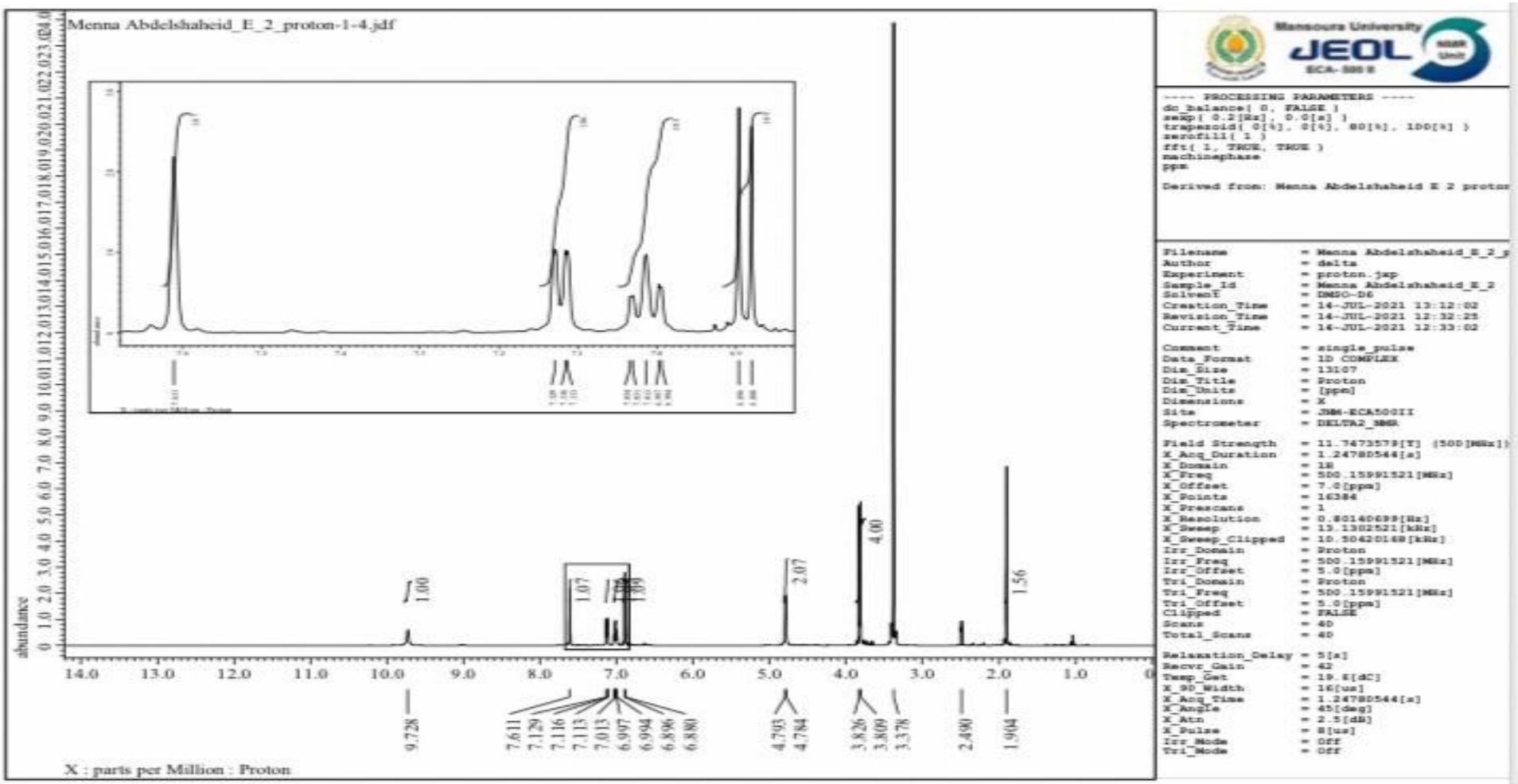
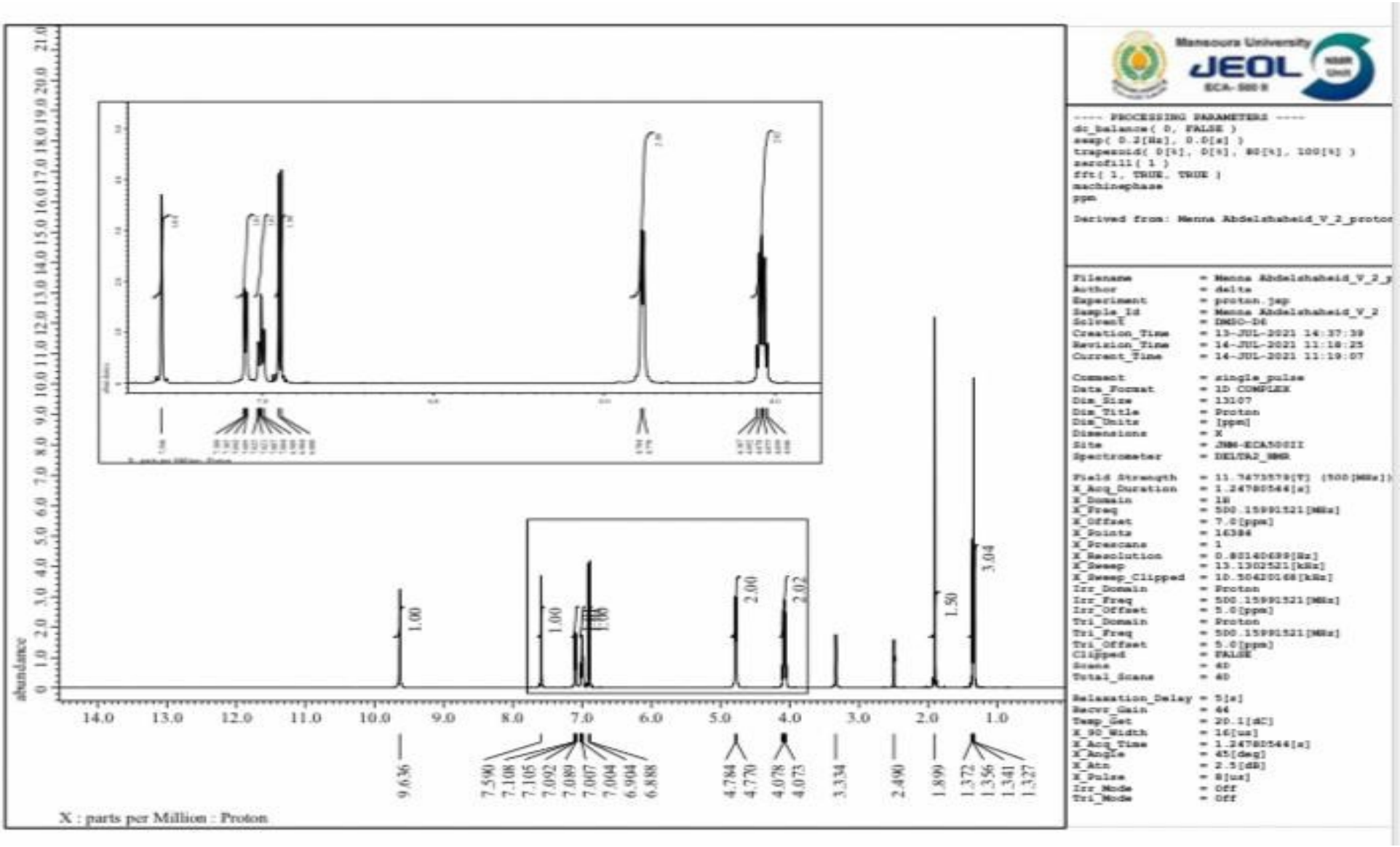
Electronic Supplementary Material (ESI) for RSC Advances.

Supplementary material

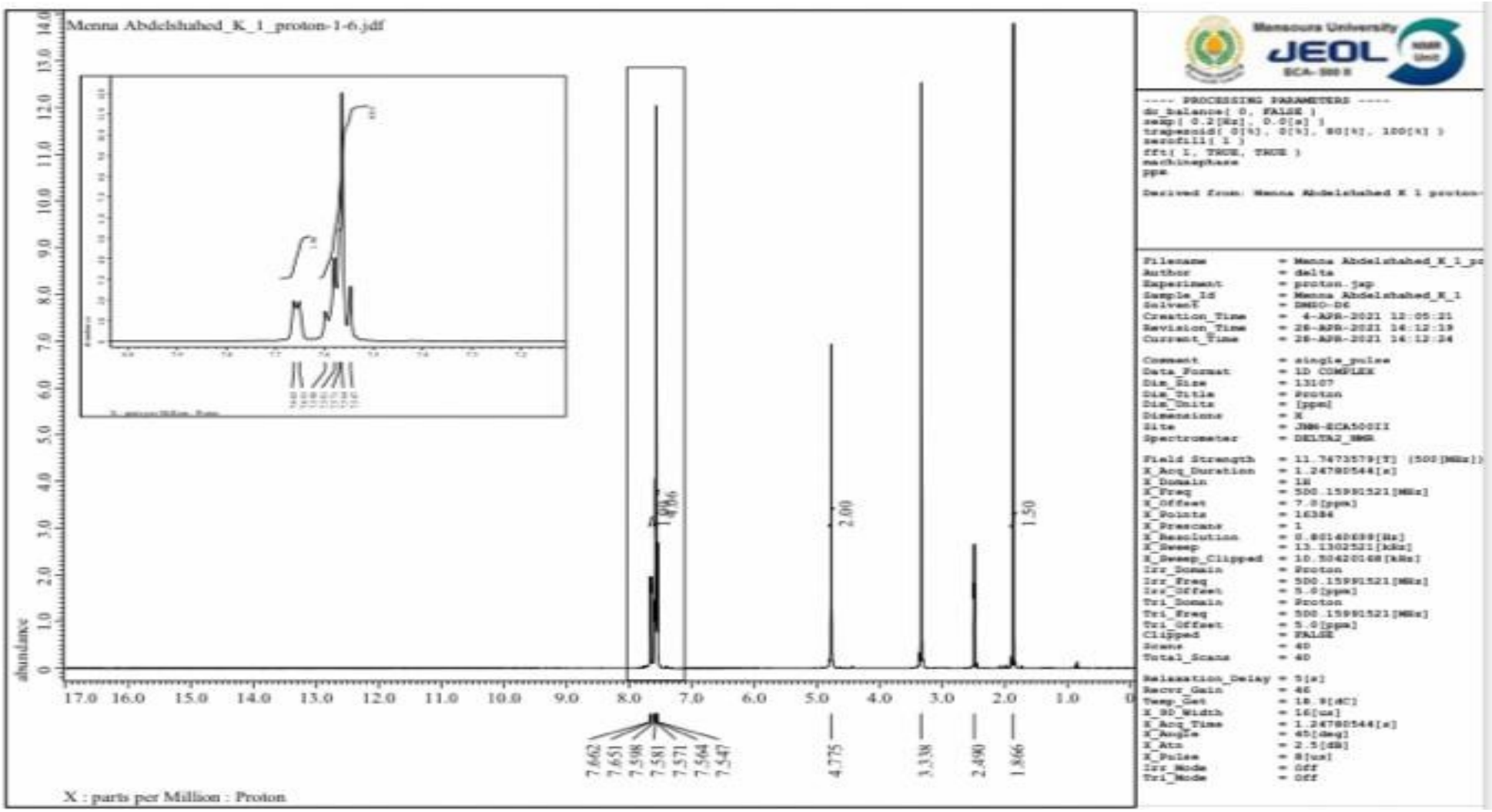
S1: ^{1}H-NMR of 3a:



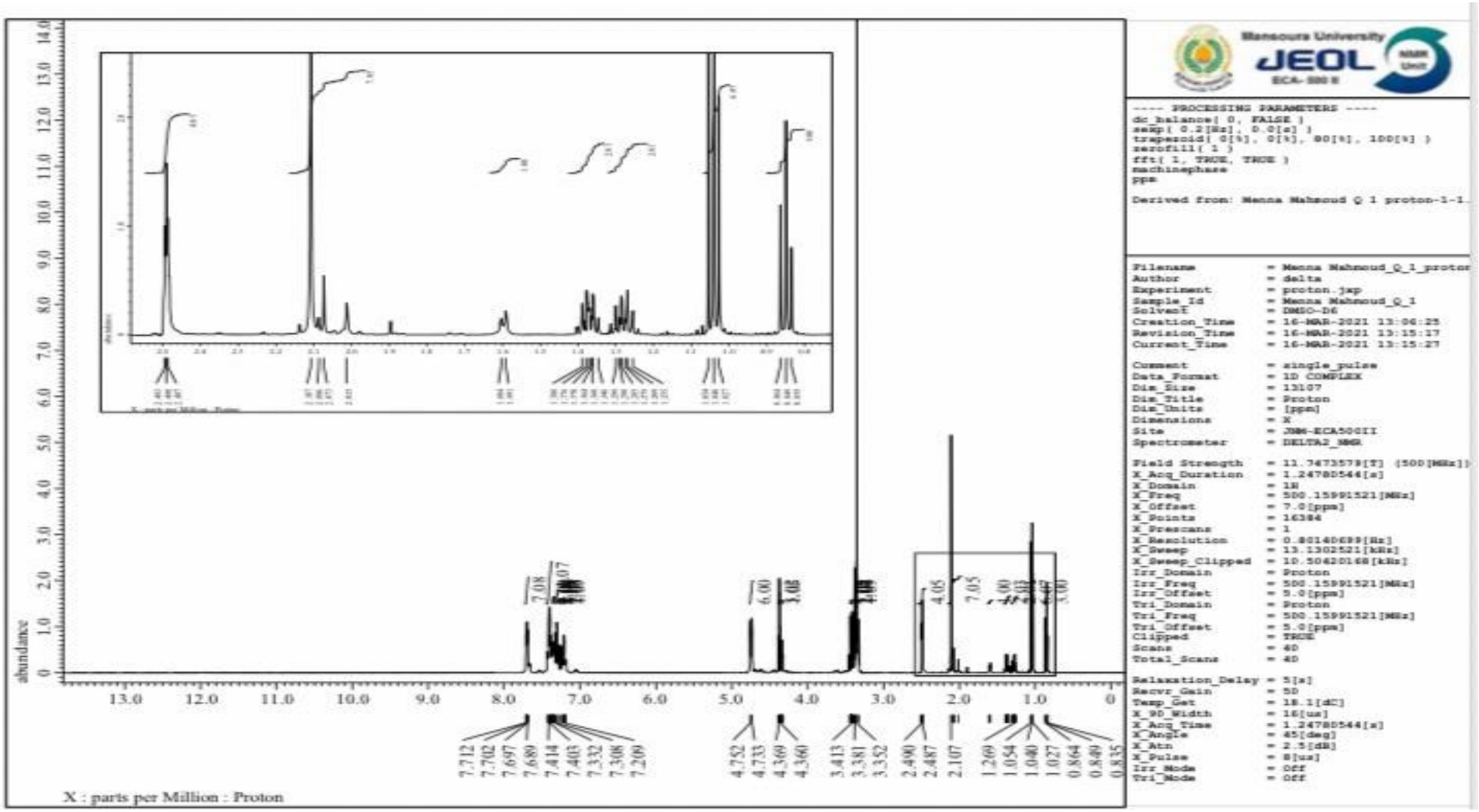
S2: ^{1}H-NMR of 3b:



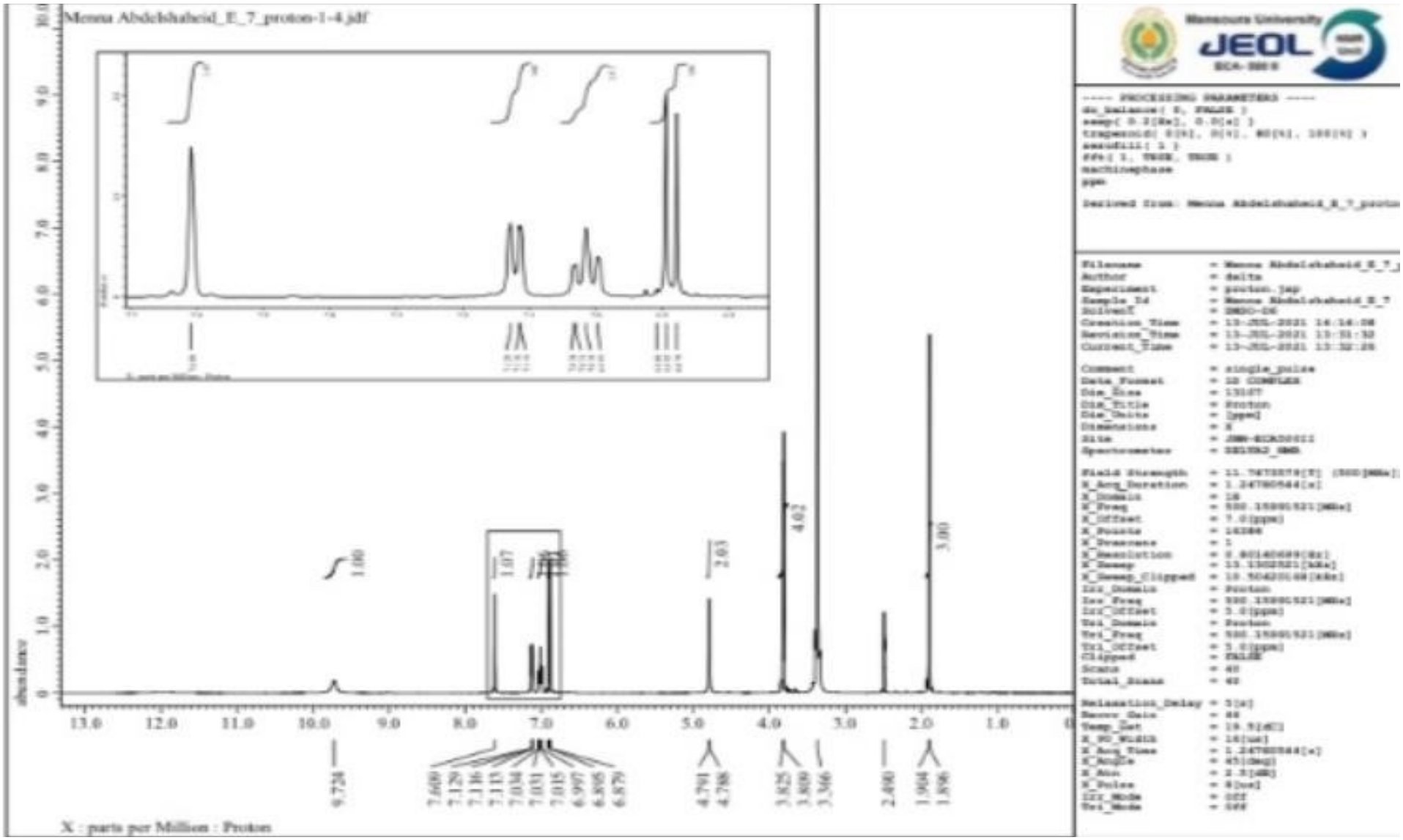
S3: ^{1}H-NMR of 3c:



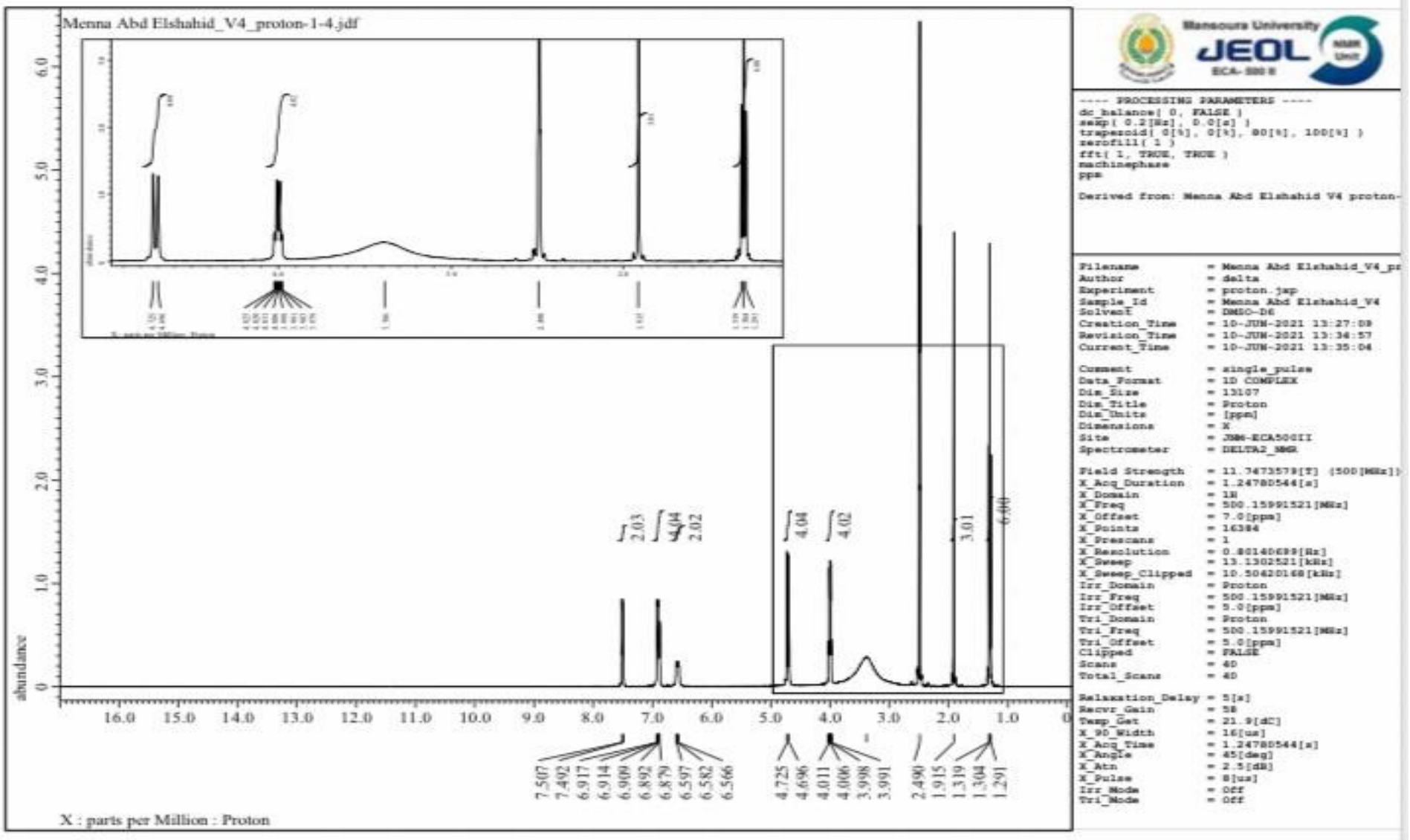
S4: ^{1}H-NMR of 3d:



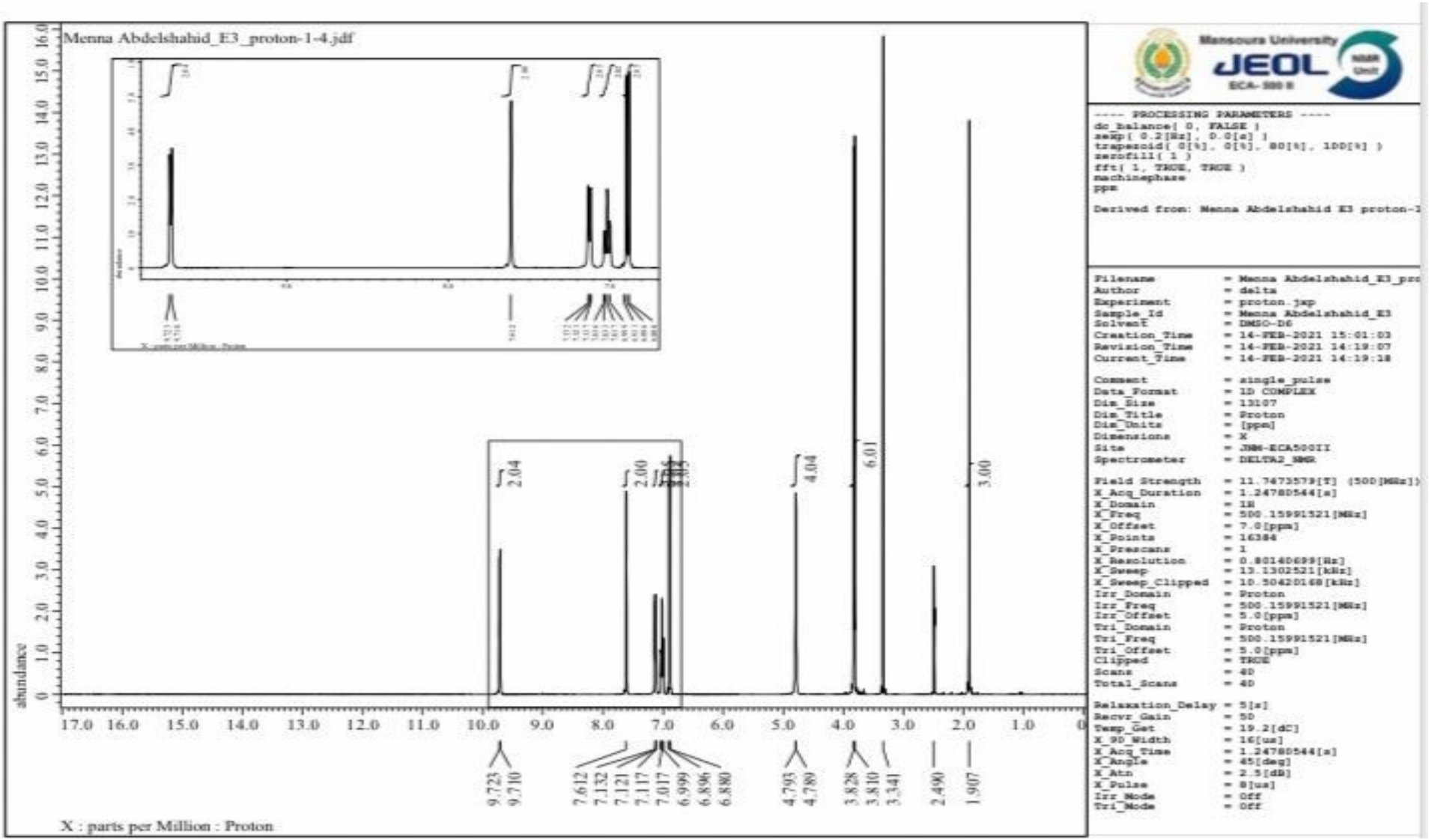
S5: ^{1}H-NMR of 4a:



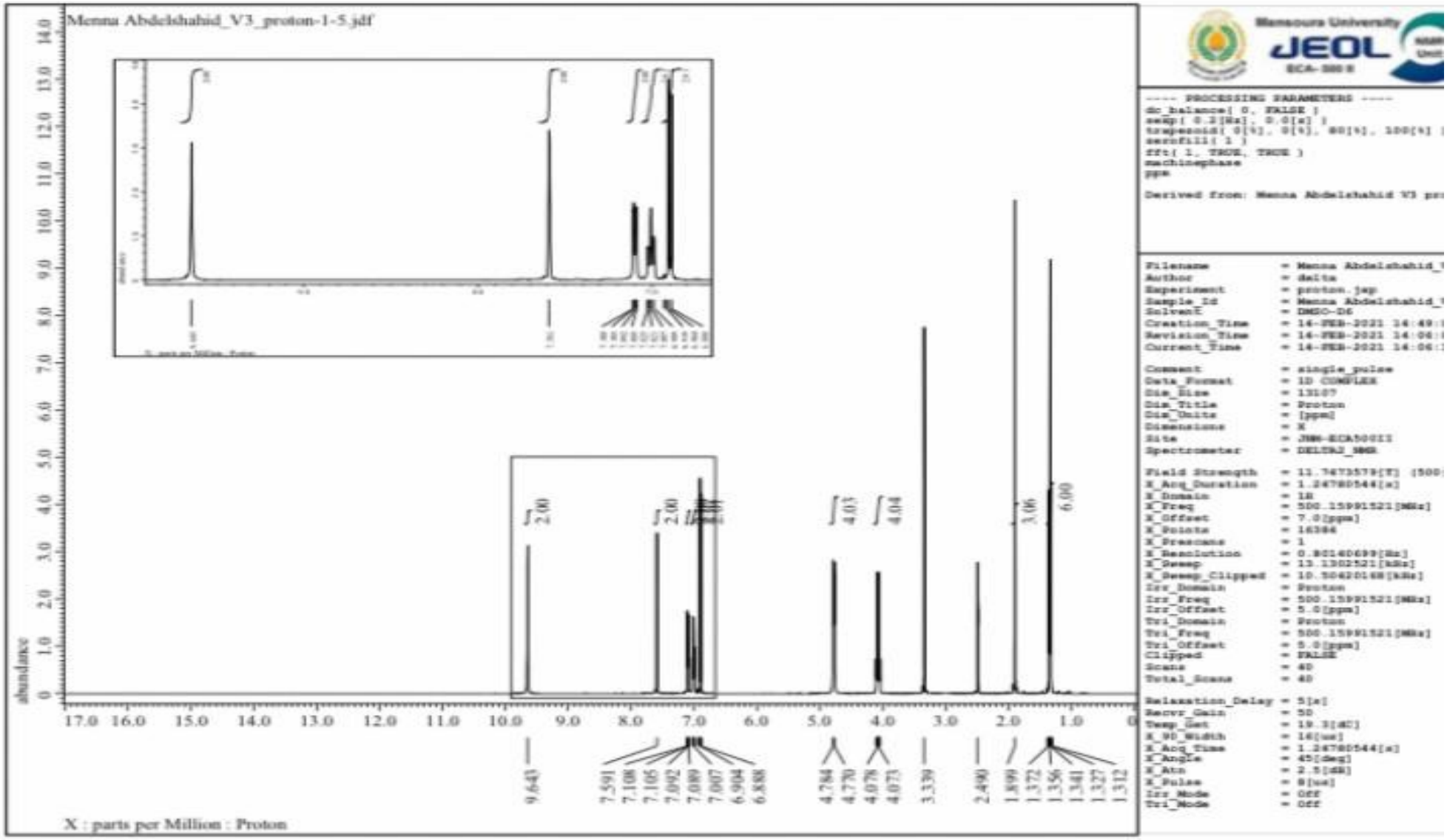
S6: ^{1}H-NMR of 4b:



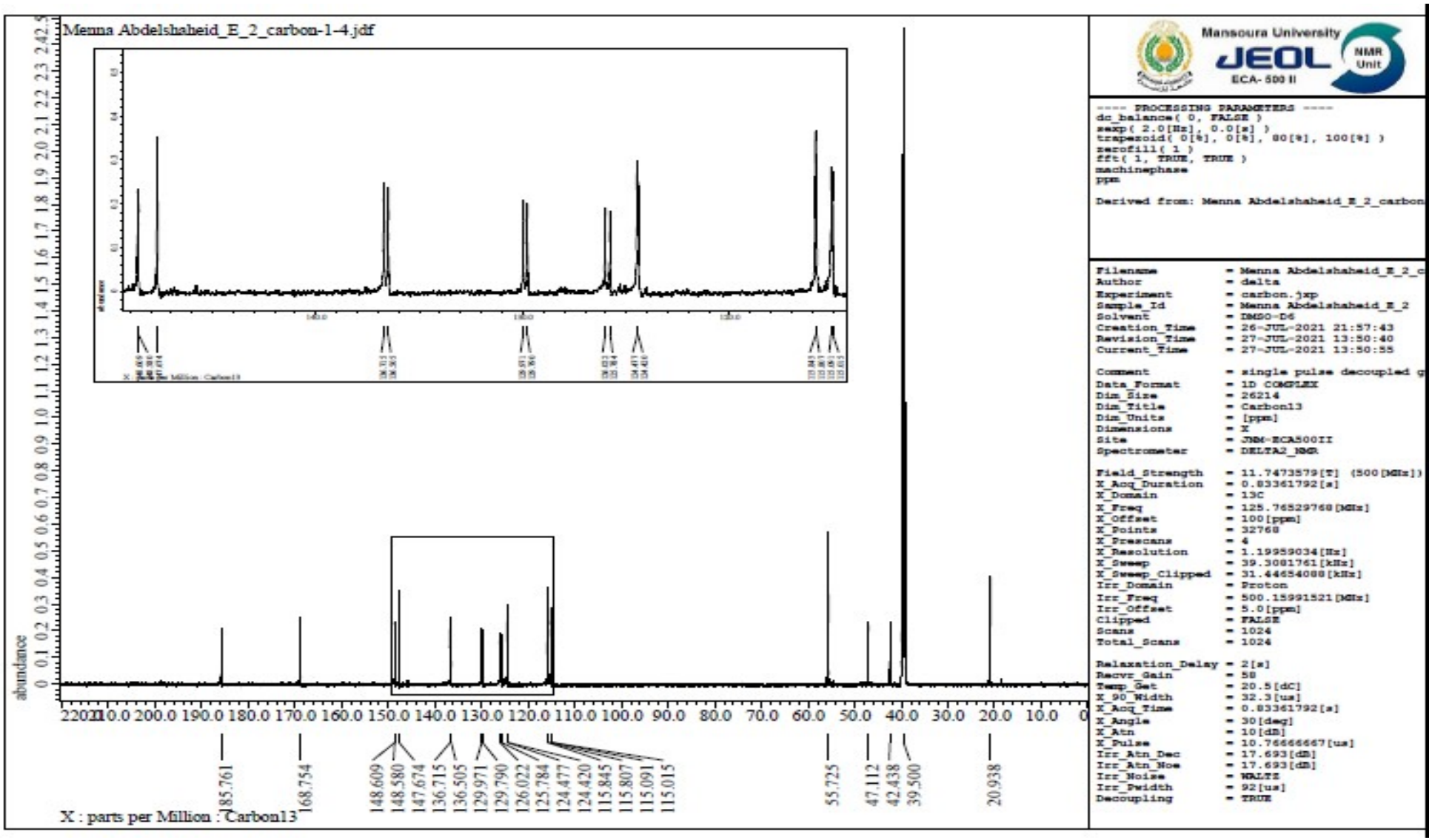
S7: ^{1}H-NMR of 5a:



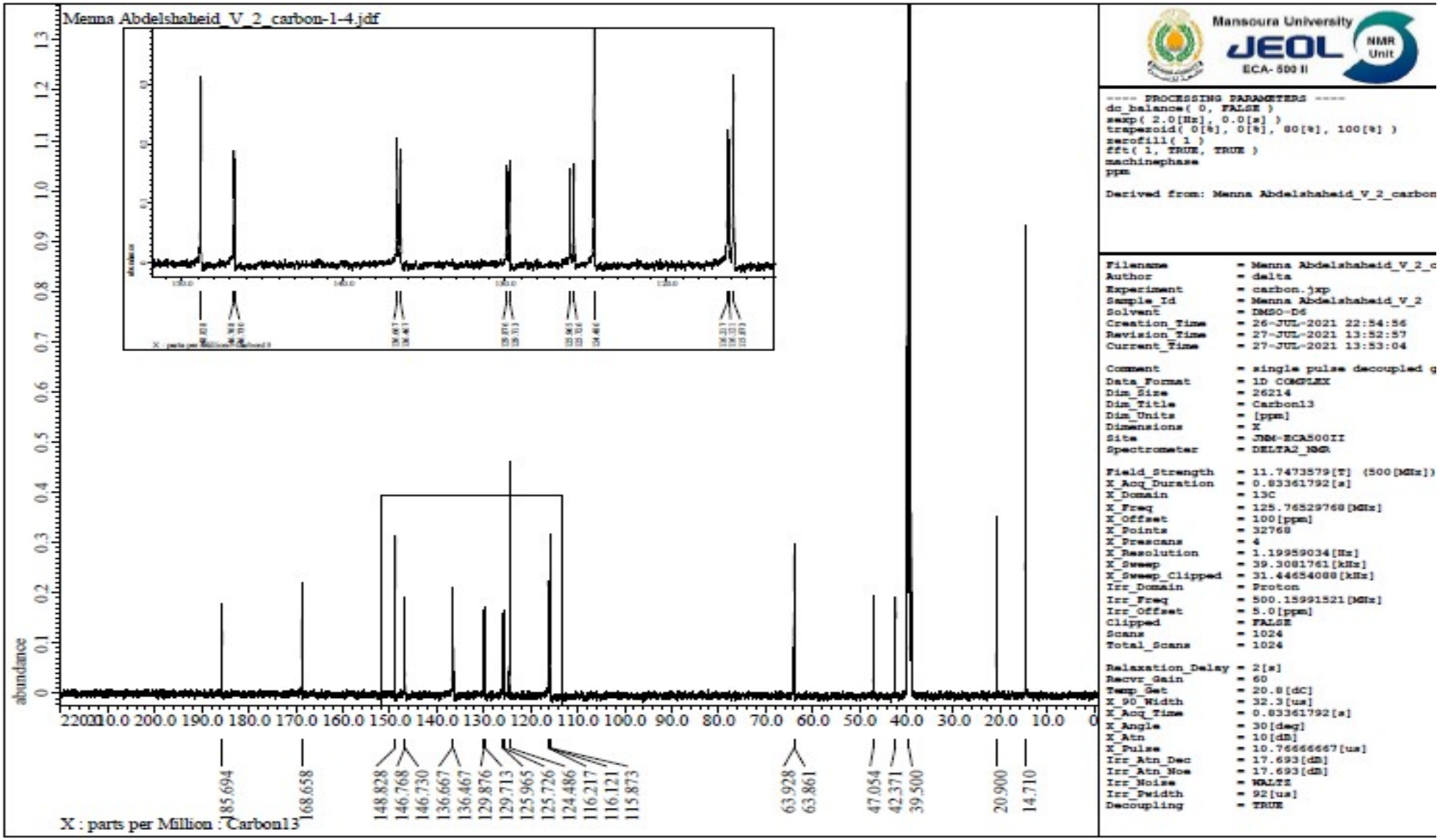
S8: ^{1}H-NMR of 5b:



S9: ^{13}C-NMR of 3a:



S10: ^{13}C-NMR of 3b:



Mansoura University
JEOL ECA-500 II NMR Unit

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==== PROCESSING PARAMETERS ====
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trapezoid( 0[%], 0[%], 80[%], 100[%] )
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fft( 1, TRUE, TRUE )
machinephase
ppm

Derived from: Menna Abdelshaheid_V_2_carbon
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Author	= delta
Experiment	= carbon.jxp
Sample_Id	= Menna Abdelshaheid_V_2
Solvent	= DMSO-D6
Creation_Time	= 26-JUL-2021 22:54:56
Revision_Time	= 27-JUL-2021 13:52:57
Current_Time	= 27-JUL-2021 13:53:04
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Dim_Size	= 26214
Dim_Title	= Carbon13
Dim_Units	= [ppm]
Dimensions	= X
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Spectrometer	= DELTA2_NMR
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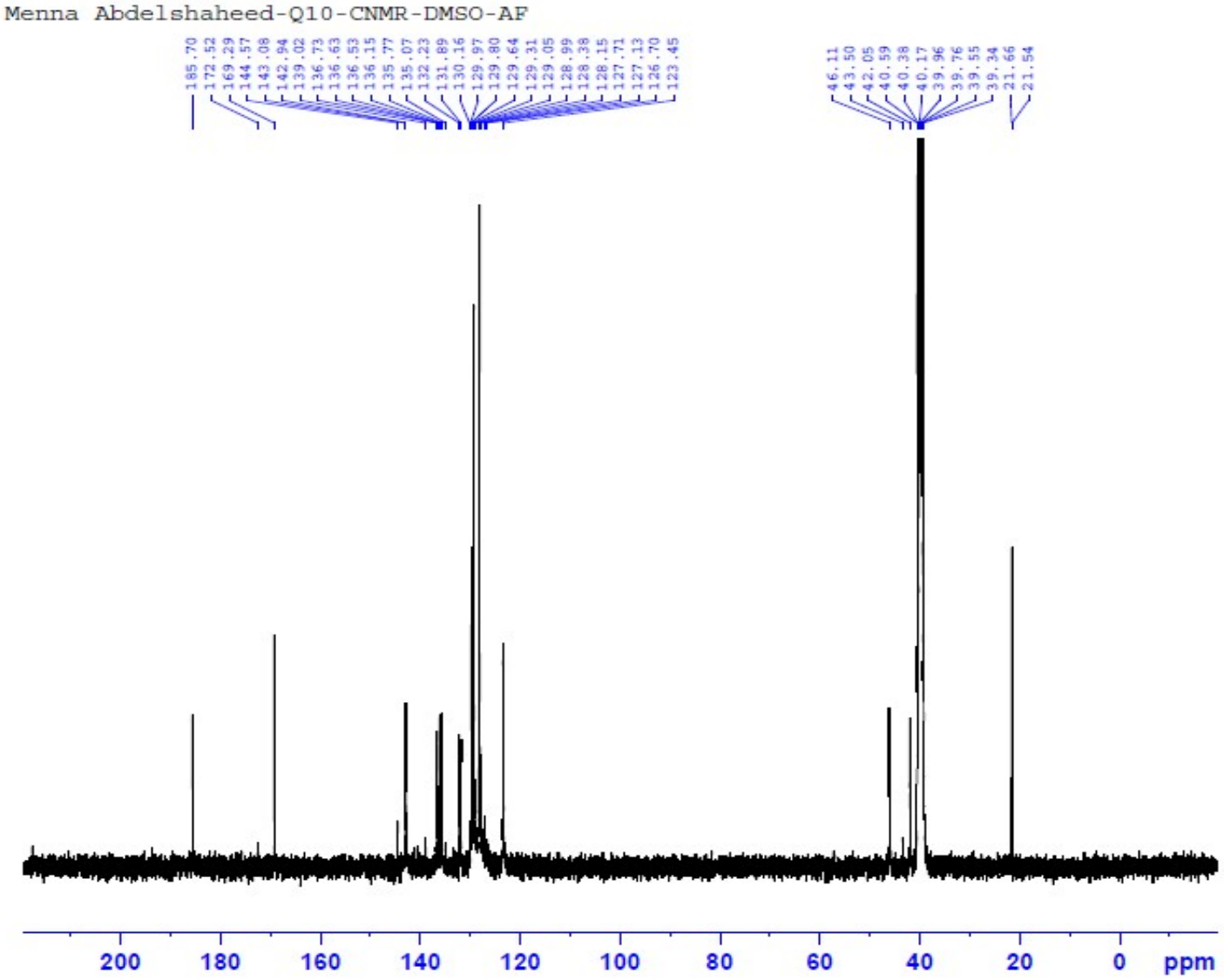
S11: ^{13}C-NMR of 3d:

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PROCNO                 1

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NS                  2200
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FIDRES         0.733596 Hz
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RG                197.77
DW                20.800 usec
DE                 6.50 usec
TE                296.8 K
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TD0                    1
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NUC1                13C
P1                 10.00 usec
PLW1          47.00000000 W
SFO2         400.2016008 MHz
NUC2                1H
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PCPD2              90.00 usec
PLW2          13.00000000 W
PLW12          0.29249999 W
PLW13          0.14713000 W

F2 - Processing parameters
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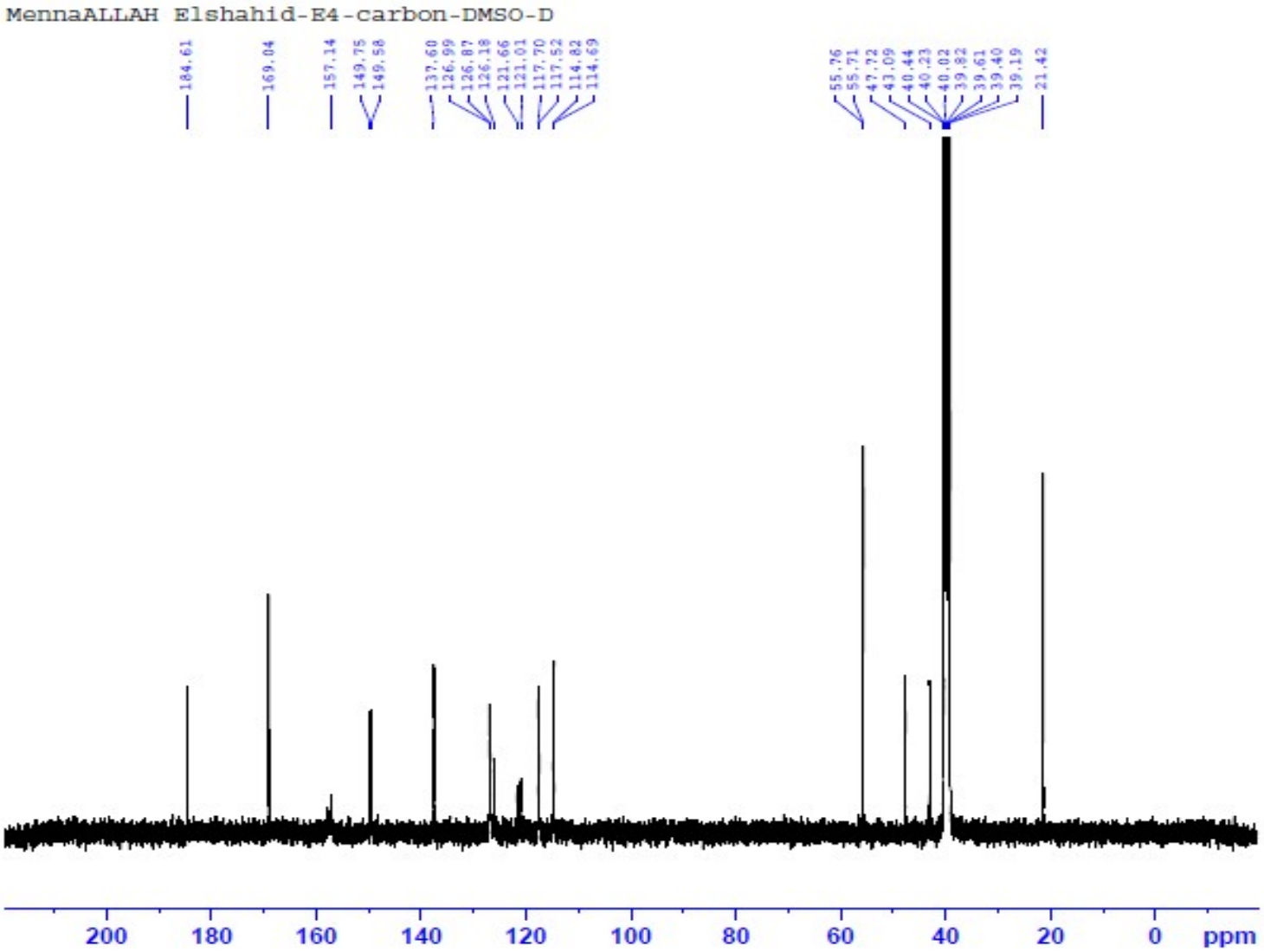
S12: ^{13}C-NMR of 4b:



BRUKER

Faculty of Pharmacy

```
Current Data Parameters
NAME      MennaALLAH Elshahid-E4-carbon-DMSO-D
EXPNO                 10
PROCNO                 1

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TD                65536
SOLVENT             DMSO
NS                  2200
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FIDRES             0.733596 Hz
AQ                1.3631488 sec
RG                  197.77
DW                 20.800 usec
DE                  6.50 usec
TE                 293.8 K
D1              2.00000000 sec
D11             0.03000000 sec
TD0                    1
SFO1           100.6404331 MHz
NUC1                  13C
P1                  10.00 usec
PLW1           47.00000000 W
SFO2           400.2016008 MHz
NUC2                  1H
CPDPRG[2          waltz16
PCPD2              90.00 usec
PLW2           13.00000000 W
PLW12           0.29249999 W
PLW13           0.14713000 W

F2 - Processing parameters
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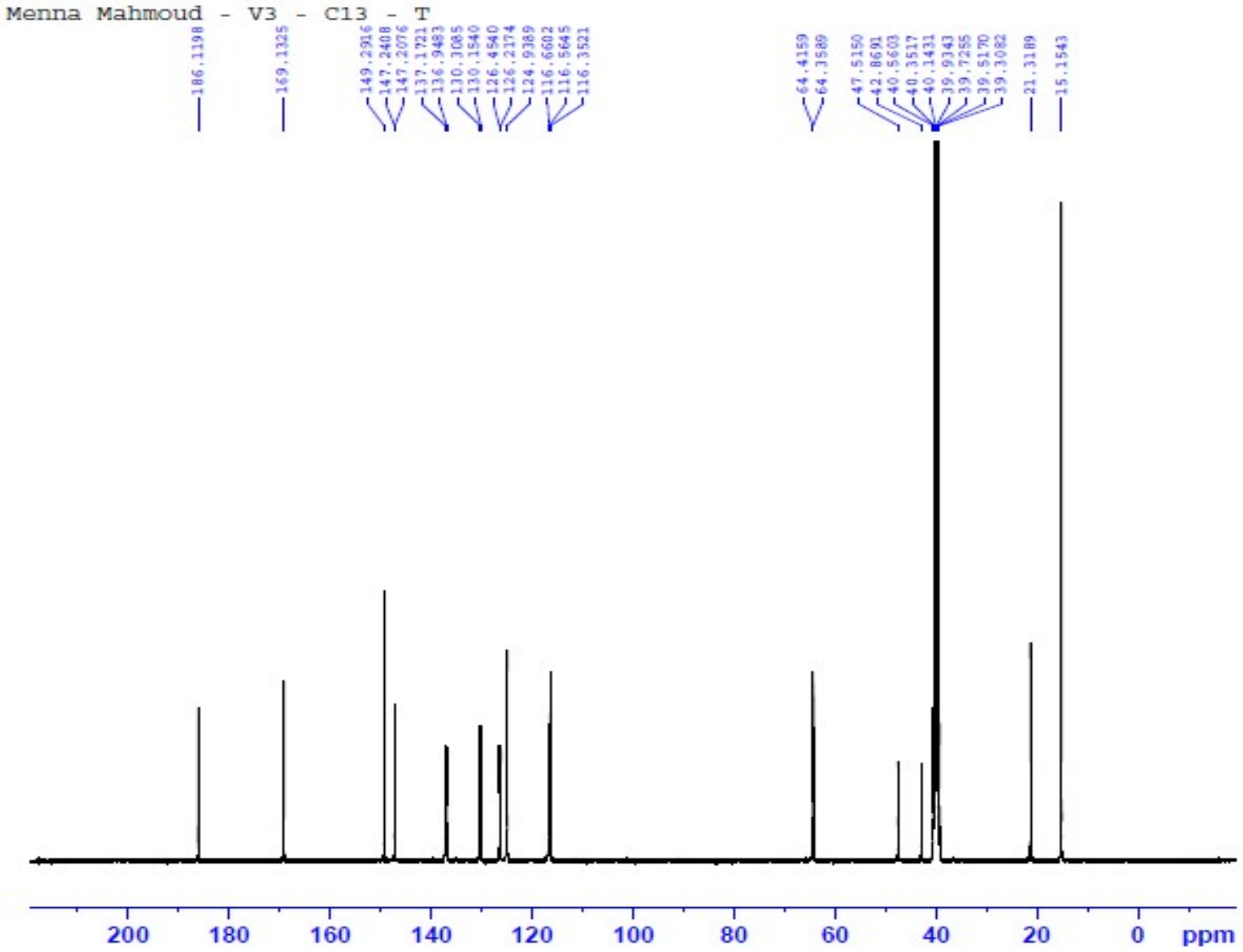
S13: ^{13}C-NMR of 5b:

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PROCNO                 1

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TE                  297.6 K
D1               2.00000000 sec
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TD0                     1
SFO1           100.6404331 MHz
NUC1                  13C
P1                  10.00 usec
PLW1           47.00000000 W
SFO2           400.2016008 MHz
NUC2                  1H
CPDPRG[2           waltz16
PCPD2               90.00 usec
PLW2           13.00000000 W
PLW12           0.29245999 W
PLW13           0.14713000 W

F2 - Processing parameters
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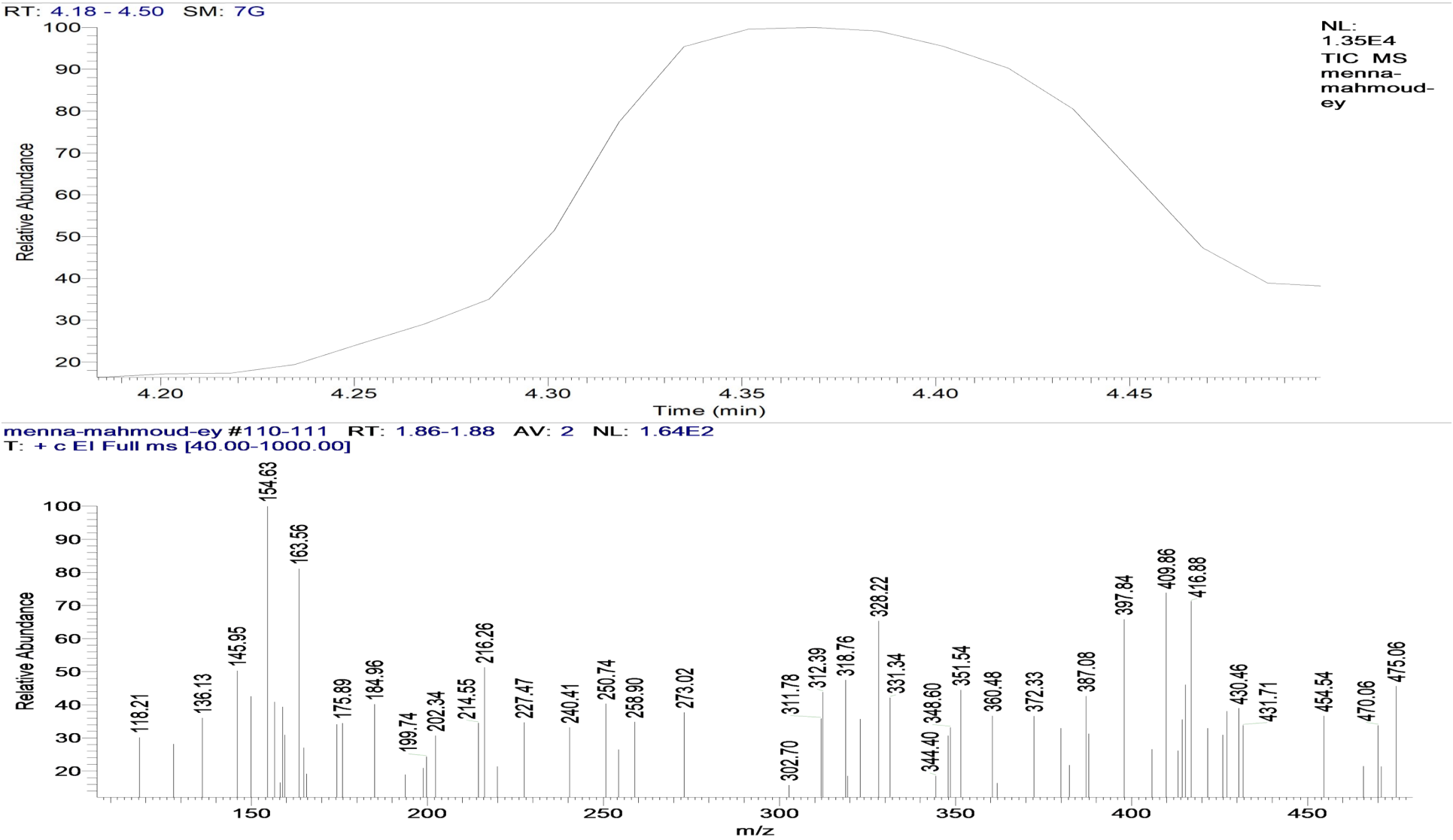
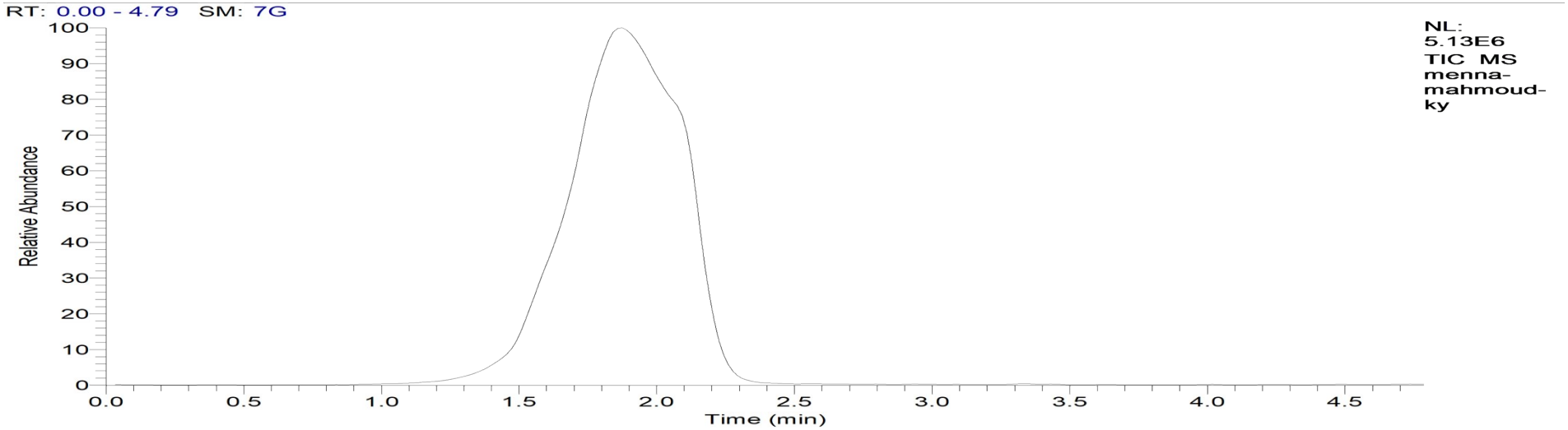
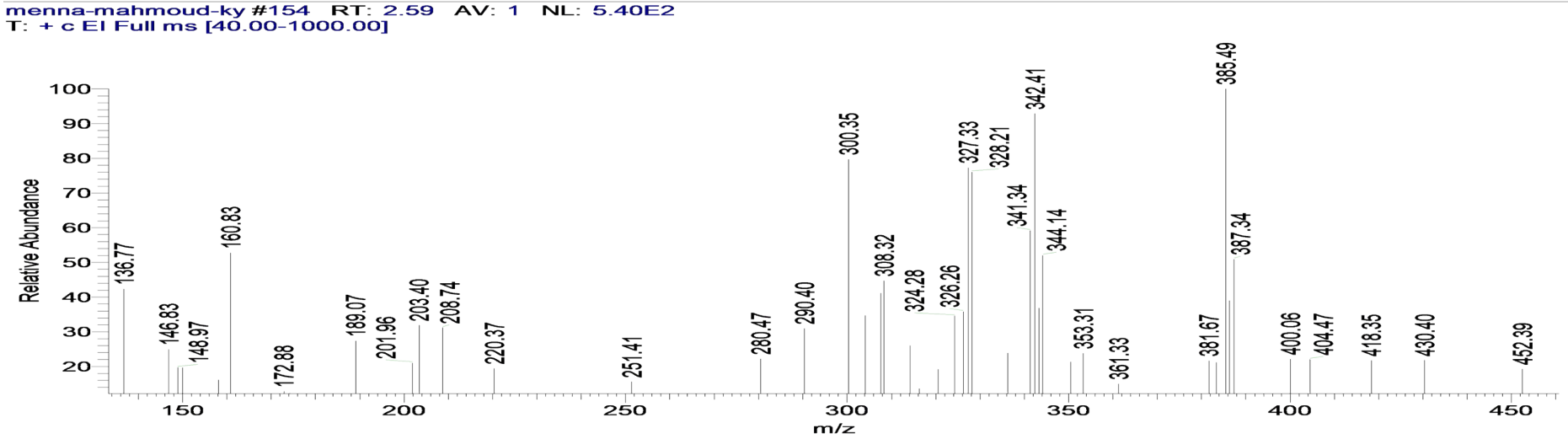
S14: Mass Spectrum of 3a:

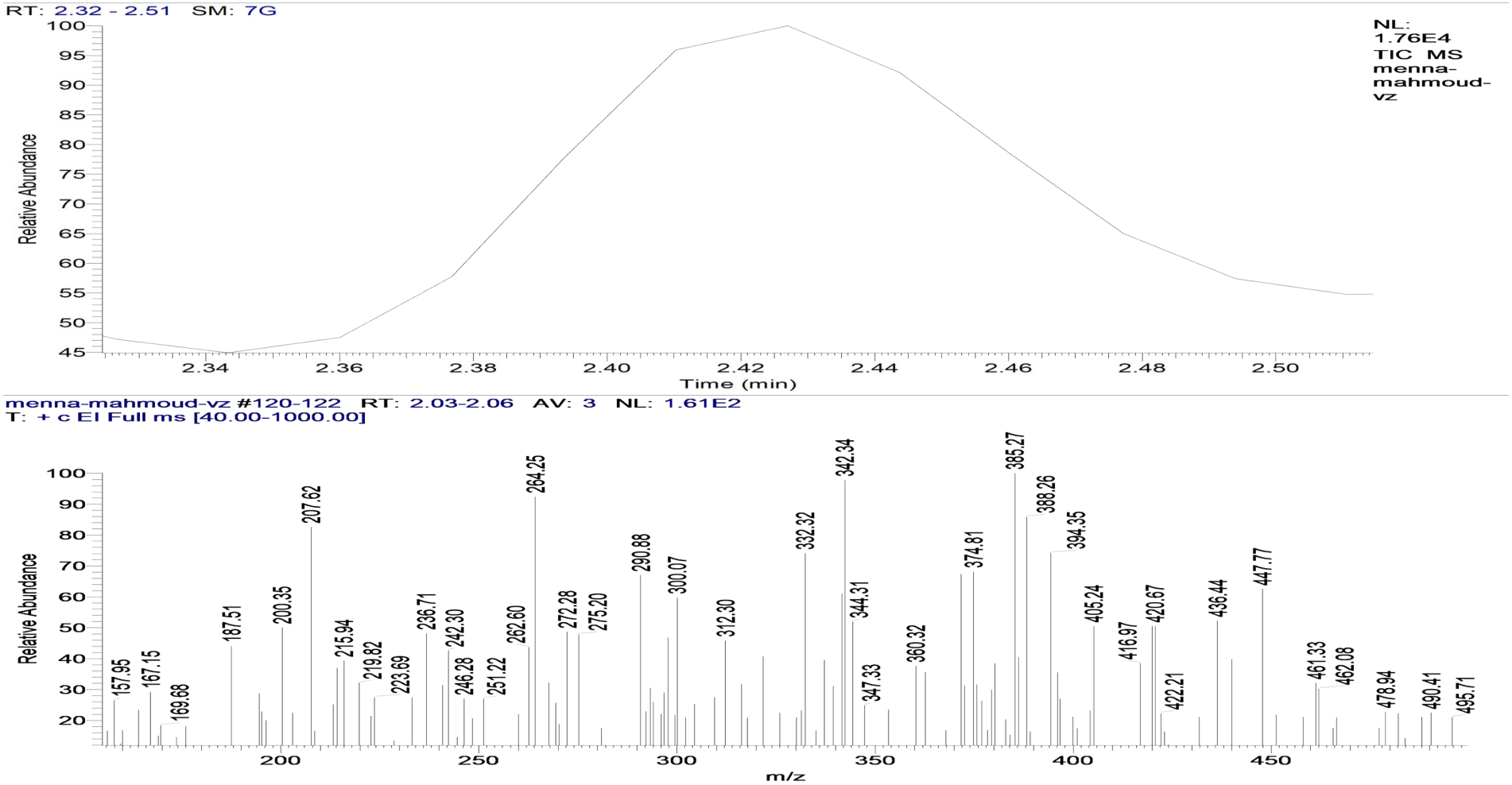


S15: Mass Spectrum of 3c:

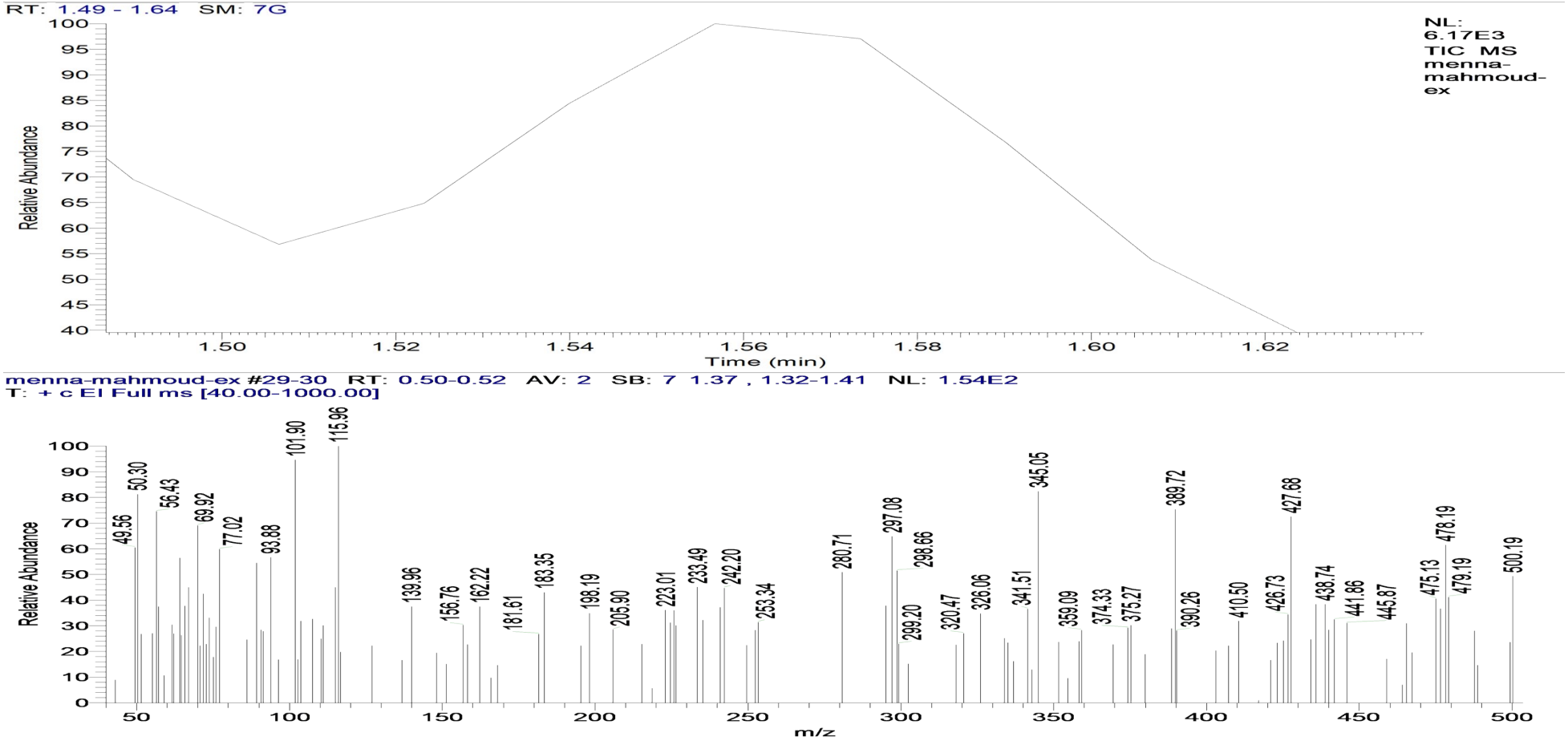




S16: Mass Spectrum of 4b:



S17: Mass Spectrum of 5a:



S18: Results of Elemental Analysis:

Al-Azhar University
The Regional Center for Mycology and Biotechnology

Requester Data:

Name: Dr. Menna Mahmoud Abdel-Shahid
Authority: Faculty of Pharmacy,
Future University

Sample Data:

Ten samples had been submitted for elemental analysis.

Analysis Report:

Sample Code	C%	H%	N%	S%
E_2	65.82	5.41	9.07	0
E_4	63.24	6.08	8.70	6.53
E_5	66.28	4.97	8.12	6.17
E_7	63.27	6.14	8.71	6.49
Q_2	67.05	5.97	8.50	0
O_4	72.09	5.56	9.21	6.97
S_1	62.17	4.70	4.47	19.61
S_2	60.95	4.51	10.85	16.29
S_3	66.08	5.23	10.29	15.40
V_2	73.25	6.08	9.16	7.61

INVESTIGATOR M. Elkassas

جامعة الأزهر المركز الإقليمي للفطريات وتطبيقاتها

DIRECTOR

Al-Azhar University Campus - Nasr City, Cairo, Egypt.
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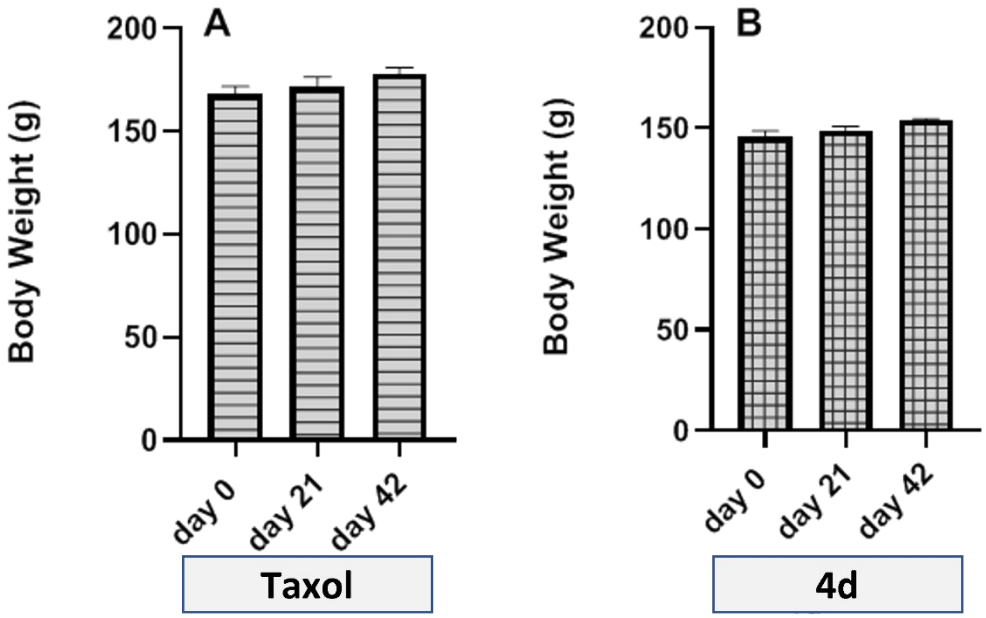
E.mail:rcmb@azhar.edu.eg
Website: http://www.azhar.edu.eg.htm * http://www.azhar.edu.eg/pages/fungi_center.htm
Facebook : RCMB AZHAR P.O. box mail : 11751 Nasr City Cairo, Egypt.

S19: Tumor volume and body weight:



S19 figure: Rats body weight. Body weight in diseased rats after the end of the induction phase, at day 0, day 21 and day 42 of treatment with A) Taxol and B) the synthetic drug 4d. Data are presented as mean ± SEM (n=6). Statistical analysis was carried out using one-way ANOVA followed by Tukey's Multiple comparison test at p-value <0.05. no significance difference was found between different groups.

S20: Statistical analysis

Values were presented as mean ± SEM of 6 animals. Significant difference between groups was carried out using analysis of variance (ANOVA) followed by Tukey's post hoc test. Significance was taken as $P< 0.05$.

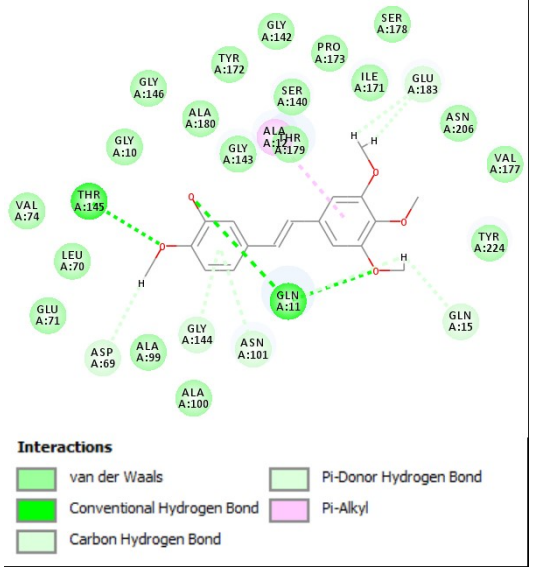
S20 A: Table: Body weight in diseased rats after the end of the induction phase, at day 0, day 21 and day 42 of treatment:

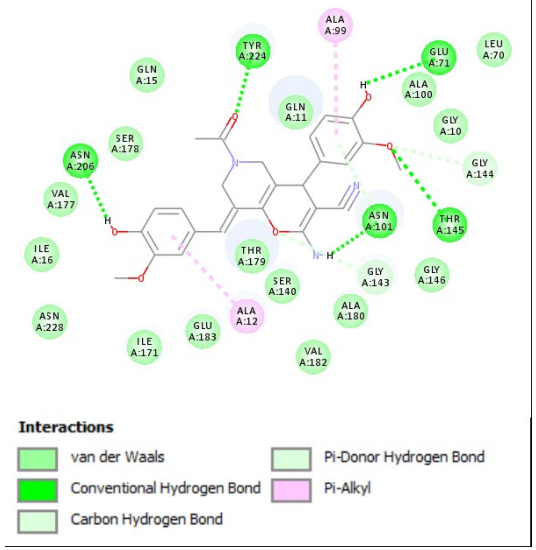
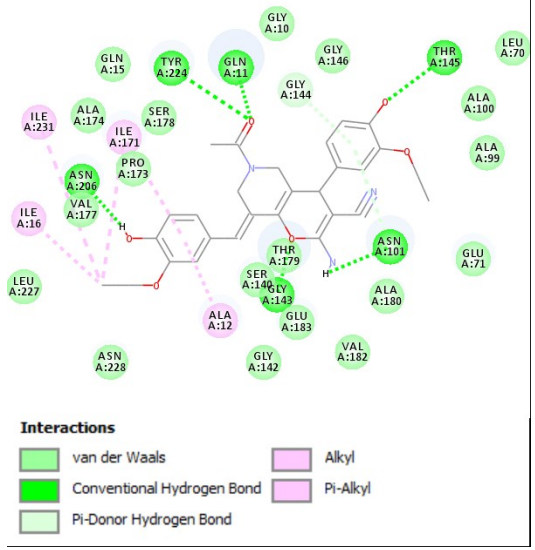
Drug/ body weight (gm)	Day 0	Day 21	Day 42
Taxol	168 ± 3.8	171.6 ± 4.7	178.3 ± 2.7
4d	145.5 ± 3	148.6 ± 2.1	154 ± 0.8

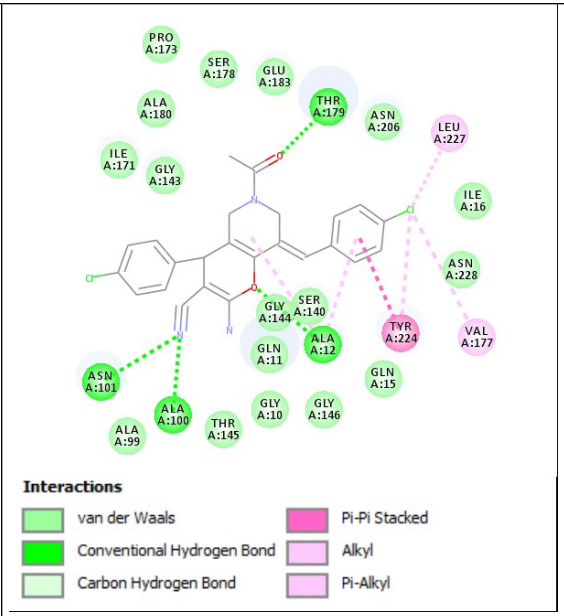
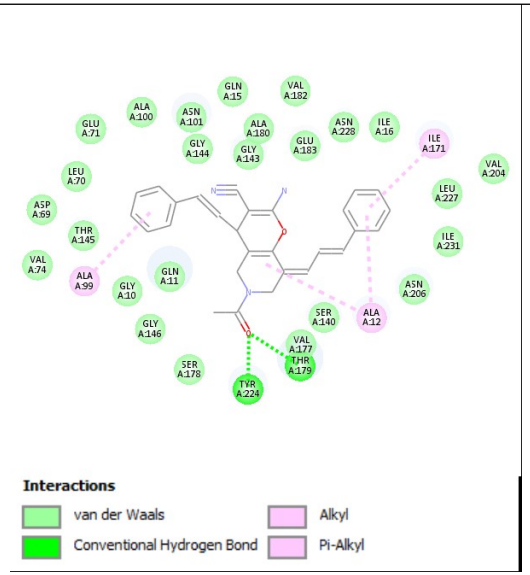
S20 B: Table: Tumor size in diseased rats after treatment at day 0, day 21 and day 42 of treatment:

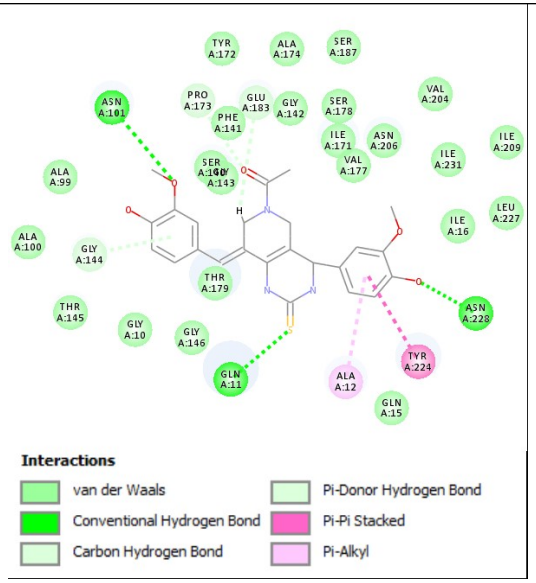
Drug/ Tumour size (cm^3)	Day 0	Day 21	Day 42
Taxol	0.05 ± 0.01	0.17 ± 0.03*	0.25 ± 0.006*
4d	0.24 ± 0.01	0.15 ± 0.006*	0.056 ± 0.007*

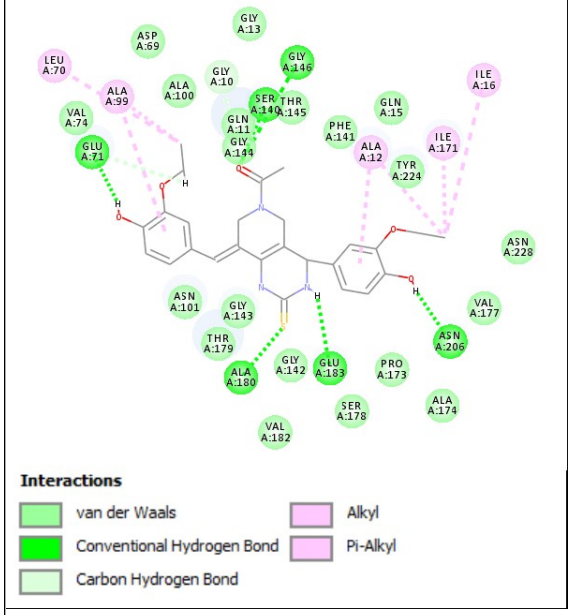
S21: Results of –(C-docker interaction energy), binding mode and 2D diagram of the molecular docking studies:

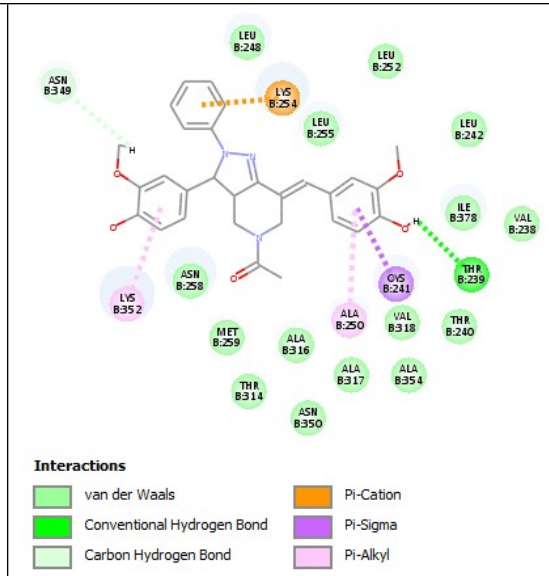
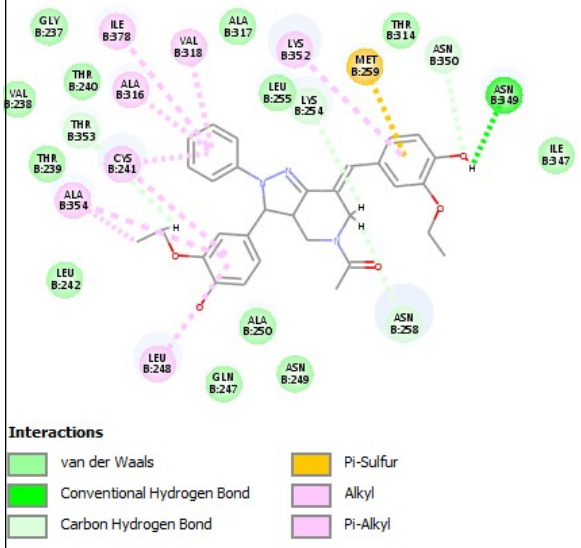
Compound	-(C-docker interaction energy) in Kcal/mol	2D binding diagram	Binding mode
Combrestatin (Reference Compound)	-38.52		: Gln 11 (x2), Gln 15, Asp 69, Gly 144, Thr 145, Glu 183 (x2) Pi-Alkyl: Ala 12

3a	-48.05		Gln 11, Glu 71, Asn 101 (x2), Gly 144, Thr 145, Thr 179, Asn 206, Tyr 224 i-Alkyl: Ala 12, Ala 99
3b	-48.22		Gln 11, Asn 101, Glu 143, Gly 144, Thr 145, Asn 206, Tyr 224 Ala 12, Ile 16, Ile 171 (x2), Ile 251

3c	-45.44		Gln 11, Ala 12, Ala 100, Asn 101, Thr 179 Pi-Pi: Tyr 224 Ala 12 (x2), Val 177, Tyr 224, Leu 277
3d	-44.87		-bond: Thr 179, Tyr 224 l: Ala 12 (x2), Ala 99, Ile 171

4a	-50.74			Gln 11, Asn 101, Phe 141, Gly 144, Glu 183, Asn 228 Pi-Pi: Tyr 224 Pi-Alkyl: Ala 12

4b	-48.59		: Gln 11, Glu 71, Ser 140, Gly 179, Ala 180, Glu 183, Asn 226 : Ala 112 (x2), Ile 16, Leu 70, Ala 99 (x2), Ile 171

5a	-47.65		Thr 259, Asn 49 Pi-Cation: Lys 254 Pi-Sigma: Cys 241 Alkyl: Ala 250, Lys 352
5b	-54.83		ys 254, Asn 258, Asn 349, Asn 350, Thr 353 Pi-Slufur: Met 259 l: Cys 241 (x2), Leu 248, Ala 318, Lys 352, Ala 354 (x2), Ile 378

S22: Table Results of Dynamic Simulation Cascades of Combrestatin-tubulin complex:

Name	Stage	Forcefield	Start Time (ps)	End Time (ps)	Initial Potential Energy (kcal/mol)	Total Energy (kcal/mol)	Potential Energy (kcal/mol)	Kinetic Energy (kcal/mol)	Temperature (K)	Van der Waals Energy (kcal/mol)	Electrostatic Energy (kcal/mol)	Initial RMS Gradient (kcal/(mol x A))	Final RMS Gradient (kcal/(mol x A))
Combrestatin	Minimization	CHARMm			5.807E+10		-18208.904			-2078.803	-25944.82	1.509E+10	0.898
Combrestatin	Minimization2	CHARMm			-18208.904		-22101.759			-3118.442	-18432.404	0.898	0.097
Combrestatin	Heating	CHARMm	0	4	-22101.759	-20536.987	-21451.036	914.05	54.267	-3109.562	-18297.805	1.574	7.692
Combrestatin	Equilibration	CHARMm	4	14	-21451.036	-12114.933	-17265.263	5150.33	305.777	-2505.498	-16660.435	7.692	18.805
Combrestatin	Production	CHARMm	14	24	-17265.263	-12289.69	-17370.043	5080.352	301.622	-2433.721	-16272.189	18.805	18.557

S23: Table Results of Dynamic Simulation Cascades of 3b-tubulin complex:

Name	Stage	Forcefield	Start Time (ps)	End Time (ps)	Initial Potential Energy (kcal/mol)	Total Energy (kcal/mol)	Potential Energy (kcal/mol)	Kinetic Energy (kcal/mol)	Temperature (K)	Van der Waals Energy (kcal/mol)	Electrostatic Energy (kcal/mol)	Initial RMS Gradient (kcal/(mol x A))	Final RMS Gradient (kcal/(mol x A))
3b	Minimization	1SA1-CHARMm			1.027E+13		-15002.708			-1101.505	-25887.553	3.238E+12	0.948
3b	Minimization2	1SA1-CHARMm			-15002.708		-18304.957			-1967.835	-18592.248	0.948	0.146
3b	Heating	1SA1-CHARMm	0	4	-18304.957	-16707.358	-17616.758	909.4	53.656	-1962.481	-18449.633	1.615	7.674
3b	Equilibration	1SA1-CHARMm	4	14	-17616.758	-8288.681	-13461.538	5172.857	305.206	-1186.345	-16416.55	7.674	18.786
3b	Production	1SA1-CHARMm	14	24	-13461.538	-8453.329	-13606.281	5152.952	304.031	-1324.499	-16147.583	18.786	18.567