Wolff/Cope Approach to the AB Ring of the Sesterterpenoid Variecolin

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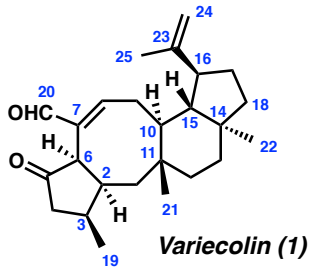
Abbreviations

Ac_2O	acetic anhydride	IRA-67	Amberlite resin with 3° amine functionality
DIAD	diisopropyl azo-dicarboxylate	*p*-Tol	*para*-tolyl; 4-methylbenzene
		sat	saturated

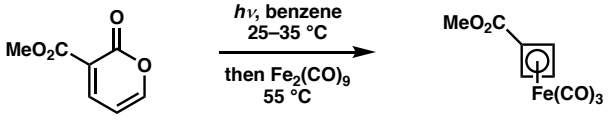
Compound Numbering Reference



Variecolin (1)

Additional Experimental Procedures for Known Compounds and Screening Reactions

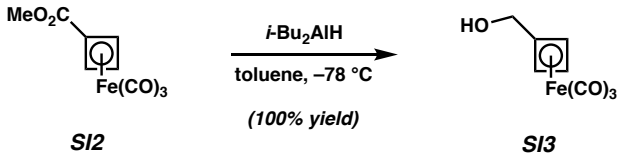
Preparation of the (Cyclobutadienyl)Tricarbonyliron Fragments



SI1 ***SI2***

(Cyclobutadiene)tricarbonyliron methyl ester (SI2).[1] Pyrone **SI1**[2] (5.086 g, 33.00 mmol, 1.0 equiv) was dissolved in spectrophotometric grade benzene (1 L, 0.033 M) in a flame-dried 1 L photochemical reactor containing a stir bar, the reactor and lamp were assembled and the solution was sparged with N_2 for 30 min. The resulting degassed solution was irradiated with a Hanovia medium-pressure mercury-vapor lamp affixed with a pyrex filter until consumption of pyrone **SI1** by TLC (5:1 CH_2Cl_2/EtOAc, typically requires 20 h to 5 d; $T_{internal}$ = 25–35 °C). The lamp was removed from the reactor and the solution was transferred to a dry 3 L flask containing a stir bar,

washing the photoreaction with excess benzene (2 x 30 mL). $Fe_2(CO)_9$ (14.4 g, 39.6 mmol, 1.2 equiv) was weighed into a glass jar in a glove box, transferred out of the box, and added to the reaction. The resulting suspension was warmed to 50 °C (internal) in an oil bath (T = 55–60 °C) and after 2 h at 50 °C, a second portion of $Fe_2(CO)_9$ (2.40 g, 6.60 mmol, 0.2 equiv) was added to the reaction. After another 1 h, the turbid reaction was cooled to room temperature and filtered through a plug of basic alumina (5 x 8 cm) capped with Celite (5 x 16 cm) washing with excess Et_2O (ca. 400 mL) until the eluent was colorless. The dark yellow solution was concentrated under reduced pressure to a turbid, yellow/brown oil. The crude material was purified by flash chromatography on SiO_2 (2.5 x 24 cm, 15:1 → 9:1 → 4:1 hexanes/Et_2O) to afford **SI2** (4.259 g, 17.03 mmol, 52% yield) as a dark yellow/brown oil that solidified in a –20 °C freezer. R_f = 0.54 (2:1 hexanes/EtOAc); ^{1}H NMR (300 MHz, C_6D_6) δ 3.84 (s, 2H), 3.22 (s, 3H), 3.20 (s, 1H). All other spectral data are consistent with reported values.

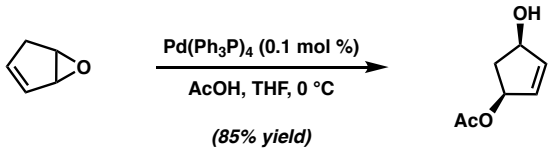


SI2 *SI3*

(Hydroxymethyl cyclobutadiene)tricarbonyliron (SI3).[3] To a solution of cyclobutadiene ester **SI2** (9.066 g, 36.27 mmol, 1.0 equiv) in toluene (120 mL, 0.3 M) at –78 °C was added neat *i*-Bu_2AlH (14.54 mL, 81.60 mmol, 2.25 equiv) dropwise over 15 min with vigorous stirring. Upon consumption of **SI2** by TLC analysis (typically as last of *i*-Bu_2AlH is added), EtOAc (3.54 mL, dried over $MgSO_4$, 1.0 equiv) was added and after 5 min the reaction was placed in a 0 °C ice bath. After 30 min, the reaction was slowly quenched with a 1 M solution of Na/K tartrate (100 mL) with vigorous stirring. After 5 min, the cooling bath was removed and EtOAc (50 mL) was added to the thick suspension. When the layers became clear (typically 5–8 h), they were separated and the aq phase was extracted with Et_2O (2 x 50 mL). The combined organic layers were dried with $MgSO_4$, filtered, and concentrated in vacuo. The thick oil was dried under high vacuum until a constant mass was achieved to afford **SI3** (8.105 g, 36.51 mmol, 100% yield) as a pale brown solid. R_f = 0.29 (2:1 hexanes/EtOAc); ^{1}H NMR (300 MHz, C_6D_6) δ 3.37 (s, 2H), 3.36 (d, J = 5.9 Hz, 2H), 3.26 (s, 1H), 0.62 (t, J = 5.9 Hz, 1H); $^{13}C\{^1H\}$ NMR (126 MHz, C_6D_6) δ 214.9, 85.0,

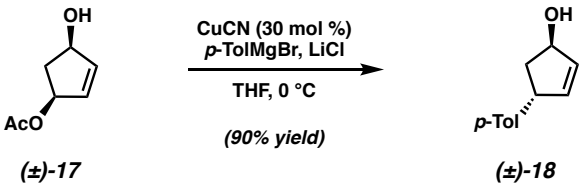
63.9, 62.2, 58.0; IR (Neat Film NaCl) 3326 (br), 2932, 2872, 2046, 1963, 1448, 1297, 1070, 997, 822, 613 cm^{-1}; HRMS (EI+) *m/z*: $[M]^+$ calc'd for $C_8H_6O_4Fe$ 221.9616, found 221.9615.

Preparation of the Model AB Ring Fragments

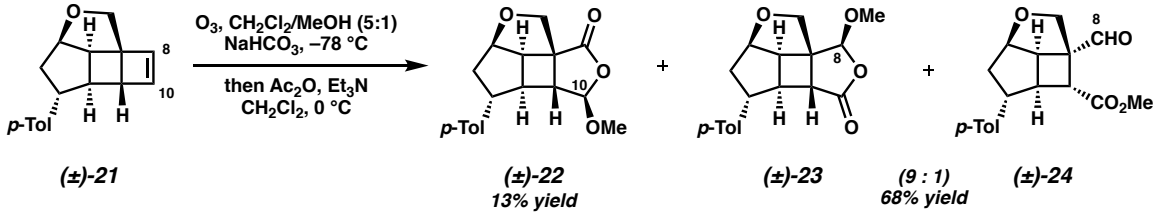


SI4 *(±)-17*

Monoacetate (±)-17.[4] A 1 L 3-neck flask fitted with an addition funnel was charged with $Pd(Ph_3P)_4$ (595 mg, 0.515 mmol, 0.001 equiv) and dissolved in THF (258 mL, 2 M) and cooled to 0 °C. The addition funnel was charged with a solution of cyclopentadiene monoepoxide (**SI4**)[5] (42.29 g corrected, 515.1 mmol, 1.0 equiv) in THF (86 mL) via cannula transfer. AcOH (29.5 mL, 515.1 mmol, 1.0 equiv) was added to the catalyst solution via syringe, followed by slow addition of **SI4** over 20 min. Upon consumption by TLC (reaction turns orange in color when complete) the solution was transferred to a flask washing with EtOAc and concentrated in vacuo. The crude material was purified by flash chromatography on SiO_2 (7 x 5 cm, dry load onto SiO_2, flush with Et_2O until product elutes by TLC) to afford (±)-**17** as a yellow semisolid. This was diluted with heptane (100 mL), concentrated and dried under high vacuum to afford a pale yellow semisolid (62.30 g, 438.3 mmol, 85.1% yield) that completely solidified in a –20 °C freezer. R_f = 0.33 (1:1 hexanes/EtOAc); ^{1}H NMR (300 MHz, $CDCl_3$) δ 6.12 (ddd, *J* = 5.61, 2.07, 1.30 Hz, 1H), 5.99 (ddd, *J* = 5.57, 2.04, 1.06 Hz, 1H), 5.52–5.47 (m, 1H), 4.76–4.69 (m, 1H), 2.81 (app dt, *J* = 14.7, 7.4 Hz, 1H), 2.06 (s, 3H), 1.72 (br s, 1H), 1.66 (dt, *J* = 14.6, 3.8 Hz, 1H). All other spectral data are consistent with reported values.

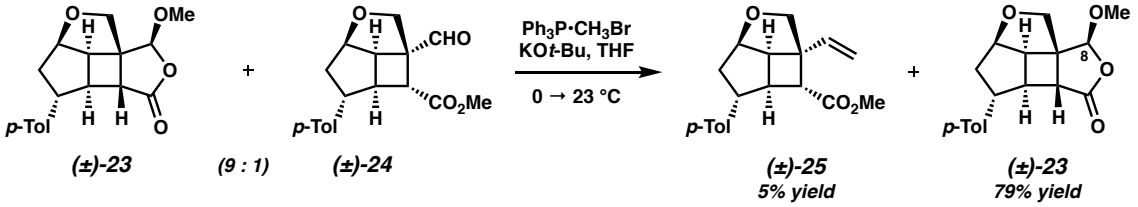


Aryl cyclopentenol 18.[6] A flask was charged with LiCl (896.4 mg, 21.1 mmol, 4.0 equiv), flame-dried under vacuum and cooled under nitrogen. To this was added CuCN (142 mg, 1.59 mmol, 0.3 equiv) and the solids were partially dissolved in THF (20 mL) and cooled to 0 °C. To this suspension was added a solution *p*-TolMgBr (15.9 mL, 15.9 mmol, 1 M in Et_2O). After 5 min, a solution of monoacetate (±)-**17** (751.5 mg, 5.29 mmol, 1.0 equiv) in THF (15 mL) over 5 min via cannulation and the flask was washed with additional THF (2 x 1 mL) for a quantitative transfer. Upon consumption of **17** by TLC (ca. 1.5 h), the reaction was slowly quenched with sat aq NH_4Cl (10 mL) and water (5 mL) and stirred vigorously for 30 min. The homogeneous phases were separated, the aq layer was extracted with EtOAc (3 x 30 mL), and the combined organics were dried over $MgSO_4$, filtered, and concentrated in vacuo. The crude material was purified by flash chromatography on SiO_2 (6:1 → 3:1 → 1:1 hexanes/Et_2O) to afford **18** (829.7 mg, 4.76 mmol, 90% yield) as a pale yellow oil. R_f = 0.63 (1:1 hexanes/EtOAc); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.10 (d, J = 7.83, 2H), 7.03 (d, J = 8.0 Hz, 2H), 6.04–6.01 (comp m, 2H), 5.05 (d, J = 5.1 Hz, 1H), 4.13–4.10 (m, 1H), 2.32 (s, 3H), 2.27 (ddd, J = 14.1, 8.0, 2.7 Hz, 1H), 2.09 (ddd, J = 14.1, 7.0, 5.5, 1H). All other spectral data are consistent with reported values.

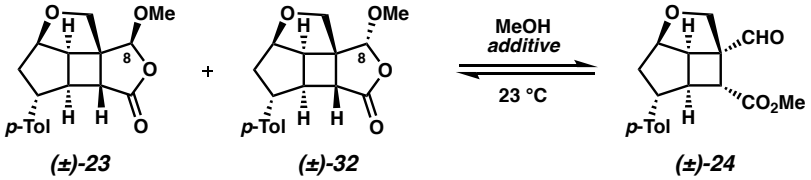


Ozonolysis of cyclobutene 21 to form acetals 22, 23 and aldehyde 24. To a solution of aryl cyclobutene **21** (49.6 mg, 0.208 mmol, 1.0 equiv) in a 5:1 mixture of CH_2Cl_2 (1.75 mL) and MeOH (0.35 mL, 0.1 M total) was added $NaHCO_3$ (5.2 mg, 63 μmol, 0.3 equiv) and a solution of Sudan Red 7b (75 μL of a 0.05 wt % solution in MeOH). The resulting pink-colored solution was cooled to –78 °C, sparged with a stream of oxygen for 1 min, then ozonolyzed until consumption of **21** by TLC (typically just as indicator turns colorless). The solution was sparged with oxygen for

1 min, the gas inlet was removed and the flask was fitted with a drying tube and warmed to room temperature. The crude reaction was filtered through a cotton plug with CH_2Cl_2 (2 x 1 mL) and benzene (1 mL). The filtrate was concentrated to ca. 0.5 mL in vacuo, diluted with 5 mL of benzene, and further concentrated to ca. 0.5 mL. This crude was dissolved in CH_2Cl_2 (2.1 mL), cooled to 0 °C, and Ac_2O (58.5 μL, 0.624 mmol, 3 equiv) and Et_3N (37.7 μL, 0.270 mmol, 1.3 equiv) were added. After 5 min the bath was removed and the reaction was stirred at room temperature for 5 h, at which point the reaction was diluted with CH_2Cl_2 (25 mL), washed with 5% H_2SO_4 (3 x 5 mL), sat aq $NaHCO_3$ (3 x 5 mL), brine, and dried over Na_2SO_4. The crude pale yellow oil was purified by flash chromatography on SiO_2 (4:1 → 3:1 → 1:1 hexanes/EtOAc) to furnish acetal **22** (8.3 mg, 27.6 μmol, 13% yield) as a colorless oil and an inseparable 9:1 mixture of acetal **23** and aldehyde **24** (42.6 mg, 0.142 mmol, 68% yield) as a pale yellow oil. The relative stereochemistry of **22** was determined by various experiments; see the compiled data below.

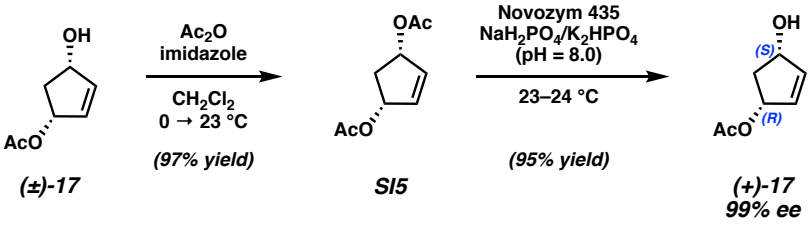


Wittig methylenation to form olefin 25 and recover acetal 23. To a suspension of $Ph_3P{\bullet}CH_3Br$ (23.6 mg, 66 μmol, 0.58 equiv) in THF (0.4 mL) at 0 °C was added KO*t*-Bu (6.4 mg, 57 μmol, 0.5 equiv) in one portion. The white suspension immediately turned bright yellow in color and was stirred for 15 min, at which point a solution of ca. 9:1 mixture acetal **23** and aldehyde **24** (34.2 mg, 114 μmol, 1.0 equiv) in THF (0.2 mL, 0.2 M total) was quantitatively transferred via cannulation. After 30 min, the reaction was quenched with 0.5 mL water and diluted with CH_2Cl_2 (3 mL). The layers were separated, the aq layer was extracted with CH_2Cl_2 (3 x 2 mL), the organics were dried over Na_2SO_4, filtered, and concentrated in vacuo. The crude material was purified by preparative TLC on SiO_2 (2:1 hexanes/EtOAc) to give olefin **25** (1.8 mg, 6.0 μmol, 5% yield) as a colorless oil and recovered acetal **23** (27.1 mg, 90.2 μmol, 79% yield) as a colorless oil. The relative stereochemistry of **23** was determined by various experiments; see the compiled data below.



Equilibration of acetal 23. To a solution of pure acetal **23** in MeOH (25 mM) was added the appropriate additive (MS = 0.5 mg/μmol; Lewis acid = 0.20 equiv). The reaction atmosphere was purged with nitrogen, capped and stirred at ambient temperature. After 20–24 h the reaction was diluted with Et_2O, filtered through a small plug of SiO_2 and concentrated in vacuo. The crude filtrate was then analyzed by ^1H NMR analysis; see Table 1 in the manuscript. In addition to acetal **23** and aldehyde **24**, acetal diastereomer **32** was identified as a minor product. The relative stereochemistry of **32** was determined by various experiments; see the compiled data below.

Preparation of the Asymmetric AB Ring Fragments



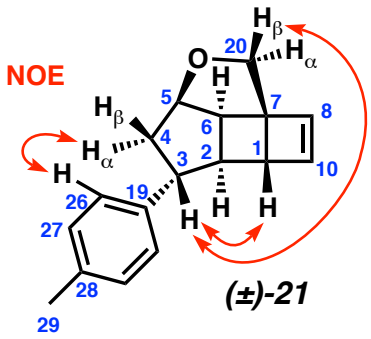
Monoacetate (+)-17.[7] To a solution of monoacetate (±)-**17** (40.43 g, 284.4 mmol, 1.0 equiv) in CH_2Cl_2 (47 mL, 6 M) was added imidazole (21.11 g, 310 mmol, 1.09 equiv), and after the contents were completely dissolved, the solution was cooled to 0 °C and Ac_2O (29.3 mL, 310 mmol, 1.09 equiv) was added over 5–7 min via syringe. After 10 min, the bath was removed and the solution was stirred for 22 h at room temperature, at which EtOAc (150 mL) was added and the contents were poured into ice-cold 1 N HCl (150 mL). The layers were separated and the aq layer was saturated with NaCl (s) and extracted with Et_2O (2 x 100 mL, 1 x 50 mL). The combined organics were washed with sat. aq $NaHCO_3$ (100 mL), this aq layer was saturated with NaCl (s) and extracted with Et_2O (2 x 100 mL). The combined organics were dried over $MgSO_4$, filtered, concentrated, and dried under high vacuum to afford **SI5** (50.88 g, 276.2 mmol, 97% yield) as a pale yellow oil. This material could be used in subsequent reactions as is, or can be purified by

short-path distillation (bp = 74–98 °C, ca. 0.8 torr) with some material loss to give **SI5** as a colorless oil in 89% yield. R_f = 0.75 (Et_2O); ^{1}H NMR (300 MHz, $CDCl_3$) δ 6.09 (d, *J* = 0.9 Hz, 2H), 5.54 (ddd, *J* = 7.6, 3.8, 0.9 Hz, 2H), 2.88 (app dt, *J* = 15.1, 7.6 Hz, 1H), 2.06 (s, 6H), 1.74 (app dt, *J* = 15.0, 3.8 Hz, 1H). All other spectral data are consistent with reported values.[7c]

meso-bisacetate **SI5** (33.15 g, 180.0 mmol, 1.0 equiv) was added to a purified water triple-rinsed 1 L Erlenmeyer flask containing a stir bar and partially dissolved in aq NaH_2PO_4/K_2HPO_4 buffer (0.05 M, pH = 8.0). To this solution was added Novozym 435 lipase (4.0 g), the flask was covered with parafilm and gently stirred at room temperature until consumption of **SI5** by TLC analysis (5–8 h). The contents were vacuum filtered and the supported enzyme was washed with water (150 mL) and EtOAc (2 x 150 mL). The filtrate layers were separated and the aq layer was saturated with NaCl (200 g), extracted with EtOAc (5 x 200 mL, follow by TLC), and the combined organics were dried over $MgSO_4$, filtered, and concentrated in vacuo. The crude oil was dissolved in Et_2O (150 mL) and heptane was added (150 mL), followed by concentration in vacuo to afford a white semisolid. This was repeated one more time and the solid was dried under high vacuum to provide (+)-**17** (24.36 g, 171 mmol, 95% yield) as a white semisolid. The crude material is > 95% pure by ^{1}H NMR, but can be purified by flash chromatography on SiO_2 (1:2 hexanes/Et_2O, dry load onto SiO_2) to provide (+)-(*1R,4S*)-**17** in 89% yield. The material displayed the same spectral properties as above; mp = 45–49 °C; $[\alpha]_D^{22.5}$ +61.2 (*c* 1.28, $CHCl_3$, 99% ee). GC conditions: 100 °C isothermal, GTA column, t_R (min): major = 30.5, minor = 27.6. We have reused the recovered Novozym 435 up to four times and observed slightly lower activity for each subsequent use with identical selectivities. It is important to control stirring as the stirbar can break apart the lipase support, further diminishing the enzyme activity.

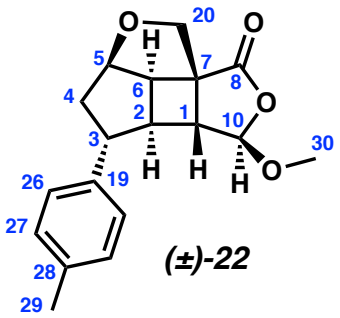
Spectral Assignment Data

Model Cycloadduct 21. Cycloadduct **21** was prepared according the manuscript procedure and isolated as a single compound. The structure was elucidated by ^{1}H, ^{13}C, HRMS, COSY, HSQC and NOESY-1D/2D NMR experiments. The assignment data is summarized below with carbon atoms 1–25 mapped onto the numbering of variecolin *(see page S2)*. The regiochemistry and relative stereochemistry resulting from the cycloaddition correlates with all known examples of intramolecular cyclobutadiene–olefin cycloadditions; see manuscript references 18, 19, 20, 36 and 48.



C atom	δ (H)	δ (C)
1	2.94	54.9
2	2.35	46.5
3	3.27	50.3
4	H_α = 2.03 H_β = 2.46	44.6
5	4.71–4.69	84.1
6	3.06	52.6
7	–	59.9
8	6.31	140.3
10	6.35	138.4
19	–	142.9 or 135.60
20	H_α = 3.87 H_β = 3.91	71.2
26	7.08	127.2
27	7.11	129.3
28	–	142.9 or 135.60
29	2.32	21.1

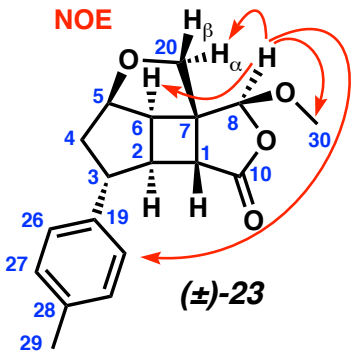
Undesired Acetal 22. Acetal **22** was prepared according the manuscript procedure (as well as described above) and isolated as a single diastereomer. The structure was elucidated by ^{1}H, ^{13}C, HRMS, COSY, NOESY-1D NMR experiments. The relative stereochemistry of C(10) could not be determined by NOESY experiments as the C(1) and C(2) resonances overlapped in the ^{1}H spectrum. The C(20) resonances do not show any correlation with C(10), however, the absence of this interaction does not confirm the structural assignment. The relative stereochemistry is therefore proposed in relation to the X-ray structural analysis of related acetal **43**.



(±)-22

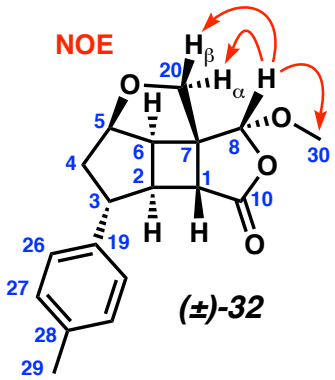
C atom	δ (H)
1	2.55–2.53
2	2.55–2.53
3	3.49
4	H_α = 1.80 H_β = 2.57
5	4.77
6	3.57
7	–
8	–
10	5.37
19	–
20	H_α = 4.03 H_β = 4.14
26	7.13 or 7.05
27	7.13 or 7.05
28	–
29	2.33
30	3.50

Desired Acetal 23. Acetal **23** was prepared according the manuscript olefination procedure (as well as above) and isolated as a single diastereomer. The structure was elucidated by ^{1}H, ^{13}C, HRMS and NOESY-1D NMR experiments. Correlations between the C(8) ^{1}H resonance and the C(20α), C(6) and C(26/27) resonances provide strong support for the relative stereochemistry.



C atom	δ (H)
1	2.89
2	2.66
3	3.55
4	H_α = 1.76 H_β = 2.53
5	4.71
6	3.31
7	–
8	5.40
10	–
19	–
20	H_α = 3.78 H_β = 4.08
26	7.08
27	7.08
28	–
29	2.31
30	3.48

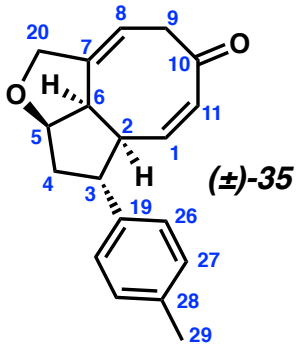
Desired Acetal 32. Acetal **32** was prepared as a minor component according the manuscript equilibration procedure (as well as above) and isolated as a single diastereomer. The structure was elucidated by ^{1}H, ^{13}C, HRMS, COSY, NOESY-1D NMR experiments. Correlations between the C(8) ^{1}H resonance and both C(20α) and C(20β) resonances provide support for the relative stereochemistry. In addition, this diastereomer can be converted to acetal **23** via the noted equilibration conditions.



(±)-32

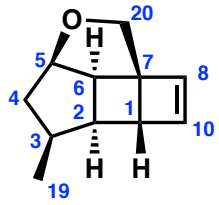
C atom	δ (H)
1	2.85
2	2.66
3	3.50
4	H_α = 1.79 H_β = 2.54
5	4.68
6	3.72
7	–
8	5.30
10	–
19	–
20	H_α = 3.69 H_β = 4.07
26	7.08
27	7.08
28	–
29	2.31
30	3.63

Cyclooctadienone 35. Wolf/Cope product **35** was prepared according the manuscript procedure and the structure was elucidated by ^{1}H, ^{13}C, HRMS and COSY NMR experiments.



C atom	δ (H) $CDCl_3$
1	5.80–5.73
2	3.23
3	3.13–3.05
4	H_α = 1.93 H_β = 2.30
5	4.76
6	3.66
7	–
8	5.63–5.59
9	3.41 and 3.13–3.05
10	–
11	5.80–5.73
19	–
20	4.49 and 4.40
26	7.15
27	7.15
28	–
29	2.34

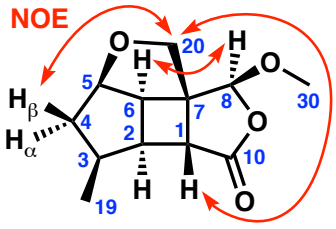
Cycloadduct 41. Cycloadduct **41** was prepared according the manuscript procedure and isolated as a single compound. The structure was elucidated by ^{1}H, ^{13}C, HRMS, COSY, HSQC and HMBC NMR experiments.



41

C atom	δ (H)	δ (C)
1	3.00	47.8
2	2.10–2.05	44.8
3	2.23	37.3
4	H_α = 2.10–2.05 H_β = 1.37	39.0
5	4.84	84.7
6	2.89	52.0
7	–	57.9
8	6.27	140.2
10	6.22	138.4
19	0.97	14.3
20	4.04, 3.94	70.3

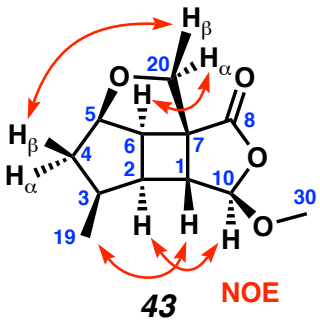
Acetal 42. Acetal **42** was prepared according the manuscript olefination procedure and isolated as a single diastereomer. The structure was elucidated by ^{1}H, ^{13}C, HRMS, COSY, HSQC, HMBC and NOESY-2D NMR experiments. Correlations between the C(8) and C(6) ^{1}H resonances, as well as the C(20) and C(4β), C(1) resonances provide strong support for the relative stereochemistry. The C(20) resonances are not distinguishable by δ in the ^{1}H spectrum.



42

C atom	δ (H)	δ (C)
1	2.89	40.8
2	2.61	44.7
3	2.39–2.30	37.2
4	H_α = 2.06 H_β = 1.60	38.6
5	4.80	86.7
6	3.13	51.5
7	–	52.4
8	5.39	107.5
10	–	179.0
19	1.11	16.9
20	3.99	70.9
30	3.48	56.8

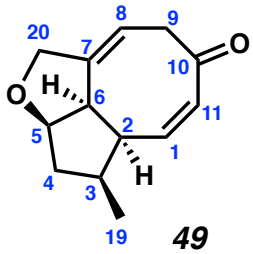
Acetal 43. Acetal **43** was prepared according the manuscript olefination procedure and isolated as a single diastereomer. The structure was elucidated by ^{1}H, ^{13}C, HRMS, COSY, HSQC, HMBC and NOESY-2D NMR experiments. Correlations between the C(10) and C(2) ^{1}H resonances, as well as the C(20β) and C(4β), C(1) resonances, C(20α) and C(6) resonances, and C(10) and C(1) resonances provide strong support for the relative stereochemistry. The structural assignment was confirmed by X-ray analysis (vide infra), although the absolute stereochemistry could not be determined.



43

C atom	δ (H)	δ (C)
1	2.58	42.8
2	2.40	41.2
3	2.26	38.2
4	H_α = 2.16 H_β = 1.55	38.7
5	4.89	86.6
6	3.33	55.5
7	–	50.1
8	–	177.2
10	5.30	108.4
19	1.03	15.3
20	H_α = 4.19 H_β = 4.11	73.2
30	3.49	56.5

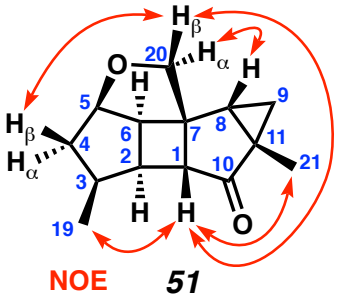
Cyclooctadienone 49. Wolf/Cope product **49** was prepared according the manuscript procedure and the structure was elucidated by ^{1}H, ^{13}C, HRMS, and COSY experiments.



49

C atom	δ (H)
1	6.08
2	3.18–3.13
3	2.36
4	2.18, 1.44
5	4.59
6	3.44
7	–
8	5.56–5.51
9	3.28, 2.99
10	–
11	5.93
19	1.11
20	4.59, 4.38

Cyclopropane 51. Cyclopropane **51** was prepared according the manuscript Wolff/Cope procedure and isolated as a single compound. The structure was elucidated by ^{1}H, ^{13}C, HRMS, COSY, HSQC, HMBC and NOESY-2D NMR experiments. Correlations between the C(1) and C(19), C(21) and C(20β) ^{1}H resonances, as well as the C(20α) and C(8) resonances, and C(20β) and C(4β) resonances provide strong support for the relative stereochemistry.



C atom	δ (H)	δ (C)
1	2.25	46.7
2	2.04	43.1
3	2.16	37.4
4	H_α = 2.12–2.07 H_β = 1.49	38.8
5	4.80	86.3
6	2.84	51.0
7	–	49.7
8	2.86	57.9
9	1.56–1.54	32.7
10	–	198.7
11	–	67.1
19	0.96	15.2
20	H_α = 3.84 H_β = 3.94	74.3
21	1.22	9.4

Notes and References

[1] Limanto, J.; Snapper, M. L. *J. Am. Chem. Soc.* **2000**, *122*, 8071–8072.

[2] Pyrone **SI1** is available from commercial sources, however, we have prepared it on large scale according to: Corey, E. J.; Watt, D. S. *J. Am. Chem. Soc.* **1973**, *95*, 2303–2311.

[3] Williams, M. J.; Deak, H. L.; Snapper, M. L. *J. Am. Chem. Soc.* **2007**, *129*, 486–487.

[4] Deardorff, D. R.; Myles, D. C. *Org. Synth.* **1989**, *67*, 114–120.

[5] Crandall, J. K.; Banks, D. B.; Colyer, R. A.; Watkins, R. J.; Arrington, J. P. *J. Org. Chem.* **1968**, *33*, 423–425.

[6] Kawamura, S.-i.; Yamakoshi, H.; Nojima, M. *J. Org. Chem.* **1996**, *61*, 5953–5958.

[7] (a) Reetz, M. T.; Eipper, A.; Tielmann, P.; Mynott, R. *Adv. Synth. Catal.* **2002**, *344*, 1008–1016. (b) Tietze, L. F.; Stadler, C.; Böhnke, N.; Brasche, G.; Grube, A. *Synlett* **2007**, 485–487. (c) For a related example, see: Deardorff, D. R.; Windham, C. Q.; Craney, C. L. *Org. Synth.* **1996**, *73*, 25–35.

X-ray Crystal Structure Data for Acetal 43

CALIFORNIA INSTITUTE OF TECHNOLOGY

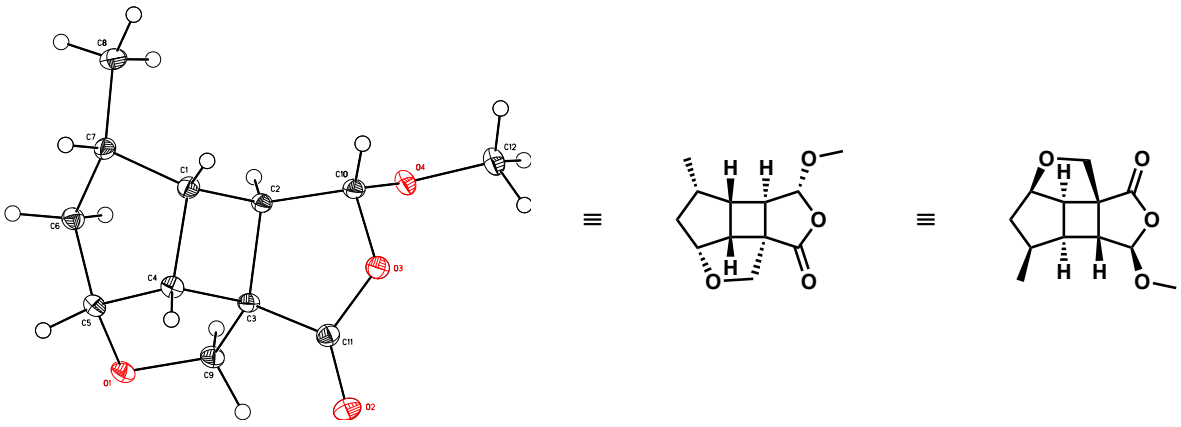
BECKMAN INSTITUTE

X-RAY CRYSTALLOGRAPHY LABORATORY

Crystal Structure Analysis of MRK03 (acetal 43)

(718289)

Contents



Acetal **43** is shown with 50% probability ellipsoids. Crystallographic data have been deposited at the CCDC, 12 Union Road, Cambridge CB2 1EZ, UK, and copies can be obtained on request, free of charge, by quoting the publication citation and the deposition number 718289.

Table SI 1. Crystal data and structure refinement for MRK03 (CCDC 718289).

Empirical formula	$C_{12}H_{16}O_4$
Formula weight	224.25
Crystallization Solvent	Chloroform/dichloromethane/diethylether
Crystal Habit	Block
Crystal size	0.30 x 0.28 x 0.20 mm^3
Crystal color	Colorless

Data Collection

Type of diffractometer	Bruker KAPPA APEX II
Wavelength	0.71073 Å MoKα
Data Collection Temperature	100(2) K
θ range for 9805 reflections used in lattice determination	3.31 to 34.80°
Unit cell dimensions	a = 6.3017(3) Å b = 11.7387(5) Å c = 14.4000(6) Å
Volume	1065.22(8) $Å^3$
Z	4
Crystal system	Orthorhombic
Space group	$P2_12_12_1$
Density (calculated)	1.398 Mg/m^3
F(000)	480
Data collection program	Bruker APEX2 v2.1-0
θ range for data collection	2.24 to 35.05°
Completeness to θ = 35.05°	97.3 %
Index ranges	$-10 \le h \le 10$, $-17 \le k \le 18$, $-23 \le l \le 22$
Data collection scan type	ω scans; 13 settings
Data reduction program	Bruker SAINT-Plus v7.34A
Reflections collected	37096
Independent reflections	4514 [R_{int}= 0.1080]
Absorption coefficient	0.104 mm^{-1}
Absorption correction	None
Max. and min. transmission	0.9794 and 0.9694

Table SI 1 (cont.)

Structure Solution and Refinement

Structure solution program	SHELXS-97 (Sheldrick, 2008)
Primary solution method	Direct methods
Secondary solution method	Difference Fourier map
Hydrogen placement	Difference Fourier map
Structure refinement program	SHELXL-97 (Sheldrick, 2008)
Refinement method	Full matrix least-squares on F^2
Data / restraints / parameters	4514 / 0 / 209
Treatment of hydrogen atoms	Unrestrained
Goodness-of-fit on F^2	1.899
Final R indices [$I>2\sigma(I)$, 4349 reflections]	R1 = 0.0286, *w*R2 = 0.0740
R indices (all data)	R1 = 0.0301, *w*R2 = 0.0744
Type of weighting scheme used	Sigma
Weighting scheme used	$w=1/\sigma^2(Fo^2)$
Max shift/error	0.001
Average shift/error	0.000
Absolute structure determination	Not able to determine reliably
Absolute structure parameter	0.1(4)
Largest diff. peak and hole	0.339 and -0.290 e.Å^{-3}

Special Refinement Details

Crystals were mounted on a glass fiber using Paratone oil then placed on the diffractometer under a nitrogen stream at 100K.

Refinement of F^2 against ALL reflections. The weighted R-factor (*w*R) and goodness of fit (S) are based on F^2, conventional R-factors (R) are based on F, with F set to zero for negative F^2. The threshold expression of $F^2 > 2\sigma(F^2)$ is used only for calculating R-factors(gt) etc. and is not relevant to the choice of reflections for refinement. R-factors based on F^2 are statistically about twice as large as those based on F, and R-factors based on ALL data will be even larger.

All esds (except the esd in the dihedral angle between two l.s. planes) are estimated using the full covariance matrix. The cell esds are taken into account individually in the estimation of esds in distances, angles and torsion angles; correlations between esds in cell parameters are only used when they are defined by crystal symmetry. An approximate (isotropic) treatment of cell esds is used for estimating esds involving l.s. planes.

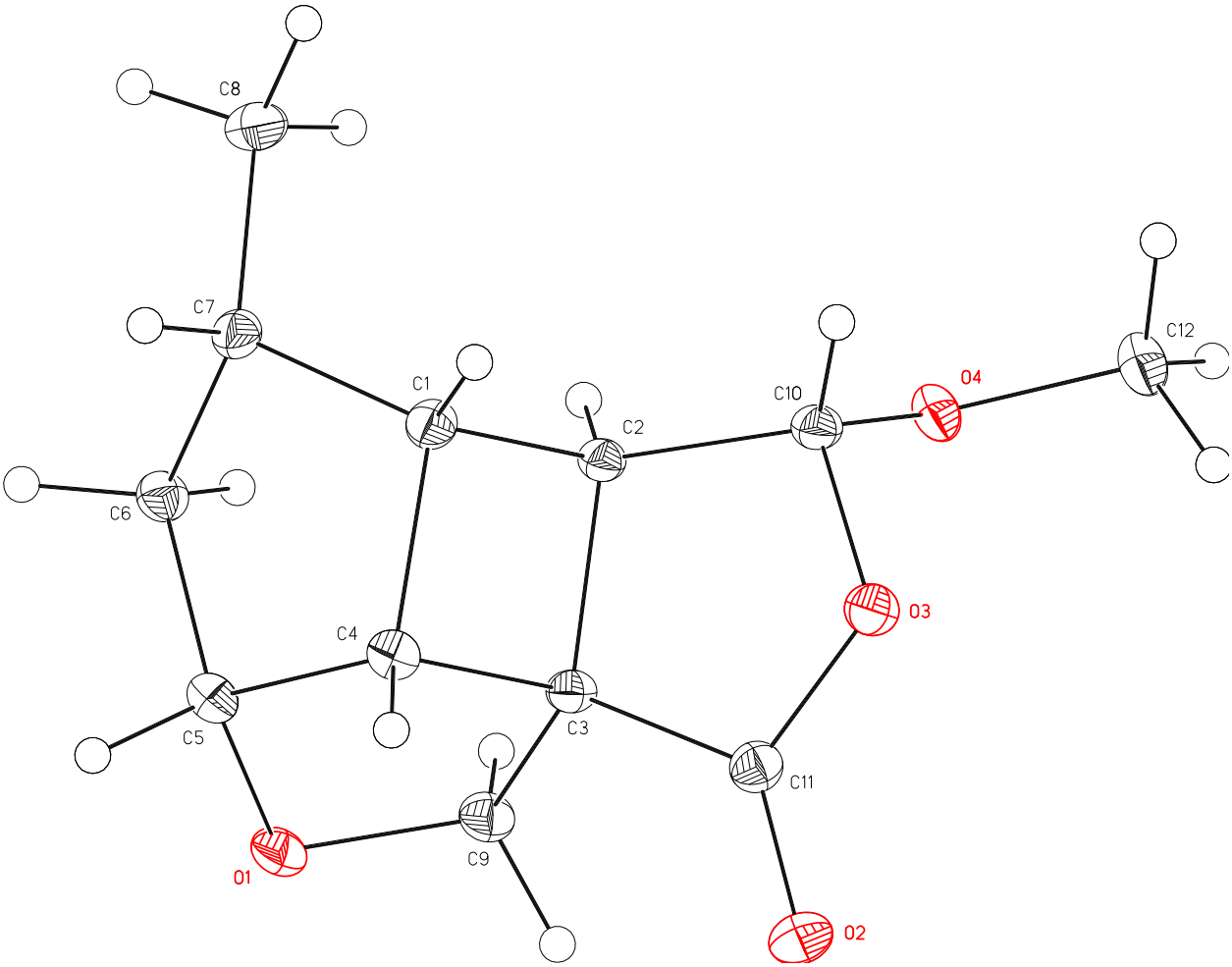

C8
C7
C1
C2
C10
O4
C12
C6
O3
C4
C5
C3
C11
O1
C9
O2

Table SI 2. Atomic coordinates (x 10^4) and equivalent isotropic displacement parameters ($Å^2$ x 10^3) for MRK03 (CCDC 718289). U(eq) is defined as the trace of the orthogonalized U^{ij} tensor.

	x	y	z	U_{eq}
O(1)	3796(1)	867(1)	1413(1)	15(1)
O(2)	-1332(1)	-917(1)	2033(1)	18(1)
O(3)	-426(1)	-1149(1)	3528(1)	14(1)
O(4)	2465(1)	-2244(1)	3980(1)	14(1)
C(1)	2711(1)	953(1)	3797(1)	12(1)
C(2)	3032(1)	-331(1)	3582(1)	11(1)
C(3)	2043(1)	-173(1)	2600(1)	11(1)
C(4)	1818(1)	1127(1)	2799(1)	12(1)
C(5)	3644(1)	1607(1)	2205(1)	12(1)
C(6)	5609(1)	1592(1)	2839(1)	12(1)
C(7)	4740(1)	1674(1)	3834(1)	13(1)
C(8)	6340(1)	1339(1)	4579(1)	19(1)
C(9)	3337(1)	-276(1)	1708(1)	13(1)
C(10)	1560(1)	-1173(1)	4061(1)	12(1)
C(11)	-47(1)	-785(1)	2646(1)	13(1)
C(12)	1362(1)	-3130(1)	4468(1)	17(1)

Table SI 3. Bond lengths [Å] and angles [°] for MRK03 (CCDC 718289).

O(1)-C(9)	1.4372(9)	C(9)-C(3)-C(4)	106.32(5)
O(1)-C(5)	1.4374(8)	C(2)-C(3)-C(4)	89.20(5)
O(2)-C(11)	1.2077(8)	C(5)-C(4)-C(1)	106.87(5)
O(3)-C(11)	1.3610(7)	C(5)-C(4)-C(3)	100.86(5)
O(3)-C(10)	1.4689(8)	C(1)-C(4)-C(3)	90.48(5)
O(4)-C(10)	1.3853(9)	C(5)-C(4)-H(4)	113.5(6)
O(4)-C(12)	1.4356(9)	C(1)-C(4)-H(4)	123.1(6)
C(1)-C(7)	1.5344(9)	C(3)-C(4)-H(4)	118.0(7)
C(1)-C(2)	1.5518(10)	O(1)-C(5)-C(6)	114.23(6)
C(1)-C(4)	1.5569(8)	O(1)-C(5)-C(4)	105.60(6)
C(1)-H(1)	0.942(11)	C(6)-C(5)-C(4)	105.50(5)
C(2)-C(10)	1.5213(9)	O(1)-C(5)-H(5)	106.8(6)
C(2)-C(3)	1.5565(8)	C(6)-C(5)-H(5)	112.0(6)
C(2)-H(2)	0.997(11)	C(4)-C(5)-H(5)	112.7(6)
C(3)-C(11)	1.5018(9)	C(7)-C(6)-C(5)	105.43(5)
C(3)-C(9)	1.5263(8)	C(7)-C(6)-H(6A)	110.2(6)
C(3)-C(4)	1.5590(10)	C(5)-C(6)-H(6A)	108.8(6)
C(4)-C(5)	1.5406(9)	C(7)-C(6)-H(6B)	111.8(6)
C(4)-H(4)	0.962(10)	C(5)-C(6)-H(6B)	111.5(6)
C(5)-C(6)	1.5385(9)	H(6A)-C(6)-H(6B)	109.1(8)
C(5)-H(5)	1.020(12)	C(8)-C(7)-C(1)	115.71(6)
C(6)-C(7)	1.5370(8)	C(8)-C(7)-C(6)	113.83(6)
C(6)-H(6A)	0.998(12)	C(1)-C(7)-C(6)	103.23(5)
C(6)-H(6B)	0.957(11)	C(8)-C(7)-H(7)	108.4(7)
C(7)-C(8)	1.5237(10)	C(1)-C(7)-H(7)	106.3(7)
C(7)-H(7)	0.960(14)	C(6)-C(7)-H(7)	108.9(7)
C(8)-H(8A)	1.004(13)	C(7)-C(8)-H(8A)	112.1(8)
C(8)-H(8B)	0.934(15)	C(7)-C(8)-H(8B)	110.6(8)
C(8)-H(8C)	0.985(15)	H(8A)-C(8)-H(8B)	110.3(11)
C(9)-H(9A)	0.919(12)	C(7)-C(8)-H(8C)	111.7(7)
C(9)-H(9B)	0.973(11)	H(8A)-C(8)-H(8C)	108.7(12)
C(10)-H(10)	0.947(13)	H(8B)-C(8)-H(8C)	103.0(11)
C(12)-H(12A)	0.977(13)	O(1)-C(9)-C(3)	106.39(5)
C(12)-H(12B)	1.005(16)	O(1)-C(9)-H(9A)	109.3(7)
C(12)-H(12C)	0.982(13)	C(3)-C(9)-H(9A)	111.9(7)
C(9)-O(1)-C(5)	108.46(4)	O(1)-C(9)-H(9B)	110.2(7)
C(11)-O(3)-C(10)	110.14(5)	C(3)-C(9)-H(9B)	111.9(7)
C(10)-O(4)-C(12)	114.65(6)	H(9A)-C(9)-H(9B)	107.2(10)
C(7)-C(1)-C(2)	115.74(6)	O(4)-C(10)-O(3)	108.92(5)
C(7)-C(1)-C(4)	105.16(5)	O(4)-C(10)-C(2)	107.47(5)
C(2)-C(1)-C(4)	89.45(5)	O(3)-C(10)-C(2)	105.66(5)
C(7)-C(1)-H(1)	113.3(8)	O(4)-C(10)-H(10)	114.1(8)
C(2)-C(1)-H(1)	114.1(8)	O(3)-C(10)-H(10)	103.9(8)
C(4)-C(1)-H(1)	116.8(7)	C(2)-C(10)-H(10)	116.2(8)
C(10)-C(2)-C(1)	117.45(5)	O(2)-C(11)-O(3)	121.58(6)
C(10)-C(2)-C(3)	104.21(5)	O(2)-C(11)-C(3)	128.11(6)
C(1)-C(2)-C(3)	90.76(5)	O(3)-C(11)-C(3)	110.21(5)
C(10)-C(2)-H(2)	109.7(6)	O(4)-C(12)-H(12A)	112.8(8)
C(1)-C(2)-H(2)	116.9(7)	O(4)-C(12)-H(12B)	106.4(8)
C(3)-C(2)-H(2)	116.1(6)	H(12A)-C(12)-H(12B)	114.0(11)
C(11)-C(3)-C(9)	117.88(5)	O(4)-C(12)-H(12C)	113.9(8)
C(11)-C(3)-C(2)	104.72(5)	H(12A)-C(12)-H(12C)	103.4(11)
C(9)-C(3)-C(2)	122.77(5)	H(12B)-C(12)-H(12C)	106.4(12)
C(11)-C(3)-C(4)	112.36(5)		

Table SI 4. Anisotropic displacement parameters ($Å^2 x 10^4$) for MRK03 (CCDC 718289). The anisotropic displacement factor exponent takes the form: $-2\pi^2[h^2 a^{*2} U^{11} + ... + 2 h k a^* b^* U^{12}]$

	U^{11}	U^{22}	U^{33}	U^{23}	U^{13}	U^{12}
O(1)	193(2)	161(2)	85(2)	11(2)	10(2)	-16(2)
O(2)	154(2)	213(3)	175(2)	3(2)	-58(2)	-25(2)
O(3)	104(2)	182(2)	129(2)	20(2)	0(2)	-20(2)
O(4)	156(2)	124(2)	128(2)	24(2)	24(2)	-6(2)
C(1)	128(3)	132(3)	98(2)	-18(2)	20(2)	-11(2)
C(2)	107(2)	125(3)	83(2)	3(2)	-1(2)	-12(2)
C(3)	101(2)	129(3)	86(2)	-2(2)	-5(2)	-1(2)
C(4)	112(2)	126(3)	115(2)	2(2)	4(2)	15(2)
C(5)	134(3)	126(3)	105(2)	14(2)	7(2)	5(2)
C(6)	116(3)	147(3)	110(2)	6(2)	12(2)	-8(2)
C(7)	138(3)	138(3)	103(2)	-12(2)	8(2)	-31(2)
C(8)	195(3)	242(4)	129(2)	6(2)	-40(2)	-61(3)
C(9)	156(3)	147(3)	94(2)	-8(2)	16(2)	-2(2)
C(10)	119(2)	139(3)	91(2)	0(2)	-2(2)	-10(2)
C(11)	119(3)	134(3)	127(2)	-5(2)	-1(2)	0(2)
C(12)	192(3)	160(3)	172(2)	49(2)	12(2)	-38(3)

Table SI 5. Hydrogen coordinates ($x 10^4$) and isotropic displacement parameters ($Å^2 x 10^3$) for MRK03 (CCDC 718289).

	x	y	z	U_{iso}
H(1)	1775(19)	1097(12)	4293(8)	21(3)
H(2)	4516(17)	-624(10)	3599(7)	11(2)
H(4)	471(15)	1482(10)	2675(7)	9(2)
H(5)	3332(18)	2403(11)	1957(8)	19(3)
H(6A)	6371(17)	854(10)	2751(7)	16(2)
H(6B)	6554(17)	2206(10)	2698(7)	13(2)
H(7)	4294(18)	2443(12)	3949(8)	22(3)
H(8A)	5740(20)	1409(13)	5221(9)	31(3)
H(8B)	7570(20)	1775(13)	4526(9)	31(3)
H(8C)	6860(20)	555(13)	4490(9)	30(3)
H(9A)	4588(18)	-661(10)	1802(7)	13(2)
H(9B)	2564(18)	-681(10)	1225(8)	20(3)
H(10)	1140(20)	-983(12)	4673(9)	25(3)
H(12A)	1180(20)	-2961(12)	5127(9)	31(3)
H(12B)	2160(20)	-3854(14)	4343(9)	34(3)
H(12C)	-90(20)	-3258(13)	4249(8)	28(3)

NMR and IR spectra

Table of Spectra Figures

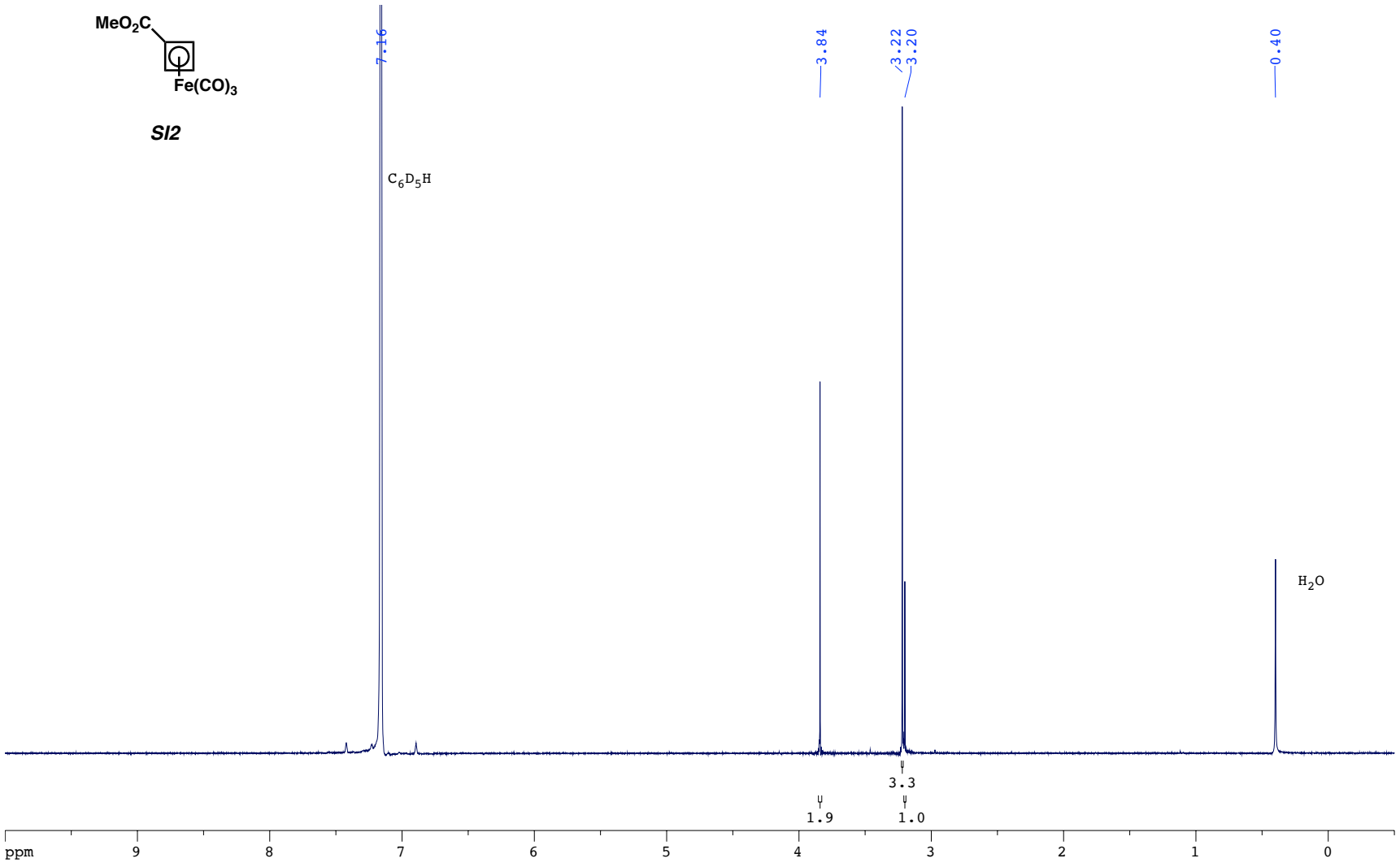


Figure SI 1. ^{1}H NMR spectrum (300 MHz, C_6D_6) of ***SI2****.*

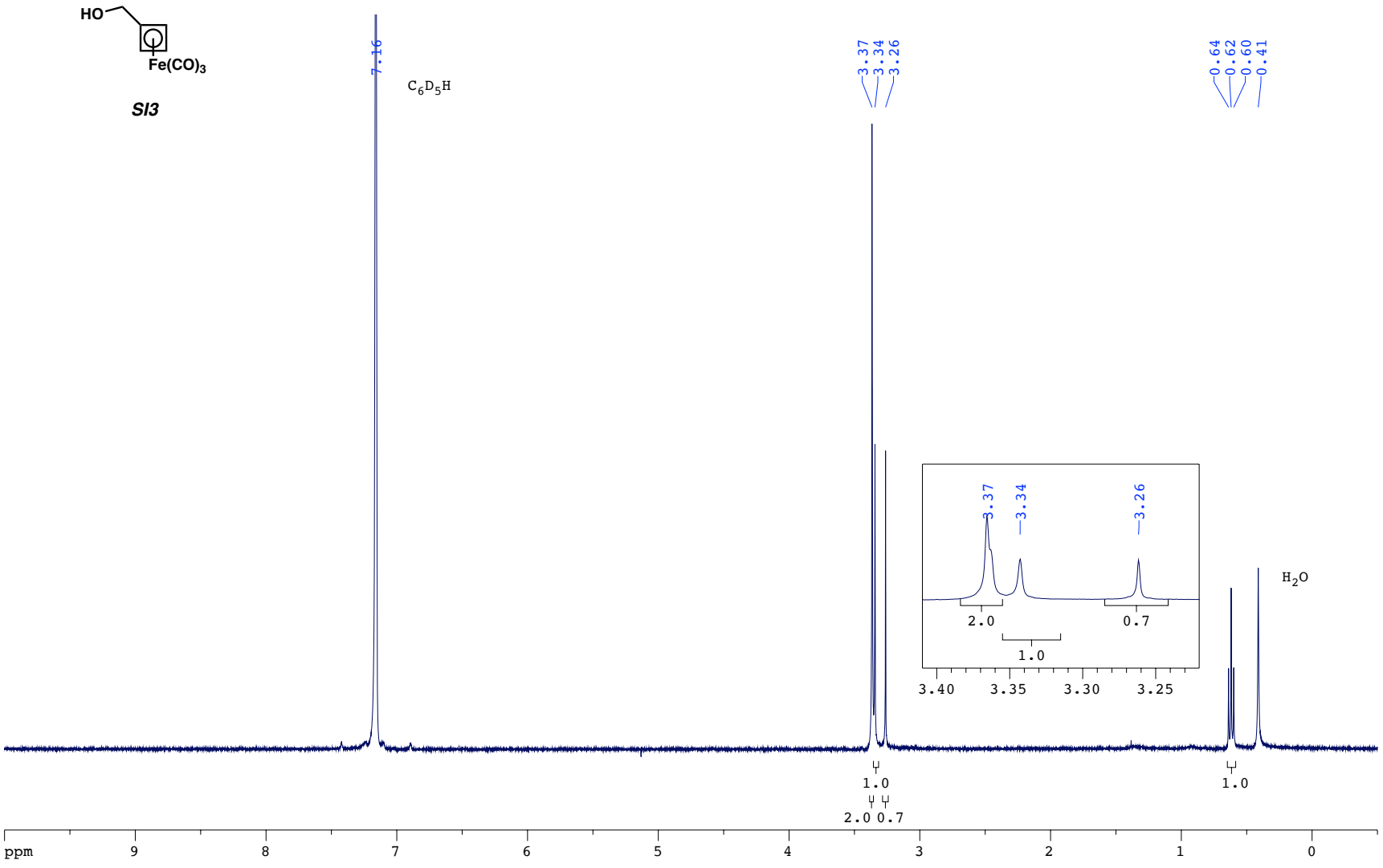


Figure SI 2. ^{1}H NMR spectrum (300 MHz, C_6D_6) of ***SI3****.*

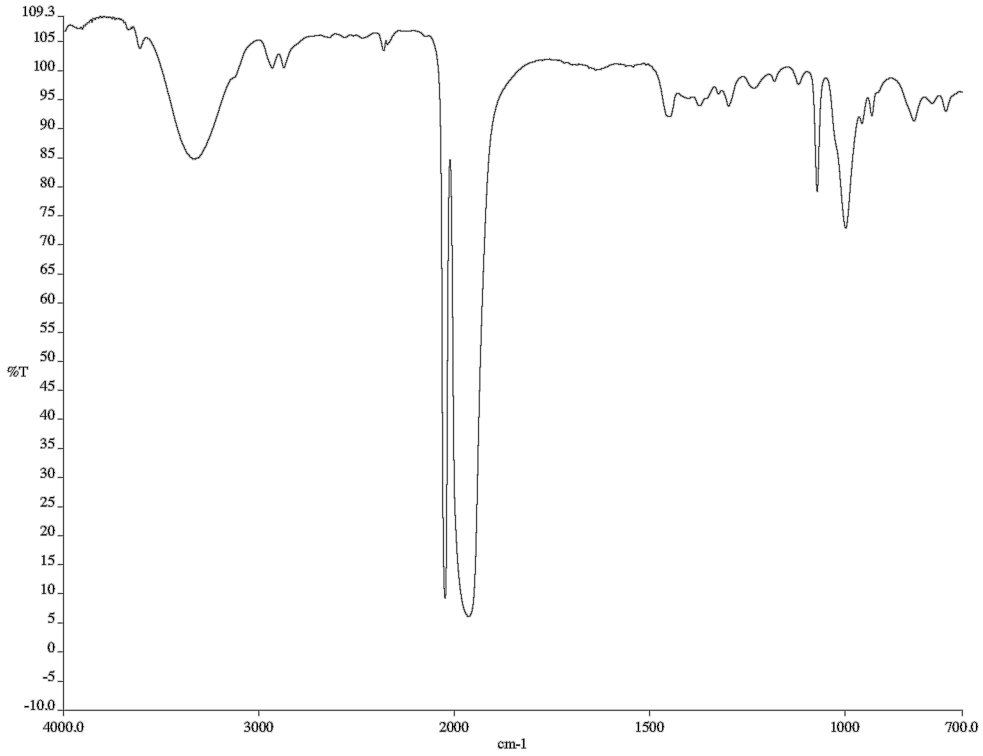


*Figure SI 3. Infrared spectrum (neat film/NaCl) of **SI3**.*

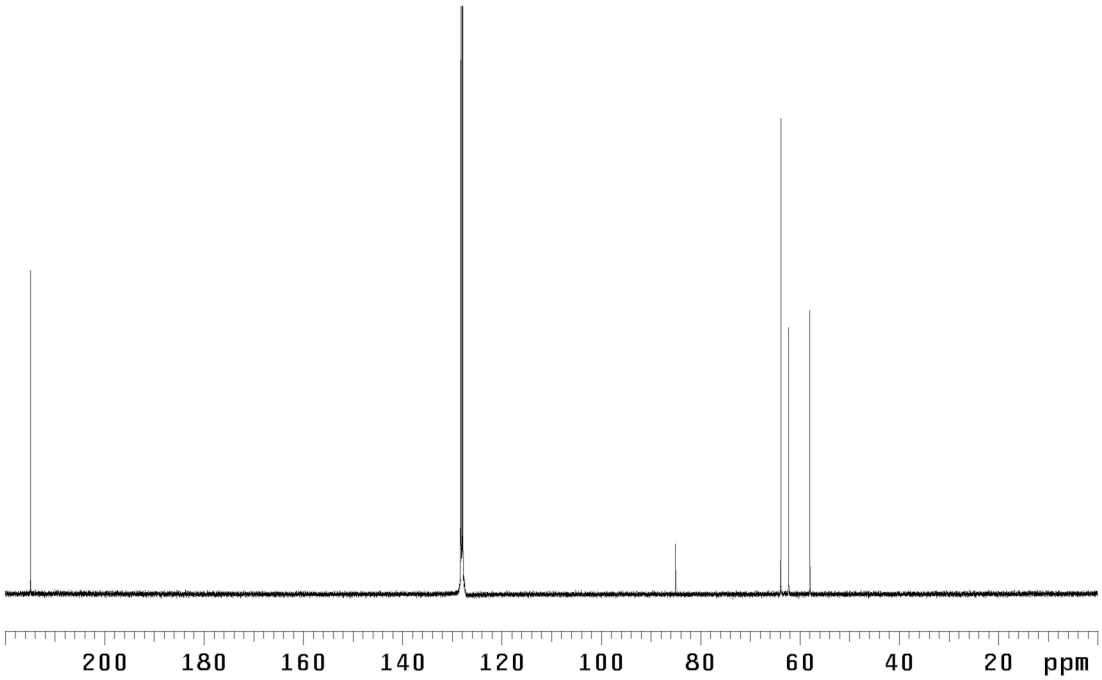


*Figure SI 4. ^{13}C NMR spectrum (126 MHz, C_6D_6) of **SI3**.*

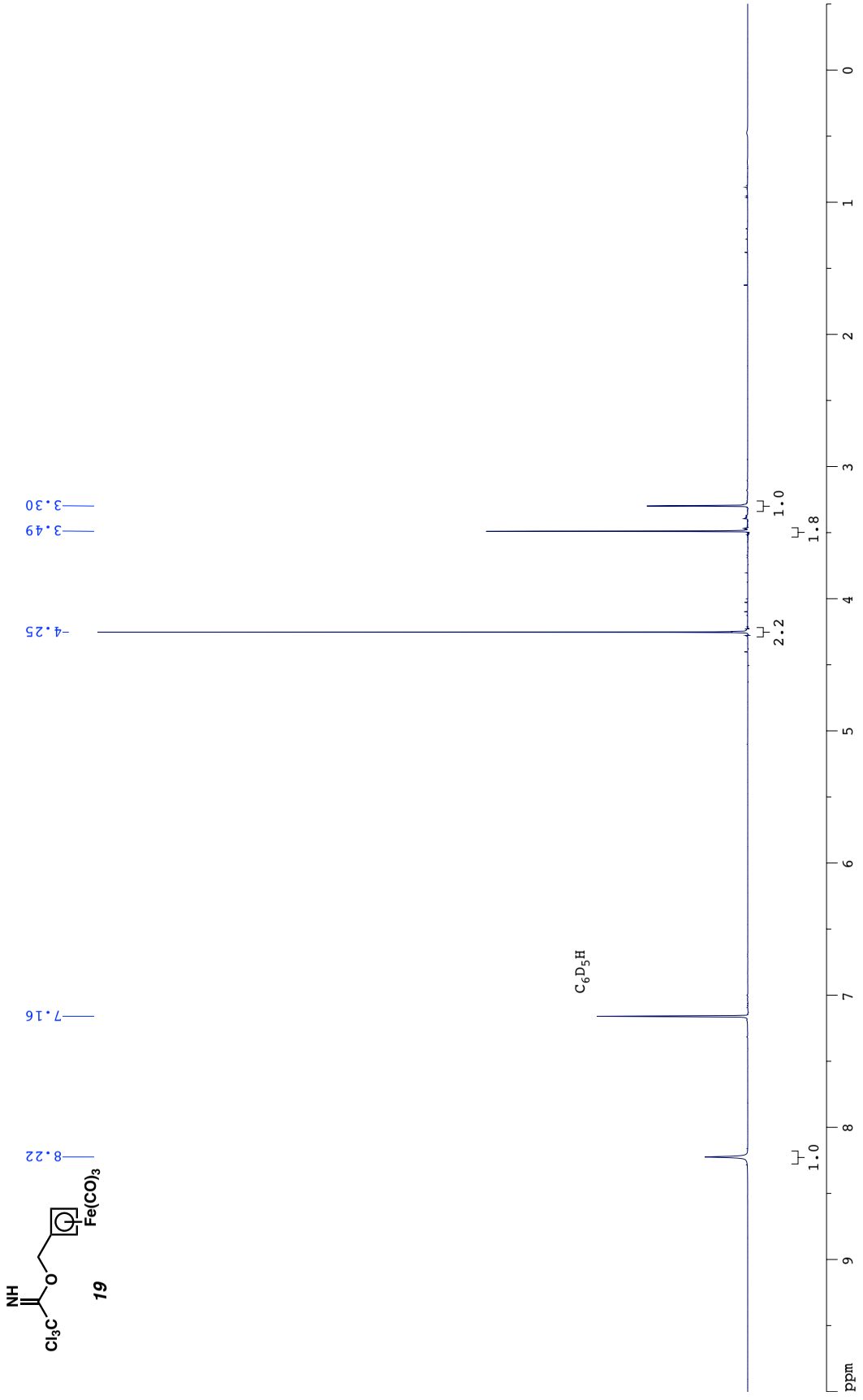


*Figure SI 5. ^1H NMR spectrum (500 MHz, C_6D_6) of **19**.*

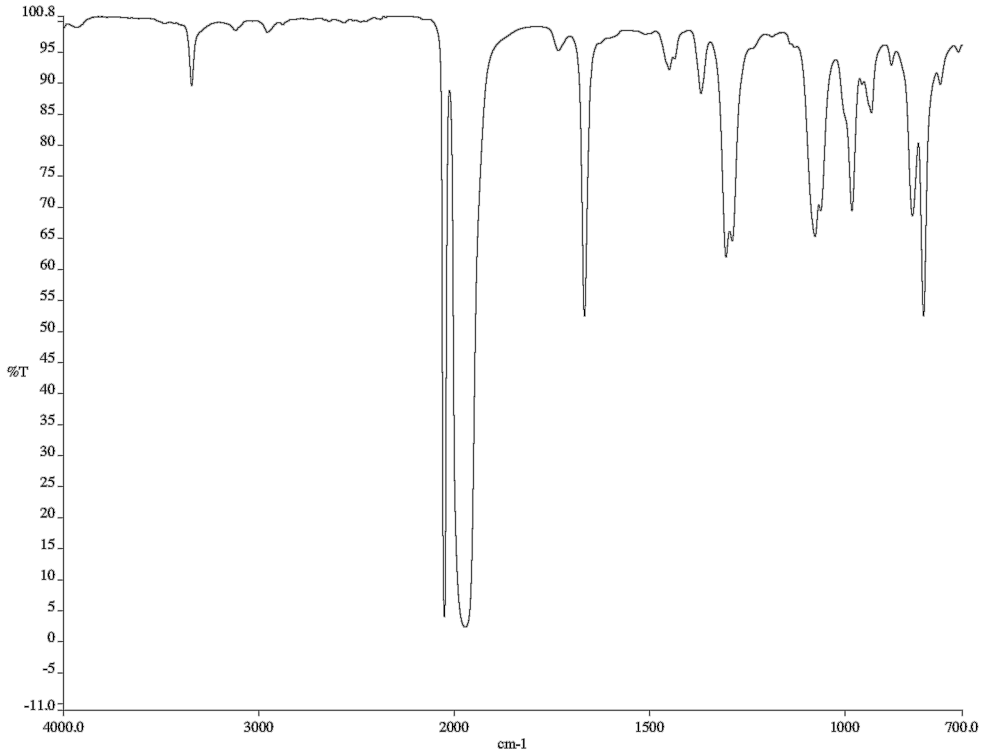


*Figure SI 6. Infrared spectrum (neat film/NaCl) of **19**.*

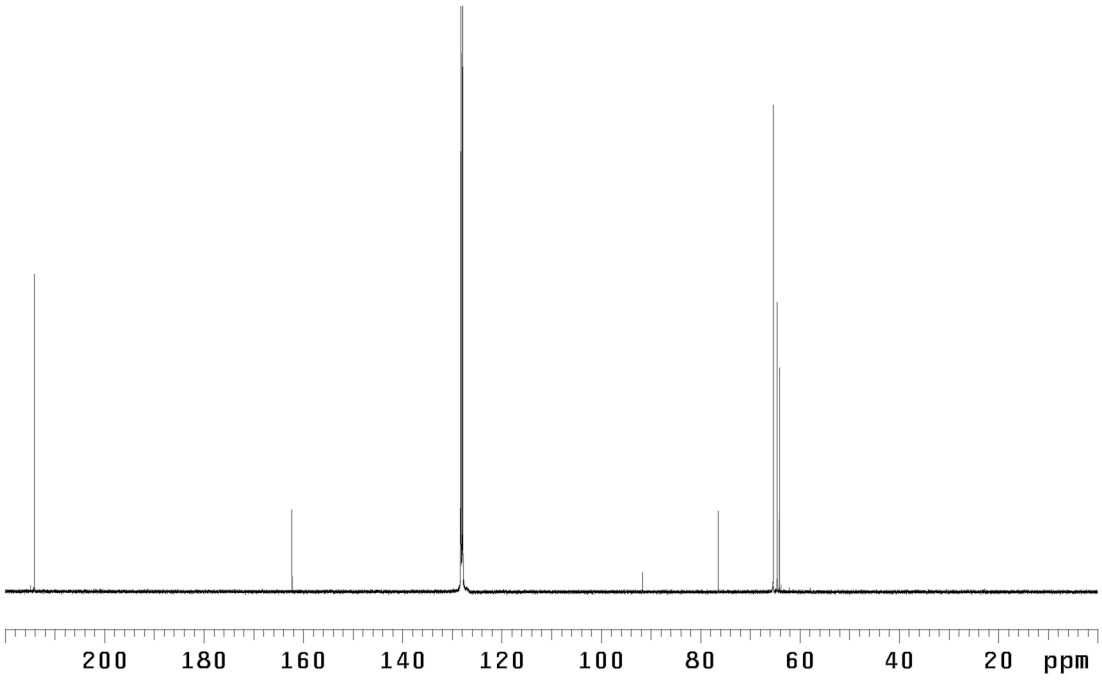


*Figure SI 7. ^{13}C NMR spectrum (126 MHz, C_6D_6) of **19**.*

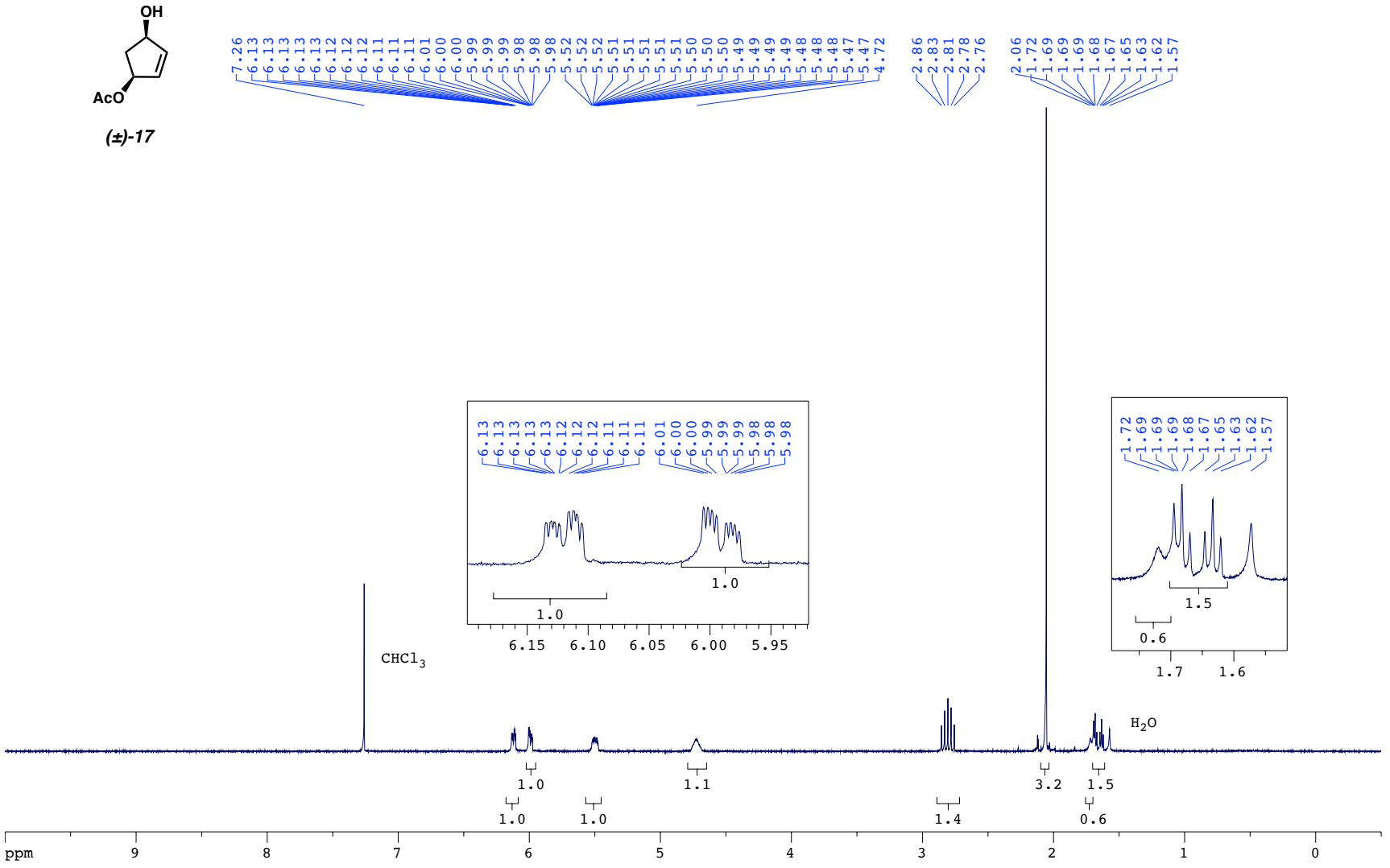


*Figure SI 8. ^{1}H NMR spectrum (300 MHz, $CDCl_3$) of **17**.*

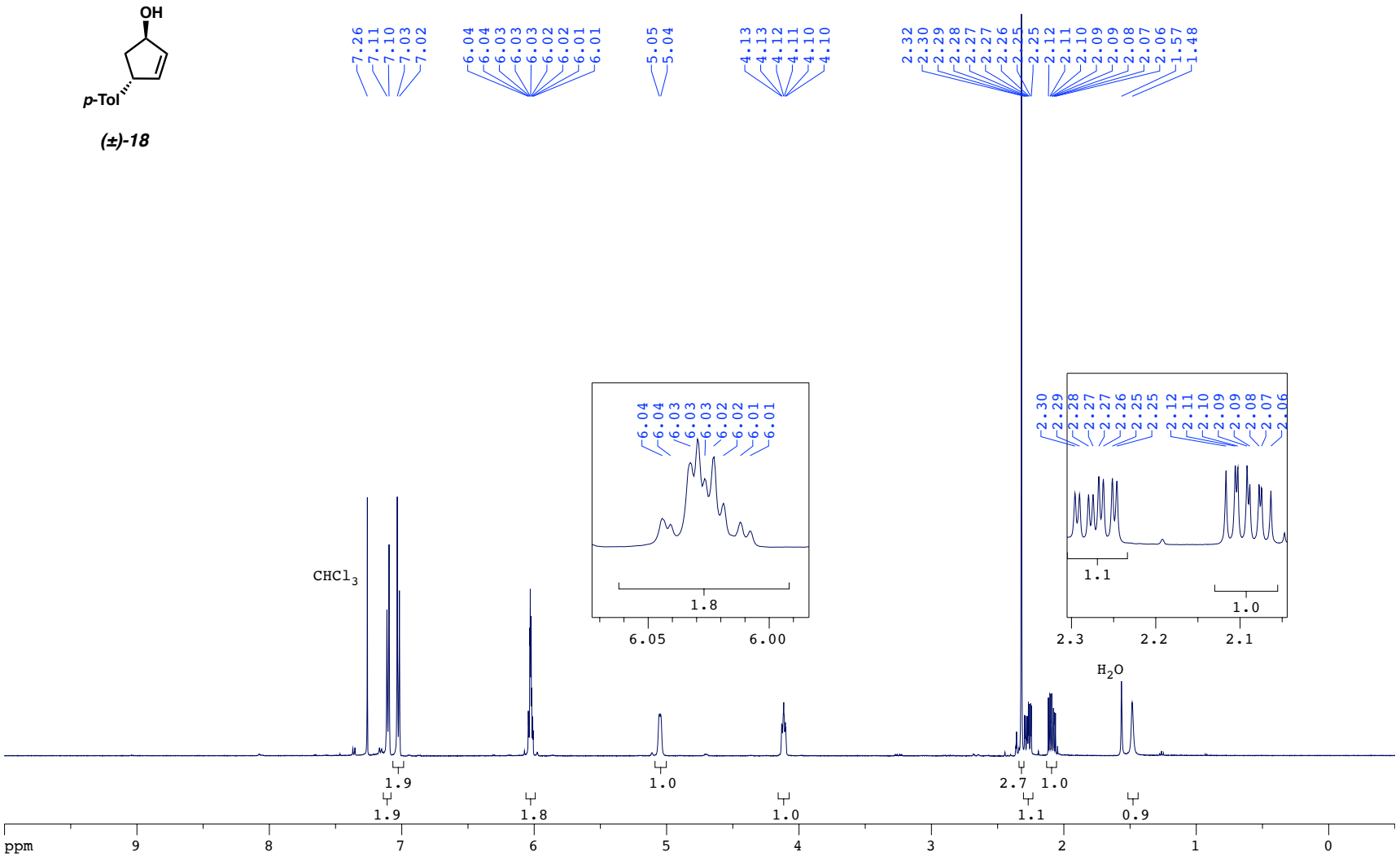


Figure SI 9. ^{1}H NMR spectrum (500 MHz, $CDCl_3$) of ***18****.*

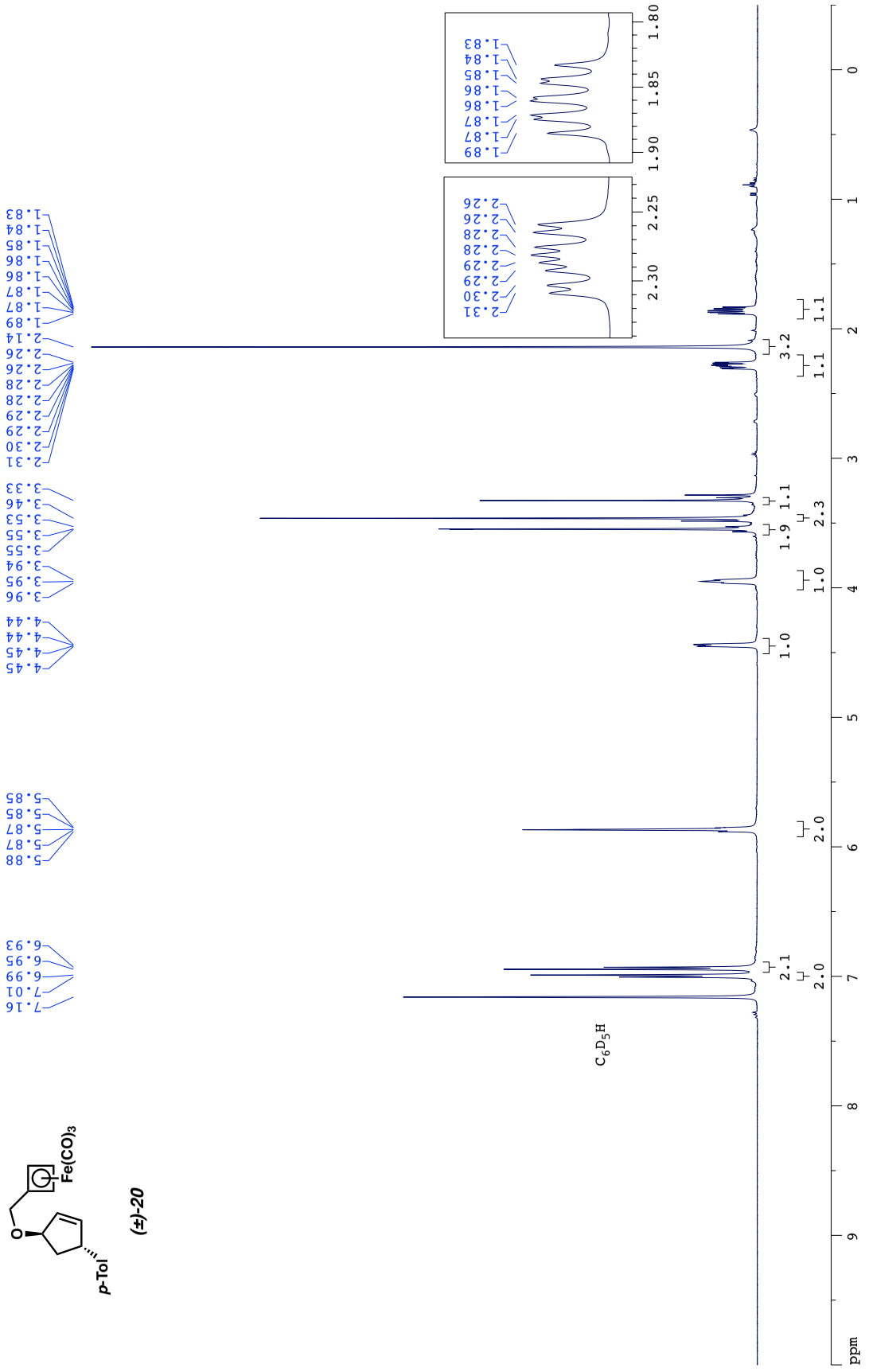


*Figure SI 10. ^1H NMR spectrum (300 MHz, C_6D_6) of **20**.*

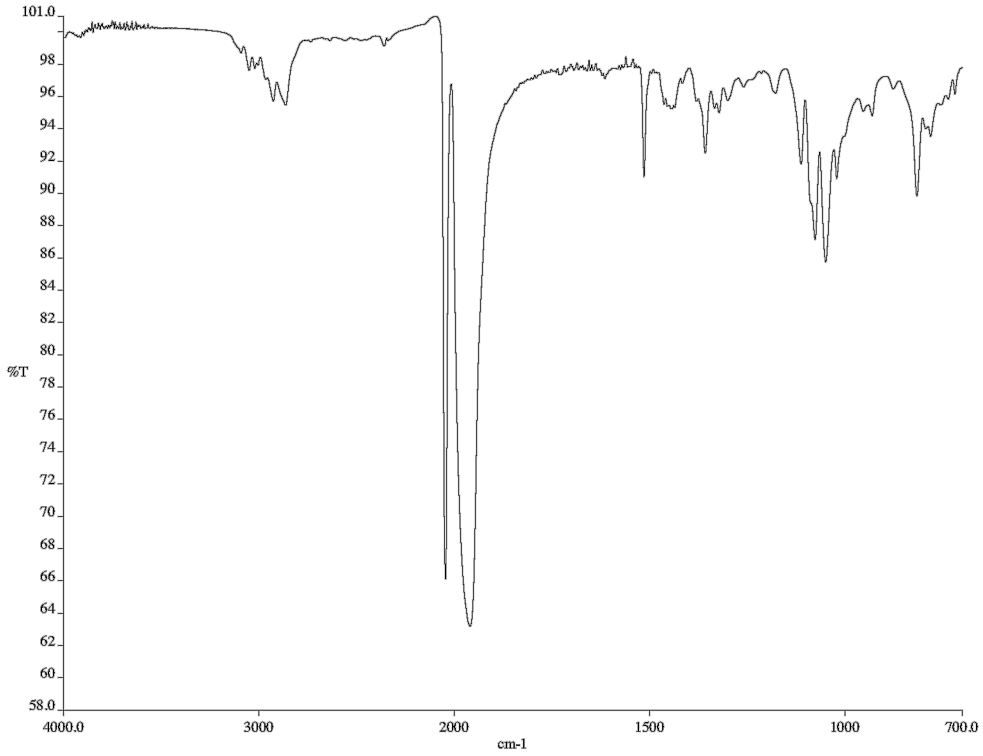


*Figure SI 11. Infrared spectrum (neat film/NaCl) of **20**.*

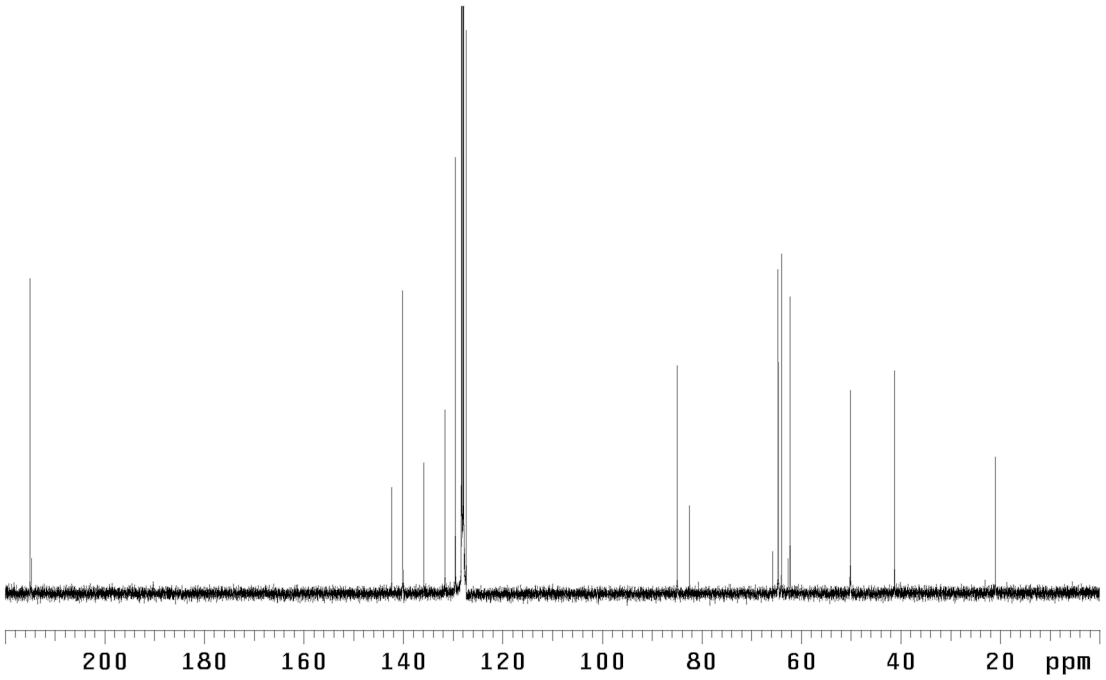


*Figure SI 12. ^{13}C NMR spectrum (126 MHz, C_6D_6) of **20**.*

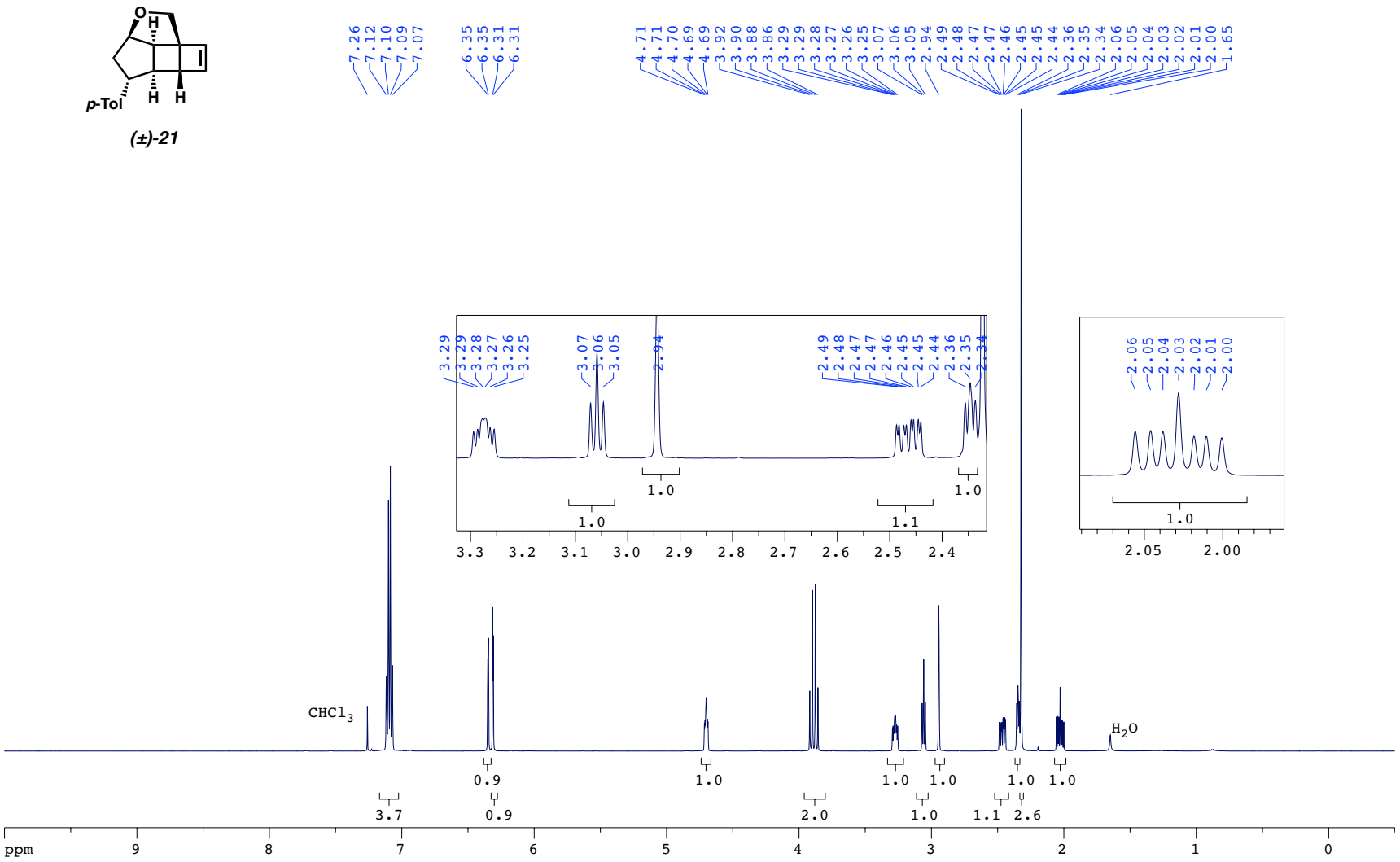


*Figure SI 13. ^{1}H NMR spectrum (500 MHz, $CDCl_3$) of **21**.*

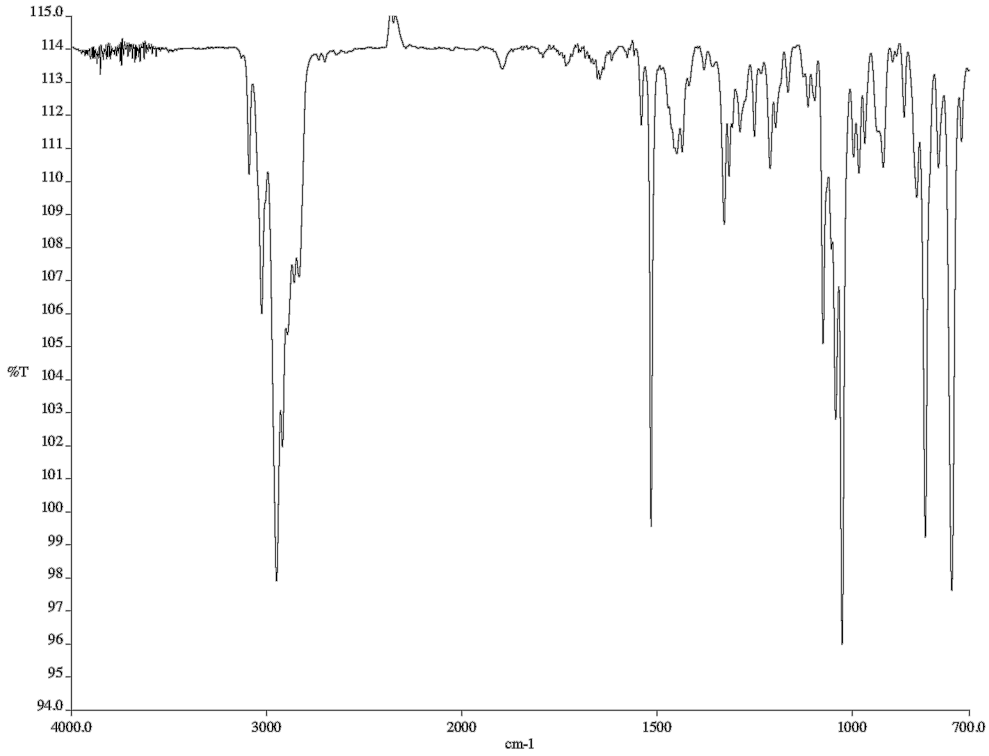


*Figure SI 14. Infrared spectrum (neat film/NaCl) of **21**.*

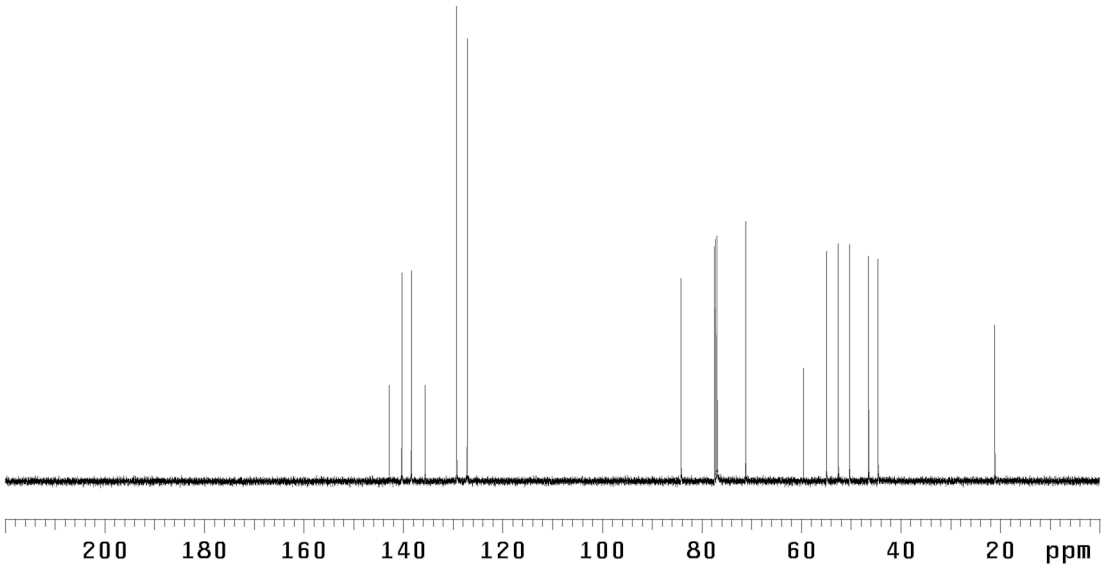


*Figure SI 15. ^{13}C NMR spectrum (126 MHz, $CDCl_3$) of **21**.*

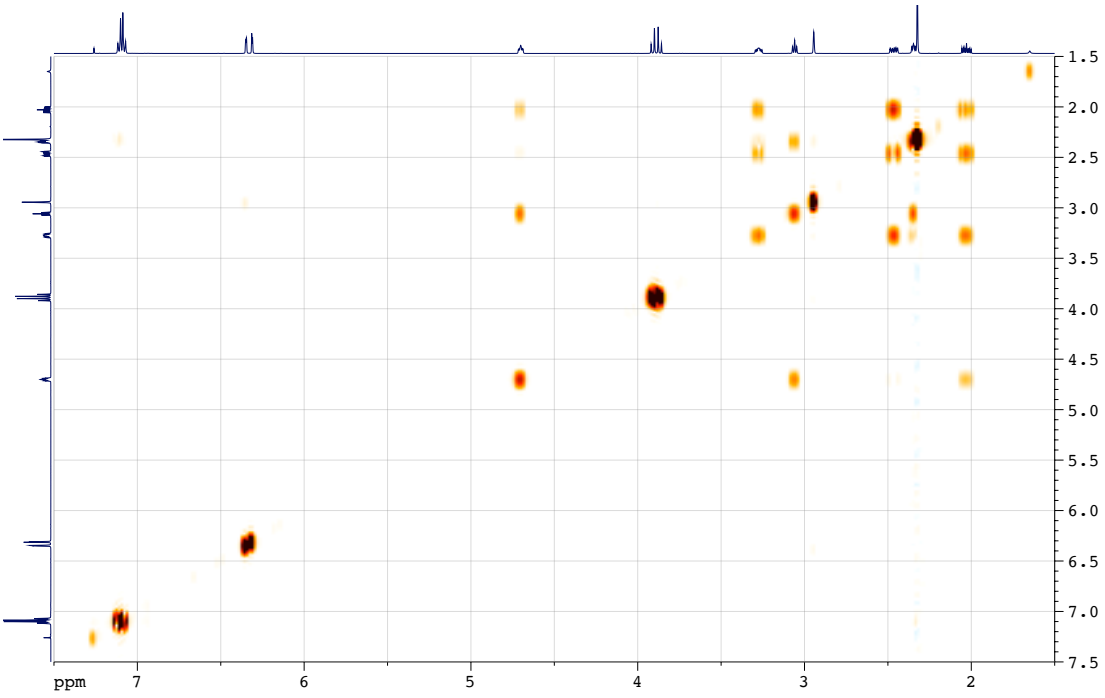


*Figure SI 16. gCOSY NMR spectrum (500 MHz, $CDCl_3$) of **21**.*

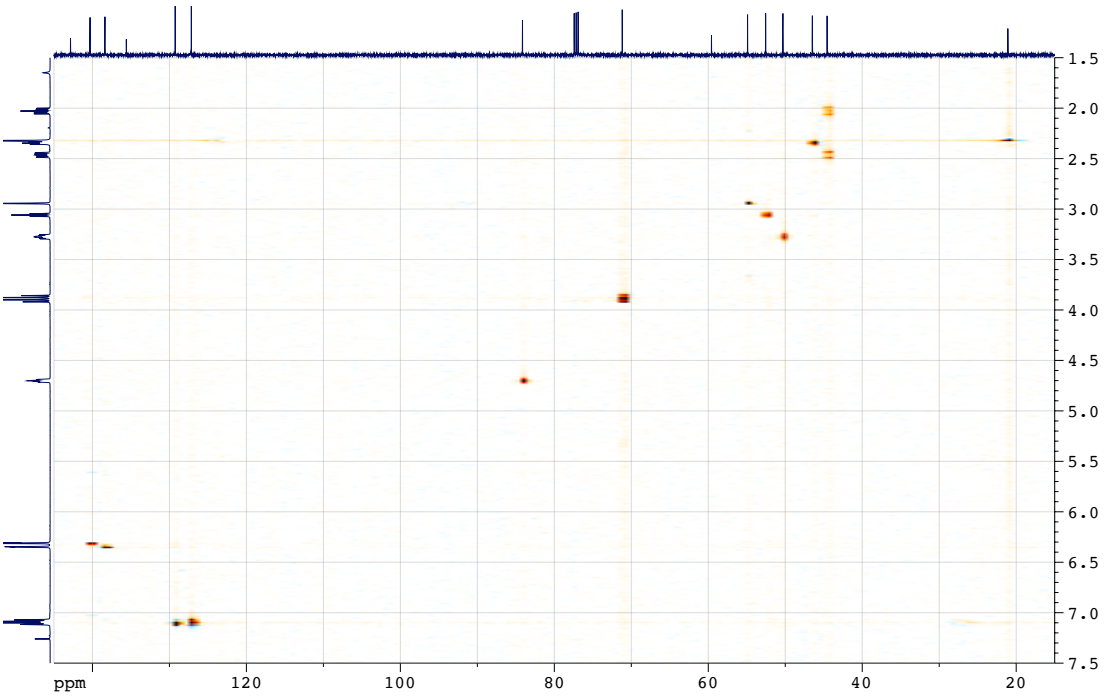


*Figure SI 17. gHSQC NMR spectrum (500, 126 MHz, $CDCl_3$) of **21**.*

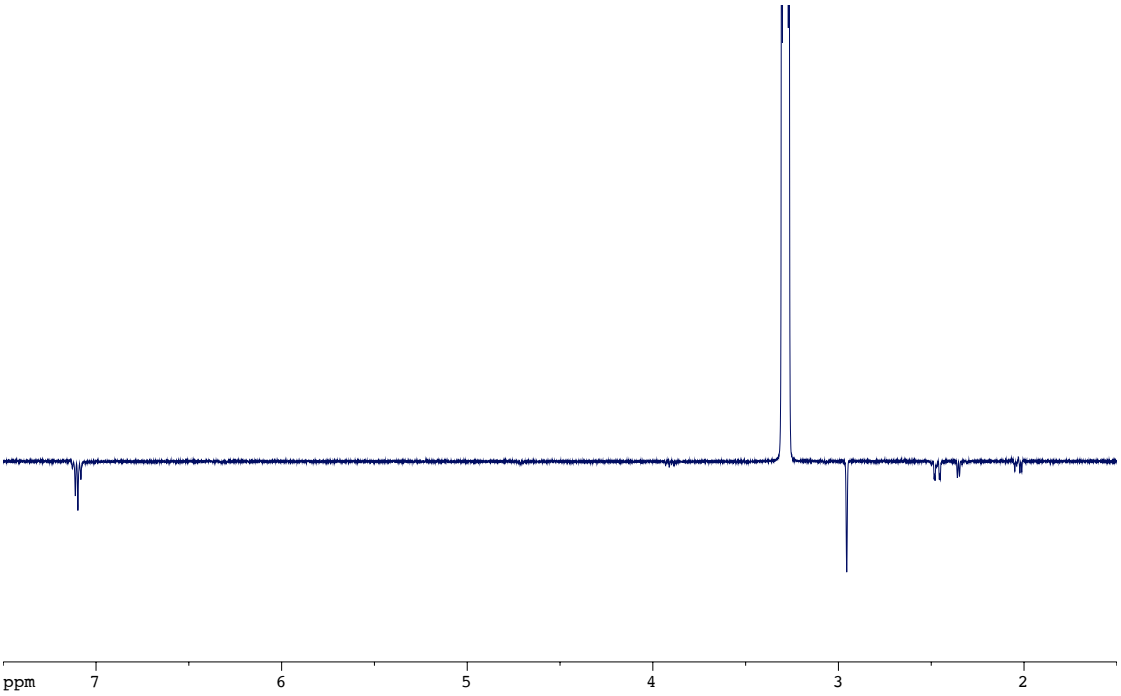


*Figure SI 18. NOESY-1D NMR spectrum (500 MHz, $CDCl_3$) of **21**.*

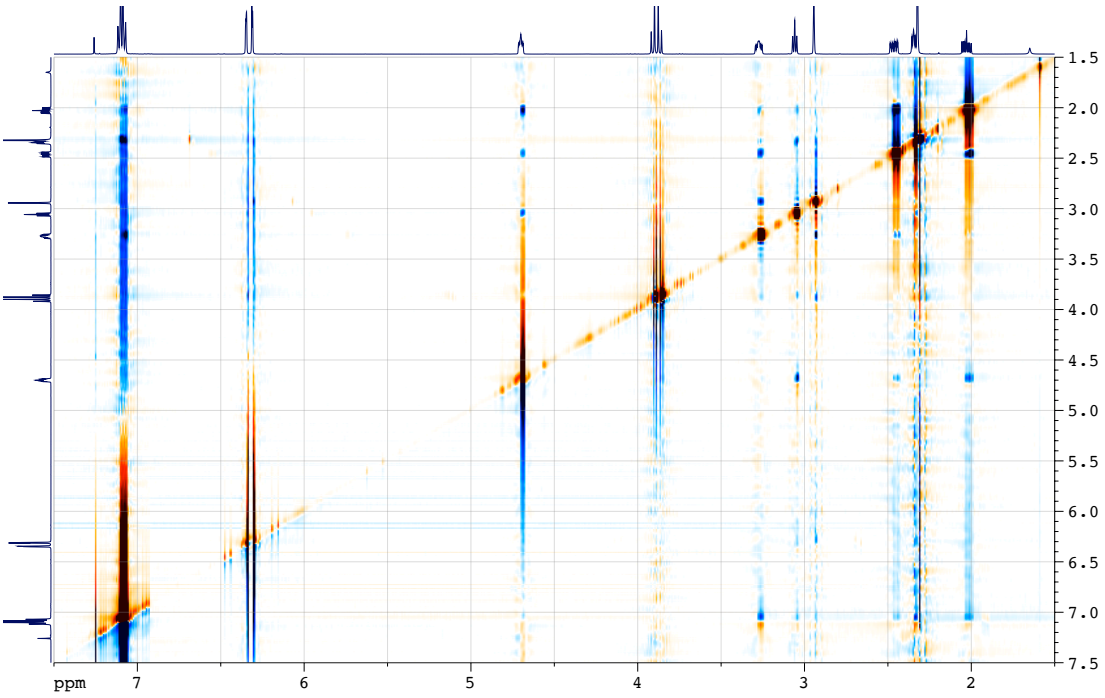


*Figure SI 19. NOESY-2D NMR spectrum (600 MHz, $CDCl_3$) of **21**.*

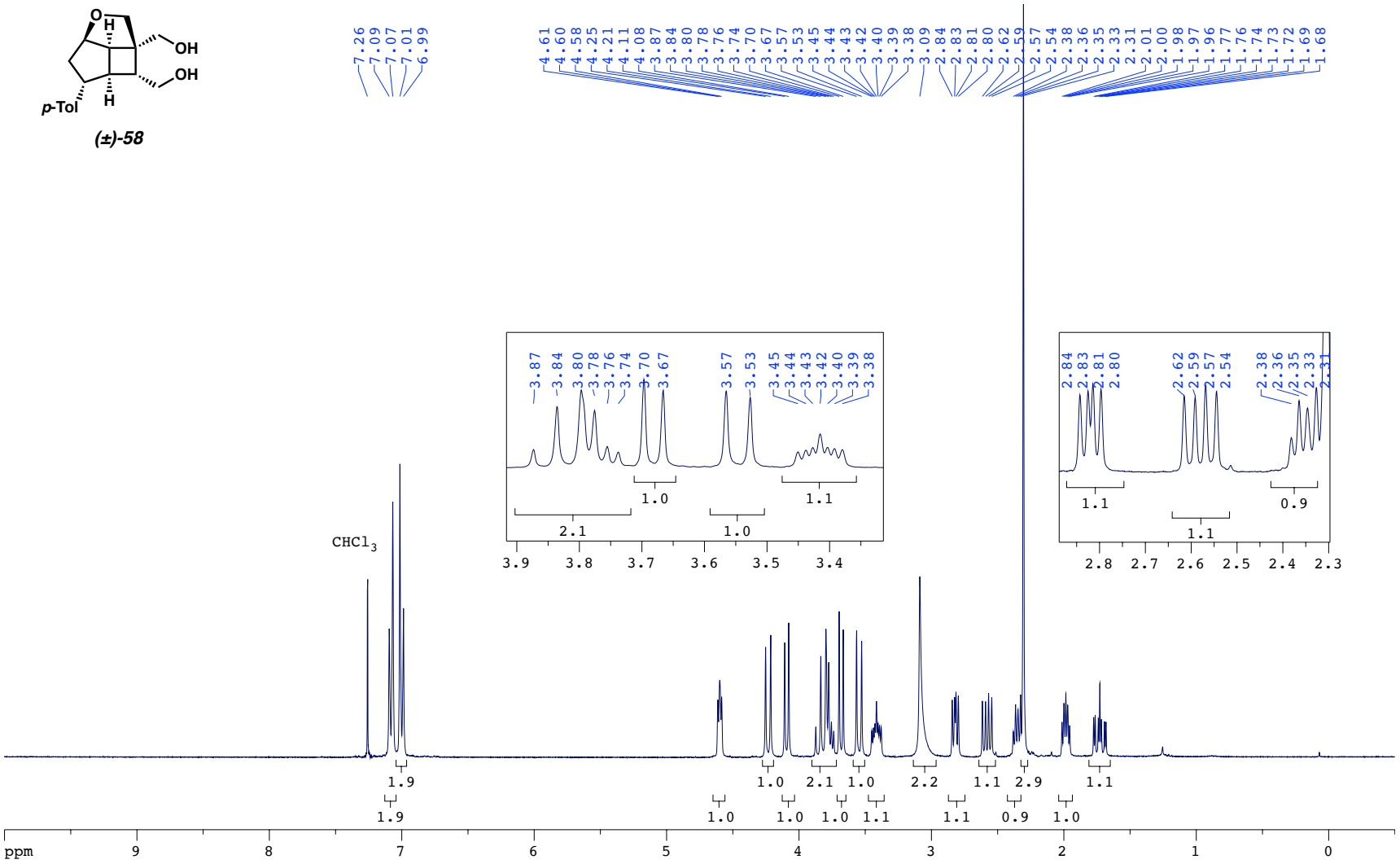


Figure SI 20. ^{1}H NMR spectrum (300 MHz, $CDCl_3$) of ***58****.*

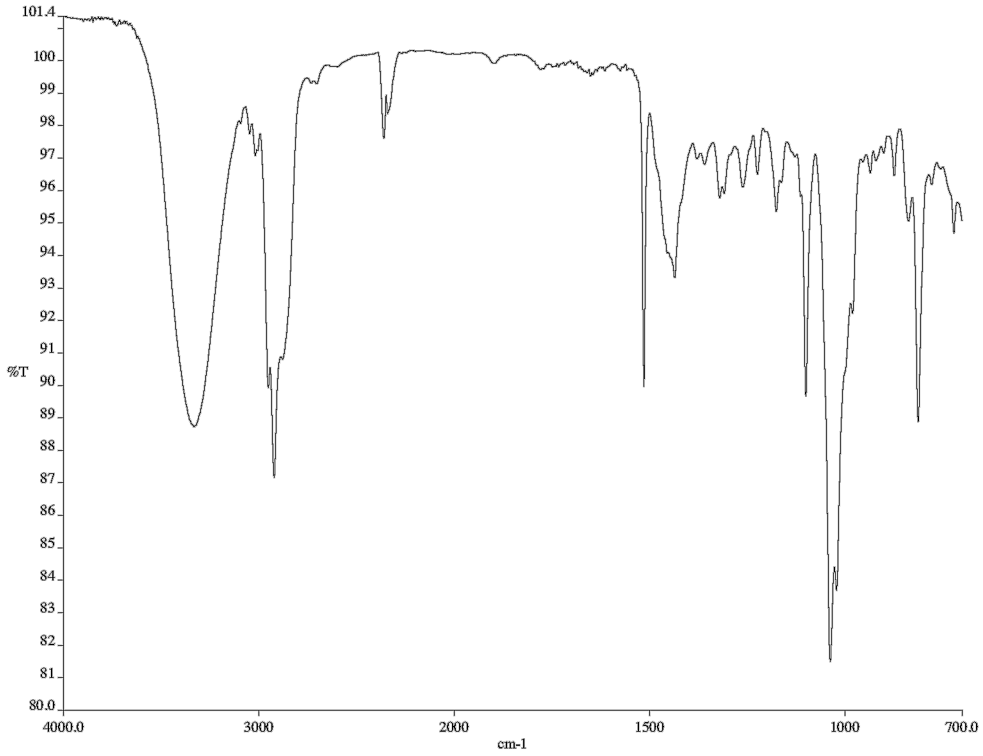


*Figure SI 21. Infrared spectrum (neat film/NaCl) of **58**.*

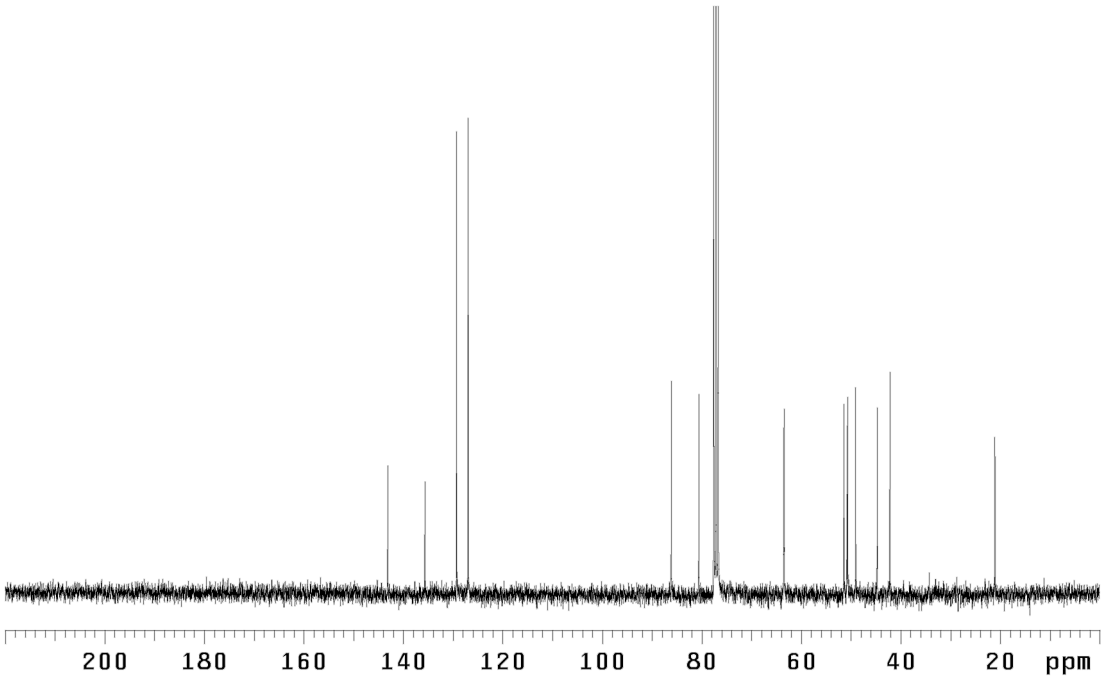


*Figure SI 22. ^{13}C NMR spectrum (75 MHz, $CDCl_3$) of **58**.*

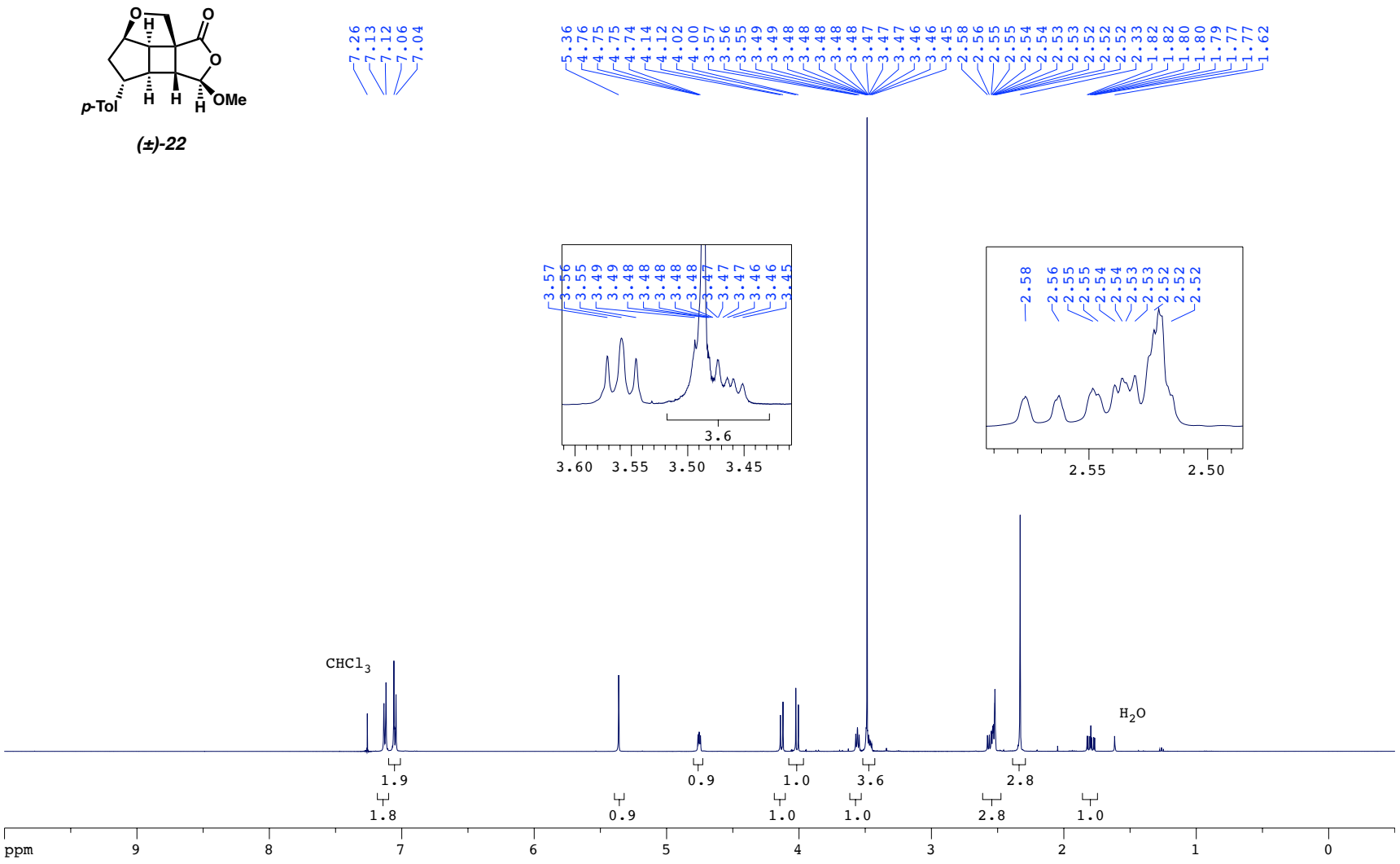


*Figure SI 23. ^{1}H NMR spectrum (500 MHz, $CDCl_3$) of **22**.*

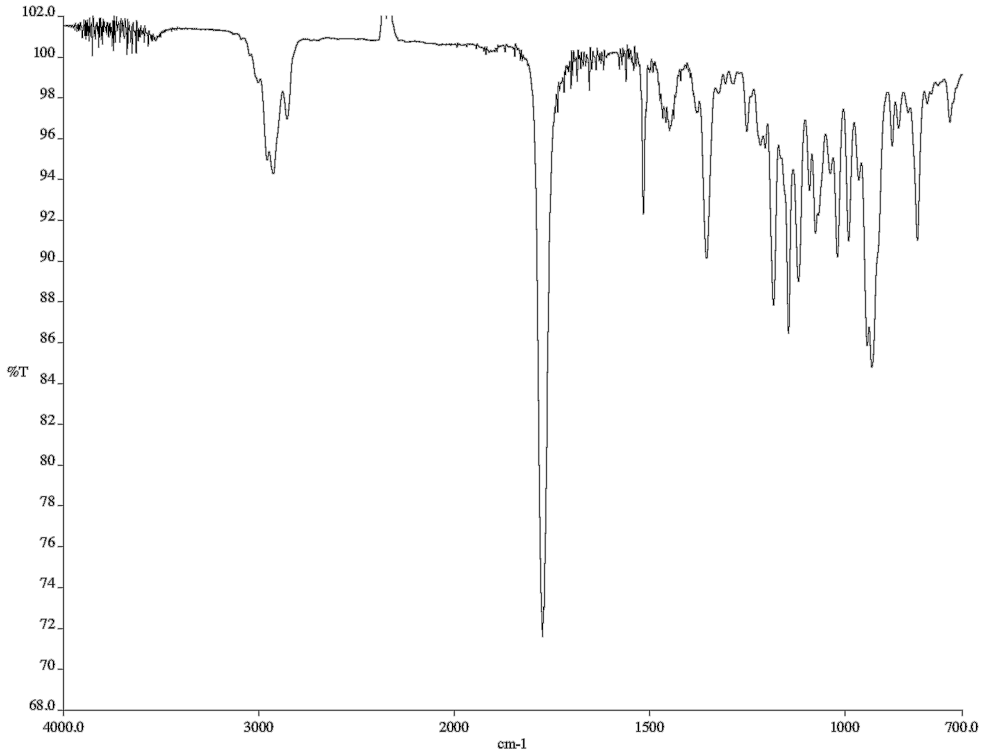


Figure SI 24. Infrared spectrum (neat film/NaCl) of ***22****.*

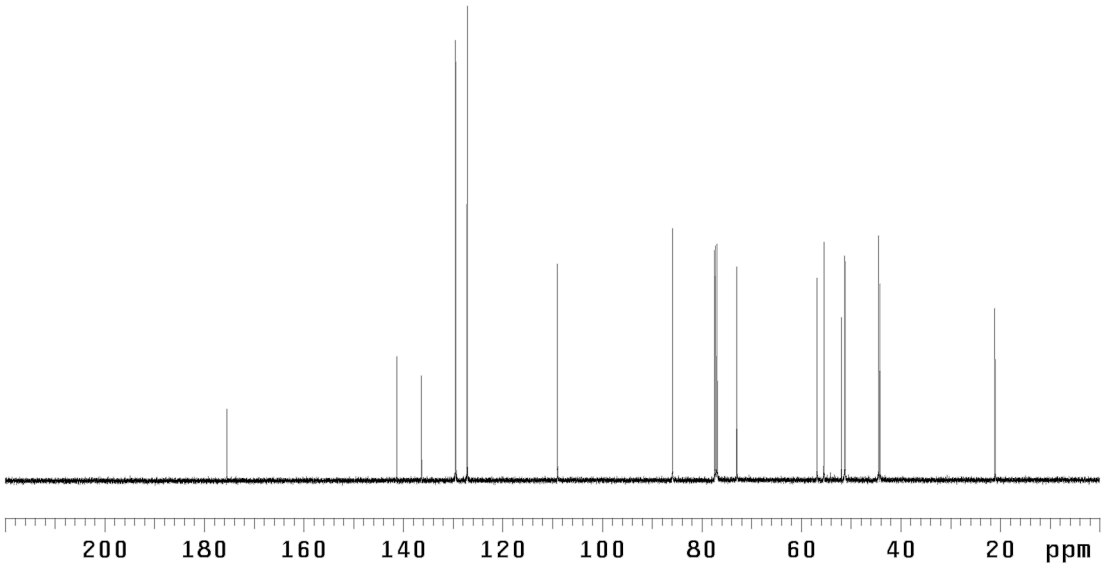


Figure SI 25. ^{13}C *NMR spectrum (126 MHz,* $CDCl_3$*) of* ***22****.*

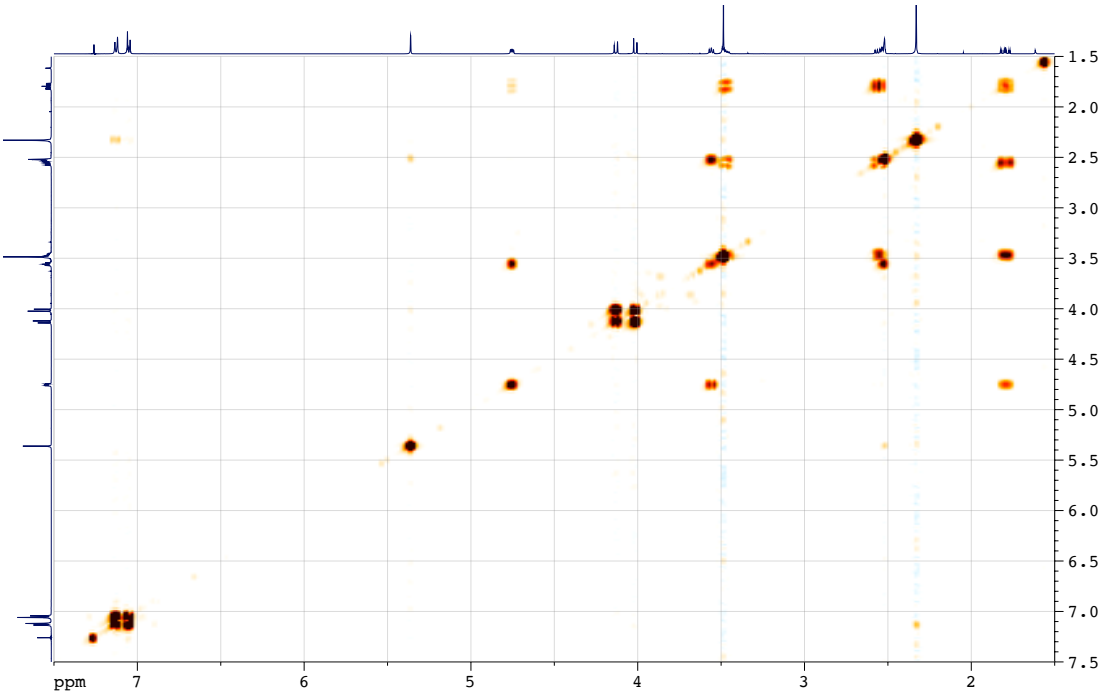


Figure SI 26. gCOSY NMR spectrum (500 MHz, $CDCl_3$) of ***22****.*

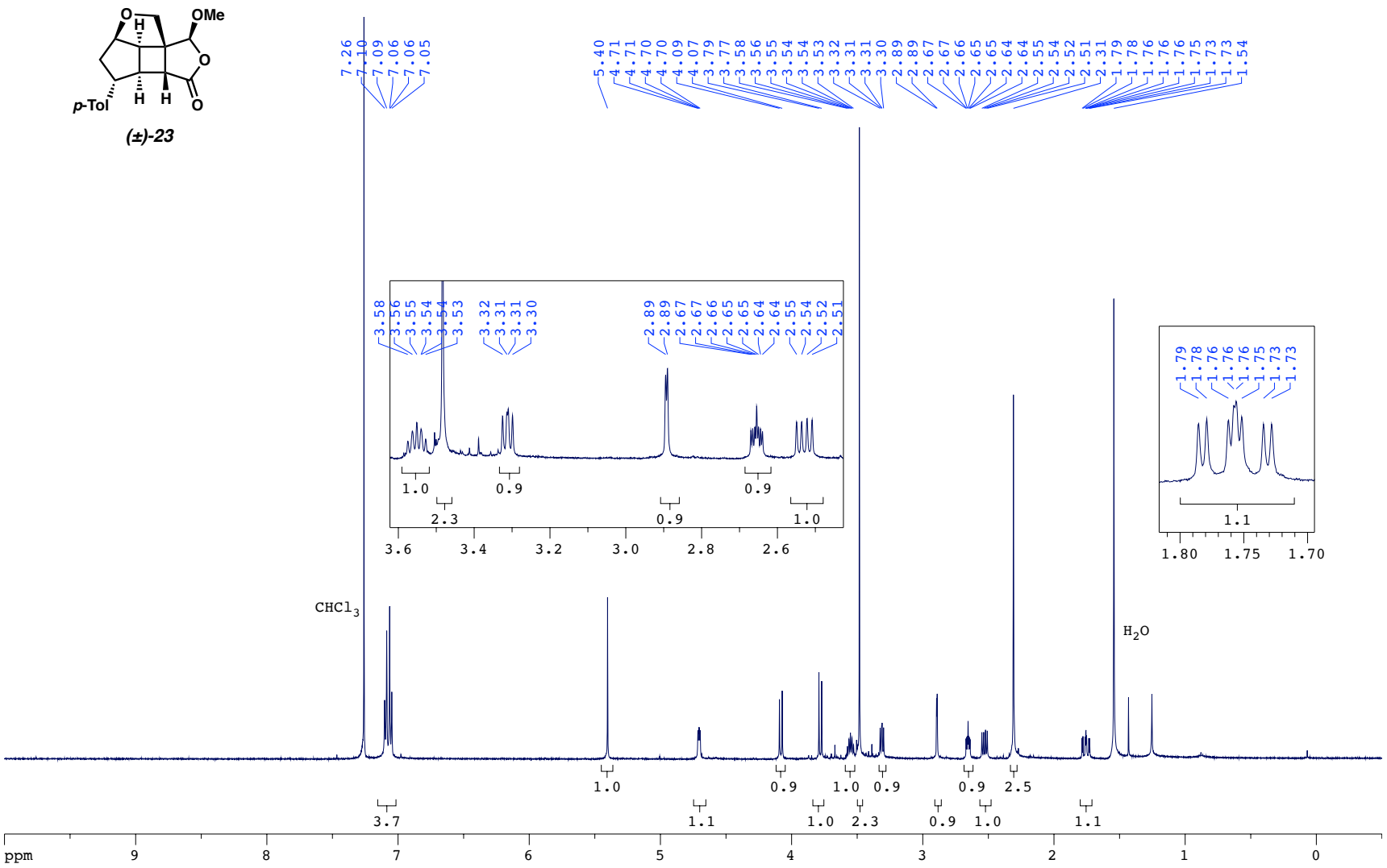


*Figure SI 27. ^{1}H NMR spectrum (500 MHz, $CDCl_3$) of **23**.*

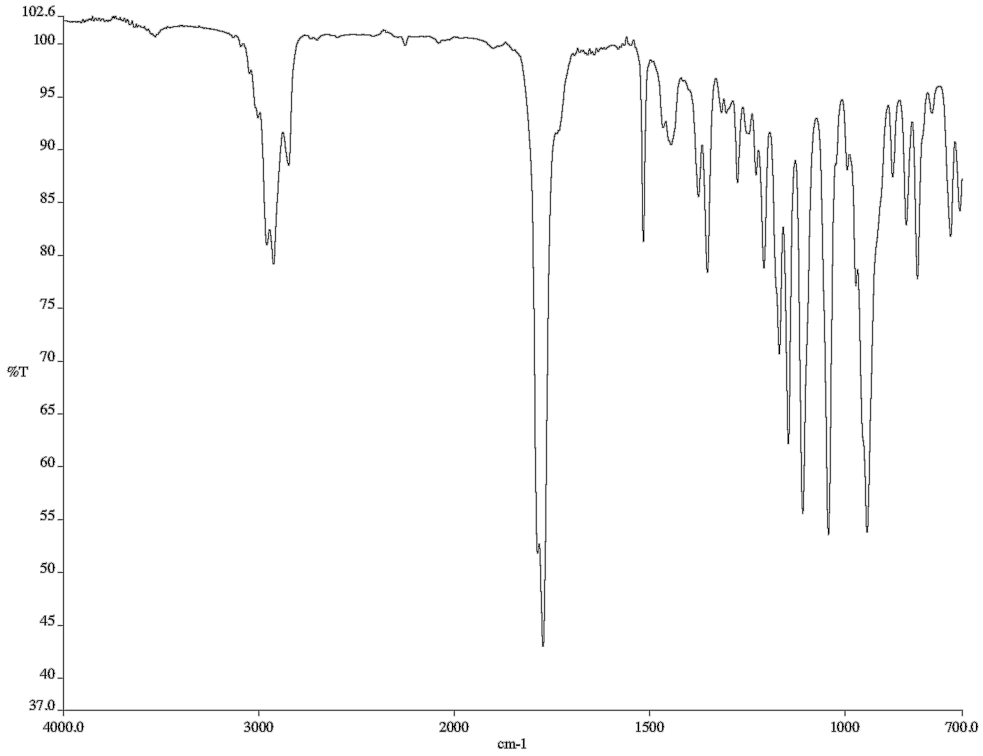


*Figure SI 28. Infrared spectrum (neat film/NaCl) of **23**.*

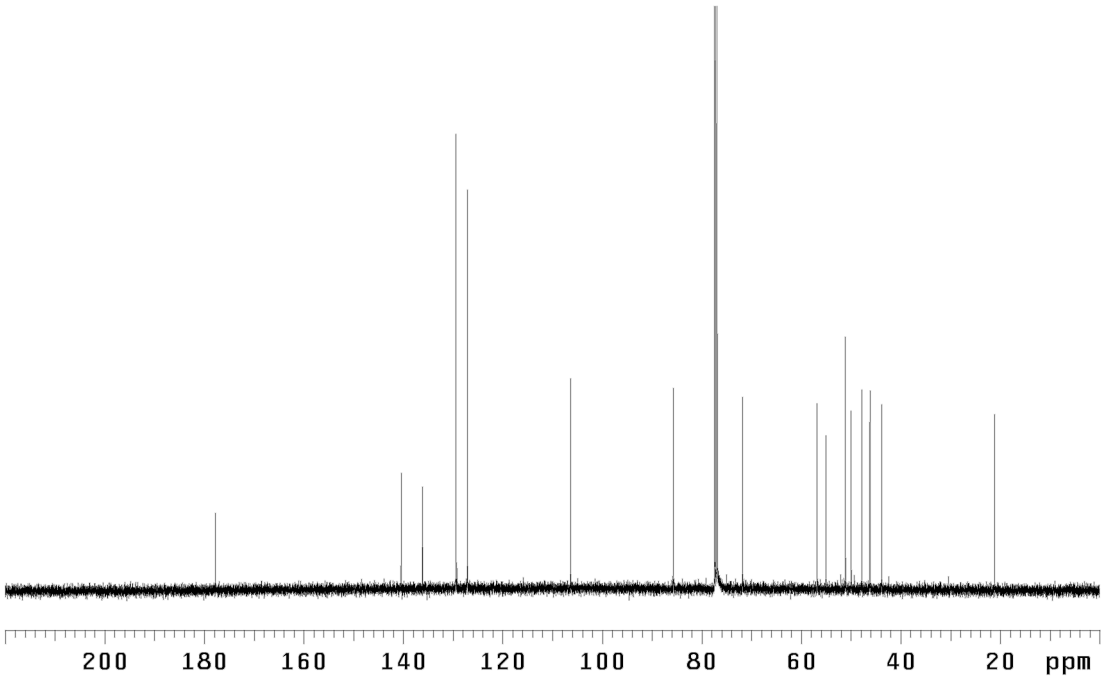


*Figure SI 29. ^{13}C NMR spectrum (126 MHz, $CDCl_3$) of **23**.*

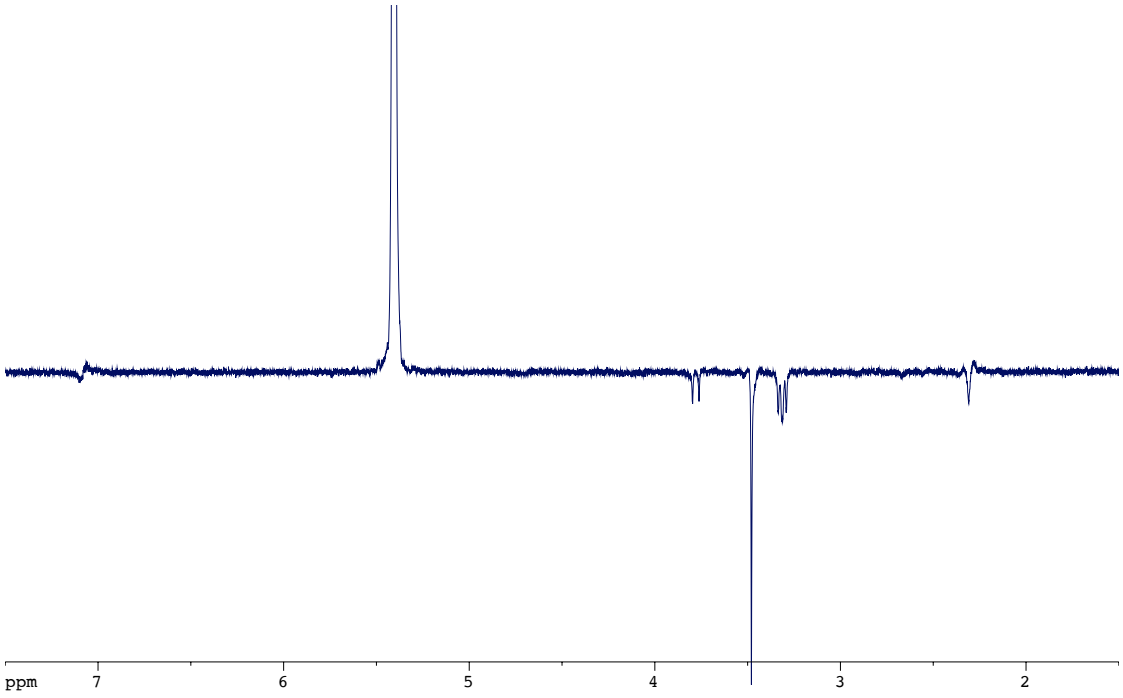


*Figure SI 30. NOESY-1D NMR spectrum (300 MHz, $CDCl_3$) of **23**.*

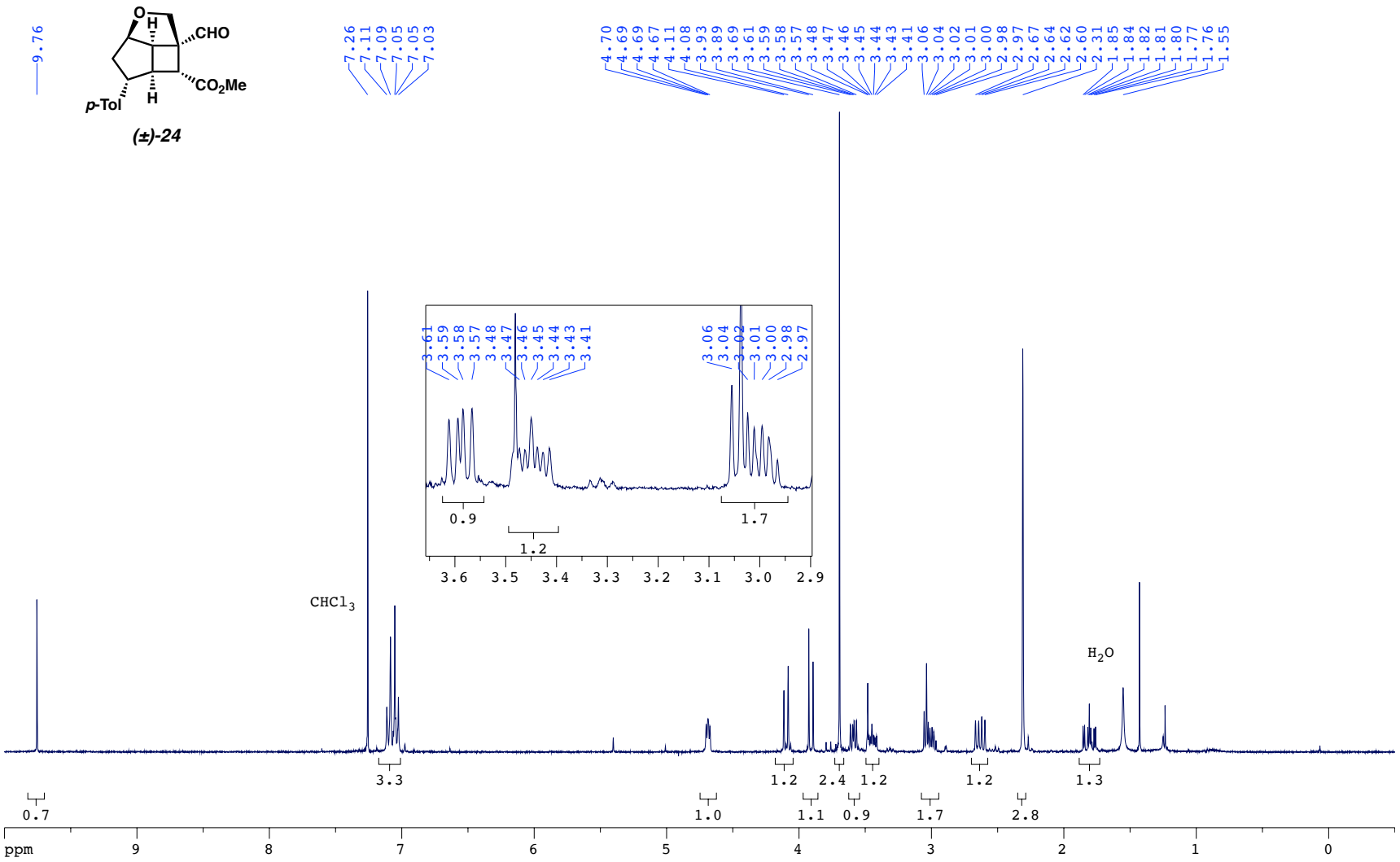


*Figure SI 31. ^1H NMR spectrum (300 MHz, $CDCl_3$) of **24**.*

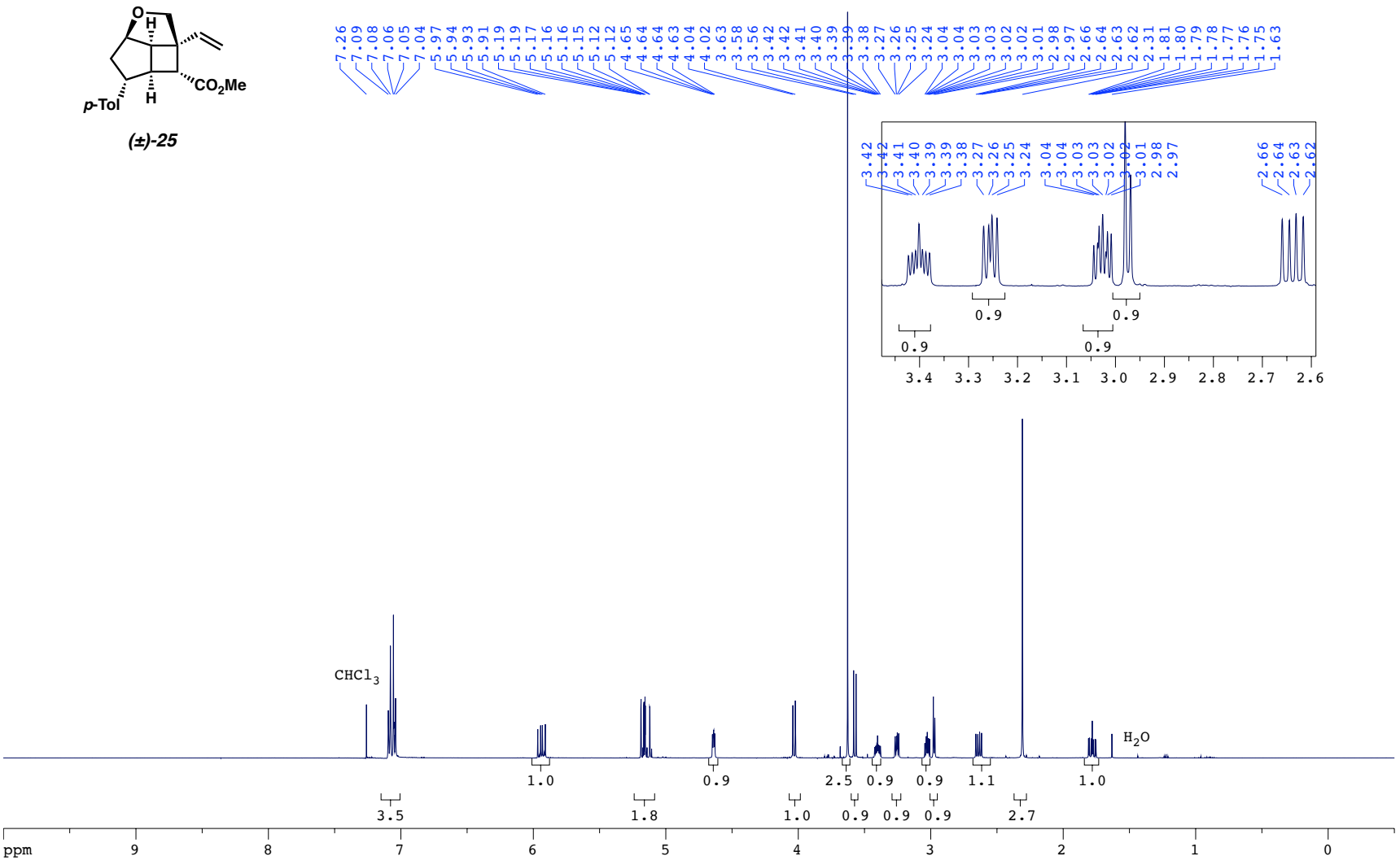


*Figure SI 32. ^{1}H NMR spectrum (500 MHz, $CDCl_3$) of **25**.*

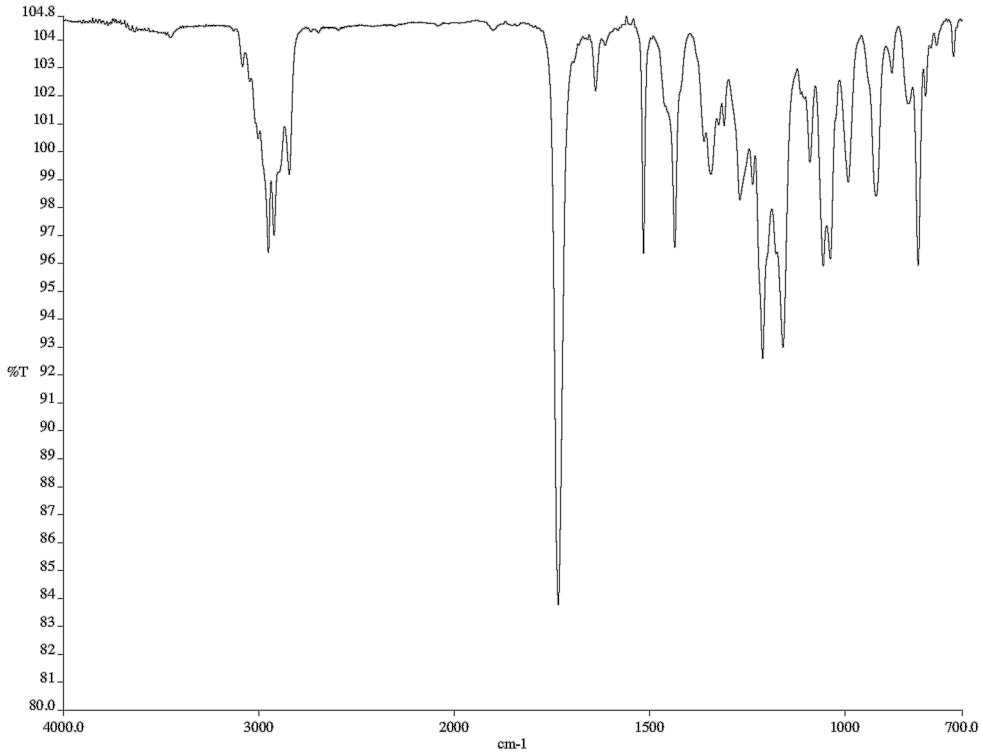


*Figure SI 33. Infrared spectrum (neat film/NaCl) of **25**.*

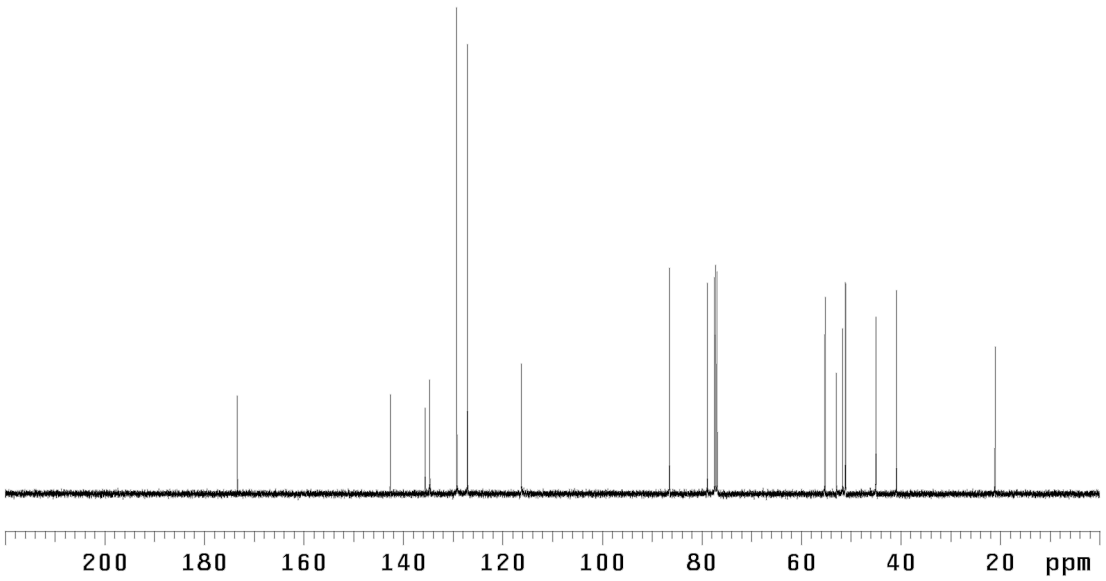


*Figure SI 34. ^{13}C NMR spectrum (126 MHz, $CDCl_3$) of **25**.*

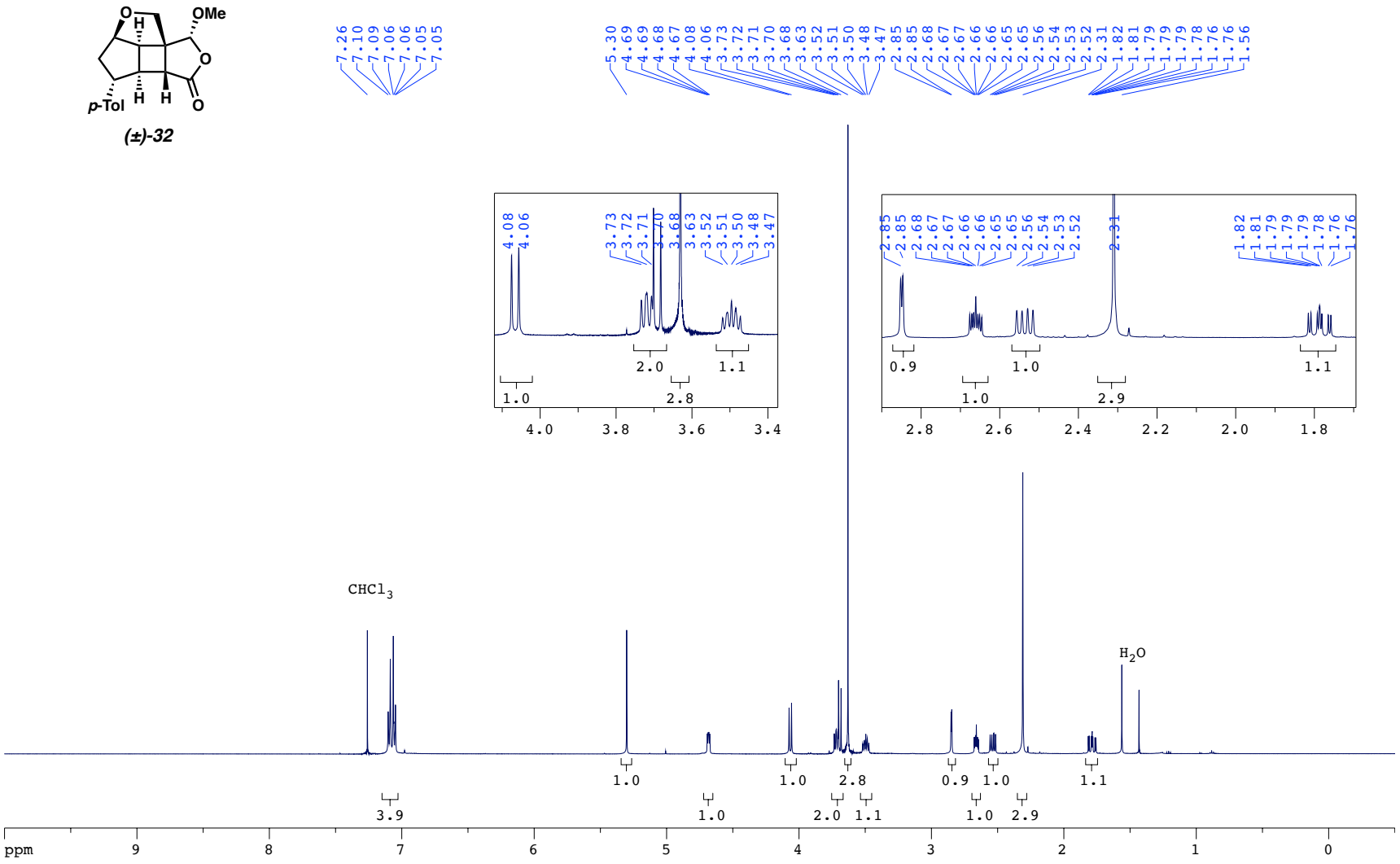


*Figure SI 35. ^{1}H NMR spectrum (500 MHz, $CDCl_3$) of **32**.*

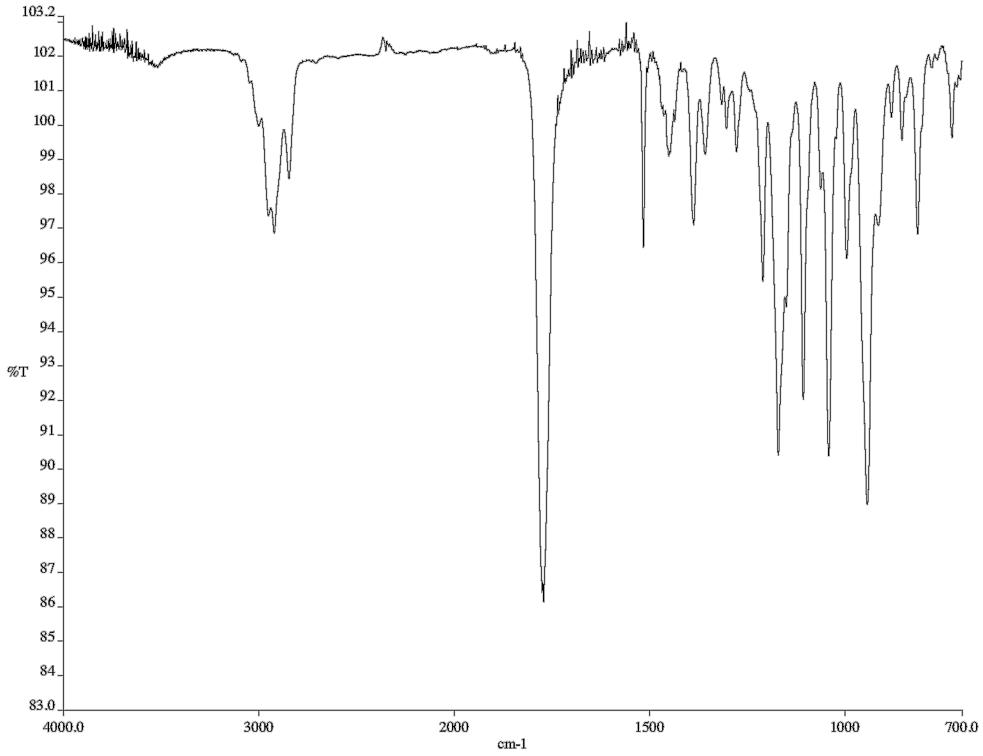


*Figure SI 36. Infrared spectrum (neat film/NaCl) of **32**.*

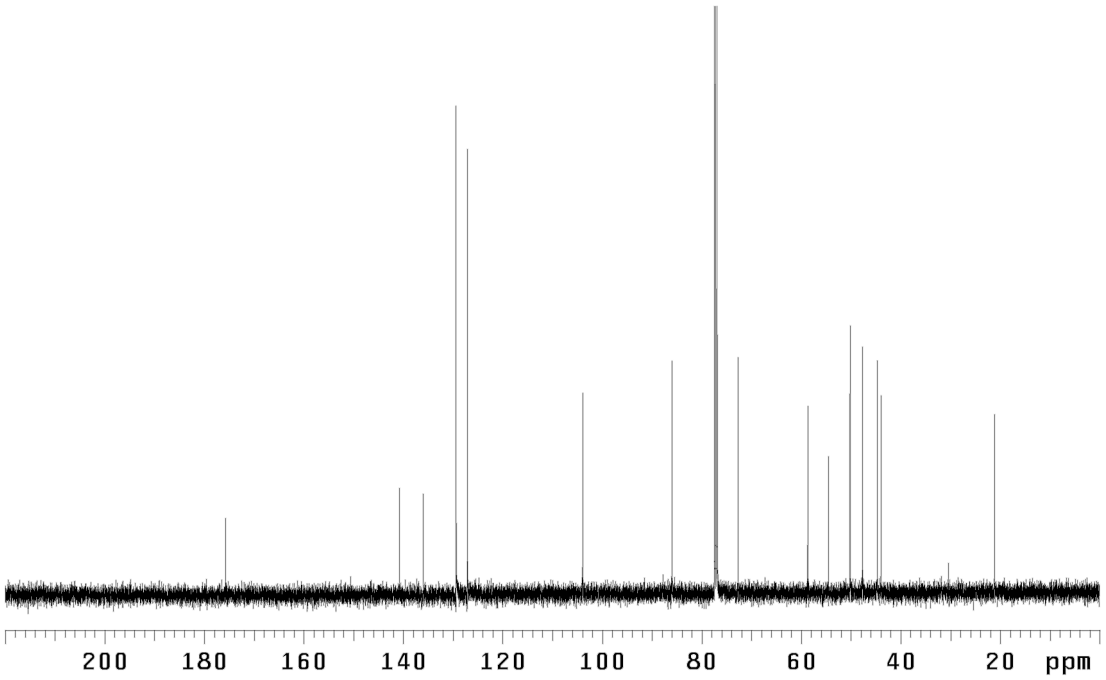


*Figure SI 37. ^{13}C NMR spectrum (126 MHz, $CDCl_3$) of **32**.*

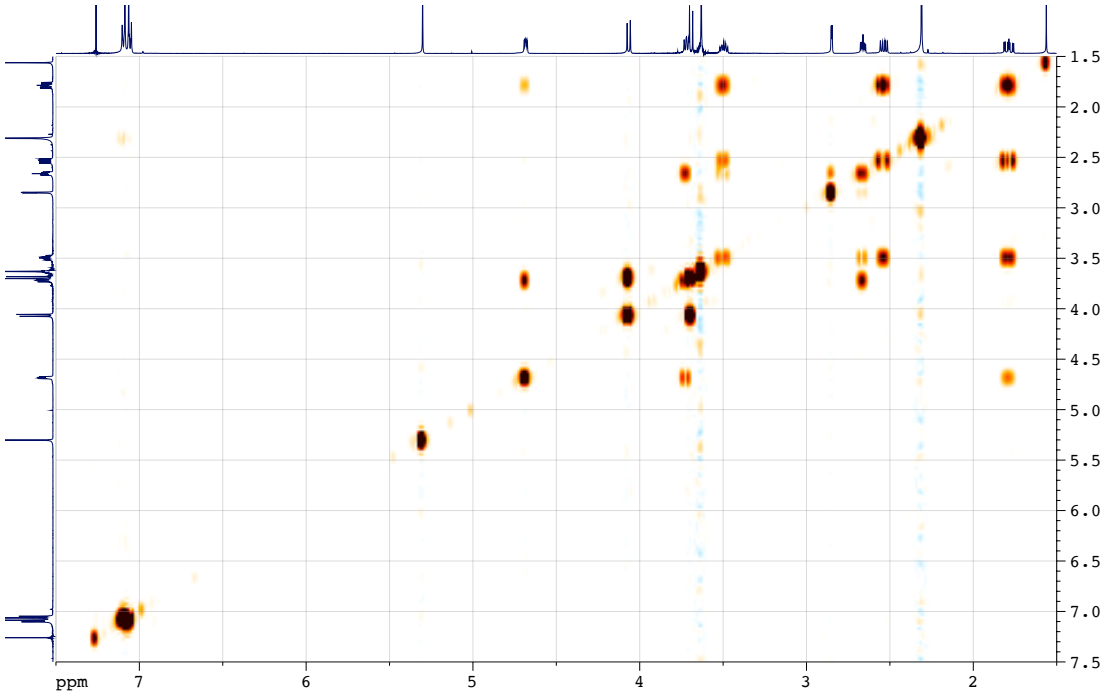


*Figure SI 38. gCOSY NMR spectrum (500 MHz, $CDCl_3$) of **32**.*

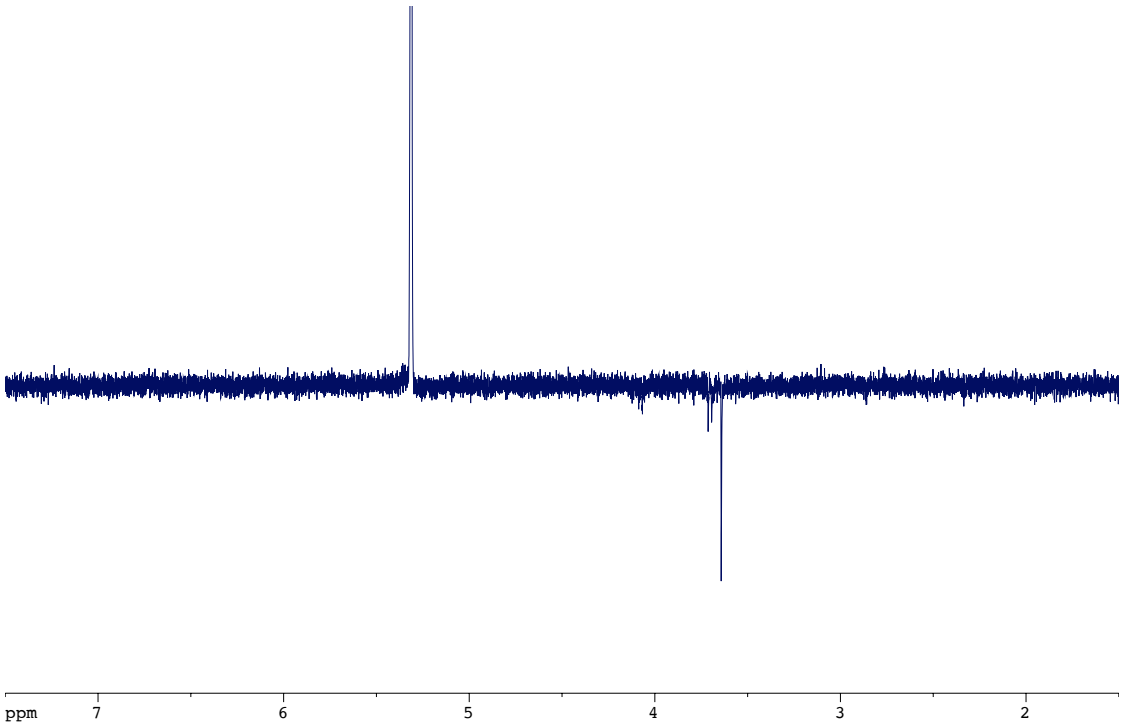


*Figure SI 39. NOESY-1D NMR spectrum (500 MHz, $CDCl_3$) of **32**.*

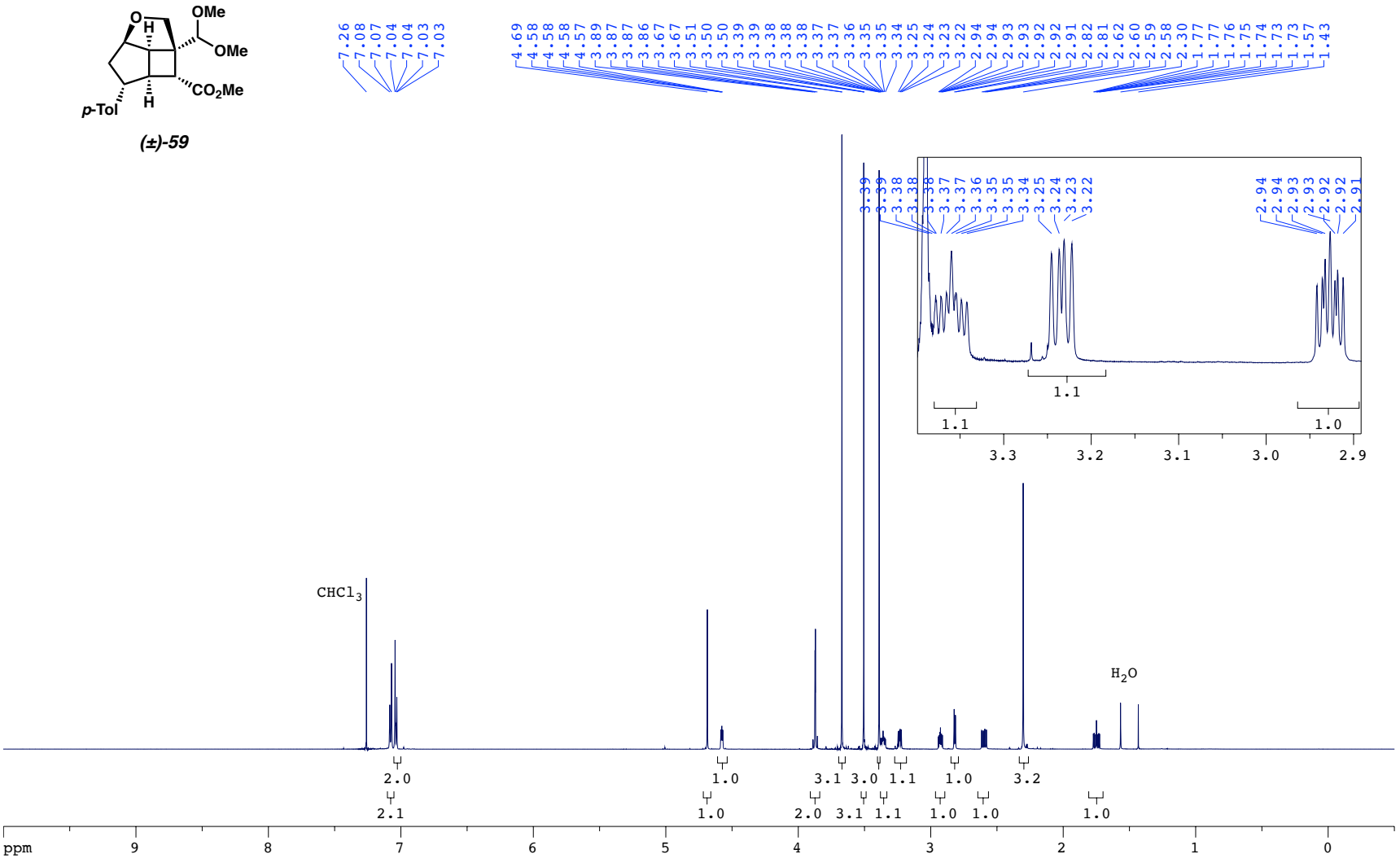


*Figure SI 40. ^{1}H NMR spectrum (600 MHz, $CDCl_3$) of **59**.*

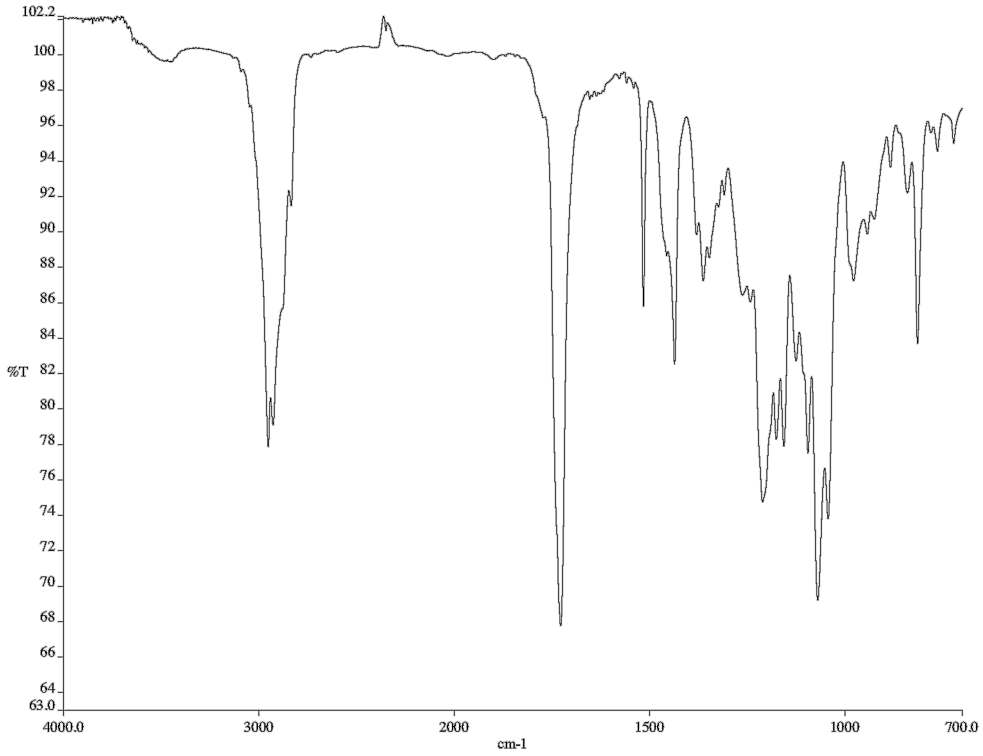


*Figure SI 41. Infrared spectrum (neat film/NaCl) of **59**.*

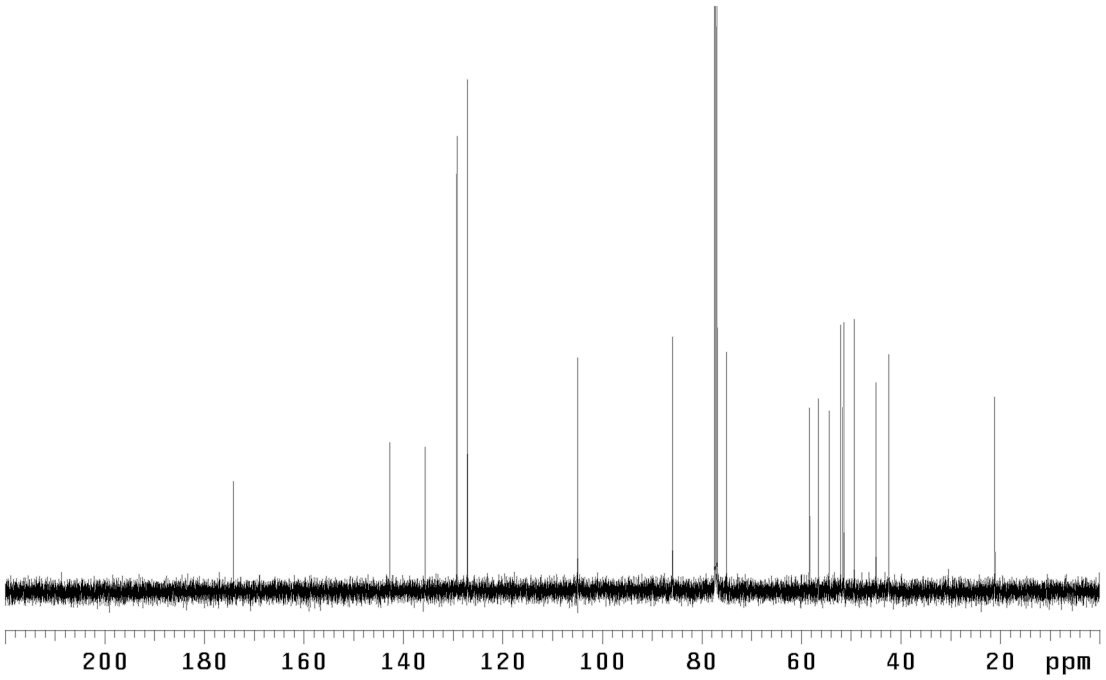


*Figure SI 42. ^{13}C NMR spectrum (126 MHz, $CDCl_3$) of **59**.*

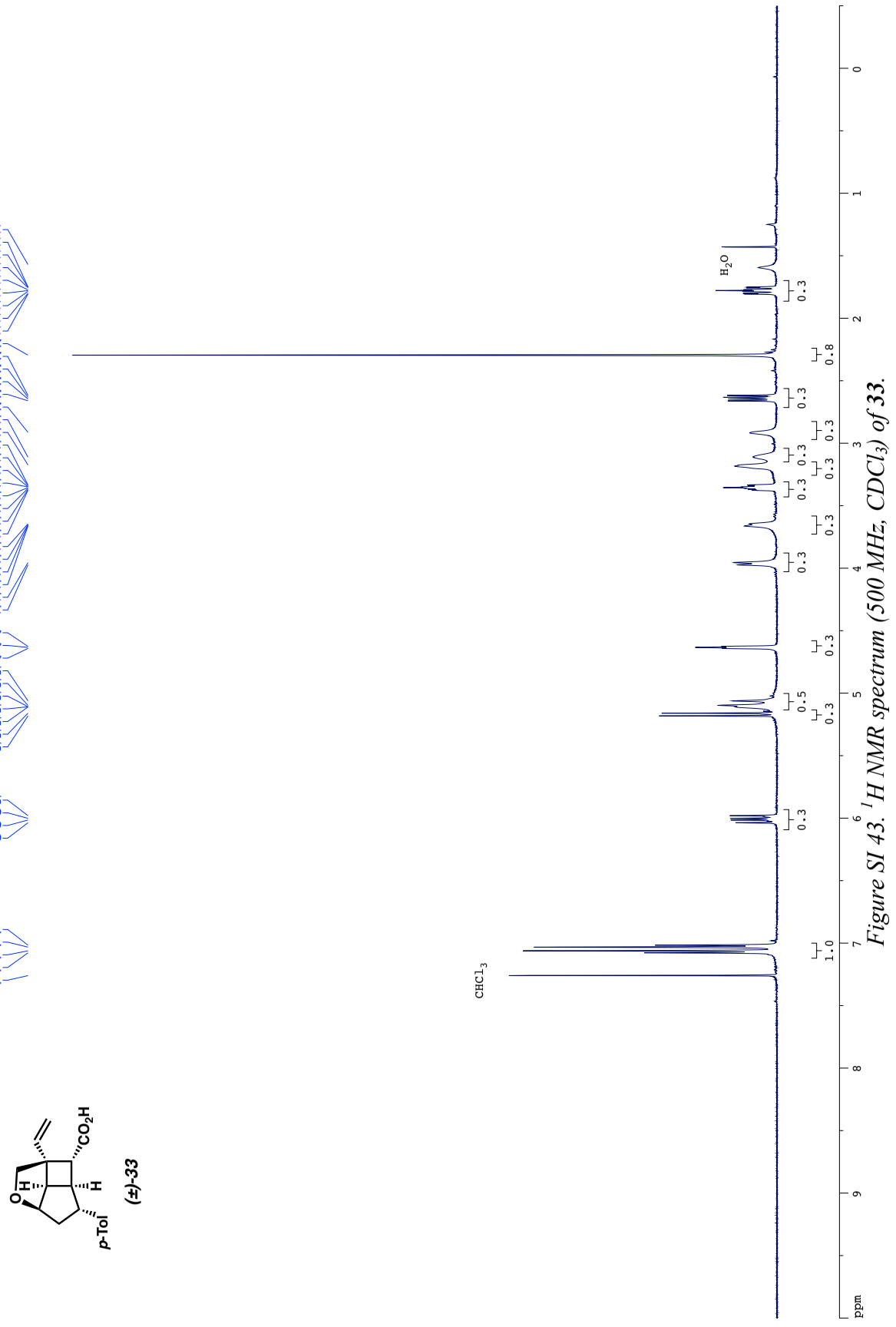


Figure SI 43. ^{1}H NMR spectrum (500 MHz, $CDCl_3$) of ***33****.*

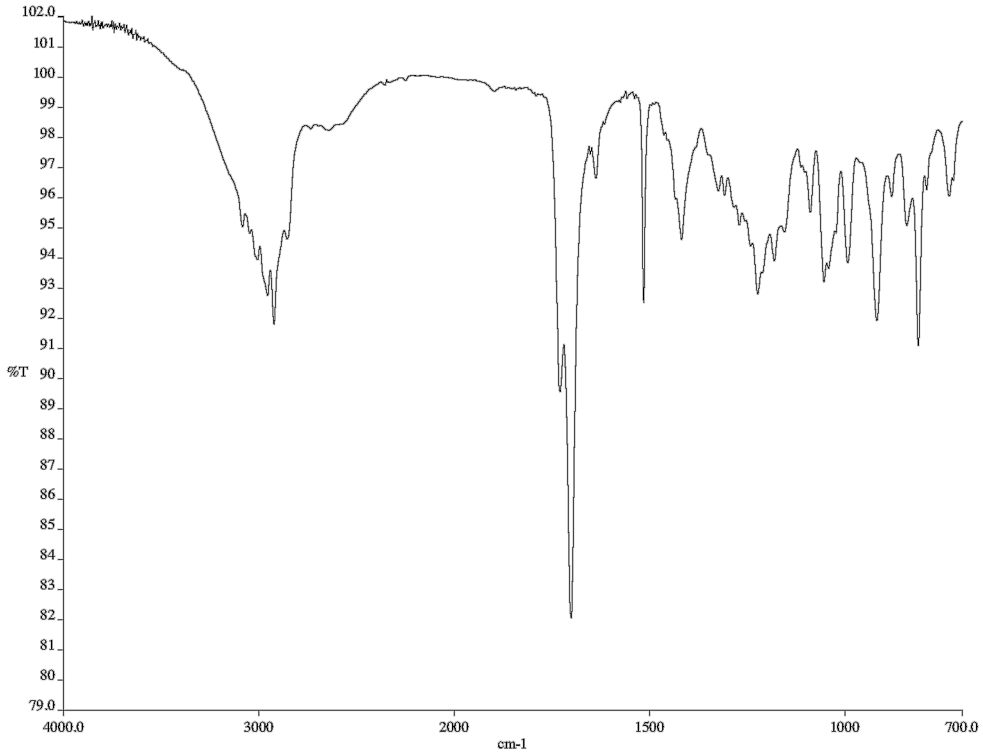


*Figure SI 44. Infrared spectrum (neat film/NaCl) of **33**.*

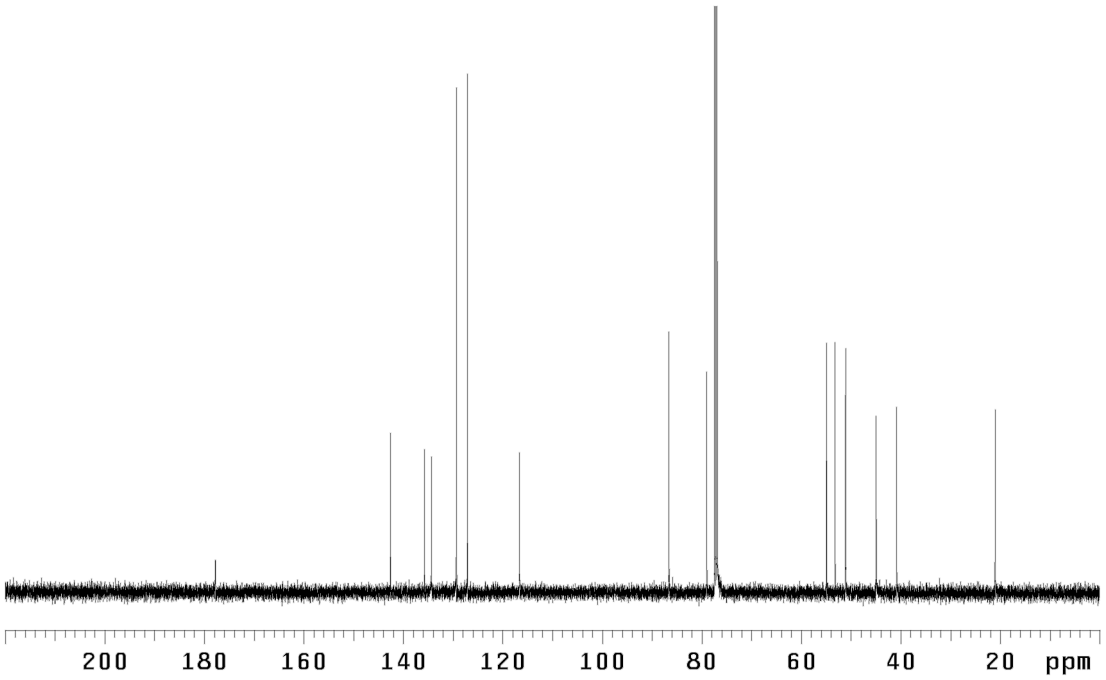


*Figure SI 45. ^{13}C NMR spectrum (126 MHz, $CDCl_3$) of **33**.*

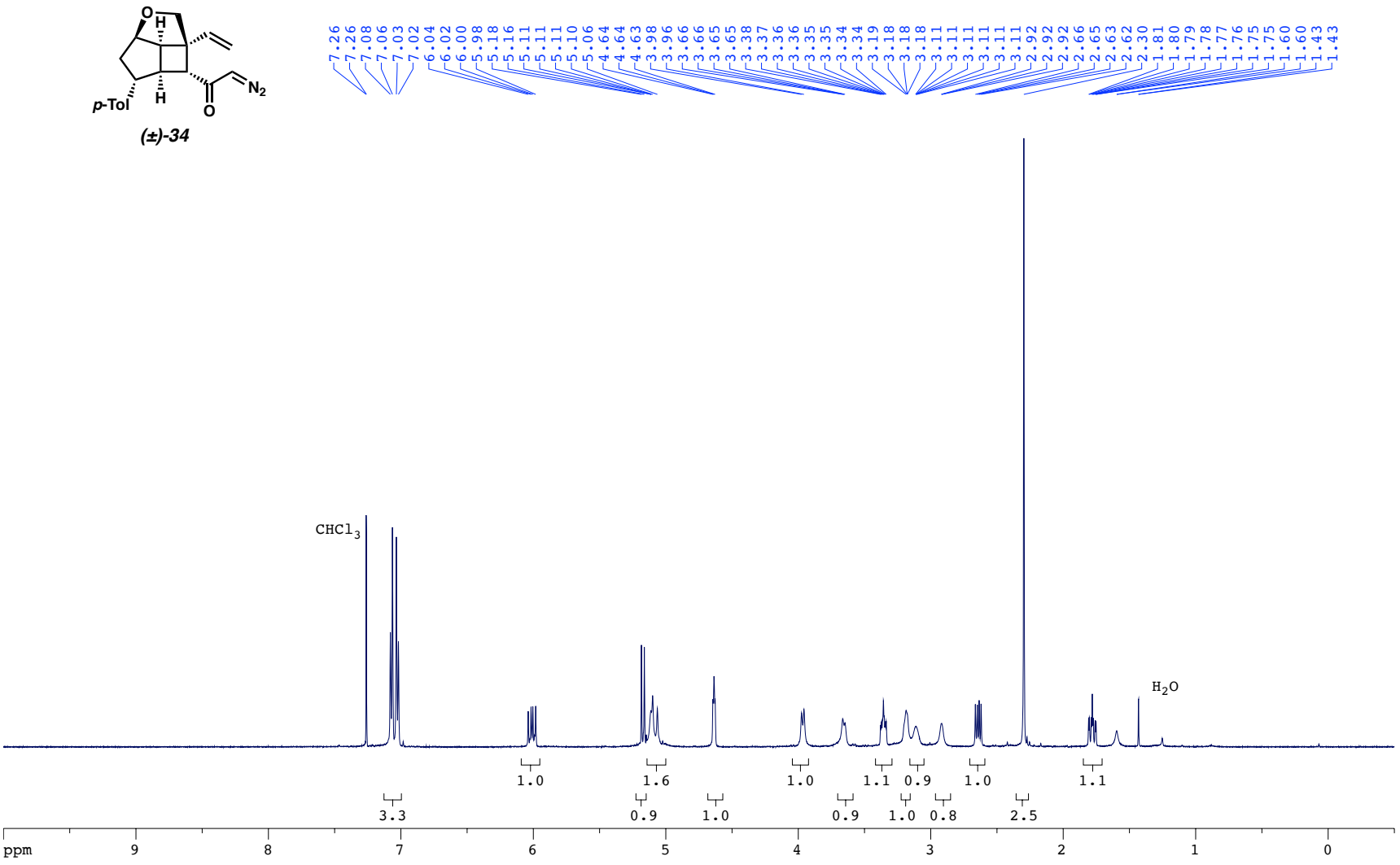


*Figure SI 46. ^1H NMR spectrum (500 MHz, $CDCl_3$) of **34**.*

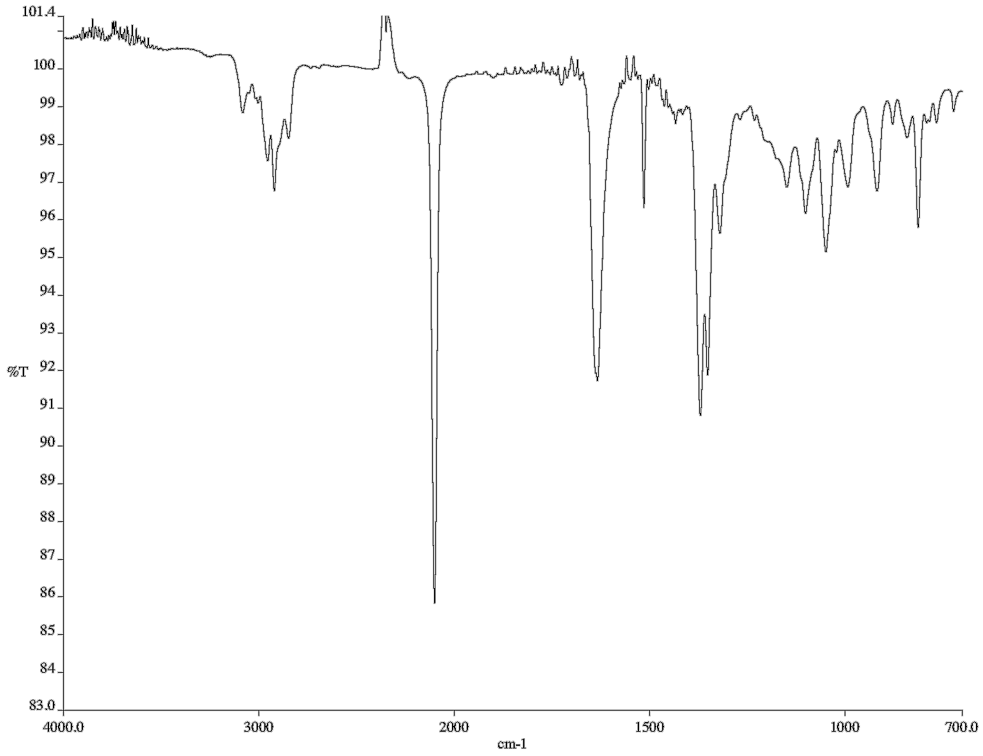


*Figure SI 47. Infrared spectrum (neat film/NaCl) of **34**.*

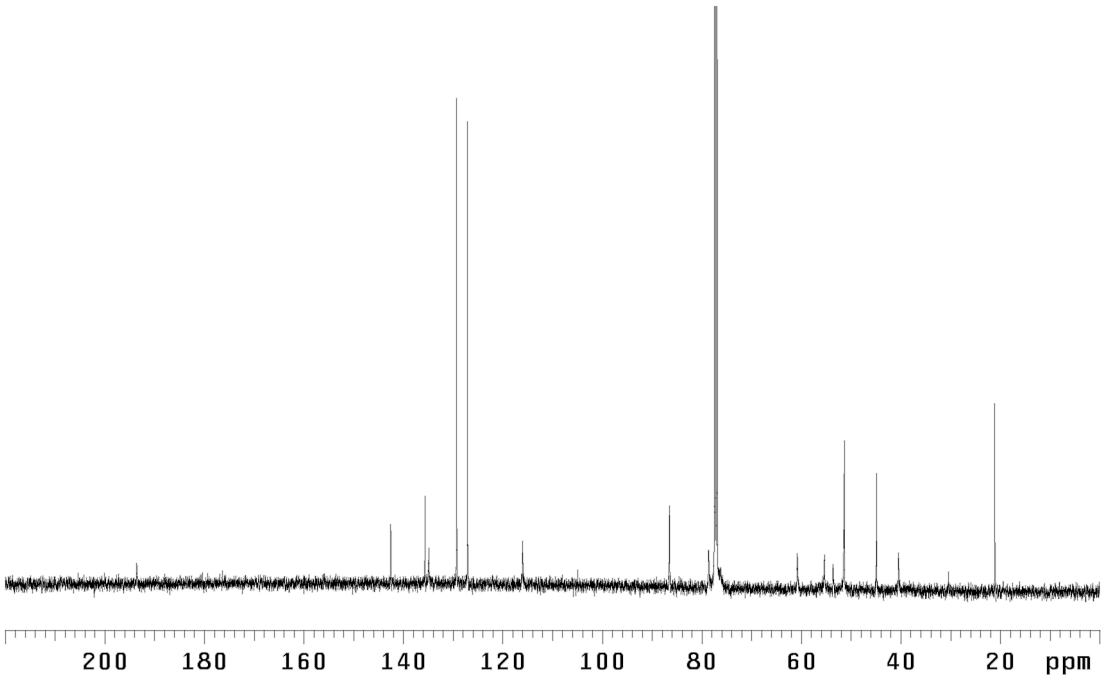


*Figure SI 48. ^{13}C NMR spectrum (126 MHz, $CDCl_3$) of **34**.*

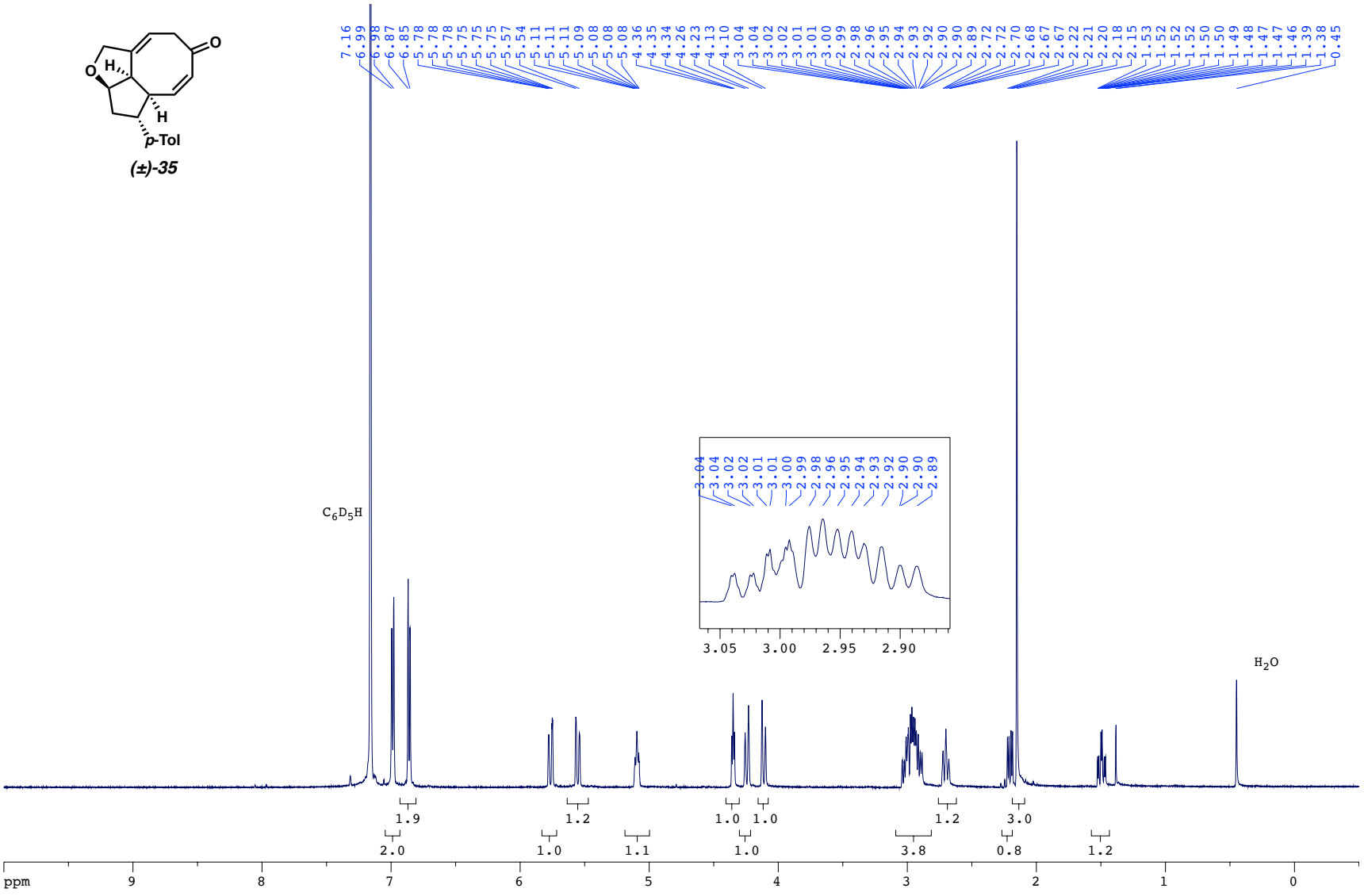


*Figure SI 49. ^{1}H NMR spectrum (500 MHz, C_6D_6) of **35**.*

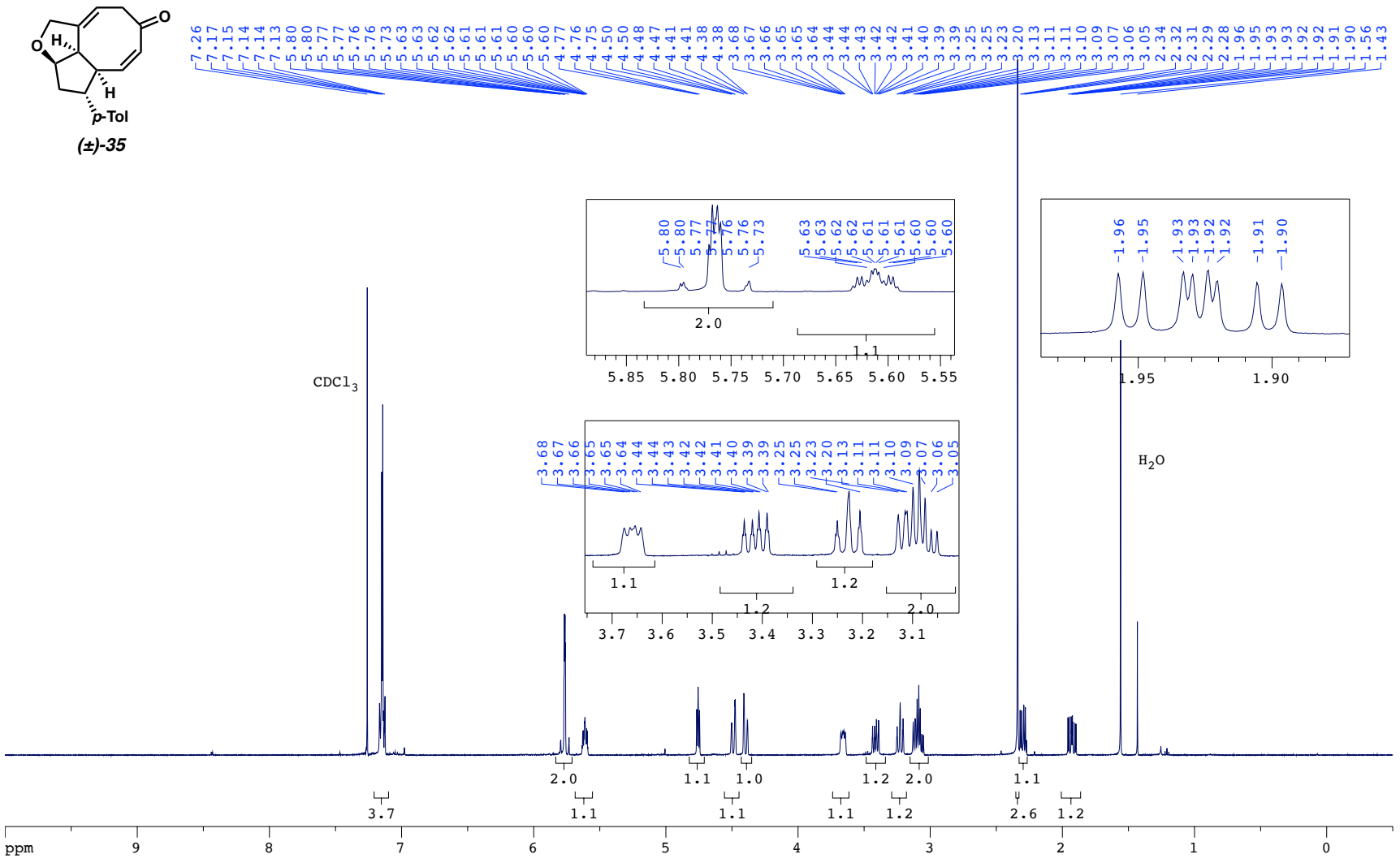


*Figure SI 50. ^{1}H NMR spectrum (500 MHz, $CDCl_3$) of **35**.*

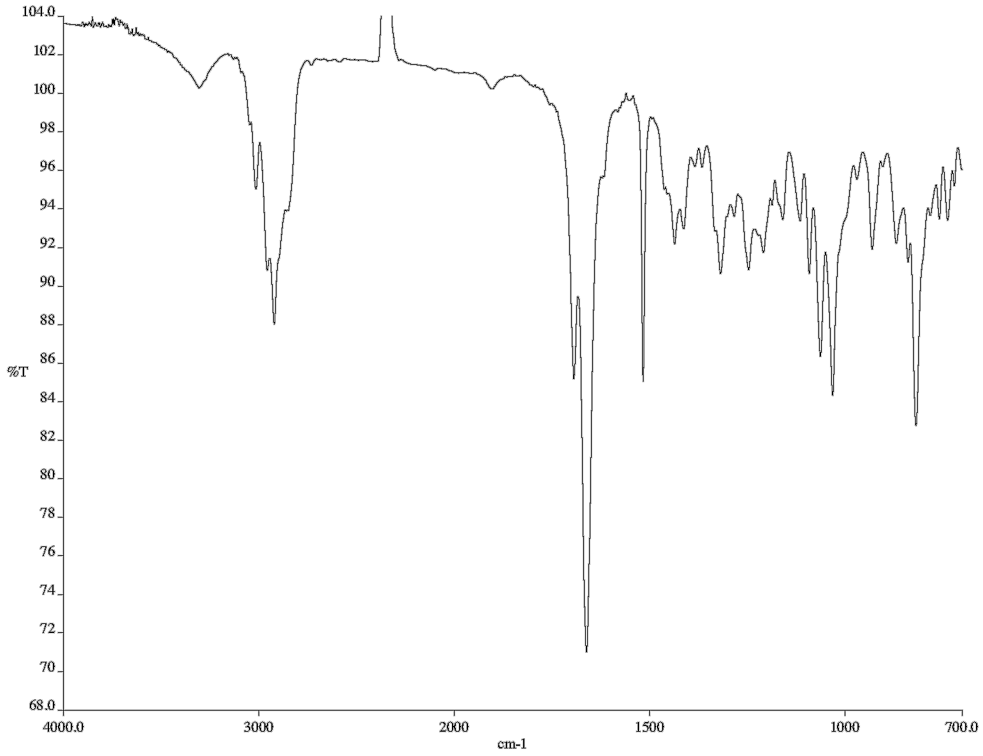


*Figure SI 51. Infrared spectrum (neat film/NaCl) of **35**.*

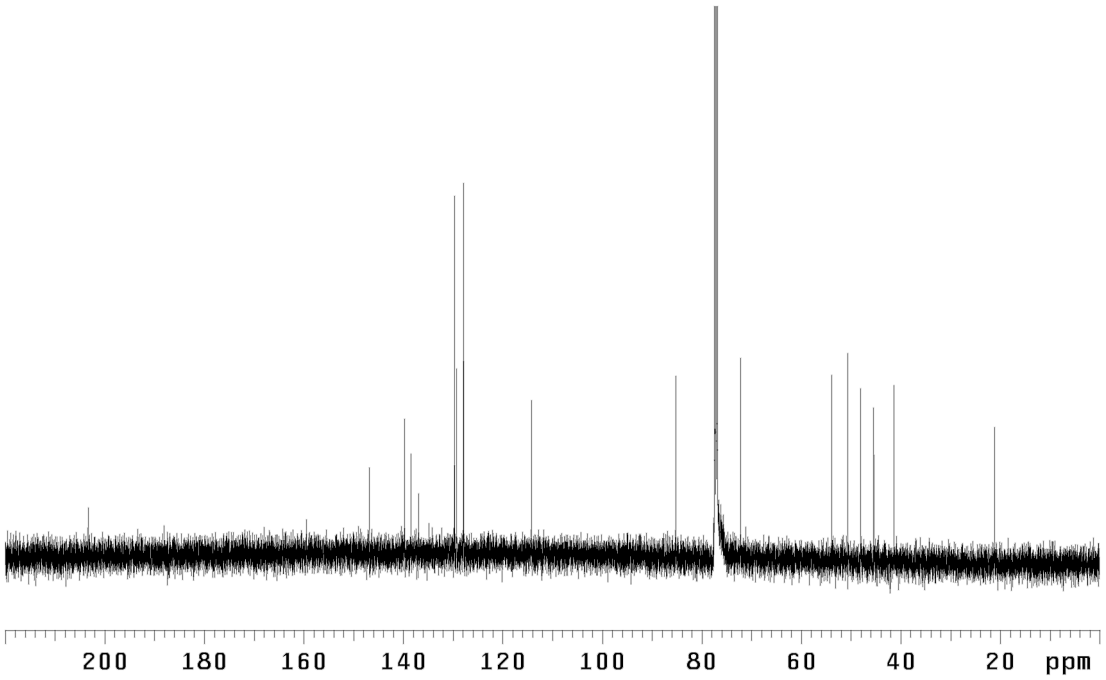


*Figure SI 52. ^{13}C NMR spectrum (126 MHz, $CDCl_3$) of **35**.*

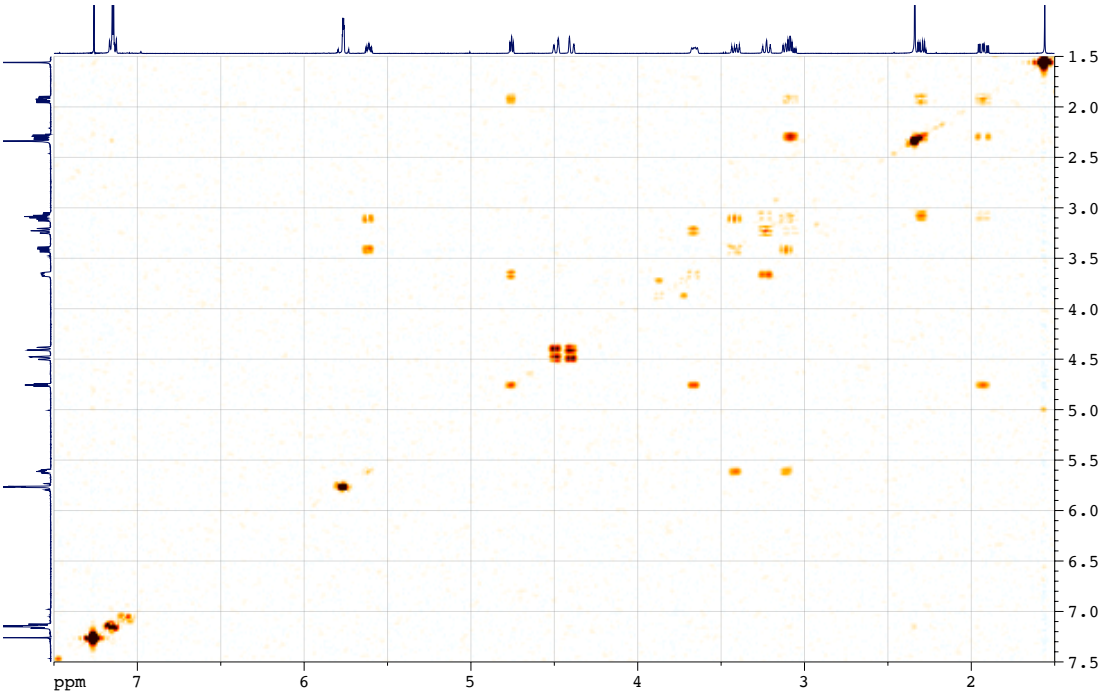


*Figure SI 53. gCOSY NMR spectrum (500 MHz, $CDCl_3$) of **35**.*

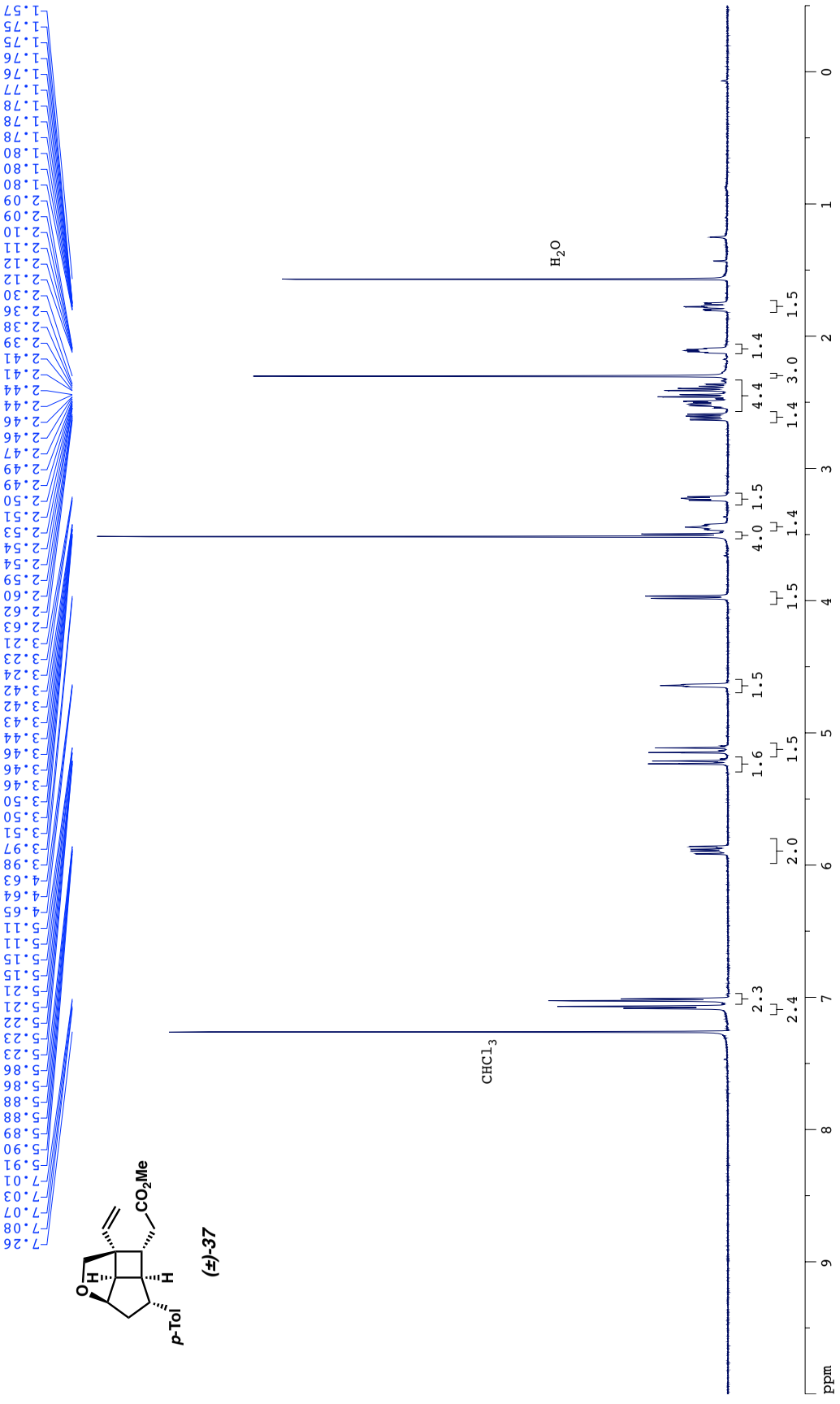


*Figure SI 54. ^1H NMR spectrum (500 MHz, $CDCl_3$) of **37**.*

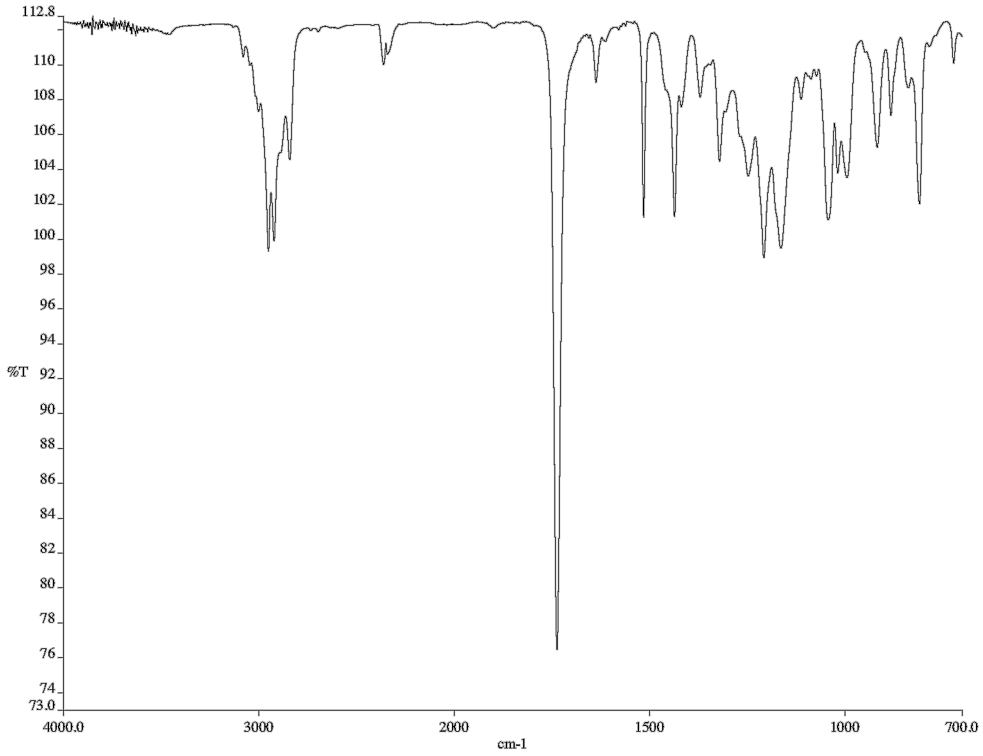


*Figure SI 55. Infrared spectrum (neat film/NaCl) of **37**.*

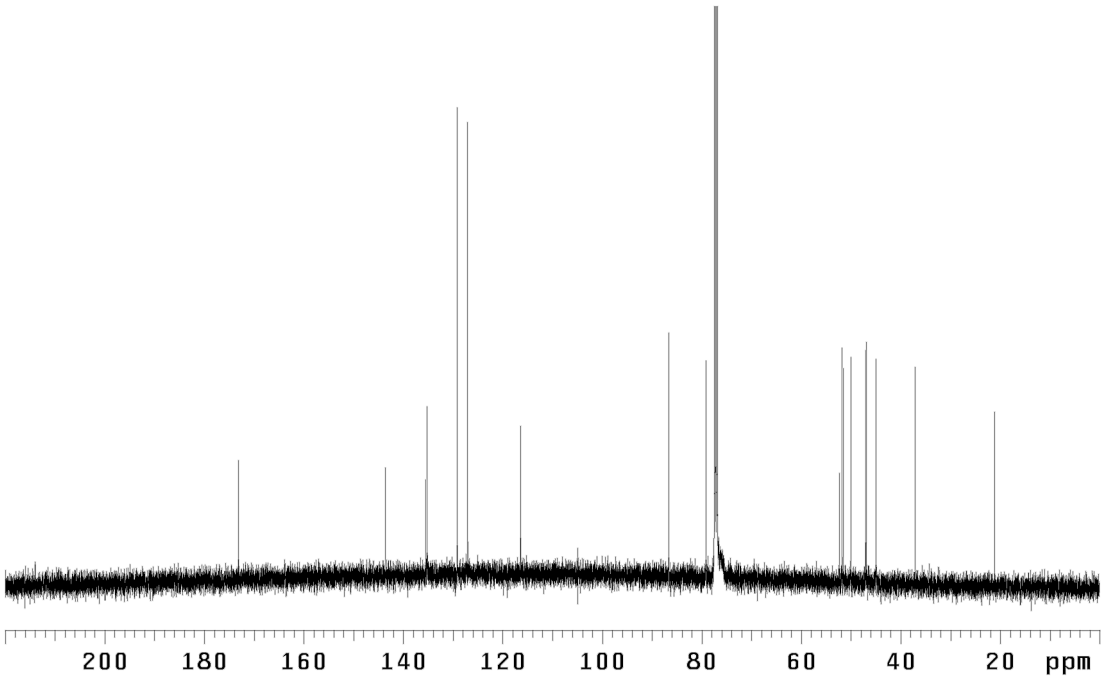


*Figure SI 56. ^{13}C NMR spectrum (126 MHz, $CDCl_3$) of **37**.*

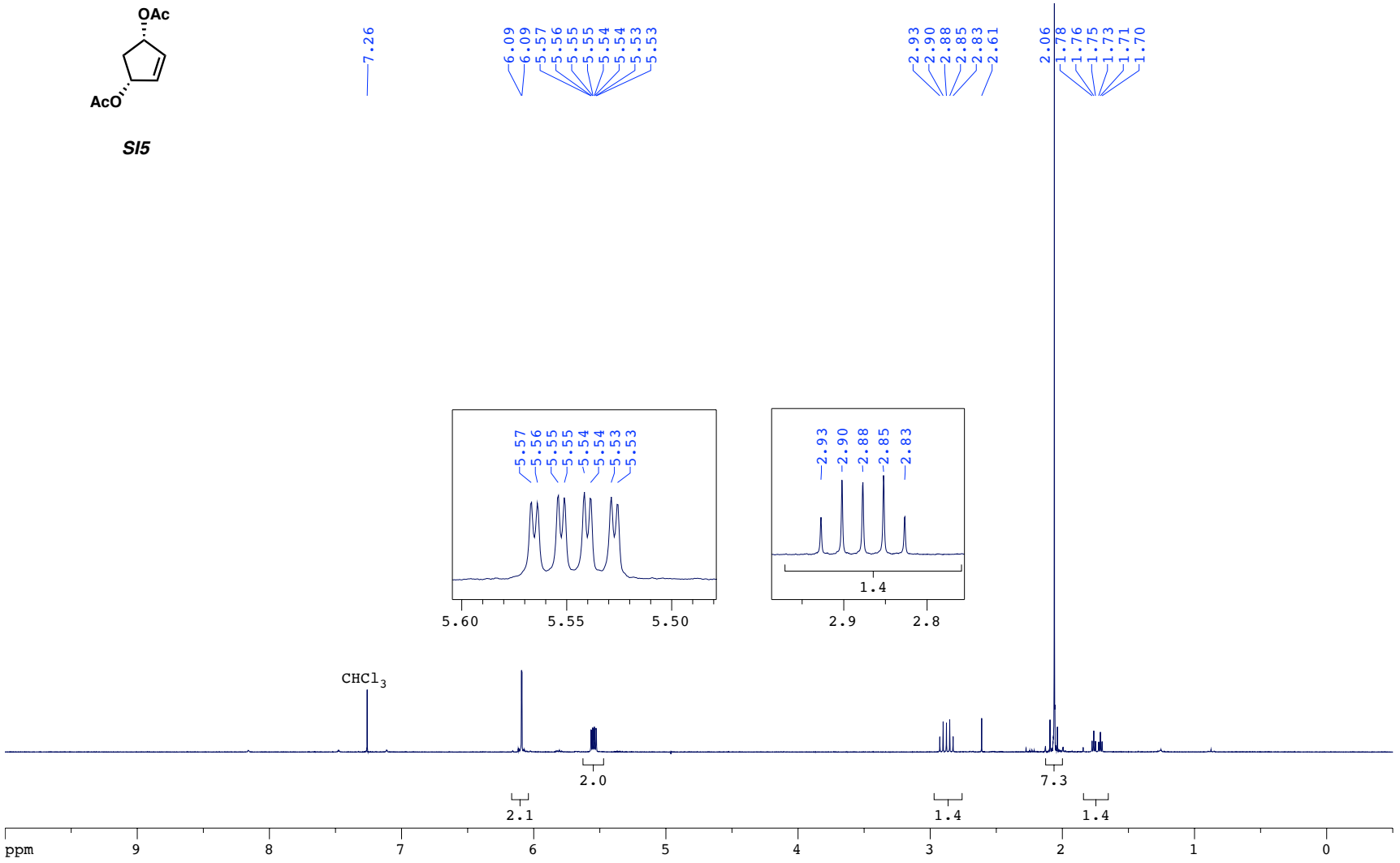


Figure SI 57. ^{1}H NMR spectrum (300 MHz, $CDCl_3$) of ***SI5****.*

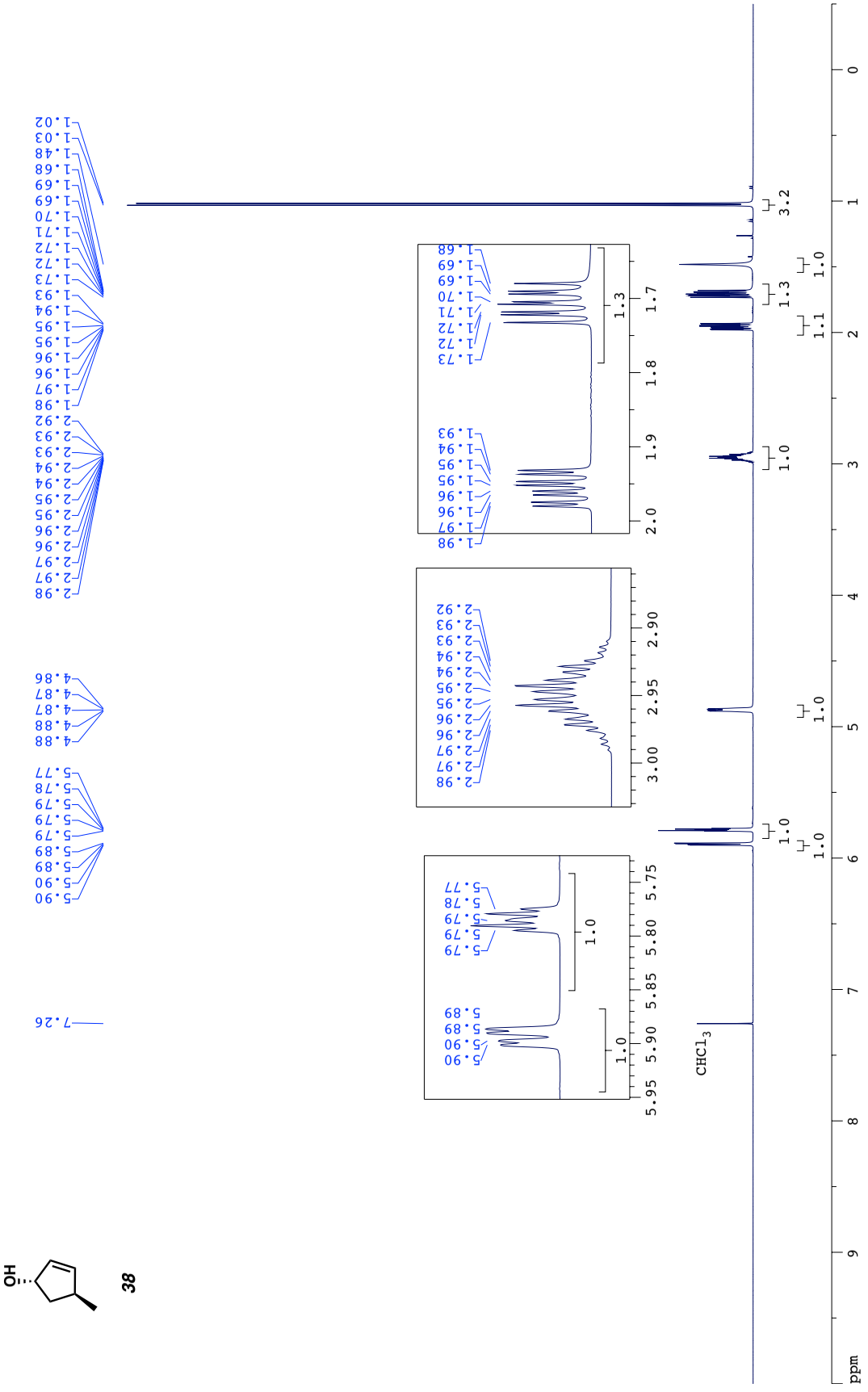


Figure SI 58. ^1H NMR spectrum (500 MHz, $CDCl_3$) of ***38****.*

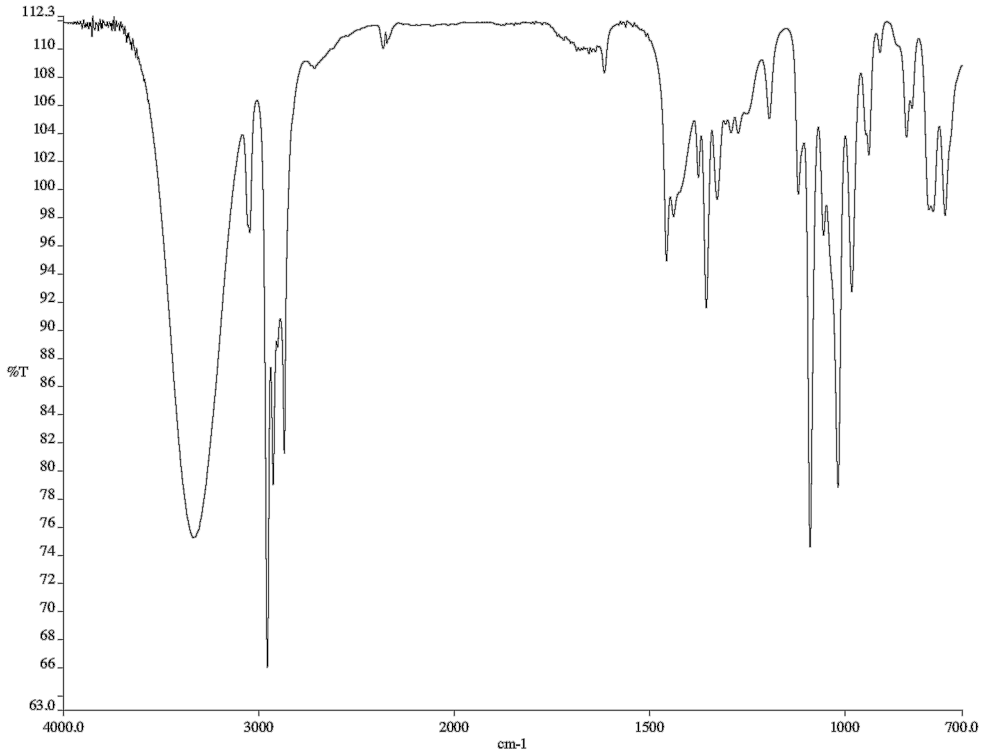


*Figure SI 59. Infrared spectrum (neat film/NaCl) of **38**.*

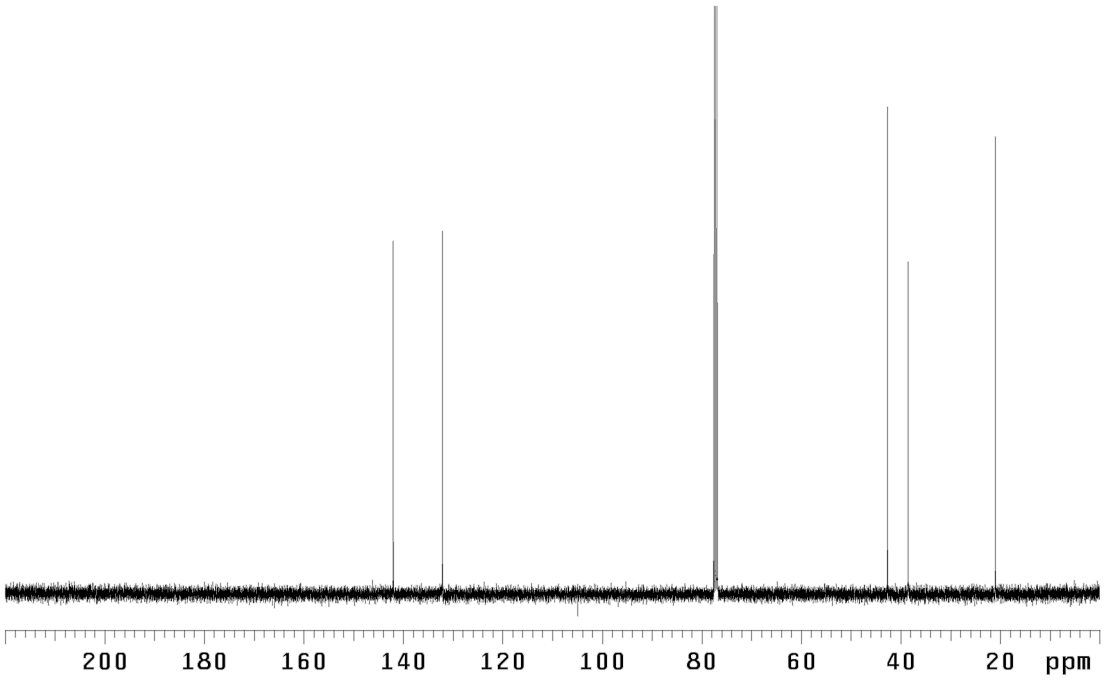


*Figure SI 60. ^{13}C NMR spectrum (126 MHz, $CDCl_3$) of **38**.*

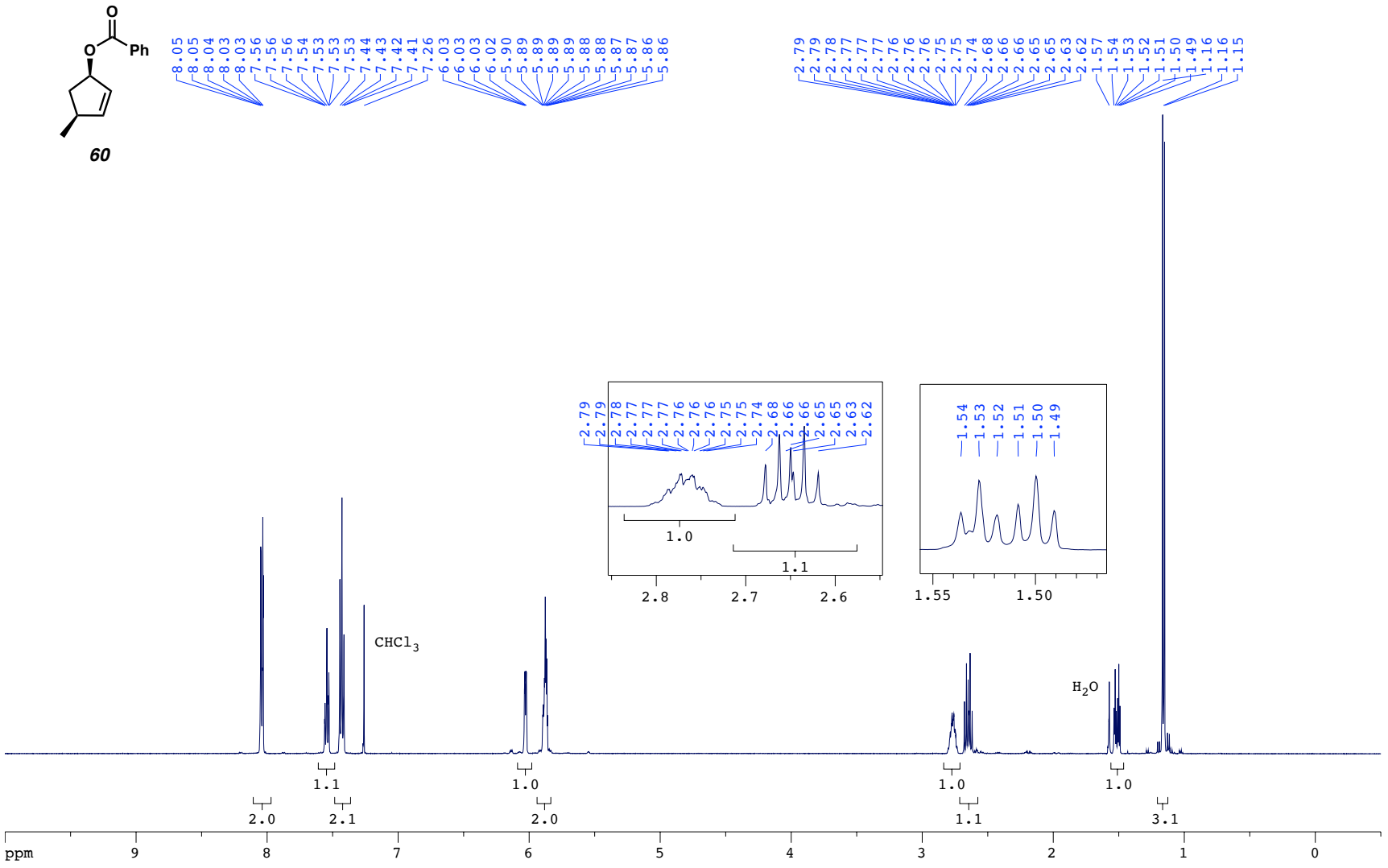


*Figure SI 61. ^1H NMR spectrum (500 MHz, $CDCl_3$) of **60**.*

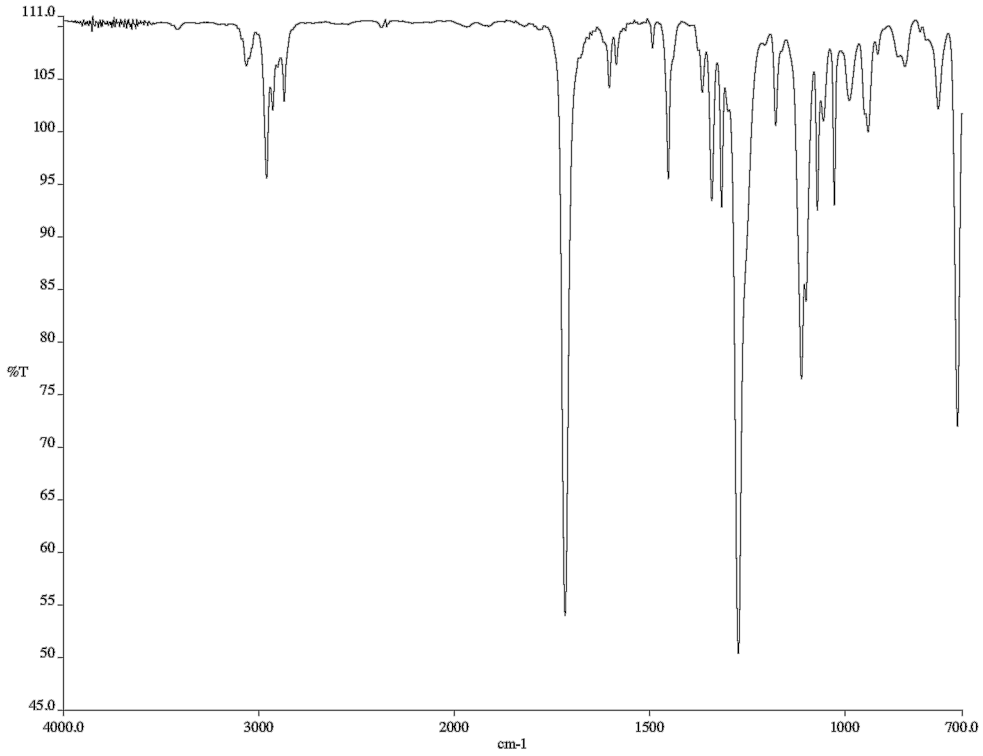


*Figure SI 62. Infrared spectrum (neat film/NaCl) of **60**.*

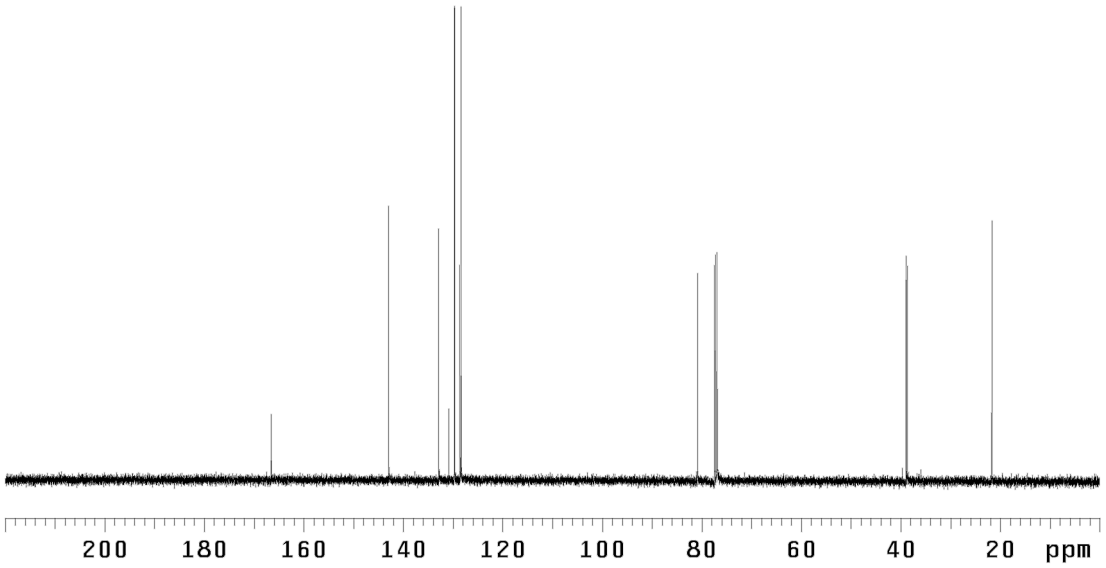


*Figure SI 63. ^{13}C NMR spectrum (126 MHz, $CDCl_3$) of **60**.*

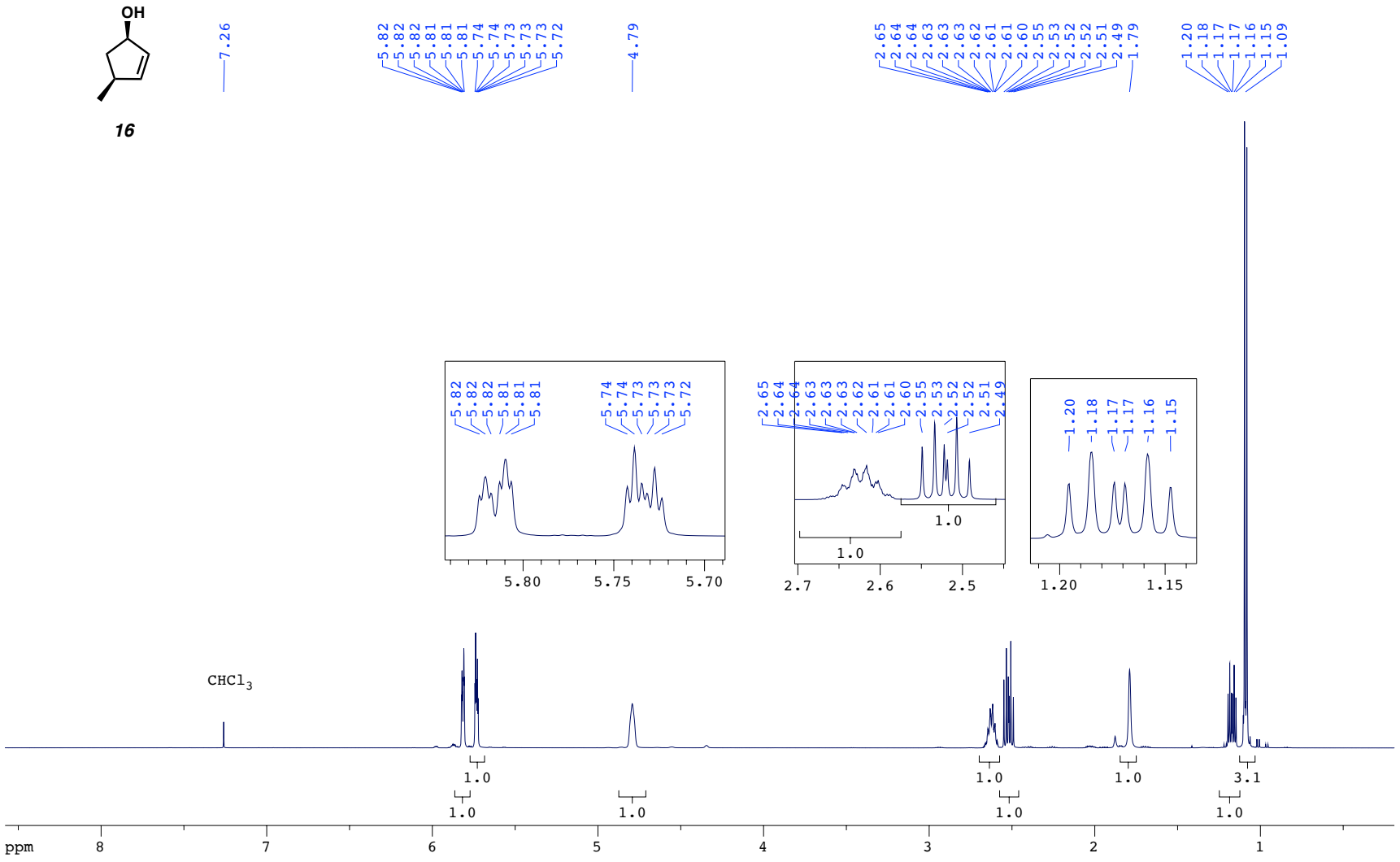


Figure SI 64. ^{1}H NMR spectrum (500 MHz, $CDCl_3$) of ***16****.*

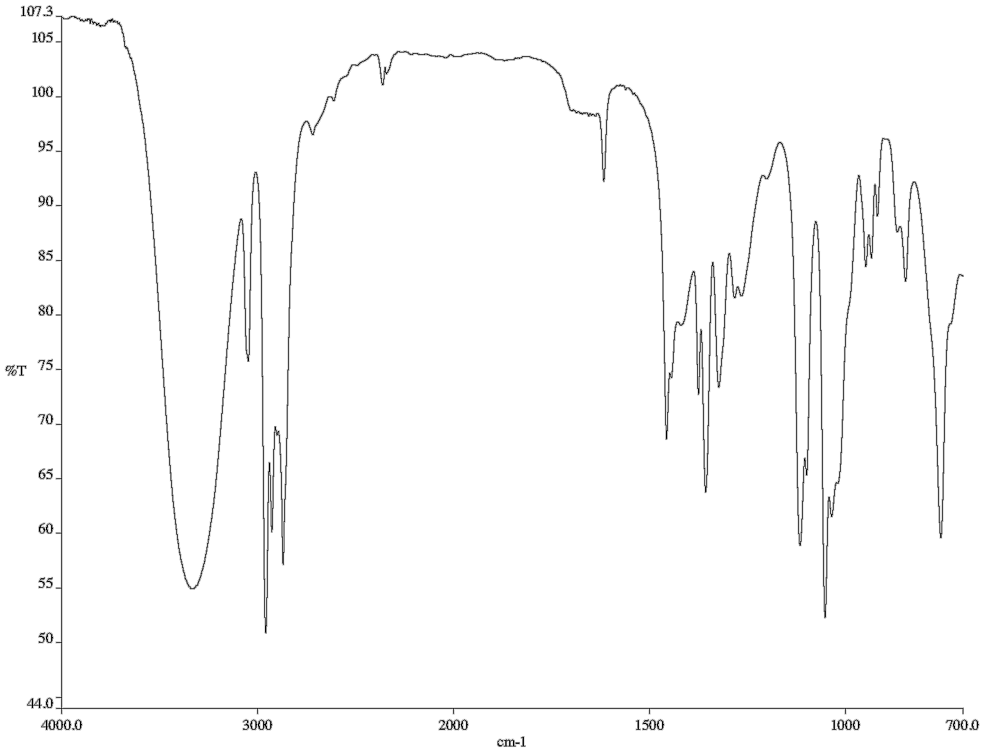


*Figure SI 65. Infrared spectrum (neat film/NaCl) of **16**.*

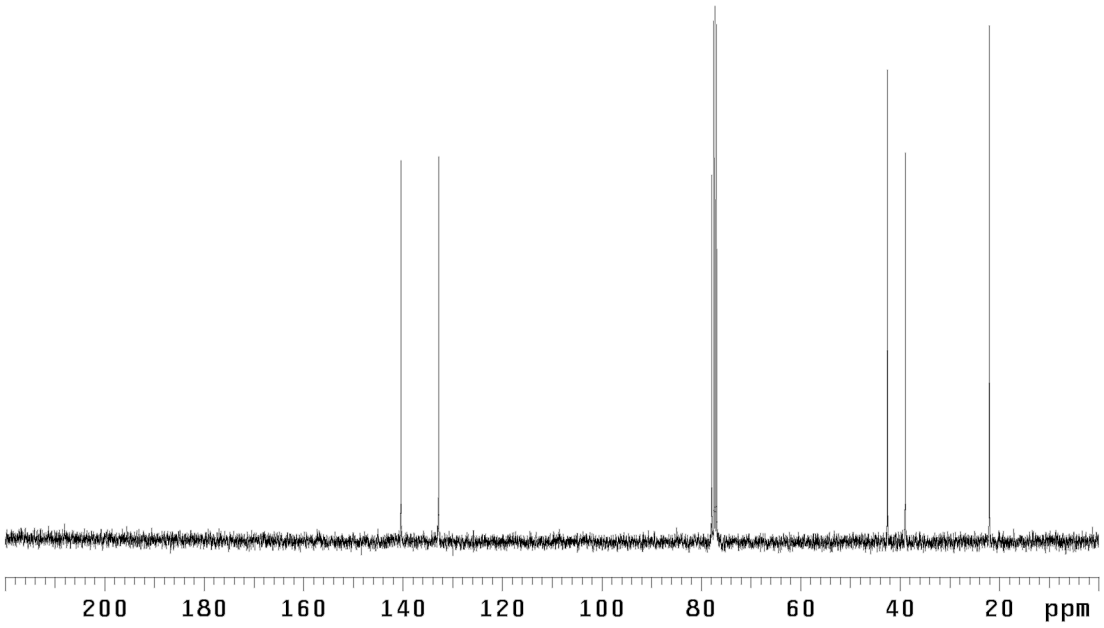


*Figure SI 66. ^{13}C NMR spectrum (126 MHz, $CDCl_3$) of **16**.*

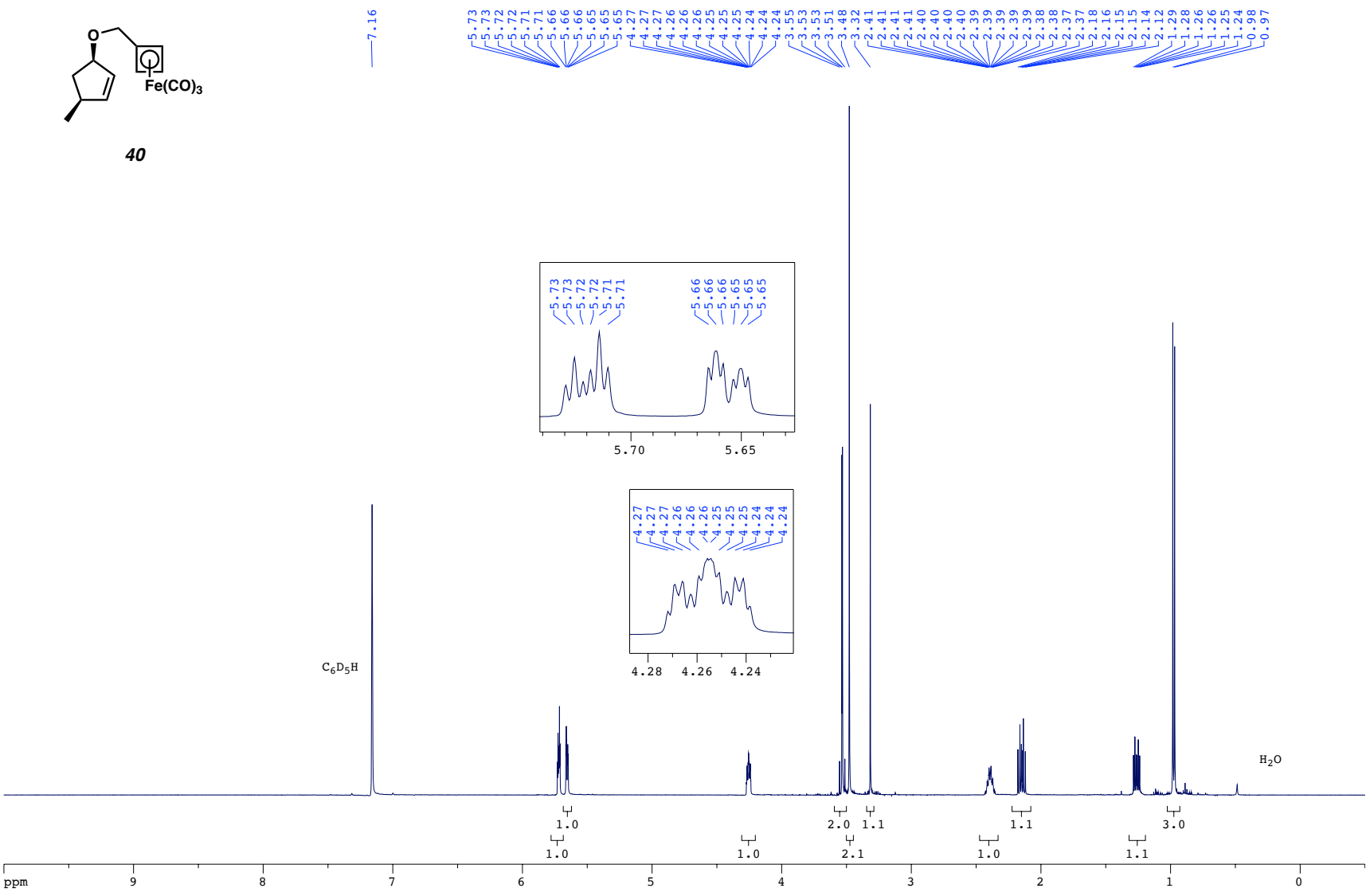


*Figure SI 67. ^{1}H NMR spectrum (500 MHz, C_6D_6) of **40**.*

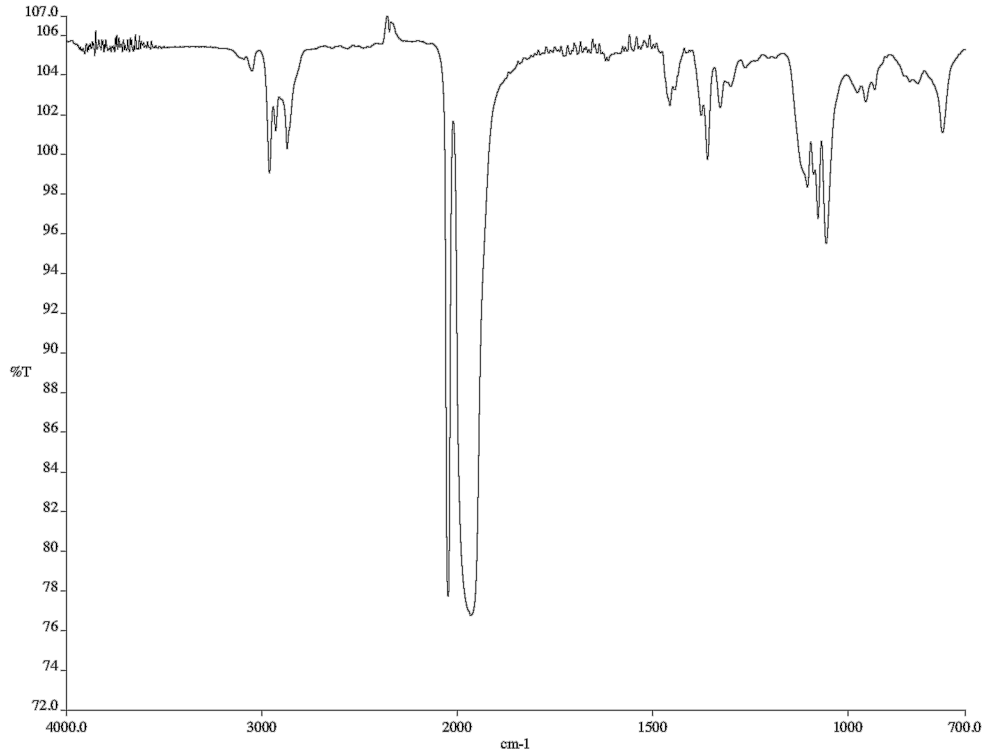


*Figure SI 68. Infrared spectrum (neat film/NaCl) of **40**.*

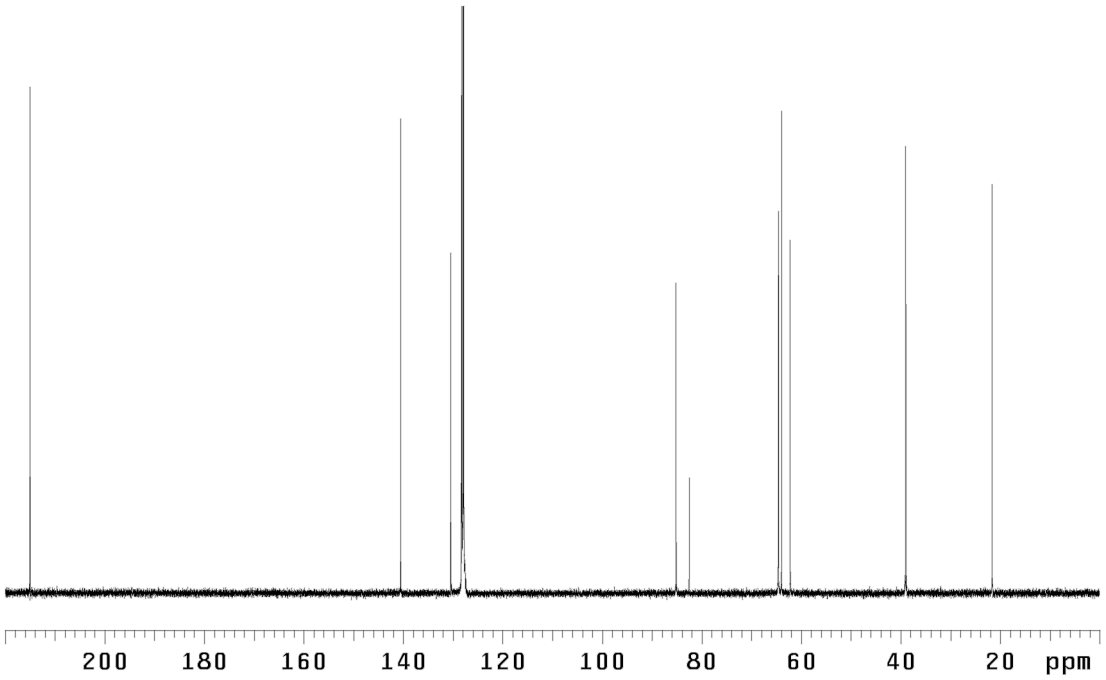


*Figure SI 69. ^{13}C NMR spectrum (126 MHz, $CDCl_3$) of **40**.*

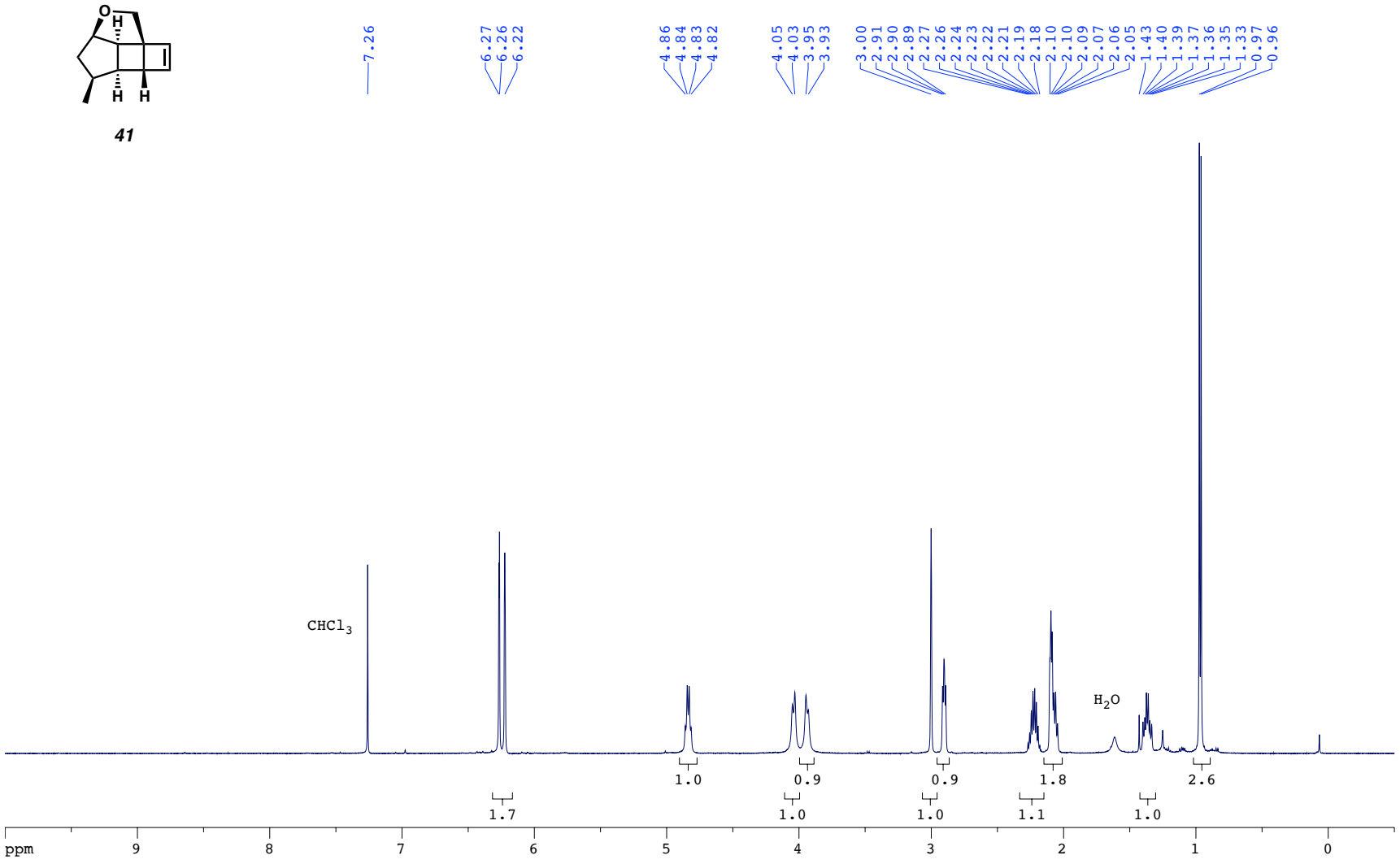


*Figure SI 70. ^{1}H NMR spectrum (500 MHz, $CDCl_3$) of **41**.*

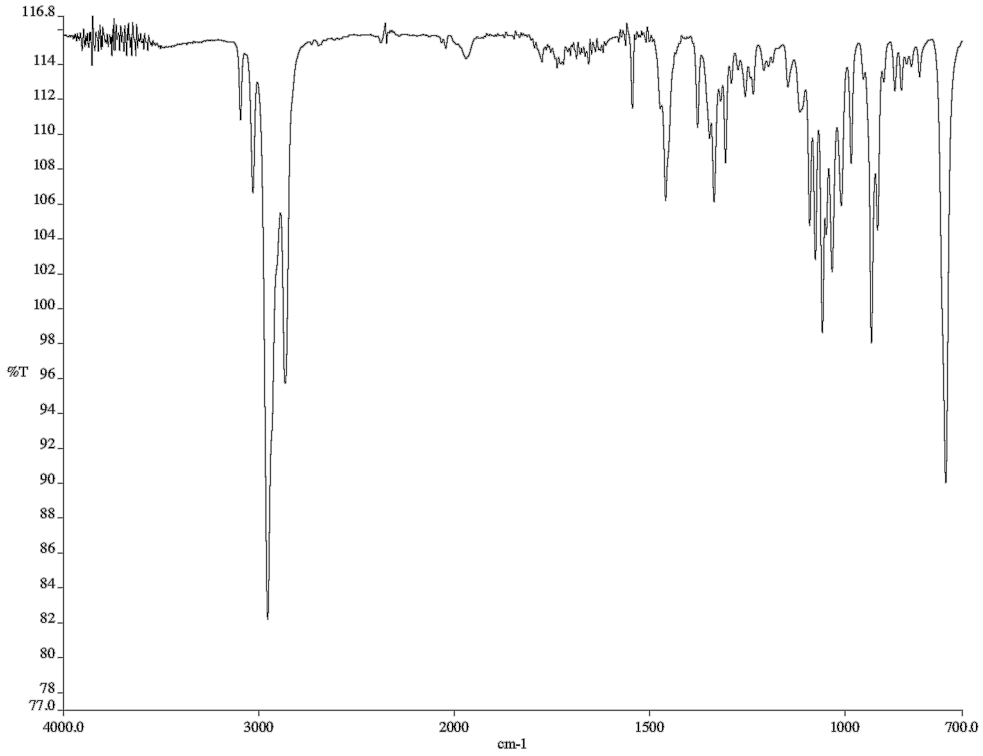


*Figure SI 71. Infrared spectrum (neat film/NaCl) of **41**.*

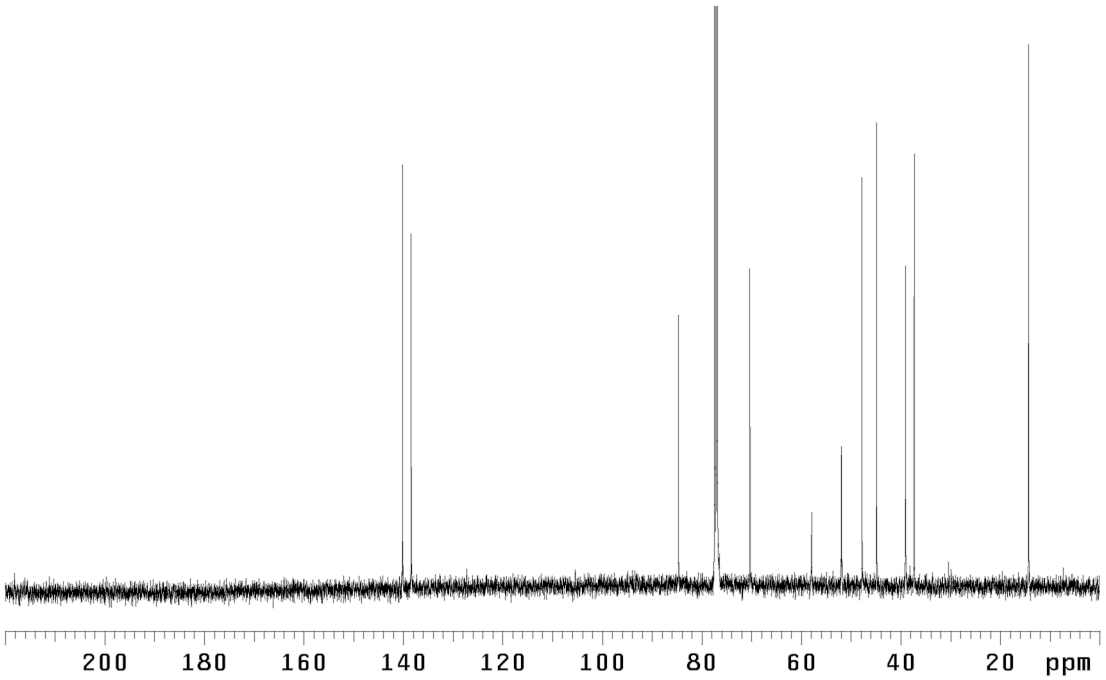


*Figure SI 72. ^{13}C NMR spectrum (126 MHz, $CDCl_3$) of **41**.*

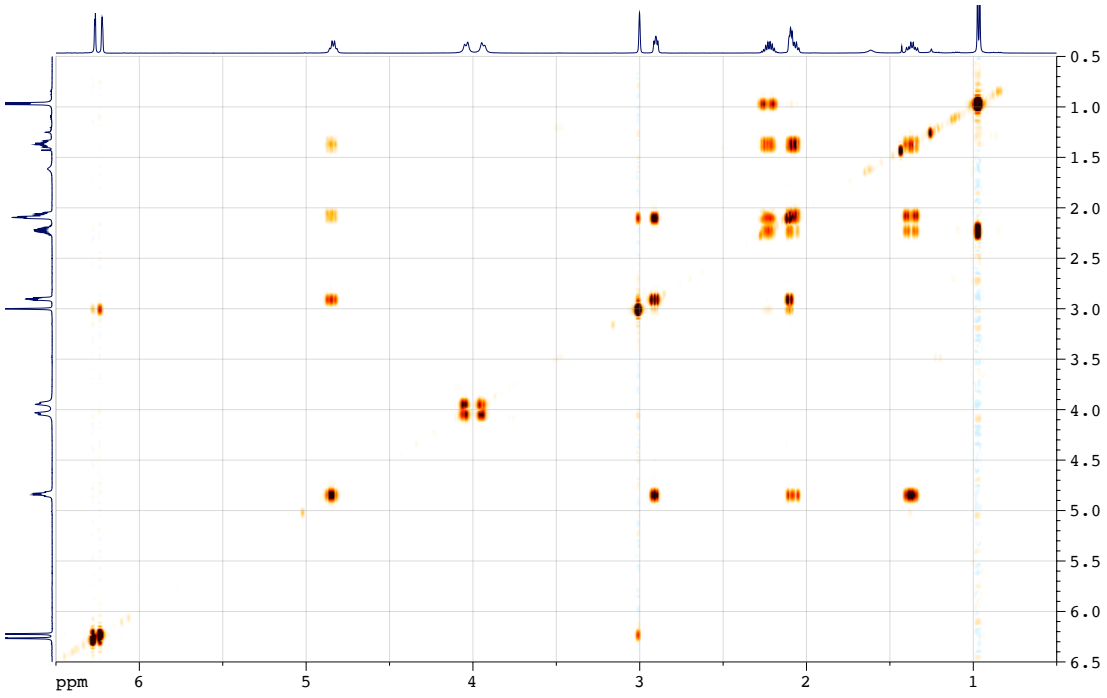


*Figure SI 73. gCOSY NMR spectrum (500 MHz, $CDCl_3$) of **41**.*

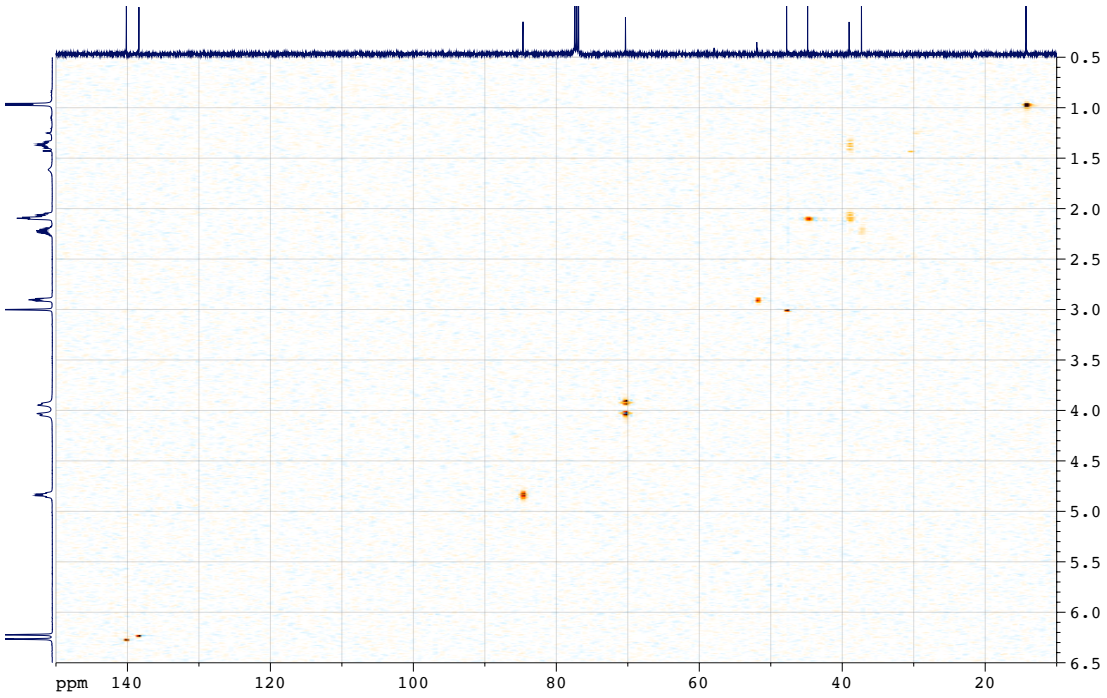


*Figure SI 74. gHSQC NMR spectrum (500, 126 MHz, $CDCl_3$) of **41**.*

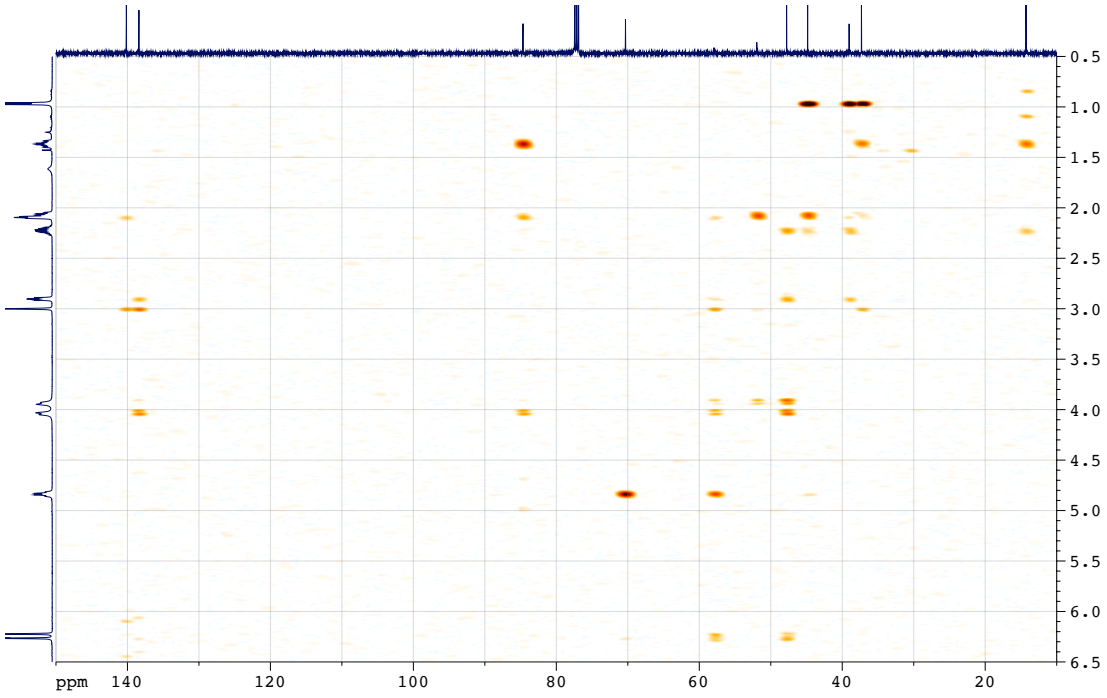


*Figure SI 75. gHMBC NMR spectrum (500, 126 MHz, $CDCl_3$) of **41**.*

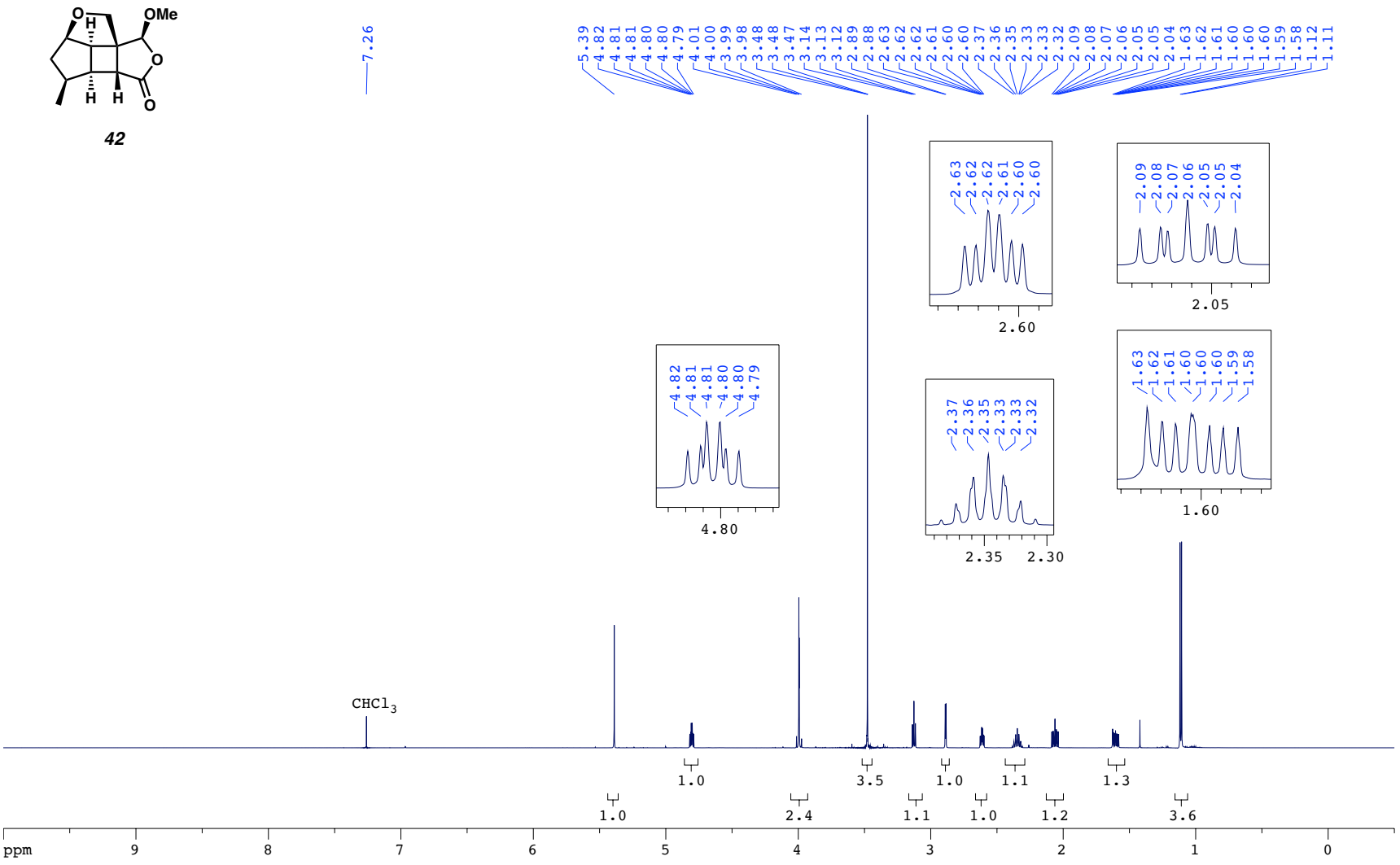


*Figure SI 76. ^{1}H NMR spectrum (500 MHz, $CDCl_3$) of **42**.*

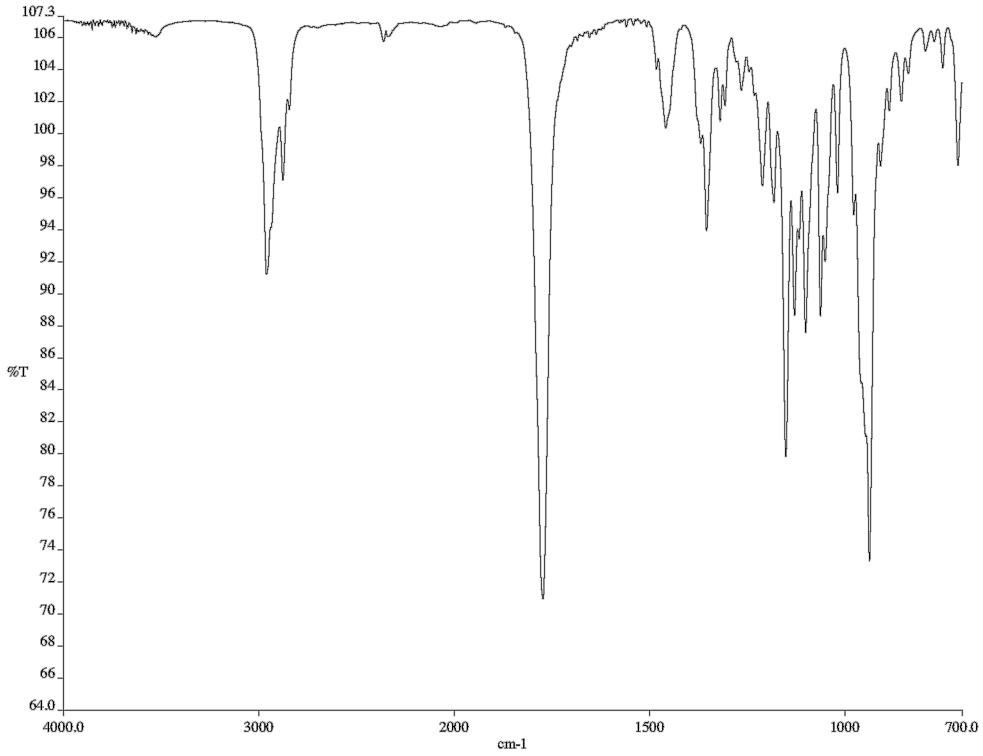


*Figure SI 77. Infrared spectrum (neat film/NaCl) of **42**.*

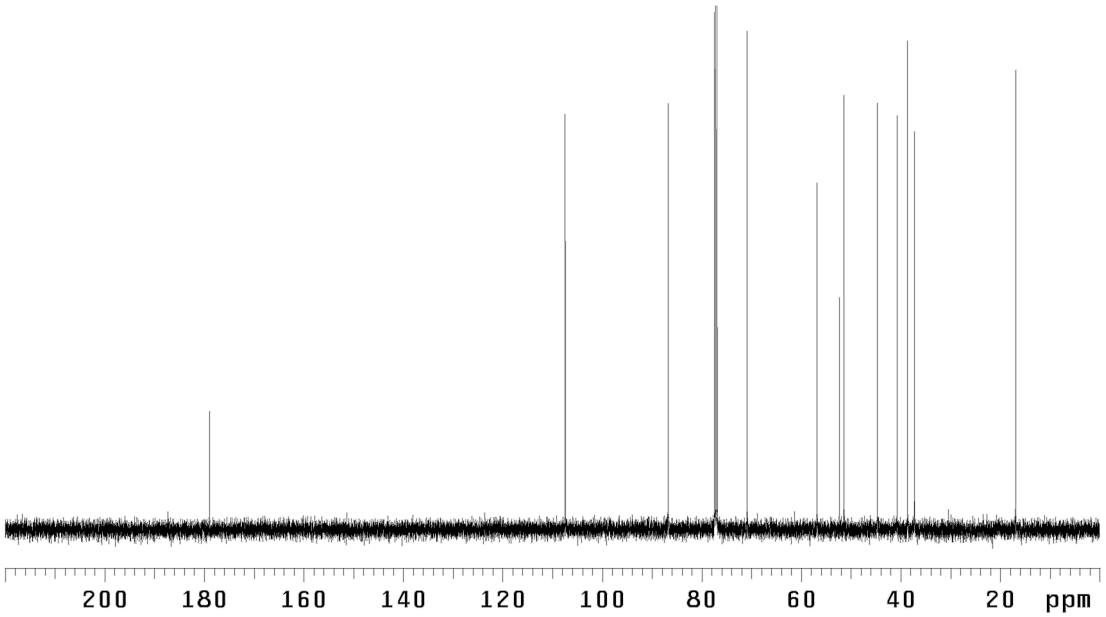


*Figure SI 78. ^{13}C NMR spectrum (126 MHz, $CDCl_3$) of **42**.*

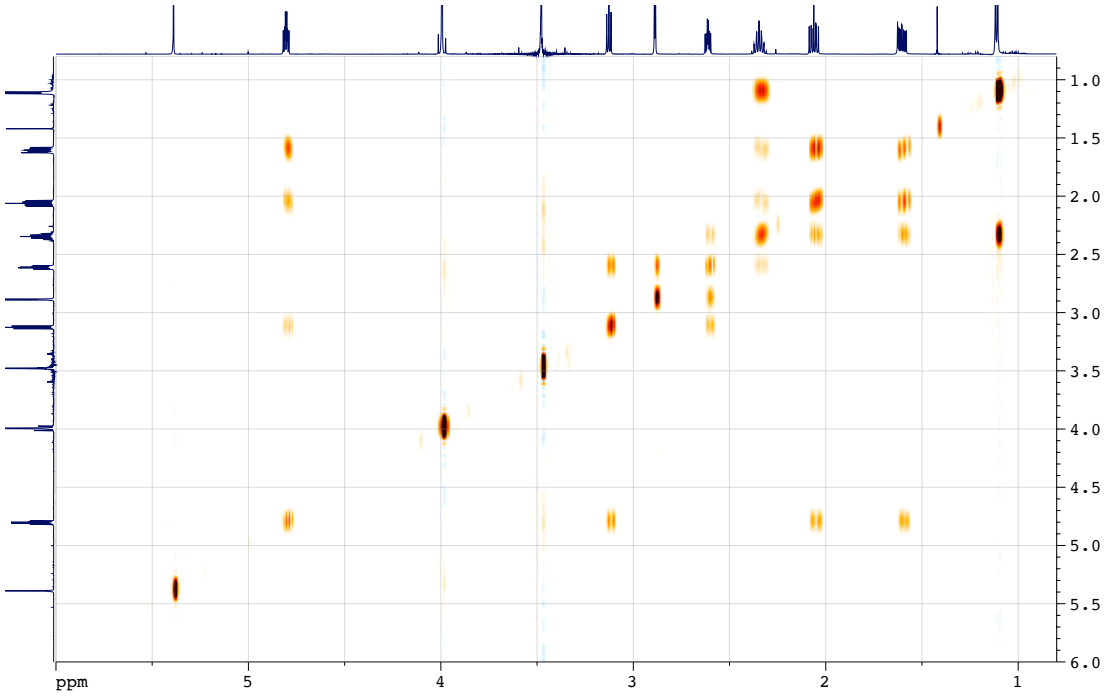


*Figure SI 79. gCOSY NMR spectrum (600 MHz, $CDCl_3$) of **42**.*

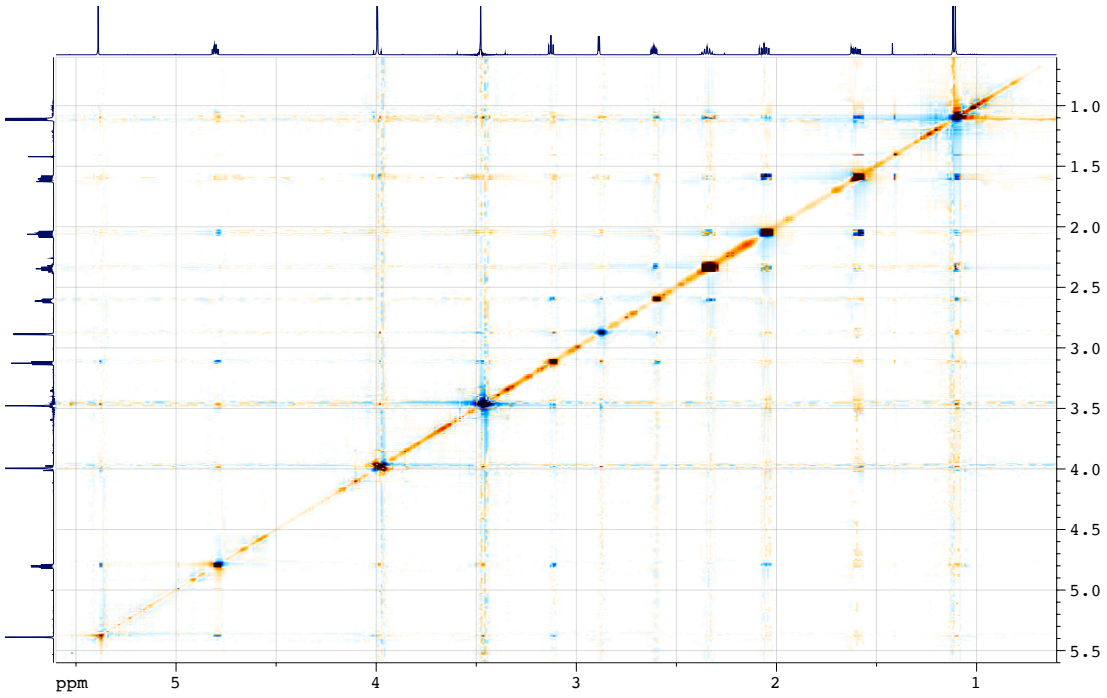


*Figure SI 80. NOESY-2D NMR spectrum (600 MHz, $CDCl_3$) of **42**.*

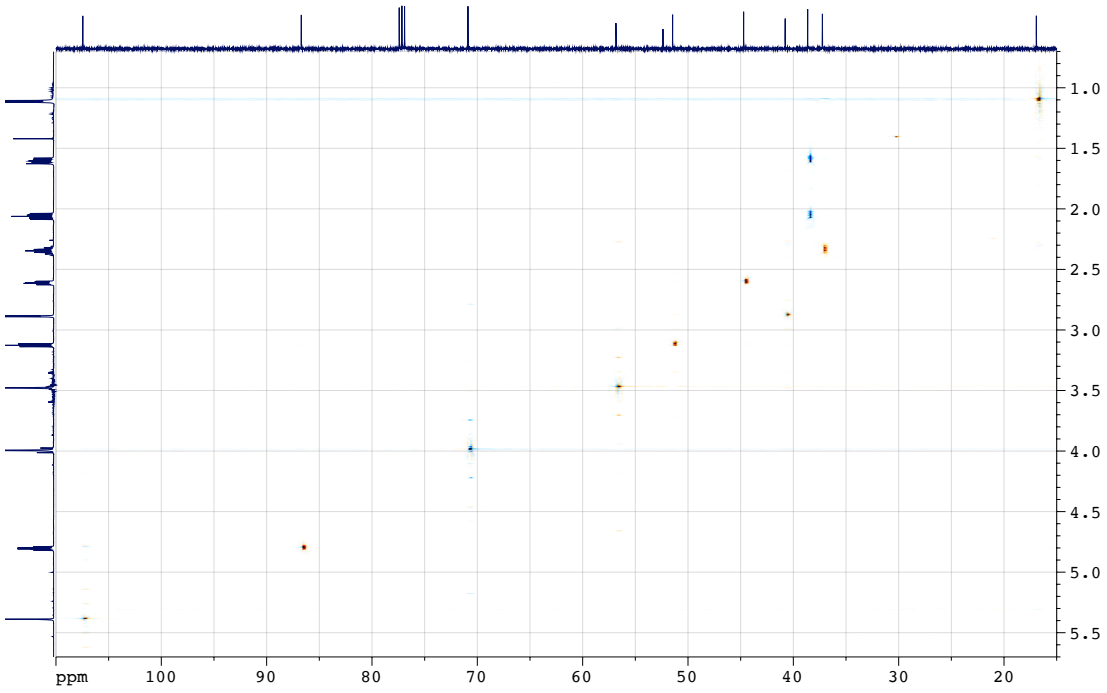


Figure SI 81. gHSQC NMR spectrum (600, 151 MHz, $CDCl_3$) of ***42****.*

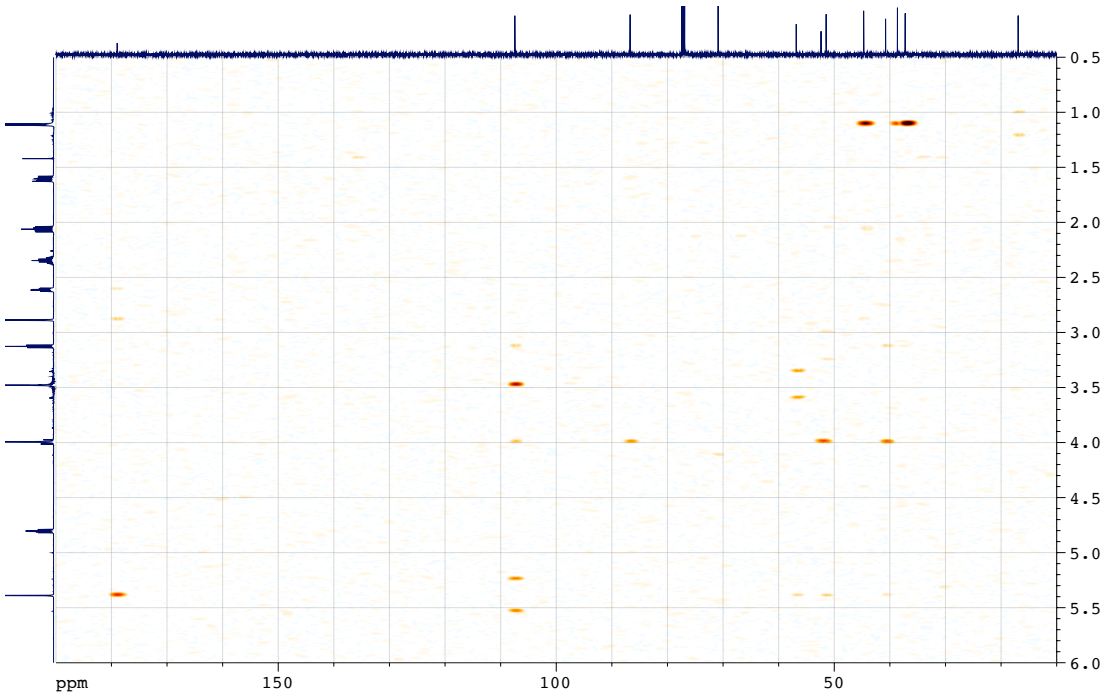


Figure SI 82. gHMBC NMR spectrum (600, 151 MHz, $CDCl_3$) of ***42****.*

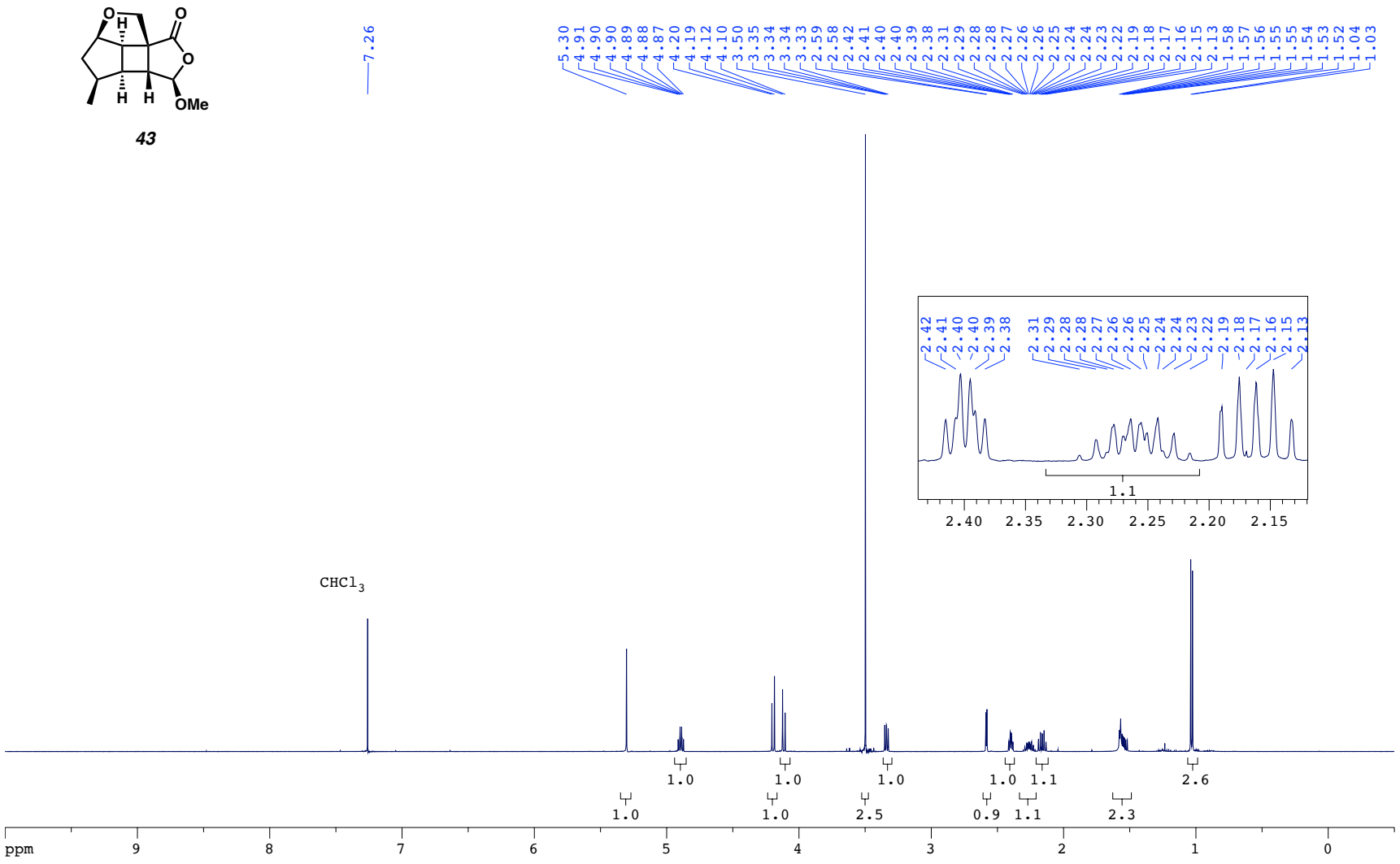


*Figure SI 83. ^{1}H NMR spectrum (600 MHz, $CDCl_3$) of **43**.*

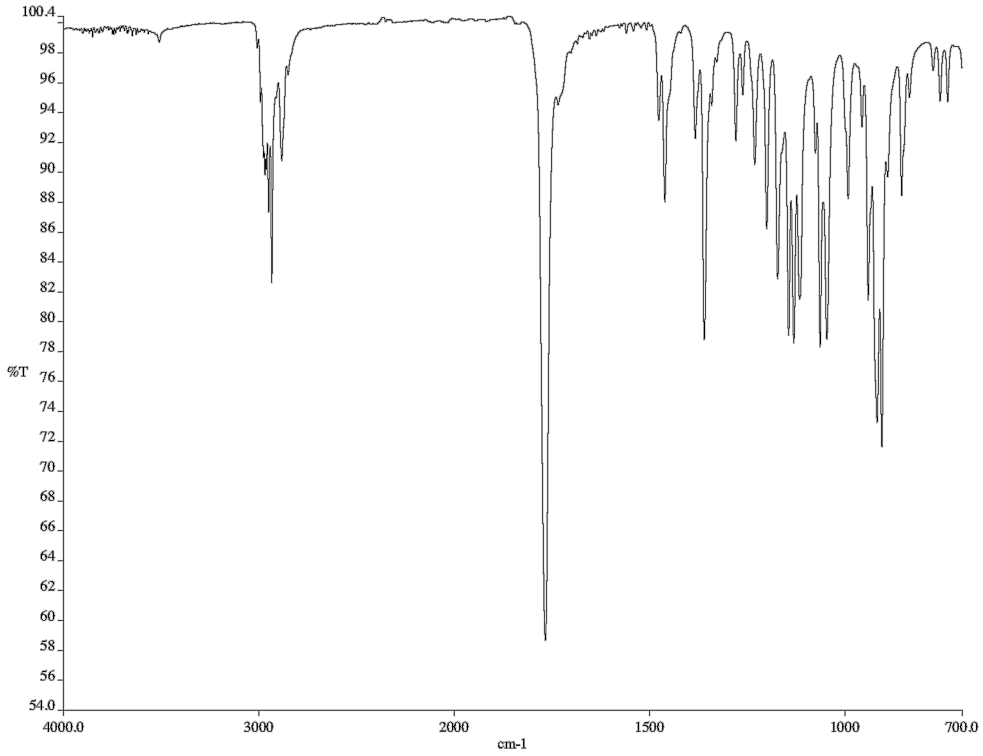


*Figure SI 84. Infrared spectrum (neat film/NaCl) of **43**.*

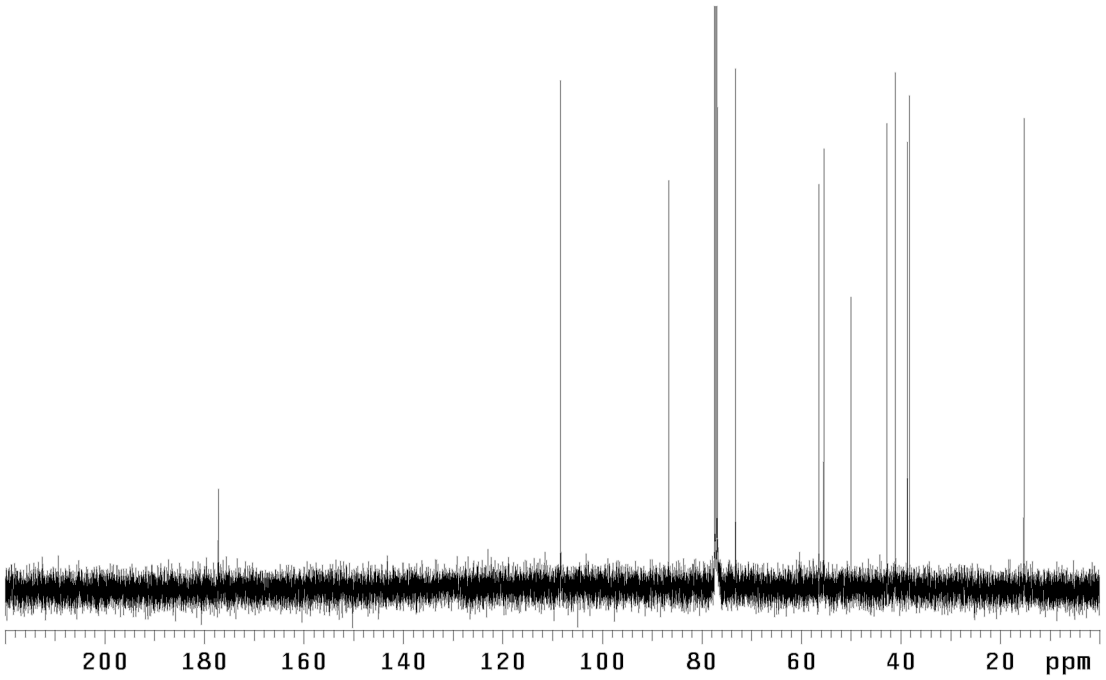


*Figure SI 85. ^{13}C NMR spectrum (126 MHz, $CDCl_3$) of **43**.*

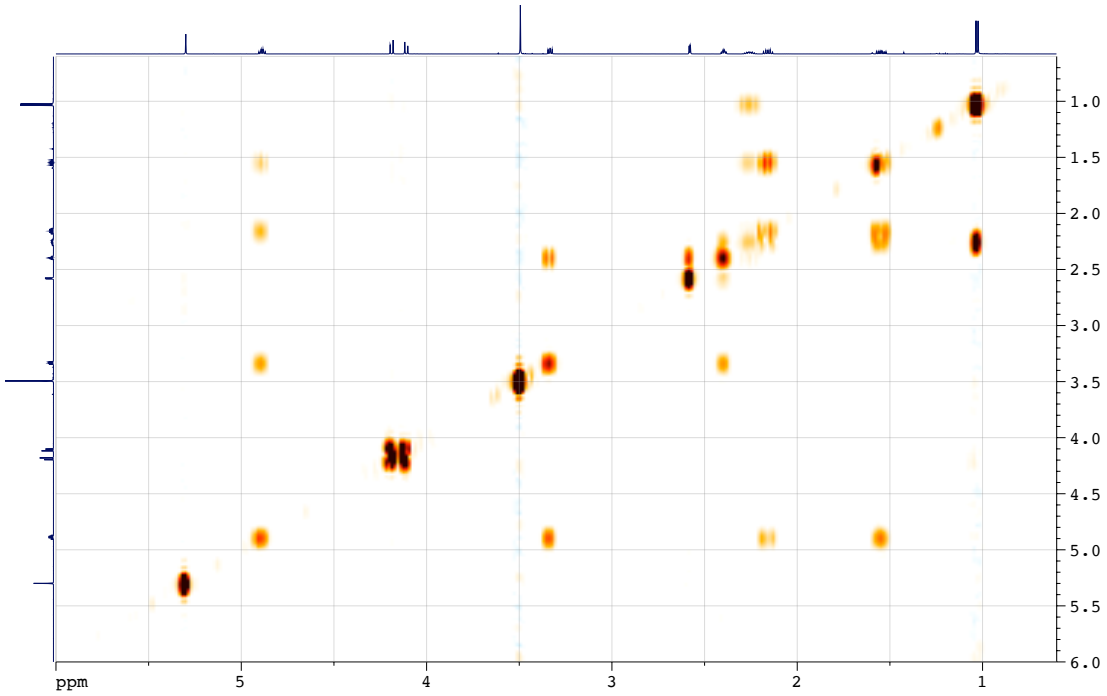


*Figure SI 86. NOESY-2D NMR spectrum (600 MHz, $CDCl_3$) of **43**.*

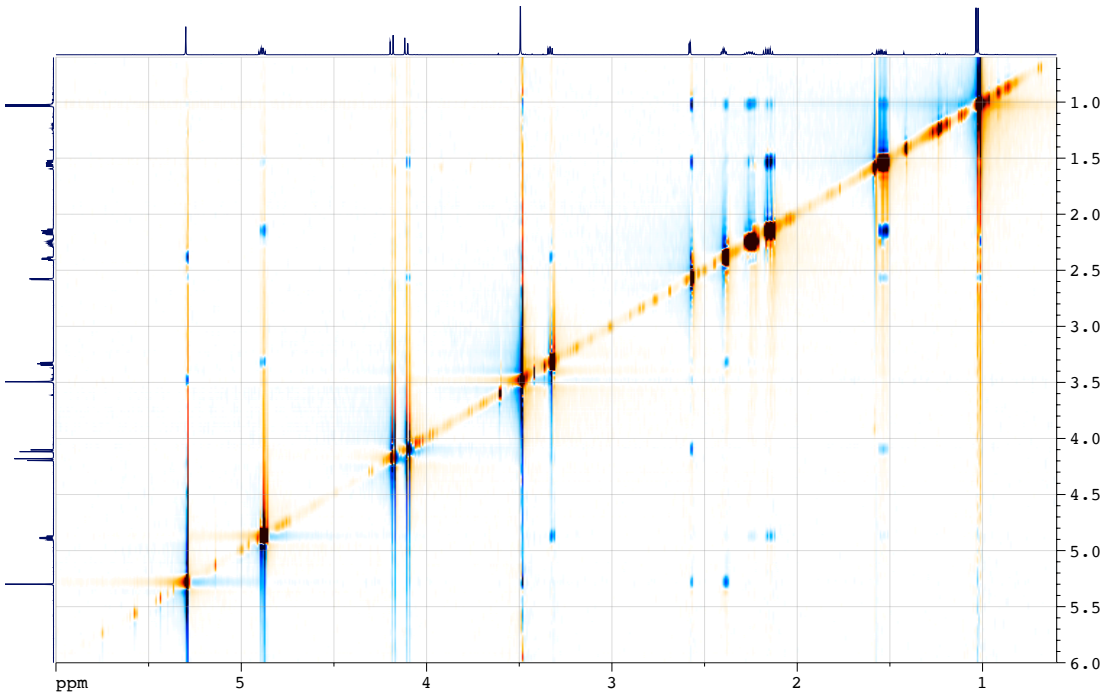


*Figure SI 87. NOESY-2D NMR spectrum (600 MHz, $CDCl_3$) of **43**.*

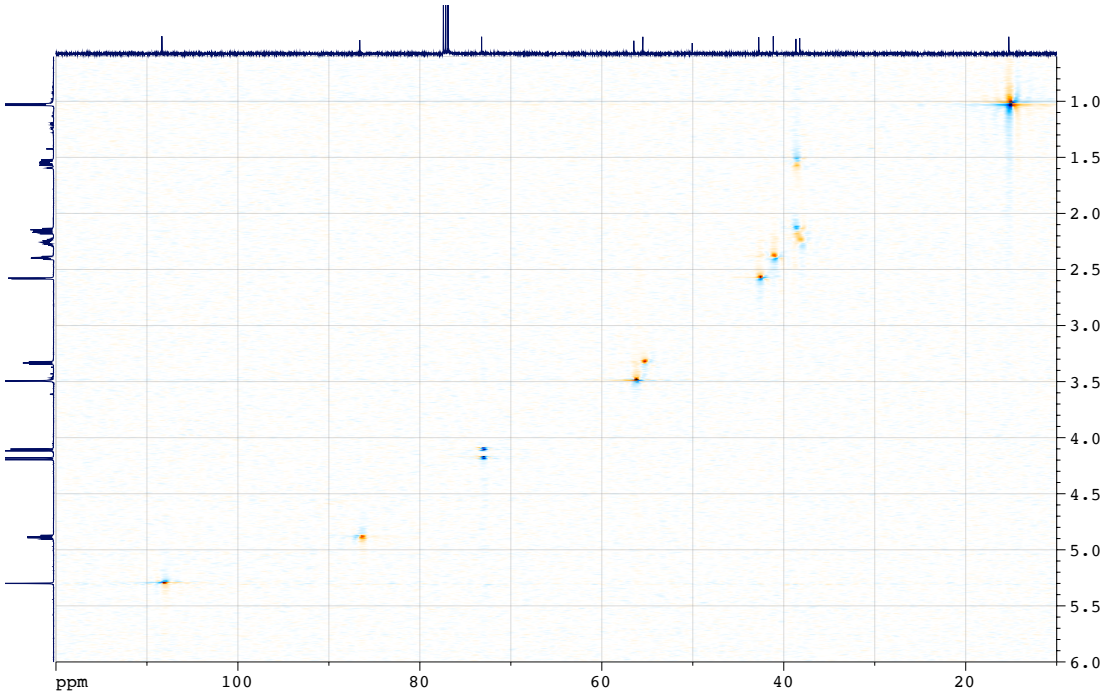


*Figure SI 88. gHSQC NMR spectrum (600, 151 MHz, $CDCl_3$) of **43**.*

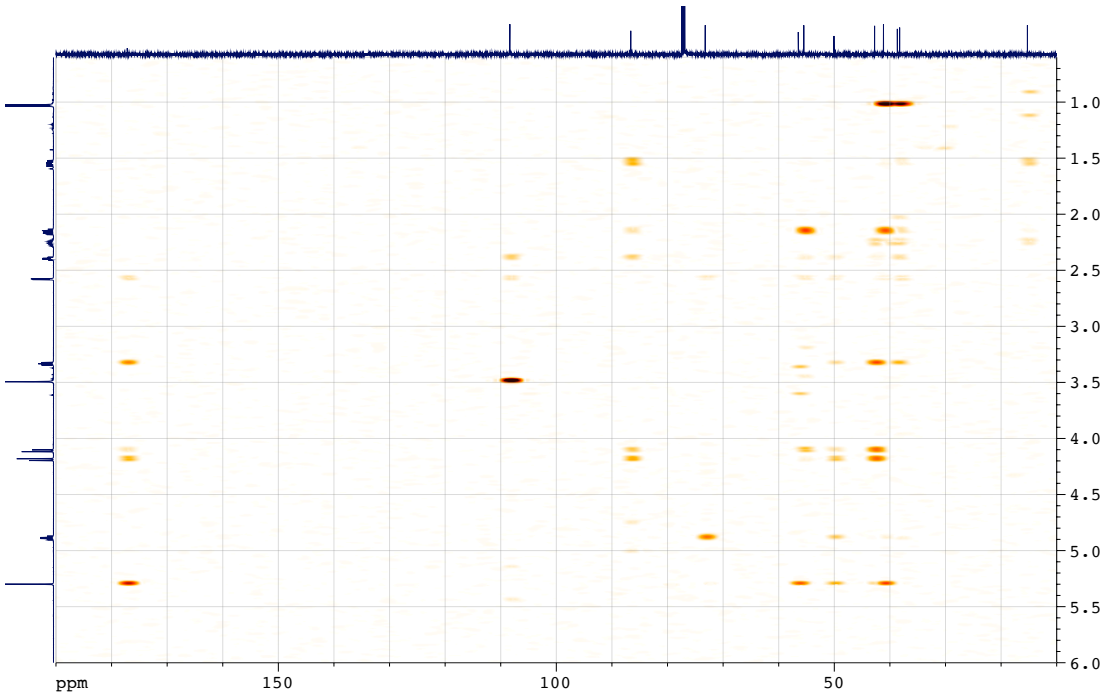


*Figure SI 89. gHMBC NMR spectrum (600, 151 MHz, $CDCl_3$) of **43**.*

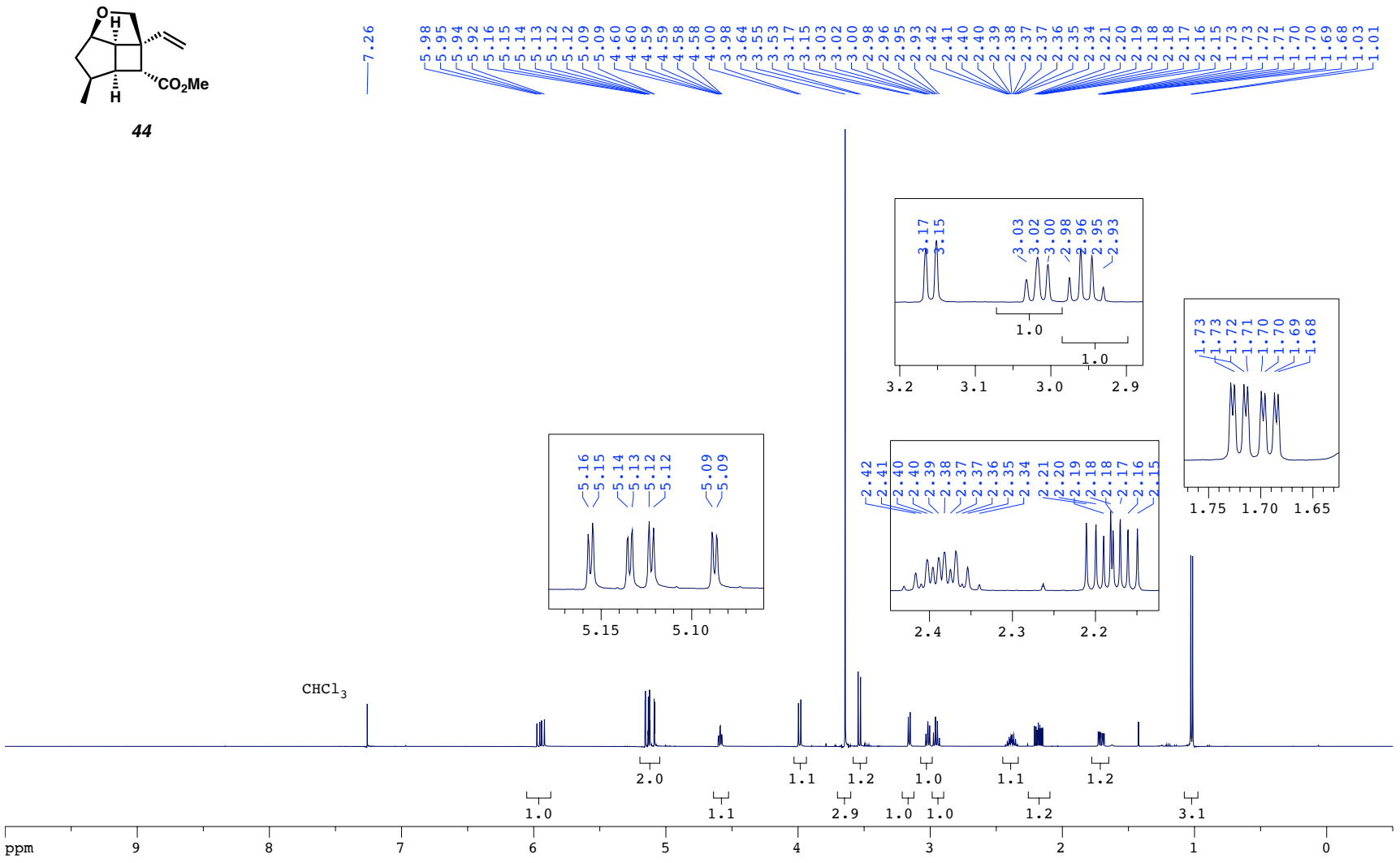


*Figure SI 90. ^{1}H NMR spectrum (500 MHz, $CDCl_3$) of **44**.*

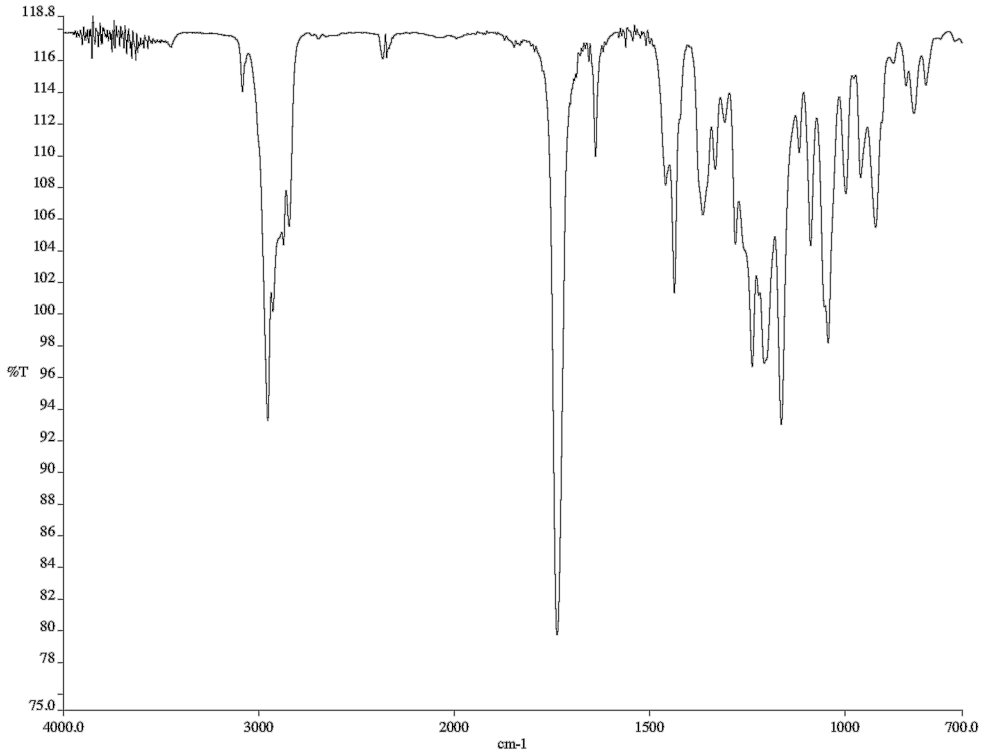


*Figure SI 91. Infrared spectrum (neat film/NaCl) of **44**.*

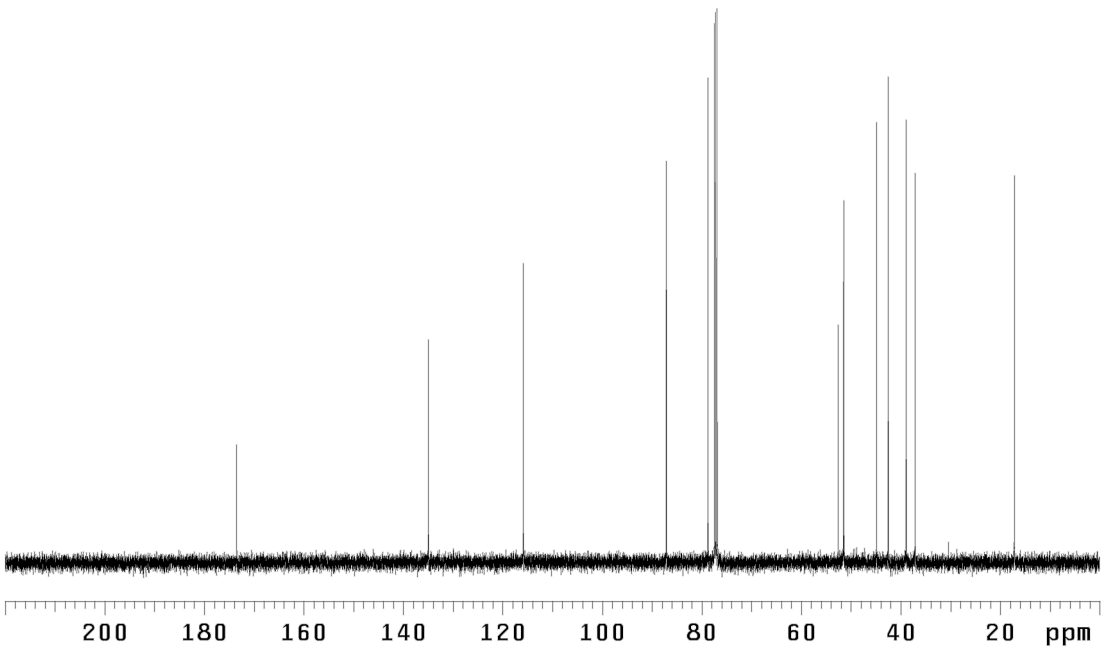


*Figure SI 92. ^{13}C NMR spectrum (126 MHz, $CDCl_3$) of **44**.*

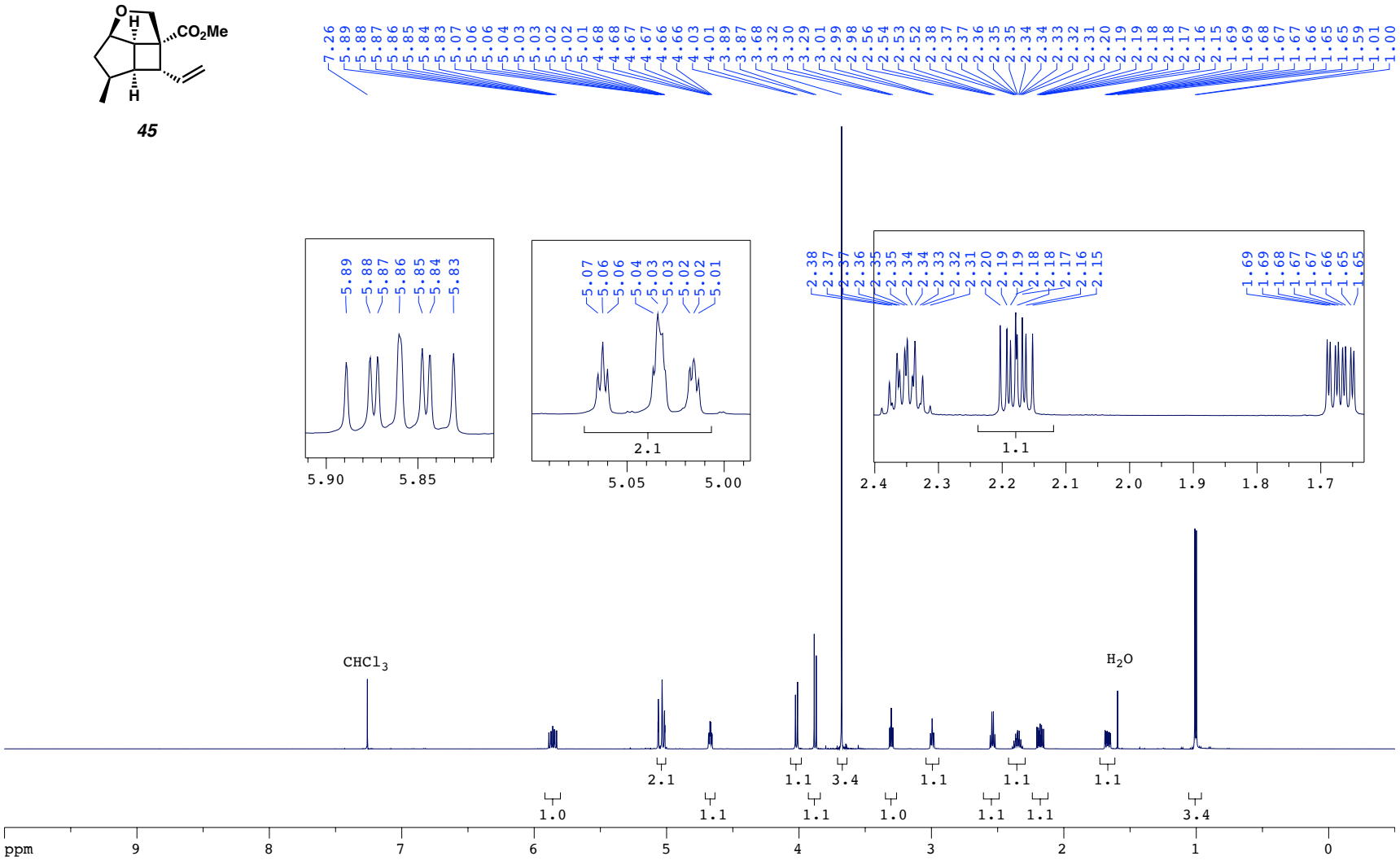


*Figure SI 93. ^{1}H NMR spectrum (500 MHz, $CDCl_3$) of **45**.*

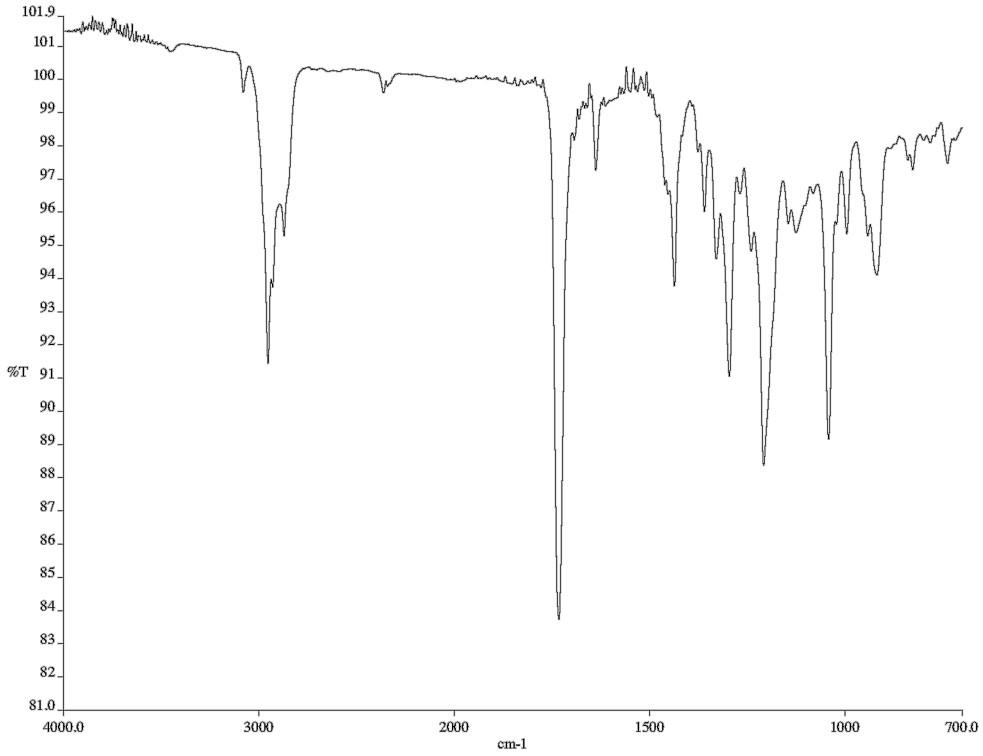


*Figure SI 94. Infrared spectrum (neat film/NaCl) of **45**.*

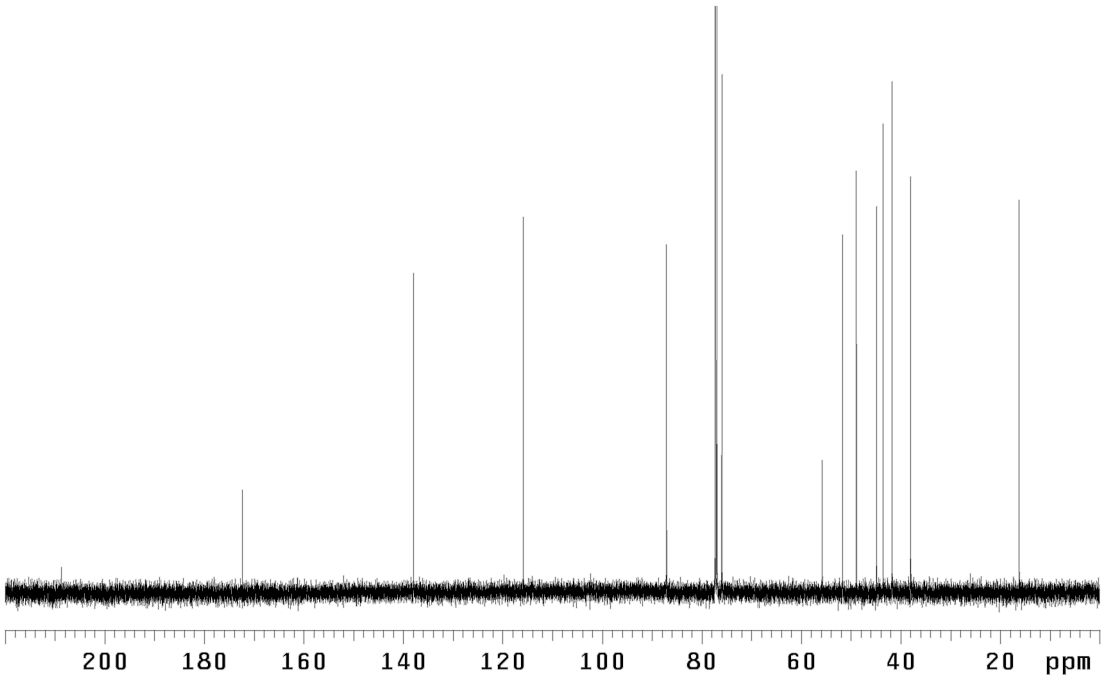


*Figure SI 95. ^{13}C NMR spectrum (126 MHz, $CDCl_3$) of **45**.*

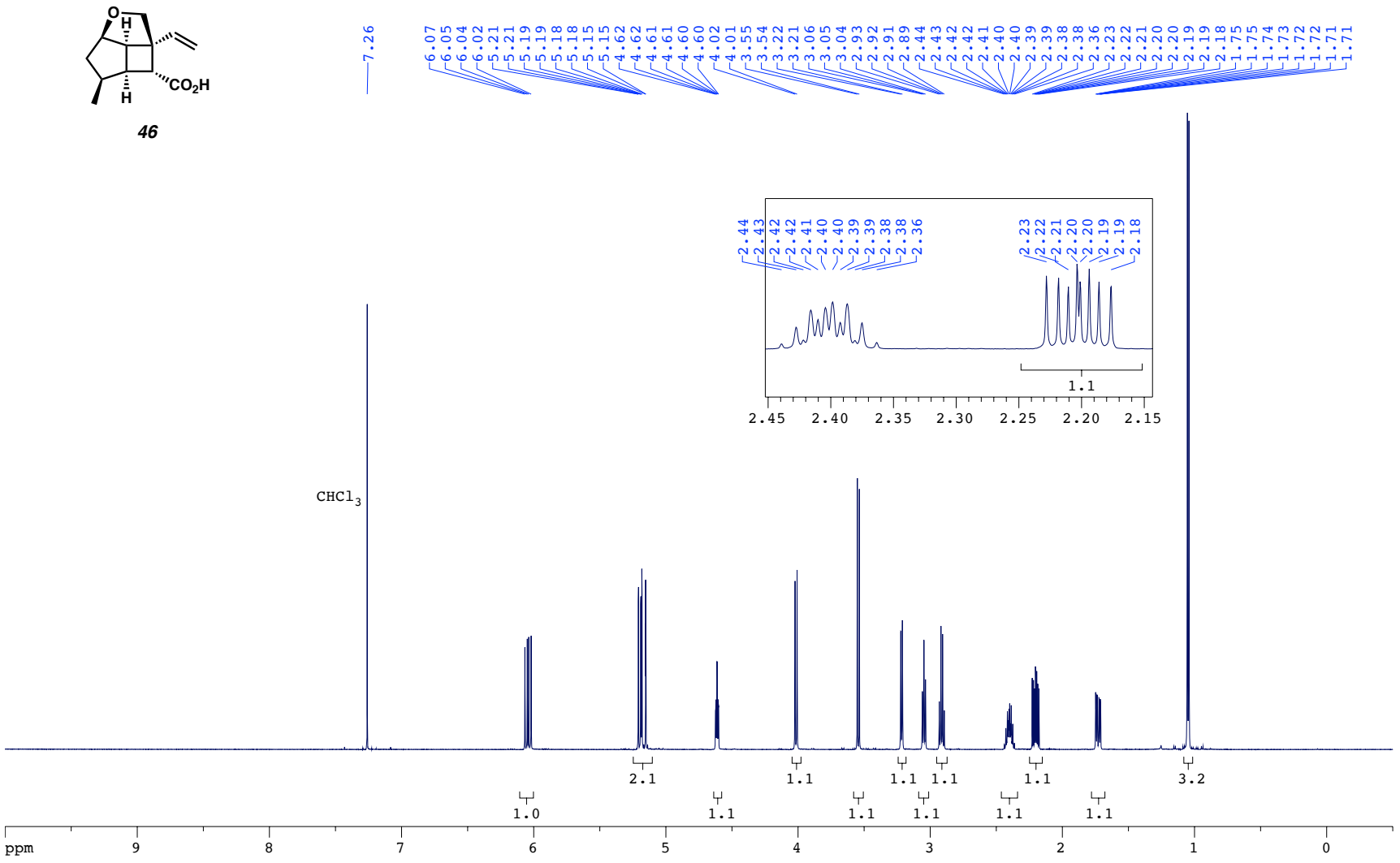


*Figure SI 96. ^{1}H NMR spectrum (600 MHz, $CDCl_3$) of **46**.*

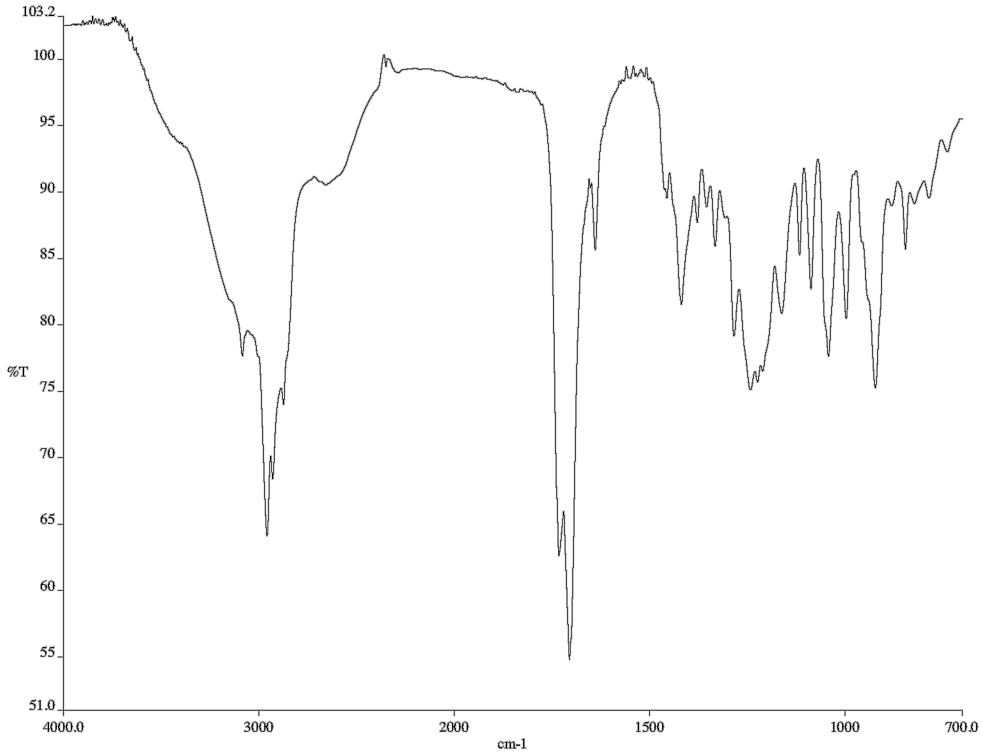


*Figure SI 97. Infrared spectrum (neat film/NaCl) of **46**.*

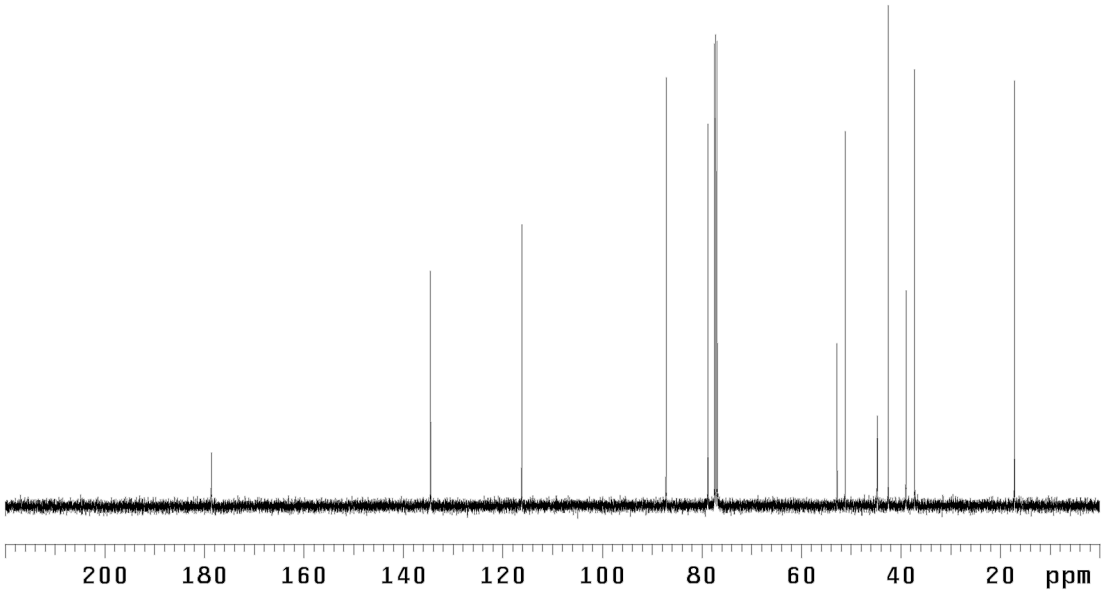


*Figure SI 98. ^{13}C NMR spectrum (126 MHz, $CDCl_3$) of **46**.*

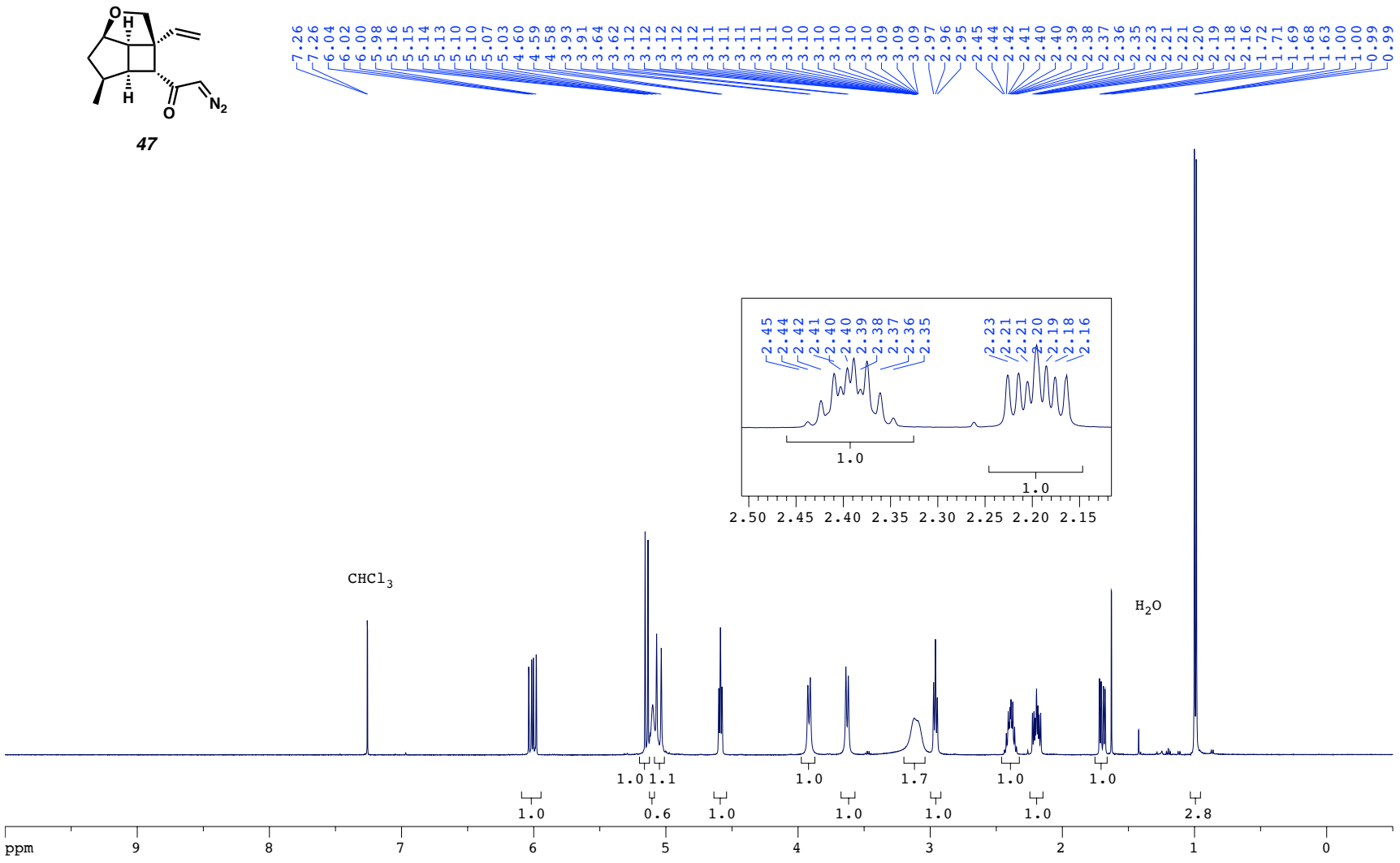


*Figure SI 99. ^{1}H NMR spectrum (500 MHz, $CDCl_3$) of **47**.*

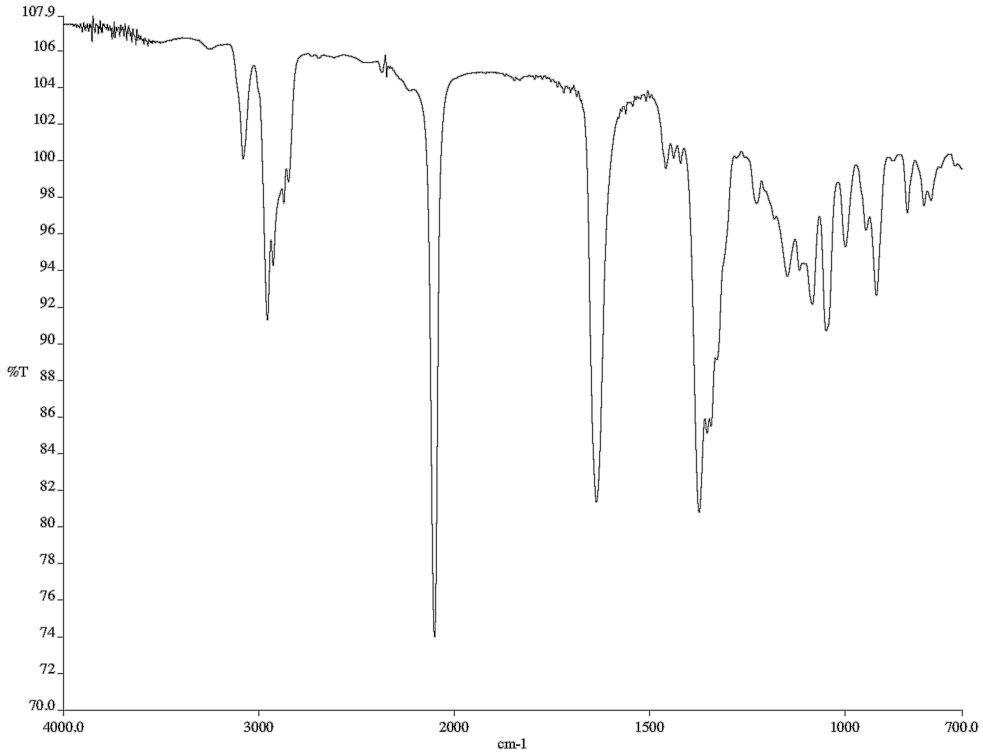


*Figure SI 100. Infrared spectrum (neat film/NaCl) of **47**.*

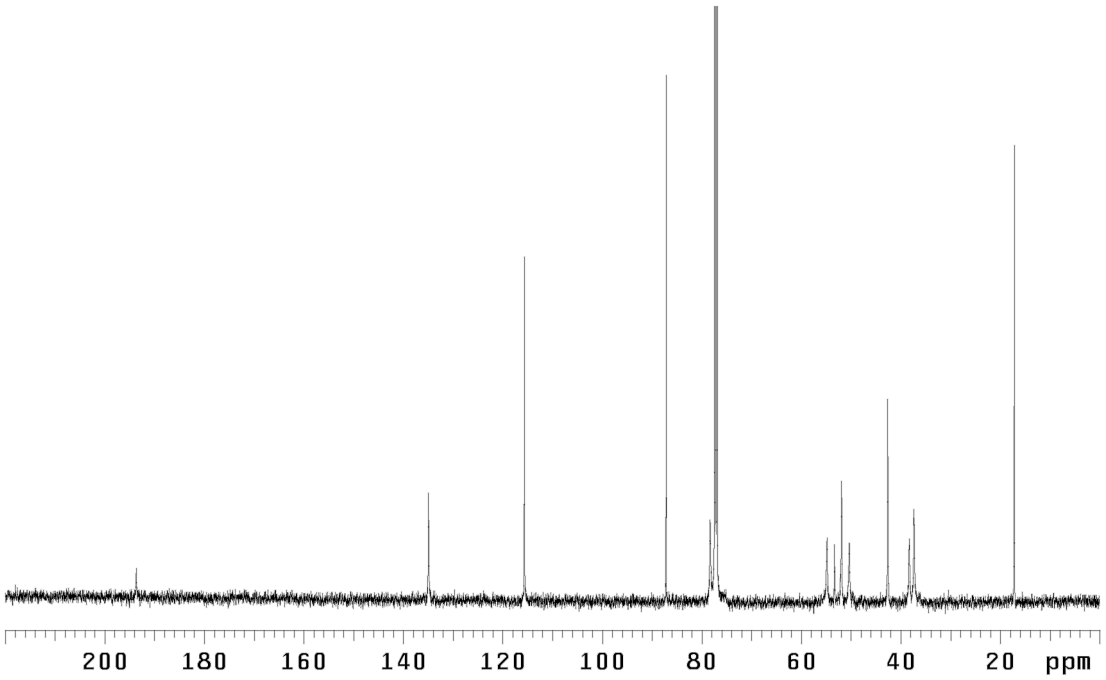


*Figure SI 101. ^{13}C NMR spectrum (126 MHz, $CDCl_3$) of **47**.*

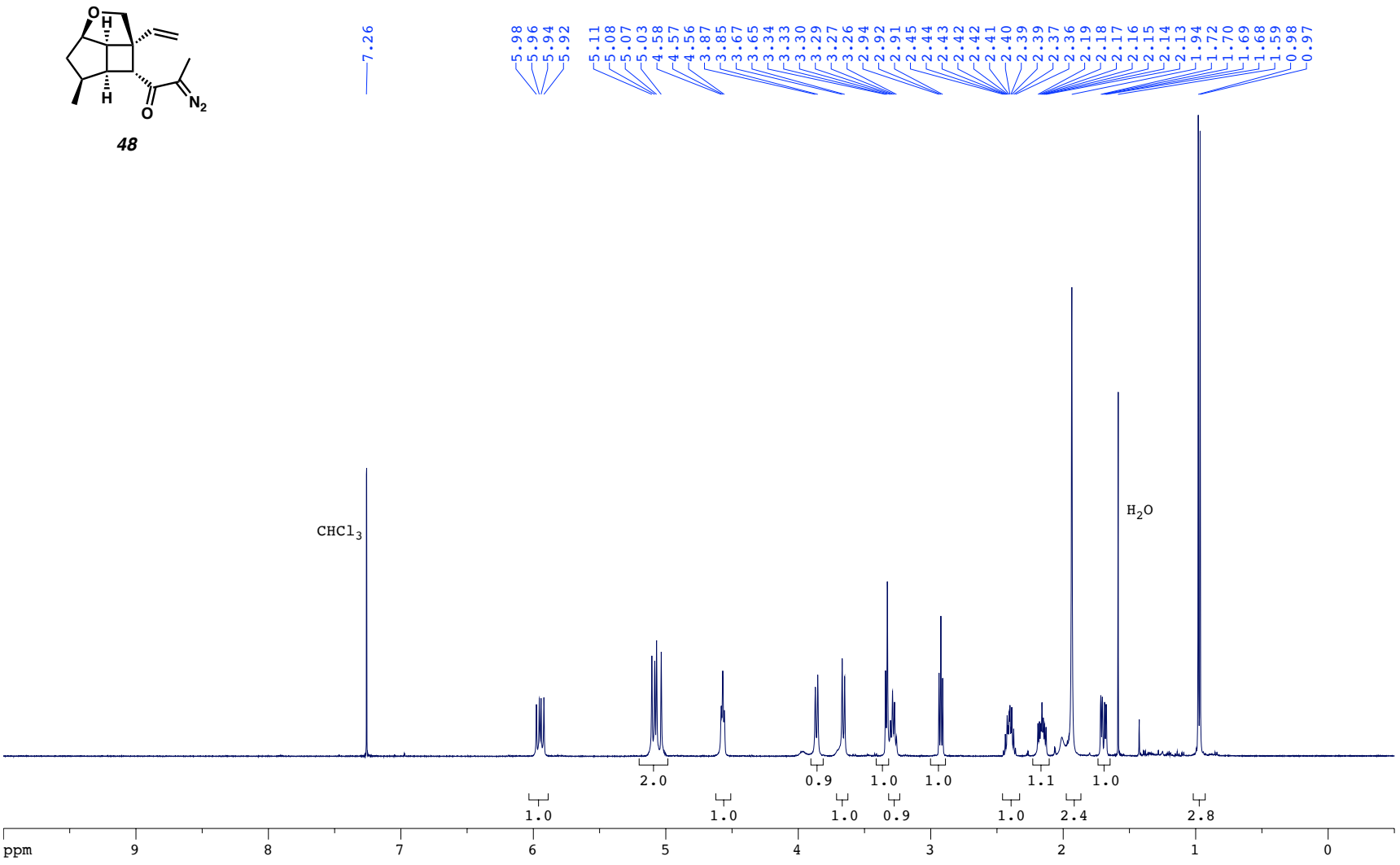


*Figure SI 102. ^{1}H NMR spectrum (500 MHz, $CDCl_3$) of **48**.*

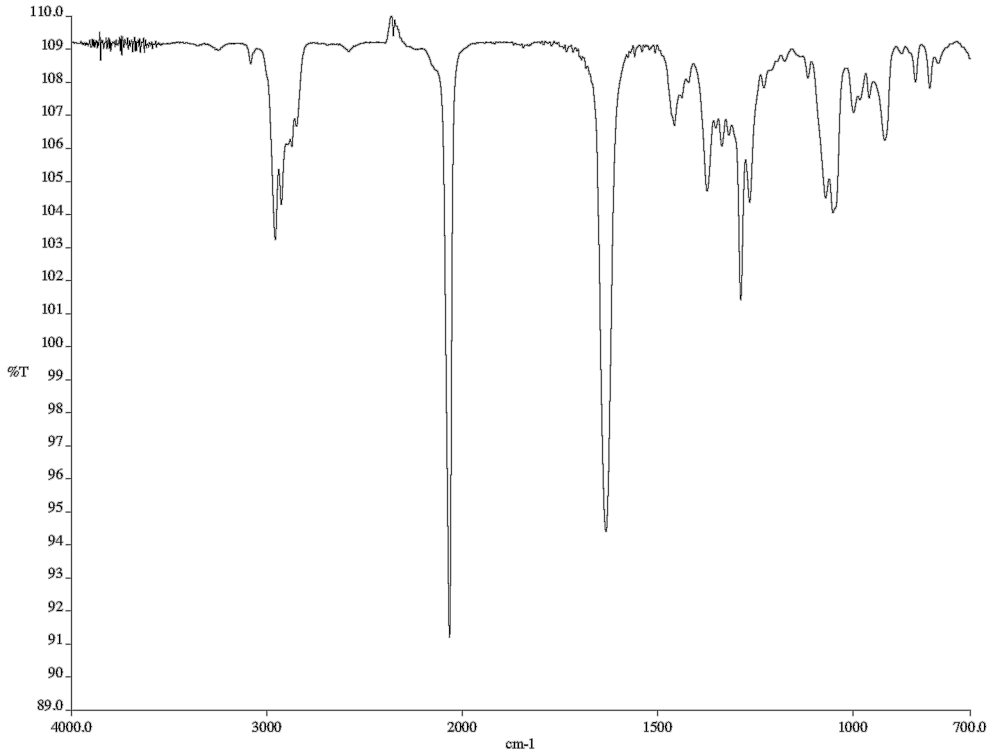


*Figure SI 103. Infrared spectrum (neat film/NaCl) of **48**.*

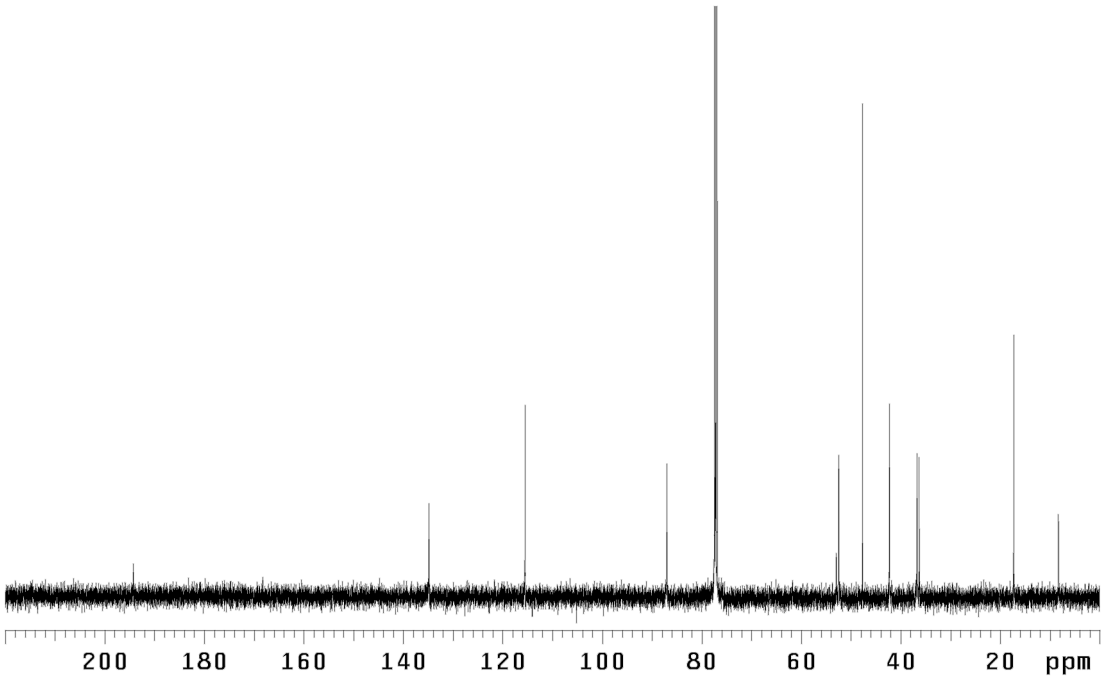


*Figure SI 104. ^{13}C NMR spectrum (126 MHz, $CDCl_3$) of **48**.*

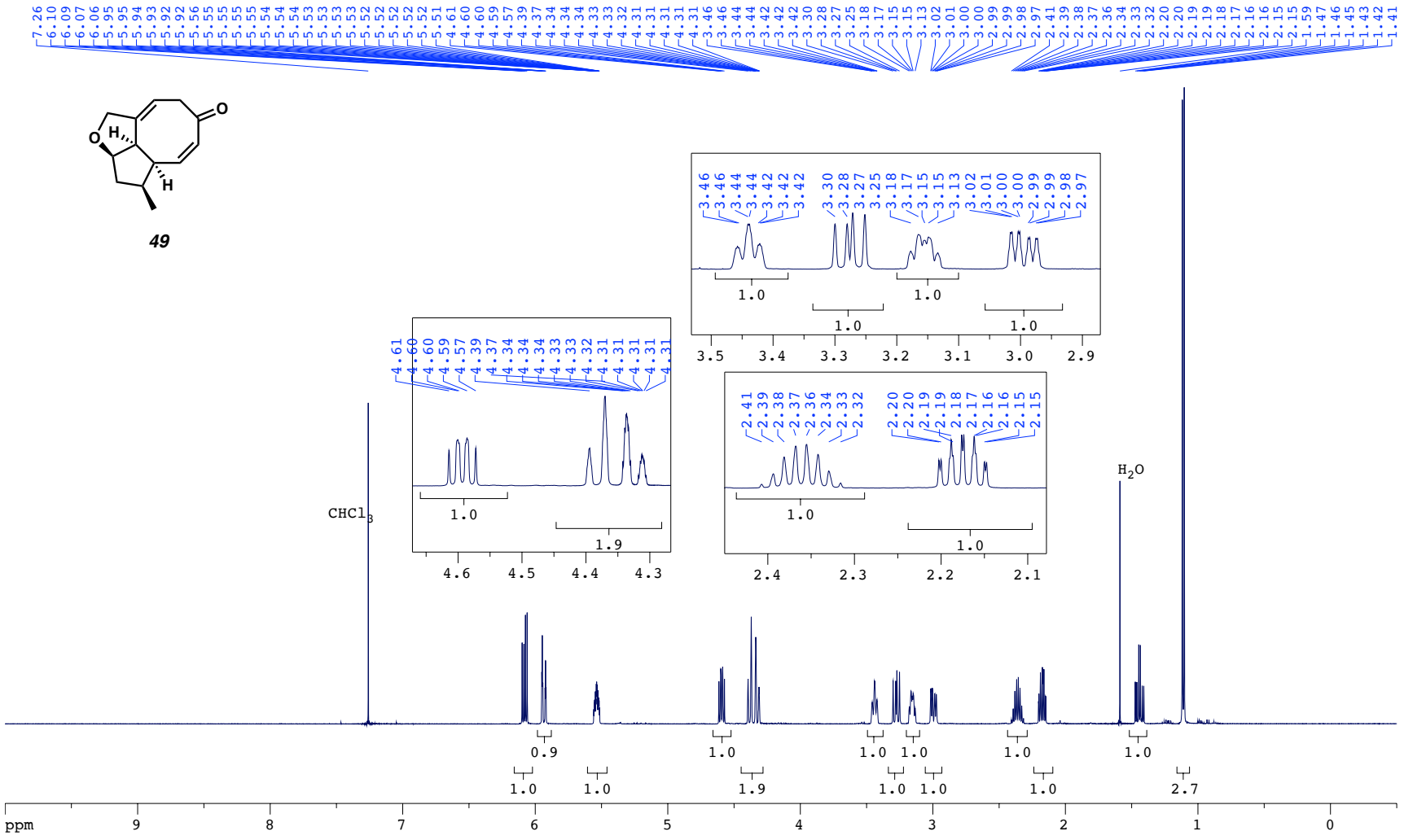


*Figure SI 105. ^{1}H NMR spectrum (500 MHz, $CDCl_3$) of **49**.*

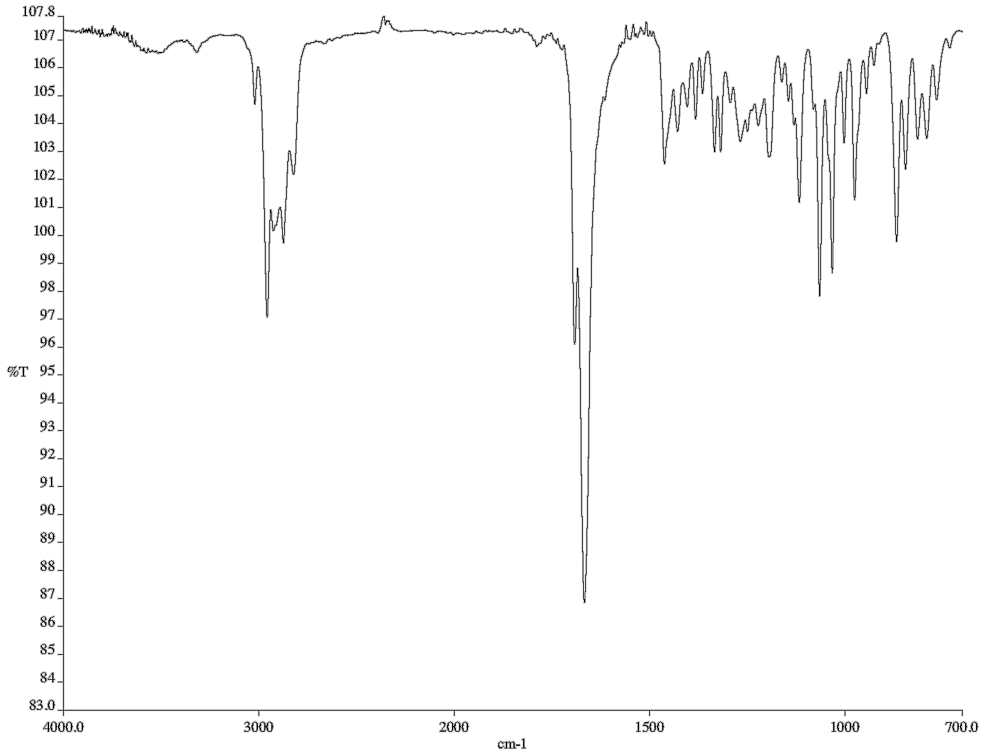


*Figure SI 106. Infrared spectrum (neat film/NaCl) of **49**.*

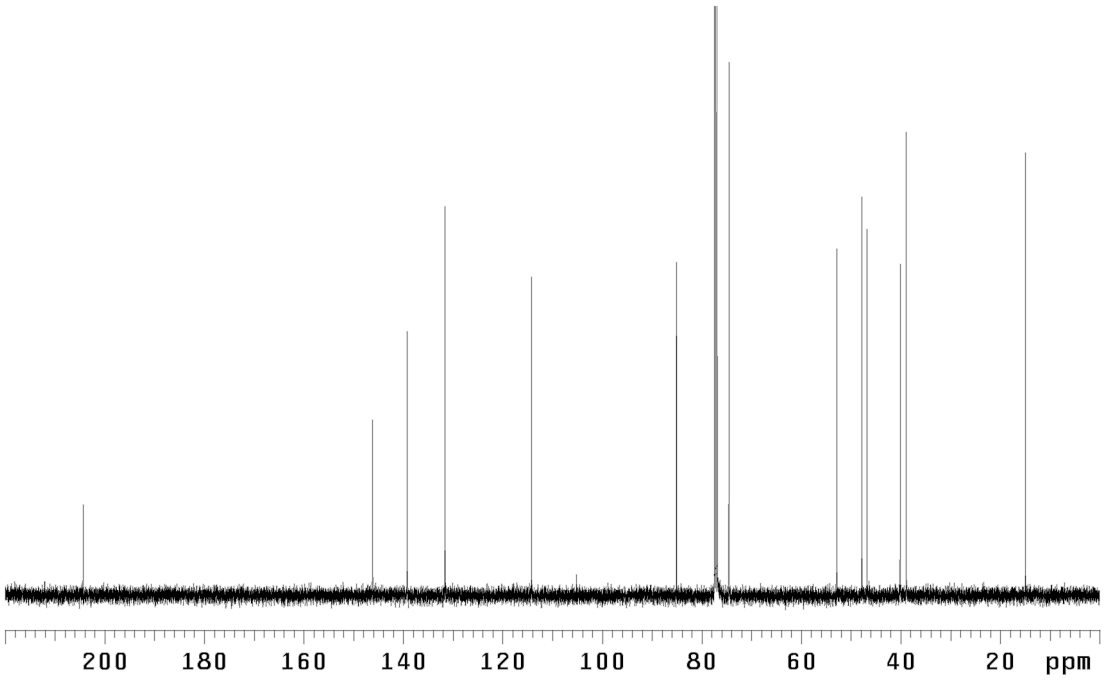


*Figure SI 107. ^{13}C NMR spectrum (126 MHz, $CDCl_3$) of **49**.*

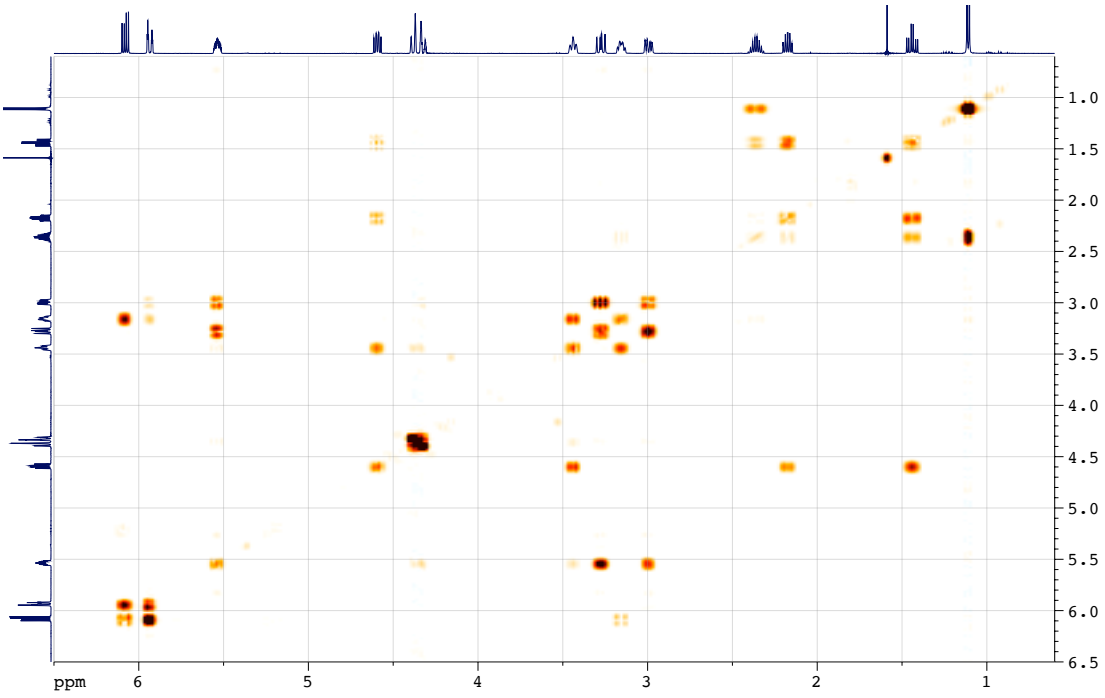


*Figure SI 108. gCOSY NMR spectrum (500 MHz, $CDCl_3$) of **49**.*

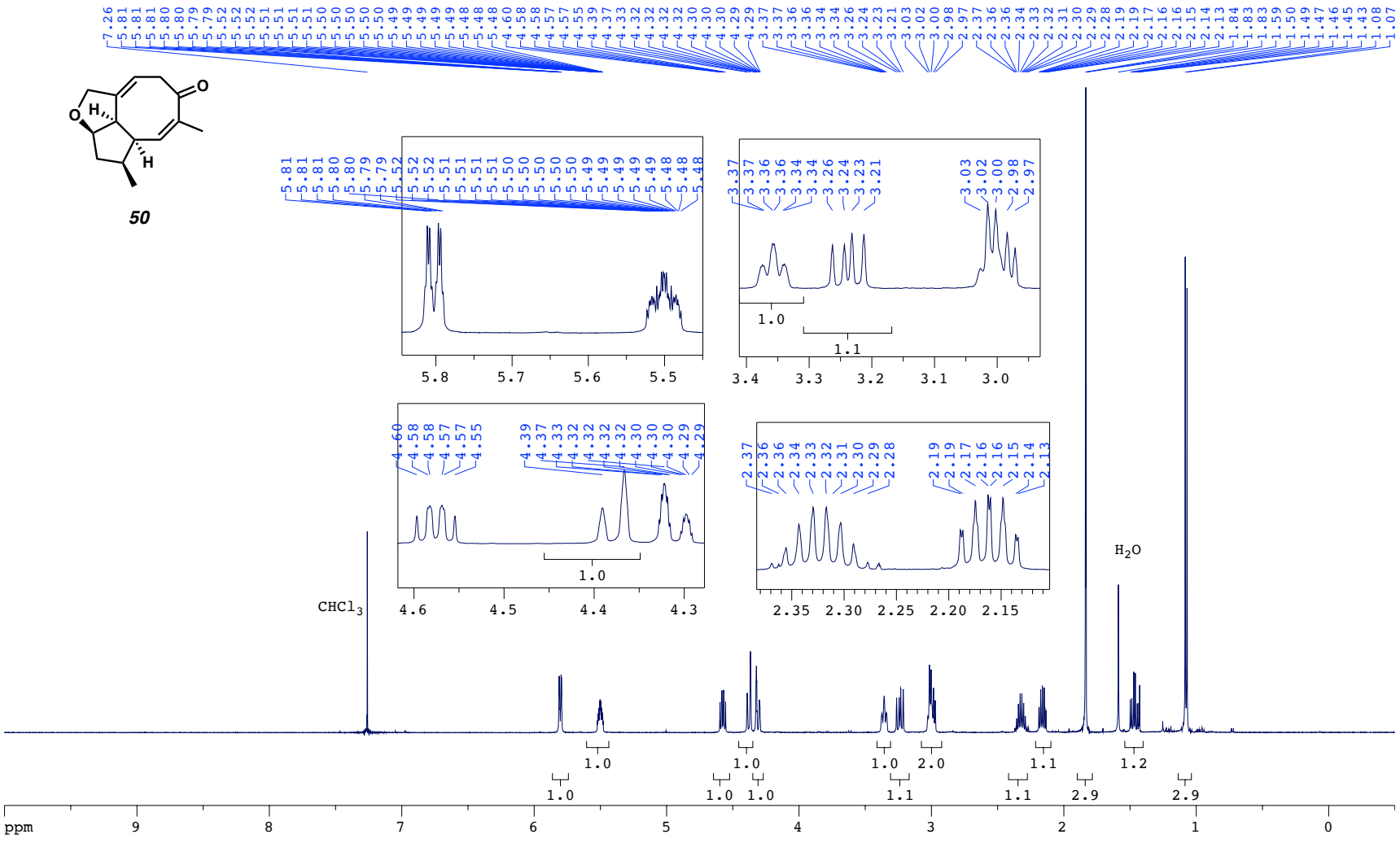


*Figure SI 109. ^{1}H NMR spectrum (600 MHz, $CDCl_3$) of **50**.*

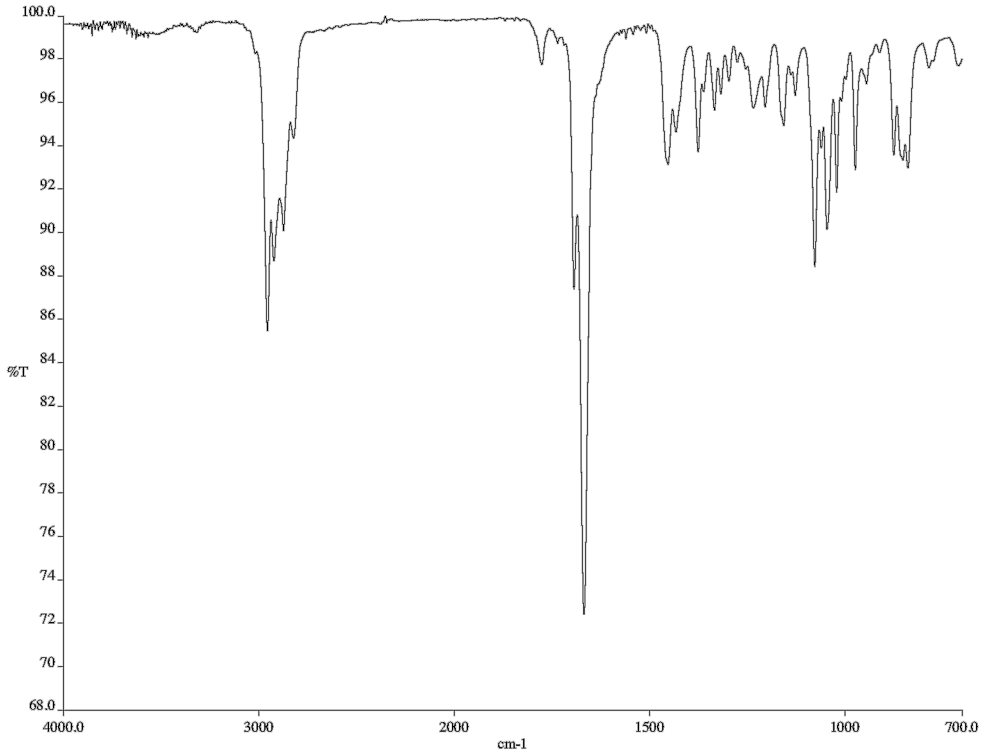


*Figure SI 110. Infrared spectrum (neat film/NaCl) of **50**.*

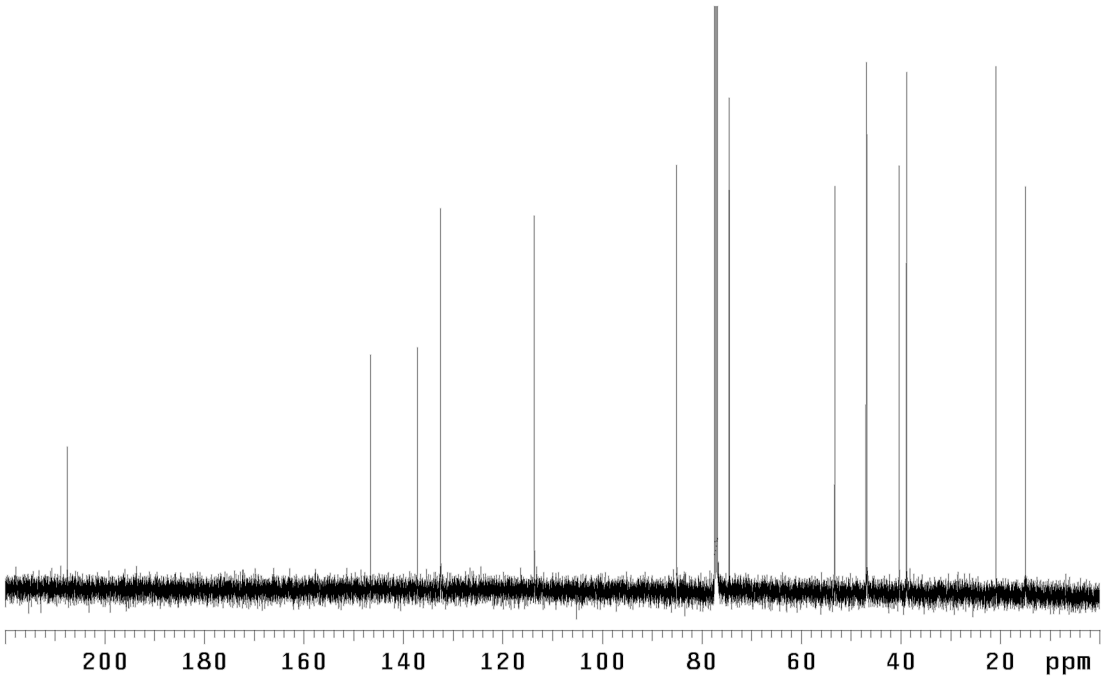


*Figure SI 111. ^{13}C NMR spectrum (126 MHz, $CDCl_3$) of **50**.*

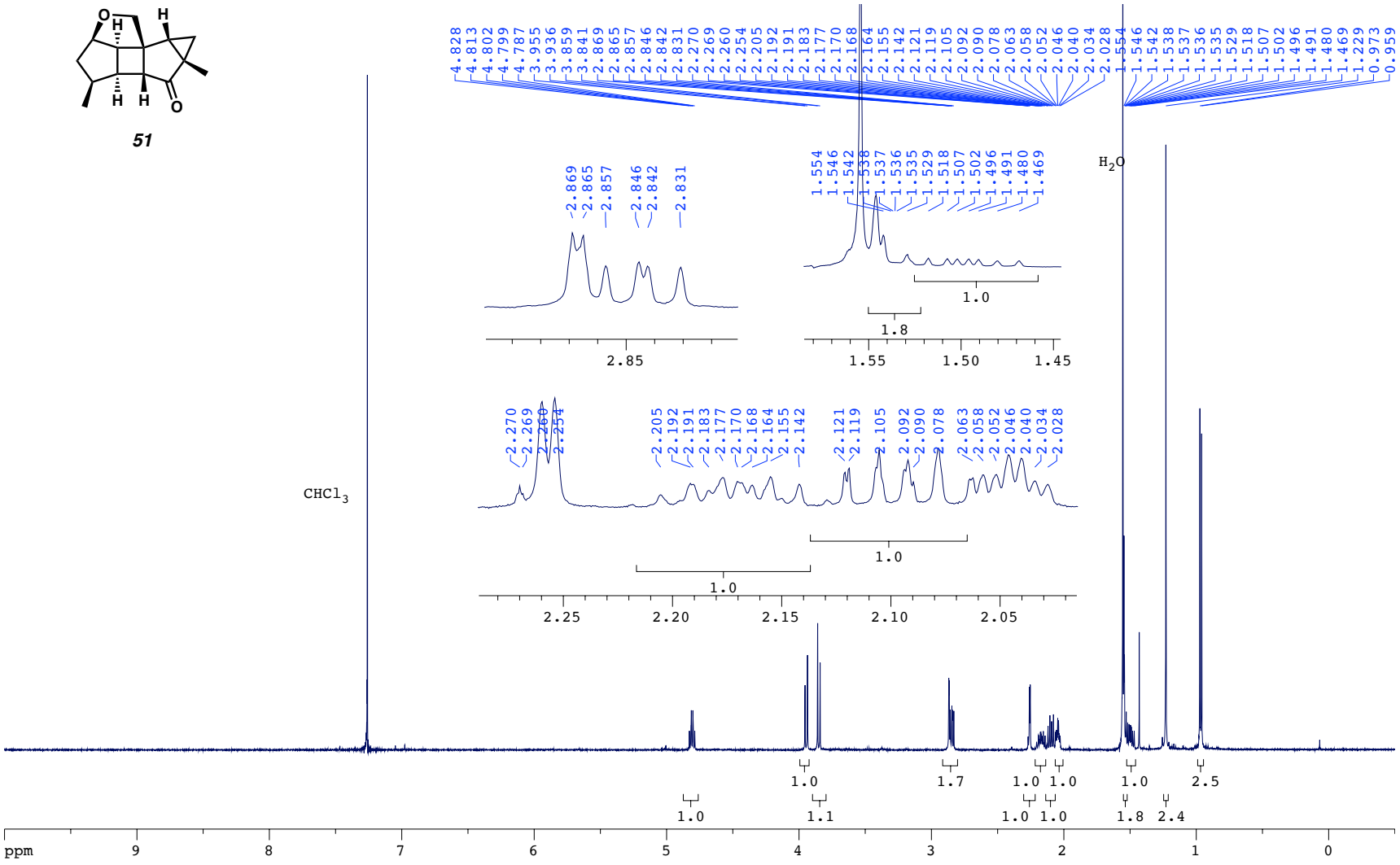


*Figure SI 112. ^{1}H NMR spectrum (500 MHz, $CDCl_3$) of **51**.*

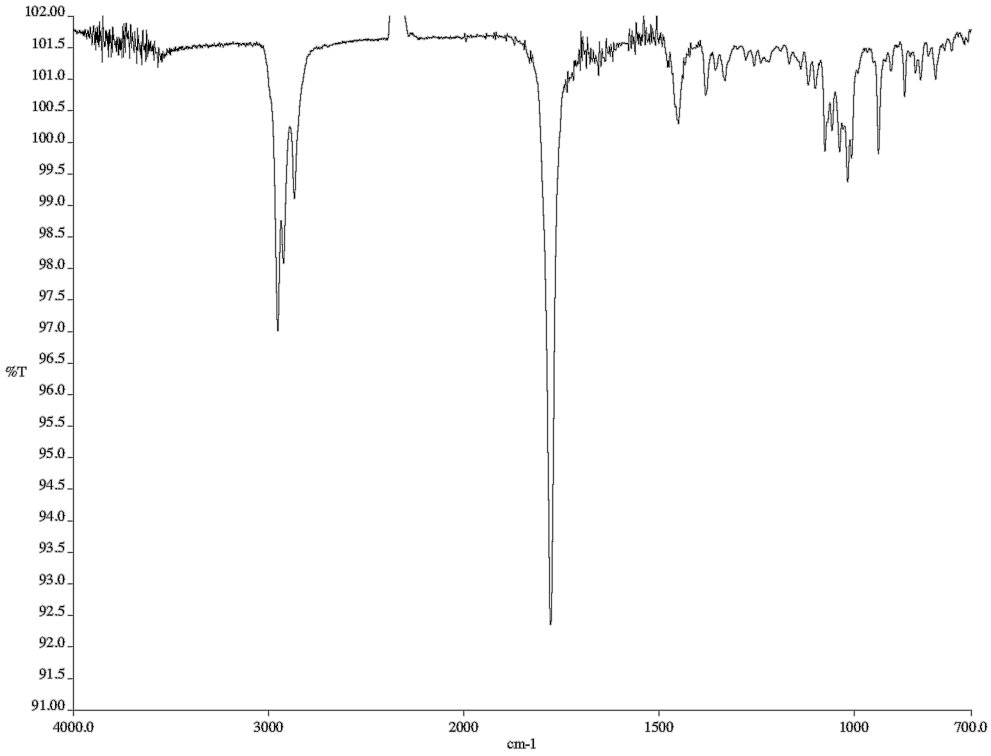


*Figure SI 113. Infrared spectrum (neat film/NaCl) of **51**.*

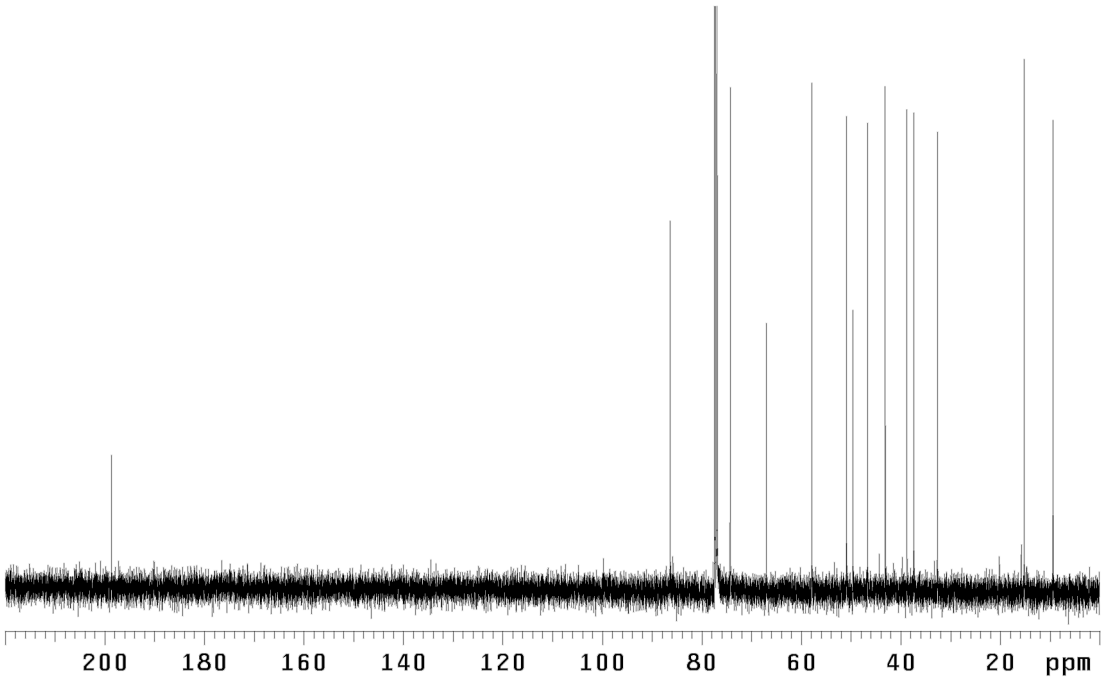


*Figure SI 114. ^{13}C NMR spectrum (126 MHz, $CDCl_3$) of **51**.*

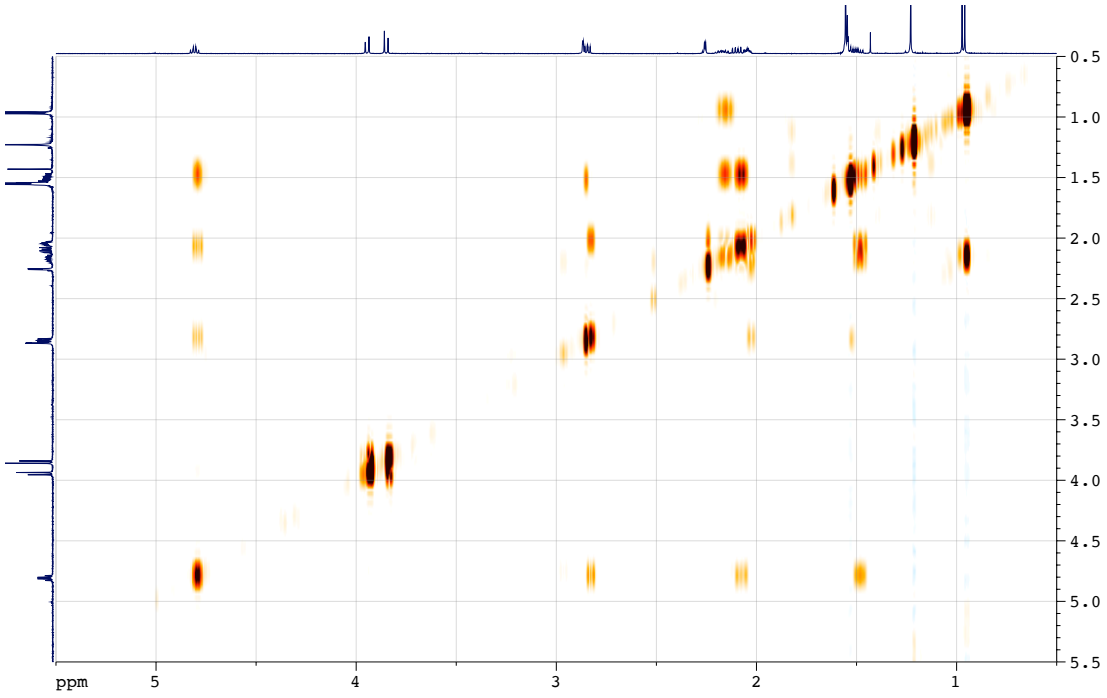


*Figure SI 115. gCOSY NMR spectrum (600 MHz, $CDCl_3$) of **51**.*

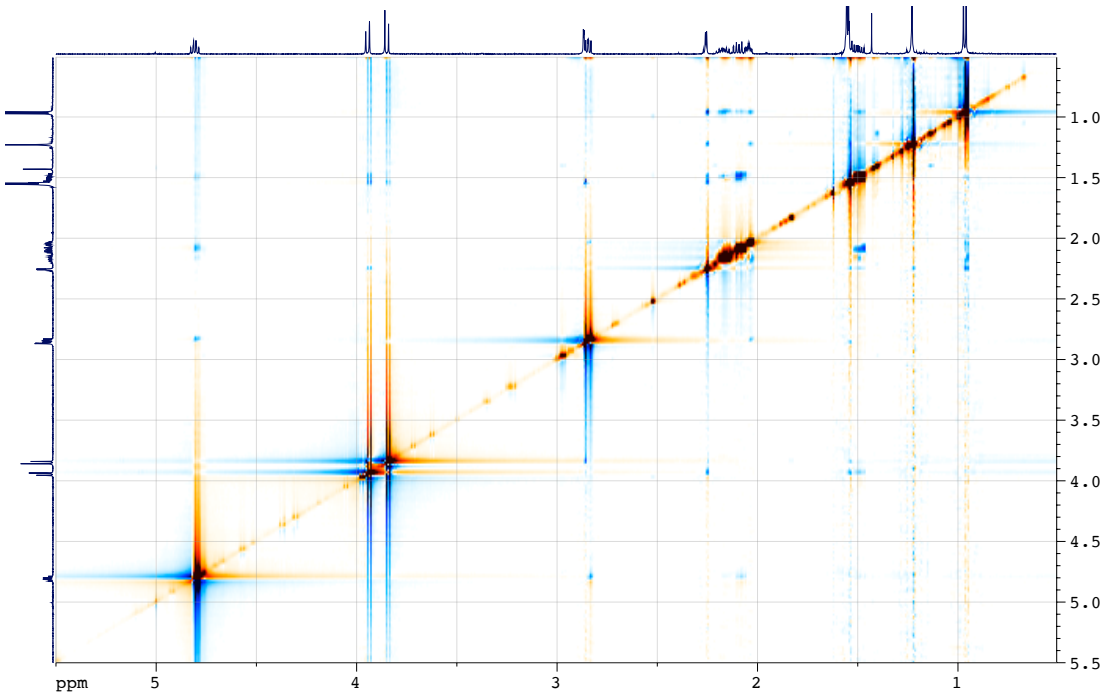


*Figure SI 116. NOESY-2D NMR spectrum (600 MHz, $CDCl_3$) of **51**.*

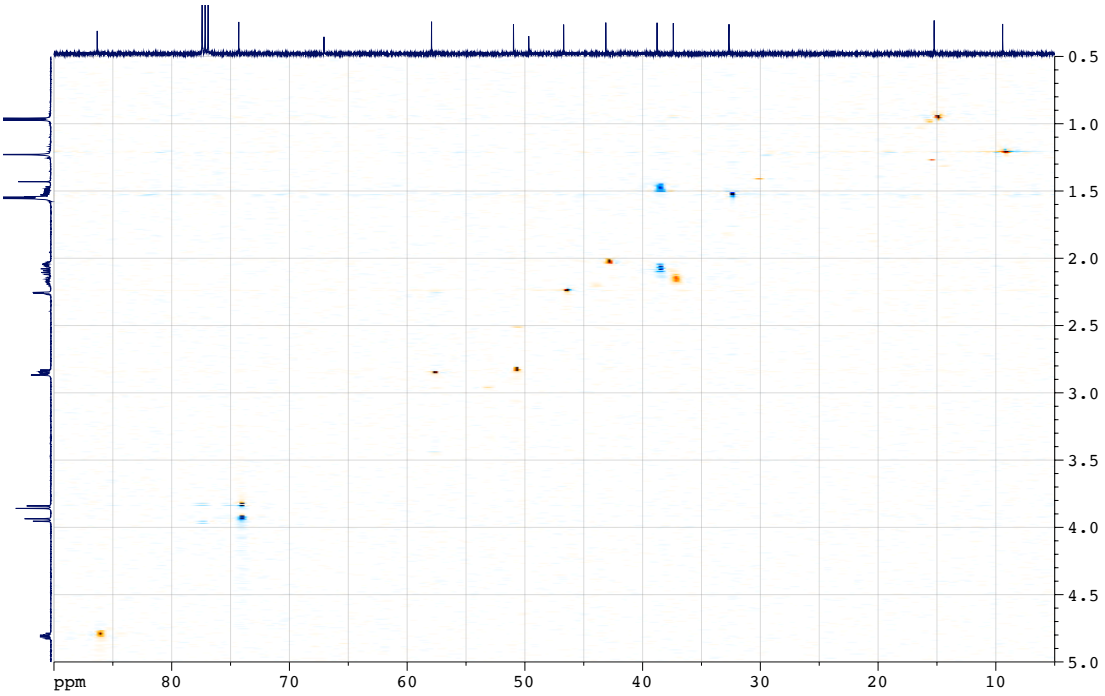


*Figure SI 117. gHSQC NMR spectrum (600, 151 MHz, $CDCl_3$) of **51**.*

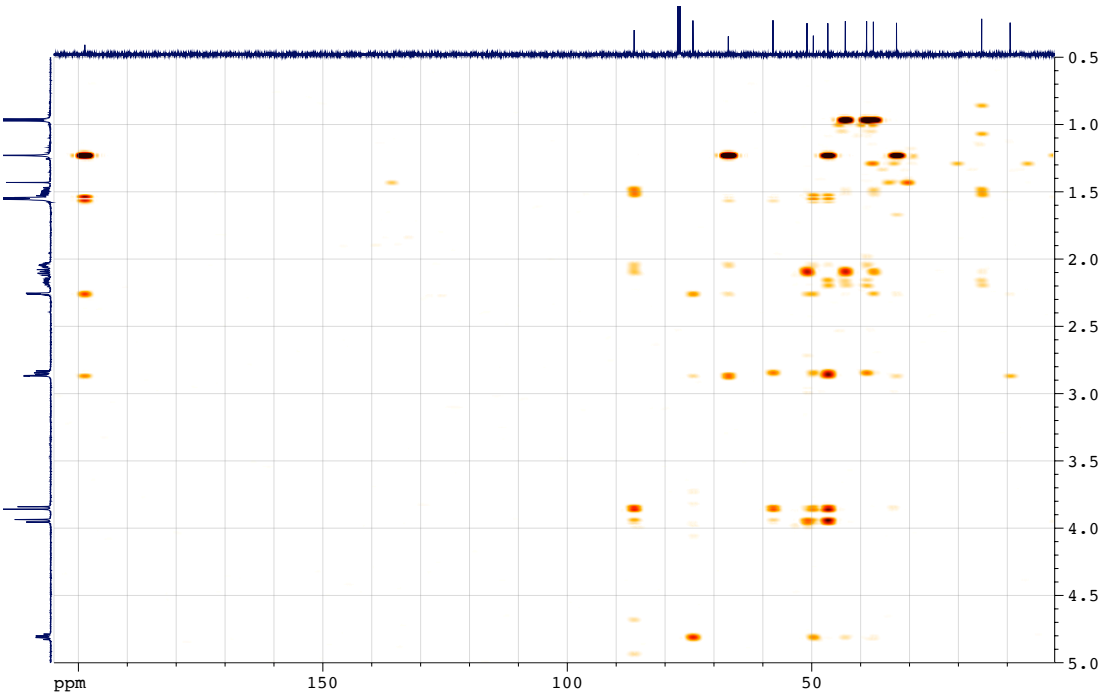


*Figure SI 118. gHMBC NMR spectrum (600, 151 MHz, $CDCl_3$) of **51**.*