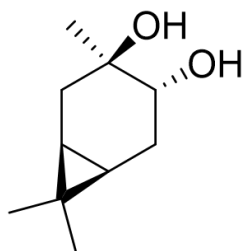


General Methods

All reagents were purchased from commercial sources and used without further purification unless otherwise noted. CHN **1** and *trans*-3-carene oxide **4** were prepared according to McKnight et al. Silica gel TLC plates (60 μ m) with a fluorescent indicator (254 nm) were used to monitor the progress of the reactions; they were visualized using UV, anisaldehyde, or KMnO₄ stain. Purification was accomplished with silica gel column chromatography using a Teledyne Isco CombiFlashC Lumen with 25 μ m SiliCycle spherical silica gel. ¹H, ¹³C, HSQC, and COSY NMR spectra were recorded on a Bruker AV400 spectrometer and referenced to the protic residue of the deuterated solvents: chloroform-*d* (7.26 ppm), methanol-*d*₄ (3.31 ppm), ethanol-*d*₆ (3.56 ppm), or dimethyl sulfoxide-*d*₆ (2.50 ppm) unless otherwise noted. IR spectra were recorded on a ThermoNicolet IR100 spectrometer using a Thunderdome Attenuated Total Reflectance (ATR) sample accessory. High-resolution mass spectroscopy data was acquired via a Vanquish UHPLC/HPLC system coupled to Q Exactive Orbitrap MS with electrospray ionization in positive mode. Abbreviations include ethyl acetate (EtOAc), column volume (CV), retention factor (R_f), singlet (s), doublet (d), doublet of doublets (dd), triplet (t), triplet of triplets (td), multiplet (m), broad (b), weak (w), medium (m), and strong (s).

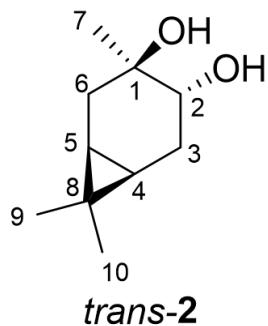
Product Isolation and Characterization



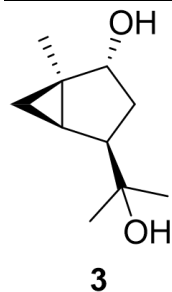
trans-**2**

CHN **1** (231 mg, 1.07 mmol) was suspended in 10% v/v H₂O/DMSO (0.5 mL D.I. water, 4.5 mL DMSO), then stirred at room temperature for 5 hours. The reaction mixture was quenched with 0.5 M NaOH (2.14 mL, 1 equiv), then transferred to a separatory funnel with diethyl ether (30 mL). The mixture was extracted with diethyl ether (4 x 10 mL), then the combined organic extracts were washed with D.I. water (3 x 50 mL), dried with anhydrous Na₂SO₄, gravity filtered, and concentrated in vacuo. The crude product was purified by column chromatography (12 g SiO₂, 0-100% EtOAc/hexane), yielding impure *trans*-**2** (47 mg, 26% yield). The impure *trans*-**2** was repurified by column chromatography (12 g SiO₂, 0-40% EtOAc/hexane over 1.5 CV, 40% for 4 CV, 40-100% over 17 CV), yielding pure *trans*-**2** as a white crystalline solid: IR (ATR) cm⁻¹ 3385 (bd m, alcoholic OH), 2929 (m), 1064 (s); HRMS ESI + *m/z* calculated for [C₁₀H₁₈O₂]⁺ (170.1293, observed; 170.1301, expected); R_f 0.11 (30% EtOAc/hexane, anisaldehyde); ¹H NMR (400 MHz, CDCl₃) δ 3.33 (dd, *J* = 10.3, 7.4 Hz, 1H), 2.53 (s, 2H), 2.08 (dd, *J* = 14.4, 7.3 Hz, 1H), 2.00 – 1.91 (m, 1H), 1.67 – 1.59 (m, 1H), 1.22 – 1.19 (m, 4H), 0.97 (s, 3H), 0.95 (s, 3H), 0.73-0.65 (m, 2H);

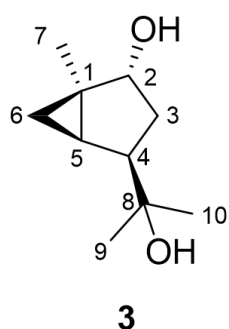
^{13}C { ^1H } NMR (101 MHz, CDCl_3) δ 74.56, 73.46, 33.88, 28.79, 27.93, 21.09, 20.10, 19.14, 17.77, 15.91.



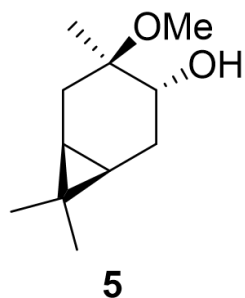
Assignment	# H	Multiplicity	^1H δ (ppm, CDCl_3)	^1H δ (ppm, $\text{MeOD-}d_4$)	^1H δ (ppm, $\text{EtOD-}d_6$)	^1H δ (ppm, 16.7% $\text{D}_2\text{O}/\text{DMSO-}d_6$)	^1H δ (ppm, $\text{DMSO-}d_6$)
2	1	dd	3.33	obscured	3.33	3.09	3.09
3 _A	1	dd	2.08	2.04	2.04	1.86 - 1.80	1.87 - 1.82
3 _B	1	m	1.67 - 1.59	1.70 - 1.62	1.72 - 1.64	1.54 - 1.46	1.55 - 1.47
4 and 5	2	m	0.73 - 0.65	0.75 - 0.67	0.74 - 0.66	0.63 - 0.56	0.64 - 0.57
6 _A	1	m	2.00 - 1.91	1.95 - 1.89	1.97 - 1.91	1.80 - 1.75	1.82 - 1.76
6 _B	1	m	1.22	1.23	1.25	1.05	1.06
7	3	s	1.22	1.18	1.19	1.00	1.02
9 and 10	3	s	0.97 and 0.95	0.99 and 0.99	1.00 and 1.00	0.91 and 0.89	0.94 and 0.92



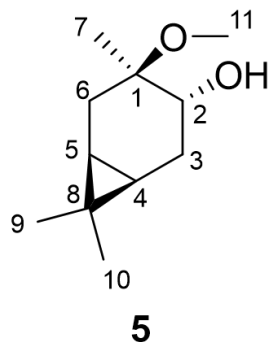
CHN **1** (101 mg, 0.469 mmol) was suspended in D.I. water (5 mL, 0.09 M), then stirred at room temperature for 16 hours. The reaction mixture was quenched with 0.5 M NaOH (0.938 mL, 1 equiv), then concentrated in vacuo. The crude product was purified by column chromatography (12 g SiO₂, 0-100% EtOAc/hexane), yielding **3** as a white crystalline solid (54 mg, 68% yield): IR (ATR) cm⁻¹ 3337 (bd m, alcoholic OH), 2968 (m); HRMS ESI+ *m/z* calculated for [C₁₀H₁₈O₂]⁺ (170.1292, observed; 170.1301, expected); R_f 0.06 (30% EtOAc/hexane, anisaldehyde); ¹H NMR (400 MHz, CDCl₃) δ 4.07 (d, *J* = 4.5 Hz, 1H), 2.51 (m, 1H), 1.89 (br-s, 2H), 1.53 – 1.37 (m, 2H), 1.25 (s, 3H), 1.21 (s, 3H), 1.14 (m, 4H), 0.58 (t, *J* = 4.5 Hz, 1H), 0.29 (dd, *J* = 5.0, 2.5 Hz, 1H) ppm; ¹³C {¹H} NMR (101 MHz, CDCl₃) δ 76.70, 72.59, 48.19, 32.45, 29.48, 27.82, 26.56, 24.09, 16.54, 13.17 ppm.



Assignment	# H	Multiplicity	¹ H δ (ppm, CDCl ₃)	¹ H δ (ppm, MeOD- <i>d</i> ₄)	¹ H δ (ppm, EtOD- <i>d</i> ₆)	¹ H δ (ppm, 16.7% D ₂ O/ DMSO- <i>d</i> ₆)
2	1	d	4.07	3.99	3.99	3.82
3	2	m	1.53 - 1.37	1.51 - 1.38	1.53 - 1.36	1.32 - 1.20
4	1	m	2.51	2.54	2.58	2.37
5	1	m	1.12	1.12	1.12	0.96
6 _A	1	t	0.58	0.57	0.55	0.42
6 _B	1	dd	0.29	0.27	0.25	0.14
7	3	s	1.21	1.20	1.20	1.09
9 and 10	3	s	1.14 and 1.25	1.18 and 1.21	1.18 and 1.21	1.04 and 1.09

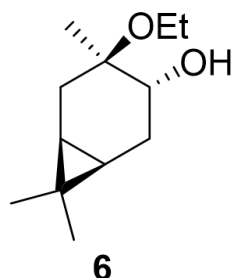


trans-3-Carene oxide **4** (152 mg, 1 mmol) and Bi(NO₃)₃ • 5 H₂O (485 mg, 1 equiv) were suspended in methanol (5 mL, 0.2 M). The reaction mixture was stirred for 1.25 hours at room temperature, then filtered through celite and rinsed with dichloromethane (2 x 10 mL). The filtrate was washed with saturated sodium bicarbonate (2 x 10 mL). The organic extracts were dried with anhydrous sodium sulfate, then gravity filtered and concentrated in vacuo to yield a clear crude oil. The crude product was purified by column chromatography (12 g, SiO₂, 0-30% EtOAc/hexane), yielding **5** as a clear oil (87 mg, 47% yield): IR (ATR) cm⁻¹ 3453 (bd w, alcoholic OH), 2934 (m), 1061 (s); HRMS ESI + *m/z* calculated for [C₁₁H₂₀O₂]⁺ (184.1450, observed; 184.1463, expected); R_f 0.50 (30% EtOAc/hexane, anisaldehyde); ¹H NMR (400 MHz, CDCl₃) δ 3.40 (dd, *J* = 10.3, 7.4 Hz, 1H), 3.21 (s, 3H), 2.14 – 2.06 (m, 2H), 1.75 – 1.67 (m, 1H), 1.16 (s, 3H), 1.10 – 1.05 (m, 1H), 0.99 (s, 3H), 0.96 (s, 3H), 0.70 – 0.63 (m, 2H); ¹³C {¹H} NMR (101 MHz, CDCl₃) δ 77.57, 73.14, 48.81, 28.89, 28.29, 26.61, 20.53, 19.67, 17.81, 15.97, 13.84.

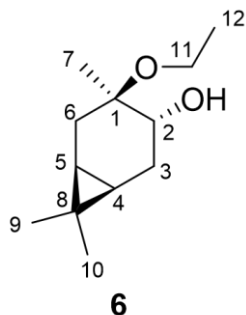


Assignment	# H	Multiplicity	¹ H δ (ppm, CDCl ₃)	¹ H δ (ppm, MeOD- <i>d</i> ₄)	¹ H δ (ppm, 16.7% D ₂ O/MeOD- <i>d</i> ₄)
2	1	dd	3.40	3.42	3.45
3 _A	1	m	2.10	2.04 - 2.01	2.05 - 2.02
3 _B	1	m	1.75 - 1.67	1.74 - 1.66	1.75 - 1.67
4 and 5	2	m	0.70 - 0.63	0.74 - 0.66	0.74 - 0.66
6 _A	1	m	2.12	2.10 - 2.04	2.08 - 2.05

6 _B	1	m	1.10-1.05	1.15	1.16
7	3	s	1.16	1.17	1.18
9 and 10	3	s	0.99 and 0.96	0.99 and 0.98	0.98 and 0.97
11	3	s	3.21	3.22	3.22

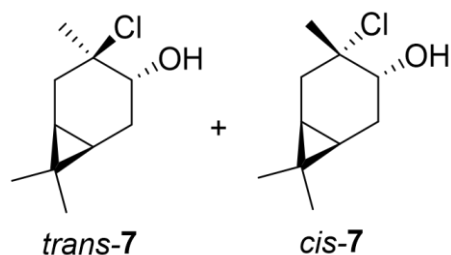


trans-3-Carene oxide **4** (152 mg, 1 mmol) and BiBr₃ (449 mg, 1 equiv) were suspended in ethanol (5 mL, 0.2 M). The reaction mixture was stirred for 1.75 hours at room temperature, then filtered through celite and rinsed with dichloromethane (2 x 10 mL). The filtrate was washed with saturated sodium bicarbonate (2 x 15 mL). The organic extracts were dried with anhydrous sodium sulfate, then gravity filtered and concentrated in vacuo to yield a clear crude oil. The crude product was purified by column chromatography (12 g, SiO₂, 0-30% EtOAc/hexane), yielding **6** as a clear oil (104 mg, 53% yield): IR (ATR) cm⁻¹ 3457 (bd w, alcoholic OH), 2930 (m), 1064 (s); HRMS ESI + *m/z* calculated for [C₁₂H₂₂O₂]⁺ (198.1604, observed; 198.1614, expected); R_f 0.67 (30% EtOAc/hexane, anisaldehyde); ¹H NMR (400 MHz, C₆D₆) δ 3.50 (dd, *J* = 10.2, 7.4 Hz, 1H), 3.17 (q, *J* = 7.0 Hz, 2H), 2.51 (br-s, 1H), 2.16 (dd, *J* = 14.6, 7.4 Hz, 1H), 1.95 – 1.84 (m, 2H), 1.18 (s, 3H), 1.06 (m, 1 H), 1.04 (t, *J* = 6.9, Hz, 3H), 0.86 (s, 3H), 0.84 (s, 3H), 0.47 – 0.40 (m, 2H); ¹³C {¹H} NMR (101 MHz, C₆D₆) δ 77.41, 73.39, 56.06, 29.05, 28.85, 26.78, 20.69, 19.99, 17.69, 16.36, 15.89, 14.50.

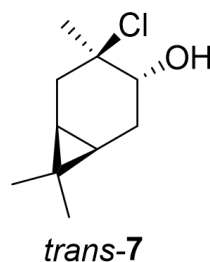


Assignment	# H	Multiplicity	¹ H δ (ppm, C ₆ D ₆)	¹ H δ (ppm, EtOD- <i>d</i> ₆)
2	1	dd	3.50	3.43

3 _A	1	dd	2.16	2.11 - 2.05
3 _B	1	m	1.88	1.77 - 1.69
4 and 5	2	m	0.47 - 0.40	0.73 - 0.65
6 _A	1	m	1.92	2.05 - 2.00
6 _B	1	m	1.06	obscured
7	3	s	1.18	1.19
9 and 10	3	s	0.86 and 0.84	1.01 and 1.00
11	2	q	3.17	3.48
12	3	t	1.04	1.14

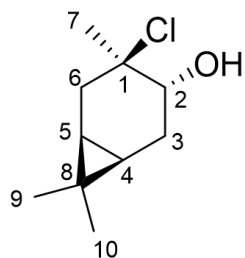


CHN **1** (250 mg, 1.16 mmol) and NaCl (339 mg, 5 equiv) were suspended in 10% v/v H₂O/DMSO (0.5 mL D.I. water, 4.5 mL DMSO). The reaction mixture was stirred at room temperature for 3 hours, then quenched with NaHCO₃ (98 mg, 1 equiv) and extracted with diethyl ether (5 x 15 mL). The combined organic extracts were washed with D.I. water (3 x 5 mL), then dried with anhydrous Na₂SO₄, gravity filtered, and concentrated in vacuo to yield a clear crude oil. The crude product was purified by column chromatography (12 g, SiO₂, 20-75% MTBE/pentane), yielding *trans*-**7** and *cis*-**7** in 17% and 10% yield, respectively.



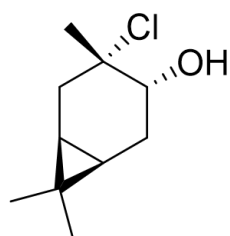
trans-**7** was isolated as a clear oil (38 mg, 17% yield): IR (ATR) cm⁻¹ 3449 (bd w, alcoholic OH), 2937 (m), 1069 (s); HRMS ESI + *m/z* calculated for [C₁₀H₁₇OCl]⁺ (188.0960, observed; 188.0968, expected); R_f 0.75 (30% EtOAc/hexane, anisaldehyde); ¹H NMR (400 MHz, CDCl₃) δ 3.58 (dd, J

= 10.2, 7.4 Hz, 1H), 2.44 – 2.37 (m, 1H), 2.10 (dd, $J = 14.7, 7.4$ Hz, 1H), 1.77 – 1.69 (m, 2H), 1.58 (s, 3H), 0.99 (d, $J = 1.1$ Hz, 6H), 0.79 – 0.71 (m, 2H); ^{13}C $\{^1\text{H}\}$ NMR (101 MHz, CDCl_3) δ 77.76, 74.96, 36.88, 28.59, 26.75, 21.29, 21.04, 20.29, 18.22, 15.90 ppm.



trans-7

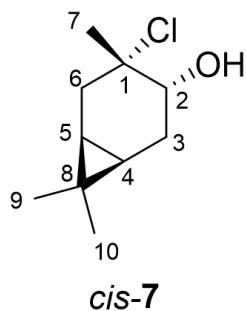
Assignment	# H	Multiplicity	^1H δ (ppm, CDCl_3)
2	1	dd	3.58
3 _A	1	dd	2.10
3 _B	1	m	1.75
4 and 5	2	m	0.79 - 0.71
6 _A	1	m	2.41
6 _B	1	m	1.73
7	3	s	1.58
9 and 10	3	s	0.99 and 0.99



cis-7

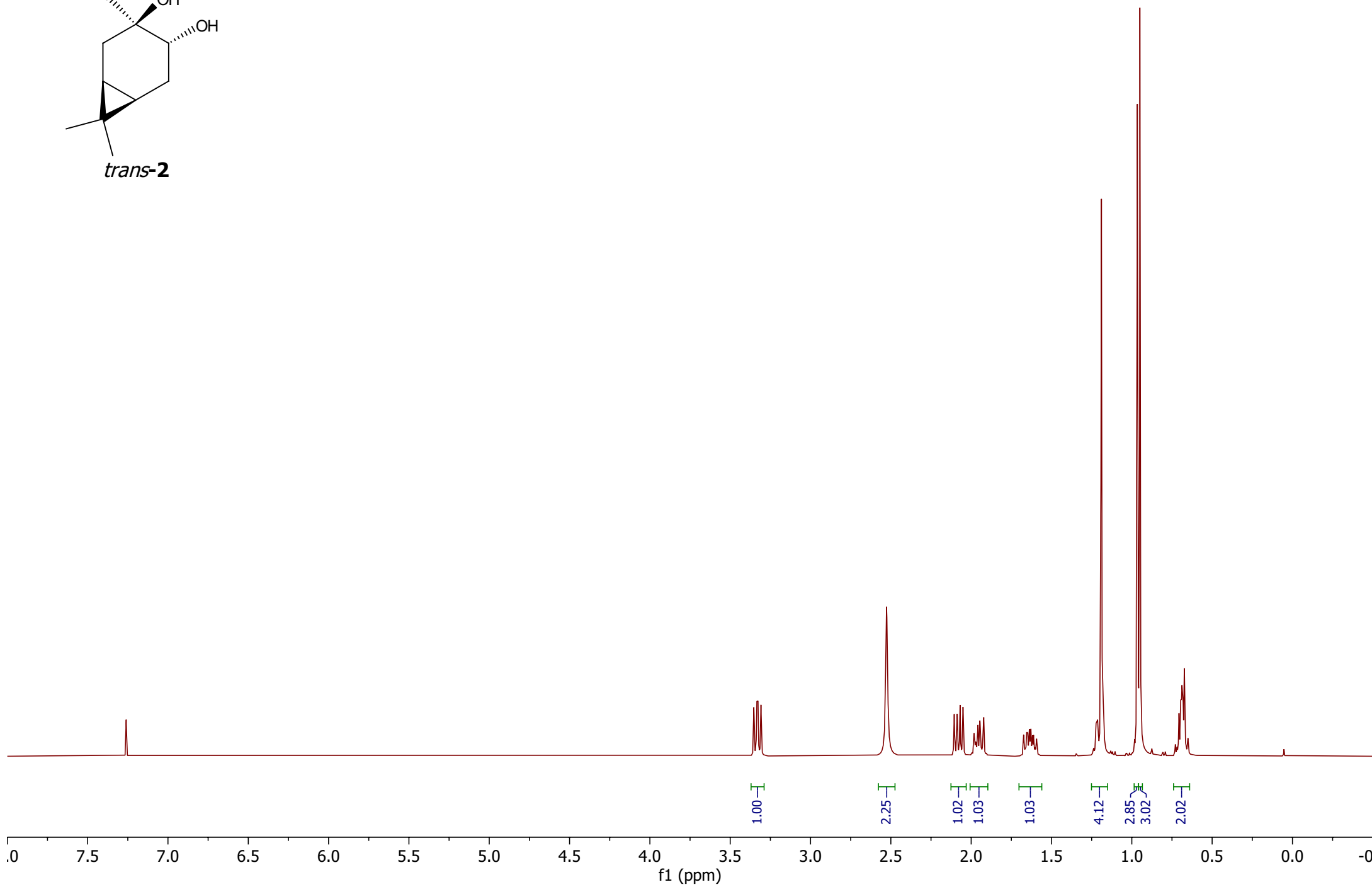
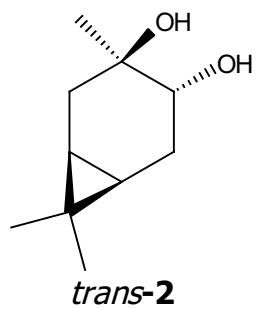
cis-7 was isolated as a clear oil (21 mg, 10% yield): IR (ATR) cm^{-1} 3409 (bd w, alcoholic OH), 2932 (m), 733 (s); HRMS ESI + m/z calculated for $[\text{C}_{10}\text{H}_{17}\text{OCl}]^+$ (188.0964, observed; 188.0968, expected); R_f 0.61 (30% EtOAc/hexane, anisaldehyde); ^1H NMR (400 MHz, CDCl_3) δ 3.94 (td, $J = 5.6, 1.3$ Hz, 1H), 2.53 (m, 1H), 1.91 (dd, $J = 6.5, 1.3$ Hz, 1H), 1.66 (ddd, $J = 16.1, 5.7, 4.2$ Hz, 1H), 1.46 (dd, $J = 15.4, 6.0$ Hz, 1H), 1.29 (s, 3H), 1.06 (s, 3H), 1.03 (s, 3H), 0.78 – 0.67 (m, 2H)

ppm; ^{13}C { ^1H } NMR (101 MHz, CDCl_3) δ 71.96, 63.73, 29.64, 28.60, 27.62, 26.74, 19.27, 18.84, 18.04, 15.67.

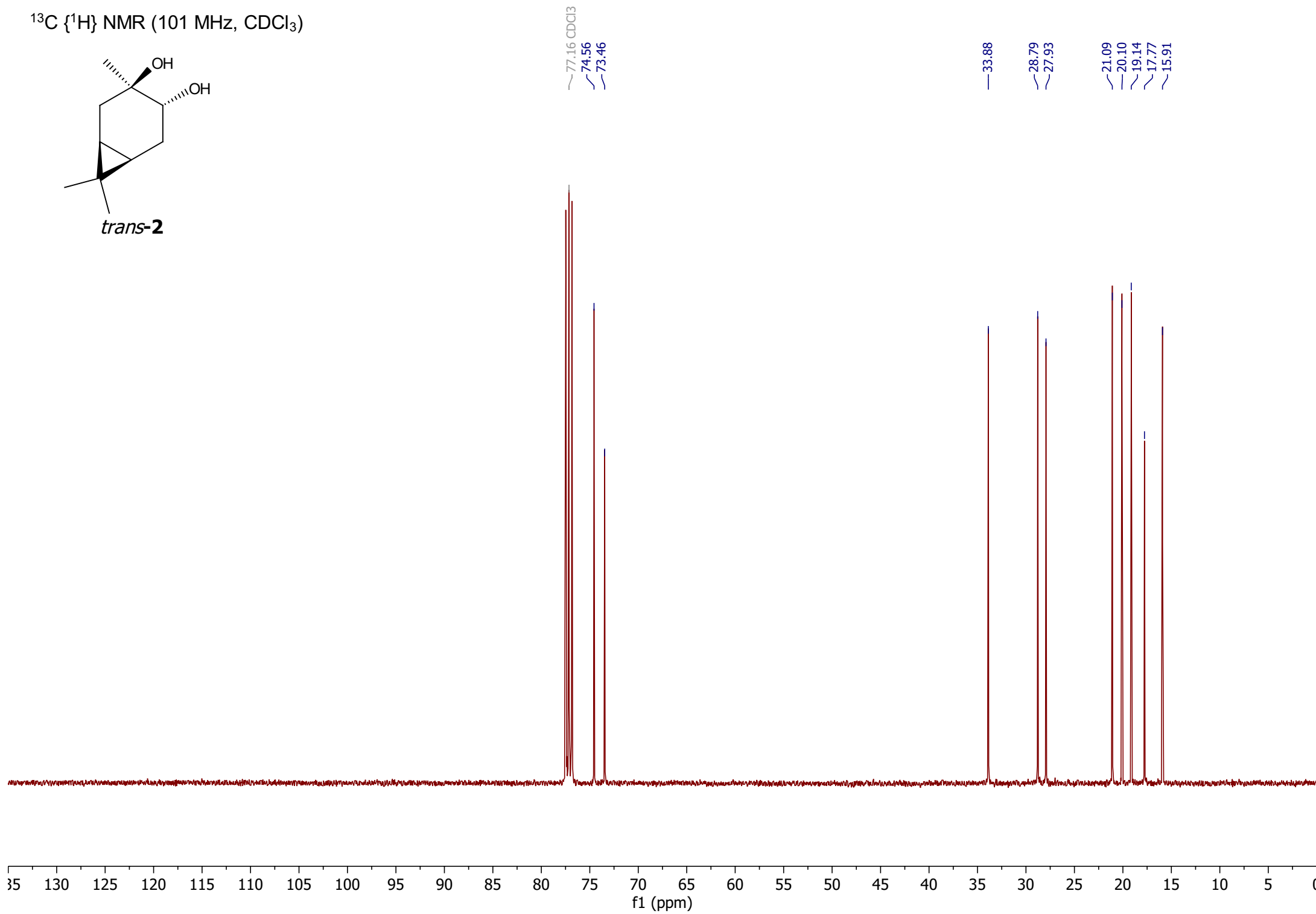
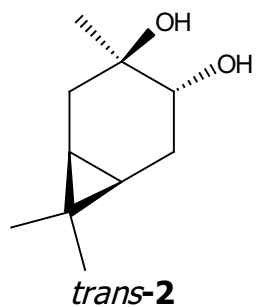


Assignment	# H	Multiplicity	^1H δ (ppm, CDCl_3)
2	1	td	3.94
3 _A	1	m	2.53
3 _B	1	m	1.66
4 and 5	2	m	0.78 - 0.687
6 _A	1	dd	1.91
6 _B	1	dd	1.46
7	3	s	1.29
9 and 10	3	s	1.06 and 1.03

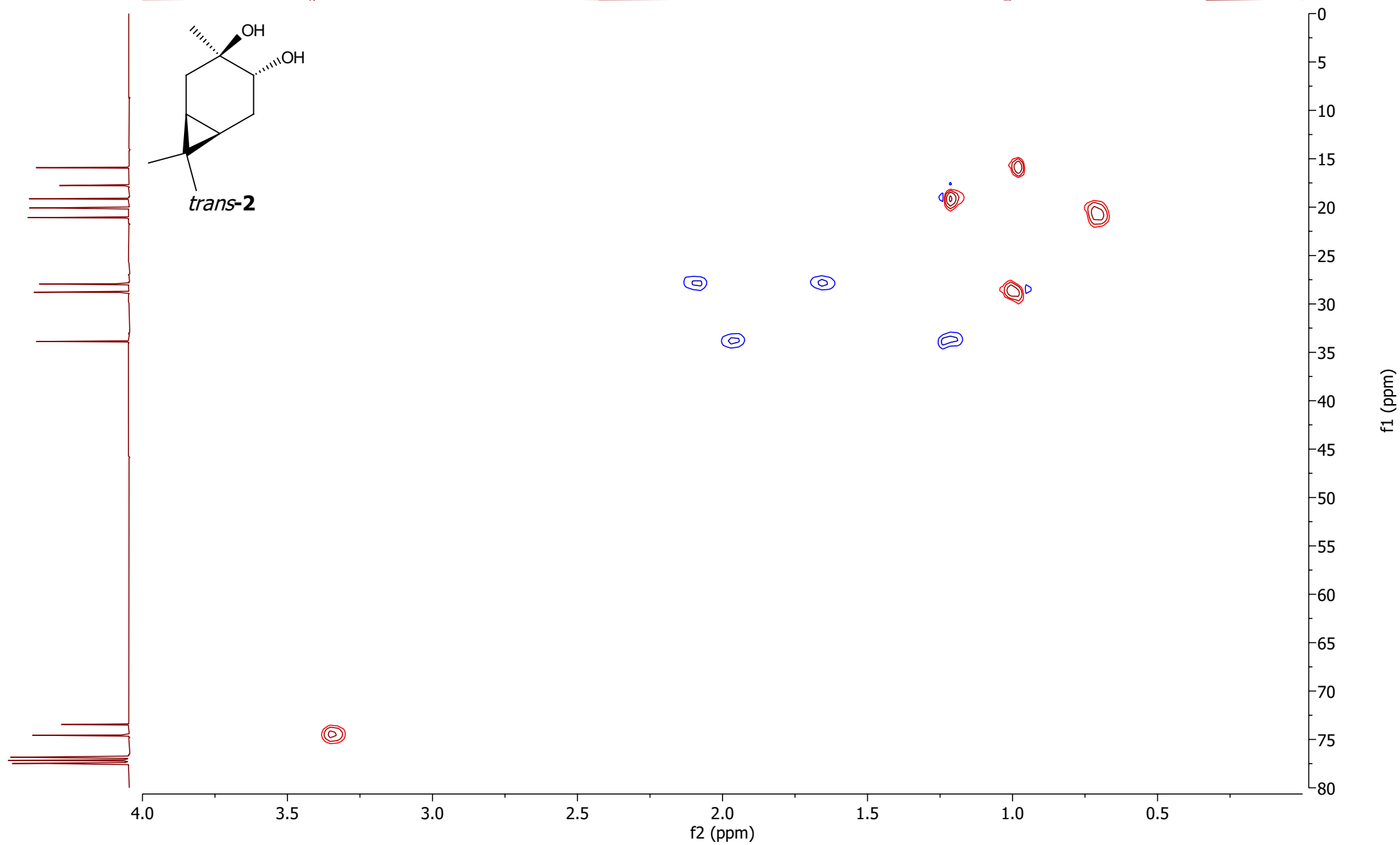
^1H NMR (400 MHz, CDCl_3)



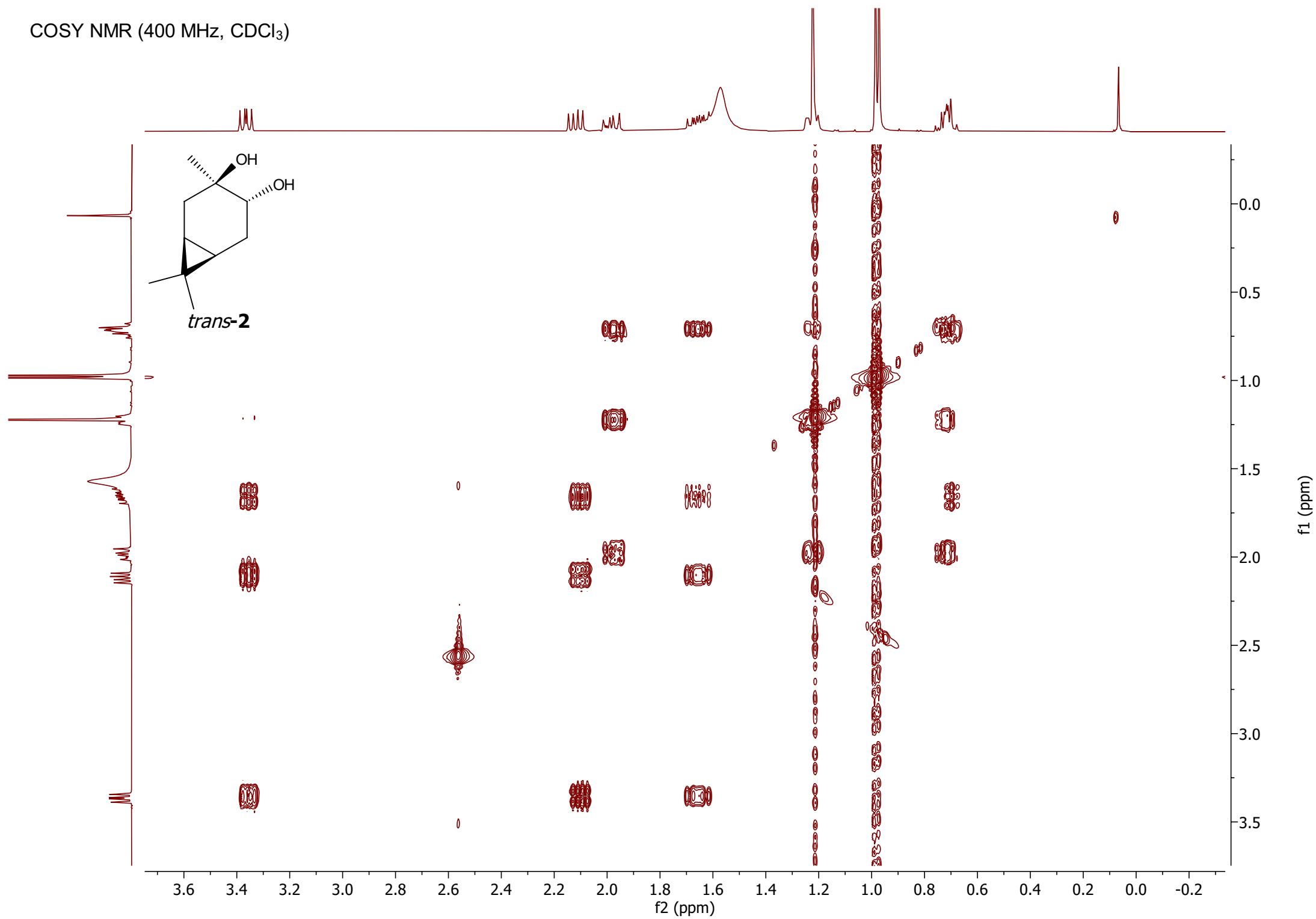
^{13}C $\{^1\text{H}\}$ NMR (101 MHz, CDCl_3)

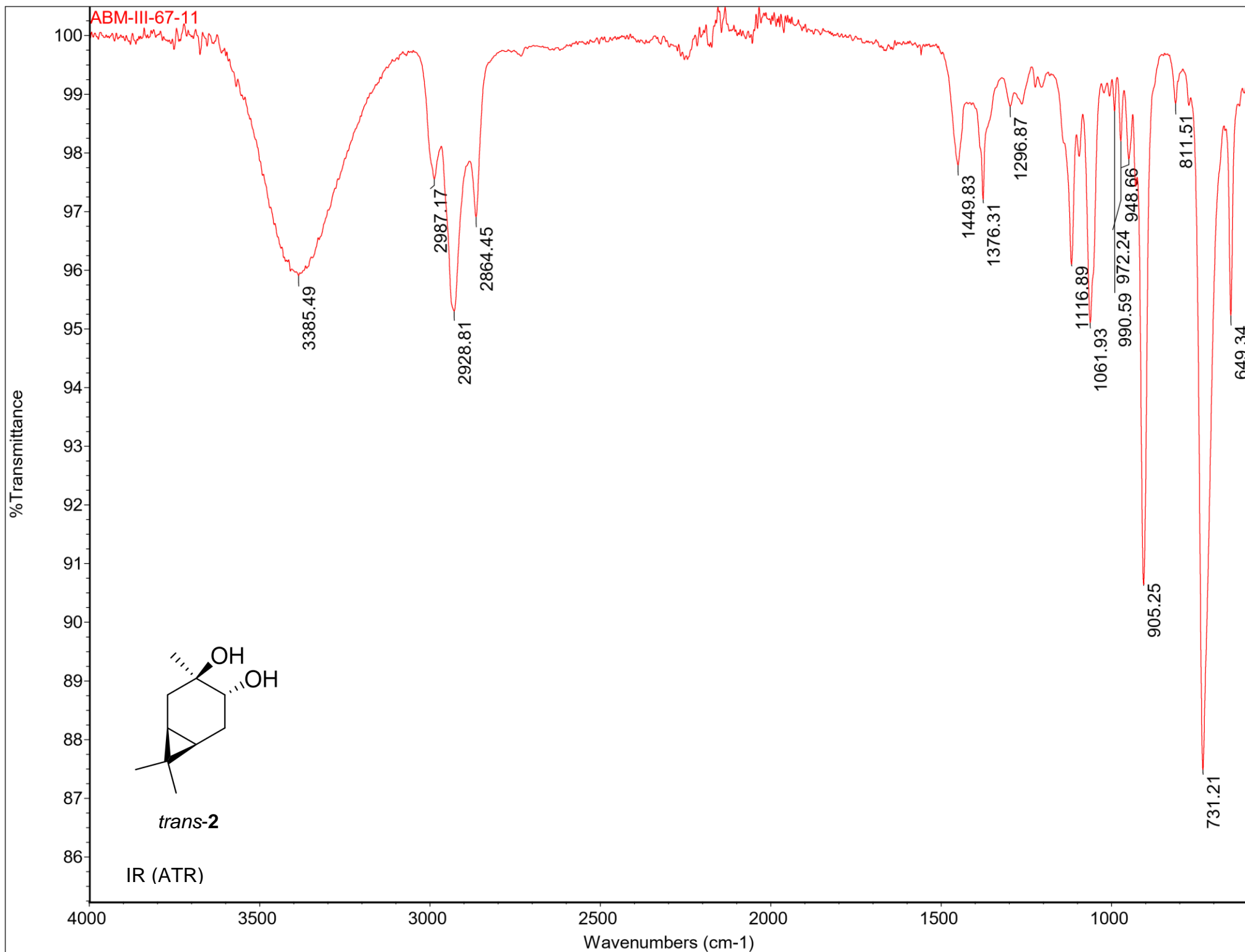


HSQC NMR (^1H - ^{13}C , CDCl_3)

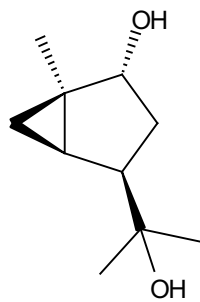


COSY NMR (400 MHz, CDCl₃)

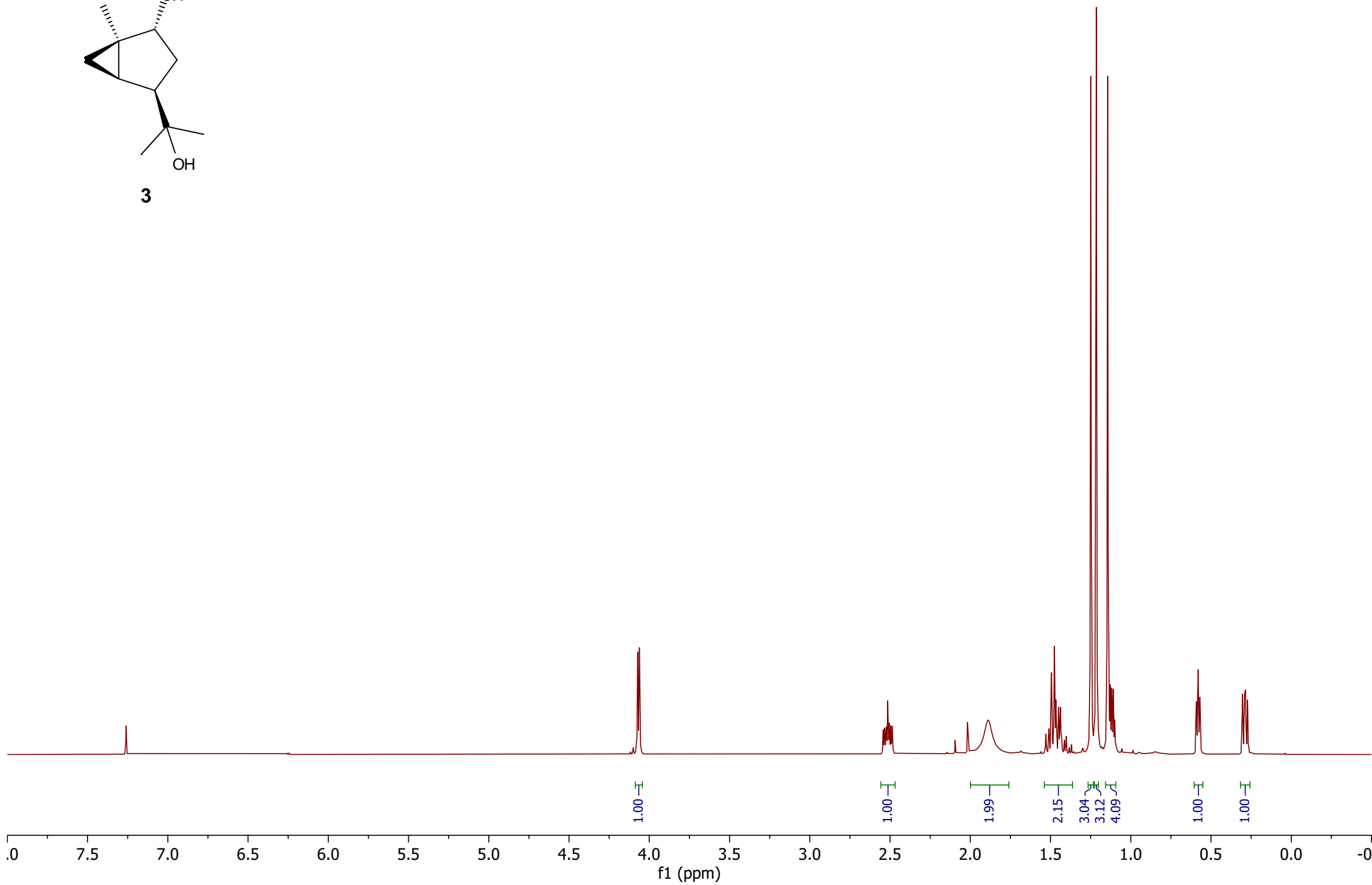




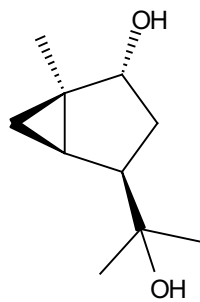
^1H NMR (400 MHz, CDCl_3)



3



^{13}C $\{^1\text{H}\}$ NMR (101 MHz, CDCl_3)



3

77.16 CDCl_3

76.70

72.59

48.19

32.45

29.48

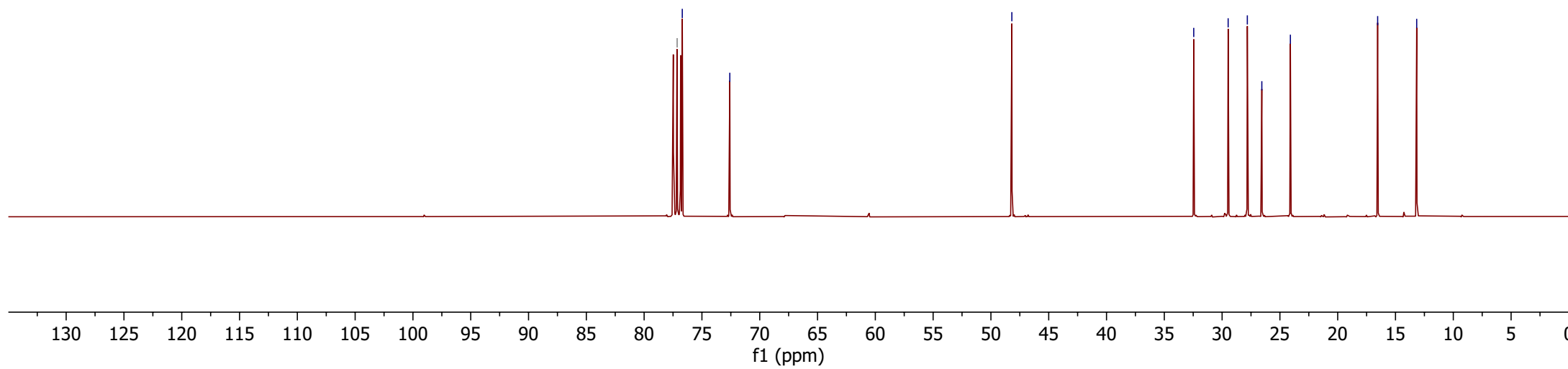
27.82

26.56

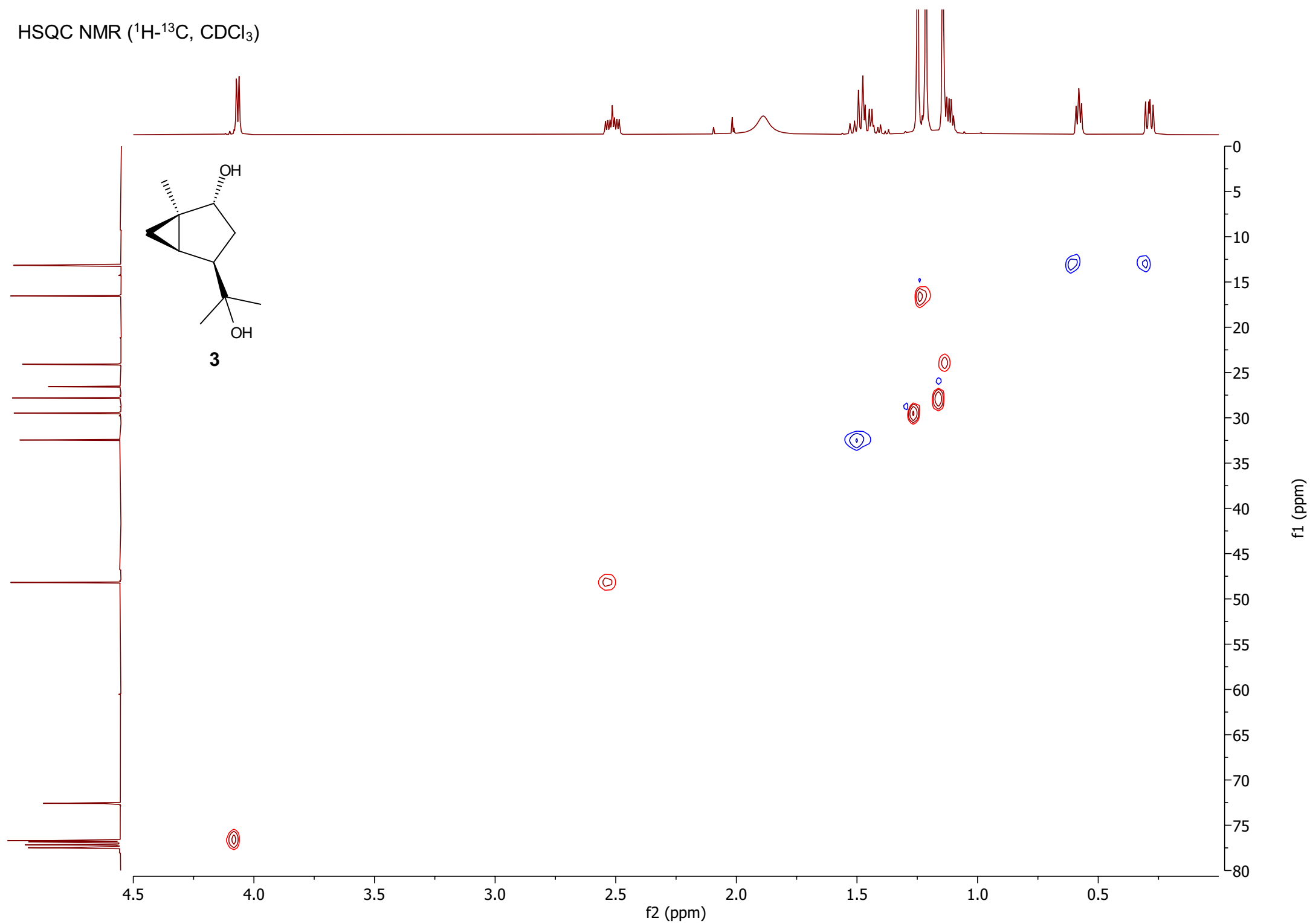
24.09

16.54

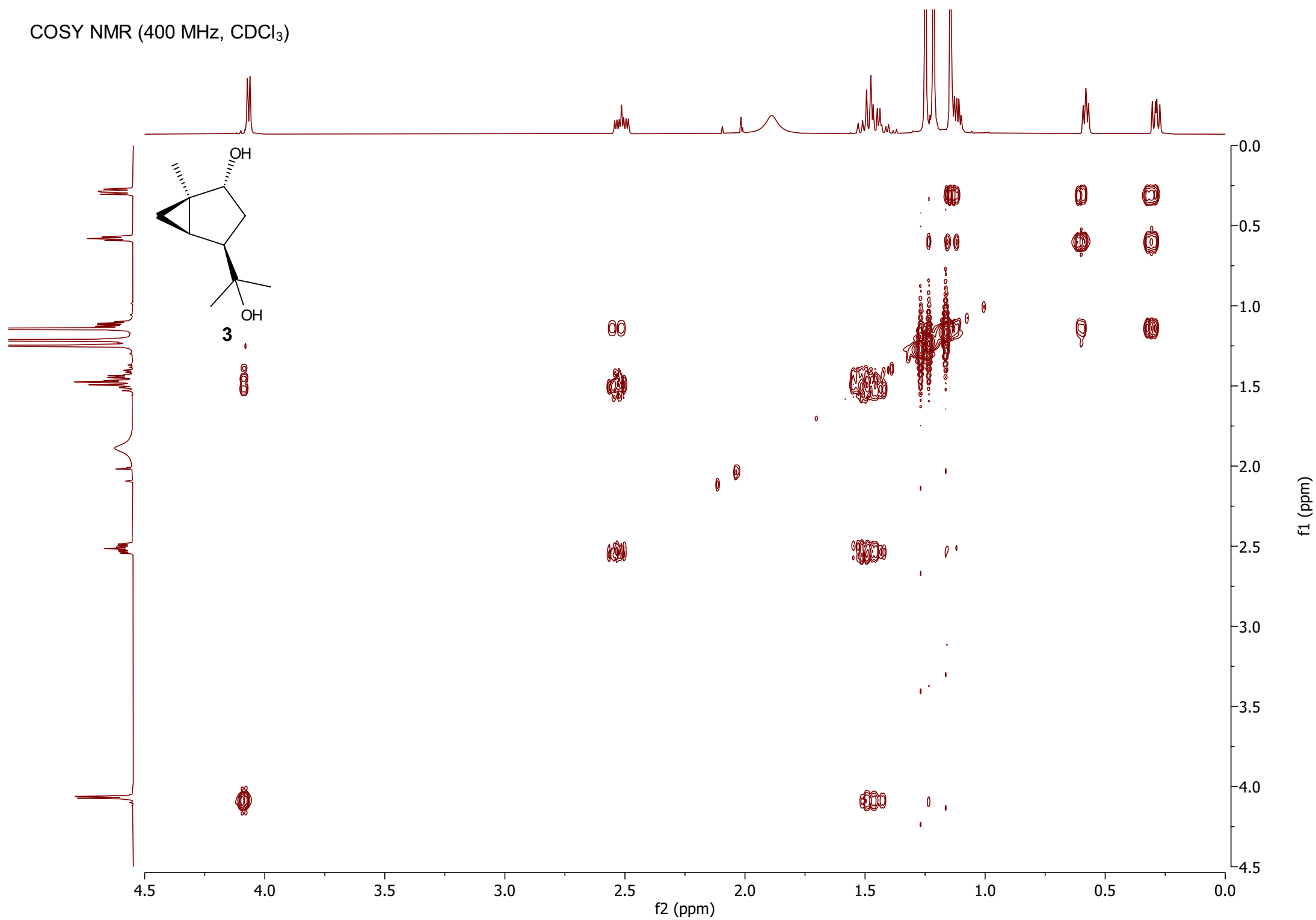
13.17



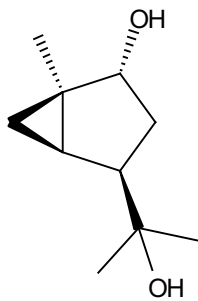
HSQC NMR (^1H - ^{13}C , CDCl_3)



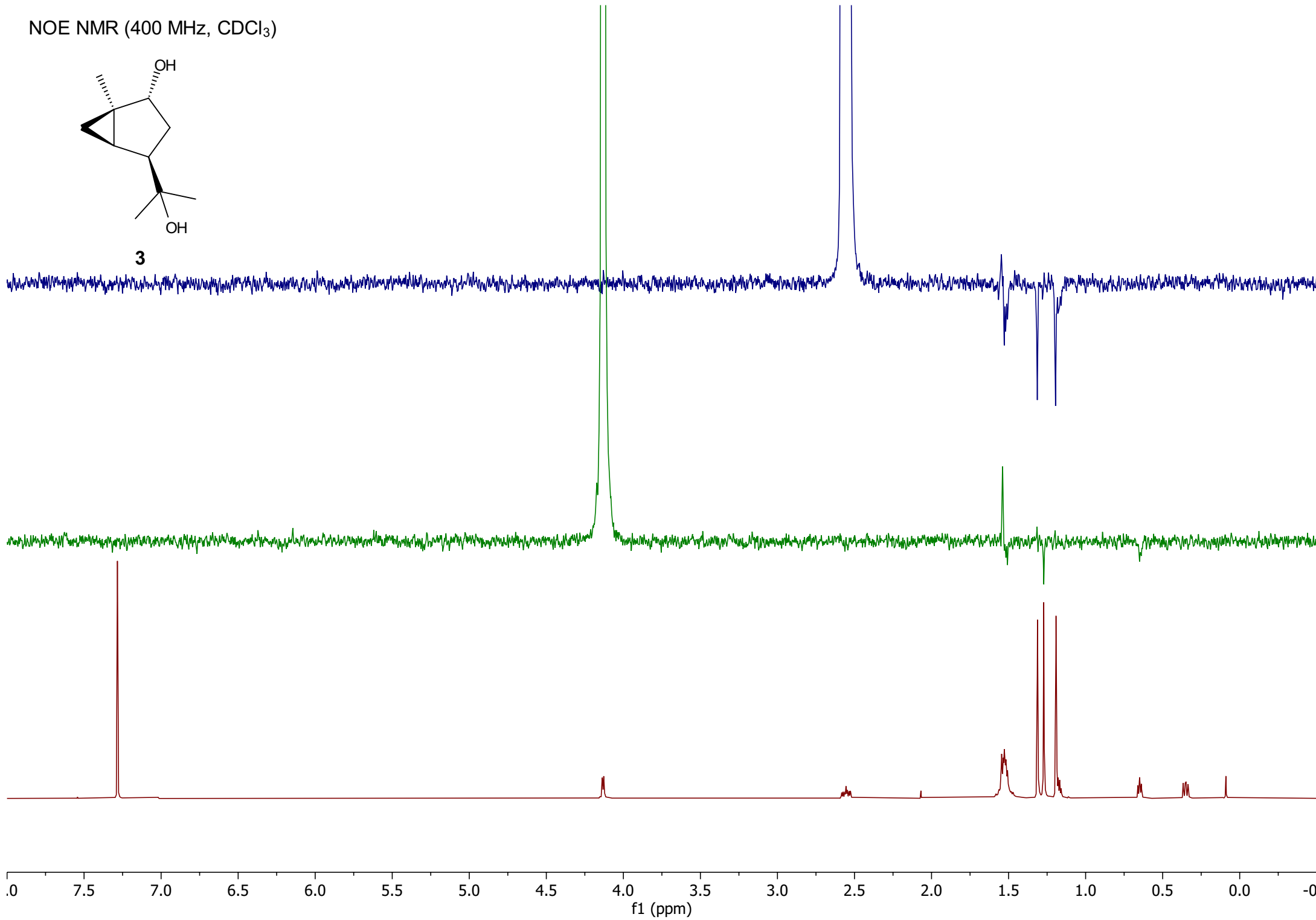
COSY NMR (400 MHz, CDCl₃)



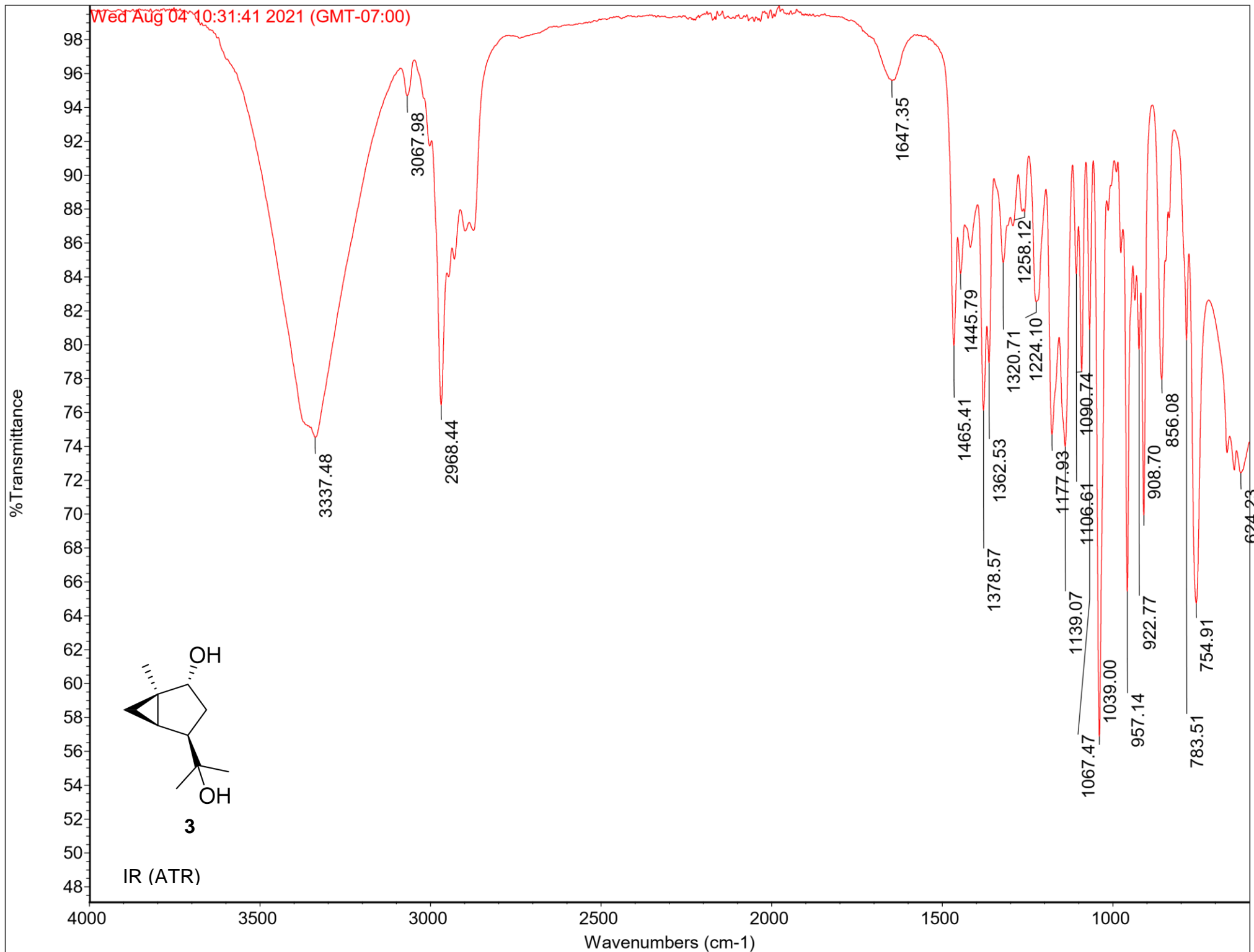
NOE NMR (400 MHz, CDCl₃)



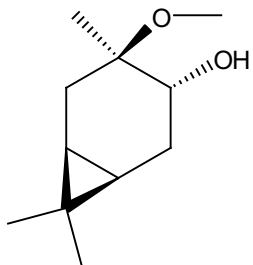
3



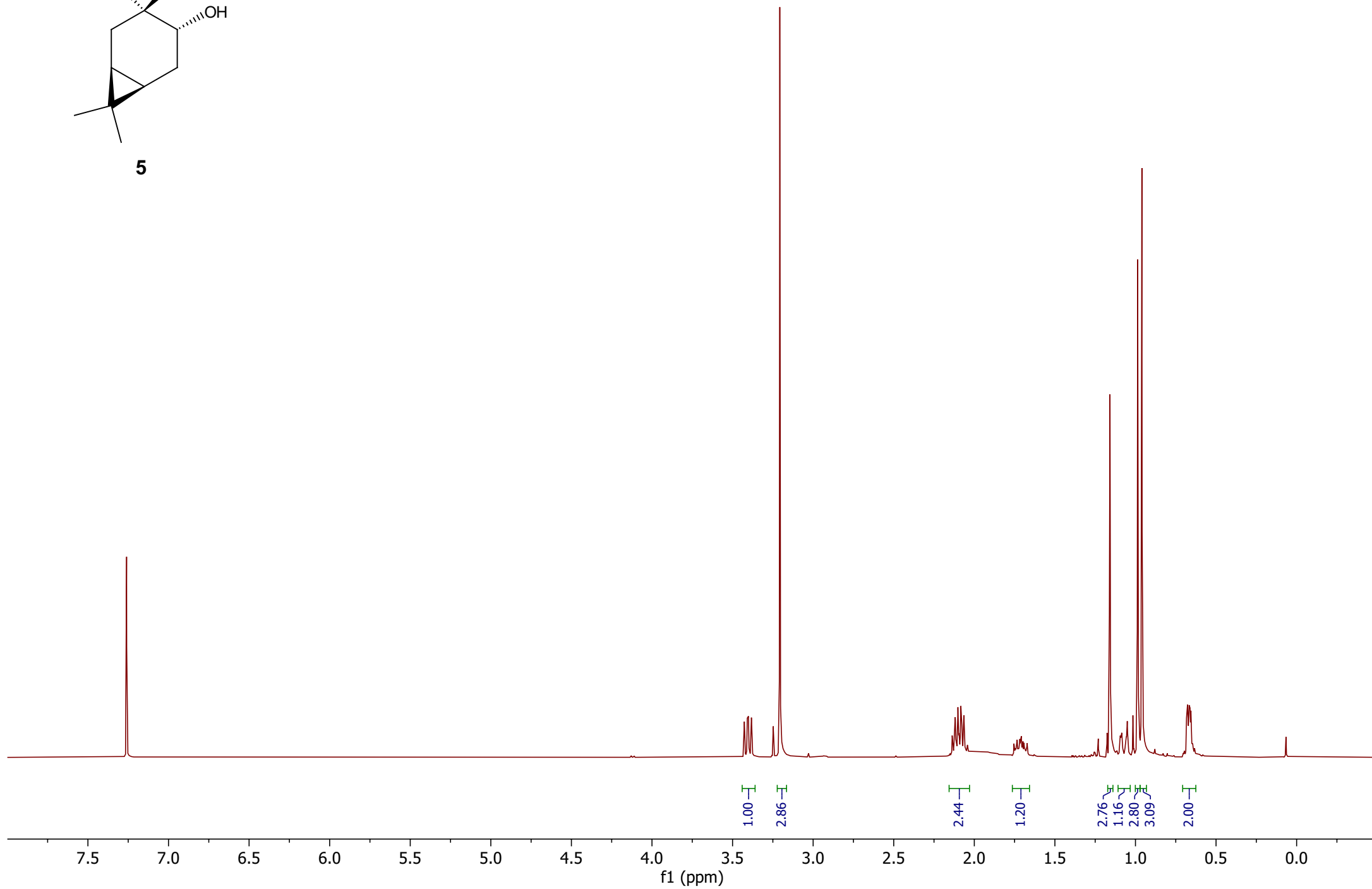
Wed Aug 04 10:31:41 2021 (GMT-07:00)



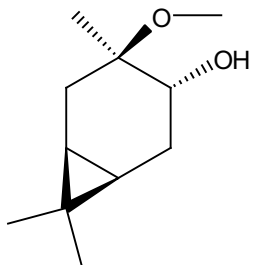
^1H NMR (400 MHz, CDCl_3)



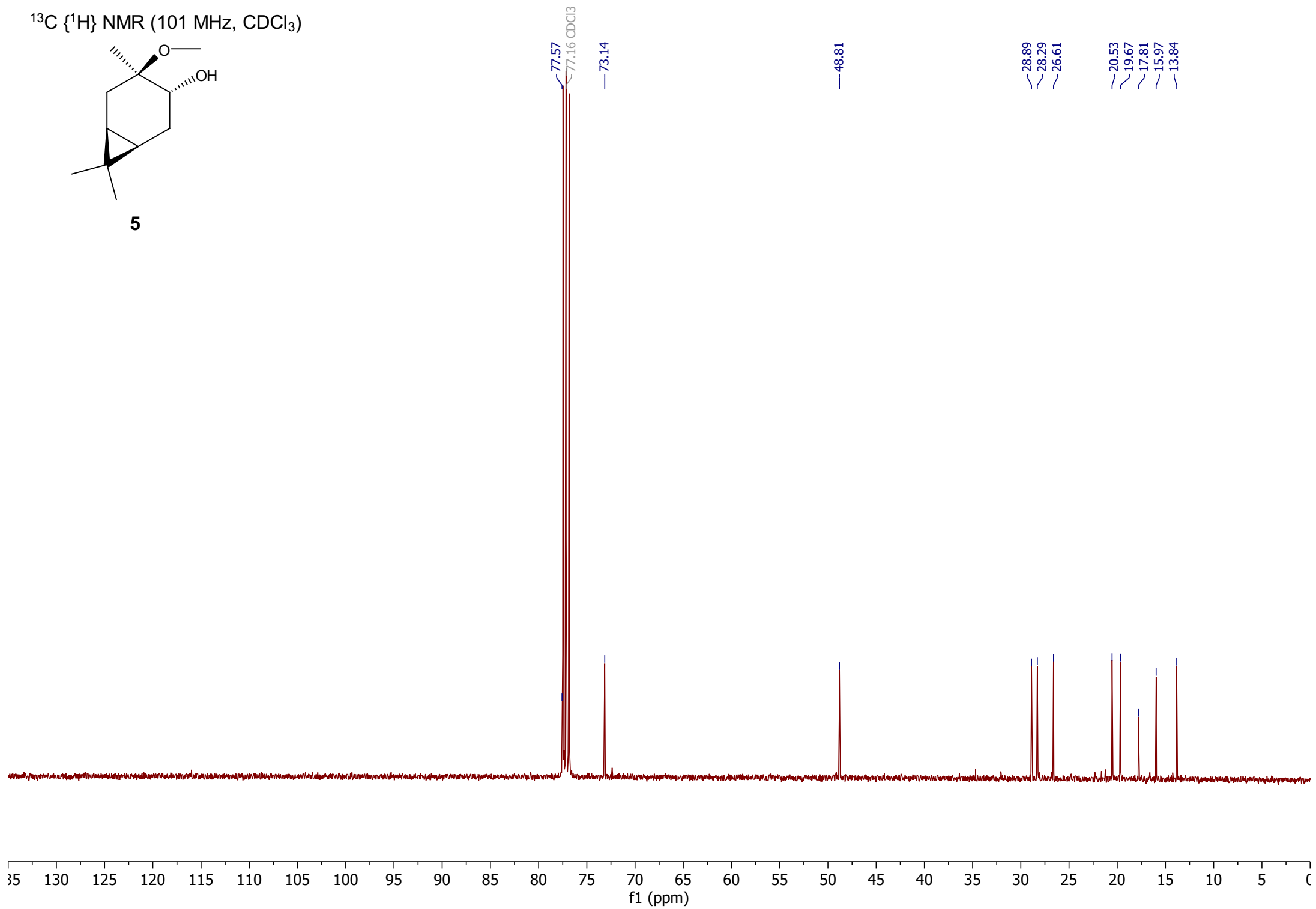
5



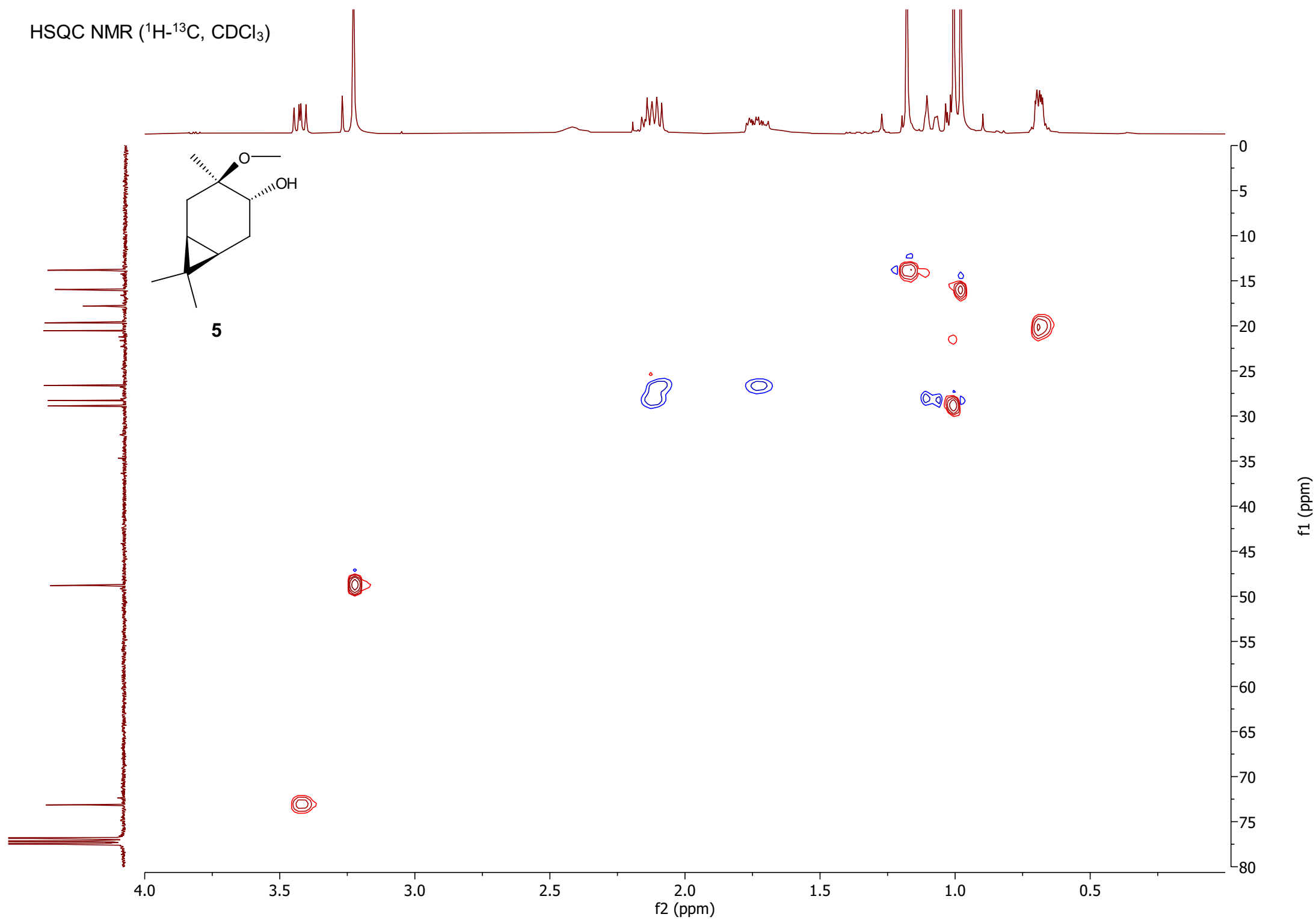
^{13}C { ^1H } NMR (101 MHz, CDCl_3)



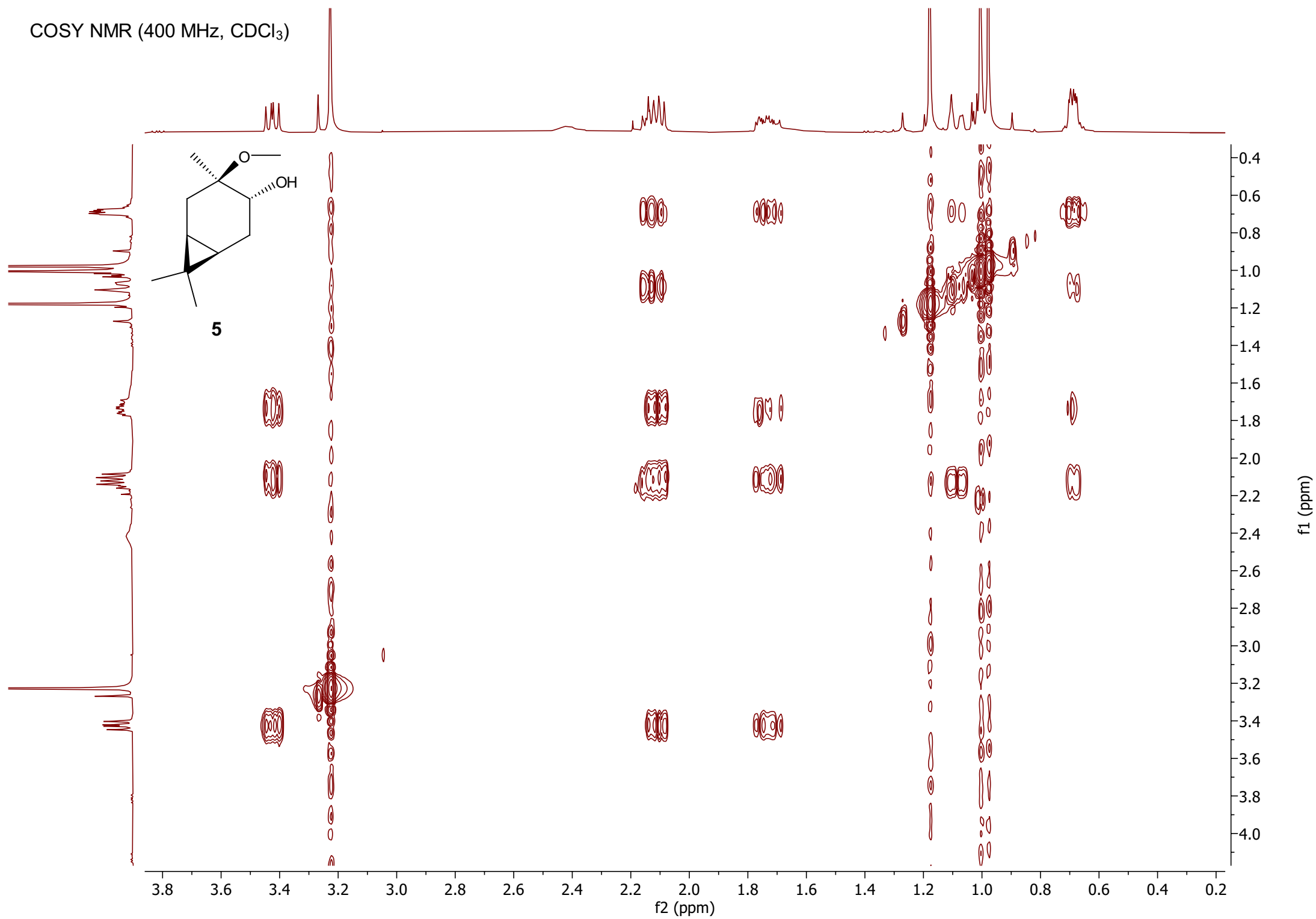
5



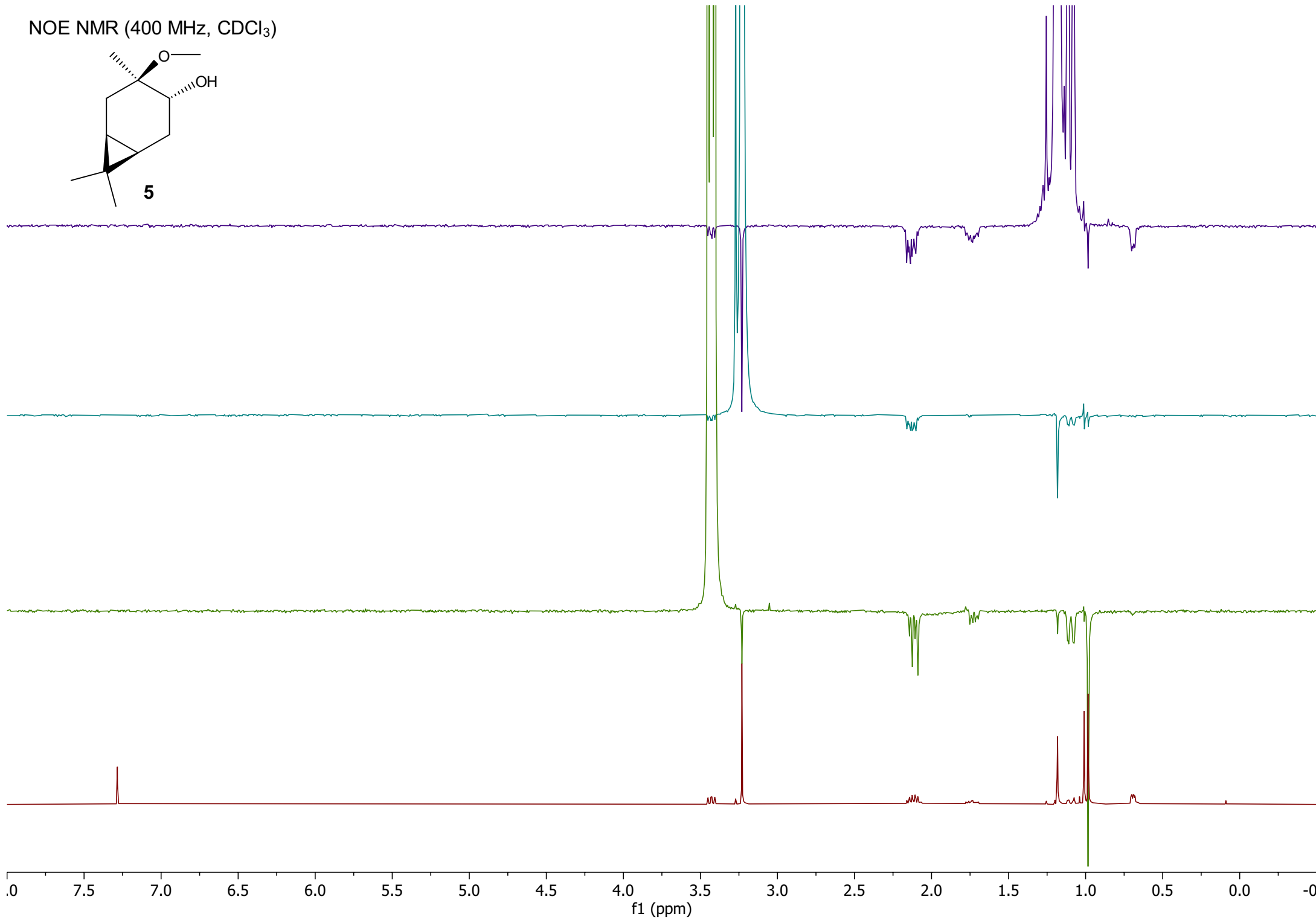
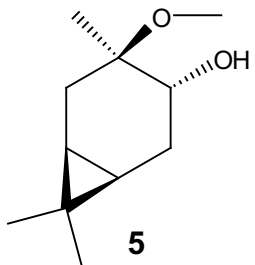
HSQC NMR (^1H - ^{13}C , CDCl_3)



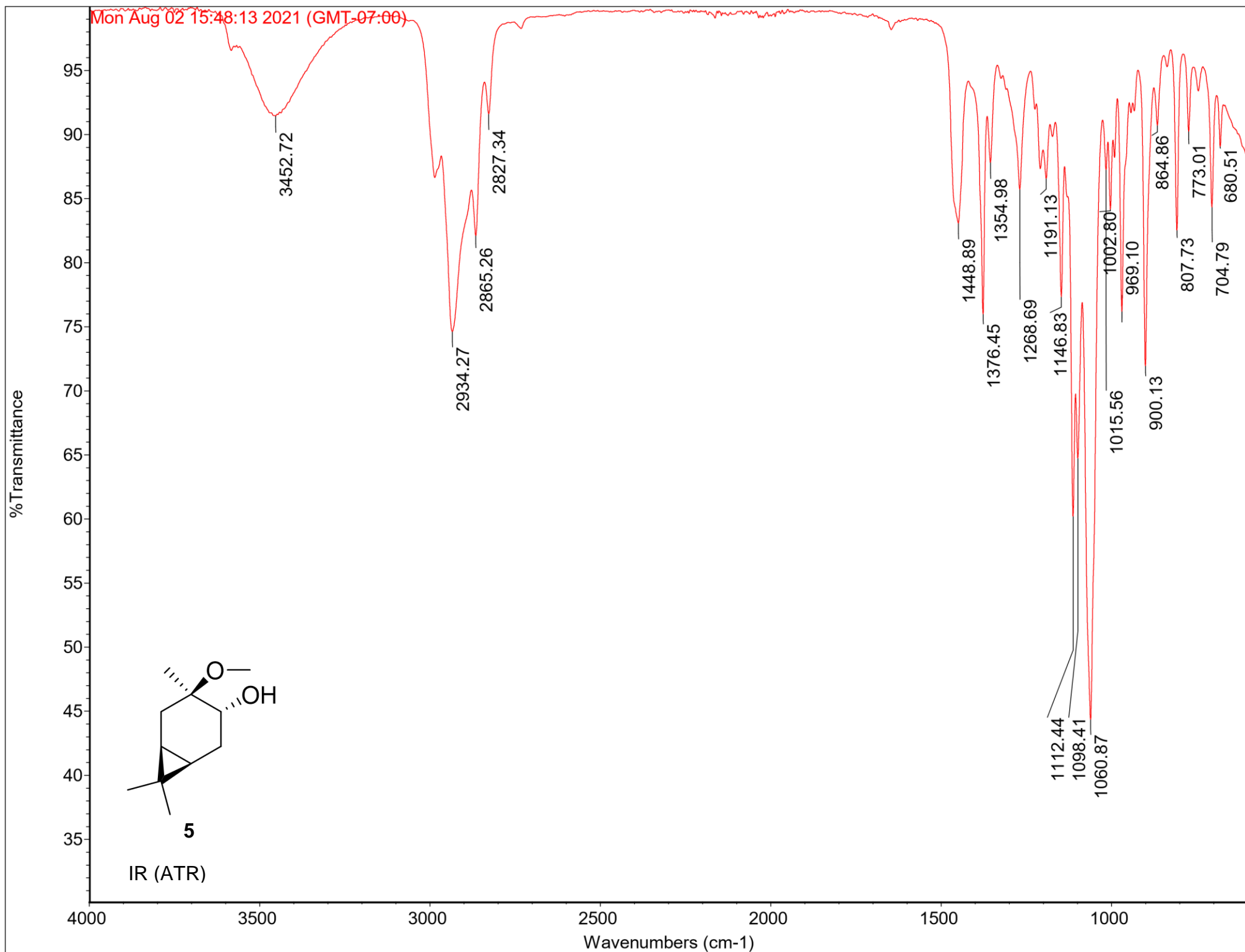
COSY NMR (400 MHz, CDCl₃)



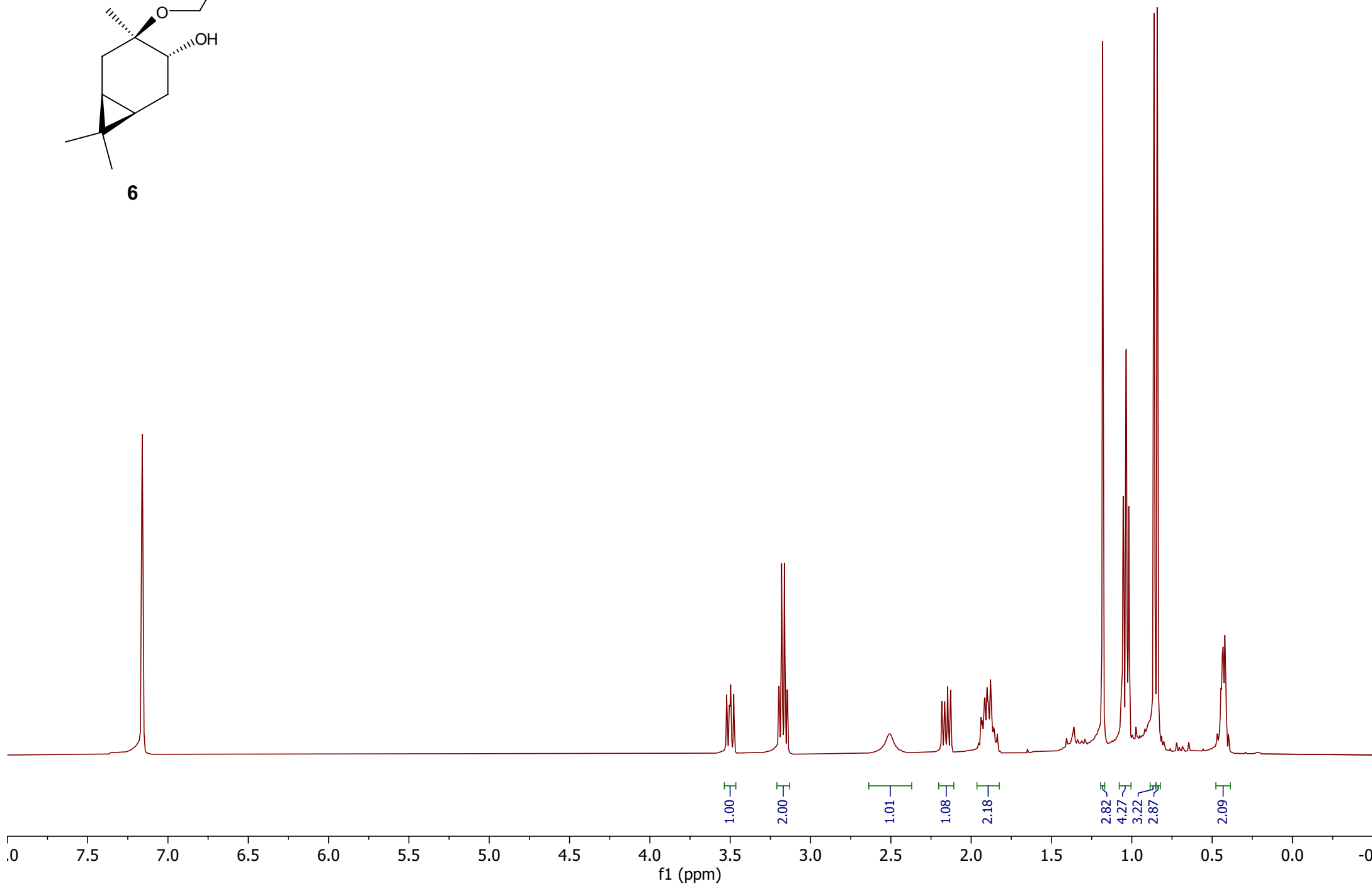
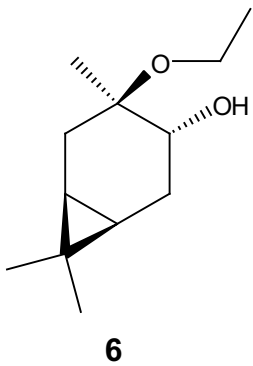
NOE NMR (400 MHz, CDCl₃)



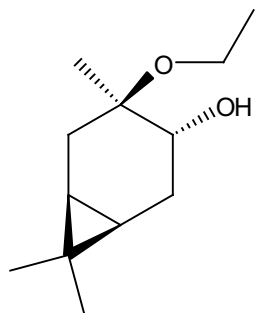
Mon Aug 02 15:48:13 2021 (GMT-07:00)



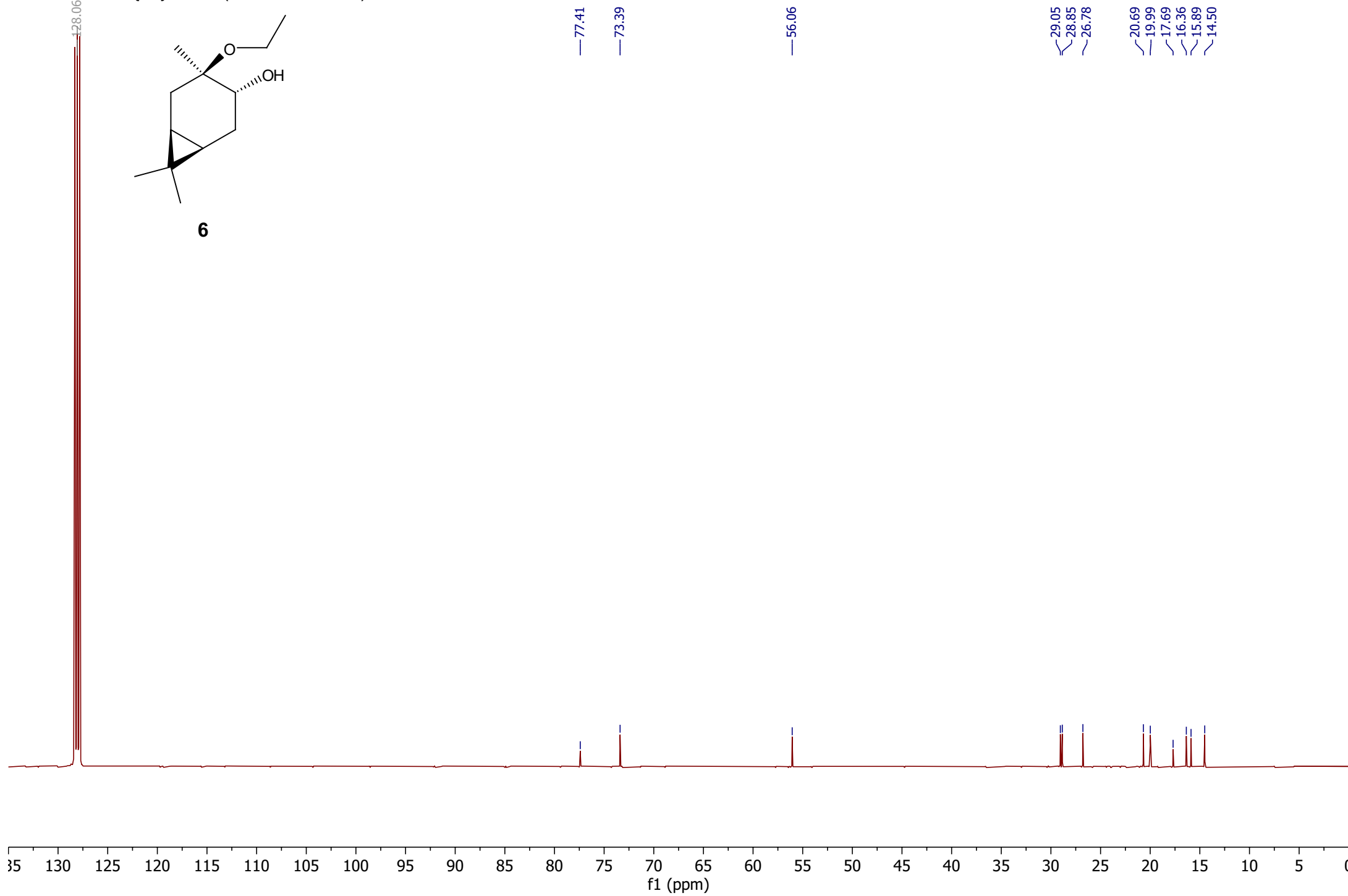
^1H NMR (400 MHz, C_6D_6)



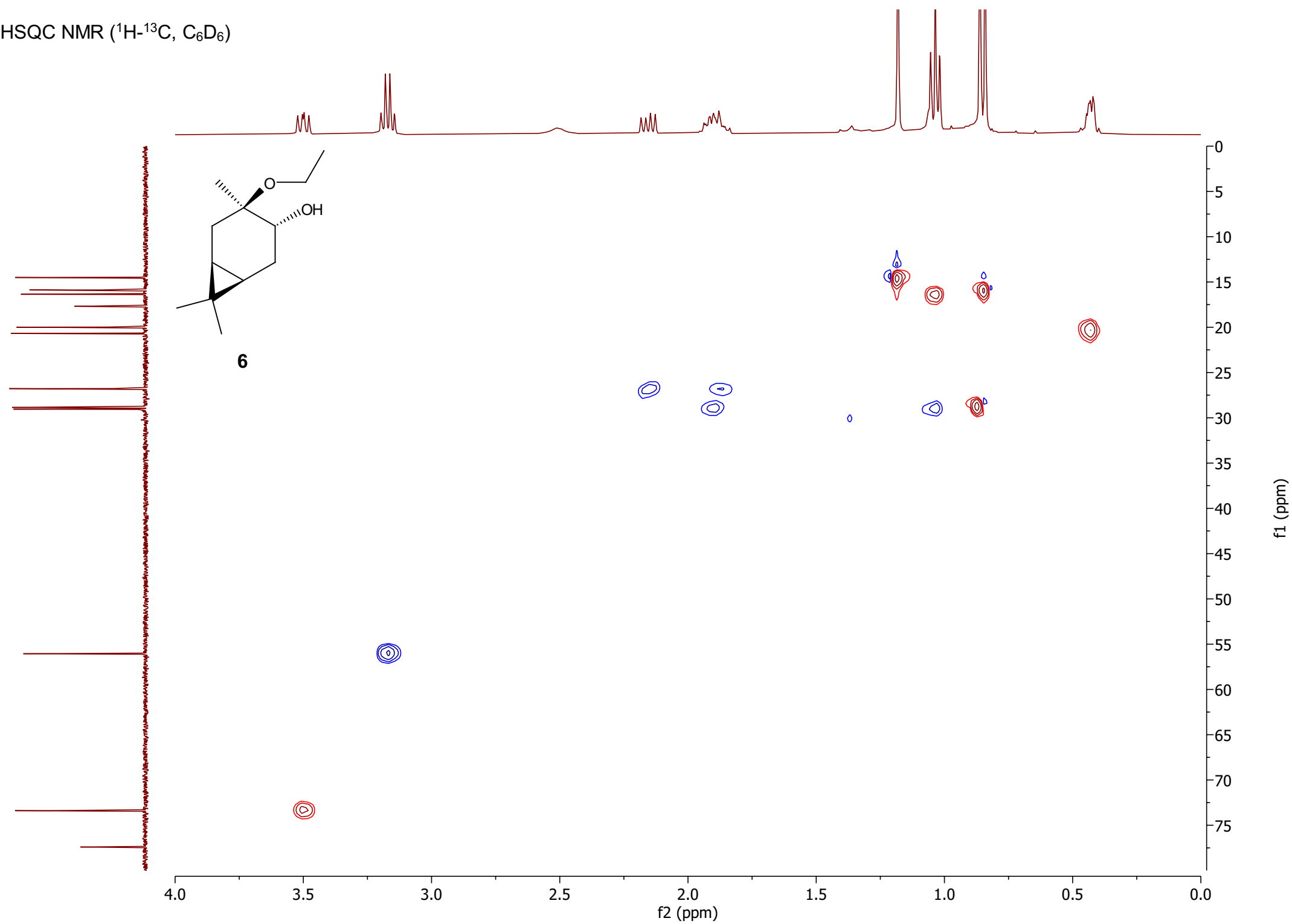
^{13}C $\{^1\text{H}\}$ NMR (101 MHz, C_6D_6)



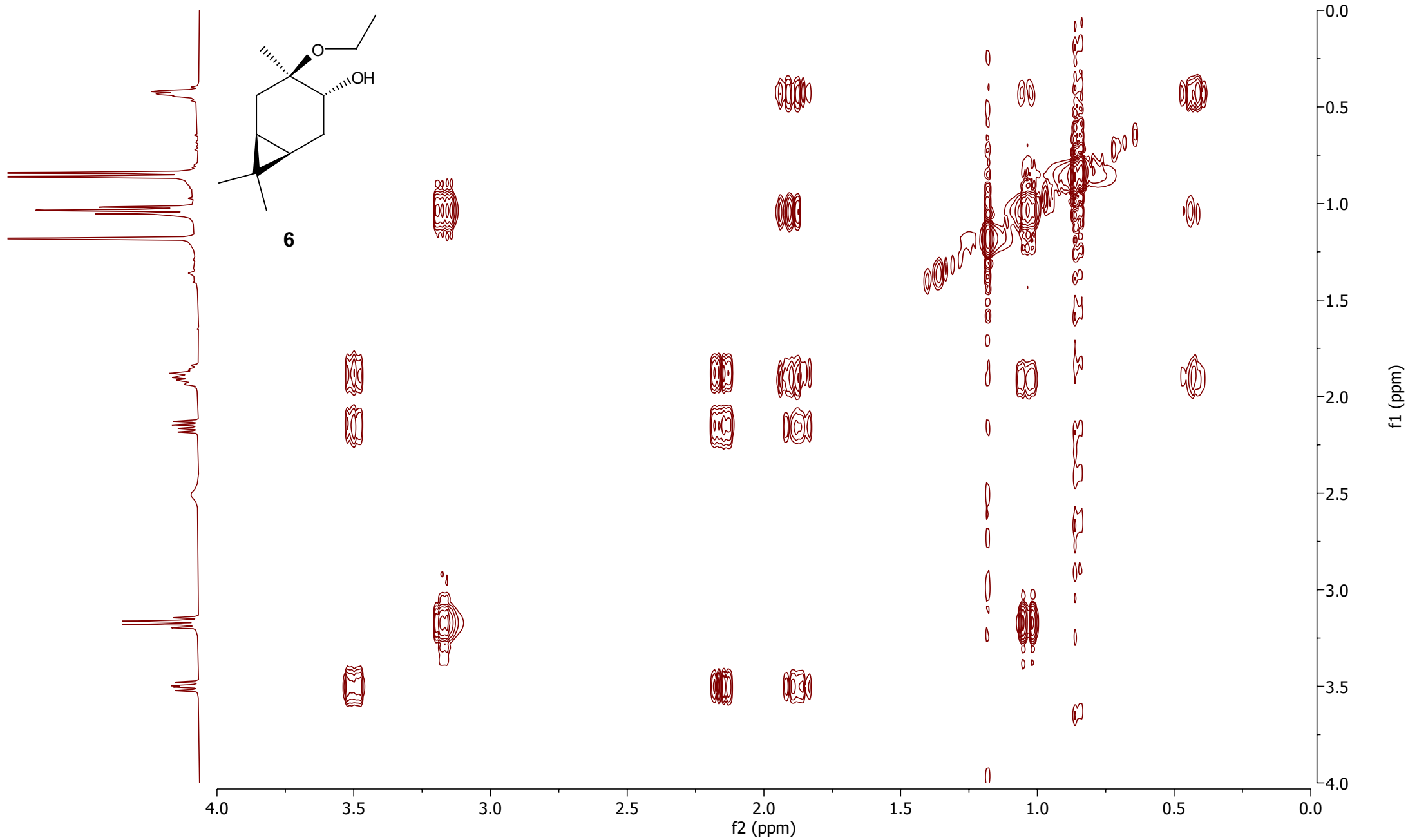
6



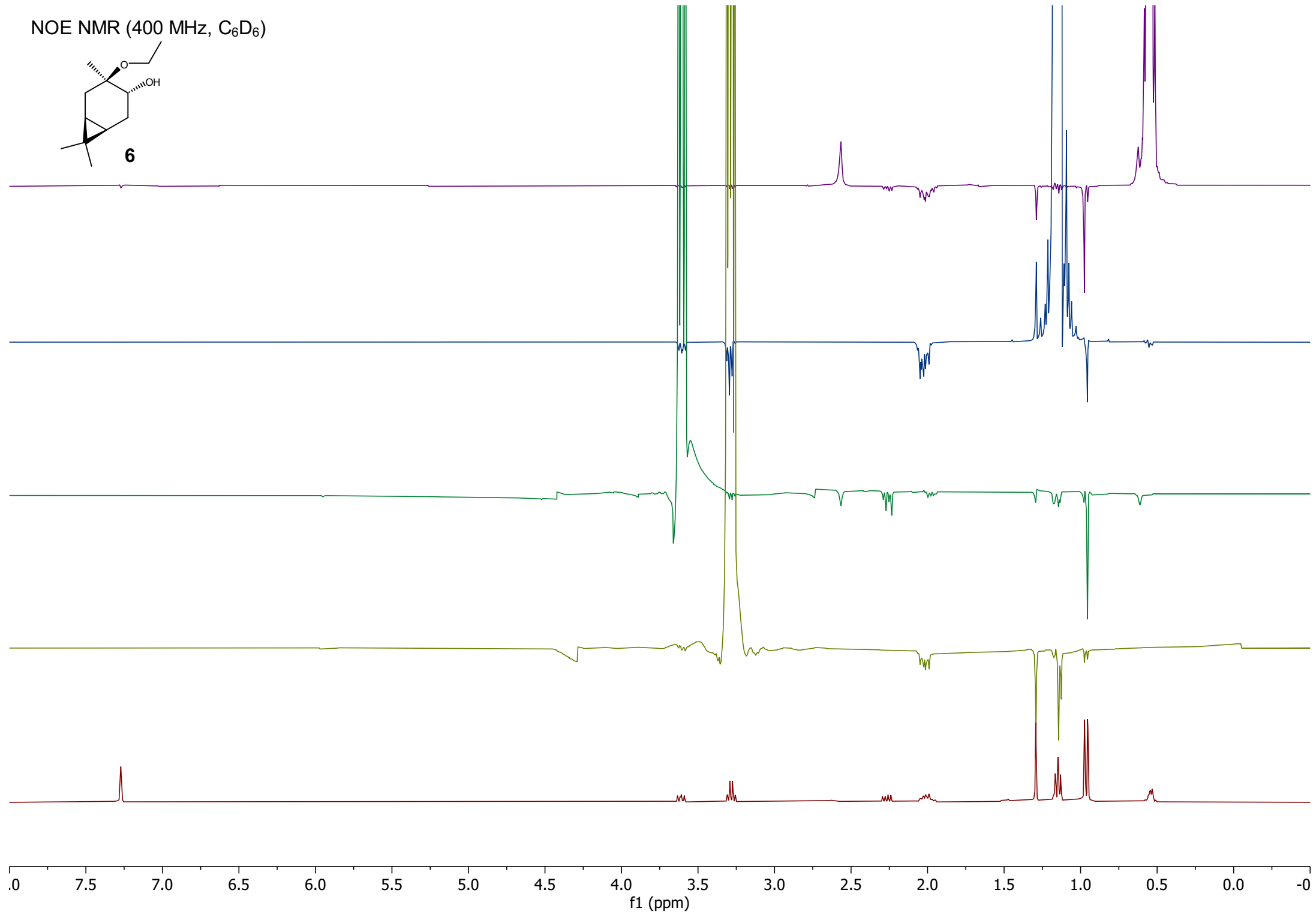
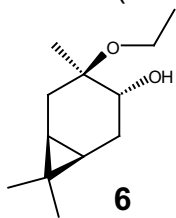
HSQC NMR (^1H - ^{13}C , C_6D_6)

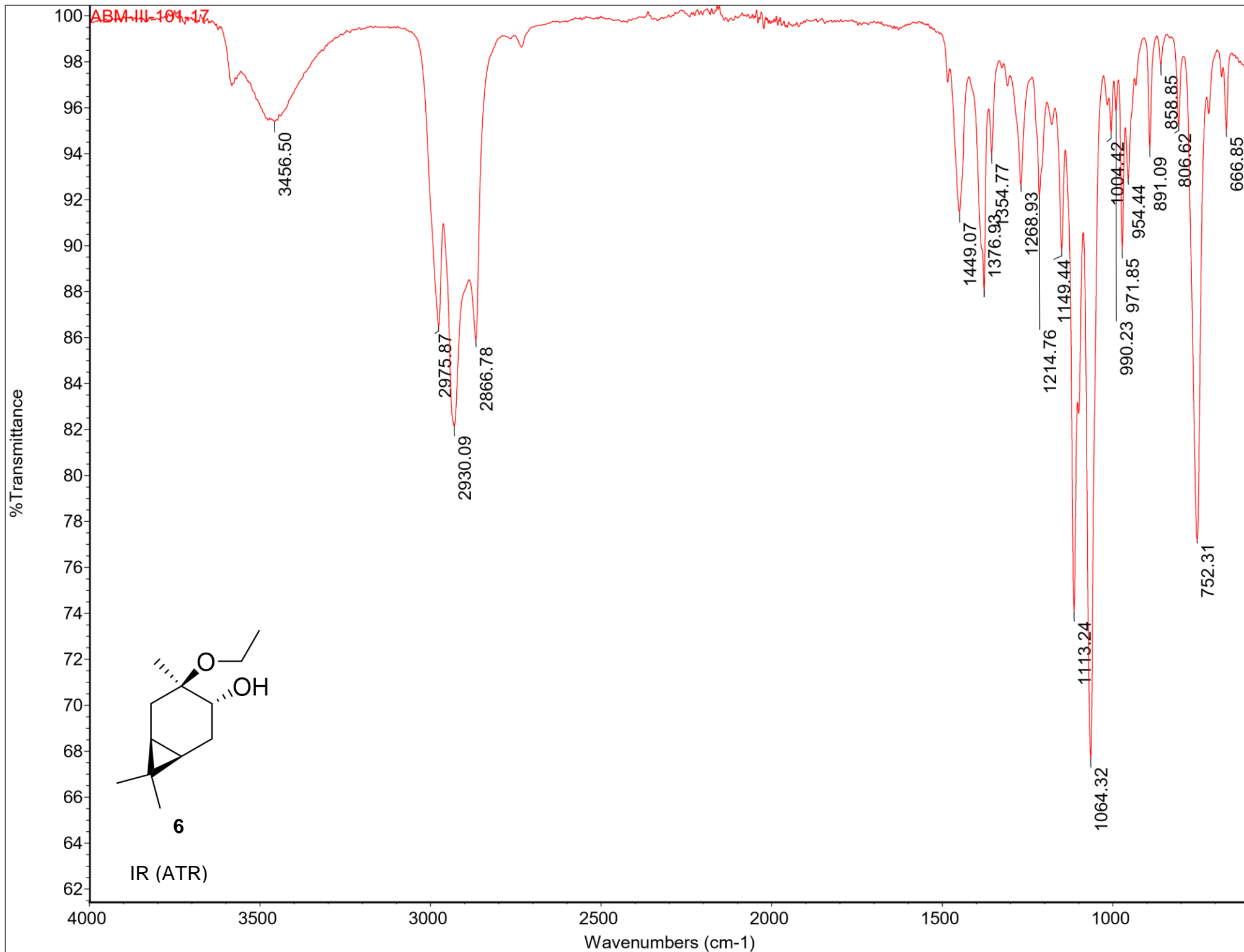


COSY NMR (400 MHz, C₆D₆)

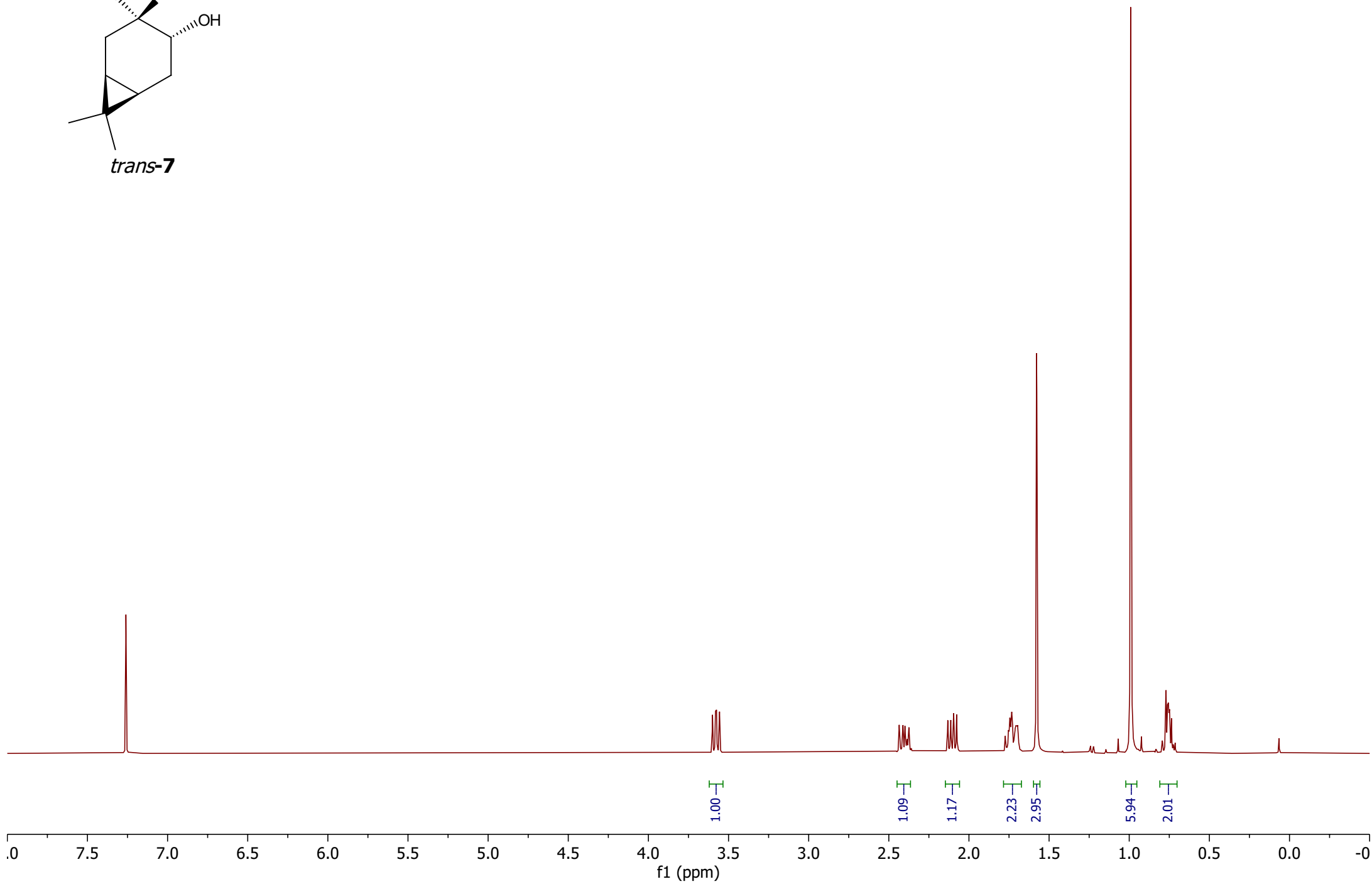
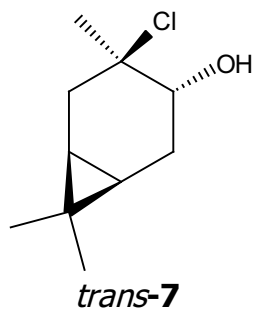


NOE NMR (400 MHz, C₆D₆)

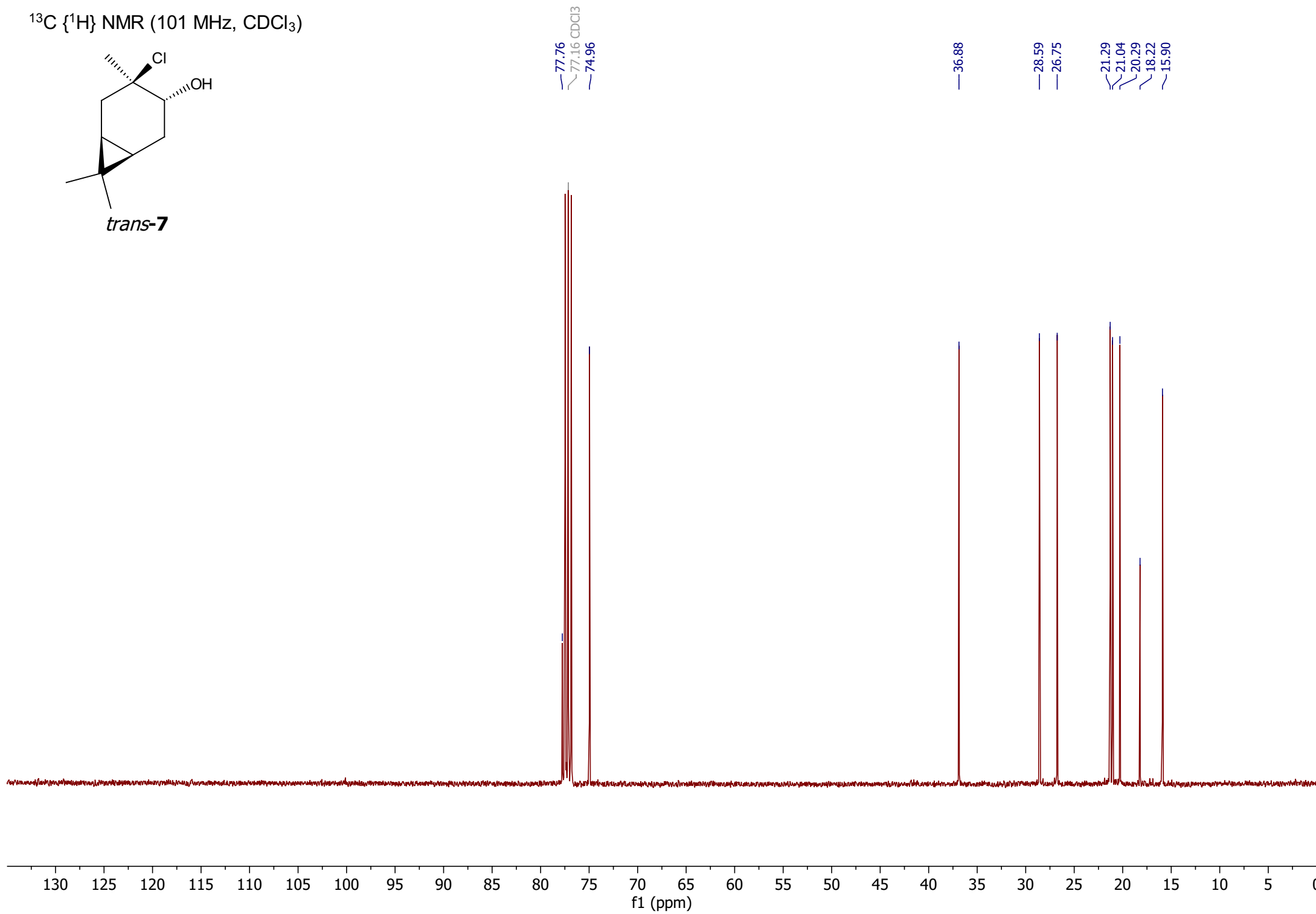
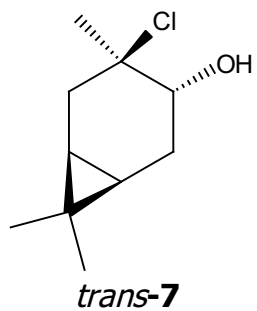




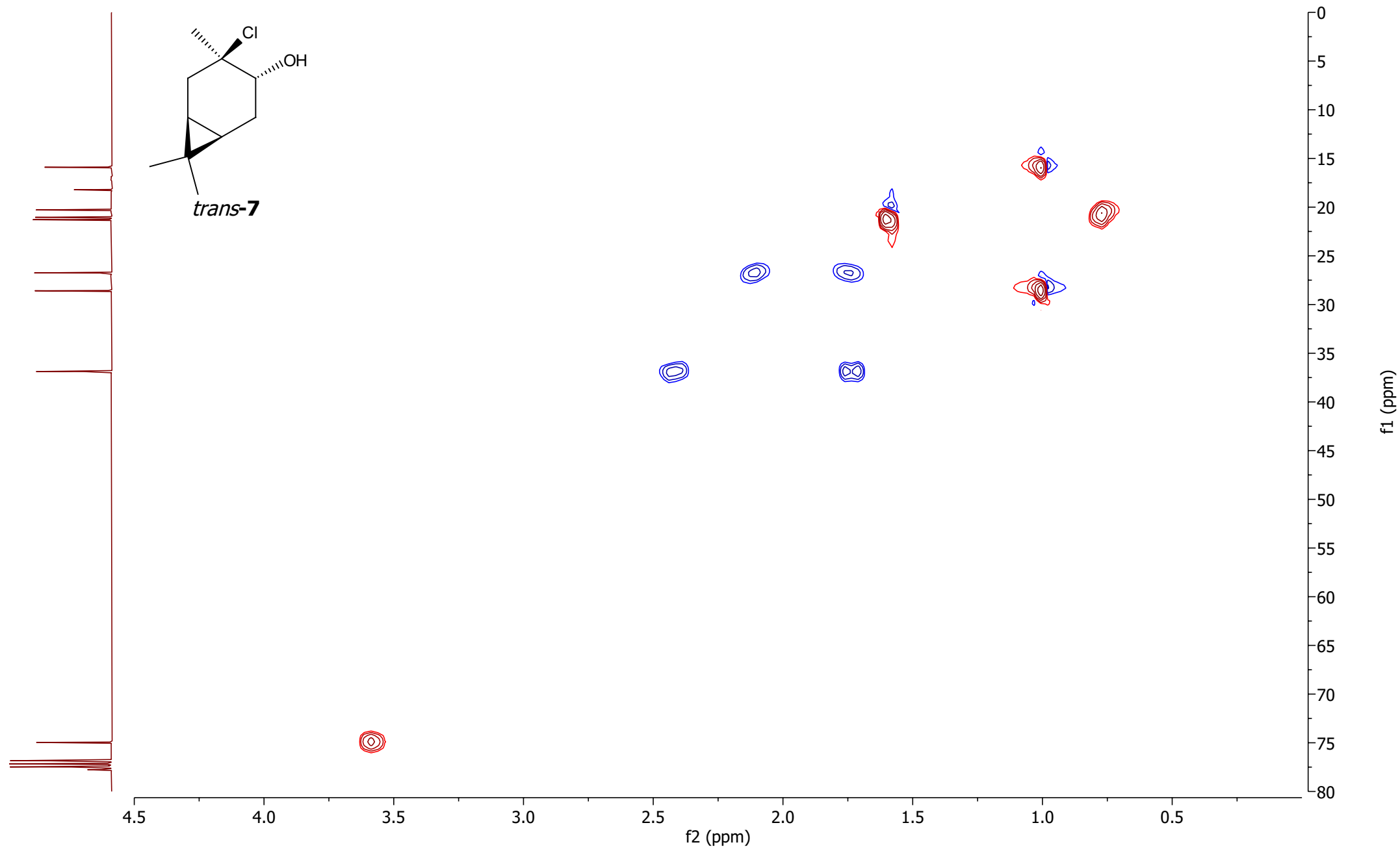
^1H NMR (400 MHz, CDCl_3)



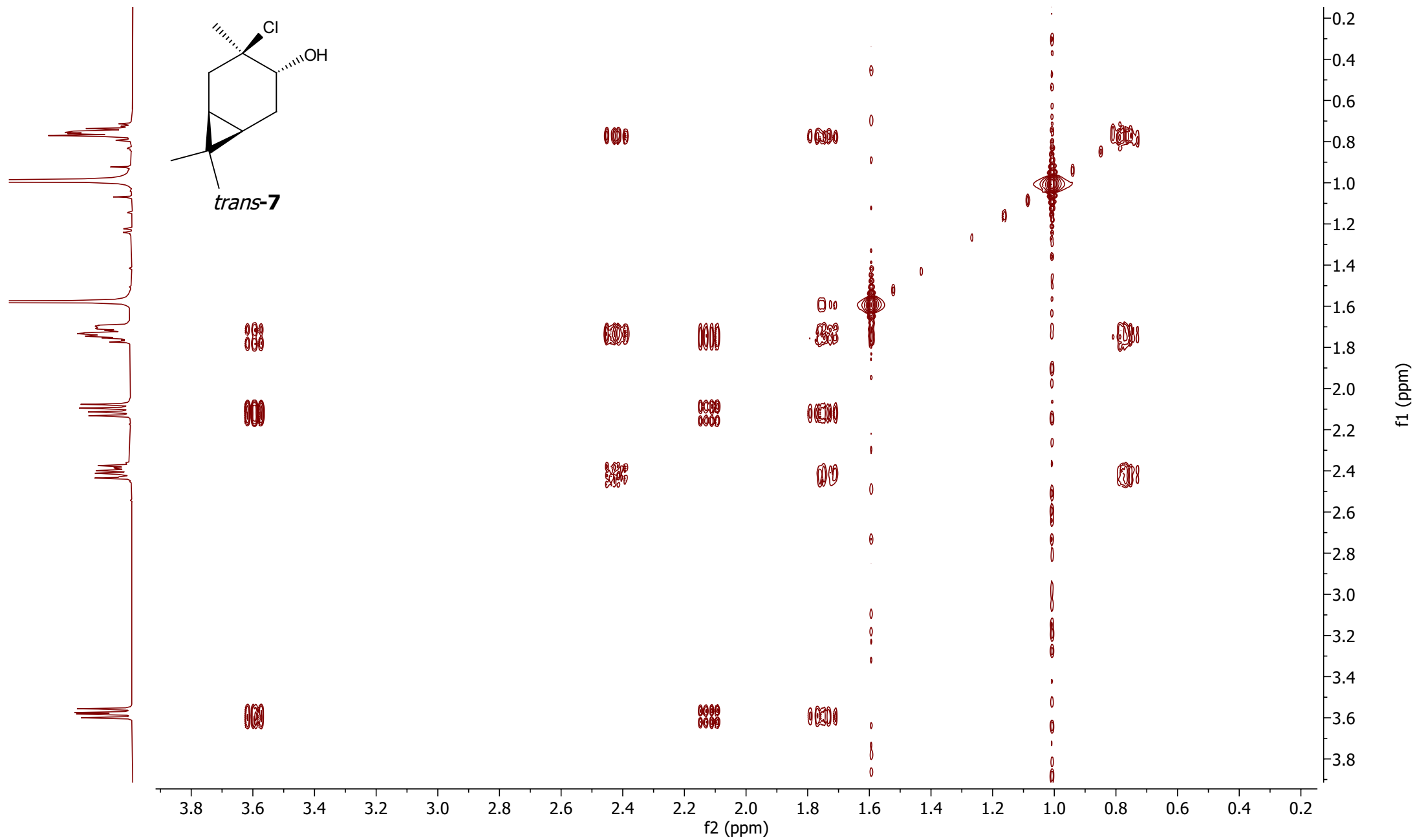
^{13}C $\{^1\text{H}\}$ NMR (101 MHz, CDCl_3)



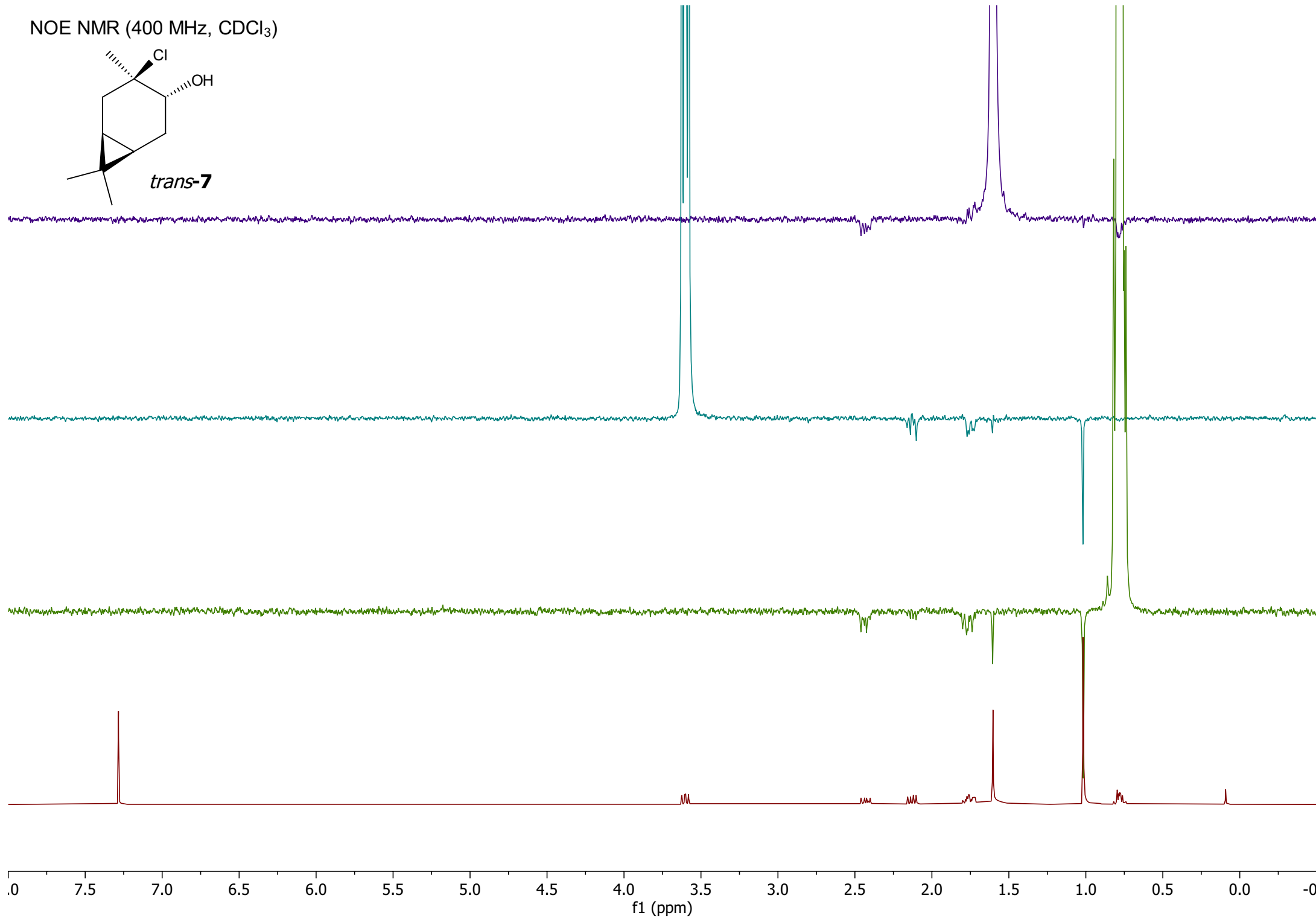
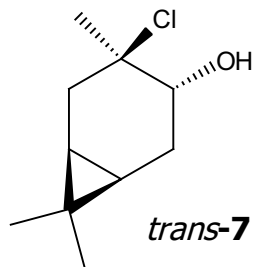
HSQC NMR (^1H - ^{13}C , CDCl_3)

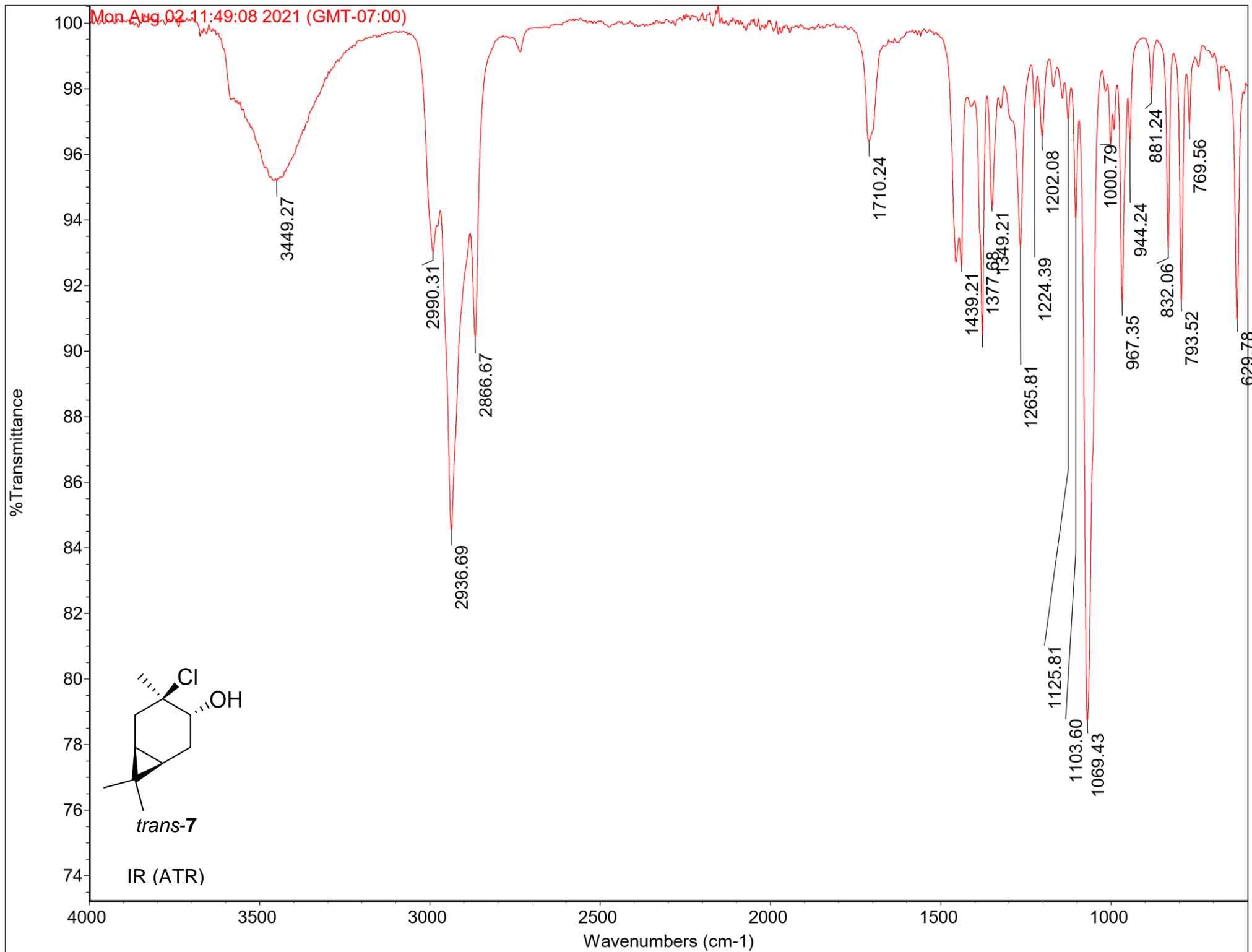


COSY NMR (400 MHz, CDCl₃)

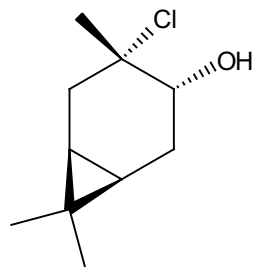


NOE NMR (400 MHz, CDCl₃)

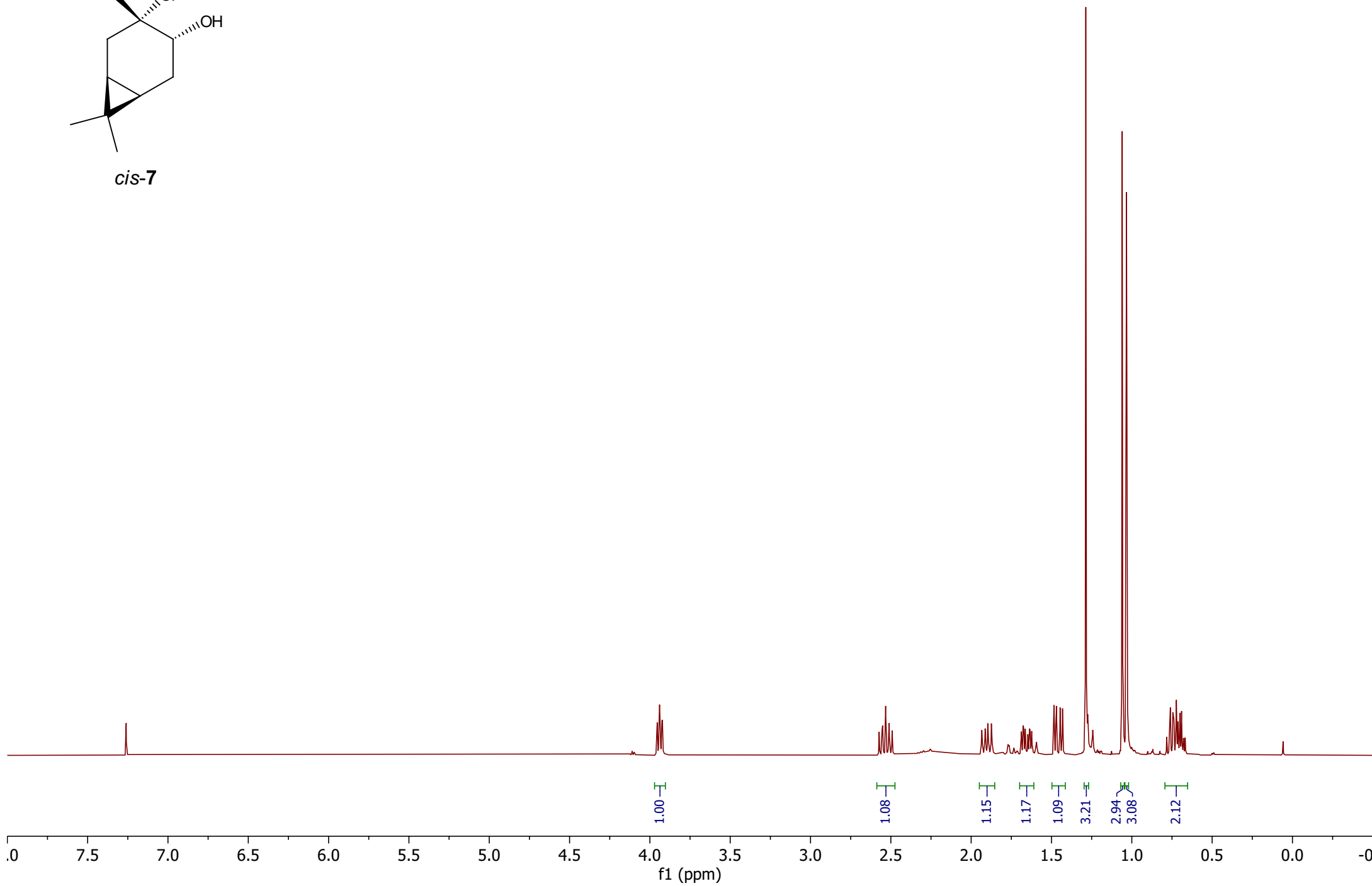




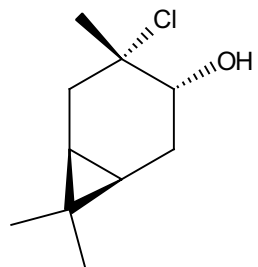
^1H NMR (400 MHz, CDCl_3)



cis-7



^{13}C $\{^1\text{H}\}$ NMR (101 MHz, CDCl_3)



cis-7

— 77.16 CDCl_3

— 71.96

— 63.73

— 29.64

— 28.60

— 27.62

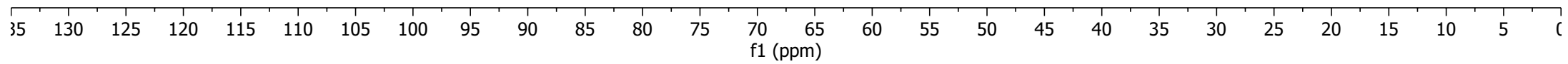
— 26.74

— 19.27

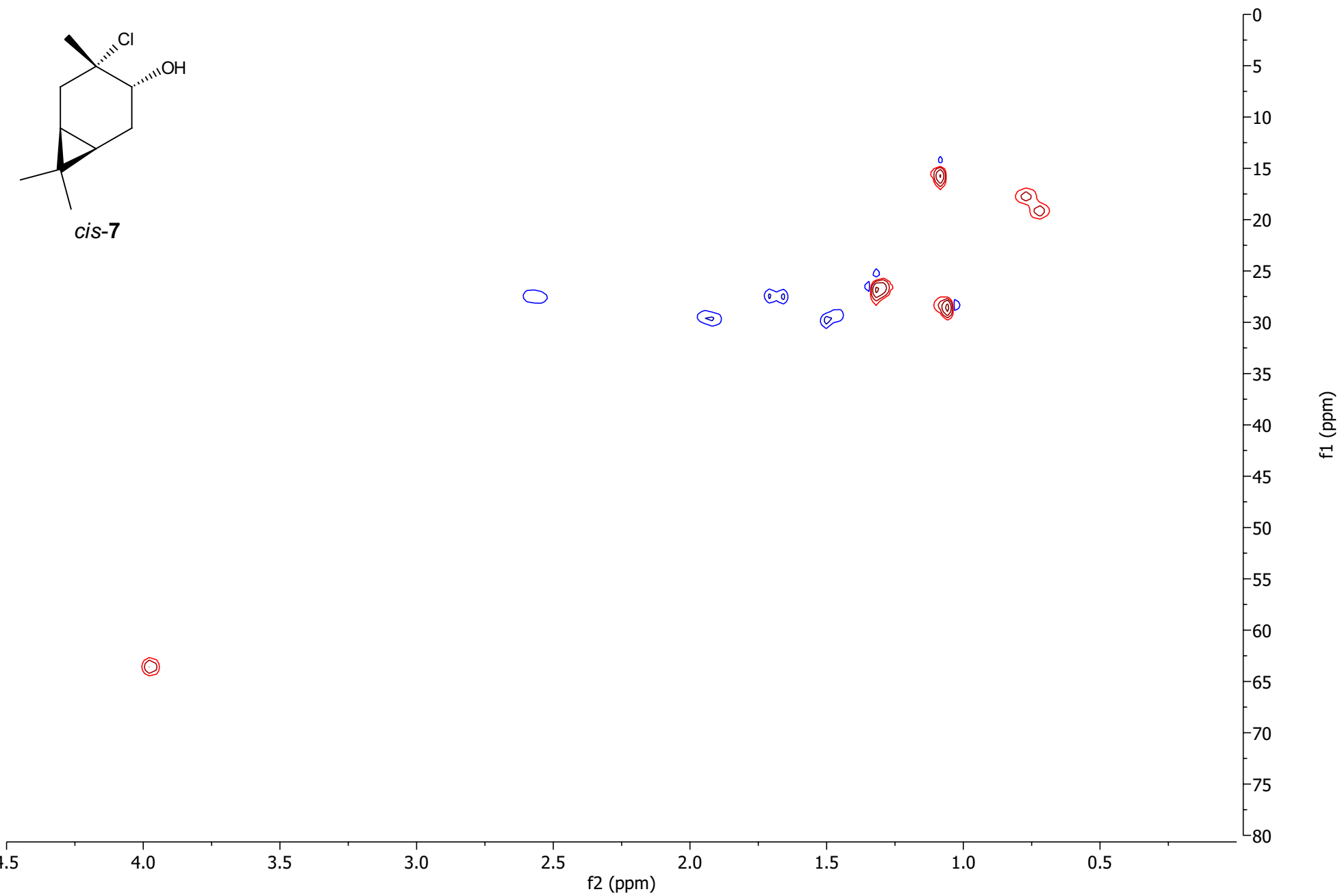
— 18.84

— 18.04

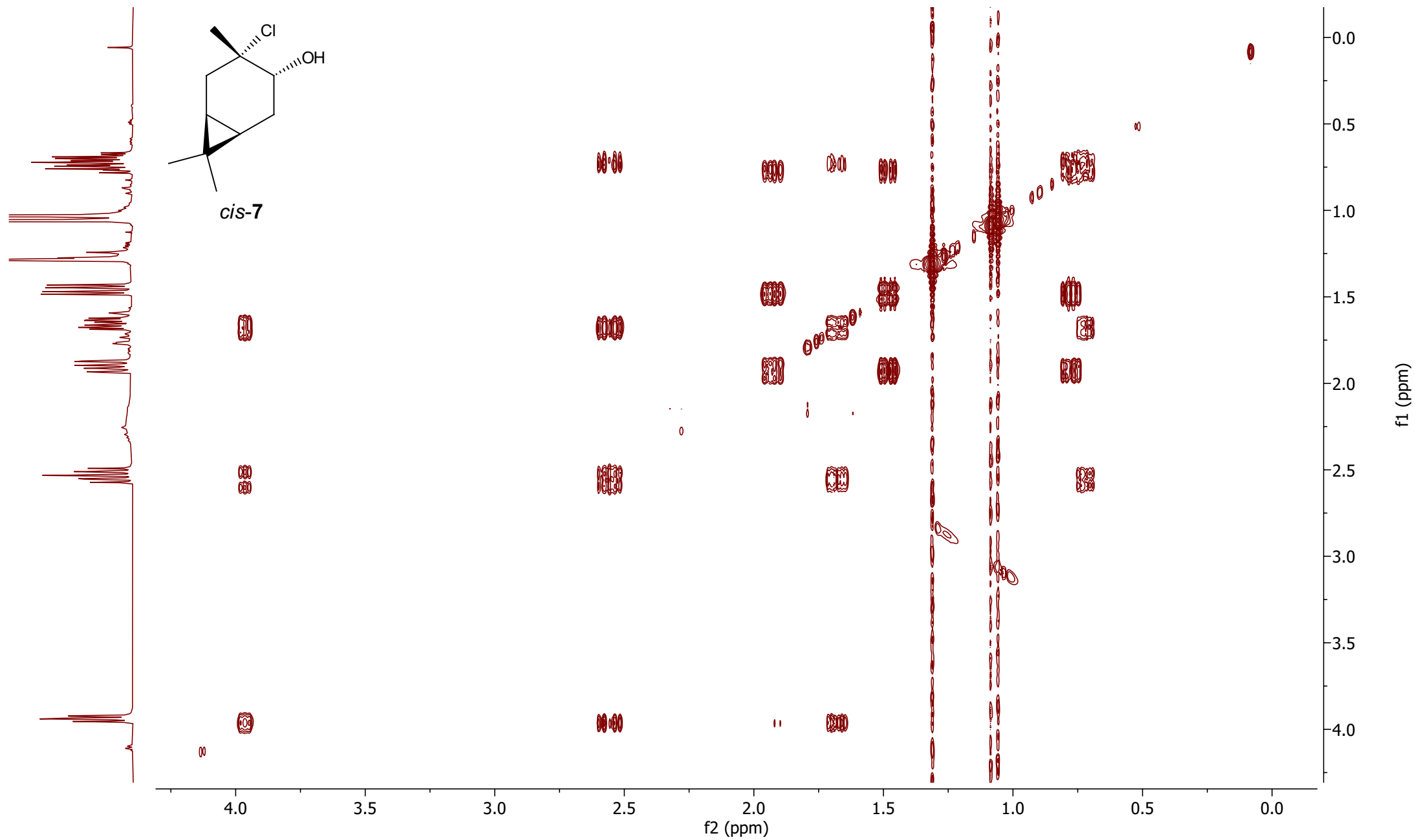
— 15.67



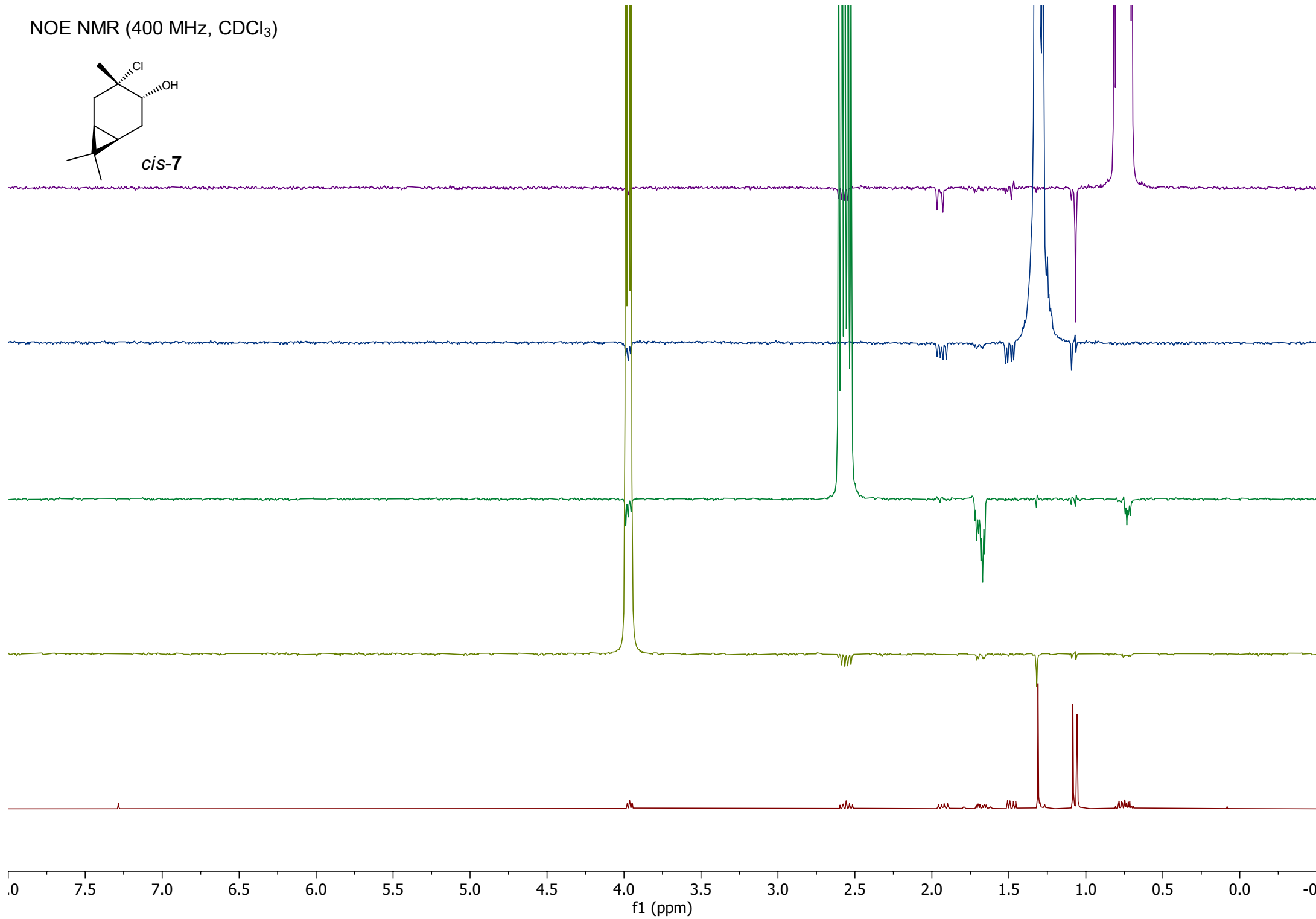
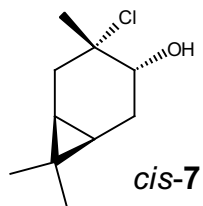
HSQC NMR (^1H - ^{13}C , CDCl_3)

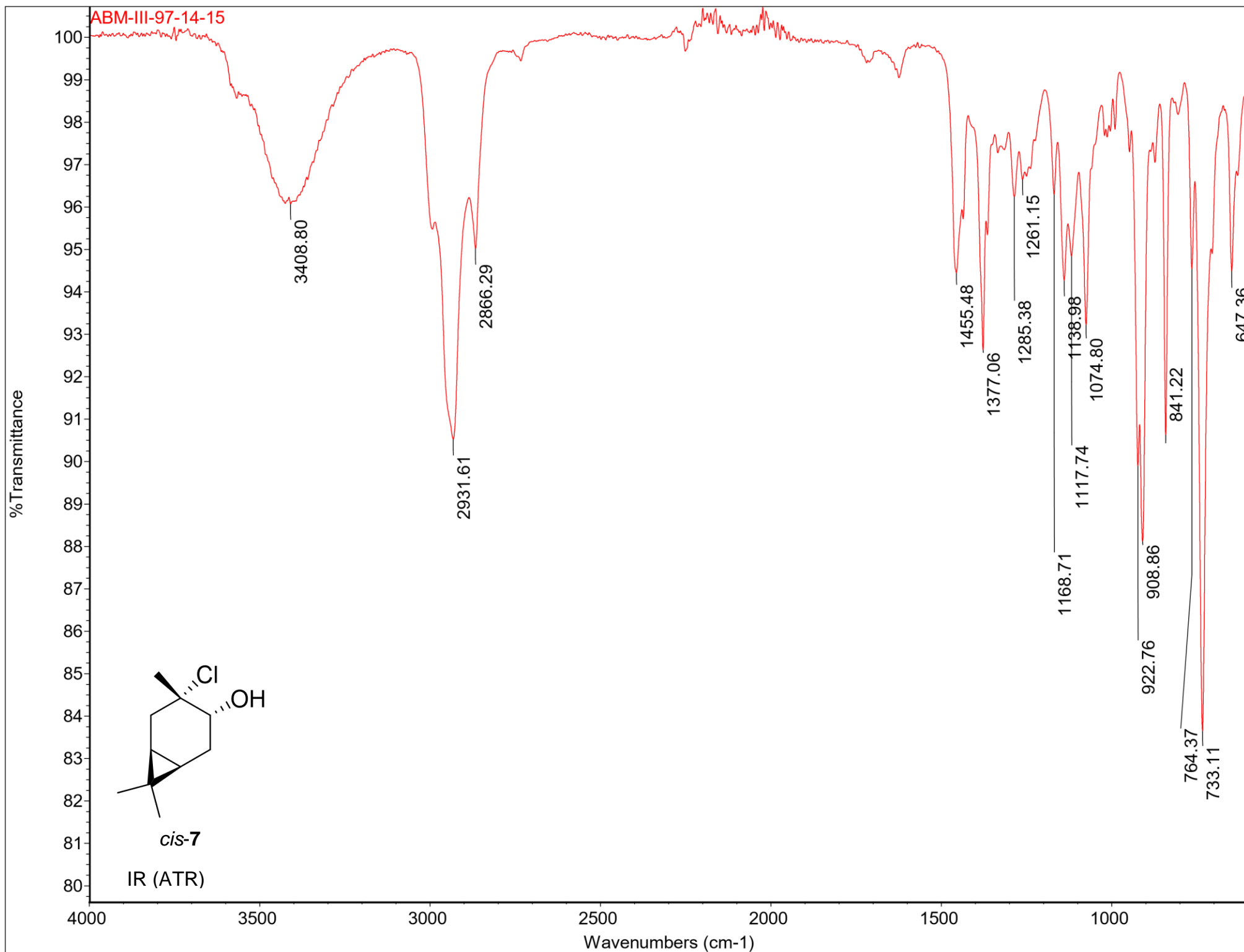


COSY NMR (400 MHz, CDCl₃)

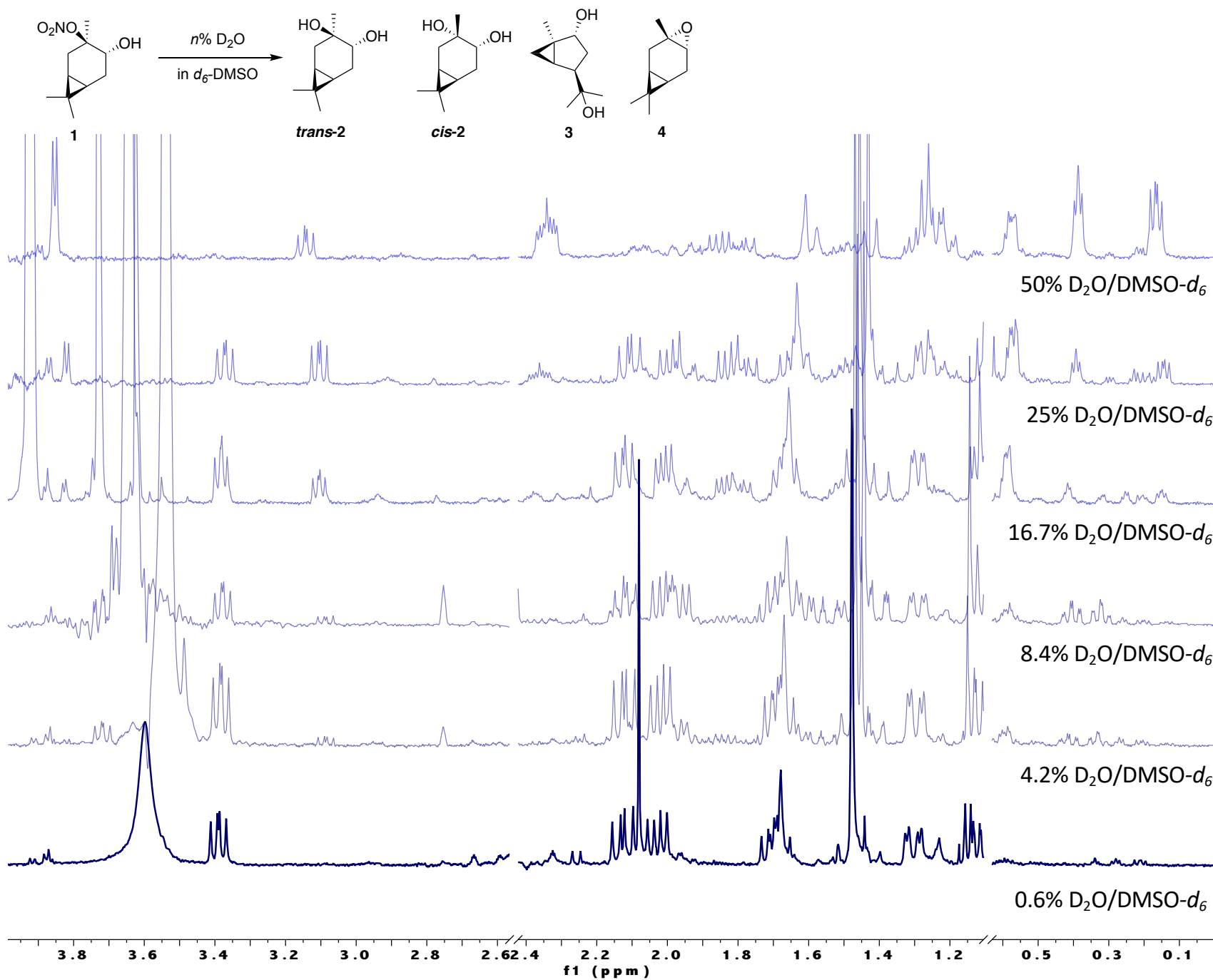


NOE NMR (400 MHz, CDCl₃)

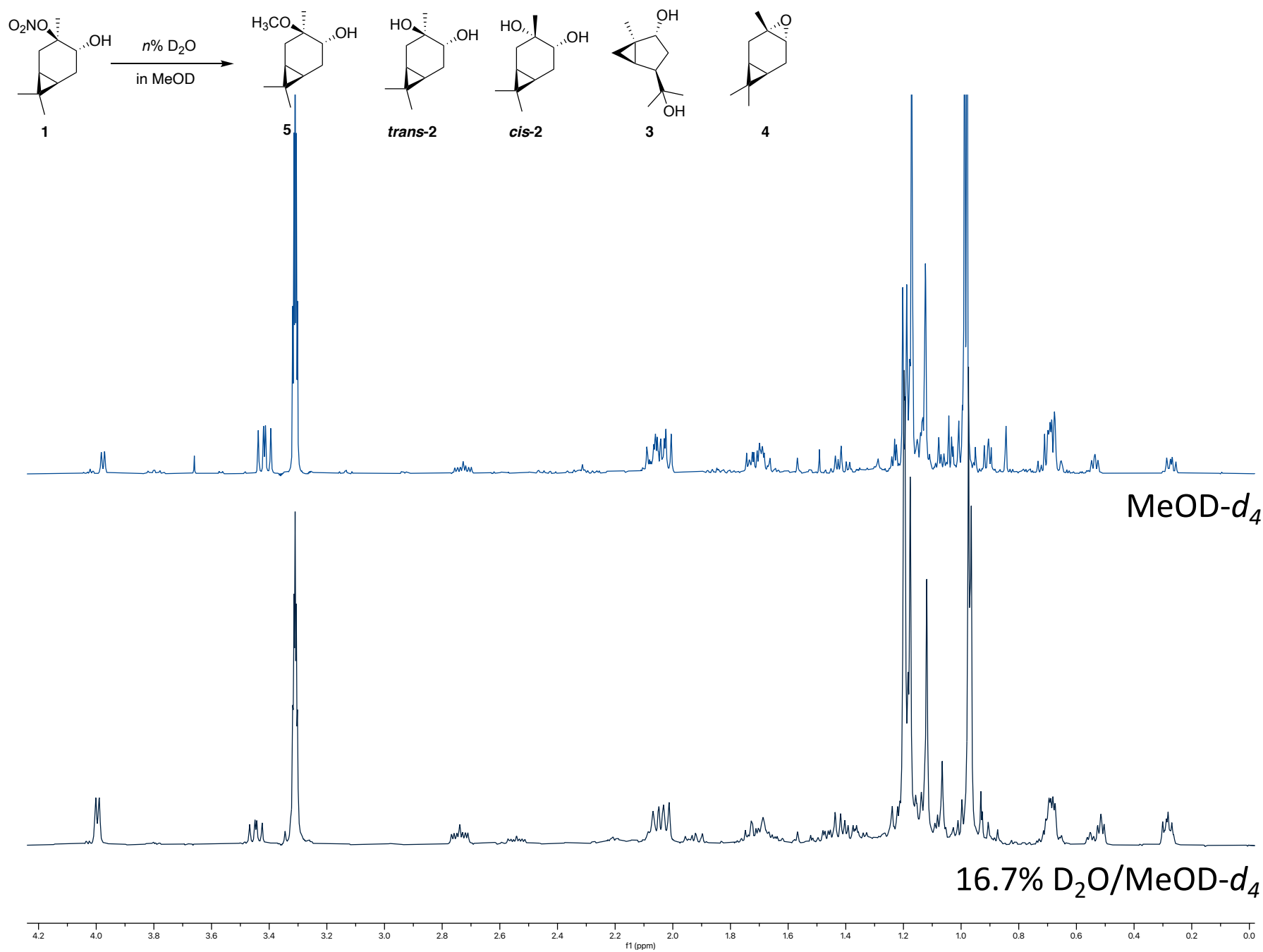




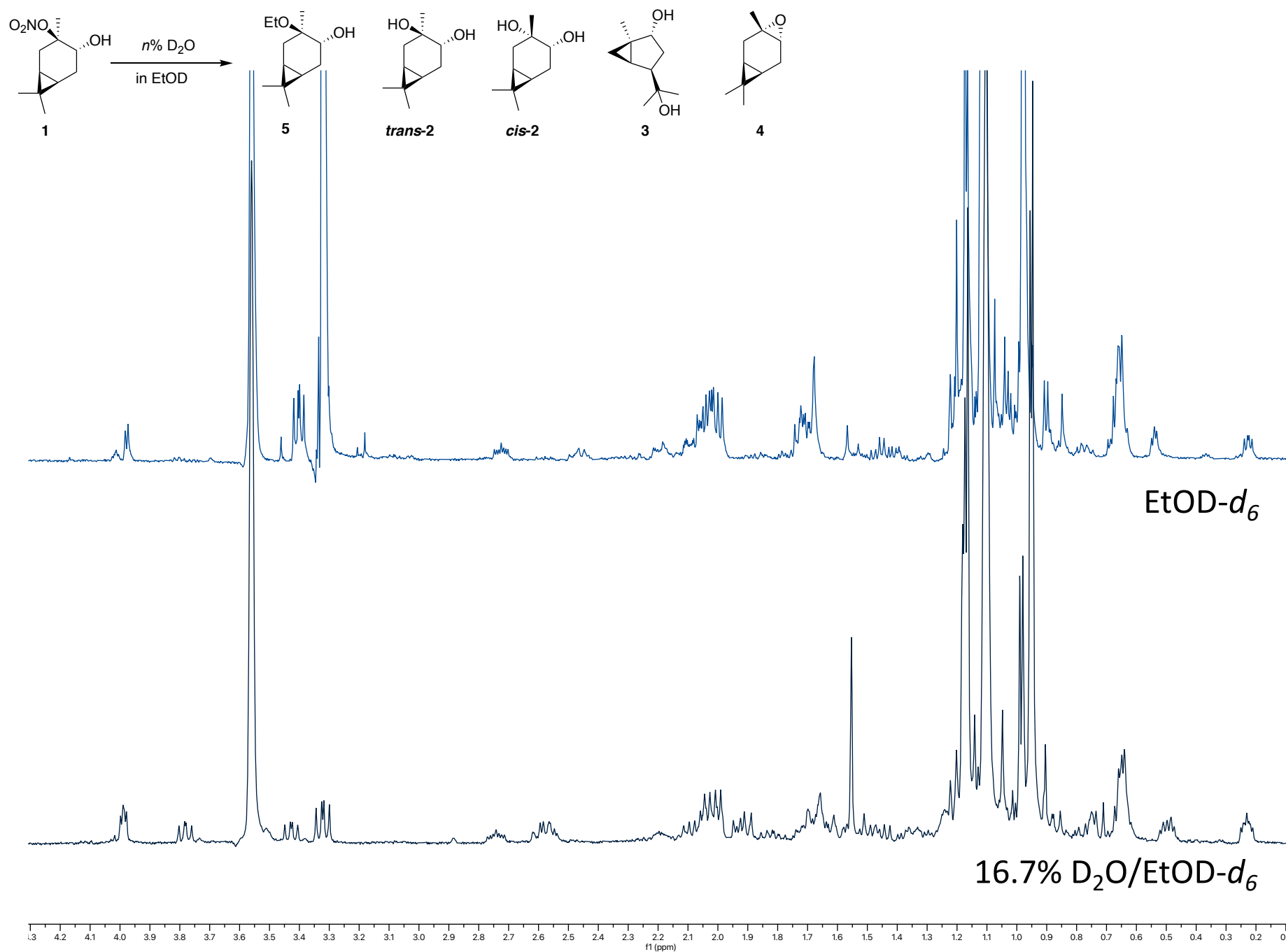
^1H NMR (400 MHz) CHN **1** Reaction Mixtures in $\text{D}_2\text{O}/\text{DMSO-}d_6$



^1H NMR (400 MHz) CHN **1** Reaction Mixtures in $\text{D}_2\text{O}/\text{MeOD-}d_4$



^1H NMR (400 MHz) CHN **1** Reaction Mixtures in $\text{D}_2\text{O}/\text{EtOD-}d_6$



^1H NMR (400 MHz) CHN **1** Reaction Mixtures with NaCl in 8.4% $\text{D}_2\text{O}/\text{DMSO}-d_6$

