Supporting Information for

Thiohydantoin and Hydantoin Derivatives from the Roots of *Armoracia rusticana* and Their Neurotrophic and Anti-neuroinflammatory Activities

Tae Hyun Lee,[†] Zahra Khan,[‡,§] Sun Yeou Kim,[‡,§] and Kang Ro Lee[*,†]

[†]Natural Products Laboratory, School of Pharmacy, Sungkyunkwan University, Suwon 16419, Republic of Korea

[‡]Gachon Institute of Pharmaceutical Science, Gachon University, Incheon 21936, Republic of Korea

[§]College of Pharmacy, Gachon University, #191, Hambakmoero, Yeonsu-gu, Incheon 21936, Republic of Korea

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S1. General Experimental Procedures

Optical rotations were measured on a JASCO P-2000 polarimeter (JASCO, Easton, MD, USA). Ultraviolet (UV) spectra were obtained utilizing a Shimadzu UV-1601 UV visible spectrophotometer (Shimadzu, Tokyo, Japan). CD spectra were acquired on a JASCO J-1500 CD spectrometer (JASCO, Easton, MD, USA). Infrared (IR) spectra were garnered using a JASCO Fourier Transform Infrared (FT/IR)-4600 spectrometer (JASCO, Easton, MD, USA). The NMR spectra (^{1}H, ^{13}C, ^{1}H-^{1}H COSY, HSQC, and HMBC) were obtained using a Bruker AVANCE III 700 MNR spectrometer at 700 MHz (^{1}H) and 175 MHz (^{13}C) (Bruker, Karlsruhe, Germany). The HRESIMS data were recorded on an Agilent 1290 Infinity LC systems (Agilent, Sant Clara, CA, USA) coupled with an Agilent G6550A Accurate-Mass Q-TOF (Agilent, Sant Clara, CA, USA). LC/MS analysis was performed with an Agilent 1200 Series HPLC embedded with a diode array detector and 6130 Series ESIMS spectrometer utilizing an analytical Kinetex C_{18} 100 Å column (Phenomenex, Torrance, CA, USA). Semipreparative high performance liquid chromatography (HPLC) was carried out using a Gilson 306 pump connected to a Shodex refractive index detector, which was equipped with an INNO column ODS(N) 120 Å (Young Jin Biochrom Co., Ltd., Seongnam-City, Kyonggi-do, Republic of Korea). Chiral-phase HPLC was conducted using a Phenomenex Lux® 5 µm Cellulose-1 column (Phenomenex, Torrance, CA, USA). Low-pressure liquid chromatography (LPLC) was subjected over a LiChroprep Lobar-A Si 60 (240 x 10 mm) column equipped with an FMI QSY-0 pump (Teledyne Isco, Lincoln, NE, USA). Open columns packed with normal-phase silica gel 60 (70-230 and 230-400 mesh; Merck, Darmstadt, Germany) or reversed-phase (RP)-C_{18} silica gel (230-400 mesh, Merck, Germany) were implemented. Thin layer chromatography (TLC) was practiced using both pre-coated normal-phase silica gel F_{254} plates and reversed-phase (RP)-C_{18} F_{254s} plates. Spots were detected under UV light or by heating after spraying with anisaldehyde-sulfuric acid on the TLC.

Table S1. NGF secretion and inhibitory effects on NO production of *A. rusticana*.

	NGF Secretion [a]	**Cell Viability (%)**[b]
80% MeOH ext.	148.29 ± 0.83	108.49 ± 1.53
Hexane Layer	35.2 ± 1.13	104.72 ± 3.82
$CHCl_3$ Layer	44.19 ± 0.19	47.17 ± 3.31
EtOAc Layer	104.66 ± 7.72	73.63 ± 2.39
BuOH Layer	138.24 ± 1.67	112.12 ± 0.55

[a]C6 cells were treated with 100 µg/ml of extracts. After 24 h, the content of NGF secretion in C6-conditioned media was measured by ELISA. The level of secreted NGF cells is expressed as percentage of the untreated control. The data shown represent the means ± SD of three independent experiments performed in triplicate; [b]Cell viability after treatment with 100 µg/ml of each extract was determined by MTT assay and is expressed in percentage (%). The results are averages of three independent experiments, and the data are expressed as mean ± SD

	IC_{50} (μM)[a]	**Cell Viability (%)**[b]
80% MeOH ext.	65.04	158.35±3.31
Hexane Layer	50.5	66.43±6.98
$CHCl_3$ Layer	27.79	72.07±3.68
EtOAc Layer	17.06	110.51±96
BuOH Layer	80.4	125.12±21.14

[a]IC_{50} value of each extract was defined as the concentration (µg/ml) that caused 50% inhibition of NO production in LPS-activated BV-2 cells; [b]Cell viability after treatment with 100 µg/ml of each extract was determined by MTT assay and is expressed in percentage (%). The results are averages of three independent experiments, and the data are expressed as mean ± SD.

Figure S1. The ECD spectrum data of **1**, **2**, **3**, and **4**.

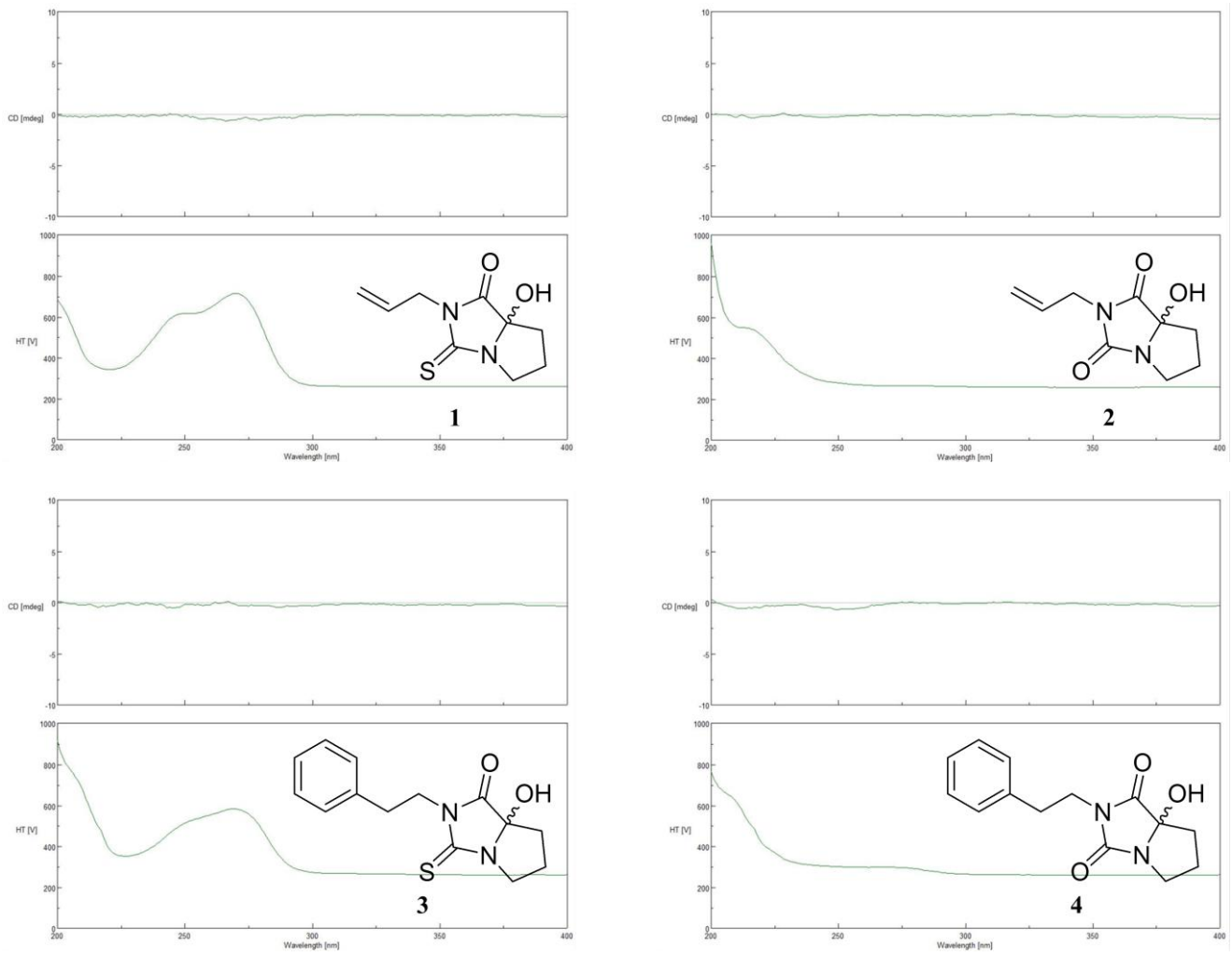

Figure S2. The chiral-phase HPLC chromatography of **1**, **2**, **3**, and **4**.

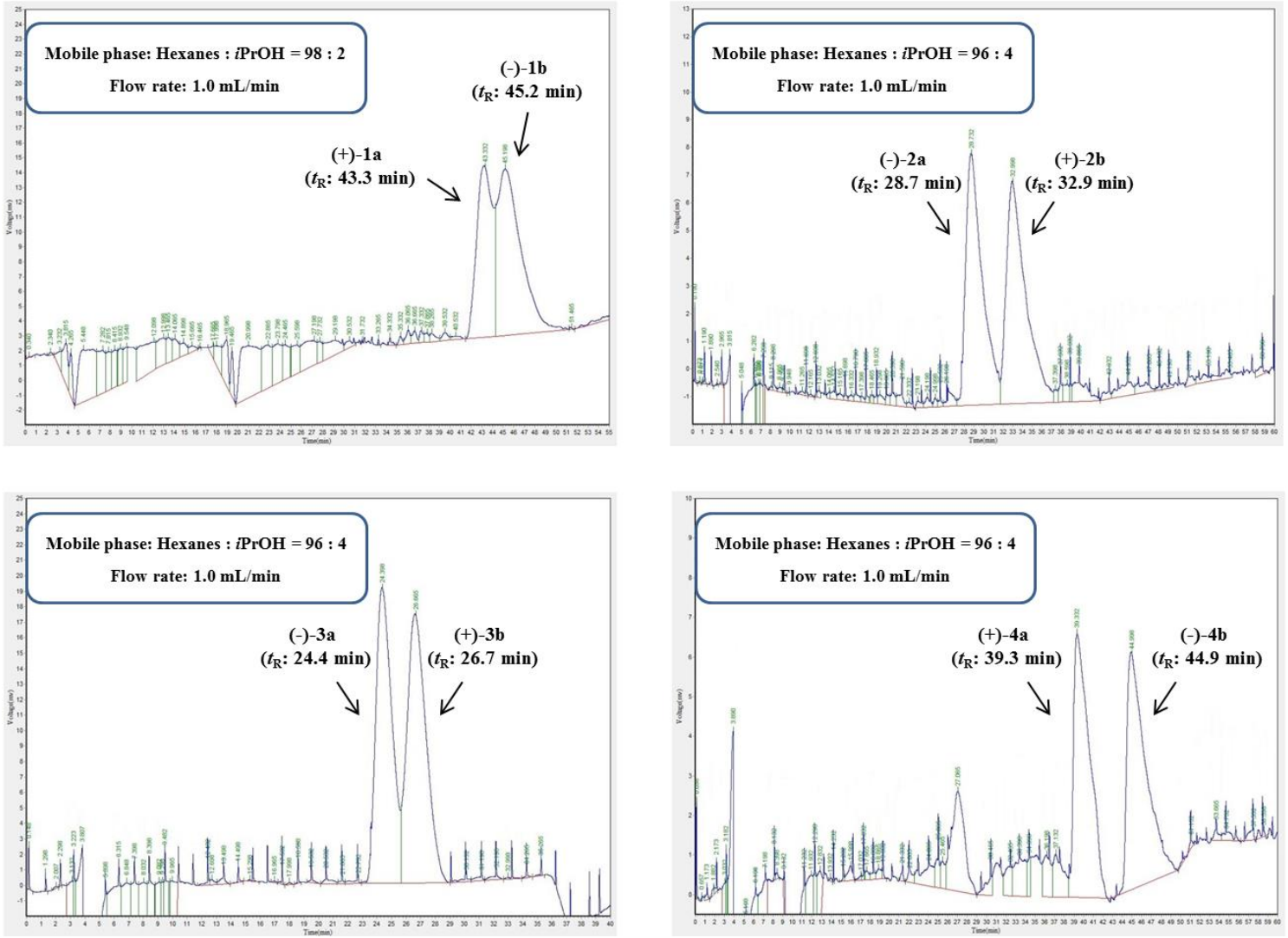

Figure S3. The ECD data analysis of **1a** and **1b**.

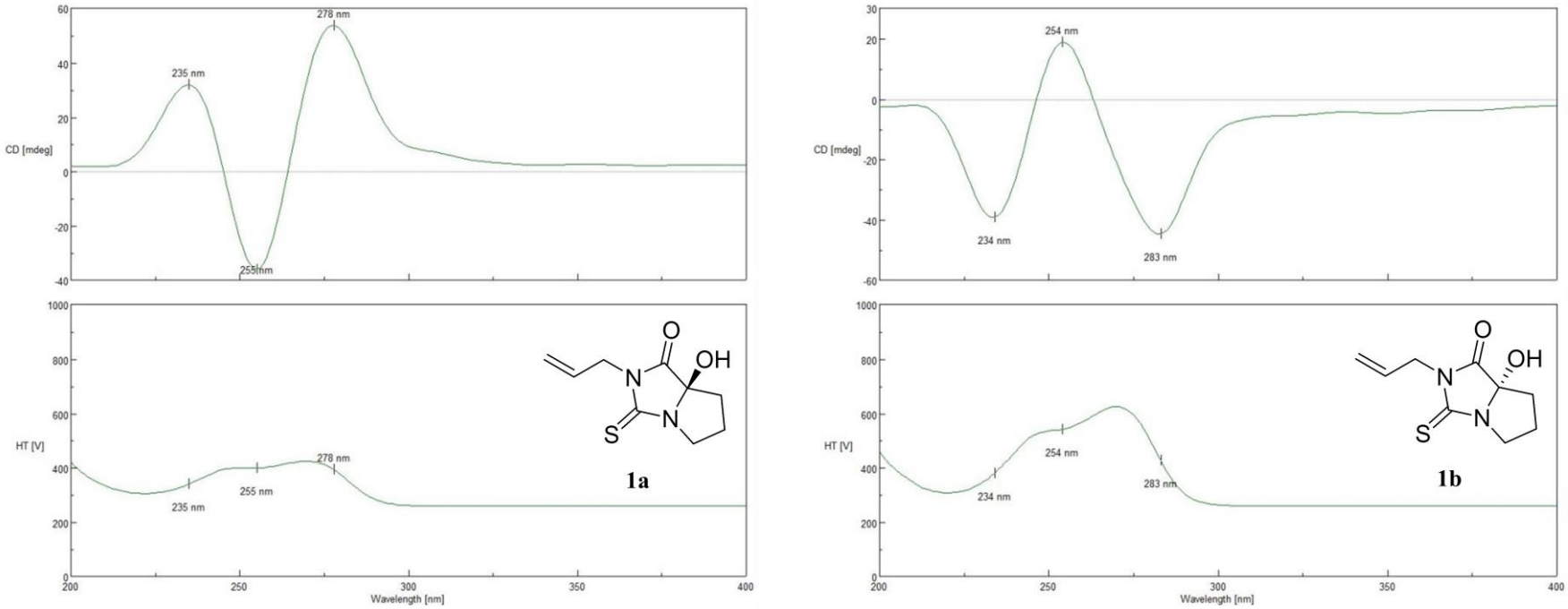

Figure S4. The ECD data analysis of **2a** and **2b**.

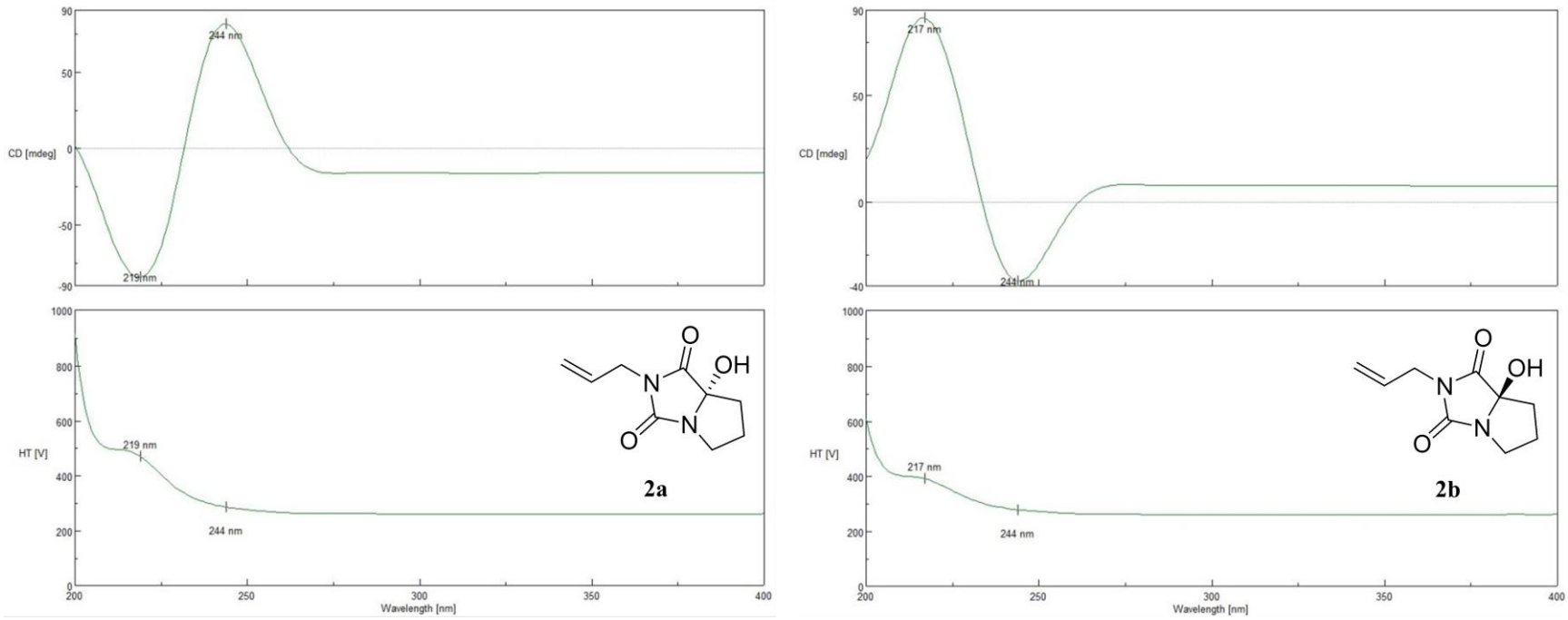

Figure S5. The ECD data analysis of **3a** and **3b**.

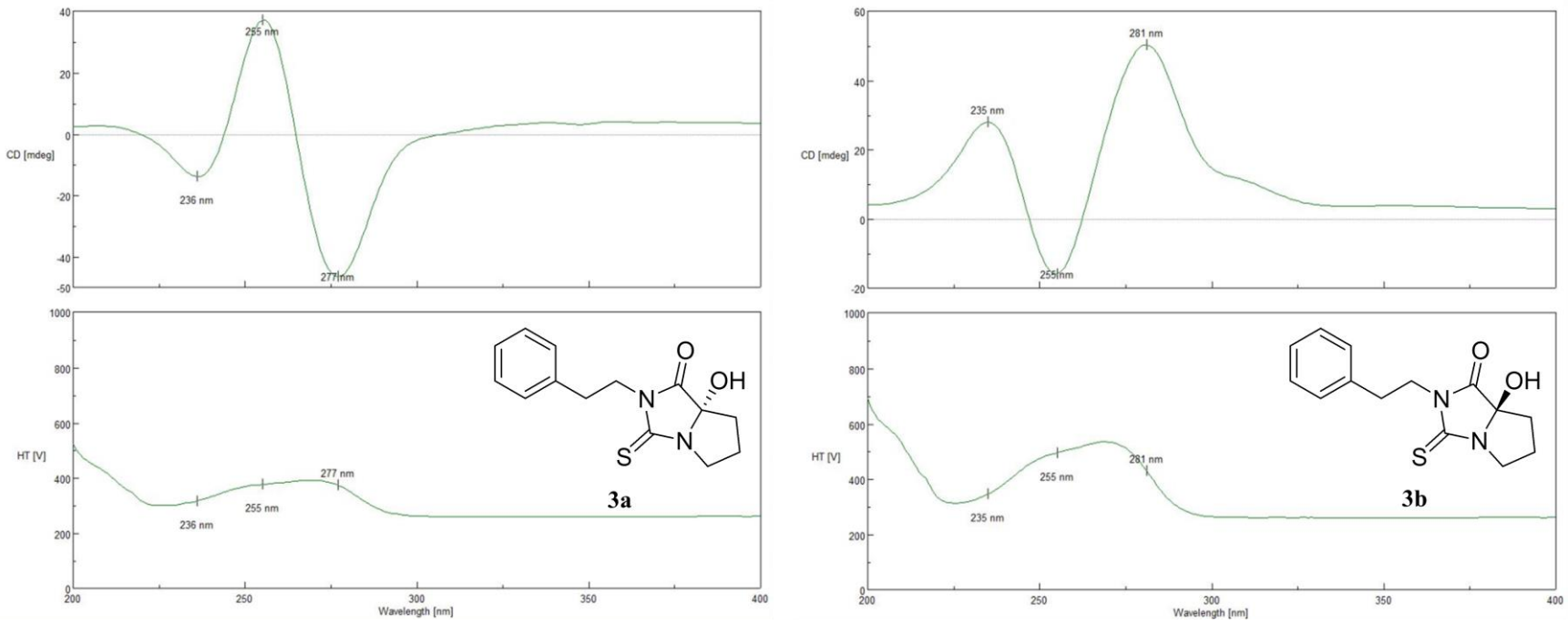

Figure S6. The ECD data analysis of **4a** and **4b**.

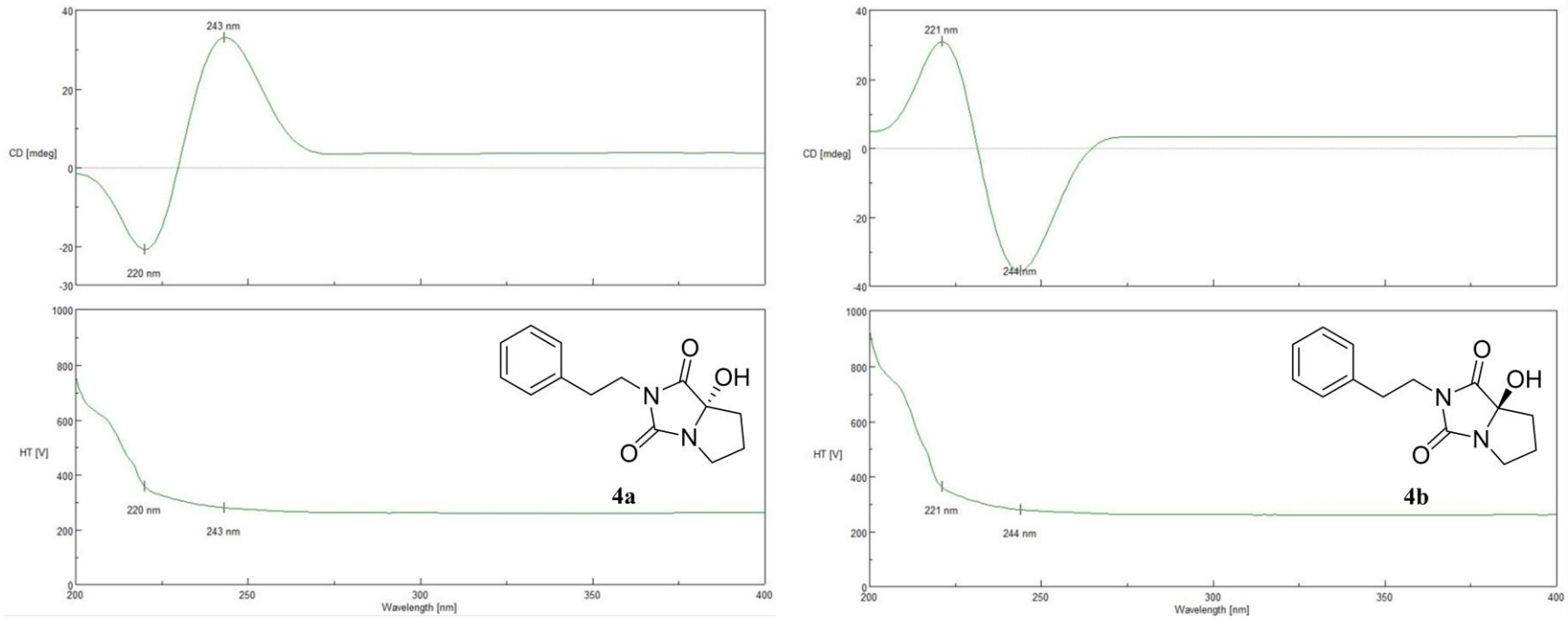

Figure S7. The ECD data analysis of **5**.

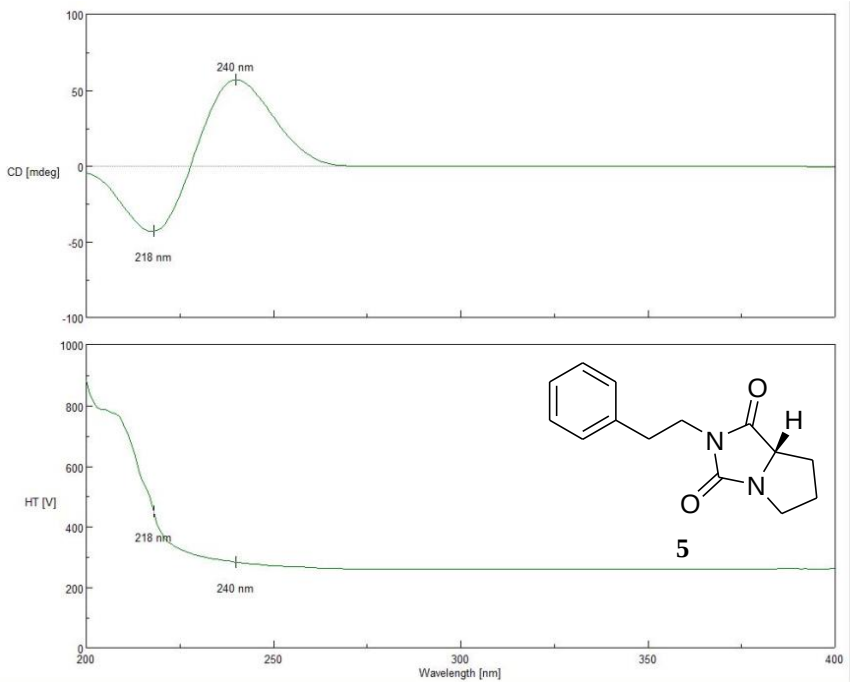

Figure S8. The HRESIMS spectrum of **1**.

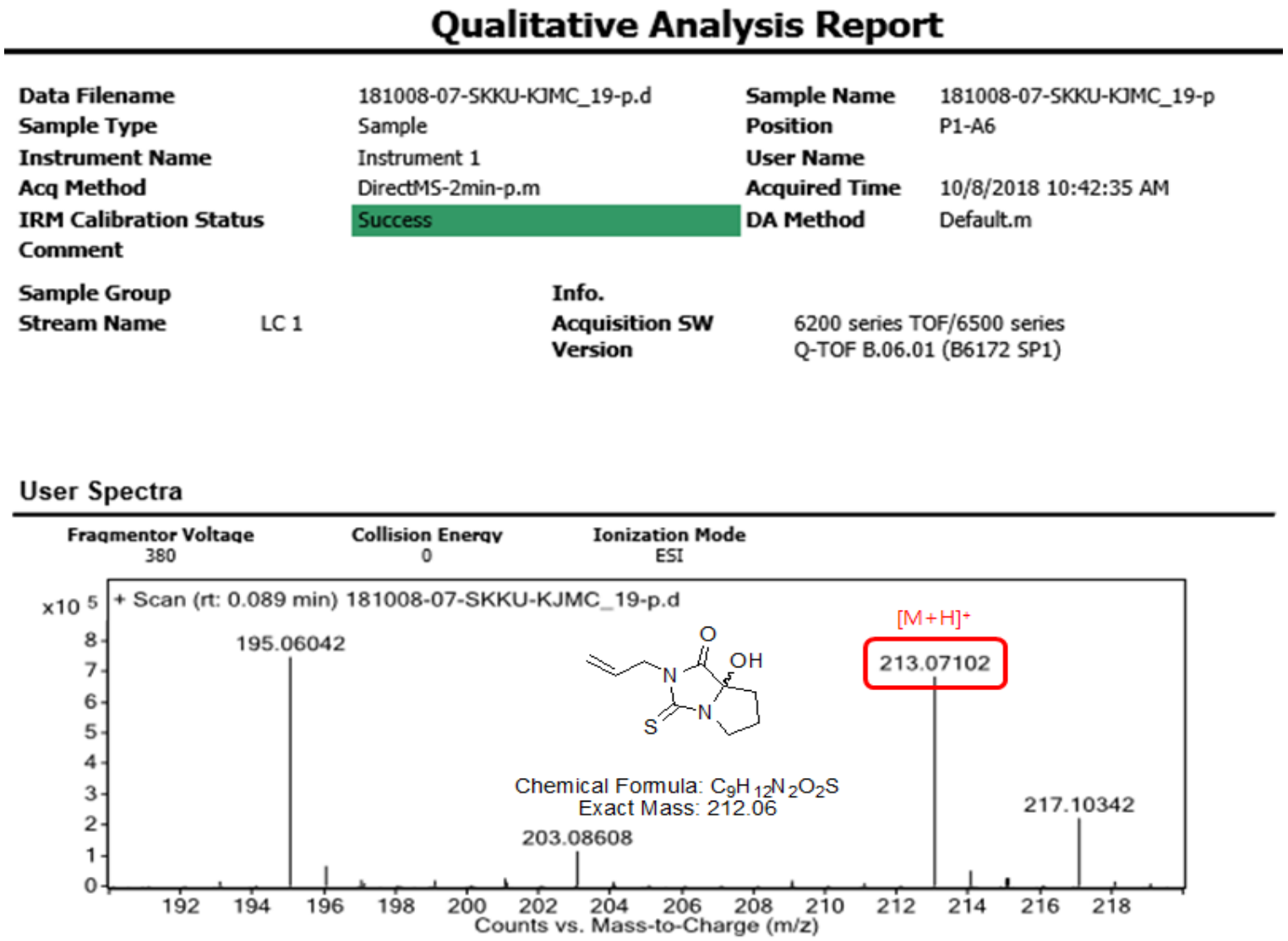

Figure S9. The ^{1}H NMR spectrum of **1** in chloroform-*d*.

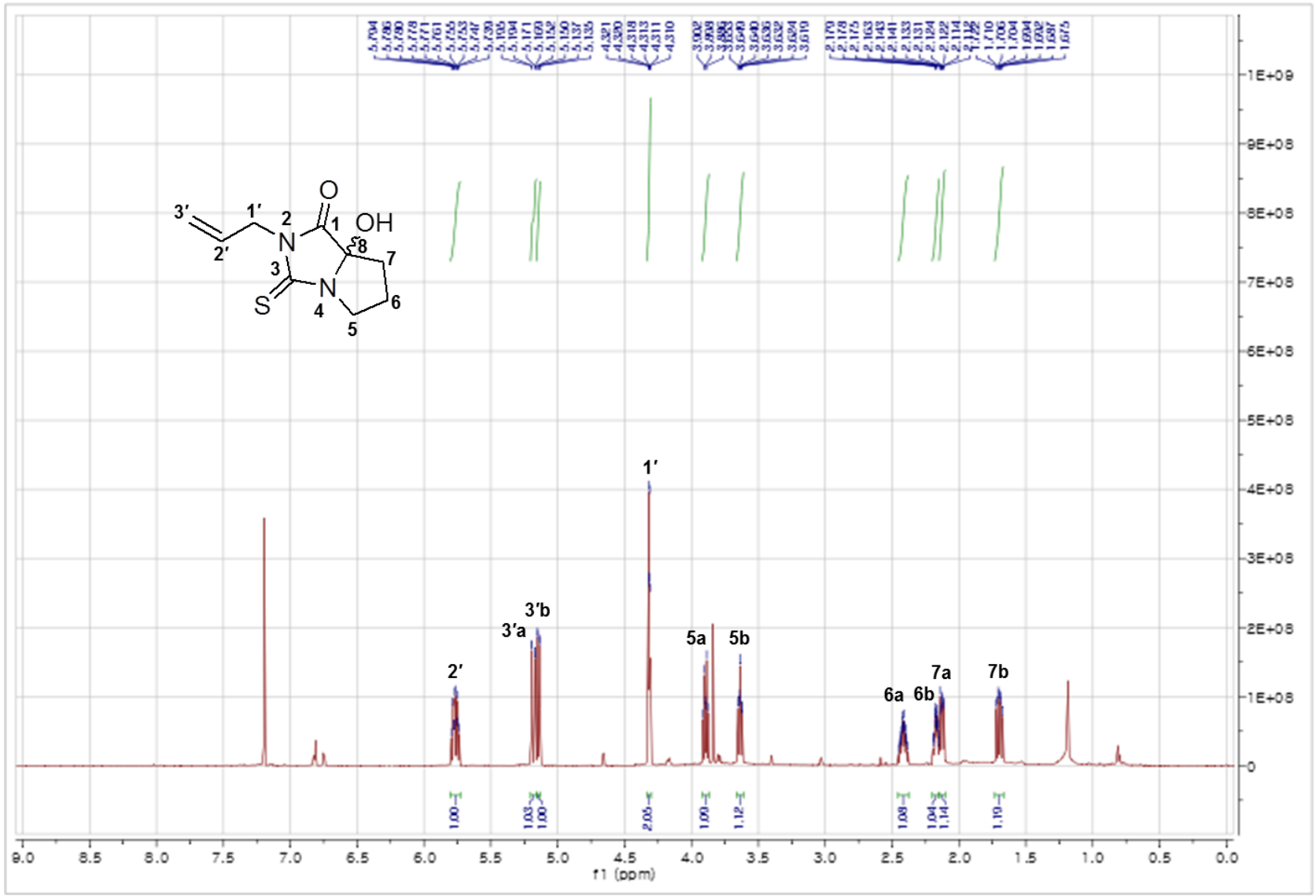

Figure S10. The ^{13}C NMR spectrum of **1** in chloroform-*d*.

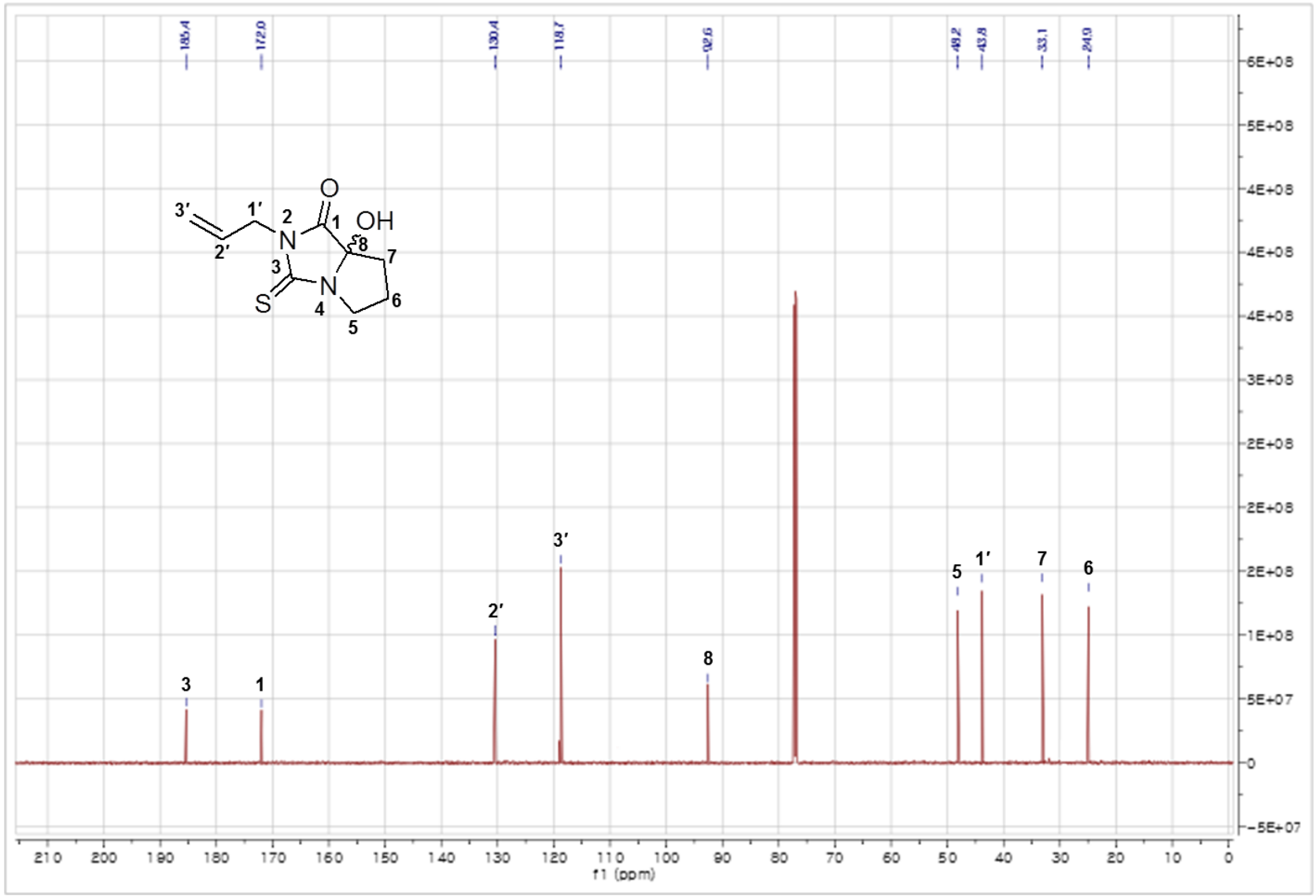

Figure S11. The COSY spectrum of **1** in chloroform-*d*.

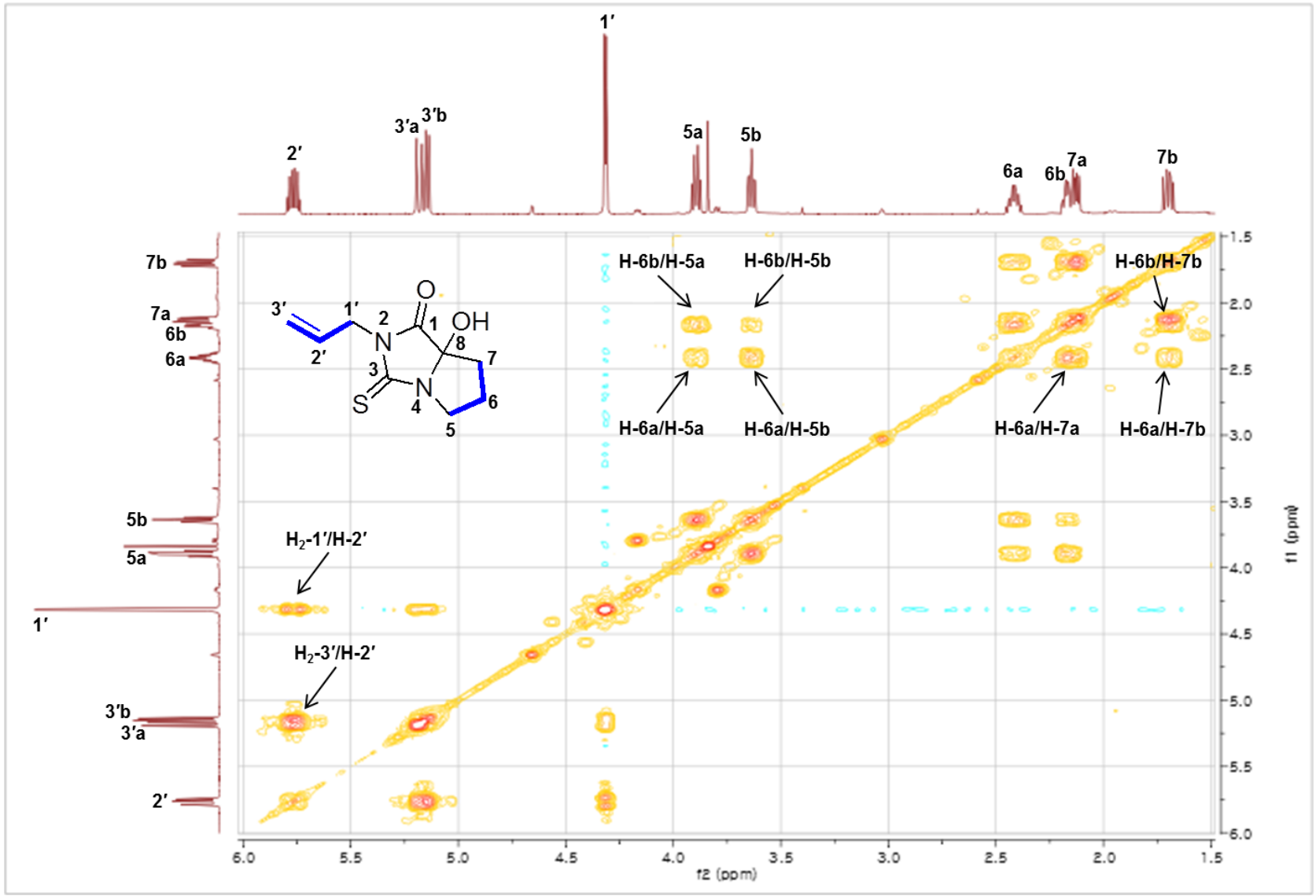

Figure S12. The HSQC spectrum of **1** in chloroform-*d*.

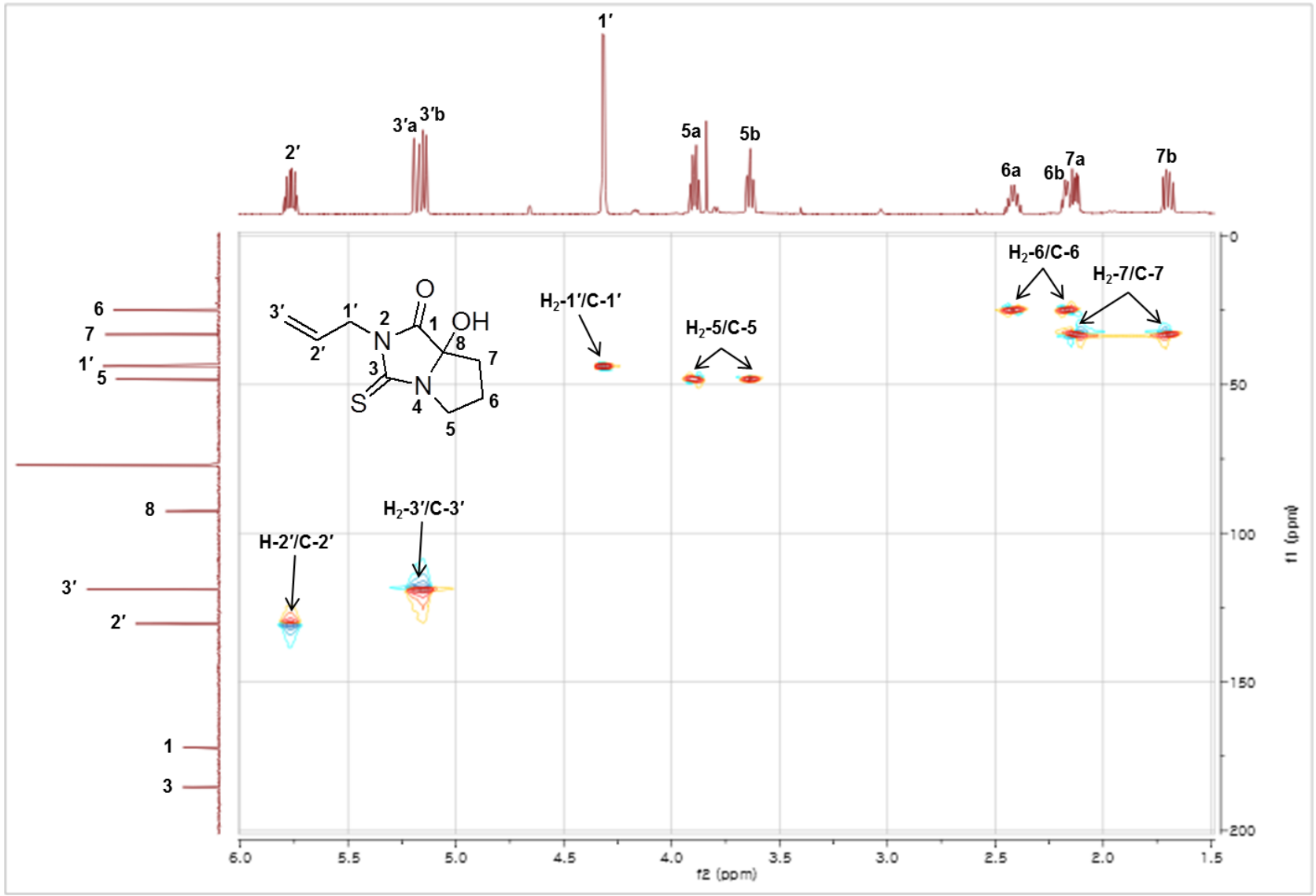

Figure S13. The HMBC spectrum of **1** in chloroform-*d*.

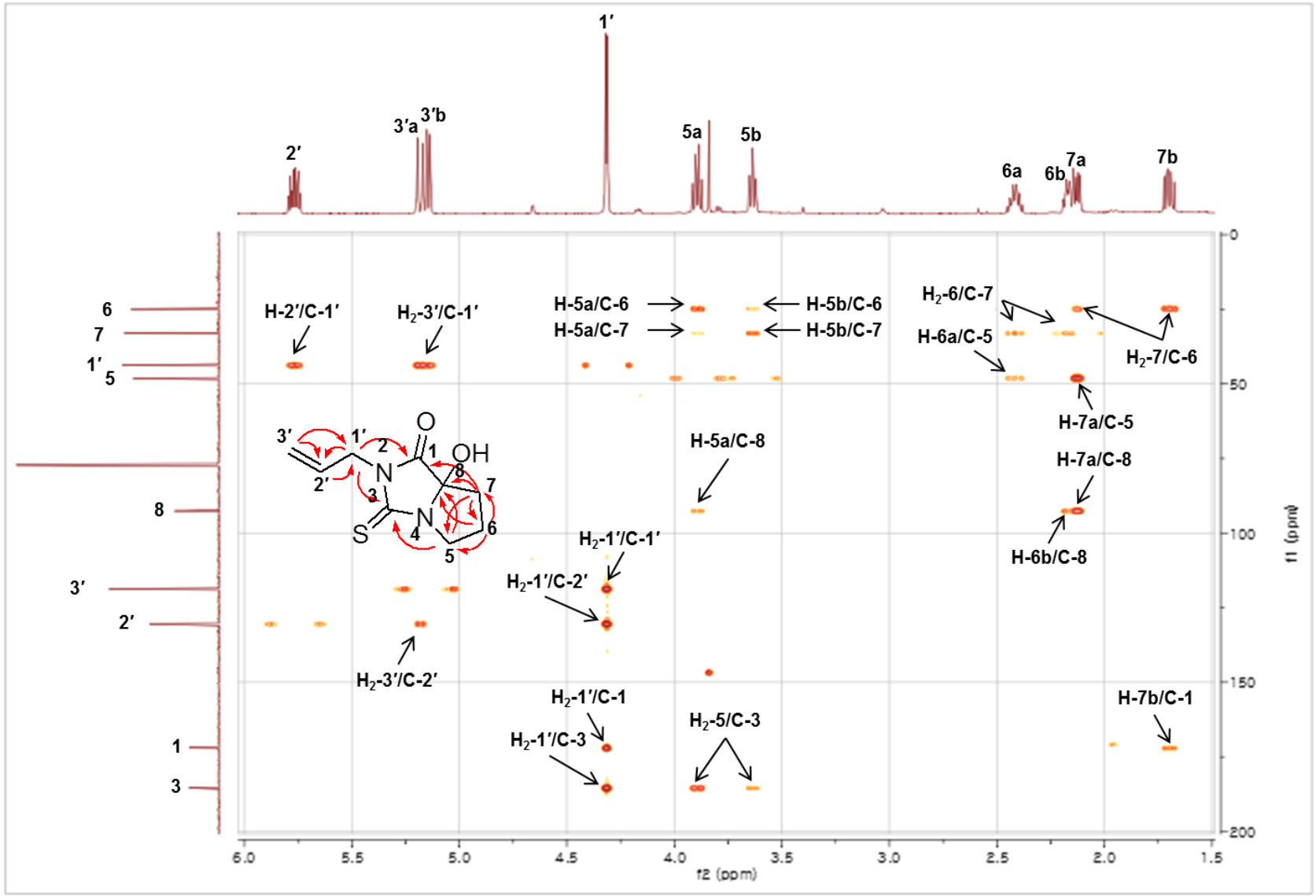

Figure S14. The HRESIMS spectrum of **2**.

Qualitative Compound Report

Data File	181008-08-SKKU-KJMC_22-p.d	**Sample Name**	181008-08-SKKU-KJMC_22-p
Sample Type	Sample	**Position**	P1-A7
Instrument Name	Instrument 1	**User Name**	
Acq Method	DirectMS-2min-p.m	**Acquired Time**	10/8/2018 10:45:22 AM
IRM Calibration Status	Success	**DA Method**	Default.m
Comment			
Sample Group		**Info.**	
Stream Name	LC 1	**Acquisition SW Version**	6200 series TOF/6500 series Q-TOF B.06.01 (B6172 SP1)

Compound Table

Compound Label	RT	Mass	Abund	Formula	Tgt Mass	Diff (ppm)
Cpd 1: 0.087	0.087	196.08549	56924	C9 H12 N2 O3	196.08479	3.53

Compound Label	m/z	RT	Algorithm	Mass
Cpd 1: 0.087	197.09273	0.087	Find By Formula	196.08549

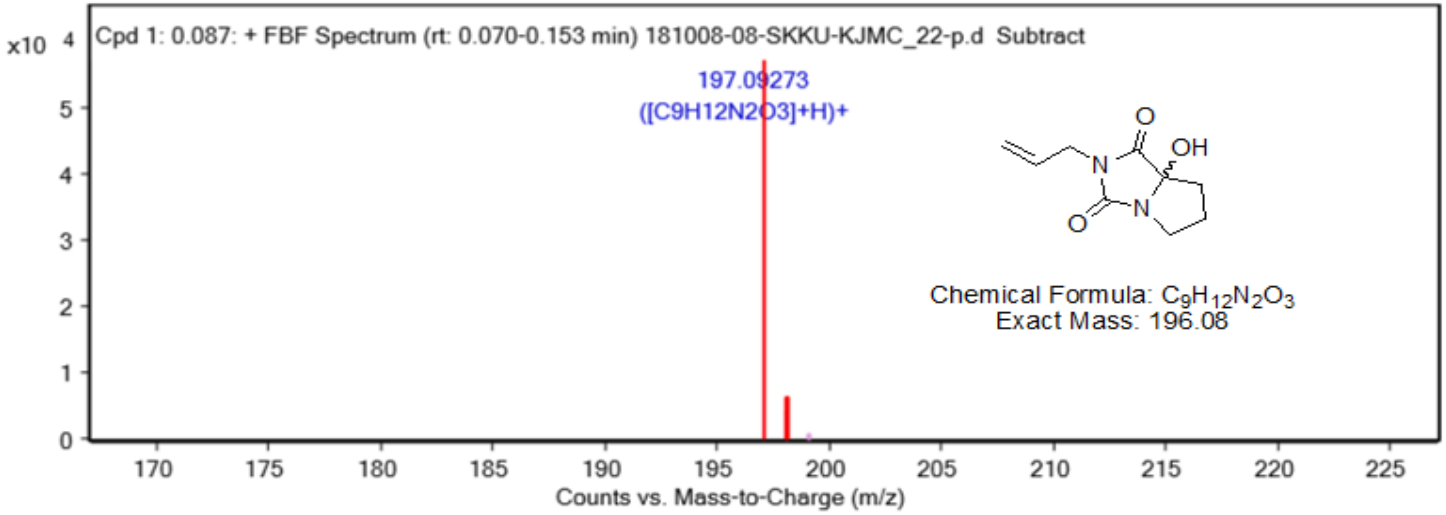

Figure S15. The ^{1}H NMR spectrum of **2** in chloroform-*d*.

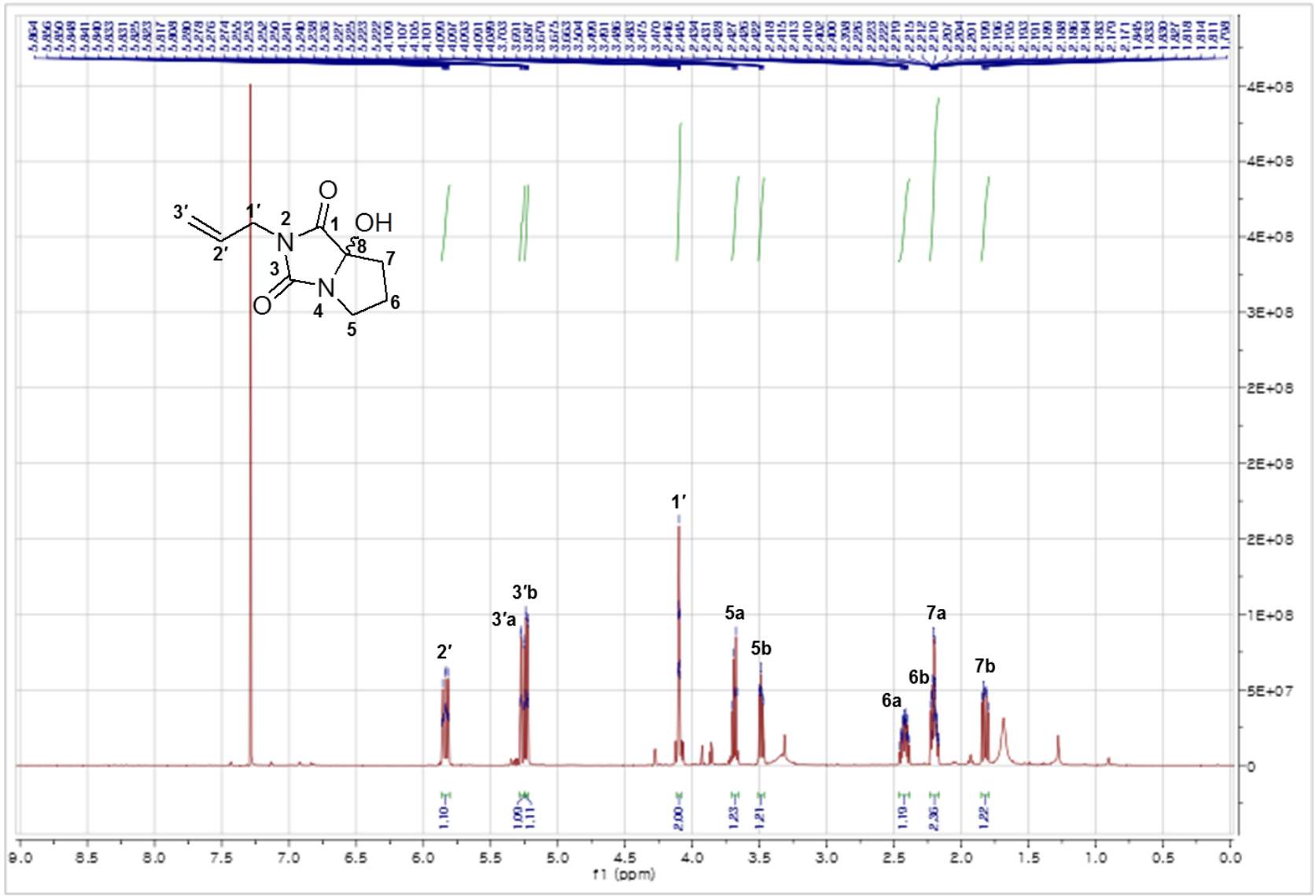

Figure S16. The ^{13}C NMR spectrum of **2** in chloroform-*d*.

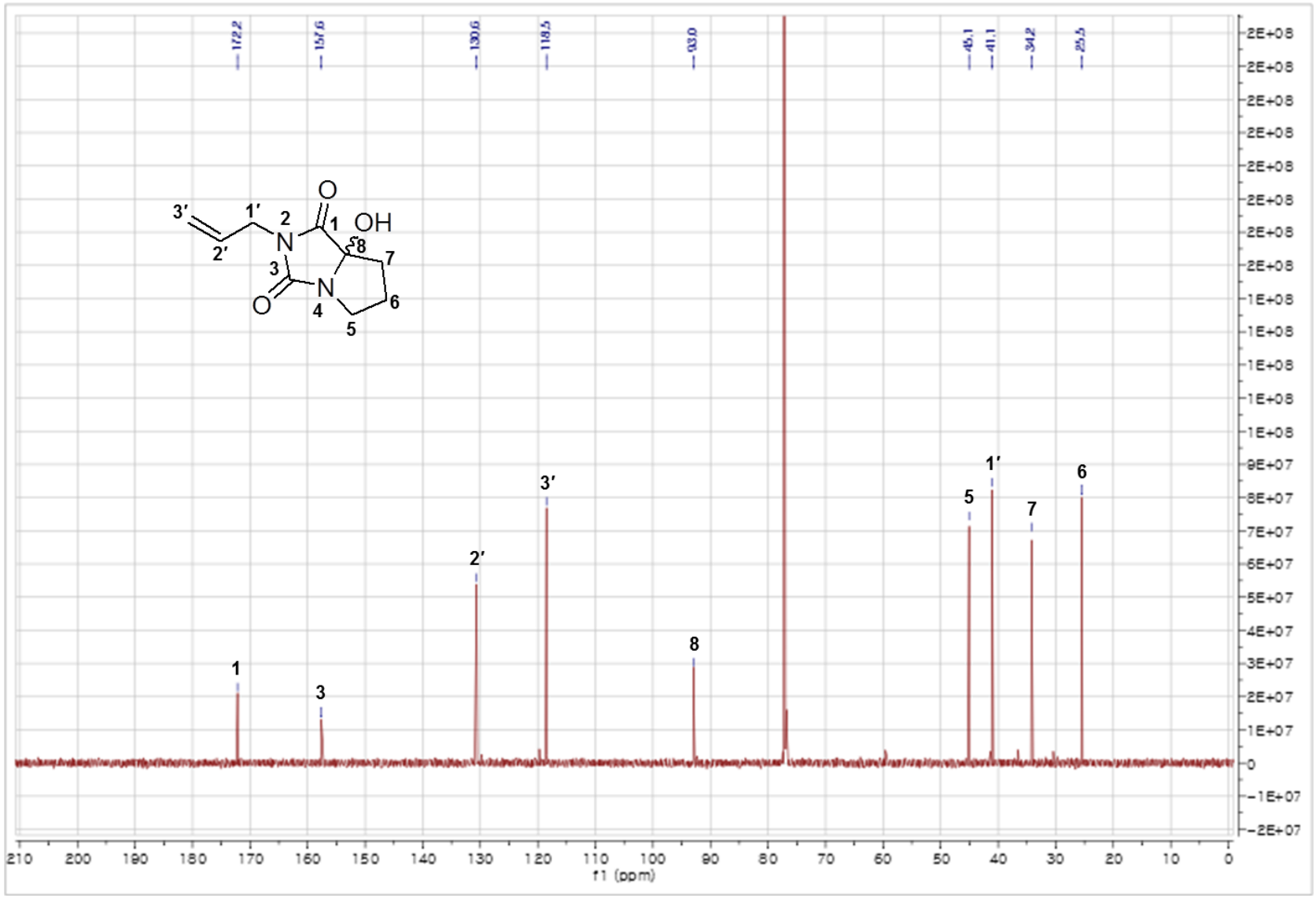

Figure S17. The COSY spectrum of **2** in chloroform-*d*.

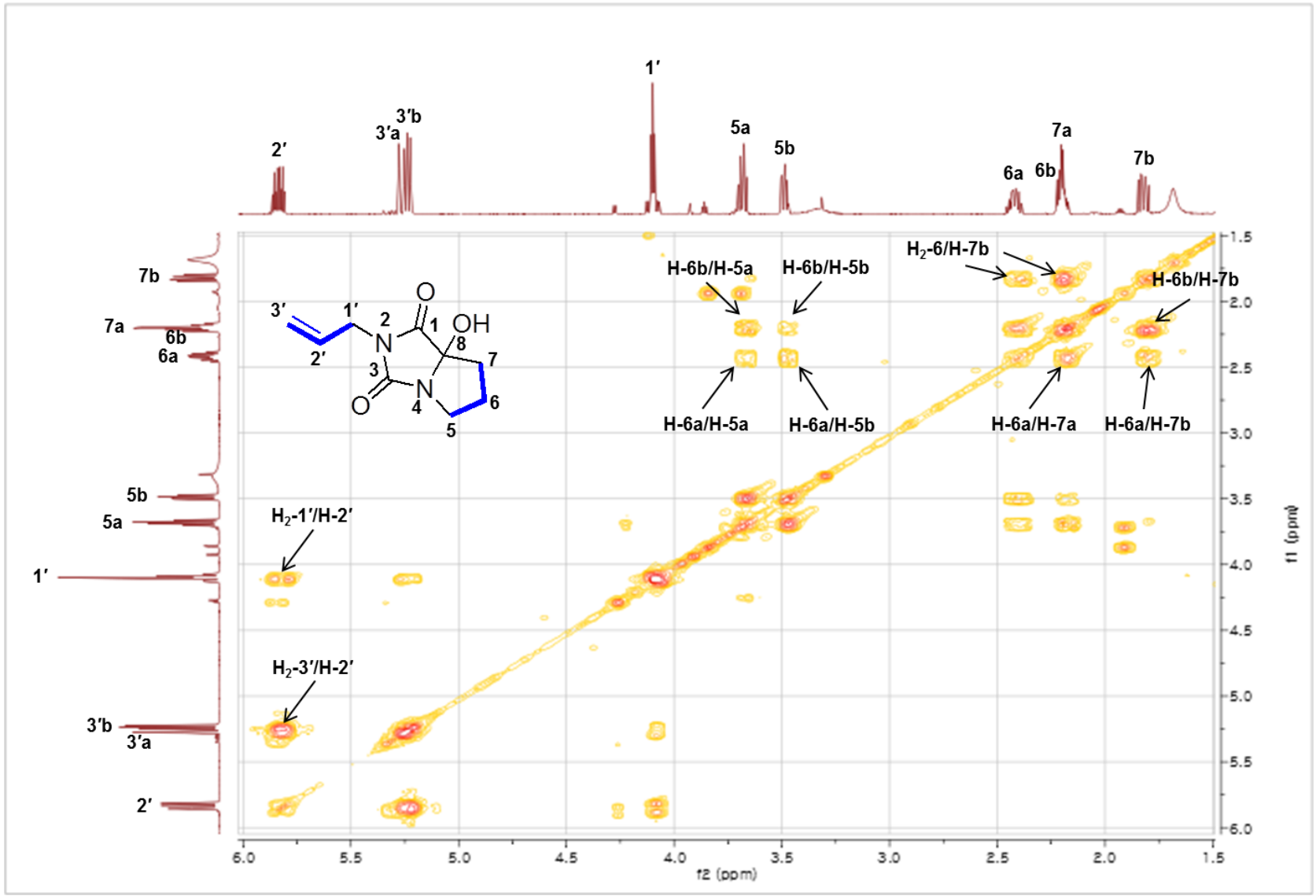

Figure S18. The HSQC spectrum of **2** in chloroform-*d*.

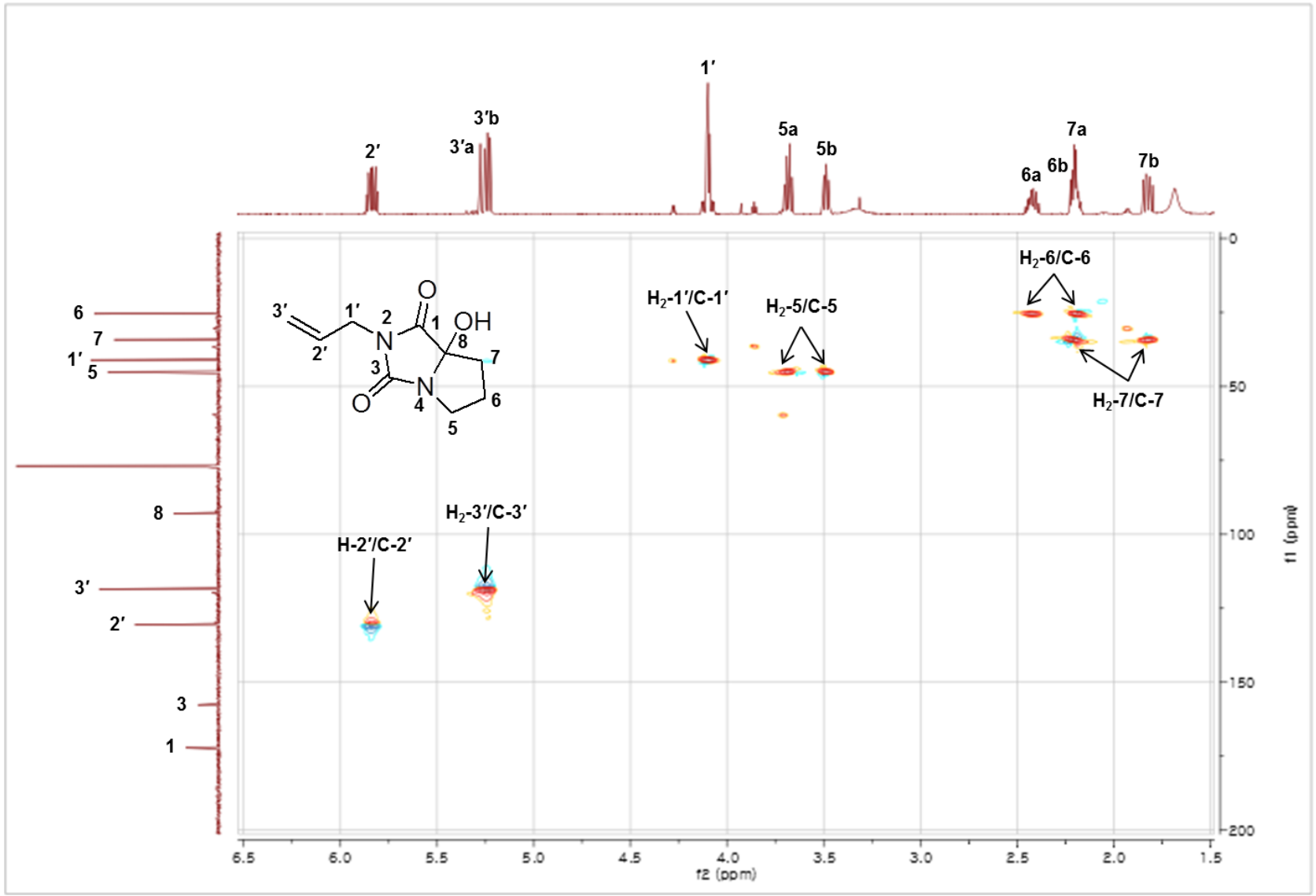

Figure S19. The HMBC spectrum of **2** in chloroform-*d*.

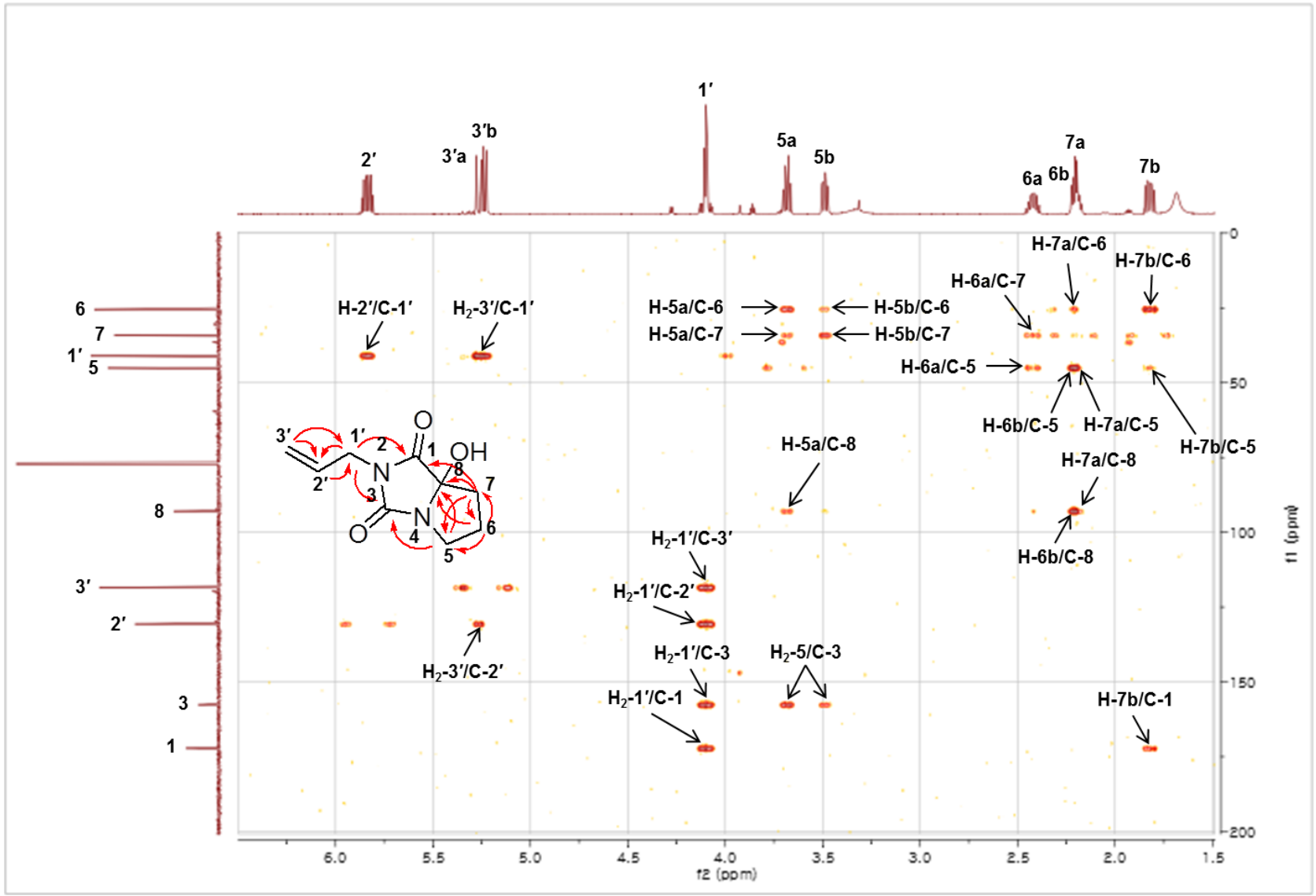

Figure S20. The HRESIMS spectrum of **3**.

Qualitative Compound Report

Data File	181008-09-SKKU-KJMC_11-p.d	**Sample Name**	181008-09-SKKU-KJMC_11-p
Sample Type	Sample	**Position**	P1-A8
Instrument Name	Instrument 1	**User Name**	
Acq Method	DirectMS-2min-p.m	**Acquired Time**	10/8/2018 10:48:09 AM
IRM Calibration Status	Success	**DA Method**	Default.m
Comment			
Sample Group		**Info.**	
Stream Name	LC 1	**Acquisition SW Version**	6200 series TOF/6500 series Q-TOF B.06.01 (B6172 SP1)

Compound Table

Compound Label	RT	Mass	Abund	Formula	Tgt Mass	Diff (ppm)
Cpd 1: 0.157	0.157	276.09383	1607	C14 H16 N2 O2 S	276.09325	2.09

Compound Label	m/z	RT	Algorithm	Mass
Cpd 1: 0.157	277.10144	0.157	Find By Formula	276.09383

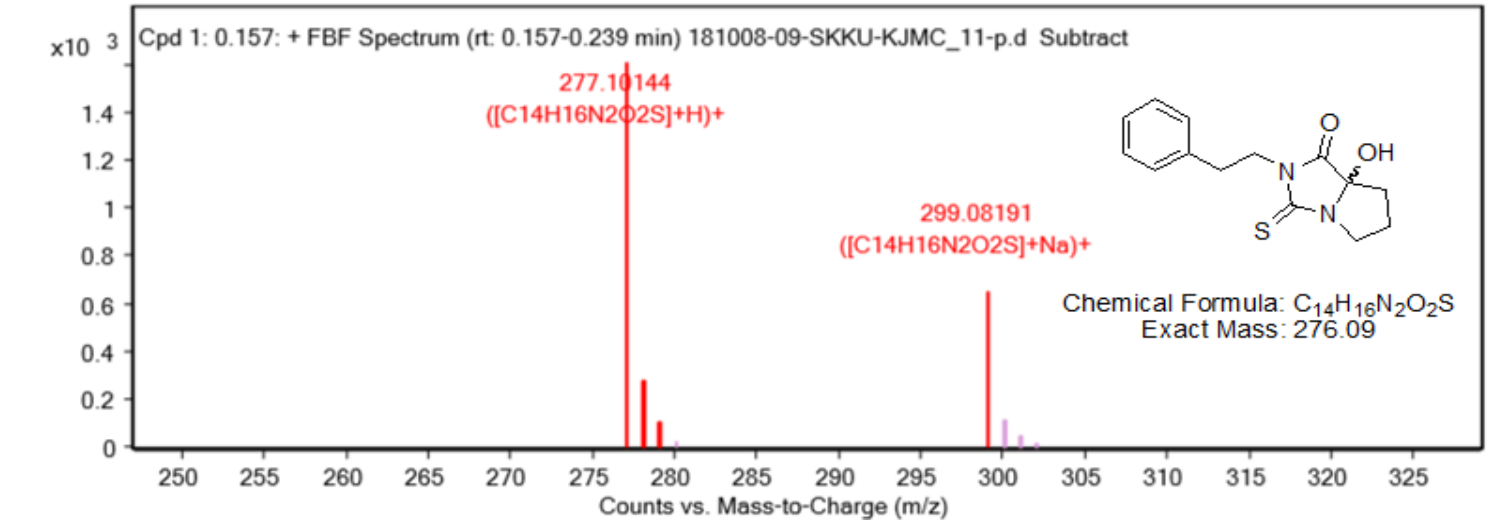

Figure S21. The ^{1}H NMR spectrum of **3** in chloroform-*d*.

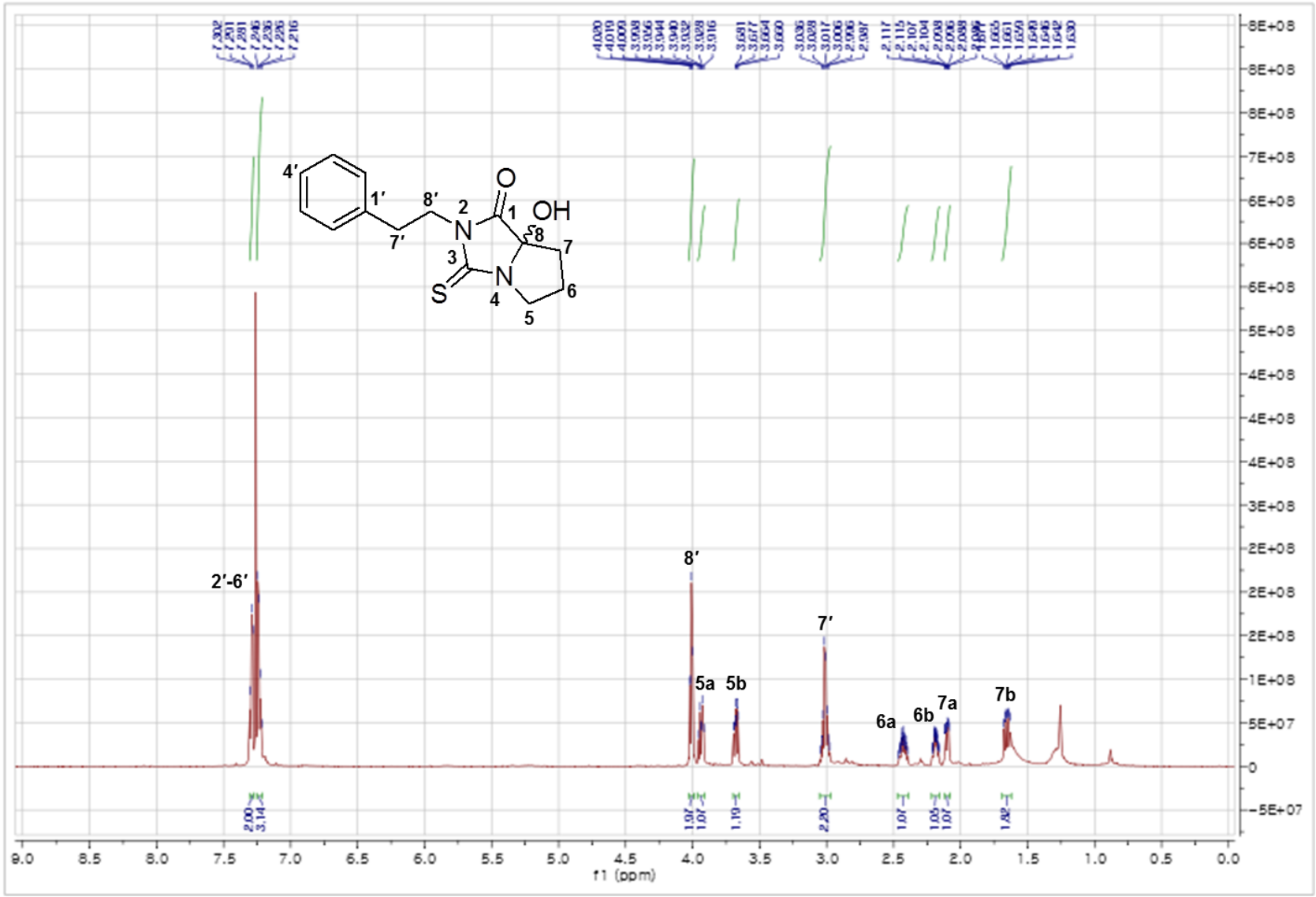

Figure S22. The ^{13}C NMR spectrum of **3** in chloroform-*d*.

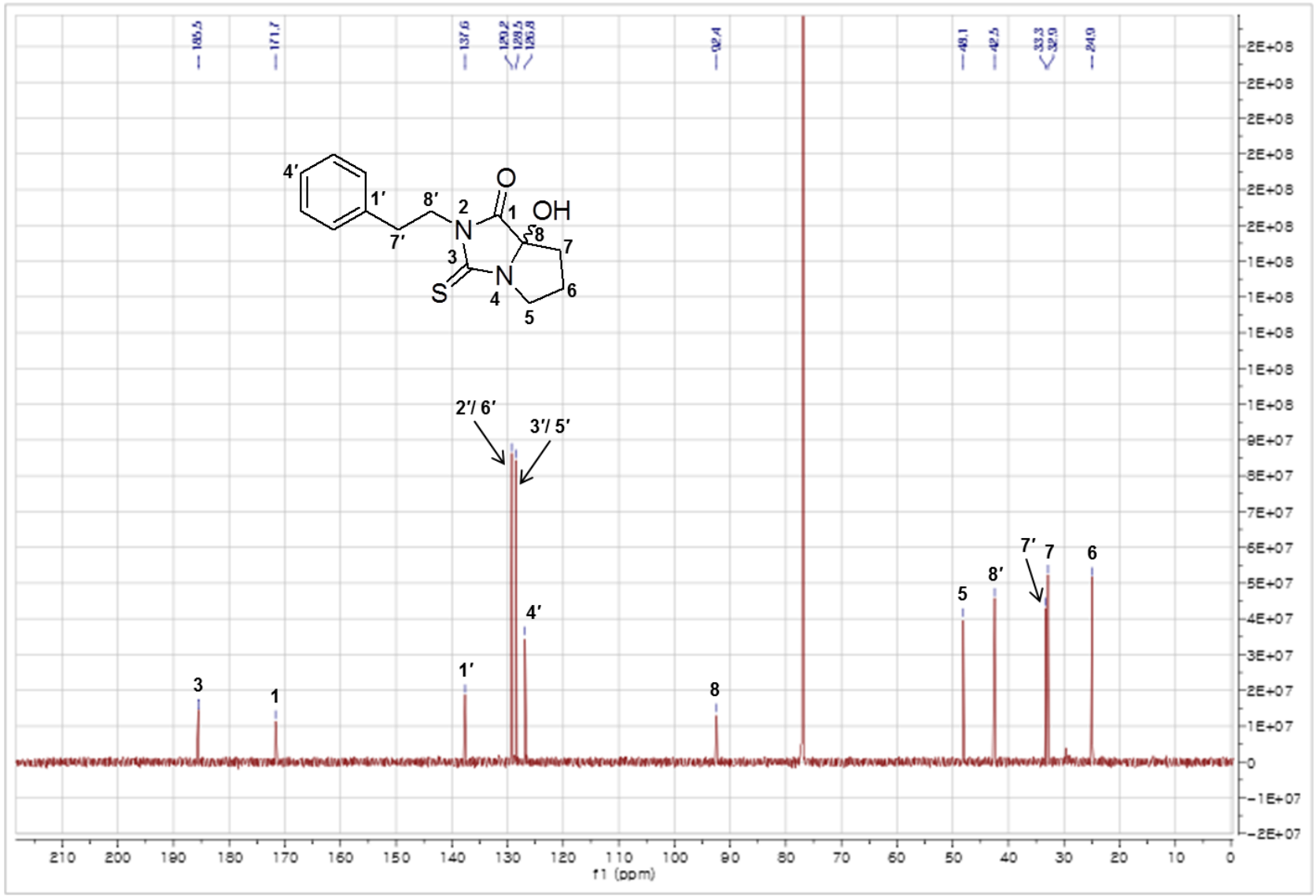

Figure S23. The COSY spectrum of **3** in chloroform-*d*.

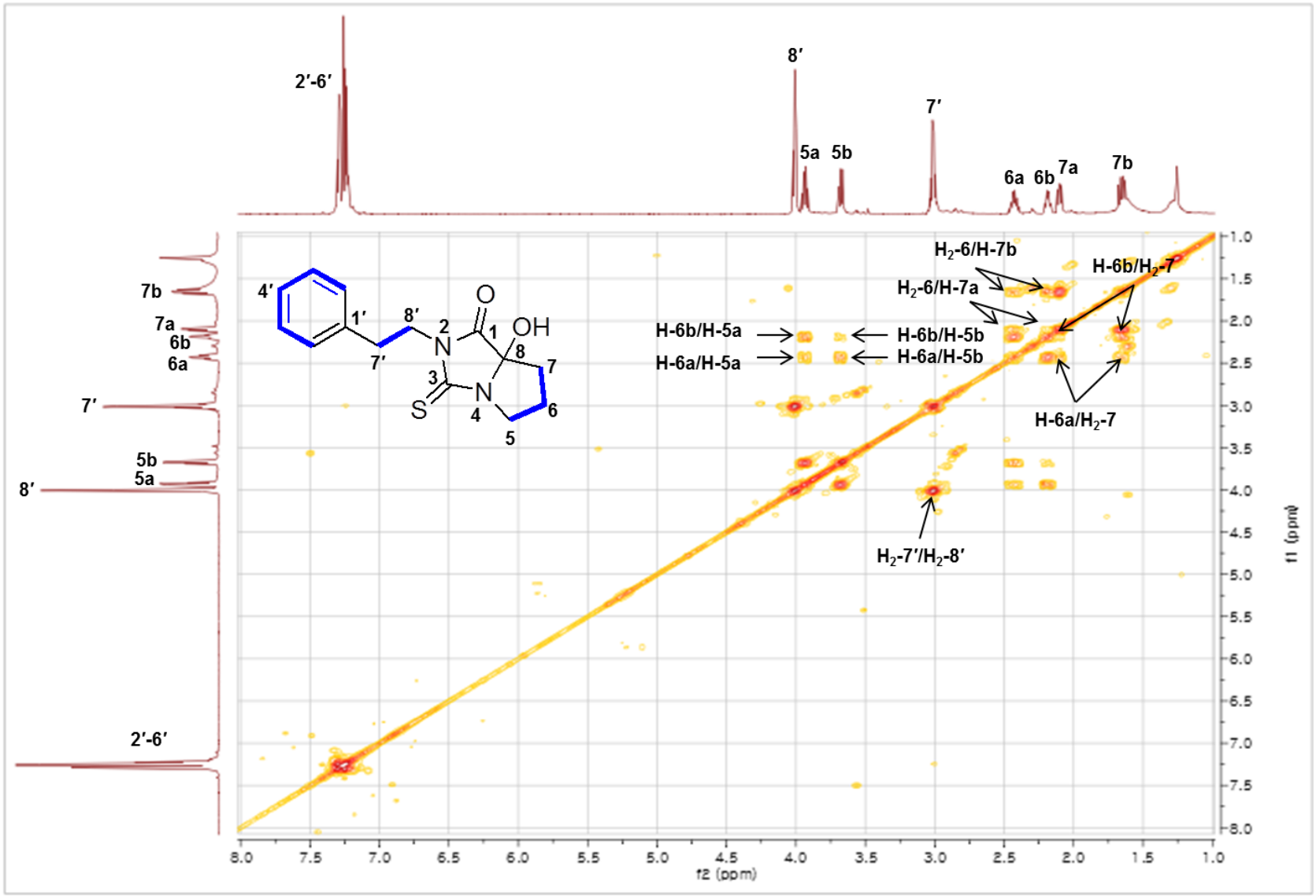

Figure S24. The HSQC spectrum of **3** in chloroform-*d*.

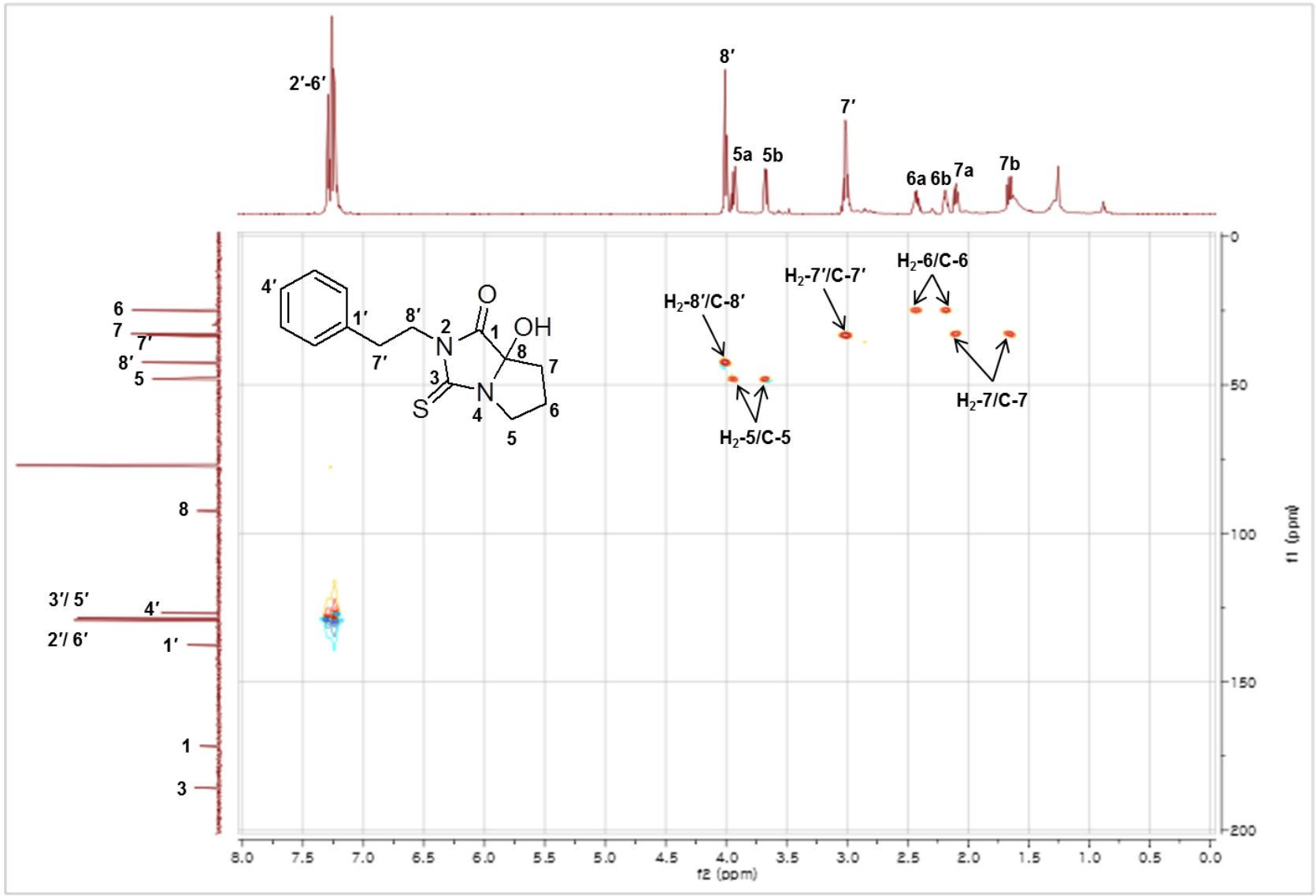

Figure S25. The HMBC spectrum of **3** in chloroform-*d*.

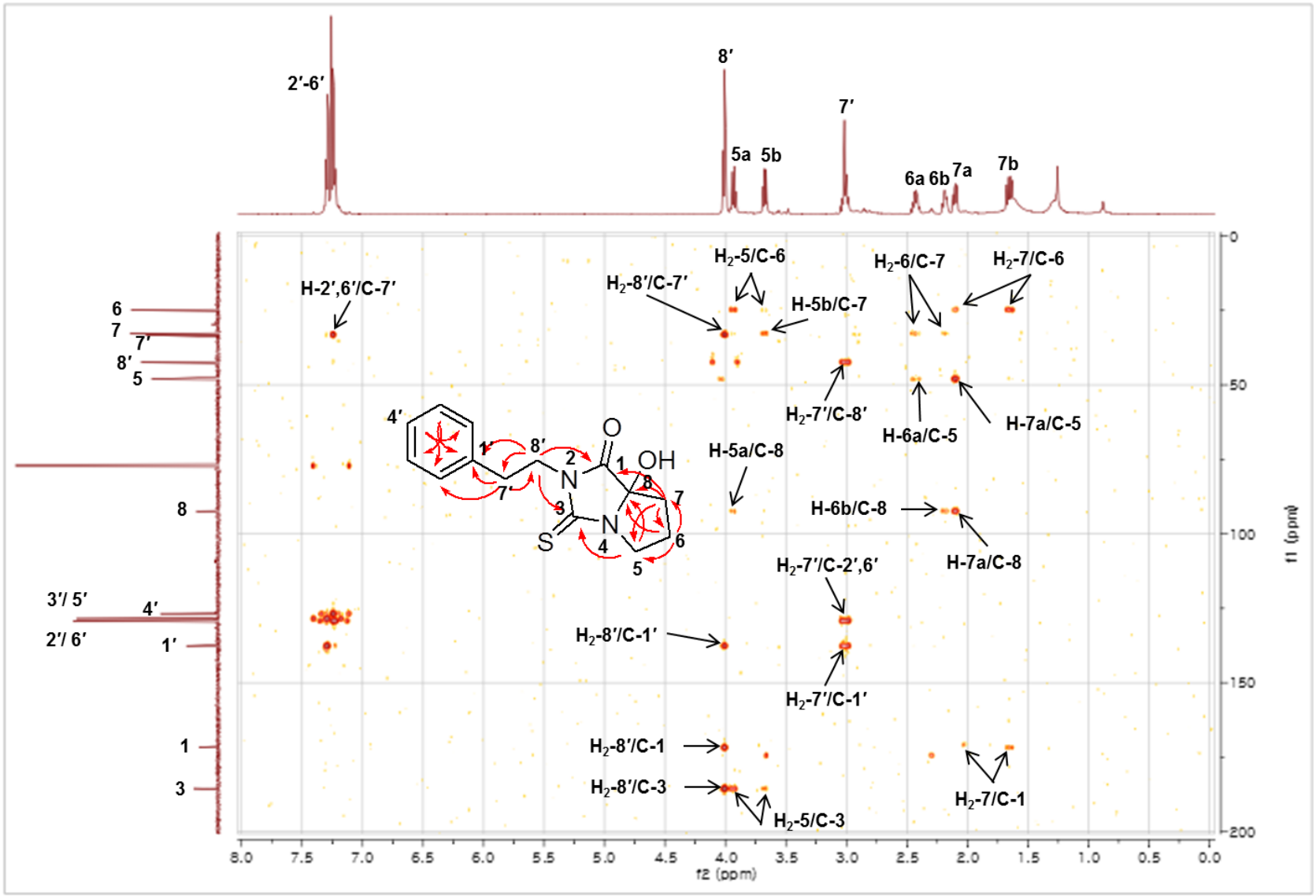

Figure S26. The HRESIMS spectrum of **4**.

Qualitative Analysis Report

Data Filename	181008-10-SKKU-KJMC_26-p.d	**Sample Name**	181008-10-SKKU-KJMC_26-p
Sample Type	Sample	**Position**	P1-A9
Instrument Name	Instrument 1	**User Name**	
Acq Method	DirectMS-2min-p.m	**Acquired Time**	10/8/2018 10:50:55 AM
IRM Calibration Status	Success	**DA Method**	Default.m
Comment			

Sample Group		**Info.**	
Stream Name	LC 1	**Acquisition SW Version**	6200 series TOF/6500 series Q-TOF B.06.01 (B6172 SP1)

User Spectra

Fragmentor Voltage	Collision Energy	Ionization Mode
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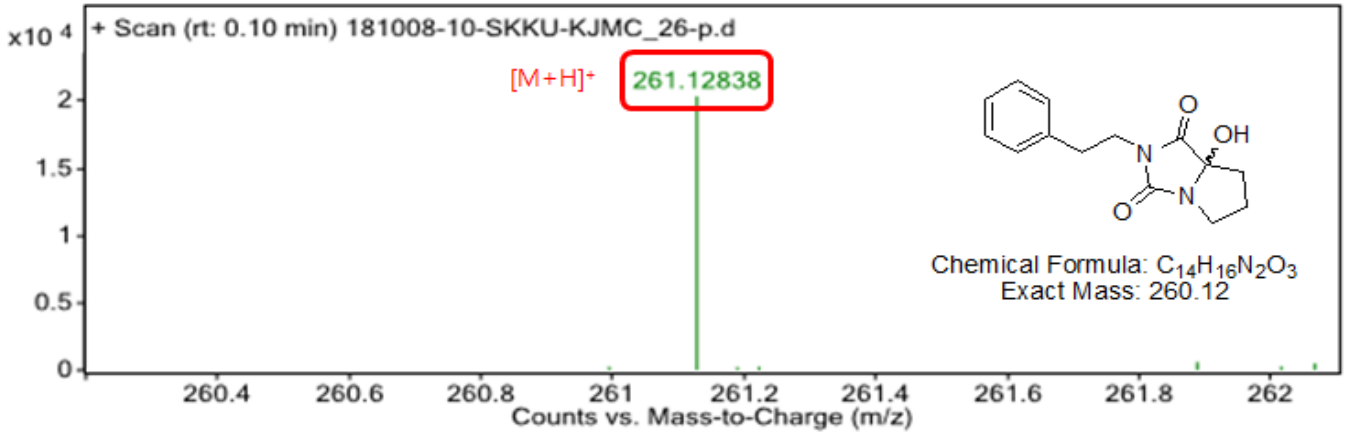

Figure S27. The ^{1}H NMR spectrum of **4** in chloroform-*d*.

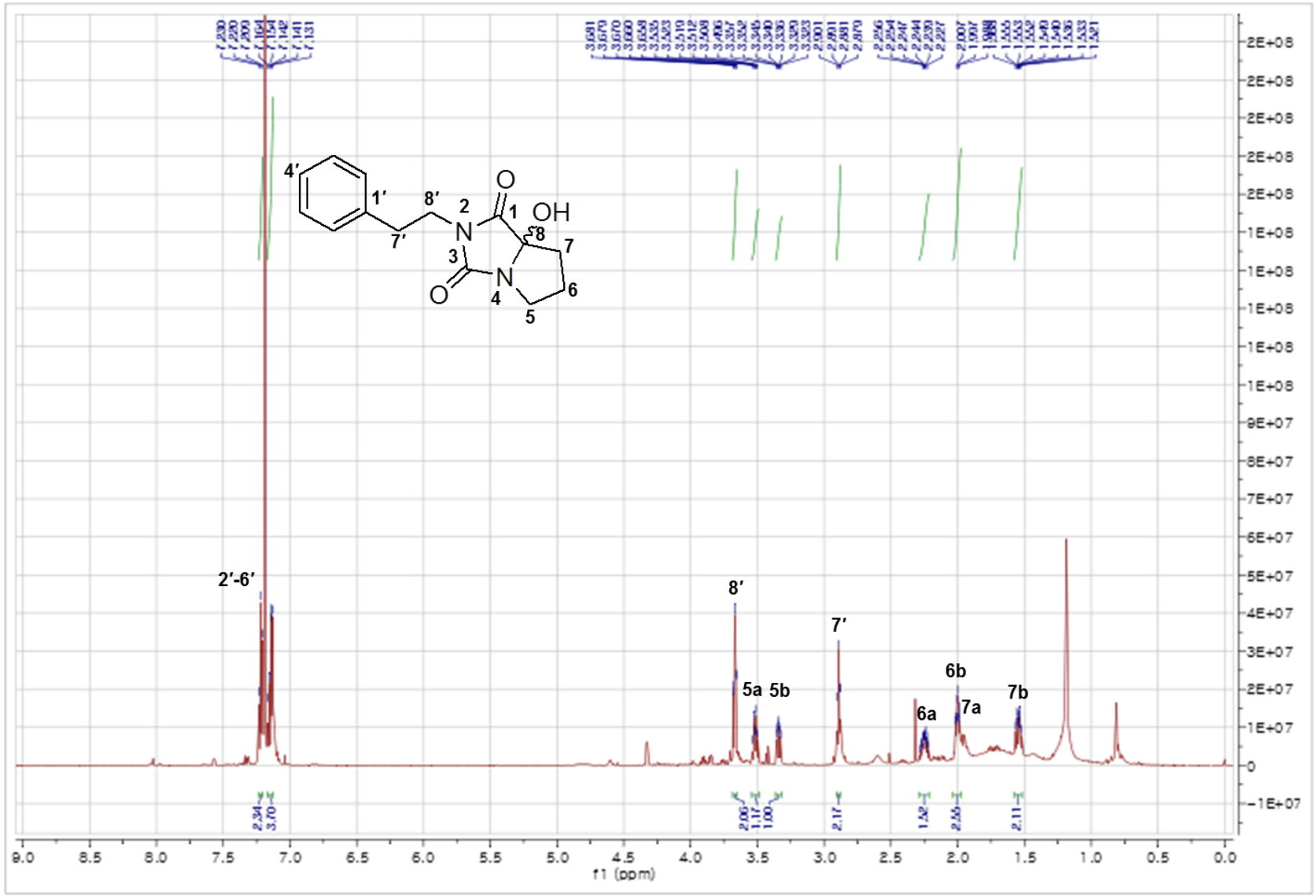

Figure S28. The ^{13}C NMR spectrum of **4** in chloroform-*d*.

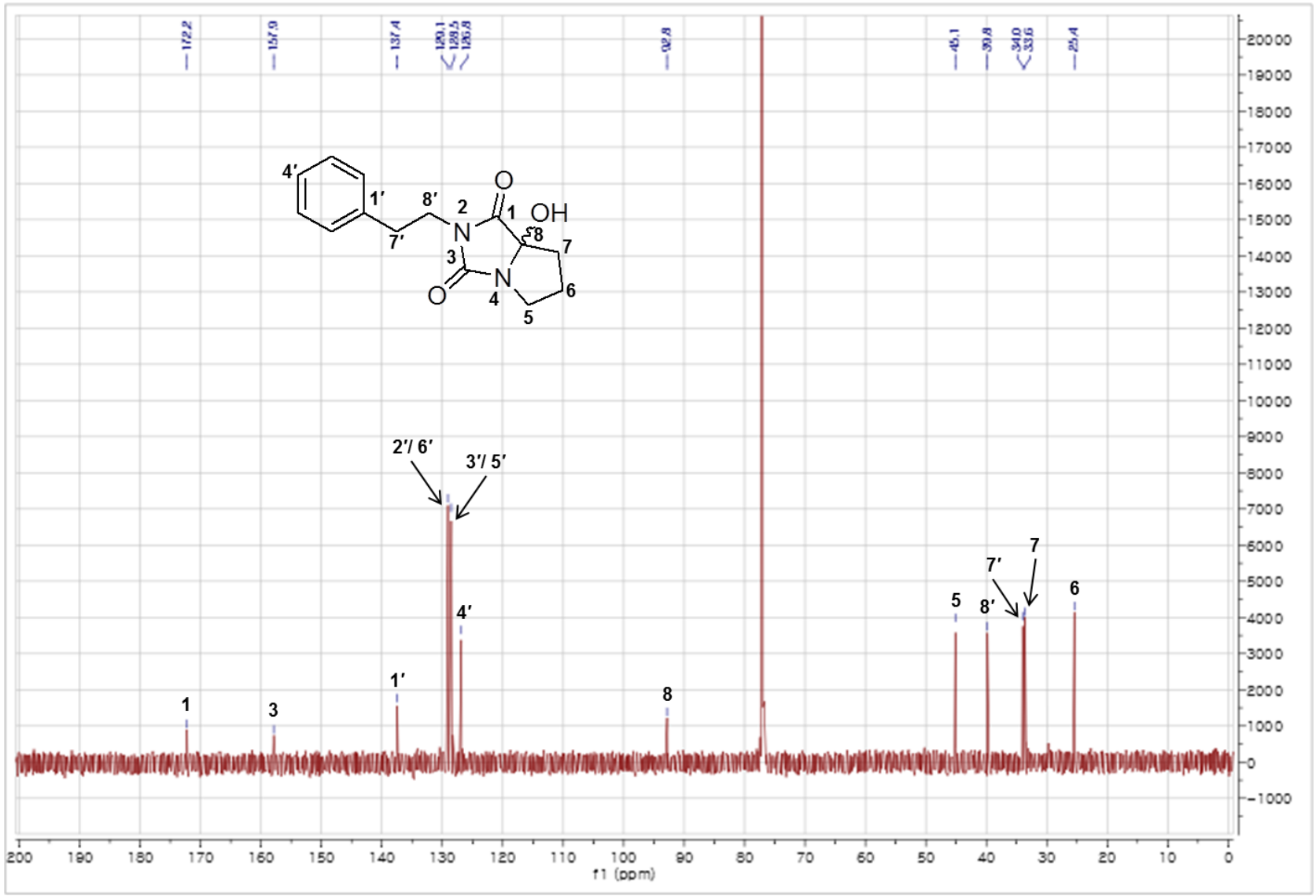

Figure S29. The COSY spectrum of **4** in chloroform-*d*.

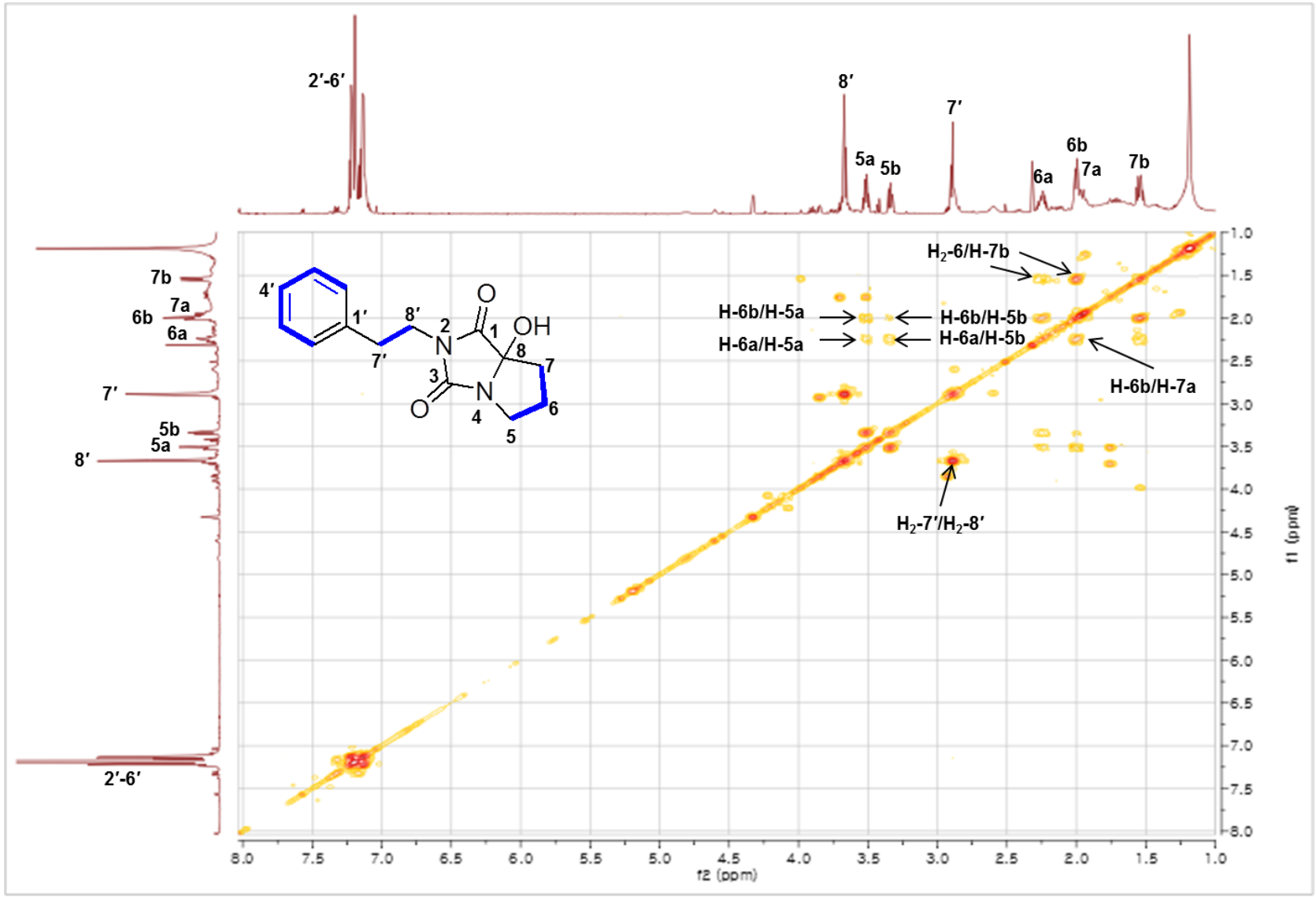

Figure S30. The HSQC spectrum of **4** in chloroform-*d*.

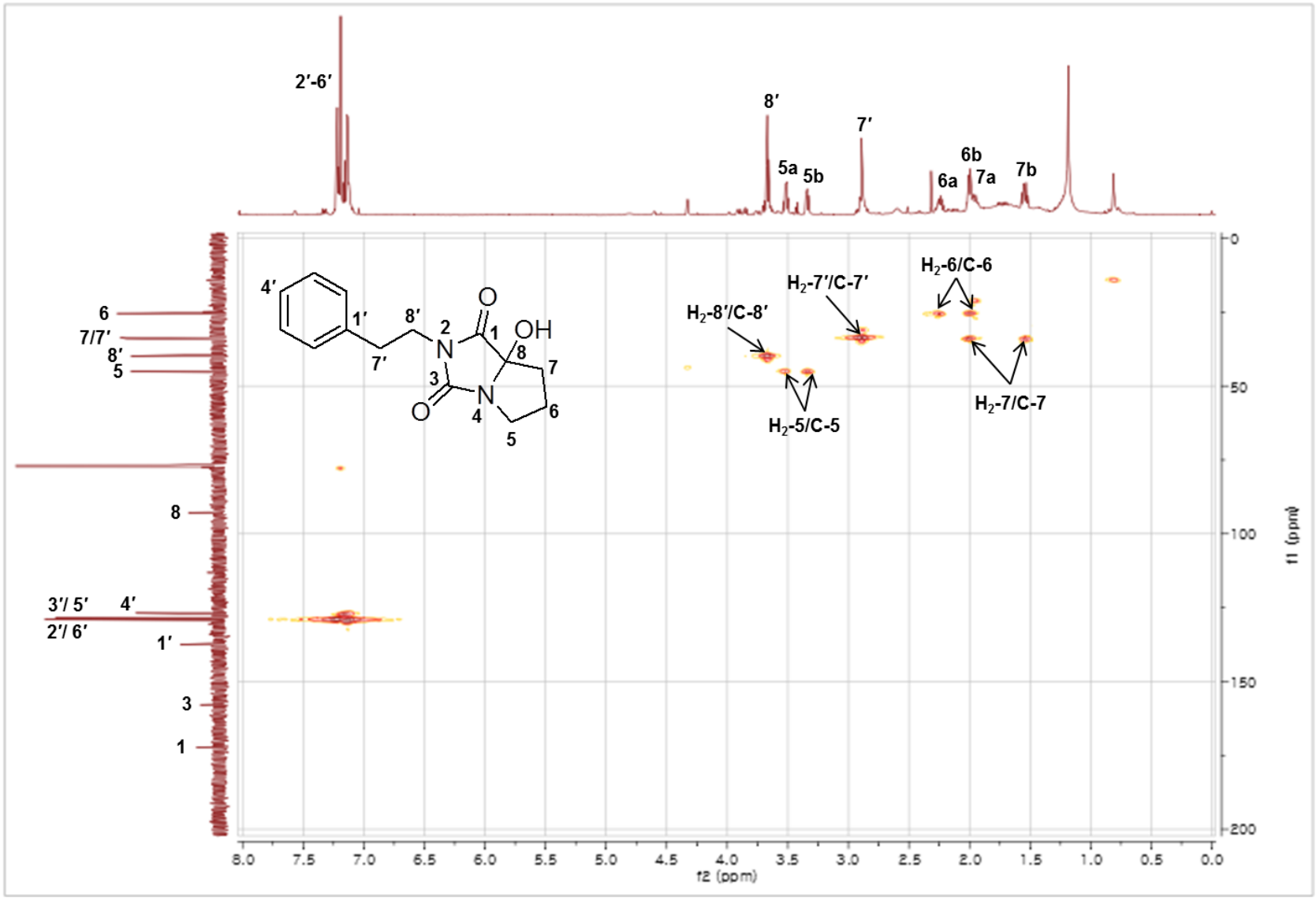

Figure S31. The HMBC spectrum of **4** in chloroform-*d*.

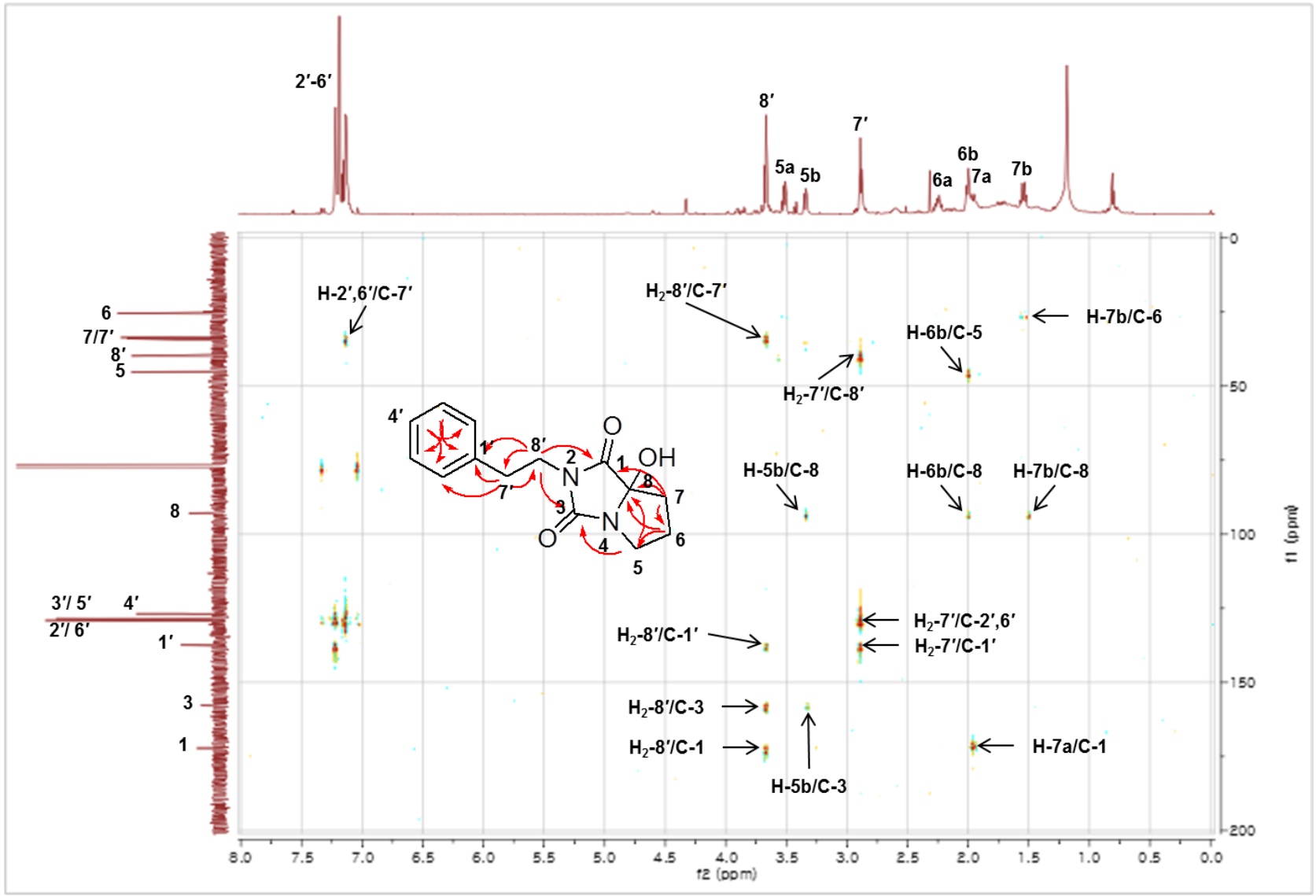

Figure S32. The HRESIMS spectrum of **5**.

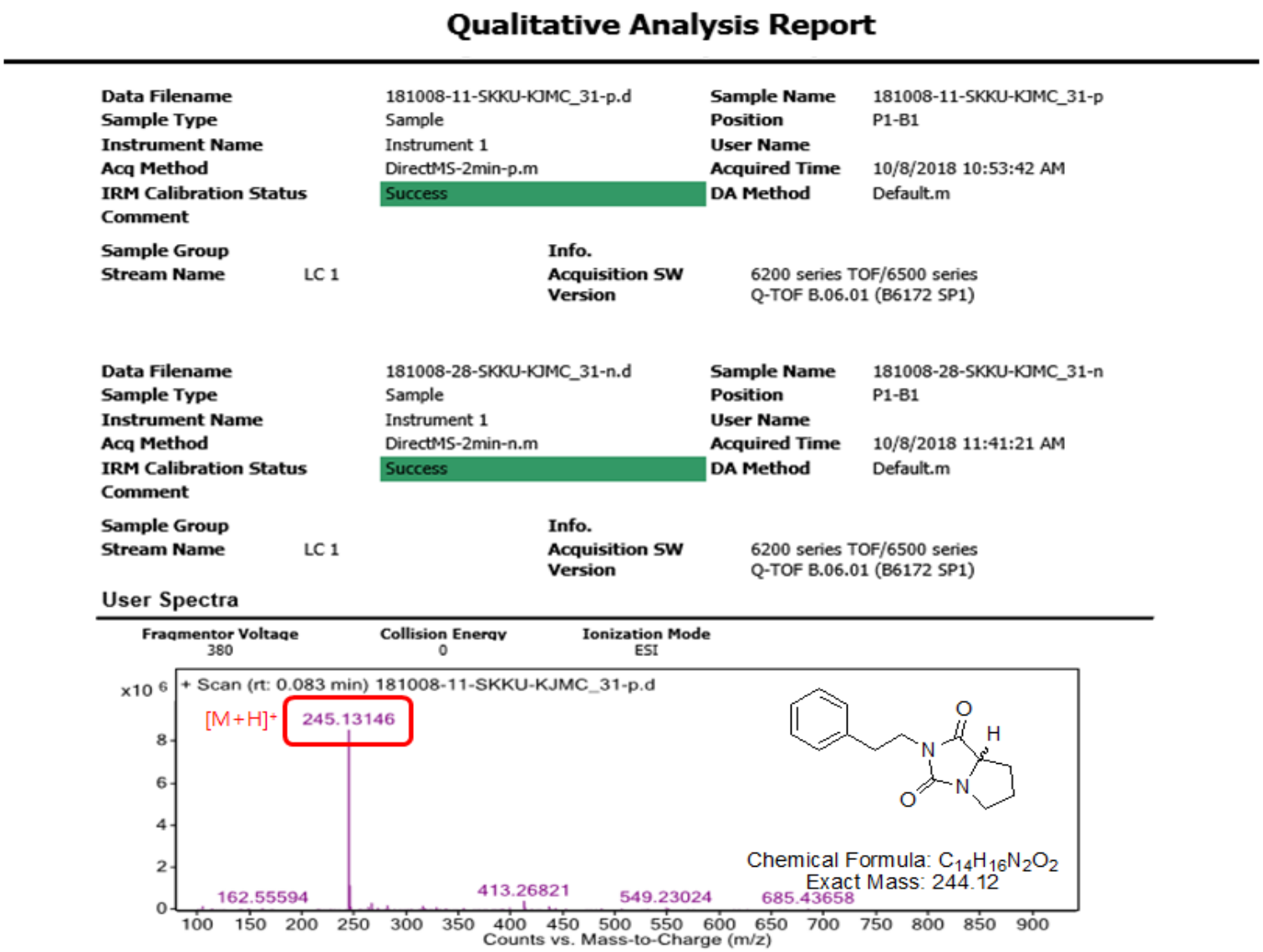

Figure S33. The ^{1}H NMR spectrum of **5** in chloroform-*d*.

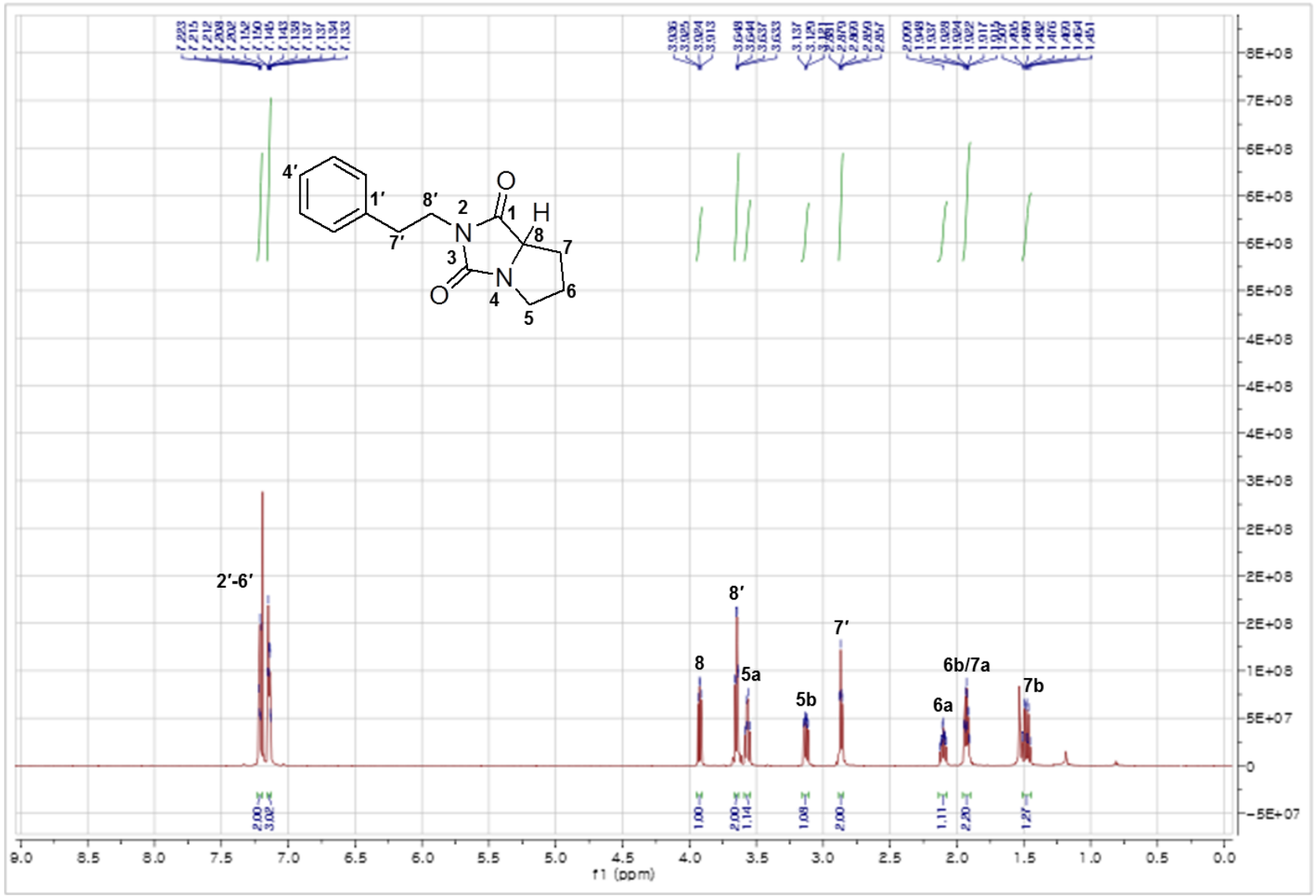

Figure S34. The ^{13}C NMR spectrum of **5** in chloroform-*d*.

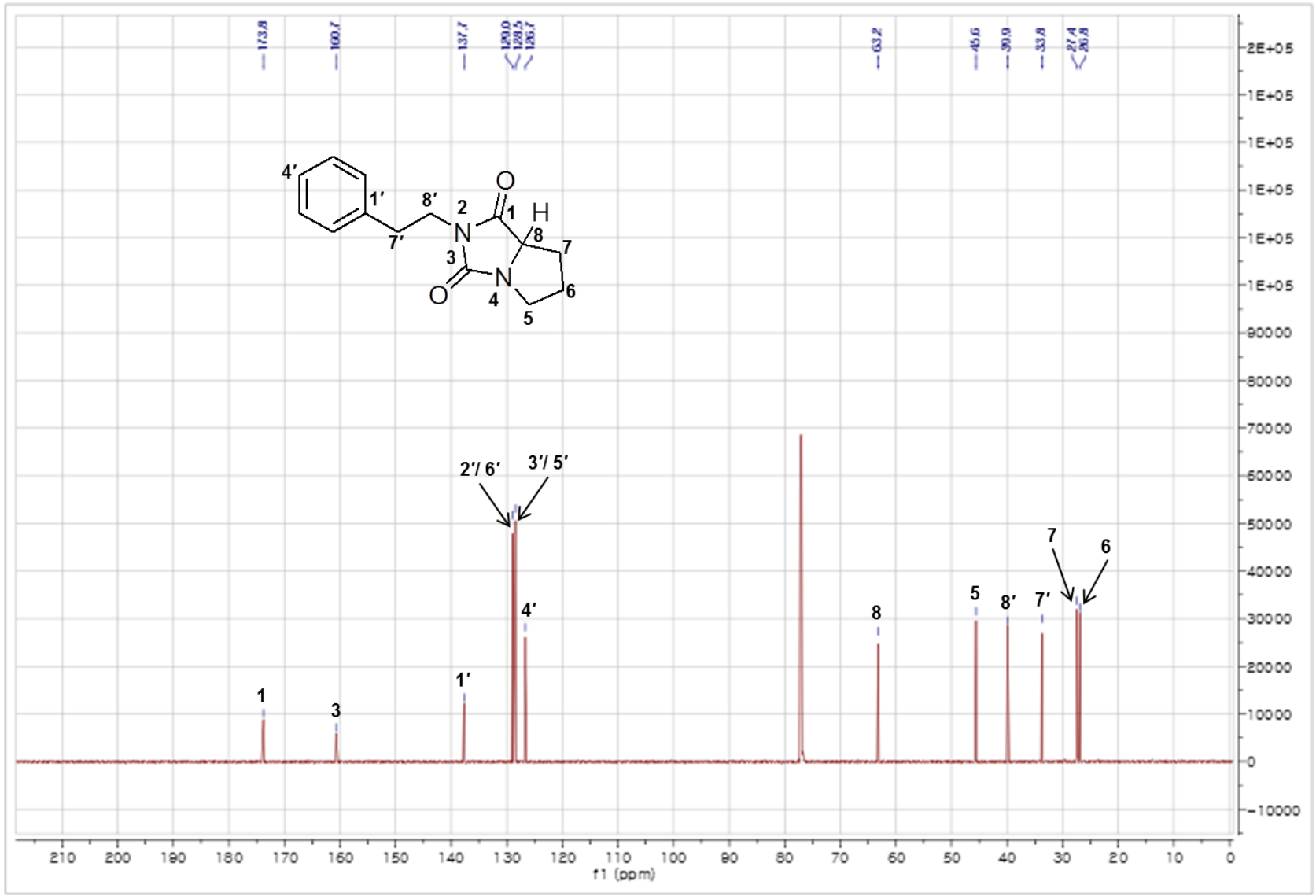

Figure S35. The COSY spectrum of **5** in chloroform-*d*.

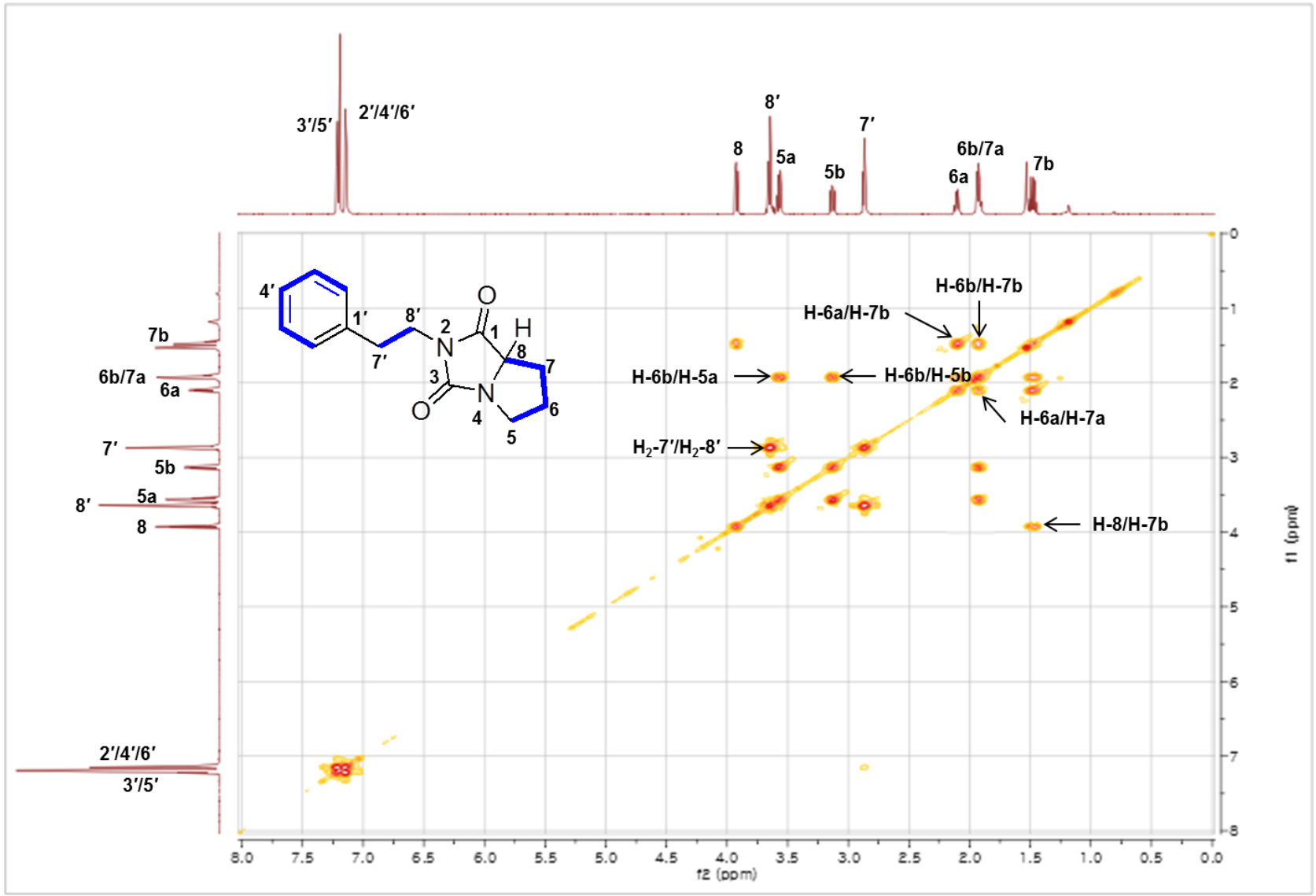

Figure S36. The HSQC spectrum of **5** in chloroform-*d*.

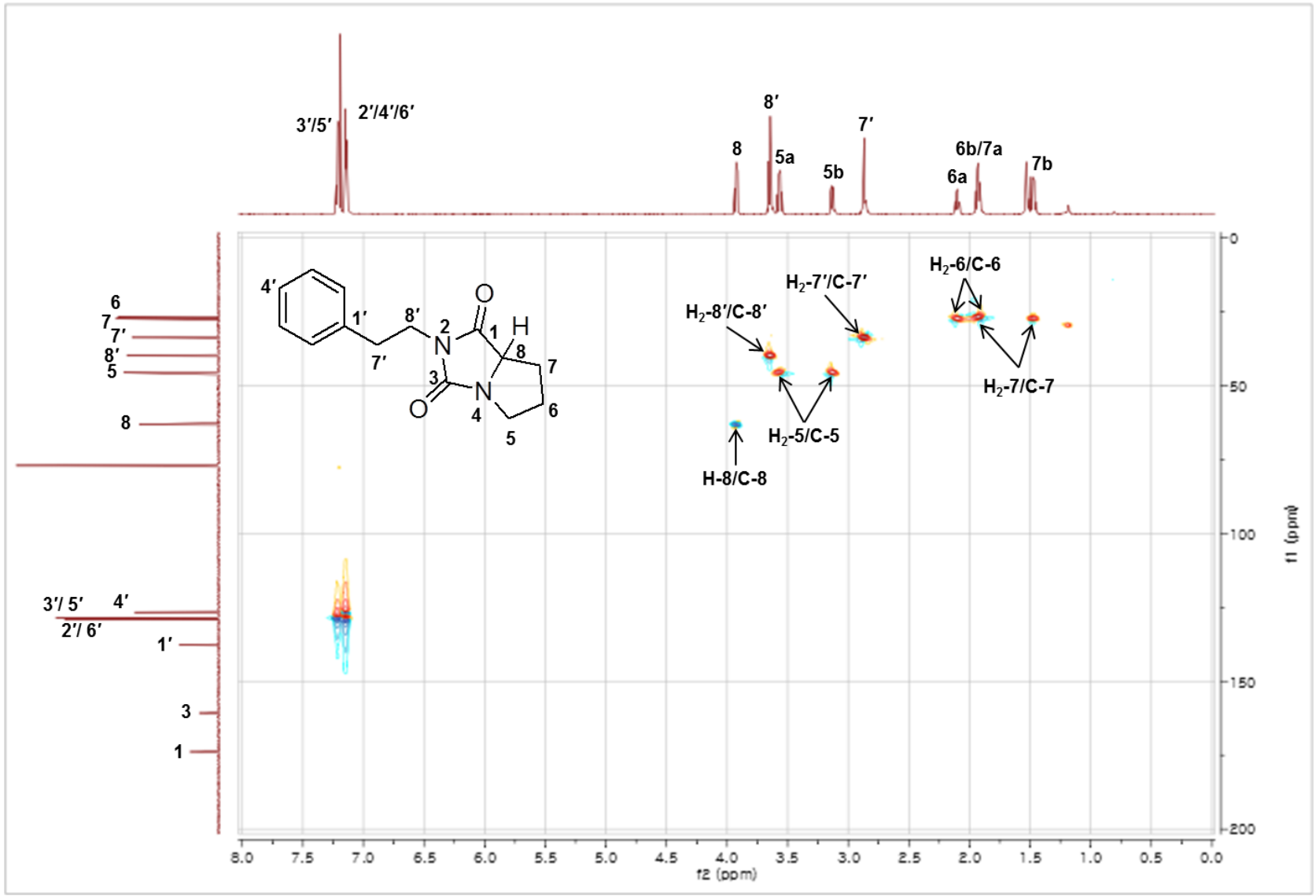

Figure S37. The HMBC spectrum of **5** in chloroform-*d*.