Electronic Supplementary Material (ESI) for RSC Advances

A Biomimetic Approach For Bicyclic Alkaloids Using Acetal Pro-nucleophile: Total synthesis of (±)-Epilupinine and Formal syntheses of (±)-Laburnine, (±)-Isoretronecanol (±)-Tashiromine

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General Procedures. Oxygen- or moisture-sensitive reactions were carried out in flame- or oven-dried glassware sealed (through standard joint) with 3-way stopcock (made of glass) under dry nitrogen atmosphere. Similarly, sensitive liquids and solutions were transferred using gas-tight syringe or cannula. Reagents were purchased and used without purification. Solvents were purified and dried following usual procedures. Reactions were monitored by thinlayer chromatography (TLC) carried out on 0.25 mm silica gel plates with UV light, I2, 7% ethanolic phosphomolybdic acid-heat and 2.5% ethanolic anisaldehyde (with 1% AcOH and 3.3% conc. H_2SO_4)-heat as developing agents. Silica gels of 60-120 and 100-200 mesh were used for chromatographic separation.

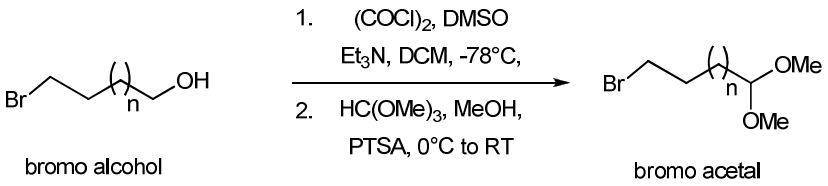
Instrumentation. Proton nuclear magnetic resonance (^{1}H NMR) spectra and carbon nuclear magnetic resonance (^{13}C NMR) spectra were recorded on a Bruker Avance-300 (300 MHz) Bruker Avance-400 (400 MHz) NMR spectrometer and carbon nuclear magnetic resonance (^{13}C NMR) spectra were recorded on a Bruker Avance -300 (75 MHz) and Bruker Avance-400 (100 MHz) NMR spectrometer. Chemical shifts for protons are reported in parts per million downfield from tetramethylsilane and are referenced to the NMR solvent residual peak ($CHCl_3$: δ 7.26). Chemical shifts for carbons are reported in parts per million downfield from tetramethylsilane and are referenced to the carbon resonances of the NMR solvent ($CDCl_3$: δ 77.0). Data are represented as follows: chemical shift, multiplicity (br = broad, s = singlet, d = doublet, t = triplet, q = quartet, quin = quintet, m = multiplet), coupling constants in Hertz (Hz), and integration. Unless noted otherwise on the spectra, NMR spectra were recorded in $CDCl_3$.

High resolution mass spectra were taken with a 3000 mass spectrometer, using Waters Agilent 6520-Q-TofMS/MS system and JEOL-AccuTOF JMST100LC. Mass spectra were obtained under electron impact ionisation (EI), liquid secondary ion mass spectrometric (LSIMS) technique and electron spray ionisation (ESI) techniques.

IR spectra were recorded as neat liquids or KBr pellets. Data are represented as follows: frequency of absorption (cm–1), intensity of absorption (s = strong, m = medium, w = weak).

Abbreviations used: TLC – thin layer chromatography, dr – diastereomeric ratio

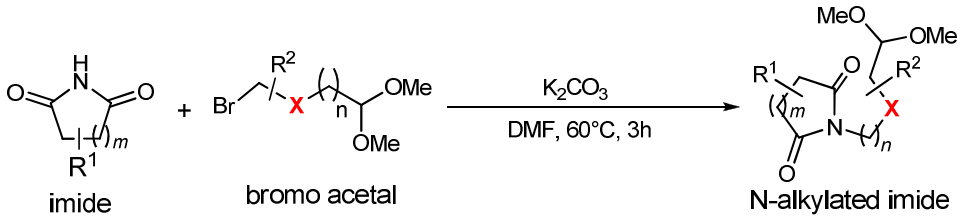
General procedure A (Synthesis of bromoalcohol to bromoacetal derivative)



To a stirring solution of oxalyl chloride (2 equiv) in dry CH_2Cl_2 (2.5 mL/mmol) at –78 ˚C, dry DMSO (4 equiv) was added dropwise with stirring under nitrogen atmosphere. After 15 min, alcohol (1 equiv) in dry CH_2Cl_2 (2 mL/mmol) was added to the reaction mixture. After 0.5 h of stirring at –78 ˚C, Et_3N (5 equiv) was added and stirred for another 0.5 h at –78 ˚C and then for 0.5 h at 0 ˚C. The reaction mixture was then quenched with saturated aqueous NH_4Cl solution and extracted with CH_2Cl_2. The combined organic extracts were washed with water, brine, dried (anhydrous Na_2SO_4) and concentrated in *vacuo*. The aldehyde, thus obtained, was used in the next step without further characterization.

To a solution of the crude aldehyde in dry MeOH (1 ml/mmol) at 0 °C was added trimethyl orthoformate (2 equiv) and PTSA (0.1 equiv) sequentially and the reaction mixture was stirred for 3 h at room temperature. The reaction mixture was then quenched with saturated aqueous $NaHCO_3$ solution, and extracted with EtOAc. The combined organic extracts were washed with water, brine, dried (anhydrous Na_2SO_4) and concentrated in *vacuo*. Purification of the residue by column chromatography on silica gel gave pure title compound.

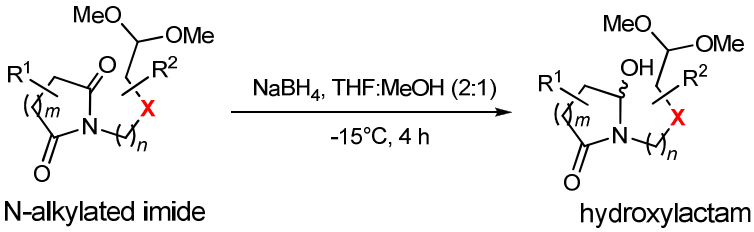
General procedure B (Coupling of bromo acetal derivatives with imide substrates to afford N-alkylated imide)



To a stirring solution of **bromo acetal** (1 equiv) and succinimide/glutarimide/3,3-dimethyl-glutarimide/pthalimide(1.5 equiv) under argon atmosphere in dry DMF (1 ml/mmol) at room temperature was added dry K_2CO_3 (1.5 equiv) and the reaction mixture was heated at 60 °C for 3 hrs. The reaction mixture was allowed to cool to rt and the reaction was quenched with saturated aqueous NH_4Cl solution and extracted with dichloromethane. The combined organic extracts were washed with

water, brine, dried (anhydrous Na_2SO_4) and concentrated in *vacuo*. Purification of the residue by column chromatography on silica gel provided pure title compound.

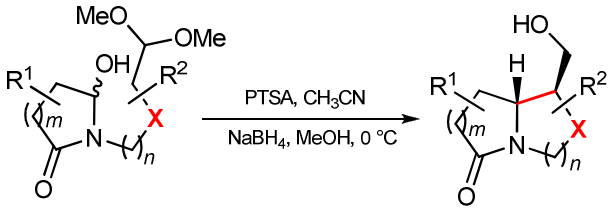
General procedure C (Selective Reduction of N-alkylated imide to the corresponding hydroxylactam derivative)



N-alkylated imide hydroxylactam

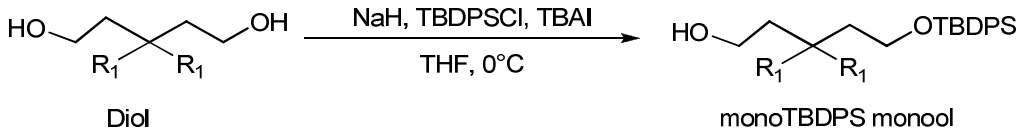
To a stirring solution of **N-alkylated imide** (1 equiv) in a mixture of dry THF and dry MeOH (with a ration of 2:1) at -15 °C $NaBH_4$ (6 equiv) was added portion wise within a span of 4 hrs and the reaction mixture was further stirred (if required, monitored by TLC) at the same temperature till the starting material disappeared completely. The reaction mixture was then quenched by saturated aqueous NH_4Cl solution and extracted with dichloromethane. The combined organic extracts were washed with water, brine, dried (anhydrous Na_2SO_4) and concentrated in *vacuo*. The residue was purified by column chromatography to give pure title product.

General procedure D (Cyclization of hydroxylactam derivative and in situ reduction to provide the hydroxymethyl substituted izidinone derivatives)



To a stirring solution of hydroxylactam (1 equiv) in acetonitrile (0.2 M) at 30 °C was added *p*-toluenesulfonic acid monohydrate (PTSA) (1 equiv) and stirred at 30 °C. The reaction mixture was cooled to 0 °C and MeOH (1 ml) was added followed by $NaBH_4$ (6 equiv). The reaction mixture was quenched by saturated aqueous $NaHCO_3$ solution (2 mL) and extracted with dichloromethane (4 x 20 mL). The combined organic extracts were washed with brine (5 mL), dried (anhydrous Na_2SO_4) and concentrated in *vacuo*. Purification of the residue by column chromatography on silica gel provided the title compound.

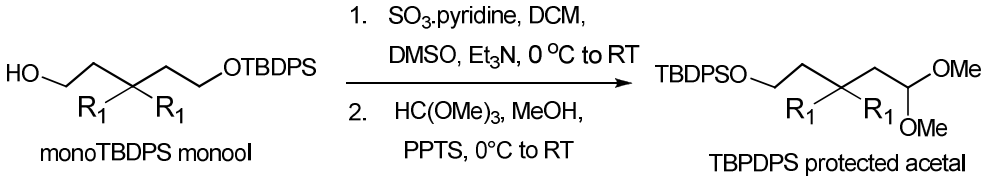
General procedure E (Synthesis of mono TBDPS protected alcohol from symmetric diol)



Diol monoTBDPS monool

To a stirring solution of the diol (1 equiv) in dry THF (2 ml/mmol) at 0 °C was added NaH (1.1 equiv 60% in hexane) portion wise under nitrogen atmosphere. It was allowed to run for 15 minute at room temperature. The reaction mixture was cooled again to 0 °C. TBDPSCl (1 equiv) was added via syringe followed by the addition of TBAI (0.1 equiv). It was allowed to run for 3 h at room temperature. The reaction mixture was then quenched with saturated aqueous NH_4Cl solution and extracted with EtOAc. The combined organic extracts were washed with water, brine, dried (anhydrous Na_2SO_4) and concentrated in *vacuo*. Purification of the residue by column chromatography on silica gel provided the title compound.

General procedure F (Synthesis of TBDPS protected acetal from TBDPS ptotected alcohol derivative)

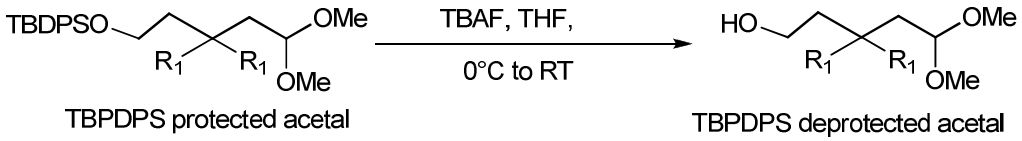


monoTBDPS monool TBPDPS protected acetal

To a solution of alcohol (1 equiv) in dry CH_2Cl_2 (2 ml/mmol) was added with stirring, DMSO (1 ml/mmol), Et_3N (5 equiv) and SO_3-Py complex (5 equiv) portion wise at 0 °C under nitrogen atmosphere. It was allowed to run for 1 h at room temperature. The reaction mixture was then quenched with saturated aqueous NH_4Cl solution and extracted with CH_2Cl_2 The combined organic extracts were washed with water, brine, dried (anhydrous Na_2SO_4) and concentrated in *vacuo*. The aldehyde, thus obtained, was used in the next step without further characterization.

To a solution of the crude aldehyde in dry MeOH (1 ml/mmol) at 0 °C was added trimethyl orthoformate (2 equiv) and PPTS (0.1 equiv) sequentially and the reaction mixture was stirred for 14 h at room temperature. The reaction mixture was then quenched with saturated aqueous $NaHCO_3$ solution, and extracted with EtOAc. The combined organic extracts were washed with water, brine, dried (anhydrous Na_2SO_4) and concentrated in *vacuo*. Purification of the residue by column chromatography on silica gel gave pure title compound.

General procedure G (Deprotection of TBDPS from the acetal derivatives)

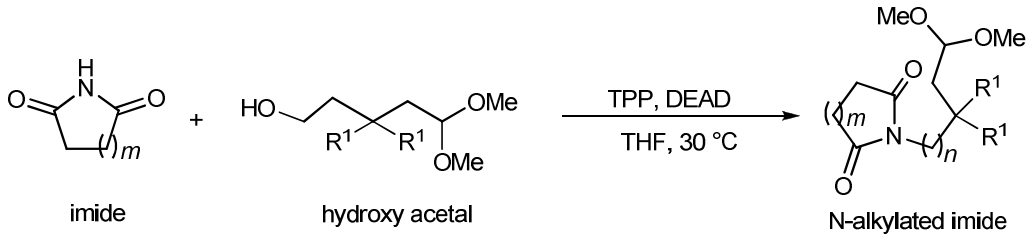


TBPDPS protected acetal

TBPDPS deprotected acetal

To a solution of TBDPS protected derivative (1.0 equiv) in THF (2 mL/mmol) was added a 1 M TBAF (1.0 equiv) solution in THF at 0 °C and stirred for 2 h at RT. Saturated aqueous NH_4Cl solution was added to quench the reaction at 0 °C. The aqueous layer was extracted with EtOAc. The combined organic layers were washed with brine, dried over Na_2SO_4 and concentrated. The crude product was purified by silica gel column chromatography to obtain the desired title compound.

<u>General procedure H</u> (Coupling of alcohol derivatives with imide substrates to afford N-alkylated imide)

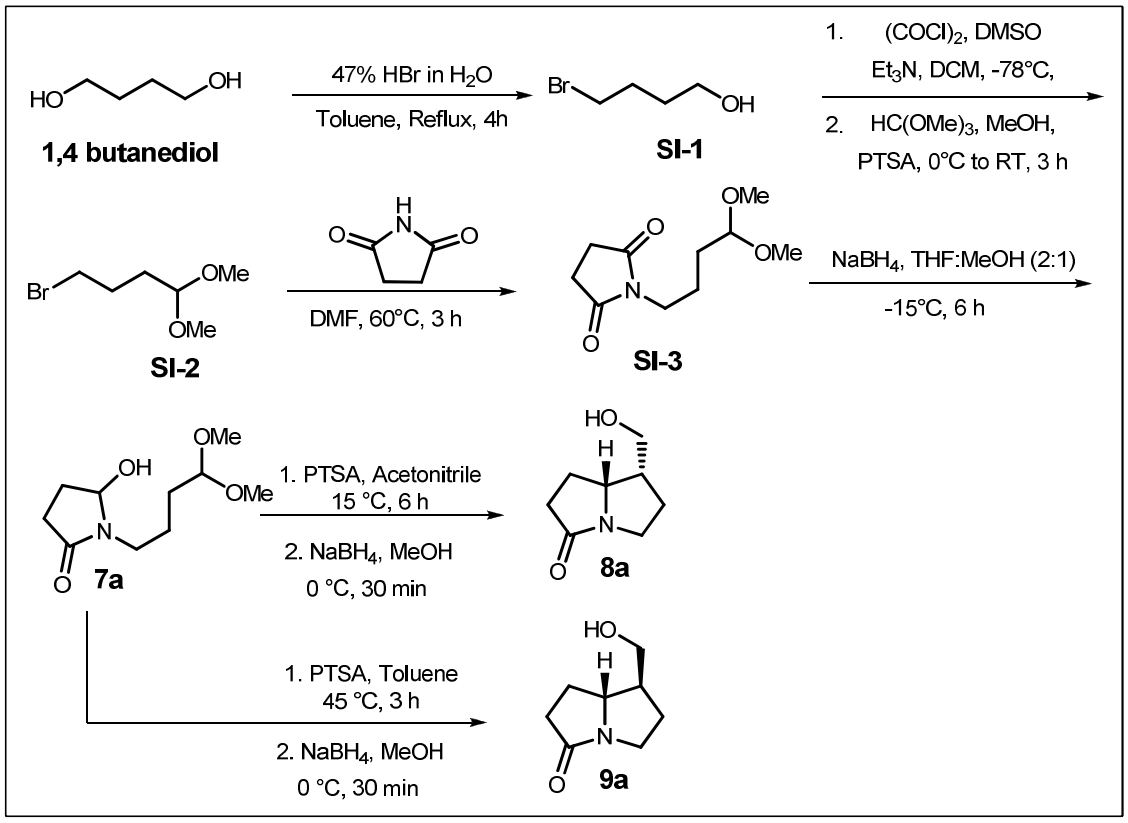


imide

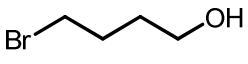
hydroxy acetal

N-alkylated imide

To a solution of alcohol (1.0 equiv), imide (1.1 equiv) and PPh_3 (1.1 equiv) in THF (10 mL/mmol) was added a solution of DEAD (1.1 equiv) in THF (3 mL/mmol) dropwise by syringe at 30 °C and stirred for 10 min. The resulting yellow solution was concentrated. The crude product was purified by silica gel column chromatography to obtain the desired alkylated imide product.



Synthesis of 4-bromo-1-butanol (SI-1): **SI-1** was synthesized using a modified procedure described in the literature[1]. To a mixture of 1, 4 butanediol (9 g, 100 mmol) and toluene (300 mL) 47% aqueous HBr (12.2 mL, 100 mmol) was added at room temperature and the mixture was refluxed using Dean Stark Apparatus for 4 hours. The reaction mixture was allowed to cool to rt and the reaction was quenched with 1 M NaOH at 0 °C. The organic layer was diluted with ethyl acetate and washed with water, brine, and dried (anhydrous Na_2SO_4). Concentration of the organic layer gave yellow oil. Purification of the residue by column chromatography on silica gel (hexane : ethyl acetate = 3:1) gave compound **S1** as an yellow oil (14 g, 92% yield). Spectral data were found in agreement with the literature data.



SI-1

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

δ **3.96** bs, 1H

3.67 (t, *J* = 6.5 Hz, 2H)

[1] J. M. Chong, M. A. Heuft, P. Rabbat, *J. Org. Chem.* **2000,** *65*, 5837

3.43 (t, *J* = 6.7 Hz, 2H)

1.99–1.89 (m, 2H)

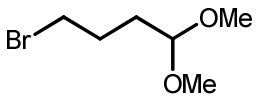
1.75–1.66 (m, 2H)

^{13}C NMR ($CDCl_3$, 75 MHz)

δ **61.9** **33.6**

31.1 **29.2**

Synthesis of 4-bromo-1,1-dimethoxybutane (SI-2)[2]: Prepared according to the **general procedure A** using SI-1 (9.4g, 62 mmol). Purification of the residue by column chromatography on silica gel (hexane: ethyl acetate = 9:1) gave product **SI-2** as a yellow oil (9.9 g, 82% yield) whose spectroscopic data are in agreement with the literature report.[3]



SI-2

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

δ **4.39** (t, *J* = 5.5 Hz, 1H)

3.43 (t, *J* = 6.7 Hz, 2H)

3.33 (s, 6H)

1.96 (m, 2H)

1.78 (m, 2H)

^{13}C NMR ($CDCl_3$, 75 MHz)

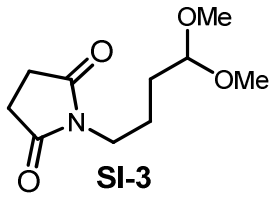
δ **103.9** **31.2**

53.0 **28.0**

33.7

Synthesis of 1-(4,4-dimethoxybutyl)pyrrolidine-2,5-dione (SI-3): Prepared according to the **general procedure B** using **SI-2** (4.5 g, 22.8 mmol) and succunimide (3.39g, 34.2 mmol). Purification of the residue by column chromatography on silica gel (hexane: acetone = 3:1) gave product **SI-3** as a yellow oil (4.8 g, 99% yield).

(2) Trost, B. M.; Chen, D. W. C. *J. Am. Chem. Soc.* **1996**, *118*, 12541–12554
(3) Lohse, C., Jaeger, L. L., Staimer, N., Sanborn, J. R., Jones, A. D., Lango, J., Gee, S. J., and Hammock, B. D. *J. Agr. Food Chem.* **2000**, *48*, 5913–5923.



SI-3

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

δ **4.35** (t, *J* = 5.3 Hz, 1H)
3.51 (t, *J* = 6.6 Hz, 2H)
3.30 (s, 6H)
2.68 (s, 4H)
1.69–1.54 (m, 4H)

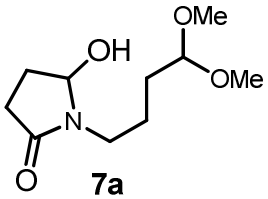
^{13}C NMR ($CDCl_3$, 75 MHz)

δ **177.1**, **104.0**, **52.9**, **38.4**, **29.8**, **28.0**, **22.9**

IR(Neat): 2945, 2832, 1771, 1701, 1368, 1193, 767 cm^{-1}

HRMS (ESI): Calculated for $C_{10}H_{17o}NaO_4$ $[M+Na]^+$: 238.1055 found 238.1054

Synthesis of 1-(4,4-dimethoxybutyl)-5-hydroxypyrrolidin-2-one (7a): Prepared according to the **general procedure C** using **SI-3** (3.6g, 16.7 mmol). Purification of the residue by column chromatography on silica gel (hexane: acetone = 6:4) to give product **7a** as a yellow oil (3.58 g, 99% yield).



7a

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

δ **5.18** (t, *J* = 6.8 Hz, 1H)
4.41–4.32 (m, 2H)
3.45–3.36 (m, 1H)
3.29 (s, 6H)
2.59–2.47 (m, 1H)
2.35 – 2.20 (m, 3H)
1.94 – 1.83 (m, 1H)
1.59 (bs, 4H)

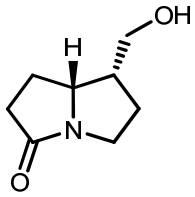
^{13}C NMR ($CDCl_3$, 75 MHz)

δ	**175.0**	**39.6**
	104.3	**29.8**
	83.0	**28.9**
	53.0	**28.0**
	52.9	**22.6**

IR(Neat): 3401, 2947, 1668, 1331, 1125, 1064, 757 cm^{-1}

HRMS (ESI): Calculated for $C_{10}H_{19}NNaO_4$ $[M+Na]^+$: 240.1212 found 240.1217

Synthesis of (7R,7aR)-7-(hydroxymethyl)tetrahydro-1H-pyrrolizin-3(2H)-one (8a): Prepared according to the **general procedure D** using **7a** (50 mg, 0.23 mmol) and 5 equivalent of PTSA for 6 h in 2.5 ml of MeCN. Purification of the residue by column chromatography on silica gel ($CHCl_3$: MeOH = 19:1) provided inseparable mixture of diastereomers of **8a** (dr 6:1) as a yellow oil (29 mg, 81% yield).



8a

^{1}H NMR ($CDCl_3$, 400 MHz)

δ	**4.08**	(q, *J* = 7.2 Hz, 1H)	**2.42**	(dd, *J* = 8.5, 3.6 Hz, 1H)
	3.65	(dd *J* = 10.1, 7.6 Hz, 1H)	**2.38**	(dd, *J* = 8.5, 3.6 Hz, 1H)
	3.58–3.50	(m, 2H)	**2.28**	(d of quint, *J* = 6.8, 3.6 Hz, 1H)
	3.00	(dddd, *J* = 12.7, 8.9, 4.7, 1.2 Hz, 1H)	**2.19 – 2.03**	(m, 2H)
			1.95 – 1.87	(m, 1H)
	2.65	(td, *J* = 16.6, 9.6 Hz, 1H)		

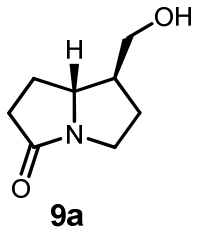
^{13}C NMR ($CDCl_3$, 75 MHz)

δ	**175.0**	**40.1**
	63.3	**34.8**
	61.4	**30.0**
	40.6	**21.4**

IR(Neat): 3412, 2933, 2343, 1663, 1425, 1216, 1049, 667 cm^{-1}

HRMS (ESI): Calculated for $C_8H_{14}NO_2$ $[M+H]^+$: 156.1025 found 156.1027

Synthesis of (7S,7aR)-7-(hydroxymethyl)tetrahydro-1H-pyrrolizin-3(2H)-one (9a): Prepared according to the **general procedure D** using **7a** (50 mg, 0.23 mmol) and 5 equivalent of PTSA in toluene for 3 h. Purification of the residue by column chromatography on silica gel ($CHCl_3$: MeOH = 19:1) provided inseparable mixture of diastereomers of **9a** (dr 9:1) as a yellow oil (31 mg, 86% yield).



9a

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

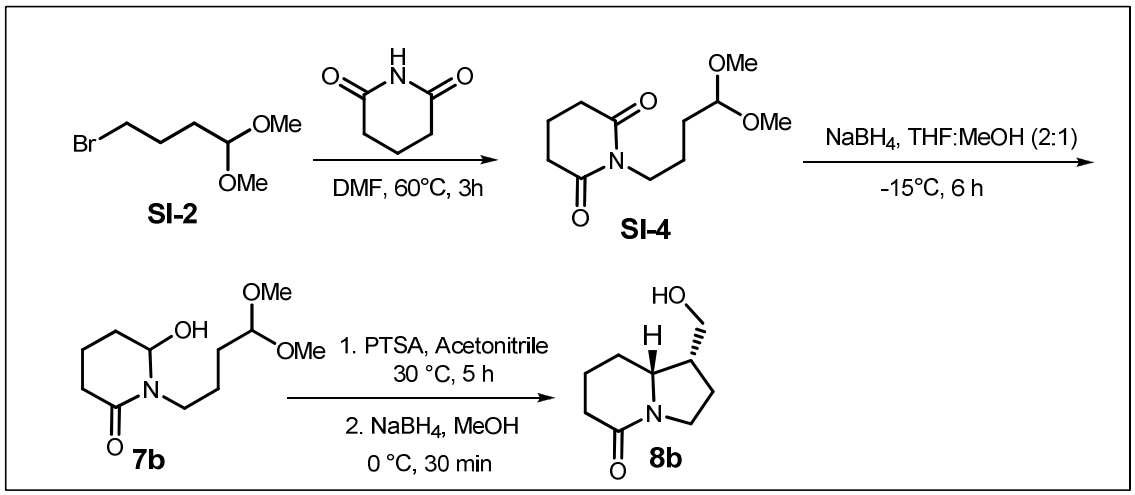
δ	**3.78 – 3.69**	(m, 2H)		**2.43**	(dd, *J* = 16.7, 9.6 Hz, 1H)
	3.66 – 3.53	(m, 2H)		**2.36 – 2.29**	(m, 1H)
	3.13	(t, *J* = 9.9 Hz, 1H)		**2.25 – 2.15**	(m, 1H)
	2.71	(td, *J* = 16.6 Hz, 9.7 Hz, 1H)		**1.95 – 1.81**	(m, 3H)

^{13}C NMR ($CDCl_3$, 75 MHz)

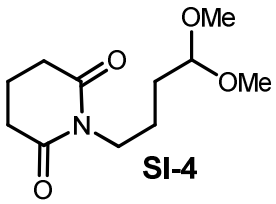
δ	**174.7**	**40.6**
	65.2	**34.9**
	63.6	**29.9**
	47.9	**26.8**

IR(Neat): 3405, 3014, 2402, 1664, 1425, 1216, 1047, 668 cm^{-1}

HRMS (ESI): Calculated for $C_8H_{14}NO_2$ $[M+H]^+$: 156.1025 found 156.1016



Synthesis of 1-(4,4-dimethoxybutyl)piperidine-2,6-dione (SI-4): Prepared according to the **general procedure B** using glutarimide (3.7 g, 32.6 mmol) and **SI-2** (4.2 g, 21.7 mmol). Purification of the residue by column chromatography on silica gel (hexane: acetone = 3:1) provided title compound as yellow oil. (4.1g, 83% yield).



SI-4

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

δ	**4.35**	(t, *J* = 5.2 Hz, 1H)	**2.62**	(t, *J* = 6.5 Hz, 4H)
	3.76	(t, *J* = 6.9 Hz, 2H)	**1.91**	(m, 2H)
	3.29	(s, 6H)	**1.57**	(m, 4H)

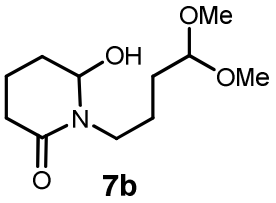
^{13}C NMR ($CDCl_3$, 75 MHz)

δ	**172.3**	**32.7**
	104.1	**29.8**
	52.7	**23.1**
	39.0	**17.1**

IR(Neat): 3019, 1669, 1435, 1358, 1216, 759 cm^{-1}

HRMS (ESI): Calculated for $C_{11}H_{19}NNaO_4$ $[M+Na]^+$: 252.1212 found 252.1202

Synthesis of 1-(4,4-dimethoxybutyl)-6-hydroxypiperidin-2-one (7b): Prepared according to the **general procedure C** using **SI-4** (2.2 g, 9.6 mmol). Purification of the residue by column chromatography on silica gel (hexane: acetone = 2:1) provided title compound as yellow oil. (2 g, 90% yield).



7b

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

δ	**4.97**	(d, *J* = 6.6 Hz, 1H)	**3.16**	(m, 1H)
	4.89	(m, 1H)	**2.89**	(bs, 1H)

4.71 (bs, 1H)
4.29 (t, *J* = 4.9 Hz, 1H)
3.54 (m, 1H)
3.24 (d, *J* = 1 Hz, 6H)
2.34 (td, *J* = 17.8, 4.8 Hz, 1H)
2.20 (ddd, *J* = 17.8, 10.1, 6.3 Hz, 1H)
1.85– 1.74 (m, 2H)
1.58– 1.46 (m, 4H)

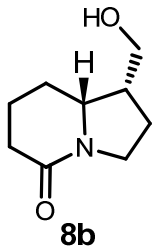
^{13}C NMR ($CDCl_3$, 75 MHz)

δ **170.5**
104.5
79.7
53.1
52.9
44.7
32.3
31.0
29.8
23.0
15.7

IR(Neat): 3358, 2951, 1623, 1368, 1333, 1158, 1127, 1077, 757 cm^{-1}

HRMS (ESI): Calculated for $C_{11}H_{21}NNaO_4$ $[M+Na]^+$: 254.1368 found 254.1357

Synthesis of (1R,8aR)-1-(hydroxymethyl)hexahydroindolizin-5(1H)-one (8b): Prepared according to the **general procedure D** using **7b** (53 mg, 0.23 mmol) and 5 equiv PTSA for 5 h. Purification of the residue by column chromatography on silica gel (1% MeOH in $CHCl_3$) provided an inseparable mixture of diastereomers of **8b** (10:1) as yellow oil. (31 mg, 82% yield).



8b

^{1}H NMR ($CDCl_3$, 400 MHz)

δ **3.72 – 3.53** (m, 3H)
3.46 – 3.40 (m, 2H)
2.90 (bs, 1H)
2.44– 2.37 (m, 2H)
2.29 – 2.20 (m, 2H)
2.00 – 1.95 (m, 2H)
1.92– 1.84 (m, 1H)
1.71– 1.56 (m, 1H)
1.48 (dq, *J* = 12.5, 4.2 Hz, 1H)

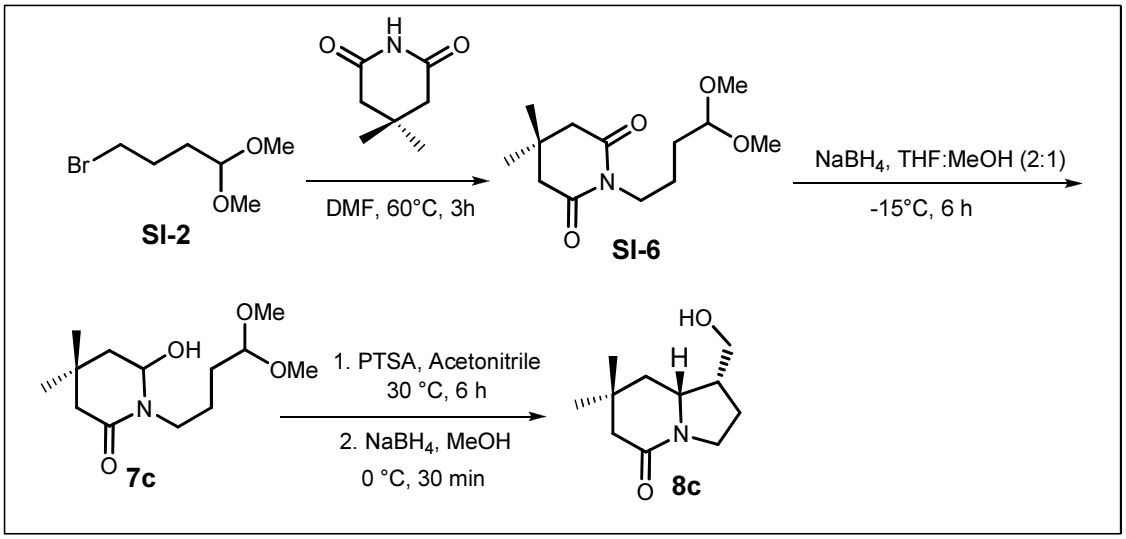
^{13}C NMR ($CDCl_3$, 100 MHz)

δ **169.5**
31.0

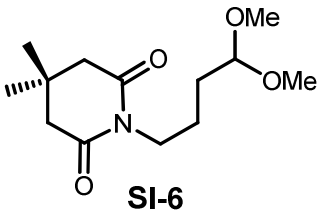
60.9	**24.8**
60.8	**24.7**
43.6	**21.3**
43.4	

IR(Neat): 3409, 2953, 1609, 1476, 1325, 1047, 756 cm^{-1}

HRMS (ESI): Calculated for $C_9H_{16}NO_2$ $[M+H]^+$: 170.1181 found 170.1182



Synthesis of 1-(4,4-dimethoxybutyl)-4,4-dimethylpiperidine-2,6-dione (SI-6): Prepared according to the **general procedure B** using **SI-2** (1.1 g, 5.5 mmol) and 3,3-dimethylglutarimide (1.2 g, 8.2 mmol). Purification of the residue by column chromatography on silica gel (hexane: acetone = 3:1) gave **SI-6** as yellow oil. (1.2g, 83% yield).



SI-6

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

δ	**4.36**	(t, *J* = 5.2 Hz, 1H)	**2.49**	(s, 4H)
	3.78	(t, *J* = 6.9 Hz, 2H)	**1.60 – 1.56**	(m, 4H)
	3.30	(s, 6H)	**1.07**	(s, 6H)

^{13}C NMR ($CDCl_3$, 75 MHz)

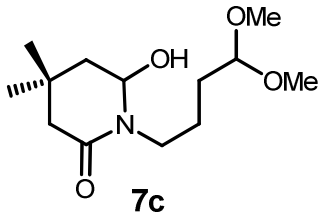
δ **171.9** **29.9**
104.1 **29.1**
52.8 **27.7**
46.4 **23.1**
39.1

IR(Neat): 2955, 2833, 1672, 1356, 1209, 770 cm^{-1}

HRMS (ESI): Calculated for $C_{13}H_{23}NNaO_4$ $[M+Na]^+$: 280.1525 found 280.1530

Physical appearance: light yellow oil

Synthesis of 1-(4,4-dimethoxybutyl)-6-hydroxy-4,4-dimethylpiperidin-2-one (7c): Prepared according to the **general procedure C** from **SI-6** (300 mg, 1.1 mmol)**.** Purification of the residue by column chromatography on silica gel (hexane: acetone = 2:1) gave title product as yellow oil (272 mg, 90% yield).



7c

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

δ **4.93** (q, *J* = 7.0 Hz, 1H) **2.16** (dd, *J* = 14.0, 3.4 Hz, 1H)
4.38 (t, *J* = 5.0 Hz, 1H) **2.01** (dd, *J* = 13.8, 5.8 Hz, 1H)
3.57–3.44 (m, 2H) **1.70– 1.55** (m, 5H)
3.40 (d, *J* = 8.3 Hz, 1H) **1.06** (s, 3H)
3.33 (s, 6H) **0.96** (s, 3H)
2.24 (d, *J* = 14.0 Hz, 1H)

^{13}C NMR ($CDCl_3$, 75 MHz)

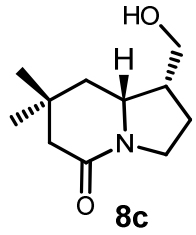
δ **169.9** **44.9**
104.6 **42.7**
79.4 **29.9**
53.2 **29.5**
52.9 **26.3**
46.1 **22.7**

IR(Neat): 3396, 2952, 1620, 1370, 1327, 1054, 756 cm^{-1}

HRMS (ESI): Calculated for $C_{13}H_{25}NNaO_4$ $[M+Na]^+$: 282.1681 found 282.1672

Synthesis of (1R,8aR)-1-(hydroxymethyl)-7,7-dimethylhexahydroindolizin-5(1H)-one (8c):

Prepared according to the **general procedure D** from **7c** (59 mg, 0.23 mmol) using 5 equivalent of PTSA at 30 °C for 6 h. Purification of the residue by column chromatography on silica gel (hexane: acetone = 2:4) gave inseparable mixture of diastereomers of **8c** (7:1) as yellow oil (41 mg, 91% yield).



8c

^{1}H NMR ($CDCl_3$, 400 MHz)

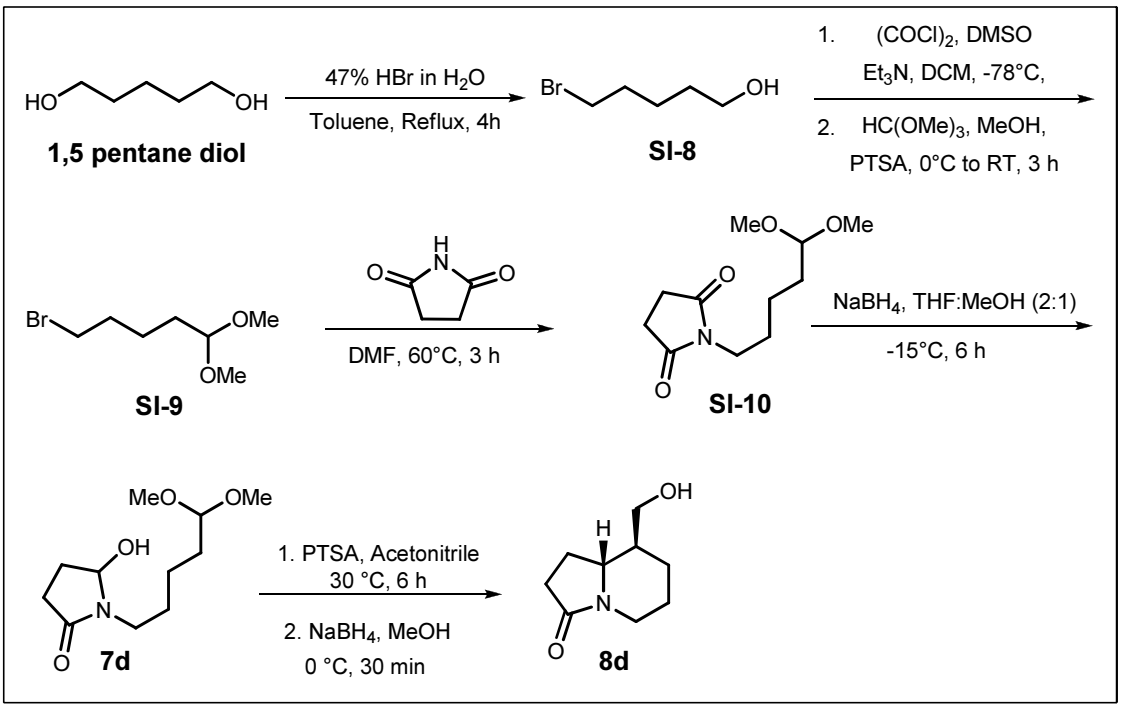
δ	**3.74 – 3.62**	(m, 2H)		**2.07**	(d, *J* = 17.6 Hz, 1H)
	3.61 – 3.54	(m, 1H)		**2.01– 1.87**	(m, 2H)
	3.43 – 3.36	(m, 2H)		**1.64**	(m, 1H)
	3.09	(bs, 1H)		**1.45**	(t, *J* = 12.7 Hz, 1H)
	2.36	(quin, *J* = 6.4 Hz, 1H)		**1.05**	(s, 3H)
	2.15	(d, *J* = 17.6 Hz, 1H)		**1.01**	(s, 3H)

^{13}C NMR ($CDCl_3$, 100 MHz)

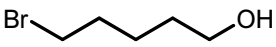
δ	**169.4**	**37.3**
	60.9	**31.4**
	57.3	**30.6**
	45.3	**25.8**
	43.2	**25.2**
	43.2	

IR(Neat): 3422, 2956, 1610, 1412, 1330, 1216, 1046, 758 cm^{-1}

HRMS (ESI): Calculated for $C_{11}H_{20}NO_2$ $[M+H]^+$: 198.1494 found 198.1492



Synthesis of 5-bromopentan-1-ol (SI-8): Prepared according to the same procedure described for **SI-1** from 1, 5 pentanediol (4.5 g, 43.2 mmol). Purification of the residue by column chromatography on silica gel (hexane: ethyl acetate = 4:1) gave title compound as yellow oil (5.92 g, 82% yield)



SI-8

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

δ **3.64** (t, *J* = 6.2 Hz, 2H) **1.88** (quin, , *J* = 7.2 Hz, 2H)

3.40 (t, *J* = 6.8 Hz, 2H) **1.65 – 1.45** (m, 4H)

^{13}C NMR ($CDCl_3$, 75 MHz)

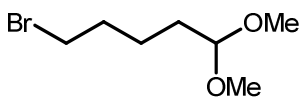
δ **62.2** **31.5**

33.7 **24.3**

32.4

Synthesis of 5-bromo-1,1-dimethoxypentane (SI-9): Prepared according to the **general procedure A** using **SI-8** (5.1 g, 30 mmol). Purification of the residue by column chromatography on silica gel

(hexane: ethyl acetate = 7:1) gave title compound as yellow oil (5.6g, 87% yield). The spectroscopic data were in full agreement with the literature report.[4]



SI-9

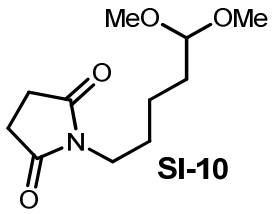
^{1}H NMR ($CDCl_3$, 300 MHz)

δ	**4.36**	(t, *J* = 5.5Hz, 1H)		**1.88**	(quin, , *J* = 7.2 Hz, 2H)
	3.40	(t, *J* = 6.8 Hz, 2H)		**1.67 – 1.57**	(m, 2H)
	3.32	(s, 6H)		**1.54 – 1.46**	(m, 2H)

^{13}C NMR ($CDCl_3$, 75 MHz)

δ	**104.4**	**32.6**
	52.9	**31.8**
	33.6	**23.4**

Synthesis of 1-(5,5-dimethoxypentyl)pyrrolidine-2,5-dione (SI-10): Prepared according to the **general procedure B** using **SI-9** (3 g, 14 mmol) and succinimide (2.1 g, 21 mmol). Purification of the residue by column chromatography on silica gel (hexane: acetone = 4:1) gave title compound as yellow oil (3.1 g, 97% yield).



SI-10

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

δ	**4.33**	(t, *J* = 5.6 Hz, 1H)		**2.68**	(s, 4H)
	3.50	(t, *J* = 7.4 Hz, 2H)		**1.65 – 1.52**	(m, 4H)
	3.30	(s, 6H)		**1.40 – 1.28**	(m, 2H)

^{13}C NMR ($CDCl_3$, 75 MHz)

δ	**177.1**	**31.9**

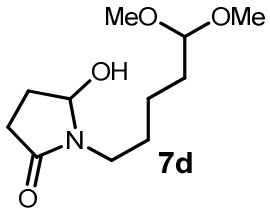
(4) Russell, M. G. N.; Matassa, V. G.; Pengilley, R. R.; van Niel, M. B.; Sohal, B.; Watt, A. P.; Hitzel, L.; Beer, M. S.; Stanton, J. A.; Broughton, H. B.; Castro, J. L. *J. Med. Chem.* **1999**, *42*, 4981-5001.

104.2	**28.0**
52.7	**27.4**
38.6	**21.8**

IR(Neat): 2945, 2869, 1773, 1701,1367, 1159, 758 cm^{-1}

HRMS (ESI): Calculated for $C_{11}H_{19}NNaO_4$ $[M+Na]^+$: 252.1212 found 252.1209

Synthesis of 1-(5,5-dimethoxypentyl)-5-hydroxypyrrolidin-2-one (7d): Prepared according to the **general procedure C** using **SI-10** (500 mg, 2.1 mmol)**.** Purification of the residue by column chromatography on silica gel (hexane: acetone = 3:1) gave title compound as yellow oil (465 mg, 95% yield).



7d

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

δ	**5.20**	(t, *J* = 6.0 Hz, 1H)	**2.61 – 2.46**	(m, 1H)
	4.34	(t, *J* = 5.6 Hz, 1H)	**2.40 – 2.24**	(m, 2H)
	3.50 – 3.40	(m, 1H)	**1.94 – 1.84**	(m, 1H)
	3.30	(s, 6H)	**1.67 – 1.50**	(m, 4H)
	3.29 – 3.13	(m, 2H)	**1.40 – 1.30**	(m, 2H)

^{13}C NMR ($CDCl_3$, 100 MHz)

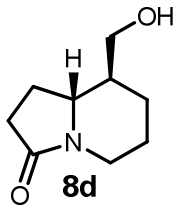
δ	**174.7**	**32.0**
	104.4	**28.9**
	83.2	**28.3**
	52.8	**27.4**
	39.8	**21.9**

IR(Neat): 3412, 3018, 1672, 1460, 1215, 1054, 759 cm^{-1}

HRMS (ESI): Calculated for $C_{11}H_{21}NNaO_4$ $[M+Na]^+$: 254.1368 found 254.1362

Synthesis of (8S,8aR)-8-(hydroxymethyl)hexahydroindolizin-3(5H)-one (8d): Prepared according to the **general procedure D** using **7d** (53 mg, 0.23 mmol) and 1 equiv of PTSA at 30 °C for 6 h.

Purification of the residue by column chromatography on silica gel (hexane: acetone = 3:1) gave an inseparable mixture of diastereomers of **8d** (14:1) as yellow oil (29 mg, 75% yield).



8d

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

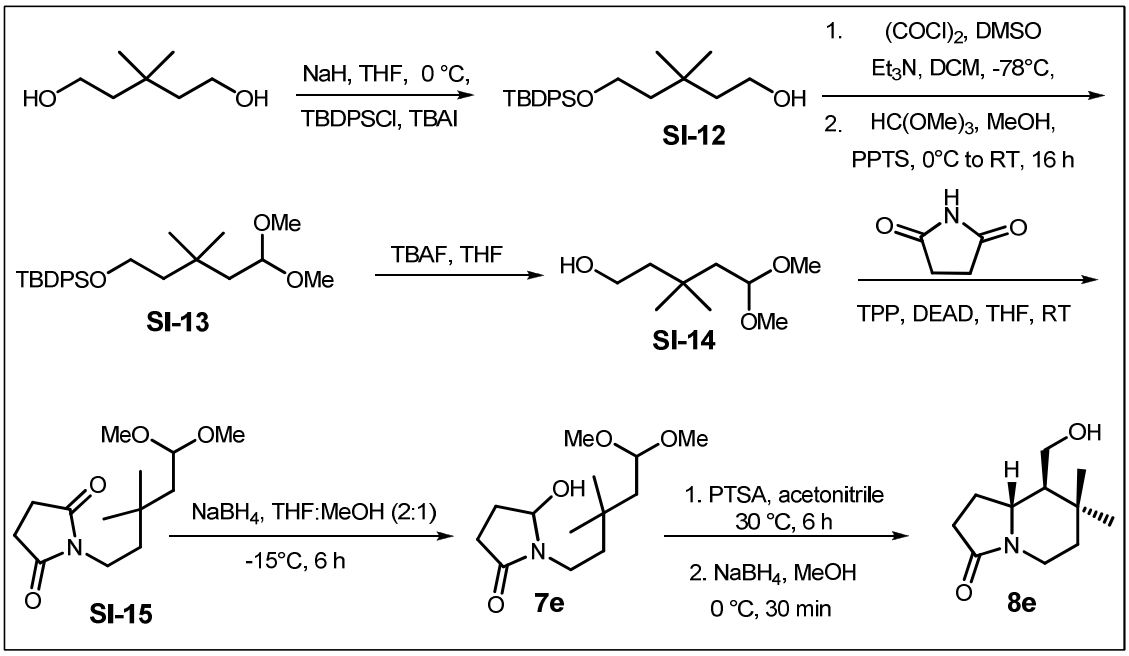
δ	**4.12**	(dd, *J* = 12.5, 4.4 Hz, 1H)	**2.42 – 2.26**	(m, 3H)
	3.66	(dd, *J* = 11.0, 4.3 Hz, 1H)	**2.11 – 1.91**	(m, 2H)
	3.58	(dd, *J* = 11.0, 4.8 Hz, 1H)	**1.80 – 1.66**	(m, 2H)
	3.25	(q, *J* = 8.2 Hz, 1H)	**1.48 – 1.21**	(m, 2H)
	2.56	(dt, *J* = 12.5, 2.8 Hz, 1H)		

^{13}C NMR ($CDCl_3$, 75 MHz)

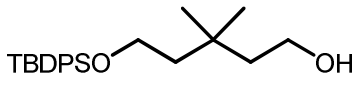
δ	**173.8**	**30.5**
	64.1	**27.0**
	59.0	**24.5**
	46.0	**24.0**
	39.9	

IR(Neat): 3430, 3019, 1664, 1460, 1215, 1047, 757 cm^{-1}

HRMS (ESI): Calculated for $C_9H_{16}NO_2$ $[M+H]^+$: 170.1181 found 170.1174



Synthesis of 5-(tert-butyldiphenylsilyloxy)-3,3-dimethylpentan-1-ol (SI-12): Prepared according to the **general procedure E** using 3,3-dimethylpentane-1,5-diol (3.2 gm, 24 mmol).[5] Purification of the residue by column chromatography on silica gel (15 % ethyl acetate in hexane) gave **SI-12** as yellow oil (8.4 g, 86% yield). Spectral data were found in agreement with the literature data.[6]



SI-12

^{1}H NMR ($CDCl_3$, 400 MHz)

δ **7.70–7.65** (m, 4H)
7.45–7.35 (m, 6H)
3.71 (t, *J* = 8.0 Hz, 2H)
3.62 (t, *J* = 8.2 Hz, 2H)
1. 60 (bs, 1H)
1.55 (t, *J* = 6.3 Hz, 2H)
1.48 (t, *J* = 6.4 Hz, 2H)
104 (s, 9H)
0.86 (s, 6H)

^{13}C NMR ($CDCl_3$, 100 MHz)

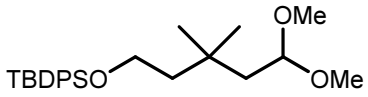
δ **135.7**
134.0
129.7
127.8
44.7
44.2
31.7
28.0

(5) L. B. D. Kelley and T. H. Lambert, *Org. Lett.* 2011, **13**, 740–743
(6) C. M. Hudson and K. D. Moeller, *J. Am. Chem. Soc.* 1994, **116**, 3347–3356

61.0 **27.0**

59.9 **19.2**

Synthesis of tert-butyl(5,5-dimethoxy-3,3-dimethylpentyloxy)diphenylsilane (SI-13): Prepared according to the **general procedure F** using **SI-12 (**3 gm, 7.82 mmol**)**. Purification of the residue by column chromatography on silica gel (10 % ethyl acetate in hexane) gave **SI-13** as yellow oil (2.66 g, 82% yield).



SI-13

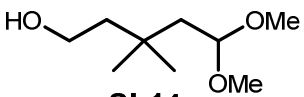
^{1}H NMR ($CDCl_3$, 400 MHz)

δ **7.70–7.65** (m, 4H)
7.43–7.35 (m, 6H)
4.40 (t, *J* = 5.3 Hz, 1H)
3.72 (t, *J* = 7.7 Hz, 2H)
3.24 (s, 6H)
1.57 (t, *J* = 7.3 Hz, 2H)
1.48 (d, *J* = 5.3 Hz, 2H)
104 (s, 9H)
0.87 (s, 6H)

^{13}C NMR ($CDCl_3$, 100 MHz)

δ **135.7**
134.2
129.6
127.7
102.7
60.9
52.3
44.9
44.4
31.3
27.9
27.0
19.2

Synthesis of 5,5-dimethoxy-3,3-dimethylpentan-1-ol (SI-14): Prepared according to the **general procedure G** using **SI-13** (1.35 gm, 3.26 mmol). Purification of the residue by column chromatography on silica gel (30% ethyl acetate in hexane) gave **SI-14** as yellow oil (300 mg, 52% yield).



SI-14

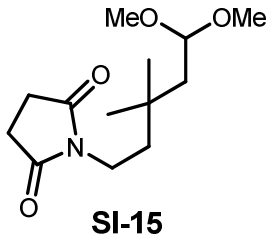
^{1}H NMR ($CDCl_3$, 400 MHz)

δ	**4.49**	(t, *J* = 5.2 Hz, 1H)	**1.61**	(d, *J* = 5.2 Hz, 2H)
	3.71	(t, *J* = 6.7 Hz, 2H)	**1. 56**	(t, *J* = 6.9 Hz, 2H)
	3.31	(s, 6H)	**0.97**	(s, 6H)

^{13}C NMR ($CDCl_3$, 100 MHz)

δ	**102.7**	**44.0**
	59.6	**31.4**
	52.5	**28.3**
	44.2	

Synthesis of 1-(5,5-dimethoxy-3,3-dimethylpentyl)pyrrolidine-2,5-dione (SI-15): Prepared according to the **general procedure H** using **SI-14** (96 mg, 0.54 mmol). Purification of the residue by column chromatography on silica gel (30% acetone in hexane) gave **SI-15** as yellow oil (135mg, 97% yield).



SI-15

^{1}H NMR ($CDCl_3$, 400 MHz)

δ	**4.46**	(t, *J* = 5.2 Hz, 1H)	**1.61**	(d, *J* = 5.2 Hz, 2H)
	3.51	(m, 2H)	**1.47**	(m, 2H)
	3.29	(s, 6H)	**0.98**	(s, 6H)
	2.66	(s, 4H)		

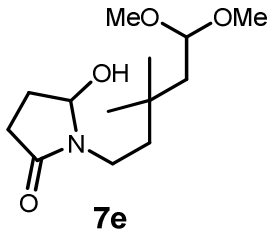
^{13}C NMR ($CDCl_3$, 100 MHz)

δ	**177.0**	**35.0**
	102.5	**31.3**
	52.4	**28.2**
	43.5	**27.4**
	39.2	

IR(Neat): 3021, 2401, 1702, 1408, 1151, 928, 670 cm^{-1}

HRMS (ESI): Calculated for $C_{13}H_{23}NO_4Na$ $[M+Na]^+$: 280.1525 found 280.1533

Synthesis of 1-(5,5-dimethoxy-3,3-dimethylpentyl)-5-hydroxypyrrolidin-2-one (7e): Prepared according to the **general procedure C** using **SI-15** (125 mg, 0.48 mmol)**.** Purification of the residue by column chromatography on silica gel (40 % acetone in hexane) gave **7e** as yellow oil Yield (125 mg, 99% yield).



7e

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

δ	**5.26**	(bs, 1H)	**2.58 – 2.47**	(m, 1H)
	4.48	(t, *J* = 4.8 Hz, 1H)	**2.34 – 2.24**	(m, 2H)
	3.77 – 3.66	(m, 1H)	**1.90 – 1.80**	(m, 1H)
	3.49	(td, *J* = 13.1, 5.6 H, 1H)	**1.62**	(dd, *J* = 14.2, 5.6 Hz, 1H)
	3.32	(s, 3H)	**1.54**	(td, *J* = 14.0, 4.7 Hz, 1H)
	3.29	(s, 3H)	**1.42**	(td, J = 14.9, 5.6 Hz, 1H)
	3.12	(td, *J* = 12.6, 4.6 Hz, 1H)	**0.96**	(s, 6H)

^{13}C NMR ($CDCl_3$, 100 MHz)

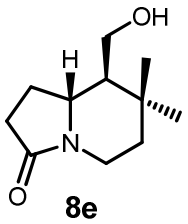
δ	**174.3**	**42.8**
	102.8	**31.2**
	82.9	**29.1**
	52.9	**28.0**
	52.1	**27.9**
	38.0	**27.8**
	35.8	

IR(Neat): 3400, 2960, 1676, 1466, 1324, 1122, 928, 626 cm^{-1}

HRMS (ESI): Calculated for $C_{13}H_{25}NO_4Na[M+Na]^+$: 282.1681 found 282.1678

Synthesis of (8S,8aR)-8-(hydroxymethyl)-7,7-dimethylhexahydroindolizin-3(5H)-one (8e): Prepared according to the **general procedure D** using **7e** (60 mg, 0.23 mmol) and 1 equiv of PTSA at

30 °C for 6 h. Purification of the residue by column chromatography on silica gel (40 % acetone in hexane) an inseparable mixture of diastereomers (3:1) of **8e** as yellow oil. Yield (37 mg, 82% yield).



8e

^{1}H NMR ($CDCl_3$, 400 MHz)

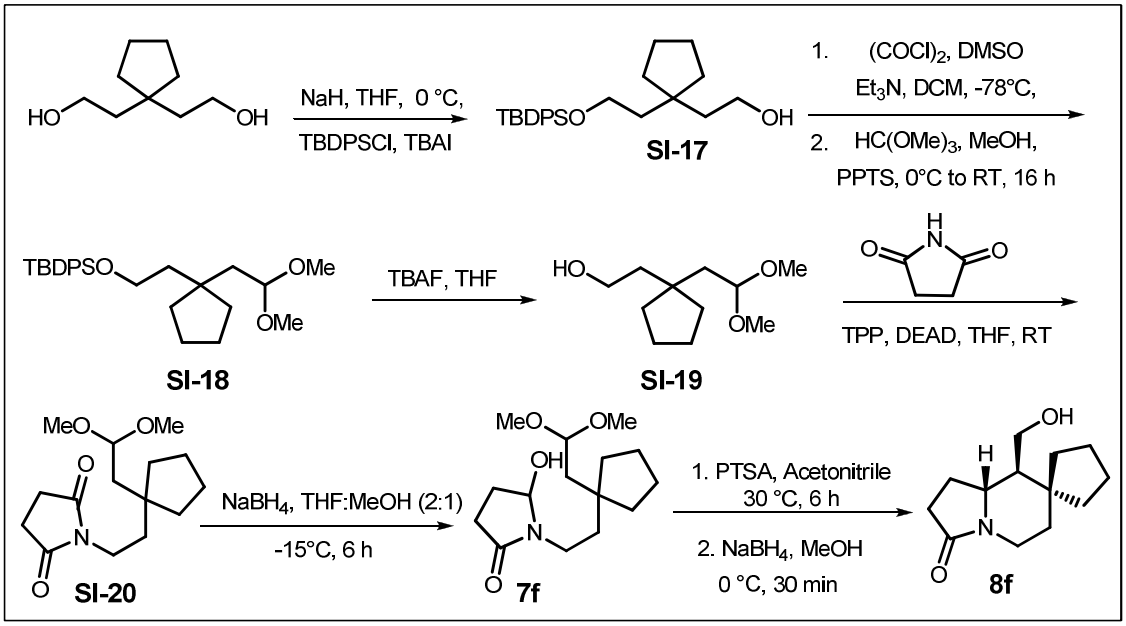
δ	**4.03**	(dt, *J* = 8.8, 4.6 Hz, 1H, minor)
	3.96	(t, *J* = 3.6 Hz, 1H, minor)
	3.93	(m, 1H, (major)
	3.88	(dd, *J* = 11.3, 3.8 Hz, 1H, major)
	3.82	(dd, *J* = 11.6, 2.2 Hz, 1H, minor)
	3.69 – 3.62	(m, 2H, (minor + major)
	3.51	(ddd, *J* = 12.5, 7.4, 2.4 Hz, 1H, major)
	2.89 – 2.76	(m, 2H, major + minor)
	2.48 – 2.29	(m, 3H, major + minor)
	2.24 – 2.15	(m, 1H, minor)
	2.12 – 2.01	(m, 1H, major)
	1.85 – 1.73	(m, 2H, major + minor)
	1.45 – 1.22	(m, 5H, major + minor)
	1.19 – 1.15	(m, 2H, major + minor)
	1.13	(s, 3H, minor)
	1.10	(s, 3H, minor)
	1.07	(s, 3H, major)
	0.96	(s, 3H, major)

^{13}C NMR ($CDCl_3$, 100 MHz)

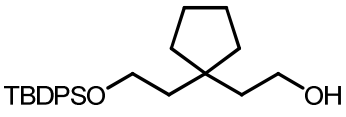
δ	**174.6, 173.9**	**32.7, 32.3**
	60.9, 58.7	**30.8, 30.6**
	56.4, 55.4	**30.1, 29.7**
	54.5, 49.9	**25.7 (two)**
	39.6, 36.4	**20.7, 19.6**
	36.0, 33.0	

IR(Neat): 3406, 2975, 2401, 1666, 1425, 1216, 1039, 761, 670 cm^{-1}

HRMS (ESI): Calculated for $C_{11}H_{20}NO_2[M+H]^+$: 198.1494 found 198.1485



Synthesis of 2-(1-(2-(tert-butyldiphenylsilyloxy)ethyl)cyclopentyl)ethanol (SI-17): Prepared according to the **general procedure E** using 2,2'-(cyclopentane-1,1-diyl)diethanol[7] (500 mg, 3.16 mmol). Purification of the residue by column chromatography on silica gel (7% ethyl acetate in hexane) gave **SI-17** as yellow oil (1.2 g, 89% yield).



SI-17

^{1}H NMR ($CDCl_3$, 400 MHz)

δ **7.72–7.66** (m, 4H)
7.45–7.36 (m, 6H)
3.71 (t, *J* = 6.5 Hz, 2H)
3.58 (t, *J* = 7.4 Hz, 2H)
1. 61 (t, *J* = 6.8 Hz, 2H)
1.58–1.51 (m, 6H)
1.39–1.33 (m, 4H)
1.06 (s, 9H)

^{13}C NMR ($CDCl_3$, 100 MHz)

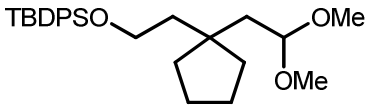
δ **135.7** **41.4**

(7) T. Hata, H. Imade and H. Urabe, *Org. Lett.* 2012, **14**, 2450–2453

133.9 **40.7**
129.7 **38.9**
127.7 **26.9**
61.6 **24.2**
60.3 **19.2**
43.0

Synthesis of tert-butyl(2-(1-(2,2-dimethoxyethyl)cyclopentyl)ethoxy)diphenylsilane (SI-18):

Prepared according to the **general procedure F** using **SI-17** (400 mg, 1 mmol). Purification of the residue by column chromatography on silica gel (5% ethyl acetate in hexane) gave **SI-18** as yellow oil (400 mg, 90% yield).



SI-18

^{1}H NMR ($CDCl_3$, 400 MHz)

δ **7.69–7.66** (m, 4H)
7.41–7.35 (m, 6H)
4.34 (t, *J* = 5.1 Hz, 1H)
3.72 (t, *J* = 7.7 Hz, 2H)
3.22 (s, 6H)
1. 65 (t, *J* = 7.6 Hz, 2H)
1.58–1.51 (m, 6H)
1.38 (t, *J* = 7.4 Hz, 4H)
1.01 (s, 9H)

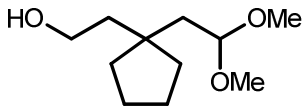
^{13}C NMR ($CDCl_3$, 100 MHz)

δ **135.6** **42.5**
134.1 **40.9**
129.5 **40.7**
127.6 **38.0**
103.3 **26.9**
61.6 **24.0**
52.5 **19.1**

IR(Neat): 3018, 2859, 2400, 1589, 1427, 1363, 1084, 929, 757, 614 cm^{-1}

HRMS (ESI): Calculated for $C_{27}H_{40}O_3SiNa[M+Na]^+$: 463.2644 found 463.2639

Synthesis of 2-(1-(2,2-dimethoxyethyl)cyclopentyl)ethanol (SI-19): Prepared according to the **general procedure G** using **SI-18** (250 mg, 0.56 mmol). Purification of the residue by column chromatography on silica gel (15% ethyl acetate in hexane) gave **SI-19** as yellow oil (108 mg, 95% yield).



SI-19

^{1}H NMR ($CDCl_3$, 400 MHz)

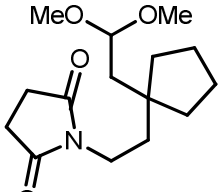
δ	**4.45**	(t, *J* = 5.0 Hz, 1H)		**1.70**	(d, *J* = 5.0 Hz, 2H)
	3.70	(t, *J* = 6.6 Hz, 2H)		**1.6–1.58**	(m, 6H)
	3.32	(s, 6H)		**1.46–1.42**	(s, 4H)

^{13}C NMR ($CDCl_3$, 100 MHz)

δ	**103.4**	**41.2**
	60.2	**40.8**
	52.6	**38.4**
	42.9	**24.0**

IR(Neat): 3401, 2930, 1673, 1404, 1127, 929, 668 cm^{-1}

Synthesis of 1-(2-(1-(2,2-dimethoxyethyl)cyclopentyl)ethyl)pyrrolidine-2,5-dione (SI-20): Prepared according to the **general procedure H** using **SI-19** (84 mg, 0.41 mmol). Purification of the residue by column chromatography on silica gel (30% acetone in hexane) gave **SI-20** as yellow oil (108 mg, 93% yield).



SI-20

^{1}H NMR ($CDCl_3$, 400 MHz)

δ	**4.48**	(t, *J* = 5.0 Hz, 1H)		**2.06**	(s, 4H)
	3.71	(m, 2H)		**1. 64–1.52**	(m, 8H)
	3.32	(s, 6H)		**1.50–1.44**	(s, 4H)

^{13}C NMR ($CDCl_3$, 75 MHz)

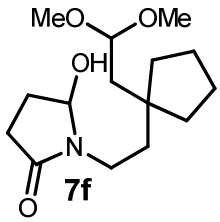
δ	**177.1**	**38.0**
	103.2	**35.9**
	52.8	**35.7**
	42.7	**28.2**
	40.6	**24.1**

IR(Neat): 2952, 2401, 1700, 1521, 1406, 1216, 1122, 928, 670 cm^{-1}

HRMS (ESI): Calculated for $C_{15}H_{25}NO_4Na[M+Na]^+$: 306.1681 found 306.1677

Synthesis of 1-(2-(1-(2,2-dimethoxyethyl)cyclopentyl)ethyl)-5-hydroxypyrrolidin-2-one (7f):

Prepared according to the **general procedure C** using **SI-20** (90 mg, 0.31 mmol)**.** Purification of the residue by column chromatography on silica gel (40% acetone in hexane) gave **7f** as yellow oil (90 mg, 99% yield).



7f

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

δ	**5.20**	(t, *J* = 5.2 Hz, 1H)	**2.55 – 2.44**	(m, 1H)
	4.45	(t, *J* = 4.5 Hz, 1H)	**2.31 – 2.15**	(m, 2H)
	4.27	(bs, 1H)	**1.91 – 1.82**	(m, 1H)
	3.45	(td, *J* = 12.4, 5.4 H, 1H)	**1.73– 1.65**	(m, 1H)
	3.31	(s, 3H)	**1.64– 1.54**	(m, 6H)
	3.29	(s, 3H)	**1.50– 1.37**	(m, 5H)
	3.12	(td, *J* = 12.5, 4.0 Hz, 1H)		

^{13}C NMR ($CDCl_3$, 100 MHz)

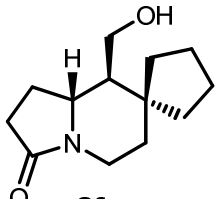
δ	**174.3**	**38.2**
	103.6	**37.9**
	82.8	**36.2**
	53.1	**35.0**

52.2	**29.2**
42.7	**27.7**
40.0	**24.0**

IR(Neat): 3406, 2958, 2401, 1679, 1423, 1216, 1047, 761, 627 cm^{-1}

HRMS (ESI): Calculated for $C_{15}H_{27o}O_4Na[M+Na]^+$: 308.1838 found 308.1826

Synthesis of (8'S,8a'R)-8'-(hydroxymethyl)tetrahydro-1'H-spiro[cyclopentane-1,7'-indolizin]-3'(2'H)-one (8f): Prepared according to the **general procedure D** using **7f** (65 mg, 0.23 mmol) and 1 equiv of PTSA at 30 °C for 6 h. Purification of the residue by column chromatography on silica gel (35 % acetone in hexane) gave an inseparable mixture of diastereomers (1:1) of **8f** as yellow oil (39 mg, 76% yield).



8f

^{1}H NMR ($CDCl_3$, 400 MHz)

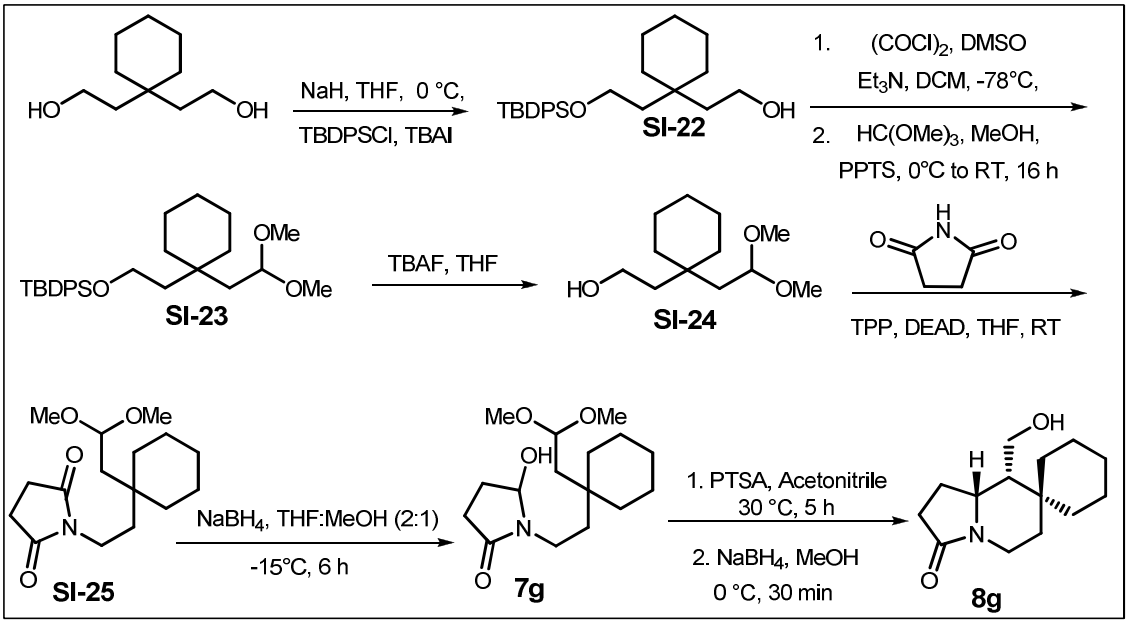
δ	**4.01– 3.93**	(m, 2H)	**2.73**	(dd, *J* = 13.4, 3.1 Hz, 1H)
	3.89– 3.83	(m, 2H)	**2.48 – 2.23**	(m, 4H)
	3.75–3.69	(m, 2H)	**2.10 – 1.98**	(m, 1H)
	3.64	(dd, *J* = 11.8, 3.6 Hz, 1H)	**1.89–1.80**	(m, 2H)
	3.42–3.35	(m, 1H)	**1.74–1.14**	(m, 23H)
	2.80	(dd, *J* = 13.2, 4.2 Hz, 1H)		

^{13}C NMR ($CDCl_3$, 100 MHz)

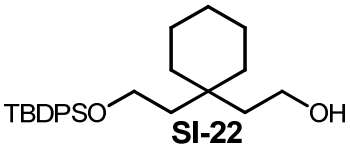
δ	**174.8, 173.9**	**36.8, 34.7**
	61.5, 60.3	**30.8, 30.6**
	58.3, 57.3	**30.3, 29.3**
	53.6, 51.6	**26.2, 25.4**
	45.1, 44.1	**25.2, 24.2**
	39.6, 38.9	**23.7, 20.8**
	37.8, 36.8	

IR(Neat): 3401, 2959, 1666, 1520, 1423, 1158, 928, 669 cm^{-1}

HRMS (ESI): Calculated for $C_{13}H_{22}NO_2[M+H]^+$: 224.1651 found 224.1644



Synthesis of 2-(1-(2-(tert-butyldiphenylsilyloxy)ethyl)cyclohexyl)ethanol (SI-22): Prepared according to the **general procedure E** using 2,2'-(cyclohexane-1,1-diyl)diethanol[8] (1.4 g, 8.1 mmol). Purification of the residue by column chromatography on silica gel (7% ethyl acetate) gave **SI-22** as yellow oil (3g, 89% yield).



^{1}H NMR ($CDCl_3$, 400 MHz)

δ **7.70–7.67** (m, 4H)
7.45–7.37 (m, 6H)
3.70 (t, *J* = 7.2 Hz, 2H)
3.57 (t, *J* = 7.7 Hz, 2H)
1. 62 (t, *J* = 7.2 Hz, 2H)
1. 53 (t, *J* = 7.7 Hz, 2H)
1.41–1.32 (m, 6H)
1.27–1.21 (m, 4H)
1.05 (s, 9H)

^{13}C NMR ($CDCl_3$, 100 MHz)

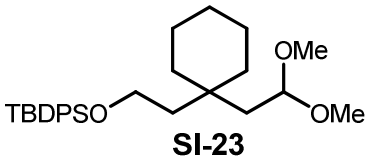
δ **135.6**
133.8
129.6
36.5
33.9
26.9

(8) F. C. Bargiggia and W. V. Murria, *Tetrahedron Lett.*, 2006, **47**, 3191

127.6	**26.3**
60.4	**21.5**
59.0	**19.0**
40.2	**14.2**
39.4	

Synthesis of tert-butyl(2-(1-(2,2-dimethoxyethyl)cyclohexyl)ethoxy)diphenylsilane (SI-23):

Prepared according to the **general procedure F** using **SI-22** (2 g, 4.8 mmol). Purification of the residue by column chromatography on silica gel (5% ethyl acetate in hexane) gave **SI-23** as yellow oil (2 g, 91% yield).



SI-23

^{1}H NMR ($CDCl_3$, 400 MHz)

δ	**7.71–7.66**	(m, 4H)	**1. 67**	(t, J = 7.6 Hz, 2H)
	7.43–7.36	(m, 6H)	**1.50**	(d, J = 5.2 Hz, 2H)
	4.39	(t, J = 5.2 Hz, 1H)	**1.42–1.19**	(m, 10H)
	3.71	(t, *J* = 7.7 Hz, 2H)	**1.04**	(s, 9H)
	3.23	(s, 6H)		

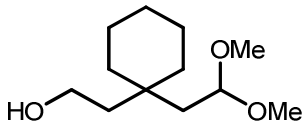
^{13}C NMR ($CDCl_3$, 100 MHz)

δ	**135.6**	**39.3**
	134.1	**36.3**
	129.5	**33.6**
	127.6	**26.9**
	102.5	**26.2**
	60.3	**21.6**
	52.5	**19.1**
	40.6	

IR(Neat): 2927, 1700, 1402, 1124, 1059, 771 cm^{-1}

HRMS (ESI): Calculated for $C_{28}H_{42}NaO_3Si$ $[M+H]^+$: 477.2801 found 477.2798

Synthesis of 2-(1-(2,2-dimethoxyethyl)cyclohexyl)ethanol (SI-24): Prepared according to the **general procedure G** using **SI-23** (1 g, 2.2 mmol). Purification of the residue by column chromatography on silica gel (15 % ethyl acetate) gave **SI-23** as yellow oil (420 mg, 88% yield).



SI-24

^{1}H NMR ($CDCl_3$, 400 MHz)

δ	**4.49**	(t, *J* = 5.2 Hz, 1H)		**1.69**	(d, *J* = 5.2 Hz, 2H)
	3.69	(t, *J* = 6.8 Hz, 2H)		**1.64**	(t, *J* = 6.8 Hz, 2H)
	3.32	(s, 6H)		**1.48–1.38**	(m, 6H)
	2.24	(bs, 1H)		**1.37–1.32**	(m, 4H)

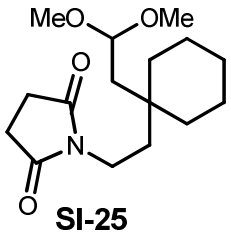
^{13}C NMR ($CDCl_3$, 100 MHz)

δ	**102.3**	**36.6**
	58.9	**33.5**
	52.5	**26.3**
	42.3	**21.4**
	39.4	

IR(Neat): 3427, 2930, 2855, 2400, 1652, 1457, 1120, 928, 669 cm^{-1}

HRMS (ESI): Calculated for $C_{12}H_{24}O_3Na[M+Na]^+$: 239.1623 found 239.1615

Synthesis of 1-(2-(1-(2,2-dimethoxyethyl)cyclohexyl)ethyl)pyrrolidine-2,5-dione (SI-25): Prepared according to the **general procedure H** using **SI-25** (200 mg, 0.86 mmol). Purification of the residue by column chromatography on silica gel (30% acetone in hexane) to gave **SI-25** as yellow oil (227 mg, 88% yield).



SI-25

^{1}H NMR ($CDCl_3$, 400 MHz)

δ	**4.54**	(t, *J* = 5.0 Hz, 1H)		**2.67**	(s, 4H)
	3.51	(m, 2H)		**1. 69–1.54**	(m, 6H)

3.33 (s, 6H) **1.49–1.32** (s, 8H)

^{13}C NMR ($CDCl_3$, 100 MHz)

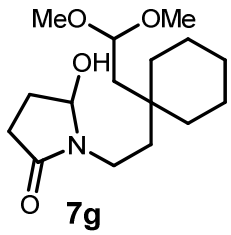
δ	**177.2**	**34.4**
	102.4	**33.7**
	52.8	**28.2**
	39.9	**26.2**
	36.6	**21.4**
	36.2	

IR(Neat): 3020, 2931, 2401, 1700, 1440, 1216, 1122, 1051, 928, 670 cm^{-1}

HRMS (ESI): Calculated for $C_{16}H_{27o}O_4Na[M+Na]^+$: 320.1838 found 320.1825

Synthesis of 1-(2-(1-(2,2-dimethoxyethyl)cyclohexyl)ethyl)-5-hydroxypyrrolidin-2-one (7g):

Prepared according to the **general procedure C** using **SI-25** (90 mg, 0.3 mmol)**.** Purification of the residue by column chromatography on silica gel (40 % acetone in hexane) gave **7g** as yellow oil (81 mg, 89% yield).



7g

^{1}H NMR ($CDCl_3$, 400 MHz)

δ	**5.24**	(m, 1H)	**3.09**	(td, *J* = 12.6, 4.0 Hz, 1H)
	4.52	(dd, *J* = 5.7, 4.2 Hz, 1H)	**2.58 – 2.47**	(m, 1H)
	3.96	(d, *J* = 5.3 Hz, 1H)	**2.34 – 2.24**	(m, 2H)
	3.46	(td, *J* = 12.3, 5.6 Hz, 1H)	**1.90 – 1.84**	(m, 3H)
	3.34	(s, 3H)	**1.70– 1.58**	(m, 3H)
	3.31	(s, 3H)	**1.55–1.24**	(m, 8H)

^{13}C NMR ($CDCl_3$, 100 MHz)

δ	**174.1**	**34.9**
	102.5	**33.7**
	82.7	**32.9**

53.2 **29.3**

52.0 **27.5**

39.2 **26.1**

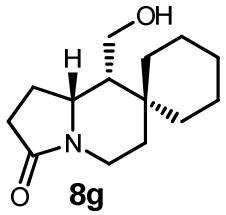
36.5 **21.4**

36.2

IR(Neat): 3402, 3019, 2400, 1678, 1422, 1215, 1047, 928, 669 cm^{-1}

HRMS (ESI): Calculated for $C_{16}H_{29}NO_2Na[M+Na]^+$: 322.1994 found 322.1993

Synthesis of (8'S,8a'R)-8'-(hydroxymethyl)tetrahydro-1'H-spiro[cyclohexane-1,7'-indolizin]-3'(2'H)-one (8g): Prepared according to the **general procedure D** using **7g** (68 mg, 0.23 mmol) and 1 equiv of PTSA at 30 °C for 5 h. Purification of the residue by column chromatography on silica gel (50 % acetone in hexane) gave an inseparable mixture of diastereomers (2:1)of **8g** as yellow oil (46 mg, 85% yield).



8g

^{1}H NMR ($CDCl_3$, 400 MHz)

δ **4.03** (ddd, *J* = 8.9, 6.0, 3.7 Hz, 1H) (major)

3.97–3.87 (m, 3H) (major + minor)

3.84 (dd, *J* = 11.4, 2.2 Hz, 1H) (major)

3.67 (dd, *J* = 11.6, 4.9 Hz, 1H) (minor)

3.63 (dd, *J* = 11.4, 5.5 Hz, 1H) (major)

3.60–3.54 (m, 1H) (minor)

2.85 (td, *J* = 13.5, 4.3 Hz, 1H) (major)

2.76 (td, *J* = 13.8, 3.2 Hz, 1H) (minor)

2.46 – 2.28 (m, 4H) (major + minor)

2.24 – 2.16 (m, 2H) (minor)

2.10 – 2.00 (m, 1H) (major)

1.81 – 1.04 (m, 26H) (major + minor)

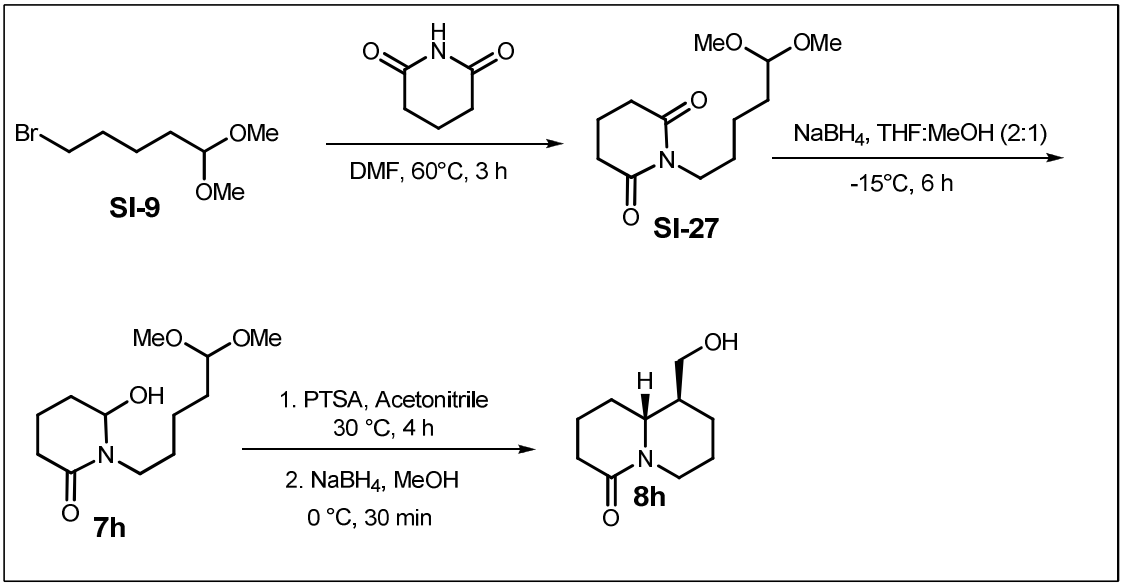
0.96 (tdd, *J* = 13.8, 5.3, 1.2 Hz, 1H)

^{13}C NMR ($CDCl_3$, 100MHz)

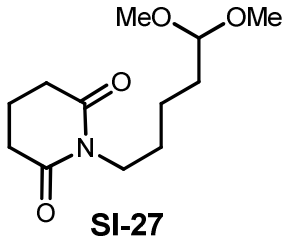
δ	**174.6, 173,7**	**32.7 (two)**
	60.4, 58.2	**30.8, 30.7**
	55.5, (two)	**30.6 (two)**
	54.6, 46.6	**26.4, 26.3**
	37.2, 36.7	**26.2, 25.8**
	35.7, 35.5	**21.3 (two)**
	35.3, 35.2	**21.0, 20.8**

IR(Neat): 3384, 3017, 2857, 1659, 1423, 1111, 756 cm^{-1}

HRMS (ESI): Calculated for $C_{14}H_{24}NO_2$ $[M+H]^+$: 238.1807 found 238.1805



Synthesis of 1-(5,5-dimethoxypentyl)piperidine-2,6-dione (SI-27): Prepared according to the **general procedure B** using glutarimide (2.4 g, 21.4 mmol) and **SI-9** (3 g, 14.2 mmol). Purification of the residue by column chromatography on silica gel (12 % acetone in hexane) gave **SI-27** as yellow oil (3.1 g, 92% yield).



SI-27

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

δ	**4.32**	(t, *J* = 5.7 Hz, 1H)		**1.91**	(quin, *J* = 6.6 Hz, 2H)
	3.74	(t, *J* = 7.5 Hz, 2H)		**1.65 – 1.55**	(m, 2H)
	3.29	(s, 6H)		**1.55 – 1.45**	(m, 2H)
	2.62	(t, *J* = 6.7 Hz, 4H)		**1.40 – 1.27**	(m, 2H)

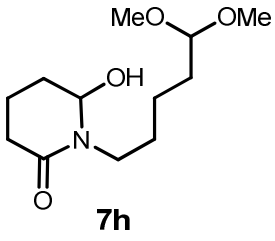
^{13}C NMR ($CDCl_3$, 75 MHz)

δ	**172.1**	**31.9**
	104.1	**27.5**
	52.4	**21.7**
	39.1	**16.9**
	32.6	

IR(Neat): 2948, 2831, 1673, 1356, 1291, 757 cm^{-1}

HRMS (ESI): Calculated for $C_{12}H_{21}NNaO_4$ $[M+Na]^+$: 266.1368 found 266.1373

Synthesis of 1-(5,5-dimethoxypentyl)-6-hydroxypiperidin-2-one (7h): Prepared according to the **general procedure C** using **SI-27** (1 g, 4.1 mmol). Purification of the residue by column chromatography on silica gel (20 % acetone in hexane) gave **7h** as yellow oil (970 mg, 95% yield).



7h

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

δ	**4.87**	(bs, 1H)		**2.33**	(td, *J* = 17.4, 4.7 Hz, 1H)
	4.26	(t, *J* = 5.6 Hz, 1H)		**2.20**	(ddd, *J* = 17.4, 9.9, 6.3 Hz, 1H)
	3.62 – 3.49	(m, 1H)		**2.03 – 1.90**	(m, 1H)

3.22	(s, 6H)	**1.87 – 1.71**	(m, 2H)
3.15 – 3.02	(m, 1H)	**1.65 – 1.43**	(m, 5H)
2.82	(bs, 1H)	**1.31 – 1.18**	(m, 2H)

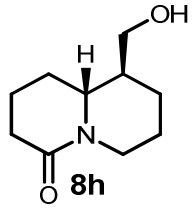
^{13}C NMR ($CDCl_3$, 75 MHz)

δ	**170.4**	**32.3**
	104.4	**32.1**
	79.6	**31.1**
	52.8	**27.7**
	52.7	**21.9**
	44.7	**15.7**

IR(Neat): 3432, 2950, 1620, 1336, 1126, 1075, 767dm^{-1}

HRMS (ESI): Calculated for $C_{12}H_{23}NNaO_4$ $[M+Na]^+$: 268.1525 found 268.1490; calculated for $C_{10}H_{16}NO_2$ $[M-2MeOH+H]^+$: 182.1181 found 182.1154

Synthesis of (9S,9aR)-9-(hydroxymethyl)hexahydro-1H-quinolizin-4(6H)-one (8h): Prepared according to the **General Procedure D** using **7h** (56 mg, 0.23 mmol) and 1 equiv of PTSA for 4 h. Purification of the residue by column chromatography on silica gel (1 % MeOH in chloroform) gave an inseparable mixture of diastereomers (9:1) of **8h** as yellow oil (32 mg, 76% yield).



8h

^{1}H NMR ($CDCl_3$, 400 MHz)

δ	**4.85–4.75**	(m, 1H)	**2.08–2.01**	(bs, 1H)
	3.64	(m, 2H)	**1.93–1.85**	(m, 1H)
	3.26 – 3.18	(m, 1H)	**1.84–1.78**	(m, 1H)
	2.46–2.41	(m, 1H)	**1.77–1.70**	(m, 1H)
	2.34–2.22	(m, 2H)	**1.66–1.57**	(m, 2H)
	2.18–2.09	(m, 1H)	**1.51–1.40**	(m, 3H)

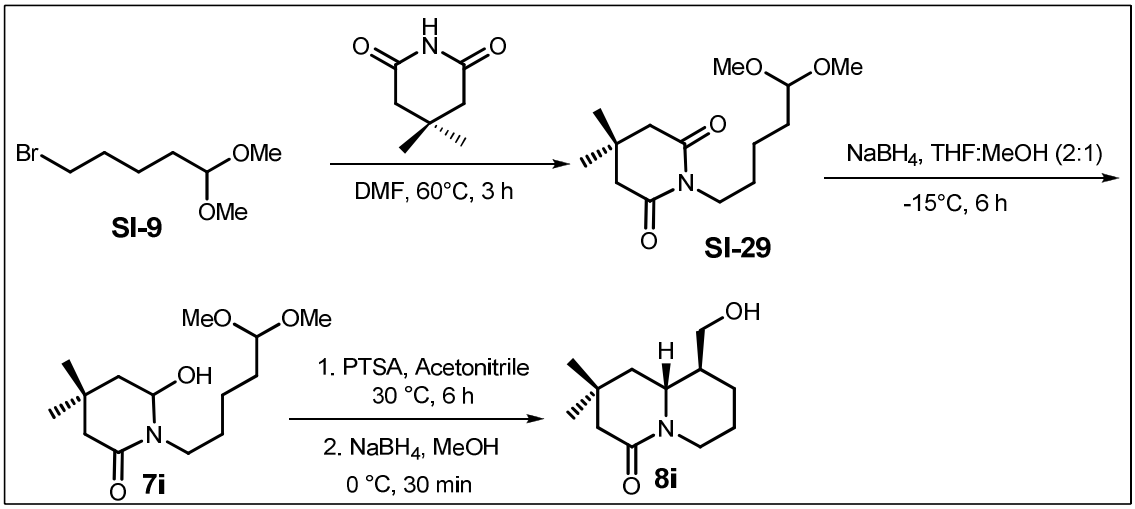
^{13}C NMR ($CDCl_3$, 100 MHz)

δ	**169.6**	**32.8**

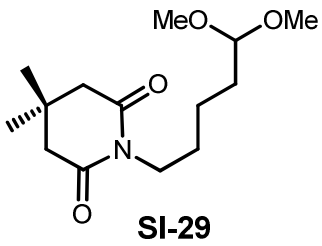
64.0	**28.2**
58.7	**27.4**
45.0	**24.8**
42.5	**18.8**

IR(Neat): 3398, 2941, 2464, 1611, 1448, 1268, 1080, 861 cm^{-1}

HRMS (ESI): Calculated for $C_{10}H_{18o}O_2$ $[M+H]^+$: 184.1338 found 184.1342



Synthesis of 1-(5,5-dimethoxypentyl)-4,4-dimethylpiperidine-2,6-dione (SI-29): Prepared according to the **general procedure B** using 3,3-dimethylglutarimide (1.5 g, 10.7 mmol) and **SI-9** (1.5 g, 7.1 mmol). Purification of the residue by column chromatography on silica gel (30 % acetone in hexane) gave **SI-29** as yellow oil (1.45 g, 75% yield).



SI-29

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

δ	**4.34**	(t, *J* = 5.7 Hz, 1H)		**1.67 – 1.48**	(m, 4H)
	3.76	(t, *J* = 7.4 Hz, 2H)		**1.40 – 1.32**	(m, 2H)
	3.30	(s, 6H)		**1.07**	(s, 6H)
	2.49	(s, 4H)			

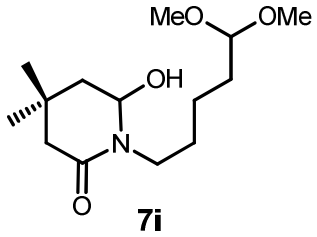
^{13}C NMR ($CDCl_3$, 75 MHz)

δ	**171.8**	**32.0**
	104.2	**29.0**
	52.6	**27.7**
	46.4	**27.6**
	39.3	**22.0**

IR(Neat): 2950, 1624, 1464, 1218, 1053 758 cm^{-1}

HRMS (ESI): Calculated for $C_{14}H_{25}NNaO_4$ $[M+Na]^+$: 294.1681 found 294.1657

Synthesis of 1-(5,5-dimethoxypentyl)-6-hydroxy-4,4-dimethylpiperidin-2-one (7i): Prepared according to the **general procedure C** using **SI-29** (400 mg, 1.47 mmol). Purification of the residue by column chromatography on silica gel (40 % acetone in hexane) gave **7i** as yellow oil (331 mg, 82% yield).



7i

^{1}H NMR ($CDCl_3$, 400 MHz)

δ	**4.92**	(dd, *J* = 13.5, 7.4 Hz, 1H)		**2.17**	(dd, *J* = 16.7, 2.0 Hz, 1H)
	4.35	(t, *J* = 5.6 Hz, 1H)		**2.01**	(ddd, *J* = 13.8, 5.6, 2.6 Hz, 1H)
	3.57	(ddd, *J* = 13.5, 9.3, 6.5 Hz, 1H)	**1.66 – 1.53**		(m, 5H)
	3.37	(ddd, *J* = 13.5, 8.9,6.5 Hz, 1H)	**1.40 – 1.32**		(m, 2H)
	3.31	(s, 6H)		**1.05**	(s, 3H)
3.26– 3.20		(m, 1H)		**0.96**	(s, 3H)
	2.22	(d, *J* = 16.7 Hz, 1H)			

^{13}C NMR ($CDCl_3$, 100 MHz)

δ	**169.8**	**42.6**
	104.5	**32.1**
	79.2	**29.9**
	52.8	**29.5**

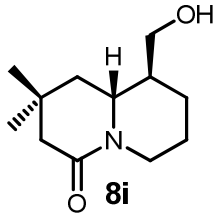
52.7	**27.2**
46.1	**26.1**
45.1	**22.2**

IR(Neat): 3385, 3010, 2951, 1624, 1645, 1383, 1216, 1052, 757 cm^{-1}

HRMS (ESI): Calculated for $C_{14}H_{27o}NaO_4$ $[M+Na]^+$: 296.1838 found 296.1829

Synthesis of (9S,9aR)-9-(hydroxymethyl)-2,2-dimethylhexahydro-1H-quinolizin-4(6H)-one (8i):

Prepared according to the **general procedure D** using **7i** (62 mg, 0.23 mmol) at 30 ° C for 6 h. Purification of the residue by column chromatography on silica gel (1% MeOH in chloroform) gave an inseparable mixture of diastereomers (17:1) of **8i** as yellow oil (39 mg, 81% yield).



8i

^{1}H NMR ($CDCl_3$, 400 MHz)

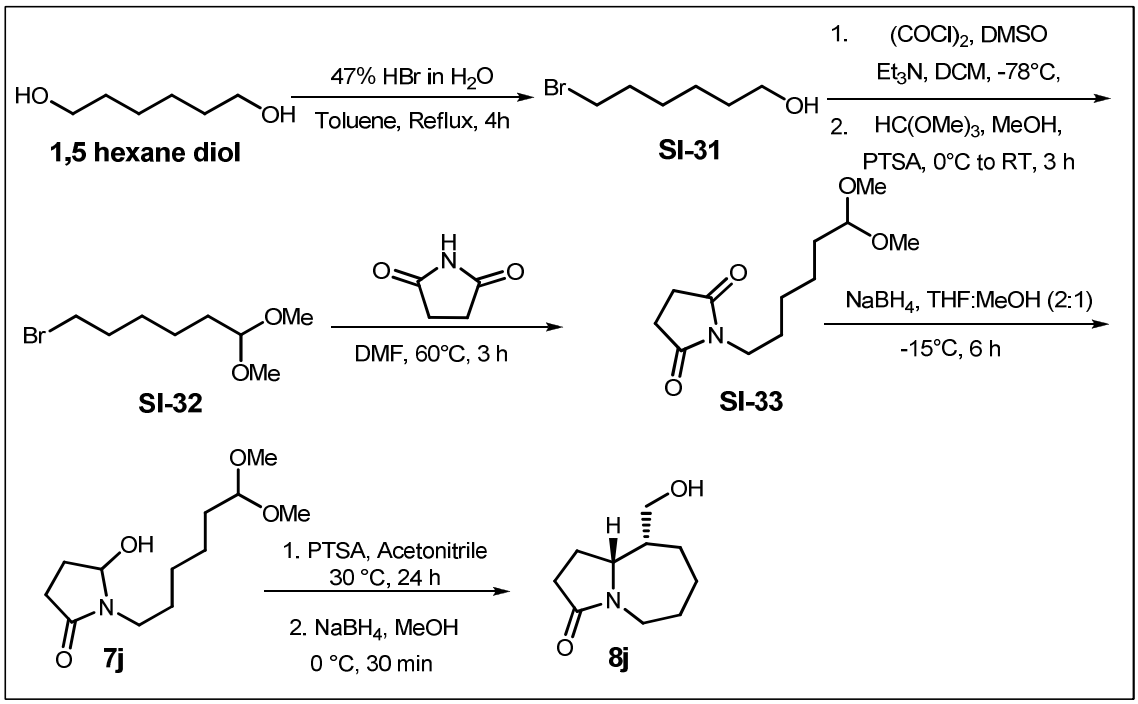
δ	**4.84 – 4.79**	(m, 1H)	**1.89**	(dd, *J* = 5.5, 3.2 Hz, 1H)
	3.65	(d, *J* = 4.0 Hz, 2H)	**1.79 – 1.74**	(m, 1H)
	3.19	(dt, *J* = 10.2, 5.6 Hz, 1H)	**1.52 – 1.41**	(m, 2H)
	2.35	(dt, *J* = 12.6, 2.6 Hz, 1H)	**1.38 – 1.31**	(m, 2H)
	2.19	(dd, *J* = 16.7, 3.1, Hz, 1H)	**1.00**	(s, 3H)
	2.12	(d, *J* = 16.7 Hz, 1H)	**0.91**	(s, 3H)
	1.92	(dd, *J* = 5.6, 3.3 Hz, 1H)		

^{13}C NMR ($CDCl_3$, 100 MHz)

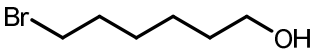
δ	**169.4**	**41.2**
	64.0	**30.9**
	56.0	**29.0**
	46.1	**28.2**
	45.9	**24.9**
	41.9	**24.6**

IR(Neat): 3435, 3019, 2400, 1620, 1403, 1215, 1058, 757, 669 cm^{-1}

HRMS (ESI): Calculated for $C_{12}H_{22}NO_2$ $[M+H]^+$: 212.1651 found 212.1648



Synthesis of 6-bromohexan-1-ol (SI-31): Prepared according to the same procedure described for **SI-1** from 1, 5 hexanediol (5 g, 42 mmol). Purification of the residue by column chromatography on silica gel (15% ethyl acetate hexane) gave **SI-31** as yellow oil (6.9 g, 91% yield)



SI-31

^{1}H NMR ($CDCl_3$, 400 MHz)

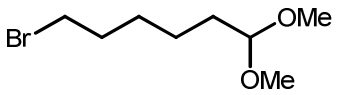
δ **3.64** (t, *J* = 6.8 Hz, 2H)
3.41 (t, *J* = 6.8 Hz, 2H)
1.87 (quin, *J* = 7.2 Hz, 2H)
1.60–1.55 (m, 2H)
1.51–1.35 (m, 4H)

^{13}C NMR ($CDCl_3$, 100 MHz)

δ **62.7**
33.8
32.7
32.5
27.9
24.9

Synthesis of 6-bromo-1,1-dimethoxyhexane (SI-32): Prepared according to the **general procedure A** using **SI-8** (5 g, 27.7 mmol). Purification of the residue by column chromatography on silica gel (10%

ethyl acetate hexane) gave **SI-32** as yellow oil (5.4 g, 87% yield). The spectroscopic data were in full agreement with the literature report.[9]



SI-32

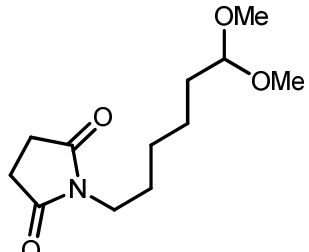
^{1}H NMR ($CDCl_3$, 400 MHz)

δ	**4.35**	(t, *J* = 5.7 Hz, 1H)	**1.63 – 1.58**	(m, 2H)
	3.40	(t, *J* = 7.0 Hz, 2H)	**1.50 – 1.42**	(m, 2H)
	3.31	(s, 6H)	**1.41 –1.33**	(m, 2H)
	1.87	(q, *J* = 7.0 Hz, 2H)		

^{13}C NMR ($CDCl_3$, 100 MHz)

δ	**104.4**	**32.3**
	52.7	**27.9**
	33.7	**23.7**
	32.7	

Synthesis of 1-(6,6-dimethoxyhexyl)pyrrolidine-2,5-dione (SI-33): Prepared according to the **general procedure B** using **SI-32** (3.1 g, 13.8 mmol) and succinimide (2.05 g, 20.7 mmol).). Purification of the residue by column chromatography on silica gel (40% ethyl acetate in hexane) gave **SI-33** as yellow oil. (3.1 g, 94% yield).



SI-33

^{1}H NMR ($CDCl_3$, 400 MHz)

δ	**4.34**	(t, *J* = 5.7 Hz, 1H)	**2.69**	(s, 4H)
	3.49	(t, *J* = 7.5 Hz, 2H)	**1.66 – 1.54**	(m, 4H)

(9) Russell, M. G. N.; Matassa, V. G.; Pengilley, R. R.; van Niel, M. B.; Sohal, B.; Watt, A. P.; Hitzel, L.; Beer, M. S.; Stanton, J. A.; Broughton, H. B.; Castro, J. L. *J. Med. Chem.* **1999**, *42*, 4981-5001.

3.30 (s, 6H) **1.41 – 1.29** (m, 4H)

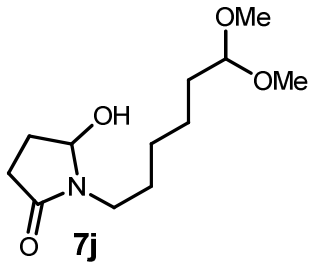
^{13}C NMR ($CDCl_3$, 100 MHz)

δ **177.3** **28.2**
104.3 **27.7**
52.6 **26.7**
38.8 **24.1**
32.3

IR(Neat): 2946, 2833, 2400, 1700, 1439, 1215, 1129, 928, 757, 668 cm^{-1}

HRMS (ESI): Calculated for $C_{12}H_{21}NO_4Na[M+Na]^+$: 266.1368 found 266.1365

Synthesis of 1-(6,6-dimethoxyhexyl)-5-hydroxypyrrolidin-2-one (7j): Prepared according to the **general procedure C** using **SI-33** (550 mg, 2.2 mmol**).**). Purification of the residue by column chromatography on silica gel (40% acetone in hexane) gave **7j** as yellow oil. (520 mg, 94% yield).



7j

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

δ **5.20** (bs, 1H) **2.56 – 2.45** (m, 1H)
4.32 (t, *J* = 5.6 Hz, 1H) **2.37 – 2.21** (m, 2H)
3.52 – 3.39 (m, 1H) **1.95 – 1.84** (m, 1H)
3.30 (s, 6H) **1.62 – 1.48** (m, 4H)
3.18 – 3.05 (m, 1H) **1.39 – 1.36** (m, 4H)

^{13}C NMR ($CDCl_3$, 100 MHz)

δ 174.8 **28.9**
104.5 **28.3**
83.2 **27.5**
52.7 (two) **26.7**

39.8 **24.1**

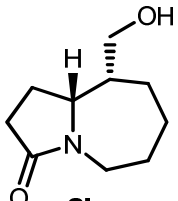
32.3

IR(Neat): 3384, 2942, 1668, 1422, 1283, 1127, 986, 756 cm^{-1}

HRMS (ESI): Calculated for $C_{12}H_{23}NO_4Na[M+Na]^+$: 268.1525 found 268.1523

Synthesis of (9S,9aR)-9-(hydroxymethyl)hexahydro-1H-pyrrolo[1,2-a]azepin-3(2H)-one (8j):

Prepared according to the **general procedure D** using **7j** (56 mg, 0.23 mmol) and 1 equiv of PTSA at 30 °C for 24 h. Purification of the residue by column chromatography on silica gel (40% acetone in hexane) gave an inseparable mixture of diastereomers (2:1) of **8j** as yellow oil (21 mg, 50%, 85% brsm).



8j

^{1}H NMR ($CDCl_3$, 400 MHz)

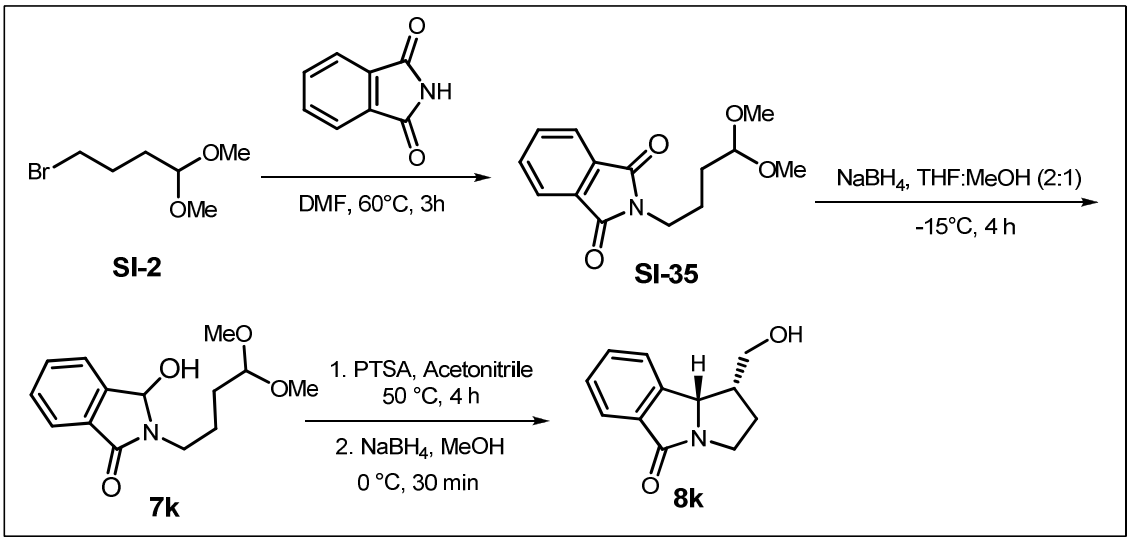
δ **3.98** (dt, *J* = 10.0, 6.0 Hz, 1H, minor)
3.93 (dt, *J* = 13.4, 3.8 Hz, 1H, minor)
3.86 (dt, *J* = 13.9, 4.7 Hz, 1H, major)
3.70 (dd, *J* = 10.6, 4.7 Hz, 1H, major)
3.64 (dd, *J* = 10.6, 6.8 Hz, 1H, major)
3.61 (dd, *J* = 11.0, 2.4 Hz, 1H, minor)
3.56 (dd, *J* = 11.0, 4.0 Hz, 1H, minor)
3.51 (dt, *J* = 7.4, 5.9 Hz, 1H, major)
2.97 (ddd, *J* = 13.9, 9.8, 3.9 Hz, 1H, major)
2.73 (ddd, *J* = 13.4, 11.4, 1.7 Hz, 1H, minor)
2.44 (dd, *J* = 9.3, 5.8 Hz, 1H, minor)
2.40 (dd, *J* = 9.0, 5.8 Hz, 1H, minor)
2.38 – 2.25 (m, 2H, major)
2.23 – 2.12 (m, 2H, major + minor)
2.02 – 1.92 (m, 1H, major)
1.84 – 1.57 (m, 12H, major + minor)
1.54 – 1.34 (m, 3H, major + minor)

^{13}C NMR ($CDCl_3$, 100 MHz)

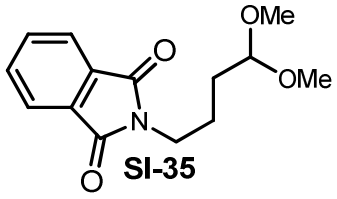
δ	**174.8, 174.4(minor)**	**30.8, 30.4(minor)**
	65.1, 36.4(minor)	**29.2, 29.1(minor)**
	62.1, 59.7(minor)	**28.4, 26.8(minor)**
	47.0, 45.2(minor)	**25.7, 24.6(minor)**
	42.2, 41.3(minor)	**24.8, 21.5(minor)**

IR(Neat): 3404, 2932, 2400, 1668, 1421, 1047, 928, 757, 626 cm^{-1}

HRMS (ESI): Calculated for $C_{10}H_{18o}O_2[M+H]^+$: 184.1338 found 184.1333



<u>Synthesis of 2-(4,4-dimethoxybutyl)isoindoline-1,3-dione (SI-35):</u> Prepared according to the **general procedure B** using phthalimide (1.1 g, 7.6 mmol) and **SI-2** (1 g, 5.1 mmol). Purification of the residue by column chromatography on silica gel (30% ethyl acetate in hexane) gave **SI-35** as yellow oil. (1 g, 78% yield).



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

δ	**7.86– 7.80**	(m, 2H)	**3.30**	(s, 6H)
	7.74–7.67	(m, 2H)	**1.80–1.70**	(m, 2H)
	4.39	(t, *J* = 5.6 Hz, 1H)	**1.80–1.70**	(m, 2H)

3.71 (t, *J* = 6.9 Hz, 2H)

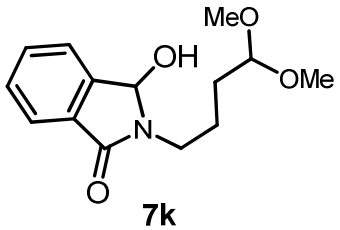
^{13}C NMR ($CDCl_3$, 75 MHz)

δ	**168.3**	**52.9**
	133.9	**37.6**
	132.1	**29.8**
	123.1	**23.8**
	104.1	

IR(Neat): 3020, 2946, 1614, 1440, 1398, 1368, 759 cm^{-1}

HRMS (ESI): Calculated for $C_{14}H_{17o}NaO_4$ $[M+Na]^+$: 286.1055 found 286.1057

Synthesis of 2-(4,4-dimethoxybutyl)-3-hydroxyisoindolin-1-one (7k): Prepared according to the **general procedure C** using **SI-35** (200 mg, 0.76 mmol). Purification of the residue by column chromatography on silica gel (50% ethyl acetate in hexane) gave **7k** as yellow oil. (197 mg, 98% yield).



7k

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

δ	**7.66–7.52**	(m, 3H)	**4.01–3.85**	(m, 1H)
	7.49–7.41	(m, 1H)	**3.57–3.32**	(m, 2H)
	5.76	(d, *J* = 11.0 Hz, 1H)	**3.26**	(s, 6H)
	4.31	(t, *J* = 5.3 Hz, 1H)	**1.80– 1.54**	(m, 4H)

^{13}C NMR ($CDCl_3$, 75 MHz)

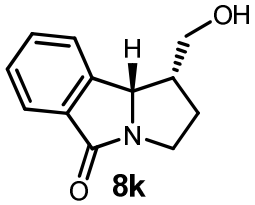
δ	**167.5**	**104.3**
	143.9	**81.9**
	132.1	**52.9**
	131.6	**52.8**
	129.7	**39.0**
	123.2	**29.8**
	123.1	**23.4**

IR(Neat): 3390, 3016, 2939, 1684, 1428, 1315, 1059, 758 cm^{-1}

HRMS (ESI): Calculated for $C_{14}H_{19}NNaO_4$ $[M+Na]^+$: 288.1212 found 288.1208

Synthesis of (1R,9bS)-1-(hydroxymethyl)-2,3-dihydro-1H-pyrrolo[2,1-a]isoindol-5(9bH)-one (8k):

Prepared according to the **general procedure D** using **7k** (61 mg, 0.23 mmol) for 4 h at 45 °C. Purification of the residue by column chromatography on silica gel (50% acetone in hexane) gave an inseparable mixture of diastereomers (9:1) of **8k** as yellow oil. (35 mg, 75% yield).



8k

^{1}H NMR ($CDCl_3$, 400 MHz)

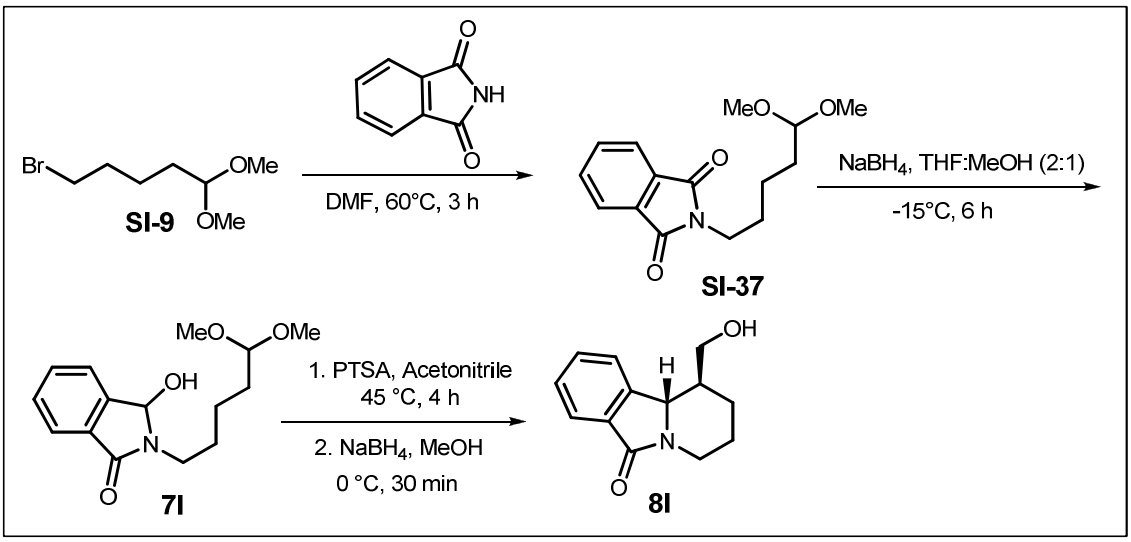
δ	**7.80**	(d, *J* = 7.5 Hz, 1H)		**3.21 – 3.16**	(m, 1H)
	7.55 – 7.44	(m, 3H)		**3.01 – 2.96**	(m, 1H)
	4.92	(d, *J* = 6.4 Hz, 1H)		**2.69**	(quint of d, *J* = 6.4, 1.4 Hz, 1H)
	3.74	(ddd, *J* = 11.6, 8.9, 2.7 Hz, 1H)		**2.49 – 2.40**	(m, 1H)
				2.37– 2.30	(m, 1H)
	3.42	(ddd, *J* = 11.6, 9.5, 2.8 Hz, 1H)			

^{13}C NMR ($CDCl_3$, 100 MHz)

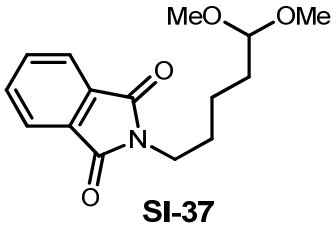
δ	**170.9**	**123.6**
	143.2	**66.2**
	135.1	**60.9**
	131.5	**40.7**
	128.6	**40.5**
	124.2	**31.1**

IR(Neat): 3415, 3015, 2892, 2401, 1671, 1400, 1331, 1046, 757 cm^{-1}

HRMS (ESI): Calculated for $C_{12}H_{14}NO_2$ $[M+H]^+$: 204.1025 found 204.1020



Synthesis 2-(5,5-dimethoxypentyl)isoindoline-1,3-dione (SI-37): Prepared according to the **general procedure B** using phthalimide (1.1 g, 7.6 mmol) and **SI-9** (1 g, 5.1 mmol). Purification of the residue by column chromatography on silica gel (30% ethyl acetate in hexane) gave **SI-37** as yellow oil. (1 g, 78% yield)



SI-37

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

δ	**7.86– 7.81**	(m, 2H)	**3.30**	(s, 6H)
	7.73–7.68	(m, 2H)	**1.76–1.61**	(m, 4H)
	4.35	(t, *J* = 5.6 Hz, 1H)	**1.46–1.35**	(m, 2H)
	3.69	(t, *J* = 7.2 Hz, 2H)		

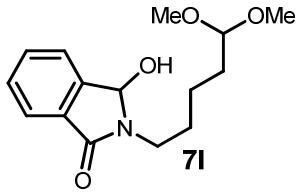
^{13}C NMR ($CDCl_3$, 75 MHz)

δ	**168.4**	**52.7**
	133.9	**37.8**
	132.1	**32.0**
	123.1	**28.4**
	104.3	**21.9**

IR(Neat): 3017, 2944, 1711, 1616, 1440, 1397, 1367, 723 cm^{-1}

HRMS (ESI): Calculated for $C_{15}H_{19}NNaO_4$ $[M+Na]^+$: 300.1212 found 300.1209

Synthesis of 2-(5,5-dimethoxypentyl)-3-hydroxyisoindolin-1-one (7l): Prepared according to the **general procedure C** using **SI-37** (200 mg, 0.76 mmol). Purification of the residue by column chromatography on silica gel (50% ethyl acetate in hexane) gave **7l** as yellow oil. (197 mg, 98% yield).



7l

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

δ	**7.63– 7.53**	(m, 3H)	**3.35 – 3.28**	(m, 1H)
	7.48– 7.41	(m, 1H)	**3.25**	(s, 6H)
	5.74	(d, *J* = 11.5 Hz, 1H)	**1.79 – 1.72**	(m, 1H)
	4.29	(t, *J* = 5.6 Hz, 1H)	**1.69 – 1.54**	(m, 3H)
	4.0–3.8	(m, 1H)	**1.38 – 1.28**	(m, 2H)
	3.53 – 3.48	(m, 1H)		

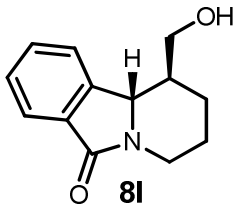
^{13}C NMR ($CDCl_3$, 75 MHz)

δ	**167.4**	**81.8**
	143.9	**52.7**
	132.0	**52.6**
	131.6	**39.1**
	129.7	**32.0**
	123.2	**28.0**
	123.1	**21.9**
	104.3	

IR(Neat): 3391, 3013, 2940, 1682, 1317, 1056, 756 cm^{-1}

HRMS (ESI): Calculated for $C_{15}H_{21}NNaO_4$ $[M+Na]^+$: 302.1368 found 302.1362

Synthesis of (1S,10bS)-1-(hydroxymethyl)-1,2,3,4-tetrahydropyrido[2,1-a]isoindol-6(10bH)-one (8l): Prepared according to the **general procedure D** using **7l** (64 mg, 0.23 mmol) for 4 h at 45 °C as an inseparable mixture of diastereomers (19:1). Purification of the residue by column chromatography on silica gel (50% ethyl acetate in hexane) gave **8l** as yellow oil. (35 mg, 70% yield).



8l

^{1}H NMR ($CDCl_3$, 400 MHz)

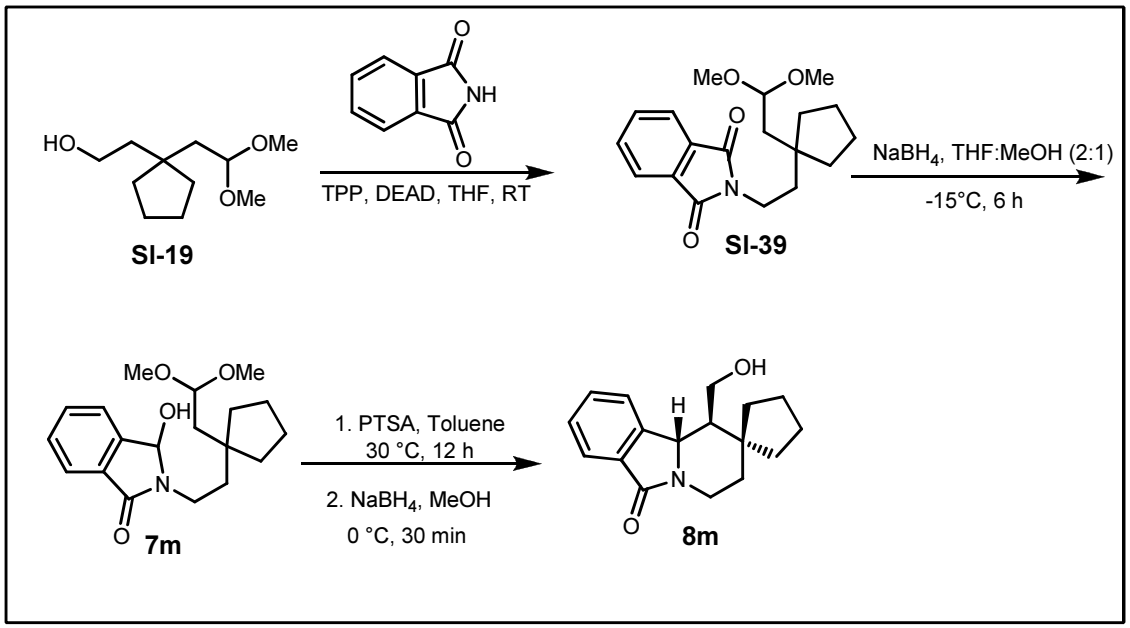
δ	**7.87**	(d, *J* = 7.1 Hz, 1H)		**3.95**	(dd, *J* = 11.0, 3.5 Hz, 1H)
	7.60	(d, *J* = 7.3 Hz, 1H)		**2.92**	(dt, *J* = 13.0, 3.6 Hz, 1H)
	7.50	(dt, *J* = 7.5, 1.4 Hz, 1H)		**2.00**	(m, 1H)
	7.45	(dt, *J* = 7.3, 0.8 Hz, 1H)		**1.89**	(m, 1H)
	4.49	(dd, *J* = 13.1, 4.5 Hz, 1H)		**1.78**	(dq, *J* = 12.8, 3.4 Hz, 1H)
	4.35	(d, *J* = 11.0 Hz, 1H)		**1.49**	(tq, *J* = 13.0, 3.4 Hz, 1H)
	4.11	(dd, *J* = 11.0, 5.0 Hz, 1H)		**1.35 – 1.25**	(m, 1H)

^{13}C NMR ($CDCl_3$, 100 MHz)

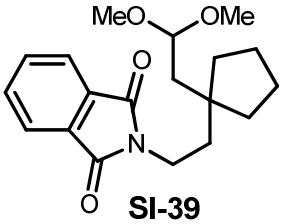
δ	**166.2**	**63.8**
	144.5	**60.1**
	132.7	**45.0**
	130.8	**39.4**
	128.1	**27.9**
	123.8	**25.5**
	123.7	

IR(Neat): 3413, 3016, 1661, 1433, 1215, 1045, 755 cm^{-1}

HRMS (ESI): Calculated for $C_{13}H_{16}NO_2$ $[M+H]^+$: 218.1181 found 218.1161



Synthesis of 2-(2-(1-(2,2-dimethoxyethyl)cyclopentyl)ethyl)isoindoline-1,3-dione (SI-39): Prepared according to the **general procedure H** using **SI-19** (100 mg, 0.49 mmol) and phthalimide (80 mg, 0.54 mmol) . Purification of the residue by column chromatography on silica gel (15% ethyl acetate in hexane) gave **SI-39** as yellow oil (150 mg, 91% yield).



^{1}H NMR ($CDCl_3$, 400 MHz)

δ **7.81** (dd, *J* = 5.4, 3.0 Hz, 2H)
7.68 (dd, *J* = 5.4, 3.0 Hz, 2H)
4.52 (t, *J* = 5.1 Hz, 1H)
3. 74–3.69 (m, 2H)
3.34 (s, 6H)
1. 70–1.65 (m, 3H)
1.64–1.59 (m, 5H)
1.54–1.48 (m, 4H)

^{13}C NMR ($CDCl_3$, 100 MHz)

δ **168.3**
133.8
132.3
123.0
42.8
40.6
38.1
36.9

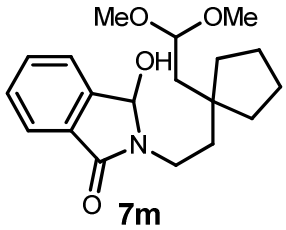
103.3	**34.9**
52.9	**24.2**

IR(Neat): 3019, 2955, 1710, 1619, 1523, 1400, 1215, 1047, 757, 669 cm^{-1}

HRMS (ESI): Calculated for $C_{17}H_{20}NO_3$ $[M+H-C_2H_6O]^+$: 286.1443 found 286.1442

Synthesis of 2-(2-(1-(2,2-dimethoxyethyl)cyclopentyl)ethyl)-3-hydroxyisoindolin-1-one (7m):

Prepared according to the **general procedure C** using **SI-39** (115 mg, 0.34 mmol)**.** Purification of the residue by column chromatography on silica gel (30% Acetone in hexane) gave **7m** as yellow oil (113 mg, 99% yield).



7m

^{1}H NMR ($CDCl_3$, 400 MHz)

δ	**7.68**	(d *J* = 7.6 Hz, 1H)		**3.90**	(bs, 1H)
	7.60	(d *J* = 7.6 Hz, 1H)		**3.53**	(td, J = 13.1, 5.4 Hz, 1H)
	7.55	(td, J = 7.4, 1.2 Hz, 1H)		**3.37–3.30**	(m, 7H)
	7.46	(td, J = 7.4, 1.2 Hz, 1H)		**1. 75–1.67**	(m, 3H)
	5.78	(d, J = 9.0 Hz, 1H)		**1.65–1.56**	(m, 6H)
	4.49	(dd, J = 5.4, 4.4 Hz, 1H)		**1.55–1.43**	(m, 3H)

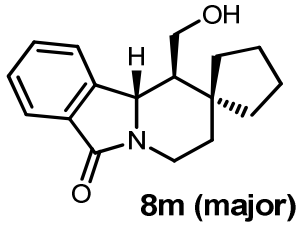
^{13}C NMR ($CDCl_3$, 100 MHz)

δ	**167.2**	**52.5**
	143.9	**42.7**
	131.9	**40.0**
	129.5	**38.2**
	123.2	**37.9**
	123.1	**36.2**
	103.5	**35.8**
	81.5	**24.2**
	52.8	**24.1**

IR(Neat): 3405, 3019, 2926, 1688, 1523, 1421, 1122, 1046, 758, 626 cm^{-1}

HRMS (ESI): Calculated for $C_{19}H_{27o}O_4Na[M+Na]^+$: 356.1838 found 356.1836

Synthesis of (1'S,10b'S)-1'-(hydroxymethyl)-3',4'-dihydro-1'H-spiro[cyclopentane-1,2'-pyrido[2,1-a]isoindol]-6'(10b'H)-one (8g): Prepared according to the **general procedure D** using **7m** (76 mg, 0.23 mmol) and 1 equiv of PTSA at 30 °C for 12 h in toluene. Purification of the residue by column chromatography on silica gel (50% ethyl acetate in hexane) gave **8m** as major isomer (35 mg) and the minor isomer (24 mg) as yellow oil. (total 94% yield)



8m (major)

^{1}H NMR ($CDCl_3$, 400 MHz)

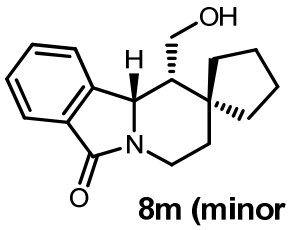
δ	**7.86**	(d, *J* = 7.2 Hz, 1H)		**4.16**	(dd, *J* = 11.7, 2.3 Hz, 1H)
	7.71	(d, *J* = 7.4 Hz, 1H)		**4.08**	(dd, *J* = 11.7, 4.0 Hz, 1H)
	7.50	(td, *J* = 7.5, 1.2 Hz, 1H)		**3.11**	(td, *J* = 13.6, 3.4 Hz, 1H)
	7.44	(t, *J* = 7.5 Hz, 1H)	**1.97 – 1.31**		(m, 9H)
	4.55	(d, *J* = 11.0 Hz, 1H)	**1.47 – 1.29**		(m, 2H)
	4.39	(ddd, *J* = 13.6, 5.4, 1.5 Hz, 1H)			

^{13}C NMR ($CDCl_3$, 100 MHz)

δ	**166.1**	**52.1**
	144.7	**45.2**
	132.7	**39.0**
	130.8	**38.9**
	128.0	**36.6**
	124.0	**30.0**
	123.7	**26.1**
	60.1	**25.5**
	58.9	

IR(Neat): 3430, 3019, 1664, 1460, 1215, 1047, 757 cm^{-1}

HRMS (ESI): Calculated for $C_{17}H_{22}NO_2[M+H]^+$: 272.1651 found 272.1647



8m (minor isomer)

^{1}H NMR ($CDCl_3$, 400 MHz)

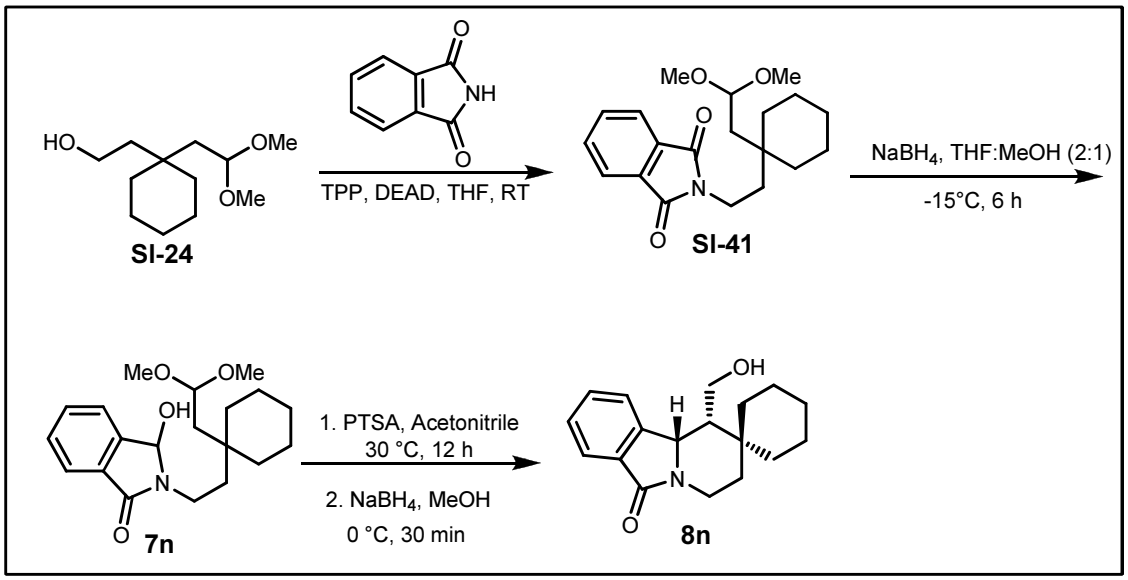
δ	**7.87**	(d, *J* = 7.4 Hz, 1H)	**3.15 – 3.06**	(m, 2H)
	7.54–7.44	(m, 3H)	**2.16 – 2.11**	(m, 1H)
	4.70	(d, *J* = 3.7 Hz, 1H)	**2.05 – 1.98**	(m, 1H)
	4.34	(dd, *J* = 13.8, 5.8 Hz, 1H)	**1.81 – 1.45**	(m, 7H)
	3.40	(d, *J* = 11.8 Hz, 1H)	**1.39 – 1.29**	(m, 2H)

^{13}C NMR ($CDCl_3$, 100 MHz)

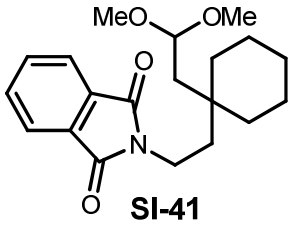
δ	**166.8**	**51.7**
	143.9	**45.3**
	133.3	**39.1**
	130.9	**36.2**
	128.4	**35.0**
	123.9	**31.0**
	123.8	**24.3**
	59.8	**23.9**
	59.2	

IR(Neat): 3408, 3019, 2957, 1675, 1470, 1215, 1047, 928, 757, 669 cm^{-1}

HRMS (ESI): Calculated for $C_{17}H_{22}NO_2[M+H]^+$: 272.1651 found 272.1643



Synthesis of 2-(2-(1-(2,2-dimethoxyethyl)cyclohexyl)ethyl)isoindoline-1,3-dione (SI-41): Prepared according to the **general procedure H** using **SI-24** (130 mg, 0.6 mmol) and phthalimide (97 mg, 0.66 mmol) . Purification of the residue by column chromatography on silica gel (15% ethyl acetate in hexane) gave **SI-41** as yellow oil (117 mg, 56% yield).



^{1}H NMR ($CDCl_3$, 400 MHz)

δ **7.82** (dd, *J* = 5.5, 3.6 Hz, 2H)
7.68 (dd, *J* = 5.5, 3.0 Hz, 2H)
4.59 (t, *J* = 5.1 Hz, 1H)
3.71–3.67 (m, 2H)
3.35 (s, 6H)
1. 70–1.65 (m, 4H)
1.51–1.32 (s, 10H)

^{13}C NMR ($CDCl_3$, 100 MHz)

δ **168.3**
133.8
132.3
123.0
102.4
36.3
35.1
33.7
33.6
26.2

52.8 **21.4**

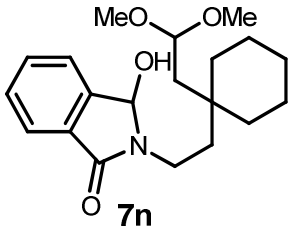
40.1

IR(Neat): 3021, 2931, 2401, 1711, 1521, 1302, 1120, 1053, 758, 532 cm^{-1}

HRMS (ESI): Calculated for $C_{20}H_{27o}O_4Na[M+Na]^+$: 368.1838 found 368.1838

Synthesis of 2-(2-(1-(2,2-dimethoxyethyl)cyclohexyl)ethyl)-3-hydroxyisoindolin-1-one (7n):

Prepared according to the **general procedure C** using **SI-41** (85 mg, 0.24 mmol)**.** Purification of the residue by column chromatography on silica gel (40% ethyl acetate in hexane) gave **7n** as yellow oil (85 mg, 99% yield).



7n

^{1}H NMR ($CDCl_3$, 400 MHz)

δ	**7.67**	(d, *J* = 7.4 Hz, 1H)	**3.53 – 3.42**	(m, 1H)
	7.59	(d, *J* = 7.2 Hz, 1H)	**3.31**	(s, 3H)
	7.54	(td, *J* = 7.3, 1.0 Hz, 1H)	**3.30**	(s, 3H)
	7.45	(td, *J* = 7.4, 1.0 Hz, 1H)	**1.82 – 1.76**	(m, 1H)
	5.78	(d, *J* = 8.4 Hz, 1H)	**1.70 – 1.55**	(m, 4H)
	4.52	(t, *J* = 5.1 Hz, 1H)	**1.50 – 1.31**	(m, 9H)
	4.21 –4.08	(m, 1H)		

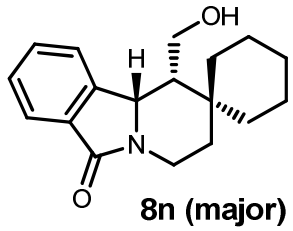
^{13}C NMR ($CDCl_3$, 100 MHz)

δ	**167.3**	**39.5**
	143.9	**36.4**
	131.9(two)	**36.1**
	129.6	**34.5**
	123.2 (two)	**34.3**
	102.5	**33.7**
	81.6	**26.1**
	52.8	**21.4**
	52.5	**21.3**

IR(Neat): 3386, 3019, 2928, 1686, 1420, 1215, 1053, 928, 669 cm^{-1}

HRMS (ESI): Calculated for $C_{20}H_{29}NO_4Na[M+Na]^+$: 370.1994 found 370.1994

Synthesis of (1'S,10b'S)-1'-(hydroxymethyl)-3',4'-dihydro-1'H-spiro[cyclohexane-1,2'-pyrido[2,1-a]isoindol]-6'(10b'H)-one (8n): Prepared according to the **general procedure D** using **7n** (80 mg, 0.23 mmol) and 1 equiv of PTSA at 30 °C for 12 h. Purification of the residue by column chromatography on silica gel (50% ethyl acetate in hexane) gave **8n** as major isomer (32 mg) and its minor isomer (22 mg) as yellow oil. (total 82% yield)



8n (major)

^{1}H NMR ($CDCl_3$, 400 MHz)

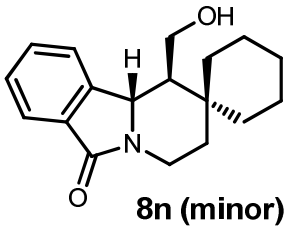
δ **7.87** (d, *J* = 7.9 Hz, 1H)
7.56–7.44 (m, 3H)
4.87 (d, *J* = 4.0 Hz, 1H)
4.28 (dd, *J* = 13.8, 6.0 Hz, 1H)
3.50 (dd, *J* = 12.1, 2.5 Hz, 1H)
3.16 (td, *J* = 13.0, 4.4 Hz, 1H)
3.06 (dd, *J* = 12.0, 5.3 Hz, 1H)
2.30–2.26 (m, 1H)
1.84–1.79 (m, 2H)
1.66–1.50 (m, 10H)

^{13}C NMR ($CDCl_3$, 100 MHz)

δ	**166.7**	**47.4**
	144.4	**36.8**
	133.4	**35.5**
	130.9	**35.0**
	128.3	**32.8**
	124.0	**31.1**
	122.6	**26.3**
	58.1	**21.4**
	56.9	**21.3**

IR(Neat): 3430, 3019, 1664, 1460, 1215, 1047, 757 cm^{-1}

HRMS (ESI): Calculated for $C_{18}H_{24}NO_2[M+H]^+$: 286.1807 found 286.1802



8n (minor)

^{1}H NMR ($CDCl_3$, 400 MHz)

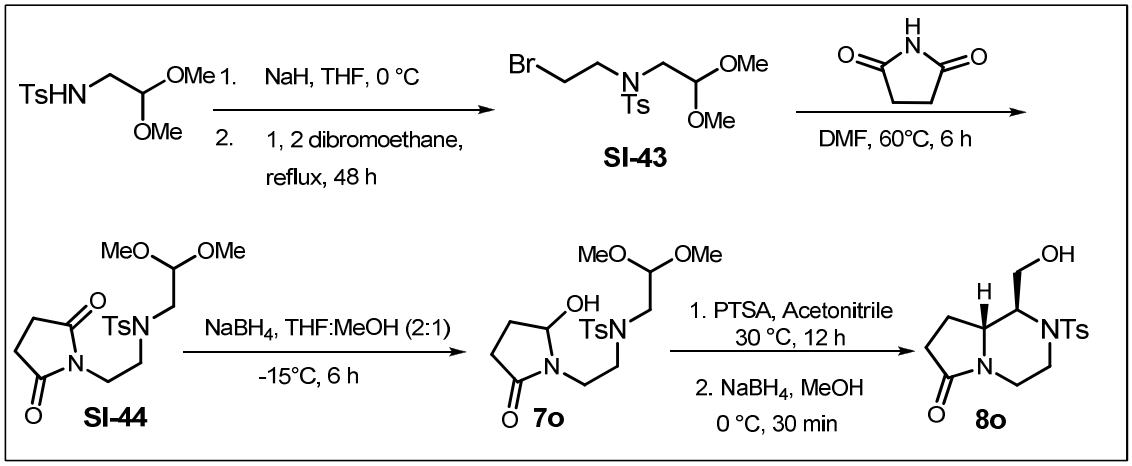
δ	**7.87**	(d, *J* = 7.0 Hz, 1H)
	7.69	(d, *J* = 7.3 Hz, 1H)
	7.54–7.48	(m, 1H)
	7.45	(t, *J* = 7.3 Hz, 1H)
	4.77	(d, *J* = 11.2 Hz, 1H)
	4.37	(ddd, *J* = 13.6, 5.6, 2.1 Hz, 1H)
	4.27	(dd, *J* = 11.8, 1.5 Hz, 1H)
	4.08	(dd, *J* = 11.8, 4.3 Hz, 1H)
	3.11	(td, *J* = 13.4, 3.5 Hz, 1H)
	2.31	(dt, *J* = 13.7, 2.8 Hz, 1H)
	2.1–2.04	(m, 1H)
	1.84–1.35	(m, 8H)
	1.07	(dd, *J* = 13.4, 5.4 Hz, 1H)
	1.04–0.96	(m, 2H)

^{13}C NMR ($CDCl_3$, 100 MHz)

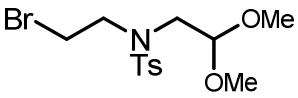
δ	**166.2**	**53.8**
	145.0	**36.8**
	132.8	**36.4**
	130.8	**35.2**
	128.0	**32.0**
	124.9	**27.2**
	123.8	**26.5**
	58.7	**21.6**
	56.2	**21.4**

IR(Neat): 3409, 2926, 2344, 1667, 1430, 1217, 1063, 755 cm^{-1}

HRMS (ESI): Calculated for $C_{18}H_{24}NO_2[M+H]^+$: 286.1807 found 286.1805



Synthesis of N-(2-bromoethyl)-N-(2,2-dimethoxyethyl)-4-methylbenzenesulfonamide (SI-43): To a solution of N-(2,2-dimethoxyethyl)-4-methylbenzenesulfonamide(2 g, 7.7 mmol) in dry THF(30 ml) was added NaH (60% in hexane 338 mg, 8.4 mmol) under nitrogen atmosphere at 0 ºC, after 5 min 1, 2 dibromoethane was added and heated to reflux for 24 h. Reaction mixture was cooled to 0 ºC and saturated aqueous NH_4Cl solution was added, extracted with EtOAc. The combined organic extracts were washed with water, brine, dried (anhydrous Na_2SO_4) and concentrated in *vacuo*. Purification of the residue by column chromatography on silica gel (15% ethyl acetate in hexane) gave pure title compound (1.7 g, 63% yield).



SI-43

^{1}H NMR ($CDCl_3$, 400 MHz)

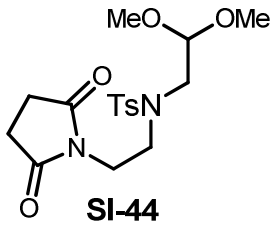
δ **7.72** (d, *J* = 8.1 Hz, 2H)
7.32 (d, *J* = 8.1 Hz, 2H)
4.47 (t, *J* = 5.4 Hz, 1H)
3.50 (s, 4H)
3.40 (s, 6H)
3.21 (d, *J* = 5.3 Hz, 2H)
2.48 (s, 3H)

^{13}C NMR ($CDCl_3$, 100 MHz)

δ **143.8**
136.0
55.1
51.8

129.9	**51.7**
127.2	**29.1**
104.5	**21.5**

Synthesis of N-(2,2-dimethoxyethyl)-N-(2-(2,5-dioxopyrrolidin-1-yl)ethyl)-4-methylbenzenesulfonamide (SI-44): Prepared according to the **general procedure B** using **SI-43** (139 mg, 0.38 mmol) and succunimide (56.5 mg, 0.57 mmol). Purification of the residue by column chromatography on silica gel (30% acetone in hexane) gave product **SI-44** as yellow oil (137 mg, 94% yield).



SI-44

^{1}H NMR ($CDCl_3$, 400 MHz)

δ	**7.64**	(d, *J* = 8.3 Hz, 2H)	**3.36**	(s, 6H)
	7.28	(d, *J* = 8.3 Hz, 2H)	**3.32**	(d, *J* = 5.3 Hz, 2H)
	4.43	(t, *J* = 5.1 Hz, 1H)	**2.72**	(s, 4H)
	3.73	(t, *J* = 5.4 Hz, 2H)	**2.41**	(s, 3H)
	3.38	(d, *J* = 5.1 Hz, 2H)		

^{13}C NMR ($CDCl_3$, 100 MHz)

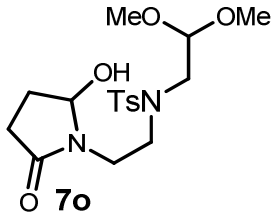
δ	**177.8**	**54.6**
	143.5	**50.7**
	136.7	**46.5**
	129.7	**36.9**
	127.1	**28.3**
	104.1	**21.4**

IR(Neat): 3021, 2939, 1720, 1403, 1215, 1157, 1078, 760, 668 cm^{-1}

HRMS (ESI): Calculated for $C_{17}H_{25}N_2O_6S$ $[M+H]^+$: 385.1433 found 385.1462

Synthesis of N-(2,2-dimethoxyethyl)-N-(2-(2-hydroxy-5-oxopyrrolidin-1-yl)ethyl)-4-methylbenzenesulfonamide (7o): Prepared according to the **general procedure C** using **SI-44** (100

mg, 0.26 mmol). Purification of the residue by column chromatography on silica gel (50% acetone in hexane) gave mixture of rotamers of **7o** as yellow oil (95 mg, 95% yield).



7o

^{1}H NMR ($CDCl_3$, 400 MHz)

δ	**7.69–7.64**	(m, 2H)	**3.38–3.35**	(m, 12H)
	7.33–7.28	(m, 4H)	**3.35–3.28**	(m, 2H)
	5.44–5.37	(m, 2H)	**3.21–3.10**	(m, 4H)
	4.54–4.49	(m, 2H)	**2.56–2.50**	(m, 2H)
	4.31–4.28	(m, 1H)	**2.43–2.40**	(m, 6H)
	4.13–4.08	(m, 1H)	**2.38–2.27**	(m, 4H)
	3.57–3.52	(m, 4H)	**1.91–1.84**	(m, 2H)
	3.50–3.43	(m, 2H)		

^{13}C NMR ($CDCl_3$, 75 MHz)

δ	**174.9**	**53.8**
	143.8	**51.0**
	135.3	**49.0**
	129.8	**39.4**
	127.3	**29.0**
	102.9	**28.1**
	84.3	**21.5**
	54.3	

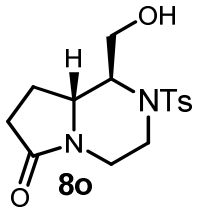
IR(Neat): 3384, 2939, 1670, 1456, 1157, 1074, 743, 658 cm^{-1}

HRMS (ESI): Calculated for $C_{17}H_{27o2}O_6SNa$ $[M+Na]^+$: 409.1409 found 409.1408

Synthesis of (1S,8aR)-1-(hydroxymethyl)-2-tosylhexahydropyrrolo[1,2-a]pyrazin-6(7*H*)-one (8o):

Prepared according to the **general procedure D** using **7o** (88 mg, 0.23 mmol) and 1 equiv of PTSA at

30 °C for 12 h. Purification of the residue by column chromatography on silica gel (40% acetone in hexane) gave separable mixture of diastereomers (3:1) of **8o** as yellow oil. (65 mg, 71%)



8o

^{1}H NMR ($CDCl_3$, 400 MHz)

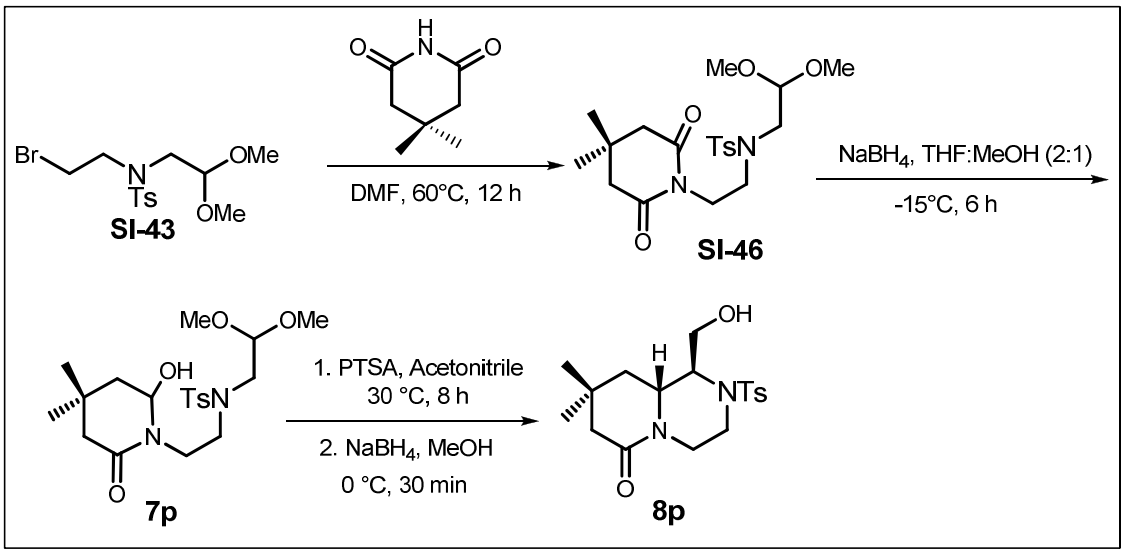
δ	**7.68**	(d, *J* = 8.1 Hz, 2H)		**3.09**	(ddd, *J* = 12.8, 8.1, 4.4 Hz, 1H)
	7.34	(d, *J* = 8.0 Hz, 2H)		**3.00 –2.92**	(m, 1H)
	4.16	(dt, *J* = 13.0, 3.0 Hz, 1H)		**2.73**	(dt, *J* = 9.7, 3.0 Hz, 1H)
	3.90 – 3.82	(m, 2H)		**2.45**	(s, 3H)
	3.75	(ddd, *J* = 10.1, 5.8, 4.4 Hz, 1H)		**2.37 – 2.22**	(m, 3H)
	3.70 – 3.61	(m, 1H)		**1.60 – 1.54**	(m, 1H)

^{13}C NMR ($CDCl_3$, 100 MHz)

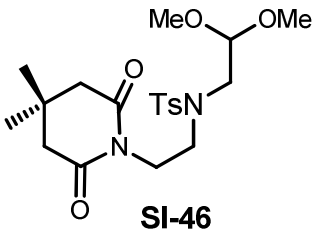
δ	**173.4**	**54.6**
	144.6	**45.1**
	134.9	**38.9**
	130.2	**29.8**
	127.1	**23.0**
	65.7	**21.6**
	60.7	

IR(Neat): 3407, 3019, 2400, 1682, 1421, 1215, 1047, 928, 757, 626 cm^{-1}

HRMS (ESI): Calculated for $C_{15}H_{21}N_2O_4S$ $[M+H]^+$: 325.1222 found 325.1219



Synthesis of N-(2,2-dimethoxyethyl)-N-(2-(4,4-dimethyl-2,6-dioxopiperidin-1-yl)ethyl)-4-methylbenzenesulfonamide (SI-46):): Prepared according to the **general procedure B** using **SI-43** (500 mg, 1.36 mmol) and 3,3-dimethylglutarimide (230 mg, 1.63 mmol). Purification of the residue by column chromatography on silica gel (20% acetone in hexane) gave product **SI-46** as yellow oil (518 mg, 89% yield).



^{1}H NMR ($CDCl_3$, 400 MHz)

δ	**7.65**	(d, *J* = 8.3 Hz, 2H)		**3.33**	(d, *J* = 5.2 Hz, 2H)
	7.27	(d, *J* = 8.3 Hz, 2H)		**3.36**	(s, 6H)
	4.38	(t, *J* = 5.2 Hz, 1H)		**2.55**	(s, 4H)
	3.99	(t, *J* = 8.3 Hz, 2H)		**2.41**	(s, 3H)
	3.38	(d, *J* = 5.7 Hz, 2H)		**1.07**	(s, 6H)

^{13}C NMR ($CDCl_3$, 100 MHz)

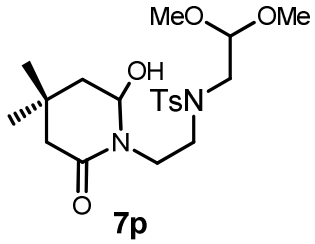
δ	**172.4**	**46.5**
	171.8	**46.3**
	134.2	**45.5**

137.2	**36.9**
129.6	**29.2**
127.1	**27.9**
103.6	**27.8**
54.4	**21.4**
49.9	

IR(Neat): 3236, 2962, 1695, 1217, 1153, 1079, 760, 667 cm^{-1}

HRMS (ESI): Calculated for $C_{20}H_{32}N_2O_6SNa$ $[M+Na]^+$: 449.1722 found 395.1640

Synthesis of N-(2,2-dimethoxyethyl)-N-(2-(2-hydroxy-4,4-dimethyl-6-oxopiperidin-1-yl)ethyl)-4-methylbenzenesulfonamide (7p): Prepared according to the **general procedure C** using **SI-46** (300 mg, 0.7 mmol). Purification of the residue by column chromatography on silica gel (30% acetone in hexane) gave mixtures of rotamers of **7p** as yellow oil (290 mg, 96% yield).



7p

^{1}H NMR ($CDCl_3$, 400 MHz)

δ	**7.69**	(d, *J* = 7.9 Hz, 2H)	**3.31–3.25**	(m, 2H)
	7.30	(d, *J* = 8.1 Hz, 2H)	**3.21**	(d, *J* = 6.0 Hz, 2H)
	5.97	(d, *J* = 7.7 Hz, 1H)	**2.41**	(s, 3H)
	4.96	(d, *J* = 7.7 Hz, 1H)	**2.32**	(s, 2H)
	4.50	(t, *J* = 5.4 Hz, 1H)	**2.10–1.87**	(m, 2H)
	3.67	(t, *J* = 6.5 Hz, 2H)	**1.04**	(s, 6H)
	3.37	(s, 6H)		

^{13}C NMR ($CDCl_3$, 100 MHz)

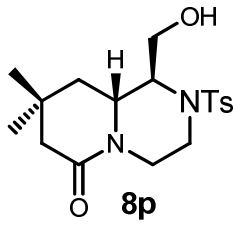
δ	**169.5**	**54.4**
	143.6	**51.2**
	136.1	**47.9**
	129.8	**45.9**

127.5	**45.6**
127.3	**31.6**
117.5	**27.9**
103.6	**21.5**

IR(Neat): 3407, 2975, 1638, 1412, 1334, 1158, 1047, 758, 669 cm^{-1}

HRMS (ESI): Calculated for $C_{20}H_{32}N_2O_6SNa$ $[M+Na]^+$: 451.1879 found 451.1868

Synthesis of (1S,9aR)-1-(hydroxymethyl)-8,8-dimethyl-2-tosylhexahydro-1H-pyrido[1,2-a]pyrazin-6(2H)-one (8p): Prepared according to the **general procedure D** using **7p** (98 mg, 0.23 mmol) and 1 equiv of PTSA at 30 °C for 8 h. Purification of the residue by column chromatography on silica gel (35% acetone in hexane) gave an inseparable mixture of diastereomers (2:1) of **8p** as yellow oil. (52 mg, 62%)



8p

^{1}H NMR ($CDCl_3$, 400 MHz)

δ	**7.75**	(d, *J* = 8.3 Hz, 2H, minor)
	7.69	(d, *J* = 8.3 Hz, 2H, major)
	7.34–7.29	(m, 4H, major + minor)
	4.43	(dt, *J* = 13.4, 3.0 Hz, 1H, minor)
	4.09	(dd, *J* = 12.8, 2.6 1Hz, 1H, major)
	4.05 – 3.96	(m, 2H, major + minor)
	3.83 – 3.62	(m, 6H, major + minor)
	3.51 – 3.41	(m, 2H, major + minor)
	3.15 – 3.05	(m, 2H, major + minor)
	2.90	(dt, *J* = 13.5, 5.2 Hz, 1H, major)
	2.64	(td, *J* = 13.0, 3.0 Hz, 1H, minor)
	2.43	(s, 3H, minor)
	2.42	(s, 3H, major)
	2.19 – 2.07	(m, 3H, major + minor)
	1.97 – 1.89	(m, 2H, major + minor)
	1.57 – 1.53	(m, 2H, minor)

1.20 – 1.04 (m, 1H, major)

1.00 (s, 3H, minor)

0.96 (s, 3H, major)

0.91 (s, 3H, major)

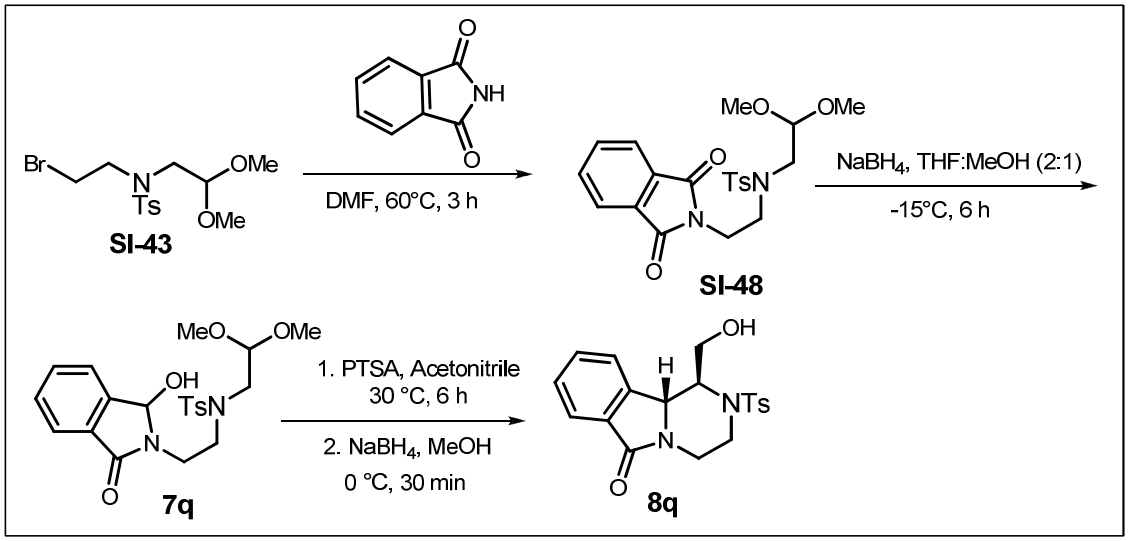
0.83 (s, 3H, minor)

^{13}C NMR ($CDCl_3$, 100 MHz)

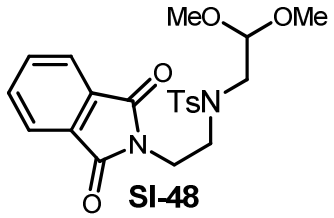
δ	**170.4, 169.5**	**45.9, 45.3**
	144.3, 144.0	**43.4, 40.7**
	137.2, 135.8	**40.6, 40.5**
	130.0, 129.9	**40.4, 37.5**
	127.2, 127.1	**30.6, 30.5**
	64.7, 57.6	**29.4, 29.2**
	61.5, 58.3	**24.5, 23.9**
	55.1, 51.3	**21.5 (two)**

IR(Neat): 3400, 3020, 2401, 1632, 1408, 1216, 1157, 1090, 762, 669 cm^{-1}

HRMS (ESI): Calculated for $C_{18}H_{27}N_2O_4S$ $[M+H]^+$: 367.1692 found 367.1686



Synthesis of N-(2,2-dimethoxyethyl)-N-(2-(1,3-dioxoisoindolin-2-yl)ethyl)-4-methylbenzenesulfonamide (SI-48): Prepared according to the **general procedure B** using **SI-43** (500 mg, 1.36 mmol) and phthalimide (220 mg, 1.63 mmol). Purification of the residue by column chromatography on silica gel (20% acetone in hexane) gave product **SI-48** as yellow oil (580 mg, 98% yield).



SI-48

^{1}H NMR ($CDCl_3$, 400 MHz)

δ	**7.83–7.79**	(m, 2H)	**3.88**	(t, *J* = 6.8 Hz, 2H)
	7.71–7.68	(m, 2H)	**3.51**	(t, *J* = 6.3 Hz, 2H)
	7.61	(d, *J* = 8.0 Hz, 2H)	**3.41**	(s, 6H)
	7.14	(d, *J* = 8.0 Hz, 2H)	**3.39**	(d, *J* = 5.5 Hz, 2H)
	4.54	(t, *J* = 5.2 Hz, 1H)	**2.41**	(s, 3H)

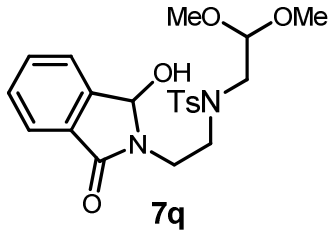
^{13}C NMR ($CDCl_3$, 100 MHz)

δ	**168.2**	**123.2**
	143.2	**104.5**
	136.7	**54.8**
	133.8	**50.1**
	132.2	**47.1**
	129.6	**36.2**
	127.0	**21.5**

IR(Neat): 3021, 2401, 1713, 1605, 1342, 1123, 761, 670 cm^{-1}

HRMS (ESI): Calculated for $C_{21}H_{24}N_2O_6SNa$ $[M+Na]^+$: 455.1253 found 455.1243

Synthesis of N-(2,2-dimethoxyethyl)-N-(2-(1-hydroxy-3-oxoisoindolin-2-yl)ethyl)-4-methylbenzenesulfonamide (7q): Prepared according to the **general procedure C** using **SI-48** (130 mg, 0.3 mmol). Purification of the residue by column chromatography on silica gel (30% acetone in hexane) gave **7q** as yellow oil (125 mg, 96% yield).



7q

^{1}H NMR ($CDCl_3$, 400 MHz)

δ	**7.72**	(d, *J* = 7.5 Hz, 1H)		**3.84–3.71**	(m, 2H)
	7.64	(d, *J* = 8.2 Hz, 2H)		**3.59–3.48**	(m, 1H)
	7.59–7.54	(m, 2H)		**3.39–3.33**	(m, 2H)
	7.47	(td, *J* = 7.1, 1,8 Hz, 1H)		**3.32**	(s, 3H)
	7.22	(d, *J* = 8.2 Hz, 2H)		**3.30**	(s, 3H)
	5.89	(d, *J* = 10.0 Hz, 1H)		**3.20**	(dd, *J* = 14.8, 5.2 Hz, 1H)
	4.49	(d, *J* = 5.2 Hz, 1H)		**2.37**	(s, 3H)
	4.19	(d, *J* = 10.0 Hz, 1H)			

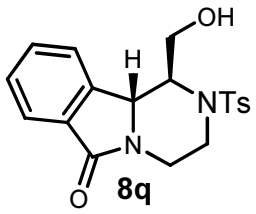
^{13}C NMR ($CDCl_3$, 100 MHz)

δ	**167.6**	**123.0**
	144.2	**103.4**
	143.6	**82.7**
	135.7	**54.5**
	132.1	**54.0**
	131.6	**50.6**
	129.7	**48.8**
	129.6	**38.9**
	127.3	**21.5**
	123.3	

IR(Neat): 3401, 3020, 1695, 1337, 1216, 1157, 761, 670 cm^{-1}

HRMS (ESI): Calculated for $C_{21}H_{26}N_2O_6SNa$ $[M+Na]^+$: 457.1409 found 457.1410

Synthesis of (1S,10bR)-1-(hydroxymethyl)-2-tosyl-1,2,3,4-tetrahydropyrazino[2,1-a]isoindol-6(10bH)-one (8q): Prepared according to the **general procedure D** using **7q** (100 mg, 0.23 mmol) and 1 equiv of PTSA at 30 °C for 6 h almost as a single diastereomers (>25:1). Purification of the residue by column chromatography on silica gel (40% acetone in hexane) gave **8q** as yellow oil. (70 mg, 82%)



8q

^{1}H NMR ($CDCl_3$, 400 MHz)

δ	**7.84**	(d, *J* = 8.2 Hz, 2H)		**4.63**	(d, *J* = 8.2 Hz, 1H)
	7.60–7.55	(m, 2H)		**4.31**	(d, *J* = 10.1 Hz, 1H)
	7.52–7.48	(m, 2H)		**3.91**	(d, *J* = 10.1 Hz, 1H)
	7.34	(d, *J* = 8.2 Hz, 2H)		**3.21 –3.08**	(m, 4H)
	4.78	(dt, *J* = 8.7, 5.0 Hz, 1H)		**2.43**	(s, 3H)

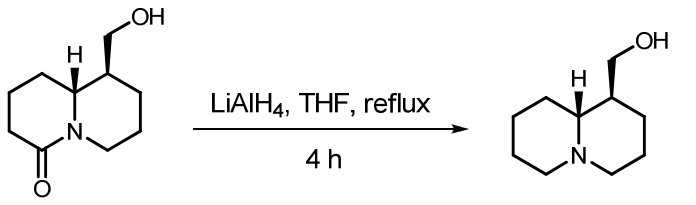
^{13}C NMR ($CDCl_3$, 100 MHz)

δ	**166.7**	**124.2**
	144.2	**122.8**
	140.4	**58.3**
	137.5	**56.8**
	132.5	**56.4**
	131.9	**39.7**
	130.1	**38.5**
	129.1	**21.6**
	127.2	

IR(Neat): 3401, 3019, 2400, 1687, 1523, 1215, 757, 669 cm^{-1}

HRMS (ESI): Calculated for $C_{19}H_{21}N_2O_4S$ $[M+H]^+$: 373.1222 found 373.1211

Synthesis of (±)-epilupinine, (±)-4



8h (±)-epilupinine, (±)-**4**

Synthesis of (±)-epilupinine, (4): To a solution of **8h** (23 mg, 0.125 mmol) in dry THF (3.5 ml) at 0 °C was added a suspension of $LiAlH_4$ (19 mg, 0.502 mmol) in dry THF(1.5 ml) and the reaction mixture was stirred at 0 °C for 15 min and then heated to reflux for 4 h. Reaction mixture was cooled to 0 °C and saturated aq. Na_2SO_4 (0.1 ml) was added carefully and stirred at room temperature for 1 h. The mixture was filtered using THF and filtrate was concentrated in *vacuo* to give (±)-epilupinine (19 mg, 90% yield) as oil. Spectral data were found in agreement with the literature data.

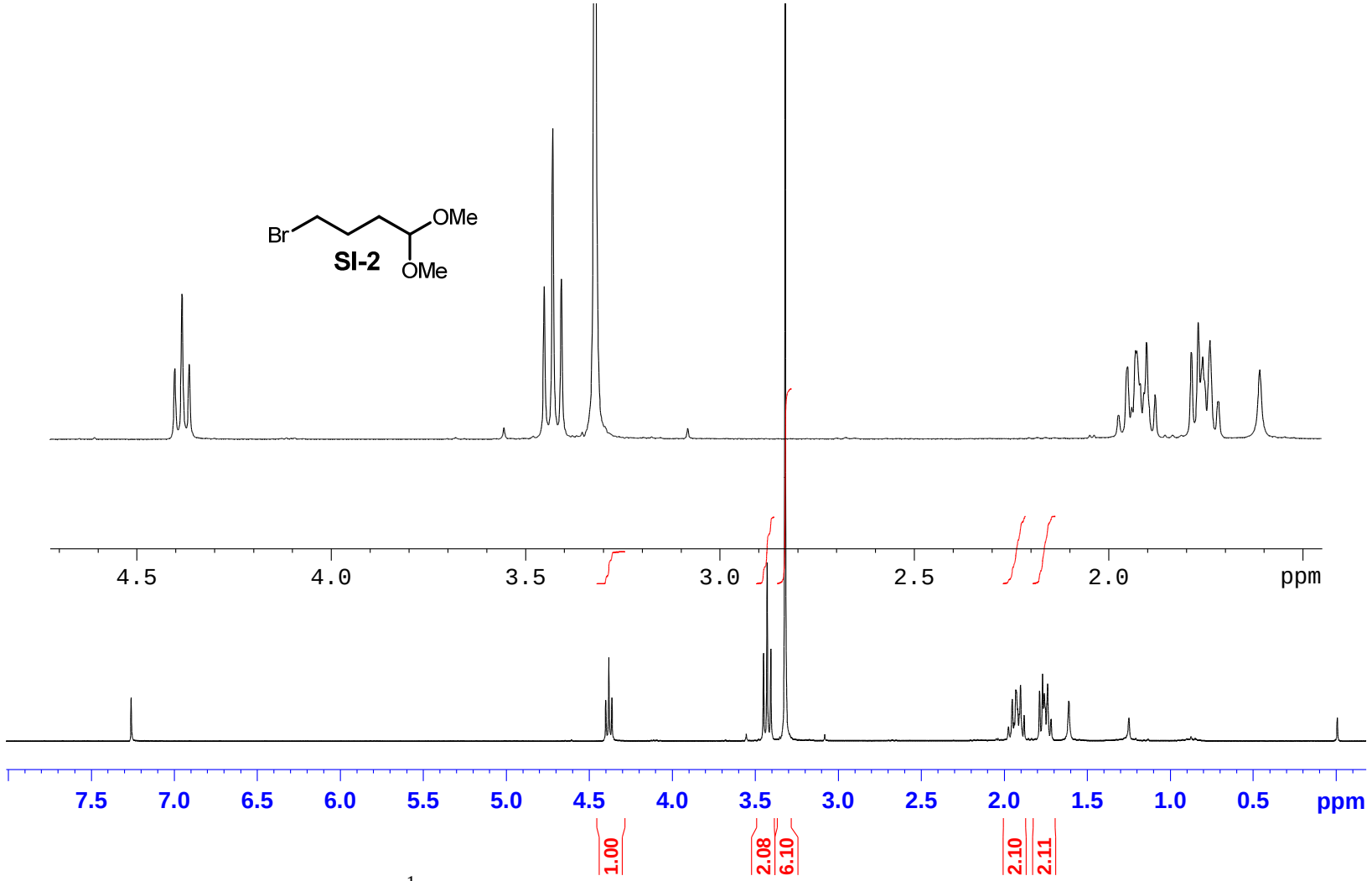
^{1}H NMR ($CDCl_3$, 400 MHz)

δ	**3.66**	(dd, *J* = 10.9, 3.6 Hz, 1H)	**1.72–1.66**	(m, 3H)
	3.57	(dd, *J* = 10.8, 5.6 Hz, 1H)	**1.63–1.57**	(m, 2H)
	2.86–2.75	(m, 2H)	**1.46–1.36**	(m, 1H)
	2.07–1.97	(m, 2H)	**1.30–1.12**	(m, 3H)
	1.93–1.73	(m, 4H)		

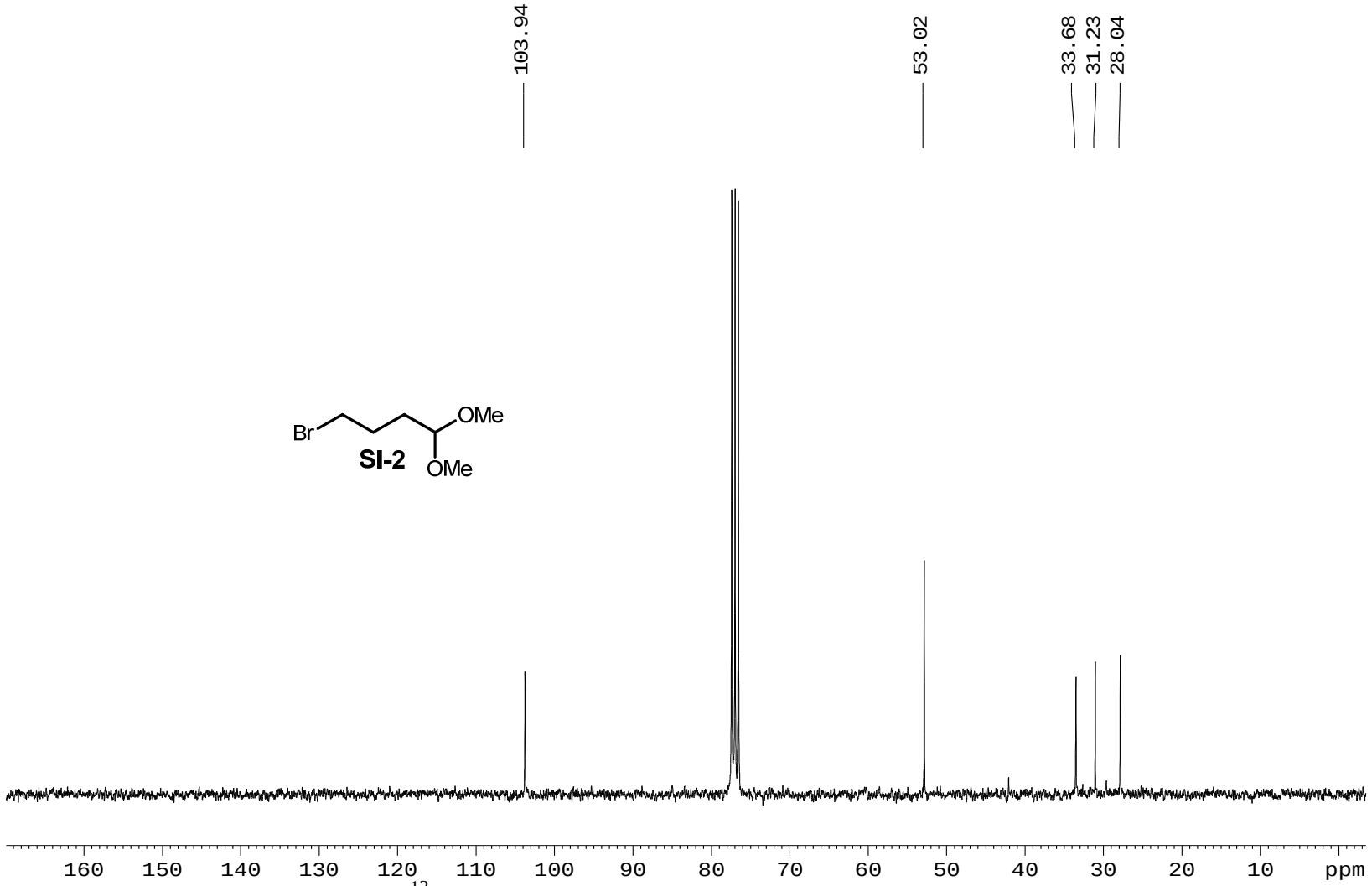
^{13}C NMR ($CDCl_3$, 100 MHz)

δ	**64.7**	**29.8**
	64.2	**28.2**
	56.9	**25.6**
	56.6	**25.0**
	43.9	**24.6**

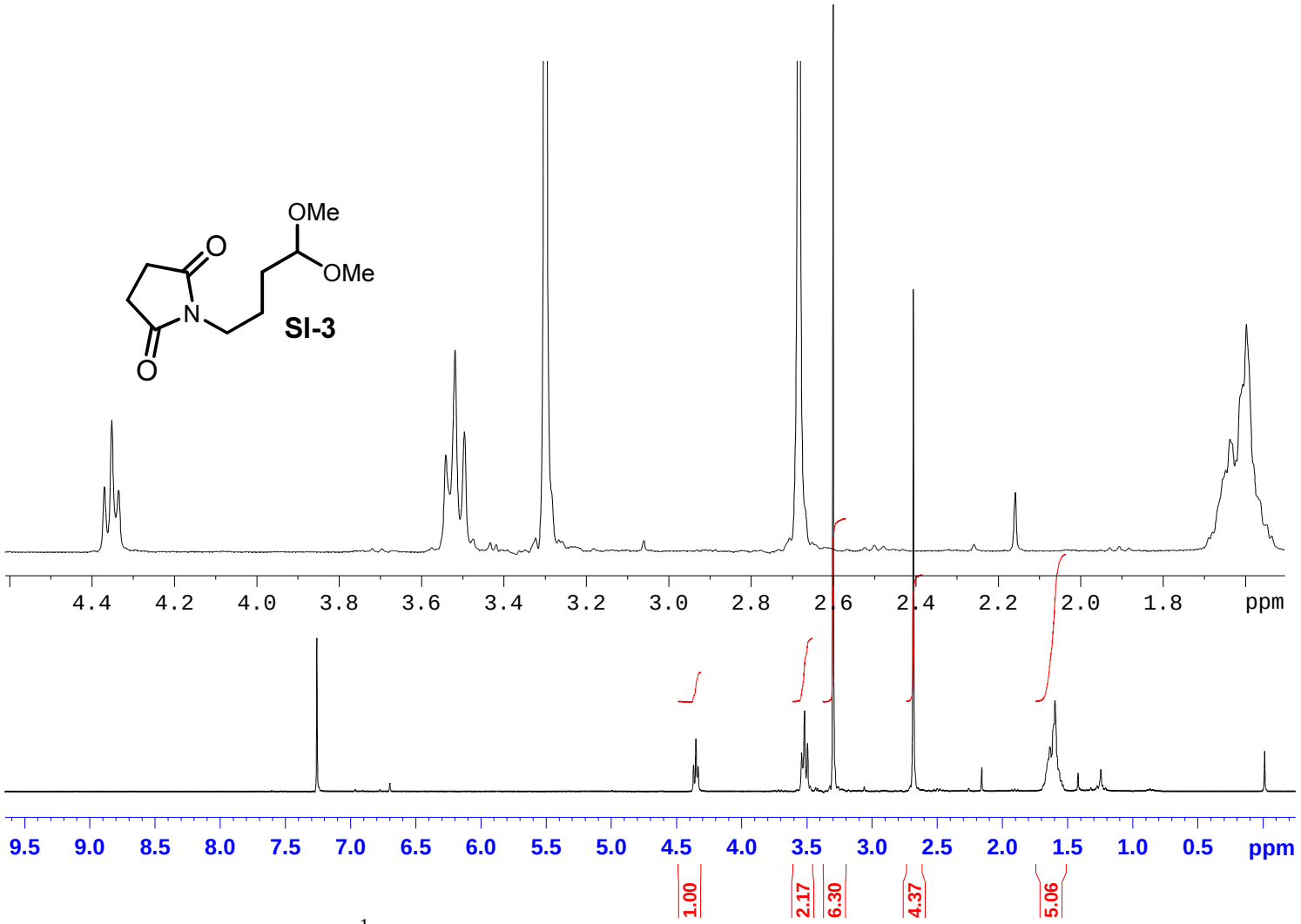
HRMS (ESI): Calculated for $C_{10}H_{20}NO$ $[M+H]^+$: 170.1545 found 170.1534



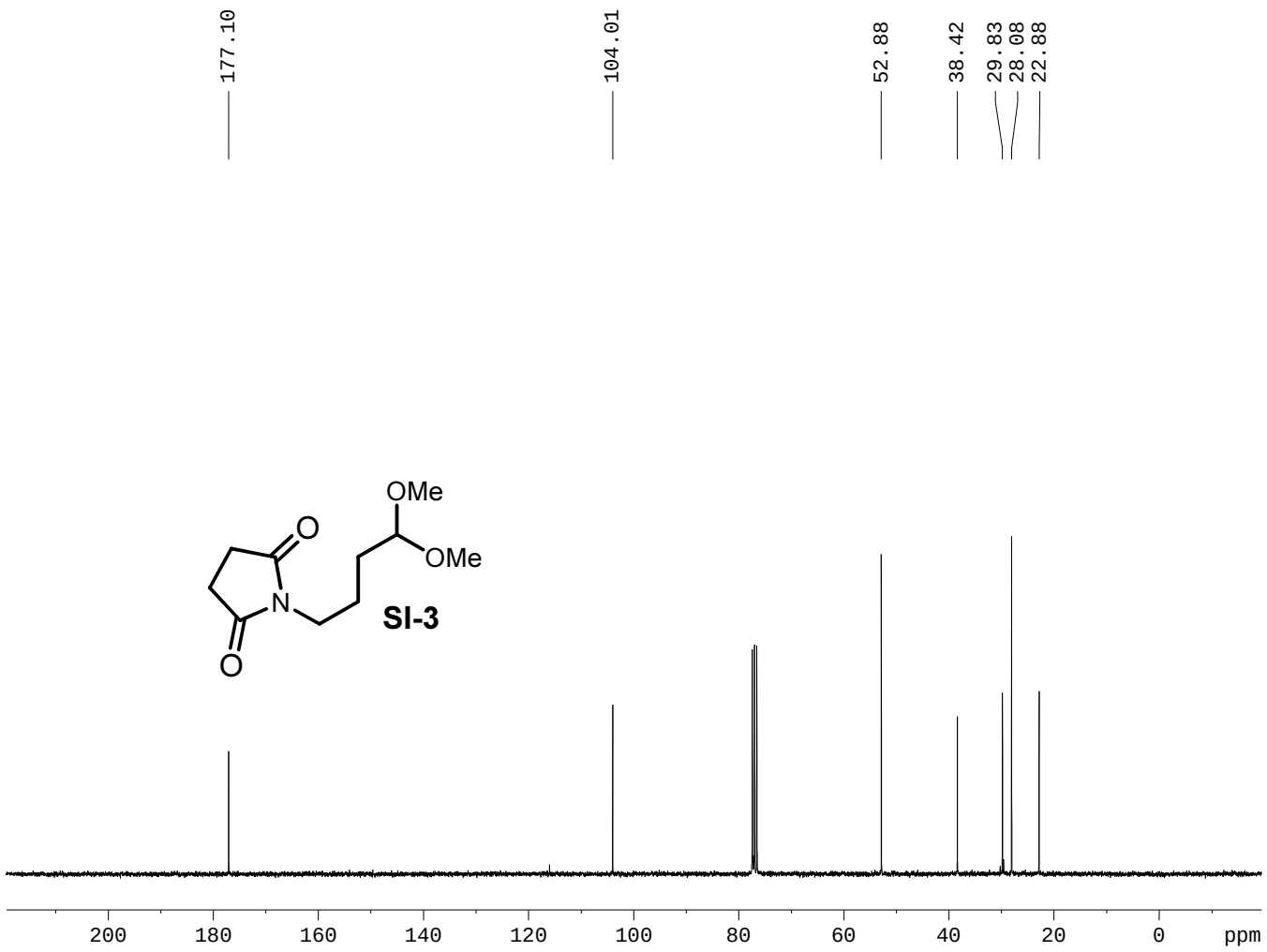
^{1}H NMR of compound **SI-2** (300 MHz, $CDCl_3$)



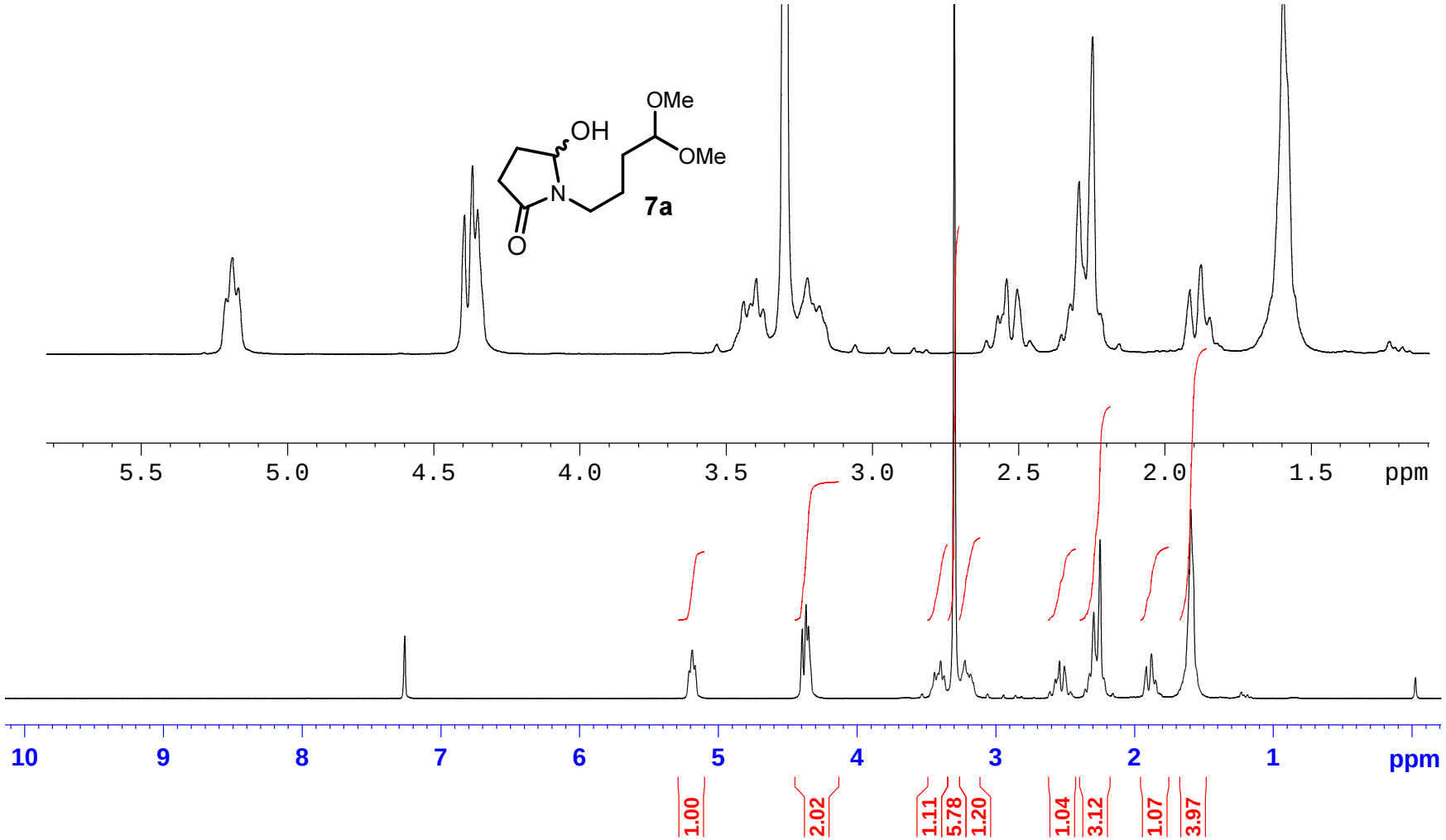
^{13}C NMR of compound **SI-2** (75 MHz, $CDCl_3$)



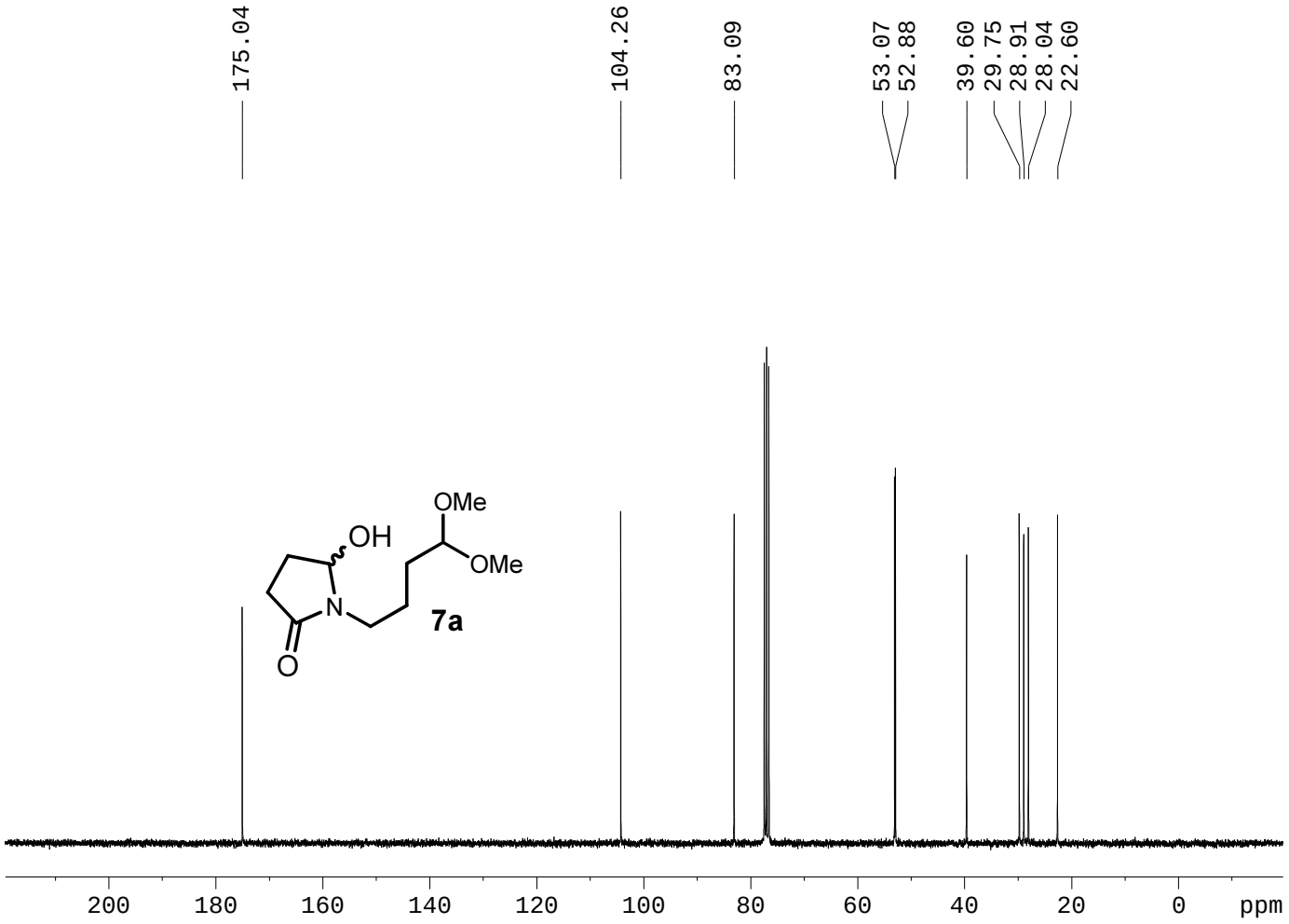
^{1}H NMR of compound **SI-3** (300 MHz, $CDCl_3$)



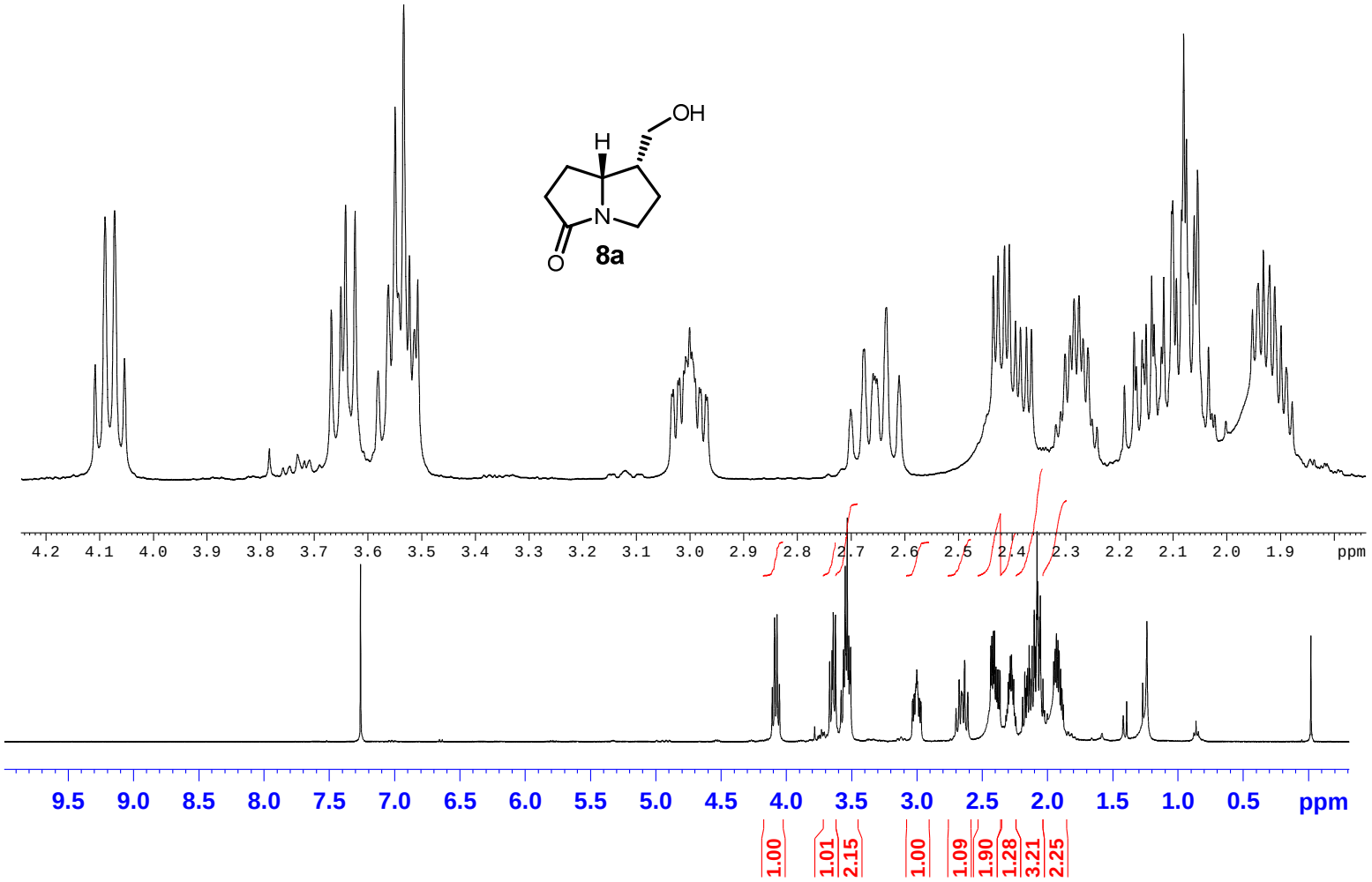
^{13}C NMR of compound **SI-3** (75 MHz, $CDCl_3$)



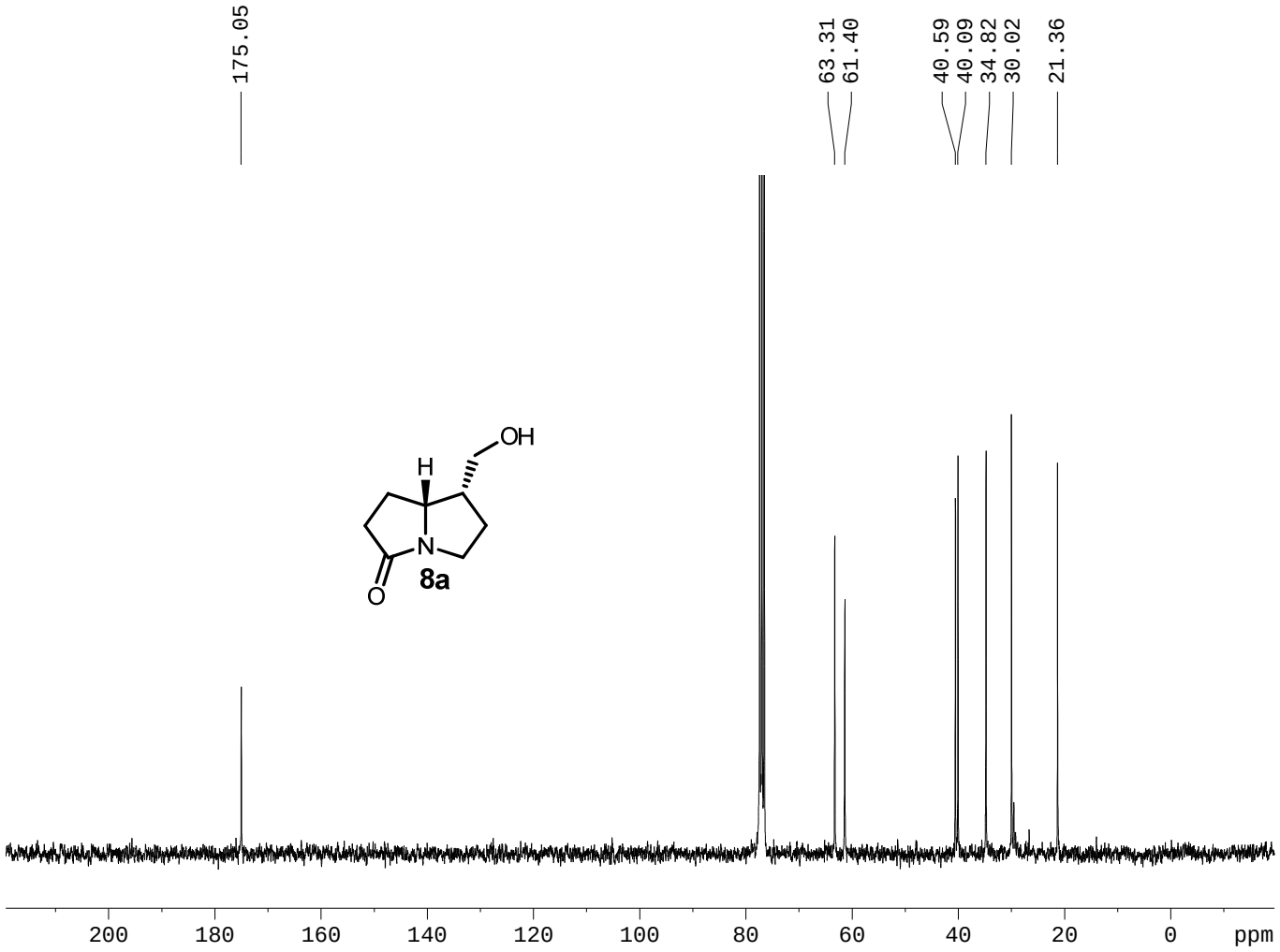
^{1}H NMR of compound **7a** (300 MHz, $CDCl_3$)



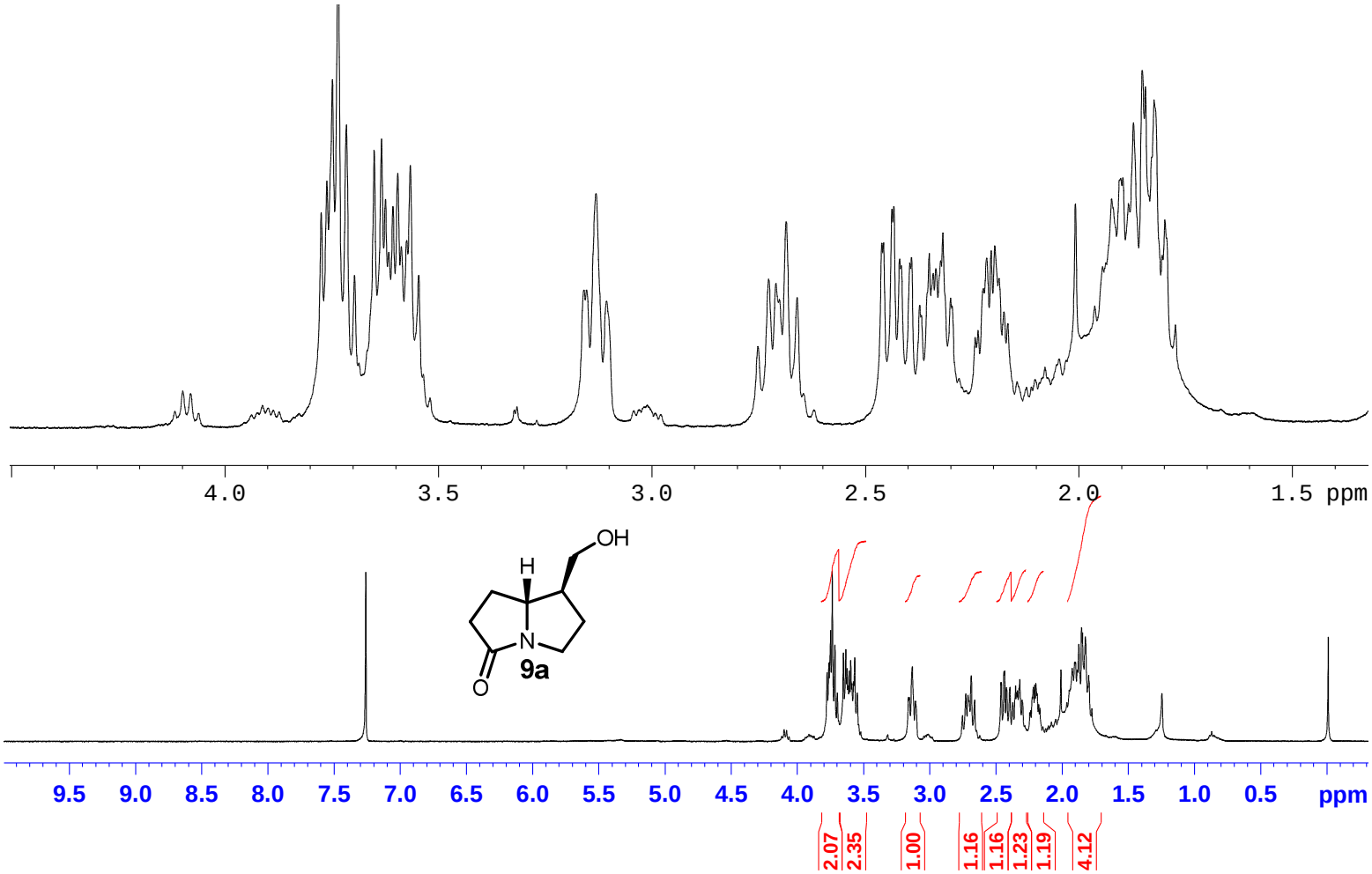
^{13}C NMR of compound **7a** (75 MHz, $CDCl_3$)



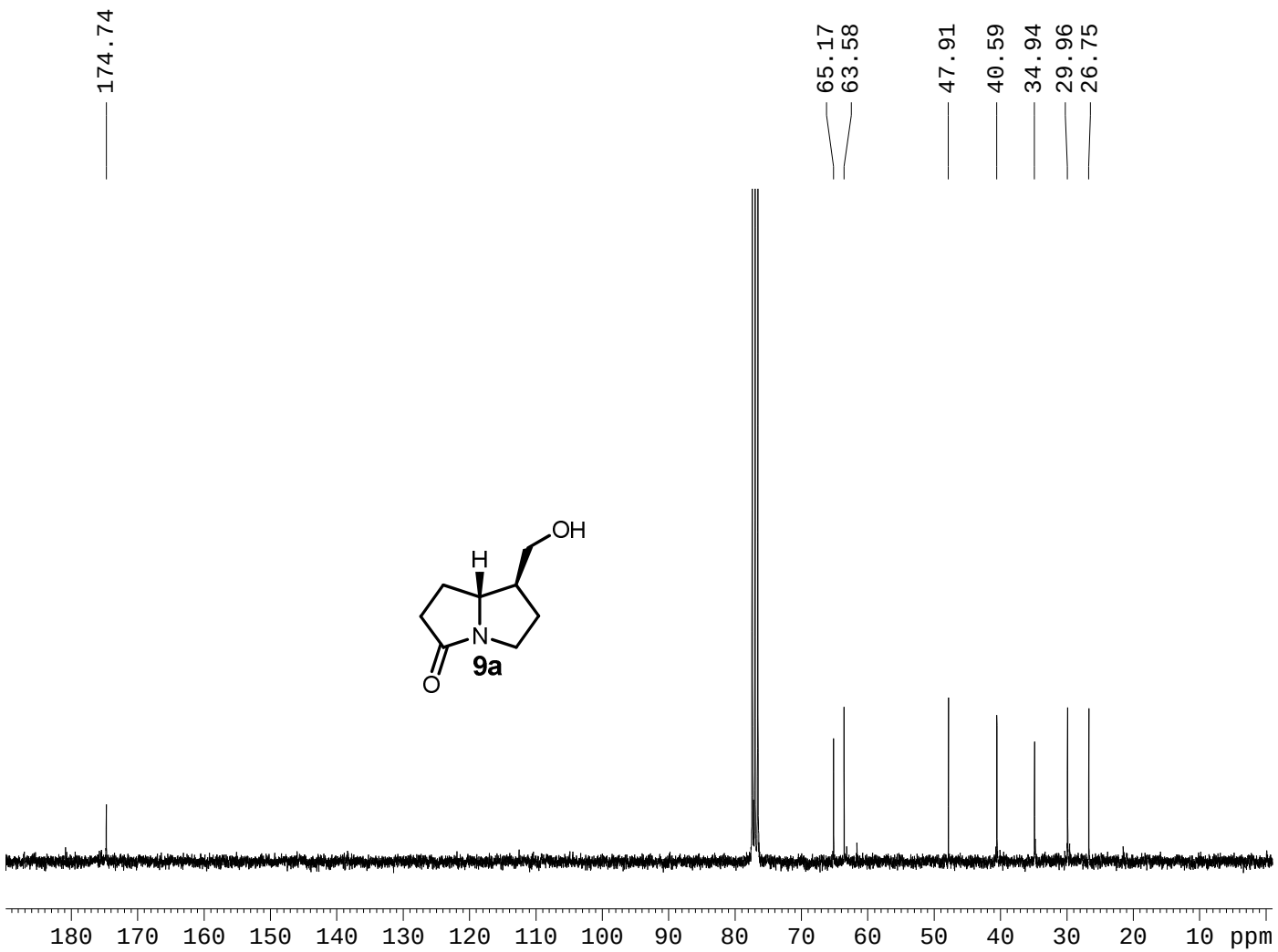
^{1}H NMR of compound **8a** (400 MHz, $CDCl_3$)



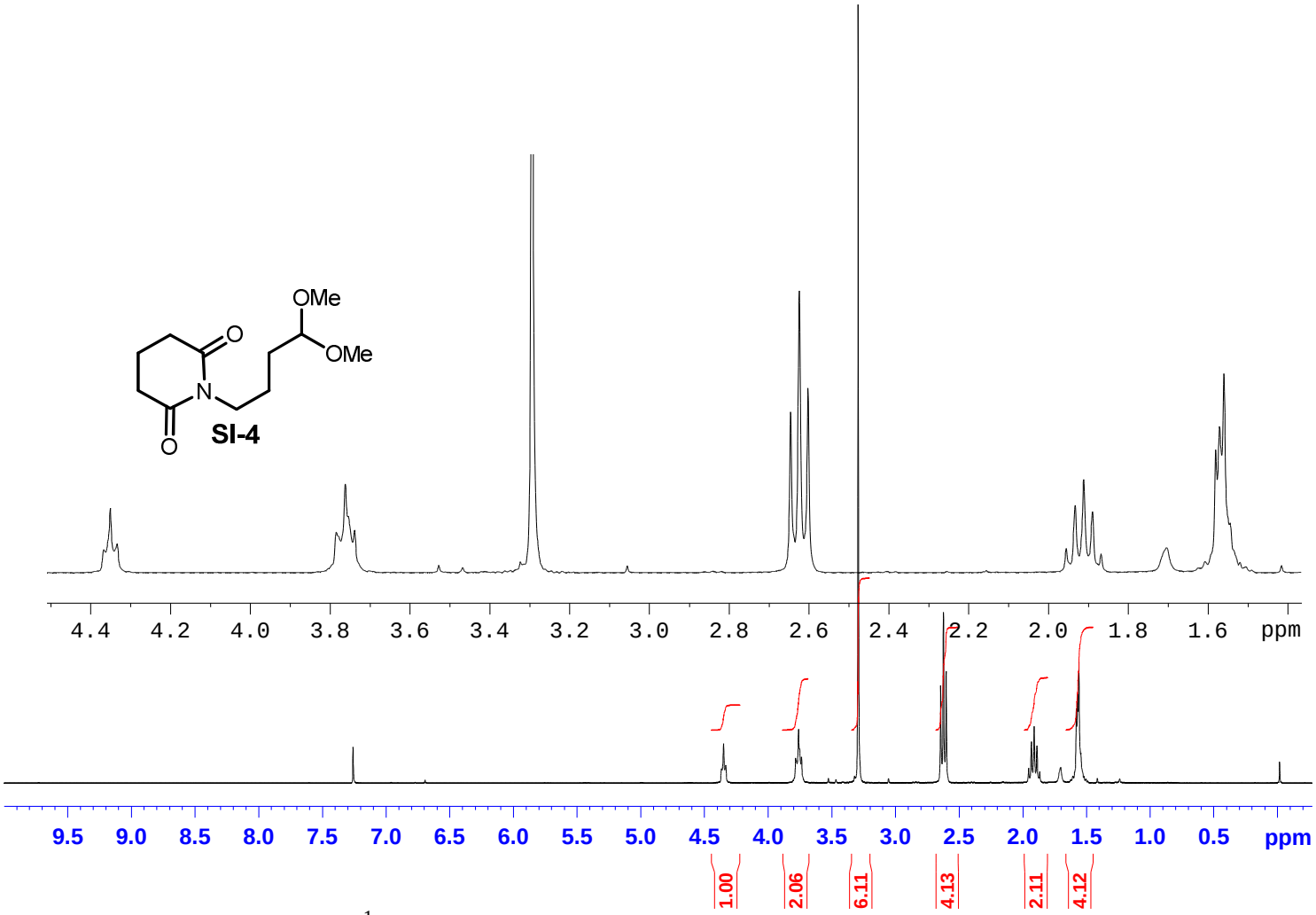
^{13}C NMR of compound **8a** (75 MHz, $CDCl_3$)



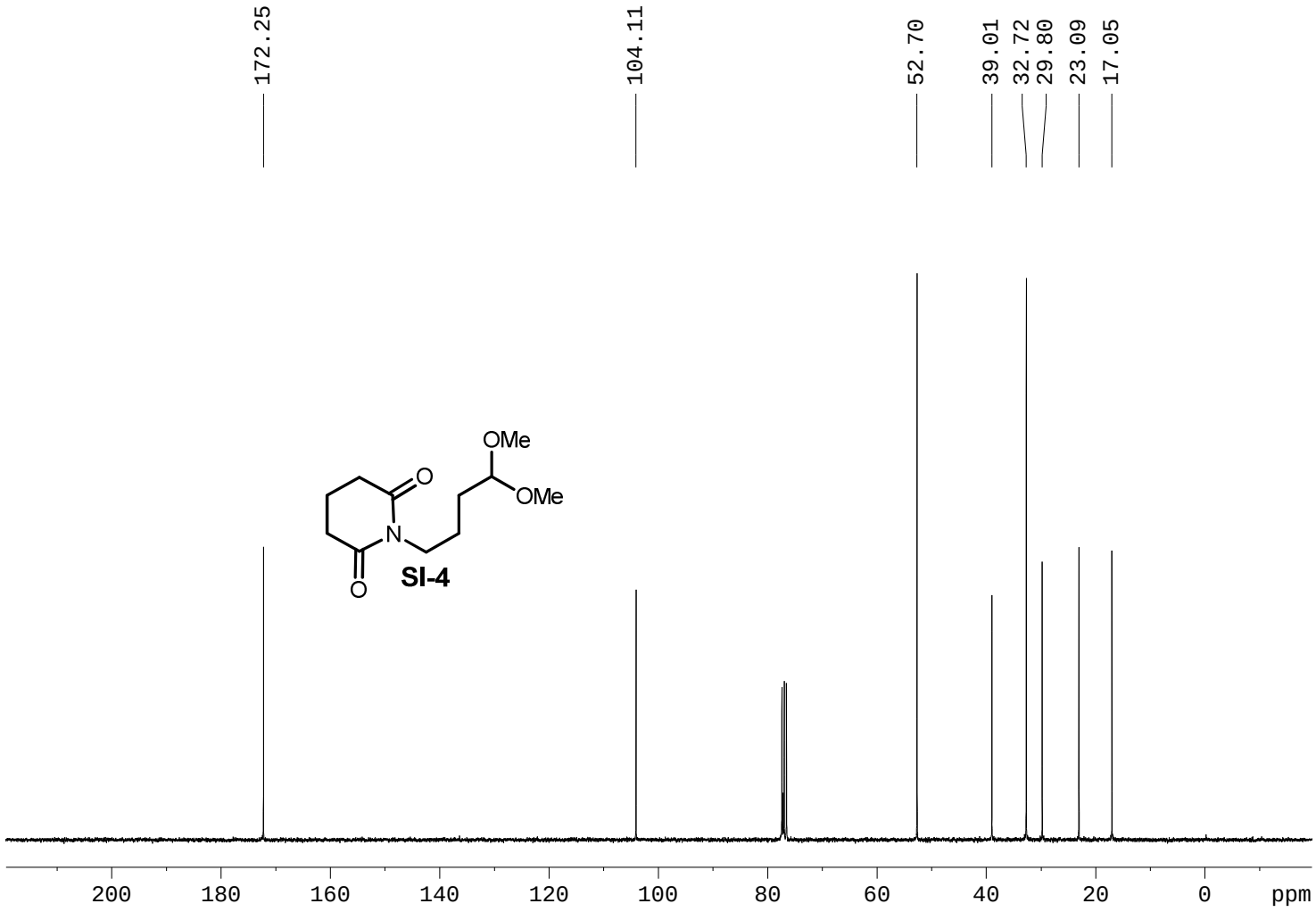
^{1}H NMR of compound **9a** (300 MHz, $CDCl_3$)



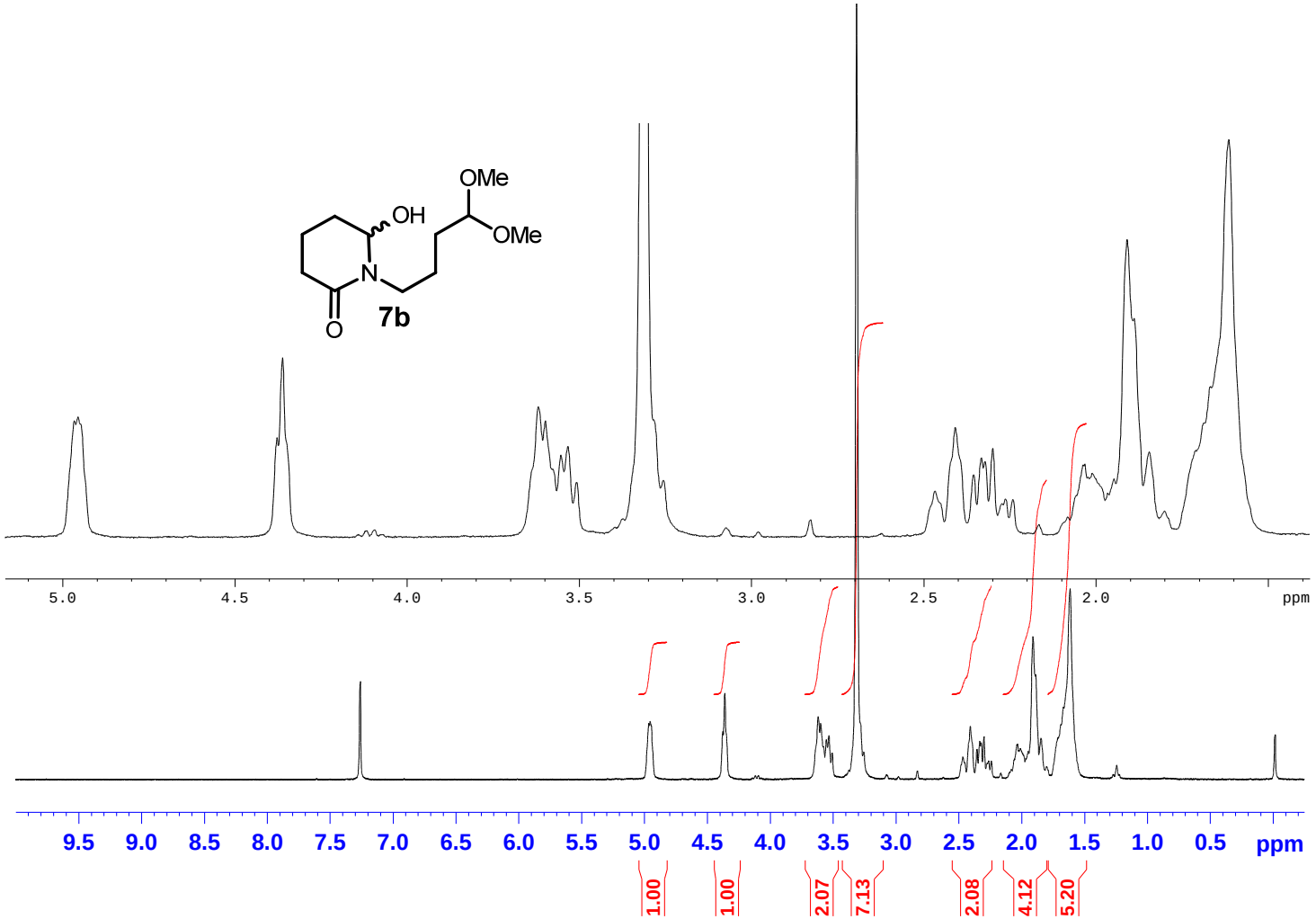
^{13}C NMR of compound **9a** (75 MHz, $CDCl_3$)



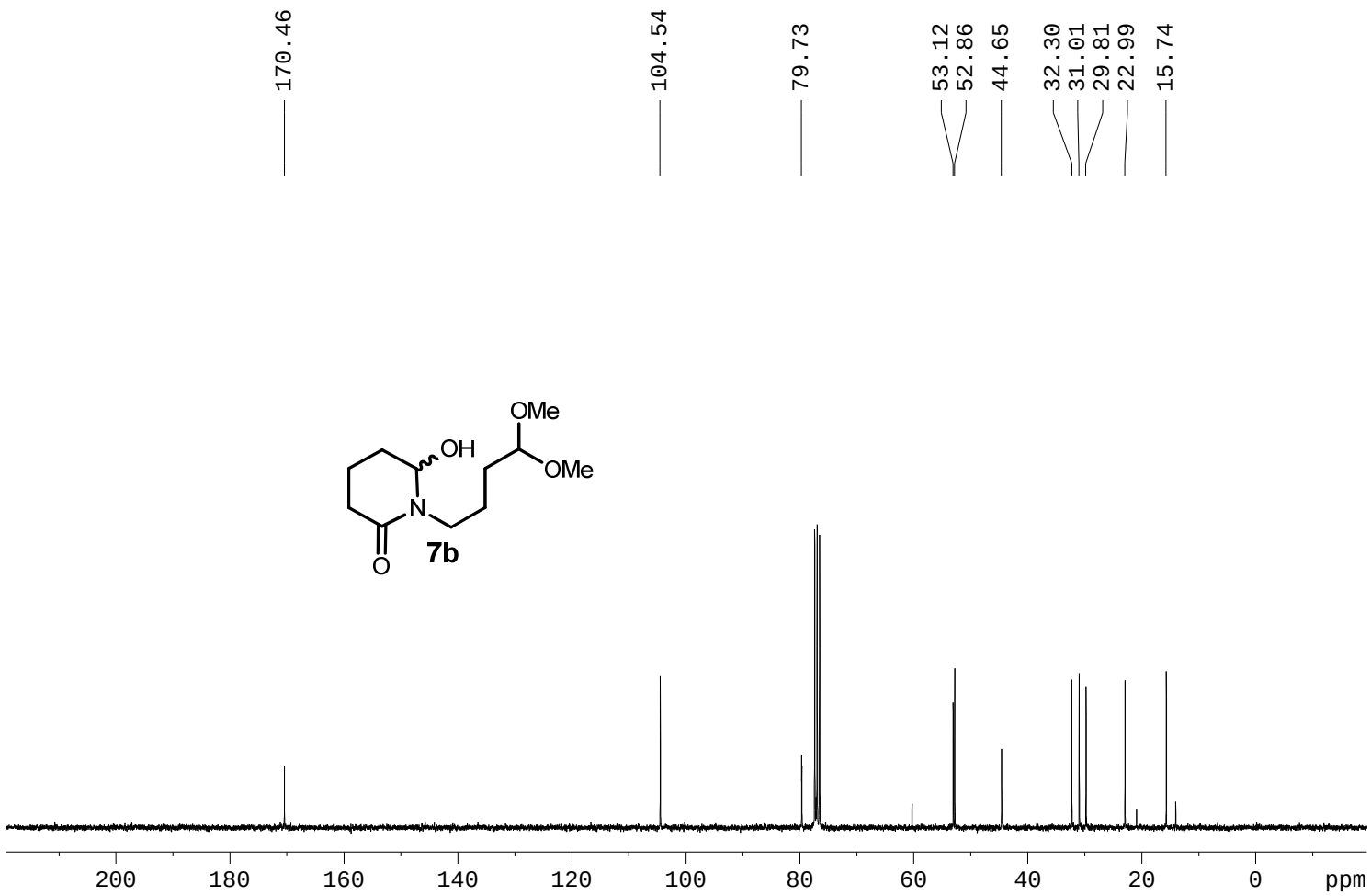
^{1}H NMR of compound SI-**4** (300 MHz, $CDCl_3$)



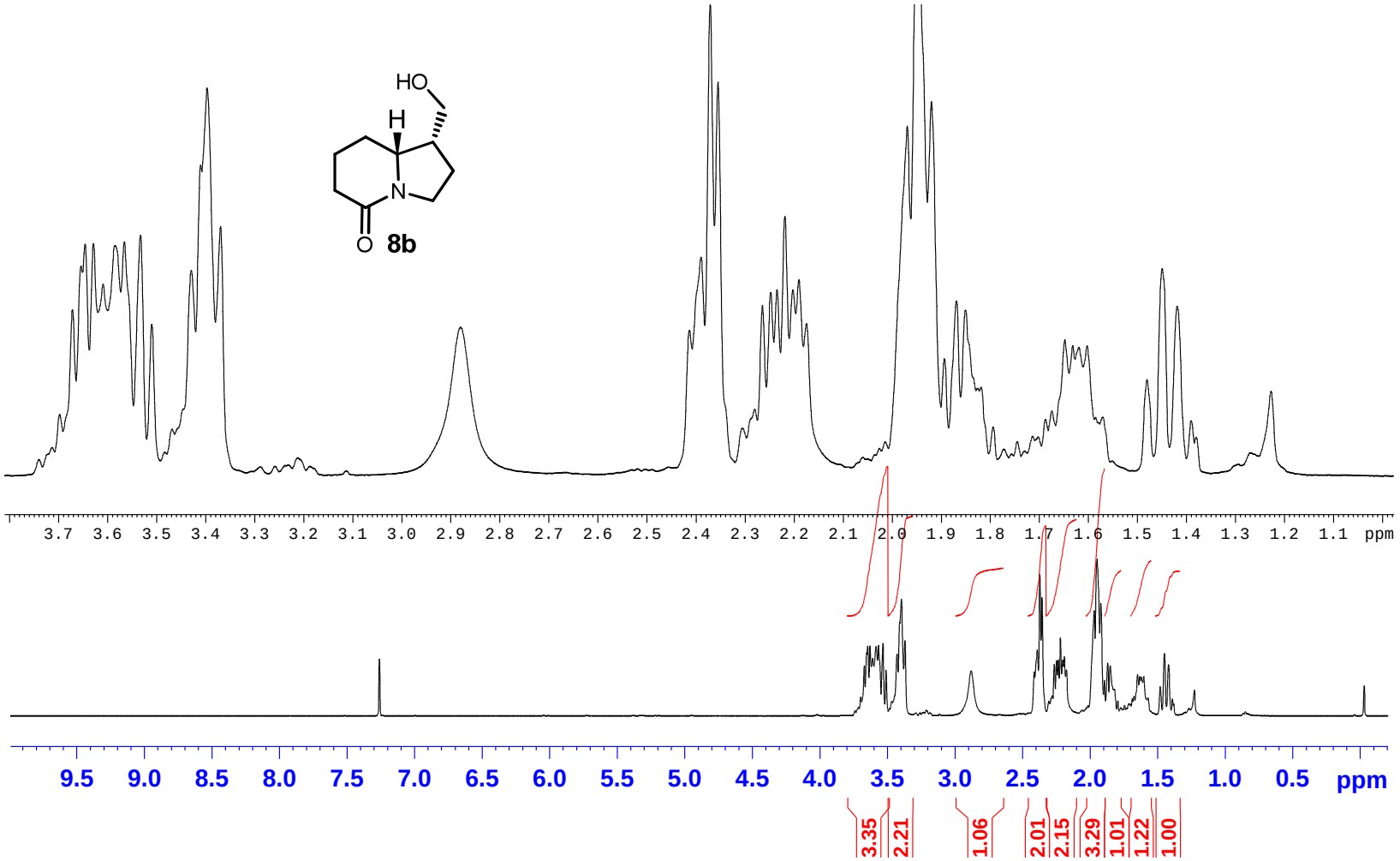
^{13}C NMR of compound **SI-4** (75 MHz, $CDCl_3$)



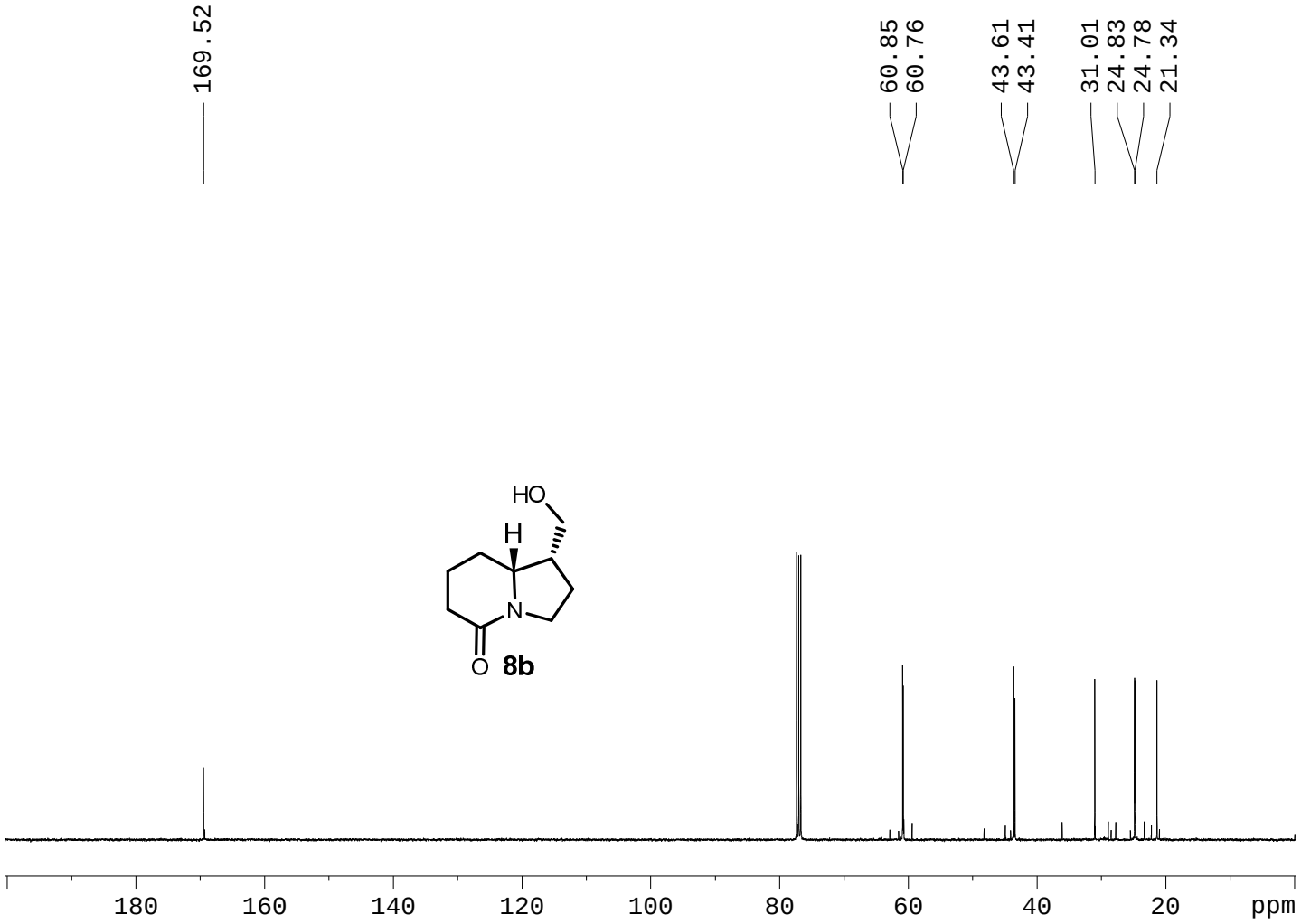
^{1}H NMR of compound **7b** (300 MHz, $CDCl_3$)



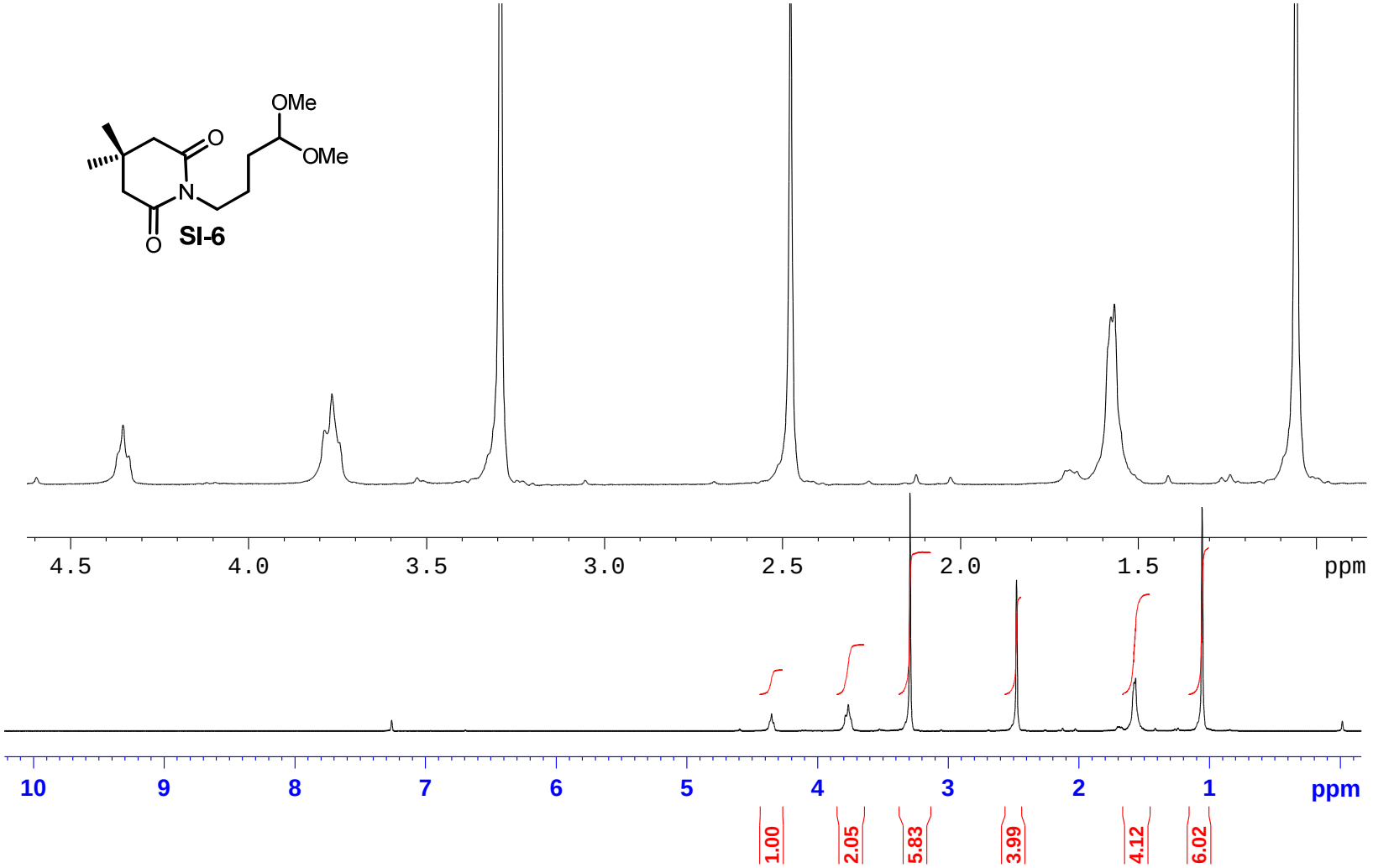
^{13}C NMR of compound **7b** (75 MHz, $CDCl_3$)



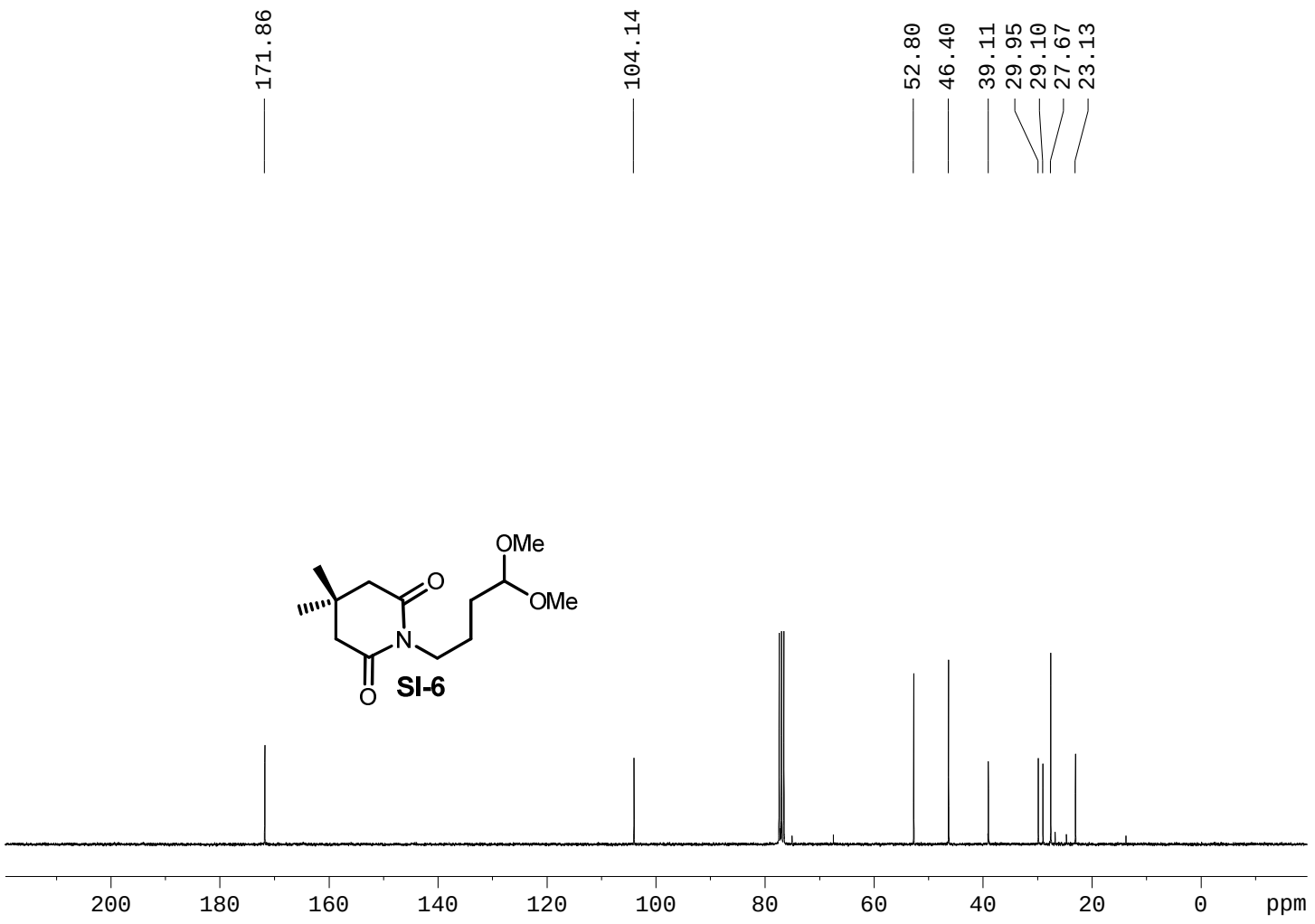
^{1}H NMR of compound **8b** (400 MHz, $CDCl_3$)



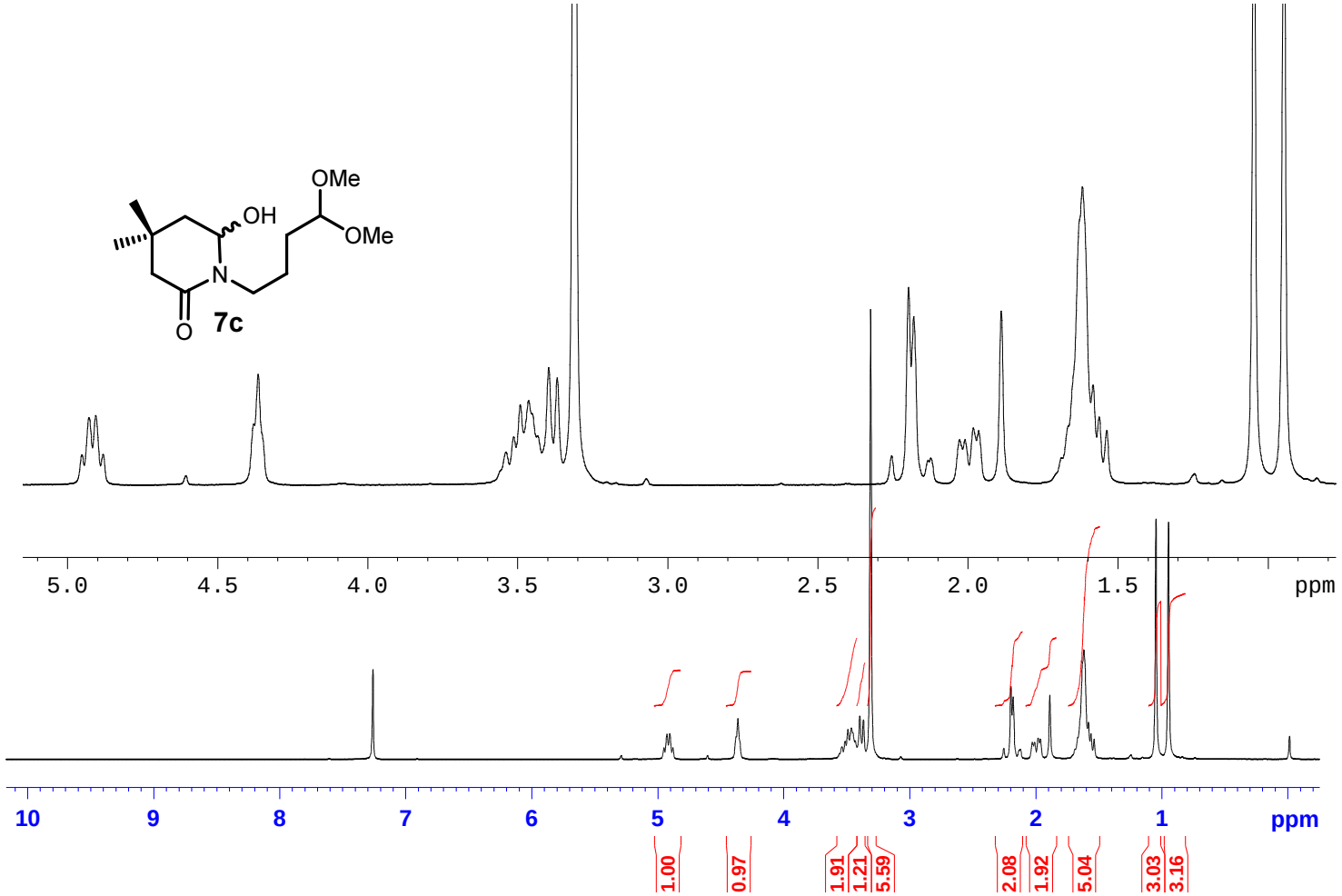
^{13}C NMR of compound **8b** (100 MHz, $CDCl_3$)



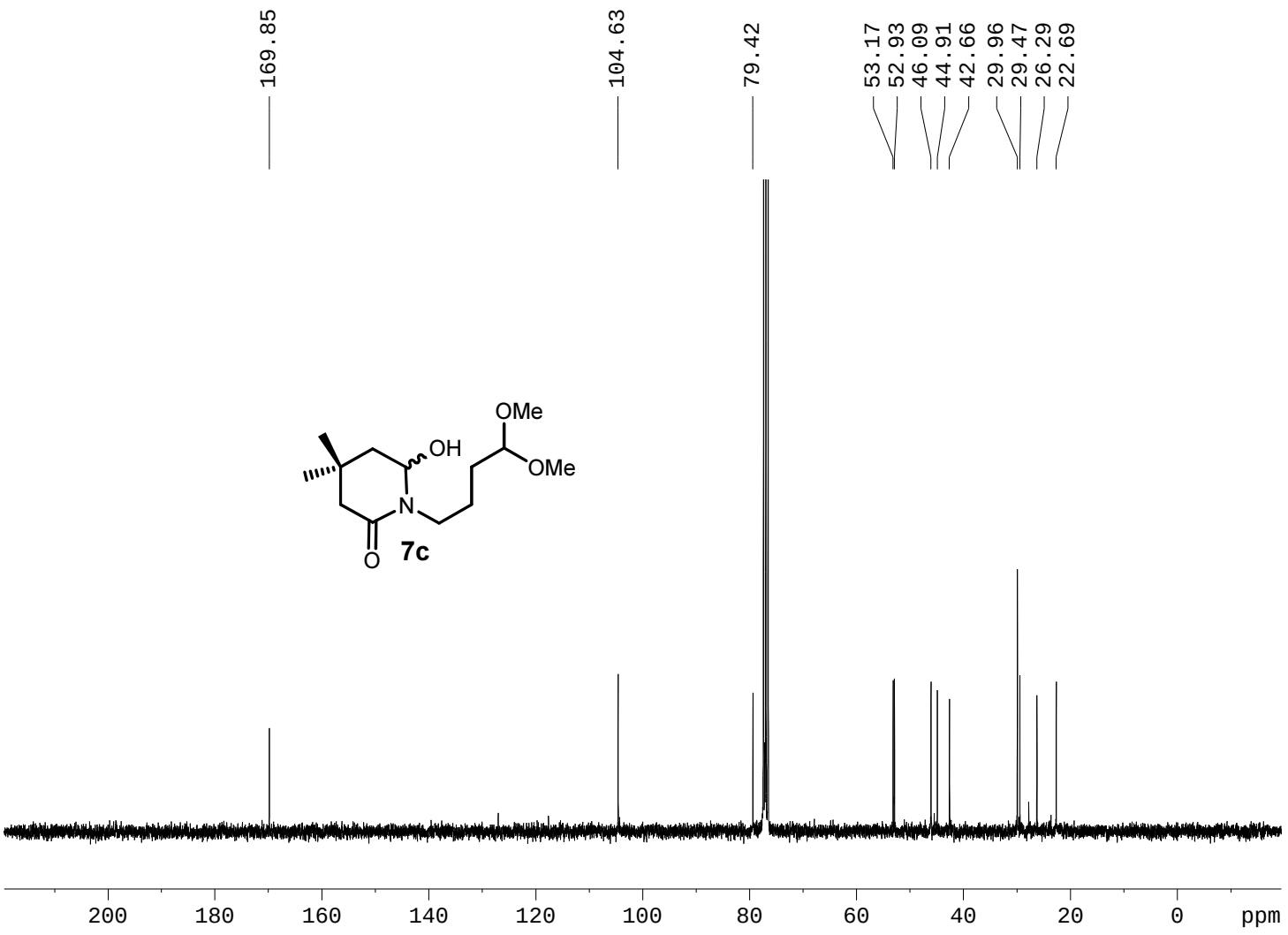
^{1}H NMR of compound **SI-6** (300 MHz, $CDCl_3$)



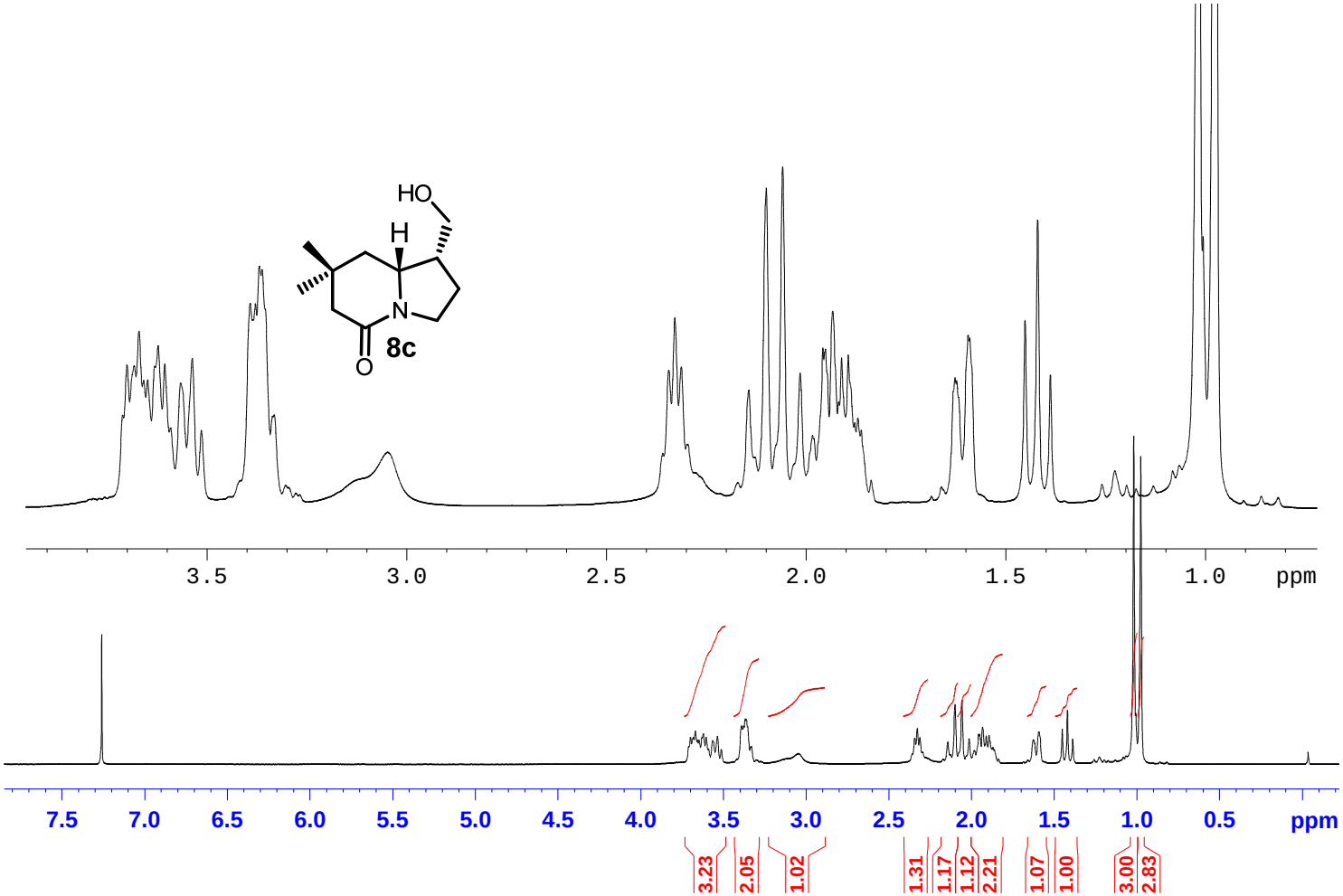
^{13}C NMR of compound **SI-6** (75 MHz, $CDCl_3$)



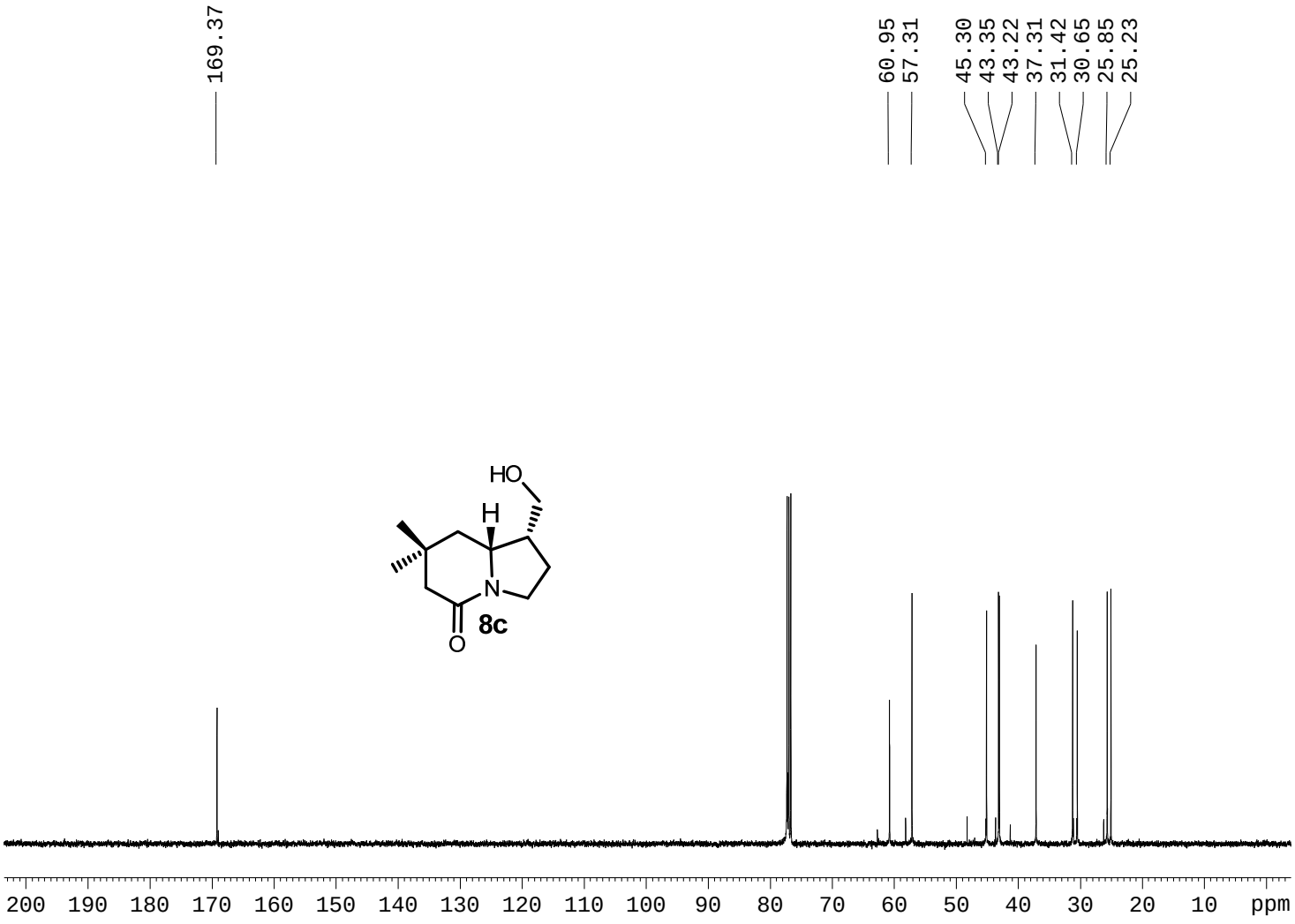
^{1}H NMR of compound **7c** (300 MHz, $CDCl_3$)



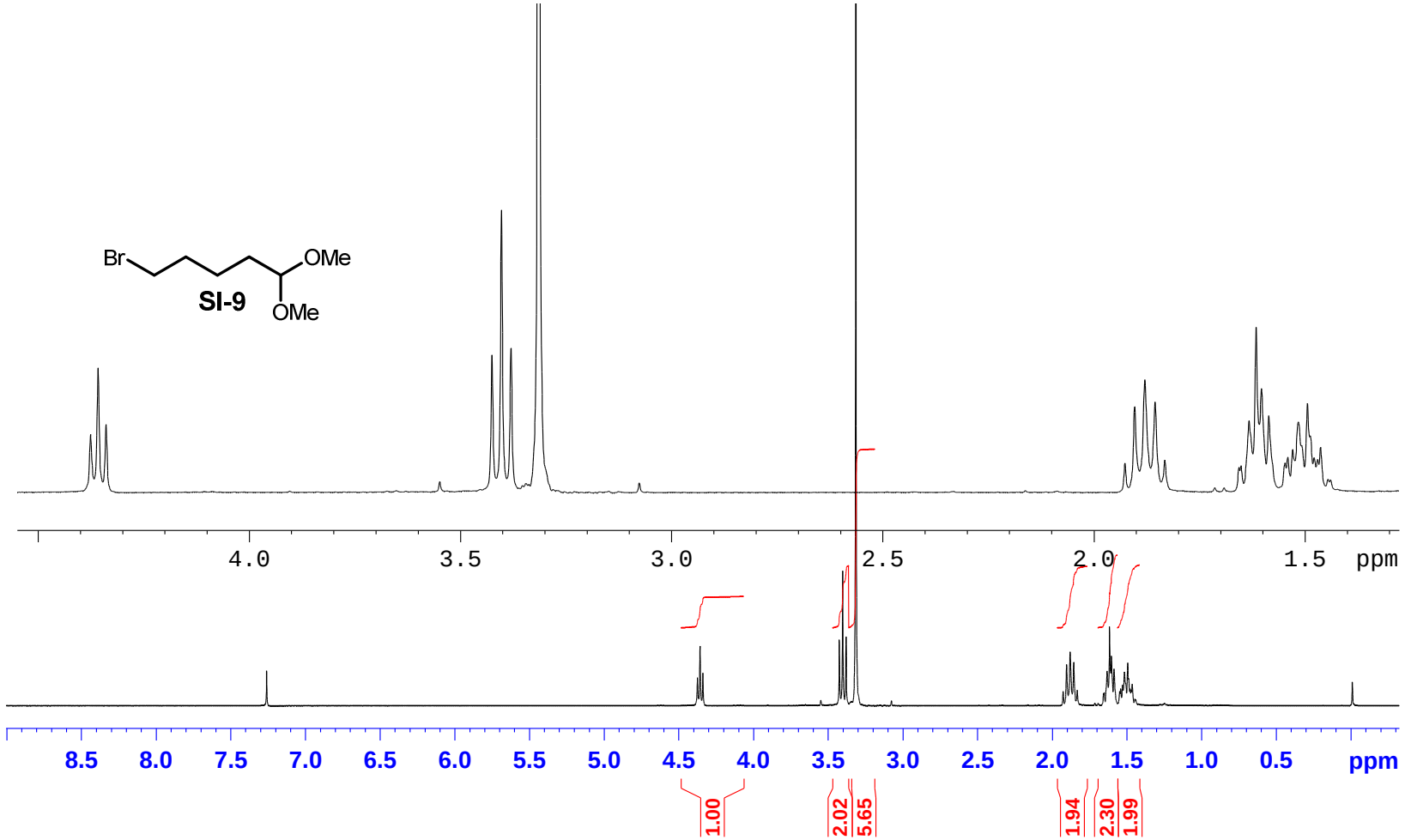
^{13}C NMR of compound **7c** (75 MHz, $CDCl_3$)



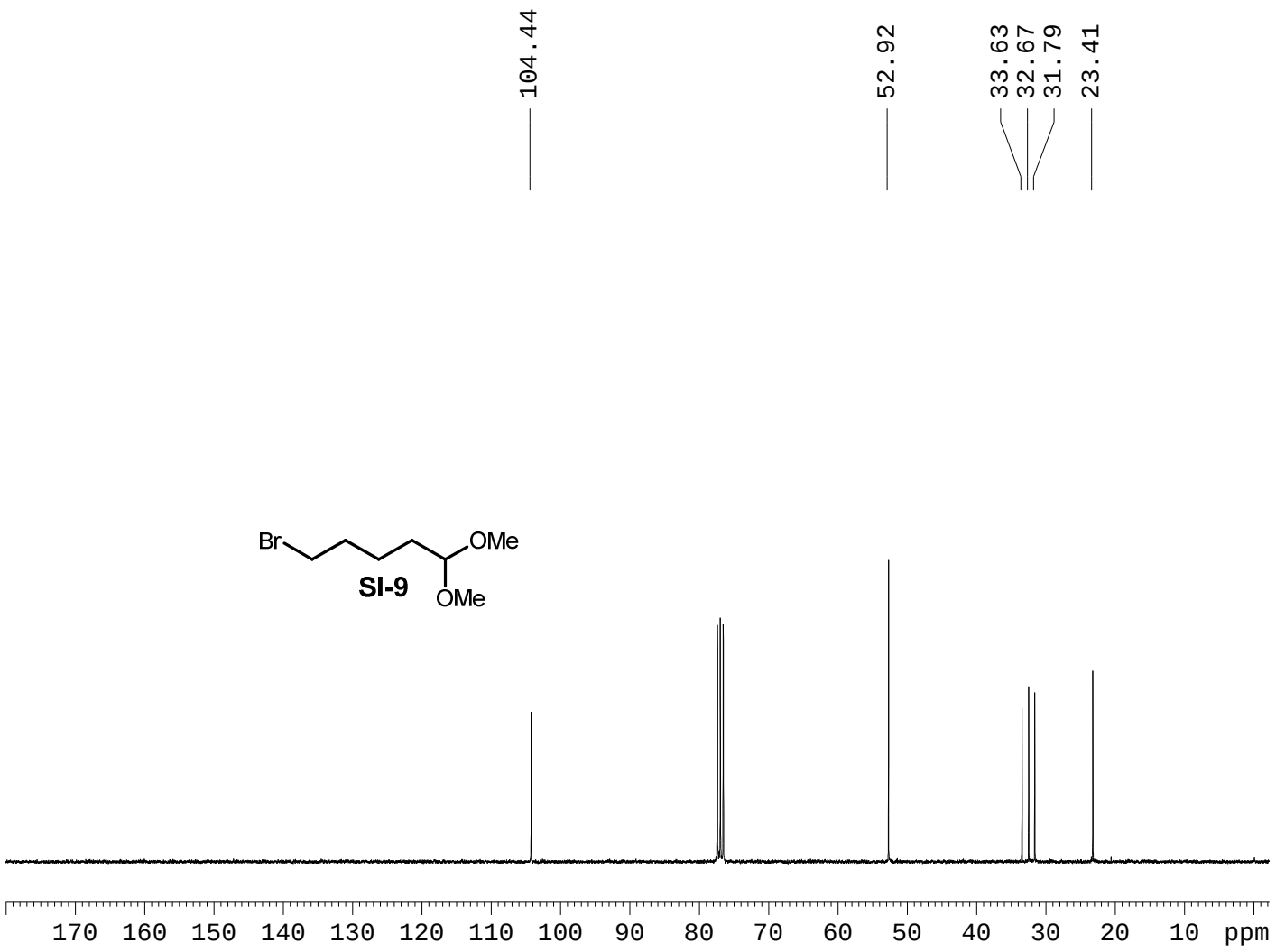
^{1}H NMR of compound **8c** (400 MHz, $CDCl_3$)



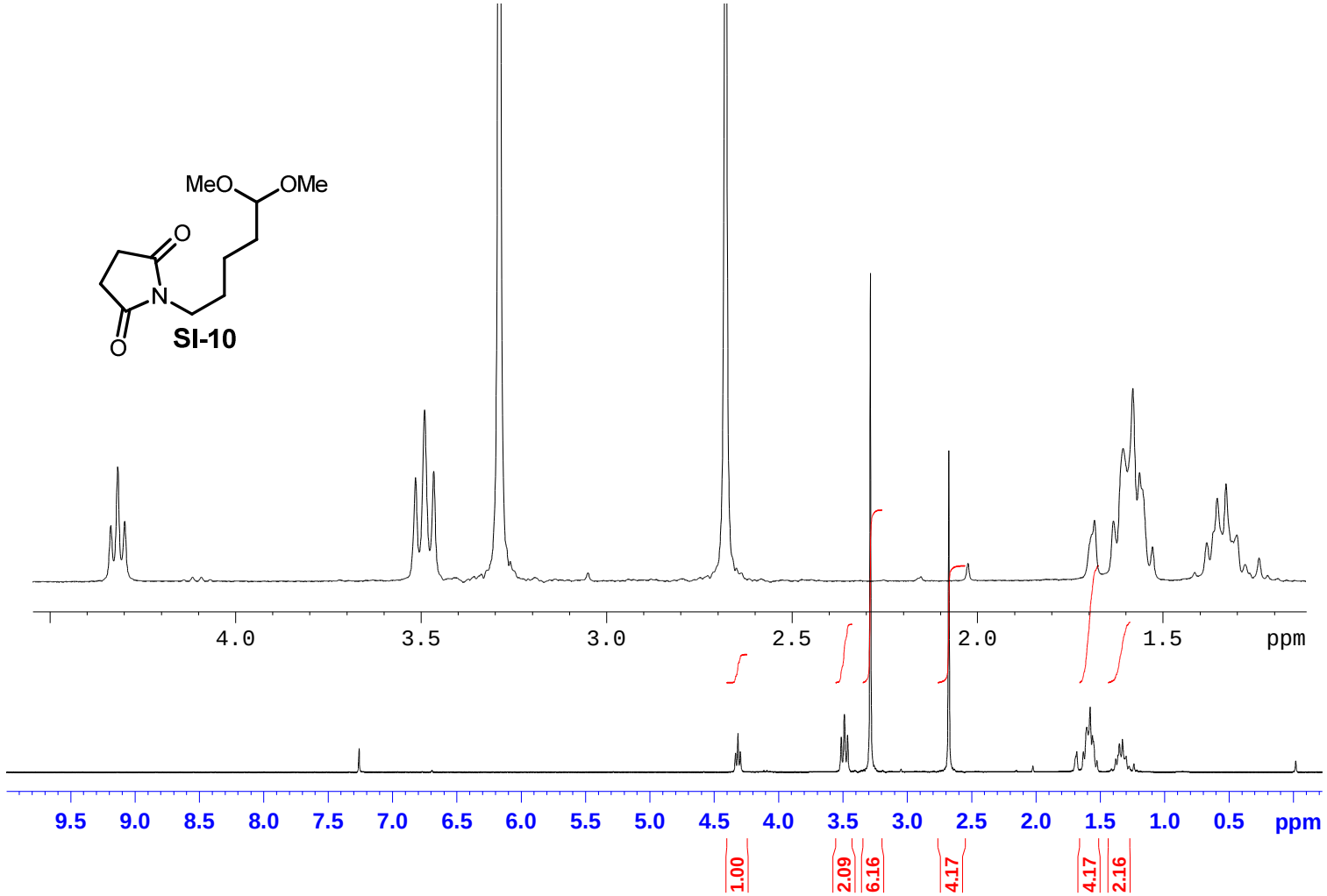
^{13}C NMR of compound **8c** (100 MHz, $CDCl_3$)



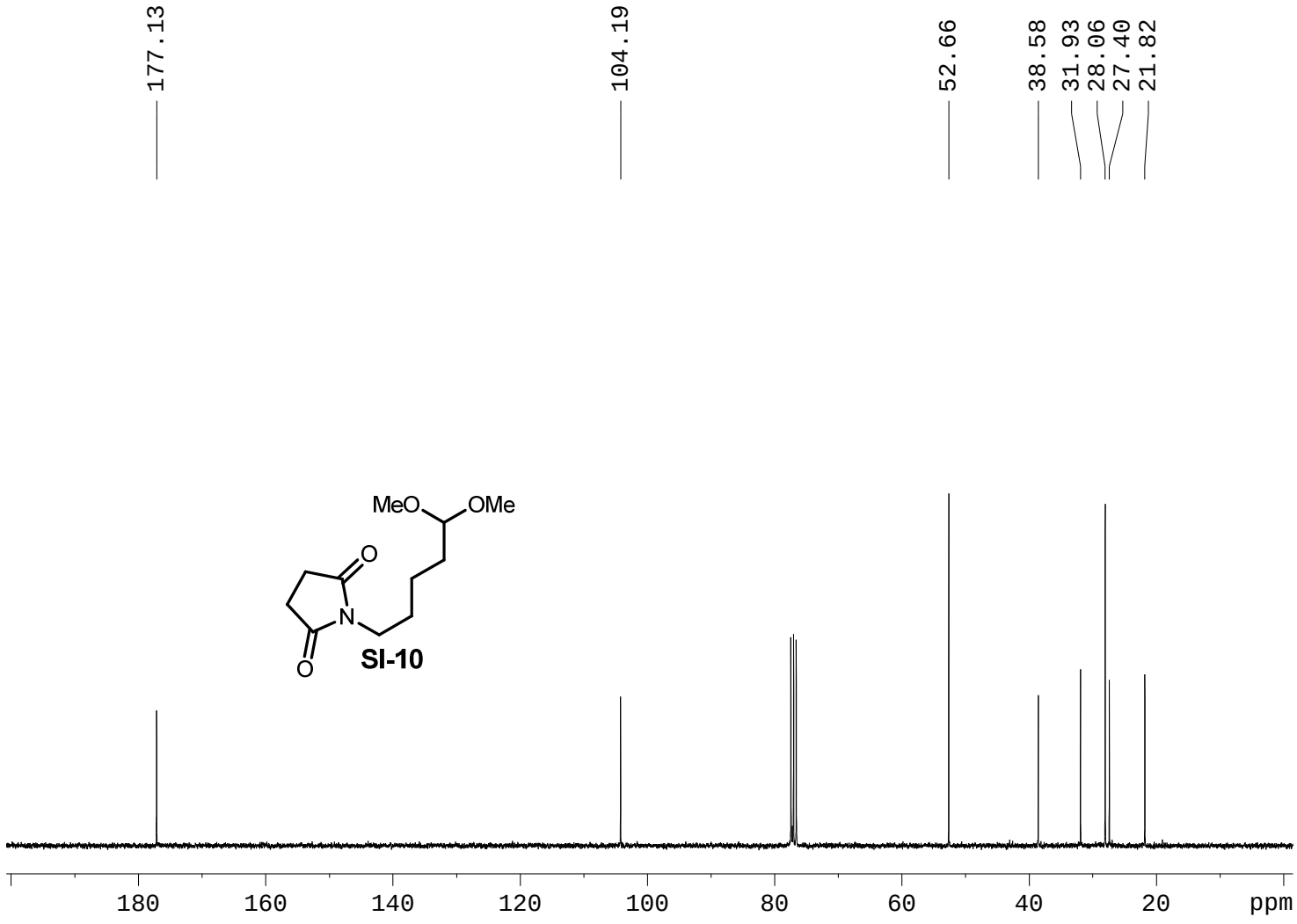
^{1}H NMR of compound **SI-9** (300 MHz, $CDCl_3$)



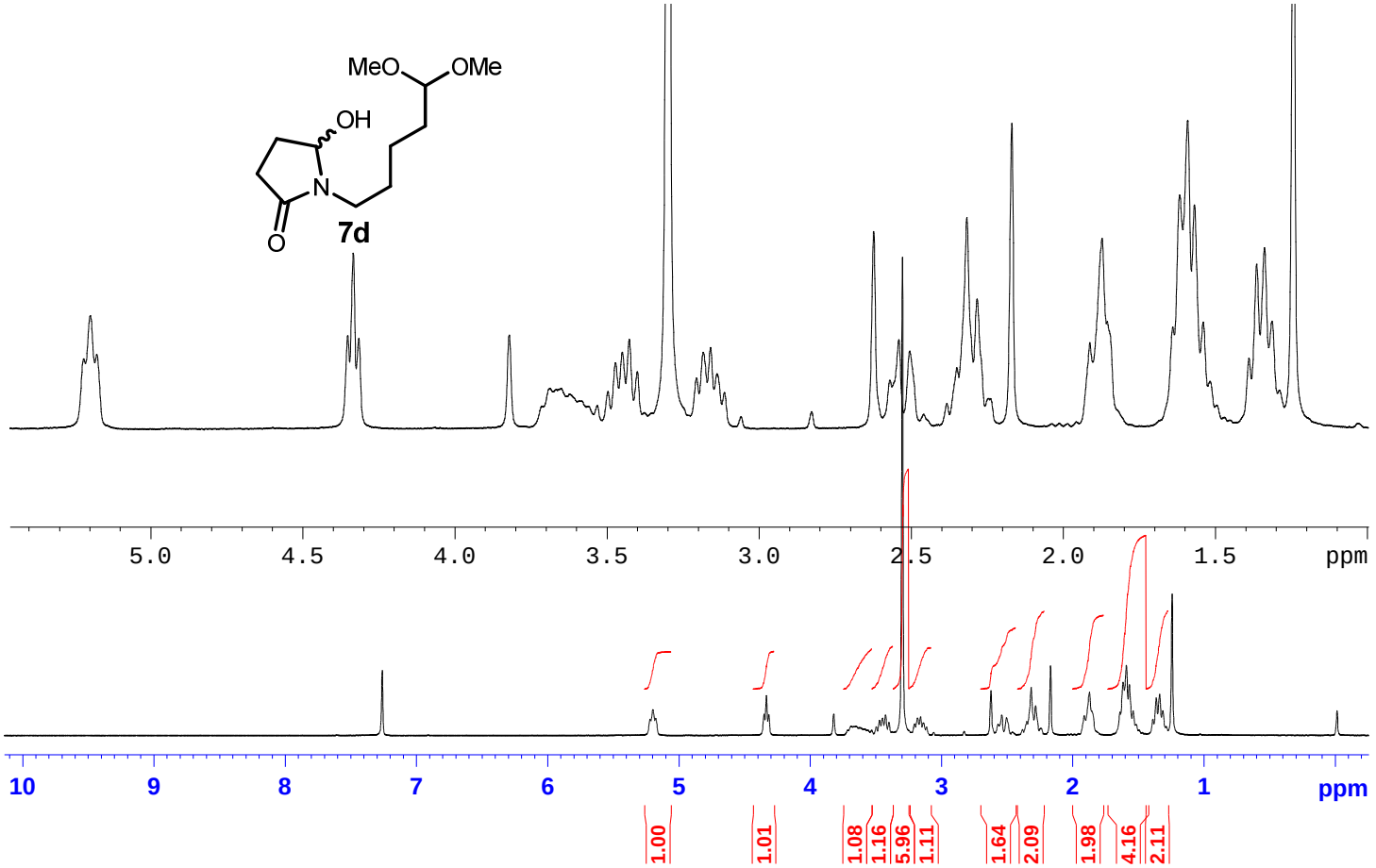
^{13}C NMR of compound **SI-9** (75 MHz, $CDCl_3$)



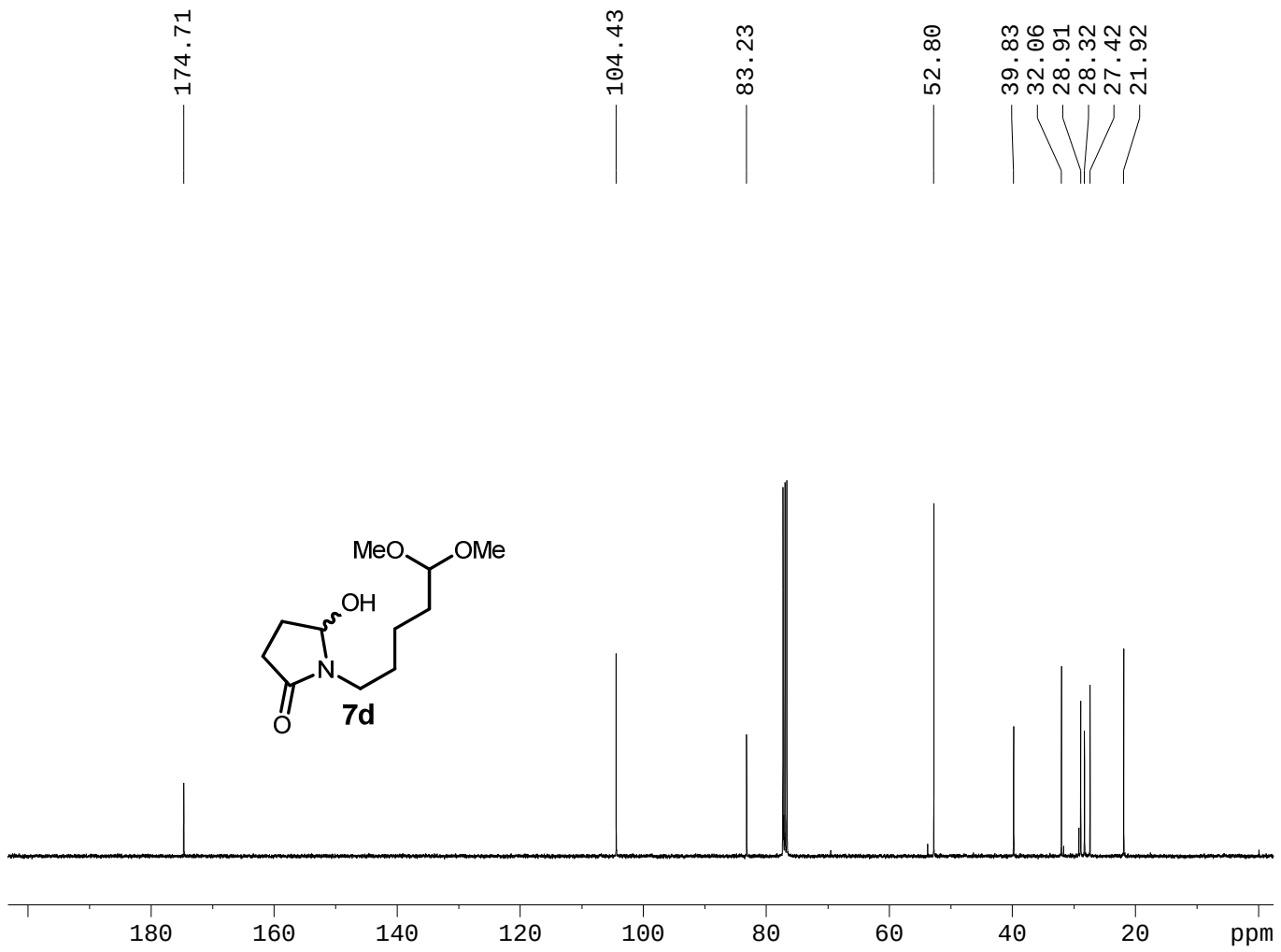
^{1}H NMR of compound **SI-10** (300 MHz, $CDCl_3$)



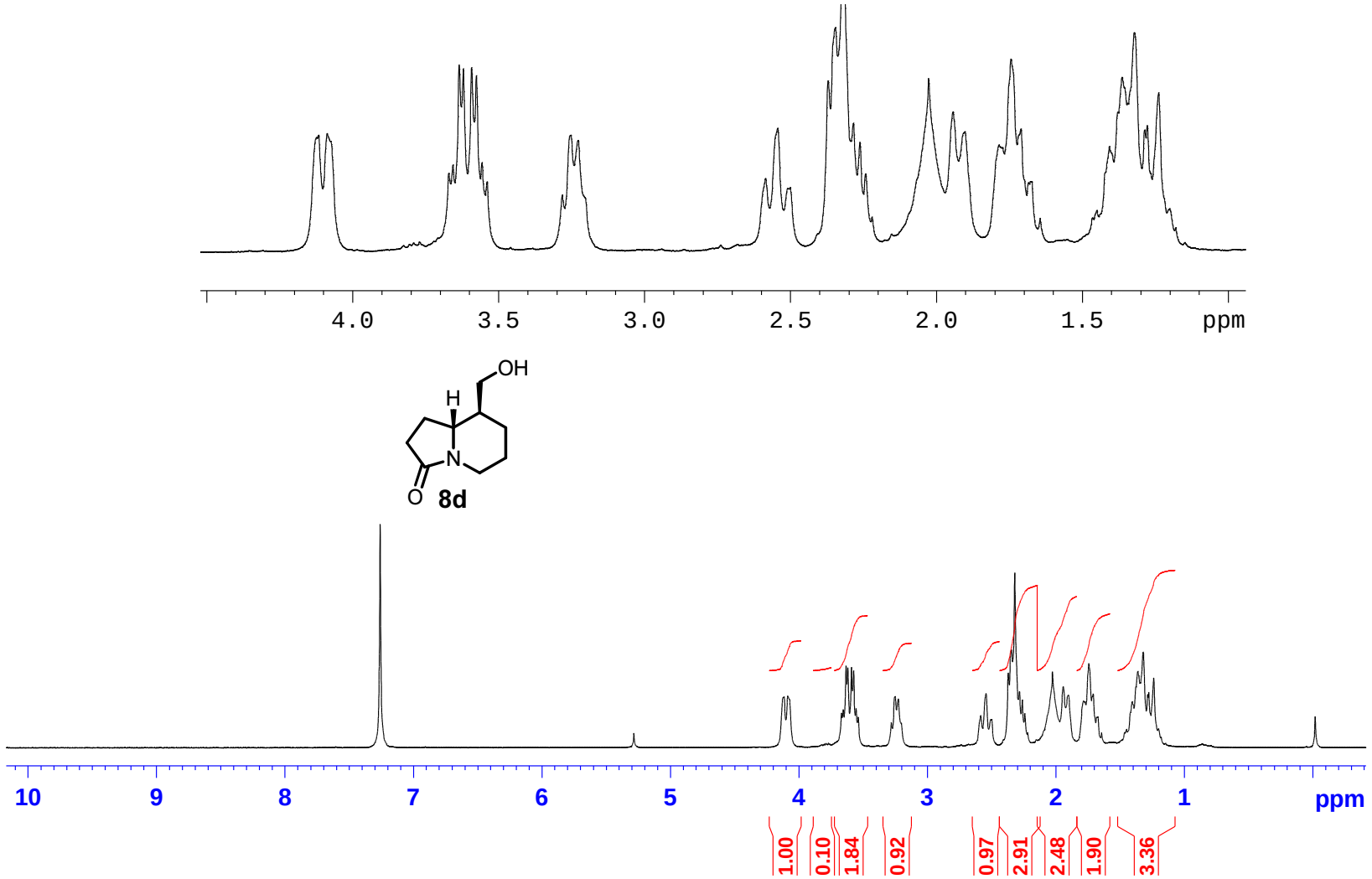
^{13}C NMR of compound **SI-10** (75 MHz, $CDCl_3$)



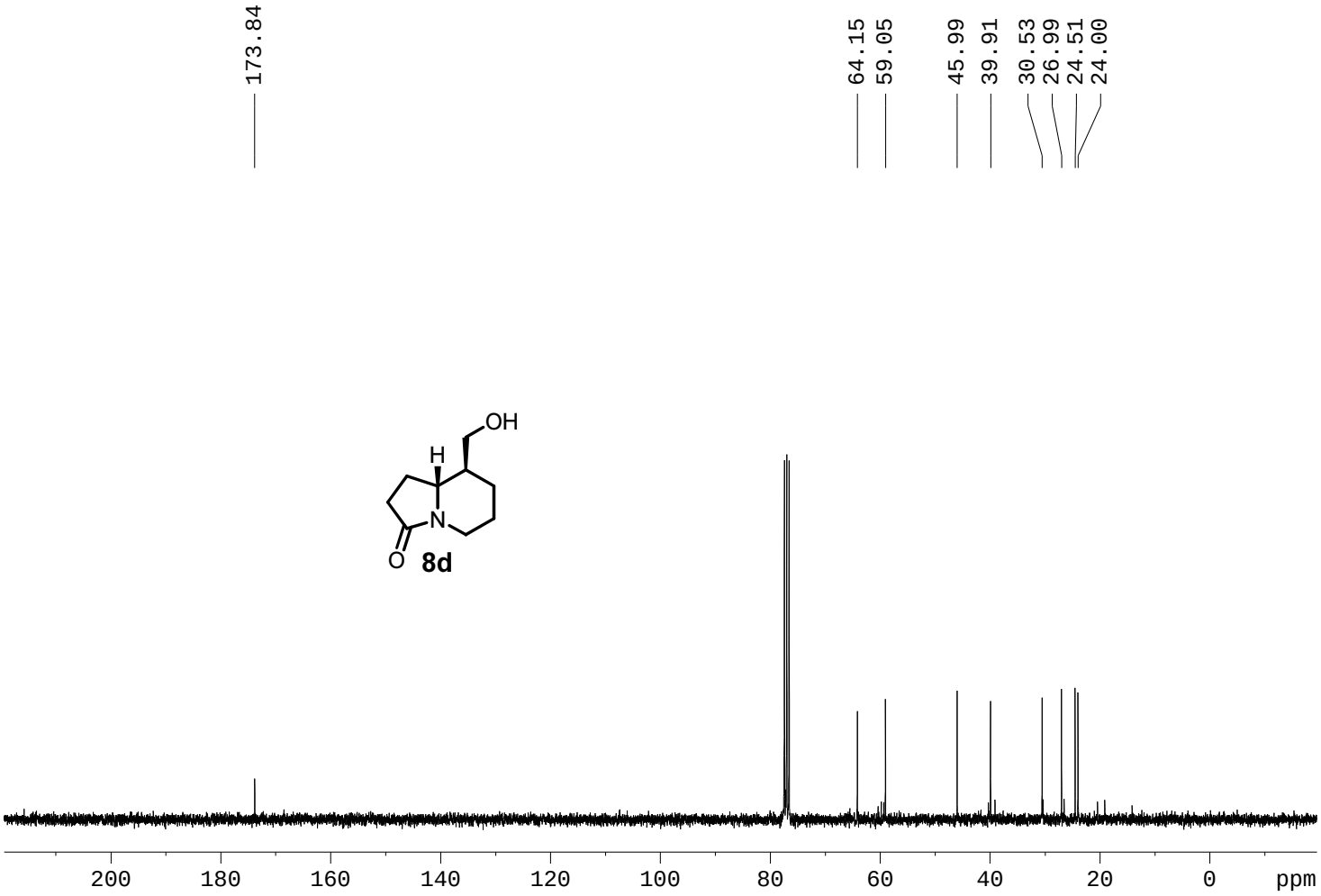
^{1}H NMR of compound **7d** (300 MHz, $CDCl_3$)



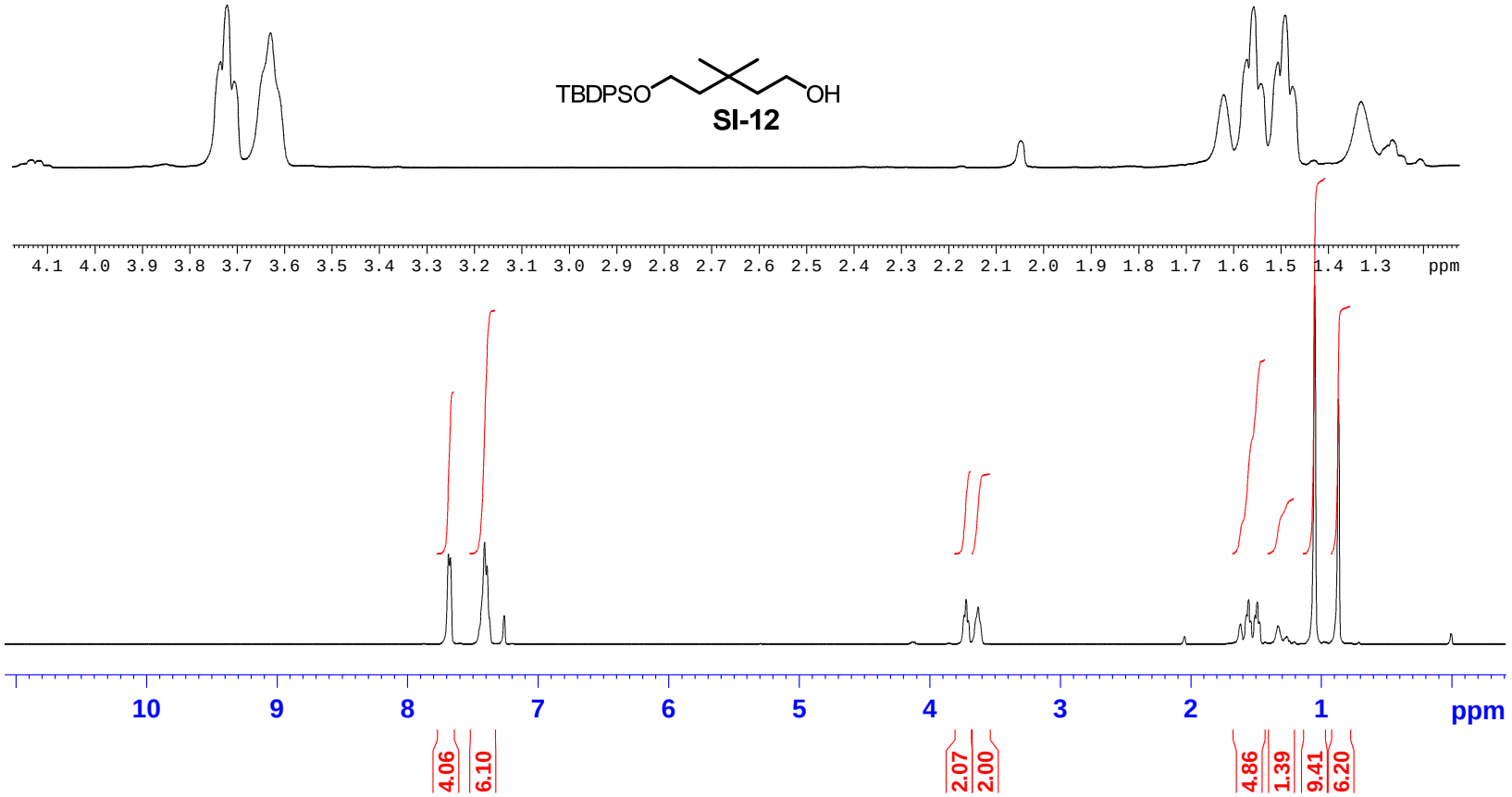
^{13}C NMR of compound **7d** (100 MHz, $CDCl_3$)



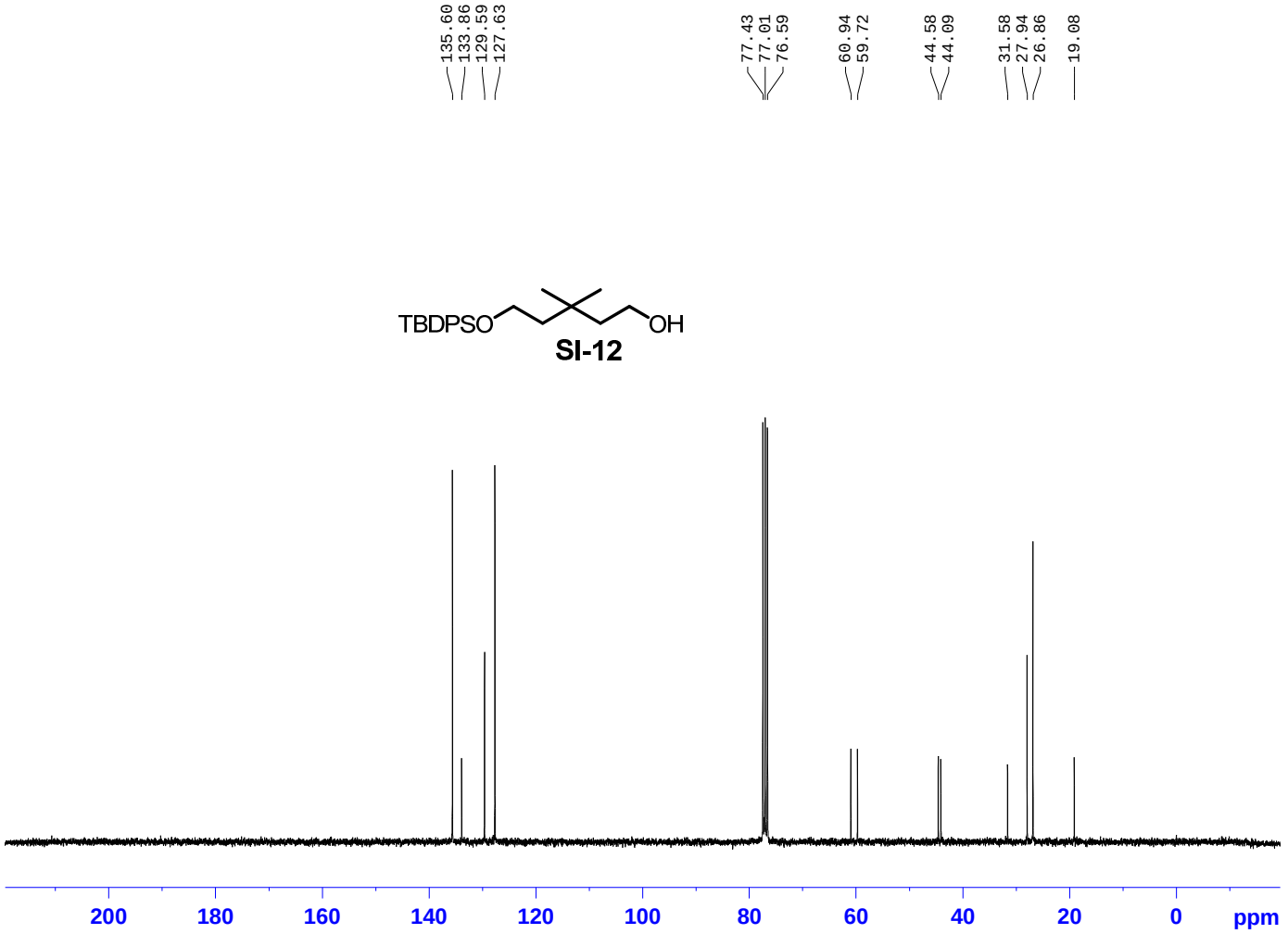
^{1}H NMR of compound **8d** (300 MHz, $CDCl_3$)



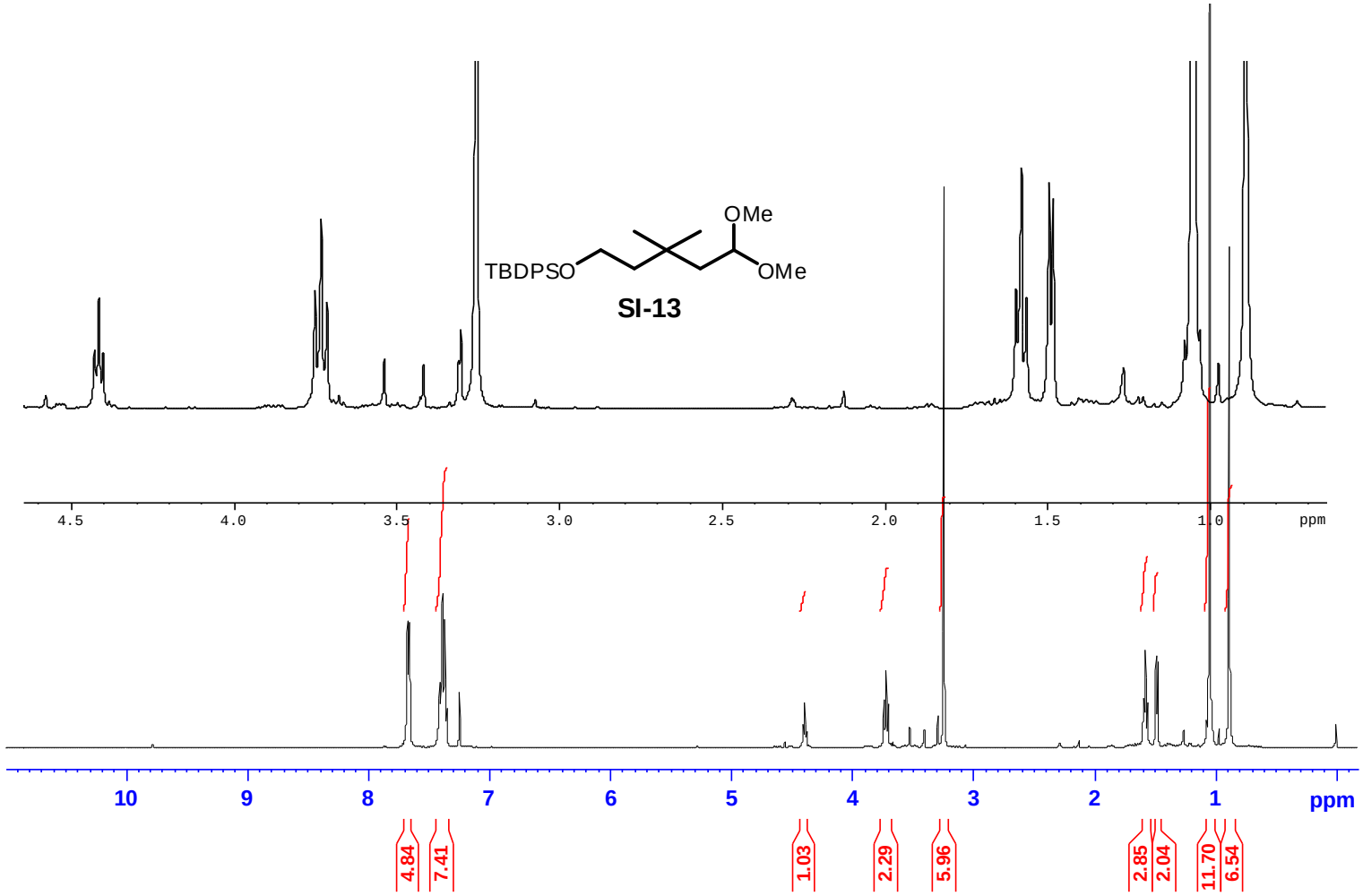
^{13}C NMR of compound **8d** (75 MHz, $CDCl_3$)



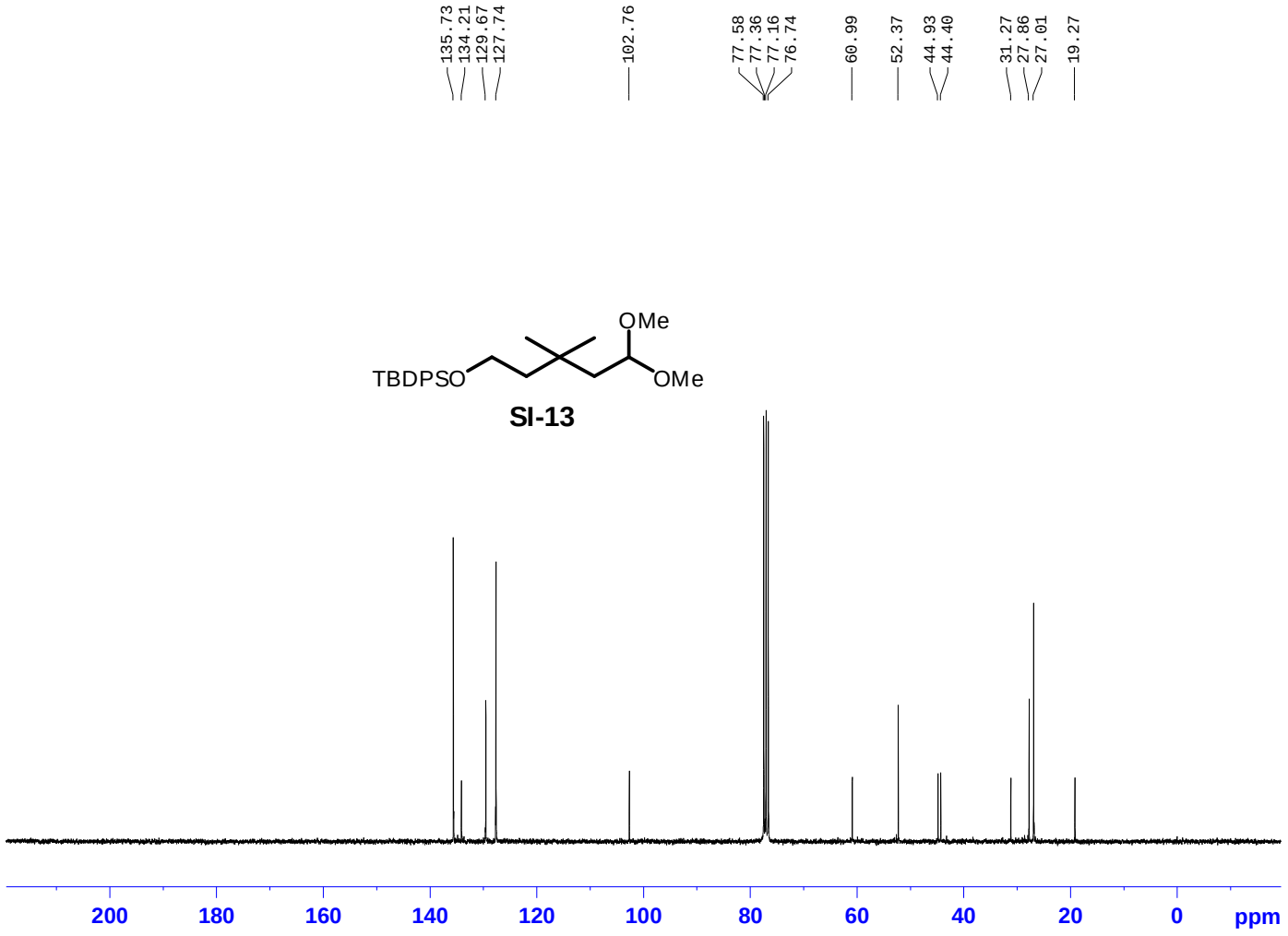
^{1}H NMR of compound **SI-12** (400 MHz, $CDCl_3$)



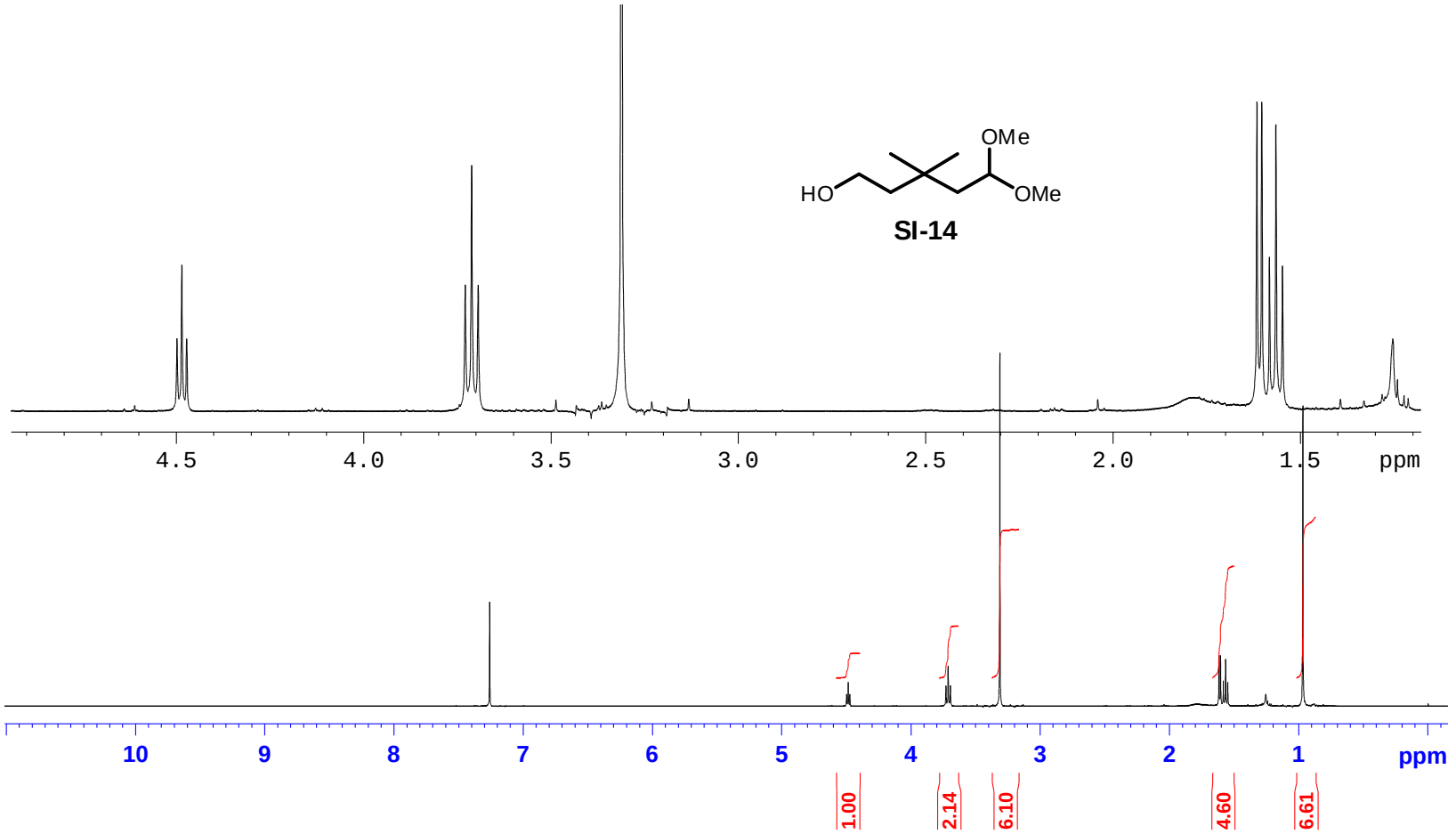
^{13}C NMR of compound **SI-12** (100 MHz, $CDCl_3$)



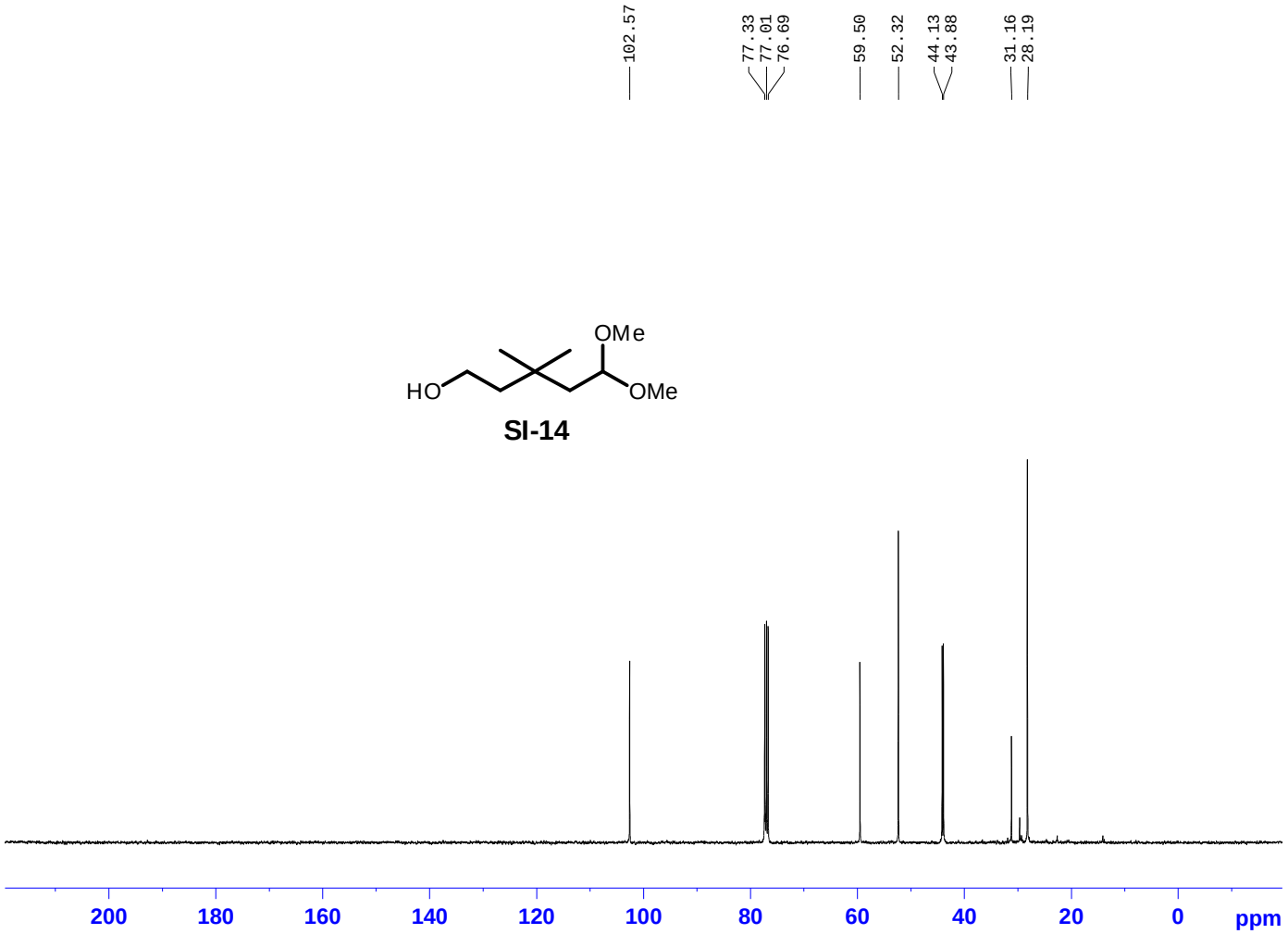
^{1}H NMR of compound **SI-13** (400 MHz, $CDCl_3$)



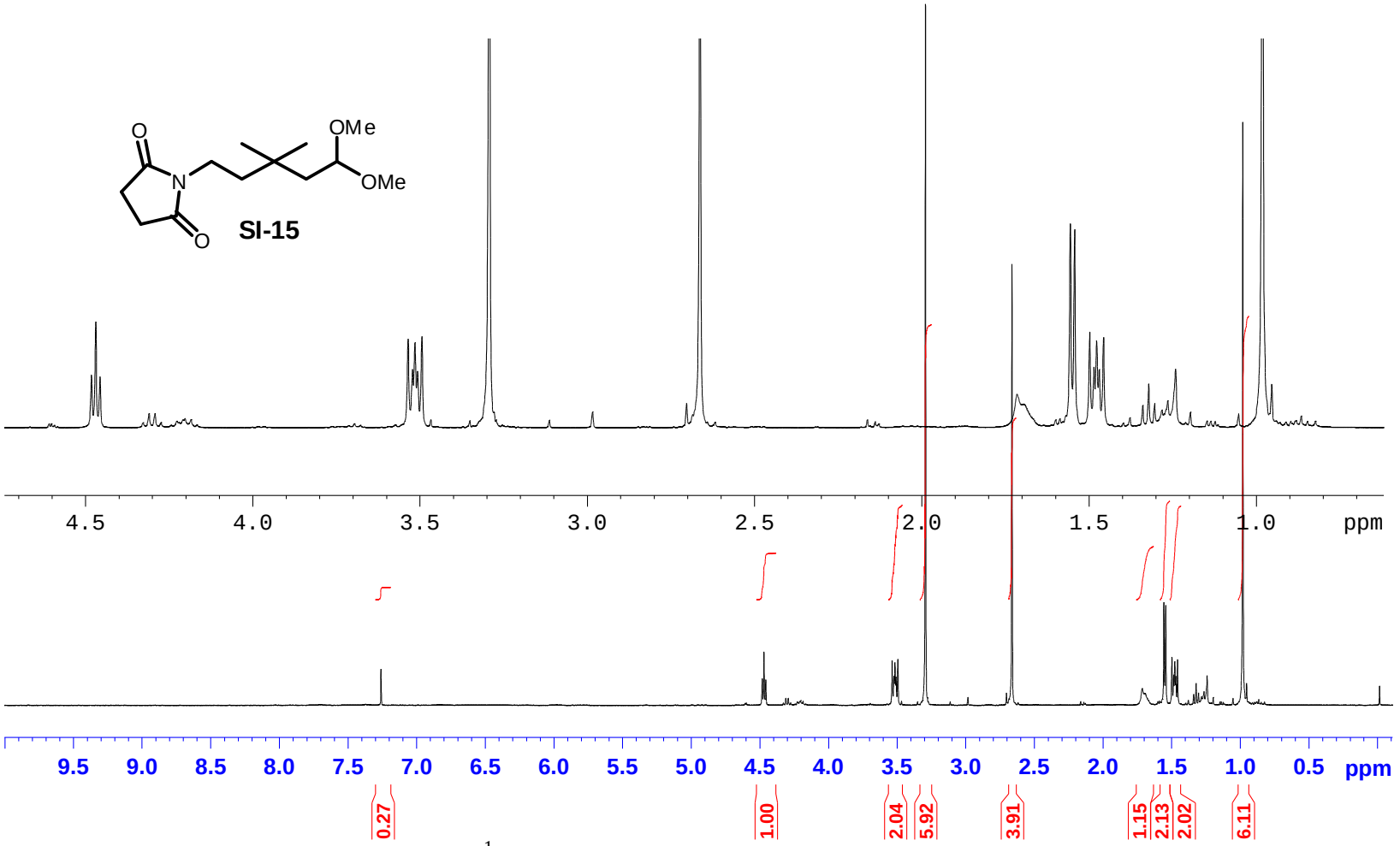
^{13}C NMR of compound **SI-13** (100 MHz, $CDCl_3$)



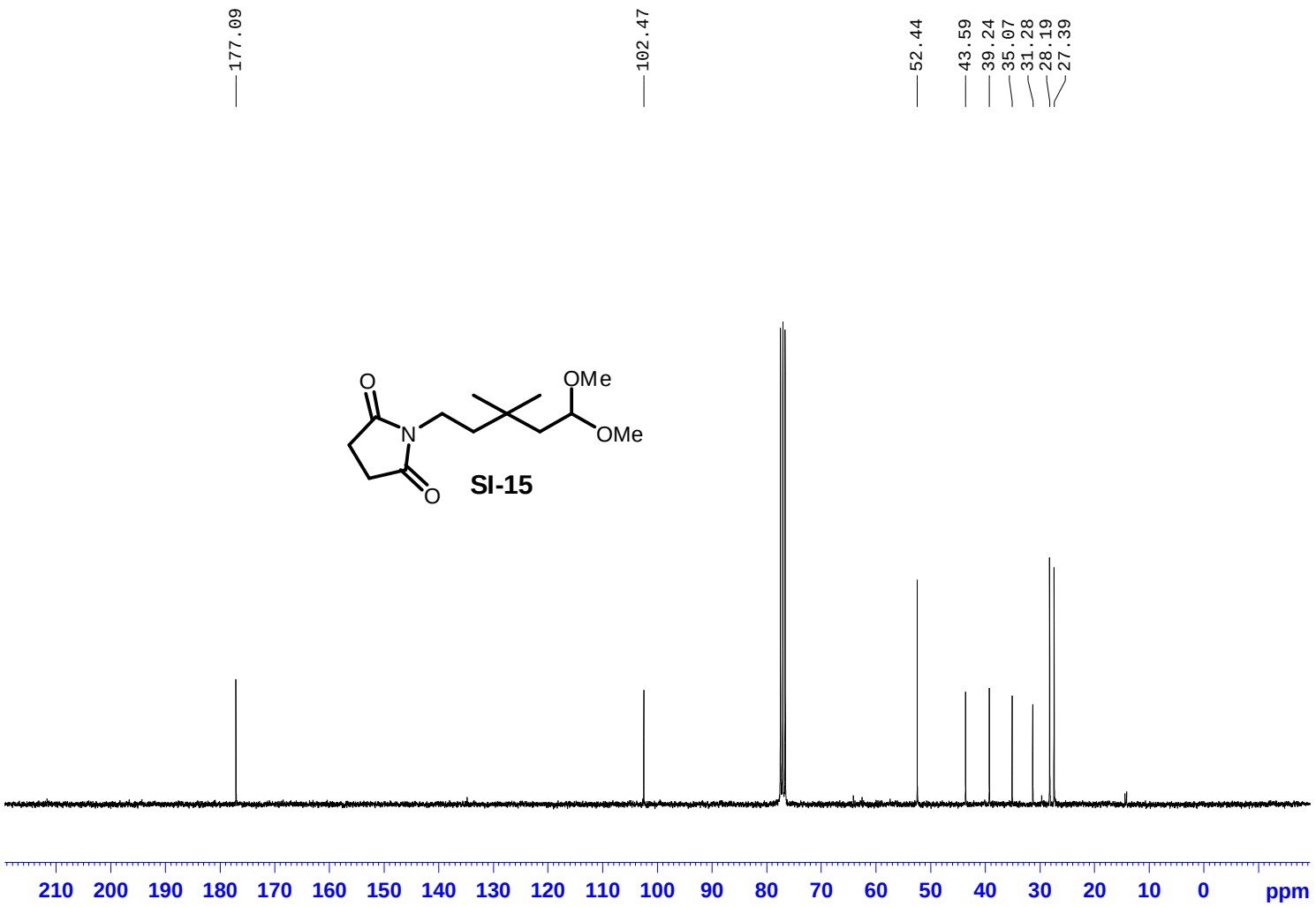
^{1}H NMR of compound **SI-14** (400 MHz, $CDCl_3$)



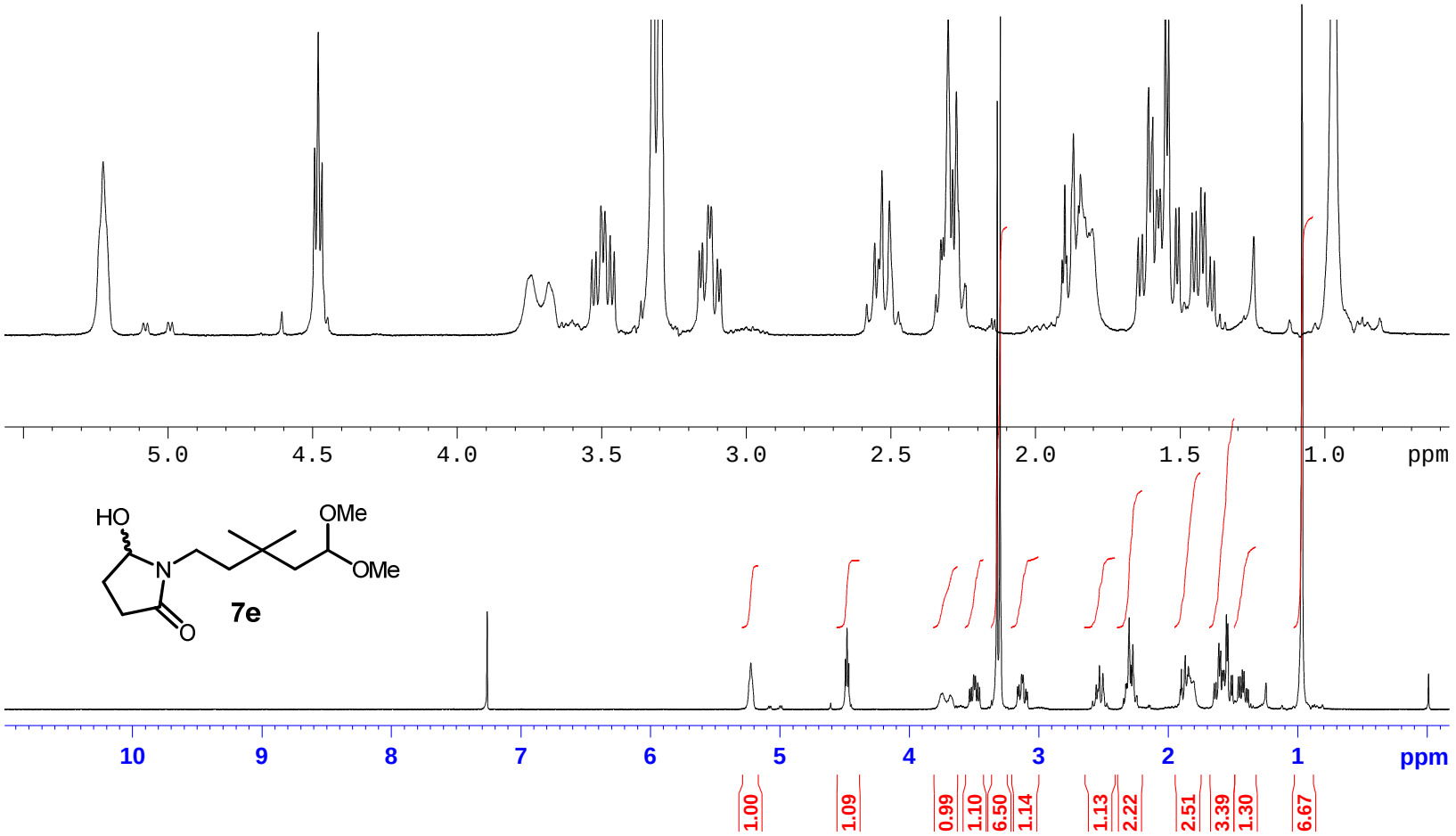
^{13}C NMR of compound **SI-14** (100 MHz, $CDCl_3$)



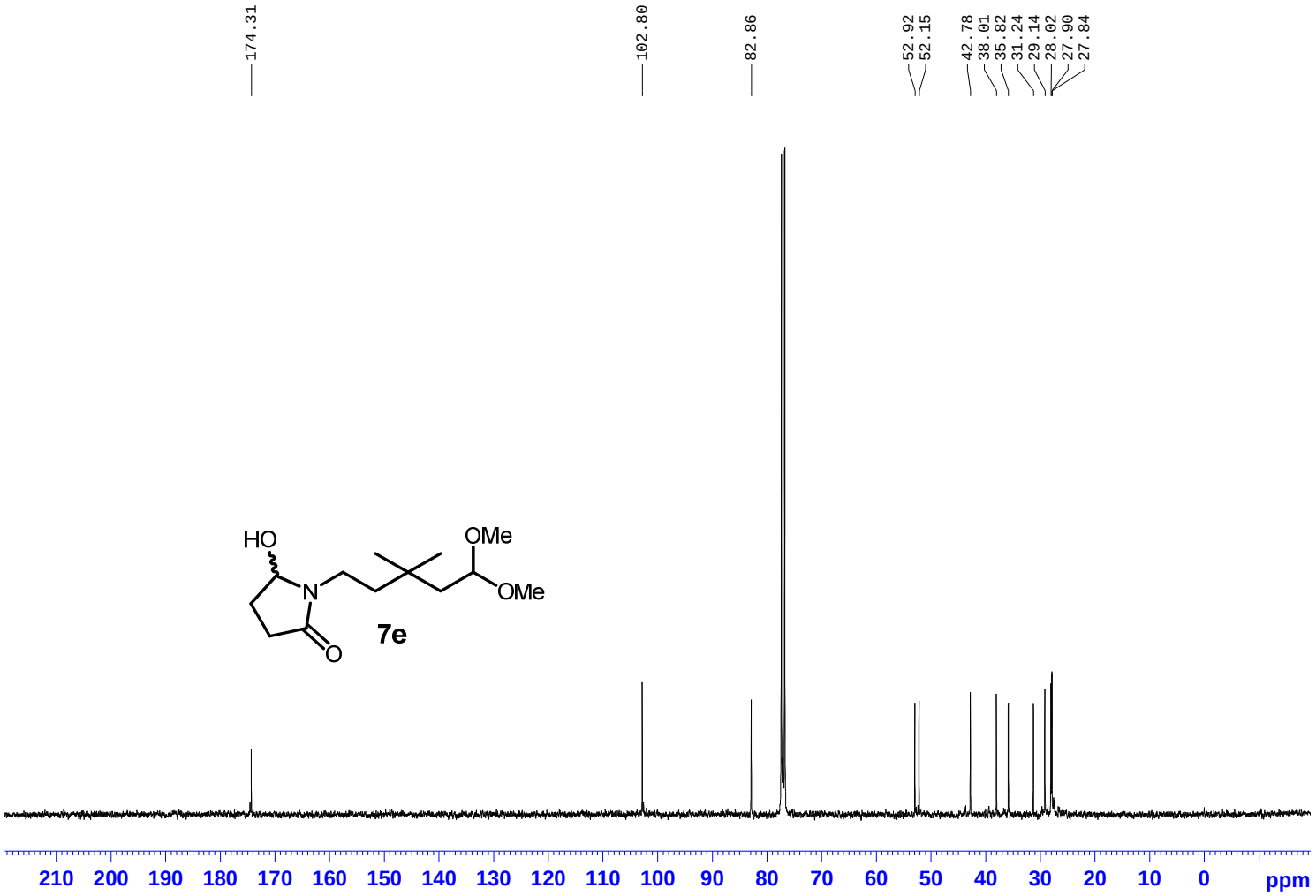
^{1}H NMR of compound **SI-15** (400 MHz, $CDCl_3$)



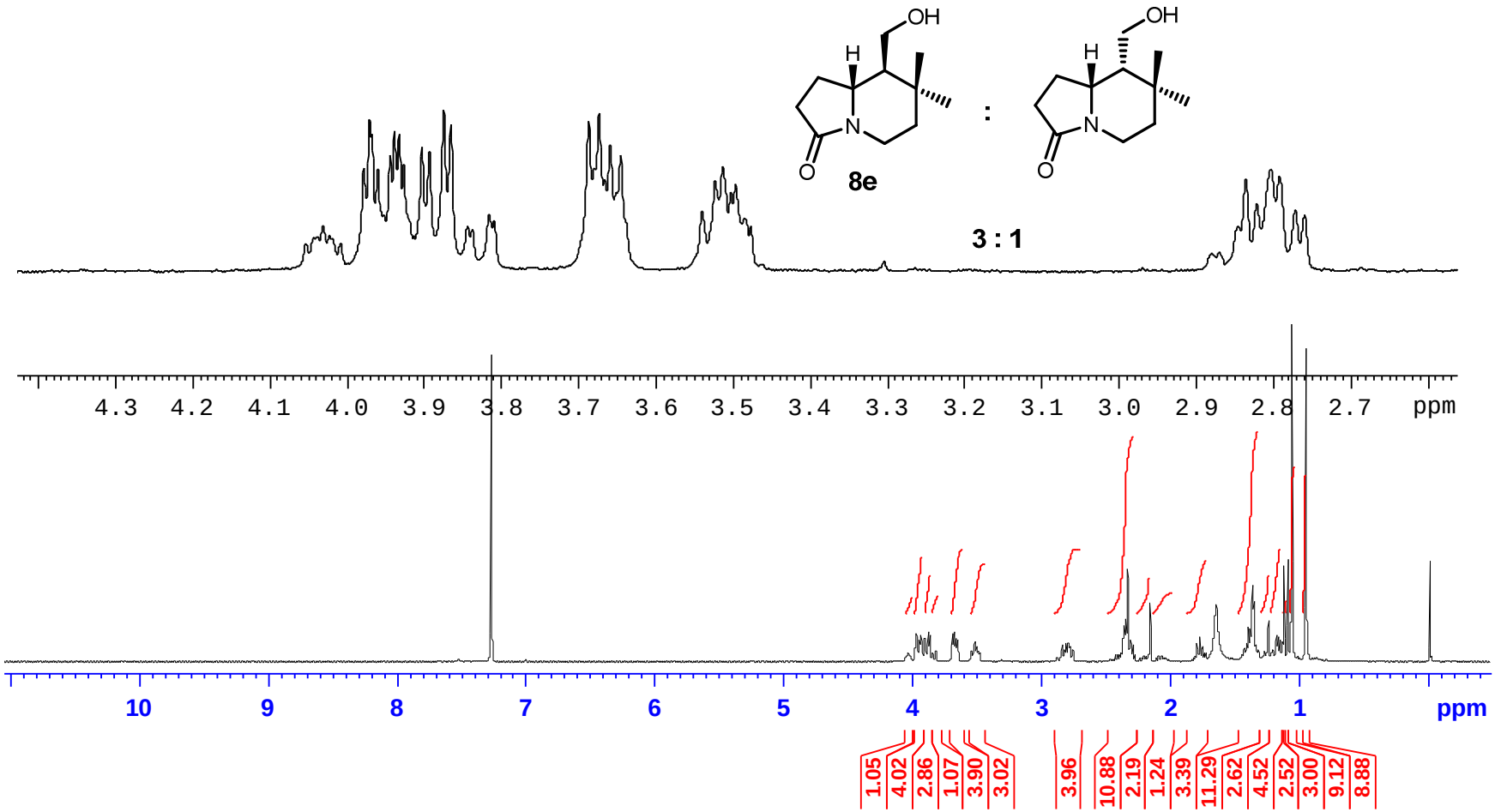
^{13}C NMR of compound **SI-15** (100 MHz, $CDCl_3$)



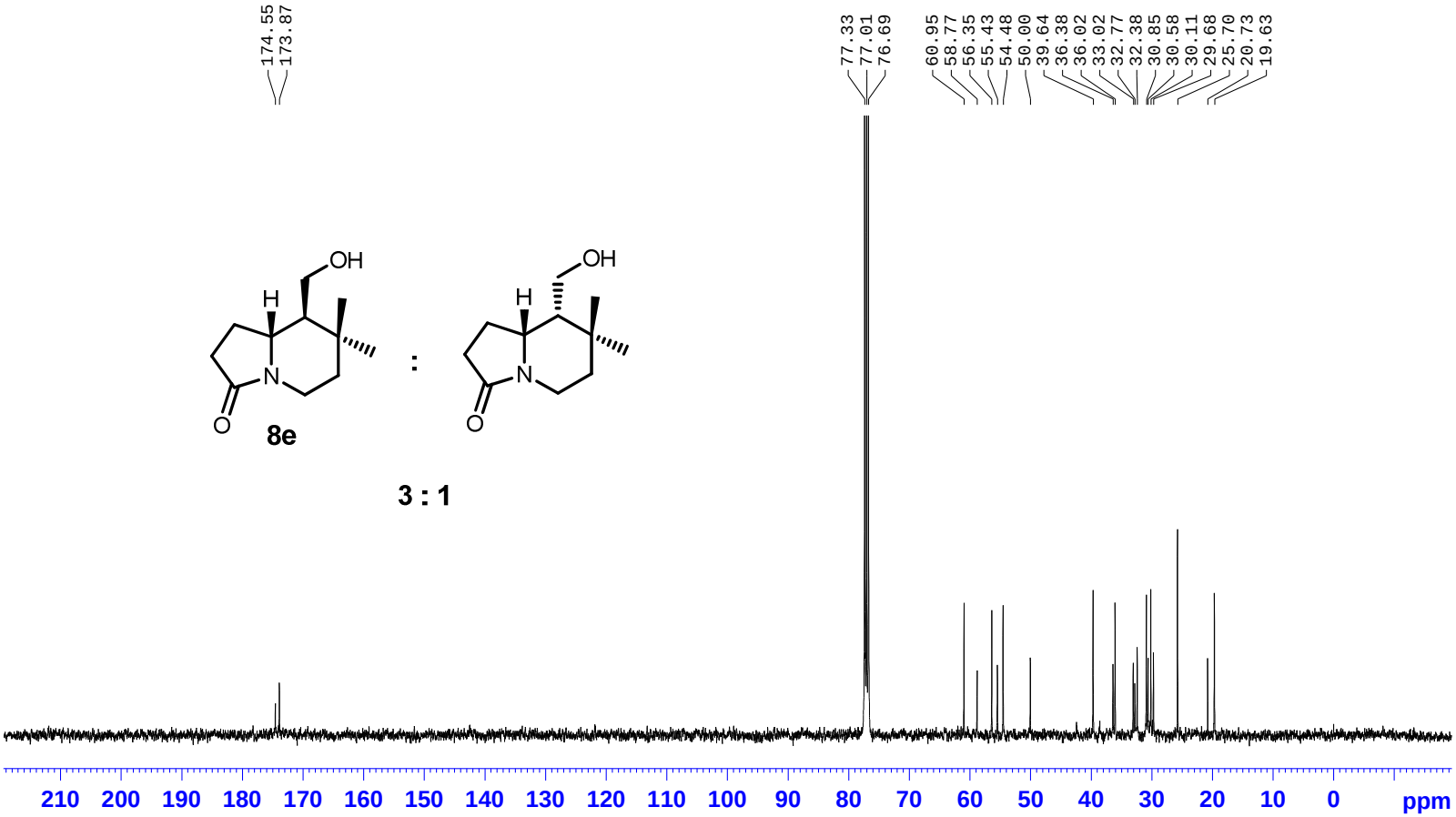
^{1}H NMR of compound **7e** (400 MHz, $CDCl_3$)



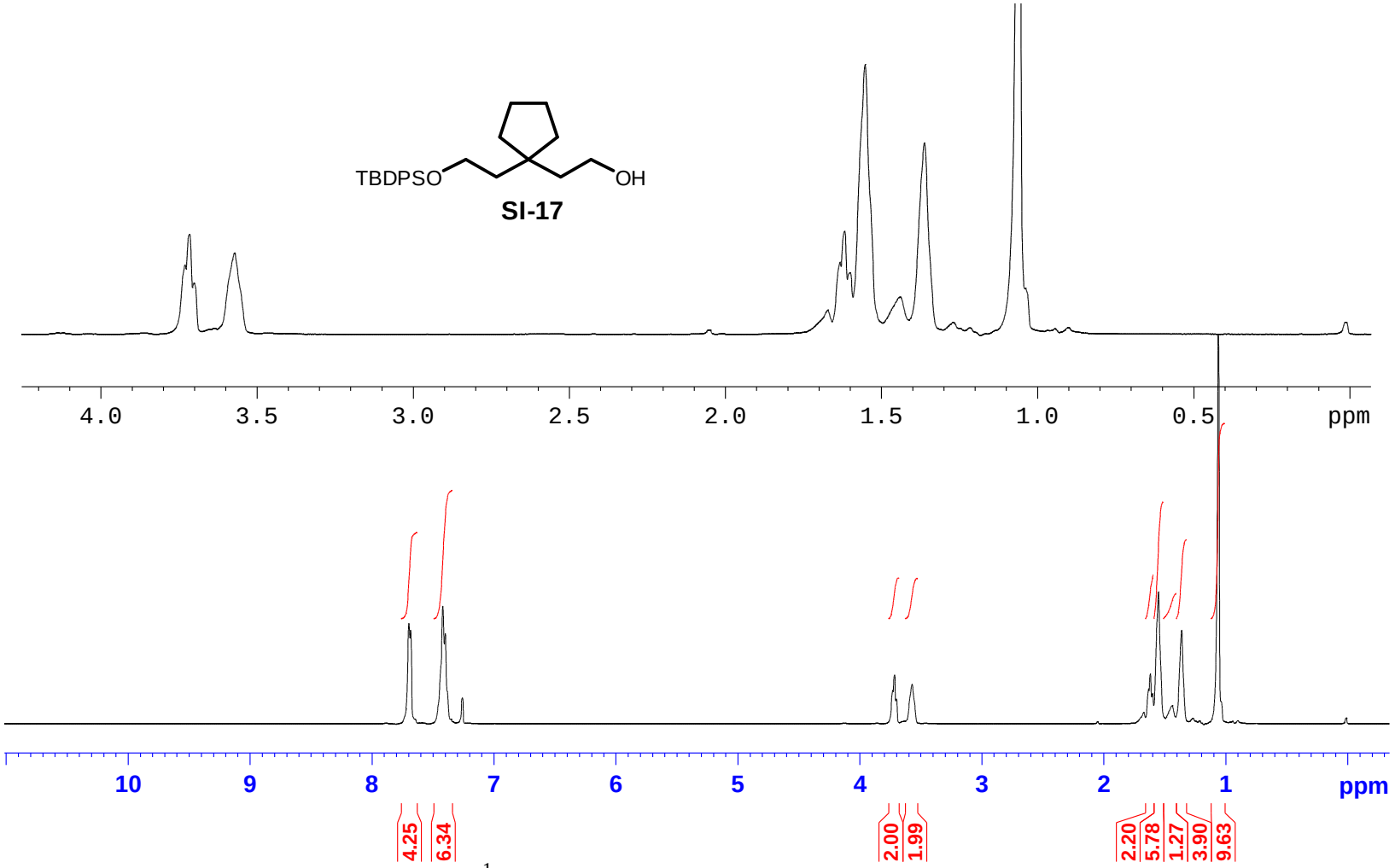
^{13}C NMR of compound **7e** (100 MHz, $CDCl_3$)



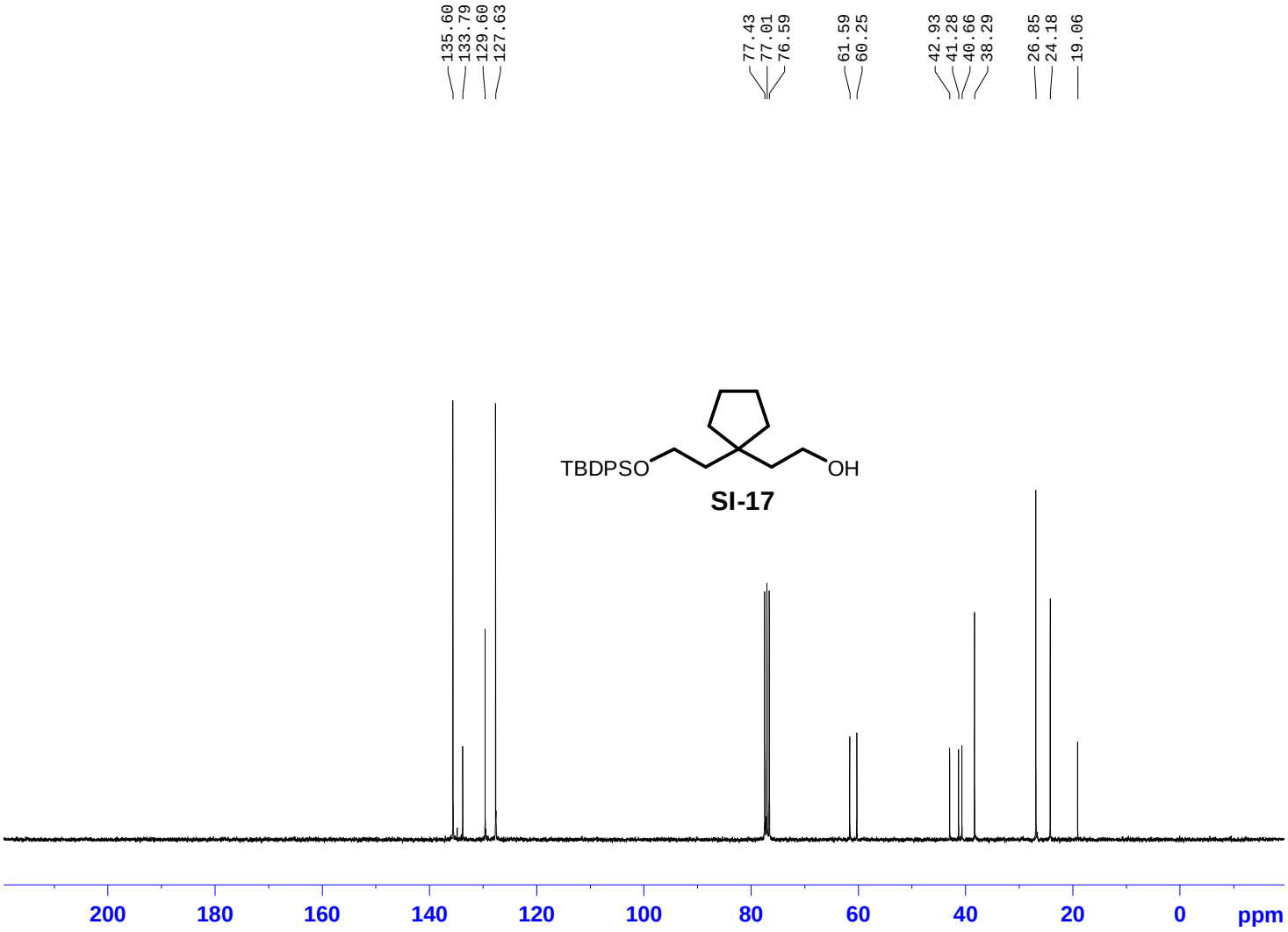
^{1}H NMR of compound **8e** (400 MHz, $CDCl_3$)



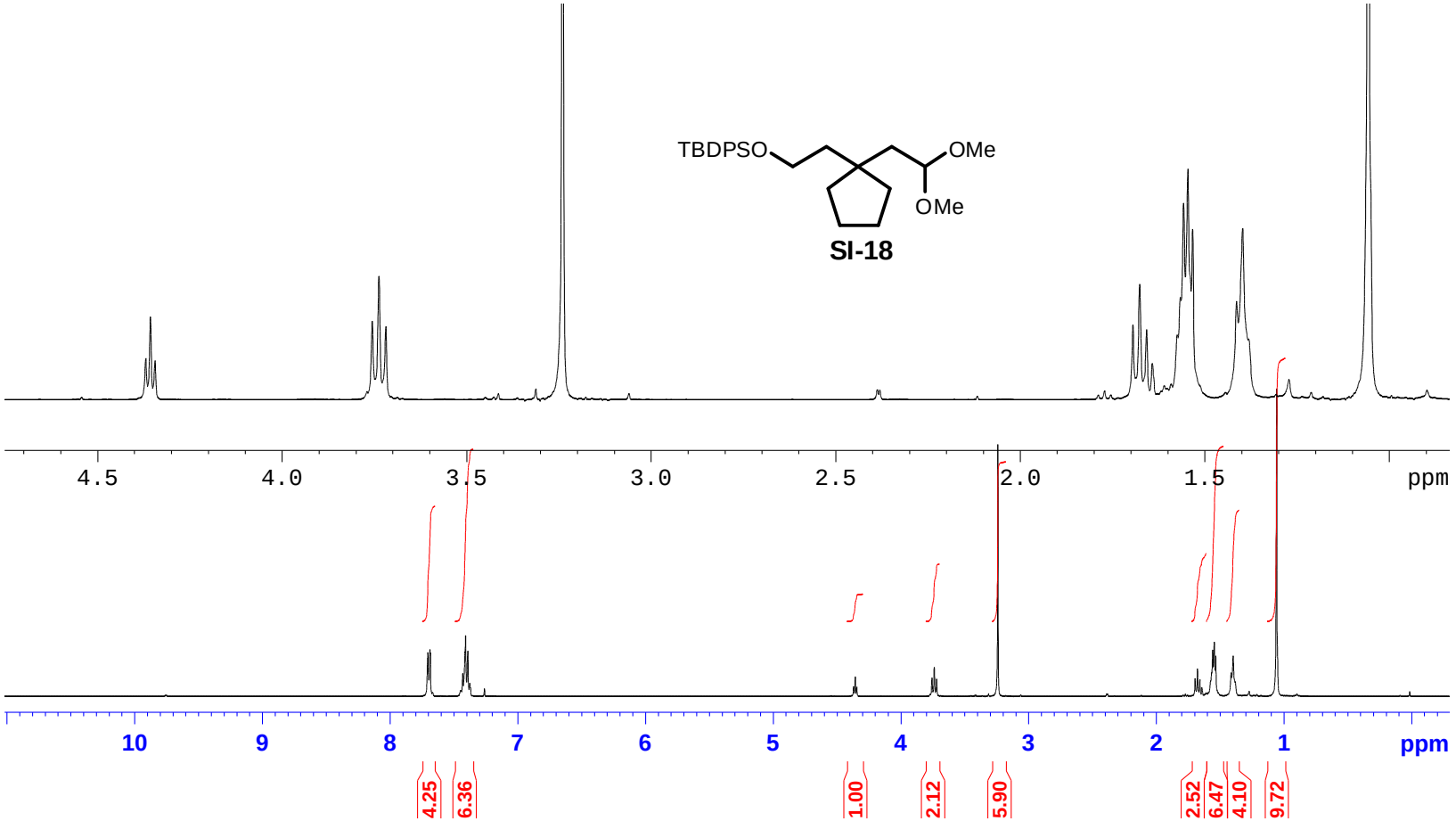
^{13}C NMR of compound **8e** (100 MHz, $CDCl_3$)



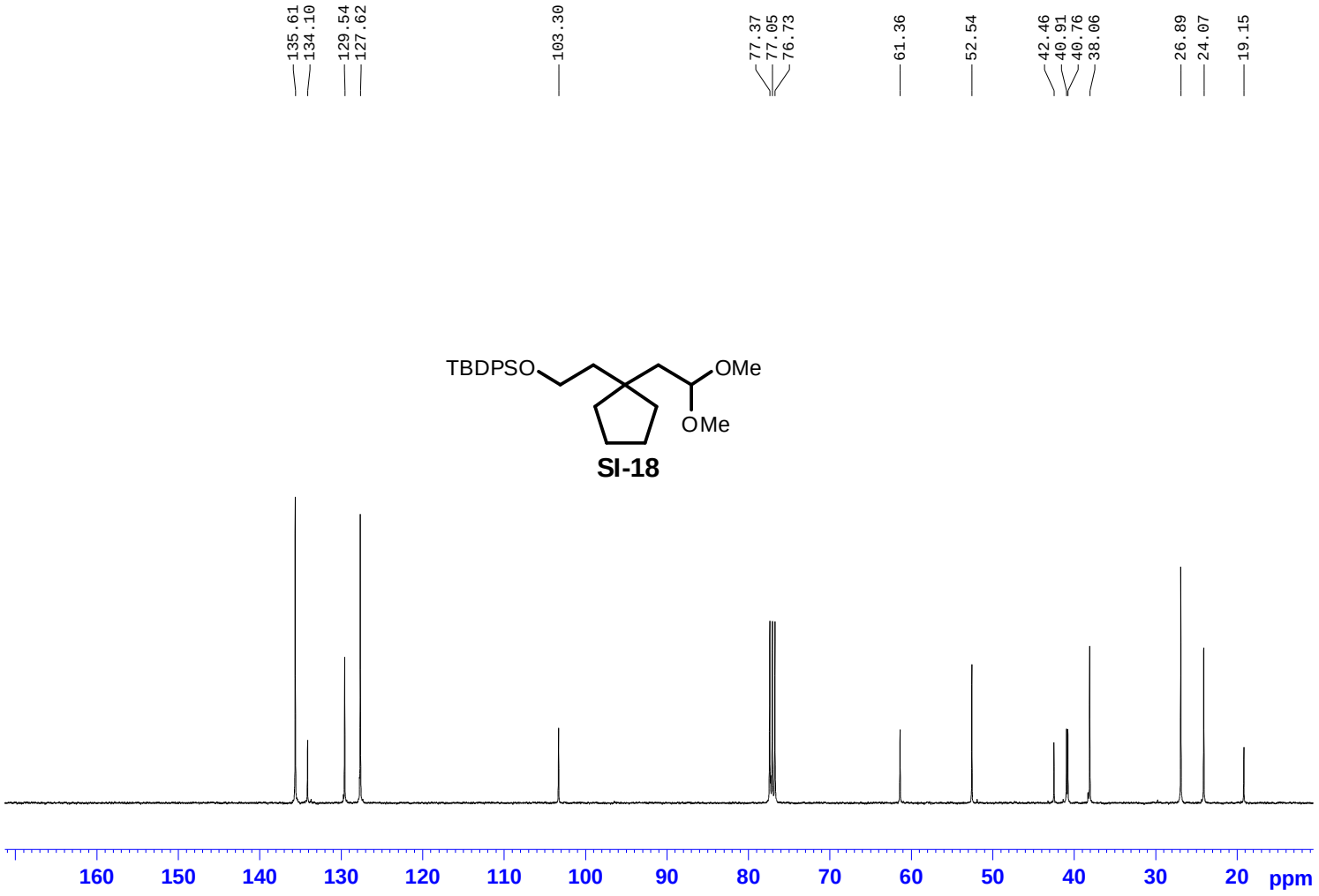
^{1}H NMR of compound **SI-17** (400 MHz, $CDCl_3$)



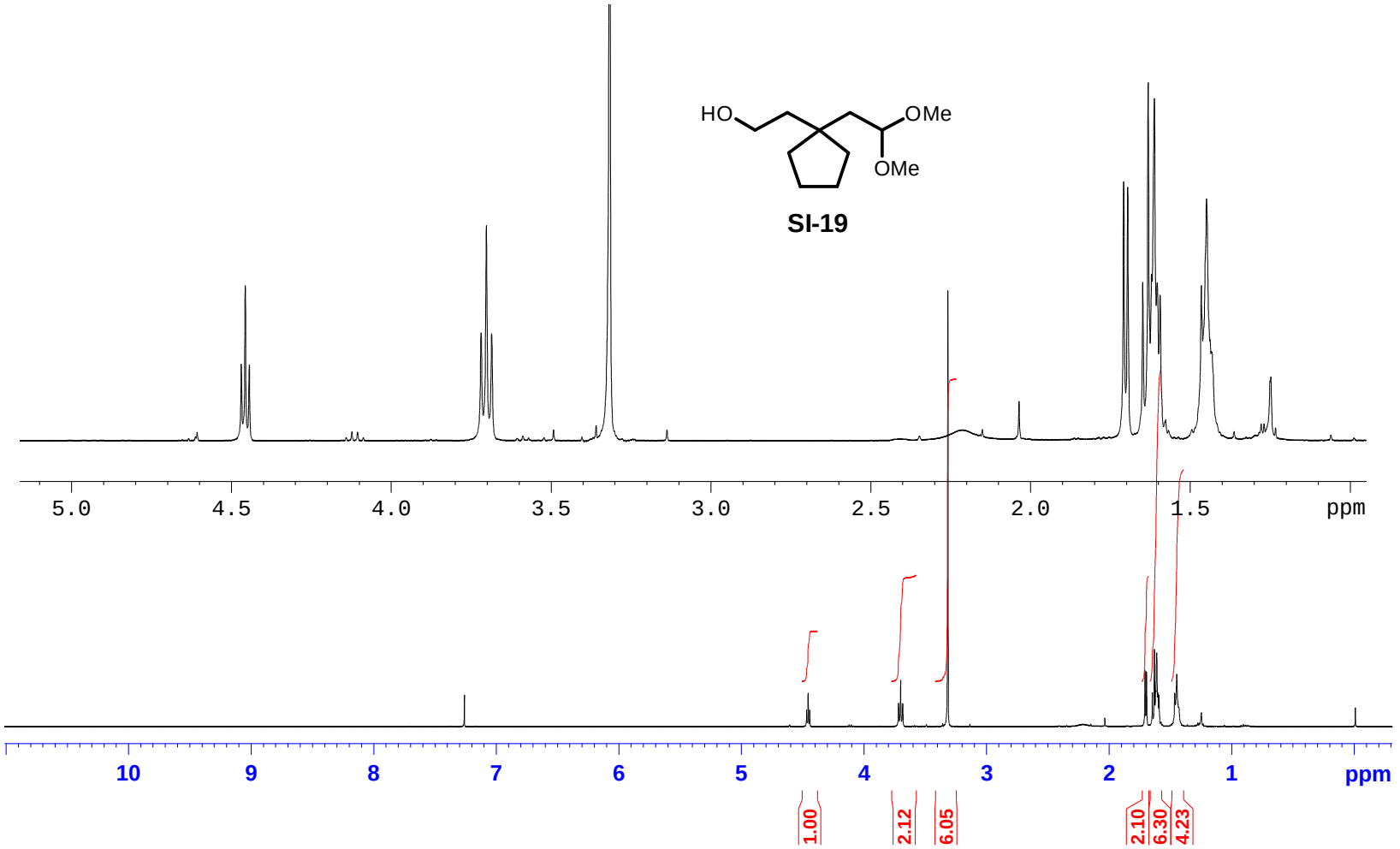
^{13}C NMR of compound **SI-17** (100 MHz, $CDCl_3$)



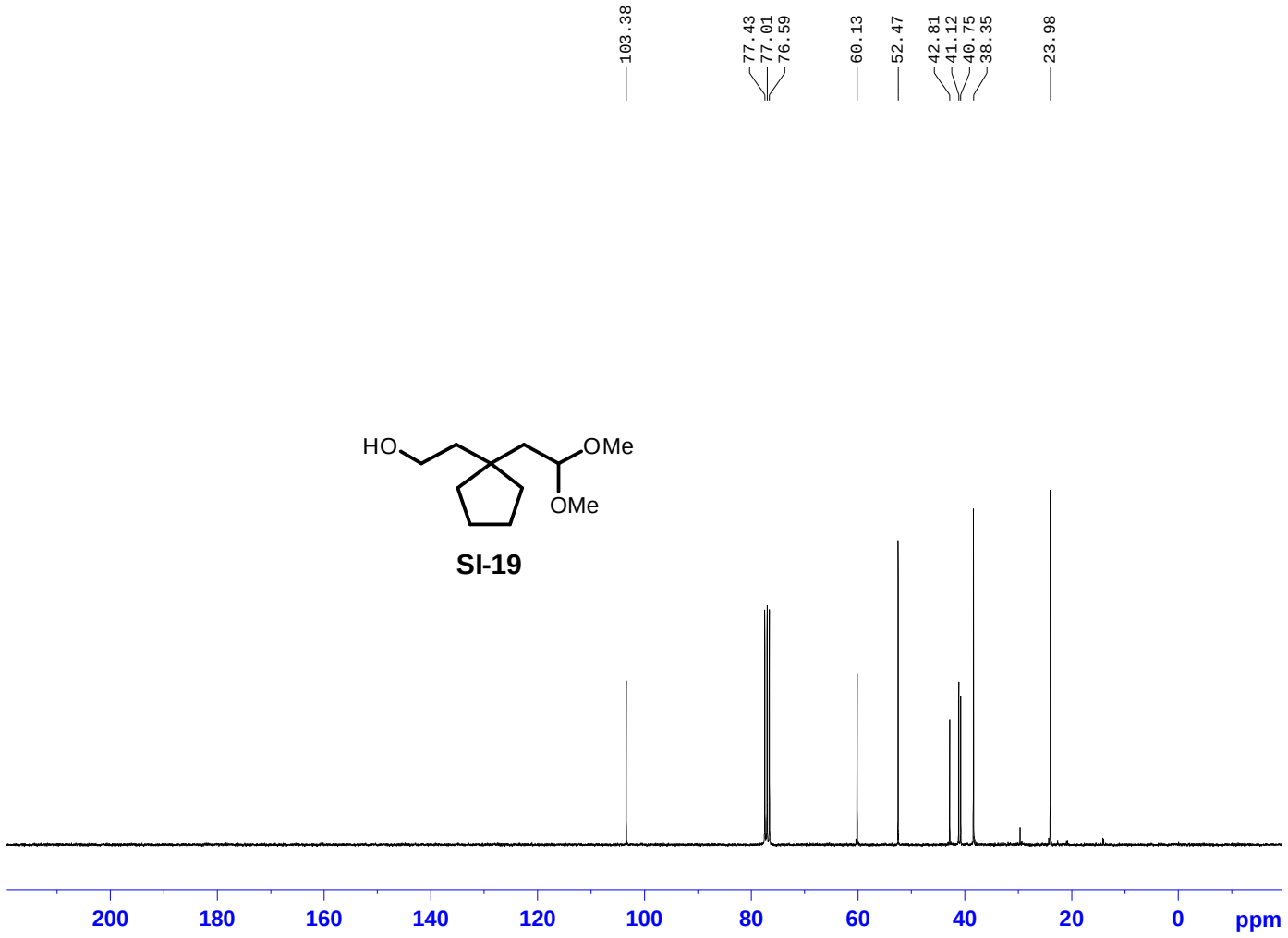
^{1}H NMR of compound **SI-18** (400 MHz, $CDCl_3$)



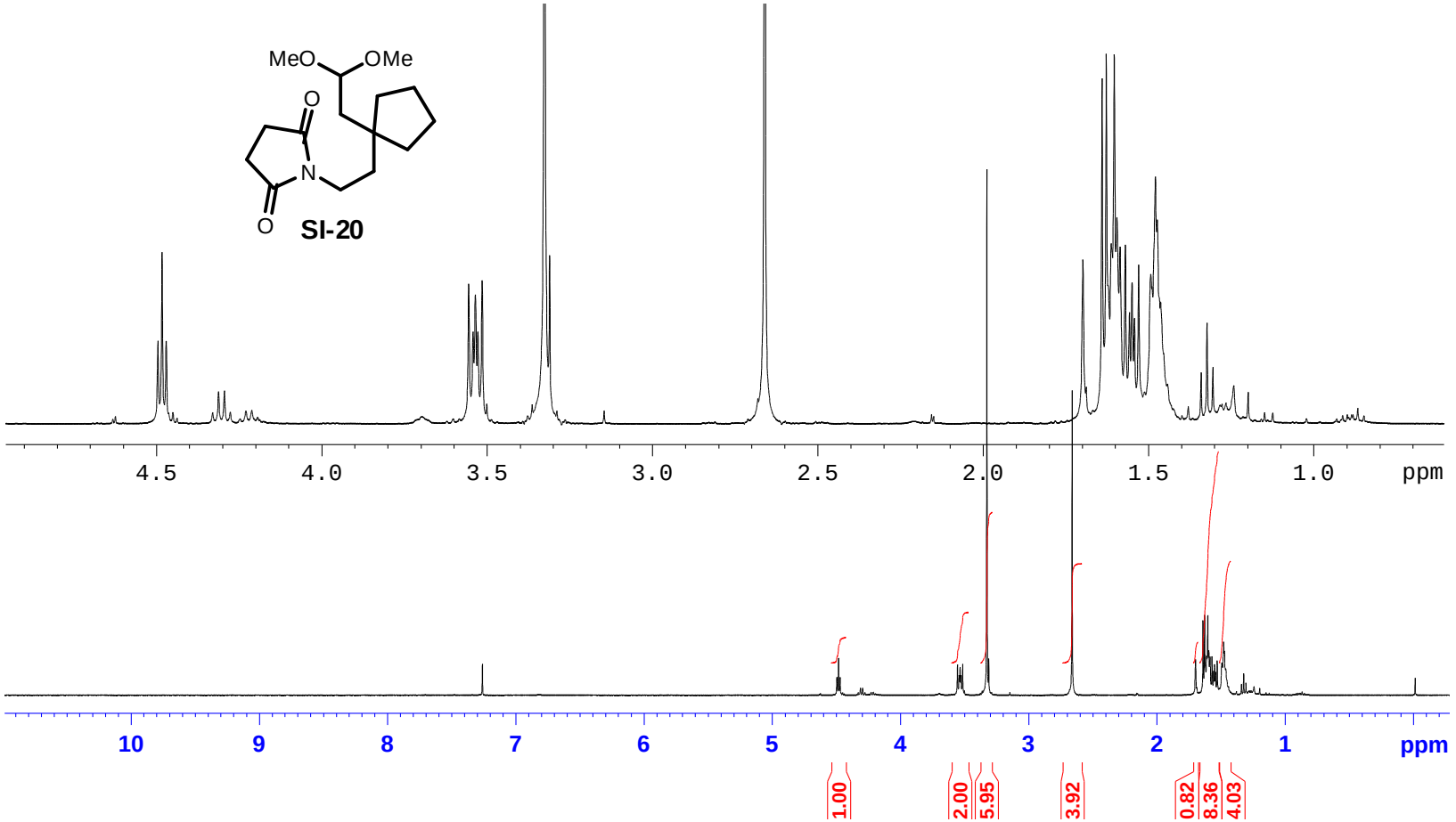
^{13}C NMR of compound **SI-18** (100 MHz, $CDCl_3$)



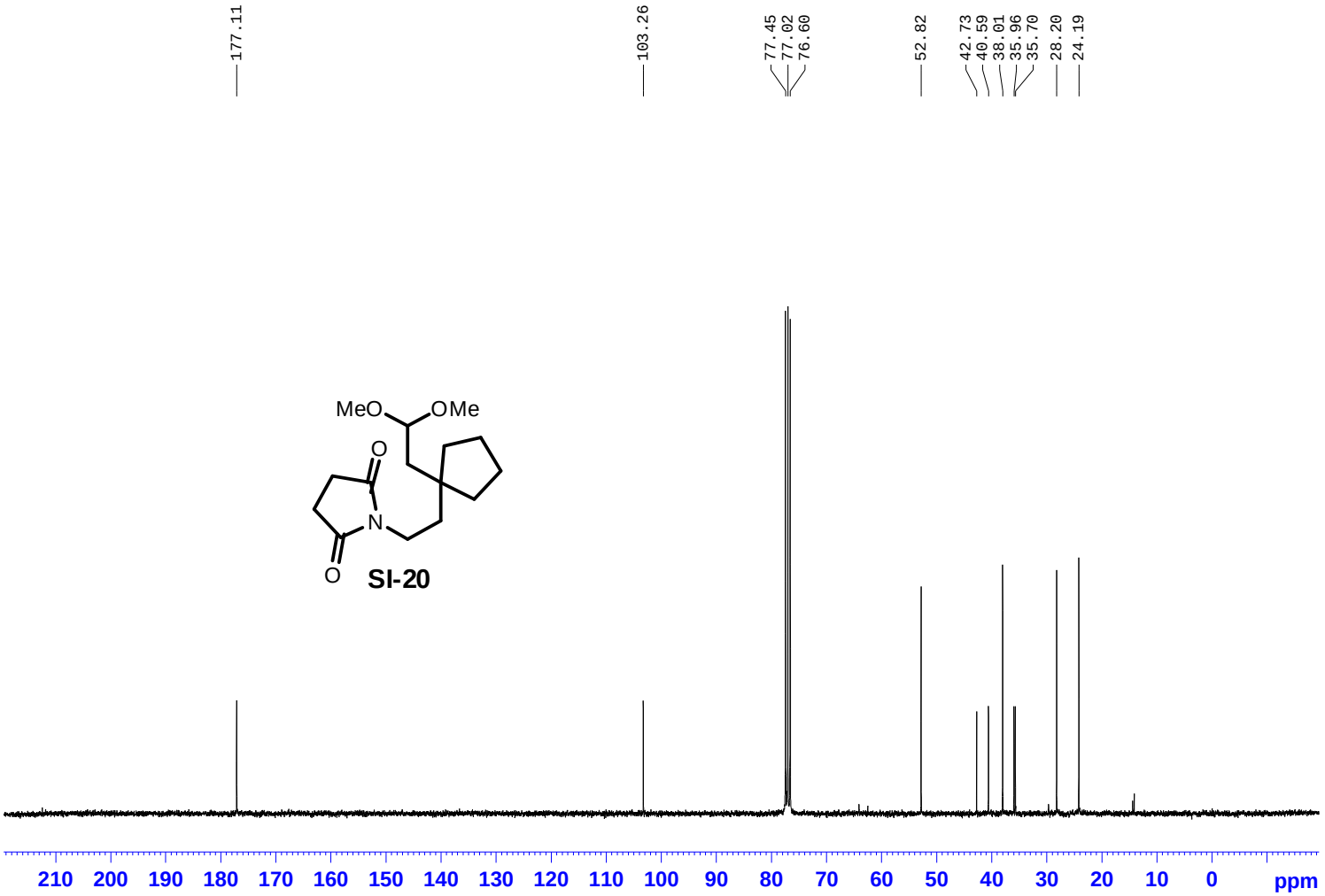
^{1}H NMR of compound **SI-19** (400 MHz, $CDCl_3$)



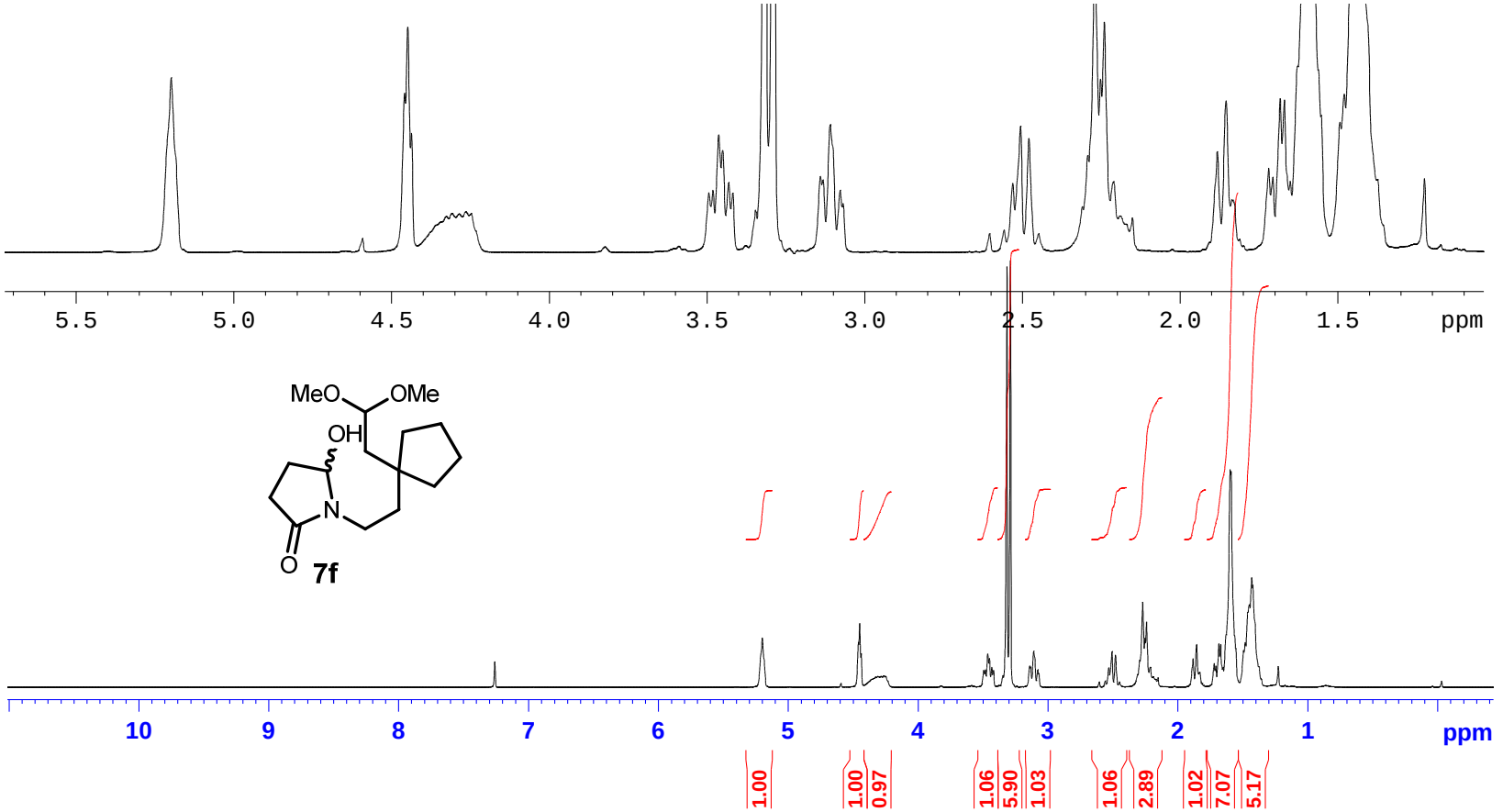
^{13}C NMR of compound **SI-19** (100 MHz, $CDCl_3$)



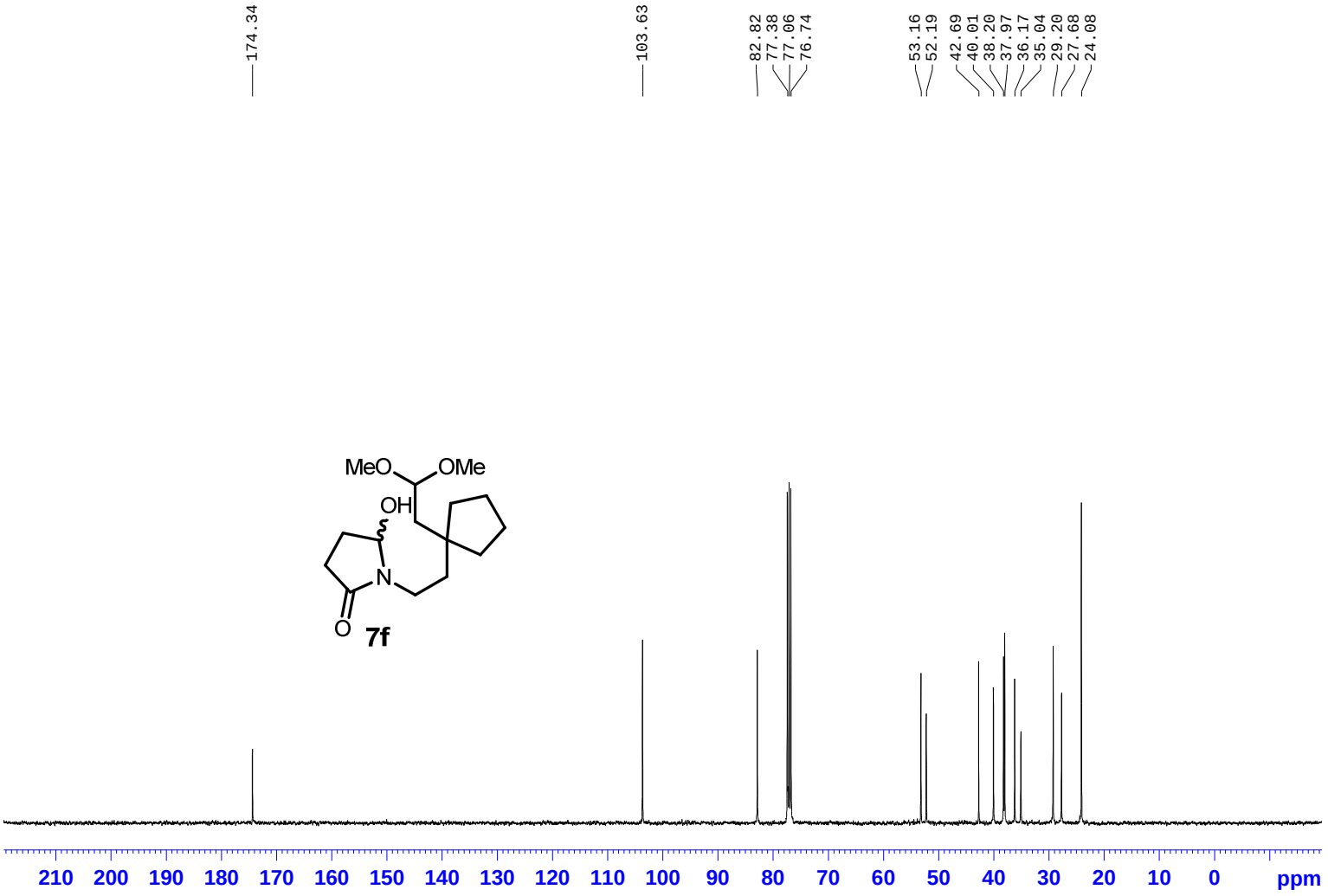
^{1}H NMR of compound **SI-20** (400 MHz, $CDCl_3$)



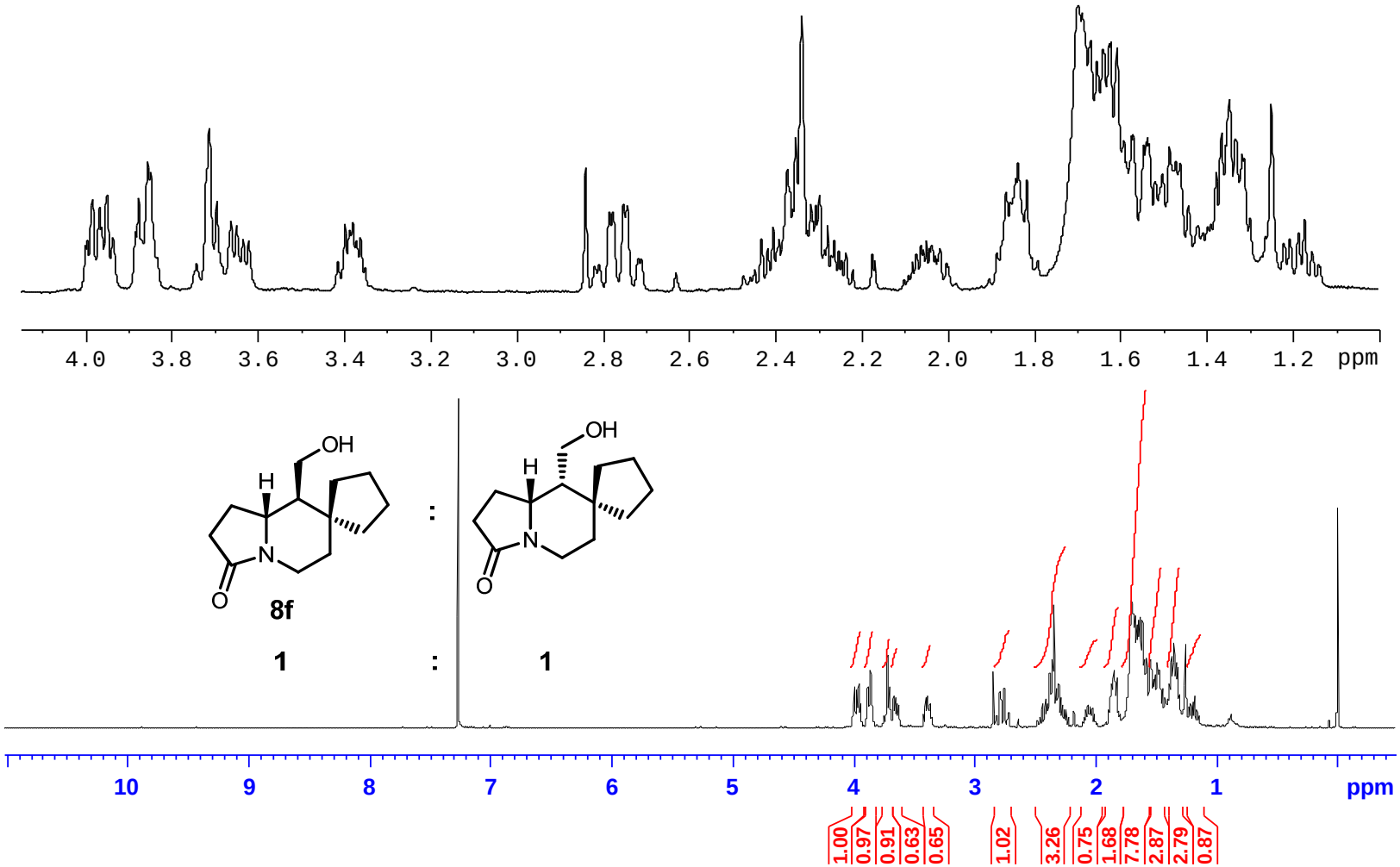
^{13}C NMR of compound **SI-20** (100 MHz, $CDCl_3$)



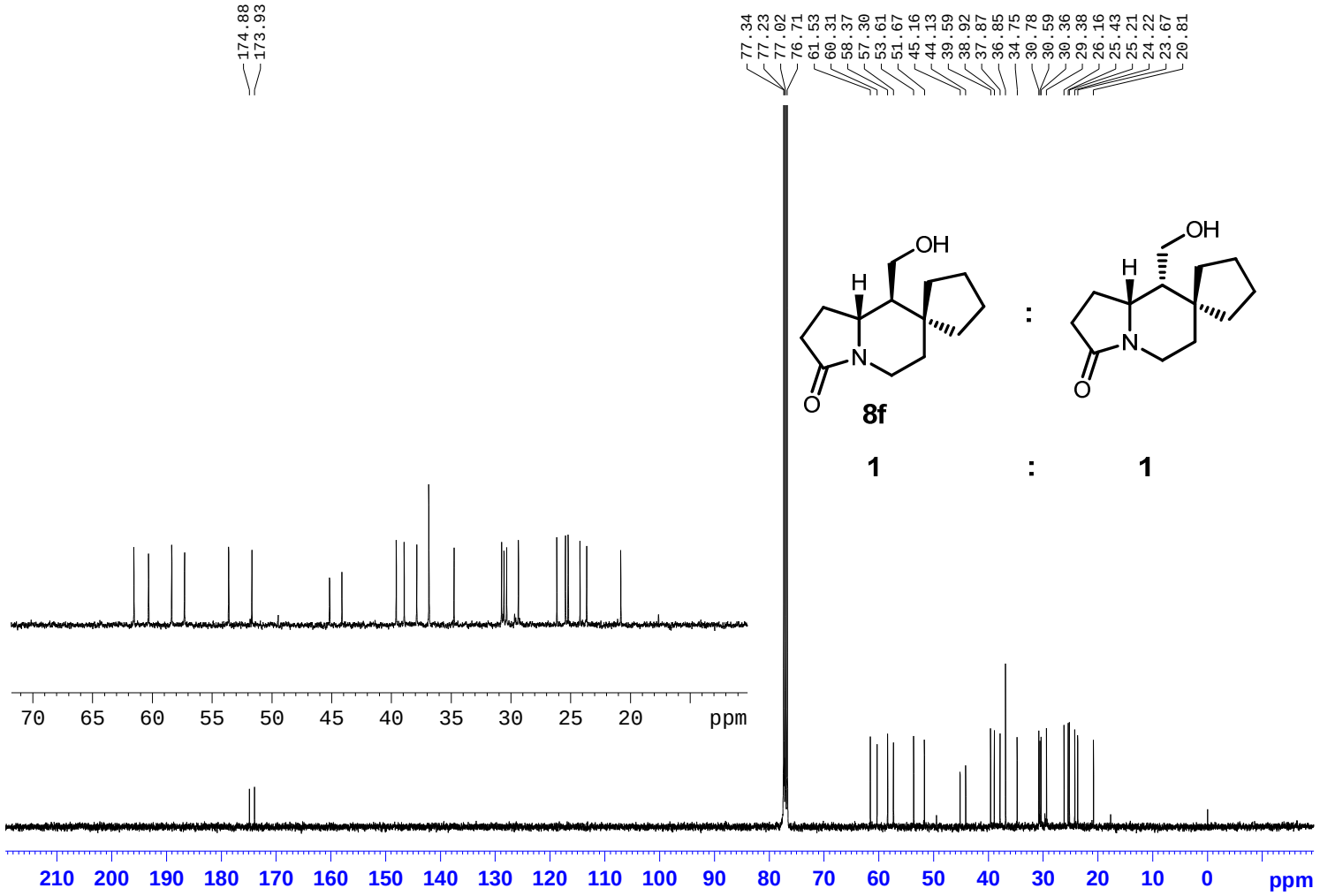
^{1}H NMR of compound **7f** (400 MHz, $CDCl_3$)



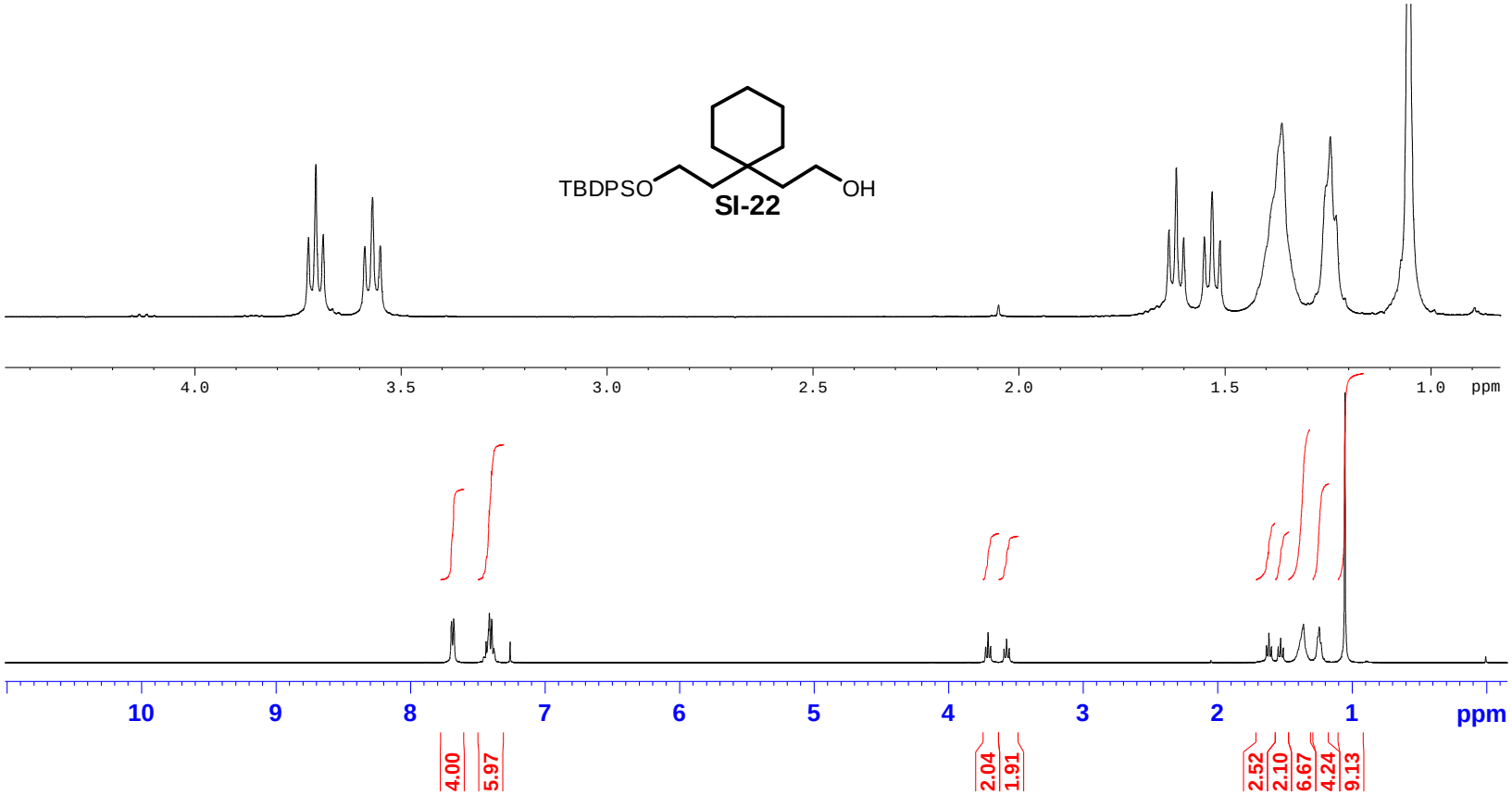
^{13}C NMR of compound **7f** (100 MHz, $CDCl_3$)



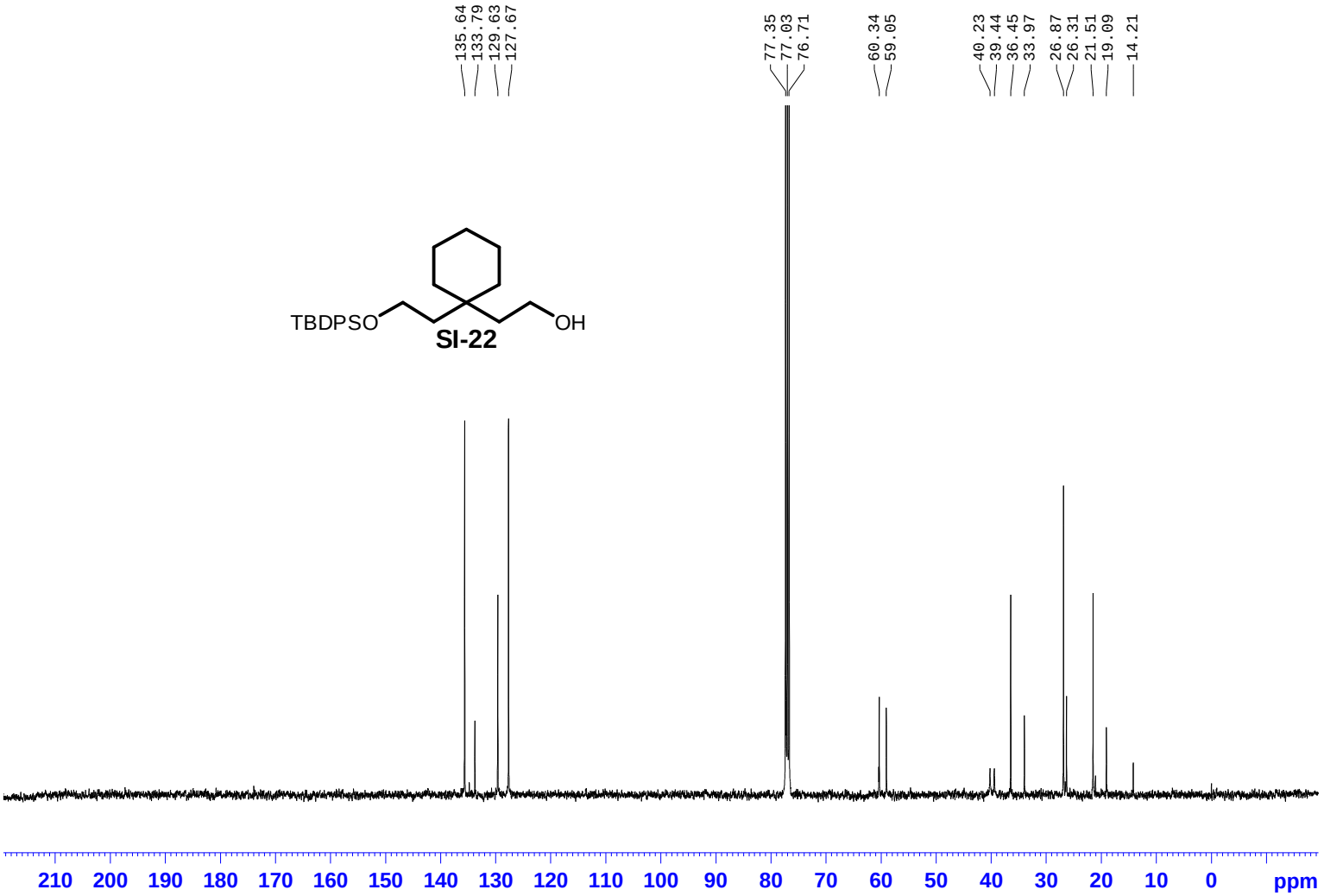
^{1}H NMR of compound **8f** (400 MHz, $CDCl_3$)



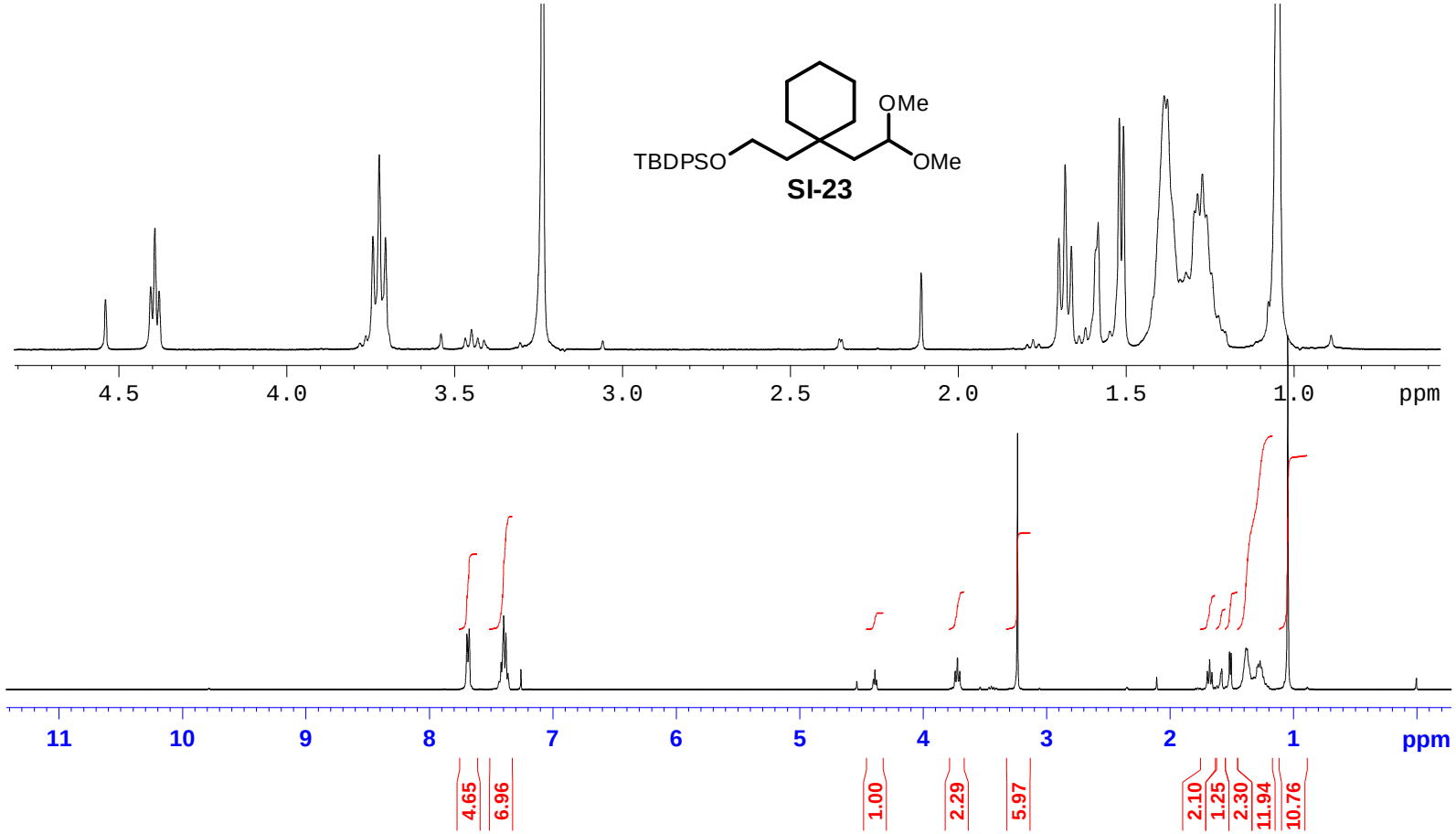
^{13}C NMR of compound **8f** (100 MHz, $CDCl_3$)



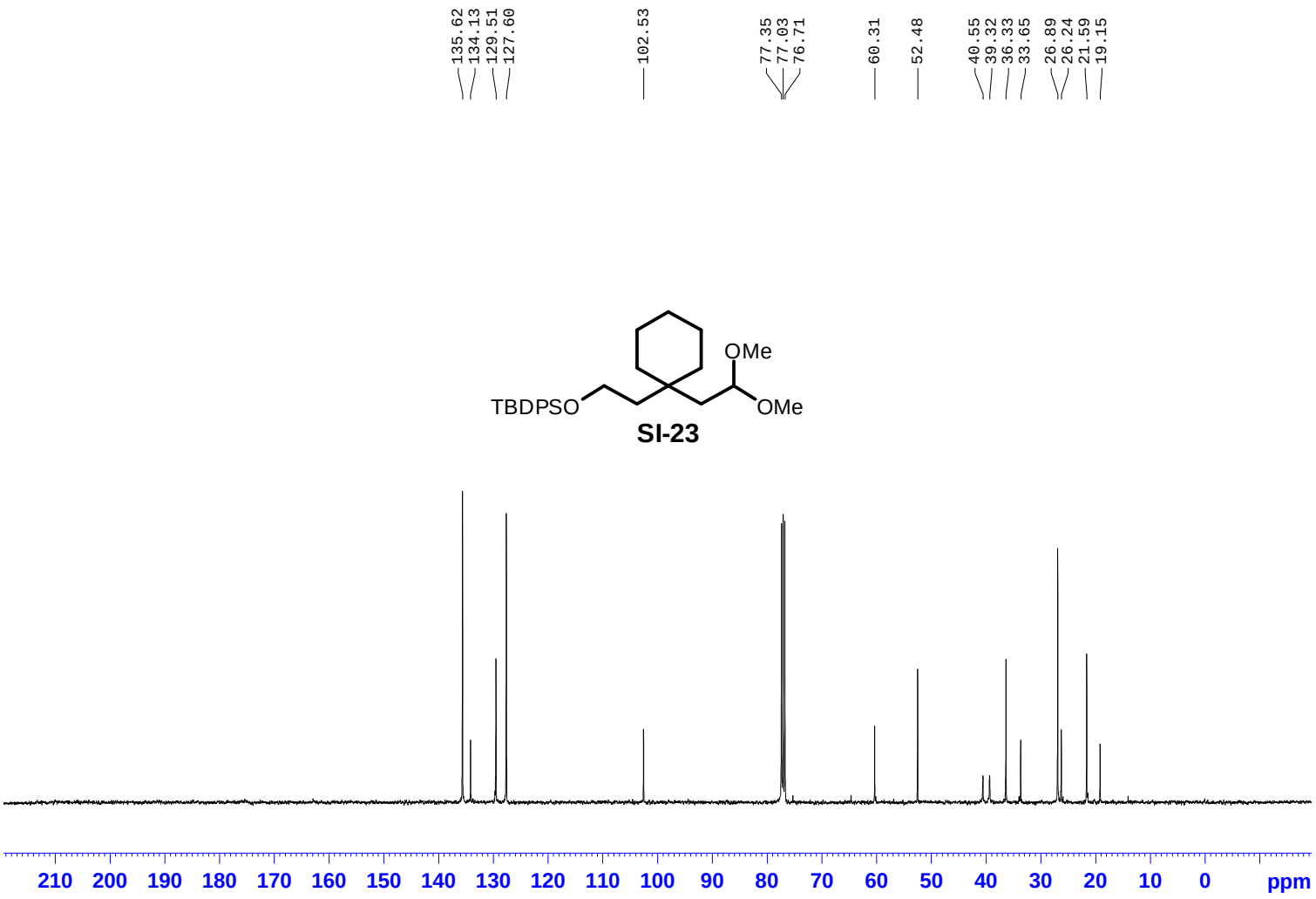
^{1}H NMR of compound **SI-22** (400 MHz, $CDCl_3$)



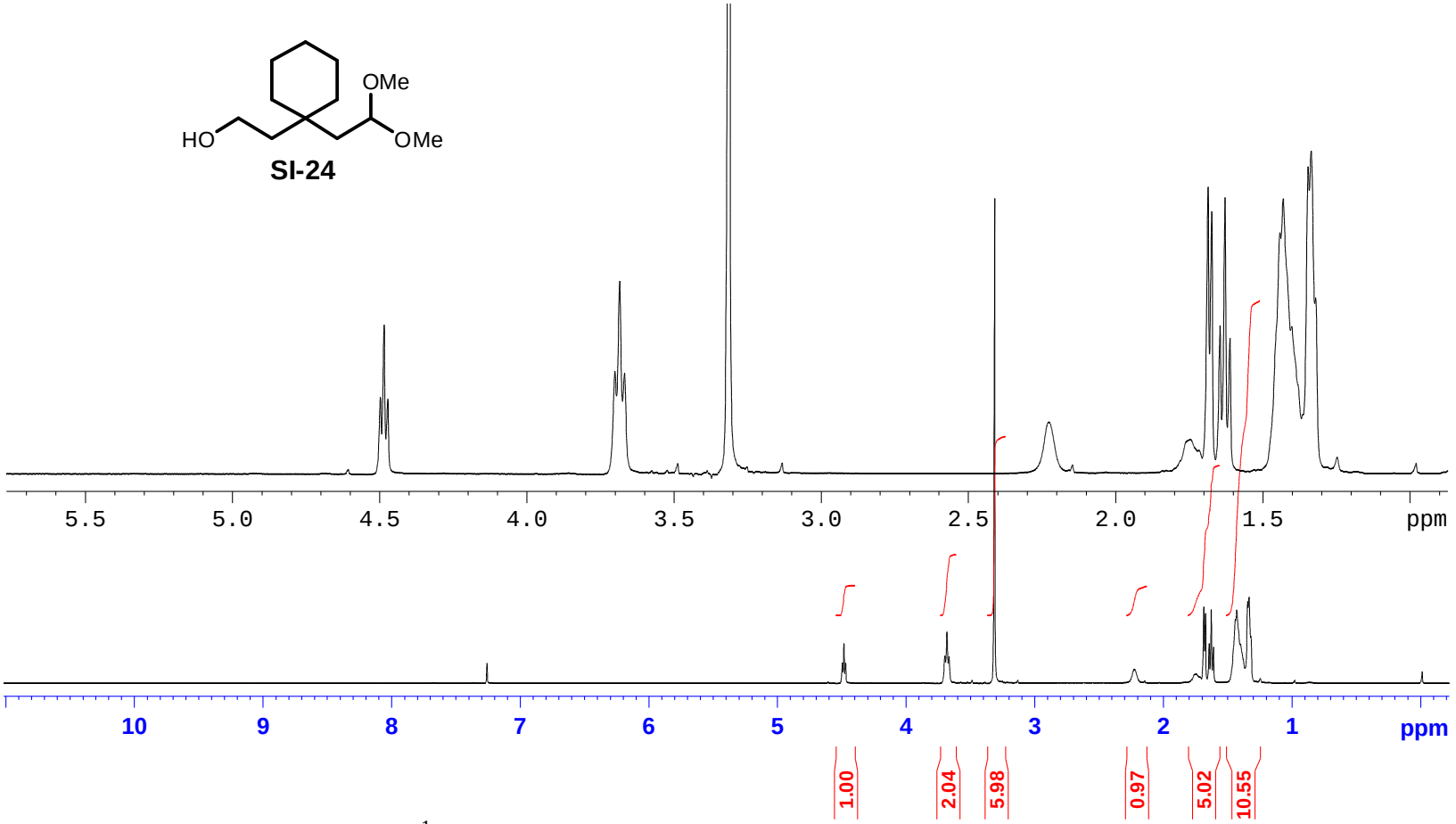
^{13}C NMR of compound **SI-22** (100 MHz, $CDCl_3$)



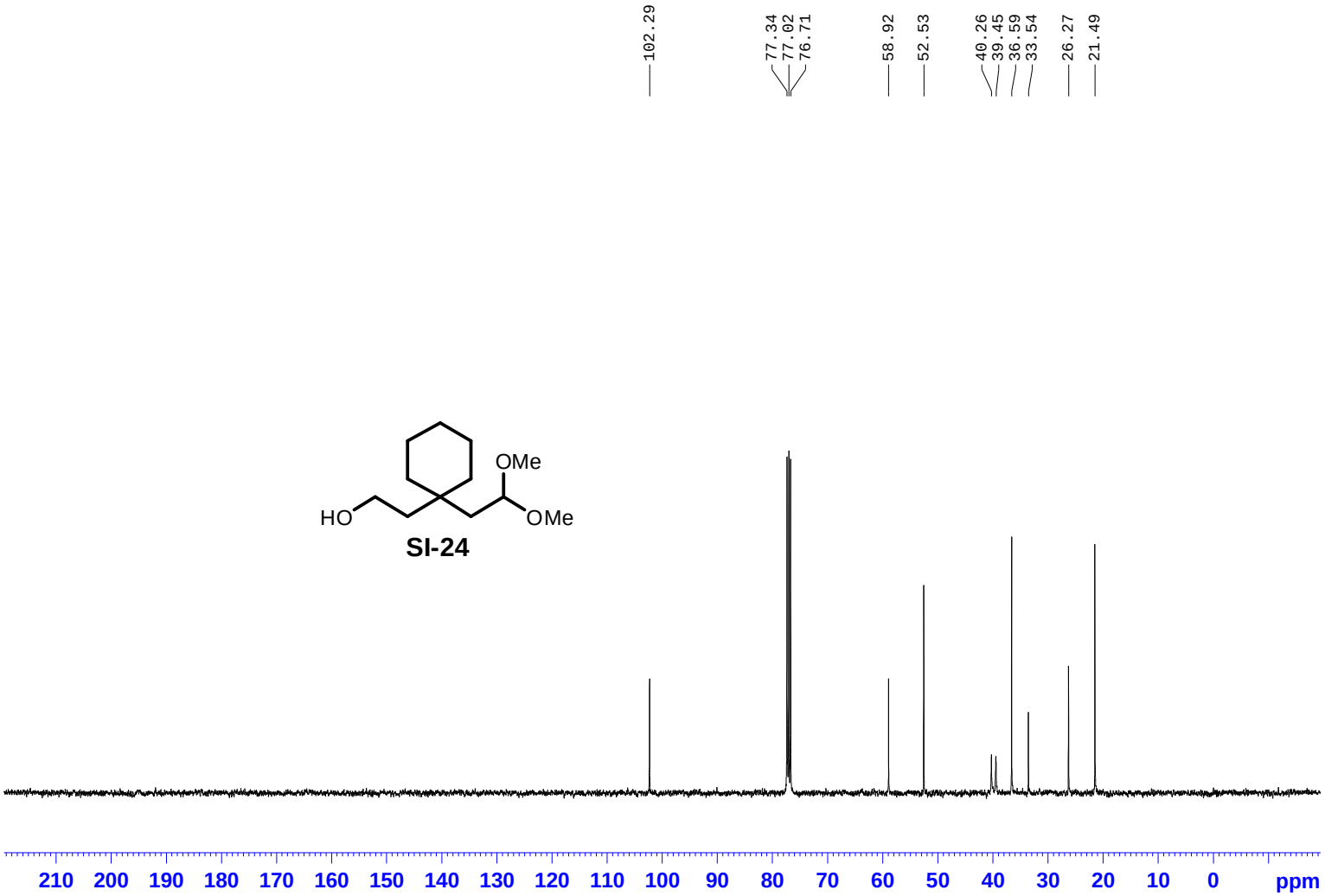
^{1}H NMR of compound **SI-23** (400 MHz, $CDCl_3$)



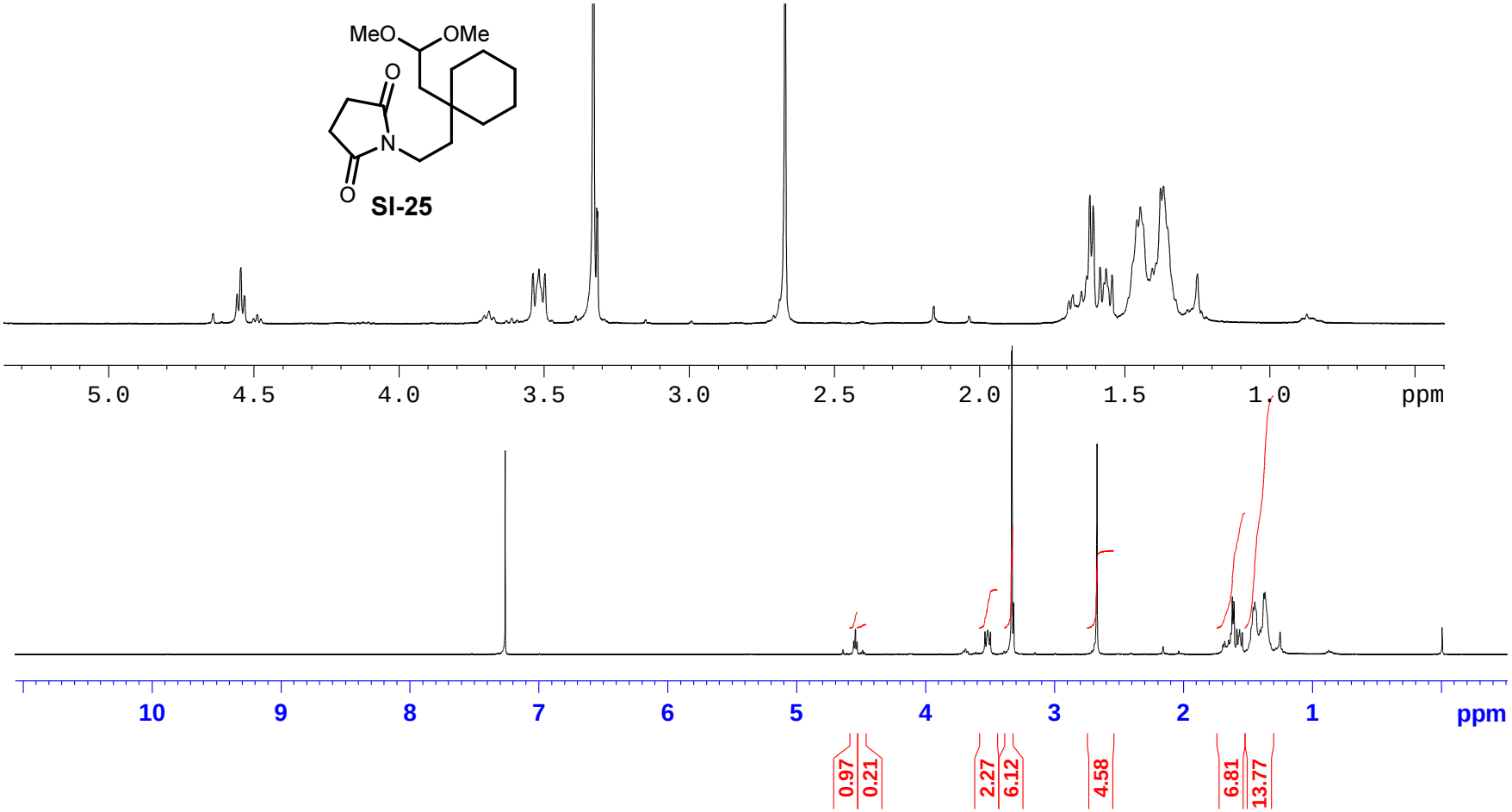
^{13}C NMR of compound **SI-23** (100 MHz, $CDCl_3$)



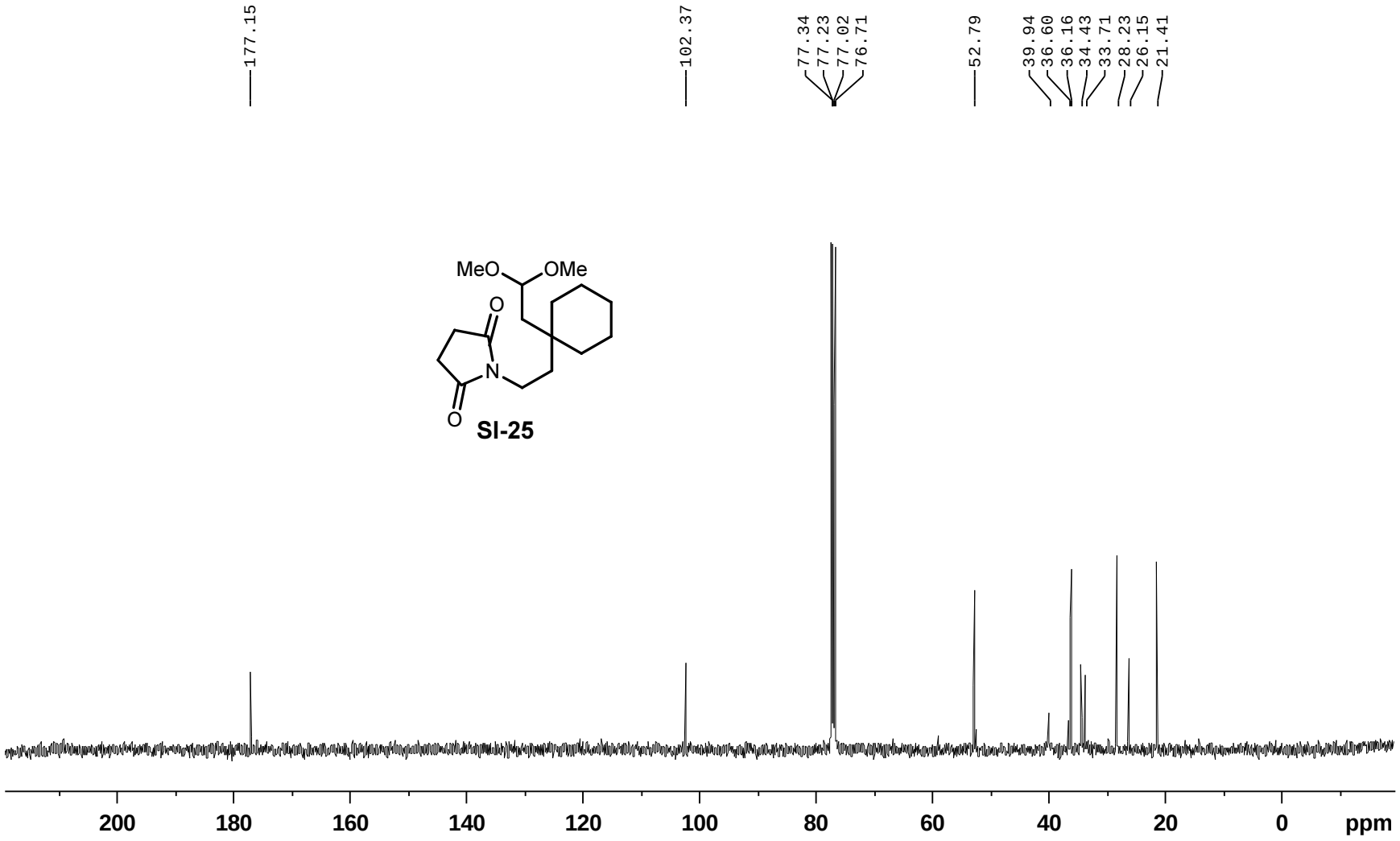
^{1}H NMR of compound **SI-24** (400 MHz, $CDCl_3$)



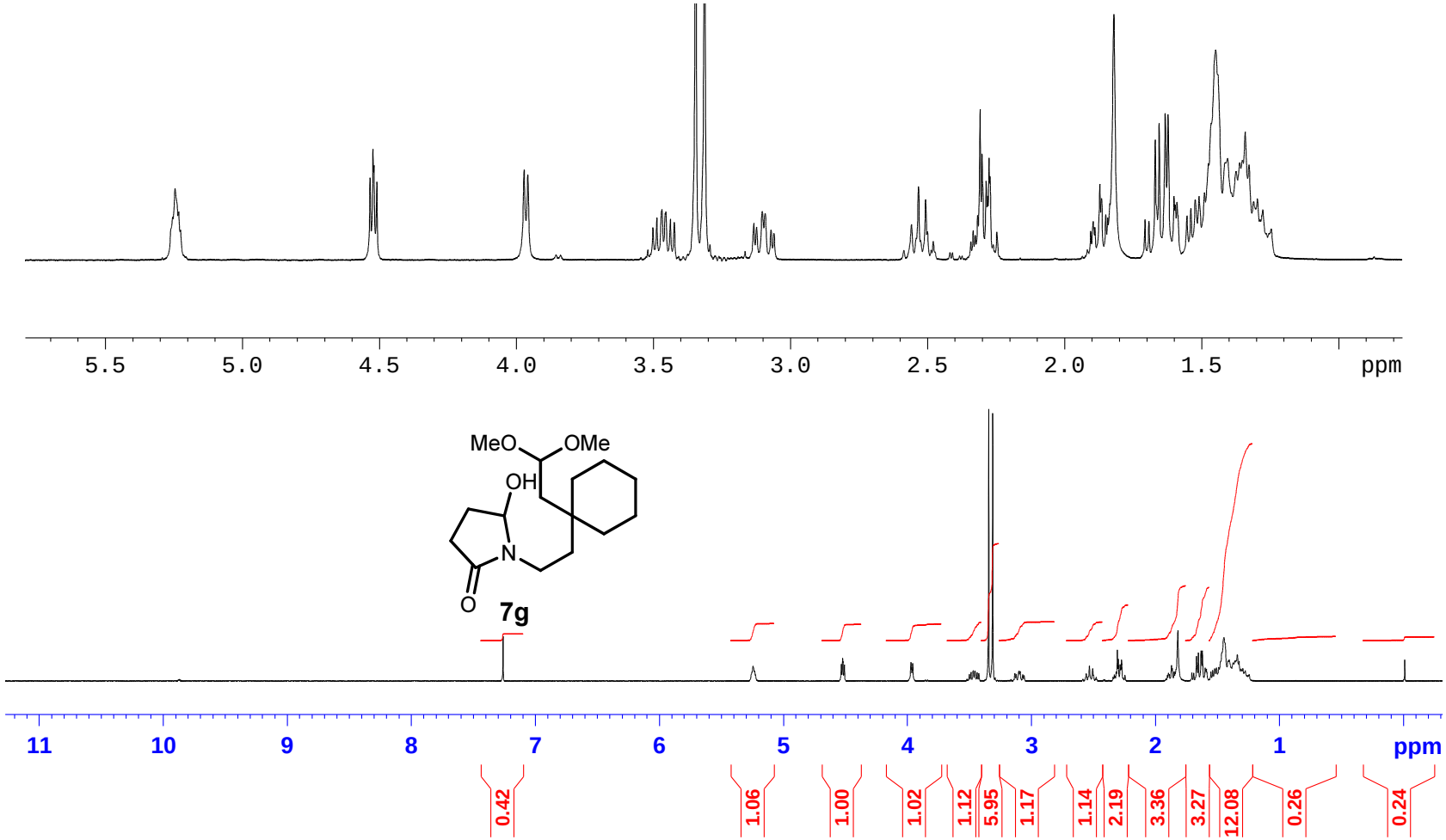
^{13}C NMR of compound **SI-24** (100 MHz, $CDCl_3$)



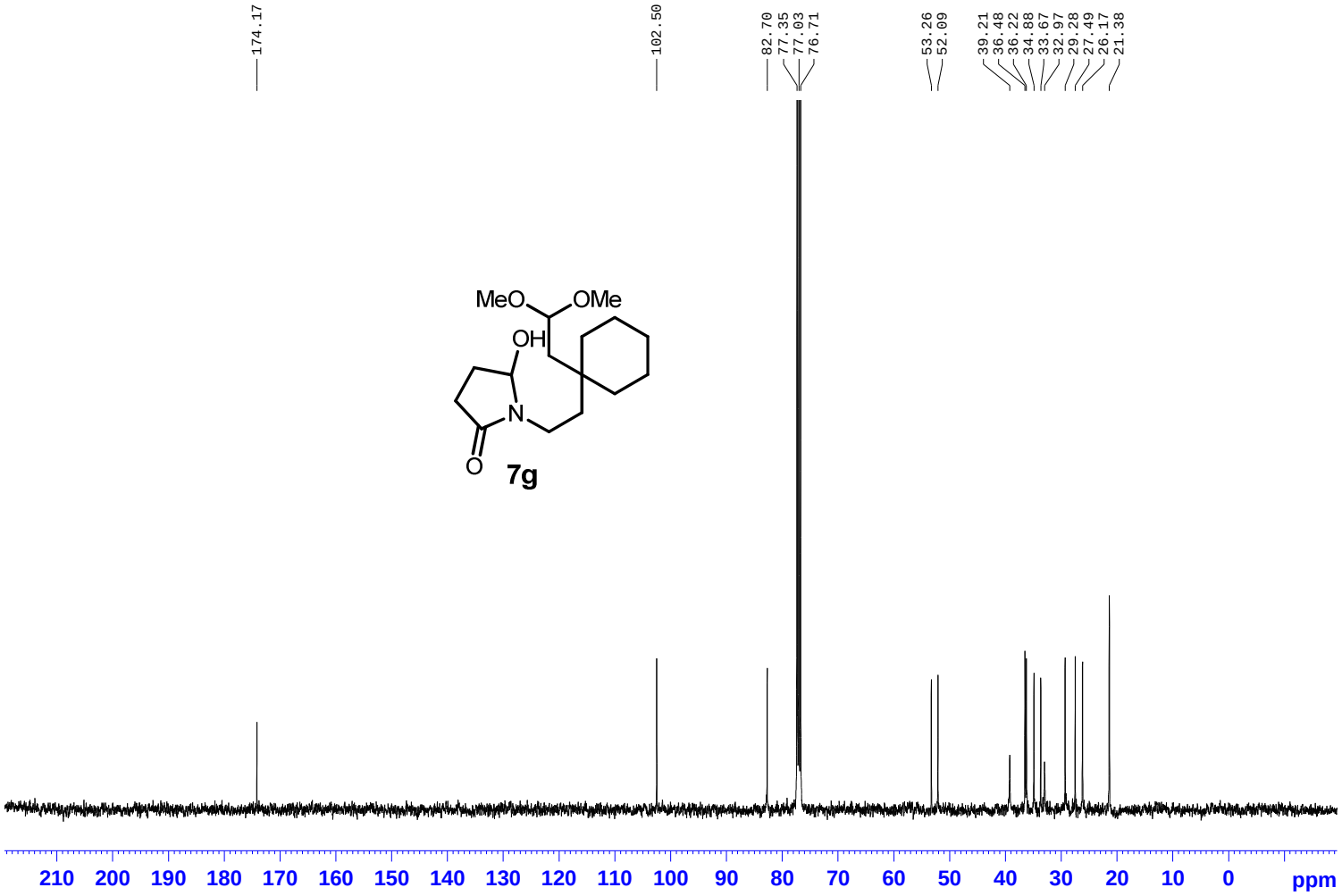
^{1}H NMR of compound **SI-25** (400 MHz, $CDCl_3$)



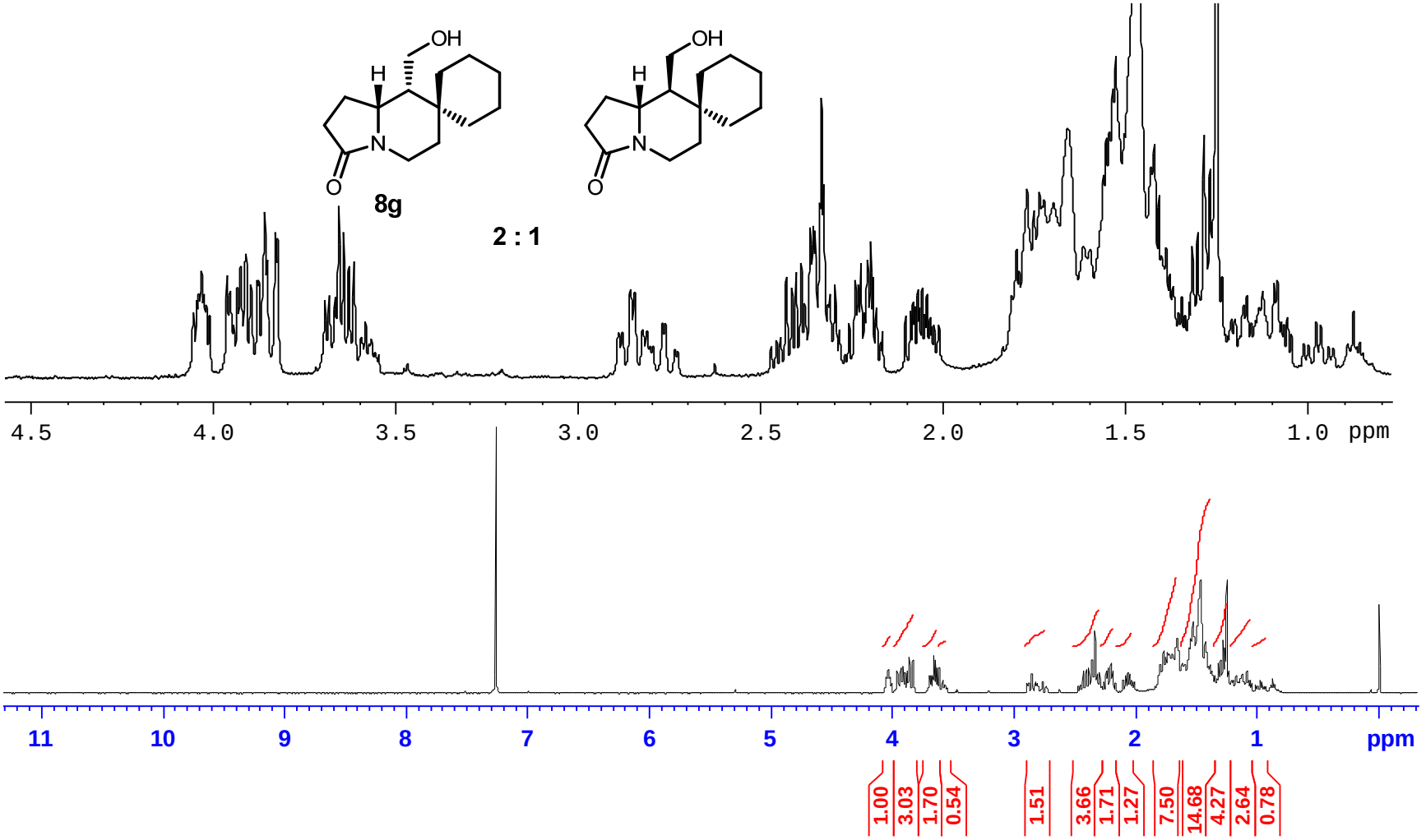
^{13}C NMR of compound **SI-25** (100 MHz, $CDCl_3$)



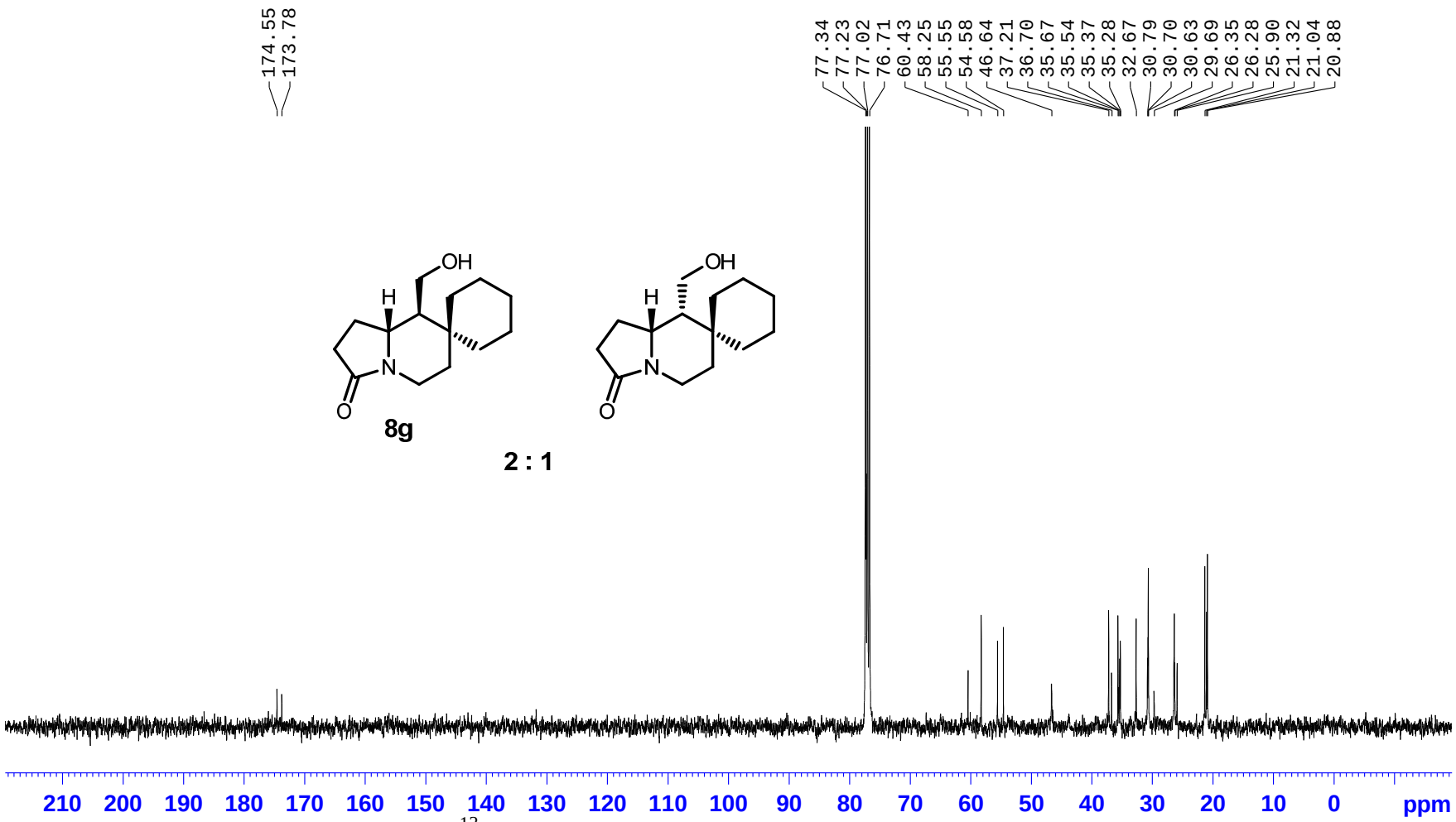
^{1}H NMR of compound **7g** (400 MHz, $CDCl_3$)



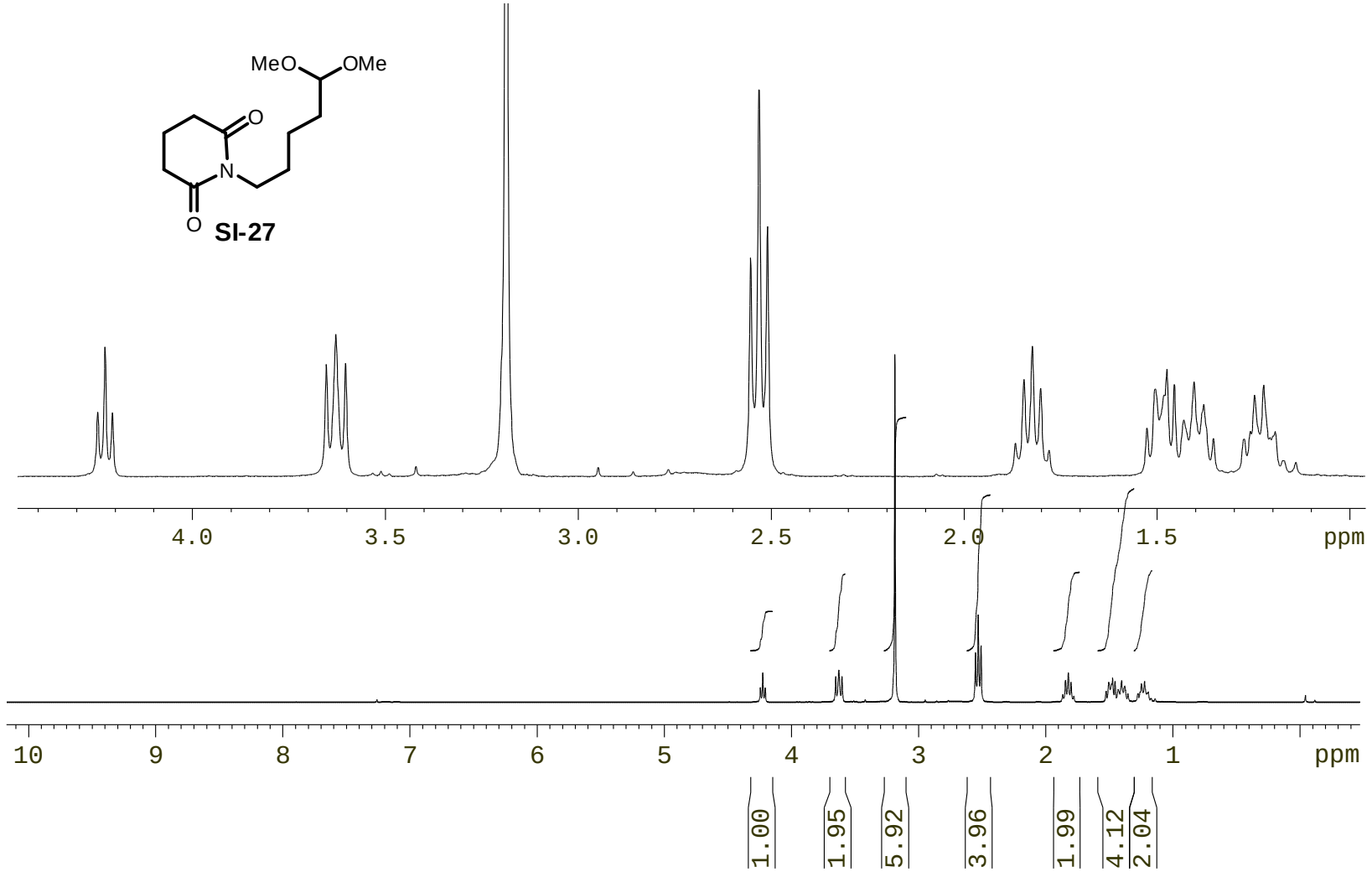
^{13}C NMR of compound **7g** (100 MHz, $CDCl_3$)



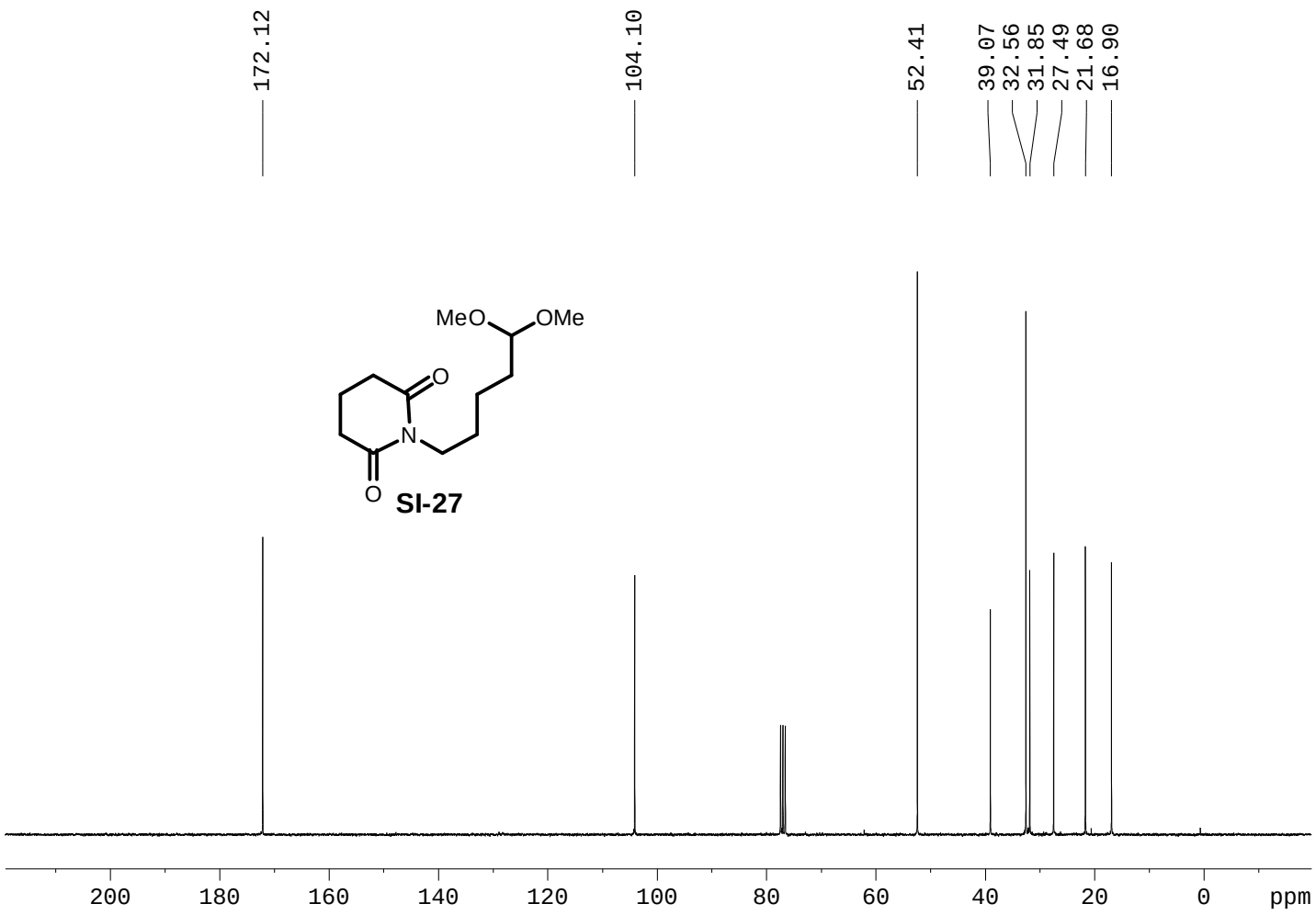
^{1}H NMR of compound **8g** (400 MHz, $CDCl_3$)



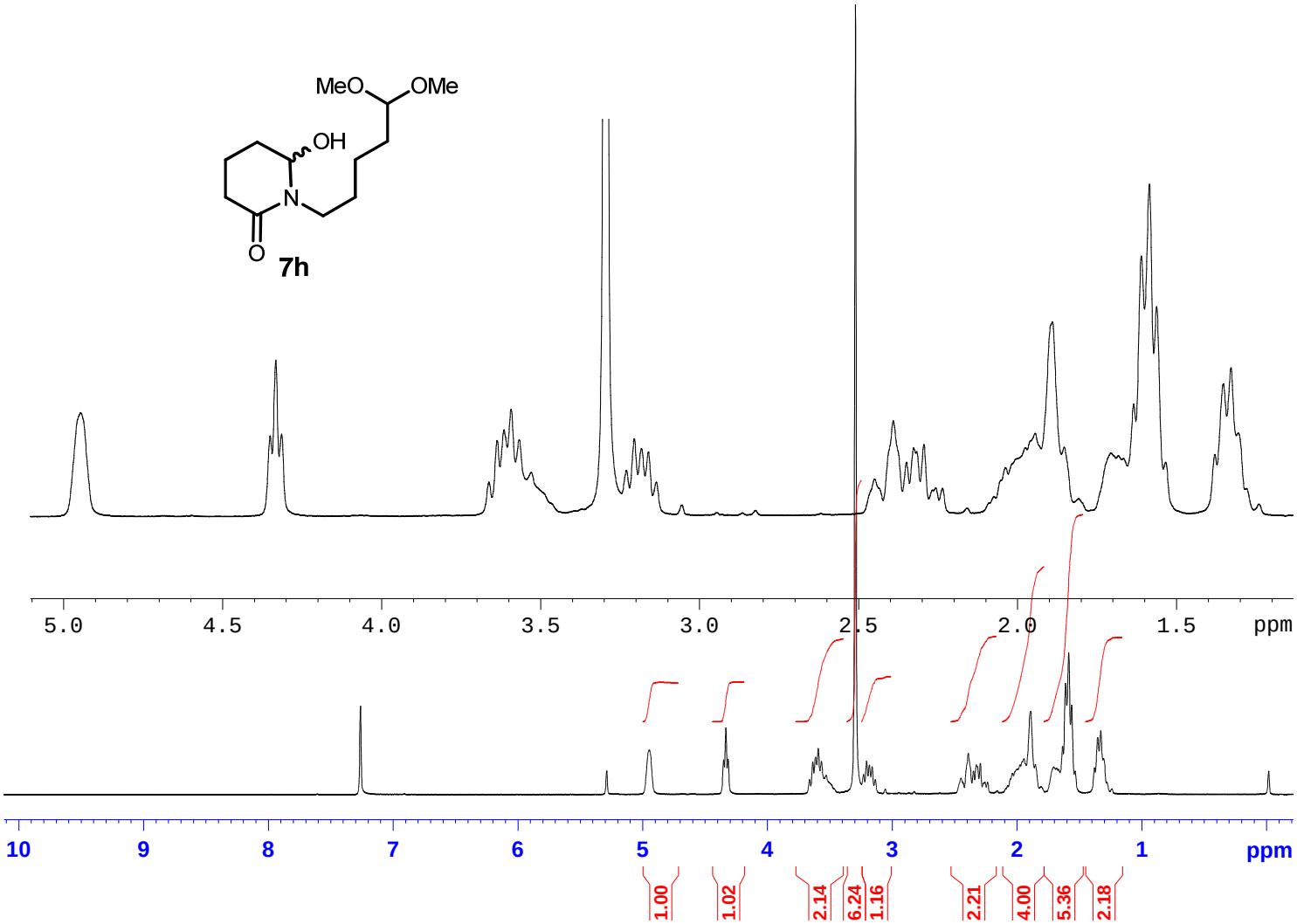
^{13}C NMR of compound **8g** (100 MHz, $CDCl_3$)



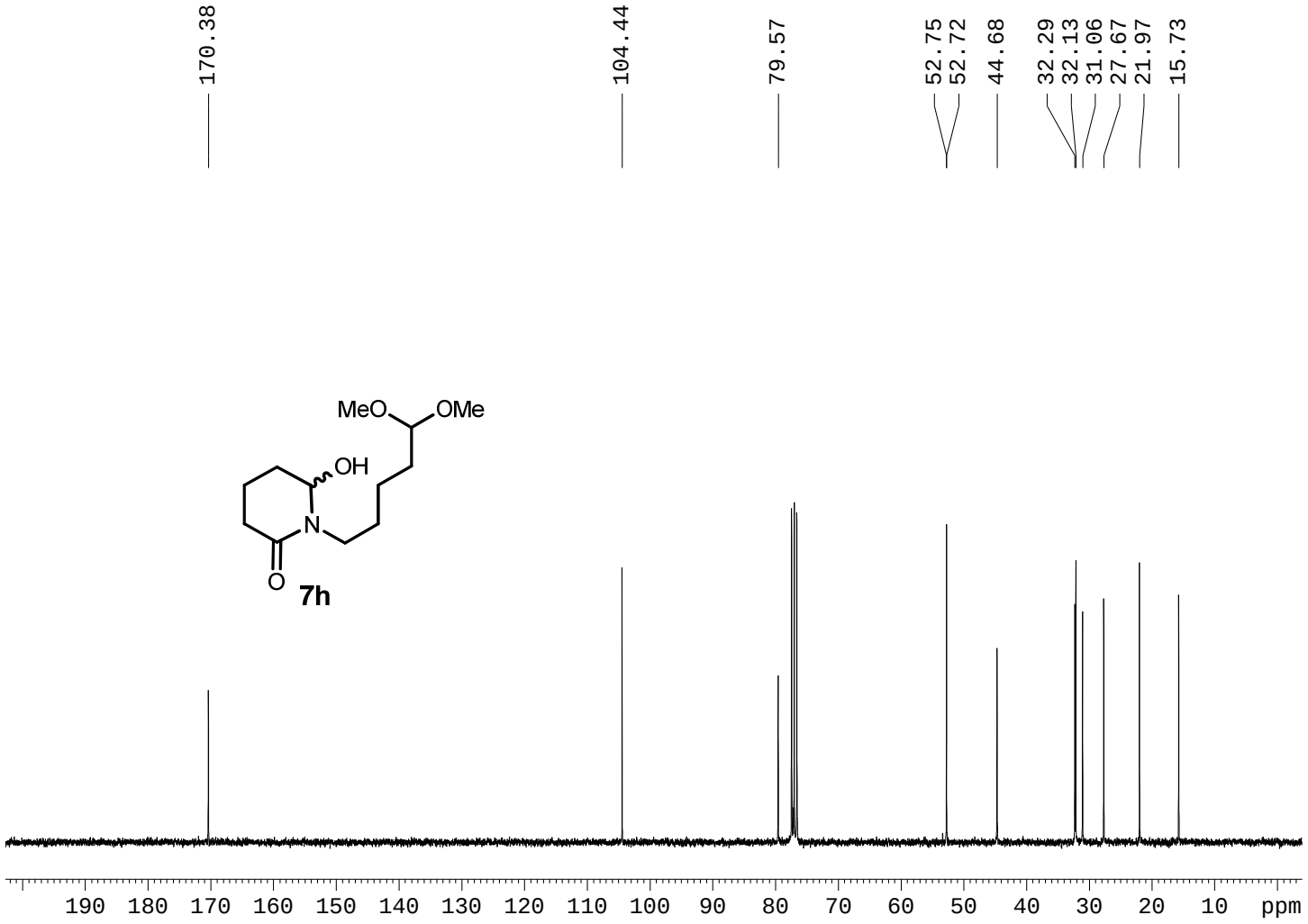
^{1}H NMR of compound **SI-27** (300 MHz, $CDCl_3$)



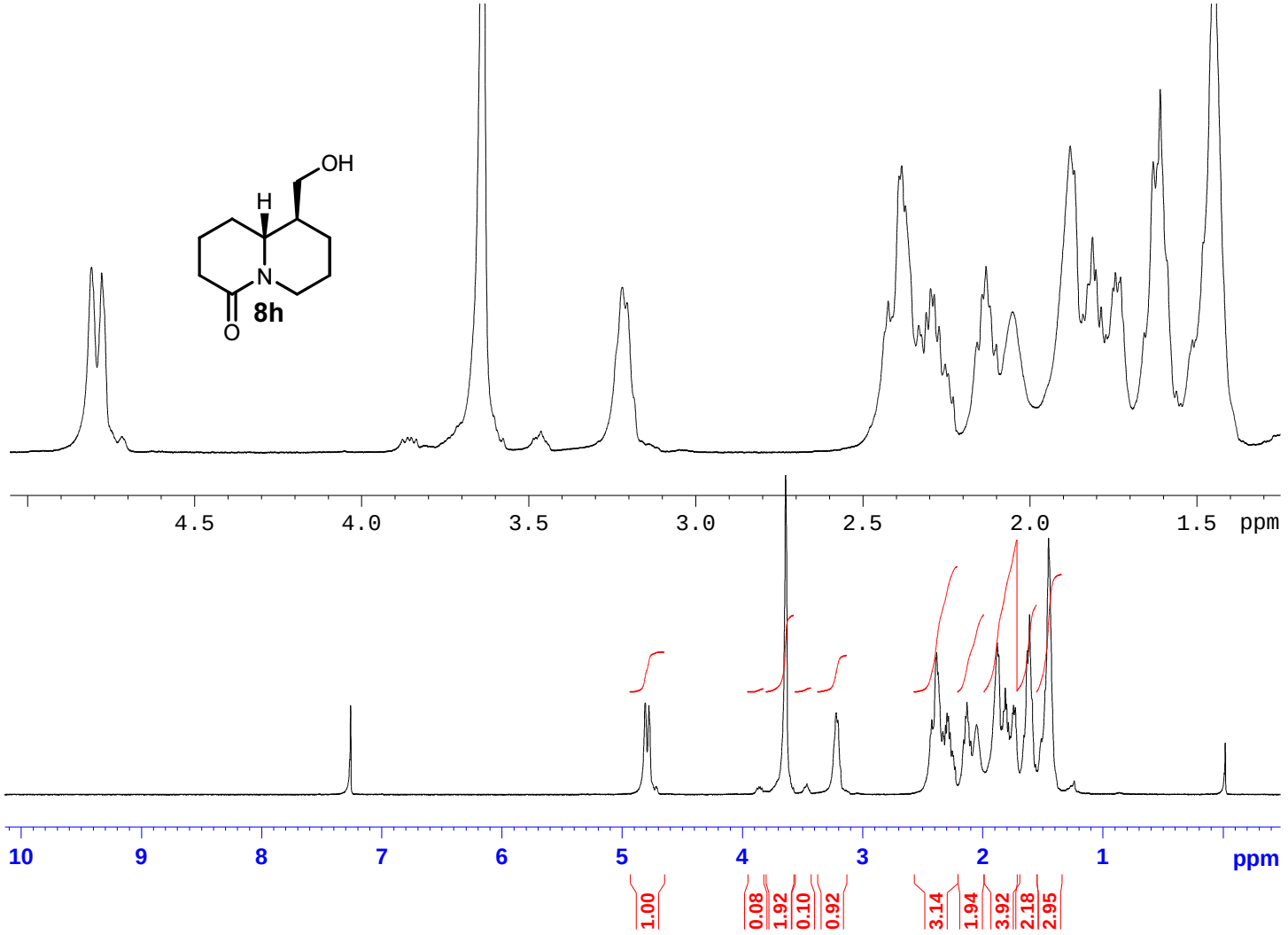
^{13}C NMR of compound **SI-27** (75 MHz, $CDCl_3$)



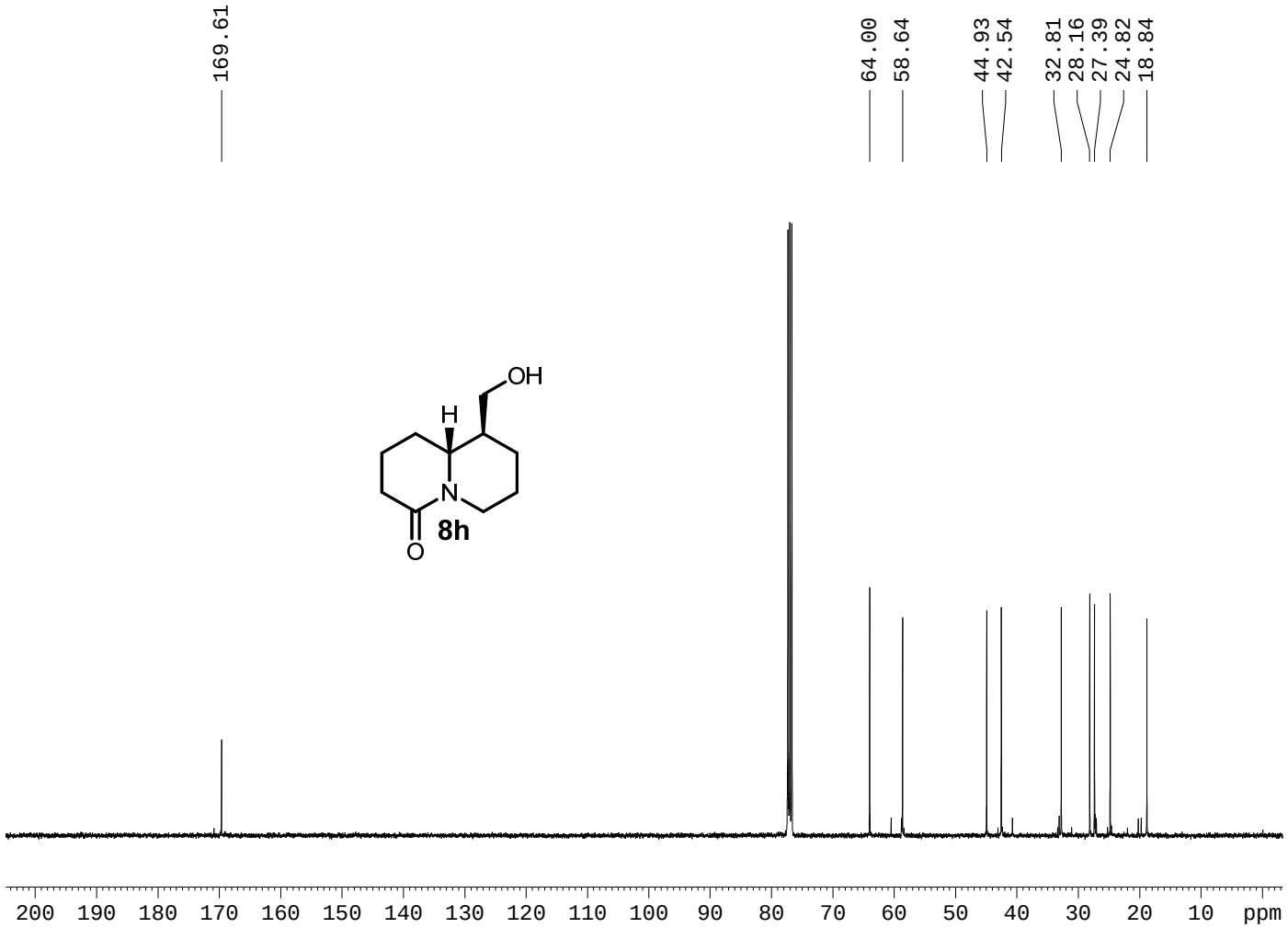
^{1}H NMR of compound **7h** (300 MHz, $CDCl_3$)



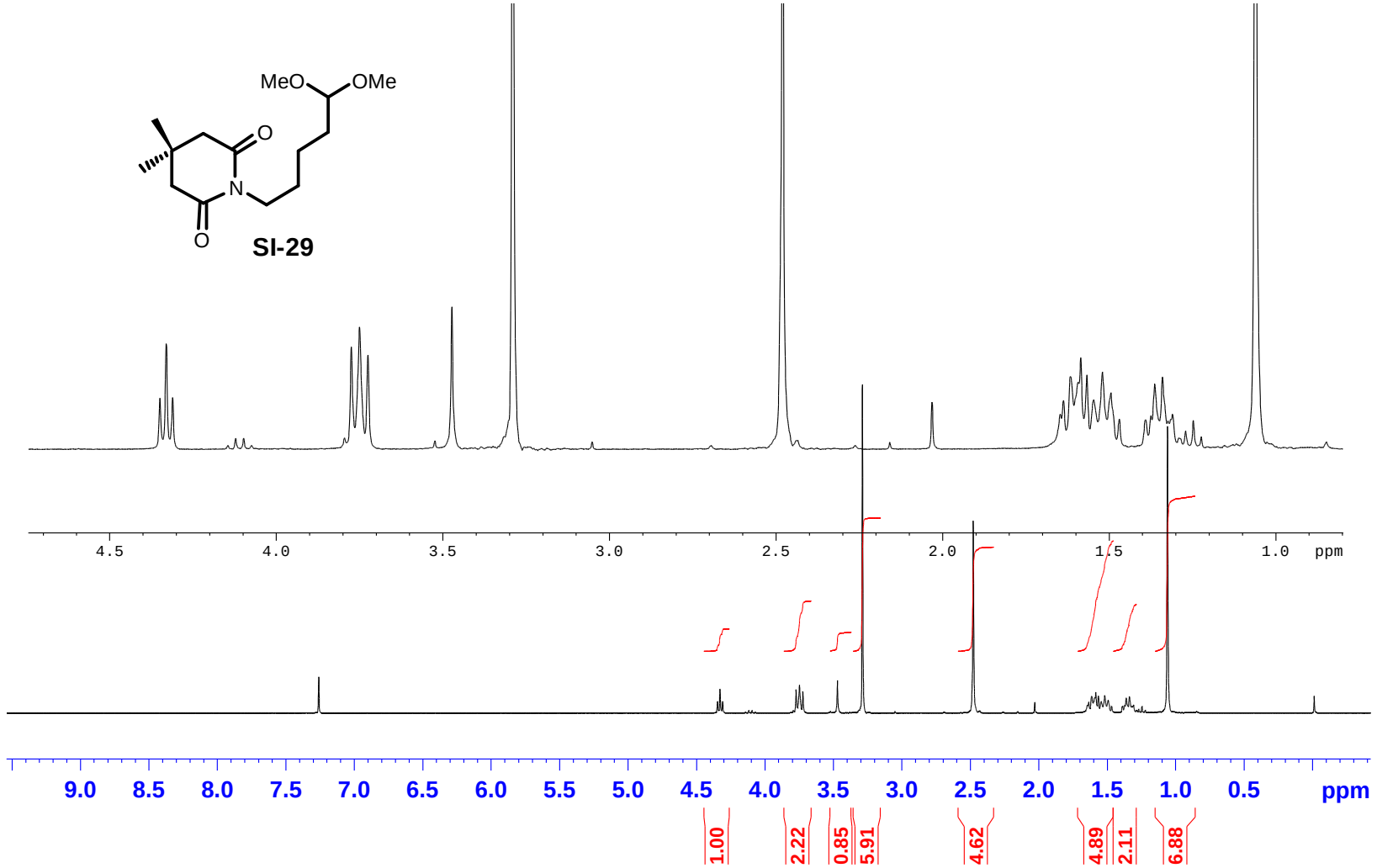
^{13}C NMR of compound **7h** (75 MHz, $CDCl_3$)



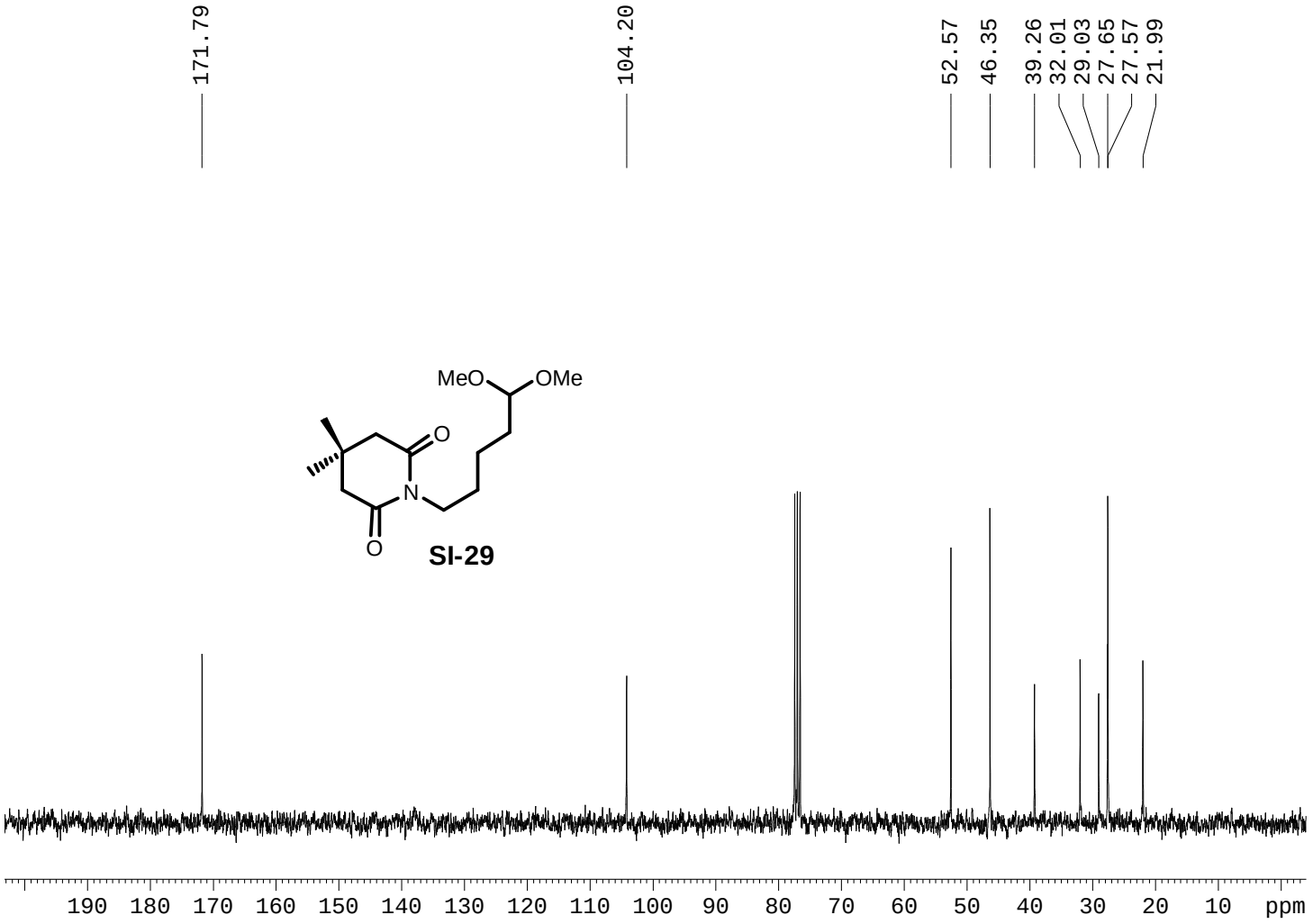
^{1}H NMR of compound **8h** (400 MHz, $CDCl_3$)



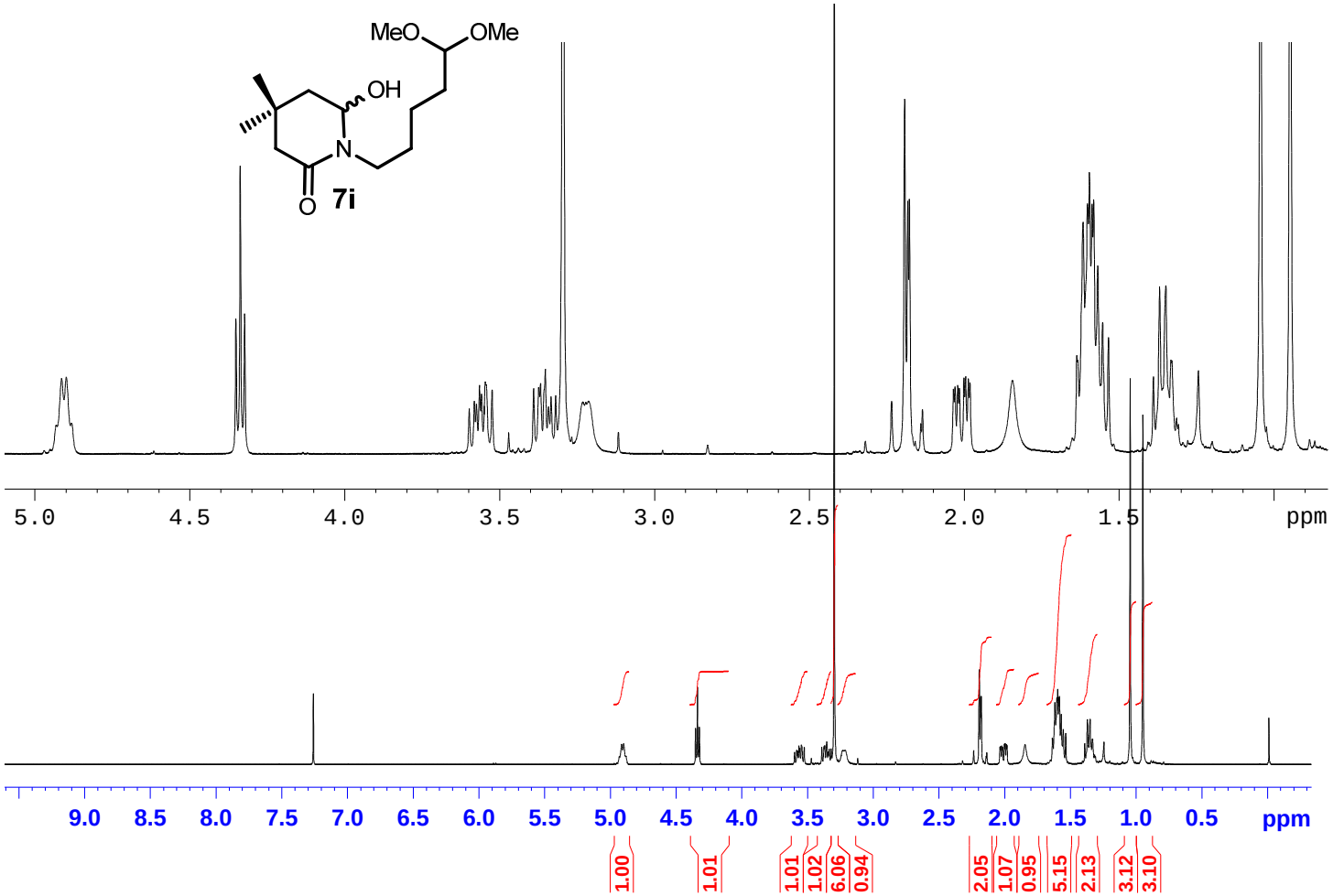
^{13}C NMR of compound **8h** (100 MHz, $CDCl_3$)



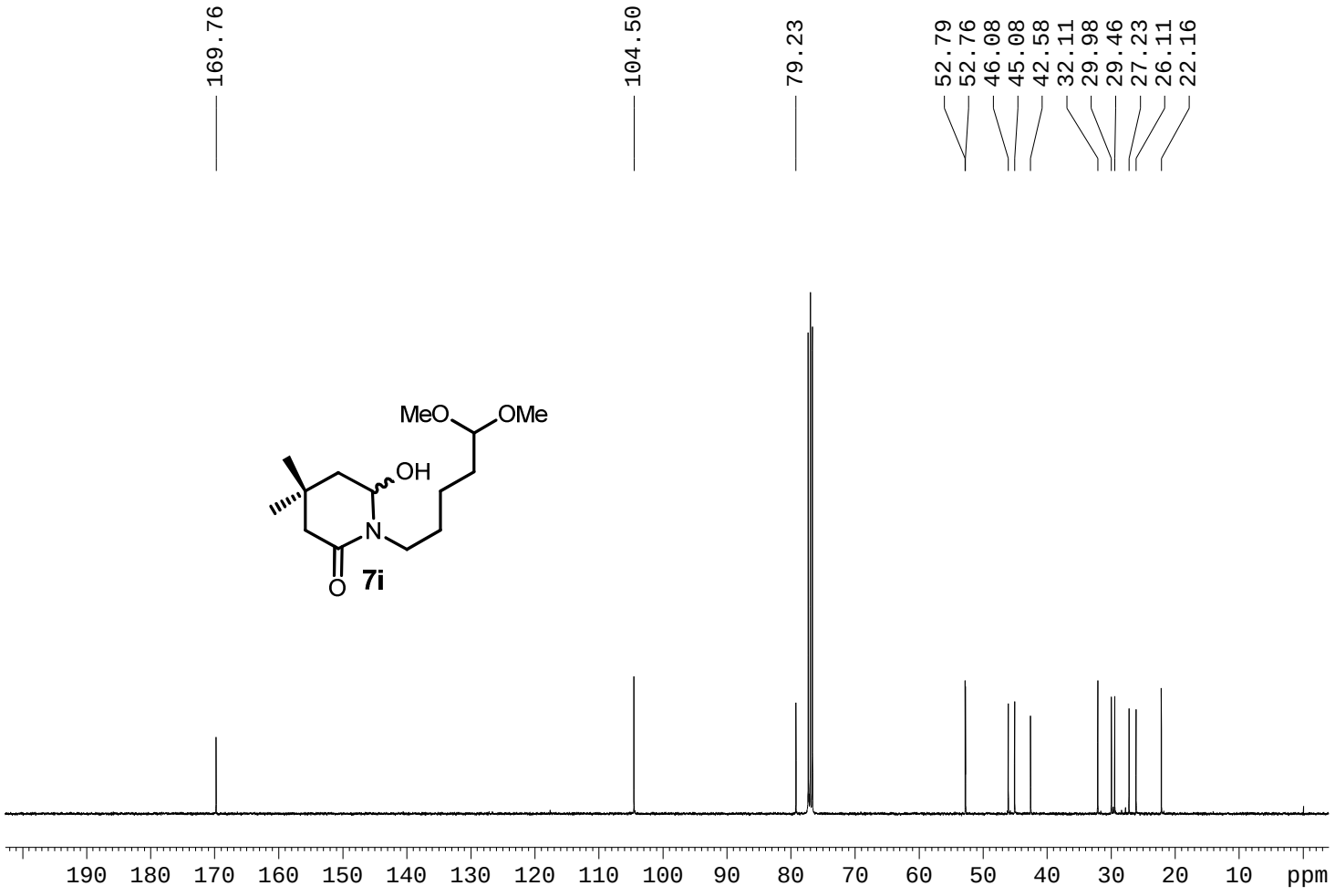
^{1}H NMR of compound **SI-29** (300 MHz, $CDCl_3$)



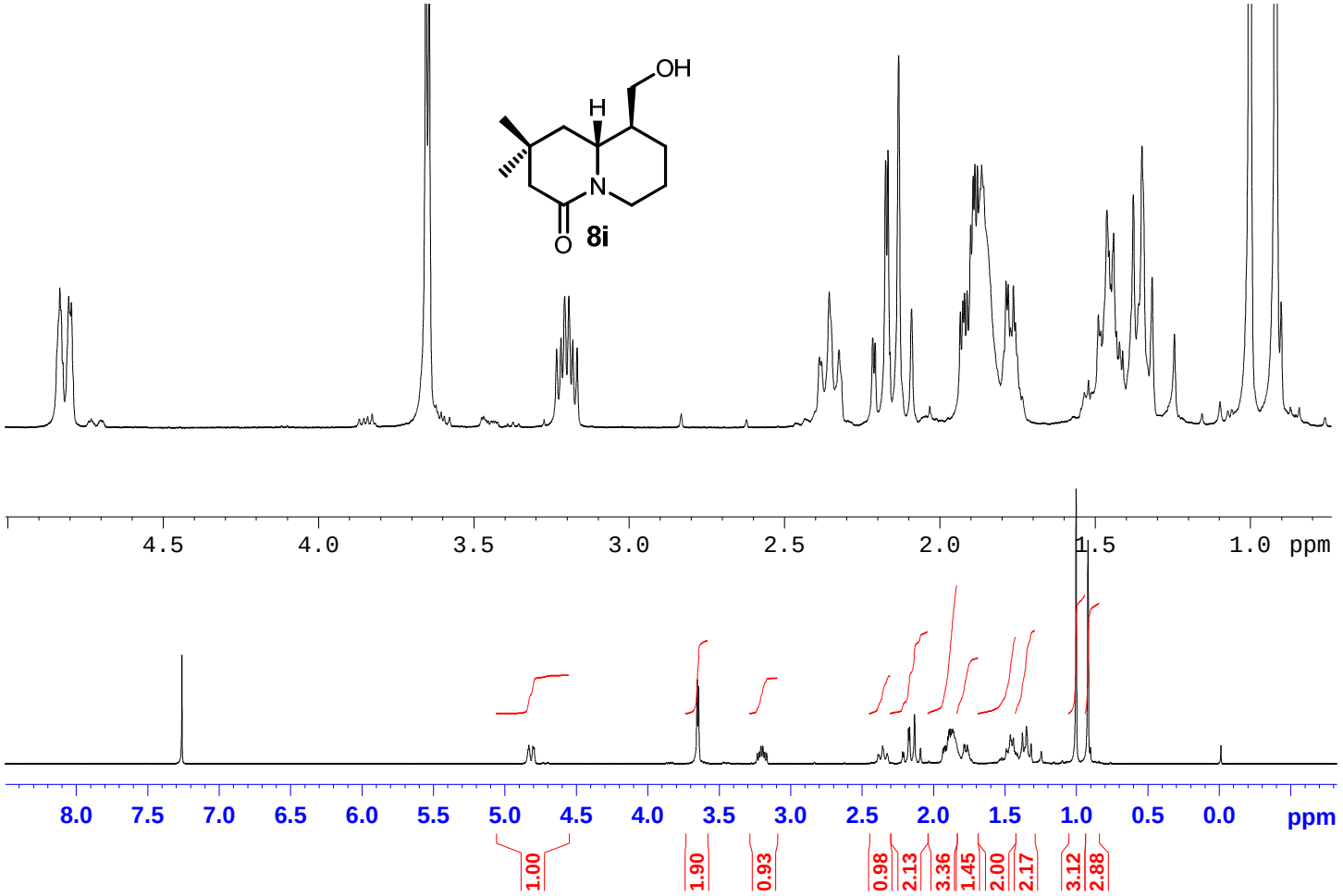
^{13}C NMR of compound **SI-29** (75 MHz, $CDCl_3$)



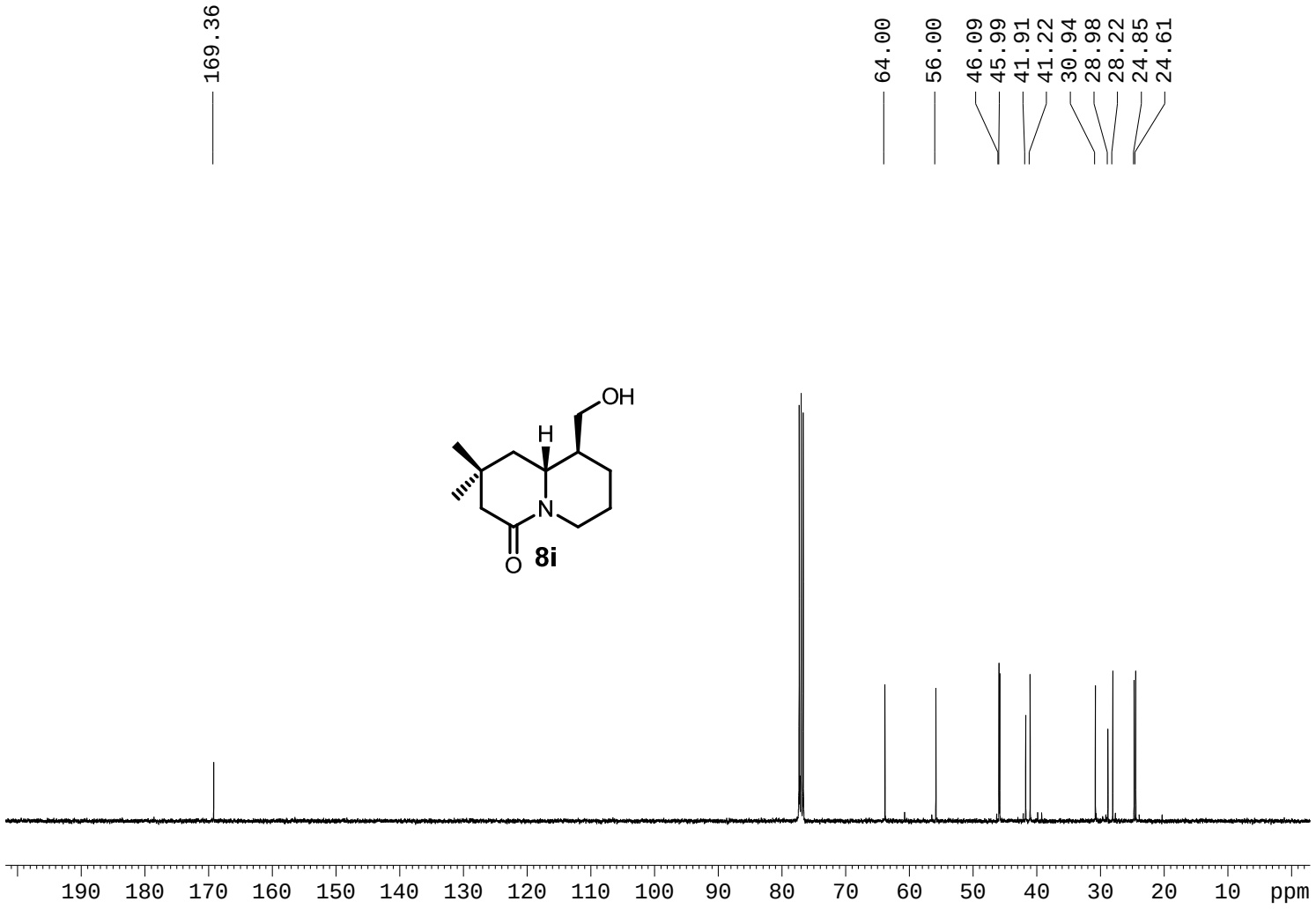
^{1}H NMR of compound **7i** (400 MHz, $CDCl_3$)



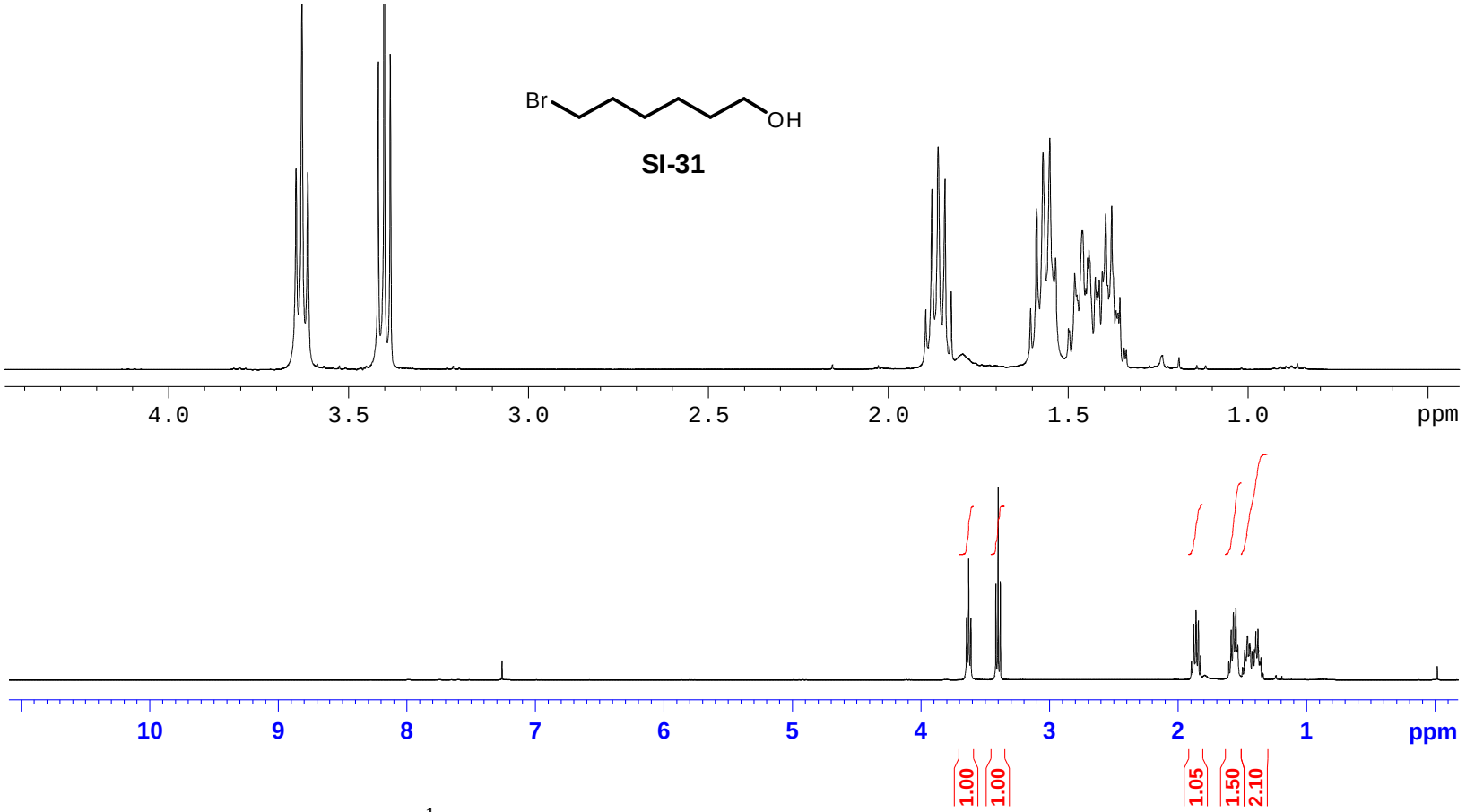
^{13}C NMR of compound **7i** (100 MHz, $CDCl_3$)



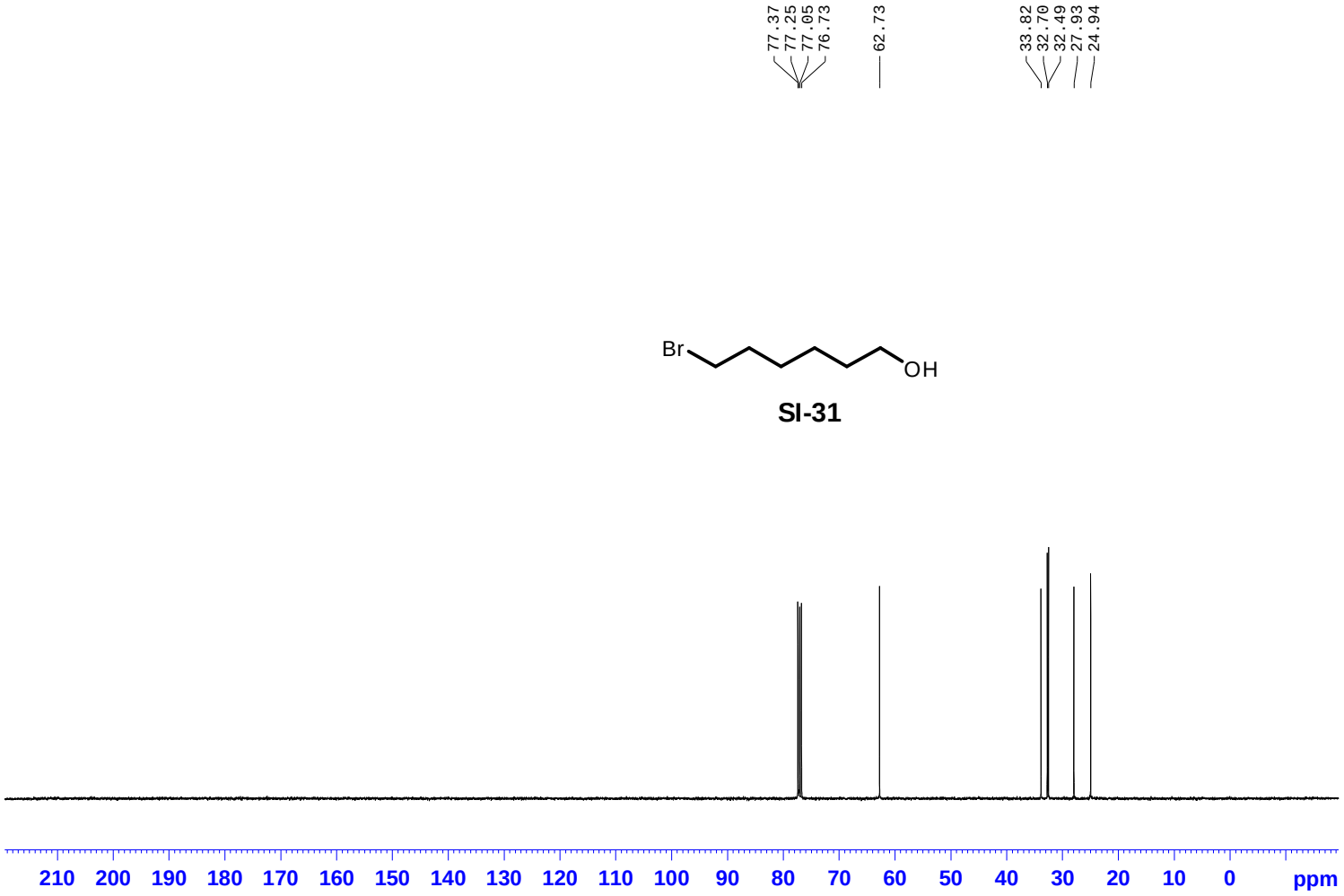
^{1}H NMR of compound **8i** (400 MHz, $CDCl_3$)



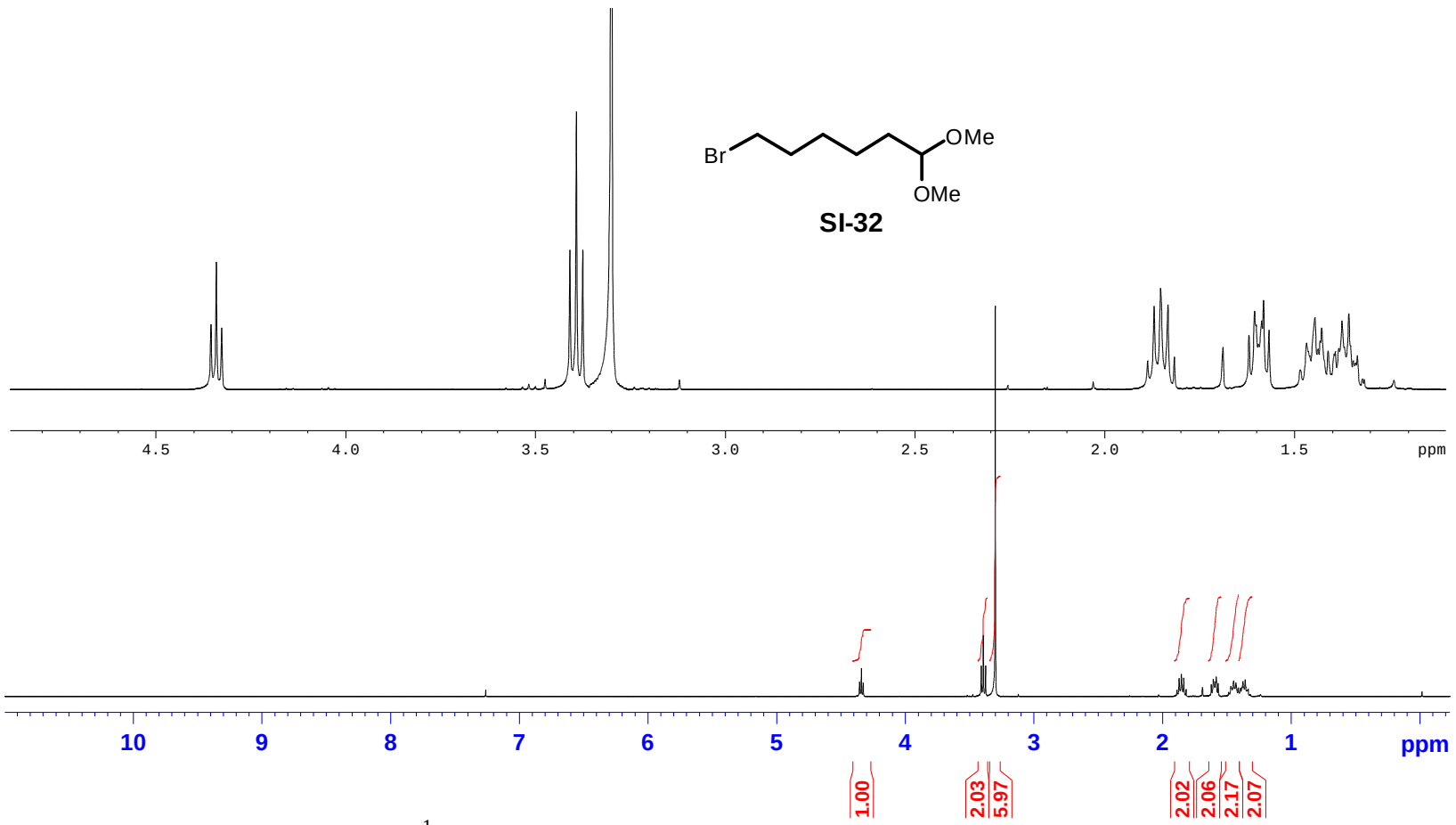
^{13}C NMR of compound **8i** (100 MHz, $CDCl_3$)



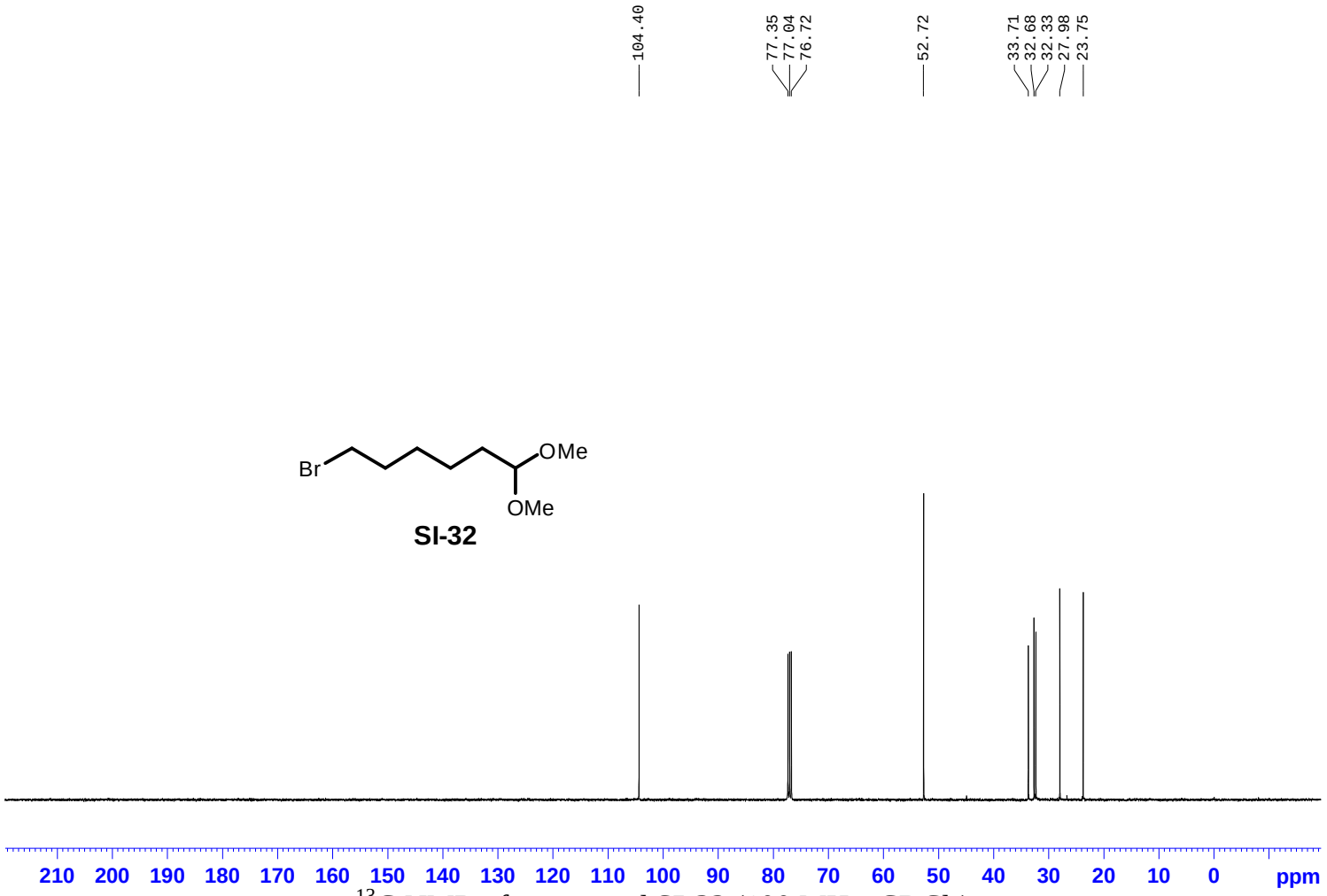
^{1}H NMR of compound **SI-31** (400 MHz, $CDCl_3$)



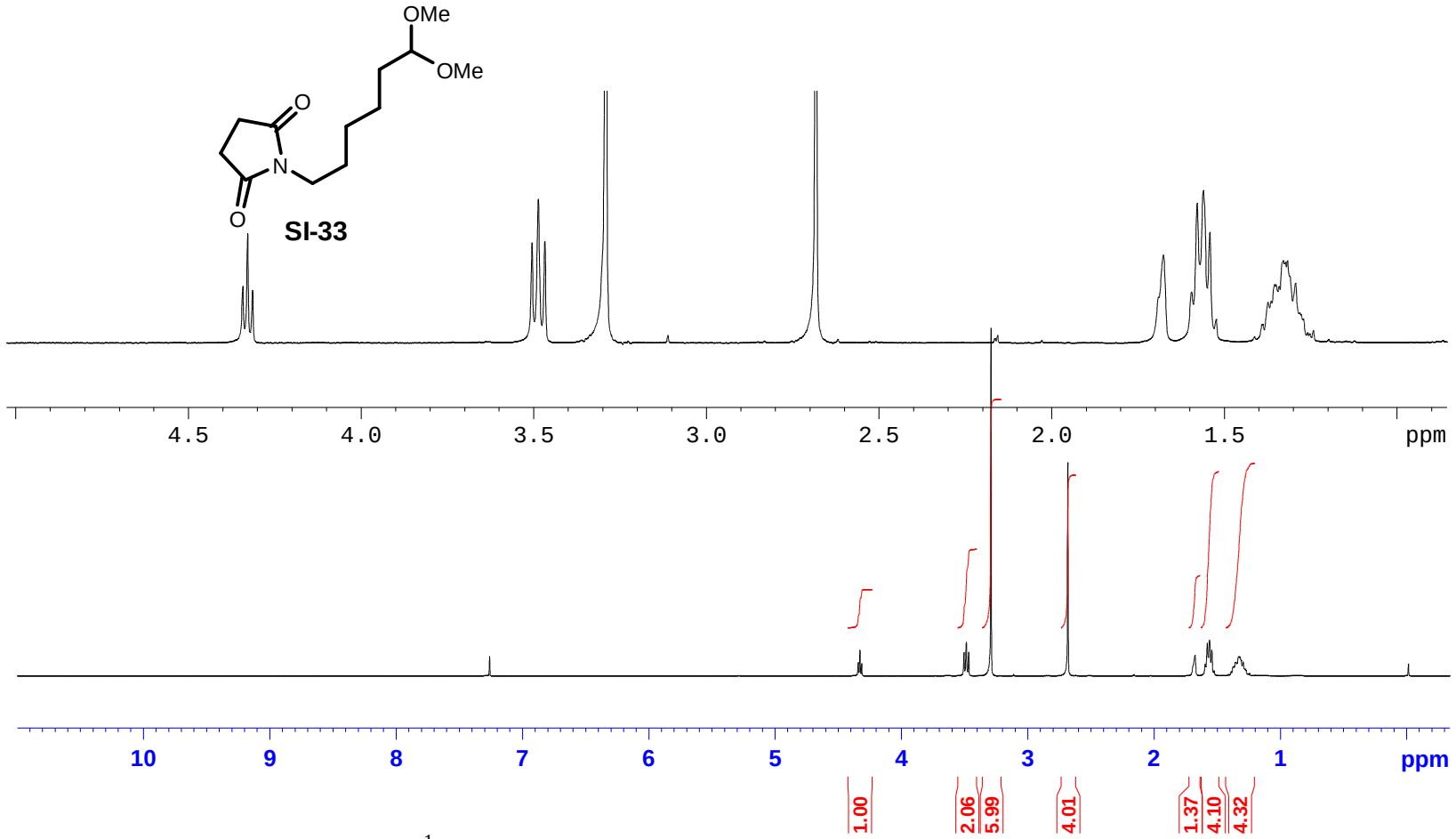
^{13}C NMR of compound **SI-31** (100 MHz, $CDCl_3$)



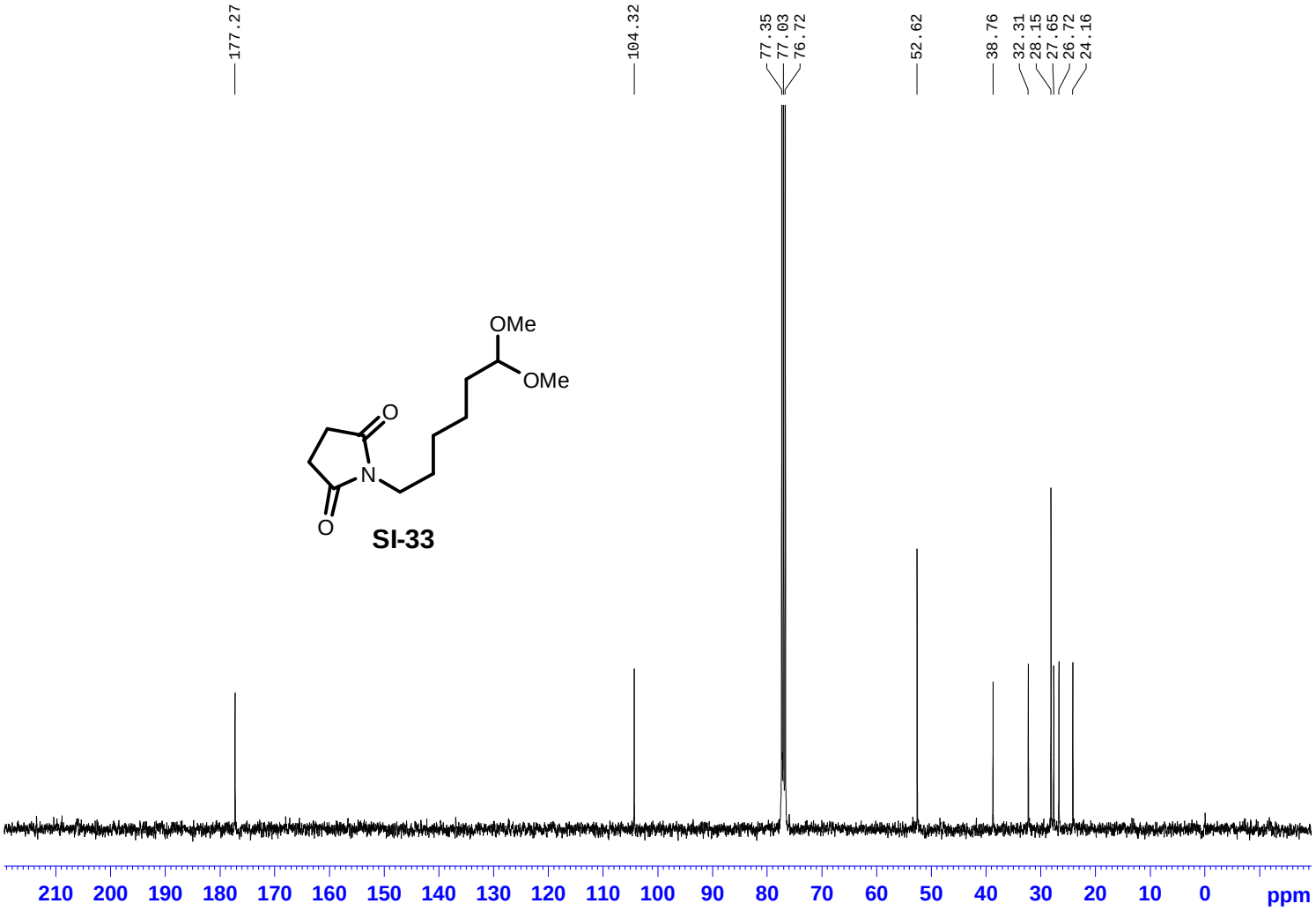
^{1}H NMR of compound **SI-32** (400 MHz, $CDCl_3$)



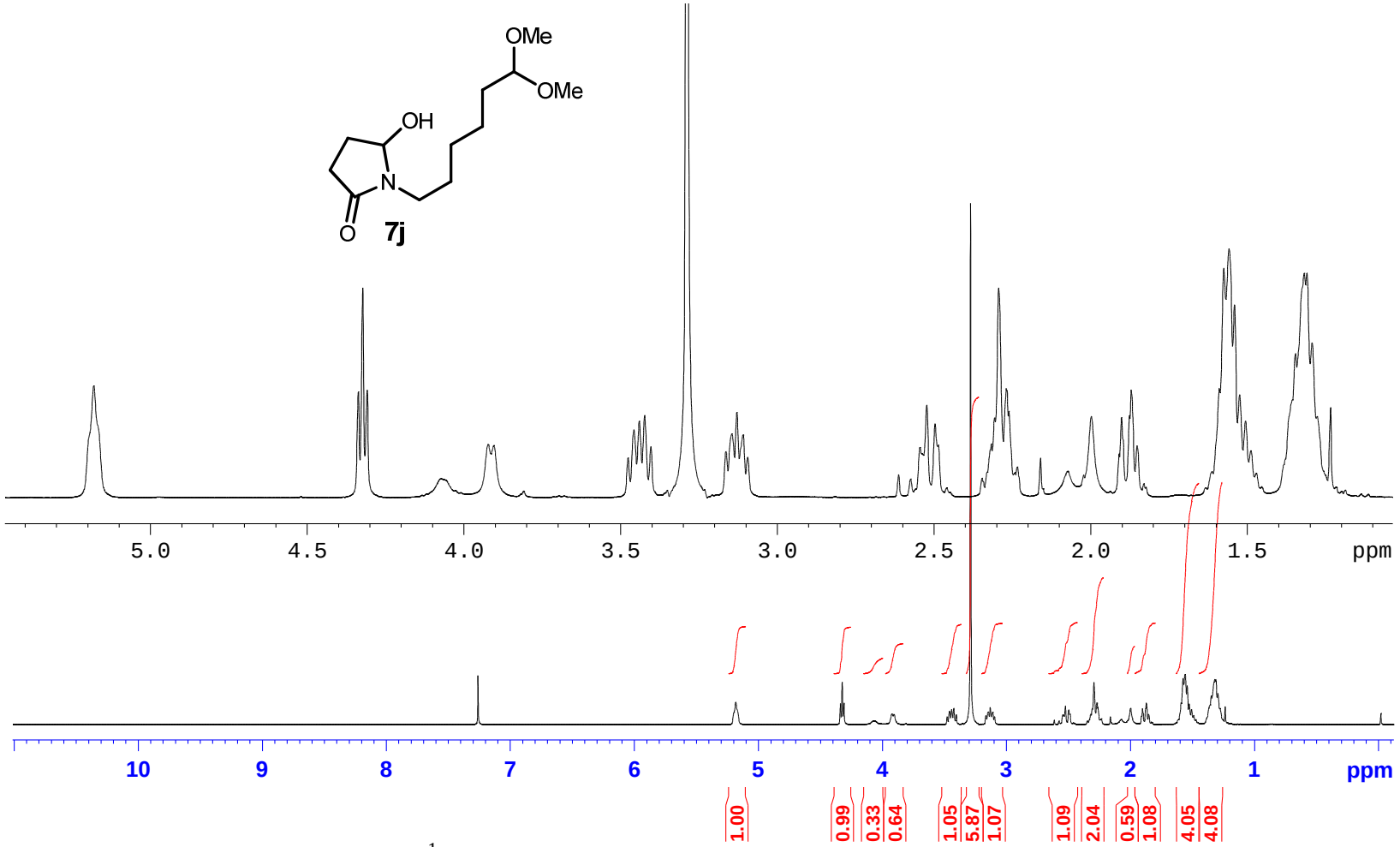
^{13}C NMR of compound **SI-32** (100 MHz, $CDCl_3$)



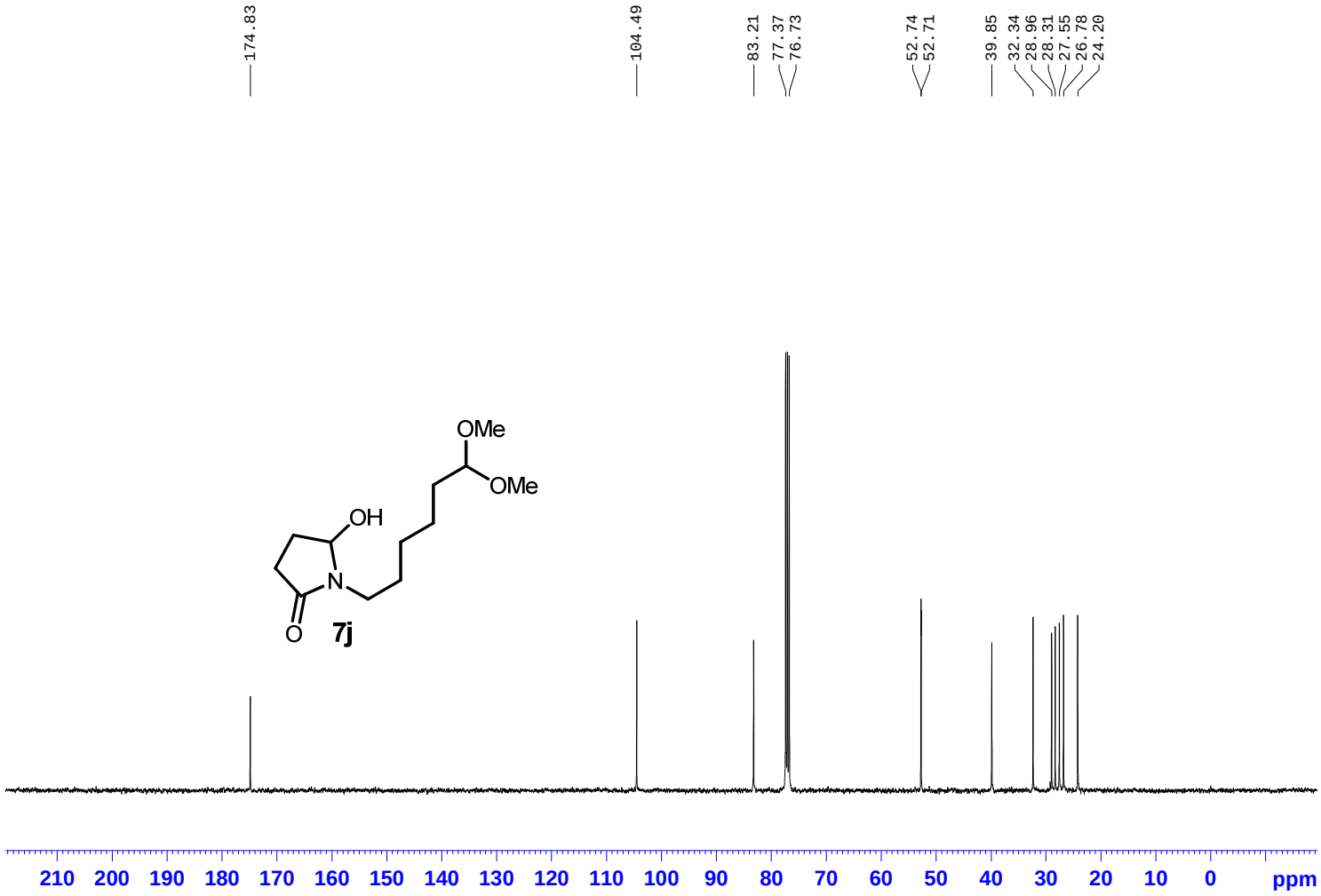
^{1}H NMR of compound **SI-33** (400 MHz, $CDCl_3$)



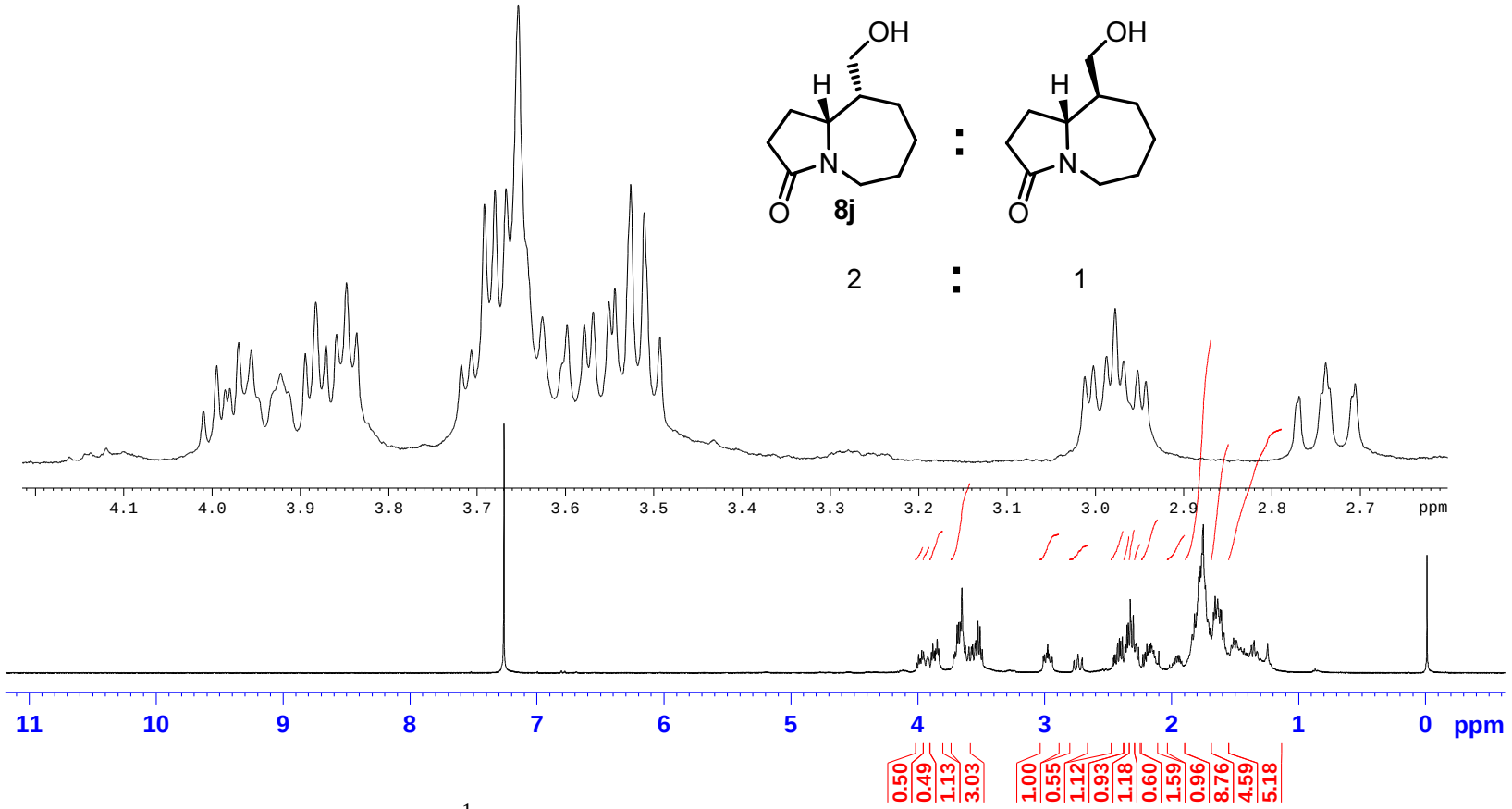
^{13}C NMR of compound **SI-33** (100 MHz, $CDCl_3$)



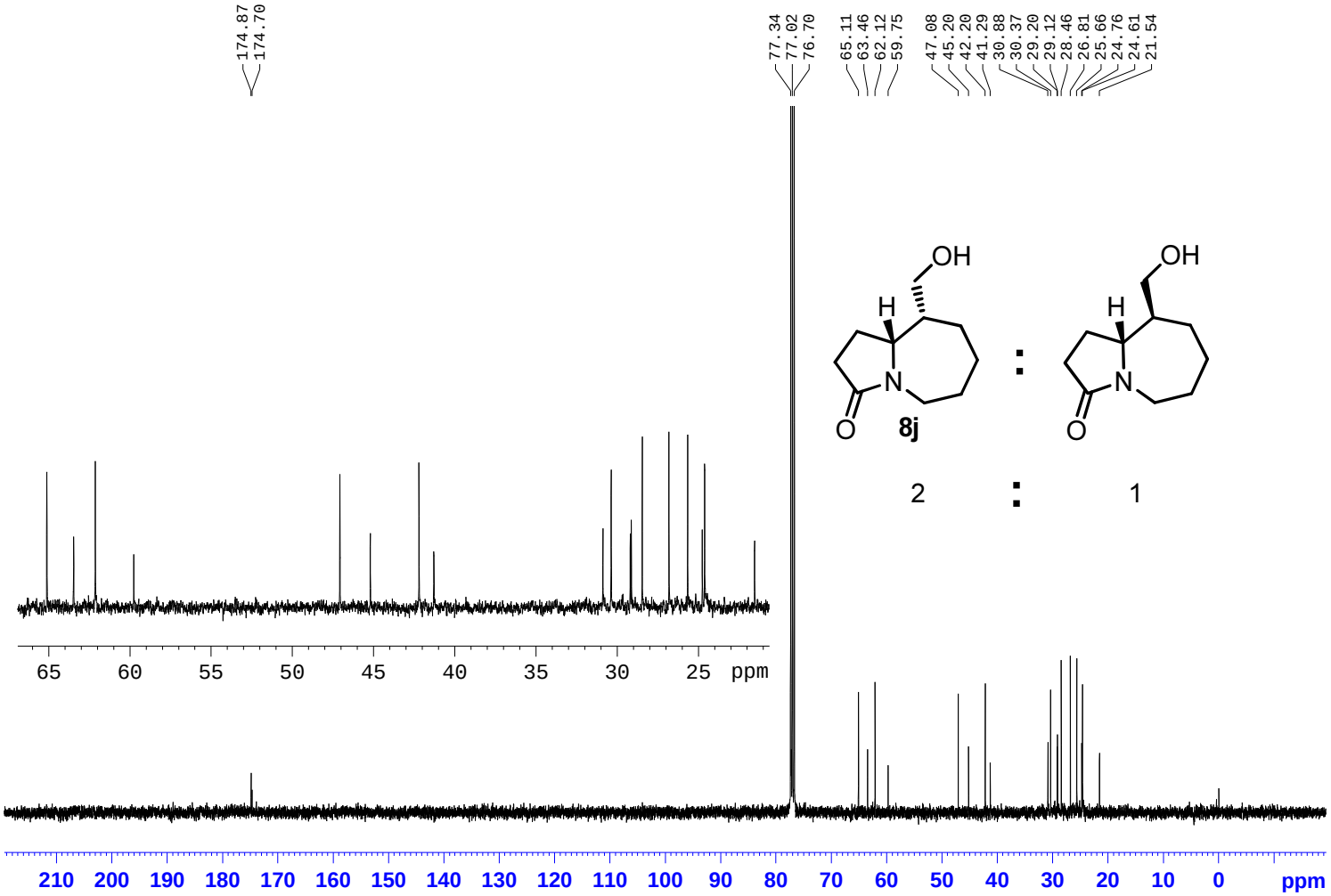
^{1}H NMR of compound **7j** (300 MHz, $CDCl_3$)



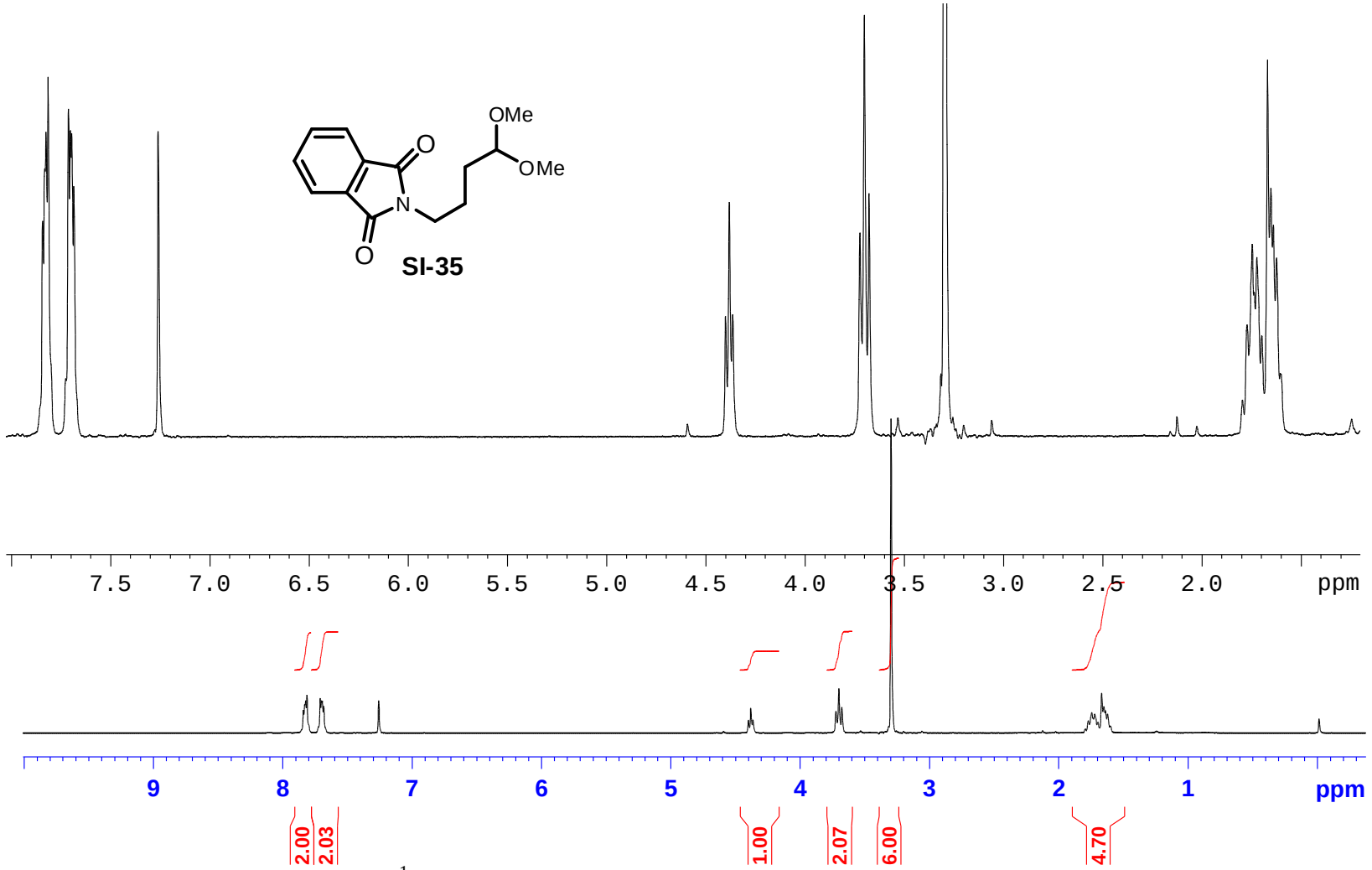
^{13}C NMR of compound **7j** (100 MHz, $CDCl_3$)



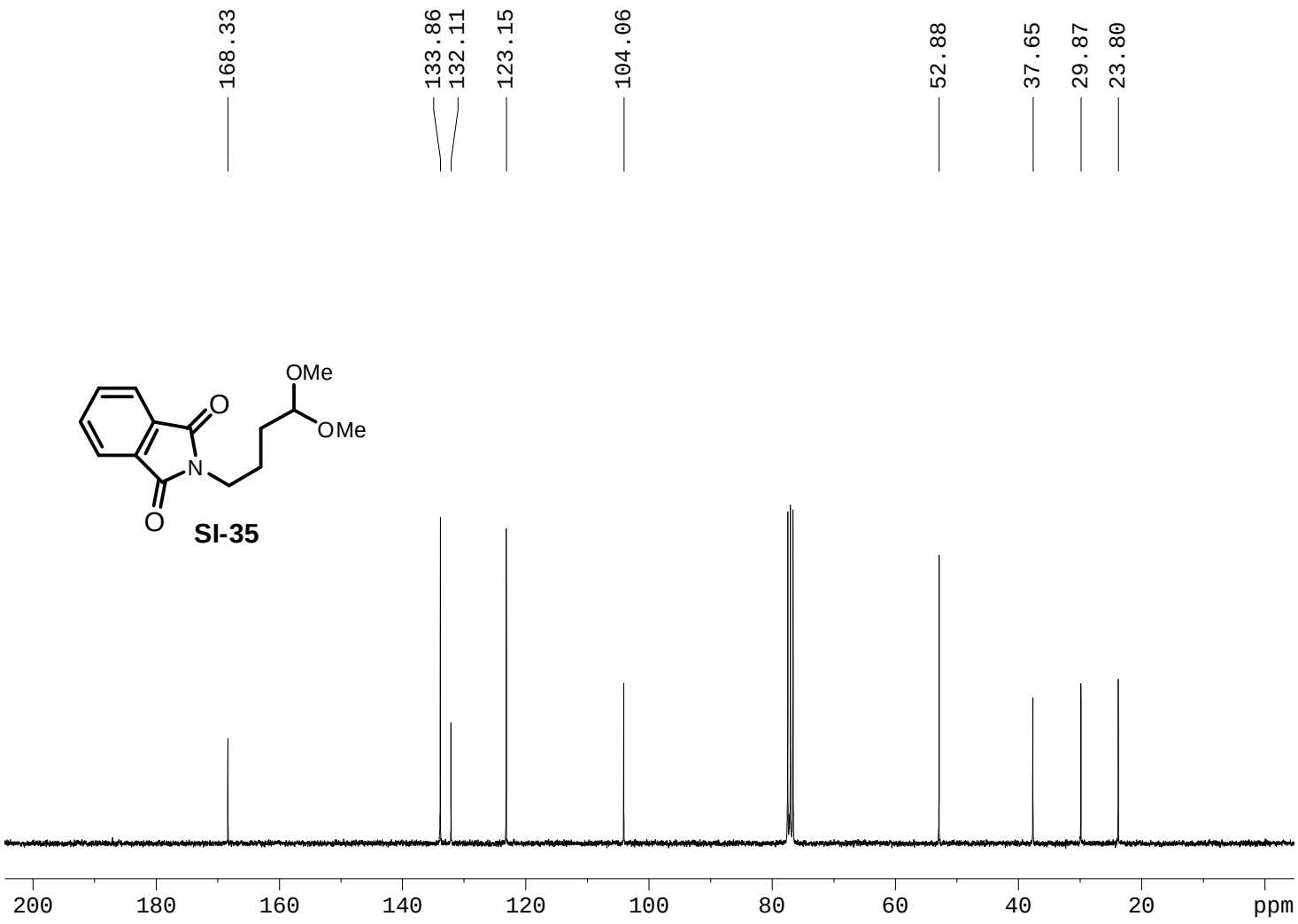
^{1}H NMR of compound **8j** (400 MHz, $CDCl_3$)



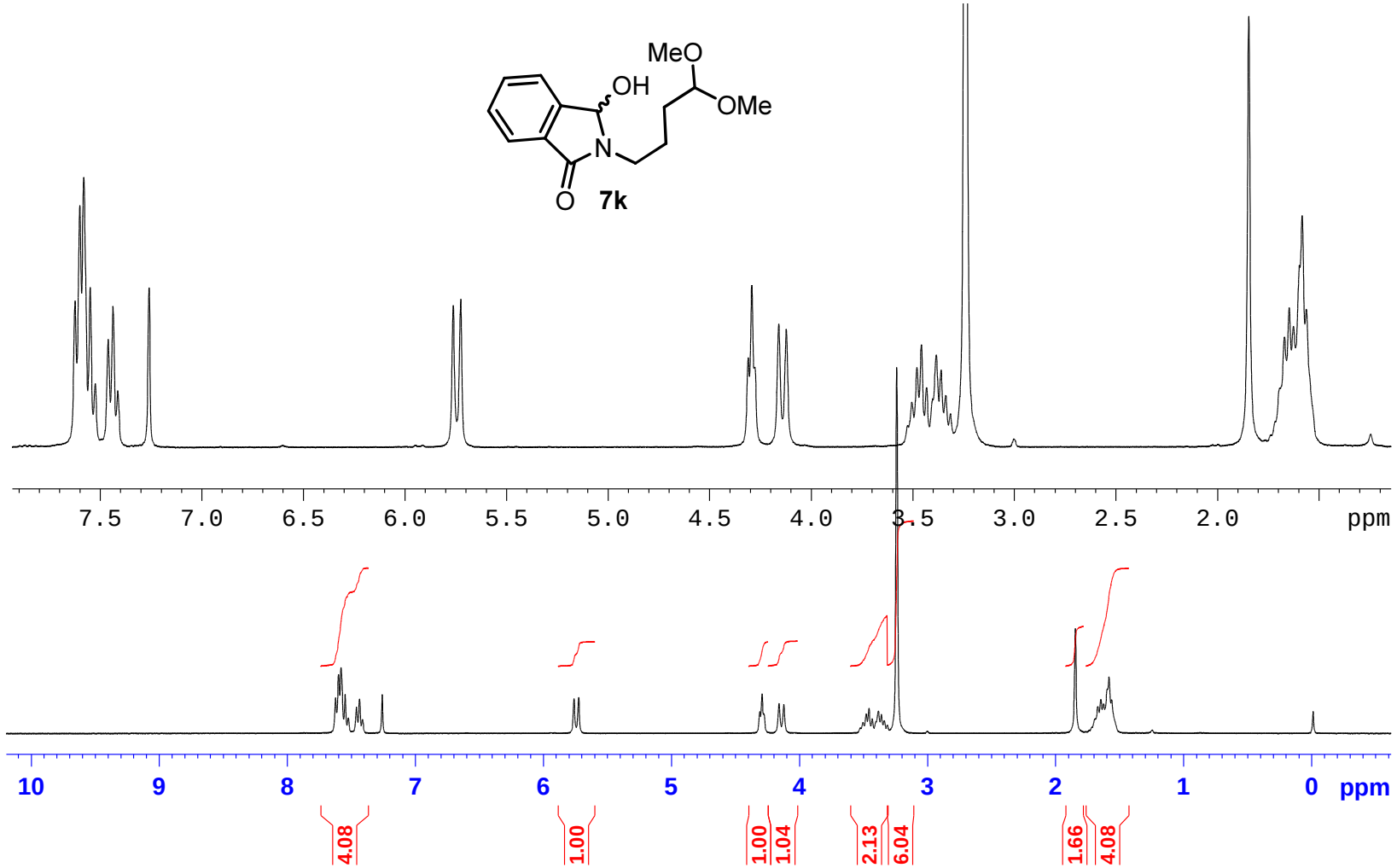
^{13}C NMR of compound **8j** (100 MHz, $CDCl_3$)



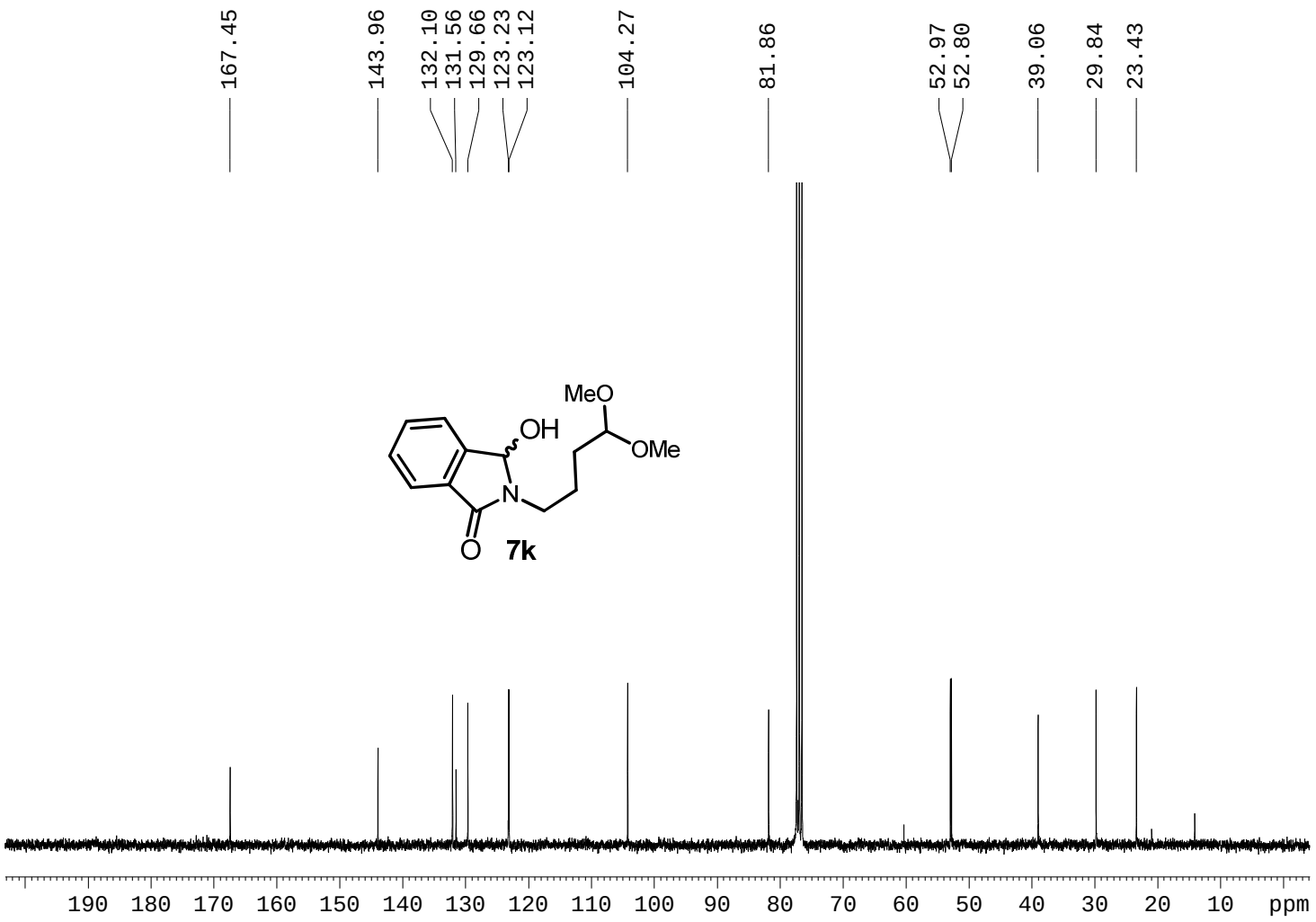
^{1}H NMR of compound **SI-35** (300 MHz, $CDCl_3$)



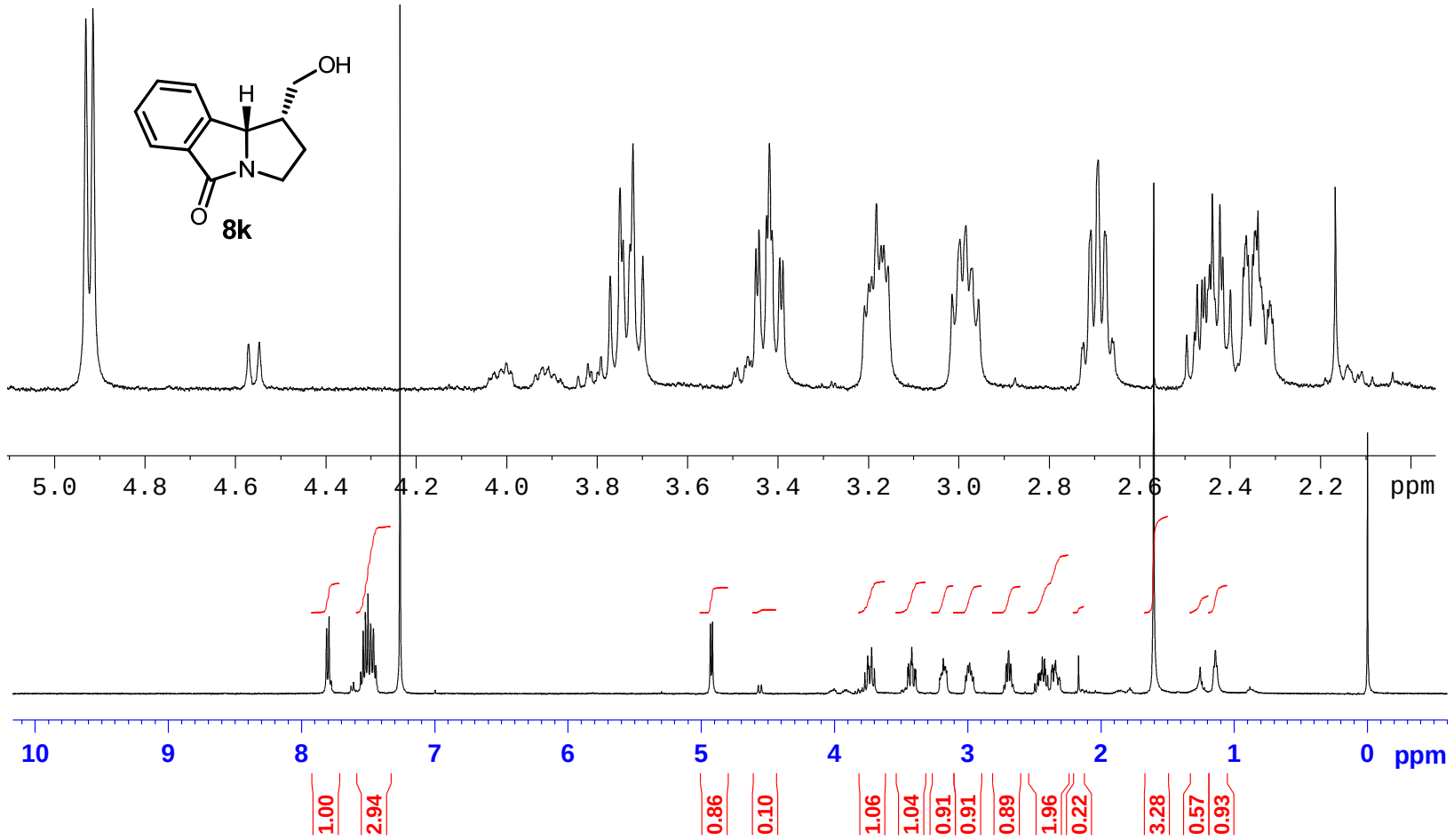
^{13}C NMR of compound **SI-35** (75 MHz, $CDCl_3$)



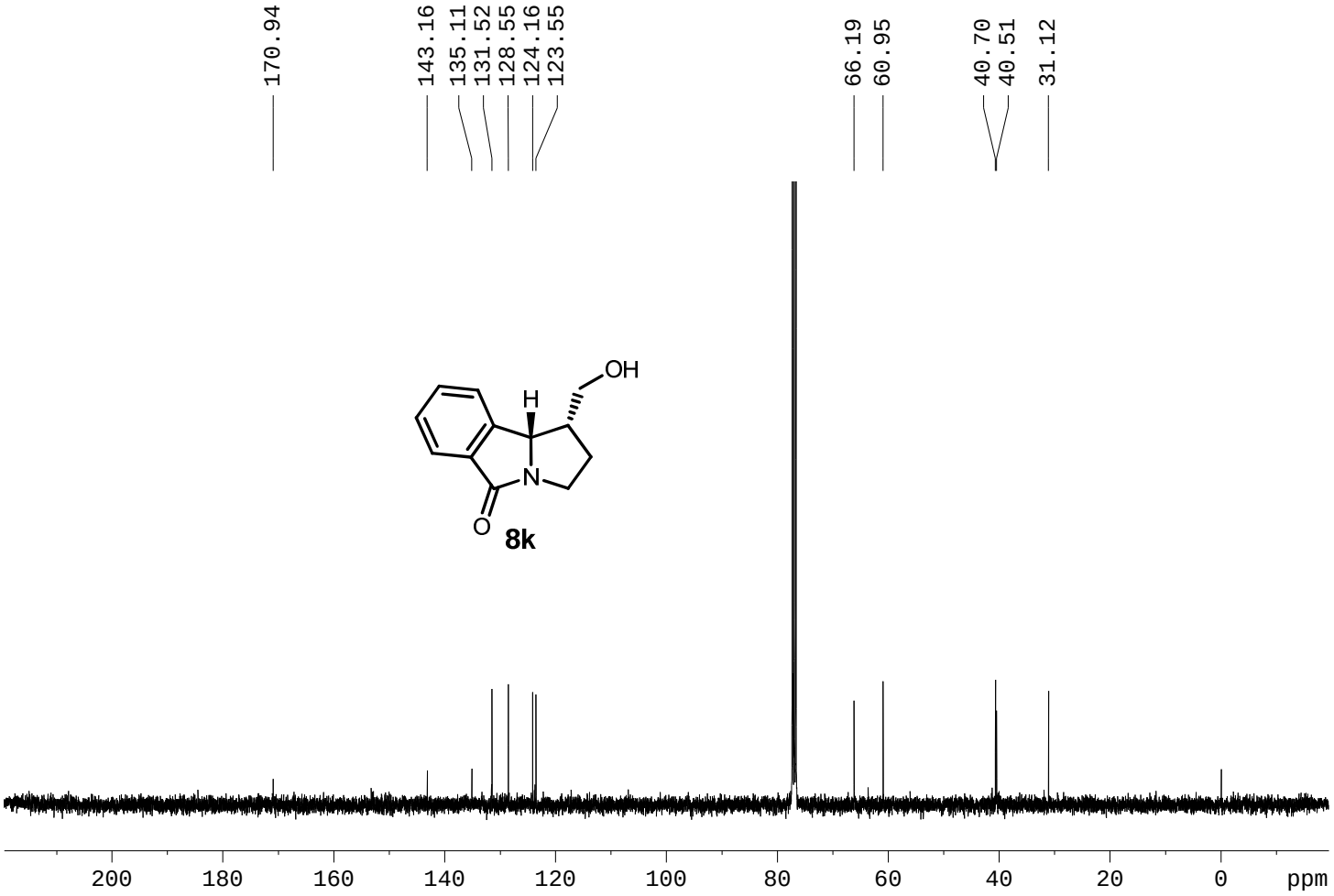
^{1}H NMR of compound **7k** (300 MHz, $CDCl_3$)



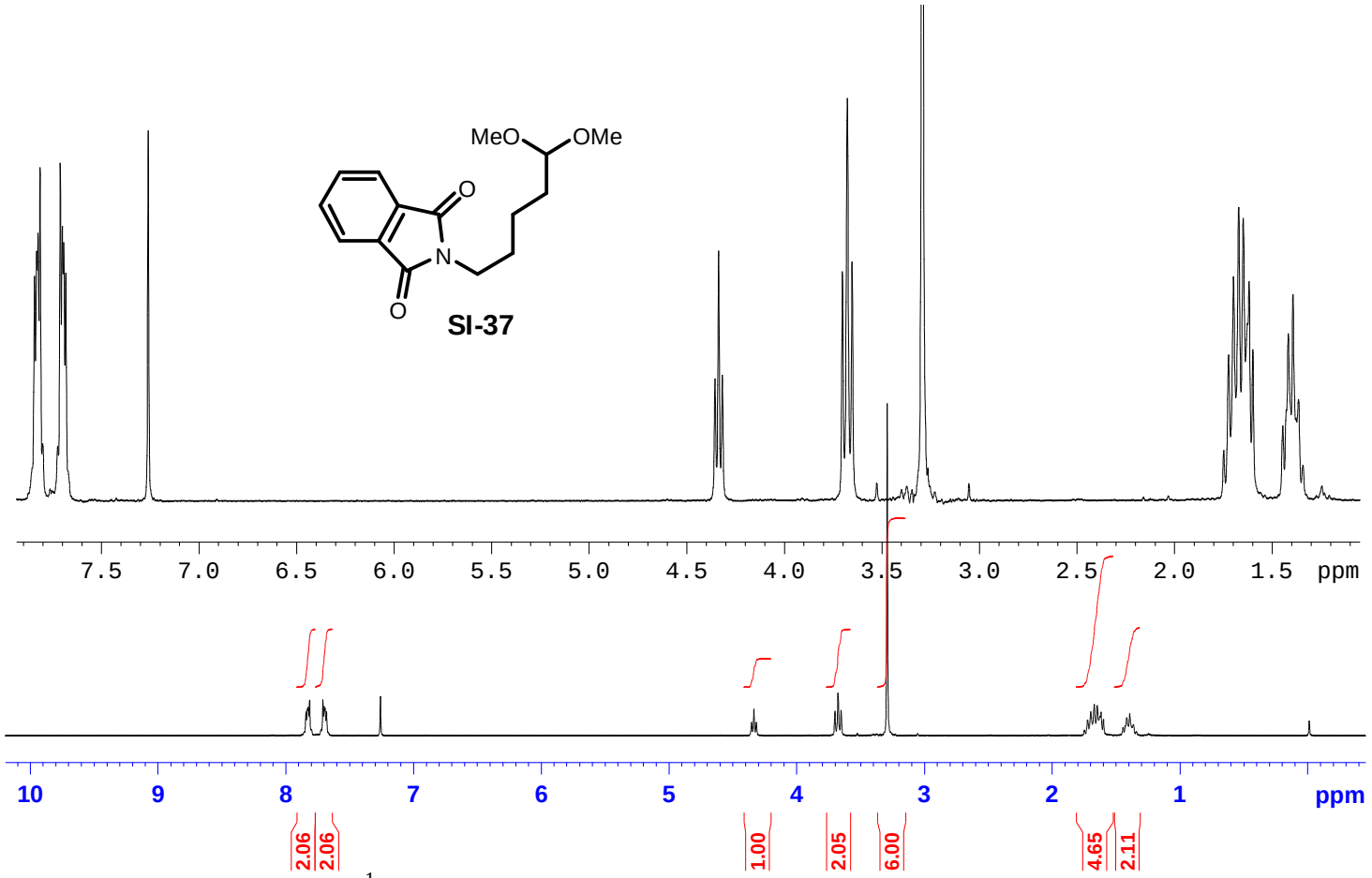
^{13}C NMR of compound **7k** (75 MHz, $CDCl_3$)



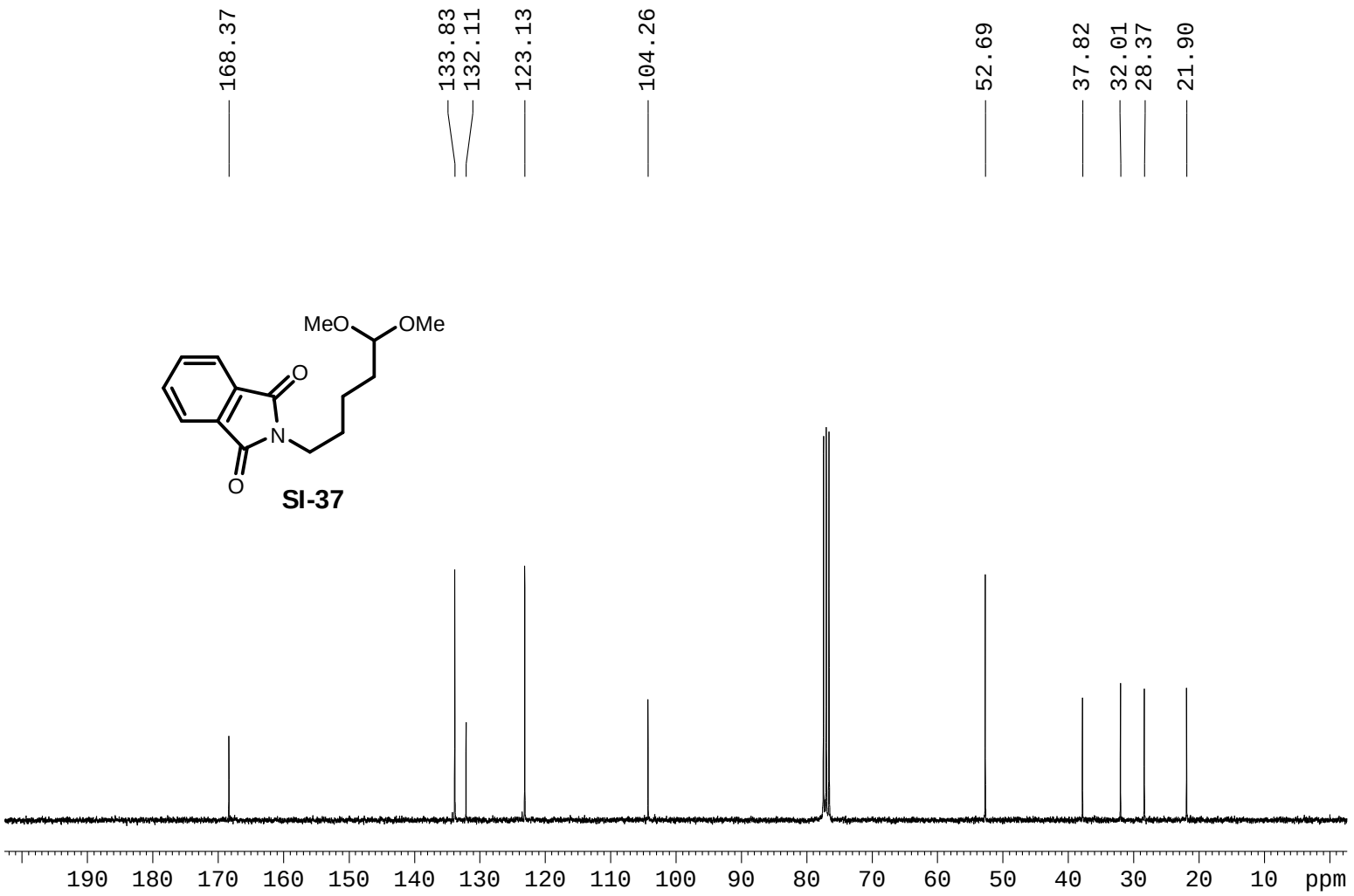
^{1}H NMR of compound **8k** (400 MHz, $CDCl_3$)



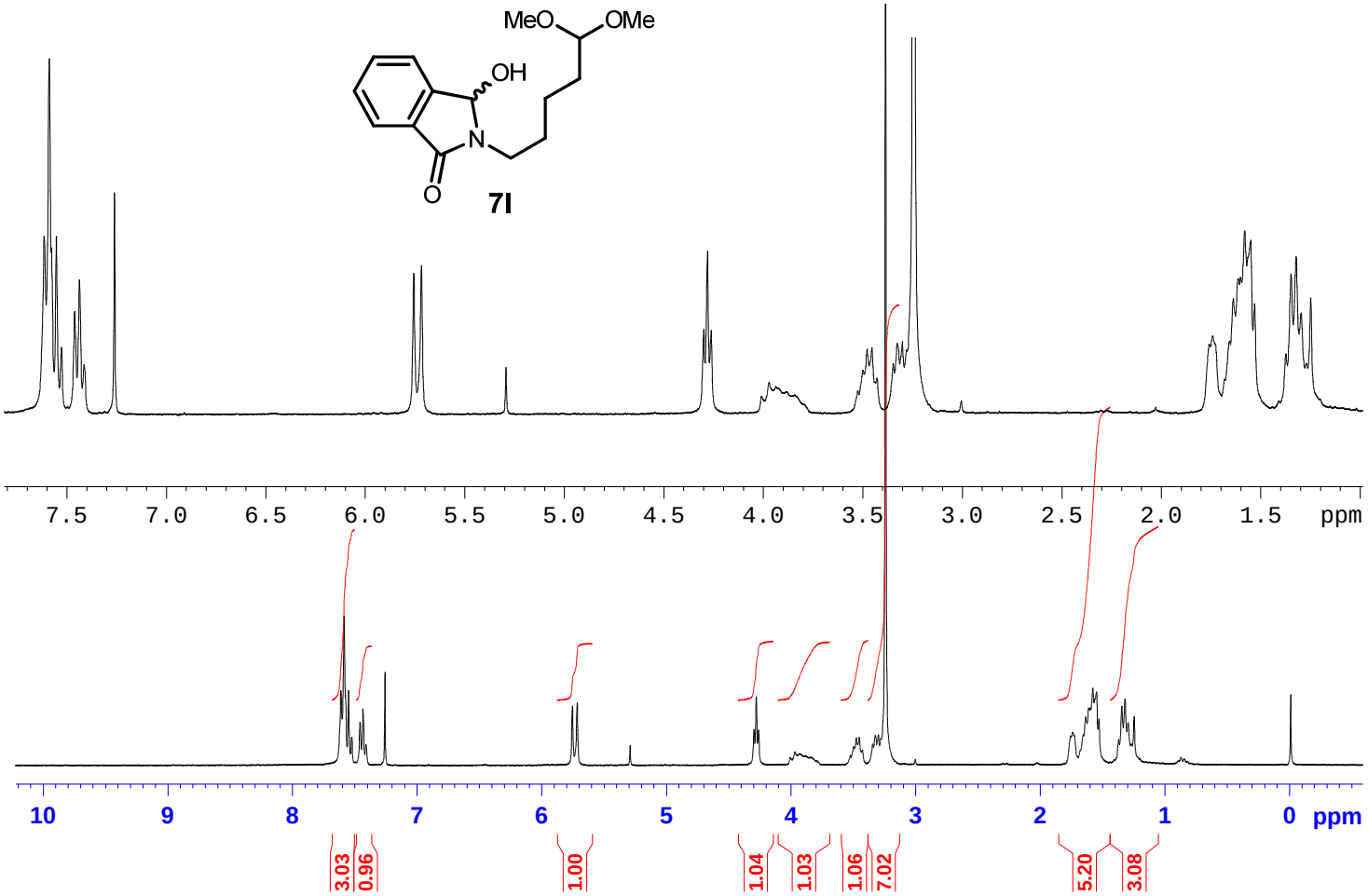
^{13}C NMR of compound **8k** (100 MHz, $CDCl_3$)



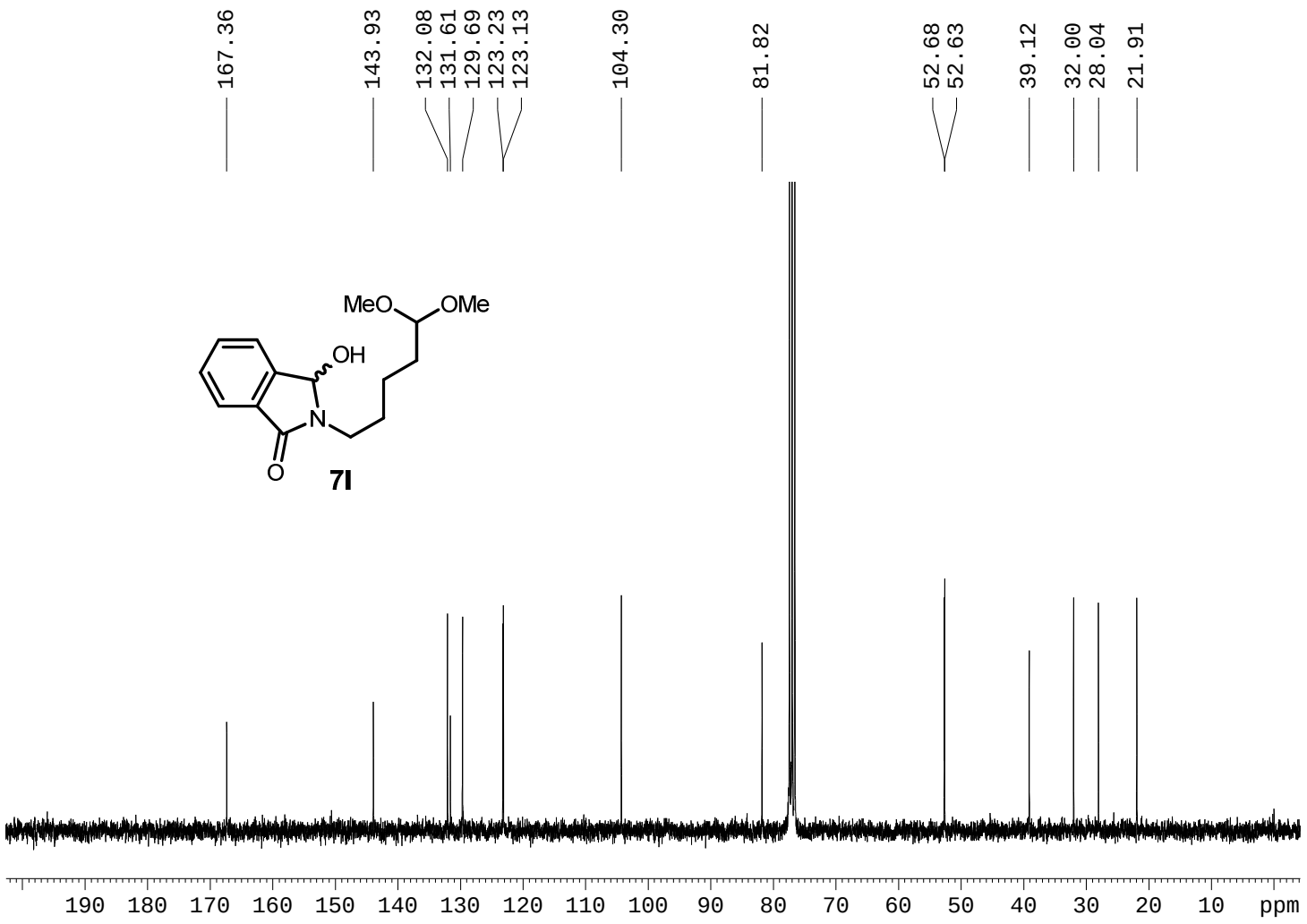
^{1}H NMR of compound **SI-37** (300 MHz, $CDCl_3$)



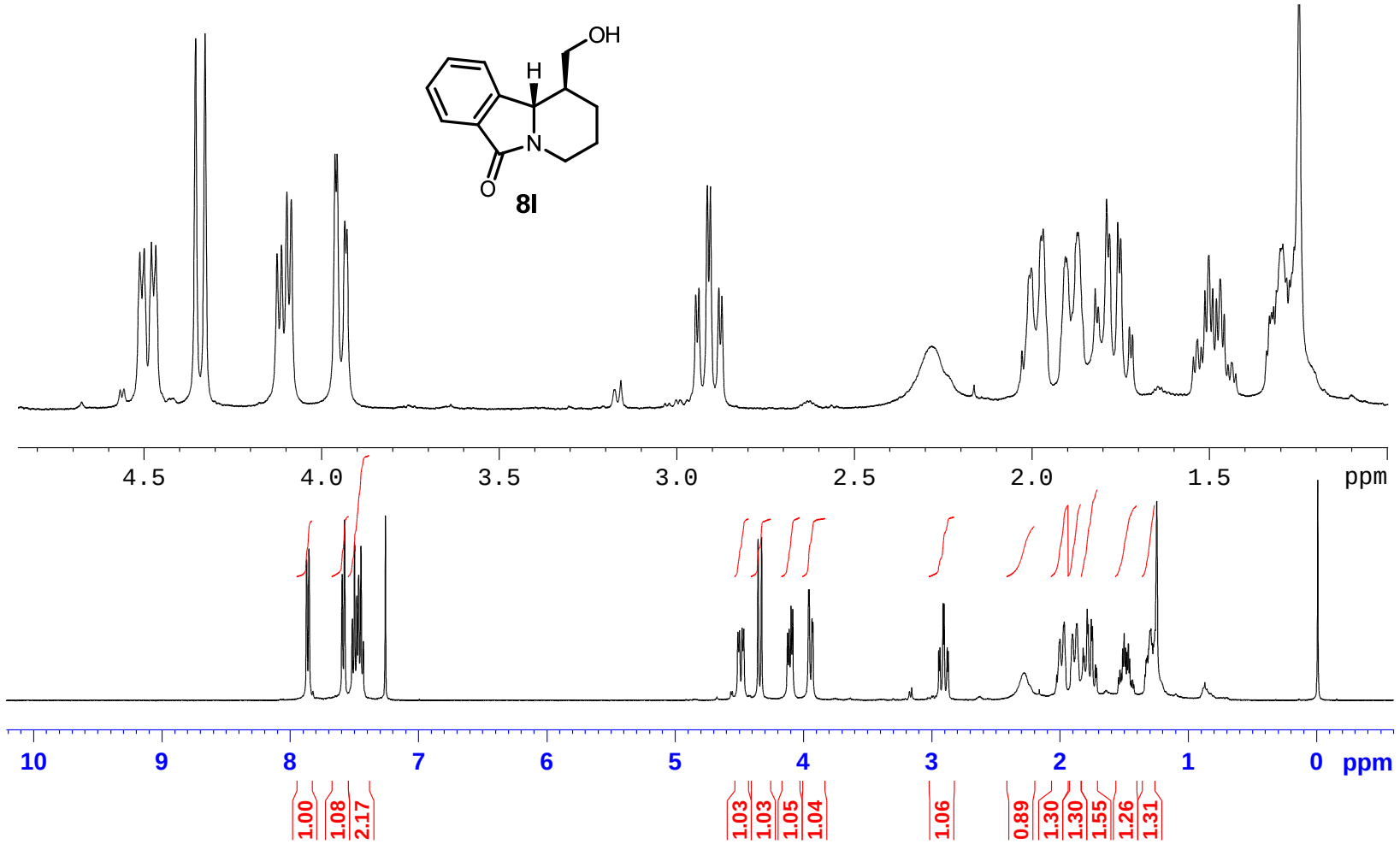
^{13}C NMR of compound **SI-37** (75 MHz, $CDCl_3$)



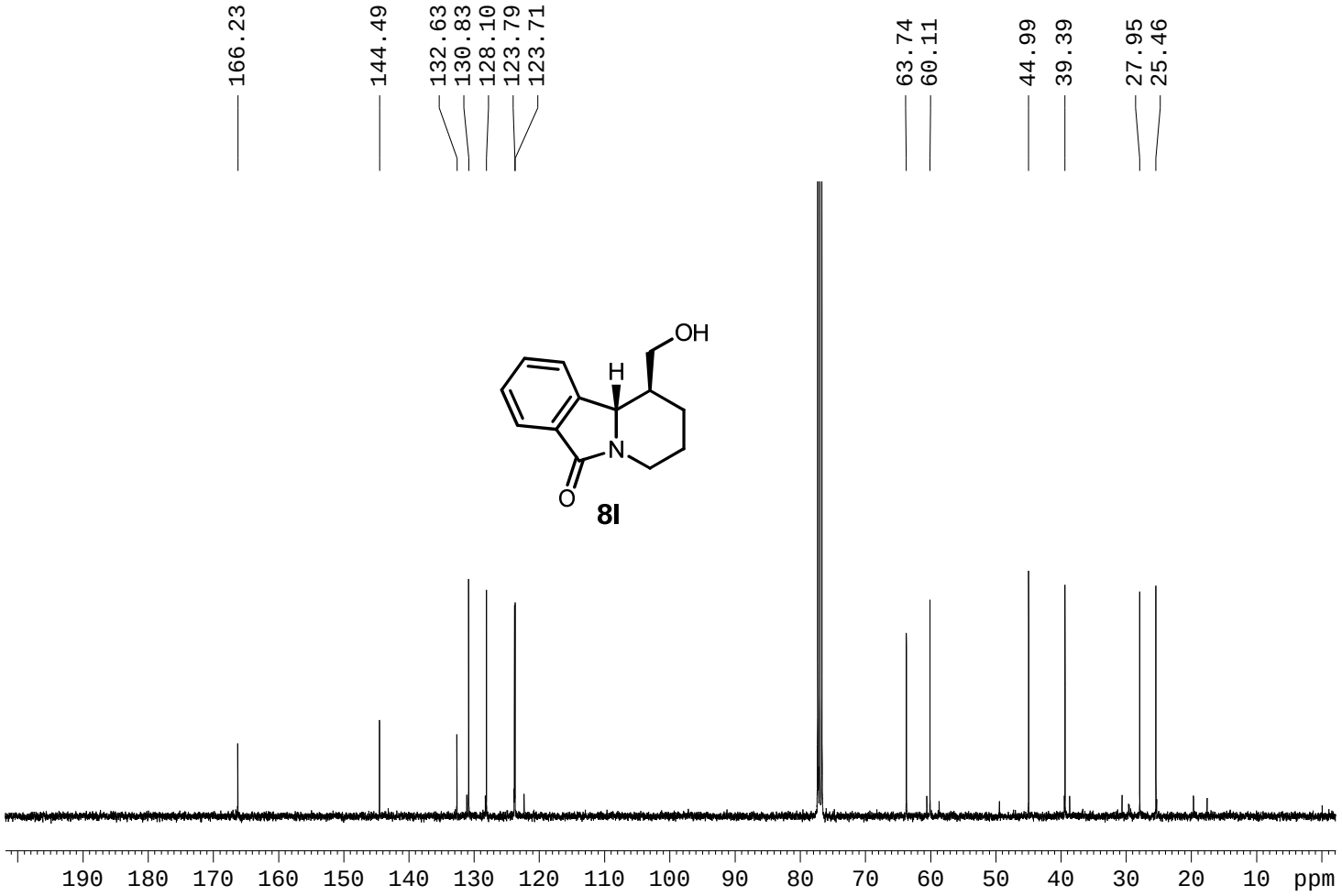
^{1}H NMR of compound **7l** (300 MHz, $CDCl_3$)



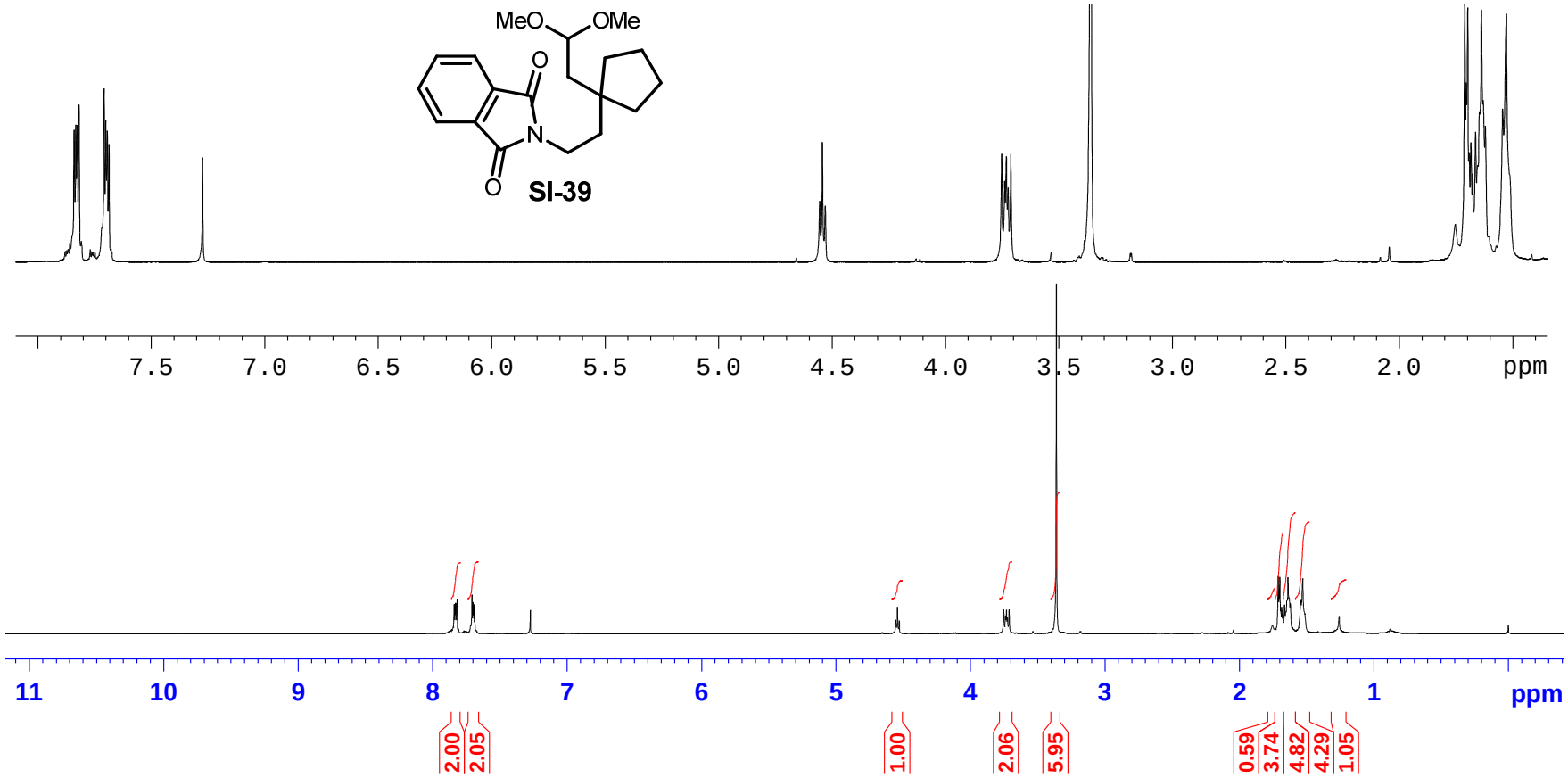
^{13}C NMR of compound **7l** (75 MHz, $CDCl_3$)



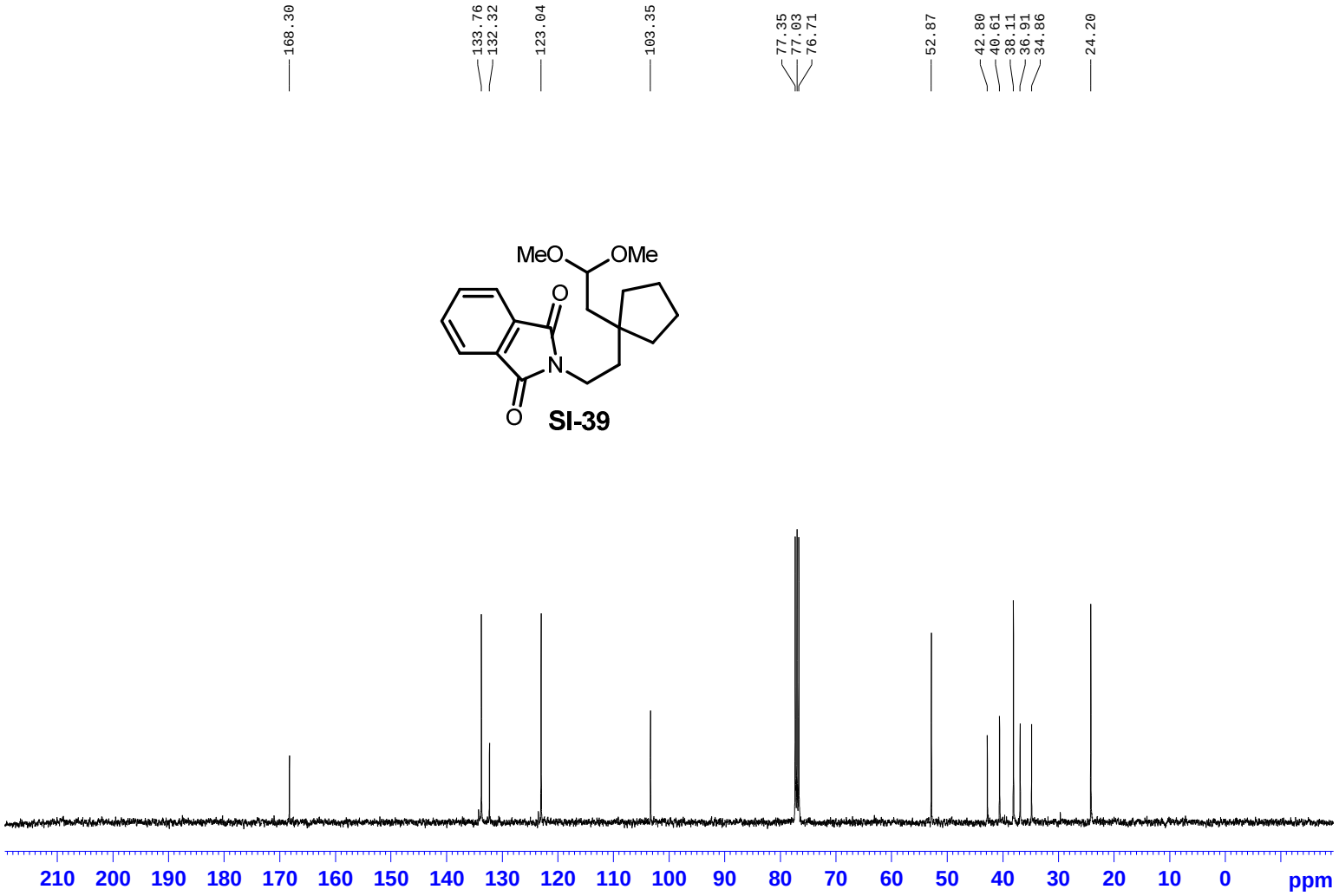
^{1}H NMR of compound **8l** (400 MHz, $CDCl_3$)



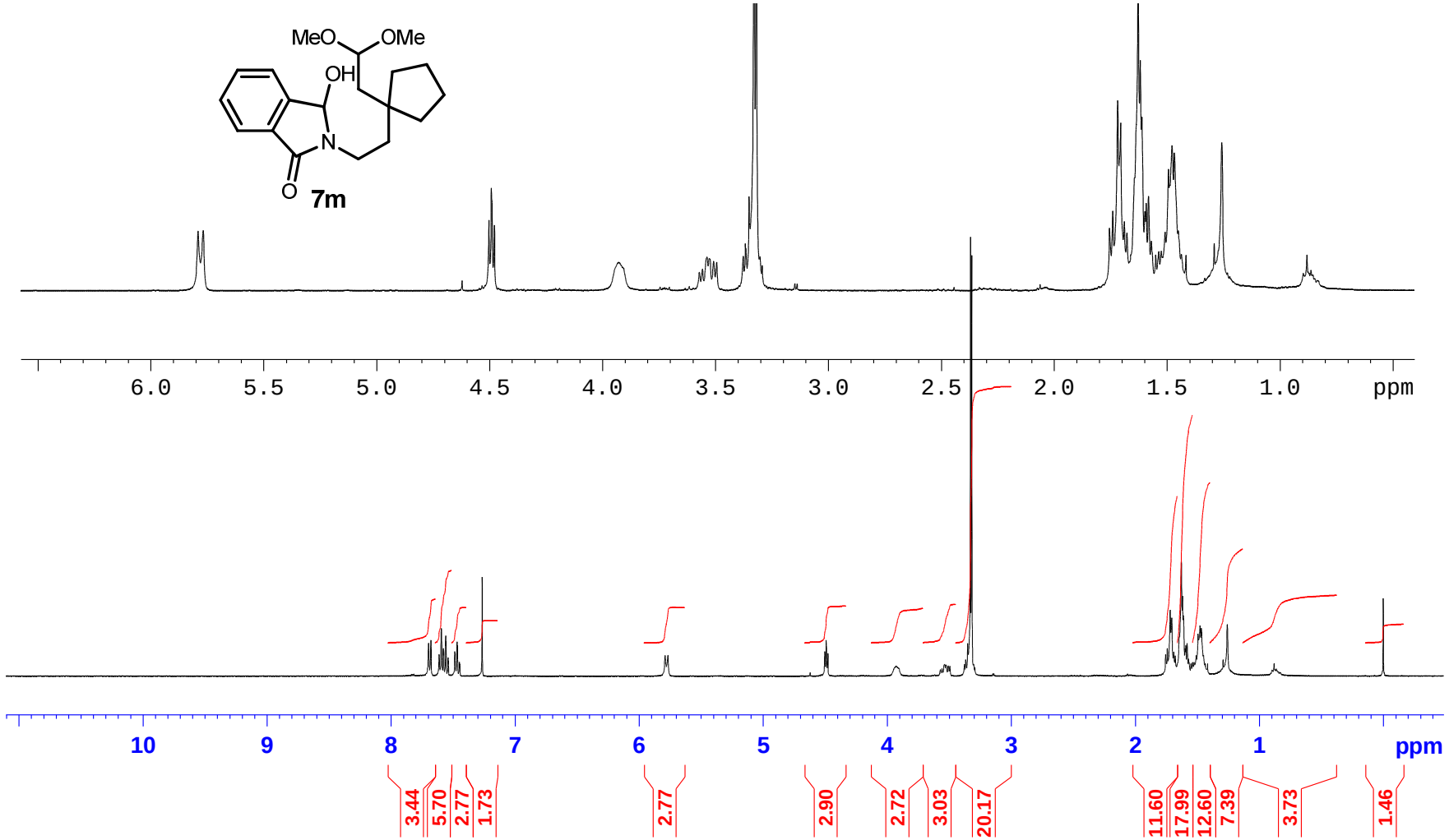
^{13}C NMR of compound **8l** (100 MHz, $CDCl_3$)



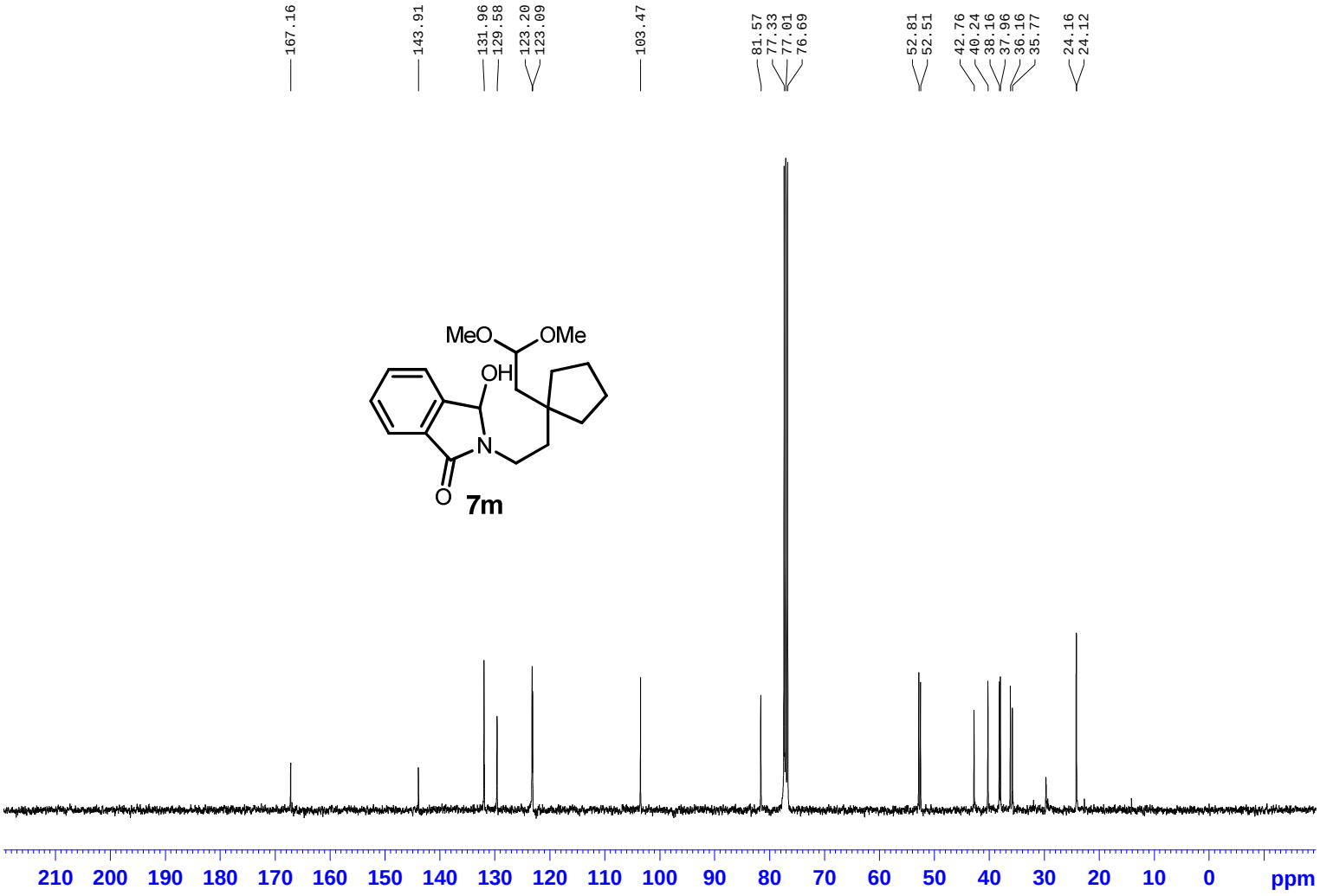
^{1}H NMR of compound **SI-39** (400 MHz, $CDCl_3$)



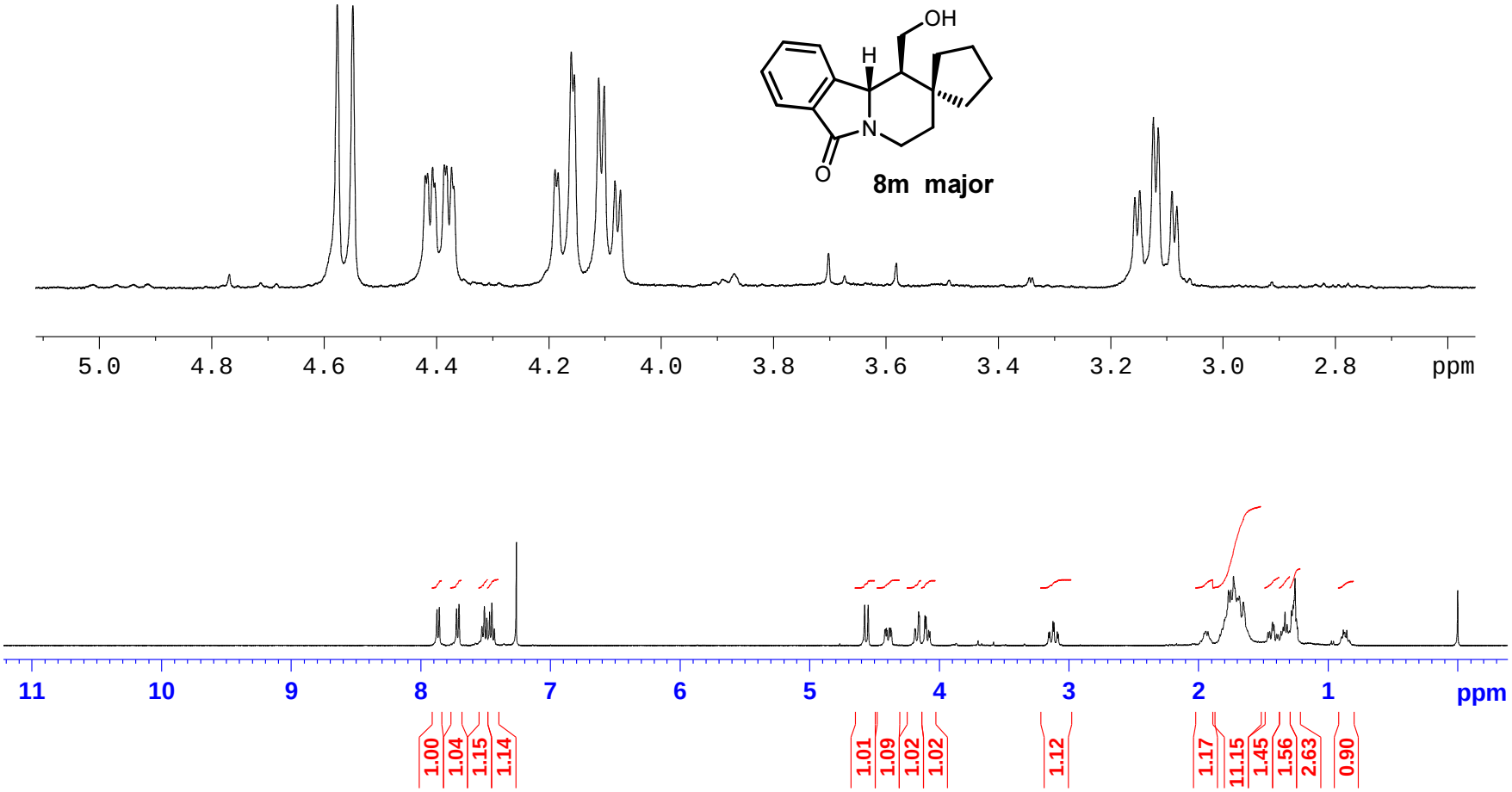
^{13}C NMR of compound **SI-39** (100 MHz, $CDCl_3$)



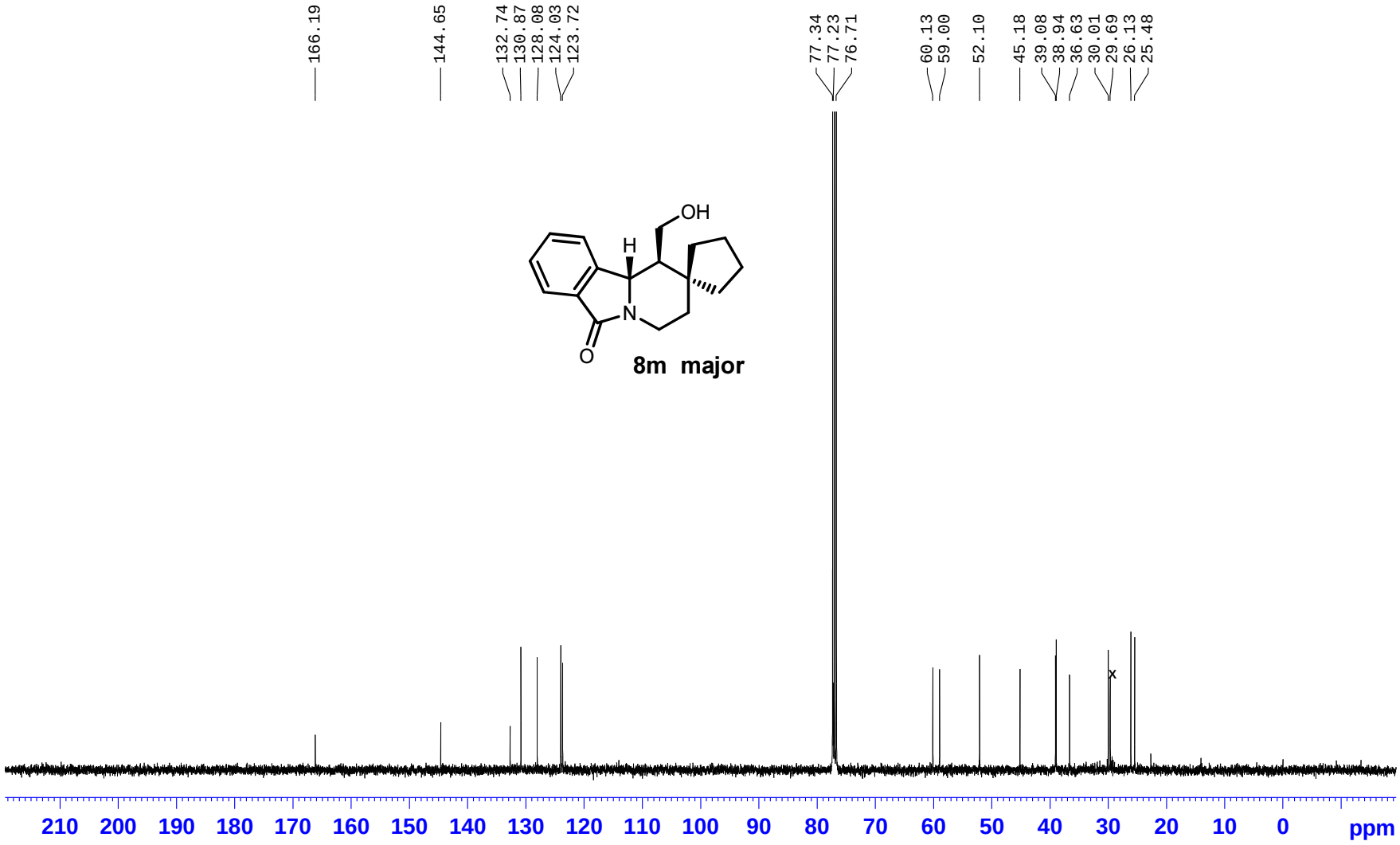
^{1}H NMR of compound **7m** (400 MHz, $CDCl_3$)



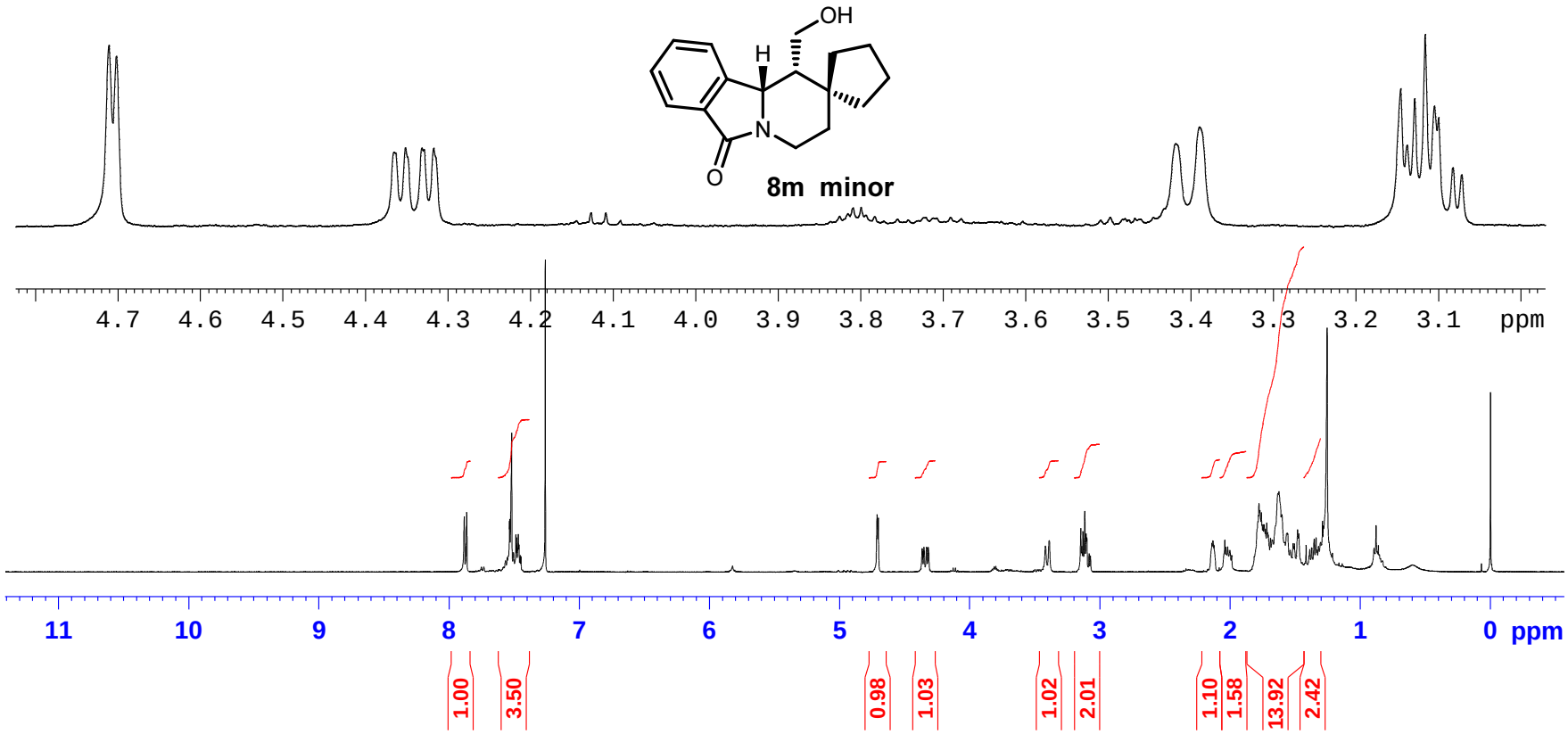
^{13}C NMR of compound **7m** (100 MHz, $CDCl_3$)



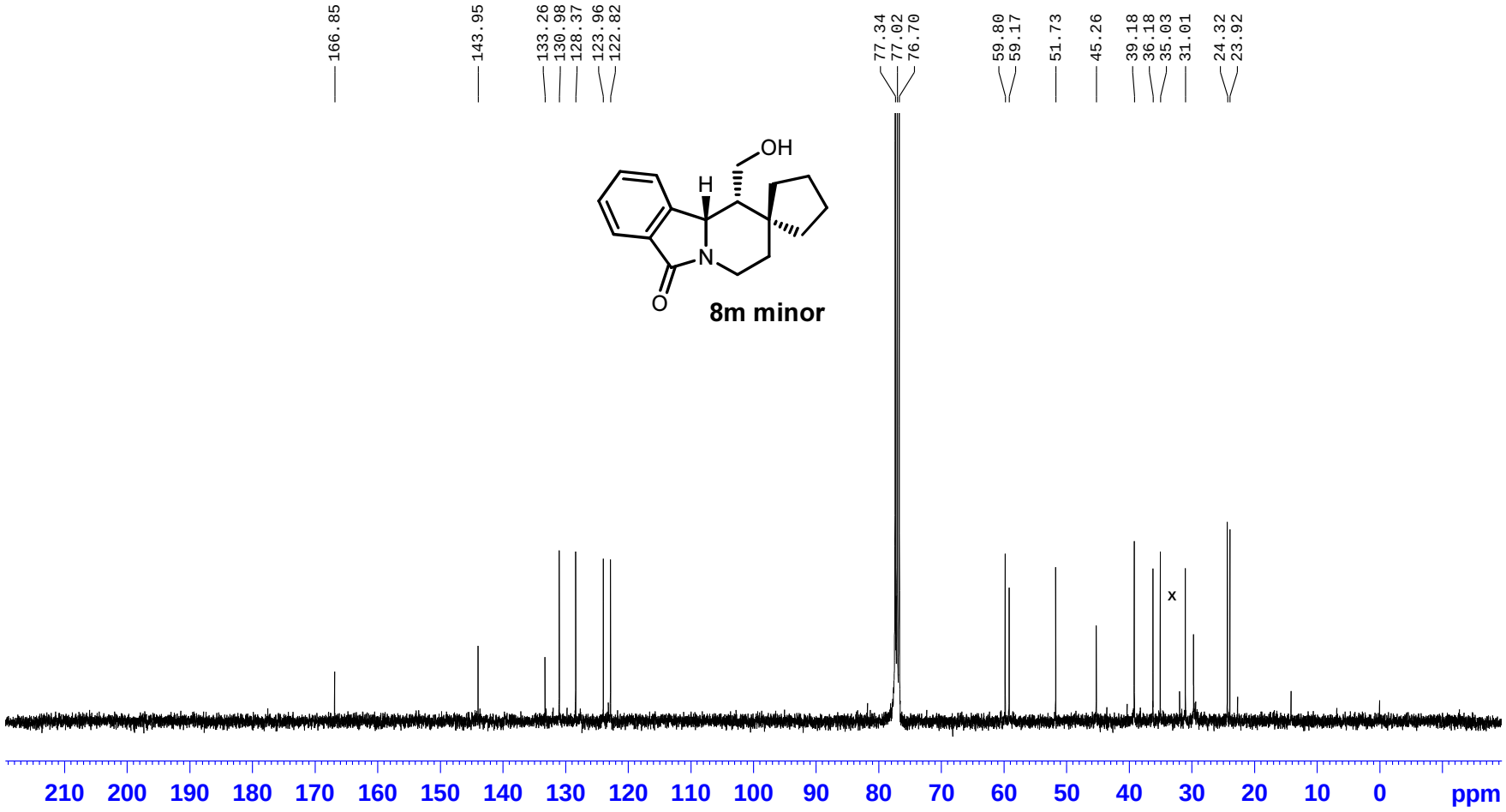
^{1}H NMR of compound **8m major** (400 MHz, $CDCl_3$)



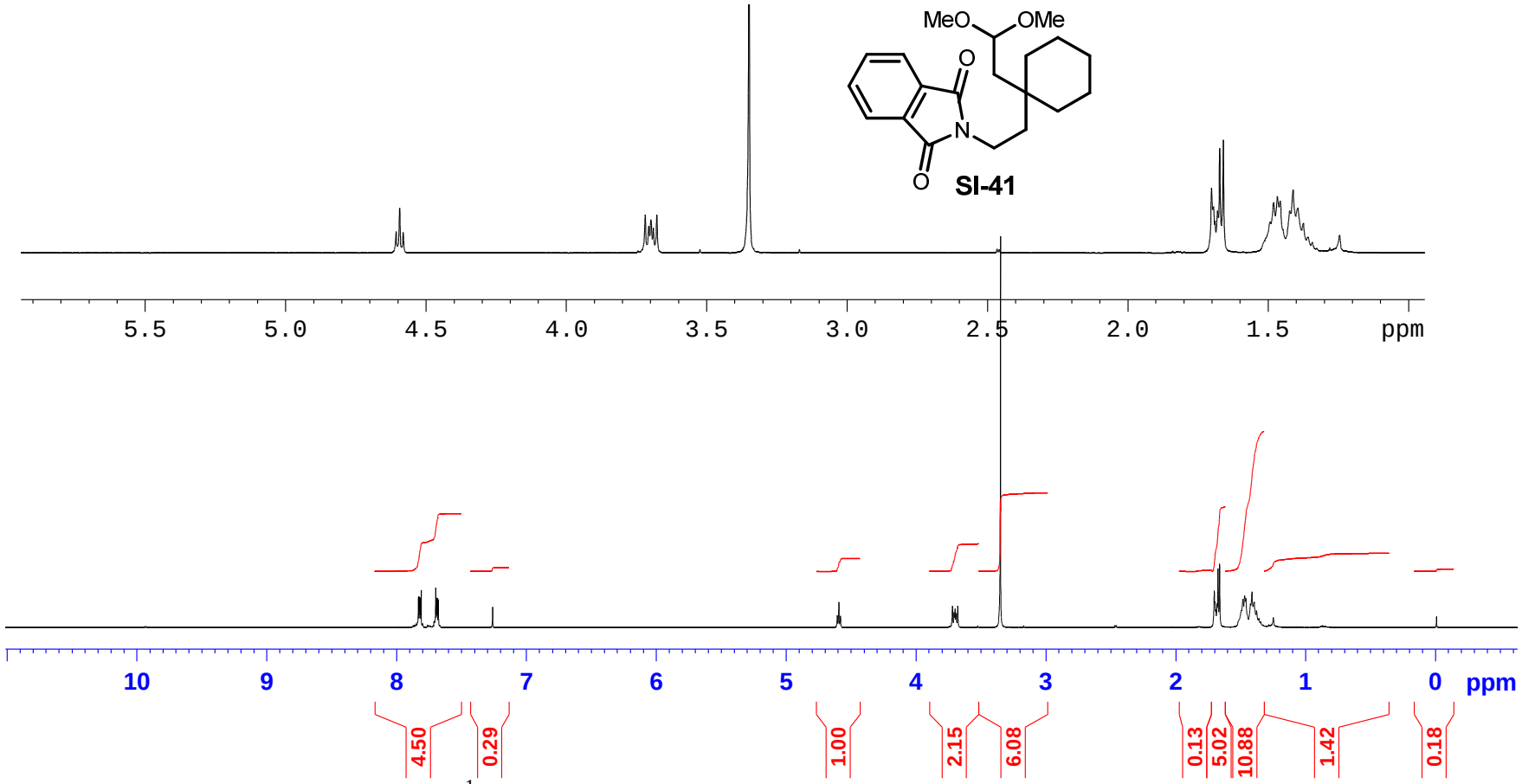
^{13}C NMR of compound **8m major** (100 MHz, $CDCl_3$)



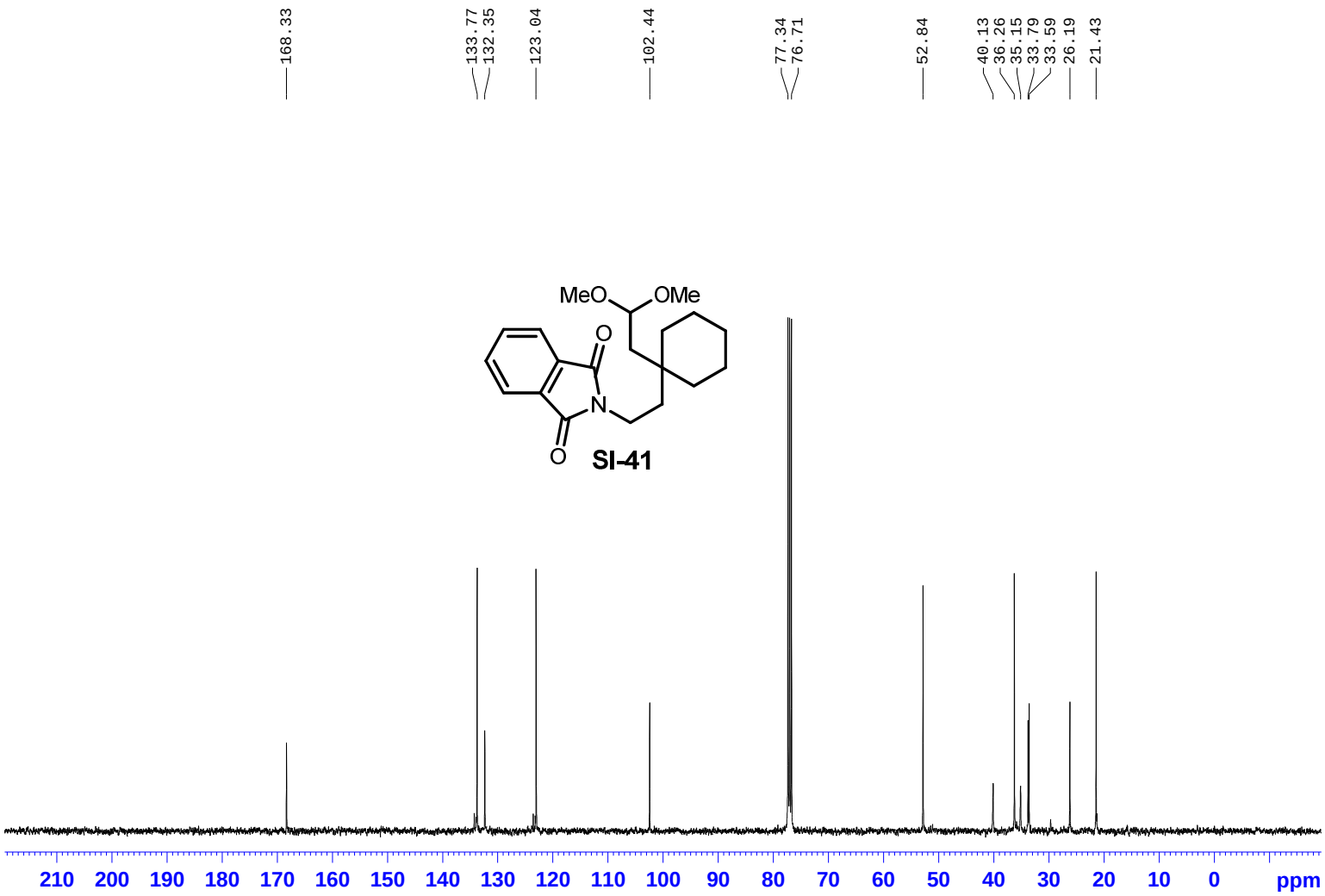
^{1}H NMR of compound **8m-minor** (400 MHz, $CDCl_3$)



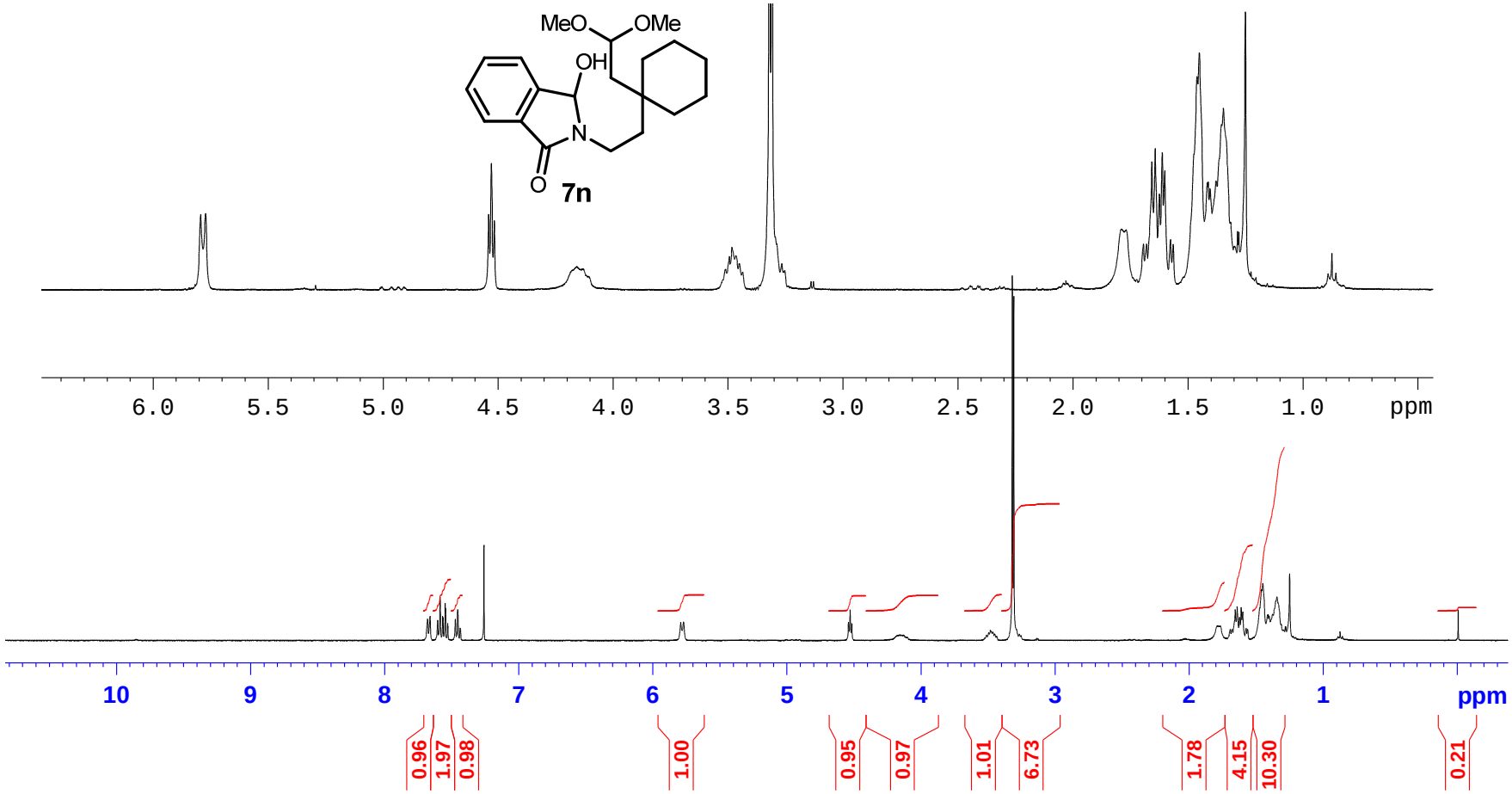
^{13}C NMR of compound **8m-minor** (100 MHz, $CDCl_3$)



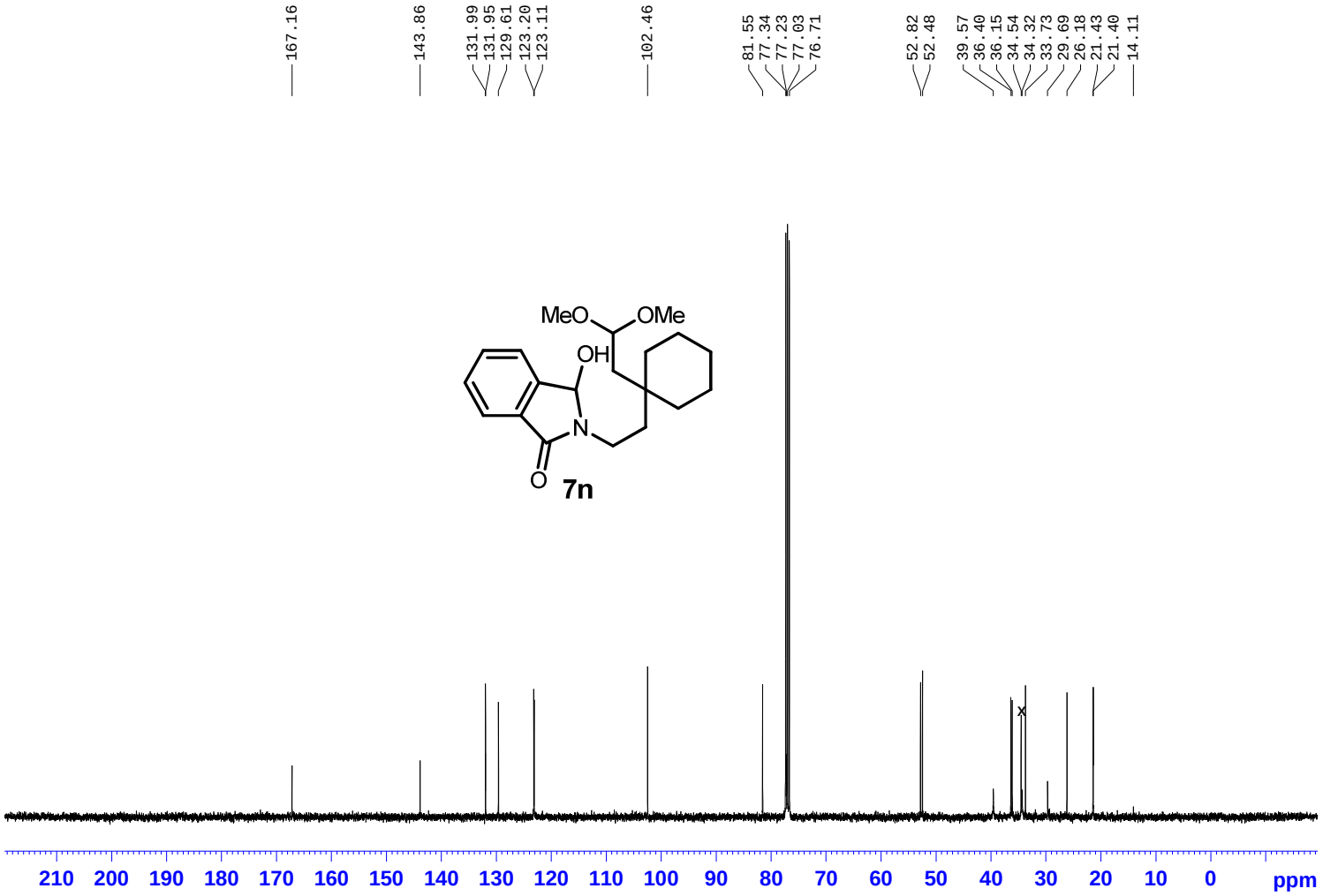
^{1}H NMR of compound **SI-41** (400 MHz, $CDCl_3$)



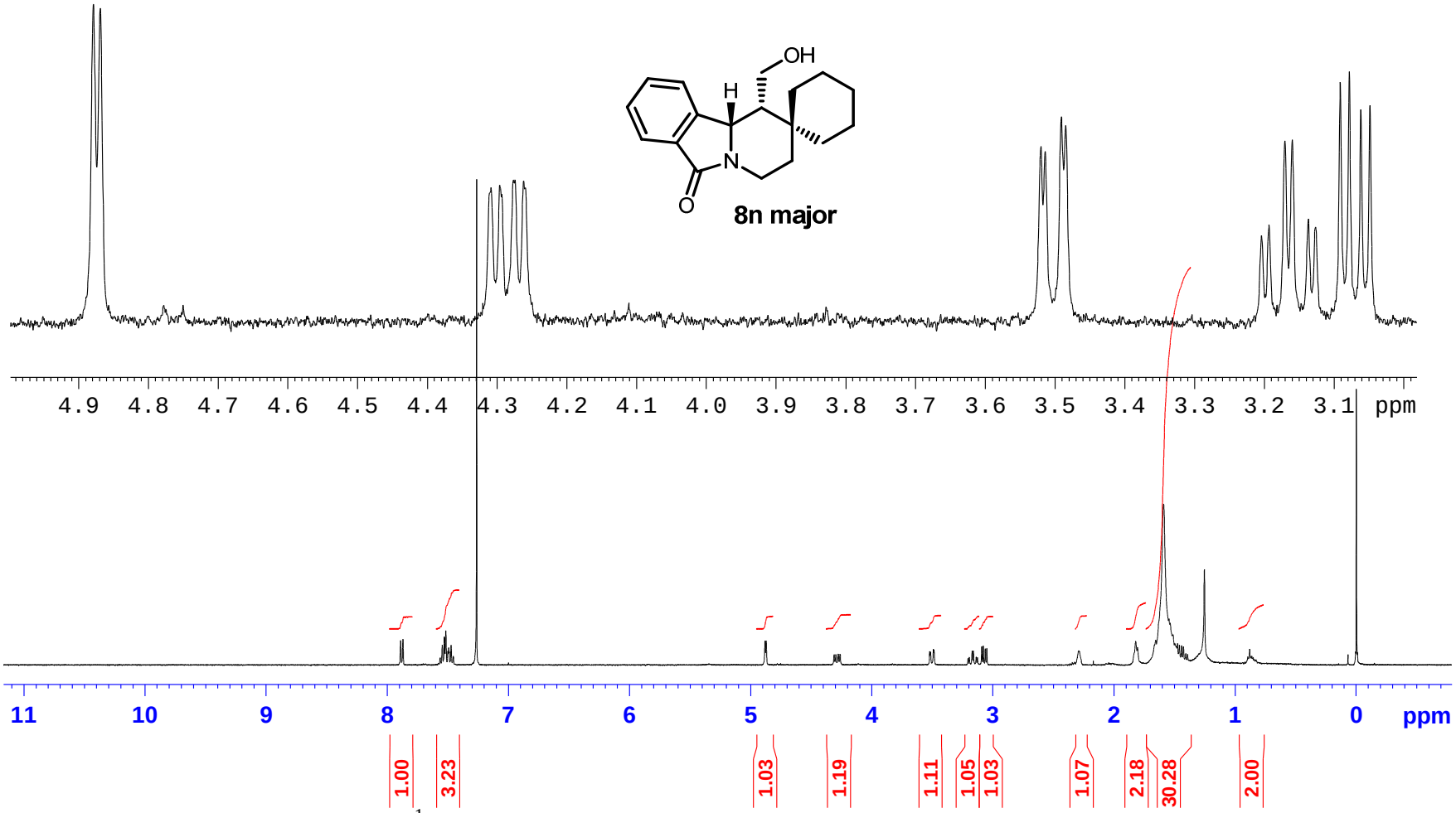
^{13}C NMR of compound **SI-41** (100 MHz, $CDCl_3$)



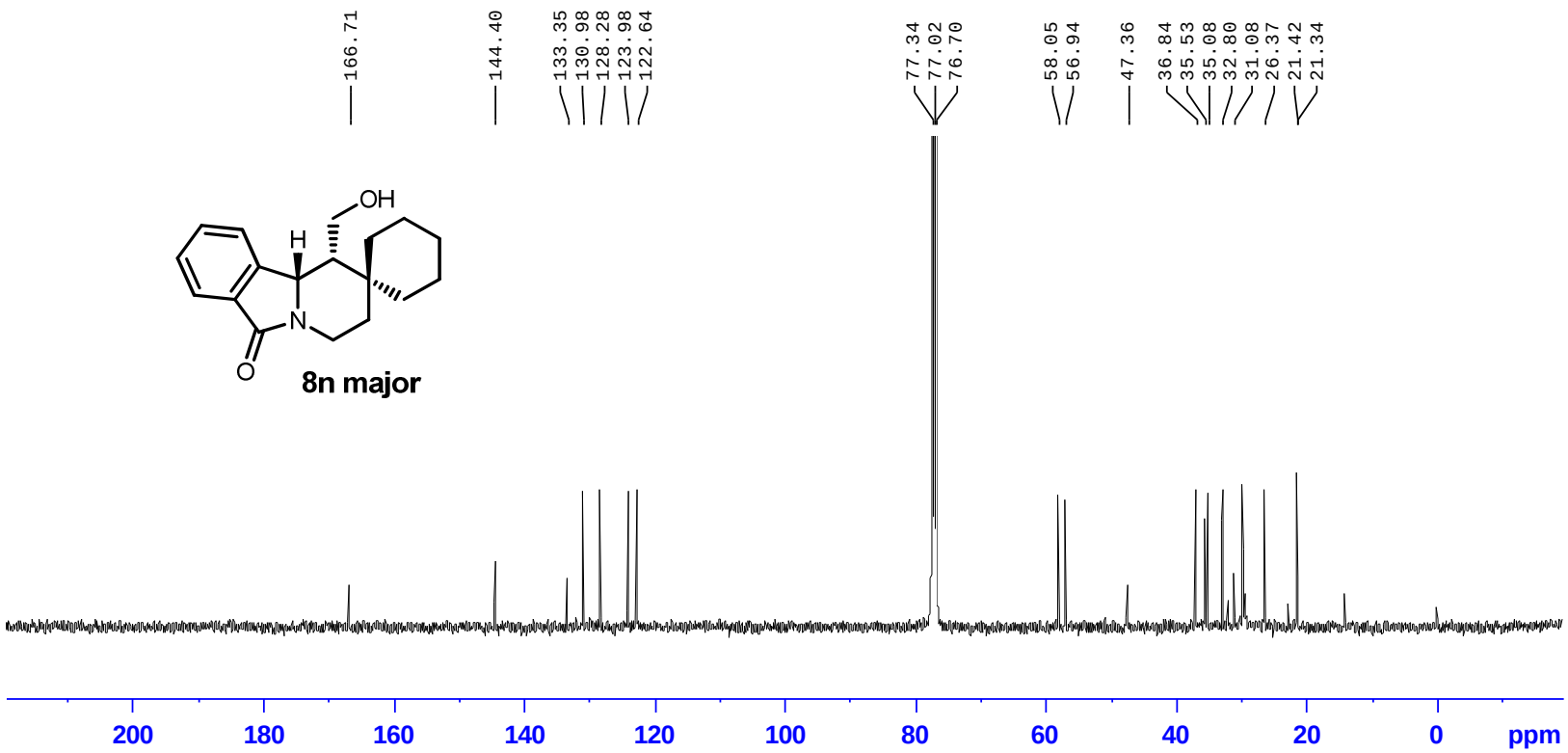
^{1}H NMR of compound **7n** (400 MHz, $CDCl_3$)



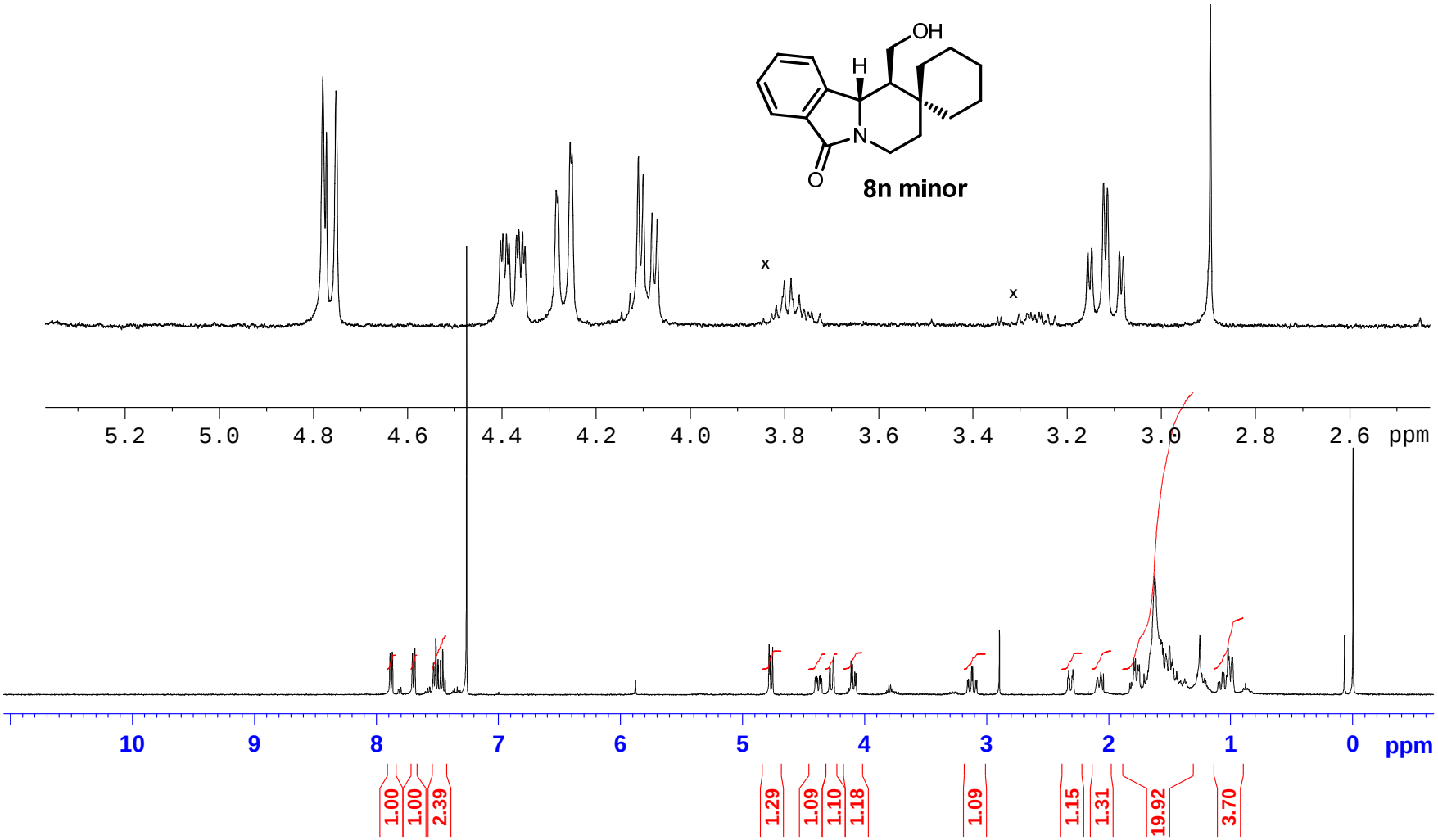
^{13}C NMR of compound **7n** (100 MHz, $CDCl_3$)



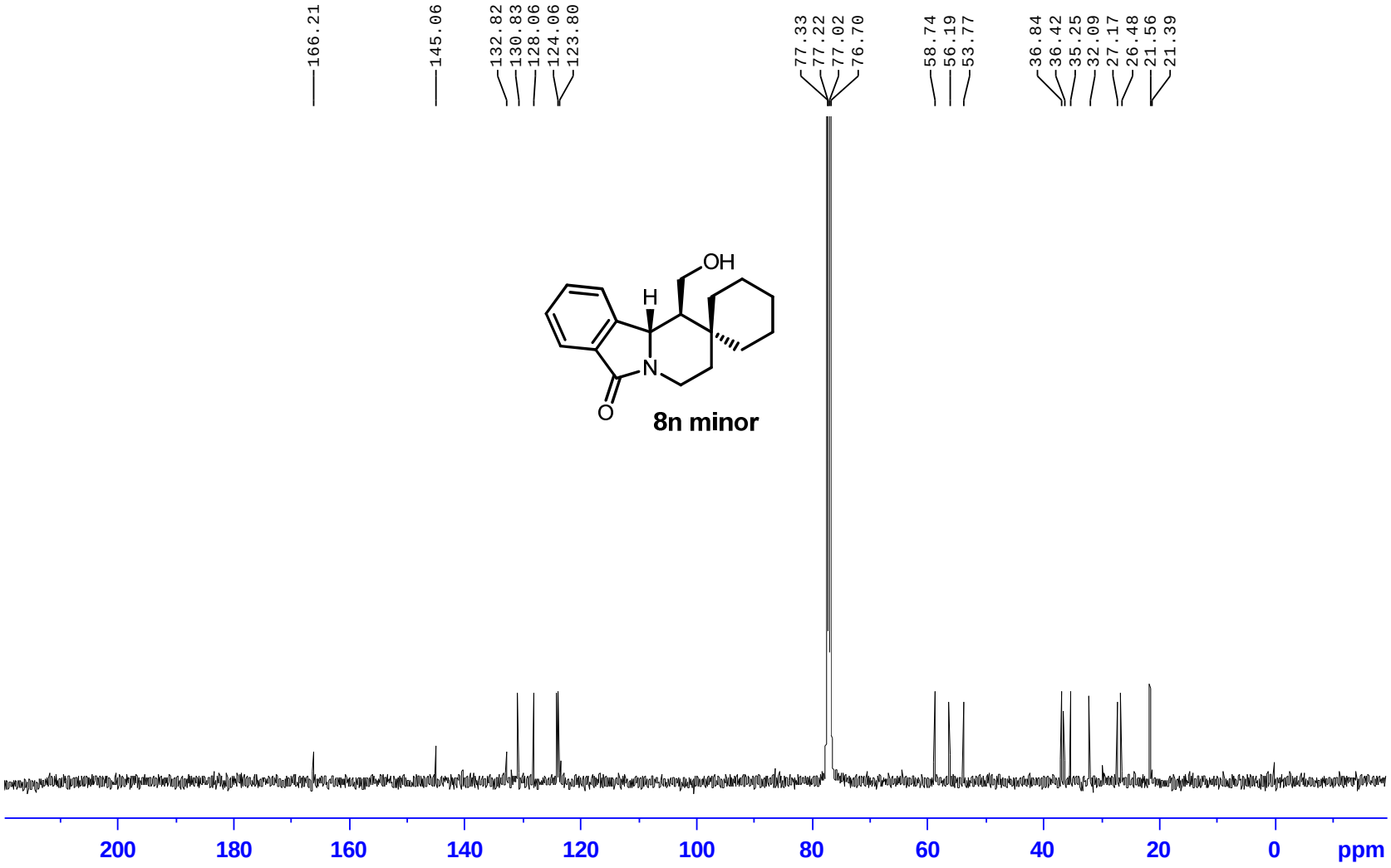
^{1}H NMR of compound **8n** (major) (400 MHz, $CDCl_3$)



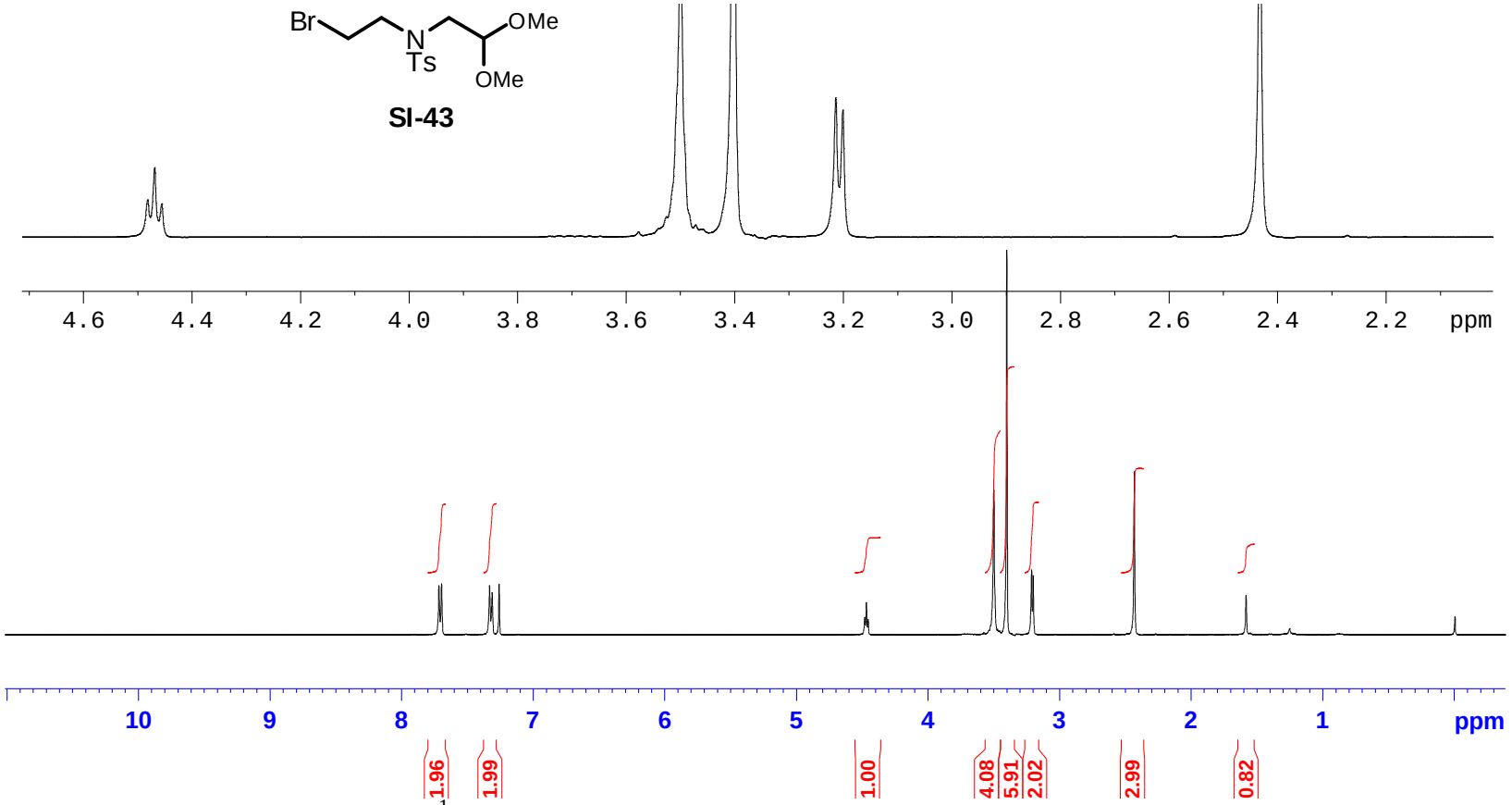
^{13}C NMR of compound **8n** (major) (100 MHz, $CDCl_3$)



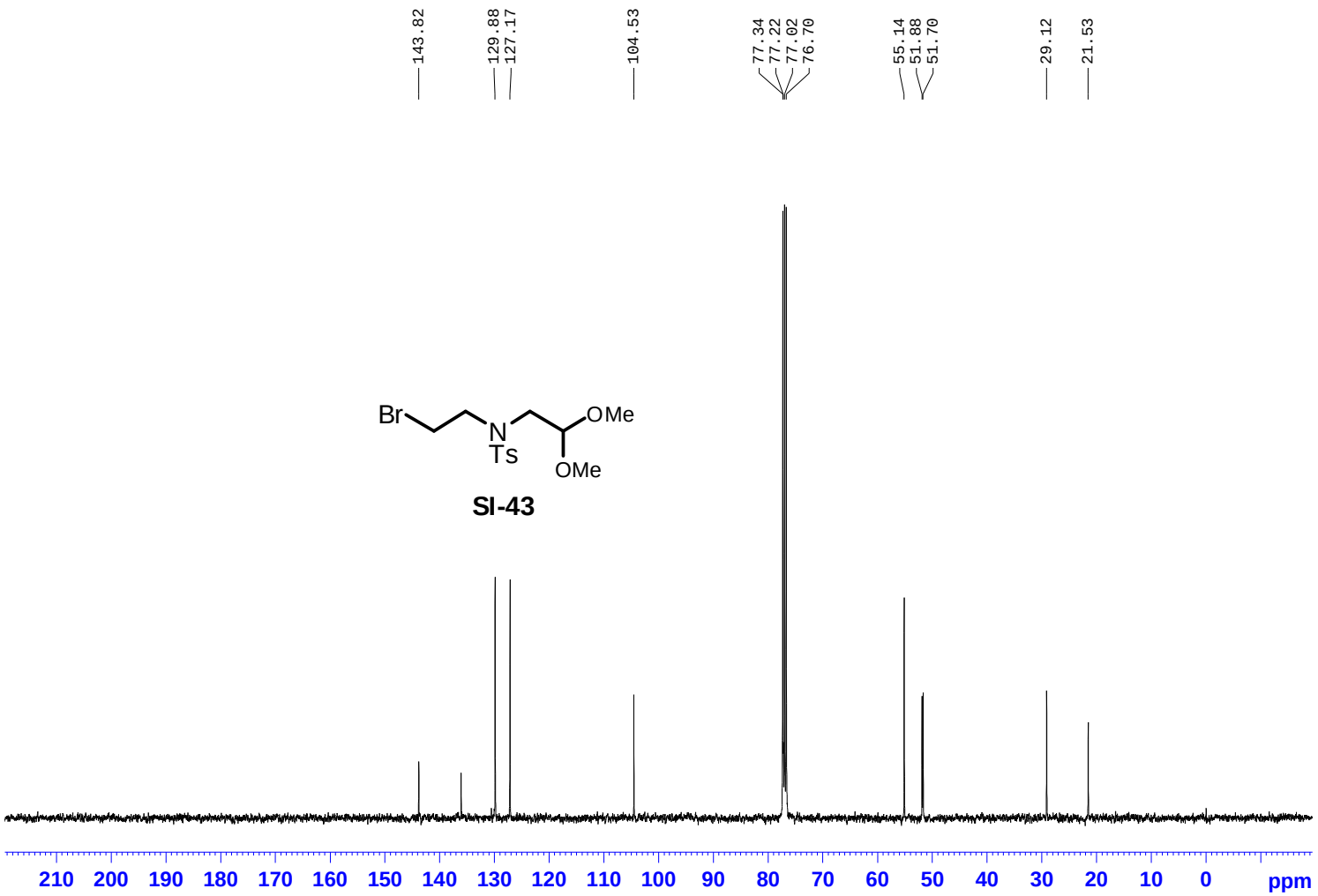
^{1}H NMR of compound **8n** (minor) (400 MHz, $CDCl_3$)



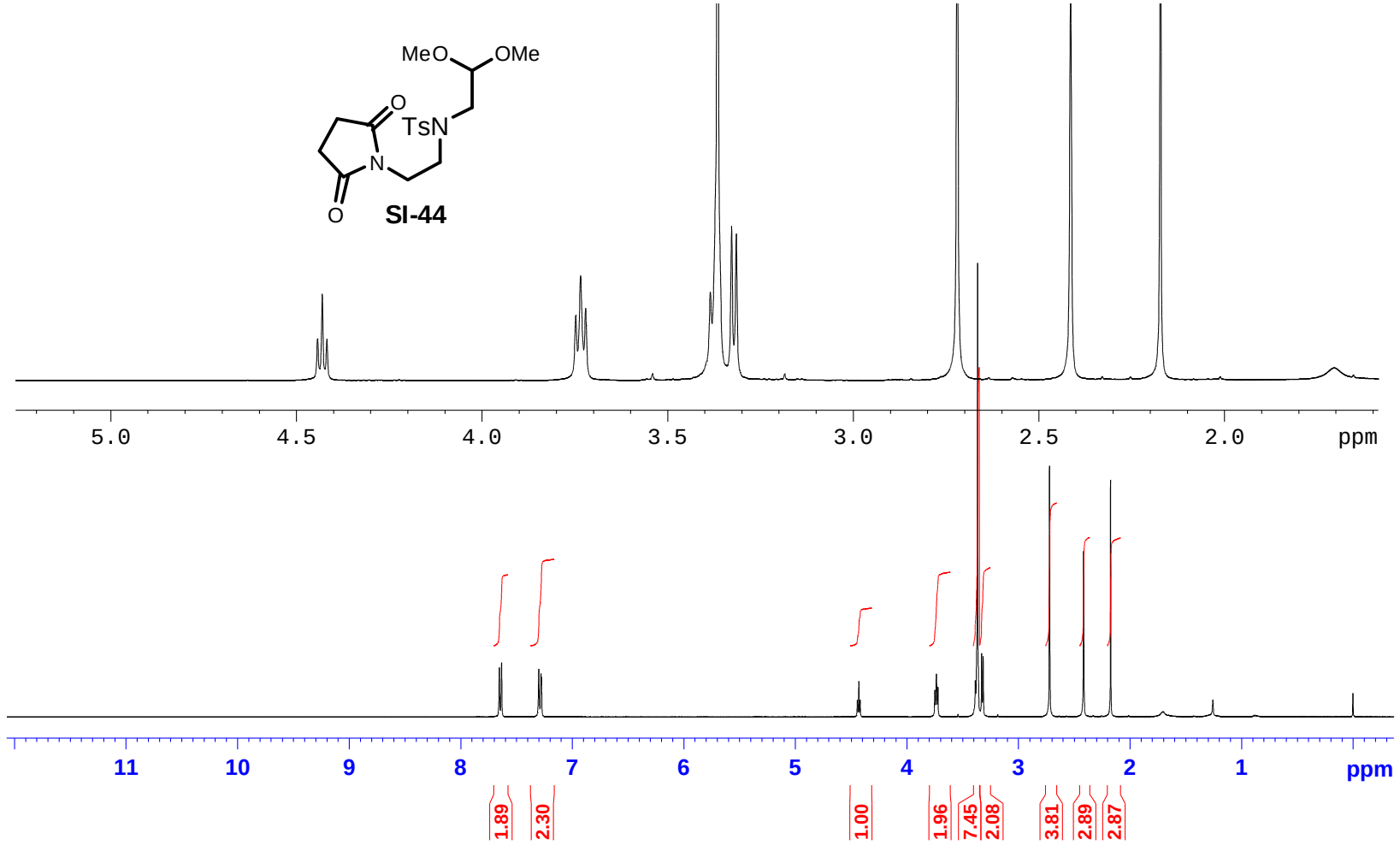
^{13}C NMR of compound **8n minor** (100 MHz, $CDCl_3$)



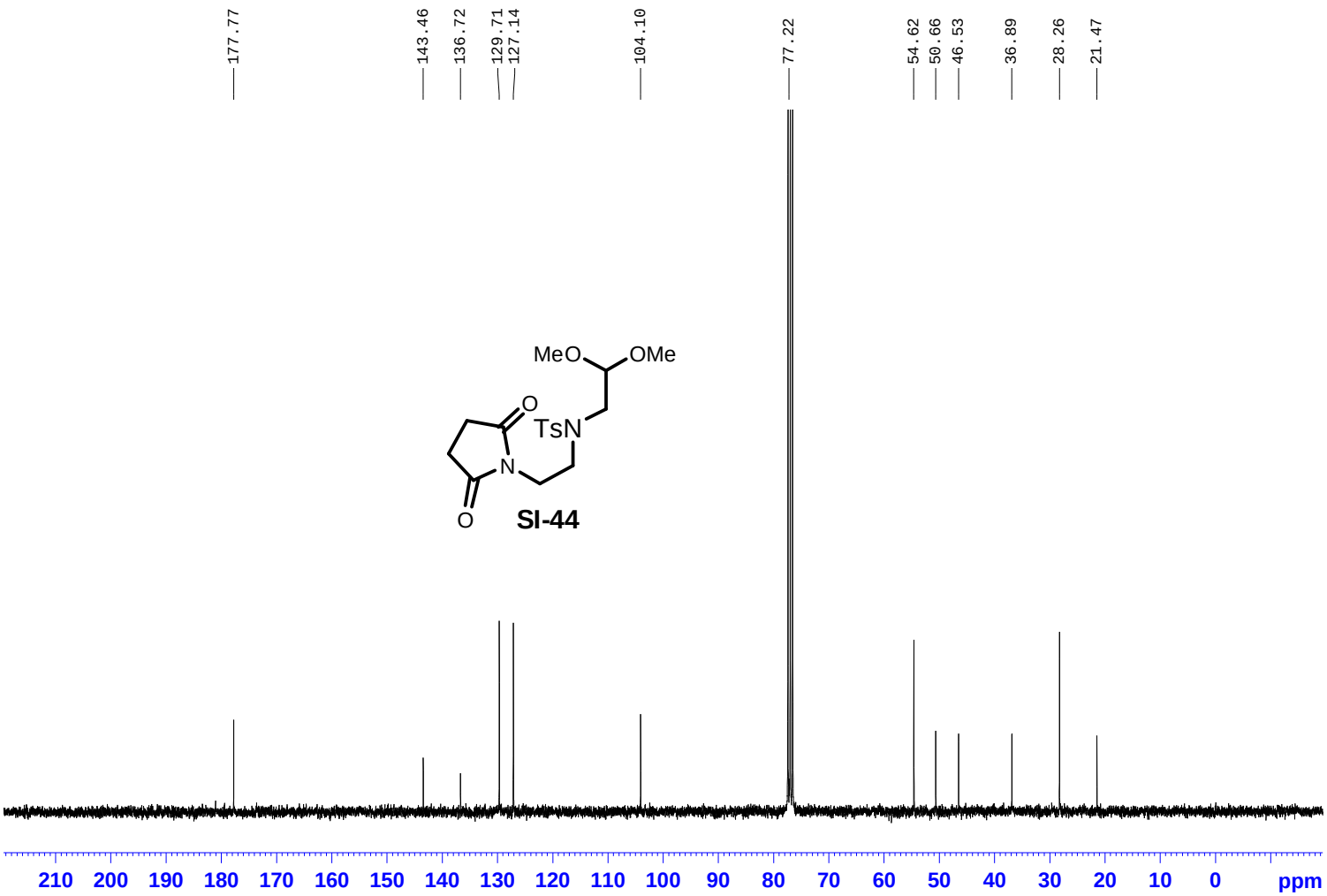
^{1}H NMR of compound **SI-43** (400 MHz, $CDCl_3$)



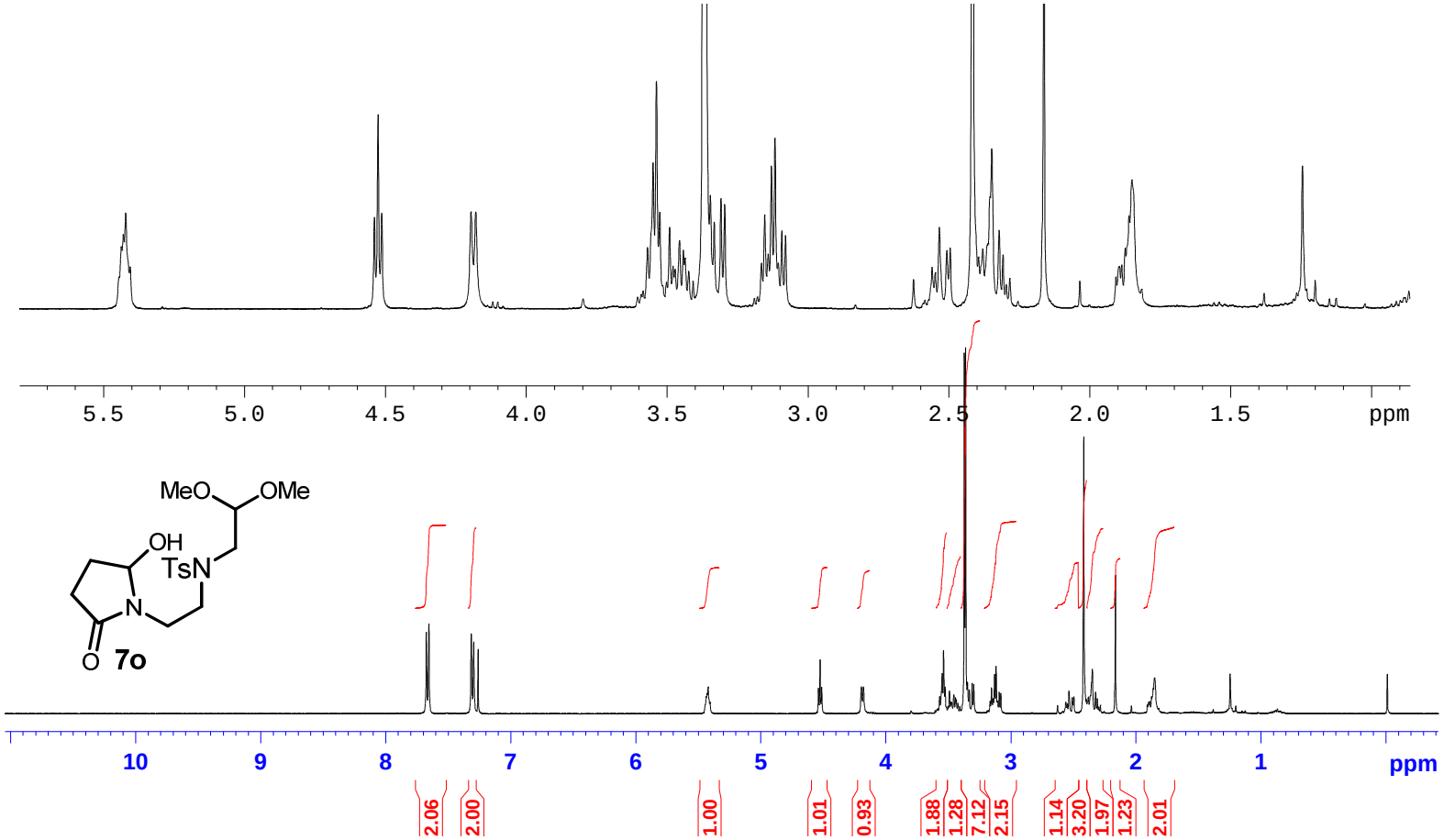
^{13}C NMR of compound **SI-43** (100 MHz, $CDCl_3$)



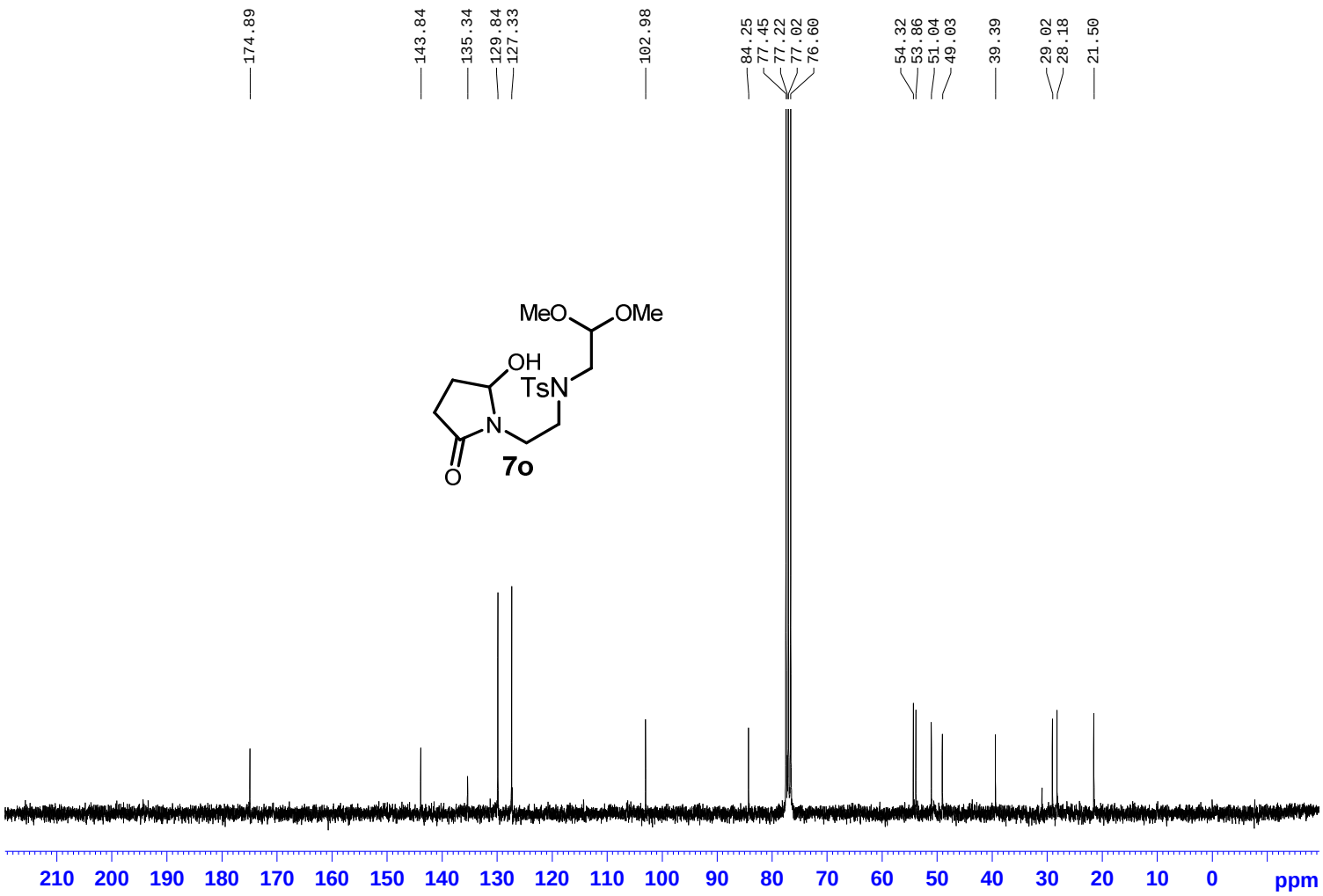
^{1}H NMR of compound **SI-44** (400 MHz, $CDCl_3$)



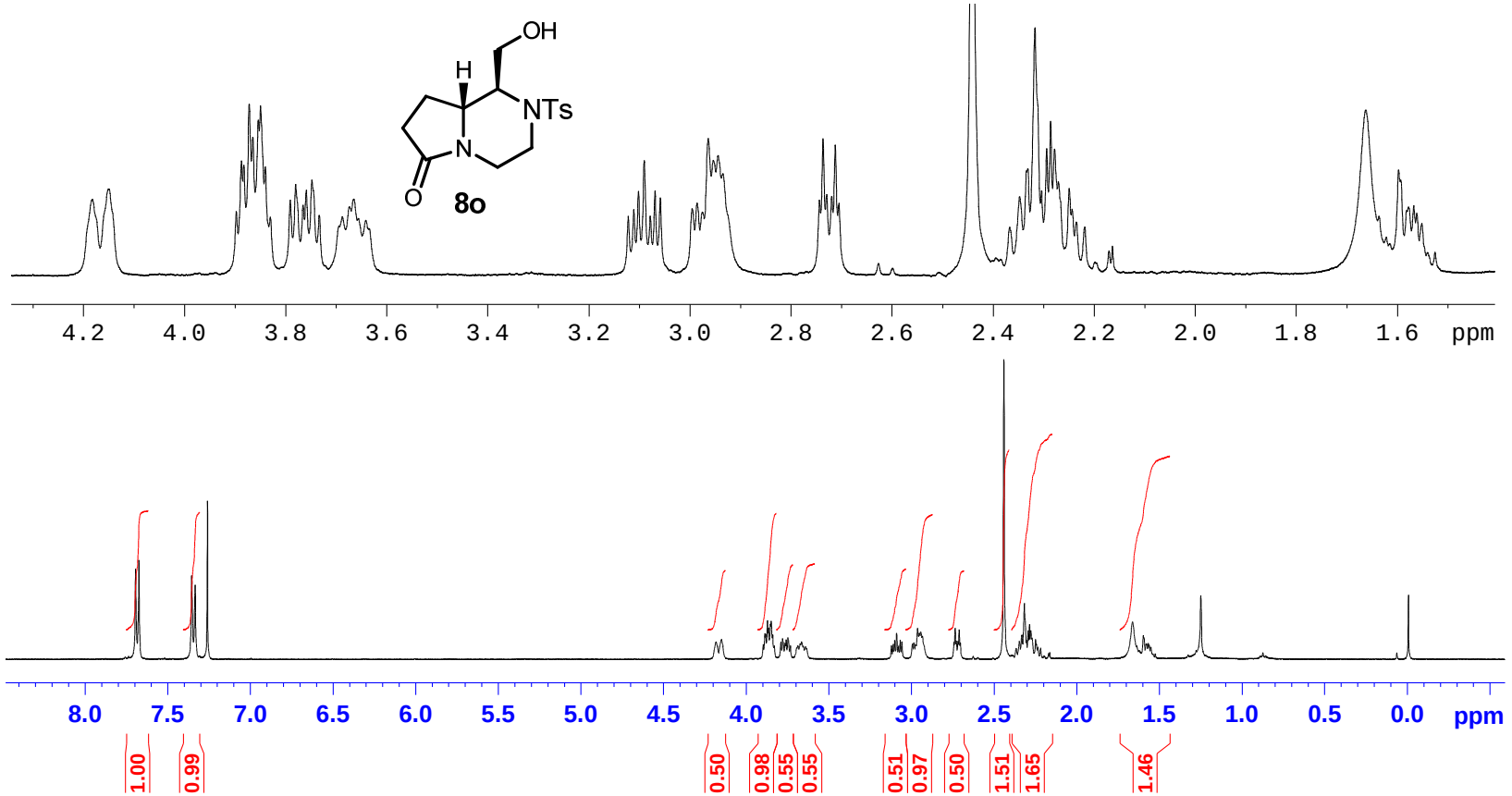
^{13}C NMR of compound **SI-44** (100 MHz, $CDCl_3$)



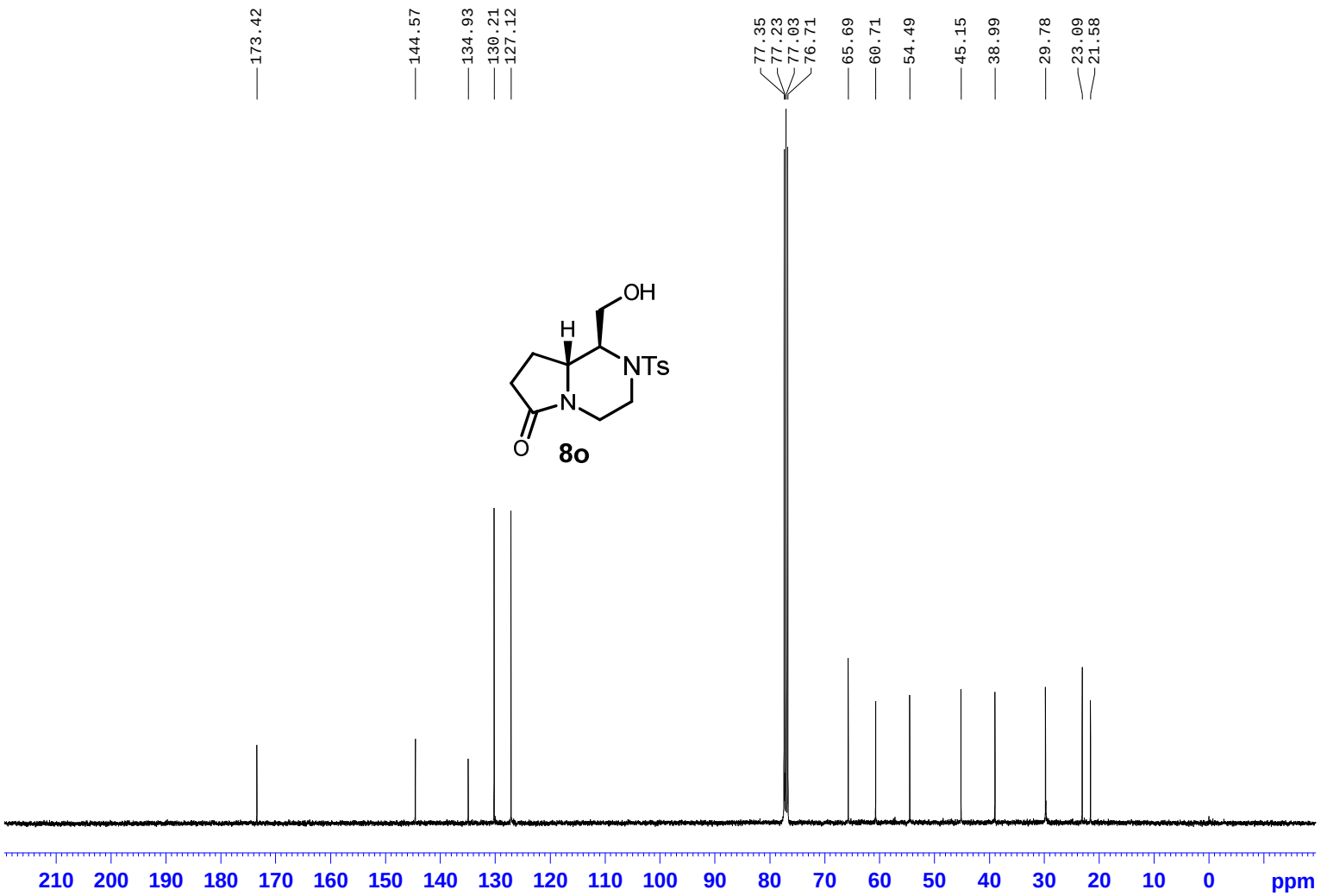
^{1}H NMR of compound **7o** (400 MHz, $CDCl_3$)



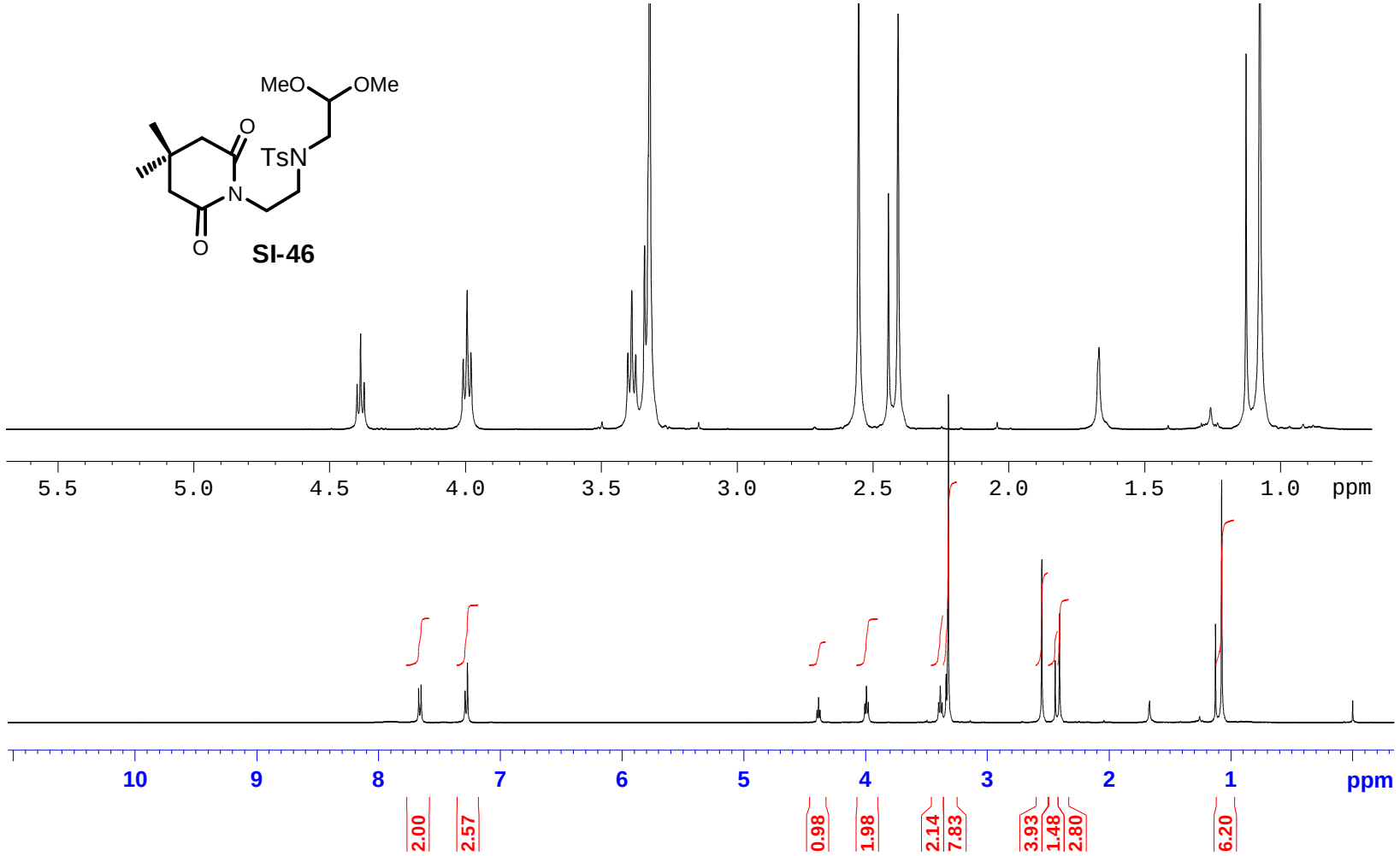
^{13}C NMR of compound **7o** (100 MHz, $CDCl_3$)



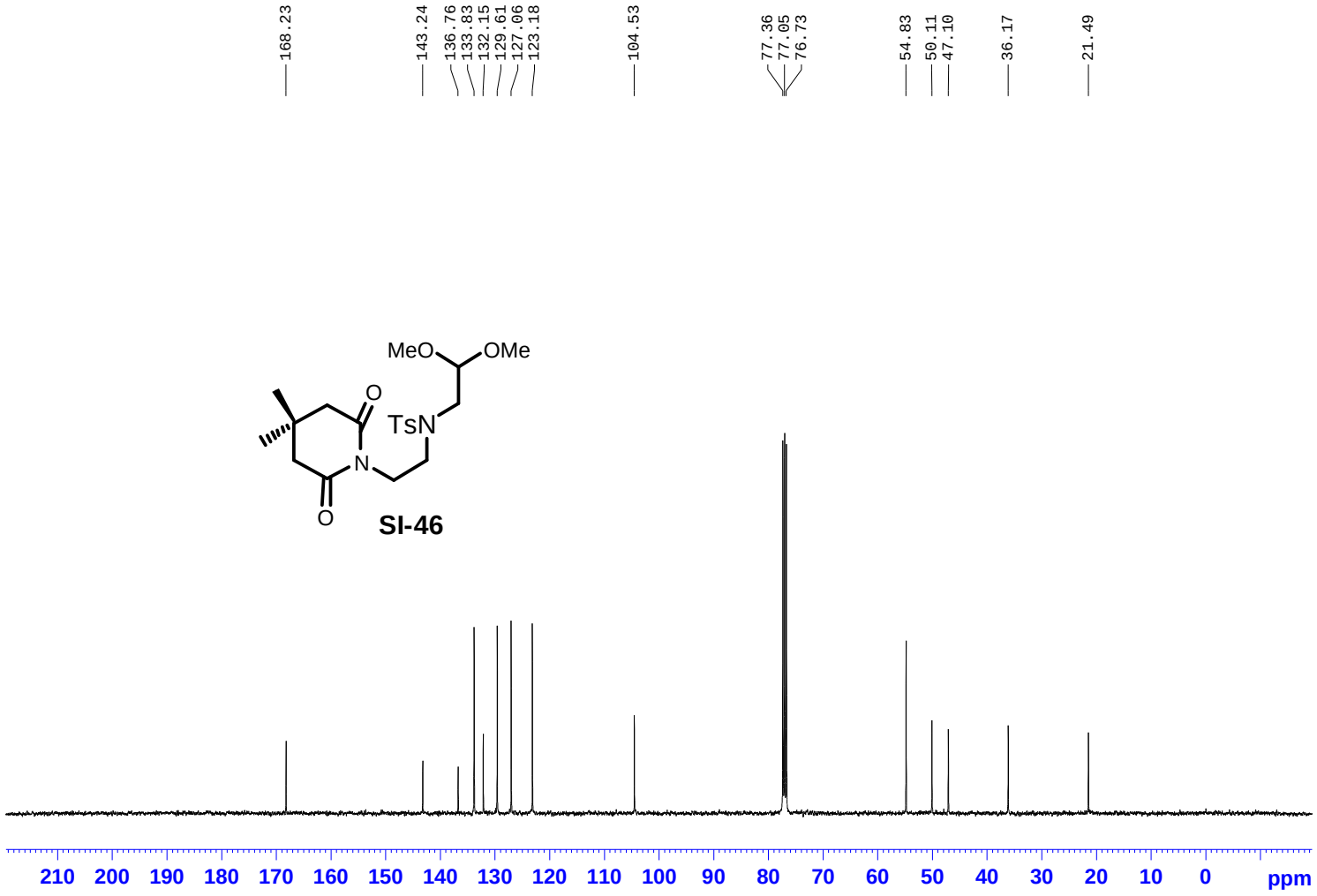
^{1}H NMR of compound **8o** (400 MHz, $CDCl_3$)



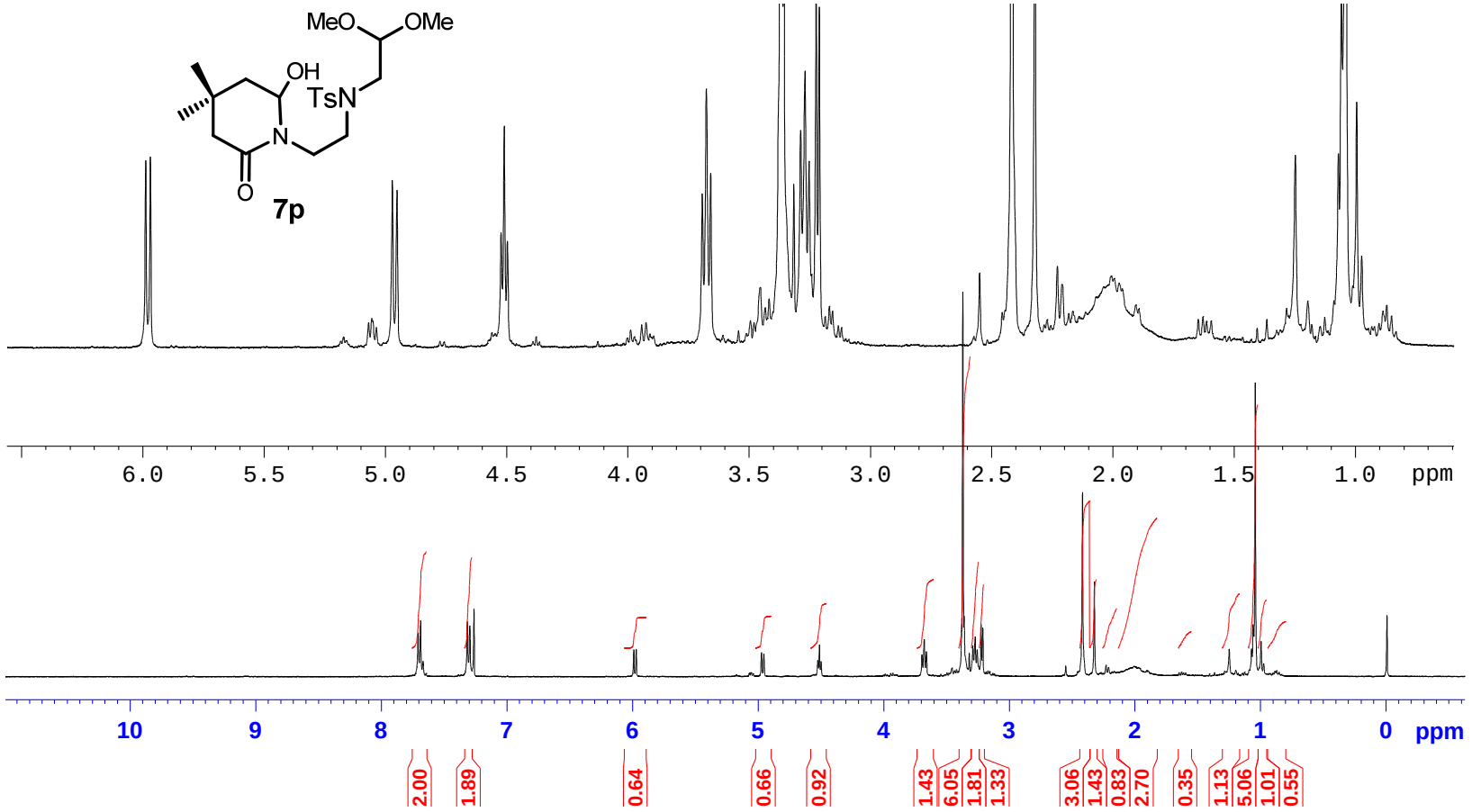
^{13}C NMR of compound **8o** (100 MHz, $CDCl_3$)



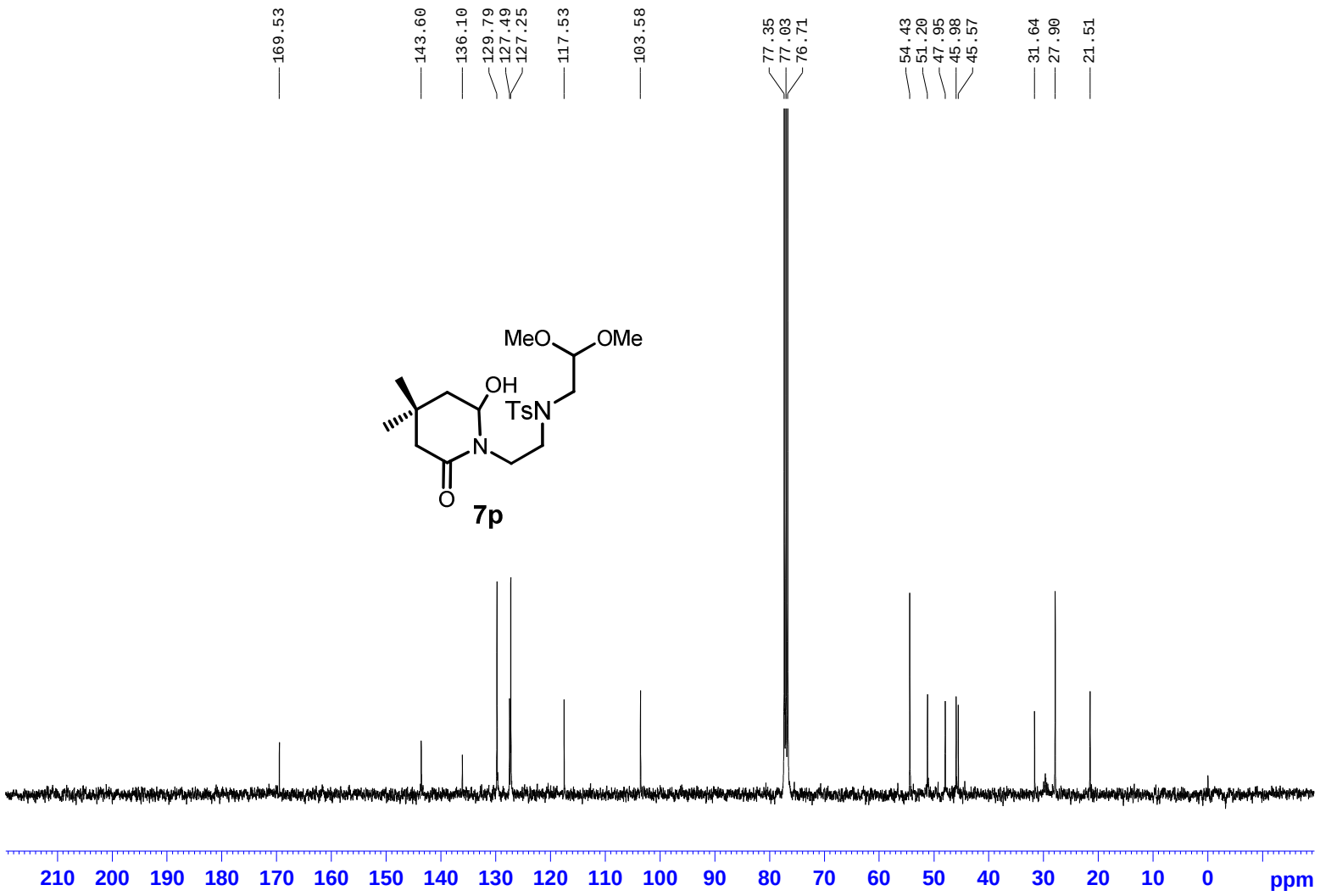
^{1}H NMR of compound **SI-46** (400 MHz, $CDCl_3$)



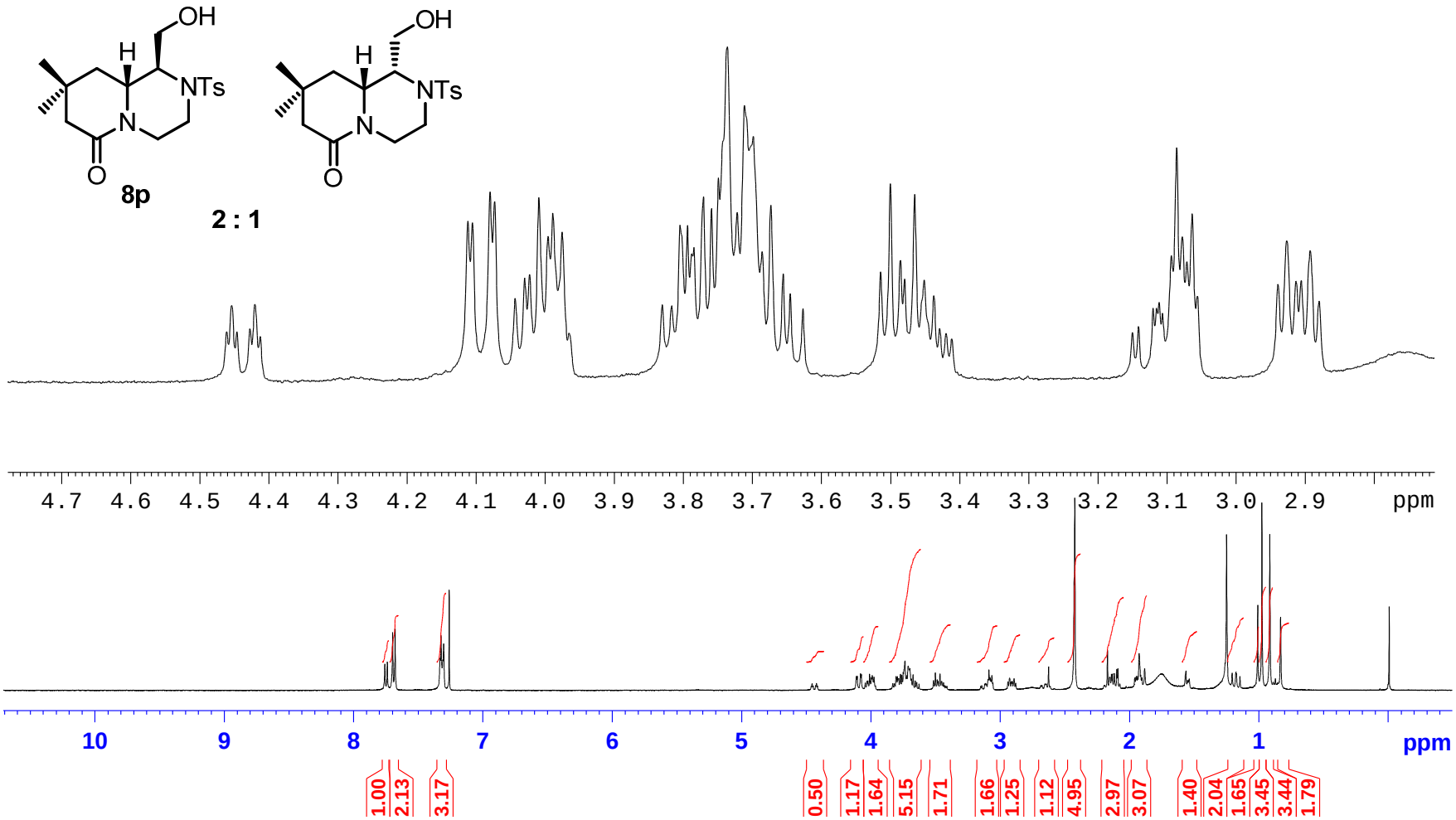
^{13}C NMR of compound **SI-46** (100 MHz, $CDCl_3$)



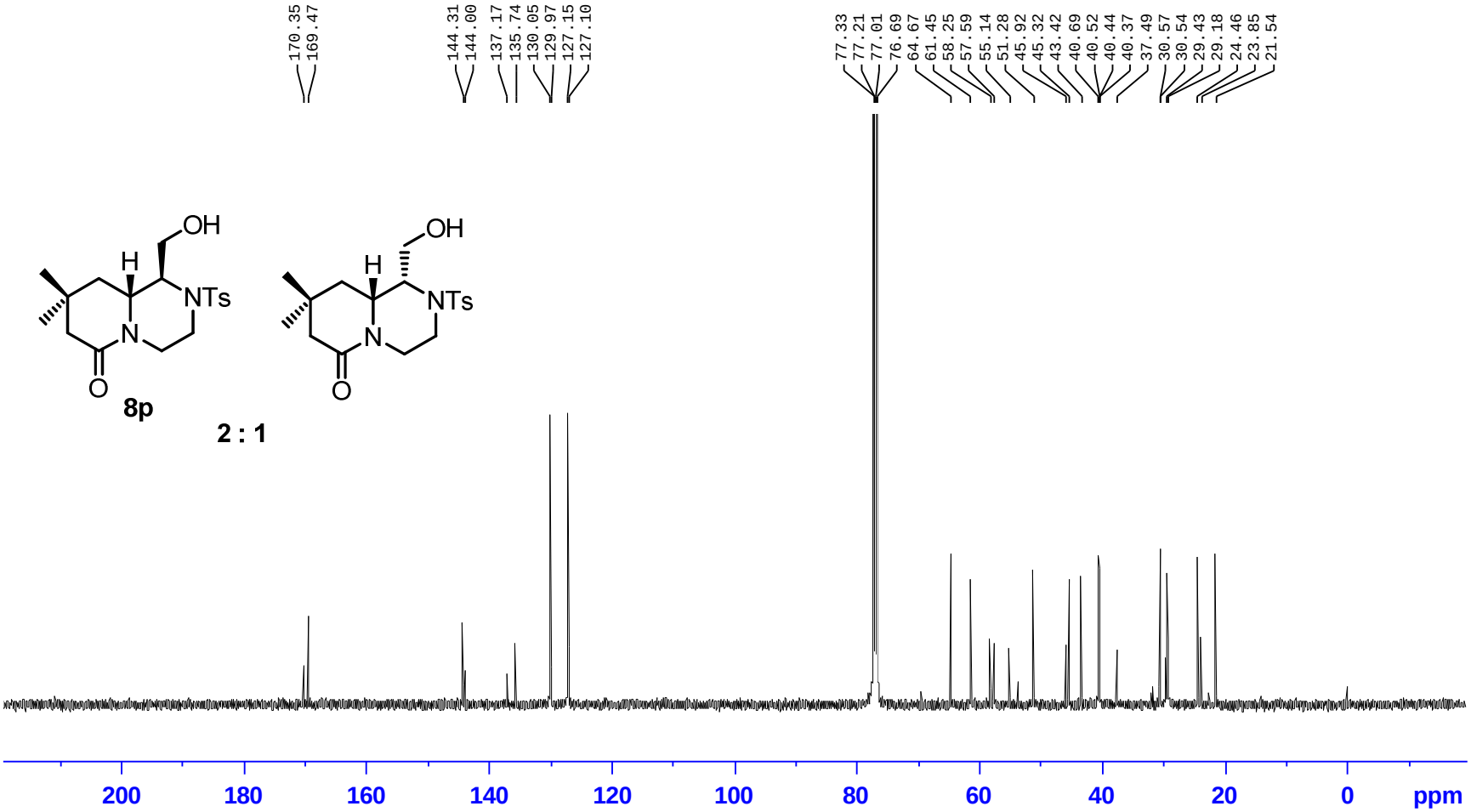
^{1}H NMR of compound **7p** (400 MHz, $CDCl_3$)



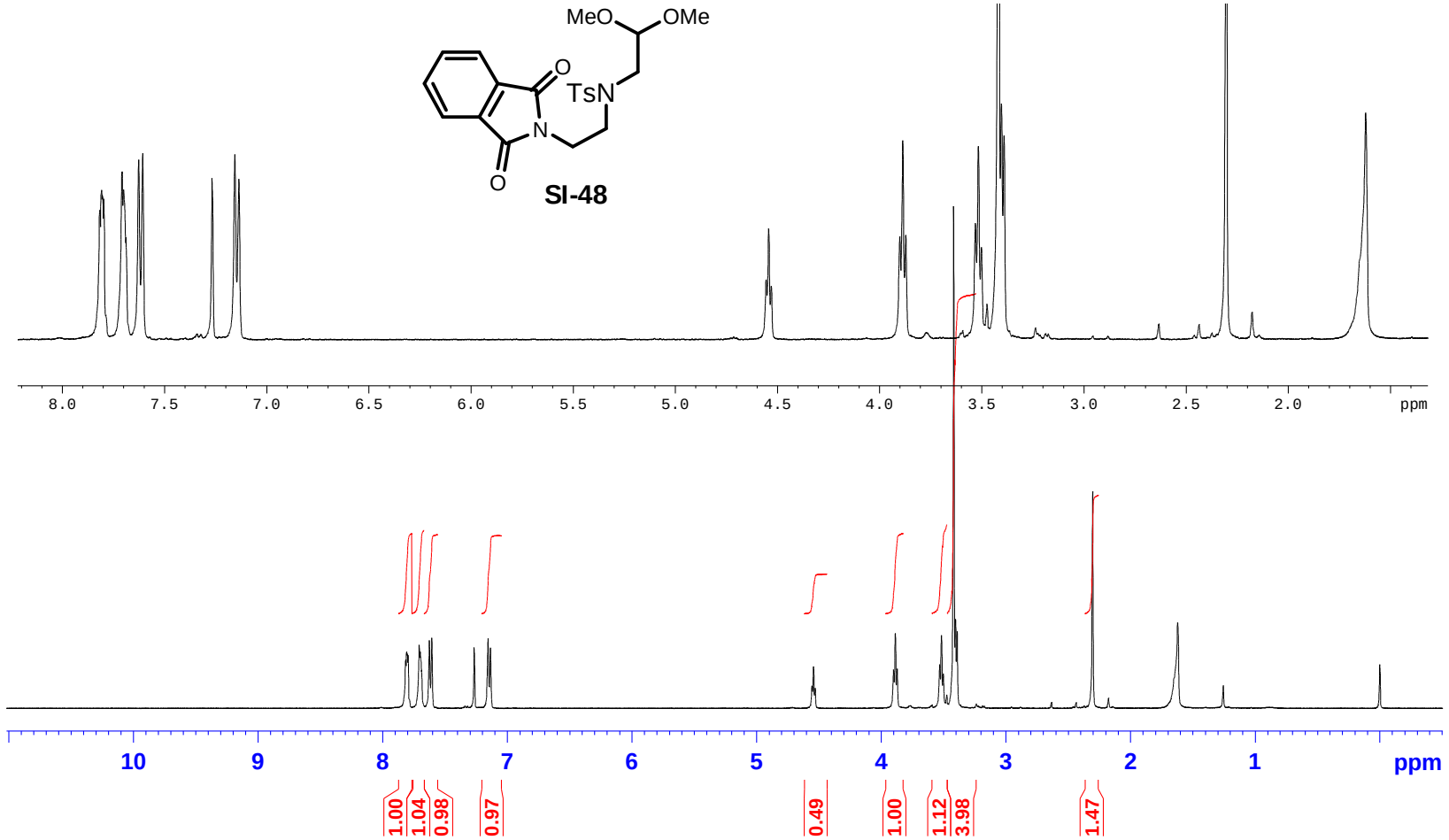
^{13}C NMR of compound **7p** (100 MHz, $CDCl_3$)



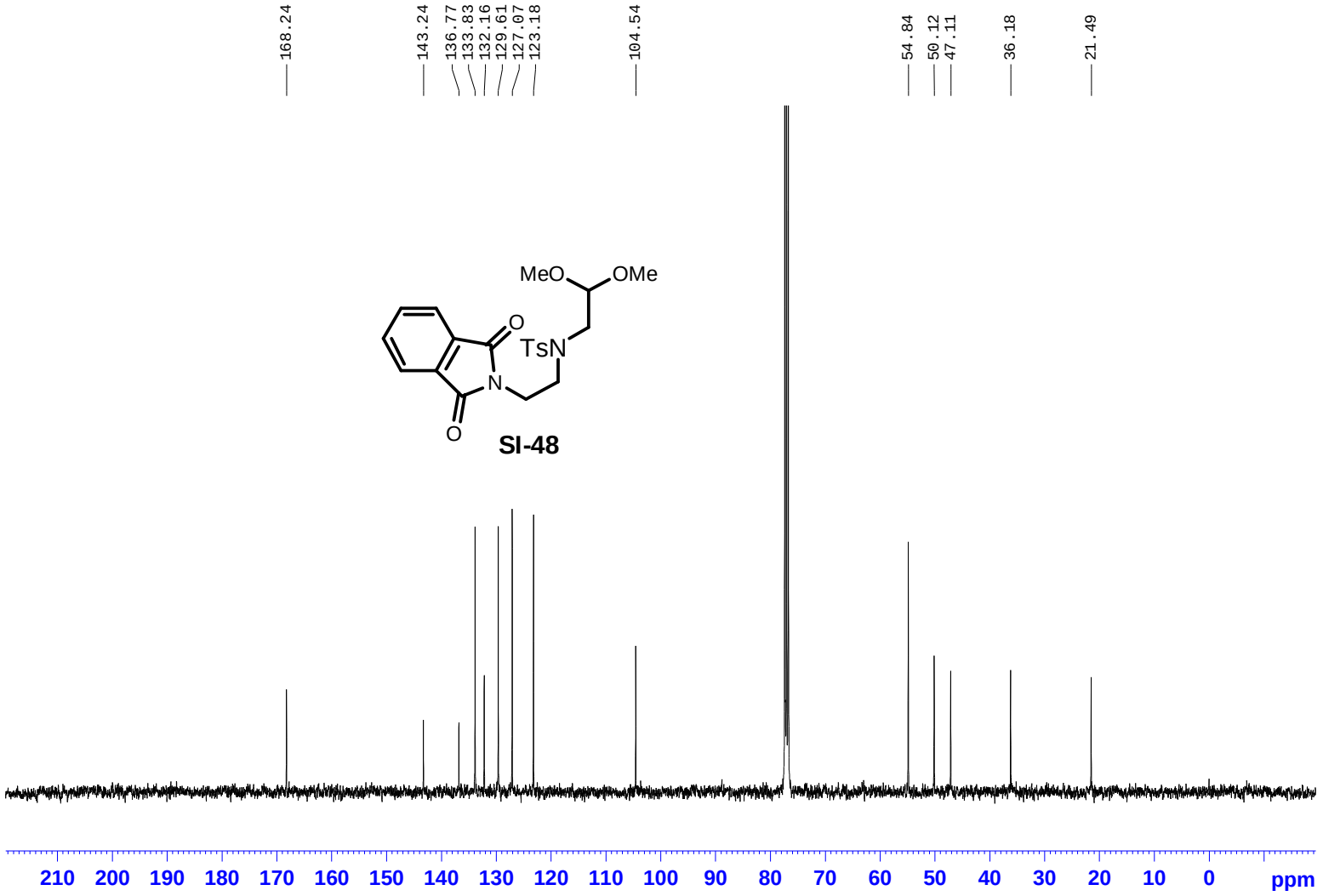
^{1}H NMR of compound **8p** (400 MHz, $CDCl_3$)



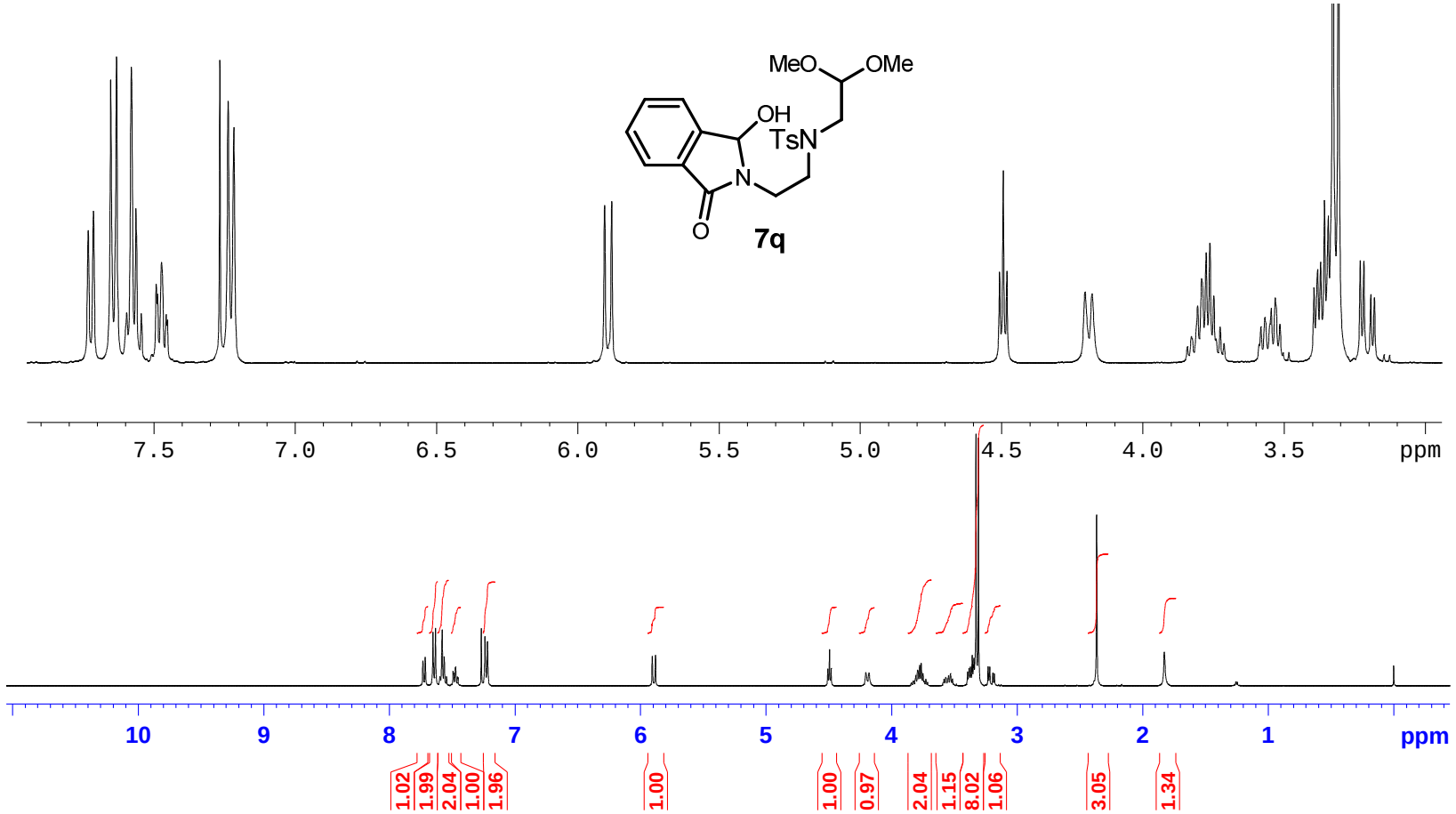
^{13}C NMR of compound **8p** (100 MHz, $CDCl_3$)



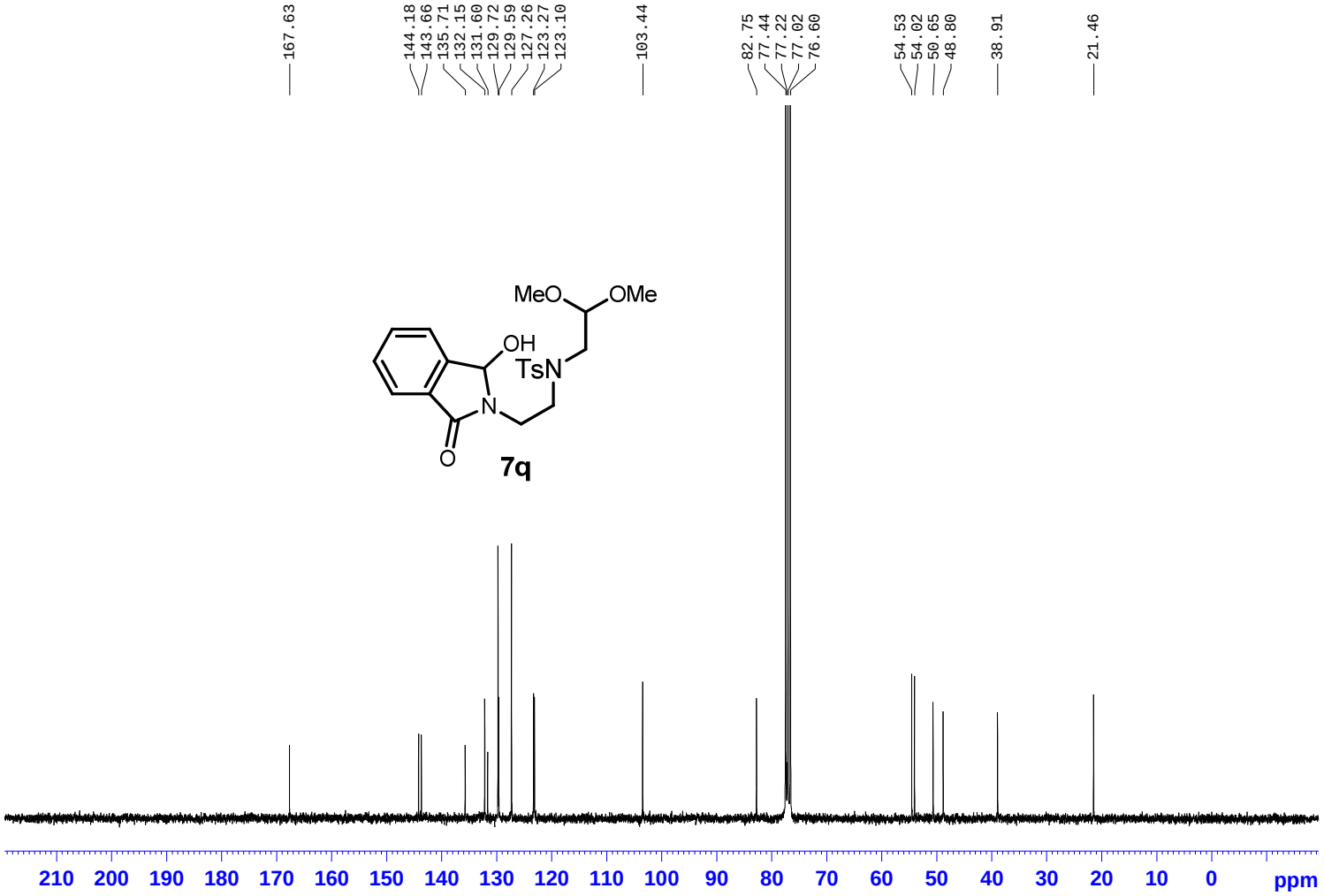
^{1}H NMR of compound **SI-48** (400 MHz, $CDCl_3$)



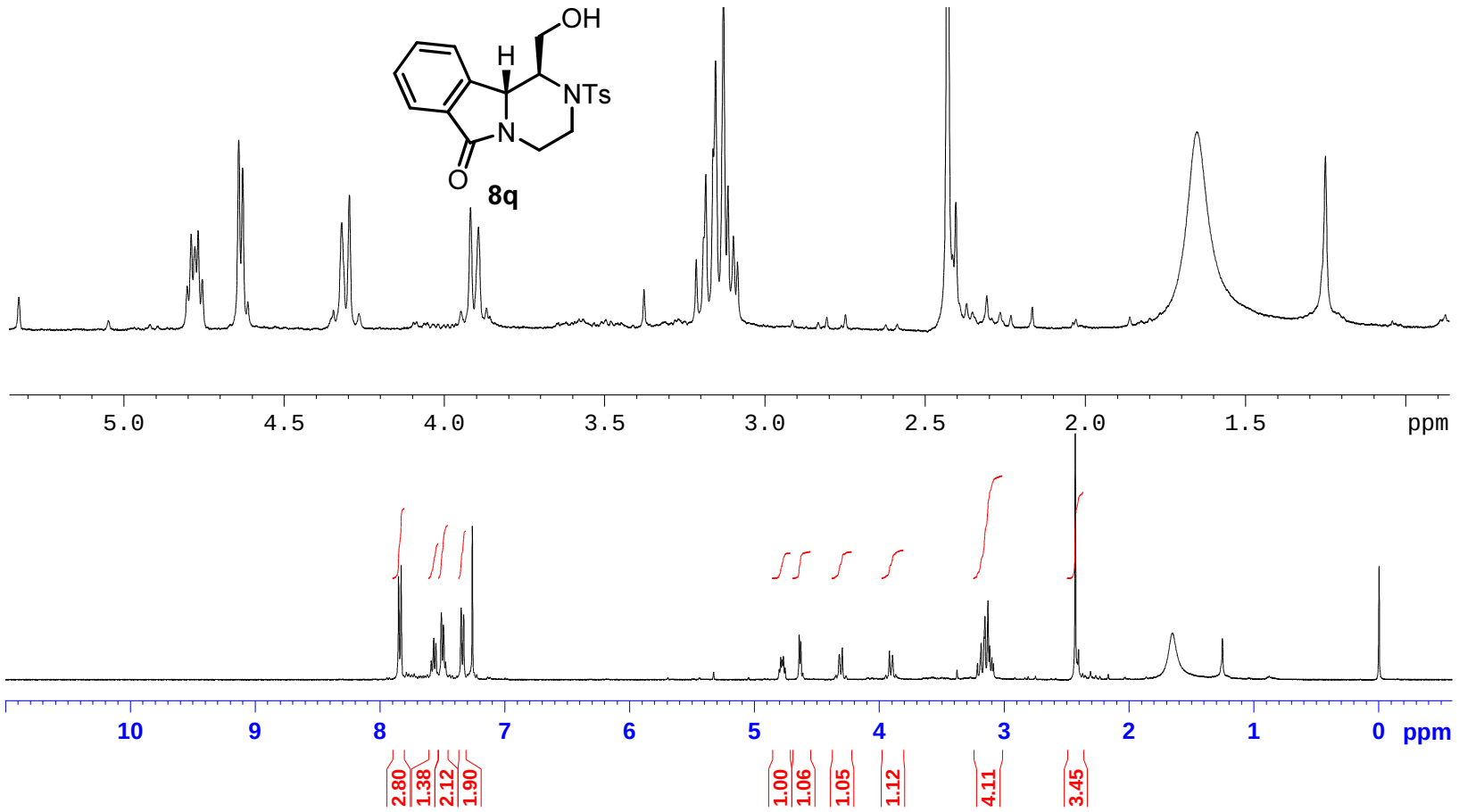
^{13}C NMR of compound **SI-48** (100 MHz, $CDCl_3$)



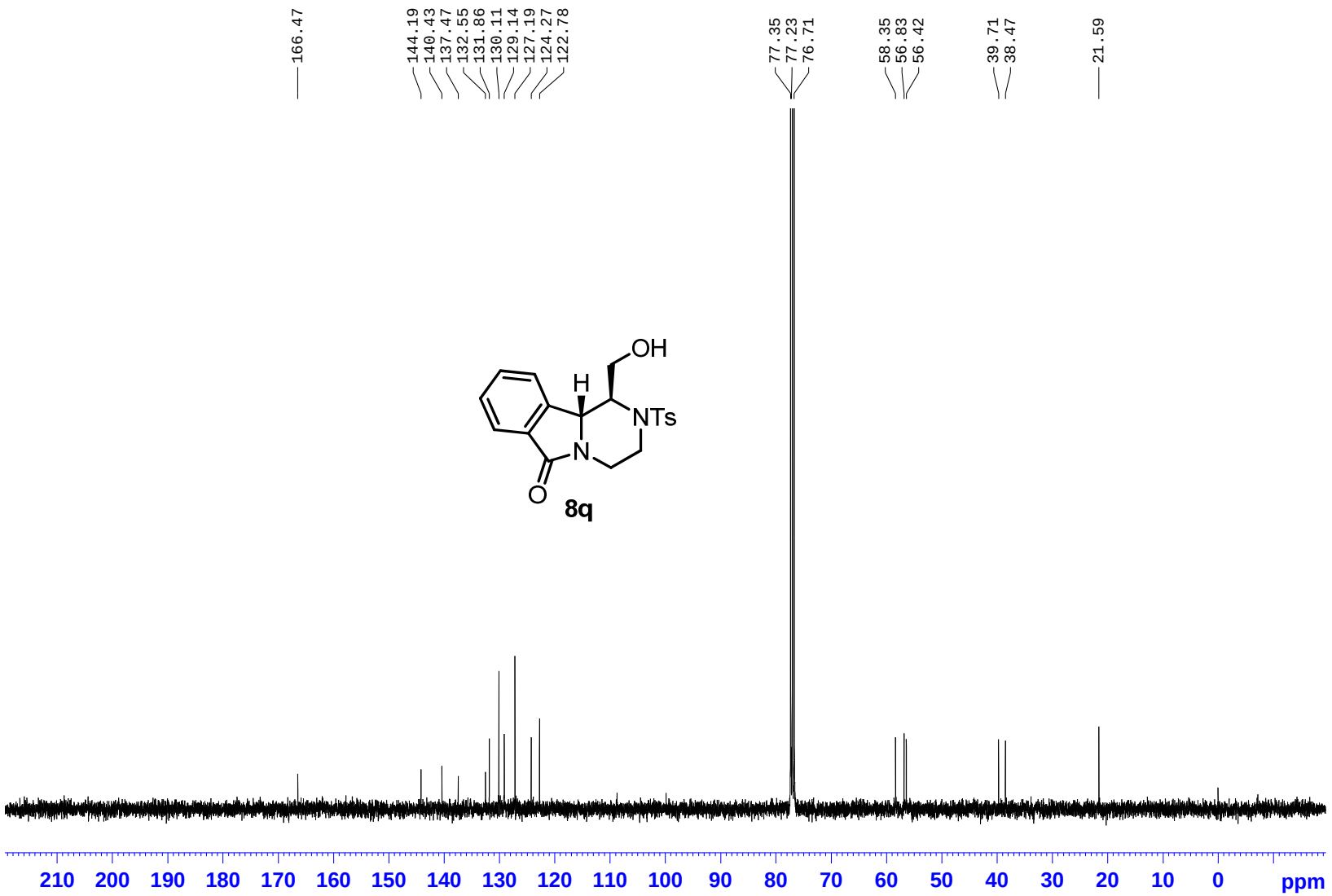
^{1}H NMR of compound **7q** (400 MHz, $CDCl_3$)



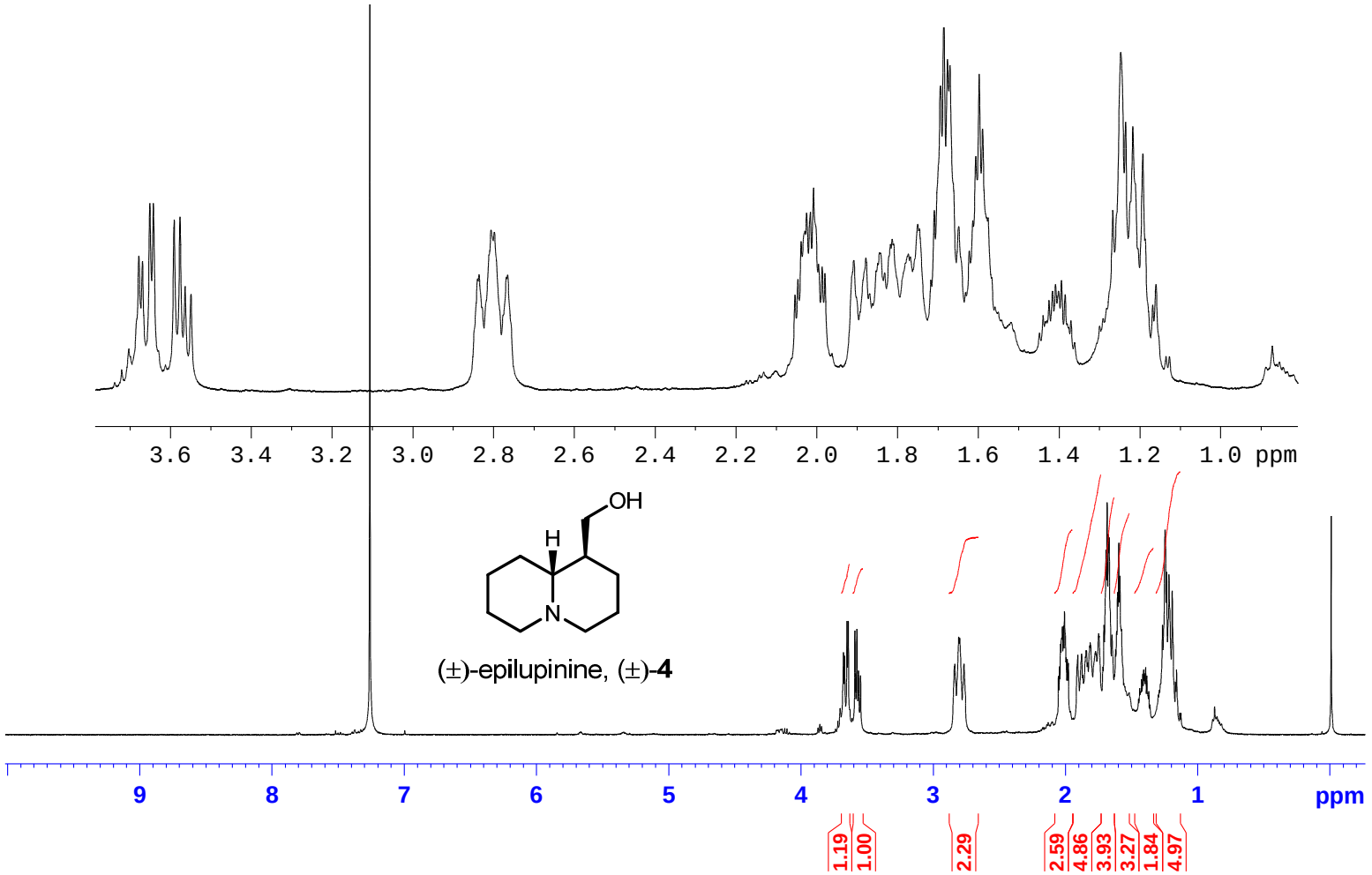
^{13}C NMR of compound **7q** (100 MHz, $CDCl_3$)



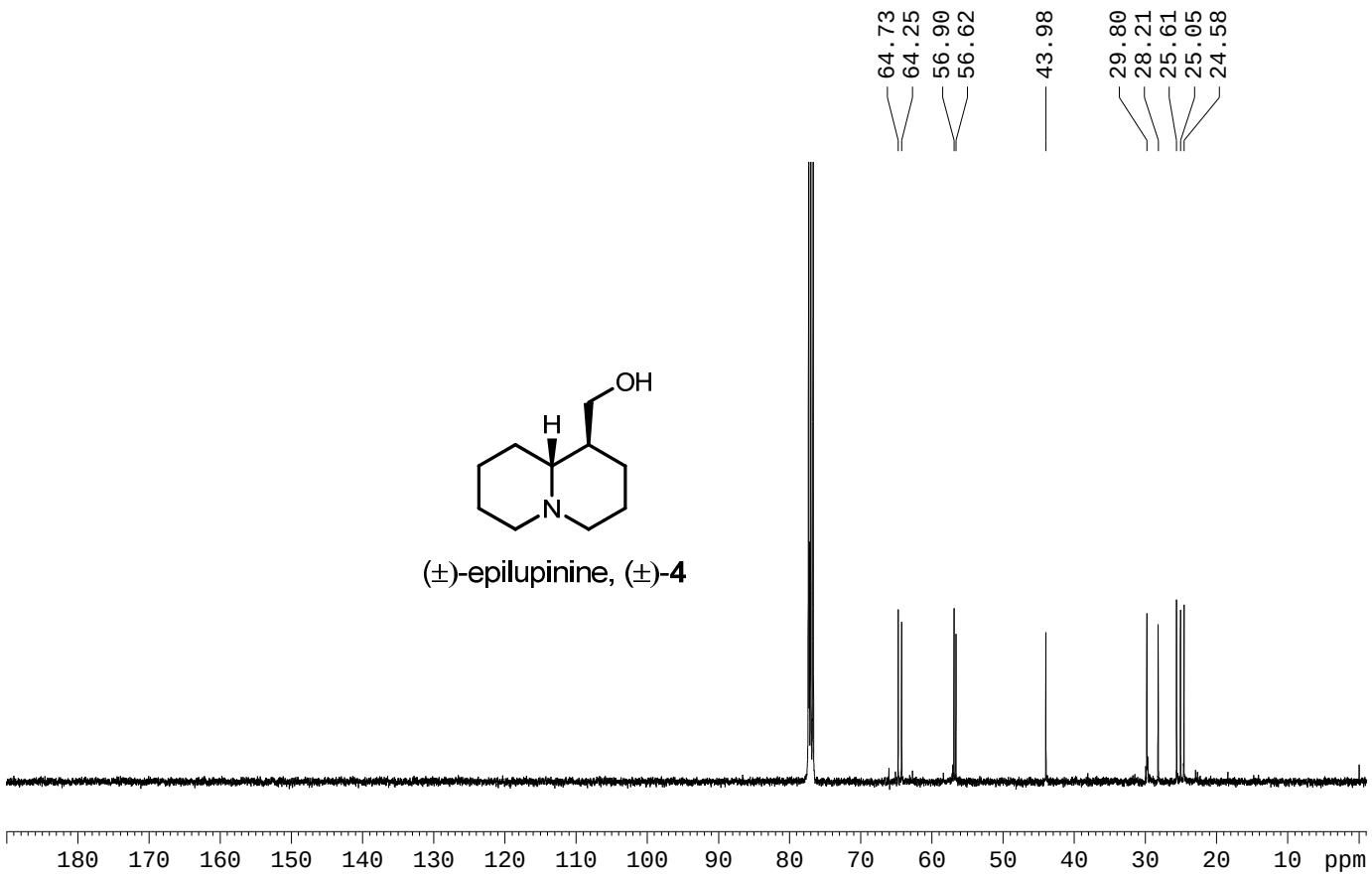
^{1}H NMR of compound **8q** (400 MHz, $CDCl_3$)



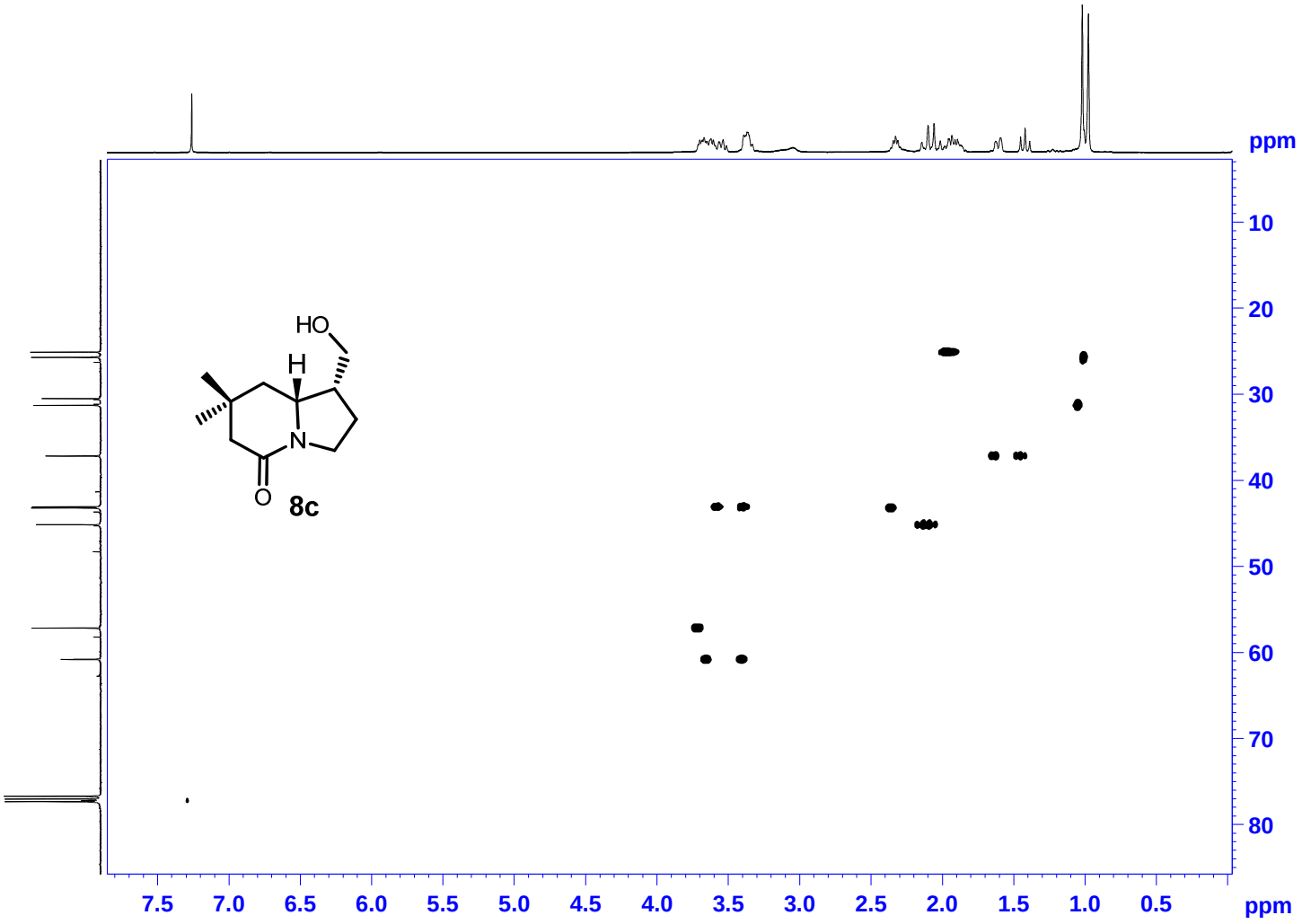
^{13}C NMR of compound **8q** (100 MHz, $CDCl_3$)



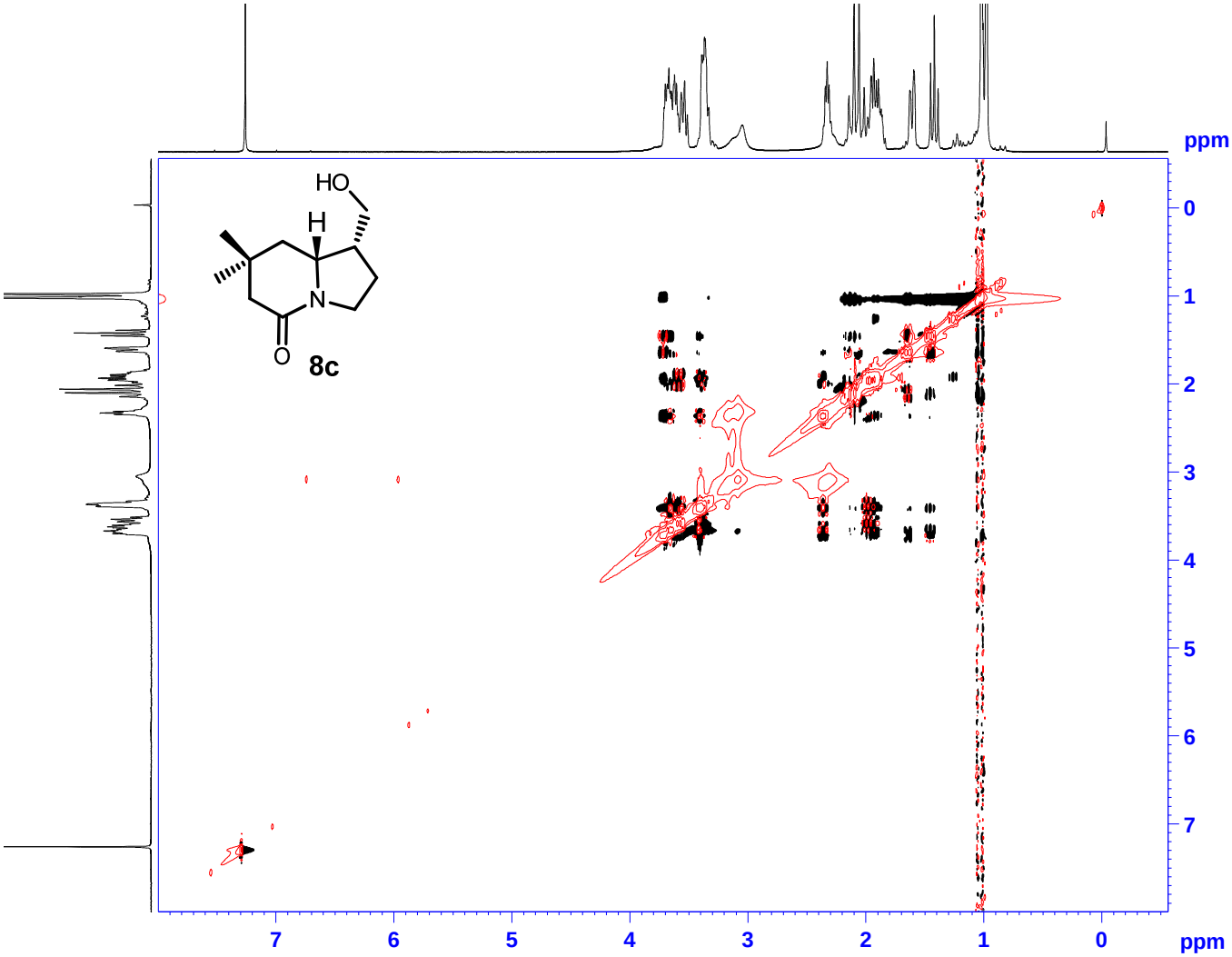
^{1}H NMR of compound **4** (epilupinine) (400 MHz, $CDCl_3$)



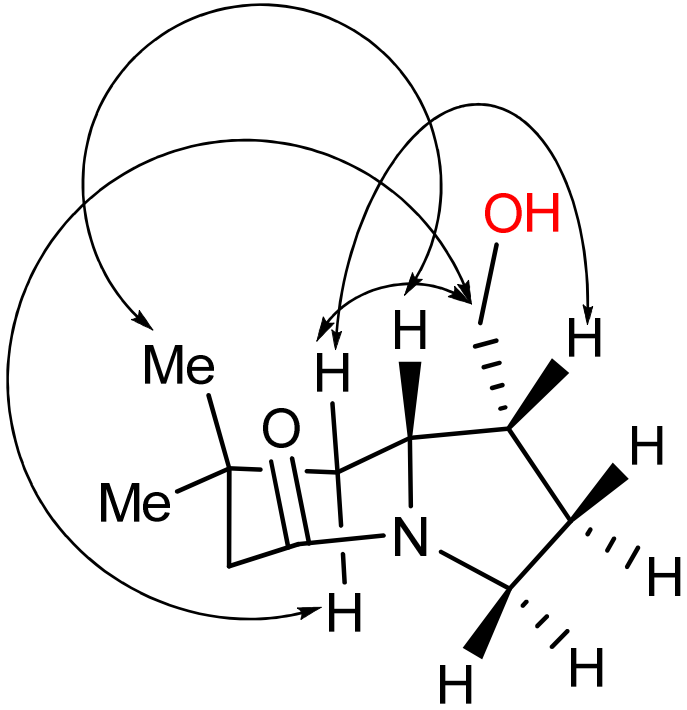
^{13}C NMR of compound **4** (epilupinine) (100 MHz, $CDCl_3$)



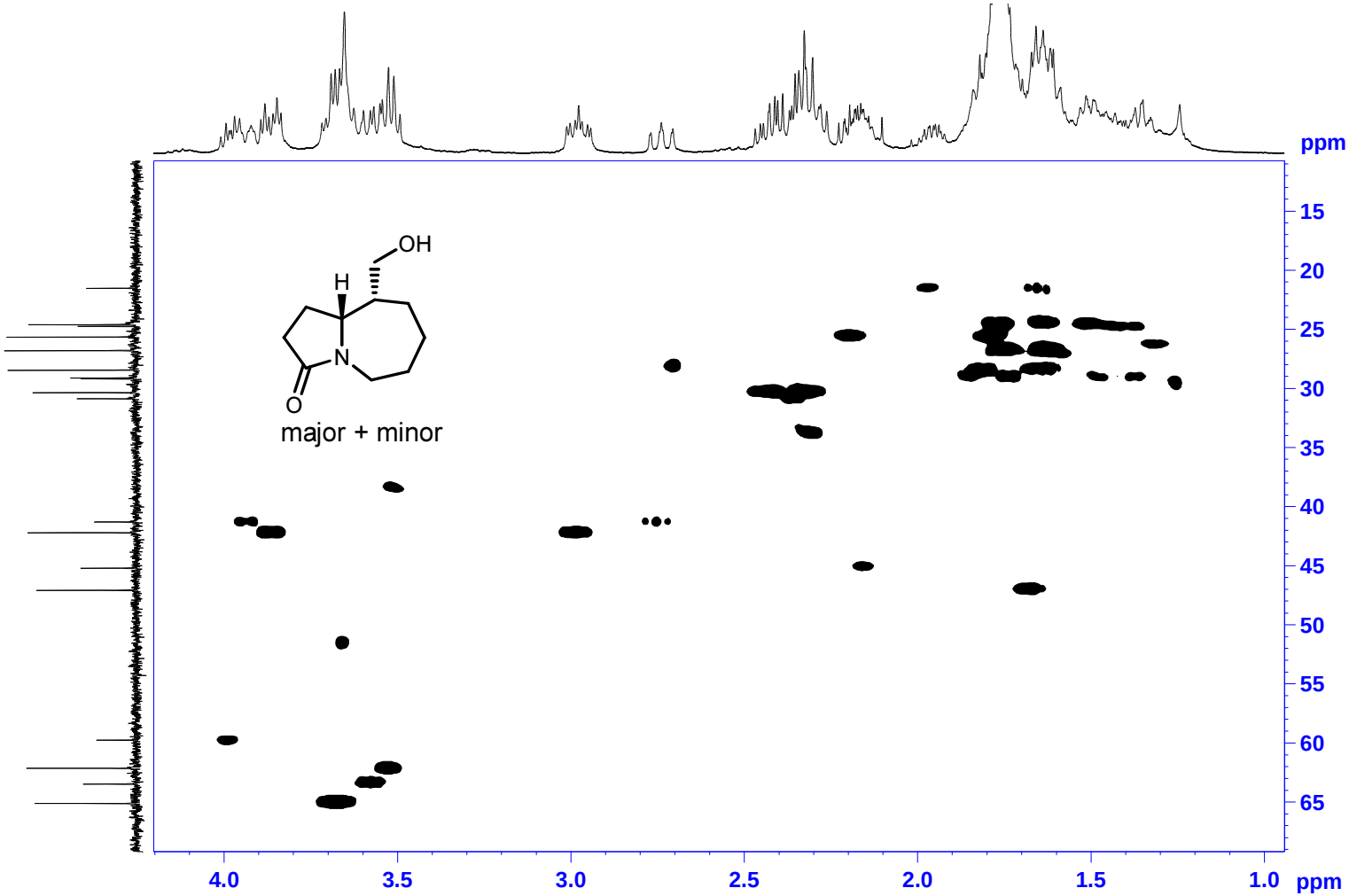
2D HSQC Spectrum of **8c** ($CDCl_3$, 298 K, 400 MHz)



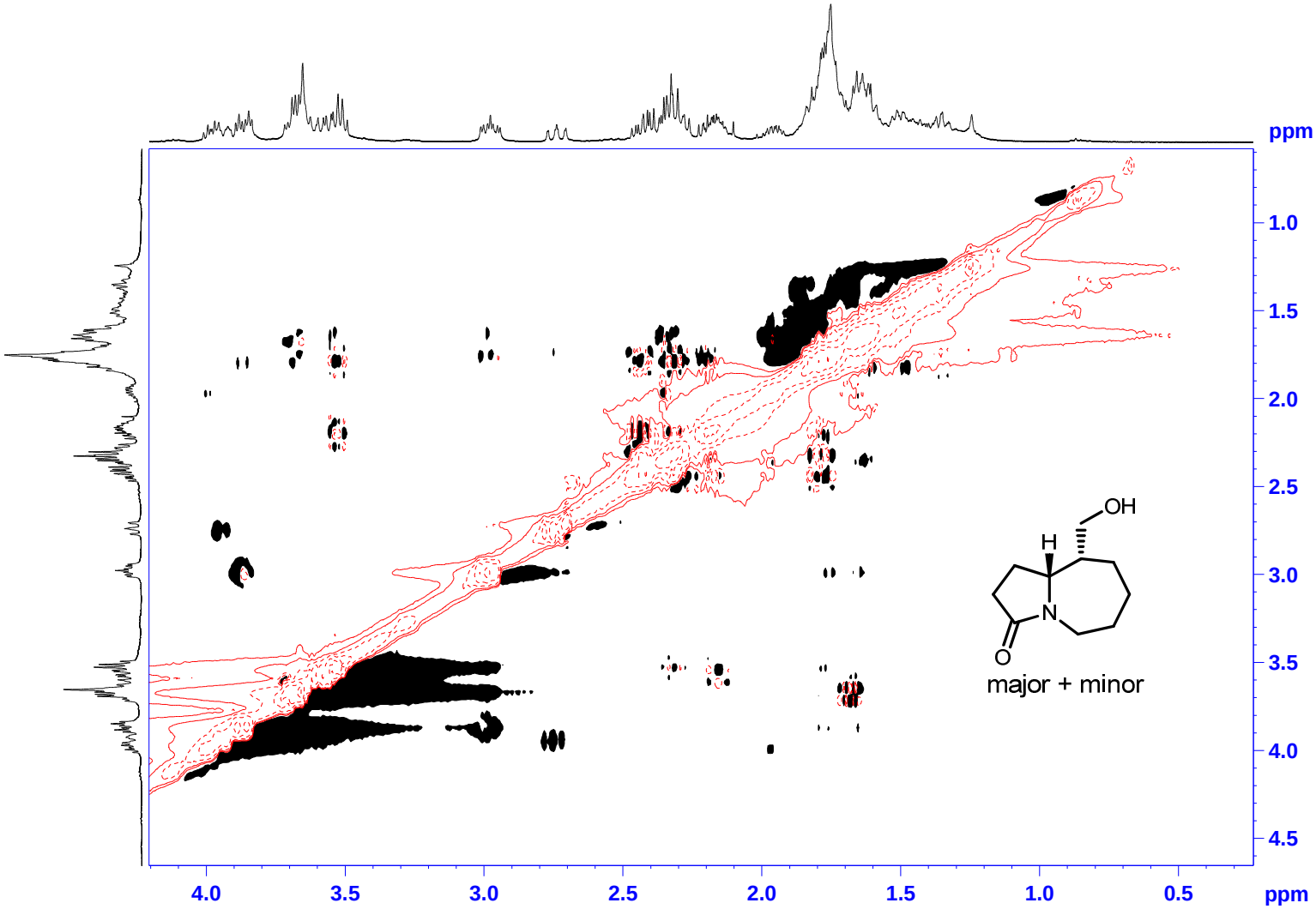
NOESY Spectrum of **8c** ($CDCl_3$, 298 K, 400 MHz)



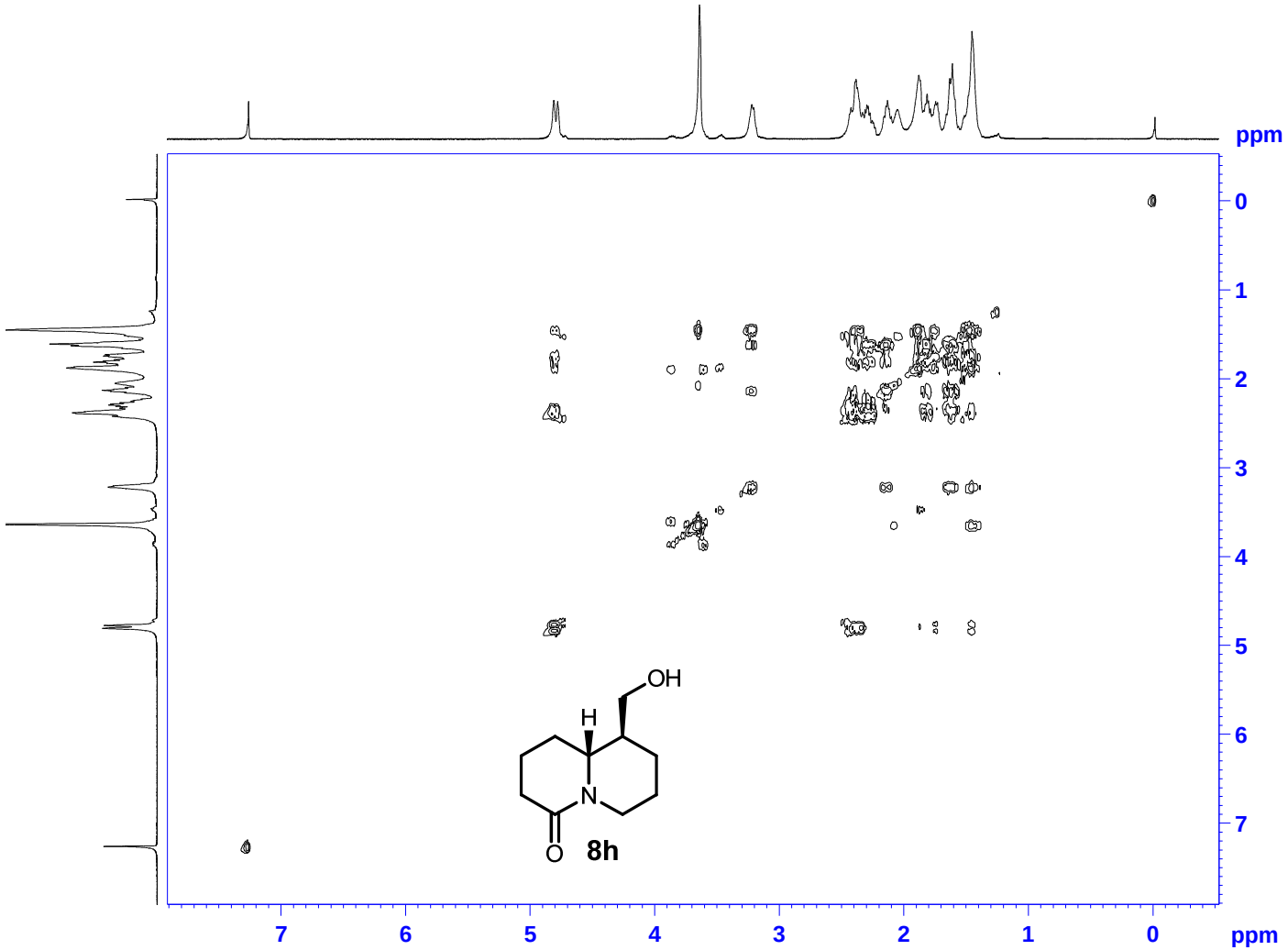
Important nOes observed in **8c**



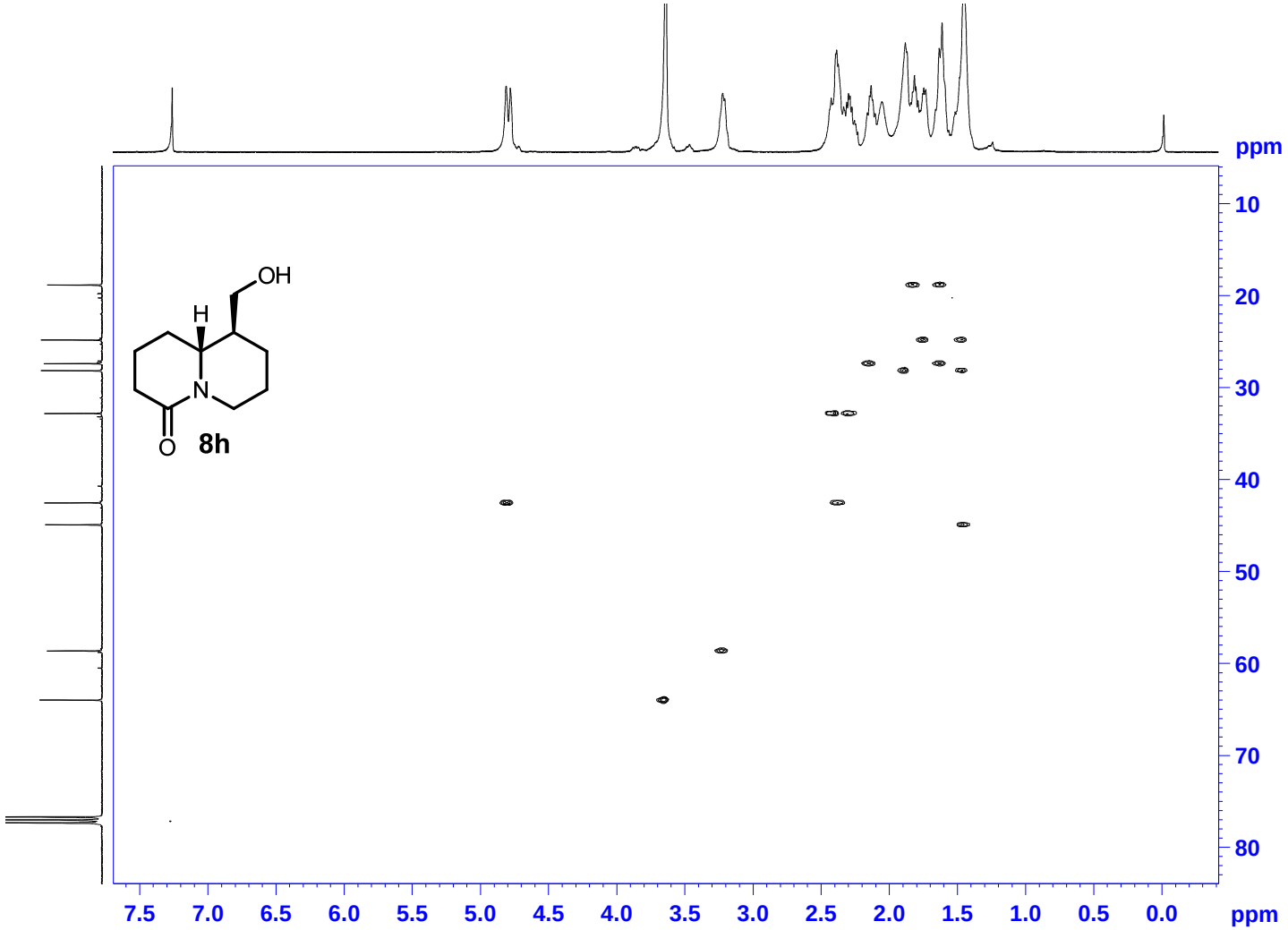
2D HSQC Spectrum of **8j** ($CDCl_3$, 298 K, 400 MHz)



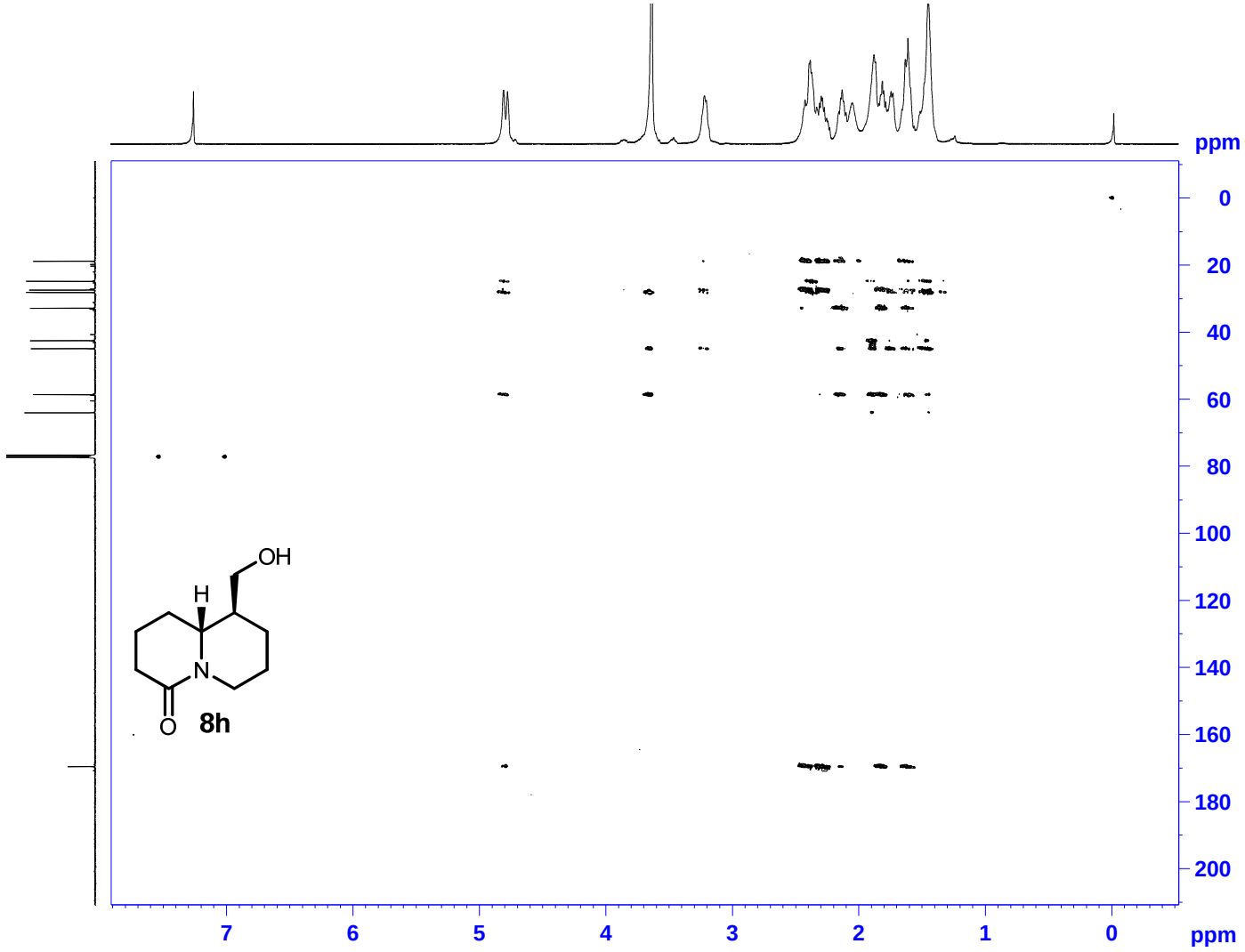
NOESY Spectrum of **8j** ($CDCl_3$, 298 K, 400 MHz)



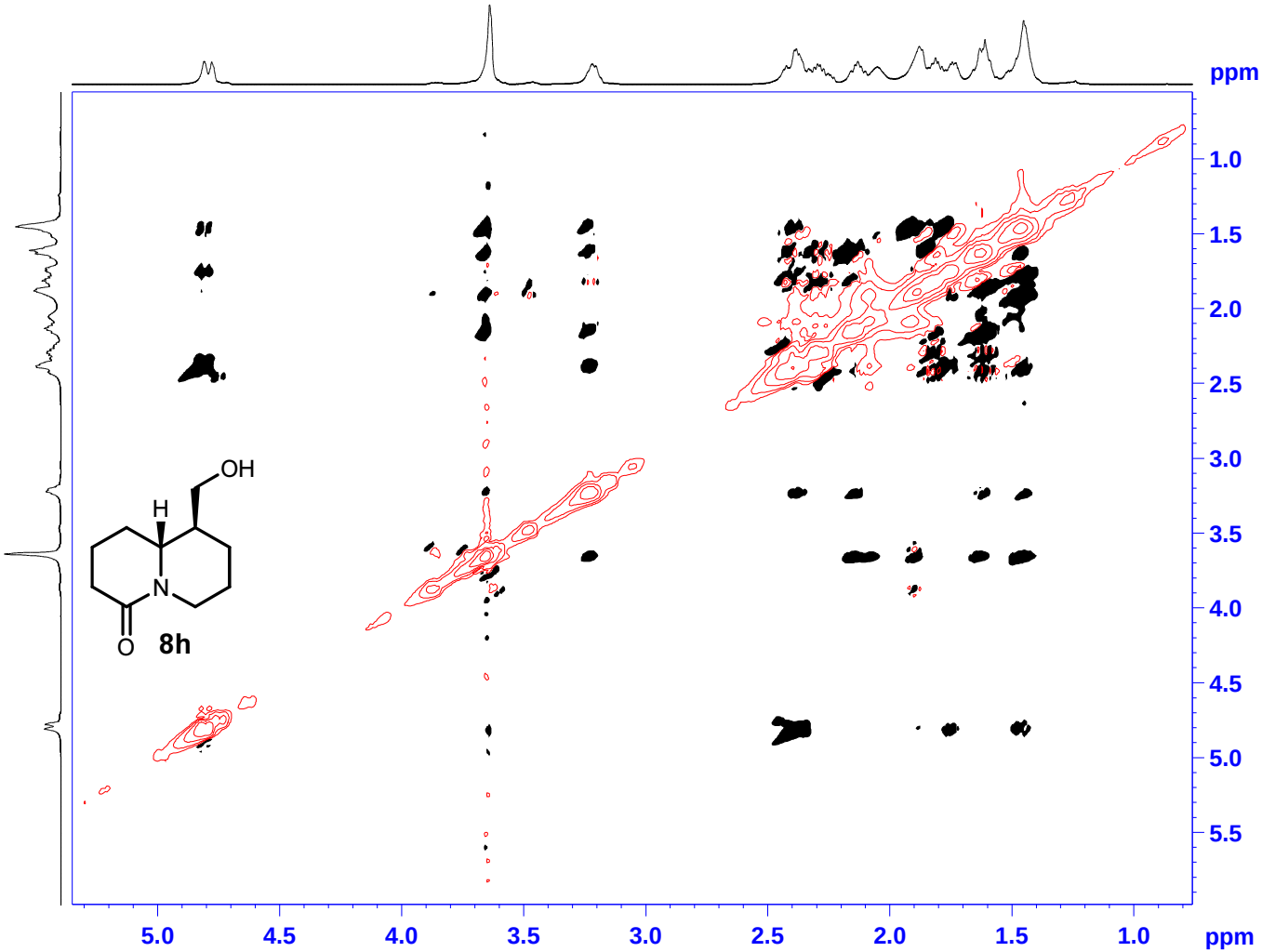
COSY Spectrum of **8h** ($CDCl_3$, 298 K, 400 MHz)



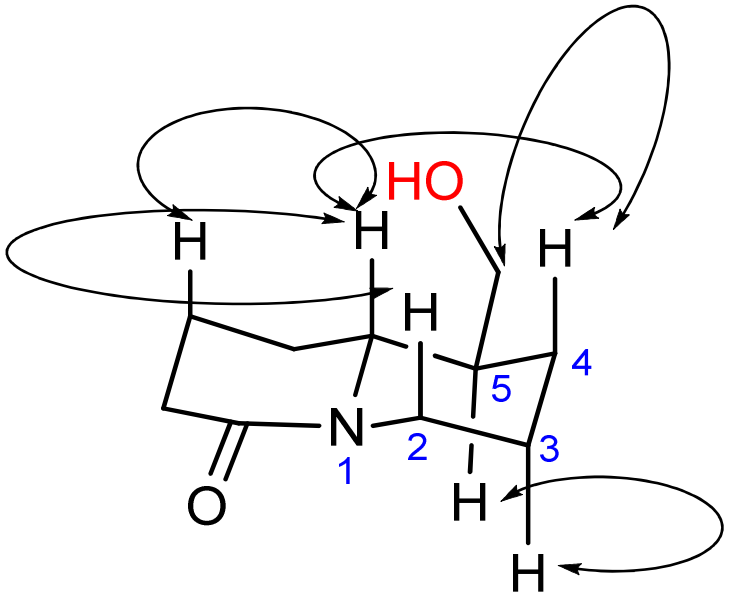
2D HSQC Spectrum of **8h** ($CDCl_3$, 298 K, 400 MHz)



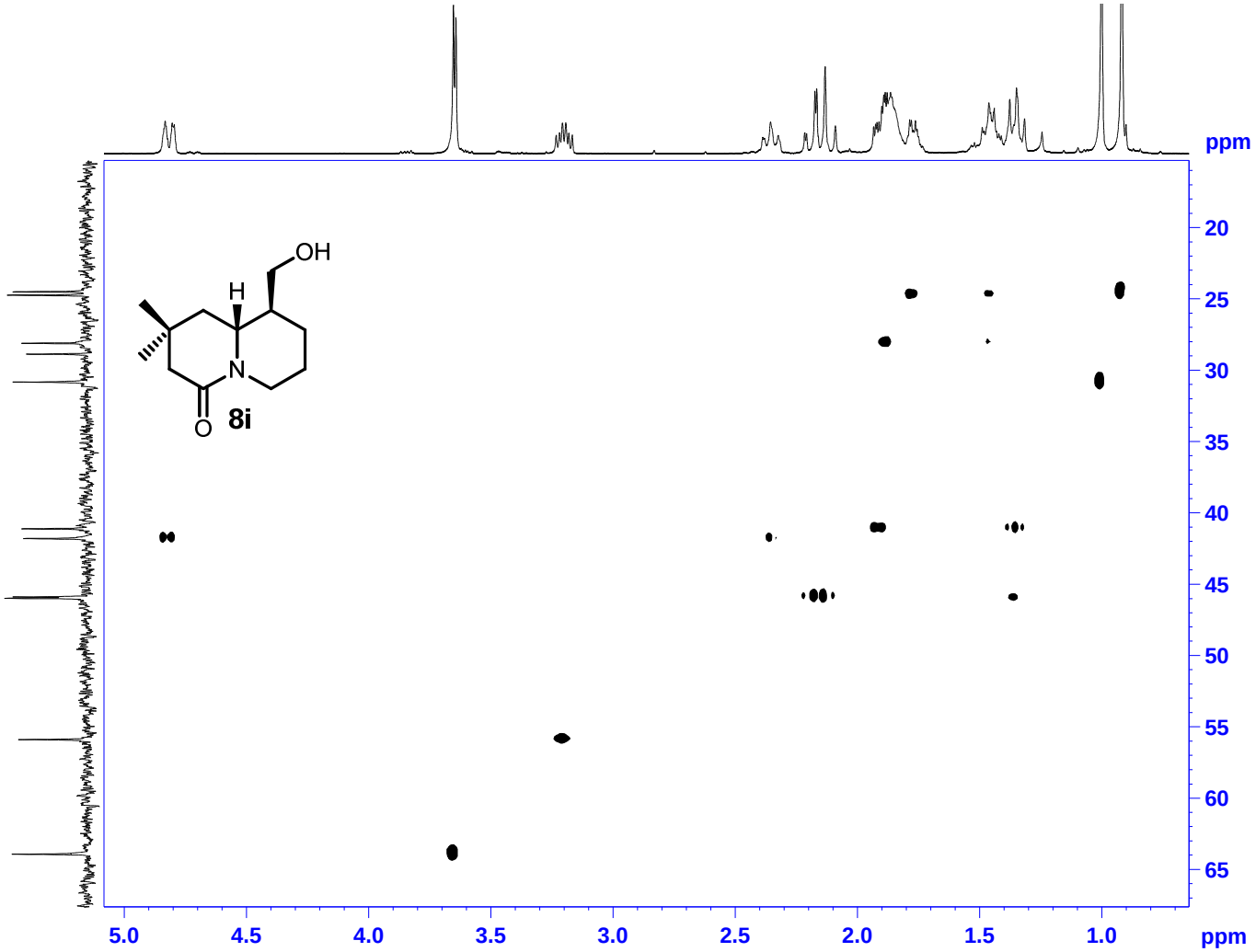
HMBC Spectrum of **8h** ($CDCl_3$, 298 K, 400 MHz)



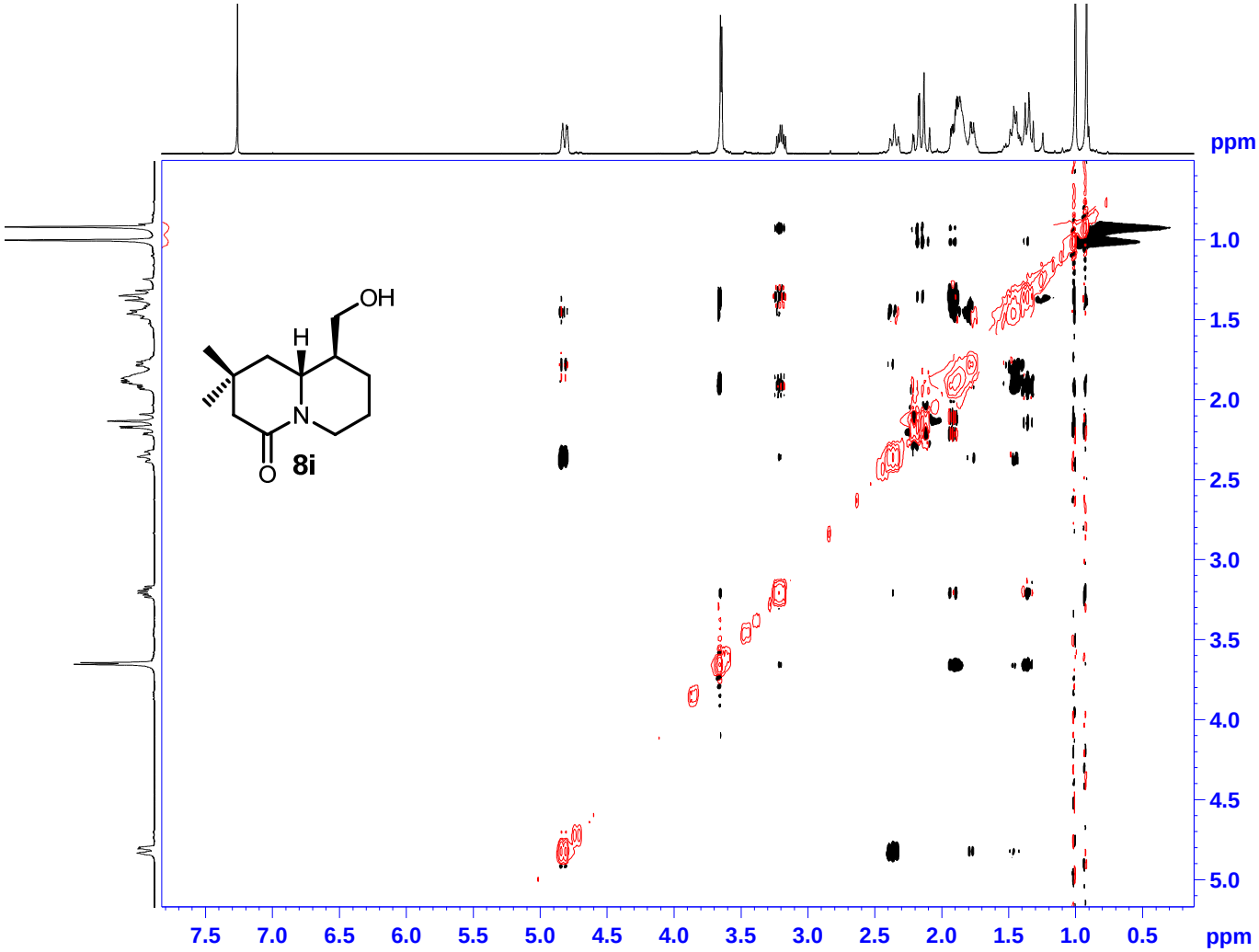
NOESY Spectrum of **8h** ($CDCl_3$, 298 K, 400 MHz)



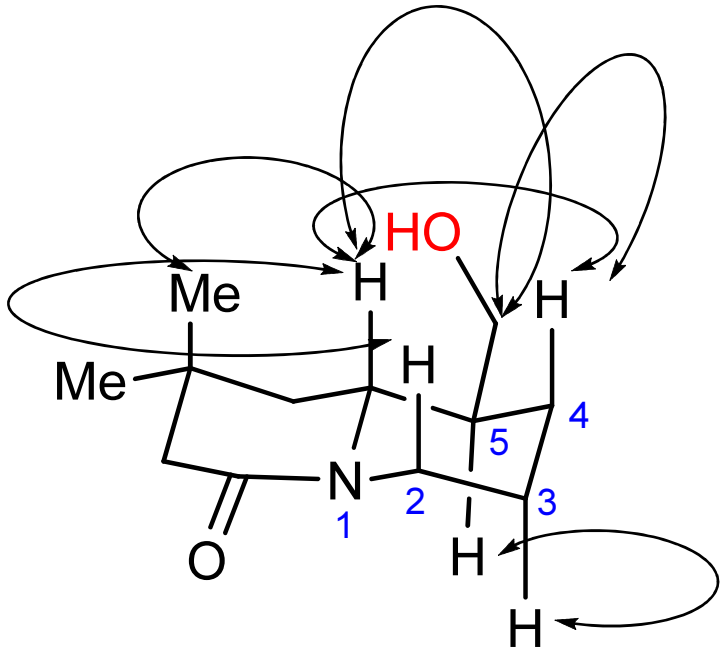
Important nOes observed in **8h**



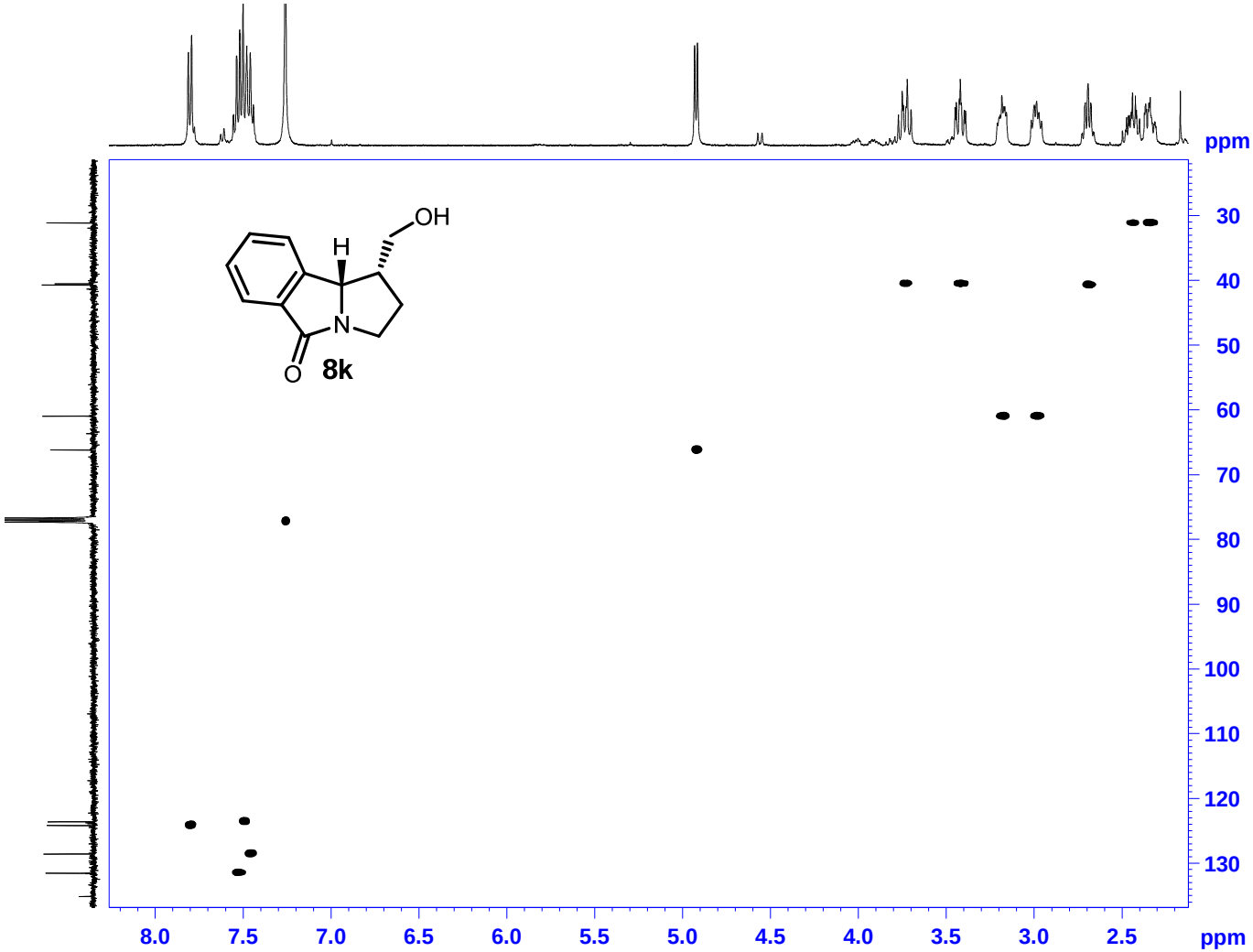
2D HSQC Spectrum of **8i** ($CDCl_3$, 298 K, 400 MHz)



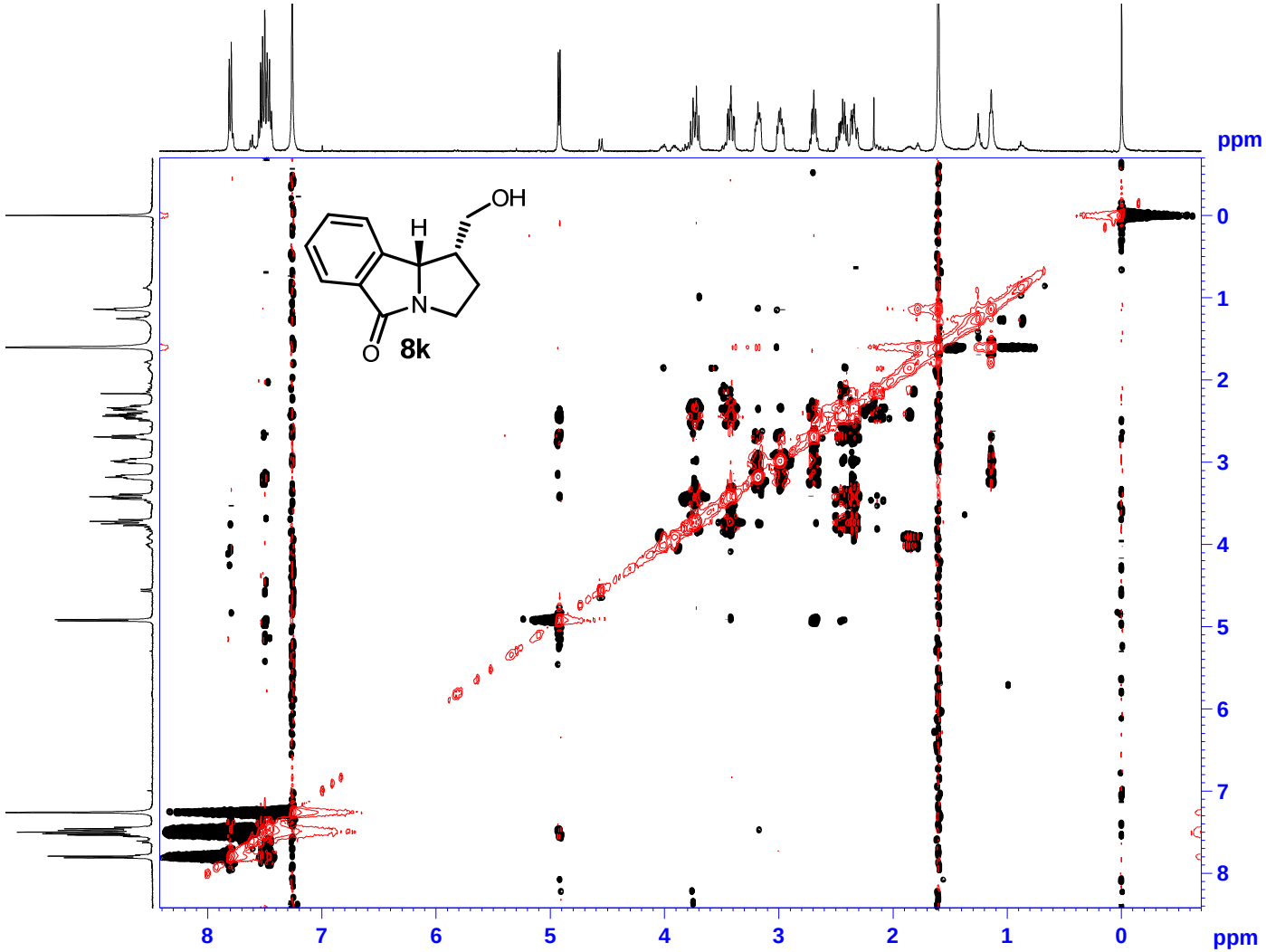
NOESY Spectrum of **8i** ($CDCl_3$, 298 K, 400 MHz)



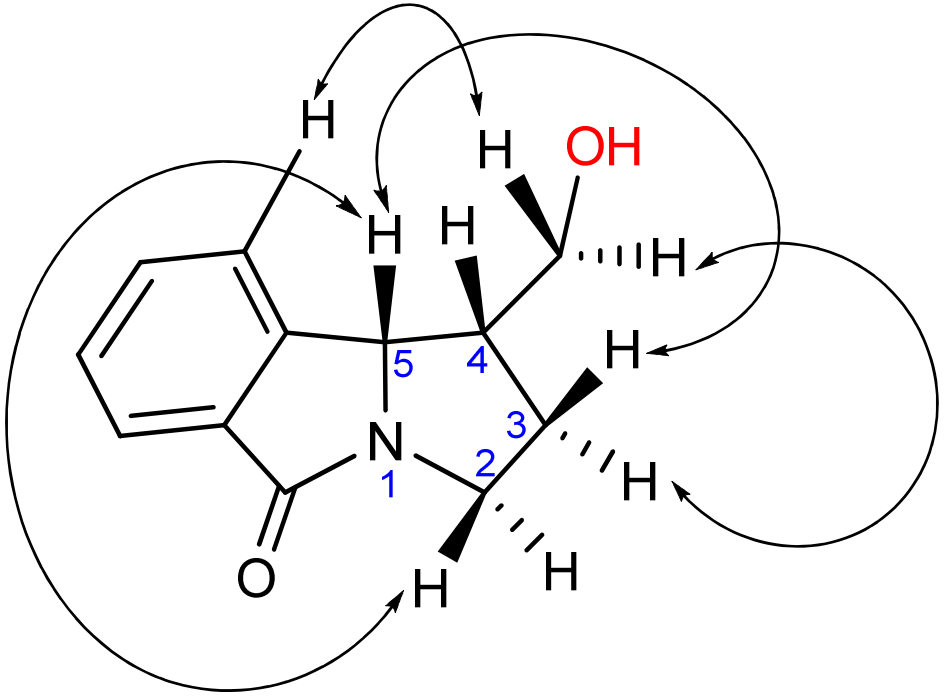
Important nOes observed in **8i**



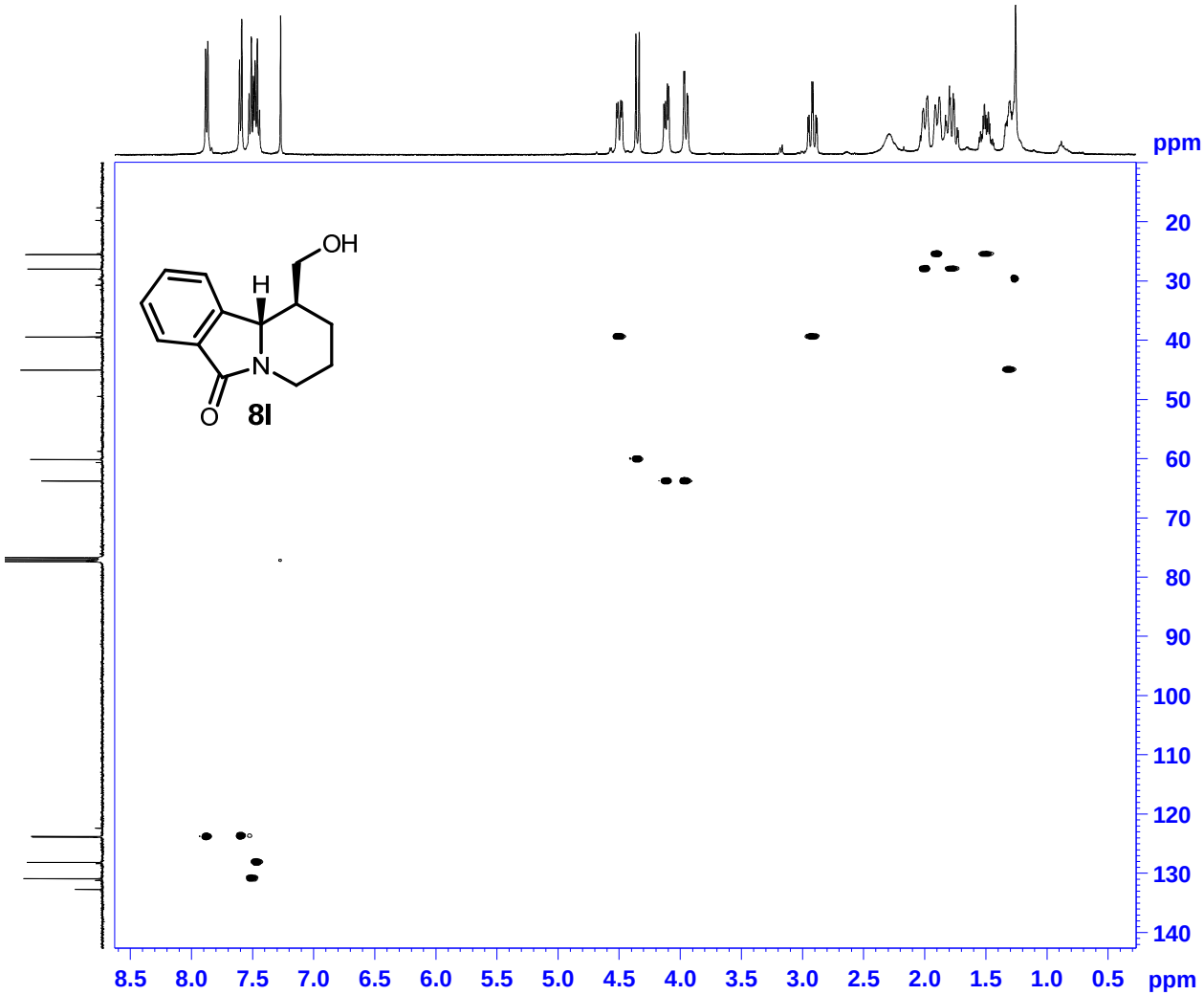
2D HSQC Spectrum of **8k** ($CDCl_3$, 298 K, 400 MHz)



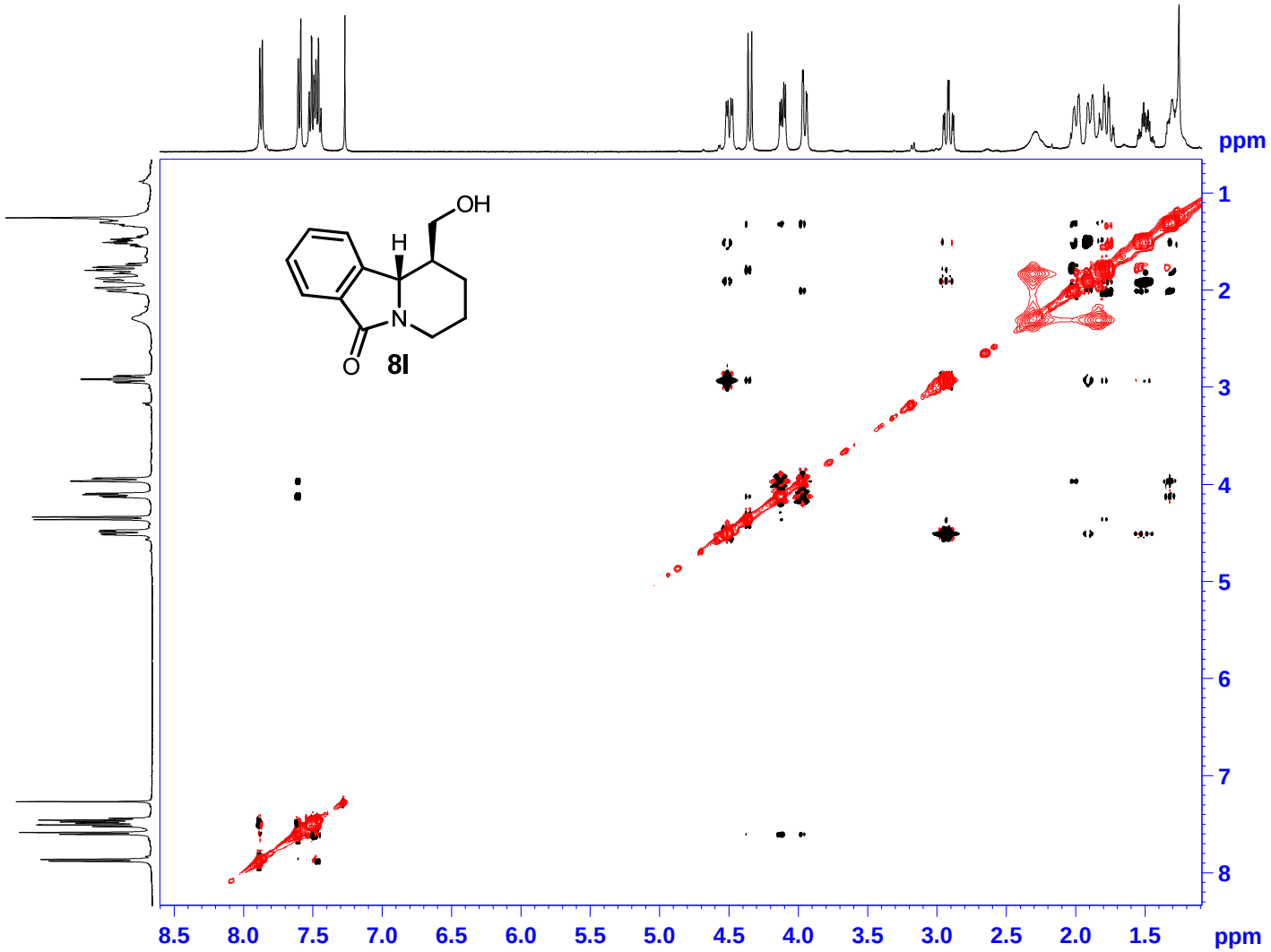
NOESY Spectrum of **8k** ($CDCl_3$, 298 K, 400 MHz)



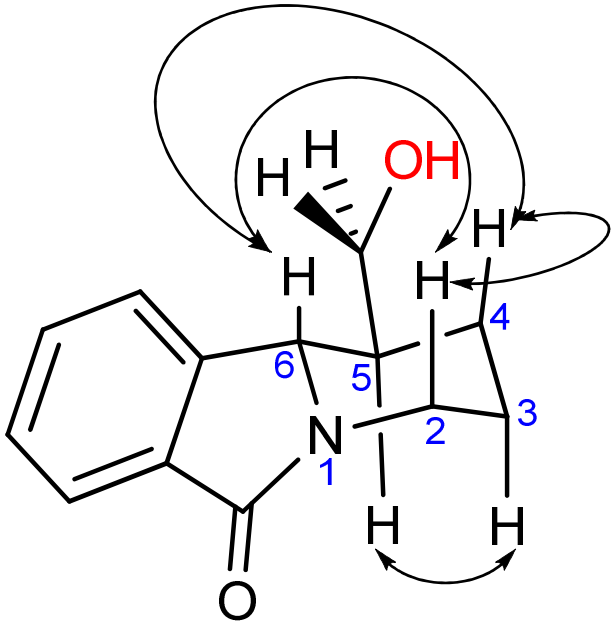
Important nOes observed in **8k**



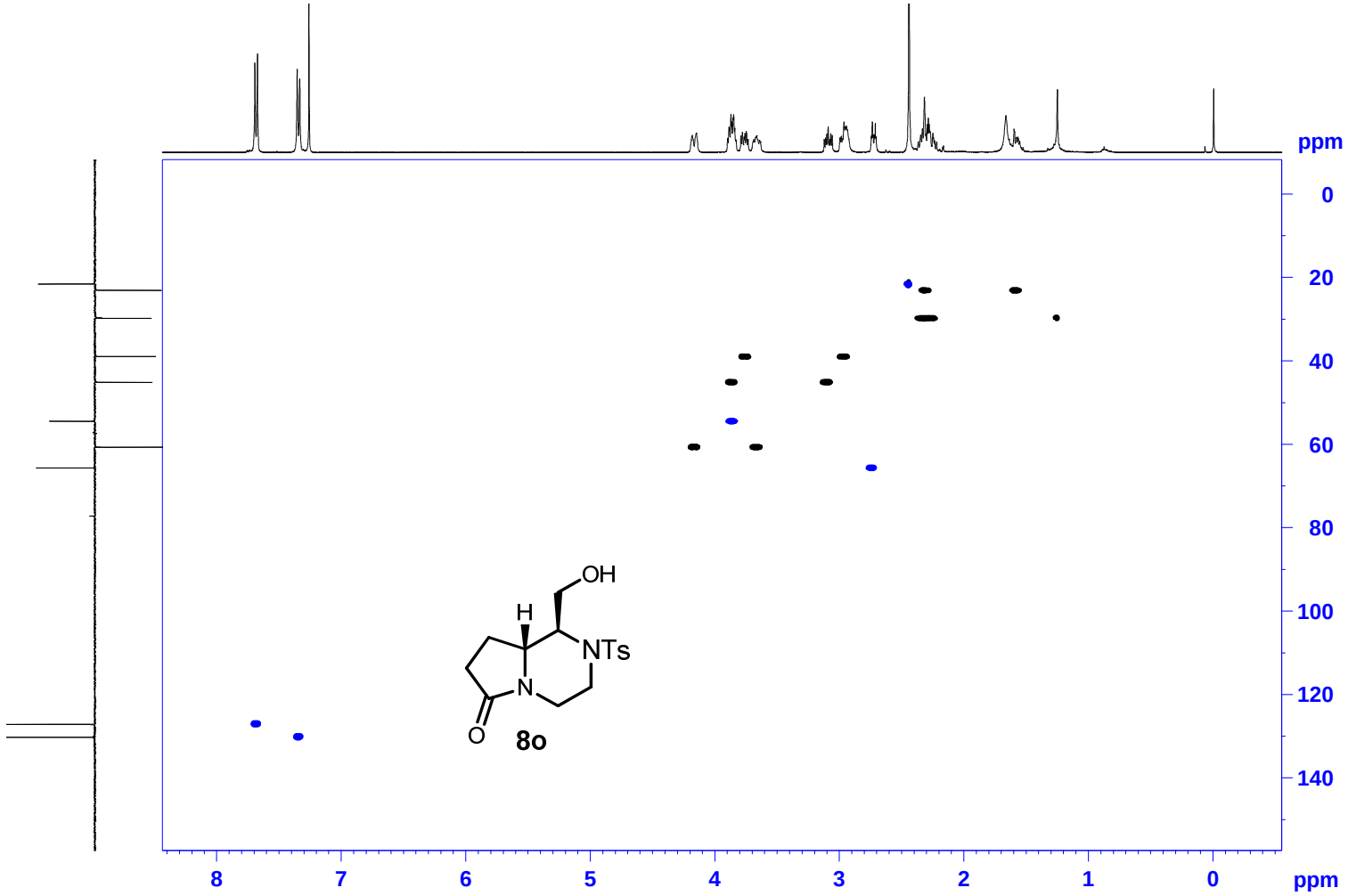
2D HSQC Spectrum of **8l** ($CDCl_3$, 298 K, 400 MHz)



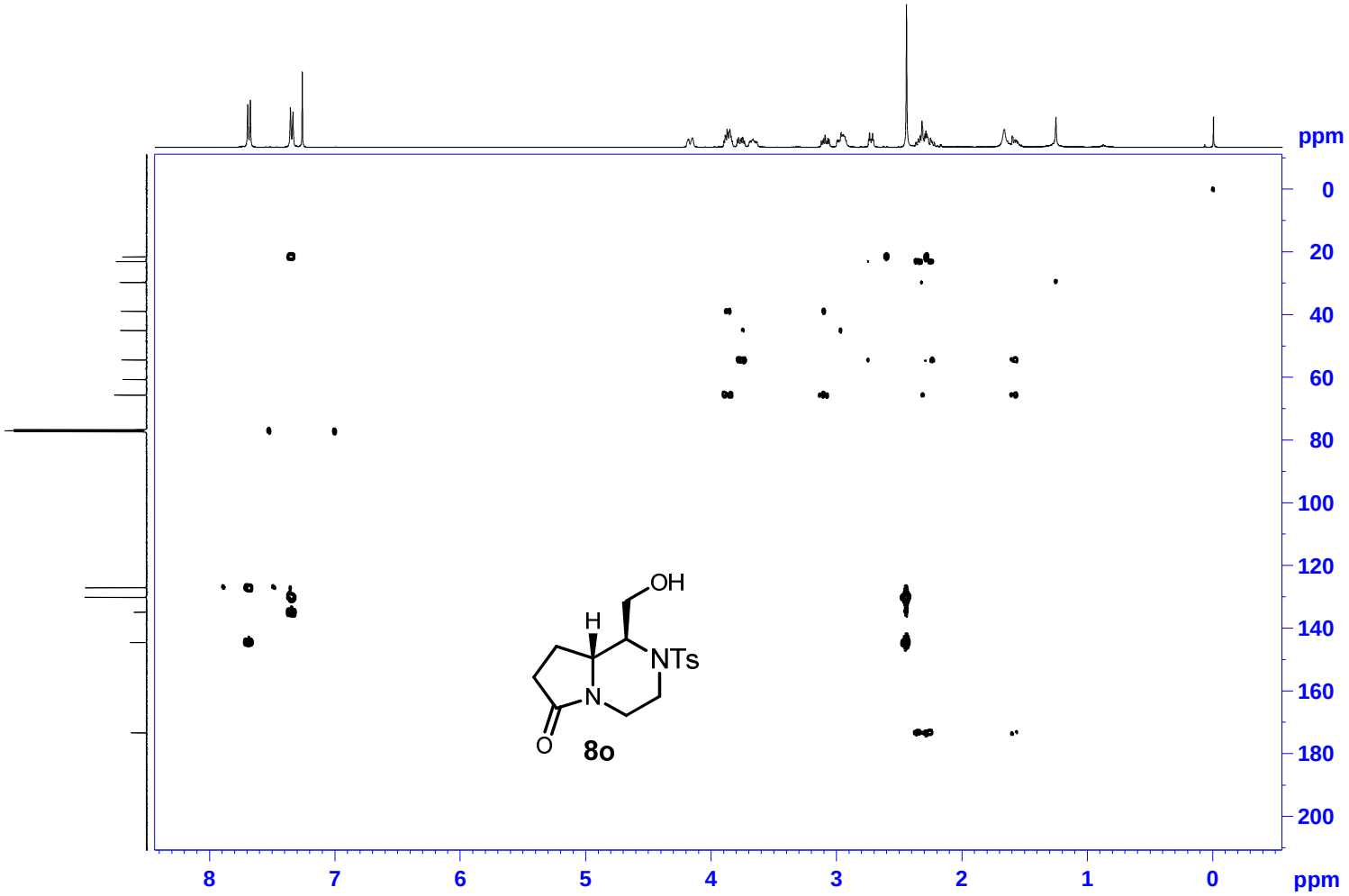
NOESY Spectrum of **8l** ($CDCl_3$, 298 K, 400 MHz)



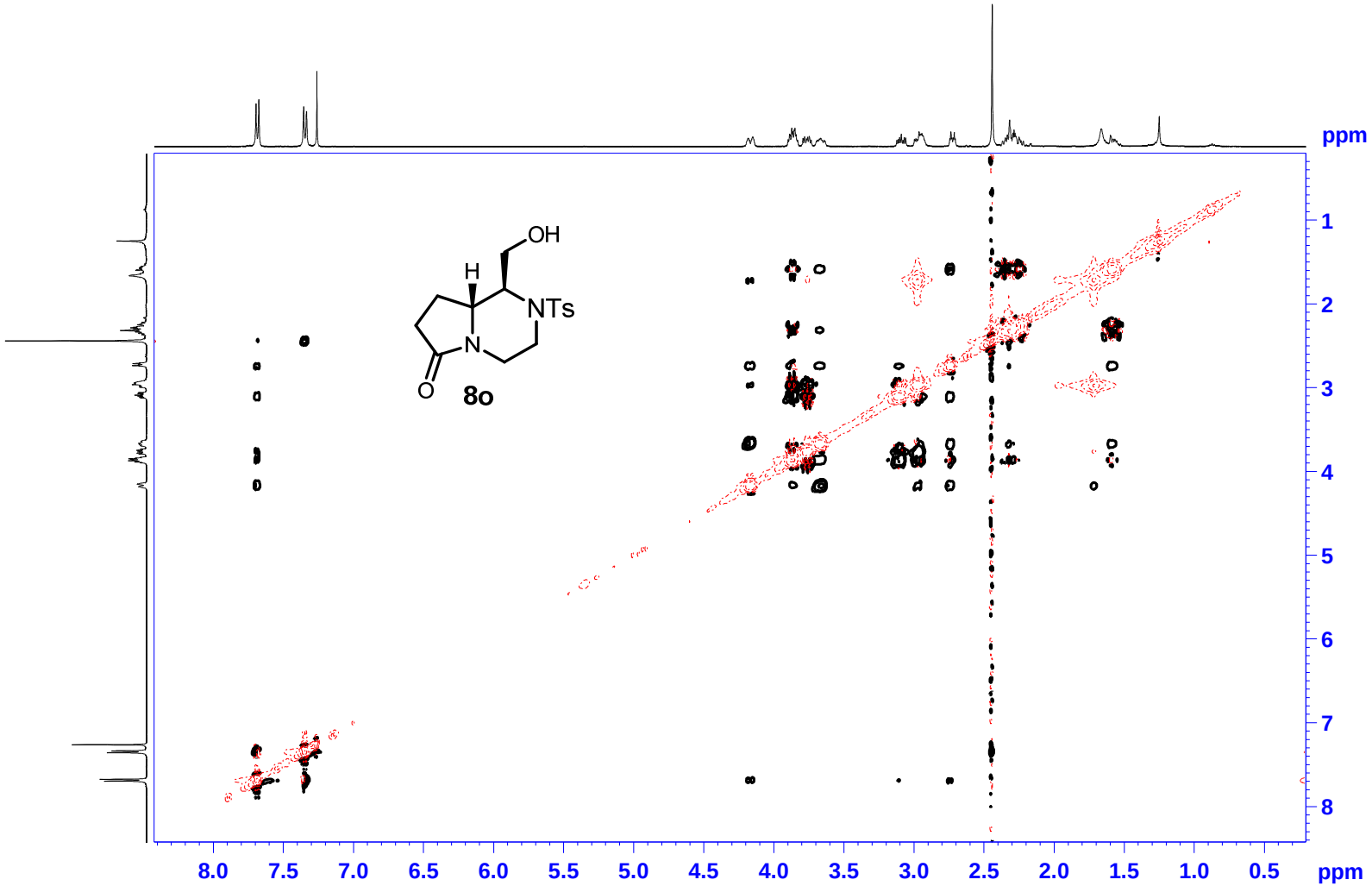
Important nOes observed in **8l**



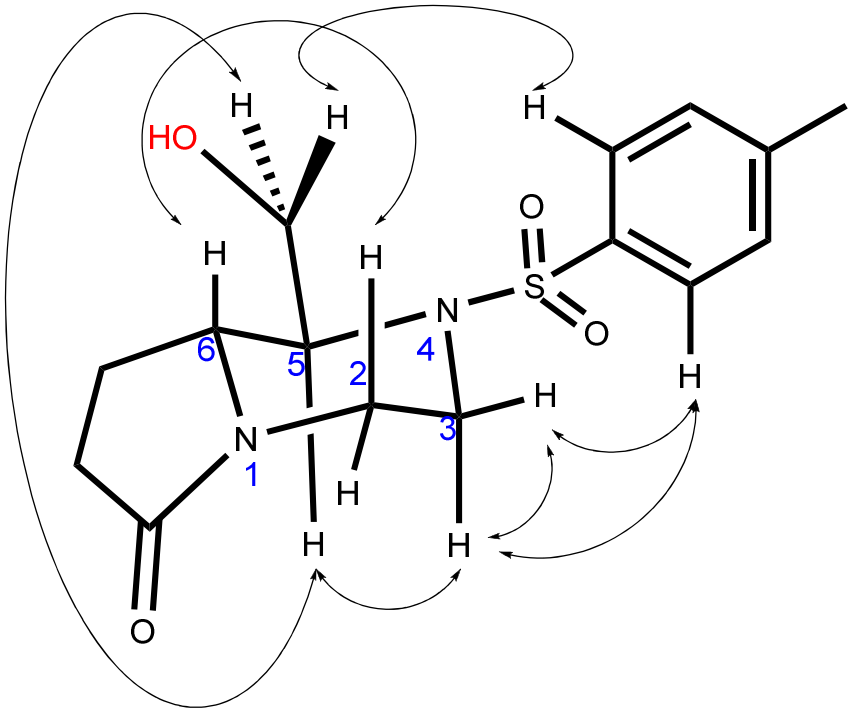
2D HSQC Spectrum of 8o ($CDCl_3$, 298 K, 400 MHz)



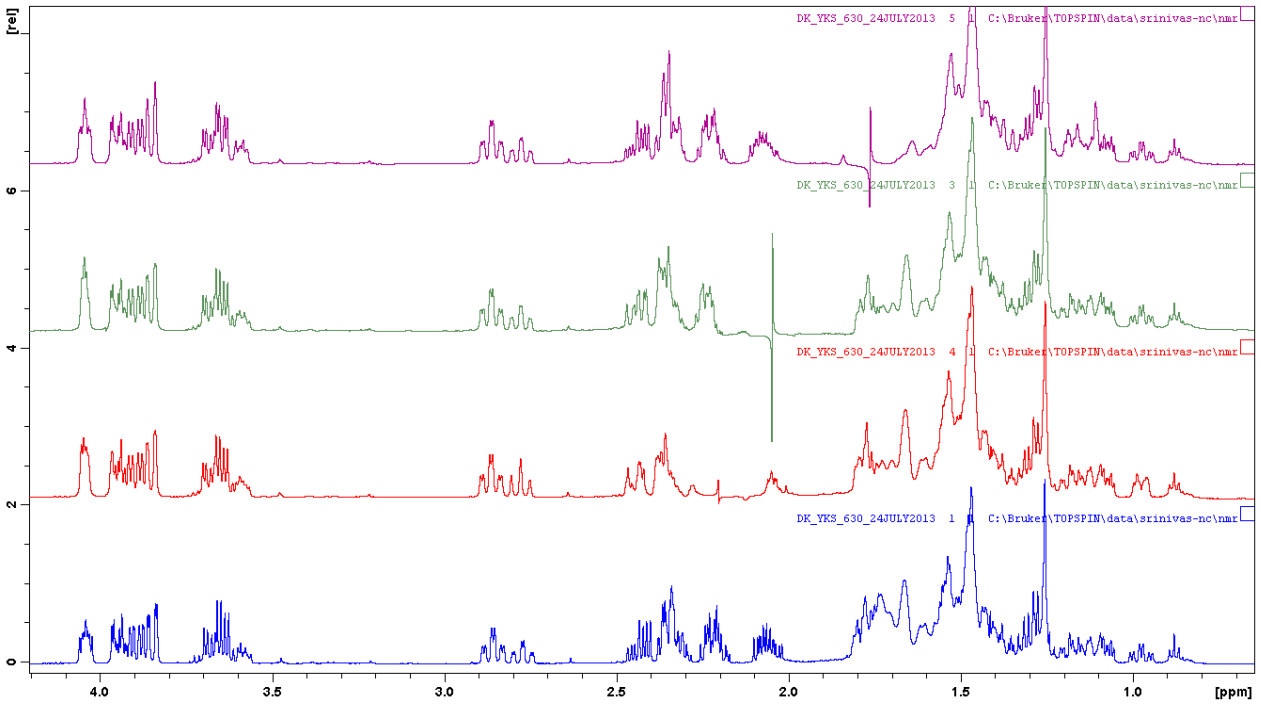
HMBC Spectrum of 8o ($CDCl_3$, 298 K, 400 MHz)

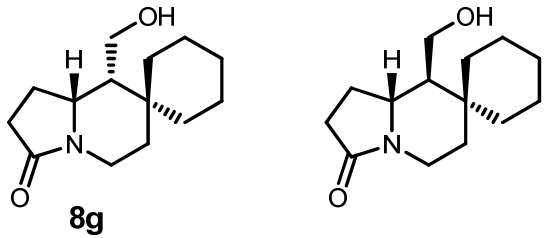


NOESY Spectrum of 8o ($CDCl_3$, 298 K, 400 MHz)



Important nOes observed in **8o**





8g

2 : 1

a :^{1}H NMR Spectrum of **8g** (mixture of isomers)
b: ^{1}H NMR Spectrum of **8g** (mixture of isomers) after irradiation at 1103.20 Hz (2.20 ppm)
c: ^{1}H NMR Spectrum of **8g** (mixture of isomers) after irradiation at 1024.95 Hz (2.04 ppm)
d: ^{1}H NMR Spectrum of **8g** (mixture of isomers) after irradiation at 882.57 Hz (1.76 ppm)