Supporting information for

A Tetramer Derived from Islet Amyloid Polypeptide

Yilin Wang, Adam G. Kreutzer, Nicholas L. Truex, and James S. Nowick*

Department of Chemistry, University of California, Irvine, Irvine, CA 92697-2025

*To whom correspondence should be addressed: jsnowick@uci.edu

I. SUPPLEMENTARY FIGURES AND TABLE

Fig. S1. ^{1}H NMR spectra of peptide $\mathbf{1_{Arg}}$ at various concentrations in 50 mM CD_3COOD and 50 mM CD_3COONa in D_2O at 500 MHz and 298 K S3

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Fig. S3. Downfield shifting of the α-protons of peptide $\mathbf{1_{Arg}}$ relative to those of random coil chemical shifts at 4 mM. S5

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Fig. S5. Tetramer structure of peptide $\mathbf{1_{Cit}}$ generated in MacroModel with the MMFFs force field with GB/SA water solvation. S6

Table S1. Crystallographic properties, crystallization conditions, data collection, and model refinement statistics for peptide$\mathbf{1_{Cit}}$. S7

II. CHARACTERIZATION DATA S8

Macrocyclic β-Sheet Peptide $\mathbf{1}_{\mathbf{Arg}}$

HPLC trace S9
mass spectrum S9
1D ^{1}H NMR spectrum at 4mM in D_2O at 500 MHz and 298 K S10
2D TOCSY spectrum at 4mM in D_2O at 500 MHz and 298 K S16
2D ROESY spectrum at 4mM in D_2O at 500 MHz and 298 K S18
2D DOSY spectrum at 4mM in D_2O at 500 MHz and 298 K S20

Macrocyclic β-Sheet Peptide $\mathbf{1}_{\mathbf{Cit}}$

HPLC trace S21
mass spectrum S21
1D ^{1}H NMR spectrum at 2.0 mM in D_2O at 500 MHz and 298 K S23
2D TOCSY spectrum at 2.0 mM in D_2O at 500 MHz and 298 K S28
2D ROESY spectrum at 2.0 mM in D_2O at 500 MHz and 298 K S30

1D ^{1}H NMR spectrum at 16.0 mM in D_2O at 500 MHz and 298 K S32
2D TOCSY spectrum at 16.0 mM in D_2O at 500 MHz and 298 K S38
2D NOESY spectrum at 16.0 mM in D_2O at 500 MHz and 298 K S42

2D DOSY spectrum at 1.0 mM in D_2O at 500 MHz and 298 K S46
2D DOSY spectrum at 2.0 mM in D_2O at 500 MHz and 298 K S47
2D DOSY spectrum at 4.0 mM in D_2O at 500 MHz and 298 K S48
2D DOSY spectrum at 8.0 mM in D_2O at 500 MHz and 298 K S49
2D DOSY spectrum at 16.0 mM in D_2O at 500 MHz and 298 K S50

Macrocyclic β-Sheet Peptide $\mathbf{2}_{\mathbf{Cit}}$

HPLC trace S51
mass spectrum S51
1D ^{1}H NMR spectrum at 1.0 mM in D_2O at 500 MHz and 298 K S53

I. SUPPLEMENTAL FIGURES

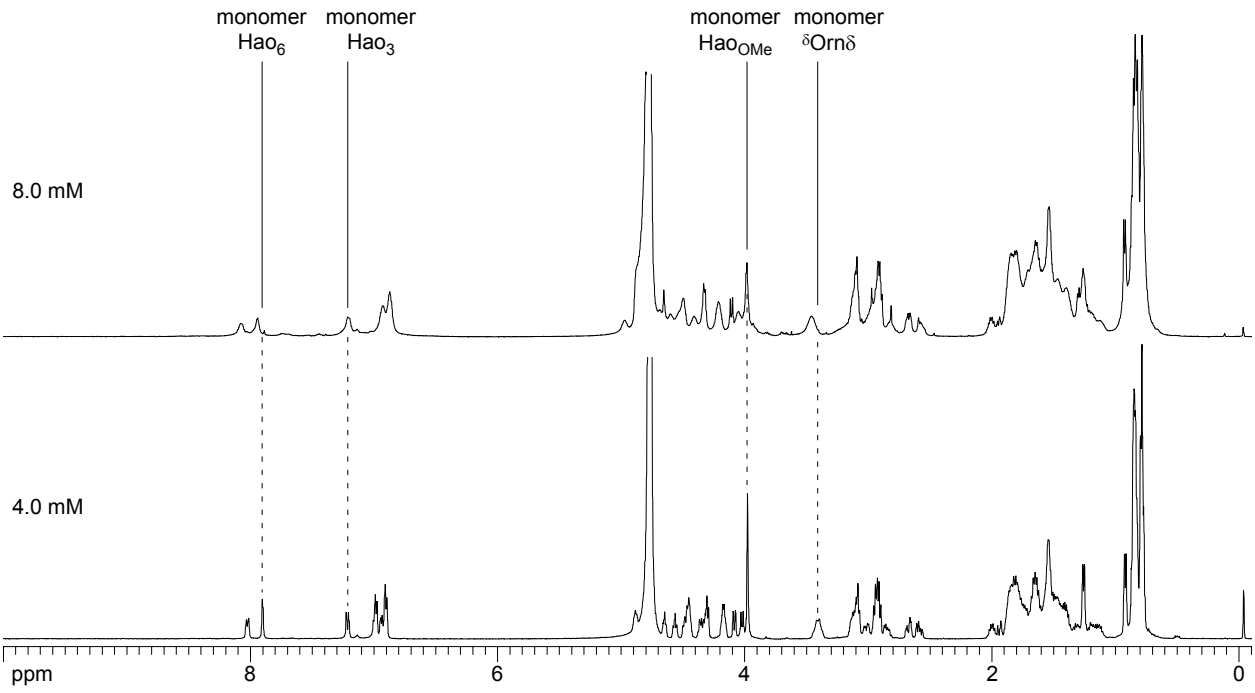


Fig S1. ^{1}H NMR spectra of peptide $\mathbf{1_{Arg}}$ at 4 mM and 8 mM in 50 mM CD_3COOD and 50 mM CD_3COONa buffer in D_2O at 500 MHz and 298 K.

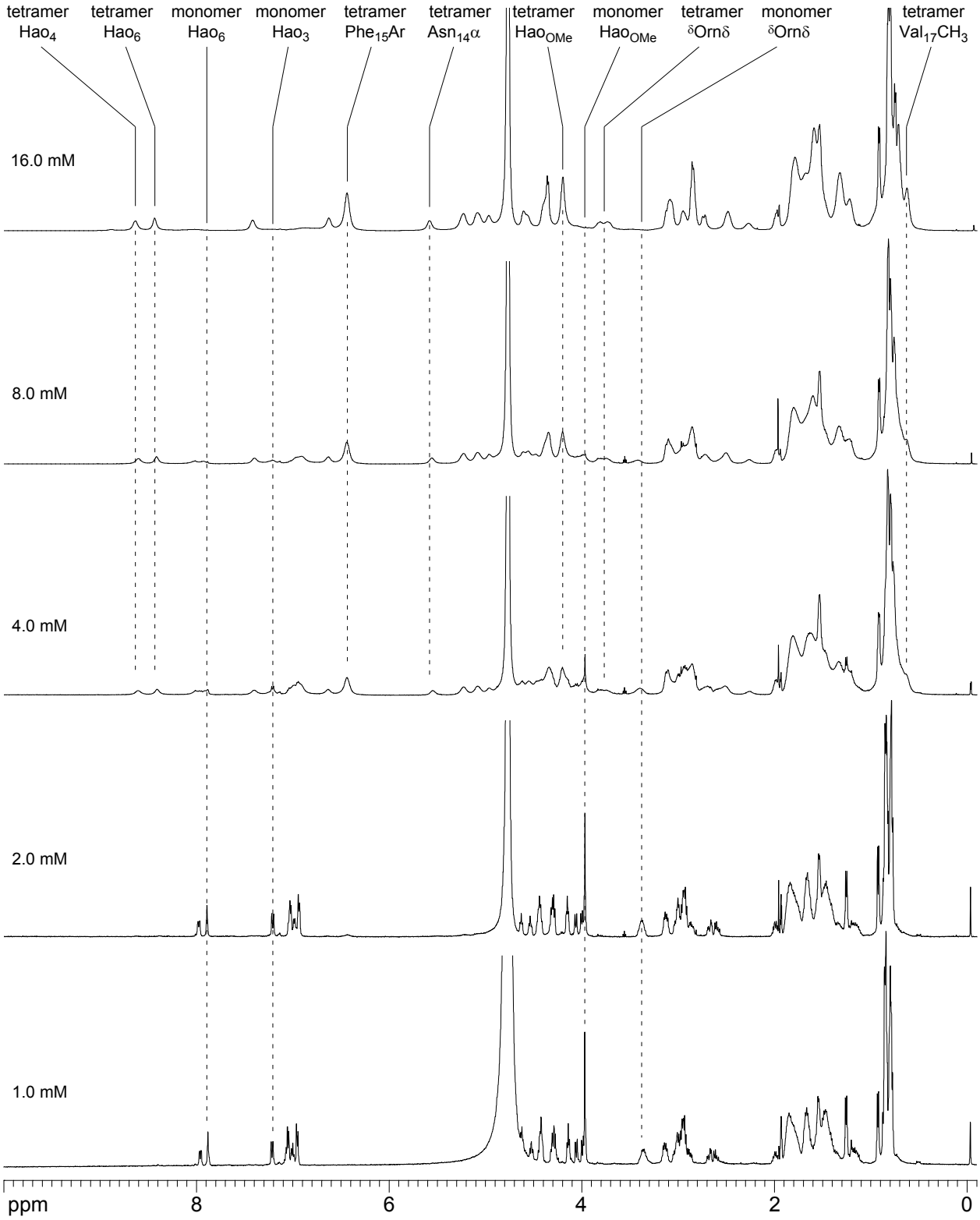


Fig S2. ^{1}H NMR spectra of peptide $\mathbf{1}_{\mathbf{Cit}}$ at various concentrations in 50 mM CD_3COOD and 50 mM CD_3COONa in D_2O at 500 MHz and 298 K.

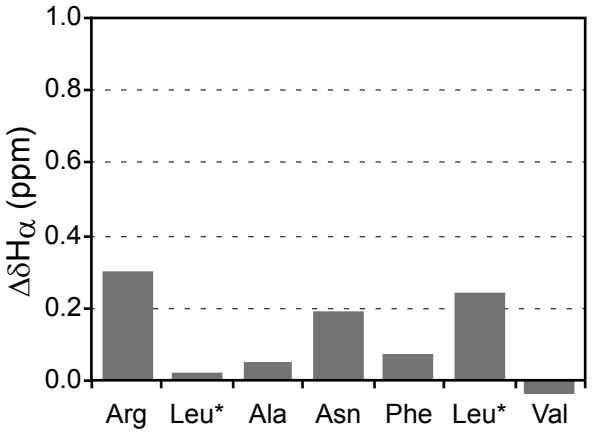


Fig. S3. Downfield shifting of the α-protons of peptide $\mathbf{1}_{\mathbf{Arg}}$ at 4 mM relative to those of random coil chemical shifts. *Leucine residues are not assigned in a sequence-specific fashion.

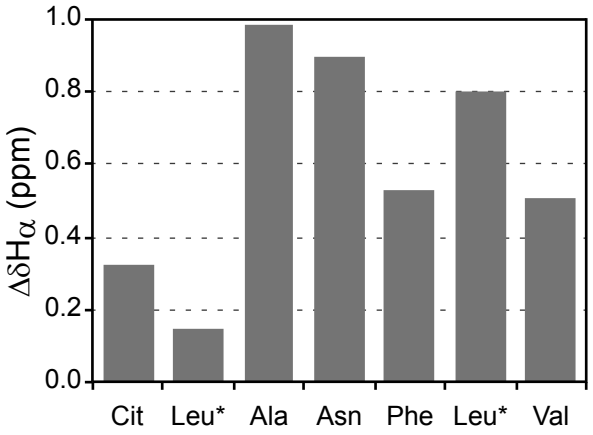


Fig. S4. Downfield shifting of the α-protons of peptide $\mathbf{1}_{\mathbf{Cit}}$ at 16 mM relative to those of random coil chemical shifts. The random coil chemical shift of arginine was used for citrulline. *Leucine residues are not assigned in a sequence-specific fashion.

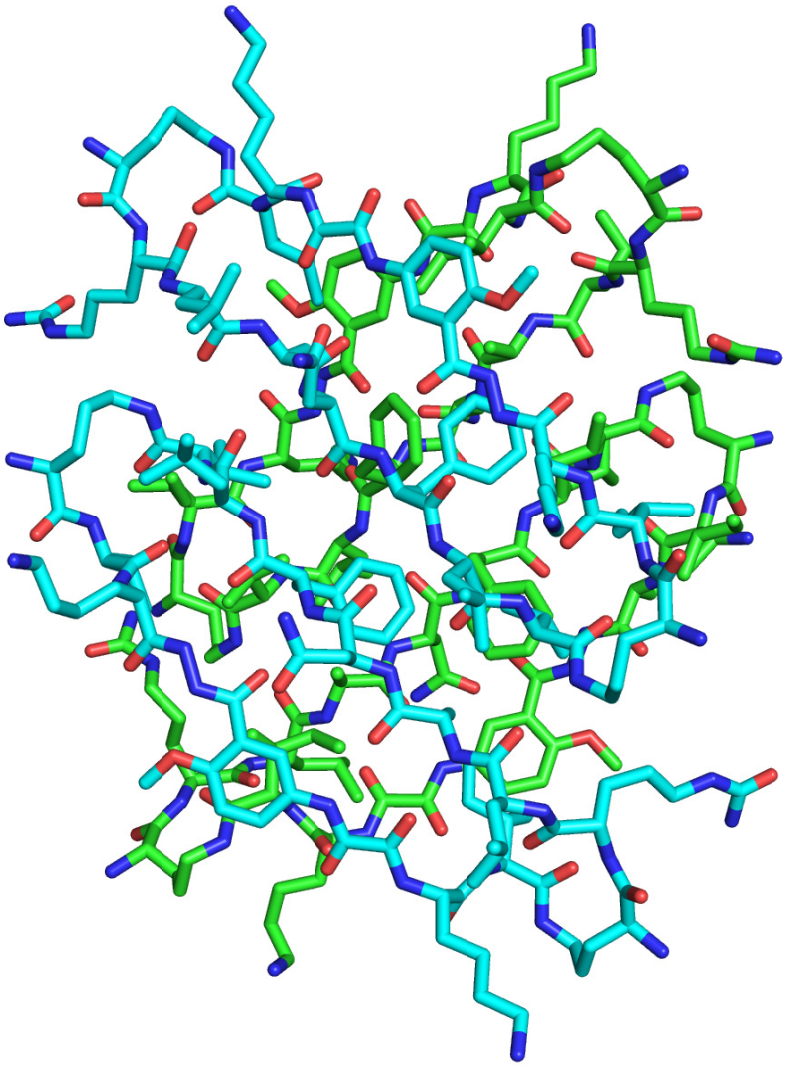


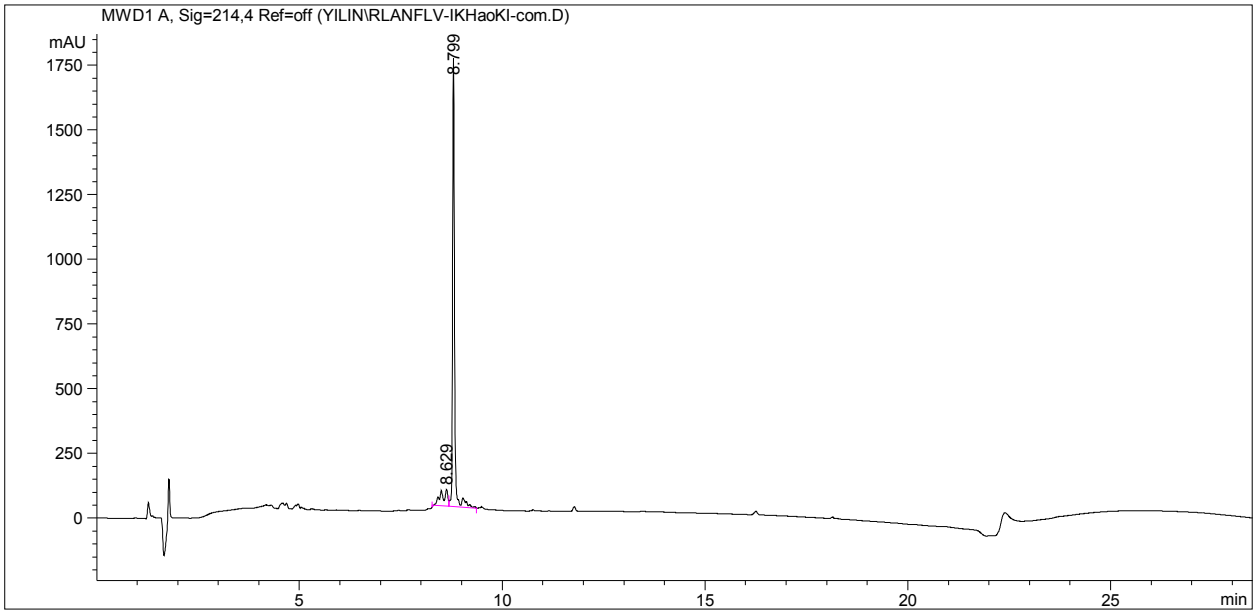
Fig. S5. Crystallographically based molecular model of the tetramer formed by peptide $\mathbf{1}_{\mathbf{Cit}}$. The model was generated in MacroModel with the MMFFs force field with GB/SA water solvation.

Table S1. Crystallographic properties, crystallization conditions, data collection, and model refinement statistics for peptide **2_{Cit}**.

peptide	peptide **2_{Cit}**
PDB ID	5UHR
space group	$P4_12_12$
a, *b*, *c* (Å)	33.88, 33.88, 99.05
α, β, λ (°)	90, 90, 90
peptides per asymmetric unit	4
crystallization conditions	0.1 M sodium citrate at pH 4.9, 20% (v/v) isopropanol, 18% PEG 4000
wavelength (Å)	0.92
resolution (Å)	27.96–1.798 (1.862–1.798)
total reflections	11672 (1079)
unique reflections	5838 (541)
multiplicity	2.0 (2.0)
completeness (%)	99.51 (95.41)
mean I/σ	41.22 (9.47)
Wilson B factor	24.70
R_{merge}	0.01553 (0.06924)
$R_{measure}$	0.02196 (0.09792)
$CC_{1/2}$	1.000 (0.988)
CC^*	1.000 (0.997)
R_{work}	0.2257 (0.2928)
R_{free}	0.2687 (0.3045)
number of non-hydrogen atoms	540
RMS_{bonds}	0.020
RMS_{angles}	2.04
Ramachandran favored (%)	100
outliers (%)	0
clashscore	3.30
average B-factor	32.91
number of TLS groups	4
ligands/ions	Cl (1)
water molecules	39

IV. CHARACTERIZATION DATA

RP-HPLC of Macrocyclic β-Sheet **1_{Arg}**



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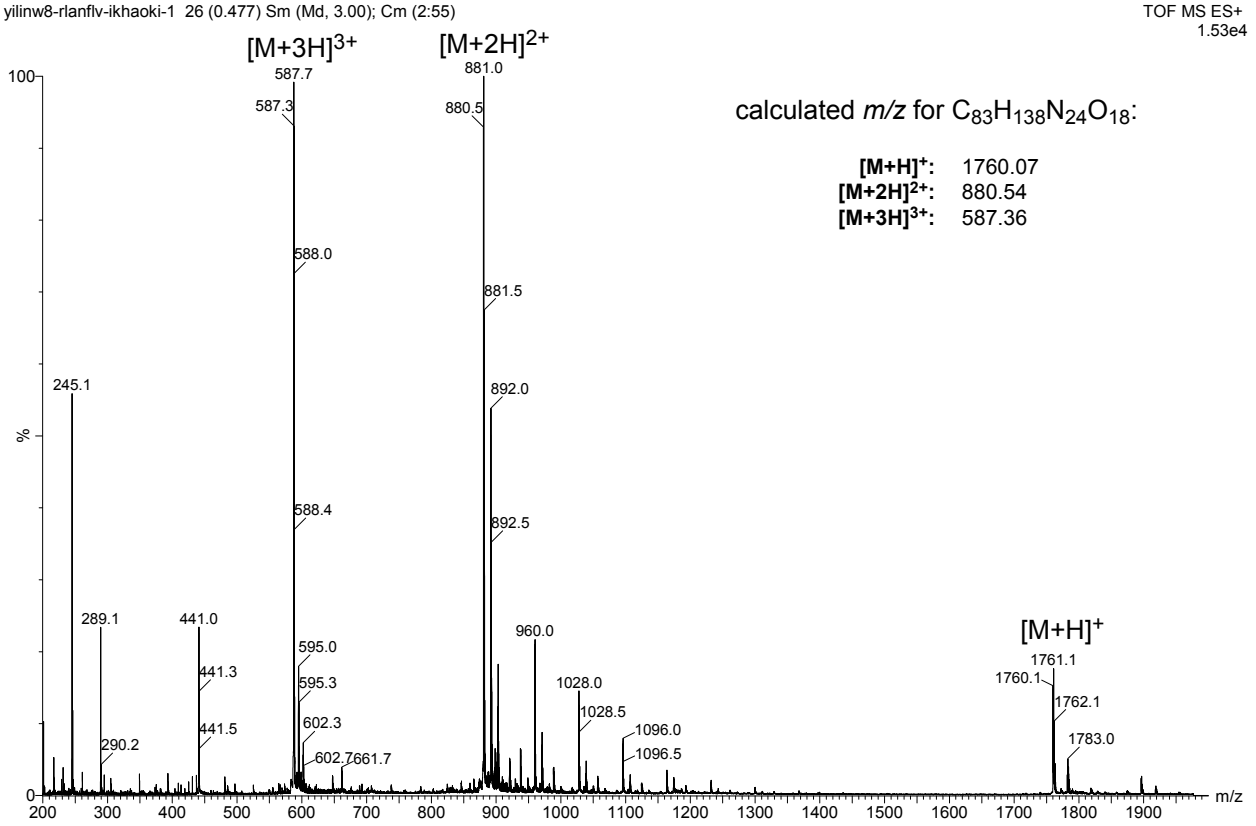
1	8.629	MF	0.1768	685.6629	64.6265	10.0330
2	8.799	FM	0.0584	6148.4335	1756.0099	89.9670

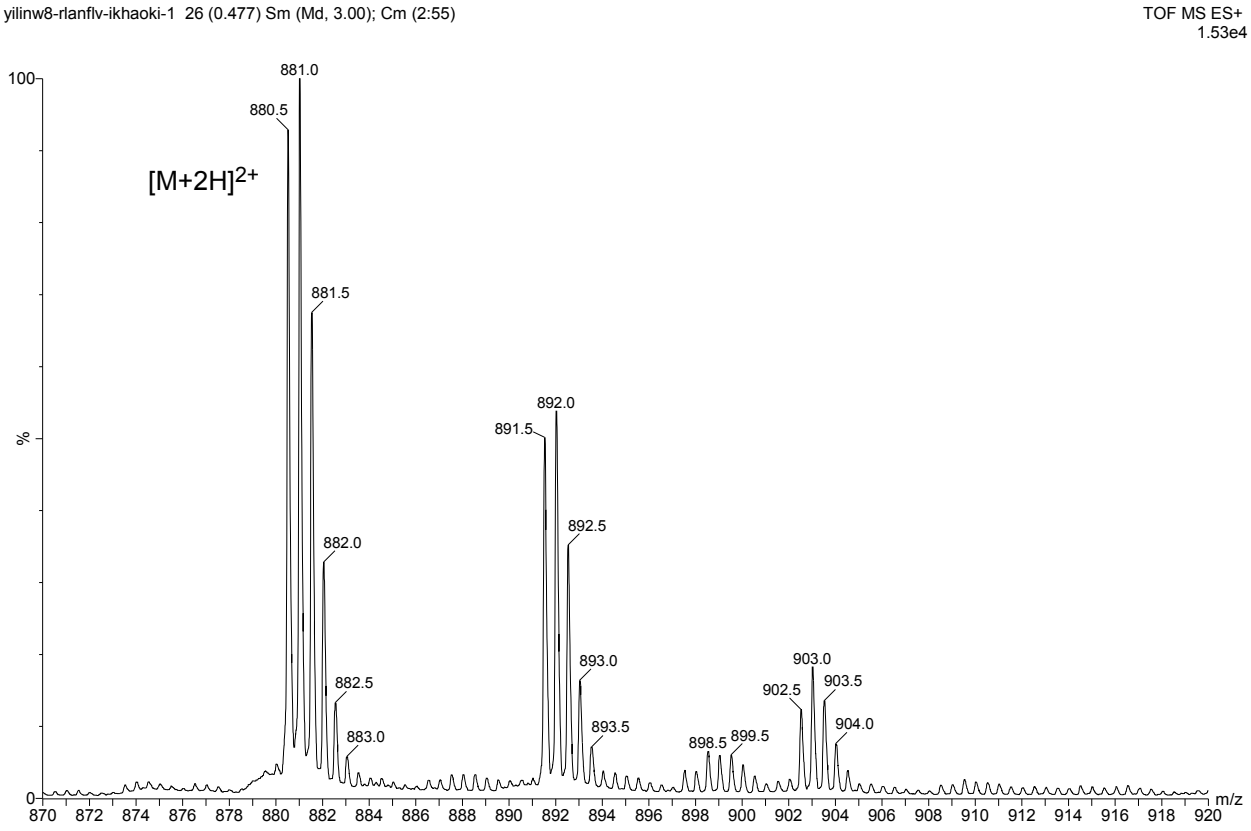
column: Aeris XB-C18 2.6µ
dimensions: 150 mm x 4.6 mm
mobile phase: A: H_2O, 0.1% TFA
B: CH_3CN, 0.1% TFA
gradient: A/B (95:5) to (0:100) in 20 min
flow rate: 1.0 mL/min
detection: VWD, wavelength = 214 nm
temperature: 298 K

MS (ESI) of Macrocyclic β-Sheet **1_{Arg}**



calculated *m/z* for $C_{83}H_{138}N_{24}O_{18}$:

$[M+H]^+$: 1760.07
$[M+2H]^{2+}$: 880.54
$[M+3H]^{3+}$: 587.36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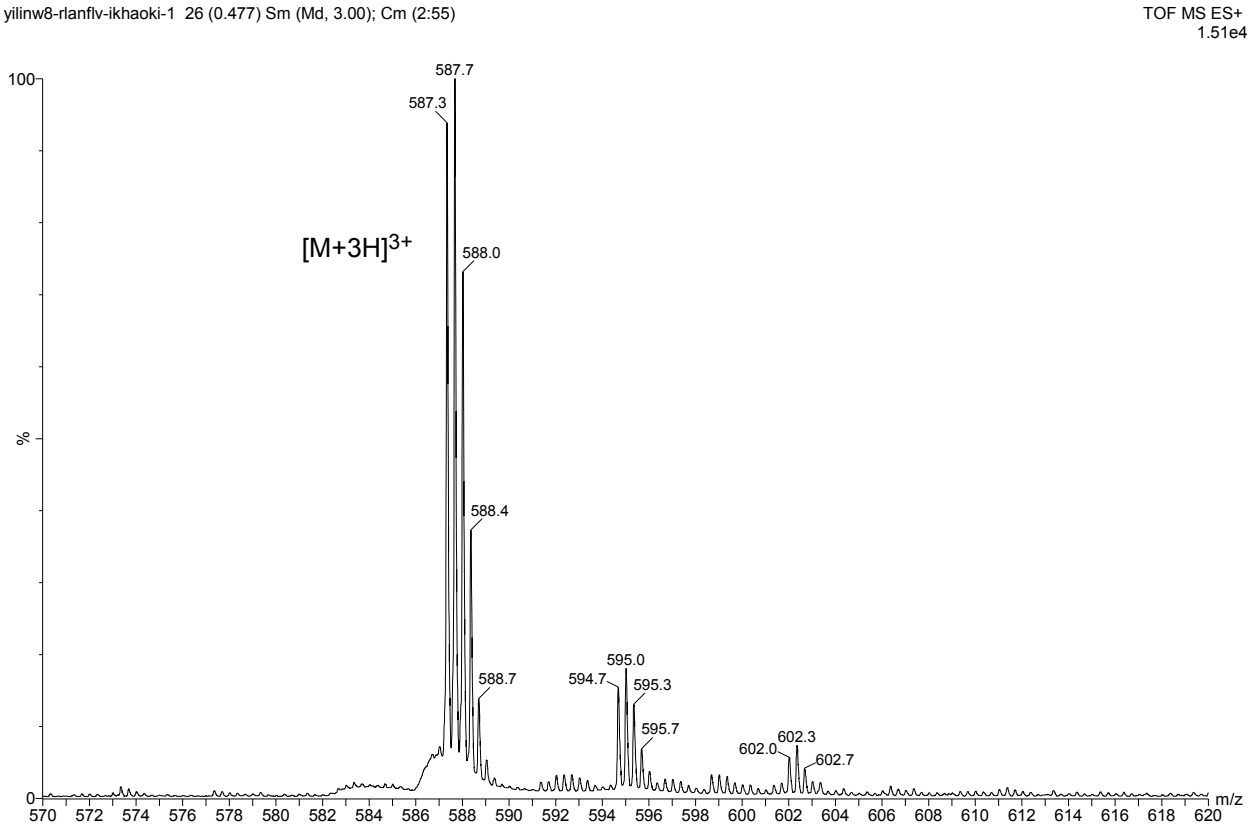
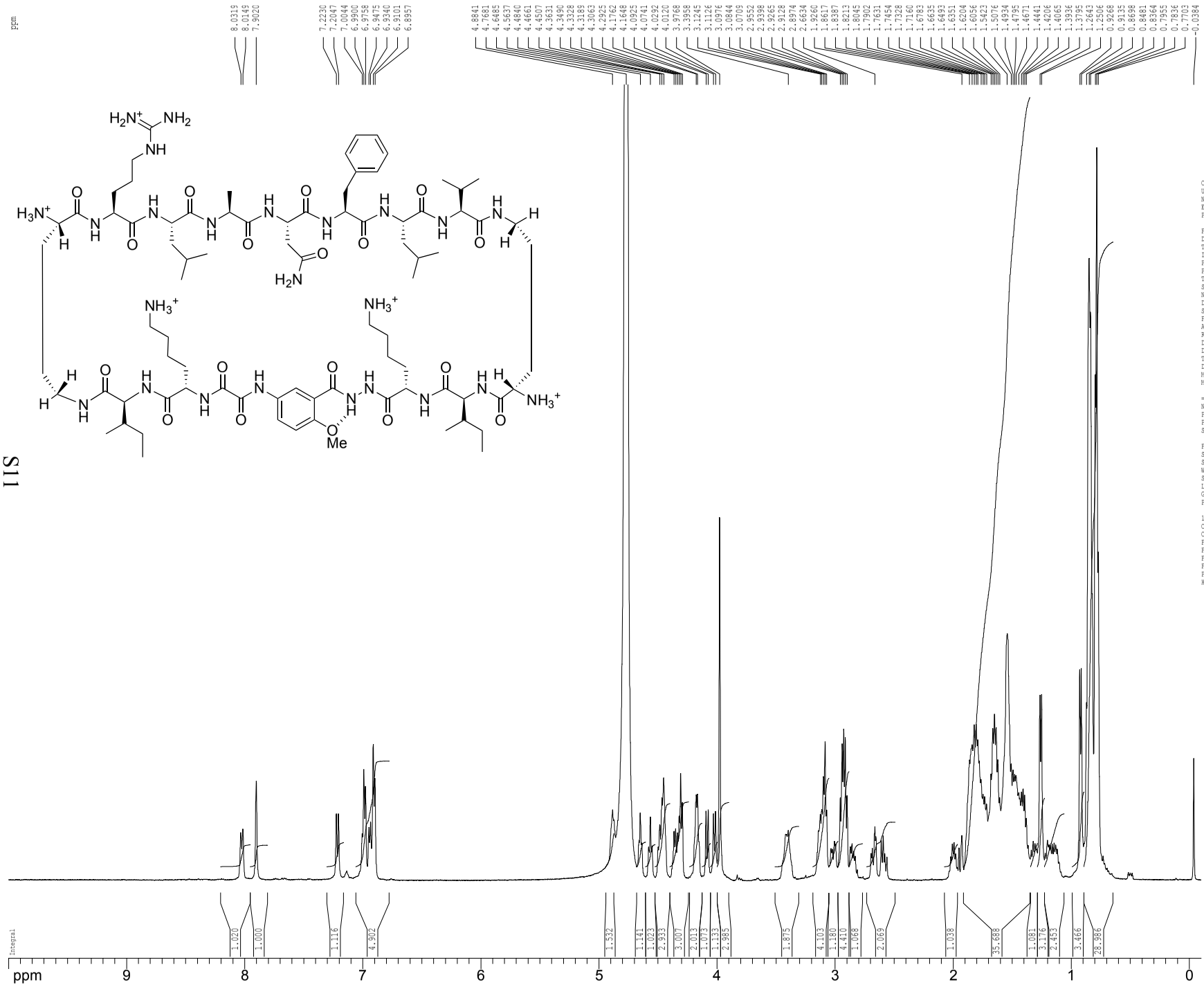
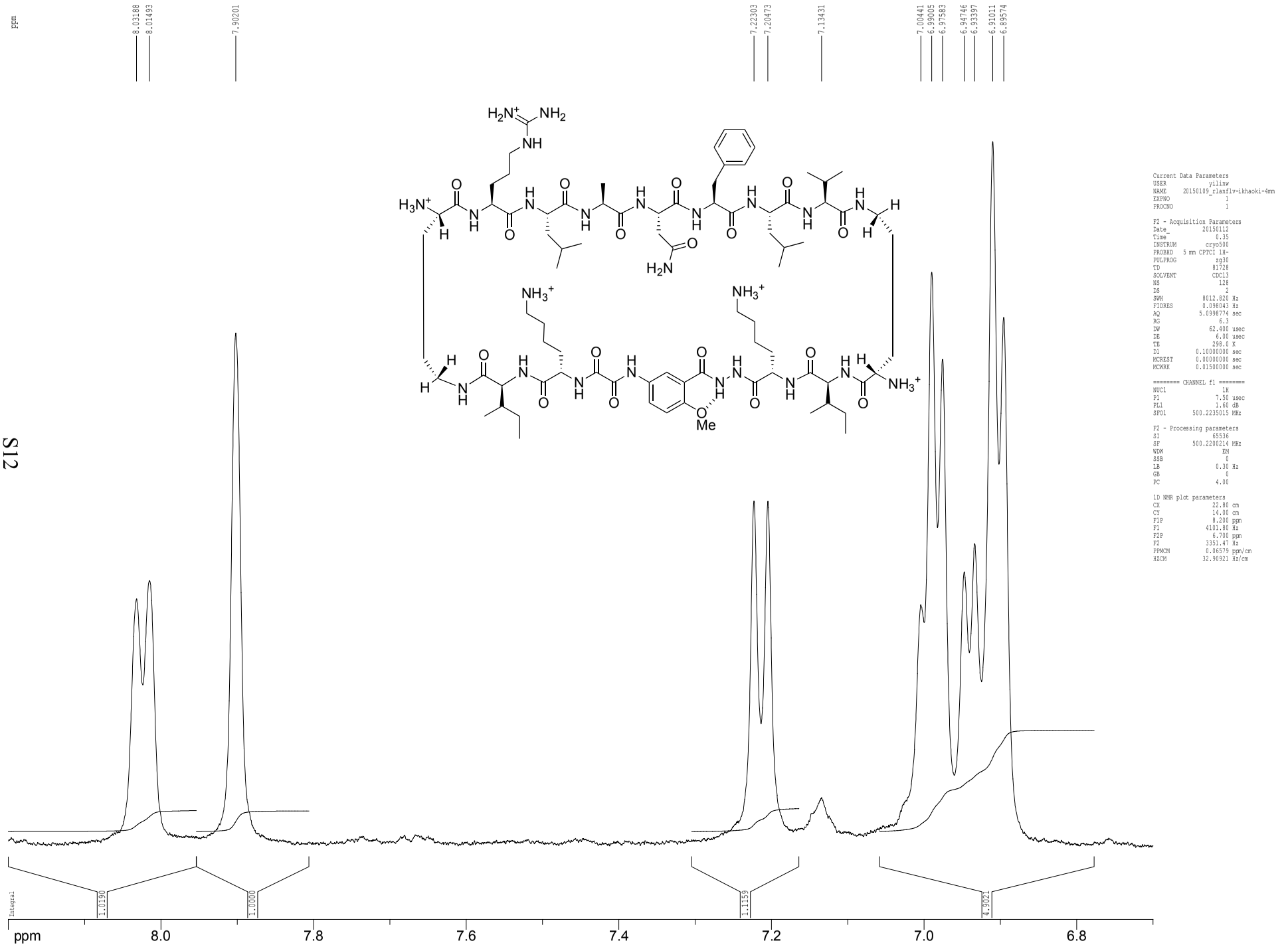
TOF MS ES+
1.53e4
100
%
0
[M+2H]2+
881.0
880.5
881.5
882.0
882.5
883.0
892.0
891.5
892.5
893.0
893.5
898.5
899.5
902.5
903.0
903.5
904.0
m/z
870 872 874 876 878 880 882 884 886 888 890 892 894 896 898 900 902 904 906 908 910 912 914 916 918 920


yilinw8-rlanflv-ikhaoki-1 26 (0.477) Sm (Md, 3.00); Cm (2:55)
TOF MS ES+
1.51e4
100
%
0
[M+3H]3+
587.7
587.3
588.0
588.4
588.7
594.7
595.0
595.3
595.7
602.0
602.3
602.7
m/z
570 572 574 576 578 580 582 584 586 588 590 592 594 596 598 600 602 604 606 608 610 612 614 616 618 620

^{1}H NMR of macrocyclic β-sheet peptide **1_{Arg}**, 4 mM in 100 mM deuterioacetate buffer in D_2O at 500 MHz and 298 K



^{1}H NMR of macrocyclic β-sheet peptide **1$_{Arg}$**, 4 mM in 100 mM deuterioacetate buffer in D_2O at 500 MHz and 298 K

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MCWRK          0.01500000 sec

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PL1                1.60 dB
SFO1          500.2235015 MHz

F2 - Processing parameters
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SF            500.2200214 MHz
WDW                    EM
SSB                     0
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GB                      0
PC                   4.00

1D NMR plot parameters
CX                  22.80 cm
CY                  14.00 cm
F1P                 8.200 ppm
F1                4101.80 Hz
F2P                 6.700 ppm
F2                3351.47 Hz
PPMCM             0.06579 ppm/cm
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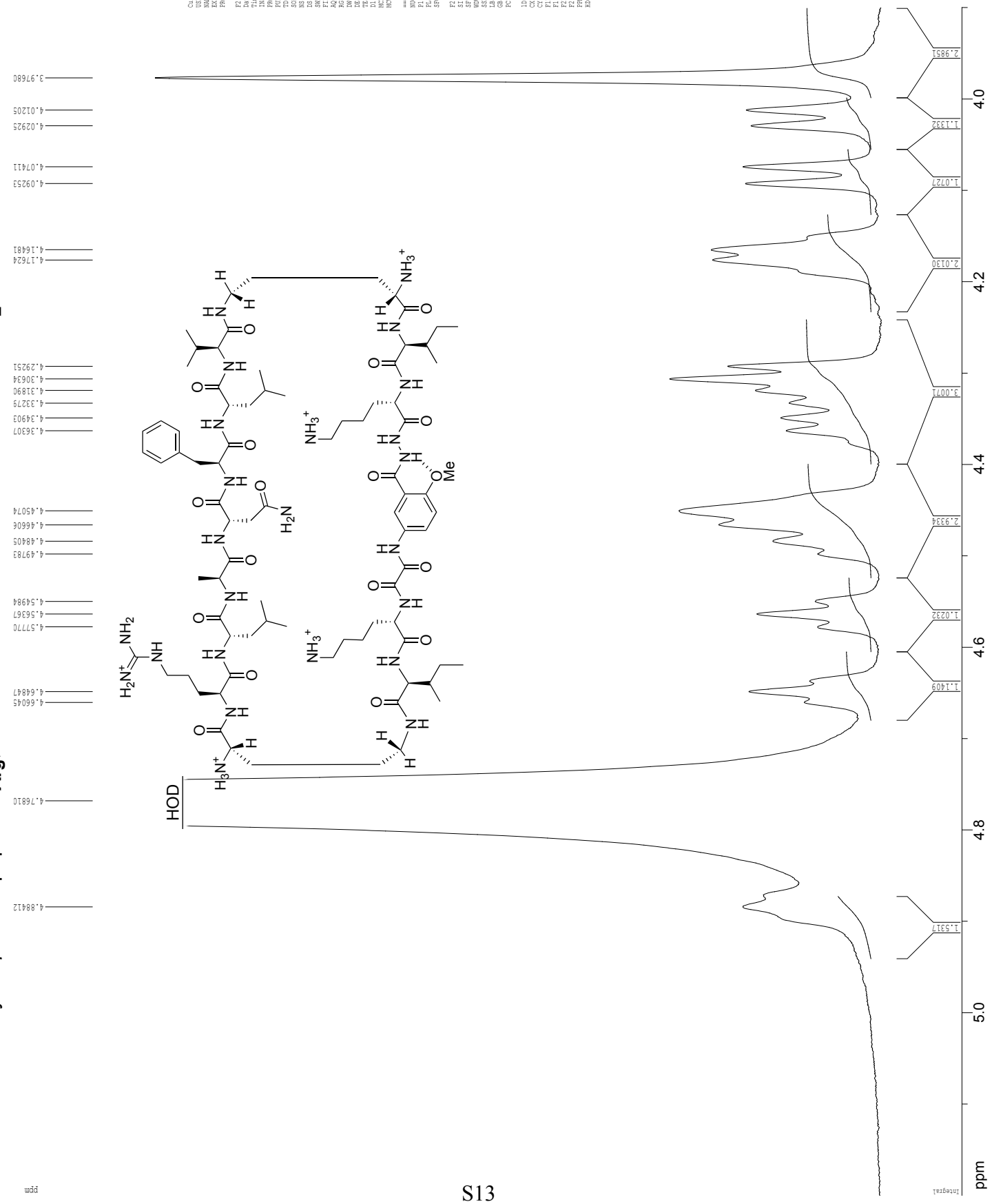
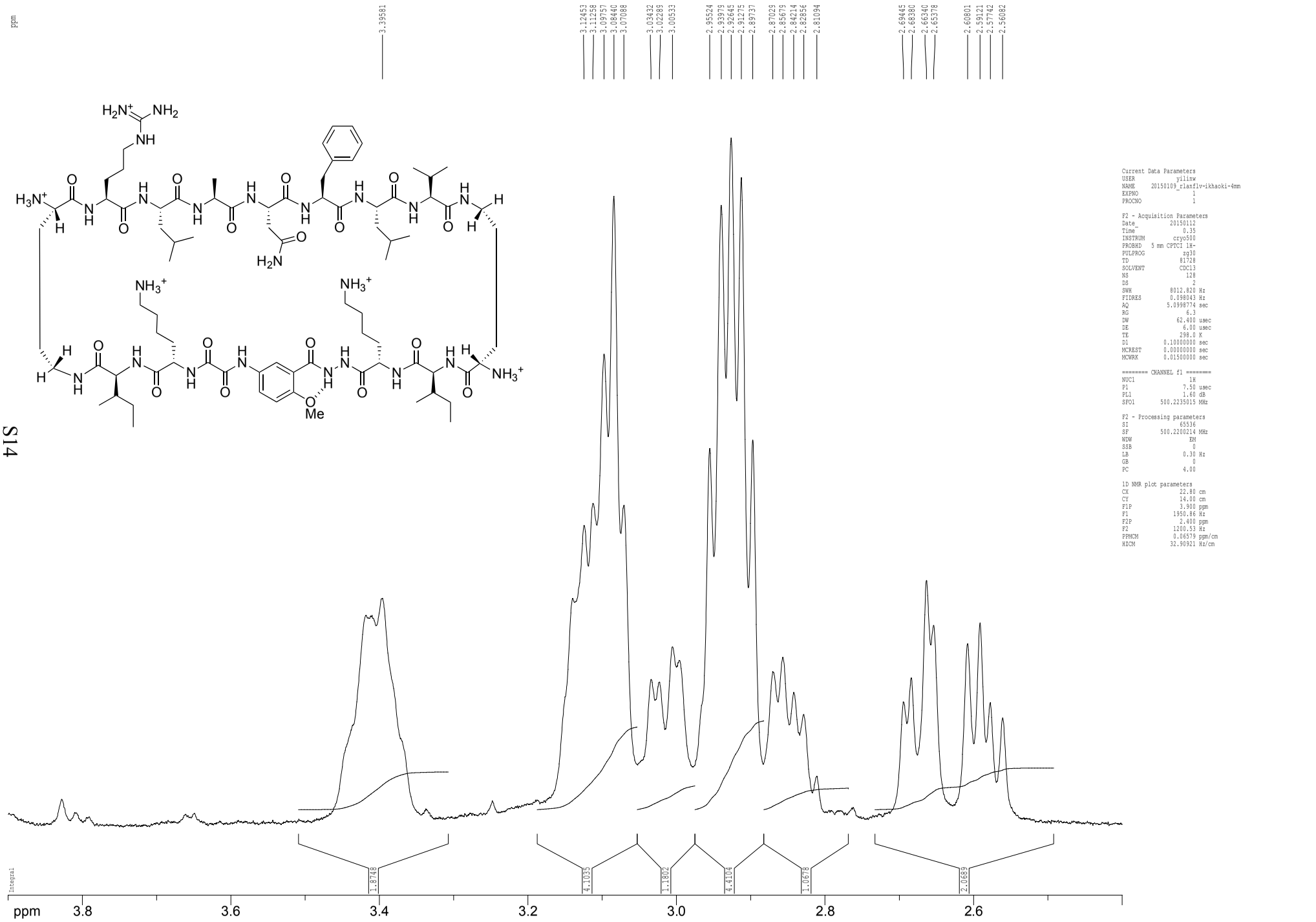
^{1}H NMR of macrocyclic β-sheet peptide **1Arg**, 4 mM in 100 mM deuterioacetate buffer in D_2O at 500 MHz and 298 K



^{1}H NMR of macrocyclic β-sheet peptide **$\mathbf{1_{Arg}}$**, 4 mM in 100 mM deuterioacetate buffer in D_2O at 500 MHz and 298 K



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PROCNO 1

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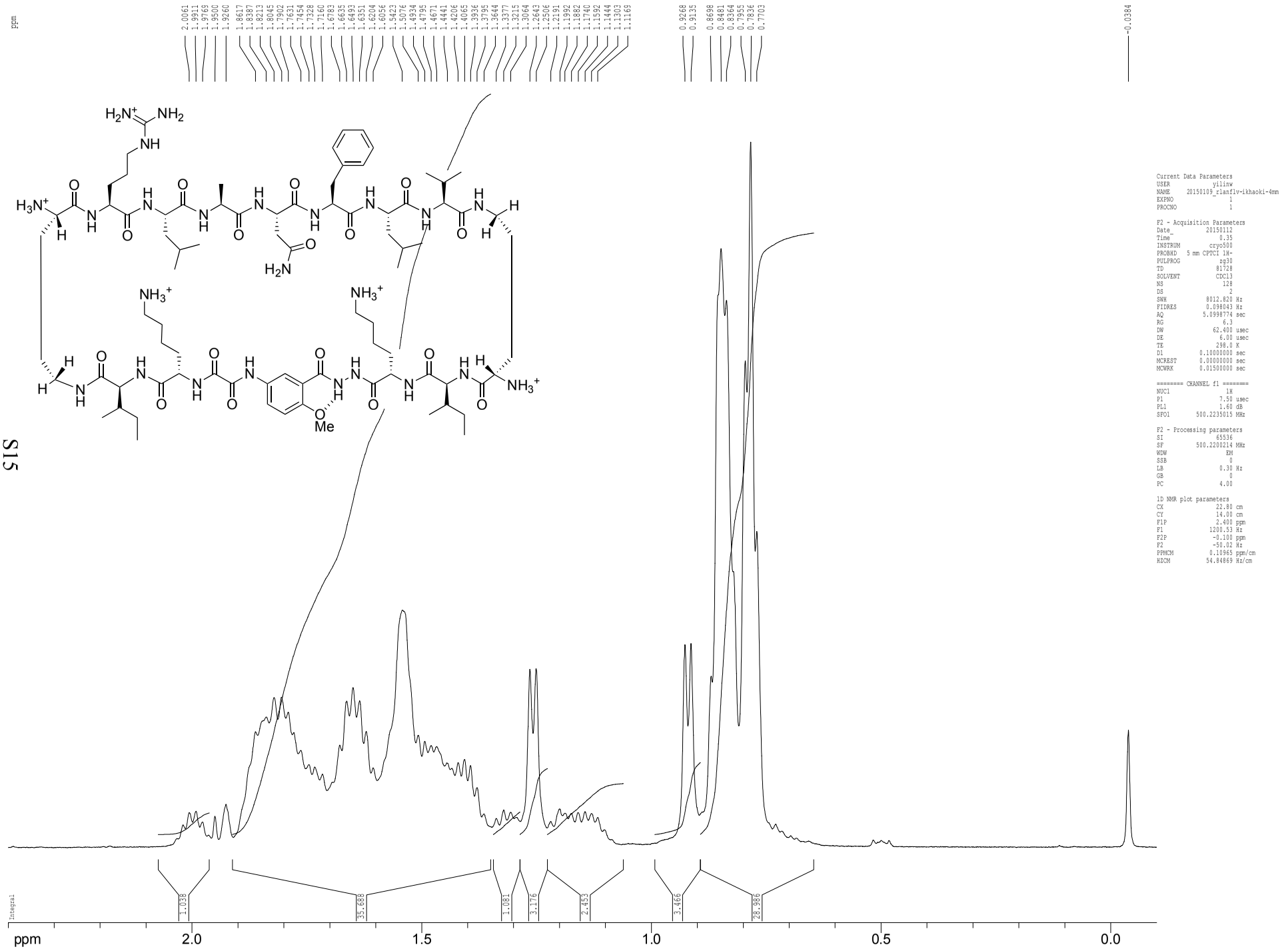
PULPROG zg30
TD 81728
SOLVENT CDCl3
NS 128
DS 2
SWH 8012.820 Hz
FIDRES 0.098043 Hz
AQ 5.0998774 sec
RG 6.3
DW 62.400 usec
DE 6.00 usec
TE 298.0 K
D1 0.10000000 sec
MCREST 0.00000000 sec
MCWRK 0.01500000 sec

======== CHANNEL f1 ========
NUC1 1H
P1 7.50 usec
PL1 1.60 dB
SFO1 500.2235015 MHz

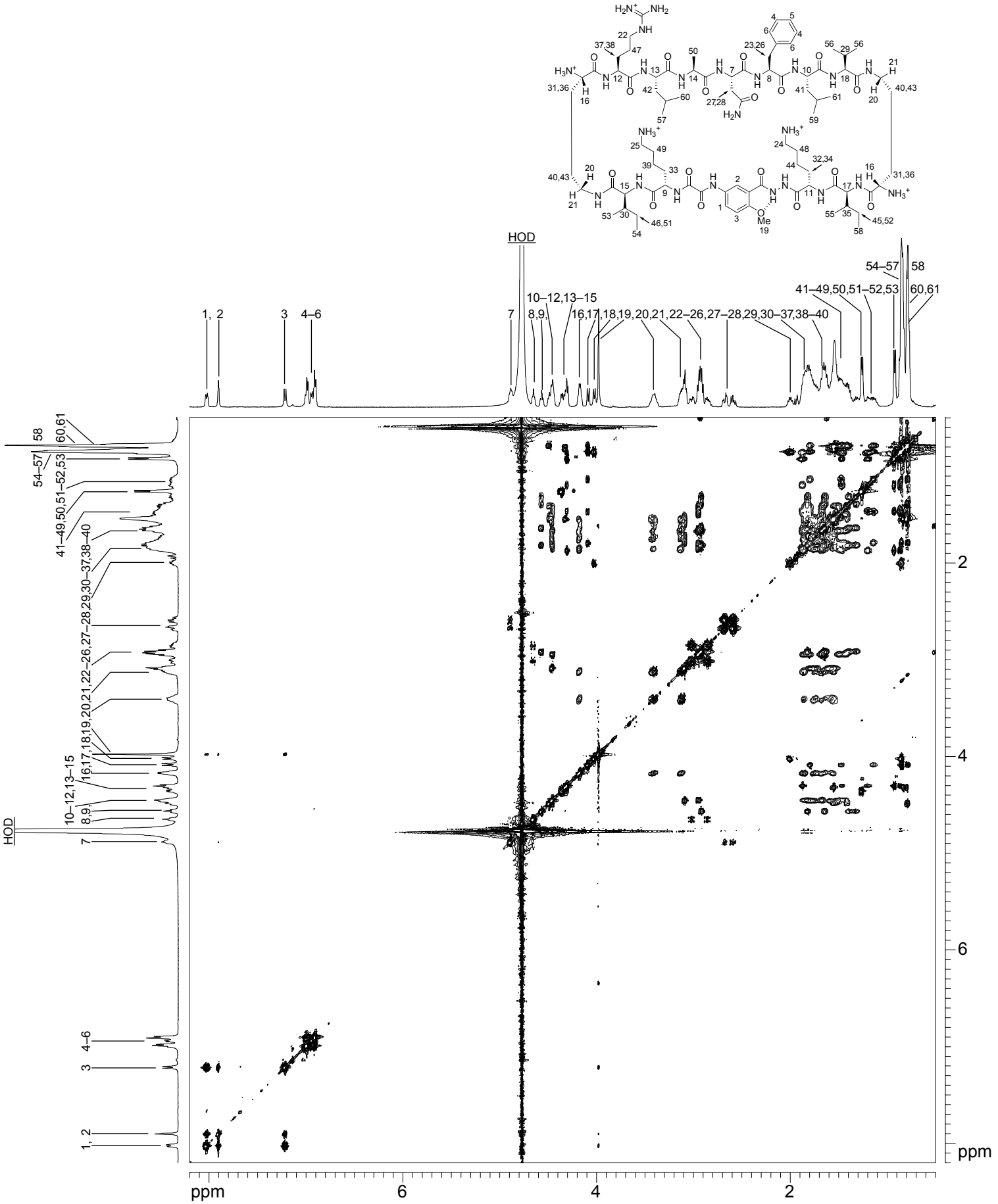
F2 - Processing parameters
SI 65536
SF 500.2200214 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 4.00

1D NMR plot parameters
CX 22.80 cm
CY 14.00 cm
F1P 3.900 ppm
F1 1950.86 Hz
F2P 2.400 ppm
F2 1200.53 Hz
PPMCM 0.06579 ppm/cm
HZCM 32.90921 Hz/cm

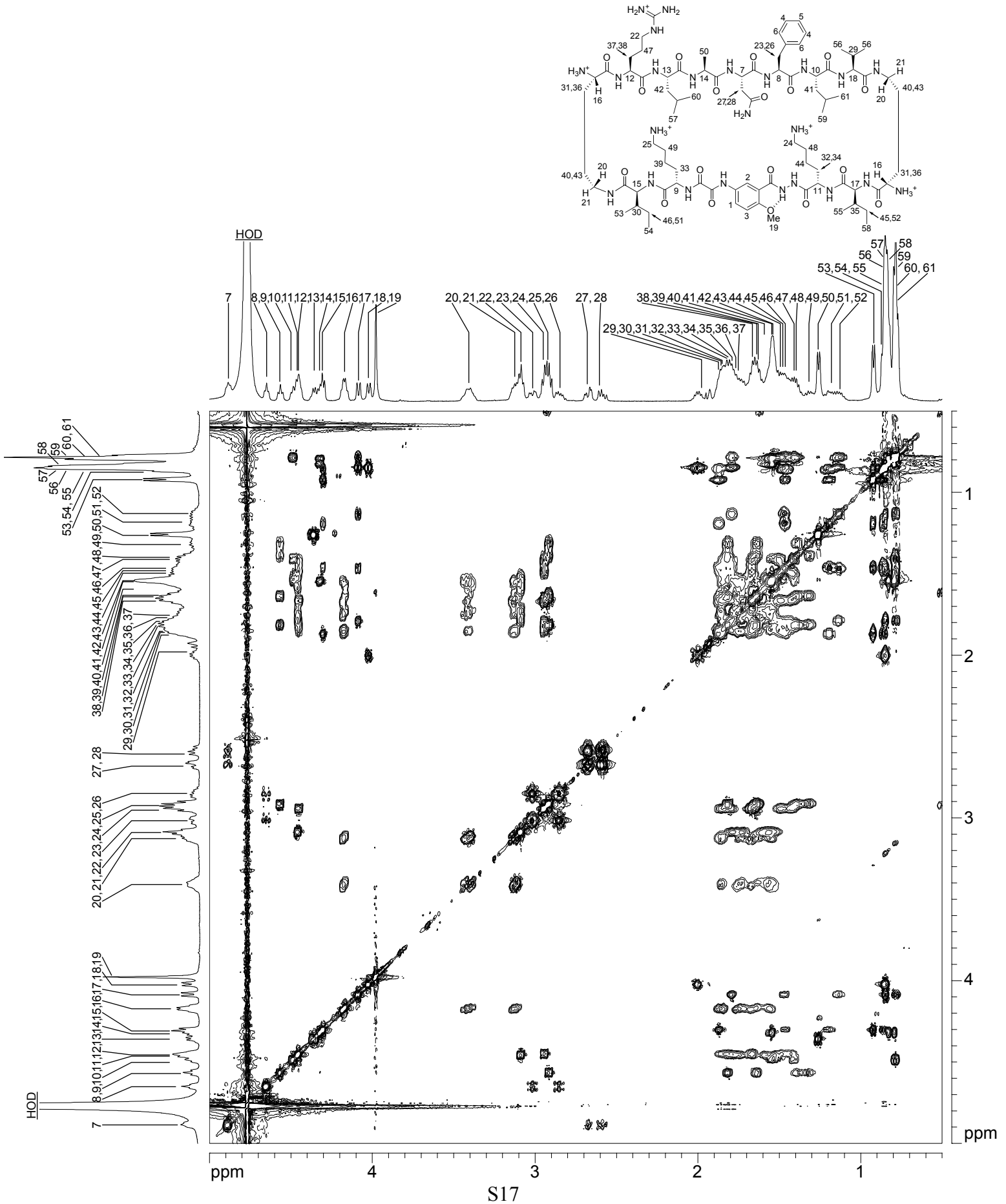
^{1}H NMR of macrocyclic β-sheet peptide **$\mathbf{1}_{Arg}$**, 4 mM in 100 mM deuterioacetate buffer in D_2O at 500 MHz and 298 K



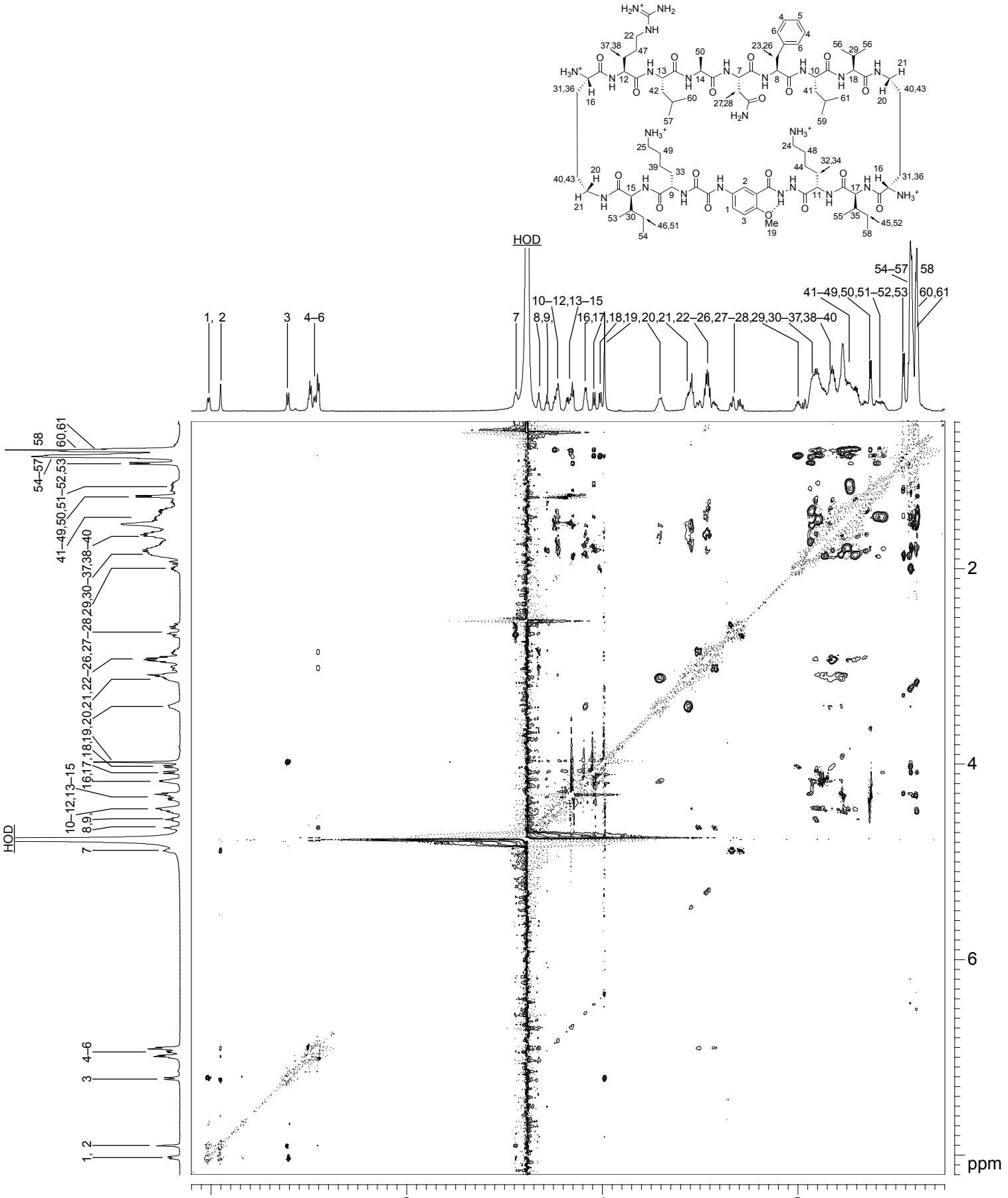
^{1}H NMR 2D TOCSY of macrocyclic β-sheet peptide **1$_{Arg}$** with 150-ms spin-lock mixing time
4 mM in 100 mM deuterioacetate buffer in D_2O at 500 MHz and 298 K



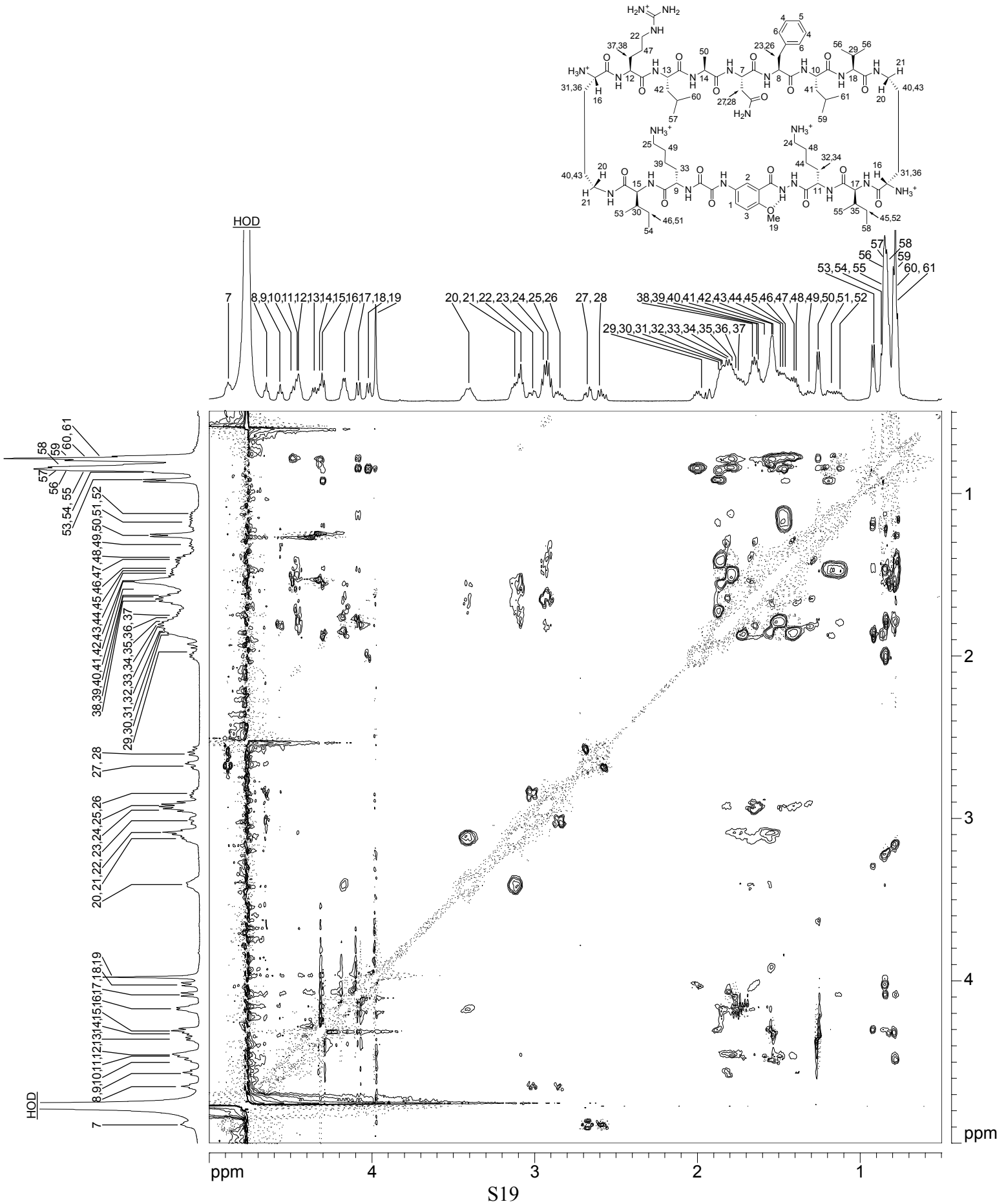
^{1}H NMR 2D TOCSY of macrocyclic β-sheet peptide **1$_{Arg}$** with 150-ms spin-lock mixing time
4 mM in 100 mM deuterioacetate buffer in D_2O at 500 MHz and 298 K



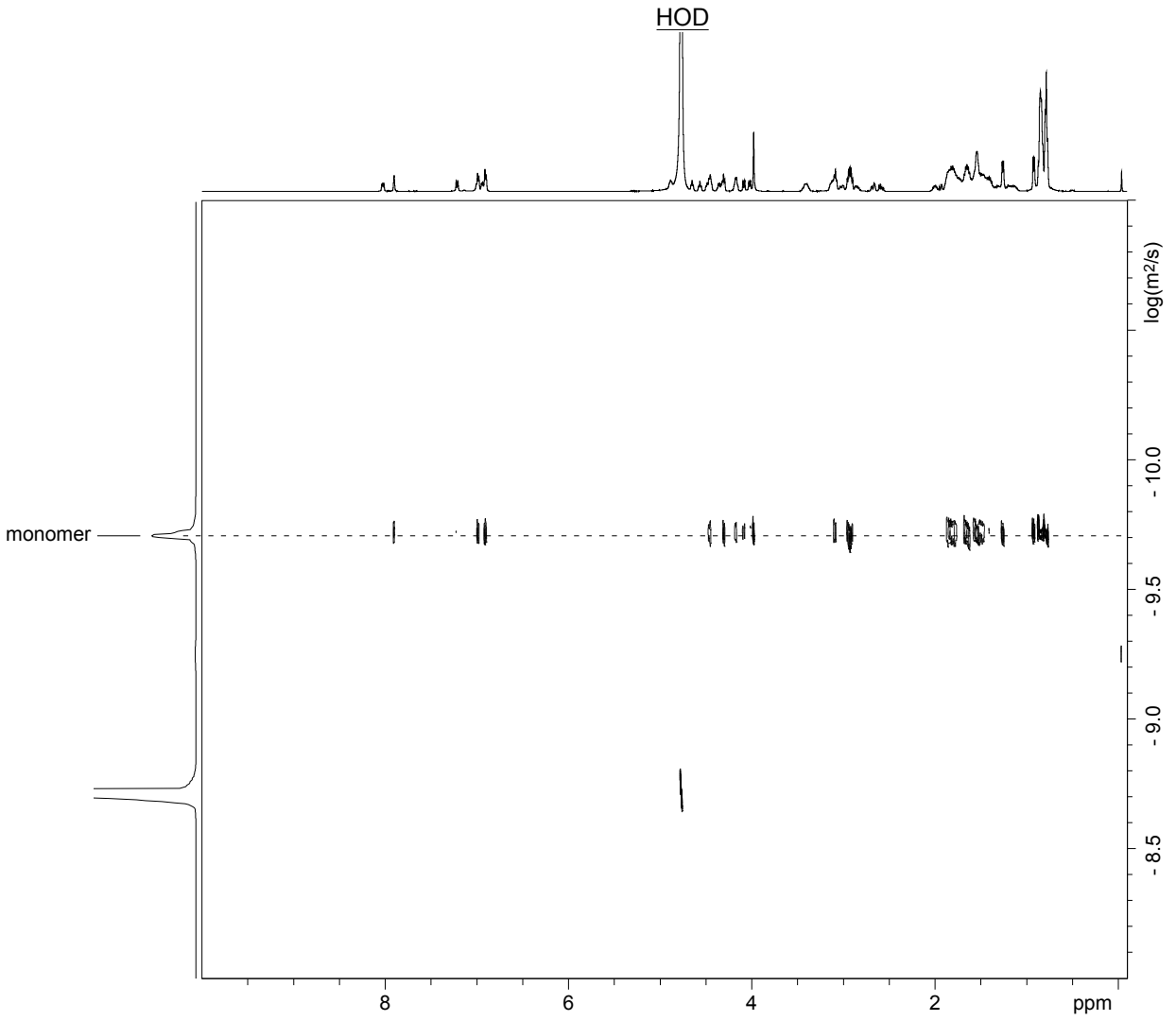
^{1}H NMR 2D ROESY of macrocyclic β-sheet peptide **1$_{Arg}$** with 150-ms spin-lock mixing time
4 mM in 100 mM deuterioacetate buffer in D_2O at 500 MHz and 298 K



^{1}H NMR 2D ROESY of macrocyclic β-sheet peptide **1$_{Arg}$** with 150-ms spin-lock mixing time
4 mM in 100 mM deuterioacetate buffer in D_2O at 500 MHz and 298 K



^{1}H NMR DOSY of macrocyclic β-sheet peptide **1$_{Arg}$** at 500 MHz and 298 K
4 mM in 100 mM deuterioacetate buffer in D_2O



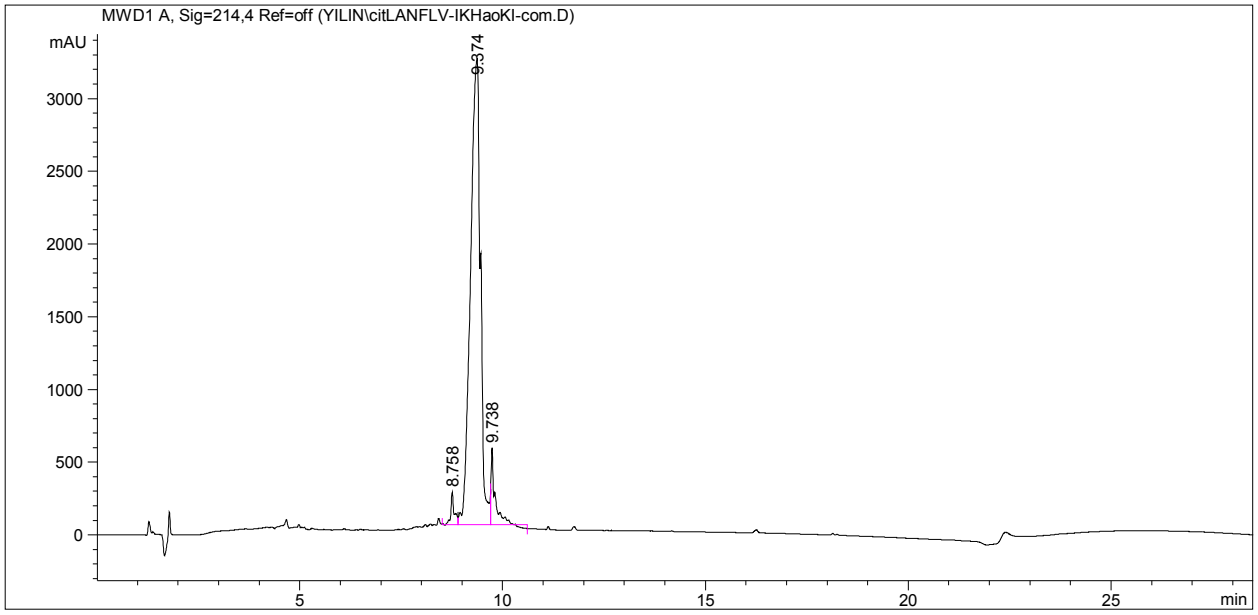
Calculations for macrocyclic β-sheet peptide **1$_{Arg}$** at 4 mM

D_{HOD} = 19.0 x 10^{-10} m^2/s [a]
log (D_{HOD}) = -8.721

$D_{monomer}$: log(D) = -9.708; D = $10^{-9.708}$ = 19.6 ± 0.6 x 10^{-11} m^2/s

[a]Longsworth, L. G. *J. Phys. Chem.* **1960**, *64*, 1914−1917.

RP-HPLC of Macrocyclic β-Sheet **1_{Cit}**



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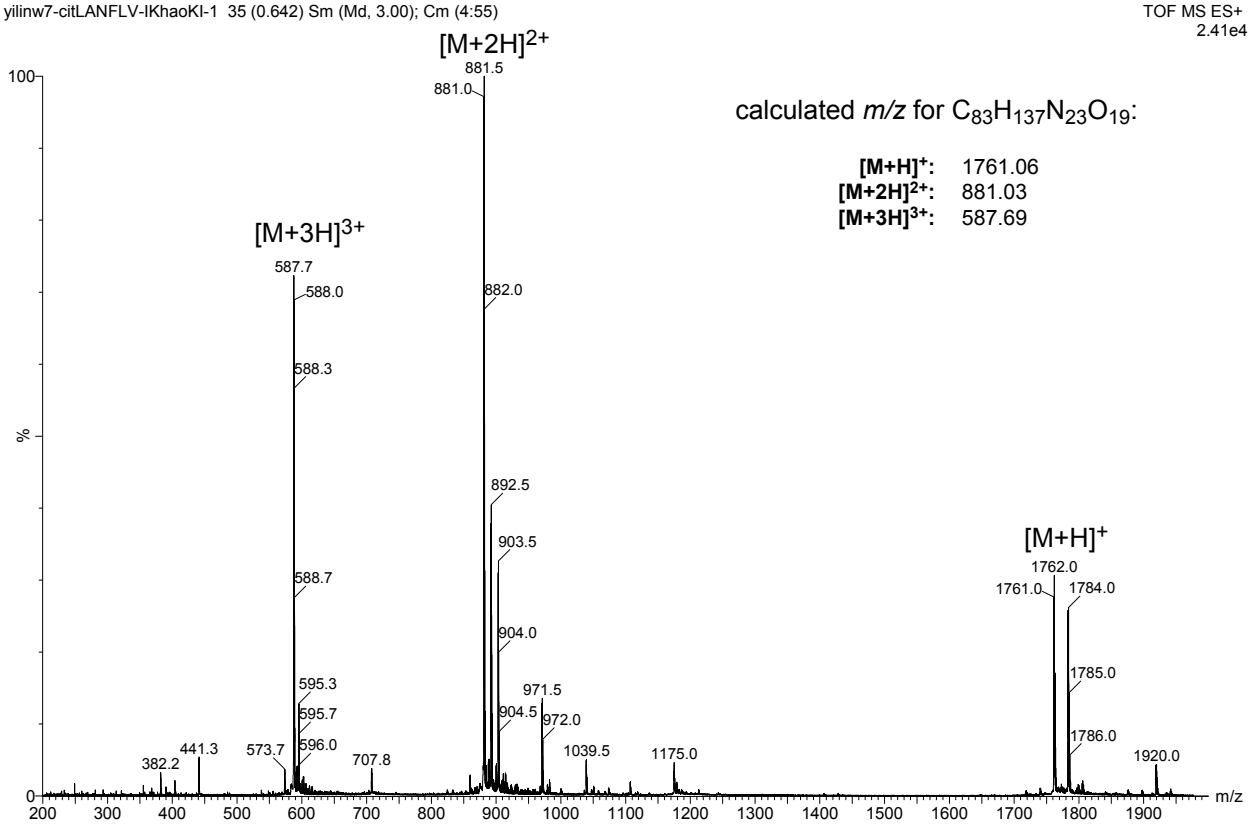
2	9.374	FM	0.2858	5.4981e4	3206.0356	91.7819
3	9.738	FM	0.1130	3599.7199	530.8340	6.0090

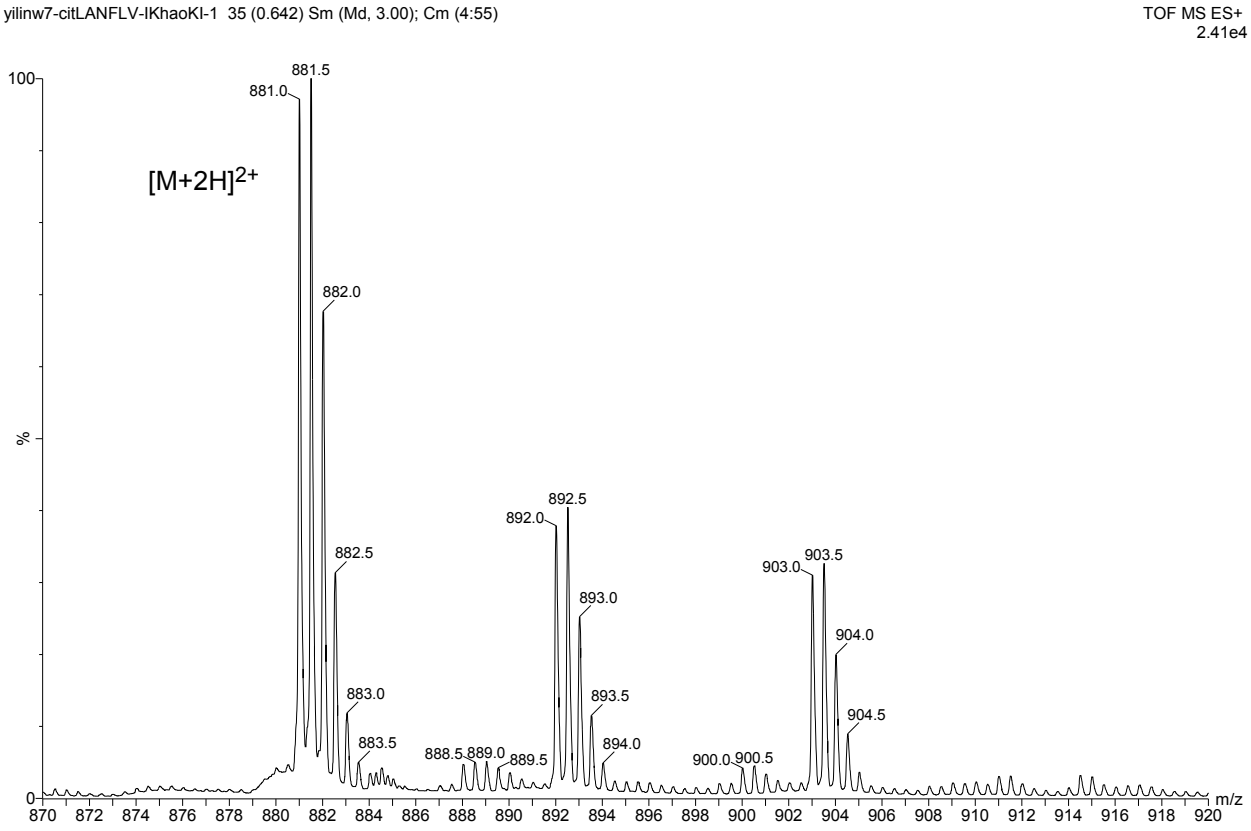
column: Aeris XB-C18 2.6µ
dimensions: 150 mm x 4.6 mm
mobile phase: A: H_2O, 0.1% TFA
B: CH_3CN, 0.1% TFA
gradient: A/B (95:5) to (0:100) in 20 min
flow rate: 1.0 mL/min
detection: VWD, wavelength = 214 nm
temperature: 298 K

MS (ESI) of Macrocyclic β-Sheet **1_{Cit}**



calculated *m/z* for $C_{83}H_{137}N_{23}O_{19}$:

$[M+H]^+$: 1761.06
$[M+2H]^{2+}$: 881.03
$[M+3H]^{3+}$: 587.69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2.41e4
[M+2H]2+
881.5
881.0
882.0
882.5
883.0
883.5
888.5
889.0
889.5
892.5
892.0
893.0
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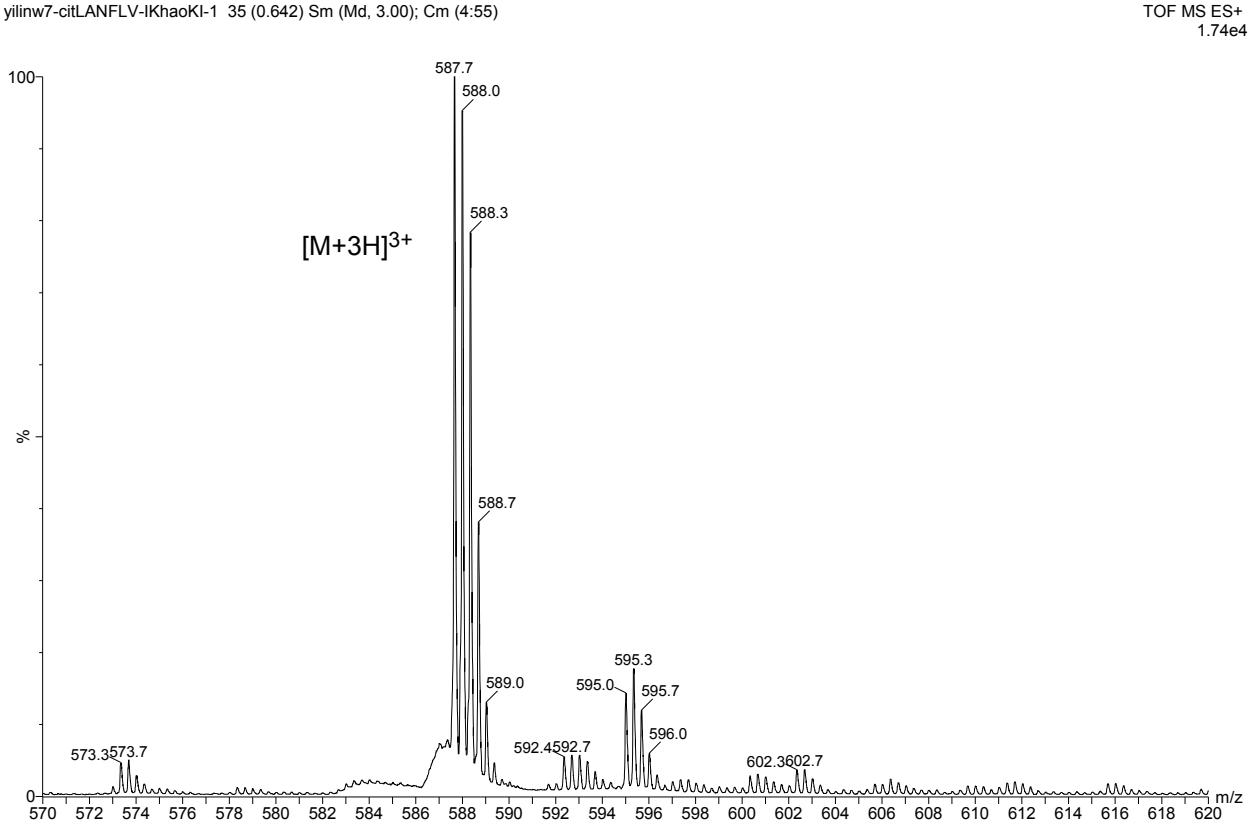
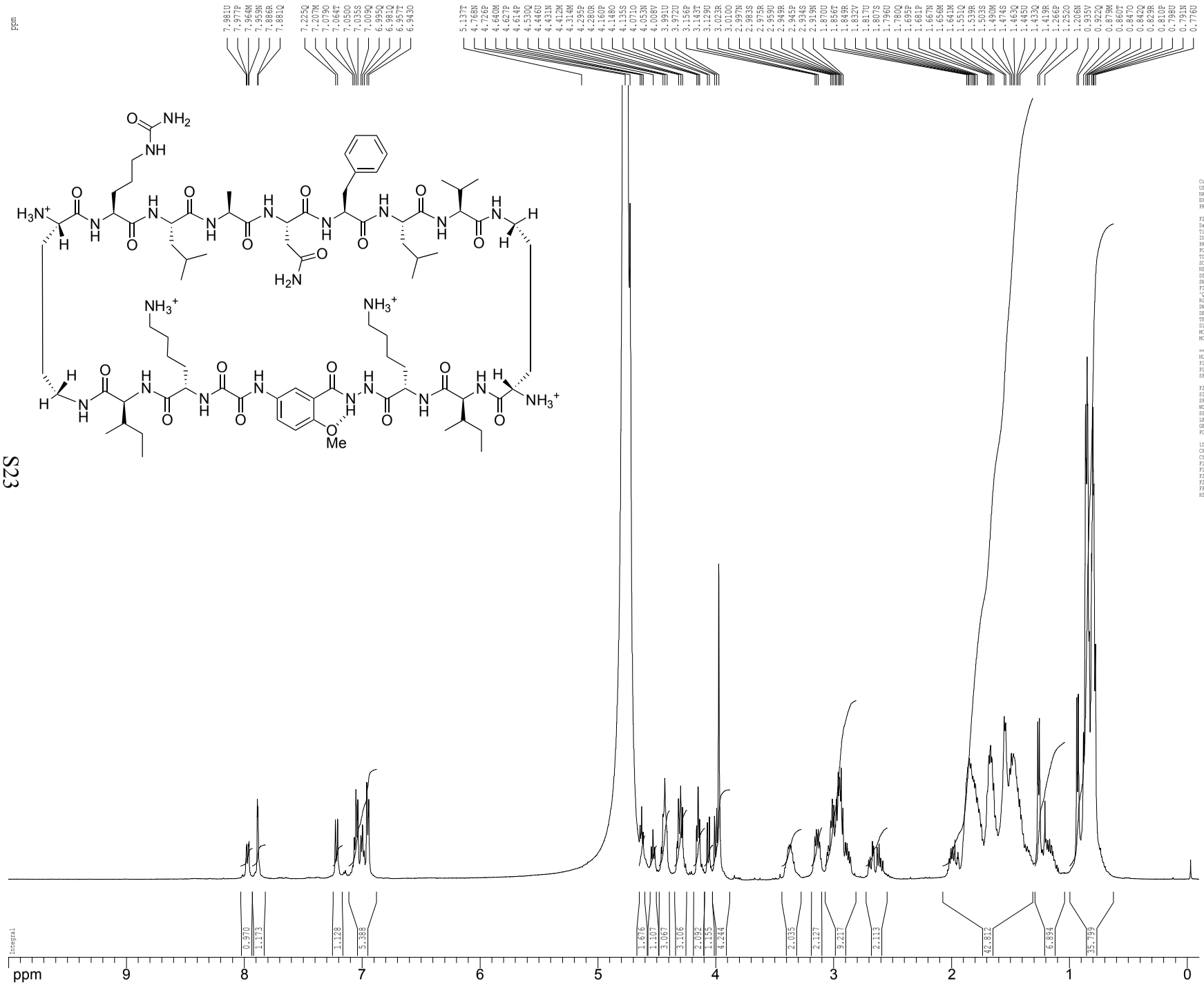
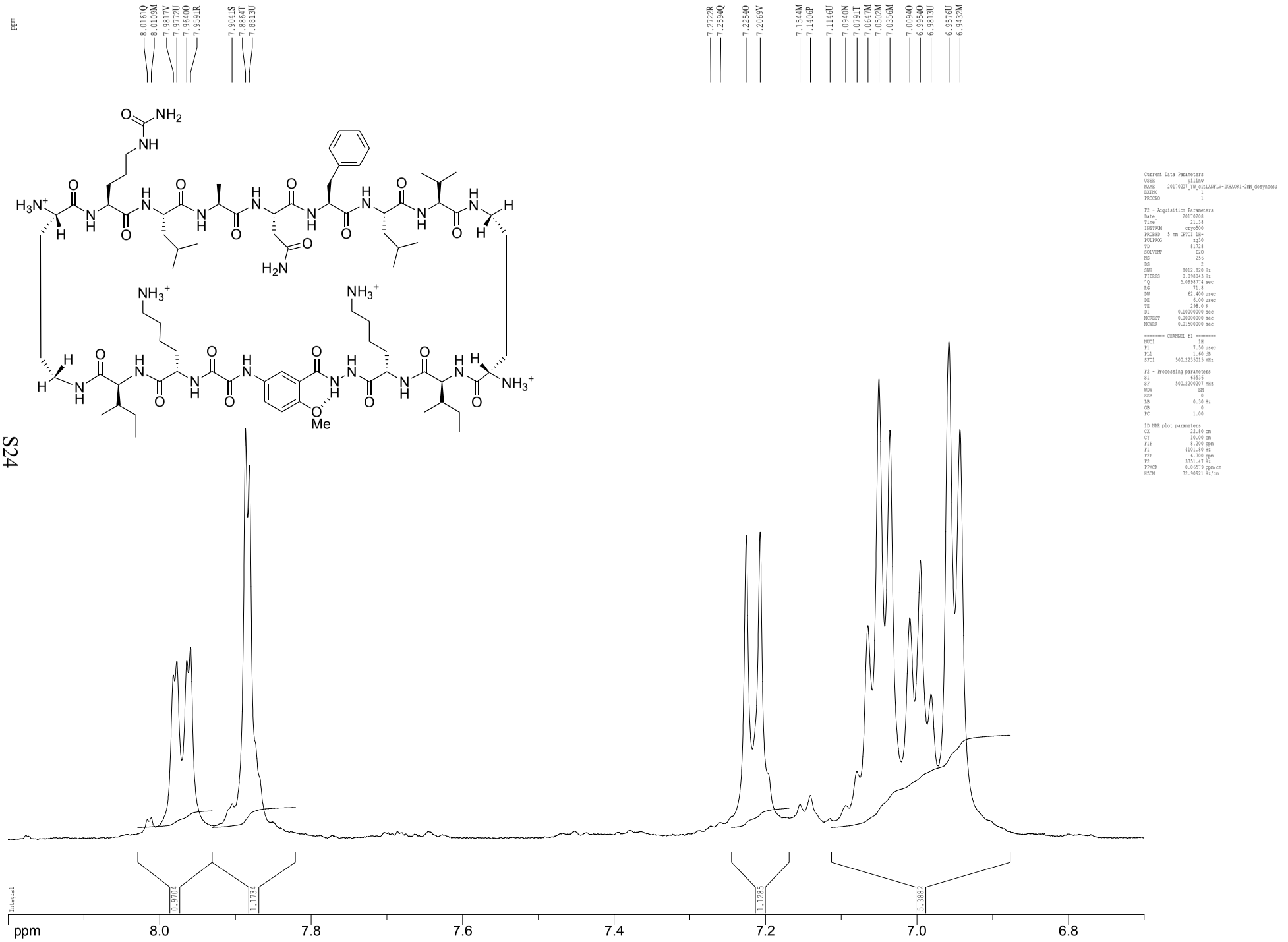
903.0
903.5
904.0
904.5
%
m/z


yilinw7-citLANFLV-IKhaoKI-1 35 (0.642) Sm (Md, 3.00); Cm (4:55)
TOF MS ES+
1.74e4
[M+3H]3+
587.7
588.0
588.3
588.7
589.0
595.3
595.0
595.7
596.0
573.3
573.7
592.4
592.7
602.3
602.7
%
m/z

^{1}H NMR of macrocyclic β-sheet peptide **1**$_{Cit}$ 2 mM in 100 mM deuterioacetate buffer in D_2O at 500 MHz and 298 K



^{1}H NMR of macrocyclic β-sheet peptide **1$_{Cit}$**, 2 mM in 100 mM deuterioacetate buffer in D_2O at 500 MHz and 298 K



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PULPROG zg30
TD 81728
SOLVENT D2O
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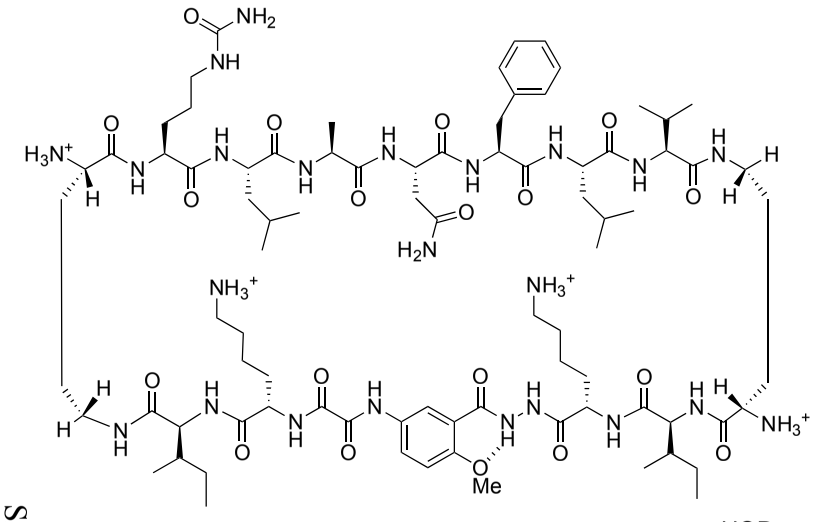
DS 2
SWH 8012.820 Hz
FIDRES 0.098043 Hz
AQ 5.0998774 sec
RG 71.8
DW 62.400 usec
DE 6.00 usec
TE 298.0 K
D1 0.10000000 sec
MCREST 0.00000000 sec
MCWRK 0.01500000 sec

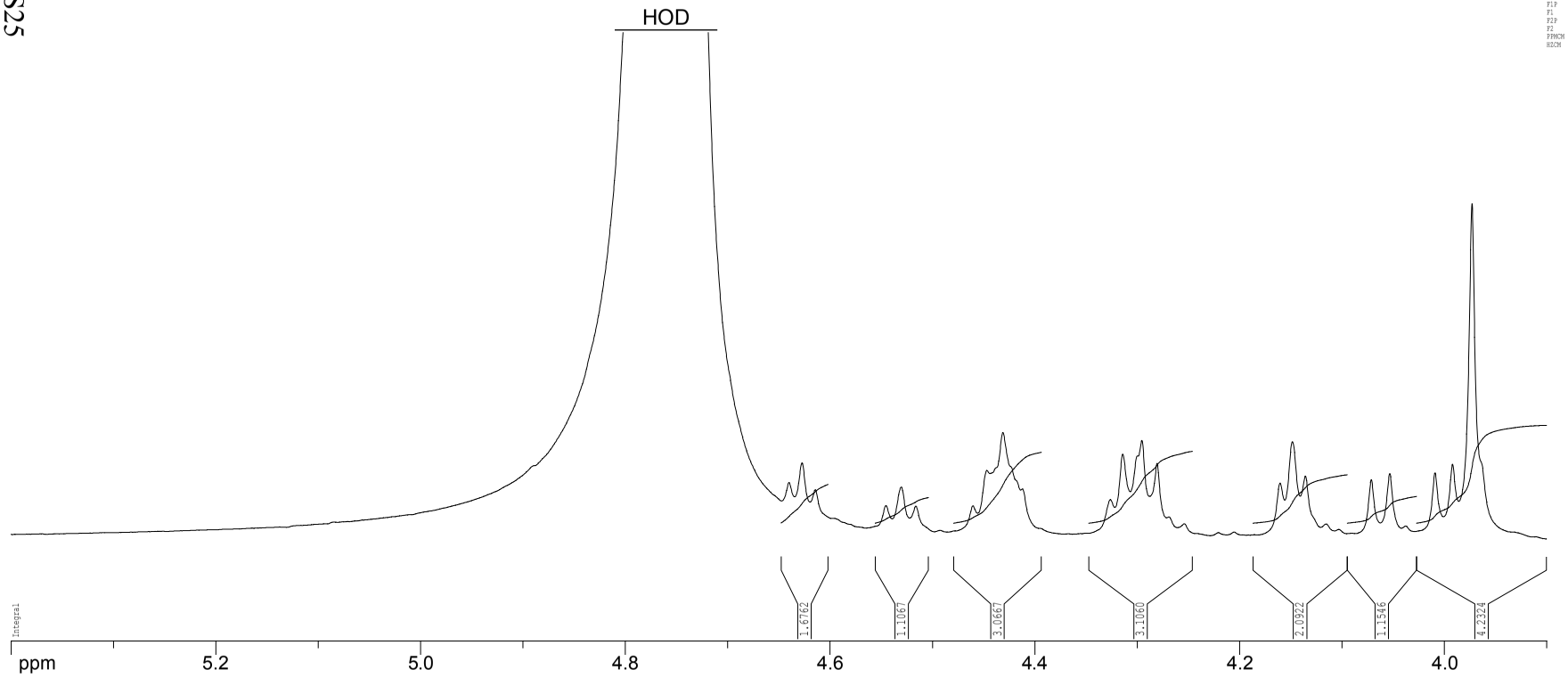
======== CHANNEL f1 ========
NUC1 1H
P1 7.50 usec
PL1 1.60 dB
SFO1 500.2235015 MHz

F2 - Processing parameters
SI 65536
SF 500.2200207 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00

1D NMR plot parameters
CX 22.80 cm
CY 10.00 cm
F1P 8.200 ppm
F1 4101.80 Hz
F2P 6.700 ppm
F2 3351.47 Hz
PPMCM 0.04579 ppm/cm
HZCM 32.90921 Hz/cm

^{1}H NMR of macrocyclic β-sheet peptide **$\mathbf{1}_{\mathbf{Cit}}$**, 2 mM in 100 mM deuterioacetate buffer in D_2O at 500 MHz and 298 K





Current Data Parameters
USER yiLiew
NAME 20170207_FW_citLAHFLV-DKHAORI-2mM_dosymoesu
EXPNO 1
PROCNO 1

F2 - Acquisition Parameters
Date 20170208
Time 21.38
INSTRUM cryo500
PROBHD 5 mm CPTCI 1H-
PULPROG zg30
TD 81728
SOLVENT D2O
NS 256
DS 2
SWH 8012.820 Hz
FIDRES 0.098043 Hz
AQ 5.0998774 sec
RG 71.8
DW 62.400 usec
DE 6.00 usec
TE 298.0 K
D1 0.10000000 sec
MCREST 0.00000000 sec
MCWRK 0.01500000 sec

======== CHANNEL f1 ========
NUC1 1H
P1 7.50 usec
PL1 1.60 dB
SFO1 500.2235015 MHz

F2 - Processing parameters
SI 65536
SF 500.2200207 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00

1D NMR plot parameters
CX 22.80 cm
CY 5.00 cm
F1P 5.400 ppm
F1 2701.19 Hz
F2P 3.900 ppm
F2 1950.86 Hz
PPMCM 0.04579 ppm/cm
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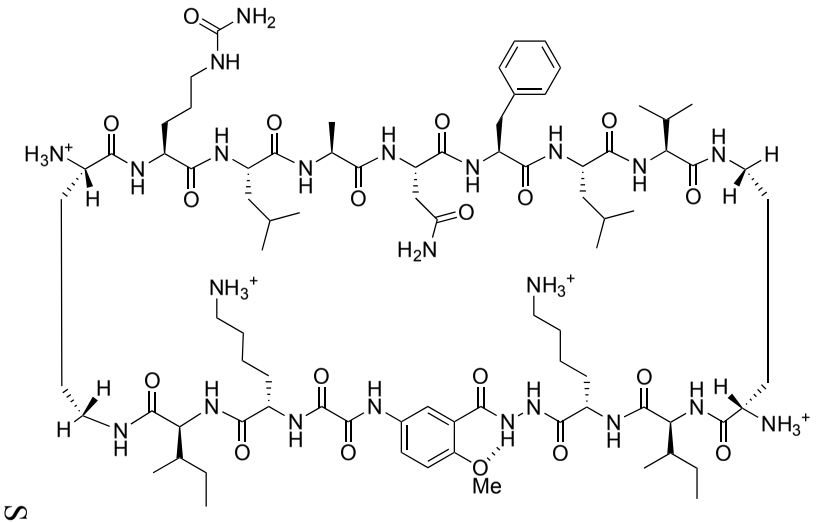
^{1}H NMR of macrocyclic β-sheet peptide **1$_{Cit}$**, 2 mM in 100 mM deuterioacetate buffer in D_2O at 500 MHz and 298 K



Current Data Parameters
USER yiLiew
NAME 20170207_FW_citLANFLV-DKHAORI-2mM_dosymoesu
EXPNO 1
PROCNO 1

F2 - Acquisition Parameters
Date 20170208
Time 21.38
INSTRUM cryo500
PROBHD 5 mm CPTCI 1H-
PULPROG zg30
TD 81728
SOLVENT D2O
NS 256
DS 2
SWH 8012.820 Hz
FIDRES 0.098043 Hz
AQ 5.0998774 sec
RG 71.8
DW 62.400 usec
DE 6.00 usec
TE 298.0 K
D1 0.10000000 sec
MCREST 0.00000000 sec
MCWRK 0.01500000 sec

======== CHANNEL f1 ========
NUC1 1H
P1 7.50 usec
PL1 1.60 dB
SFO1 500.2235015 MHz

F2 - Processing parameters
SI 65536
SF 500.2200207 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00

1D NMR plot parameters
CX 22.80 cm
CY 5.00 cm
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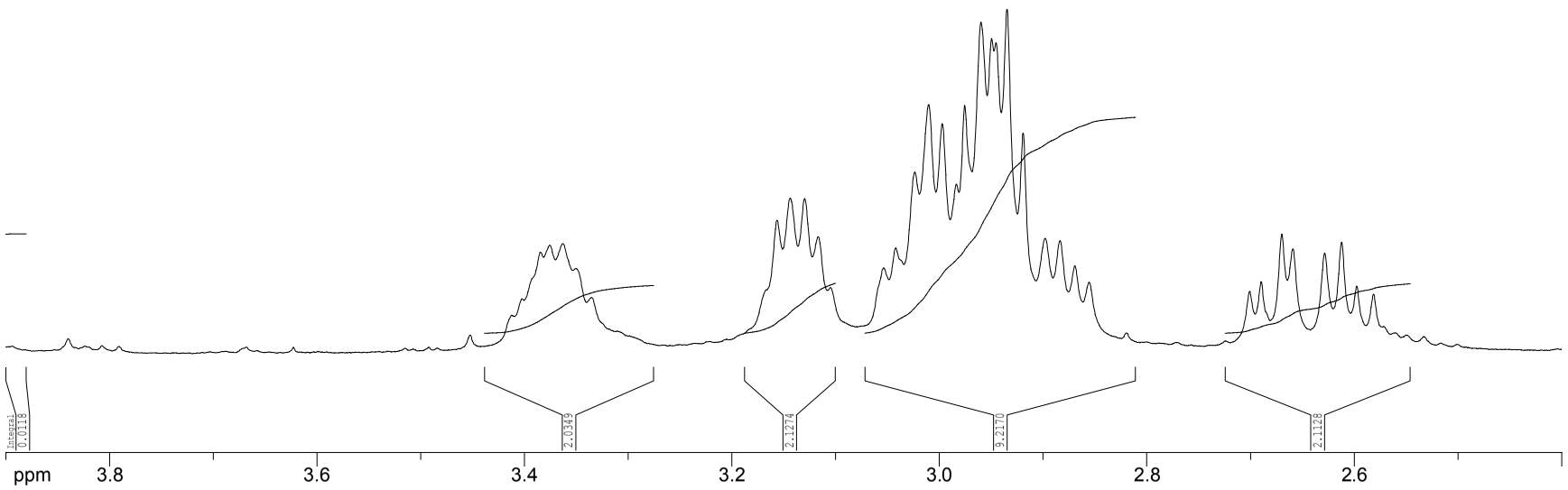
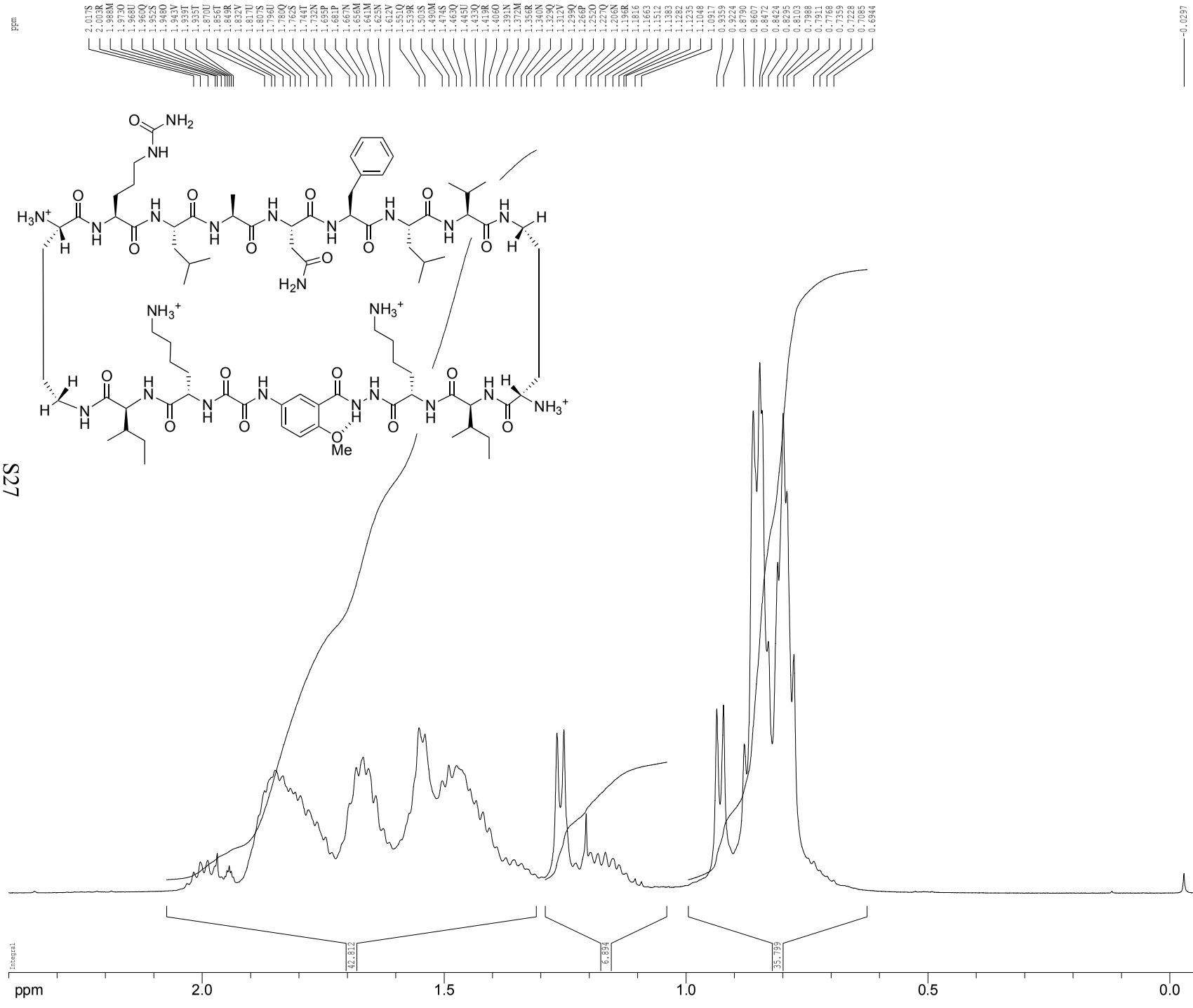
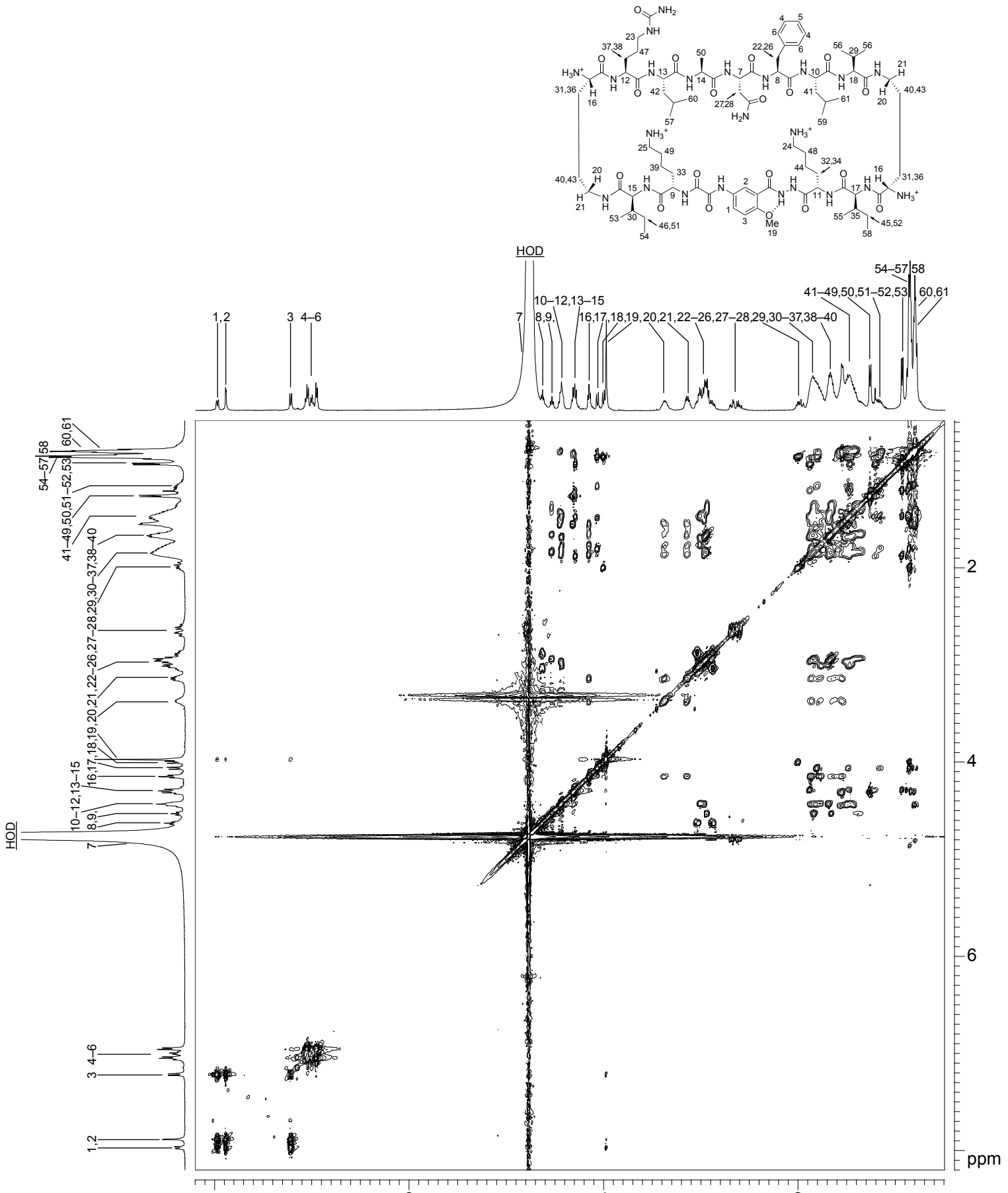
F1 1950.86 Hz
F2P 2.400 ppm
F2 1200.53 Hz
PPMCM 0.04579 ppm/cm
HZCM 32.90921 Hz/cm



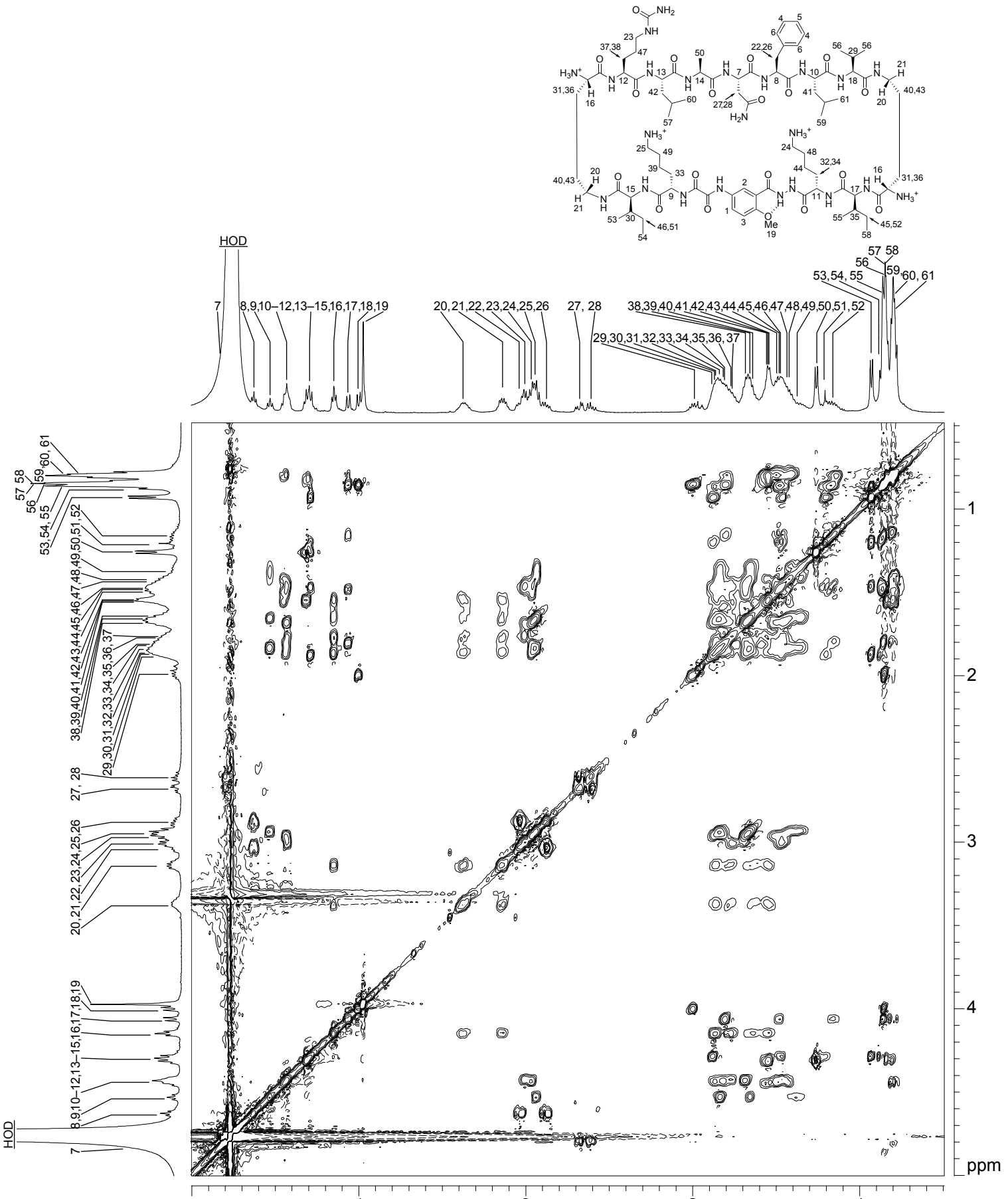
^{1}H NMR of macrocyclic β-sheet peptide **1_{Cit}**, 2 mM in 100 mM deuterioacetate buffer in D_2O at 500 MHz and 298 K



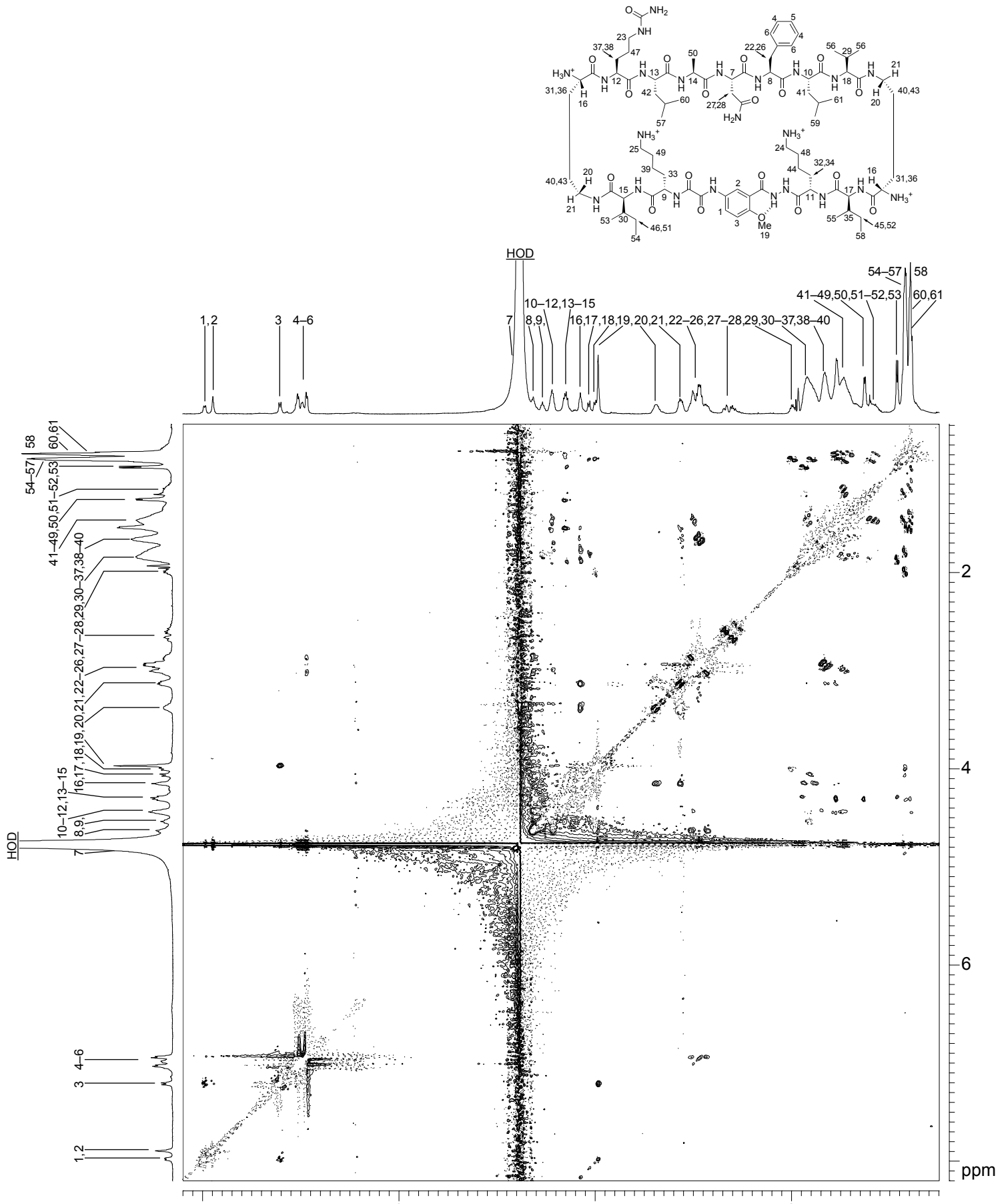
^{1}H NMR 2D TOCSY of macrocyclic β-sheet peptide **1$_{Cit}$** with 150-ms spin-lock mixing time
2 mM in 100 mM deuterioacetate buffer in D_2O at 500 MHz and 298 K



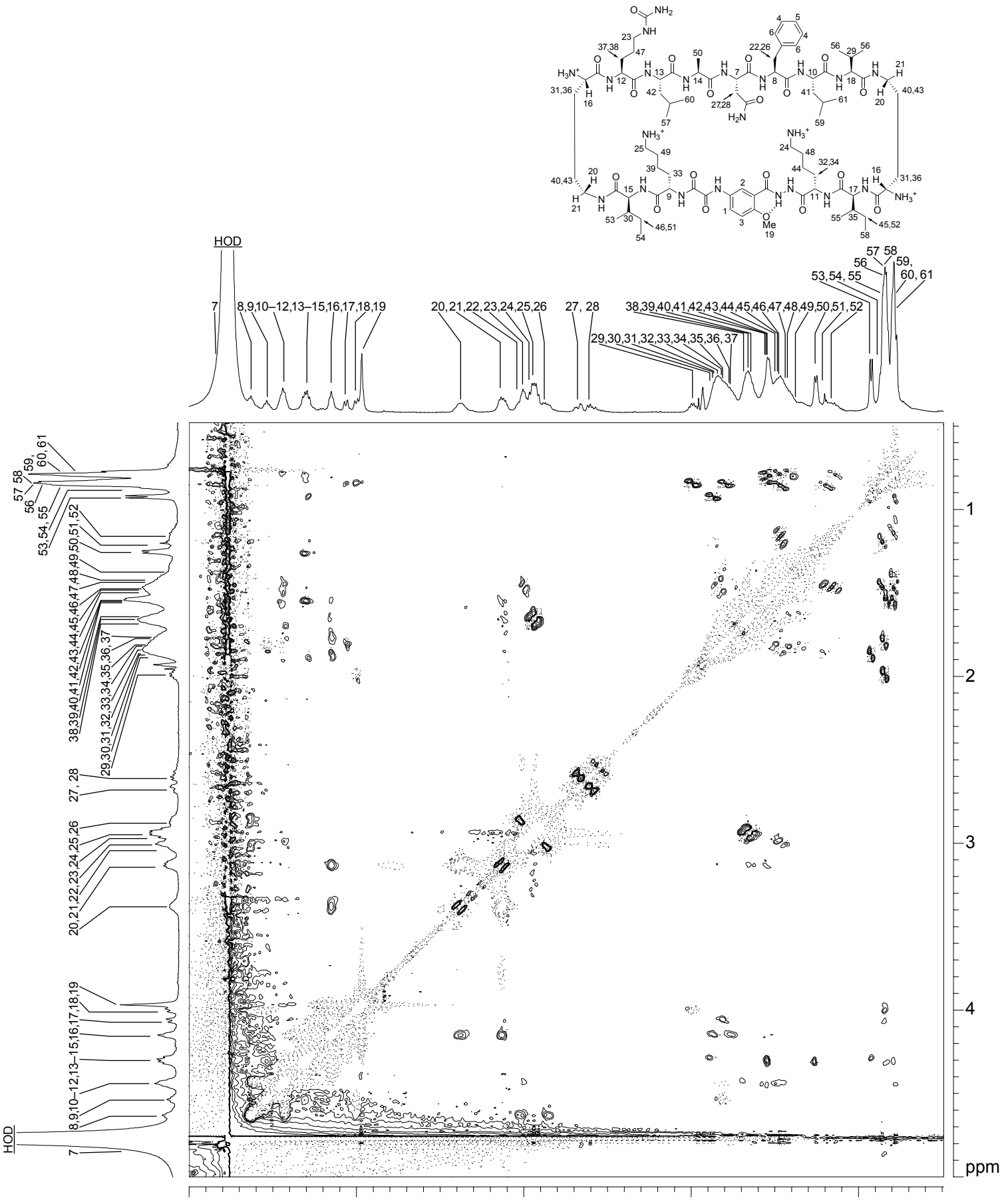
^{1}H NMR 2D TOCSY of macrocyclic β-sheet peptide **1$_{Cit}$** with 150-ms spin-lock mixing time
2 mM in 100 mM deuterioacetate buffer in D_2O at 500 MHz and 298 K



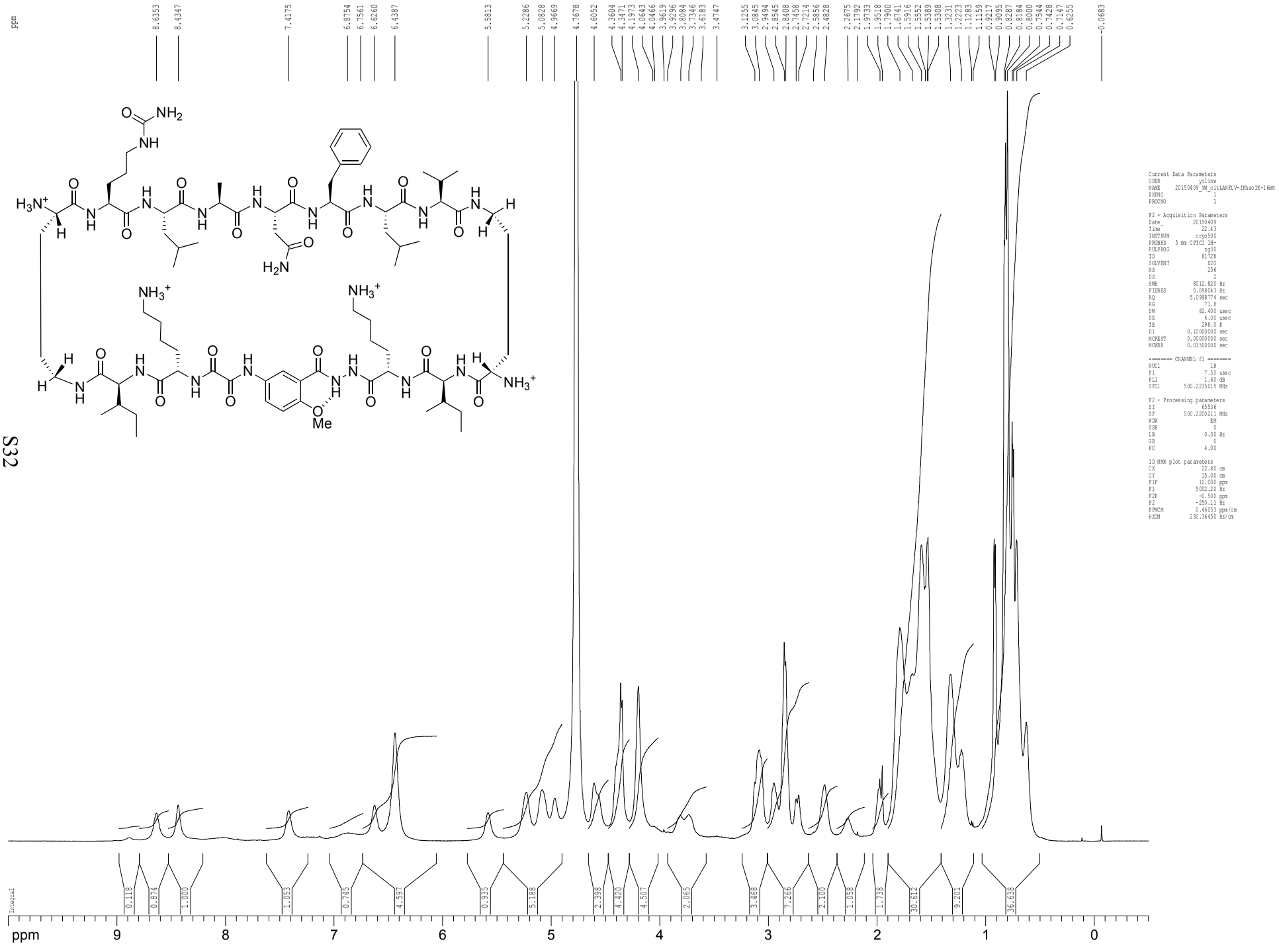
^{1}H NMR 2D ROESY of macrocyclic β-sheet peptide **1$_{Cit}$** with 100-ms spin-lock mixing time
2 mM in 100 mM deuterioacetate buffer in D_2O at 500 MHz and 298 K



^{1}H NMR 2D ROESY of macrocyclic β-sheet peptide **1$_{Cit}$** with 100-ms spin-lock mixing time
2 mM in 100 mM deuterioacetate buffer in D_2O at 500 MHz and 298 K



^{1}H NMR of macrocyclic β-sheet peptide **1_{Cit}**, 16 mM in 100 mM deuterioacetate buffer in D_2O at 500 MHz and 298 K



Current Data Parameters
USER yilinw
NAME 20150409_YM_citLANFLV-IKOhaoIK-1fnM
EXPNO 1
PROCNO 1

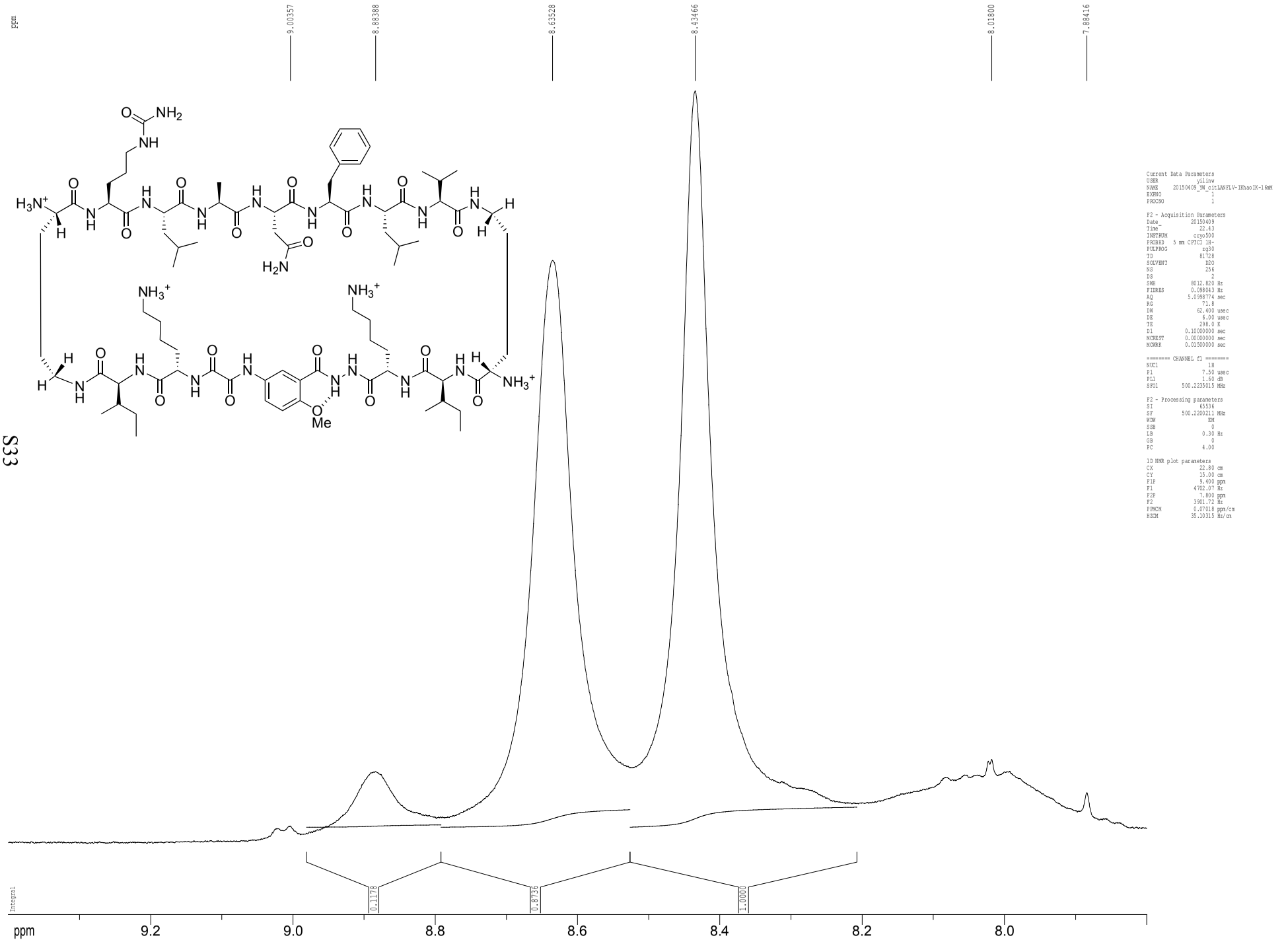
F2 - Acquisition Parameters
Date_ 20150409
Time 22.43
INSTRUM cryo500
PROBHD 5 mm CPTCI 1H-
PULPROG zg30
TD 81728
SOLVENT H2O
NS 256
DS 2
SWH 8012.820 Hz
FIDRES 0.098043 Hz
AQ 5.0998774 sec
RG 71.8
DW 62.400 usec
DE 6.00 usec
TE 298.0 K
D1 0.10000000 sec
MCREST 0.00000000 sec
MCWRK 0.01500000 sec

======= CHANNEL f1 =======
NUC1 1H
P1 7.50 usec
PL1 1.60 dB
SFO1 500.2235015 MHz

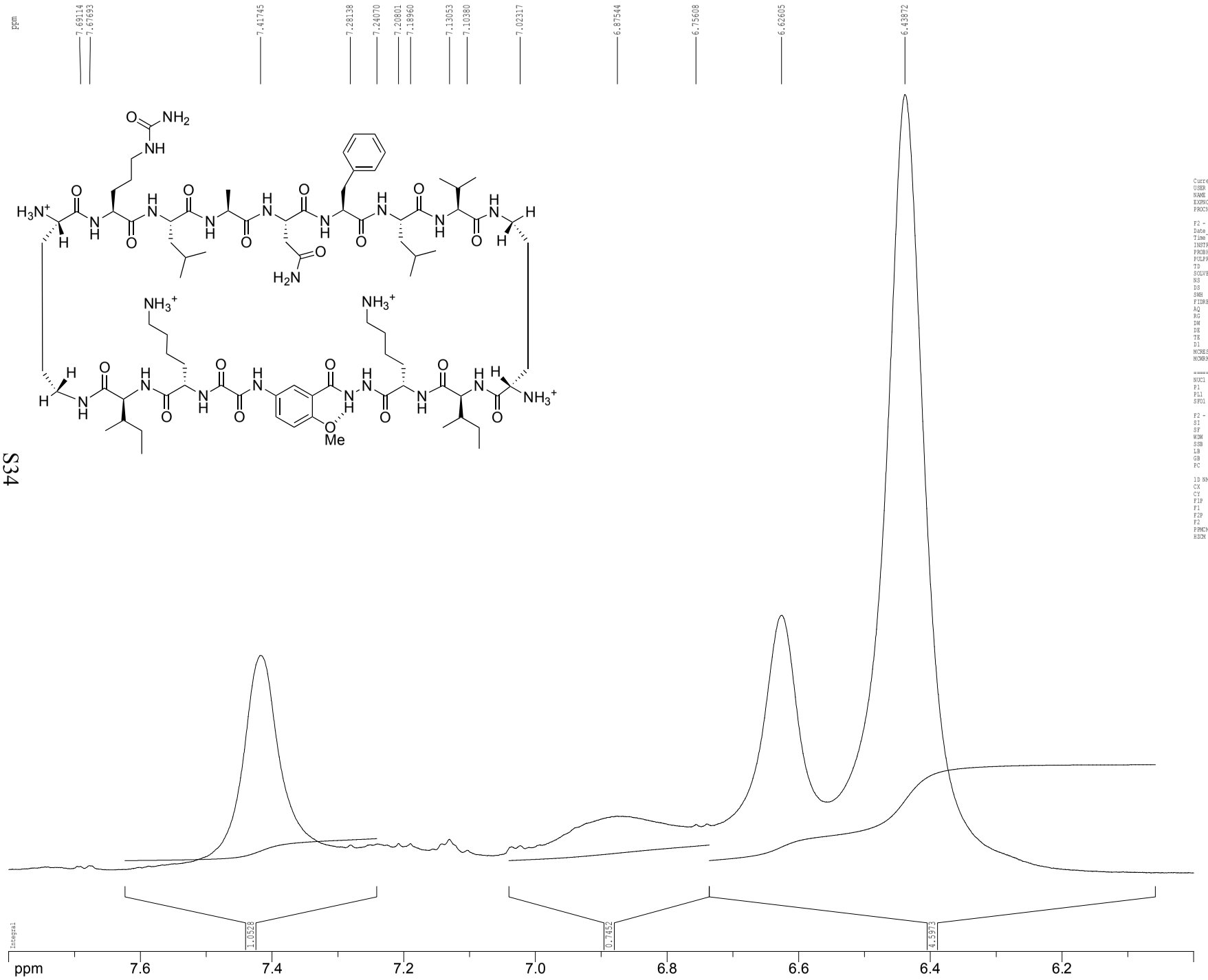
F2 - Processing parameters
SI 65536
SF 500.2200211 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 4.00

1D NMR plot parameters
CX 22.80 cm
CY 15.00 cm
F1P 10.000 ppm
F1 5002.20 Hz
F2P -0.500 ppm
F2 -250.11 Hz
PPMCM 0.46053 ppm/cm
HZCM 230.36450 Hz/cm

^{1}H NMR of macrocyclic β-sheet peptide **$\mathbf{1_{Cit}}$**, 16 mM in 100 mM deuterioacetate buffer in D_2O at 500 MHz and 298 K



^{1}H NMR of macrocyclic β-sheet peptide **$\mathbf{1}_{Cit}$**, 16 mM in 100 mM deuterioacetate buffer in D_2O at 500 MHz and 298 K



Current Data Parameters
USER yilinw
NAME 20150409_YM_cit:LAN:FLV-1KOhaoIK-1fnM
EXPNO 1
PROCNO 1

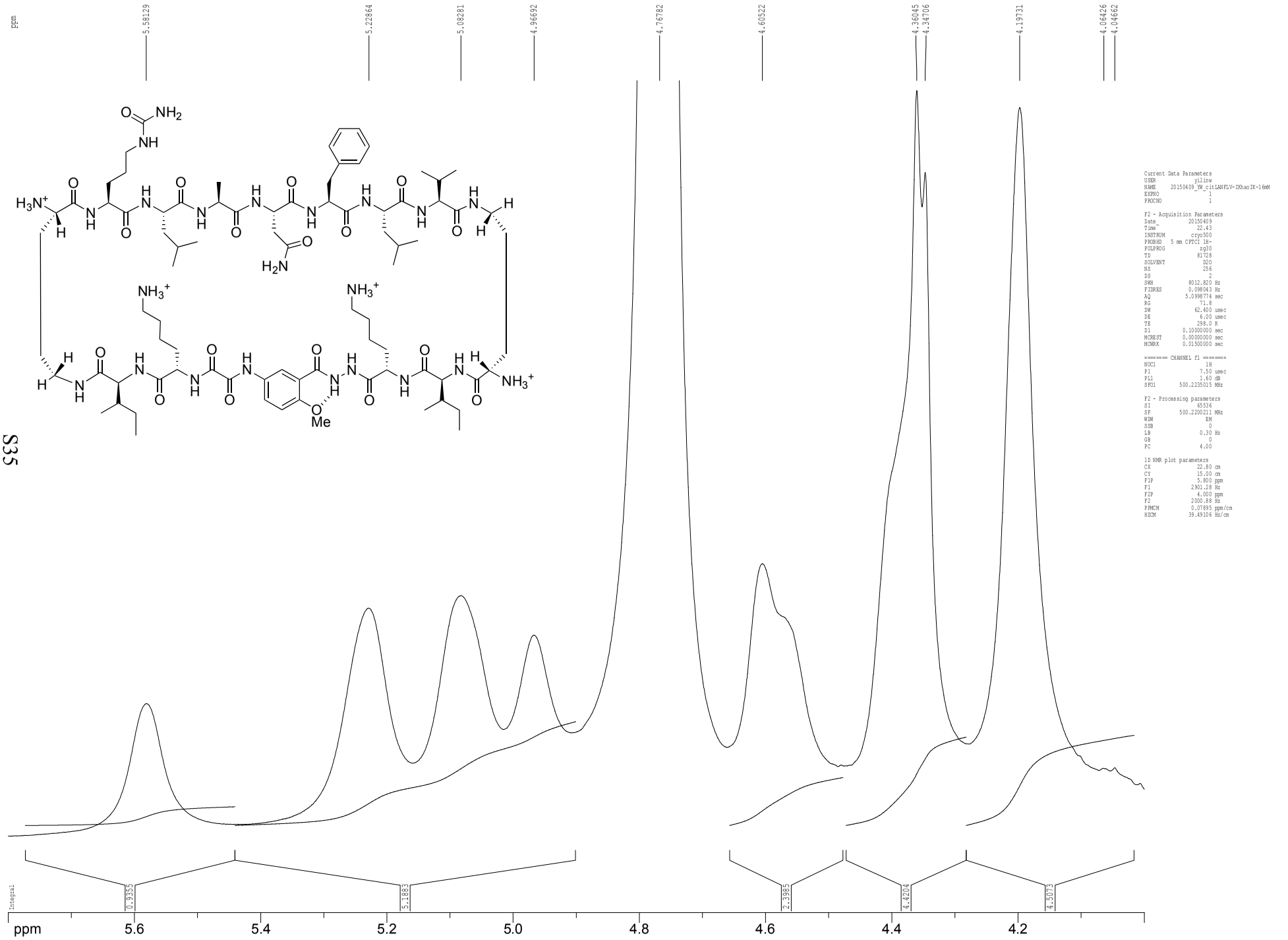
F2 - Acquisition Parameters
Date_ 20150409
Time 22.43
INSTRUM cryo500
PROBHD 5 mm CPTCI 1H-
PULPROG zg30
TD 81728
SOLVENT H2O
NS 256
DS 2
SWH 8012.820 Hz
FIDRES 0.098043 Hz
AQ 5.0998774 sec
RG 71.8
DW 62.400 usec
DE 6.00 usec
TE 298.0 K
D1 0.10000000 sec
MCREST 0.00000000 sec
MCWRK 0.01500000 sec

======= CHANNEL f1 =======
NUC1 1H
P1 7.50 usec
PL1 1.60 dB
SFO1 500.2235015 MHz

F2 - Processing parameters
SI 65536
SF 500.2200211 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 4.00

1D NMR plot parameters
CX 22.80 cm
CY 15.00 cm
F1P 7.800 ppm
F1 3901.72 Hz
F2P 6.000 ppm
F2 3001.32 Hz
PPMCM 0.07895 ppm/cm
HZCM 39.49106 Hz/cm

^{1}H NMR of macrocyclic β-sheet peptide **1$_{Cit}$**, 16 mM in 100 mM deuterioacetate buffer in D_2O at 500 MHz and 298 K



Current Data Parameters
USER yilinw
NAME 20150409_YM_citLANFLV-IKOhaoIK-1fnM
EXPNO 1
PROCNO 1

F2 - Acquisition Parameters
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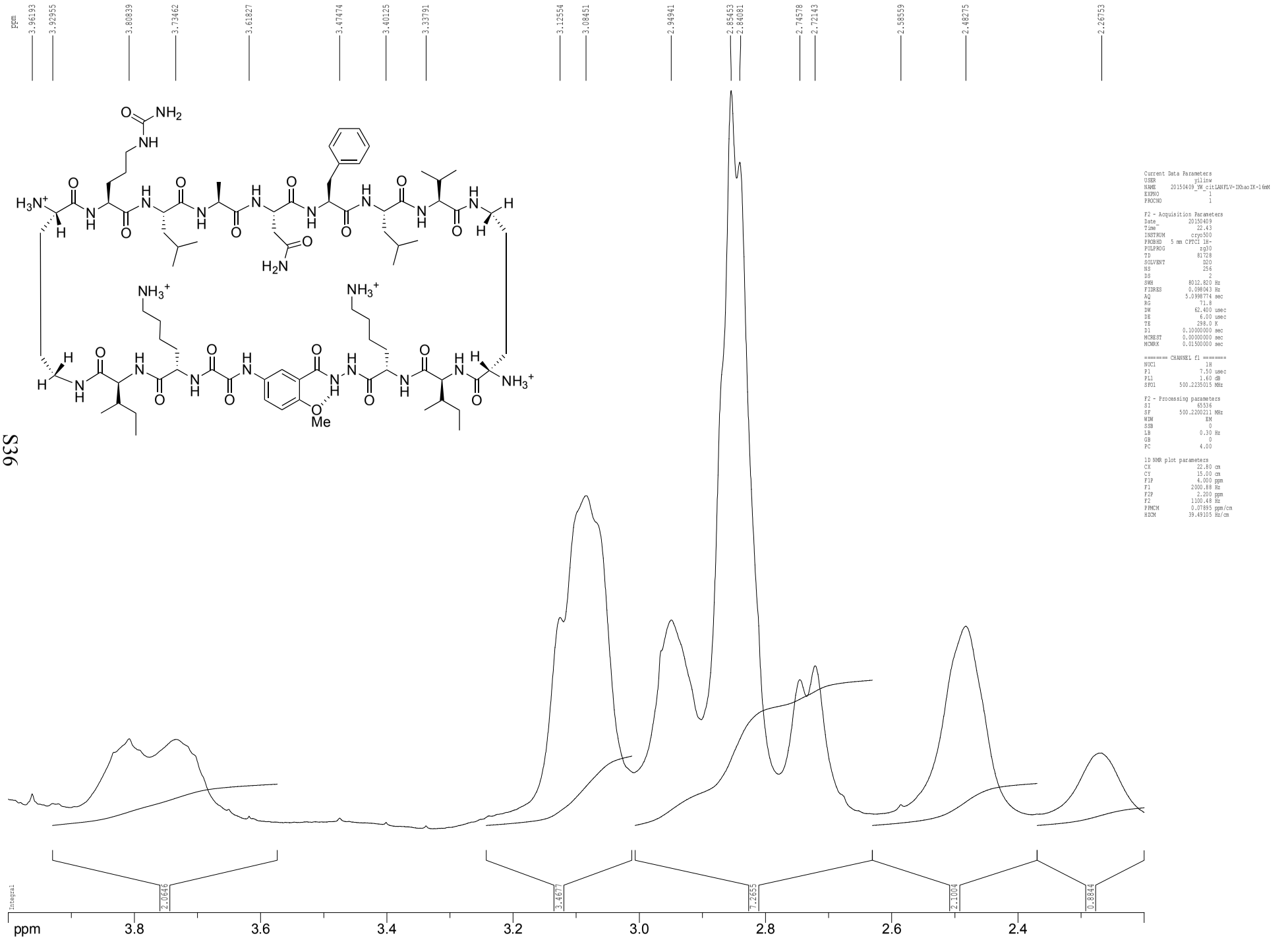
PROBHD 5 mm CPTCI 1H-
PULPROG zg30
TD 81728
SOLVENT H2O
NS 256
DS 2
SWH 8012.820 Hz
FIDRES 0.098043 Hz
AQ 5.0998774 sec
RG 71.8
DW 62.400 usec
DE 6.00 usec
TE 298.0 K
D1 0.10000000 sec
MCREST 0.00000000 sec
MCWRK 0.01500000 sec

====== CHANNEL f1 ======
NUC1 1H
P1 7.50 usec
PL1 1.60 dB
SFO1 500.2235015 MHz

F2 - Processing parameters
SI 65536
SF 500.2200211 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 4.00

1D NMR plot parameters
CX 22.80 cm
CY 15.00 cm
F1P 5.800 ppm
F1 2901.28 Hz
F2P 4.000 ppm
F2 2000.88 Hz
PPMCM 0.07895 ppm/cm
HZCM 39.49106 Hz/cm

^{1}H NMR of macrocyclic β-sheet peptide **$\mathbf{1}_{Cit}$**, 16 mM in 100 mM deuterioacetate buffer in D_2O at 500 MHz and 298 K



Current Data Parameters
USER yilinw
NAME 20150409_YM_citLANFLV-1KOhaoIK-1fnM
EXPNO 1
PROCNO 1

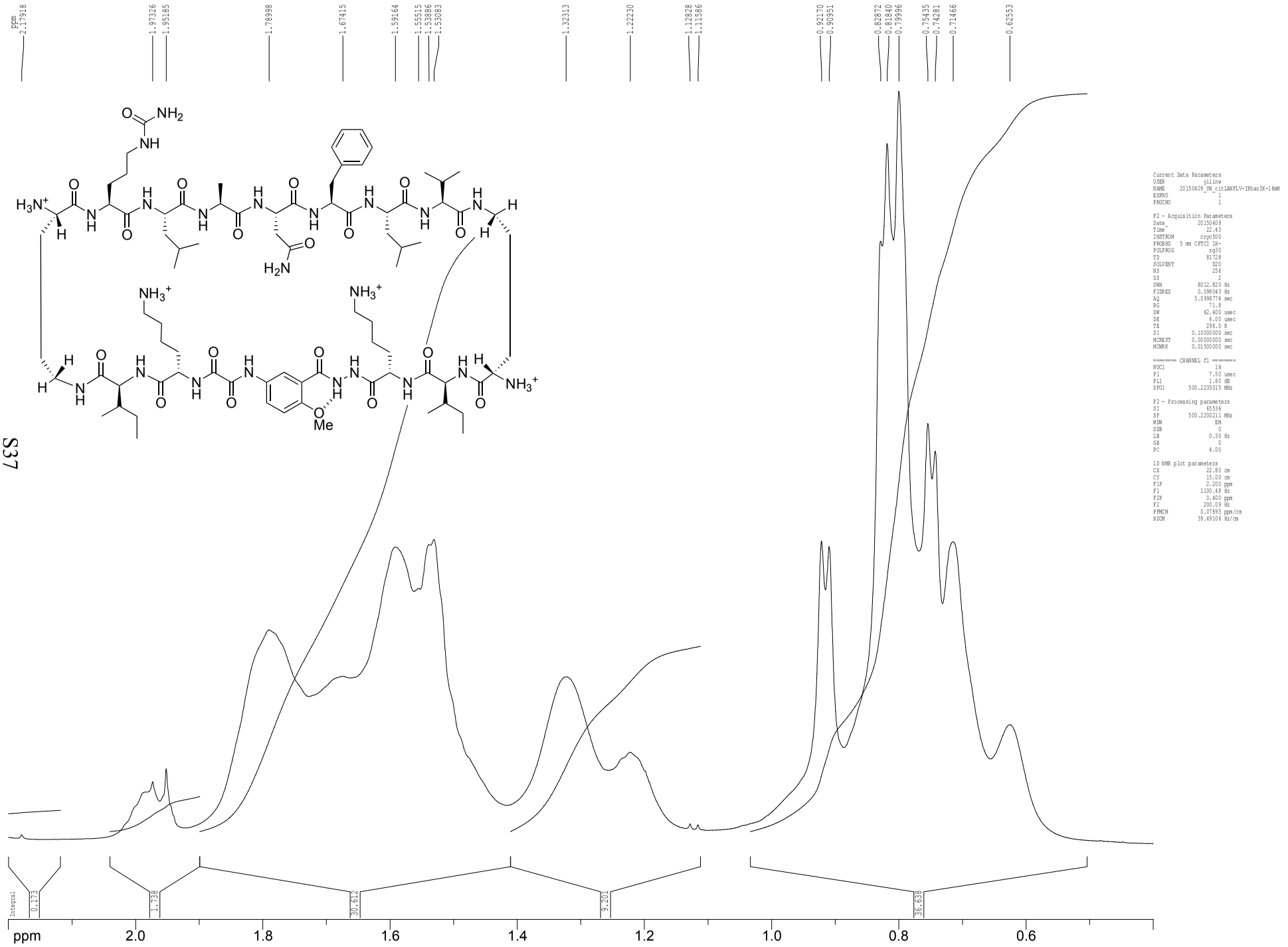
F2 - Acquisition Parameters
Date_ 20150409
Time 22.43
INSTRUM cryo500
PROBHD 5 mm CPTCI 1H-
PULPROG zg30
TD 81728
SOLVENT H2O
NS 256
DS 2
SWH 8012.820 Hz
FIDRES 0.098043 Hz
AQ 5.0998774 sec
RG 71.8
DW 62.400 usec
DE 6.00 usec
TE 298.0 K
D1 0.10000000 sec
MCREST 0.00000000 sec
MCWRK 0.01500000 sec

======== CHANNEL f1 ========
NUC1 1H
P1 7.50 usec
PL1 1.60 dB
SFO1 500.2235015 MHz

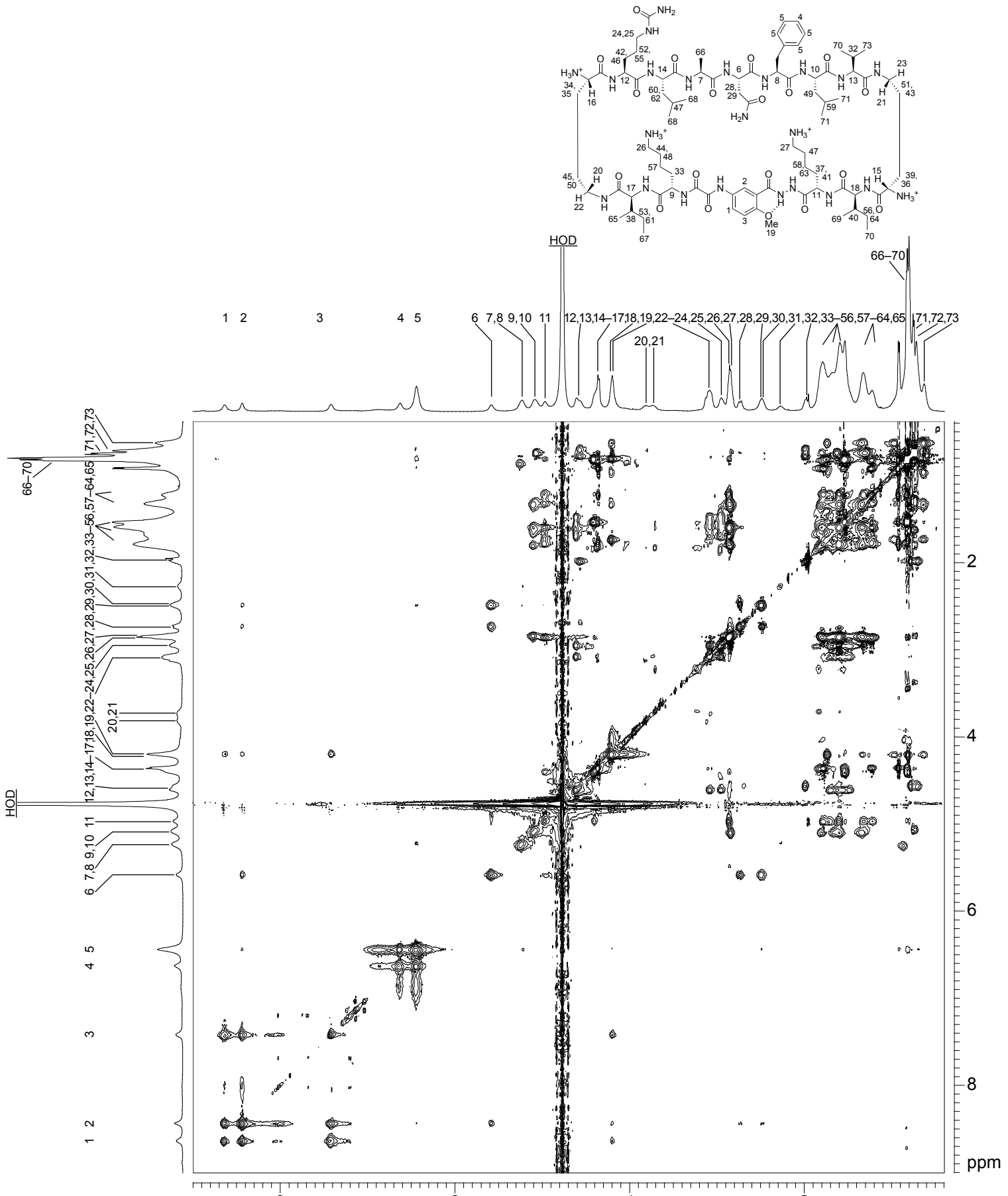
F2 - Processing parameters
SI 65536
SF 500.2200211 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 4.00

1D NMR plot parameters
CX 22.80 cm
CY 15.00 cm
F1P 4.000 ppm
F1 2000.88 Hz
F2P 2.200 ppm
F2 1100.48 Hz
PPMCM 0.07895 ppm/cm
HZCM 39.49105 Hz/cm

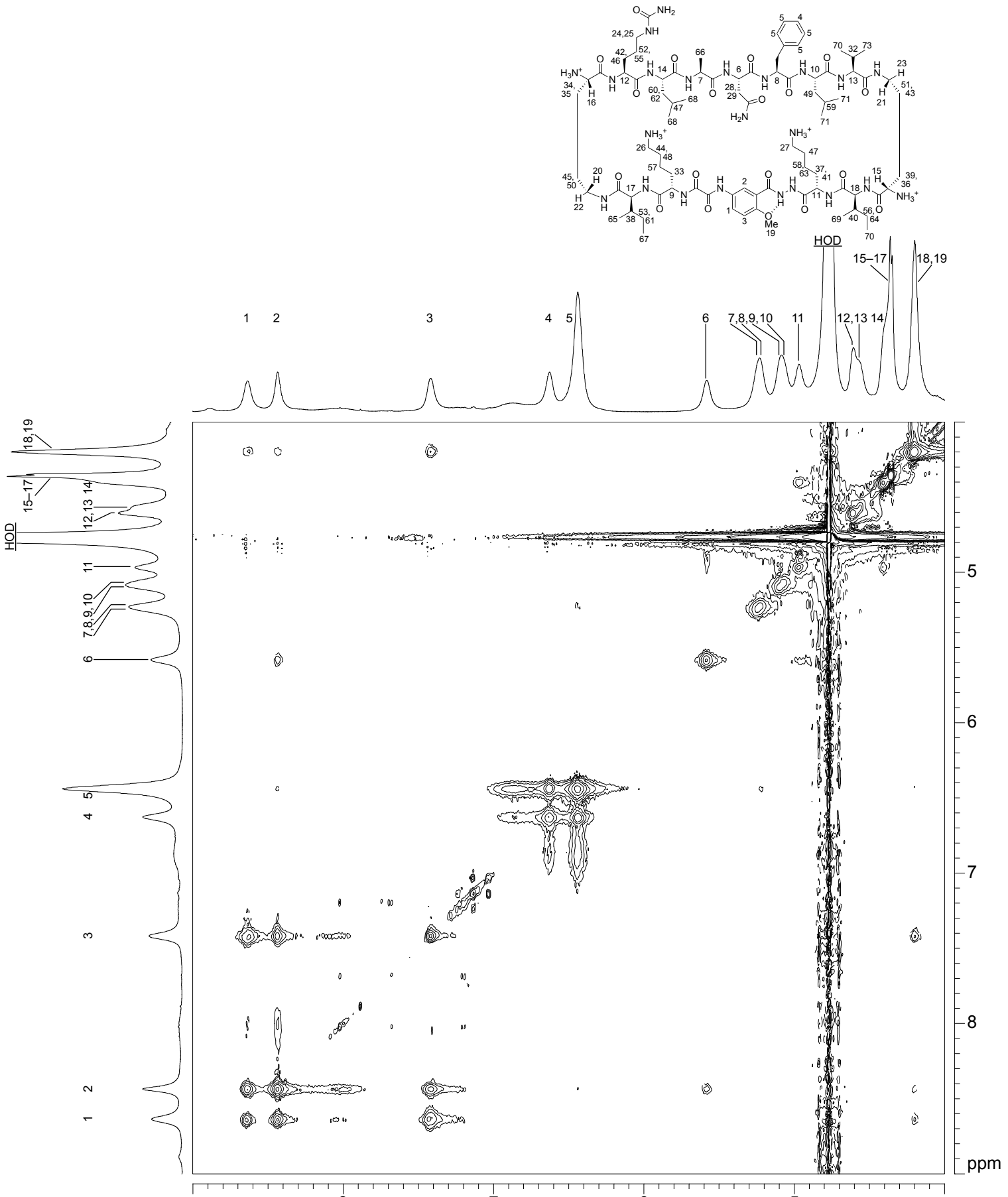
^{1}H NMR of macrocyclic β-sheet peptide **1_{Cit}**, 16 mM in 100 mM deuterioacetate buffer in D_2O at 500 MHz and 298 K



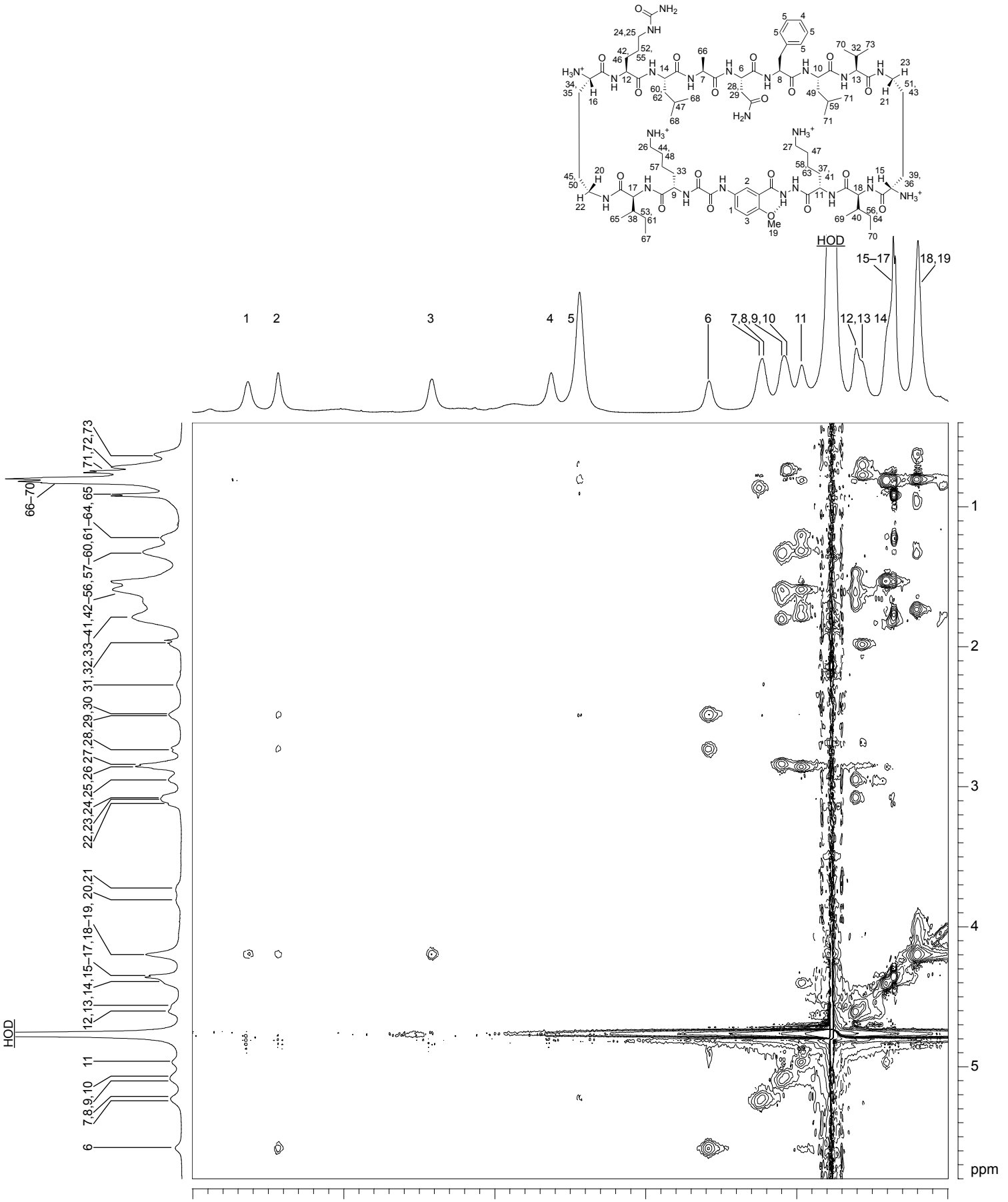
^{1}H NMR 2D TOCSY of macrocyclic β-sheet peptide **1$_{Cit}$** with 150-ms spin-lock mixing time
16 mM in 100 mM deuterioacetate buffer in D_2O at 500 MHz and 298 K



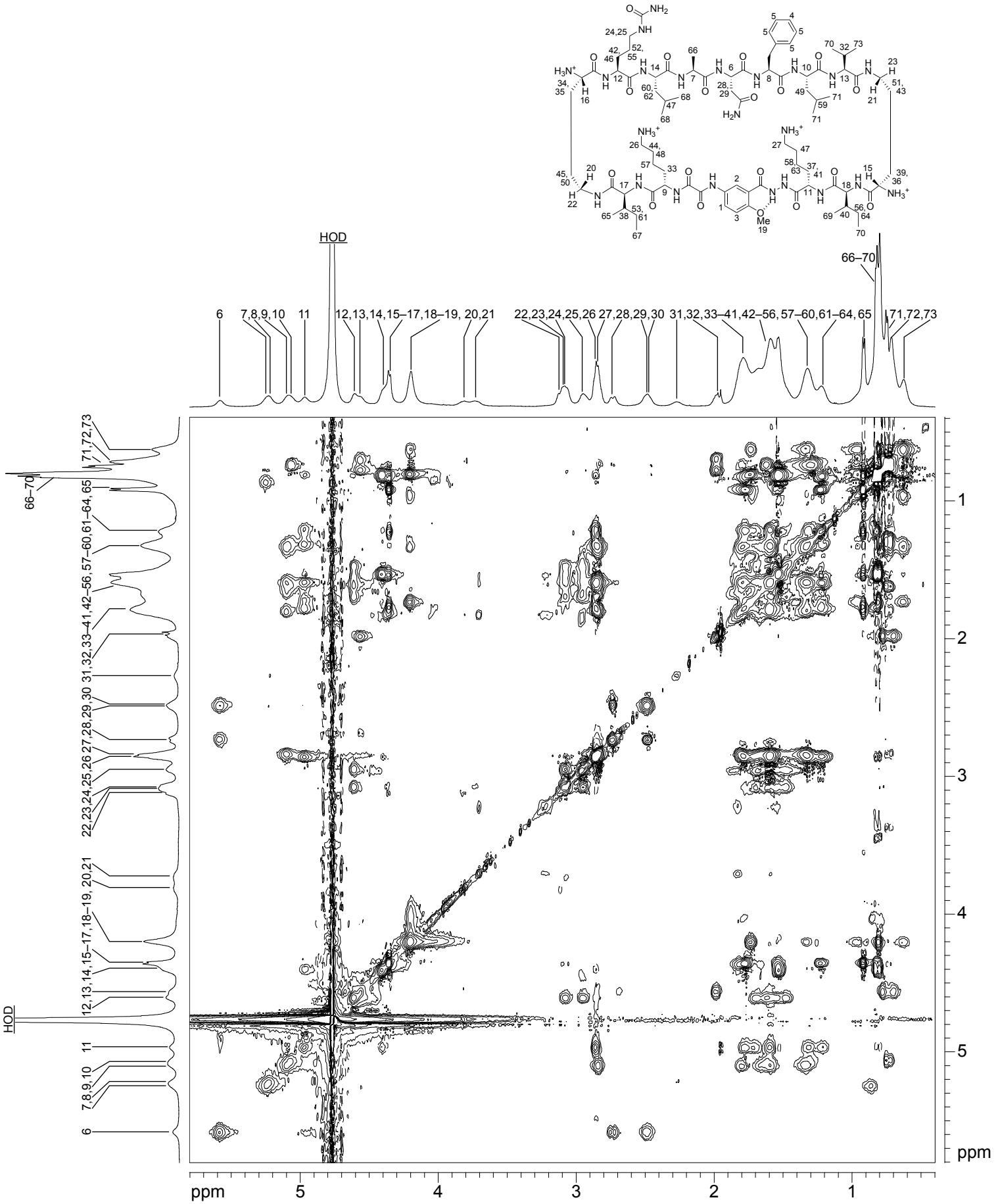
^{1}H NMR 2D TOCSY of macrocyclic β-sheet peptide **1$_{Cit}$** with 150-ms spin-lock mixing time
16 mM in 100 mM deuterioacetate buffer in D_2O at 500 MHz and 298 K



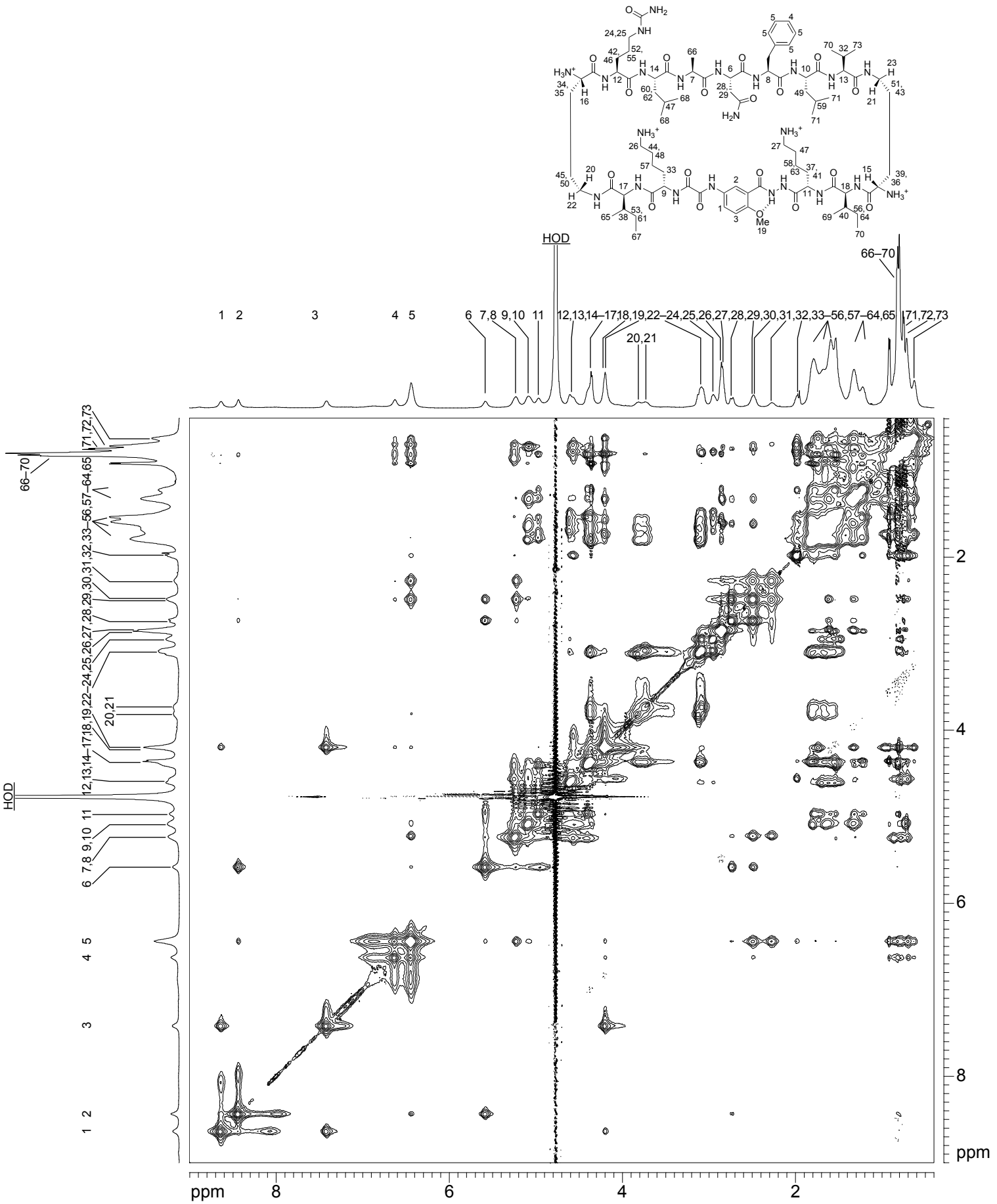
^{1}H NMR 2D TOCSY of macrocyclic β-sheet peptide **1$_{Cit}$** with 150-ms spin-lock mixing time
16 mM in 100 mM deuterioacetate buffer in D_2O at 500 MHz and 298 K



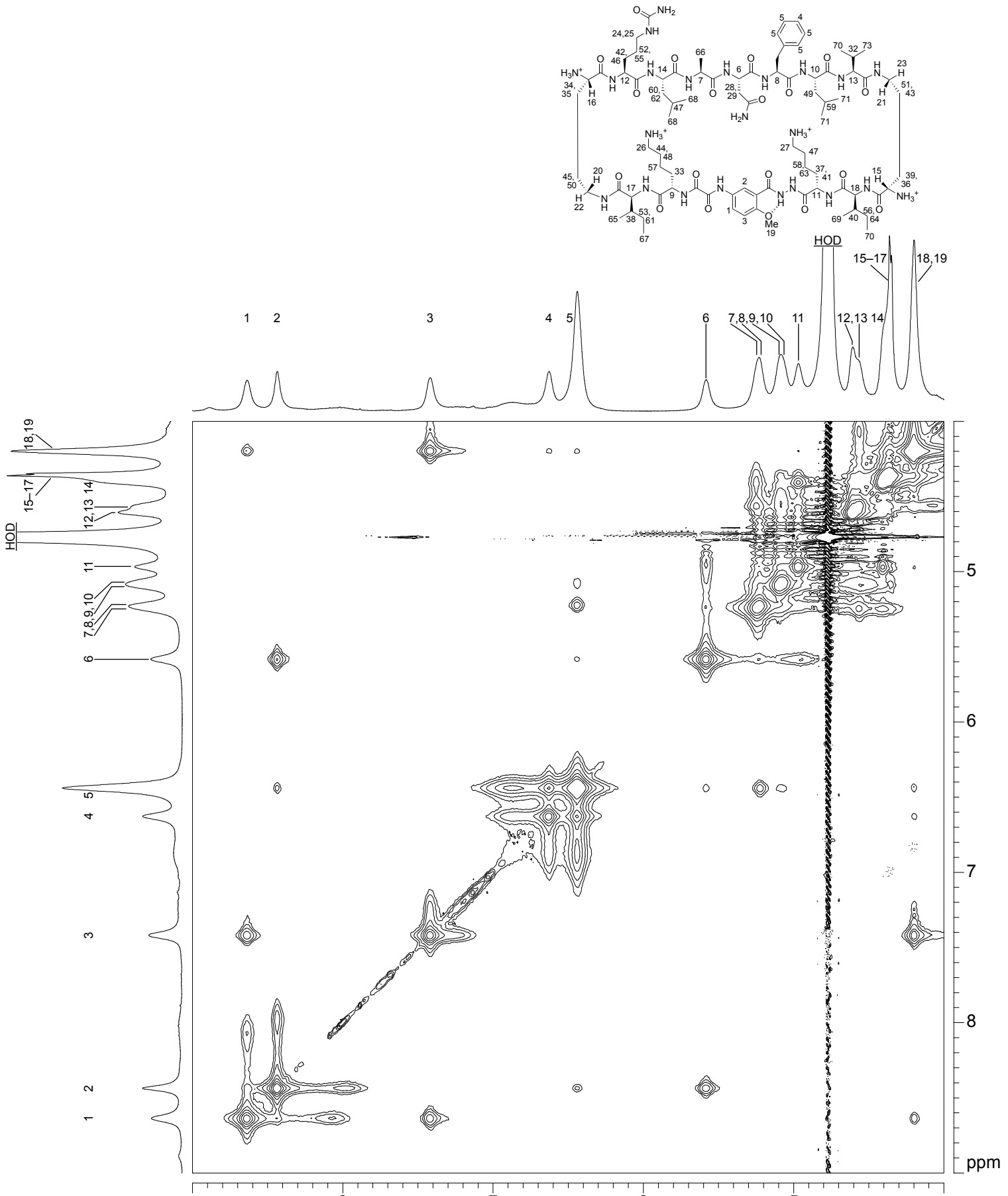
^{1}H NMR 2D TOCSY of macrocyclic β-sheet peptide **1$_{Cit}$**
16 mM in D_2O at 500 MHz and 298 K with 150-ms spin-lock mixing time



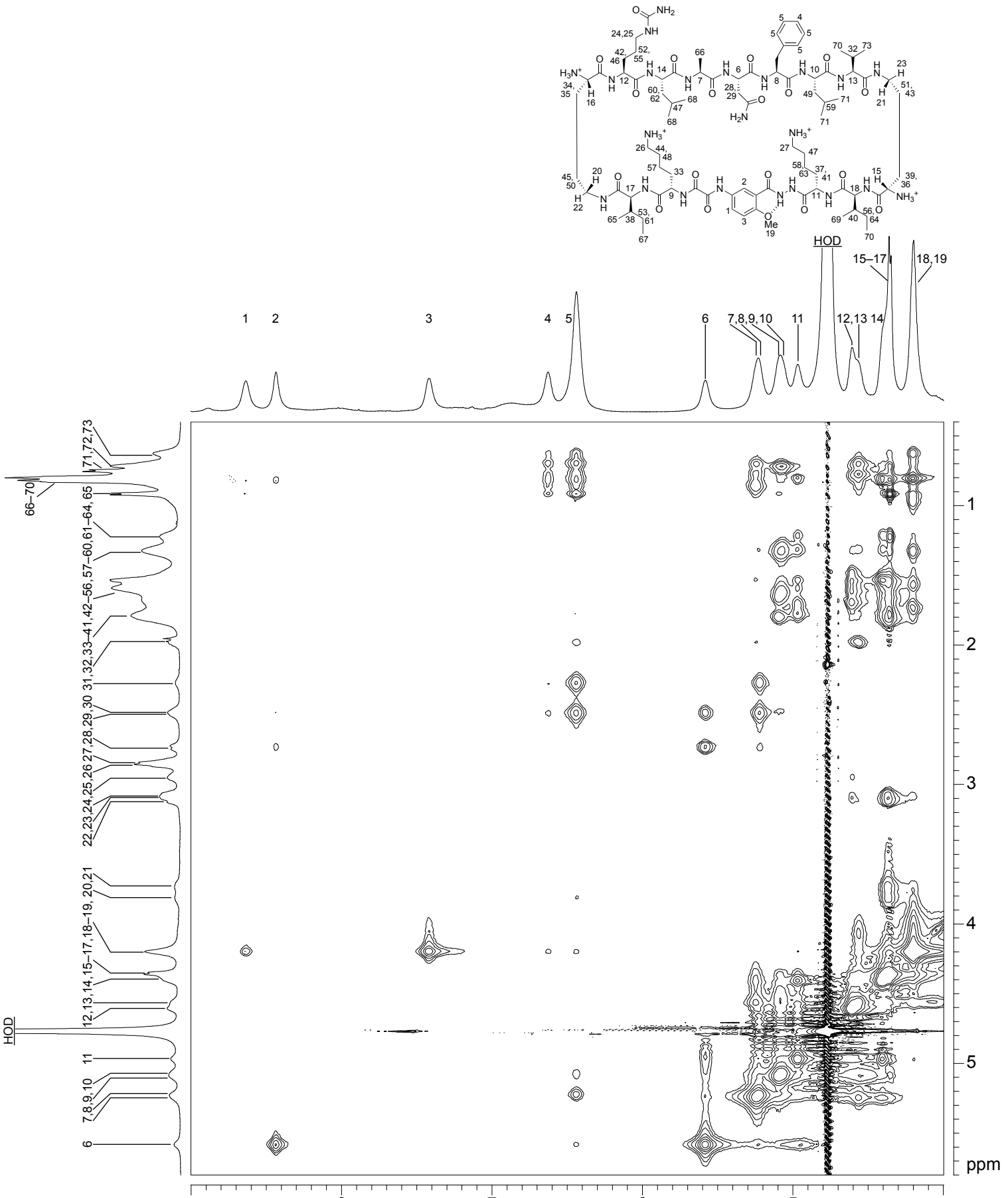
^{1}H NMR 2D NOESY of macrocyclic β-sheet peptide **$\mathbf{1}_{Cit}$** with 150-ms mixing time
16 mM in 100 mM deuterioacetate buffer in D_2O at 500 MHz and 298 K



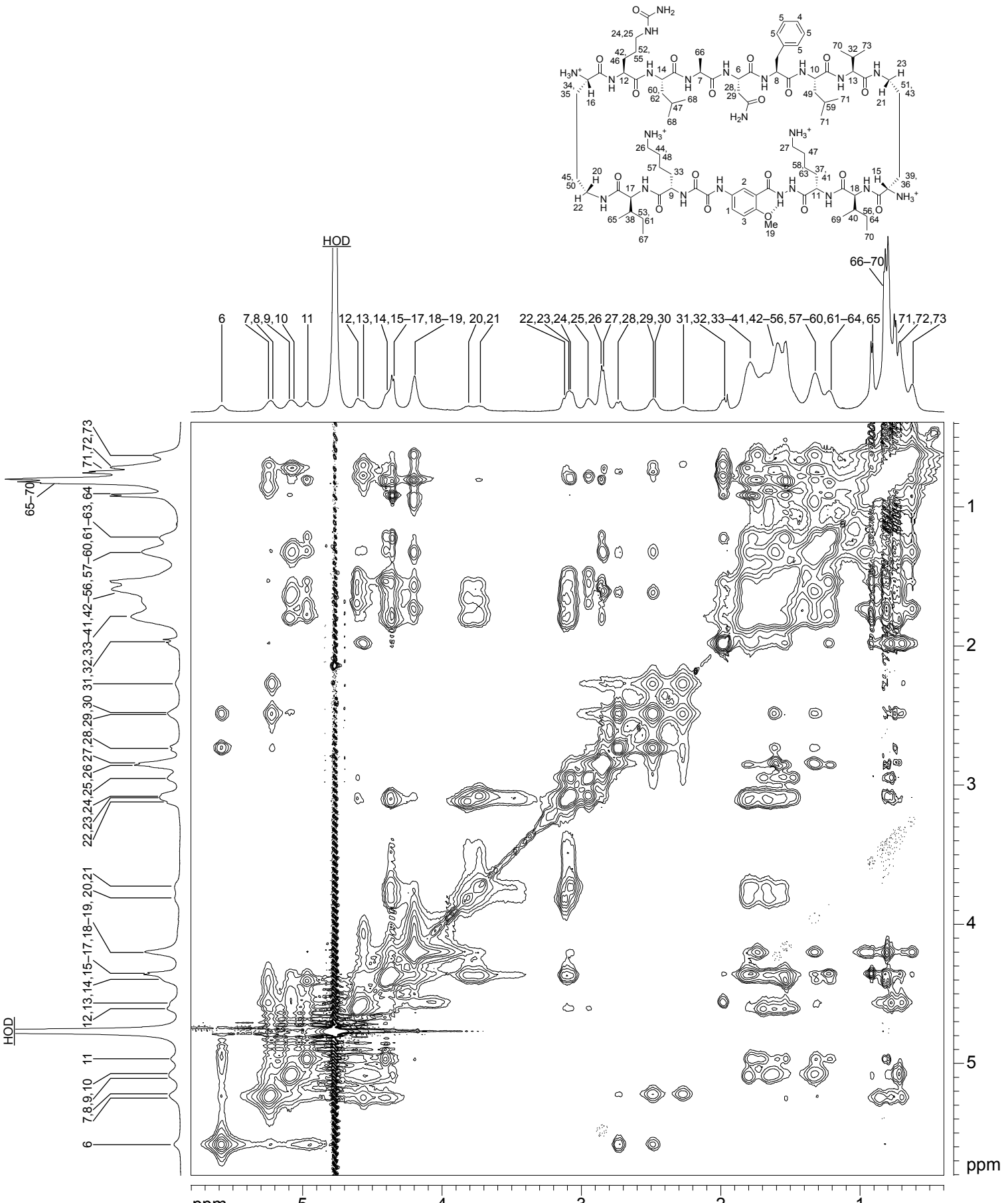
^{1}H NMR 2D NOESY of macrocyclic β-sheet peptide **$\mathbf{1}_{\mathbf{Cit}}$** with 150-ms mixing time
16 mM in 100 mM deuterioacetate buffer in D_2O at 500 MHz and 298 K



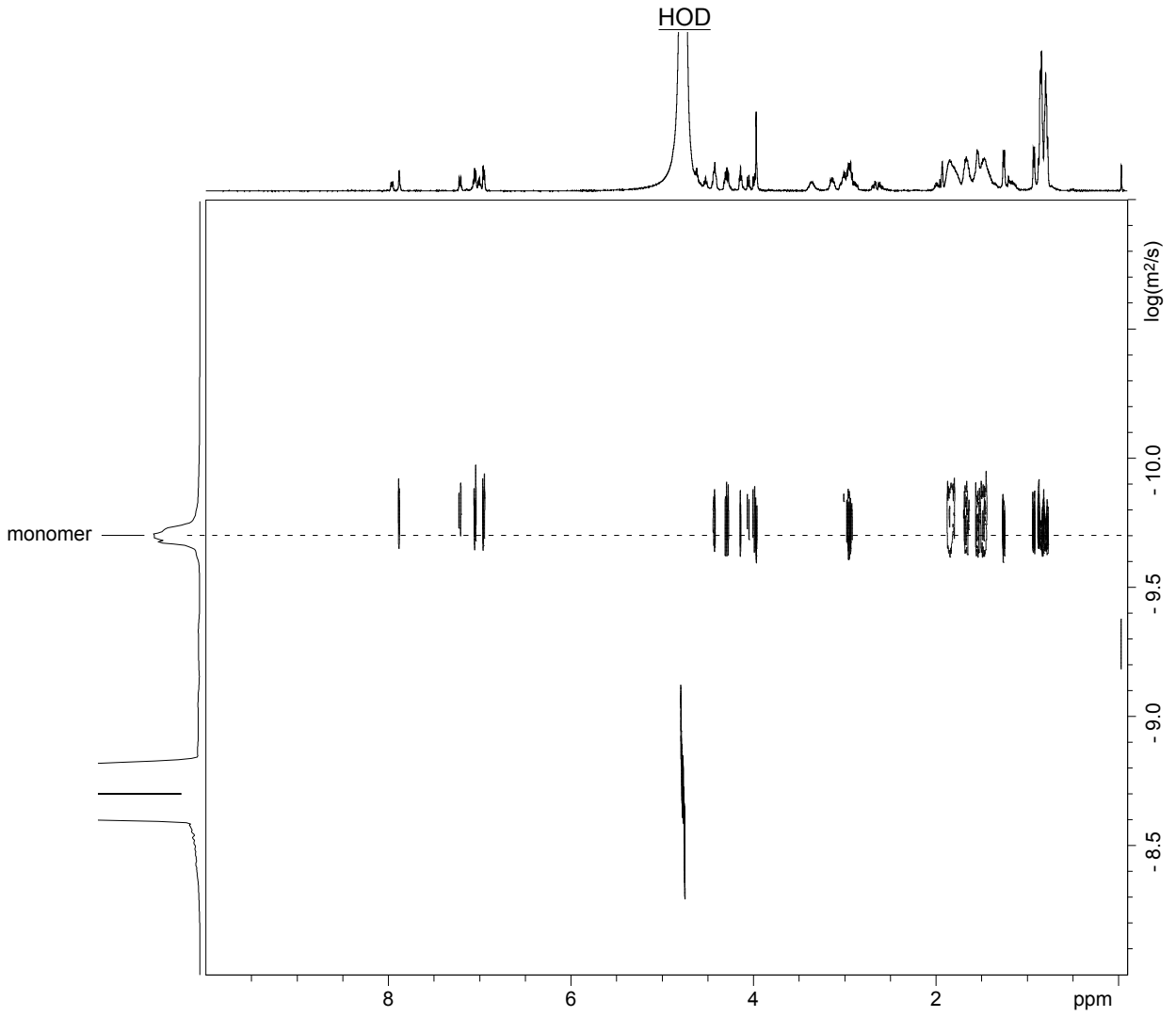
^{1}H NMR 2D NOESY of macrocyclic β-sheet peptide **1$_{Cit}$** with 150-ms mixing time
16 mM in 100 mM deuterioacetate buffer in D_2O at 500 MHz and 298 K



^{1}H NMR 2D NOESY of macrocyclic β-sheet peptide **$\mathbf{1}_{\mathbf{Cit}}$** with 150-ms mixing time
16 mM in 100 mM deuterioacetate buffer in D_2O at 500 MHz and 298 K



^{1}H NMR DOSY of macrocyclic β-sheet peptide **1$_{Cit}$** at 500 MHz and 298 K
1 mM in 100 mM deuterioacetate buffer in D_2O



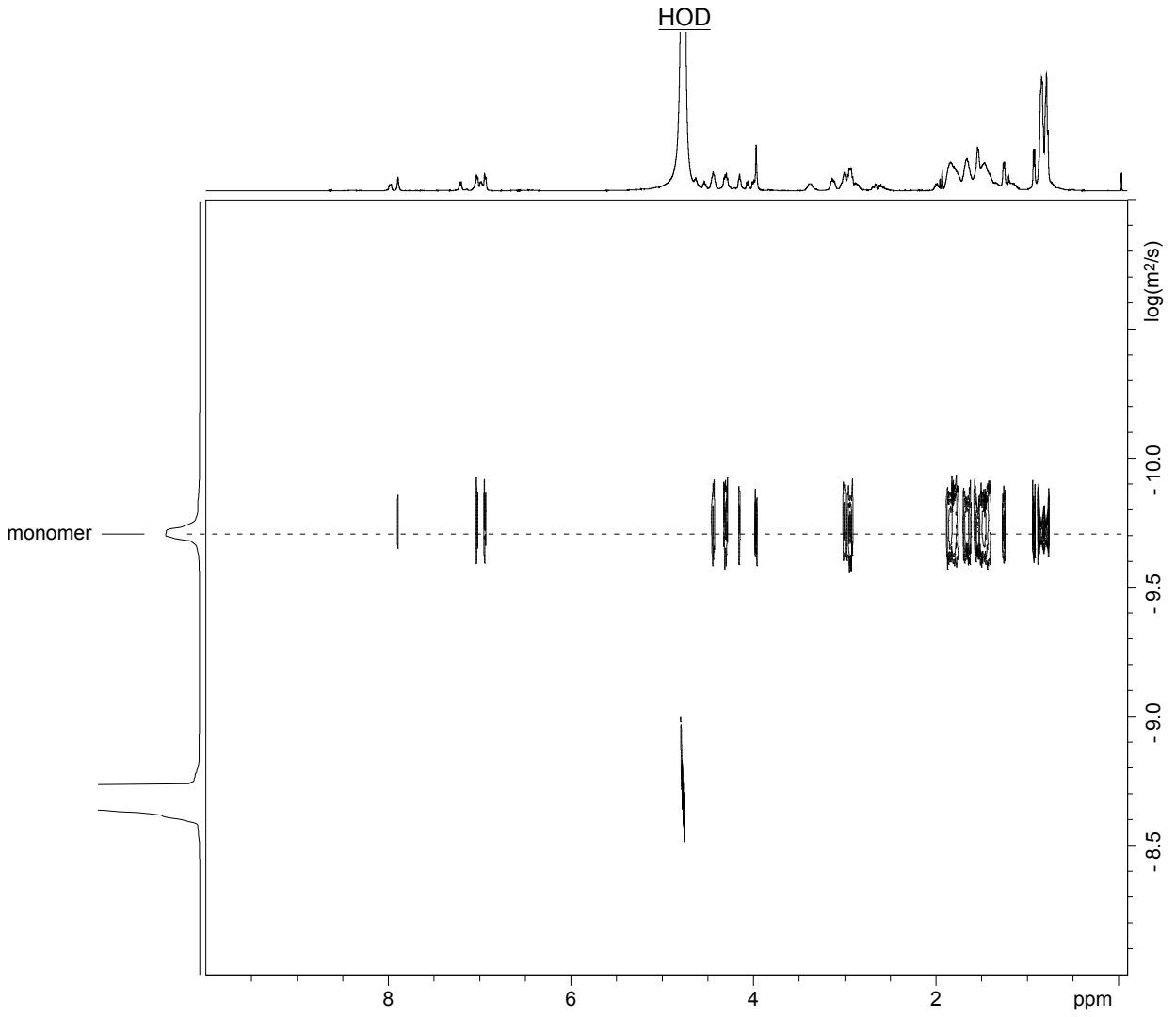
Calculations for macrocyclic β-sheet peptide **1$_{Cit}$** at 1 mM

D_{HOD} = 19.0 x 10^{-10} m^2/s [a]
log (D_{HOD}) = -8.721

$D_{monomer}$: log(D) = -9.700; D = $10^{-9.700}$ = 20.0 ± 2.0 x 10^{-11} m^2/s

[a]Longsworth, L. G. *J. Phys. Chem.* **1960**, *64*, 1914−1917.

^{1}H NMR DOSY of macrocyclic β-sheet peptide **1$_{Cit}$** at 500 MHz and 298 K
2 mM in 100 mM deuterioacetate buffer in D_2O



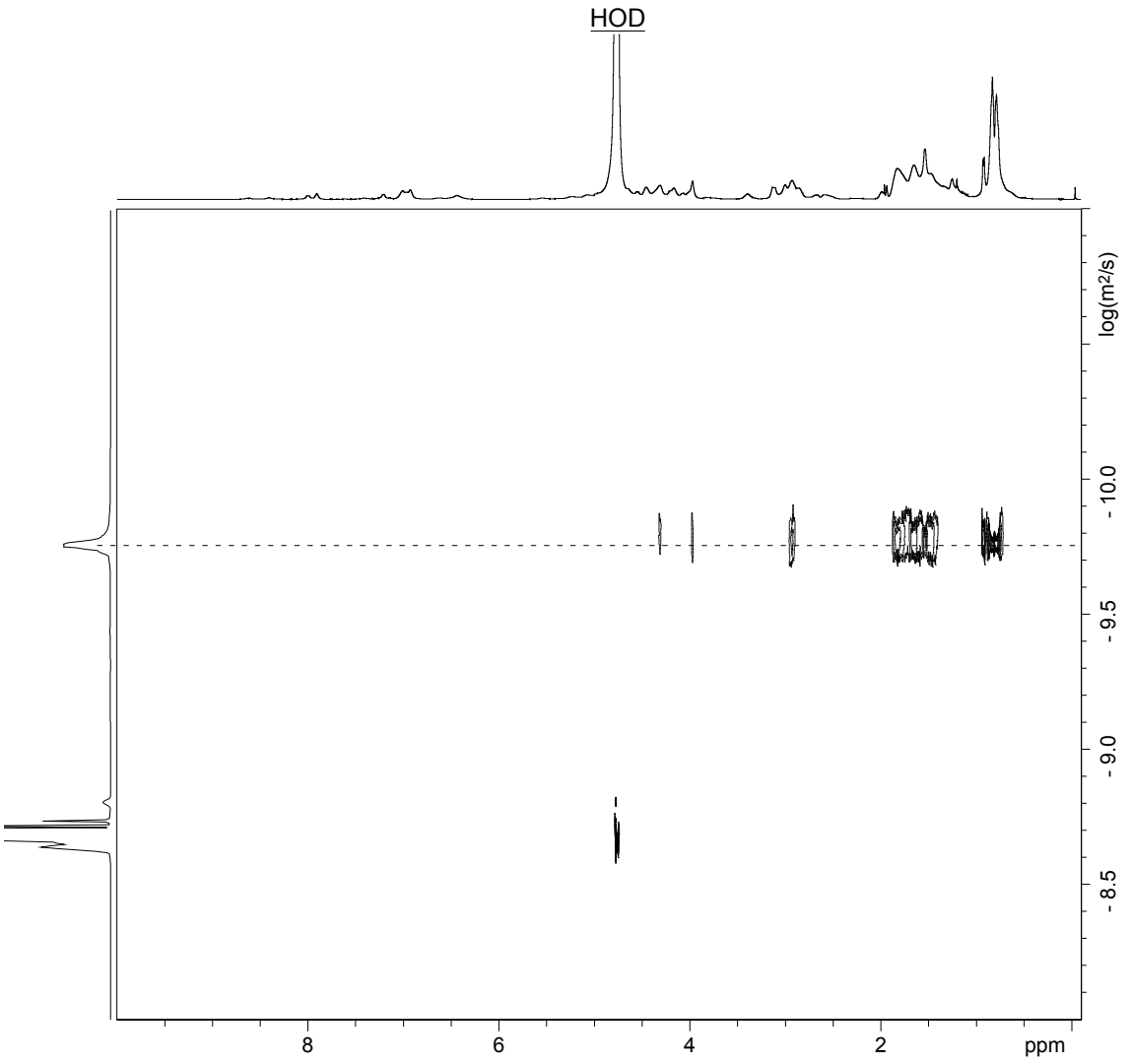
Calculations for macrocyclic β-sheet peptide **1$_{Cit}$** at 2 mM

D_{HOD} = 19.0 x 10^{-10} m^2/s [a]
log (D_{HOD}) = -8.721

$D_{monomer}$: log(D) = -9.723; D = $10^{-9.723}$ = 18.9 ± 1.2 x 10^{-11} m^2/s

[a]Longsworth, L. G. *J. Phys. Chem.* **1960**, *64*, 1914−1917.

^{1}H NMR DOSY of macrocyclic β-sheet peptide **1$_{Cit}$** at 500 MHz and 298 K
4 mM in 100 mM deuterioacetate buffer in D_2O



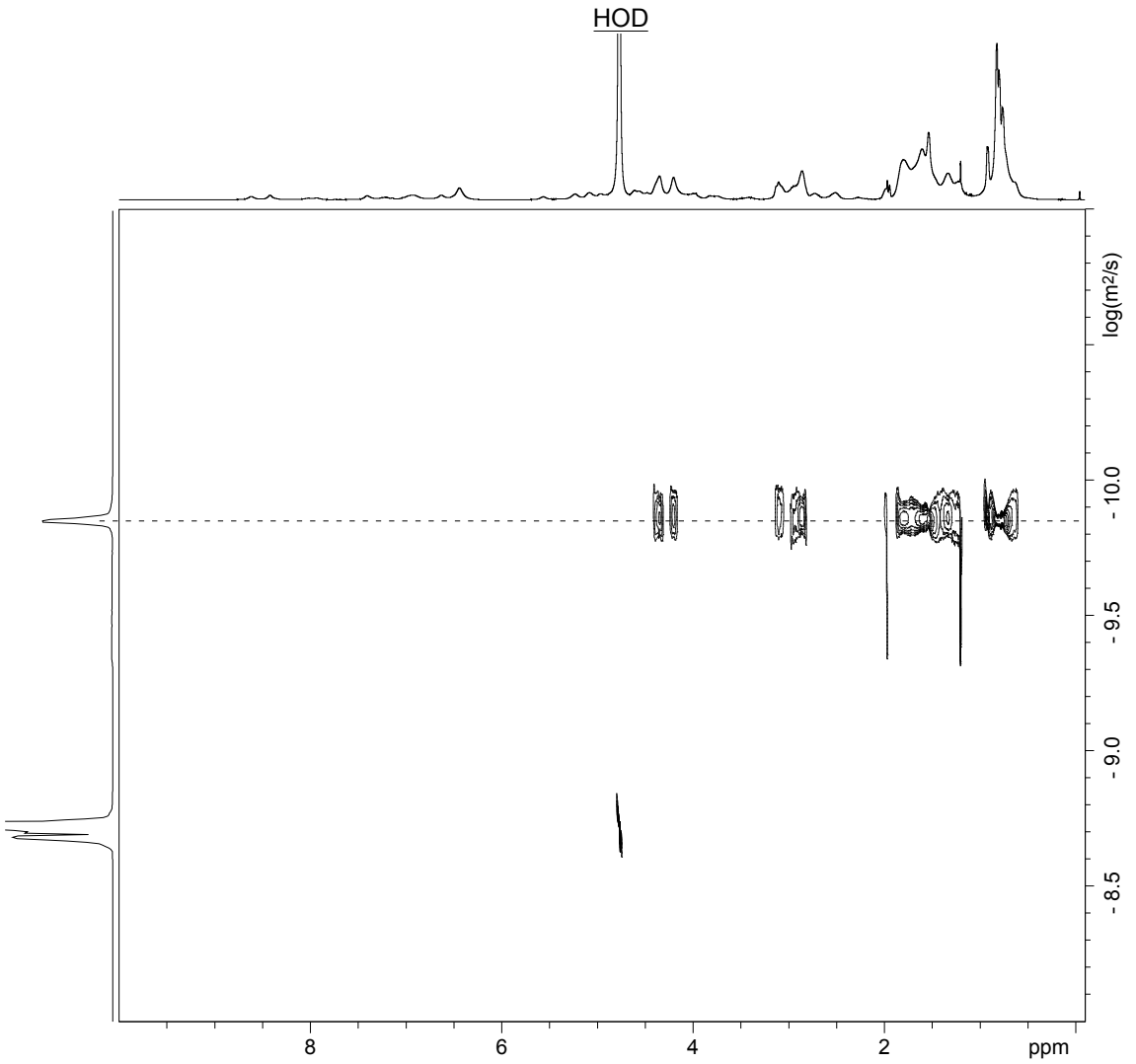
Calculations for macrocyclic β-sheet peptide **1$_{Cit}$** at 4 mM

D_{HOD} = 19.0 x 10^{-10} m^2/s [a]
log (D_{HOD}) = -8.721

$D_{monomer}$: log(D) = -9.759; D = $10^{-9.759}$ = 17.4 ± 1.2 x 10^{-11} m^2/s

[a]Longsworth, L. G. *J. Phys. Chem.* **1960**, *64*, 1914−1917.

^{1}H NMR DOSY of macrocyclic β-sheet peptide **1$_{Cit}$** at 500 MHz and 298 K
8 mM in 100 mM deuterioacetate buffer in D_2O



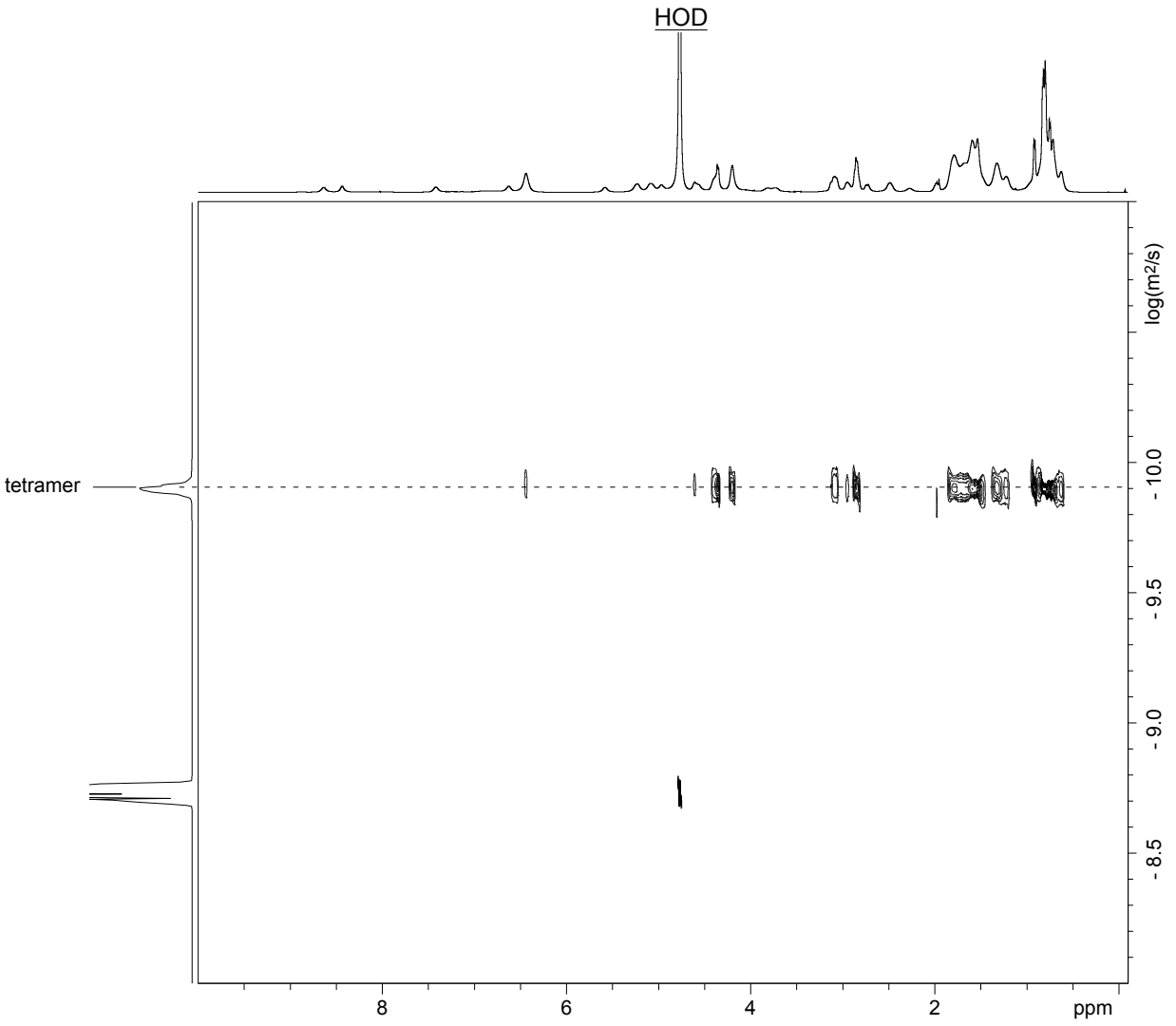
Calculations for macrocyclic β-sheet peptide **1$_{Cit}$** at 8 mM

D_{HOD} = 19.0 x 10^{-10} m^2/s [a]
log (D_{HOD}) = -8.721

$D_{monomer}$: log(D) = -9.849; D = $10^{-9.849}$ = 14.2 ± 0.3 x 10^{-11} m^2/s

[a]Longsworth, L. G. *J. Phys. Chem.* **1960**, *64*, 1914−1917.

^{1}H NMR DOSY of macrocyclic β-sheet peptide **1$_{Cit}$** at 500 MHz and 298 K
16 mM in 100 mM deuterioacetate buffer in D_2O



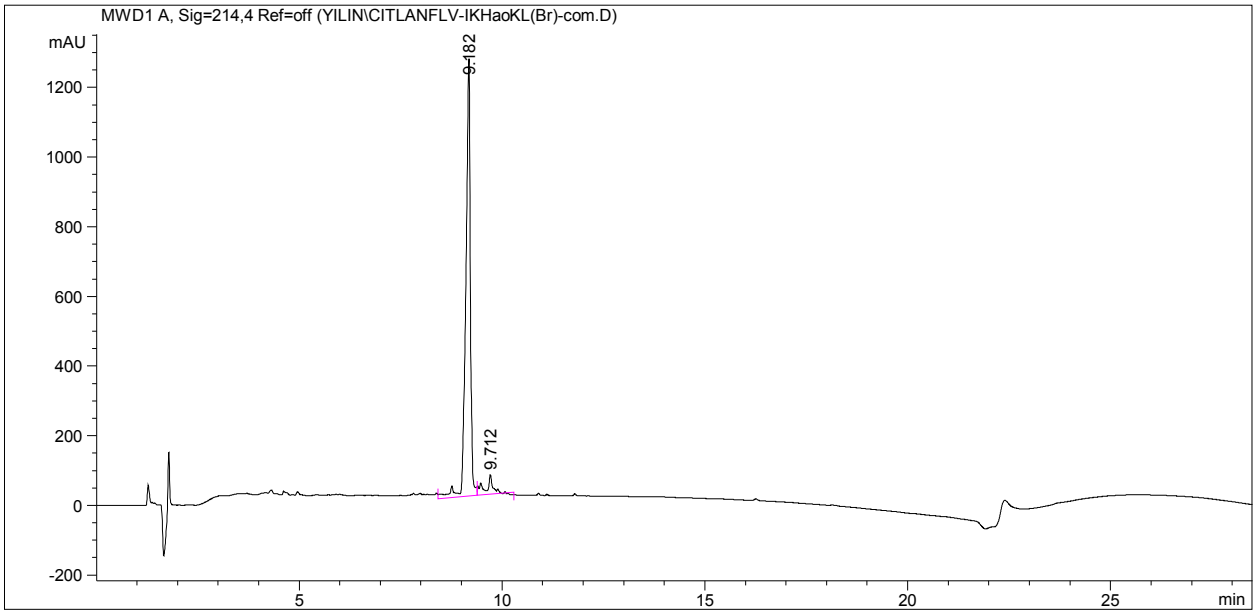
Calculations for macrocyclic β-sheet peptide **1$_{Cit}$** at 16 mM

D_{HOD} = 19.0 x 10^{-10} m^2/s [a]
log (D_{HOD}) = -8.721

$D_{monomer}$: log(D) = -9.905; D = $10^{-9.905}$ = 12.4 ± 0.3 x 10^{-11} m^2/s

[a]Longsworth, L. G. *J. Phys. Chem.* **1960**, *64*, 1914−1917.

RP-HPLC of Macrocyclic β-Sheet **2_{Cit}**



Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
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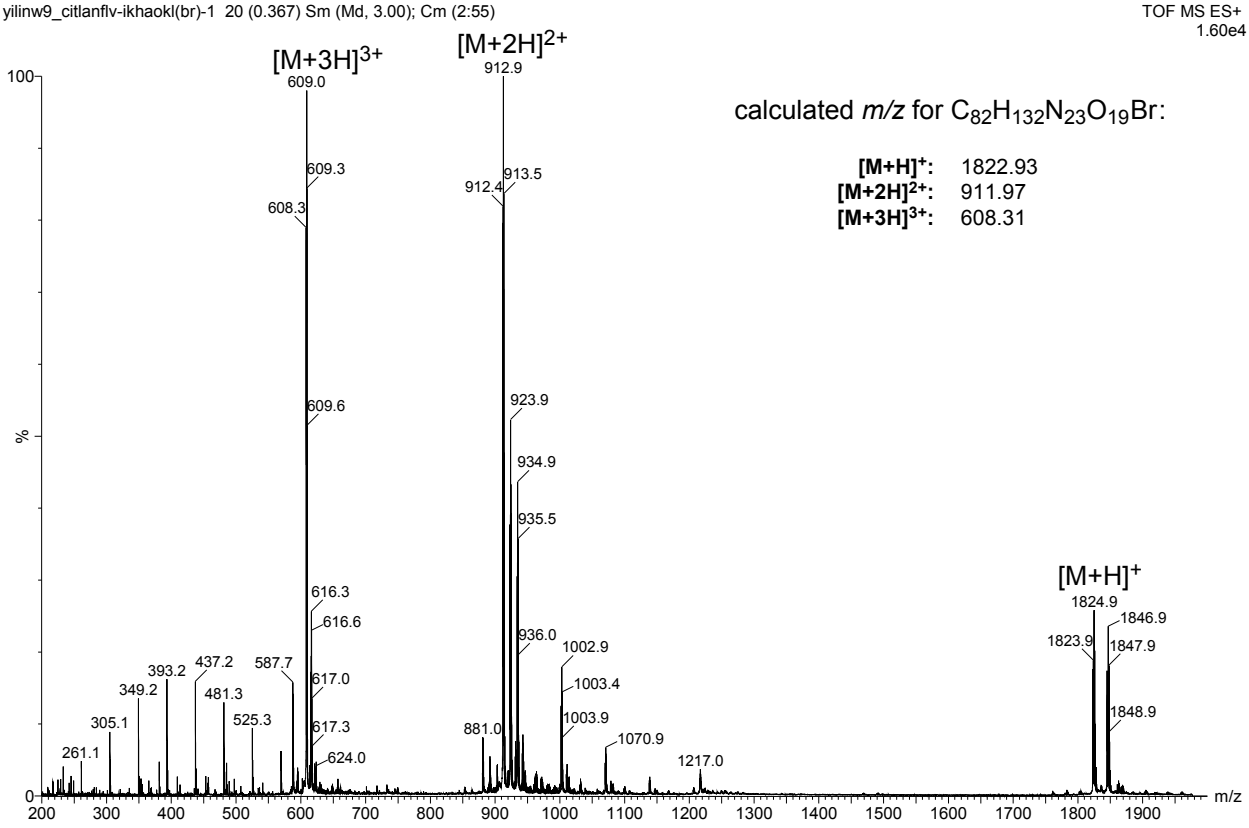
2	9.712	FM	0.1955	664.1050	56.6224	6.3666

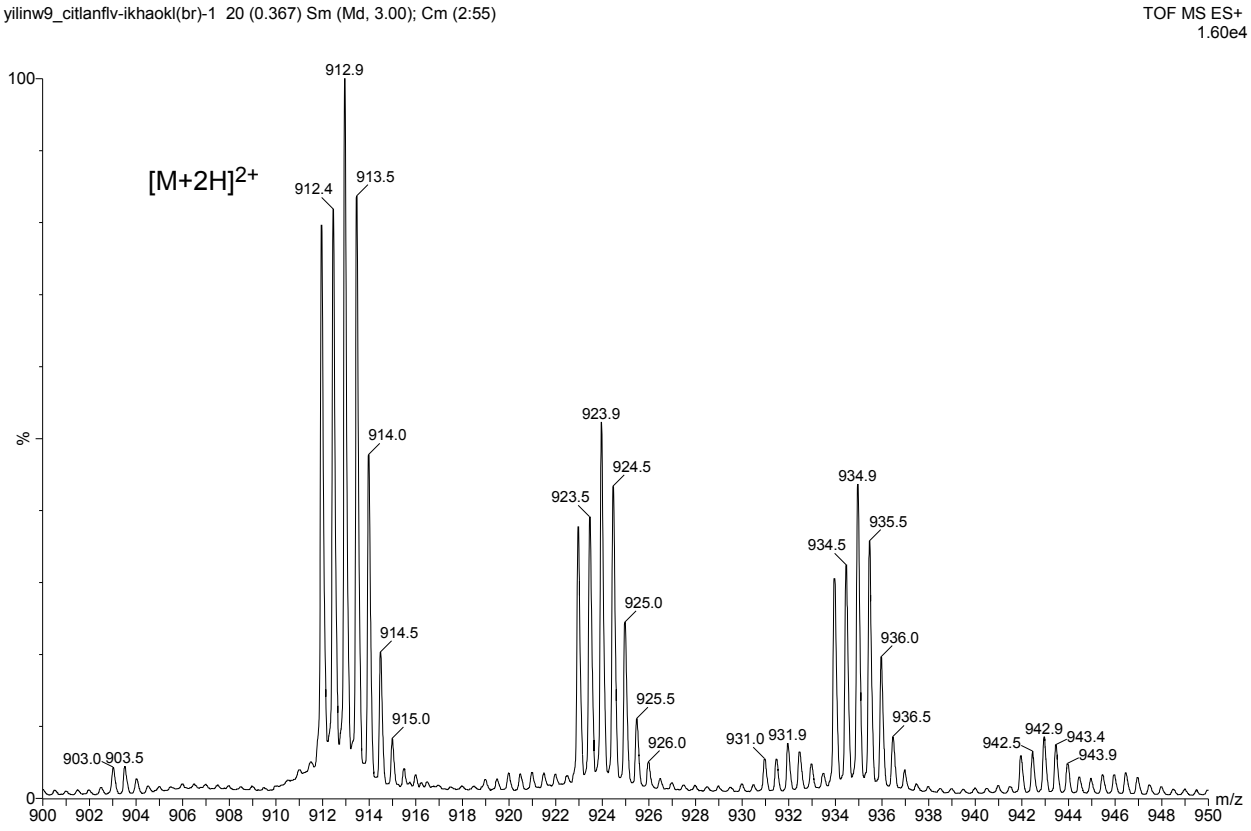
column: Aeris XB-C18 2.6µ
dimensions: 150 mm x 4.6 mm
mobile phase: A: H_2O, 0.1% TFA
B: CH_3CN, 0.1% TFA
gradient: A/B (95:5) to (0:100) in 20 min
flow rate: 1.0 mL/min
detection: VWD, wavelength = 214 nm
temperature: 298 K

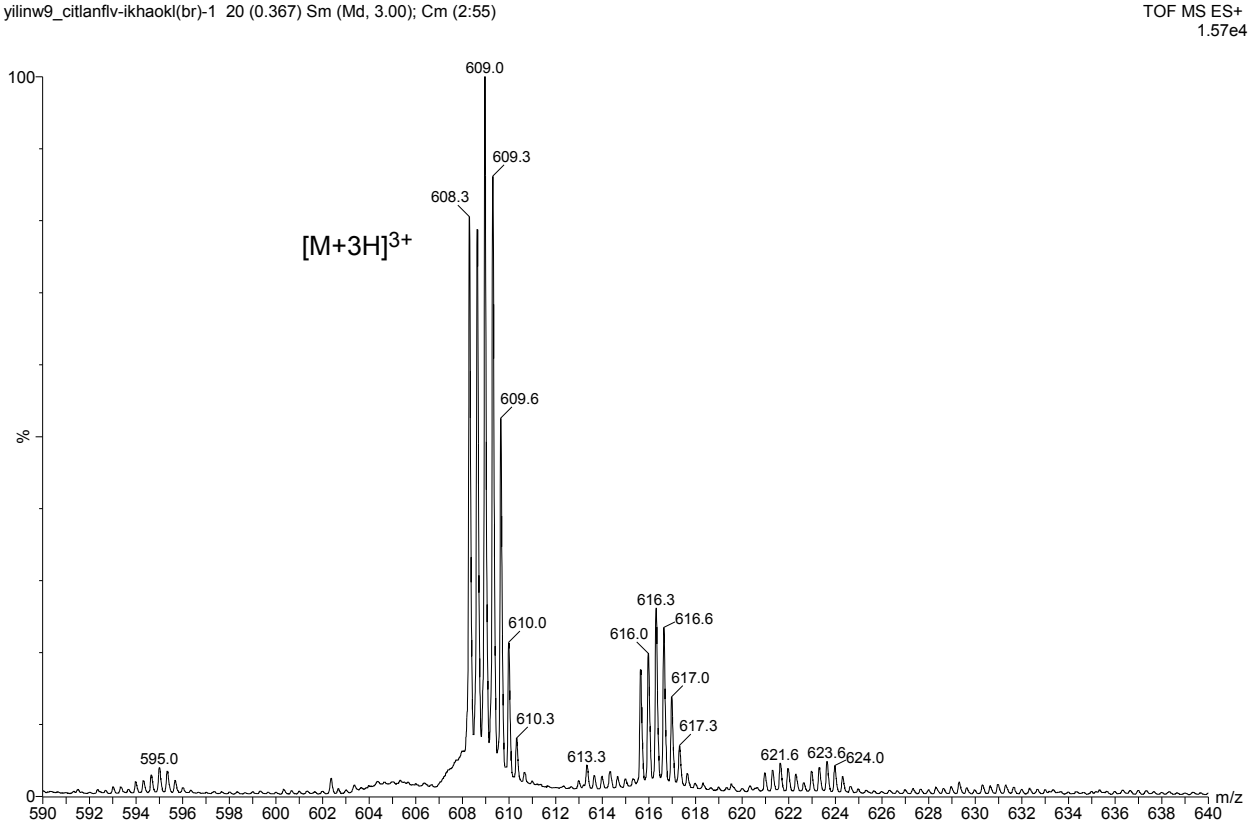
MS (ESI) of Macrocyclic β-Sheet **2_{Cit}**



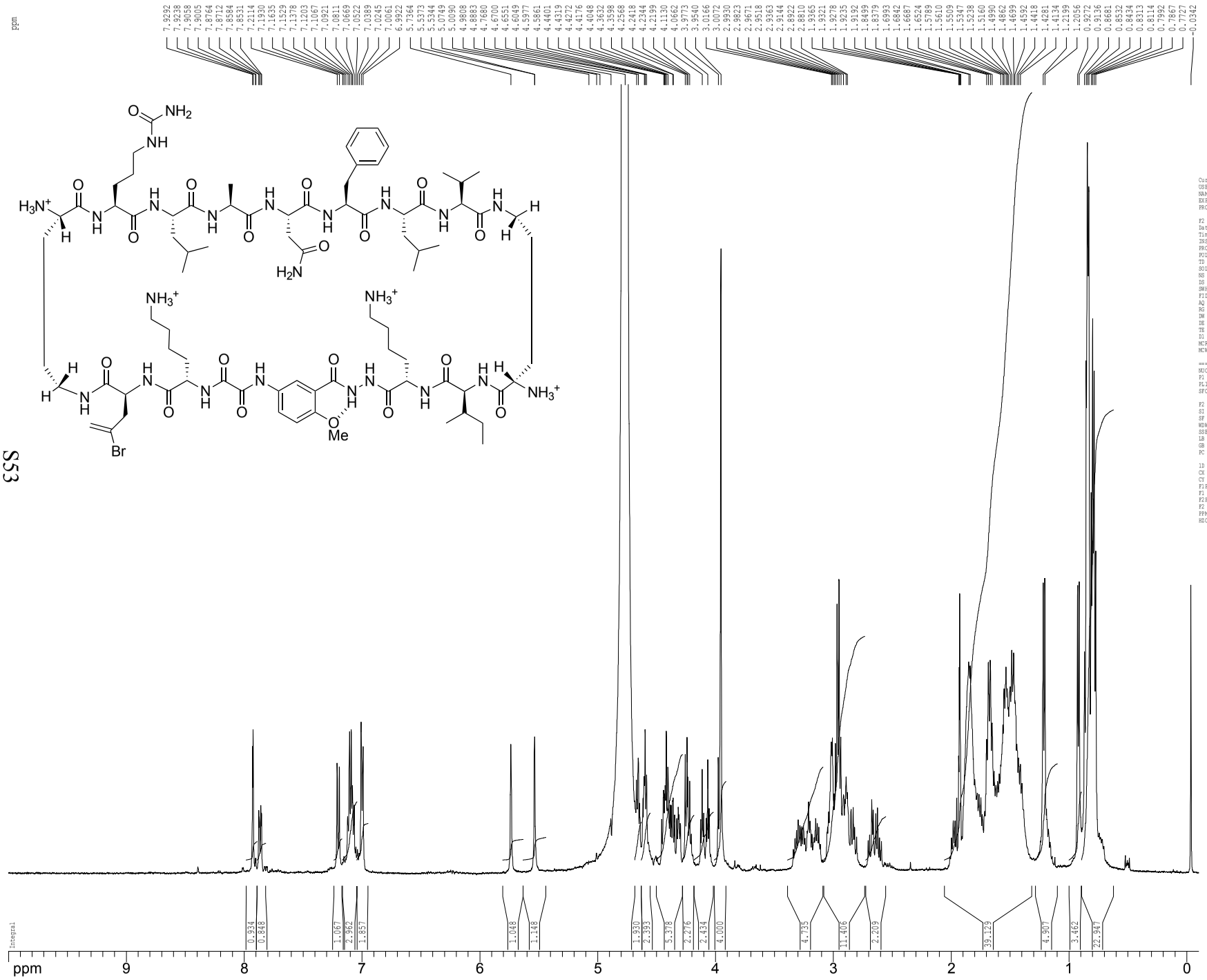
calculated *m/z* for $C_{82}H_{132}N_{23}O_{19}Br$:

$[M+H]^+$: 1822.93
$[M+2H]^{2+}$: 911.97
$[M+3H]^{3+}$: 608.31

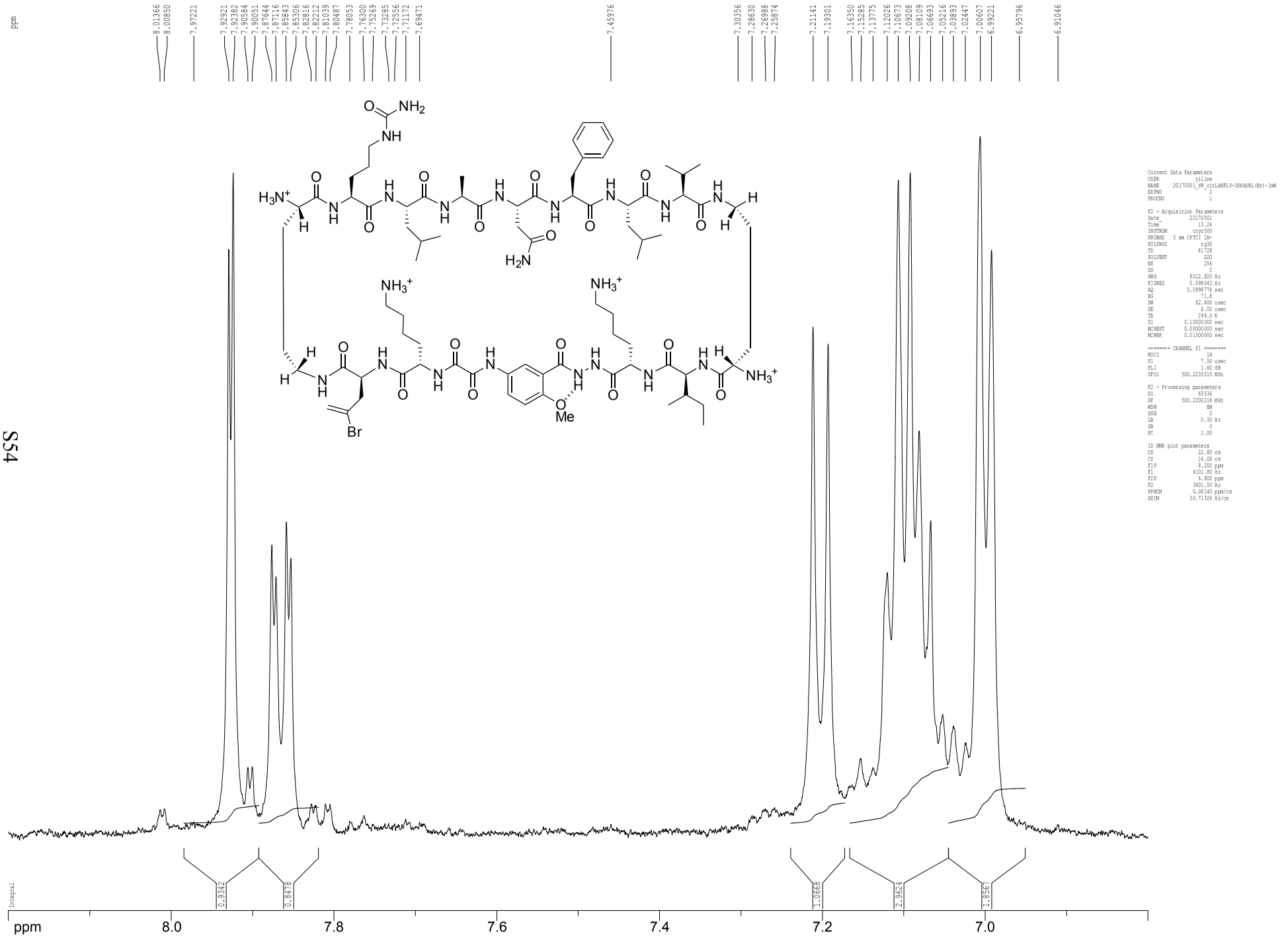

yilinw9_citlanflv-ikhaokl(br)-1 20 (0.367) Sm (Md, 3.00); Cm (2:55)
TOF MS ES+
1.60e4
[M+2H]2+
912.9
912.4
913.5
914.0
914.5
915.0
903.0
903.5
923.9
923.5
924.5
925.0
925.5
926.0
931.0
931.9
934.9
934.5
935.5
936.0
936.5
942.5
942.9
943.4
943.9
%
m/z


yilinw9_citlanflv-ikhaokl(br)-1 20 (0.367) Sm (Md, 3.00); Cm (2:55)
TOF MS ES+
1.57e4
[M+3H]3+
609.0
609.3
608.3
609.6
610.0
610.3
595.0
613.3
616.3
616.6
616.0
617.0
617.3
621.6
623.6
624.0
%
m/z

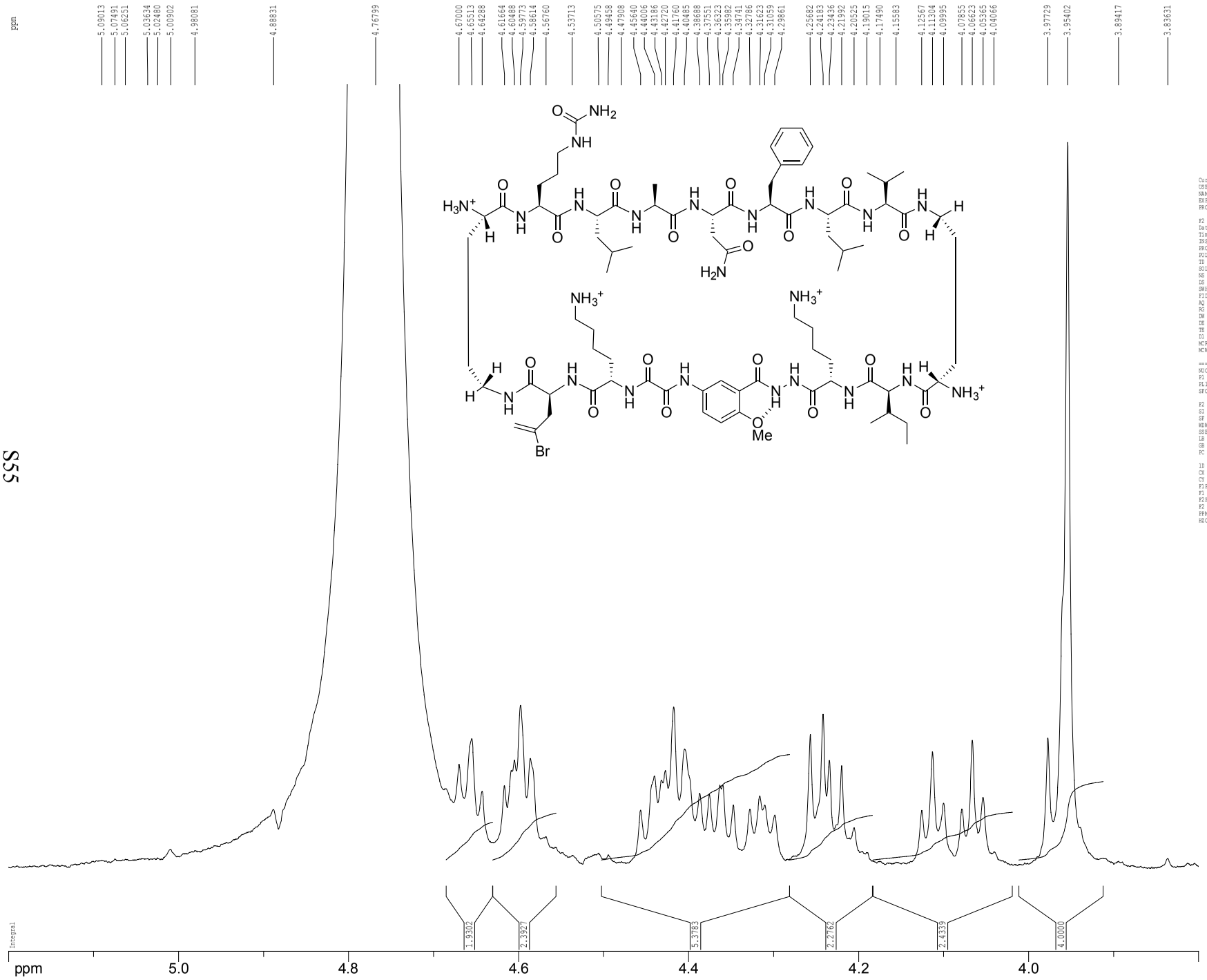
^{1}H NMR of macrocyclic β-sheet peptide **2_{Cit}**, 1 mM in 100 mM deuterioacetate buffer in D_2O at 500 MHz and 298 K



^{1}H NMR of macrocyclic β-sheet peptide **2_{Cit}**, 1 mM in 100 mM deuterioacetate buffer in D_2O at 500 MHz and 298 K



^{1}H NMR of macrocyclic β-sheet peptide **2_{Cit}**, 1 mM in 100 mM deuterioacetate buffer in D_2O at 500 MHz and 298 K



Current Data Parameters
USER yilinw
NAME 20170501_YW_citLANFLV-IKHAOKL(Br)-1mM
EXPNO 2
PROCNO 1

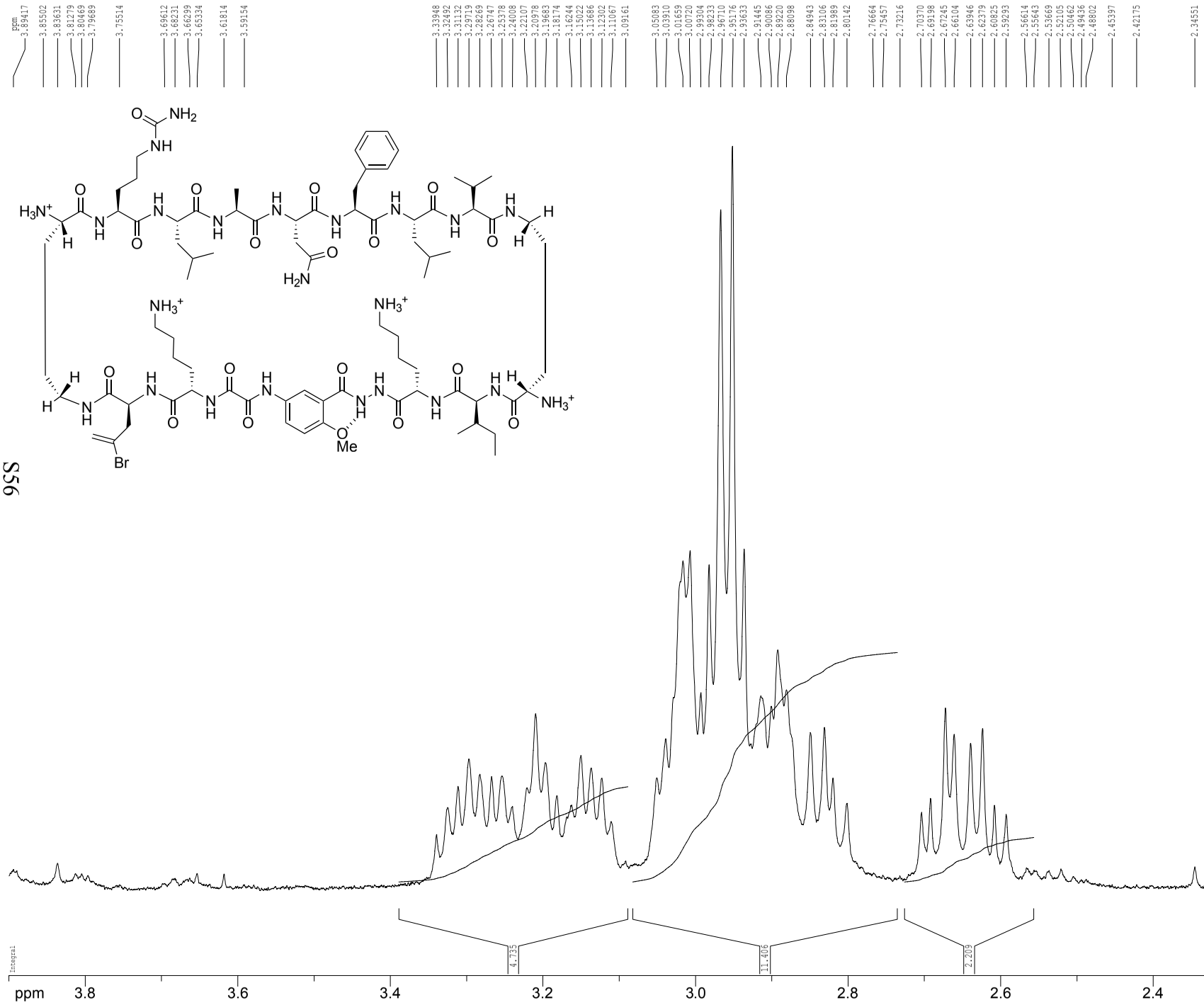
F2 - Acquisition Parameters
Date_ 20170501
Time 13.24
INSTRUM cryo500
PROBHD 5 mm CPTCI 1H-
PULPROG zg30
TD 81728
SOLVENT D2O
NS 256
DS 2
SWH 8012.820 Hz
FIDRES 0.098043 Hz
AQ 5.0998774 sec
RG 71.8
DW 62.400 usec
DE 6.00 usec
TE 298.0 K
D1 0.10000000 sec
MCREST 0.00000000 sec
MCWRK 0.01500000 sec

======= CHANNEL f1 =======
NUC1 1H
P1 7.50 usec
PL1 1.60 dB
SFO1 500.2235015 MHz

F2 - Processing parameters
SI 65536
SF 500.2200218 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00

1D NMR plot parameters
CX 22.80 cm
CY 14.00 cm
F1P 5.200 ppm
F1 2601.14 Hz
F2P 3.800 ppm
F2 1900.84 Hz
PPMCM 0.06140 ppm/cm
HZCM 30.71526 Hz/cm

^{1}H NMR of macrocyclic β-sheet peptide **2$_{Cit}$**, 1 mM in 100 mM deuterioacetate buffer in D_2O at 500 MHz and 298 K



Current Data Parameters
USER yilinw
NAME 20170501_YW_citLANFLV-IKHAOKL(Br)-1mM
EXPNO 2
PROCNO 1

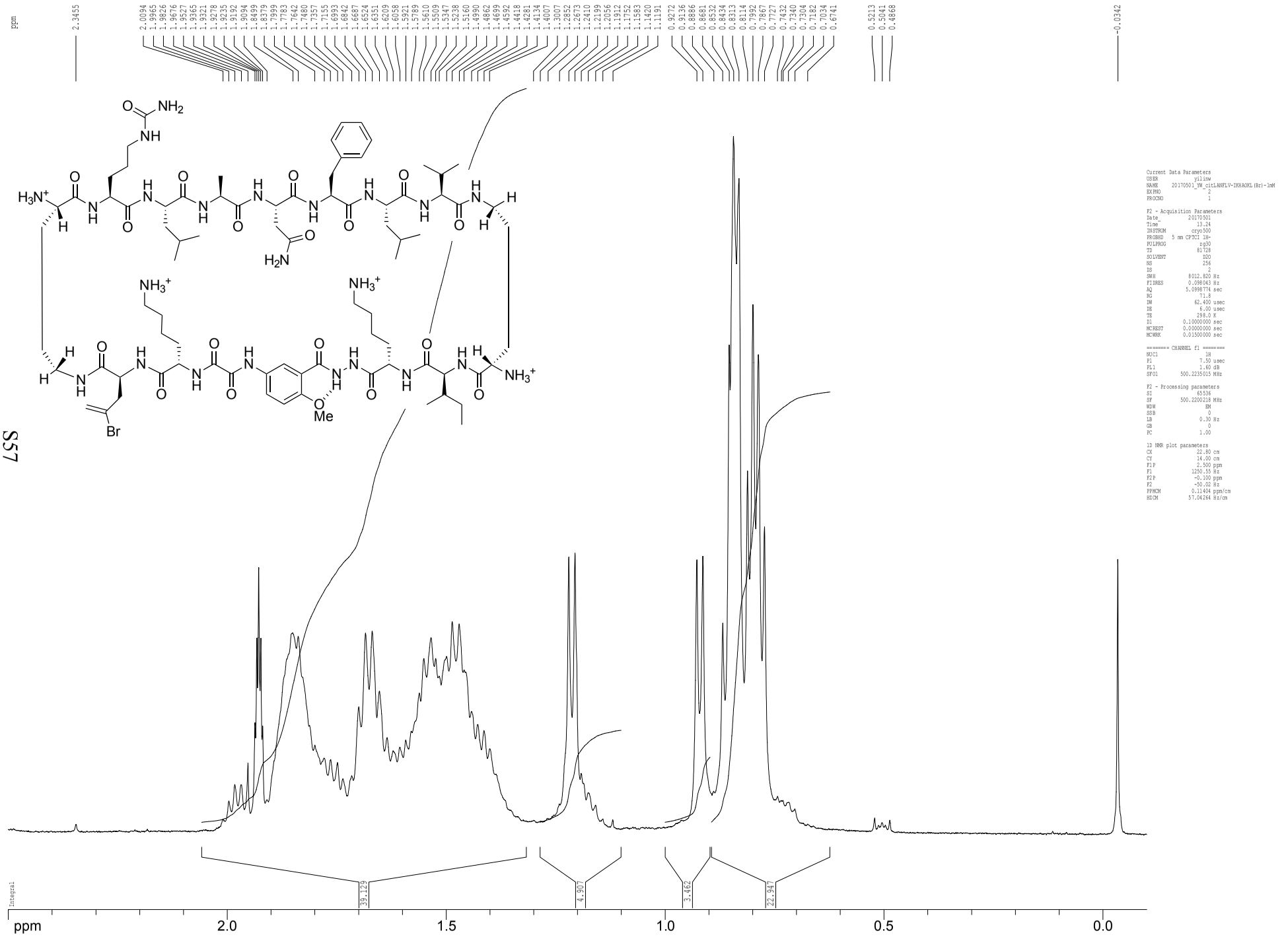
F2 - Acquisition Parameters
Date_ 20170501
Time 13.24
INSTRUM cryo500
PROBHD 5 mm CPTCI 1H-
PULPROG zg30
TD 81728
SOLVENT D2O
NS 256
DS 2
SWH 8012.820 Hz
FIDRES 0.098043 Hz
AQ 5.0998774 sec
RG 71.8
DW 62.400 usec
DE 6.00 usec
TE 298.0 K
D1 0.10000000 sec
MCREST 0.00000000 sec
MCWRK 0.01500000 sec

======= CHANNEL f1 =======
NUC1 1H
P1 7.50 usec
PL1 1.60 dB
SFO1 500.2235015 MHz

F2 - Processing parameters
SI 65536
SF 500.2200218 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00

1D NMR plot parameters
CX 22.80 cm
CY 14.00 cm
F1P 3.900 ppm
F1 1950.86 Hz
F2P 2.300 ppm
F2 1150.51 Hz
PPMCM 0.07018 ppm/cm
HZCM 35.10316 Hz/cm

^{1}H NMR of macrocyclic β-sheet peptide **2_{Cit}**, 1 mM in 100 mM deuterioacetate buffer in D_2O at 500 MHz and 298 K



Current Data Parameters
USER yilinw
NAME 20170501_YW_citLANFLV-IKHAOKL(Br)-1mM
EXPNO 2
PROCNO 1

F2 - Acquisition Parameters
Date_ 20170501
Time 13.24
INSTRUM cryo500
PROBHD 5 mm CPTCI 1H-
PULPROG zg30
TD 81728
SOLVENT D2O
NS 256
DS 2
SWH 8012.820 Hz
FIDRES 0.098043 Hz
AQ 5.0998774 sec
RG 71.8
DW 62.400 usec
DE 6.00 usec
TE 298.0 K
D1 0.10000000 sec
MCREST 0.00000000 sec
MCWRK 0.01500000 sec

======= CHANNEL f1 =======
NUC1 1H
P1 7.50 usec
PL1 1.60 dB
SFO1 500.2235015 MHz

F2 - Processing parameters
SI 65536
SF 500.2200218 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00

1D NMR plot parameters
CX 22.80 cm
CY 14.00 cm
F1P 2.500 ppm
F1 1250.55 Hz
F2P -0.100 ppm
F2 -50.02 Hz
PPMCM 0.11404 ppm/cm
HZCM 57.04264 Hz/cm