**Supporting Information**

# New peptaibiotics and a cyclodepsipeptide from *Ijuhya vitellina:* Isolation, identification, cytotoxic and nematicidal activities.


**Ashaimaa Y. Moussa[1,2], Christopher Lambert[3], Theresia E.B. Stradal[3], Samad Ashrafi[4], Wolfgang Maier[4] , Marc Stadler[1], Soleiman Helaly[1,5]***

[1] Department of Microbial Drugs, Helmholtz Centre for Infection Research, Inhoffenstraße 7, 38124 Braunschweig, Germany.

[2] Department of Pharmacognosy, Faculty of Pharmacy, Ain shams University, Abbassia, 11566, Cairo, Egypt.

[3] Department of Cell Biology, Helmholtz Centre for Infection Research (HZI), Inhoffenstraße 7, 38124, Braunschweig, Germany.

[4] Institute for Epidemiology and Pathogen Diagnostics, Julius Kühn-Institut (JKI)– Federal Research Centre for Cultivated Plants, Braunschweig, Germany.

[5] Department of Chemistry, Faculty of Science, Aswan University, Aswan, Egypt.
*Correspondence: soleiman.helaly@helmholtz-hzi.de.

**Contents**

**LIST OF TABLES**

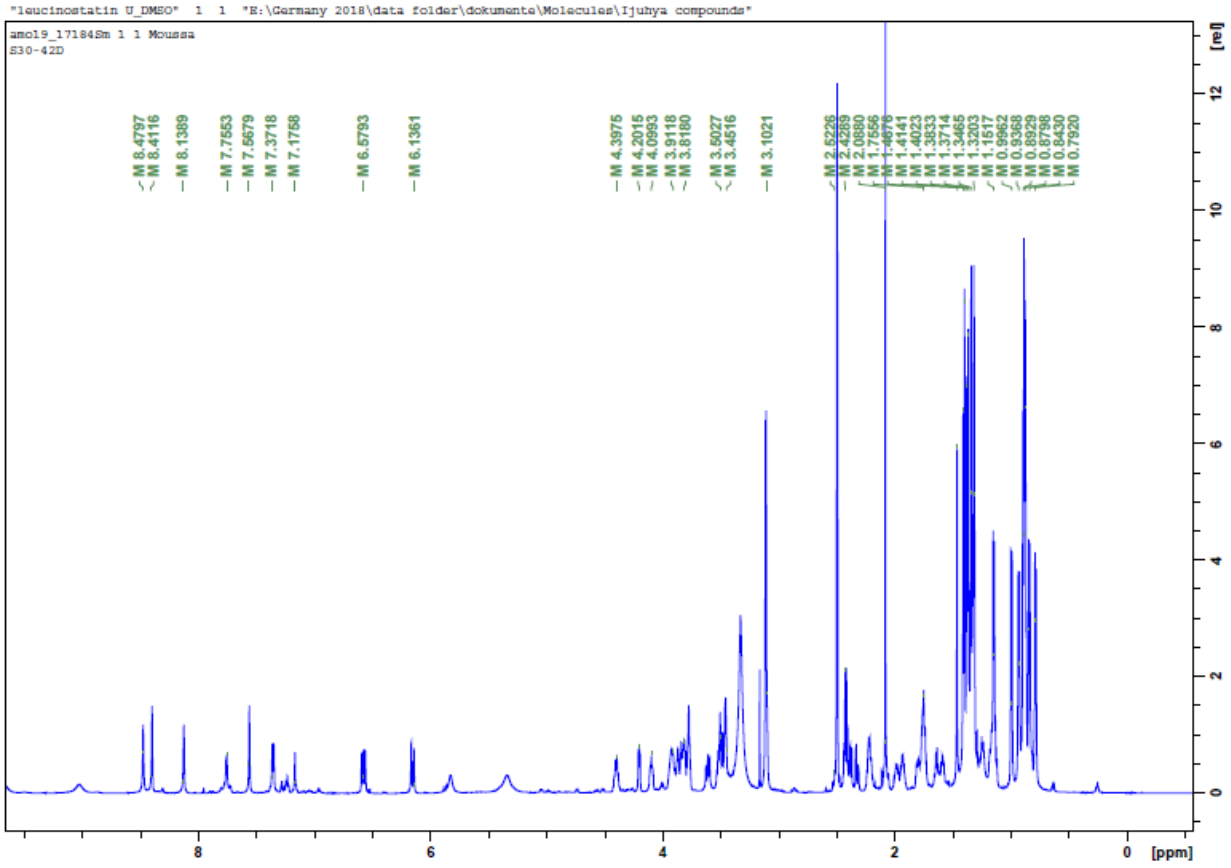
**LIST OF FIGURES**

**LIST OF TEXT:**

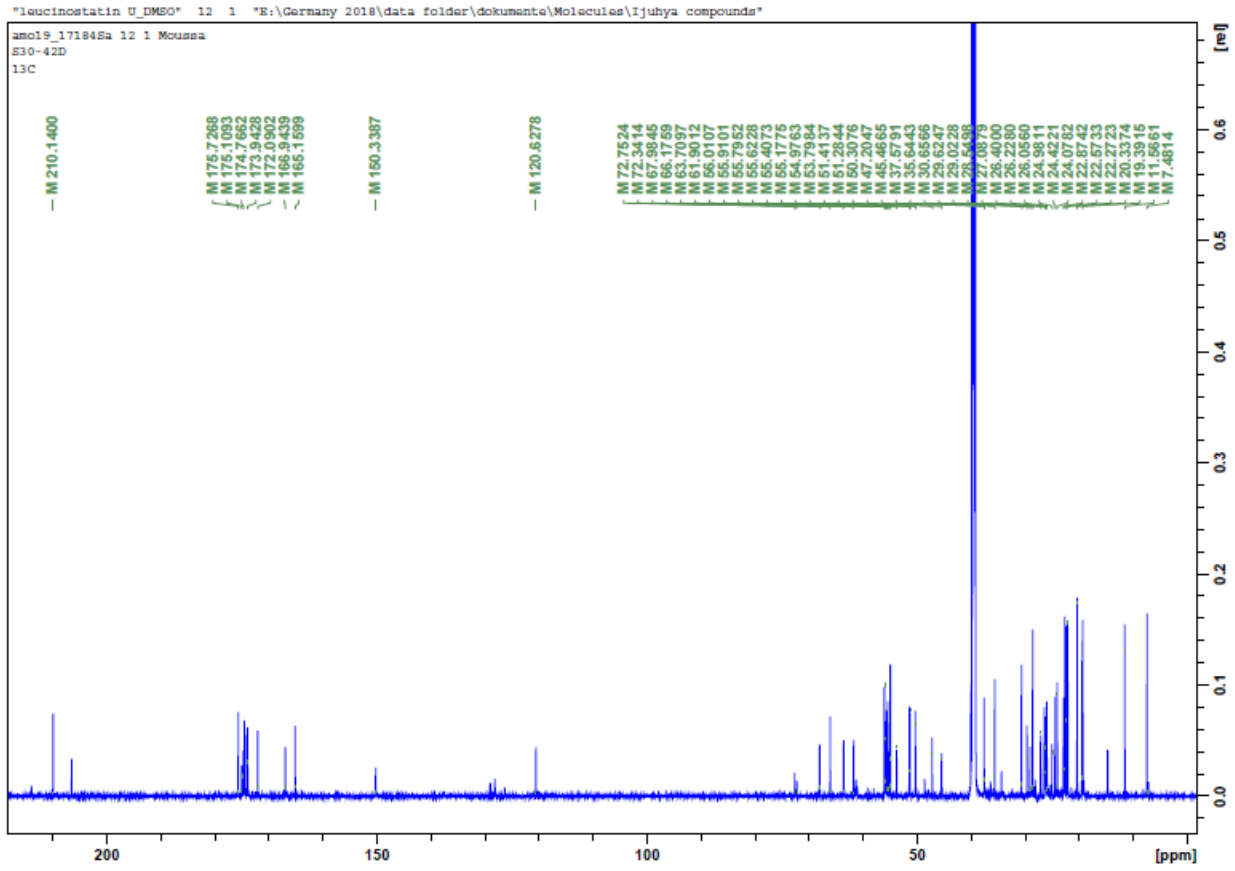
**S1 Table**. $^{1}H$ NMR and $^{13}C$ NMR data of **1 & 2** and the characteristic chemical shift values.

| | | leucinostatin U (1) | | leucinostatin Q (2) | |
|---|---|---|---|---|---|
| **residue** | position | δC, type | δH( J in Hz) | δC, type | δH( J in Hz) |
| **ΔMHA** | 1 | 165.15, C | | 165.45,C | |
| | 2 | 120.27, CH | 6.14, (15.04) | 120.65,CH | 6.25 |
| | 3 | 150.02,CH | 6.58 (7.7, 15.0) | 151.24,CH | 6.66 |
| | 4 | 38.10,CH | 2.22 | 37.82,CH | 2.26 |
| | 5 | 29.23,CH2 | 1.36 | 28.86,CH2 | 1.38 |
| | 6 | 12.10,CH3 | 0.88 | 11.88,CH3 | 0.87 |
| | 7 | 19.86,CH3 | 0.99(6.3) | 18.85,CH3 | 1.04 |
| **Pro** | 1 | 174.76,C | | 173.6,C | |
| | 2 | 62.28,CH | 4.2(4.12, 8.9) | 61.61,CH | 4.26 |
| | 3 | 30.22,CH2 | 2.22 | 29.84,CH2 | 2.19 |
| | | | 1.8 | | 1.82 |
| | 4 | 24.80,CH2 | 1.94 | 24.80,CH2 | 1.94 |
| | 5 | 47.75,CH2 | 3.91 | 47.53,CH2 | 3.81 |
| | | | 3.52 | | 3.6 |
| **AHMOD** | 1 | 175.05, C | | 173.5,C | |
| | 2 | 54.38,CH | 4.09 | 52.84,CH | 4.17 |
| | 3 | 34.82, CH2 | 2.07 | 36.01,CH2 | 1.88 |
| | | | 1.16 | | 1.36 |
| | 4 | 25.47,CH | 1.76 | 26.18,CH | 1.68 |
| | 5 | 46.19,CH2 | 1.25 | 45.58,CH2 | 1.29 |
| | | | 1.17 | | 1.24 |
| | 6 | 64.23,CH | 3.94 | 64.86,CH | 3.97 |
| | 7 | 50.98,CH2 | 2.39(3.4,14.3) | 50.57,CH2 | 2.42 |
| | | | 2.33(8.7,14.3) | | |
| | 8 | 210.41,C | | 210.12,C | |
| | 9 | 36.14,CH2 | 2.42 | 36.26,CH2 | 2.44 |
| | 10 | 7.89,CH3 | 0.89(7.4) | 7.79,CH3 | 0.9 |
| | 11 | 22.91,CH3 | 0.89 | 23.32,CH3 | 0.9 |
| | NH | | 9.68 | | 6.97 |
| **Hyleu** | 1 | 172.10,C | | 172.16 | |
| | 2 | 61.77,CH | 3.81 | 58.64,CH | 4.11 |
| | 3 | 73.24,CH | 3.76 | 75.05,CH | 3.64 |
| | 4 | 29.67,CH | 1.59 | 30.34,CH | 1.58 |
| | 5 | 15.13,CH3 | 0.88 | 17.48,CH3 | 0.91 |
| | 6 | 19.88,CH3 | 0.79 | 19.70,CH3 | 0.83 |
| | NH | | 9.03 | | 7.74 |
| **Aib1** | 1 | 174.56,C | | 174.6 | |

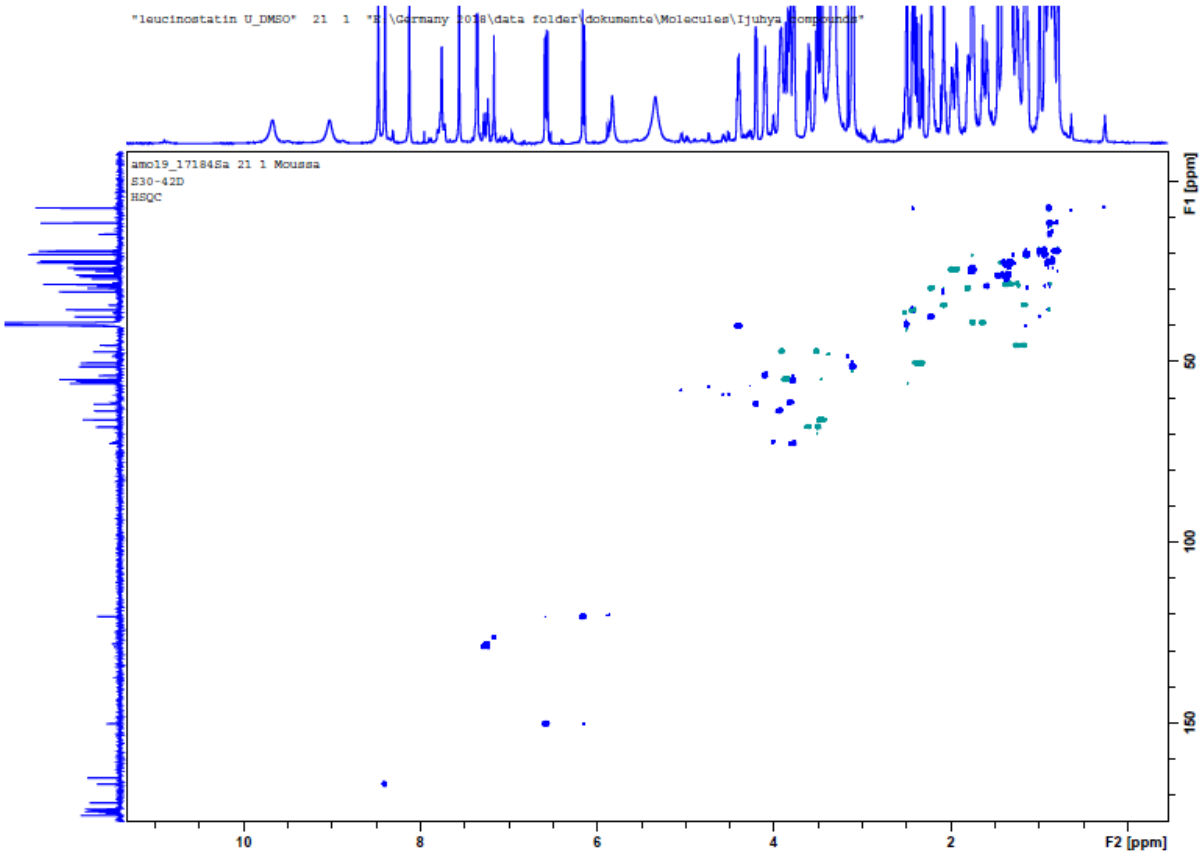
| | | | | | |
|---|---|---|---|---|---|
| | 2 | 55.7,C | | 55.80,C | |
| | 3 | 22.30,CH3 | 1.34 | 23.39,CH3 | 1.38 |
| | 4 | 26.10,CH3 | 1.41 | 25.14,CH3 | 1.34 |
| | NH | | 8.47 | | 8.16 |
| **Aib2** | 1 | 175.64,C | | 173.24,C | |
| | 2 | 56.0,C | | 55.94,C | |
| | 3 | 22.6,CH3 | 1.32 | 25.63,CH3 | 1.31 |
| | 4 | 25.83,CH3 | 1.46 | 23.32,CH3 | 1.38 |
| | NH | | 7.56 | | 7.43 |
| **Leu** | 1 | 174.43,C | | 173.16,C | |
| | 2 | 55.82,CH | 3.78 | 53.76,CH | 3.83 |
| | 3 | 39.80,CH2 | 1.75 | 39.41,CH2 | 1.77 |
| | | | 1.64 | | 1.58 |
| | 4 | 24.54,CH | 1.76 | 24.55,CH | 1.76 |
| | 5 | 22.57,CH3 | 0.84(6.3) | 21.75,CH3 | 0.84 |
| | 6 | 22.91,CH3 | 0.89 | 23.32,CH3 | 0.9 |
| | NH | | 7.75 | | 6.92 |
| **Aib3** | 1 | 173.97,C | | 175.2,C | |
| | 2 | 56.04,C | | 56.09,C | |
| | 3 | 22.3,CH3 | 1.36 | 22.90,CH3 | 1.38 |
| | 4 | 26.54,CH3 | 1.4 | 25.66,CH3 | 1.35 |
| | NH | | 8.12 | | 7.57 |
| **Aib4** | 1 | 173.90,C | | 173.31,C | |
| | 2 | 55.73,C | | 55.97,C | |
| | 3 | 26.79,CH3 | 1.47 | 25.76,CH3 | 1.34 |
| | 4 | 22.90,CH3 | 1.38 | 23.44,CH3 | 1.37 |
| | NH | | 7.16 | | 7.57 |
| **C-terminal** | 1 | 40.64,CH | 4.4(m) | 43.15,CH | 3.81 |
| | 2 | 68.65,CH2 | 3.61(9.8) | 63.31,CH2 | 2.31 |
| | | | 3.5(7.6) | | |
| | 3 | 66.59,CH2 | 3.46 (5.3) | 60.21,CH2 | 2.45 |
| | 4 | 55.48,CH2 | 3.86 (5.3) | 59.22,CH2 | 3.44 |
| | 5 | 51.91,CH3 | 3.11(5.9) | 19.27,CH3 | 1.02 |
| | 6 | 51.91,CH3 | 3.11(5.9) | | |
| | 7 | 20.86,CH3 | 1.15(6.4) | | |
| | NH | | 7.36 | | 7.75 |
| | N-CH3 | | | 43.41,CH3 | 2.2 |



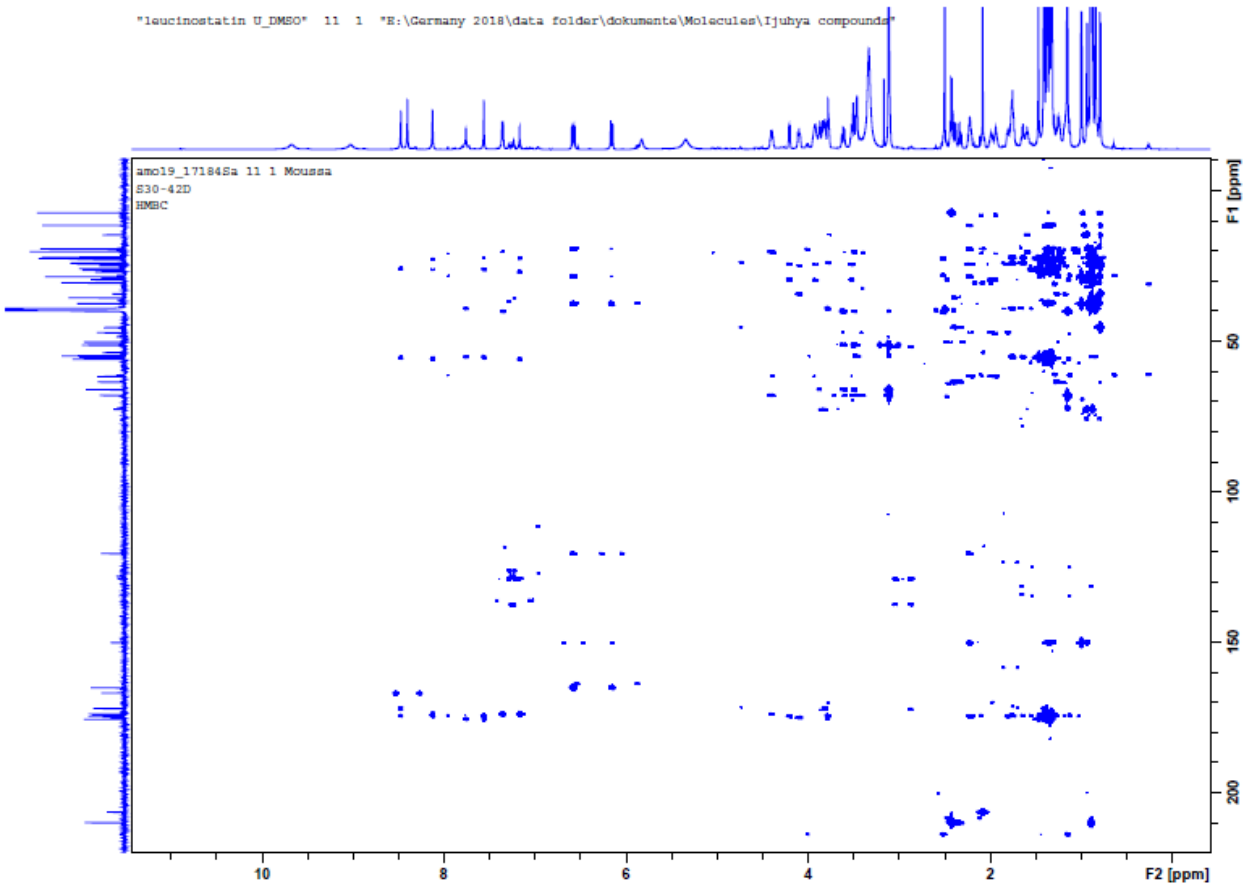

**S1 figure:** $^{1}$HNMR spectra of **leucinostatin U 1.**



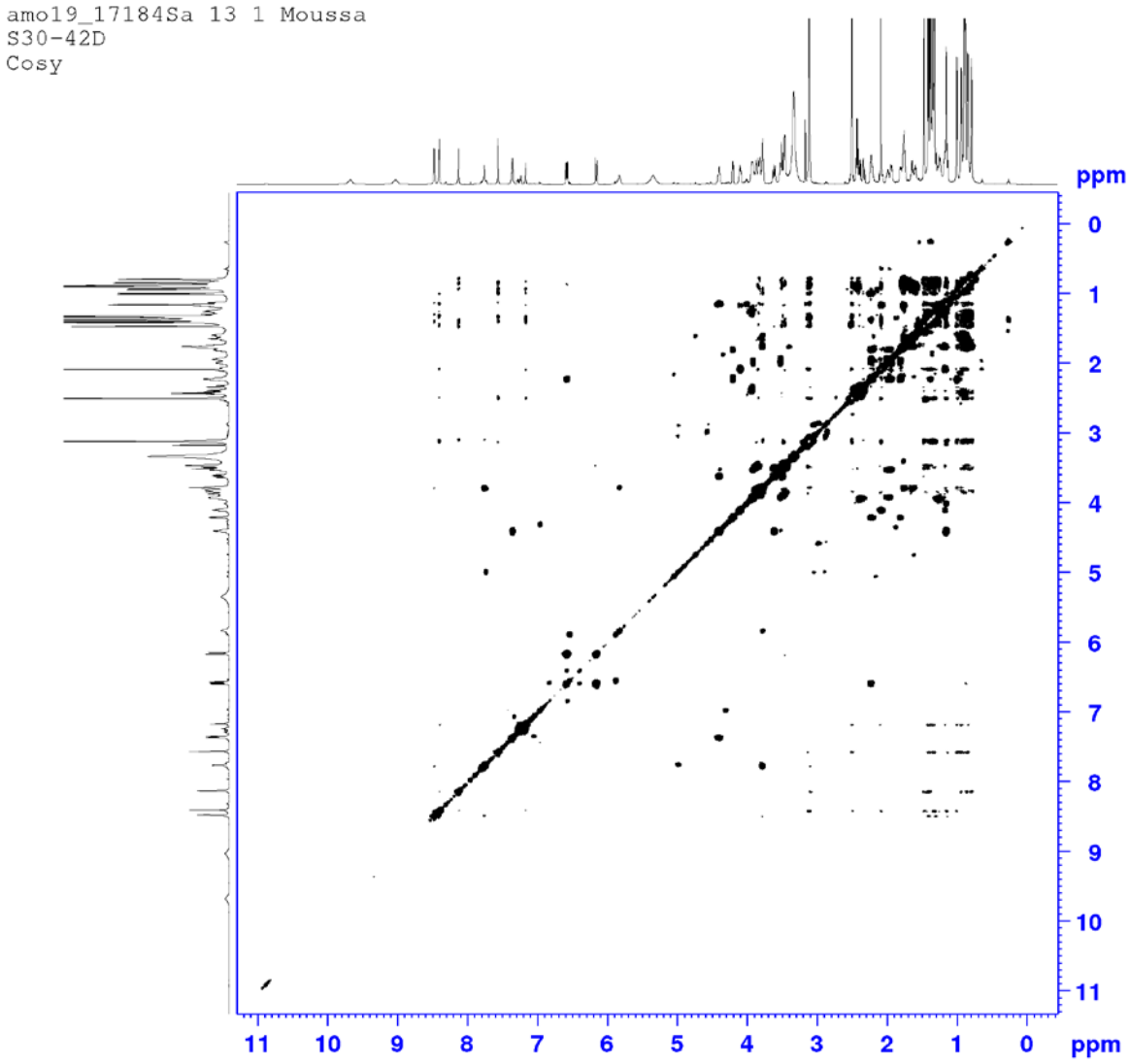

**S2. Figure:** $^{13}$CNMR spectra of **leucinostatin U.1.**



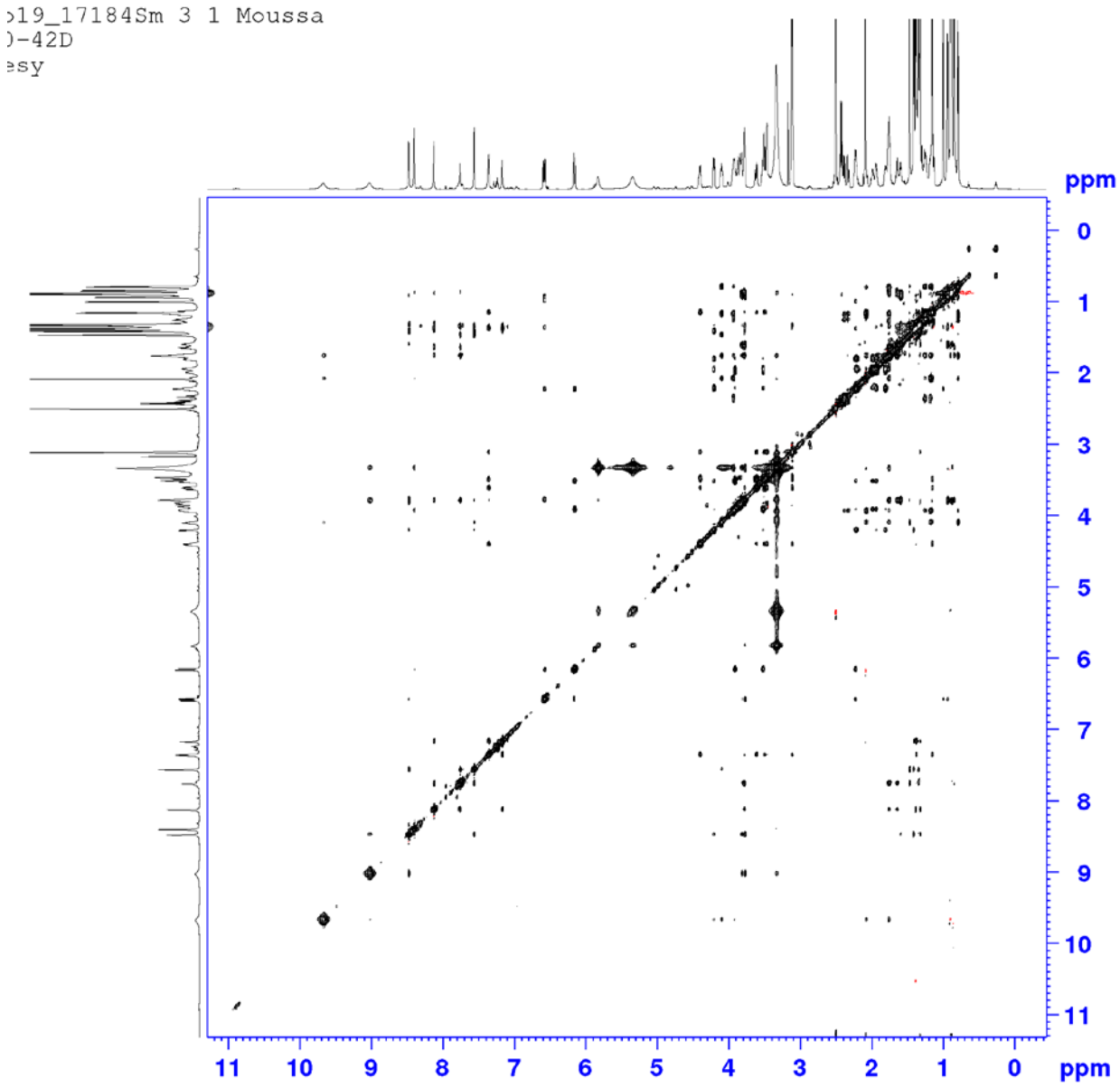

**S3 Figure:** HSQC spectra **of leucinostatin U 1.**



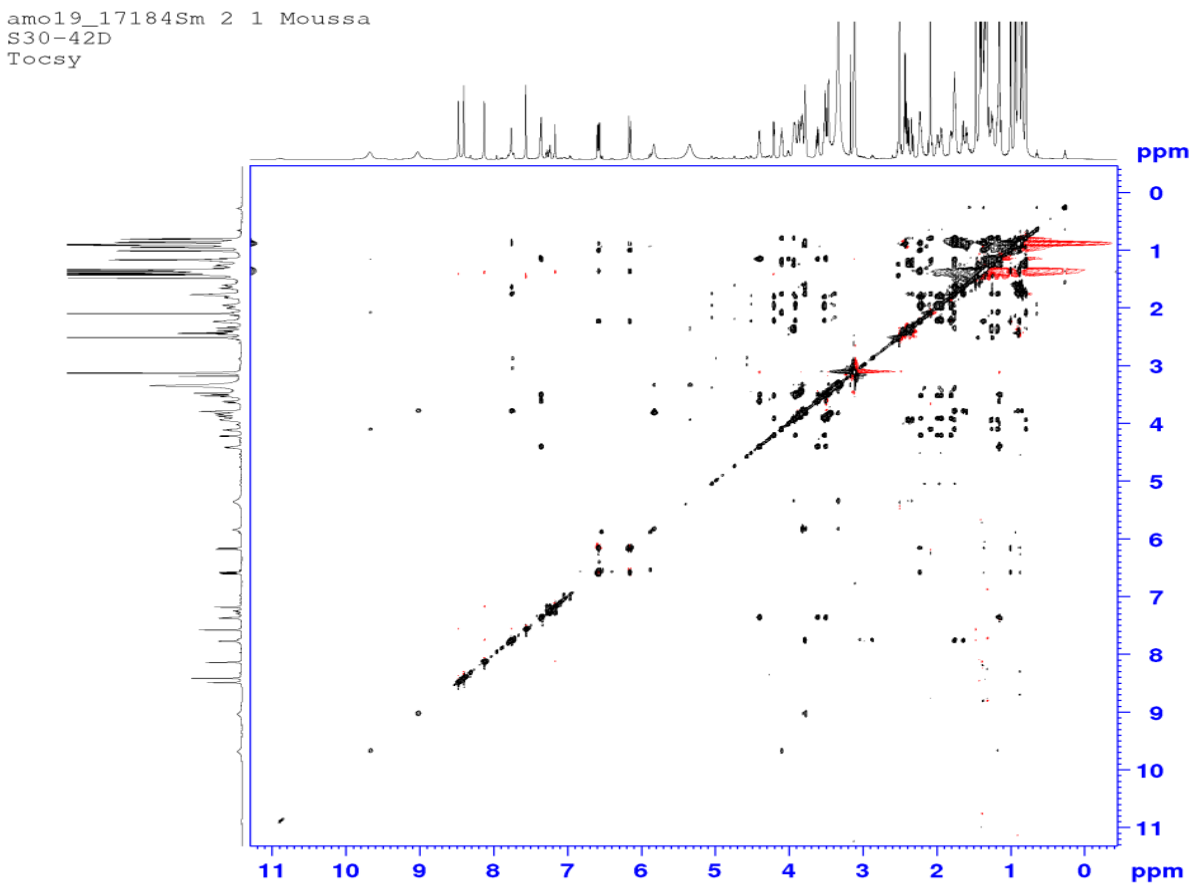

**S4 Figure:** HMBC spectra **of leucinostatin U 1**




**S5 Figure:** COSY spectra **of leucinostatin U 1.**

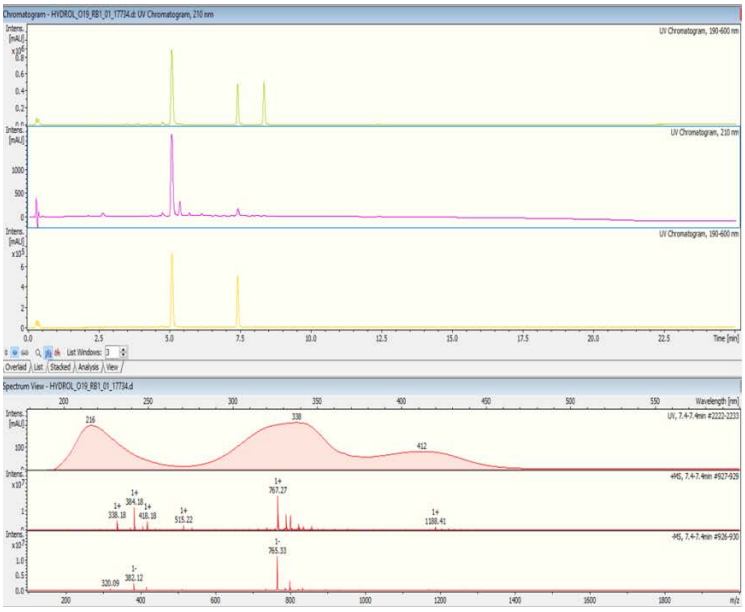


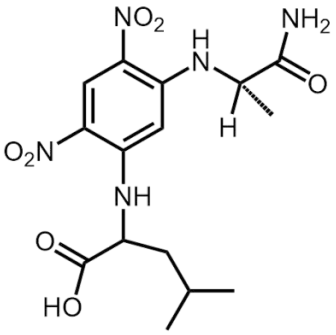

**S6 Figure:** NOESY spectra **of leucinostatin U 1**




**S7 Figure:** TOCSY spectra **of leucinostatin U 1.**

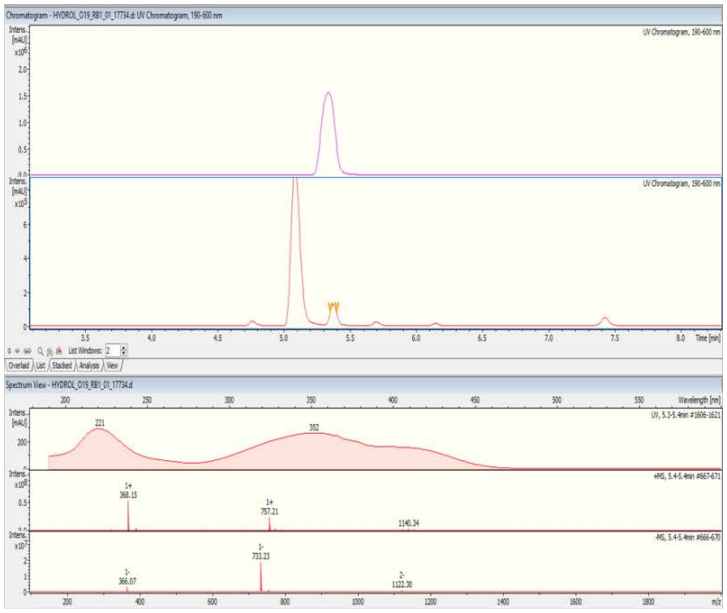
.

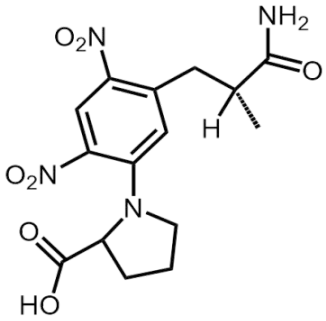





Chemical Formula: C15H21N5O7
Exact Mass: 383,14
Molecular Weight: 383,36

**FDLA- D-leucine and DL-leucine**

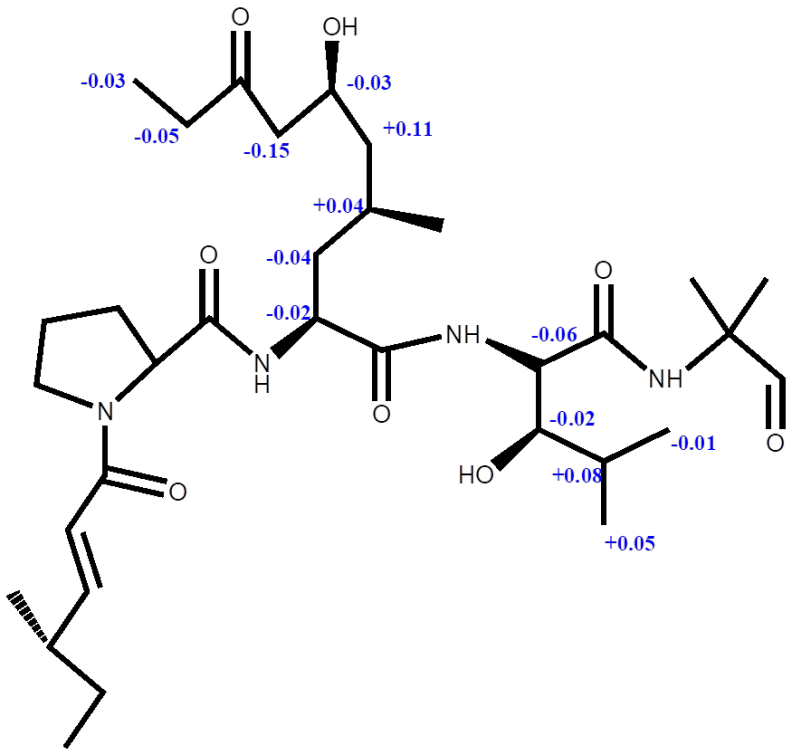




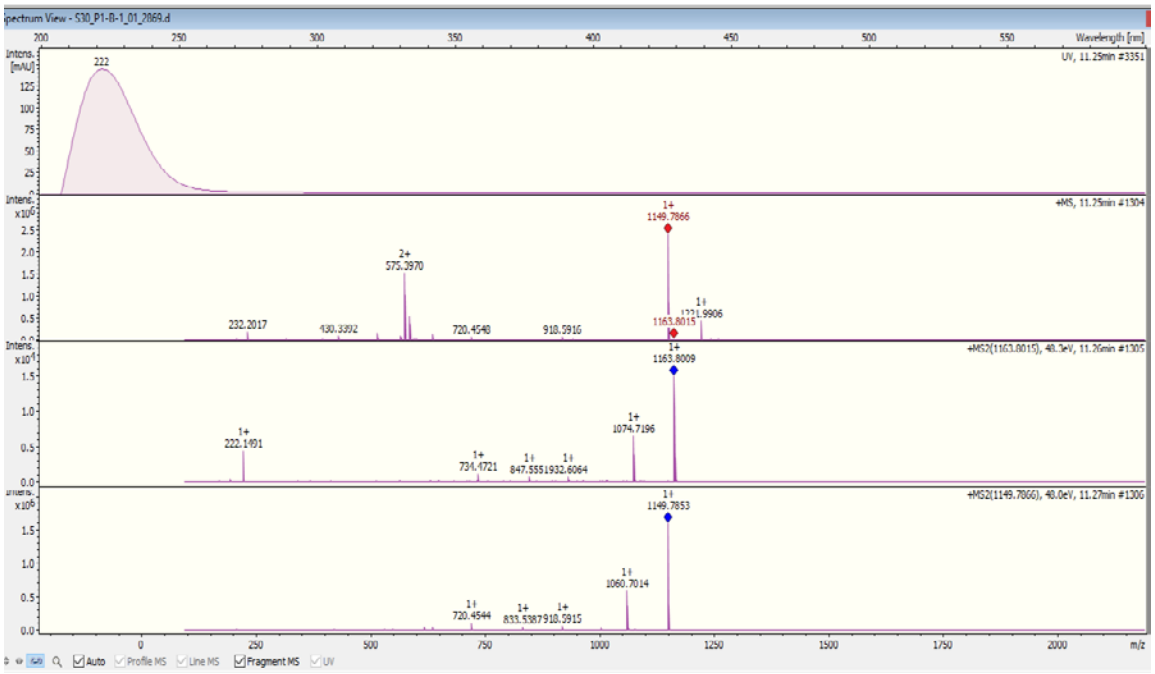

Chemical Formula: C15H18N4O7
Exact Mass: 366,12
Molecular Weight: 366,33

**FDLA-L- Proline and D-proline**

**S8 Figure.** HR-ESI-MS of Marfay's reaction products of **leucinostatin U 1.**



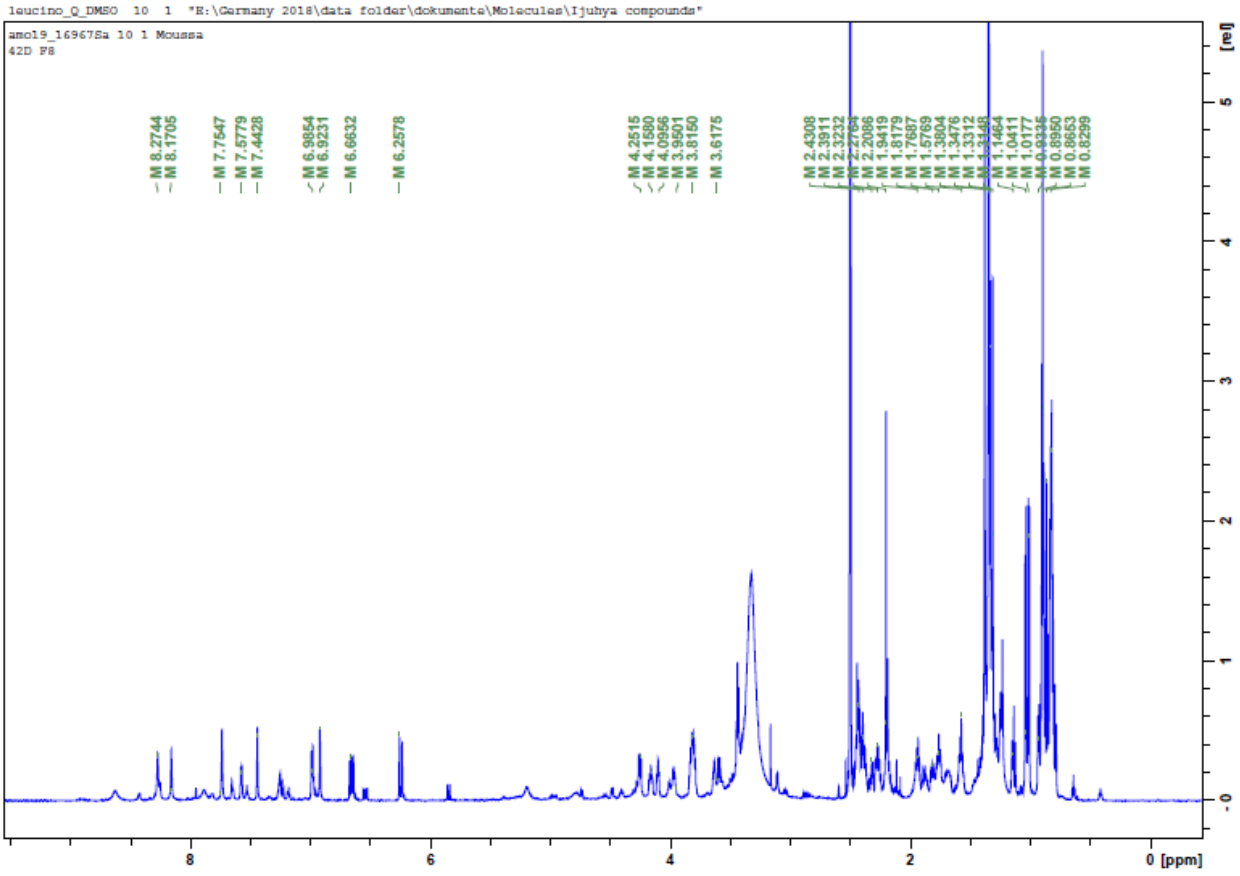

**S9 Figure.** ΔδSR chemical shifts of MTPA (*α*-methoxy-*α*-trifluoromethylphenylacetic acid) (Mosher) derivatives of the proline, AHMOD and Hy-Leu of **1.**



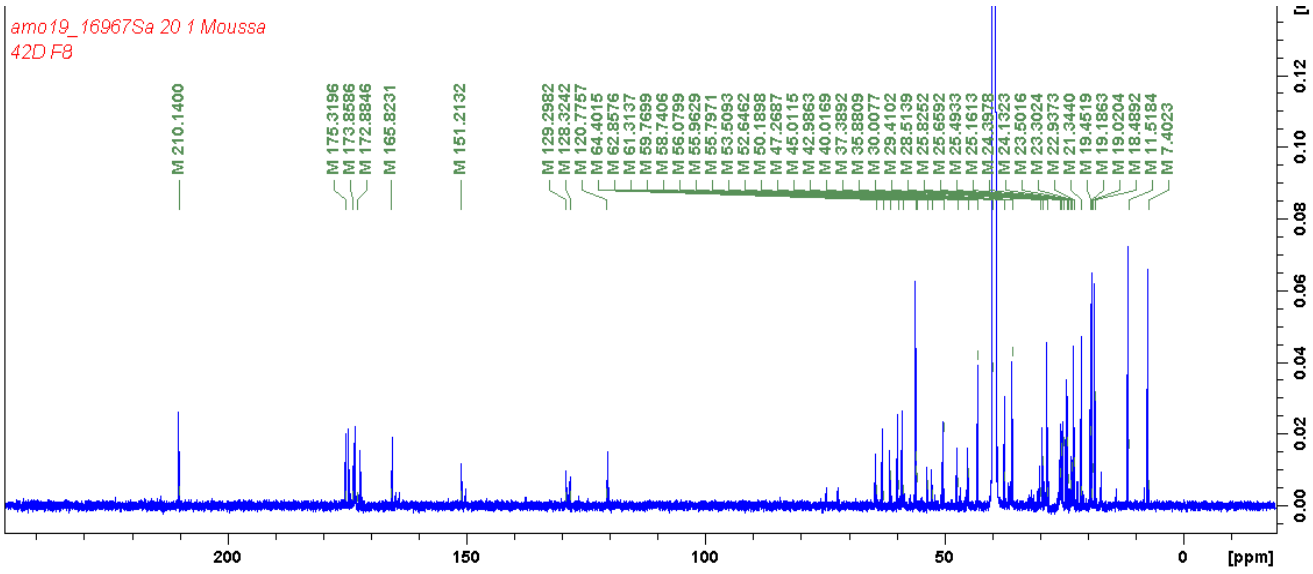

**S10 Figure**. HR-ESI-MS-MS fragmentation pattern of leucinostatin U **1**.

**S2.Table**. 1H NMR data of **leucinostatin U 1** and the characteristic chemical shift value differences ΔδSR of the corresponding Mosher esters, recorded at 700 MHz (75% CH3CN/D2O).

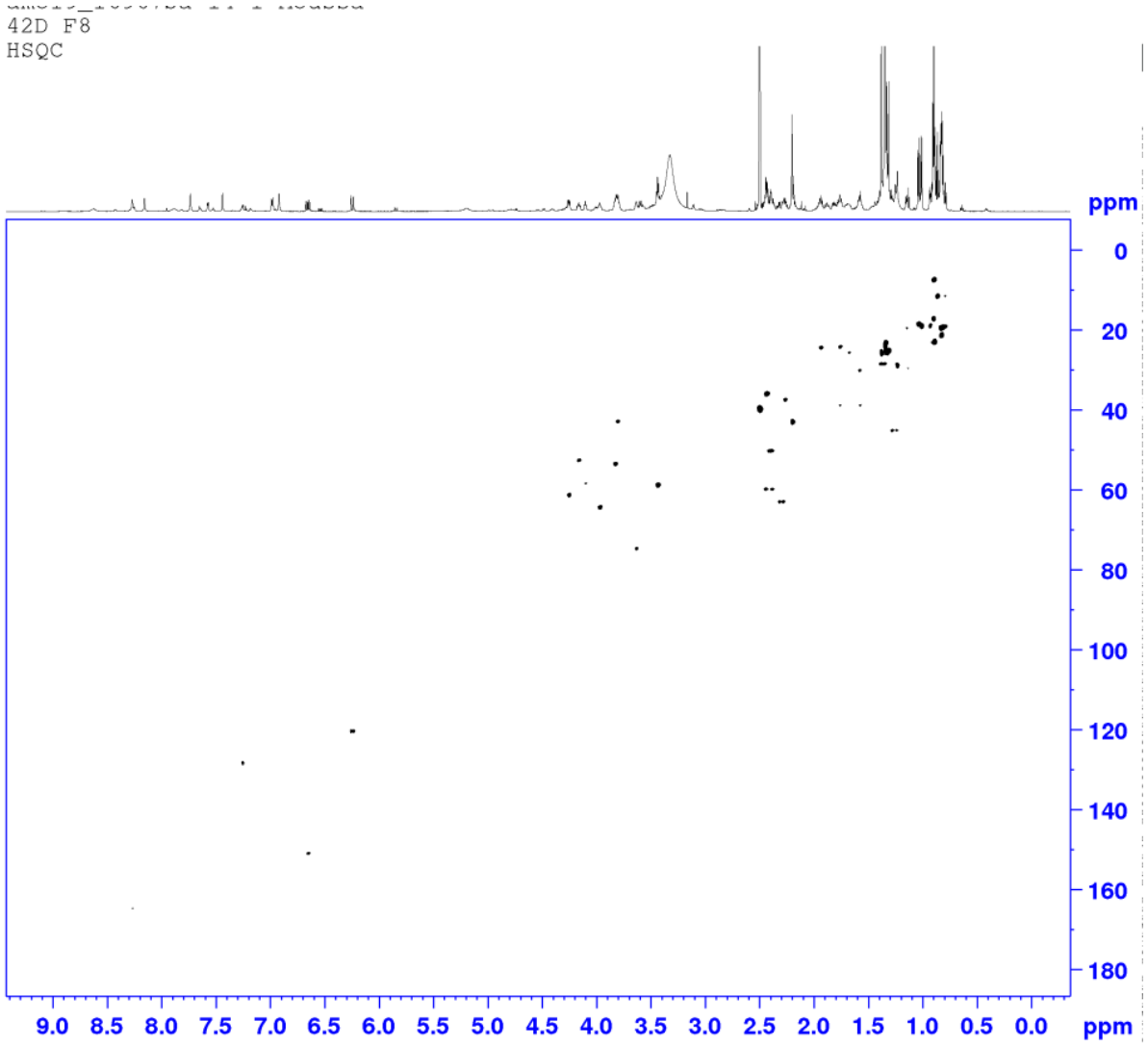
| position | δH leucinostatin U (1) | δH of leucinostatin U (1) reacted with R-MTPA-Cl | δH of leucinostatin U (1) reacted with S-MTPA-Cl | ΔS-ΔR(ppm) | ΔS-ΔR (Hz) |
|---|---|---|---|---|---|
| **AHMOD** | | | | | |
| **2** | 4.67 | 4.73,CH | 4.71,CH | -0.02 | -14 |
| **3** | 2.57, 1.29 | 1.52, 2.51CH2 | 1.92, 2.76,CH2 | -0.04 | -28 |
| **4** | 1.74 | 1.72 | 1.68, CH2 | 0.04 | 28 |
| **10** | 1 | 0.98 | 0.97 | 0.01 | 7 |
| **5** | 1.55, 1.19 | 1.62, 1.30 | 1.73 | 0.11 | 77 |
| **6** | 4.58 | 4.68 | 4.51,CH2 | -0.03 | -21 |
| **7** | 2.98 | 2.56, 2.72 | 3.22, 2.99, CH2 | -0.15 | -105 |
| **8** | 2.57, 1.29 | 2.64, 2.53 | 2.59,2.45,CH2 | -0.05 | -35 |
| **9** | 1.06 | 0.99 | 1.02 | -0.03 | -21 |
| **Hyleu** | | | | | |
| **2** | 4.39 | 4.60,CH | 4.55,CH | -0.06 | -42 |
| **3** | 4.52 | 4.45,CH | 4.47,CH | -0.02 | -14 |
| **4** | 1.88 | 1.86,CH | 1.94,CH | 0.08 | 56 |
| **5** | 0.85 | 0.88,CH3 | 0.93,CH3 | 0.05 | 35 |
| **6** | 1.42 | 1.34,CH3 | 1.35,CH3 | -0.01 | -1 |



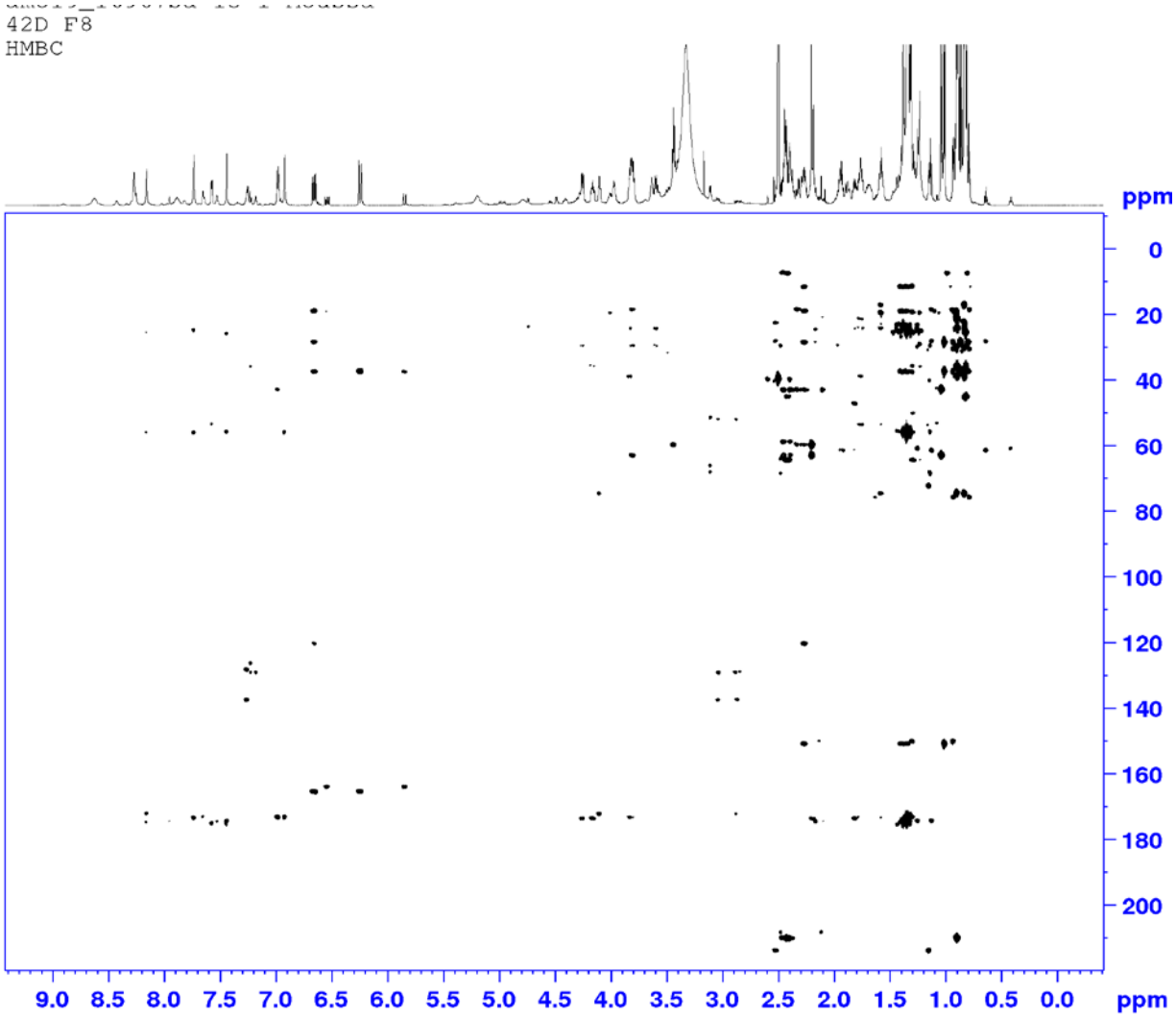

**S11 figure:** [1]HNMR spectra of **leucinostatin Q 2**



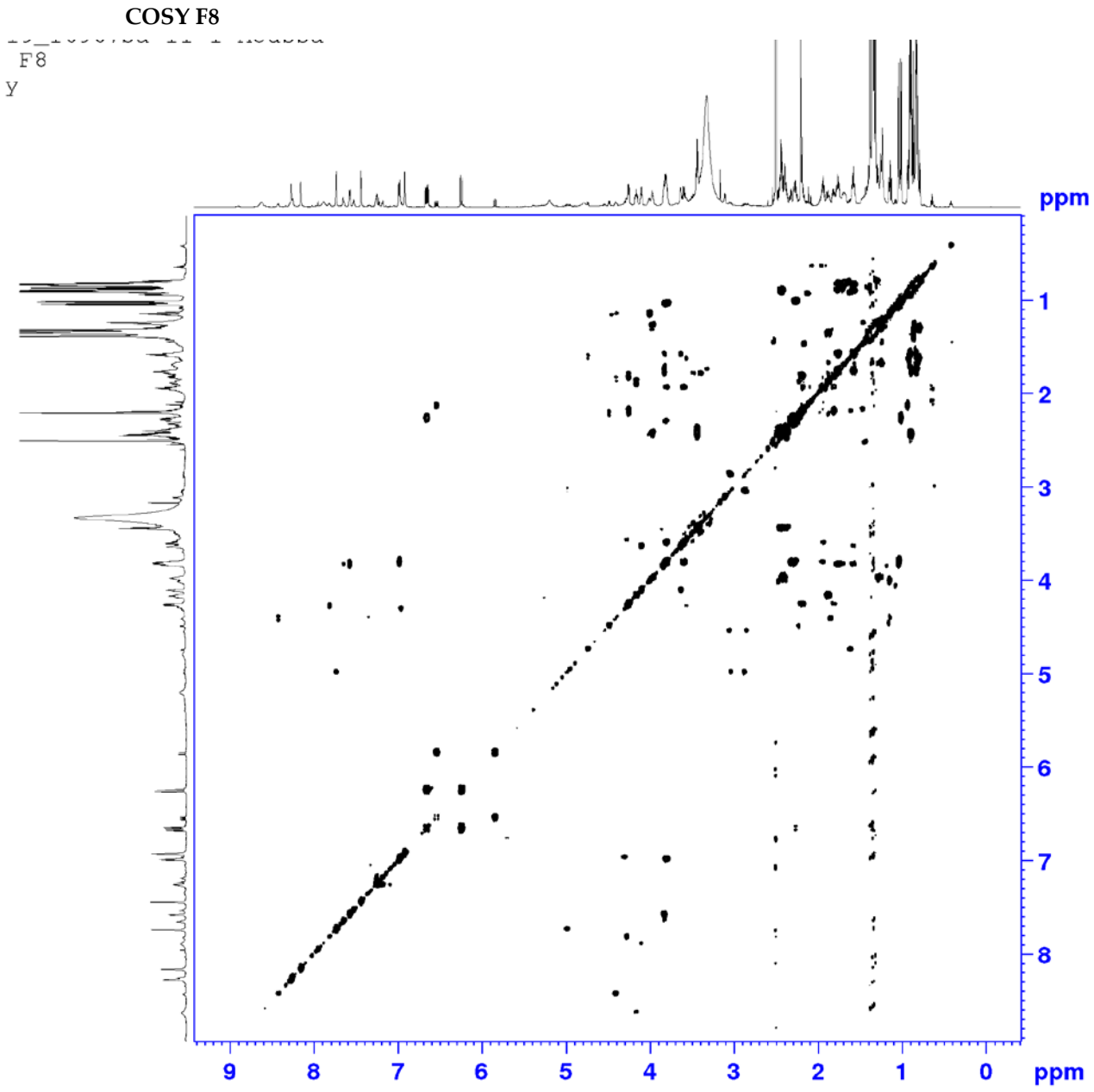

**S12. Figure:** $^{13}$CNMR spectra of **leucinostatin Q 2.**.


42D F8
HSQC
ppm
0
20
40
60
80
100
120
140
160
180
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
ppm

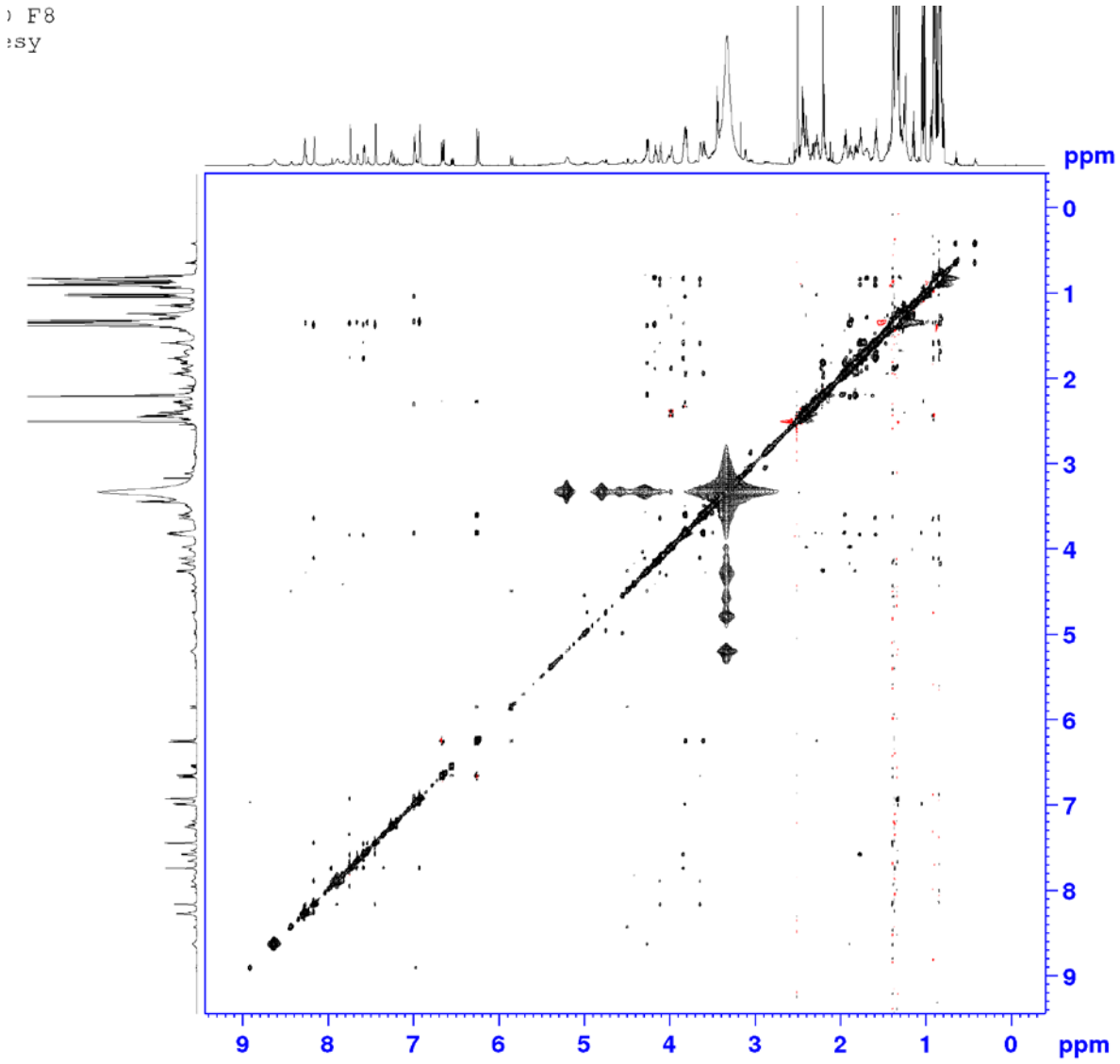
**S13 Figure:** HSQC spectra of **leucinostatin Q 2**



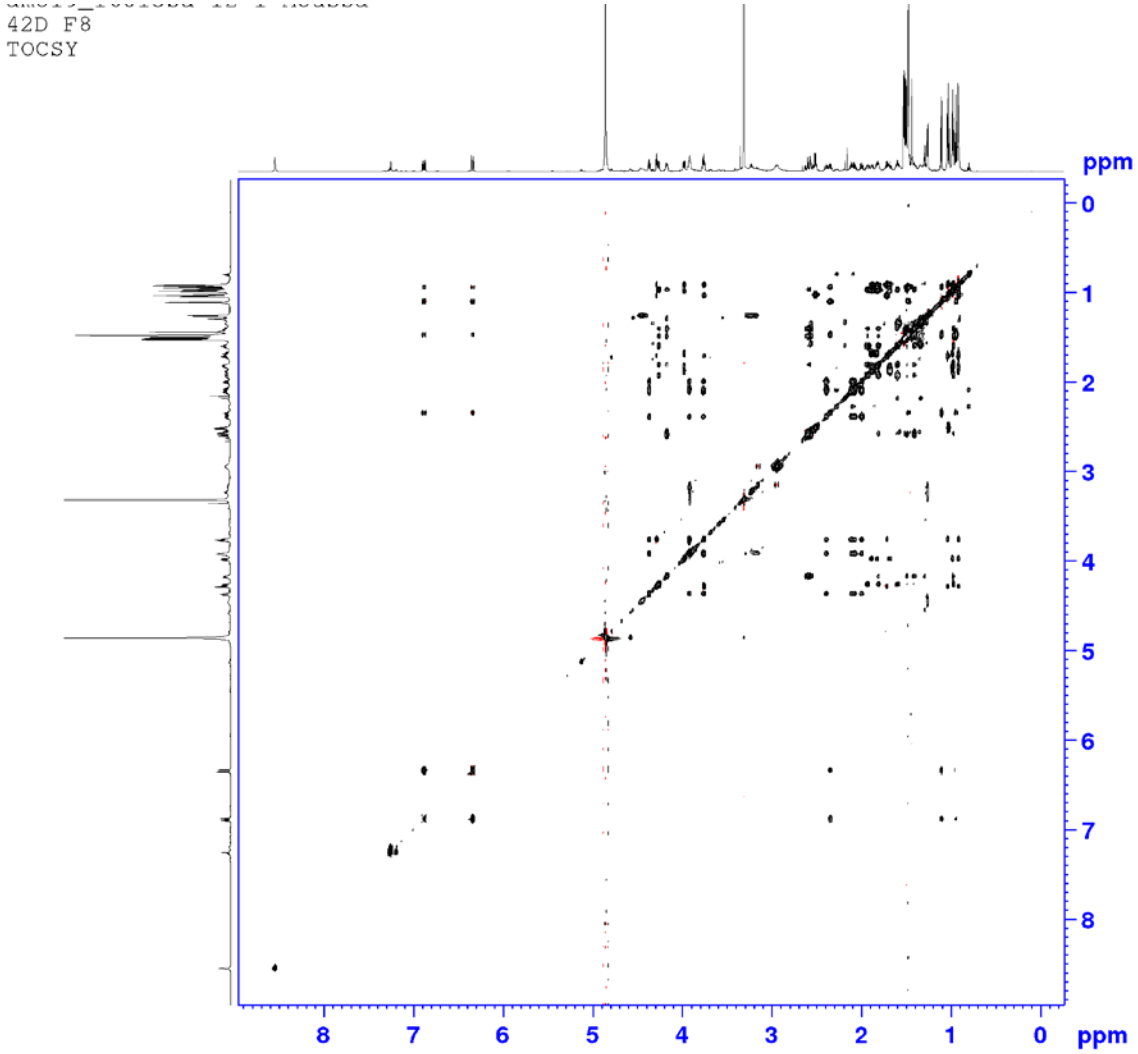

**S14 Figure:** HMBC spectra **of leucinostatin Q 2**



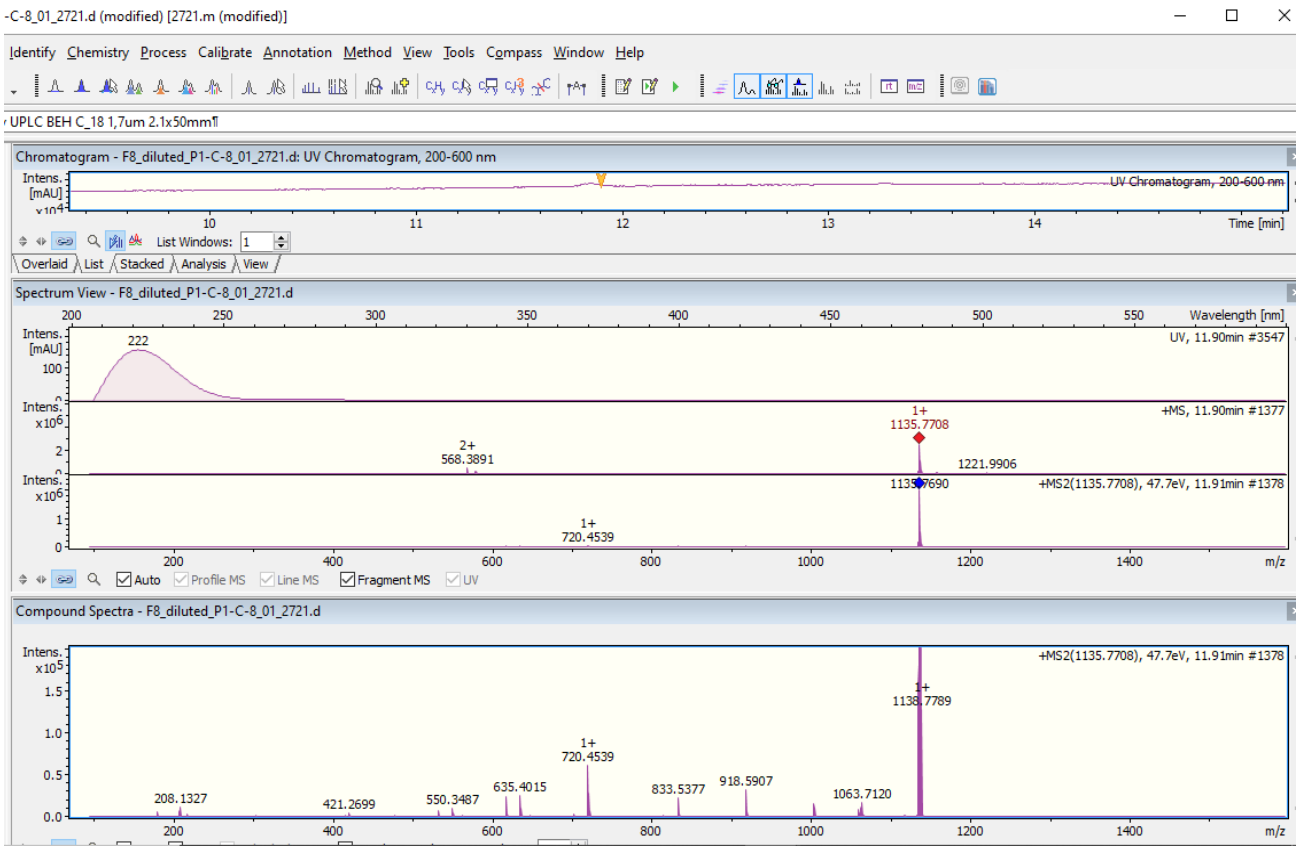

**S15 Figure:** COSY spectra **of leucinostatin Q 2**




**S16 Figure:** NOESY spectra **of leucinostatin Q 2**


42D F8
TOCSY
ppm
0
1
2
3
4
5
6
7
8
8
7
6
5
4
3
2
1
0
ppm

**S17 Figure:** TOCSY spectra **of leucinostatin Q 2**

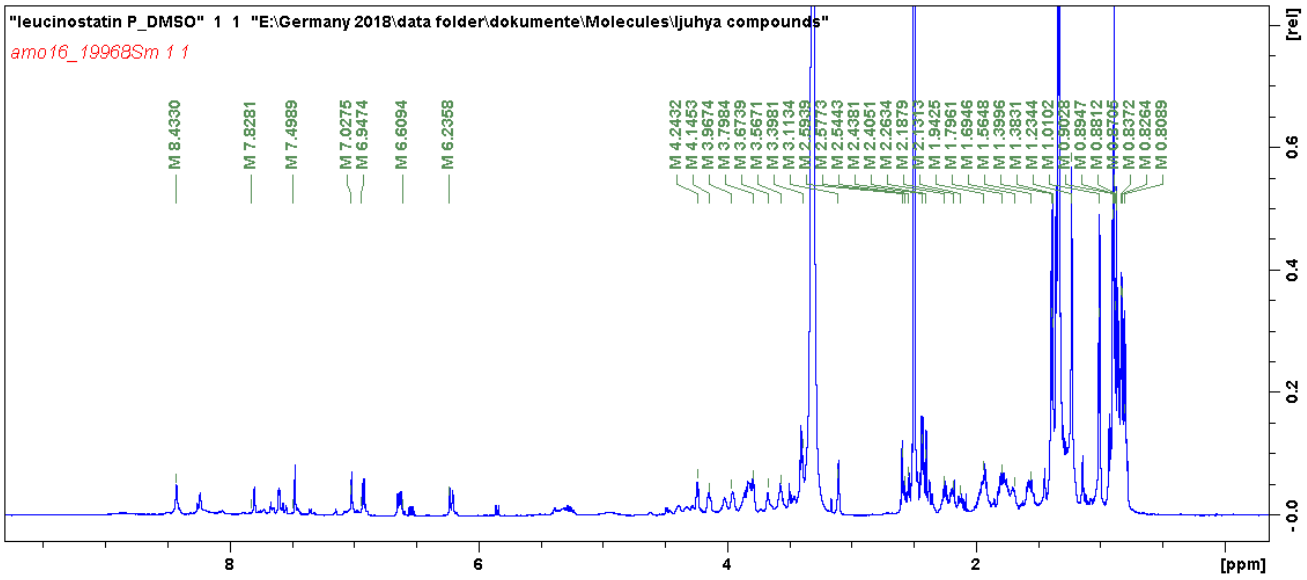



**S18 Figure**: HR-ESI-MS-MS fragmentation pattern of **leucinostatin Q 2.**

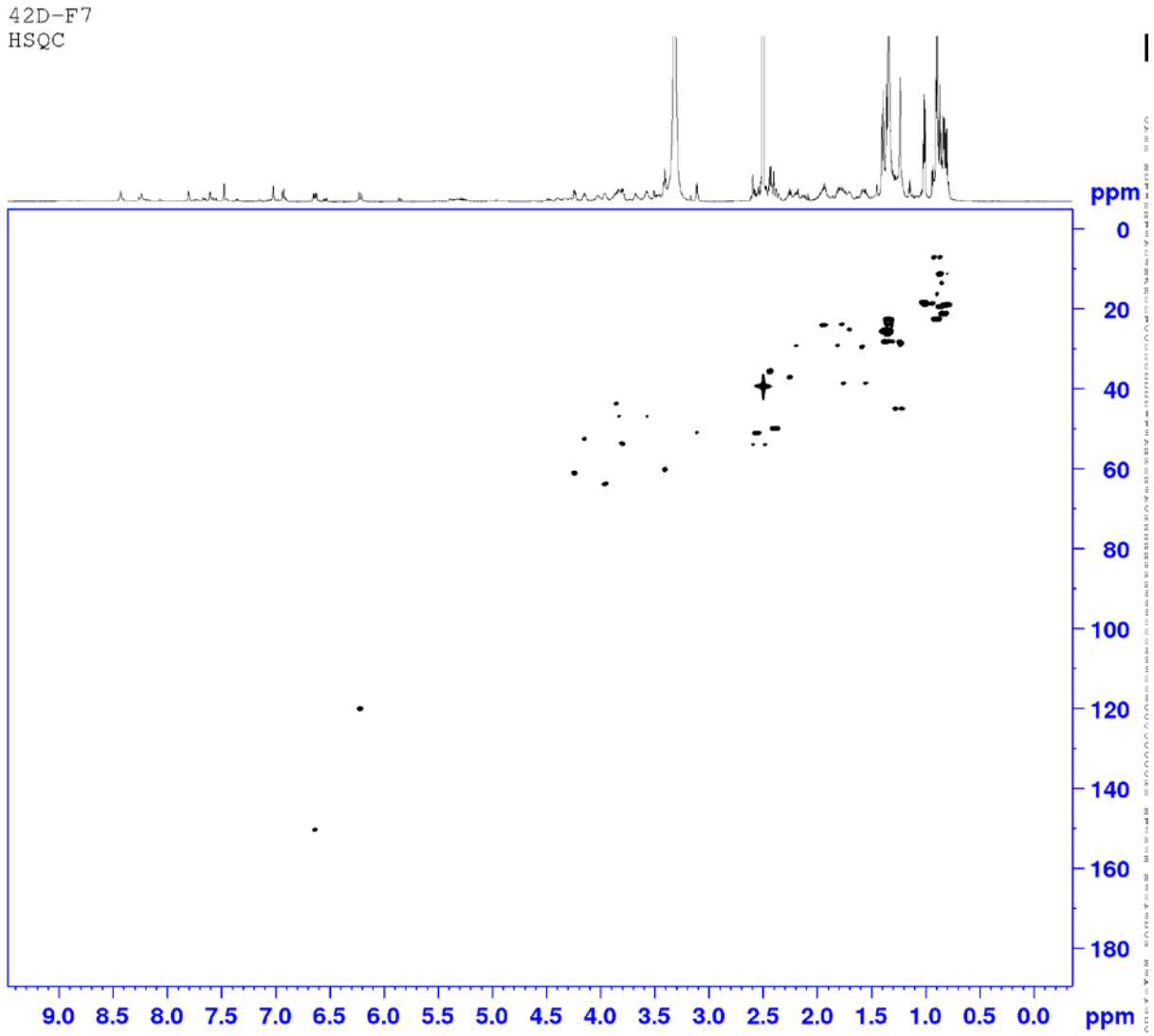
**S3 Table.** $^{1}H$ NMR and $^{13}C$ NMR data of **leucinostatin P 3** and its characteristic chemical shift values.

| residue | position | δC, type | δH( J in Hz) | residue | position | δC, type | δH( J in Hz) |
|---|---|---|---|---|---|---|---|
| **ΔMHA** | **1** | 165.28,C | | **Aib2** | **1** | 173.23,C | |
| | **2** | 120.19,CH | 6.22 | | **2** | 55.8,C | |
| | **3** | 150.59,CH | 6.64 | | **3** | 25.18,CH3 | 1.39 |
| | **4** | 37.17,CH | 2.25 | | **4** | 23.06,CH3 | 1.33 |
| | **5** | 28.22,CH2 | 1.36 | | **NH** | | 7.47 |
| | **6** | 11.29,CH3 | 0.87 | **Leu** | **1** | 173.78,C | |
| | **7** | 18.62,CH3 | 1.01 | | **2** | 53.88,CH | 3.79 |
| **Pro** | **1** | 173.16,C | | | **3** | 38.74,CH2 | 1.55 |
| | **2** | 61.28,CH | 4.24 | | | | 1.75 |
| | **3** | 29.19,CH2 | 1.81 | | **4** | 23.79,CH | 1.77 |
| | | | 2.19 | | **5** | 21.27,CH3 | 0.85 |
| | **4** | 24.10,CH2 | 1.95 | | **6** | 22.58,CH3 | 0.91 |
| | **5** | 46.90,CH2 | 3.82 | | NH | | 7.02 |
| | | | 3.56 | **Aib3** | **1** | 175.23,C | |
| **AHMOD** | **1** | 173.63,C | | | **2** | 24.30,CH3 | 1.34 |
| | **2** | 52.65,CH | 4.15 | | **3** | 25.01,CH3 | 1.33 |
| | **3** | | | | **4** | 56.5,C | |
| | | | | | **NH** | | 7.6 |
| | **4** | 25.11,CH | 1.7 | **Aib4** | **1** | 171.4,C | |
| | **5** | 44.90,CH2 | 1.21 | | **2** | 55.7,C | |
| | | | 1.28 | | **3** | 23.85,CH3 | 1.35 |
| | **6** | 64.02,CH | 3.96 | | **4** | 24.10,CH3 | 1.32 |
| | **7** | 51.12,CH2 | 2.57 | | **NH** | | 7.6 |
| | | | | **C-terminal** | **1** | 43.62,CH | 3.85 |
| | | | 2.54 | | | | |

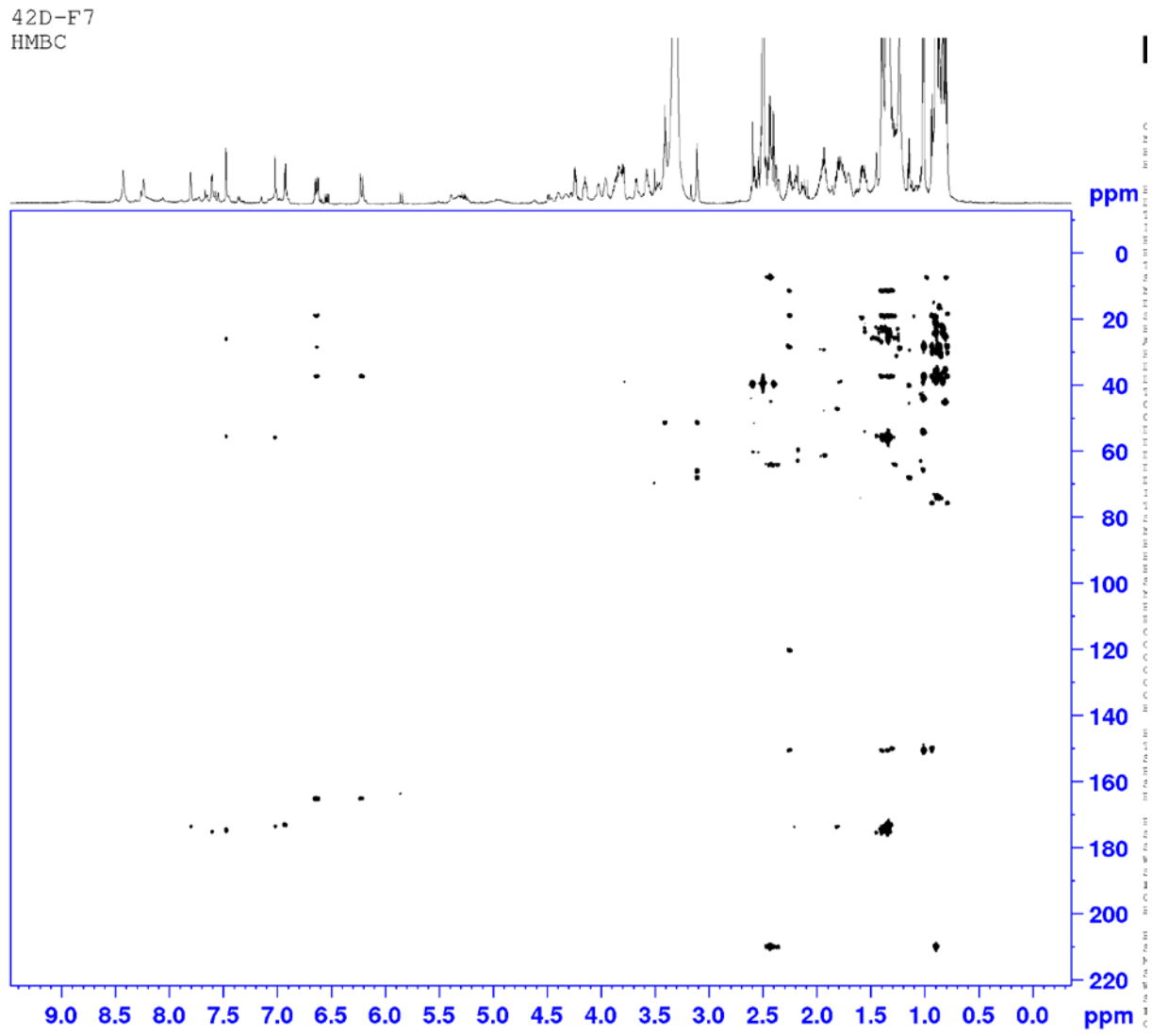
| | | | | | | |
|---|---|---|---|---|---|---|
| | **8** | 209.95,C | | **2** | 54.13,CH2 | 2.5 |
| | **9** | 35.66,CH2 | 2.43 | | | 2.48 |
| | **10** | 7.20,CH3 | 0.9 | **3** | 51.12,CH2 | 2.57 |
| | **11** | 22.58,CH3 | 0.91 | | | 2.54 |
| | **NH** | | 6.93 | **4** | 60.18,CH2 | 3.4 |
| **Hyleu** | **1** | 172.16,C | | **NH** | | 8.25 |
| | **2** | 63.85,CH | 4.01 | | | |
| | **3** | 73.88,CH | 3.67 | | | |
| | **4** | 29.57,CH | 1.58 | | | |
| | **5** | 13.50,CH3 | 0.85 | | | |
| | **6** | 18.98,CH3 | 0.81 | | | |
| | **NH** | | 7.8 | | | |
| **Aib1** | **1** | 174.68,C | | | | |
| | **2** | 56.03,C | | | | |
| | **3** | 23.57,CH3 | 1.33 | | | |
| | **4** | 26.01,CH3 | 1.36 | | | |
| | **NH** | | | | | |
| | | 8.43 | | | | |



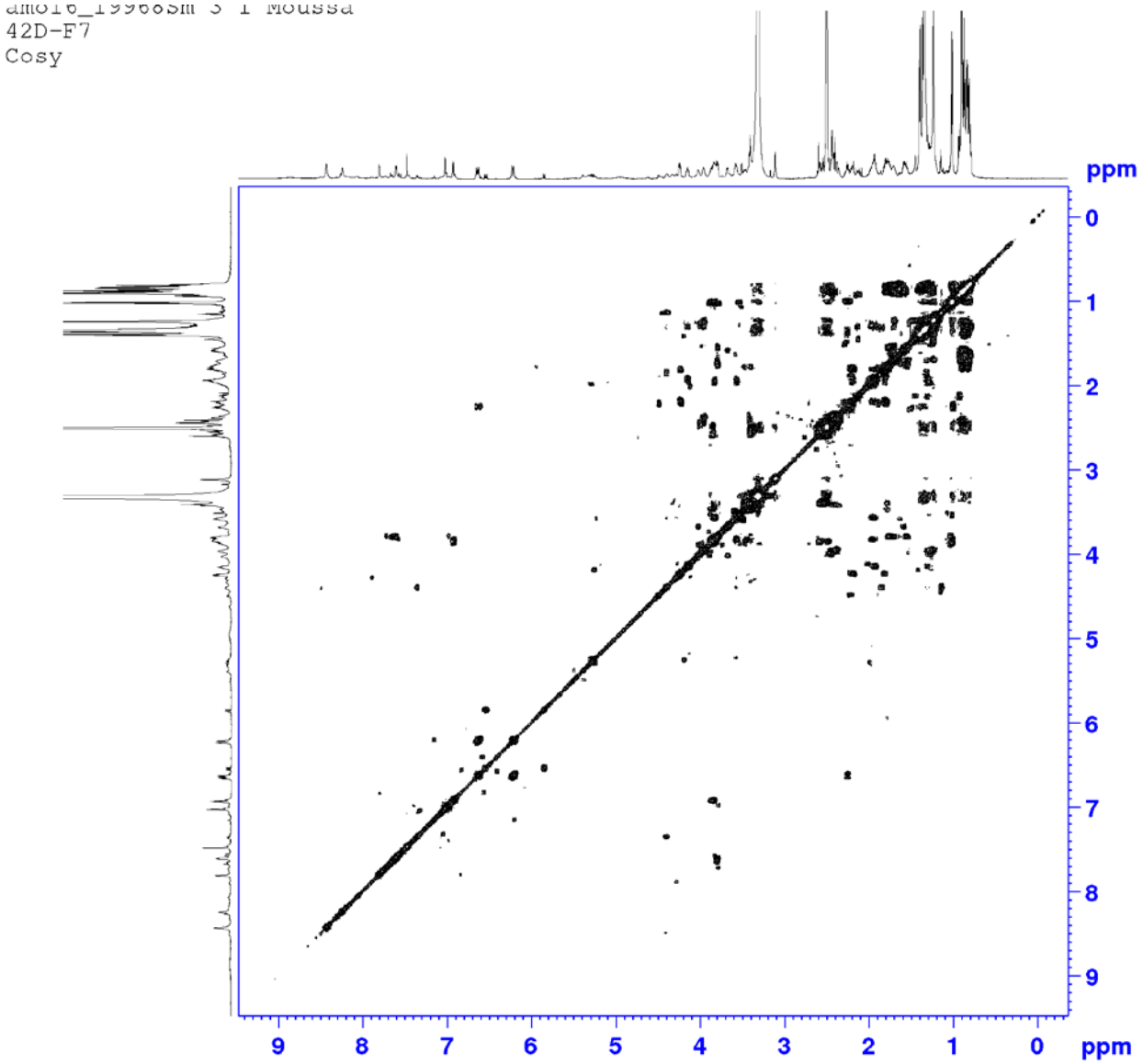

**S19 figure:** 1HNMR spectra of **leucinostatin P 3**



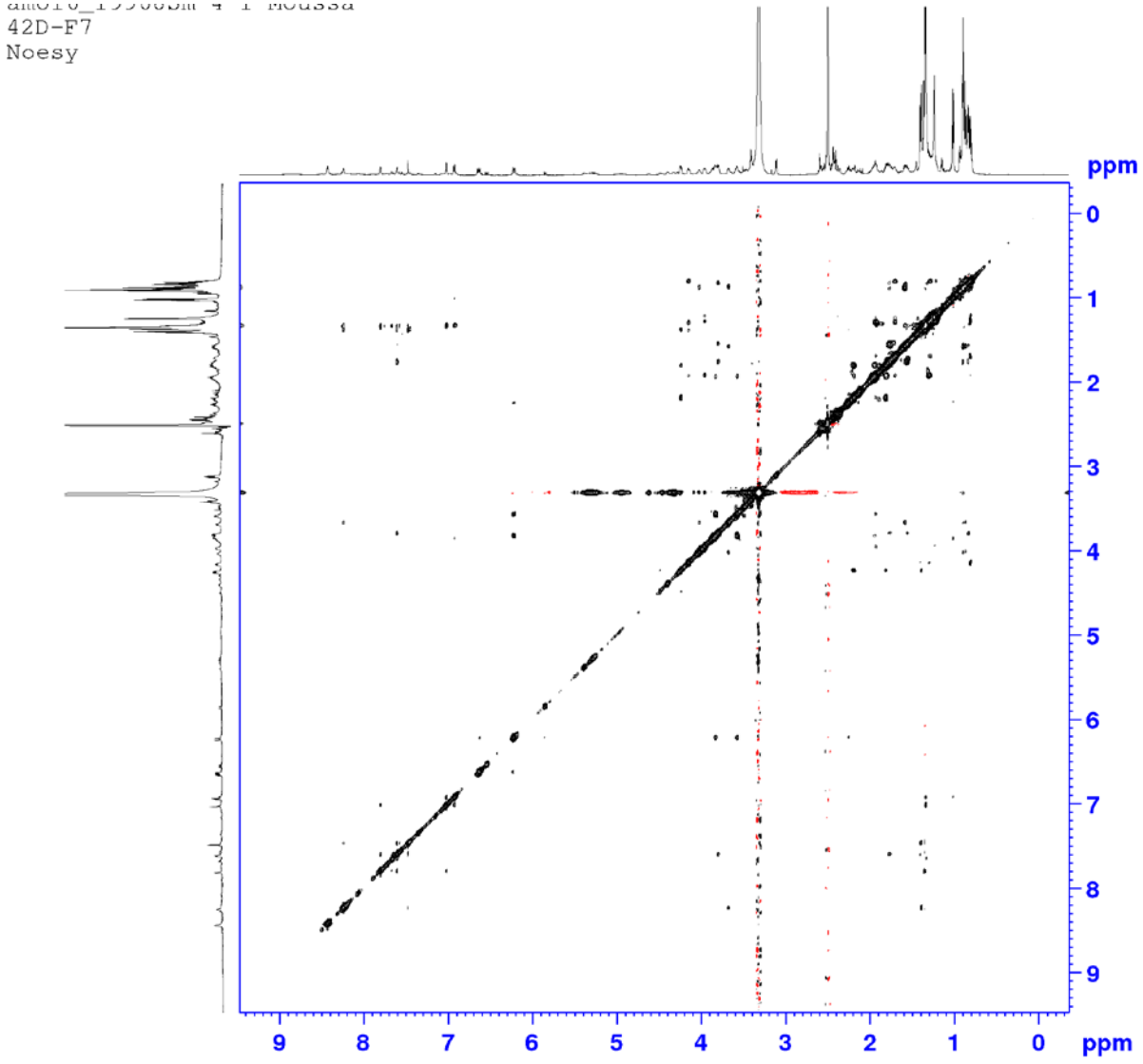

**S20 Figure:** HSQC spectra of **leucinostatin P 3**



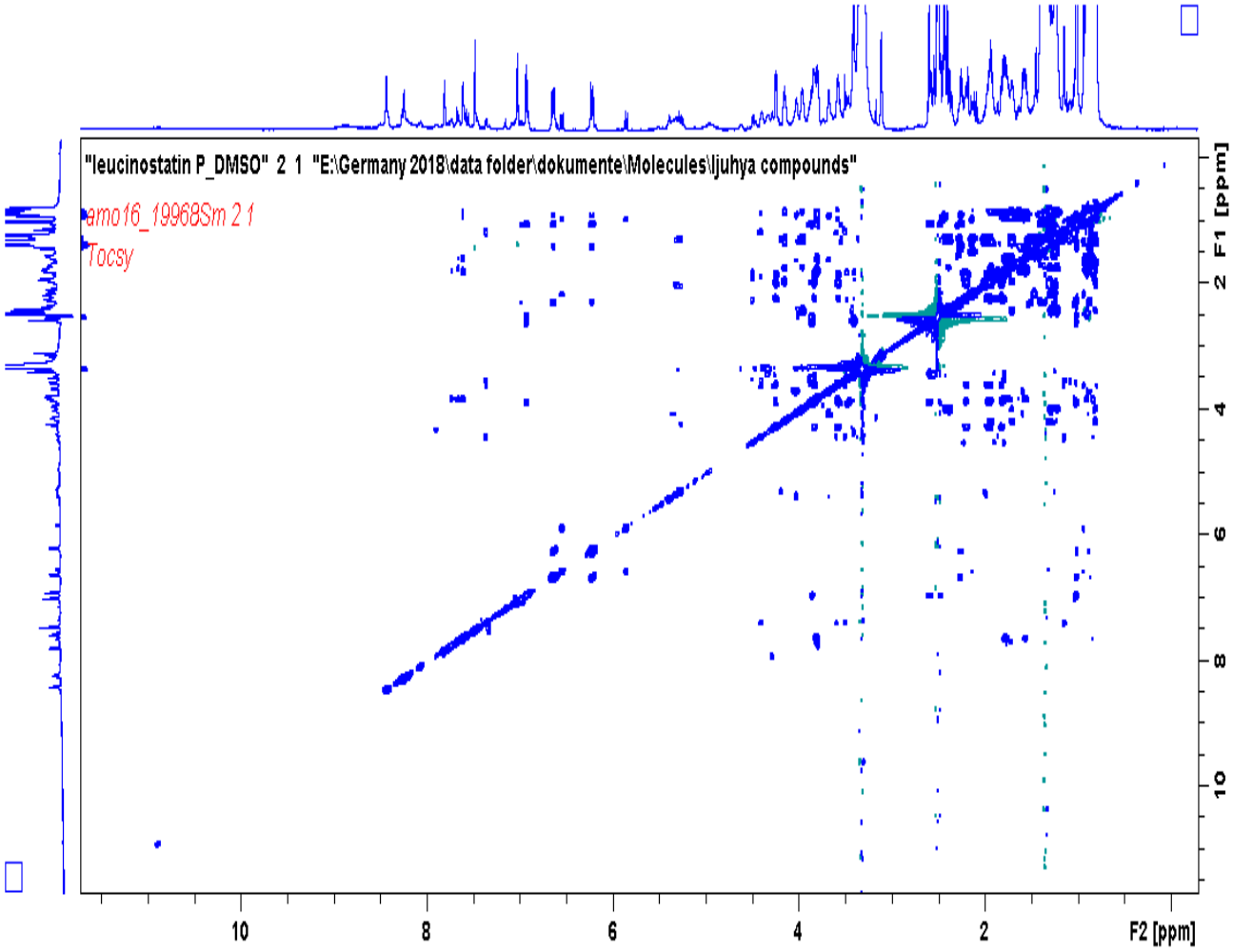

**S21 Figure:** HMBC spectra **of leucinostatin P 3**



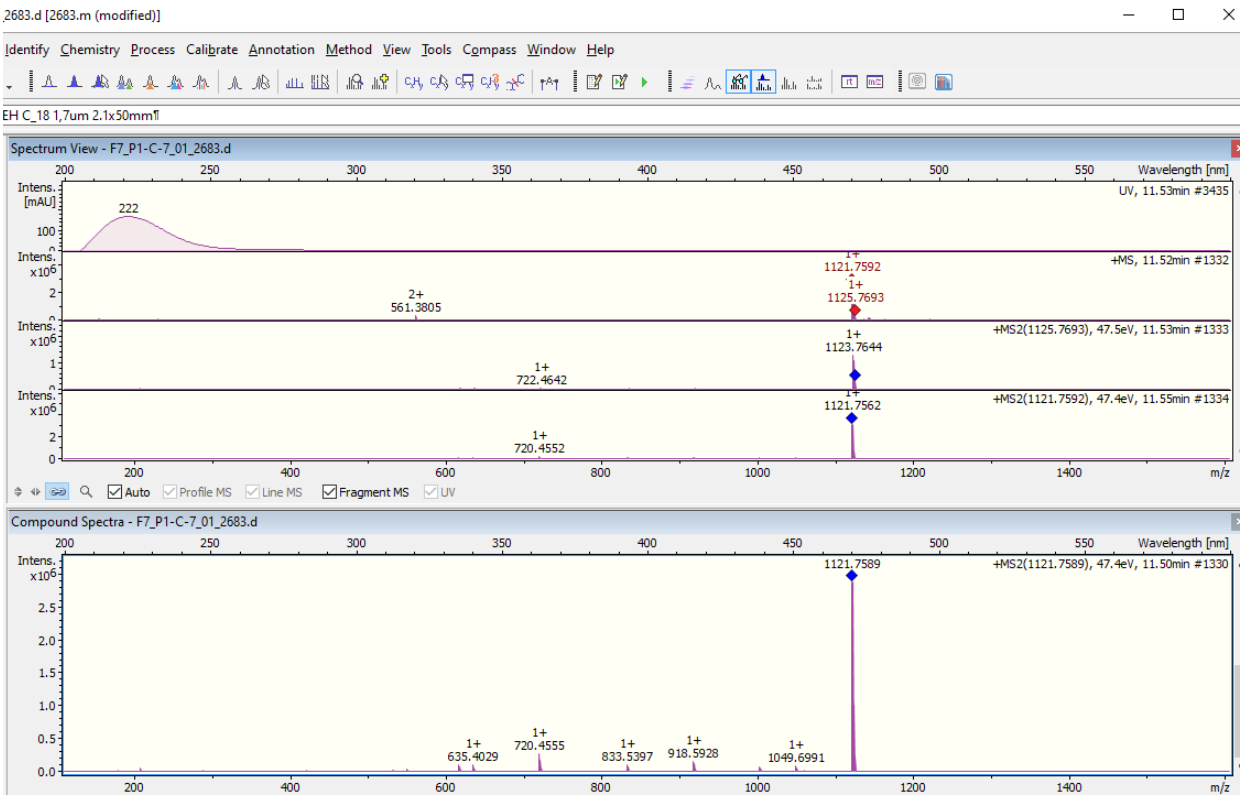

**S22 Figure:** COSY spectra **of leucinostatin P 3.**



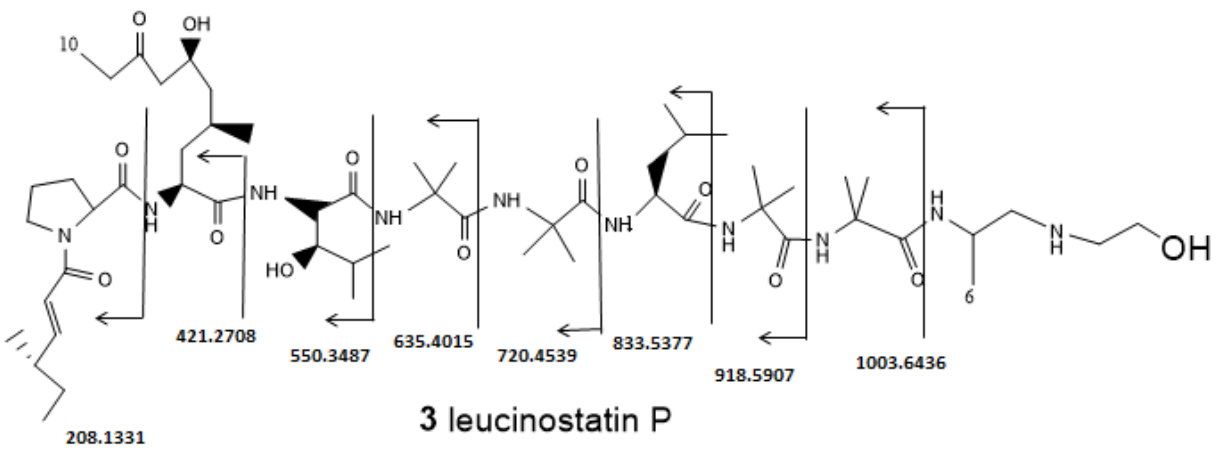

**S23 Figure:** NOESY spectra **of leucinostatin P 3**




**S24 Figure:** TOCSY spectra **of leucinostatin P 3.**



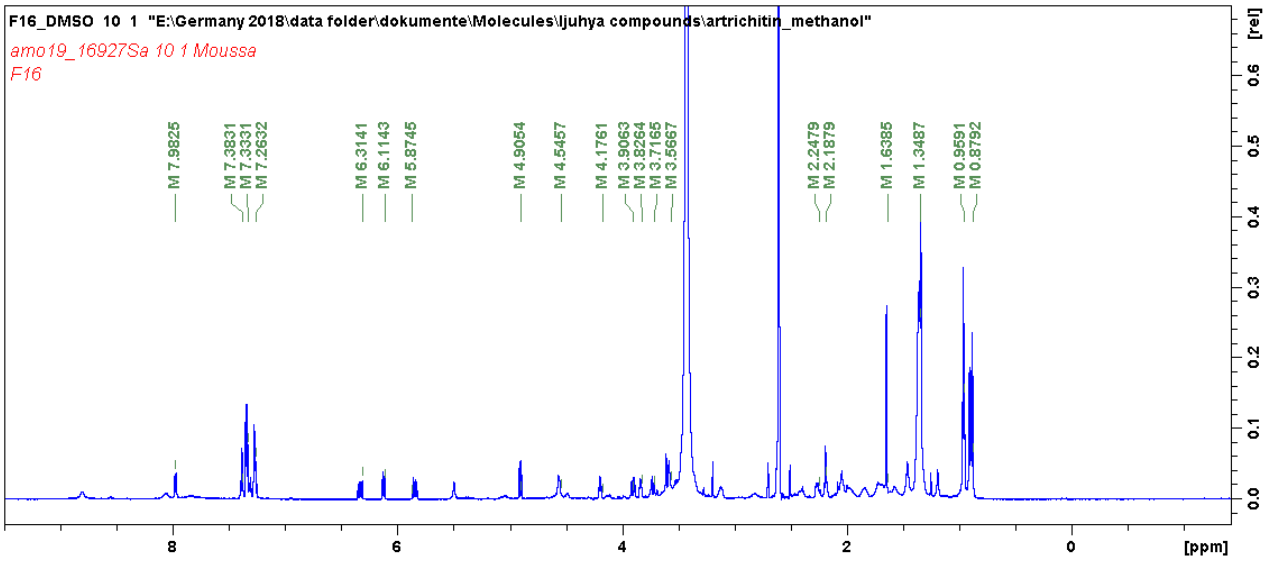

**S25 Figure**: HR-ESI-MSMS fragmentation pattern of **leucinostatin P 3.**



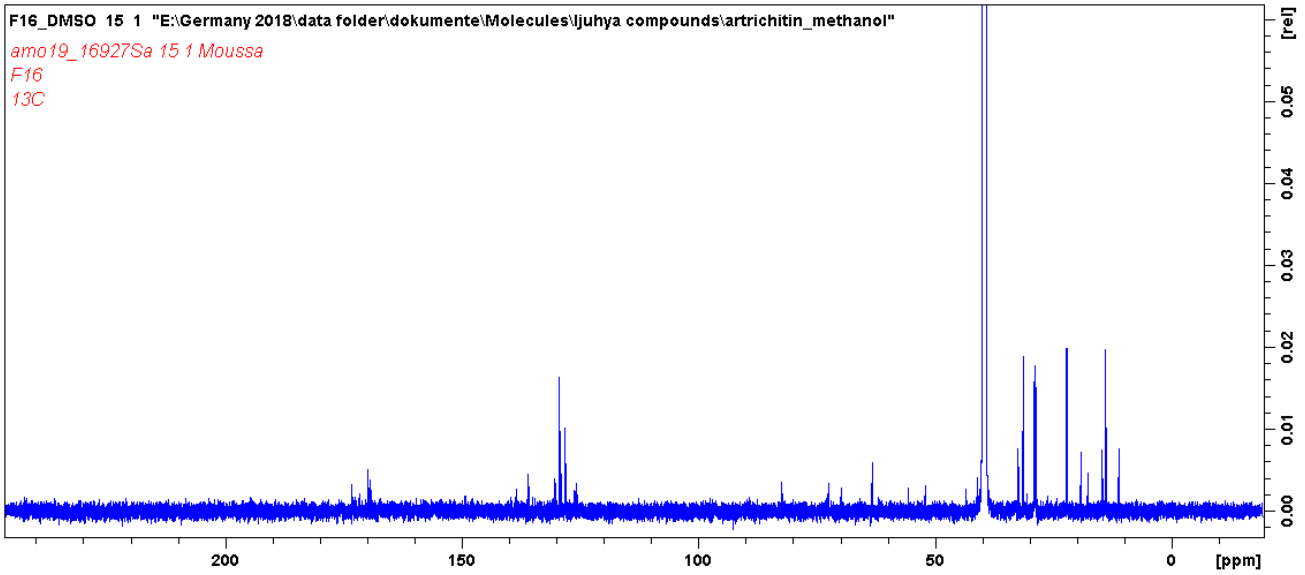

**S26 Figure:** HR-ESI-MS-MS fragments of **leucinostatin P 3.**

**S4 Table**. $^{1}H$ NMR and $^{13}C$ NMR data of **arthrichitin D 4** and its characteristic chemical shift values

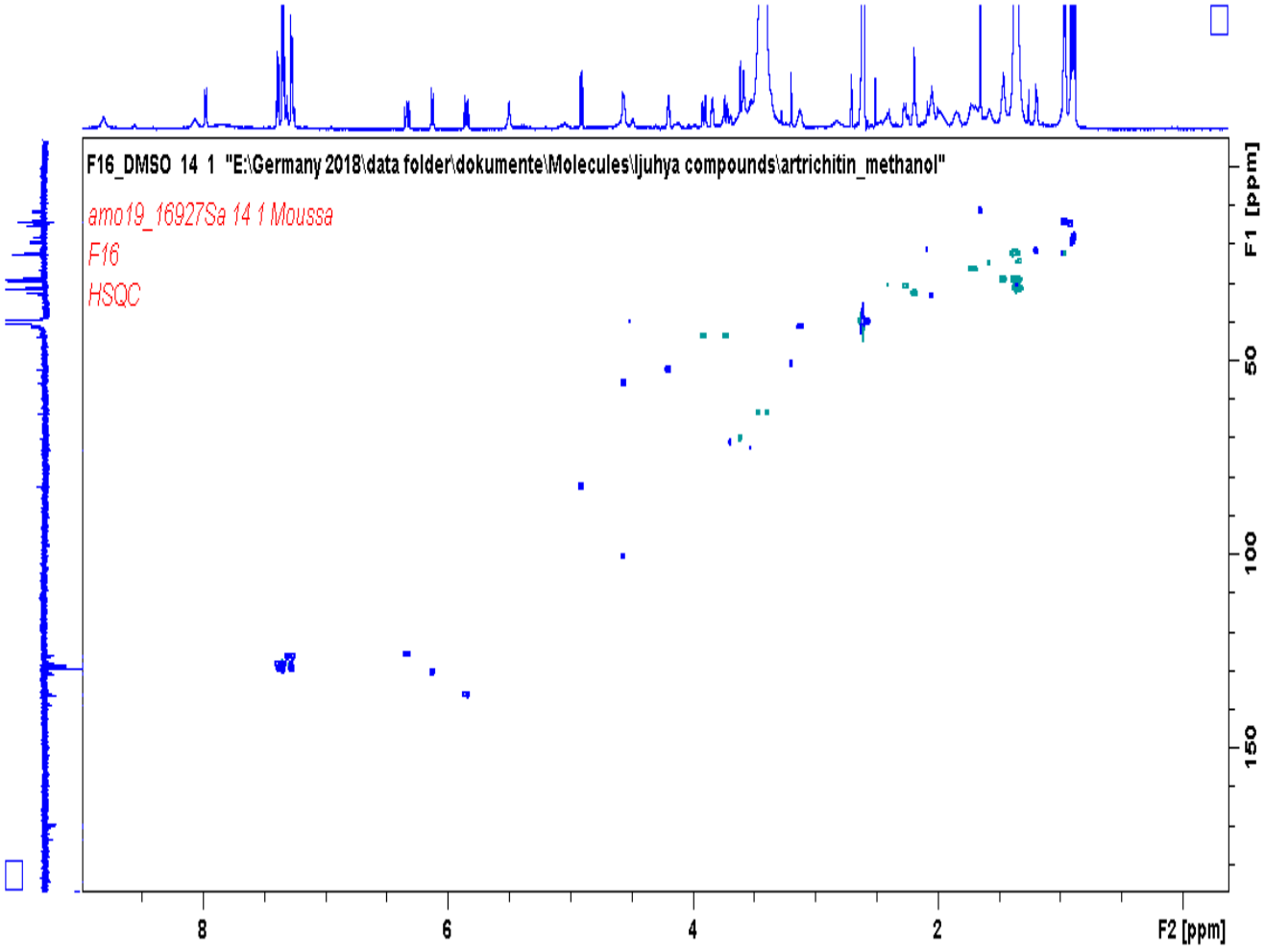
| Arthrichitin D | | | | | | |
|---|---|---|---|---|---|---|
| residue | position | δC, type | δH( J in Hz) | | δH( J in Hz) | δC, type |
| **L-Glu** | **1** | 169.92,C | | | **Dimethyl-oxy-hexadecanoyl** | |
| | **2** | 52.50,CH | 4.19 | **27** | 173.19,C | |
| | **3** | 25.20,CH2 | 1.82 | **28** | 40.70,CH | 3.11 |
| | | | 2.04 | **29** | 82.30,CH | 4.91 |
| | **4** | 30.50,CH2 | 2.25 | **30** | 130.20,C | |
| | | | 2.4 | **31** | 129.9,CH | 6.12 |
| | **5** | 173.02,C | | **32** | 125.70,CH | 6.33 |
| | **NH** | | 7.35 | **33** | 136.50,CH | 5.84 |
| **L-Gly** | **6** | 169.30,C | 4.05 | **34** | 32.10,CH2 | 2.19 |
| | **7** | 43.40,CH2 | 3.73 | **35** | 31.50,CH2 | 1.34 |
| | | | 3.9 | **36** | 28.9,CH2 | 1.35 |
| | **NH** | | 8.06 | **37** | 24.40,CH2 | 1.33 |
| **L-Phe** | **8** | 171.50,C | | **38-40** | 22.10,CH2 | 1.36 |
| | **9** | 55.01,CH | 4.13 | **42** | 14.74,CH3 | 0.9 |
| | **10** | 36.60,CH2 | 3.43 | **43** | 14.04,CH3 | 0.96 |
| | | | | **44** | 11.25,CH3 | 1.64 |
| | **11** | 138.55,C | | | | |
| | **12** | 129.40,CH | 7.34 | | | |
| | **13** | 128.34,CH | 7.34 | | | |
| | **14** | 126.25,CH | 7.26 | | | |
| | **15** | 128.22,CH | 7.38 | | | |
| | **16** | 129.30,CH | 7.27 | | | |
| | **NH** | | 8.81 | | | |
| **L-Gln** | **17** | 171.60,C | | | | |
| | **18** | 56.60,CH | 3.83 | | | |
| | **19** | 26.00,CH2 | 1.71 | | | |
| | **20** | 32.37,CH2 | 2.18 | | | |
| | **21** | 170.13,C | | | | |
| | **NH** | | 7.97 | | | |
| **L-Val** | | | | | | |
| | **22** | 170.0,C | | | | |
| | **23** | 55.6,CH | 4.56 | | | |
| | **24** | 33.27,CH | 2.04 | | | |
| | **25** | 19.17,CH3 | 0.89 | | | |
| | **26** | 17.79,CH3 | 0.88 | | | |
| | **NH** | | 7.98 | | | |



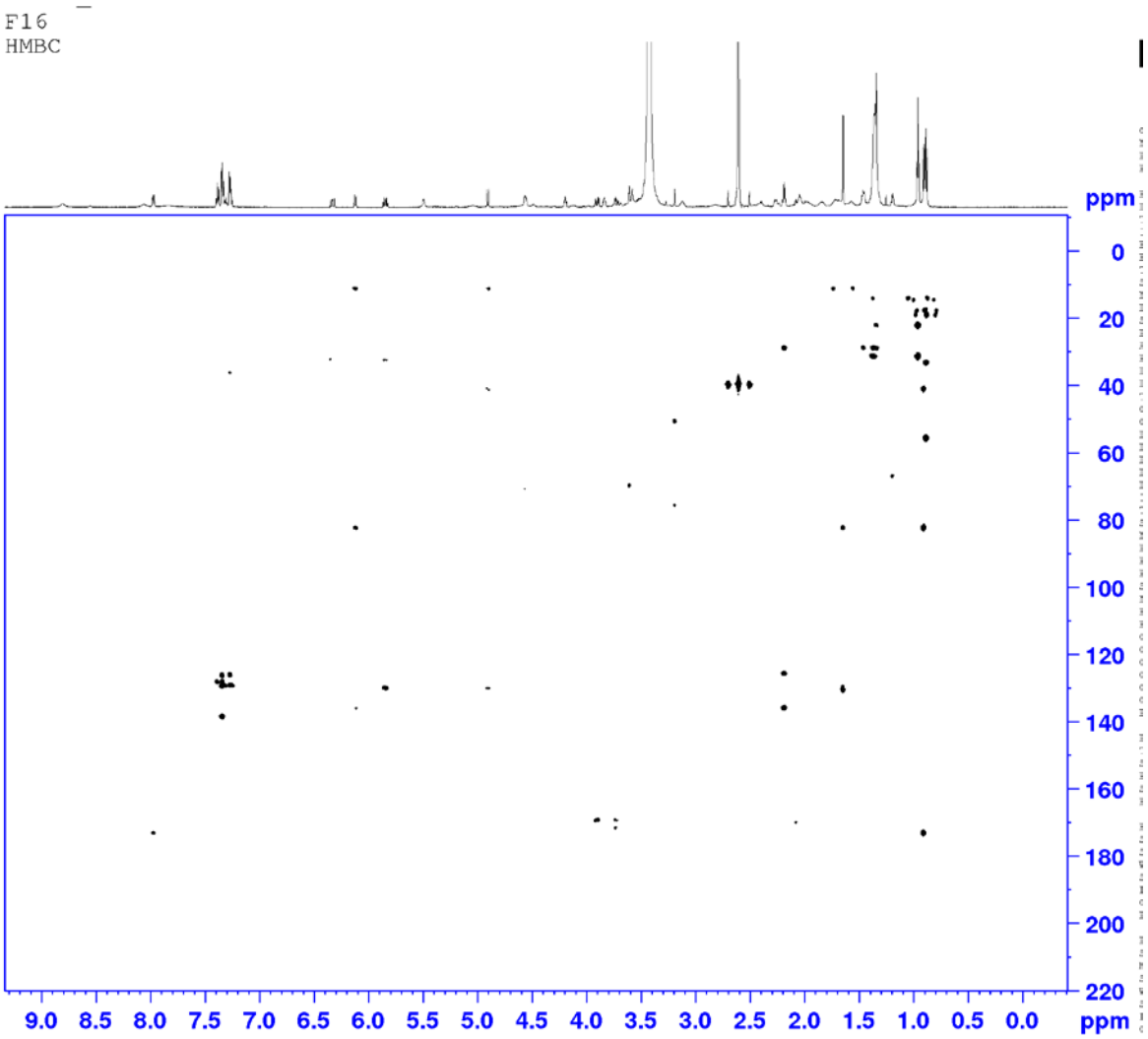

**S27.Figure:** [1]H NMR spectra of **arthrichitin D 4**



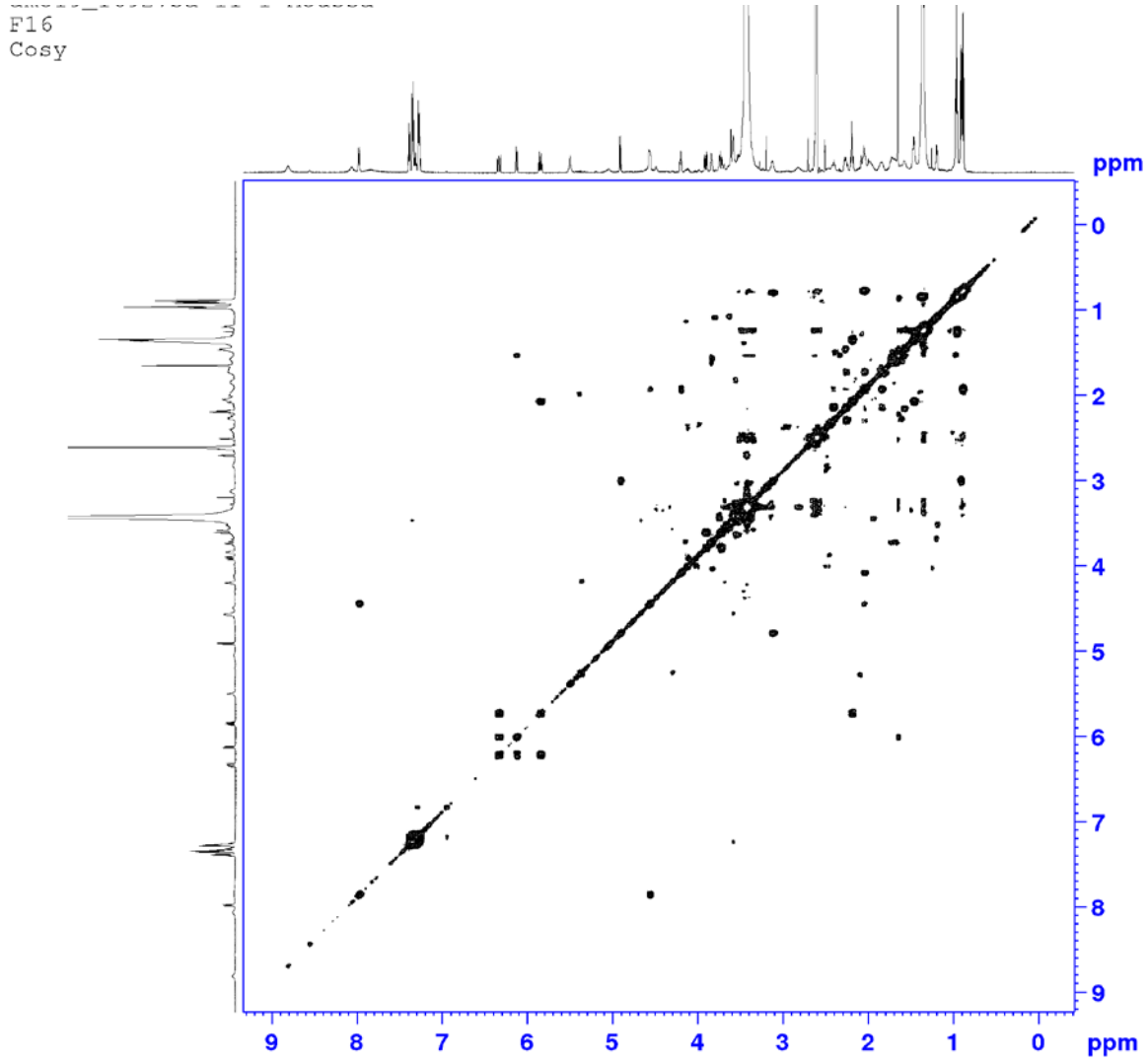

**S28 Figure:** $^{13}$CNMR spectra of **arthrichitin D 4**



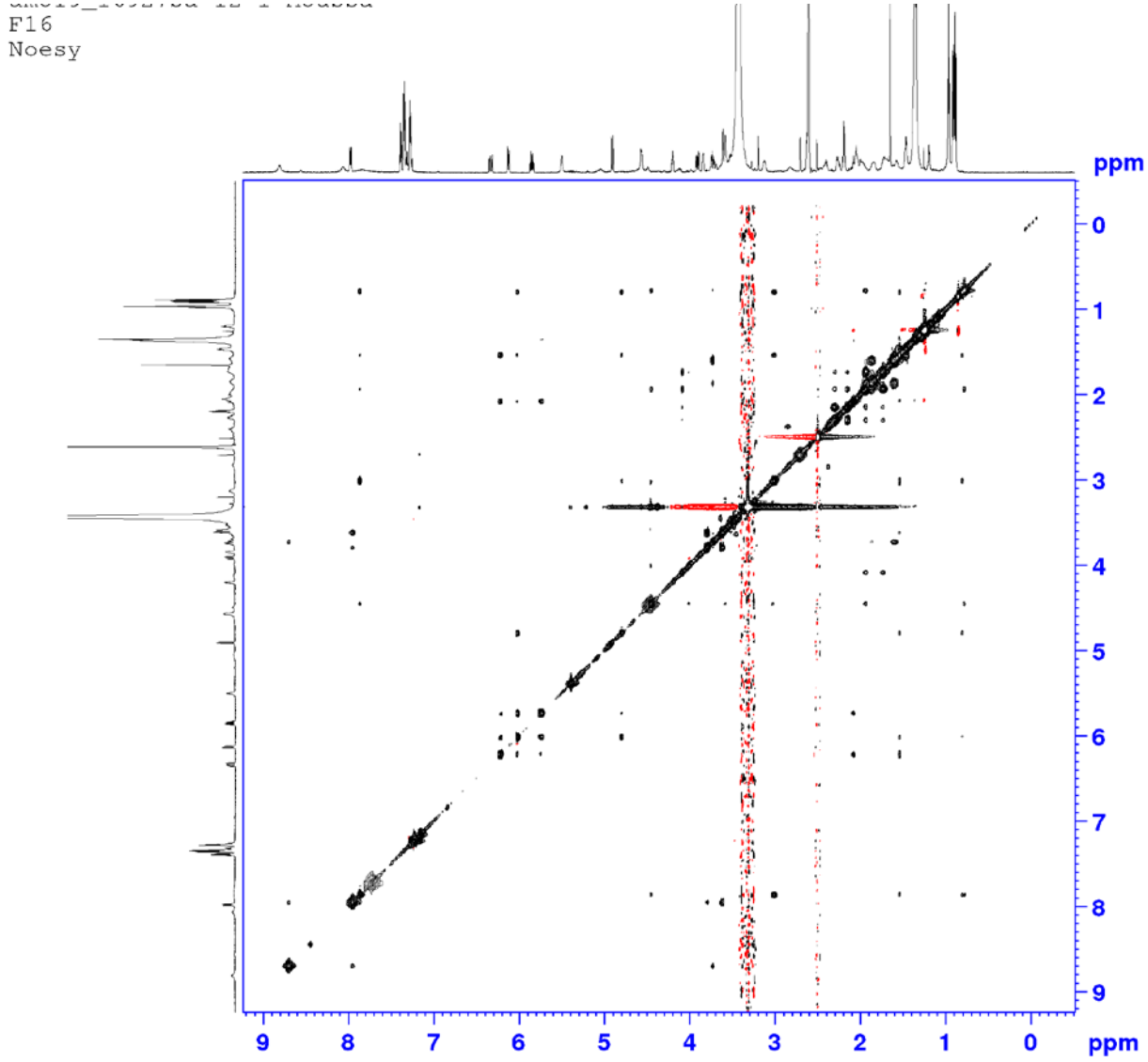

**S29 Figure:** HSQC spectra of **arthrichitin D 4**



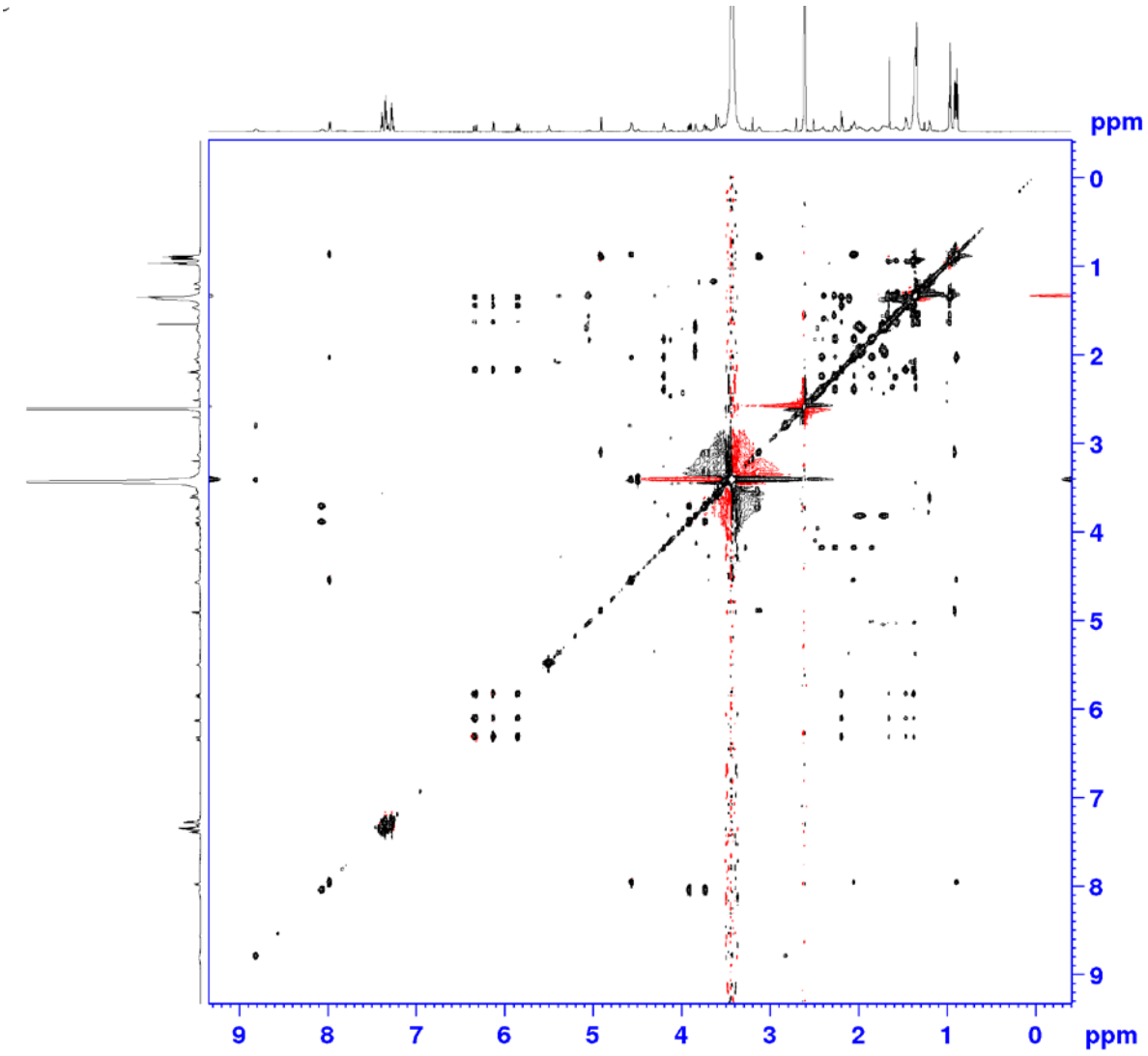

**S30 Figure:** HMBC spectra **of arthrichitin D 4..**



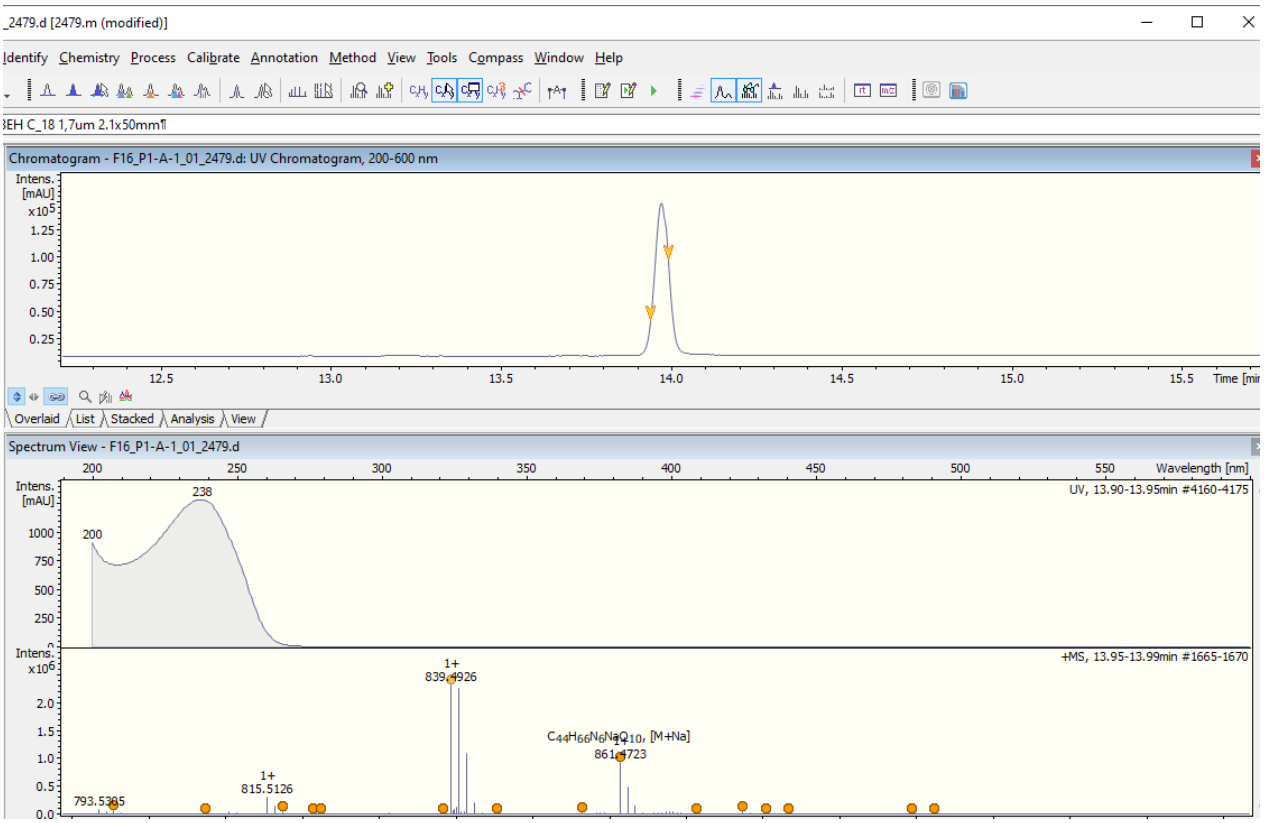

**S31 Figure:** COSY spectra **of arthrichitin D 4**




**S32 Figure:** NOESY spectra **of arthrichitin D 4**




**S33 Figure:** ROESY spectra **of arthrichitin D 4**




**S34.Figure:** HR-ESI-MS of **arthrichitin D 4.**

**S12 Text:** $^{1}$H NMR and $^{13}$C NMR data of **chaetoglobosin B 5** and its characteristic chemical shift values.

**Chaetoglobosin B 5**

Yellow powder, UV absorption $\lambda_{max}$ 200, 222, 281 nm , HR-ESI-MS m/z 1057.5321 $[2M+H]^+$ (calcd for $C_{32}H_{36}N_2O_5$ ); $^{1}$H NMR (700 MHz, methanol-d4) δH 3.53 (H-3, dd, J=8.4, 5.2 Hz), 3.84 (H-7, d, J= 9.4 Hz), 2.07 (H-8, dd, J= 9.4, 12.3 Hz), 2.87 (H-10a, dd, J=5.3, 14.5 Hz), 2.57 (H-10b, dd, J=5.3, 14.5 Hz), 1.28 (H-11, s), 1.65 (H-12, s), 6.05 (H-13, dd, J=9.4, 15.9 Hz), 5.15 (H-14, ddd, J=3.5, 10.2, 15.5 Hz), 2.32(H-15a, m), 2.01 (H-15b,m), 2.58 (H-16, m), 5.57(H-17, d, J=9.6 Hz), 5.11 (H-19,s), 6.68 (H-21, d, J=16.2 Hz), 7.46 (H-22,d J=5.6 Hz), 7.02 (H-2′, brs), 7.48 (H-4′, m), 7.01 (H-5′, t, J=7.1 Hz), 7.07(H-6′, t, J= 7.3 Hz), 7.32 (H-7′, d, J= 8.3Hz ), 1.01(Me-16, d, J=6.8 Hz), 1.42 (Me-18, s).

**S13 Text:** $^{1}$H NMR and $^{13}$C NMR data of **19-O-acetyl chaetoglobosin B (6)** and its characteristic chemical shift values.

**19-O-acetyl chaetoglobosin B 6**

Yellow powder, UV absorption $\lambda_{max}$ 199, 223, 280 nm, HR-ESI-MS m/z 571.2801 $[M+H]^+$, HR-ESI-MS m/z (calcd for $C_{34}H_{38}N_2O_6$); $^{1}$H NMR (700 MHz, methanol-d4) δH 3.60 (H-3, dd, J=3.2,8.5 Hz), 3.26 (H-4, m), 3.89 (H-7, d, J= 9.4 Hz), 2.10 (H-8, m), 2.89 (H-10a,dd, J=14.3, 4.3 Hz), 2.60 (H-10b,dd, J=14.3, 4.3 Hz), 1.32 (H-11, s), 1.65 (H-12, s), 6.17 (H-13, dd, J=15.3, 9.5 Hz), 5.19 (H-14, ddd, J= 3.5, 9.5, 15.4 Hz), 2.01 (H-15a, m), 2.32 (H-15b, m), 2.61 (H-16, m), 5.77 (H-17, d, J=9.4 Hz), 5.92 (H-19, s), 6.80 (H-21, m), 7.66 (H-22, m), 7.15 (H-2′, brs), 7.53 (H-4′, d, J=7.9 Hz), 7.01 (H-5′, 7.09 (H-6′, t), 7.38 (H-7′, d, J= 8.15 Hz), 2.11 ( 19-O-acetyl);$^{13}$C NMR (175 MHz, methanol-d4) δH$^{13}$C 59.0 (C-3), 48.4 (C-4), 127.1 (C-5), 134.0 (C-6), 69.2 (C-7), 52.3 ( C-8), 62.2 (C-9), 33.2 (C-10), 17.7 (C-11), 14.6 (C-12), 129.1 (C-13), 135.5 (C-14), 41.9 (C-15), 33.0 (C-16), 143.3 (C-17), 127.9 (C-18), 84.2 (C-19), 194.9 (C-20), 135.0 (C-21), 136.8 (C-22), 199.7 (C-23), 172.5 ( C-24), 124.5 (C-2′), 111.7 (C-3′), 119.2(C-4′), 119.6 (C-5′), 122.3 (C-6′), 112.3 (C-7′), 169.4 ( 19-O-acetyl C=O), 20.2 ( 19-O-acetyl –Me), 137.1 (C-1a′), 128.0 (C-3a′).