Electronic Supplementary Material (ESI) for Chemical Communications.

Discovery, absolute assignments, total synthesis of asperversiamides A–C and their potent activity against *Mycobacterium marinum*

Content of Supporting Information

Materials and Methods

1. General Experimental Procedures

Optical rotations were measured on a JASCO P-1020 digital polarimeter (JASCO Ltd., Tokyo, Japan). UV spectra were obtained on a Beckman DU 640 spectrophotometer (Beckman Instruments Ltd., California, USA). IR spectrawere recorded on a Nicolet-Nexus-470 spectrometer (Perkin Elmer Ltd., Boston, MA, USA) using KBr pellets. NMR spectra were recorded on a JEOL JEM-ECP NMR spectrometer (JEOL Ltd., Tokyo, Japan; 500MHz for ^{1}H and 125MHz for ^{13}C), using TMS as internal standard. The ESI-MS spectra were obtained from a Micromass Q-TOF spectrometer (Waters Ltd., Boston, MA, USA). Semi-preparative HPLC was performed on a Hitachi L-2000 system (Hitachi Ltd., Tokyo, Japan) using a C18 column (Kromasil (Eka Ltd., Bohus, Sweden) 250 × 10 mm, 5 μm, 2.0 mL/min). HPLC-MS was performed on an Agilent series 1290 Infinity HPLC instrument (Agilent, Technologies, Santa Clara, CA, USA), coupled with a Q-TOF Mass spectrometer (Thermo Scientific, Bremen, Germany), with a YMC C_{18} column [(YMC Co., Ltd., Tokyo, Japan) YMC-Park, ODS-A, 250 × 2.1 mm, S-5 μm, 12 nm, 0.5 mL/min]. UPLC-MS was performed on Waters UPLC® system (Waters Ltd., Massachusetts, America) using a C_{18} column [(Waters Ltd., Massachusetts, America) ACQUITY UPLC® BEH C18, 2.1 × 50 mm, 1.7 μm; 0.5 mL/min] and ACQUITY QDa ESIMS scan from 150 to 1000 Da. Silica gel (Qingdao Haiyang Chemical Group Co., Qingdao, China; 200–300 mesh), octadecylsilyl silica gel (YMC Co., Ltd., Tokyo, Japan; 45–60 μm), and Sephadex LH-20 (GE Ltd., Hartford, CT, USA) were used for column chromatography (CC). Precoated silica gel plates (Yantai Zhifu Chemical Group Co., Yantai, China; G60, F-254) were used for thin layer chromatography.

2. Fungal Material

The fungal strain CHNSCLM-0063 was isolated from the gorgonian coral *Rumphella aggregata* (NSM02) collected from Nansha Islands in the South China Sea in April 2015. The strain was identified as *Aspergillus versicolor* according to morphologic traits and molecular identification. Its 617 base pair ITS sequence had 100% sequence identity to that of *Aspergillus versicolor* (AY373882). The sequence data have been submitted to GenBank with the accession number MG736310. The strain was deposited at the Key Laboratory of Marine Drugs, the Ministry of Education of China, School of Medicine and Pharmacy, Ocean University of China, Qingdao, China.

3. Fermentation, Extraction, and Isolation

The fungus was cultured for 50 days on sea water-added rice solid medium (two hundred 1000 mL Erlenmeyer flasks, each containing 50 g of rice and 50 mL of sea water) at room temperature. The fermented rice substrate was extracted three times with ethyl acetate (EtOAc) (200 mL per flask) to give an organic extract (50 g). The organic extract was subjected to silica gel vacuum liquid chromatography (VLC) and eluted by a gradient of petroleum ether (PE)−EtOAc (PE, 100%−0), EtOAc−MeOH (v:v, 9:1), and then MeOH to afford six fractions (Fr.1–Fr.6) on the basis of TLC analysis. Fr.6 was subjected to Sephadex LH-20 column chromatography (CC) and eluted with a mixture of CH_2Cl_2–MeOH (v:v, 1:1) to obtain four sub-fractions (Fr.6-1–Fr.6-4). Fr.6-3 was then repeatedly separated by reversed-phase C18 CC, and then purified by HPLC (MeCN–H_2O, 20–80) to afford compounds **1** (50 mg), **2** (2 mg), and **3** (2 mg).

4. Acid Hydrolysis and Marfey's Analysis of 1–3

A solution of **1** (or **2** and **3**, 0.1 mg) with HCl (6 M, 1 mL) was hydrolyzed by heating for 10 h at 70 °C. The solution was evaporated to dryness under vacuum and redissolved in H_2O (250 μL). The acid

hydrolysate solution (50 μL) was treated with 1% solution of L-FDAA (20 μL) in acetone followed by a solution of $NaHCO_3$ (1M, 10 μL). The mixture was heated at 60 °C for 1 h. The reaction was stopped by HCl (2M, 5 μL). The amino acid standards, L-Ala, L/D-Ala, L-Val, L/D-Val, L-Phe, L/D-Phe, L-Trp, L/D-Trp, L-Ser, and L/D-Ser, were derivatized with L-FDAA in the same manner as that of **1**. All L-FDAA derivatives were analyzed and detected by HPLC (MeCN (A), H_2O (B); 0–30 min 23.5% A, 30–45 min 23.5%–30% A, 45–125 min 30%–40% A; 2 mL/min; UV 340 nm). The retention times of the L-FDAA-derivatized amino acid standards were as follows: L-Ser (26.1 min), D-Ser (28.2 min), Gly (44.1 min), L-Ala (50.1 min), D-Ala (61.6 min), L-Val (76.9 min), L-Trp (97.7 min), D-Val (100.3 min), L-Phe (102.8 min), D-Trp (111.4 min), D-Phe (123.5 min). The retention times of the acid hydrolysate derivatives of **1**–**3** were as follows: **1**: L-Ser (26.0 min), D-Ser (28.1 min), D-Ala (61.8 min), D-Val (100.1 min), L-Phe (102.8 min), and D-Trp (111.4 min); **2**: D-Ser (28.3 min), L-Ala (50.2 min), D-Ala (61.5 min), D-Val (100.1 min), L-Phe (102.9 min), and D-Trp (111.2 min); **3**: L-Ser (26.1 min), D-Ala (61.7 min), D-Val (100.3 min), L-Phe (102.9 min), and D-Trp (111.7 min).

5. Total synthesis

5.1 *Cyclo*-[(NH)D-Val–D-Ser–D-Trp–L-Ser–D-Ala–D-Val–L-Phe(CO)] (syn-1) and *Cyclo*-[(NH)D-Val–L-Ser–D-Trp–D-Ser–D-Ala–D-Val–L-Phe(CO)] (*iso*-1)

Resin preparation: Wang resin (100–200 mesh) preloaded with Fmoc-L-phenylalanine (0.26 mmol/g) was dissolved in CH_2Cl_2 and agitated for 1 h, then drained and washed with dimethyl formamide (DMF, 3 mL×3 times, 1 min/time).

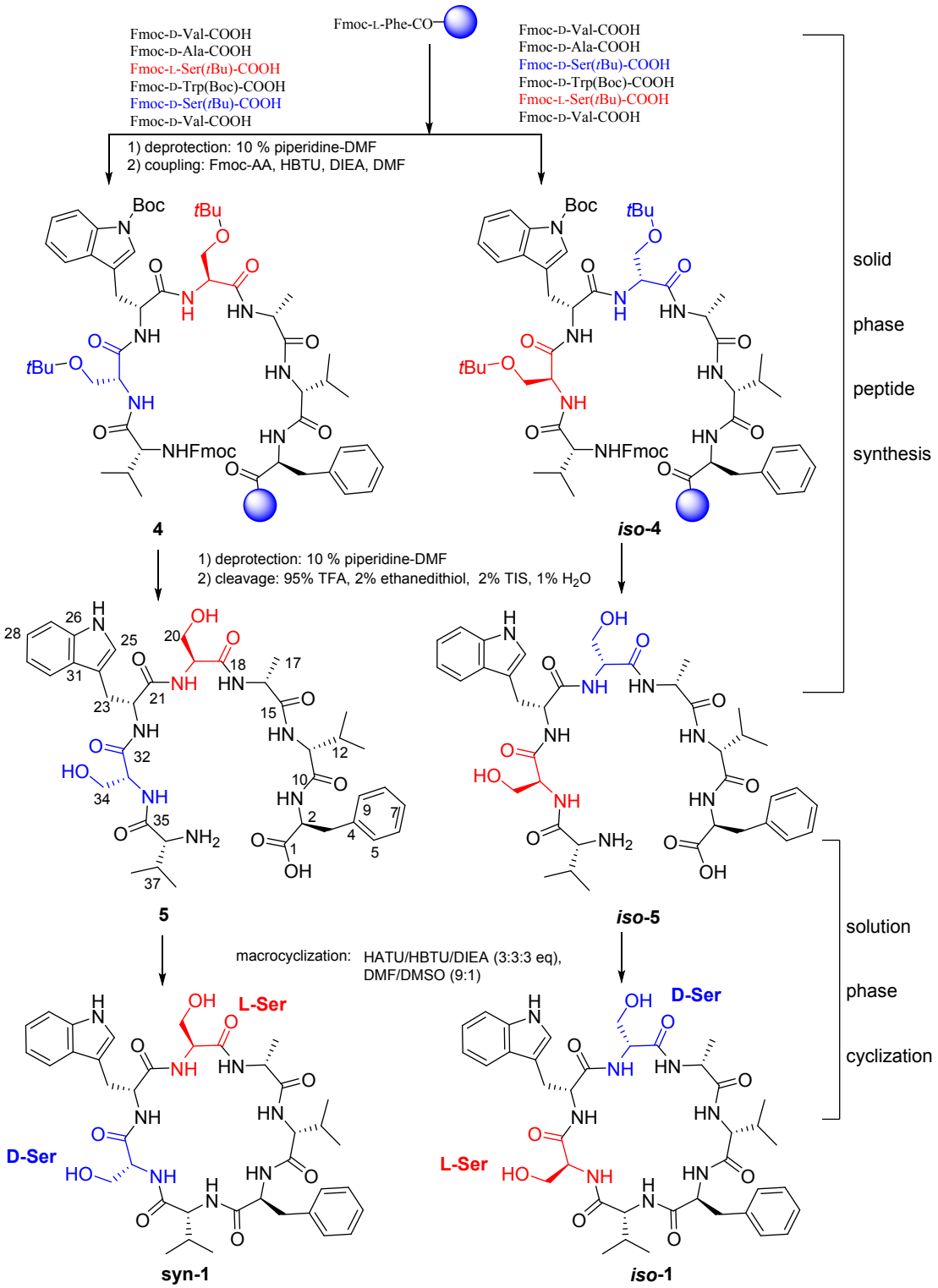
Fmoc deprotection: The resin was agitated in 10% piperidine/DMF (3 mL×3 times, 1 min/time), then washed with DMF (3 mL×3 times, 1 min/time), CH_2Cl_2 (3 mL×3 times, 1 min/time), and then DMF (3 mL×3 times, 1 min/time). The collected deprotection solutions were diluted 100-fold with 10% piperidine/DMF, and the resin loading was estimated by measuring the adsorbance of the piperidine-fulvene adduct at 301 nm.

Peptide coupling: A solution was prepared of the appropriate Fmoc-protected amino acid (5 eq to resin loading) and HBTU (3 eq) in DMF (2 mL). After adding DIEA (6 eq), the resulting solution was immediately added to the resin and agitated for 1 h at N_2 protection. The resin was then drained and washed with DMF (3 mL×3 times, 1 min/time), CH_2Cl_2 (3 mL×3 times, 1 min/time), and then DMF (3 mL×3 times, 1 min/time).

Cleavage: After the last Fmoc deprotection, the resin was washed with DCM (3 mL×3 times, 1 min/time) and then dried in vacuum. A solution of TFA/H_2O/triisopylsilane (96:2:2) was added to the resin and agitated for 2 h, then the resin was drained and washed with TFA (3 mL×2 times, 1 min/time). The combined cleavage solutions were concentrated in vacuum to give a clear glassy solid, and then recrystallization by diethyl ether to afford **5**.

Macrocyclization: A solution of linear peptide **5** (20 mg, 0.025 mmol) in DMF/DMSO (9:1, 20 mL) was slowly dropped into a stirring solution of HBTU (28.6 mg, 0.076 mmol), HATU (28.6 mg, 0.076 mmol), DIEA (28 μL) in DMF/DMSO (9:1, 20 mL) in N_2 protection at 28 °C. After 2 h reaction, the mixture was poured into saturated $NaHCO_3$ and the solvent layer was extracted with EtOAc. The organic extract was concentrated in vacuum and diluted with MeCN/H_2O, and then purified by HPLC to afford compound **syn-1**.

Compound ***iso*-1** was synthesized by the same method.



Compound **5**: white, amorphous powder; [α]20 D + 35 (*c* 0.29, MeOH); IR (KBr) ν_{max} 3304, 1669, 1527 cm^{-1}; ^{1}H NMR (DMSO-d_6, 500 MHz, *J* in Hz) δ_H 12.80 (1H, s, COOH), 10.80 (1H, s, 25-NH), 8.50 (1H, d, *J* = 7.6 Hz, 33-NH), 8.29 (1H, d, *J* = 8.2 Hz, 2-NH), 8.20 (1H, d, *J* = 7.2 Hz, 22-NH), 8.02-8.11 (3H, overlapped, 19-NH/36-NH$_2$), 7.91 (1H, d, *J* = 7.3 Hz, 16-NH), 7.66 (1H, d, *J* = 9.2 Hz, 11-NH), 7.56 (1H, d, *J* = 7.7 Hz, H-30), 7.31 (1H, d, *J* = 7.7 Hz, H-27), 7.24 (2H, overlapped, H-6/8), 7.22 (2H, overlapped, H-5/9), 7.17 (1H, m, H-7), 7.14 (1H, m, H-25), 7.05 (1H, t, *J* = 7.7 Hz, H-28), 6.95 (1H, t, *J* = 7.7 Hz, H-29), 5.15 (1H, br s, OH), 4.88 (1H, br s, OH), 4.59 (1H, dd, *J* = 8.1, 7.2 Hz, H-22), 4.45 (1H, m, H-2), 4.42 (1H,

m, H-33), 4.32 (1H, m, H-16), 4.24 (1H, m, H-19), 4.17 (1H, dd, *J* = 9.2, 6.2 Hz, H-11), 3.66 (1H, m, H-36), 3.62 (1H, m, Ha-34), 3.57 (1H, m, Hb-34), 3.51 (1H, m, Ha-20), 3.44 (1H, m, Hb-20), 3.14 (1H, m, Ha-23), 3.09 (1H, m, Ha-3), 2.98 (1H, dd, *J* = 14.7, 8.1 Hz, Hb-23), 2.83 (1H, dd, *J* = 13.5, 10.6 Hz, Hb-3), 2.01 (1H, m, H-37), 1.80 (1H, m, H-12), 1.18 (3H, d, *J* = 7.0 Hz, H-17), 0.88 (3H, d, *J* = 6.0 Hz, H-38), 0.87 (3H, d, *J* = 6.0 Hz, H-39), 0.63 (3H, d, *J* = 6.7 Hz, H-14), 0.56 (3H, d, *J* = 6.7 Hz, H-13); ^{13}C NMR (DMSO-d_6, 125 MHz) δ_C 172.9 (C, C-1), 171.8 (C, C-15), 171.2 (C, C-21), 170.7 (C, C-10), 169.7 (C, C-18), 169.5 (C, C-32), 167.9 (C, C-35), 137.6 (C, C-26), 136.0 (C, C-4), 129.1 (CH, C-5/9), 128.1 (CH, C-6/8), 127.4 (C, C-31), 126.4 (CH, C-7), 123.5 (CH, C-25), 120.8 (CH, C-28), 118.4 (CH, C-30), 118.2 (CH, C-29), 111.3 (CH, C-27), 109.8 (C, C-24), 61.7 (CH_2, C-20/34), 57.2 (CH, C-11), 55.1 (CH, C-19), 54.9 (CH, C-33), 53.8 (CH, C-22), 53.4 (CH, C-2), 48.3 (CH, C-16), 36.8 (CH_2, C-3), 30.8 (CH, C-12), 29.9 (CH, C-37), 27.6 (CH_2, C-23), 19.1 (CH_3, C-14), 18.4 (CH_3, C-39), 18.0 (CH_3, C-17), 17.6 (CH_3, C-38), 17.4 (CH_3, C-13); (+)-HR-ESI-MS *m/z* 795.4039 $[M + H]^+$, *m/z* 817.3841 $[M + Na]^+$ (calcd. for $C_{39}H_{55}N_8O_{10}$, 795.4036 $[M + H]^+$, $C_{39}H_{54}N_8O_{10}Na$, *m/z* 817.3855 $[M + Na]^+$).

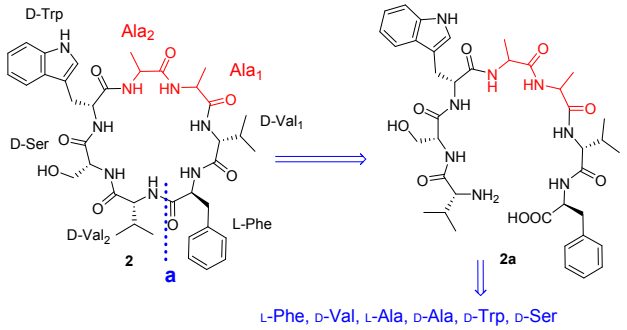
Compound ***iso*-5**: white, amorphous powder; [α]20 D + 82 (*c* 0.22, MeOH); IR (KBr) ν_{max} 3305, 1670, 1526 cm^{-1}; ^{1}H NMR (DMSO-d_6, 500 MHz, *J* in Hz) δ_H 12.72 (1H, s, COOH), 10.81 (1H, s, 25-NH), 8.52 (1H, d, *J* = 8.4 Hz, 33-NH), 8.33 (1H, d, *J* = 8.3 Hz, 2-NH), 8.27 (1H, d, *J* = 8.2 Hz, 22-NH), 8.24 (1H, d, *J* = 7.7 Hz, 19-NH), 8.02-8.11 (3H, overlapped, 16-NH/36-NH_2), 7.69 (1H, d, *J* = 9.3 Hz, 11-NH), 7.64 (1H, d, *J* = 7.9 Hz, H-30), 7.31 (1H, d, *J* = 7.9 Hz, H-27), 7.24 (2H, overlapped, H-6/8), 7.22 (2H, overlapped, H-5/9), 7.17 (1H, m, H-7), 7.15 (1H, m, H-25), 7.04 (1H, t, *J* = 7.9 Hz, H-28), 6.96 (1H, t, *J* = 7.9 Hz, H-29), 5.03 (1H, br s, OH), 4.90 (1H, br s, OH), 4.64 (1H, td, *J* = 9.1, 8.2 Hz, H-22), 4.50 (1H, dd, *J* = 8.4, 6.8 Hz, H-33), 4.43 (1H, m, H-2), 4.36 (1H, m, H-16), 4.33 (1H, dd, *J* = 8.4, 7.2 Hz, H-19), 4.20 (1H, dd, *J* = 9.3, 6.1 Hz, H-11), 3.71 (1H, m, H-36), 3.61 (1H, m, Ha-34), 3.55 (1H, m, Ha-20), 3.38 (1H, m, Hb-34), 3.34 (1H, m, Hb-20), 3.14 (1H, dd, *J* = 14.7, 4.2 Hz, Ha-23), 3.09 (1H, dd, *J* = 13.7, 4.2 Hz, Ha-3), 2.94 (1H, dd, *J* = 14.7, 9.1 Hz, Hb-23), 2.81 (1H, m, Hb-3), 2.05 (1H, m, H-37), 1.77 (1H, m, H-12), 1.20 (3H, d, *J* = 7.0 Hz, H-17), 0.93 (3H, d, *J* = 8.0 Hz, H-38), 0.91 (3H, d, *J* = 8.0 Hz, H-39), 0.62 (3H, d, *J* = 6.7 Hz, H-14), 0.53 (3H, d, *J* = 6.7 Hz, H-13); ^{13}C NMR (DMSO-d_6, 125 MHz) δ_C 172.9 (C, C-1), 171.9 (C, C-15), 171.5 (C, C-21), 170.7 (C, C-10), 169.7 (C, C-18), 169.0 (C, C-32), 167.9 (C, C-35), 137.6 (C, C-26), 136.0 (C, C-4), 129.1 (CH, C-5/9), 128.1 (CH, C-6/8), 127.4 (C, C-31), 126.4 (CH, C-7), 123.9 (CH, C-25), 120.8 (CH, C-28), 118.6 (CH, C-30), 118.1 (CH, C-29), 111.2 (CH, C-27), 109.6 (C, C-24), 63.9 (CH_2, C-34), 61.9 (CH_2, C-20), 57.2 (CH, C-36), 57.1 (CH, C-11), 55.04 (CH, C-33) , 54.95 (CH, C-19), 53.5 (CH, C-22), 53.2 (CH, C-2), 48.3 (CH, C-16), 36.8 (CH_2, C-3), 30.9 (CH, C-12), 29.8 (CH, C-37), 28.0 (CH_2, C-23), 19.1 (CH_3, C-14), 18.3 (CH_3, C-39), 18.1 (CH_3, C-17), 17.6 (CH_3, C-38), 17.3 (CH_3, C-13); (+)-HR-ESI-MS *m/z* 795.4044 $[M + H]^+$, *m/z* 817.3845 $[M + Na]^+$ (calcd. for $C_{39}H_{55}N_8O_{10}$, 795.4036 $[M + H]^+$, $C_{39}H_{54}N_8O_{10}Na$, *m/z* 817.3855 $[M + Na]^+$).

Compound **syn-1**: white, amorphous powder; ^{1}H NMR data (Pyridine-d_5, 500 MHz, *J* in Hz) δ_H 11.99 (1H), 9.75 (1H), 9.68 (1H), 9.52 (1H), 9.31 (1H), 9.06 (1H), 9.00 (1H), 8.86 (1H), 7.73 (1H), 7.56 (2H), 7.37 (2H), 7.32 (2H), 7.24 (2H), 7.09 (1H), 5.33 (1H), 5.12 (4H), 4.99 (1H), 4.60 (1H), 4.44 (1H), 4.42 (1H), 4.32 (1H), 4.13 (1H), 3.79 (1H), 3.77 (1H), 3.66 (1H), 3.06 (1H), 2.56 (1H), 2.25 (1H), 1.60 (3H), 1.01 (3H), 0.96 (3H), 0.90 (3H), 0.84 (3H); ^{13}C NMR (Pyridine-d_5, 125 MHz) δ_C 174.1 (C), 173.8 (C), 173.6 (C), 173.0 (C), 172.9 (C), 172.7 (C), 171.3 (C), 138.9 (C), 137.9 (C), 130.0 (CH×2), 129.2 (CH×2), 128.6 (C), 127.3 (CH), 125.2 (CH), 122.2 (CH), 119.6 (CH), 119.3 (CH), 112.4 (CH), 111.0 (C), 62.6 (CH_2), 62.4 (CH_2), 61.8 (CH), 61.3 (CH), 57.9 (CH), 57.2 (CH), 56.5 (CH), 56.2 (CH), 50.3 (CH), 37.9 (CH_2), 31.6 (CH), 29.9 (CH), 27.7 (CH_2), 20.2 (CH_3), 20.1 (CH_3), 19.5 (CH_3), 19.0 (CH_3), 18.3 (CH_3); (+)-HR-ESI-MS *m/z* 777.3930 $[M + H]^+$, *m/z* 799.3751 $[M + Na]^+$ (calcd. for $C_{39}H_{53}N_8O_9$, 777.3930 $[M + H]^+$, $C_{39}H_{52}N_8O_9Na$, *m/z* 799.3749 $[M + Na]^+$).

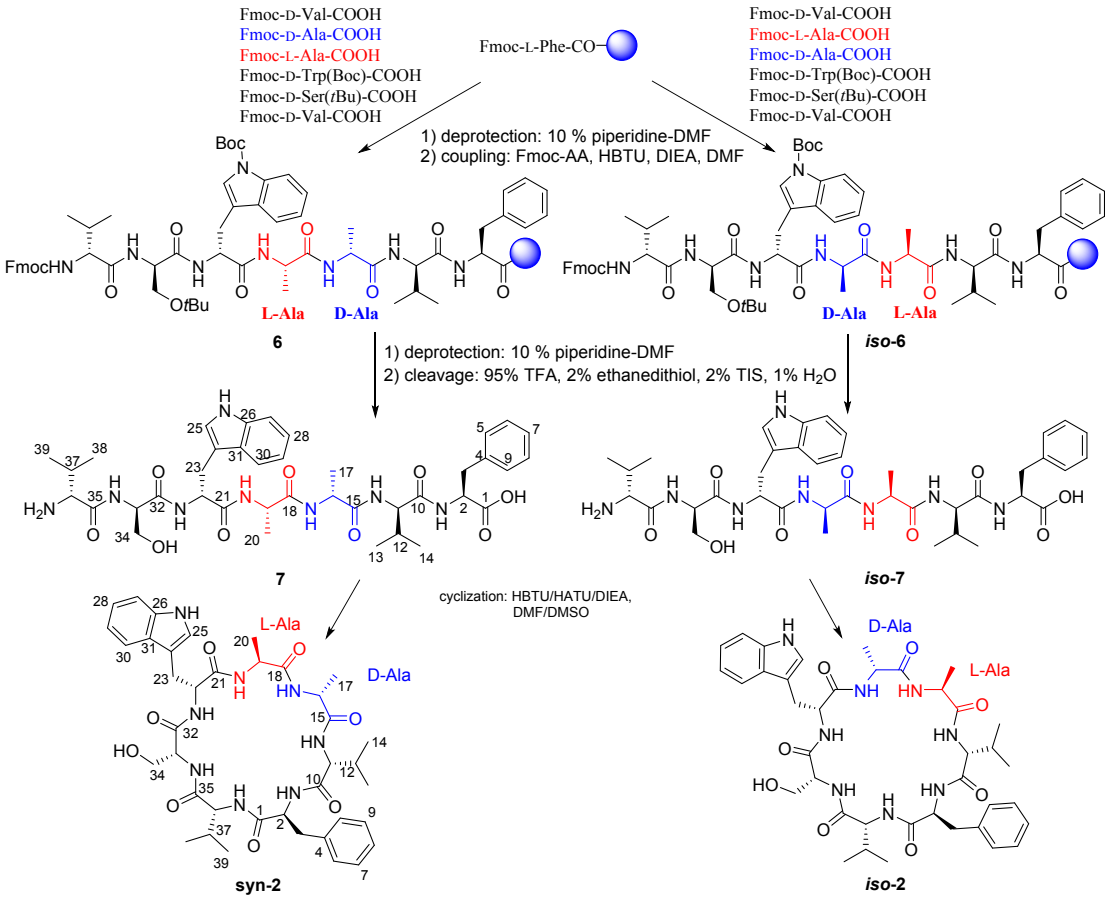
Compound ***iso*-1**: white, amorphous powder; ^{1}H NMR (prydine-d_5, 500 MHz, *J* in Hz) δ_H 11.90 (1H), 10.23 (1H), 9.64 (1H), 9.59 (1H), 9.52 (1H), 8.33 (1H), 8.31 (1H), 8.02 (1H), 7.89 (1H), 7.48 (1H), 7.46 (1H), 7.30-7.27-7.20 (5H), 7.16 (1H), 7.13 (1H), 5.72 (1H), 5.33 (1H), 5.25 (1H), 5.21 (1H), 4.78 (1H), 4.72 (1H), 4.56 (2H), 4.46 (1H), 4.43 (1H), 4.41 (1H), 4.02 (1H), 3.83 (1H), 3.80 (1H), 3.29 (1H), 2.70 (1H), 2.19 (1H), 1.63 (3H), 1.12 (3H), 1.01 (3H), 1.00 (3H), 0.93 (3H); (+)-HR-ESI-MS *m/z* 777.3931 $[M + H]^+$, *m/z* 799.3748 $[M + Na]^+$ (calcd. for $C_{39}H_{53}N_8O_9$, 777.3930 $[M + H]^+$, $C_{39}H_{52}N_8O_9Na$, *m/z* 799.3749 $[M + Na]^+$).

5.2 Total synthesis of asperversiamide B (2)

5.2.1. Retrosynthetic analysis of asperversiamide B (2)



5.2.2. *Cyclo*-[(NH)D-Val–D-Ser–D-Trp–L-Ala–D-Ala–D-Val–L-Phe(CO)] (syn-2) and *cyclo*-[(NH)D-Val–D-Ser–D-Trp–D-Ala–L-Ala–D-Val–L-Phe(CO)] (*iso*-2)



Compounds **syn-2** and ***iso*-2** were synthesized by the same method as that of **syn-1**.

Compound **7**: white, amorphous powder; [α]20 D + 11.9 (*c* 0.24, MeOH); IR (KBr) ν_{max} 3299, 1668, 1522 cm^{-1}; ^{1}H NMR (DMSO-d_6, 500 MHz, *J* in Hz) δ_H 12.76 (1H, s, COOH), 10.80 (1H, s, 25-NH), 8.50 (1H, d, *J* = 7.7 Hz, 33-NH), 8.28 (1H, d, *J* = 8.3 Hz, 2-NH), 8.25 (1H, d, *J* = 7.3 Hz, 22-NH), 8.00-8.10 (3H, overlapped, 19-NH/36-NH$_2$), 7.90 (1H, d, *J* = 7.4 Hz, 16-NH), 7.64 (1H, d, *J* = 9.2 Hz, 11-NH), 7.53 (1H, d, *J* = 7.5 Hz, H-30), 7.31 (1H, d, *J* = 7.5 Hz, H-27), 7.24 (2H, overlapped, H-6/8), 7.22 (2H, overlapped, H-5/9), 7.17 (1H, m, H-7), 7.13 (1H, m, H-25), 7.05 (1H, t, *J* = 7.5 Hz, H-28), 6.96 (1H, t, *J* = 7.5 Hz, H-29), 5.17 (1H, br s, OH), 4.51 (1H, dd, *J* = 8.0, 7.3 Hz, H-22), 4.45 (1H, m, H-2), 4.43 (1H, m, H-33), 4.30 (1H, m, H-16), 4.20 (1H, m, H-19), 4.16 (1H, m, H-11), 3.66 (1H, m, H-36), 3.63 (1H, m, Ha-34), 3.56 (1H, dd, *J* = 10.5, 6.2 Hz, Hb-34), 3.12 (1H, m, Ha-23), 3.09 (1H, m, Ha-3), 2.97 (1H, dd, *J* = 14.7, 8.0 Hz, Hb-23), 2.83 (1H, dd, *J* = 13.7, 10.5 Hz, Hb-3), 2.01 (1H, m, H-37), 1.80 (1H, m, H-12), 1.16 (3H, d, *J* = 7.0 Hz, H-17), 1.05 (3H, d, *J* = 7.1 Hz, H-20), 0.88 (3H, d, *J* = 3.9 Hz, H-38), 0.87 (3H, d, *J* = 3.9 Hz, H-39), 0.63 (3H, d, *J* = 6.8 Hz, H-14), 0.56 (3H, d, *J* = 6.8 Hz, H-13); ^{13}C NMR (DMSO-d_6, 125 MHz) δ_C 172.9 (C, C-1), 171.8 (C, C-18), 171.7 (C, C-15), 170.73 (C, C-21), 170.68 (C, C-10), 169.5 (C, C-32), 167.8 (C, C-35), 137.6 (C, C-26), 136.0 (C, C-4), 129.1 (CH, C-5/9), 128.1 (CH, C-6/8), 127.3 (C, C-31), 126.4 (CH, C-7), 123.5 (CH, C-25), 120.8 (CH, C-28), 118.3 (CH, C-30), 118.2 (CH, C-29), 111.3 (CH, C-27), 109.8 (C, C-24), 61.7 (CH$_2$, C-34), 57.21 (CH, C-11), 57.18 (CH, C-36), 54.8 (CH, C-33), 53.9 (CH, C-22), 53.4 (CH, C-2), 48.3 (CH, C-19), 48.1 (CH, C-16), 36.8 (CH$_2$, C-3), 30.8 (CH, C-12), 29.9 (CH, C-37), 27.5 (CH$_2$, C-23), 19.1 (CH$_3$, C-14), 18.3 (CH$_3$, C-17), 18.1 (CH$_3$, C-20), 17.9 (CH$_3$, C-39), 17.6 (CH$_3$, C-38), 17.4 (CH$_3$, C-13); (+)-HR-ESI-MS *m*/*z* 779.4097 [M + H]$^+$ (calcd. for $C_{39}H_{55}N_8O_9$, 779.4087 [M + H]$^+$).

Compound ***iso*-7**: white, amorphous powder; [α]20 D + 7.8 (*c* 0.27 , CH_3OH); IR (KBr) ν_{max} 3305, 1669, 1522 cm^{-1}; ^{1}H NMR (DMSO-d_6, 500 MHz, *J* in Hz) δ_H 12.73 (1H, s, COOH), 10.76 (1H, s, 25-NH), 8.48 (1H, d, *J* = 7.7 Hz, 33-NH), 8.34 (1H, d, *J* = 8.3 Hz, 2-NH), 8.20 (1H, d, *J* = 7.7 Hz, 22-NH), 8.00-8.10 (3H, overlapped, 19-NH/36-NH$_2$), 7.89 (1H, d, *J* = 7.5 Hz, 16-NH), 7.79 (1H, d, *J* = 9.3 Hz, 11-NH), 7.55 (1H, d, *J* = 7.4 Hz, H-30), 7.31 (1H, d, *J* = 7.4 Hz, H-27), 7.24 (2H, overlapped, H-6/8), 7.22 (2H, overlapped, H-5/9), 7.16 (1H, m, H-7), 7.13 (1H, m, H-25), 7.04 (1H, t, *J* = 7.4 Hz, H-28), 6.94 (1H, t, *J* = 7.4 Hz, H-29), 5.20 (1H, br s, OH), 4.55 (1H, dd, *J* = 8.2, 7.7 Hz, H-22), 4.46 (1H, m, H-2), 4.42 (1H, m, H-33), 4.36 (1H, m, H-16), 4.26 (1H, m, H-19), 4.24 (1H, m, H-11), 3.66 (1H, m, H-36), 3.62 (1H, m, Ha-34), 3.57 (1H, dd, *J* = 10.5, 6.2 Hz, Hb-34), 3.19 (1H, m, Ha-23), 3.08 (1H, m, Ha-3), 2.95 (1H, dd, *J* = 14.8, 8.2 Hz, Hb-23), 2.83 (1H, dd, *J* = 13.5, 10.5 Hz, Hb-3), 1.99 (1H, m, H-37), 1.81 (1H, m, H-12), 1.19 (3H, d, *J* = 7.0 Hz, H-17), 1.16 (3H, d, *J* = 7.1 Hz, H-20), 0.87 (3H, d, *J* = 1.5 Hz, H-38), 0.85 (3H, d, *J* = 1.5 Hz, H-39), 0.62 (3H, d, *J* = 6.7 Hz, H-14), 0.53 (3H, d, *J* = 6.7 Hz, H-13); ^{13}C NMR (DMSO-d_6, 125 MHz) δ_C 172.9 (C, C-1), 172.0 (C, C-15), 171.7 (C, C-18), 170.9 (C, C-21), 170.6 (C, C-10), 169.7 (C, C-32), 167.8 (C, C-35), 137.6 (C, C-26), 136.1 (C, C-4), 129.1 (CH, C-5/9), 128.1(CH, C-6/8), 127.3 (C, C-31), 126.4 (CH, C-7), 123.5 (CH, C-25), 120.8 (CH, C-28), 118.4 (CH, C-30), 118.2 (CH, C-29), 111.2 (CH, C-27), 109.9 (C, C-24), 61.8 (CH$_2$, C-34), 57.2 (CH, C-36), 56.9 (CH, C-11), 54.7 (CH, C-33), 53.5 (CH, C-22), 53.5 (CH, C-2), 48.6 (CH, C-19), 48.3 (CH, C-16), 36.9 (CH$_2$, C-3), 30.9 (CH, C-12), 29.9 (CH, C-37), 27.3 (CH$_2$, C-23), 19.1 (CH$_3$, C-14), 18.9 (CH$_3$, C-17), 18.3 (CH$_3$, C-39), 18.0 (CH$_3$, C-20), 17.6 (CH$_3$, C-38), 17.2 (CH$_3$, C-13); (+)-HR-ESI-MS *m*/*z* 779.4100 [M + H]$^+$ (calcd. for $C_{39}H_{55}N_8O_9$, 779.4087 [M + H]$^+$).

Compound **syn-2**: white, amorphous powder; ^{1}H NMR (Pyridine-d_5, 500 MHz, *J* in Hz) δ_H 11.99 (1H), 9.71 (2H), 9.59 (1H), 9.29 (1H), 9.14 (1H), 9.00 (1H), 8.64 (1H), 7.71 (1H), 7.60 (1H), 7.44 (1H), 7.41 (2H), 7.30 (2H), 7.27 (2H), 7.11 (1H), 5.36 (1H), 5.10 (2H), 4.99 (1H), 4.91 (1H), 4.87 (1H), 4.67 (1H), 4.41 (1H), 4.33 (1H), 3.72 (1H), 3.81 (1H), 3.60 (1H), 3.06 (1H), 2.52 (1H), 2.27 (1H), 1.58 (3H), 1.36 (3H), 1.04 (3H), 1.00 (3H), 0.89 (3H), 0.83 (3H); ^{13}C NMR (DMSO-d_6, 125 MHz) δ_C 173.9 (C), 173.8 (C), 173.6 (C), 173.0

(C), 172.9 (C), 172.9 (C), 172.8 (C), 139.1 (C), 138.0 (C), 130.0 (CH×2), 129.3 (CH×2), 128.6 (C), 127.3 (CH), 125.2 (CH), 122.3 (CH), 119.7 (CH), 119.4 (CH), 112.5 (CH), 111.1 (C), 62.8 (CH_2), 62.1 (CH), 61.7 (CH), 57.7 (CH), 56.6 (CH), 56.1 (CH), 50.6 (CH), 50.1 (CH), 38.0 (CH_2), 31.9 (CH), 29.9 (CH), 27.8 (CH_2), 20.2 (CH_3×2), 19.5 (CH_3), 19.1 (CH_3), 18.3 (CH_3), 17.5 (CH_3); (+)-HR-ESI-MS *m/z* 761.3971 $[M + H]^+$, *m/z* 783.3795 $[M + Na]^+$ (calcd. for $C_{39}H_{53}N_8O_8$, *m/z* 761.3981 $[M + H]^+$, $C_{39}H_{52}N_8O_8Na$, *m/z* 783.3800 $[M + Na]^+$).

Compound ***iso*-2**: white, amorphous powder; ^1H NMR (prydine-d_5, 500 MHz, *J* in Hz) δ_H 12.02 (1H), 10.08 (1H), 9.53 (1H), 9.30 (1H), 8.85-8.87 (2H), 8.26 (1H), 8.16 (1H), 7.84 (1H), 7.65 (1H), 7.54 (1H), 7.30-7.25 (5H), 7.15 (2H), 5.18-5.12 (2H) 5.03-4.97 (2H), 4.77 (1H), 4.71 (1H), 4.44 (1H), 4.39 (1H), 3.73 (1H), 3.68 (1H), 3.63 (1H), 3.43 (1H), 3.31 (1H), 2.39 (1H), 2.21 (1H), 1.69 (3H), 1.63 (3H), 0.98 (3H), 0.91 (3H), 0.77 (6H); (+)-HR-ESI-MS *m/z* 761.3974 $[M + H]^+$, *m/z* 783.3801 $[M + Na]^+$ (calcd. for $C_{39}H_{53}N_8O_8$, *m/z* 761.3981 $[M + H]^+$, $C_{39}H_{52}N_8O_8Na$, *m/z* 783.3800 $[M + Na]^+$).

5.3 Cyclization reaction

A solution of linear peptide **5** (1.0 mg, 1.26 μmol) in solvent (2 mL) was slowly dropped (1 mL/h) into a stirring solvent with coupling reagent and DIEA in N_2 protection, then for HPLC analysis. The results were summarized in table S3.

6. Bioactivity assay

The bioactivity of compounds **1**–**3**, **syn-1**, ***iso*-1**, **syn-2**, ***iso*-2**, **5**, ***iso*-5**, **7**, and ***iso*-7** against *Mycobacterium marinum* was conducted using a broth dilution method.[1] These compounds were dissolved in DMSO to give 3200 μg/mL stock solutions. The stock solutions were then serially diluted to concentrations of 0.0625–128 μg/mL with MH broth or 7H9 broth (added with 0.2% glycerol, 0.05% Tween 80). DMSO in MH broth or 7H9 broth was used as a negative control, and broth-containing bacteria was used as positive control. All experiments were performed in triplicate with rifampicin, streptomycin, and isoniazid as control agents.

The anti-TB activity of compounds **1**–**3**, **syn-1**, ***iso*-1**, **syn-2**, ***iso*-2**, **5**, ***iso*-5**, **7**, and ***iso*-7** against *M. tuberculosis* H37Rv were also tested using the same method as that of against *M. marinum*.

(1) CLSI (Clinical and Laboratory Standards Institute). Performance standards for antimicrobial susceptibility testing; nineteenth informational supplement. M100-S19 (Wayne, 2009).

Table S1. NMR data of asperversiamide A (**1**). [a]

No.	δ_H (*J* in Hz)	δ_C	HMBC
1		173.1	
2	5.34 (1H, m)	56.2	4
3a	3.08 (1H, dd, *J* = 16.0, 10.0 Hz)	38.0	1, 5, 9
3b	3.75(1H, dd, *J* = 16.0, 6.0 Hz)		
4		138.9	
5/9	7.38 (2H, overlapped)	129.2	
6/8	7.32 (2H, overlapped)	130.0	
7	7.25 (1H, overlapped)	127.3	
2-NH	9.68 (1H, d, *J* = 6.0 Hz)		3, 10
10		172.9	
11	4.32 (1H, dd, *J* = 8.0, 3.5 Hz)	61.8	13, 14
12	2.27 (1H, m)	29.9	10
13	0.83 (3H, d, *J* = 7.0 Hz)	19.5	11
14	0.89 (3H, d, *J* = 7.0 Hz)	20.1	11
11-NH	9.08 (1H, d, *J* = 3.5 Hz)		15, 12
15		173.8	
16	5.10 (1H, overlapped)	50.3	
17	1.60 (3H, d, *J* = 6.5 Hz)	18.3	15
16-NH	8.86 (1H, d, *J* = 9.0 Hz)		17, 18
18		171.3	
19	5.10 (1H, overlapped)	56.6	
20a	4.14 (1H, m)	62.6	18
20b	4.43 (1H, overlapped)		
19-NH	9.77 (1H, d, *J* = 7.5 Hz)		20, 21
21		174.2	
22	5.10 (1H, overlapped)	57.8	24
23a	3.66 (1H, dd, *J* = 14.0, 8.0 Hz)	27.7	21, 25, 31
23b	3.78 (1H, dd, *J* = 14.0, 7.0 Hz)		
24		138.0	
25	7.58 (1H, overlapped)	125.2	26, 31
NH	11.99 (1H, s)		
26		128.6	
27	7.56 (1H, overlapped)	112.5	
28	7.09 (1H, t, *J* = 7.5 Hz)	119.6	26
29	7.25 (1H, overlapped)	122.2	31
30	7.71 (1H, d, *J* = 8.0 Hz)	119.3	24, 26
31		111.0	
22-NH	9.56 (1H, d, *J* = 4.5 Hz)		23, 32
32		173.6	
33	5.10 (1H, overlapped)	57.3	
34a	4.43 (1H, overlapped)	62.7	32
34b	4.60 (1H, m)		

33-NH	9.01 (1H, d, *J* = 6.0 Hz)		34, 35
35		172.7	
36	4.98 (1H, overlapped)	61.4	38,39
37	2.54 (1H, m)	31.6	35
38	0.96 (3H, d, *J* = 6.5 Hz)	20.1	36
39	1.01 (3H, d, *J* = 6.5 Hz)	18.9	36
36-NH	9.30 (1H, d, *J* = 9.5 Hz)		1

[a] Measured in pyridine-d_5, 500 MHz for ^{1}H NMR and 125 MHz for ^{13}C NMR

Table S2. NMR data of asperversiamides B (**2**) and C (**3**). [a]

No.	**2**		**3**	
	δ_H (*J* in Hz)	δ_C	δ_H (*J* in Hz)	δ_C
1		172.9		173.4
2	5.37 (1H, m)	56.2	5.25 (1H, m)	56.7
3a	3.04 (1H, m)	38.0	3.15 (1H, dd, *J* = 13.5, 8.0 Hz)	38.1
3b	3.80 (1H, overlapped)		3.63 (1H, overlapped)	
4		139.1		138.6
5/9	7.33 (2H, overlapped)	130.1	7.33 (2H, overlapped)	130.2
6/8	7.39 (2H, overlapped)	129.3	7.33 (2H, overlapped)	129.3
7	7.27 (1H, overlapped)	127.4	7.26 (1H, overlapped)	127.5
2-NH	9.72 (1H, overlapped)		9.72 (1H, d, *J* = 6.5 Hz)	
10		172.9		172.9
11	4.34 (1H, m)	62.13	4.46 (1H, overlapped)	60.9
12	2.27 (1H, m)	29.9	2.37 (1H, m)	30.5
13	0.83 (3H, d, *J* = 6.5 Hz)	19.5	0.91 (3H, overlapped)	19.9
14	0.89 (3H, d, *J* = 6.5 Hz)	20.2	0.95 (3H, overlapped)	19.4
11-NH	9.14 (1H, d, *J* = 4.0 Hz)		8.75 (1H, overlapped)	
15		173.8		173.5
16	5.10 (1H, overlapped)	50.2	5.13 (1H, overlapped)	50.7
17	1.58 (3H, d, *J* = 6.5 Hz)	18.3	1.62 (3H, d, *J* = 7.0 Hz)	19.09
16-NH	8.64 (1H, d, *J* = 8.0 Hz)		8.90 (1H, overlapped)	
18		173.1		171.0
19	4.87 (1H, overlapped)	50.7	5.13 (1H, overlapped)	57.6
20a	1.36 (3H, d, *J* = 6.0 Hz)	17.6	4.07 (1H, m)	62.6
20b			4.41 (1H, overlapped)	
19-NH	9.72 (1H, overlapped)		9.41 (1H, d, *J* = 7.5 Hz)	
21		173.9		173.5
22	4.90 (1H, overlapped)	57.7	4.96 (1H, overlapped)	57.5
23a	3.59 (1H, m)	27.8	3.68 (1H, overlapped)	27.6
23b	3.74 (1H, overlapped)		3.83 (1H, dd, *J* = 14.5, 7.5 Hz)	
24		138.0		138.0
25	7.46 (1H, overlapped)	125.2	7.48 (1H, overlapped)	125.1
NH	11.99 (1H, s)		11.97 (1H, s)	
26		128.7		129.3
27	7.61 (1H, overlapped)	112.5	7.58 (1H, overlapped)	112.5
28	7.10 (1H, m)	119.5	7.11 (1H, t, *J* = 7.5 Hz)	119.7
29	7.27 (1H, overlapped)	122.3	7.26 (1H, overlapped)	122.3
30	7.70 (1H, d, *J* = 8.0 Hz)	119.8	7.72 (1H, d, *J* = 8.0 Hz)	119.5
31		111.1		111.4
22-NH	9.59 (1H, d, *J* = 4.5 Hz)		9.66 (1H, d, *J* = 4.0 Hz)	
32		173.7		174.9
33	5.10 (1H, overlapped)	56.2	4.96 (1H, overlapped)	50.2
34a	4.40 (1H, overlapped)	62.9	1.74 (3H, d, *J* = 7.0 Hz)	18.4

34b	4.65 (1H, m)			
33-NH	9.01 (1H, d, *J* = 6.0 Hz)		8.90 (1H, overlapped)	
35		172.8		172.5
36	4.97 (1H, overlapped)	61.7	4.89 (1H, m)	60.6
37	2.52 (1H, m)	32.0	2.56 (1H, m)	31.0
38	1.00 (3H, d, *J* = 6.0 Hz)	19.2	0.89 (3H, overlapped)	20.2
39	1.04 (3H, d, *J* = 6.0 Hz)	19.5	0.95 (3H, overlapped)	18.6
36-NH	9.30 (1H, d, *J* = 8.5 Hz)		9.16 (1H, d, *J* = 9.5 Hz)	

[a] Measured in pyridine-d_5, 500 MHz for ^{1}H NMR and 125 MHz for ^{13}C NMR

Table S3. Cyclization conditions for linear heptapeptide.

Entry	Coupling reagent	Solvent	Temp. (°C)	t_{react} (h)	Yield (%)	Epimer (%)
1	DMTMM/DIEA	DMF	25	4	14	ND
2	(3:3 eq)			16	14	ND
3	HOAT/DIEA	DMF	25	1.5	ND	ND
4	(3:3 eq)			2.5	ND	ND
5				4	ND	ND
6				6.5	ND	ND
7				20	ND	ND
8				24	ND	ND
9	HOBT/DIEA	DMF	25	2	ND	ND
10	(3:3 eq)			4	ND	ND
11	HATU/DIEA	DMF	25	3	15	ND
12	(3:3 eq)			17	15	ND
13	HBTU/DIEA	DMF	25	1.5	15	ND
14	(3:3 eq)			2.5	15	ND
15				4	15	ND
16				6	15	ND
17				20	15	ND
18				24	15	ND
19		DMSO	25	2	21	ND
20				4	21	ND
21				5.5	21	ND
22				6.5	21	ND
23				24	21	ND
24		CH_2Cl_2	25	1	ND	ND
25				8	ND	ND
26				24	ND	ND
27	HATU/HOAT	CH_2Cl_2/DMF	25	2	ND	ND
28	(3:3 eq)	DMF		2	15	ND
29		DMSO		2	21	ND
30	HATU/HBTU/DIEA	DMF/DMSO	25	I	43	ND
31	(3:3:3 eq)	(9:1)		1	43	ND
32			28	3h	43	ND
33				15	43	ND
34		DMF	25	I	43	ND
35				1	43	ND
36				3	43	ND
37			28	2	43	ND
38				15	43	ND
39	HATU/HBTU/DIEA	DMF	25	I	43	ND
40	(4:4:2 eq)			2	43	ND

41			28	1.5	43	ND
42				16.5	43	ND
43	HATU/HBTU/DIEA	DMSO	30	I	29	ND
44	(3:3:3 eq)			1	29	ND
45			35	2	29	3
46			38	2.5	29	3
47				5.5	29	3
48				24	29	3
49		DMF/DMSO	38	I	29	4
50		(1:1)		1.5	29	5
51				4	29	6
52				6.5	29	5
53				24	29	19
54		DMF/DMSO	38	I	28	7
55		(9:1)		1	28	11
56				4.5	28	16
57				7.5	28	18
58				24	28	20
59			50	2	43	29
60		DMF/DMSO	35	I	41	13
61		(1:9)		2	40	15
62				5	41	15
63				24	41	16

I: Detected immediately after dropping.

ND: Not detected.

Optimum reaction condition: HATU/HBTU/DIEA (3:3:3 eq), DMF/DMSO (9:1), 28^{o}C.

Under the optimum condition, the yields of **syn-1**, ***iso*-1**, **syn-2**, and ***iso*-2** were 43%, 44%, 43%, and 66%.

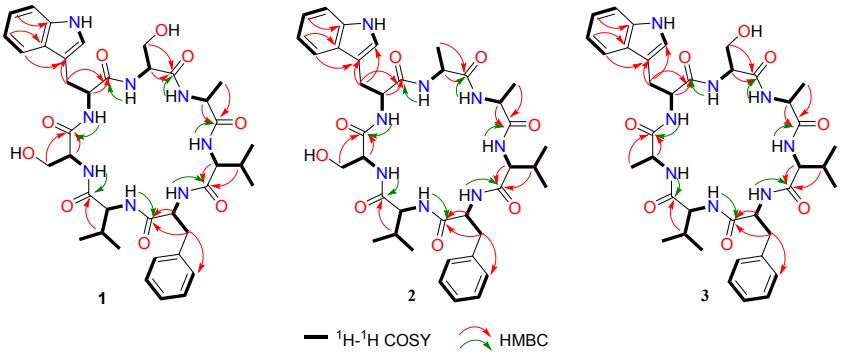


Fig. S1. The ^{1}H-^{1}H COSY and key HMBC correlations of **1**–**3**.

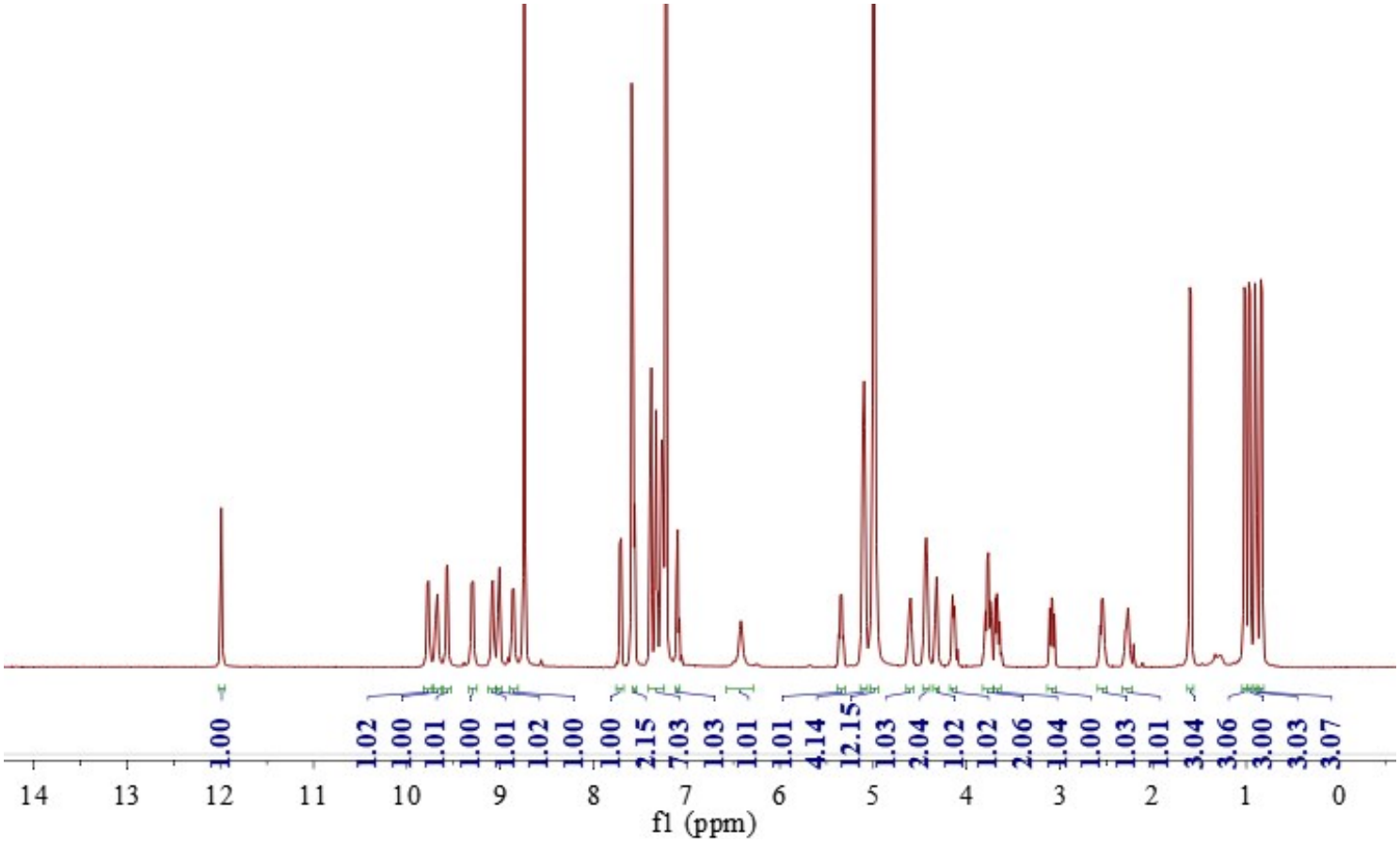


Fig. S2. ^{1}H NMR (500 MHz, pyridine-d_5) spectrum of **1**.

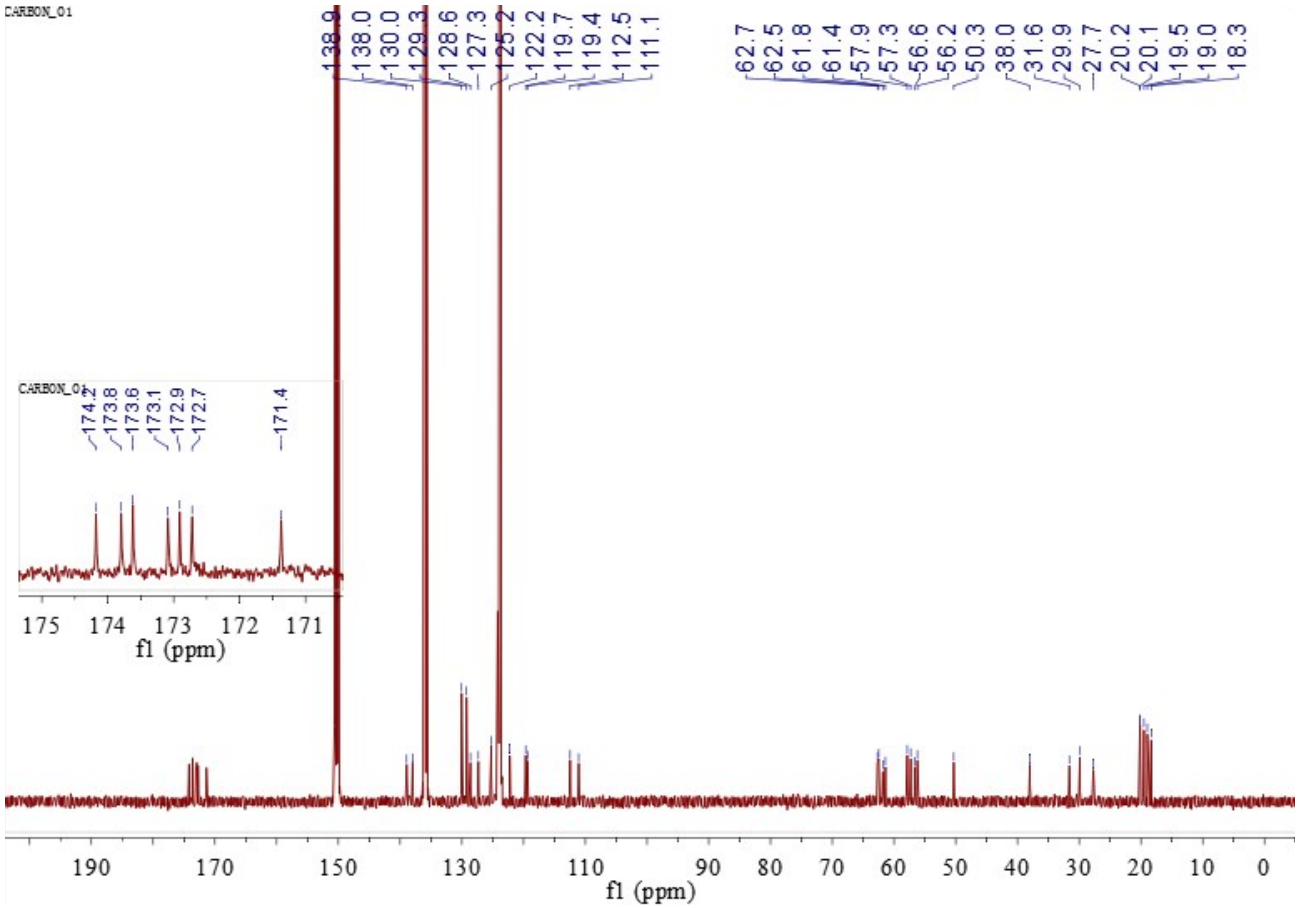


Fig. S3. ^{13}C NMR (125 MHz, pyridine-d_5) spectrum of **1**.

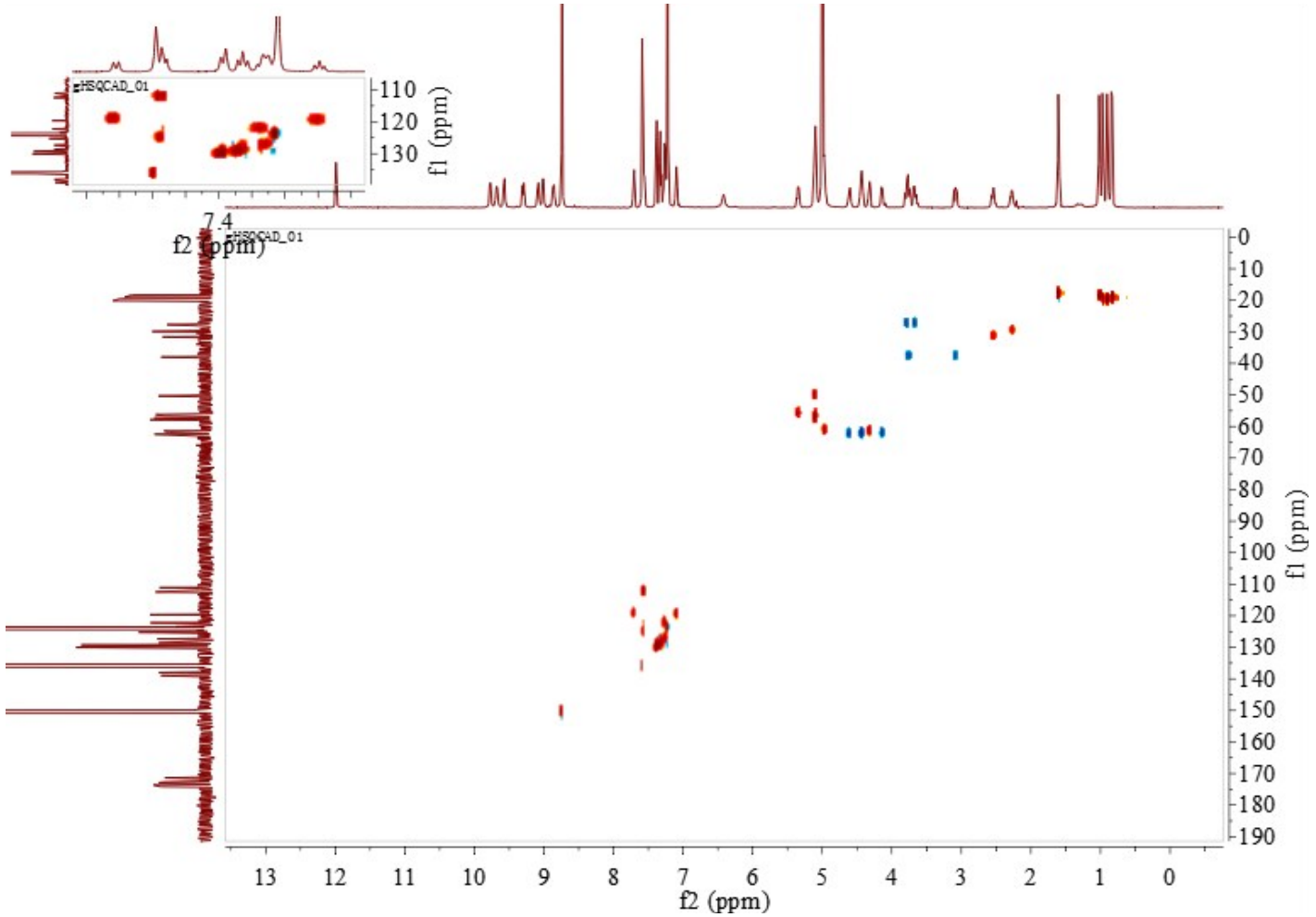


Fig. S4. HSQC (pyridine-d_5) spectrum of **1**.

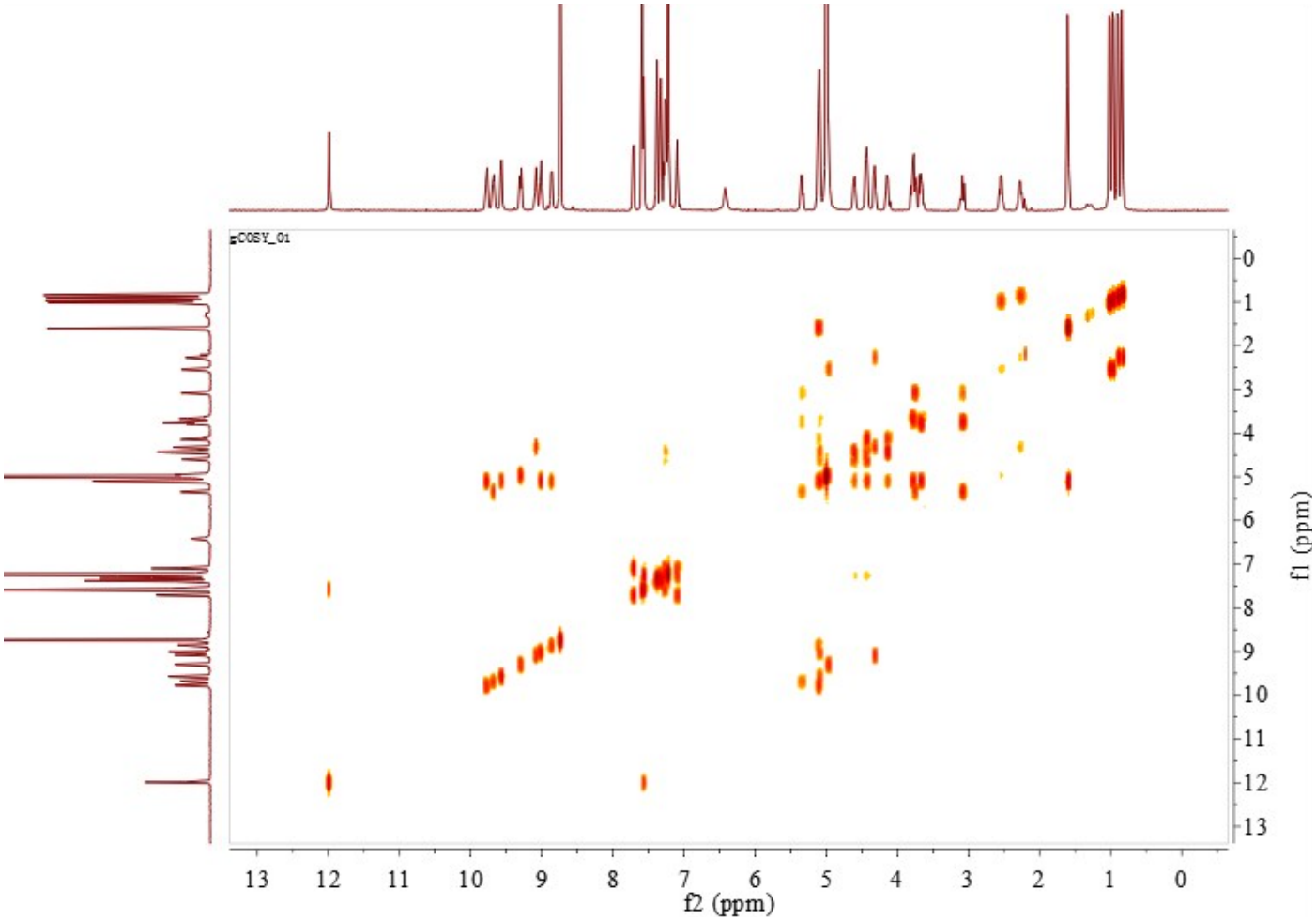


Fig. S5. ^{1}H-^{1}H COSY (pyridine-d_5) spectrum of **1**.

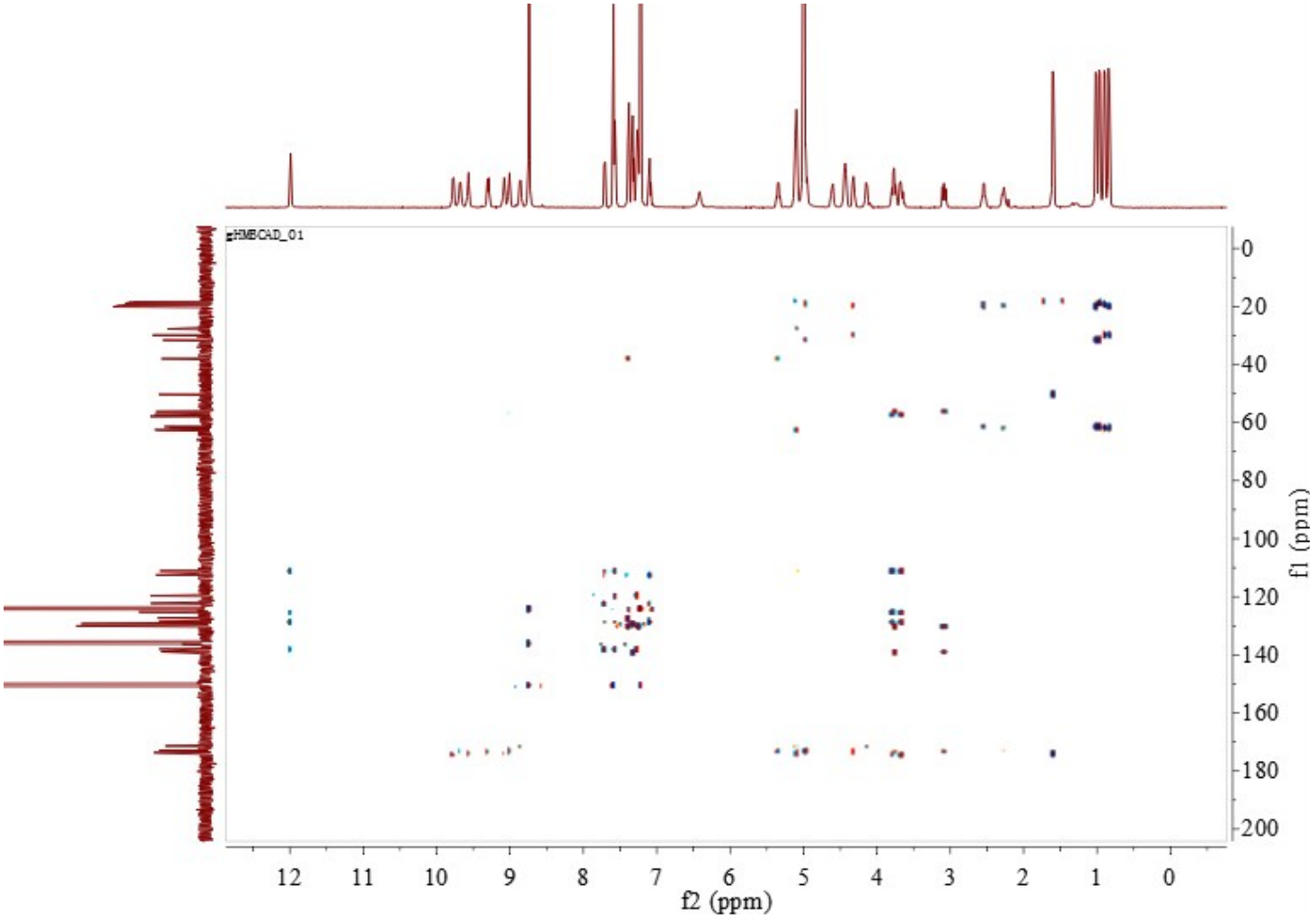


Fig. S6. HMBC (pyridine-d_5) spectrum of **1**.

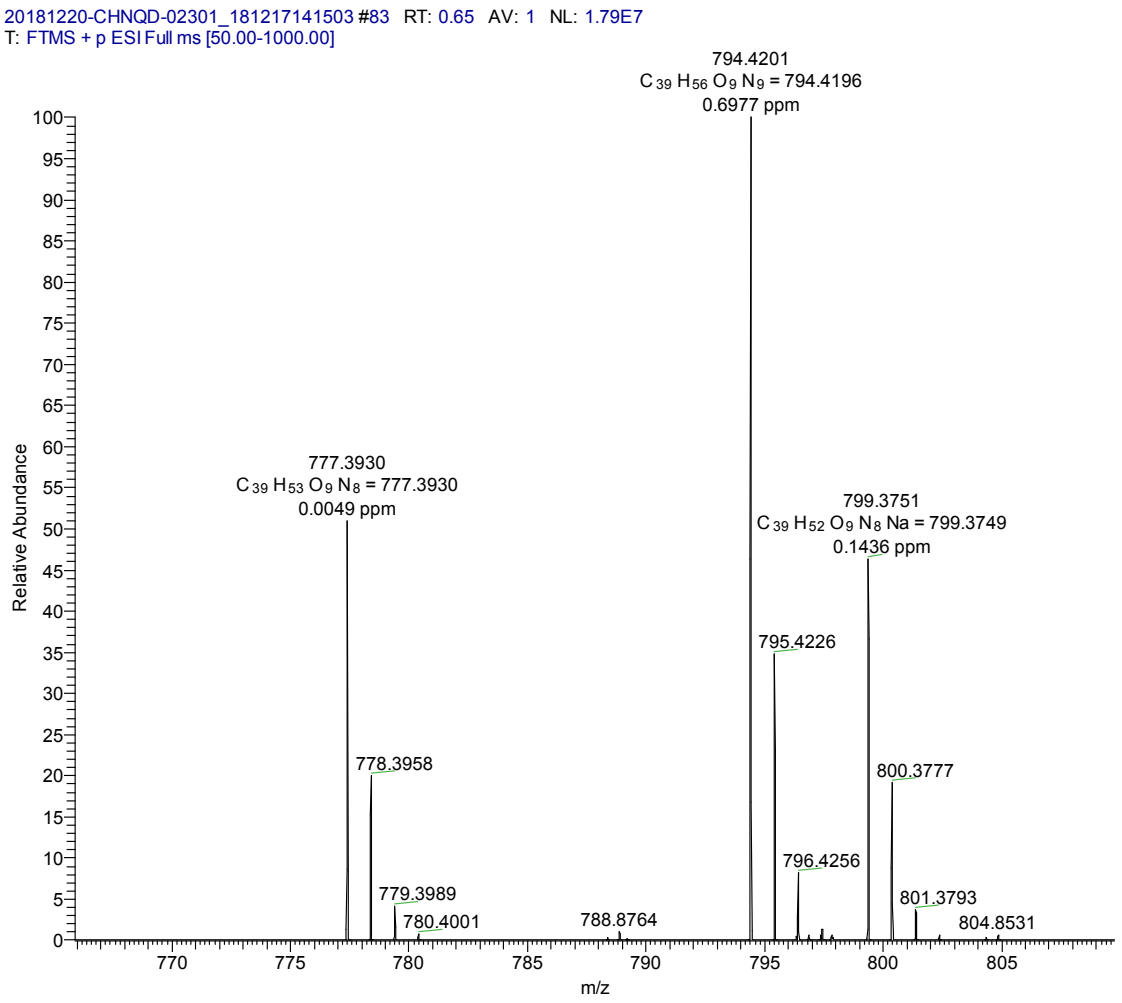


Fig. S7. HR-ESI-MS spectrum of **1**.

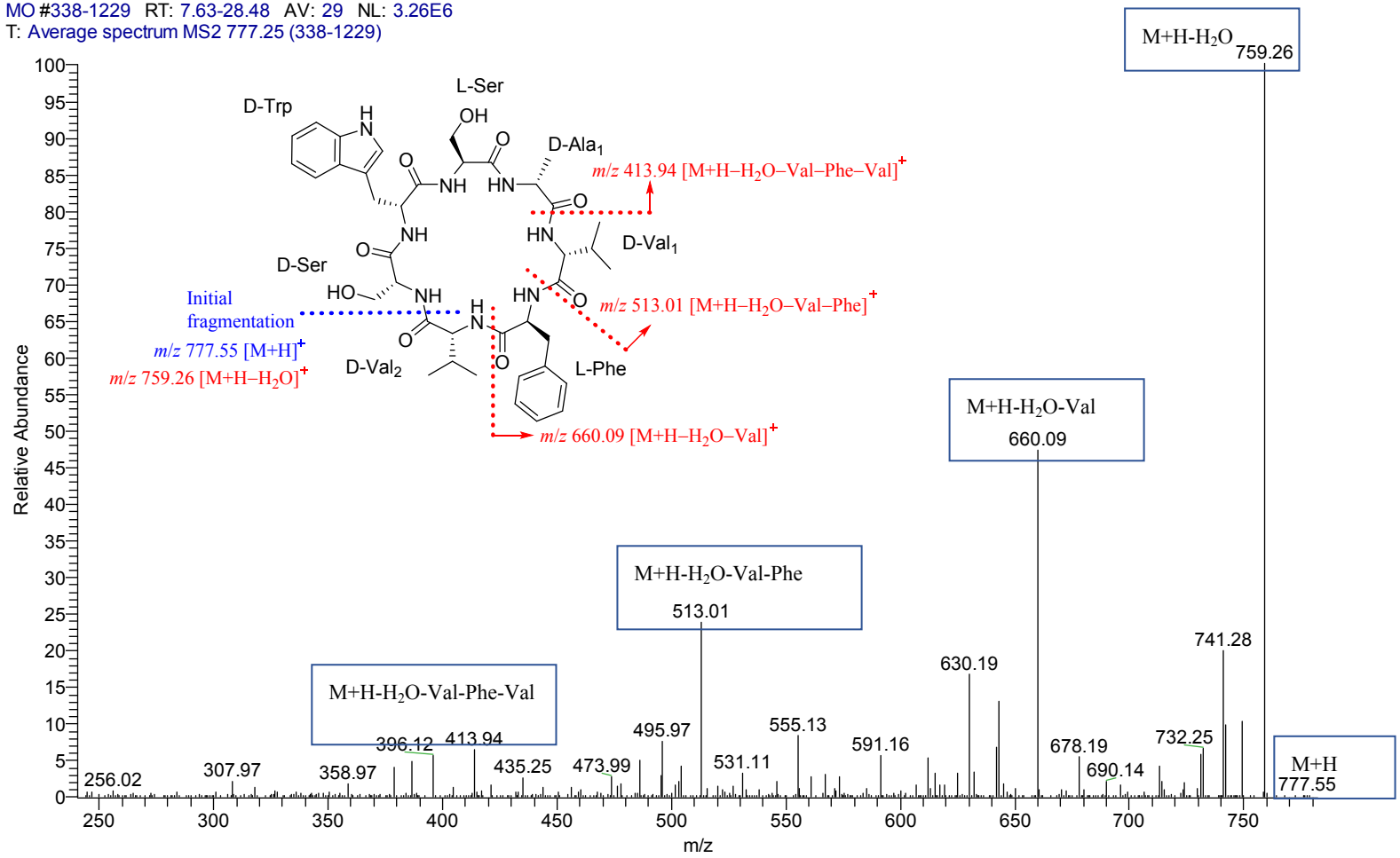


Fig. S8. ESI-MS/MS spectrum of **1**.

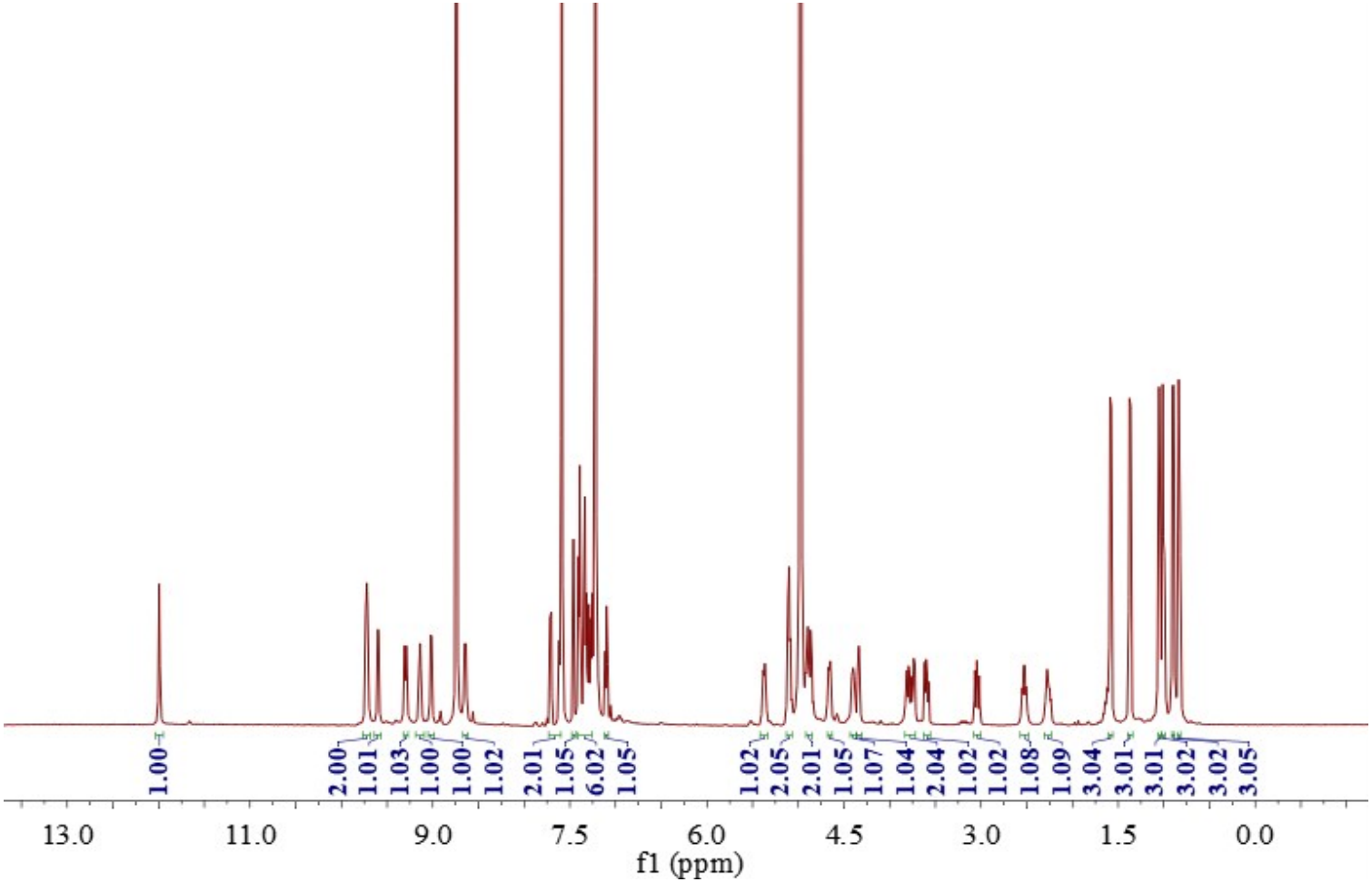


Fig. S9. ^{1}H NMR (500 MHz, pyridine-d_5) spectrum of **2**.

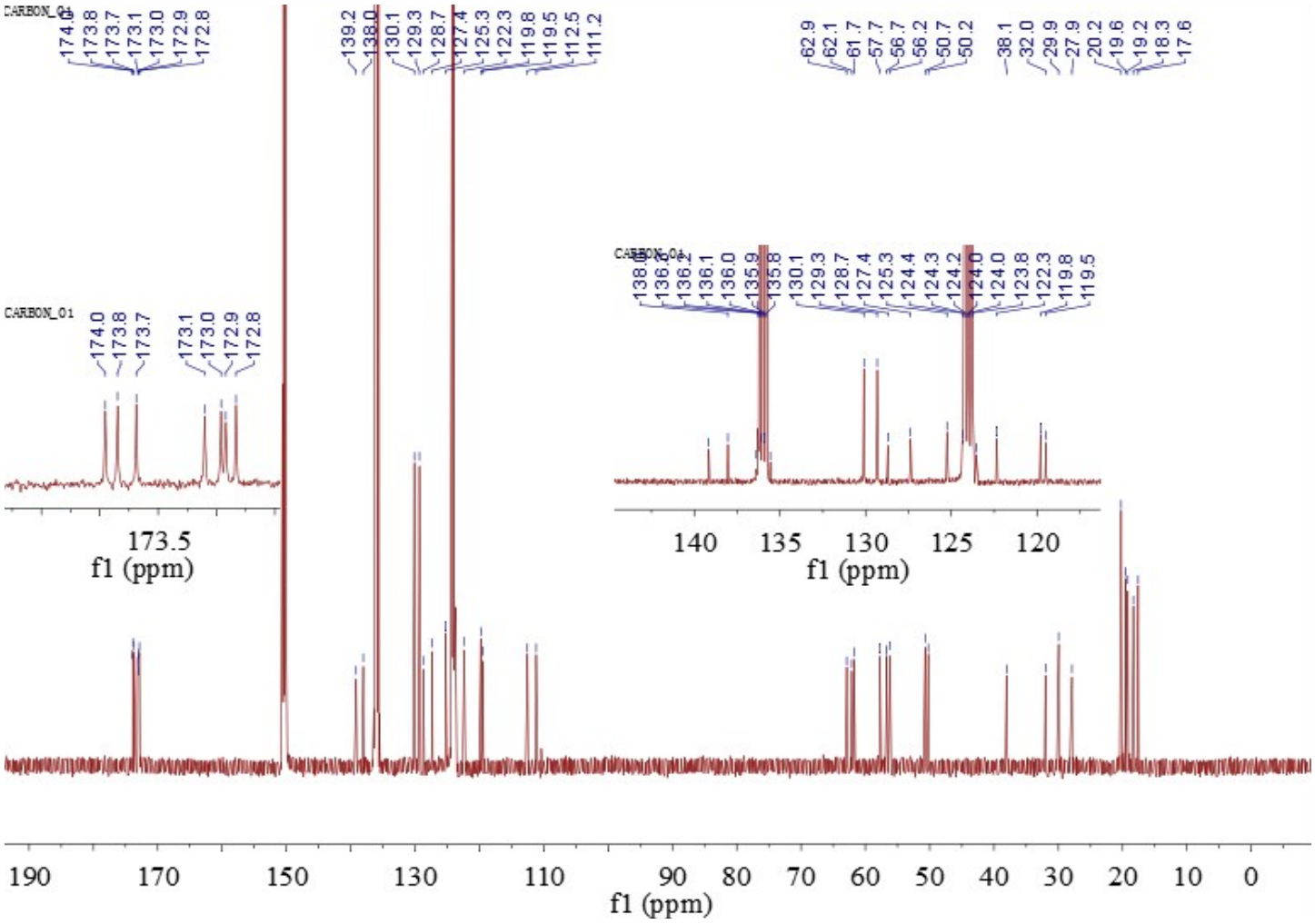


Fig. S10. ^{13}C NMR (125 MHz, pyridine-d_5) spectrum of **2**.

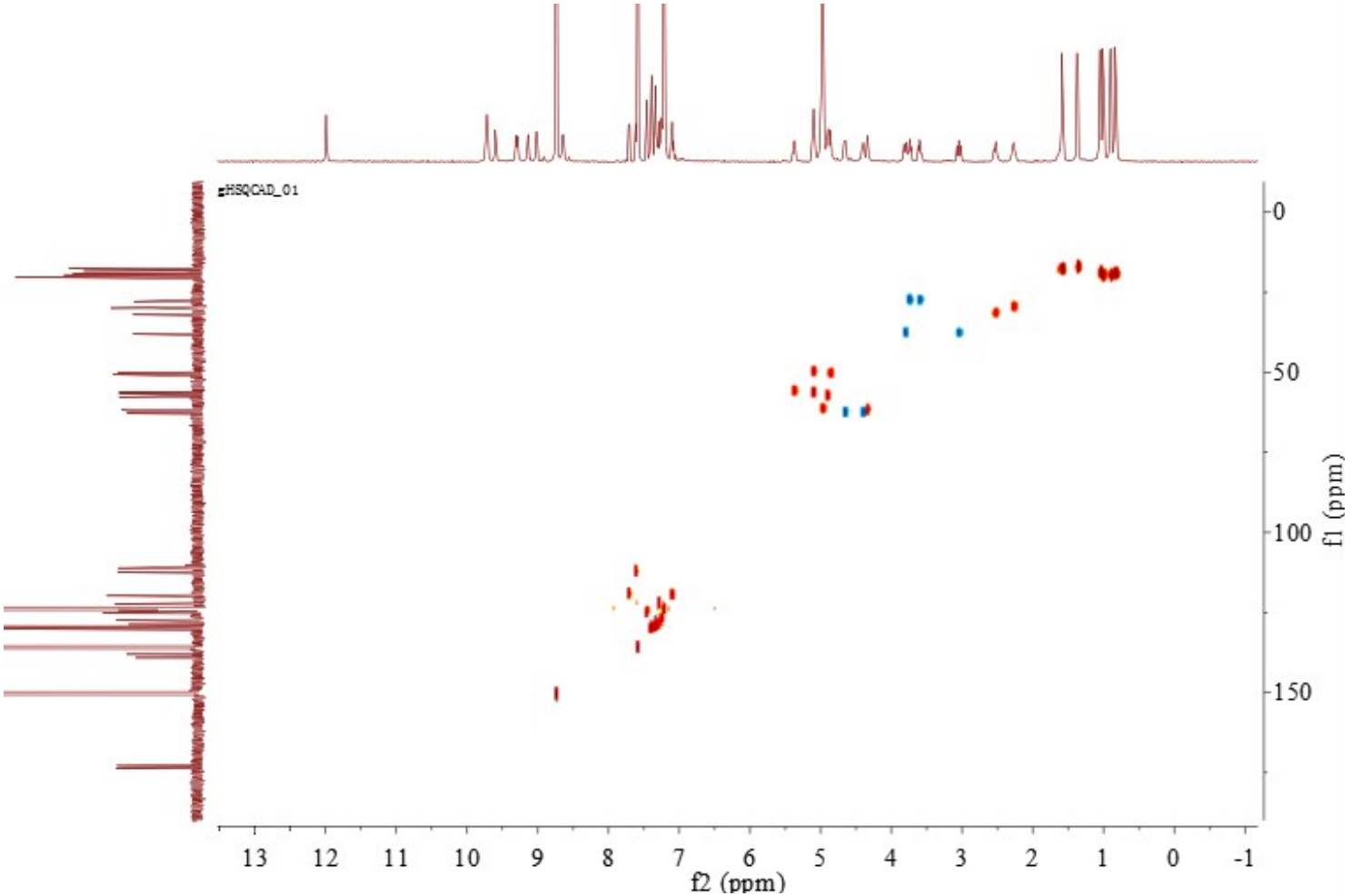


Fig. S11. HSQC (pyridine-d_5) spectrum of **2**.

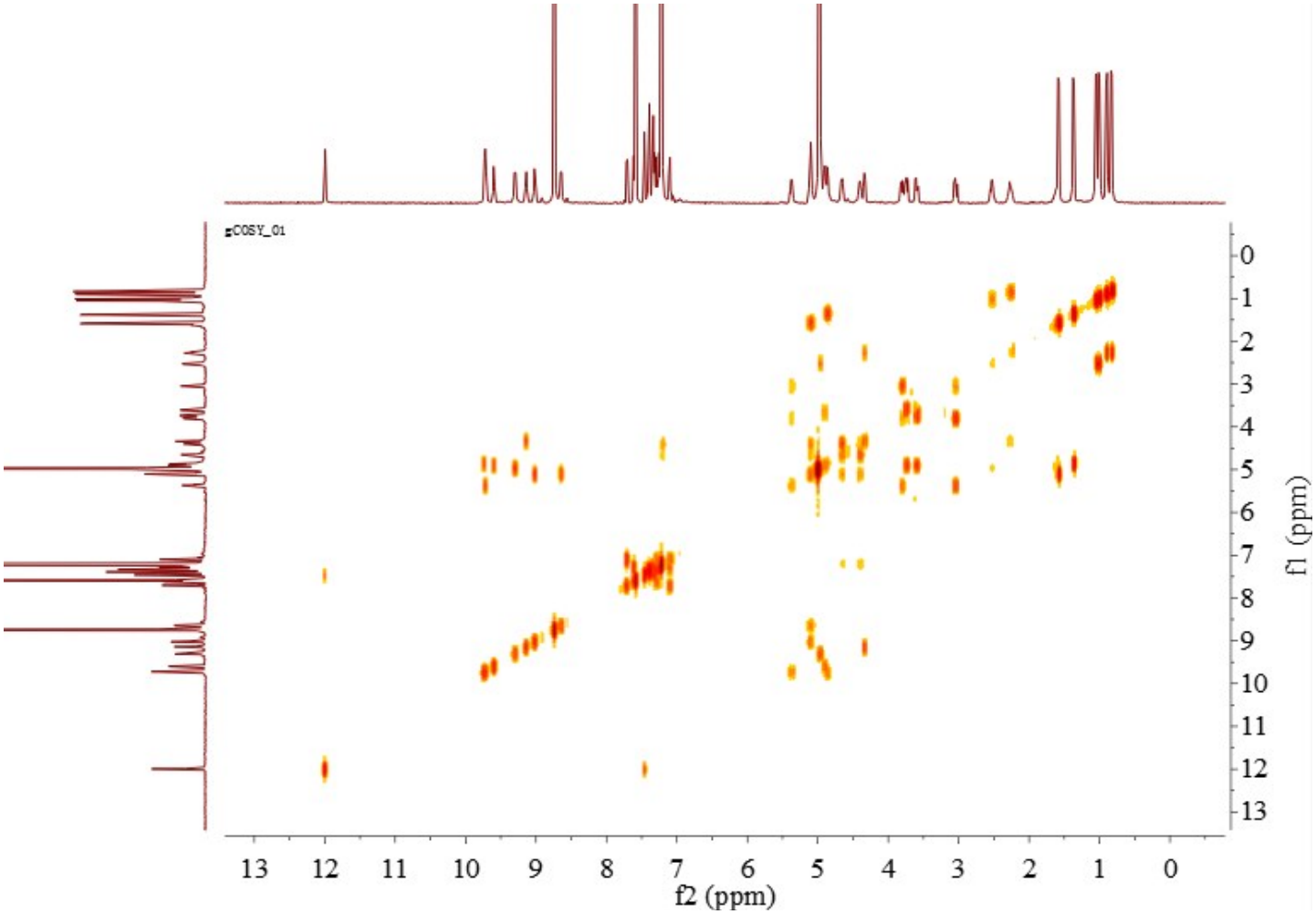


Fig. S12. ^{1}H-^{1}H COSY (pyridine-d_5) spectrum of **2**.

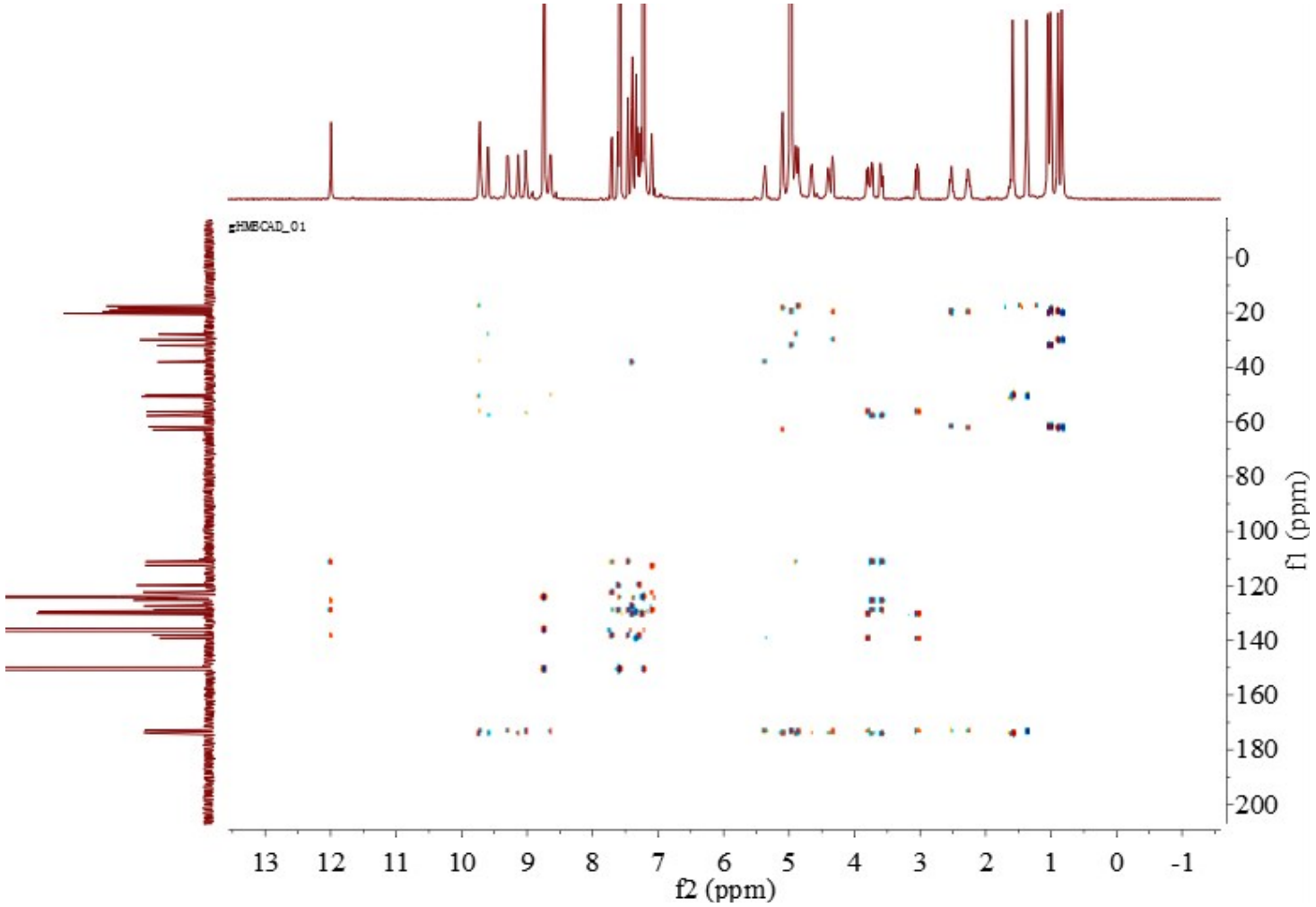


Fig. S13. HMBC (pyridine-d_5) spectrum of **2**.

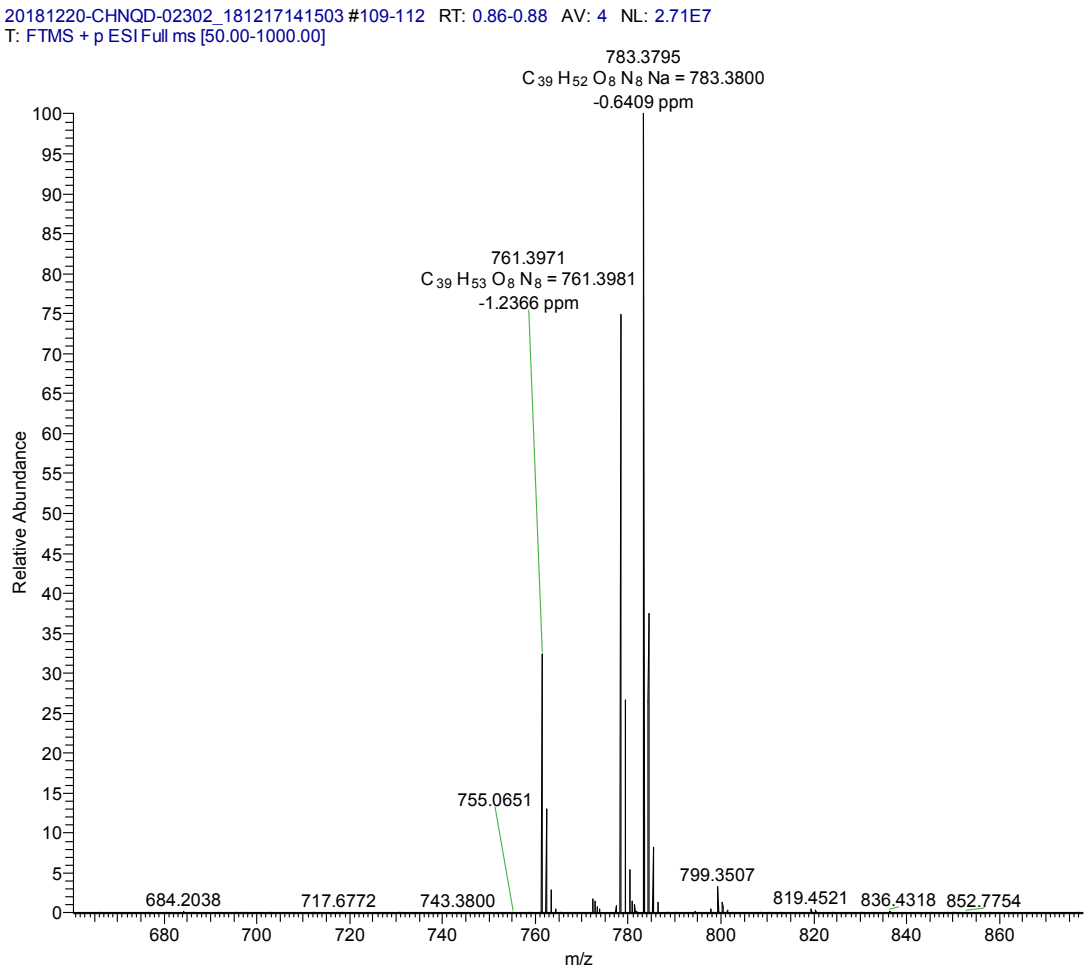


Fig. S14. HR-ESI-MS spectrum of **2**.

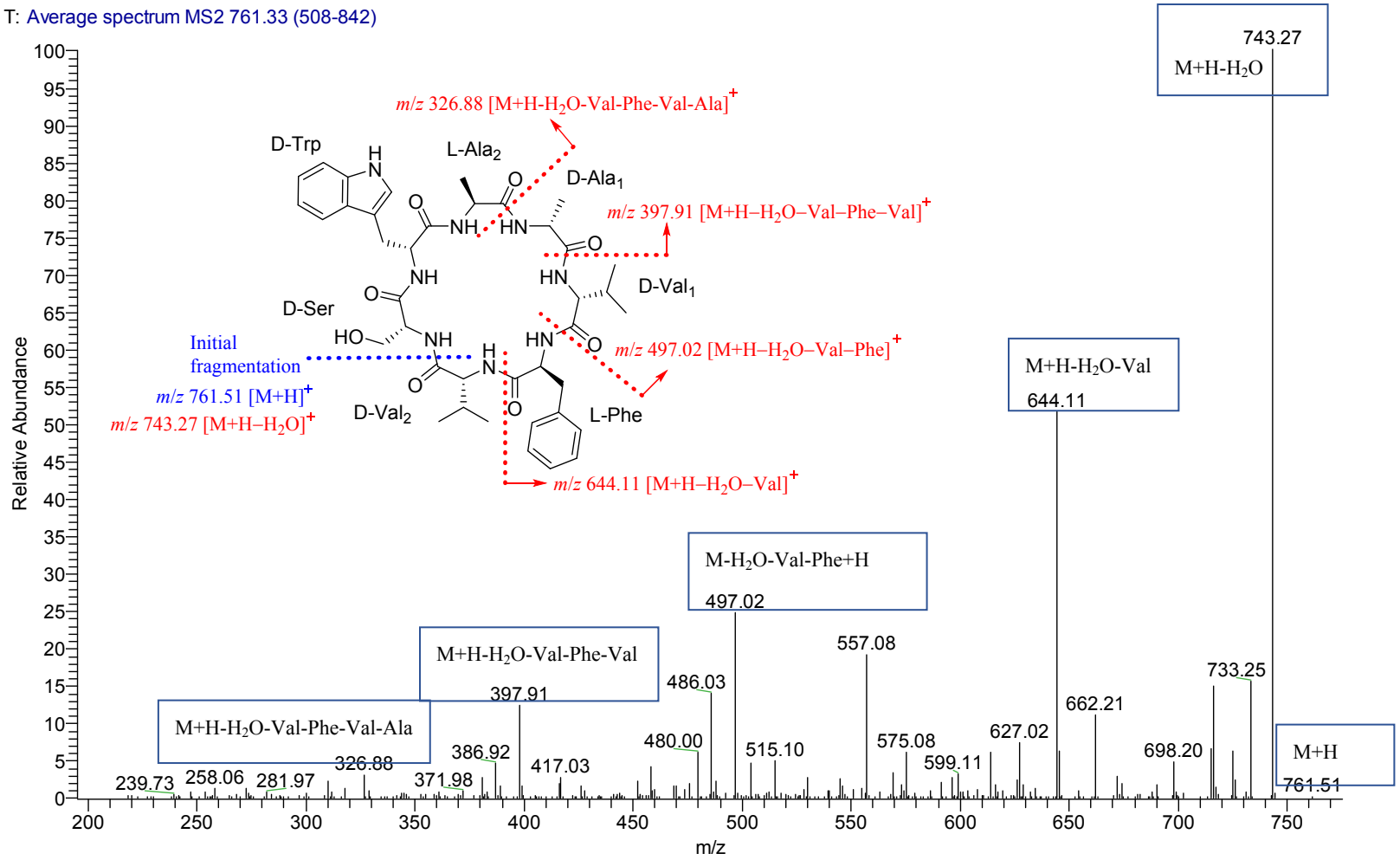


Fig. S15. ESI-MS/MS spectrum of **2**.

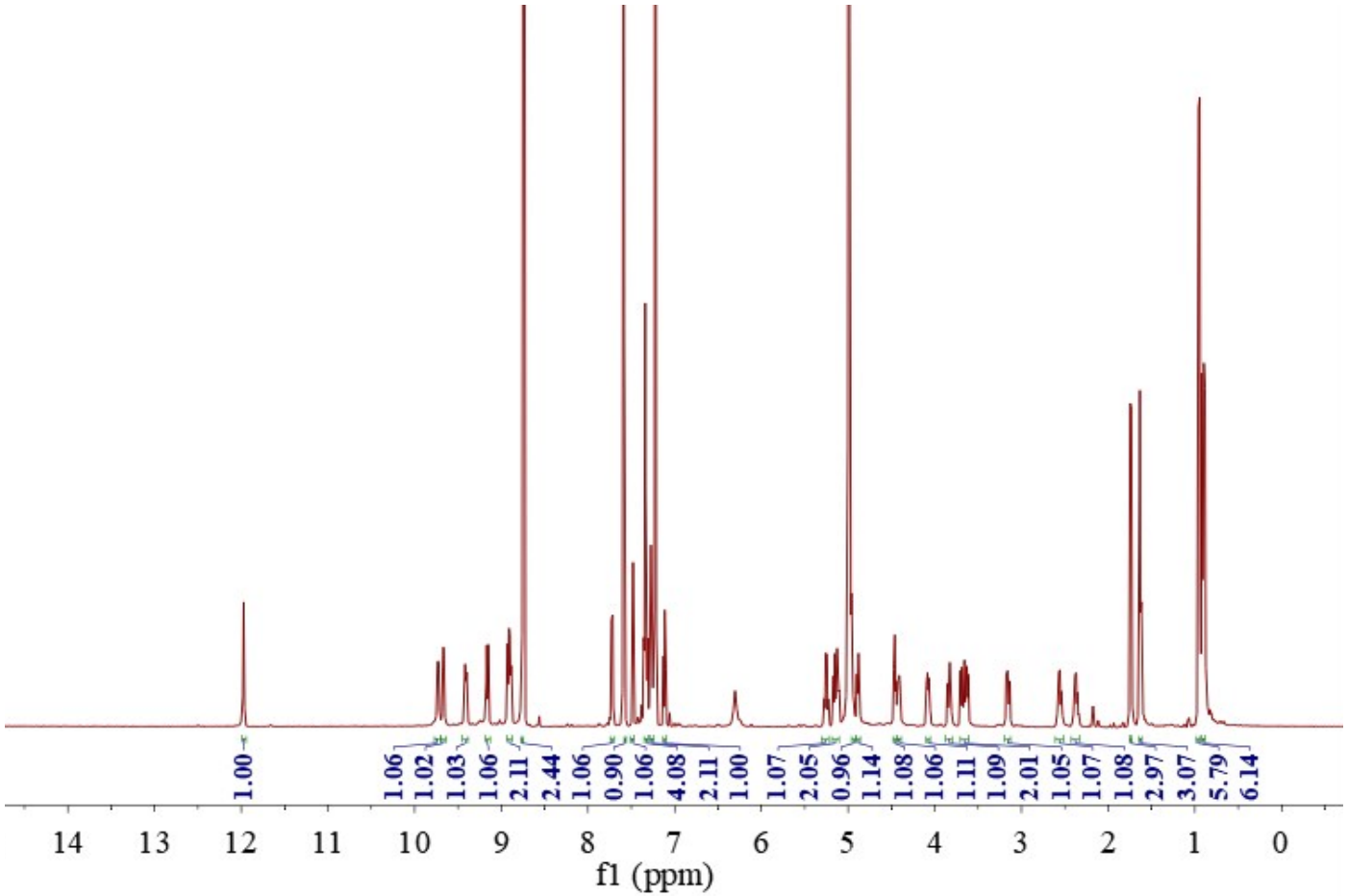


Fig. S16. ^{1}H NMR (500 MHz, pyridine-d_5) spectrum of **3**.

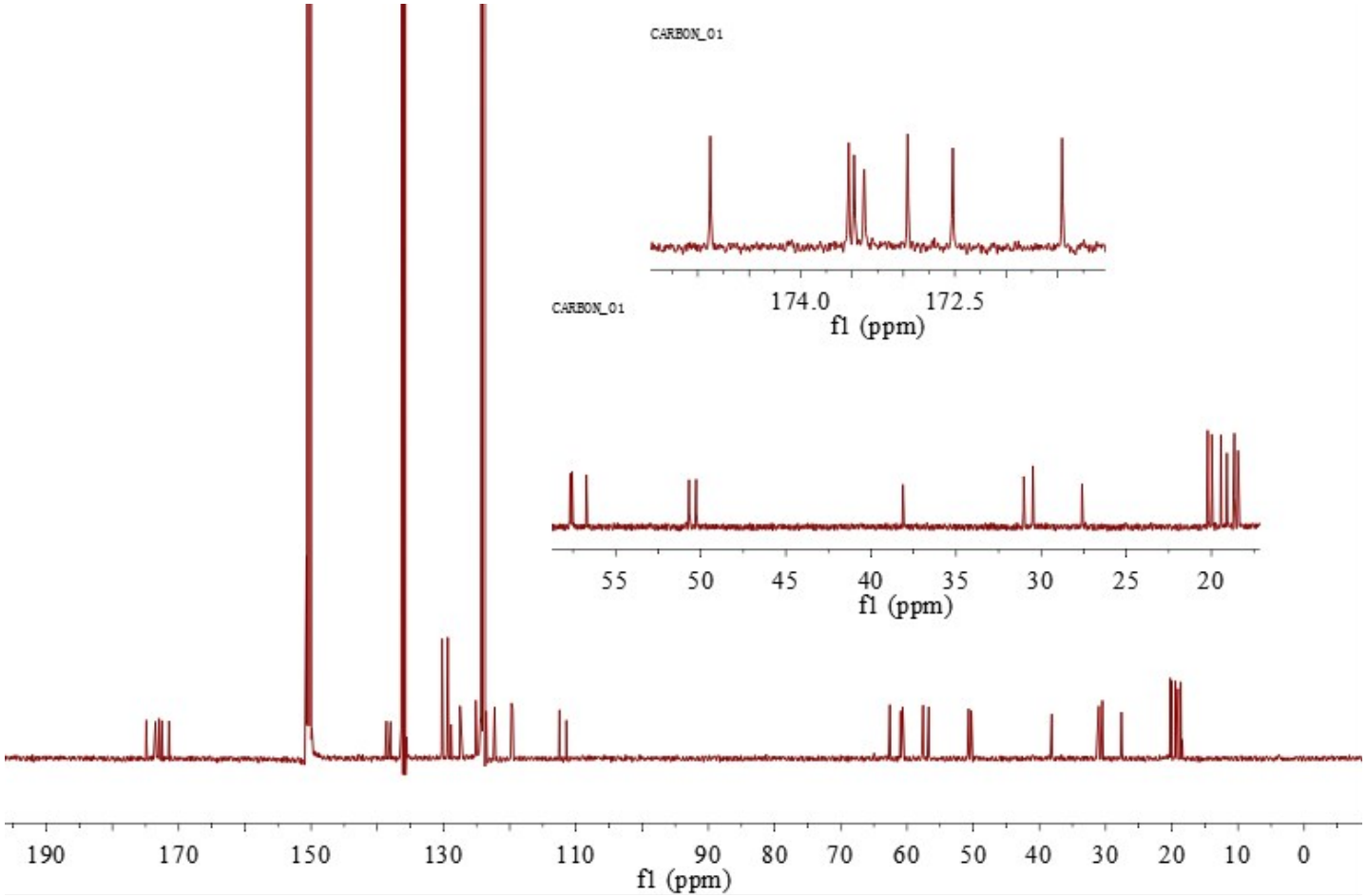


Fig. S17. ^{13}C NMR (125 MHz, pyridine-d_5) spectrum of **3**.

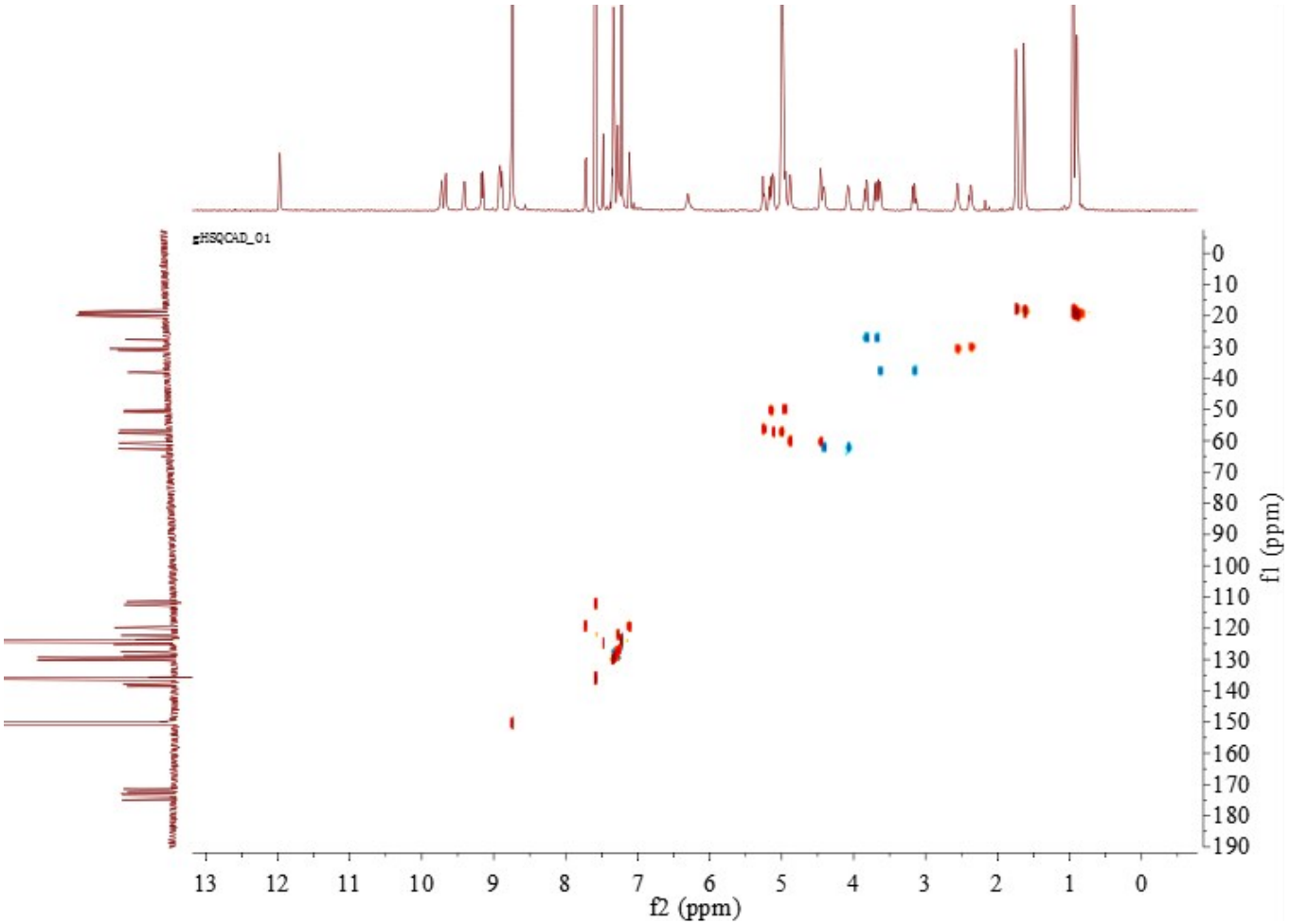


Fig. S18. HSQC (pyridine-d_5) spectrum of **3**.

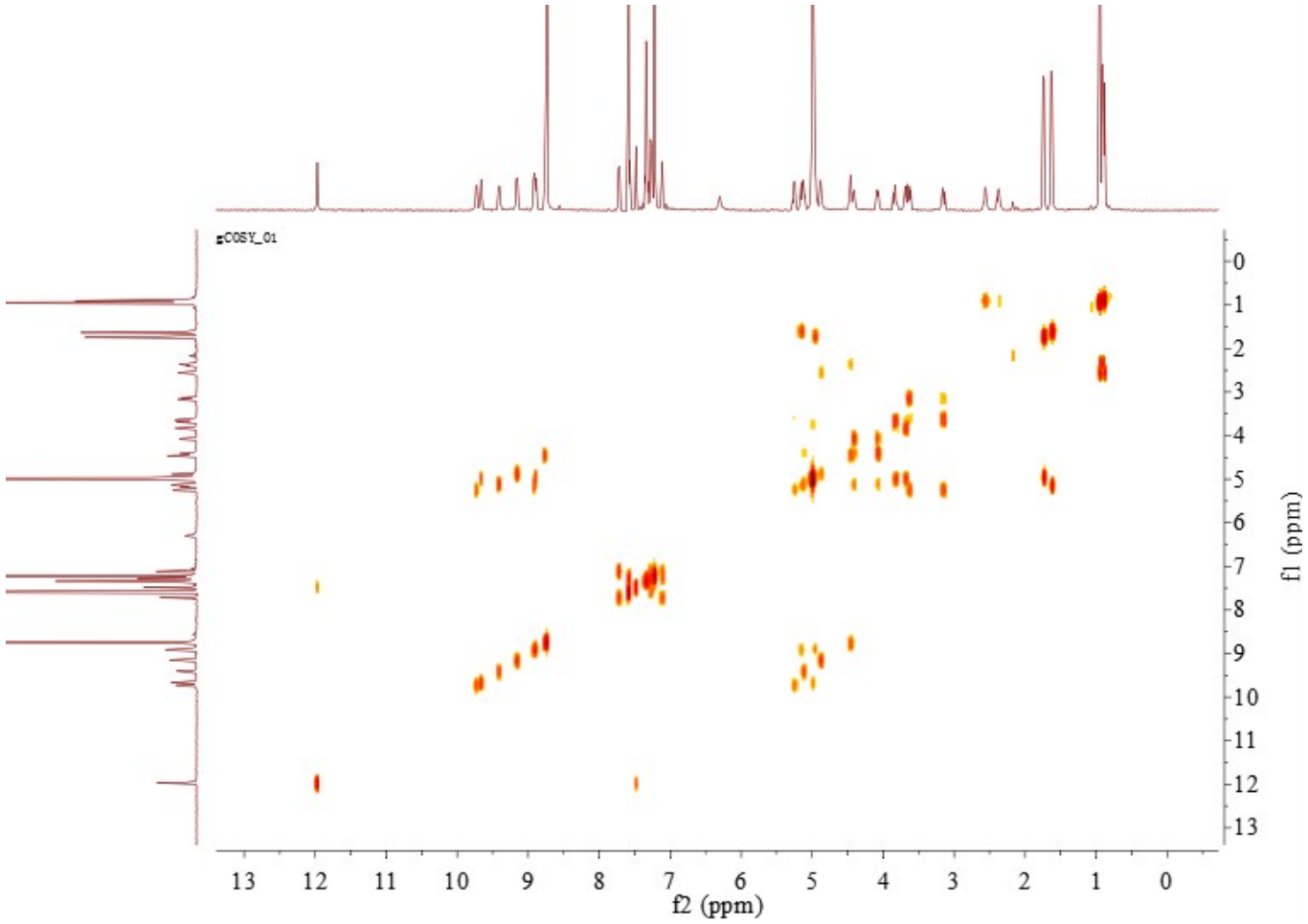


Fig. S19. ^{1}H-^{1}H COSY (pyridine-d_5) spectrum of **3**.

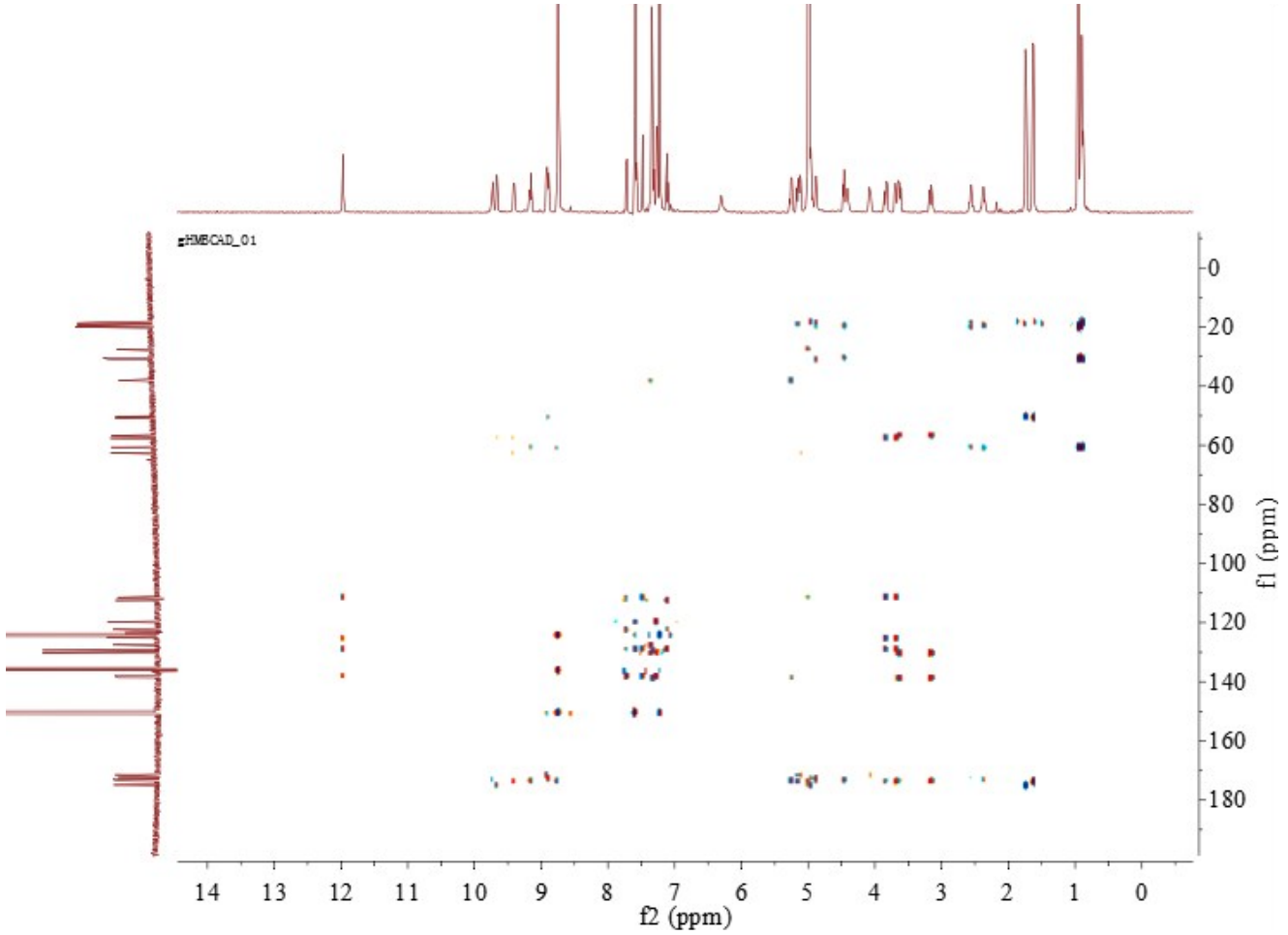


Fig. S20. HMBC (pyridine-d_5) spectrum of **3**.

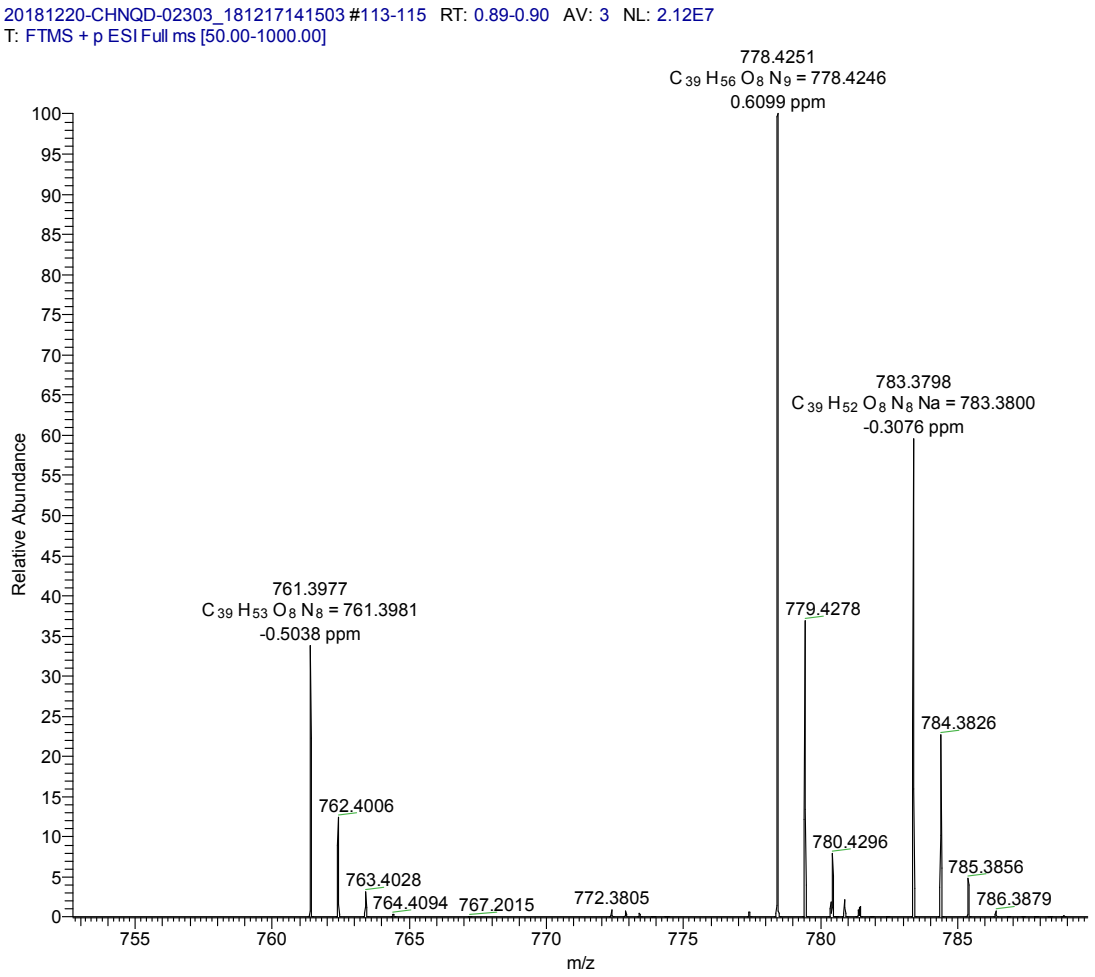


Fig. S21. HR-ESI-MS spectrum of **3**.

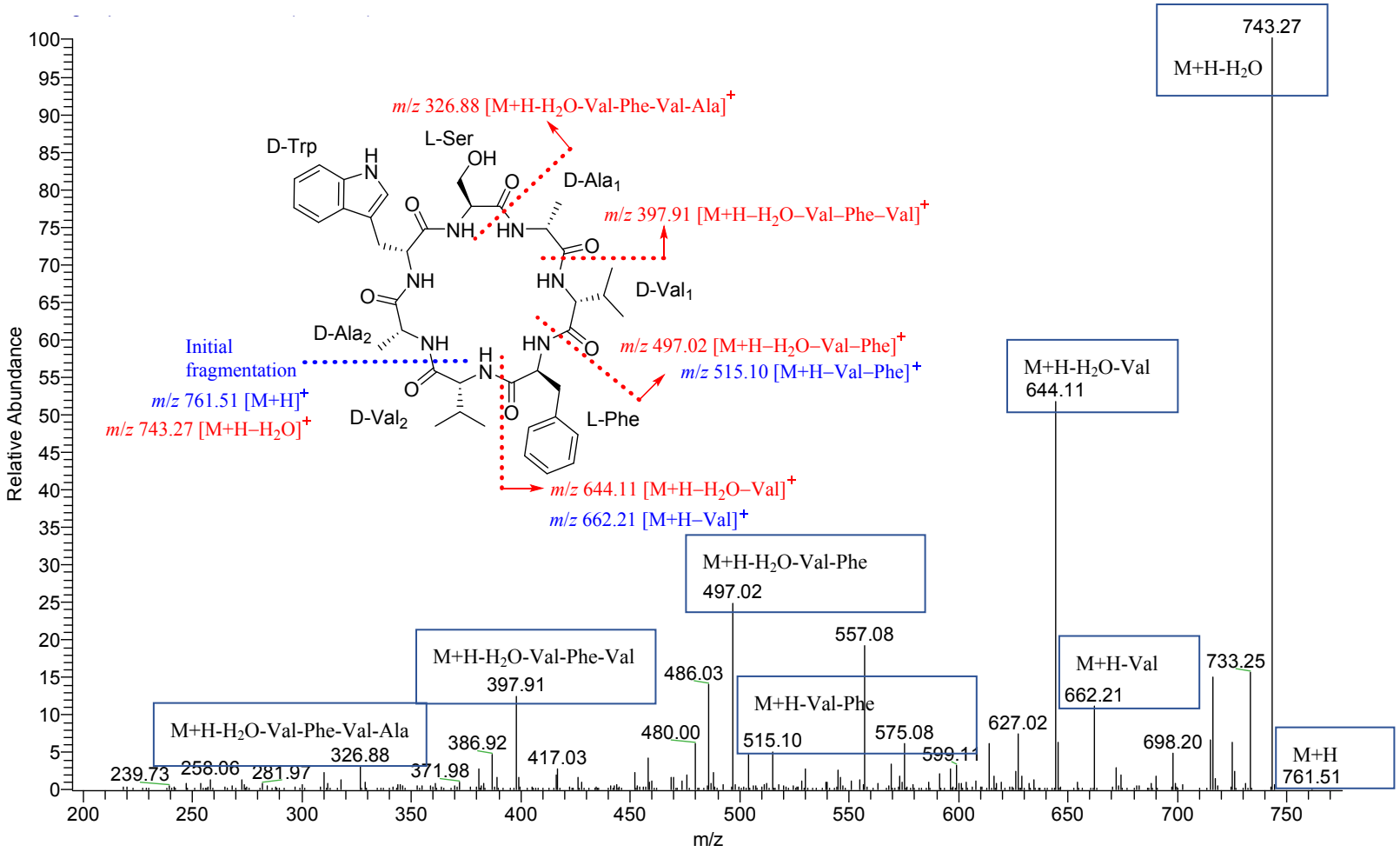


Fig. S22. ESI-MS/MS spectrum of **3**.

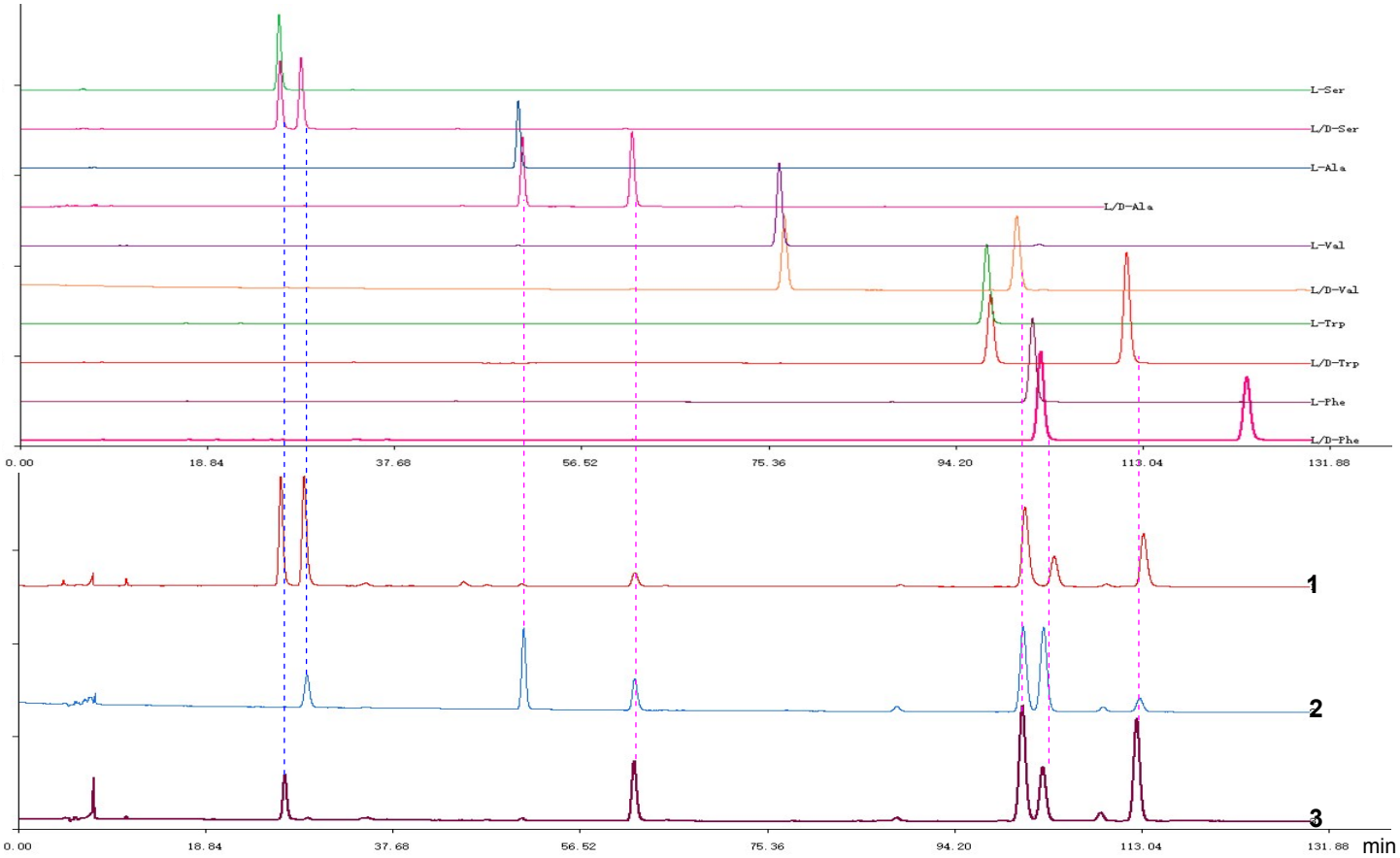


Fig. S23. HPLC analysis of *L*-FDAA derivatized with standard amino acids and **1–3**.

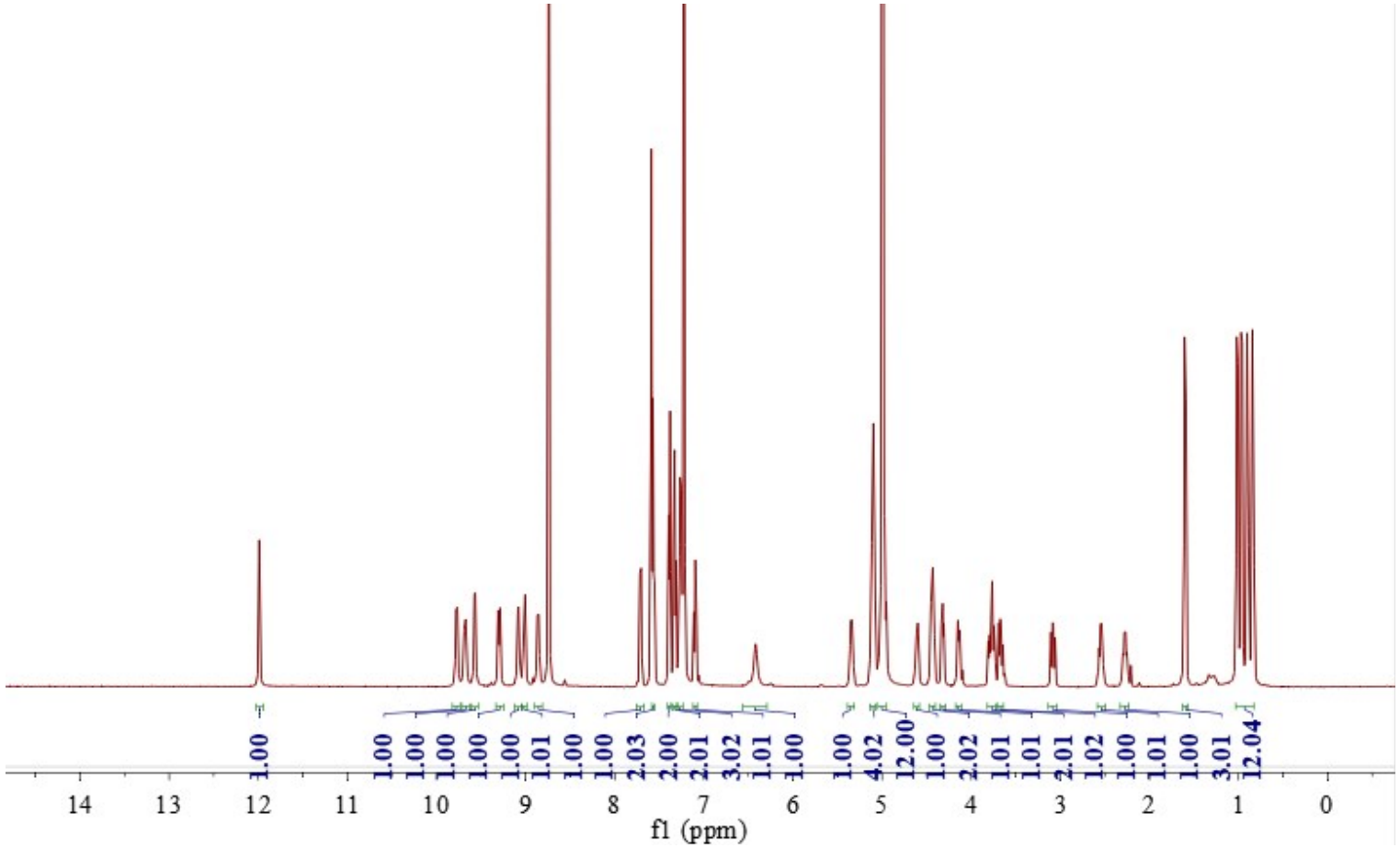


Fig. S24. ^{1}H NMR (500 MHz, pyridine-d_5) spectrum of **syn-1**.

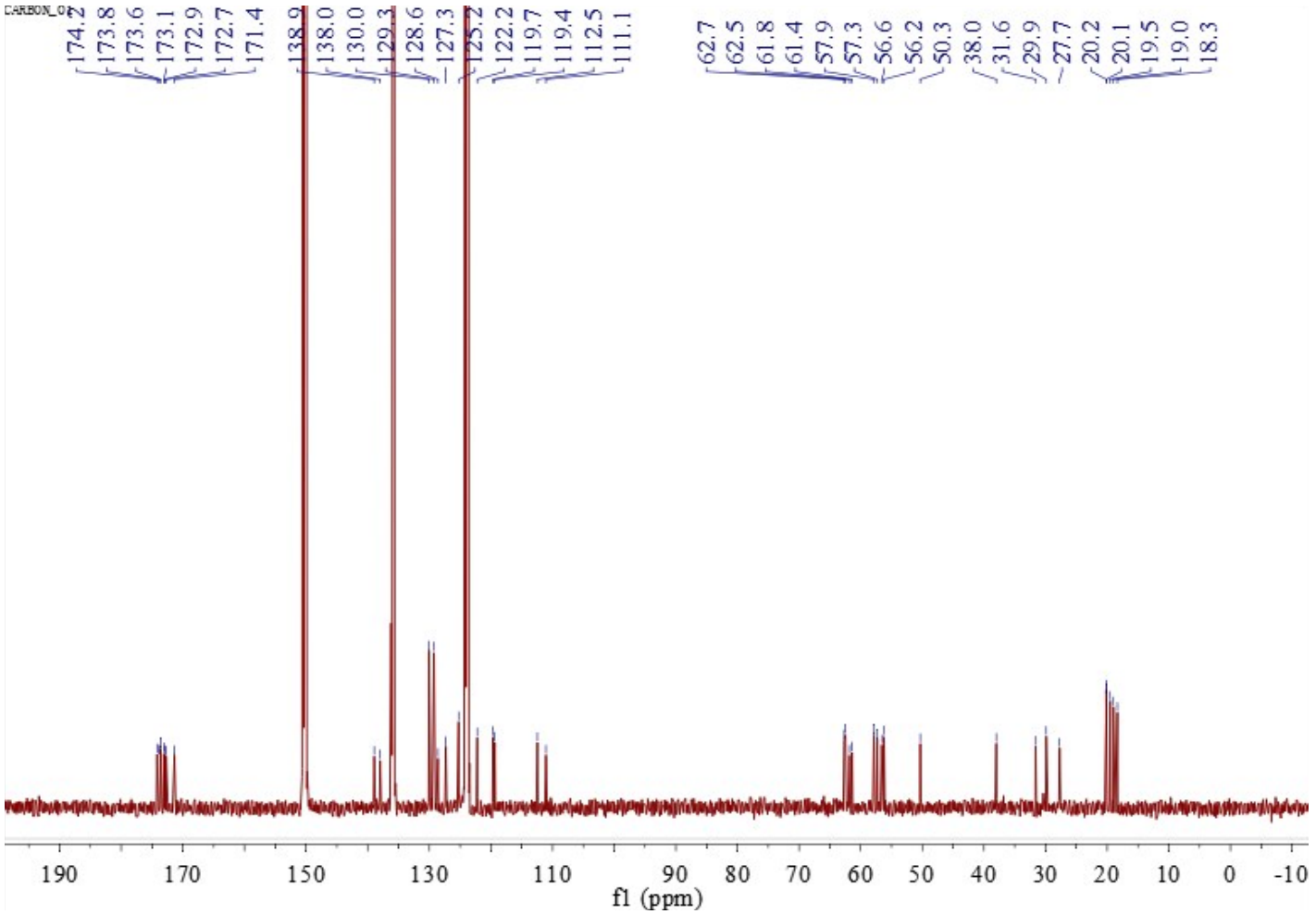


Fig. S25. ^{13}C NMR (125 MHz, pyridine-d_5) spectrum of **syn-1**.

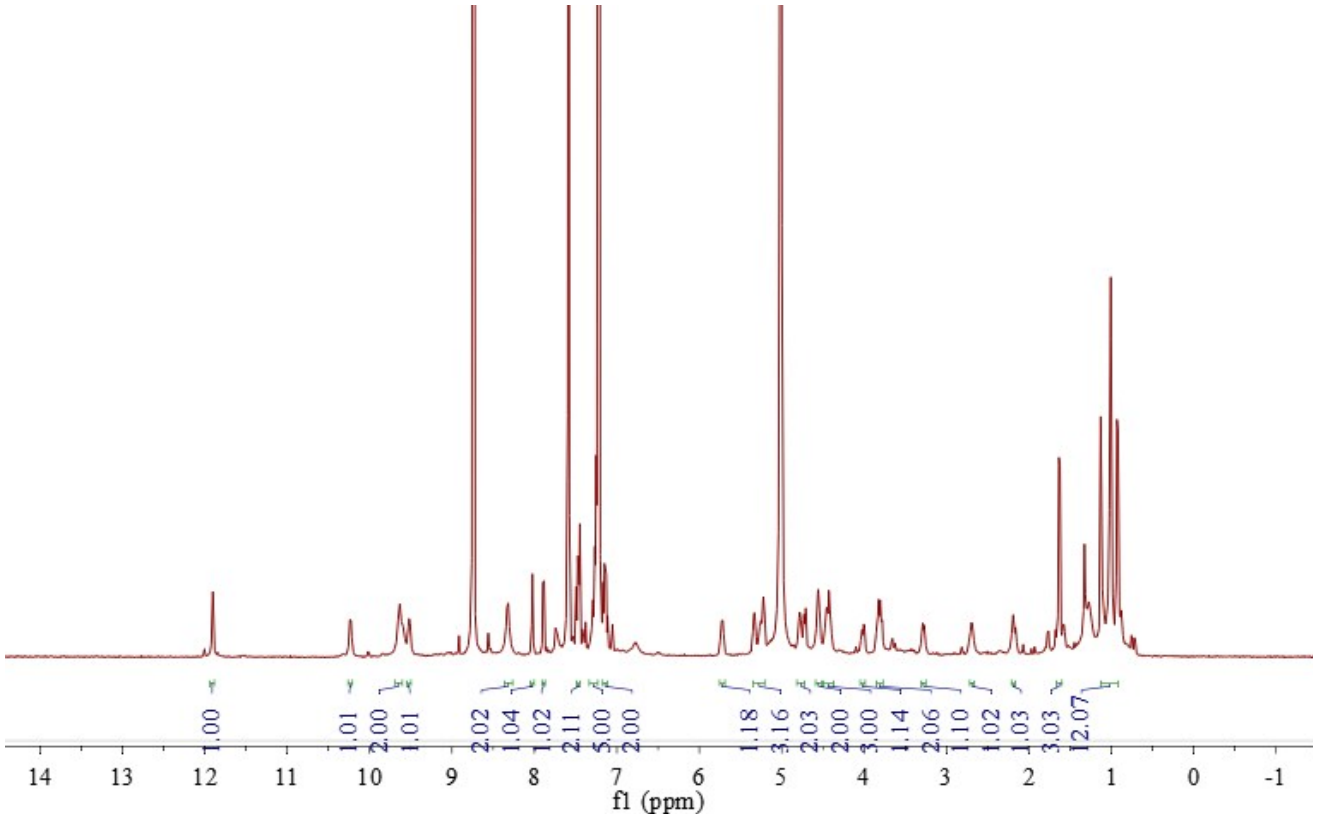


Fig. S26. ^{1}H NMR (500 MHz, pyridine-d_5) spectrum of ***iso*-1**.

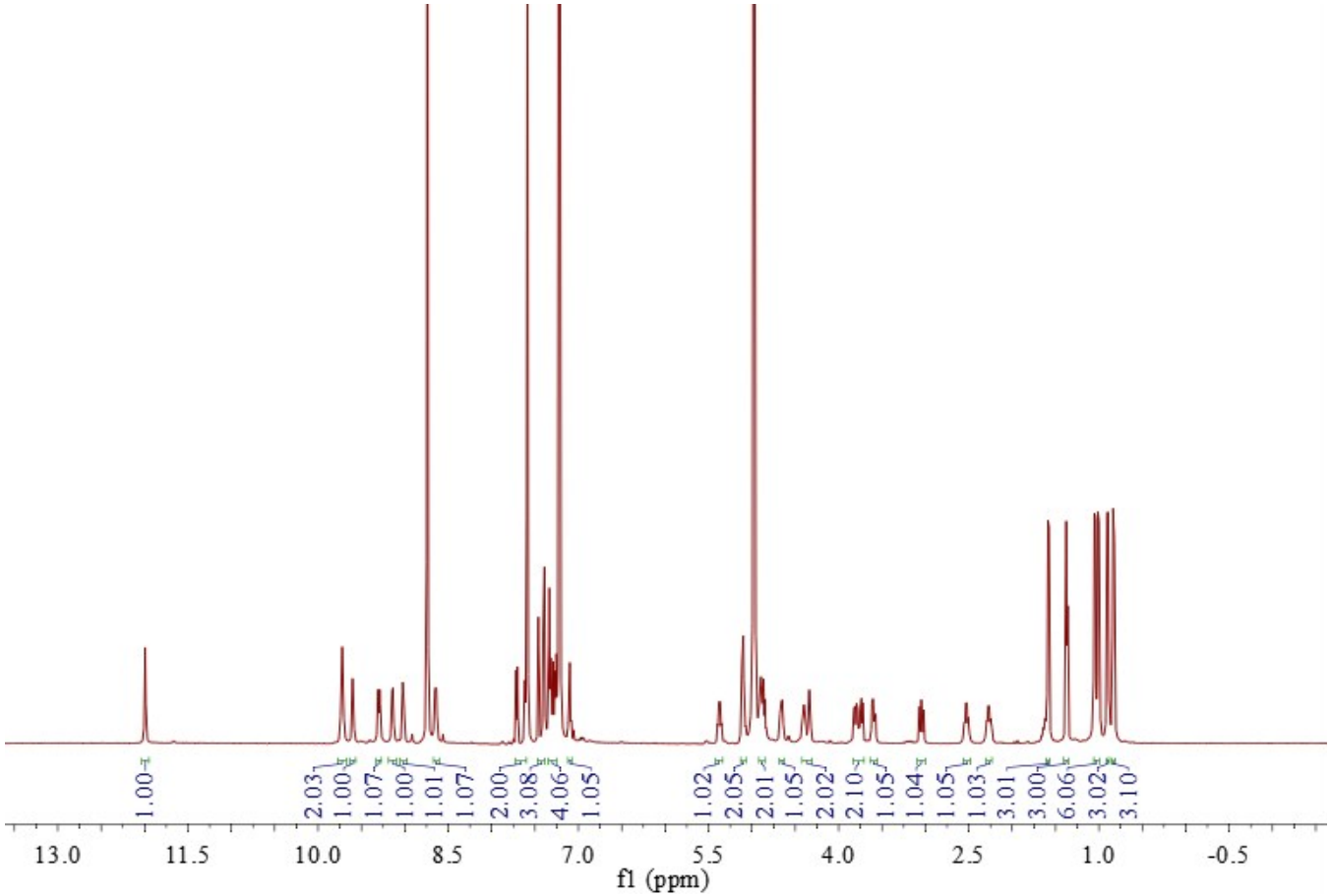


Fig. S27. ^{1}H NMR (500 MHz, pyridine-d_5) spectrum of **syn-2**.

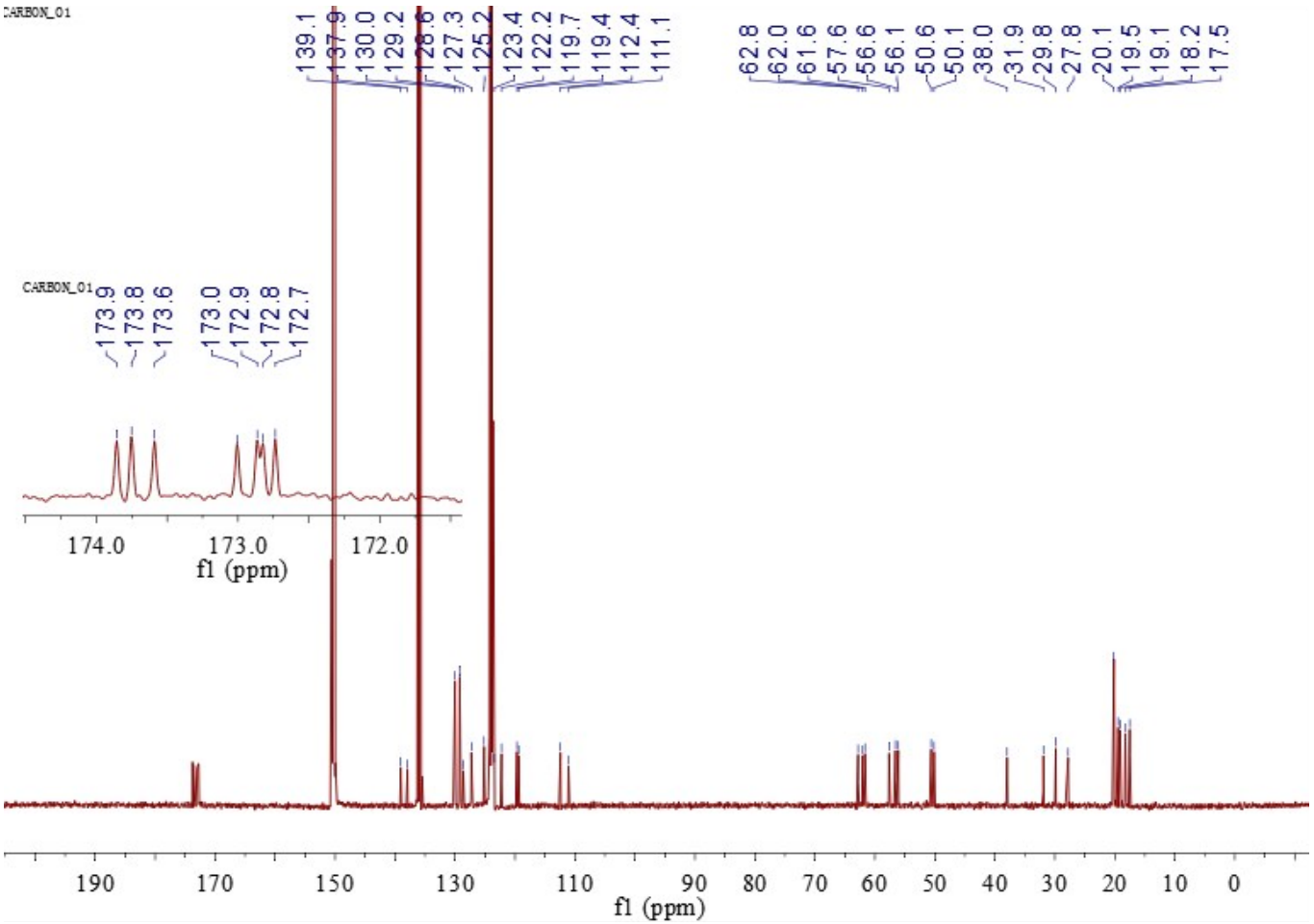


Fig. S28. ^{13}C NMR (125 MHz, pyridine-d_5) spectrum of **syn-2**.

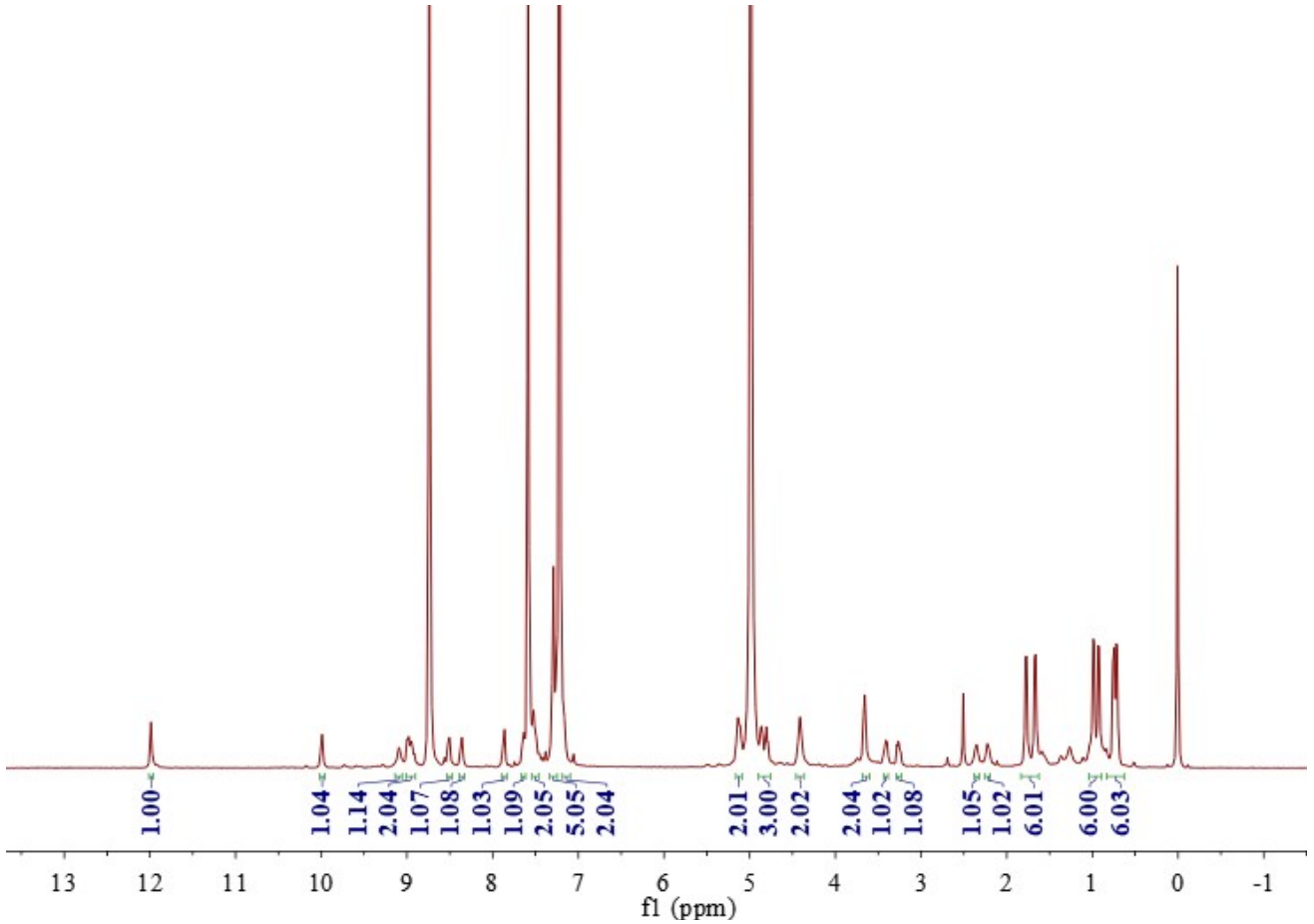


Fig. S29. ^{1}H NMR (500 MHz, pyridine-d_5) spectrum of ***iso*-2**.

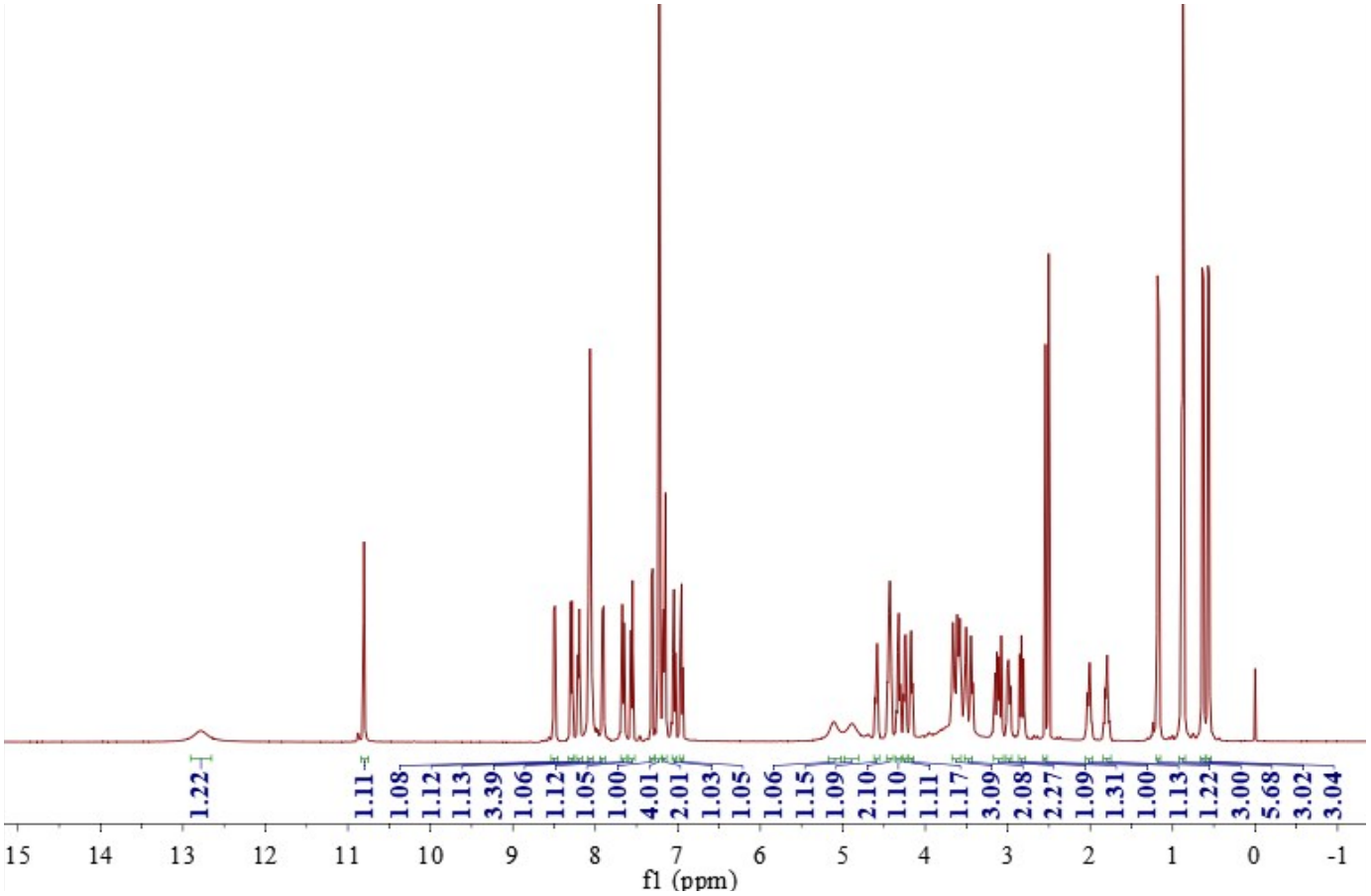


Fig. S30. ^{1}H NMR (500 MHz, DMSO-d_6) spectrum of **5**.

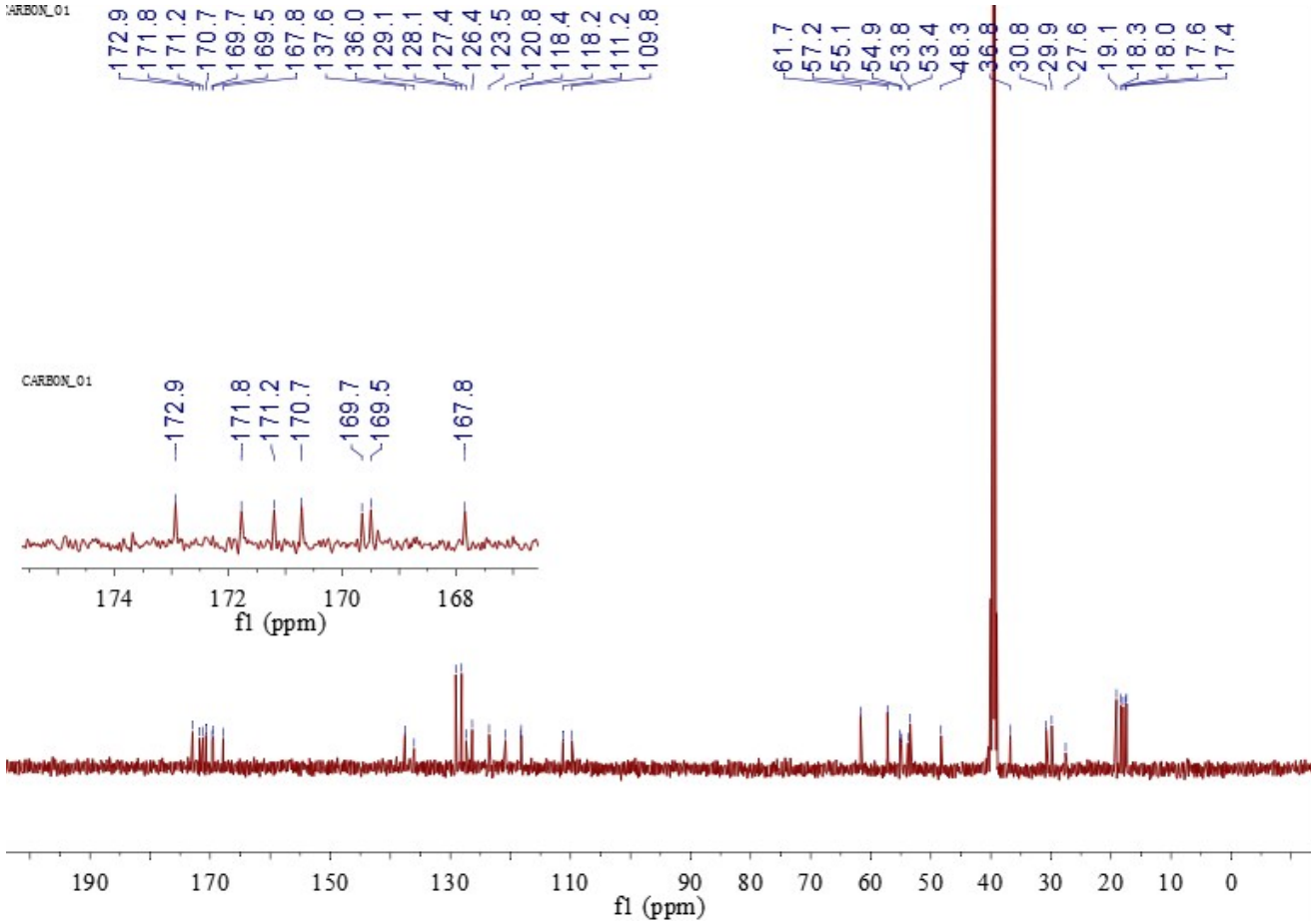


Fig. S31. ^{13}C NMR (125 MHz, DMSO-d_6) spectrum of **5**.

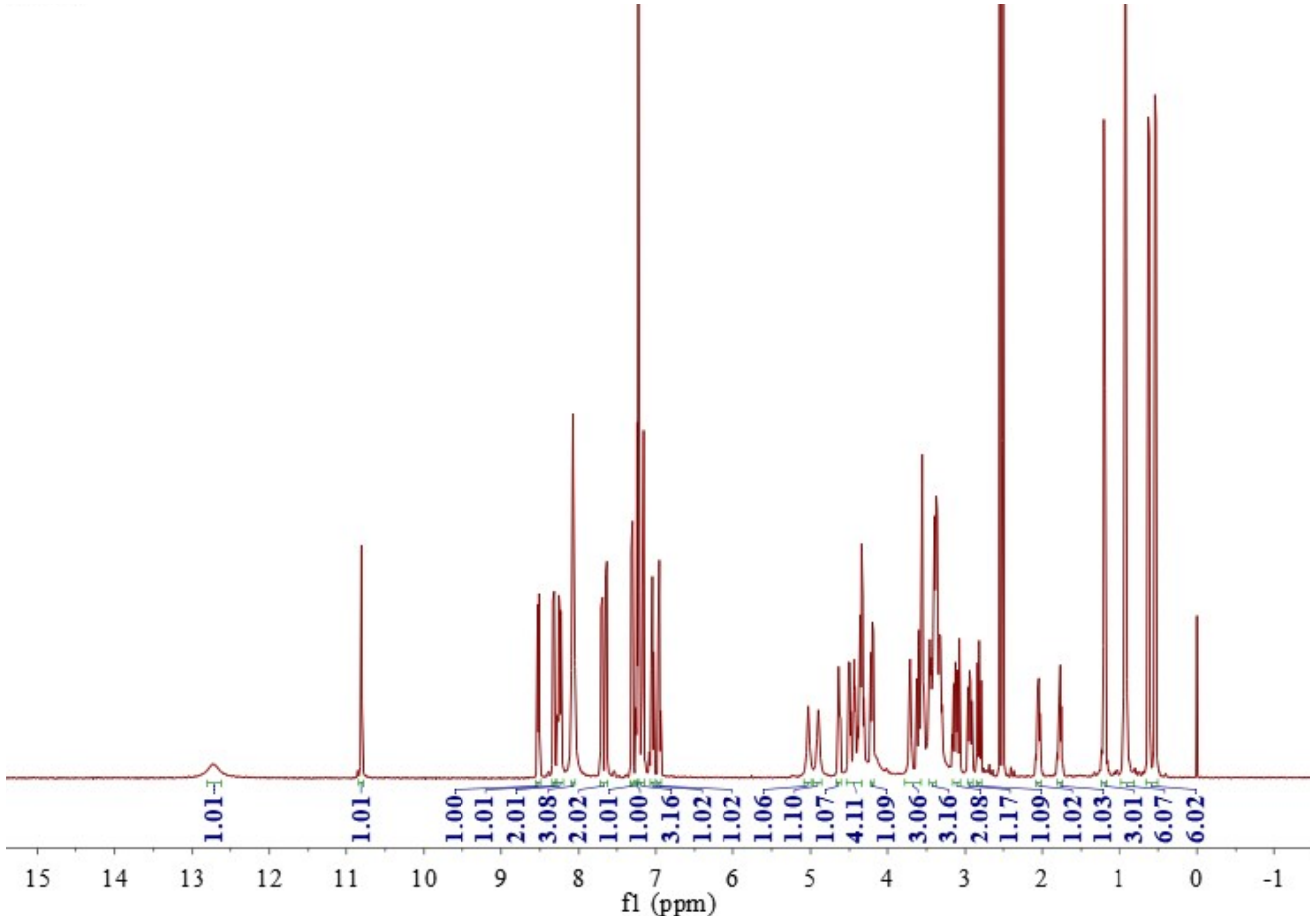


Fig. S32. ^{1}H NMR (500 MHz, DMSO-d_6) spectrum of ***iso*-5**.

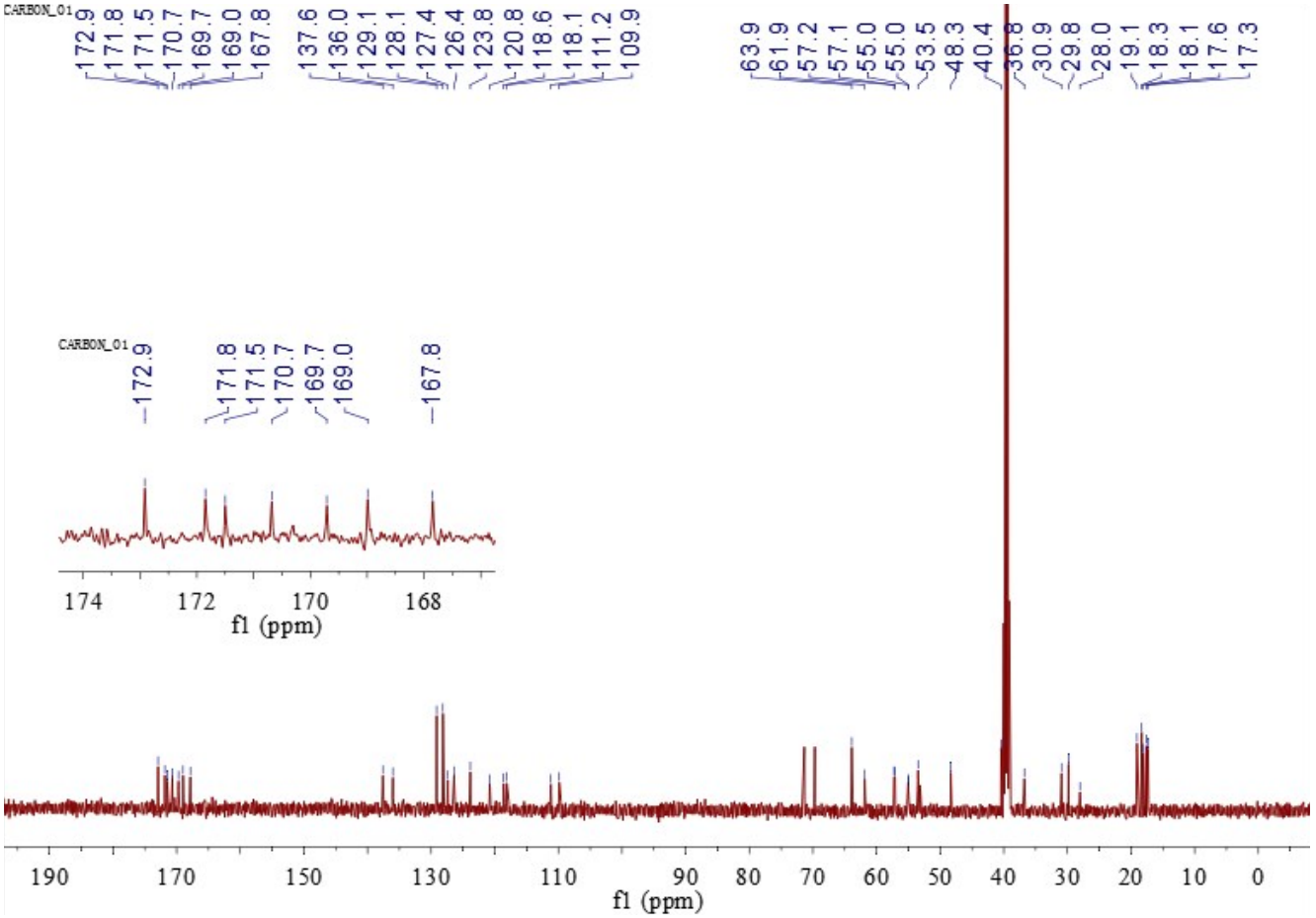


Fig. S33. ^{13}C NMR (125 MHz, DMSO-d_6) spectrum of ***iso*-5**.

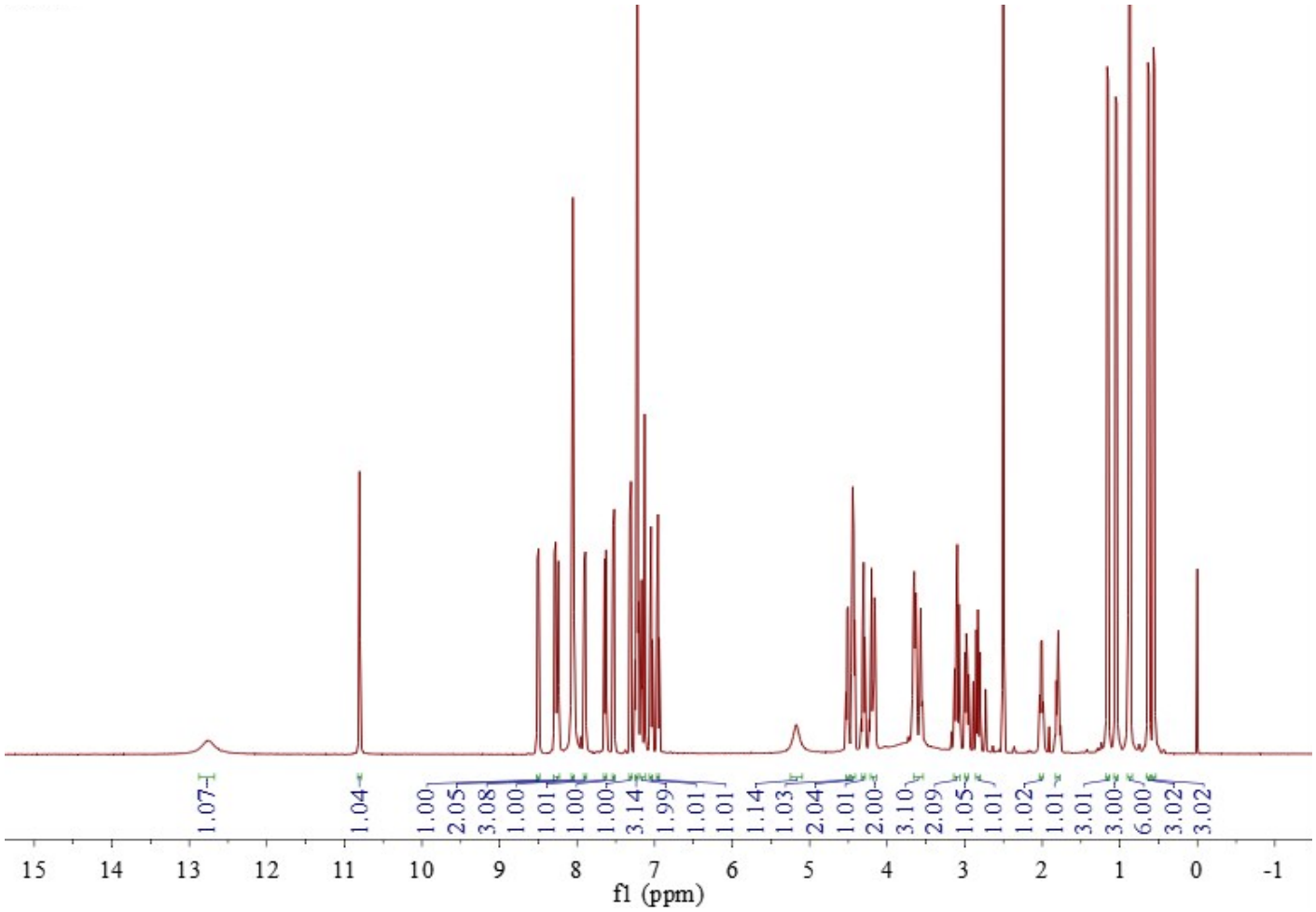


Fig. S34. ^{1}H NMR (500 MHz, DMSO-d_6) spectrum of **7**.

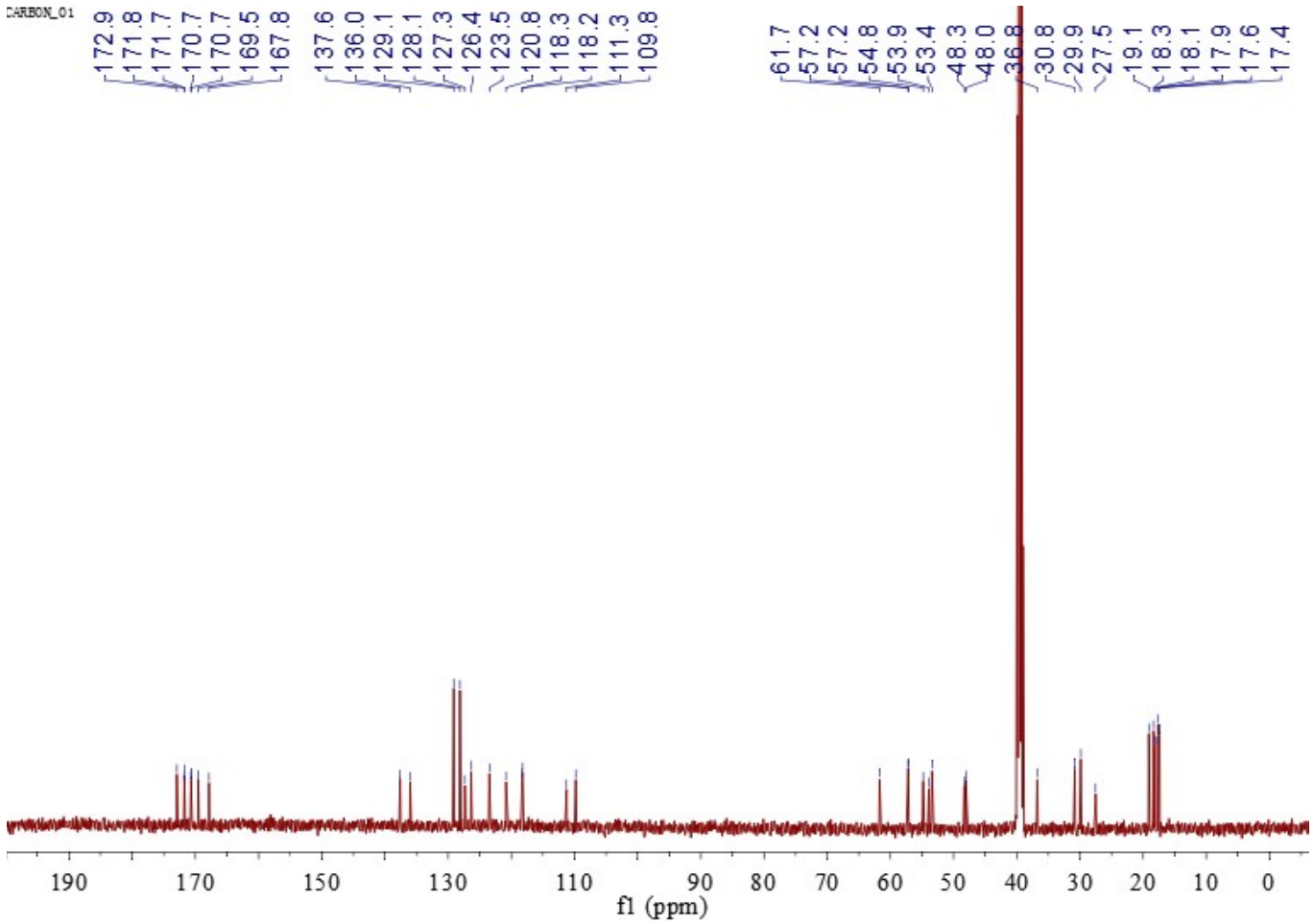


Fig. S35. ^{13}C NMR (125 MHz, DMSO-d_6) spectrum of **7**.

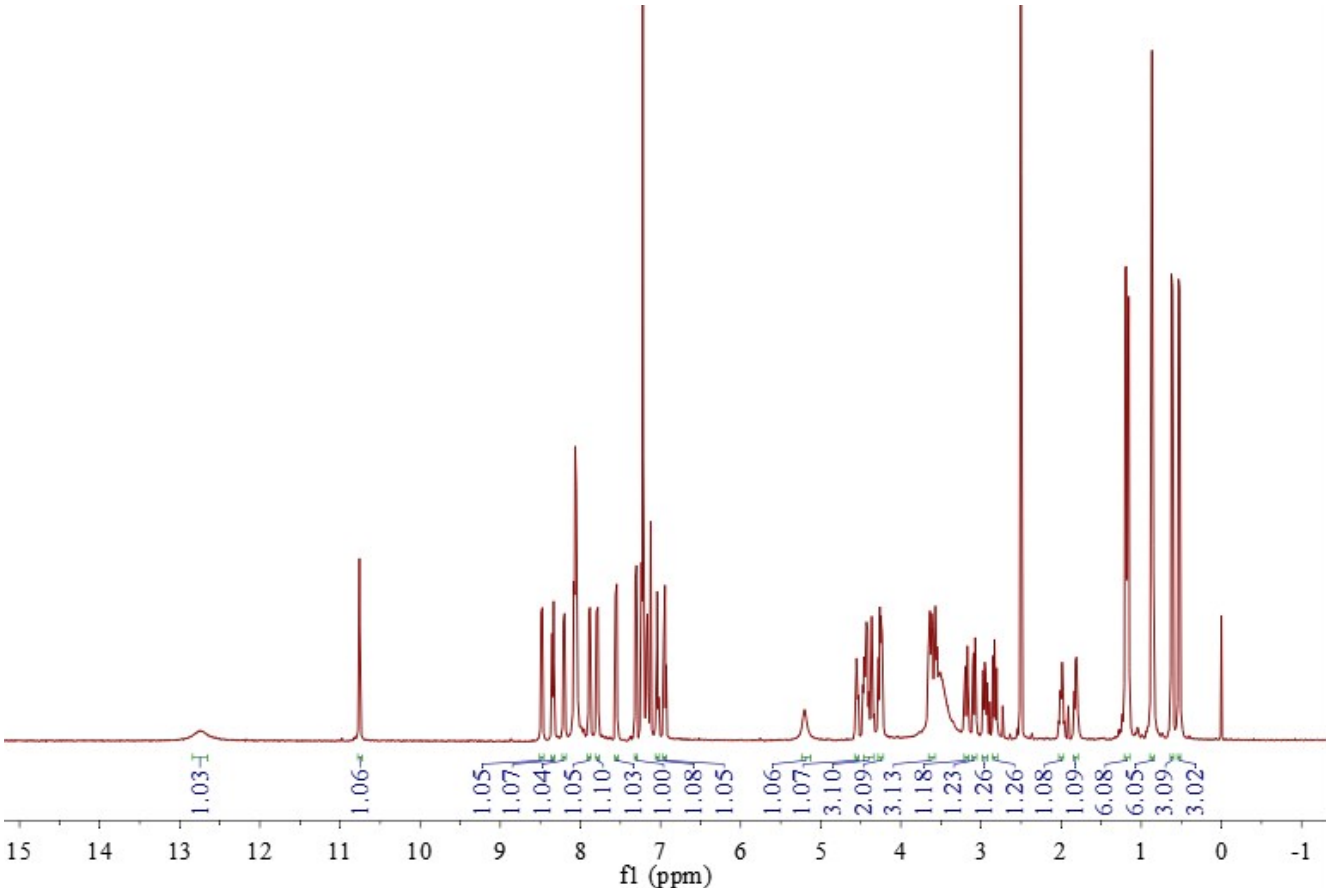


Fig. S36. ^{1}H NMR (500 MHz, DMSO-d_6) spectrum of ***iso*-7**.

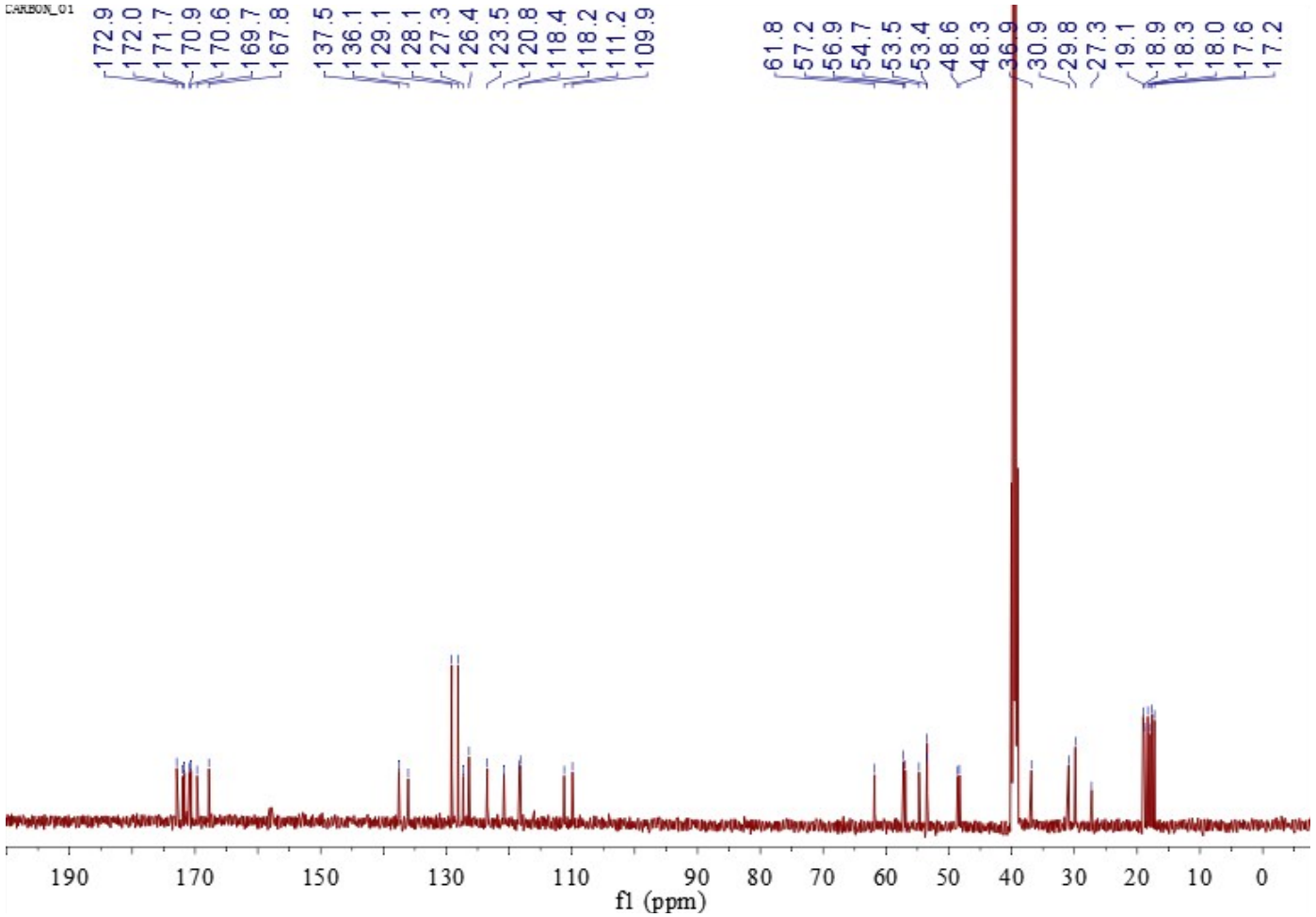


Fig. S37. ^{13}C NMR (125 MHz, DMSO-d_6) spectrum of ***iso*-7**.

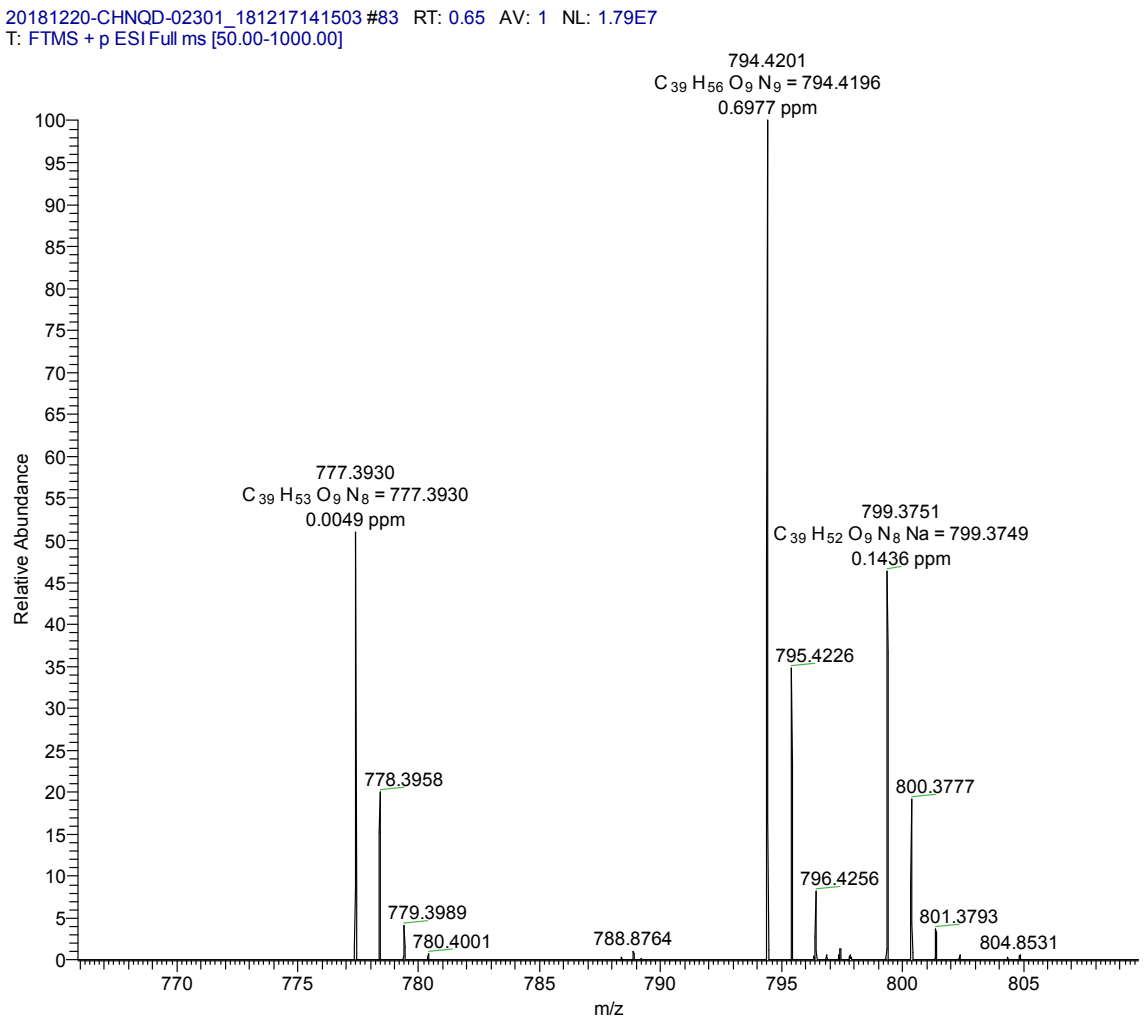


Fig. S38. HR-ESI-MS spectrum of **syn-1**.

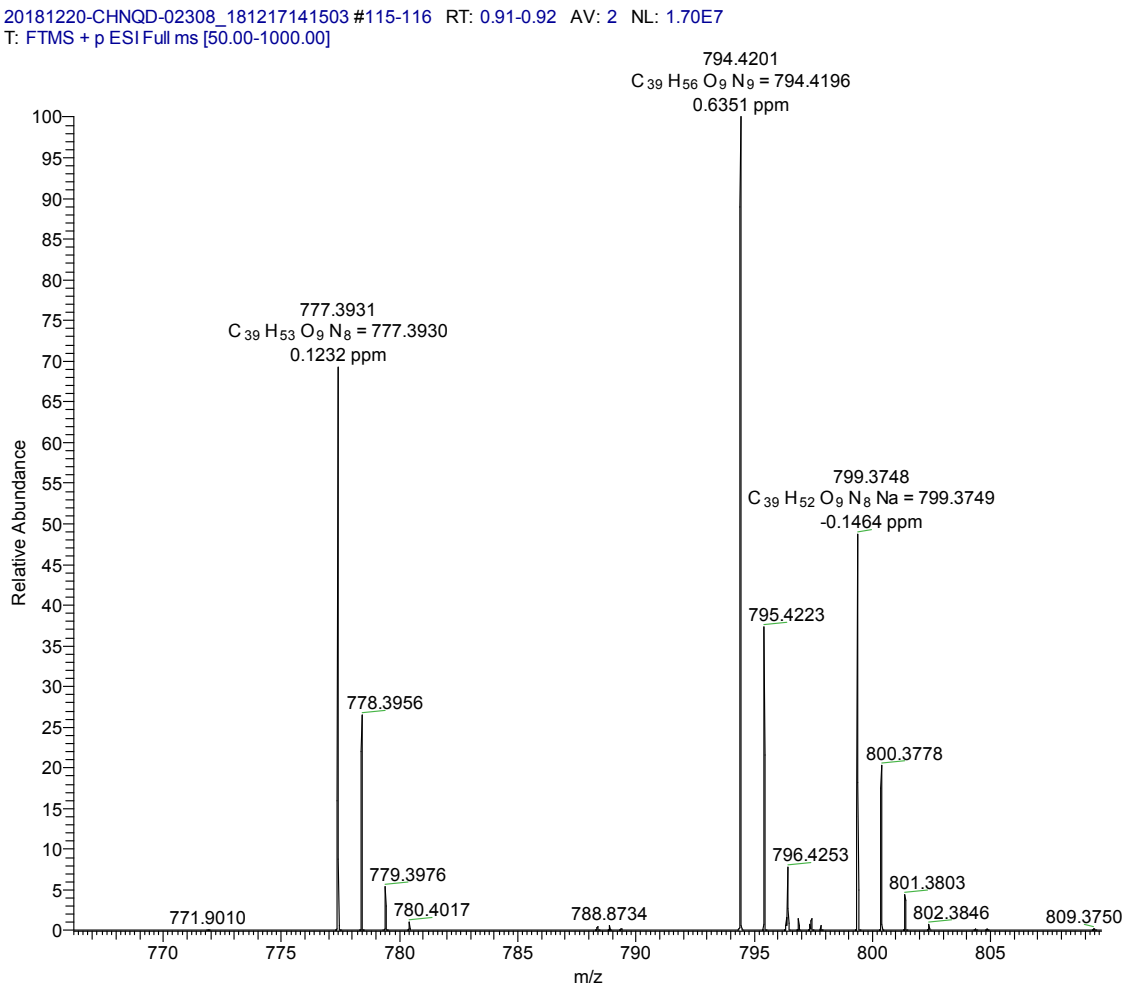


Fig. S39. HR-ESI-MS spectrum of ***iso*-1**.

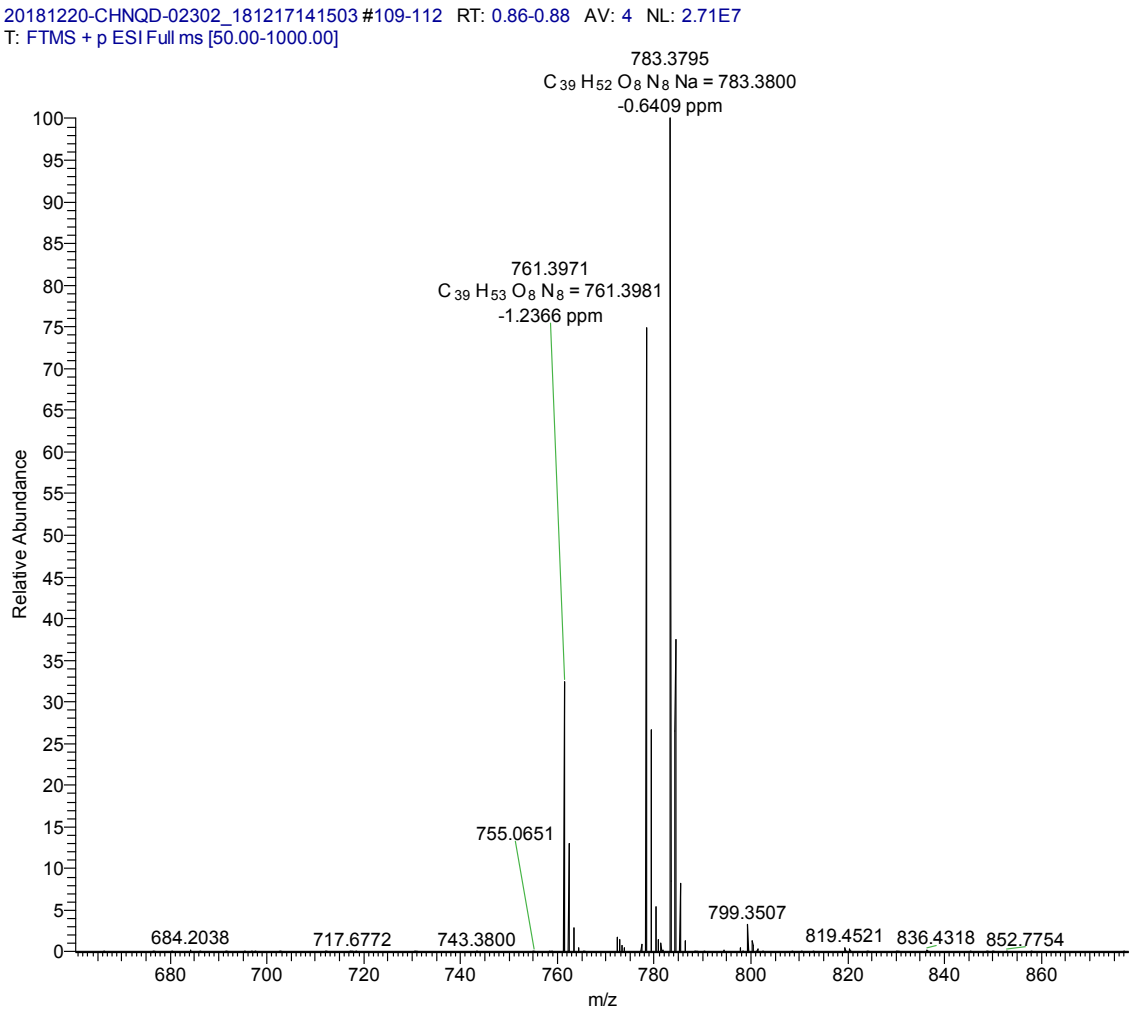


Fig. S40. HR-ESI-MS spectrum of **syn-2**.

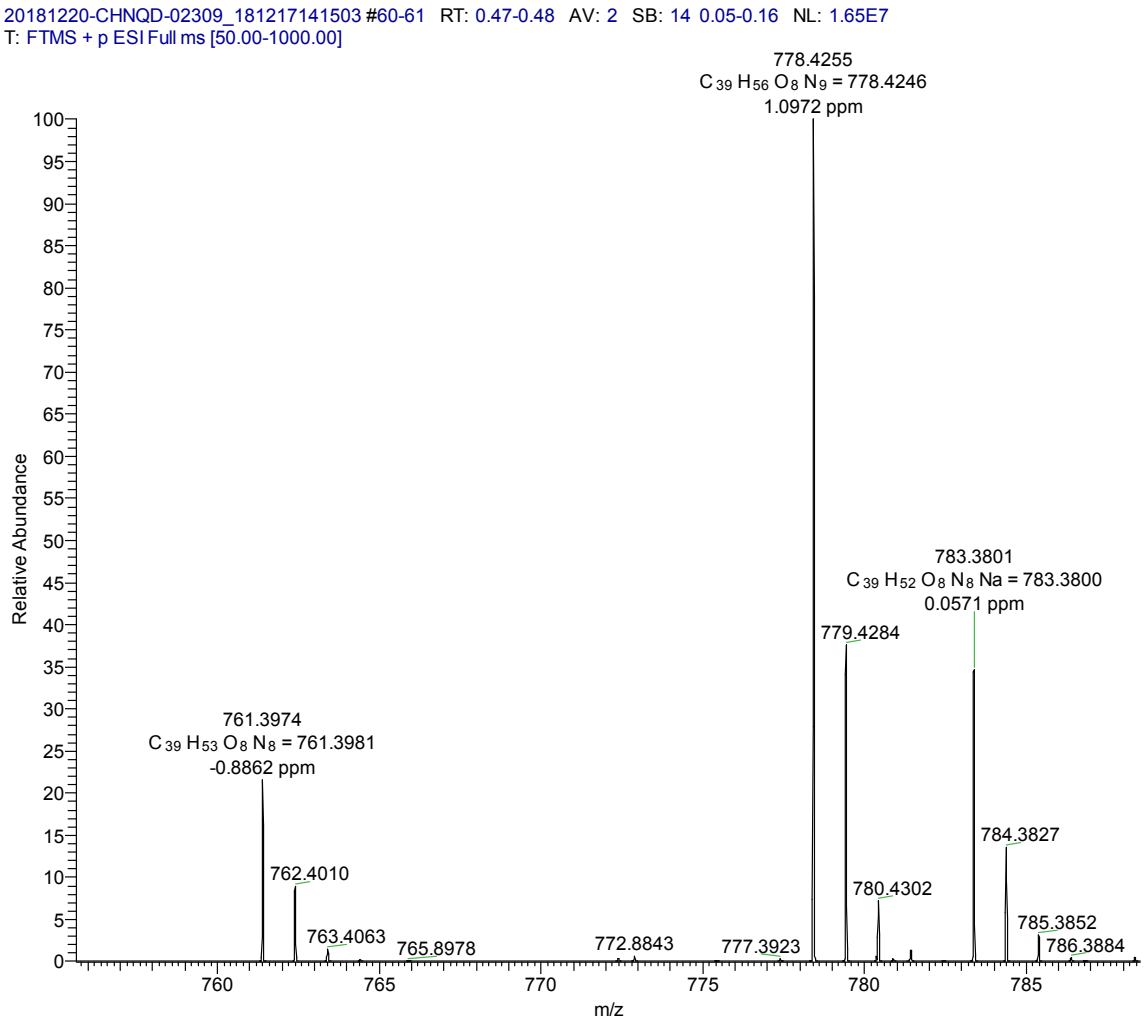


Fig. S41. HR-ESI-MS spectrum of ***iso*-2**.

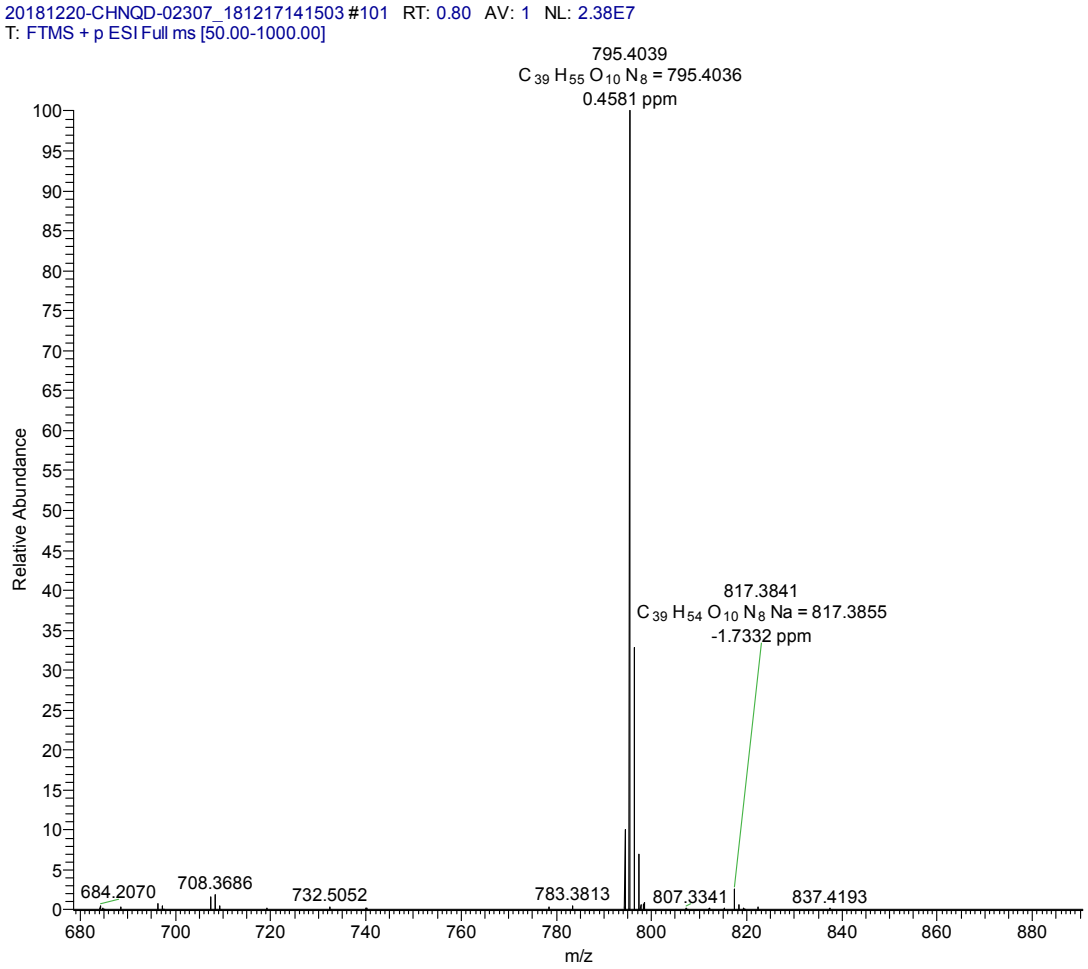


Fig. S42. HR-ESI-MS spectrum of **5**.

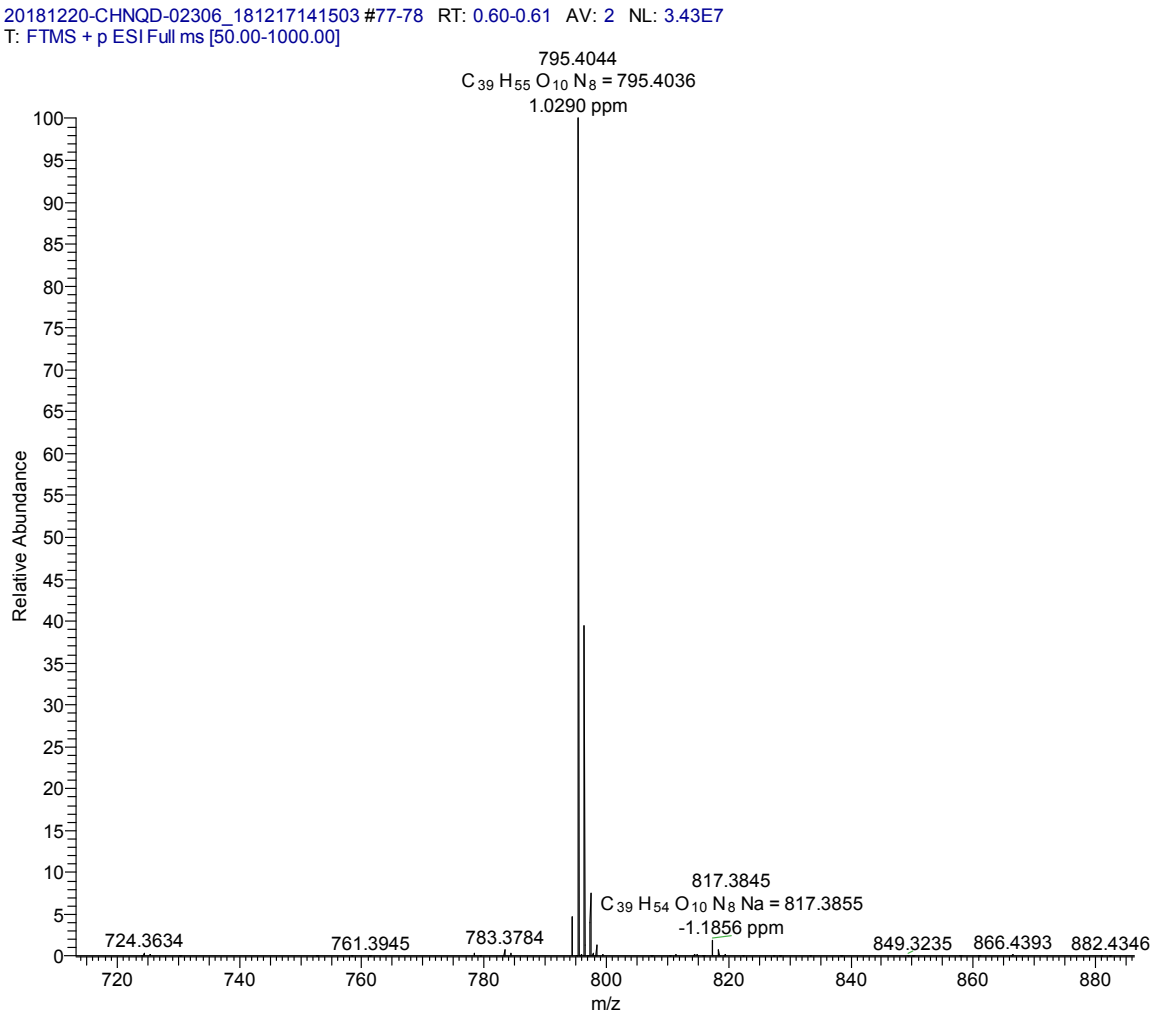


Fig. S43. HR-ESI-MS spectrum of ***iso*-5**.

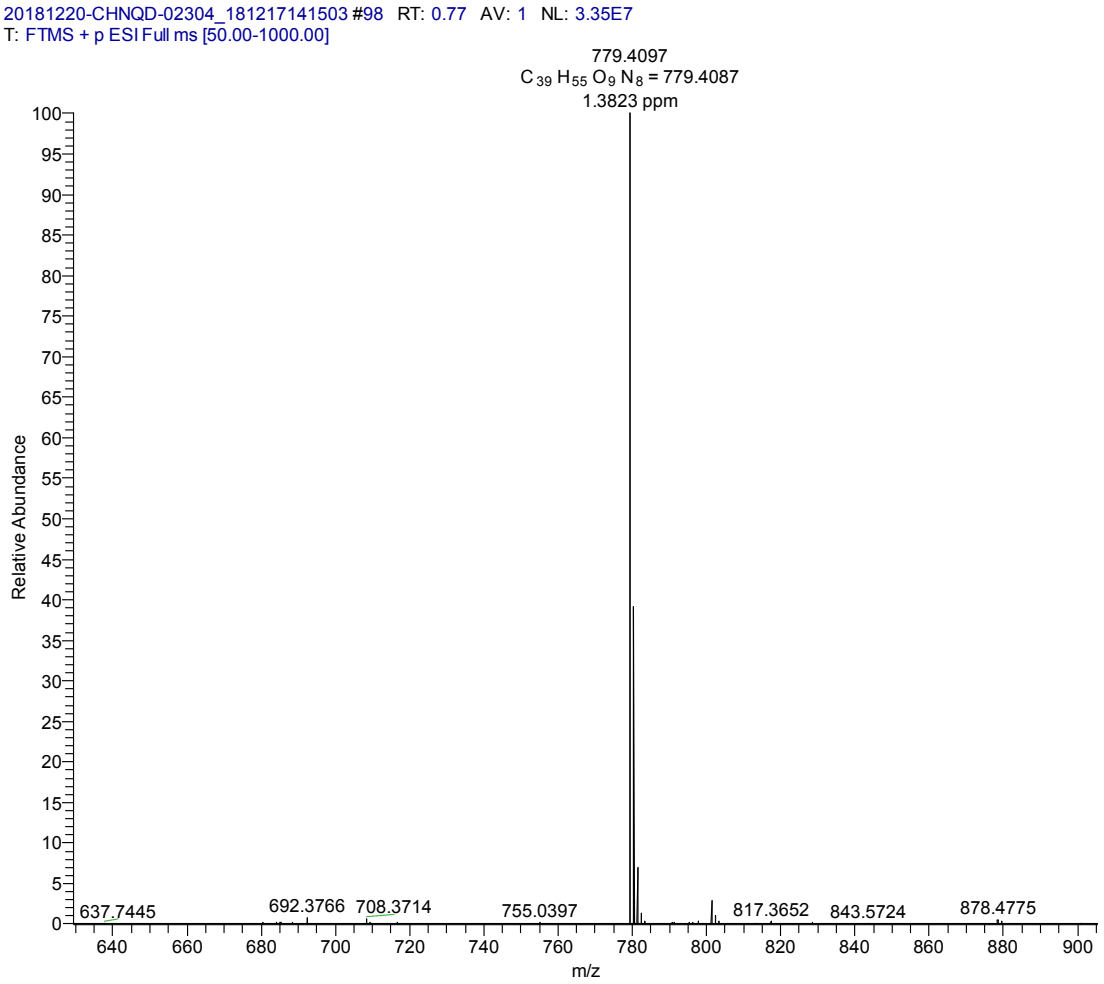


Fig. S44. HR-ESI-MS spectrum of **7**.

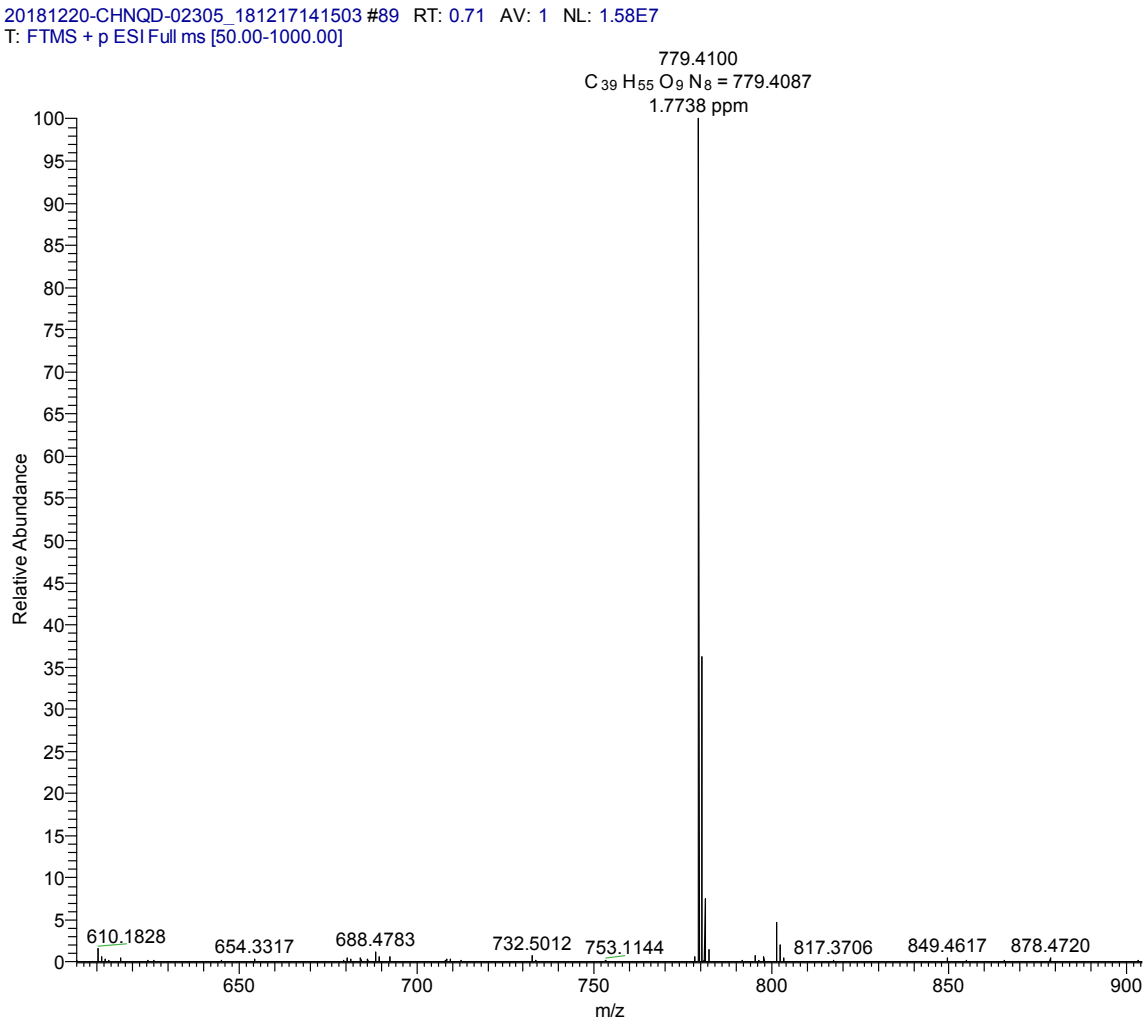


Fig. S45. HR-ESI-MS spectrum of ***iso*-7**.

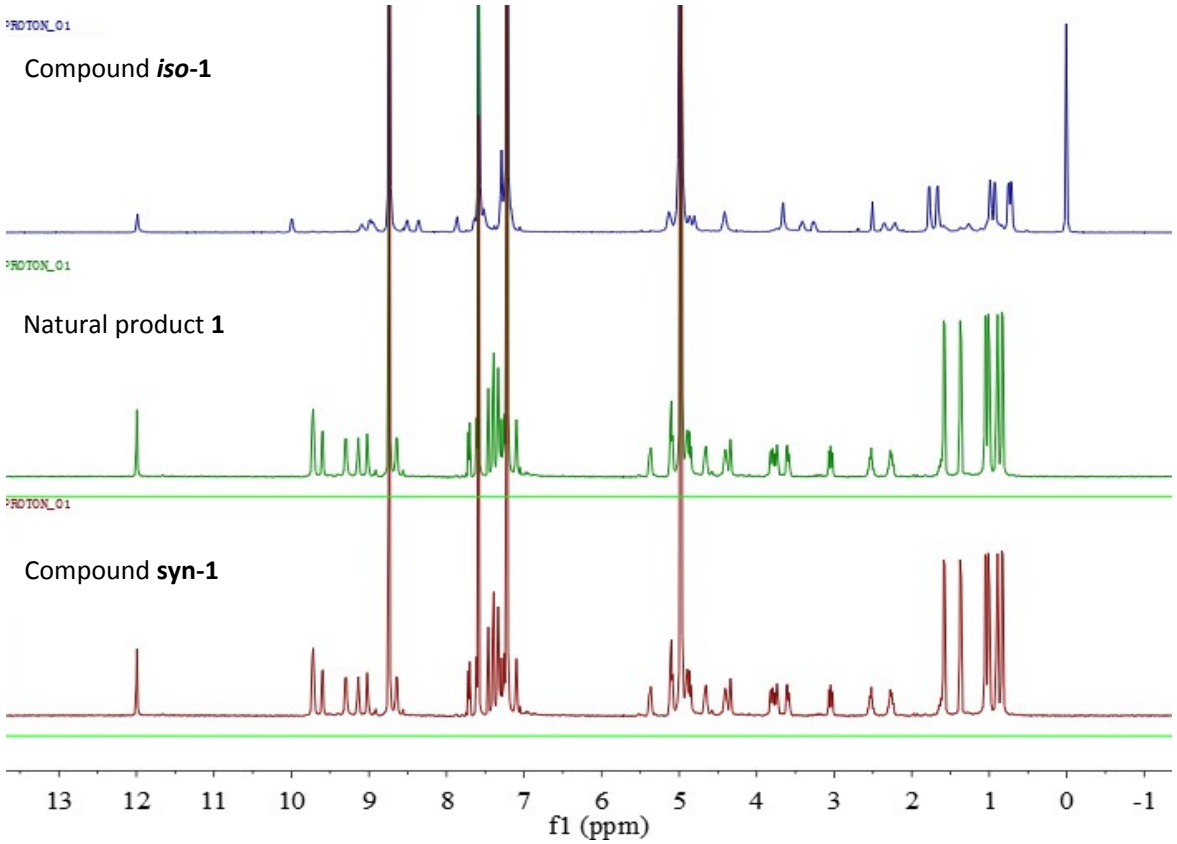


Fig. S46. ^{1}H NMR (500 MHz, pyridine-d_5) spectrum comparison of natural product **1** with **syn-1** and ***iso*-1**.

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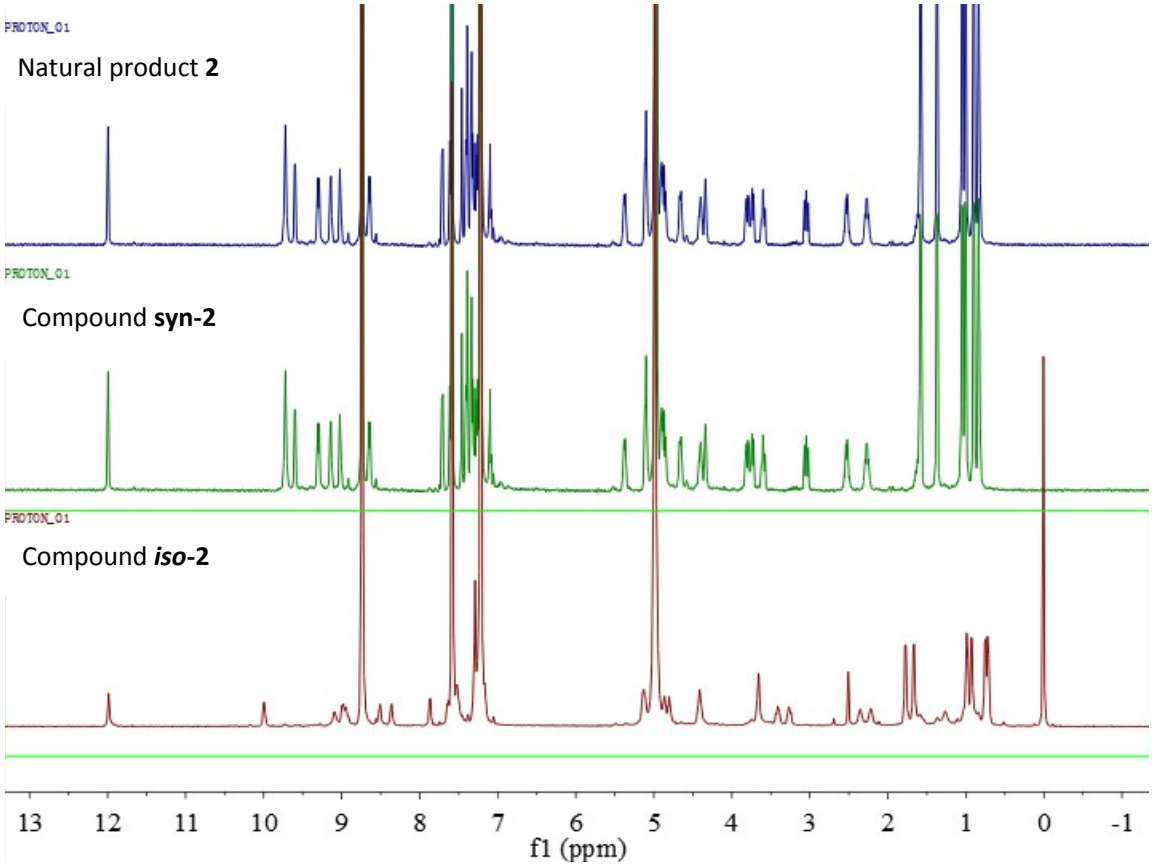

Fig. S47. ^{1}H NMR (500 MHz, pyridine-d_5) spectrum comparison of natural product **2** with **syn-2** and ***iso*-2**.

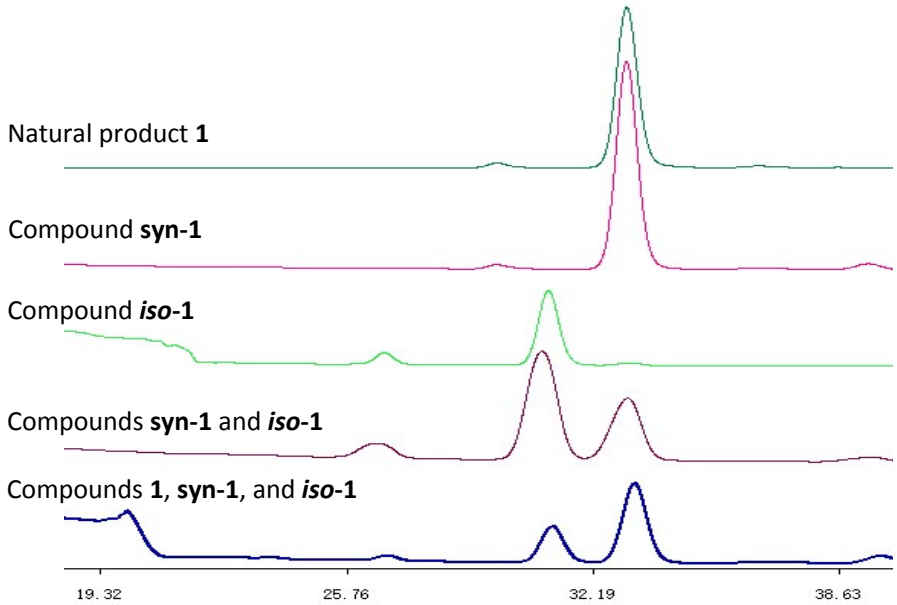

Fig. S48. HPLC analysis of natural product **1** and the synthesized **syn-1** and ***iso*-1** (CH_3OH-H_2O, 60:40; 2 mL/min; UV 212 nm).

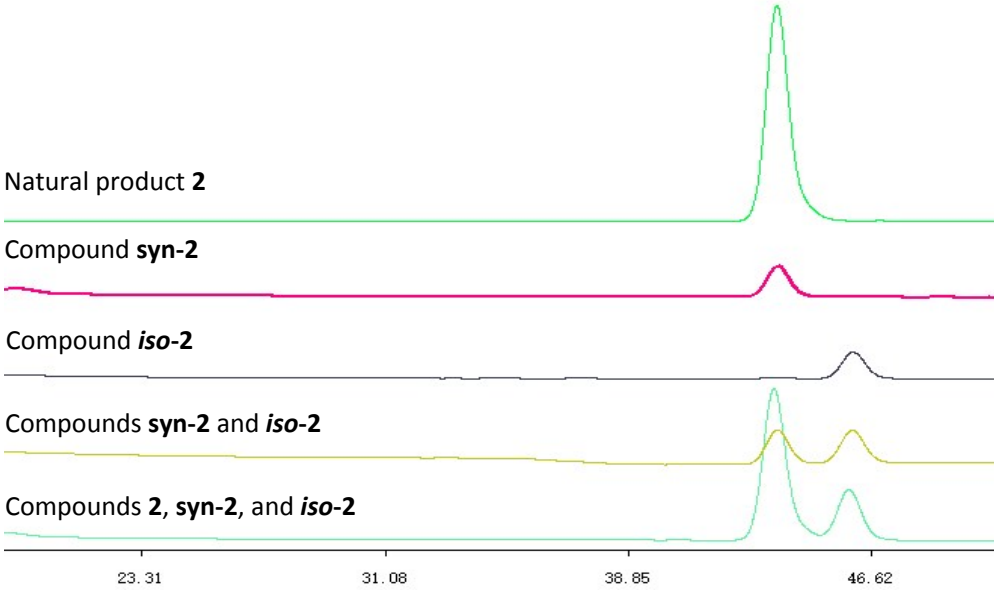

Fig. S49. HPLC analysis of natural product **2** and the synthesized **syn-2** and ***iso*-2** (CH_3OH-H_2O, 60:40; 2 mL/min; UV 212 nm).

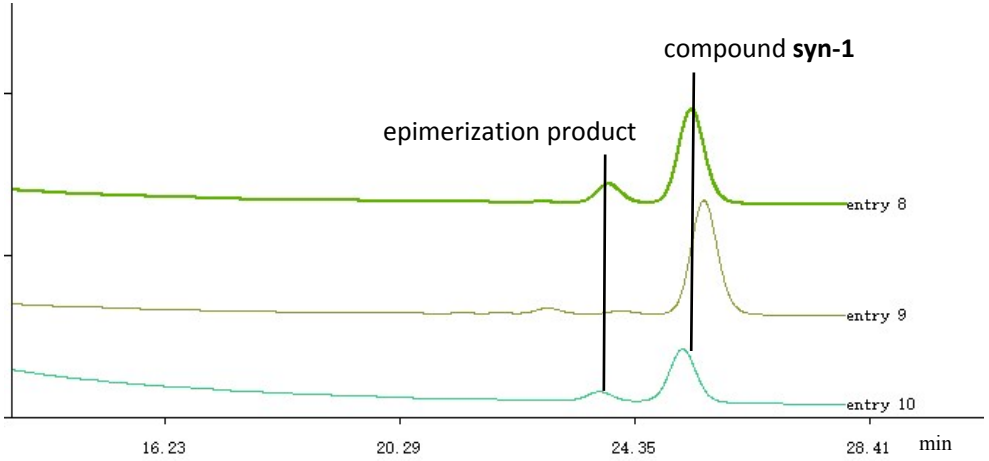

Fig. S50. UPLC analysis of reacted cyclization solvents (MeCN-H_2O (0.1% THF), 45:55; 0.5 mL/min; UV 212 nm).