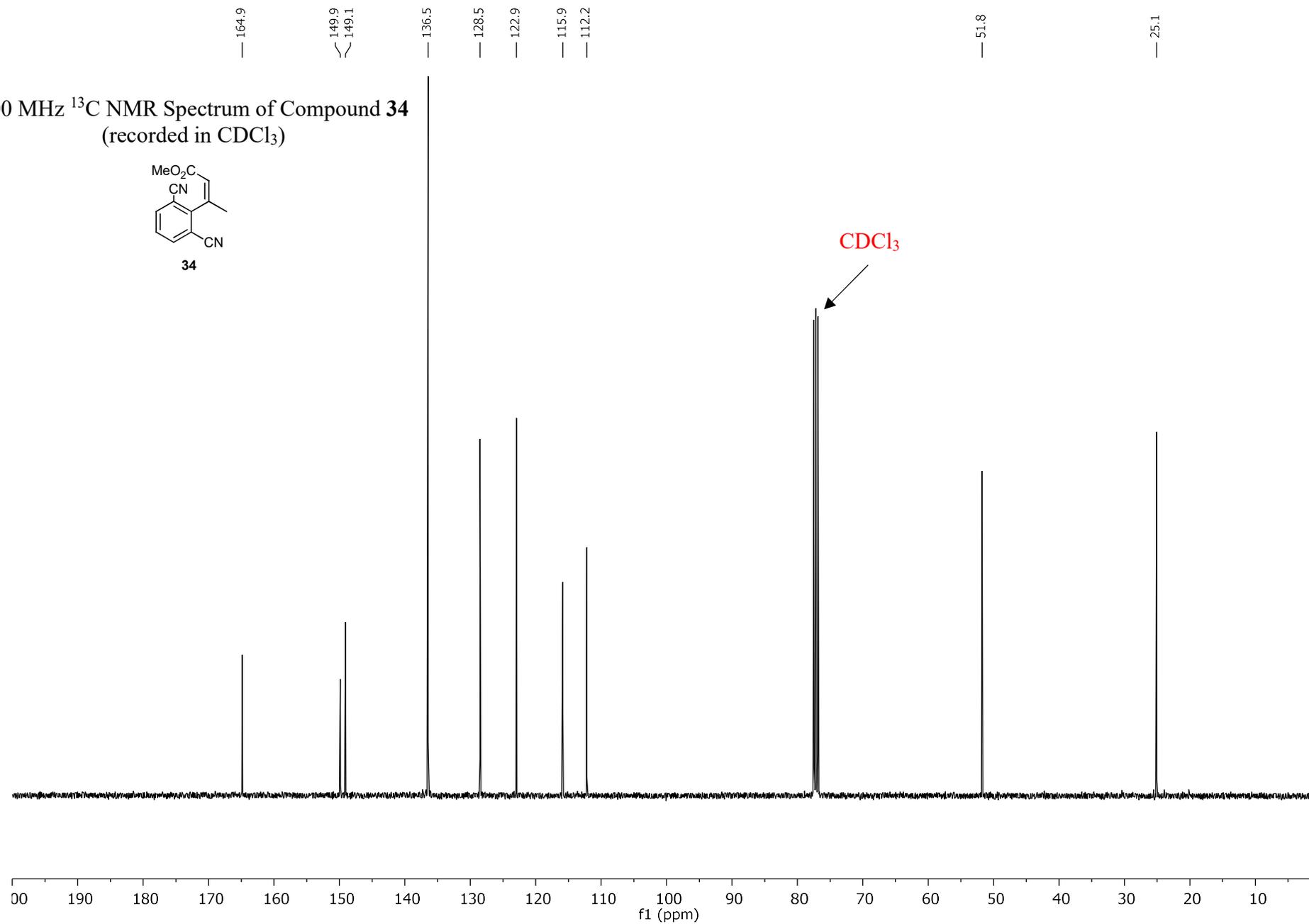
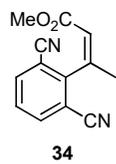
100 MHz ^{13}C NMR Spectrum of Compound **33**
(recorded in CDCl_3)



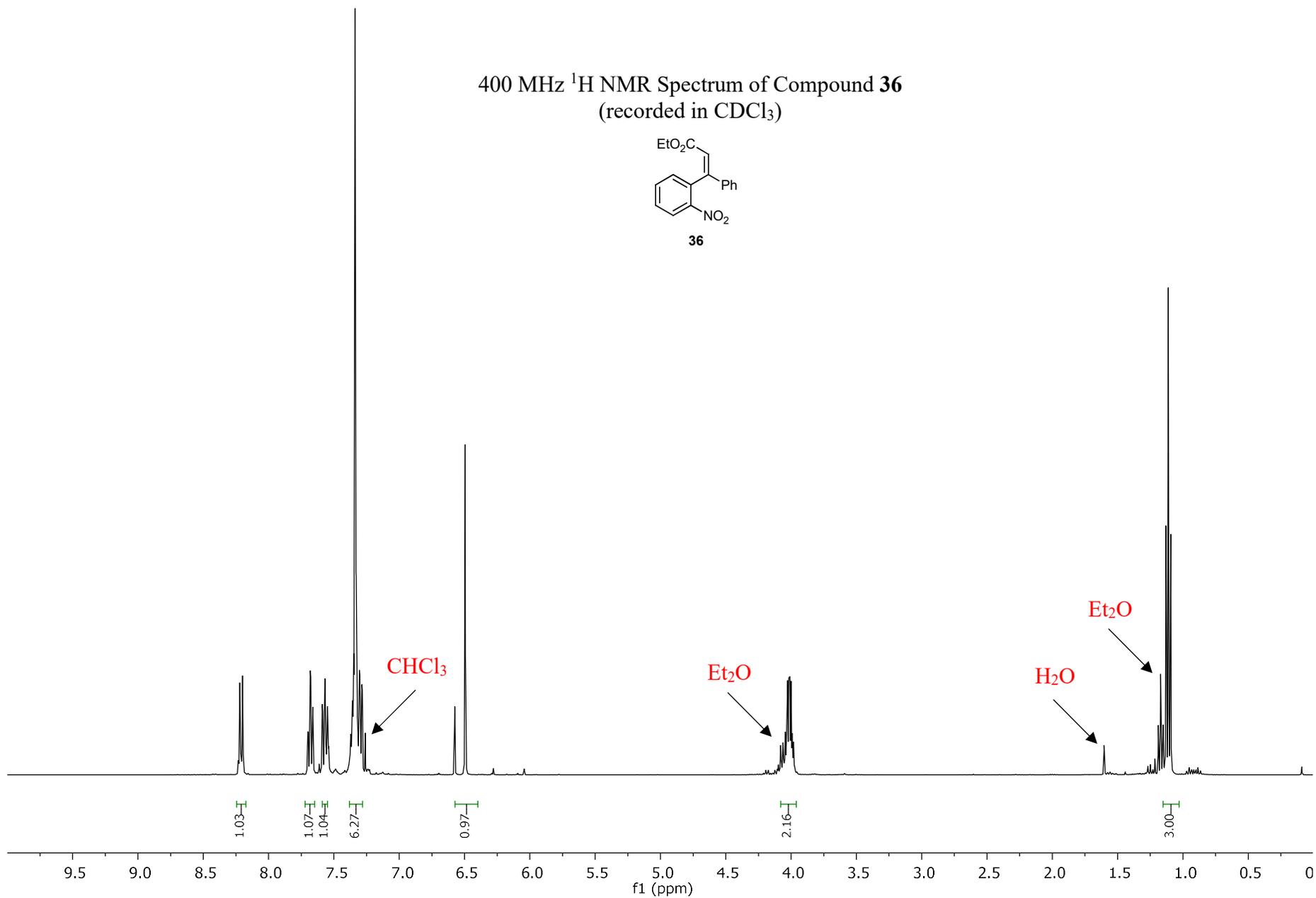
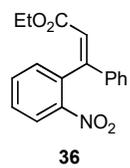
400 MHz ^1H NMR Spectrum of Compound **34**
(recorded in CDCl_3)

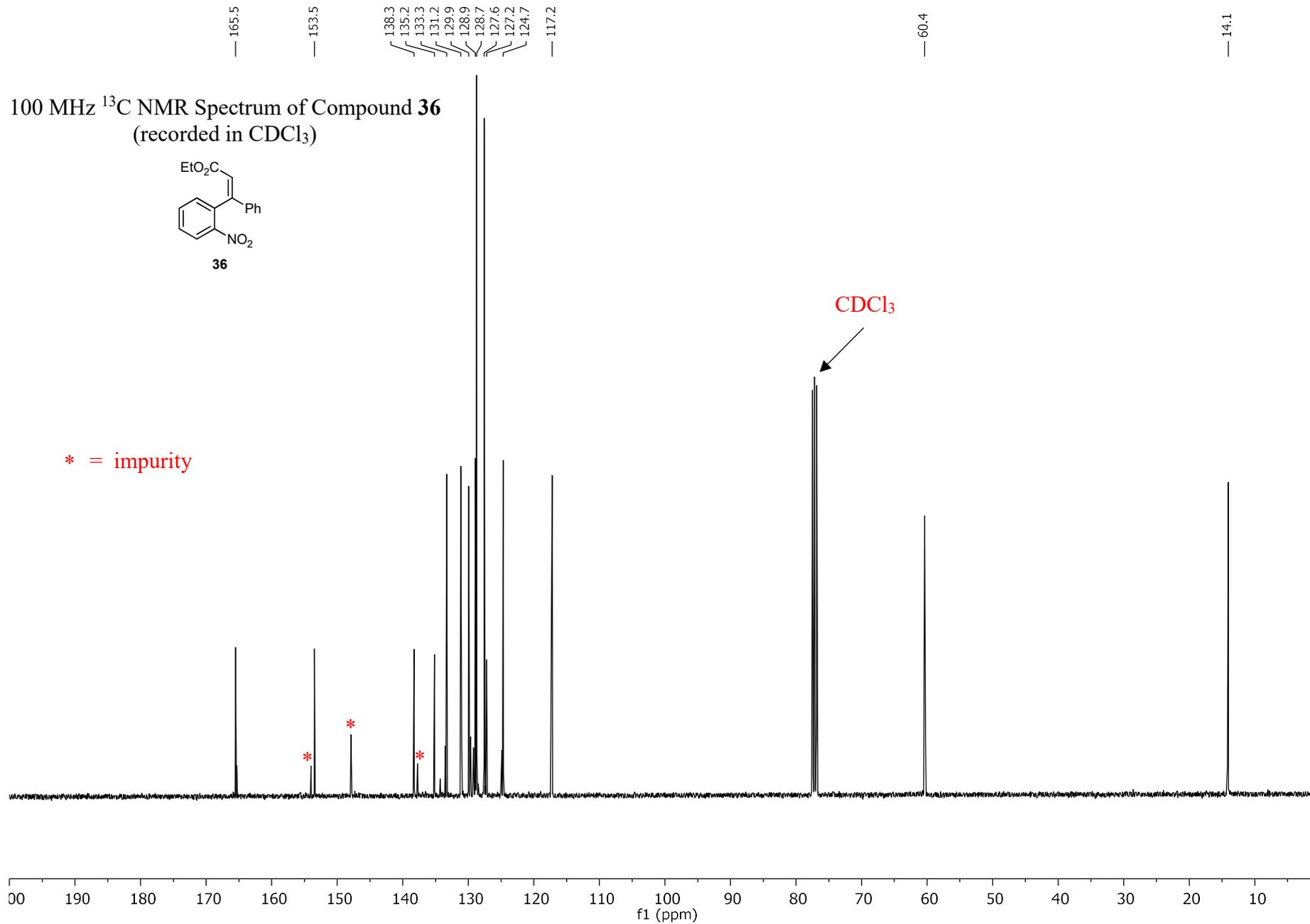


100 MHz ^{13}C NMR Spectrum of Compound **34**
(recorded in CDCl_3)

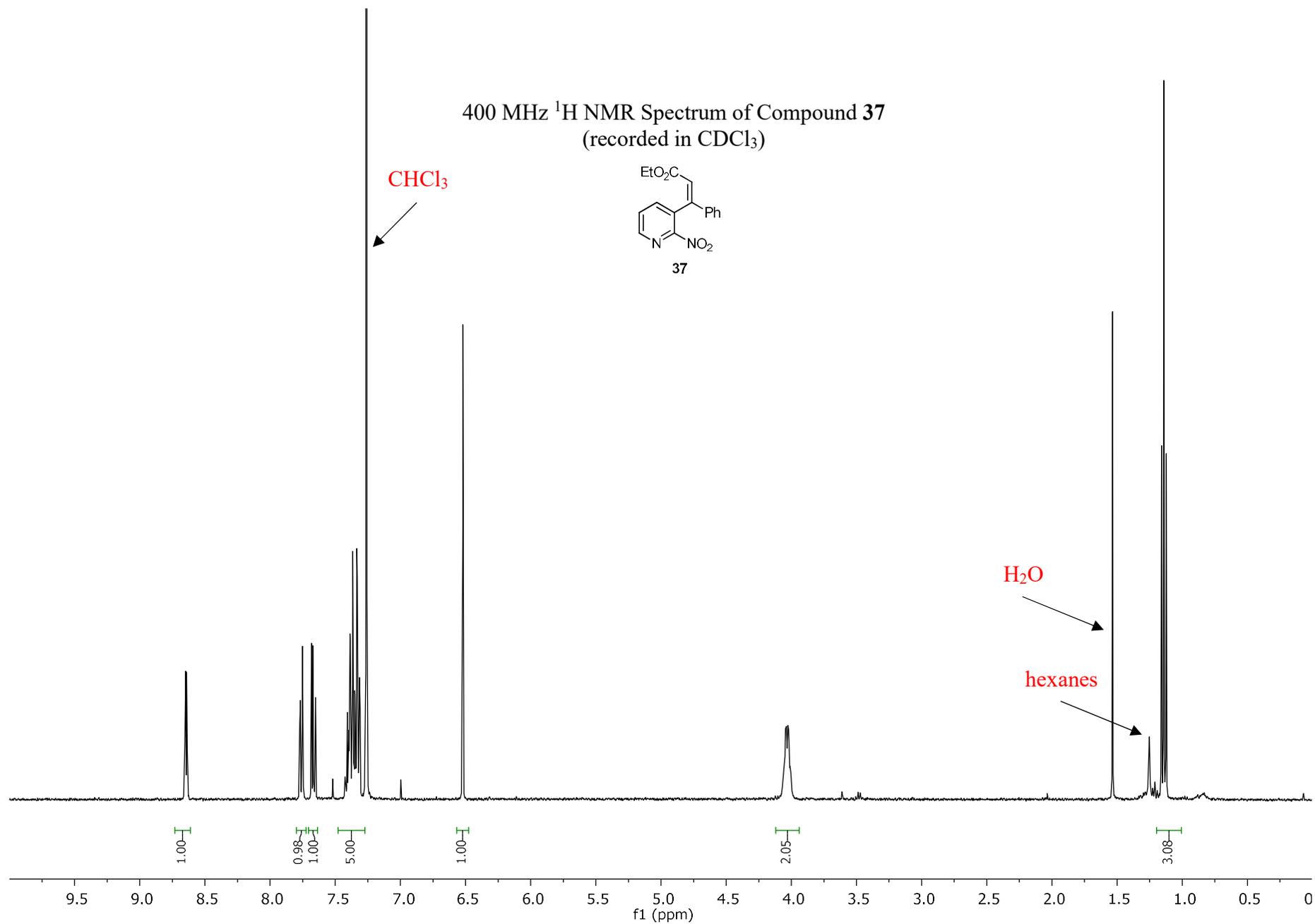
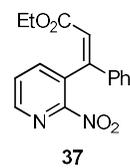


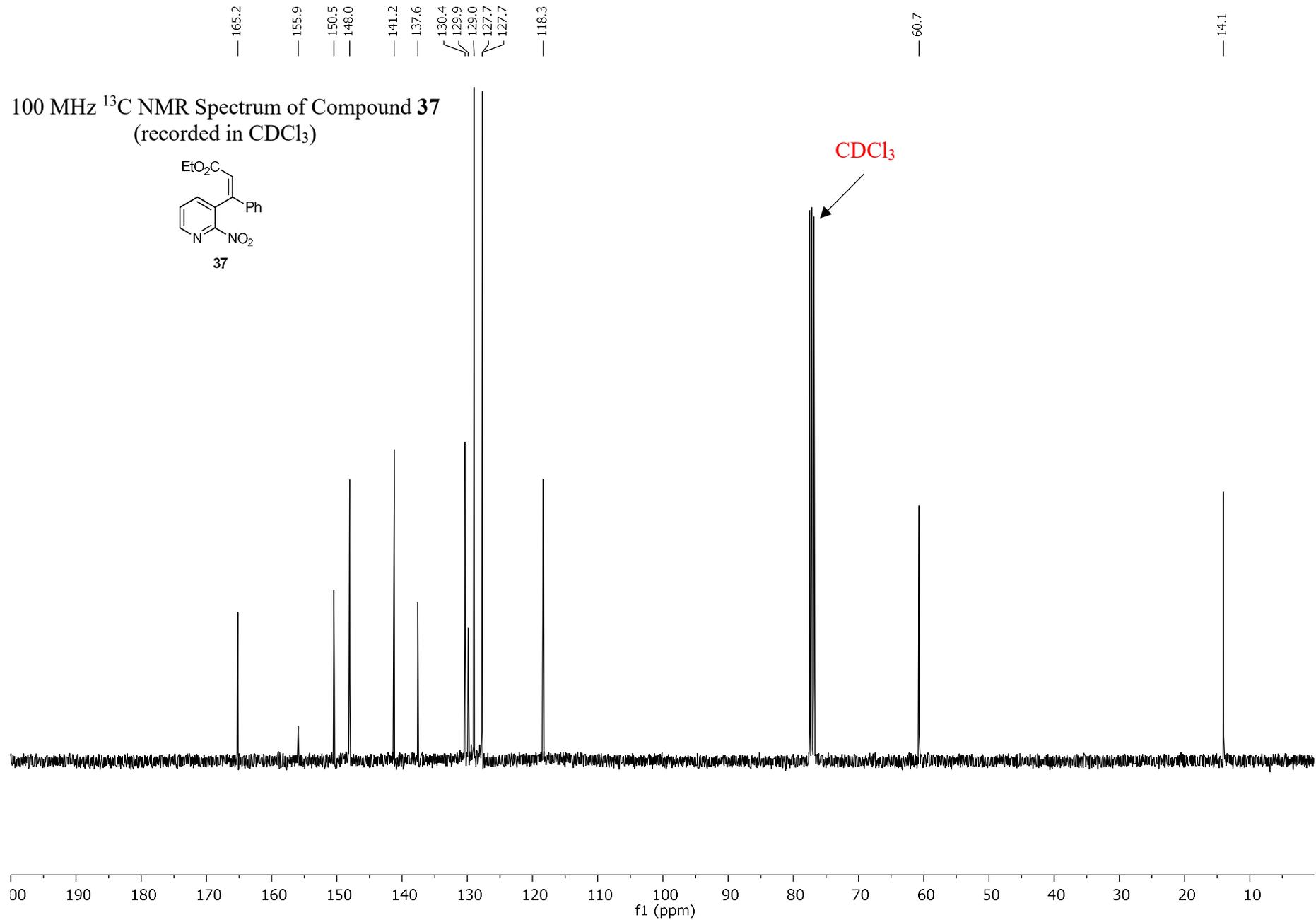
400 MHz ^1H NMR Spectrum of Compound **36**
(recorded in CDCl_3)



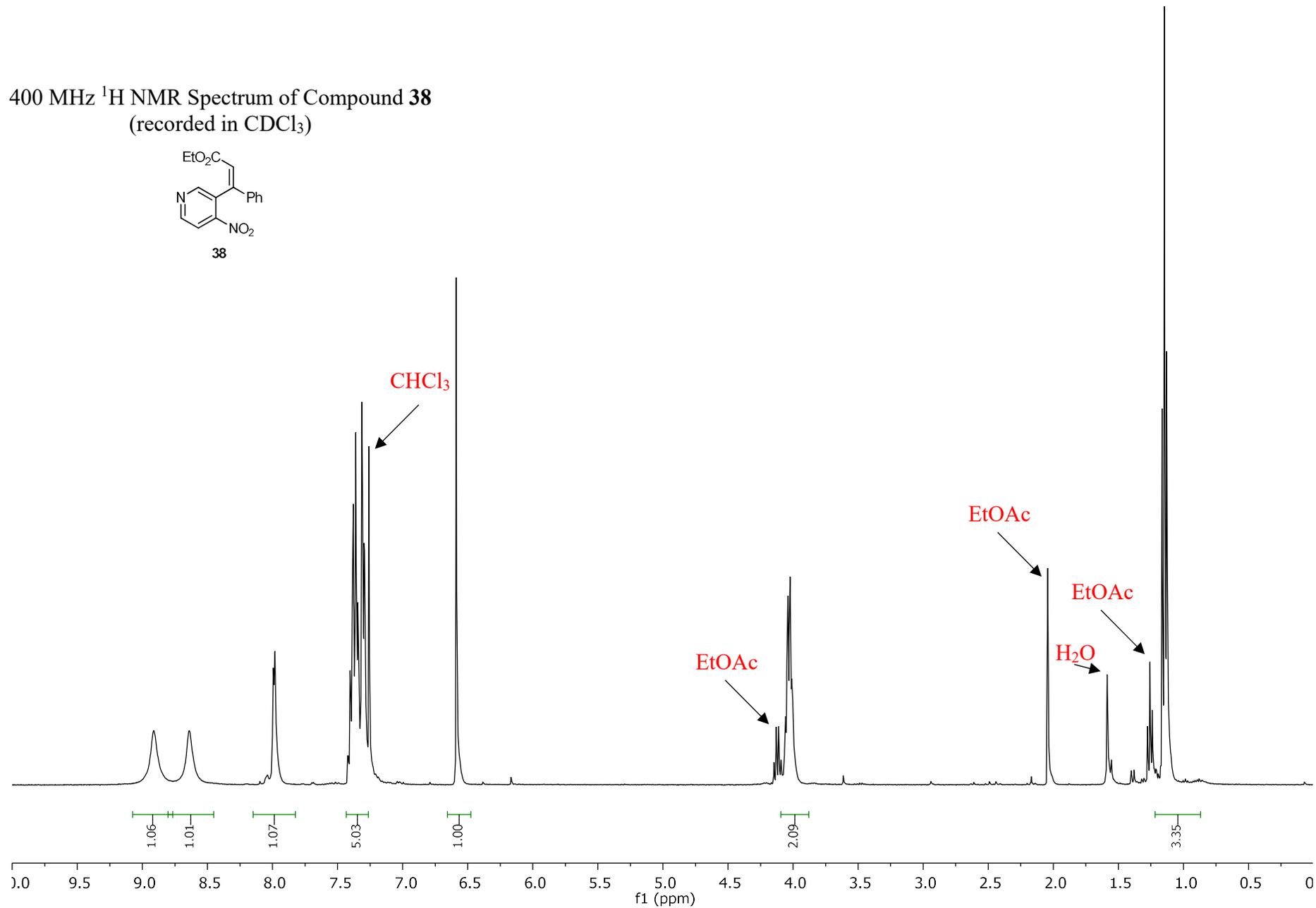
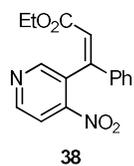


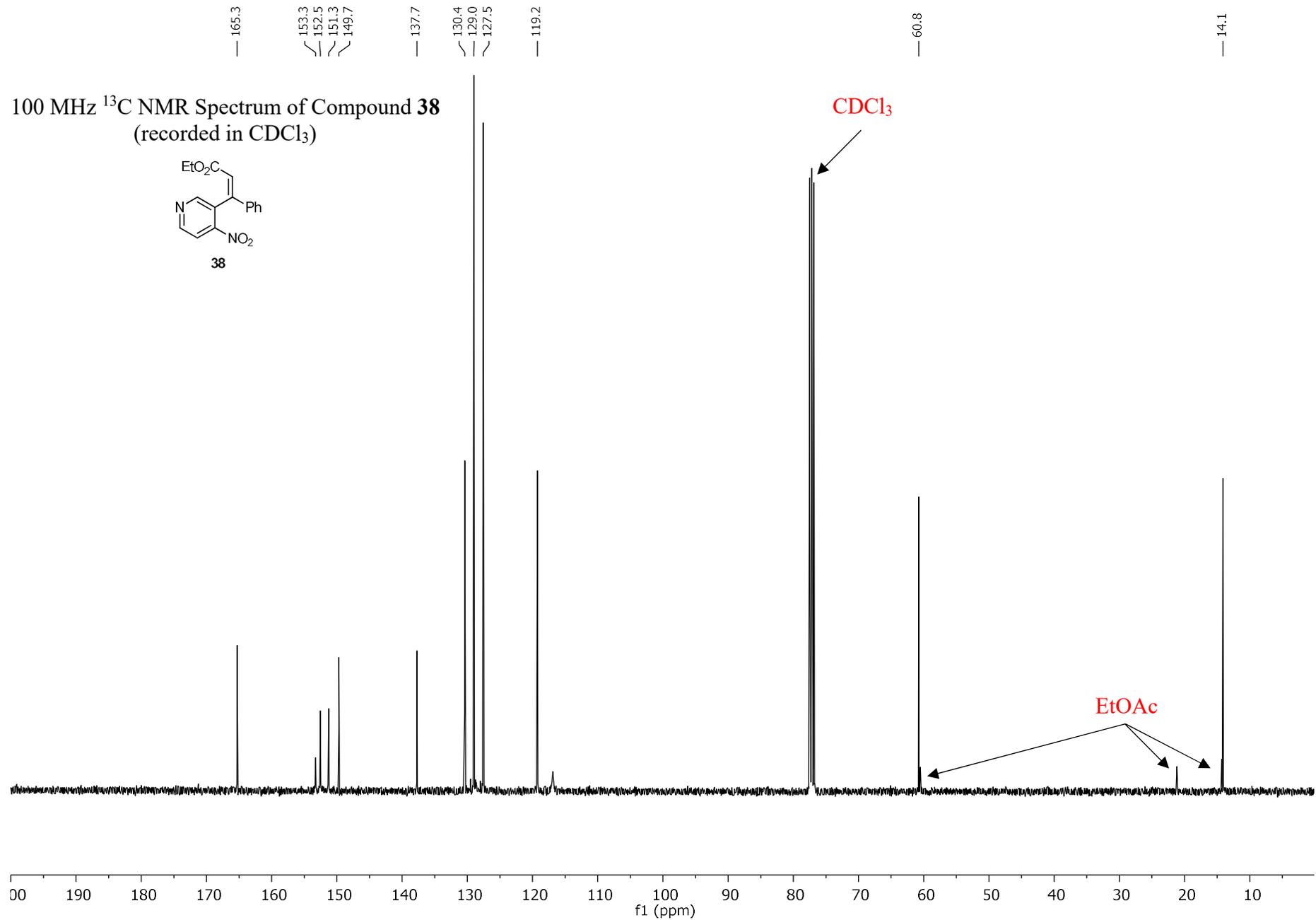
400 MHz ^1H NMR Spectrum of Compound **37**
(recorded in CDCl_3)



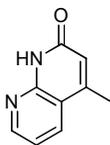


400 MHz ^1H NMR Spectrum of Compound **38**
(recorded in CDCl_3)





400 MHz ^1H NMR Spectrum of Compound **39**
(recorded in CDCl_3)



39

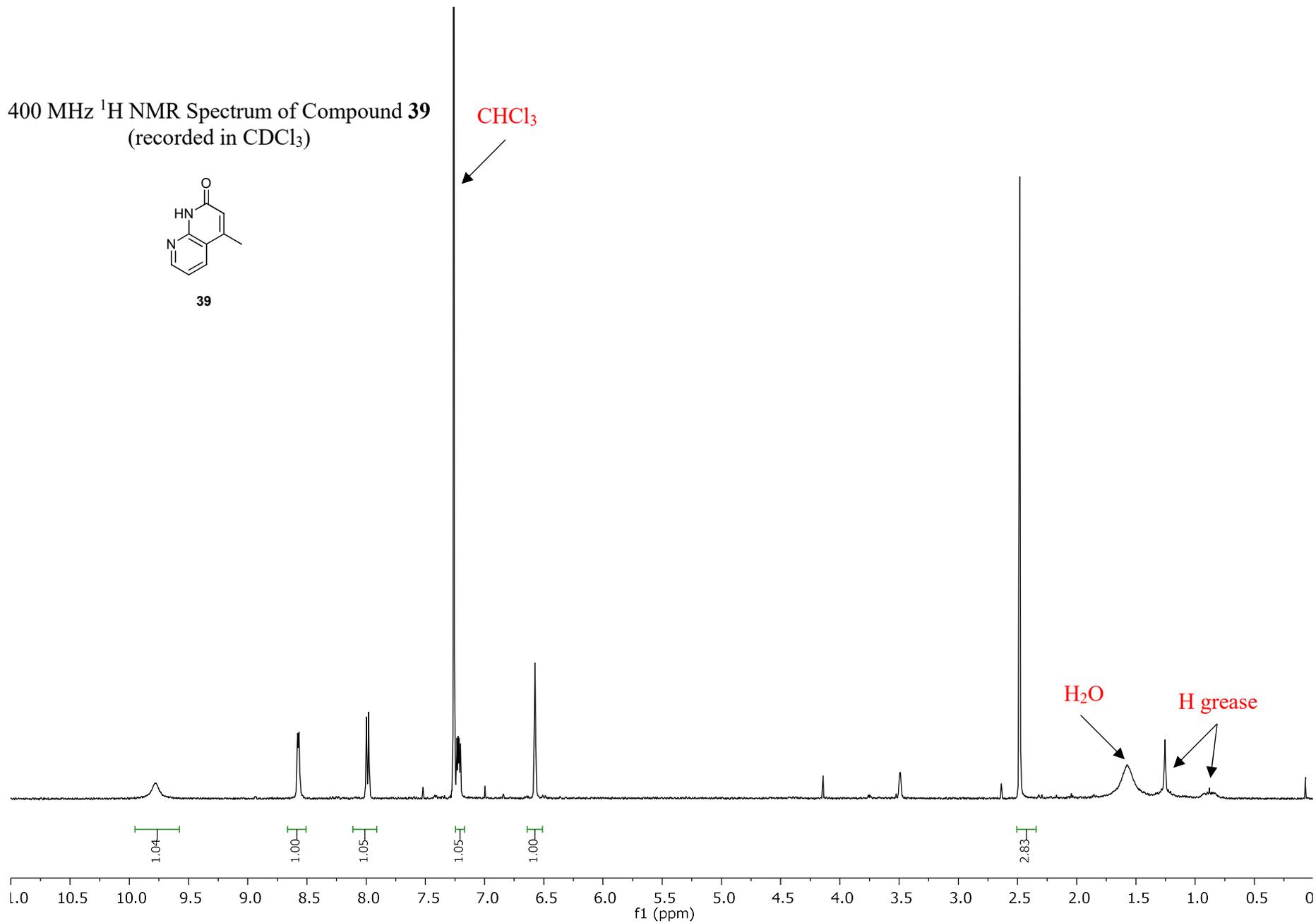
CHCl_3

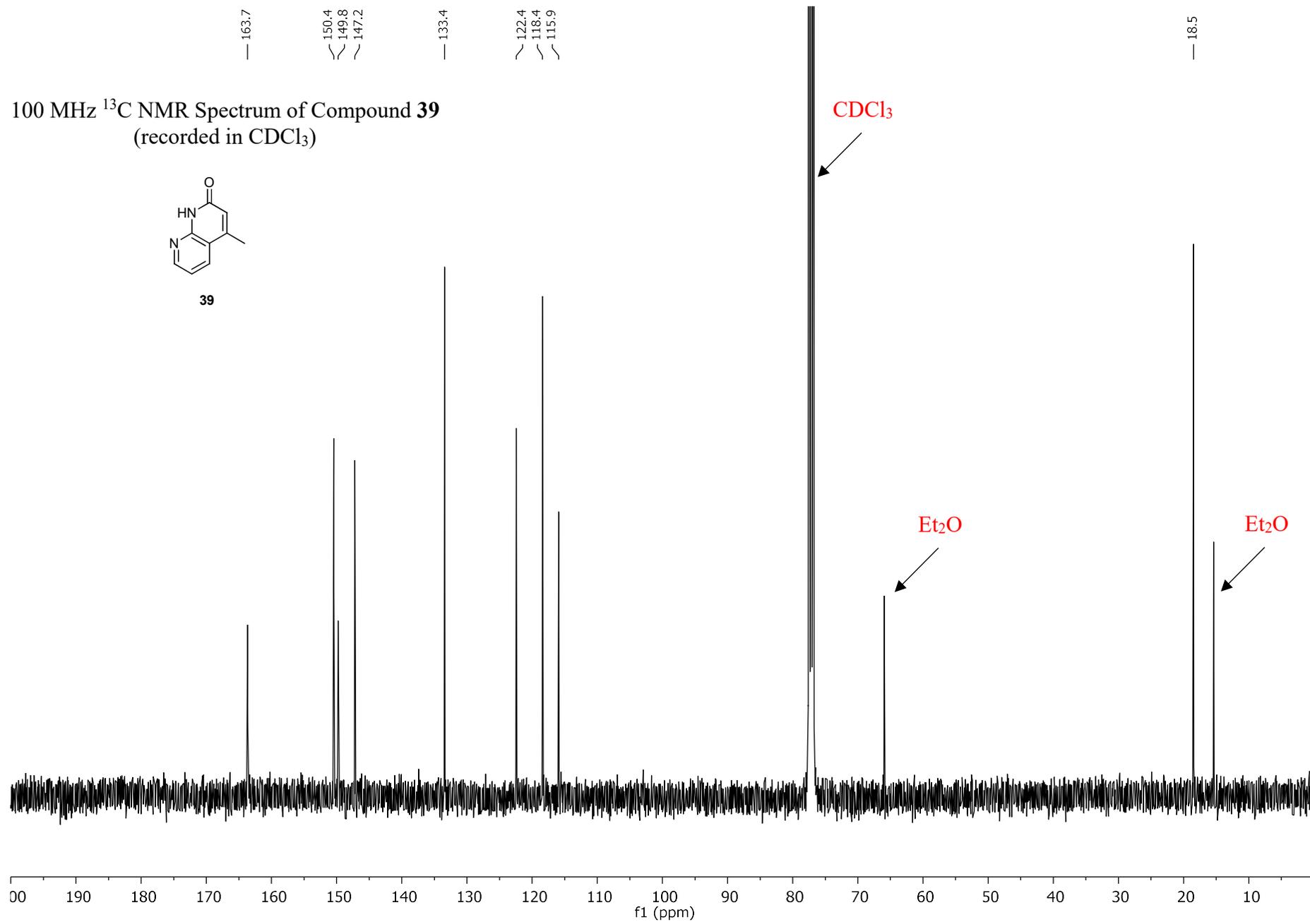


H_2O

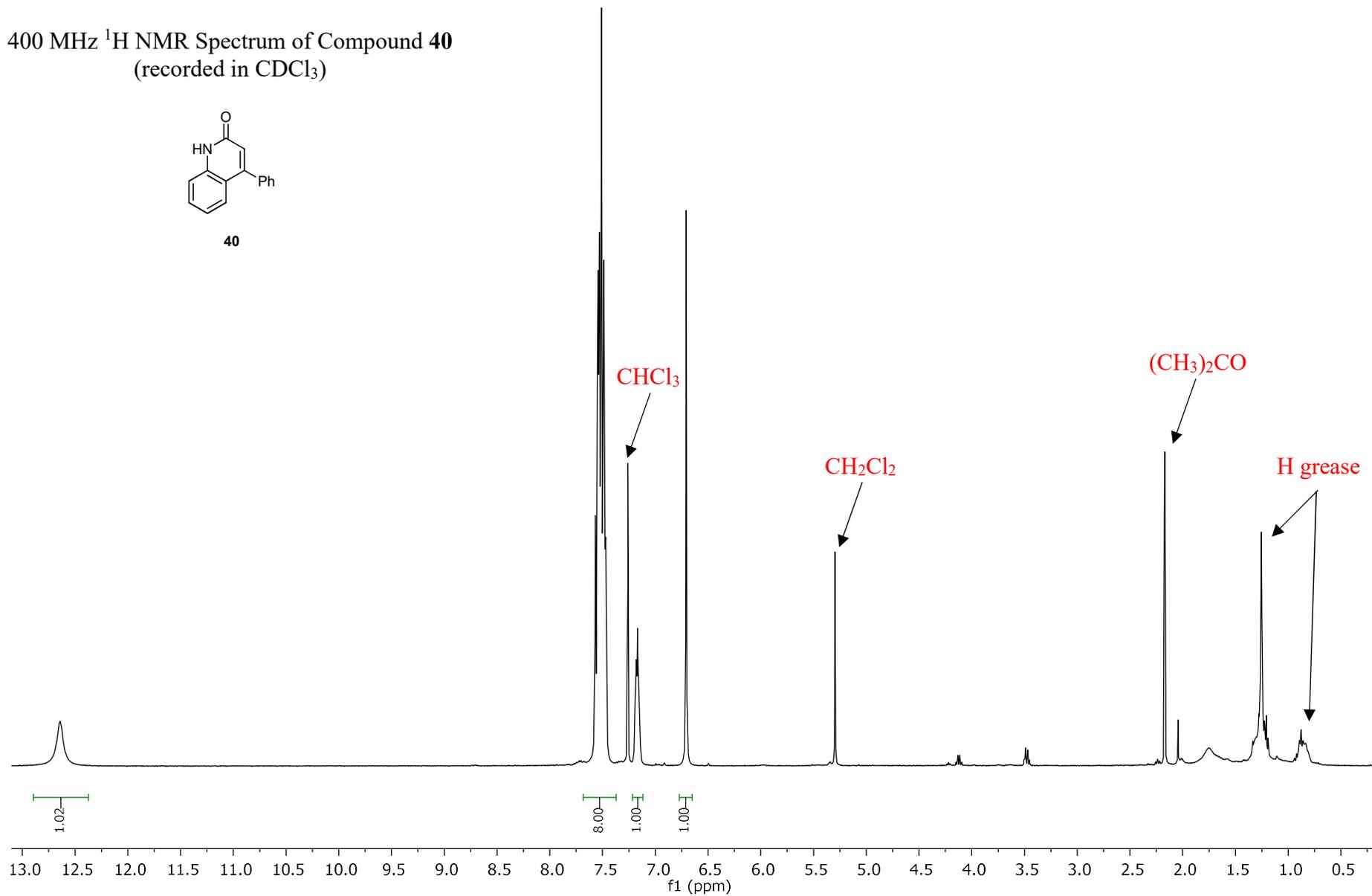
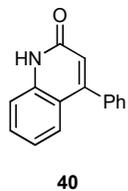


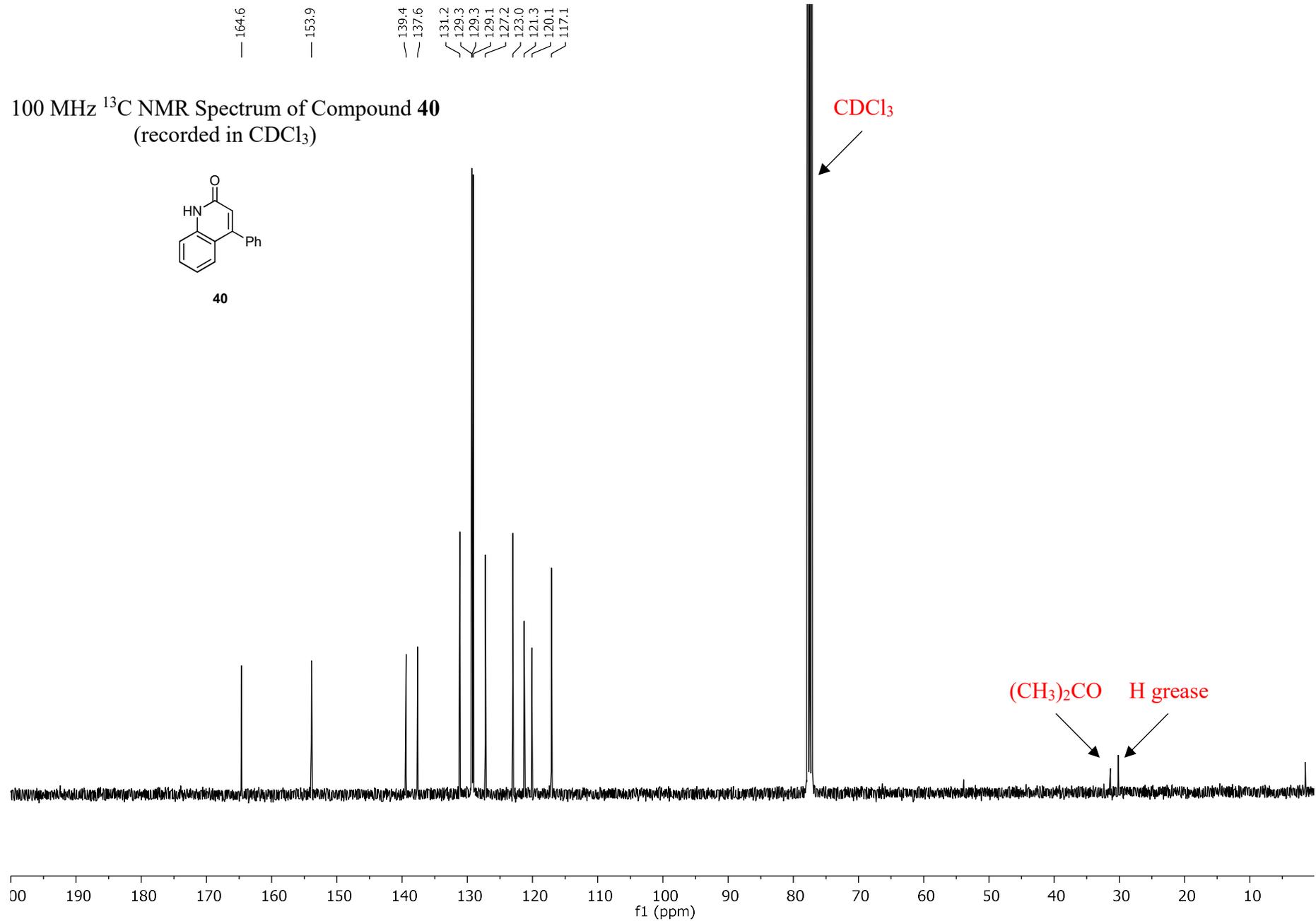
H grease





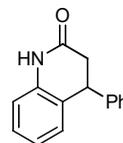
400 MHz ^1H NMR Spectrum of Compound **40**
(recorded in CDCl_3)





CHCl₃

400 MHz ¹H NMR Spectrum of Compound 41
(recorded in CDCl₃)

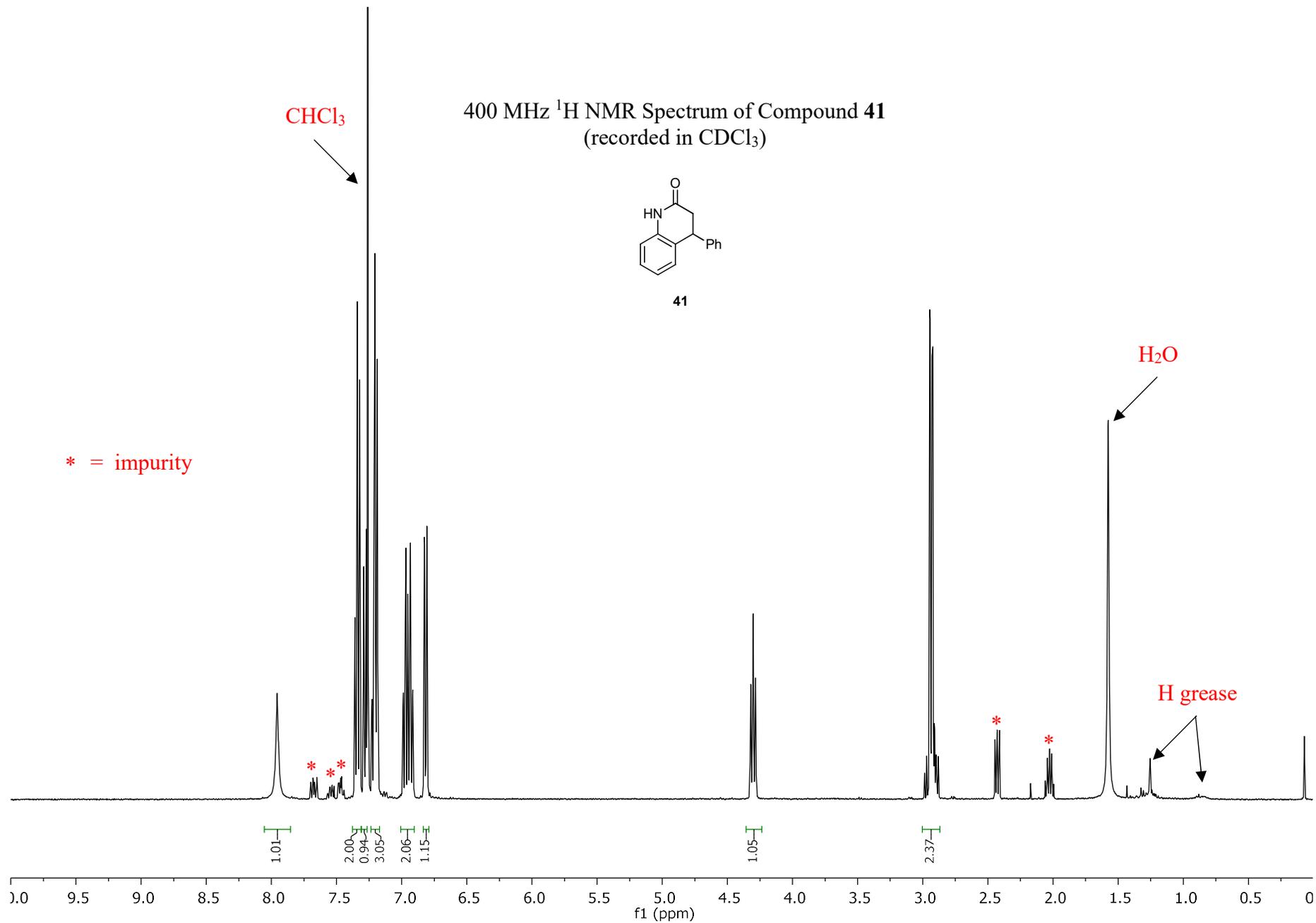


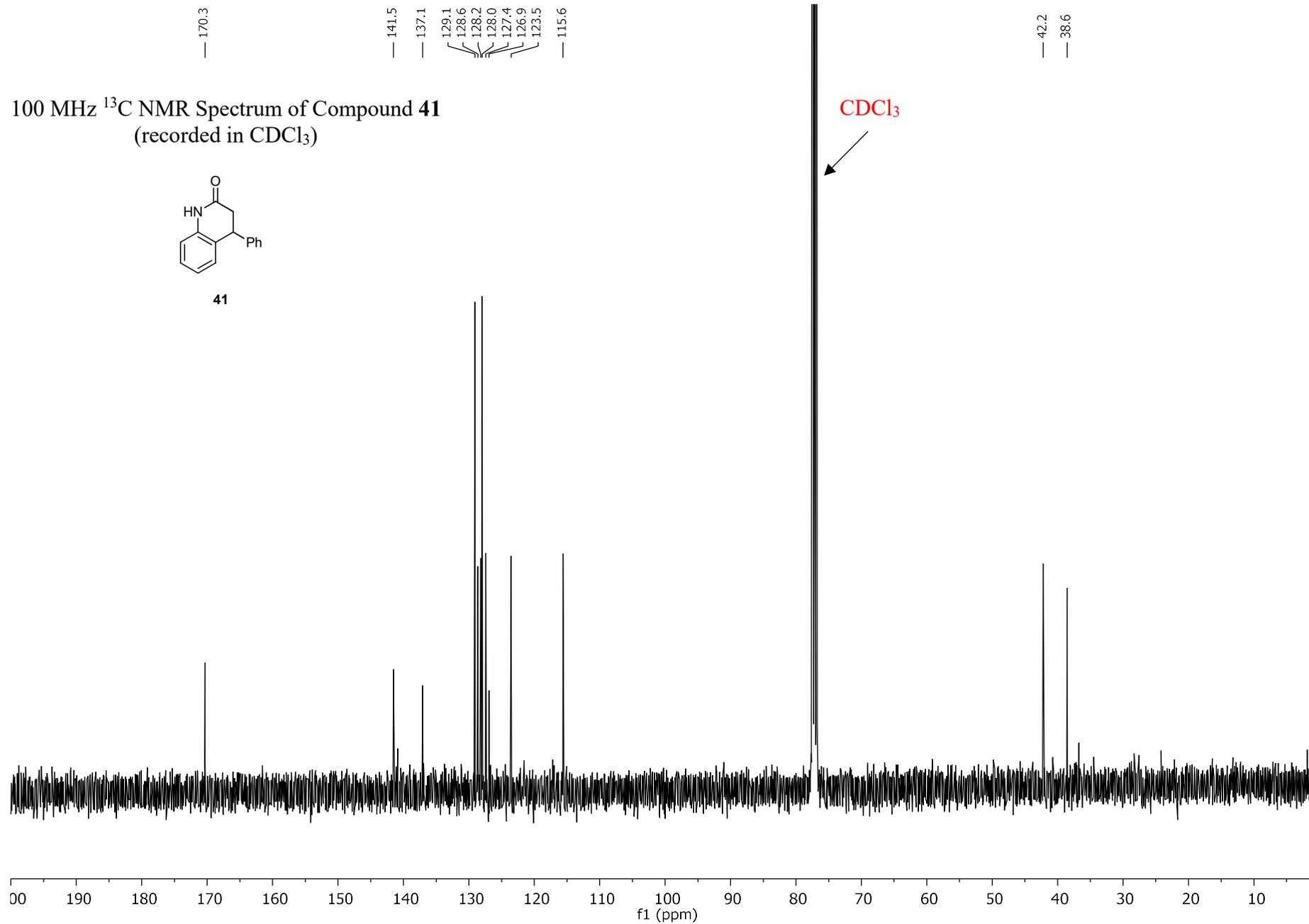
41

H₂O

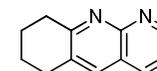
* = impurity

H grease

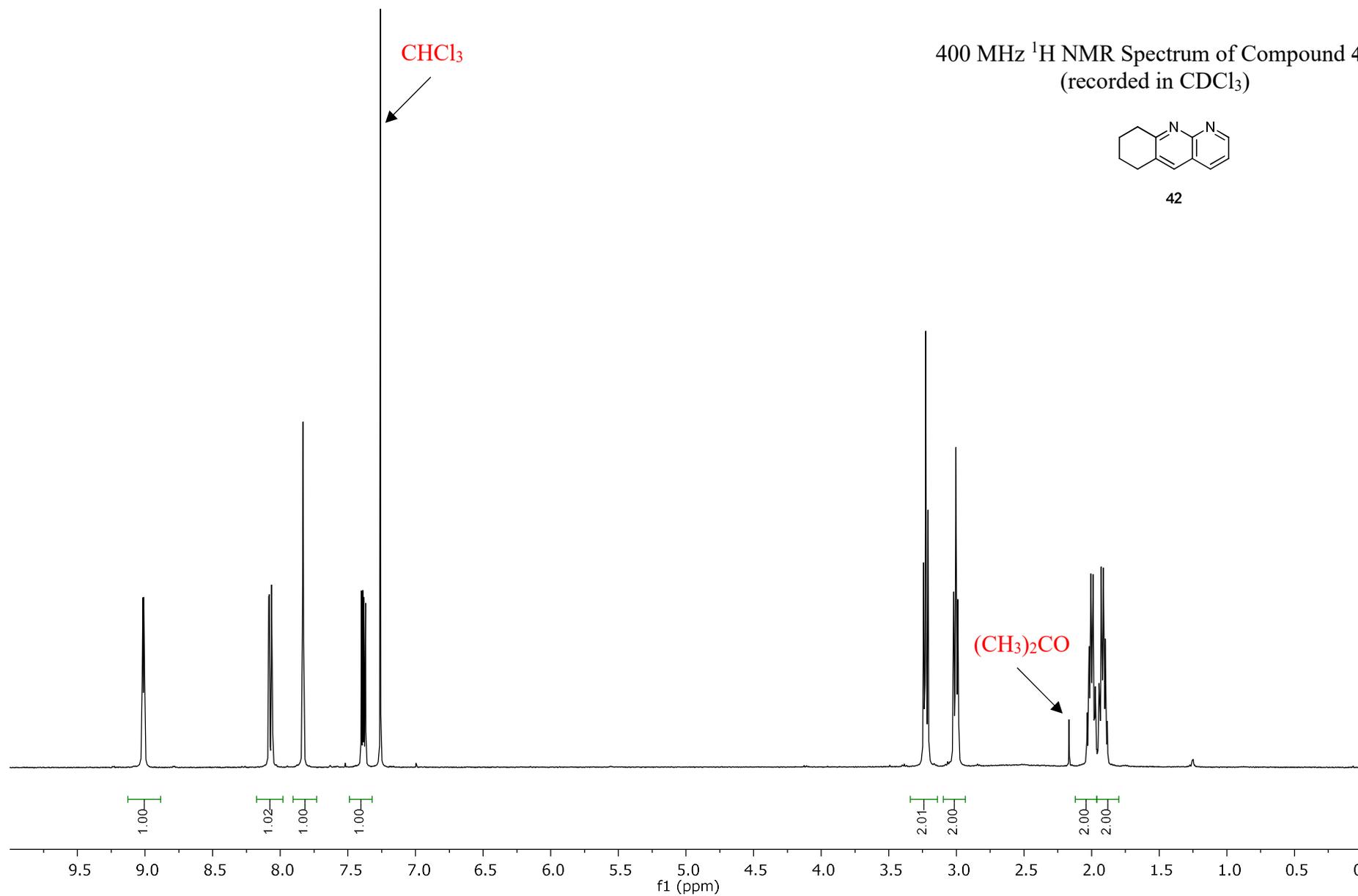




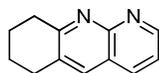
400 MHz ^1H NMR Spectrum of Compound **42**
(recorded in CDCl_3)



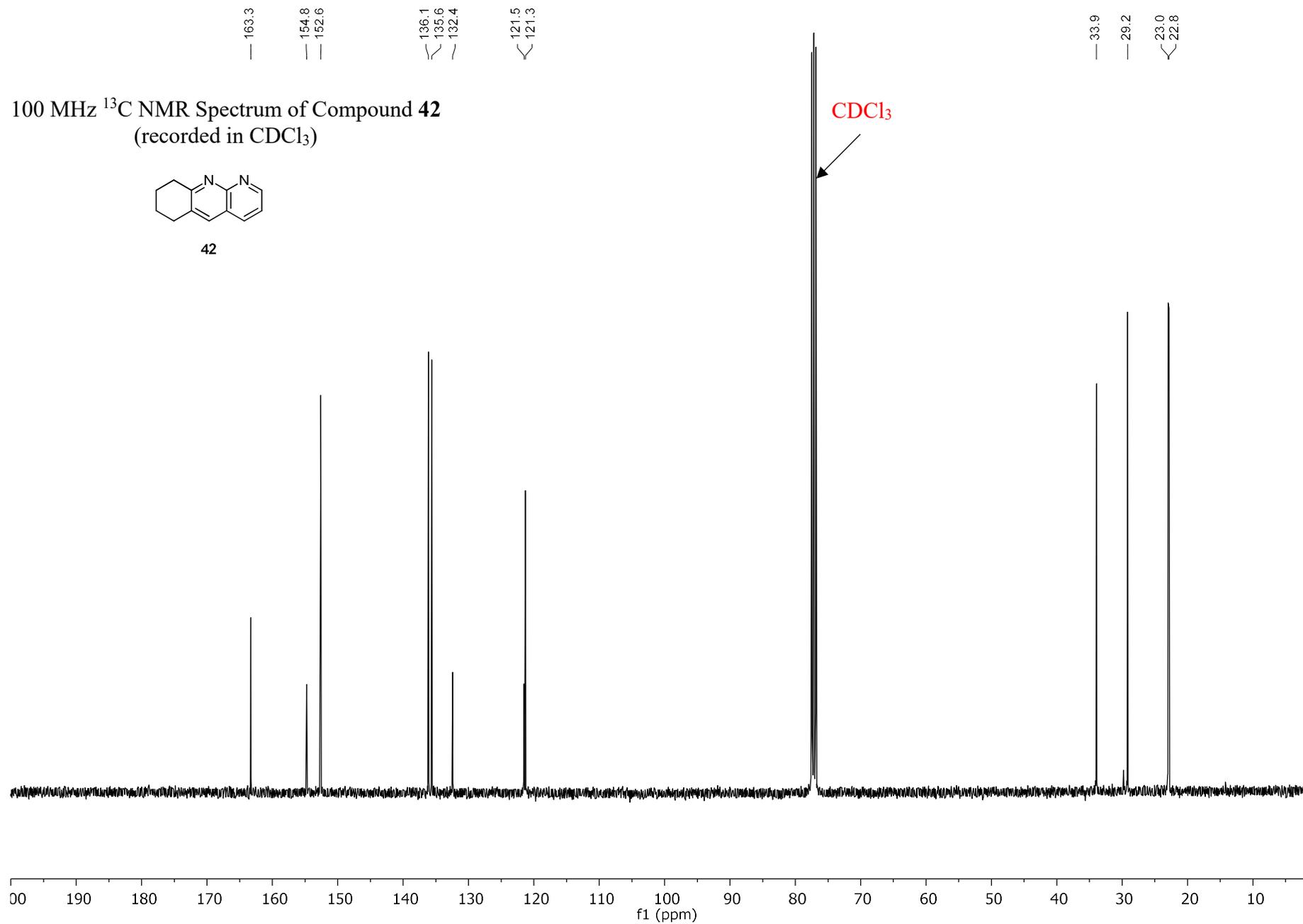
42



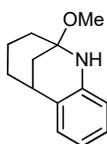
100 MHz ^{13}C NMR Spectrum of Compound **42**
(recorded in CDCl_3)



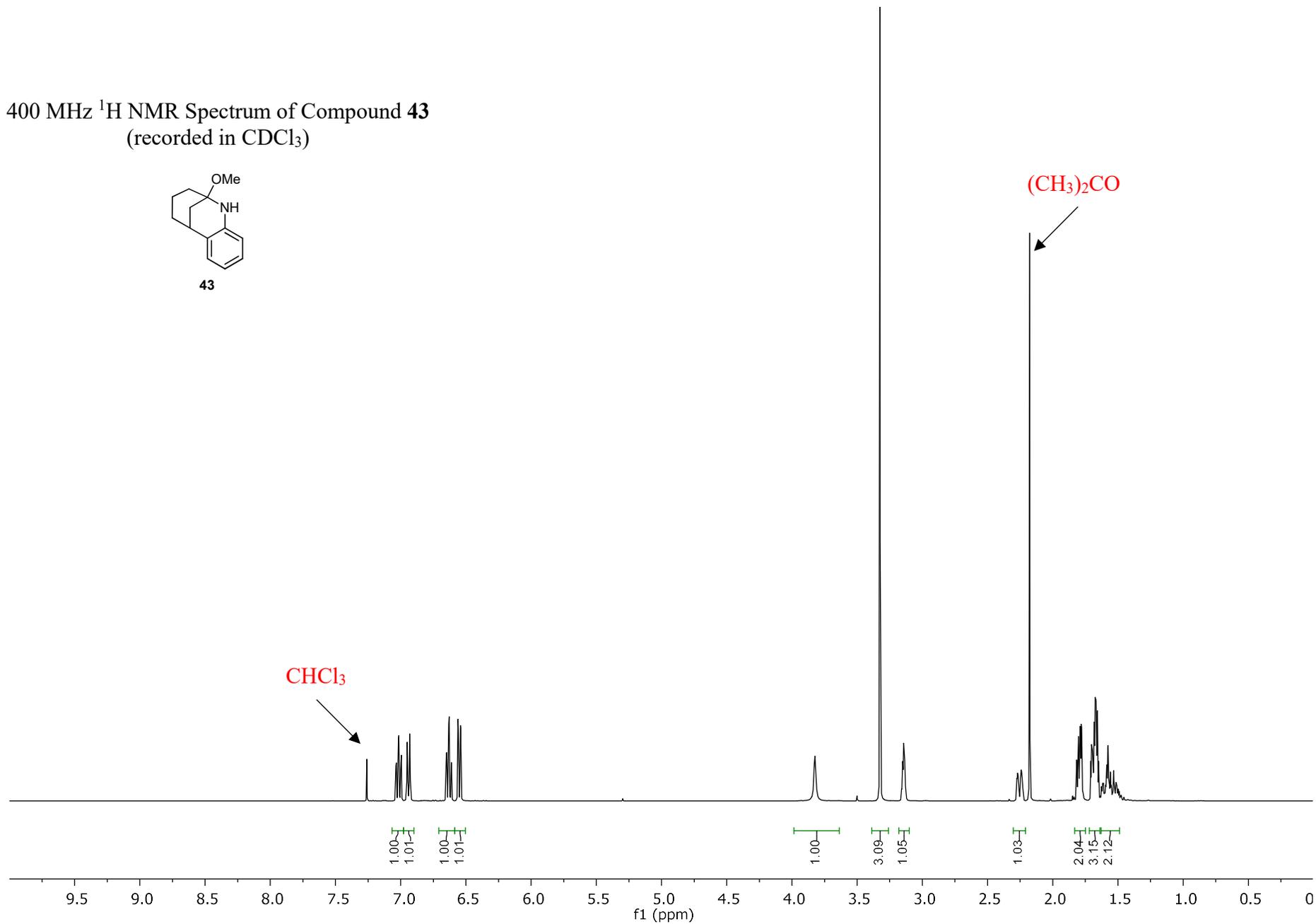
42



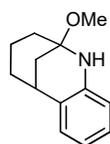
400 MHz ^1H NMR Spectrum of Compound **43**
(recorded in CDCl_3)



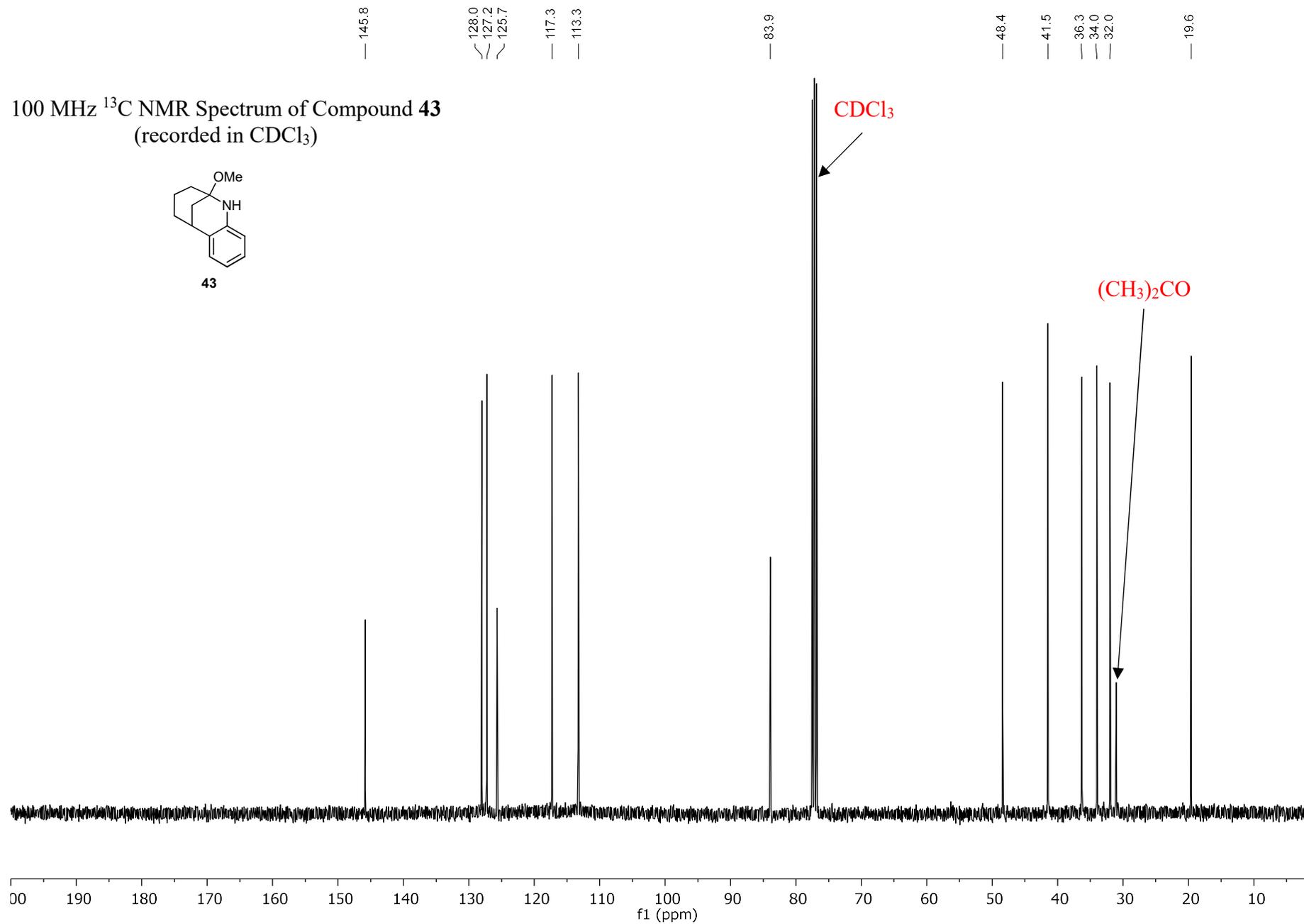
43



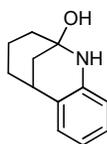
100 MHz ^{13}C NMR Spectrum of Compound **43**
(recorded in CDCl_3)



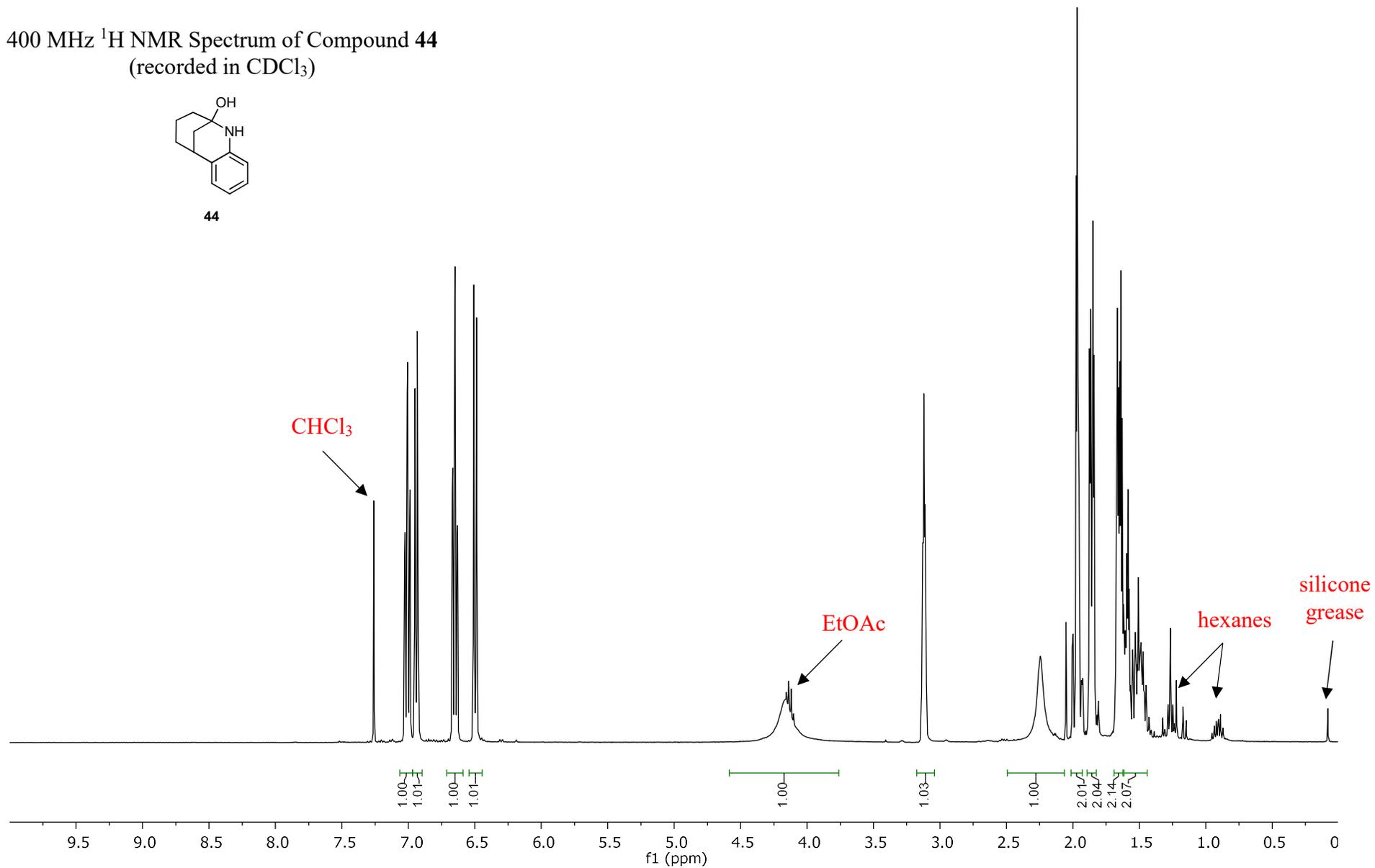
43



400 MHz ^1H NMR Spectrum of Compound 44
(recorded in CDCl_3)

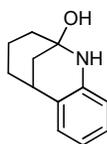


44

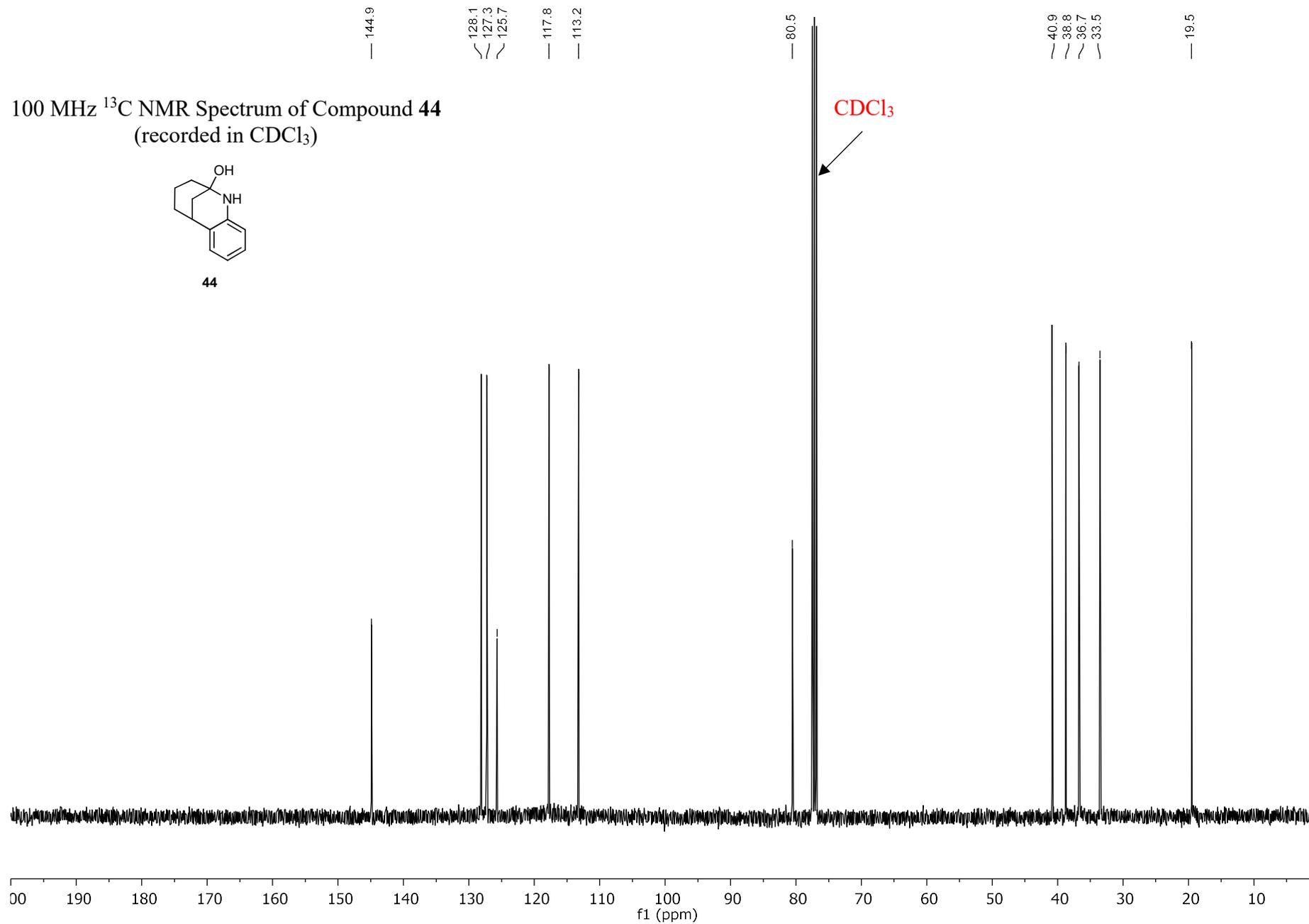


v

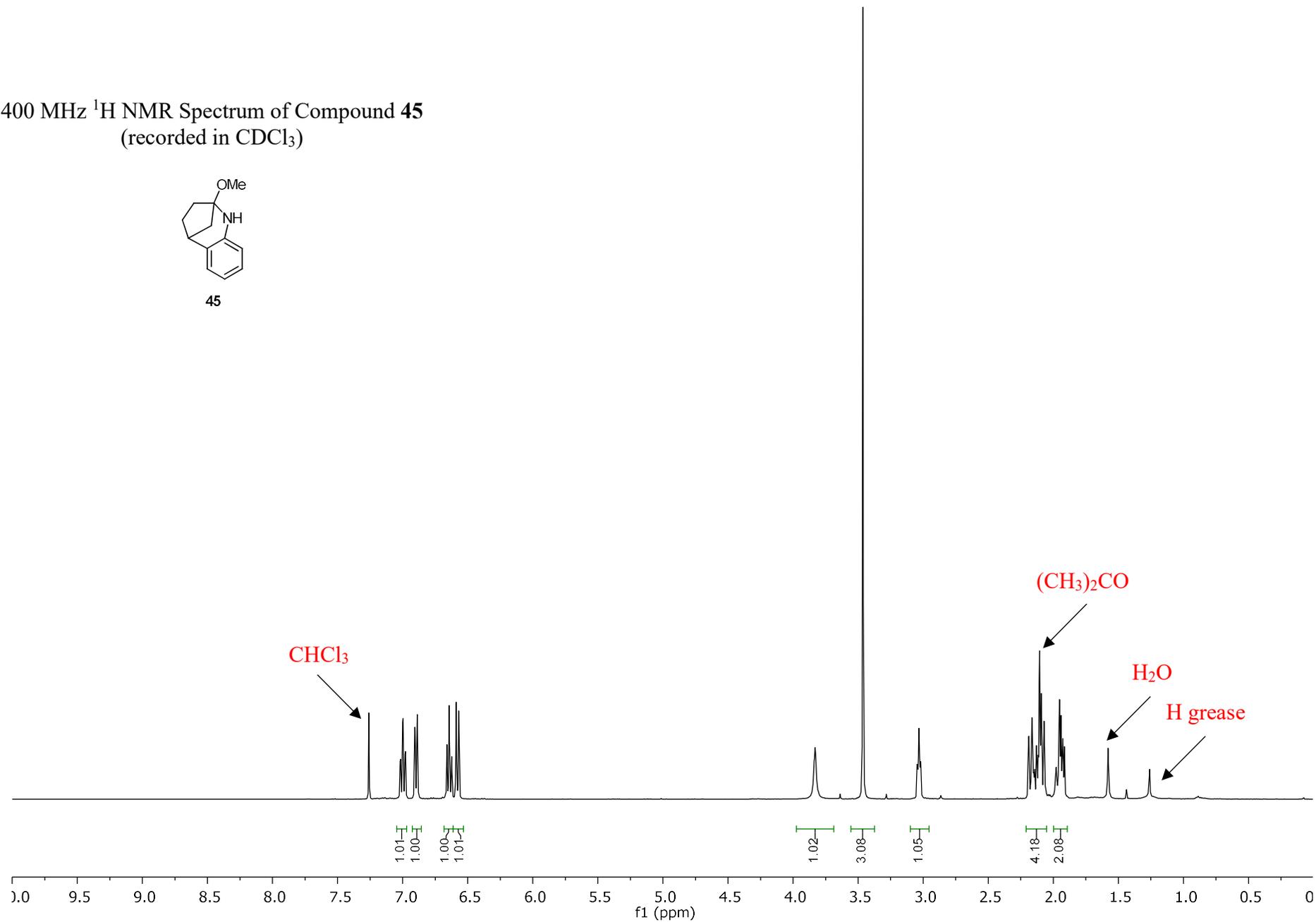
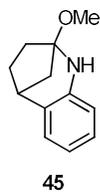
100 MHz ^{13}C NMR Spectrum of Compound **44**
(recorded in CDCl_3)



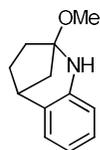
44



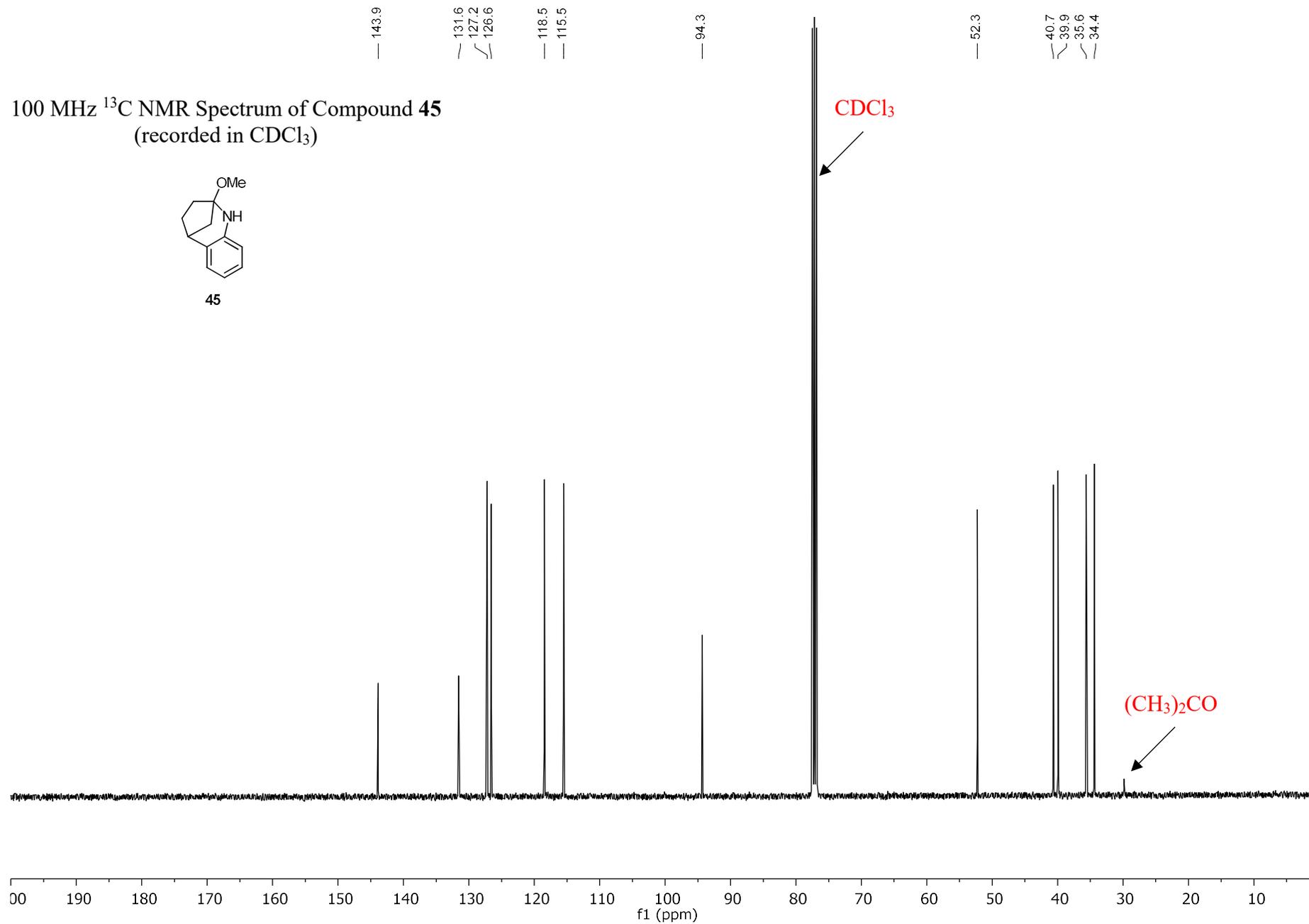
400 MHz ^1H NMR Spectrum of Compound **45**
(recorded in CDCl_3)



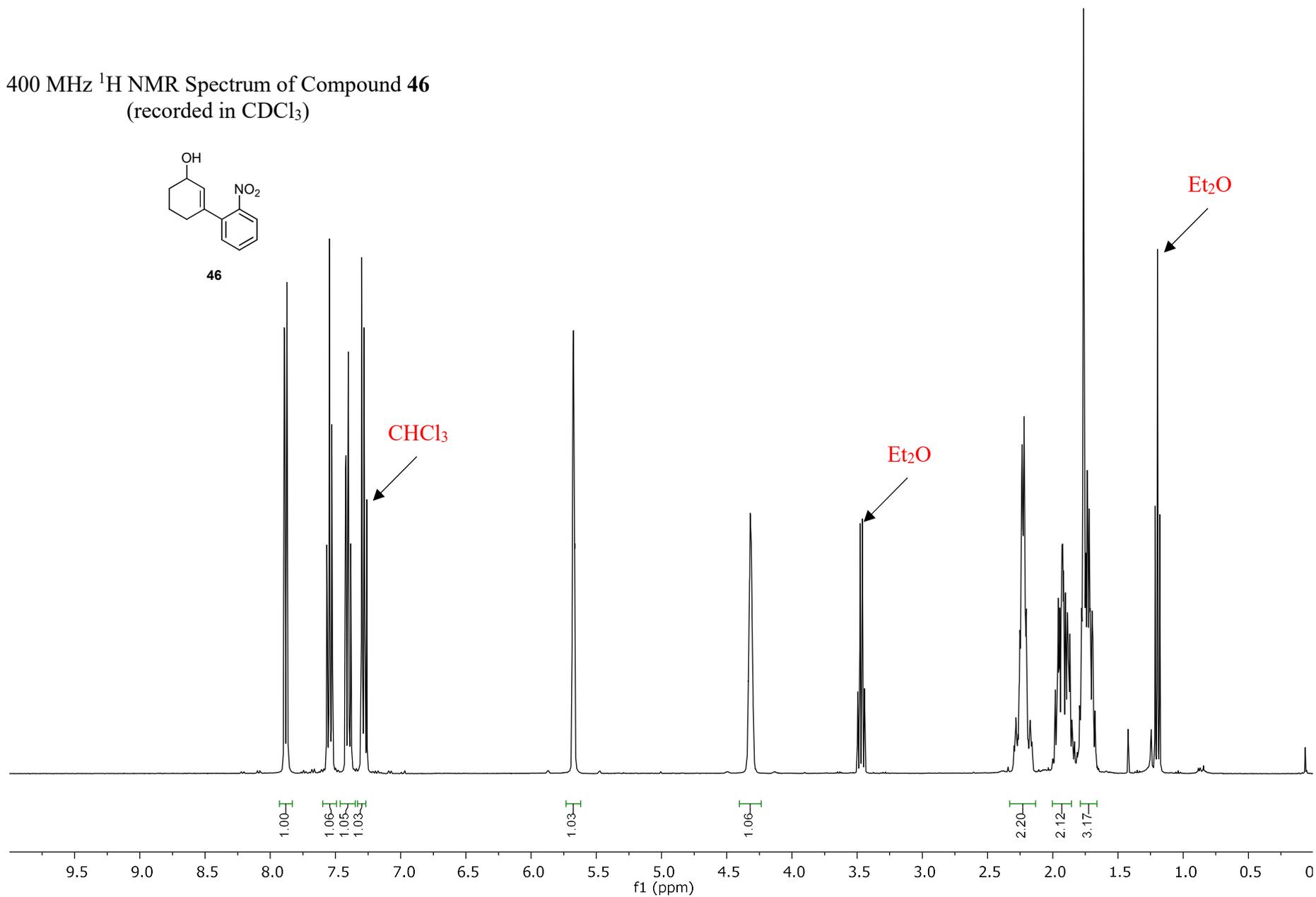
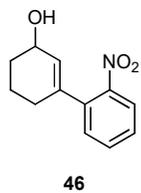
100 MHz ^{13}C NMR Spectrum of Compound **45**
(recorded in CDCl_3)



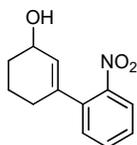
45



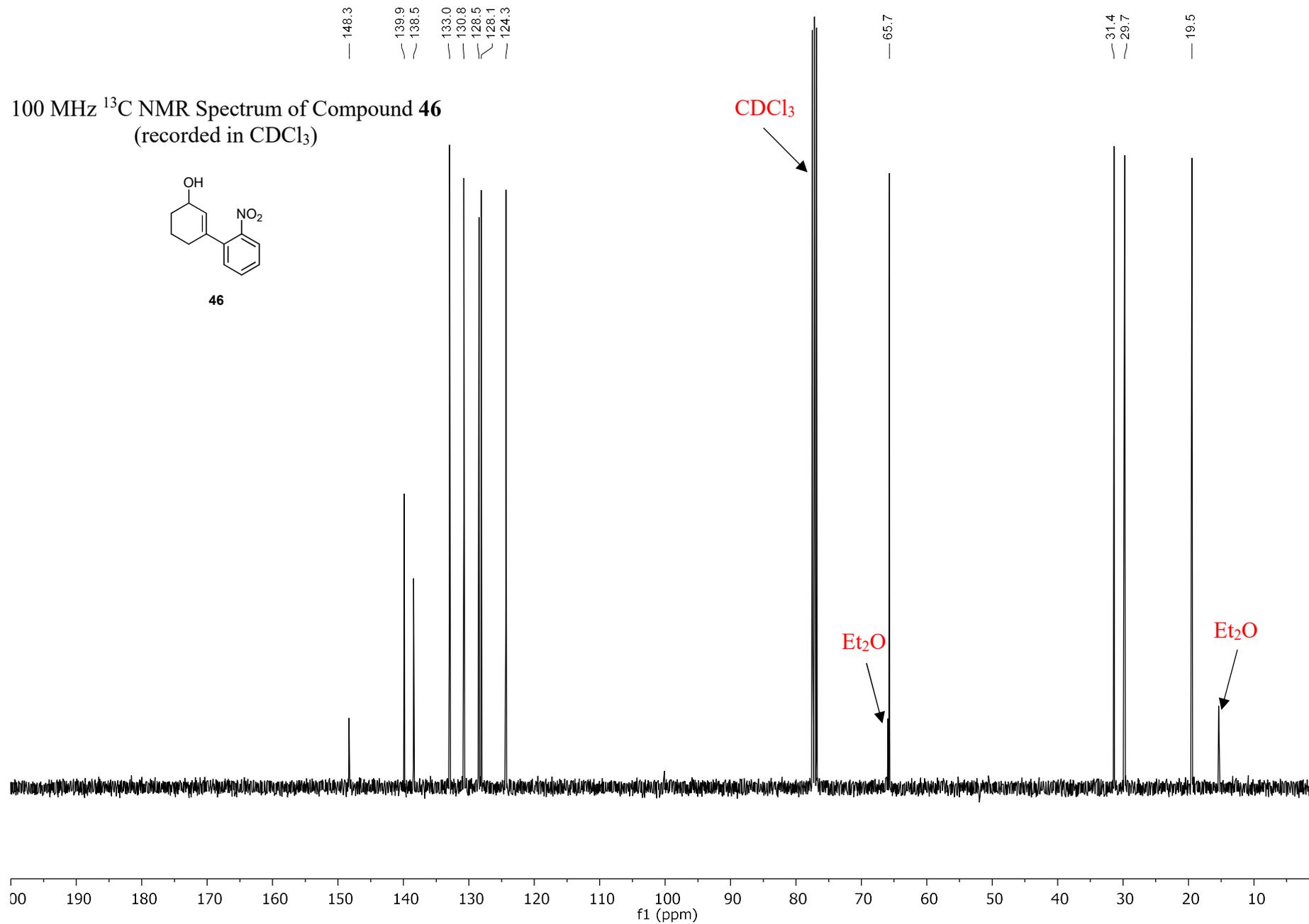
400 MHz ^1H NMR Spectrum of Compound **46**
(recorded in CDCl_3)



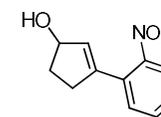
100 MHz ^{13}C NMR Spectrum of Compound **46**
(recorded in CDCl_3)



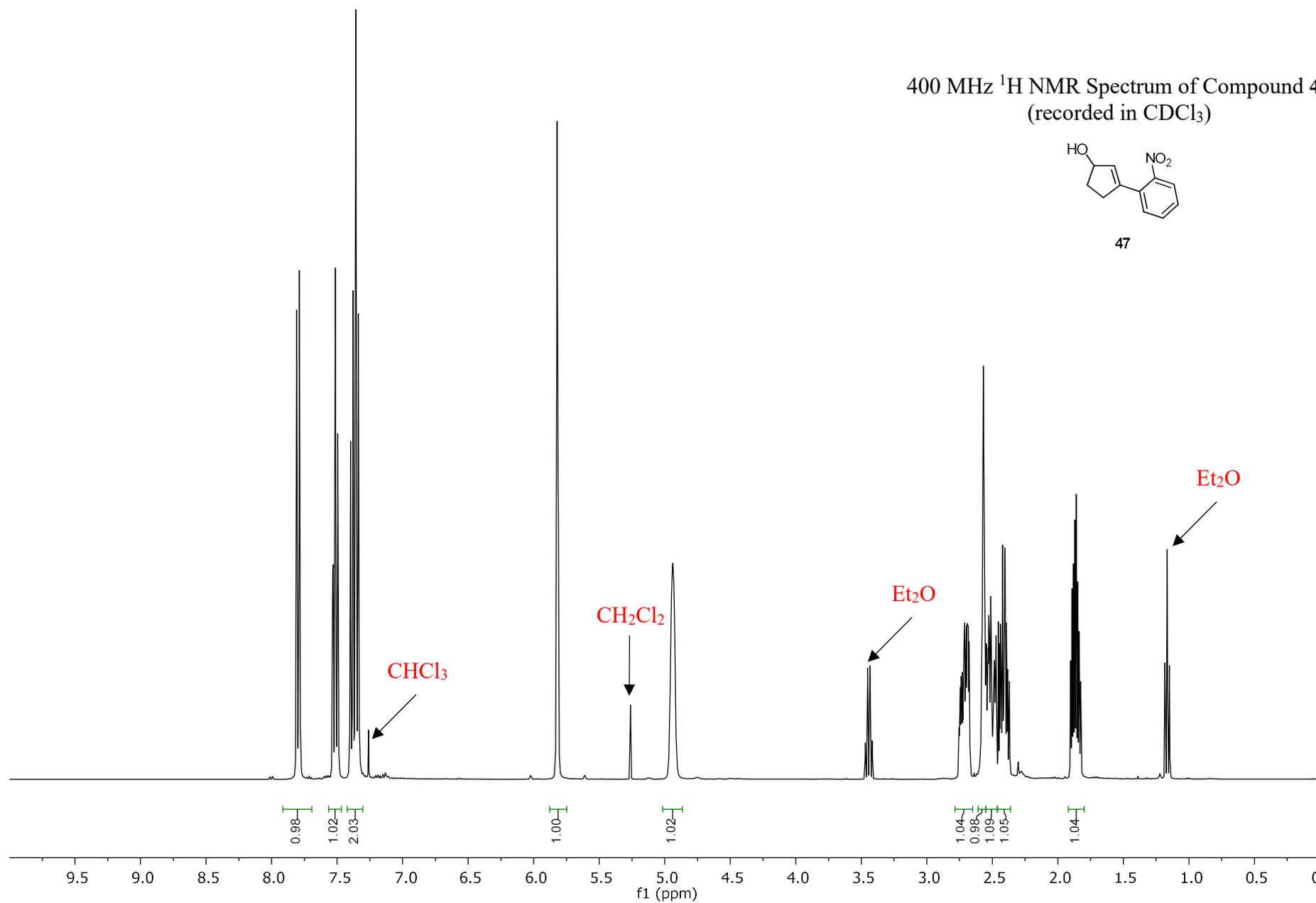
46



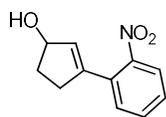
400 MHz ^1H NMR Spectrum of Compound **47**
(recorded in CDCl_3)



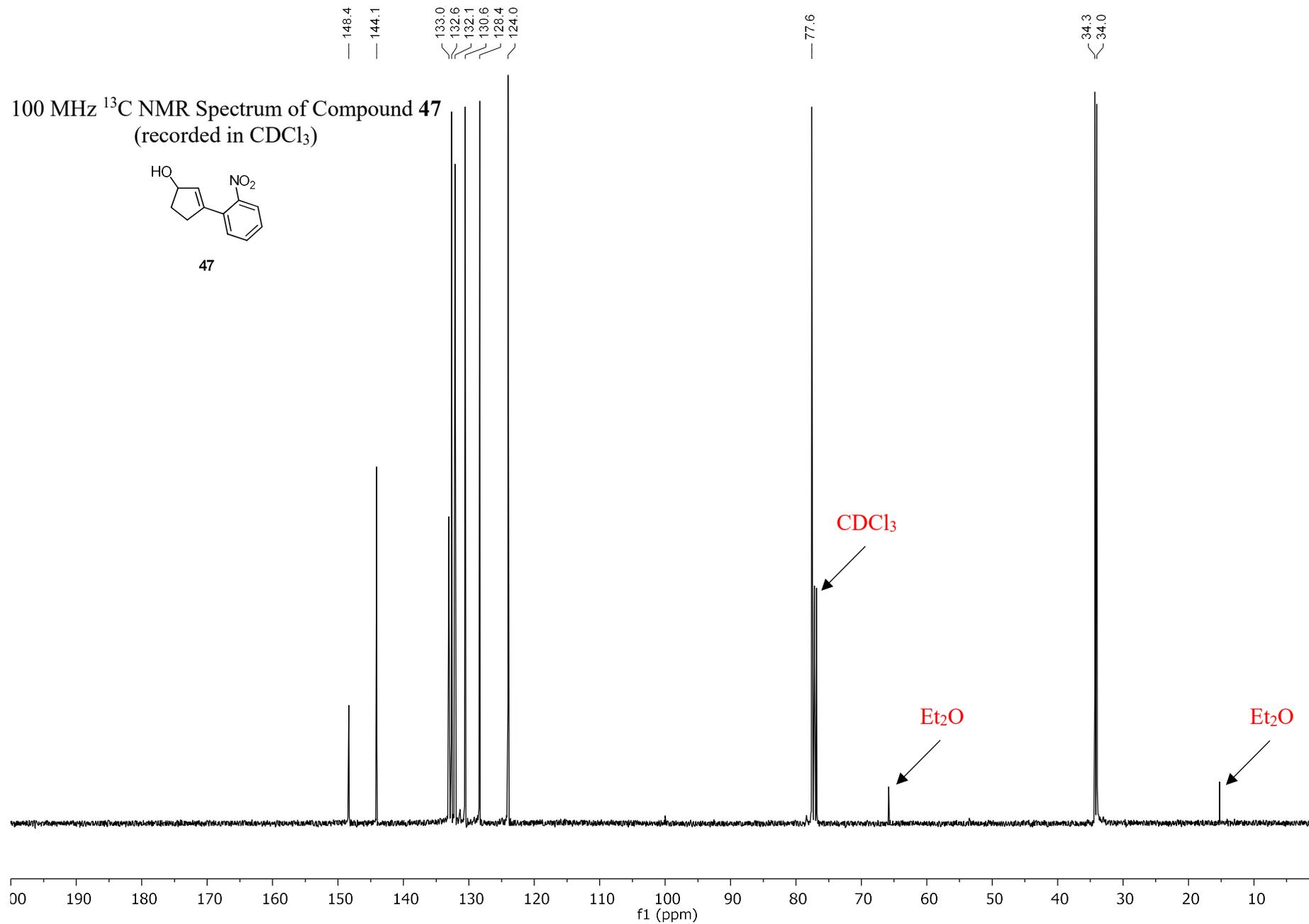
47



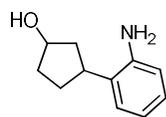
100 MHz ^{13}C NMR Spectrum of Compound **47**
(recorded in CDCl_3)



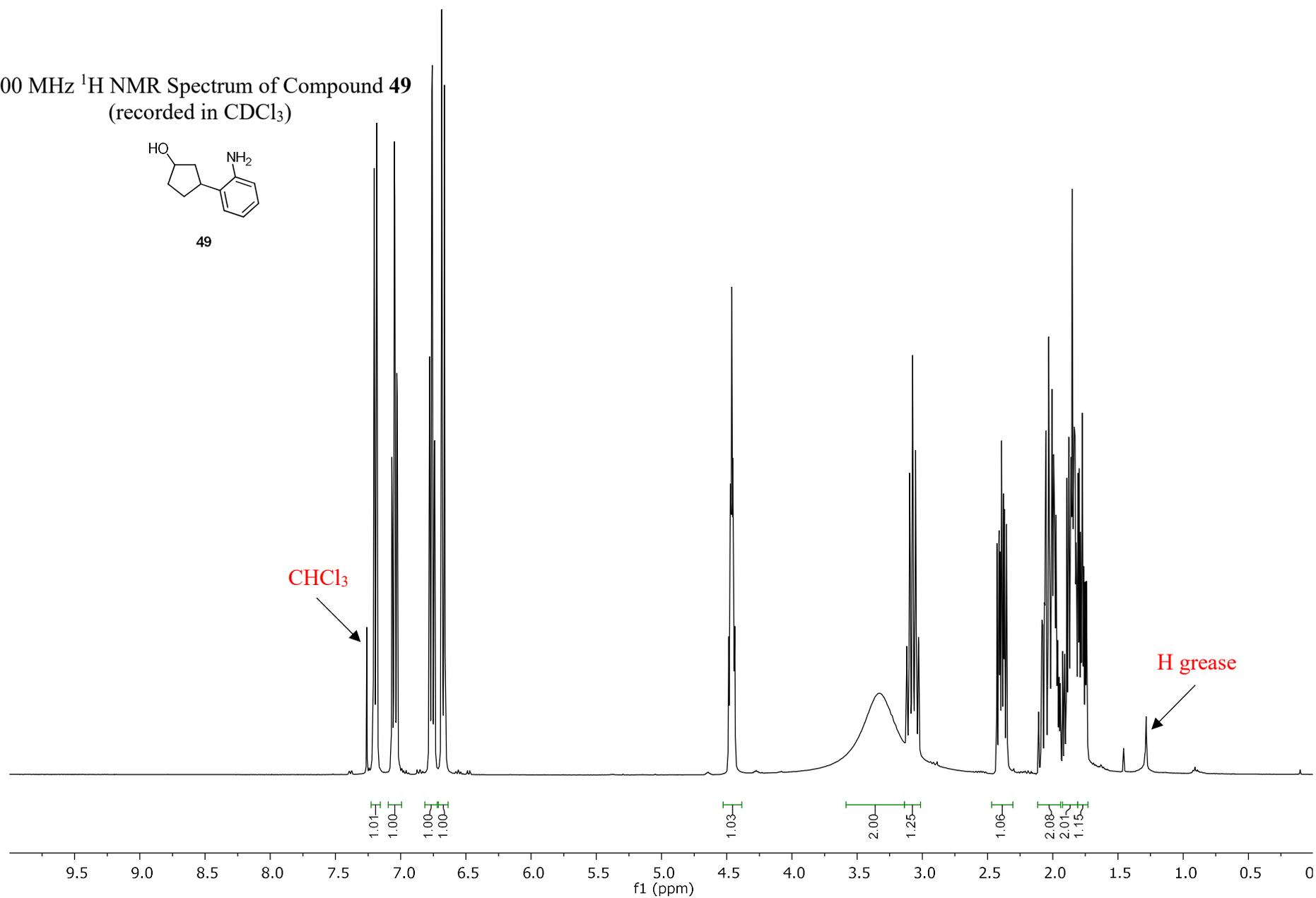
47



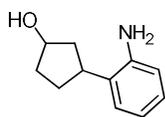
400 MHz ^1H NMR Spectrum of Compound **49**
(recorded in CDCl_3)



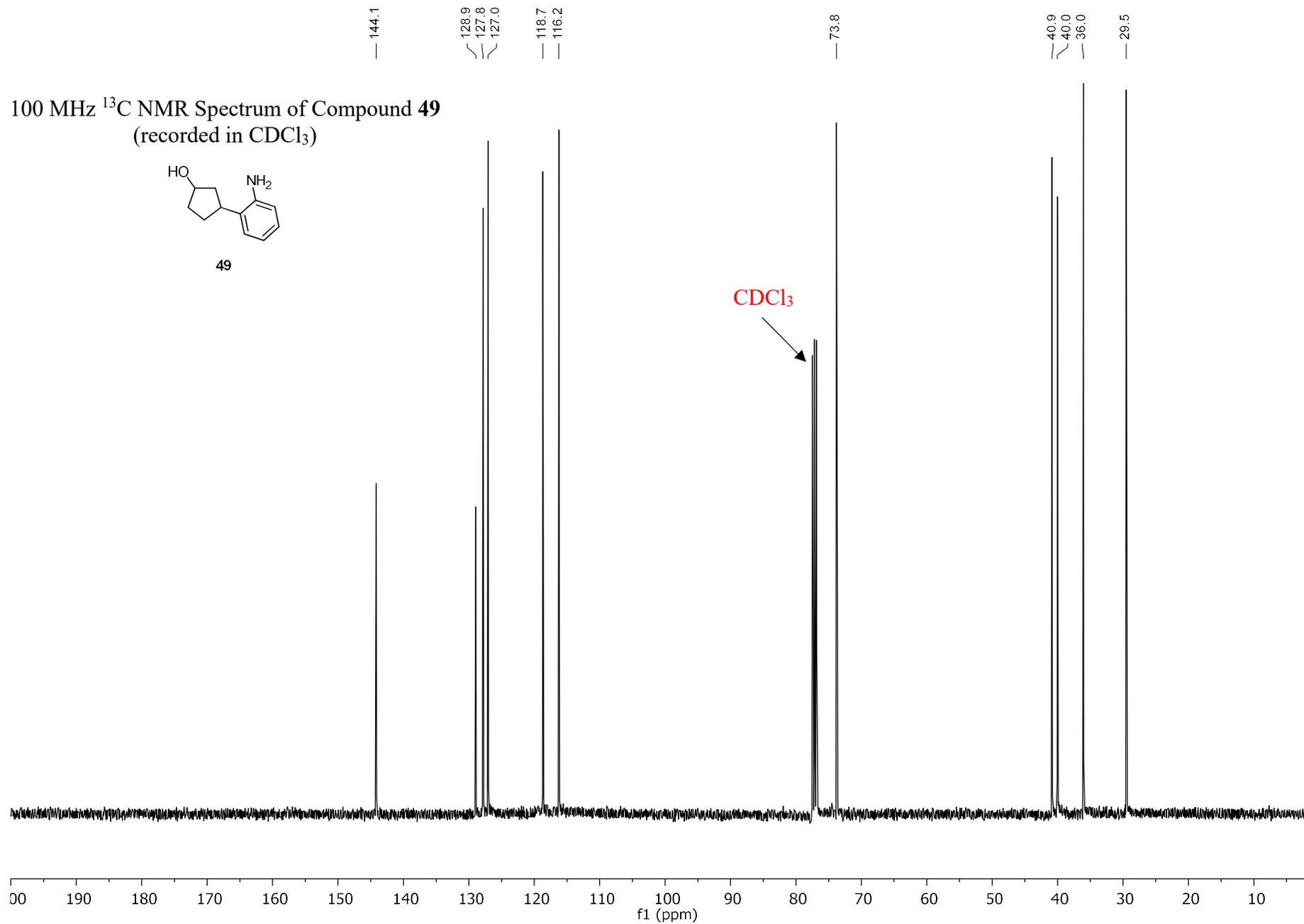
49



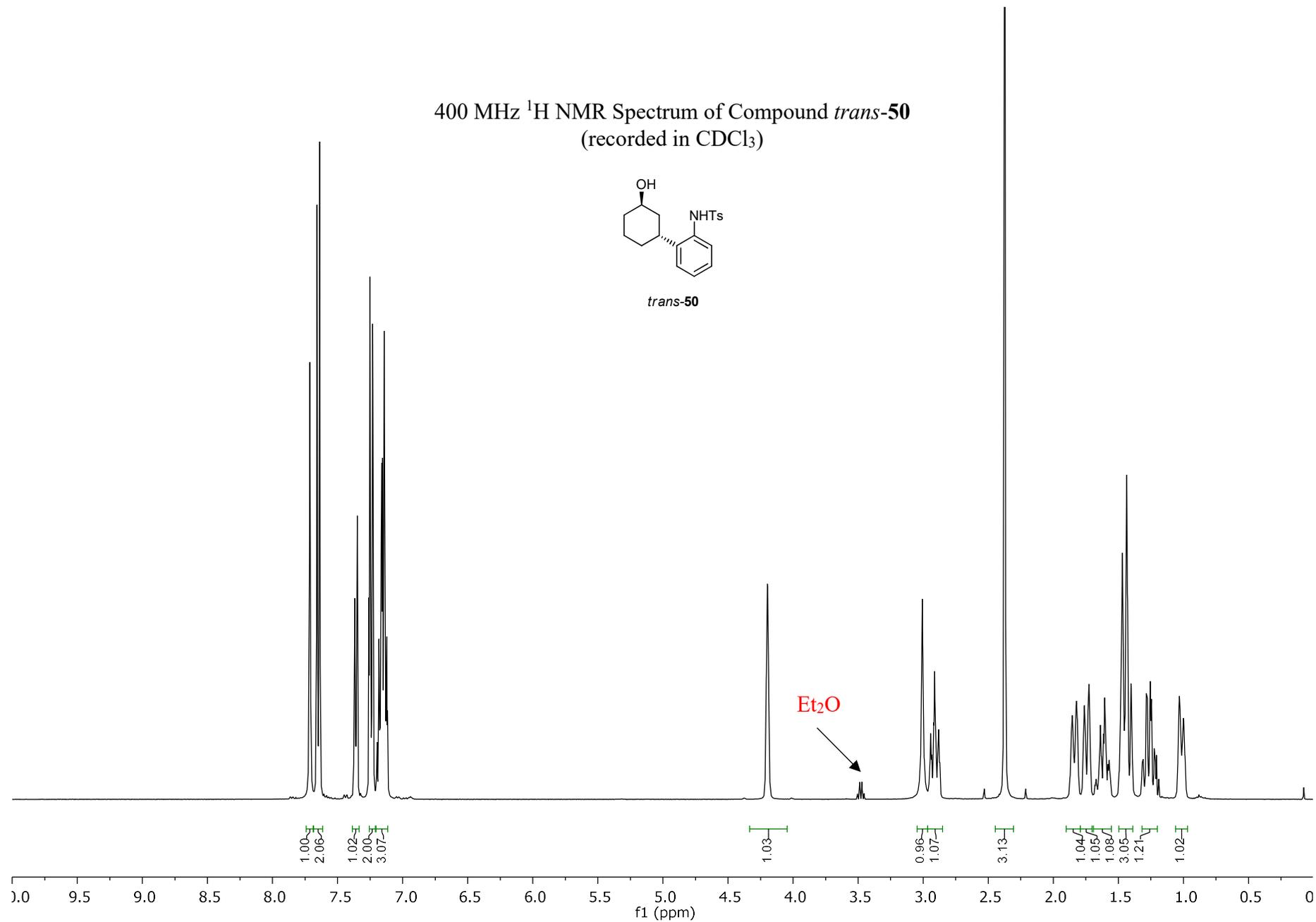
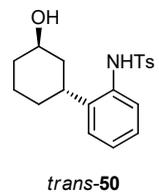
100 MHz ^{13}C NMR Spectrum of Compound **49**
(recorded in CDCl_3)



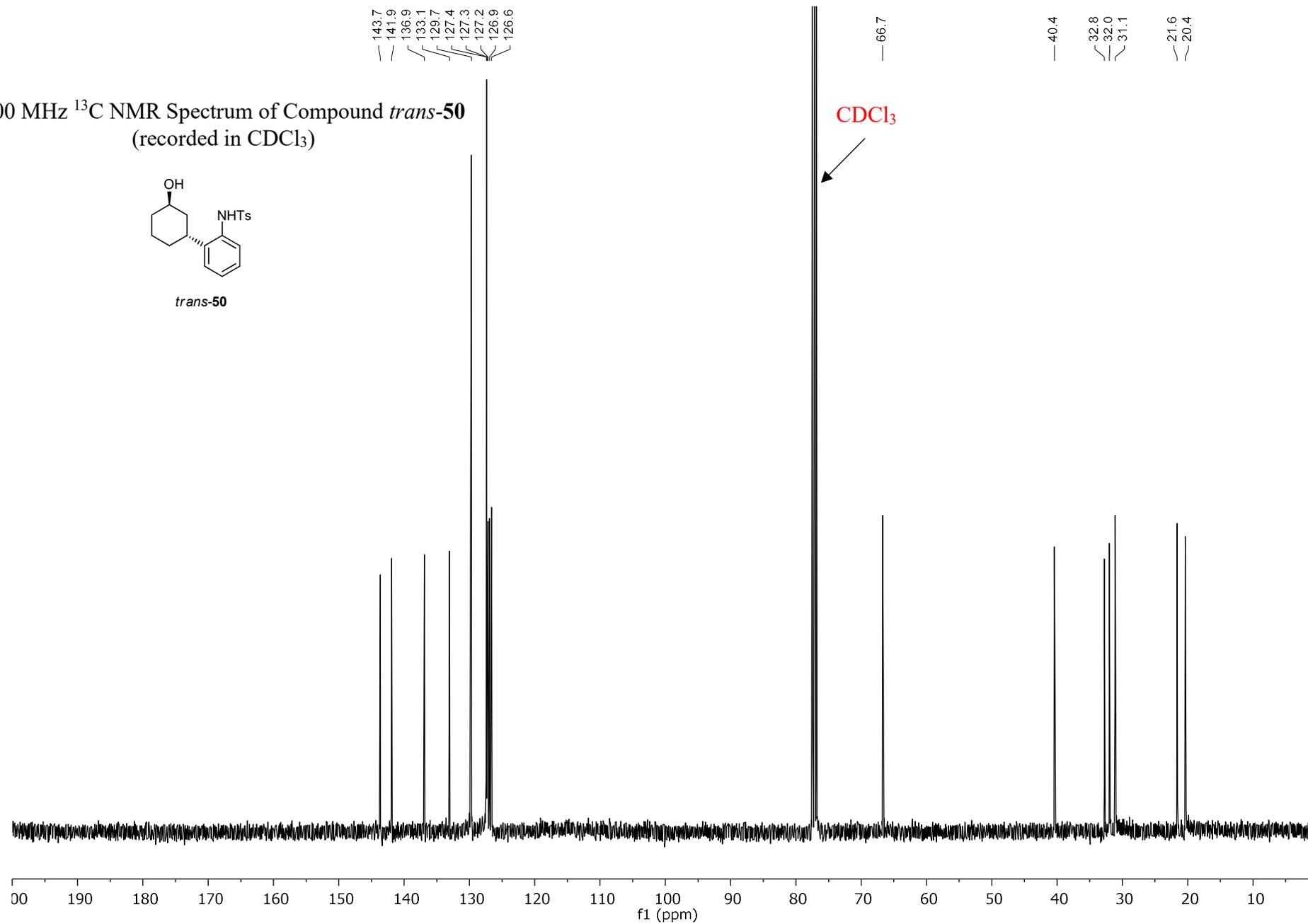
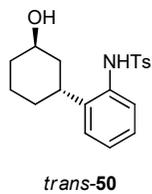
49



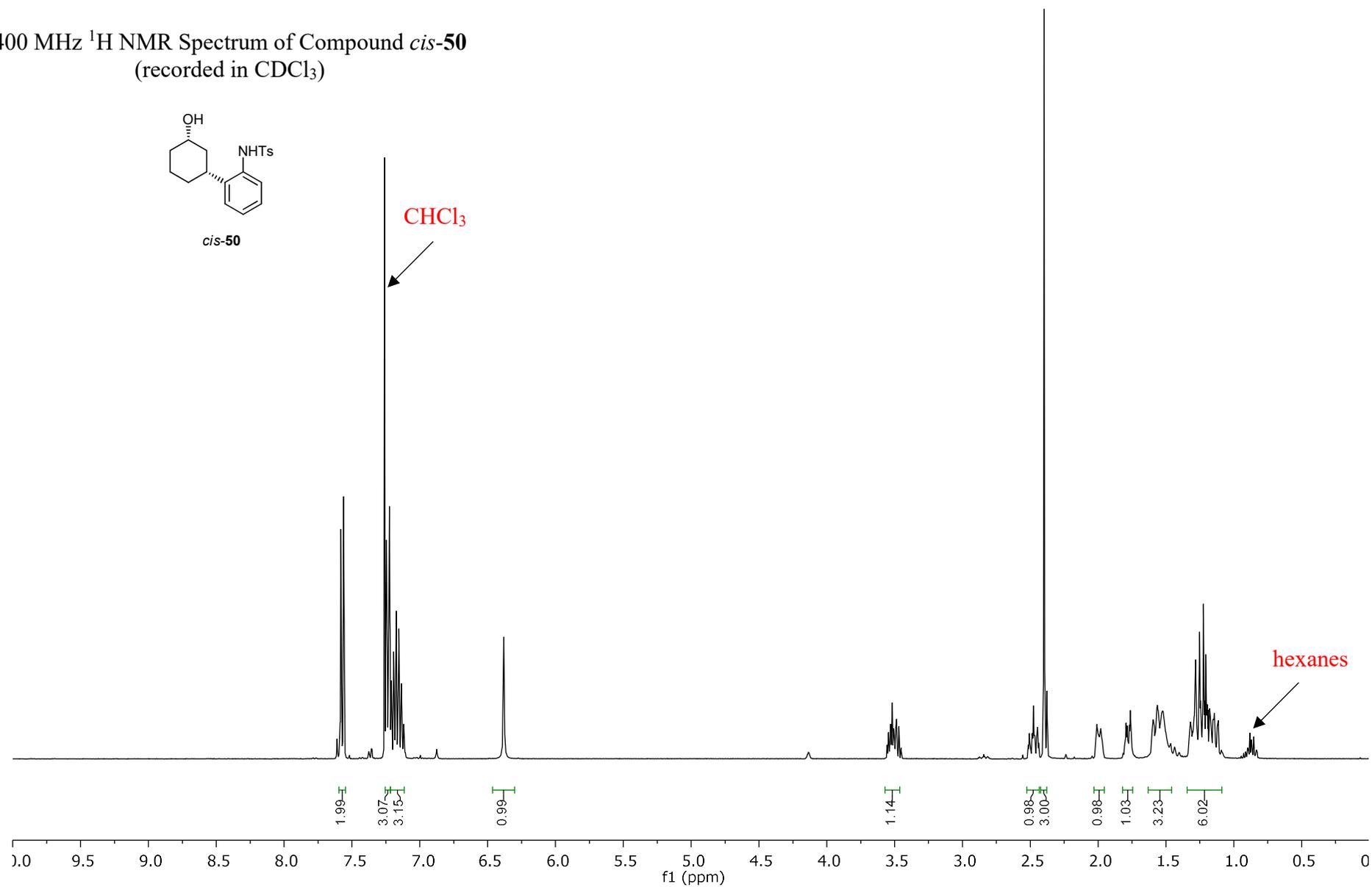
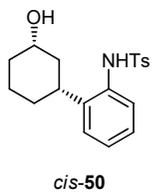
400 MHz ^1H NMR Spectrum of Compound *trans*-50
(recorded in CDCl_3)



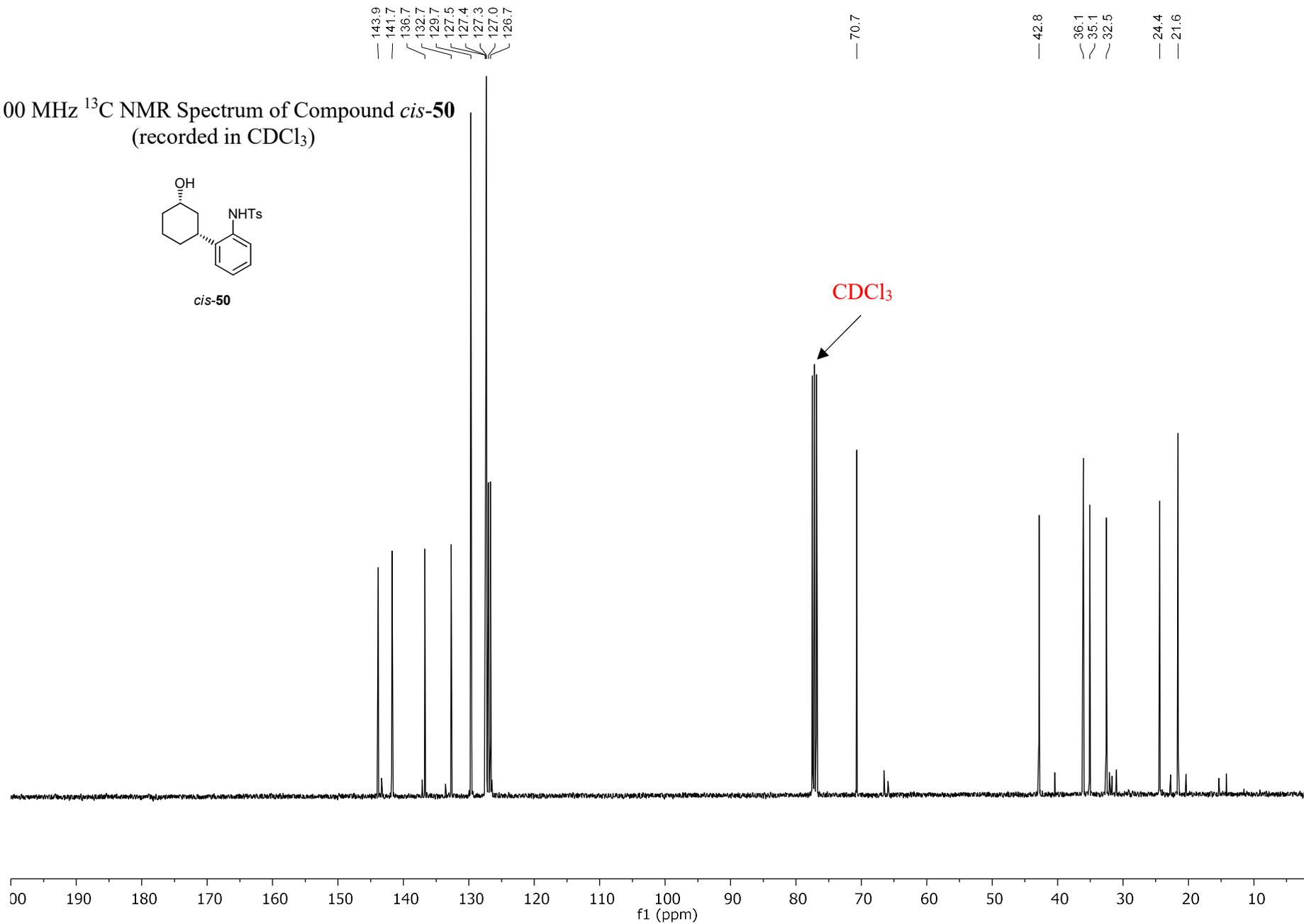
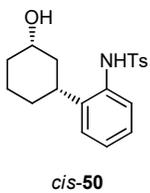
100 MHz ^{13}C NMR Spectrum of Compound *trans*-**50**
(recorded in CDCl_3)



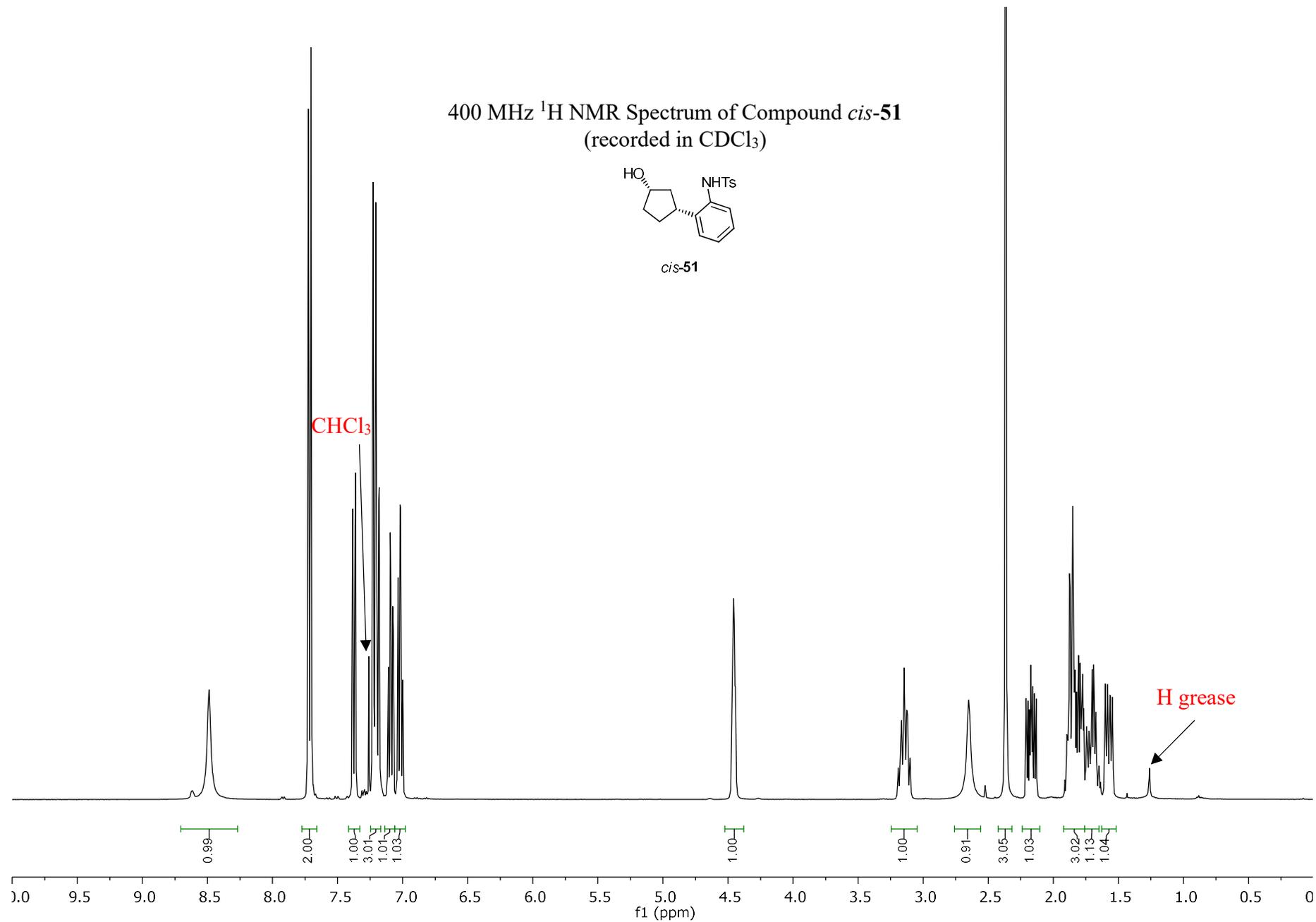
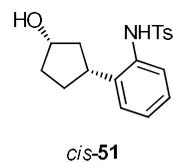
400 MHz ^1H NMR Spectrum of Compound *cis*-50
(recorded in CDCl_3)

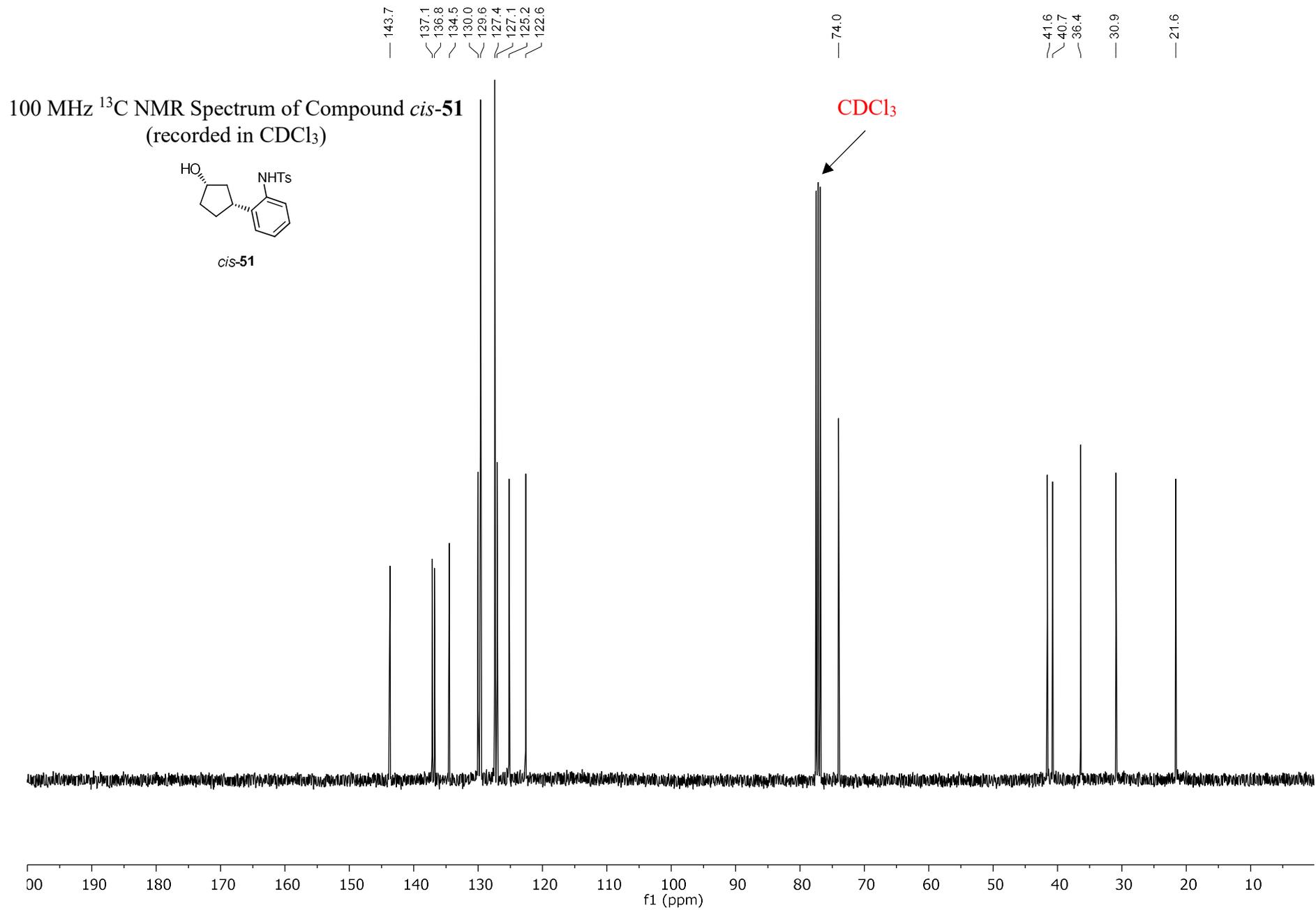


100 MHz ^{13}C NMR Spectrum of Compound *cis-50*
(recorded in CDCl_3)

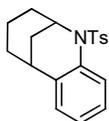


400 MHz ^1H NMR Spectrum of Compound *cis*-**51**
(recorded in CDCl_3)

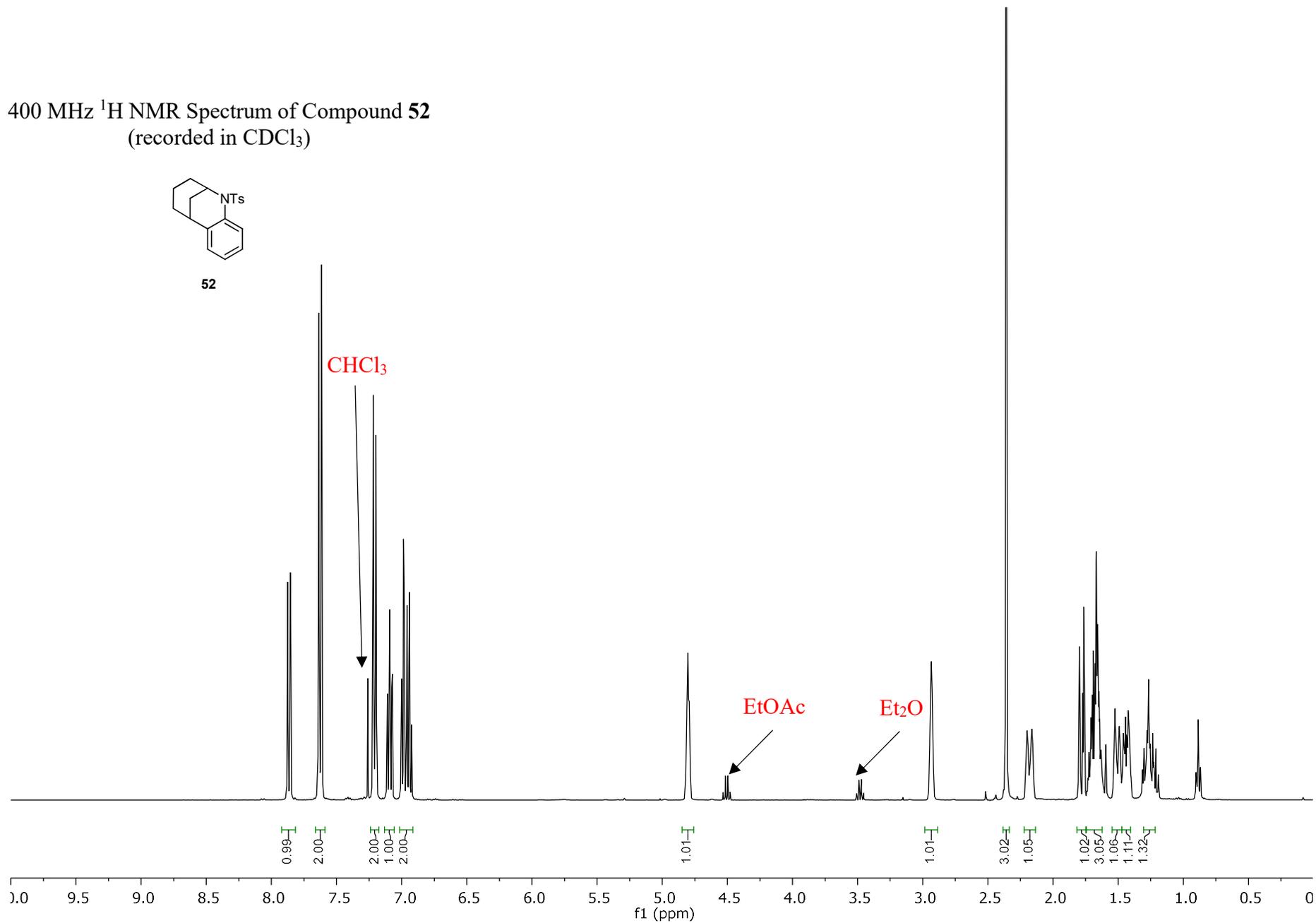




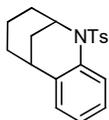
400 MHz ^1H NMR Spectrum of Compound **52**
(recorded in CDCl_3)



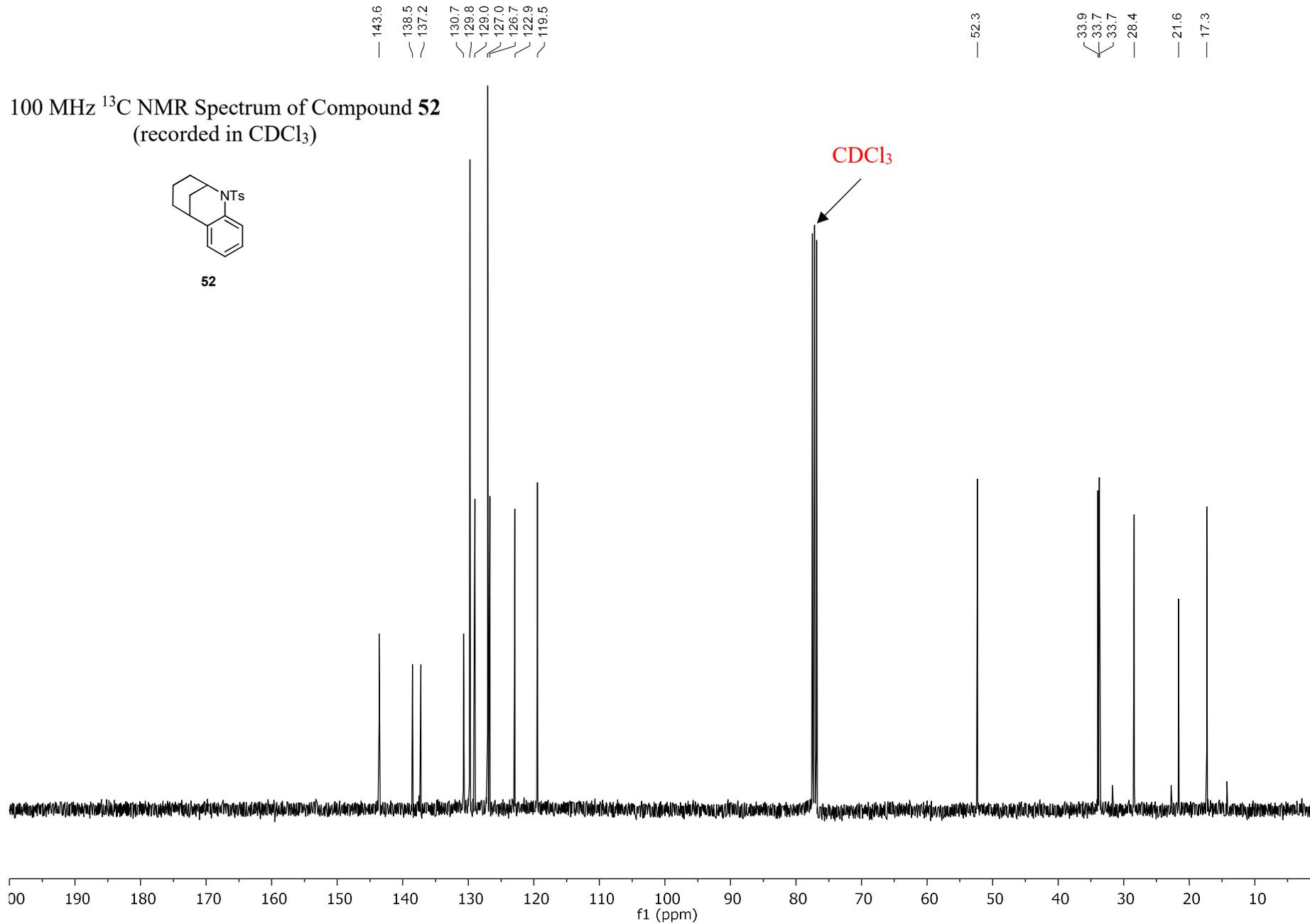
52



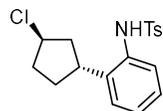
100 MHz ^{13}C NMR Spectrum of Compound **52**
(recorded in CDCl_3)



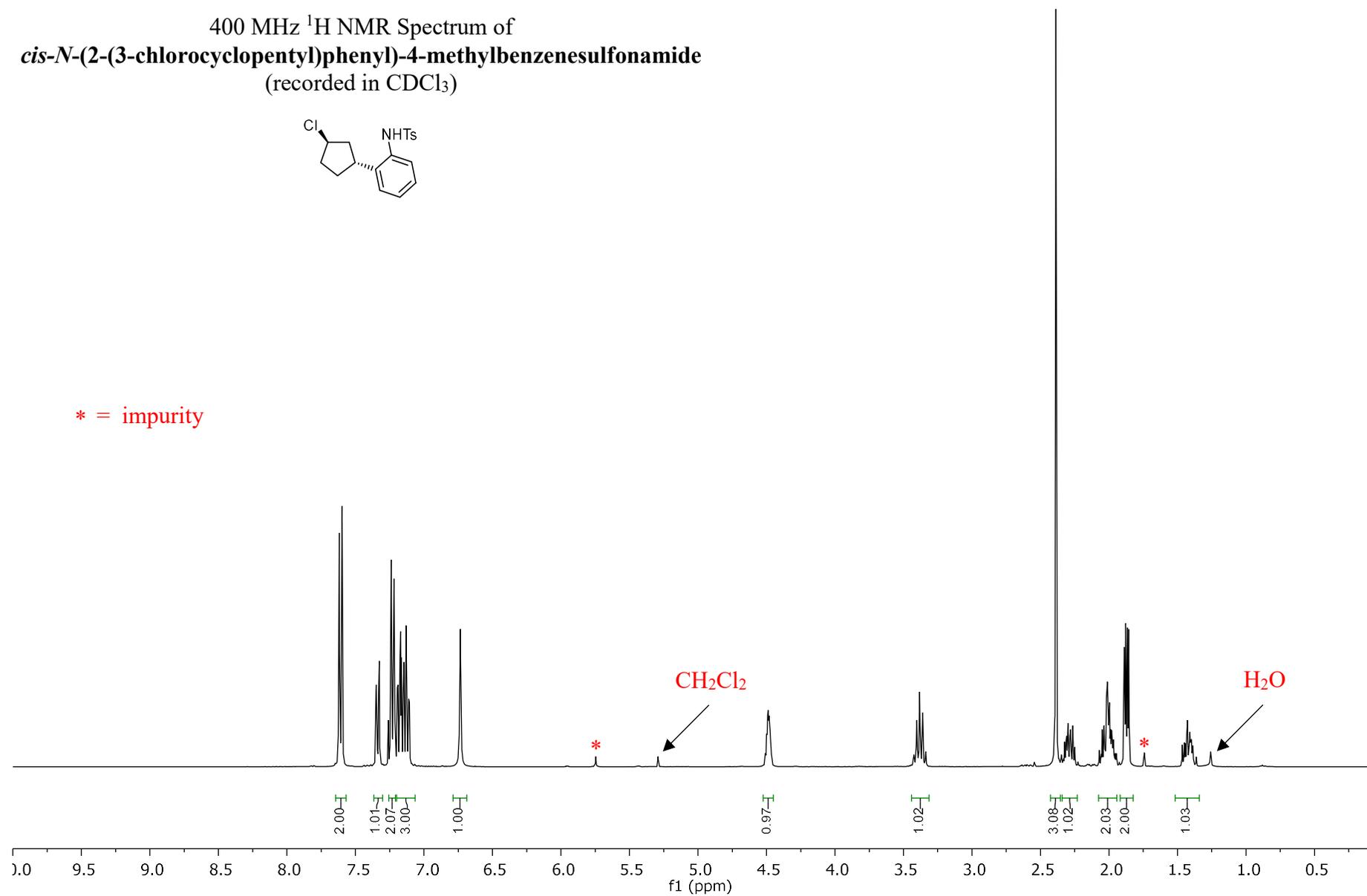
52

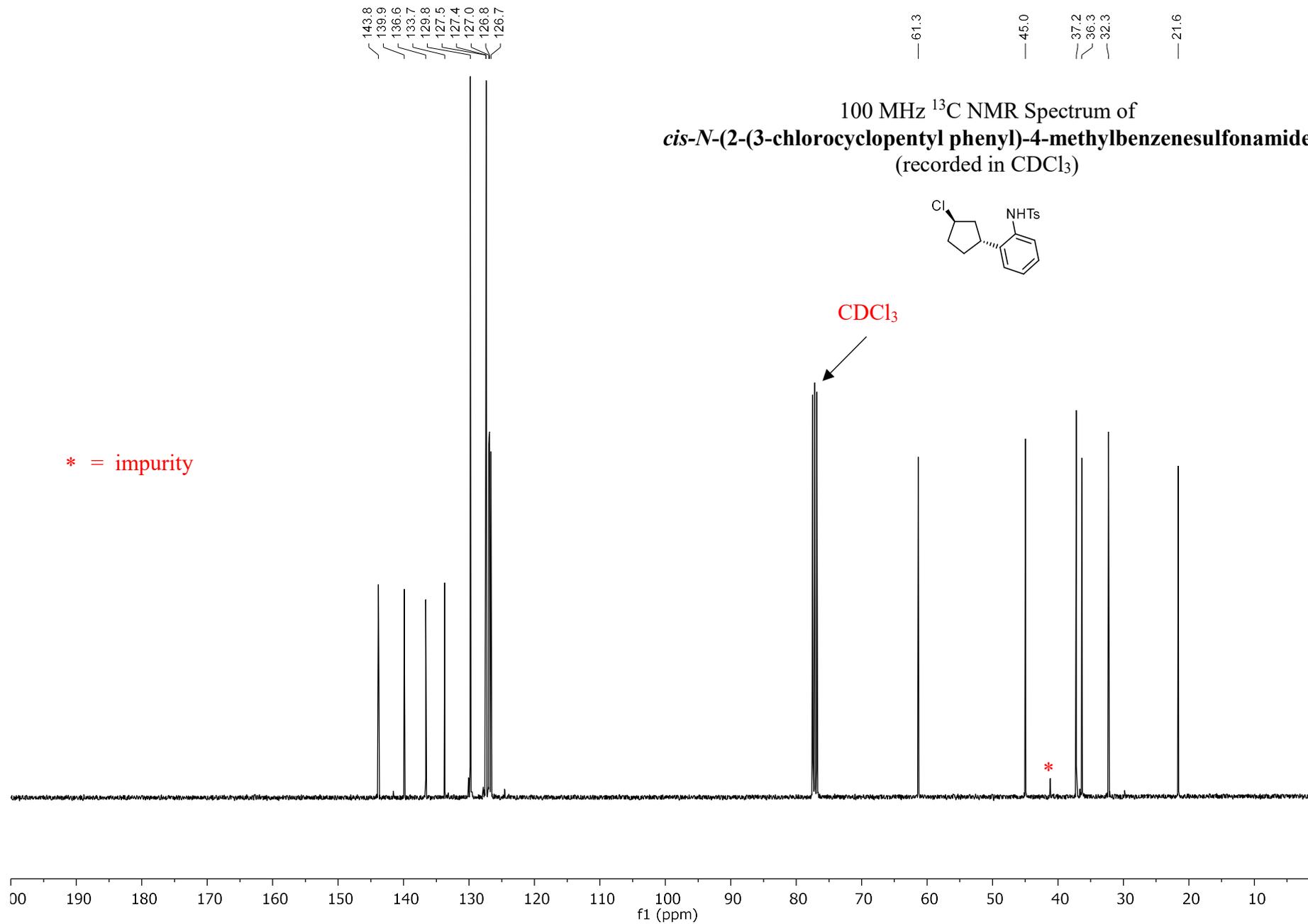


400 MHz ^1H NMR Spectrum of
cis-*N*-(2-(3-chlorocyclopentyl)phenyl)-4-methylbenzenesulfonamide
(recorded in CDCl_3)

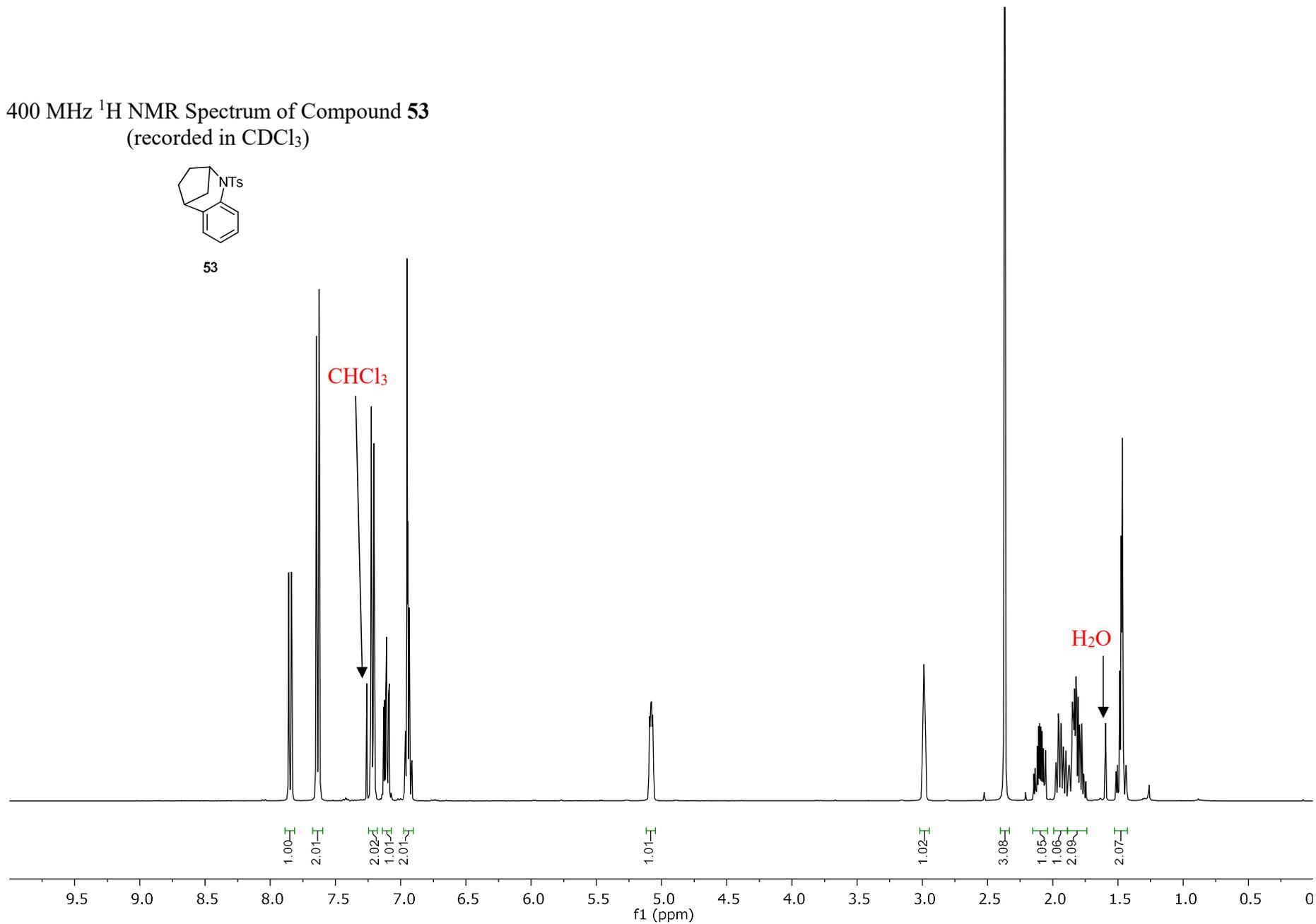
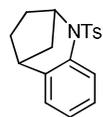


* = impurity

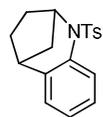




400 MHz ^1H NMR Spectrum of Compound **53**
(recorded in CDCl_3)



400 MHz ^1H NMR Spectrum of Compound **53**
(recorded in CDCl_3)



53

