

Phenylalanyl tRNA synthetase (PheRS) substrate mimics: Design, synthesis, molecular dynamics and antimicrobial evaluation

Nada A. Nouredin^{a,b,*}, Jennifer Richards^c, Hend Kothayer^b, Mohammed M. Baraka^b, Sobhy M. Eladl^b, Mandy Wootton^c, Claire Simons^a

^a*School of Pharmacy and Pharmaceutical Sciences, Cardiff University, Cardiff CF10 3NB, U.K.*

^b*Department of Medicinal Chemistry, Faculty of Pharmacy, Zagazig University, Zagazig P.C. 44519, Egypt*

^c*Specialist Antimicrobial Chemotherapy Unit, University Hospital of Wales, Heath Park, Cardiff CF14 4XW, U.K.*

*Correspondence: NaNouredine@pharmacy.zu.edu.eg

¹ School of Pharmacy and Pharmaceutical Sciences, Cardiff University, Cardiff CF10 3NB, United Kingdom

² Department of Medicinal Chemistry, Faculty of Pharmacy, Zagazig University, Zagazig P.C. 44519, Egypt

Electronic supplementary information

1. Microbiological evaluation results:

Table. S1| MIC (µg/mL) for the synthesised compounds (5a-b), (6a-e), (7a-d) and (9a-e)

Compound	<i>S. aureus</i> ATCC 29213	<i>E. faecalis</i> ATCC 29212	<i>P. aeruginosa</i> ATCC 29853	<i>E. coli</i> ATCC 25922	<i>K. pneumoniae</i> ATCC 700603
5a	>128	128	128	>128	>128
5b	>128	128	128	>128	128
6a	128	128	128	>128	128
6b	128	128	128	>128	128
6c	128	128	128	>128	128
6d	128	128	128	>128	128
6e	128	128	128	128	128
7a	128	128	128	128	128
7b	128	128	128	>128	128
7c	>128	128	128	>128	128
7d	128	128	128	128	128
9a	128	128	128	>128	128
9b	128	64	128	>128	128
9c	128	128	128	>128	>128
9d	128	64	128	>128	128
9e	64	32	128	>128	128
ciprofloxacin	0.25	1	0.5	0.008	0.25

Table. S2| MIC ($\mu\text{g/mL}$) for the synthesised compounds (16a-c)

Compound	<i>S. aureus</i> ATCC 29213	MRSA NCTC 12493	<i>E. faecalis</i> ATCC 29212	<i>E. faecium</i> 16568
16a	128	64	64	32
16b	128	64	128	64
16c	128	64	32	32
ciprofloxacin	0.25	0.5	0.5	1

2. Computational studies supplementary information:

2.1. Flexible alignment studies:

Flexible alignment and docking studies were performed using MOE 2015.10 software¹. Flexible alignment was performed using MMFF94 forcefield, flexible alignment mode and the resulted conformations were examined according to their grand alignment score (S). The latter is the sum of the similiraity measure of configuration (F) and the average strain energy of the molecules in the alignment in kcal/mol (U). The lower S value indicates better alignment.

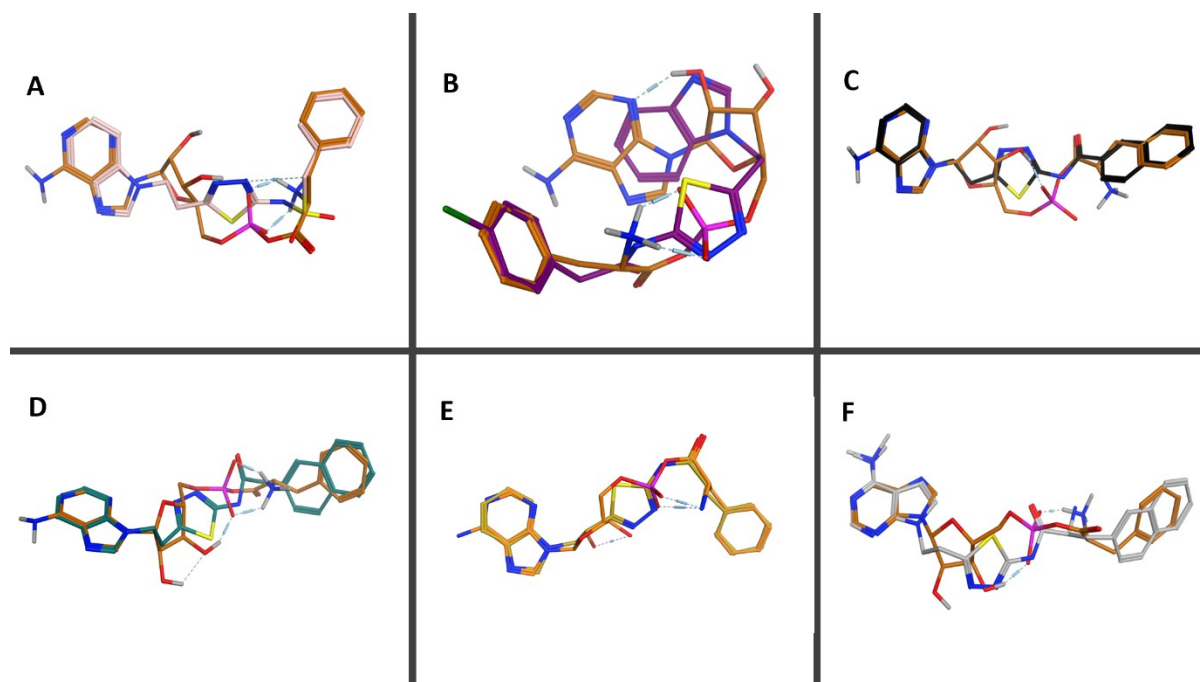


Fig. S1. 3D molecular alignment results. Phe-AMP is presented in orange colour. (A) **5a** (pink colour) $S = -170.1604$, (B) **6c** (purple colour) $S = -154.4615$, (C) **6e** (black colour) $S = -159.4926$, (D) **7d** (green colour) $S = -162.6272$, (E) **9a** (yellow colour) $S = -190.7823$ and (F) **16c** (grey colour) $S = -206.69$

2.2. Multiple sequence alignment:

CLUSTAL O(1.2.4) multiple sequence alignment

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sp|Q9I0A3|SYFA_PSEAE  --MENLDALVSQALEAVRHTEDVNALQIRVHYLGKKGELTQVMKTLGDLPAEERPKVG  57
sp|A6TAI3|SYFA_KLEP7  --MSHLAELVASAKAAINEASDVAALDNVRVEYLGKKGHLTLQMTTLRELPPPEERPAAG  57
sp|P08312|SYFA_ECOLI  --MSHLAELVASAKAAISQASDVAALDNVRVEYLGKKGHLTLQMTTLRELPPPEERPAAG  57
sp|P68849|SYFA_STAAU  MSEQQTMSELKQQALVDINEANDERALQEVKVKYLGKKGSVSGLMKMLKDLNPEEKPAFG  60
sp|Q836J6|SYFA_ENTFA  MTLQAQLEALRDNTLKEIAQVATLKELNQIRVETLGKKGPITEVLRGMKNLSPEERPVVG  60
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sp|A6TAI3|SYFA_KLEP7  AVINEAKEVQQALNARKAELEGAALNARLAAETIDVSLPGRRIENGGLHPVTRTIDRIE  117
sp|P08312|SYFA_ECOLI  AVINEAKEVQQALNARKAELESAALNARLAAETIDVSLPGRRIENGGLHPVTRTIDRIE  117
sp|P68849|SYFA_STAAU  QKVNELRQTIQNELDERQQMLVKEKLNQLAEETIDVSLPGRHIEIGSKHPLRTTIEEIE  120
sp|Q836J6|SYFA_ENTFA  GFANEIRDLLTEATEARKVYLEALNAALKEESLDVTLPGKQMPQGRHILTQVMEIEIE  120
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sp|P08312|SYFA_ECOLI  SFFGELGFTVATGPEIEDDYHNFALNIPGHHPARADHDTFWFDRLLRTQTSVGQVIRT  177
sp|P68849|SYFA_STAAU  DLFLGLGYEIVNGYEVEQDHYNFEMNLNPKSHPARDMQDSFYITDEILLRTHTSVPVQART  180
sp|Q836J6|SYFA_ENTFA  DIFLGMGYQVVEGYEVESDHYNFERMNLPKDHPARDMQDTFYISDEMLIRTHTSVPVQART  180
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sp|Q9I0A3|SYFA_PSEAE  MESQ--QPPRIIVCPGRVYRCDS-LTHSPMFHQVEGLLVDEGVSFADLKGTIEEFLRA  233
sp|A6TAI3|SYFA_KLEP7  MENQ--QPPRIIAPGRVYRNDYD-QTHTPMFHQMEGLIVDKNISFTNLKGTLDHFLNN  233
sp|P08312|SYFA_ECOLI  MKAQ--QPPRIIAPGRVYRNDYD-QTHTPMFHQMEGLIVDTNISFTNLKGTLDHFLRN  233
sp|P68849|SYFA_STAAU  MESR-HGQGPVKIICPGKVYRDSDDATHSHQFTQIEGLVVDKNVKMSDLKGTLELLAKK  239
sp|Q836J6|SYFA_ENTFA  MEKHDFSGALRMISPGKVFRDRTDDATHSHQFHQIEGLVVDKNVTMGDLKGTLEVMKK  240
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sp|Q9I0A3|SYFA_PSEAE  FFEKQLEVRFRPSFFPTEPSAEVDIQVCISGNGCRVCKQTGWLEVMGCMVHPNVLRM  293
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sp|P08312|SYFA_ECOLI  FFEEDLQIRFRPSYFPFTEPSAEVDVM-----GKNGKWLLEVLGCGMVHPNVLRN  282
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sp|Q9I0A3|SYFA_PSEAE  SNIDPEKFQGFAGFMGAERLAMLRYGVNDLRLFFDNDLRLFLGQFR-----  338
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                        . : * : : * : : * : : * : : * : : * : : * : : *

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Fig. S2. Multiple sequence alignment² of PheRS α subunit amino acid sequences from *P. aeruginosa* (Q9I0A3), *K. pneumoniae* (A6TAI3), *E. coli* (P08312), *S. aureus* (P68849) and *E. faecalis* (Q836J6). Yellow boxes show residues responsible for hydrophobic interactions. While green boxes show residues responsible for hydrophilic interaction. A high level of conservation among sequences could be observed.

2.3. Homology model evaluation:

2.3.1. Ramachandran plot:

Almost 98% of the amino acids are in the allowed region with only 3 amino acids observed in the outlier region which are Asp 185, Leu 191 and Gly 273 and all of them are not a part of the enzyme's active site.

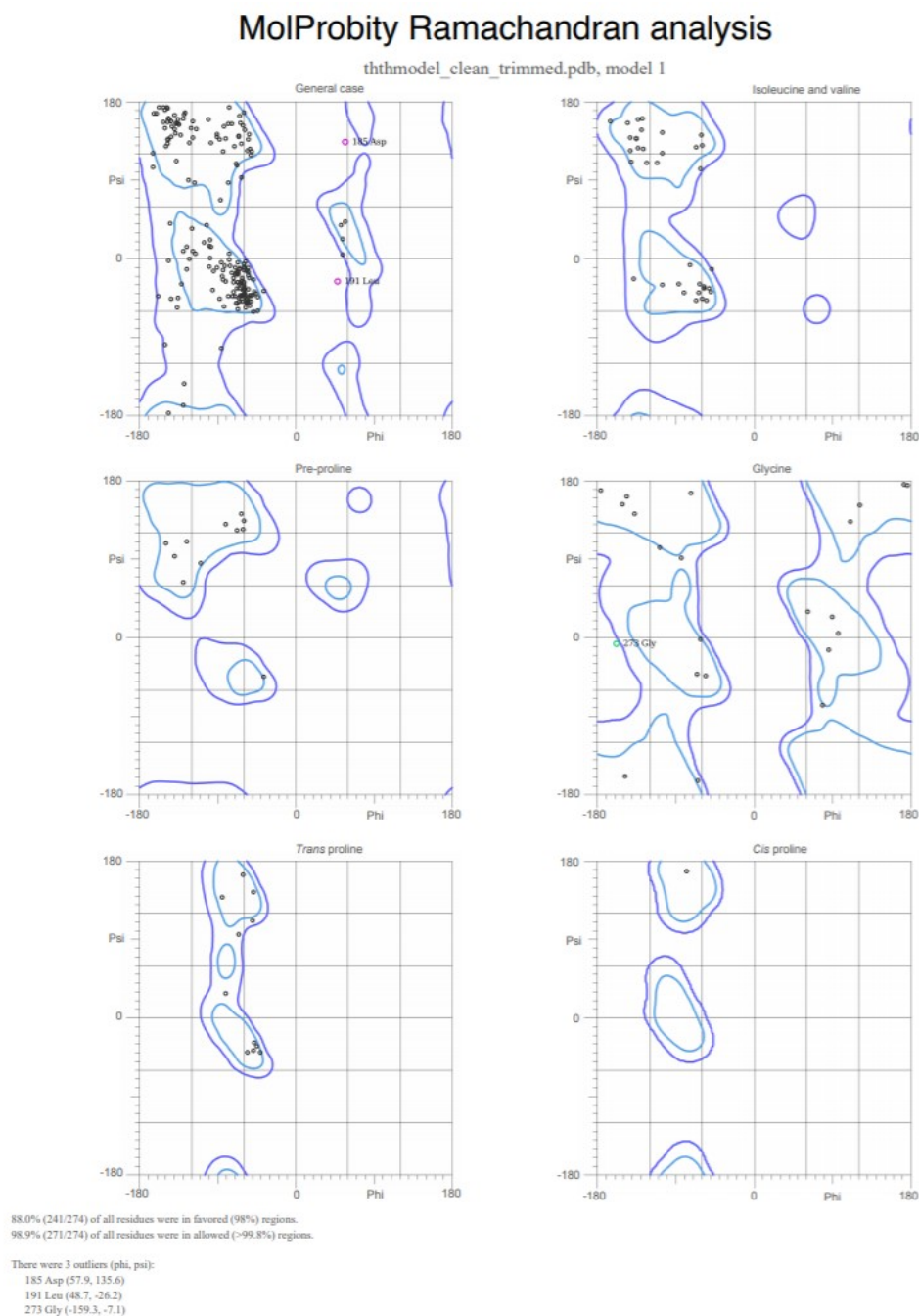
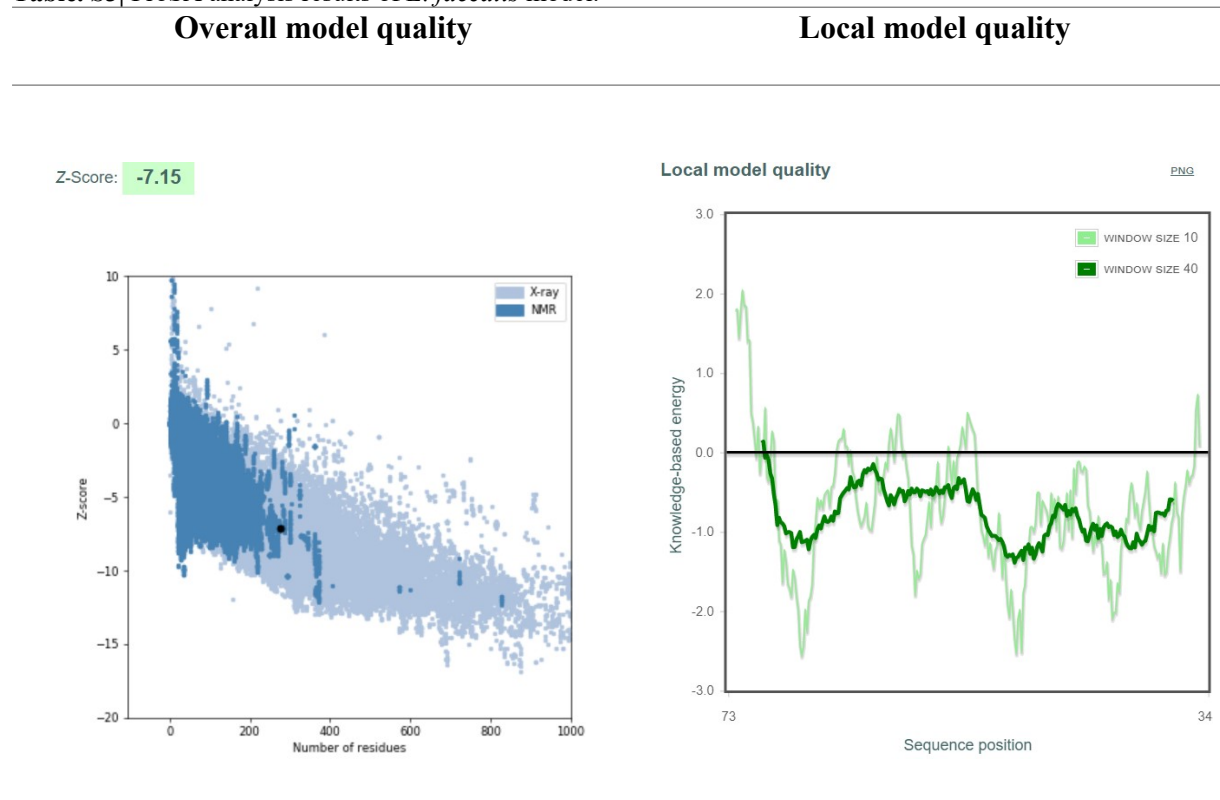


Fig. S3| Ramachandran plot of *E. faecalis* model.³

2.3.2. ProSA analysis:

ProSA analysis revealed good quality model as its Z-score is among the same sized solved protein structures and equal to -7.15 and the internal energy of each amino acid in the protein 3D structure is with negative value (Table. S3).

Table. S3 ProSA analysis results of *E. faecalis* model. ^{4, 5}



2.3.3. Verify 3D:

The newly constructed model passed the 3D verification as 86.32% of its amino acids have scored more than or equal to 0.2.

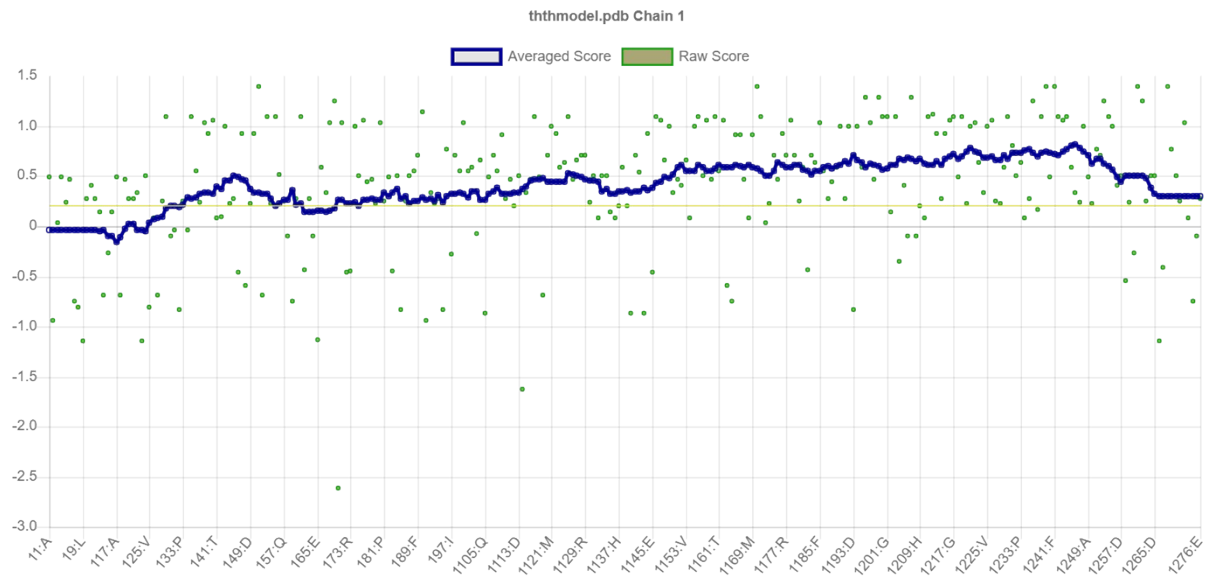


Fig. S4| 3D profile of *E. faecalis* model. ⁶

3. Chemistry supplementary information:

3.1. Preparation methods for compounds 3,4 and 12:

3.1.1. 3-(1*H*-Benzo[d]imidazol-1-yl) propanehydrazide (**3**)^{7,8}

To a solution of the methyl propanoate ester (**2**) (3 g, 14.69 mmol) in EtOH (125 mL) was added hydrazine monohydrate (10 equivalents) and the reaction mixture was stirred at room temperature overnight. The formed solid was collected by filtration and recrystallised from EtOAc and petroleum ether to give the pure hydrazide compound (**3**) as white crystals; yield 2.5 g (84%); m.p. 105-110 °C; TLC CH₂Cl₂-MeOH 9:1 v/v, R_f = 0.29; ¹H NMR (DMSO-*d*₆) δ: 2.60 (t, *J* = 6.7 Hz, 2H, CH₂CO), 4.19 (s, 2H, NH₂), 4.47 (t, *J* = 6.6 Hz, 2H, CH₂CH₂), 7.21 (t, *J* = 7.2 Hz, 1H, Ar), 7.26 (t, *J* = 8.1 Hz, 1H, Ar), 7.58 (d, *J* = 8.00 Hz, 1H, Ar), 7.62 (d, *J* = 7.9 Hz, 1H, Ar), 8.11 (s, 1H, H-imidazole), 9.06 (s, 1H, NH). ¹³C NMR (DMSO-*d*₆) δ: 34.1 (CH₂CO), 40.9 (NCH₂CH₂), 110.9 (CH), 119.8 (CH), 122.1 (CH), 122.9 (CH), 134.0 (C), 143.6 (C), 144.4 (CH-imidazole), 169.5 (CO).

3.1.2. 5-(2-(1*H*-Benzo[d]imidazol-1-yl)ethyl)-1,3,4-thiadiazol-2-amine (**4**)⁷

To a stirred mixture of the hydrazide (0.5 g, 2.45 mmol) in dry IPA (20 mL), was added (trimethylsilyl)isothiocyanate (TMSNCS) (1.38 mL, 9.8 mmol), then the mixture was heated under reflux overnight. The solvent was then concentrated under vacuum and c.H₂SO₄ (10 mL) was added, and the reaction stirred at room temperature for 2 h. The reaction was poured into crushed ice and neutralised using NH₄OH in -70°C dry ice/acetone bath. The resulting solid was collected by filtration, washed with H₂O and petroleum ether and dried *in vacuo* at 40 °C to afford the product as a yellow solid. Yield 0.3 g (53%); m.p. 208- 210°C (Lit. m.p. 182-184²); TLC CH₂Cl₂-MeOH 9:1 v/v, R_f 0.49. ¹H NMR (DMSO-*d*₆) δ: CH₂ signal is obscured by DMSO-*d*₆ signal, 4.59 (t, *J* = 6.8 Hz, 2H, CH₂CH₂), 7.03 (s, 2H, NH₂), 7.21 (t, *J* = 7.3 Hz, 1H, Ar), 7.26 (t, *J* = 7.6 Hz, 1H, Ar), 7.63 (t, *J* = 8.6 Hz, 2H, Ar), 8.15 (s, 1H, H-imidazole). ¹³C NMR (DMSO-*d*₆) δ: 30.3 (NCH₂CH₂), 43.7 (NCH₂), 110.9 (CH), 119.9 (CH), 122.0 (CH), 122.8 (CH), 134.1 (C), 143.9 (C), 144.6 (CH-imidazole), 154.7 (C), 169.1 (C).

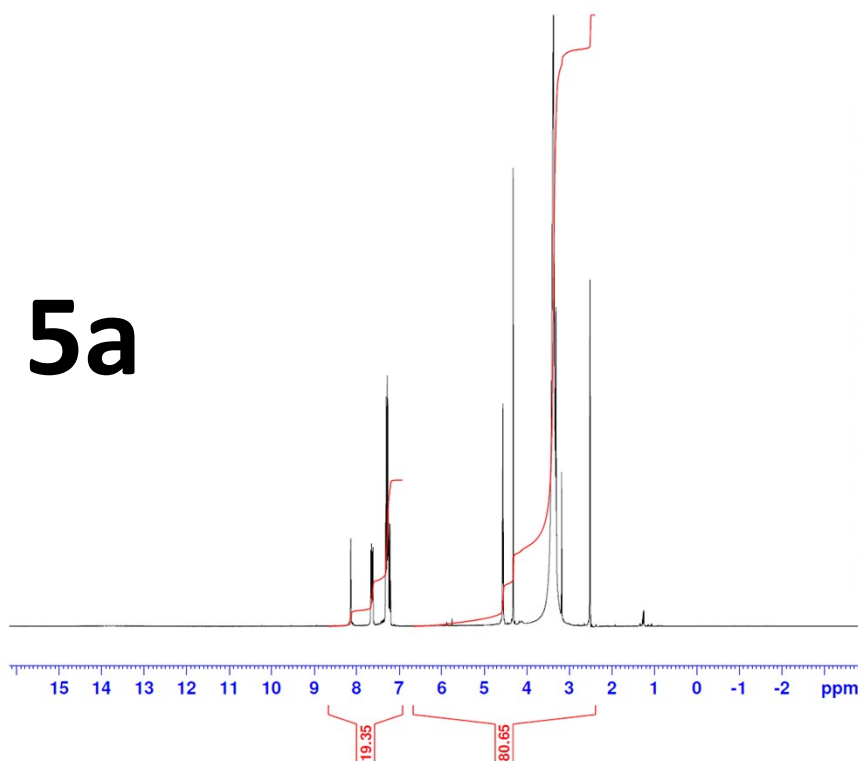
3.1.3. Methyl 3-(4-(dimethylamino)-7*H*-pyrrolo[2,3-*d*]pyrimidin-7-yl)propanoate (**12**)⁹

Prepared using *N,N*-dimethyl-7*H*-pyrrolo[2,3-*d*]pyrimidin-4-amine (**11**) (2 g, 12.33 mmol). The product was pure enough to be used in next steps with any further purification needed and separated as yellow low melting solid. Yield: 2.54 g, 83%; m.p. 52-54 °C; TLC: CH₂Cl₂-MeOH

9:1 v/v, R_f 0.75. ^1H NMR ($\text{DMSO-}d_6$) δ : 2.85 (t, $J = 7.0$ Hz, 2H, CH_2CO), 3.28 (s, 6H, $\text{N}(\text{CH}_3)_2$), 3.58 (s, 3H, OCH_3), 4.38 (t, $J = 7.0$ Hz, 2H, NCH_2), 6.62 (d, $J = 3.6$ Hz, 1H, Ar), 7.18 (d, $J = 3.7$ Hz, 1H, Ar), 8.14 (s, 1H, Ar). ^{13}C NMR ($\text{DMSO-}d_6$) δ : 34.6 ($\underline{\text{C}}\text{H}_2\text{CO}$), 39.1 ($\text{N}(\text{CH}_3)_2$), CH_2 peak is obscured by $\text{DMSO-}d_6$ peak, 52.0 (OCH_3), 101.7 (CH), 102.9 (C), 124.2 (CH), 150.5 (C), 151.2 (CH), 157.4 (C), 171.7 (CO).

3.2. NMR Charts for compounds (5a-b), (6a-e), (7a-d), (9a-e) and (16a-c)

5a

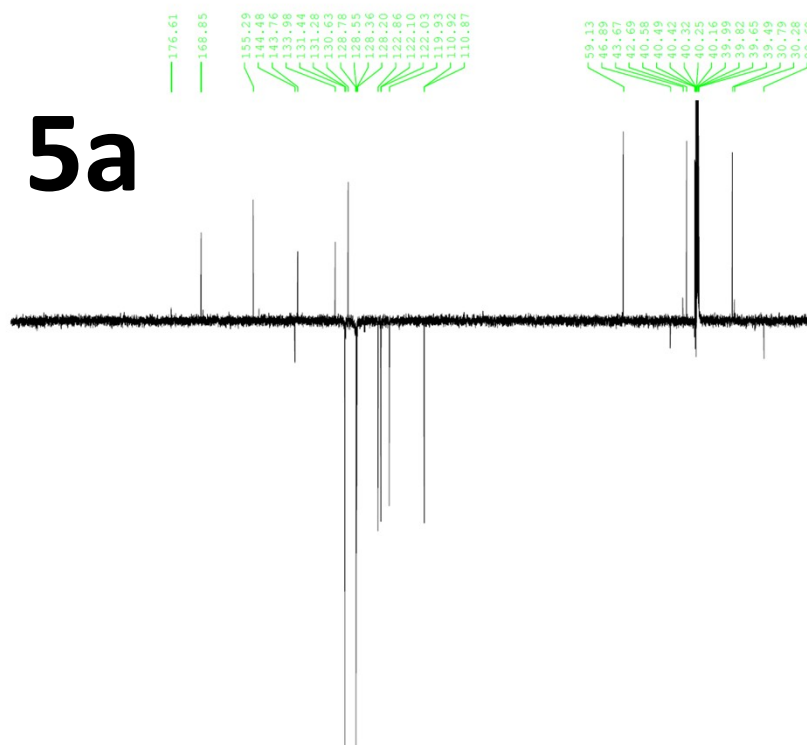


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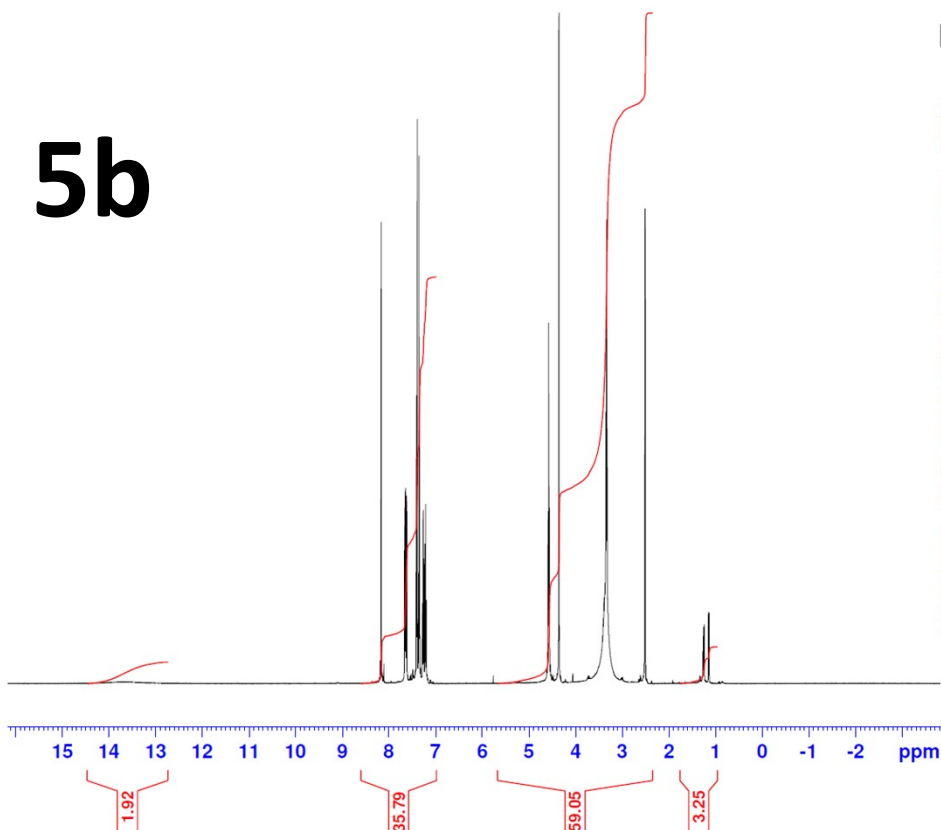
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5a



5b

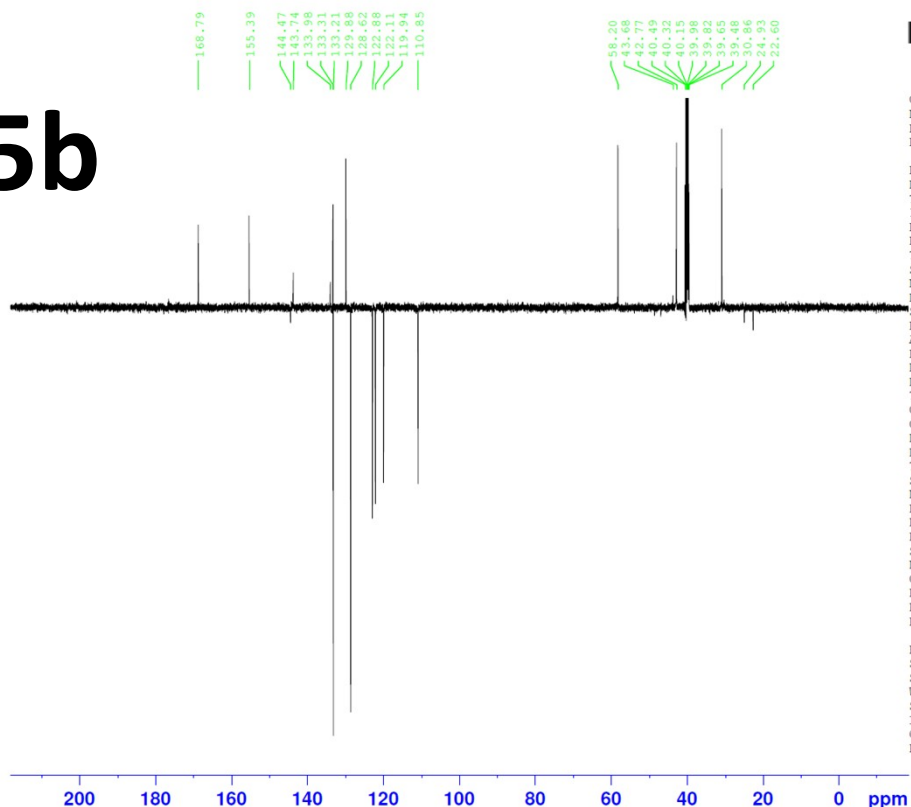


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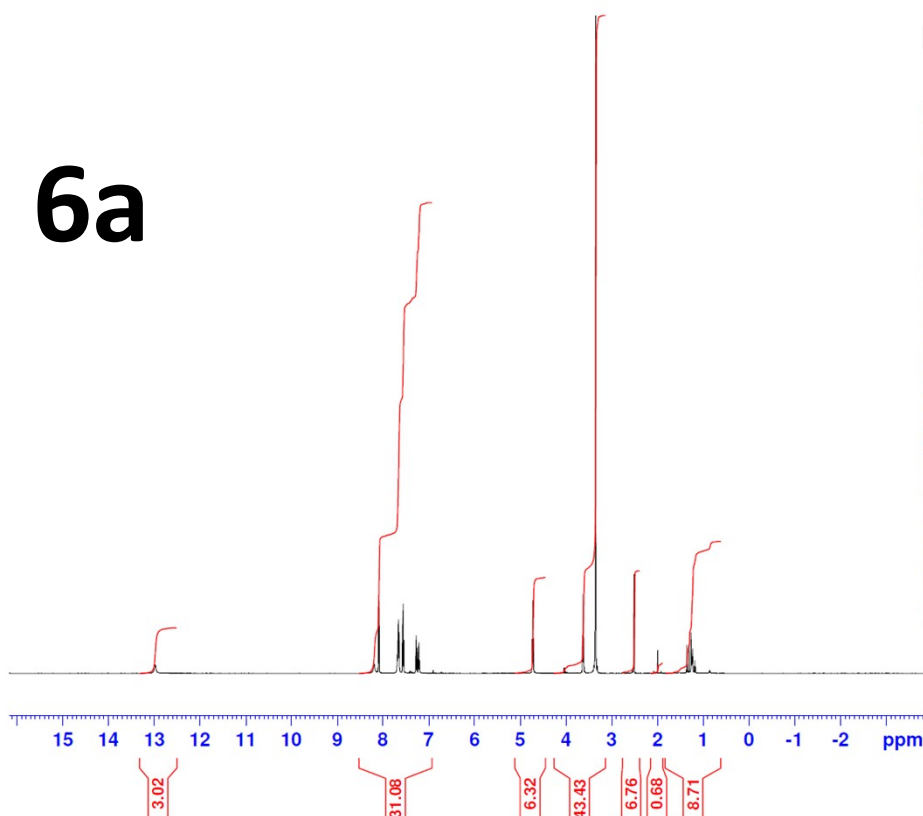


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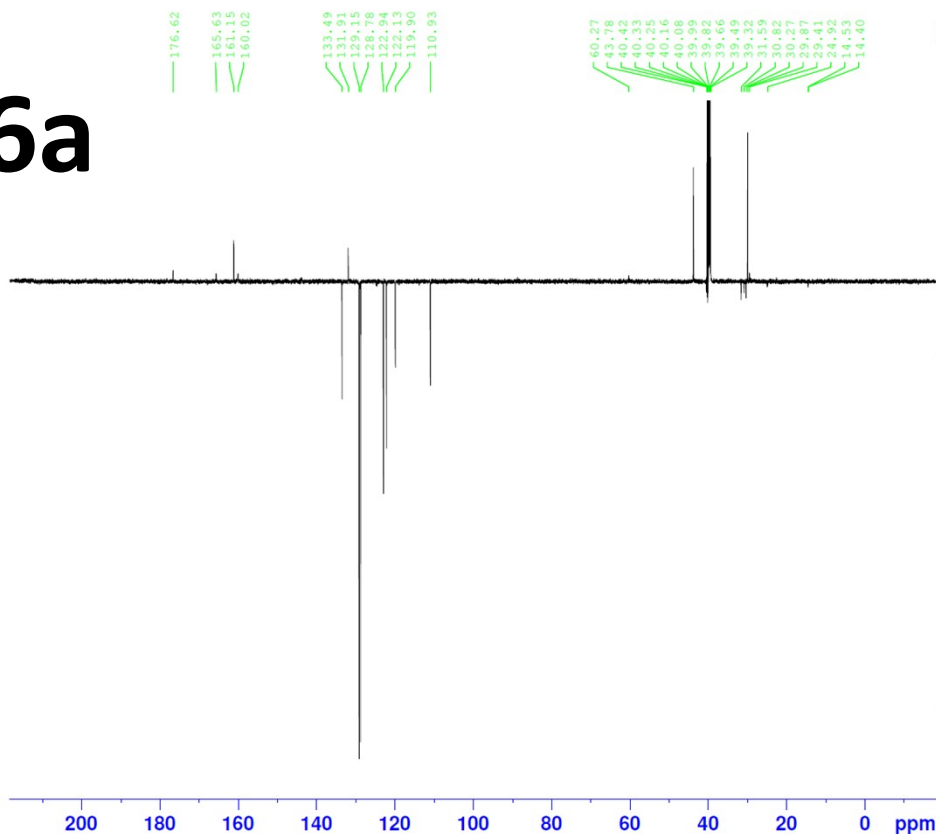


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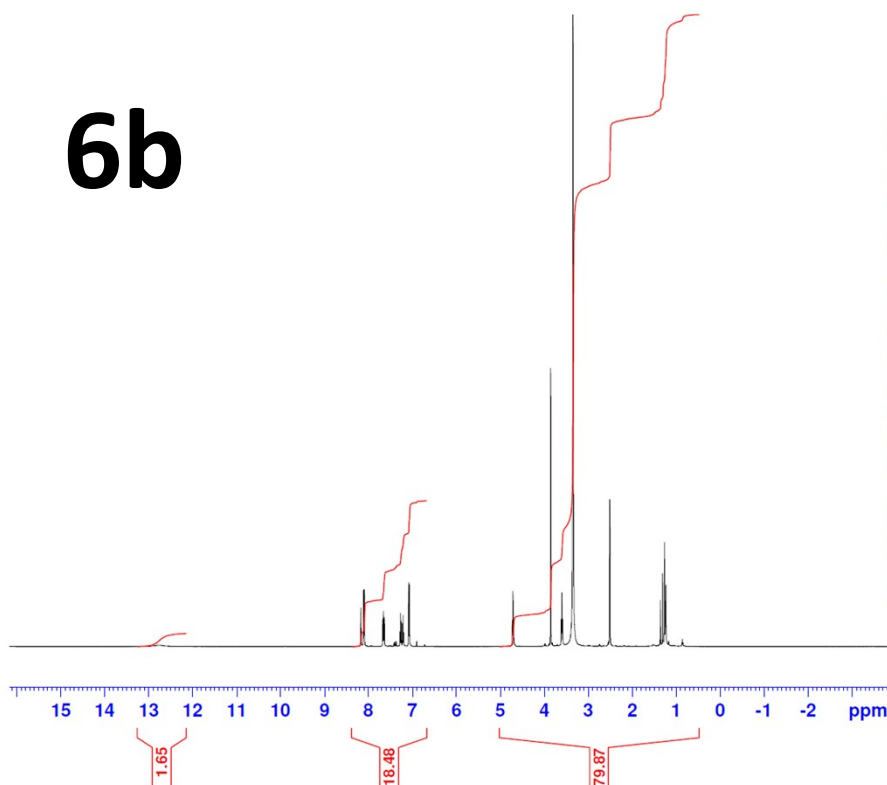


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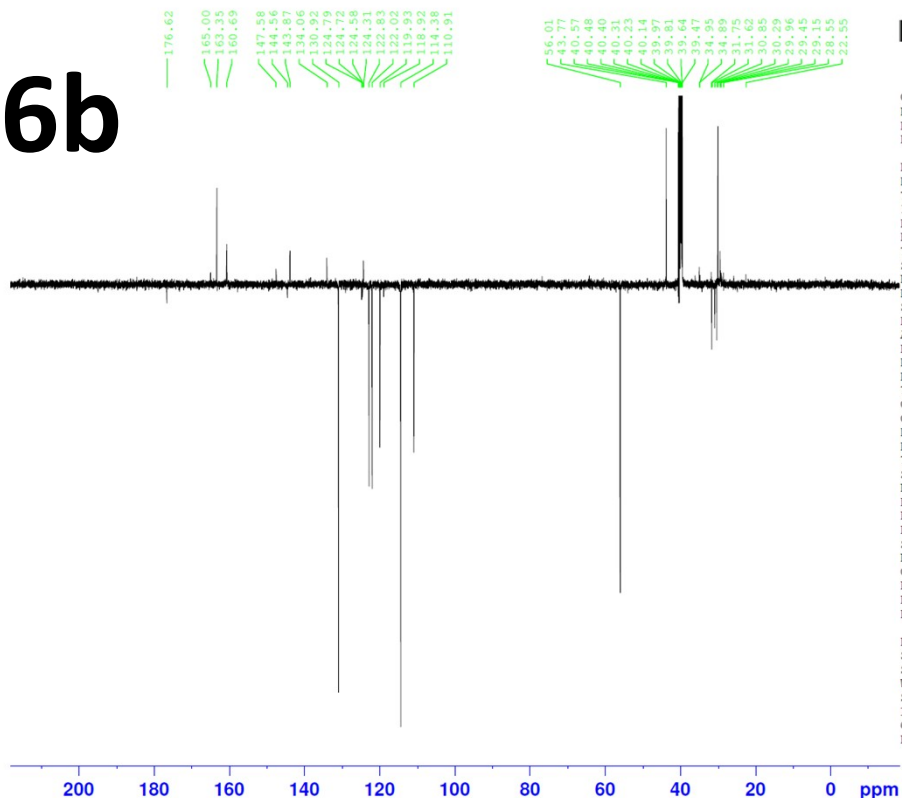


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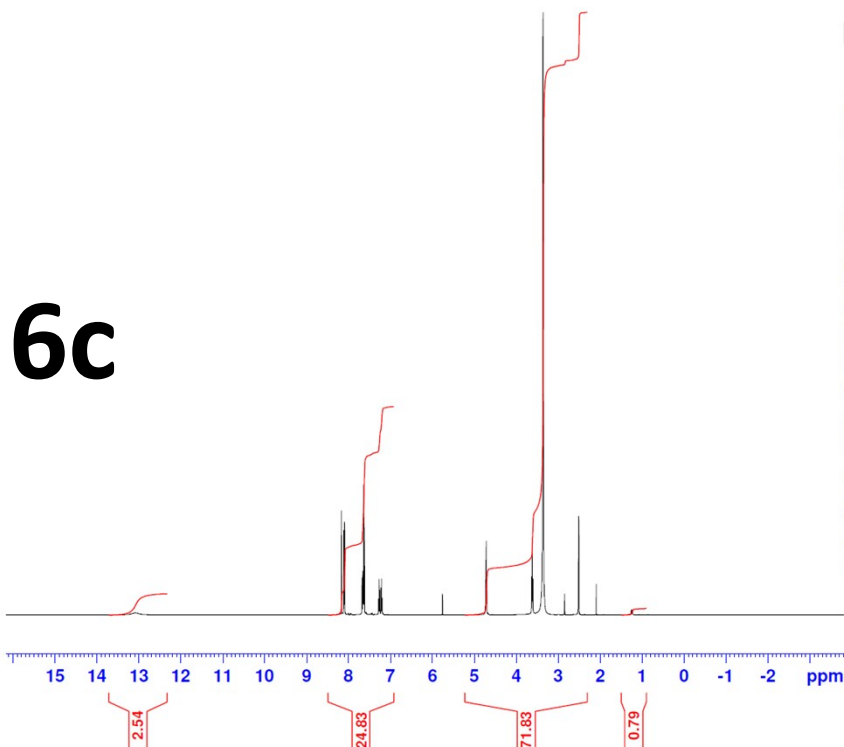
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NUC1 13C
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P2 20.00 usec
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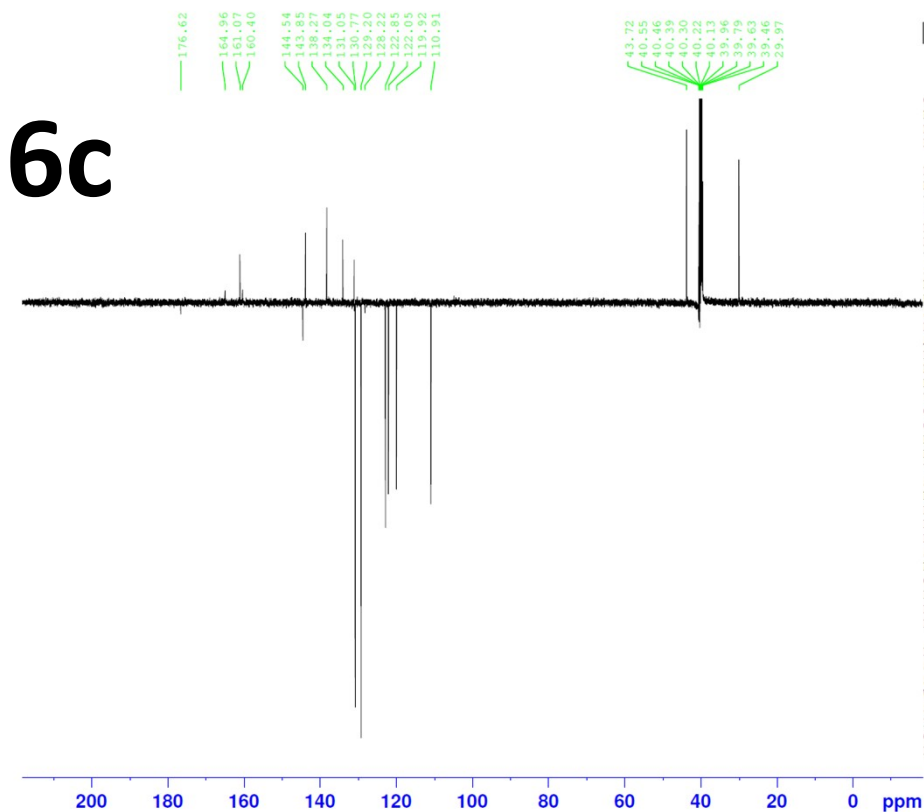
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DE 13.50 usec
TE 298.1 K
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NUC1 1H
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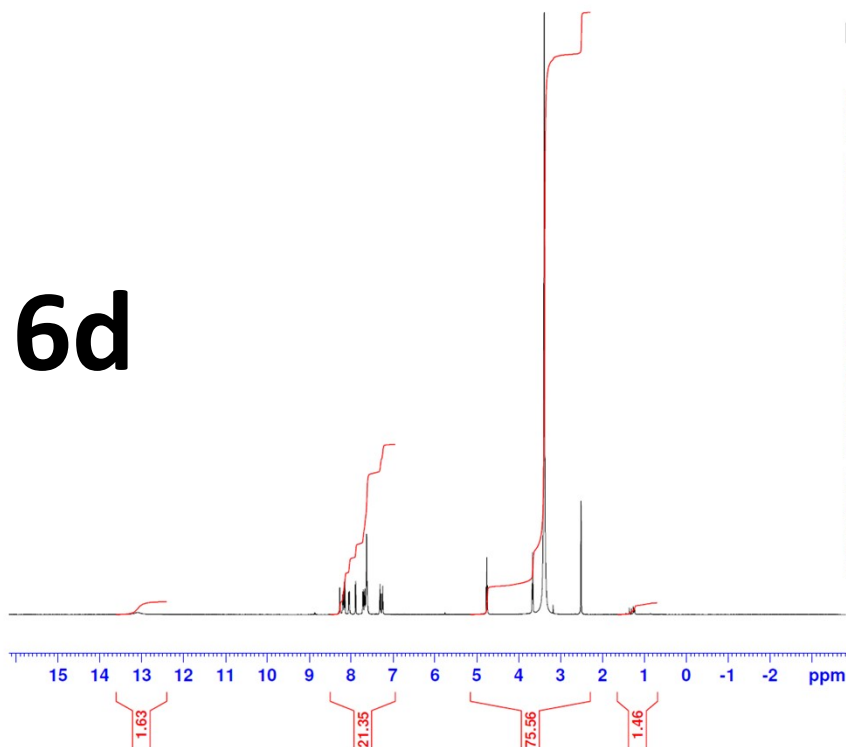


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PROCNO 1

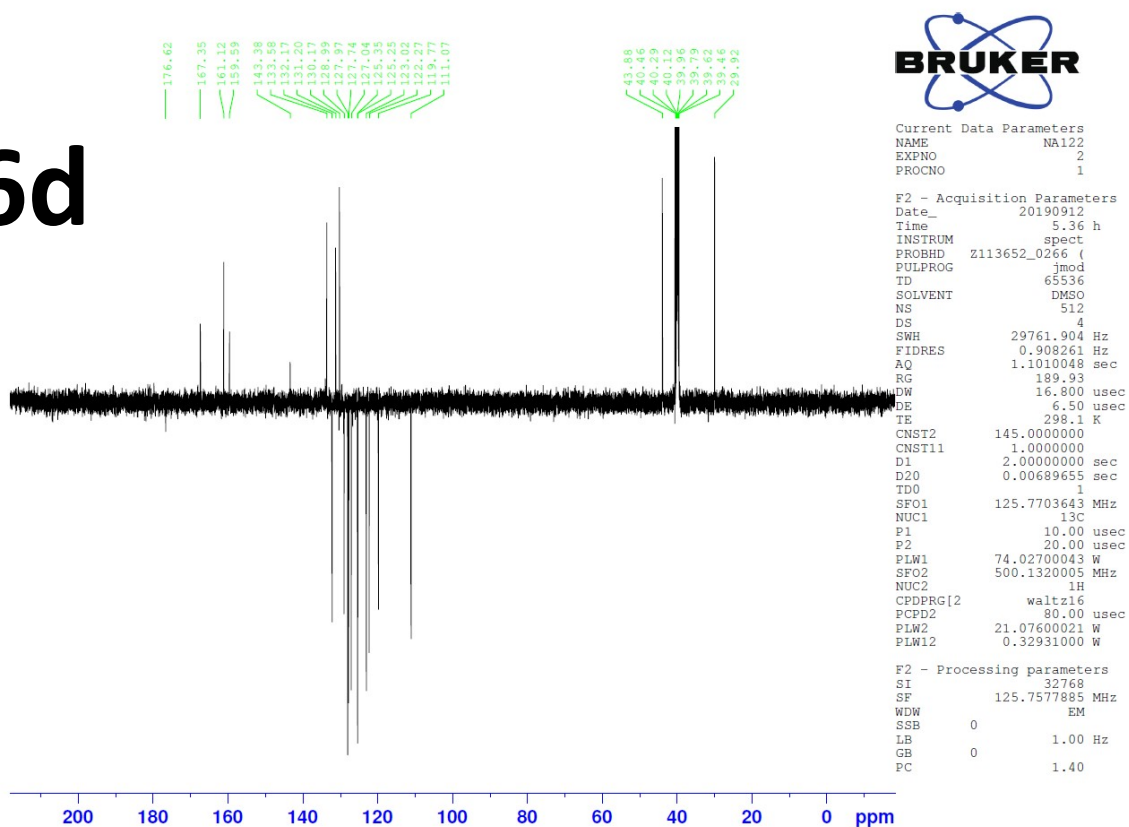
F2 - Acquisition Parameters
Date_ 20190906
Time 21.31 h
INSTRUM spect
PROBHD Z113652_0266 (
PULPROG jmod
TD 65536
SOLVENT DMSO
NS 1024
DS 4
SWH 29761.904 Hz
FIDRES 0.908261 Hz
AQ 1.1010048 sec
RG 189.93
DW 16.800 usec
DE 6.50 usec
TE 298.1 K
CNST2 145.0000000
CNST11 1.0000000
D1 2.00000000 sec
D20 0.00689655 sec
TD0 1
SFO1 125.7703643 MHz
NUC1 13C
P1 10.00 usec
P2 20.00 usec
PLW1 74.02700043 W
SFO2 500.1320005 MHz
NUC2 1H
CPDPRG2 waltz16
PCPD2 80.00 usec
PLW2 21.07600021 W
PLW12 0.32931000 W

F2 - Processing parameters
SI 32768
SF 125.7577885 MHz
WDW EM
SSB 0
LB 1.00 Hz
GB 0
PC 1.40

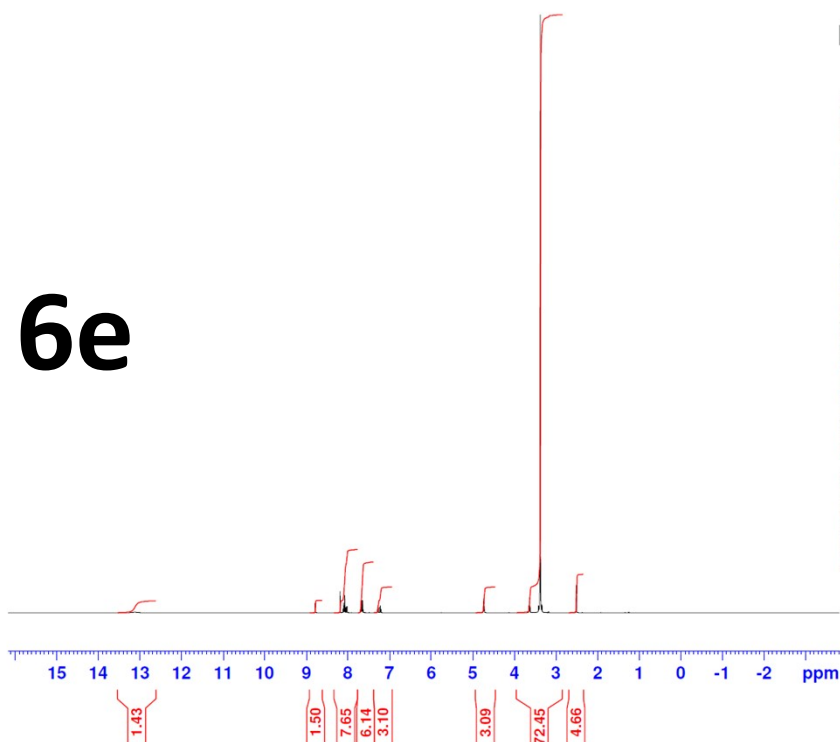
6d



6d



6e

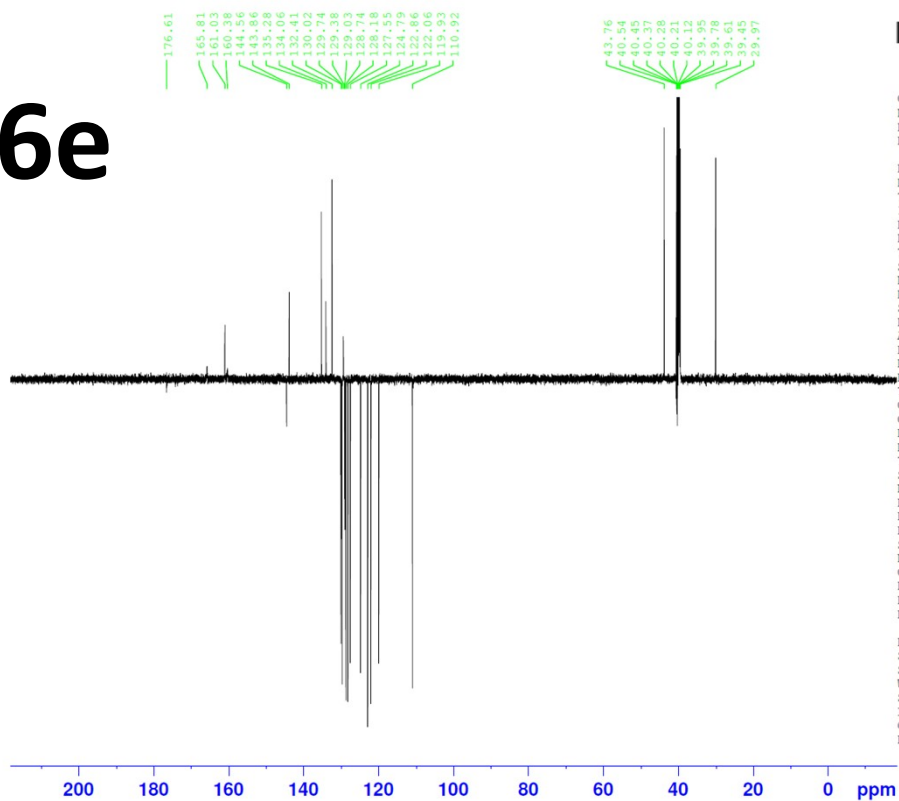


Current Data Parameters
NAME NA121
EXPNO 1
PROCNO 1

F2 - Acquisition Parameters
Date_ 20190910
Time 11.01 h
INSTRUM spect
PROBHD Z113652_0266 (
PULPROG zg30
TD 65536
SOLVENT DMSO
NS 16
DS 2
SWH 10000.000 Hz
FIDRES 0.305176 Hz
AQ 3.2767999 sec
RG 85.54
DW 50.000 usec
DE 13.50 usec
TE 298.1 K
D1 1.00000000 sec
TD0 1
SFO1 500.1330883 MHz
NUC1 1H
P1 10.00 usec
PLW1 21.07600021 W

F2 - Processing parameters
SI 65536
SF 500.1300000 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00

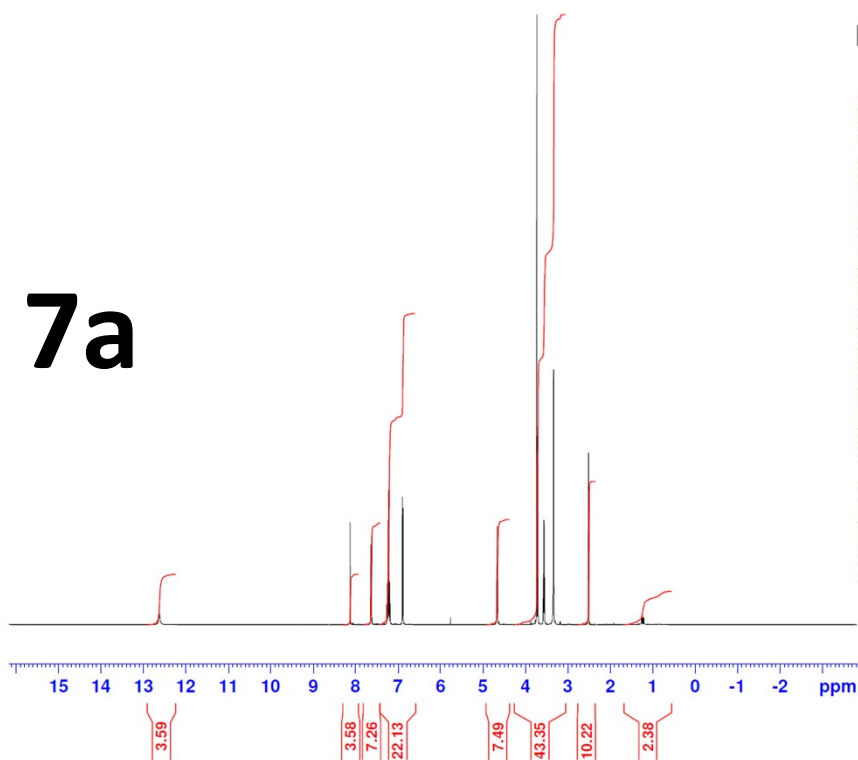
6e



Current Data Parameters
NAME NA121
EXPNO 3
PROCNO 1

F2 - Acquisition Parameters
Date_ 20190919
Time 2.05 h
INSTRUM spect
PROBHD Z113652_0266 (
PULPROG jmod
TD 65536
SOLVENT DMSO
NS 3072
DS 4
SWH 29761.904 Hz
FIDRES 0.908261 Hz
AQ 1.1010048 sec
RG 189.93
DW 16.800 usec
DE 6.50 usec
TE 298.1 K
CNS12 145.0000000
CNS11 1.0000000
D1 2.00000000 sec
D20 0.00689655 sec
TD0 1
SFO1 125.7703643 MHz
NUC1 13C
P1 10.00 usec
P2 20.00 usec
PLW1 74.02700043 W
SFO2 500.1320005 MHz
NUC2 1H
CPDPRG2 waltz16
PCPD2 80.00 usec
PLW2 21.07600021 W
PLW12 0.32931000 W

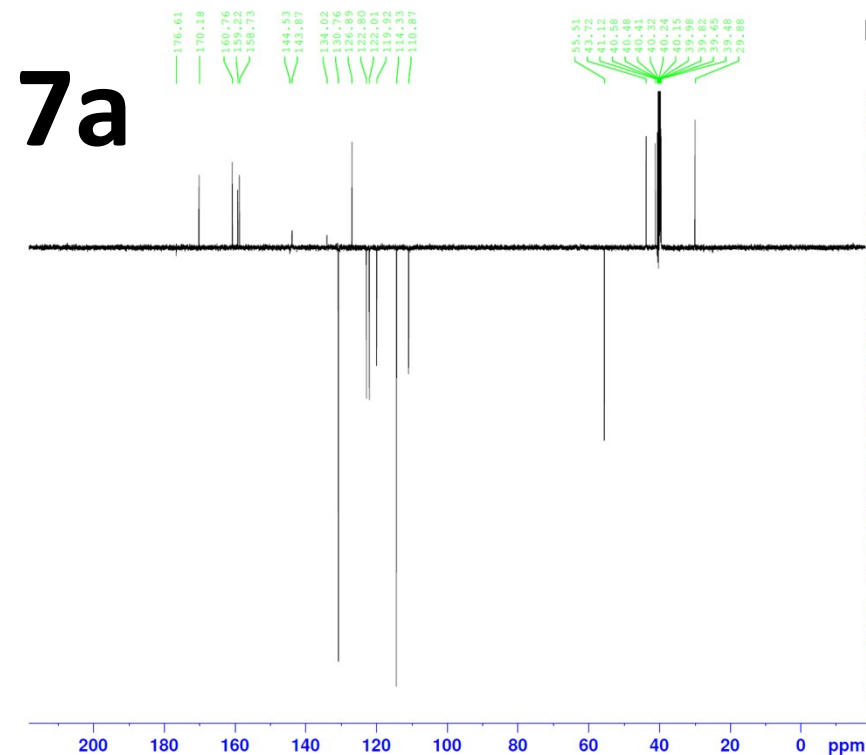
F2 - Processing parameters
SI 32768
SF 125.7577885 MHz
WDW EM
SSB 0
LB 1.00 Hz
GB 0
PC 1.40



Current Data Parameters
NAME NA124
EXPNO 1
PROCNO 1

F2 - Acquisition Parameters
Date_ 20190920
Time 16.38 h
INSTRUM spect
PROBHD Z113652_0266 (
PULPROG zg30
TD 65536
SOLVENT DMSO
NS 16
DS 2
SWH 10000.000 Hz
FIDRES 0.305176 Hz
AQ 3.2767999 sec
RG 119.43
DW 50.000 usec
DE 13.50 usec
TE 298.1 K
D1 1.00000000 sec
TD0 1
SFO1 500.1330883 MHz
NUC1 1H
P1 10.00 usec
PLW1 21.07600021 W

F2 - Processing parameters
SI 65536
SF 500.1300000 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00

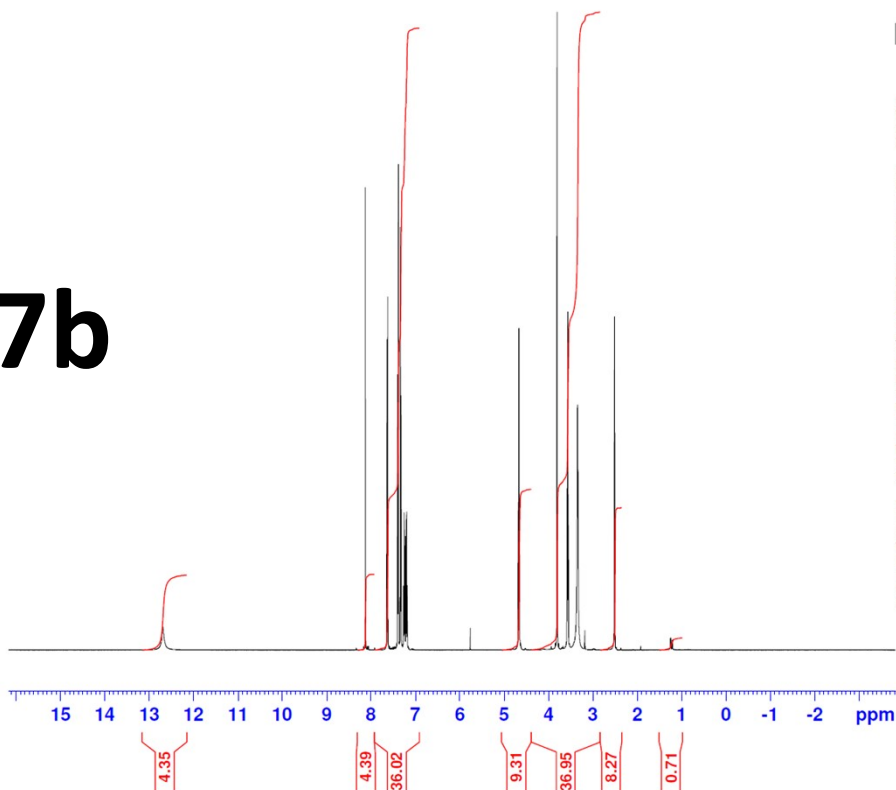


Current Data Parameters
NAME NA124
EXPNO 3
PROCNO 1

F2 - Acquisition Parameters
Date_ 20191007
Time 22.47 h
INSTRUM spect
PROBHD Z113652_0266 (
PULPROG jmod
TD 65536
SOLVENT DMSO
NS 2048
DS 4
SWH 29761.904 Hz
FIDRES 0.908261 Hz
AQ 1.1010048 sec
RG 189.93
DW 16.800 usec
DE 6.50 usec
TE 298.2 K
CNST2 145.0000000
CNST11 1.0000000
D1 2.00000000 sec
D20 0.00689655 sec
TD0 1
SFO1 125.7703643 MHz
NUC1 13C
P1 10.00 usec
P2 20.00 usec
PLW1 74.02700043 W
SFO2 500.1320005 MHz
NUC2 1H
CPDPRG[2] waltz16
PCPD2 80.00 usec
PLW2 21.07600021 W
PLW12 0.32931000 W

F2 - Processing parameters
SI 32768
SF 125.7577885 MHz
WDW EM
SSB 0
LB 1.00 Hz
GB 0
PC 1.40

7b

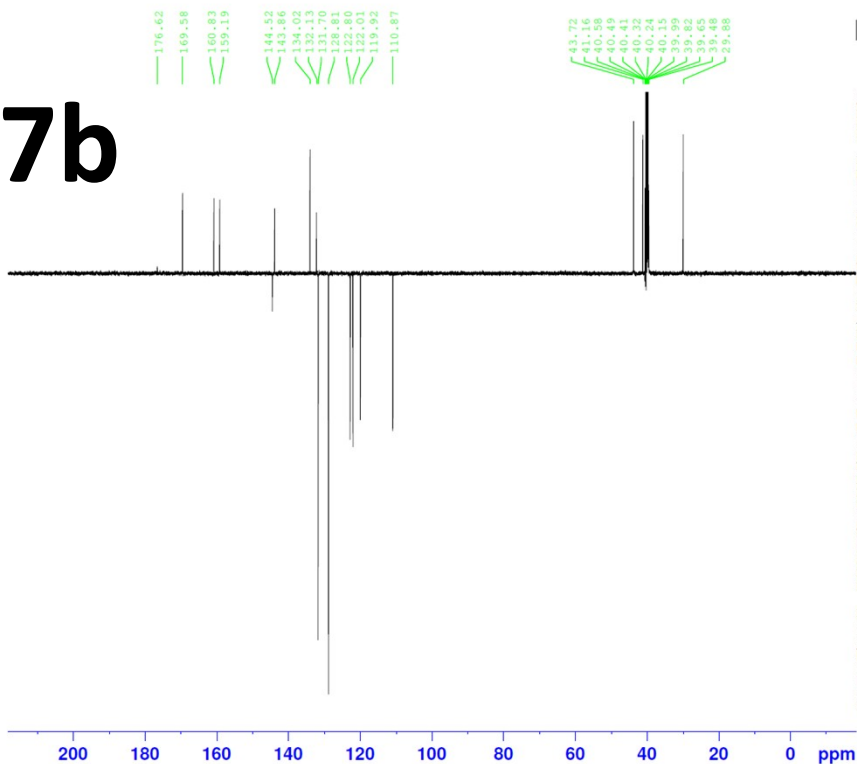


Current Data Parameters
 NAME NA123
 EXPNO 1
 PROCNO 1

F2 - Acquisition Parameters
 Date_ 20190920
 Time 15.54 h
 INSTRUM spect
 PROBHD Z113652_0266 (zg30)
 PULPROG 65536
 TD 16
 SOLVENT DMSO
 NS 2
 DS 10000.000 Hz
 SWH 0.305176 Hz
 FIDRES 3.2767999 sec
 AQ 118.43
 RG 50.000 usec
 DW 13.50 usec
 DE 298.1 K
 TE 1.00000000 sec
 D1 1
 TD0 500.1330883 MHz
 SFO1 1H
 NUC1 10.00 usec
 F1 21.07600021 W
 PLW1

F2 - Processing parameters
 SI 65536
 SF 500.1300000 MHz
 WDW EM
 SSB 0
 LB 0.30 Hz
 GB 0
 PC 1.00

7b

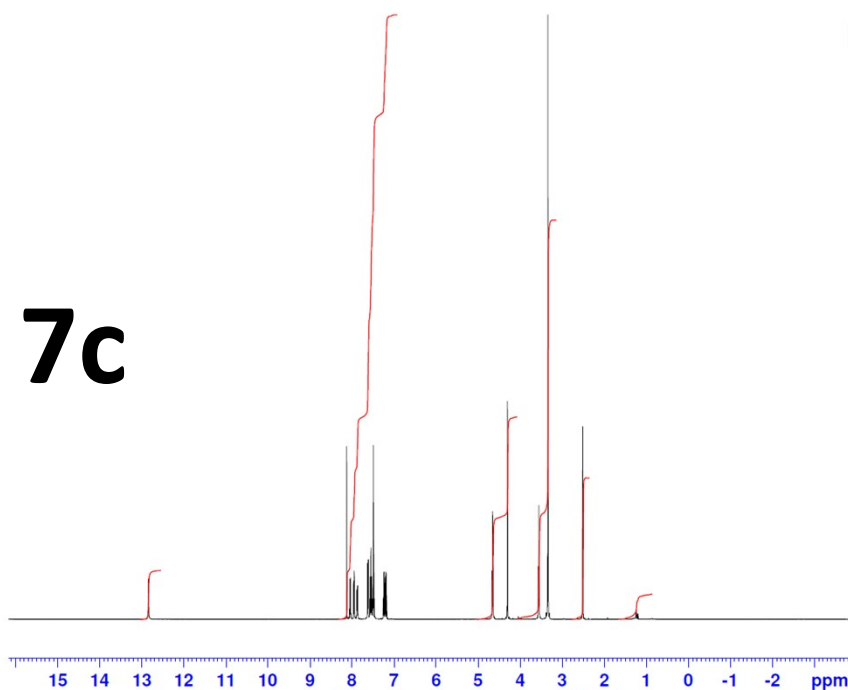


Current Data Parameters
 NAME NA123
 EXPNO 2
 PROCNO 1

F2 - Acquisition Parameters
 Date_ 20191001
 Time 23.45 h
 INSTRUM spect
 PROBHD Z113652_0266 (jmod)
 PULPROG 65536
 TD 2048
 SOLVENT DMSO
 NS 4
 DS 29761.904 Hz
 SWH 0.908261 Hz
 FIDRES 1.1010048 sec
 AQ 189.93
 RG 16.800 usec
 DW 6.50 usec
 DE 298.1 K
 TE 145.0000000
 CNST2 1.0000000
 D1 2.00000000 sec
 D20 0.00689655 sec
 TD0 1
 SFO1 125.7703643 MHz
 NUC1 13C
 P1 10.00 usec
 P2 20.00 usec
 PLW1 74.02700043 W
 SFO2 500.1320005 MHz
 NUC2 1H
 CPDPRG2 waltz16
 PCPD2 80.00 usec
 PLW2 21.07600021 W
 PLW12 0.32931000 W

F2 - Processing parameters
 SI 32768
 SF 125.7577885 MHz
 WDW EM
 SSB 0
 LB 1.00 Hz
 GB 0
 PC 1.40

7c

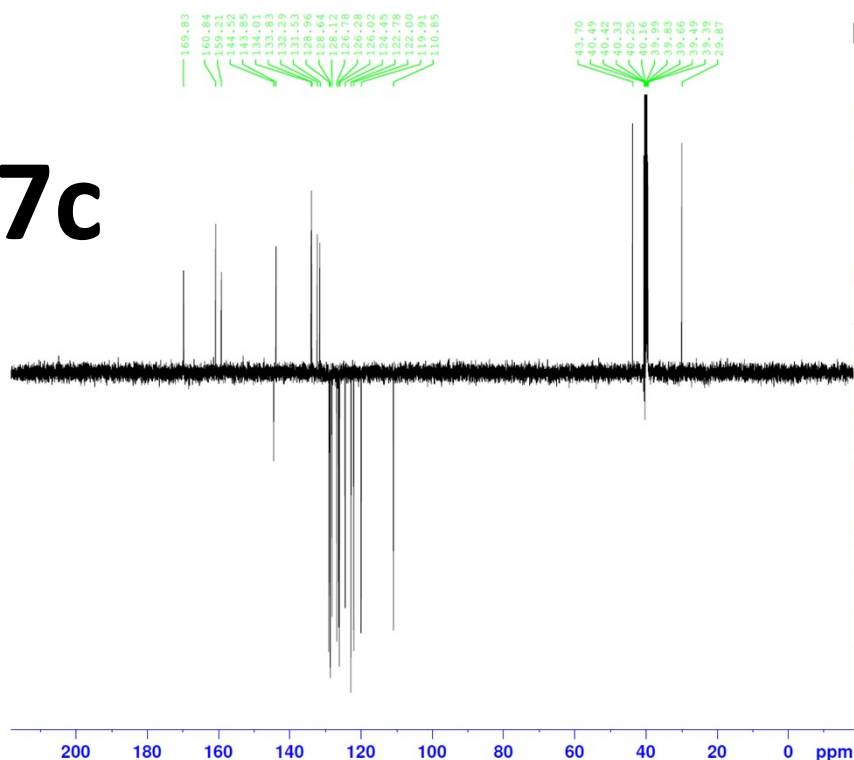


Current Data Parameters
NAME NA126
EXPNO 1
PROCNO 1

F2 - Acquisition Parameters
Date_ 20191016
Time 15.50 h
INSTRUM spect
PROBHD Z113652_0266 (
PULPROG zg30
TD 65536
SOLVENT DMSO
NS 16
DS 2
SWH 10000.000 Hz
FIDRES 0.305176 Hz
AQ 3.2767999 sec
RG 118.43
DW 50.000 usec
DE 13.50 usec
TE 298.1 K
D1 1.00000000 sec
TD0 1
SFO1 500.1330883 MHz
NUC1 1H
P1 10.00 usec
PLW1 21.07600021 W

F2 - Processing parameters
SI 65536
SF 500.1300000 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00

7c

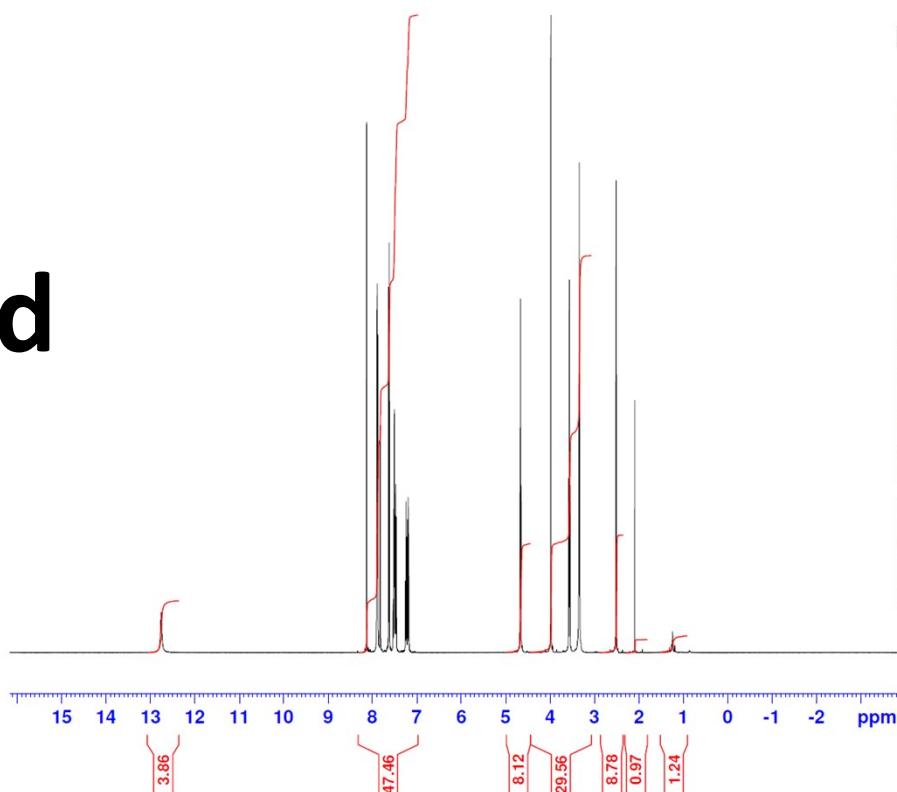


Current Data Parameters
NAME NA126
EXPNO 2
PROCNO 1

F2 - Acquisition Parameters
Date_ 20191016
Time 20.02 h
INSTRUM spect
PROBHD Z113652_0266 (
PULPROG jmod
TD 65536
SOLVENT DMSO
NS 512
DS 4
SWH 29761.904 Hz
FIDRES 0.908261 Hz
AQ 1.1010048 sec
RG 189.93
DW 16.800 usec
DE 6.50 usec
TE 298.2 K
CNST2 145.0000000
CNST11 1.0000000
D1 2.00000000 sec
D20 0.00689655 sec
TD0 1
SFO1 125.7703643 MHz
NUC1 13C
P1 10.00 usec
P2 20.00 usec
PLW1 74.02700043 W
SFO2 500.1320005 MHz
NUC2 1H
CPDPRG2 waltz16
PCPD2 80.00 usec
PLW2 21.07600021 W
PLW12 0.32931000 W

F2 - Processing parameters
SI 32768
SF 125.7577885 MHz
WDW EM
SSB 0
LB 1.00 Hz
GB 0
PC 1.40

7d

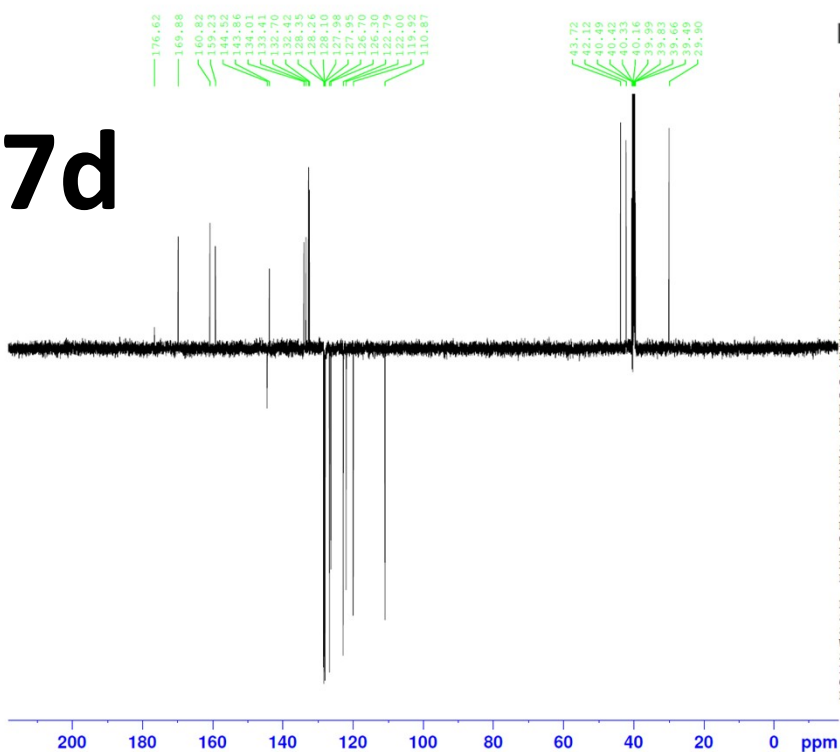


Current Data Parameters
NAME NA125
EXPNO 1
PROCNO 1

F2 - Acquisition Parameters
Date_ 20191016
Time 15.35 h
INSTRUM spect
PROBHD Z113652_0266 ()
PULPROG zg30
TD 65536
SOLVENT DMSO
NS 16
DS 2
SWH 10000.000 Hz
FIDRES 0.305176 Hz
AQ 3.2767999 sec
RG 118.43
DW 50.000 usec
DE 13.50 usec
TE 298.1 K
D1 1.00000000 sec
TD0 1
SFO1 500.1330883 MHz
NUC1 1H
P1 10.00 usec
PLW1 21.07600021 W

F2 - Processing parameters
SI 65536
SF 500.1300000 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00

7d

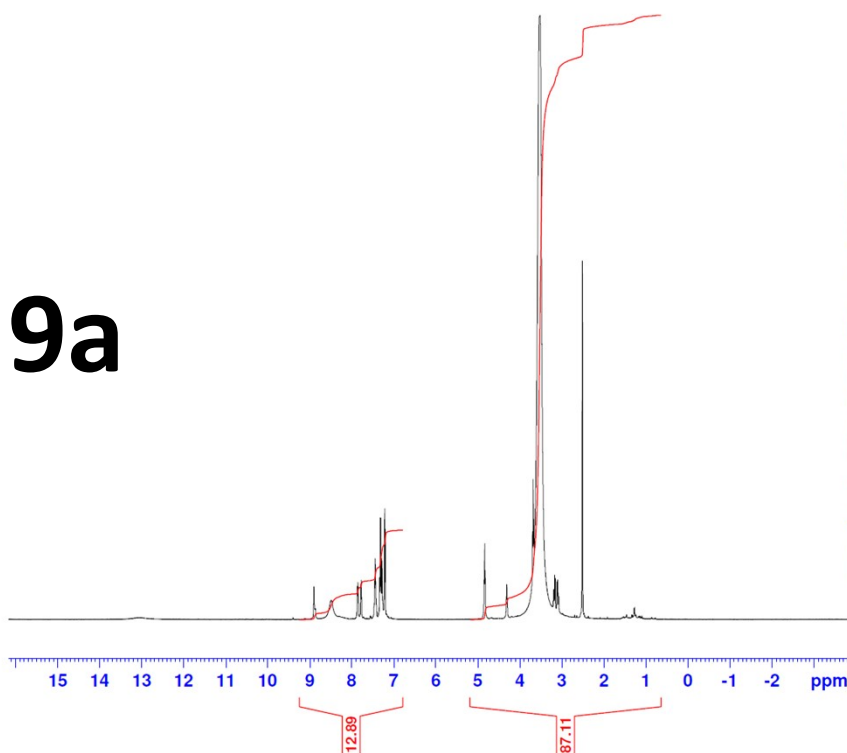


Current Data Parameters
NAME NA125
EXPNO 2
PROCNO 1

F2 - Acquisition Parameters
Date_ 20191016
Time 19.32 h
INSTRUM spect
PROBHD Z113652_0266 ()
PULPROG jmod
TD 65536
SOLVENT DMSO
NS 512
DS 4
SWH 29761.904 Hz
FIDRES 0.908261 Hz
AQ 1.1010048 sec
RG 189.93
DW 16.800 usec
DE 6.50 usec
TE 298.2 K
CNST2 145.0000000
CNST11 1.0000000
D1 2.00000000 sec
D20 0.00689655 sec
TD0 1
SFO1 125.7703643 MHz
NUC1 13C
P1 10.00 usec
P2 20.00 usec
PLW1 74.02700043 W
SFO2 500.1320005 MHz
NUC2 1H
CPDPRG2 waltz16
PCPD2 80.00 usec
PLW2 21.07600021 W
PLW12 0.32931000 W

F2 - Processing parameters
SI 32768
SF 125.7577885 MHz
WDW EM
SSB 0
LB 1.00 Hz
GB 0
PC 1.40

9a

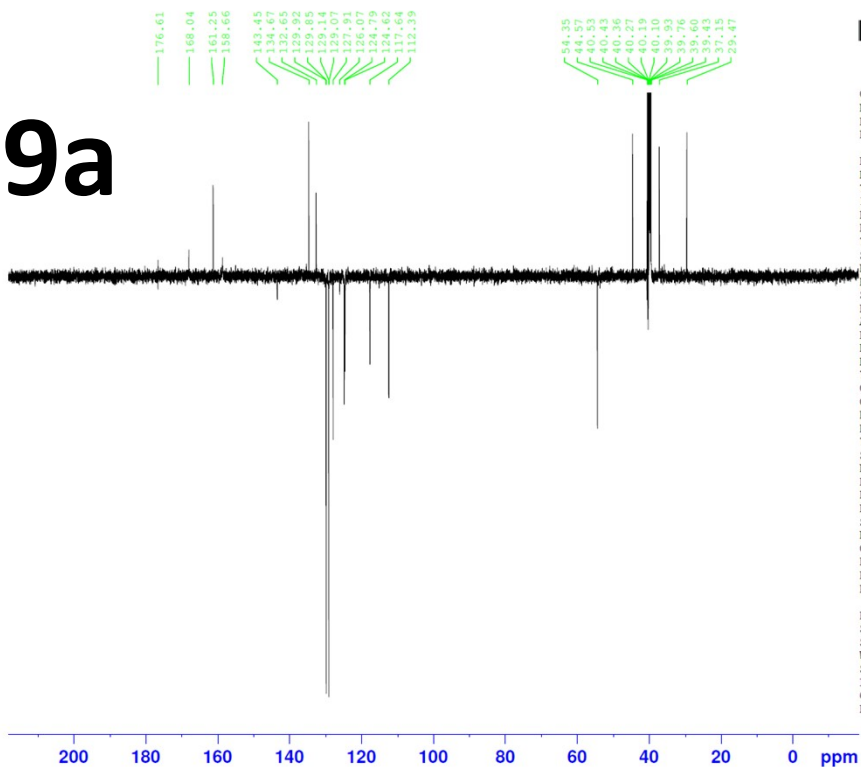


Current Data Parameters
 NAME NA110 melted
 EXPNO 1
 PROCNO 1

F2 - Acquisition Parameters
 Date_ 20190809
 Time 11.27 h
 INSTRUM spect
 PROBHD Z113652_0266 (Zg30
 PULPROG 65536
 TD 16
 SOLVENT DMSO
 NS 2
 DS 10000.000 Hz
 SWH 0.305176 Hz
 FIDRES 3.2767999 sec
 AQ 76.2
 RG 50.000 usec
 DW 13.50 usec
 DE 298.1 K
 TE 1.00000000 sec
 D1 1
 TD0 500.1330883 MHz
 SFO1 1H
 NUC1 10.00 usec
 P1 21.07600021 W
 PLW1

F2 - Processing parameters
 SI 65536
 SF 500.1300000 MHz
 WDW EM
 SSB 0
 LB 0.30 Hz
 GB 0
 PC 1.00

9a

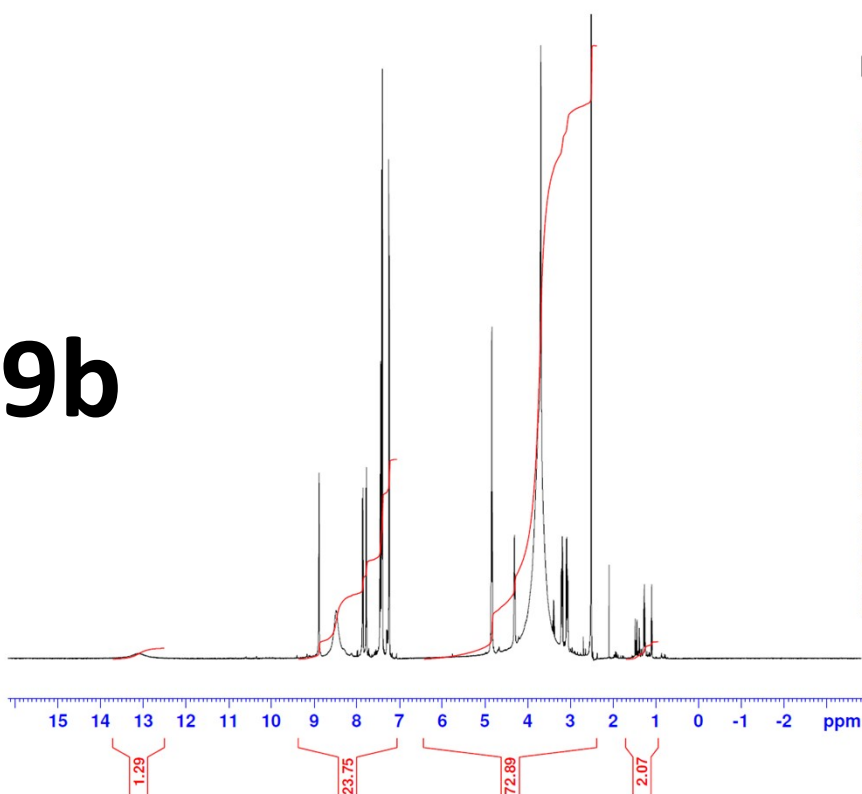


Current Data Parameters
 NAME NA110
 EXPNO 5
 PROCNO 1

F2 - Acquisition Parameters
 Date_ 20190821
 Time 1.03 h
 INSTRUM spect
 PROBHD Z113652_0266 (jmod
 PULPROG 65536
 TD 3072
 SOLVENT DMSO
 NS 4
 DS 29761.904 Hz
 SWH 0.908261 Hz
 FIDRES 1.1010048 sec
 AQ 189.93
 RG 16.800 usec
 DW 6.50 usec
 DE 298.1 K
 TE 145.0000000
 CNST1 1.0000000
 D1 2.00000000 sec
 D20 0.00689655 sec
 TD0 1
 SFO1 125.7703643 MHz
 NUC1 13C
 P1 10.00 usec
 P2 20.00 usec
 PLW1 74.02700043 W
 SFO2 500.1320005 MHz
 NUC2 1H
 CPDPRG2 waltz16
 PCPD2 80.00 usec
 PLW2 21.07600021 W
 PLW12 0.32931000 W

F2 - Processing parameters
 SI 32768
 SF 125.7577885 MHz
 WDW EM
 SSB 0
 LB 1.00 Hz
 GB 0
 PC 1.40

9b

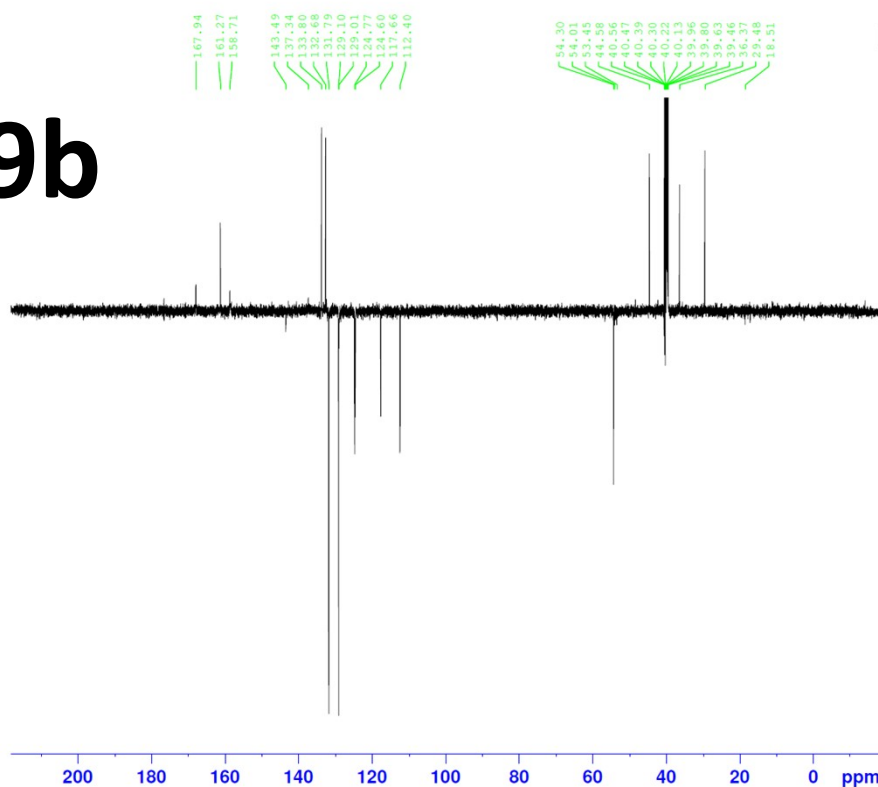


Current Data Parameters
NAME NAl18
EXPNO 1
PROCNO 1

F2 - Acquisition Parameters
Date_ 20190904
Time 16.53 h
INSTRUM spect
PROBHD Z113652_0266 ()
PULPROG zg30
TD 65536
SOLVENT DMSO
NS 16
DS 2
SWH 10000.000 Hz
FIDRES 0.305176 Hz
AQ 3.2767999 sec
RG 104.67
DW 50.000 usec
DE 13.50 usec
TE 298.1 K
D1 1.00000000 sec
TD0 1
SFO1 500.1330883 MHz
NUC1 1H
P1 10.00 usec
PLW1 21.07600021 W

F2 - Processing parameters
SI 65536
SF 500.1300000 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00

9b

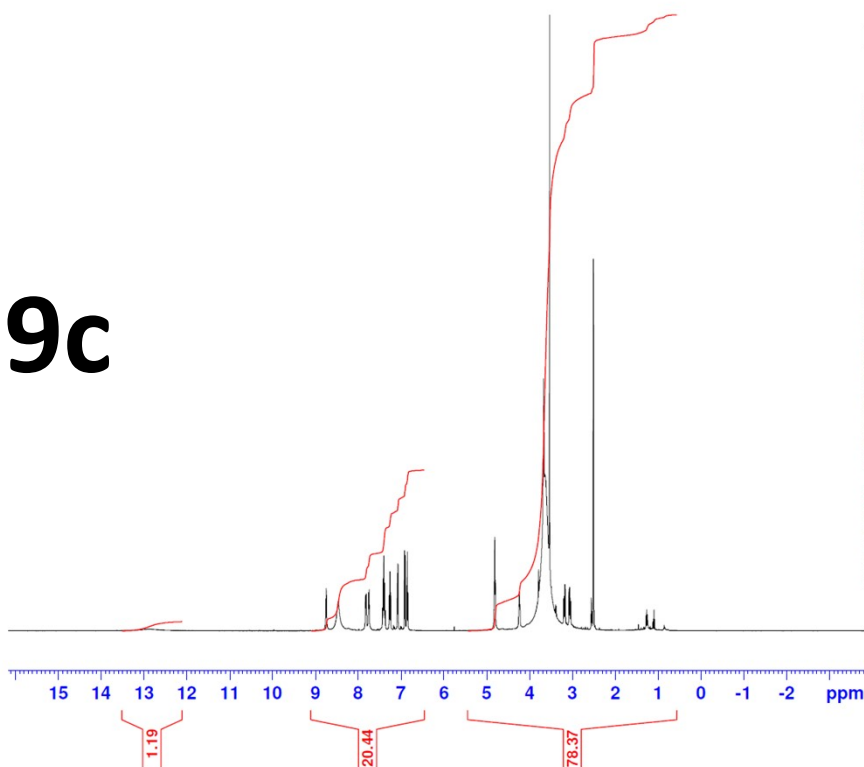


Current Data Parameters
NAME NAl18
EXPNO 5
PROCNO 1

F2 - Acquisition Parameters
Date_ 20190914
Time 3.47 h
INSTRUM spect
PROBHD Z113652_0266 ()
PULPROG jmod
TD 65536
SOLVENT DMSO
NS 3072
DS 4
SWH 29761.904 Hz
FIDRES 0.908261 Hz
AQ 1.1010048 sec
RG 189.93
DW 16.800 usec
DE 6.50 usec
TE 298.2 K
CNST2 145.0000000
CNST11 1.00000000
D1 2.00000000 sec
D20 0.00689655 sec
TD0 1
SFO1 125.7703643 MHz
NUC1 13C
P1 10.00 usec
F2 20.00 usec
PLW1 74.02700043 W
SFO2 500.1320005 MHz
NUC2 1H
CPDPRG2 waltz16
PCPD2 80.00 usec
PLW2 21.07600021 W
PLW12 0.32931000 W

F2 - Processing parameters
SI 32768
SF 125.7577885 MHz
WDW EM
SSB 0
LB 1.00 Hz
GB 0
PC 1.40

9c

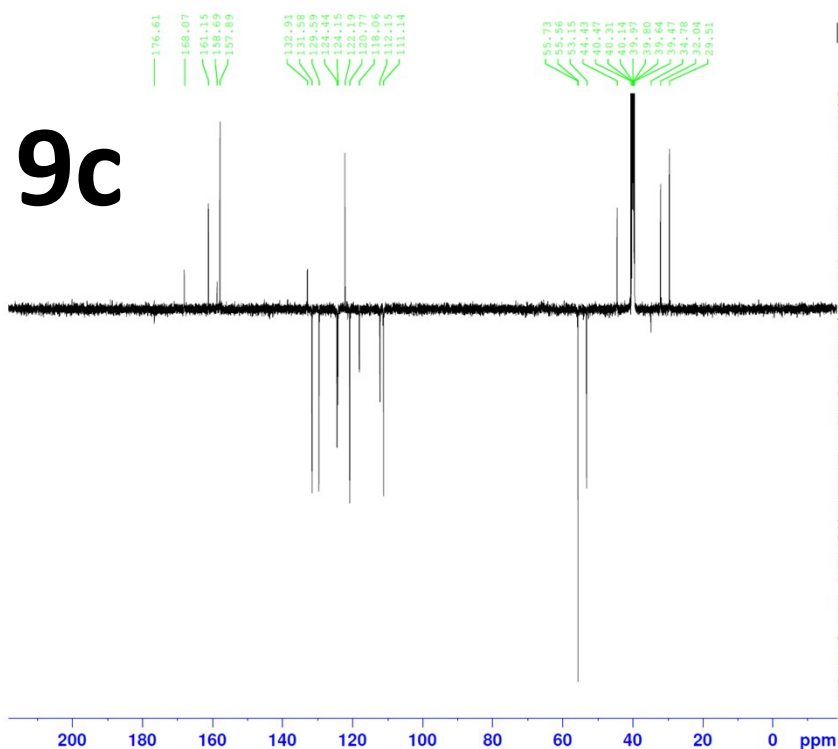


Current Data Parameters
NAME NA119
EXPNO 1
PROCNO 1

F2 - Acquisition Parameters
Date_ 20190910
Time 10.49 h
INSTRUM spect
PROBHD Z113652_0266 (
PULPROG zg30
TD 65536
SOLVENT DMSO
NS 16
DS 2
SWH 10000.000 Hz
FIDRES 0.305176 Hz
AQ 3.2767999 sec
RG 91.87
DW 50.000 usec
DE 13.50 usec
TE 298.1 K
D1 1.00000000 sec
TD0 1
SFO1 500.1330883 MHz
NUC1 1H
P1 10.00 usec
PLW1 21.07600021 W

F2 - Processing parameters
SI 65536
SF 500.1300000 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00

9c

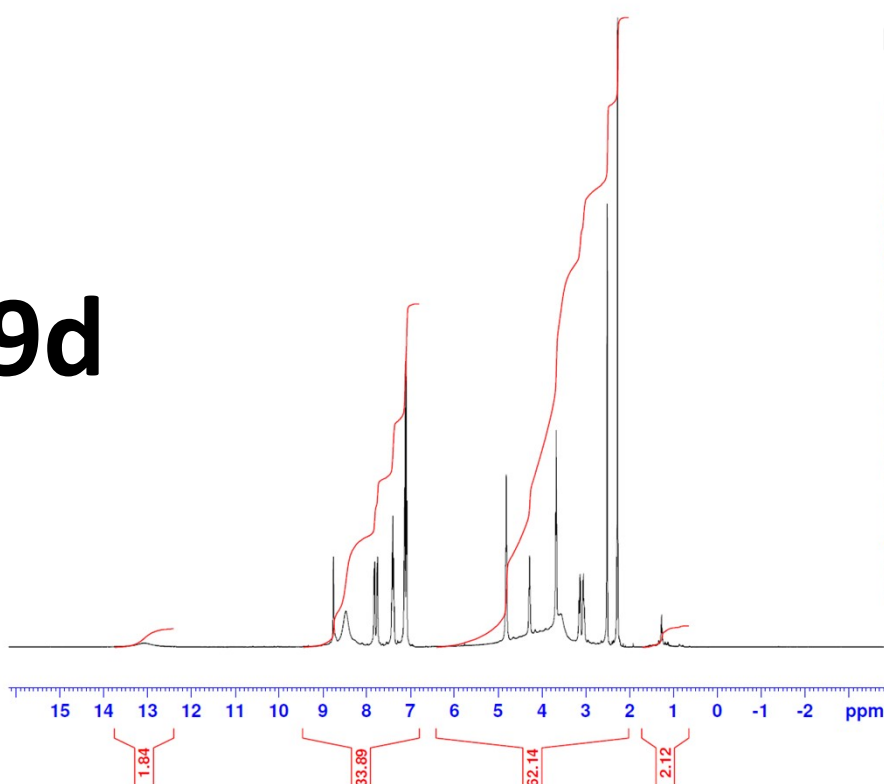


Current Data Parameters
NAME NA119
EXPNO 3
PROCNO 1

F2 - Acquisition Parameters
Date_ 20190918
Time 1.36 h
INSTRUM spect
PROBHD Z113652_0266 (
PULPROG jmod
TD 65536
SOLVENT DMSO
NS 3072
DS 4
SWH 29761.904 Hz
FIDRES 0.908261 Hz
AQ 1.1010048 sec
RG 189.93
DW 16.800 usec
DE 6.50 usec
TE 298.2 K
CNST2 145.0000000
CNST11 1.0000000
D1 2.00000000 sec
D20 0.00689655 sec
TD0 1
SFO1 125.7703643 MHz
NUC1 13C
P1 10.00 usec
P2 20.00 usec
PLW1 74.02700043 W
SFO2 500.1320005 MHz
NUC2 1H
CPDPRG2 waltz16
PCPD2 80.00 usec
PLW2 21.07600021 W
PLW12 0.32931000 W

F2 - Processing parameters
SI 32768
SF 125.7577885 MHz
WDW EM
SSB 0
LB 1.00 Hz
GB 0
PC 1.40

9d

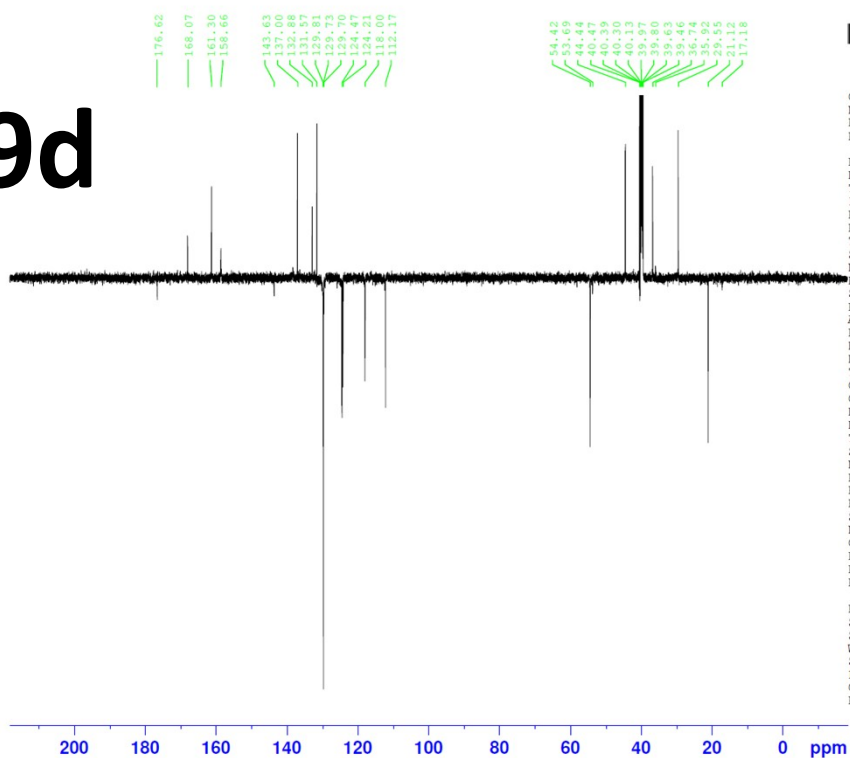


Current Data Parameters
 NAME NA128
 EXPNO 1
 PROCNO 1

F2 - Acquisition Parameters
 Date_ 20190920
 Time 16.44 h
 INSTRUM spect
 PROBHD Z113652_0266 ()
 PULPROG zg30
 TD 65536
 SOLVENT DMSO
 NS 16
 DS 2
 SWH 10000.000 Hz
 FIDRES 0.305176 Hz
 AQ 3.2767999 sec
 RG 104.67
 DW 50.000 usec
 DE 13.50 usec
 TE 298.1 K
 D1 1.0000000 sec
 TD0 1
 SFO1 500.1330883 MHz
 NUC1 1H
 P1 10.00 usec
 PLW1 21.07600021 W

F2 - Processing parameters
 SI 65536
 SF 500.1300000 MHz
 WDW EM
 SSB 0
 LB 0.30 Hz
 GB 0
 PC 1.00

9d



Current Data Parameters
 NAME NA128
 EXPNO 3
 PROCNO 1

F2 - Acquisition Parameters
 Date_ 20191008
 Time 1.33 h
 INSTRUM spect
 PROBHD Z113652_0266 ()
 PULPROG jmod
 TD 65536
 SOLVENT DMSO
 NS 3072
 DS 4
 SWH 29761.904 Hz
 FIDRES 0.908261 Hz
 AQ 1.1010048 sec
 RG 189.93
 DW 16.800 usec
 DE 6.50 usec
 TE 298.1 K
 CNST2 145.0000000
 CNST11 1.0000000
 D1 2.0000000 sec
 D20 0.00689655 sec
 TD0 1
 SFO1 125.7703643 MHz
 NUC1 13C
 P1 10.00 usec
 P2 20.00 usec
 PLW1 74.02700043 W
 SFO2 500.1320005 MHz
 NUC2 1H
 CPDPRG2 waltz16
 PCPD2 80.00 usec
 PLW2 21.07600021 W
 PLW12 0.32931000 W

F2 - Processing parameters
 SI 32768
 SF 125.7577885 MHz
 WDW EM
 SSB 0
 LB 1.00 Hz
 GB 0
 PC 1.40

9d



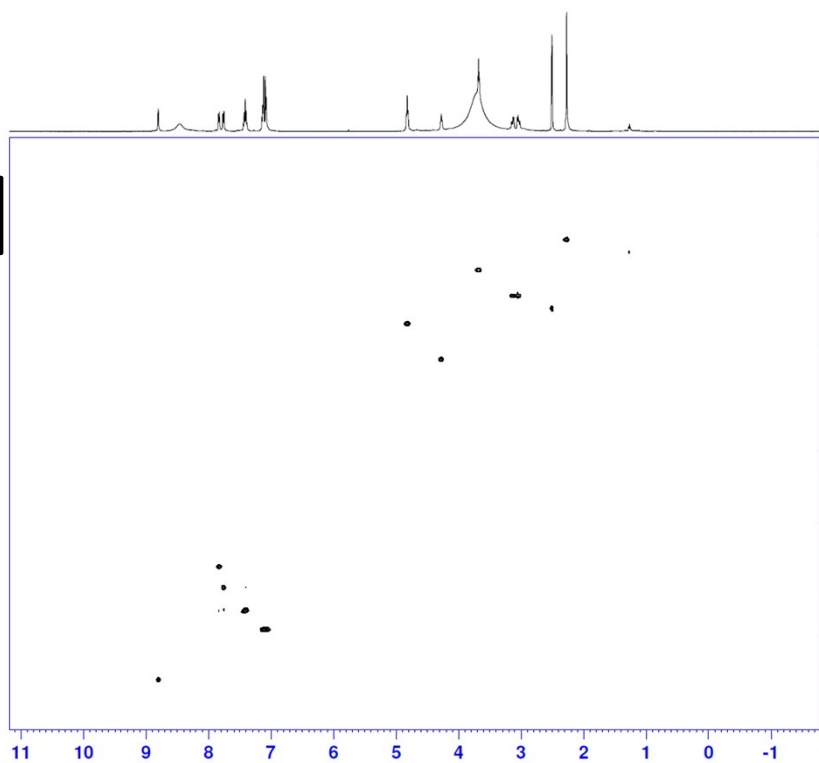
Current Data Parameters
NAME NA128
EXPNO 2
PROCNO 1

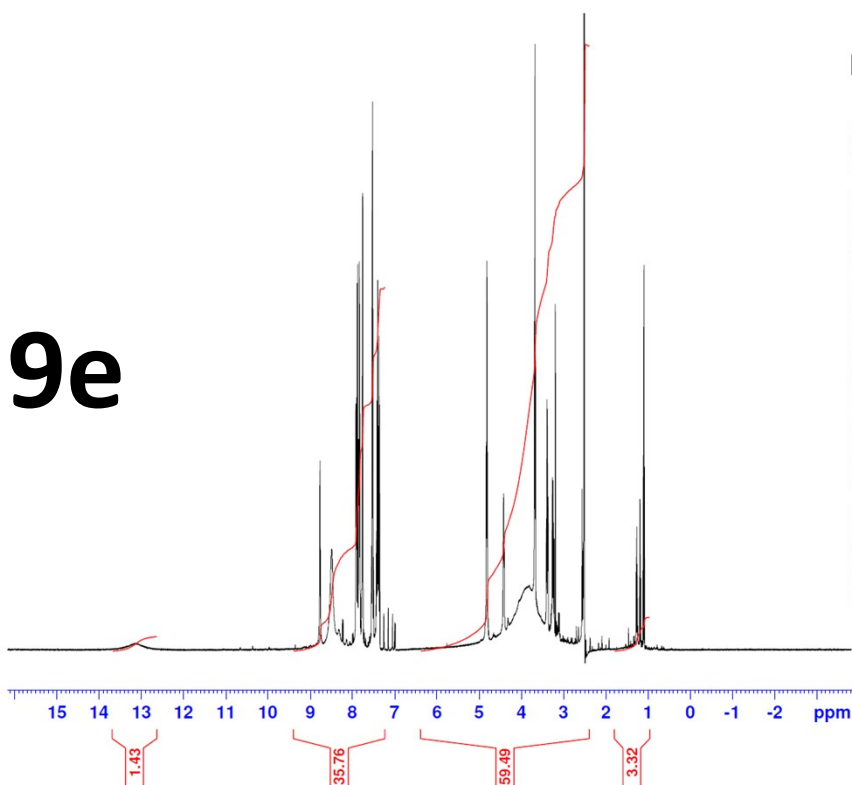
F2 - Acquisition Parameters
Date_ 20191009
Time 1.36 h
INSTRUM spect
PROBHD 513652_0246 f
PULPROG zgpg30
TD 65536
SOLVENT DMSO
NS 2
DS 2
SWH 6480.306 Hz
FIDRES 6.341315 Hz
AQ 0.191660 sec
RG 189.93
RW 77.000 usec
DE 6.90 usec
TE 300.2 K
CMT2 149.0000000
CMT11 -0.0000000
D0 0.0000300 sec
D1 1.0000000 sec
D11 0.00172414 sec
D14 0.0000000 sec
D16 0.0000000 sec
D18 0.0000000 sec
IN0 0.0000410 sec
TD0 500.132304 MHz
NUC1 1H
P1 10.00 usec
P2 20.00 usec
P2A 0 usec
P2B 11.07600021 W
P2C 125.7672204 MHz
P2D 13C
CPCPRG2 gpg30
P3 10.00 usec
P4 500.00 usec
P4A 2000.00 usec
PCPD2 70.00 usec
PMA0 0 W
PMA2 74.02700043 W
PMA12 1.51069999 W
SPRAME3 Cpr60, 0.5, 20.1
SPOAL3 0 Hz
SPW3 11.31000042 W
SPRAME7 Cpr50000, 4
SPOAL7 0 Hz
SPW7 11.31000042 W
GPRAME11 ENDQ15, 100
GPR1 80.00 Hz
GPRAME12 ENDQ15, 100
GPR2 20.10 Hz
GPRAME13 ENDQ15, 100
GPR3 11.00 Hz
GPRAME14 ENDQ15, 100 Hz
GPR4 1000.00 usec
P16 600.00 usec
P19 0 Hz

F1 - Acquisition parameters
TD 294
SF01 125.767170 MHz
FIDRES 162.095048 Hz
SW 144.862 ppm
FPMODE Echo-AntiEcho

F2 - Processing parameters
SI 3274
SF 500.130000 MHz
WDW QFTUNE
SSB 2
LB 0 Hz
GB 0
PC 1.40

F1 - Processing parameters
SI 3274
MC2 echo-anti-echo
SF 125.7577880 MHz
WDW QFTUNE
SSB 2
LB 0 Hz
GB 0

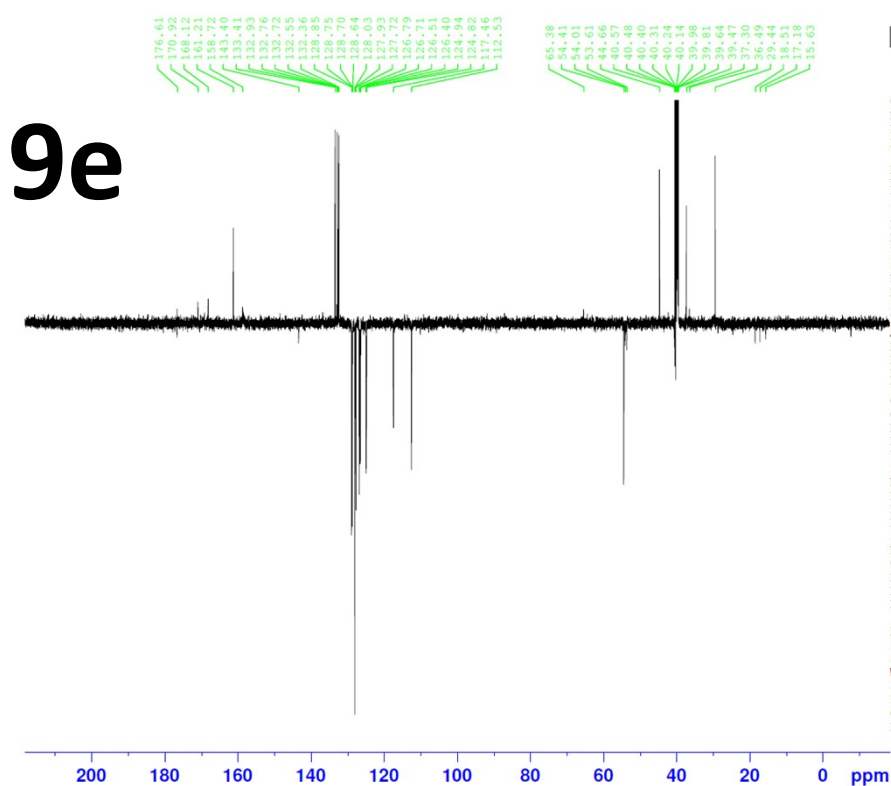




Current Data Parameters
 NAME NA120 repeat
 EXPNO 1
 PROCNO 1

F2 - Acquisition Parameters
 Date_ 20200219
 Time 18.16 h
 INSTRUM spect
 PROBHD Z113652_0266 ()
 PULPROG zg30
 TD 65536
 SOLVENT DMSO
 NS 16
 DS 2
 SWH 10000.000 Hz
 FIDRES 0.305176 Hz
 AQ 3.2767999 sec
 RG 133.44
 DW 50.000 usec
 DE 13.50 usec
 TE 298.1 K
 D1 1.00000000 sec
 TD0 1
 SFO1 500.1330883 MHz
 NUC1 1H
 P1 10.00 usec
 PLW1 21.07600021 W

F2 - Processing parameters
 SI 65536
 SF 500.1300000 MHz
 WDW EM
 SSB 0
 LB 0.30 Hz
 GB 0
 PC 1.00

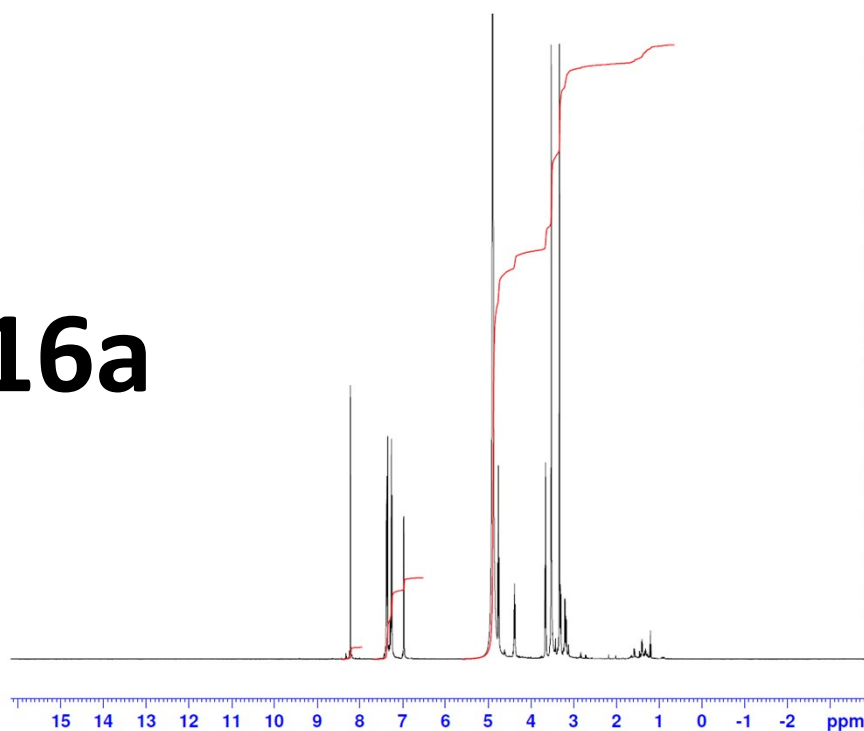


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 EXPNO 3
 PROCNO 1

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 Time 4.21 h
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 PROBHD Z113652_0266 ()
 PULPROG jmod
 TD 65536
 SOLVENT DMSO
 NS 3072
 DS 4
 SWH 29761.904 Hz
 FIDRES 0.908261 Hz
 AQ 1.1010048 sec
 RG 189.93
 DW 16.800 usec
 DE 6.50 usec
 TE 298.2 K
 CNST2 145.0000000
 CNST11 1.00000000
 D1 2.00000000 sec
 D20 0.00689655 sec
 TD0 1
 SFO1 125.7703643 MHz
 NUC1 13C
 P1 10.00 usec
 P2 20.00 usec
 PLW1 74.02700043 W
 SFO2 500.1320005 MHz
 NUC2 1H
 CPDPRG2 waltz16
 PCPD2 80.00 usec
 PLW2 21.07600021 W
 PLW12 0.32931000 W

F2 - Processing parameters
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 WDW EM
 SSB 0
 LB 1.00 Hz
 GB 0
 PC 1.40

16a

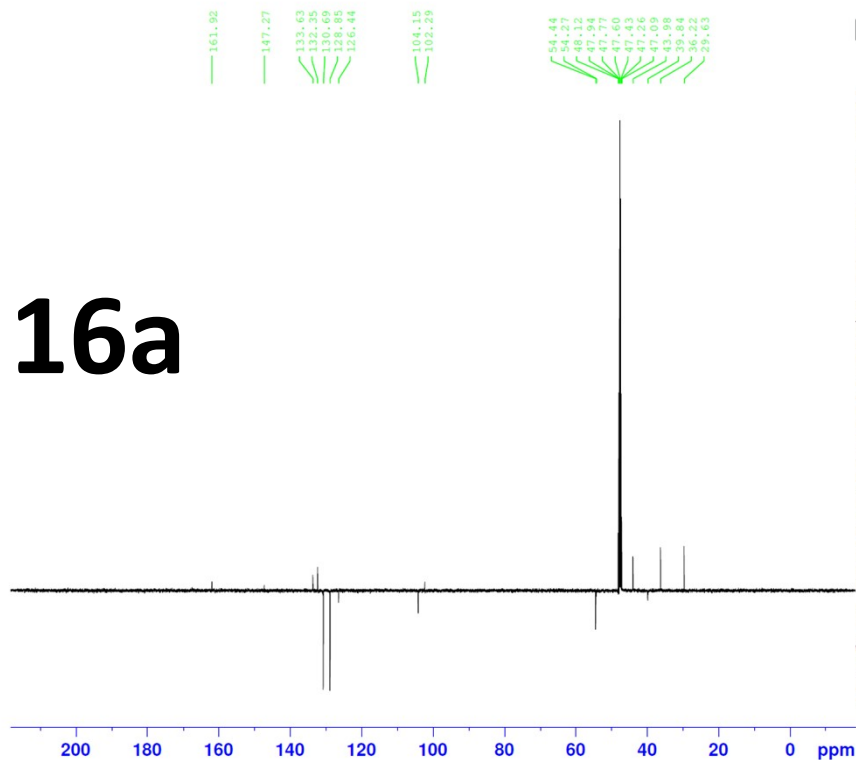


Current Data Parameters
NAME NA1111 MeOD
EXPNO 1
PROCNO 1

F2 - Acquisition Parameters
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Time 16.13 h
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PULPROG zg30
TD 65536
SOLVENT MeOD
NS 16
DS 2
SWH 10000.000 Hz
FIDRES 0.305176 Hz
AQ 3.2767999 sec
RG 91.87
DW 50.000 usec
DE 13.50 usec
TE 298.1 K
D1 1.00000000 sec
TD0 1
SFO1 500.1330883 MHz
NUC1 1H
P1 10.00 usec
PLW1 21.07600021 W

F2 - Processing parameters
SI 65536
SF 500.1300000 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00

16a

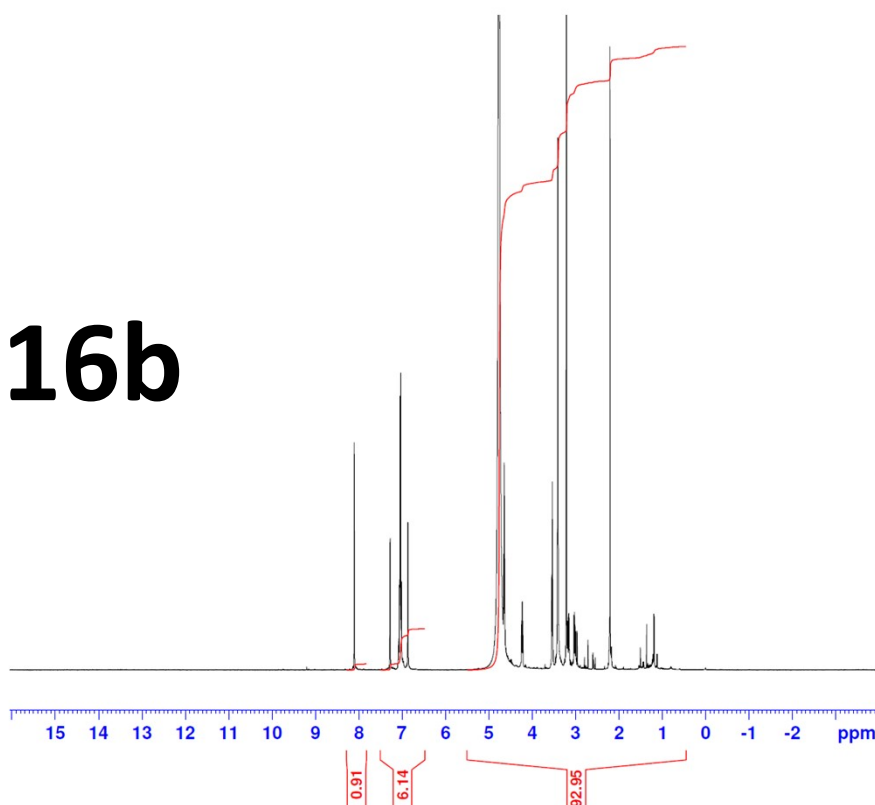


Current Data Parameters
NAME NA1111 MeOD
EXPNO 2
PROCNO 1

F2 - Acquisition Parameters
Date_ 20200226
Time 22.49 h
INSTRUM spect
PROBHD Z113652_0266 ()
PULPROG jmod
TD 65536
SOLVENT MeOD
NS 1024
DS 4
SWH 29761.904 Hz
FIDRES 0.908261 Hz
AQ 1.1010048 sec
RG 189.93
DW 16.800 usec
DE 6.50 usec
TE 298.1 K
CNST2 145.0000000
CNST11 1.0000000
D1 2.00000000 sec
D20 0.00689655 sec
TD0 1
SFO1 125.7703643 MHz
NUC1 13C
P1 10.00 usec
P2 20.00 usec
PLW1 74.02700043 W
SFO2 500.1320005 MHz
NUC2 1H
CPDPRG2 waltz16
PCPD2 80.00 usec
PLW2 21.07600021 W
PLW12 0.32931000 W

F2 - Processing parameters
SI 32768
SF 125.7577885 MHz
WDW EM
SSB 0
LB 1.00 Hz
GB 0
PC 1.40

16b

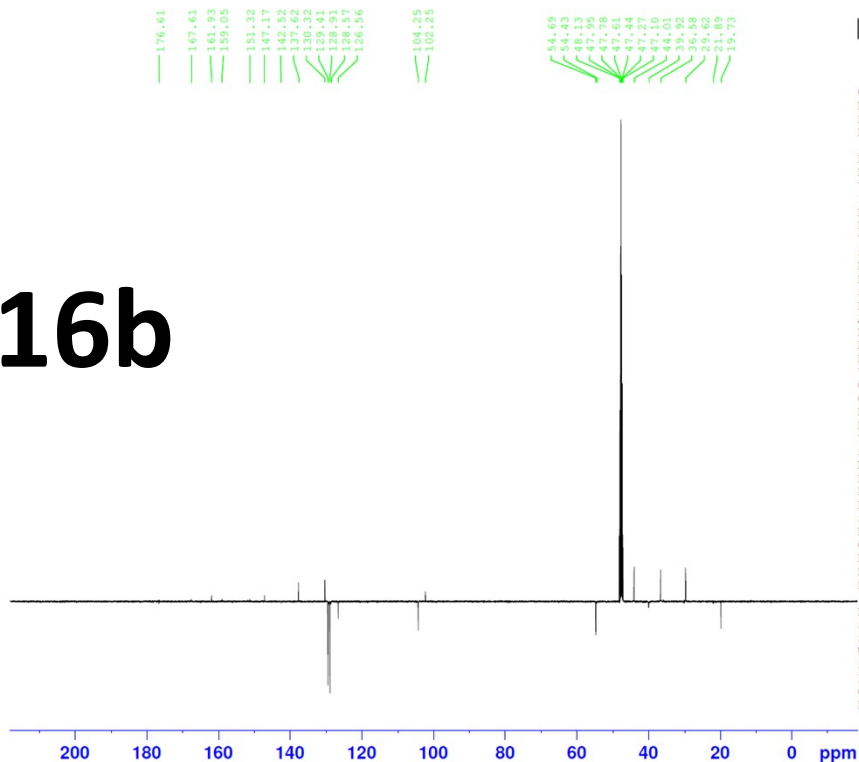


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 PROCNO 1

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 PULPROG zg30
 ID 65536
 SOLVENT MeOD
 NS 16
 DS 2
 SWH 10000.000 Hz
 FIDRES 0.305176 Hz
 AQ 3.2767999 sec
 RG 76.2
 DW 50.000 usec
 DE 13.50 usec
 TE 298.1 K
 D1 1.00000000 sec
 TD0 1
 SFO1 500.1330883 MHz
 NUC1 1H
 P1 10.00 usec
 PLW1 21.07600021 W

F2 - Processing parameters
 SI 65536
 SF 500.1300594 MHz
 WDW EM
 SSB 0
 LB 0.30 Hz
 GB 0
 PC 1.00

16b

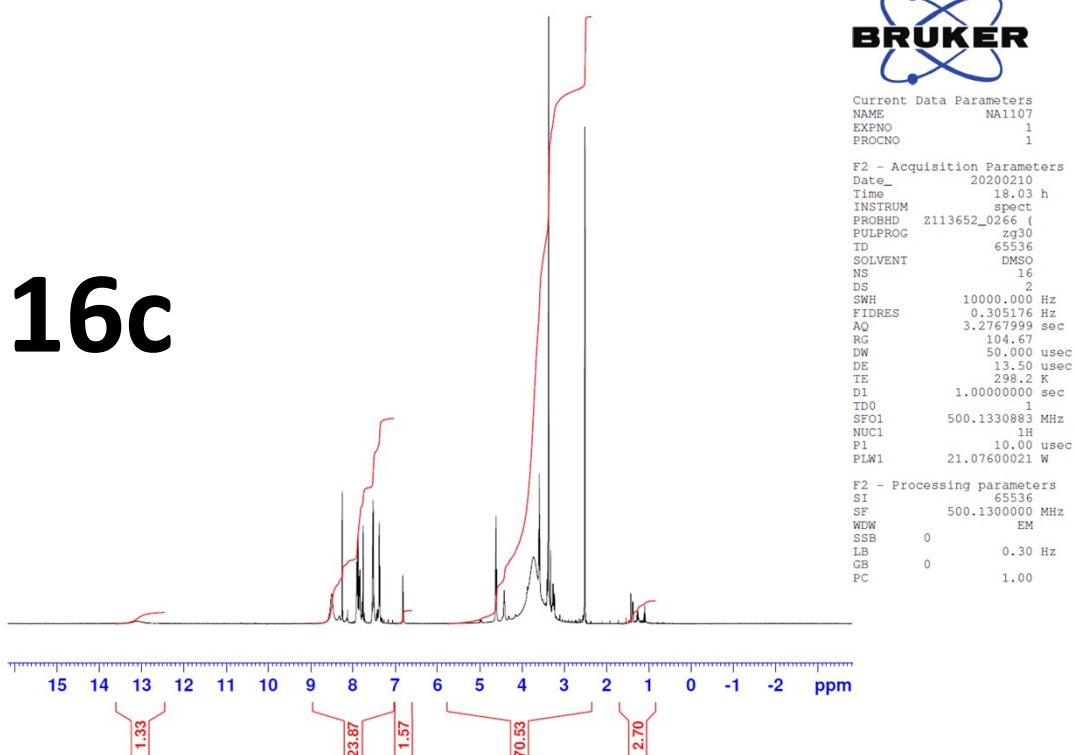


Current Data Parameters
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 EXPNO 2
 PROCNO 1

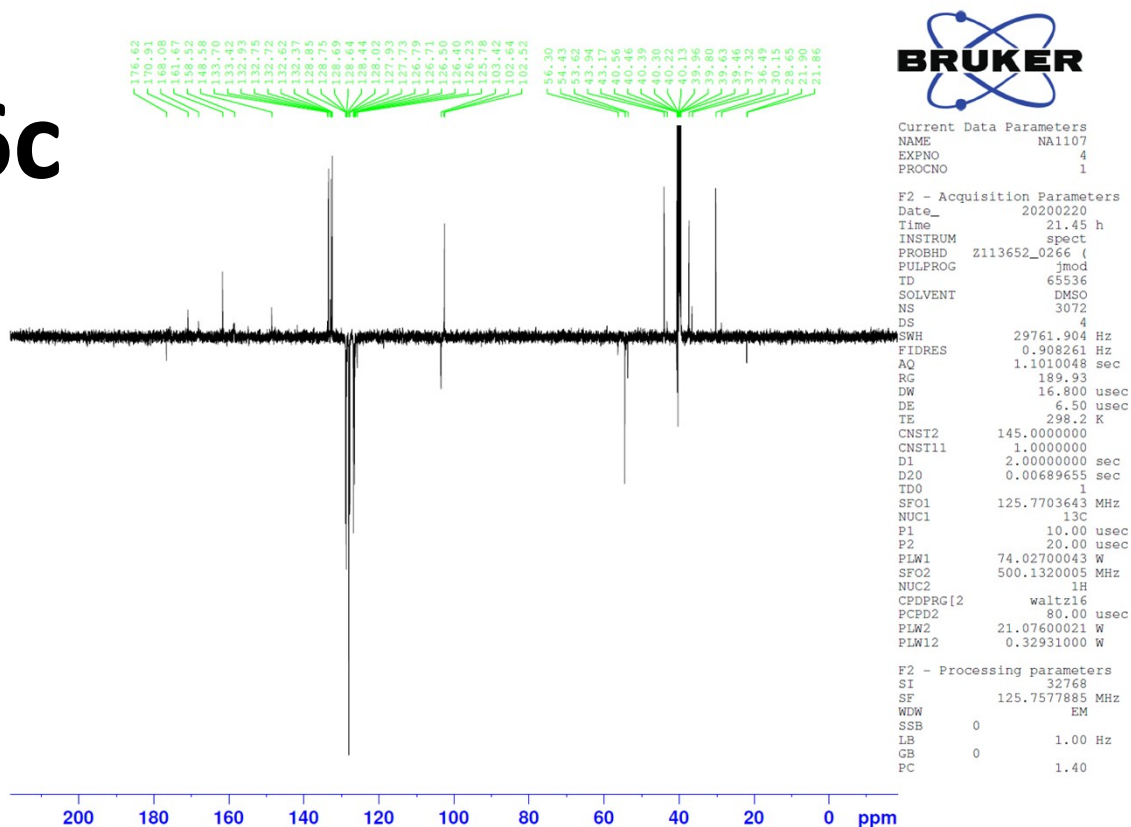
F2 - Acquisition Parameters
 Date_ 20200226
 Time 0.40 h
 INSTRUM spect
 PROBHD Z113652_0266 (
 PULPROG jmod
 ID 65536
 SOLVENT MeOD
 NS 3072
 DS 4
 SWH 29761.904 Hz
 FIDRES 0.908261 Hz
 AQ 1.1010048 sec
 RG 189.93
 DW 16.800 usec
 DE 6.50 usec
 TE 298.1 K
 CNST2 145.0000000
 CNST11 1.0000000
 D1 2.00000000 sec
 D20 0.00689655 sec
 TD0 1
 SFO1 125.7703643 MHz
 NUC1 13C
 P1 10.00 usec
 P2 20.00 usec
 PLW1 74.02700043 W
 SFO2 500.1320005 MHz
 NUC2 1H
 CPDPRG[2] waltz16
 PCPD2 80.00 usec
 PLW2 21.07600021 W
 PLW12 0.32931000 W

F2 - Processing parameters
 SI 32768
 SF 125.7577885 MHz
 WDW EM
 SSB 0
 LB 1.00 Hz
 GB 0
 PC 1.40

16c



16c



3.3. HPLC Charts:

5a

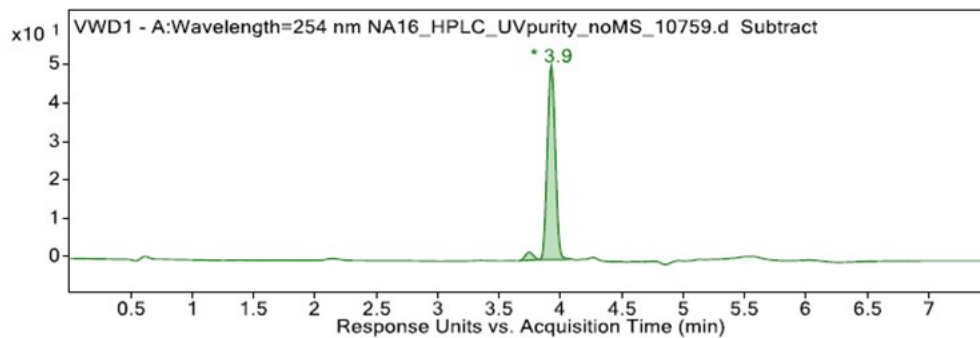


Figure: Base peak or HPLC chromatogram (indicated in left hand corner)

User Chromatogram Peak List

RT (min)	Area	Area %	Area Sum (%)	Symmetry	Width (min)
3.70	9.62	4.21	4.04	1.25	0.200
3.90	228.55	100.00	95.96	1.02	0.200

5b

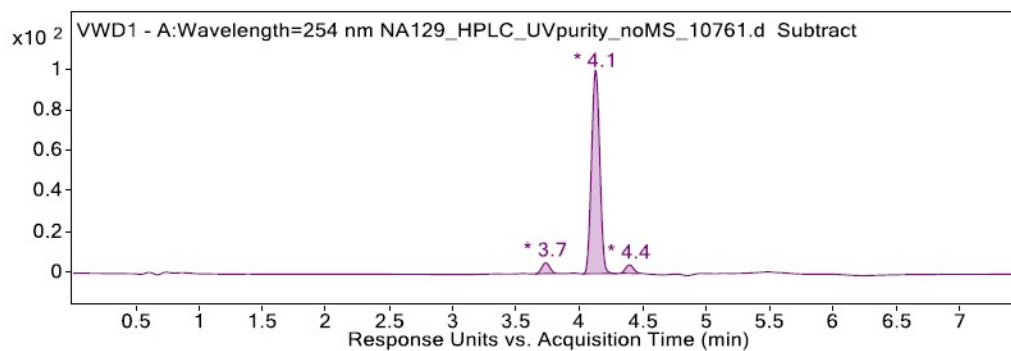
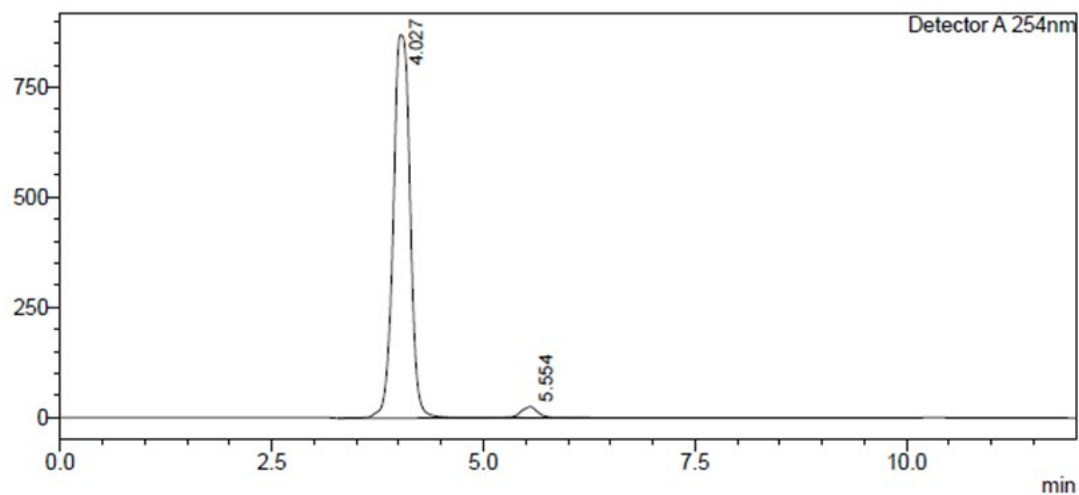


Figure: Base peak or HPLC chromatogram (indicated in left hand corner)

User Chromatogram Peak List

RT (min)	Area	Area %	Area Sum (%)	Symmetry	Width (min)
3.70	23.51	5.17	4.73	1.19	0.200
4.10	454.63	100.00	91.53	1.14	0.300
4.40	18.54	4.08	3.73	1.23	0.100

6a

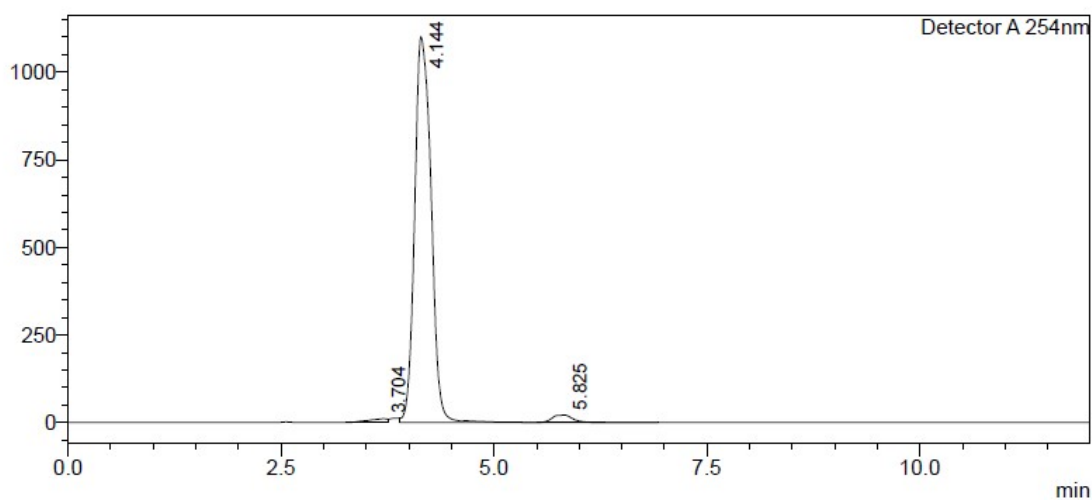


<Peak Table>

Detector A 254nm

Peak#	Ret. Time	Area	Height	Conc.	Area%	Unit	Mark
1	4.027	12067622	869684	97.334	97.334		S
2	5.554	330540	24671	2.666	2.666		TV
Total		12398162	894354		100.000		

6b

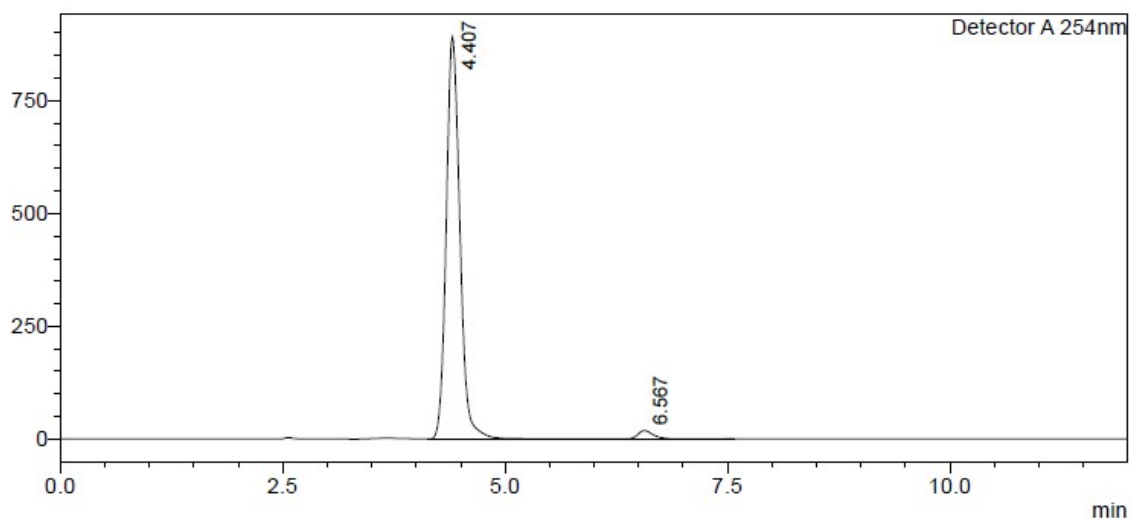


<Peak Table>

Detector A 254nm

Peak#	Ret. Time	Area	Height	Conc.	Area%	Unit	Mark
1	3.704	172783	10747	1.123	1.123		
2	4.144	14873977	1100700	96.664	96.664		SV
3	5.825	340571	21063	2.213	2.213		T
Total		15387331	1132510		100.000		

6c

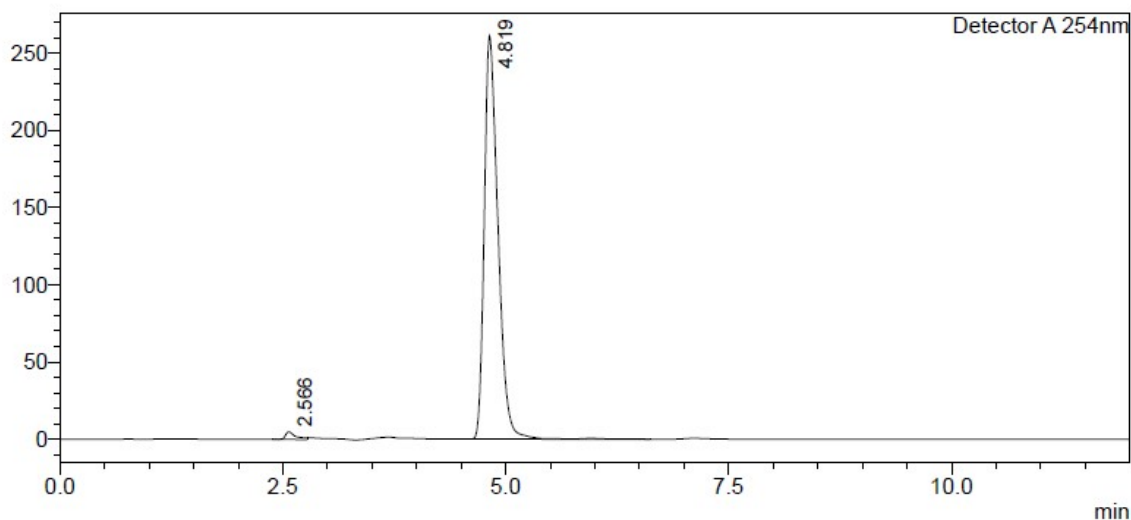


<Peak Table>

Detector A 254nm

Peak#	Ret. Time	Area	Height	Conc.	Area%	Unit	Mark
1	4.407	9583264	891048	97.632	97.632		SV
2	6.567	232408	18956	2.368	2.368		T
Total		9815672	910004		100.000		

6d

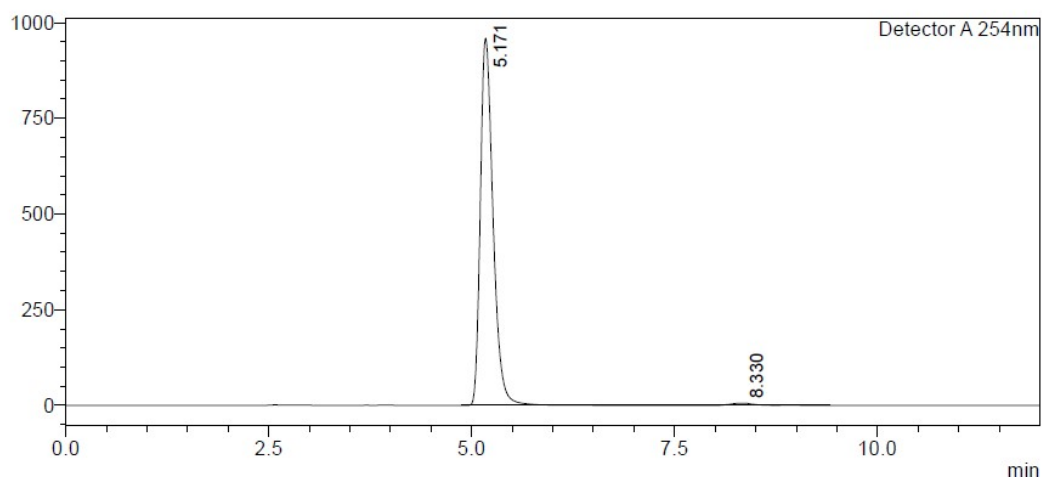


<Peak Table>

Detector A 254nm

Peak#	Ret. Time	Area	Height	Conc.	Area%	Unit	Mark
1	2.566	38346	4863	1.353	1.353		
2	4.819	2794845	261036	98.647	98.647		S
Total		2833191	265899		100.000		

6e



<Peak Table>

Detector A 254nm

Peak#	Ret. Time	Area	Height	Conc.	Area%	Unit	Mark
1	5.171	10438829	958772	98.975	98.975		S
2	8.330	108114	5998	1.025	1.025		T
Total		10546943	964770		100.000		

7a

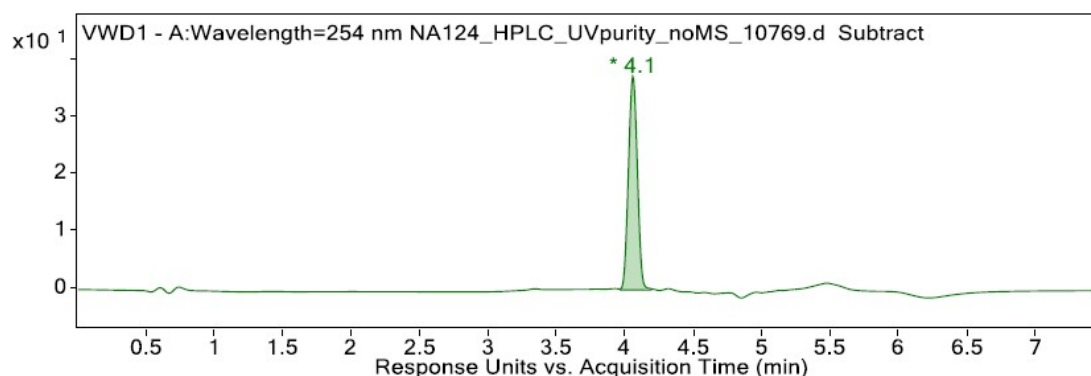


Figure: Base peak or HPLC chromatogram (indicated in left hand corner)

User Chromatogram Peak List

RT (min)	Area	Area %	Area Sum (%)	Symmetry	Width (min)
4.10	169.54	100.00	100.00	1.09	0.200

7b

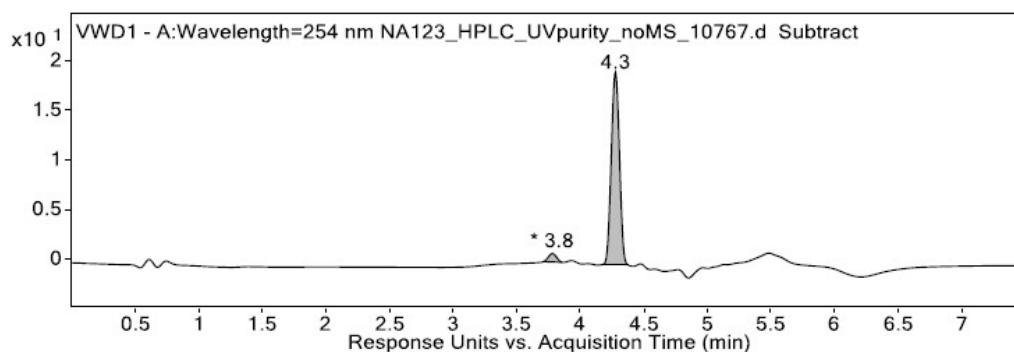


Figure: Base peak or HPLC chromatogram (indicated in left hand corner)

User Chromatogram Peak List

RT (min)	Area	Area %	Area Sum (%)	Symmetry	Width (min)
3.80	3.72	4.30	4.12	1.06	0.100
4.30	86.49	100.00	95.88	0.96	0.200

7c

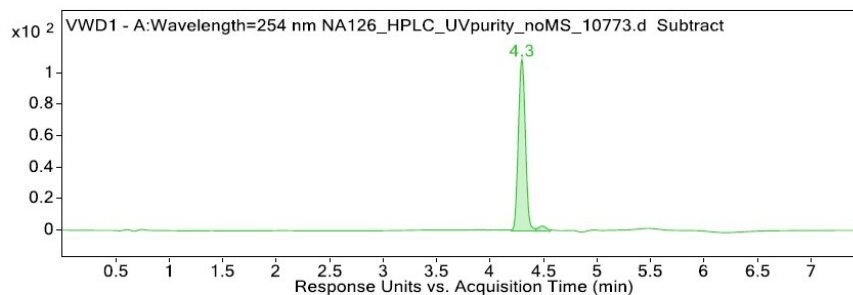


Figure: Base peak or HPLC chromatogram (indicated in left hand corner)

User Chromatogram Peak List

RT (min)	Area	Area %	Area Sum (%)	Symmetry	Width (min)
4.30	500.35	100.00	96.79	1.03	0.200
4.50	16.59	3.32	3.21	1.22	0.100

7d

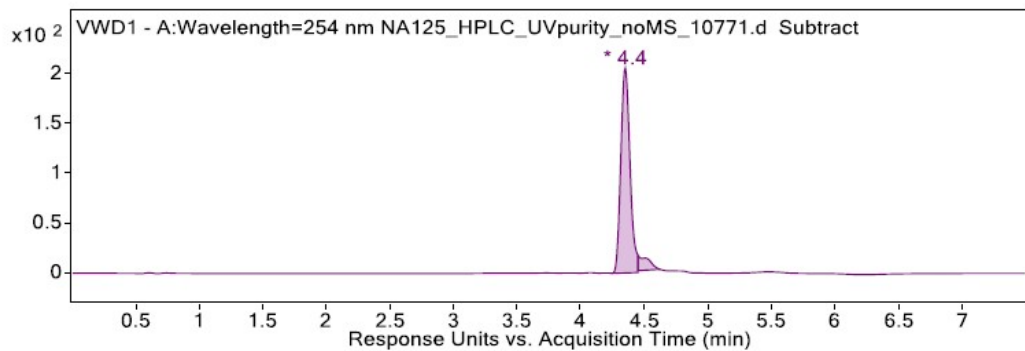
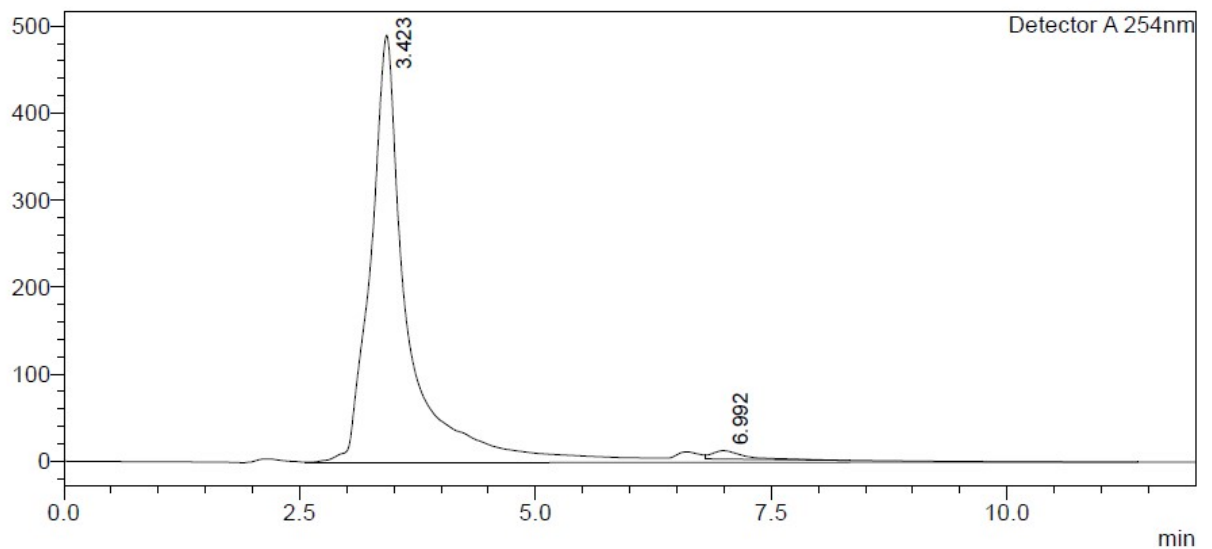


Figure: Base peak or HPLC chromatogram (indicated in left hand corner)

User Chromatogram Peak List

RT (min)	Area	Area %	Area Sum (%)	Symmetry	Width (min)
4.40	1031.23	100.00	92.43	1.36	0.200
4.50	84.51	8.20	7.57	Infinity	0.200

9a

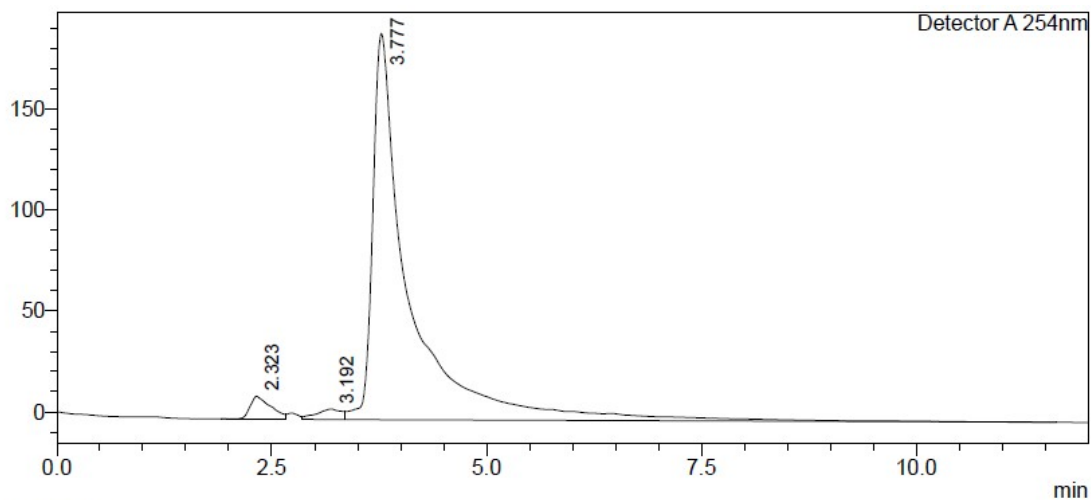


<Peak Table>

Detector A 254nm

Peak#	Ret. Time	Area	Height	Conc.	Unit	Mark	Name
1	3.423	14074909	491002	98.420		SV	
2	6.992	225940	9393	1.580		TV	
Total		14300849	500395				

9b

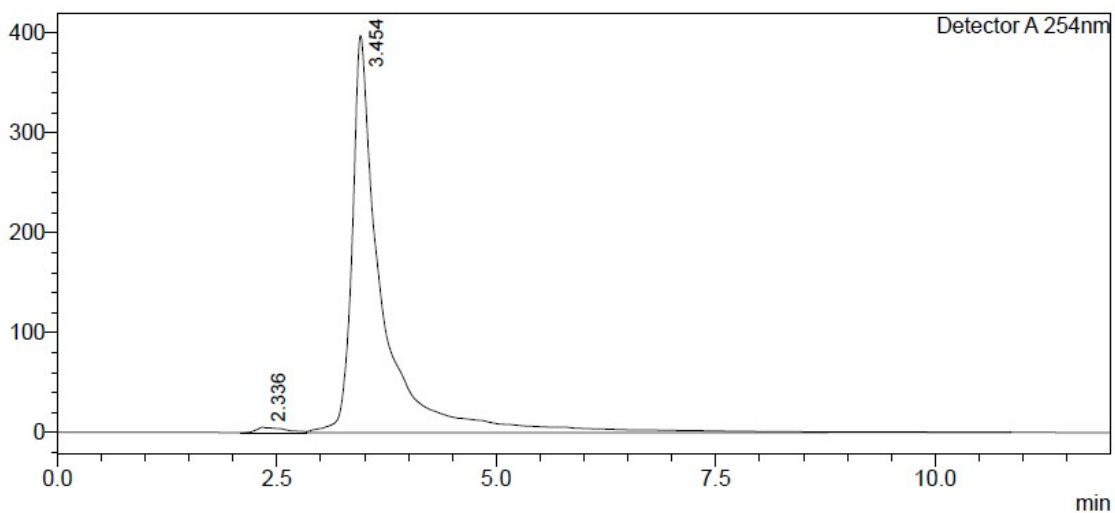


<Peak Table>

Detector A 254nm

Peak#	Ret. Time	Area	Height	Conc.	Area%	Unit	Mark
1	2.323	187965	11295	3.135	3.135		
2	3.192	102866	5150	1.716	1.716		V
3	3.777	5705411	190986	95.150	95.150		SV
Total		5996242	207430		100.000		

9c



<Peak Table>

Detector A 254nm

Peak#	Ret. Time	Area	Height	Conc.	Area%	Unit	Mark
1	2.336	115196	5326	1.199	1.199		
2	3.454	9492896	397489	98.801	98.801		SV
Total		9608093	402815		100.000		

9d

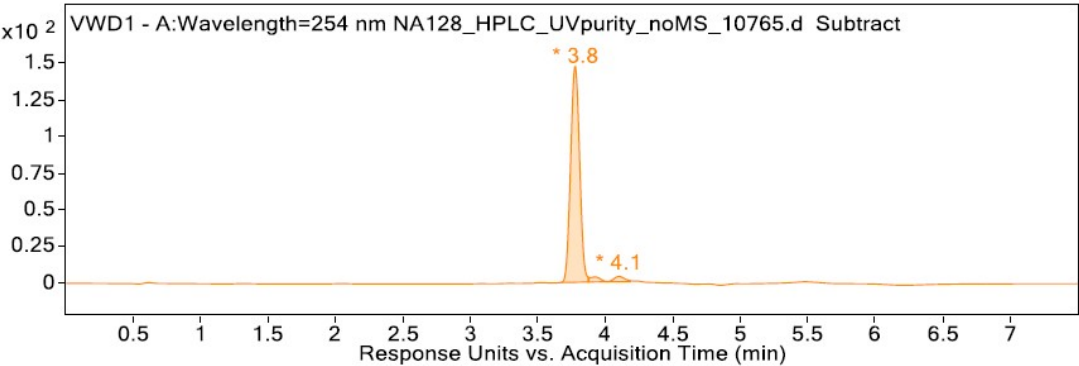


Figure: Base peak or HPLC chromatogram (indicated in left hand corner)

User Chromatogram Peak List

RT (min)	Area	Area %	Area Sum (%)	Symmetry	Width (min)
3.80	684.74	100.00	94.81	0.98	0.200
3.90	17.91	2.62	2.48	1.79	0.100
4.10	19.57	2.86	2.71	1.29	0.200

9e

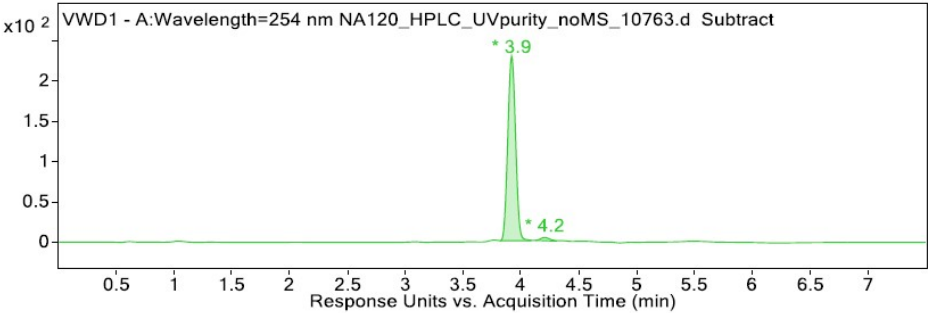


Figure: Base peak or HPLC chromatogram (indicated in left hand corner)

User Chromatogram Peak List

RT (min)	Area	Area %	Area Sum (%)	Symmetry	Width (min)
3.90	1072.78	100.00	97.96	1.09	0.300
4.20	22.36	2.08	2.04	0.95	0.200

16a

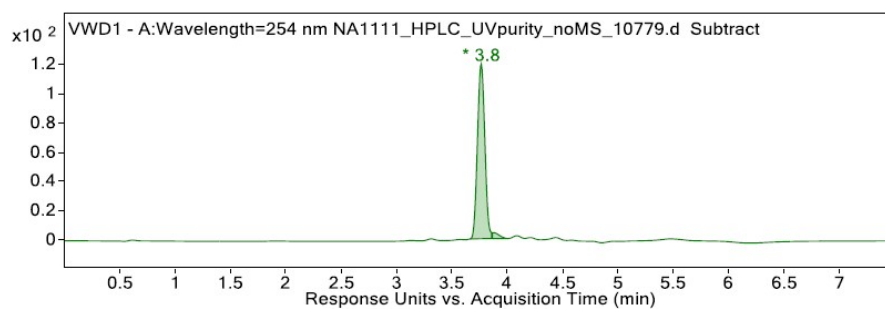


Figure: Base peak or HPLC chromatogram (indicated in left hand corner)

User Chromatogram Peak List

RT (min)	Area	Area %	Area Sum (%)	Symmetry	Width (min)
3.80	552.97	100.00	97.05	1.03	0.200
3.90	16.78	3.04	2.95	Infinity	0.100

16b

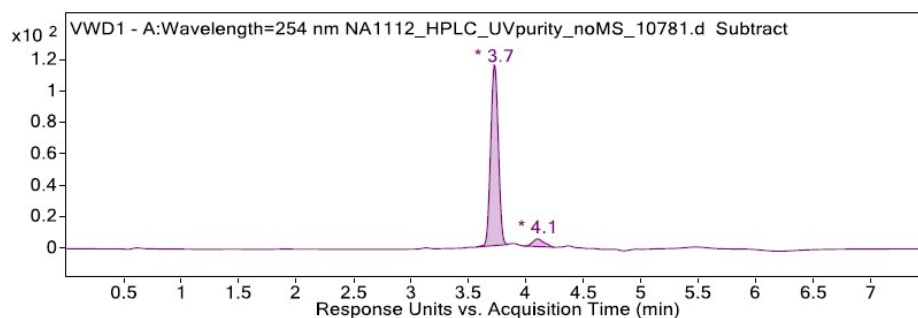


Figure: Base peak or HPLC chromatogram (indicated in left hand corner)

User Chromatogram Peak List

RT (min)	Area	Area %	Area Sum (%)	Symmetry	Width (min)
3.70	532.75	100.00	94.03	1.15	0.300
4.10	33.81	6.35	5.97	1.15	0.300

16c

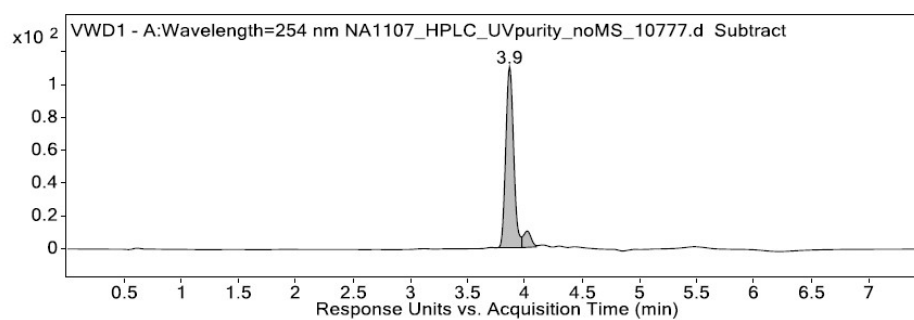


Figure: Base peak or HPLC chromatogram (indicated in left hand corner)

User Chromatogram Peak List

RT (min)	Area	Area %	Area Sum (%)	Symmetry	Width (min)
3.90	528.3	100.00	91.73	1.19	0.200
4.00	47.6	9.01	8.27	1.71	0.100

References:

1. P. Labute, C. Williams, M. Feher, E. Sourial and J. M. Schmidt, *J. Med. Chem.*, 2001, **44**, 1483-1490.
2. F. Madeira, Y. M. Park, J. Lee, N. Buso, T. Gur, N. Madhusoodanan, P. Basutkar, A. R. N. Tivey, S. C. Potter, R. D. Finn and R. Lopez, *Nucleic Acids Res.*, 2019, **47**, 636-641, Accessible from: [<https://www.ebi.ac.uk/Tools/msa/clustalo/>].
3. C. J. Williams, J. J. Headd, N. W. Moriarty, M. G. Prisant, L. L. Videau, L. N. Deis, V. Verma, D. A. Keedy, B. J. Hintze and V. B. Chen, *Protein Sci.*, 2018, **27**, 293-315.
4. M. Wiederstein and M. J. Sippl, *Nucleic Acids Res.*, 2007, **35**, W407-W410, Accessible from: [<https://prosa.services.came.sbg.ac.at/prosa.php>].
5. M. J. Sippl, *Proteins: Struct., Funct., Bioinf.*, 1993, **17**, 355-362.
6. D. Eisenberg, R. Lüthy and J. U. Bowie, *Meth. Enzymol*, 1997, **277**, 396-404.
7. S. S. Elbaramawi, C. Hughes, J. Richards, A. Gupta, S. M. Ibrahim, E.-S. M. Lashine, M. E. El-Sadek, A. J. O'Neill, M. Wootton and J. M. Bullard, *Egypt. J. Chem.*, 2018, **61**, 9-25.
8. Ş. Demirayak, K. Benkli and K. Güven, *Eur. J. Med. Chem.*, 2000, **35**, 1037-1040.
9. G. H. Hitchings, K. W. Ledig and R. A. West, *US Pat.*, US3037980A , 1962.