Angewandte Chemie
Eine Zeitschrift der Gesellschaft Deutscher Chemiker

Supporting Information

The Structure of Cyclodecatriene Collinolactone, its Biosynthesis, and Semisynthetic Analogues: Effects of Monoastral Phenotype and Protection from Intracellular Oxidative Stress

*Julian C. Schmid, Kerstin Frey[+], Matthias Scheiner[+], Jaime Felipe Guerrero Garzón[+], Luise Stafforst, Jan-Niklas Fricke, Michaela Schuppe, Hajo Schiewe, Axel Zeeck, Tilmann Weber, Isabel Usón, Ralf Kemkemer, Michael Decker, and Stephanie Grond**

anie_202106802_sm_miscellaneous_information.pdf
anie_202106802_sm_JCSchmid_Collazulen.cif

SUPPORTING INFORMATION

Table of Contents

Experimental Procedures

General Remarks:

NMR spectra were recorded on a Bruker Avance III HDX 700 instrument at 298 K, if not stated otherwise. High resolution mass spectrometry data were acquired on a Bruker MaXis 4G ESI-QTOF instrument coupled to a Dionex Ultimate 3000 HPLC system (Thermo Fisher Scientific). Each analysis was calibrated using sodium formiate as internal calibrant.

The nebulizer pressure of the ESI source was set to 2.0 bar and dry gas was set to 8.0 L min^{-1} at an operating temperature of 200 °C. For MS/MS spectra acquisition, the auto MS/MS mode with collision energy stepping was used. The routine gradient was 10% methanol to 100% methanol in 20 min with a flow rate of 0.3 mL/min on a Nucleoshell® EC RP-C18 (150 x 2 mm, 2.7 µm) from Macherey-Nagel. Analytical TLC was performed on TLC Silica gel 60 RP-18 $F_{254}S$, obtained from Merck and sprayed with a solution of anisaldehyde. Preparative HPLC was performed on a Dionex Ultimate 3000 (Thermo Fisher Scientific), using a Kromasil 100 C_{18}, 250 x 20 mm, 7 µm particle size (Dr. Maisch GmbH). Flash chromatography was performed on a Varian 971-FP Flash Purification System, using Chromabond® Flash RS 25 15 SiOH (15 - 40 µm) cartridges from Machery-Nagel GmbH & Co. KG. All reactions, unless otherwise stated, were performed under argon inert gas. Solvents for synthesis were dried over molecular sieves and degassed using the freeze-thaw method before use. Sodium [1-^{13}C, 99%] acetate, sodium [1,2-$^{13}C_2$, 99%] acetate and sodium [1-^{13}C] propionate were obtained from Cambridge Isotope Laboratories, sodium [1,2,3-$^{13}C_3$] propionate was obtained from Sigma-Aldrich and $^{18}O_2$ (93.3% atom purity) was obtained from Eurisotop. Parts of the following procedures have been published in several doctoral theses (available in german).[1]

Fermentation of *Streptomyces* Gö 40/10

Streptomyces Gö 40/10 was isolated from a soil sample taken in Bolivia and identified as *Streptomyces coelescens*/ *Streptomyces cinerochromogenes* (100% matched).

Based on mannitol soya flour media (MS), an optimized composition (containing the following components: reduced-fat soy flour 20 g/L, D-Mannitol 20 g/L, starch from potato (soluble) 20 g/L, D-glucose 10 g/L, yeast extract 5 g/L and calcium carbonate 1 g/L) with 75 g/L of Amberlite XAD-16 was used in 1 L shaking flasks (150 mL of media) with baffled-bottom. The pH value was adjusted to 7.0 by addition of sodium hydroxide. Sterilization was done using an autoclave at 121 °C for 20 min. Before addition to the media, Amberlite XAD-16 was thoroughly washed with 1 N HCl in methanol, followed by aceton, 1 N aqueous sodium hydroxide and finally deionized water until the pH value of the washing solution became neutral again.

The production culture was inoculated with 10 mL per shaking flask of a 48 hours old culture grown in mannitol soya flour media (MS). The fermentation was run for 72 hours at 28 °C and 200 rpm. To further increase the production of **1**, a sterile-filtered solution of the biosynthetic precursors sodium propionate and malonic acid (each 500 mg/L culture broth) with the pH adjusted by addition of sodium hydroxide to 7.0 was added to the culture 8 hours after the fermentation started.

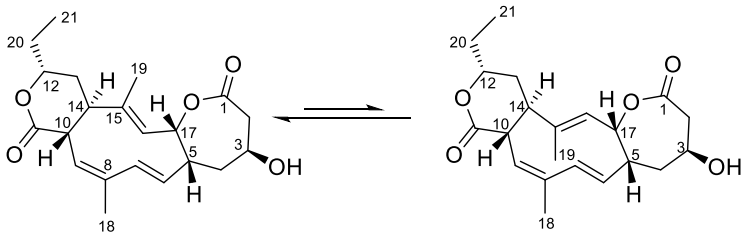
Isolation of collinolactone (1)

The viridescent colored culture broth was centrifuged to separate the bacteria and the Amberlite XAD-16 from the supernatant. Due to the quantitative absorbing of **1** to the absorbing resin, the supernatant did not contain any product (TLC control) and was discarded. The pellet, together with the resin was then extracted three times with 2 L of acetone while stirring. The solid material was separated by filtration through a Büchner funnel. The solvent of the combined organic extracts was removed *in vacuo* using a rotary evaporator with water bath temperature set to 40 °C.

The obtained viscous black residue was dissolved in 300 mL of water and extracted three times with 200 mL of toluene. The solvent was removed *in vacuo* again. The oily residue was purified by chromatography over silica gel (2 L of cyclohexan/aceton 3:2, 200 g silica gel, 6 cm column diameter). The fractions containing **1** were identified by TLC (RP-18, methanol/water 7:3, R_f = 0.4) and concentrated *in vacuo*. The enriched extract was further purified by flash chromatography (A: diisopropylether, B: aceton, 25 g silica gel, column dimensions: 13 x 2.5 cm, 20 mL/min, fraction size 20 mL) using the following gradient: 5 min 2% B, 10 min 8% B, 20 min 8% B, 25 min 16% B, 35 min 16% B, 40 min 20% B, 45 min 20% B. The crude product was finally purified by preparative HPLC (Kromasil 100 C_{18}) with 34% acetonitrile/water at 17.5 mL/min. The pure compound **1** eluted at R_t = 25 - 27 min. Fractions containing the product were lyophilized to give a white, fluffy solid. The obtained yields varied between 15-30 mg per liter media. Compound **4** was isolated using the same purification workflow (R_t = 19.5 - 22 min) in yields of 0.3 mg per liter media.

Characterization of collinolactone (1):

Please note: In the following part, the numbers differ from the main manuscript.



HR-ESI-MS: (m/z):
$[M+H]^+$ calculated for $C_{21}H_{29}O_5$: 361.2010; found 361.2004 (1.6 ppm err, 26.5 mSigma)
$[M+Na]^+$ calculated for $C_{21}H_{28}NaO_5$: 383.1829; found 383.1824 (1.3 ppm err, 2.6 mSigma)

Table S1: ^{1}H-NMR and ^{13}C-NMR data of **1** in DCM-d_2 at 298K, 700 MHz

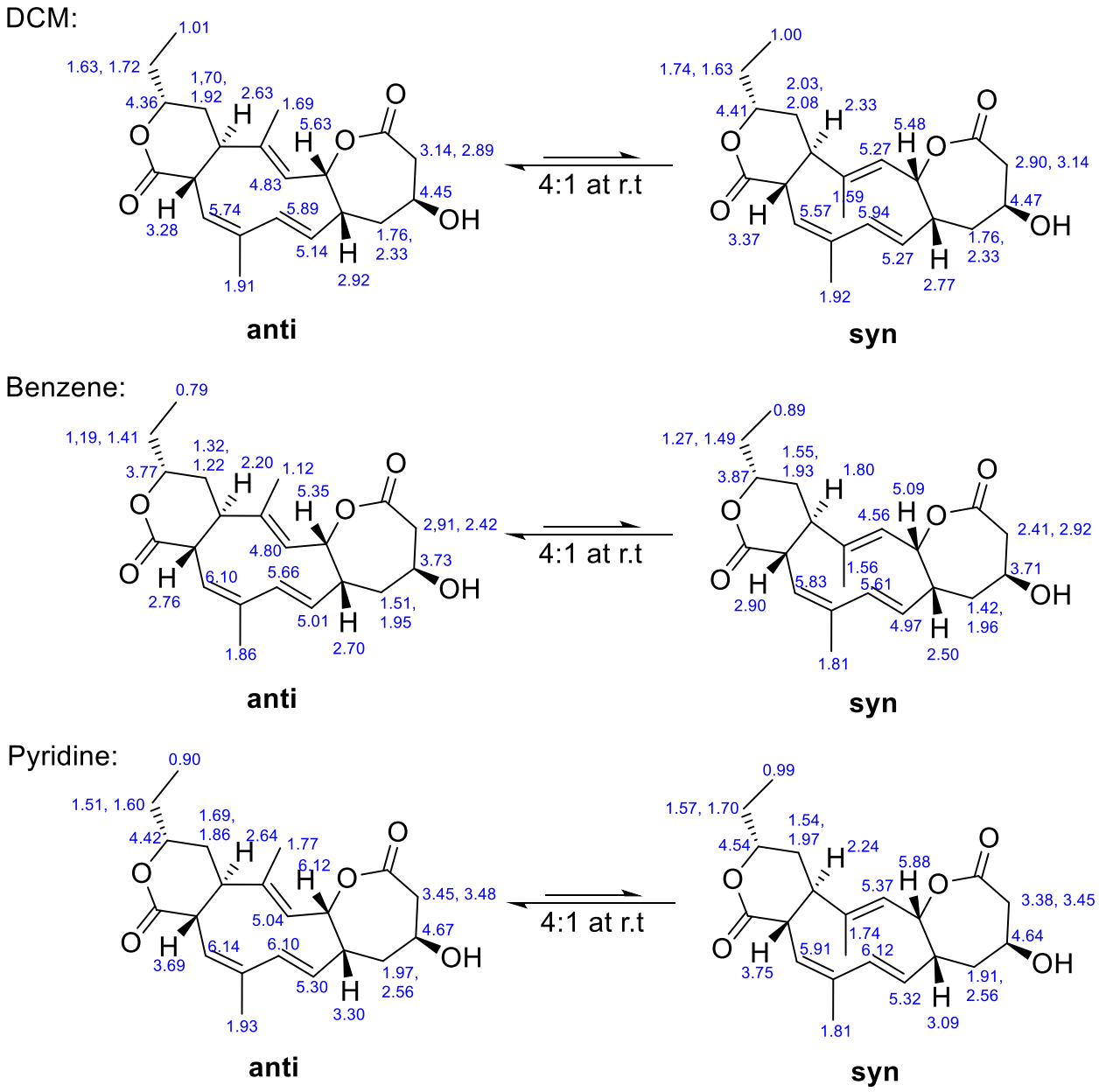
Rotamere I (anti)			Rotamere II (syn)		
C-Atom	δ_C	δ_H (mult., J in Hz)	δ_H (mult., J in Hz)	δ_C	C-Atom
1	171.9			171.9	1
2	42.9	H_a: 3.14 (dd, *J* = 15.0, 9.8 Hz, 1H) H_b: 2.93 – 2.85 (m, 1H)	H_a: 3.14 (dd, *J* = 15.3, 9.5 Hz, 1H) H_b: 2.92 – 2.87 (m, 1H)	43.1	2
3	62.8	4.50 – 4.41 (m, 1H)	4.47 – 4.43 (m, 1H)	62.6	3
4	35.1	H_a: 2.33 (dt, *J* = 15.1, 4.9 Hz, 1H) H_b: 1.76 (dt, *J* = 11.7, 3.3, 2.4 Hz, 1H)	H_a: 2.38 – 2.34 (m, 1H) H_b: 1.73 – 1.70 (m, 1H)	35.7	4
5	43.1	2.92 (dd, *J* = 14.7, 4.7 Hz, 1H)	2.77 (hept, *J* = 5.1 Hz, 1H)	44.6	5
6	127.2	5.14 (dd, J = 16.4, 10.2 Hz, 1H)	5.27 (dd, *J* = 5.4, 1.5 Hz, 1H)	124.5	6
7	138.8	5.89 (d, J = 16.4 Hz, 1H)	5.94 (d, *J* = 16.3 Hz, 1H)	138.4	7
8	136.0			133.8	8
9	123.5	5.74 (dt, J = 7.6, 1.5 Hz, 1H)	5.57 (dt, *J* = 8.4, 1.6 Hz, 1H)	120.5	9
10	40.7	3.28 (t, *J* = 8.0 Hz, 1H)	3.37 (dd, *J* = 11.9, 8.4 Hz, 1H)	46.7	10
11	174.2			174.2	11
12	78.6	4.39 – 4.34 (m, 1H)	4.43 – 4.39 (m, 1H)	78.8	12
13	32.5	H_a: 1.94 – 1.89 (m, 1H) H_b: 1.83 – 1.77 (m, 1H)	H_a: 2.08 (ddd, *J* = 14.6, 7.0, 4.7 Hz, 1H) H_b: 2.03 (dt, *J* = 14.5, 9.3 Hz, 1H)	35.0	13
14	46.8	2.63 (td, *J* = 8.5, 3.0 Hz, 1H)	2.23 (ddd, *J* = 11.9, 9.2, 7.0 Hz, 1H)	45.4	14
15	138.1			148.1	15
16	133.9	4.83 (d, *J* = 6.6 Hz, 1H)	5.27 (dd, *J* = 5.4, 1.5 Hz, 1H)	122.0	16
17	82.4	5.63 (t, J = 6.3 Hz, 1H)	5.48 (t, *J* = 4.8 Hz, 1H)	80.3	17
18	19.9	1.91 (s, 3H)	1.92 (s, 3H)	20.4	18
19	13.2	1.69 (d, *J* = 1.2 Hz, 3H)	1.59 (s, 3H)	23.6	19
20	28.4	H_a: 1.66 – 1.60 (m, 1H) H_b: 1.72 (q, *J* = 7.4, 6.9 Hz, 1H)	H_a: 1.67 – 1.60 (m, 1H) H_b: 1.76 – 1.73 (m, 1H)	28.6	20
21	9.7	1.01 (t, *J* = 7.6 Hz, 3H)	1.00 (t, *J* = 7.6 Hz, 3H)	10.0	21

Table S2: ^{1}H-NMR and ^{13}C-NMR data of **1** in benzene-d_6 at 298K, 700 MHz

Rotamere I (anti)			Rotamere II (syn)		
C-Atom	δ_C	δ_H (mult., J in Hz)	δ_H (mult., J in Hz)	δ_C	C-Atom
1	170.6			170.5	1
2	42.8	H_a: 2.91 (ddd, J = 15.4, 9.6, 1.7 Hz, 1H) H_b: 2.42 (dd, J = 15.0, 4.6 Hz, 1H)	H_a: 2.92 (dd, J = 9.7, 1.5 Hz, 1H) H_b: 2.41 (d, J = 4.6 Hz, 1H)	43.0	2
3	62.4	3.73 (d, J = 16.9 Hz, 1H)	3.75 – 3.68 (m, 1H)	62.3	3
4	34.7	H_a: 1.95 (dq, J = 14.9, 5.2, 4.8 Hz, 1H) H_b: 1.53 – 1.49 (m, 1H)	H_a: 1.98 – 1.94 (m, 1H) H_b: 1.45 – 1.39 (m, 1H)	35.3	4
5	43.1	2.70 (hept, J = 5.2 Hz,1H)	2.50 (hept, J = 5.2 Hz, 1H)	44.3	5
6	126.7	5.01 (dd, J = 16.4, 10.2 Hz, 1H)	4.97 (dd, J = 16.4, 9.4 Hz, 1H)	124.0	6
7	139.1	5.66 (d, J = 16.4 Hz, 1H)	5.61 (d, J = 16.4 Hz, 1H)	138.4	7
8	135.1			137.2	8
9	124.4	6.10 (dt, J = 7.3, 1.5 Hz, 1H)	5.83 (dt, J = 8.4, 1.6 Hz, 1H)	121.4	9
10	40.4	2.76 (t, J = 8.1 Hz, 1H)	2.90 (dd, J = 9.7, 2.0 Hz, 1H)	46.2	10
11	172.6			172.8	11
12	77.1	3.79 – 3.75 (m, 1H)	3.87 (qd, J = 7.5, 5.2 Hz, 1H)	77.3	12
13	32.4	H_a: 1.32 (dt, J = 14.9, 2.3 Hz, 1H) H_b: 1.25 – 1.19 (m, 1H)	H_a: 1.93 (d, J = 4.8 Hz, 1H) H_b: 1.58 – 1.53 (m, 1H)	34.9	13
14	46.4	2.20 (td, J = 8.7, 2.4 Hz, 1H)	1.83 – 1.76 (m, 1H)	45.1	14
15	133.2			147.9	15
16	134.1	4.80 (d, J = 6.5 Hz, 1H)	4.56 (dd, J = 5.4, 1.5 Hz, 1H)	121.7	16
17	81.8	5.35 (t, J = 6.1 Hz, 1H)	5.11 – 5.07 (m, 1H)	79.7	17
18	20.0	1.86 (s, 3H)	1.81 (s, 3H)	20.3	18
19	12.6	1.12 (s, 3H)	1.56 (s, 3H)	23.7	19
20	28.3	H_a: 1.44 – 1.38 (m, 1H) H_b: 1.23 – 1.15 (m, 1H)	H_a: 1.53 – 1.47 (m, 1H) H_b: 1.30 – 1.24 (m, 1H)	28.5	20
21	9.6	0.79 (t, J = 7.4 Hz, 3H)	0.89 (t, J = 7.4 Hz, 3H)	9.9	21

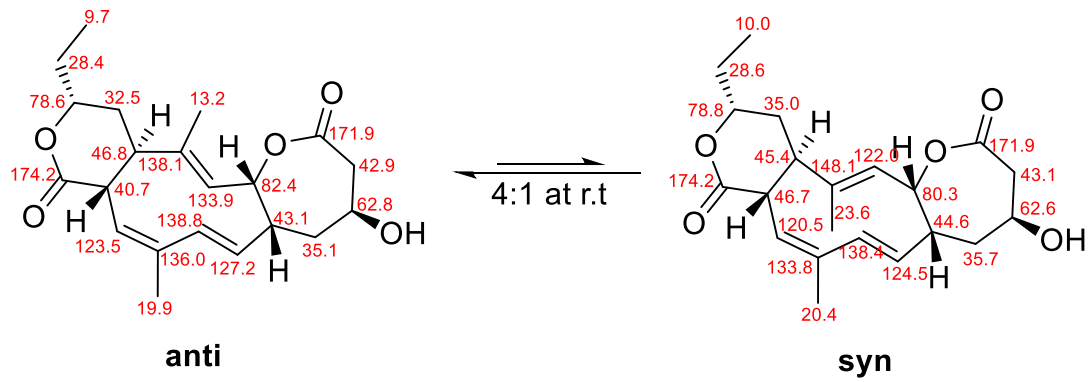
Table S3: ^{1}H-NMR and ^{13}C-NMR data of **1** in pyridine-d_5 at 298K, 700 MHz

Rotamere I (anti)			Rotamere II (syn)		
C-Atom	δ_C	δ_H (mult., J in Hz)	δ_H (mult., J in Hz)	δ_C	C-Atom
1	172.6			172.5	1
2	44.1	H_a: 3.48 (dd, J = 13.3, 5.6 Hz 1H) H_b: 3.47 – 3.44 (m, 1H)	H_a: 3.48 – 3.43 (m, 1H) H_b: 3.38 (dd, J = 15.1, 4.2 Hz, 1H)	44.4	2
3	62.3	4.67 (d, J = 6.2 Hz,1H)	4.64 (dt, J = 8.5, 3.6 Hz, 1H)	62.1	3
4	36.0	H_a: 2.02 – 1.95 (m, 1H) H_b: 2.56 (dt, J = 14.6, 5.0 Hz, 1H)	H_a: 2.56 (dt, J = 14.6, 5.0 Hz, 1H) H_b: 1.91 (d, J = 1.5 Hz, 1H)	36.5	4
5	43.8	3.30 (tt, J = 10.9, 5.4 Hz, 1H)	3.09 (dp, J = 10.1, 5.0 Hz, 1H)	45.2	5
6	128.0	5.30 (dt, J = 16.4, 10.0 Hz, 1H)	5.35 – 5.28 (m, 1H)	125.1	6
7	139.2	6.10 (d, J = 10.4 Hz, 1H)	6.12 (d, J = 6.2 Hz, 1H)	138.6	7
8	135.7			137.9	8
9	124.7	6.16 – 6.13 (m, 1H)	5.91 (dt, J = 8.4, 1.5, Hz, 1H)	121.6	9
10	40.9	3.69 (t, J = 8.0 Hz, 1H)	3.75 (dd, J = 12.0, 8.3 Hz, 1H)	46.6	10
11	174.1			174.2	11
12	78.1	4.42 (dddd, J = 10.8, 7.2, 5.2, 1.8 Hz, 1H)	4.54 (ddt, J = 9.8, 7.5, 4.8 Hz, 1H)	78.3	12
13	33.0	H_a: 1.86 (dq, J = 14.8, 2.8, 2.1 Hz, 1H) H_b: 1.73 – 1.66 (m, 1H)	H_a: 2.02 – 1.95 (m, 1H) H_b: 1.58 – 1.53 (m, 1H)	35.6	13
14	47.2	2.64 (td, J = 8.7, 2.2 Hz, 1H)	2.24 (ddd, J = 11.9, 9.7, 6.6 Hz, 1H)	45.9	14
15	136.2			147.7	15
16	134.4	5.04 (d, J = 6.5 Hz, 1H)	5.37 (dd, J = 5.3, 1.4 Hz, 1H)	123.2	16
17	82.8	6.12 (d, J = 6.2 Hz, 1H)	5.88 (t, J = 4.8 Hz, 1H)	80.6	17
18	20.3	1.93 (s, 3H)	1.81 (s, 3H)	20.6	18
19	13.2	1.77 (s, 3H)	1.74 (s, 3H)	24.0	19
20	28.7	H_a: 1.65 – 1.56 (m, 1H) H_b: 1.51 (dqd, J = 14.7, 7.4, 5.3 Hz, 1H)	H_a: 1.74 – 1.65 (m, 1H) H_b: 1.60 – 1.55 (m, 1H)	28.9	20
21	9.9	0.90 (t, J = 7.4 Hz, 3H)	0.99 (t, J = 7.4 Hz, 3H)	10.3	21



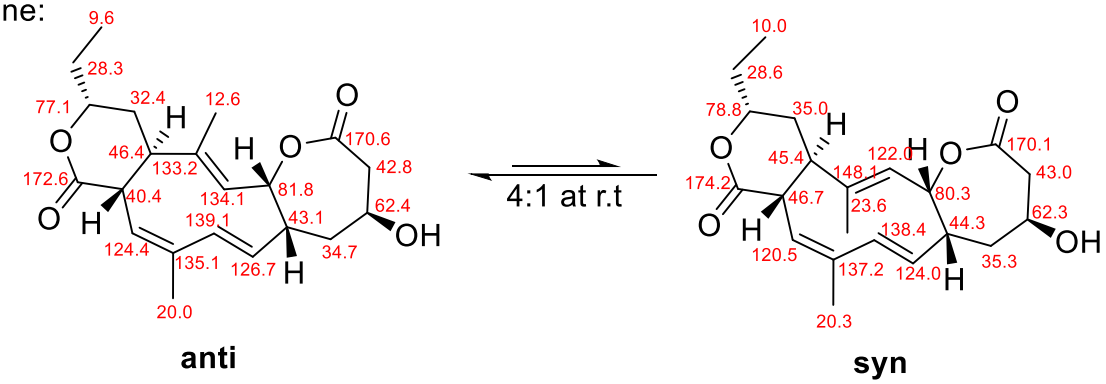
Scheme 1: ^{1}H NMR shifts of **1** in DCM-d_2, benzene-d_6 and pyridine-d_5

DCM:



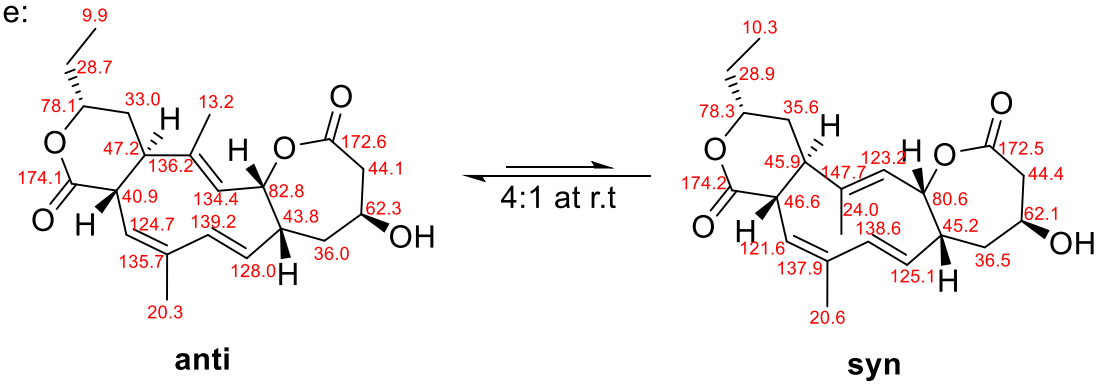
anti syn

Benzene:



anti syn

Pyridine:



anti syn

Scheme 2: ^{13}C NMR shifts of **1** in DCM-d_2, benzene-d_6 and pyridine-d_5

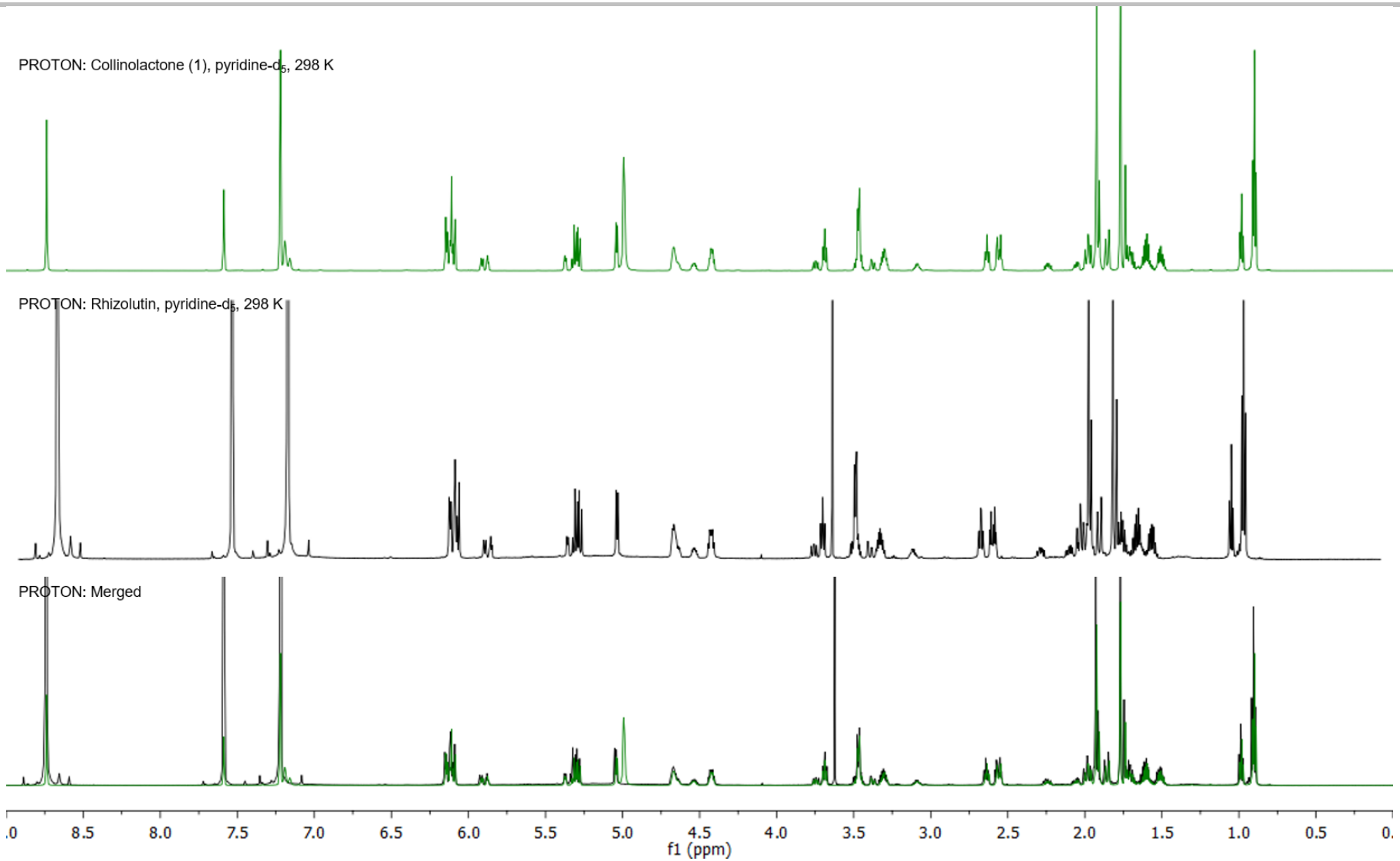


Figure S1A: Proton spectra of collinolactone (**1**), displayed in green (top) and rhizolutin,[2] displayed in black (middle) and overlay of both spectra (bottom). Spectra were recorded in pyridine-d_5 at 298 K. The source data files (Mnova) of the experimental NMR-data of rhizolutin were kindly provided by Prof. Dr. Oh and coworkers from the Natural Products Research Institute, College of Pharmacy, Seoul National University.

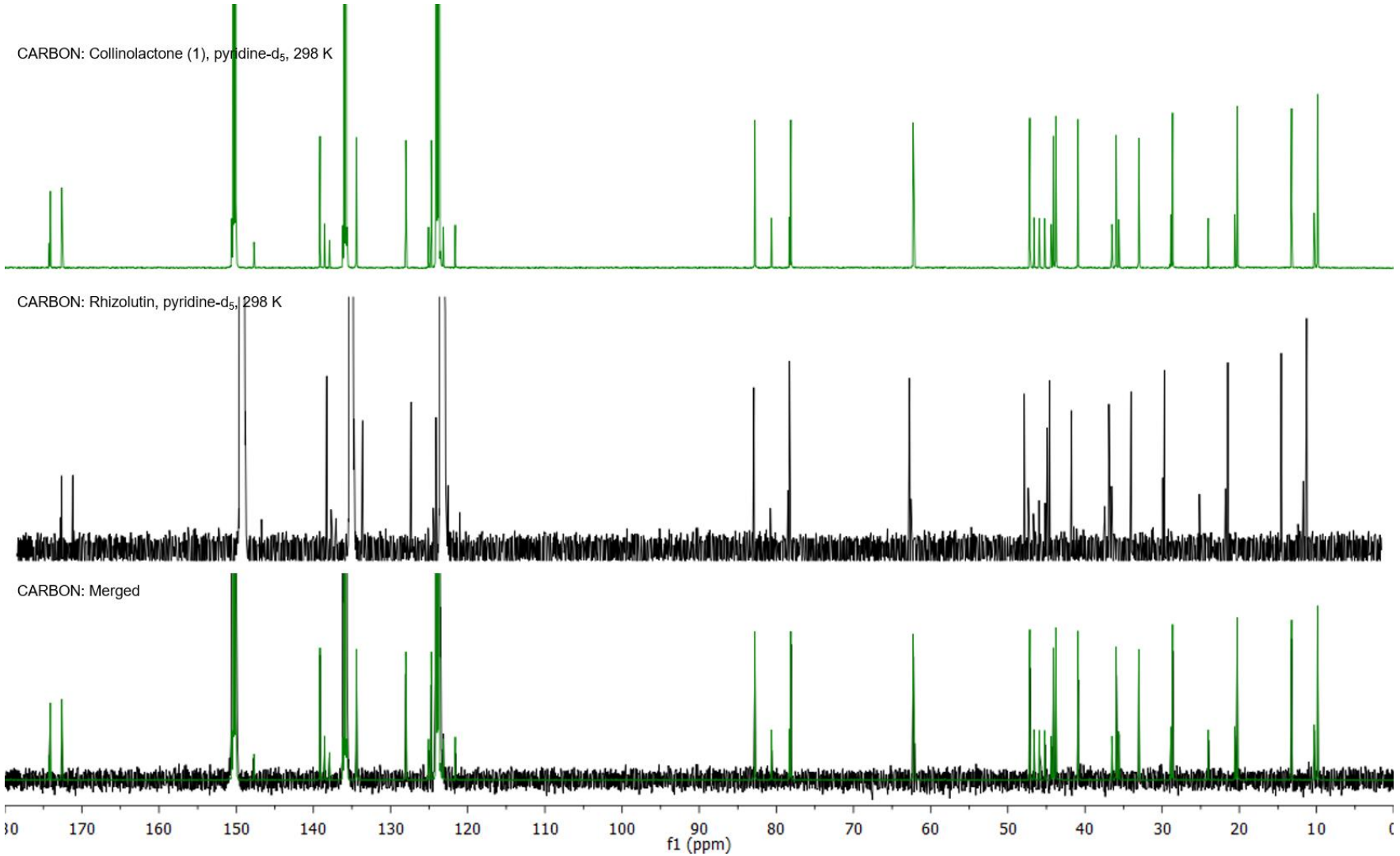


Figure S1B: Carbon spectra of collinolactone (**1**), displayed in green (top) and rhizolutin,[2] displayed in black (middle) and overlay of both spectra (bottom). Spectra were recorded in pyridine-d_5 at 298 K. The source data files (Mnova) of the experimental NMR-data of rhizolutin were kindly provided by Prof. Dr. Oh and coworkers from the Natural Products Research Institute, College of Pharmacy, Seoul National University.

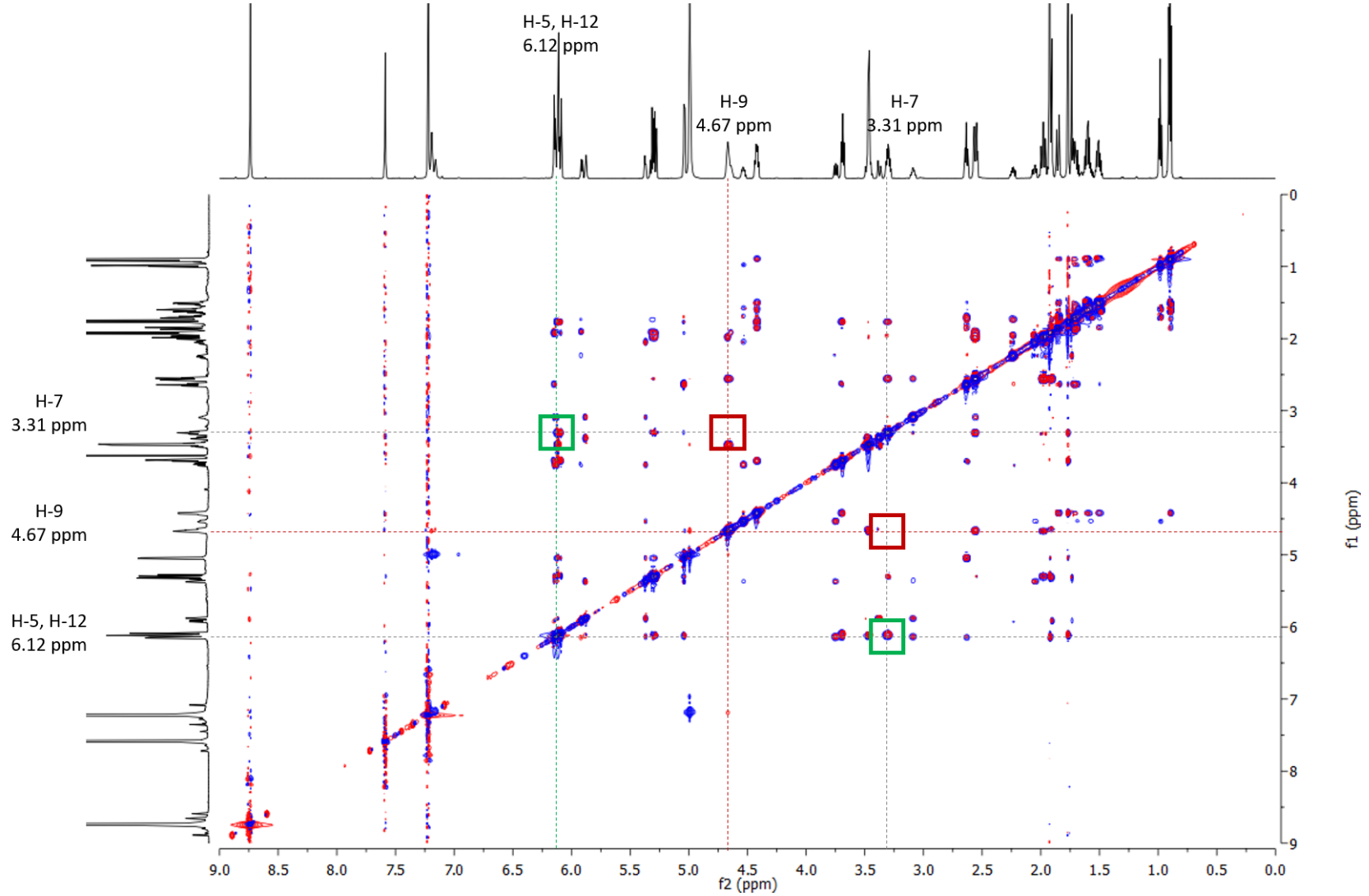


Figure S1C: ROESY spectra of collinolactone (**1**), displayed in red and rhizolutin,[2] displayed in blue. Spectra were recorded in pyridine-d_5 at 298 K. Red boxes show the missing correlation between H-9 and H-7, green boxes show the existing correlation between H-7 and H-5 or H-12, which are overlapping and cannot be distinguished in pyridine-d_5. The source data files (Mnova) of the experimental NMR-data of rhizolutin were kindly provided by Prof. Dr. Oh and coworkers from the Natural Products Research Institute, College of Pharmacy, Seoul National University.

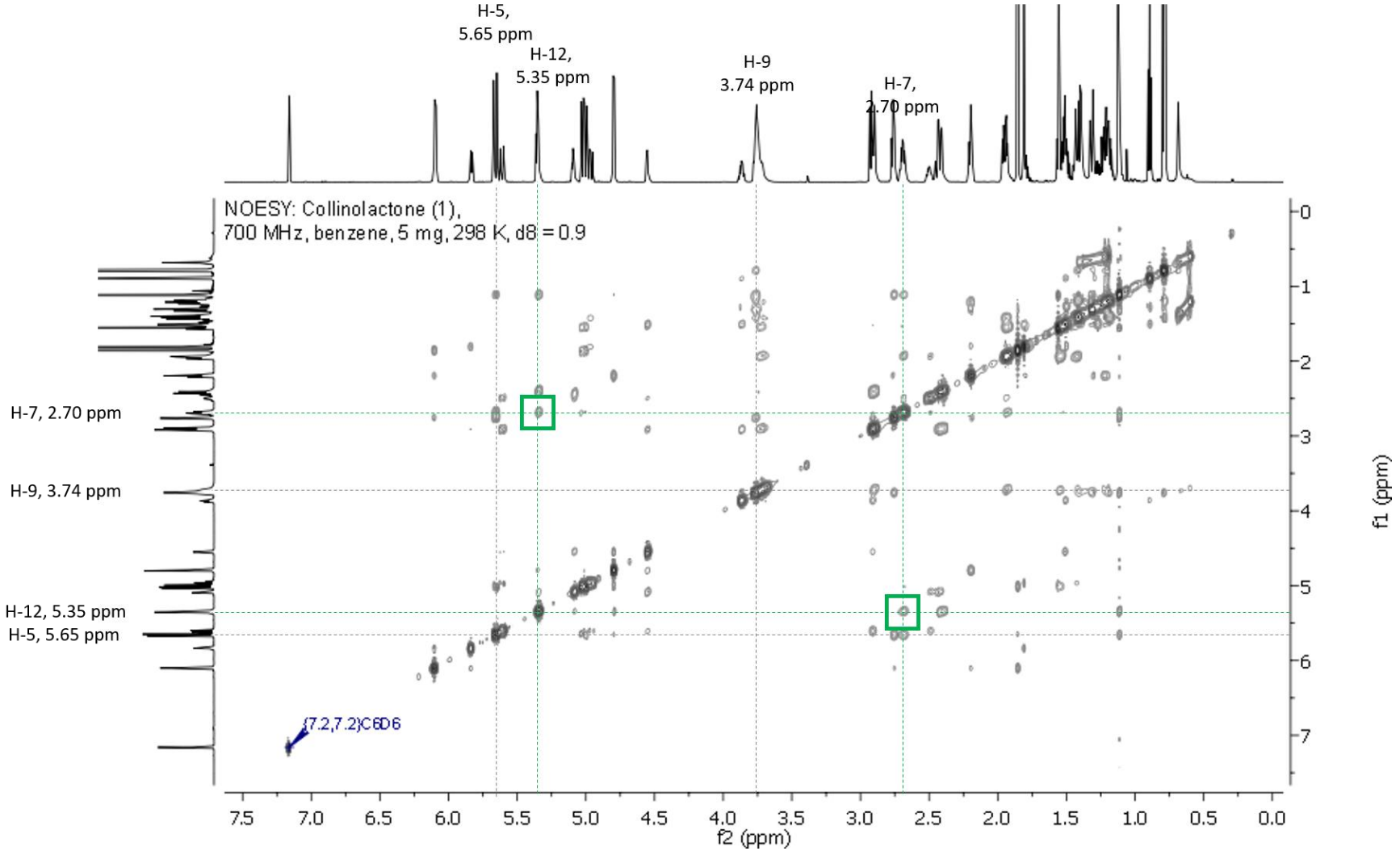


Figure S2: NOESY spectra in benzene for **1**; green boxes show the correlation between H-7 and H-12, indicating that these protons are in the same plane. No correlation was observed between H-9 and H-12.

Determination of coalescence temperature

^{1}H-NMR spectra for **1** were acquired at temperatures between 230 K and 350 K in steps of 20 K in toluene-d8. For determination of the coalescence temperature, the distance (in Hz) of the proton signals in position 16 (4.80 ppm for **1a** and 4.56 ppm for **1b** at 298 K) were measured after calibration using the solvent signal. Due to instrument limitations, the coalescence temperature had to be extrapolated from the obtained data using a one phase decay model for curve fitting (GraphPad Prism 9).

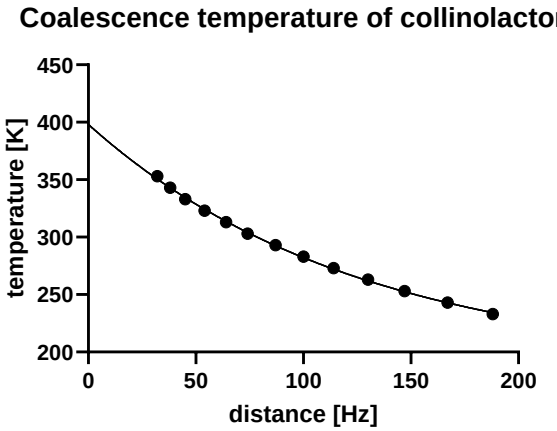
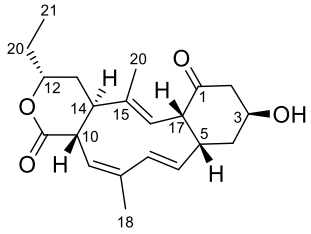


Figure S3. Extrapolation of coalescence temperature of **1** based on proton signal shifts at temperatures between 230 K and 350 K.

Characterization of collinoketone (4):



4

HR-ESI-MS (m/z): $[M+H]^+$ calculated for $C_{21}H_{29}O_4$: 345.2060; found 345.2058 (0.6 ppm err, 4.0 mSigma)

^{1}H NMR (700 MHz, CD_2Cl_2) δ = 6.01 (ddt, *J* = 11.2, 2.1, 1.0, 1H, 7-H), 5.53 – 5.39 (m, 1H, 9-H), 5.27 (dd, *J* = 11.3, 9.5, 1H, 6-H), 5.01 (d, *J* = 10.1, 1H, 16-H), 4.25 (dddd, *J* = 11.3, 7.4, 5.4, 2.2, 1H, 12-H), 3.93 (tt, *J* = 11.3, 4.6, 1H, 3-H), 2.89 – 2.81 (m, 2H,10-H, 17-H), 2.74 (ddd, *J* = 12.7, 4.8, 2.2, 1H, 2-H_a), 2.45 (ddd, *J* = 12.7, 11.6, 1.1, 1H, 2-H_b), 2.36 (td, *J* = 10.0, 2.3, 1H, 14-H), 2.28 (dtd, *J* = 12.9, 4.0, 2.2, 1H, 4-H_a), 2.18 – 2.09 (m, 1H, 5-H), 1.99 (dt, *J* = 14.9, 2.4, 1H, 13-H_a), 1.85 (s, 3H, 18-H), 1.80 – 1.73 (m, 1H, 13-H_b), 1.73 – 1.67 (m, 2H, 20-H_a,4-H_b), 1.65 – 1.56 (m, 1H, 20-H_b), 1.49 (d, *J* = 1.3, 3H, 19-H), 1.00 (t, *J* = 7.4, 3H, 21-H).

^{13}C NMR (176 MHz, CD_2Cl_2) δ = 207.6 (C-1), 174.1 (C-11), 138.1 (C-8), 136.9 (C-15), 134.28 (C-6), 132.4 (C-7), 124.3 (C-9, C-16), 78.7 (C-12), 69.3 (C-3), 54.2 (C-17), 52.0 (C-2), 45.91 (C-14), 43.3 (C-10), 41.1 (C-5), 40.7 (C-4), 31.6 (C-13), 28.5 (C-20), 24.6 (C-18), 13.3 (C-19), 9.9 (C-21).

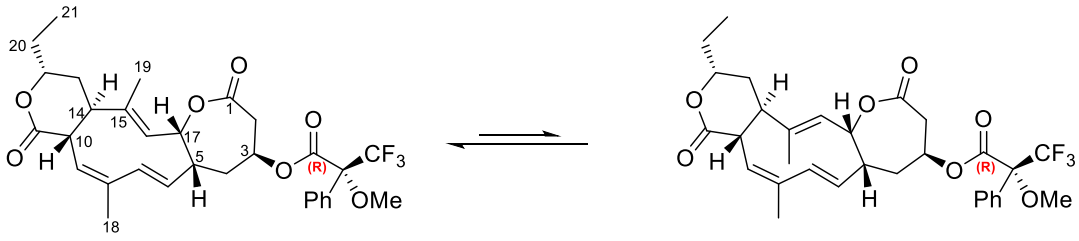
Feeding experiments with stable isotope precursors

Feeding experiments were performed in a total of 1 L of mannitol soya flour media (MS) equally distributed to five 1L baffled flasks. Equilibrated Amberlite XAD-16 was added as described above before autoclaving at 121 °C for 20 min.
The fed cultures were inoculated with 10 mL per shaking flask of a 48 hours old culture grown in mannitol soya flour media (MS). The fermentation was run for 72 hours at 28 °C and 200 rpm.
After 6 hours, 2 mM of ^{13}C-labeled sodium acetate and non-labeled sodium propionate (2 mM) or ^{13}C-labeled sodium propionate with non-labeled malonic acid (2 mM, pH-value adjusted by adding sodium hydroxide), respectively, was added. The addition was repeated after 12 and 24 hours with 1 mM of each labeled and non-labeled component. Purification procedure is the same for labeled and non-labeled collinolactone (**1**) and was already described above. At the end, about 19 mg of each labeled pure compound was isolated.

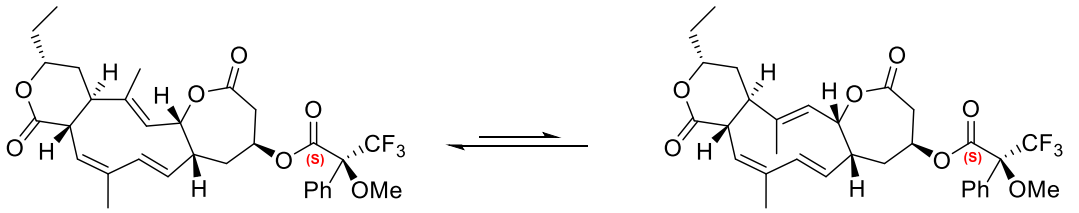
Feeding experiment in $^{18}O_2$-enriched atmosphere

Seven 250 mL baffled flasks with 100 mL of mannitol soya flour media (MS) with pH adjusted to 7 were autoclaved at 121 °C for 20 min. After cooling to room temperature, they were inoculated with 5 mL of a 48 hours old culture grown in mannitol soya flour media (MS). The fermentation was run for 72 hours in total at 28 °C and 250 rpm.
After 36 hours, the flasks were connected to an oxygen cultivation apparatus[3], and flushed three times with nitrogen to reduce the amount of unlabeled oxygen in the apparatus.1.2 L of ^{18}O-oxygen were injected initially and additional 800 mL were injected during the ongoing fermentation process to replace the consumed oxygen. After 72 hours, the cultures were harvested and **1** was purified using the procedure described above.

Synthesis of MTPA-collinolactone (2)



2a (anti) **2a** (syn)



2b (anti) **2b** (syn)

10 mg of compound **1** (27.7 µmol, 1 Eq.) was dissolved in 20 mL of dry dichloromethane. DCC (N,N'-Dicyclohexylcarbodiimide, 28.6 mg, 138.7 µmol, 5 Eq.) and DMAP (4-Dimethylaminopyridine, 0.68 mg, 5.5 µmol, 0.2 Eq.) were added, followed by α-methoxy-α-trifluoromethylphenylacetic acid (32.5 mg, 138.7 µmol, 5 Eq.). The reaction mixture was allowed to stir for 30 minutes at room temperature before heating up to 40 °C for additional 16 hours. The solvent was then removed *in vacuo* and the raw product was purified by preparative HPLC on a Kromasil 100 C_{18} with 65% acetonitrile/water at 17.5 mL/min (R_t = 20.1 min) to afford 4.9 mg (30%) of **2** as a white powder after lyophilization.

HR-ESI-MS (m/z): $[M+H]^+$ calculated for $C_{31}H_{36}O_7F_3$: 577.2408; found 577.2411 (0.5 ppm err, 14.9 mSigma)

R-MTPA-Ester (**2a**):

anti-form:
^{1}H NMR (700 MHz, CD_2Cl_2) δ = 7.54 – 7.50 (m, 2H, H_a-27, H_b-27), 7.49 – 7.44 (m, 3H, H_a-28, H_b-28, H-29), 5.81 (d, *J* = 16.4 Hz, 1H, H-7), 5.76 (dp, *J* = 7.6, 1.4 Hz, 1H, H-9), 5.57 (dtd, *J* = 10.5, 4.6, 1.8 Hz, 1H, H-3), 5.30 (t, *J* = 6.0 Hz, 1H, H-17), 5.14 – 5.08 (m, 1H, H-6), 4.77 (dd, *J* = 6.4, 1.3 Hz, 1H, H-16), 4.36 – 4.29 (m, 1H, H-12), 3.54 (s, 3H, H-25), 3.46 (dd, *J* = 15.7, 10.2 Hz, 1H, H_a-2), 3.21 (t, *J* = 8.1 Hz, 1H, H-10), 2.84 (dd, *J* = 15.6, 4.3 Hz, 1H, H_b-2), 2.62 (ddd, *J* = 14.9, 10.2, 4.4 Hz, 1H, H-5), 2.59 – 2.57 (m, 1H, H-14), 2.55 (q, *J* = 5.1 Hz, 1H, H_a-4), 1.95 – 1.92 (m, 1H, H_b-4), 1.91 (s, 3H, H-18), 1.88 (dt, *J* = 15.0, 2.5 Hz, 1H, H_a-13), 1.80 – 1.75 (m, 1H, H_b-13), 1.75 – 1.69 (m, 1H, H_a-20), 1.62 (ttd, *J* = 14.9, 7.3, 5.6 Hz, 1H, H_b-20), 1.42 (s, 3H, H-19), 1.01 (t, *J* = 7.5 Hz, 3H, H-21).

^{13}C NMR (176 MHz, CD_2Cl_2) δ = 173.6 (C-11), 169.7 (C-1), 166.1 (C-22), 139.7 (C-7), 135.8 (C-8), 134.3 (C-15), 133.3 (C-16), 132.2 (C-26), 130.5 (C-29), 129.2 (C_a-28, C_b-28), 127.7 (C_a-27, C_b-27), 125.6 (C-6), 124.0 (C-9), 123.9 (q, *J* = 288 Hz, C-24), 85.2 (C-23), 82.1 (C-17), 78.5 (C-12), 67.9 (C-3), 55.8 (C-25), 46.7 (C-14), 44.0 (C-5), 40.6 (C-10), 40.3 (C-2), 32.4 (C-13), 32.1 (C-4), 28.5 (C-20), 19.8 (C-18), 12.8 (C-19), 9.7 (C-21).

syn-form:
^{1}H NMR (700 MHz, CD_2Cl_2) δ = 7.55 – 7.49 (m, 2H, H_a-27, H_b-27), 7.49 – 7.43 (m, 3H, H_a-28, H_b-28, H-29), 5.87 (d, *J* = 16.3, 1.3 Hz, 1H, H-7), 5.60 (dt, *J* = 8.4, 1.5 Hz, 1H, H-9), 5.54 (dddd, *J* = 9.5, 5.5, 3.8, 1.7 Hz, 1H, H-3), 5.16 – 5.11 (m, 1H, H-6), 5.10 – 5.08 (m, 1H, H-17), 5.03 – 5.00 (m, 1H, H-16), 4.40 (qd, *J* = 7.2, 5.3 Hz, 1H, H-12), 3.54 (s, 3H, H-25), 3.39 (dd, *J* = 16.2, 9.9 Hz, 1H, H_a-2), 3.30 (dd, *J* = 11.9, 8.4 Hz, 1H, H-10), 2.89 – 2.85 (m, 1H, H_b-2), 2.65 – 2.58 (m, 1H, H_a-4), 2.49 – 2.40 (m, 1H, H-5), 2.26 – 2.19 (m, 1H, H-14), 2.03 (dd, *J* = 8.2, 7.1 Hz, 2H, H-13), 1.92 (s, 3H, H-18), 1.88 – 1.83 (m, 1H, H_b-4), 1.81 – 1.69 (m, 1H, H_a-20), 1.67 – 1.58 (m, 1H, H_b-20), 1.57 (s, 3H, H-19), 1.03 (t, *J* = 7.5 Hz, 3H, H-21).

^{13}C NMR (176 MHz, CD_2Cl_2) δ = 173.7 (C-11), 169.6 (C-1), 165.9 (C-22), 148.9 (C-15), 139.1 (C-7), 137.9 (C-8), 132.3 (C-26), 130.3 (C-29), 129.2 (C_a-28, C_b-28), 127.7 (C_a-27, C_b-27), 123. 9 (q, *J* = 288 Hz, C-24), 123.4 (C-6), 121.2 (C-16), 120.9 (C-9), 85.0 (C-23), 80.1 (C-17), 78.6 (C-12), 67.9 (C-3), 55.8 (C-25), 46.7 (C-10), 45.5 (C-14), 45.0 (C-5), 40.3 (C-2), 34.9 (C-13), 32.7 (C-4), 28.7 (C-20), 23.7 (C-19), 20.4 (C-18), 10.0 (C-21).

(S)-MTPA-Ester (**2b**):

anti-form:
^{1}H NMR (700 MHz, CD_2Cl_2) δ = 7.55 – 7.52 (m, 2H, H_a-27, H_b-27), 7.49 – 7.46 (m, 1H, H-29), 7.46 – 7.43 (m, 2H, H_a-28, H_b-28), 5.76 – 5.73 (m, 1H, H-9), 5.66 (d, *J* = 16.3 Hz, 1H, H-7), 5.63 (ddd, *J* = 10.6, 4.6, 1.7 Hz, 1H, H-3), 5.37 (t, *J* = 6.0 Hz, 1H, H-17), 5.07 (m, 1H, H-6), 4.76 (dd, *J* = 6.6, 1.3 Hz, 1H, H-16), 4.35 – 4.29 (m, 1H, H-12), 3.59 (s, 3H, H-25), 3.42 – 3.34 (m, 1H, H_a-2), 3.17 (t, *J* = 8.0 Hz, 1H, H-10), 3.02 (dd, *J* = 15.3, 4.3 Hz, 1H, H_b-2), 2.59 – 2.54 (m, 2H, H_a-4, H-14), 2.34 – 2.27 (m, 1H, H-5), 1.90 (s, 3H, H-18), 1.88 – 1.81 (m, 2H, H_b-4, H_a-13), 1.81 – 1.75 (m, 1H, H_b-13), 1.73 (dd, *J* = 14.3, 7.2 Hz, 1H, H_a-20), 1.67 – 1.58 (m, 1H, H_b-20), 1.35 (s, 3H, H-19), 1.01 (t, *J* = 7.4 Hz, 3H, H-21).

^{13}C NMR (176 MHz, CD_2Cl_2) δ = 173.6 (C-11), 169.7 (C-1), 166.0 (C-22), 139.5 (C-7), 135.8 (C-8), 134.3 (C-15), 133.3 (C-16), 132.6 (C-26), 130.4 (C-29), 129.1 (C_a-28, C_b-28), 127.5 (C_a-27, C_b-27), 125.6 (C-6), 123.8 (q, *J* = 288 Hz),123.9 (C-9), 85.1 (C-23), 82.2 (C-17), 78.5 (C-12), 67.9 (C-3), 56.0 (C-25), 46.7 (C-14), 43.7 (C-5), 40.6 (C-10), 40.0 (C-2), 32.4 (C-13), 31.6 (C-4), 28.5 (C-20), 19.8 (C-18), 12.9 (C-19), 9.7 (C-21).

syn-form:
^{1}H NMR (700 MHz, CD_2Cl_2) δ = 7.58 – 7.55 (m, 2H, H_a-27, H_b-27), 7.49 – 7.46 (m, 2H, H_a-28, H_b-28), 7.45 – 7.42 (m, 1H, H-29), 5.78 – 5.75 (m, 1H, H-7), 5.59 (dp, *J* = 8.6, 1.6 Hz, 1H, H-9), 5.57 – 5.54 (m, 1H, H-3), 5.17 (t, *J* = 4.8 Hz, 1H, H-17), 5.09 (dd, *J* = 19.1, 9.7 Hz, 1H, H-6), 4.98 – 4.94 (m, 1H, H-16), 4.42 – 4.36 (m, 1H, H-12), 3.57 (s, 3H, H-25), 3.38 – 3.34 (m, 1H, H_a-2), 3.26 (dd, *J* = 11.9, 8.4 Hz, 1H, H-10), 3.02 – 2.98 (m, 1H, H_b-2), 2.61 – 2.58 (m, 1H, H_a-4), 2.22 (dt, *J* = 11.9, 8.1 Hz, 1H, H-14), 2.17 (tt, *J* = 10.2, 5.3 Hz, 1H, H-5), 2.04 – 2.00 (m, 2H, H_a-13, H_b-13), 1.90 (s, 3H, H-18), 1.89 – 1.83 (m, 1H, H_b-4), 1.75 – 1.70 (m, 1H, H_a-20), 1.67 – 1.61 (m, 1H, H_b-20), 1.56 (s, 3H, H-19), 1.03 (t, *J* = 7.5, 7.0 Hz, 3H, H-21).

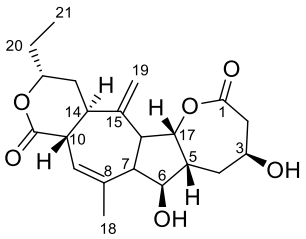
^{13}C NMR (176 MHz, CD_2Cl_2) δ = 173.7 (C-11), 169.6 (C-1), 165.9 (C-22), 148.9 (C-15), 139.0 (C-7), 137.9 (C-8), 132.6 (C-26), 130.3 (C-29), 129.1 (C_a-28, C_b-28), 127.6 (C_a-27, C_b-27), 123.8 (q, *J* = 288 Hz), 123.3 (C-6), 121.2 (C-16), 120.8 (C-9), 85.0 (C-23), 80.1 (C-17), 78.7 (C-12), 68.0 (C-3), 56.0 (C-25), 46.7 (C-10), 45.4 (C-14), 44.7 (C-5), 40.1 (C-2), 35.0 (C-13), 32.2 (C-4), 28.7 (C-20), 23.6 (C-19), 20.4 (C-18), 10.0 (C-21).

Determination of stereo configuration using MTPA-collinolactone (2)

Derivatization with (R)- or (S)-α-methoxy-α-trifluoromethylphenylacetic acid (MTPA) represents a valid and well described method for determination of stereochemical configurations of hydroxyl groups.[4] We used this method to determine the configuration of the hydroxyl group at C4 as an initial starting point (yielding in **2a** and **2b**) for relative stereo configuration assignment. But obtained values are relatively small and signals of hydrogen atoms close to the hydroxyl group at C4 overlap with other signals, making the precise determination of chemical shifts rather difficult and prone to errors.

2 (anti) **2** (syn)

Synthesis of collazulen (3)



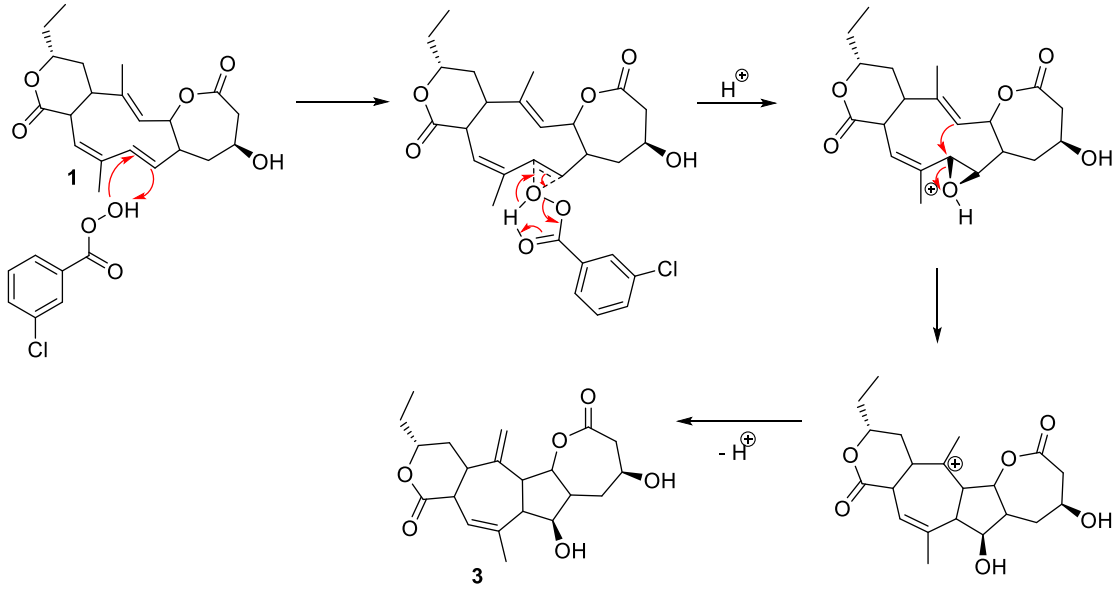
3

30 mg of compound **1** (83.2 µmol, 1 Eq.) was dissolved in 20 mL of dry dichloromethane and cooled to 0 °C. 3-chloroperbenzoic acid (17.67 mg, 83.2 µmol, 1 Eq.) was dissolved in 20 mL of dry DCM and slowly added over 1 hour. The reaction mixture was allowed to warm up to room temperature and was stirred for another 4 hours. Saturated sodium bicarbonate solution was added to the reaction which was then extracted three times with dichloromethane (20 mL each). The combined organic fractions were evaporated *in vacuo* and the raw product was purified by preparative HPLC on a Kromasil 100 C_{18} with 30% acetonitrile/water at 17.5 mL/min. The pure compound **3** eluted at R_t = 14.0 – 15.0 min. Lyophilizing the product containing fractions yielded 14.9 mg (47%) of a white, fluffy powder. Crystals of X-Ray quality were obtained by dissolving the pure product in DCM-d_2 in an NMR tube and long-term storage at -20 °C.

HR-ESI-MS (m/z): $[M+H]^+$ calculated for $C_{21}H_{29}O_6$: 377.1959; found 377.1956 (0.8 ppm err, 6.3 mSigma)

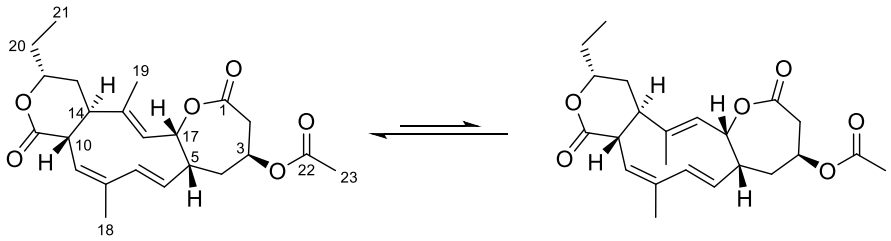
^{1}H NMR (700 MHz, CD_2Cl_2) δ = 6.23 (dt, *J* = 5.5, 1.7 Hz, 1H, 9-H), 5.16 (dd, *J* = 8.6, 4.2 Hz, 1H, 17-H), 5.07 (d, *J* = 71.6 Hz, 2H, H-19), 4.41 – 4.35 (m, 2H, H-12, H-3), 3.99 (t, *J* = 9.1 Hz, 1H, H-6), 2.95 (dd, *J* = 13.1, 8.2 Hz, 1H, H_a-2), 2.92 – 2.88 (m, 1H, H-10), 2.75 (dd, *J* = 12.9, 7.9 Hz, 1H, H_b-2), 2.65 (s, 1H, OH-3), 2.42 – 2.39 (m, 2H, H-7, H-16), 2.39 – 2.34 (m, 1H, H-5), 2.29 (td, *J* = 8.4, 3.5 Hz, 1H, H-14), 2.20 (ddd, *J* = 14.9, 3.5, 2.0 Hz, 1H, H_a-13), 2.16 (dt, *J* = 14.8, 3.4 Hz, 1H, H_a-4), 2.01 (s, 3H, H-18), 1.83 (s, 1H, OH-6), 1.80 – 1.75 (m, 1H, H_b-13), 1.76 – 1.73 (m, 1H, H_a-20), 1.72 – 1.67 (m, 1H, H_b-20), 1.67 – 1.62 (m, 1H, H_b-4), 1.03 (t, *J* = 7.4 Hz, 3H, H-21).

^{13}C NMR (176 MHz, CD_2Cl_2) δ = 173.7 (C-11), 171.3 (C-1), 153.4 (C-15), 138.9 (C-8), 127.9 (C-9), 105.2 (C-19), 79.7 (C-17), 79.1 (C-6), 78.9 (C-12), 64.2 (C-3), 54.6 (C-7), 53.0 (C-16), 45.5 (C-10), 43.2 (C-15), 42.0 (C-2), 41.9 (C-14), 34.4 (C-4), 32.9 (C-13), 28.3 (C-20), 21.4 (C-18), 9.7 (C-21).



Scheme 3: Proposed mechanism of transannular cyclization

Synthesis of acetylcollinolactone (5)



5 (anti) **5** (syn)

10 mg of compound **1** (27.7 µmol, 1 Eq.) was dissolved in 5 mL of dry pyridine. At 0 °C acetic acid anhydride (2 mL) was slowly added over 10 min. The reaction mixture was stirred for 20 hours at room temperature before 5 mL of water was added to quench the reaction. The solvent was removed *in vacuo* and the raw product was purified by preparative HPLC on a Kromasil 100 C_{18} with 50% acetonitrile/water at 17.5 mL/min (R_t = 16.8 min) to afford 9.4 mg (84%) of **5** as white, fluffy powder after lyophilization.

HR-ESI-MS (m/z): $[M+H]^+$ calculated for $C_{23}H_{31}O_6$: 403.2115; found 403.2118 (0.6 ppm err, 1.2 mSigma)

anti-form:
^{1}H NMR (700 MHz, CD_2Cl_2) δ = 5.90 (dt, *J* = 16.5, 1.1, 1H, H-7), 5.76 (dp, *J* = 7.5, 1.4, 1H, H-9), 5.56 (t, *J* = 6.1, 1H, H-17), 5.31 – 5.26 (m, 1H, H-3), 5.16 – 5.10 (m, 1H, H-6), 4.86 – 4.83 (m, 1H, H-16), 4.39 – 4.33 (m, 1H, H-12), 3.33 – 3.25 (m, 2H, H_a-2, H-10), 2.92 (dt, *J* = 15.8, 4.6, 1H, H_b-2), 2.80 – 2.73 (m, 1H, H-5), 2.64 (td, *J* = 8.5, 3.0, 1H, H-14), 2.48 (dt, *J* = 15.3, 5.1, 1H, H_b-4), 2.11 (s, 3H, H-23), 1.94 – 1.92 (m, 1H, H_a-13), 1.92 – 1.91 (m, 3H, H-18), 1.85 – 1.79 (m, 2H, H_a-4, H_b-13), 1.77 – 1.70 (m, 1H, H_a-20), 1.69 (d, *J* = 1.1, 3H, H-19), 1.67 – 1.58 (m, 1H, H_b-20), 1.01 (td, *J* = 7.4, 1.2, 3H, H-21).

^{13}C NMR (176 MHz, CD_2Cl_2) δ = 173.7 (C-11), 170.6 (C-1), 170.3 (C-22), 139.2 (C-7), 135.9 (C-8), 133.9 (C-15), 133.6 (C-16), 126.3 (C-6), 123.8 (C-9), 82.2 (C-17), 78.5 (C-12), 65.4 (C-3), 46.7 (C-14), 43.9 (C-5), 40.6 (C-10), 40.5 (C-2), 32.4 (C-13), 31.9 (C-4), 28.5 (C-20), 21.2 (C-23), 19.8 (C-18), 13.3 (C-19), 9.7 (C-21).

syn-form:
^{1}H NMR (700 MHz, CD_2Cl_2) δ = 5.95 (dt, *J* = 16.4, 1.3, 1H, H-7), 5.60 (dp, *J* = 8.4, 1.6, 1H, H-9), 5.39 (t, *J* = 4.9, 1H, H-17), 5.29 – 5.28 (m, 1H, H-3), 5.27 (dt, *J* = 4.9, 1.8, 1H, H-16), 5.15 (d, *J* = 5.8, 1H, H-6), 4.41 (ddt, *J* = 9.1, 7.4, 5.2, 1H, H-12), 3.36 (dd, *J* = 11.9, 8.4, 1H, H-10), 3.30 – 3.26 (m, 1H, H_a-2), 2.92 (dt, *J* = 15.8, 4.6, 1H, H_b-2), 2.70 – 2.66 (m, 1H, H-5), 2.52 (dd, *J* = 10.4, 4.8, 1H, H_a-4), 2.24 (ddd, *J* = 11.9, 9.2, 7.0, 1H, H-14), 2.09 (s, 3H, H-23), 2.08 – 2.02 (m, 2H, H-13), 1.92 – 1.91 (m, 3H, H-18), 1.79 – 1.75 (m, 2H, H_b-4, H_b-20), 1.67 – 1.58 (m, 1H, H_a-20), 1.60 (d, *J* = 1.5, 3H, H-19), 1.01 (td, *J* = 7.4, 1.2, 3H, H-21).

^{13}C NMR (176 MHz, CD_2Cl_2) δ = 173.8 (C-11), 170.5 (C-1), 170.3 (C-22), 148.9 (C-15), 138.7 (C-7), 138.0 (C-8), 124.1 (C-6), 121.5 (C-16), 120.6 (C-9), 80.2 (C-17), 78.7 (C-12), 65.2 (C-3), 46.7 (C-10), 45.4 (C-14), 44.9 (C-5), 40.6 (C-2), 35.1 (C-13), 32.6 (C-4), 28.6 (C-20), 23.7 (C-19), 21.2 (C-23), 20.4 (C-18), 10.0 (C-21).

Synthesis of benzoylcollinolactone (6)

6 (anti) **6** (syn)

10 mg of **1** (27.7 µmol, 1 Eq.) was dissolved in 20 mL of dry dichloromethane. DIC (*N,N'*-Diisopropylcarbodiimide, 10.7 µL,69.3 µmol, 2.5 Eq.) and DMAP (4-Dimethylaminopyridine, 0.68 mg, 5.5 µmol, 0.2 Eq.) were added, followed by benzoic acid (8.47 mg, 69.3 µmol, 2.5 Eq.). The reaction mixture was allowed to stir for 30 minutes at room temperature before heating up to 40 °C for additional 20 hours. The solvent was then removed *in vacuo* and the raw product was purified by preparative HPLC on a Kromasil 100 C_{18} with 65% acetonitrile/water at 17.5 mL/min (R_t = 12.9 min) to afford 9.6 mg (74%) of **6** as white, fluffy powder after lyophilization.

HR-ESI-MS (m/z): $[M+H]^+$ calculated for $C_{28}H_{33}O_6$: 465.2272; found 465.2280 (1.8 ppm err, 3.2 mSigma)

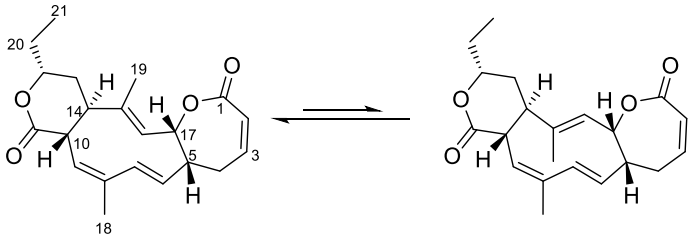
anti-form:
^{1}H NMR (700 MHz, CD_2Cl_2) δ = 8.07 (ddd, *J* = 8.4, 5.0, 1.4, 2H, H-24), 7.64 (tdd, *J* = 7.6, 2.3, 1.0, 1H, H-26), 7.53 – 7.48 (m, 2H, H-25), 5.93 (dt, *J* = 16.4, 1.1, 1H, H-7), 5.78 (dt, *J* = 7.5, 1.4, 1H, H-9), 5.68 (t, *J* = 6.0, 1H, H-17), 5.56 (dtd, *J* = 9.7, 4.6, 1.9, 1H, H-3), 5.19 (dd, *J* = 16.4, 10.1, 1H, H-6), 4.88 (dd, *J* = 6.2, 1.4, 1H, H-16), 4.39 – 4.33 (m, 1H, H-12), 3.49 – 3.44 (m, 1H, H_a-2), 3.28 (t, *J* = 8.0, 1H, H-10), 3.09 (dd, *J* = 15.7, 4.4, 1H, H_b-2), 2.93 – 2.86 (m, 1H, H-5), 2.69 – 2.63 (m, 2H, H_b-4, H-14), 1.96 (d, *J* = 2.0, 2H, H_a-4, H_a-13), 1.95 – 1.91 (m, 3H, H-18), 1.81 (ddd, *J* = 15.0, 10.2, 8.6, 1H, H_b-13), 1.74 (dd, *J*=14.3, 7.2, 1H, H_a-20), 1.71 (s, 3H, H-19), 1.66 – 1.59 (m, 1H, H-20), 1.01 (td, *J* = 7.5, 2.0, 3H, H-21).

^{13}C NMR (176 MHz, CD_2Cl_2) δ = 173.7 (C-11), 170.6 (C-1), 165.7 (C-22), 139.4 (C-7), 135.9 (C-8), 133.8 (C-23), 133.7 (C-16), 130.2 (C-15), 129.8 (C-24), 129.0 (C-25), 126.1 (C-6), 123.8 (C-9), 82.3 (C-17), 78.4 (C-12), 66.1 (C-3), 46.7 (C-14), 44.2 (C-5), 40.8 (C-2), 40.6 (C-10), 32.5 (C-13), 32.1 (C-4), 28.5 (C-20), 19.8 (C-18), 13.3 (C-19), 9.7 (C-21).

syn-form:
^{1}H NMR (700 MHz, CD_2Cl_2) δ = 8.07 (ddd, *J* = 8.4, 5.0, 1.4, 2H, H-24), 7.64 (tdd, *J* = 7.6, 2.3, 1.0, 1H, H-26), 7.53 – 7.48 (m, 2H, H-25), 5.98 (dt, *J* = 16.2, 1.3, 1H, H-7), 5.61 (dp, *J* = 8.4, 1.5, 1H, H-9), 5.52 (dt, *J* = 9.5, 4.4, 2H, H-3, H-17), 5.30 (dd, *J* = 5.4, 1.5, 1H, H-16), 5.21 (s, 1H, H-6), 4.44 – 4.40 (m, 1H, H-12), 3.46 – 3.41 (m, 1H, H_a-2), 3.37 (dd, *J*=11.9, 8.4, 1H, H-10), 3.09 (dd, *J* = 15.7, 4.4, 1H, H_b-2), 2.82 – 2.76 (m, 1H, H-5), 2.67 (t, *J*=5.1, 1H, H_b-4), 2.26 (ddd, *J* = 12.0, 9.2, 7.0, 1H, H-14), 2.11 – 2.02 (m, 1H, H-13), 1.95 – 1.93 (m, 3H, H-18), 1.88 (ddd, *J*=14.2, 3.5, 1.4, 1H, H_a-4), 1.85 – 1.69 (m, 3H, H_a-20), 1.64 – 1.62 (m, 3H, H-19), 1.01 (td, *J* = 7.5, 2.0, 3H, H-21).

^{13}C NMR (176 MHz, CD_2Cl_2) δ = 173.8 (C-11), 170.4 (C-1), 165.9 (C-22), 149.0 (C-15), 138.9 (C-7), 138.0 (C-8), 133.8 (C-26), 130.2 (C-23), 129.9 (C-24), 128.9 (C-25), 124.0 (C-6), 121.5 (C-16), 120.7 (C-9), 80.3 (C-17), 78.6 (C-12), 66.1 (C-3), 46.6 (C-10), 45.4 (C-14), 45.1 (C-5), 40.7 (C-2), 35.1 (C-13), 32.8 (C-4), 28.6 (C-20), 23.7 (C-19), 20.4 (C-18), 10.0 (C-21).

Synthesis of collinolactenone (7)



7 (anti) **7** (syn)

25 mg of **1** (69.4 µmol, 1 Eq.) was dissolved in 50 mL of dry acetonitrile. Burgess reagent (1-Methoxy-N-triethylammoniosulfonyl-methanimidate, 66.1 mg, 277.4 µmol, 4 Eq.) was added slowly over 1 hour before the reaction solution was refluxed for 20 hours. After removal of the solvent *in vacuo*, the product was purified by preparative HPLC on a Kromasil 100 C_{18} with 50% acetonitrile/water at 17.5 mL/min. The pure compound collinolactenone (**7**) eluted at R_t = 16.0 min. Lyophilizing the product containing fractions yielded 17.1 mg (72%) of **7** as a white, fluffy powder.

HR-ESI-MS (m/z): $[M+H]^+$ calculated for $C_{21}H_{27}O_4$: 343.1904; found 343.1904 (0 ppm err, 10.5 mSigma)

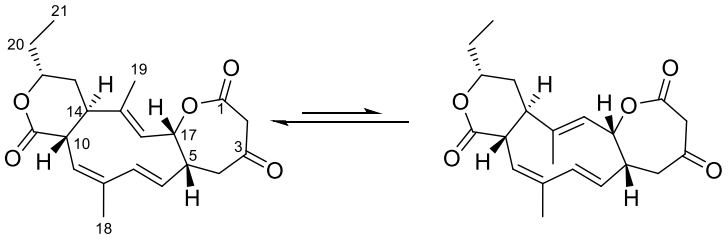
anti-form:
^{1}H-NMR (700 MHz, CD_2Cl_2): δ (ppm) = 6.67 – 6.62 (m, 1H, H-3), 6.07 (ddd, J = 10.8, 2.4, 1.1 Hz, 1H, H-2), 5.86 (dt, J = 16.4, 1.0 Hz, 1H, H-7), 5.76 (dp, J = 7.5, 1.5 Hz, 1H, H-9), 5.38 (dd, J = 7.1, 5.6 Hz, 1H, H-17), 4.89 – 4.85 (m, 1H, H-6), 4.35 (tdd, J = 7.5, 6.6, 5.7, 2.1 Hz, 1H, H-16), 3.25 (ddd, J = 8.6, 7.5, 1.1 Hz, 1H, H-12), 2.78 – 2.71 (m, 2H, 5-H, H_a-4), 2.63 (td, J = 8.5, 3.0 Hz, 1H, H-14), 2.56 – 2.48 (m, 1H, H_b-4), 1.94 (s, 3H, H-18), 1.90 (dd, J = 3.0, 2.2 Hz, 1H, H_a-13), 1.82 – 1.86 (m, 1H, H-20), 1.80 - 1.86 (m, 1H, H_b-13), 1.63 - 1.76 (m, 1H), 1.60 (s, 3H, H-19), 1.00 (t, J = 7.5, 2.4 Hz, 3H, H-21).

^{13}C-NMR (176 MHz, CD_2Cl_2): δ (ppm) = 173.8 (C-11), 169.5 (C-1), 140.93 (C-7), 139.3 (C-8), 135.9 (C-2), 133.9 (C-15), 133.3 (C-4), 126.8 (C-3), 125.45 (C-6), 123.8 (C-9), 83.0 (C-17), 78.5 (C-12), 54.2 (C-14), 49.5 (C-5), 40.6 (C-10), 32.5 (C-16), 29.2 (C-13), 28.5 (C-20), 19.9 (C-18), 13.2 (C-19), 9.7 (C-21).

syn-form:
^{1}H-NMR (700 MHz, CD_2Cl_2): δ (ppm) = 6.62 – 6.58 (m, 1H, H-3), 6.03 (ddd, J = 10.9, 2.5, 1.2 Hz, 1H, H-2), 5.92 (dt, J = 16.4, 1.3 Hz, 1H, H-7), 5.60 (dp, J = 8.4, 1.5 Hz, 1H, H-9), 5.20 (m, 3H, 6-H, 15-H, H-17), 4.36 – 4.43 (m, 1H, H-12), 3.33 (dd, J = 11.9, 8.4 Hz, 1H, H-10), 2.82 – 2.78 (m, 1H, H_a-4$_a$), 2.70 – 2.64 (m, 1H, H-5), 2.45 – 2.39 (m, 1H, H_b-4), 2.24 – 2.28 (m, 1H, H-14), 2.10 – 2.06 (m, 2H, H-13), 1.92 (s, 3H, H-18), 1.65 – 1.86 (m, 1H, H-20), 1.58 (s, 3H, H-19), 1.00 (td, J = 7.5, 2.4 Hz, 3H, H-21).

^{13}C-NMR (176 MHz, CD_2Cl_2): δ (ppm) = 173.8 (C-11), 149.4 (C-1), 140.6 (C-7), 133.3 (C-8), 125.3 (C-2), 124.8 (C-3), 121.7 (C-6), 120.6 (C-9), 81.1 (C-17), 78.8 (C-12), 54.2 (C-14), 49.7 (C-5), 44.9 (C-10), 35.1 (C-16), 29.7 (C-13), 28.6 (C-20), 23.7 (C-18), 20.5 (C-19), 10.0 (C-21).

Synthesis of ketocollinolactone (8)



8 (anti) **8** (syn)

10 mg of **1** (27.7 µmol, 1 Eq.) was dissolved in 10 mL of dry dichloromethane and Dess–Martin periodinane (3-Oxo-1,3-dihydro-11λ5,2-benziodoxole-1,1,1-triyl triacetate, 12.94 mg, 30.5 µmol, 1.1 Eq.) were added. The reaction mixture was stirred for 4 hours at room temperature before saturated sodium bicarbonate solution was added and extracted three times with dichloromethane (20 mL each). The combined organic fractions were evaporated *in vacuo* and the raw product was purified by preparative HPLC on a Kromasil 100 C_{18} with 34% acetonitrile/water at 17.5 mL/min (R_t = 29.3 min) to afford 14.9 mg (47%) of **8** as white, fluffy powder after lyophilization.

HR-ESI-MS (m/z): $[M+H]^+$ calculated for $C_{21}H_{27}O_5$: 359.1853; found 377.1851 (0.4 ppm err, 14.7 mSigma)

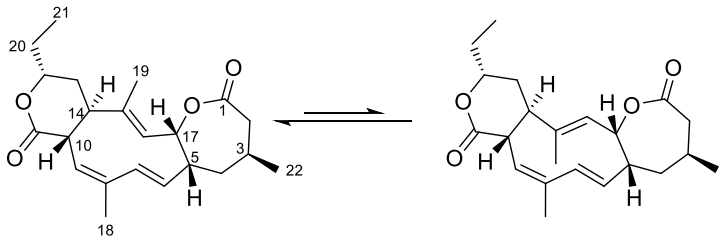
anti-form:
^{1}H-NMR (700 MHz, CD_2Cl_2): δ (ppm) = 5.91 (d, J = 16.4 Hz, 1H, H-7), 5.80 (dt, J = 7.5, 1.1, 1.1 Hz, 1H, H-9), 5.52 (t, J = 5.7 Hz, 1H, H-17), 5.15 – 5.24 (m, 1H, H-6), 4.86 (d, J = 6.4 Hz, 1H, H-16), 4.30 – 4.36 (m, 1H, H-12), 3.83 (d, J = 19.5 Hz, 1H, H_a-4), 3.56 (d, J = 19.5 Hz, 1H, H_b-4), 3.25 (t, J = 8.1 Hz, 1H, H-10), 2.81 - 3.01 (m, 1H, H-2), 2.77 (m, 1H, H-5), 2.64 (m, 1H, H-14), 1.92 – 1.93 (m, 3H, H-16), 1.87 – 1.91 (m, 1H, H_a-13), 1.79 - 1.84 (m, 1H, H_b-13), 1.67 – 1.79 (m, 1H, H_a-20), 1.63 (s, 3H, H-19), 1.58 - 1.64 (m, 1H, H_b-20), 1.01 (t, J = 7.4 Hz, 3H, H-21).

^{13}C-NMR (176 MHz, CD_2Cl_2): anti, δ (ppm) = 200.8 (C-3), 173.4 (C-11), 168.3 (C-1), 140.3 (C-7), 135.6 (C-8), 134.9 (C-15), 132.9 (C-16), 124.5 (C-6), 124.4 (C-9), 82.6 (C-17), 78.5 (C-12), 49.7 (C-4), 47.4 (C-5), 46.9 (C-14), 45.0 (C-2), 40.8 (C-10), 32.6 (C-13), 28.7 (C-20), 20.0 (C-18), 13.6 (C-19), 9.9 (C-21)

syn-form:
^{1}H-NMR (700 MHz, CD_2Cl_2): δ (ppm) = 5.96 (d, J = 16.2 Hz, 1H, H-7), 5.63 (dt, J = 8.4, 1.4, 1.4 Hz, 1H, H-9), 5.31 (dd, J = 10.0, 5.1 Hz, 1H, H-17), 5.15 – 5.24 (m, 2H, H-6, H-16), 4.40 (m, 1H, H-12), 3.76 (d, J = 20.3 Hz, 1H, H_a-4), 3.53 (d, J = 19.9 Hz, 1H, H_b-4), 3.34 (dd, J = 11.8, 8.3 Hz, 1H, H-10), 2.82 – 2.91 (m, 2H, H-2), 2.66– 2.71 (m, 1H, H-5), 2.29 (m, 1H, H-14), 2.01 – 2.06 (m, 1H, H-13), 1.95 (d, J = 1.3 Hz, 3H, H-18), 1.69 – 1.78 (m, 1H, H_a-20), 1.64 (s, 3H, H-19), 1.59 - 1.65 (m, 1H, H_b-20), 1.01 (t, J = 7.5 Hz, 3H, H-21).

^{13}C-NMR (176 MHz, CD_2Cl_2): syn, δ (ppm) = 201.1 (4-CO), 173.5 (C-10), 167.9 (C-2), 150.0 (C-14), 139.7 (C-7), 137.8 (C-8), 122.5 (C-6), 121.2 (C-9), 120.5 (C-15), 80.9 (C-15a), 78.6 (C-12), 49.3 (C-5), 48.3 (C-5a), 46.9 (C-9a), 45.8 (C-13a), 45.4 (C-3), 35.1 (C-13), 28.8 (C-17), 23.9 (C-19), 20.5 (C-16), 10.2 (C-18)

Synthesis of methylcollinolactone (9)



9 (anti) **9** (syn)

To heat-dried Copper(I)-iodine (16.6 mg, 87.6 µmol, 4 Eq.) a solution of methyllithium (0.08 M) in diethyl ether (1 mL, 87.6 µmol, 4 Eq.) was added at -30 °C and stirred for 1h before adding **7** (7.5 mg, 21.9 µmol, 1 Eq.) at -78 °C. The reaction mixture was allowed to heat to -10 °C over the course of 4 hours. Saturated ammonium chloride solution was added and stirred at room temperature for another hour for quenching. The organic phase was extracted three times with DCM. The combined organic phases were dried with sodium sulfate and the solvent was removed *in vacuo*. The raw product was purified by preparative HPLC on a Kromasil 100 C_{18} with 55% acetonitrile/water at 17.5 mL/min (R_t = 16.9 min) to afford 3.1 mg (39%) of **9** after lyophilization.

HR-ESI-MS (m/z): $[M+H]^+$ calculated for $C_{22}H_{31}O_4$: 359.2217; found 359.2225 (2.2 ppm err, 3.7 mSigma)

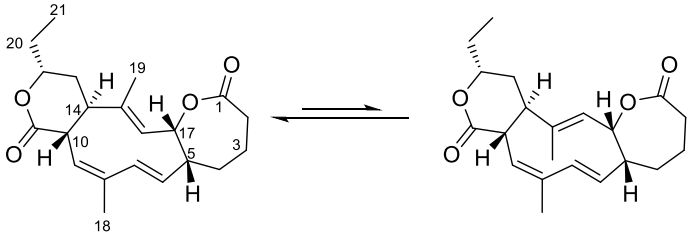
anti-form:
^{1}H NMR (700 MHz, C_6D_6) δ = 6.13 (dq, *J* = 7.4, 1.5 Hz, 1H, H-9), 5.59 (dd, *J* = 16.5, 1.9 Hz, 1H, H-7), 4.99 – 4.95 (m, 1H, H-6), 4.95 – 4.92 (m, 1H, H-17), 4.79 (d, *J* = 6.6 Hz, 1H, H-16), 3.82 – 3.76 (m, 1H, H-12), 2.78 (t, *J* = 7.5 Hz, 1H, H-10), 2.54 – 2.50 (m, 1H, H_a-2), 2.29 (tt, *J* = 10.9, 5.4 Hz, 1H, H-5), 2.20 (td, *J* = 8.7, 2.5 Hz, 1H, H-14), 1.88 – 1.81 (m, 1H, H-3), 1.84 (s, 3H, H-18), 1.83 – 1.75 (m, 1H, H_b-2), 1.70 (ddd, *J* = 14.6, 11.9, 4.1 Hz, 1H, H_a-4), 1.64 – 1.56 (m, 1H, H_b-4), 1.48 – 1.40 (m, 1H, H_a-20), 1.36 – 1.30 (m, 1H, H_a-13), 1.26 – 1.18 (m, 2H, H_b-13, H_b-20), 1.03 (s, 3H, H-19), 0.81 (t, *J* = 7.4 Hz, 3H, H-21), 0.62 – 0.59 (m, 3H, H-22).

^{13}C NMR (176 MHz, C_6D_6) δ = 172.1 (C-11), 171.4 (C-1), 138.5 (C-7), 135.1 (C-8), 134.2 (C-16), 132.7 (C-15), 127.5 (C-6), 124.4 (C-9), 81.1 (C-17), 77.0 (C-12), 46.4 (C-14), 43.6 (C-5), 40.4 (C-10), 39.8 (C-2), 33.5 (C-4), 32.5 (C-13), 28.4 (C-20), 24.8 (C-3), 20.2 (C-22), 20.1 (C-18), 12.5 (C-19), 9.6 (C-21).

syn-form:
^{1}H NMR (700 MHz, C_6D_6) δ = 5.87 (dq, *J* = 8.3, 1.5 Hz, 1H, H-9), 5.54 (d, *J* = 16.3 Hz, 1H, H-7), 5.01 – 4.96 (m, 1H, H-6), 4.59 – 4.55 (m, 1H, H-17), 4.55 – 4.50 (m, 1H, H-16), 3.92 – 3.86 (m, 1H, H-12), 2.97 – 2.90 (m, 1H, H-10), 2.47 (dd, *J* = 14.1, 7.5 Hz, 1H, H_a-2), 2.00 (dp, *J* = 9.4, 4.4 Hz, 1H, H-5), 1.88 – 1.84 (m, 1H, H-14), 1.85 – 1.81 (m, 1H, H_b-2), 1.80 (s, 3H, H-18), 1.79 – 1.74 (m, 1H, H-3), 1.64 – 1.61 (m, 1H, H_a-4), 1.58 (s, 3H, H-19), 1.58 – 1.56 (m, 1H, H_a-13), 1.55 – 1.49 (m, 2H, H_b-13, H_a-20), 1.45 – 1.40 (m, 1H, H_b-4), 1.30 – 1.25 (m, 1H, H_b-20), 0.88 (t, *J* = 7.4 Hz, 3H, H-21), 0.62 (dd, *J* = 9.0, 6.8 Hz, 3H, H-22).

^{13}C NMR (176 MHz, C_6D_6) δ = 172.3 (C-11), 171.4 (C-1), 147.5 (C-15), 138.2 (C-7), 137.0 (C-8), 123.2 (C-6), 121.9 (C-16), 121.7 (C-9), 79.8 (C-17), 77.2 (C-12), 46.4 (C-10), 46.3 (C-5), 45.4 (C-14), 40.2 (C-2), 36.0 (C-4), 34.7 (C-13), 28.6 (C-20), 24.9 (C-3), 23.9 (C-19), 21.1 (C-22), 20.2 (C-18), 10.0 (C-21).

Synthesis of dehydrocollinolactone (10)



10 (anti) **10** (syn)

Commercially obtained Stryker reagent (from Sigma-Aldrich) did not lead to the desired product, so fresh Strykers had to be prepared according to a previously described procedure.[5]
Compound **7** (7 mg, 20.4 µmol, 1 Eq.) and the synthesized stryker reagent (13.3 mg, 6.78 µmol, 0.4 Eq.) were dissolved in 10 mL of abs. benzene. After 12 h of stirring at room temperature the reaction was quenched by addition of saturated ammonium chloride solution and extracted three times with toluene. The combined organic phases were dried with sodium sulfate and purified by preparative HPLC on a Kromasil 100 C_{18} with 50% acetonitrile/water at 17.5 mL/min (R_t = 16.2 min) to afford 3.4 mg (48%) of **10** after lyophilization.

HR-ESI-MS (m/z): $[M+H]^+$ calculated for $C_{21}H_{29}O_4$: 345.2060; found 345.2067 (1.9 ppm err, 18.6 mSigma)

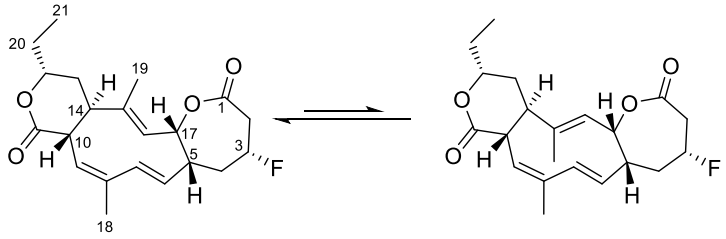
anti-form:
^{1}H NMR (700 MHz, CD_2Cl2) δ = 5.85 (dt, *J* = 16.5, 1.0 Hz, 1H, H-7), 5.74 (dp, *J* = 7.5, 1.4 Hz, 1H, H-9), 5.44 (t, *J* = 6.3 Hz, 1H, H-17), 5.15 (dd, *J* = 16.5, 10.0 Hz, 1H, H-6), 4.83 – 4.78 (m, 1H, H-16), 4.38 – 4.33 (m, 1H, H-12), 3.30 – 3.23 (m, 1H, H-10), 3.00 – 2.94 (m, 1H, H-2_a), 2.73 – 2.65 (m, 1H, H-2_b), 2.62 (td, *J* = 8.6, 3.0 Hz, 1H, H-14), 2.48 (ddt, *J* = 10.8, 9.2, 5.6 Hz, 1H, H-5), 2.22 – 2.16 (m, 1H, H-20_a), 2.03 – 1.95 (m, 1H, H-3_a), 1.92 – 1.91 (m, 3H, H-18), 1.90 (dd, *J* = 3.0, 2.2 Hz, 1H, H-13_a), 1.83 – 1.77 (m, 1H, H-13_b), 1.76 – 1.69 (m, 2H,H-4_a, H-3_b), 1.67 (d, *J* = 1.1, 3H Hz, H-19), 1.65 – 1.59 (m, 2H, H-20_b, H-4_b), 1.01 (td, *J* = 7.5, 1.4 Hz, 3H, H-21).

^{13}C NMR (176 MHz, CD_2Cl2) δ = 174.0 (C-11), 173.5 (C-1), 138.6 (C-7), 136.2 (C-8), 134.1 (C-16), 133.7 (C-15), 127.9 (C-6), 123.7 (C-9), 82.4 (C-17), 78.6 (C-12), 49.3 (C-5), 47.0 (C-14), 40.8 (C-10), 32.7 (C-13), 32.6 (C-2), 28.6 (C-4), 27.6 (C-20), 20.1 (C-18), 18.6 (C-3), 13.4 (C-19), 9.8 (C-21).

syn-form:
^{1}H NMR (700 MHz, CD_2Cl_2) δ = 5.89 (dt, *J* = 16.3, 1.2, 1H, H-7), 5.58 (dp, *J* = 8.3, 1.5, 1H, H-9), 5.26 (t, *J* = 4.7, 1H, H-17), 5.21 (tt, *J* = 2.8, 1.4, 1H, H-16), 5.20 – 5.17 (m, 1H, H-6), 4.42 – 4.36 (m, 1H, H-12), 3.35 (dd, *J* = 11.9, 8.4, 1H, H-14), 2.94 – 2.85 (m, 1H, H_a-2), 2.73 – 2.65 (m, 1H, H_b-2), 2.41 – 2.35 (m, 1H, H-5), 2.22 (s, 1H, H-10), 2.21 – 2.16 (m, 1H, H_b-4), 2.09 – 2.03 (m, 2H, H-13), 1.98 – 1.93 (m, 1H, H_a-3), 1.92 (dd, *J* = 3.5, 1.9, 3H, H-18), 1.82 – 1.77 (m, 1H, H_b-3), 1.75 – 1.69 (m, 1H, H_b-20), 1.67 – 1.62 (m, 2H, H_a-4, H_a-20), 1.59 (d, *J* = 1.3, 3H, H-19), 1.01 (td, *J* = 7.5, 1.4, 3H, H-21).

^{13}C NMR (176 MHz, CD_2Cl_2) δ = 174.1 (C-11), 173.4 (C-1), 148.4 (C-15), 138.3 (C-8), 138.3 (C-7), 124.8 (C-6), 122.0 (C-16), 120.6 (C-9), 80.6 (C-17), 78.8 (C-12), 50.3 (C-5), 46.8 (C-14), 45.6 (C-10), 35.1 (C-13), 32.8 (C-2), 28.8 (C-4, C-20), 23.8 (C-19), 20.6 (C-18), 18.4 (C-3), 10.2 (C-21).

Synthesis of fluorocollinolactone (11)



11 (anti) **11** (syn)

N,N-Diethylaminosuflur trifluoride (DAST, 16.5 µL, 124.82 µmol, 3 Eq.) was added to a solution of **1** (15 mg, 41.6 µmol, 1 Eq.) in 2 mL of abs. DCM at -78 °C. After 3 h of stirring at -78 °C the reaction was quenched by addition of water. Removal of solvent and purification by preparative HPLC on a Kromasil 100 C_{18} with 45% acetonitrile/water at 17.5 mL/min (R_t = 27.5 min) to afford 6.1 mg (40%) of **11** after lyophilization.

HR-ESI-MS (m/z): $[M+H]^+$ calculated for $C_{21}H_{28}O_4F$: 363.1966; found 363.1967 (2.8 ppm err, 5.5 mSigma)

anti-form:
^{1}H NMR (700 MHz, CD_2Cl_2) δ = 5.88 (d, *J* = 16.4, 1H, H-7), 5.77 (dt, *J* = 7.5, 1.5, 1H, H-9), 5.24 (t, *J* = 6.3, 1H, H-17), 5.14 (dd, *J* = 16.4, 9.7, 1H, H-6), 5.08 – 4.95 (m, 1H, H-3), 4.82 (dd, *J* = 6.9, 1.4, 1H, H-16), 4.35 (tdd, *J* = 7.4, 6.5, 2.1, 1H, H-12), 3.42 (dddd, *J* = 24.6, 16.3, 8.1, 2.3, 1H, H_a-2), 3.25 (t, *J* = 8.0, 1H, H-10), 2.98 (dd, *J* = 30.2, 16.1, 1H, H_b-2), 2.63 (qt, *J* = 7.7, 3.3, 2H, H_b-4, H-14), 2.60 – 2.55 (m, 1H, H-5), 2.00 – 1.94 (m, 1H, H_a-4), 1.92 (s, 3H, H-18), 1.92 – 1.88 (m, 1H, H_b-13), 1.83 – 1.76 (m, 1H, H_a-13), 1.76 – 1.68 (m, 1H, H_b-20), 1.65 (s, 3H, H-19), 1.64 – 1.60 (m, 1H, H_a- 20), 1.01 (td, *J* = 7.4, 1.9, 3H, H-21).

^{13}C NMR (176 MHz, CD_2Cl_2) δ = 173.6 (C-11), 170.0 (C-1), 139.4 (C-7), 135.8 (C-8), 134.3 (C-15), 133.1 (C-16), 126.2 (C-6), 124.0 (C-9), 86.0 (C-3), 81.8 (C-17), 78.5 (C-12), 46.8 (C-14), 44.0 (C-5), 41.3 (C-2), 40.6 (C-10), 34.1 (C-4), 32.4 (C-13), 28.5 (C-20), 20.0 (C-18), 13.3 (C-19), 9.7 (C-21).

syn-form:
^{1}H NMR (700 MHz, CD_2Cl_2) δ = 5.92 (d, J = 16.4, 1H, H-7), 5.61 (dt, J = 8.4, 1.6, 1H, H-9), 5.22 – 5.17 (m, 2H, H-6, H-16), 5.08 – 4.95 (m, 1H, H-3), 5.03 – 5.00 (m, 1H, H-17), 4.41 – 4.37 (m, 1H, H-12), 3.45 – 3.42 (m, 1H, H_a-2), 3.33 (dd, J = 12.0, 8.4, 1H, H-10), 3.05 – 2.98 (m, 1H, H_b-2), 2.63 (qt, J = 7.7, 3.3, 1H, H_a-4), 2.54 – 2.49 (m, 1H, H-5), 2.25 (ddd, J = 11.9, 9.0, 7.3, 1H, H-14), 2.08 – 2.00 (m, 3H, H-13), 1.99 – 1.94 (m, 1H, H_b-4), 1.92 (s, 3H, H-18), 1.79 – 1.75 (m, 1H, H_a-20), 1.63 – 1.60 (m, 1H, H_b-20), 1.60 (d, J = 1.3, 3H, H-19), 1.01 (td, J = 7.4, 1.9, 3H, H-21).

^{13}C NMR (176 MHz, CD_2Cl_2) δ = 173.7 (C-11), 169.8 (C-1), 149.2 (C-15), 139.0 (C-7), 137.9 (C-8), 123.2 (C-6), 121.0 (C-16), 120.8 (C-9), 85.0 (C-3), 80.2 (C-17), 78.7 (C-12), 46.7 (C-10), 45.8 (C-5), 45.5 (C-14), 41.2 (C-2), 34.9 (C-13), 34.3 (C-4), 28.6 (C-20), 23.7 (C-19), 20.3 (C-18), 10.0 (C-21).

SUPPORTING INFORMATION

Sequencing and genetic engineering

General remarks:
Streptomyces Gö 40/10 was isolated from a soil sample collected in Bolivia. The sequence can be found at NCBI BioProject: SAMN18970196.

Bacterial Strains and Growth Conditions:
Commercial *E. coli* DH5alpha and Mach1 T1 were used to maintain plasmids. *E. coli* ET12567/pUZ8002 was used to perform conjugations of plasmids into streptomycetes. All *E. coli* strains were cultivated in liquid and solid LB-medium at 37 °C. *Streptomyces* sp. were grown at 30 °C in soy flour medium (SFM)[6] followed by preparation of spore suspensions in 20% glycerol. Appropriate antibiotics were supplemented as necessary (50 µg/mL apramycin; 50 µg/mL hygromycin; 50 µg/mL nalidixic acid; 0.5 µg/mL thiostrepton; 25 µg/mL kanamycin; and 25 µg/mL chloramphenicol).

Construction of knock-out mutants in *S.* Gö 40/10 strain:
Two strategies to generate knock-out mutants in *S.* Gö 40/10 were implemented in this study. CRISPR-cBEST system was used to knock-out the following genes: LLPMBPKK_00314, LLPMBPKK_00542, *colL* and LLPMBPKK_06915. The identification of protospacers compatible with CRISPR-cBEST was done using CRISPy-web[7] (Table S1). The protospacers were cloned in the linearized pCRISPR-cBEST plasmid as specified previously.[8] The resulting constructs were individually introduced in *S*. Gö 40/10 via conjugation from *E. coli* ET12567/pUZ8002.[6] Apramycin (50 µg/mL) was used for selection of recombinant *Streptomyces* strains. Primers amplifying several-hundred base pairs region containing the base editing window were designed (Table S2). Colony PCR was used to amplify the designed DNA fragments directly from the *S.* Gö 40/10 colonies. Lastly, the PCR products were cleaned up by GeneJET PCR Purification Kit (Thermo Fisher Scientific, USA) and then Sanger sequenced by Mix2Seq kit (Eurofins Genomics, Germany).
DNA fragments (874 bp and 794 bp), containing the central parts of LLPMBPKK_00537 and LLPMBPKK_07936 genes were amplified by PCR from gDNA of *S*. Gö 40/10; the primers GoR3_0537_R_Fw, GoR3_0537_R_Rv, GoR39_07936_R_Fw and GoR39_07936_R_Rv were used (Table S2). These primers included the restriction sites EcoRI and HindIII respectively, to allow proper ligation with the 3.0 kb EcoRI-HindIII fragment from pSOK201 plasmid containing ColE1, oriT and AmR.[9] The resulting constructs were conjugated in *S*. Gö 40/10 as above mentioned.

Construction of *S*. Gö 40/10 strain that overexpresses a transcriptional factor luxR from collinolactone cluster:
A putative trancriptional activator gene (*colA*) that belongs to the luxR family was identified in the cluster of **1**. A synthetic cassette (1012 bp) containing the luxR gene (888 bp) under the control of kasOp* promoter (63 bp) and flanking restriction sites (HindIII/XbaI) was synthesized and cloned in plasmid pUC57 by GenScript company. The synthetic cassette kasOp*_LuxR_G23_luxR was subcloned in the hygromycin resistant pKC1218 plasmid.[10] The resulting construct and the empty pKC1218 plasmid were introduced in *S*. Gö 40/10 via conjugation from *E. coli* ET12567/pUZ8002 as above mentioned. Hygromycin (50 µg/mL) was used for selection of positive recombinant strains.

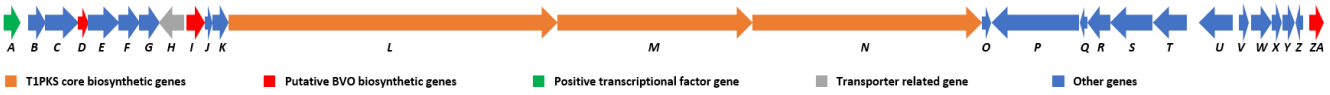
SUPPORTING INFORMATION

Table S1. List of protospacers used for CRISPR-BEST system

Name	Sequence (5´-3´)	Target
GoR1_0314	CGGTTGGTAGGATCGACGGCTTCCAGGAGAAGGGCAGGCGGTTTTA GAGCTAGAAATAGA	LLPMBPKK_00314, Region 1
GoR3_0542	CGGTTGGTAGGATCGACGGCGAGGTCCAGGAACGCCAGATGTTTTA GAGCTAGAAATAGA	LLPMBPKK_00542, Region 3
GoR23_*colL*	CGGTTGGTAGGATCGACGGCCAGGCCCAGCTGTGGGGACTGTTTTA GAGCTAGAAATAGA	LLPMBPKK_*colL*, Region 23
GoR31_06915	CGGTTGGTAGGATCGACGGCGGGTCTCAACGGGCTGGTATGTTTTA GAGCTAGAAATAGA	LLPMBPKK_06915, Region 31

Table S2. List of oligonucleotide primers used in this work

Name	Sequence (5´-3´)	Characteristics
GoR1_0314_Fw	GTCCAGGTCGTTGCGTAG	Screening of KO mutant, LLPMBPKK_00314
GoR1_0314_Rv	GTGTATGCGGGTGGTGTG	Screening of KO mutant, LLPMBPKK_00314
GoR3_0542_Fw	TGCAGGGCGATGAGGTAGA	Screening of KO mutant, LLPMBPKK_00542
GoR3_0542_Rv	GAGAGCATGAGCGACGAAGA	Screening of KO mutant, LLPMBPKK_00542
GoR23_*colL*_Fw	CCTGCTGTCCCGTTGGTA	Screening of KO mutant, LLPMBPKK_06003
GoR23_*colL*_Rv	CCGGTATCGCGGCGAGTA	Screening of KO mutant, LLPMBPKK_06003
GoR31_06915_Fw	GCGCACGTCATCCTGGAA	Screening of KO mutant, LLPMBPKK_06915
GoR31_06915_Rv	CAAGTCCACACCGTCACC	Screening of KO mutant, LLPMBPKK_06915
GoR3_0537_R_Fw	GTCAAAGCTTCATGAAGACGAGTTCGGT	Construction of pSOK201- GoR3_0537_R vector
GoR3_0537_R_Rv	GTCAGAATTCGCTGTTCGAGAAGTTCCC	Construction of pSOK201- GoR3_0537_R vector
GoR39_07936_R_Fw	GTCAAAGCTTCTCGGTTCCTGGGGGATA	Construction of pSOK201- GoR3_07936_R vector
GoR39_07936_R_Rv	GTCAGAATTCTAGTGCTGGTGCTGGAAG	Construction of pSOK201- GoR3_07936_R vector



Gene	Predicted gene product
colA	Positive transcriptional regulator (luxR family)
colB	Unknown protein
colC	Asparagine synthase
colD	Flavin reductase
colE	Anthranilate 3-monooxygenase (4-hydroxyphenylacetate 3-monooxygenase)
colF	Methyltransferase
colG	DNA-binding protein
colH	Purine efflux pump PbuE
colI	Luciferase like monooxygenase
colJ	Class-II DAHP synthetase family protein
colK	Methylenetetrahydrofolate reductase
colL	T1PKS subunit
colM	T1PKS subunit
colN	T1PKS subunit
colO	Polyketide cyclase (SnoaL family)
colP	Chaperone protein HtpG
colQ	Unknown protein
colR	Methylmalonyl Co-A mutase (associated GTPase MeaB)
colS	Methylmalonyl Co-A mutase
colT	Methylmalonyl Co-A mutase (subunit beta)
colU	Membrane protein
colV	Cell division protein SepF
colW	bldA-regulated nucleotide-binding protein
colX	Nucleotide pyrophosphohydrolase
colY	Unknown protein
colZ	Unknown protein
colZA	Luciferase like monooxygenase

Figure S4. Region 1.23 is a T1PKS cluster presumably involved in biosynthesis of **1** from *Streptomyces* Gö 40/10: Organization of genes and predicted functions of their products.

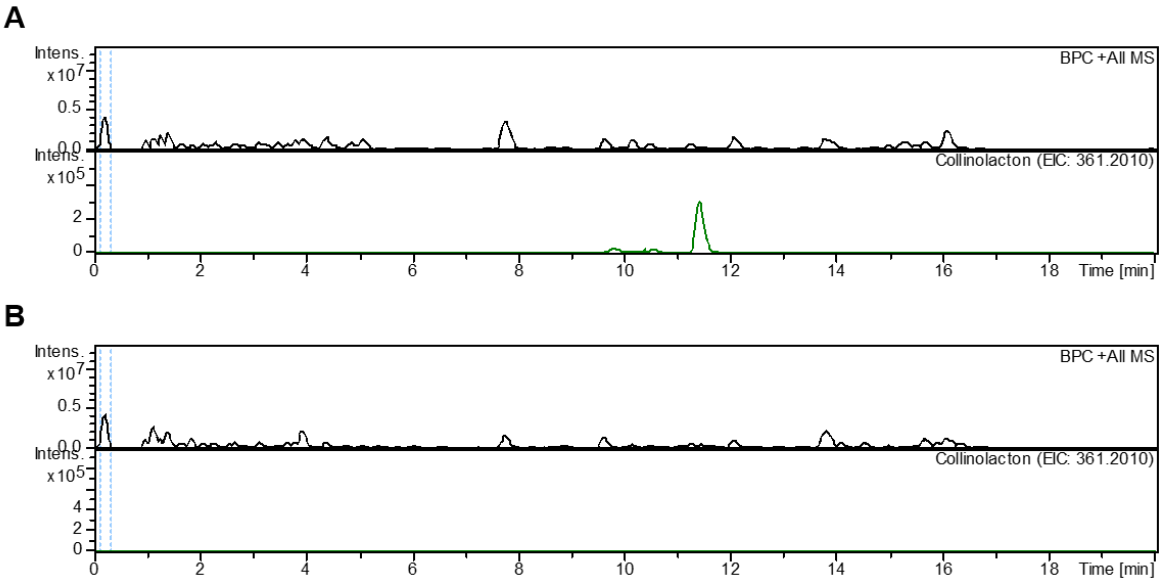
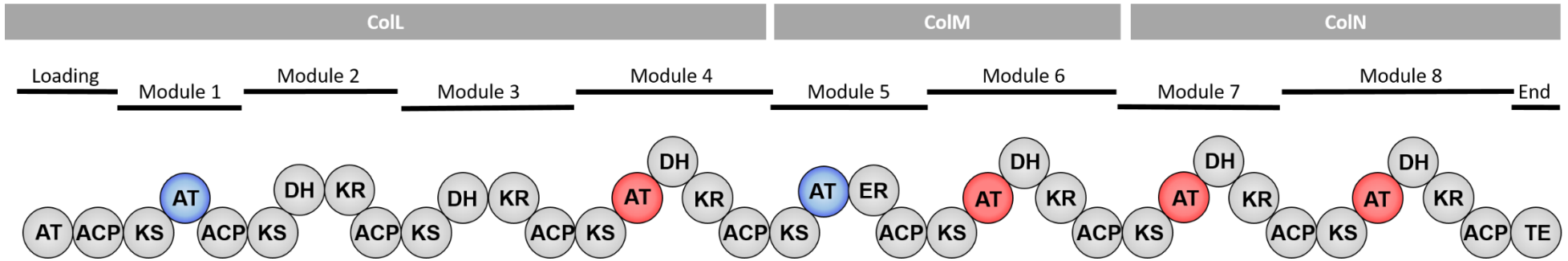


Figure S5: LC-MS chromatograms of supernatant from wild type strain Gö 40/10 (A) and mutant strain Gö 40/10 *colL*- (B). Displayed in black is the base peak chromatogram (BPC), in green the extracted ion chromatogram (EIC) of **1** (361.2010 ± 0.005 Da). Both chromatograms are scaled equally.

SUPPORTING INFORMATION



Abbreviation	Gene name
AT (red)	Acyltransferase domain (prediction: malonyl)
AT (blue)	Acyltransferase domain (prediction: methylmalonyl)
ACP	Acyl-carrier protein domain
KS	Keto-synthase domain
DH	Dehydratase domain
ER	Enoylreductase domain
TE	Thioesterase domain

Figure S6: Domain organization of the putative collinolactone (**1**) PKS. Blue colored AT domains indicate a predicted specificity for methylmalonyl-CoA and red colored domains for malonyl-CoA extender units.

Production curve of strain Gö 40/10 with pKC1218-KasOp_luxR construct

To quantify the increased production of **1** in strain Gö 40/10 with pKC1218-KasOp_luxR construct, five independent colonies were transferred onto agar plates, incubated for 7 days and used for cryo stock preparation. Similarly, cryo stocks for the Gö 40/10 wild type strain and Gö 40/10 with the hygromycin resistant pKC1218 plasmid were prepared.
A standard colony forming unit test was performed: 100 µL of spore stock solutions were serially diluted. The spore dilutions were used to inoculate agar plates (20 g/L soy flour meal, 20 g/L D-mannit, 20 g/L agar and hygromycin 50 µg/mL when required). After incubation for 72 h at 28 °C formed colonies were counted.
An equal amount of spores was then used to inoculate 250 mL baffled flasks with 100 mL of SM media (20 g/L soy flour meal, 20 g/L D-mannit, pH = 7), which were incubated at 28 °C and 165 rpm. Samples were taken every 24 hours for 144 hours in total, centrifuged and directly analyzed by LC-MS. EICs (extracted ion chromatograms) for **1** were generated (m/z = 361.2010 ± 0.005 Da) and the area was calculated automatically using Brukers DataAnalysis 4.2.
All experiments were performed in triplicates.

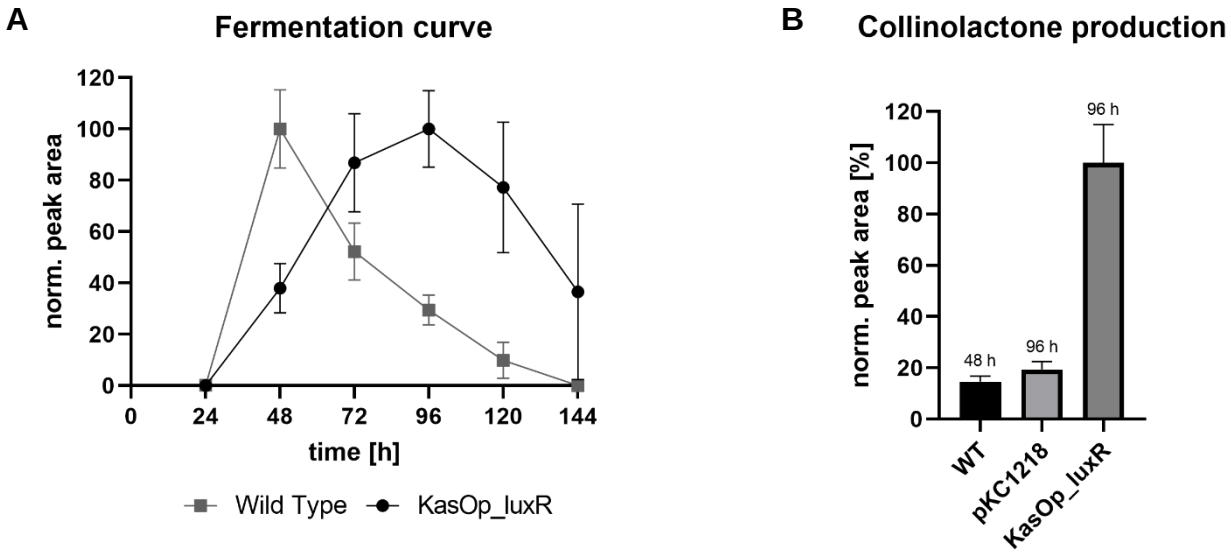


Figure S7: A: Fermentation curve of wild type producer strain Gö 40/10 and overproducer Gö 40/10 pKC1218-KasOp_luxR. Intensities are normalized and scaled separately for both data sets. B: Production of wild type strain Gö 40/10, control strain with hygromycin resistant plasmid pKC1218 and overproducer Gö 40/10 pKC1218-KasOp_luxR. Intensities were collected at the apax of collinolactone (**1**) yield and normalized to the global maximum in the data sets.

Cell viability assays on L929 cells

General remarks:
Assay was performed according to ISO 10993-5:2009 (Biological evaluation of medical devices - Part 5: Tests for in vitro cytotoxicity).

Cell culture:
RPMI 1640 GlutaMAX (Gibco by life technologies) containing 110 mg/L sodium pyruvate and supplemented with 10% (v/v) fetal calf serum (FCS, Gibco by life technologies) and 1% (v/v) penicillin/streptomycin (Gibco by life technologies) was used for experiments. L929 cells (DSMZ Leibniz) were cultivated at 37 °C with 5% CO_2 in a humidified incubator and subcultivated every two to three days (approx. 80% confluency) using trypsine/EDTA (Gibco by life technologies) for detaching.

Cell viability:
Cells were seeded to a sterile, clear 96-well plate (10.000 cells/well, 100 µL total volume, Ependorf). After cultivation for 24 h, cells were incubated with the compounds.
Compounds were dissolved in pure DMSO and diluted with medium to get the final test concentrations. Tested concentrations ranged from 0.12 µM to 250 µM.
The maximum DMSO concentration was set to 0.1% to avoid cytotoxic effects caused by the DMSO. The growth medium was discarded and replaced by the medium containing the desired compound concentrations. DMSO (10%) served as a positive control for reduced viability, cells without compound were used as a negative control.
Cells were incubated for 24 h with the compound dilutions, then cell viability was determined using MTS assay.

MTS Assay:
Cell viability was investigated by MTS assay (CellTiter96 AQueous One Solution Cell Proliferation Assay from Promega). After cell cultivation for 24 h and incubation with the compounds, medium was discarded and MTS diluted in RPMI cultivation medium without phenol red (20 µL in 100 µL/well) was added (total volume of 120 µL per well) and incubated for 1.5 hours. Absorbance at 490 nm was determined with a multiwell plate photometer (BMG, Plate Reader Omega), values were blank corrected (only MTS in RPMI) and normalized by negative control (cells without compound and without DMSO). Following the ISO 10993-5:2009 specifications, a reduction of cell viability by more than 30% was considered as a cytotoxic effect. Concentration dependent values were plotted, and the half maximal effective concentration (EC_{50}) values were determined as shown below.

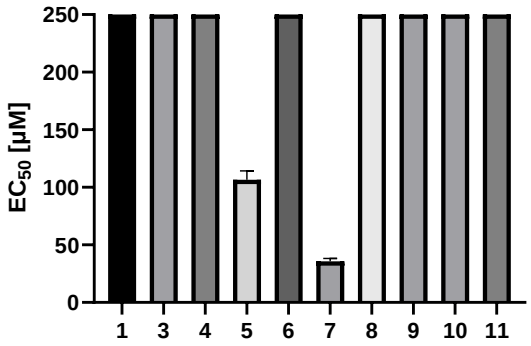


Figure S8: Cell viability assay on L929 cell line with collinolactone (**1**) and derivatives **3-11**. Cutoff was set to 250 µM, all data are represented as mean ± standard error of the mean (SEM).

Fluorescence microscopy of Ptk2 cells

Cell culture:
RPMI 1640 GlutaMAX (Gibco by life technologies) containing 110 mg/L sodium pyruvate and supplemented with 10% (v/v) fetal calf serum (FCS, Gibco by life technologies) and 1% (v/v) penicillin/streptomycin (Gibco by life technologies) was used for experiments. Ptk2 cells (CLS Cell Line Services) were cultivated at 37 °C with 5% CO_2 in a humidified incubator. Growth medium was replaced every two to three days and cells were subcultured once a week at approx. 80% confluency using trypsine/EDTA for detaching.

Compound incubation:
PtK2 cells were seeded into a sterile µ-slide 8 Well Glass Bottom chamber (ibidi) (10.000 cells/well) and used for experiments after 30 h of cultivation.
Compounds were dissolved in pure DMSO and diluted with medium to get the final test concentrations with a maximum DMSO concentration of 0.2%. The growth medium was discarded and replaced by the medium containing the desired compound concentrations. DMSO (0.2%) served as a negative control.
After incubation for 12 h, cells were fixed and stained for fluorescence microscopy.

Fixation, permeabilization and blocking:
Cells were fixed using 4% para-formaldehyde solution for 15 min at room temperature. After washing with PBS, cells were incubated for 10 minutes at room temperature with 0.1% (v/v) Triton X-100 in PBS for permeabilization of the cell membrane
Cells were washed 3 times and blocked with 3% (w/v) BSA in PBS-Tween20 0.05% (v/v) for 30 min at room temperature before washing once with PBS.

Immunostaining:
Mouse Anti-beta-tubulin (Tub 41 mono T4026, sigma-aldrich T4026), 1:300 in PBS was added and incubated for 1 h. Antibody solution was removed and cells were washed 3 times with 0.05% Tween20 in PBS (v/v) containing 1% BSA (w/v).
Goat anti mouse Alexa 488 (ab150113, abcam) secondary antibody was used at 1:400 in PBS and incubated for 1 h in the dark.
Antibody solution was removed and cells were washed 3 times with PBS.
NucBlue LiveReadyProbes Reagent (Hoechst 33342, Molecular Probes) and Actin Red 555 Ready Probes Reagent (Rhodamine phalloidin, Molecular Probes) were used for staining DNA and F-Actin. The applied concentration was two droplets of each solution per 1 mL of PBS and the incubation time was set to 30 min at room temperature in the dark.
After a final washing step, PBS was replaced by mounting media (ibidi).
Slides were stored at 8 °C in the dark until used for fluorescence imaging.

Fluorescence microscopy:
Fluorescence microscopy was used to visualize DNA and tubulin structures (microtubule, spindle apparatus and monoastral spindle apparatus) using an inverted microscope (Axio Observer Z1, Carl Zeiss, Germany with LED-Colibri illumination unit) with a 20× objective (Plan-Apochromat 20x/0.80 Ph2 M27). For each compound, 8 randomly selected regions across the well were selected and images were acquired using z-Stack mode.

Image analysis:
For image processing, software ZEN 2 Blue was used. Z-stacks were merged using the wavelet method. Histogram intensities were optimized using the Min/Max function.

Cell stage determination:
Images were acquired and processed according to the published protocol which allows to determine the cell stage distribution using fluorescence images.[11]
DAPI channel was extracted from images of 8 randomly selected regions across the well and exported using ZEN 2 Blue export function with no compression and intensity scaling.
CellProfiler[12] (version 4.1.3) was used for image analysis, using default primary object detection settings. For object detection, image rescaling was performed before, but integrated DAPI intensity was calculated from raw data.
Object diameter was adjusted to range from 40-90, thresholding method was set to manual and a threshold of 0.15 was used. The integrated DAPI intensity of each cell was automatically exported to Excel, normalized and visualized using GraphPadPrism 9.1.2 Smoothing parameter was set to high.

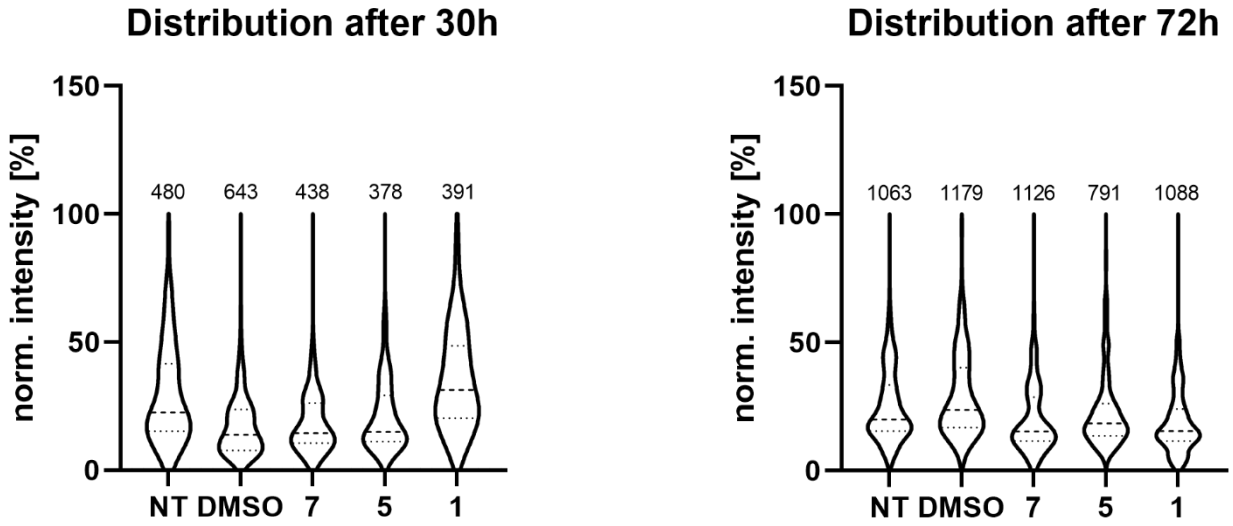


Figure S9: Cell stage distribution determined by fluorescence microscopy imaging. Displayed are the normalized integrated intensities of non-treated cells (NT), cells treated with DMSO (0.2%), and cells treated with either **1**, **5** or **7** dissolved in 0.2% DMSO. Cells were incubated for 30 hours or 72 hours respectively, before treated with compounds for additional 12 hours and fixed afterwards. Dotted lines represent the quartiles, the dashed line represents the mean. Numbers on each violin correspond to the number of cells considered for the analysis representation.

SUPPORTING INFORMATION

Neurotoxicity and neuroprotection on HT22 cells

Cell Culture:
HT22 cells were grown in Dulbecco's modified Eagle's medium (DMEM, Sigma-Aldrich, Munich, Germany) supplemented with 10% (v/v) heat inactivated fetal calf serum (FCS) and 1% (v/v) penicillin/streptomycin. Cells were passaged every two days (1:10) and incubated at 37 °C with 5% CO_2 in a humidified incubator. Compounds were dissolved in pure DMSO and then diluted with medium. Generally, 80% confluent cells were detached using trypsine/EDTA and seeded with into a sterile, clear 96-well plate (100 µL, 50 000 cells/mL). After incubation in humidor for 24 h, cells were used for experiments.

Neurotoxicity:
The growth medium was discarded, and different concentrations of the compound, diluted in growth medium, were added to the wells (100 µL). DMSO (0.5%) in DMEM served as control. SDS (1%) served as positive control for cell death. Cells were incubated for 24 h with the compound dilutions, then cell viability was determined using MTT assay.

Neuroprotection:
The growth medium was discarded, and different concentrations of the compound, diluted in growth medium containing 5 mM glutamate (monosodium-L-glutamate, Sigma-Aldrich, Munich, Germany). DMSO (0.5%) in growth medium served as control. Glutamate 5 mM in growth medium served as negative control. Quercetin (25 µM, Sigma-Aldrich, Munich, Germany) served as positive control for neuroprotection. After incubation in humidor for 24 h, cell viability was determined using MTT assay.

MTT Assay:
Cell viability was investigated using MTT assay. Therefore, a 4 mg/mL stock of MTT (Sigma-Aldrich, Munich, Germany) in PBS was freshly prepared and diluted 1:10 with growth medium. After incubating the cells for 24 h, the dilutions were discarded and MTT dilution in growth medium (100 µL) was added. Cells were incubated for 3 h, then the MTT solution was carefully discarded and replaced with an aqueous 10% SDS solution. After incubation for 12 h, absorbance at 560 nm of lysed cells was determined with a multiwell plate photometer (Tecan, SpectraMax 250).

Statistical Analysis:
Results are presented as percentage of 0.5% DMSO treated control cells. Data are expressed as means ± SEM of three independent experiments, each performed in sextuplicate. Analysis was accomplished using GraphPad Prism 5 software applying one-way ANOVA followed by Dunnett's multiple comparison post-test.

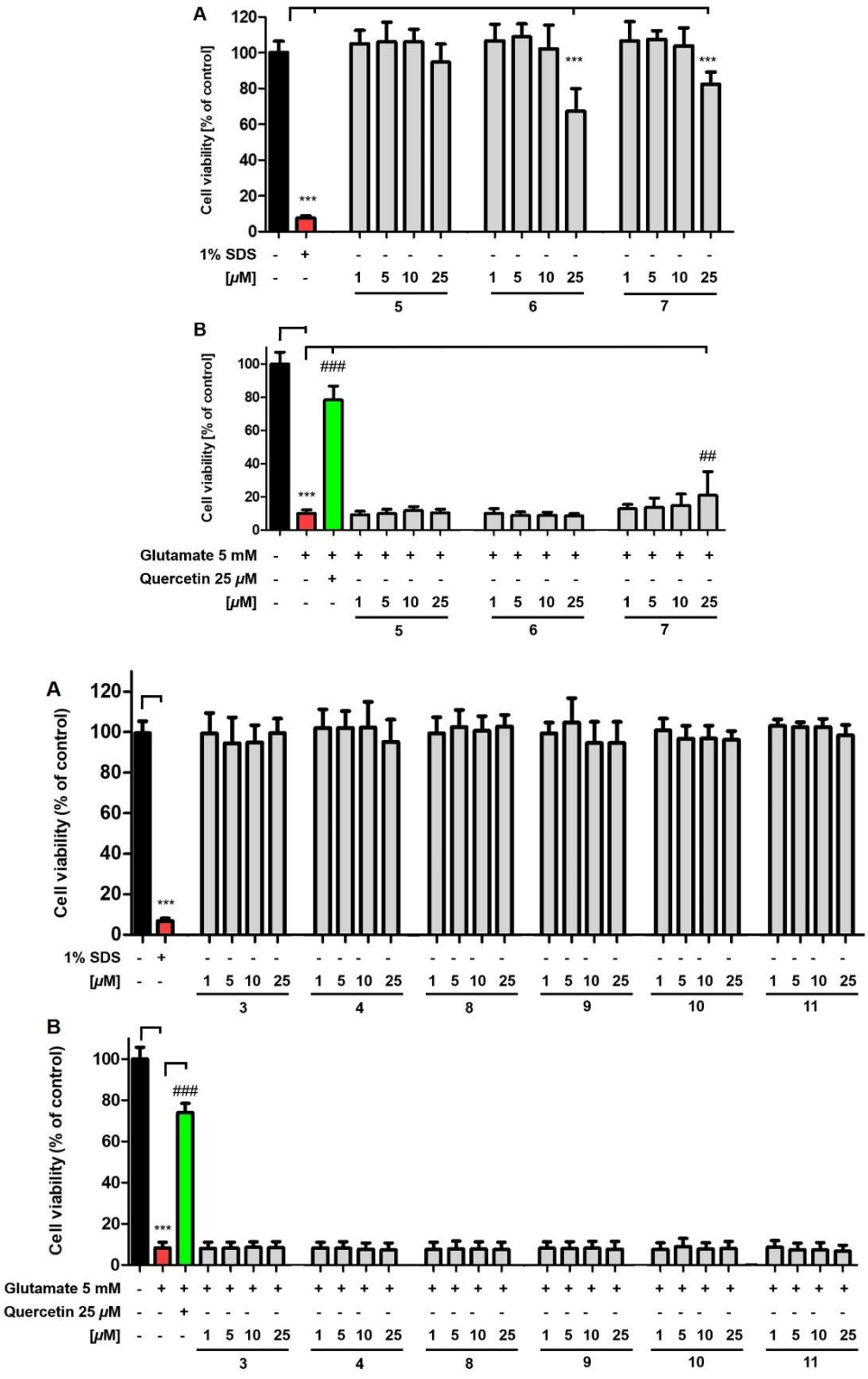


Figure S10: Derivatives of collinolactone **3-11** were studied for neurotoxic effects (A) and neuroprotection (B) against glutamate induced oxidative stress at 1 – 25 µM using HT22 cell line. 1% SDS served as positive control for neurotoxic effects whereas Quercetin (25 µM) served as a positive control for neuroprotection. Results of the modified MTT tests are presented as means ± SEM of three independent experiments, each performed in sextuplicate and refer to untreated control cells which were set as 100% values. Levels of significance: *$p < 0.05$; **$p < 0.01$; ***$p < 0.001$; $^{\#}p < 0.05$; $^{\#\#}p < 0.01$; $^{\#\#\#}p < 0.001$.

β-amyloid aggregation assay

The aggregation assay was performed according to the previously described procedure.[13] Commercially available β-amyloid peptide (1-42) from Bachem was used for experiments.
Purchased β-amyloid was treated with HFIP (Hexafluoro-2-propanol; obtained from Carl Roth) following a previously published protocol to obtain monomeric β-amyloid peptides only.[14]
0.5 mg β-amyloid peptide (1-42) was dissolved in 400 µL HFIP and aliquoted into 4 PCR tubes. HFIP was evaporated over night at room temperature in a fume hood. To remove remaining HFIP and moisture, the samples were evaporated for additional 2 hours in a lyophilizer before frozen at -20 °C until usage.
Prior usage, one aliquot was allowed to warm up to room temperature. DMSO (from Carl Roth) was added to prepare 1 mM stock which was vortexed for 30 seconds and sonicated for 10 min before diluted with deionized water to obtain 50 µM concentration. Compounds were dissolved in DMSO to obtain 25 mM stocks which were further diluted with deionized water to obtain 2 mM stocks.
12.5 µL of β-amyloid stock (50 µM) and 12.5 µL of compounds stocks (2 mM) were mixed in a 96 PCR Plate (Biodeal Thermo-Fast) obtain final concentrations of 25 µM for β-amyloid and 1 mM for compounds.
25 µM for β-amyloid with similar concentrations of DMSO served as negative control, while 20 mM of EPPS, which has been described as disaggregation reagent[15] was used as positive control. Sealed PCR plate was incubated for 5 days in an Eppendorf Thermocycler at 37 °C, before 75 µL of freshly prepared ThT (from Sigma Aldrich) solution (5 µM ThT in 50 mM glycine buffer, pH 8.8) was added. Samples were transferred into a 96 well plate (Sarstedt, 96 well plate, flat bottom, black) and fluorescence intensity was determined at 450 nm (excitation) and 485 nm (emission) using a microplate reader (Tecan Infinite 200 Pro).
All experiments were performed in triplicates.

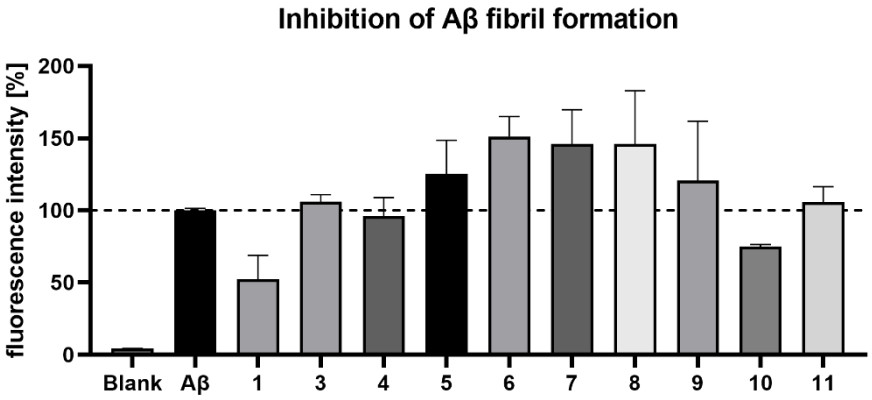
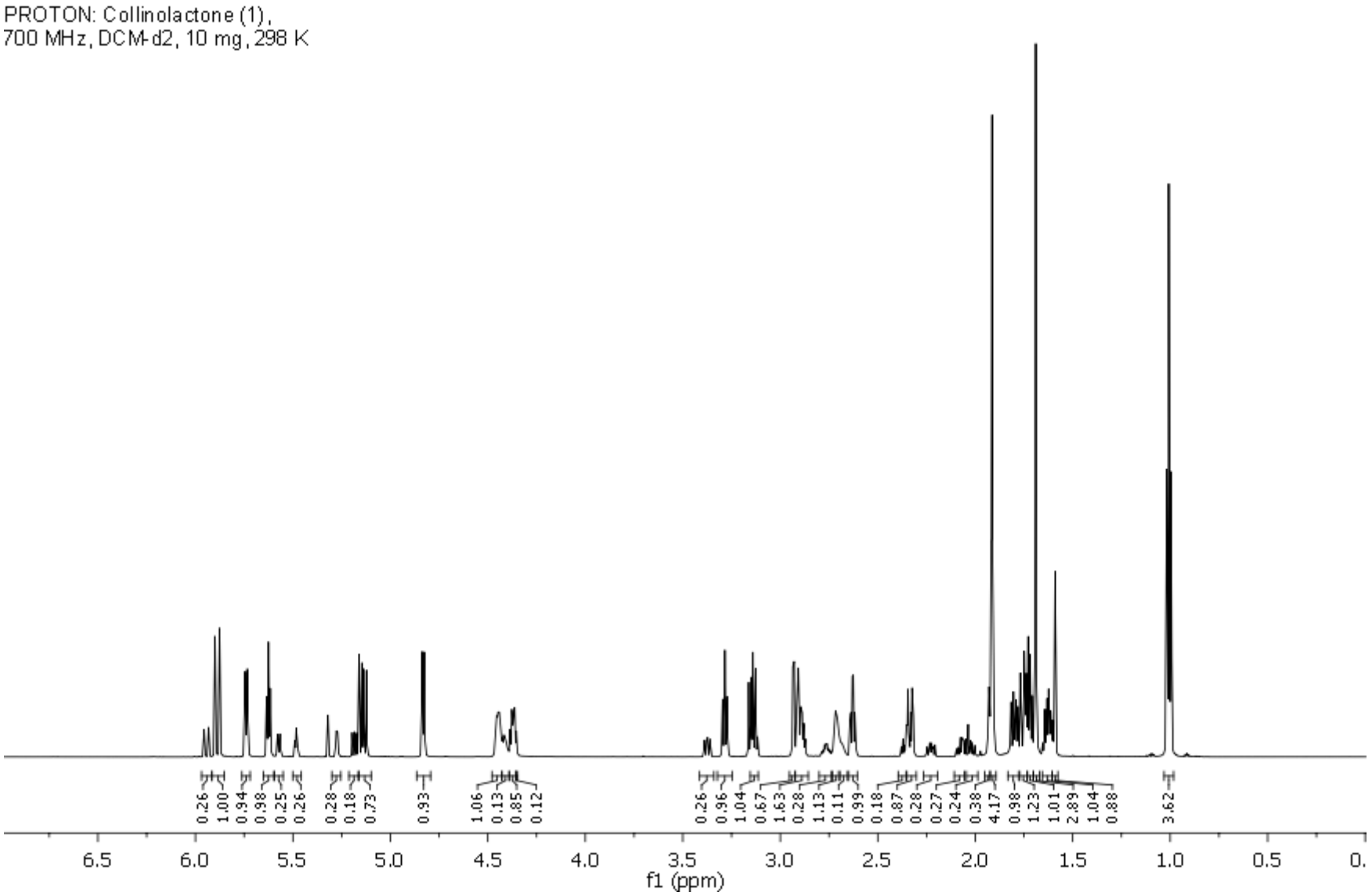
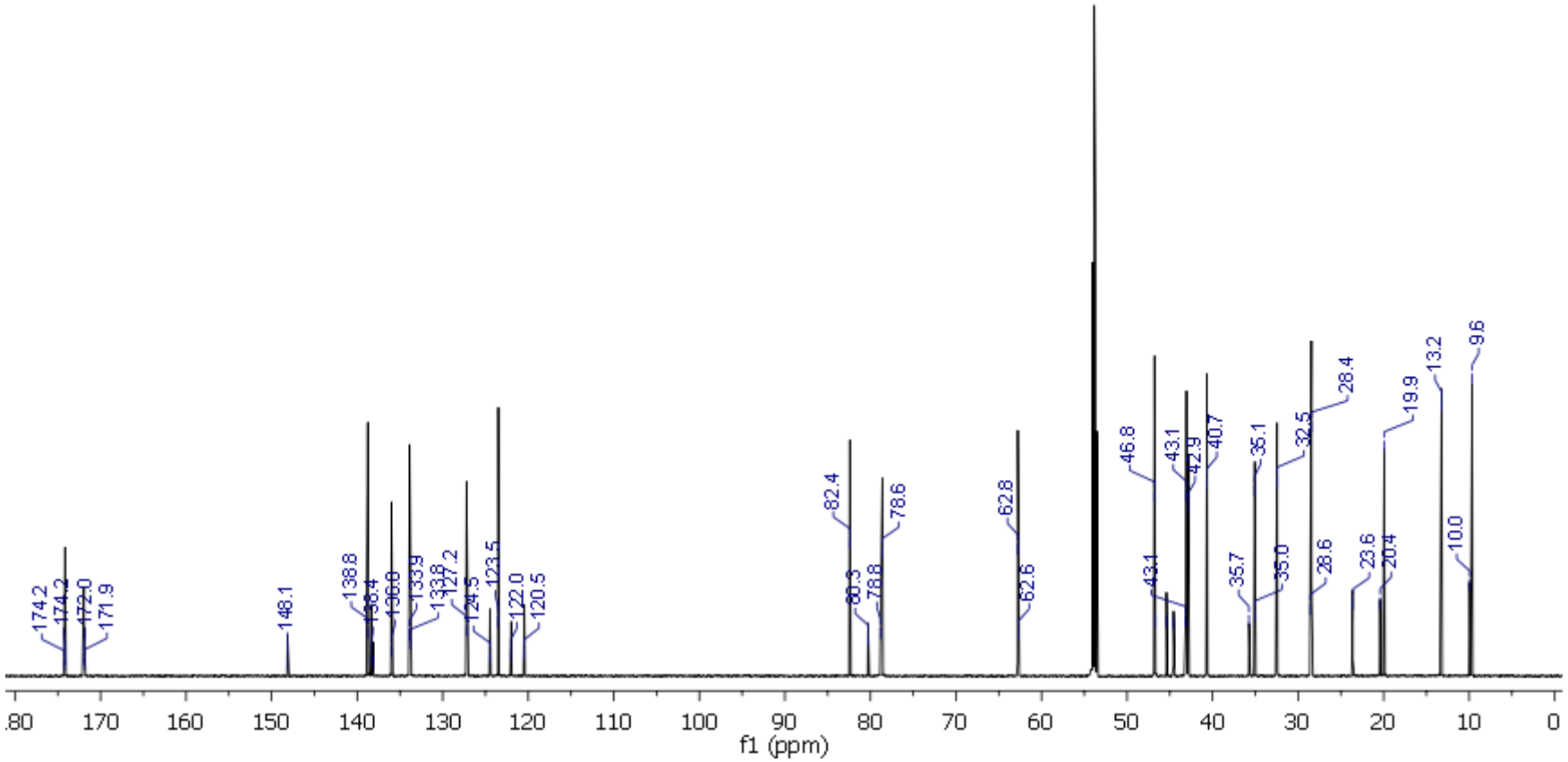


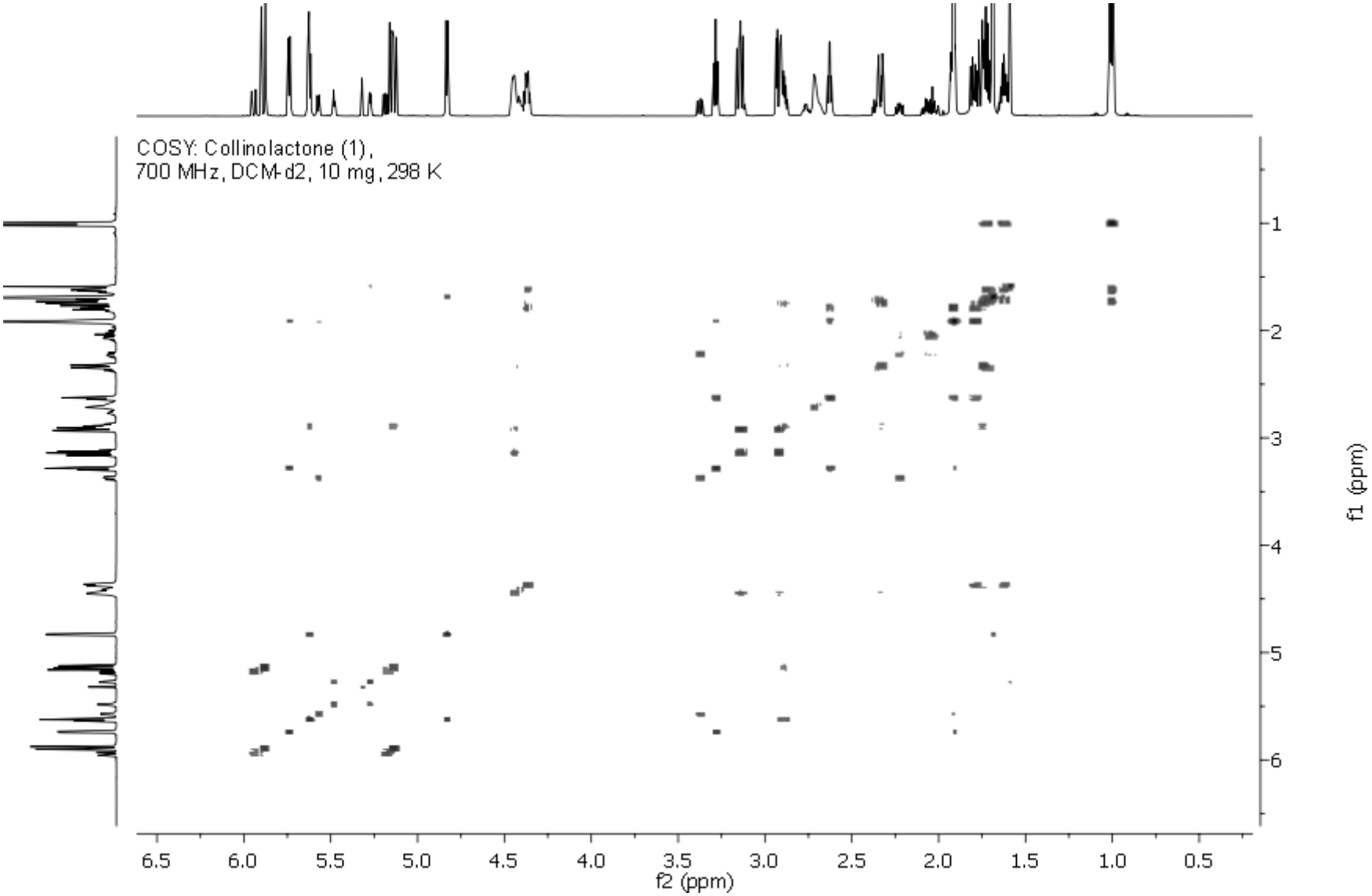
Figure S11: Inhibition of β-amyloid formation by collinolactone (**1**) and derivatives. Presented data were normalized by the mean of Aβ control samples. 5 µM ThT in 50 mM glycine buffer served as blank.

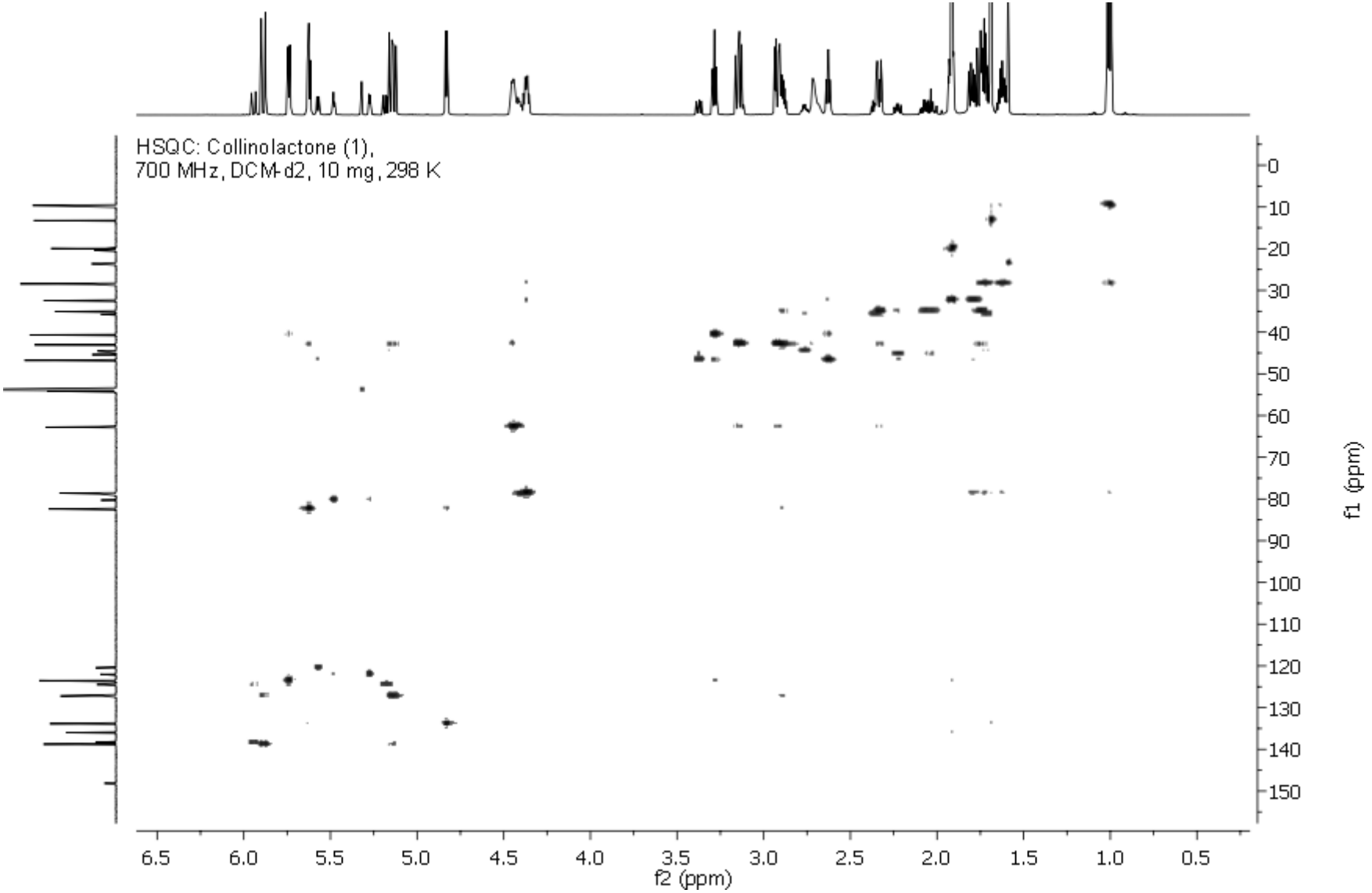
NMR spectra

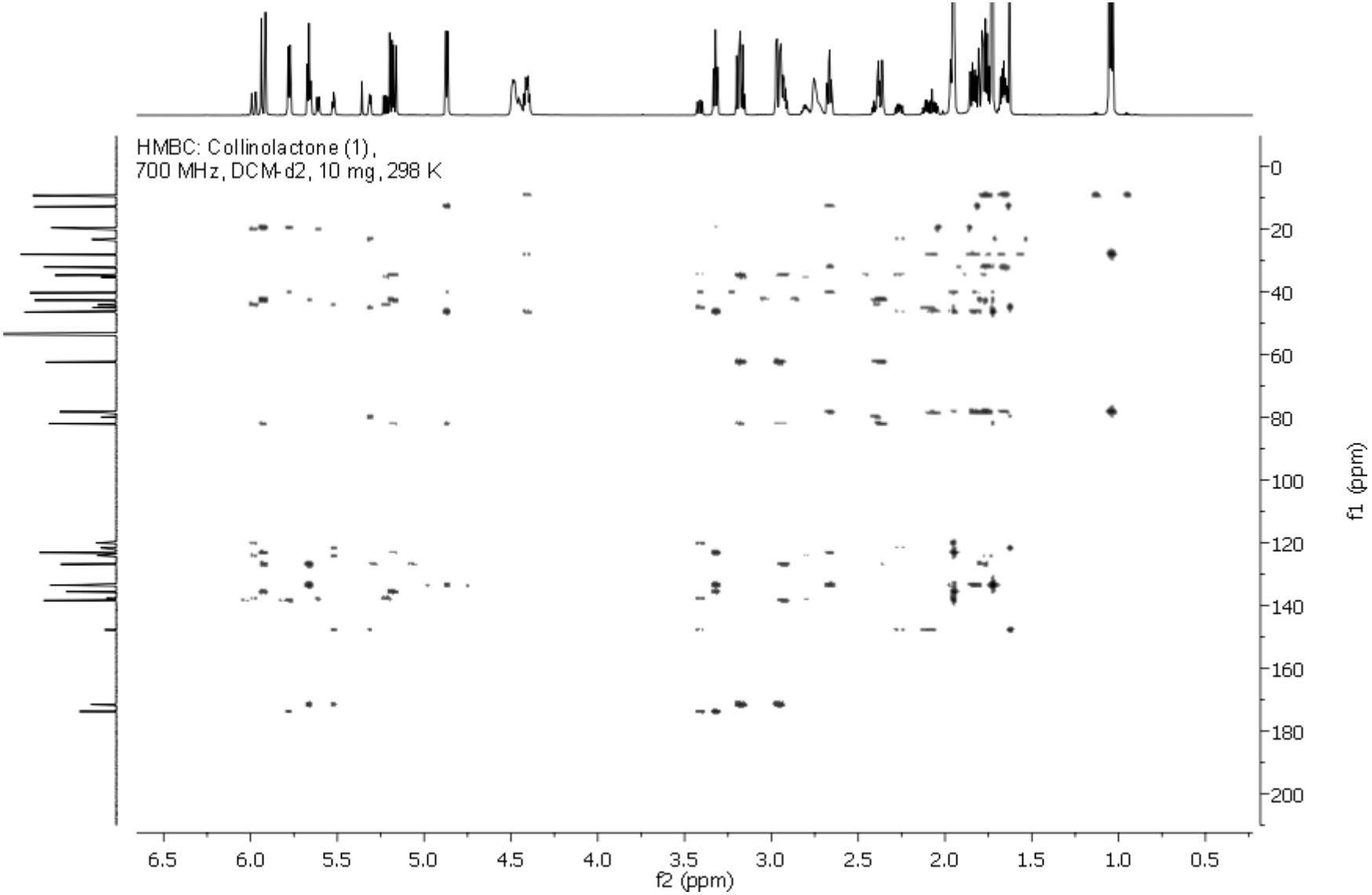

PROTON: Collinolactone (1),
700 MHz, DCM-d2, 10 mg, 298 K
0.26
1.00
0.94
0.98
0.25
0.26
0.28
0.18
0.73
0.93
1.06
0.13
0.85
0.12
0.26
0.96
1.04
0.67
1.63
0.28
1.13
0.11
0.99
0.18
0.87
0.28
0.27
0.24
0.38
4.17
0.98
1.23
1.01
2.89
1.04
0.88
3.62
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.
f1 (ppm)

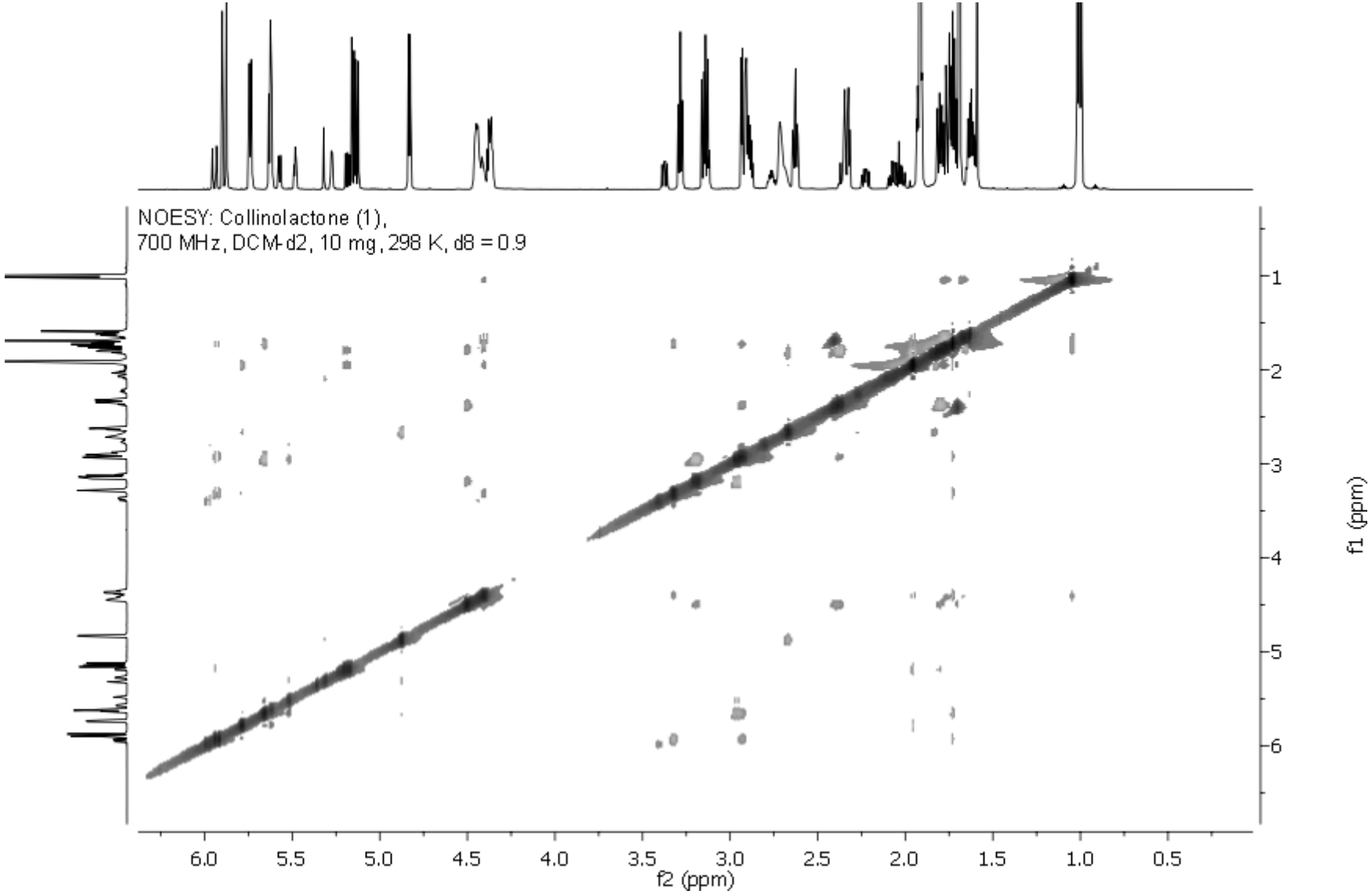
CARBON: Collinolactone (1),
700 MHz, DCM-d2, 10 mg, 298 K

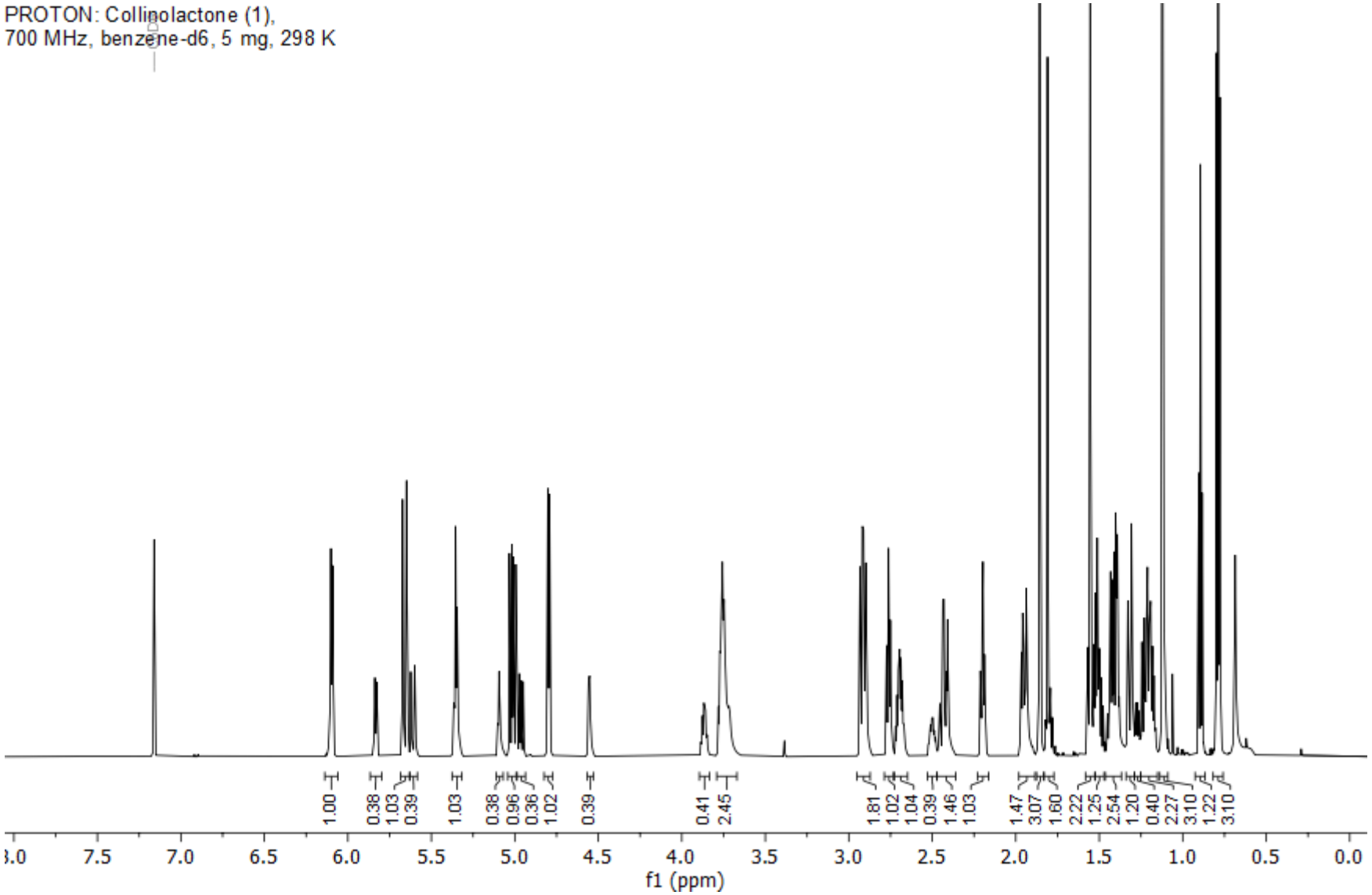


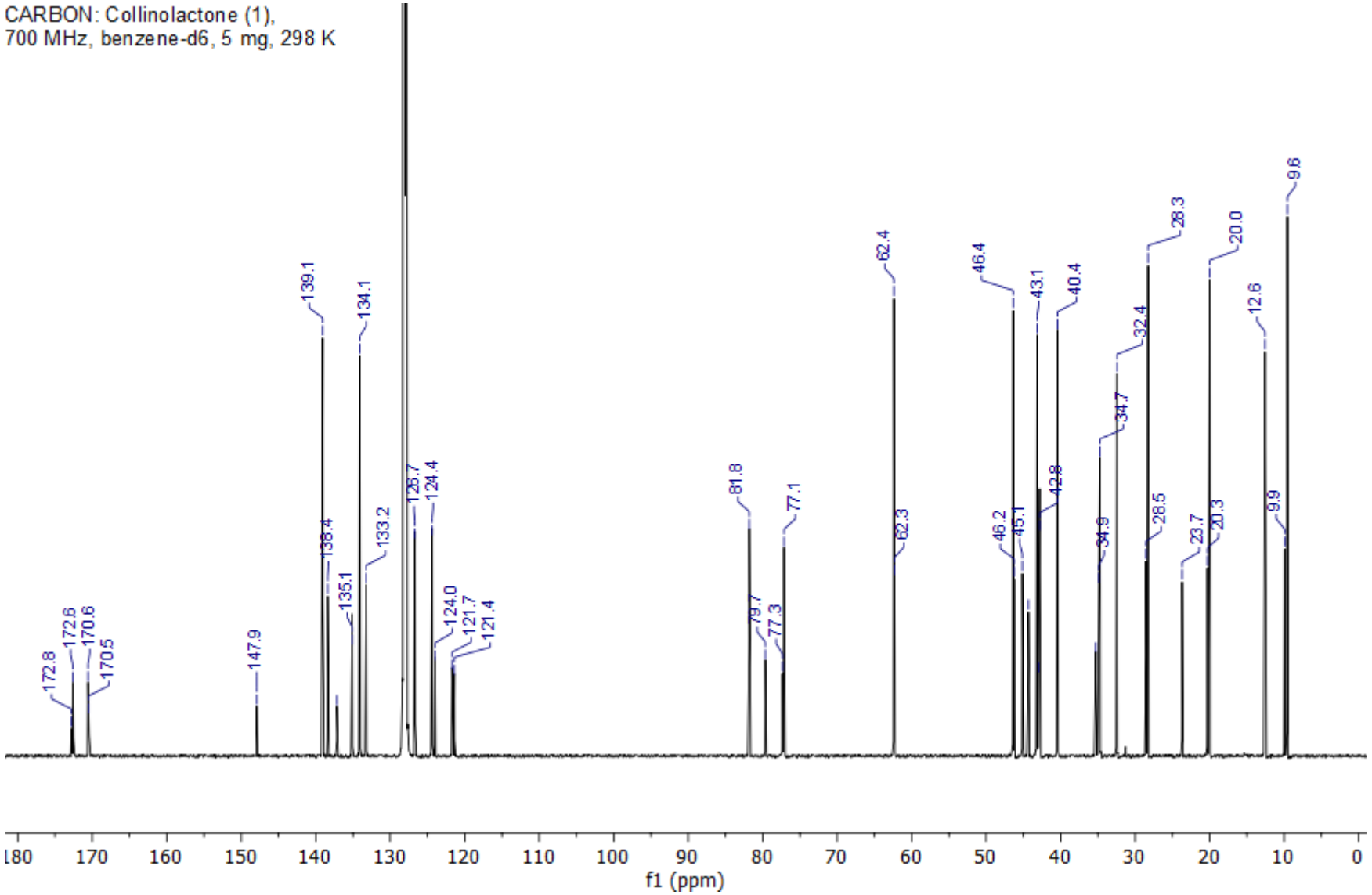

COSY: Collinolactone (1),
700 MHz, DCM-d2, 10 mg, 298 K
f1 (ppm)
f2 (ppm)
1
2
3
4
5
6
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5

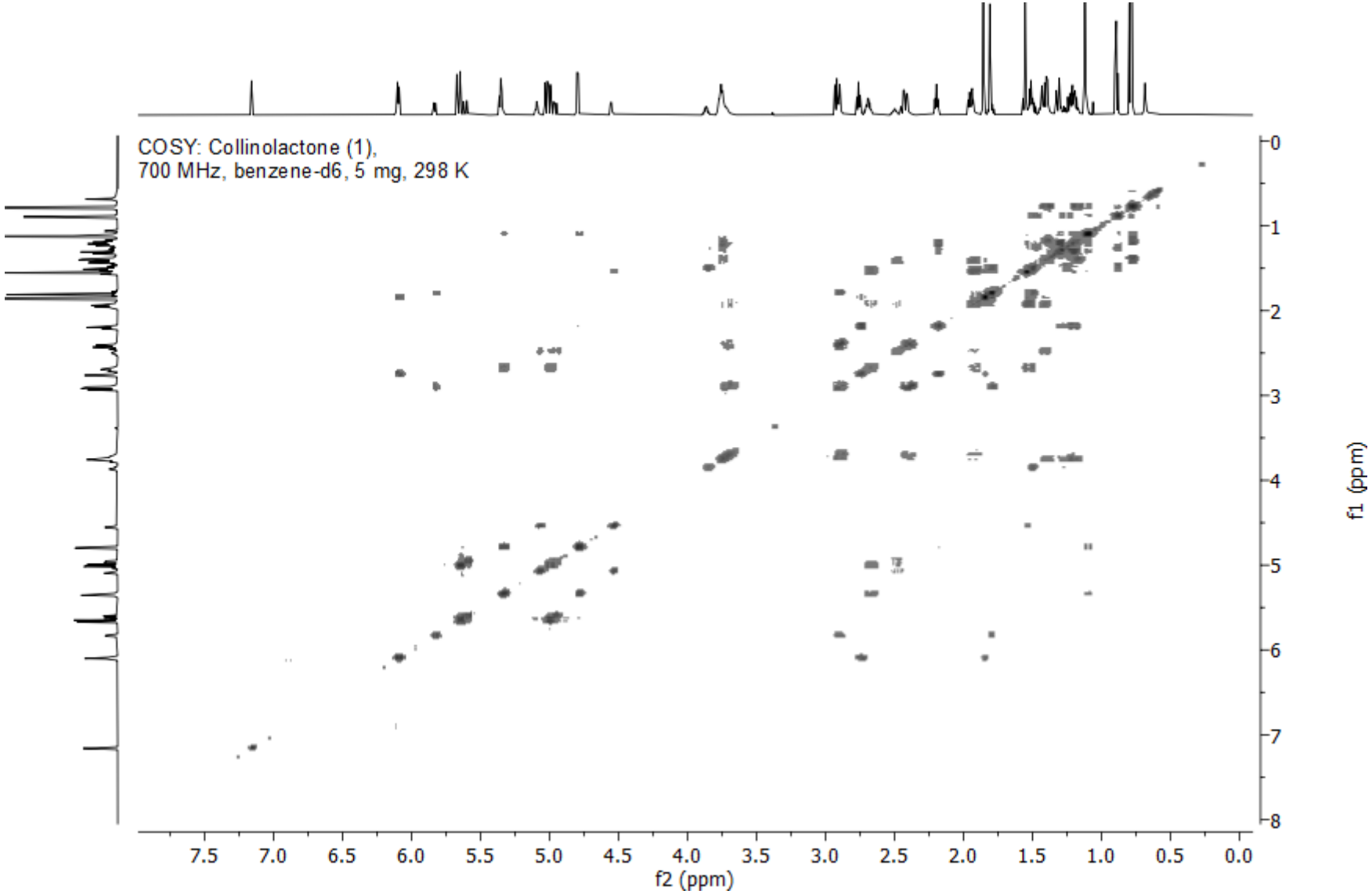

HSQC: Collinolactone (1),
700 MHz, DCM-d2, 10 mg, 298 K
f2 (ppm)
f1 (ppm)

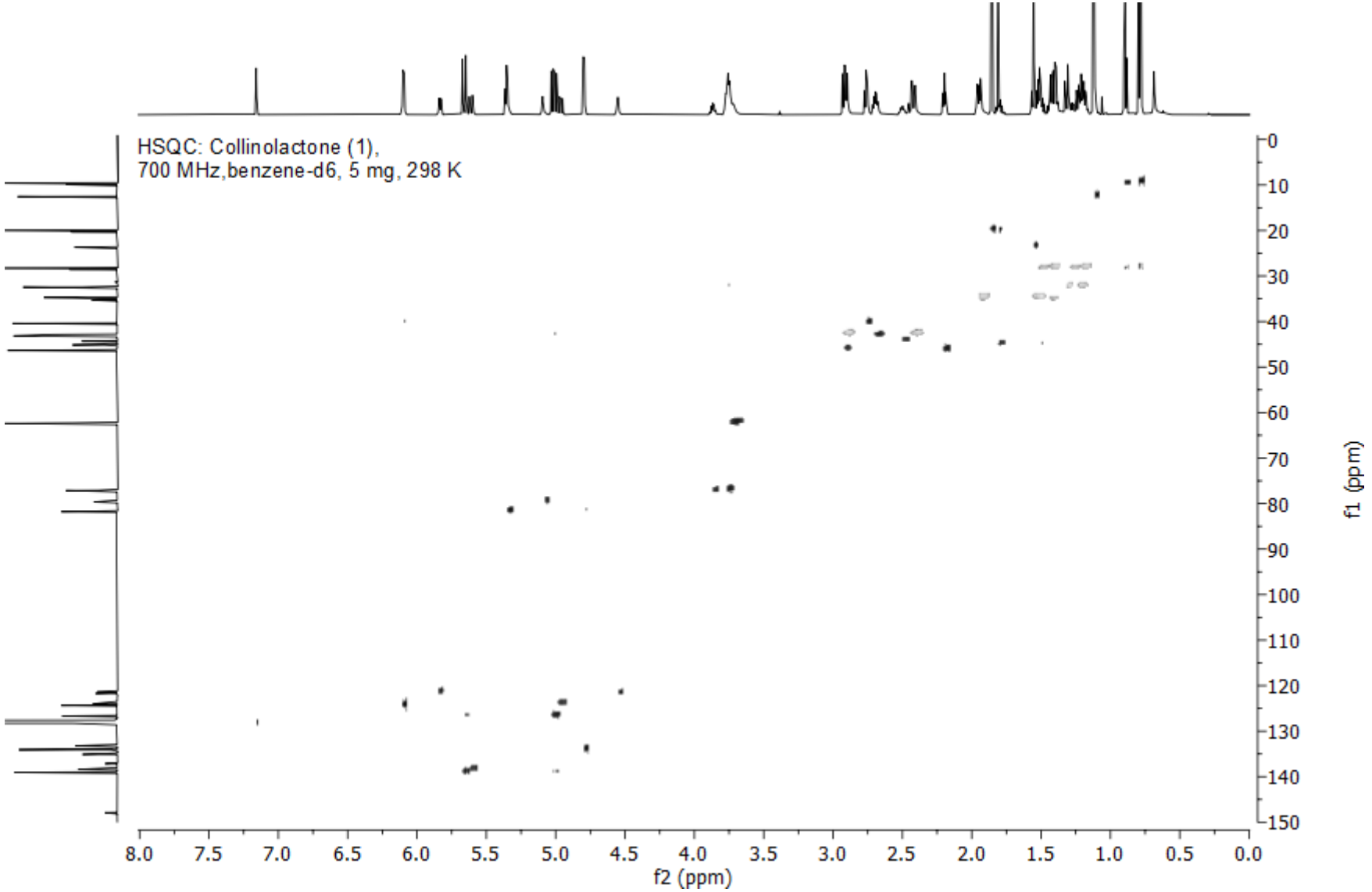

HMBC: Collinolactone (1),
700 MHz, DCM-d2, 10 mg, 298 K
f2 (ppm)
f1 (ppm)
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0
20
40
60
80
100
120
140
160
180
200

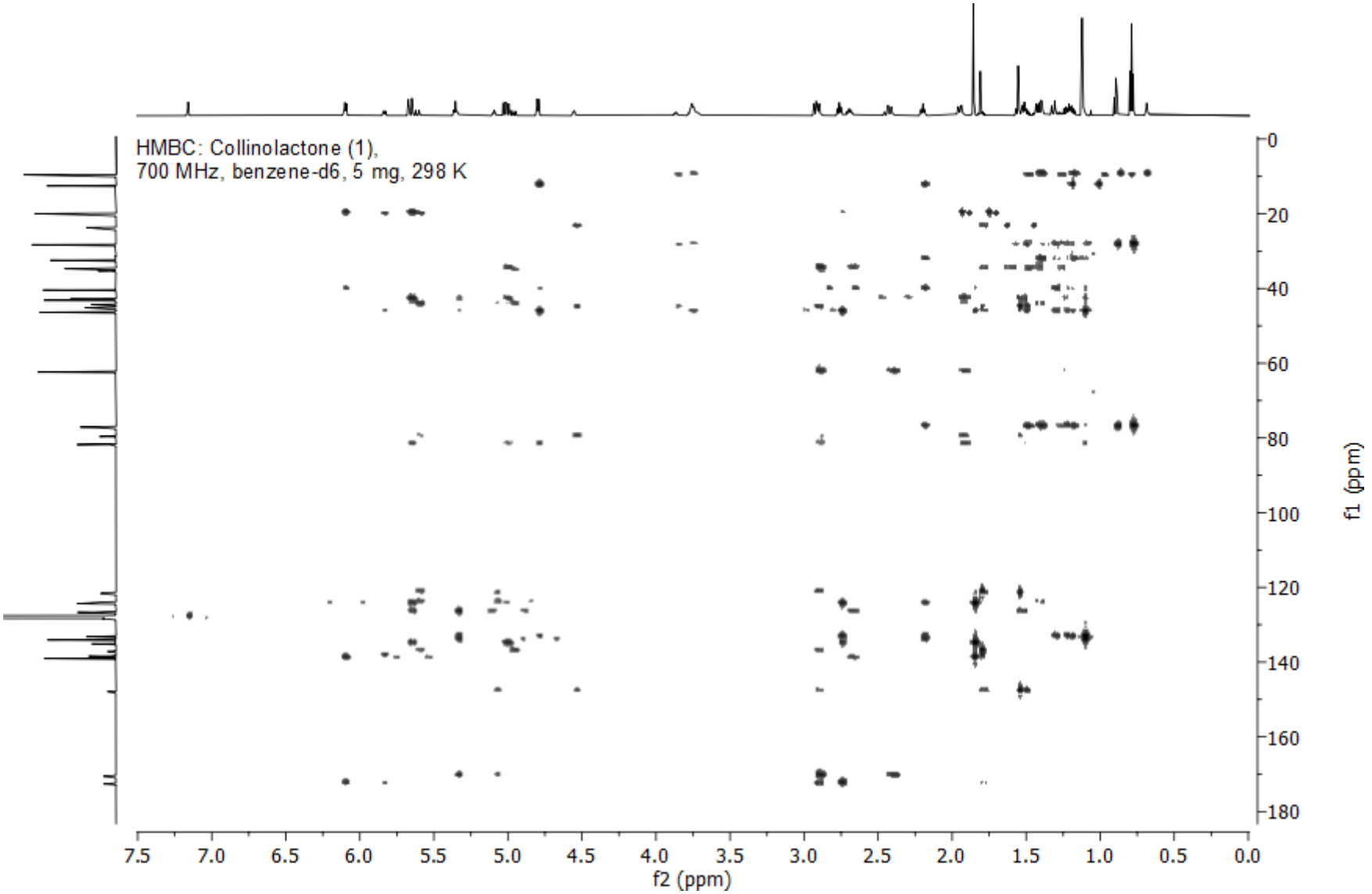

NOESY: Collinolactone (1),
700 MHz, DCM-d2, 10 mg, 298 K, d8 = 0.9
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
f2 (ppm)
1
2
3
4
5
6
f1 (ppm)

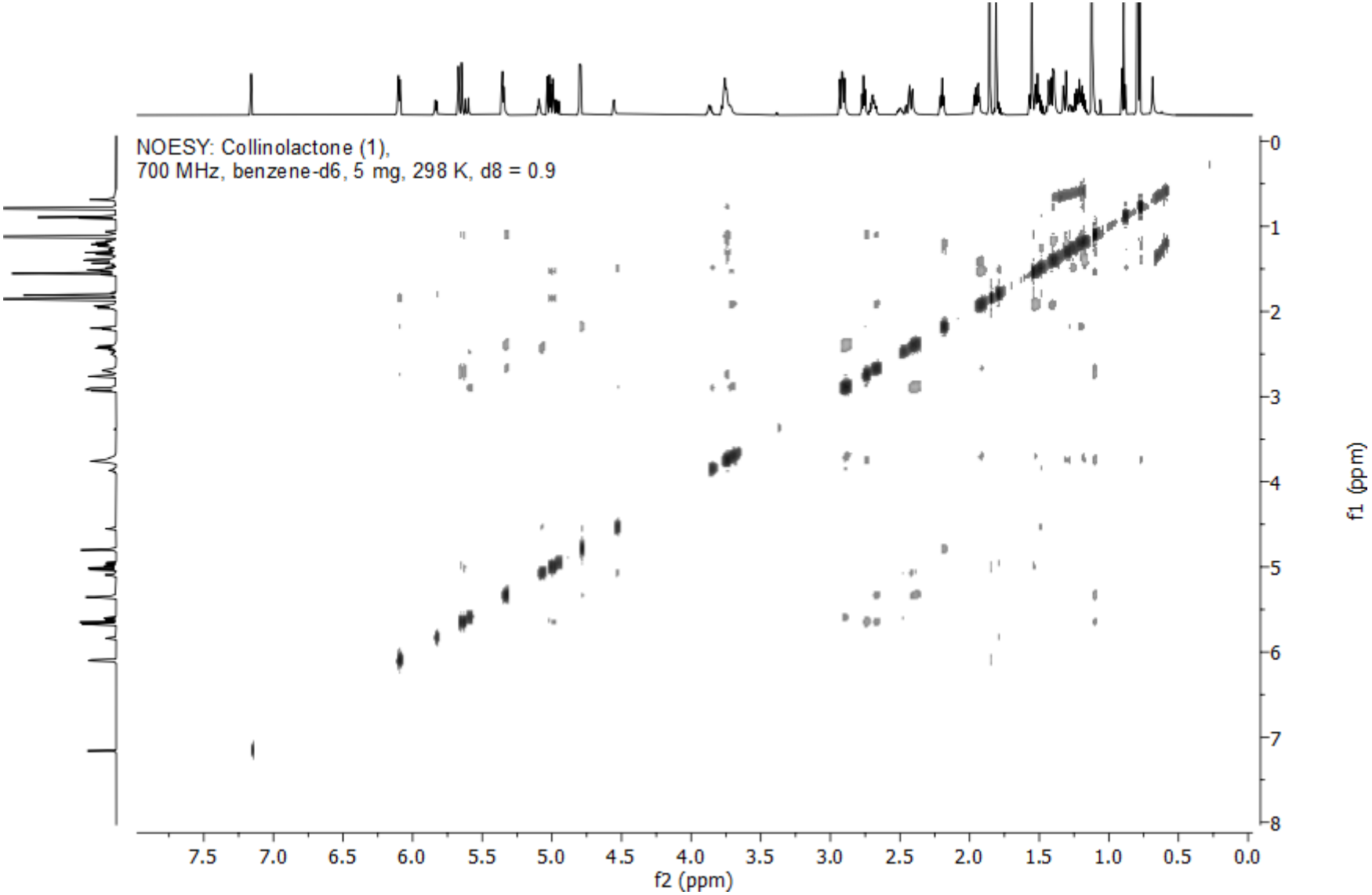

PROTON: Collinolactone (1),
700 MHz, benzene-d6, 5 mg, 298 K
1.00
0.38
1.03
0.39
1.03
0.38
0.96
0.36
1.02
0.39
0.41
2.45
1.81
1.02
1.04
0.39
1.46
1.03
1.47
3.07
1.60
2.22
1.25
2.54
1.20
0.40
2.27
3.10
1.22
3.10
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

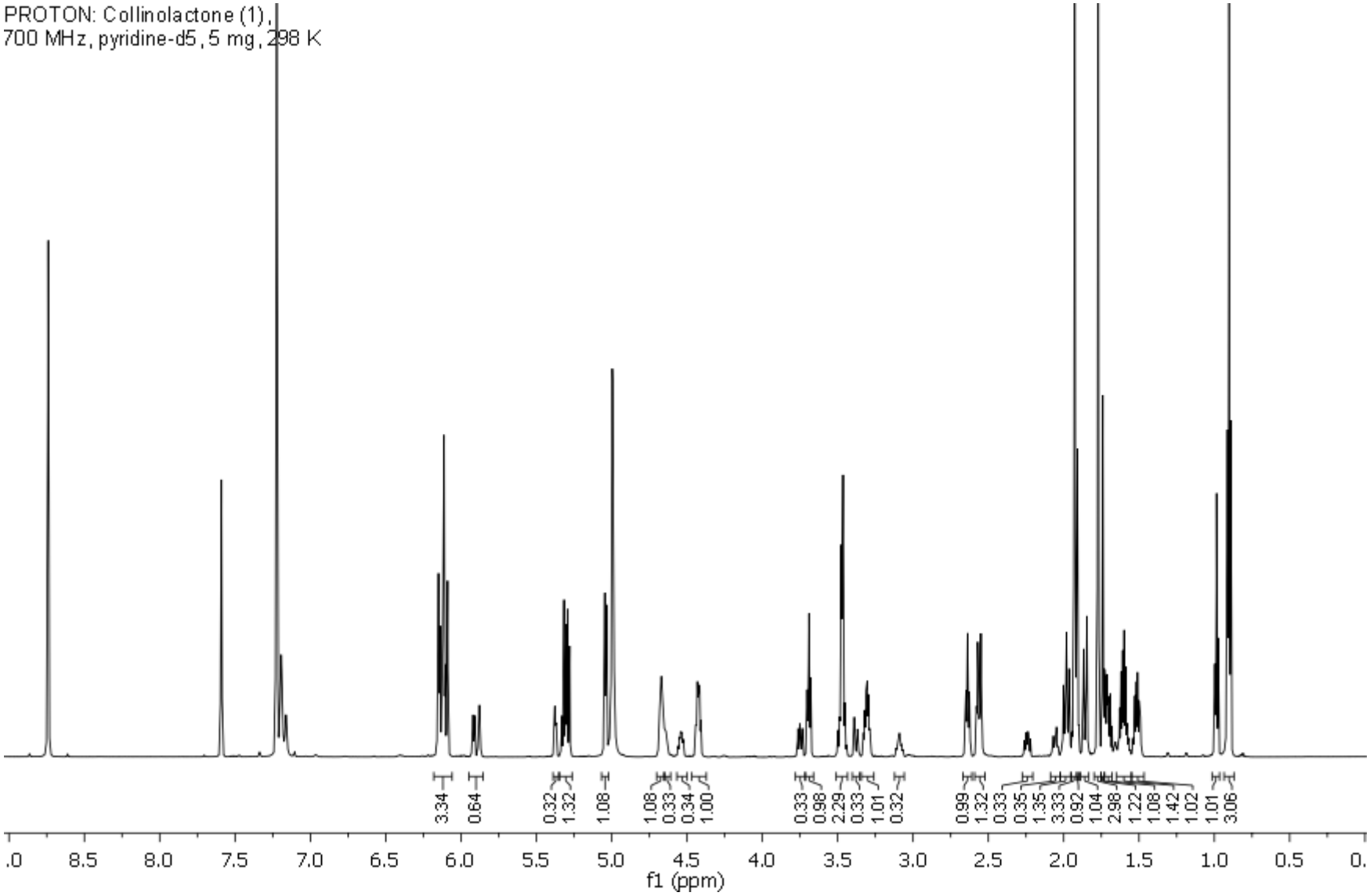

CARBON: Collinolactone (1),
700 MHz, benzene-d6, 5 mg, 298 K
172.8
172.6
170.6
170.5
147.9
139.1
138.4
135.1
134.1
133.2
125.7
124.4
124.0
121.7
121.4
81.8
79.7
77.3
77.1
62.4
62.3
46.4
46.2
45.1
43.1
42.8
40.4
34.9
34.7
32.4
28.5
28.3
23.7
20.3
20.0
12.6
9.9
9.6
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

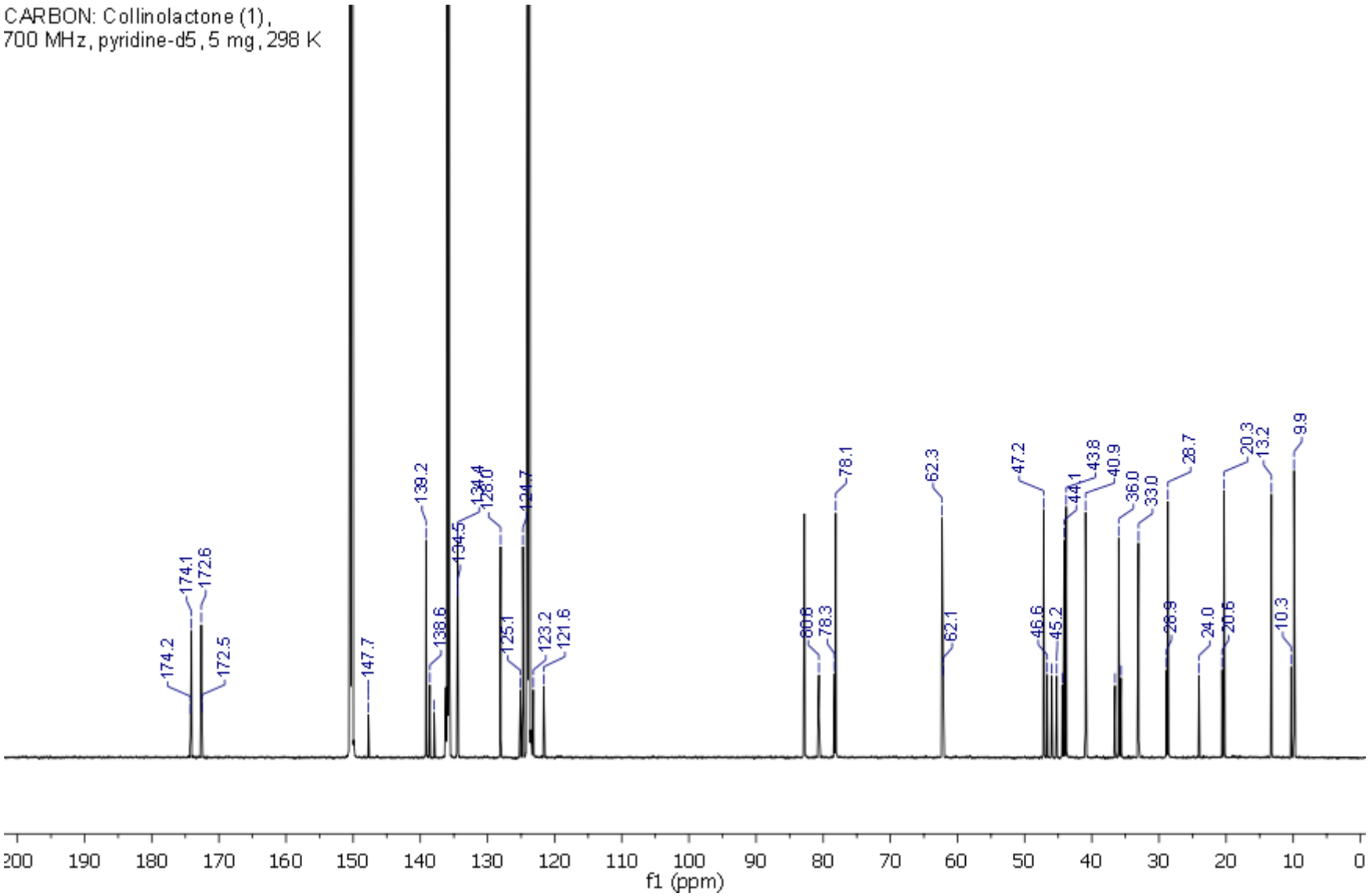

COSY: Collinolactone (1),
700 MHz, benzene-d6, 5 mg, 298 K
f2 (ppm)
f1 (ppm)
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
0
1
2
3
4
5
6
7
8

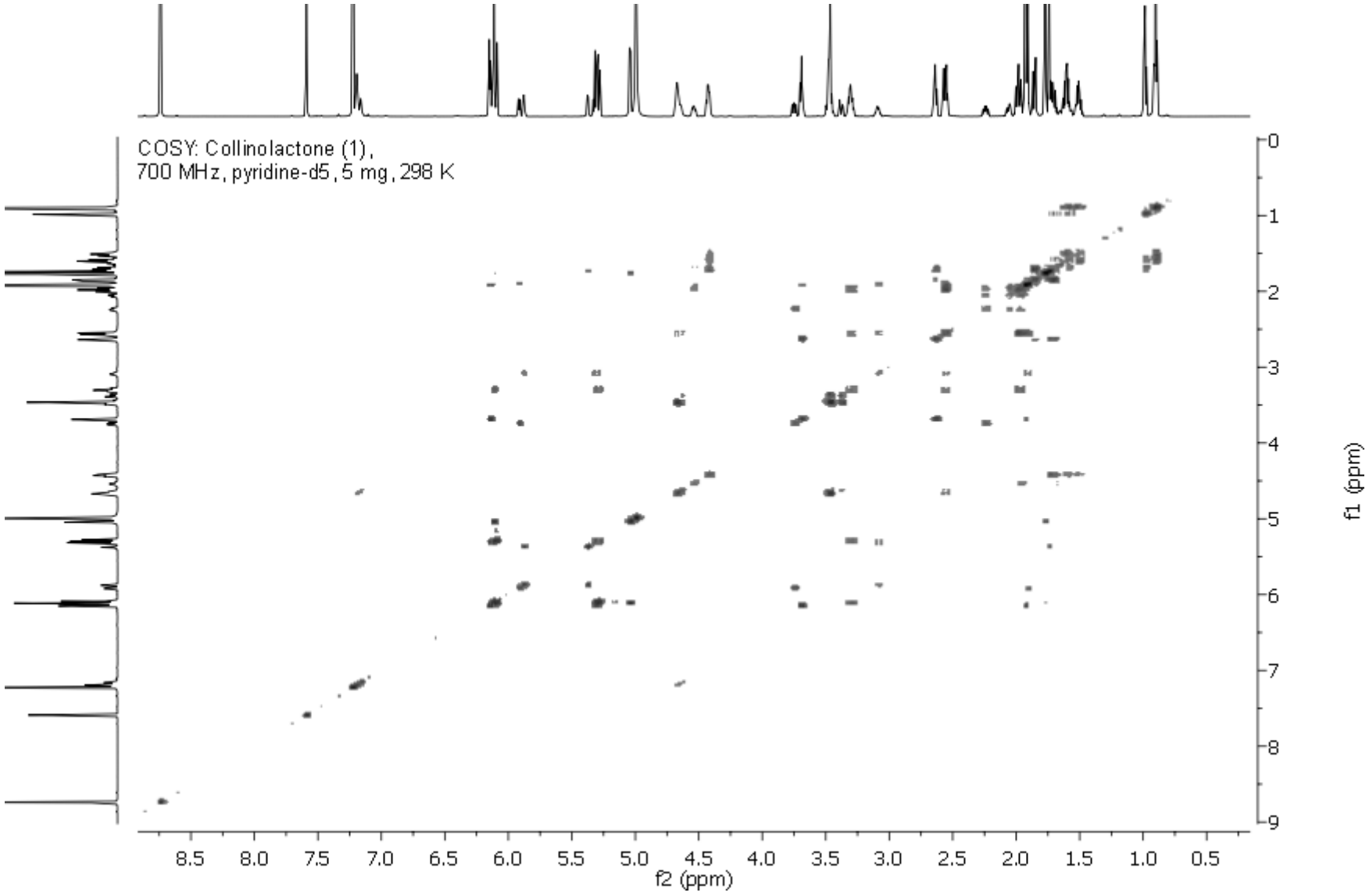

HSQC: Collinolactone (1),
700 MHz,benzene-d6, 5 mg, 298 K
f2 (ppm)
f1 (ppm)

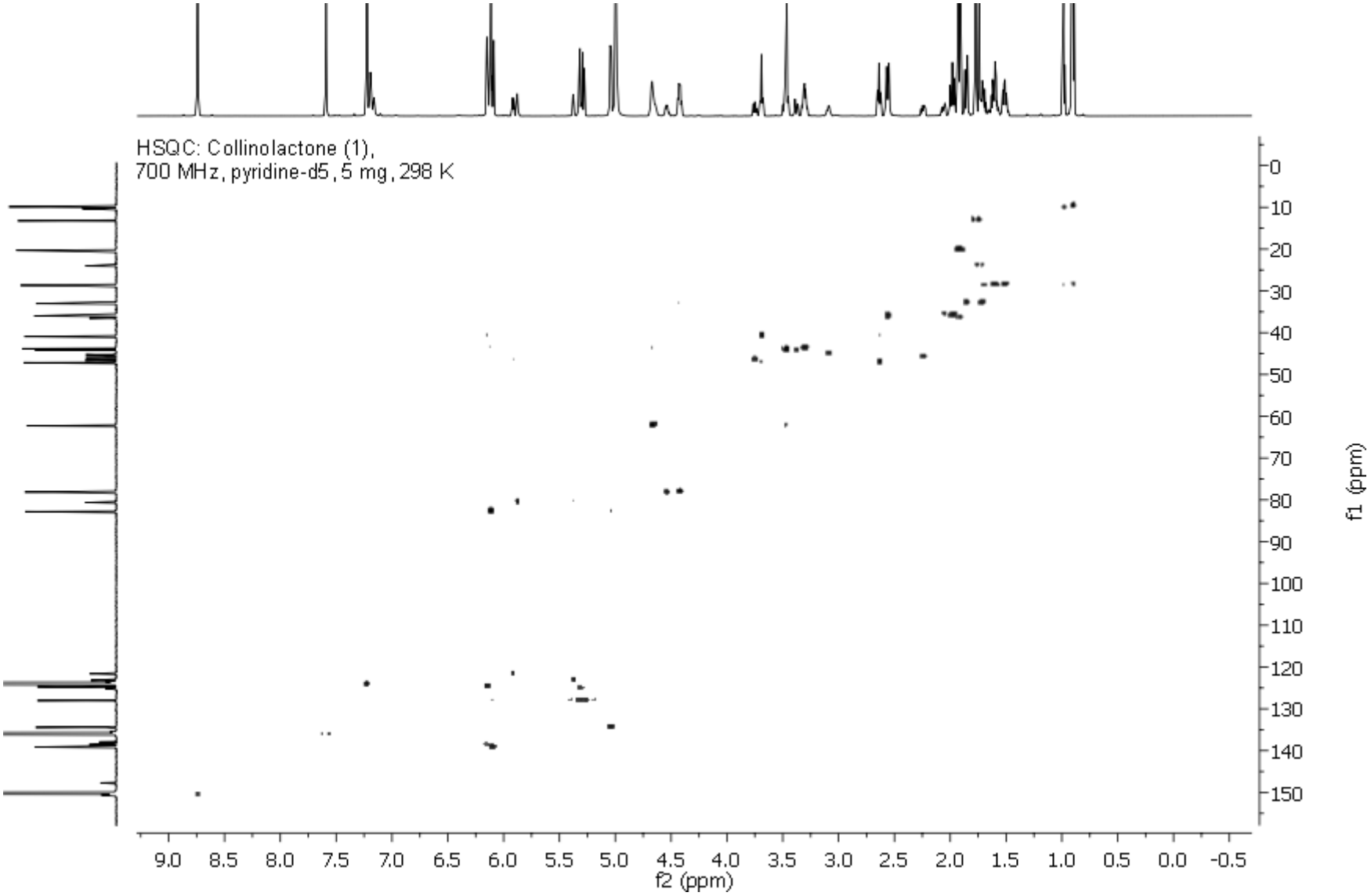

HMBC: Collinolactone (1),
700 MHz, benzene-d6, 5 mg, 298 K
f2 (ppm)
f1 (ppm)
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
0
20
40
60
80
100
120
140
160
180

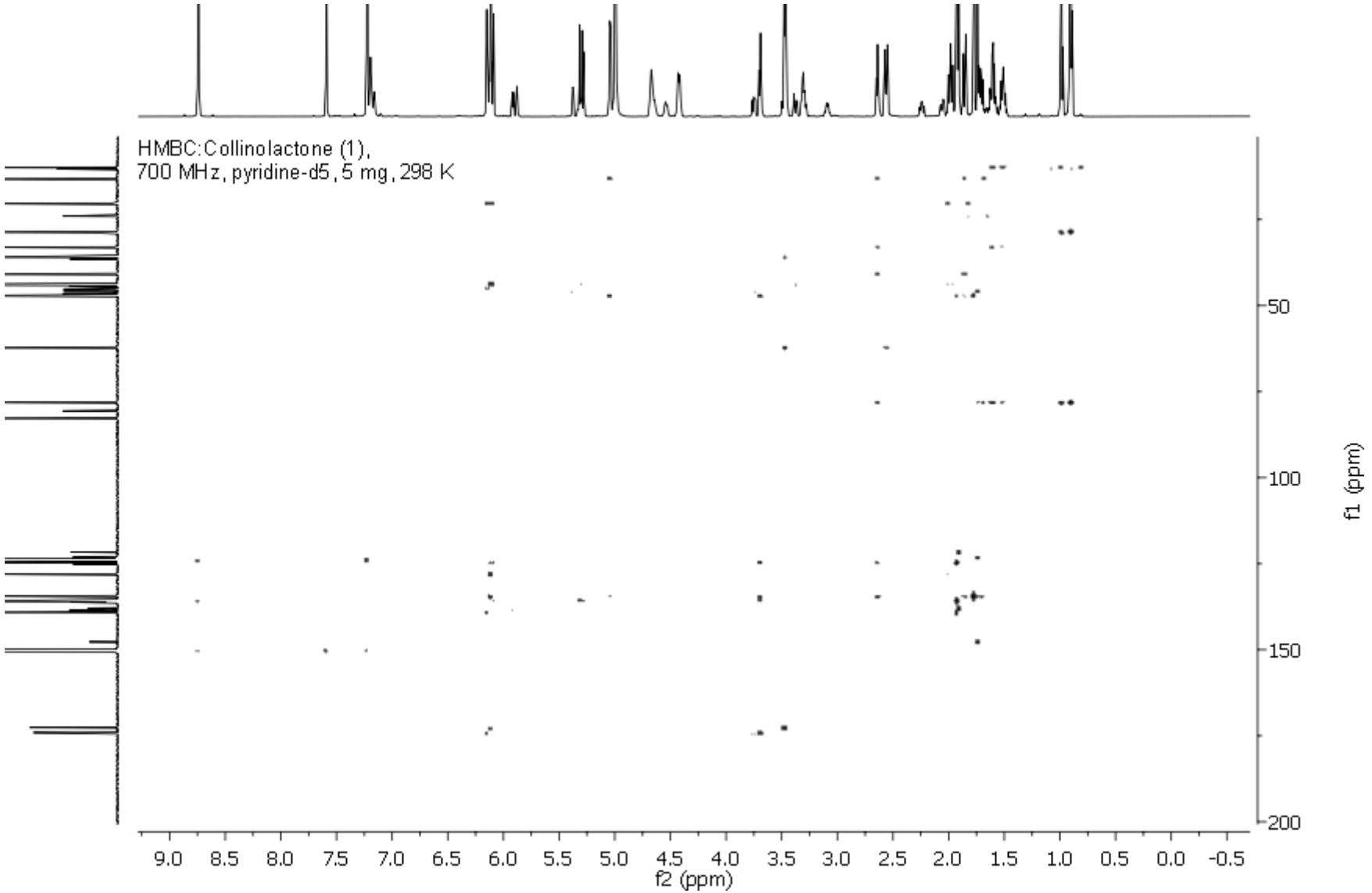

NOESY: Collinolactone (1),
700 MHz, benzene-d6, 5 mg, 298 K, d8 = 0.9
f2 (ppm)
f1 (ppm)
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
0
1
2
3
4
5
6
7
8

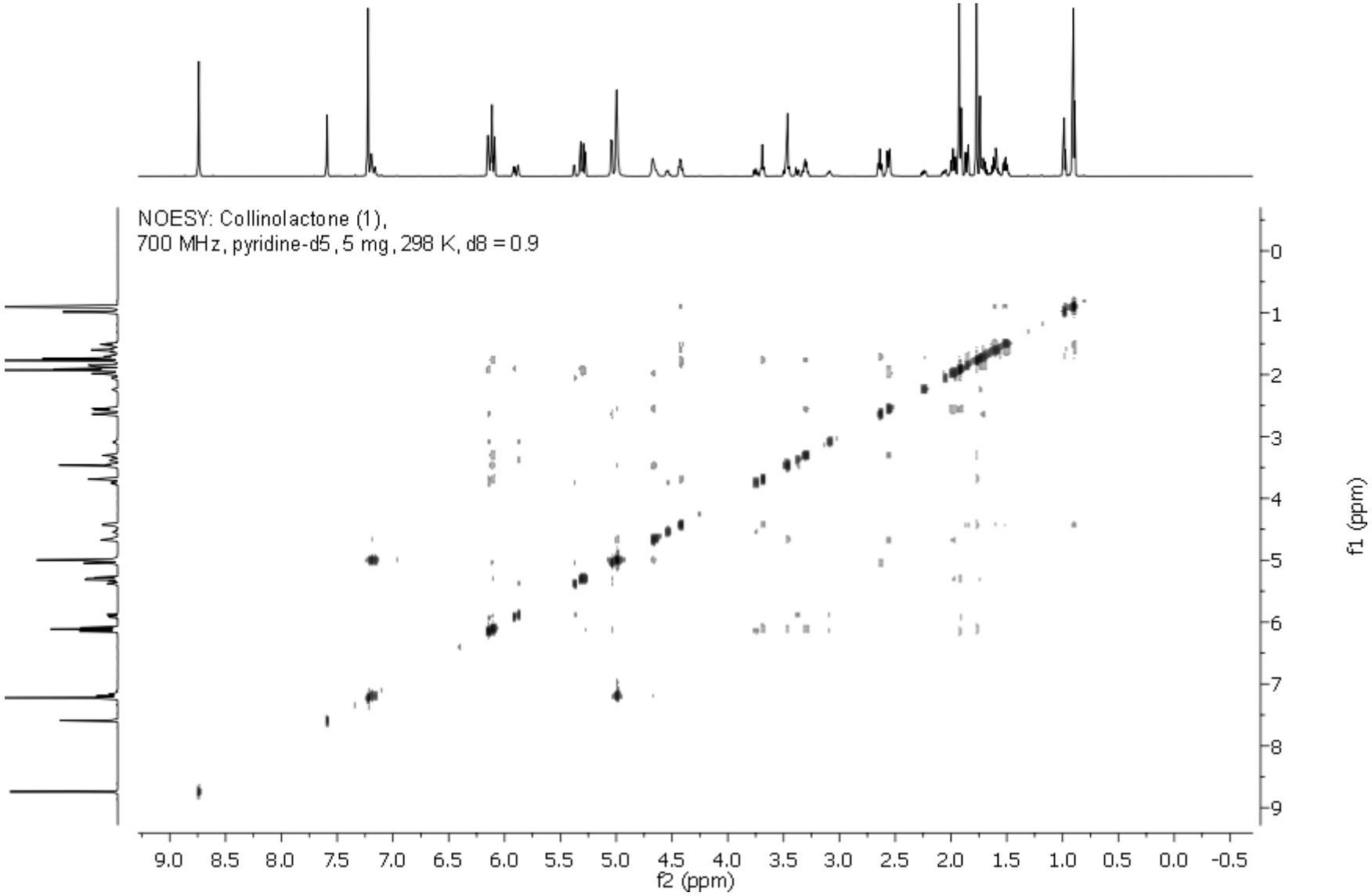

PROTON: Collinolactone (1),
700 MHz, pyridine-d5, 5 mg, 298 K
3.34
0.64
0.32
1.32
1.08
1.08
0.33
0.34
1.00
0.33
0.98
2.29
0.33
1.01
0.32
0.99
1.32
0.33
0.35
1.35
3.33
0.92
1.04
2.98
1.22
1.08
1.42
1.02
1.01
3.06
.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.
f1 (ppm)

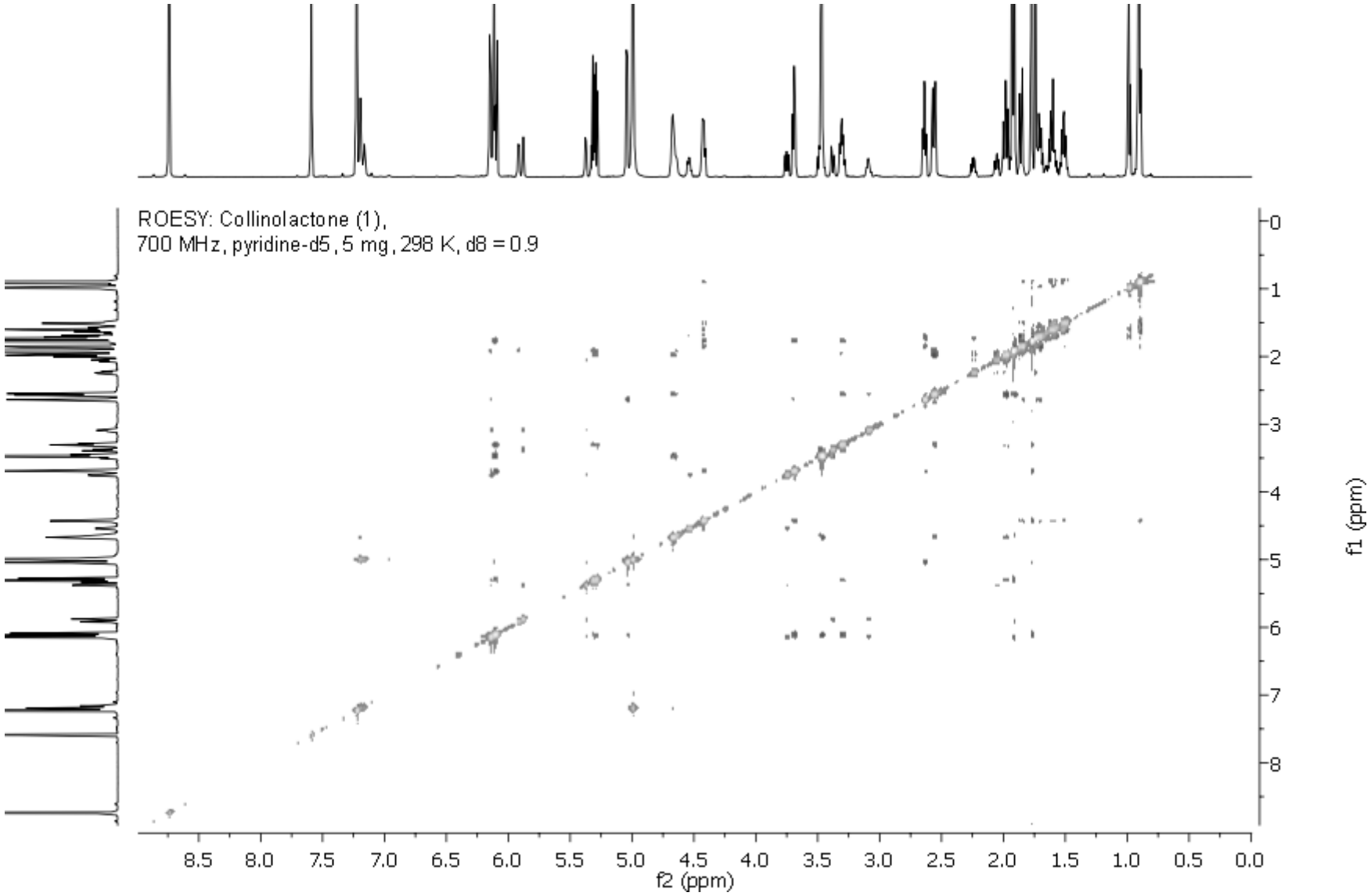

CARBON: Collinolactone (1),
700 MHz, pyridine-d5, 5 mg, 298 K
174.2
174.1
172.6
172.5
147.7
139.2
138.6
134.5
134.4
128.0
125.1
124.7
123.2
121.6
80.8
78.3
78.1
62.3
62.1
47.2
46.6
45.2
44.1
43.8
40.9
36.0
33.0
28.9
28.7
24.0
20.6
20.3
13.2
10.3
9.9
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

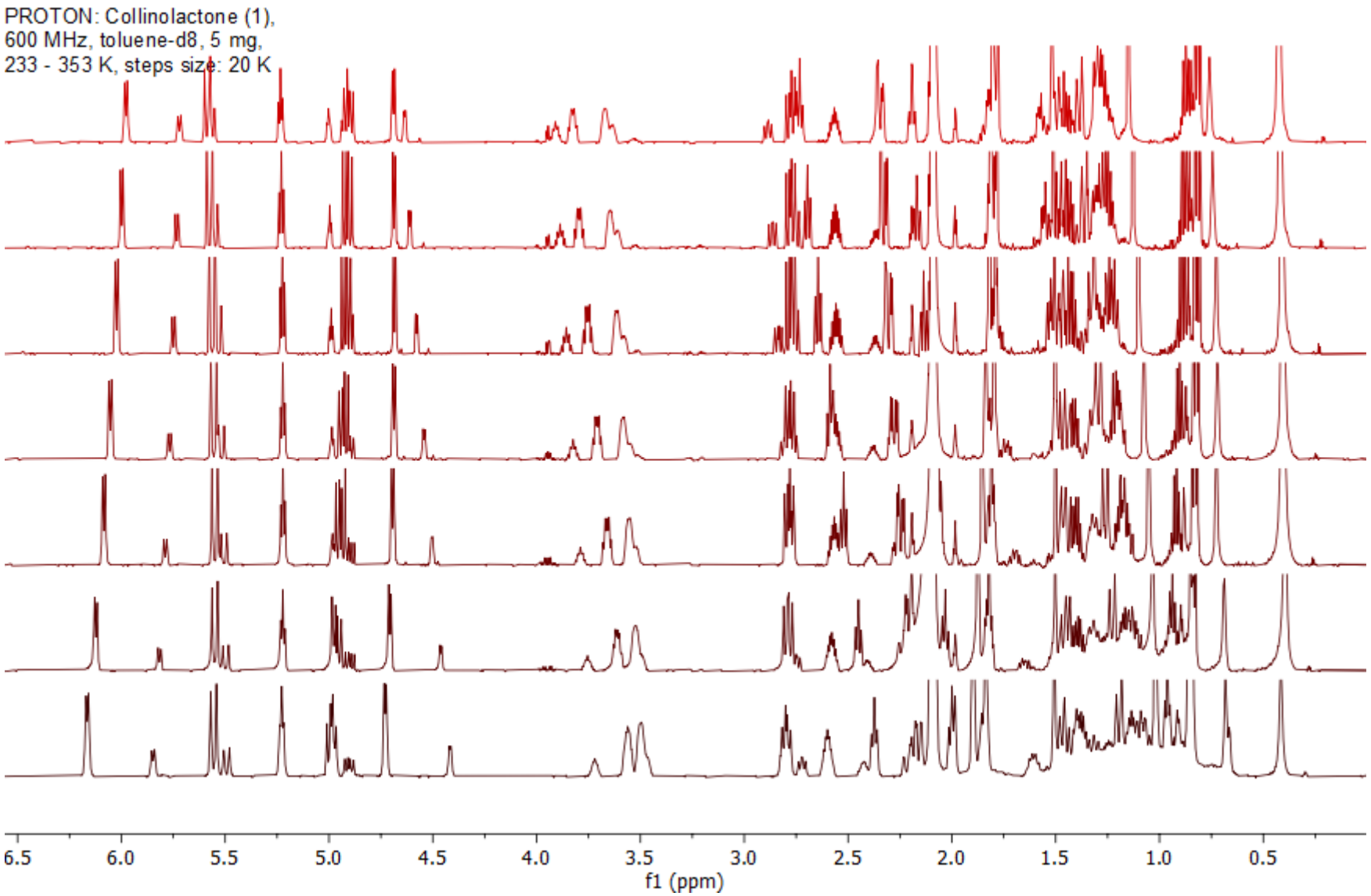

COSY: Collinolactone (1),
700 MHz, pyridine-d5, 5 mg, 298 K
f2 (ppm)
f1 (ppm)
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0
1
2
3
4
5
6
7
8
9


HSQC: Collinolactone (1),
700 MHz, pyridine-d5, 5 mg, 298 K
f2 (ppm)
f1 (ppm)

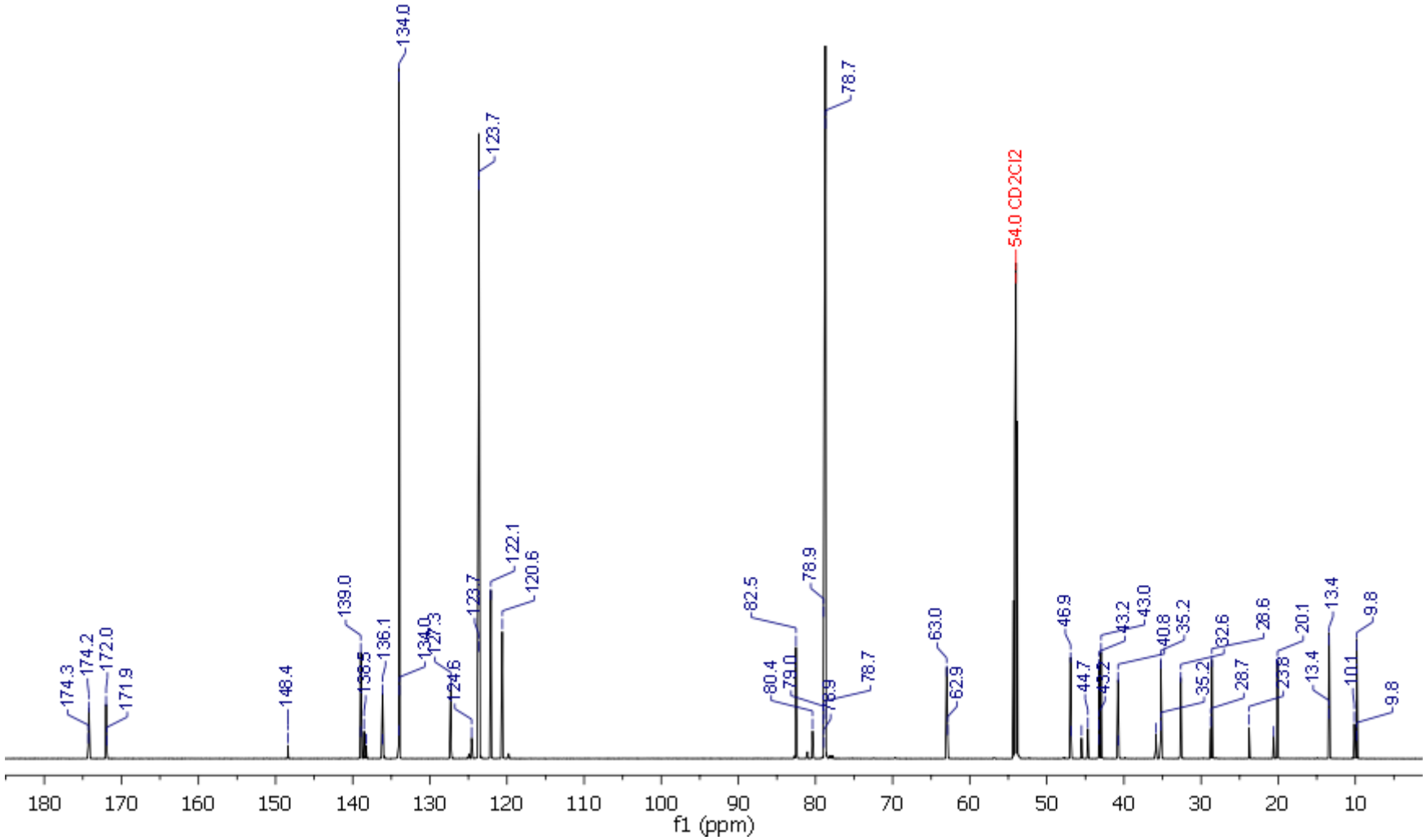

HMBC:Collinolactone (1),
700 MHz, pyridine-d5, 5 mg, 298 K
f2 (ppm)
f1 (ppm)
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
50
100
150
200

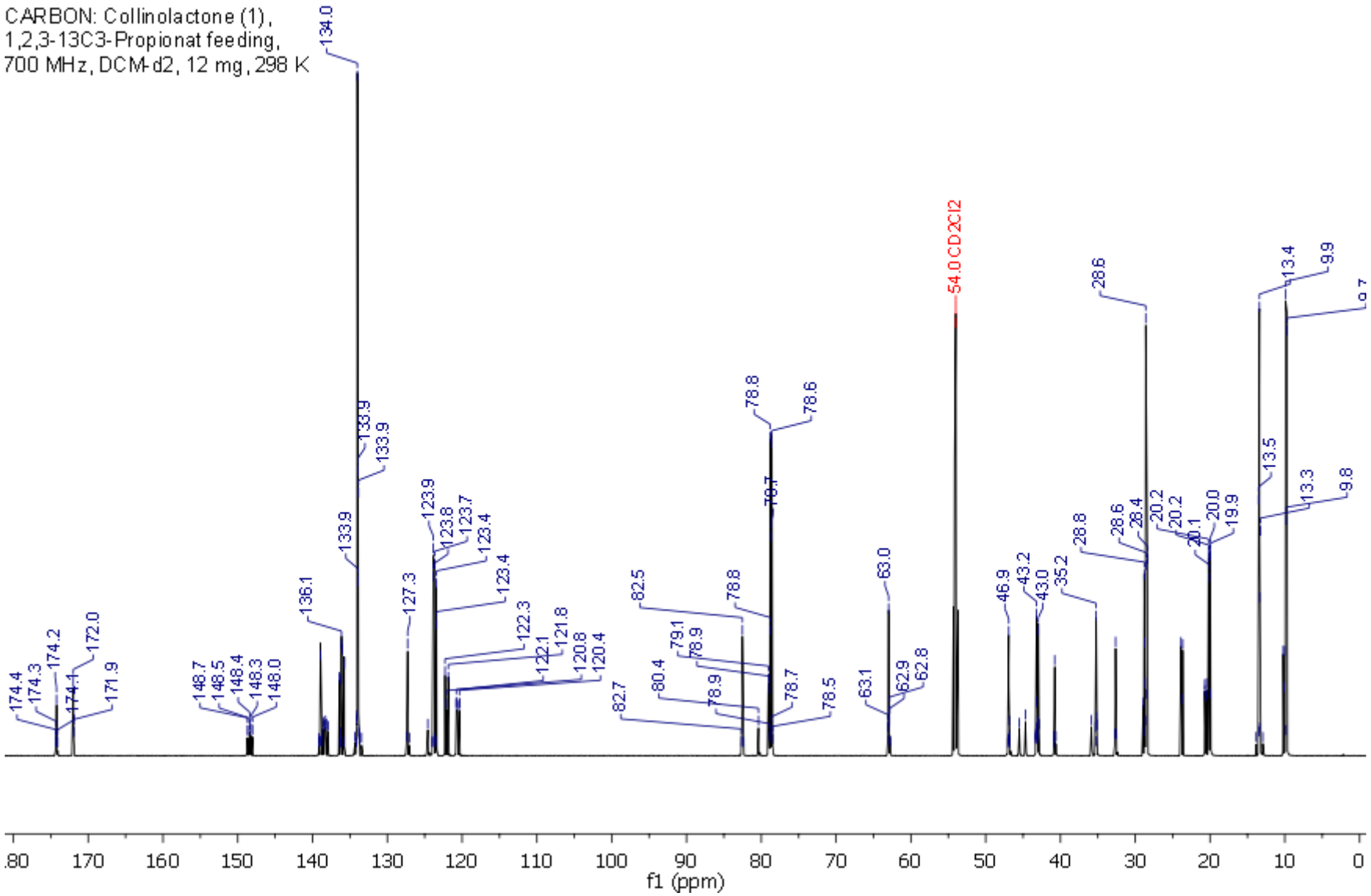

NOESY: Collinolactone (1),
700 MHz, pyridine-d5, 5 mg, 298 K, d8 = 0.9
f2 (ppm)
f1 (ppm)

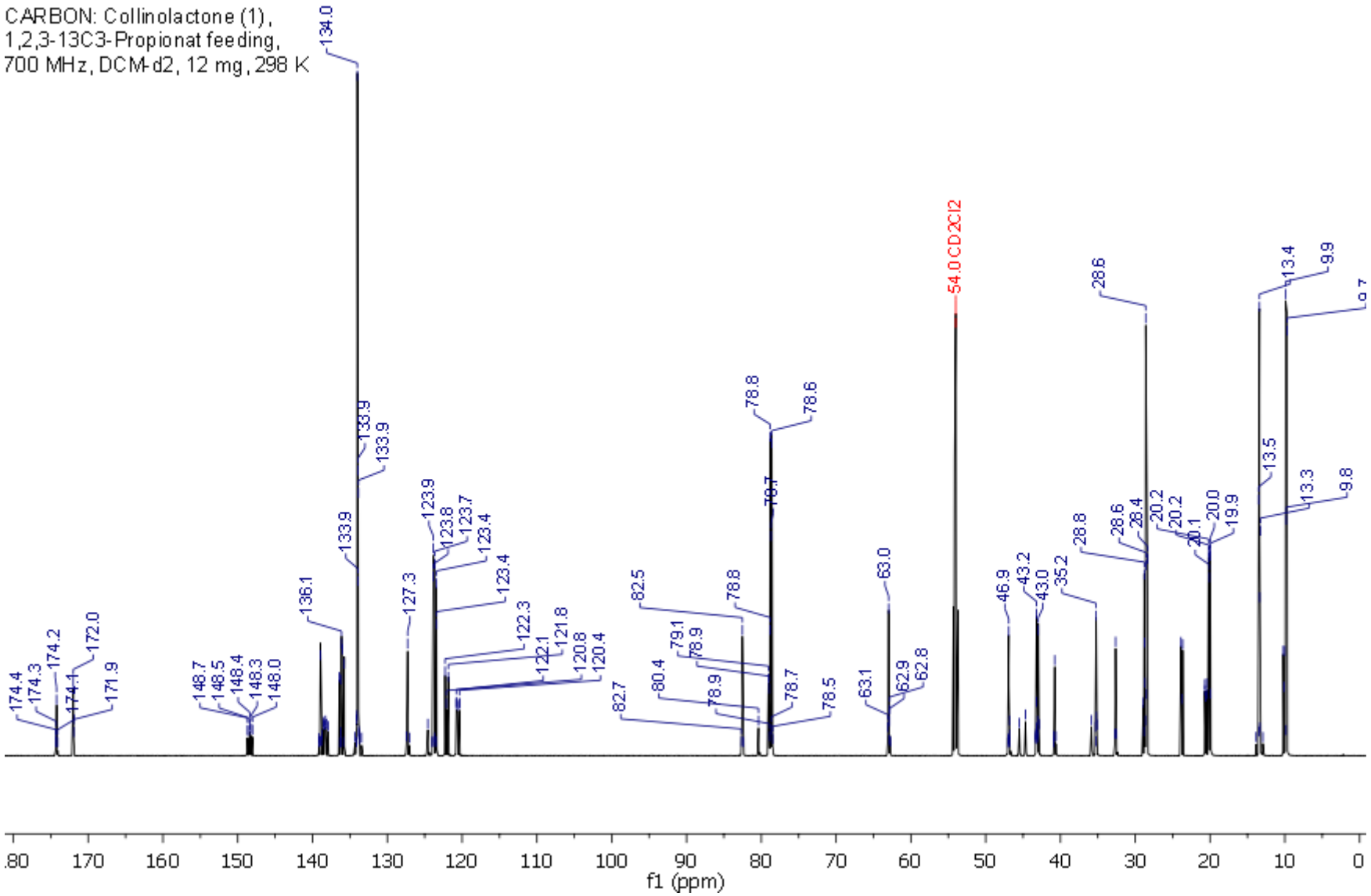

ROESY: Collinolactone (1),
700 MHz, pyridine-d5, 5 mg, 298 K, d8 = 0.9
f2 (ppm)
f1 (ppm)

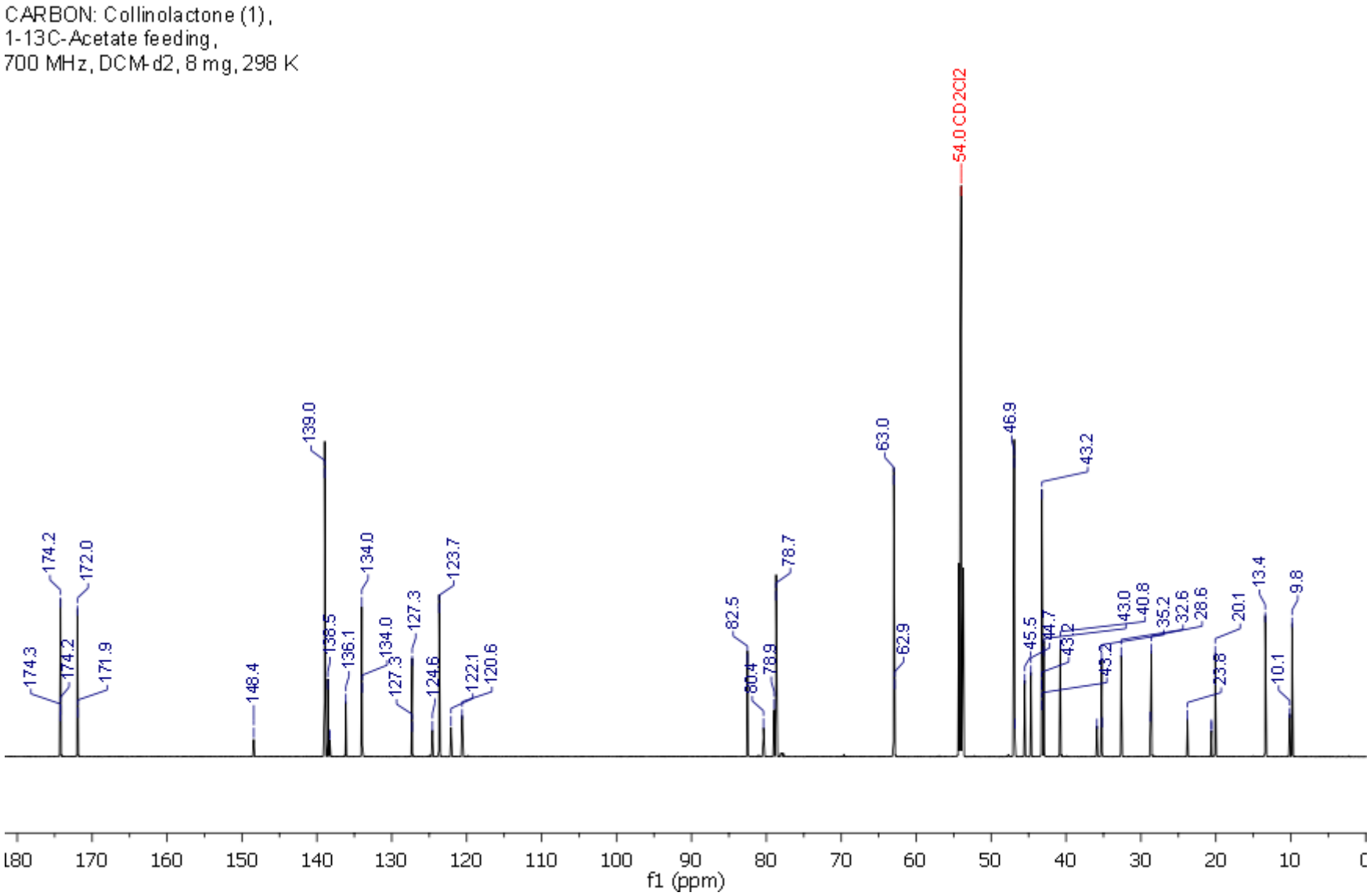

PROTON: Collinolactone (1),
600 MHz, toluene-d8, 5 mg,
233 - 353 K, steps size: 20 K
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
f1 (ppm)

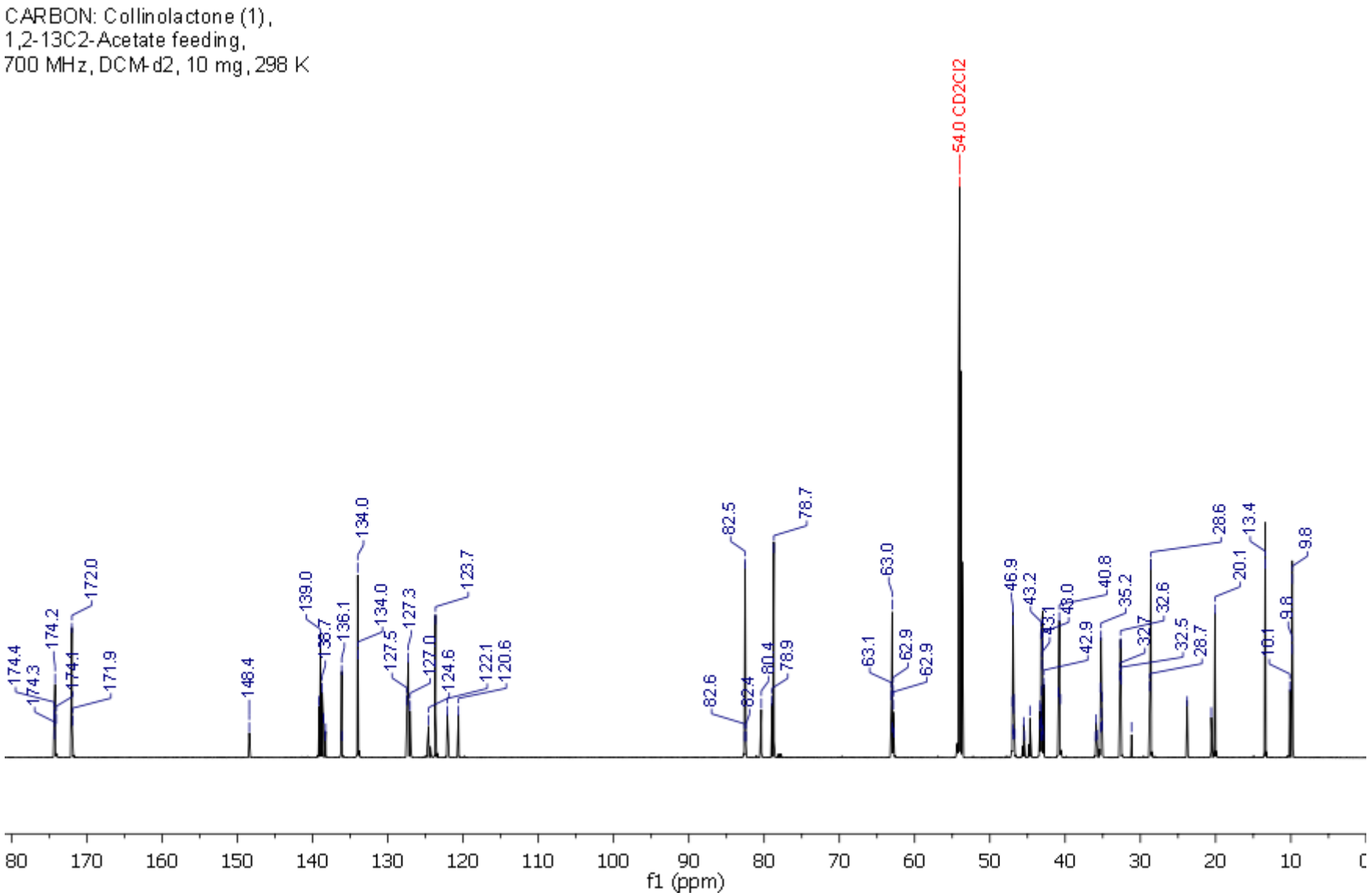
CARBON: Collinolactone (1),
1-13C-Propionate feeding,
700 MHz, DCM-d2, 19 mg, 298 K



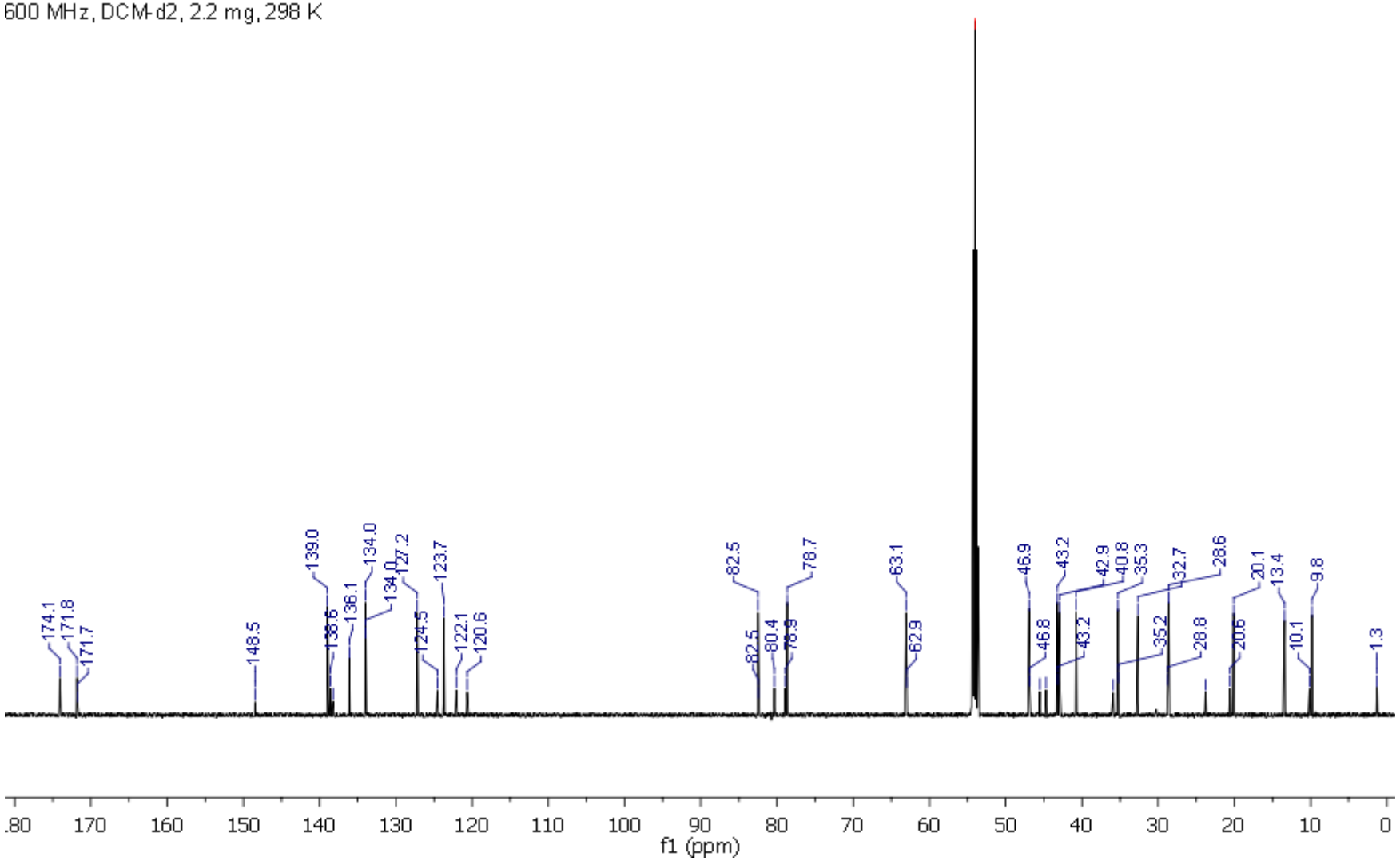

CARBON: Collinolactone (1),
1,2,3-13C3-Propionat feeding,
700 MHz, DCM-d2, 12 mg, 298 K
f1 (ppm)

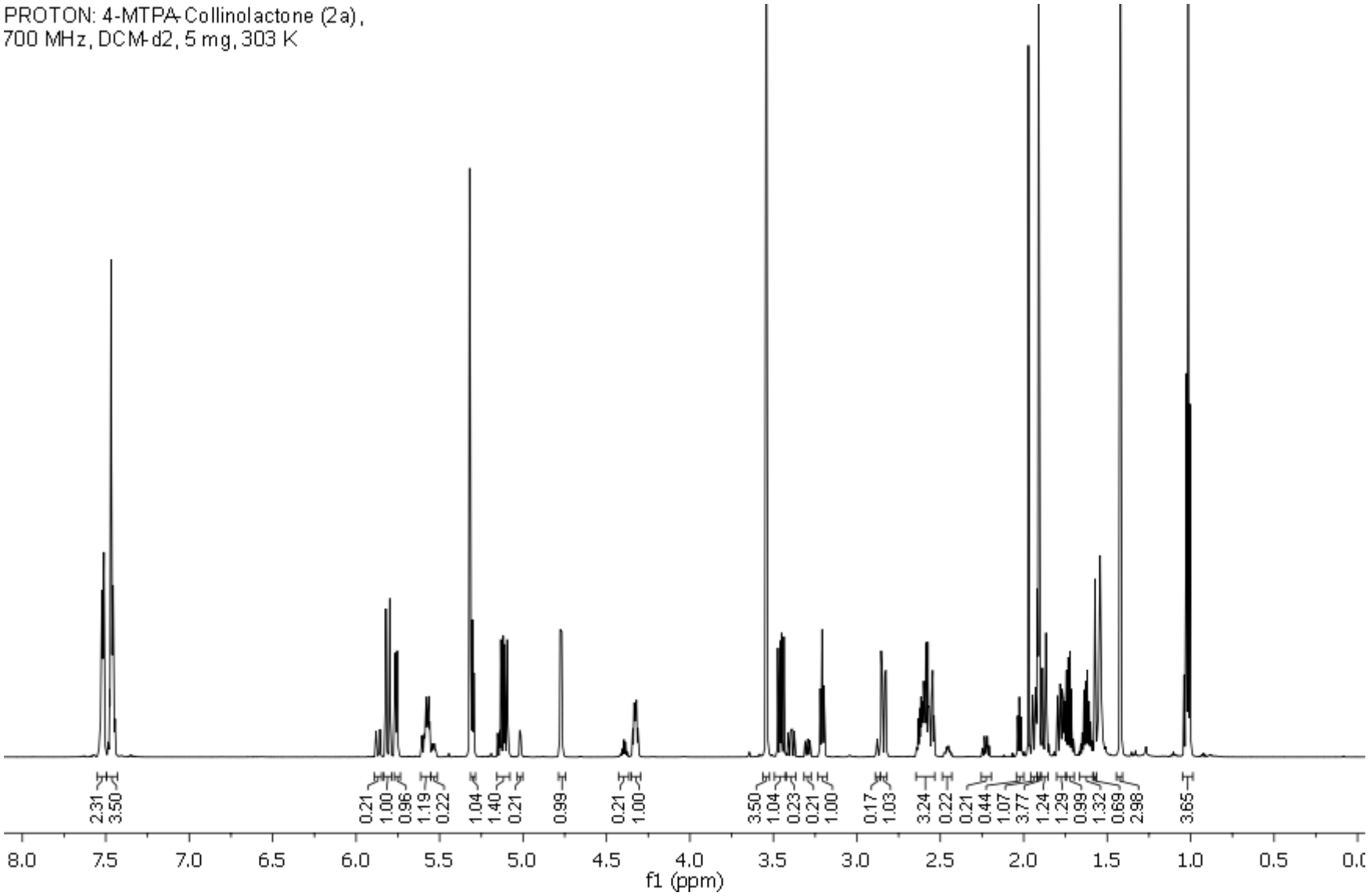

CARBON: Collinolactone (1),
1,2,3-13C3-Propionat feeding,
700 MHz, DCM-d2, 12 mg, 298 K
f1 (ppm)

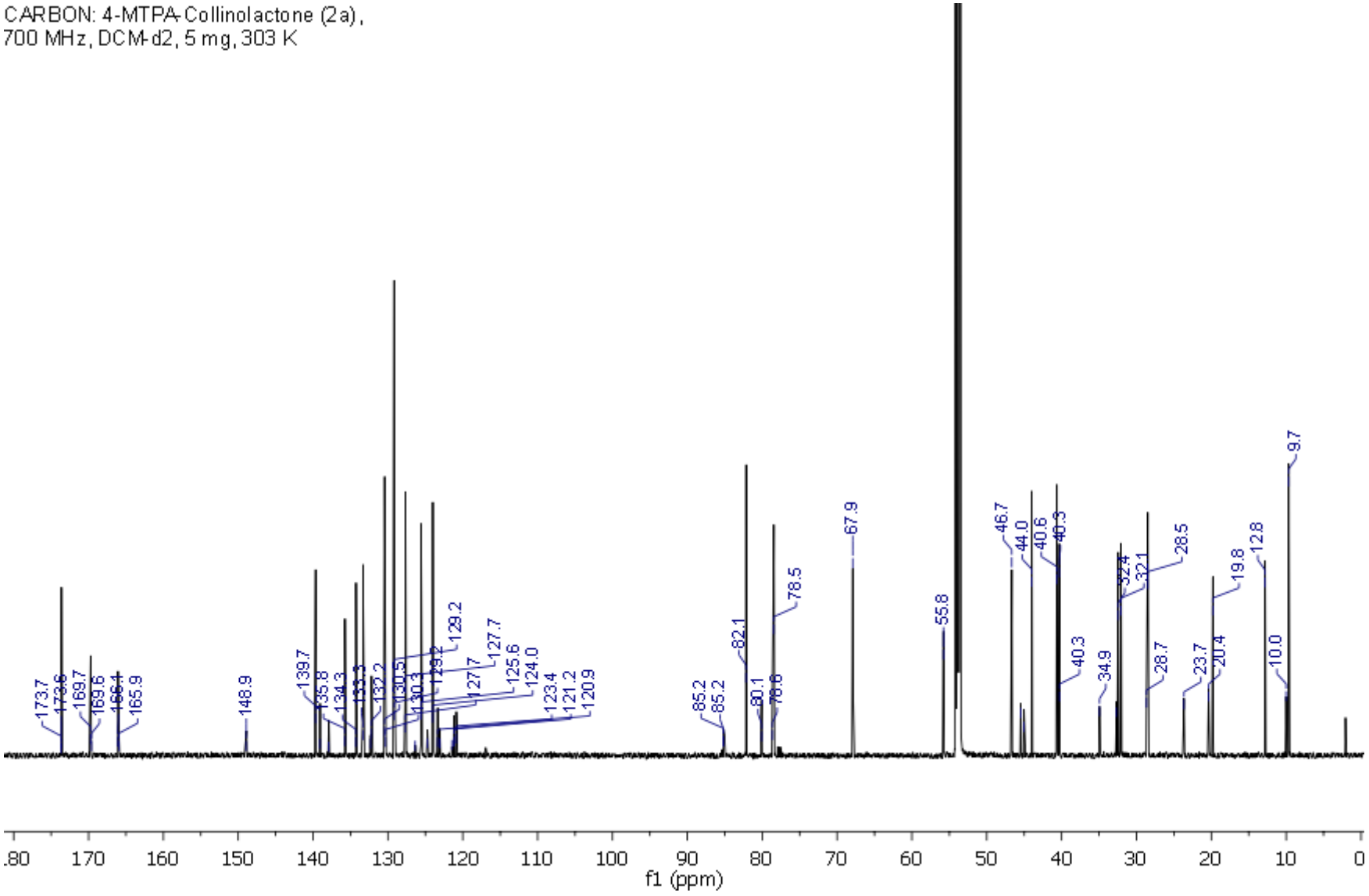

CARBON: Collinolactone (1),
1-13C-Acetate feeding,
700 MHz, DCM-d2, 8 mg, 298 K
54.0 CD2Cl2
174.3
174.2
172.0
171.9
148.4
139.0
136.5
136.1
134.0
134.0
127.3
127.3
124.6
123.7
122.1
120.6
82.5
80.4
78.9
78.7
63.0
62.9
46.9
45.5
44.7
43.2
43.2
43.0
40.8
35.2
32.6
28.6
23.8
20.1
13.4
10.1
9.8
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

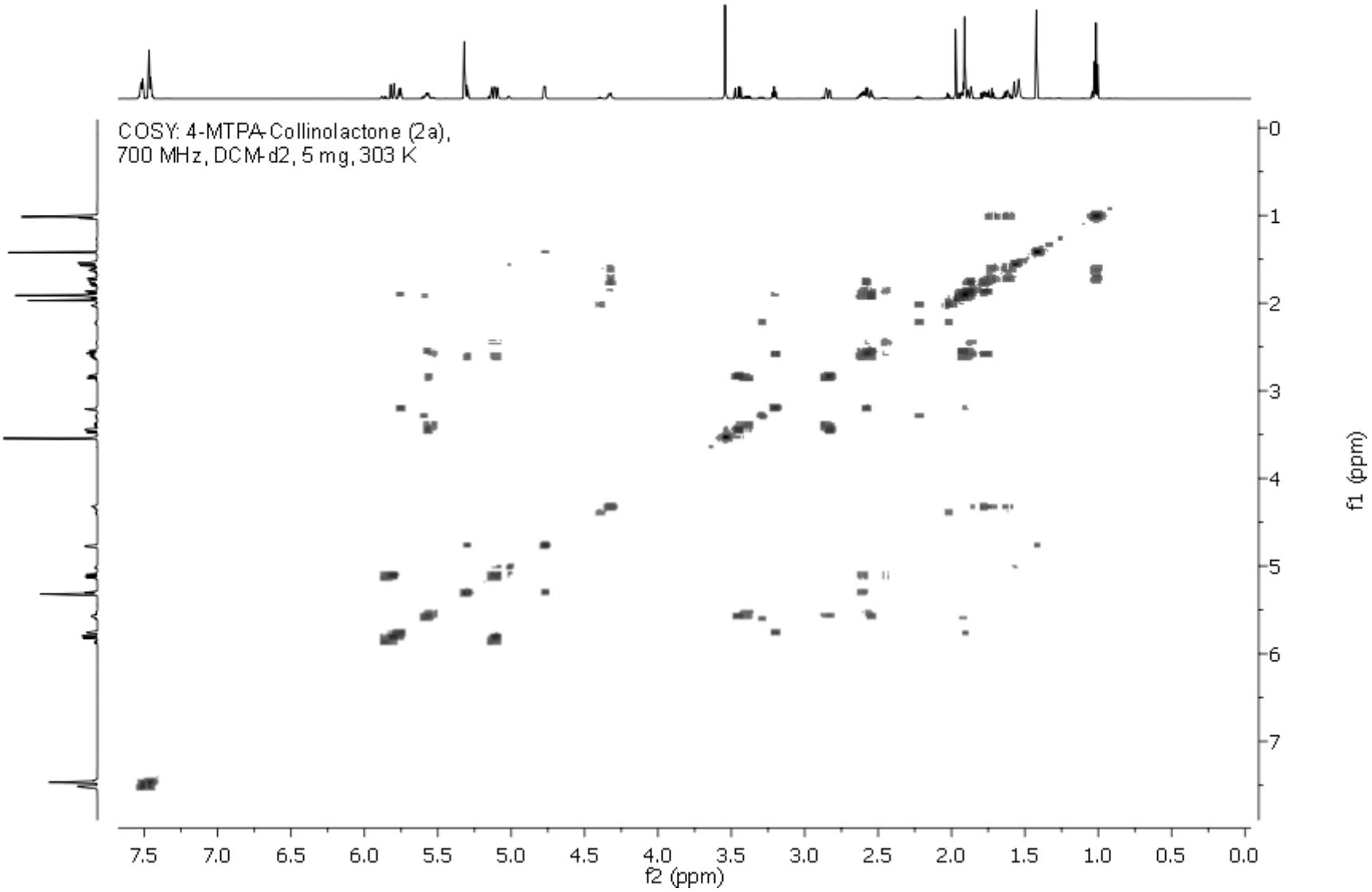

CARBON: Collinolactone (1),
1,2-13C2-Acetate feeding,
700 MHz, DCM-d2, 10 mg, 298 K
54.0 CD2Cl2
174.4
174.3
174.2
174.1
172.0
171.9
148.4
139.0
136.7
136.1
134.0
134.0
127.5
127.3
127.0
124.6
123.7
122.1
120.6
82.6
82.5
82.4
80.4
78.9
78.7
63.1
63.0
62.9
62.9
46.9
43.2
43.1
43.0
42.9
40.8
35.2
32.7
32.6
32.5
28.7
28.6
20.1
13.4
10.1
9.8
9.8
80
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
f1 (ppm)

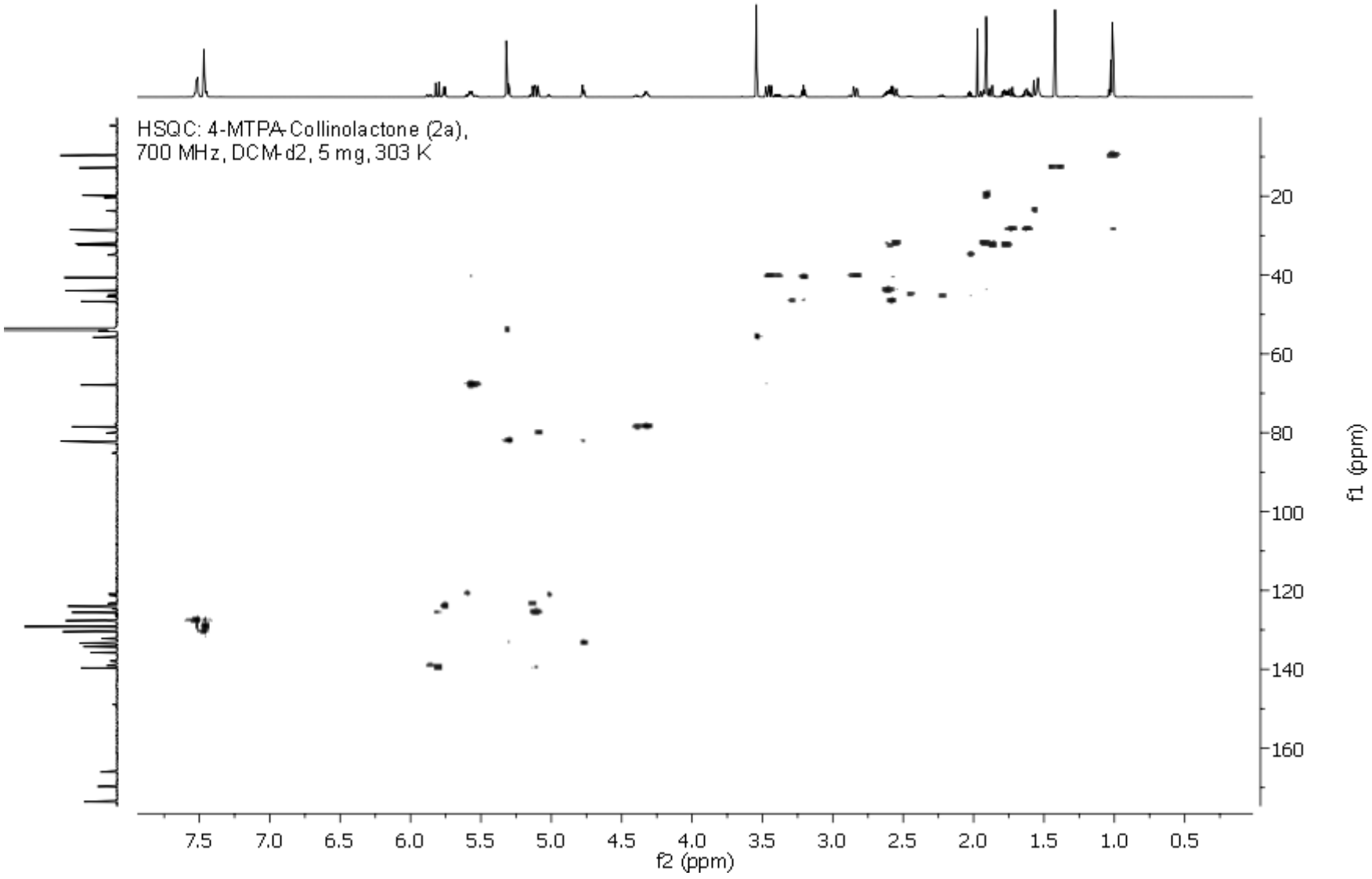
CARBON: Collinolactone (1),
18O2 feeding,
600 MHz, DCM-d2, 2.2 mg, 298 K

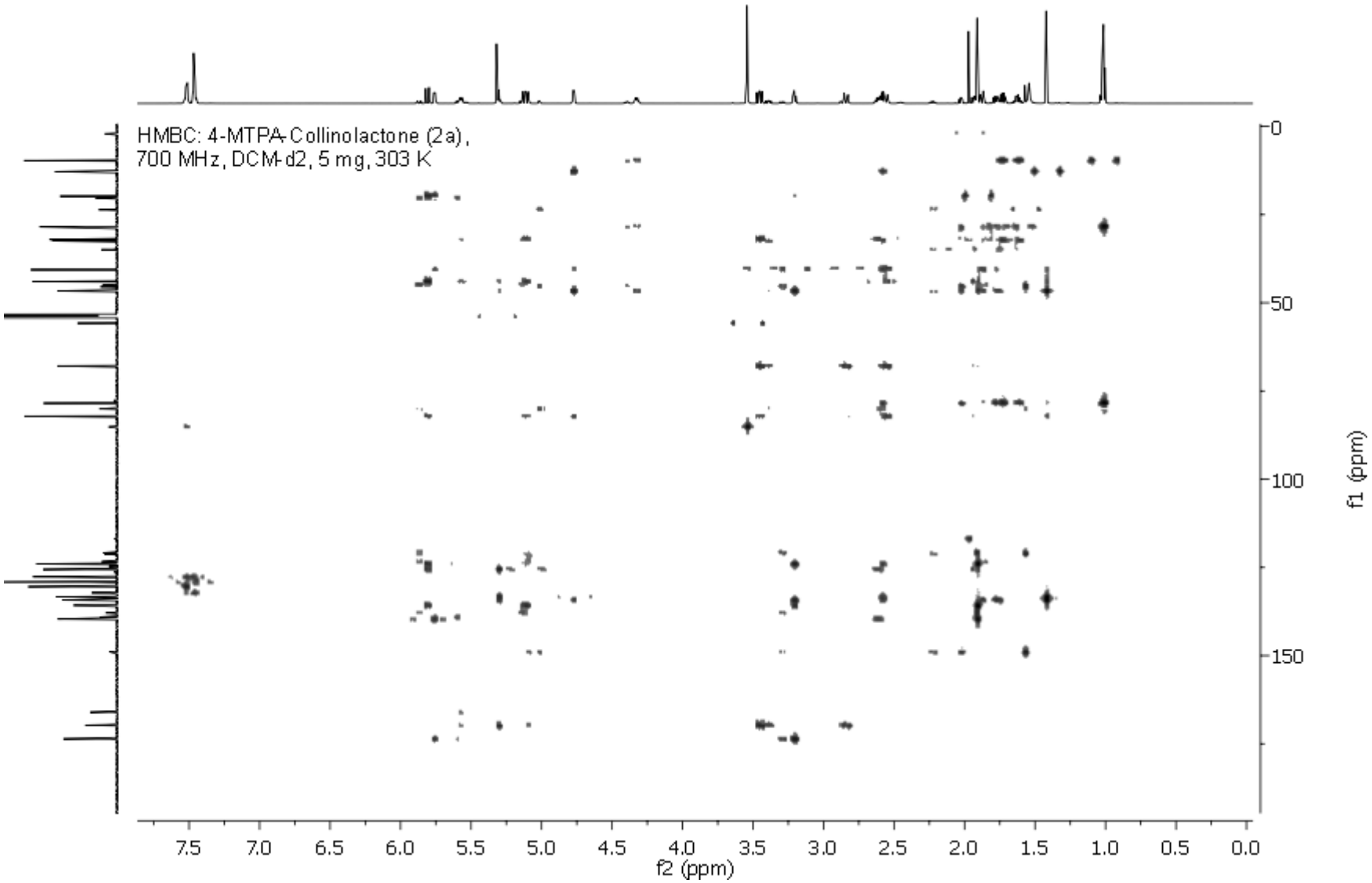



PROTON: 4-MTPA-Collinolactone (2a),
700 MHz, DCM-d2, 5 mg, 303 K
2.31
3.50
0.21
1.00
0.96
1.19
0.22
1.04
1.40
0.21
0.99
0.21
1.00
3.50
1.04
0.23
0.21
1.00
0.17
1.03
3.24
0.22
0.21
0.44
1.07
3.77
1.24
1.29
0.99
1.32
0.69
2.98
3.65
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
f1 (ppm)

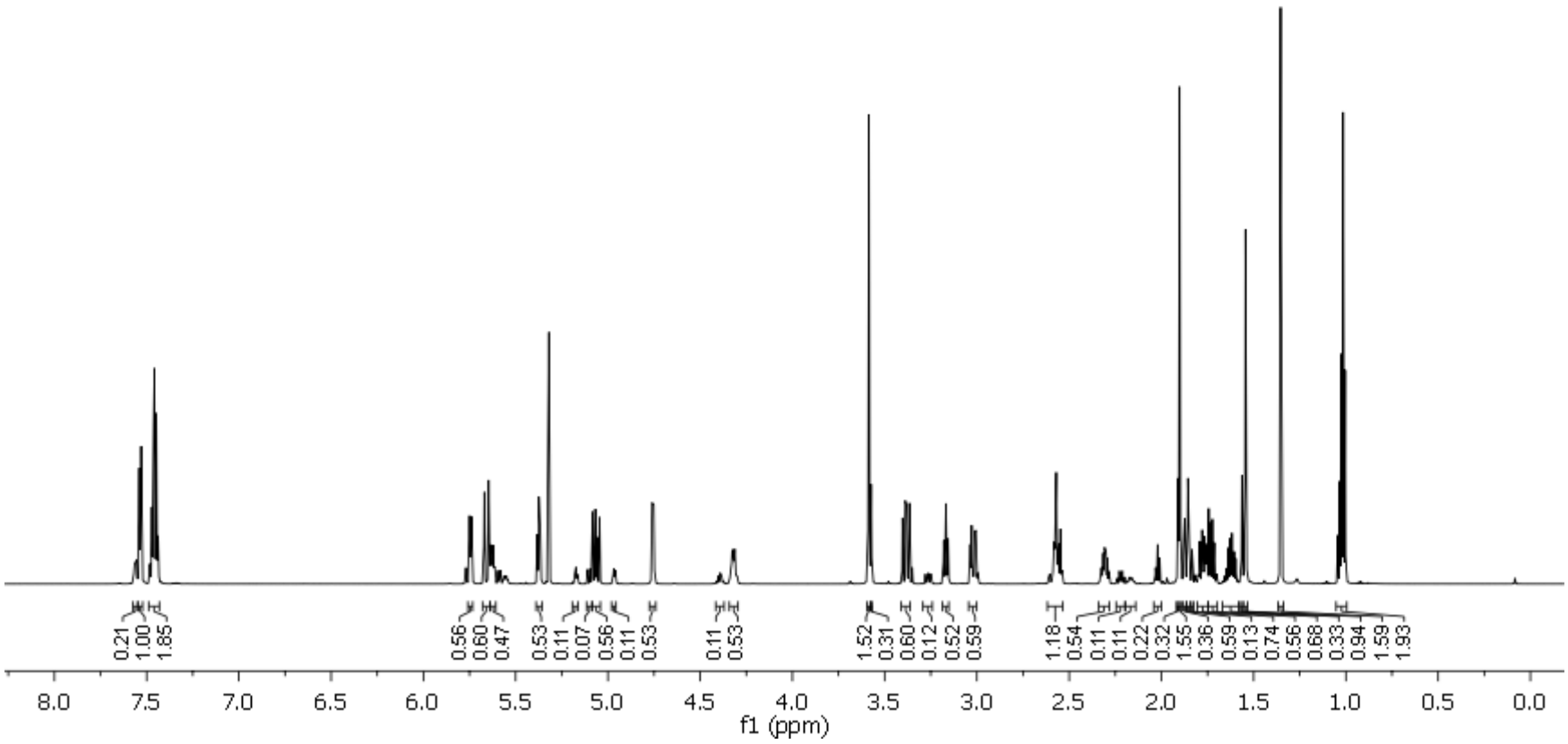

CARBON: 4-MTPA-Collinolactone (2a),
700 MHz, DCM-d2, 5 mg, 303 K
173.7
169.7
169.6
166.4
165.9
148.9
139.7
135.8
134.3
133.3
132.2
130.5
130.3
129.2
129.2
127.7
127.7
125.6
124.0
123.4
121.2
120.9
85.2
85.2
82.1
80.1
78.6
78.5
67.9
55.8
46.7
44.0
40.6
40.3
40.3
34.9
32.4
32.1
28.7
28.5
23.7
20.4
19.8
12.8
10.0
9.7
f1 (ppm)

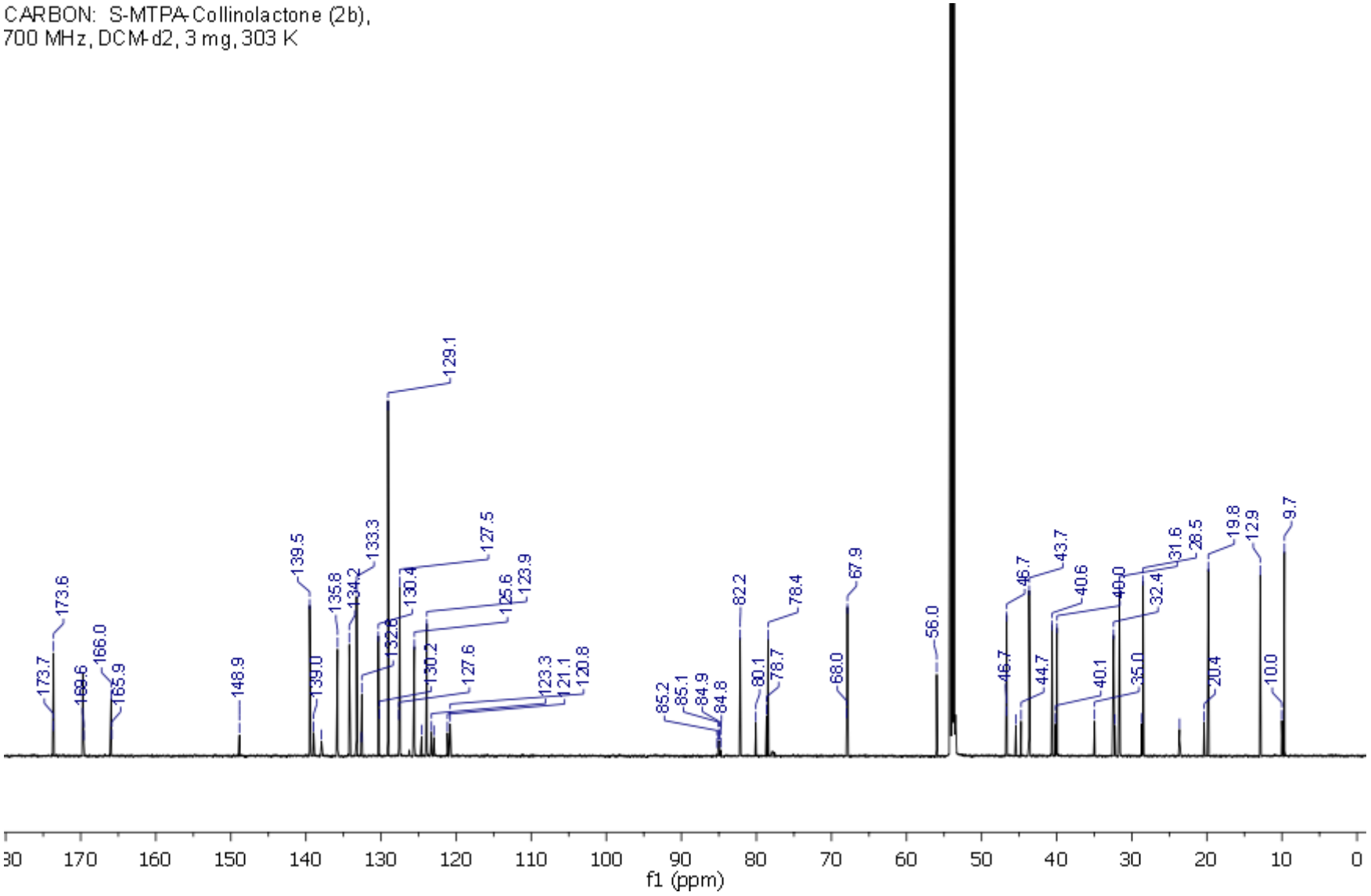

COSY: 4-MTPA-Collinolactone (2a),
700 MHz, DCM-d2, 5 mg, 303 K
f2 (ppm)
f1 (ppm)

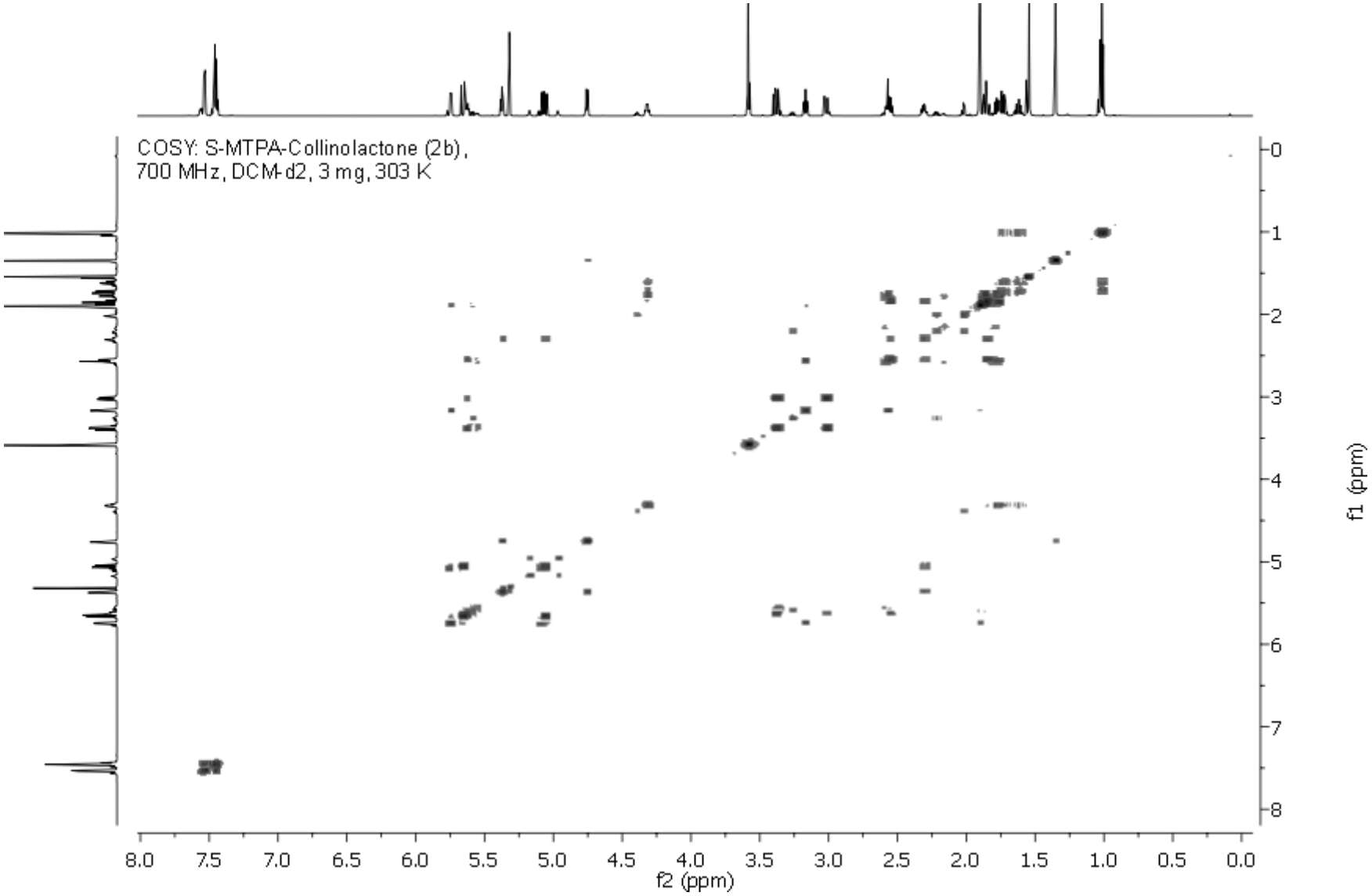

HSQC: 4-MTPA-Collinolactone (2a),
700 MHz, DCM-d2, 5 mg, 303 K
f2 (ppm)
f1 (ppm)

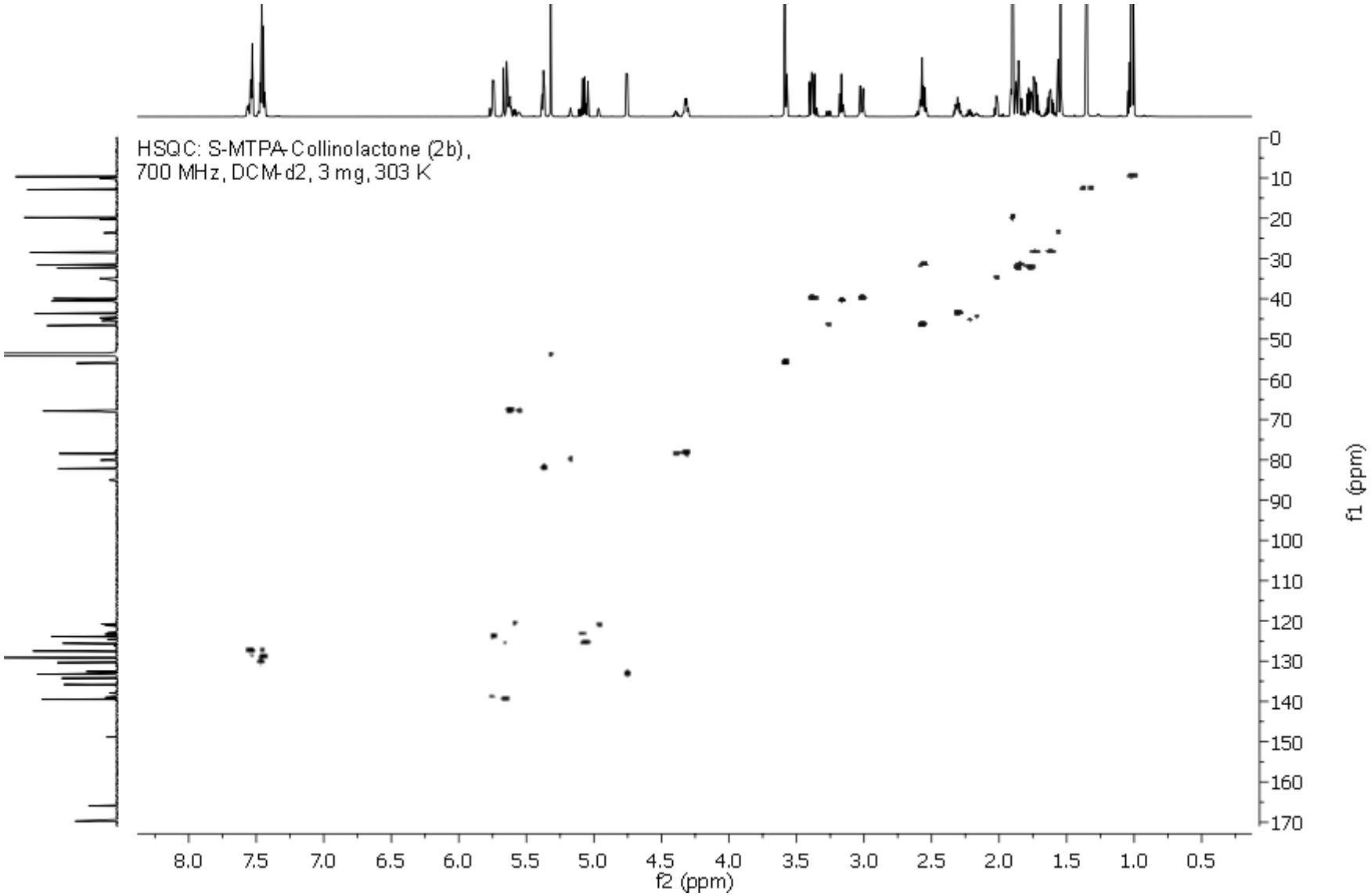

HMBC: 4-MTPA-Collinolactone (2a),
700 MHz, DCM-d2, 5 mg, 303 K
f2 (ppm)
f1 (ppm)
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
0
50
100
150

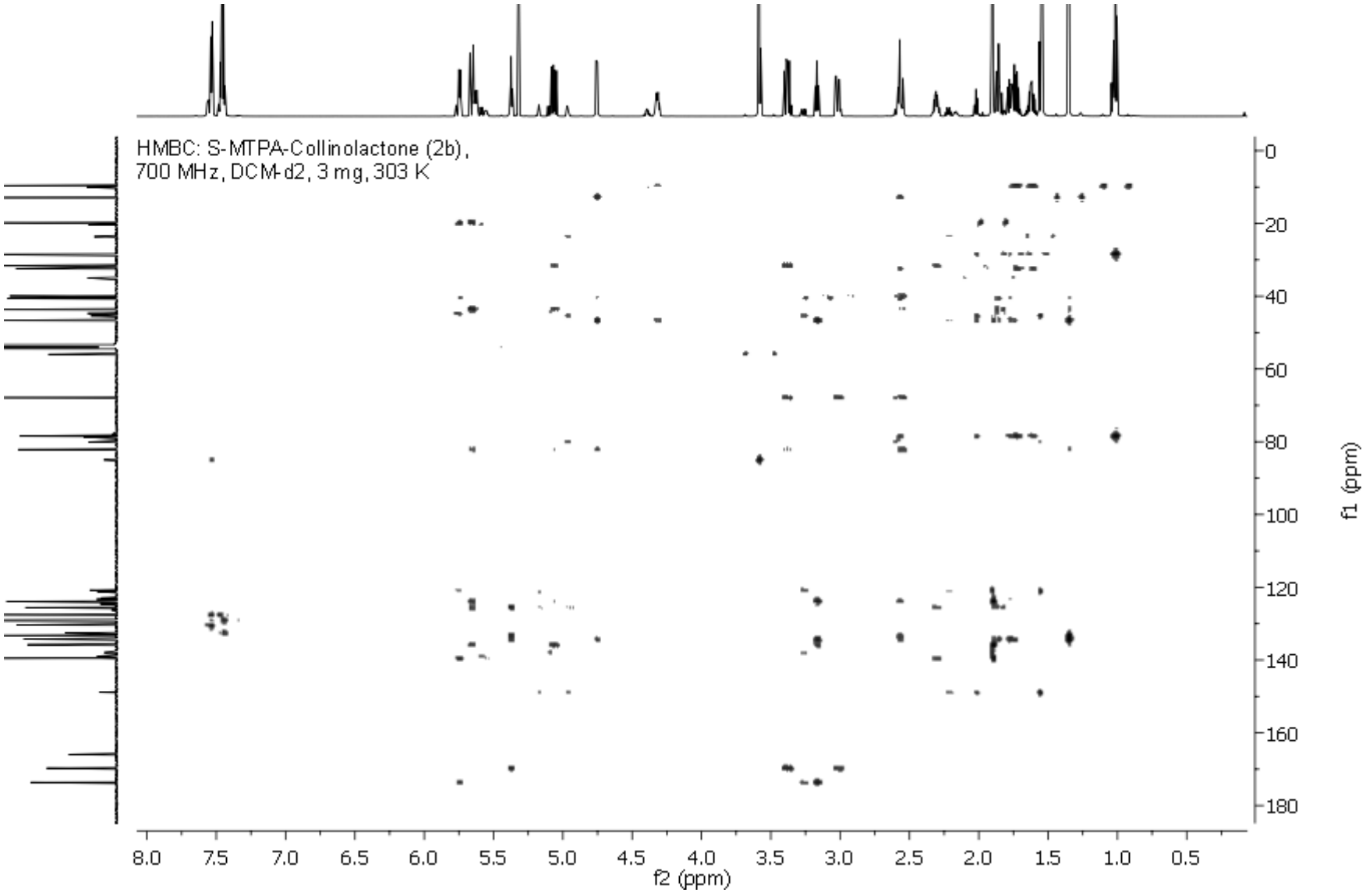
PROTON: S-MTPA-Collinolactone (2b),
700 MHz, DCM-d2, 3 mg, 303 K

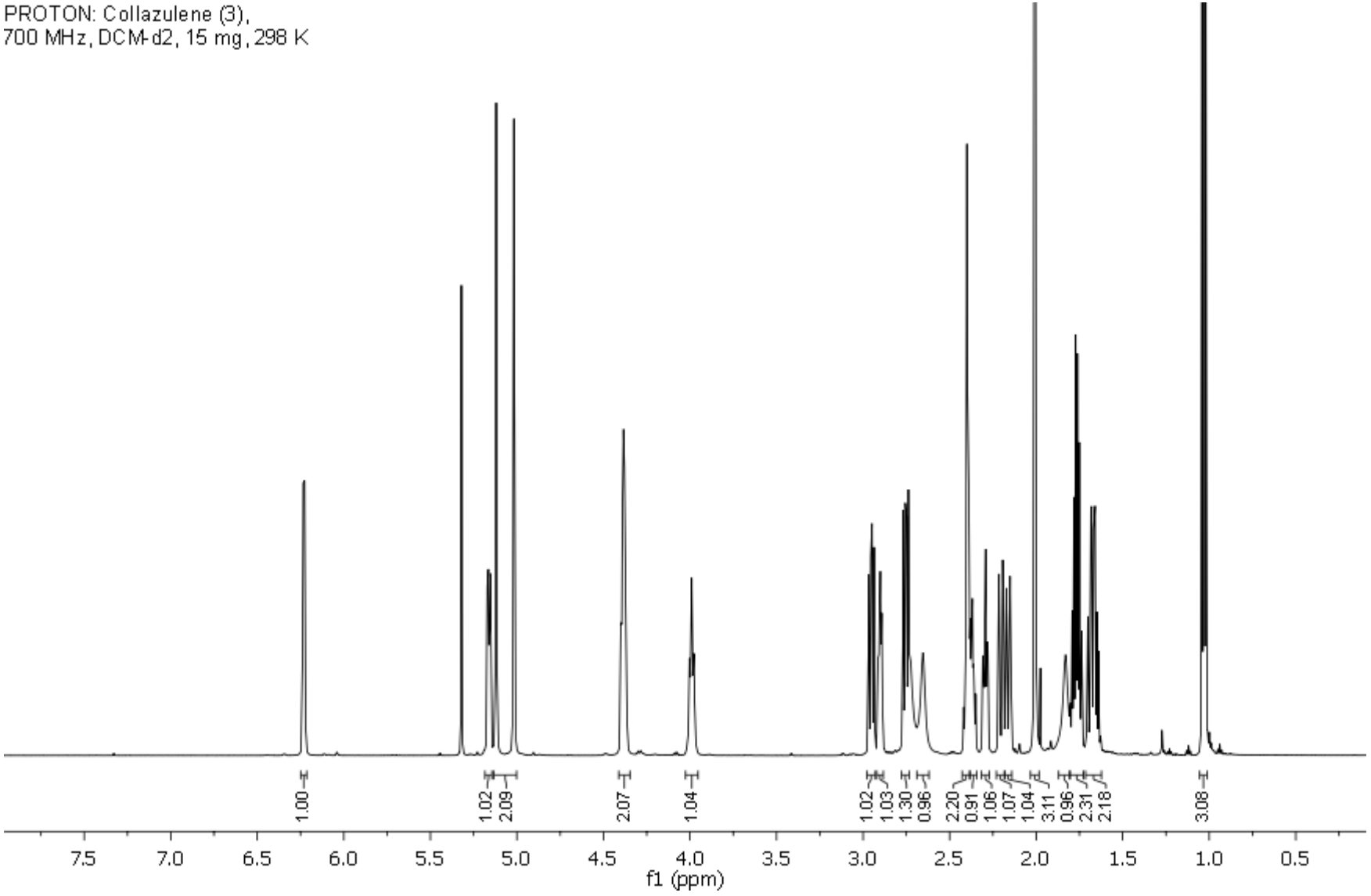


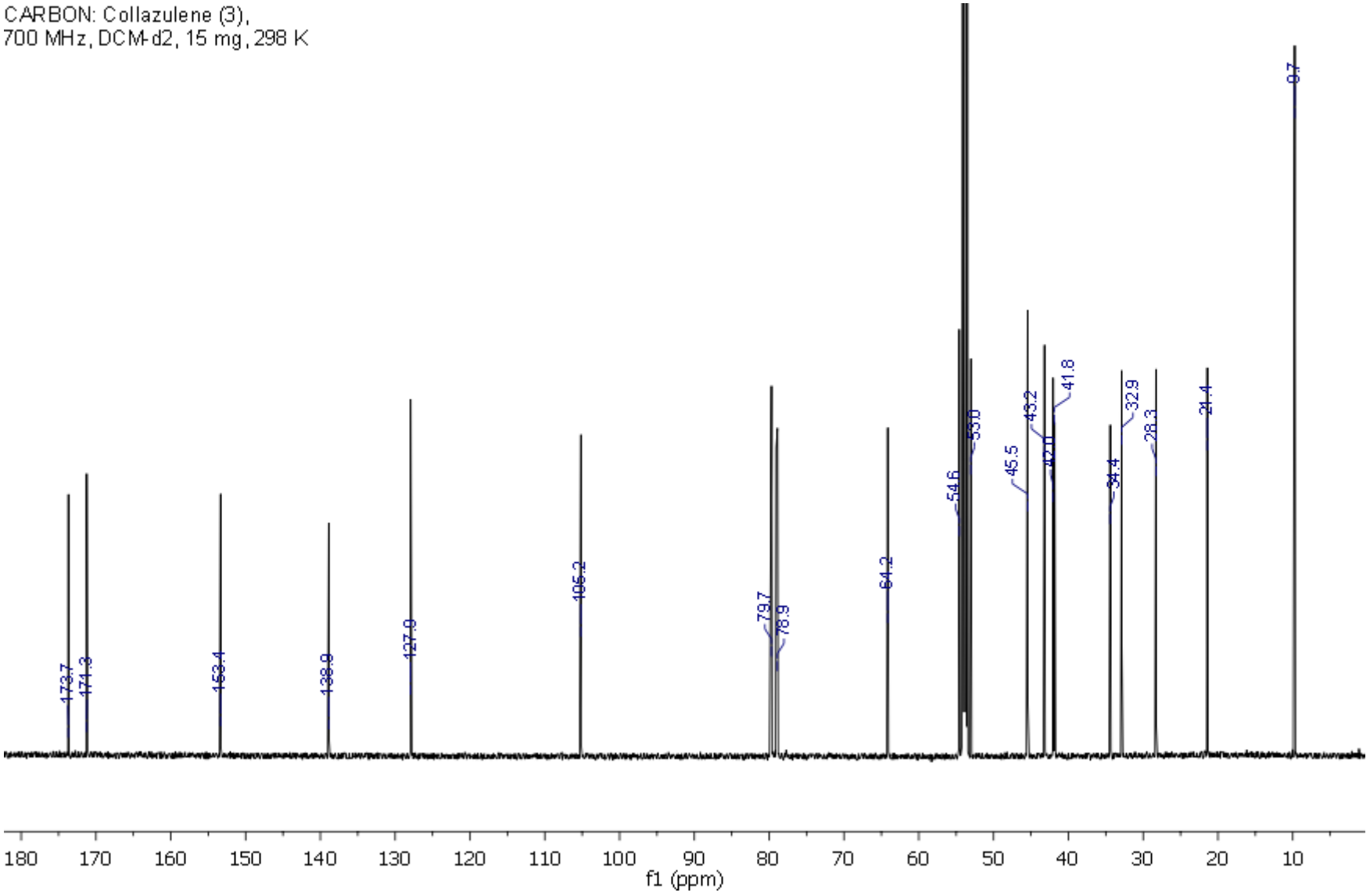

CARBON: S-MTPA-Collinolactone (2b),
700 MHz, DCM-d2, 3 mg, 303 K
173.7
173.6
169.6
166.0
165.9
148.9
139.5
139.0
135.8
134.2
133.3
132.8
130.4
130.2
129.1
127.6
127.5
125.6
123.9
123.3
121.1
120.8
85.2
85.1
84.9
84.8
82.2
80.1
78.7
78.4
68.0
67.9
56.0
46.7
46.7
44.7
43.7
40.6
40.1
40.0
35.0
32.4
31.6
28.5
20.4
19.8
12.9
10.0
9.7
f1 (ppm)

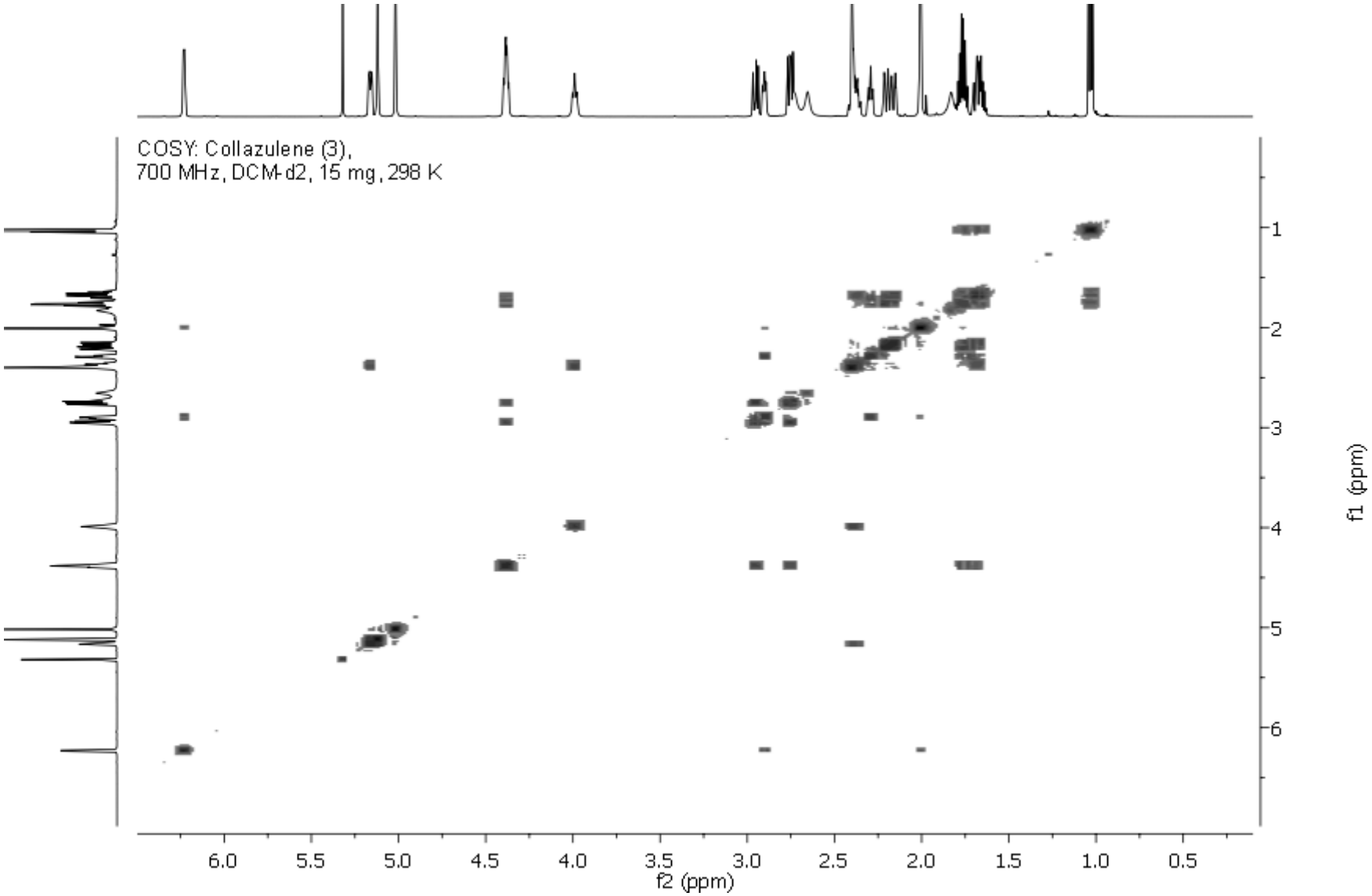

COSY: S-MTPA-Collinolactone (2b),
700 MHz, DCM-d2, 3 mg, 303 K
f2 (ppm)
f1 (ppm)
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
0
1
2
3
4
5
6
7
8

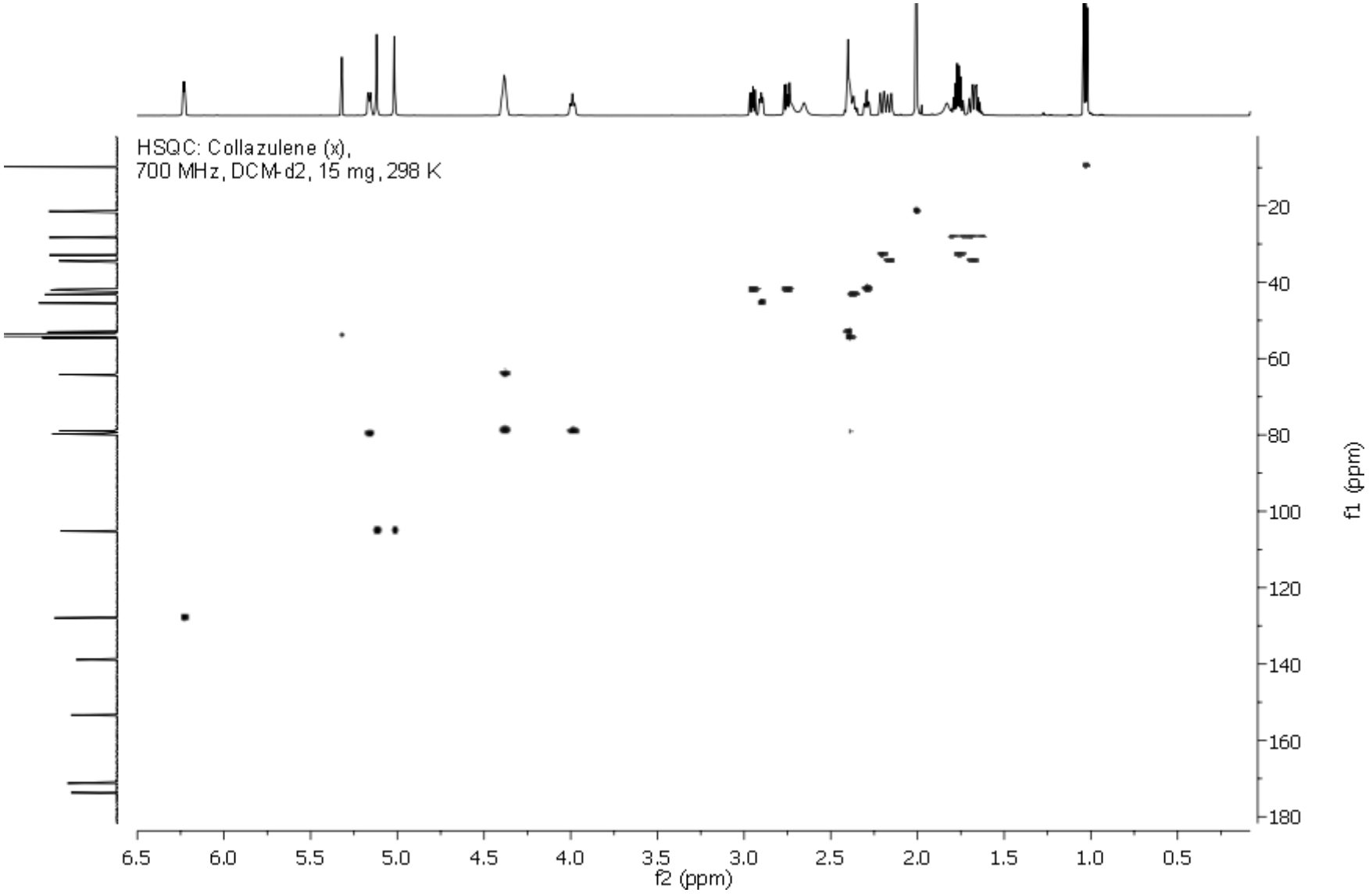

HSQC: S-MTPA-Collinolactone (2b),
700 MHz, DCM-d2, 3 mg, 303 K
f2 (ppm)
f1 (ppm)

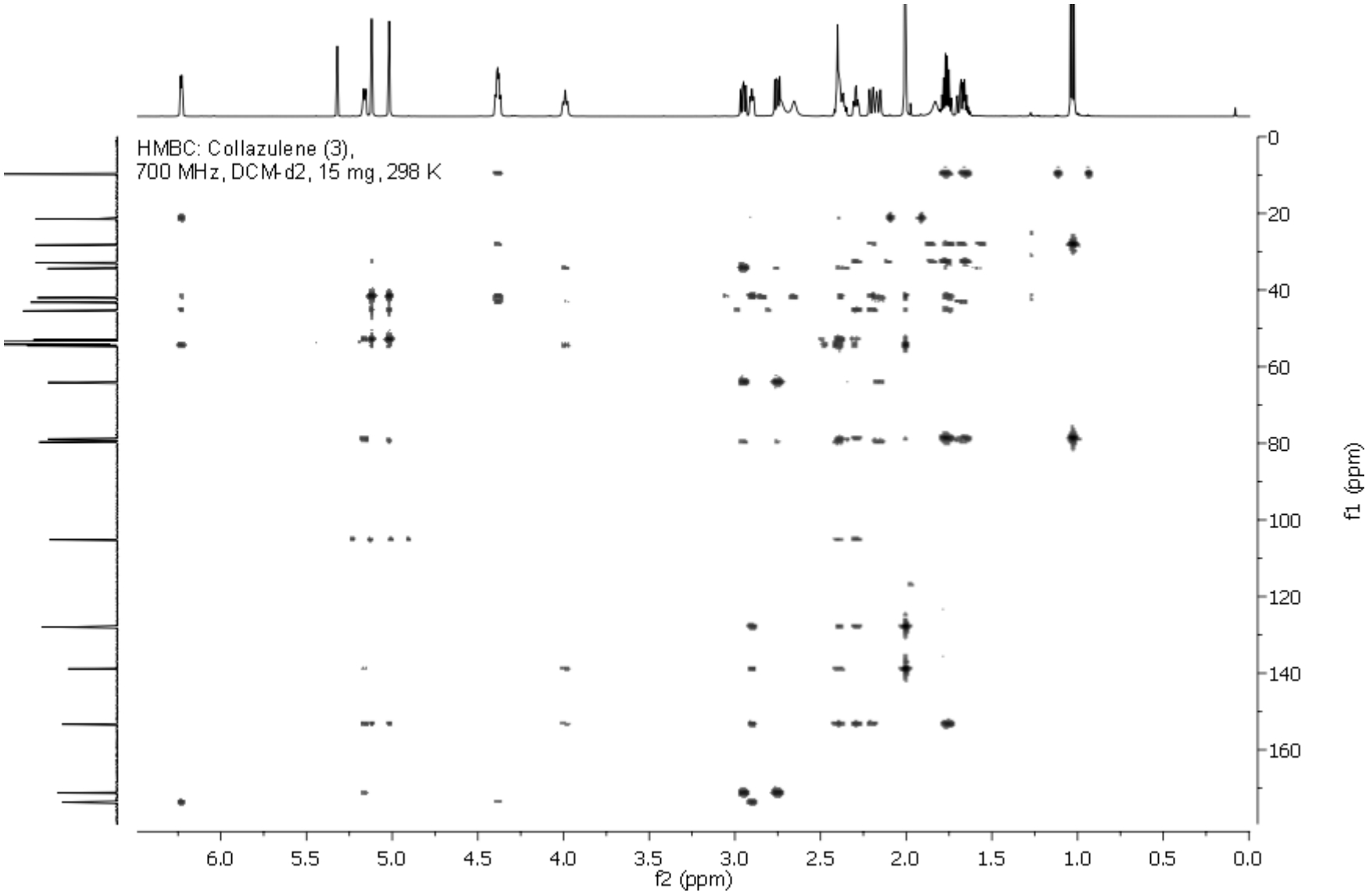

HMBC: S-MTPA-Collinolactone (2b),
700 MHz, DCM-d2, 3 mg, 303 K
f2 (ppm)
f1 (ppm)

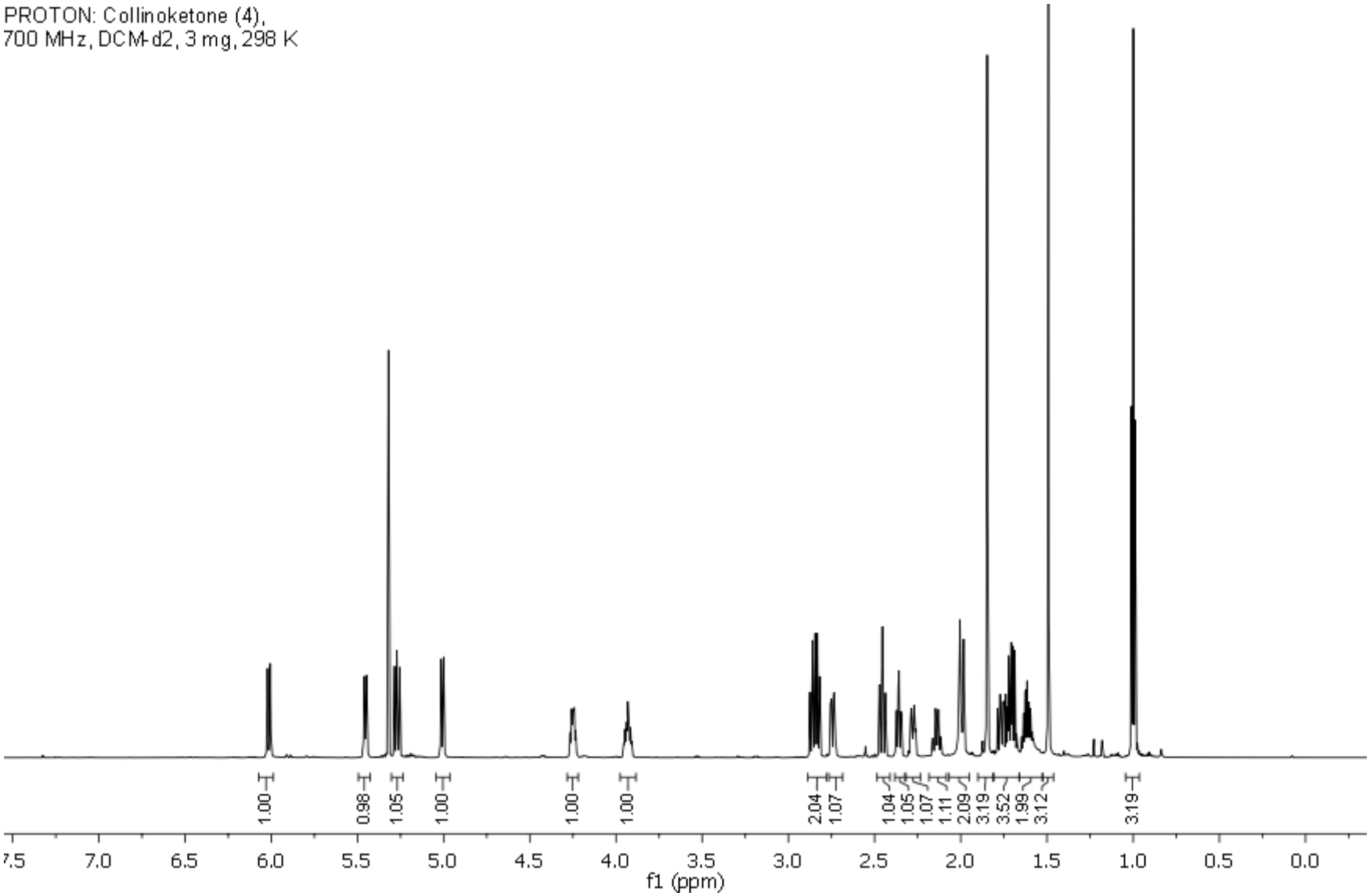

PROTON: Collazulene (3),
700 MHz, DCM-d2, 15 mg, 298 K
1.00
1.02
2.09
2.07
1.04
1.02
1.03
1.30
0.96
2.20
0.91
1.06
1.07
1.04
3.11
0.96
2.31
2.18
3.08
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
f1 (ppm)

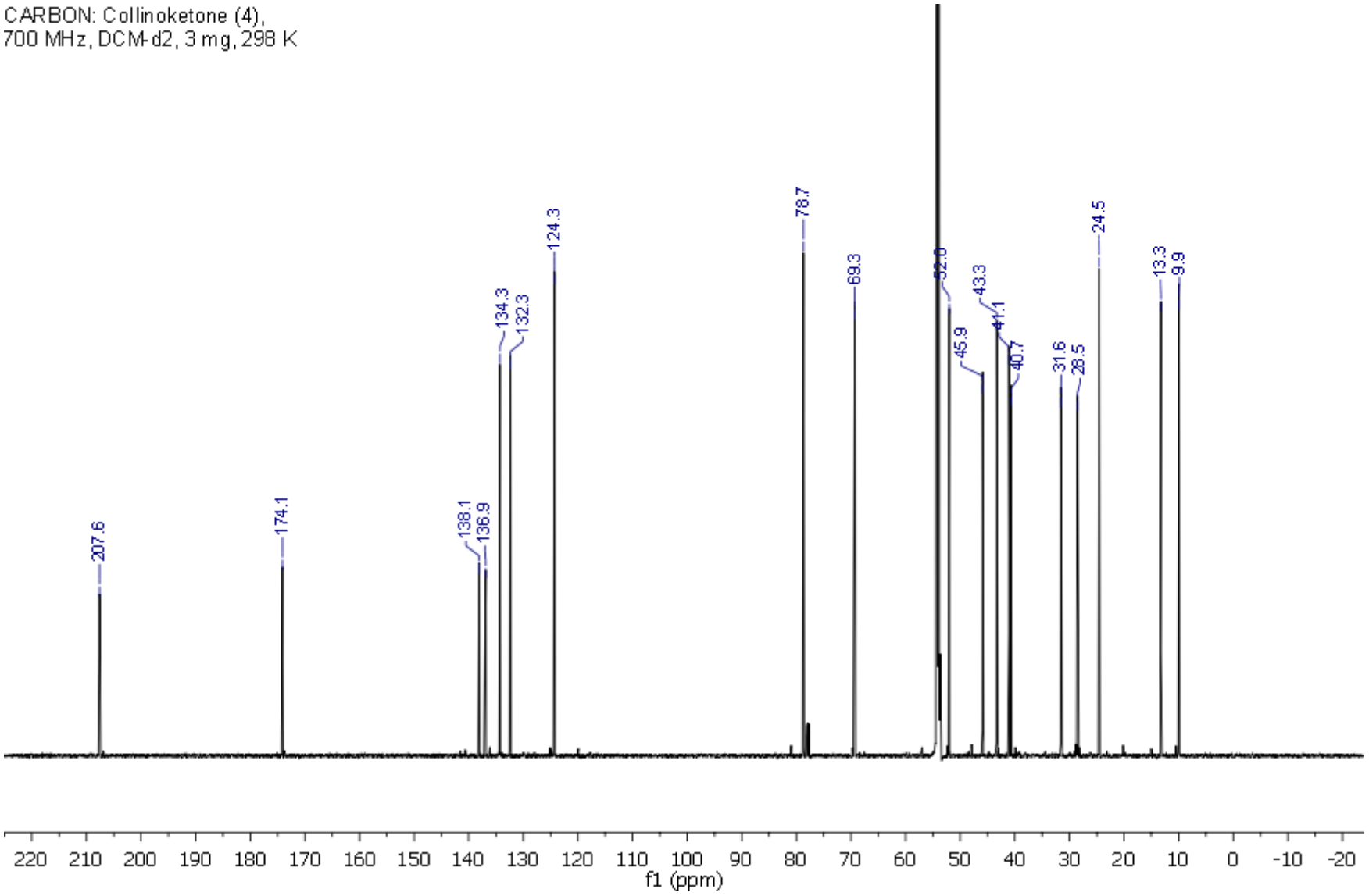

CARBON: Collazulene (3),
700 MHz, DCM-d2, 15 mg, 298 K
173.7
171.3
153.4
138.9
127.9
106.2
79.7
78.9
64.2
54.6
53.0
45.5
43.2
42.0
41.8
34.4
32.9
28.3
21.4
9.7
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
f1 (ppm)

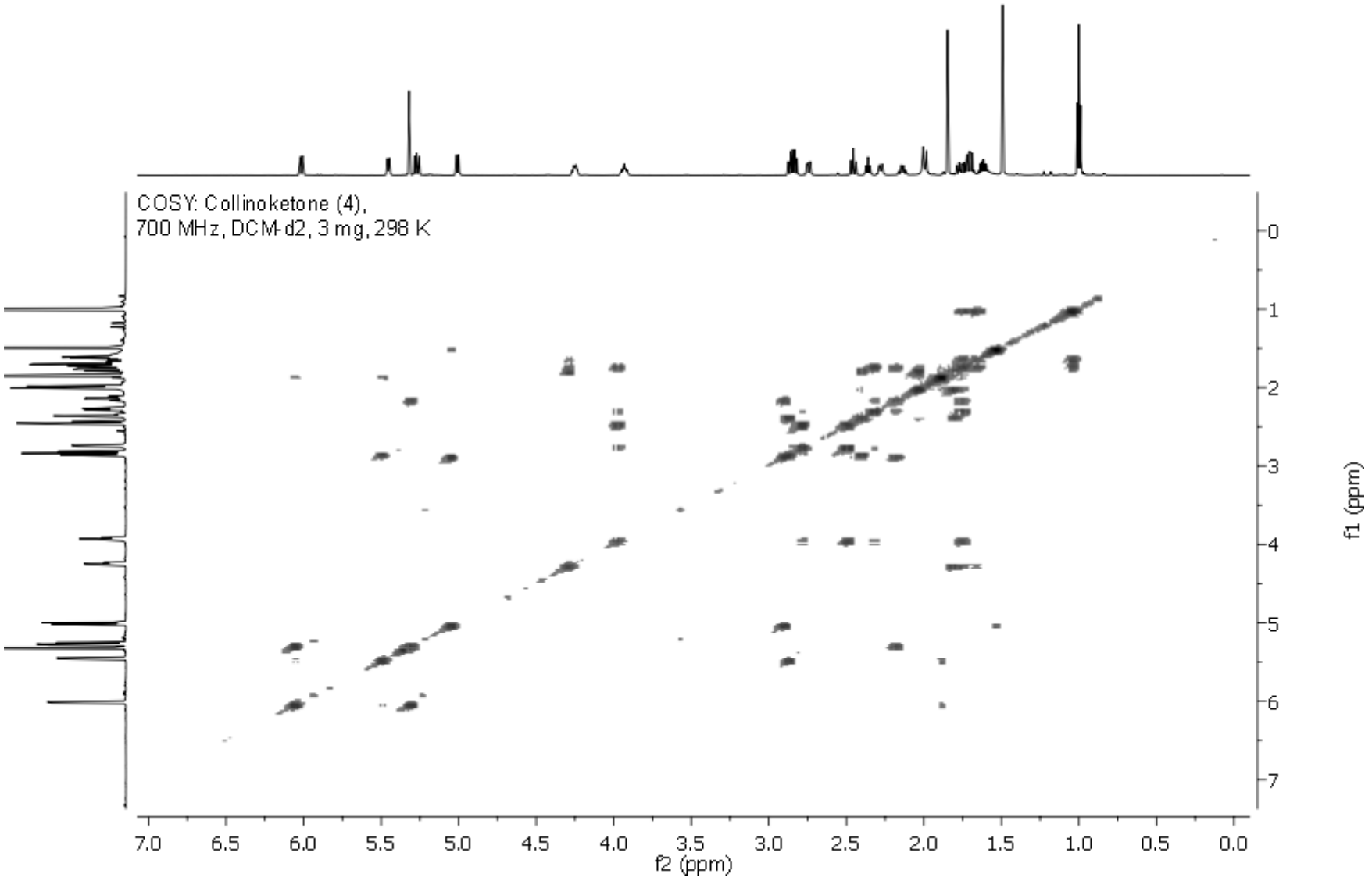

COSY: Collazulene (3),
700 MHz, DCM-d2, 15 mg, 298 K
f2 (ppm)
f1 (ppm)
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
1
2
3
4
5
6

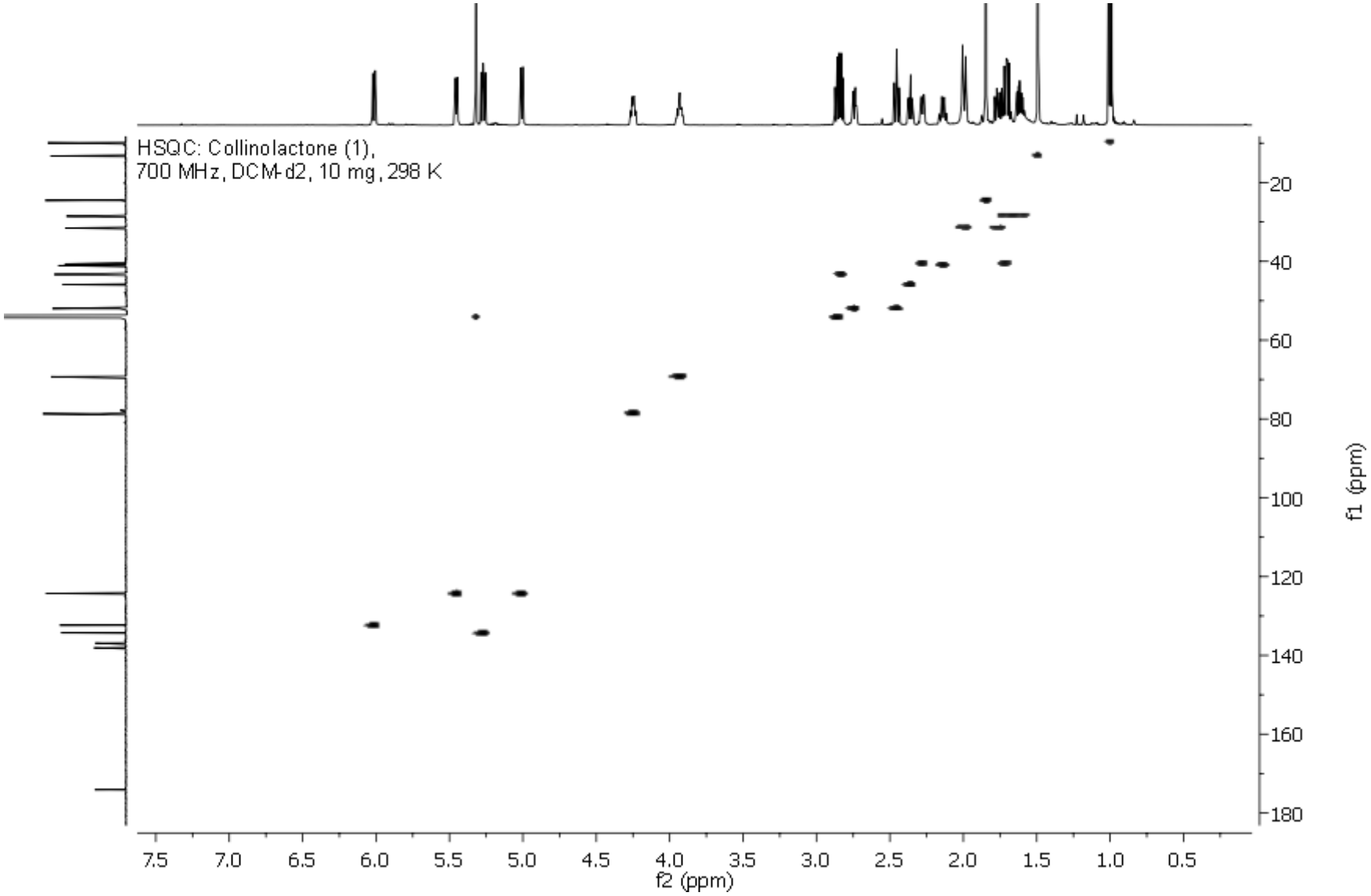

HSQC: Collazulene (x),
700 MHz, DCM-d2, 15 mg, 298 K
f2 (ppm)
f1 (ppm)

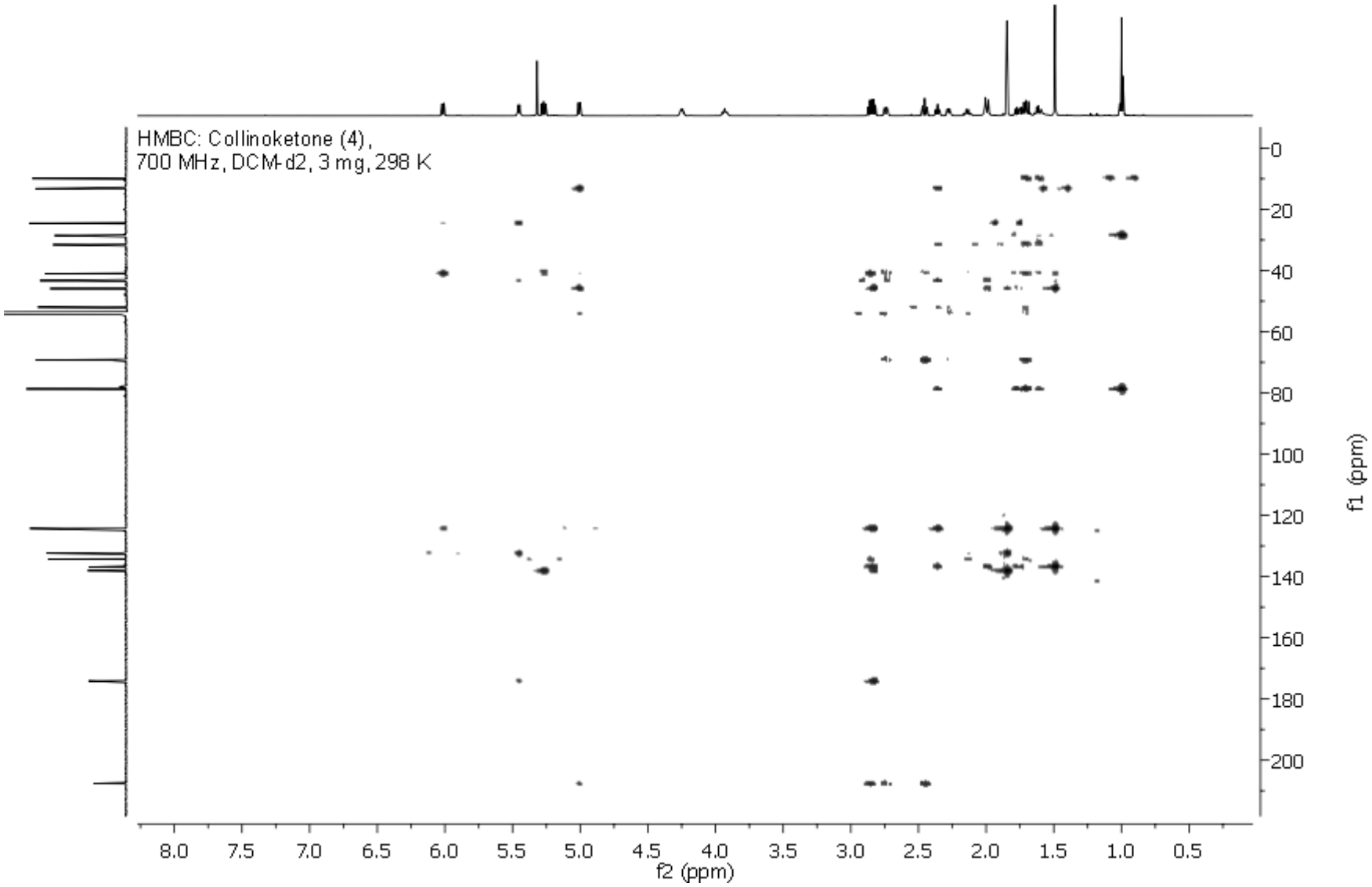

HMBC: Collazulene (3),
700 MHz, DCM-d2, 15 mg, 298 K
f2 (ppm)
f1 (ppm)
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
0
20
40
60
80
100
120
140
160

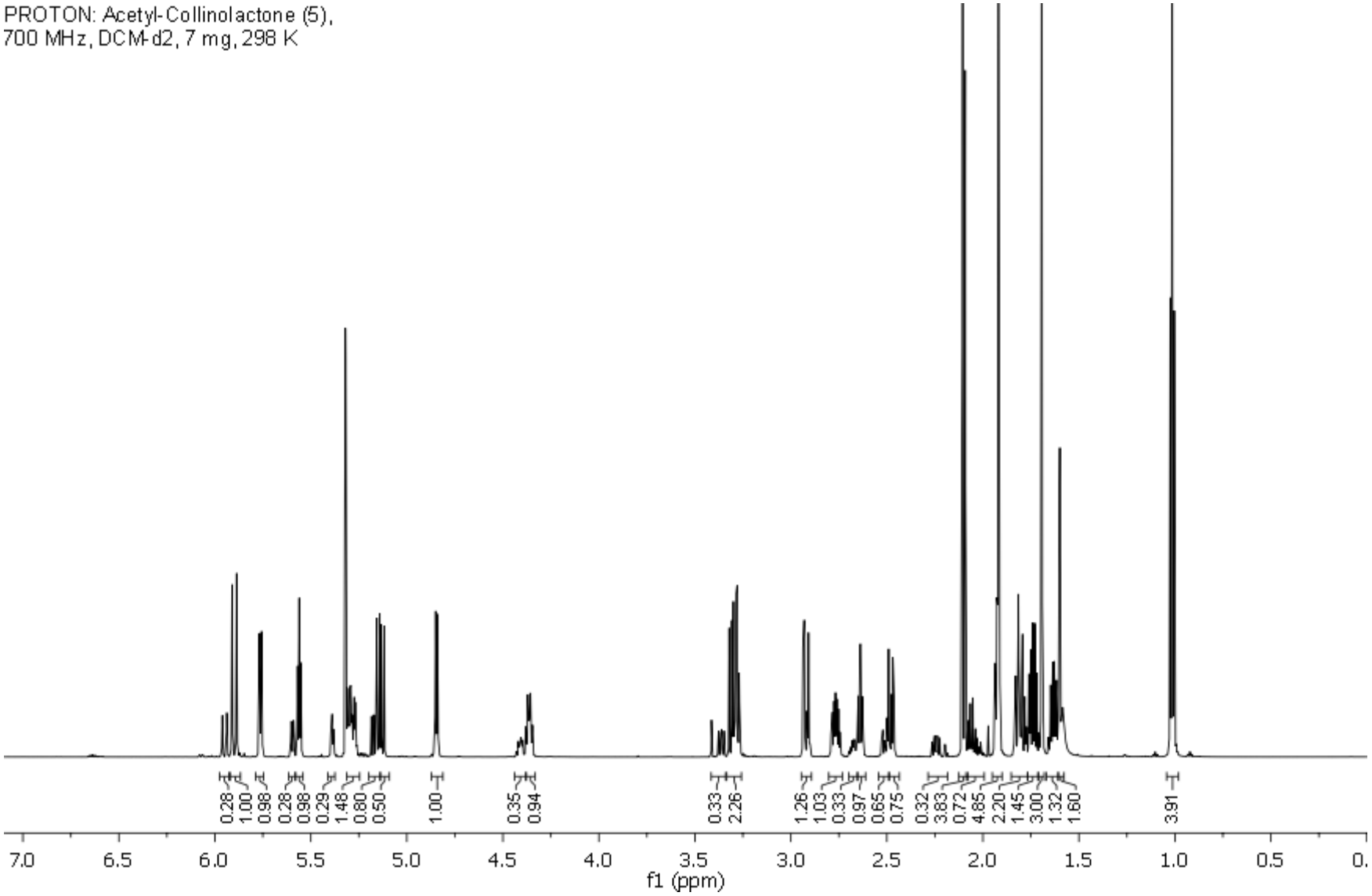

PROTON: Collinoketone (4),
700 MHz, DCM-d2, 3 mg, 298 K
1.00
0.98
1.05
1.00
1.00
1.00
2.04
1.07
1.04
1.05
1.07
1.11
2.09
3.19
3.52
1.99
3.12
3.19
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

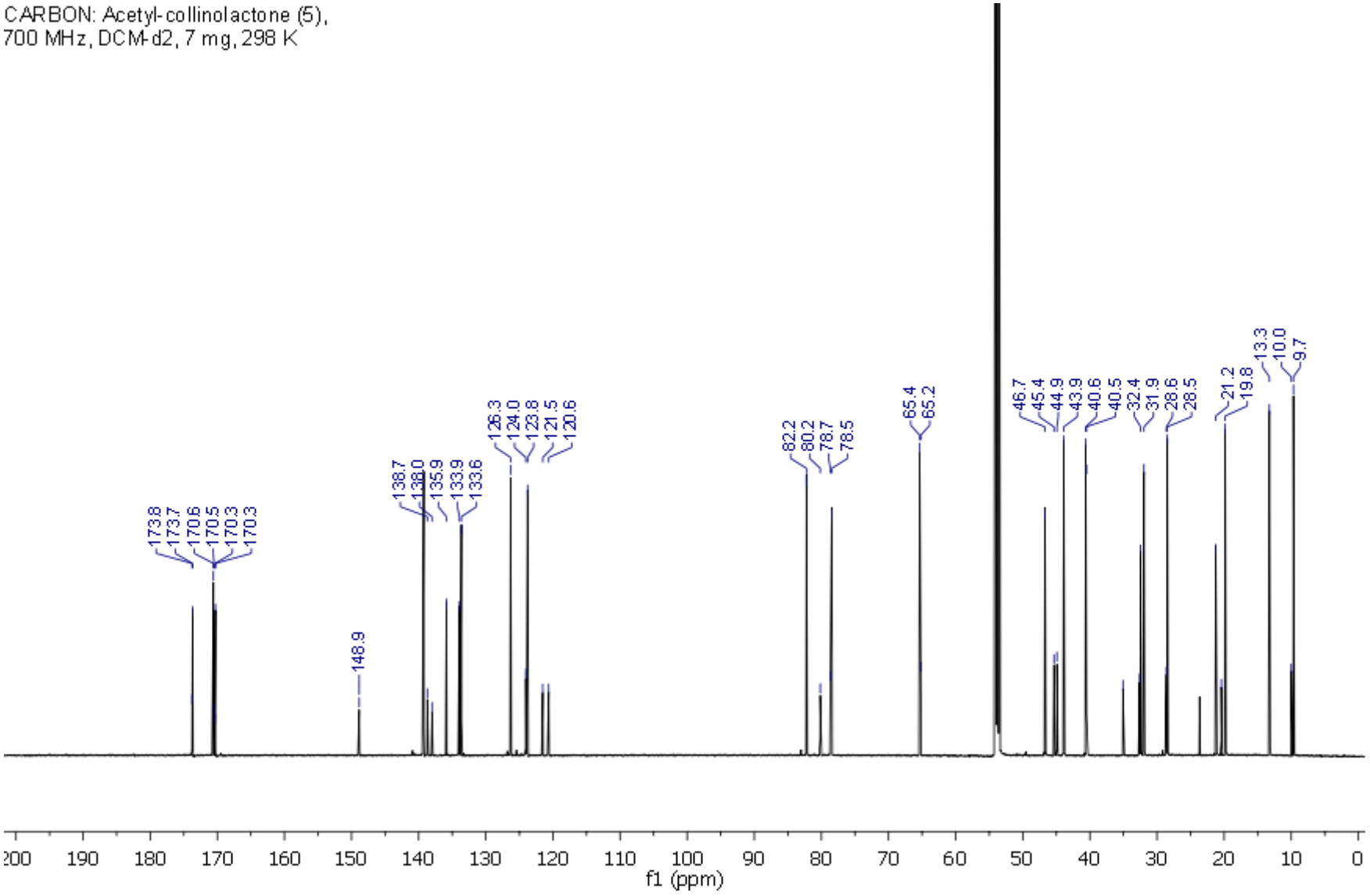

CARBON: Collinoketone (4),
700 MHz, DCM-d2, 3 mg, 298 K
207.6
174.1
138.1
136.9
134.3
132.3
124.3
78.7
69.3
52.0
45.9
43.3
41.1
40.7
31.6
28.5
24.5
13.3
9.9
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10 -20
f1 (ppm)

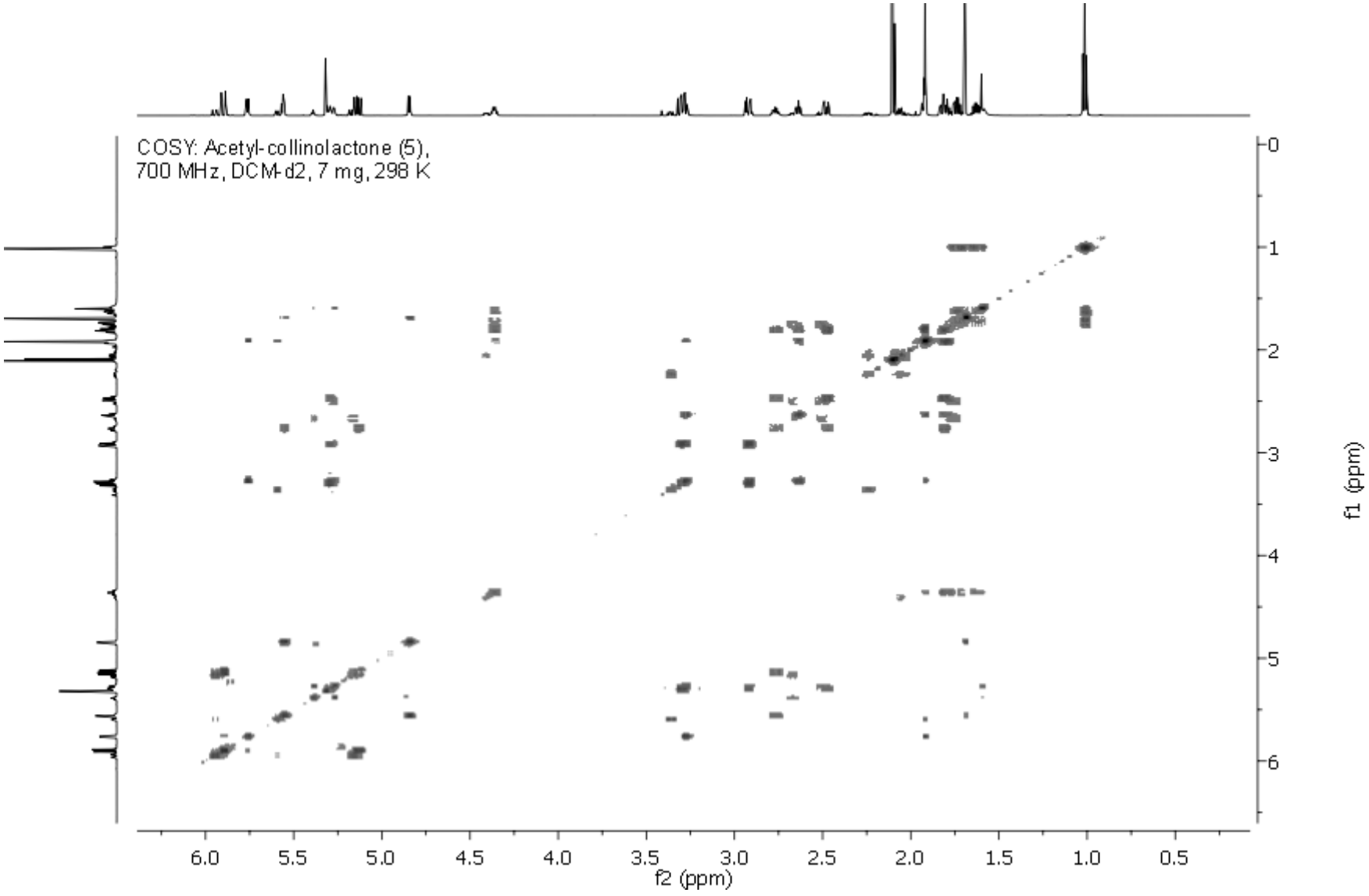

COSY: Collinoketone (4),
700 MHz, DCM-d2, 3 mg, 298 K
f2 (ppm)
f1 (ppm)

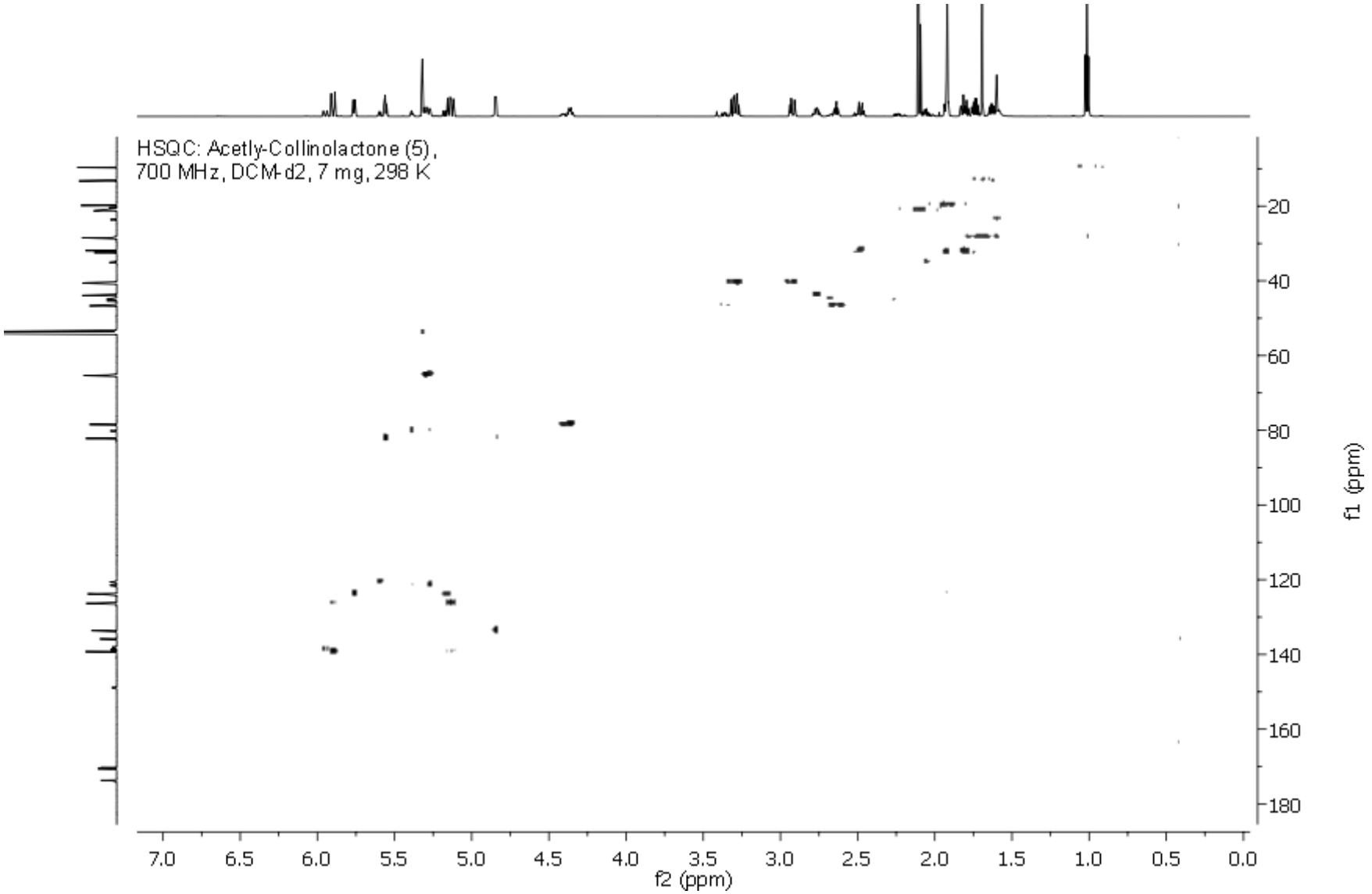

HSQC: Collinolactone (1),
700 MHz, DCM-d2, 10 mg, 298 K
f2 (ppm)
f1 (ppm)

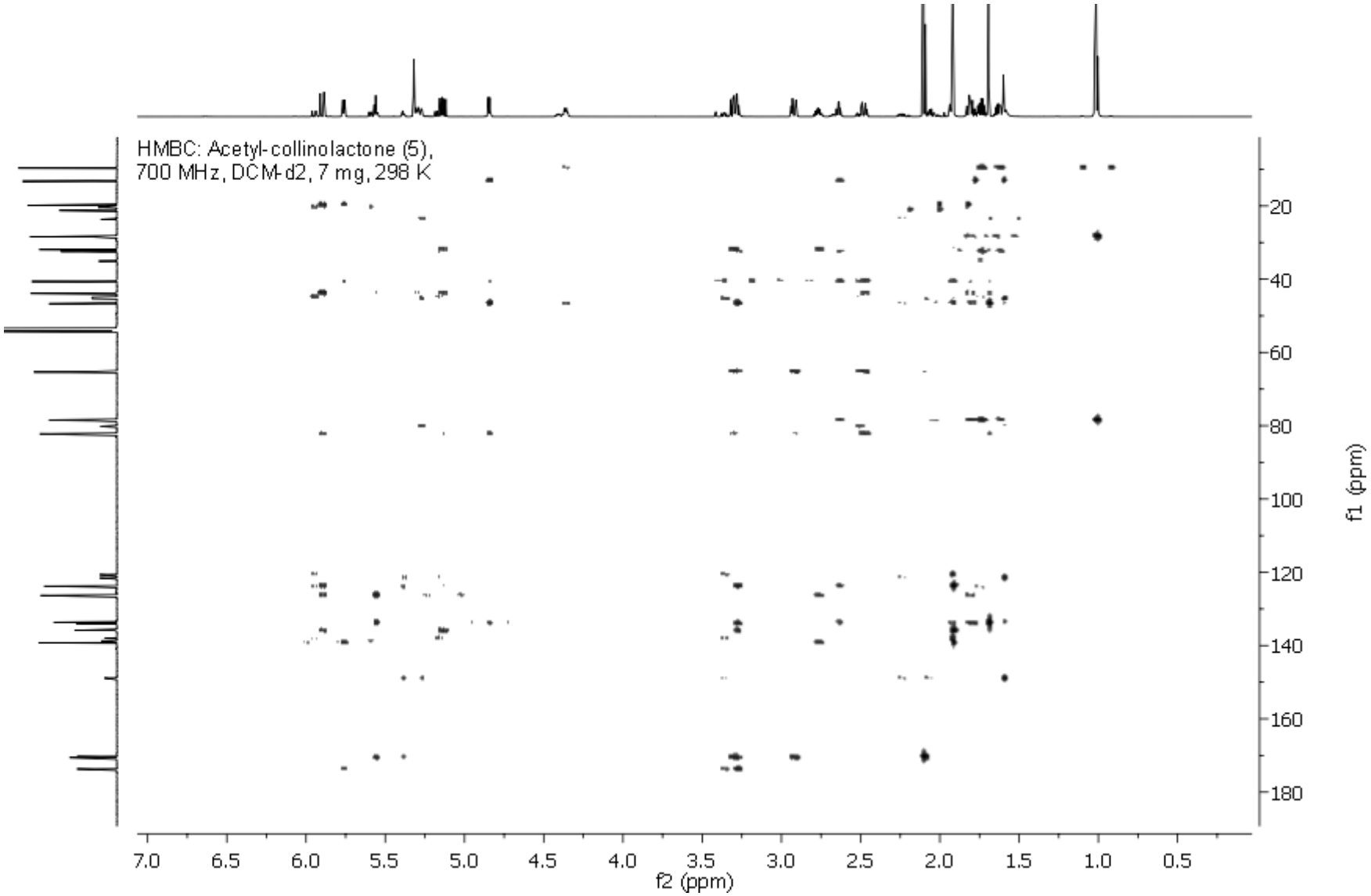

HMBC: Collinoketone (4),
700 MHz, DCM-d2, 3 mg, 298 K
f2 (ppm)
f1 (ppm)

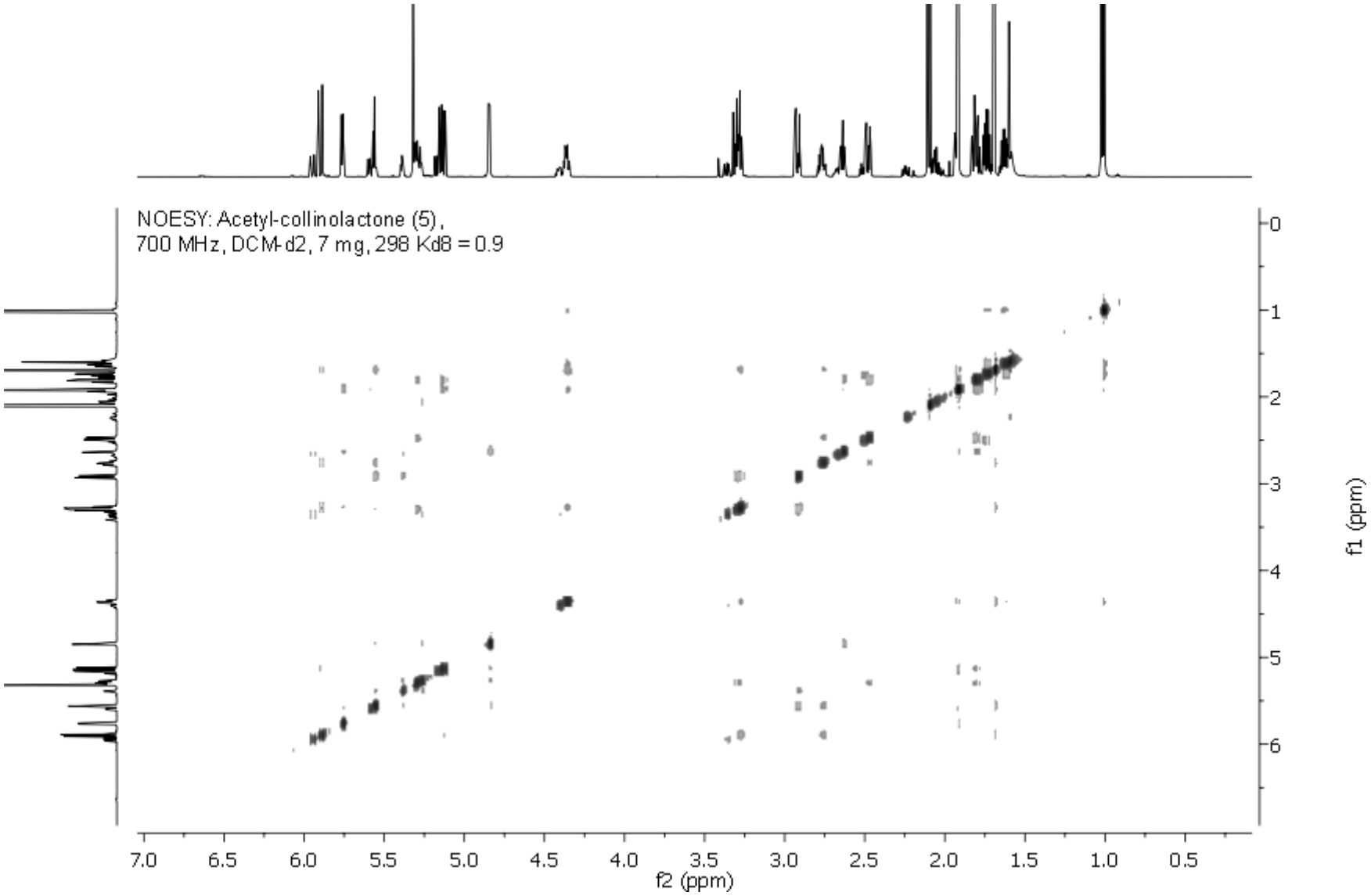

PROTON: Acetyl-Collinolactone (5),
700 MHz, DCM-d2, 7 mg, 298 K
0.28
1.00
0.98
0.28
0.98
0.29
1.48
0.80
0.50
1.00
0.35
0.94
0.33
2.26
1.26
1.03
0.33
0.97
0.65
0.75
0.32
3.83
0.72
4.85
2.20
1.45
3.00
1.32
1.60
3.91
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
f1 (ppm)

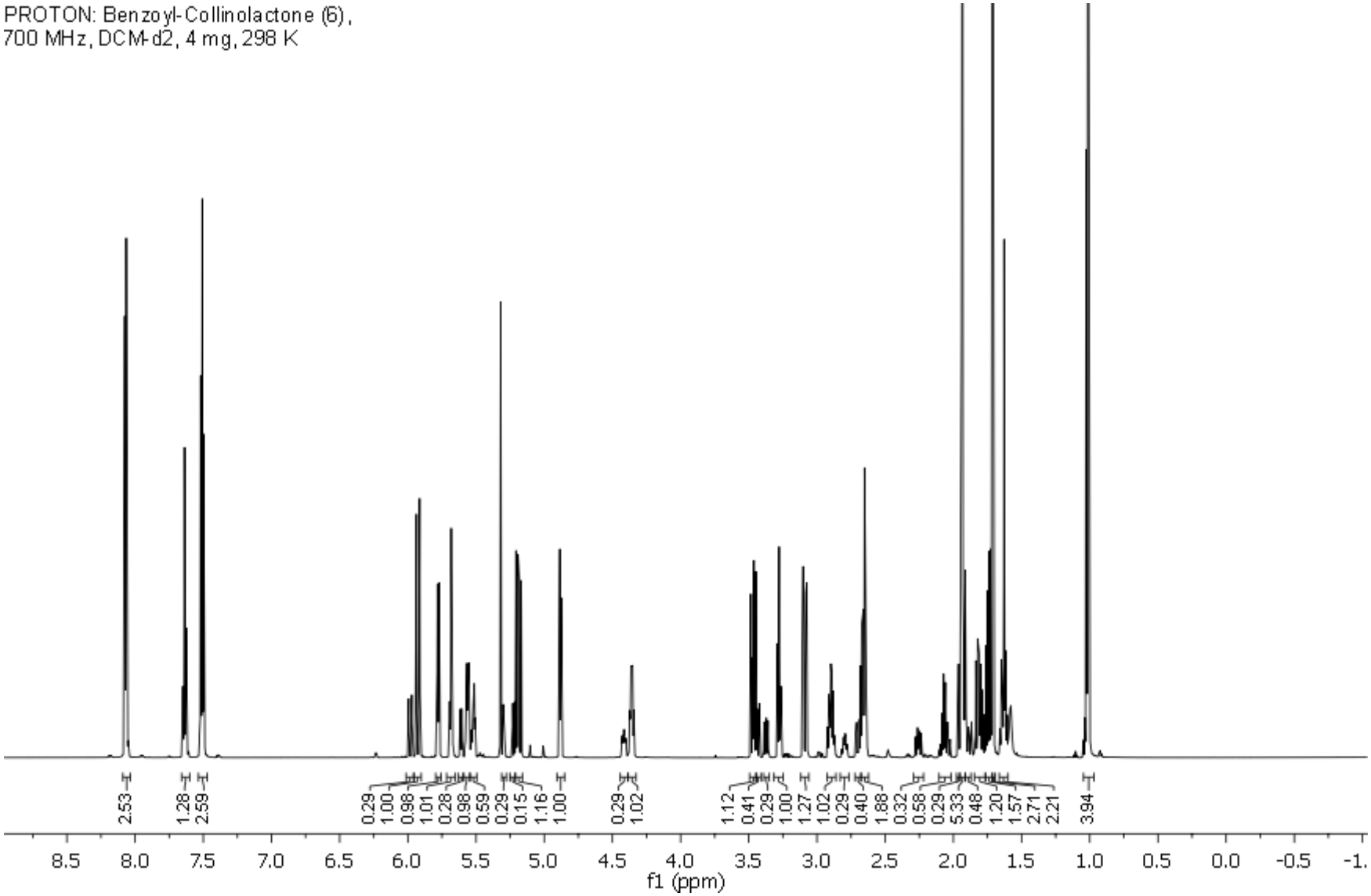

CARBON: Acetyl-collinolactone (5),
700 MHz, DCM-d2, 7 mg, 298 K
173.8
173.7
170.6
170.5
170.3
170.3
148.9
138.7
138.0
135.9
133.9
133.6
126.3
124.0
123.8
121.5
120.6
82.2
80.2
78.7
78.5
65.4
65.2
46.7
45.4
44.9
43.9
40.6
40.5
32.4
31.9
28.6
28.5
21.2
19.8
13.3
10.0
9.7
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

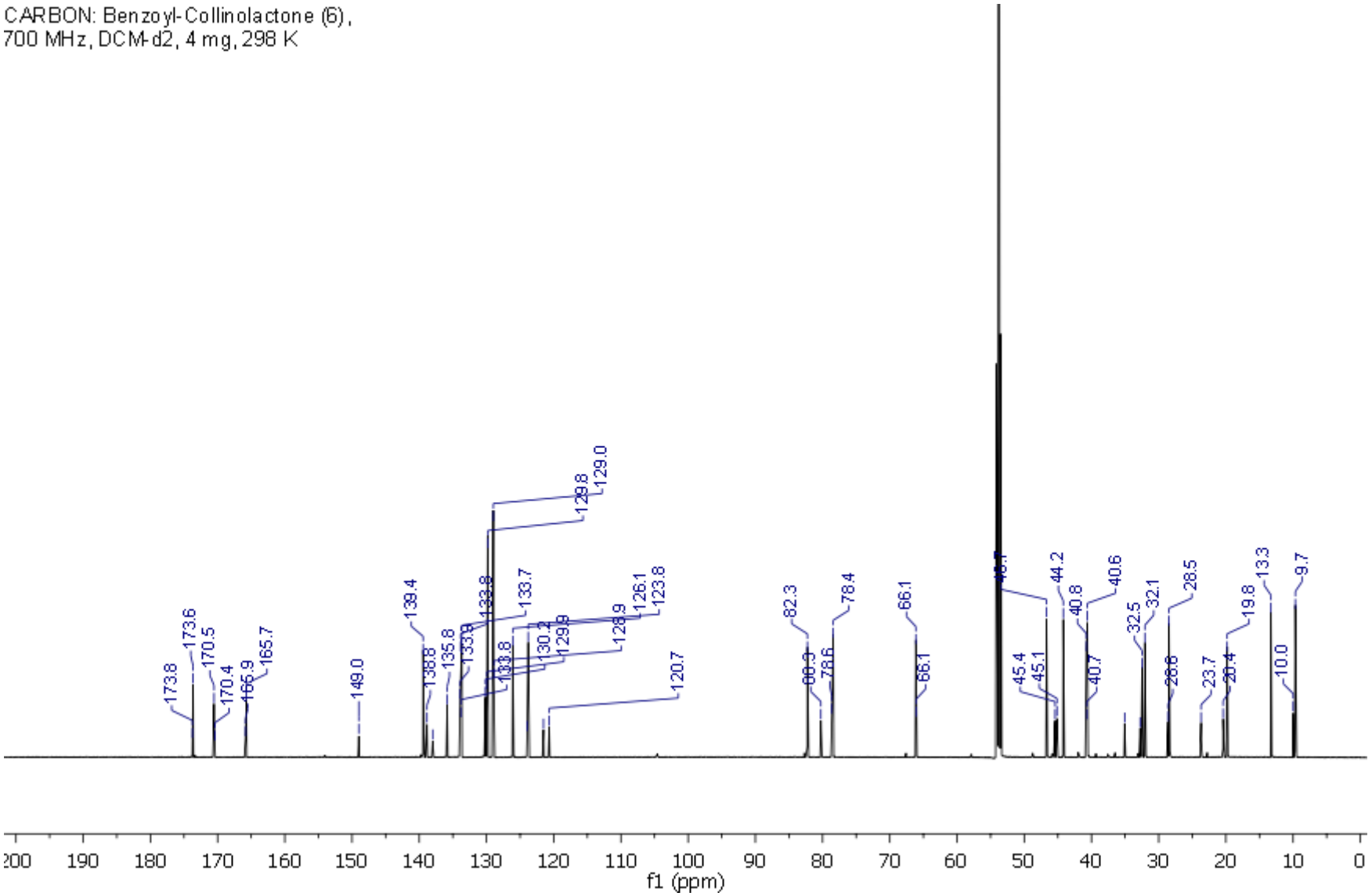

COSY: Acetyl-collinolactone (5),
700 MHz, DCM-d2, 7 mg, 298 K
f2 (ppm)
f1 (ppm)
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0
1
2
3
4
5
6

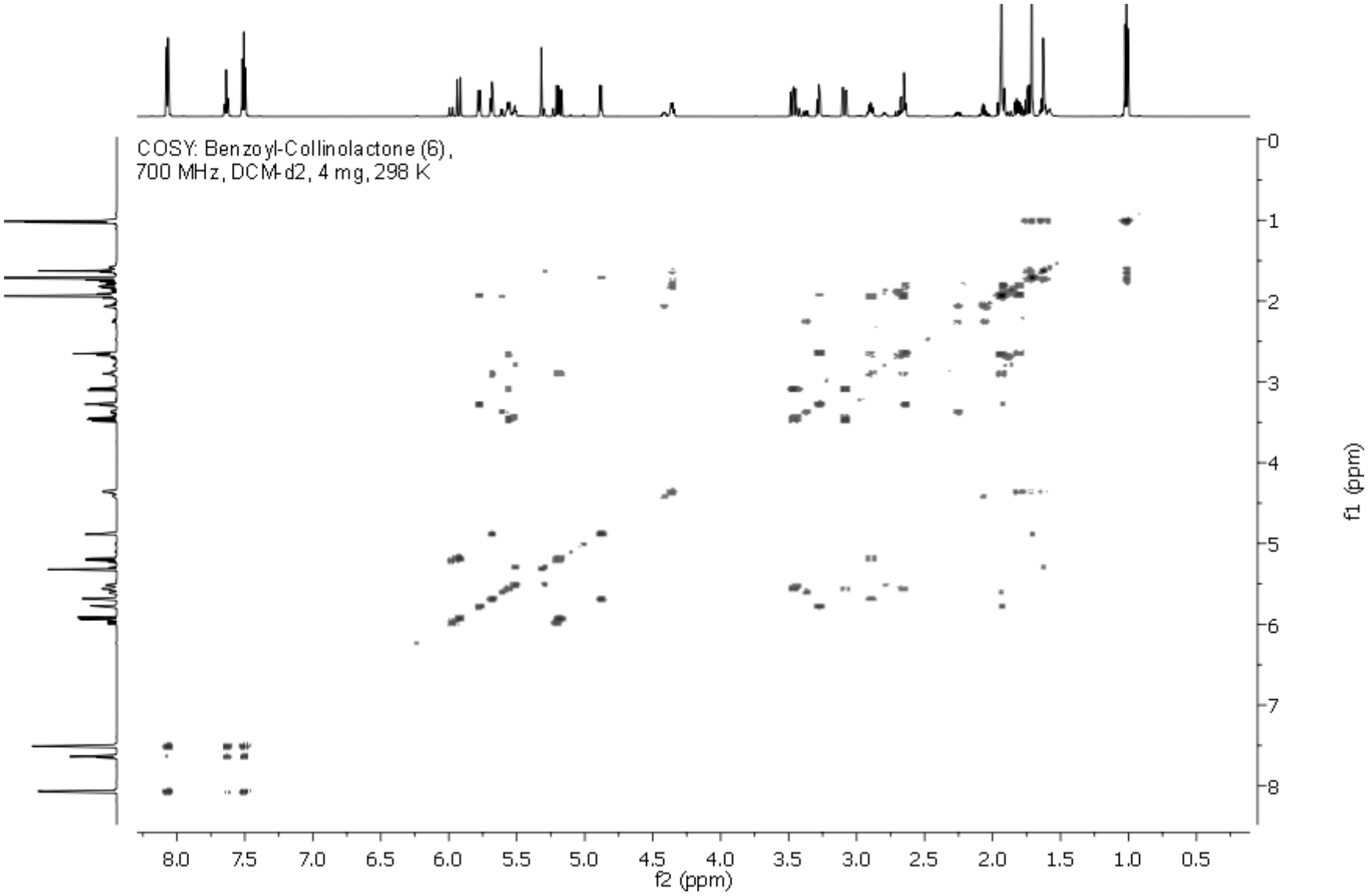

HSQC: Acetly-Collinolactone (5),
700 MHz, DCM-d2, 7 mg, 298 K
20
40
60
80
100
120
140
160
180
f1 (ppm)
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f2 (ppm)

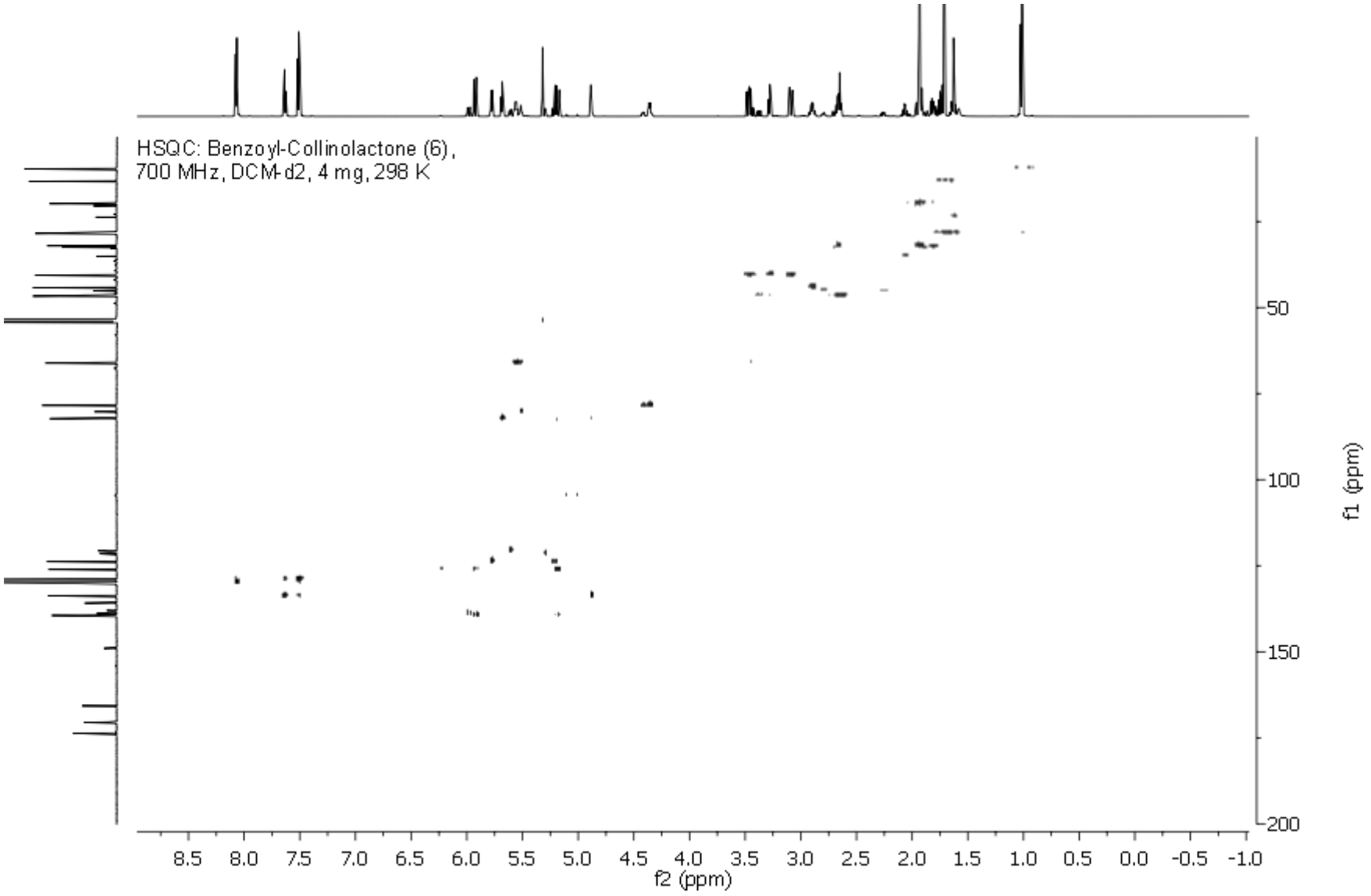

HMBC: Acetyl-collinolactone (5),
700 MHz, DCM-d2, 7 mg, 298 K
f2 (ppm)
f1 (ppm)
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
20
40
60
80
100
120
140
160
180

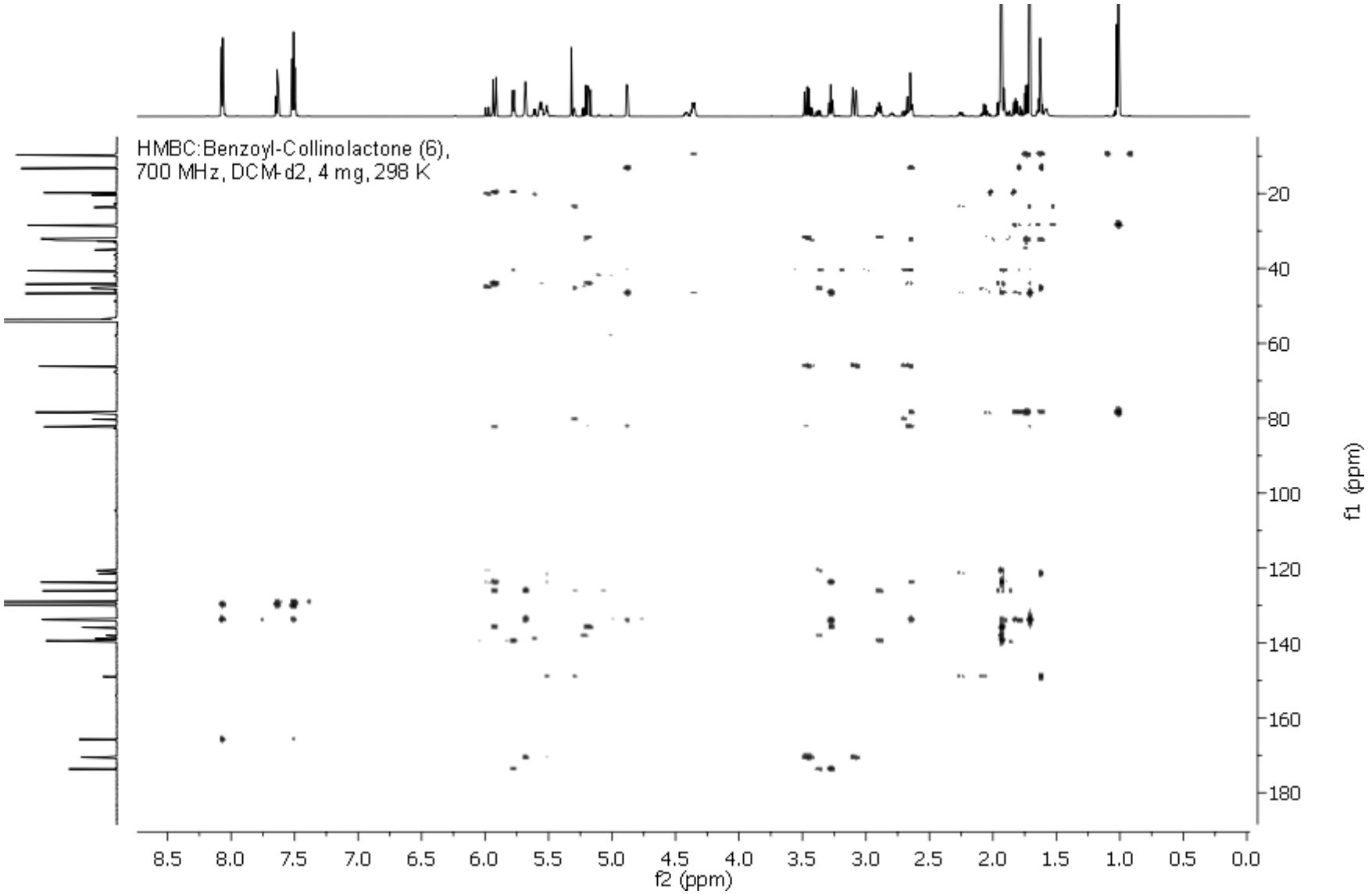

NOESY: Acetyl-collinolactone (5),
700 MHz, DCM-d2, 7 mg, 298 Kd8 = 0.9
f2 (ppm)
f1 (ppm)

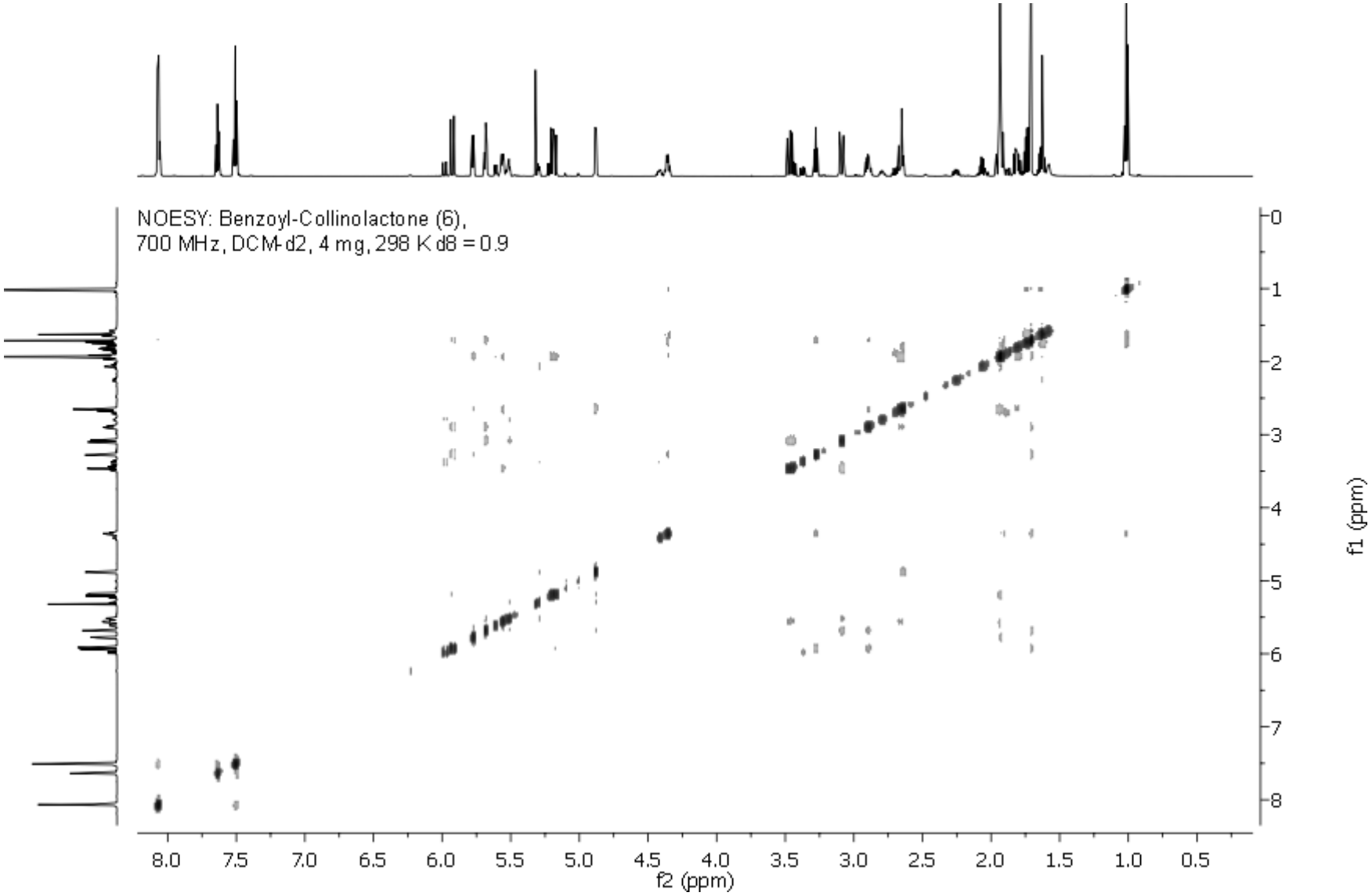

PROTON: Benzoyl-Collinolactone (6),
700 MHz, DCM-d2, 4 mg, 298 K
2.53
1.28
2.59
0.29
1.00
0.98
1.01
0.28
0.98
0.59
0.29
0.15
1.16
1.00
0.29
1.02
1.12
0.41
0.29
1.00
1.27
1.02
0.29
0.40
1.88
0.32
0.58
0.29
5.33
0.48
1.20
1.57
2.71
2.21
3.94
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
-1.
f1 (ppm)

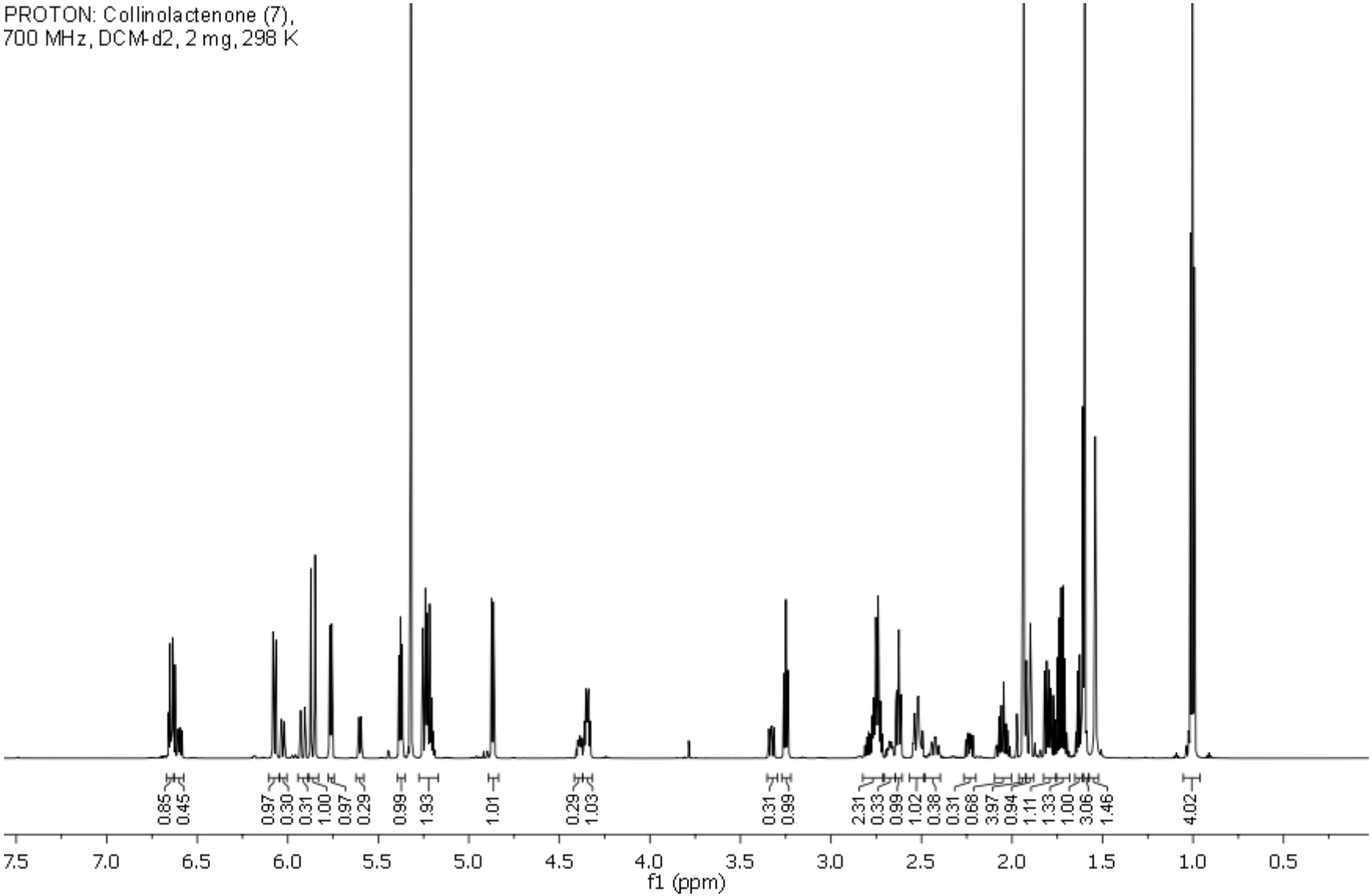

CARBON: Benzoyl-Collinolactone (6),
700 MHz, DCM-d2, 4 mg, 298 K
173.8
173.6
170.5
170.4
166.9
165.7
149.0
139.4
138.8
135.8
133.9
133.8
133.7
130.4
129.8
129.0
128.9
126.1
123.8
120.7
82.3
80.3
78.6
78.4
66.1
66.1
45.4
45.1
44.2
40.8
40.7
40.6
32.5
32.1
28.5
28.6
23.7
20.4
19.8
13.3
10.0
9.7
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

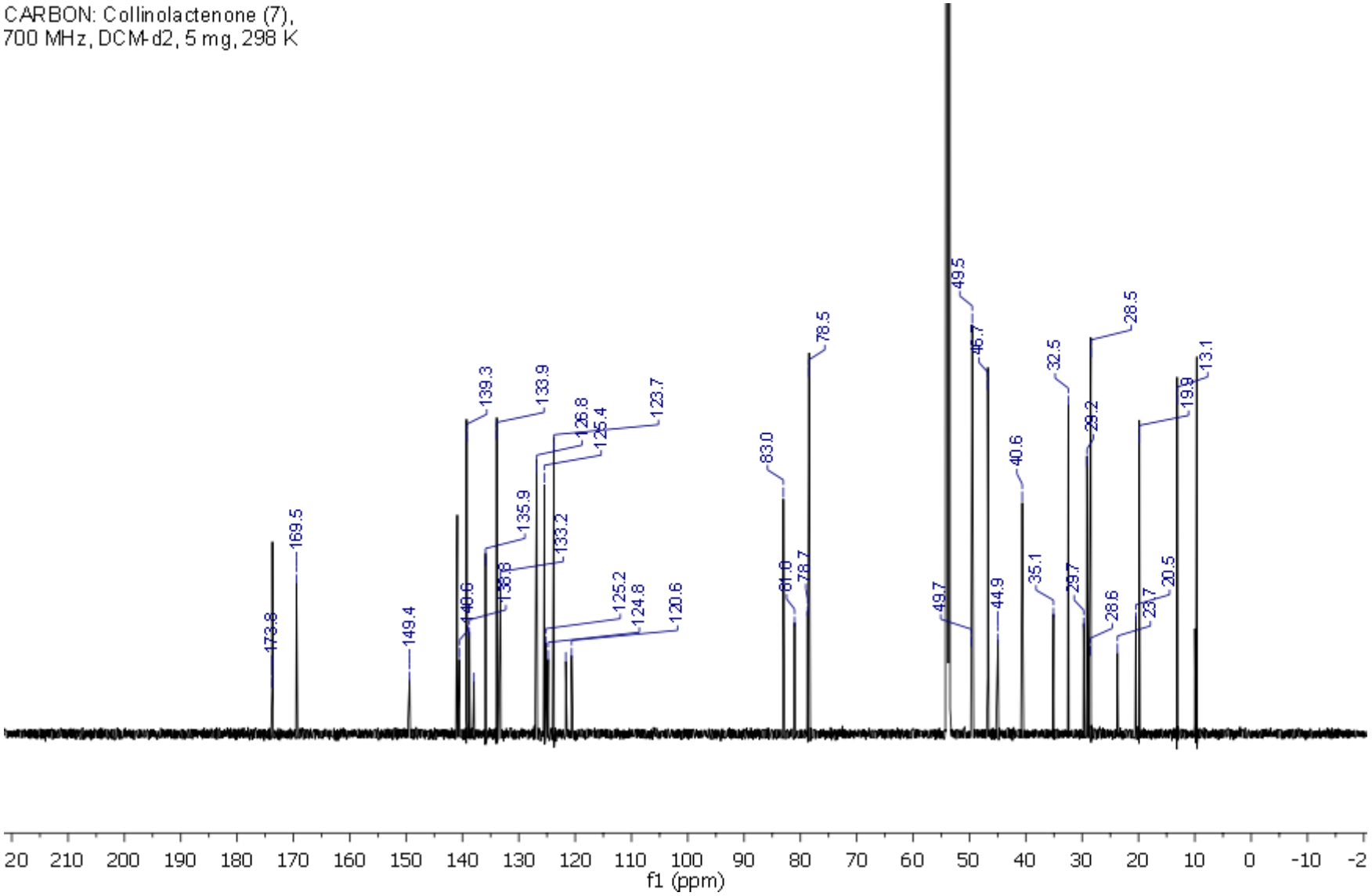

COSY: Benzoyl-Collinolactone (6),
700 MHz, DCM-d2, 4 mg, 298 K
f2 (ppm)
f1 (ppm)
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0
1
2
3
4
5
6
7
8

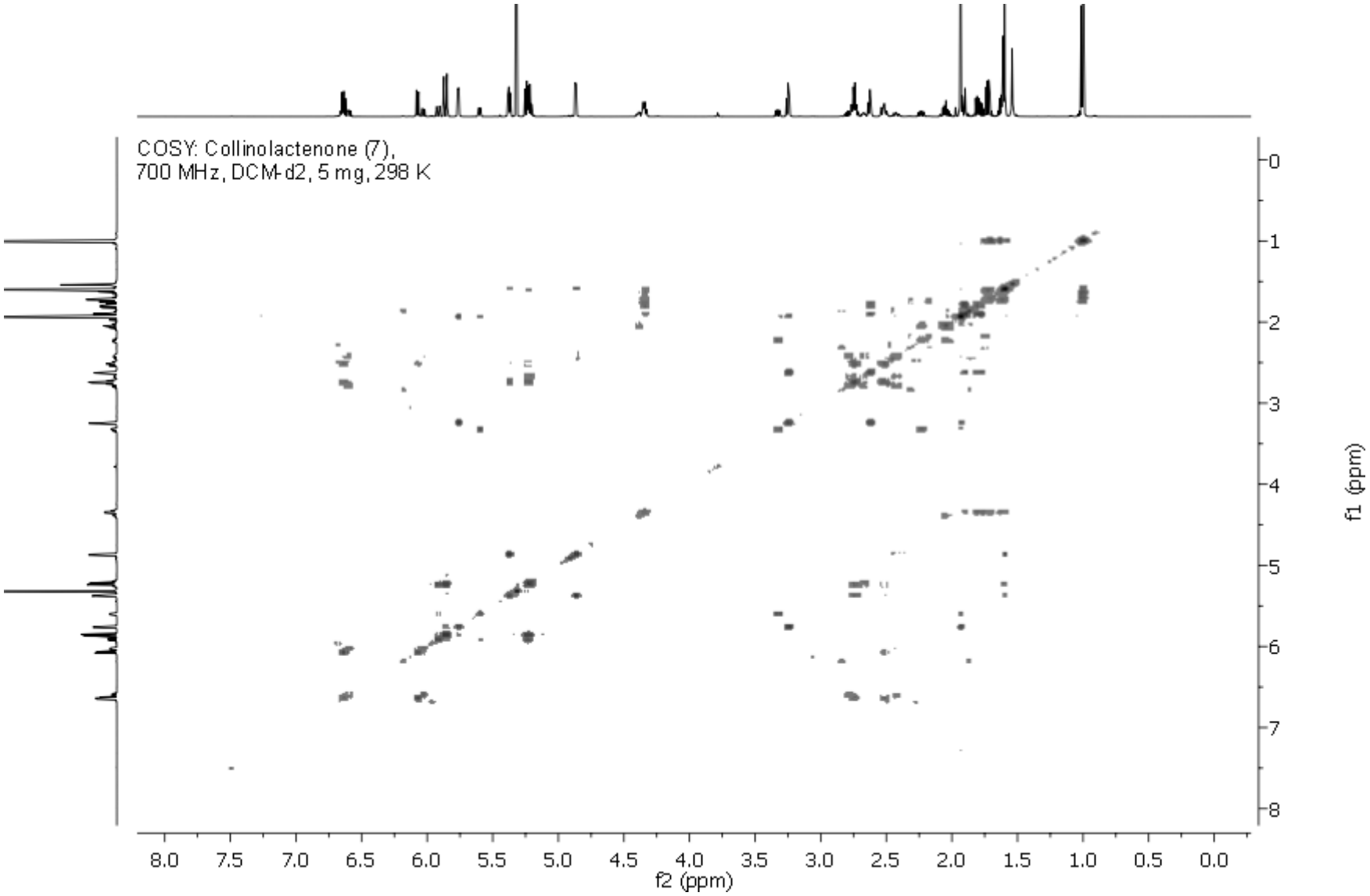

HSQC: Benzoyl-Collinolactone (6),
700 MHz, DCM-d2, 4 mg, 298 K
50
100
150
200
f1 (ppm)
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
-1.0
f2 (ppm)

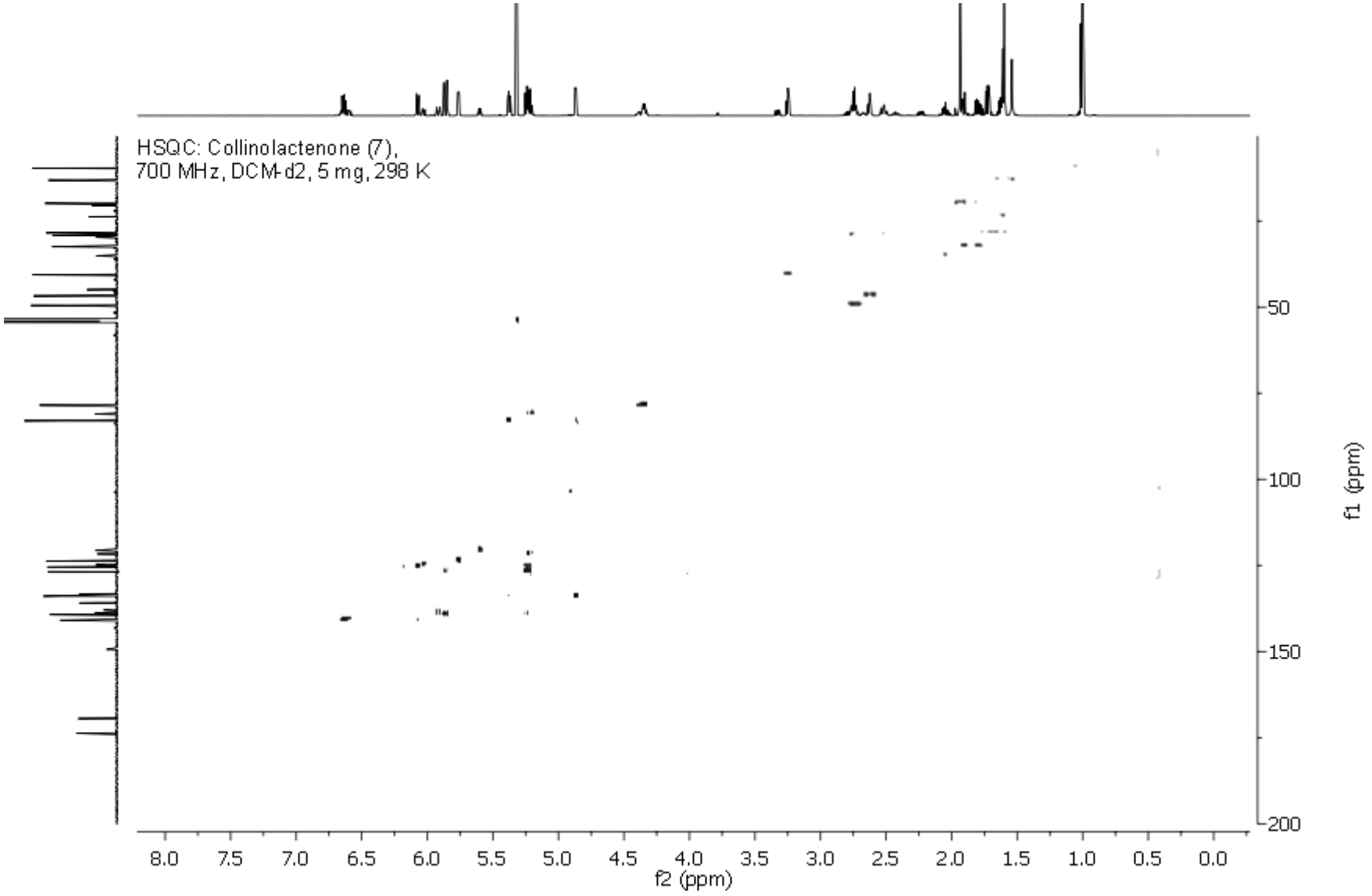

HMBC:Benzoyl-Collinolactone (6),
700 MHz, DCM-d2, 4 mg, 298 K
f2 (ppm)
f1 (ppm)
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
20
40
60
80
100
120
140
160
180

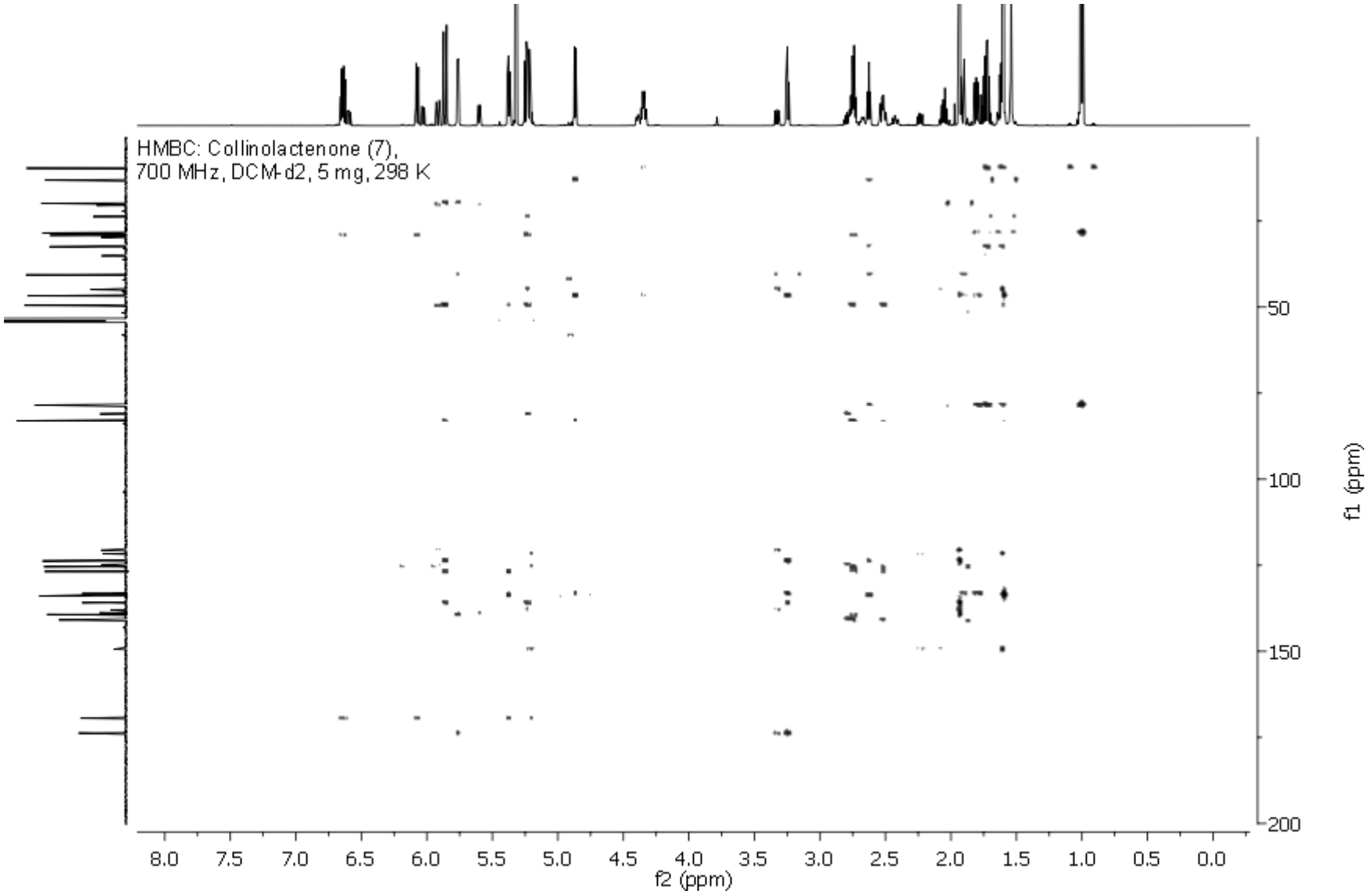

NOESY: Benzoyl-Collinolactone (6),
700 MHz, DCM-d2, 4 mg, 298 K d8 = 0.9
f2 (ppm)
f1 (ppm)

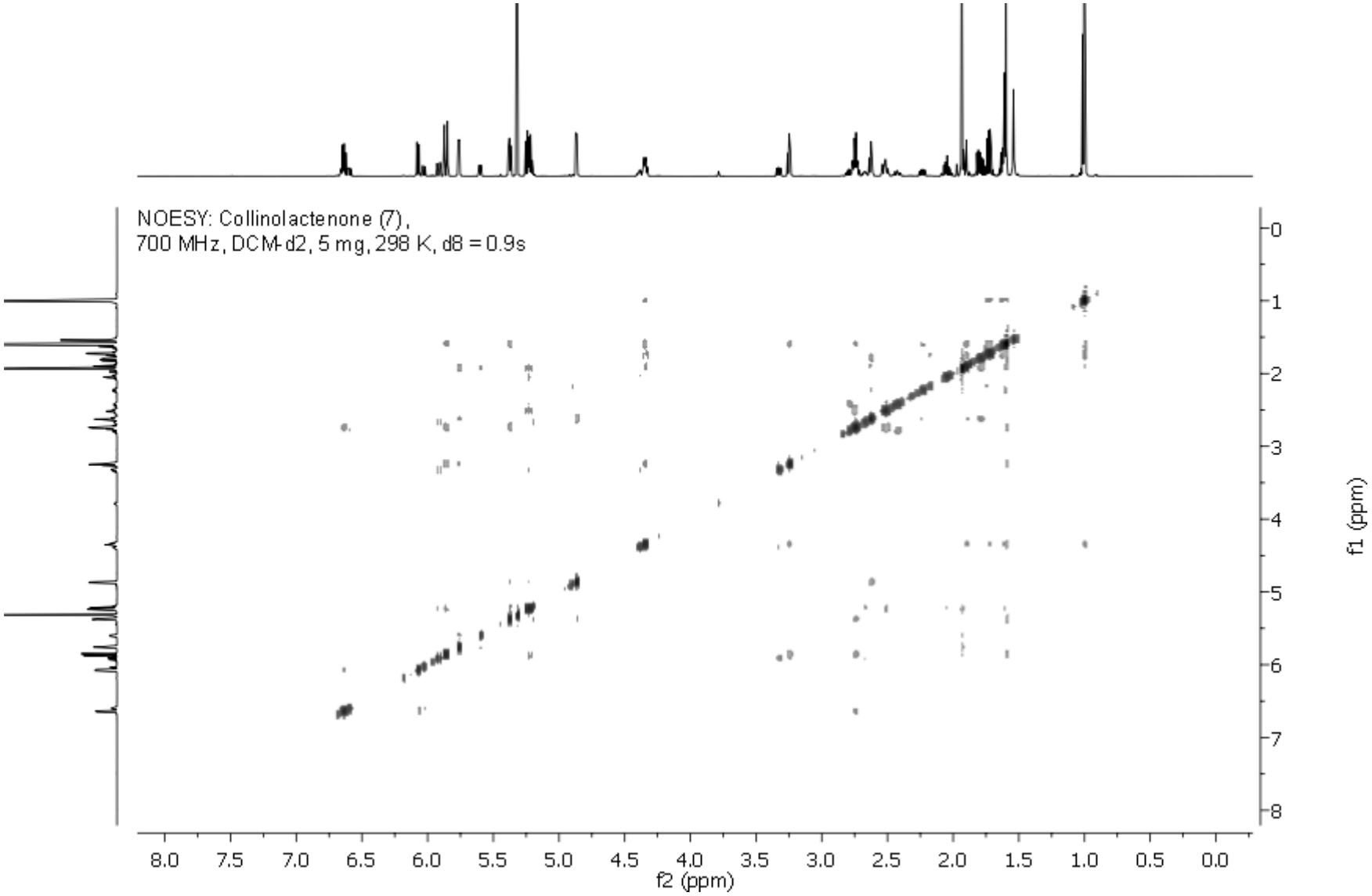

PROTON: Collinolactenone (7),
700 MHz, DCM-d2, 2 mg, 298 K
0.85
0.45
0.97
0.30
0.31
1.00
0.97
0.29
0.99
1.93
1.01
0.29
1.03
0.31
0.99
2.31
0.33
0.99
1.02
0.38
0.31
0.68
3.97
0.94
1.11
1.33
1.00
3.06
1.46
4.02
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
f1 (ppm)

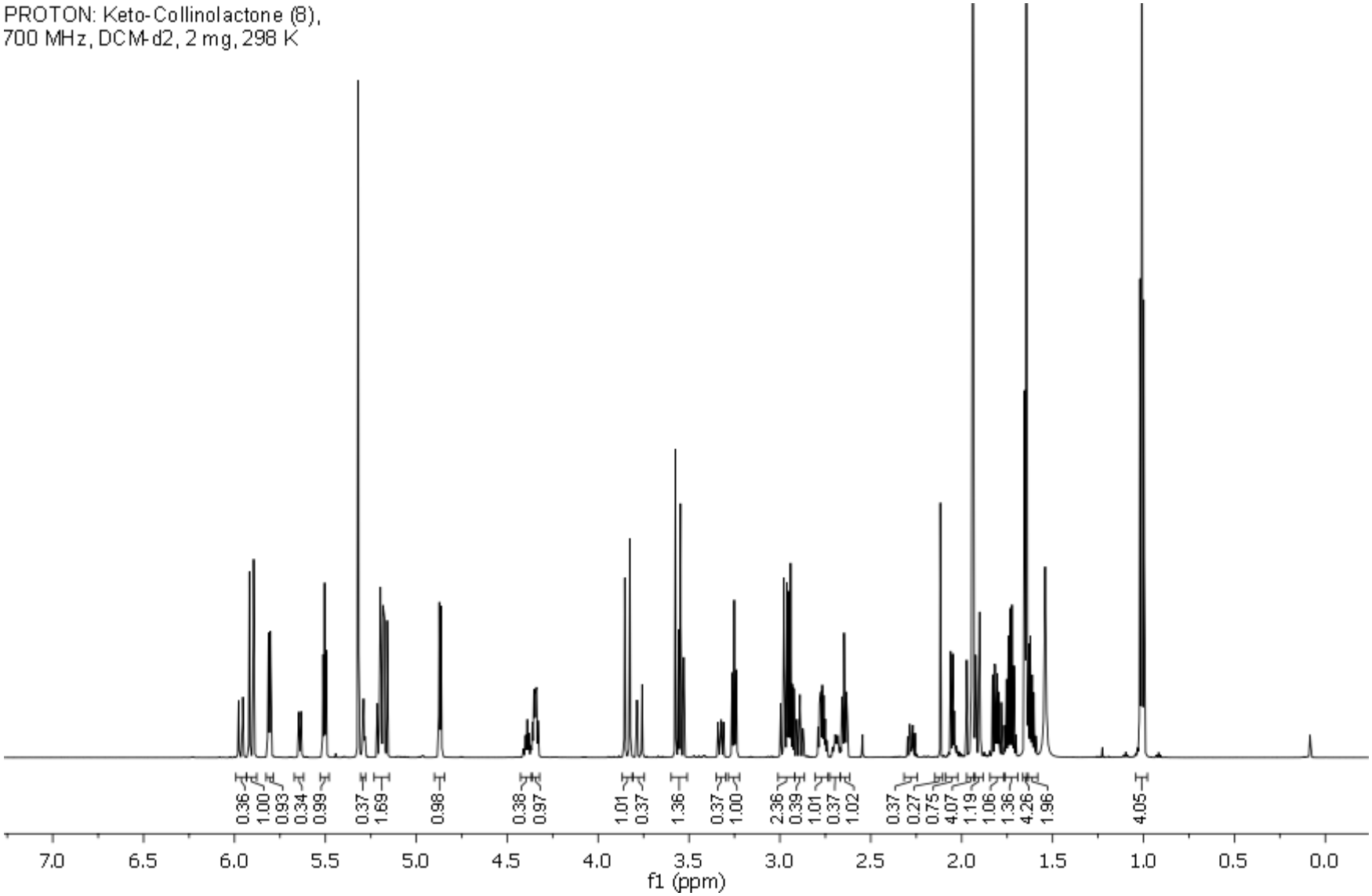

CARBON: Collinolactenone (7),
700 MHz, DCM-d2, 5 mg, 298 K
173.8
169.5
149.4
140.6
139.3
136.8
135.9
133.9
133.2
126.8
125.4
125.2
124.8
123.7
120.6
83.0
81.6
78.7
78.5
49.7
49.5
46.7
44.9
40.6
35.1
32.5
29.7
29.2
28.6
28.5
23.7
20.5
19.9
13.1
20 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10 -2
f1 (ppm)

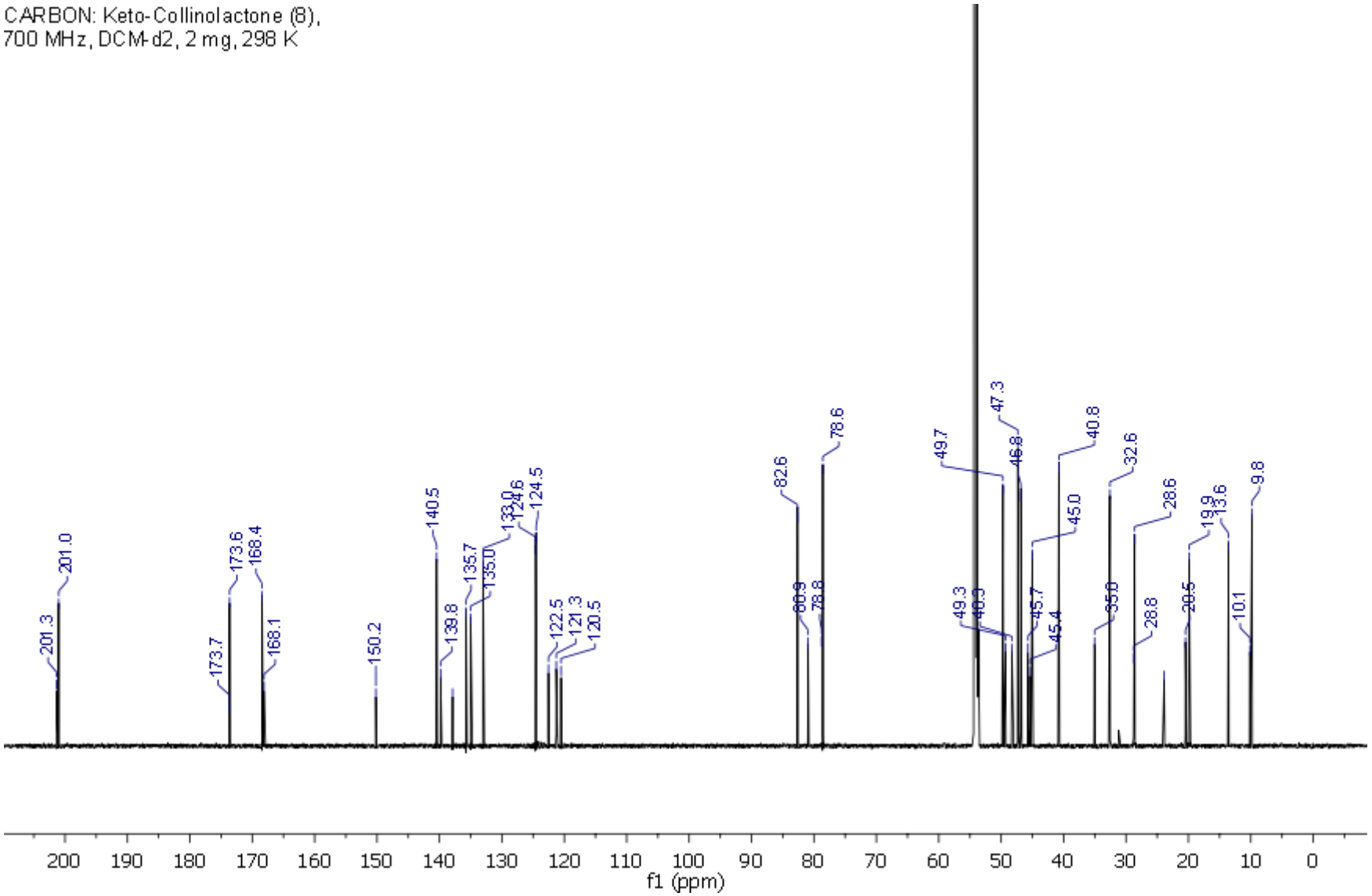

COSY: Collinolactenone (7),
700 MHz, DCM-d2, 5 mg, 298 K
f2 (ppm)
f1 (ppm)

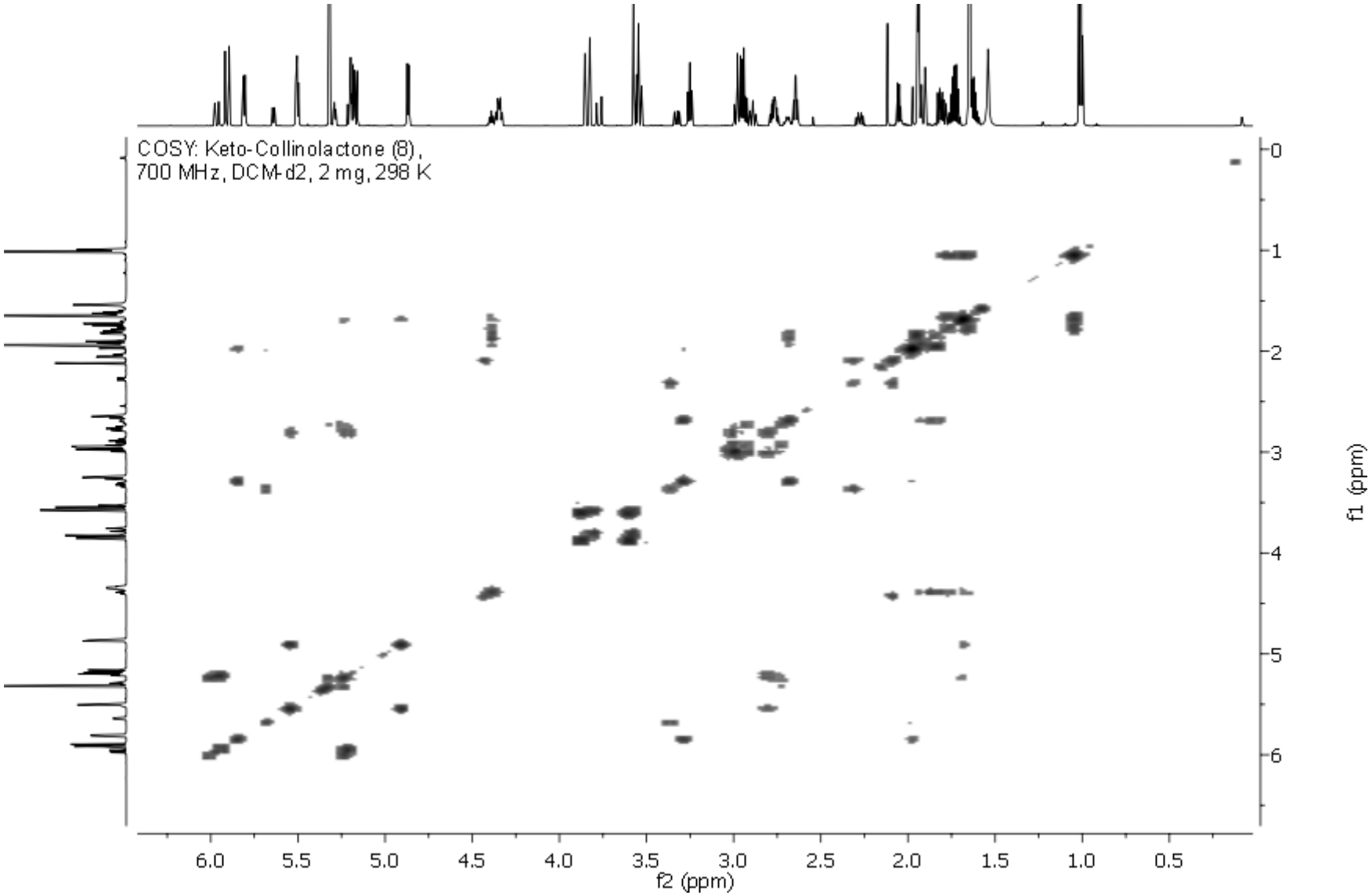

HSQC: Collinolactenone (7),
700 MHz, DCM-d2, 5 mg, 298 K
50
100
150
200
f1 (ppm)
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f2 (ppm)

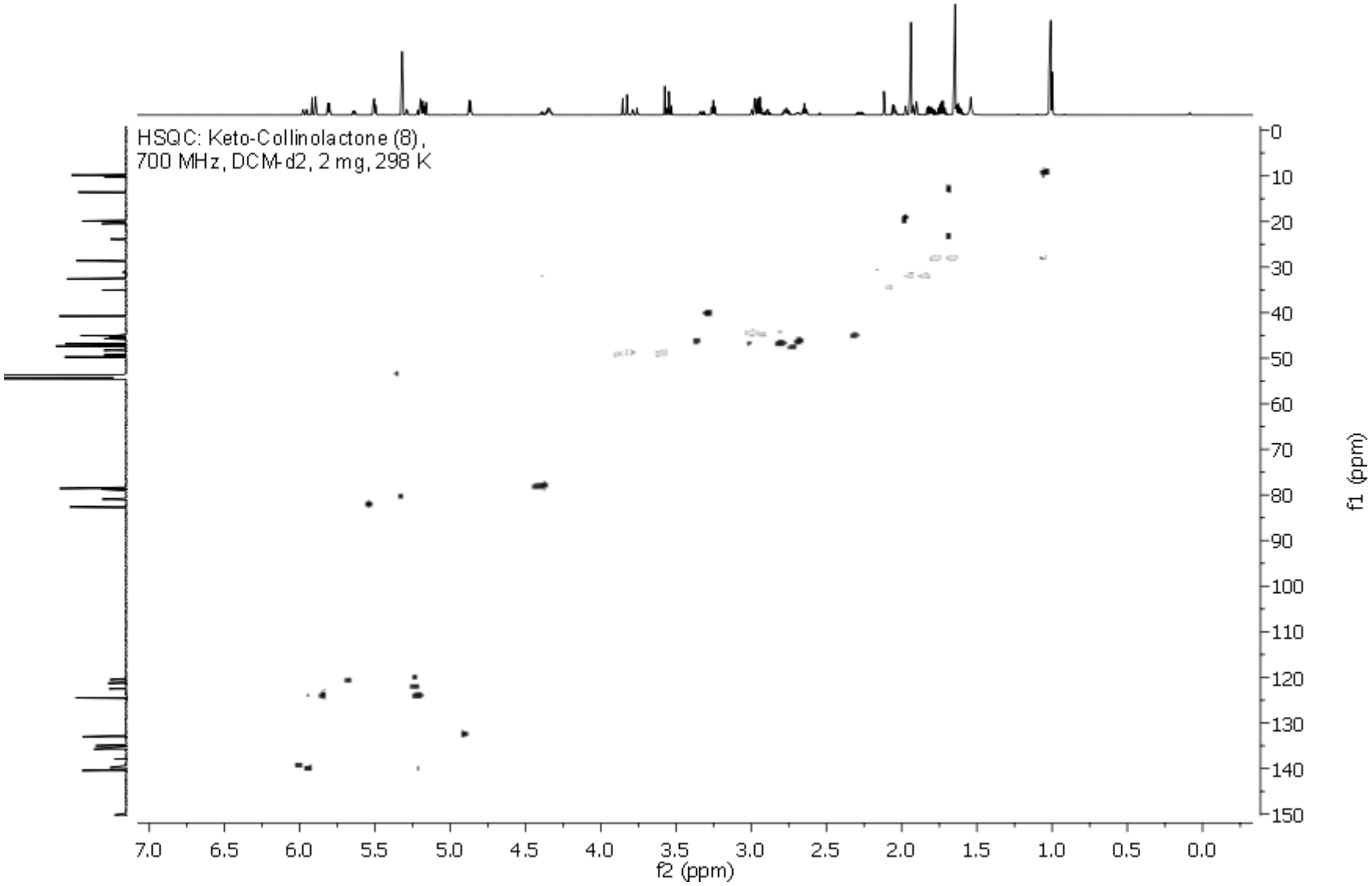

HMBC: Collinolactenone (7),
700 MHz, DCM-d2, 5 mg, 298 K
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f2 (ppm)
50
100
150
200
f1 (ppm)

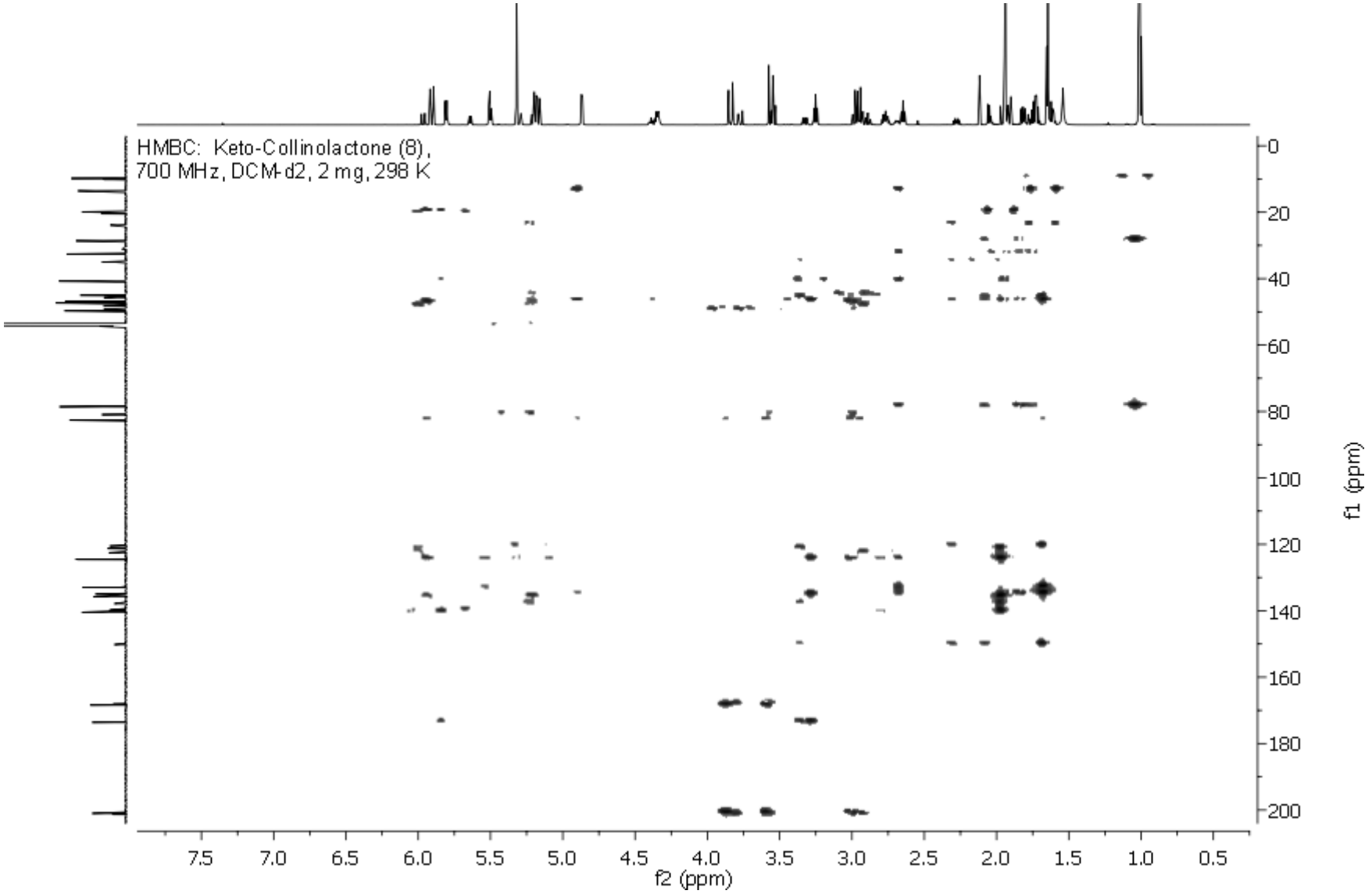

NOESY: Collinolactenone (7),
700 MHz, DCM-d2, 5 mg, 298 K, d8 = 0.9s
f2 (ppm)
f1 (ppm)

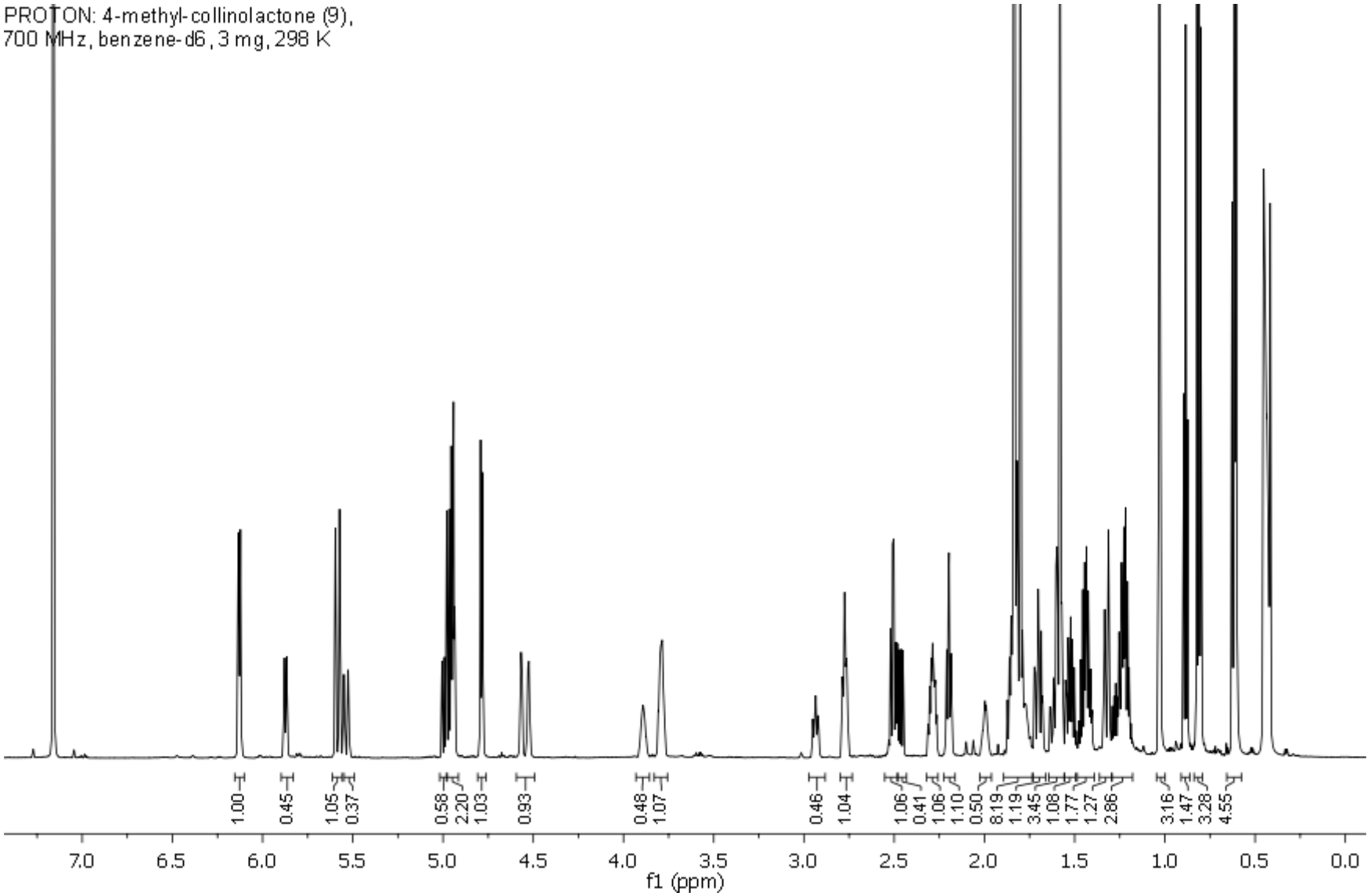

PROTON: Keto-Collinolactone (8),
700 MHz, DCM-d2, 2 mg, 298 K
0.36
1.00
0.93
0.34
0.99
0.37
1.69
0.98
0.38
0.97
1.01
0.37
1.36
0.37
1.00
2.36
0.39
1.01
0.37
1.02
0.37
0.27
0.75
4.07
1.19
1.06
1.36
4.26
1.96
4.05
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

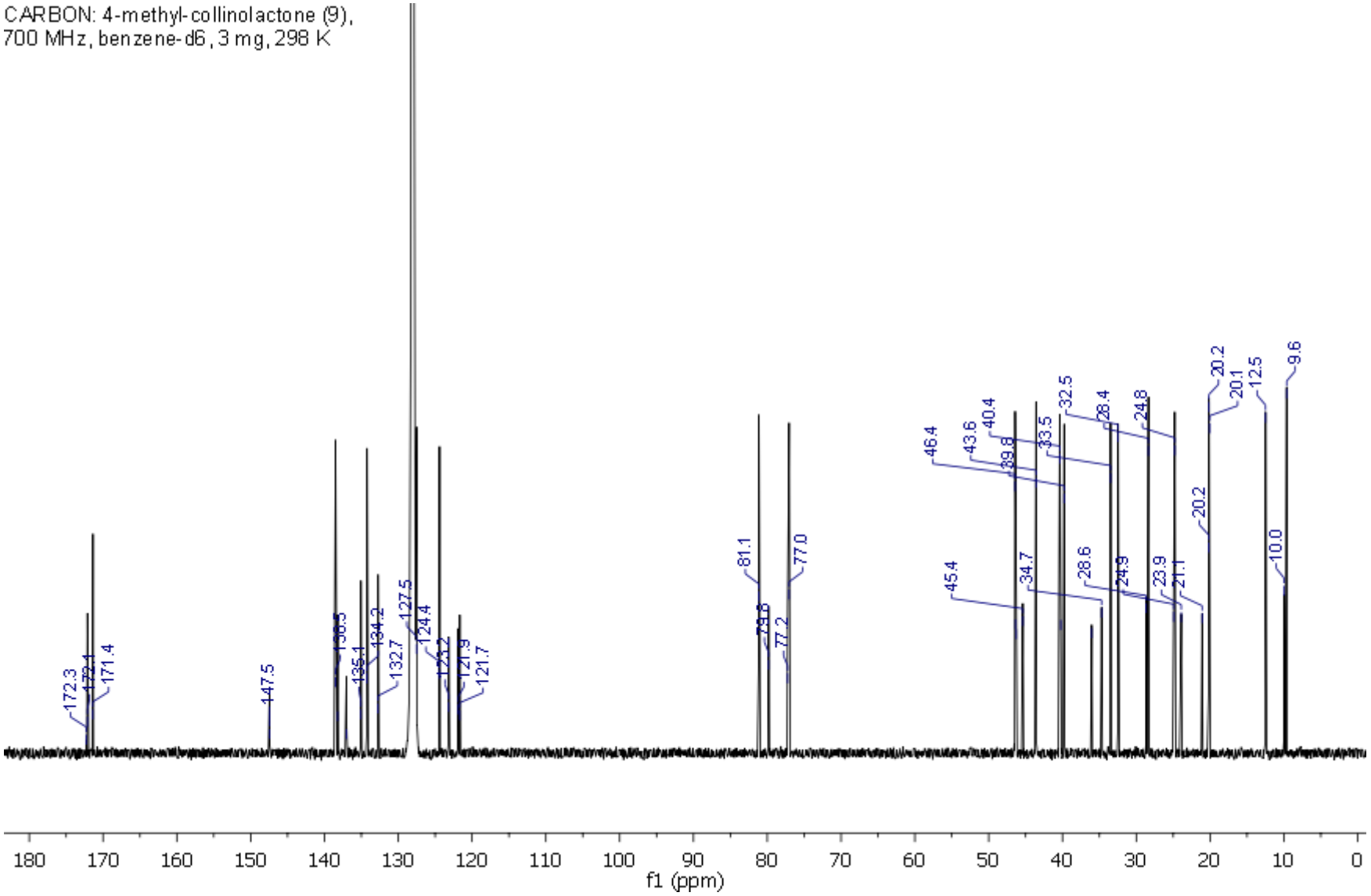

CARBON: Keto-Collinolactone (8),
700 MHz, DCM-d2, 2 mg, 298 K
201.3
201.0
173.7
173.6
168.4
168.1
150.2
140.5
139.8
135.7
135.0
133.0
124.6
124.5
122.5
121.3
120.5
82.6
80.9
78.8
78.6
49.7
49.3
47.3
46.8
45.7
45.4
45.0
40.8
35.0
32.6
28.8
28.6
20.5
19.9
13.6
10.1
9.8
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

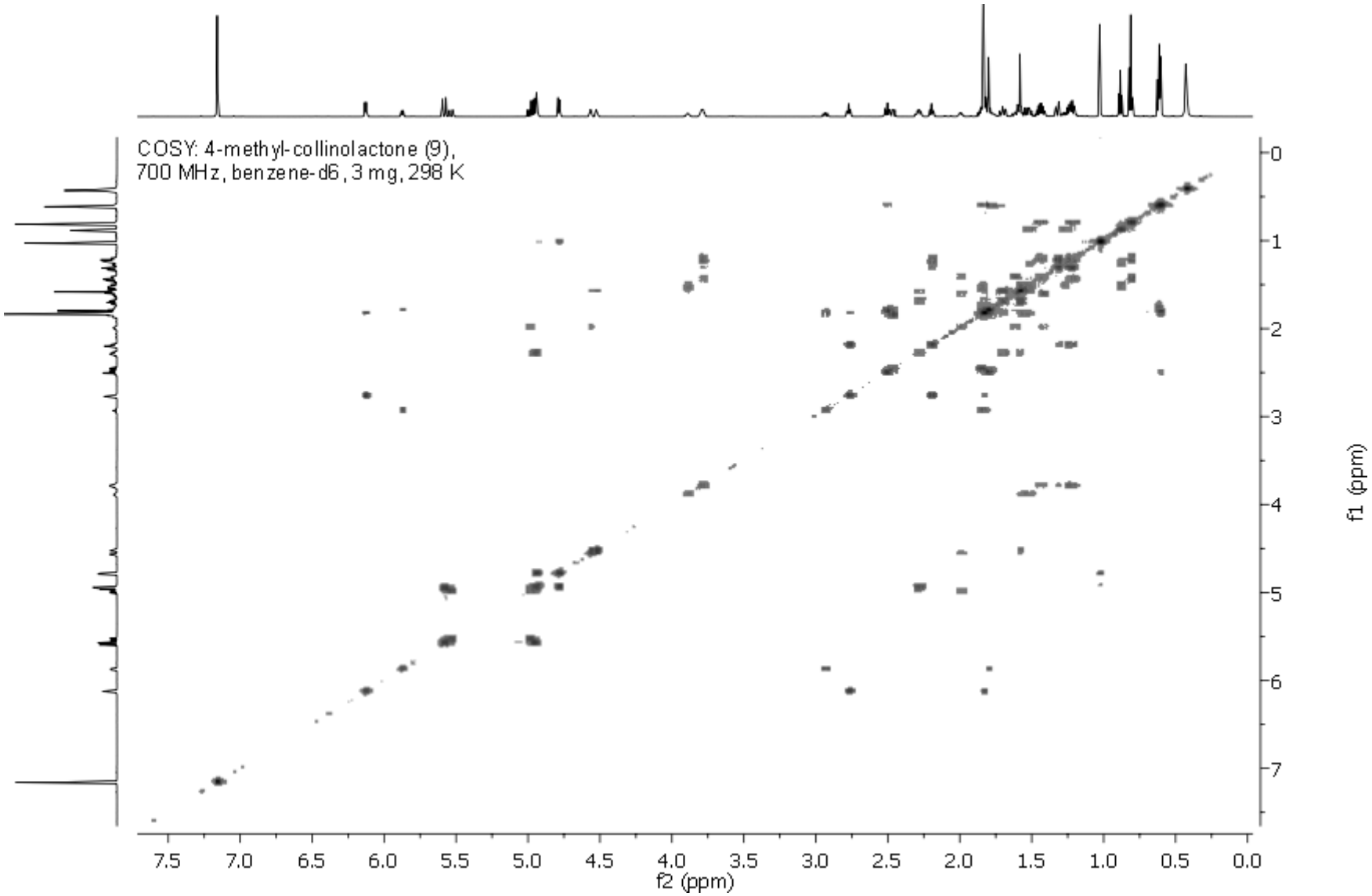

COSY: Keto-Collinolactone (8),
700 MHz, DCM-d2, 2 mg, 298 K
f2 (ppm)
f1 (ppm)
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0
1
2
3
4
5
6

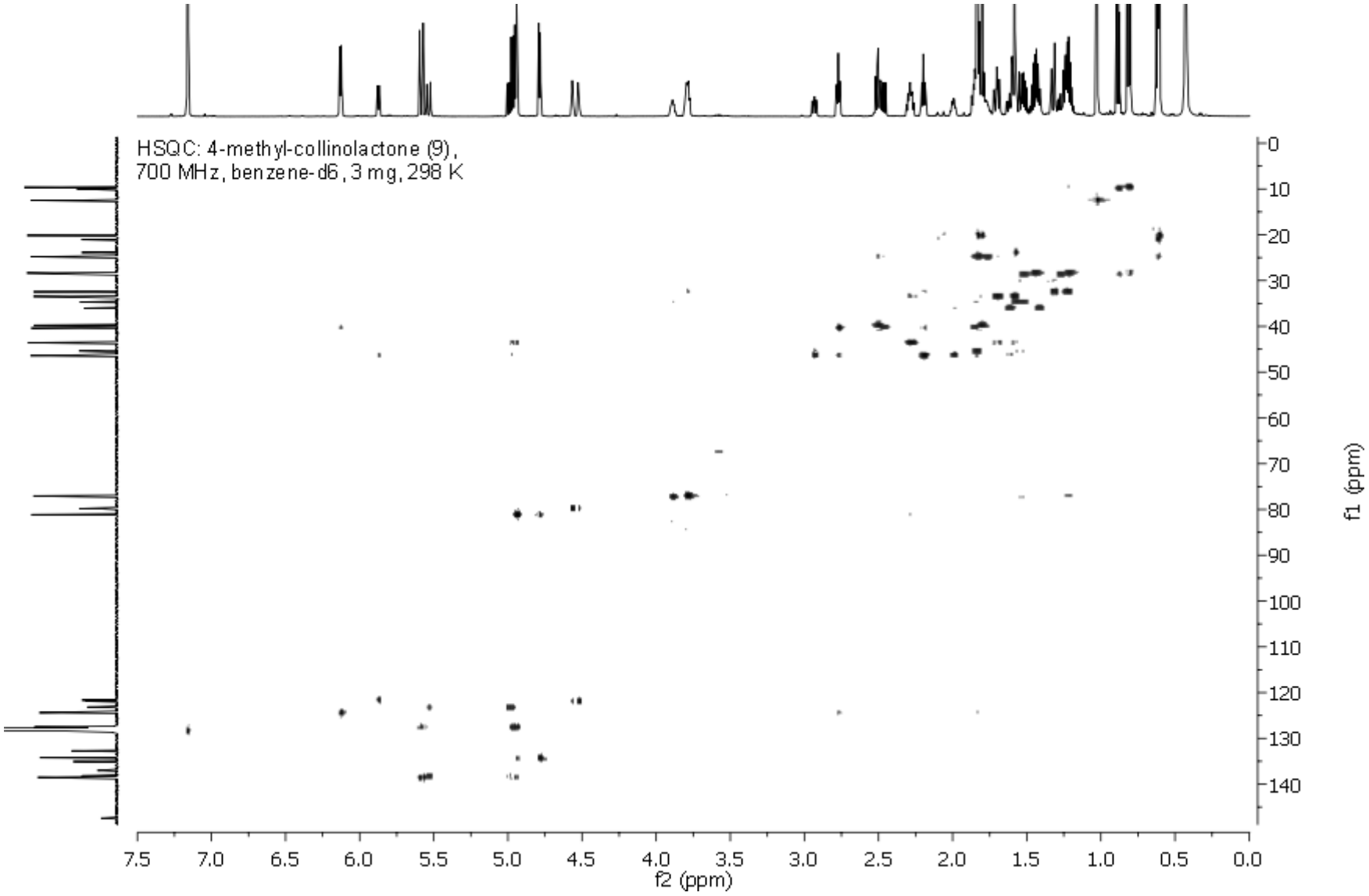

HSQC: Keto-Collinolactone (8),
700 MHz, DCM-d2, 2 mg, 298 K
f2 (ppm)
f1 (ppm)

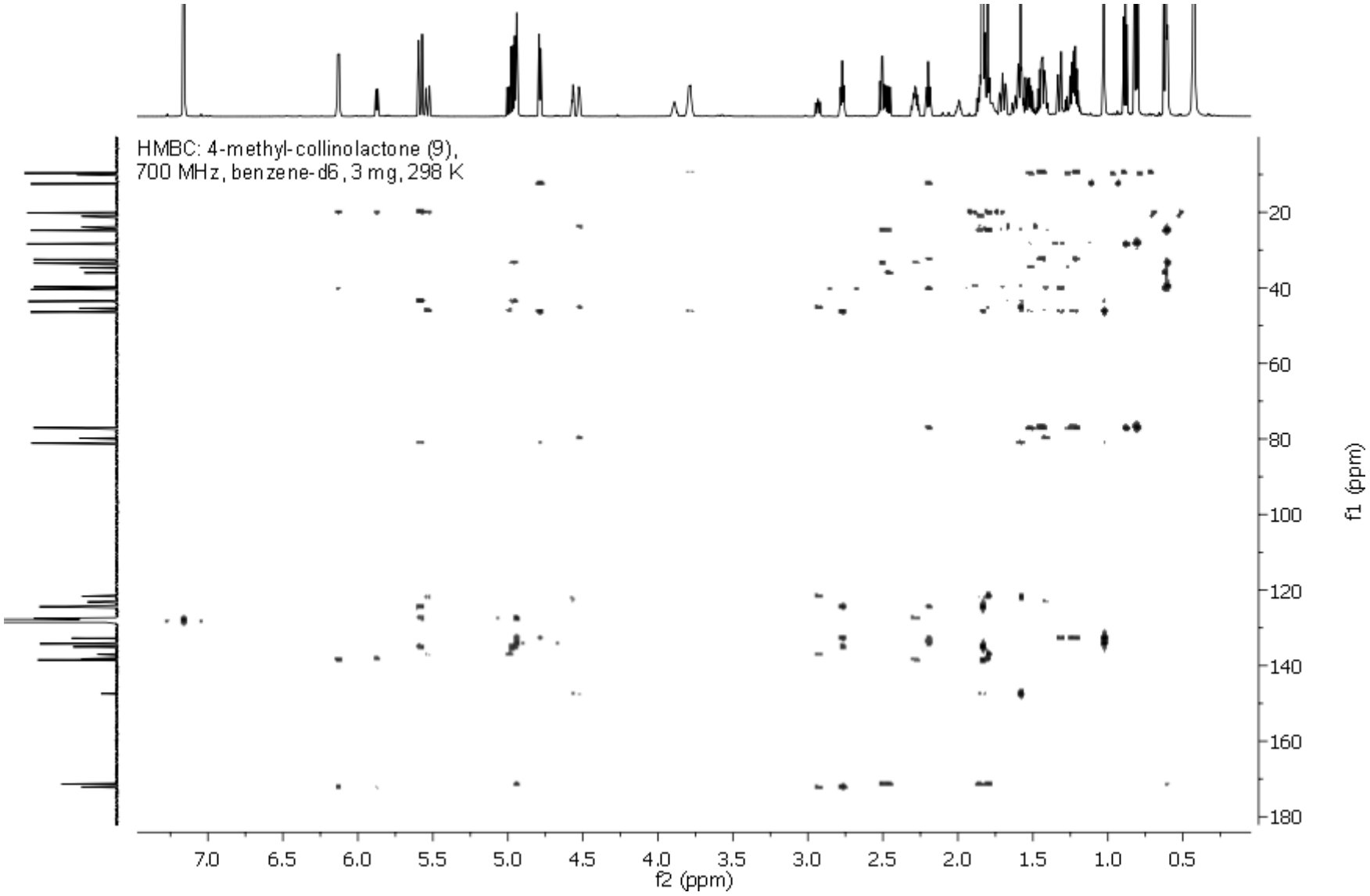

HMBC: Keto-Collinolactone (8),
700 MHz, DCM-d2, 2 mg, 298 K
f2 (ppm)
f1 (ppm)
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0
20
40
60
80
100
120
140
160
180
200

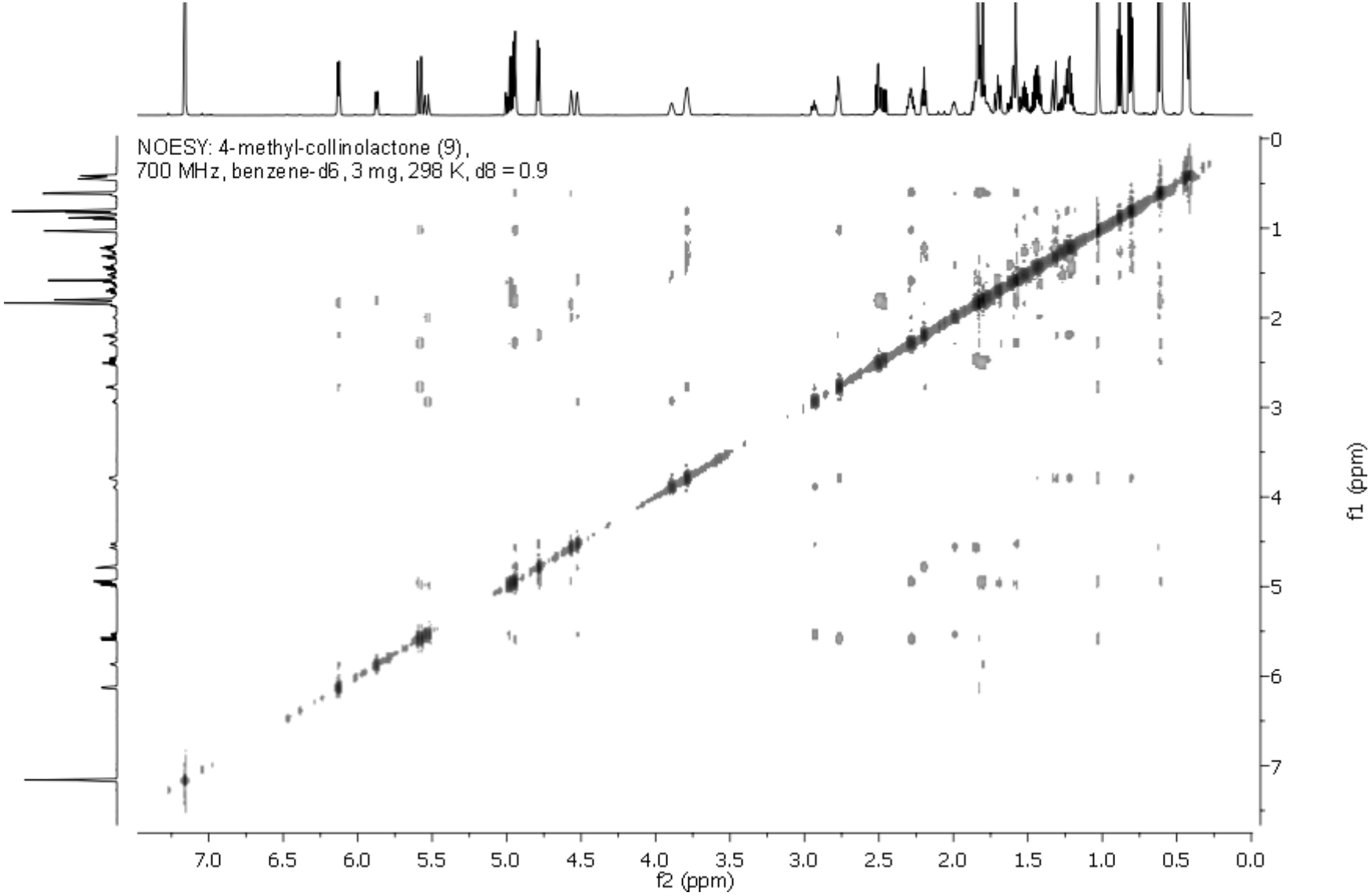

PROTON: 4-methyl-collinolactone (9),
700 MHz, benzene-d6, 3 mg, 298 K
1.00
0.45
1.05
0.37
0.58
2.20
1.03
0.93
0.48
1.07
0.46
1.04
1.06
0.41
1.06
1.10
0.50
8.19
1.19
3.45
1.08
1.77
1.27
2.86
3.16
1.47
3.28
4.55
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

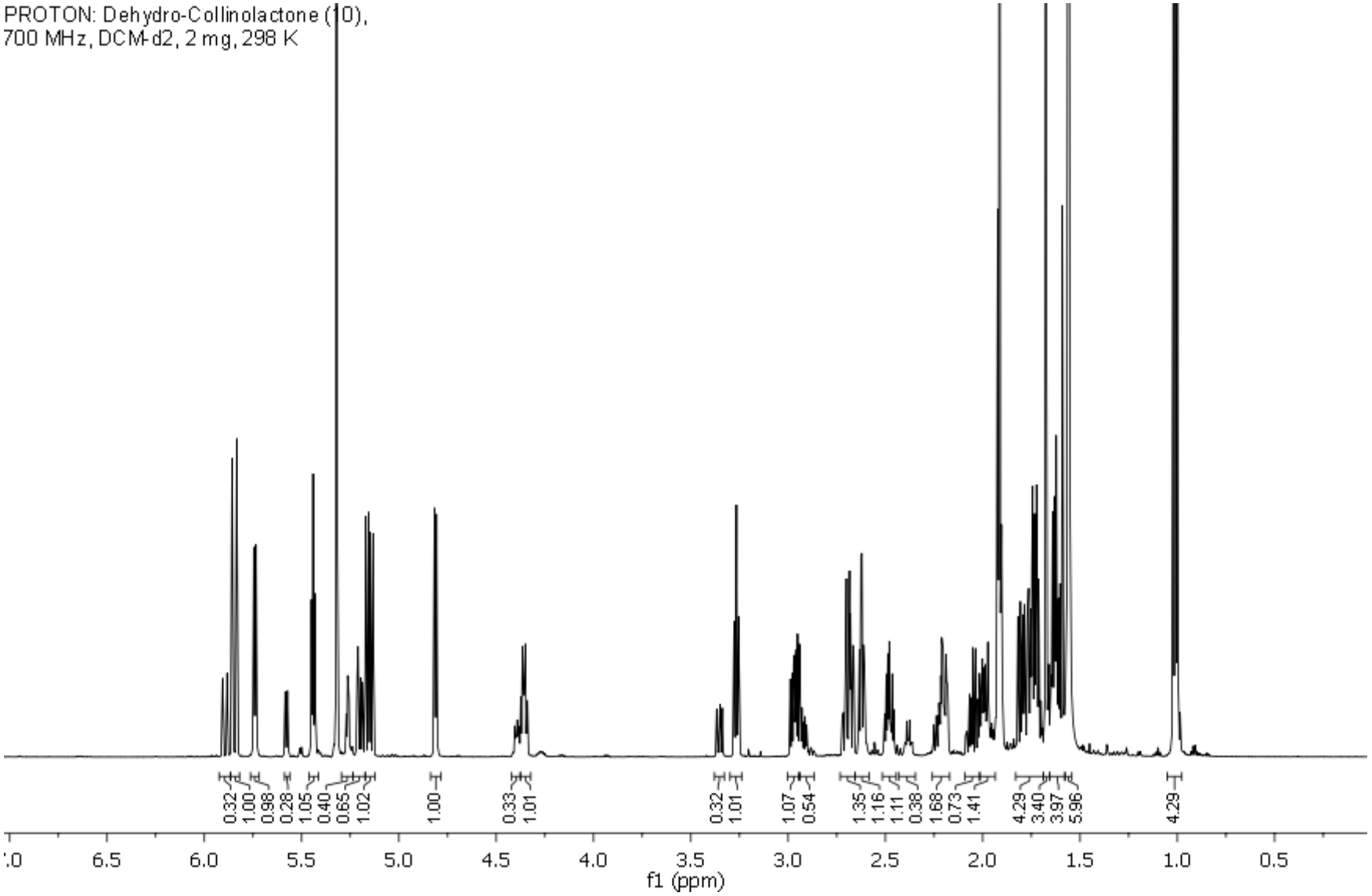

CARBON: 4-methyl-collinolactone (9),
700 MHz, benzene-d6, 3 mg, 298 K
172.3
171.4
147.5
135.1
132.7
127.5
124.4
121.9
121.7
81.1
77.0
46.4
43.6
40.4
39.8
34.7
33.5
32.5
28.6
28.4
24.9
24.8
23.9
21.1
20.2
20.1
12.5
10.0
9.6
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

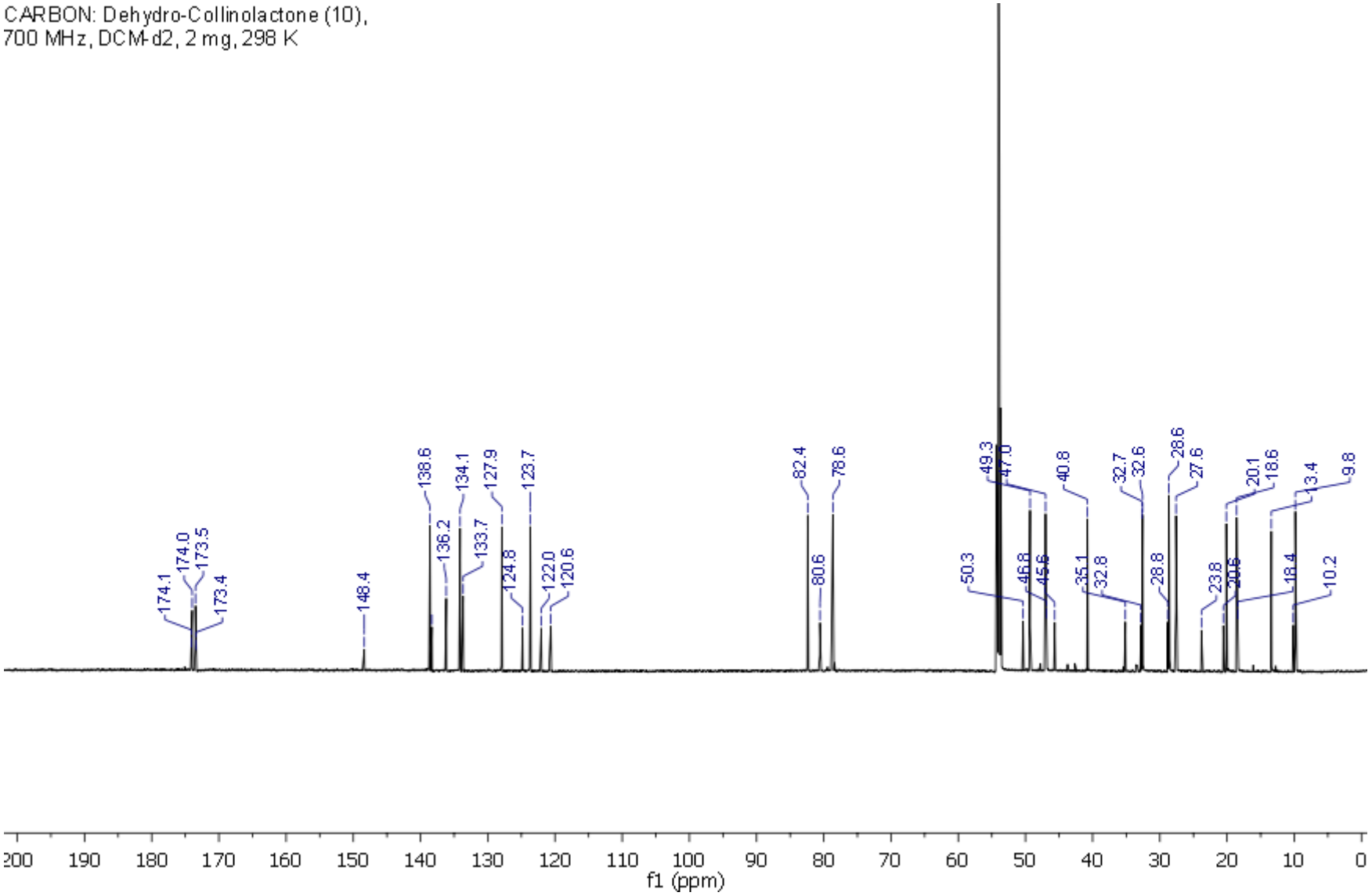

COSY: 4-methyl-collinolactone (9),
700 MHz, benzene-d6, 3 mg, 298 K
f2 (ppm)
f1 (ppm)
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
0
1
2
3
4
5
6
7

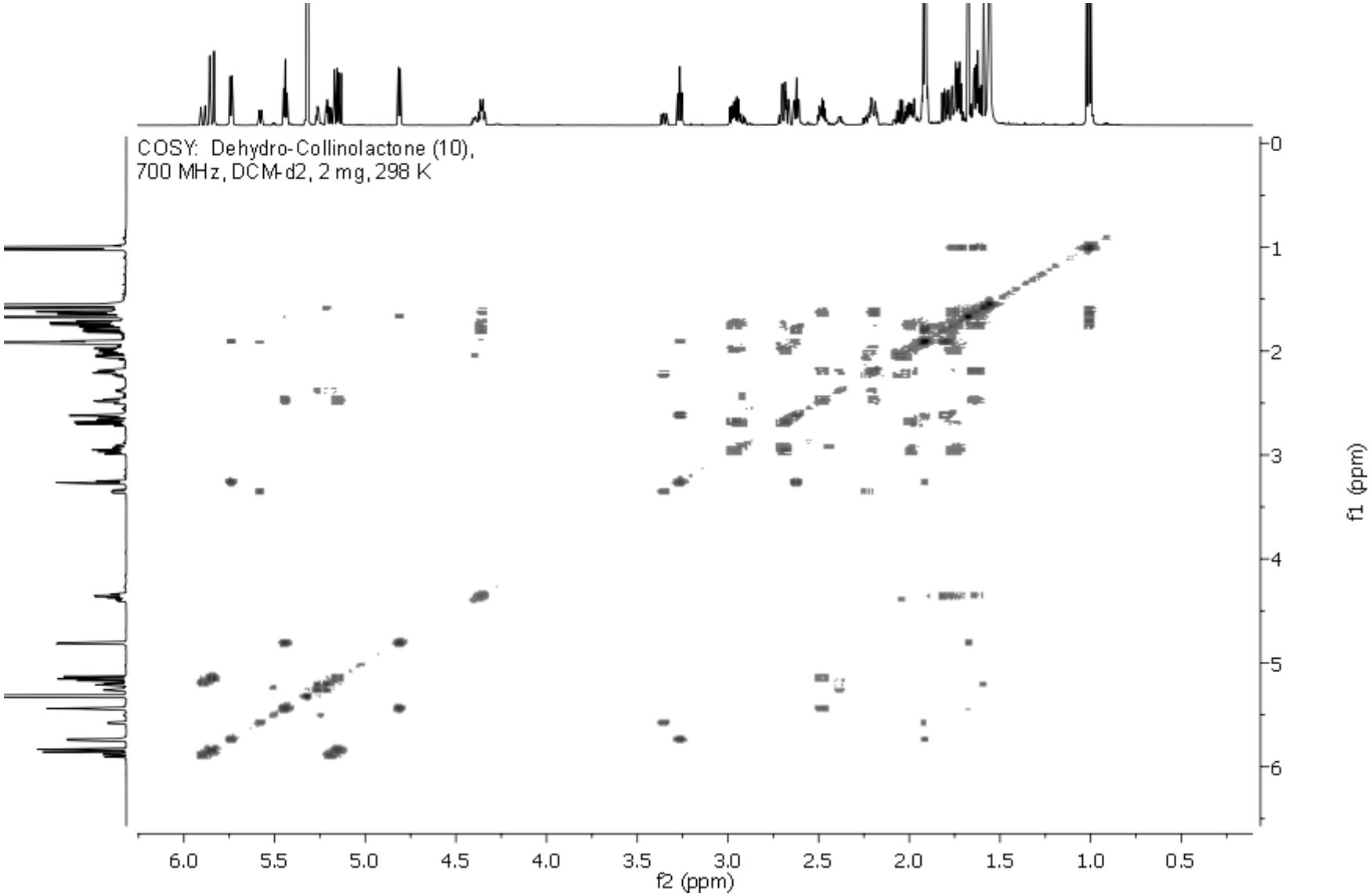

HSQC: 4-methyl-collinolactone (9),
700 MHz, benzene-d6, 3 mg, 298 K
f2 (ppm)
f1 (ppm)

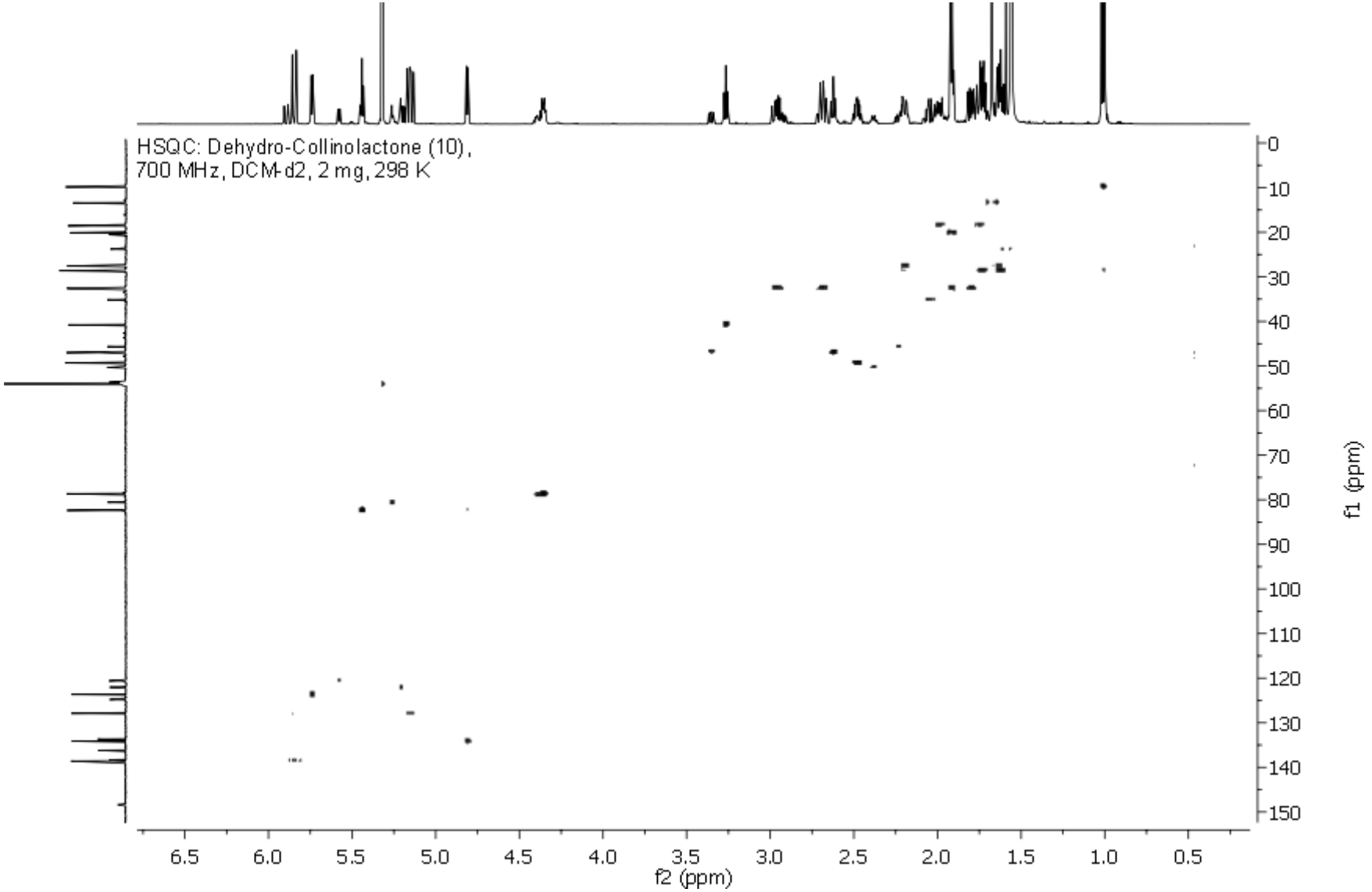

HMBC: 4-methyl-collinolactone (9),
700 MHz, benzene-d6, 3 mg, 298 K
f2 (ppm)
f1 (ppm)

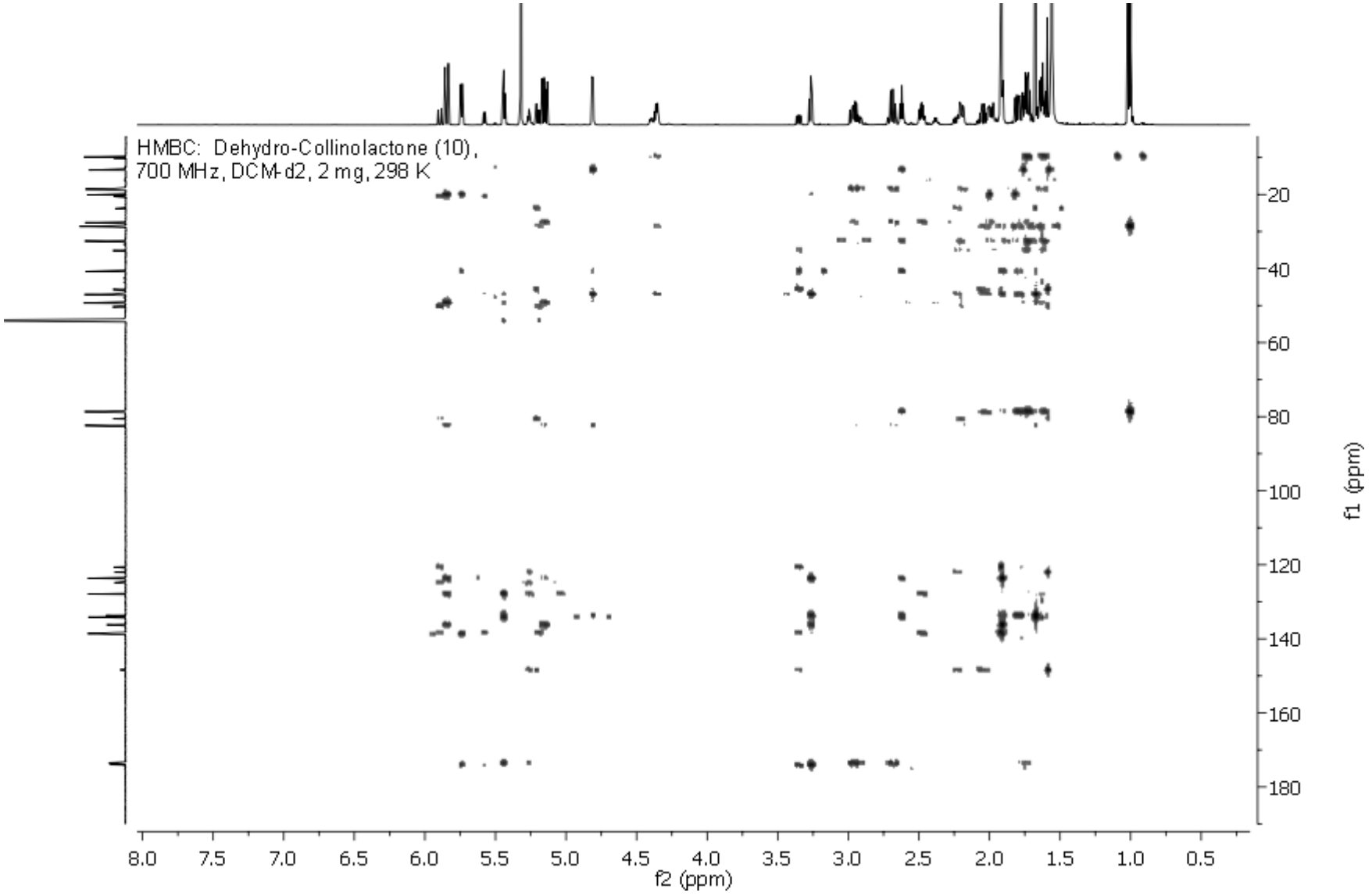

NOESY: 4-methyl-collinolactone (9),
700 MHz, benzene-d6, 3 mg, 298 K, d8 = 0.9
f2 (ppm)
f1 (ppm)
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
0
1
2
3
4
5
6
7

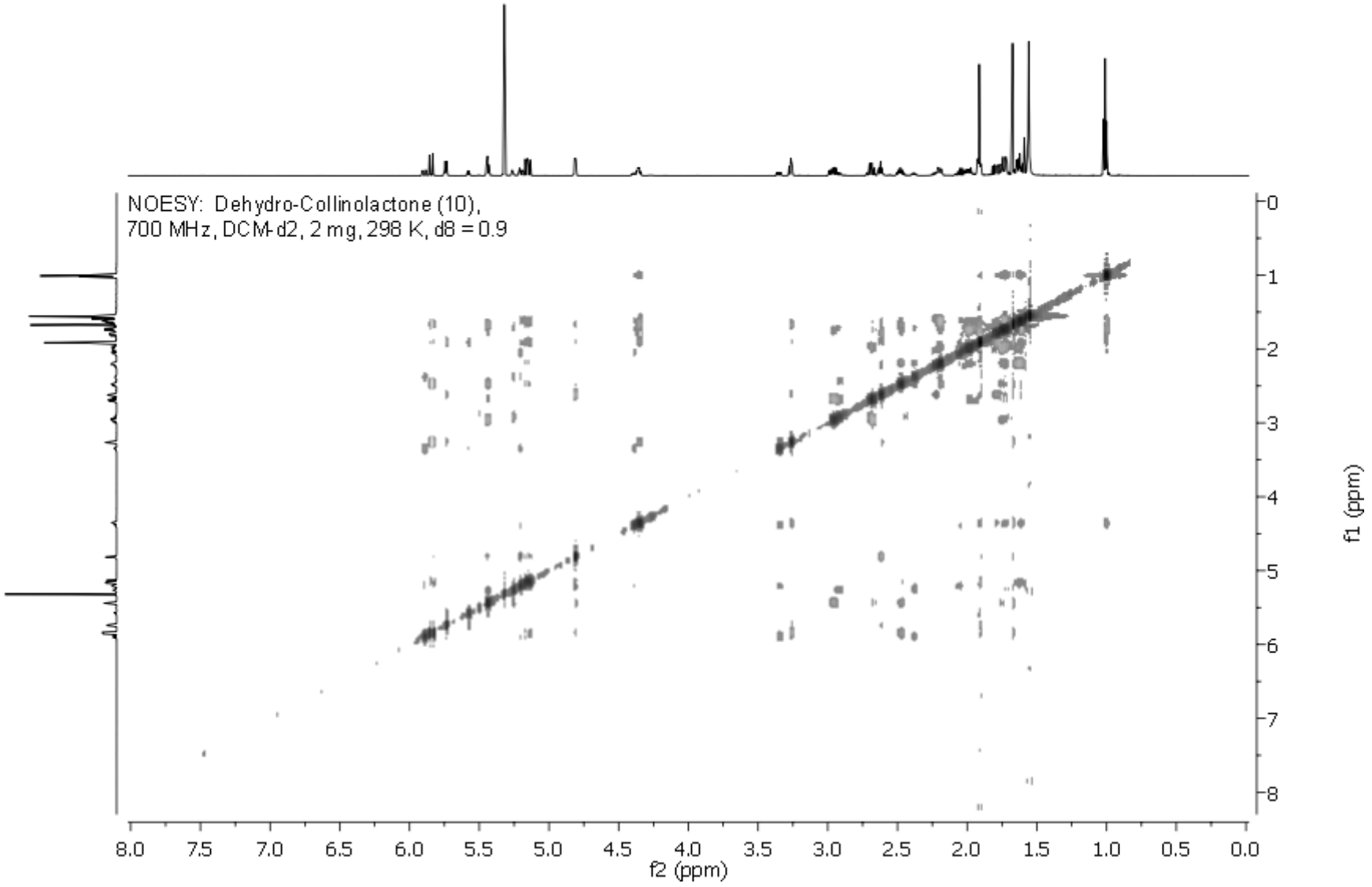

PROTON: Dehydro-Collinolactone (10),
700 MHz, DCM-d2, 2 mg, 298 K
0.32
1.00
0.98
0.28
1.05
0.40
0.65
1.02
1.00
0.33
1.01
0.32
1.01
1.07
0.54
1.35
1.16
1.11
0.38
1.68
0.73
1.41
4.29
3.40
3.97
5.96
4.29
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
f1 (ppm)

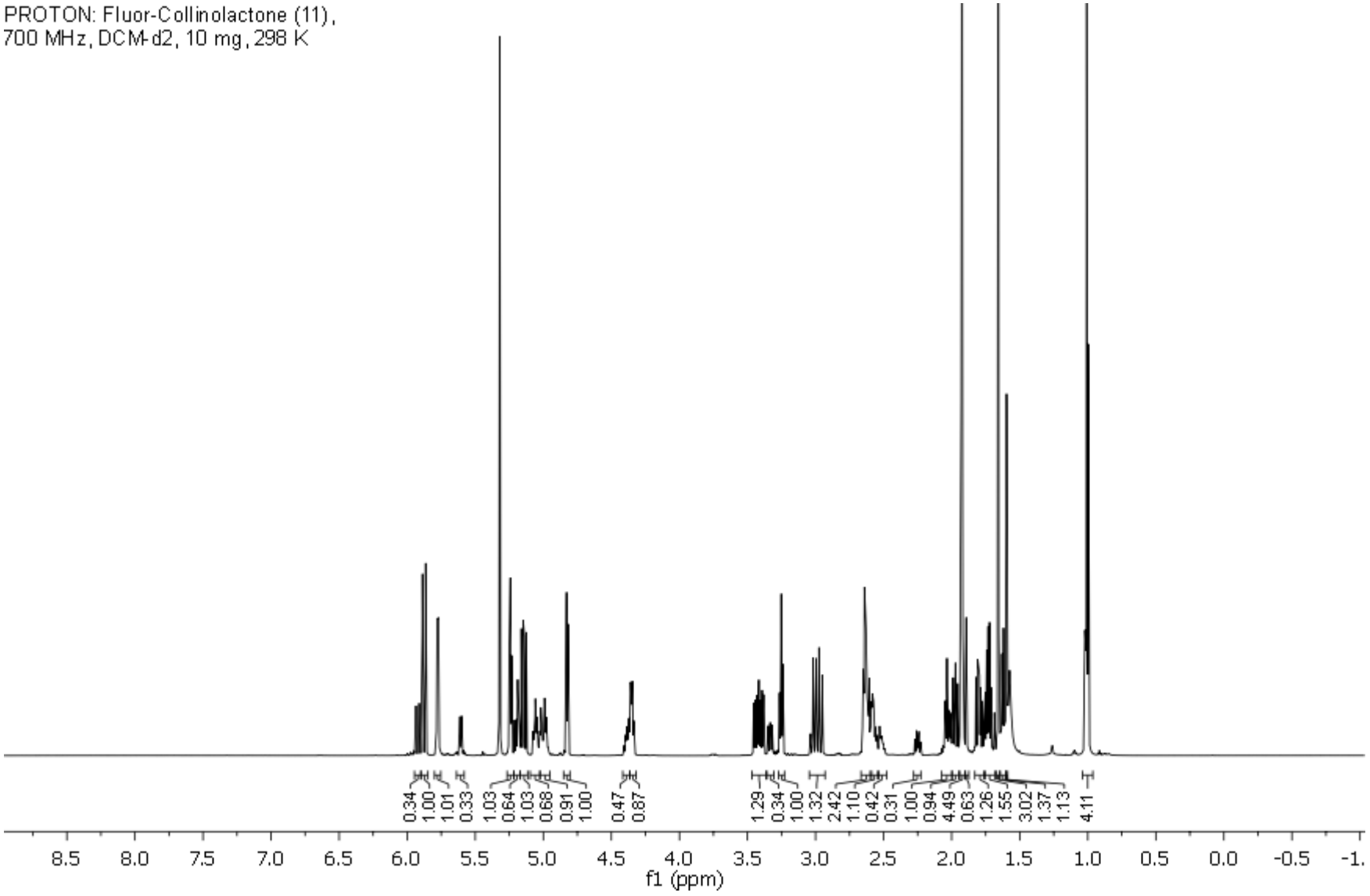

CARBON: Dehydro-Collinolactone (10),
700 MHz, DCM-d2, 2 mg, 298 K
174.1
174.0
173.5
173.4
148.4
138.6
136.2
134.1
133.7
127.9
124.8
123.7
122.0
120.6
82.4
80.6
78.6
50.3
49.3
47.0
46.8
45.6
40.8
35.1
32.8
32.7
32.6
28.8
28.6
27.6
23.8
20.6
20.1
18.6
18.4
13.4
10.2
9.8
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

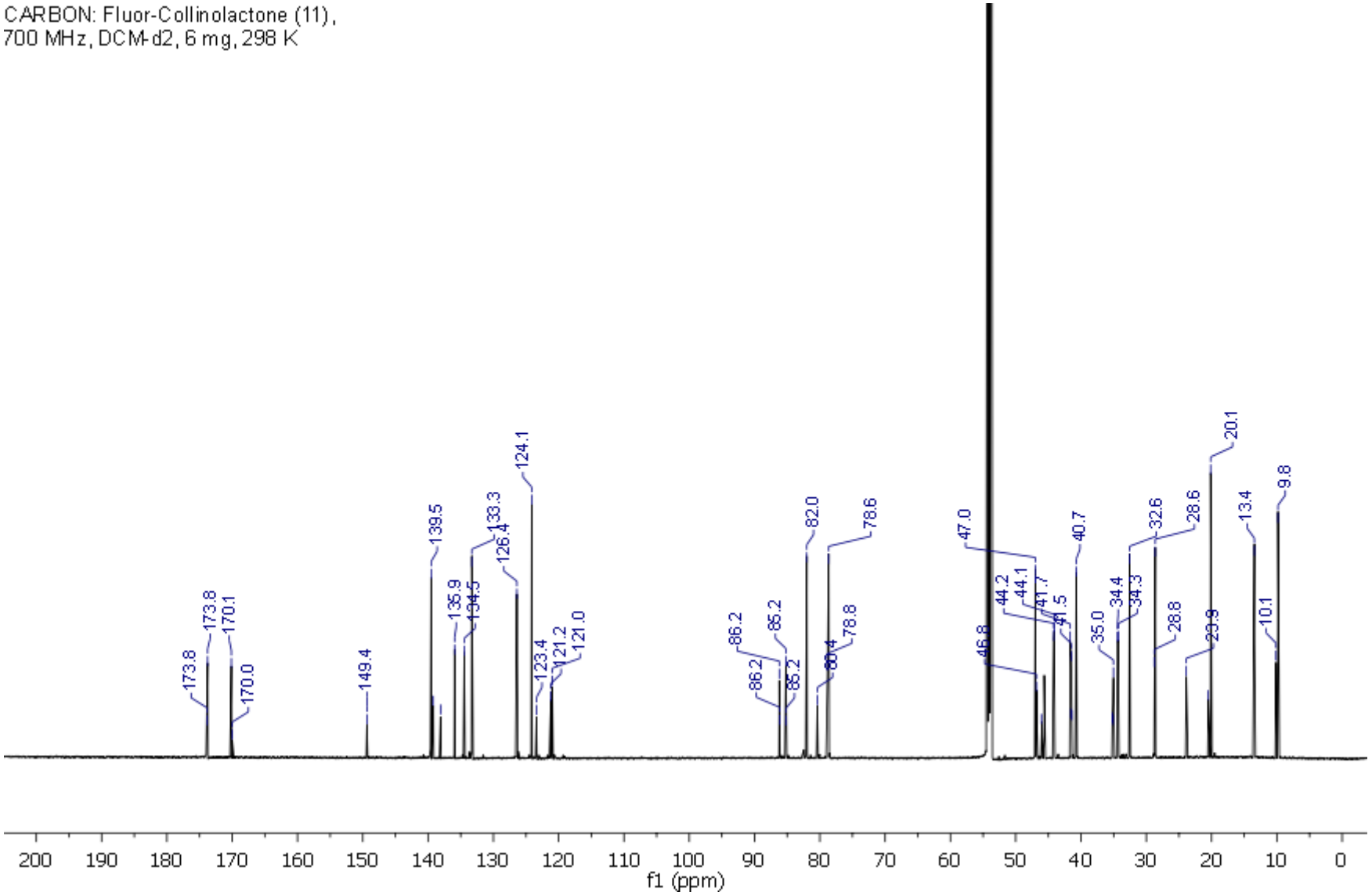

COSY: Dehydro-Collinolactone (10),
700 MHz, DCM-d2, 2 mg, 298 K
f2 (ppm)
f1 (ppm)
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0
1
2
3
4
5
6

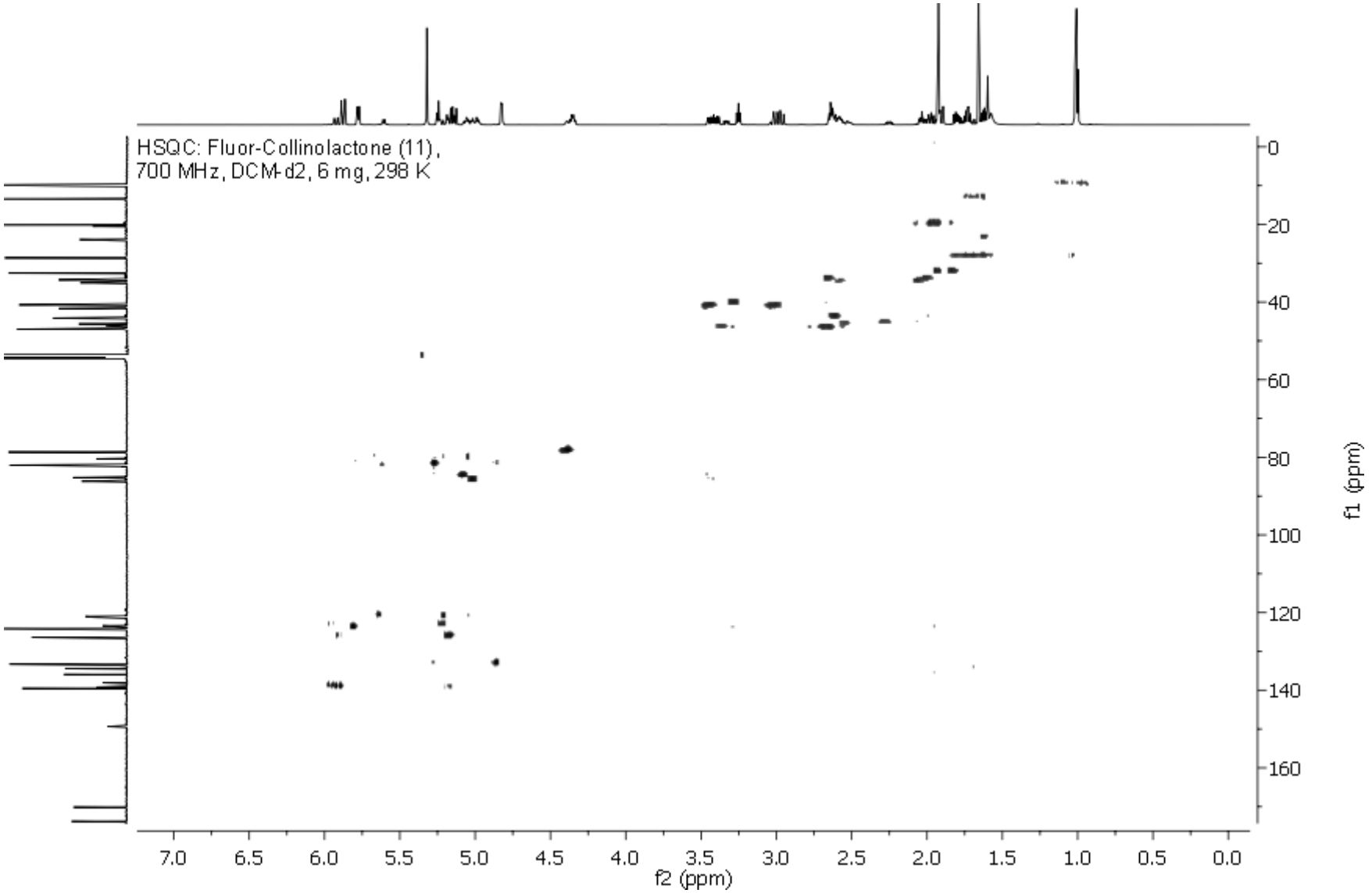

HSQC: Dehydro-Collinolactone (10),
700 MHz, DCM-d2, 2 mg, 298 K
f2 (ppm)
f1 (ppm)

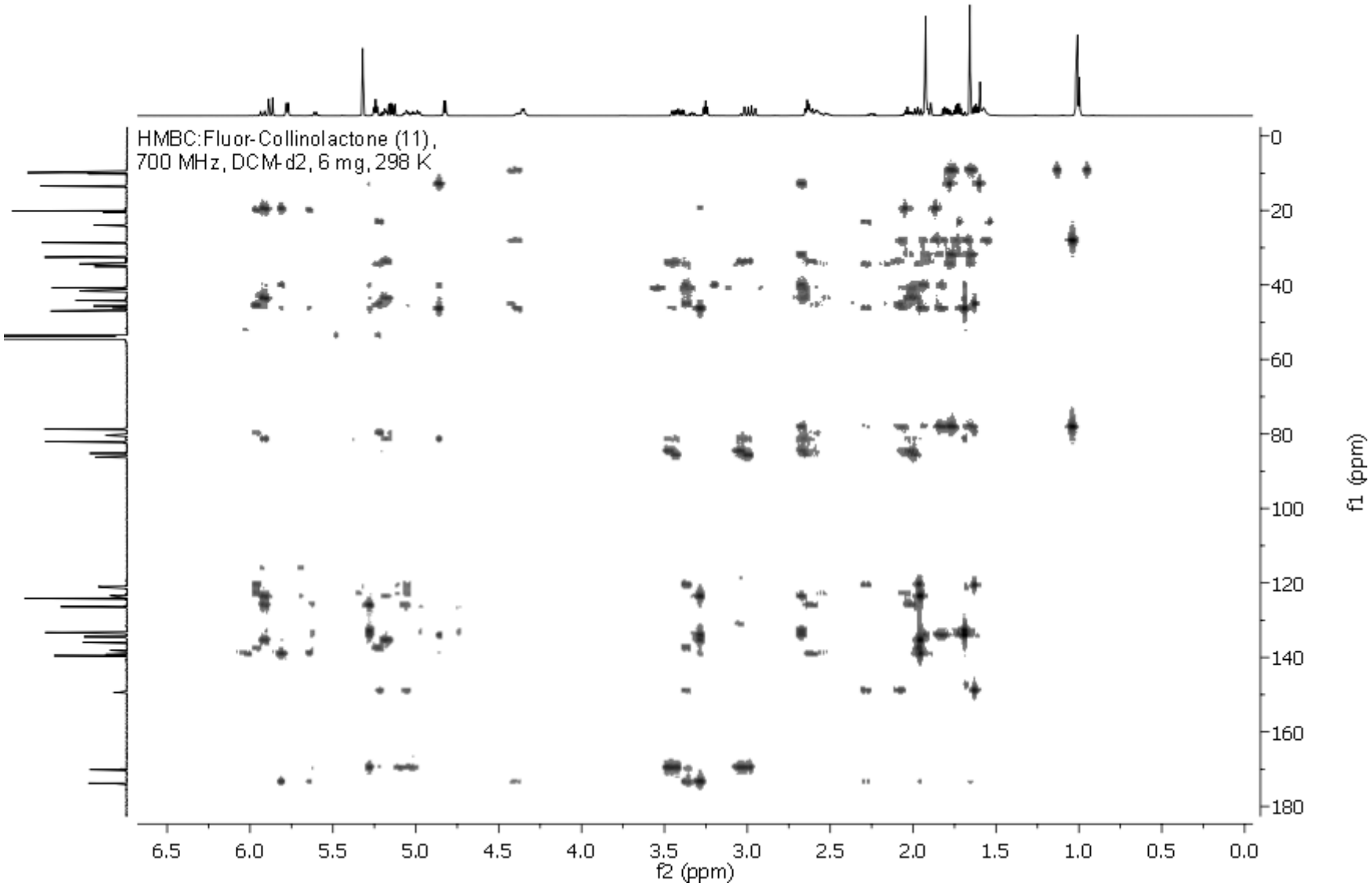

HMBC: Dehydro-Collinolactone (10),
700 MHz, DCM-d2, 2 mg, 298 K
f2 (ppm)
f1 (ppm)
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
20
40
60
80
100
120
140
160
180

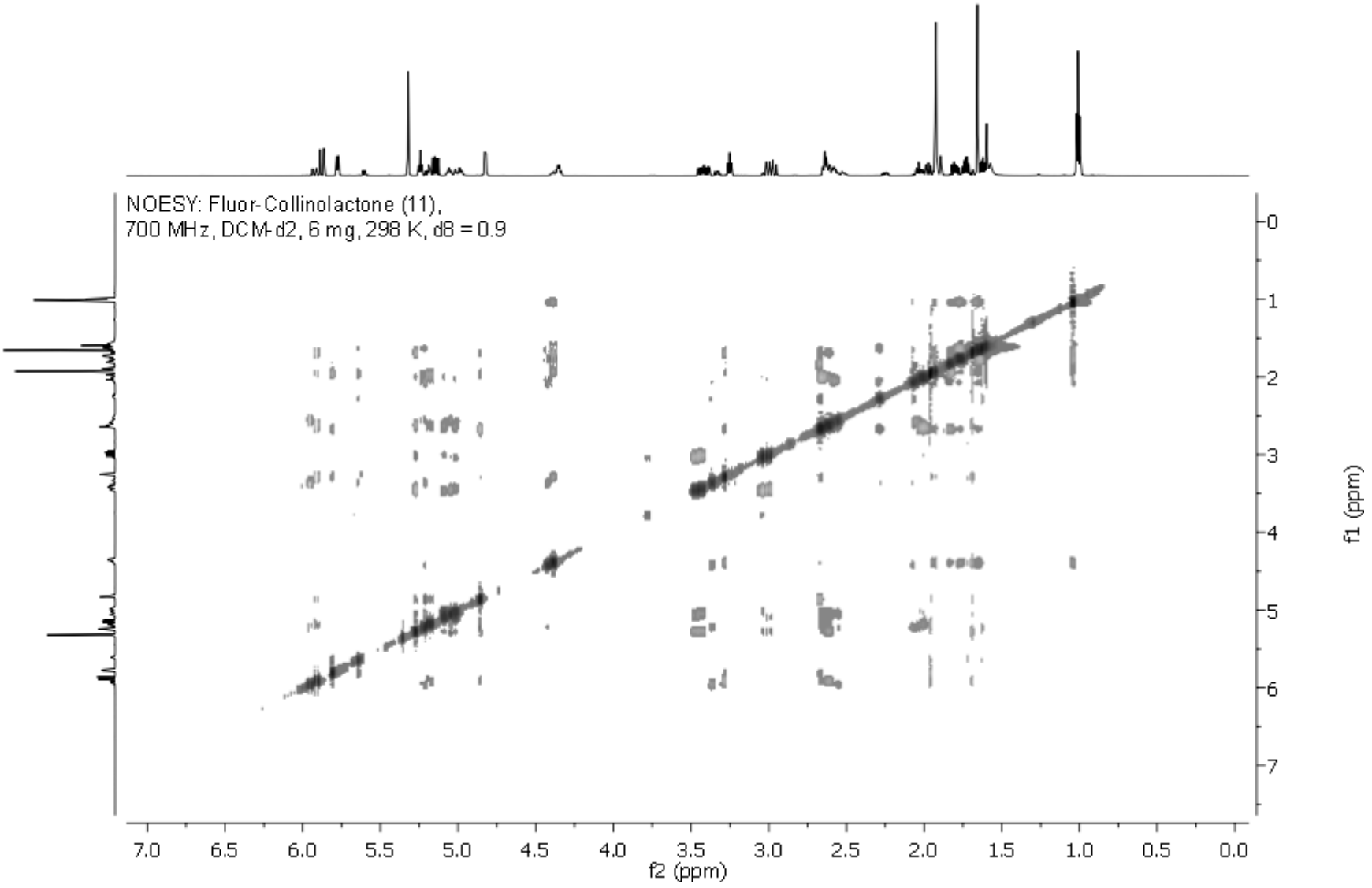

NOESY: Dehydro-Collinolactone (10),
700 MHz, DCM-d2, 2 mg, 298 K, d8 = 0.9
f2 (ppm)
f1 (ppm)


PROTON: Fluor-Collinolactone (11),
700 MHz, DCM-d2, 10 mg, 298 K
0.34
1.00
1.01
0.33
1.03
0.64
1.03
0.68
0.91
1.00
0.47
0.87
1.29
0.34
1.00
1.32
2.42
1.10
0.42
0.31
1.00
0.94
4.49
0.63
1.26
1.55
3.02
1.37
1.13
4.11
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
-1.
f1 (ppm)


CARBON: Fluor-Collinolactone (11),
700 MHz, DCM-d2, 6 mg, 298 K
173.8
173.8
170.1
170.0
149.4
139.5
135.9
134.5
133.3
126.4
124.1
123.4
121.2
121.0
86.2
85.2
82.0
80.4
78.8
78.6
47.0
46.8
44.2
44.1
41.7
41.5
40.7
35.0
34.4
34.3
32.6
28.8
28.6
23.9
20.1
13.4
10.1
9.8
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)


HSQC: Fluor-Collinolactone (11),
700 MHz, DCM-d2, 6 mg, 298 K
f2 (ppm)
f1 (ppm)
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
0
20
40
60
80
100
120
140
160


HMBC:Fluor-Collinolactone (11),
700 MHz, DCM-d2, 6 mg, 298 K
f2 (ppm)
f1 (ppm)
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
0
20
40
60
80
100
120
140
160
180


NOESY: Fluor-Collinolactone (11),
700 MHz, DCM-d2, 6 mg, 298 K, d8 = 0.9
f2 (ppm)
f1 (ppm)

Crystal data and structure refinement

Table S4: Crystal data and structure refinement[16] for compound **3**.

Identification code	Collinolactone	
Empirical formula	C21 H28 O6	
Formula weight	376.43	
Temperature	100(2) K	
Wavelength	1.54178 Å	
Crystal system	Orthorhombic	
Space group	$P2_12_12_1$	
Unit cell dimensions	a = 5.0349(10) Å	α = 90º
	b = 15.383(3) Å	β = 90º
	c = 23.783(5) Å	γ = 90º
Volume	1842.0(6) $Å^3$	
Z	4	
Density (calculated)	1.357 Mg/m^3	
Absorption coefficient	0.810 mm^{-1}	
F(000)	808	
Crystal size	0.01 x 0.005 x 0.005 mm^3	
Theta range for data collection	3.422 to 66.130º	
Index ranges	-4<=h<=5, -12<=k<=12, -20<=l<=20	
Reflections collected	2882	
Independent reflections	2882 [R(int) = ?]	
Completeness to theta = 66.130º	56.6%	
Absorption correction	Empirical	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	2882 / 408 / 251	
Goodness-of-fit on F^2	1.103	
Final R indices [I>2sigma(I)]	R1 = 0.0693, wR2 = 0.1707	
R indices (all data)	R1 = 0.0704, wR2 = 0.1729	
Absolute structure parameter	0.2(3)	
Largest diff. peak and hole	0.295 and -0.326 e.$Å^{-3}$	

CCDC 2006674 contains the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/structures

Table S5: Atomic coordinates (x 10^4) and equivalent isotropic displacement parameters (≈^{2}x 10^3) for 3. U(eq) is defined as one third of the trace of the orthogonalized U^{ij} tensor.

	x	y	z	U(eq)
O(3)	998(8)	4557(3)	5690(2)	30(1)
C(3)	2835(12)	5898(5)	6606(3)	33(2)
O(1)	-1525(8)	4170(3)	6392(2)	33(1)
C(1)	515(11)	4515(4)	6253(3)	27(2)
O(2)	3879(8)	7133(3)	4894(2)	33(1)
C(2)	2530(13)	4891(4)	6647(4)	30(2)
O(4)	5474(9)	6149(3)	6716(3)	39(2)
C(4)	2074(12)	6272(5)	6042(3)	31(2)
O(5)	7366(9)	3346(3)	2928(2)	34(1)
C(5)	3676(12)	5908(5)	5557(3)	28(2)
O(6)	8299(9)	4710(3)	2777(2)	40(2)
C(6)	3484(12)	4915(5)	5477(3)	26(2)
C(9)	2957(11)	6255(5)	4982(3)	27(2)
C(8)	4190(12)	5625(4)	4561(3)	26(2)
C(7)	3487(11)	4729(4)	4841(3)	25(2)
C(10)	3296(12)	5713(4)	3962(3)	28(2)
C(11)	1293(13)	6401(5)	3800(3)	35(2)
C(12)	4253(12)	5191(4)	3555(3)	30(2)
C(13)	6169(12)	4453(4)	3654(3)	29(2)
C(14)	7313(13)	4173(5)	3096(3)	31(2)
C(15)	5954(12)	2680(5)	3255(3)	29(2)
C(16)	6228(12)	2860(4)	3869(3)	30(2)
C(17)	4949(12)	3719(4)	4032(3)	28(2)
C(18)	5113(12)	3946(4)	4649(3)	27(2)
C(19)	6517(12)	3459(4)	5001(3)	33(2)
C(20)	3161(13)	2616(5)	3021(3)	35(2)
C(21)	3003(16)	2160(5)	2451(4)	47(2)

Table S6: Bond lengths [≈] and angles [∞] for compound **3**.

O(3)-C(1)	1.363(9)
O(3)-C(6)	1.457(8)
C(3)-O(4)	1.409(8)
C(3)-C(4)	1.510(11)
C(3)-C(2)	1.559(10)
C(3)-H(3)	1.0000
O(1)-C(1)	1.203(8)
C(1)-C(2)	1.497(10)
O(2)-C(9)	1.443(8)
O(2)-H(2)	0.90(8)
C(2)-H(2A)	0.9900
C(2)-H(2AB)	0.9900
O(4)-H(4)	0.83(10)
C(4)-C(5)	1.515(10)
C(4)-H(4A)	0.9900
C(4)-H(4AB)	0.9900
O(5)-C(14)	1.335(8)
O(5)-C(15)	1.470(8)
C(5)-C(9)	1.514(10)
C(5)-C(6)	1.542(11)
C(5)-H(5)	1.0000
O(6)-C(14)	1.226(9)
C(6)-C(7)	1.539(10)
C(6)-H(6)	1.0000
C(9)-C(8)	1.526(10)
C(9)-H(9)	1.0000
C(8)-C(10)	1.500(10)
C(8)-C(7)	1.571(9)
C(8)-H(8)	1.0000
C(7)-C(18)	1.526(9)
C(7)-H(7)	1.0000
C(10)-C(12)	1.346(10)
C(10)-C(11)	1.511(9)
C(11)-H(11A)	0.9800
C(11)-H(11B)	0.9800
C(11)-H(11C)	0.9800

C(12)-C(13)	1.509(9)
C(12)-H(12)	0.9500
C(13)-C(14)	1.509(11)
C(13)-C(17)	1.569(9)
C(13)-H(13)	1.0000
C(15)-C(16)	1.492(10)
C(15)-C(20)	1.515(10)
C(15)-H(15)	1.0000
C(16)-C(17)	1.520(10)
C(16)-H(16A)	0.9900
C(16)-H(16B)	0.9900
C(17)-C(18)	1.511(11)
C(17)-H(17)	1.0000
C(18)-C(19)	1.327(10)
C(19)-H(19A)	0.9500
C(19)-H(19B)	0.9500
C(20)-C(21)	1.530(12)
C(20)-H(20A)	0.9900
C(20)-H(20B)	0.9900
C(21)-H(21A)	0.9800
C(21)-H(21B)	0.9800
C(21)-H(21C)	0.9800

C(1)-O(3)-C(6)	120.8(5)
O(4)-C(3)-C(4)	107.4(6)
O(4)-C(3)-C(2)	110.7(6)
C(4)-C(3)-C(2)	114.1(6)
O(4)-C(3)-H(3)	108.1
C(4)-C(3)-H(3)	108.1
C(2)-C(3)-H(3)	108.1
O(1)-C(1)-O(3)	116.4(6)
O(1)-C(1)-C(2)	125.2(7)
O(3)-C(1)-C(2)	118.4(6)
C(9)-O(2)-H(2)	109.5
C(1)-C(2)-C(3)	114.3(6)
C(1)-C(2)-H(2A)	108.7
C(3)-C(2)-H(2A)	108.7
C(1)-C(2)-H(2AB)	108.7

C(3)-C(2)-H(2AB)	108.7
H(2A)-C(2)-H(2AB)	107.6
C(3)-O(4)-H(4)	109.5
C(3)-C(4)-C(5)	113.6(6)
C(3)-C(4)-H(4A)	108.8
C(5)-C(4)-H(4A)	108.8
C(3)-C(4)-H(4AB)	108.8
C(5)-C(4)-H(4AB)	108.8
H(4A)-C(4)-H(4AB)	107.7
C(14)-O(5)-C(15)	119.7(5)
C(9)-C(5)-C(4)	115.5(6)
C(9)-C(5)-C(6)	102.9(6)
C(4)-C(5)-C(6)	115.3(6)
C(9)-C(5)-H(5)	107.6
C(4)-C(5)-H(5)	107.6
C(6)-C(5)-H(5)	107.6
O(3)-C(6)-C(7)	105.8(5)
O(3)-C(6)-C(5)	112.6(5)
C(7)-C(6)-C(5)	107.8(6)
O(3)-C(6)-H(6)	110.2
C(7)-C(6)-H(6)	110.2
C(5)-C(6)-H(6)	110.2
O(2)-C(9)-C(5)	112.6(6)
O(2)-C(9)-C(8)	111.7(5)
C(5)-C(9)-C(8)	105.8(6)
O(2)-C(9)-H(9)	108.9
C(5)-C(9)-H(9)	108.9
C(8)-C(9)-H(9)	108.9
C(10)-C(8)-C(9)	116.3(5)
C(10)-C(8)-C(7)	114.5(5)
C(9)-C(8)-C(7)	100.8(5)
C(10)-C(8)-H(8)	108.2
C(9)-C(8)-H(8)	108.2
C(7)-C(8)-H(8)	108.2
C(18)-C(7)-C(6)	116.2(6)
C(18)-C(7)-C(8)	116.4(5)
C(6)-C(7)-C(8)	104.8(5)
C(18)-C(7)-H(7)	106.3

C(6)-C(7)-H(7)	106.3
C(8)-C(7)-H(7)	106.3
C(12)-C(10)-C(8)	121.4(6)
C(12)-C(10)-C(11)	118.2(7)
C(8)-C(10)-C(11)	120.4(6)
C(10)-C(11)-H(11A)	109.5
C(10)-C(11)-H(11B)	109.5
H(11A)-C(11)-H(11B)	109.5
C(10)-C(11)-H(11C)	109.5
H(11A)-C(11)-H(11C)	109.5
H(11B)-C(11)-H(11C)	109.5
C(10)-C(12)-C(13)	124.4(7)
C(10)-C(12)-H(12)	117.8
C(13)-C(12)-H(12)	117.8
C(12)-C(13)-C(14)	108.7(6)
C(12)-C(13)-C(17)	112.4(5)
C(14)-C(13)-C(17)	116.6(6)
C(12)-C(13)-H(13)	106.1
C(14)-C(13)-H(13)	106.1
C(17)-C(13)-H(13)	106.1
O(6)-C(14)-O(5)	116.6(7)
O(6)-C(14)-C(13)	120.5(7)
O(5)-C(14)-C(13)	122.9(6)
O(5)-C(15)-C(16)	110.1(6)
O(5)-C(15)-C(20)	107.5(6)
C(16)-C(15)-C(20)	117.1(6)
O(5)-C(15)-H(15)	107.2
C(16)-C(15)-H(15)	107.2
C(20)-C(15)-H(15)	107.2
C(15)-C(16)-C(17)	111.8(6)
C(15)-C(16)-H(16A)	109.2
C(17)-C(16)-H(16A)	109.2
C(15)-C(16)-H(16B)	109.2
C(17)-C(16)-H(16B)	109.2
H(16A)-C(16)-H(16B)	107.9
C(18)-C(17)-C(16)	115.2(6)
C(18)-C(17)-C(13)	111.6(5)
C(16)-C(17)-C(13)	108.3(6)

C(18)-C(17)-H(17)	107.1
C(16)-C(17)-H(17)	107.1
C(13)-C(17)-H(17)	107.1
C(19)-C(18)-C(17)	120.7(6)
C(19)-C(18)-C(7)	122.8(7)
C(17)-C(18)-C(7)	116.4(5)
C(18)-C(19)-H(19A)	120.0
C(18)-C(19)-H(19B)	120.0
H(19A)-C(19)-H(19B)	120.0
C(15)-C(20)-C(21)	113.7(6)
C(15)-C(20)-H(20A)	108.8
C(21)-C(20)-H(20A)	108.8
C(15)-C(20)-H(20B)	108.8
C(21)-C(20)-H(20B)	108.8
H(20A)-C(20)-H(20B)	107.7
C(20)-C(21)-H(21A)	109.5
C(20)-C(21)-H(21B)	109.5
H(21A)-C(21)-H(21B)	109.5
C(20)-C(21)-H(21C)	109.5
H(21A)-C(21)-H(21C)	109.5
H(21B)-C(21)-H(21C)	109.5

Symmetry transformations used to generate equivalent atoms:

Table S7: Anisotropic displacement parameters ($\approx^2$x 10^3) for compound **3**. 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(3)	38(2)	15(3)	38(4)	0(2)	1(2)	-4(2)
C(3)	40(3)	23(5)	35(6)	-4(4)	1(3)	0(3)
O(1)	38(2)	22(3)	40(4)	2(2)	5(2)	-1(2)
C(1)	37(3)	16(4)	28(5)	-1(3)	1(3)	7(2)
O(2)	40(2)	10(3)	49(4)	-1(2)	0(2)	0(2)
C(2)	42(3)	16(5)	33(5)	1(3)	1(3)	2(3)
O(4)	48(2)	26(4)	44(4)	2(3)	-10(2)	-9(2)
C(4)	36(3)	18(5)	39(6)	-1(3)	1(3)	0(3)
O(5)	50(3)	14(3)	38(4)	-2(2)	7(2)	0(2)
C(5)	35(3)	14(5)	36(5)	-2(3)	-2(3)	-2(3)
O(6)	57(3)	22(4)	41(4)	5(3)	13(2)	-2(2)
C(6)	31(3)	14(5)	34(5)	2(3)	1(3)	-2(2)
C(9)	32(3)	10(4)	38(5)	4(3)	2(3)	-3(2)
C(8)	34(3)	10(5)	32(5)	1(3)	0(3)	0(2)
C(7)	35(3)	11(4)	30(5)	7(3)	-1(3)	-2(2)
C(10)	38(3)	8(5)	39(5)	-1(3)	1(3)	-1(2)
C(11)	46(4)	24(5)	34(6)	0(4)	-6(3)	5(3)
C(12)	40(3)	16(5)	35(5)	2(3)	-2(3)	-4(2)
C(13)	35(3)	19(5)	32(5)	1(3)	1(3)	-3(2)
C(14)	37(3)	20(5)	36(6)	0(4)	0(3)	-1(3)
C(15)	46(3)	8(4)	33(5)	1(3)	4(3)	3(2)
C(16)	34(3)	17(4)	37(5)	-2(3)	-1(3)	2(3)
C(17)	31(3)	20(4)	32(5)	-1(3)	-1(3)	-1(3)
C(18)	34(3)	8(4)	39(5)	0(3)	-1(3)	-2(2)
C(19)	46(3)	16(5)	36(6)	-3(3)	0(3)	6(3)
C(20)	49(4)	18(5)	38(6)	-4(4)	-5(3)	2(3)
C(21)	68(5)	26(6)	47(6)	-7(4)	-11(4)	6(3)

Table S8: Hydrogen coordinates (x 10^4) and isotropic displacement parameters (≈^{2}x 10 ^{3}) for compound **3**.

	x	y	z	U(eq)
H(3)	1668	6167	6899	39
H(2)	2490(130)	7500(30)	4900(40)	49
H(2A)	4274	4619	6569	36
H(2AB)	2026	4737	7037	36
H(4)	5940(80)	5960(60)	7030(40)	59
H(4A)	2314	6911	6053	38
H(4AB)	168	6155	5973	38
H(5)	5583	6053	5627	34
H(6)	5028	4621	5661	32
H(9)	982	6242	4938	32
H(8)	6162	5699	4572	31
H(7)	1603	4602	4736	30
H(11A)	2043	6978	3871	52
H(11B)	-325	6325	4024	52
H(11C)	862	6344	3400	52
H(12)	3682	5294	3180	36
H(13)	7681	4704	3873	34
H(15)	6849	2111	3179	35
H(16A)	8136	2875	3969	35
H(16B)	5386	2383	4084	35
H(17)	3022	3676	3934	33
H(19A)	7433	2961	4866	39
H(19B)	6607	3609	5388	39
H(20A)	2422	3210	2983	42
H(20B)	2038	2296	3294	42
H(21A)	4368	2396	2200	71
H(21B)	1244	2256	2285	71
H(21C)	3296	1535	2501	71

References

[1] a) H.-J. Schiewe, Dissertation thesis, Georg-August-Universität Göttingen **1997**, ISBN: 3-932325-30-3;
b) J.-N. Fricke, Dissertation thesis, Eberhard Karls Universität Tübingen (Tübingen), **2012**, http://hdl.handle.net/10900/49954;
c) L. Hoffmann, Dissertation thesis, Georg-August-Universität zu Göttingen **2006**, http://hdl.handle.net/11858/00-1735-0000-0006-AEA6-0;
d) D. Vollmar, Dissertation thesis, Georg-August-Universität zu Göttingen **2010**, http://hdl.handle.net/11858/00-1735-0000-0006-B07C-3.
[2] Y. Kwon, J. Shin, K. Nam, J. S. An, S. H. Yang, S. H. Hong, M. Bae, K. Moon, Y. Cho, J. Woo, K. Park, K. Kim, J. Shin, B. Y. Kim, Y. Kim, D. C. Oh, *Angew Chem Int Ed Engl* **2020**, *59*, 22994-22998.
[3] C. R. McIntyre, F. E. Scott, T. J. Simpson, L. A. Trimble, J. C. Vederas, *Tetrahedron* **1989**, *45*, 2307-2321.
[4] T. R. Hoye, C. S. Jeffrey, F. Shao, *Nat. Protoc.* **2007**, *2*, 2451.
[5] P. Chiu, Z. Li, K. C. M. Fung, *Tetrahedron Letters* **2003**, *44*, 455-457.
[6] T. Kieser, M. J. Bibb, M. J. Buttner, K. F. Chater, D. A. Hopwood, *Practical Streptomyces genetics: A Laboratory Manual*, The John Innes Foundation, Norwich, **2000**.
[7] K. Blin, L. E. Pedersen, T. Weber, S. Y. Lee, *Synth Syst Biotechnol* **2016**, *1*, 118-121.
[8] Y. Tong, C. M. Whitford, H. L. Robertsen, K. Blin, T. S. Jørgensen, A. K. Klitgaard, T. Gren, X. Jiang, T. Weber, S. Y. Lee, *Proc. Natl. Acad. Sci. USA* **2019**, *116*, 20366-20375.
[9] S. Zotchev, K. Haugan, O. Sekurova, H. Sletta, T. E. Ellingsen, S. Valla, *Microbiology (Reading)* **2000**, *146 (Pt 3)*, 611-619.
[10] M. Bierman, R. Logan, K. O'Brien, E. T. Seno, R. N. Rao, B. E. Schoner, *Gene* **1992**, *116*, 43-49.
[11] V. Roukos, G. Pegoraro, T. C. Voss, T. Misteli, *Nat. Protoc.* **2015**, *10*, 334-348.
[12] C. McQuin, A. Goodman, V. Chernyshev, L. Kamentsky, B. A. Cimini, K. W. Karhohs, M. Doan, L. Ding, S. M. Rafelski, D. Thirstrup, W. Wiegraebe, S. Singh, T. Becker, J. C. Caicedo, A. E. Carpenter, *PLoS Biol.* **2018**, *16*, e2005970.
[13] D. Kim, G. H. Bae, H. Y. Kim, H. Jeon, K. Kim, J. Shin, S. Lee, S. Hong, I. Kim, Y. Kim, *ACS Chem. Neurosci.* **2021**, *12*, 99-108.
[14] W. B. Stine, L. Jungbauer, C. Yu, M. J. LaDu, *Methods Mol. Biol.* **2011**, *670*, 13-32.
[15] H. Y. Kim, H. V. Kim, S. Jo, C. J. Lee, S. Y. Choi, D. J. Kim, Y. Kim, *Nature communications* **2015**, *6*, 8997-8997.
[16] M. Sevvana, M. Ruf, I. Usón, G. M. Sheldrick, R. Herbst-Irmer, *Acta Crystallogr D Struct Biol* **2019**, *75*, 1040-1050.

Author Contributions

Julian C. Schmid optimized production and isolation procedures, developed and performed synthesis and purification, performed cell viability assays on L929 cell line and fluorescence microscopy on PtK2 cell line, performed cell free assays, designed and coordinated the study, analyzed NMR data and wrote the initial manuscript.
Kerstin Frey established protocols for immunostaining of Ptk2 cell line and fluorescence microscopy and supervised cell culture experiments on L929.
Matthias Scheiner performed neuroprotection and neurotoxicity assays on HT22 cell line and edited the manuscript.
Jaime Felipe Guerrero Garzón performed strain sequencing and genetic engineering of the strain and edited the manuscript.
Luise Stafforst performed crystallization and $^{18}O_2$ feeding experiments.
Jan-Niklas Fricke performed structure elucidation and chemical derivatization.
Michaela Schuppe isolated and purified collinolactone and supported cell culture experiments on L929 cell line.
Hajo Schiewe performed initial isolation and structure elucidation.
Axel Zeeck supervised the initial studies and acquired funding.
Tilmann Weber supervised sequencing and genetic engineering and acquired funding.
Isabel Usón performed x-ray crystallography refinements and analysis.
Ralf Kemkemer supervised cell culture experiments on L929 and PtK2 cell lines, fluorescence microscopy and acquired funding.
Michael Decker supervised cell culture experiments on HT22 cell line and acquired funding.
Stephanie Grond coordinated the study, supervised experiments, and acquired funding.
All authors contributed by analyzing and discussing data and commenting on the manuscript.