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Electronic Supplementary Information

Synthesis of 1,4-ketoaldehydes and 1,4-diketones by Mo-catalyzed oxidative cleavage of cyclobutane-1,2-diols

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CONTENTS

GENERAL METHODS:

Materials: All reactions involving air-sensitive compounds were carried out under N_2 atmosphere in oven-dried glassware. All common reagents and solvents were obtained from commercial suppliers and used without any further purification. The catalyst, $MoO_2Cl_2(DMSO)_2$, was prepared as reported.[1]

Chromatography: TLC was performed on alumina-backed plates coated with silica gel 60 with F_{254} indicator, using UV light or Ce/Mo solution and heat as visualizing agent. Flash silica gel chromatography was realized using Merk silica gel 60, 230-240 mesh.

Characterization: NMR spectra were recorded on a Varian Mercury Plus, Bruker Advanced III HD (300 MHz ^{1}H; 75.4 MHz ^{13}C) or Bruker Advanced NEO 4500 (500 MHz ^{1}H; 126 MHz ^{13}C) instruments at room temperature. Chemical shifts (δ) are reported in ppm, using residual solvent peak as internal reference ($CDCl_3$: δ_H = 7.26 and δ_C = 77.16, $(CD_3)_2SO$: δ_H = 2.50 and δ_C = 39.52). Coupling constants (J) are given in Hertz (Hz). Data are reported as follows: chemical shift, multiplicity (s: singlet, bs: broad single, d: doublet, dd: double of doublets, ddd: doublet of doublet doublets, dddd: double of doublets of doublets of doublets, dq: doublet of quartets, dt: double of triplets, ddt: doublet of doublets of triplets, dtd: doublet of triplets of doublets, td: triplet of doublets, t: triplet, tt: triplet of triplets, q: quartet, m: multiplet), coupling constants and integration. Carbon multiplicities were assigned by DEPT experiments. Low-resolution electron impact mass spectra (EI-LRMS) were obtained at 70 eV and only the molecular ions and/or base peaks as well as significant peaks in MS are given. High resolution mass spectra (HRMS) were recorded on an instrument equipped with a QTOF analyser using ESI (+) or APCI (+).
Melting points were measured on a Gallenkamp apparatus using open capillary tubes and are uncorrected.

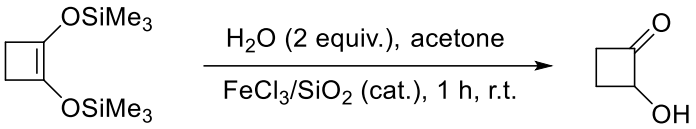
Experimental details: Microwave irradiation was realized with a CEM Discover S-Class reactor or CEM Discover 2.0 reactor with a single-mode microwave cavity producing continuous

[1] F. J. Arnáiz R. Aguado, M. R. Pedrosa and A. De Cian, *Inorg. Chim. Acta*, 20043, **347**, 33–40.

irradiation. Temperature measurements were conducted using an IR sensor below the microwave cavity floor. The maximum wattage supplied was 80 W.

SYNTHESIS and CHARACTERIZATION DATA for 2-HYDROXYCYCLOBUTANONES 1

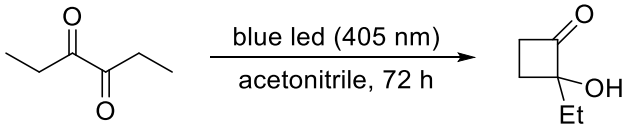
Synthesis of 2-hydroxycyclobutan-1-one (1a):



1a

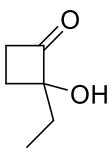
To a solution of 1,2-bis(trimethylsilyloxy)cyclobutene (461 mg, 2 mmol) in acetone (2 mL) was added water (36 mg, 2 mmol) and a catalytic amount (5 mg) of $FeCl_3/SiO_2$ (6/100). After stirring at room temperature for 1 h, the solvent was eliminated, and the residue was filtered through a 2-cm pad of SiO_2 using Et_2O as eluent. After concentration the desire product **1a** was obtained as a colourless oil (0.1636 g, 95 %).[2]

Synthesis of 2-hydroxycyclobutan-1-one 1b:



1b

In a schlenk tube, hexan-3,4-dione (2.3 g, 20 mmol) was dissolved in acetonitrile (10 mL) under N_2 atmosphere and were irradiated at 405 nm (blue LED) for 72 h. After completion of the reaction, followed by GC-MS, the solvent was removed, and the residue was purified by flash column chromatography using a 2/1 mixture of hexane/EtOAc as eluent to obtain the corresponding 2-hydroxyxycyclobutanone **1b** (1.83 g, 80% yield).



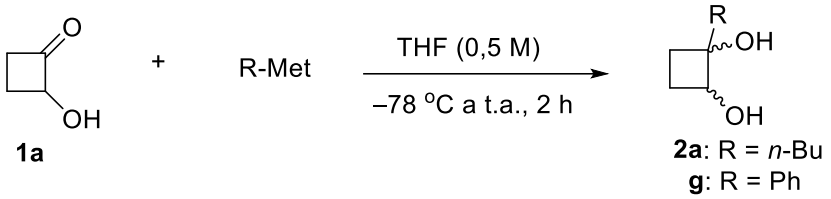
2-Ethyl-2-hydroxycyclobutan-1-one (1b): yellowish oil. ^{1}H-NMR (300 MHz, $CDCl_3$): δ (ppm) = 2.87–2.62 (m, 2H), 2.08 (ddd, J = 11.6, 10.6, 5.6 Hz, 1H), 1.92 (ddd, J = 11.3, 10.3, 0.5 Hz, 1H), 1.72–1.62 (m, 2H), 0.92 (t, J = 7.4 Hz, 3H). ^{13}C-NMR (75,4 MHz, $CDCl_3$): δ (ppm) = 213.0 (C), 91.7 (C), 39.5 (CH_2), 28.4 (CH_2), 26.2 (CH_2), 7.7 (CH_3).

OPTIMIZATION of the SYNTHESIS of CYCLOBUTANE-1,2-DIOLS 2

To optimize the synthesis of cyclobutane-1,2-diols **2**, a brief study of the reaction conditions was performed (Table S1).

[2] F. Cuccu, L. Serusi, A. Luridiana, F. Secii, P. Caboni, D. J. Aitken and A. Frongia, *Org. Lett.,* 2019, **21**, 7755−7758.

Table S1. Optimization of the reaction conditions for the synthesis of **2a,g**[a]



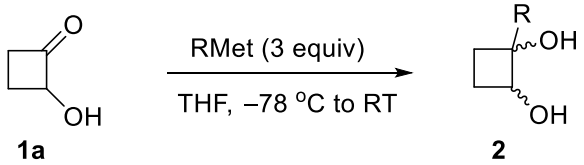
Entry	RMet	Additive	Product	dr[b]	Yield (%)[c]
1	*n*-BuLi (2 equiv)	---	**2a**	1.6/1	45
2	*n*-BuLi (3 equiv)	---	**2a**	2/1	55
3	*n*-BuLi (1.2 equiv)	*i*-PrMgCl (1 equiv)	**2a**	1/1	35
4	*n*-BuLi (4 equiv)	---	**2a**	2/1	50
5	*n*-BuLi (3 equiv)	LiCl (1 equiv)	**2a**	1.5/1	48
6	PhLi (3 equiv)	---	**2g**	3/1	54
7	PhMgCl (3 equiv)	---	**2g**	3/1	51

[a] Reaction conditions: **1a** (0.2 mmol) in THF (0.5 mL) from −78 °C to RT. [b] Determined by 1H-NMR analysis of the crude reaction mixture. [c] Yield referred to **1a** determined by ^{1}H-NMR using dibromomethane as internal standard.

Initially, 2 equivalents (entry 1) of the model organolithium compound (*n*-BuLi) were essayed obtaining a 45% yield of the corresponding diol **2a** as a 1.6/1 mixture of *cis*/*trans*-diastereoisomers. We decided to try 3 and 4 equivalents (entry 2 and 4), obtaining better results when 3 equivalents were used and a slightly better diastereoselectivity (2/1). Other experiments adding LiCl or *i*-PrMgCl were conducted but no improvement was observed, and selectivity decreased (entries 3 and 5). When *n*-BuLi was substituted by PhLi a similar result was obtained (entries 6 vs 2). Finally, we decided to test the use of an organomagnesium reagent (PhMgCl) instead of the corresponding organolithium (PhLi), obtaining similar results and diastereoselectivity in both cases (entries 6 vs 7). So, the optimal conditions established for the synthesis of cyclobutanediols **2** were 3 equivalents of the corresponding organolithium or organomagnesium compound.

SYNTHESIS and CHARACTERIZATION DATA for CYCLOBUTANE-1,2-DIOLS 2

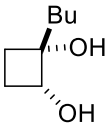
Synthesis of cyclobutane-1,2-diols 2a-m. General procedure I:



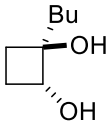
To a stirred solution of 2-hydroxycyclobutan-1-one **1a** (172 mg, 2 mmol) in anhydrous THF (4 mL), the corresponding organometallic reagent (6 mmol) was added at −78 °C and the resulted

solution was stirred at room temperature for 2 h (monitored by TLC). Then, the mixture was quenched with aq. NH_4Cl (5 mL). THF was removed under reduced pressure and the aqueous layer was extracted with EtOAc (3 × 15 mL). The combined organic layers were dried over anhydrous Na_2SO_4, filtered and concentrated in vacuo. The residue was purified by flash column chromatography using deactivated silica gel and mixtures of hexane/EtOAc as eluent to afford the corresponding cyclobutane-1,2-diols **2a-m**.

1-Butylcyclobutane-1,2-diol (2a). General procedure I was followed using *n*-BuLi (3.8 mL, 6 mmol, 1.6 M solution in hexane), obtaining **2a** as a ca. 2/1 mixture of *cis*/*trans* diastereoisomers, which were isolated independently by flash column chromatography in hexane/EtOAc (1/1).

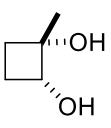


***cis*-1-Butylcyclobutane-1,2-diol (*cis*-2a):** yellow oil (118 mg, 41 %). R_f = 0.3 (hexane/EtOAc = 1/1). ^{1}H-NMR (300 MHz, $CDCl_3$): δ (ppm) = 3.91–3.95 (m, 1H), 2.64–2.93 (m, 2H), 2.08–2.17 (m, 1H), 1.80–1.88 (m, 2H), 1.68–1.73 (m, 1H), 1.50–1.53 (m, 2H), 1.30–1.36 (m, 4H), 0.90 (t, J = 7.1 Hz, 3H). ^{13}C-NMR (75.4 MHz, $CDCl_3$): δ (ppm) = 78.4 (C), 71.7 (CH), 39.2 (CH_2), 29.2 (CH_2), 27.1 (CH_2), 25.6 (CH_2), 23.2 (CH_2), 14.2 (CH_3). LRMS (EI): *m/z* (%) 124 (M^+, 7), 74 (31), 58 (100). HRMS (ESI+) calcd for $C_8H_{16}NaO_2^+$ $[M+Na]^+$ 167.1043, found 167.1043.

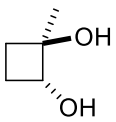


***trans*-1-Butylcyclobutane-1,2-diol (*trans*-2a)**: white solid (54 mg, 19 %). Slightly contaminated with *cis*-**2a**. M. p.: 47–49 °C. R_f = 0.15 (hexane/EtOAc = 1/1). ^{1}H-NMR (300 MHz, $CDCl_3$): δ (ppm) = 4.08 (t, J = 8.0 Hz, 1H), 3.65 (bs, 1H), 3.20 (bs, 1H), 2.05–1.95 (m, 1H), 1.91–1.75 (m, 1H), 1.59–1.47 (m, 2H), 1.47–1.27 (m, 6H), 1.10–0.83 (t, J = 7.2 Hz, 3H). ^{13}C-NMR (75.4 MHz, $CDCl_3$): δ (ppm) = 79.7 (C), 76.0 (CH), 32.0 (CH_2), 26.4 (CH_2), 24.8 (CH_2), 23.4 (CH_2), 22.7 (CH_2), 14.3 (CH_3). LRMS (EI): *m/z* (%) 124 (M^+, 7), 74 (31), 58 (100). HRMS (ESI+) calcd for $C_8H_{16}NaO_2^+$ $[M+Na]^+$ 167.1043, found 167.1043.

1-Methylcyclobutane-1,2-diol (2b). General procedure I was followed using MeLi (3.8 mL, 6 mmol, 1.6 M solution in Et_2O), obtaining **2b** as a ca. 3/1 mixture of *cis*/*trans* diastereoisomers, which were isolated independently by flash column chromatography in hexane/EtOAc (1/2).

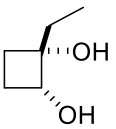


***cis* 1-Methylcyclobutane-1,2-diol (*cis*-2b):** yellowish oil (84 mg, 41 %). R_f = 0.26 (hexane/EtOAc = 1/2).^{1}H-NMR (300 MHz, $CDCl_3$): δ (ppm) = 4.07 (td, J = 8.5, 1.0 Hz, 1H), 2.63 (bs, 2H), 2.04 (dtd, J = 10.9, 8.5, 2.0 Hz, 1H), 1.81–1.69 (m, 1H), 1.62–1.46 (m, 2H), 1.40–1.26 (m, 3H). ^{13}C-NMR (75.4 MHz, $CDCl_3$): δ (ppm) = 77.4 (C), 75.7 (CH), 29.0 (CH_2), 23.0 (CH_2), 20.1 (CH_3). LRMS (EI) could not be recorded. HRMS (ESI+) calcd for $C_5H_{10}NaO_2^+$ $[M+Na]^+$ 125.0573, found 125.0575.

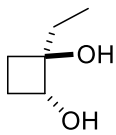


***trans*-1-Methylcyclobutane-1,2-diol (*trans*-2b)**: yellowish oil (28 mg, 14 %). R_f = 0.16 (hexane/EtOAc = 1/2). ^{1}H-NMR (300 MHz, $CDCl_3$): δ (ppm) = 4.13 (s, 1H), 4.07 (s, 1H), 3.93–3.75 (m, 1H), 2.07–1.53 (m, 4H), 1.23 (d, J = 1.8 Hz, 3H). ^{13}C-NMR (75.4 MHz, $CDCl_3$): δ (ppm) = 75.7 (C), 73.1 (CH), 30.9 (CH_2), 25.7 (CH_2), 25.7 (CH_3). LRMS (EI) could not be recorded. HRMS (ESI+) calcd for $C_5H_{10}NaO_2^+$ $[M+Na]^+$ 125.0573, found 125.0575.

1-Ethylcyclobutane-1,2-diol (2c). General procedure I was followed using EtMgCl (3 mL, 6 mmol, 2 M solution in THF), obtaining **2c** as a ca. 2/1 mixture of *cis*/*trans* diastereoisomers, which were isolated independently by flash column chromatography in hexane/EtOAc (1/1).

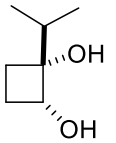


***cis*-1-Ethylcyclobutane-1,2-diol (*cis*-2c):** colourless oil (95 mg, 41%). R_f = 0.26 (hexane/EtOAc = 1/1). ^{1}H-NMR (300 MHz, $CDCl_3$): δ (ppm) = 3.93–3.89 (m, 2H), 3.46 (bs, 1H), 2.08–2.05 (m, 1H), 1.91–1.71 (m, 2H), 1.71–1.60 (m, 1H), 1.53 (q, J = 7.4 Hz, 2H), 0.87 (t, J = 7.4 Hz, 3H). ^{13}C-NMR (75.4 MHz, $CDCl_3$): δ (ppm) = 78.7 (C), 71.5 (CH), 31.8 (CH_2), 28.5 (CH_2), 26.4 (CH_2), 7.6 (CH_3). LRMS (EI) and HRMS could not be recorded.



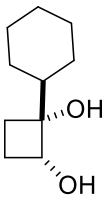
***trans*-1-Ethylcyclobutane-1,2-diol (*trans*-2c):** colourless oil (51 mg, 22%). R_f = 0.1 (hexane/EtOAc = 1/1). ^{1}H-NMR (300 MHz, $CDCl_3$): δ (ppm) = 4.11 (t, J = 8.2 Hz, 1H), 3.59 (bs, 1H), 2.04–1.95 (m, 1H), 1.86–1.75 (m, 1H), 1.71–1.53 (m, 2H), 1.45–1.28 (m, 2H), 0.97 (td, J = 7.4, 1.0 Hz, 3H), one hydroxyl proton does not appear. ^{13}C-NMR (75,4 MHz, $CDCl_3$): δ (ppm) = 79.9 (CH), 75.8 (C), 25.8 (CH_2), 24.8 (CH_2), 22.6 (CH_2), 6.8 (CH_3). LRMS (EI) and HRMS could not be recorded.

1-Isopropylcyclobutane-1,2-diol (2d). General procedure I was followed using *i*-PrMgCl (3 mL, 6 mmol, 2 M solution in THF), obtaining **2d** as a ca. 1.2/1 mixture of *cis*/*trans* diastereoisomers. After column chromatography in hexane/EtOAc (2/1) only the *cis*-diastereoisomer was isolated.

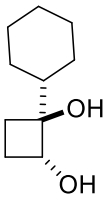


***cis*-1-Isopropylcyclobutane-1,2-diol (*cis*-2d):** yellowish oil (86 mg, 33%). R_f = 0.40 (hexane/EtOAc = 2/1). ^{1}H-NMR (300 MHz, $CDCl_3$): δ (ppm) = 3.97 (q, J = 6.9 Hz, 1H), 2.73–2.58 (m, 1H), 2.32 (d, J = 9.0 Hz, 1H), 2.22–2.07 (m, 1H), 1.94–1.81 (m, 1H), 1.82–1.68 (m, 1H), 1.72–1.56 (m, 2H), 0.88 (d, J = 6.9 Hz, 6H). ^{13}C-NMR (75.4 MHz, $CDCl_3$): δ (ppm) = 81.5 (C), 70.2 (CH), 36.13 (CH_2), 27.3 (CH_2), 27.2 (CH), 16.0 (CH_3), 15.7 (CH_3). LRMS (EI) could not be recorded. HRMS (ESI+) calcd for $C_7H_{14}NaO_2^+$ $[M+Na]^+$ 153.0886, found 153.0888.

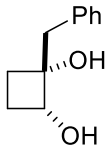
1-Cyclohexylcyclobutane-1,2-diol (2e). General procedure I was followed using cyclohexylmagnesium chloride (3 mL, 6 mmol, 2 M solution in Et_2O), obtaining **2e** as c.a. 1.2/1 mixture of *cis*/*trans* diastereoisomers, which were isolated independently by flash column chromatography in hexane/EtOAc (1/1).



***cis*-1-Cyclohexylcyclobutane-1,2-diol (*cis*-2e):** colourless oil (118 mg, 35%). R_f = 0.4 (hexane/EtOAc = 1/1). ^{1}H-NMR (300 MHz, $CDCl_3$): δ (ppm) = 4.00 (q, J = 7.3 Hz, 1H), 2.40 (d, J = 7.9 Hz, 1H), 2.10–2.21 (m, 2H), 1.63–1.90 (m, 7H), 1.01–1.33 (m, 6H). ^{13}C-NMR (75.4 MHz, $CDCl_3$): δ (ppm) = 81.3 (C), 69.9 (CH), 46.4 (CH), 27.4 (CH_2), 26.7 (CH_2), 26.5 (CH_2), 26.4 (CH_2), 26.3 (CH_2), 26.2 (CH_2), 26.0 (CH_2). LRMS (EI): *m/z* (%) 170 (M^+, 3), 71 (100), 55 (94). HRMS (ESI+) calcd for $C_{10}H_{18}NaO_2^+$ $[M+Na]^+$ 193.1199, found 193.1203.

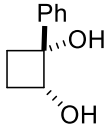


***trans*-1-Cyclohexylcyclobutane-1,2-diol (*trans*-2e):** colourless oil (95 mg, 28%). R_f = 0.19 (hexane/EtOAc = 1/1). ^{1}H-NMR (300 MHz, $CDCl_3$): δ (ppm) = 4.23 (q, J = 7.8 Hz, 1H), 1.99–2.20 (m, 3H), 1.65–1.86 (m, 7H), 1.11–1.53 (m, 7H). ^{13}C-NMR (75.4 MHz, $CDCl_3$): δ (ppm) = 101.6 (CH), 82.0 (C), 40.5 (CH), 27.5 (CH_2), 26.90 (CH_2), 26.86 (CH_2), 26.6 (CH_2), 26.5 (CH_2), 26.1 (CH_2), 23.3 (CH_2). LRMS (EI): *m/z* (%) 170 (M^+, 3), 71 (100), 55 (94). HRMS (ESI+) calcd for $C_{10}H_{18}NaO_2^+$ $[M+Na]^+$ 193.1199, found 193.1203.

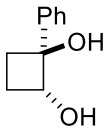


***cis*-1-Benzylcyclobutane-1,2-diol (*cis*-2f)**. General procedure I was followed using benzylmagnesium chloride (3 mL, 6 mmol, 2 M solution in THF), obtaining selectively ***cis*-2f**, which was purified by flash column chromatography in hexane/EtOAc (1/1). Yellowish oil (216 mg, 61%). R_f = 0.3 (hexane/EtOAc = 1/1). ^{1}H-NMR (300 MHz, $CDCl_3$): δ (ppm) = 7.41–7.13 (m, 5H), 4.05 (t, J = 6.8 Hz, 1H), 2.84 (s, 2H), 2.75 (bs, 1H), 2.24–2.02 (m, 1H), 1.98–1.64 (m, 3H), one hydroxyl proton does not appear. ^{13}C-NMR (75.4 MHz, $CDCl_3$): δ (ppm) = 137.0 (C), 130.0 (2 × CH), 128.5 (2 × CH), 126.7 (CH), 78.4 (C), 70.9 (CH), 45.4 (CH_2), 28.6 (CH_2), 27.3 (CH_2). LRMS (EI): *m/z* (%) 178 (M^+, 4), 91 (100), 78 (44). HRMS (ESI+) calcd for $C_{11}H_{14}NaO_2^+$ $[M+Na]^+$ 203.0944, found 209.0943.

1-Phenylcyclobutane-1,2-diol (2g). General procedure I was followed using PhLi (3.5 mL, 6.6 mmol, 1.9 M solution in Bu_2O), obtaining **2g** as a ca. 3/1 mixture of *cis*/*trans* diastereoisomers, which were isolated independently by flash column chromatography in hexane/EtOAc (1/1).



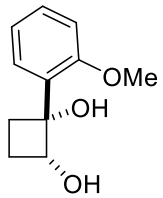
***cis*-1-Phenylcyclobutane-1,2-diol (*cis*-2g):** orange solid (138 mg, 42 %). M. p.: 88–92 °C. R_f = 0.5 (hexane/EtOAc = 1/1). ^{1}H-NMR (300 MHz, $CDCl_3$): δ (ppm) = 7.47–7.20 (m, 5H), 4.31 (d, J = 6.8 Hz, 1H), 3.00–2.64 (m, 2H), 2.36–2.21 (m, 1H), 2.20–1.98 (m, 3H). ^{13}C-NMR (75.4 MHz, $CDCl_3$): δ (ppm) = 144.8 (C), 128.6 (2 × CH), 127.7 (CH), 125.1 (2 × CH), 80.0 (C), 72.1 (CH), 28.6 (CH_2), 28.3 (CH_2). LRMS (EI): *m/z* (%) 164 (M^+, 3), 105 (89), 77 (100). HRMS (ESI+) calcd for $C_{10}H_{12}NaO_2^+$ $[M+Na]^+$ 187.073, found 187.0724.



***trans*-1-Phenylcyclobutane-1,2-diol (*trans*-2g):** orange oil. (42 mg, 13 %). Slightly contaminated with *cis*-**2g**. R_f = 0.3 (hexane/EtOAc = 1/1). ^{1}H-NMR (300 MHz, $CDCl_3$): δ (ppm) = 7.58–7.42 (m, 2H), 7.44–7.26 (m, 3H), 4.20 (t, J = 8.3 Hz, 1H), 3.14 (bs, 1H), 2.59–2.40 (m, 1H), 2.21–2.10 (m, 1H), 2.08–1.95 (m, 1H), 1.82–1.71 (m, 1H),

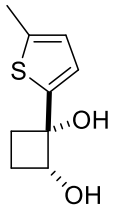
1.43–1.30 (m, 1H). ^{13}C-NMR (75.4 MHz, $CDCl_3$): δ (ppm) = 139.3 (C), 128.6 (2 × CH), 128.0 (CH), 127.1 (2 × CH), 81.8 (C), 75.8 (CH), 27.8 (CH_2), 24.5 (CH_2). LRMS (EI): *m/z* (%) 164 (M^+, 3), 105 (89), 77 (100). HRMS (ESI+) calcd for $C_{10}H_{12}NaO_2^+$ $[M+Na]^+$ 187.073, found 187.0724.

1-(2-Methoxyphenyl)cyclobutane-1,2-diol (2h). General procedure I was followed using (2-methoxyphenyl)lithium (6 mmol, prepared by treatment of 1-bromo-2-methoxybenzene (6 mmol, 1.23 g) with *t*-BuLi (12 mmol, 7 mL of a 1.7 M solution in pentane)), obtaining **2h** as a c.a. 3/1 mixture of *cis*/*trans* diastereoisomers. After column chromatography in hexane/EtOAc (1/1) only the *cis*-diastereoisomer was isolated.

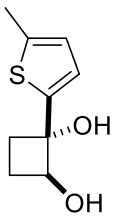


***cis*-1-(2-Methoxyphenyl)cyclobutane-1,2-diol (*cis*-2h)**: yellowish oil (177 mg, 44%). R_f = 0.24 (hexane/EtOAc = 1/1). ^{1}H-NMR (300 MHz, $CDCl_3$): δ (ppm) = 7.36–7.16 (m, 2H), 7.03–6.84 (m, 2H), 4.43–4.27 (t, *J* = 4.1 Hz, 1H), 3.87 (s, 3H), 2.37–2.01 (m, 4H), the two hydroxyl protons do not appear. ^{13}C-NMR (75.4 MHz, $CDCl_3$): δ (ppm) = 156.9 (C), 132.4 (C), 129.0 (CH), 127.0 (CH), 121.0 (CH), 111.0 (CH), 79.0 (C), 70.6 (CH), 55.6 (CH_3), 27.2 (CH_2), 27.1 (CH_2). LRMS (EI): *m/z* (%) 135 (100), 77 (60), 150 (31). HRMS (ESI+) calcd for $C_{11}H_{14}NaO_3^+$ $[M+Na]^+$ 218.0869, found 218.0873.

1-(5-Methylthiophen-2-yl)cyclobutane-1,2-diol (2i). General procedure I was followed using (5-methylthiophen-2-yl)lithium (6 mmol, prepared by treatment of 2-methylthiophene (6 mmol, 0.59 g) with *n*-BuLi (6 mmol, 3.75 mL of a 1.6 M solution in hexane)), obtaining **2i** as a c.a. 2/1 mixture of *cis*/*trans* diastereoisomers, which were isolated independently by flash column chromatography in hexane/EtOAc (2/1).

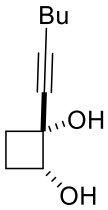


***cis*-1-(5-Methylthiophen-2-yl)cyclobutane-1,2-diol (*cis*-2i):** orange solid (110 mg, 30%). M. p.: 85–89 °C. R_f = 0.28 (hexane/EtOAc = 2/1). ^{1}H-NMR (300 MHz, $CDCl_3$): δ (ppm) = 6.72 (d, *J* = 3.5 Hz, 1H), 6.59 (dq, 1H, *J* = 3.4, 1.1 Hz), 4.21–4.26 (m, 1H), 3.00 (bs, 1H), 2.75 (bs, 1H), 2.43 (d, *J* = 1.1 Hz, 3H), 2.17–2.26 (m, 1H), 1.97–2.14 (m, 3H). ^{13}C-NMR (75.4 MHz, $CDCl_3$): δ (ppm) = 147.2 (C), 139.2 (C), 125.0 (CH), 122.5 (CH), 77.8 (C), 73.6 (CH), 30.7 (CH_2), 27.2 (CH_2), 15.4 (CH_3). LRMS (EI): *m/z* (%) 166 (M^+, 22), 140 (100), 97 (77). HRMS (ESI+) calcd for $C_9H_{12}NaO_2S^+$ $[M+Na]^+$ 207.045, found 207.0452.

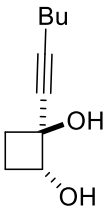


***trans*-1-(5-Methylthiophen-2-yl)cyclobutane-1,2-diol (*trans*-2i):** orange oil (44 mg, 12%). R_f = 0.18 (hexane/EtOAc = 2/1). ^{1}H-NMR (300 MHz, $CDCl_3$): δ (ppm) = 6.95 (d, *J* = 3.5 Hz, 1H), 6.82–6.61 (m, 1H), 4.30 (q, *J* = 8.8 Hz, 1H), 2.62 (d, *J* = 11.2 Hz, 1H), 2.51 (d, *J* = 0.9 Hz, 3H), 2.49–2.39 (m, 1H), 2.32–2.15 (m, 1H), 1.98–1.81 (m, 2H), 1.60–1.41 (m, 1H). ^{13}C-NMR (75.4 MHz, $CDCl_3$): δ (ppm) = 141.5 (C), 140.9 (C), 125.5 (CH), 125.0 (CH), 80.4 (C), 75.4 (CH), 29.8 (CH_2), 24.8 (CH_2), 15.51 (CH_3). LRMS (EI): *m/z* (%) 166 (M^+, 22), 140 (100), 97 (77). HRMS (ESI+) calcd for $C_9H_{12}NaO_2S^+$ $[M+Na]^+$ 207.045, found 207.0452.

1-(Hex-1-yn-1-yl)cyclobutane-1,2-diol (2j). General procedure I was followed using hex-1-yn-1yllithium (6 mmol, prepared by treatment of hex-1-yne (6 mmol, 0.49 g) with *n*-BuLi (6 mmol, 3.75 mL of a 1.6 M solution in hexane)), obtaining **2j** as a ca. 2/1 mixture of *cis*/*trans* diastereoisomers, which were isolated independently by flash column chromatography in hexane/EtOAc (1/1).

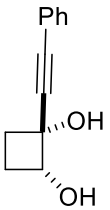


***cis*-1-(Hex-1-yn-1-yl)cyclobutane-1,2-diol (*cis*-2j):** yellowish solid (148 mg, 44 %). M. p.: 84–88 °C. R_f = 0.45 (hexane/EtOAc = 1/1). ^{1}H-NMR (300 MHz, $CDCl_3$): δ (ppm) = 4.32–4.00 (m, 1H), 3.31 (bs, 2H), 2.30–2.11 (m, 3H), 2.10–1.89 (m, 3H), 1.54–1.19 (m, 4H), 0.88 (t, J = 7.2 Hz, 3H). ^{13}C-NMR (75.4 MHz, $CDCl_3$): δ (ppm) = 85.7 (C), 82.0 (C), 73.0 (CH), 70.8 (C), 30.9 (CH_2), 30.8 (CH_2), 27.9 (CH_2), 22.0 (CH_2), 18.5 (CH_2), 13.7 (CH_3). LRMS (EI): *m/z* (%) 167 (M^+, 3), 79 (100), 77 (66). HRMS (ESI+) calcd for $C_{10}H_{17}O_2^+$ $[M+H]^+$ 169.1223, found 169.1216.

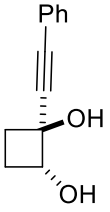


***trans*-1-(Hex-1-yn-1-yl)cyclobutane-1,2-diol (*trans*-2j):** yellowish solid (77 mg, 23 %). M. p.: 84–88 °C. R_f = 0.32 (hexane/EtOAc = 1/1). ^{1}H-NMR (300 MHz, $CDCl_3$): δ (ppm) = 3.99 (t, J = 8.4 Hz, 1H), 2.37 (bs, 2H), 2.30 (t, J = 7.0 Hz, 2H), 2.19–2.03 (m, 2H), 1.74–1.64 (m, 1H), 1.60–1.50 (m, 2H), 1.48–1.37 (m, 3H), 0.92 (t, J = 7.2 Hz, 3H). ^{13}C-NMR (75.4 MHz, $CDCl_3$): δ (ppm) = 89.7 (C), 78.4 (C), 75.7 (C), 75.2 (CH), 30.9 (CH_2), 29.0 (CH_2), 24.7 (CH_2), 22.1 (CH_2), 18.6 (CH_2), 13.7 (CH_3). LRMS (EI): *m/z* (%) 167 (M^+, 3), 79 (100), 77 (66). HRMS (ESI+) calcd for $C_{10}H_{17}O_2^+$ $[M+H]^+$ 169.1223, found 169.1216.

1-(Phenylethynyl)cyclobutane-1,2-diol (2k). General procedure I was followed using (phenylethynyl)lithium (6 mmol, prepared by treatment of phenylacetylene (6 mmol, 0.61 g) with *n*-BuLi (6 mmol, 3.75 mL of a 1.6 M solution in hexane)), obtaining **2k** as a ca. 2/1 mixture of *cis*/*trans* diastereoisomers, which were isolated independently by flash column chromatography in hexane/EtOAc (1/1).



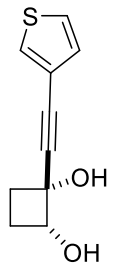
***cis*-1-(Phenylethynyl)cyclobutane-1,2-diol (*cis*-2k):** white solid (173mg, 46%). M. p.: 119–121 °C. R_f = 0.42 (hexane/EtOAc = 1/1). ^{1}H-NMR (300 MHz, $CDCl_3$): δ (ppm) = 7.45–7.39 (m, 2H), 7.33–7.27 (m, 3H), 4.36 (q, J = 7.6 Hz, 1H), 2.88 (s, 1H), 2.73 (d, J = 8.5 Hz, 1H), 2.39–2.26 (m, 1H), 2.21–2.10 (m, 2H), 2.09–1.97 (m, 1H). ^{13}C-NMR (75.4 MHz, $CDCl_3$): δ (ppm) = 131.7 (2 × CH), 128.4 (CH), 128.3 (2 × CH), 122.6 (C), 90.7 (C), 84.8 (C), 72.9 (CH), 71.1 (C), 30.6 (CH_2), 27.9 (CH_2). LRMS (EI): *m/z* (%) 188 (M^+, 6), 129 (100), 75 (44). HRMS (ESI+) calcd for $C_{12}H_{13}O_2^+$ $[M+H]^+$ 189.091, found 189.0906.



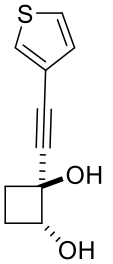
***trans*-1-(Phenylethynyl)cyclobutane-1,2-diol (trans-2k):** white solid (75 mg, 20%). M. p.: 119–121 °C. R_f = 0.27 (hexane/EtOAc = 1/1). ^{1}H-NMR (300 MHz, $CDCl_3$): δ (ppm) = 7.53–7.43 (m, 2H), 7.39–7.28 (m, 3H), 4.16-4.07 (m, 1H), 2.75 (d, J = 16.9 Hz, 1H), 2.50–2.34 (m, 1H), 2.36–2.22 (m, 1H), 2.26–2.10 (m, 1H), 1.81 (td, J = 11.0, 8.7 Hz, 1H), 1.67–1.51 (m, 1H). ^{13}C-NMR (75.4 MHz, $CDCl_3$): δ (ppm) = 132.0 (2

× CH), 128.9 (CH), 128.5 (2 × CH), 122.0 (C), 88.2 (C), 87.3 (C), 75.8 (C), 75.5 (CH), 28.9 (CH_2), 24.6 (CH_2). LRMS (EI): *m/z* (%) 188 (M^+, 6), 129 (100), 75 (44). HRMS (ESI+) calcd for $C_{12}H_{13}O_2^+$ $[M+H]^+$ 189.091, found 189.0906.

1-(Thiophen-3-ylethynyl)cyclobutane-1,2-diol (2l). General procedure I was followed using (thiophen-3-ylethynyl)lithium (6 mmol, prepared by treatment of 3-(prop-1-yn-1-yl)thiophene (6 mmol, 0.65 g) with *n*-BuLi (6 mmol, 3.75 mL of a 1.6 M solution in hexane)), obtaining **2l** as a ca. 2/1 mixture of *cis*/*trans* diastereoisomers, which were isolated independently by flash column chromatography in hexane/EtOAc (1/1).

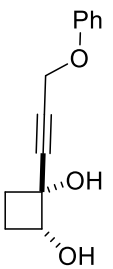


***cis*-1-(Thiophen-3-ylethynyl)cyclobutane-1,2-diol (*cis*-2l):** yellowish oil (163 mg, 42%). R_f = 0.40 (hexane/EtOAc = 1/1). ^{1}H-NMR (300 MHz, $CDCl_3$): δ (ppm) = 7.42 (dd, *J* = 3.0, 1.2 Hz, 1H), 7.22 (dd, *J* = 5.0, 3.0 Hz, 1H), 7.08 (dd, *J* = 5.0, 1.2 Hz, 1H), 4.33 (s, 1H), 3.64 (bs, *1*H), 3.54 (bs, 1H), 2.36–2.20 (m, 1H), 2.18–2.00 (m, 3H). ^{13}C-NMR (75.4 MHz, $CDCl_3$): δ (ppm) = 130.0 (CH), 129.2 (CH), 125.5 (CH), 121.6 (C), 90.1 (C), 80.2 (C), 72.8 (CH), 71.1 (C), 30.6 (CH_2), 28.2 (CH_2). LRMS (EI): *m/z* (%) 194 (M^+, 7), 137 (99), 109 (100). HRMS (ESI+) calcd for $C_{10}H_{11}O_2S^+$ $[M+H]^+$ 196.0506, found 196.0511.

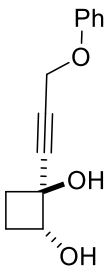


***trans*-1-(Thiophen-3-ylethynyl)cyclobutane-1,2-diol (*trans*-2l):** yellowish oil (37 mg, 19%). Slightly contaminated with ***cis*-2l**. R_f = 0.25 (hexane/EtOAc = 1/1). ^{1}H-NMR (300 MHz, $CDCl_3$): δ (ppm) = 7.51 (dd, *J* = 3.0, 1.2 Hz, 1H), 7.30–7.25 (m, 1H), 7.13 (dd, *J* = 5.0, 1.2 Hz, 1H), 4.15–4.07 (m, 1H), 2.96 (s, 1H), 2.51 (d, *J* = 9.8 Hz, 1H), 2.35–2.05 (m, 2H), 1.79 (td, *J* = 11.0, 8.7 Hz, 1H), 1.56 (tt, *J* = 11.0, 9.2 Hz, 1H). ^{13}C-NMR (75.4 MHz, $CDCl_3$): δ (ppm) = 130.1 (CH), 130.0 (CH), 125.7 (CH), 121.0 (C), 86.9 (C), 83.5 (C), 76.0 (C), 75.5 (CH), 28.9 (CH_2), 24.7 (CH_2). LRMS (EI): *m/z* (%) 194 (M^+, 7), 137 (99), 109 (100). HRMS (ESI+) calcd for $C_{10}H_{11}O_2S^+$ $[M+H]^+$ 196.0506, found 196.0511.

1-(3-Phenoxyprop-1-yn-1-yl)cyclobutane-1,2-diol (2m). General procedure I was followed using (3-phenoxyprop-1-yn-1-yl)lithium (6 mmol, prepared by treatment of (prop-2-yn-1-yloxy)benzene (6 mmol, 0.79 g) with EtMgBr (6 mmol, 3 mL of a 2 M solution in THF)), obtaining **2m** as a ca. 2/1 mixture of *cis*/*trans* diastereoisomers, which were isolated independently by flash column chromatography in hexane/EtOAc (1/1).



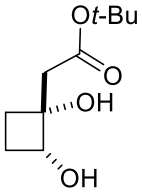
***cis*-1-(3-Phenoxyprop-1-yn-1-yl)cyclobutane-1,2-diol (*cis*-2m):** yellowish oil (174 mg, 39%). R_f = 0.45 (hexane/EtOAc = 1/1). ^{1}H-NMR (300 MHz, $CDCl_3$): δ (ppm) = 7.37–7.23 (m, 2H), 7.05–6.88 (m, 3H), 4.70 (s, 2H), 4.21 (s, 1H), 3.58–3.13 (m, 2H), 2.25–2.19 (m, 1H), 2.08–1.93 (m, 3H). ^{13}C-NMR (75.4 MHz, $CDCl_3$): δ (ppm) = 157.7 (C), 129.6 (2 × CH), 121.6 (CH), 115.0 (2 × CH), 88.7 (C), 79.8 (C), 72.4 (CH), 70.4 (C), 56.3 (CH_2), 30.3 (CH_2), 28.1 (CH_2). LRMS (EI): *m/z* (%) 218 (M^+, 2), 94 (100), 77 (42). HRMS (ESI+) calcd for $C_{13}H_{15}O_3^+$ $[M+H]^+$ 219.1016, found 219.1013.



***trans*-1-(3-Phenoxyprop-1-yn-1-yl)cyclobutane-1,2-diol (*trans*-2m):** colourless oil (75 mg, 16%). R_f = 0.24 (hexane/EtOAc = 1/1).^{1}H-NMR (300 MHz, $CDCl_3$): δ (ppm) = 7.34-7.26 (m, 2H), 7.03-6.96 (m, 3H), 4.80 (s, 2H), 3.99 (q, *J* = 9.1 Hz, 1H), 2.85 (bs, 1H), 2.29 (d, *J* = 10.4 Hz, 1H), 2.23–1.97 (m, 2H), 1.77–1.60 (m, 1H), 1.49–1.39 (m, 1H). ^{13}C-NMR (75.4 MHz, $CDCl_3$): δ (ppm) = 157.4 (C), 129.7 (2 × CH), 122.0 (CH), 115.3 (2 × CH), 86.2 (C), 83.2 (C), 75.4 (CH), 56.2 (CH_2), 28.5 (CH_2), 24.4 (CH_2), one quaternary carbon is missing due to overlapping of signals. LRMS (EI): *m/z* (%) 218 (M^+, 2), 94 (100), 77 (42). HRMS (ESI+) calcd for $C_{13}H_{15}O_3^+$ $[M+H]^+$ 219.1016, found 219.1013.

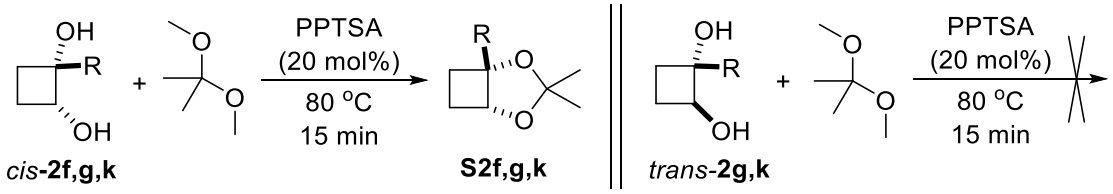
Synthesis of *tert*-butyl 2-(1,2-dihydroxycyclobutyl)acetate 2n:

A solution of LDA (6 mmol), prepared by the addition of *n*-BuLi (2.4 mL, 6 mmol, 2.5 M solution in hexane) to a stirred solution of diisopropylamine (607 mg, 6 mmol) in THF (3 mL) at 0 °C, was added slowly to a solution of *tert*-butyl acetate (697 mg, 6 mmol) in THF (2 mL) at −78 °C. The mixture was allowed to stir at room temperature for 15 minutes. Then, 2-hydroxycyclobutan-1-one **1a** (172 mg, 2 mmol) was added at −78 °C and the resulted solution was stirred at reflux for 6 h (monitored by TLC). The resulting mixture was quenched with aq. NH_4Cl (5 mL). THF was removed under reduced pressure and the aqueous layer was extracted with EtOAc (3 × 15 mL). The combined organic layers were dried over anhydrous Na_2SO_4, filtered and concentrated in vacuo. The residue was purified by flash column chromatography using a 3/1 mixture of hexane/EtOAc as eluent to afford **2n** as a ca. 2/1 mixture of *cis*/*trans* diastereoisomers. Only the *cis*-diastereoisomer was isolated.



***cis*-*tert*-Butyl 2-(1,2-dihydroxycyclobutyl)acetate (*cis*-2n)**: yellowish oil (150 mg, 37%). R_f = 0.40 (hexane/EtOAc = 2/1). ^{1}H-NMR (300 MHz, $CDCl_3$): δ (ppm) = 4.03 (q, *J* = 6.8 Hz, 1H), 3.73 (s, 1H), 3.02 (d, *J* = 6.1 Hz, 1H), 2.55 (q, *J* = 16.2 Hz, 2H), 2.29–2.13 (m, 1H), 2.12–1.82 (m, 2H), 1.78–1.57 (m, 1H), 1.44 (s, 9H). ^{13}C-NMR (75.4 MHz, $CDCl_3$): δ (ppm) = 172.0 (C), 81.8 (C), 75.8 (C), 70.8 (CH), 44.7 (CH_2), 28.3 (CH_2), 28.22 (3 × CH_3), 27.46 (CH_2). LRMS (EI) and HRMS could not be recorded.

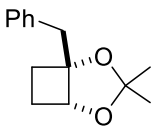
<u>STEREOCHEMICAL ASSIGNMENT of CYCLOBUTANE-1,2-DIOLS 2</u>



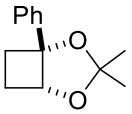
General procedure II

Cyclobutane-1,2-diols **2** are obtained as mixtures of *cis*/*trans* diastereoisomers which, in most cases, could be isolated independently. For the stereochemical assignment of diols **2,** we used

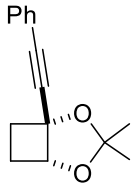
the fact that *cis*-cyclobutane-1,2-diols could easily produce acetals, whereas *trans*-diastereoisomers do not.[3] Taking into account this consideration, we performed independent acetalization experiments with *cis*-cyclobutane-1,2-diols (**2f,g,k**) and *trans*-cyclobutane-1,2-diols (**2g,k**) The corresponding cyclobutane-1,2-diol (0.1 mmol) was treated with 2,2-dimethoxypropane as reagent and solvent (2 mL) and PPTSA (5 mg, 20 mol%). The reaction was stirred at 80 °C for 15 minutes. Then, the resulting mixture was extracted with brine and EtOAc (3 × 5 mL). The combined organic layers were dried over Na_2SO_4, filtered, and concentrated under reduced pressure. The residue was analysed by ^{1}H-NMR. After analysing the NMR spectra, we could determine that the *cis*-diols give the corresponding acetals **S2**, whereas the corresponding *trans*-diols do not react.



1-Benzyl-3,3-dimethyl-2,4-dioxabicyclo[3.2.0]heptane (S2f): General procedure II was followed using *cis*-**2f** (0.1 mmol, 18 mg), obtaining **S2f**. ^{1}H-NMR (300 MHz, $CDCl_3$): δ (ppm) = 7.44–7.19 (m, 5H), 4.52 (dt, J = 4.7, 2.4 Hz, 1H), 3.12–2.89 (m, 2H), 2.24–2.03 (m, 2H), 1.98–1.76 (m, 2H), 1.57 (s, 3H), 1.08 (s, 3H). ^{13}C-NMR (75.4 MHz, $CDCl_3$): δ (ppm) = 137.1 (C), 130.3 (2 × CH), 128.2 (2 × CH), 126.6 (CH), 113.1 (C), 86.0 (CH), 79.5 (C), 42.6 (CH_2), 31.7 (CH_2), 28.6 (CH_2), 27.5 (CH_3), 21.7 (CH_3).



3,3-Dimethyl-1-phenyl-2,4-dioxabicyclo[3.2.0]heptane (S2g): General procedure III was followed using *cis*-**2g** (0.1 mmol, 16 mg) obtaining **S2'g**. ^{1}H-NMR (300 MHz, $CDCl_3$): δ (ppm) = 7.51–7.44 (m, 2H), 7.43–7.35 (m, 2H), 7.33–7.29 (m, 1H), 4.89–4.71 (m, 1H), 2.56–2.42 (m, 1H), 2.38–2.20 (m, 2H), 2.12–1.99 (m, 1H), 1.71 (t, J = 0.7 Hz, 3H), 1.30 (t, J = 0.7 Hz, 3H).



3,3-Dimethyl-1-(phenylethynyl)-2,4-dioxabicyclo[3.2.0]heptane (S2k): General procedure II was followed using *cis*-**2k** (0.1 mmol, 19 mg) obtaining the **S2k** . ^{1}H-NMR (300 MHz, $CDCl_3$): δ (ppm) = 7.53–7.42 (m, 2H), 7.41–7.29 (m, 3H), 4.95–4.66 (m, 1H), 2.44–2.25 (m, 3H), 2.06–1.86 (m, 1H), 1.63 (d, J = 0.7 Hz, 3H), 1.53 (d, J = 0.7 Hz, 3H).

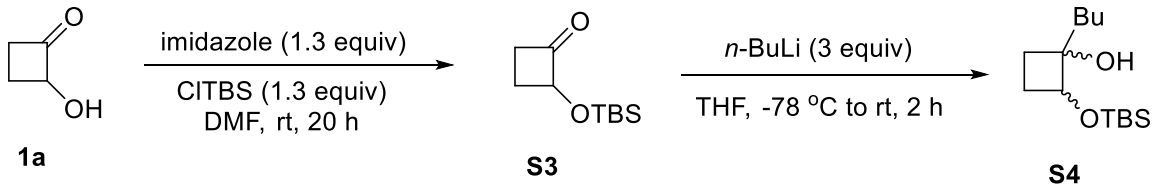
[3] M. J. Brown, T. Harrison, P. M. Herrinton, M. H. Hopkins, K. D. Hutchinson, P. Mishra and L. E. Overman, *J. Am. Chem. Soc.*, 1991, **113**, 5365–5378.

Table S2. Chemical shifts of C*H*OH signals for *cis*- and *trans*-diols **2**

Entry	R		Product	C*H*OH δ for *cis*-**2**	C*H*OH δ for *trans*-**2**
1	*n*-Bu	aliphatic	**2a**	3.93	4.08
2	Me	aliphatic	**2b**	4.07	4.13
3	Et	aliphatic	**2c**	3.91	4.11
4	*i*-Pr	aliphatic	**2d**	3.97	4.19
5	*c*-C_6H_{11}	aliphatic	**2e**	4.00	4.23
6	$PhCH_2$	aliphatic	**2f**	4.05	–
7	Ph	aromatic	**2g**	4.31	4.20
8	2-$MeOC_6H_4$	aromatic	**2h**	4.36	4.29
9	5-Me-2-Th	aromatic	**2i**	4.22	–
10	BuC≡C	alkynyl	**2j**	4.16	4.00
11	PhC≡C	alkynyl	**2k**	4.36	4.11
12	3-ThC≡C	alkynyl	**2l**	4.33	4.12
13	$PhOCH_2C$≡C	alkynyl	**2m**	4.21	3.99
14	CH_2CO_2t-Bu	aliphatic	**2n**	4.03	–

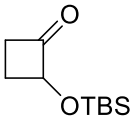
The stereochemical assignment for the rest of diols **2a-n** was extrapolated considering the chemical shift (δ) of the C*H*OH signals. We observed that the shift of this C*H*OH signal was affected by the nature of the R substituent. When R is an aliphatic group the C*H*OH shift of *cis*-**2** is lower than the corresponding of *trans*-**2**. On the other hand, when R is an aromatic or alkynyl group, the C*H*OH shift of *cis*-**2** is higher than the corresponding of *trans*-**2** (Table S2).

SYNTHESIS of CYCLOBUTANE-1,2-DIOL DERIVATIVE S4



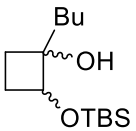
1a **S3** **S4**

To a solution of 2-hydroxycyclobutanone **1a** (861 mg, 1 mmol) in anhydrous DMF (2 mL) was added imidazole (102 mg, 1.3 mmol) and *tert*-butyldimethylsilyl chloride (225 mg, 1.3 mmol) and the resulted solution was stirred at room temperature for 20 h. Then, the mixture was quenched with water (5 mL) and extracted with Et_2O (3×5 mL). The combined organic layers were washed with brine (2×5 mL), dried over Na_2SO_4, filtered and concentrated under reduce pressure. The residue was purified by flash column chromatography using a 10/1 mixture of hexane/EtOAc as eluent to afford **S3**.



2-((*tert*-butyldimethylsilyl)oxy)cyclobutan-1-one (S3):[4] colourless oil (160 mg, 80%). R_f = 0.40 (hexane/EtOAc = 10/1). ^{1}H-NMR (300 MHz, $CDCl_3$): δ (ppm) = 4.84 (ddt, J = 10.2, 8.0, 2.3 Hz, 1H), 3.08–2.55 (m, 2H), 2.47–2.20 (m, 1H), 1.95–1.60 (m, 1H), 0.88 (d, J = 1.0 Hz, 9H), 0.09 (d, J = 5.9 Hz, 6H). ^{13}C-NMR (75.4 MHz, $CDCl_3$): δ (ppm) = 207.0 (C), 82.0 (CH), 38.3 (CH_2), 25.8 (3 $\times$ CH_3), 22.3 (CH_2), 18.23 (C), −4.7 (CH_3), −4.9 (CH_3).

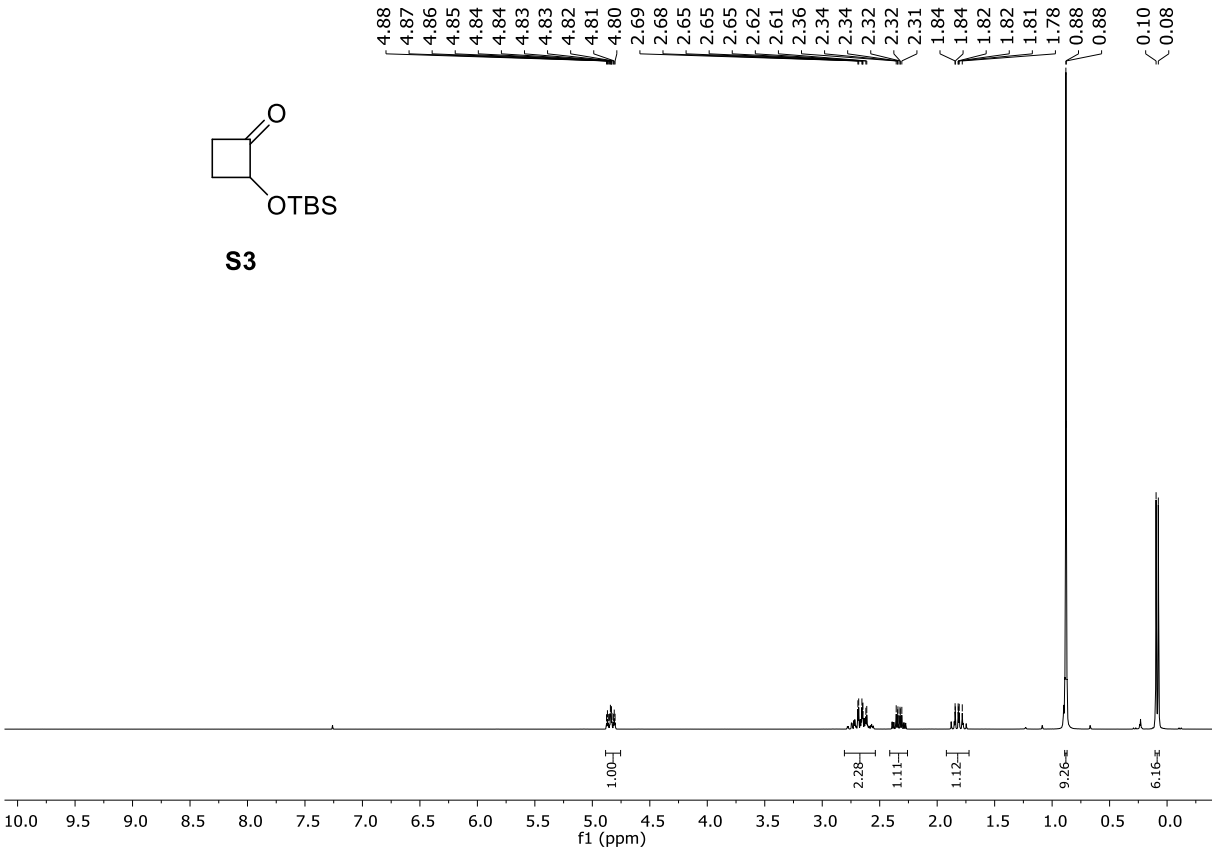
To a solution of 2-((*tert*-butyldimethylsilyl)oxy)cyclobutan-1-one **S3** (102 mg, 0.5 mmol) in anhydrous THF (1 mL) was added *n*-BuLi (0.94 mL, 1.5 mmol, 1.6 M solution in hexane) at −78 °C and the resulted solution was stirred at room temperature for 2 h (monitored by TLC). Then, the mixture was quenched with aq. NH_4Cl (5 mL) and extracted with Et_2O (3 $\times$ 5 mL). The combined organic layers were dried over anhydrous Na_2SO_4, filtered and concentrated in vacuo. The residue was purified by flash column chromatography using deactivated silica gel and a 5/1 mixture of hexane/EtOAc as eluent to afford **S4** as a c.a. 3/1 mixture of *cis*/*trans* diastereoisomers.



1-Butyl-2-((*tert*-butyldimethylsilyl)oxy)cyclobutan-1-ol (S4): colourless oil (60 mg, 52%). R_f = 0.35 (hexane/EtOAc = 10/1). Data for the major *cis*-diastereoisomer: ^{1}H-NMR (300 MHz, $CDCl_3$): δ (ppm) = 3.95 (d, J = 5.1 Hz, 1H), 3.19 (s, 1H), 2.09–1.23 (m, 17H), 0.89 (d, J = 5.1 Hz, 10H), 0.06 (s, 9H). ^{13}C-NMR (75.4 MHz, $CDCl_3$): δ (ppm) = 77.4 (C), 72.0 (CH), 39.4 (CH_2), 29.6 (CH_2), 27.34 (CH_2), 25.7 (CH_2), 25.9 (3 $\times$ CH_3), 23.2 (CH_2), 18.2 (C), 14.6 (CH_3), −4.4 (CH_3), −4.8 (CH_3).

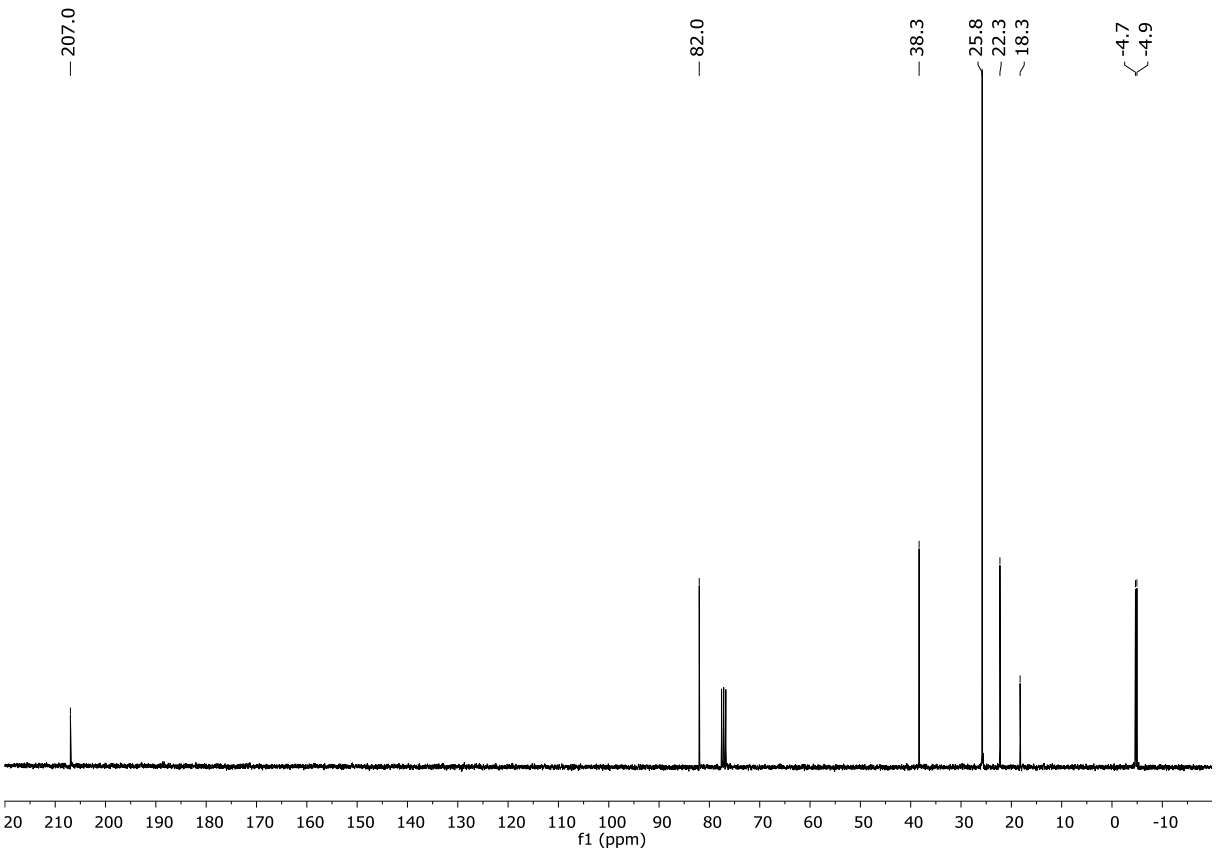
[4] S. Danappe, A. Pal, C. Alexandre, A. Aubertin, N. Bourgougnon and F. Huet, *Tetrahedron* 2005, **61**, 5782−5787.

^{1}H-NMR (300 MHz, $CDCl_3$)

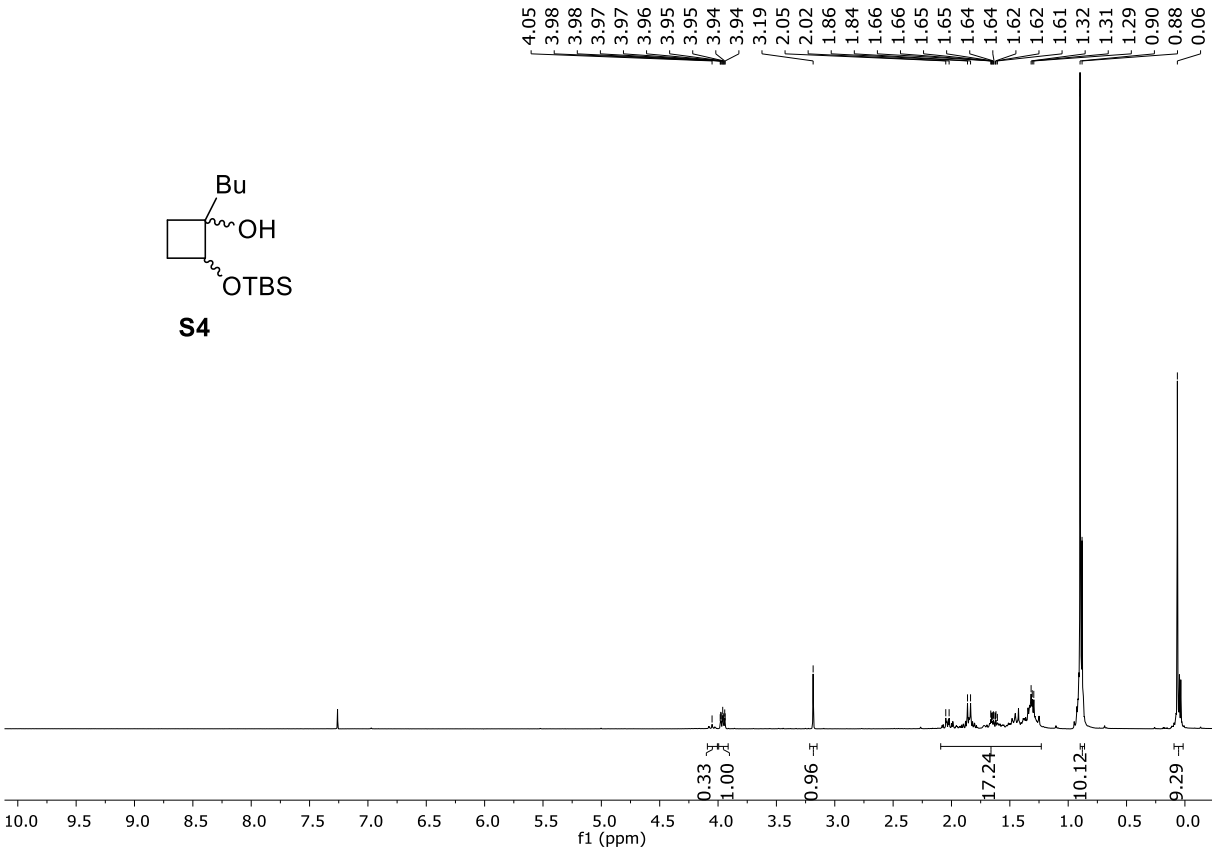


S3

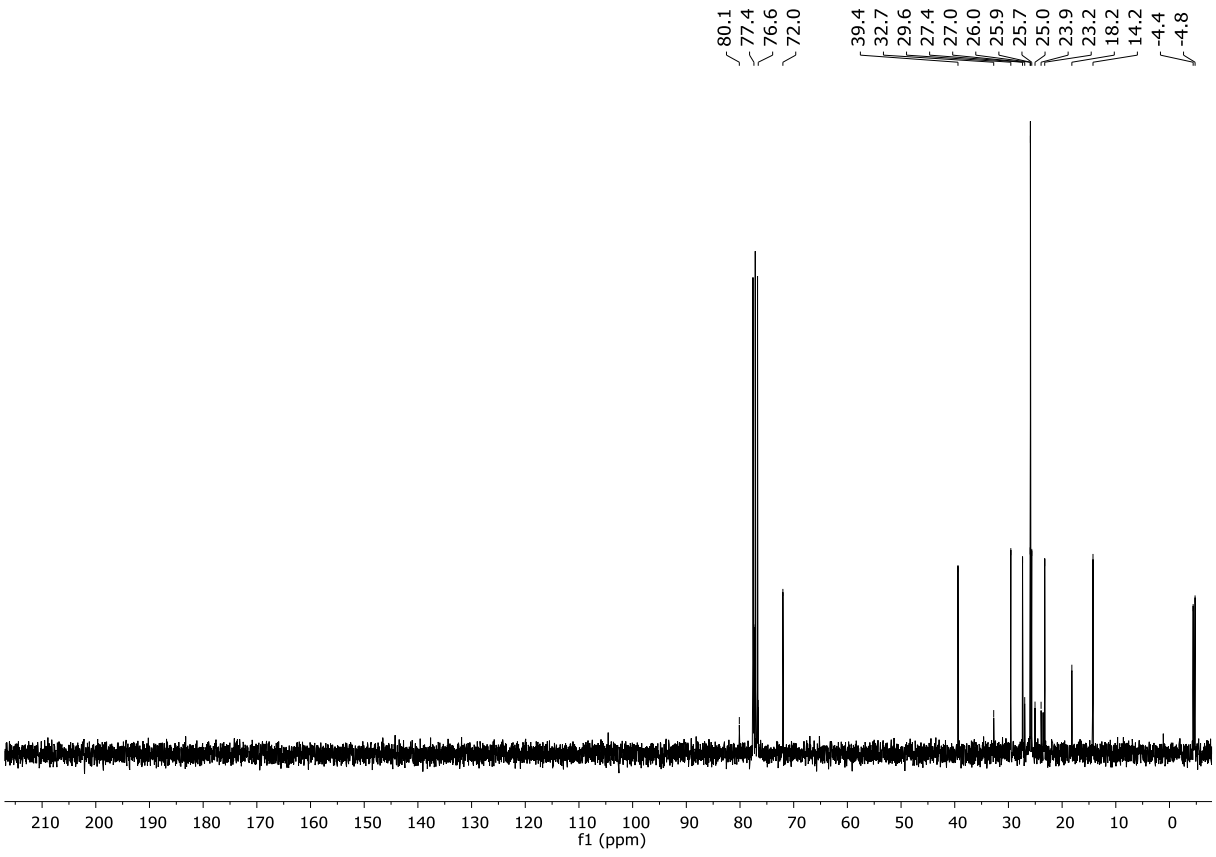
^{13}C-NMR (75.4 MHz, $CDCl_3$)



^{1}H-NMR (300 MHz, $CDCl_3$)



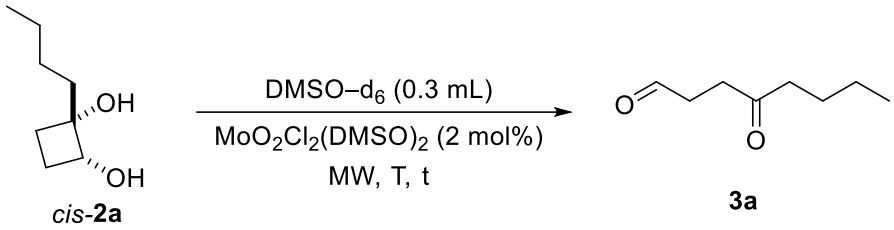
^{13}C-NMR (75.4 MHz, $CDCl_3$)



OPTIMIZATION of the OXIDATIVE CLEAVAGE of CYCLOBUTANE-1,2-DIOL 2a

As already mentioned in the manuscript, a brief study of the reaction conditions for achieving the oxidative cleavage with DMSO, under dioxomolybdenum(VI)-catalysis, of both *cis*- and *trans*-cyclobutane-1,2-diol **2a** was performed (Tables S3 and S4).

Table S3. Study of the reaction conditions for the oxidative cleavage of *cis*-**2a**.[a]



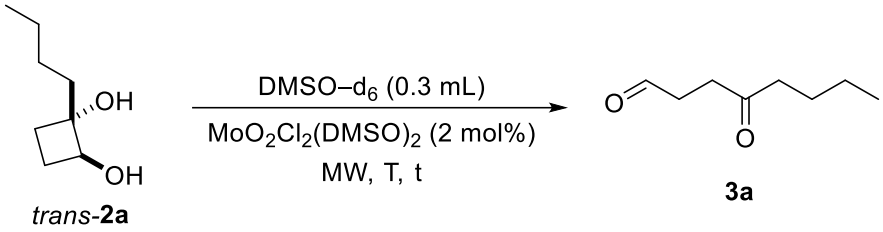
cis-**2a** → **3a**

Entry	Temperature (^{o}C)	Time (min)	Conversion (%)[b]
1	130	10	100
2	110	10	100
3	90	10	100
4[c]	90	10	10
5	70	10	100
6	50	10	40
7	70	5	55
8[d]	70	10	65
9[d]	90	10	100

[a] Reaction conditions: *cis*-**2a** (14 mg, 0.1 mmol) in DMSO-d_6 (0.3 mL) under microwave irradiation (80 W). [b] Conversion determined by ^{1}H-NMR analysis of the crude mixture. [c] Performed in absence of catalyst. [d] Performed with *cis*-**2a** (0.5 mmol) in DMSO-d_6 (1 mL).

For experiments carried out at high temperatures (>100 ^{o}C) (entries 1 and 2), full conversion was achieved. Some tests at lower temperatures were carried out and total conversion was achieved even at 70 ^{o}C for 10 min (entry 5). The essential role of the catalyst was also checked (entries 3 vs 4). Further lowering of the temperature or reaction time led to not complete conversion (entries 6 and 7). However, when the reaction scale was increased, slightly higher temperatures were needed (90 ^{o}C) to get complete conversion (entries 8 and 9). In addition, the oxidative cleavage of *cis*-**2a** also works under conventional heating (90 ^{o}C) for 1 h.

Table S4. Study of the reaction conditions for the oxidative cleavage of *trans*-**2a**.[a]



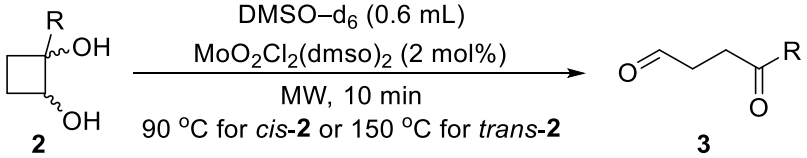
trans-**2a** **3a**

Entry	Temperature (^{o}C)	Time (min)	Conversion (%)[b]
1	70	10	5
2	90	10	10
3	110	10	25
4	130	10	55
5	150	10	100
6	130	15	100
7[c]	130	15	15

[a] Reaction conditions: *trans*-**2a** (14 mg, 0.1 mmol) in DMSO-d_6 (0.3 mL) under microwave irradiation (80 W). [b] Conversion determined by ^{1}H-NMR analysis of the crude mixture. [c] Performed in absence of catalyst. [d] Performed with *trans*-**2a** (0.5 mmol) in DMSO-d_6 (1 mL).

With temperatures from 70 to 130 ^{o}C (entries 1–4), no total conversion for *trans*-diol **2a** is achieved. Therefore, we performed another experiment at 150 ^{o}C obtaining total conversion after 10 minutes (entry 5). It is also observed that, at 130 ^{o}C, 15 minutes were needed to complete the reaction (entry 6). However, when reaction scale was increased, a higher temperature was required (entry 7). Therefore, next experiments will be carried at 150 ^{o}C for 10 minutes under microwave irradiation, except *trans*-diols with an alkynyl group as substituent, which will be carried at 130 ^{o}C for 15 minutes since at higher temperatures some decomposition was observed.

SYNTHESIS and CHARACTERIZATION DATA for 1,4-KETOALDEHYDES 3

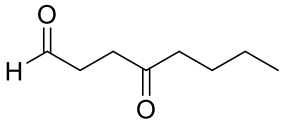


2 **3**

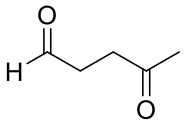
General procedure III-a

In a 10 mL microwave tube, the corresponding *cis*-**2** (0.3 mmol), DMSO-d_6 (0.6 mL) and $MoO_2Cl_2(dmso)_2$ (21 mg, 0.006 mmol) were added, and the tube was sealed with a septum. The reaction mixture was stirred at 90 ^{o}C for 10 minutes under microwave irradiation (80 W). After completion of the reaction, the corresponding γ-ketoaldehyde **3** is obtained pure

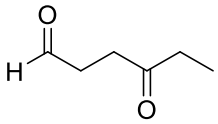
without further purification. The yields were determined using dibromomethane as internal standard. For those *trans*-**2** diols that could be isolated in pure form the oxidative cleavage was carried out at 150 °C for 10 minutes leading to the same 1,4-ketoaldehydes **3**.



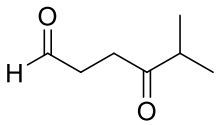
4-Oxooctanal (3a): General procedure III-a was followed using *cis*-1-butylcyclobutane-1,2-diol **2a** (43 mg, 0.3 mmol). Yield = 92%. ^{1}H-NMR (300 MHz, DMSO-d_6): δ (ppm) = 9.60 (s, 1H), 2.71–2.62 (m, 2H), 2.60–2.53 (m, 2H), 2.40 (t, J = 7.2 Hz, 2H), 1.47–1.33 (m, 2H), 1.26–1.15 (m, 2H), 0.81 (t, J = 7.2 Hz, 3H). ^{13}C-NMR (75.4 MHz, DMSO-d_6): δ (ppm) = 209.0 (C), 202.1 (CH), 41.3 (CH_2), 37.0 (CH_2), 34.4 (CH_2), 25.4 (CH_2), 21.7 (CH_2), 13.7 (CH_3). LRMS (EI): *m/z* (%) 142 (M^+, 2), 85 (74), 57 (100). HRMS (ESI+) calcd for $C_8H_{15}O_2^+$ $[M+H]^+$ 143.1067, found 143.1066.



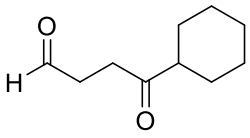
4-Oxopentanal (3b):[5] General procedure III-a was followed using *cis*-1-methylcyclobutane-1,2-diol **2b** (31 mg, 0.3 mmol). Yield = 94%. ^{1}H-NMR (300 MHz, DMSO-d_6): δ (ppm) = 9.60 (s, 1H), 2.68 (t, J = 6.1 Hz, 2H), 2.62–2.50 (m, 2H), 2.07 (s, 3H). ^{13}C-NMR (75.4 MHz, DMSO-d_6): δ (ppm) = 206.9 (C), 202.1 (CH), 37.0 (CH_2), 35.3 (CH_2), 29.5 (CH_3). LRMS (EI) and HRMS could not be recorded.



4-Oxohexanal (3c):[6] General procedure III-a was followed using *cis*-1-ethylcyclobutane-1,2-diol **2c** (35 mg, 0.3 mmol). Yield = 92%. ^{1}H-NMR (300 MHz, DMSO-d_6): δ (ppm) = 9.20 (s, 1H), 2.29–2.12 (m, 4H), 2.04–1.95 (m, 2H), 0.48 (t, J = 7.3 Hz, 3H). ^{13}C-NMR (75.4 MHz, DMSO-d_6): δ (ppm) = 209.5 (C), 202.3 (CH), 37.1 (CH_2), 34.9 (CH_2), 34.1 (CH_2), 7.7 (CH_3). LRMS (EI): *m/z* (%) could not be recorded. HRMS (APCI+) calcd for $C_6H_{11}O_2^+$ $[M+H]^+$ 116.0788, found 116.0783.



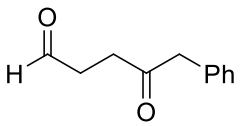
5-Methyl-4-oxohexanal (3d):[6] General procedure III-a was followed using *cis*-1-isopropylcyclobutane-1,2-diol **2d** (39 mg, 0.3 mmol). Yield = 89%. ^{1}H-NMR (300 MHz, DMSO-d_6): δ (ppm) = 9.64 (s, 1H), 2.76 (dd, J = 6.9, 5.2 Hz, 2H), 2.67–2.55 (m, 3H), 1.01 (d, J = 6.9 Hz, 6H). ^{13}C-NMR (75.4 MHz, DMSO-d_6): δ (ppm) = 212.6 (C), 202.2 (CH), 39.7 (CH), 37.0 (CH_2), 32.3 (CH_2), 18.10 (2 x CH_3). LRMS (EI): *m/z* (%) could not be recorded. HRMS (ESI+) calcd for $C_7H_{13}O_2^+$ $[M+H]^+$ 129.0910, found 129.0910.



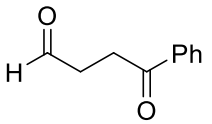
4-Cyclohexyl-4-oxobutanal (3e):[7] General procedure III-a was followed using *cis*-1-cyclohexylcyclobutane-1,2-diol **2e** (51 mg, 0.3 mmol). Yield = 92%. ^{1}H-NMR (300 MHz, DMSO-d_6): δ (ppm) = 9.64 (t, J = 1.0 Hz, 1H), 2.79–2.71 (m, 2H), 2.63–2.57 (m, 2H), 1.86–1.56 (m, 6H), 1.31–1.15 (m,

[5] S. D. Schnell, A. Linden and K. Gademann, *Org. Lett.*, 2019, **21**, 1144−1147.
[6] H. Tan, X. Chen, H. Chen, H. Lui and S. Qiu, *Eur. J. Org. Chem.*, 2015, 4956−4963.
[7] S. Muthusamy and P. Srinivasan, *Tetrahedron Lett.*, 2006, **47**, 6297−6300.

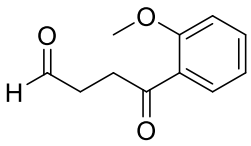
5H). ^{13}C-NMR (75.4 MHz, DMSO-d_6): δ (ppm) = 211.7 (C), 202.1 (CH), 49.4 (CH), 36.9 (CH_2), 32.5 (CH_2), 28.1 (2 × CH_2), 25.5 (CH_2), 25.1 (2 × CH_2). LRMS (EI): *m/z* (%) 168 (M^+, 3), 83 (100), 55 (90). HRMS (ESI+) calcd for $C_{10}H_{17}O_2^+$ $[M+H]^+$ 170.1257, found 170.1257.



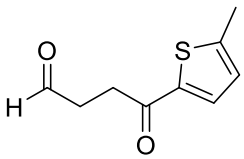
4-Oxo-5-phenylpentanal (3f): General procedure III-a was followed using *cis*-1-benzylcyclobutane-1,2-diol **2f** (54 mg, 0.3 mmol). Yield = 90%. ^{1}H-NMR (300 MHz, DMSO-d_6): δ (ppm) = 9.63 (s, 1H), 7.36–7.27 (m, 2H), 7.27–7.14 (m, 3H), 3.79 (s, 2H), 2.77 (t, *J* = 6.6 Hz, 2H), 2.61 (t, *J* = 6.6 Hz, 2H). ^{13}C-NMR (75.4 MHz, DMSO-d_6): δ (ppm) = 206.7 (C), 202.1 (CH), 134.8 (C), 129.6 (2 × CH), 128.3 (2 × CH), 126.6 (CH), 48.6 (CH_2), 37.01 (CH_2), 34.30 (CH_2). LRMS (EI): *m/z* (%) 176 (M^+, 7), 91 (54), 85 (100). HRMS (ESI+) calcd for $C_{11}H_{13}O_2^+$ $[M+H]^+$ 178.0944, found 178.0943.



4-Oxo-4-phenylbutanal (3g):[8] General procedure III-a was followed using *cis*-1-phenylcyclobutane-1,2-diol **2g** (49 mg, 0.3 mmol). Yield = 93%. ^{1}H-NMR (300 MHz, DMSO-d_6): δ (ppm) = 9.70 (s, 1H), 7.95 (d, *J* = 7.4 Hz, 2H), 7.60 (d, *J* = 7.2 Hz, 1H), 7.49 (t, *J* = 7.4 Hz, 2H), 3.37–3.20 (m, 2H), 2.87–2.67 (m, 2H).^{13}C-NMR (75.4 MHz, DMSO-d_6): δ (ppm) = 202.2 (CH), 198.3 (C), 136.2 (C), 133.3 (CH), 128.7 (2 × CH), 127.9 (2 × CH), 37.1 (CH_2), 31.0 (CH_2). LRMS (EI): *m/z* (%) 162 (M^+, 5), 105 (85), 77 (100). HRMS (APCI+) calcd for $C_{10}H_{11}O_2^+$ $[M+H]^+$ 187.0754, found 187.0749.

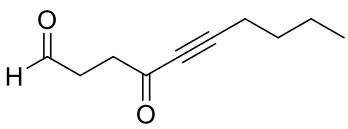


4-(2-Methoxyphenyl)-4-oxobutanal (3h): General procedure III-a was followed using *cis*-1-(2-methoxyphenyl)cyclobutane-1,2-diol **2h** (58 mg, 0.3 mmol). Yield = 91%. ^{1}H-NMR (300 MHz, DMSO-d_6): δ (ppm) = 9.71 (t, *J* = 1.0 Hz, 1H), 7.70–7.46 (m, 2H), 7.18 (dd, *J* = 8.4, 0.9 Hz, 1H), 7.03 (td, *J* = 7.5, 0.9 Hz, 1H), 3.89 (s, 3H), 3.31–3.13 (m, 2H), 2.76–2.71 (m, 2H). ^{13}C-NMR (75.4 MHz, DMSO-d_6): δ (ppm) = 202.7 (CH), 200.2 (C), 158.9 (C), 134.4 (CH), 130.1 (CH), 127.6 (C), 120.9 (CH), 113.0 (CH), 56.3 (CH_3), 38.0 (CH_2), 36.6 (CH_2). LRMS (EI): *m/z* (%) 192 (M^+, 2), 135 (80), 77 (100). HRMS (ESI+) calcd for $C_{11}H_{13}O_3^+$ $[M+H]^+$ 194.0893, found 194.0894.

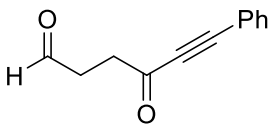


4-(5-Methylthiophen-2-yl)-4-oxobutanal (3i): General procedure III-a was followed using *cis*-1-(5-methylthiophen-2-yl)cyclobutane-1,2-diol **2i** (55 mg, 0.3 mmol). Yield = 88%. ^{1}H-NMR (300 MHz, DMSO-d_6): δ (ppm) = 9.71 (d, *J* = 0.8 Hz, 1H), 7.81 (d, *J* = 3.7 Hz, 1H), 6.96 (dd, *J* = 3.7, 0.8 Hz, 1H), 3.25–3.13 (m, 2H), 2.83–2.70 (m, 2H), 2.54 (s, 3H). ^{13}C-NMR (75.4 MHz, DMSO-d_6): δ (ppm) = 202.0 (CH), 190.9 (C), 149.3 (C), 141.0 (C), 133.8 (CH), 127.5 (CH), 37.2 (CH_2), 30.8 (CH_2), 15.6 (CH_3). LRMS (EI): *m/z* (%) 182 (M^+, 2), 125 (100), 53 (60). HRMS (ESI+) calcd for $C_9H_{11}O_2S^+$ $[M+H]^+$ 183.0474, found 183.0474.

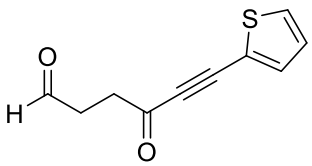
[8] I. Kumar, N. A. Mir, P. Ramaraju, D. Singh, V. K. Gupta and Rajnikant, *RCS Adv.*, 2014, **4**, 34548–34551



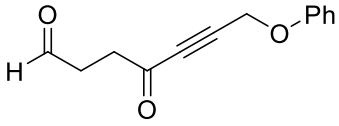
4-Oxodec-5-ynal (3j): General procedure III-a was followed using *cis*-1-(hex-1-yn-1-yl)cyclobutane-1,2-diol **2j** (51 mg, 0.3 mmol). Yield = 94%. ^{1}H-NMR (300 MHz, DMSO-d_6): δ (ppm) = 9.61 (s, 1H), 2.80–2.72 (m, 2H), 2.68 (dd, J = 6.9, 5.0 Hz, 2H), 2.44 (t, J = 6.9 Hz, 2H), 1.55–1.27 (m, 5H), 0.85 (t, J = 7.2 Hz, 1H). ^{13}C-NMR (75.4 MHz, DMSO-d_6): δ (ppm) = 201.5 (CH), 185.6 (C), 94.7 (C), 80.5 (C), 37.6 (CH_2), 37.0 (CH_2), 29.2 (CH_2), 21.3 (CH_2), 17.7 (CH_2), 13.3 (CH_3). LRMS (EI): *m/z* (%) 166 (M^+, 5), 109 (100), 79 (77). HRMS (ESI+) calcd for $C_4H_5O_2^+$ $[M–C_6H_9]^+$ 85.0284, found 85.0285.



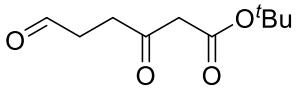
4-Oxo-6-phenylhex-5-ynal (3k): General procedure III-a was followed using *cis*-1-(phenylethynyl)cyclobutane-1,2-diol **2k** (56 mg, 0.3 mmol). Yield = 93%. ^{1}H-NMR (300 MHz, DMSO-d_6): δ (ppm) = 9.66 (s, 1H), 7.69–7.59 (m, 2H), 7.59–7.46 (m, 3H), 2.98 (t, J = 6.1 Hz, 2H), 2.78 (t, J = 6.1 Hz, 2H). ^{13}C-NMR (75.4 MHz, DMSO-d_6): δ (ppm) = 201.5 (CH), 185.6 (C), 132.9 (2 × CH), 131.3 (CH), 129.1 (2 × CH), 118.9 (C), 90.1 (C), 87.3 (C), 37.56 (CH_2), 37.07 (CH_2). LRMS (EI): *m/z* (%) 186 (M^+, 10), 129 (100), 79 (77). HRMS (ESI+) calcd for $C_{12}H_{11}O_2^+$ $[M+H]^+$ 188.0787, found 188.0791.



4-Oxo-6-(thiophen-2-yl)hex-5-ynal (3l). General procedure III-a was followed using *cis*-1-(thiophen-3-ylethynyl)cyclobutane-1,2-diol **2l** (58 mg, 0.3 mmol). Yield = 92%. ^{1}H-NMR (300 MHz, DMSO-d_6): δ (ppm) = 9.68 (d, J = 0.7 Hz, 1H), 8.22 (dd, J = 2.9, 1.2 Hz, 1H), 7.70 (dd, J = 5.0, 2.9 Hz, 1H), 7.34 (dd, J = 5.0, 1.2 Hz, 1H), 2.96–2.92 (m, 2H), 2.85–2.74 (m, 2H). ^{13}C-NMR (75.4 MHz, DMSO-d_6): δ (ppm) = 201.7 (CH), 185.7 (C), 135.7 (CH), 130.2 (CH), 128.0 (CH), 118.0 (C), 87.6 (C), 86.2 (C), 37.5(CH_2), 37.2 (CH_2). LRMS (EI): *m/z* (%) 192 (M^+, 8), 135 (100), 63 (47). HRMS (ESI+) calcd for $C_{10}H_9O_2S^+$ $[M+H]^+$ 193.0318, found 193.0318.



4-Oxo-7-phenoxyhept-5-ynal (3m): General procedure III-a was followed using *cis*-1-(3-phenoxyprop-1-yn-1-yl)cyclobutane-1,2-diol **2m** (66 mg, 0.3 mmol). Yield = 90%. ^{1}H-NMR (300 MHz, DMSO-d_6): δ (ppm) = 9.61 (s, 1H), 7.40–7.24 (m, 2H), 7.07–6.92 (m, 3H), 5.08 (s, 2H), 2.83 (t, J = 6.5 Hz, 2H), 2.71 (t, J = 6.5 Hz, 2H). ^{13}C-NMR (75.4 MHz, DMSO-d_6): δ (ppm) = 201.4 (CH), 185.2 (C), 157.0 (C), 129.7 (2 × CH), 121.7 (CH), 114.9 (2 × CH), 87.6 (C), 84.9 (C), 55.2 (CH_2), 37.4 (CH_2), 36.9 (CH_2). LRMS (EI): *m/z* (%) 216 (M^+, 4), 65 (100), 39 (99). HRMS (ESI+) calcd for $C_{13}H_{13}O_3^+$ $[M+H]^+$ 217.0859, found 217.0857.

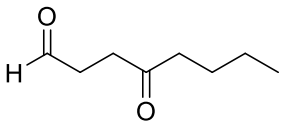


***tert*-Butyl 3,6-dioxohexanoate (3n).** General procedure III-a was followed using *cis-tert*-butyl 2-(1,2-dihydroxycyclobutyl)acetate **2n** (61 mg, 0.3 mmol). Yield = 89%.^{1}H-NMR (300 MHz, DMSO-d_6): δ (ppm) = 9.63 (s, 1H), 5.73 (s, 2H), 2.79 (t, J = 6.2 Hz, 2H), 2.63 (t, J = 6.2 Hz, 2H), 1.40 (s, 9H). ^{13}C-NMR (75.4 MHz, DMSO-d_6): δ (ppm) = 202.5 (CH), 201.9 (C), 166.4 (C), 80.9 (C), 49.9 (CH_2),

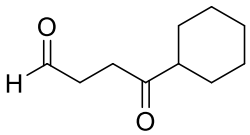
36.8 (CH_2), 34.9 (CH_2), 27.7 (3 × CH_3). LRMS (EI): *m/z* (%) 146 (M^+, 2), 85 (57), 57 (100). HRMS (ESI+) calcd for $C_{10}H_{16}NaO_4^+$ $[M+Na]^+$ 223.0941, found 223.0931.

General procedure III-b

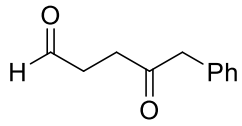
In a 10 mL microwave tube, the corresponding *cis*-cyclobutane-1,2-diol **2a,e,g** (0.3 mmol), DMSO-d_6 (0.6 mL) and $MoO_2Cl_2(dmso)_2$ (21 mg, 0.006 mmol) were added, and the tube was sealed with a septum. The reaction mixture was stirred at 90 °C for 10 minutes under microwave irradiation (80 W). After completion of the reaction, monitored by ^{1}H-NMR, the reaction is diluted with EtOAc (5 mL) and washed with brine (3 × 5 mL). The aqueous layer was further extracted with EtOAc (2 × 5 mL). The combined organic layers were dried over anhydrous Na_sSO_4, filtered, and concentrated under reduced pressure affording the corresponding γ-ketoaldehydes **3a,e,g**.



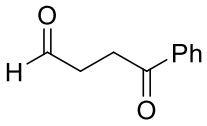
4-Oxooctanal (3a): General procedure III-b was followed using *cis*-1-butylcyclobutane-1,2-diol **2a** (43 mg, 0.3 mmol), obtaining **3a** as an orange oil (37 mg, 86%). ^{1}H-NMR (300 MHz, $CDCl_3$): δ (ppm) = 9.61 (s, 1H), 2.57 (d, J = 2.4 Hz, 3H), 2.30 (t, J = 7.3 Hz, 2H), 1.47–1.34 (m, 2H), 1.20−1.08 (m, 3H), 0.73 (t, J = 7.3 Hz, 3H). ^{13}C-NMR (75.4 MHz, $CDCl_3$): δ (ppm) = 208.7 (C), 200.4 (CH), 42.1 (CH_2), 37.1 (CH_2), 34.4 (CH_2), 25.6 (CH_2), 22.0 (CH_2), 13.6 (CH_3). LRMS (EI) and HRMS (ESI+) data have been reported above.



4-Cyclohexyl-4-oxobutanal (3e): General procedure III-b was followed using *cis*-1-cyclohexylcyclobutane-1,2-diol **2e** (51 mg, 0.3 mmol), obtaining **3e** as an orange oil (44 mg, 87%). ^{1}H-NMR (300 MHz, $CDCl_3$): δ (ppm) = 9.75 (d, J = 0.6 Hz, 1H), 2.80–2.73 (m, 2H), 2.61–2.57 (m, 2H) 2.45−2.37 (m, 1H), 1.85–1.60 (m, 6H), 1.41–1.06 (m, 4H). ^{13}C-NMR (75.4 MHz, $CDCl_3$): δ (ppm) = 211.9 (C), 200.8 (CH), 50.7 (CH), 37.5 (CH_2), 32.7 (CH_2), 28.6 (2 × CH_2), 25.9 (CH_2), 25.6 (2 × CH_2). LRMS (EI) and HRMS (ESI+) data have been reported above.

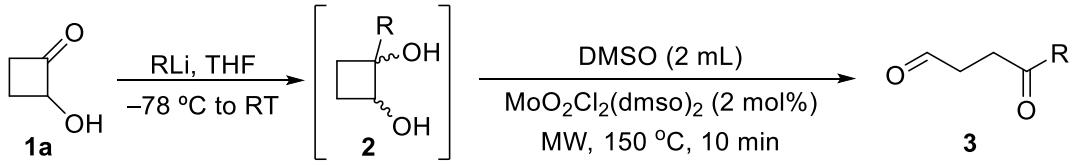


4-Oxo-5-phenylpentanal (3f): General procedure III-b was followed using *cis*-1-benzylcyclobutane-1,2-diol **2g** (53 mg, 0.3 mmol), obtaining **3g** as an orange oil (46 mg, 86%). ^{1}H-NMR (300 MHz, $CDCl_3$): δ (ppm) = 9.78 (d, J = 0.7 Hz, 1H), 7.59–7.16 (m, 5H), 3.77 (s, 2H), 2.95–2.55 (m, 4H). ^{13}C-NMR (75.4 MHz, $CDCl_3$): δ (ppm) = 206.4 (C), 200.5 (CH), 134.1 (C), 129.5 (2 × CH), 128.9 (2 × CH), 127.2 (CH), 50.1 (CH_2), 37.6 (CH_2), 34.1 (CH_2). LRMS (EI) and HRMS (ESI+) data have been reported above.



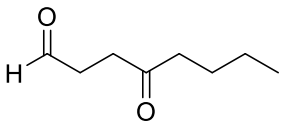
4-Oxo-4-phenylbutanal (3g): General procedure II-b was followed using *cis*-1-phenylcyclobutane-1,2-diol **2g** (49 mg, 0.3 mmol), obtaining **3g** as an orange oil (43 mg, 88%). ^{1}H-NMR (300 MHz, $CDCl_3$): δ (ppm) = 9.91 (s, 1H), 8.30–7.93 (m, 2H), 7.67–7.52 (m, 1H), 7.47 (dd, *J* = 8.3, 6.7 Hz, 2H), 3.33 (t, *J* = 6.3 Hz, 2H), 2.94 (t, *J* = 6.3 Hz, 2H). ^{13}C-NMR (75.4 MHz, $CDCl_3$): δ (ppm) = 200.8 (C), 198.0 (C), 136.6 (C), 133.5 (CH), 128.8 (2 × CH), 128.2 (2 × CH), 37.7 (CH_2), 31.2 (CH_2). LRMS (EI) and HRMS (APCI+) data has been reported above.

DIRECT SYNTHESIS of 1,4-KETOALDEHYDES 3 from 1a

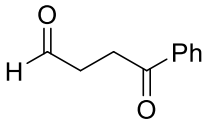


General procedure IV

To a stirred solution of 2-hydroxycyclobutan-1-one **1a** (87 mg, 1 mmol), in anhydrous THF (3 mL), the corresponding organometallic reagent (3 mmol) was added at −78 °C and the resulted solution was stirred at room temperature for 2 h (monitored by TLC). Then, the mixture was quenched with aq. NH_4Cl (5 mL). THF was removed under reduced pressure and the aqueous layer was extracted with EtOAc (3 × 15 mL). The combined organic layers were dried over anhydrous Na_2SO_4, filtered and concentrated in vacuo. The residue was used in the next step without further purification. Then, in a 10 mL microwave tube, the corresponding crude cyclobutane-1,2-diol **2**, DMSO (2 mL) and $MoO_2Cl_2(dmso)_2$ (7 mg, 0.02 mmol) were added, and the tube was sealed with a septum. The reaction mixture was stirred at 150 °C for 10 minutes under microwave irradiation (80 W). After completion of the reaction, the residue was purified by flash column chromatography using mixtures of hexane/EtOAc as eluent to afford the corresponding 1,4-ketoaldehyde **3a**, **3g** and **3h** in yields reported in Scheme 3, referred to 2-hydroxycyclobutanone **1a**.

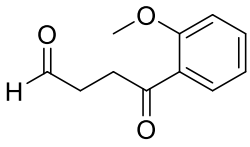


4-Oxooctanal (3a): General procedure IV was followed using *n*-BuLi (1.9 mL, 3 mmol, 1.6 M solution in hexane), obtaining **3a**, which was isolated by flash column chromatography in hexane/EtOAc (5/1) as an orange oil (18 mg, 42%). R_f = 0.32 (hexane/EtOAc = 5/1). Characterization data has been reported above.



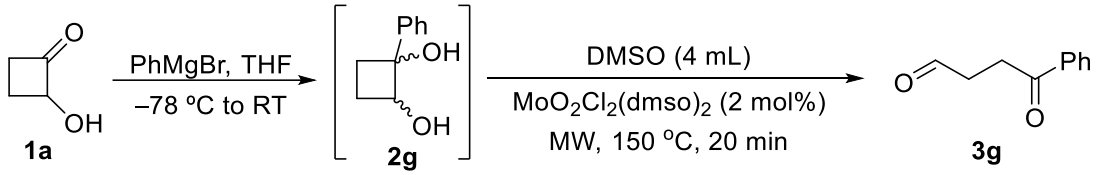
4-Oxo-4-phenylbutanal (3g): General procedure IV was followed using PhLi (1.6 mL, 3 mmol, 1.9 M solution in dibutyl ether), obtaining the **3g**, which was isolated by flash column chromatography in hexane/EtOAc (4/1) as an

orange oil (22 mg, 44%). R_f = 0.29 (hexane/EtOAc = 4/1). Characterization data has been reported above.



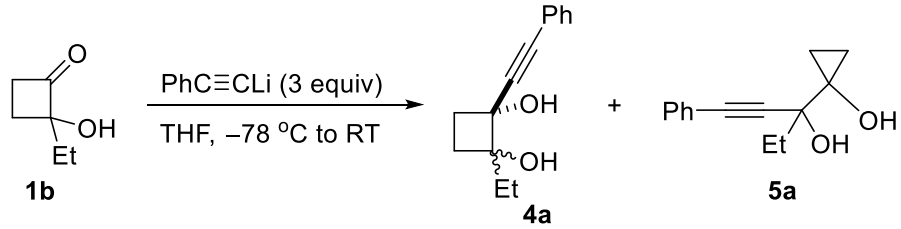
4-(2-Methoxyphenyl)-4-oxobutanal (3h): General procedure IV was followed using (2-methoxyphenyl)lithium (6 mmol, prepared by treatment of 1-bromo-2-methoxybenzene (1.234 g, 6 mmol) with *t*-BuLi (7 mL, 12 mmol of a 1.7 M solution in pentane)), obtaining **3h**, which was purified by flash column chromatography in hexane/EtOAc (3/1) as an orange oil (88 mg, 46%). R_f = 0.35 (hexane/EtOAc = 3/1). ^{1}H-NMR (300 MHz, $CDCl_3$): δ (ppm) = 9.88 (t, *J* = 1.0 Hz, 1H), 7.75 (ddd, *J* = 7.5, 1.8, 0.4 Hz, 1H), 7.47 (ddd, *J* = 8.3, 7.5, 1.8 Hz, 1H), 7.11–6.84 (m, 2H), 3.91 (s, 3H), 3.41–3.18 (t, *J* = 6.4 Hz, 2H), 2.85 (td, *J* = 6.4, 1.0 Hz, 2H). ^{13}C-NMR (75.4 MHz, $CDCl_3$): δ (ppm) = 201.4 (CH), 199.8 (C), 159.1 (C), 134.0 (CH), 130.7 (CH), 127.4 (C), 120.8 (CH), 111.7 (CH), 55.7 (CH_3), 38.2 (CH_2), 36.7 (CH_2). LRMS (EI): *m/z* (%) 192 (M^+, 2), 135 (80), 77 (100). HRMS (ESI+) calcd for $C_{11}H_{13}O_3^+$ $[M+H]^+$ 194.0893, found 194.0894.

LARGE SCALE SYNTHESIS of 1,4-KETOALDEHYDE 3g

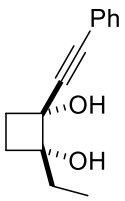


To a stirred solution of 2-hydroxycyclobutan-1-one **1a** (87 mg, 8 mmol), in anhydrous THF (3 mL) was added PhMgBr (24 mL, 24 mmol, 1 M in THF) at –78 °C and the resulted solution was stirred at room temperature for 2 h (monitored by TLC). Then, the mixture was quenched with aq. NH_4Cl (10 mL). THF was removed under reduced pressure and the aqueous layer was extracted with EtOAc (3 × 15 mL). The combined organic layers were dried over anhydrous Na_2SO_4, filtered and concentrated in vacuo. The residue was used in the next step without further purification. Then, in a 10 mL microwave tube, the corresponding crude cyclobutane-1,2-diol **2g**, DMSO (4 mL) and $MoO_2Cl_2(dmso)_2$ (57 mg, 0.16 mmol) were added, and the tube was sealed with a septum. The reaction mixture was stirred at 150 °C for 20 minutes under microwave irradiation (80 W). After completion of the reaction, the residue was purified by flash column chromatography using a 10/1 mixture of hexane/EtOAc as eluent to afford the corresponding 1,4-ketoaldehyde **3g** (558 mg, 43%). Characterization data has been reported above.

SYNTHESIS and CHARACTERIZATION DATA of *cis*-1-ETHYL-2-(PHENYLETHYNYL)CYCLOBUTANE-1,2-DIOL (*cis*-4a)



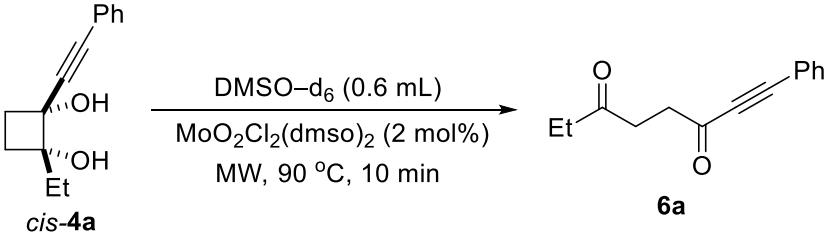
To a stirred solution of phenylacetylene (306.4 mg, 3 mmol), in anhydrous THF (2 mL), *n*-BuLi (1.9 mL, 3 mmol, 1.6 M solution in hexane) was added at −78 °C and allowed to stir at room temperature for 30 minutes. Then, 2-ethyl-2-hydroxycyclobutan-1-one **1b** (114.1 mg, 1 mmol) was added at −78 °C and the solution was stirred at room temperature for 2 h (monitored by TLC). After completion, the resulting mixture was quenched with aq. NH_4Cl (5 mL). THF was removed under reduced pressure and the aqueous layer was extracted with EtOAc (3 × 15 mL). The combined organic layers were dried over anhydrous Na_2SO_4, filtered and concentrated in vacuo. The residue was a *cis*/*trans* mixture of diol **4a** along with minor amounts of diol **5a**. After column chromatography in hexane/EtOAc (3/1) only *cis*-**4a** was isolated.



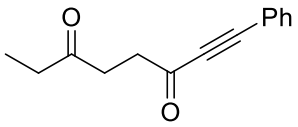
***cis*-1-Ethyl-2-(phenylethynyl)cyclobutane-1,2-diol (*cis*-4a):** yellowish oil (58 mg, 27%). R_f = 0.27 (hexane/EtOAc = 2/1). ^{1}H-NMR (300 MHz, $CDCl_3$): δ (ppm) = 7.49–7.35 (m, 2H), 7.33–7.24 (m, 3H), 3.71 (bs, 1H), 3.28 (bs, 1H), 2.24–2.09 (m, 2H), 2.08−2.02 (m, 2H), 1.92–1.70 (m, 2H), 1.05 (t, J = 7.4 Hz, 3H). ^{13}C-NMR (75.4 MHz, $CDCl_3$): δ (ppm) = 131.7 (2 × CH), 128.5 (CH), 128.4 (2 × CH), 122.7 (C), 88.8 (C), 86.3 (C), 78.8 (C), 73.4 (C), 31.3 (CH_2), 30.8 (CH_2), 29.5 (CH_2), 7.5 (CH_3). LRMS (EI): *m/z* (%) 216 (M^+, 4), 187 (87), 103 (100). HRMS (ESI+) calcd for $C_{14}H_{16}NaO_2^+$ $[M+Na]^+$ 239.1043, found 249.1037.

SYNTHESIS and CHARACTERIZATION DATA of 1,4-DIKETONES 6

Synthesis of 6a from *cis*-4a

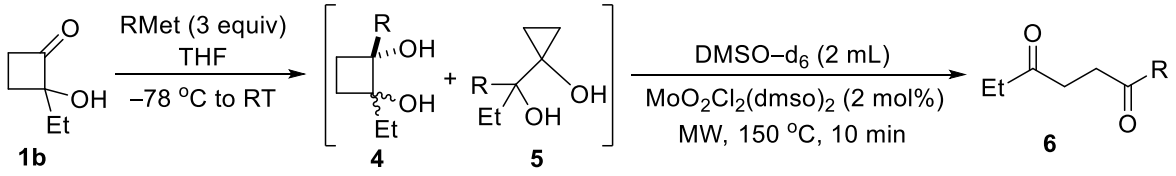


In a 10 mL microwave tube *cis*-cyclobutane-1,2-diol *cis*-**4a** (0.3 mmol), DMSO-d_6 (0.6 mL) and $MoO_2Cl_2(dmso)_2$ (21 mg, 0.006 mmol) were added, and the tube was sealed with a septum. The reaction mixture was stirred at 90 °C for 10 minutes under microwave irradiation (80 W). After completion of the reaction, monitored by ^{1}H-NMR, the crude was diluted with EtOAc (5 mL) and washed with brine (3 × 5 mL). The aqueous layer was further extracted with EtOAc (2 × 5 mL). The combined organic layers were dried over anhydrous Na_sSO_4, filtered, and concentrated under reduced pressure affording pure 1,4-diketone **6a** that was not further purified (58 mg, 90% yield).

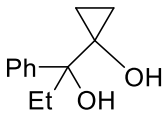


1-Phenyloct-1-yne-3,6-dione (6a): R_f = 0.32 (hexane/EtOAc = 5/1). ^{1}H-NMR (300 MHz, $CDCl_3$): *δ* (ppm) = 7.63–7.51 (m, 2H), 7.49–7.33 (m, 3H), 3.26 (t, *J* = 6.3 Hz, 2H), 2.83 (t, *J* = 6.3 Hz, 2H), 2.54 (q, *J* = 7.3 Hz, 2H), 1.07 (t, *J* = 7.3 Hz, 3H). ^{13}C-NMR (75.4 MHz, $CDCl_3$): *δ* (ppm) = 209.2 (C), 186.1 (C), 133.1 (2 × CH), 130.8 (CH), 128.7 (2 × CH), 120.0 (C), 91.1 (C), 87.7 (C), 39.2 (CH_2), 36.0 (CH_2), 35.6 (CH_2), 7.9 (CH_3). LRMS (EI): *m/z* (%) 214 (M^+, 2), 129 (100), 57 (40). HRMS (ESI+) calcd for $C_{14}H_{14}NaO_2^+$ $[M+Na]^+$ 215.1043, found 215.1034.

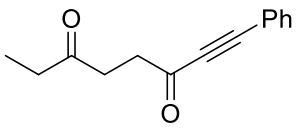
Synthesis of 1,4-diketones 6 from 1b. General procedure V



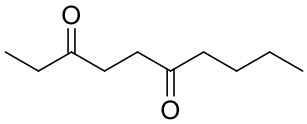
To a stirred solution of 2-ethyl-2-hydroxycyclobutan-1-one (**1b**) (114.1 mg, 1 mmol), in anhydrous THF (3 mL), the corresponding organometallic reagent (3 mmol) was added at −78 °C and the resulted solution was stirred at room temperature for 2 h (monitored by TLC). Then, the mixture was quenched with aq. NH_4Cl (5 mL). THF was removed under reduced pressure and the aqueous layer was extracted with EtOAc (3 × 15 mL). The combined organic layers were dried over anhydrous Na_2SO_4, filtered and concentrated in vacuo. The residue was a mixture of cyclobutanediols **4** (*cis*- and *trans*-diastereoisomers) and variable amounts of glycols **5** (minor), which was used in the next step without further purification. Then, in a 10 mL microwave tube, the residue was dissolved in DMSO (2 mL) and $MoO_2Cl_2(dmso)_2$ (0.02 mmol, 7 mg) was added, and the tube was sealed with a septum. The reaction mixture was stirred at 150 °C for 10 minutes under microwave irradiation (80 W). The crude was diluted with EtOAc (5 mL) and washed with brine (3 × 5 mL). The aqueous layer was further extracted with EtOAc (2 × 5 mL). The combined organic layers were dried over anhydrous Na_sSO_4, filtered, and concentrated under reduced pressure. The residue was purified by flash column chromatography using mixtures of hexane/EtOAc as eluent, to afford the corresponding 1,4-ketones **6a-f**. In the case of using PhLi, the corresponding minor glycol **5e** could be isolated.



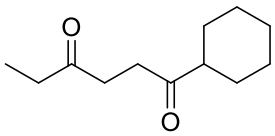
1-(1-Hydroxy-1-phenylpropyl)cyclopropan-1-ol (5e): colourless oil (19 mg, 10%). R_f = 0.21 (hexane/EtOAc = 5/1). ^{1}H-NMR (300 MHz, $CDCl_3$): δ (ppm) = 7.54-7.51 (m, 2H), 7.41–7.31 (m, 2H), 7.32–7.24 (m, 1H), 2.44 (bs, 1H), 2.18 (bs, 1H), 1.84 (m, 3H), 0.93–0.64 (m, 6H). ^{13}C-NMR (75.4 MHz, $CDCl_3$): δ (ppm) = 143.5 (C), 128.3 (2 × CH), 127.2 (CH), 126.5 (2 × CH), 78.5 (C), 62.6 (C), 29.6 (CH_2), 12.5 (CH_2), 9.5 (CH_2), 7.7 (CH_3). LRMS (EI): *m/z* (%) 174 (M^+, 3), 120 (100), 105 (83). HRMS (ESI+) calcd for $C_{12}H_{16}NaO_2^+$ $[M+Na]^+$ 215.1043, found 215.1034.



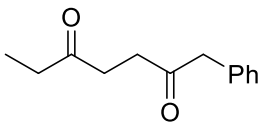
1-Phenyloct-1-yne-3,6-dione (6a): General procedure V was followed using phenylethynyl lithium, obtaining **6a** as a yellowish oil (103 mg, 48%). Characterization data have just shown above.



Decane-3,6-dione (6b): General procedure V was followed using *n*-BuLi (1.9 mL, 3 mmol, 1.6 M solution in hexane), obtaining **6b** as a colourless oil (72 mg, 42%). R_f = 0.53 (hexane/EtOAc = 5/1). ^{1}H-NMR (300 MHz, $CDCl_3$): δ (ppm) = 2.65 (d, *J* = 1.9 Hz, 4H), 2.51–2.36 (m, 4H), 1.63–1.46 (m, 2H), 1.36–1.15 (m, 2H), 1.09–0.97 (m, 3H), 0.87 (td, *J* = 7.4, 1.9 Hz, 3H). ^{13}C-NMR (75.4 MHz, $CDCl_3$): δ (ppm) = 210.2 (C), 209.9 (C), 42.6 (CH_2), 36.1 (CH_2), 36.0 (CH_2), 35.7 (CH_2), 26.0 (CH_2), 22.4 (CH_2), 13.9 (CH_3), 7.9 (CH_3). LRMS (EI): *m/z* (%) could not be recorded. HRMS (ESI+) calcd for $C_{10}H_{19}O_2^+$ $[M+H]^+$ 171.1380, found 171.1377.



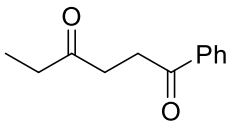
1-Cyclohexylhexane-1,4-dione (6c): General procedure V was followed using cyclohexylmagnesium chloride (1.5 mL, 3 mmol, 2 M solution in Et_2O), obtaining **6c** as a colourless oil (77 mg, 39%). R_f = 0.33 (hexane/EtOAc = 5/1). ^{1}H-NMR (300 MHz, $CDCl_3$): δ (ppm) = 2.75–2.59 (m, 4H), 2.45 (q, *J* = 7.3 Hz, 2H), 2.41–2.30 (m, 1H), 1.94–1.57 (m, 5H), 1.44–1.12 (m, 5H), 1.02 (t, *J* = 7.4 Hz, 3H). ^{13}C-NMR (75.4 MHz, $CDCl_3$): δ (ppm) = 212.8 (C), 210.2 (C), 50.8 (CH), 36.0 (CH_2), 35.7 (CH_2), 34.2 (CH_2), 28.6 (CH_2), 25.9 (2 × CH_2), 25.7 (2 × CH_2), 7.9 (CH_3). LRMS (EI): *m/z* (%) 196 (M^+, 3), 113 (79), 55 (100). HRMS (ESI+) calcd for $C_{12}H_{21}O_2^+$ $[M+H]^+$ 197.1536, found 197.1536.



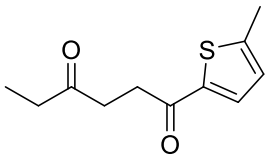
1-Phenylheptane-2,5-dione (6d):[9] General procedure V was followed using benzylmagnesium chloride (1.5 mL, 3 mmol, 2 M solution in THF), obtaining **6d** as a colourless oil (82 mg, 40%). R_f = 0.30 (hexane/EtOAc = 5/1). ^{1}H-NMR (300 MHz, $CDCl_3$): δ (ppm) = 7.36–7.25 (m, 3H), 7.23–7.18 (m, 2H), 3.75 (s, 2H), 3.09–2.62 (m, 4H), 2.46 (q, *J* = 7.4 Hz, 2H), 1.05 (t, *J* = 7.4 Hz, 3H). ^{13}C-NMR (75.4 MHz, $CDCl_3$): δ (ppm) = 210.1 (C), 207.3 (C), 134.3 (C), 129.6 (2 × CH), 128.8 (2

[9] Z. Shen, K. Goh, H. Cheong, C. Hong An Wong, Y. Lai, Y. Yang and T. Loh, *J. Am. Chem. Soc.,* 2010, **132**, 15852−15855.

× CH), 127.2 (CH), 50.2 (CH_2), 36.0 (CH_2), 35.9 (CH_2), 35.7 (CH_2), 7.9 (CH_3). LRMS (EI): *m/z* (%) 204 (M^+, 2), 113 (93), 57 (100).



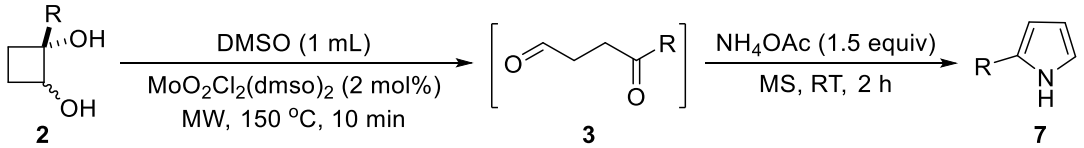
1-Phenylhexane-1,4-dione (6e):[10] General procedure V was followed using PhLi (1.6 mL, 3 mmol, 1.9 M solution in Bu_2O), obtaining **6e** as a colourless oil (72 mg, 38%). R_f = 0.32 (hexane/EtOAc = 5/1). ^{1}H-NMR (300 MHz, $CDCl_3$): δ (ppm) = 8.01–7.88 (m, 2H), 7.60–7.48 (m, 1H), 7.47–7.36 (m, 2H), 3.26 (t, *J* = 6.3 Hz, 2H), 2.83 (t, *J* = 6.3 Hz, 2H), 2.54 (q, *J* = 7.3 Hz, 2H), 1.07 (t, *J* = 7.3 Hz, 3H). ^{13}C-NMR (75.4 MHz, $CDCl_3$): δ (ppm) = 210.2 (C), 198.8 (C), 136.7 (C), 133.2 (CH), 128.6 (2 × CH), 128.1 (2 × CH), 36.1 (CH_2), 35.8 (CH_2), 32.5 (CH_2), 7.9 (CH_3). LRMS (EI): *m/z* (%) 190 (M^+, 1), 105 (91), 77 (100).



1-(5-Methylthiophene-2-yl)hexane-1,4-dione (6f): General procedure V was followed using (5-methylthiophen-2-yl)lithium (6 mmol, prepared by treatment of 2-methylthiophene (295 mg, 3 mmol) with *n*-BuLi (1.9 mL, 3 mmol, 1.6 M solution in hexane)), obtaining **6f** as a colourless oil (78 mg, 37%). R_f = 0.25 (hexane/EtOAc = 5/1). ^{1}H-NMR (300 MHz, $CDCl_3$): δ (ppm) = 7.62–7.46 (m, 1H), 6.74 (dd, *J* = 3.8, 1.0 Hz, 1H), 3.12 (t, *J* = 6.4 Hz, 2H), 2.92–2.69 (m, 2H), 2.55–2.41 (m, 5H), 1.03 (t, *J* = 7.3 Hz, 3H). ^{13}C-NMR (75.4 MHz, $CDCl_3$): δ (ppm) = 209.9 (C), 191.2 (C), 149.5 (C), 141.5 (C), 132.6 (CH), 126.7 (CH), 36.0 (CH_2), 35.8 (CH_2), 32.5 (CH_2), 16.0 (CH_3), 7.8 (CH_3). LRMS (EI): *m/z* (%) 210 (M^+, 2), 125 (100), 53 (54). HRMS (ESI+) calcd for $C_{11}H_{15}O_2S^+$ $[M+H]^+$ 212.0819, found 212.0818.

SYNTHESIS of PYRROLES 7 from 2

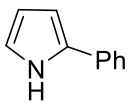
General procedure VI:



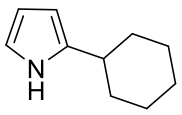
In a 10 mL microwave tube, the corresponding cyclobutane-1,2-diol **2** (as mixtures of *cis*- and *trans*-diastereoisomers) (0.5 mmol), DMSO (1 mL) and $MoO_2Cl_2(dmso)_2$ (3.5 mg, 0.01 mmol) were added, and the tube was sealed with a septum. The reaction mixture was stirred at 150 °C for 10 minutes under microwave irradiation (80 W). Then, after cooling, NH_4OAc (57.8 mg, 0.75 mmol), 4 Å molecular sieves (2 mg) were added, followed by a drop of glacial acetic acid. The reaction was allowed to stir for 2 h at room temperature. Then, the reaction was quenched by adding solid Na_2CO_3 and the resulting mixture was purified by flash column

[10] H. Imagaka, T. Kurisaki and M. Nishizawa, *Org. Lett.,* 2004, **6**, 3679–3681.

chromatography using different mixtures of hexane/EtOAc as eluent affording the corresponding pyrroles **7**.

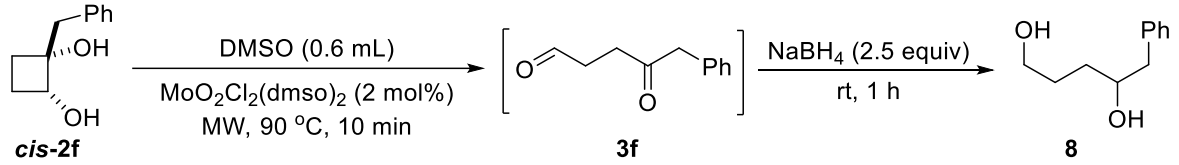


2-Phenyl-1*H*-pyrrole (7a):[11] General procedure VI was followed using 1-phenylcyclobutane-1,2-diol (0.0821 g, 0.5 mmol), obtaining **7a** as a brown oil (25 mg, 35%). R_f = 0.32 (hexane/EtOAc = 5/1). ^{1}H-NMR (300 MHz, $CDCl_3$): δ (ppm) = 8.43 (s, 1H), 7.56–7.46 (m, 2H), 7.44–7.30 (m, 2H), 7.35–7.17 (m, 1H), 6.86 (td, *J* = 2.7, 1.5 Hz, 1H), 6.57 (ddd, *J* = 3.6, 2.6, 1.3 Hz, 1H), 6.43–6.26 (m, 1H). ^{13}C-NMR (75.4 MHz, $CDCl_3$): δ (ppm) = 132.9 (C), 129.0 (2 × CH), 126.3 (CH), 124.0 (2 × CH), 119.0 (C), 110.2 (CH), 106.1 (CH), one CH is missing due to overlapping of signals. LRMS (EI): *m/z* (%) 143 (M^+,100) 115 (56), 71 (15).



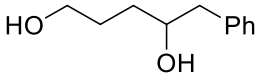
2-Cyclohexyl-1*H*-pyrrole (7b): General procedure VI was followed using 1-cyclohexylcyclobutane-1,2-diol (0.0851 g, 0.5 mmol), obtaining **7b** as a brown oil (28 mg, 37%). R_f = 0.28 (hexane/EtOAc = 5/1). ^{1}H-NMR (300 MHz, $CDCl_3$): δ (ppm) = 7.98 (bs, 1H), 6.67 (td, *J* = 2.7, 1.6 Hz, 1H), 6.16–6.13 (m, 1H), 5.94–5.91 (m, 1H), 2.66–2.45 (m, 1H), 2.18–1.93 (m, 2H), 1.89–1.66 (m, 3H), 1.46–1.26 (m, 5H). ^{13}C-NMR (75.4 MHz, $CDCl_3$): δ (ppm) = 115.8 (CH), 108.0 (CH), 103.0 (CH), 36.8 (CH), 33.2 (2 × CH_2), 26.3 (2 × CH_2), 26.2 (CH_2), one quaternary carbon is missing due to overlapping of signals. LRMS (EI): *m/z* (%) 119 (M^+, 15) 106 (100), 80 (53). HRMS (ESI+) calcd for $C_{10}H_{16}N^+$ $[M+H]^+$ 151.1309, found 151.1304.

SYNTHESIS of DIOL 8 from *cis*-2f:



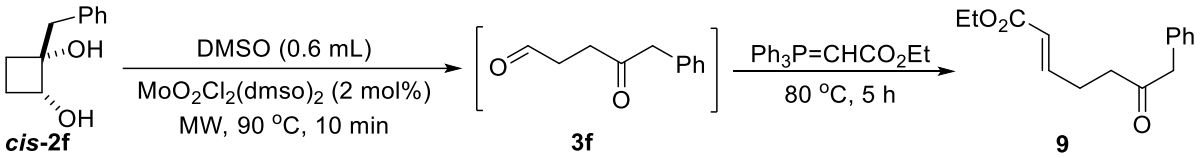
In a 10 mL microwave tube, the corresponding cyclobutane-1,2-diol ***cis*-2f** (54 mg, 0.3 mmol), DMSO (0.6 mL) and $MoO_2Cl_2(dmso)_2$ (2 mg, 0.006 mmol) were added, and the tube was sealed with a septum. The reaction mixture was stirred at 90 °C for 10 minutes under microwave irradiation (80 W). Then, after cooling, $NaBH_4$ (28 mg, 0.75 mmol), was added. The reaction was allowed to stir for 1 h at room temperature. Then, the reaction was diluted with EtOAc (5 mL) and washed with brine (3 × 5 mL). The combined organic layers were dried over anhydrous Na_sSO_4, filtered, and concentrated under reduced pressure. The residue was purified by flash column chromatography in deactivated silica using a mixture 1/2 of hexane/EtOAc as eluent affording diol **8**.

[11] N. R. Deprez, D. Kalyani, A. Krause, M. S. Sanford, *J. Am. Chem. Soc.* **2006**, *128*, 4972-4973.

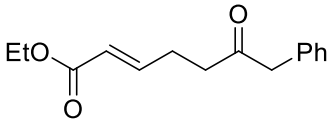


5-Phenylpentane-1,4-diol (8):[12] brown oil (32 mg, 60%). R_f = 0.22 (hexane/EtOAc = 1/2). ^{1}H-NMR (300 MHz, $CDCl_3$): δ (ppm) = 7.40–7.28 (m, 2H), 7.31–7.19 (m, 3H), 3.98–3.83 (m, 1H), 3.69 (q, *J* = 5.3 Hz, 2H), 2.83–2.69 (bm, 2H), 2.48–2.33 (bm, 2H), 1.79–1.70 (m, 3H), 1.68–1.48 (m, 1H). ^{13}C-NMR (75.4 MHz, $CDCl_3$): δ (ppm) = 138.6 (C), 129.6 (2 × CH), 128.7 (2 × CH), 126.7 (CH), 72.8 (CH), 63.1 (CH_2), 44.3 (CH_2), 33.9 (CH_2), 29.4 (CH_2). LRMS (EI): *m/z* (%) 180 (M^+, 1), 92 (100), 71 (75). HRMS (ESI+) calcd for $C_{11}H_{17}O_2$ $[M+H]^+$ 183.1282, found 183.1283.

SYNTHESIS of KETOESTER 9 from *cis*-2f:



In a 10 mL microwave tube, the corresponding cyclobutane-1,2-diol *cis*-**2f** (54 mg, 0.3 mmol), DMSO (0.6 mL) and $MoO_2Cl_2(dmso)_2$ (2 mg, 0.006 mmol) were added, and the tube was sealed with a septum. The reaction mixture was stirred at 90 °C for 10 minutes under microwave irradiation (80 W). Then, after cooling, (carbethoxymethylene)triphenylphosphorane (157 mg, 0.45 mmol), was added. The reaction was allowed to stir for 5 h at 80 °C. The crude was purified by flash column chromatography using a mixture 4/1 of hexane/EtOAc as eluent affording ketoester **9**.

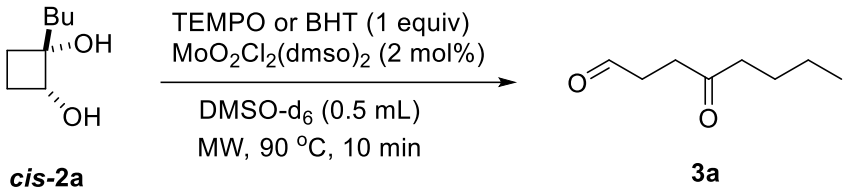


(*E*)-Ethyl 6-oxo-7-phenylhept-2-enoate (9): colourless oil (33 mg, 43%). R_f = 0.31 (hexane/EtOAc = 4/1). ^{1}H-NMR (300 MHz, $CDCl_3$): δ (ppm) = 7.39–7.28 (m, 3H), 7.25–7.18 (m, 2H), 6.89 (dt, *J* = 15.7, 6.7 Hz, 1H), 5.78 (dt, *J* = 15.7, 1.6 Hz, 1H), 4.18 (q, *J* = 7.1 Hz, 2H), 3.71 (s, 2H), 2.62 (t, *J* = 7.1 Hz, 2H), 2.51–2.32 (m, 2H), 1.29 (t, *J* = 7.1 Hz, 3H). ^{13}C-NMR (75.4 MHz, $CDCl_3$): δ (ppm) = 206.6 (C), 166.5 (C), 147.1 (CH), 134.0 (C), 129.5 (2 x CH), 128.6 (2 x CH), 127.3 (CH), 122.2 (CH), 60.4 (CH_2), 50.4 (CH_2), 39.9 (CH_2), 26.0 (CH_2), 14.4 (CH_3). LRMS (EI): *m/z* (%) 246 (M^+, 8), 155 (94), 91 (100). HRMS (ESI+) calcd for $C_{15}H_{19}O_3$ $[M+H]^+$ 247.1329, found 247.1334.

[12] B. D. Kelly, T. H. Lambert, *Org. Lett.*, 2011, **13**, 740–743.

STUDY of the REACTION MECHANISM

For the mechanism study, we design two experiments with two radical acceptors, TEMPO and BHT, and see if they are able to supress the reaction.



***cis*-2a** **3a**

After analysing the NMR spectra, the corresponding γ-ketoaldehyde **3a** was obtained in both cases with similar efficiency. This result suggests that the transformation does not follow a radical pathway.

We also investigated the formation of the proposed diolate complex **A** (Scheme 5 of the manuscript). According to the ^{1}H-NMR spectra of an equimolecular mixture of diols *cis*- or *trans*-**2a** and the Mo(VI) catalyst in DMSO-d_6 (Figures S1 and S2), recorded at different temperatures, the suggested complex **A** should be thought as existing only in the instant of its formation as it could not be detected by NMR. Furthermore, the spatial arrangement of both OH groups are crucial for the energy needed to afford the diolate complex **A**, with the *trans* configuration requiring more energy, since oxidative cleavage of *cis*-**2a** takes places at 40 °C while a temperature of 150 °C is needed to perform the oxidation of *trans*-**2a**.

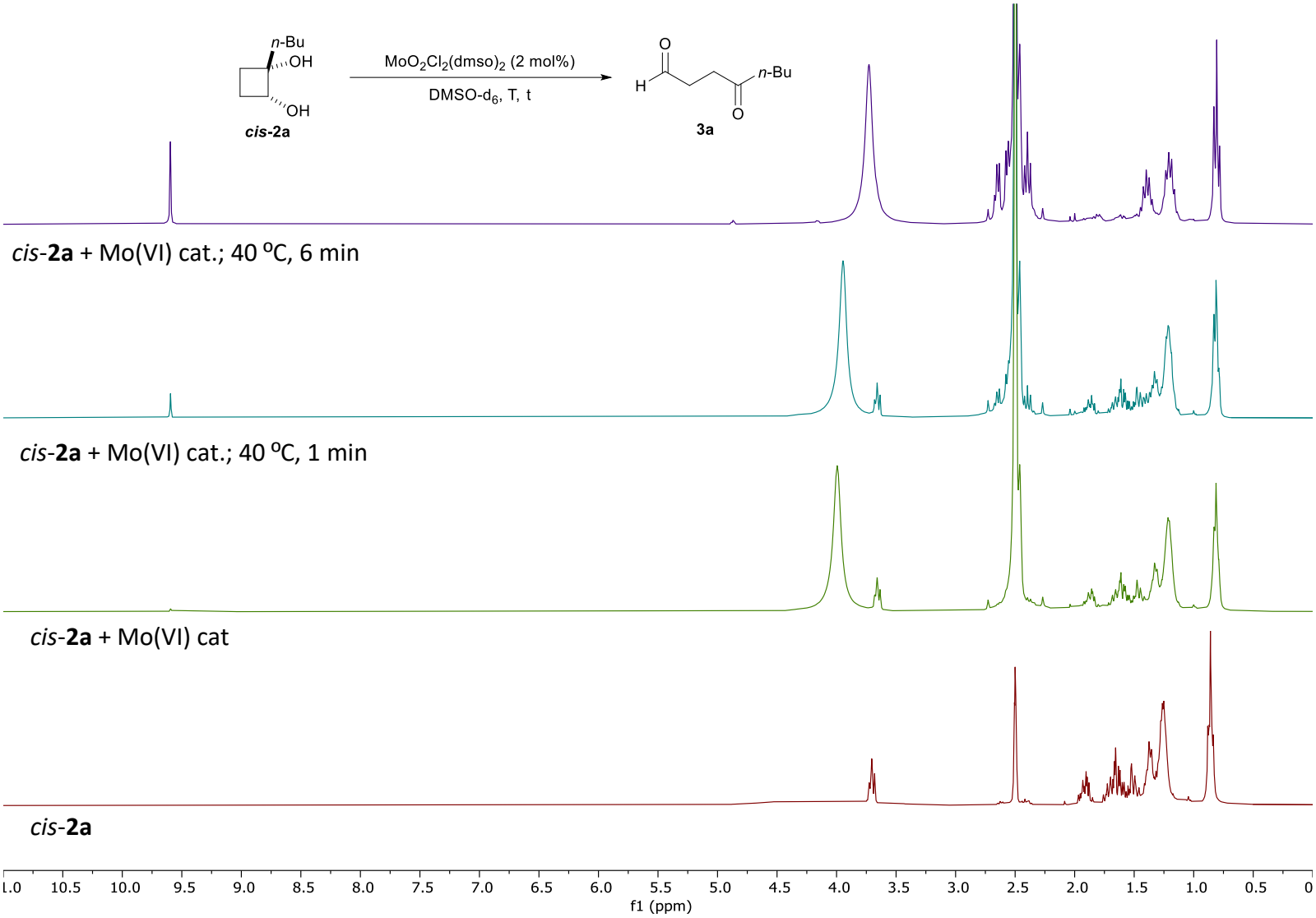

n-Bu
OH
OH
cis-2a
MoO2Cl2(dmso)2 (2 mol%)
DMSO-d6, T, t
O
H
n-Bu
O
3a
cis-2a + Mo(VI) cat.; 40 °C, 6 min
cis-2a + Mo(VI) cat.; 40 °C, 1 min
cis-2a + Mo(VI) cat
cis-2a
10.5
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0
f1 (ppm)

Figure S1.

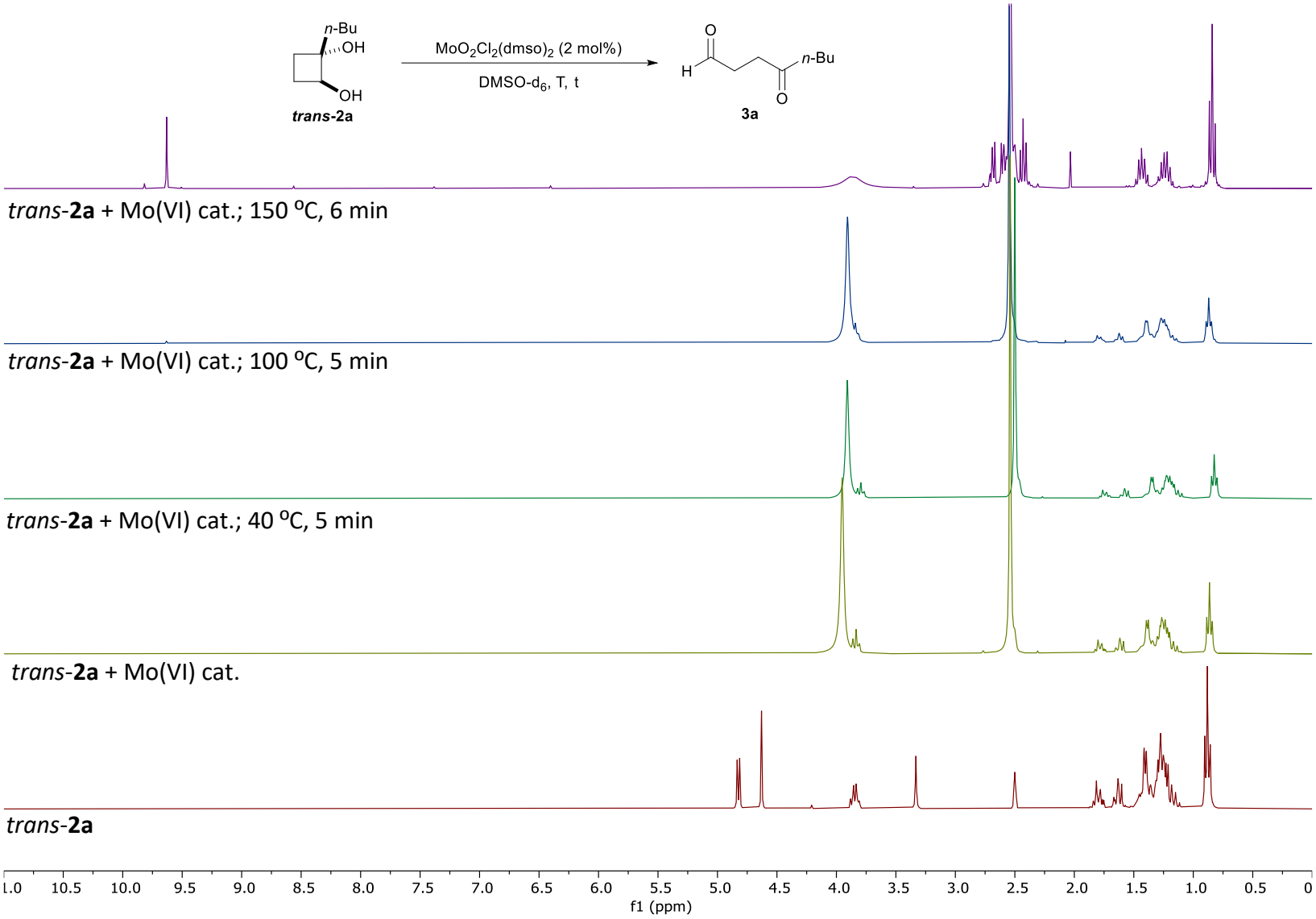
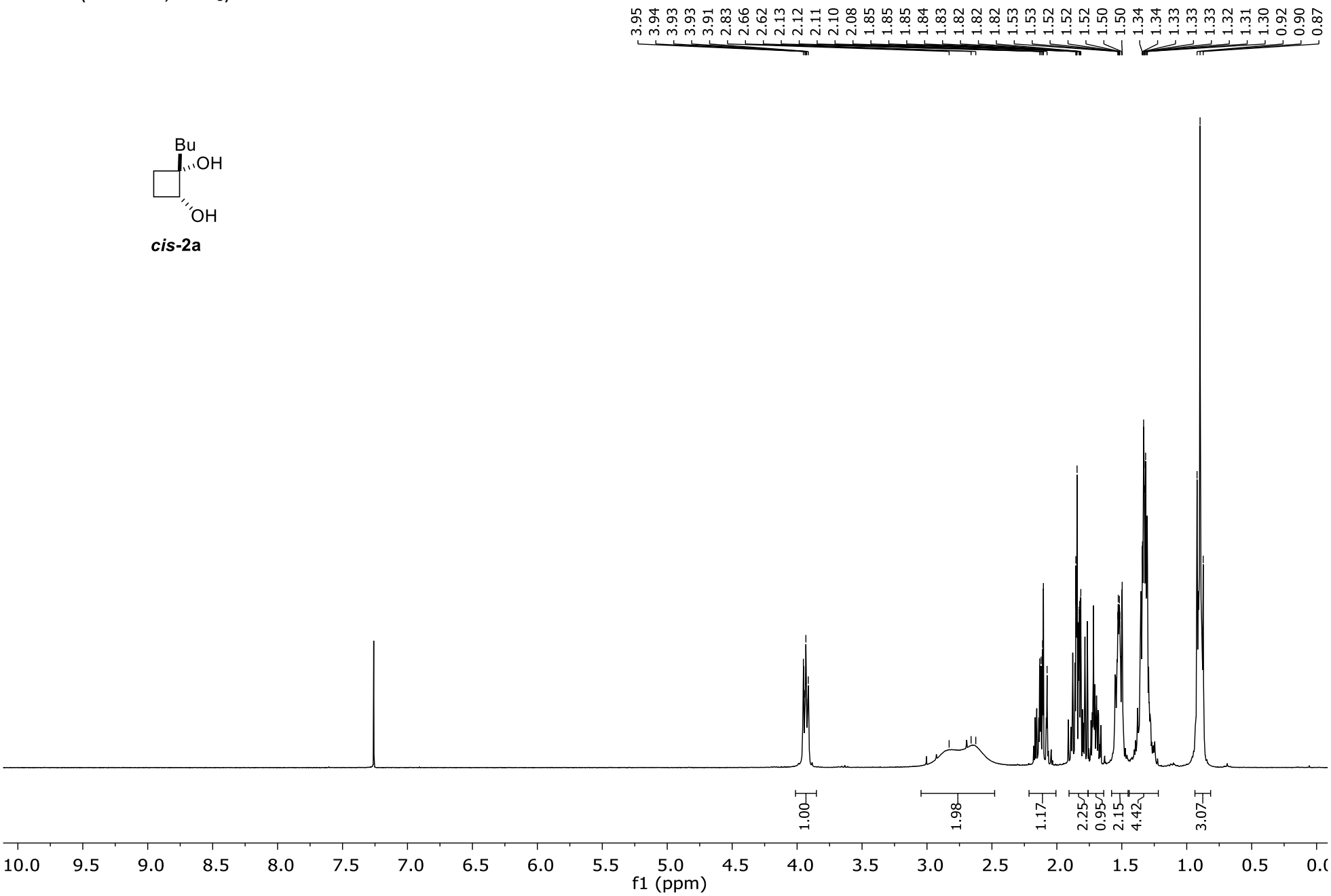

n-Bu
OH
OH
trans-2a
MoO2Cl2(dmso)2 (2 mol%)
DMSO-d6, T, t
O
H
n-Bu
O
3a
trans-2a + Mo(VI) cat.; 150 °C, 6 min
trans-2a + Mo(VI) cat.; 100 °C, 5 min
trans-2a + Mo(VI) cat.; 40 °C, 5 min
trans-2a + Mo(VI) cat.
trans-2a
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0
f1 (ppm)

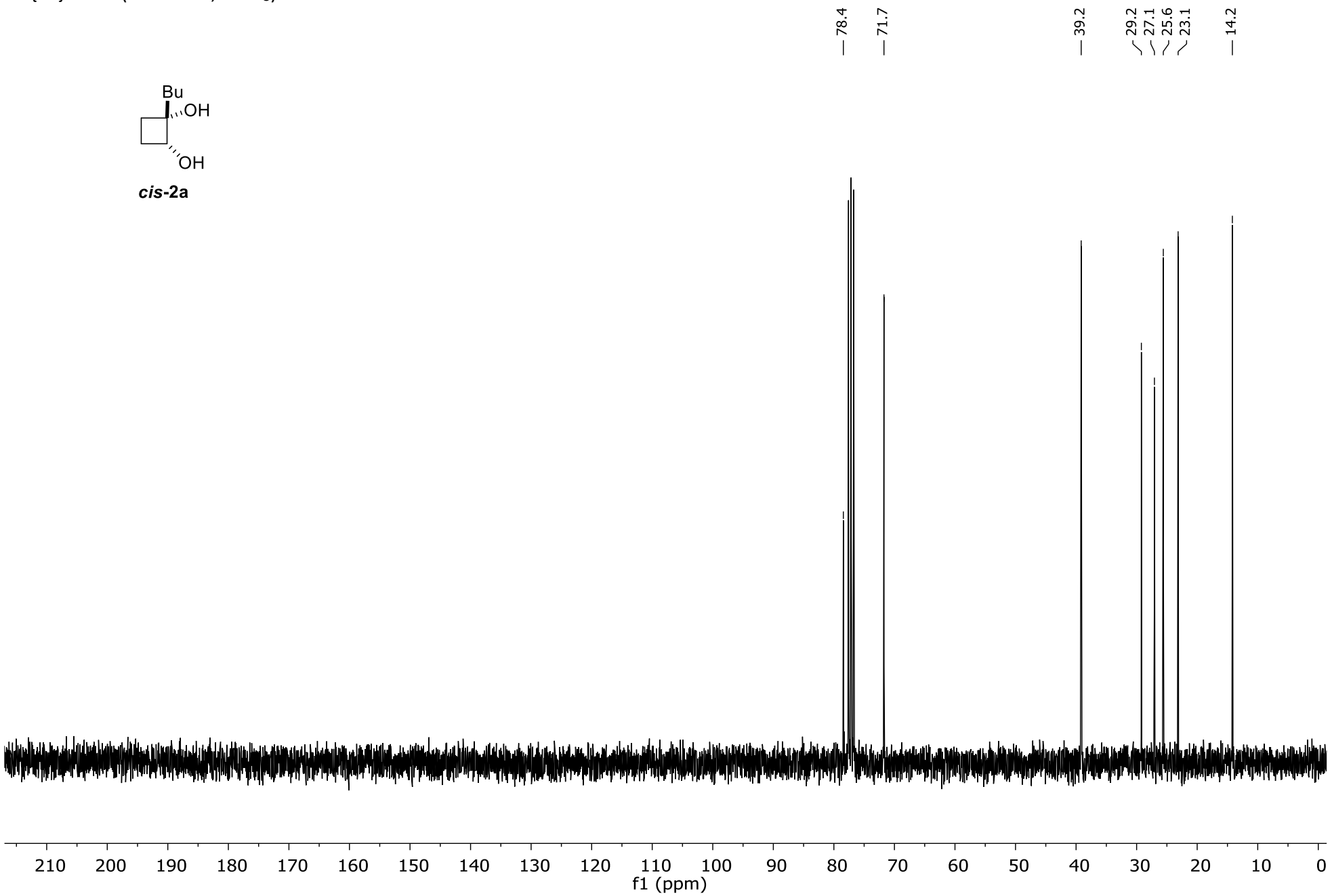
Figure S2.

^{1}H and ^{13}C NMR Spectra

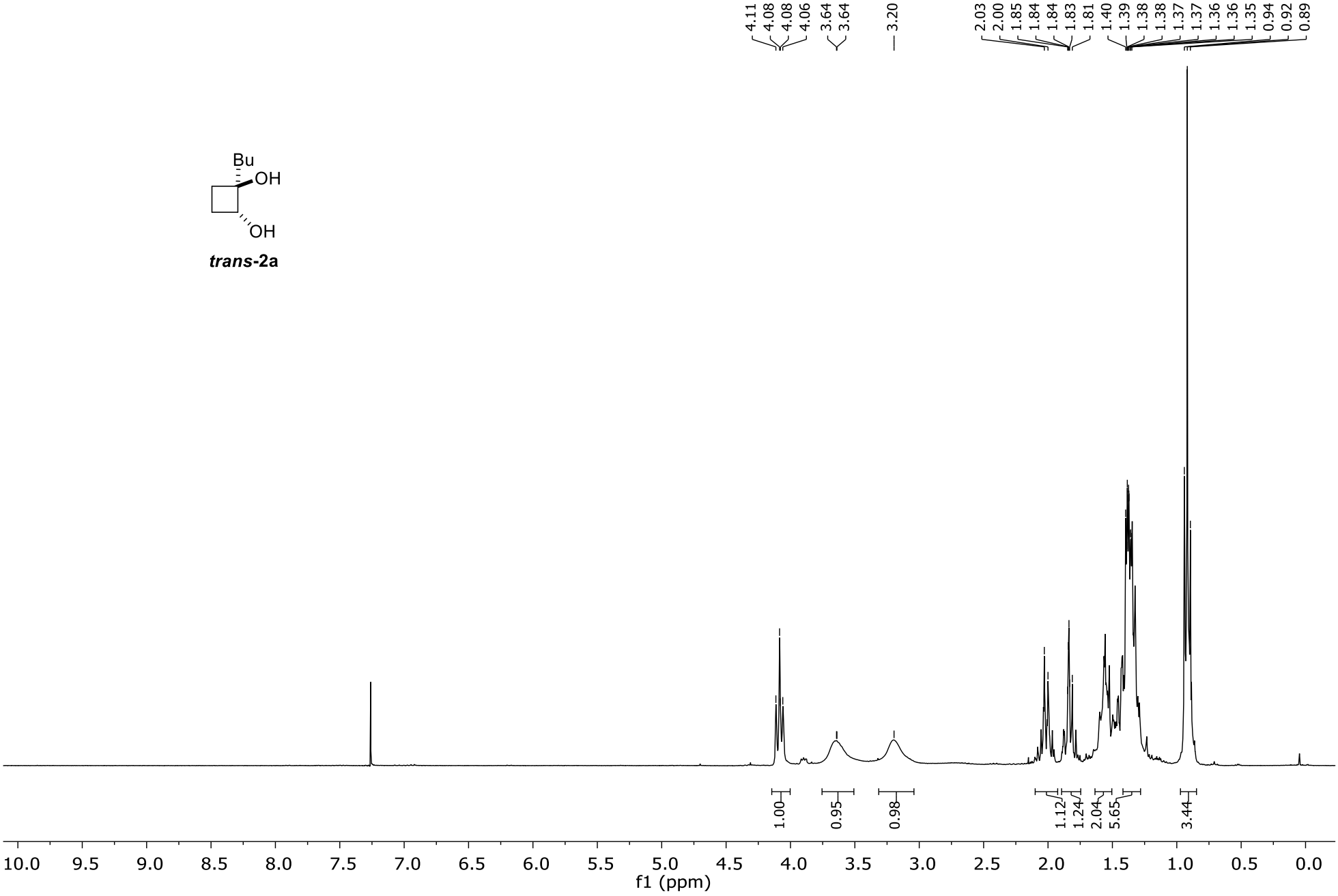
^{1}H-NMR (300 MHz, $CDCl_3$)



$^{13}C\{^{1}H\}$-RMN (75.4 MHz, $CDCl_3$)

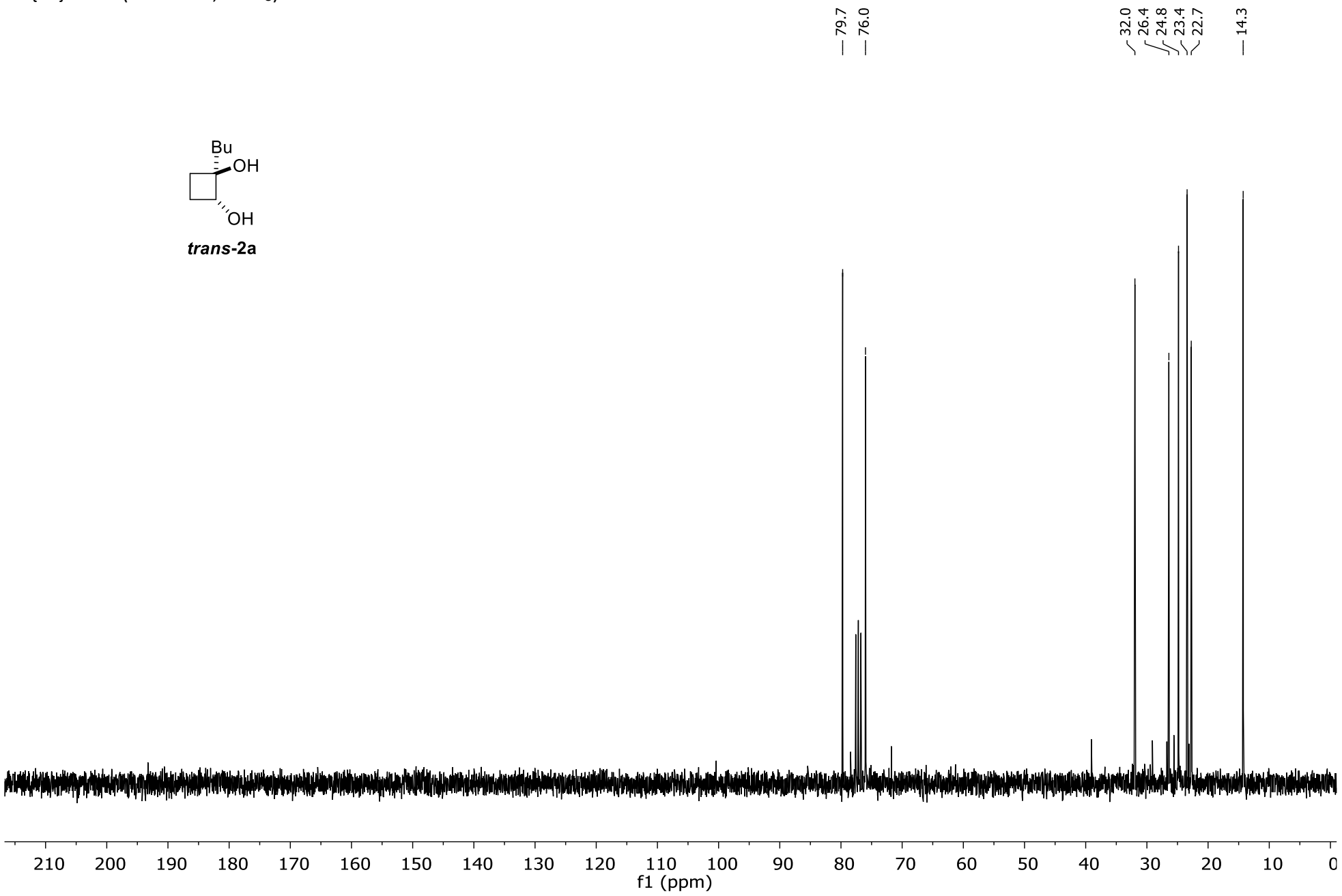


^{1}H-NMR (300 MHz, $CDCl_3$)

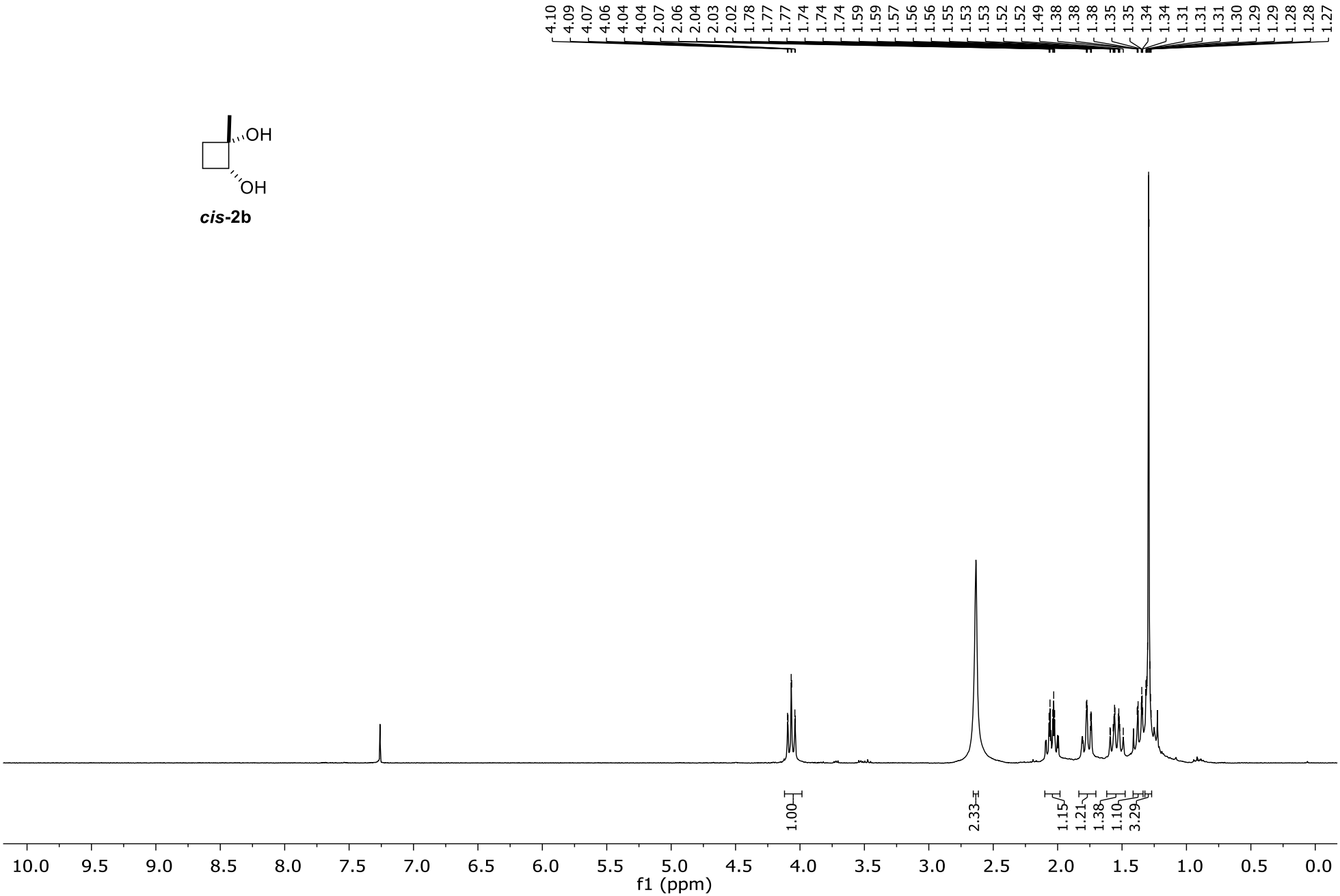


***trans*-2a**

$^{13}C\{^{1}H\}$-RMN (75.4 MHz, $CDCl_3$)

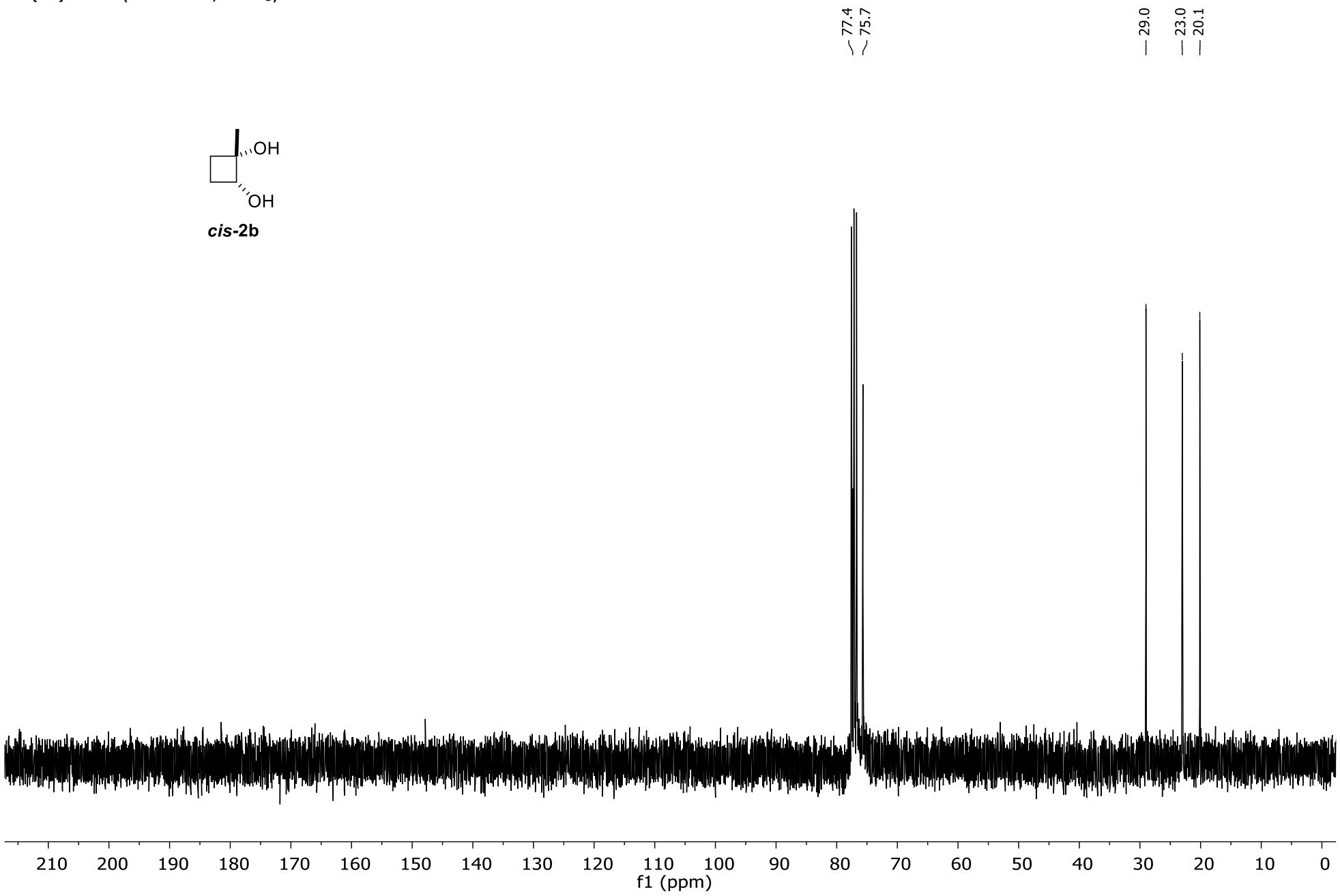


^{1}H-NMR (300 MHz, $CDCl_3$)

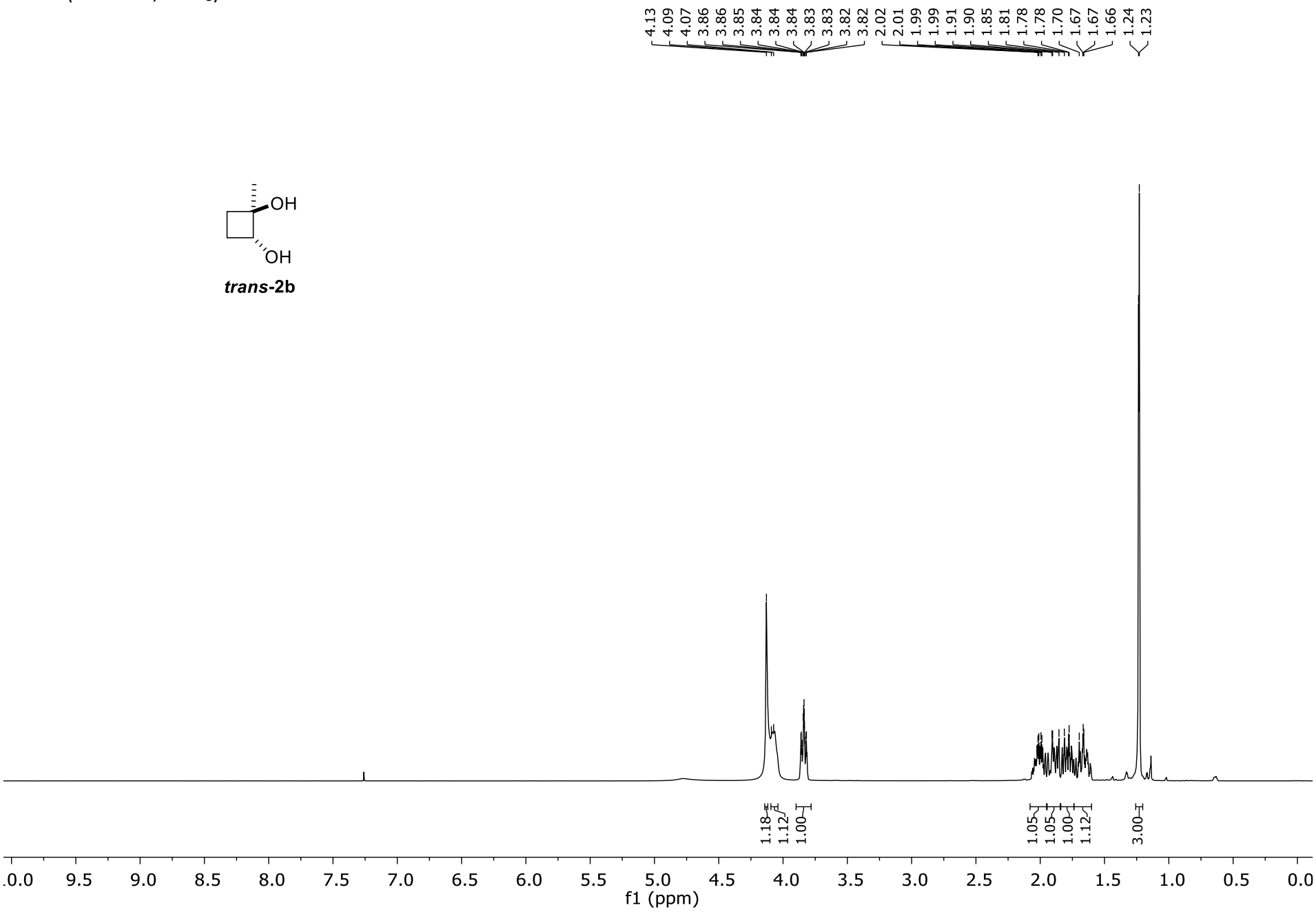


***cis*-2b**

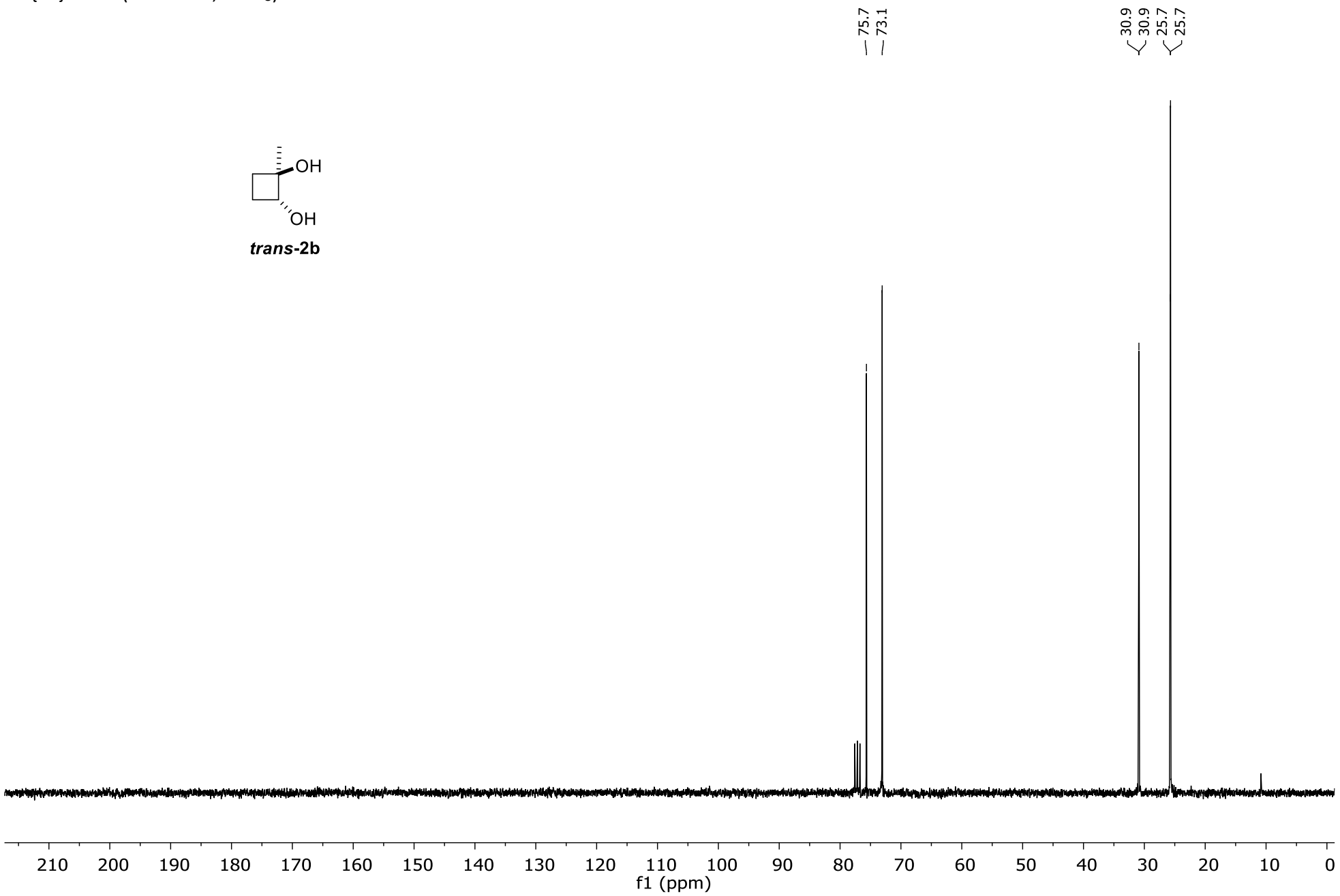
$^{13}C\{^{1}H\}$-RMN (75.4 MHz, $CDCl_3$)



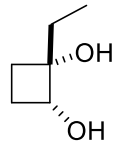
^{1}H-NMR (300 MHz, $CDCl_3$)



$^{13}C\{^{1}H\}$-RMN (75.4 MHz, $CDCl_3$)

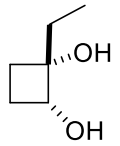


^{1}H-NMR (300 MHz, $CDCl_3$)



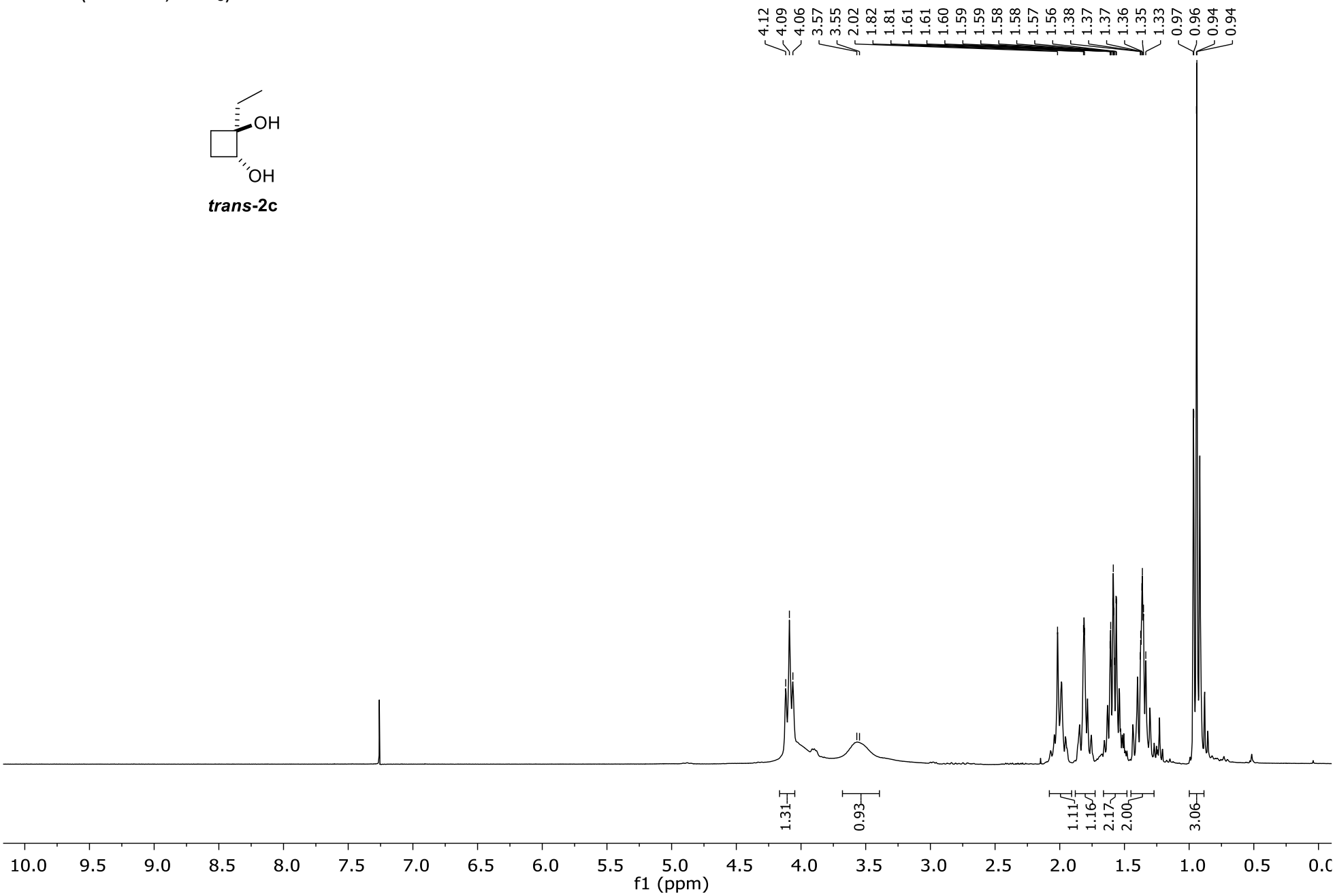
***cis*-2c**

$^{13}C\{^{1}H\}$-RMN (75.4 MHz, $CDCl_3$)



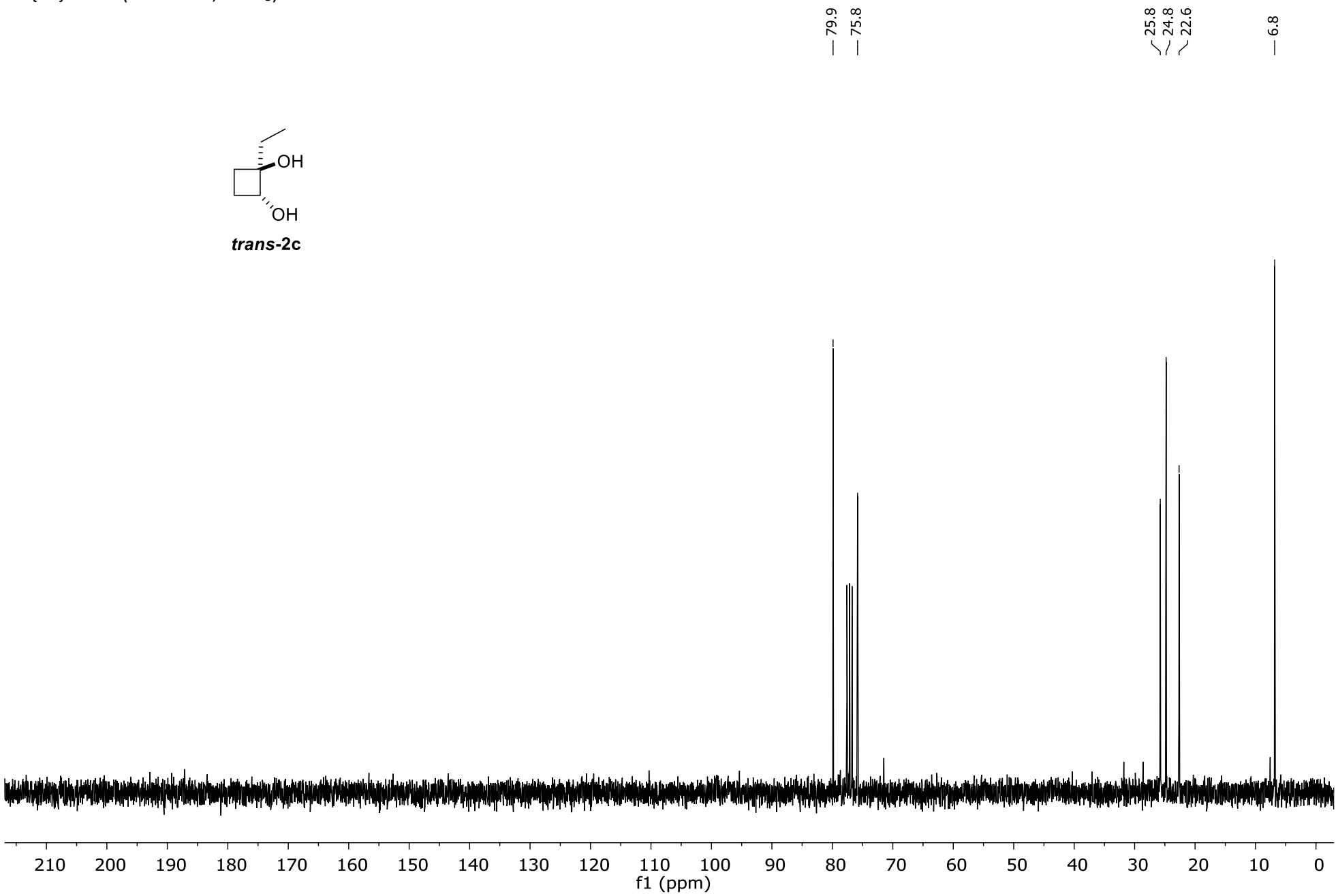
***cis*-2c**

^{1}H-NMR (300 MHz, $CDCl_3$)



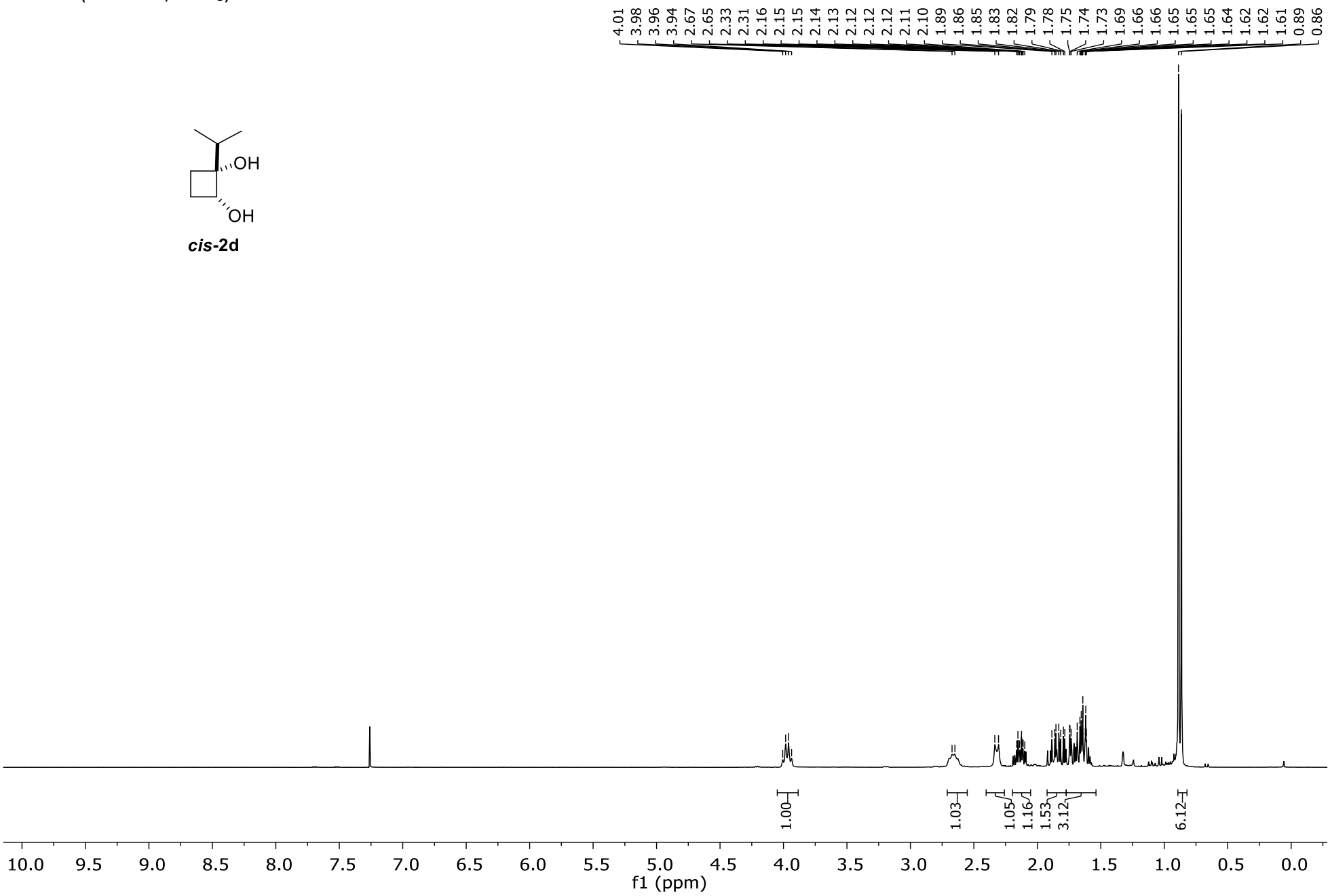
***trans*-2c**

$^{13}C\{^{1}H\}$-RMN (75.4 MHz, $CDCl_3$)



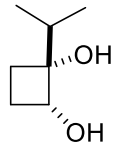
***trans*-2c**

^{1}H-NMR (300 MHz, $CDCl_3$)



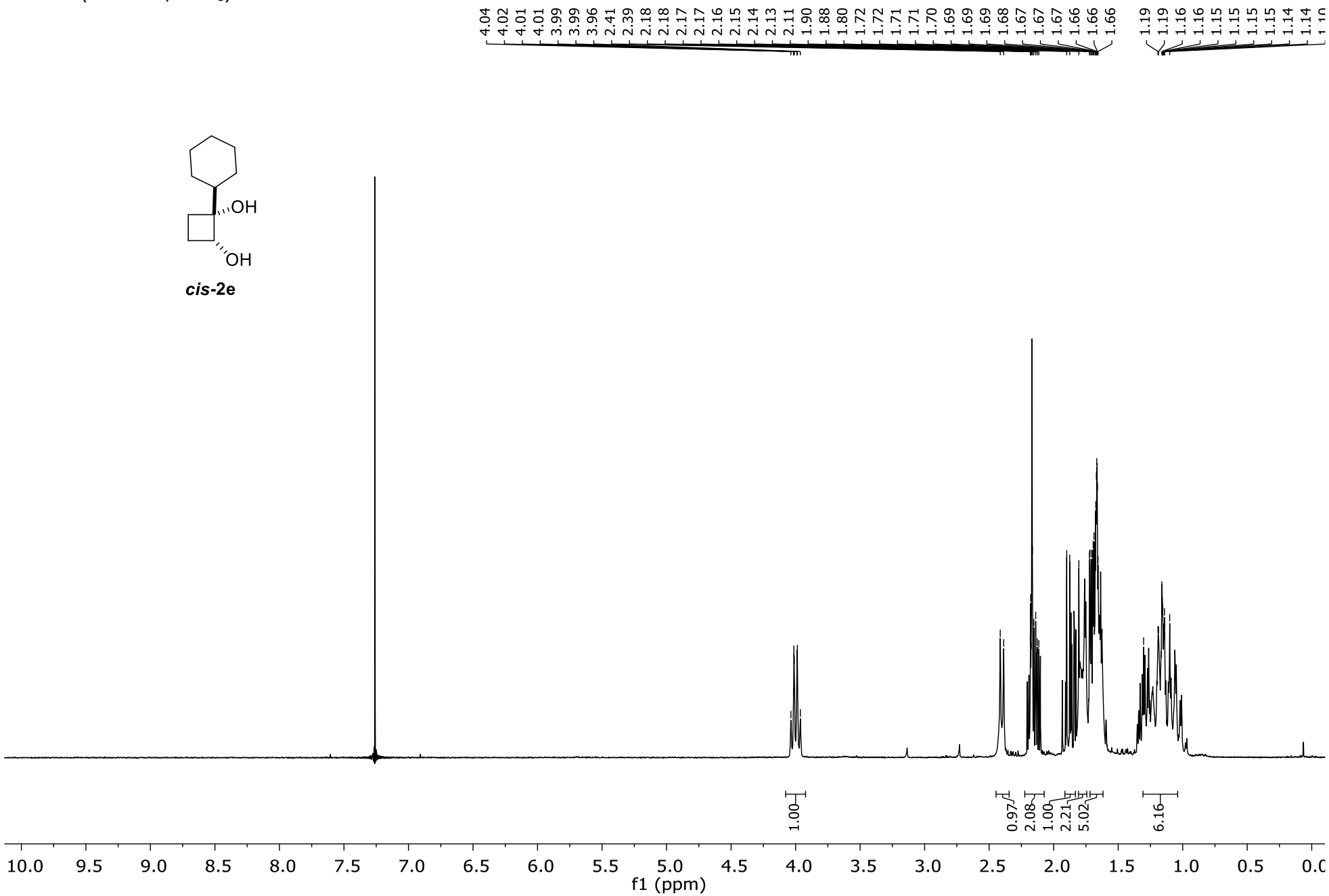
***cis*-2d**

$^{13}C\{^{1}H\}$-RMN (75.4 MHz, $CDCl_3$)

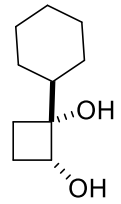


***cis*-2d**

^{1}H-NMR (300 MHz, $CDCl_3$)

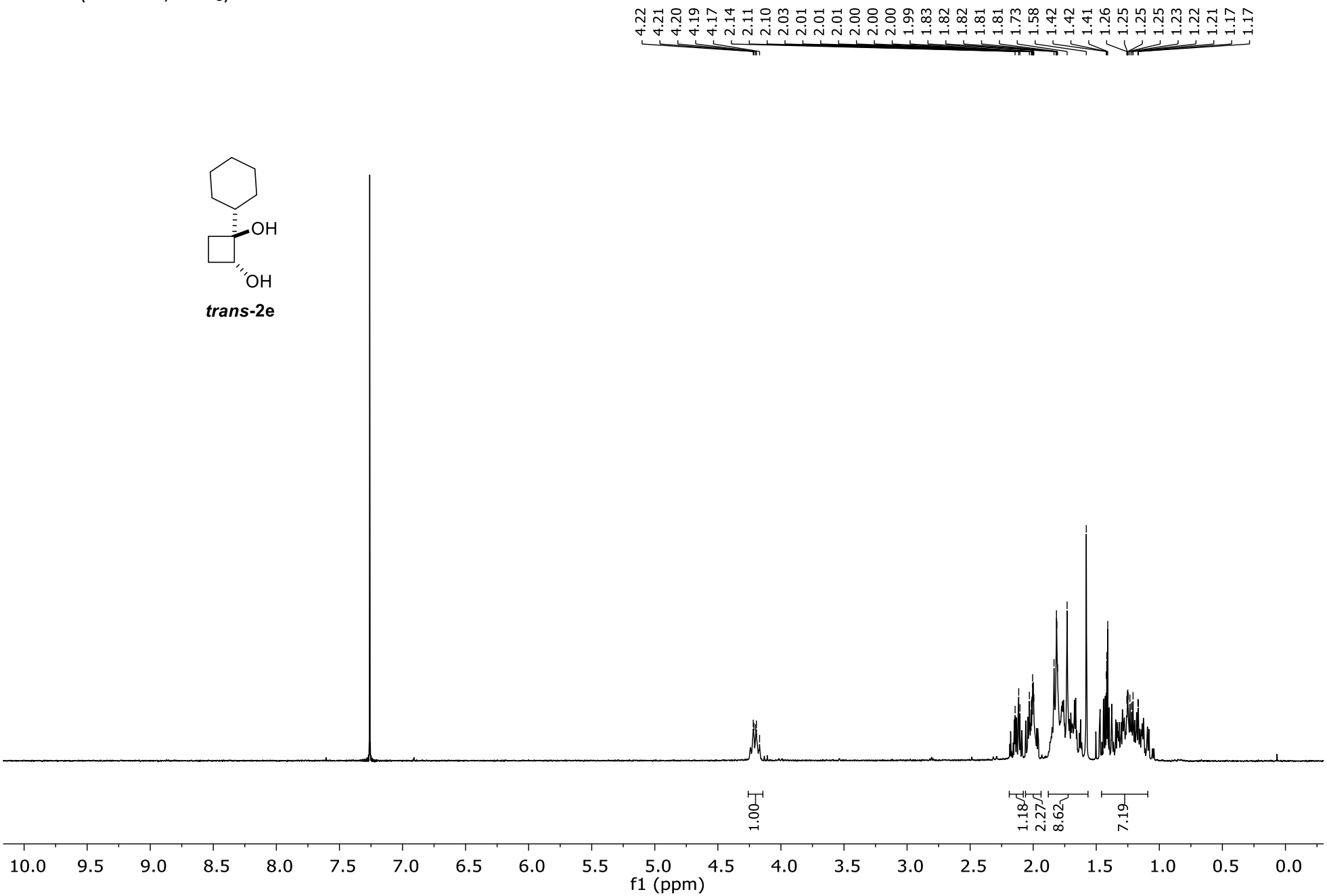


$^{13}C\{^{1}H\}$-RMN (75.4 MHz, $CDCl_3$)

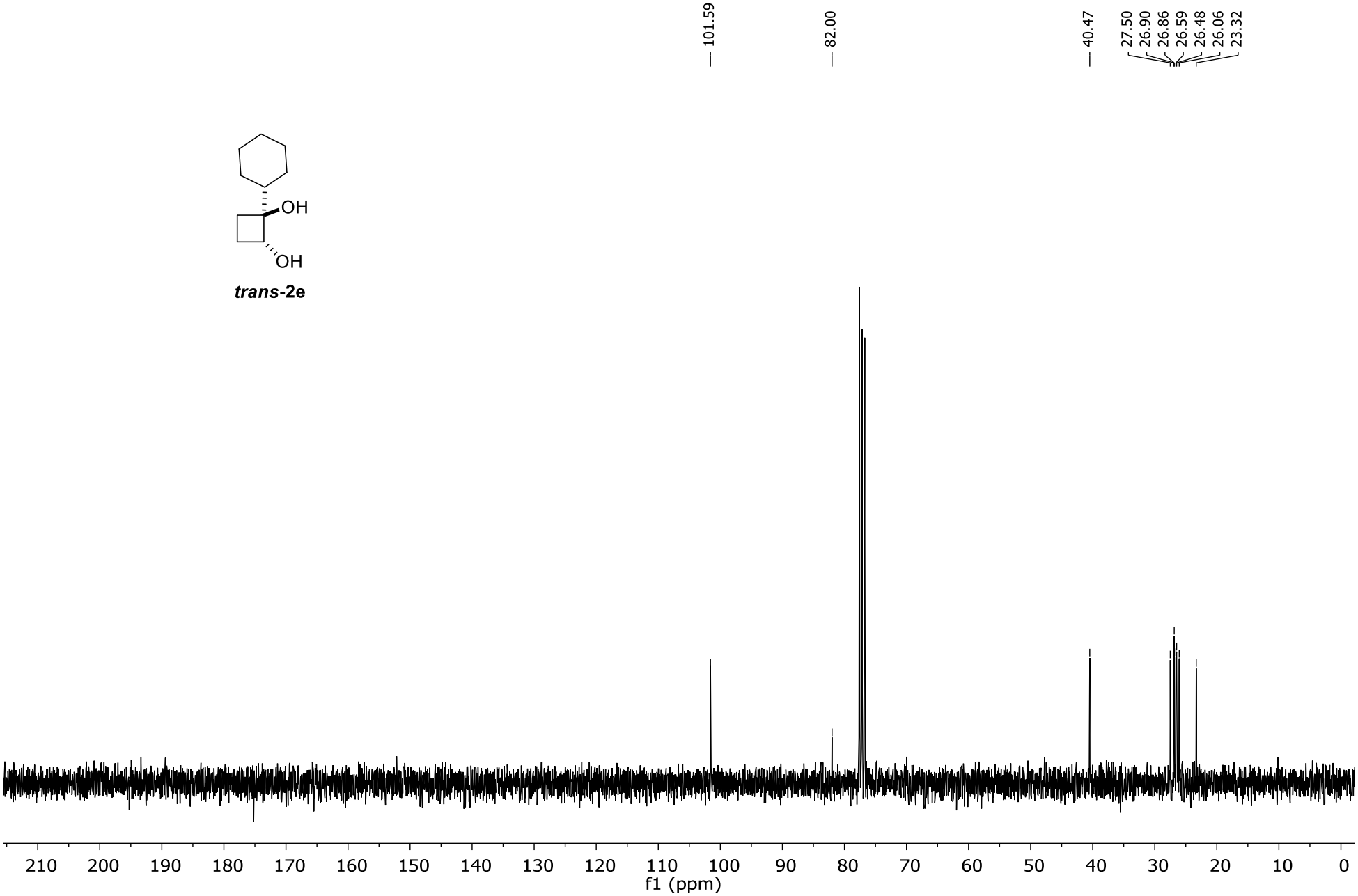


***cis*-2e**

^{1}H-NMR (300 MHz, $CDCl_3$)

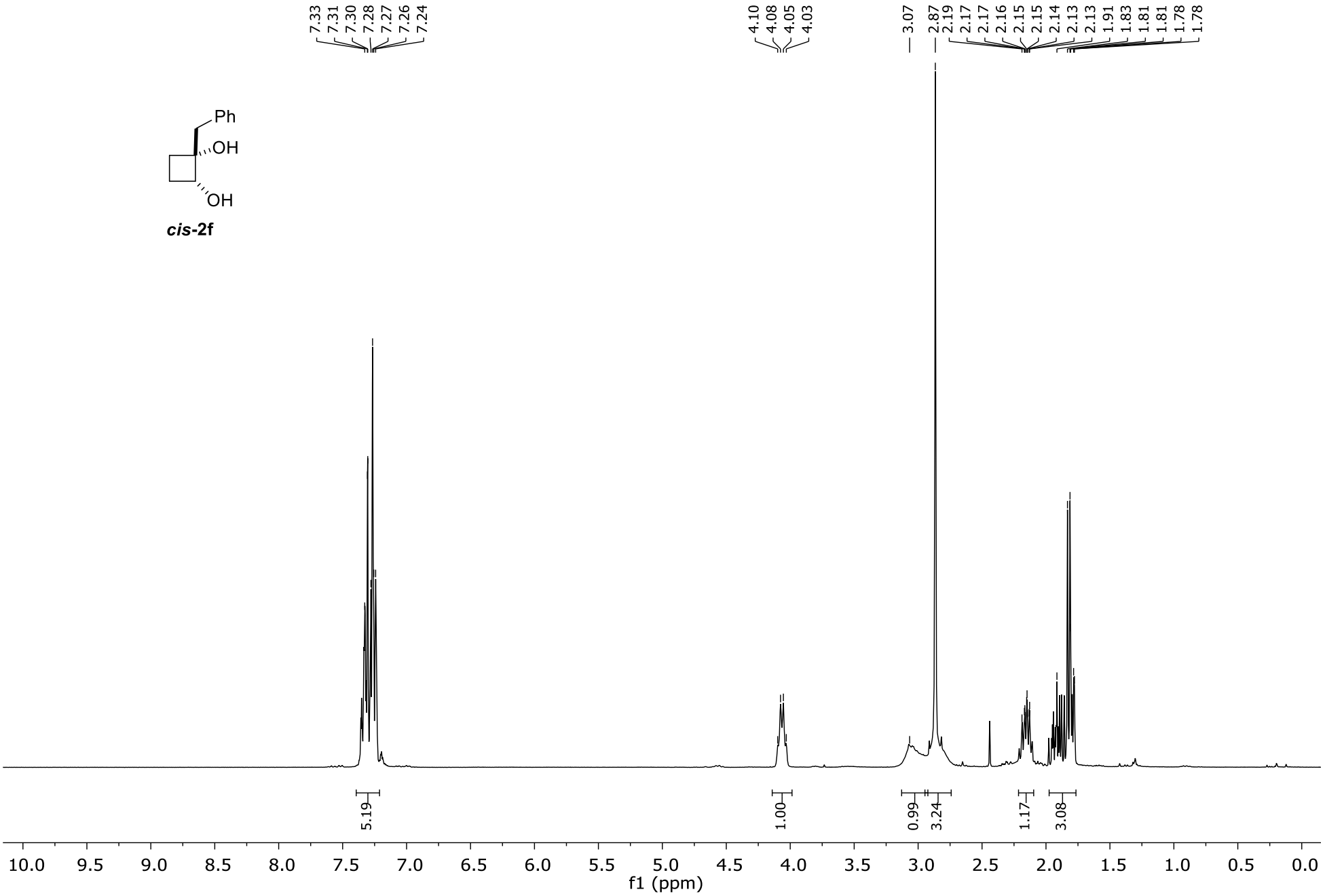


$^{13}C\{^{1}H\}$-RMN (75.4 MHz, $CDCl_3$)

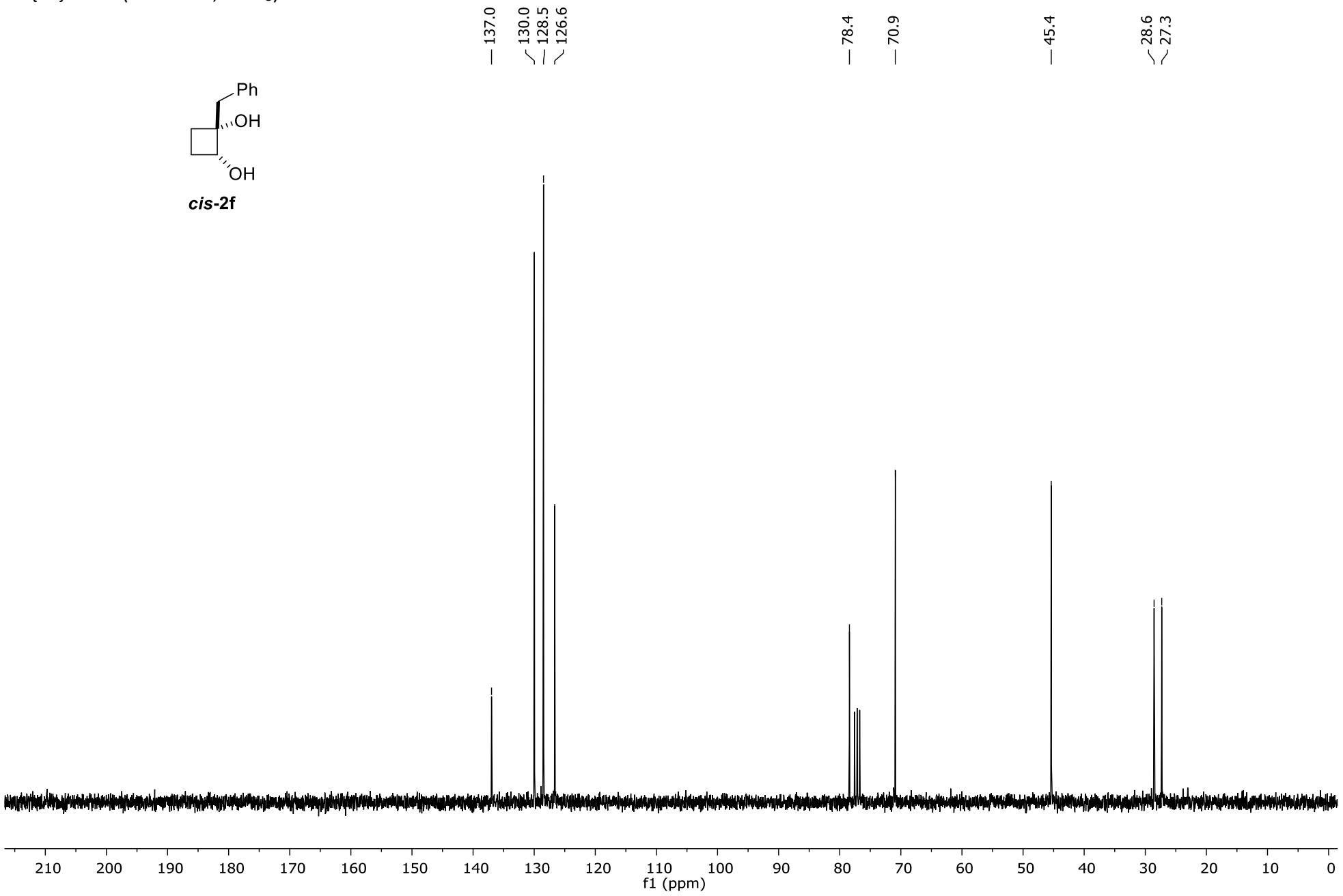


***trans*-2e**

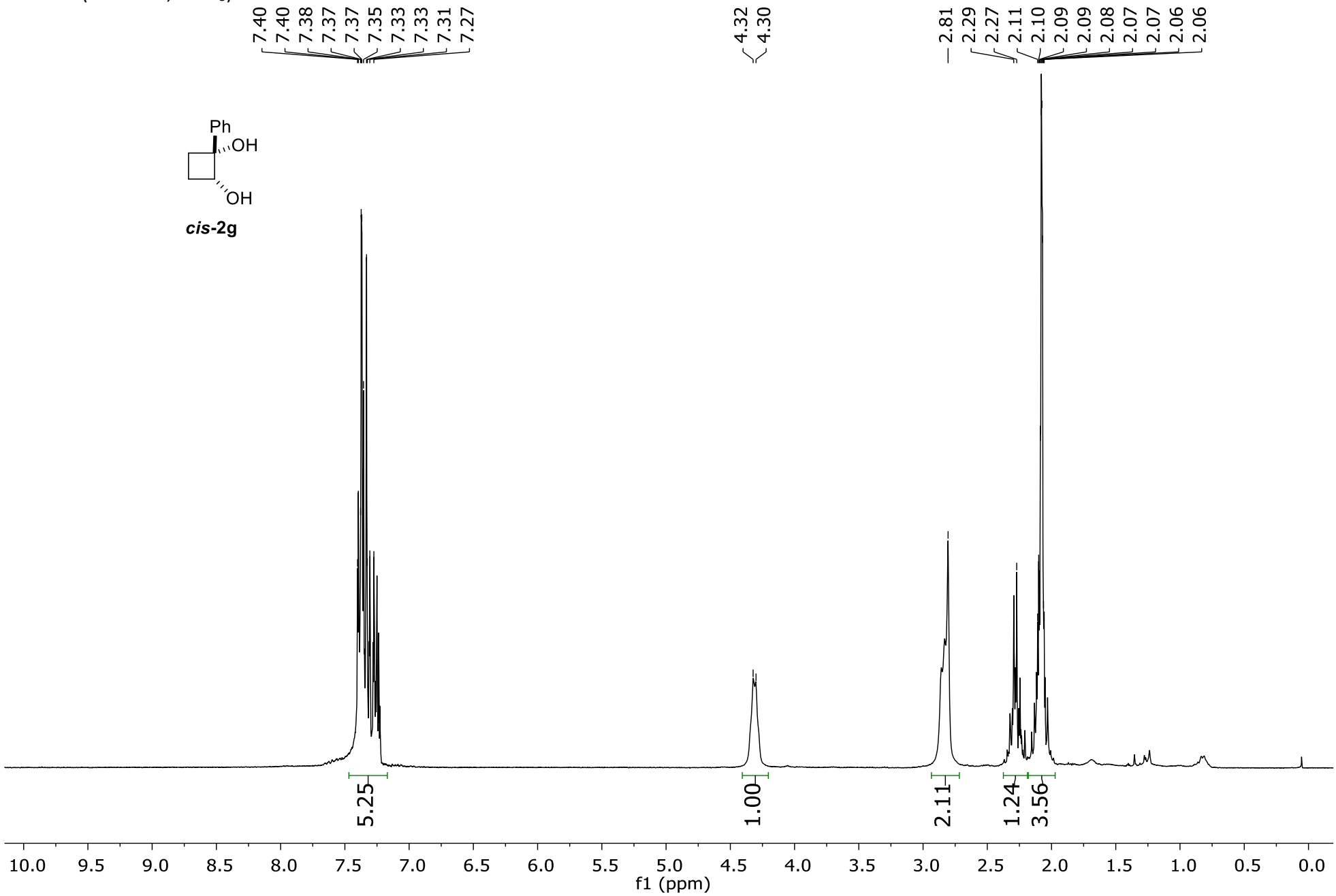
^{1}H-NMR (300 MHz, $CDCl_3$)



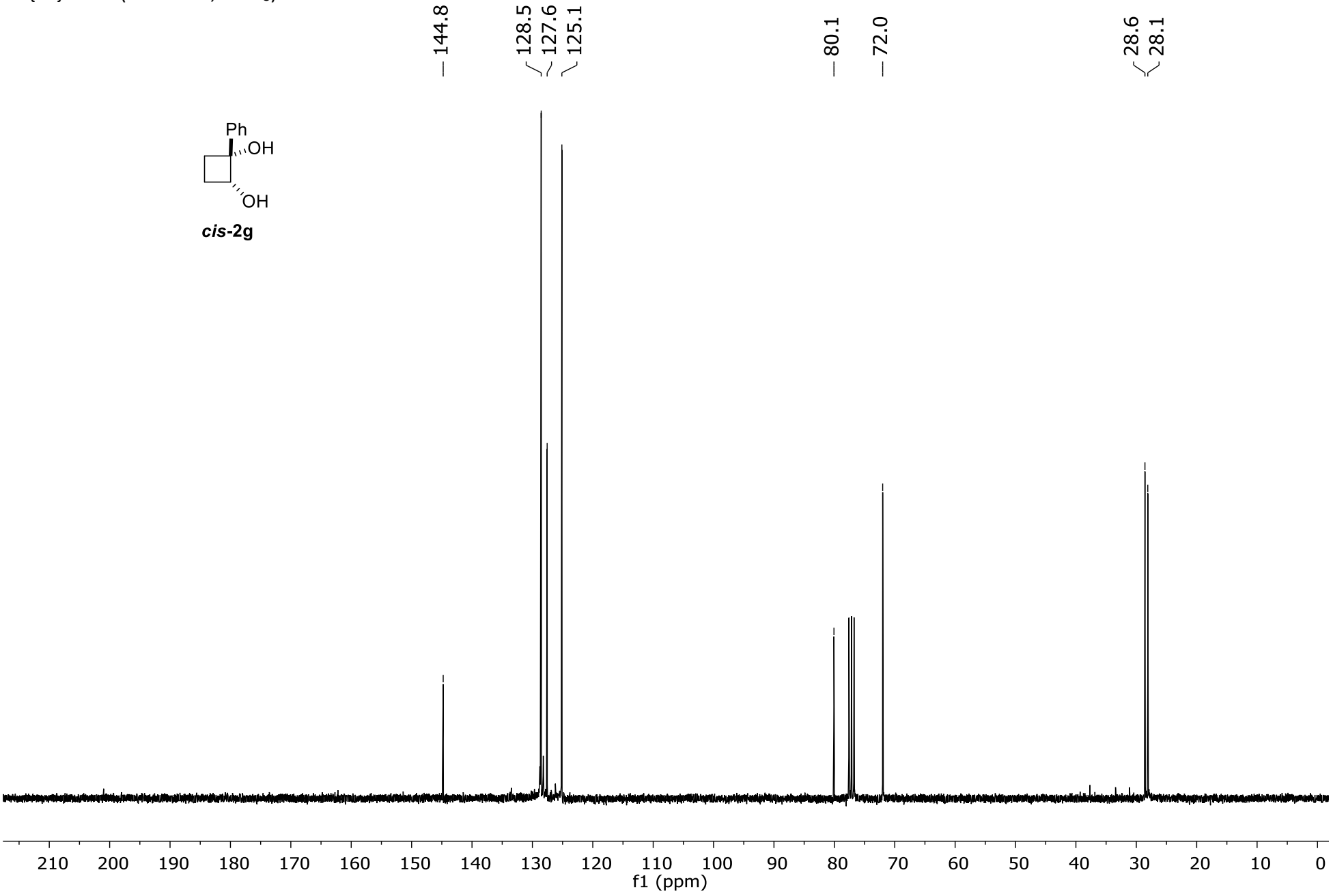
$^{13}C\{^{1}H\}$-RMN (75.4 MHz, $CDCl_3$)



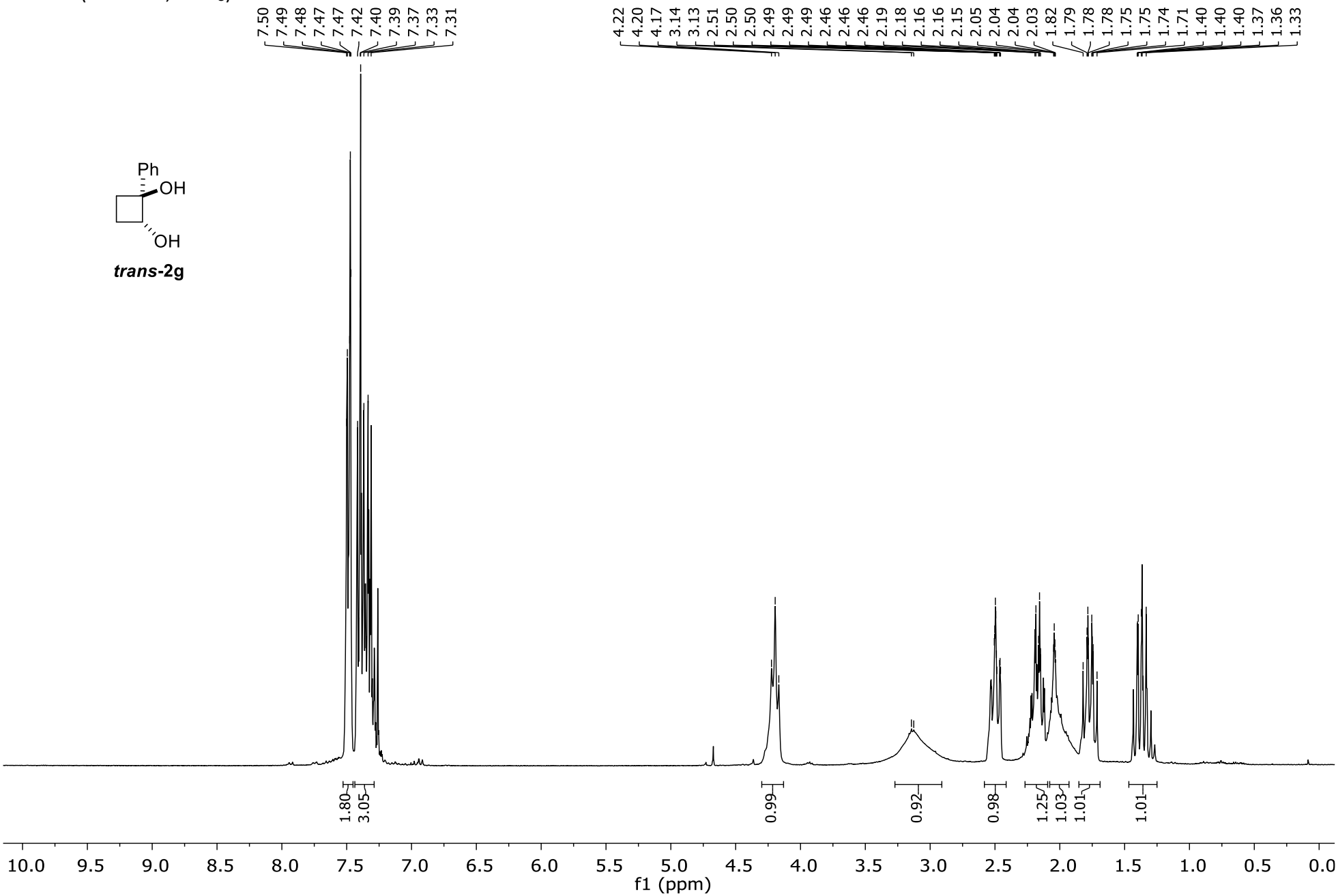
^{1}H-NMR (300 MHz, $CDCl_3$)



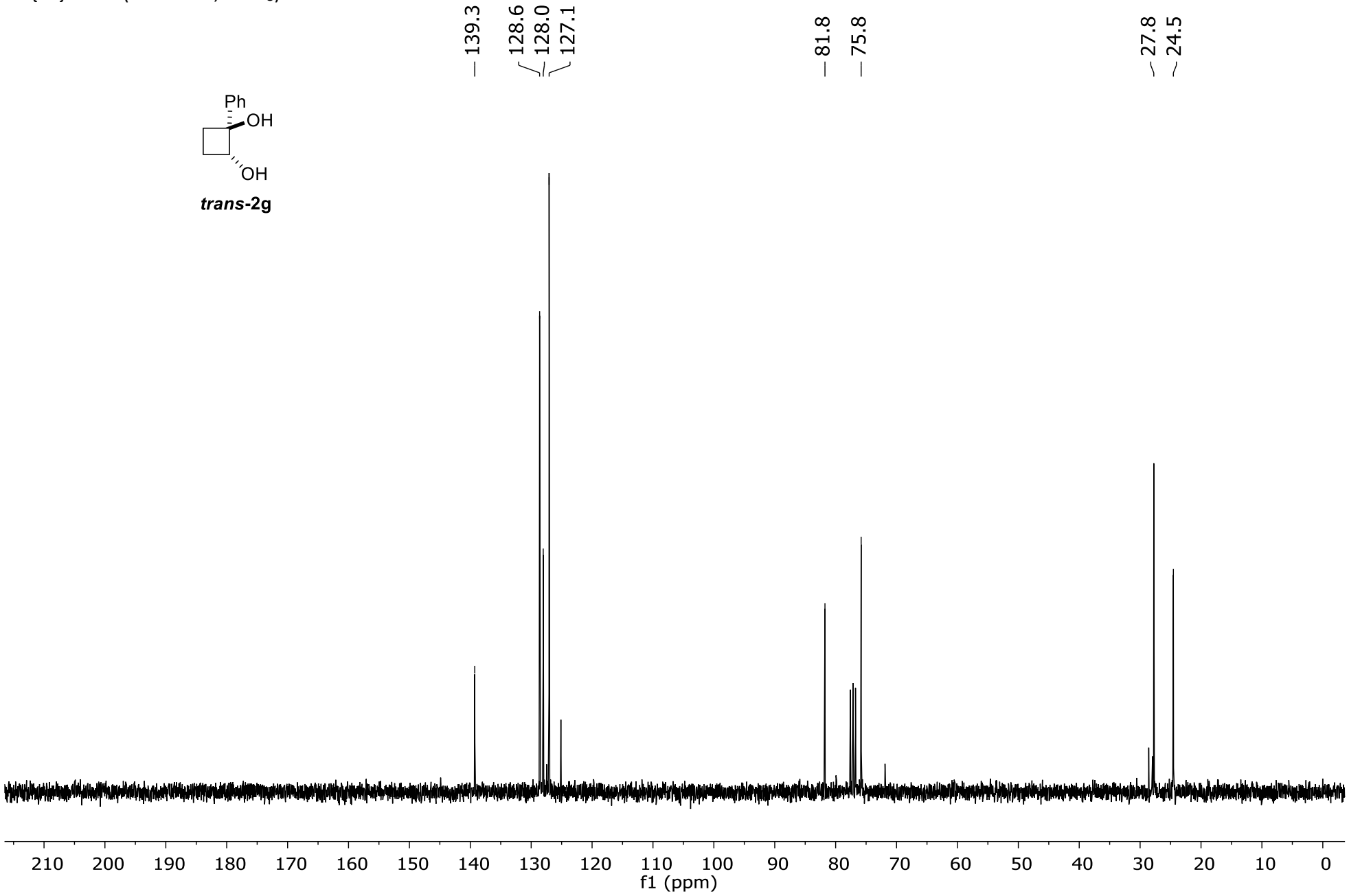
$^{13}C\{^{1}H\}$-RMN (75.4 MHz, $CDCl_3$)



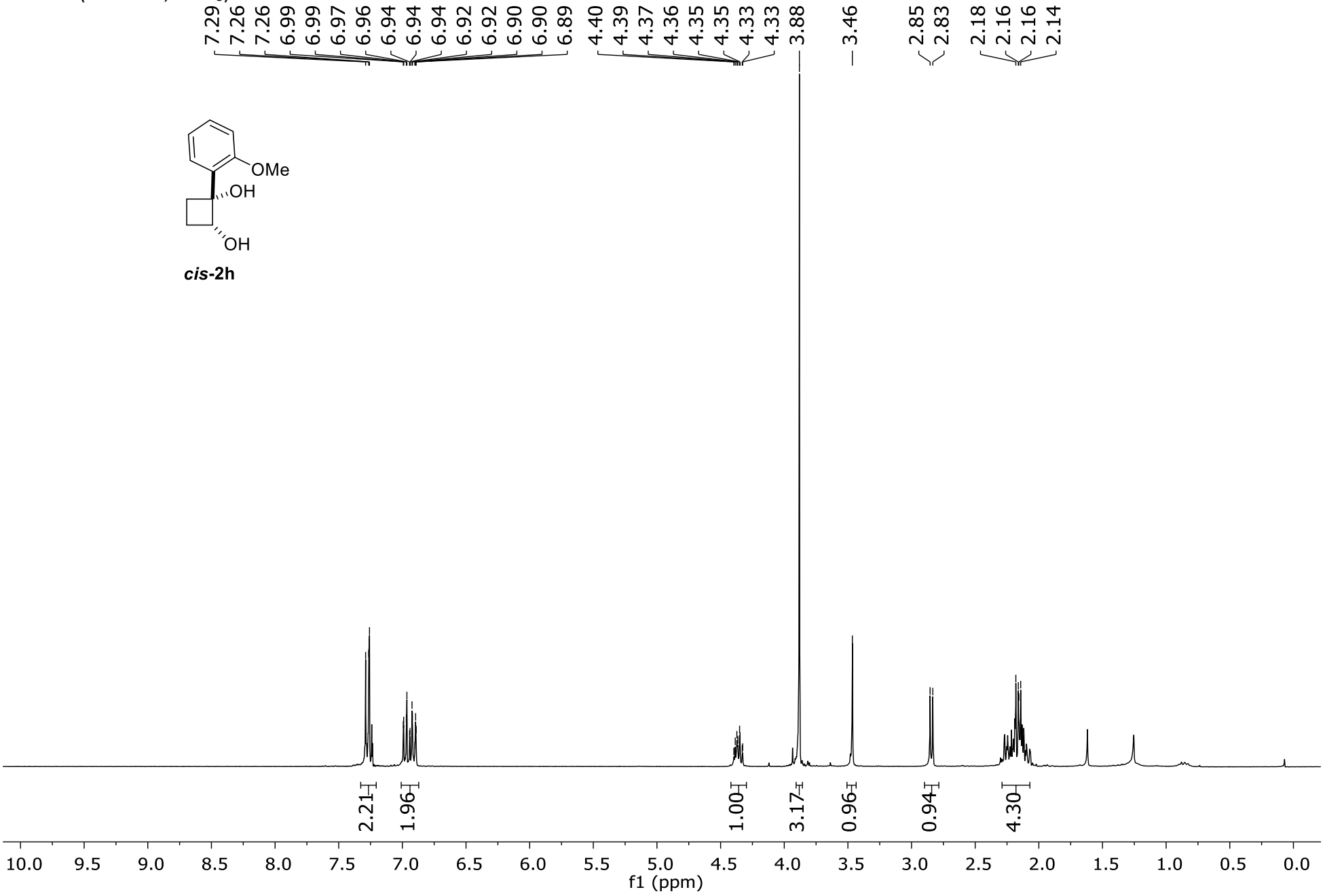
^{1}H-NMR (300 MHz, $CDCl_3$)



$^{13}C\{^{1}H\}$-RMN (75.4 MHz, $CDCl_3$)

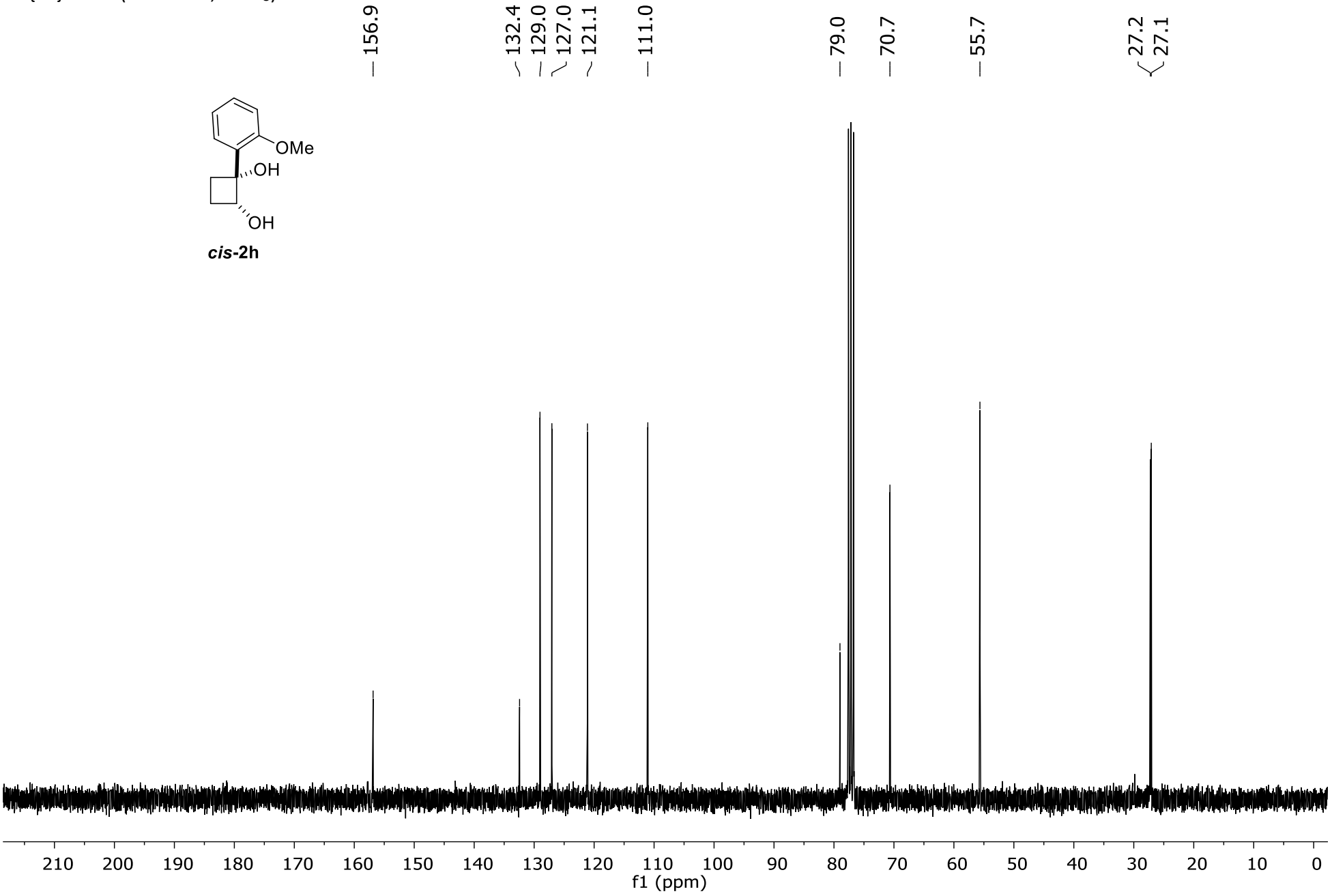


^{1}H-NMR (300 MHz, $CDCl_3$)



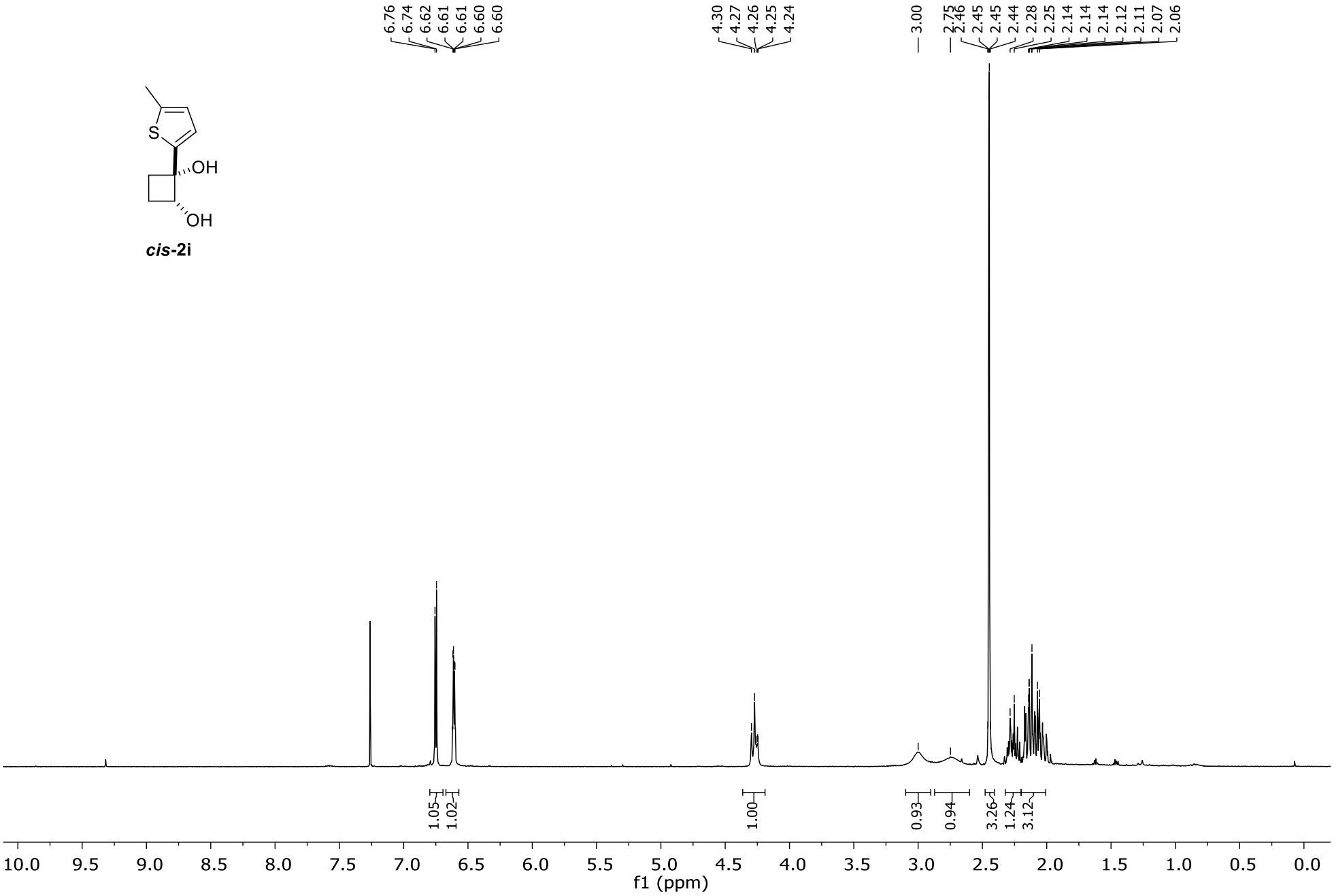
***cis*-2h**

$^{13}C\{^{1}H\}$-RMN (75.4 MHz, $CDCl_3$)



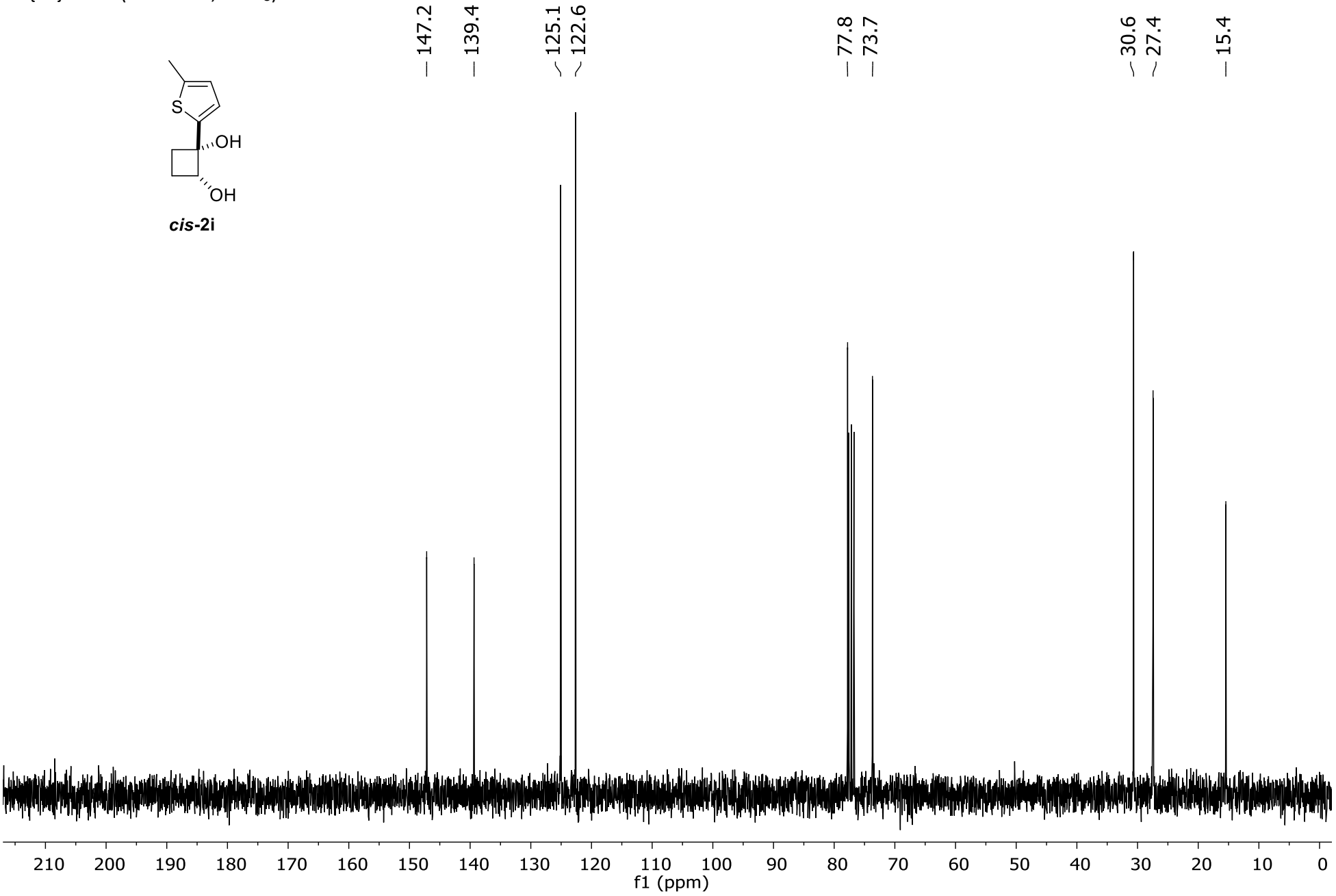
***cis*-2h**

^{1}H-NMR (300 MHz, $CDCl_3$)



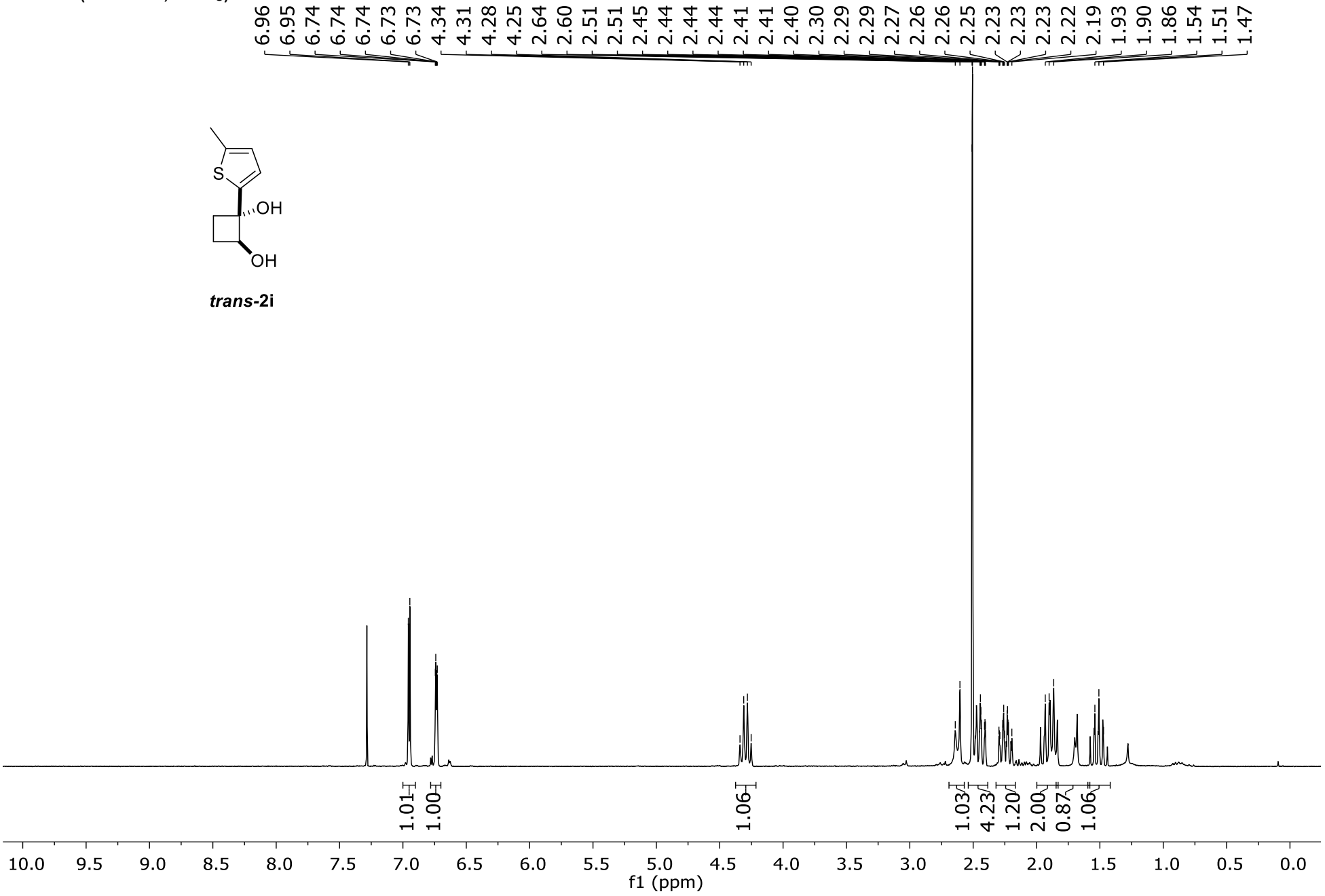
***cis*-2i**

$^{13}C\{^{1}H\}$-RMN (75.4 MHz, $CDCl_3$)



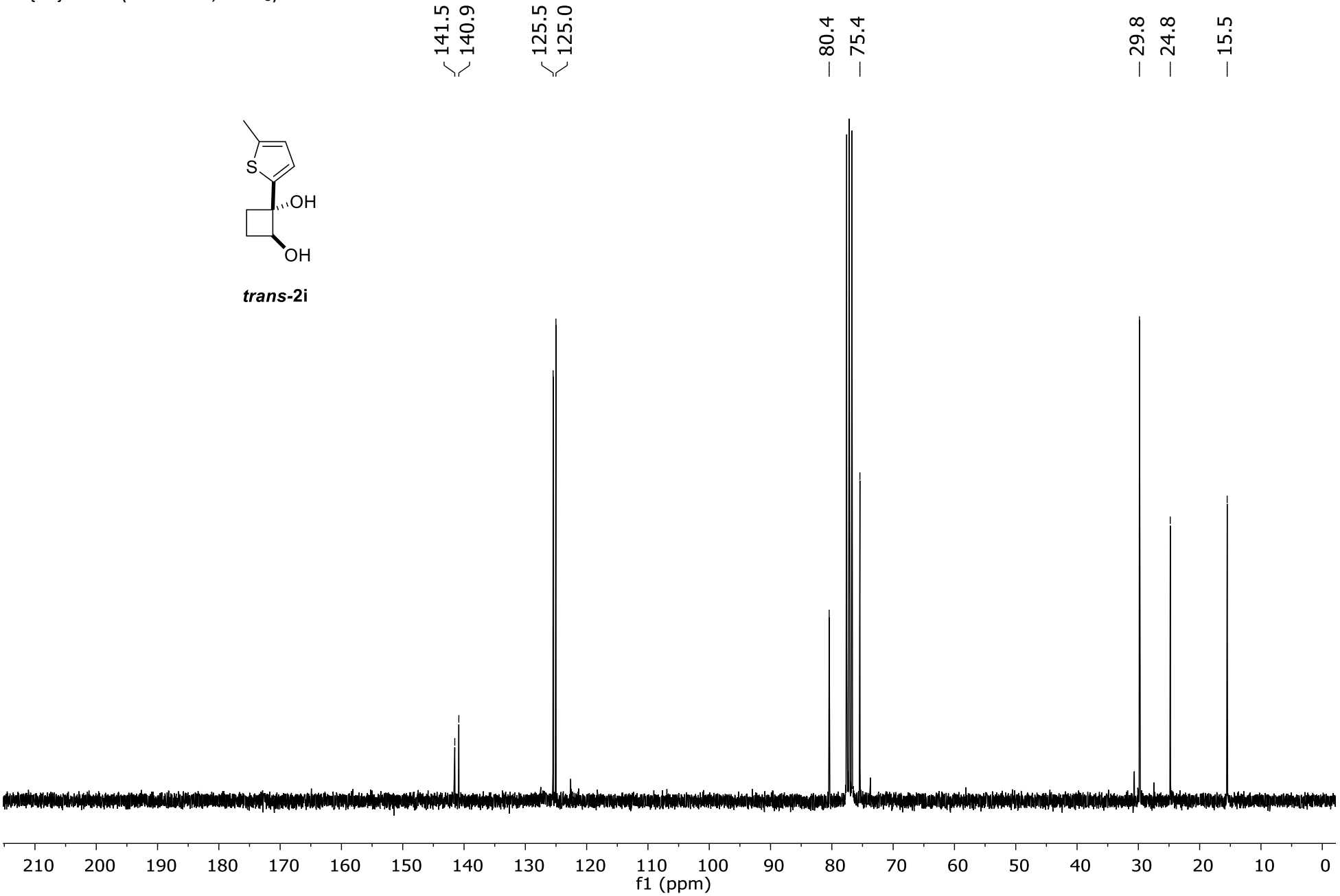
***cis*-2i**

^{1}H-NMR (300 MHz, $CDCl_3$)



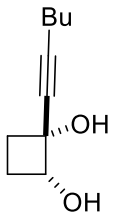
***trans*-2i**

$^{13}C\{^{1}H\}$-RMN (75.4 MHz, $CDCl_3$)



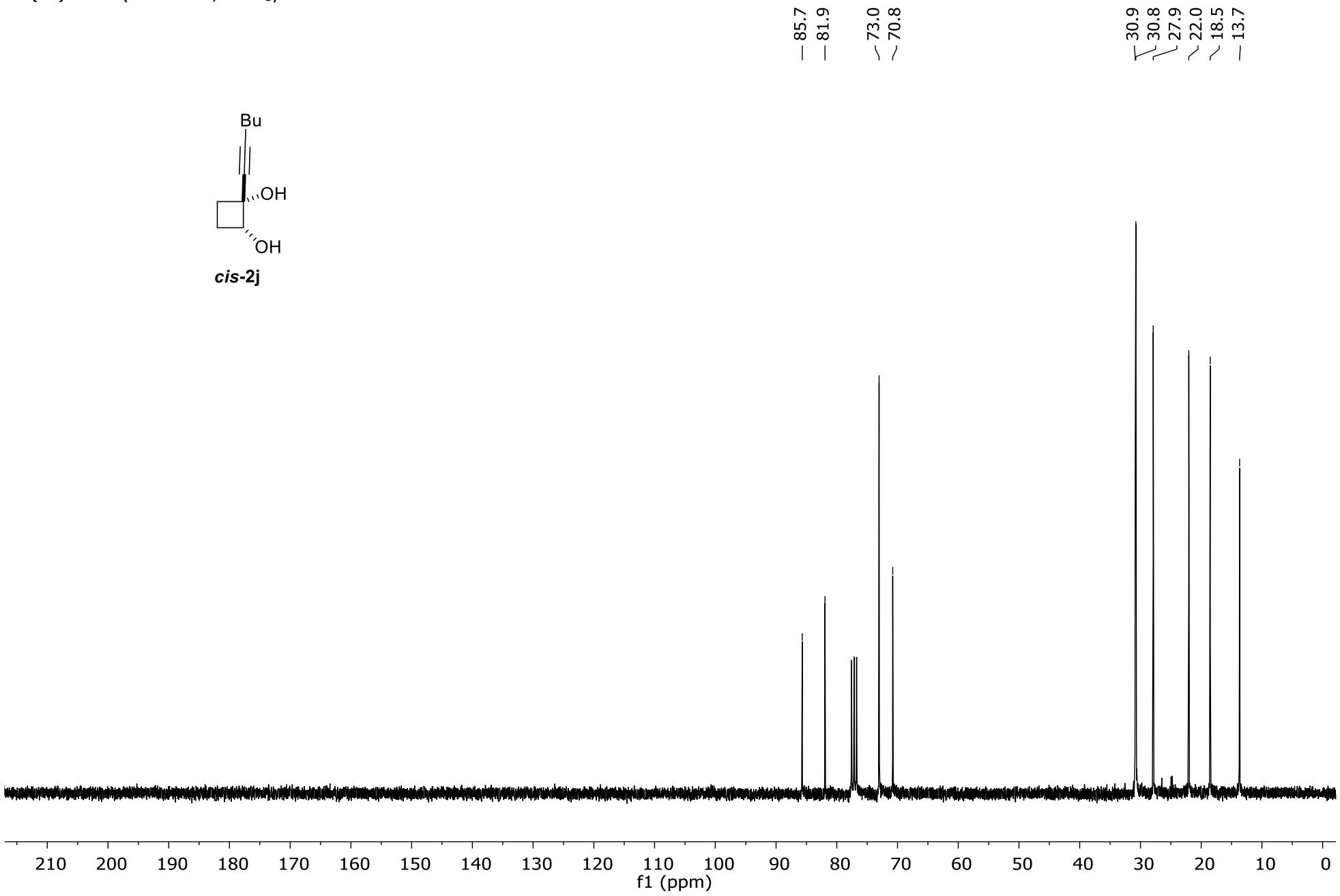
***trans*-2i**

^{1}H-NMR (300 MHz, $CDCl_3$)



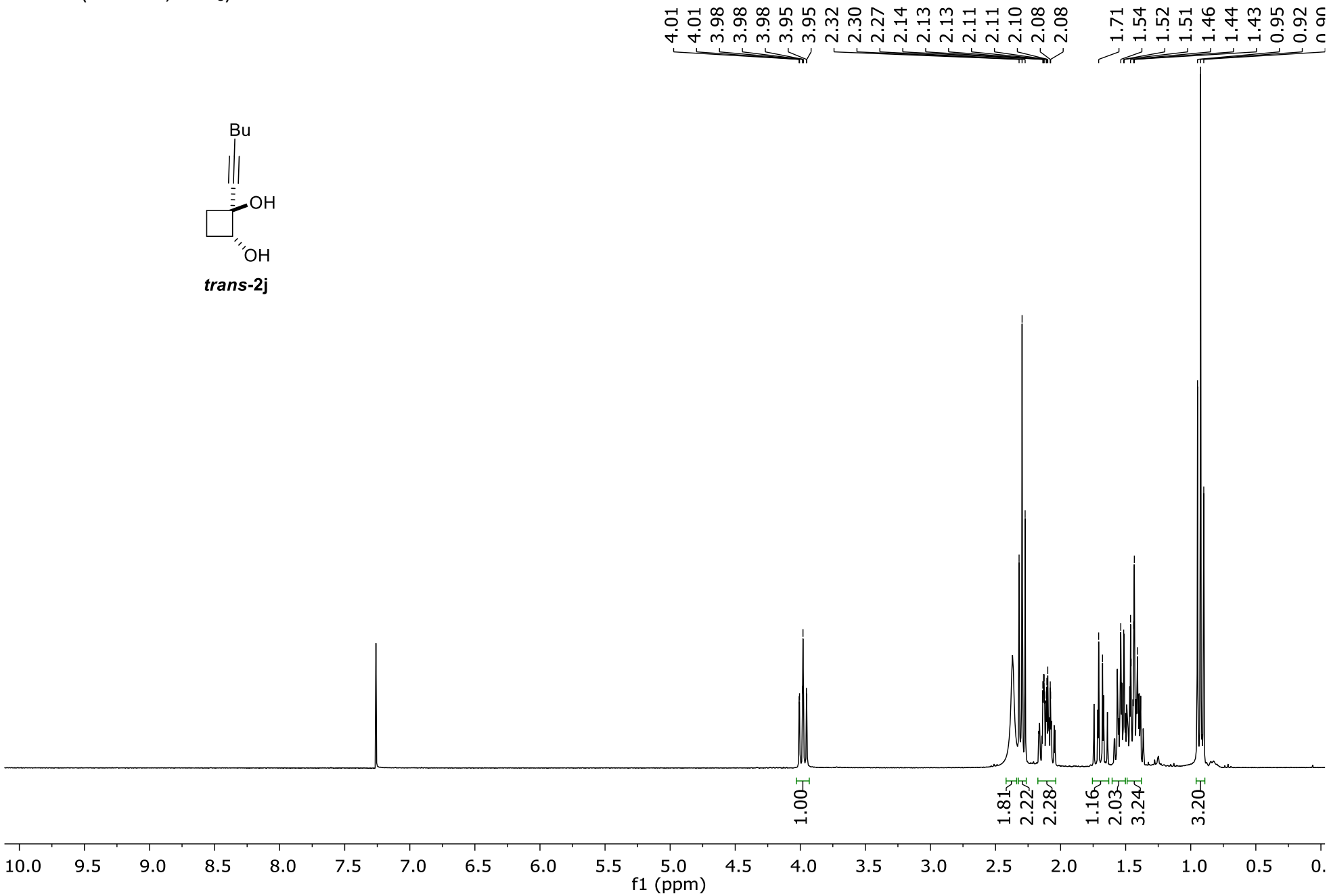
***cis*-2j**

$^{13}C\{^{1}H\}$-RMN (75.4 MHz, $CDCl_3$)



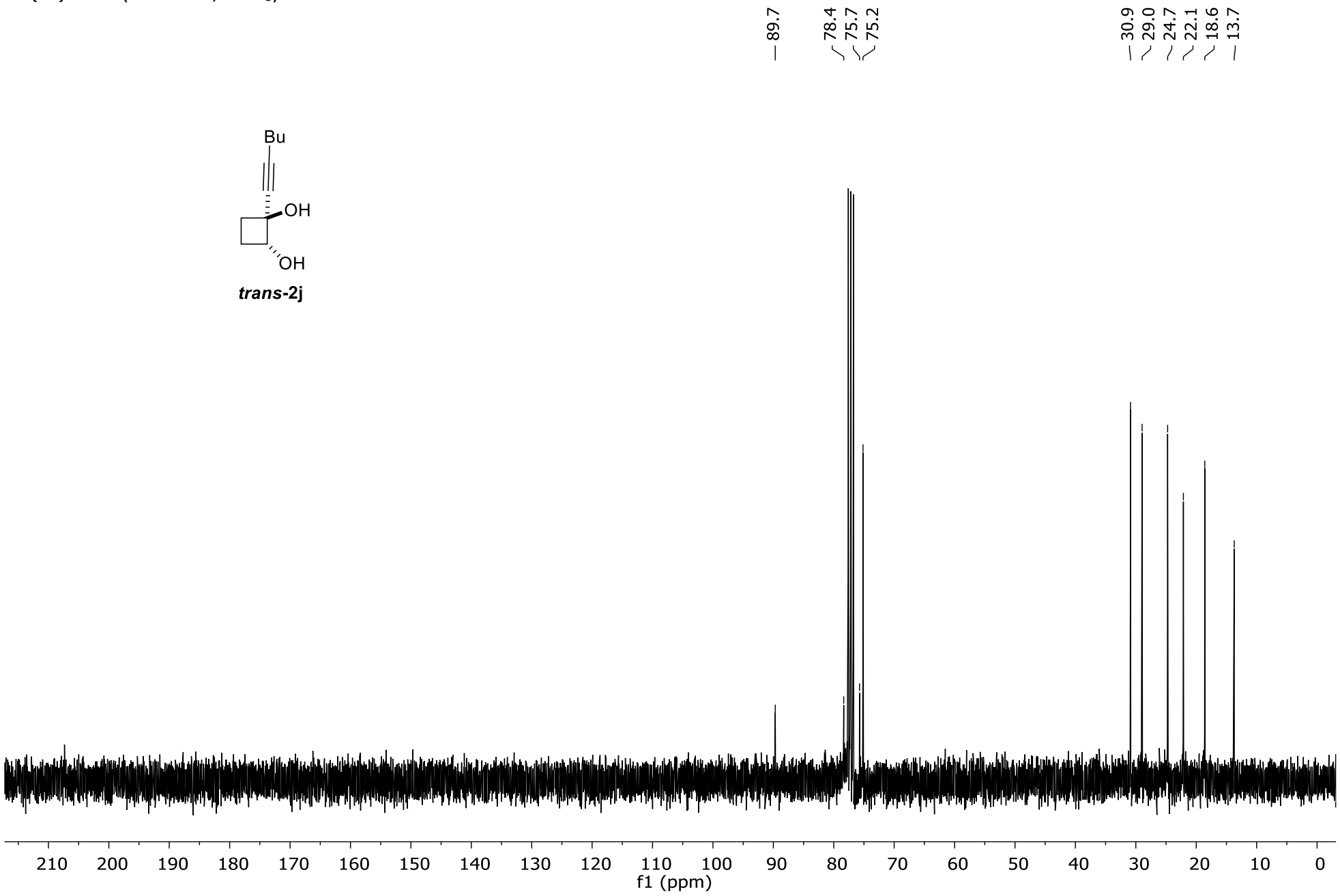
***cis*-2j**

^{1}H-NMR (300 MHz, $CDCl_3$)

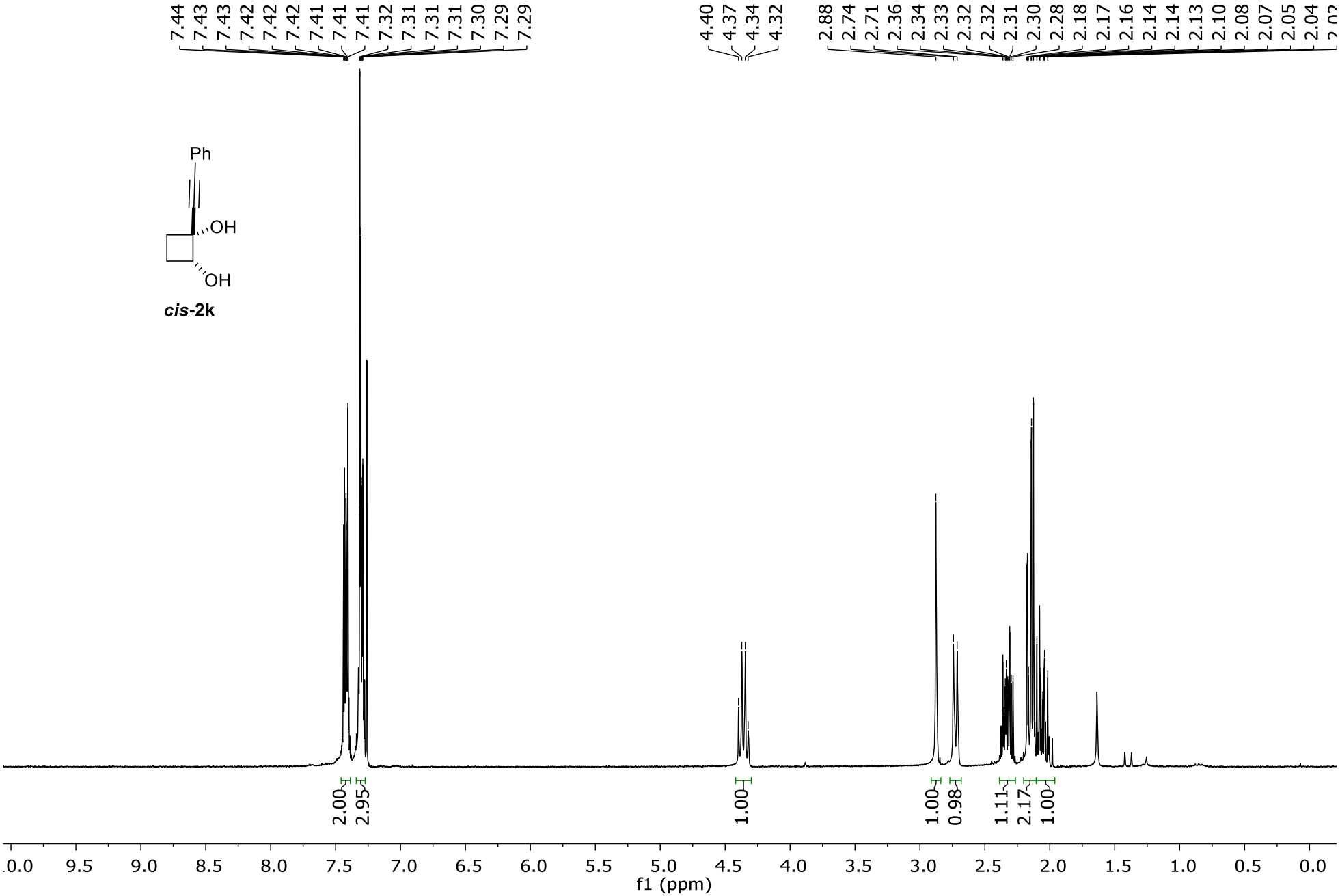


***trans*-2j**

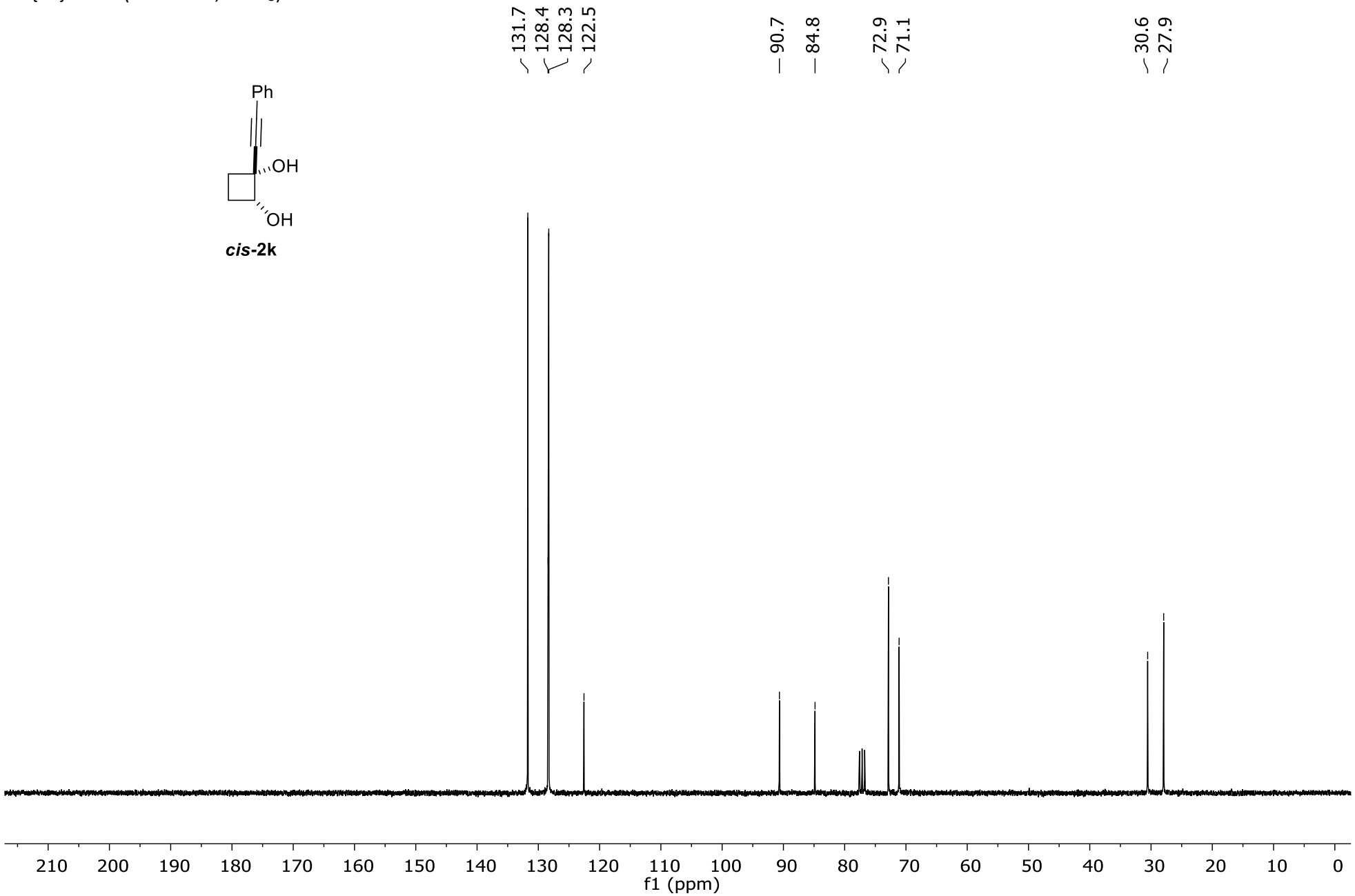
$^{13}C\{^{1}H\}$-RMN (75.4 MHz, $CDCl_3$)



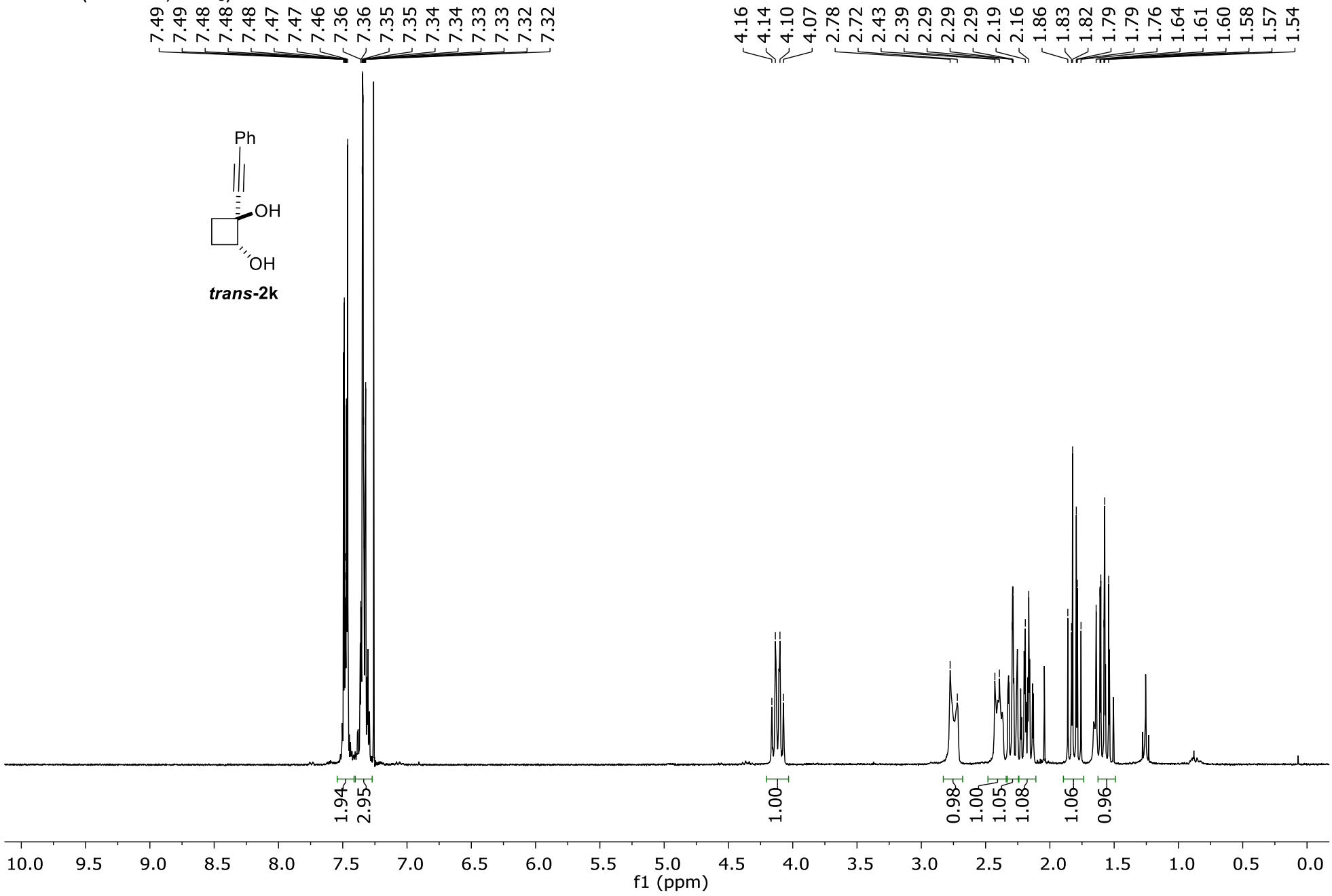
^{1}H-NMR (300 MHz, $CDCl_3$)



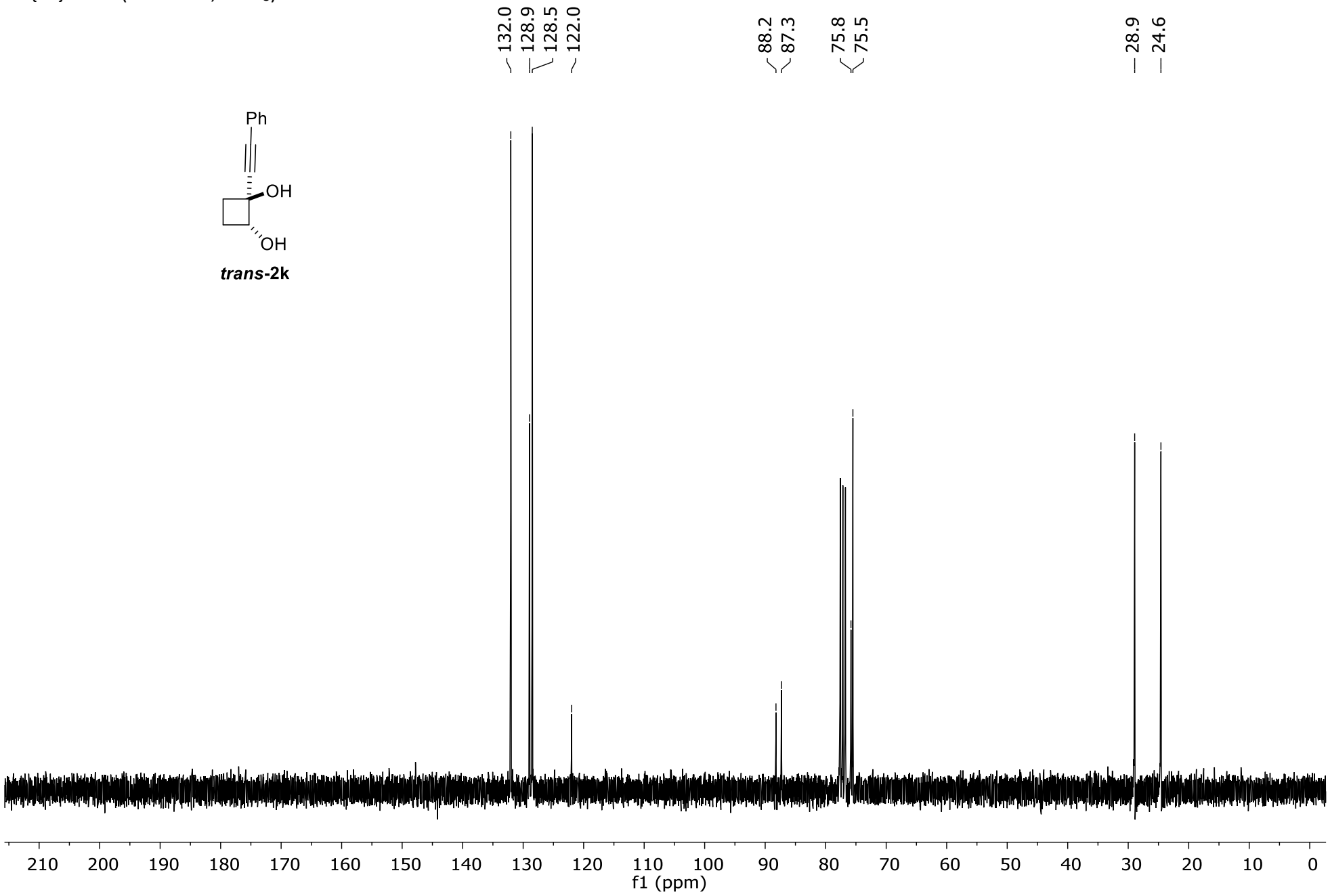
$^{13}C\{^{1}H\}$-RMN (75.4 MHz, $CDCl_3$)



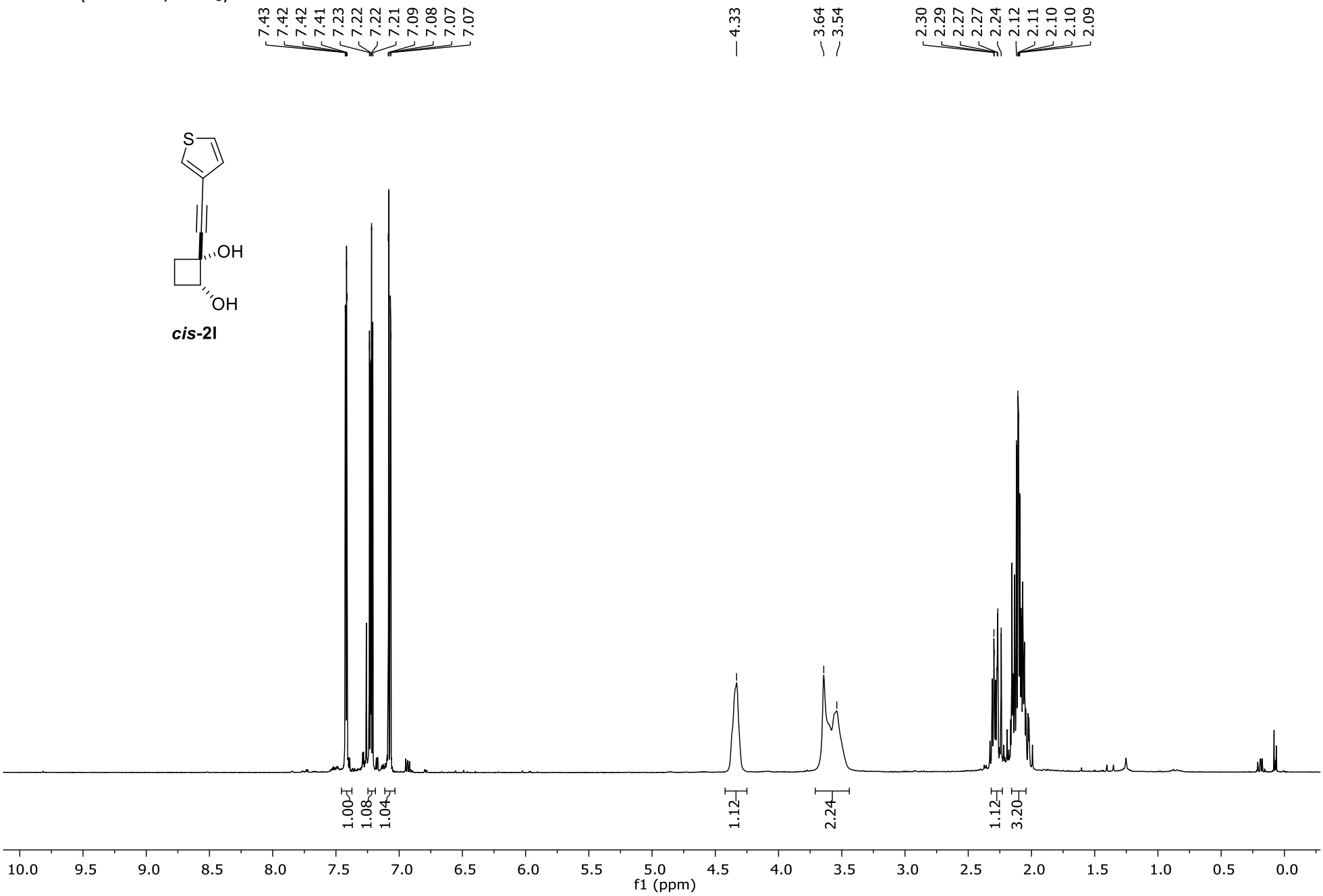
^{1}H-NMR (300 MHz, $CDCl_3$)



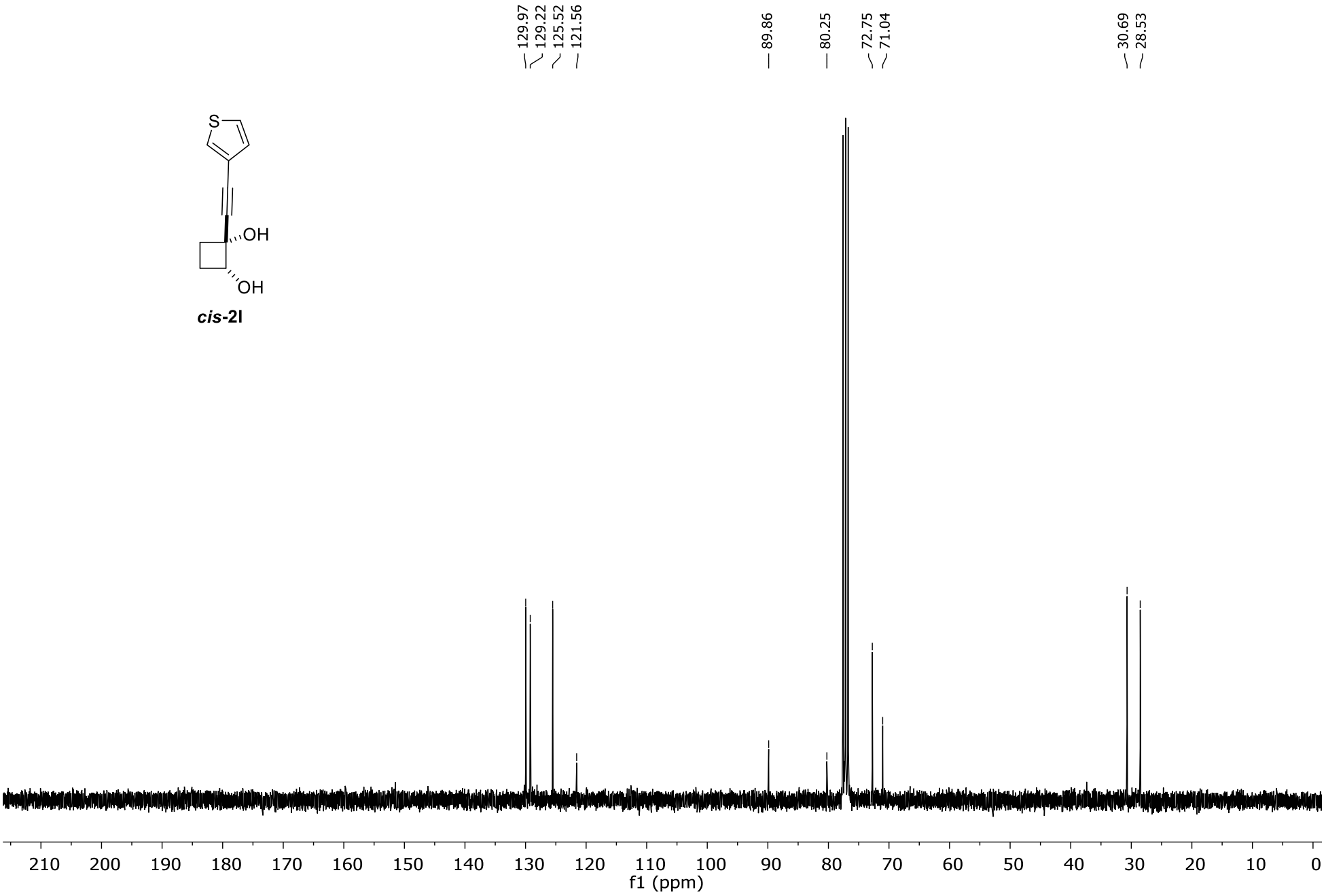
$^{13}C\{^{1}H\}$-RMN (75.4 MHz, $CDCl_3$)



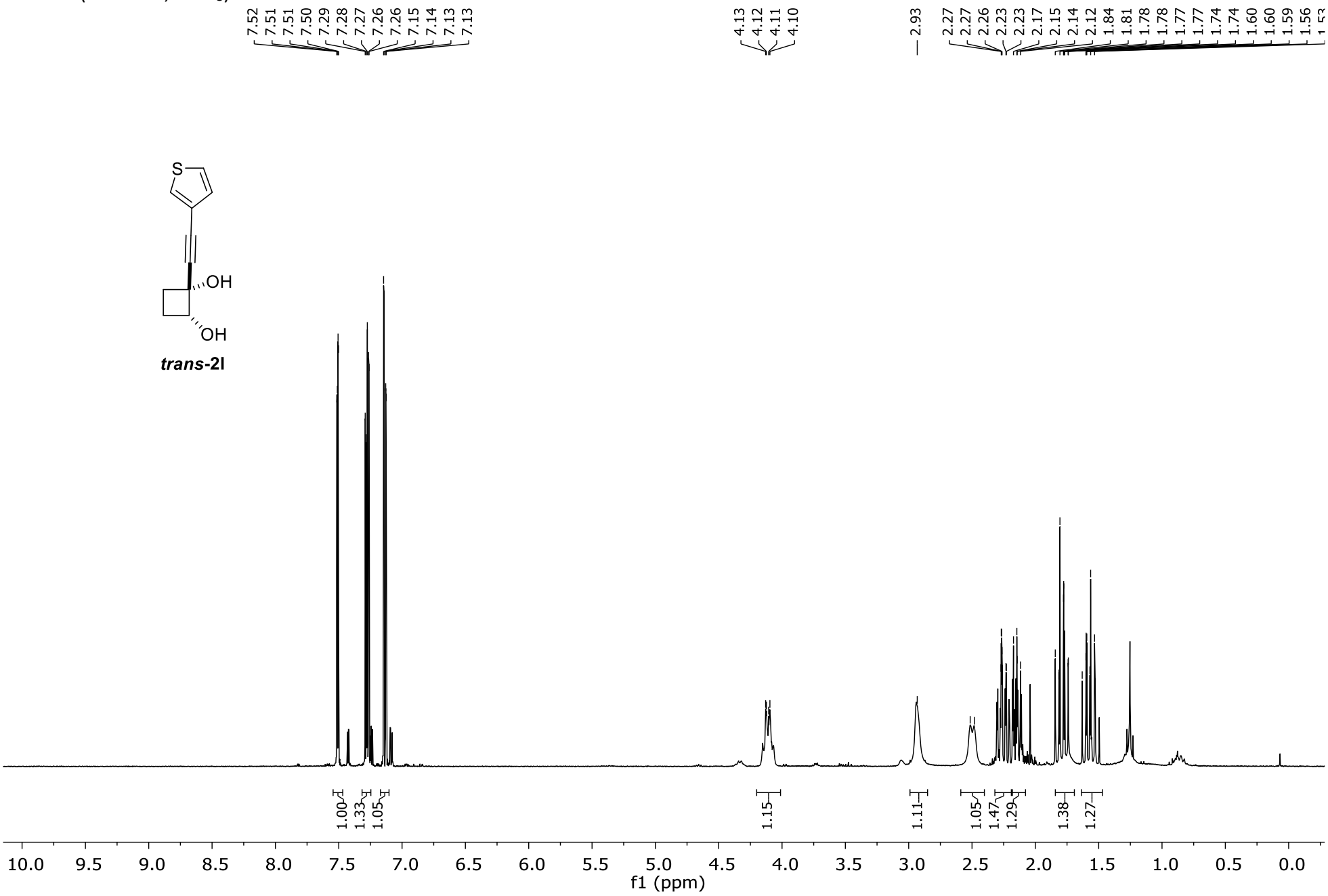
^{1}H-NMR (300 MHz, $CDCl_3$)



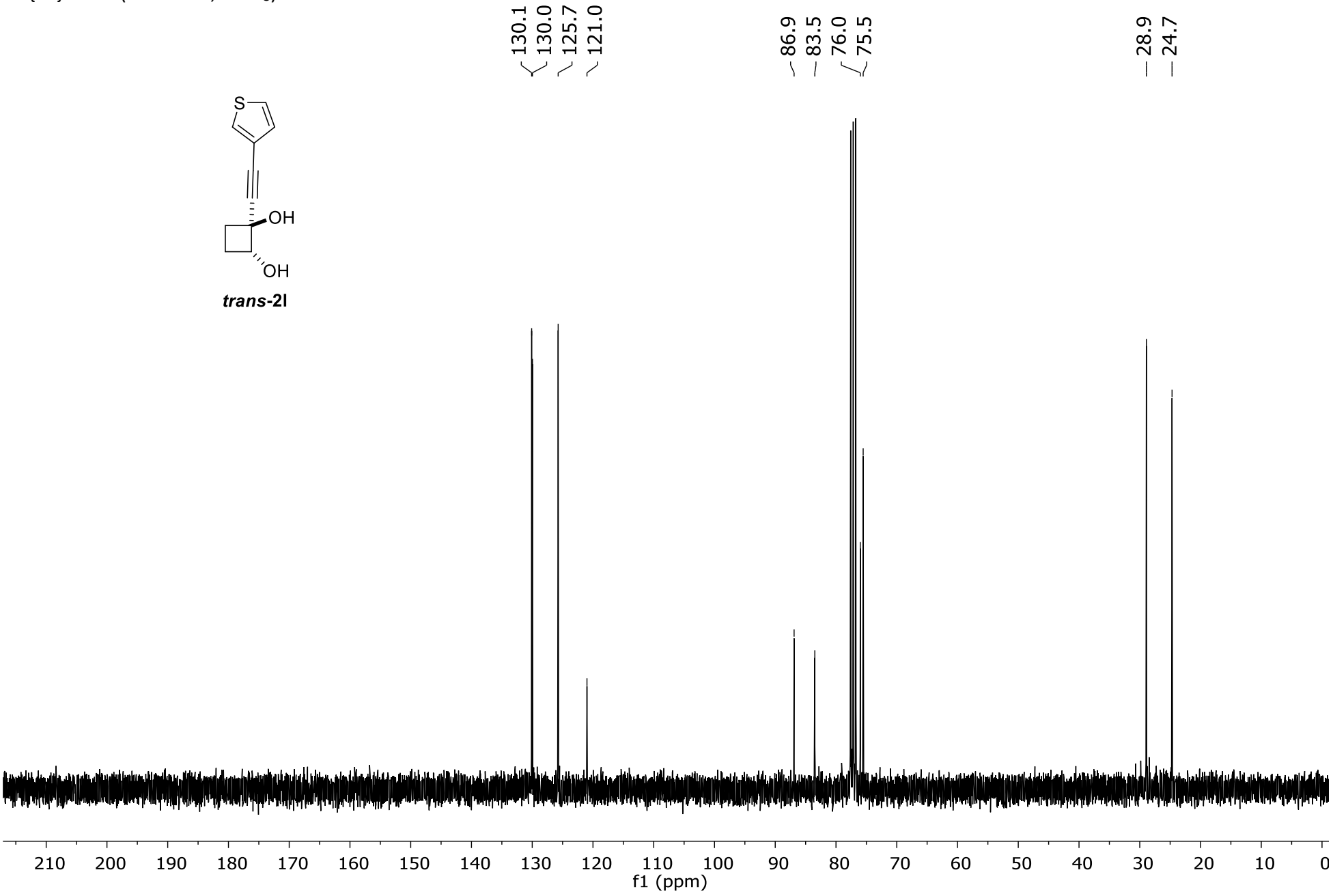
$^{13}C\{^{1}H\}$-RMN (75.4 MHz, $CDCl_3$)



^{1}H-NMR (300 MHz, $CDCl_3$)

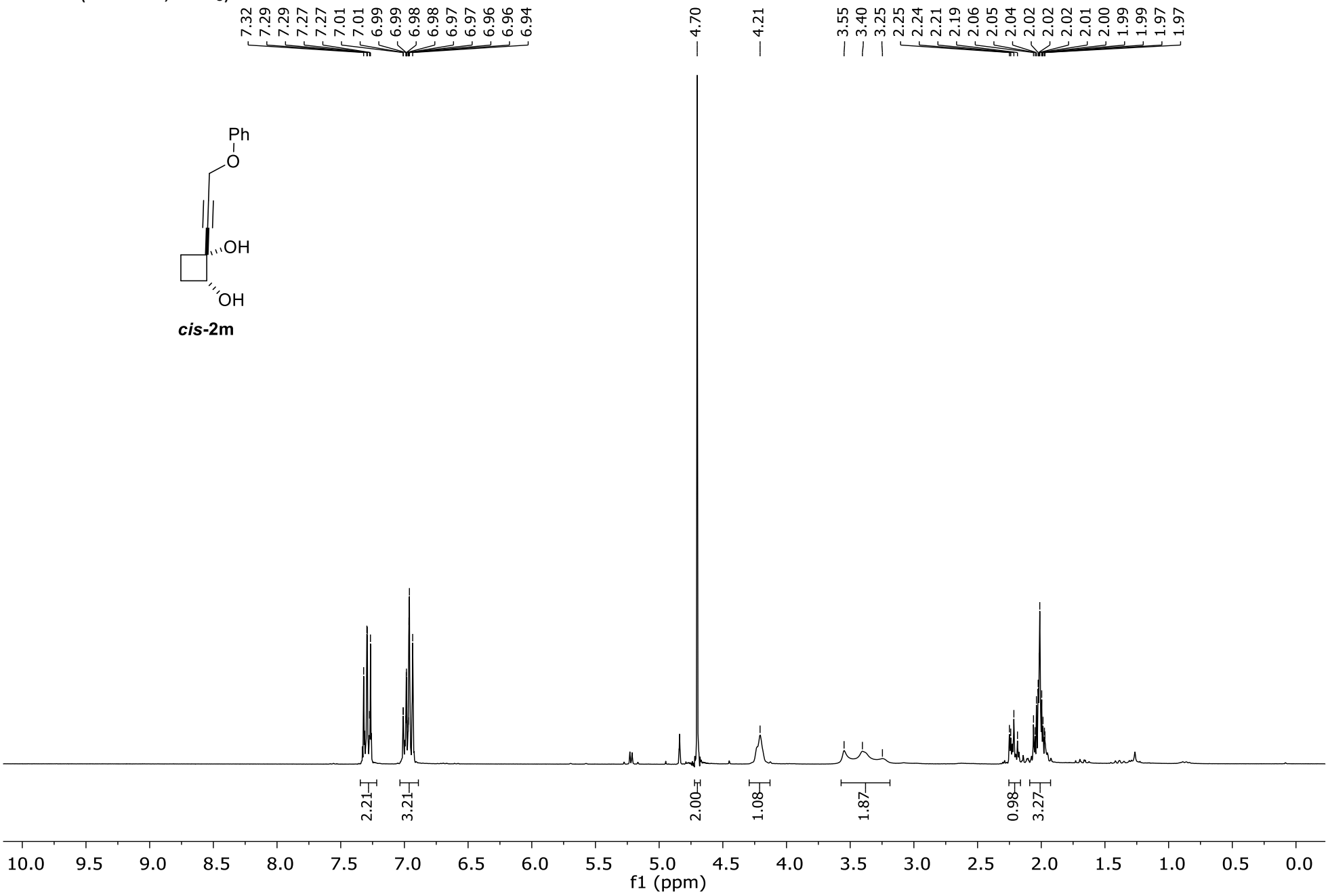


$^{13}C\{^{1}H\}$-RMN (75.4 MHz, $CDCl_3$)

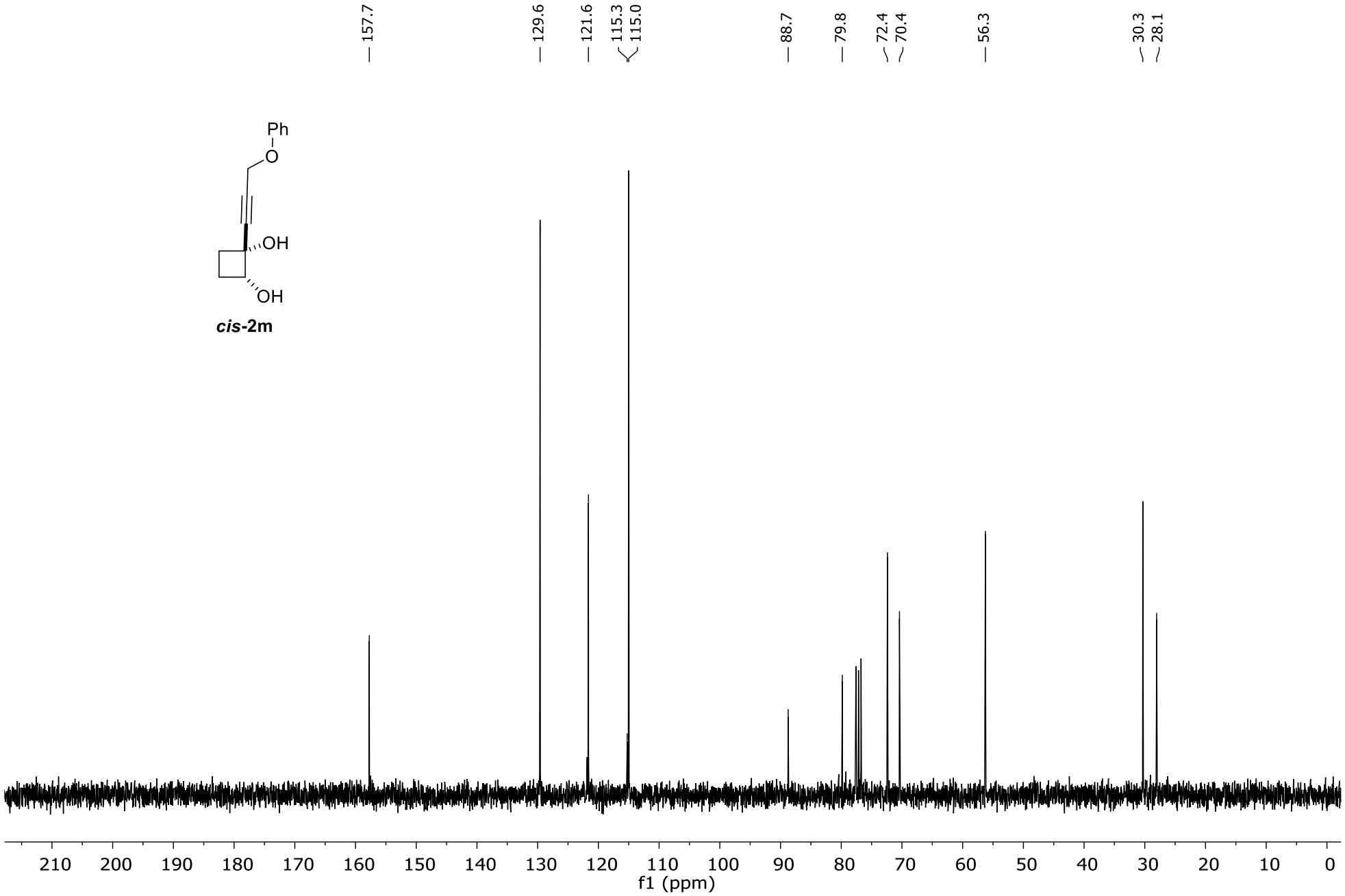


***trans*-2l**

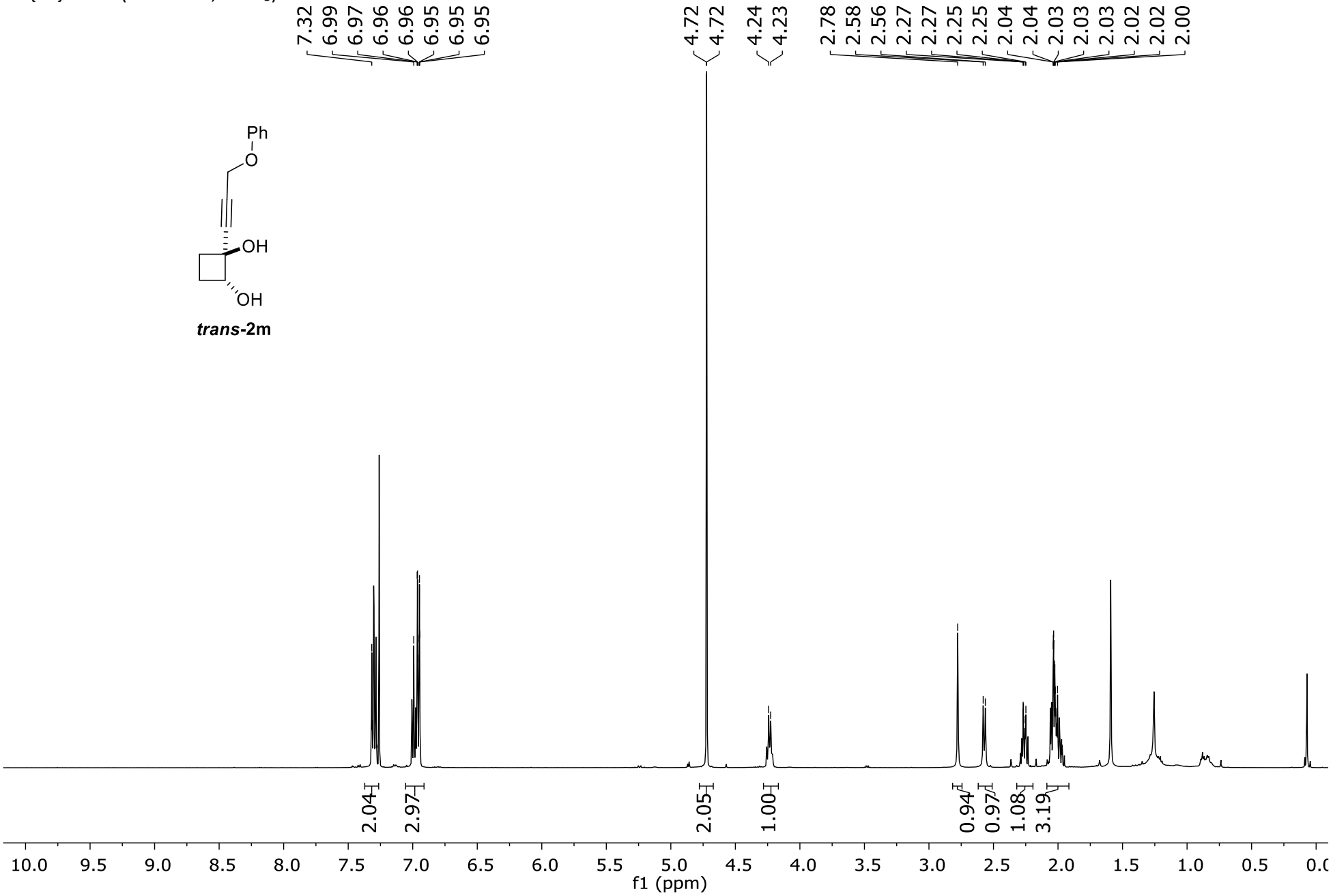
^{1}H-NMR (300 MHz, $CDCl_3$)



$^{13}C\{^{1}H\}$-RMN (75.4 MHz, $CDCl_3$)

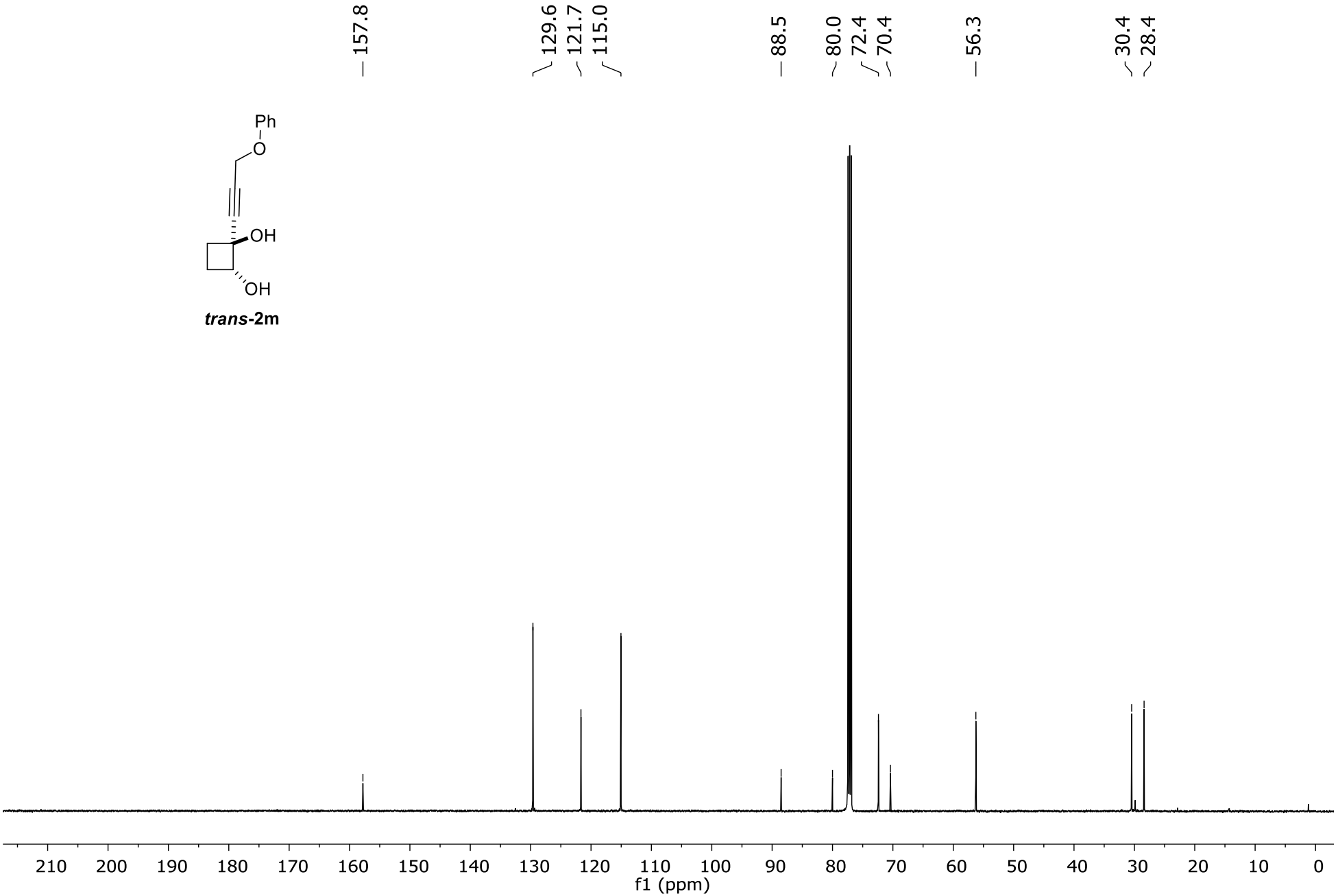


$^{13}C\{^{1}H\}$-RMN (75.4 MHz, $CDCl_3$)



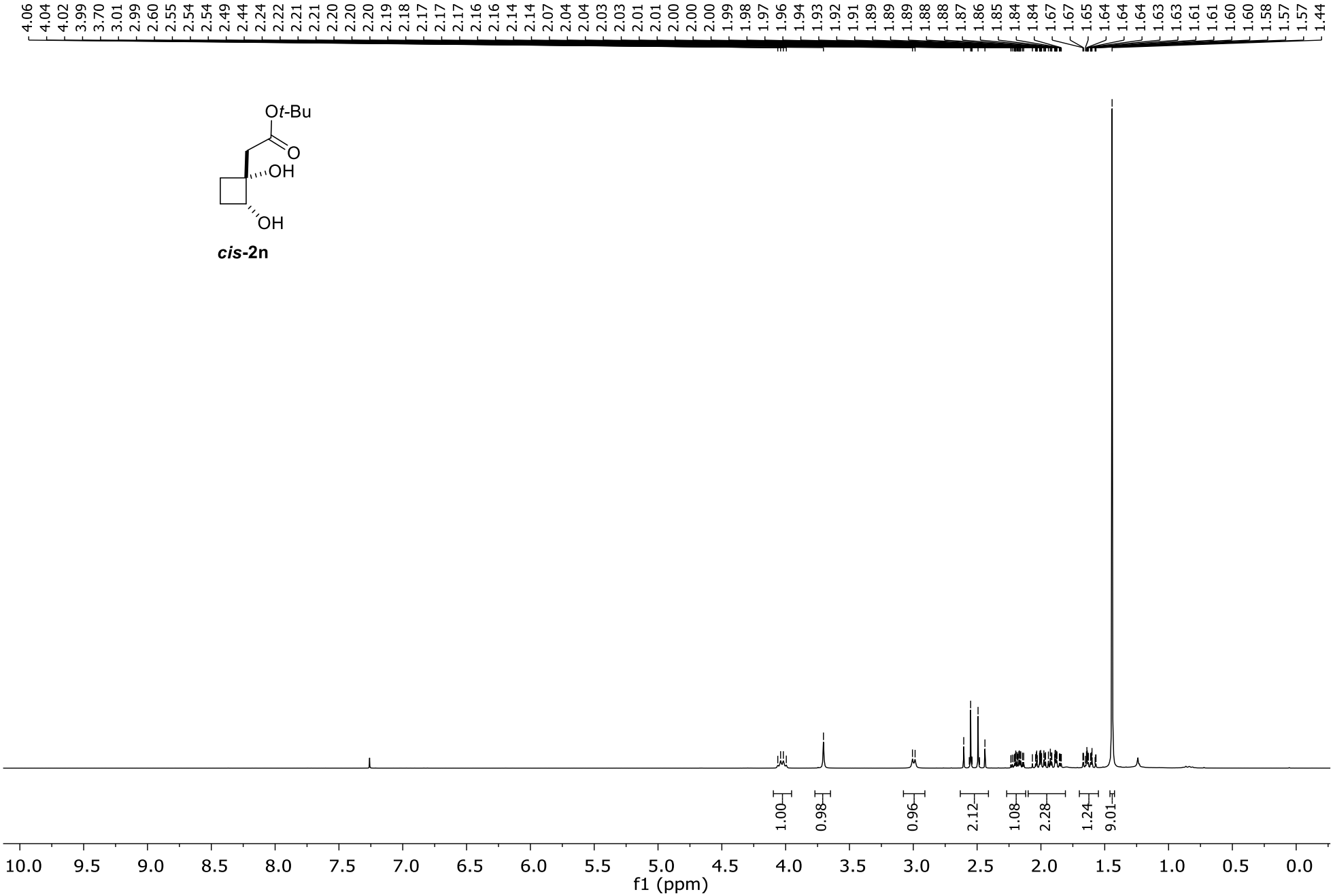
***trans*-2m**

^{1}H-RMN (500 MHz, $CDCl_3$)



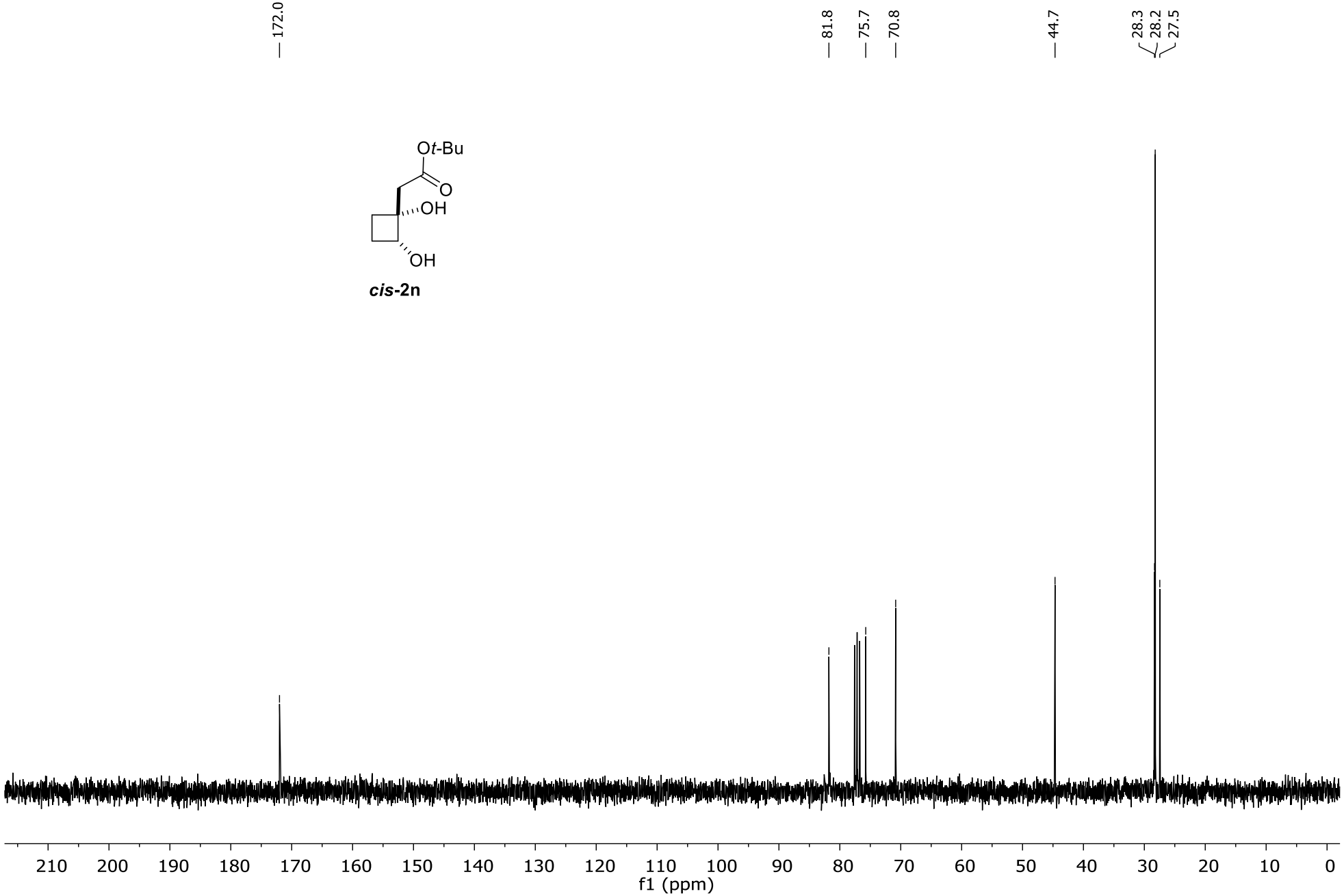
***trans*-2m**

$^{13}C\{^{1}H\}$-RMN (75.4 MHz, $CDCl_3$)

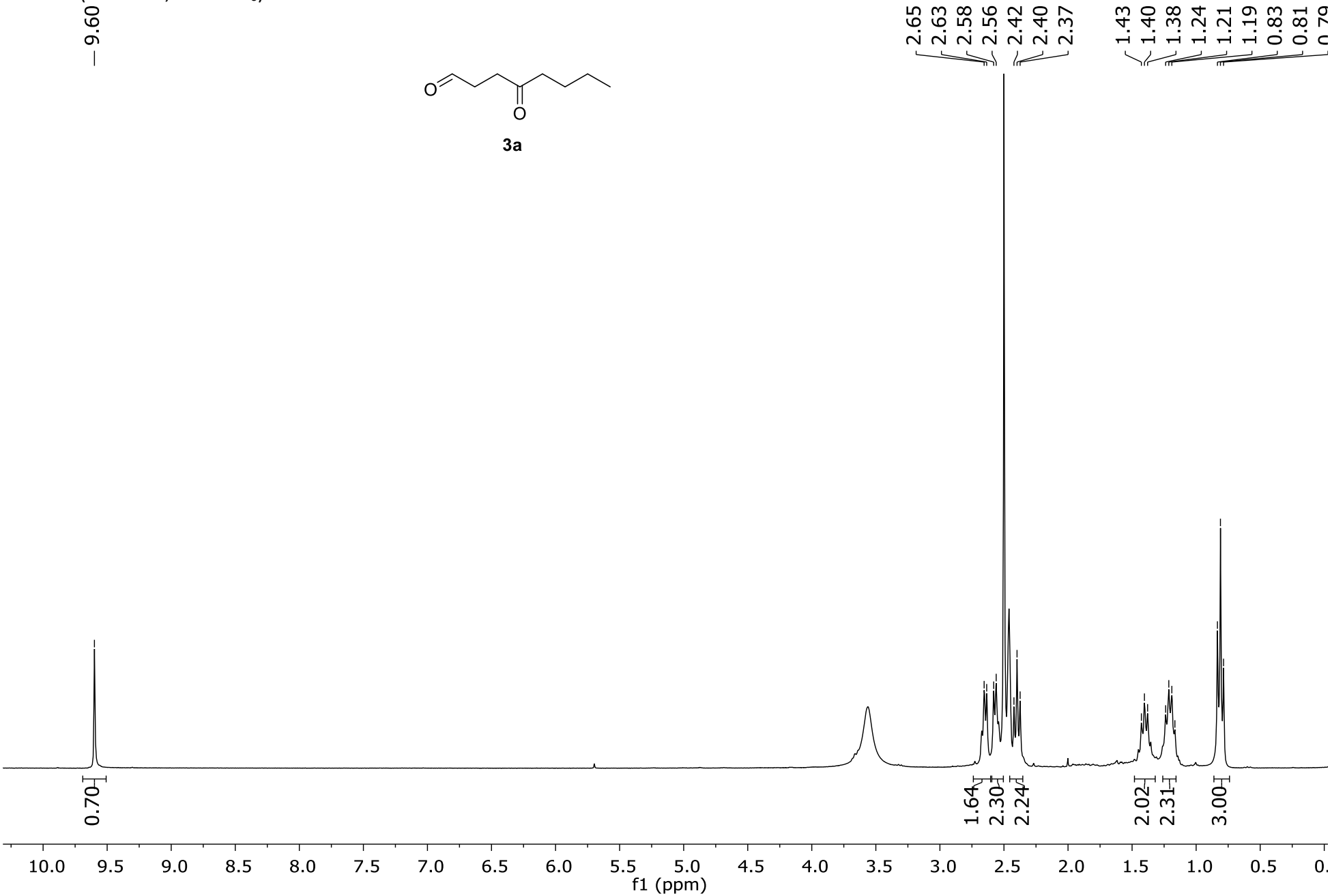


***cis*-2n**

^{1}H-RMN (300 MHz, $CDCl_3$)

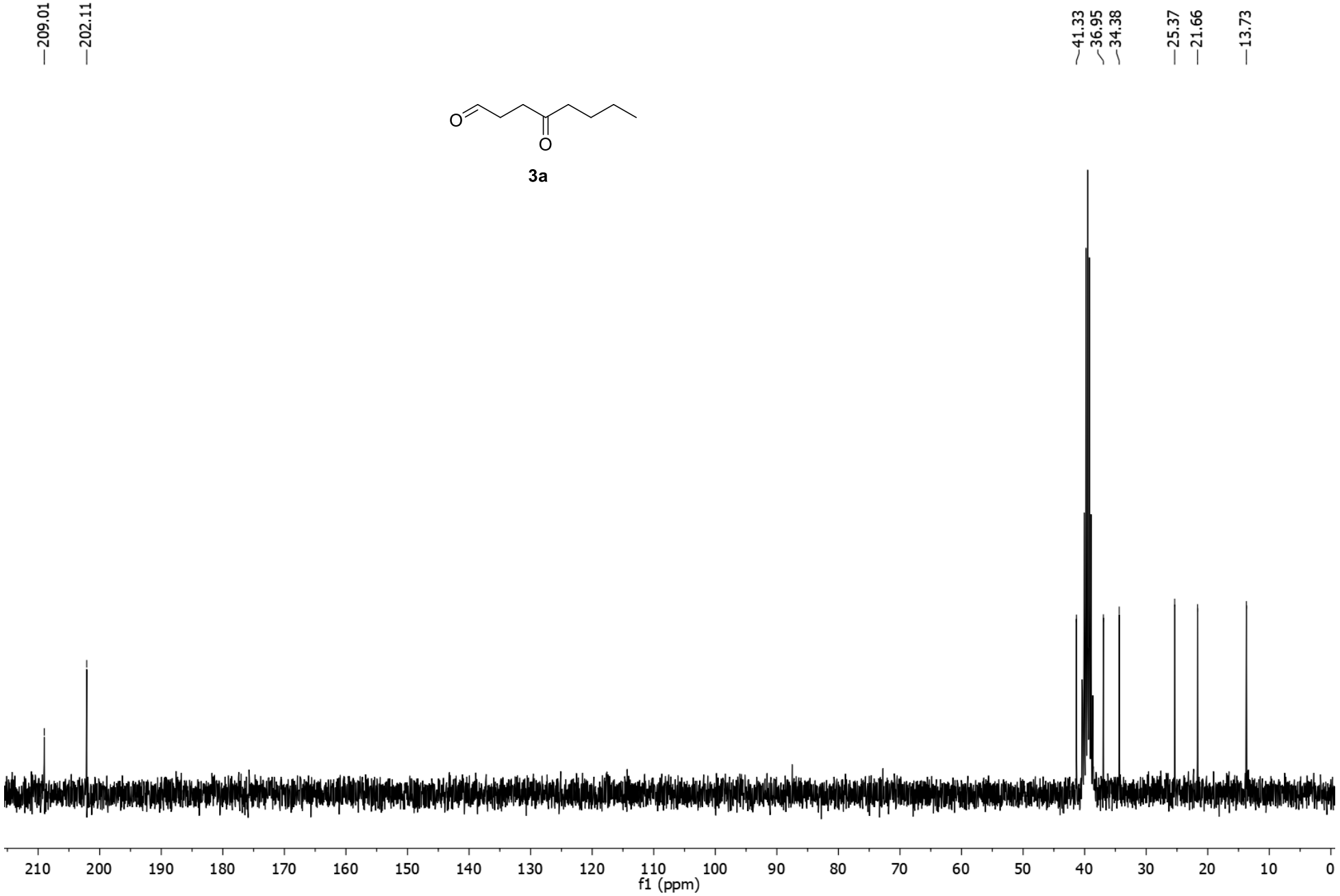


^{1}H-NMR (300 MHz, DMSO-d_6)

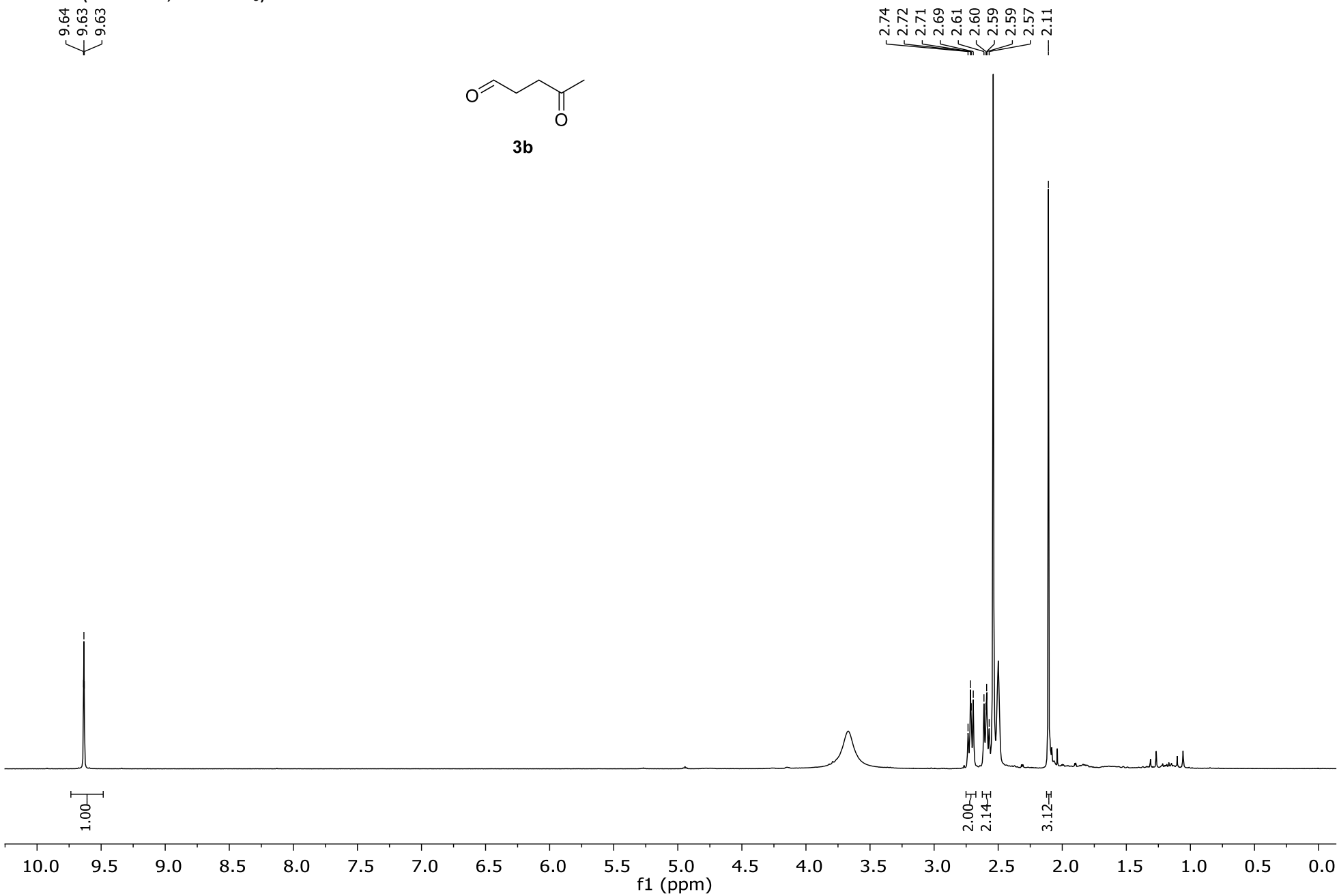


3a

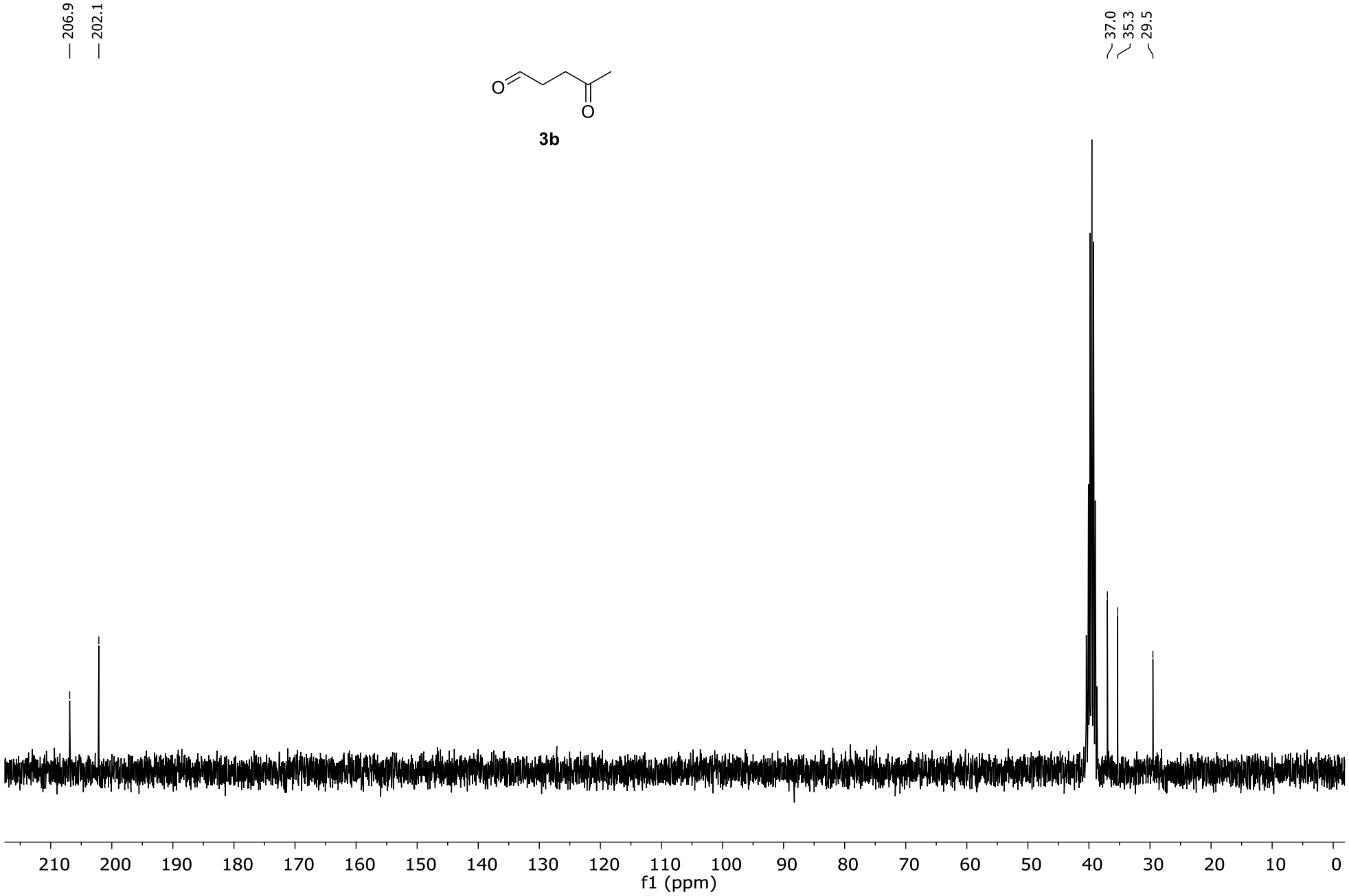
$^{13}C\{^{1}H\}$-RMN (75.4 MHz, DMSO-d_6)



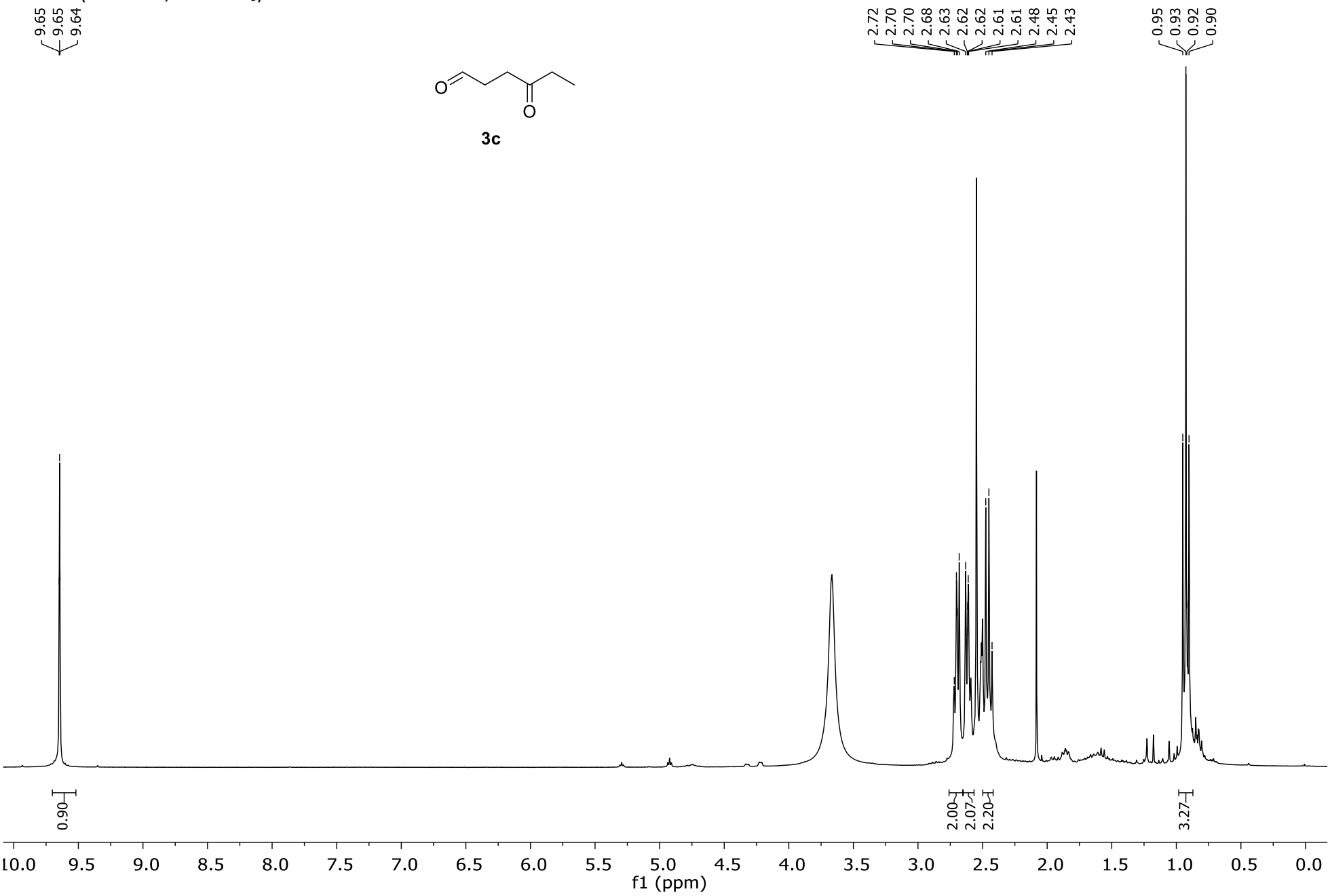
^{1}H-NMR (300 MHz, DMSO-d_6)



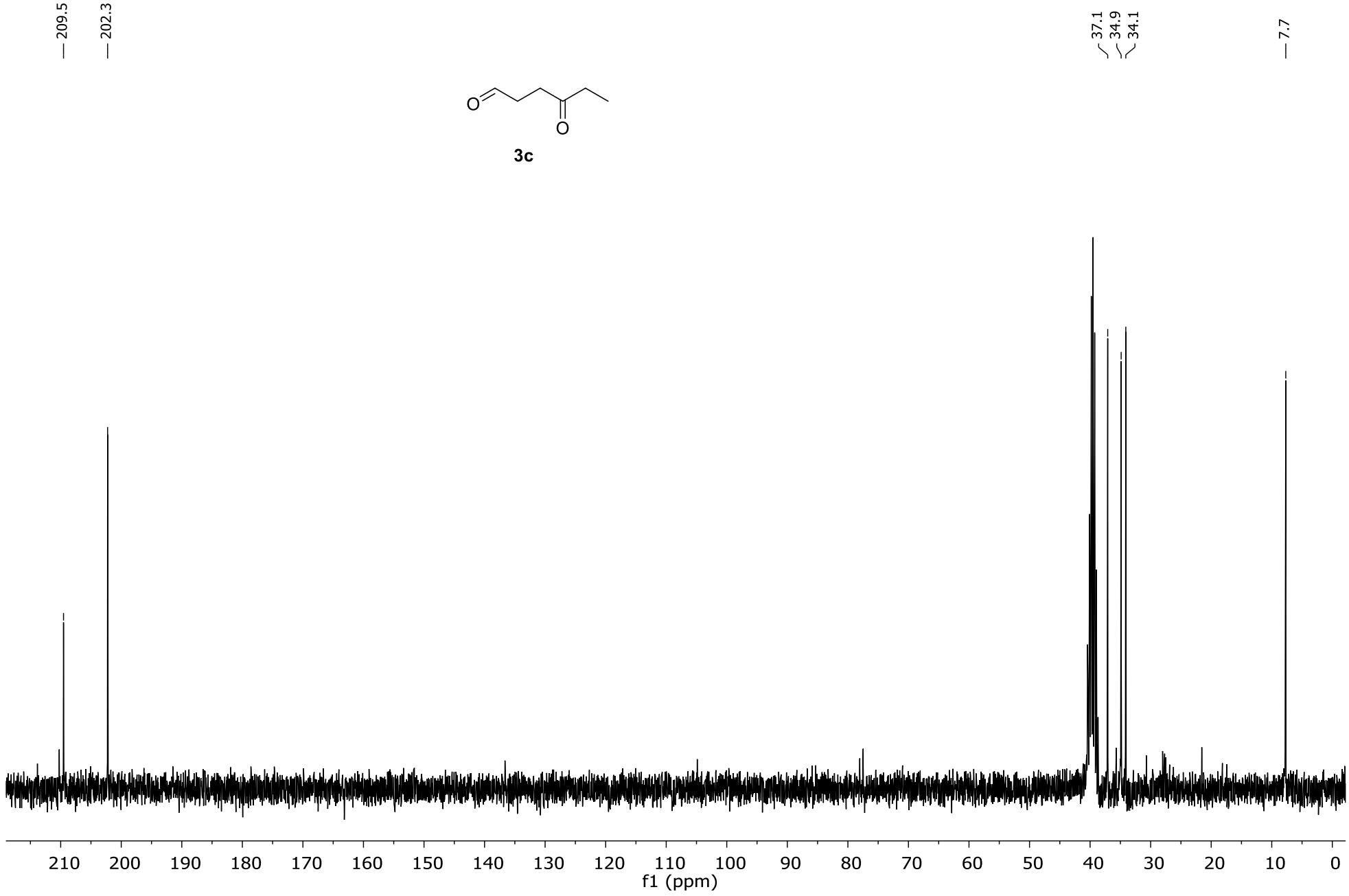
$^{13}C\{^{1}H\}$-RMN (75.4 MHz, DMSO-d_6)



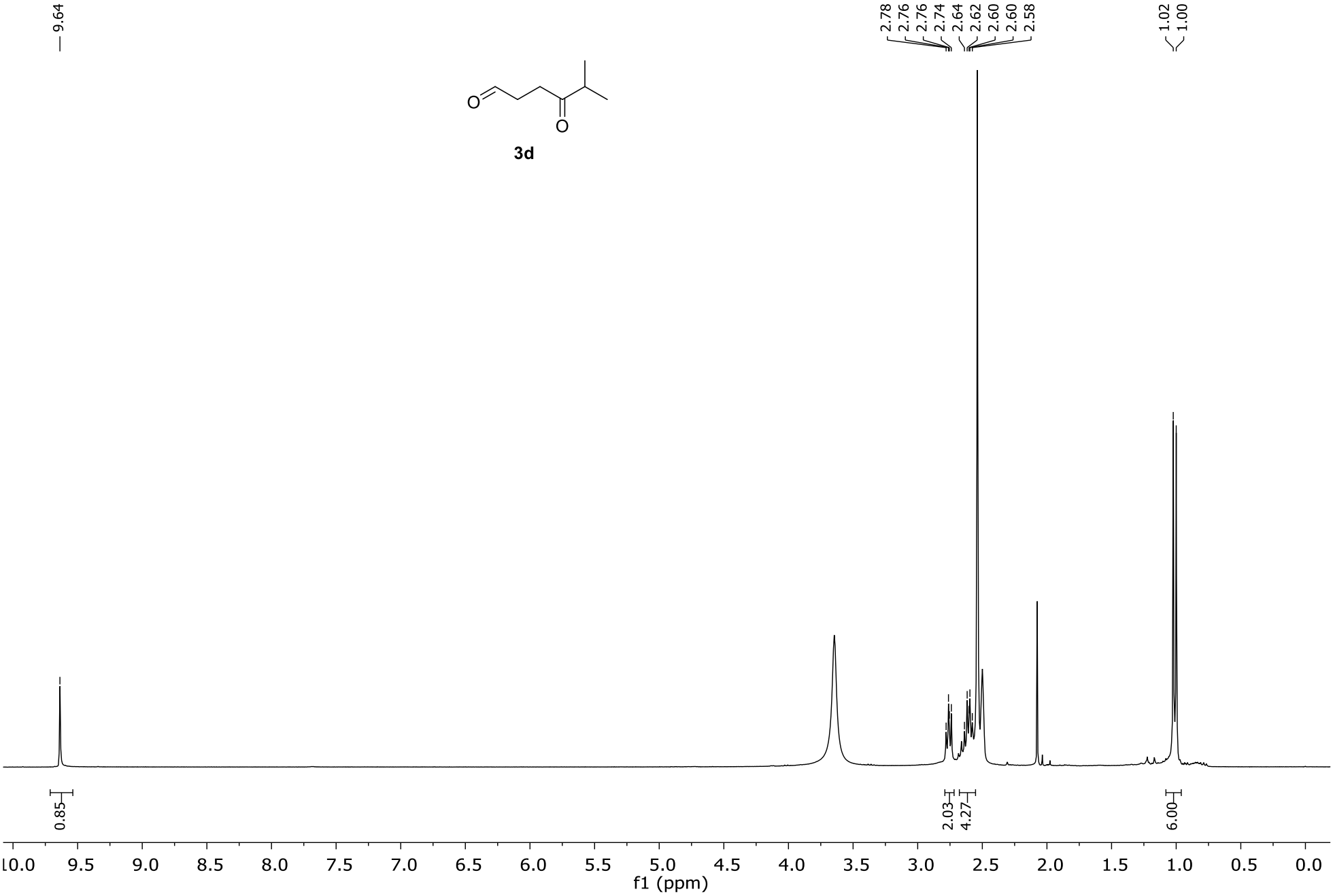
^{1}H-NMR (300 MHz, DMSO-d_6)



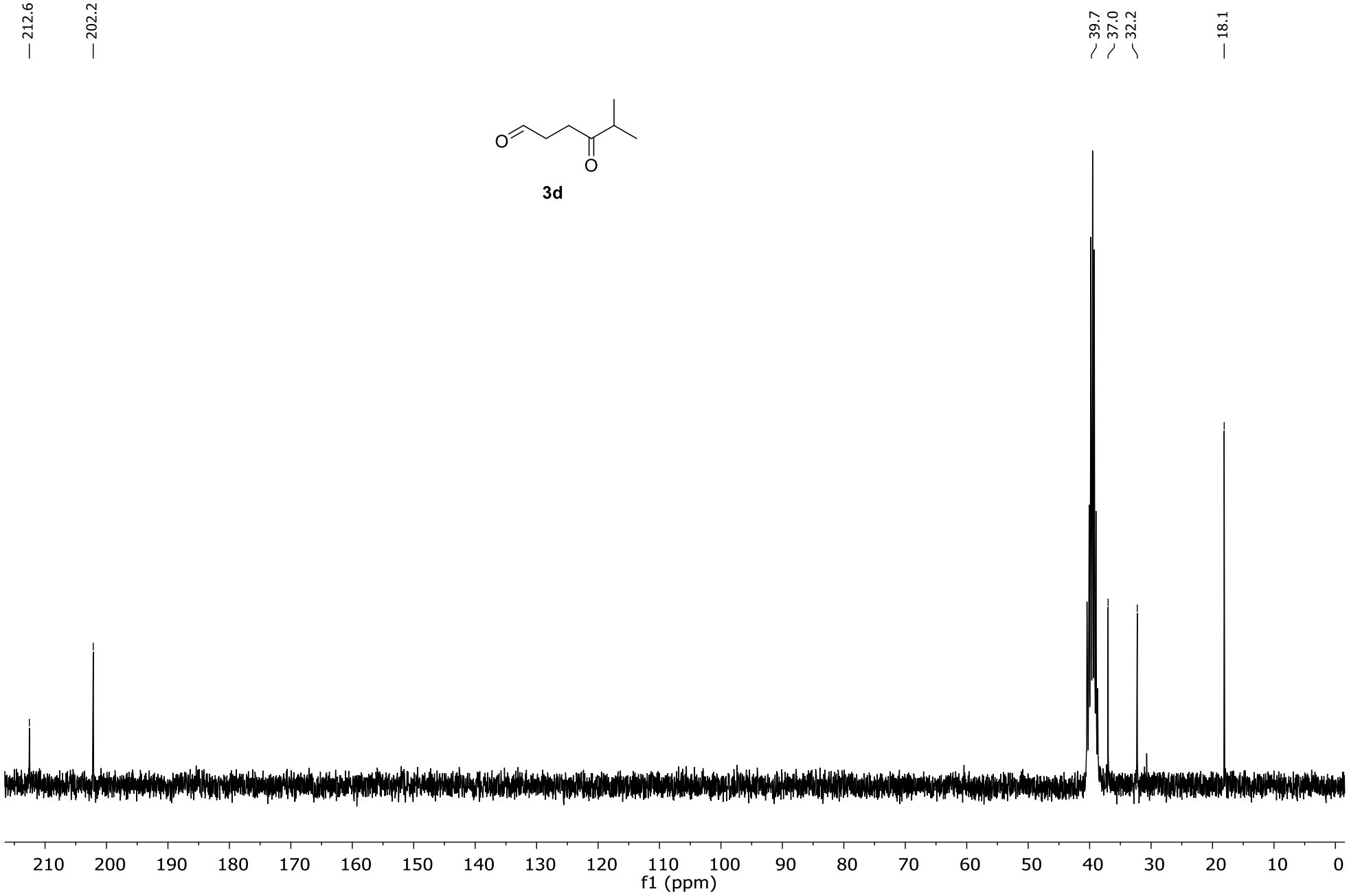
$^{13}C\{^{1}H\}$-RMN (75.4 MHz, DMSO-d_6)



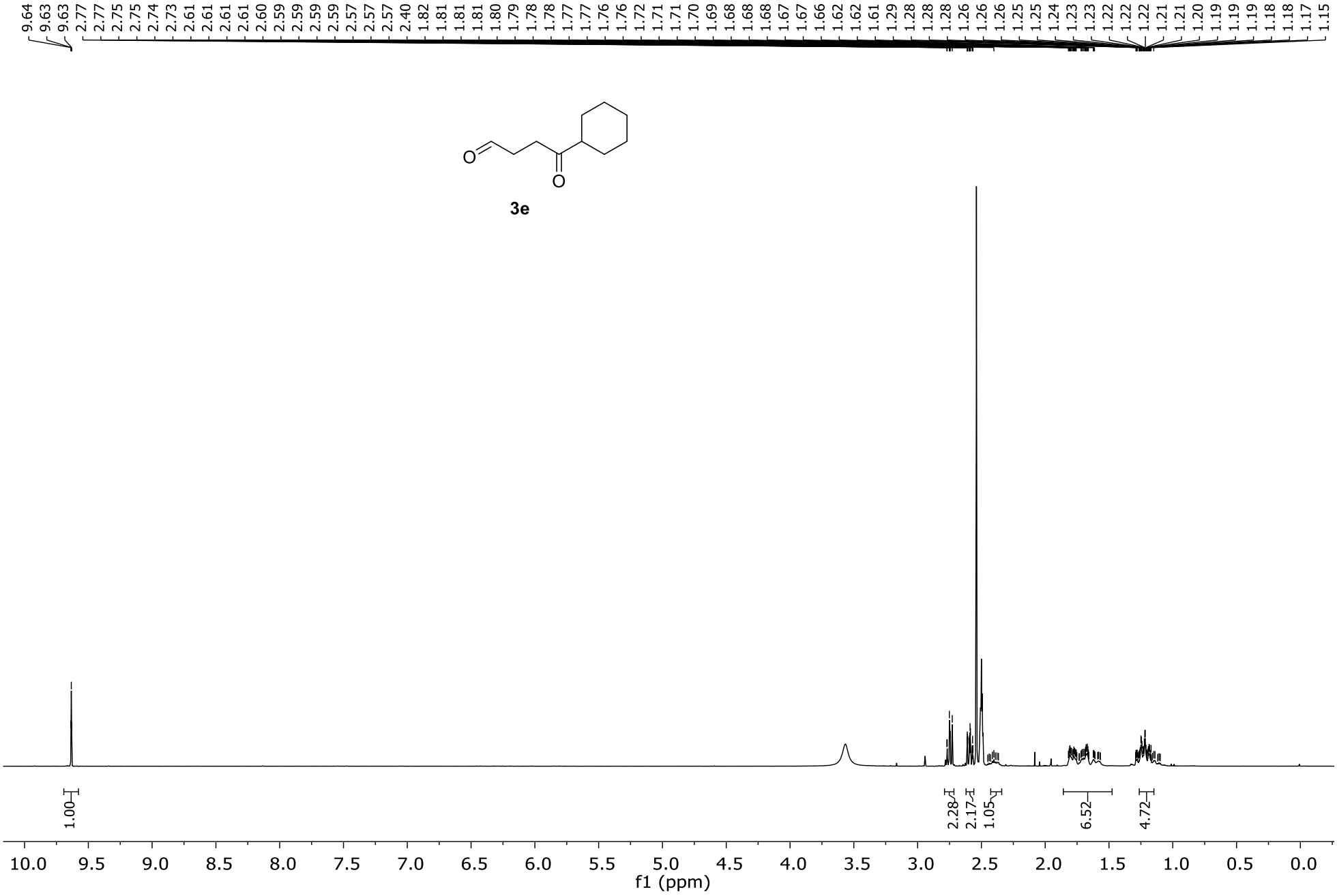
^{1}H-NMR (300 MHz, DMSO-d_6)



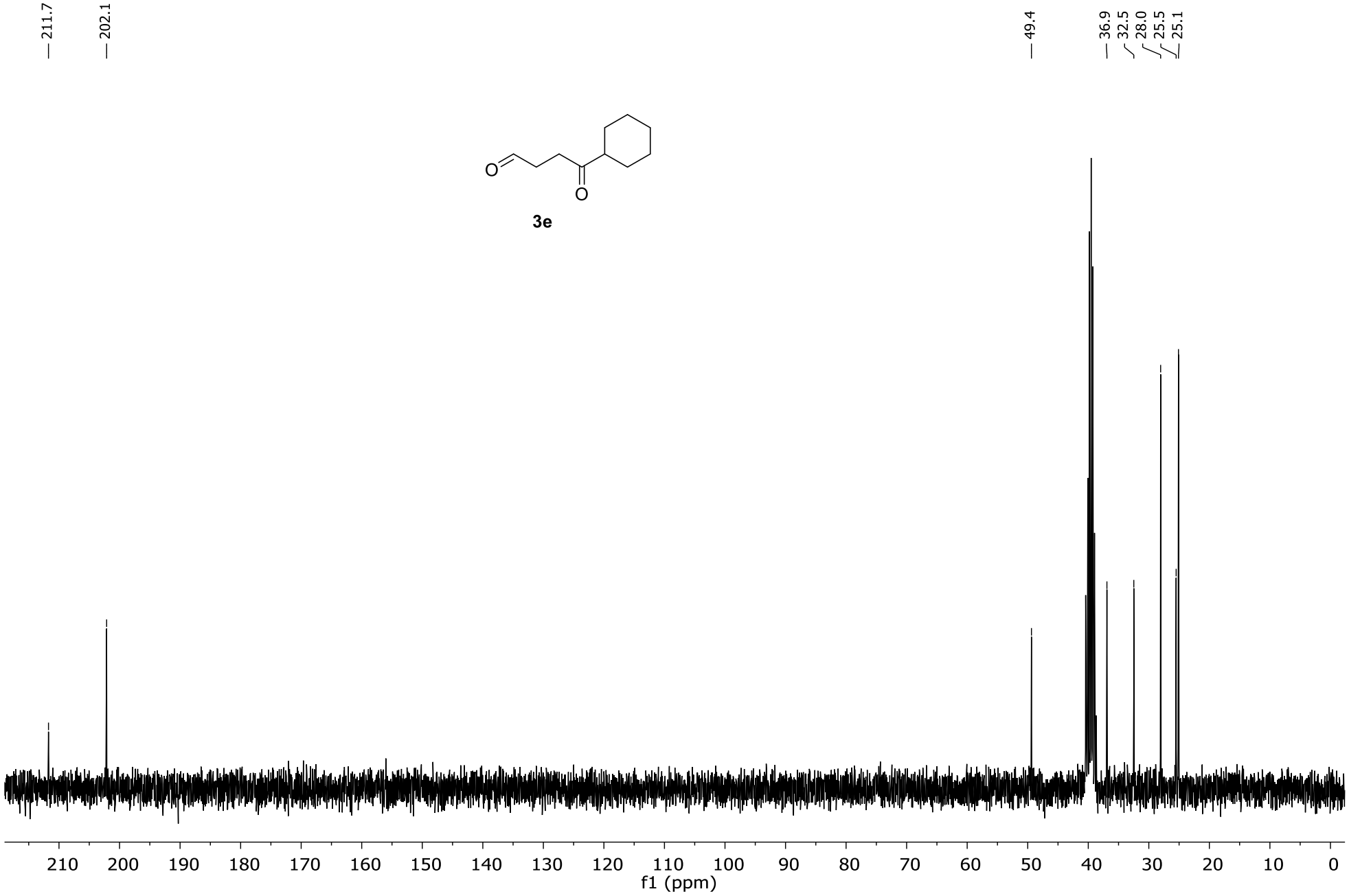
$^{13}C\{^{1}H\}$-RMN (75.4 MHz, DMSO-d_6)



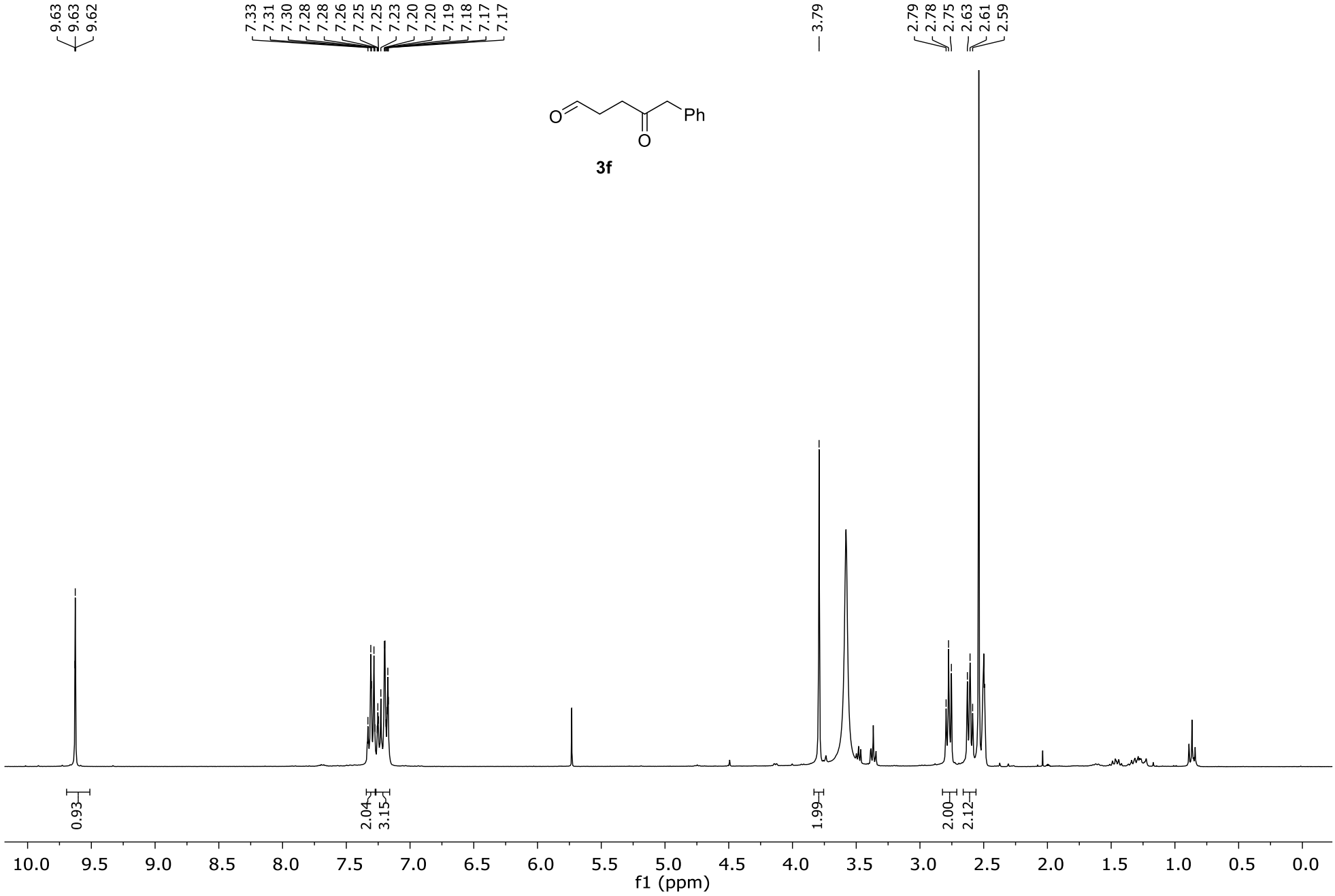
^{1}H-NMR (300 MHz, DMSO-d_6)



$^{13}C\{^{1}H\}$-RMN (75.4 MHz, DMSO-d_6)

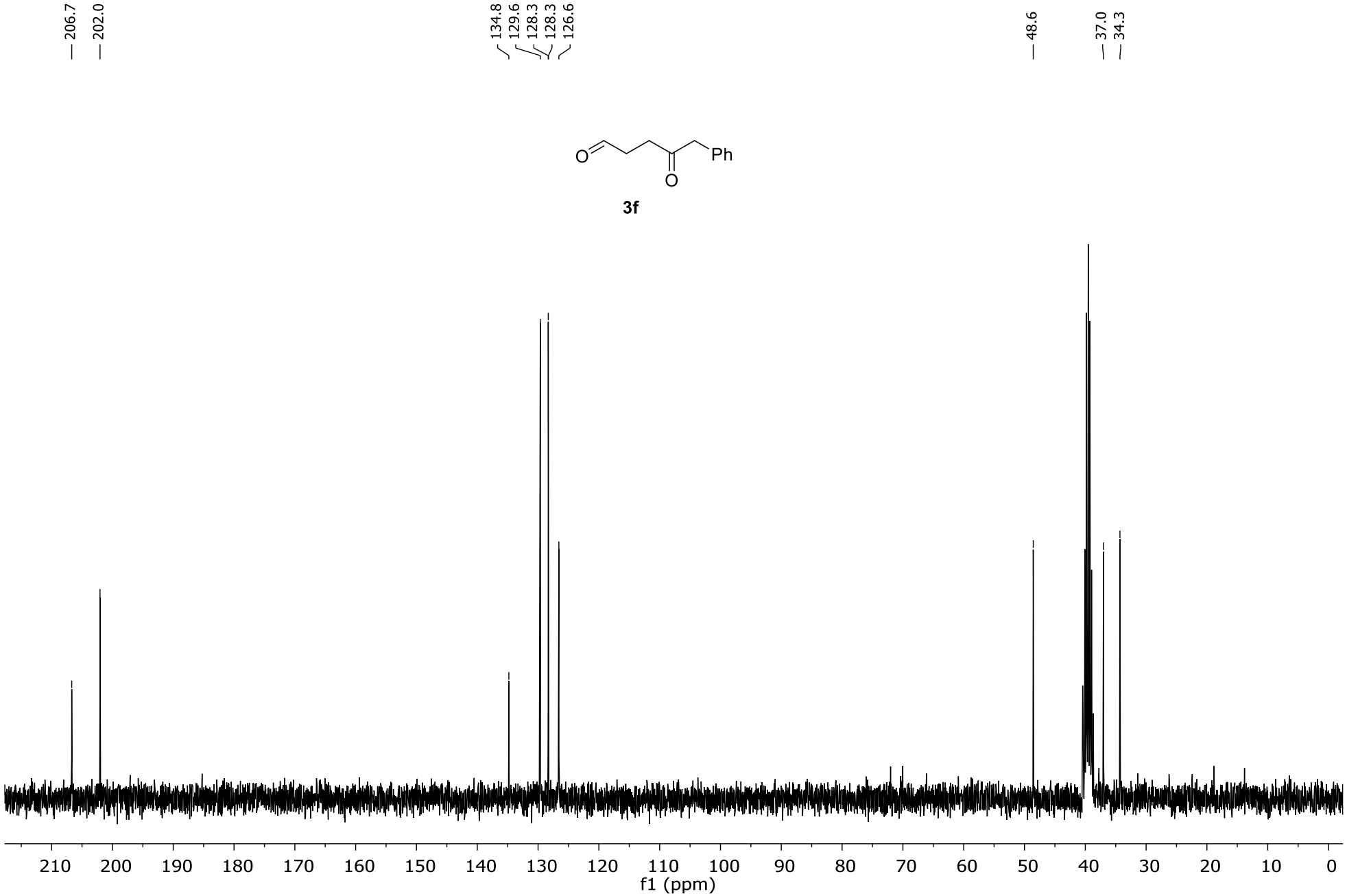


^{1}H-NMR (300 MHz, DMSO-d_6)

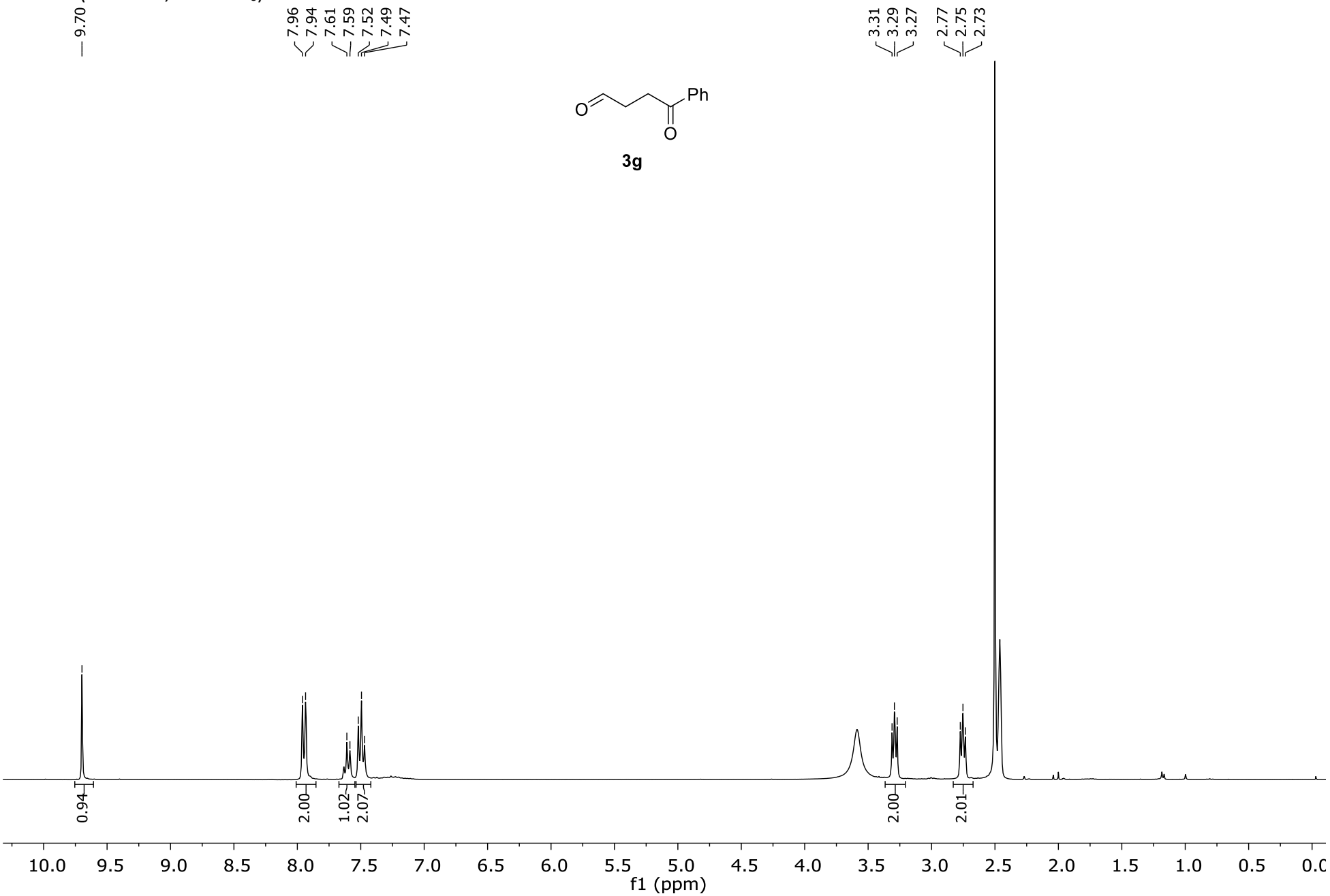


3f

$^{13}C\{^{1}H\}$-RMN (75.4 MHz, DMSO-d_6)

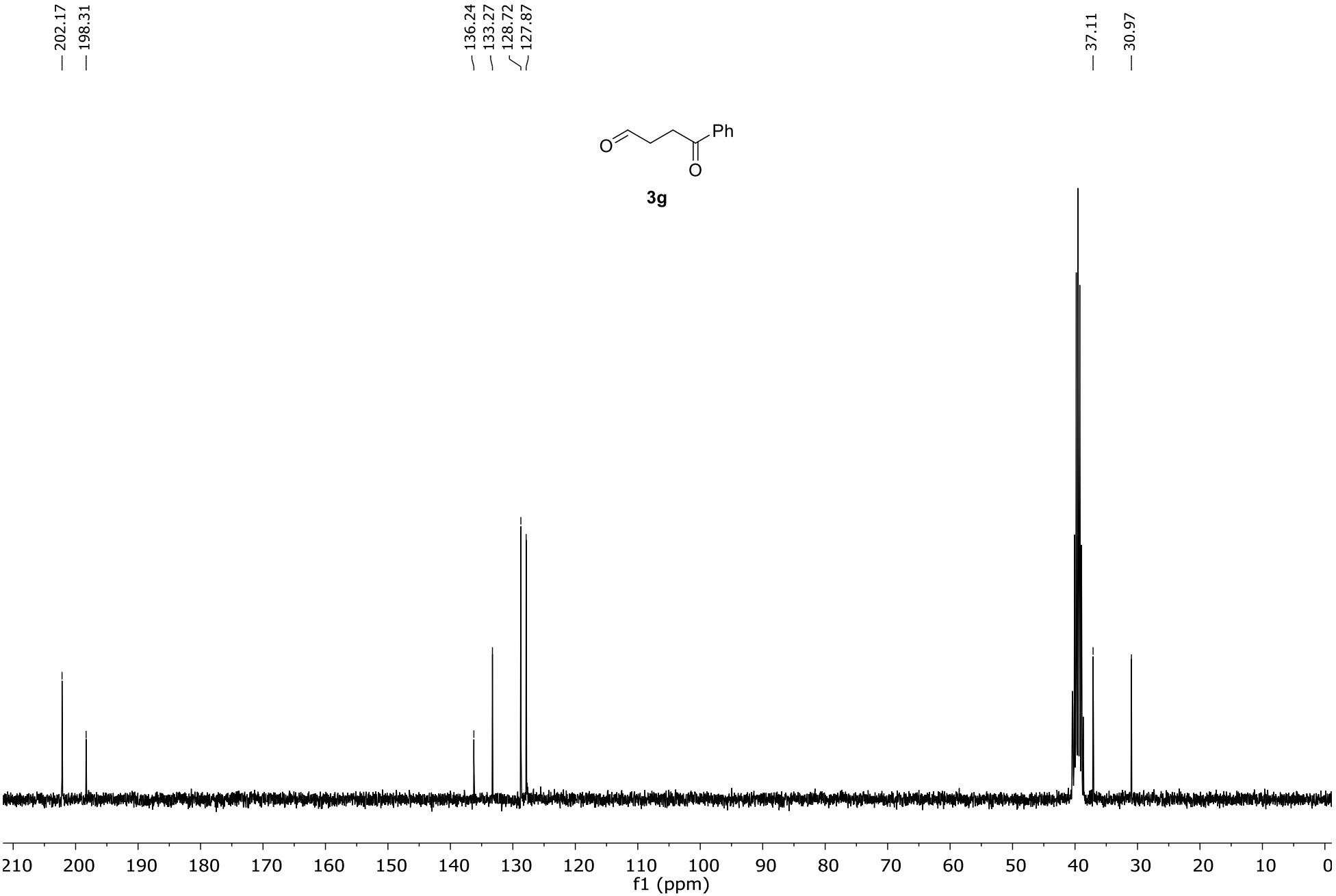


^{1}H-NMR (300 MHz, DMSO-d_6)

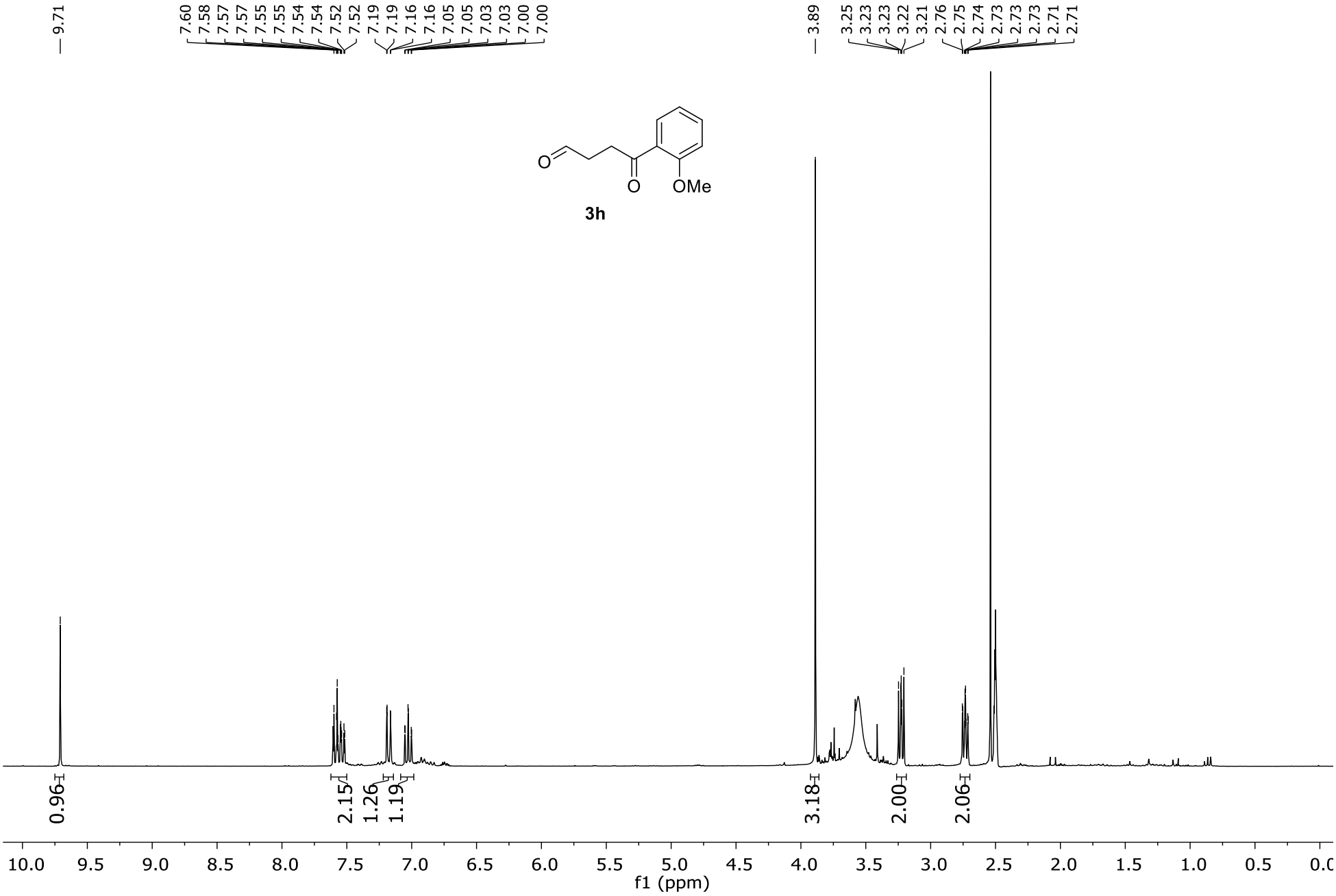


3g

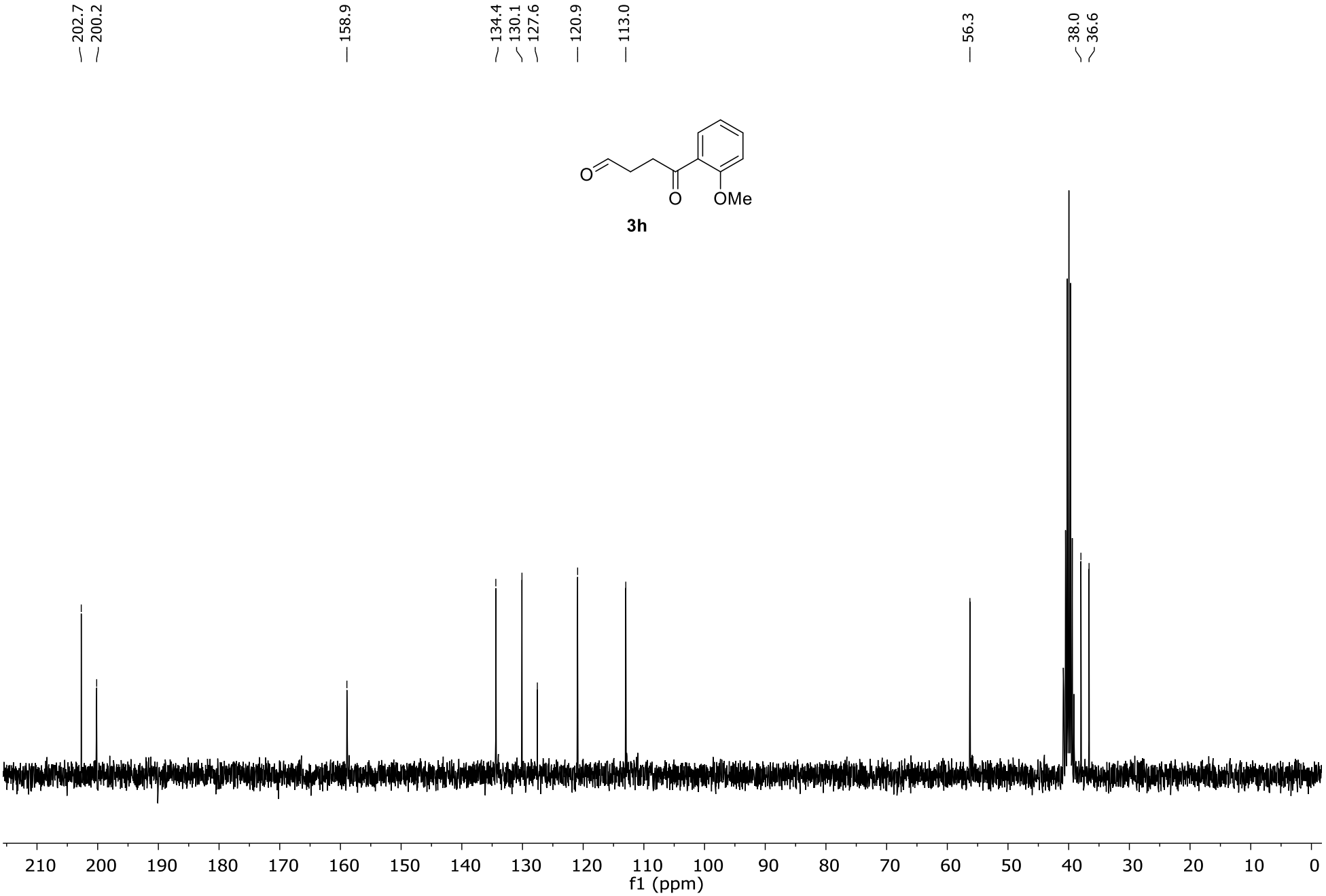
$^{13}C\{^{1}H\}$-RMN (75.4 MHz, DMSO-d_6)



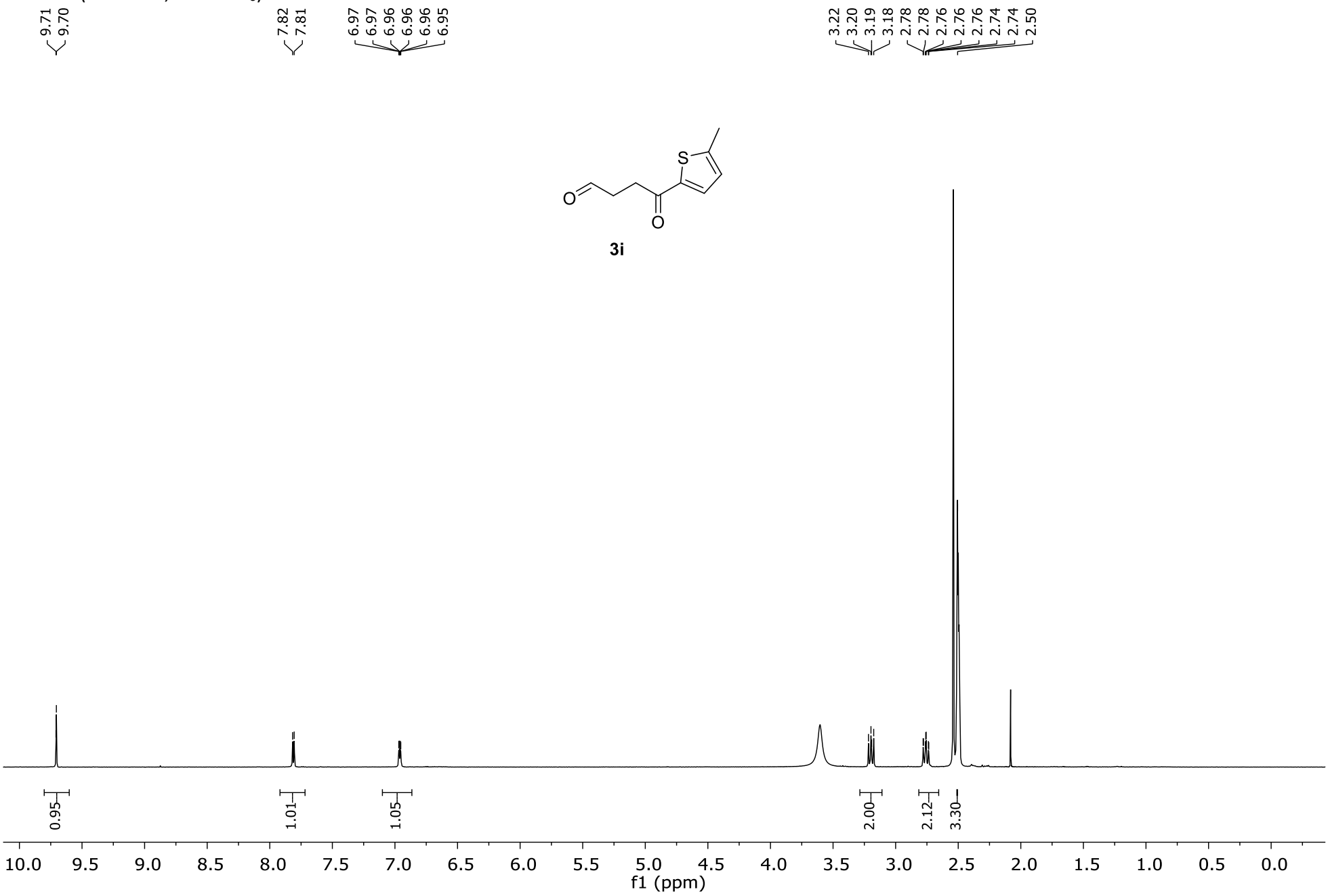
^{1}H-NMR (300 MHz, DMSO-d_6)



$^{13}C\{^{1}H\}$-RMN (75.4 MHz, DMSO-d_6)

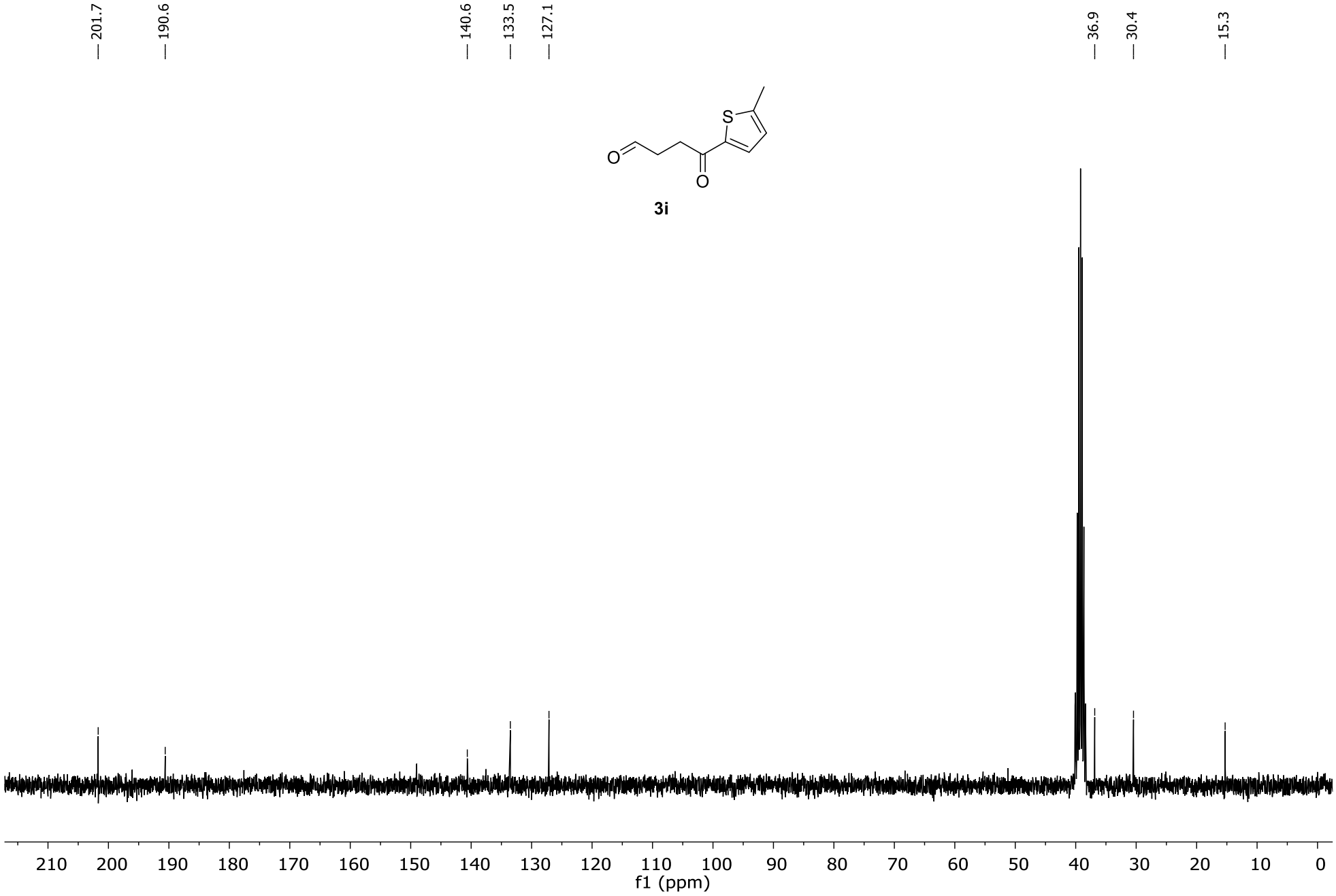


^{1}H-NMR (300 MHz, DMSO-d_6)

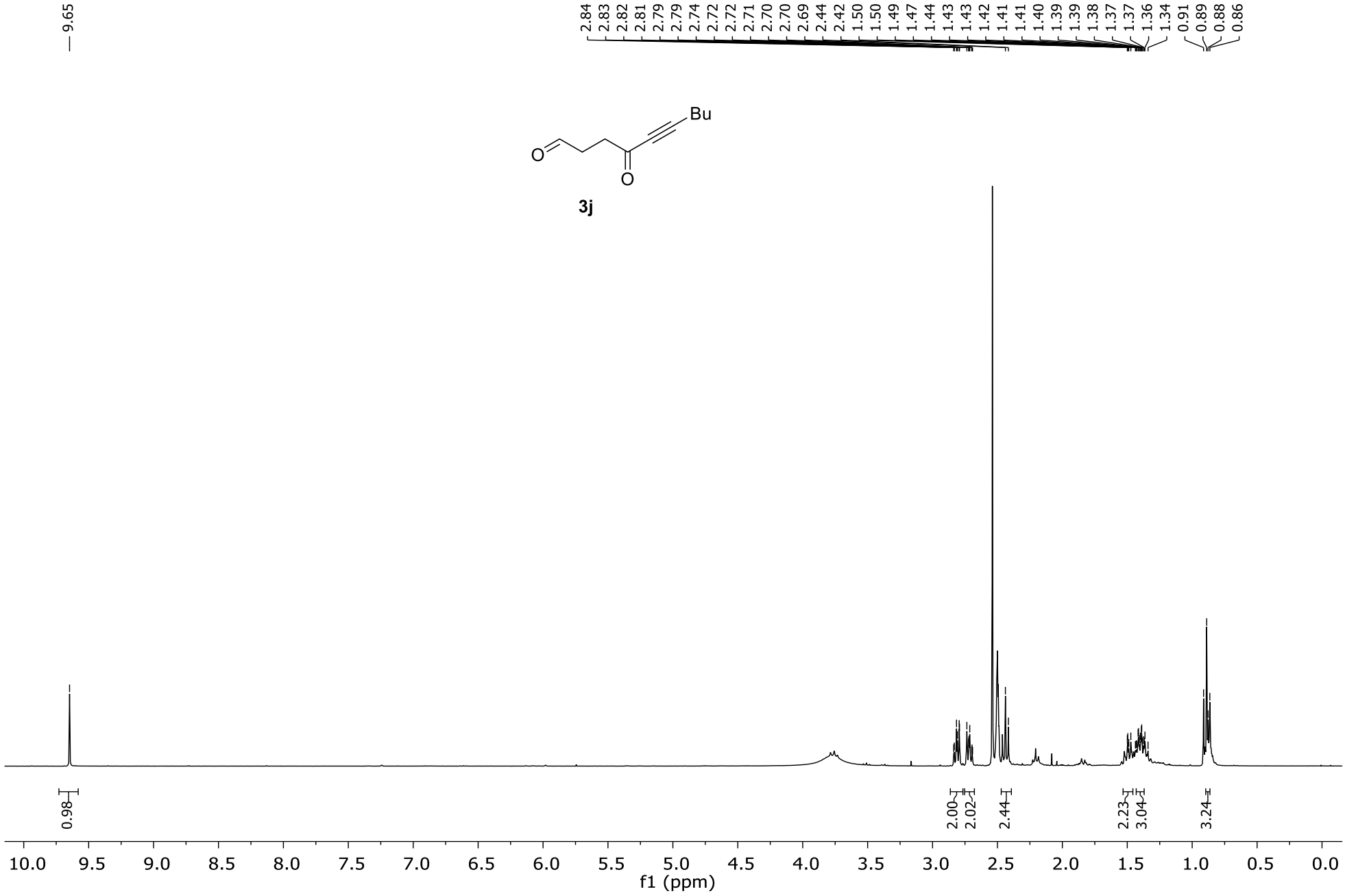


3i

$^{13}C\{^{1}H\}$-RMN (75.4 MHz, DMSO-d_6)

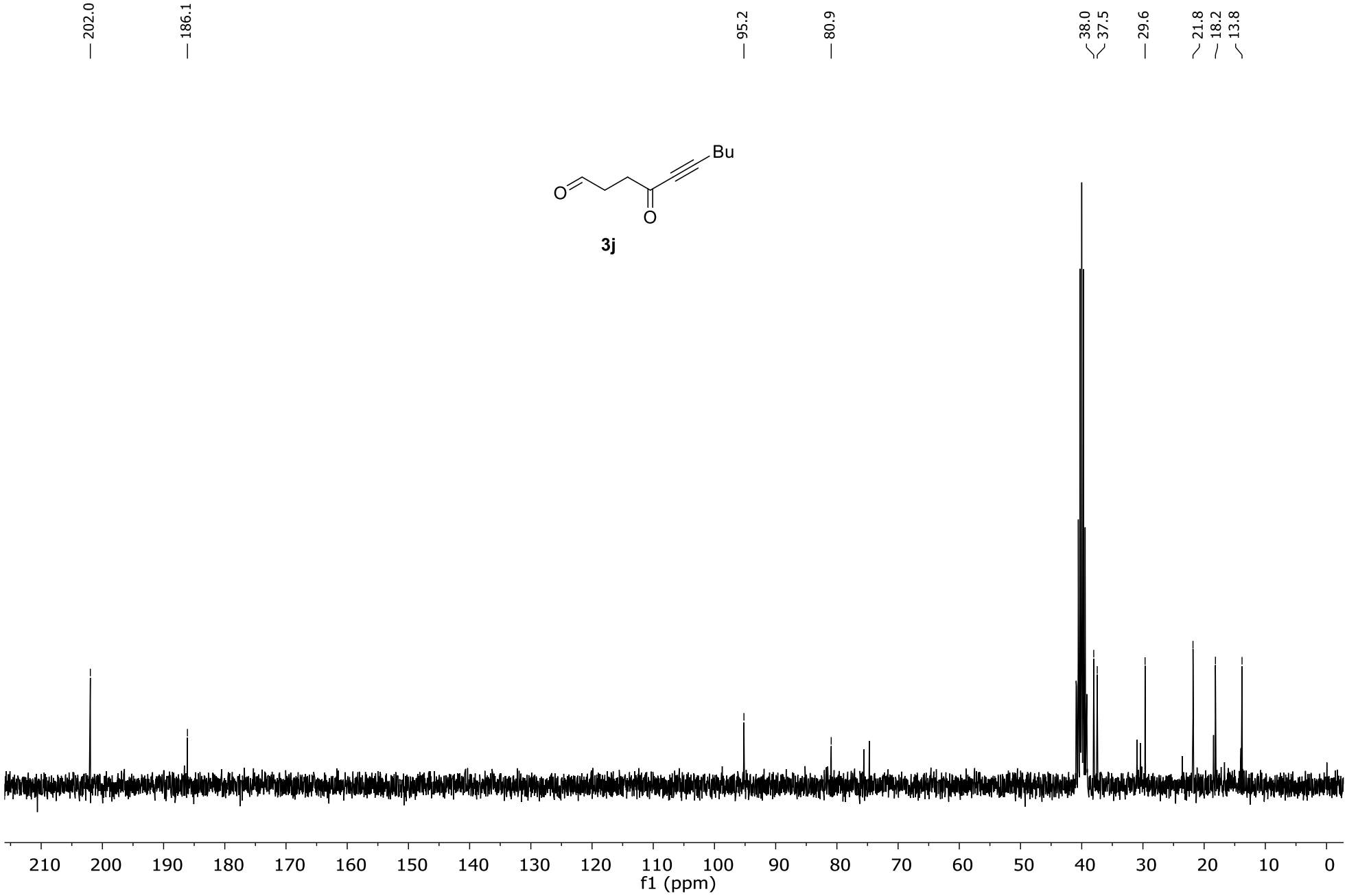


^{1}H-NMR (300 MHz, DMSO-d_6)

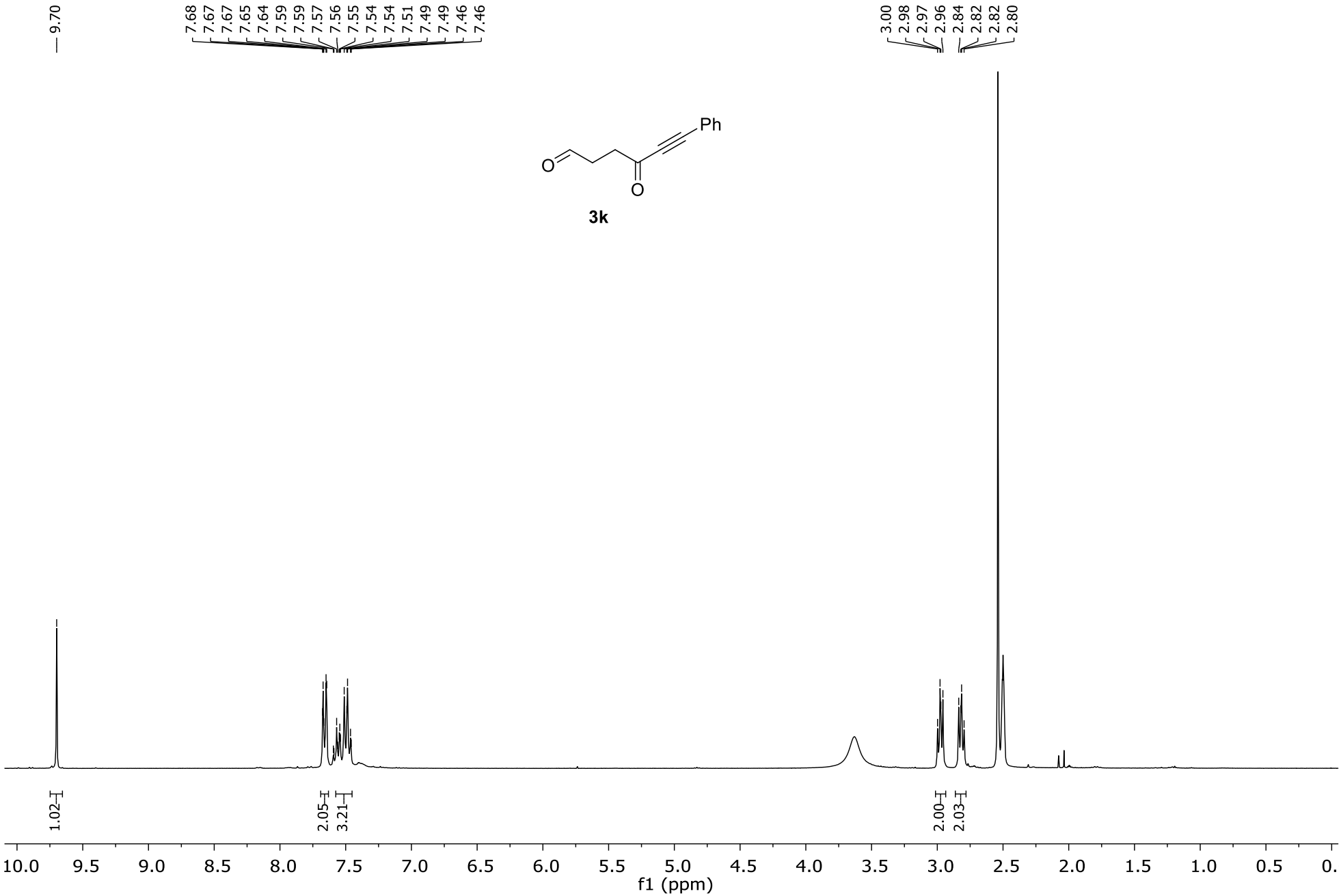


3j

$^{13}C\{^{1}H\}$-RMN (75.4 MHz, DMSO-d_6)

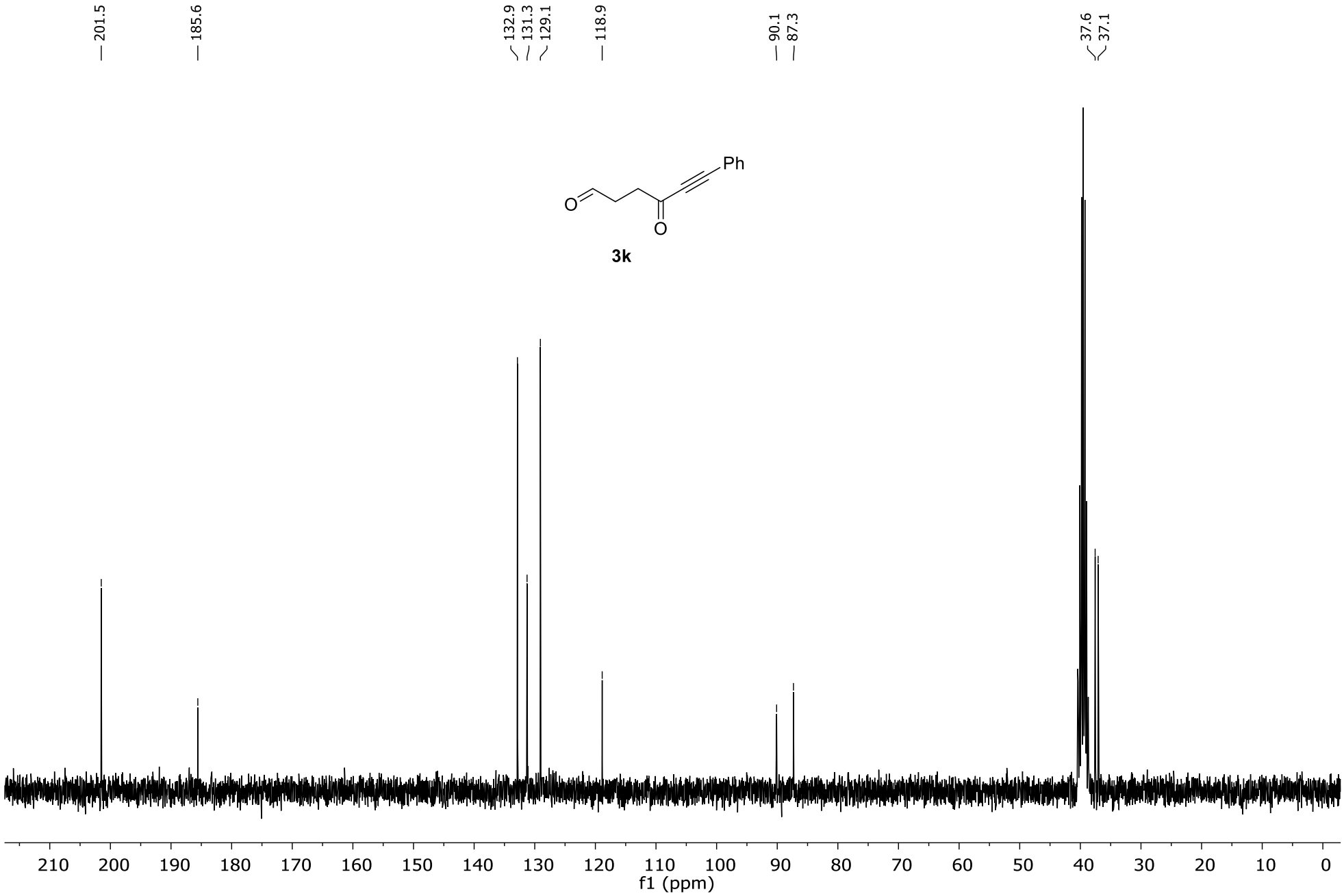


^{1}H-NMR (300 MHz, DMSO-d_6)

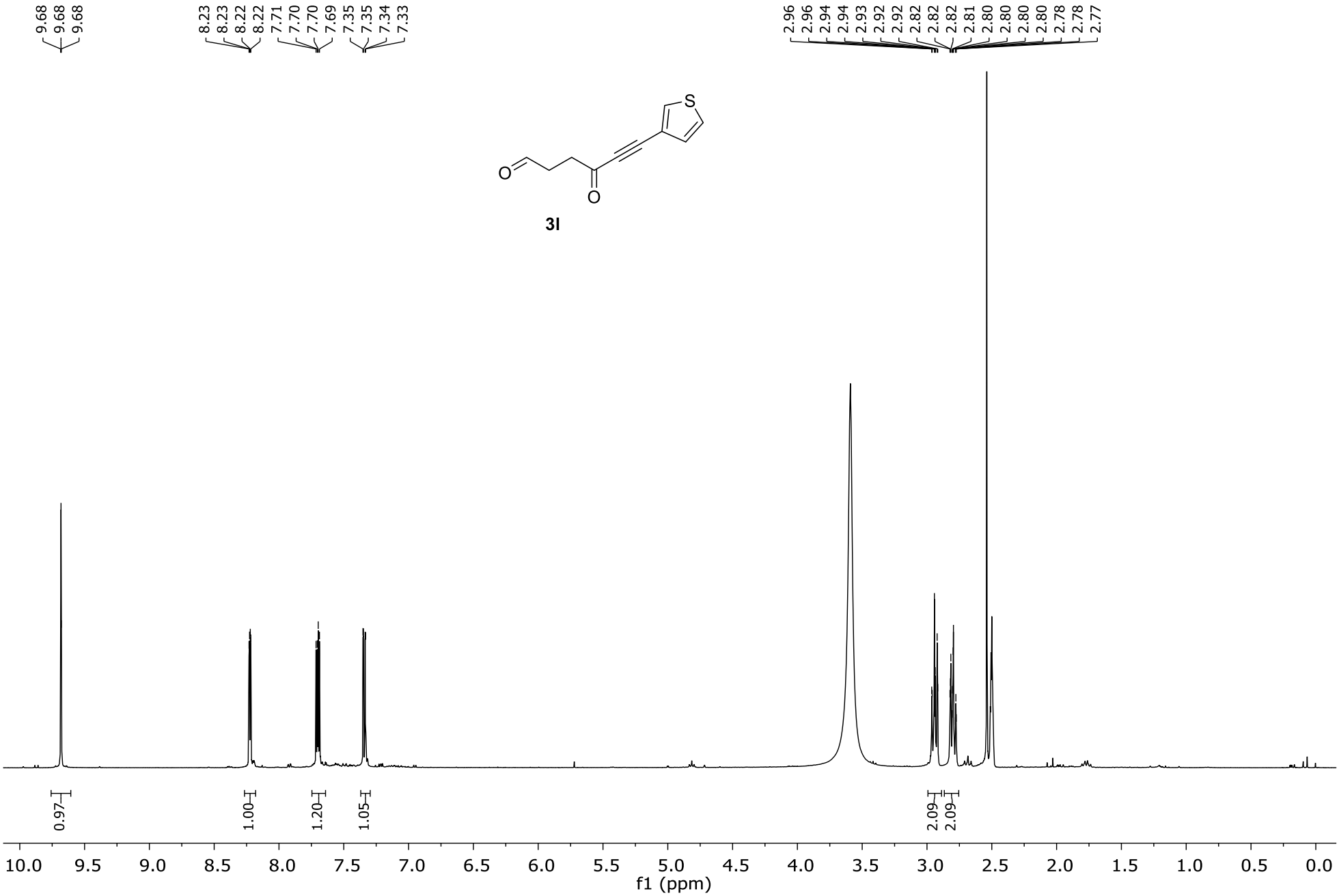


3k

$^{13}C\{^{1}H\}$-RMN (75.4 MHz, DMSO-d_6)

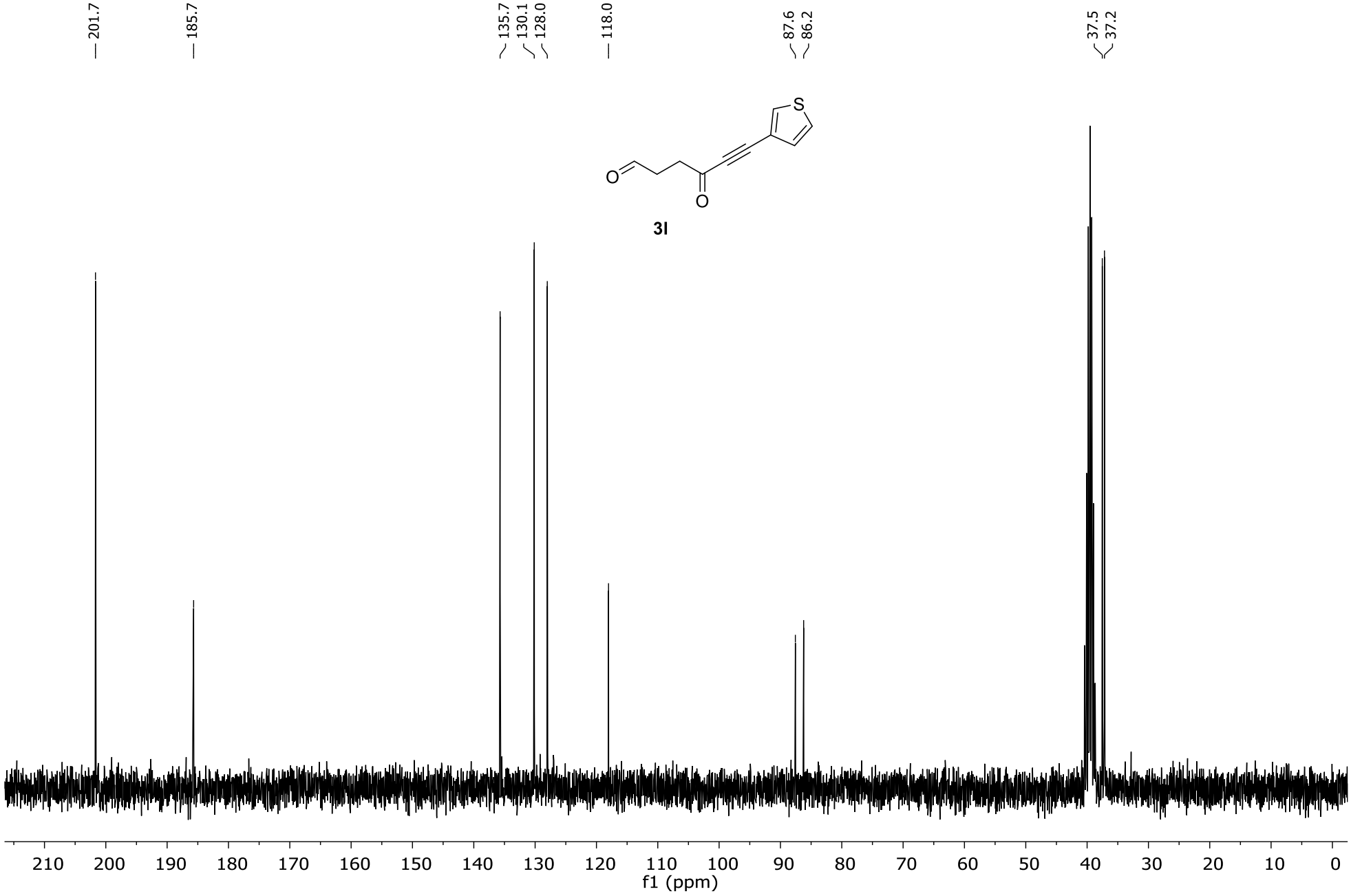


^{1}H-NMR (300 MHz, DMSO-d_6)

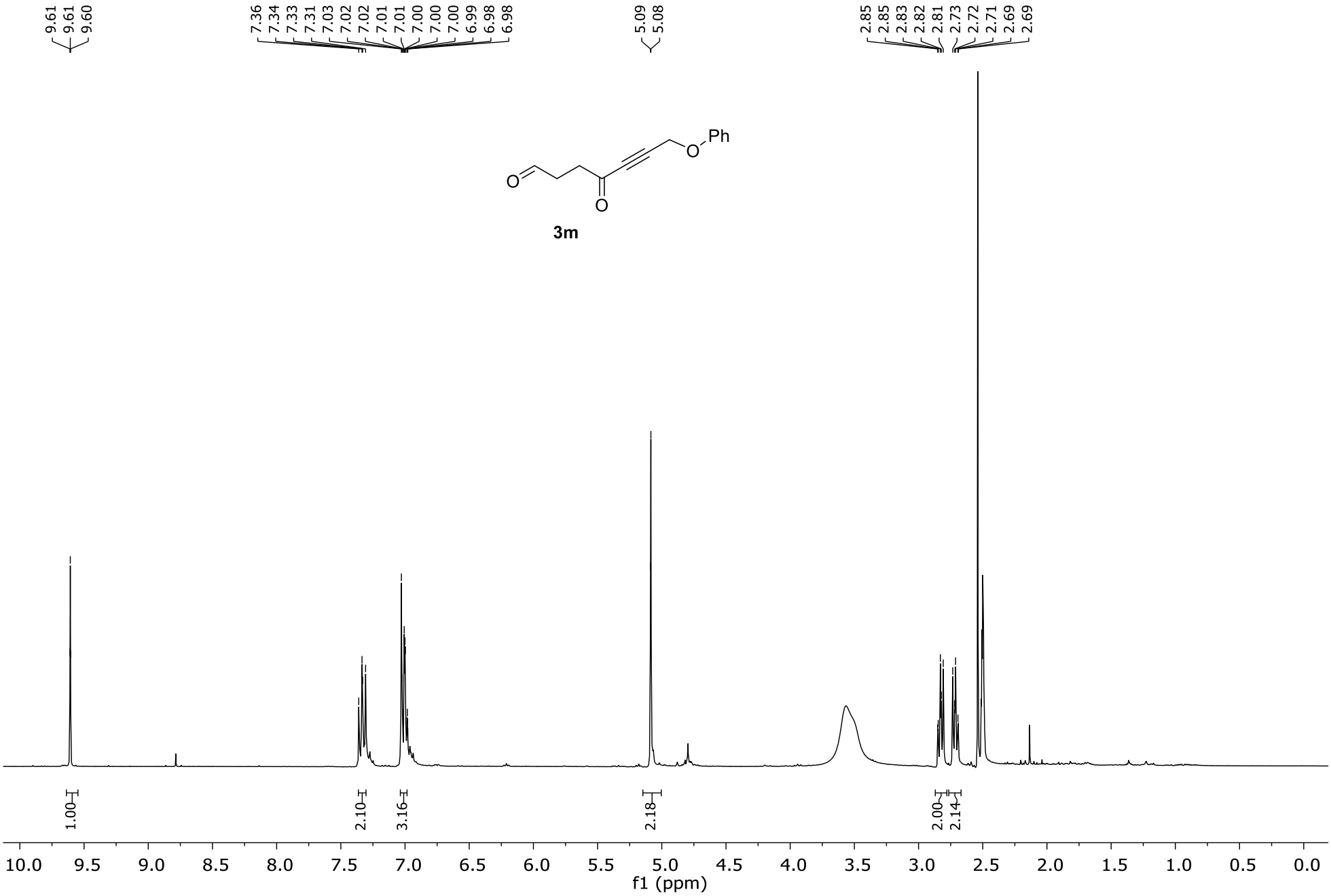


3l

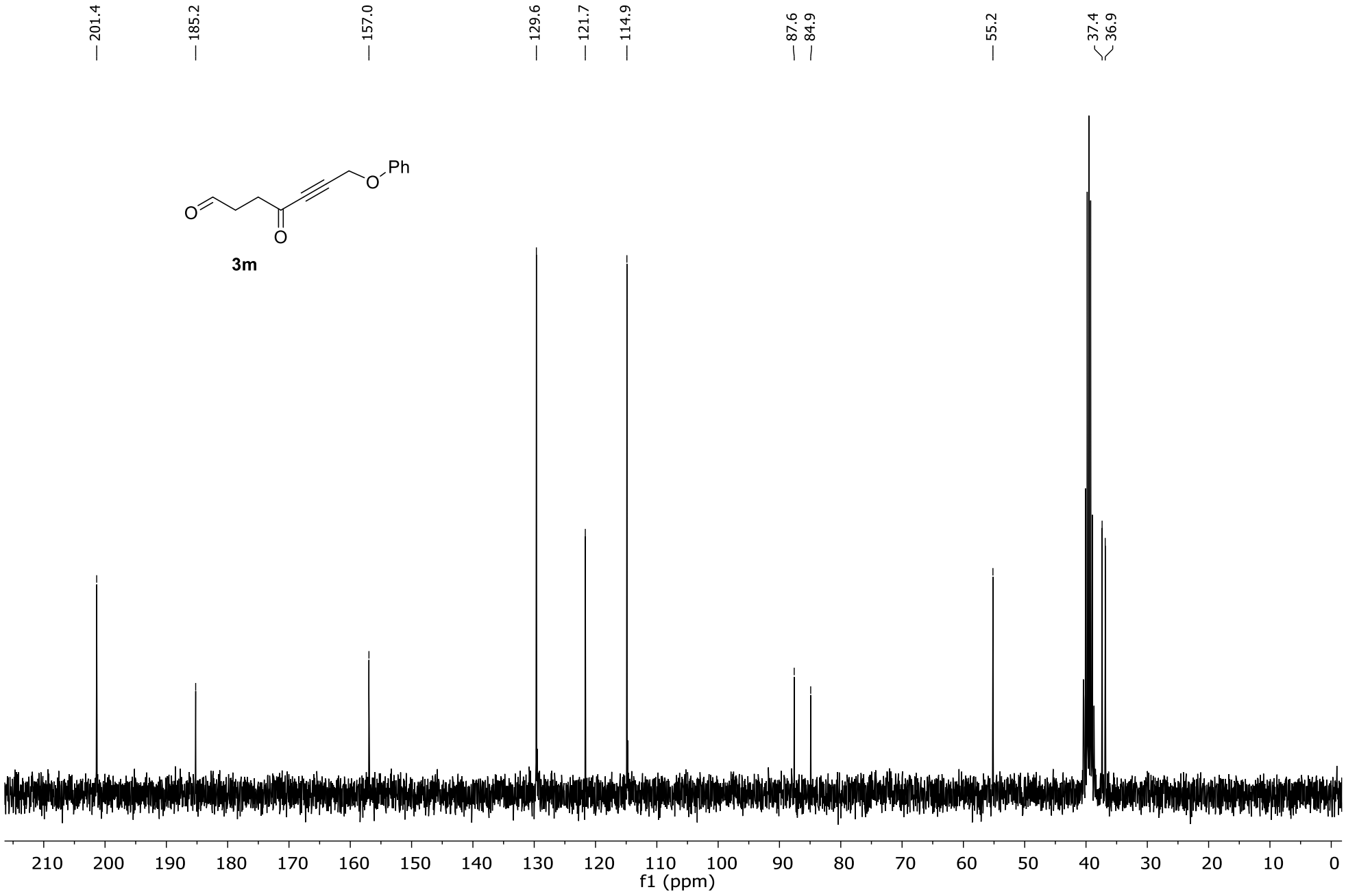
$^{13}C\{^{1}H\}$-RMN (75.4 MHz, DMSO-d_6)



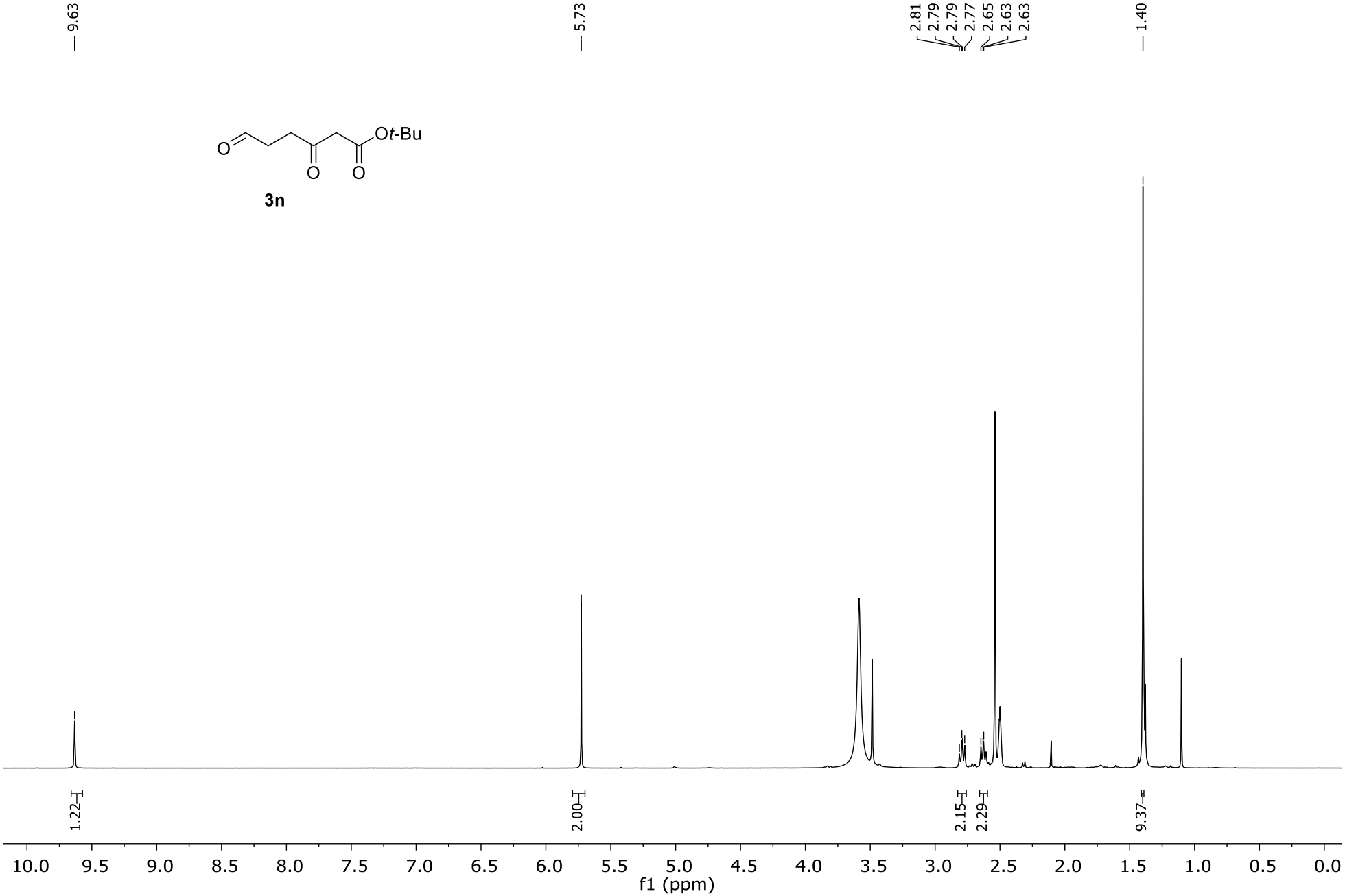
^{1}H-NMR (300 MHz, DMSO-d_6)



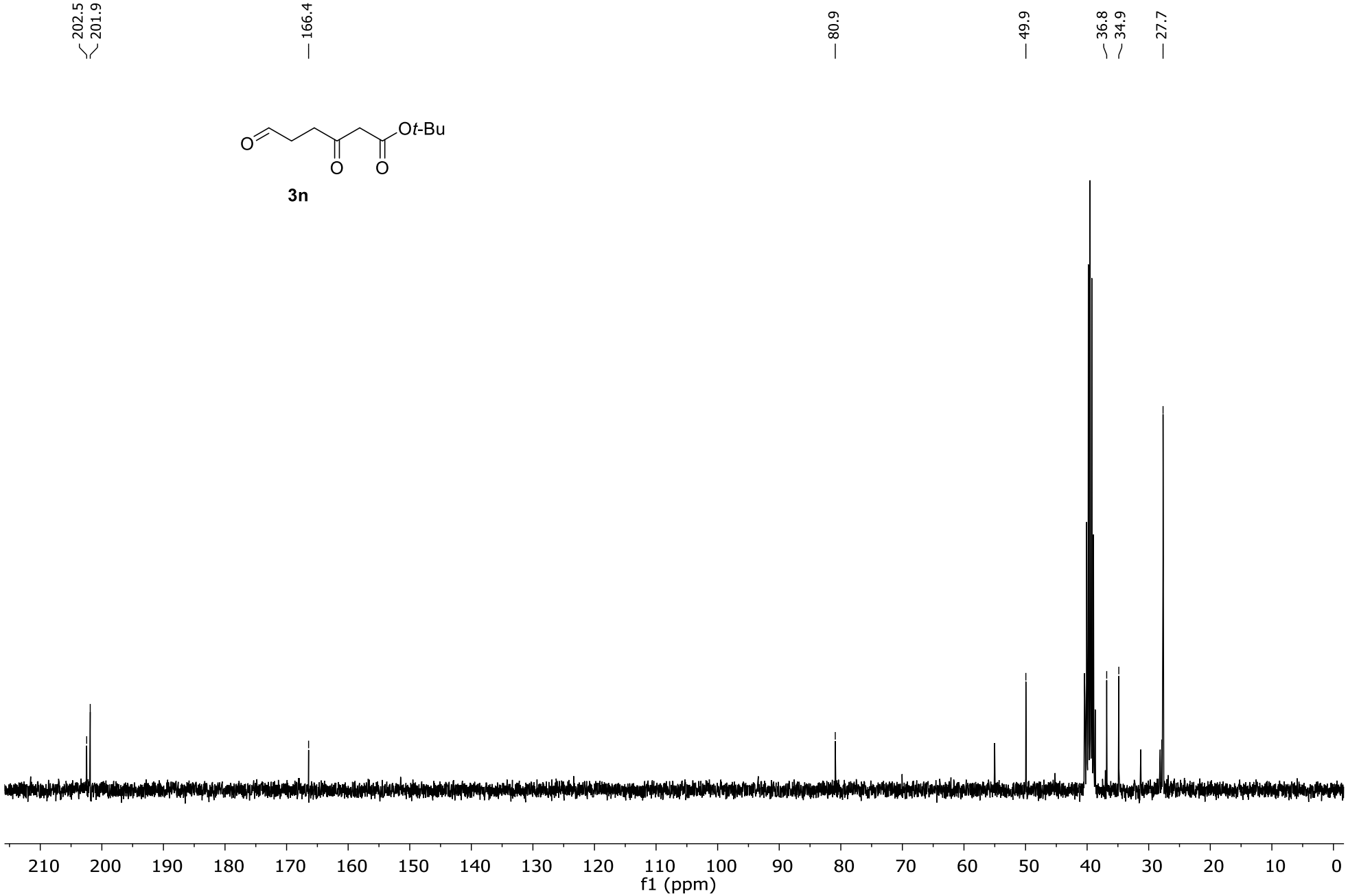
$^{13}C\{^{1}H\}$-RMN (75.4 MHz, DMSO-d_6)



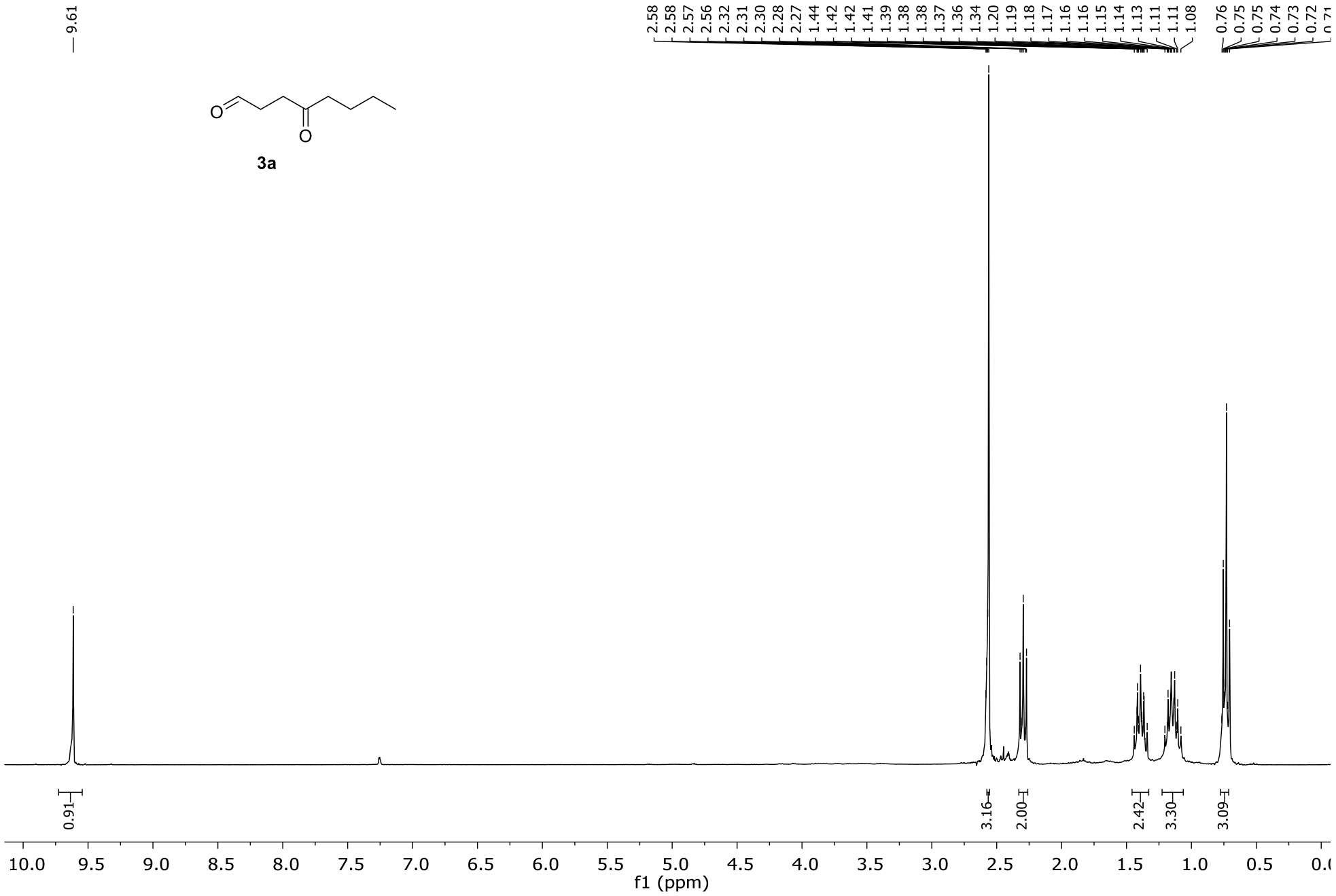
^{1}H-NMR (300 MHz, DMSO-d_6)



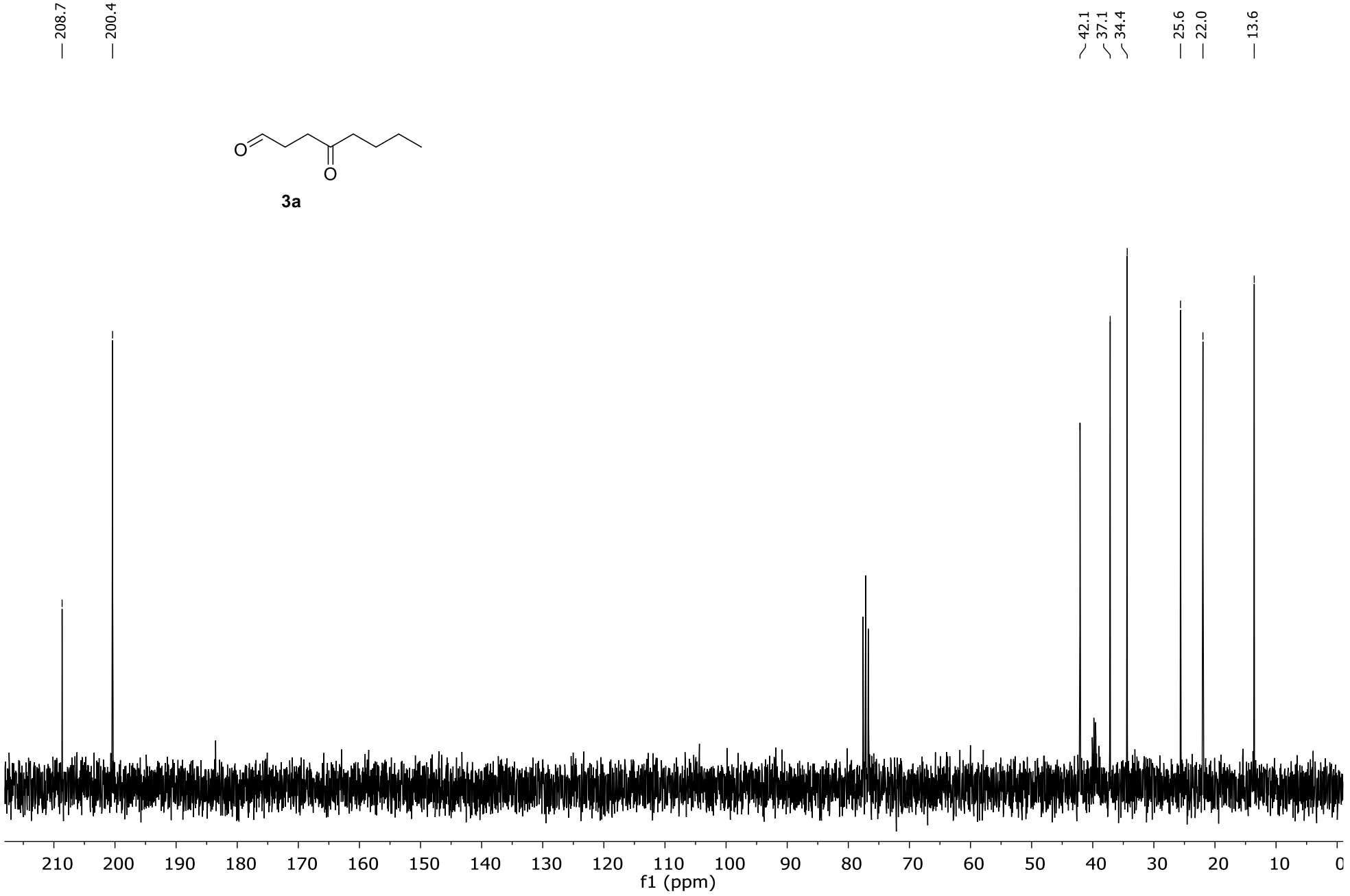
$^{13}C\{^{1}H\}$-RMN (75.4 MHz, DMSO-d_6)



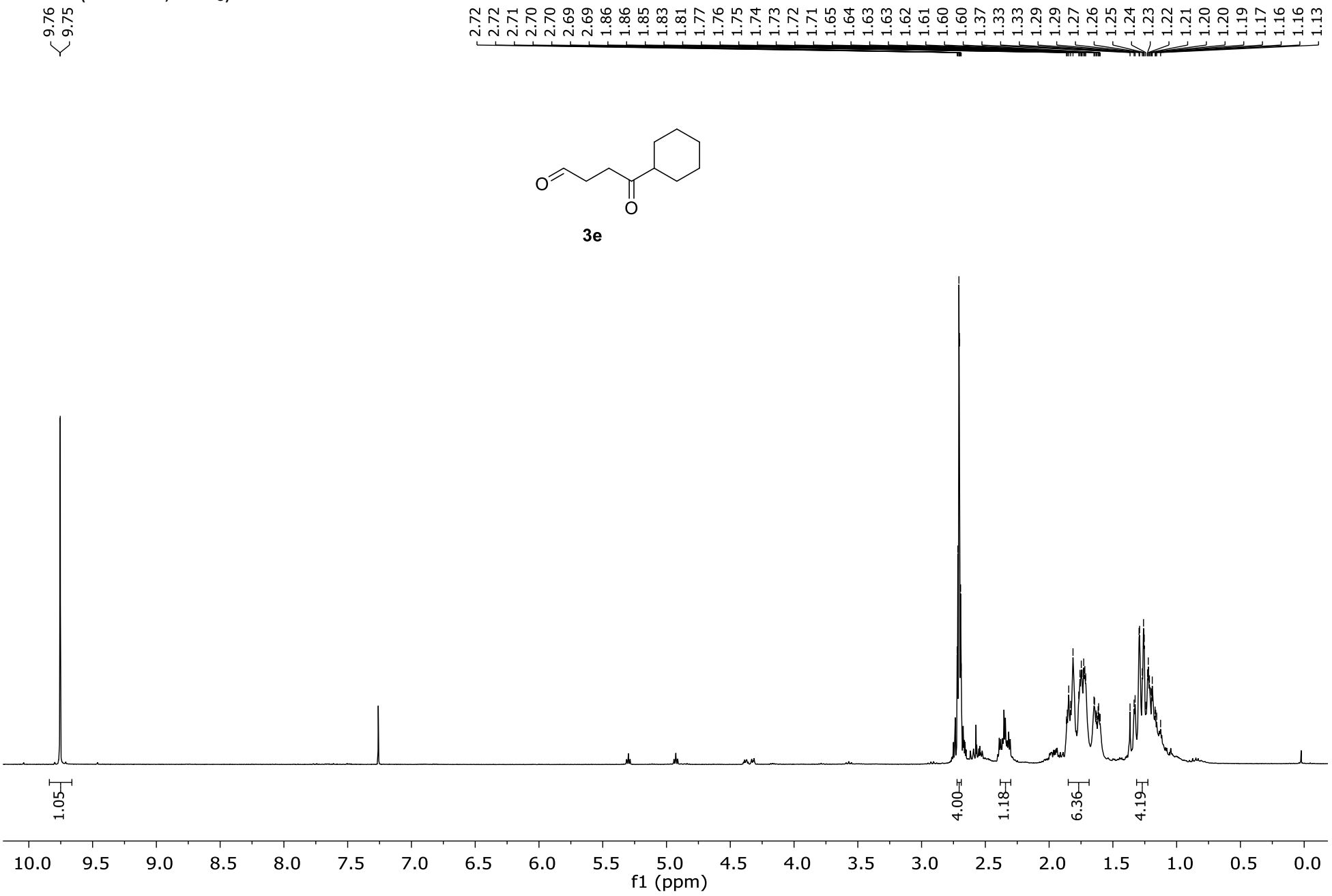
^{1}H-RMN (300 MHz, $CDCl_3$)



$^{13}C\{^{1}H\}$-RMN (75.4 MHz, $CDCl_3$)

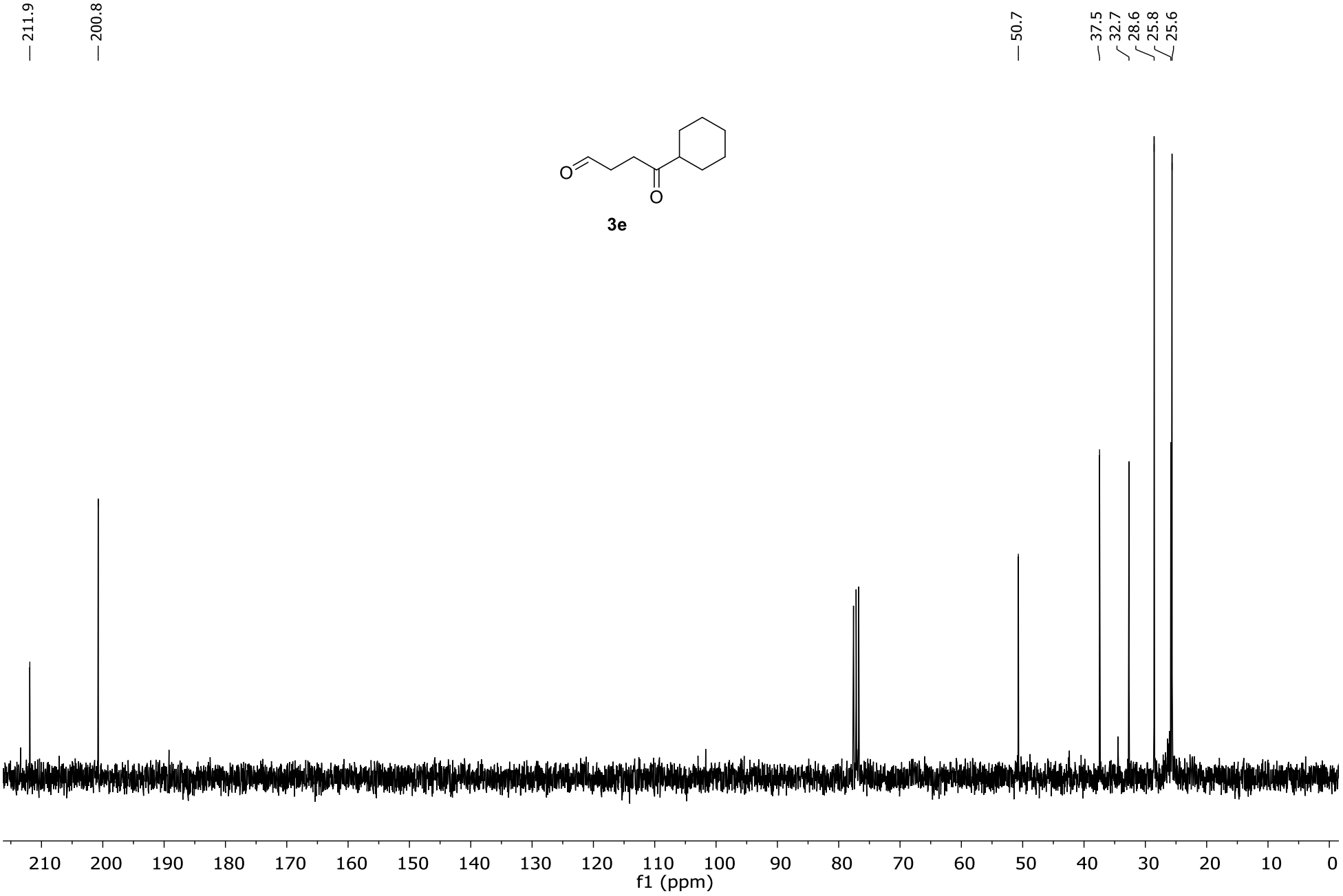


^{1}H-RMN (300 MHz, $CDCl_3$)

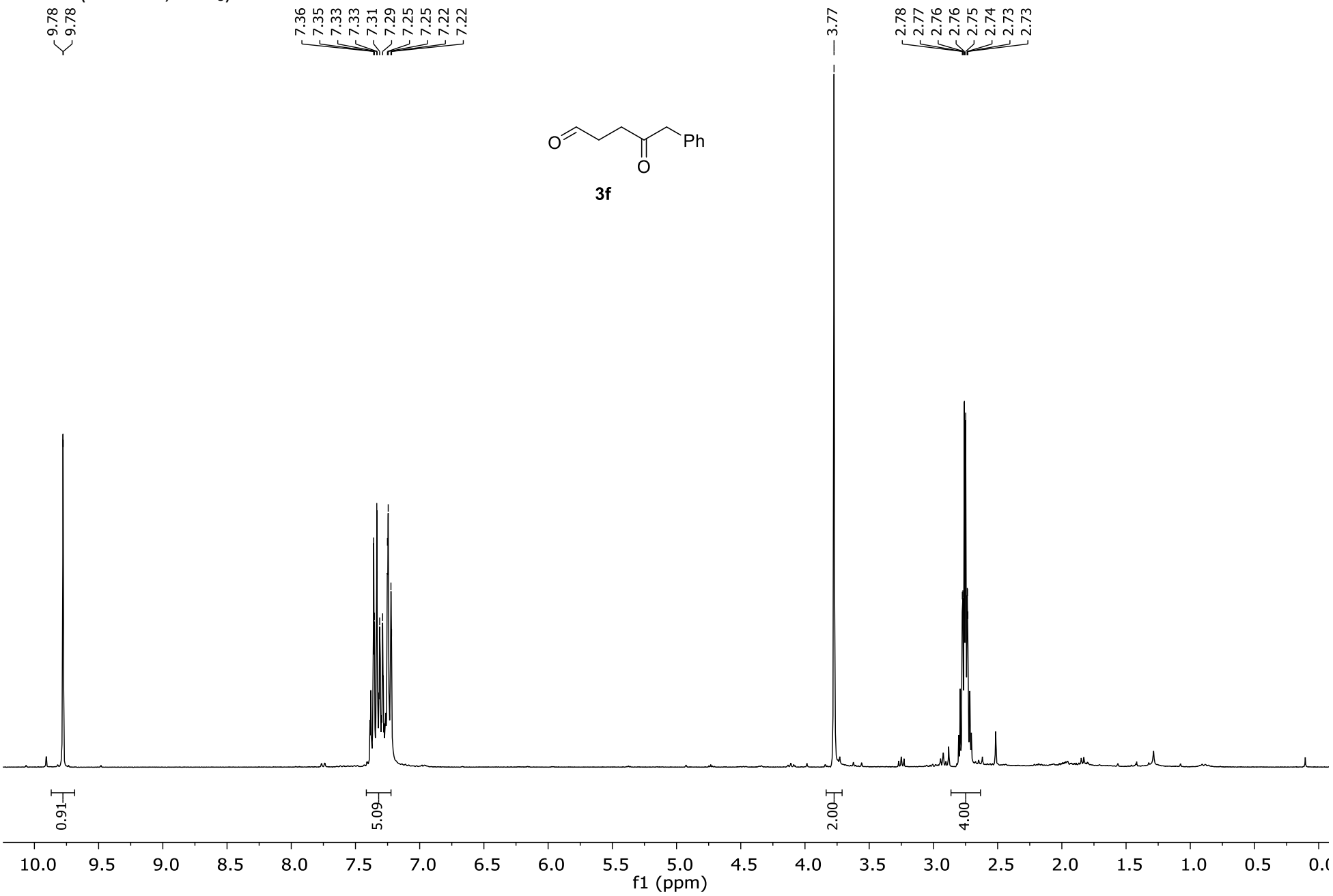


3e

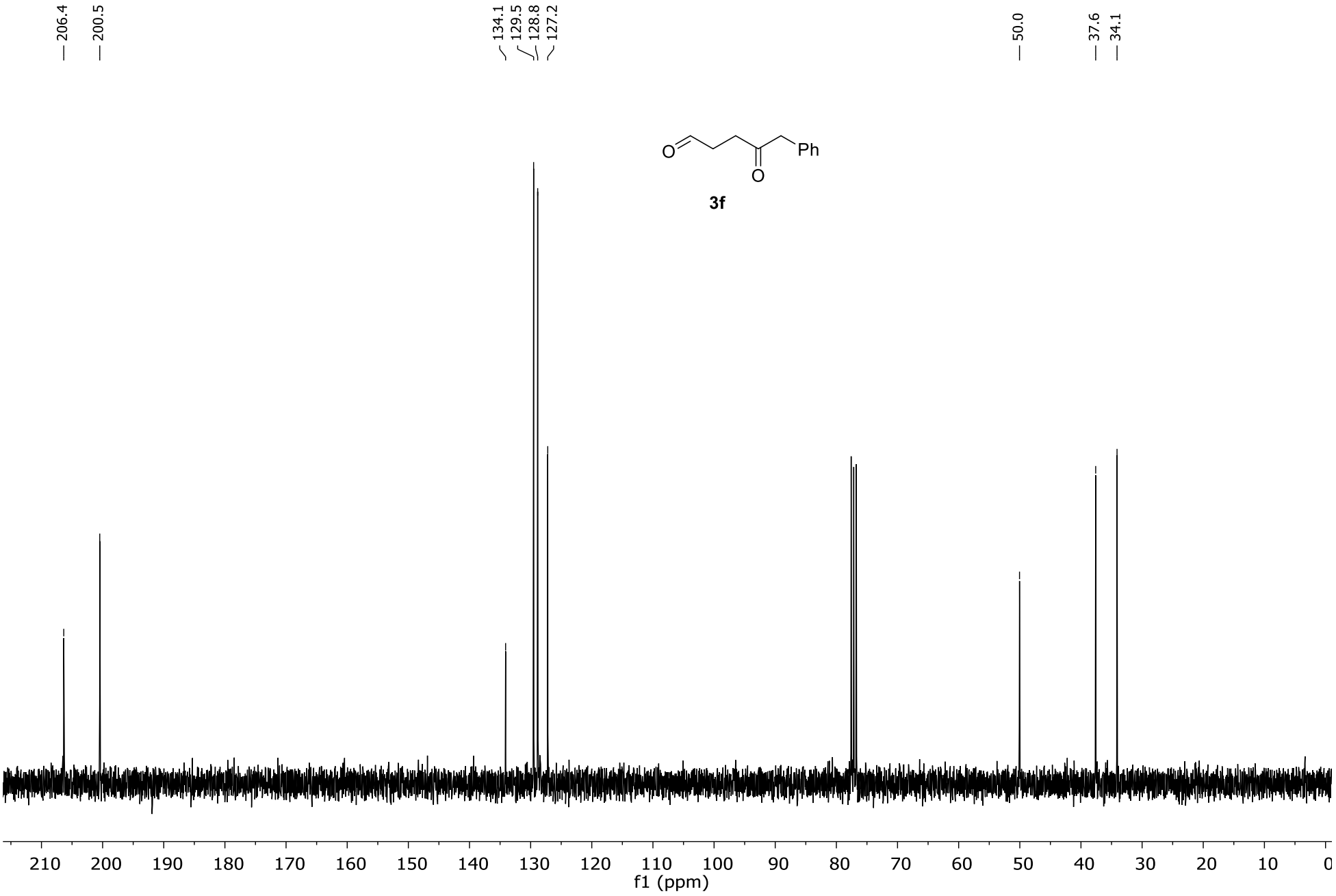
$^{13}C\{^{1}H\}$-RMN (75.4 MHz, $CDCl_3$)



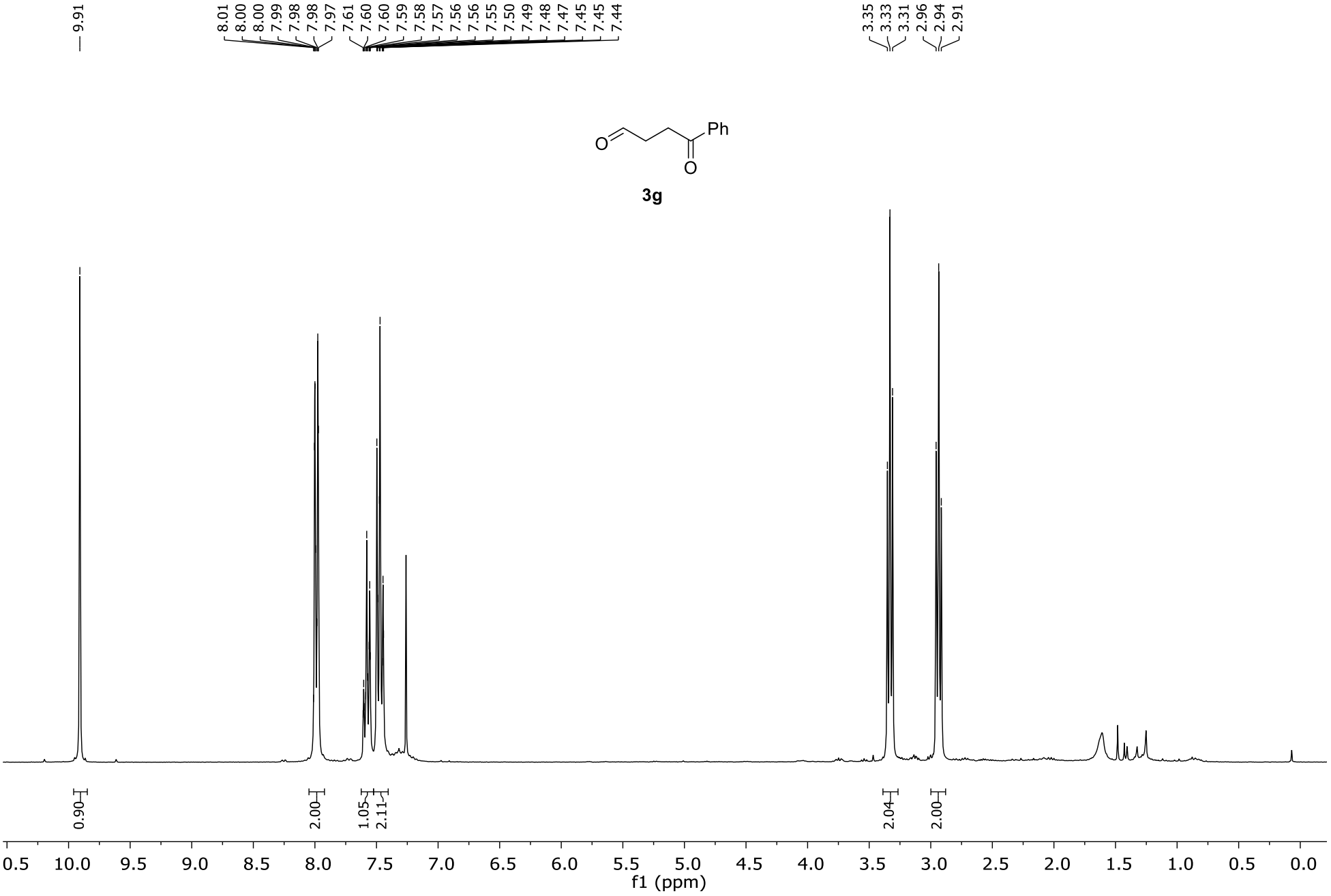
^{1}H-RMN (300 MHz, $CDCl_3$)



$^{13}C\{^{1}H\}$-RMN (75.4 MHz, $CDCl_3$)

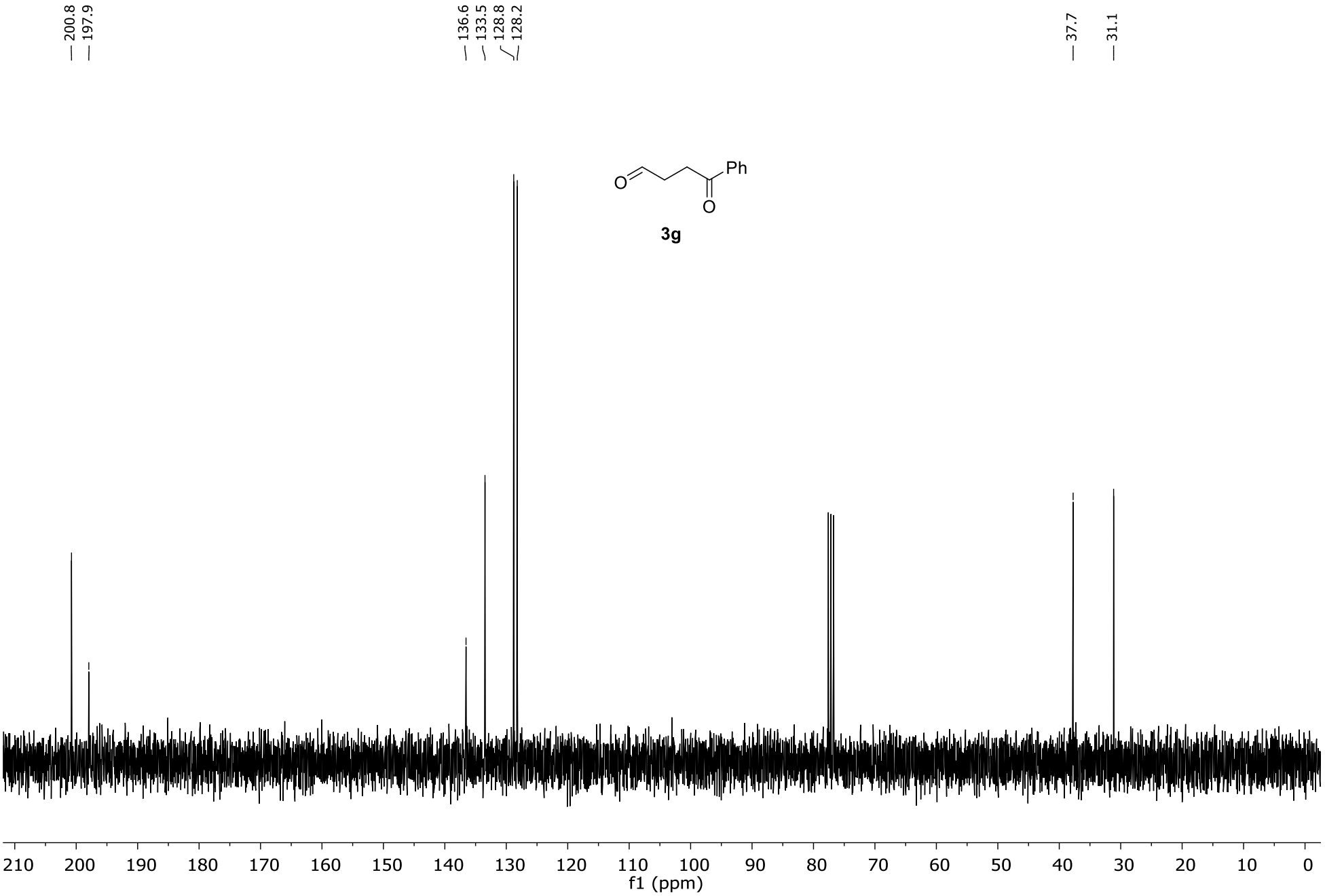


^{1}H-RMN (300 MHz, $CDCl_3$)

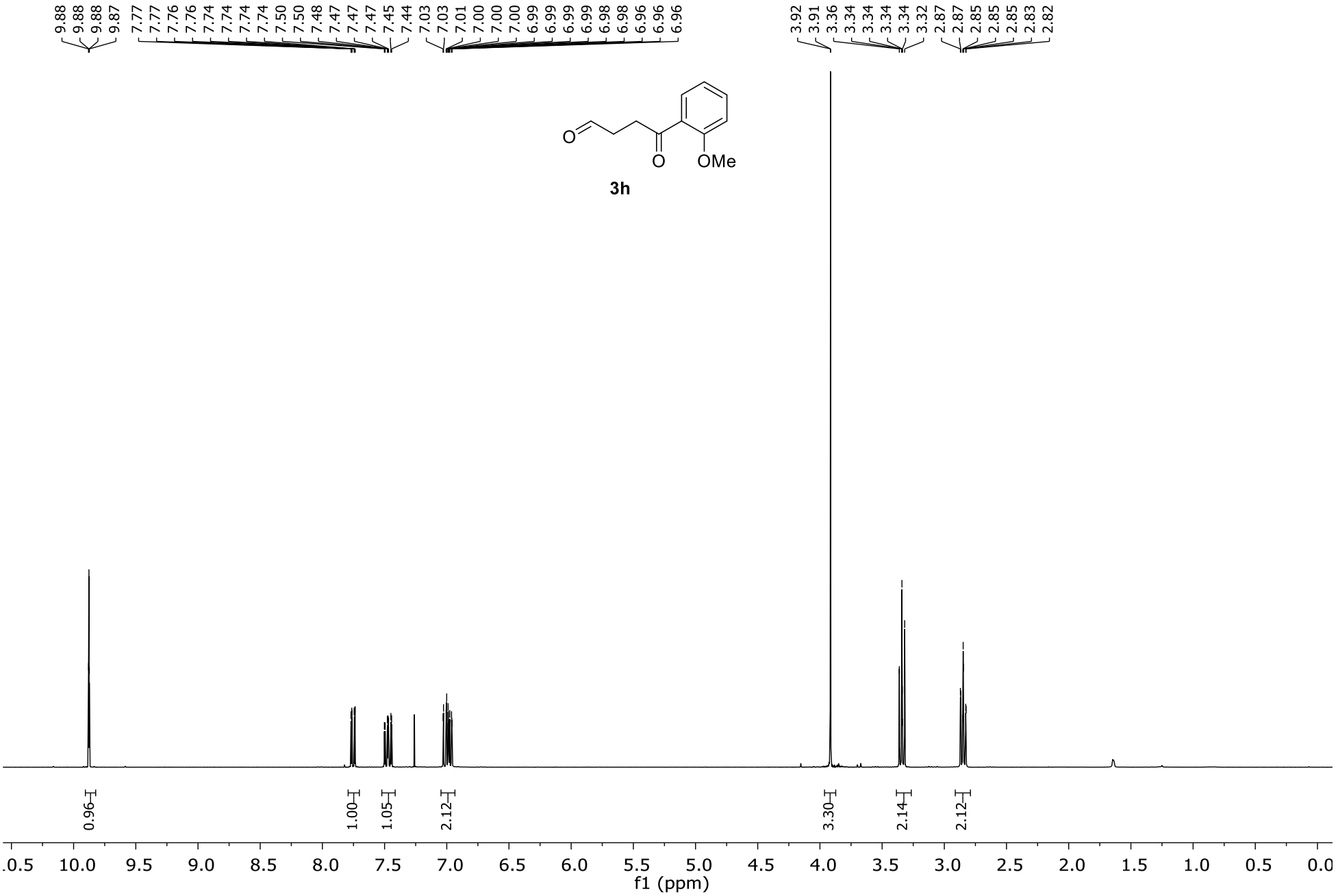


3g

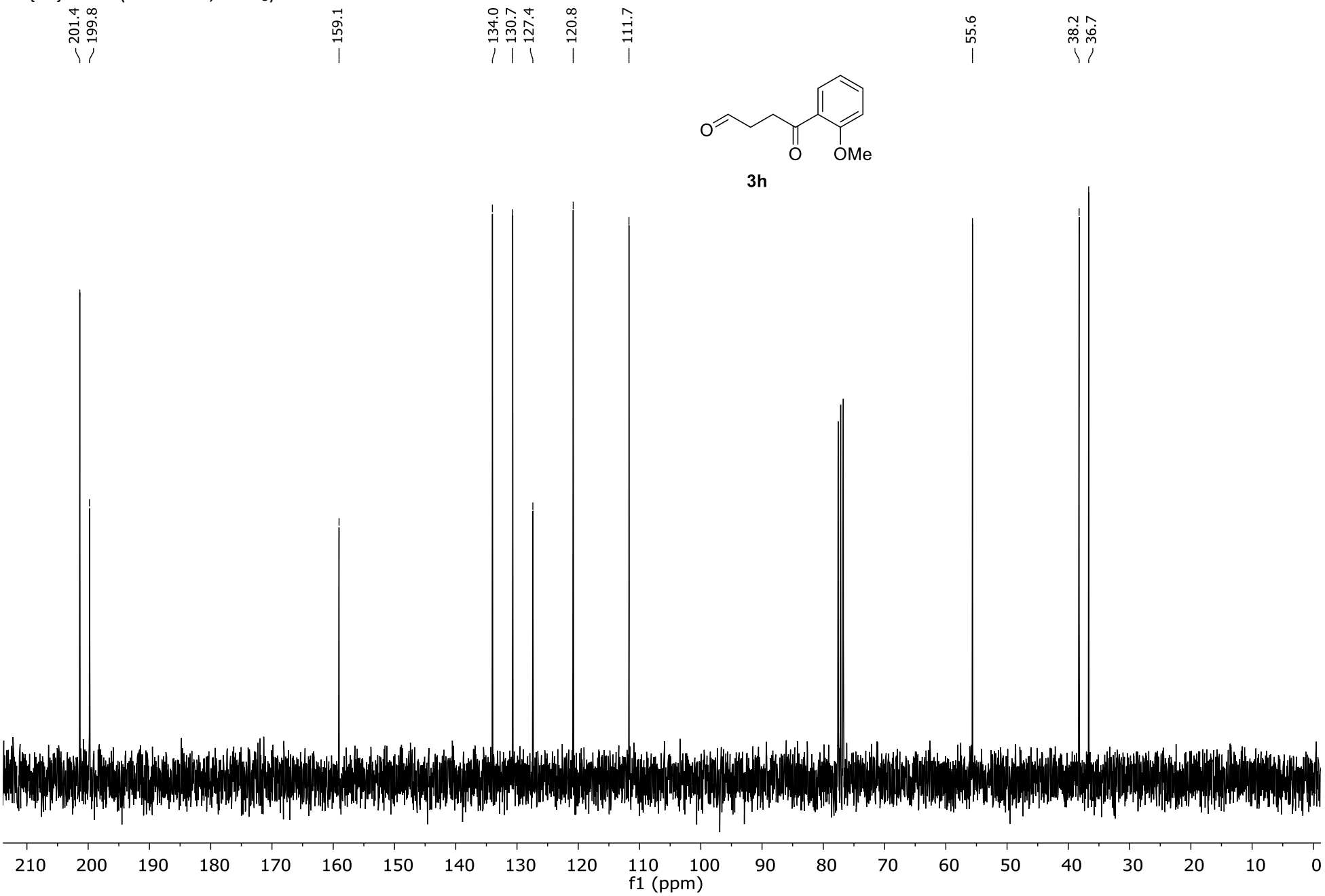
$^{13}C\{^{1}H\}$-RMN (75.4 MHz, $CDCl_3$)



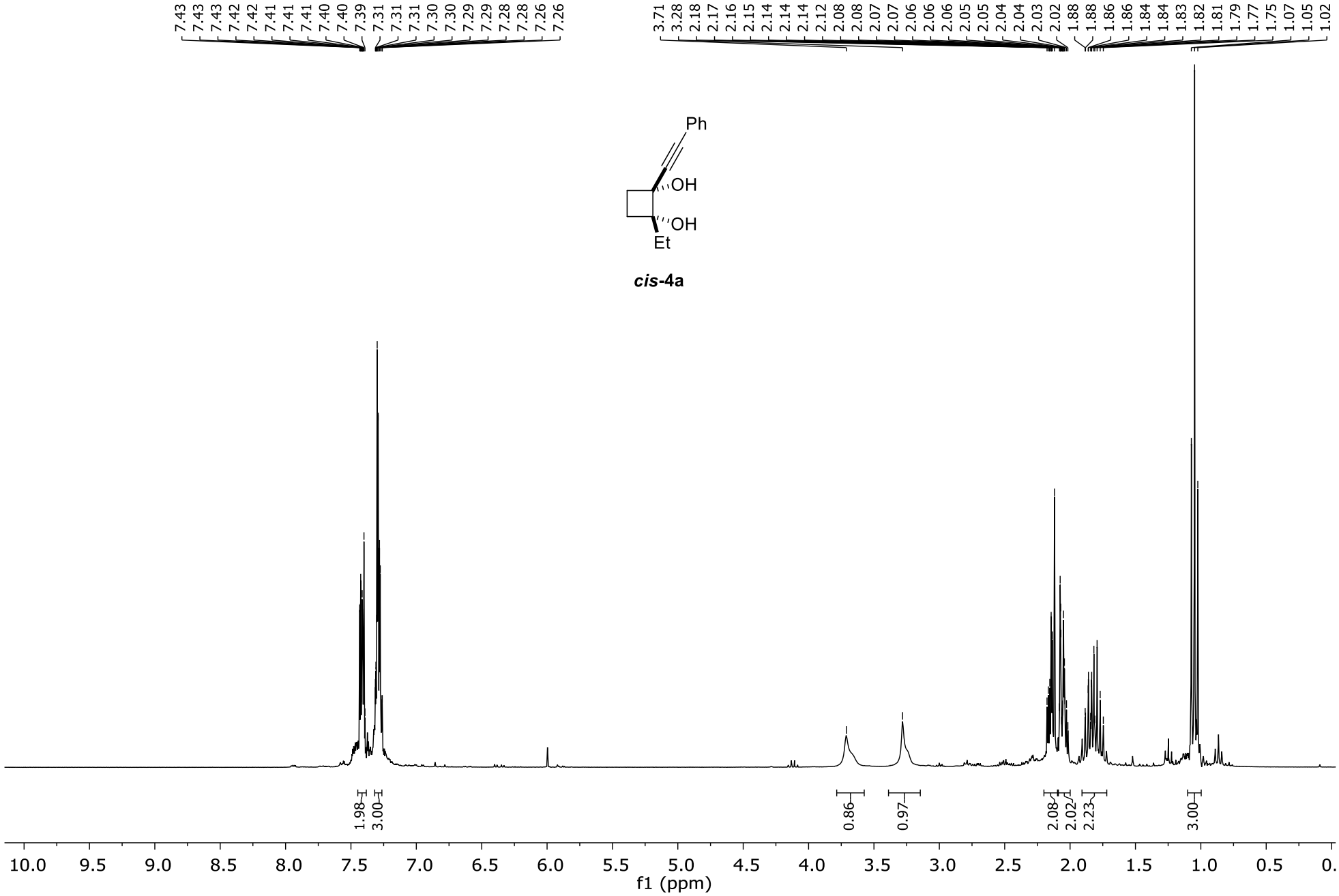
^{1}H-RMN (300 MHz, $CDCl_3$)



$^{13}C\{^{1}H\}$-RMN (75.4 MHz, $CDCl_3$)

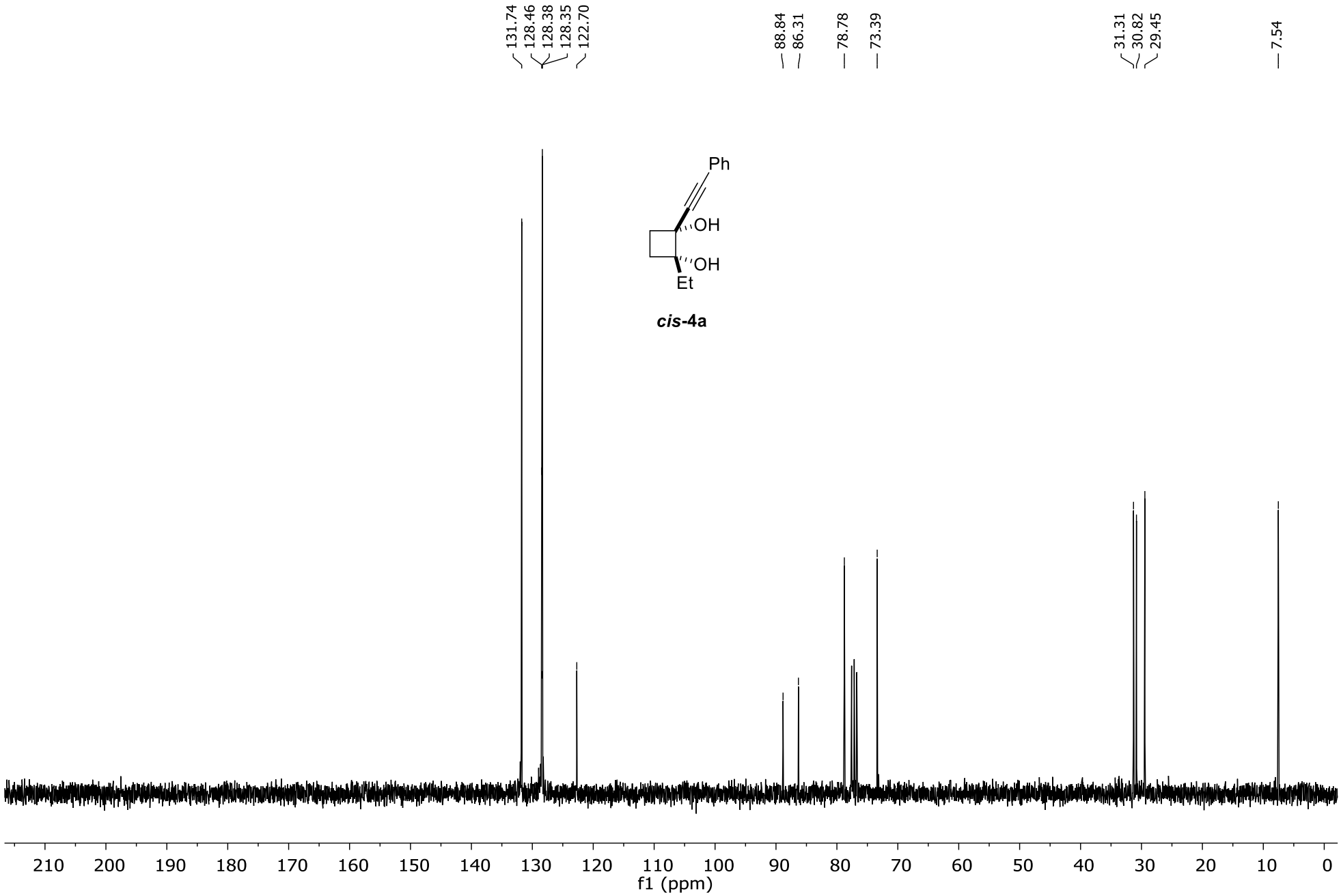


^{1}H-RMN (300 MHz, $CDCl_3$)

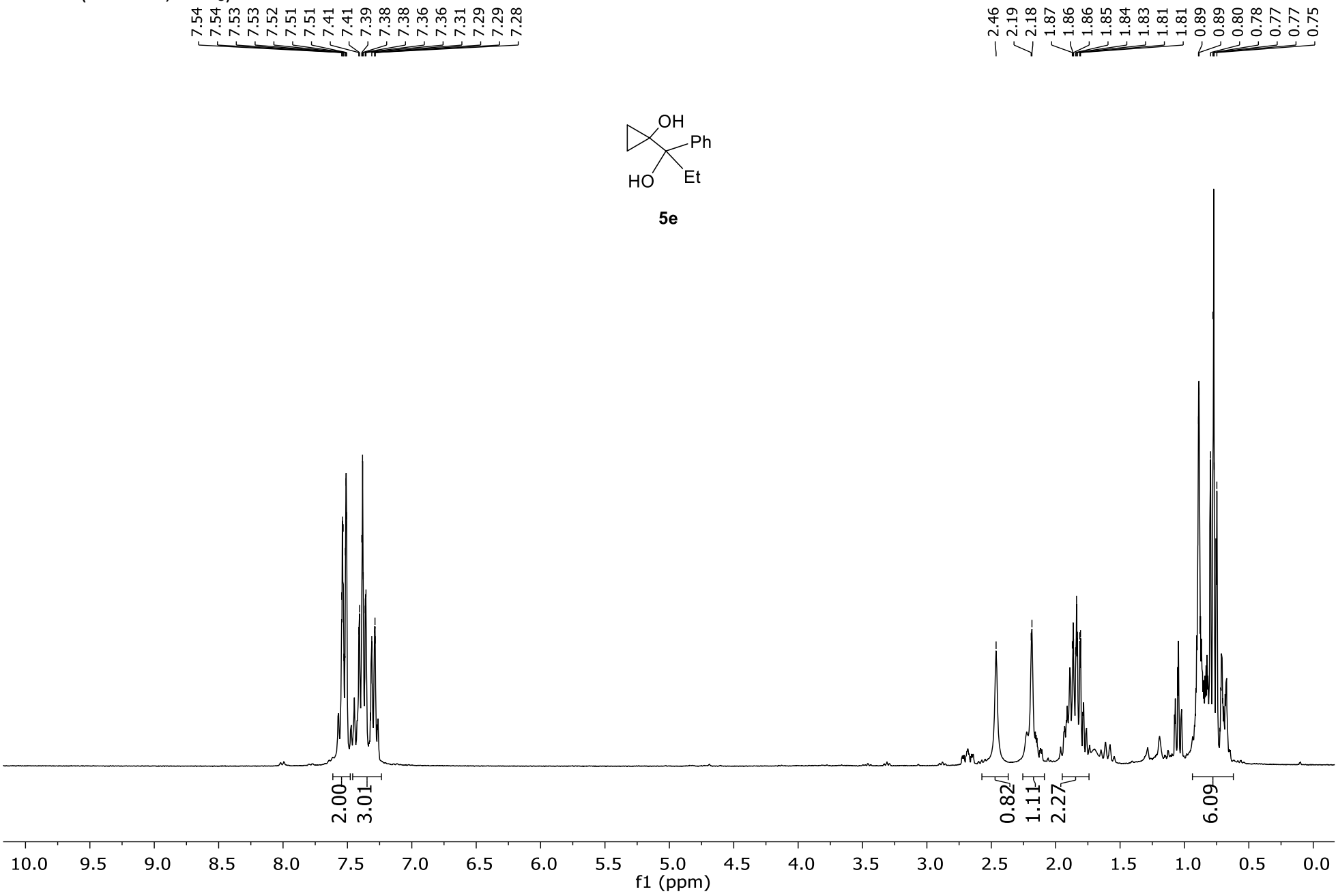


***cis*-4a**

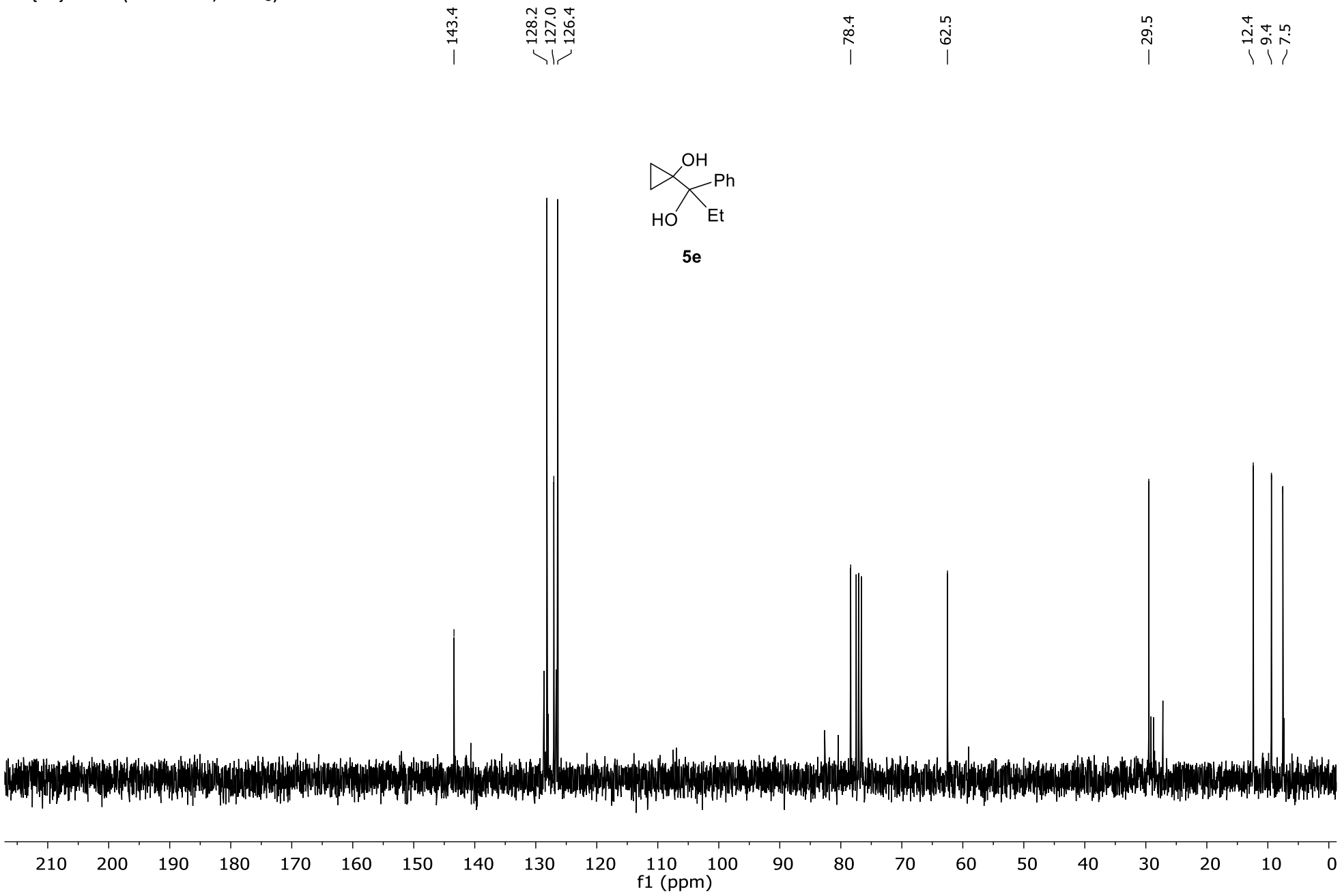
$^{13}C\{^{1}H\}$-RMN (75.4 MHz, $CDCl_3$)



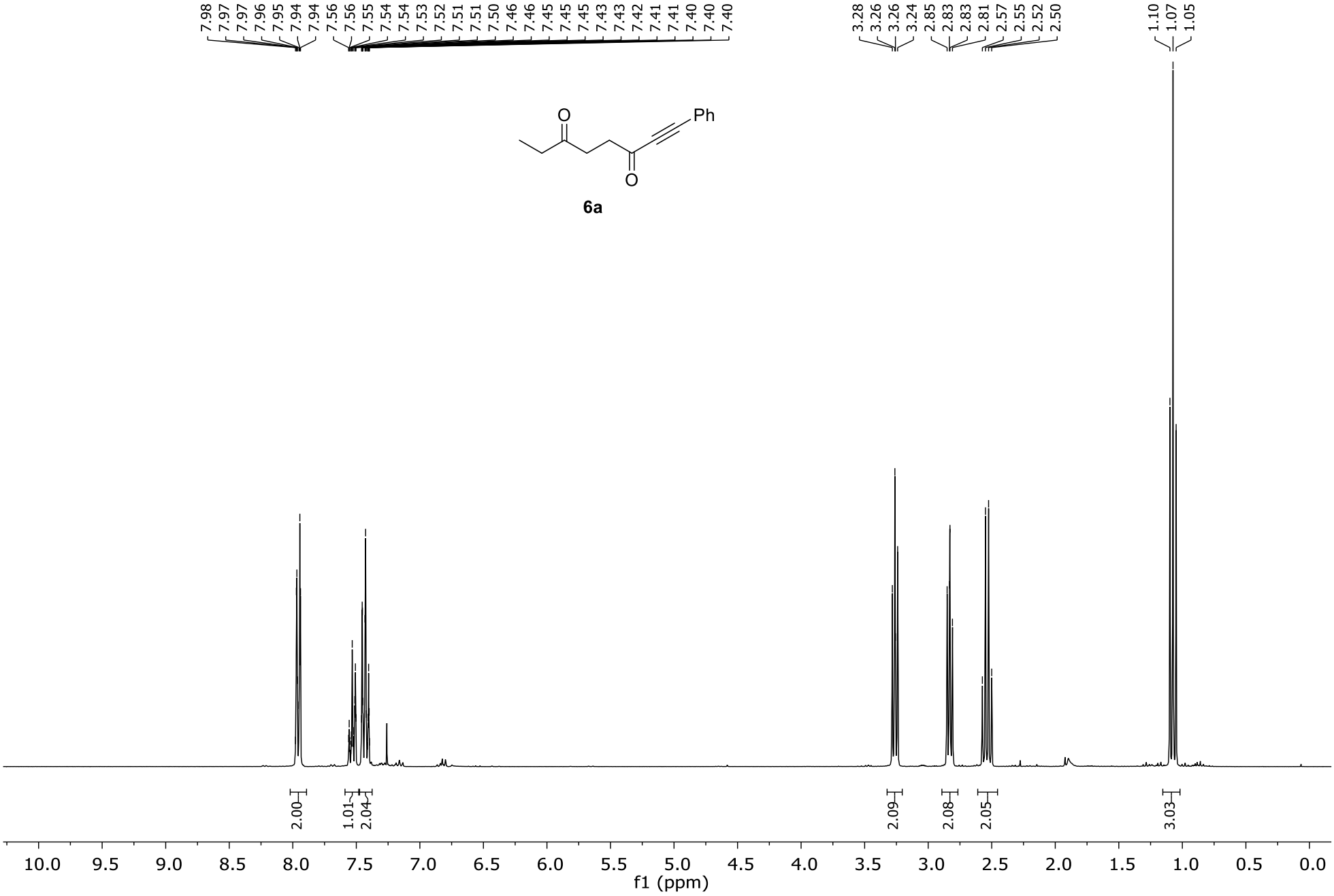
^{1}H-RMN (300 MHz, $CDCl_3$)



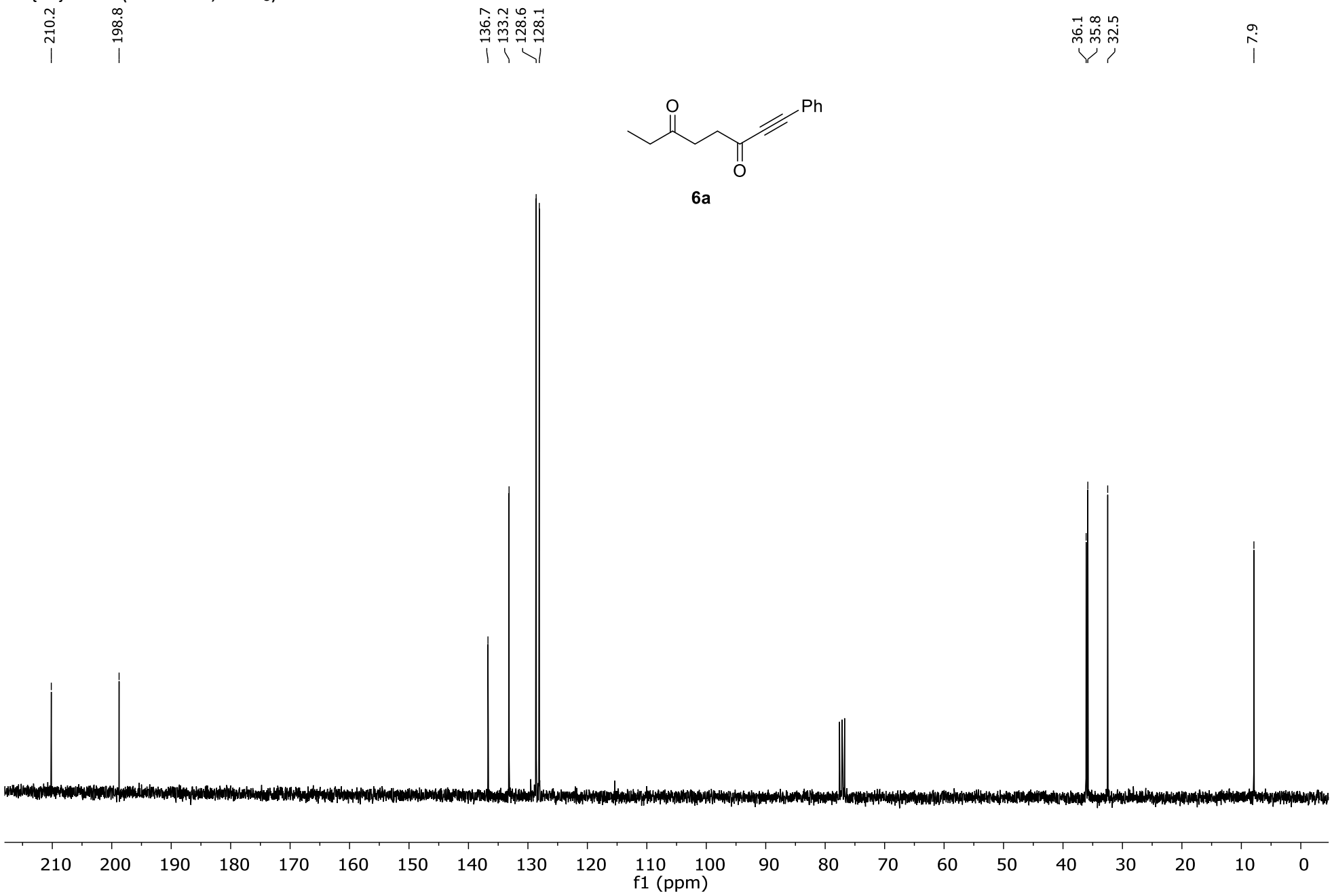
$^{13}C\{^{1}H\}$-RMN (75.4 MHz, $CDCl_3$)



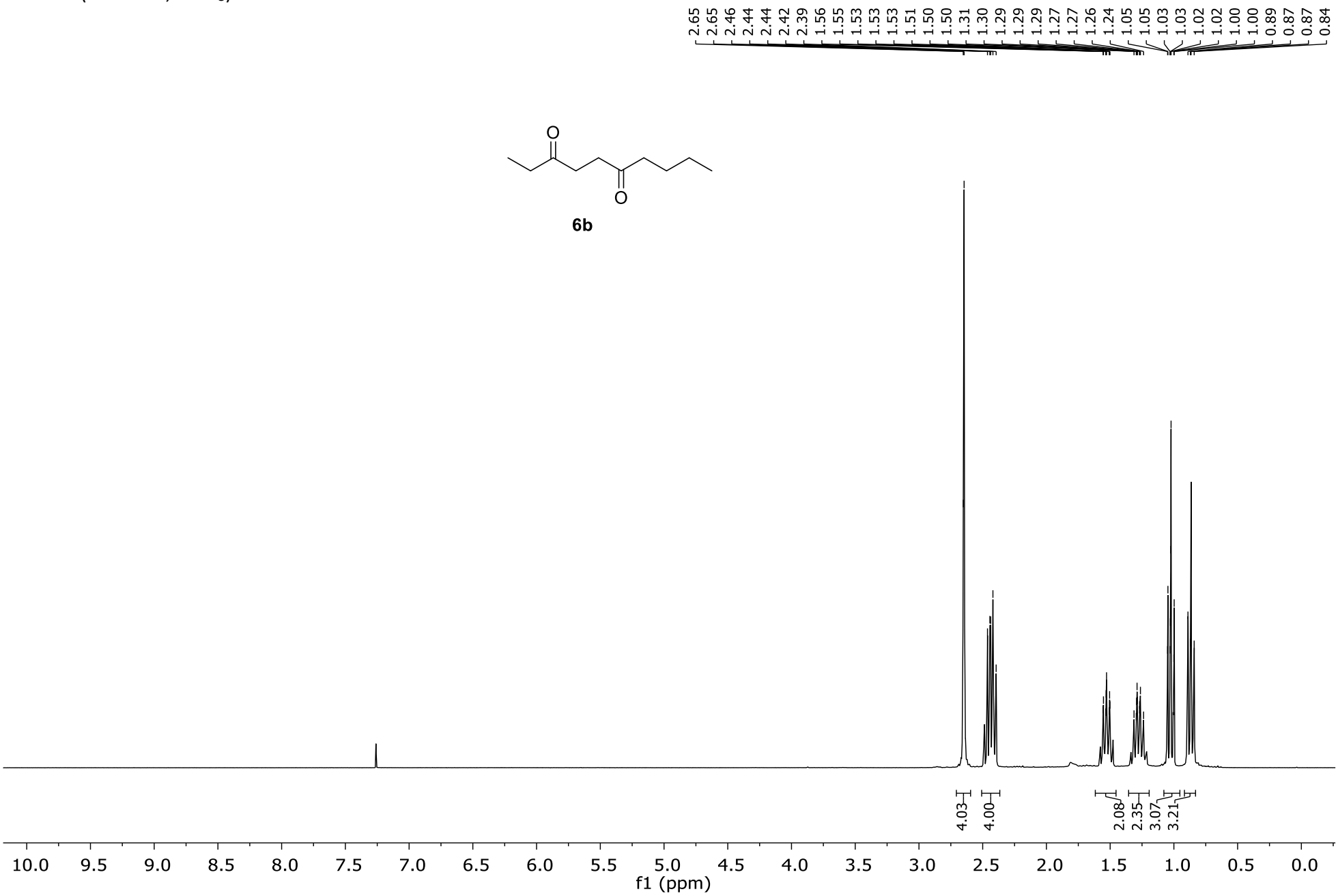
^{1}H-RMN (300 MHz, $CDCl_3$)



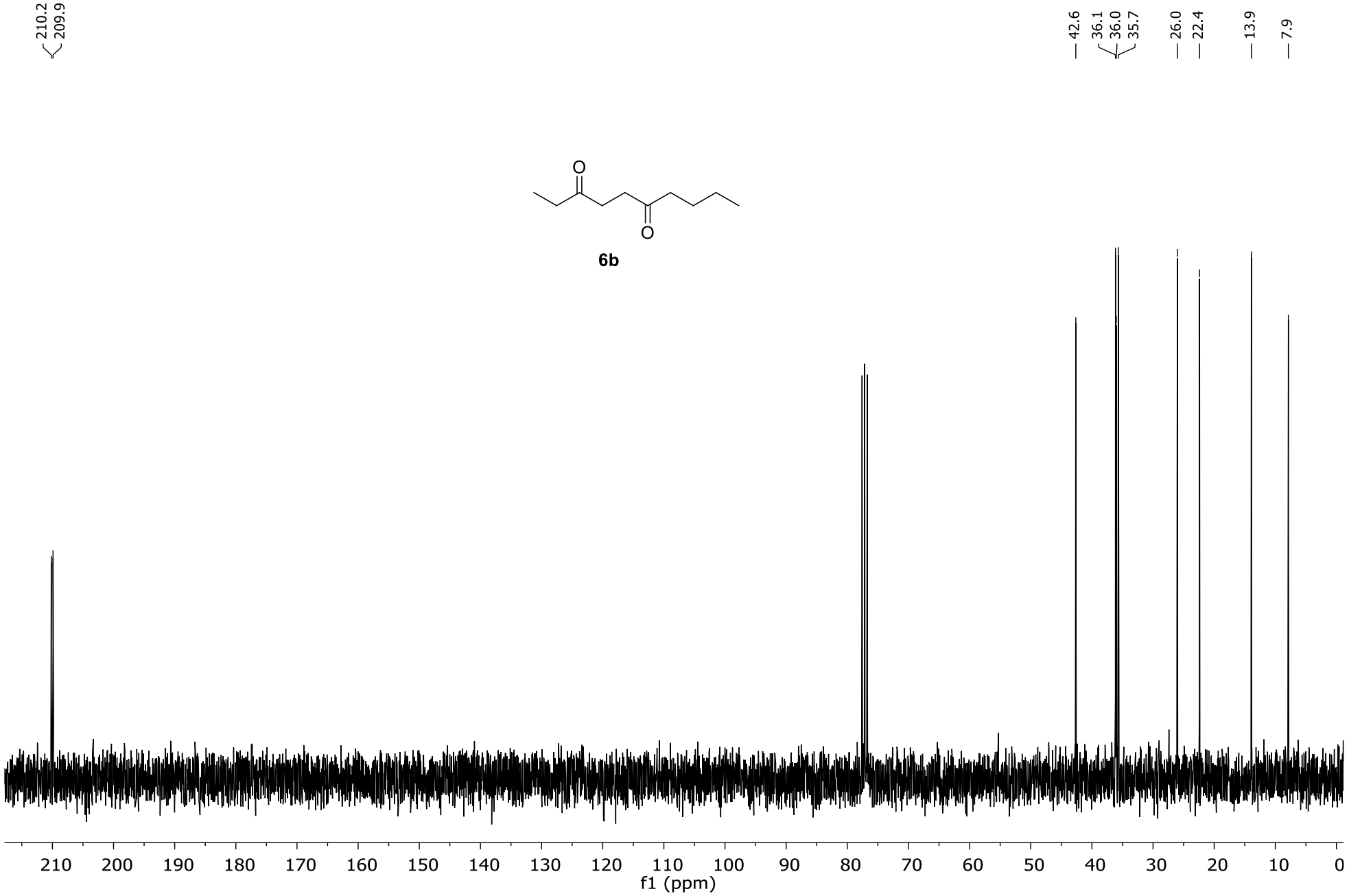
$^{13}C\{^{1}H\}$-RMN (75.4 MHz, $CDCl_3$)



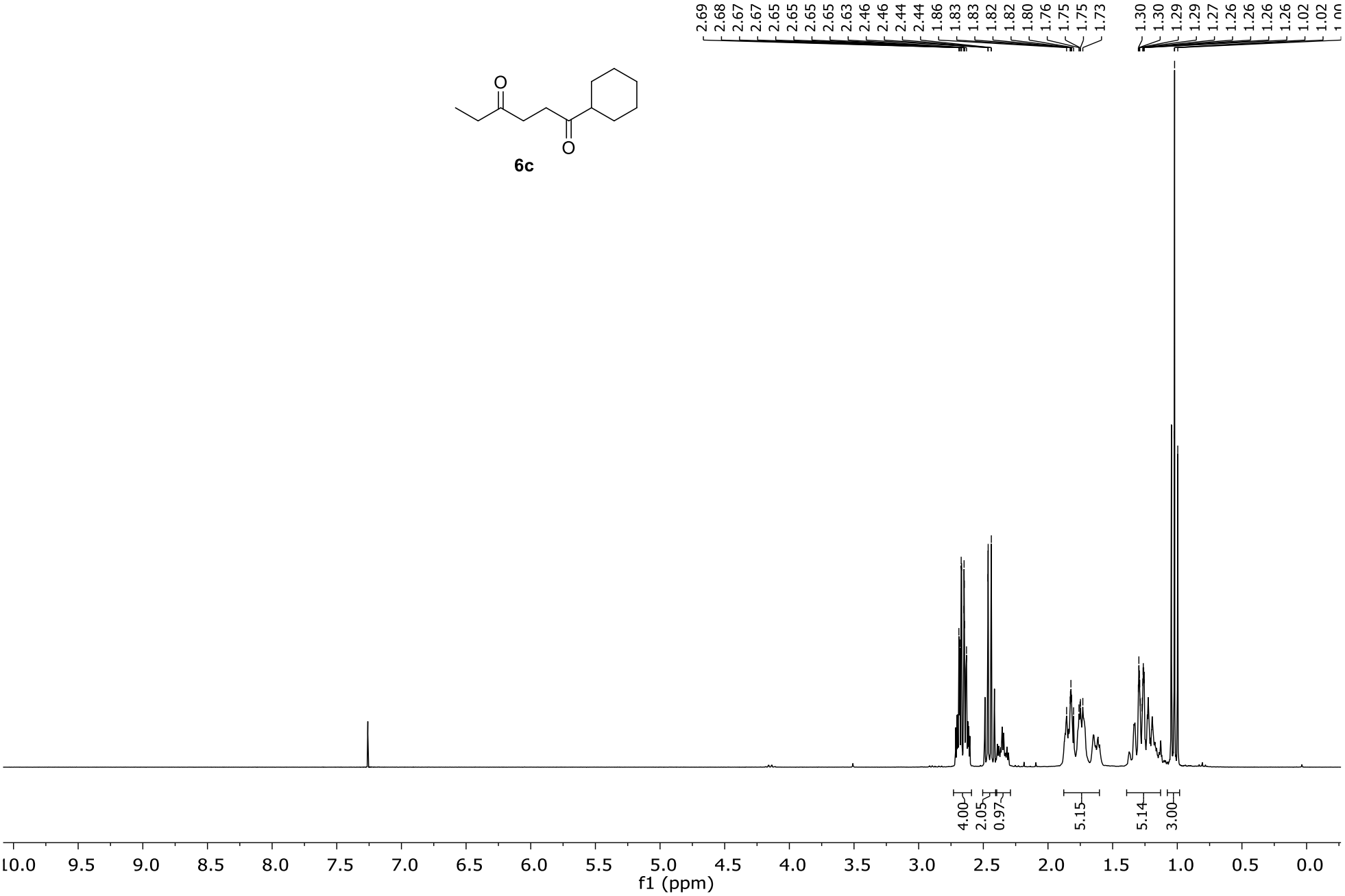
^{1}H-RMN (300 MHz, $CDCl_3$)



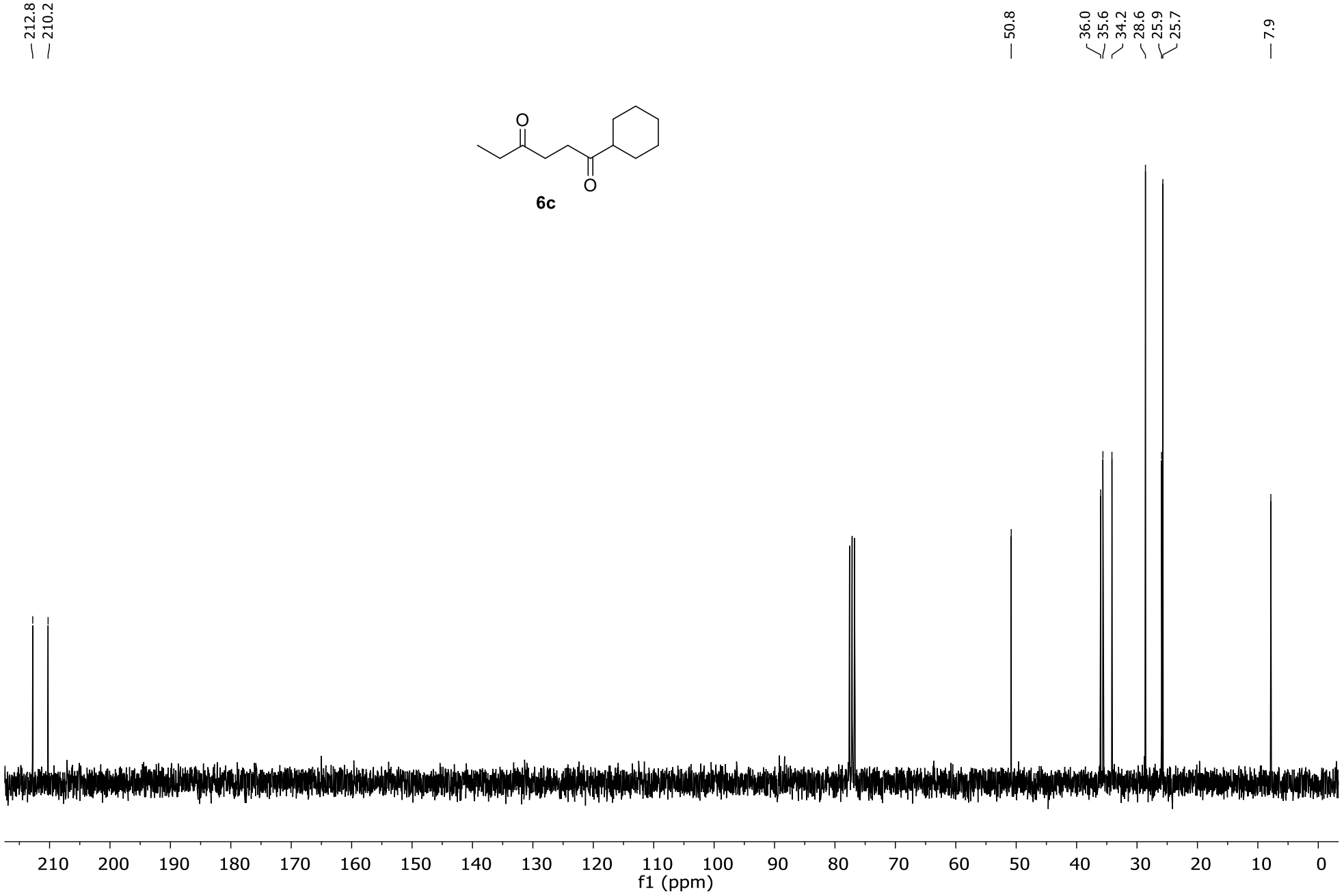
$^{13}C\{^{1}H\}$-RMN (75.4 MHz, $CDCl_3$)



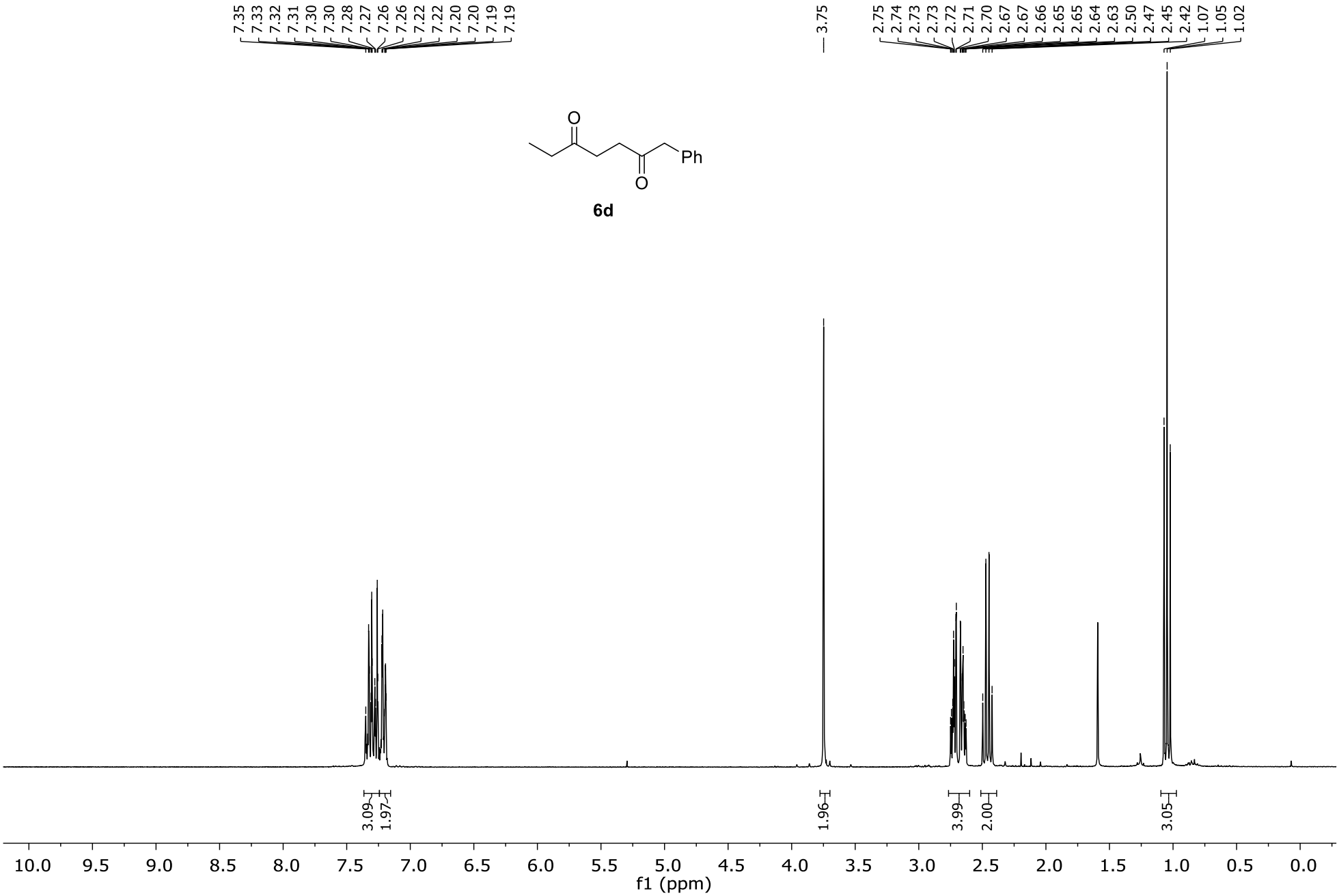
^{1}H-RMN (300 MHz, $CDCl_3$)



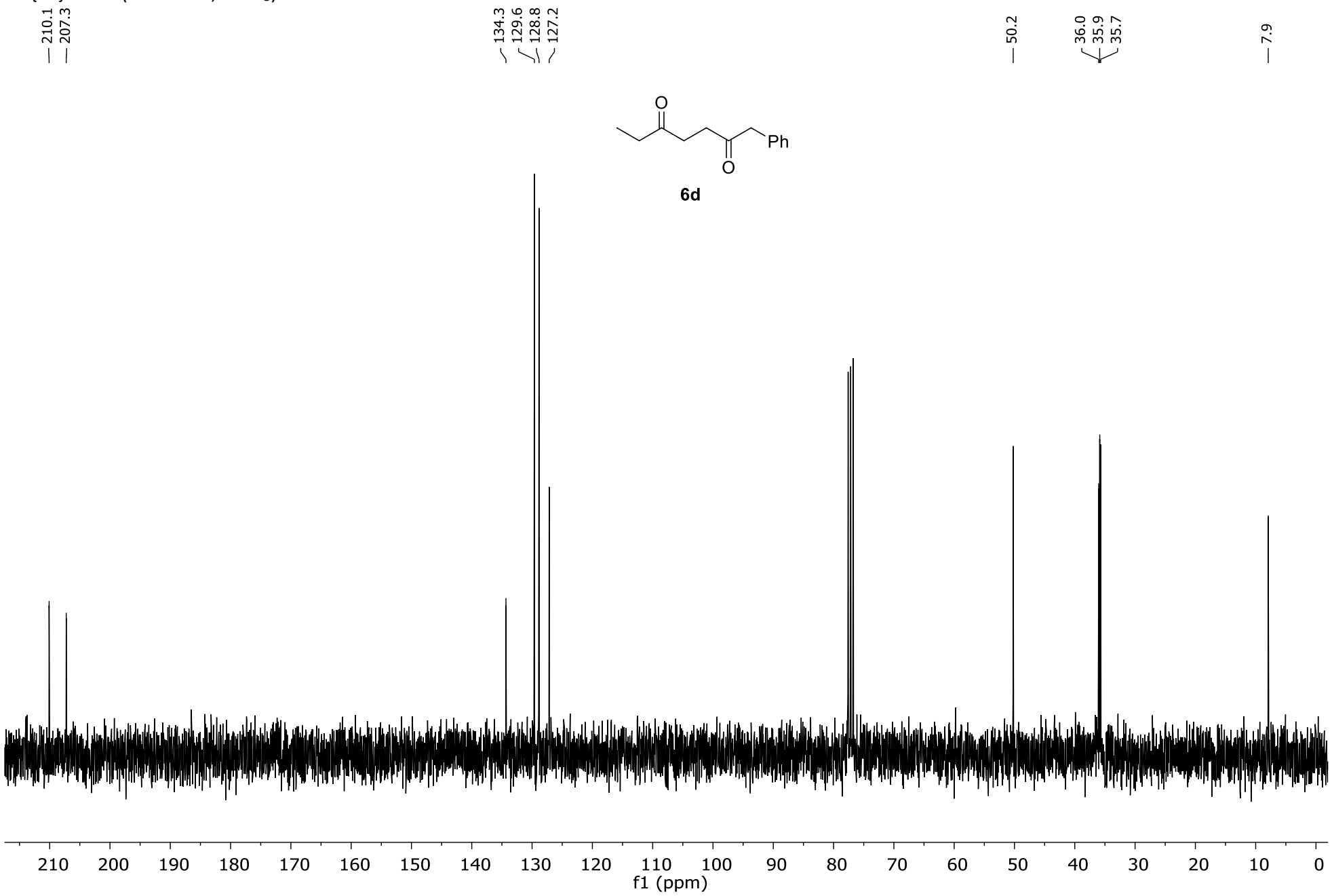
$^{13}C\{^{1}H\}$-RMN (75.4 MHz, $CDCl_3$)



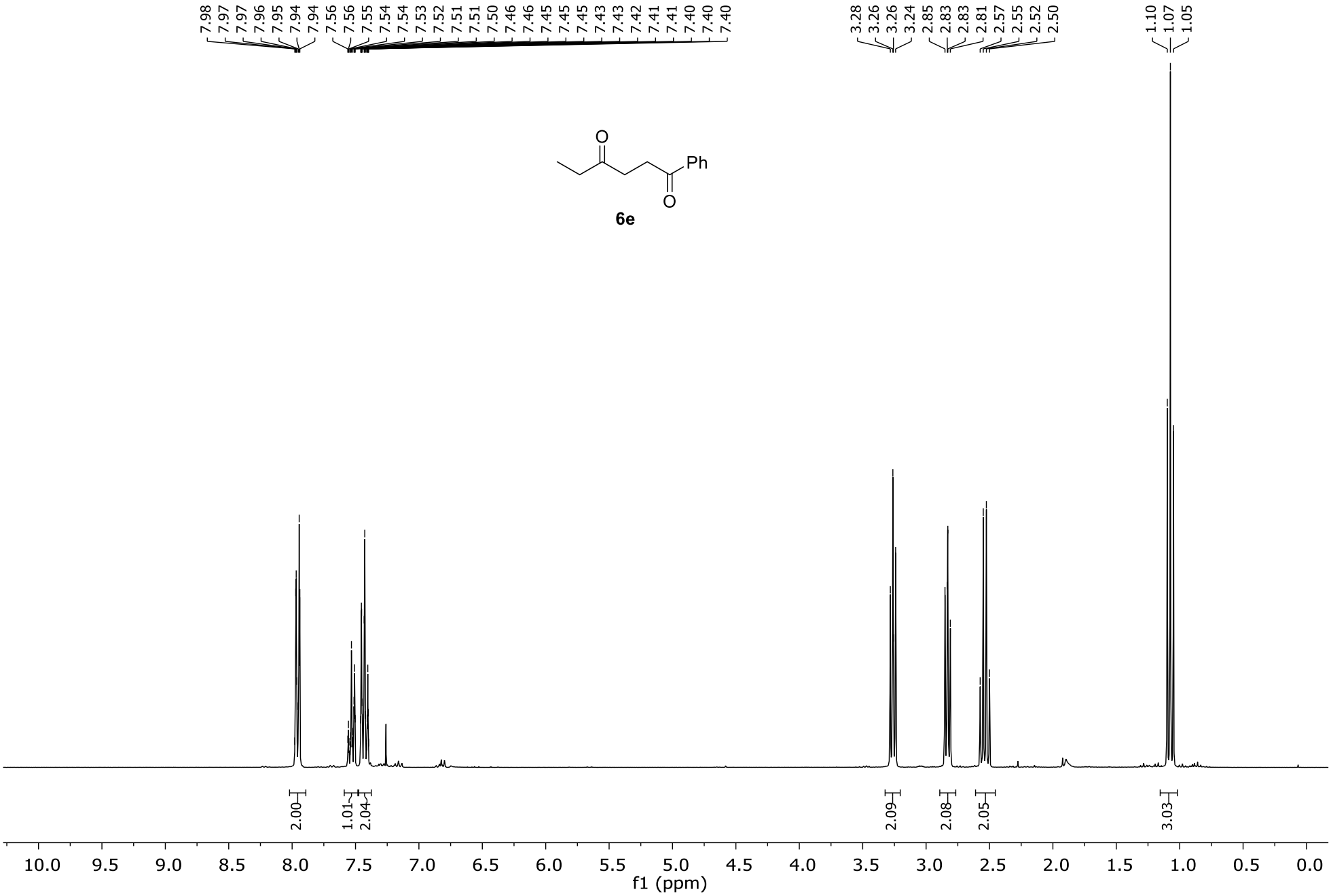
^{1}H-RMN (300 MHz, $CDCl_3$)



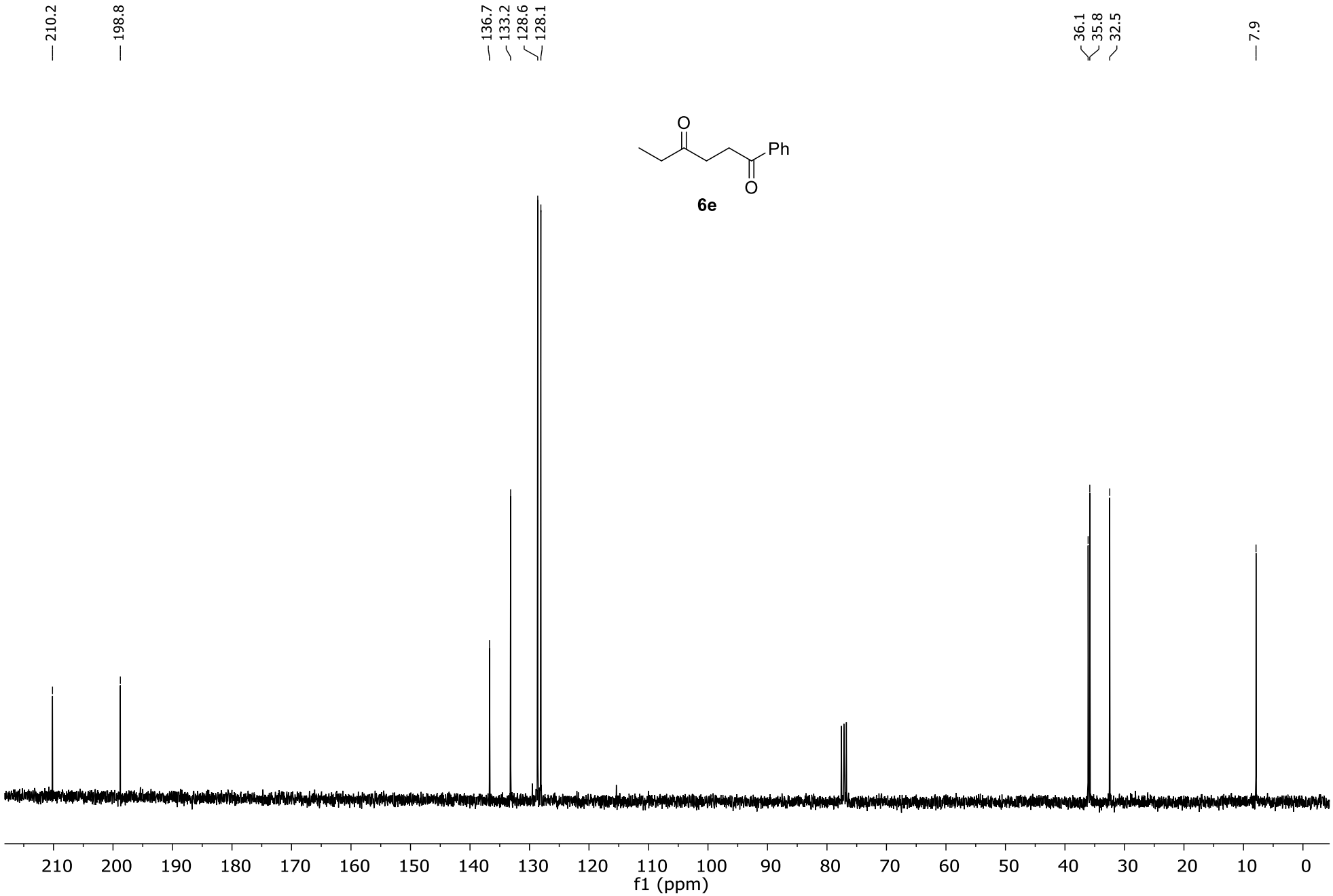
$^{13}C\{^{1}H\}$-RMN (75.4 MHz, $CDCl_3$)



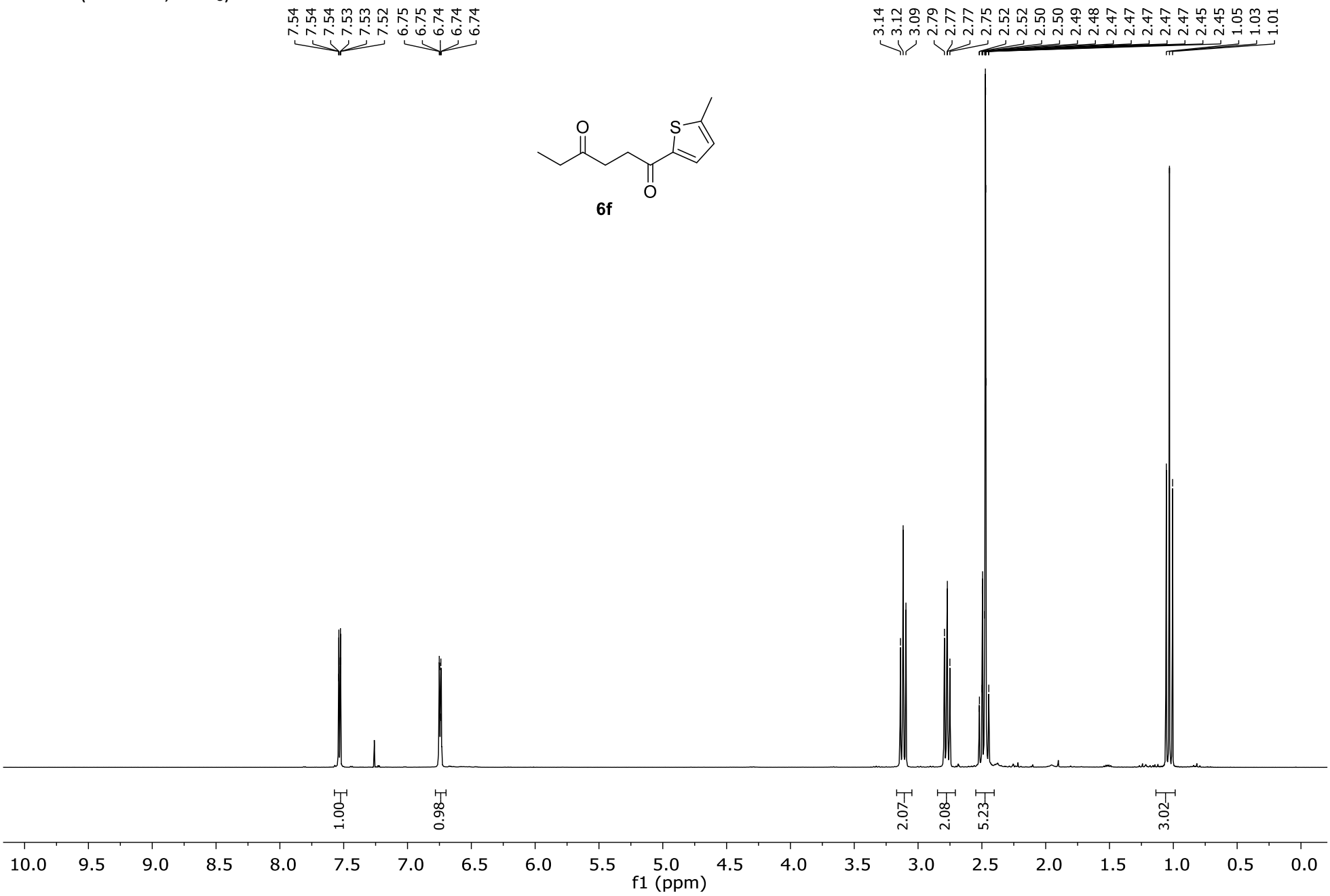
^{1}H-RMN (300 MHz, $CDCl_3$)



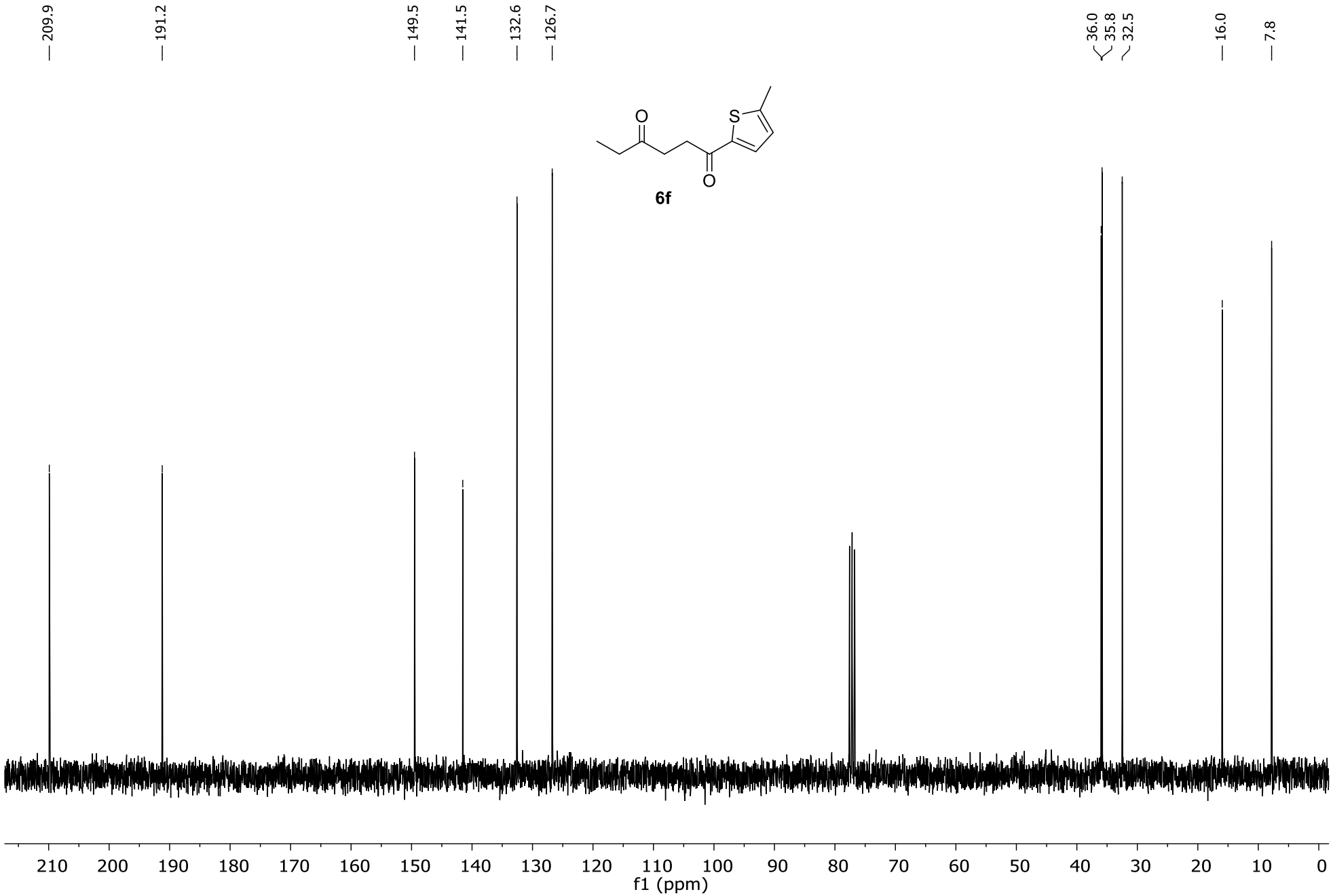
$^{13}C\{^{1}H\}$-RMN (75.4 MHz, $CDCl_3$)



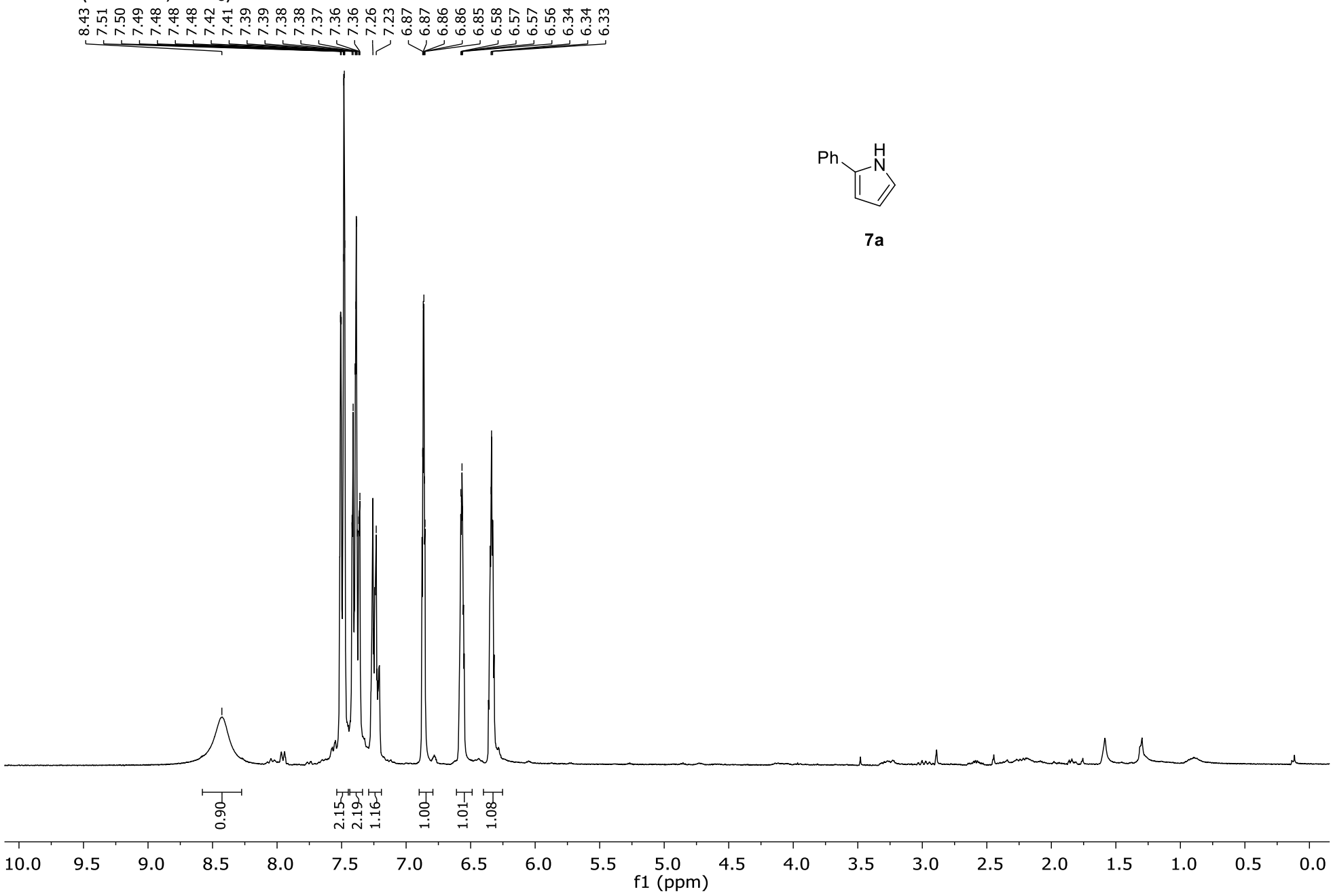
^{1}H-RMN (300 MHz, $CDCl_3$)



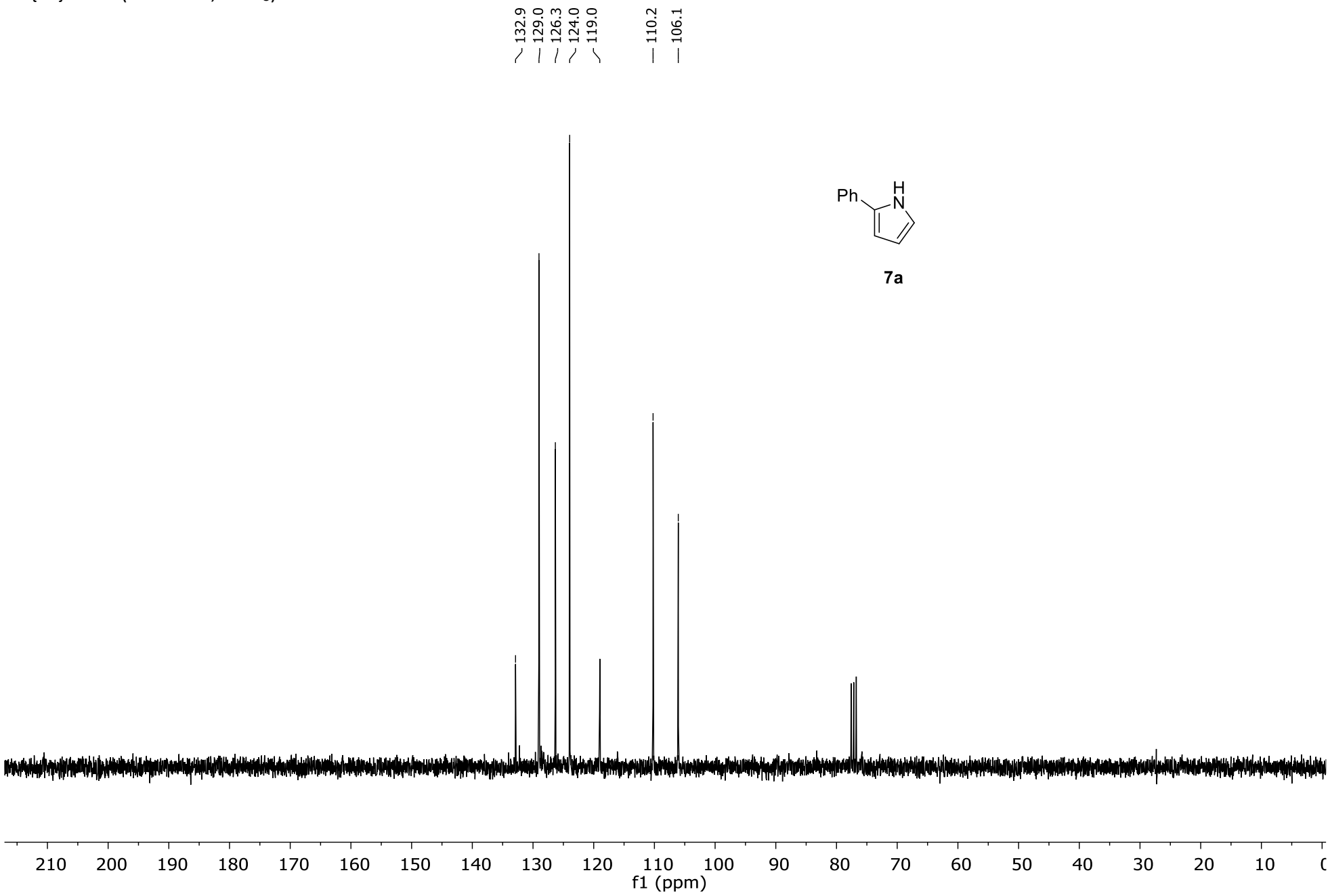
$^{13}C\{^{1}H\}$-RMN (75.4 MHz, $CDCl_3$)



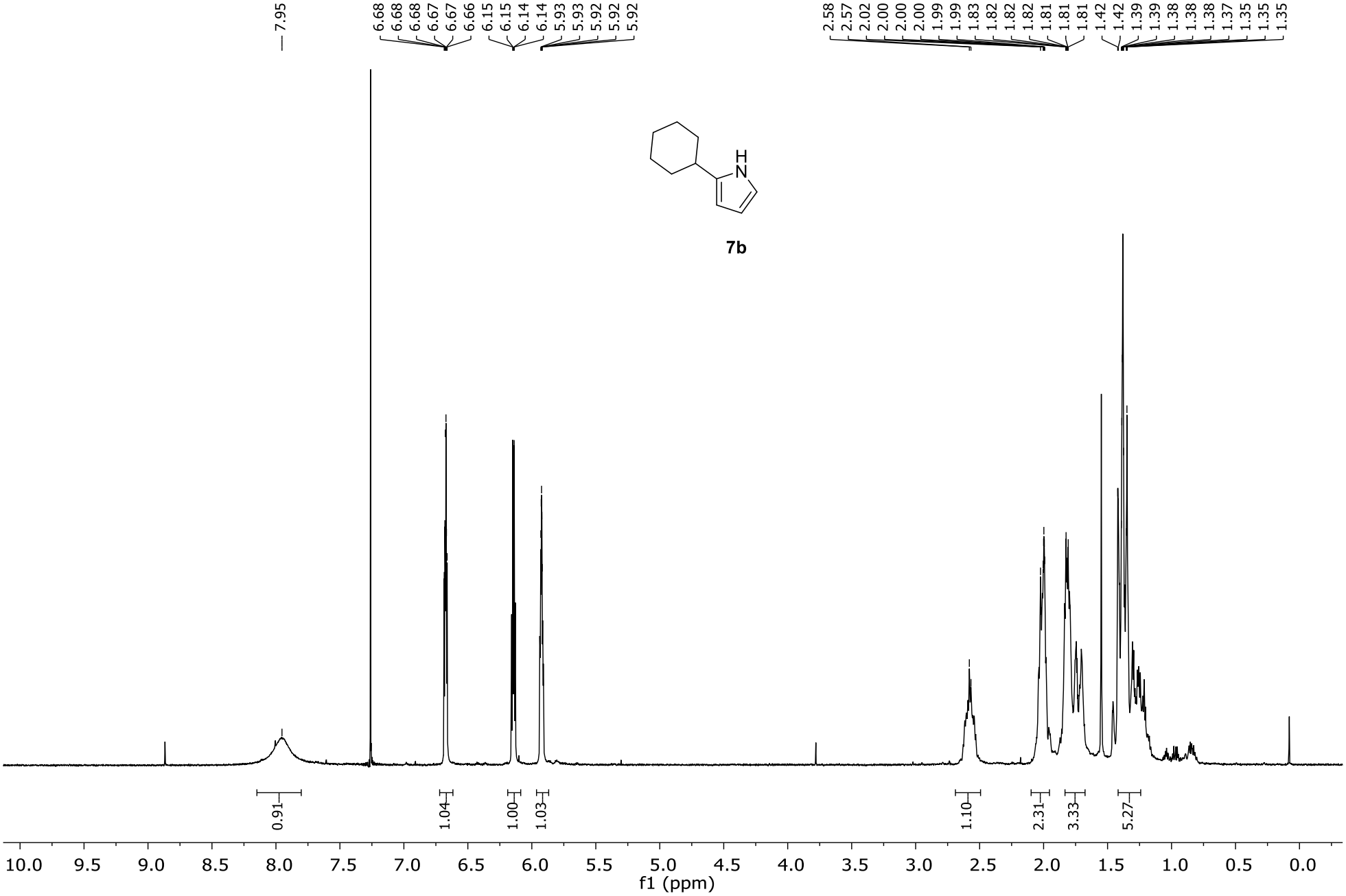
^{1}H-RMN (300 MHz, $CDCl_3$)



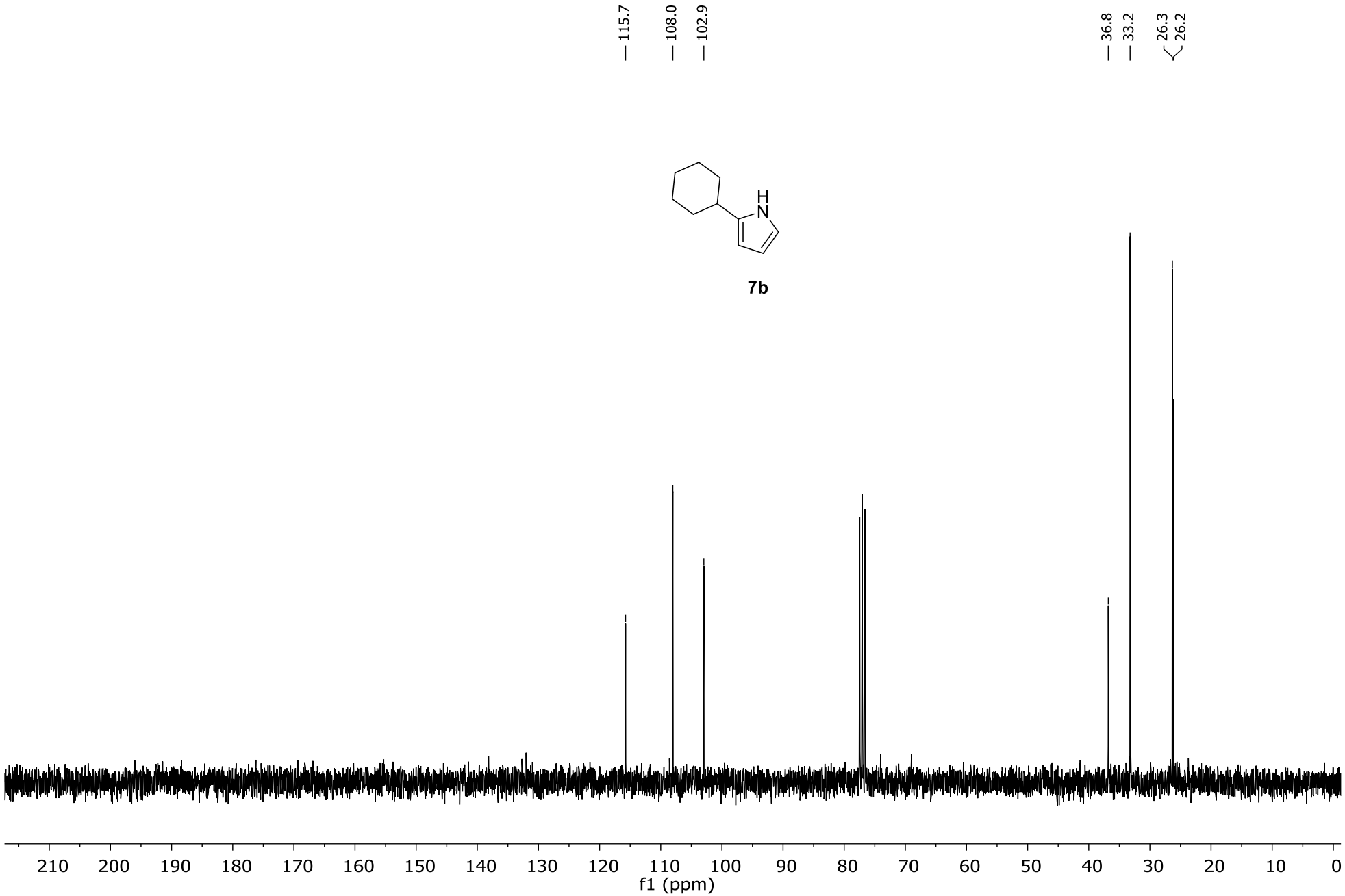
$^{13}C\{^{1}H\}$-RMN (75.4 MHz, $CDCl_3$)



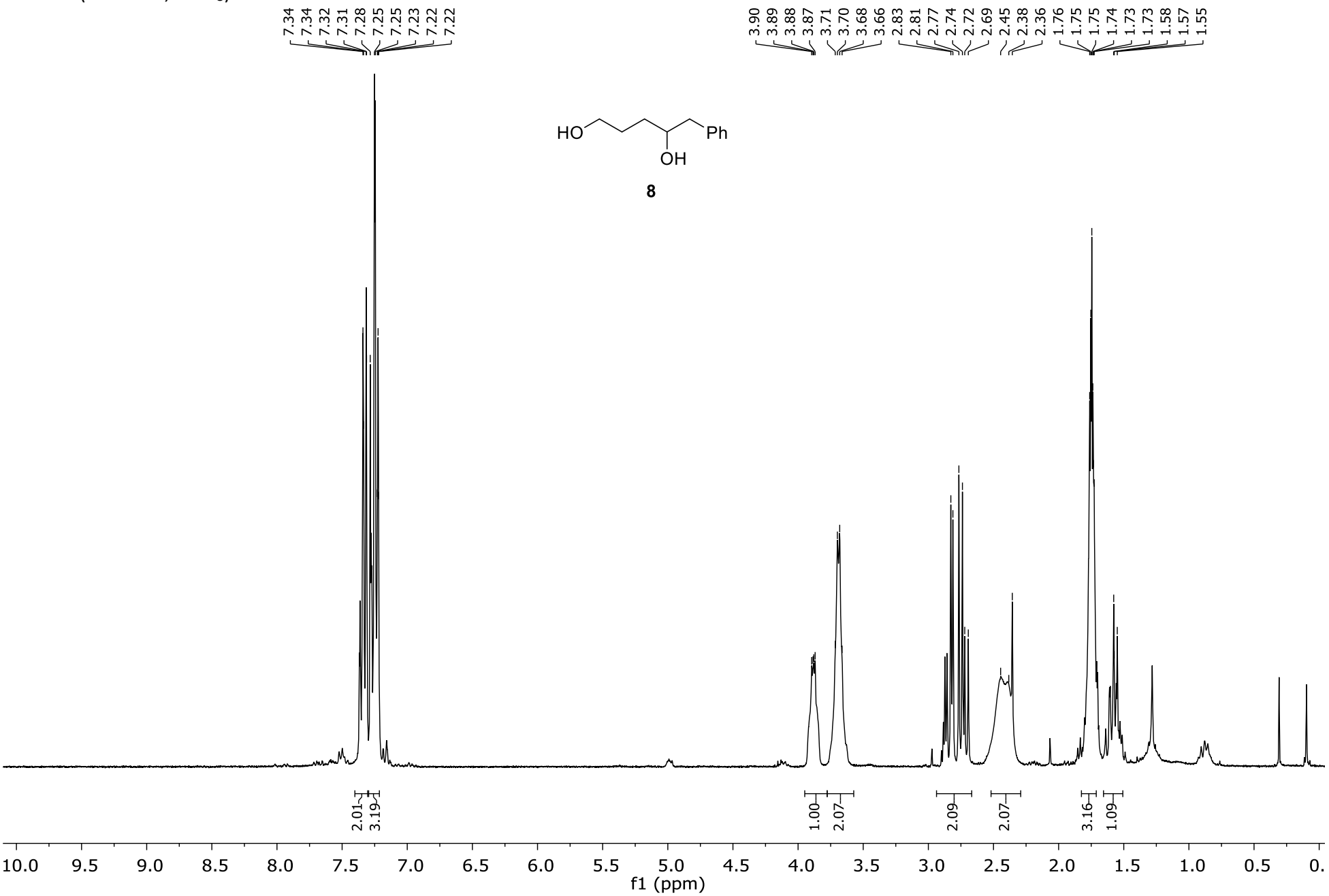
^{1}H-RMN (300 MHz, $CDCl_3$)



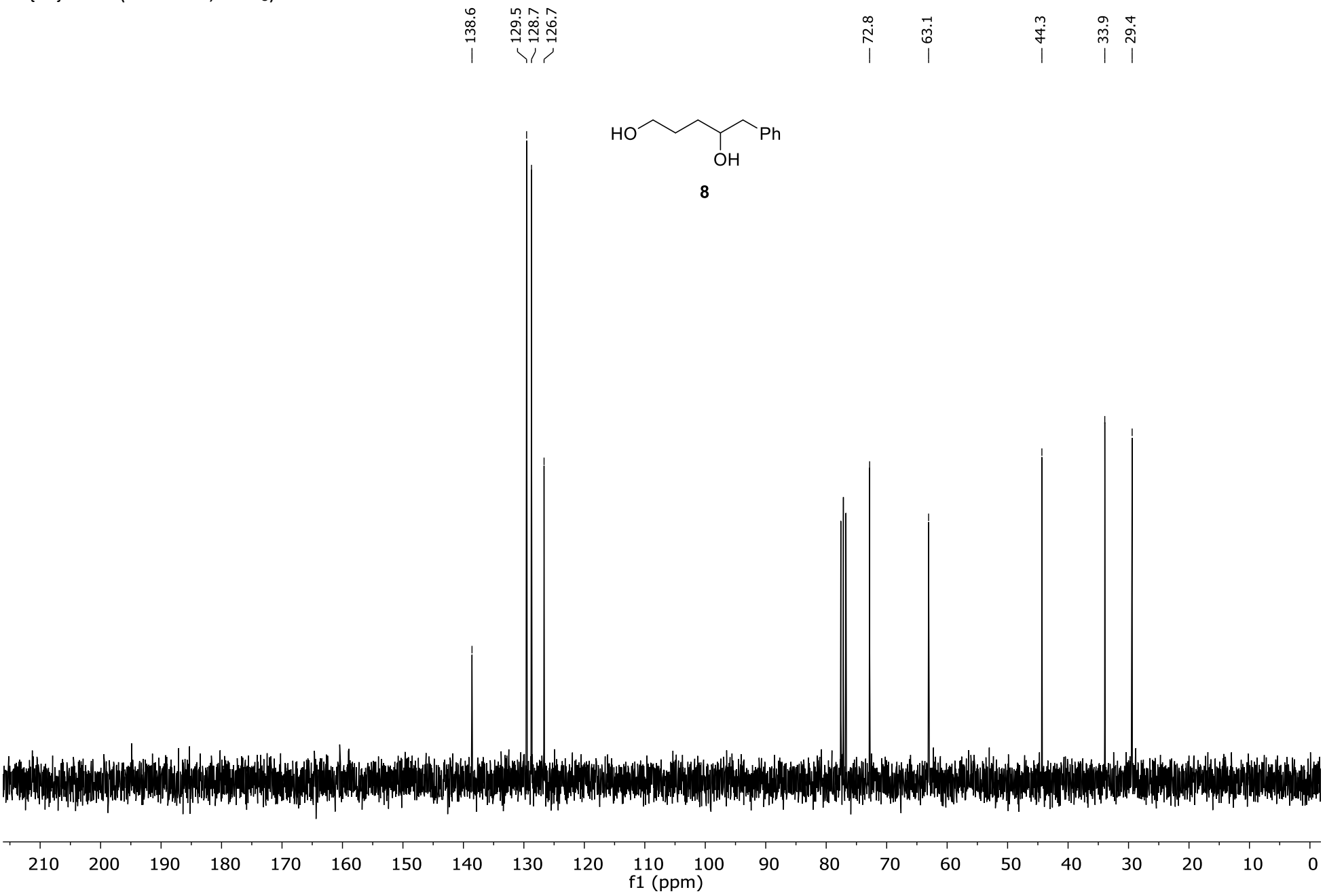
$^{13}C\{^{1}H\}$-RMN (75.4 MHz, $CDCl_3$)



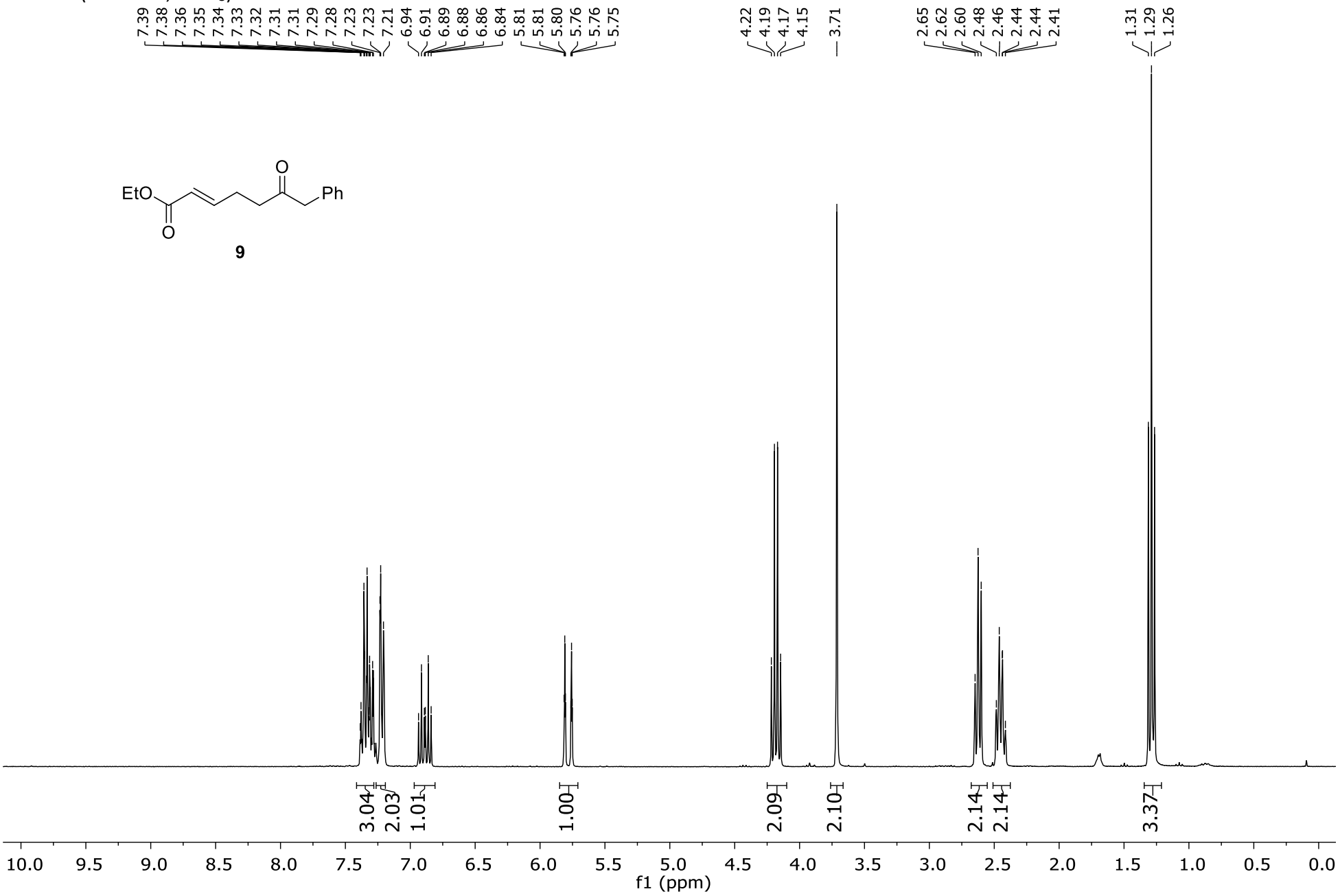
^{1}H-RMN (300 MHz, $CDCl_3$)



$^{13}C\{^{1}H\}$-RMN (75.4 MHz, $CDCl_3$)



^{1}H-RMN (300 MHz, $CDCl_3$)



$^{13}C\{^{1}H\}$-RMN (75.4 MHz, $CDCl_3$)