Synthesis, molecular structure, anticancer activity and QSAR study of *N*-(aryl/heteroaryl)-4-(1*H*-pyrrol-1-yl)benzenesulfonamide derivatives

Beata Żołnowska [1*], Jarosław Sławiński [1], Zdzisław Brzozowski [1], Anna Kawiak [2,3], Mariusz Belka [4], Joanna Zielińska [4], Tomasz Bączek [4] and Jarosław Chojnacki [5]**

[1] Department of Organic Chemistry, Medical University of Gdańsk, Al. Gen. J. Hallera 107, 80-416 Gdańsk, Poland; brzozowskigumed@gmail.com (Z.B.)

[2] Department of Biotechnology, Intercollegiate Faculty of Biotechnology, University of Gdańsk and Medical University of Gdańsk, ul. Abrahama 58, 80-307 Gdańsk, Poland; kawiak@biotech.ug.edu.pl (A.K.)

[3] Laboratory of Human Physiology, Medical University of Gdańsk, ul. Tuwima 15, 80-210 Gdańsk, Poland

[4] Department of Pharmaceutical Chemistry, Medical University of Gdańsk, Al. Gen. J. Hallera 107, 80-416 Gdańsk, Poland; mariusz.belka@gumed.edu.pl (M.B.); joanna.zielinska@gumed.edu.pl (J.Z.); tomasz.baczek@gumed.edu.pl (T.B.)

[5] Department of Inorganic Chemistry, Gdańsk University of Technology, ul. Narutowicza 11/12, 80-233 Gdańsk, Poland; jarekch@pg.gda.pl (J.Ch.)

***** Correspondence: beata.zolnowska@gumed.edu.pl (B.Ż.); jaroslaw.slawinski@gumed.edu.pl (J.S.); Tel.: +48-58-349-1098; +48-58-349-1229 (B.Ż. & J.S.); Fax: +48-58-349-1277 (B.Ż. & J.S.)

Table of contents

Spectrum 11. ^{1}H NMR of compd **19** (500 MHz, DMSO-d_6).

Spectrum 12. ^{13}C NMR of compd **19** (125 MHz, DMSO-d_6).

Spectrum 13. ^{1}H NMR of compd **23** (500 MHz, DMSO-d_6).

Spectrum 14. ^{13}C NMR of compd **23** (125 MHz, DMSO-d_6).

Spectrum 15. ^{1}H NMR of compd **25** (500 MHz, DMSO-d_6).

Spectrum 16. ^{13}C NMR of compd **25** (125 MHz, DMSO-d_6).

Spectrum 17. ^{1}H NMR of compd **27** (500 MHz, DMSO-d_6).

Spectrum 18. ^{13}C NMR of compd **27** (125 MHz, DMSO-d_6).

Spectrum 19. ^{1}H NMR of compd **30** (500 MHz, DMSO-d_6).

Spectrum 20. ^{13}C NMR of compd **30** (125 MHz, DMSO-d_6).

Table S1
The most influential molecular descriptors based on VIP values derived from OPLS models

Molecular descriptor	VIP value
HCT-116	
F08[C-O]	2.04000
RBF	2.00536
CATS2D_07_DL	1.96385
B09[C-O]	1.96385
F09[C-O]	1.96385
RBN	1.91183
NRS	1.91183
CATS2D_06_DL	1.91183
F03[C-N]	1.89564
CATS2D_08_AL	1.76264
RFD	1.73683
RCI	1.73683
Rbrid	1.73397
NNRS	1.73397
C-028	1.63053
HeLa	
CATS2D_07_DL	2.35529
B09[C-O]	2.35529
F09[C-O]	2.35529
F08[C-O]	2.17873
CATS2D_08_AL	2.01828
B08[C-S]	1.88821
RBN	1.75819
NRS	1.75819
CATS2D_06_DL	1.75819
MCF-7	
nO	2.30514
O-060	2.30514
T(O..O)	2.30514
B01[C-O]	2.30514
B04[O-S]	2.30514
B05[O-O]	2.30514
B09[N-O]	2.30514
B10[C-O]	2.30514
F04[O-S]	2.30514
F05[O-O]	2.30514
F09[N-O]	2.30514
F10[C-O]	2.30514
B03[N-O]	2.28874

Table S2

Values of descriptors characterized by high VIP values for OPLS model for HCT-116 cell line. Table is sorted with descending activity towards HCT-116.

ID	HCT116 IC50	F08[C-O]	RBF	CATS2D_07_DL	B09[C-O]	F09[C-O]	RBN	NRS	CATS2D_06_DL	F03[C-N]	CATS2D_08_AL	RFD	RCI	Rbrid	NNRS	C-028
28	4	4	0.093	0	0	0	4	3	0	9	5	0.095	1.095	1	0.75	1
29	9	4	0.087	0	0	0	4	3	0	9	5	0.095	1.095	1	0.75	2
30	19	4	0.087	0	0	0	4	3	0	10	5	0.095	1.095	1	0.75	1
33	23	4	0.103	0	0	0	4	3	0	10	7	0.1	1.1	1	0.75	2
37	46	4	0.105	0	0	0	4	3	0	8	4	0	1	0	1	1
38	69	4	0.098	0	0	0	4	3	0	8	4	0	1	0	1	2
23	71	4	0.108	0	0	0	4	3	0	6	6	0	1	0	1	0
31	105	6	0.087	1	1	2	4	3	0	9	8	0.095	1.095	1	0.75	2
35	135	4	0.111	0	0	0	4	3	0	7	5	0	1	0	1	0
24	140	8	0.122	1	1	2	6	4	2	6	9	0	1	0	1	0
25	145	9	0.122	1	1	2	6	4	2	6	9	0	1	0	1	0
27	175	9	0.125	1	1	2	6	4	2	7	9	0	1	0	1	0

Table S3

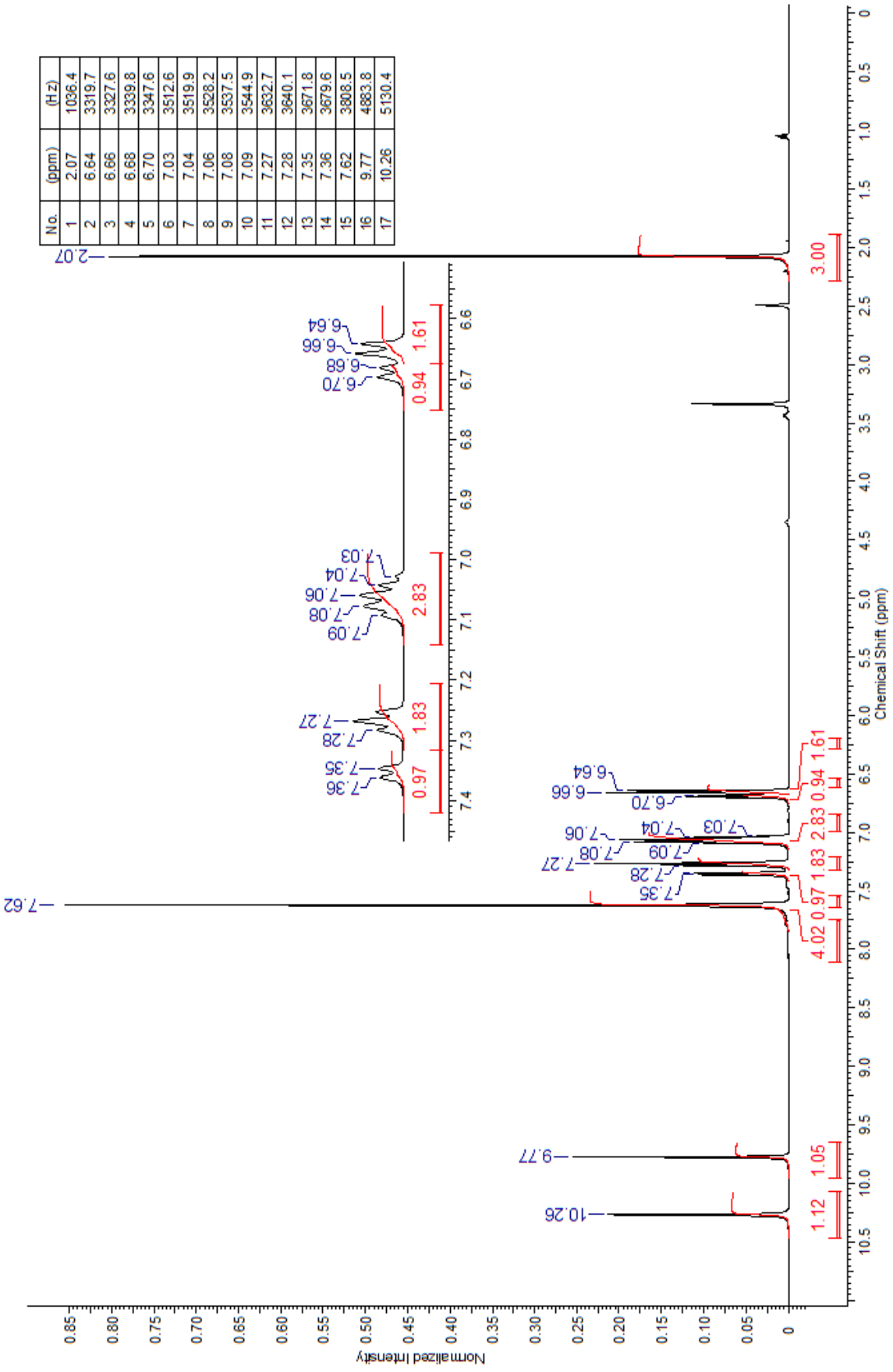
Values of descriptors characterized by high VIP values for OPLS model for HeLa cell line. Table is sorted with descending activity towards HeLa.

ID	HeLa IC50	CATS2D_07_DL	B09[C-O]	F09[C-O]	F08[C-O]	CATS2D_08_AL	B08[C-S]	RBN	NRS	CATS2D_06_DL
28	7	0	0	0	4	5	0	4	3	0
30	20	0	0	0	4	5	0	4	3	0
29	25	0	0	0	4	5	0	4	3	0
33	42	0	0	0	4	7	1	4	3	0
37	62	0	0	0	4	4	0	4	3	0
23	73	0	0	0	4	6	0	4	3	0
38	83	0	0	0	4	4	0	4	3	0
35	115	0	0	0	4	5	0	4	3	0
24	125	1	1	2	8	9	1	6	4	2
25	145	1	1	2	9	9	1	6	4	2
31	190	1	1	2	6	8	1	4	3	0
27	220	1	1	2	9	9	1	6	4	2

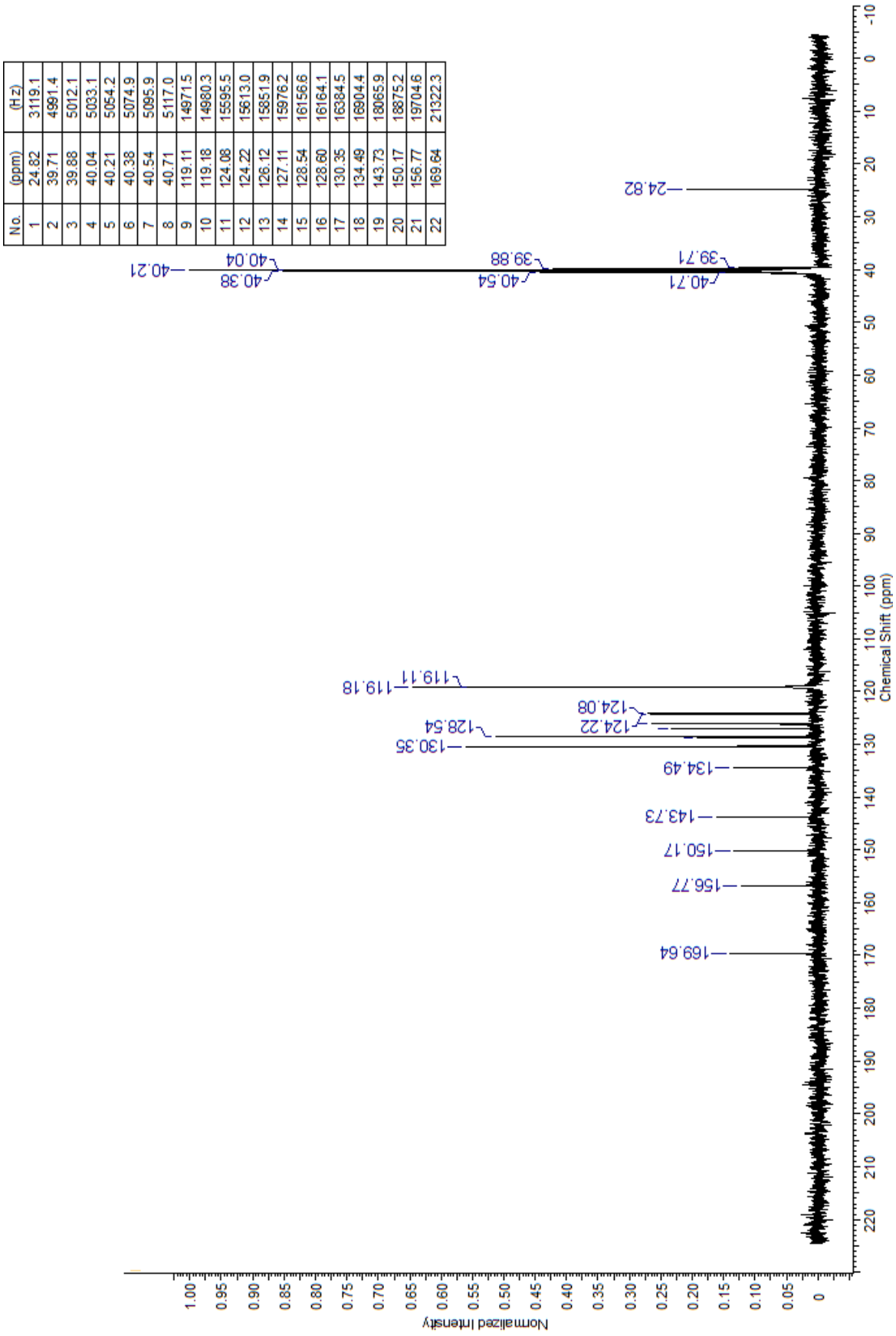
Table S4

Values of descriptors characterized by high VIP values for OPLS model for MCF-7 cell line. Table is sorted with descending activity towards MCF-7.

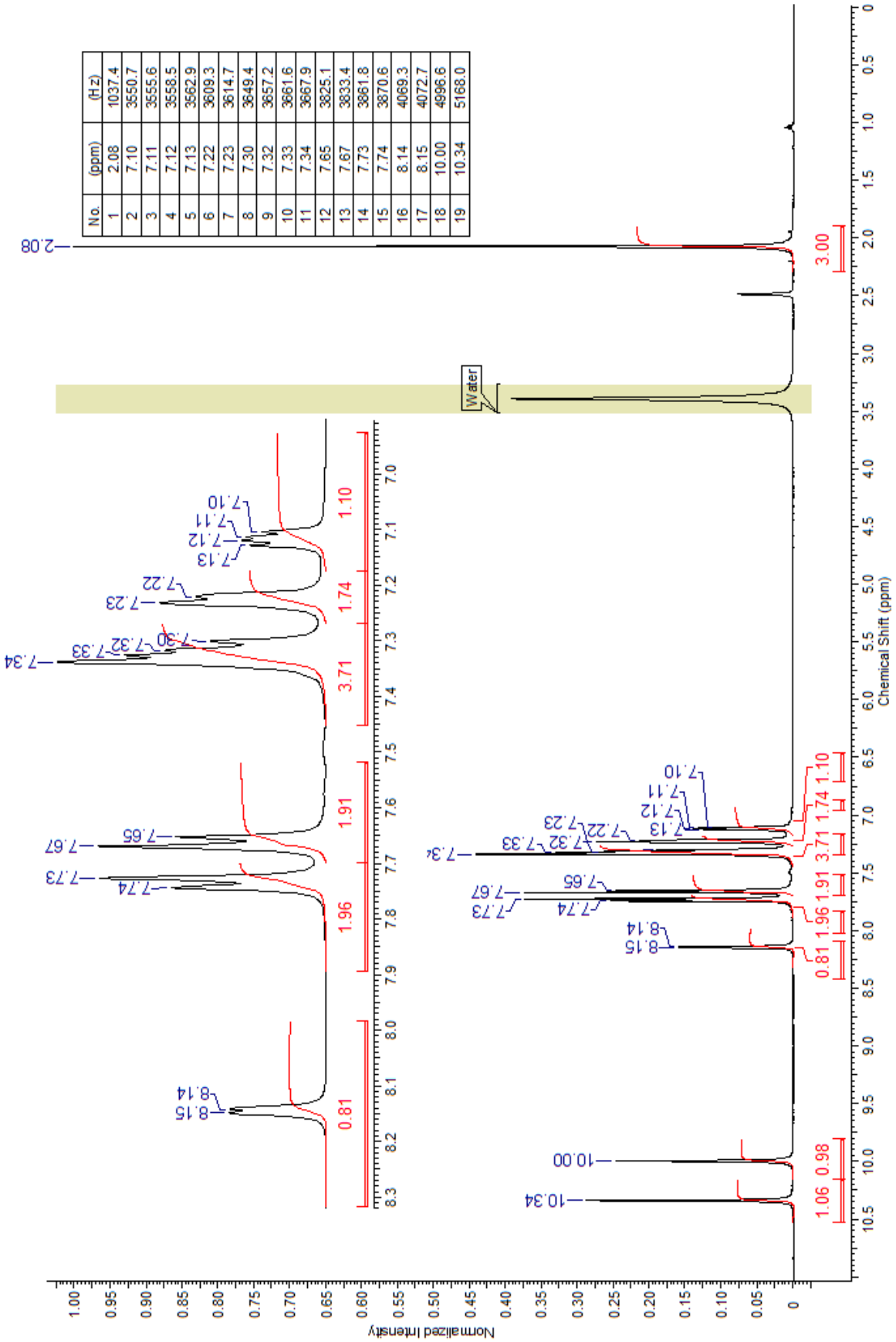
ID	MCF-7	nO	O-060	T(O..O)	B01[C-O]	B04[O-S]	B05[O-O]	B09[N-O]	B10[C-O]	F04[O-S]	F05[O-O]	F09[N-O]	F10[C-O]	B03[N-O]
28	4.5	2	0	2	0	0	0	0	0	0	0	0	0	0
33	23	2	0	2	0	0	0	0	0	0	0	0	0	0
30	50	2	0	2	0	0	0	0	0	0	0	0	0	0
37	68	2	0	2	0	0	0	0	0	0	0	0	0	0
23	82	2	0	2	0	0	0	0	0	0	0	0	0	0
29	93	2	0	2	0	0	0	0	0	0	0	0	0	0
38	135	2	0	2	0	0	0	0	0	0	0	0	0	0
24	140	2	0	2	0	0	0	0	0	0	0	0	0	0
35	140	2	0	2	0	0	0	0	0	0	0	0	0	0
32	170	2	0	2	0	0	0	0	0	0	0	0	0	1
25	180	3	1	12	1	1	1	1	1	1	2	1	2	1
31	220	2	0	2	0	0	0	0	0	0	0	0	0	0
34	275	3	1	12	1	1	1	1	1	1	2	1	2	1
27	320	3	1	12	1	1	1	1	1	1	2	1	2	1



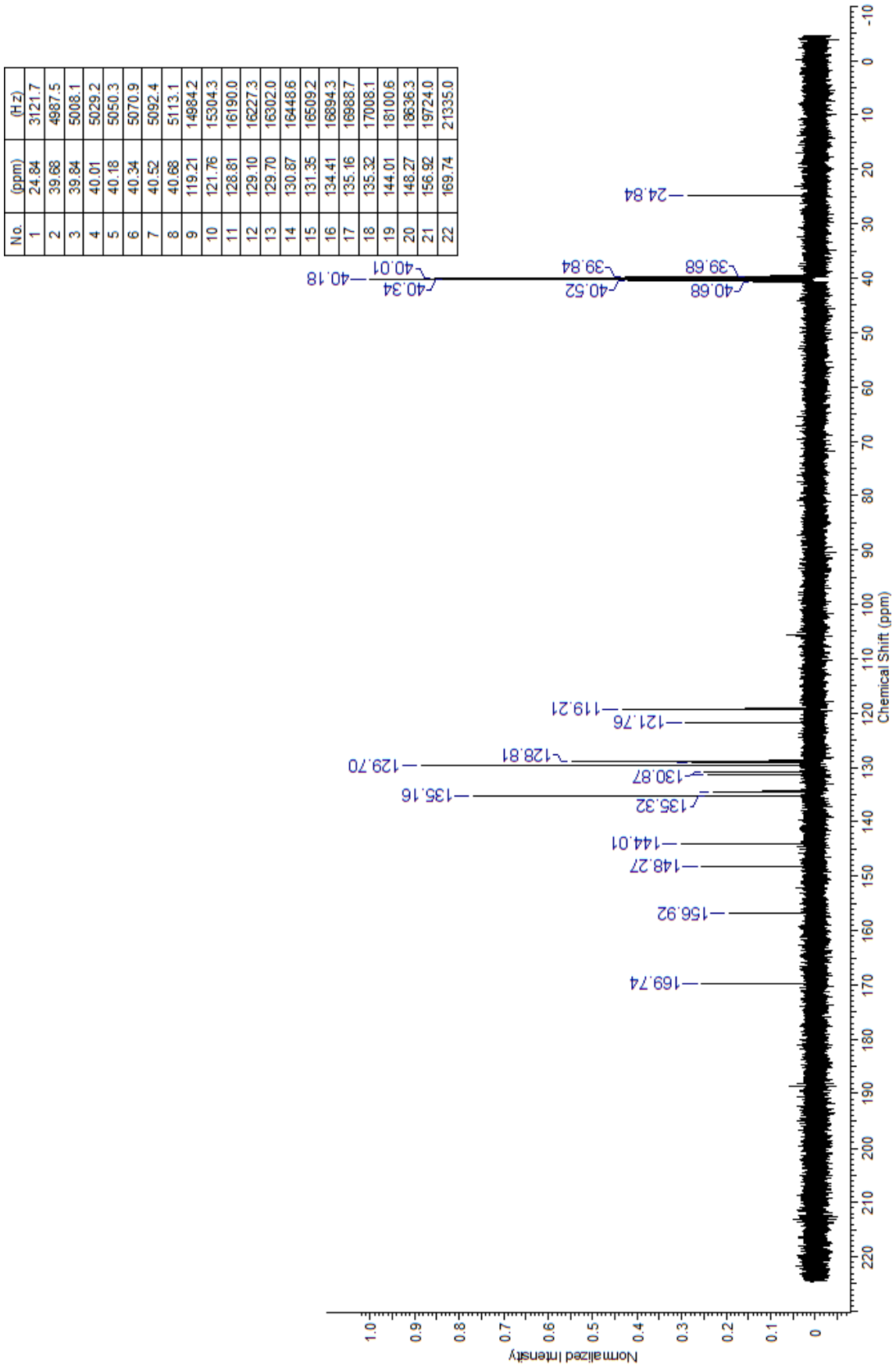
Spectrum 1. ^{1}H NMR of compd **3** (500 MHz, DMSO-d_6).



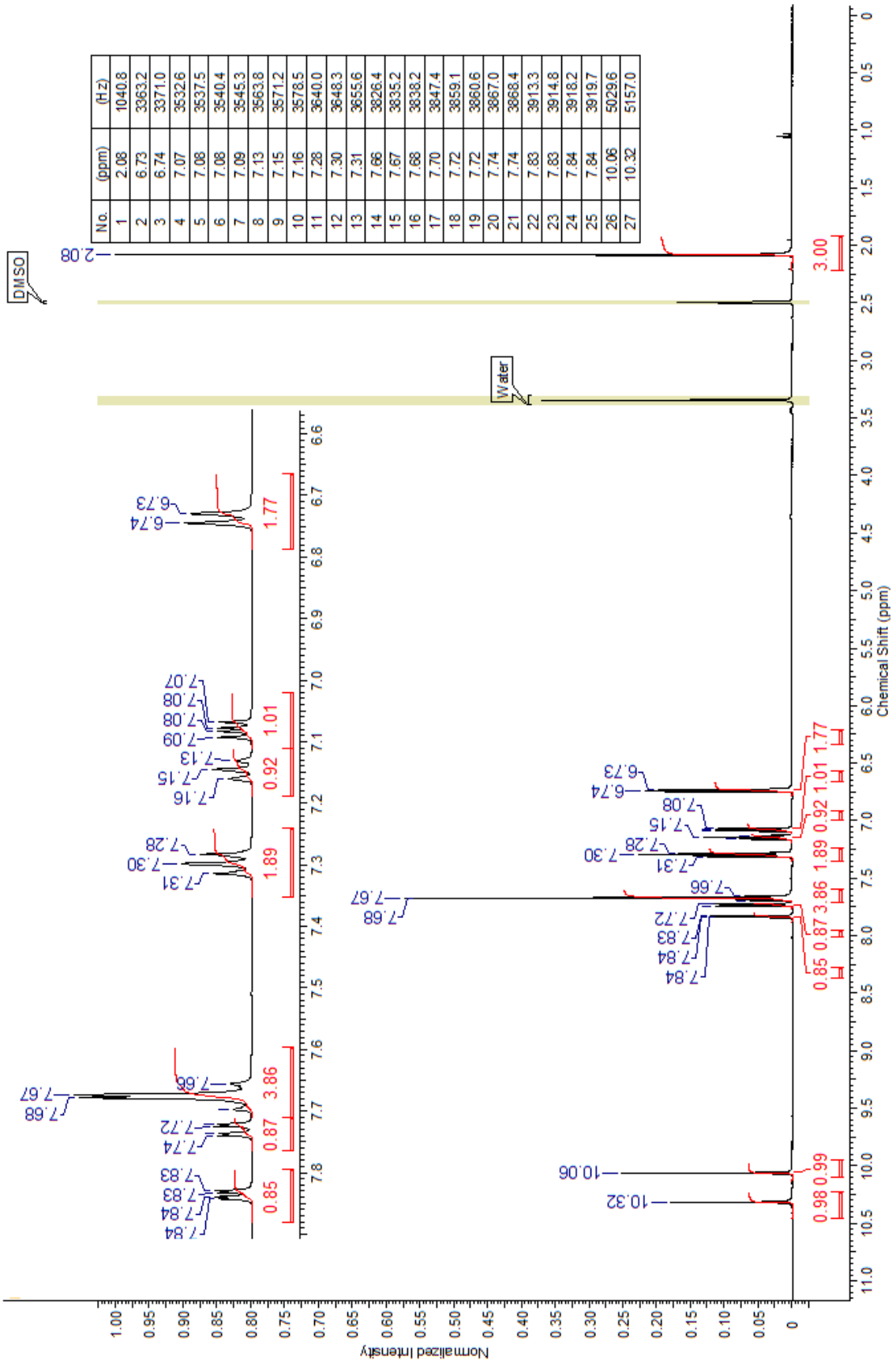
Spectrum 2. ^{13}C NMR of compd **3** (125 MHz, DMSO-d_6).



Spectrum 3. ^{1}H NMR of compd **4** (500 MHz, DMSO-d_6).

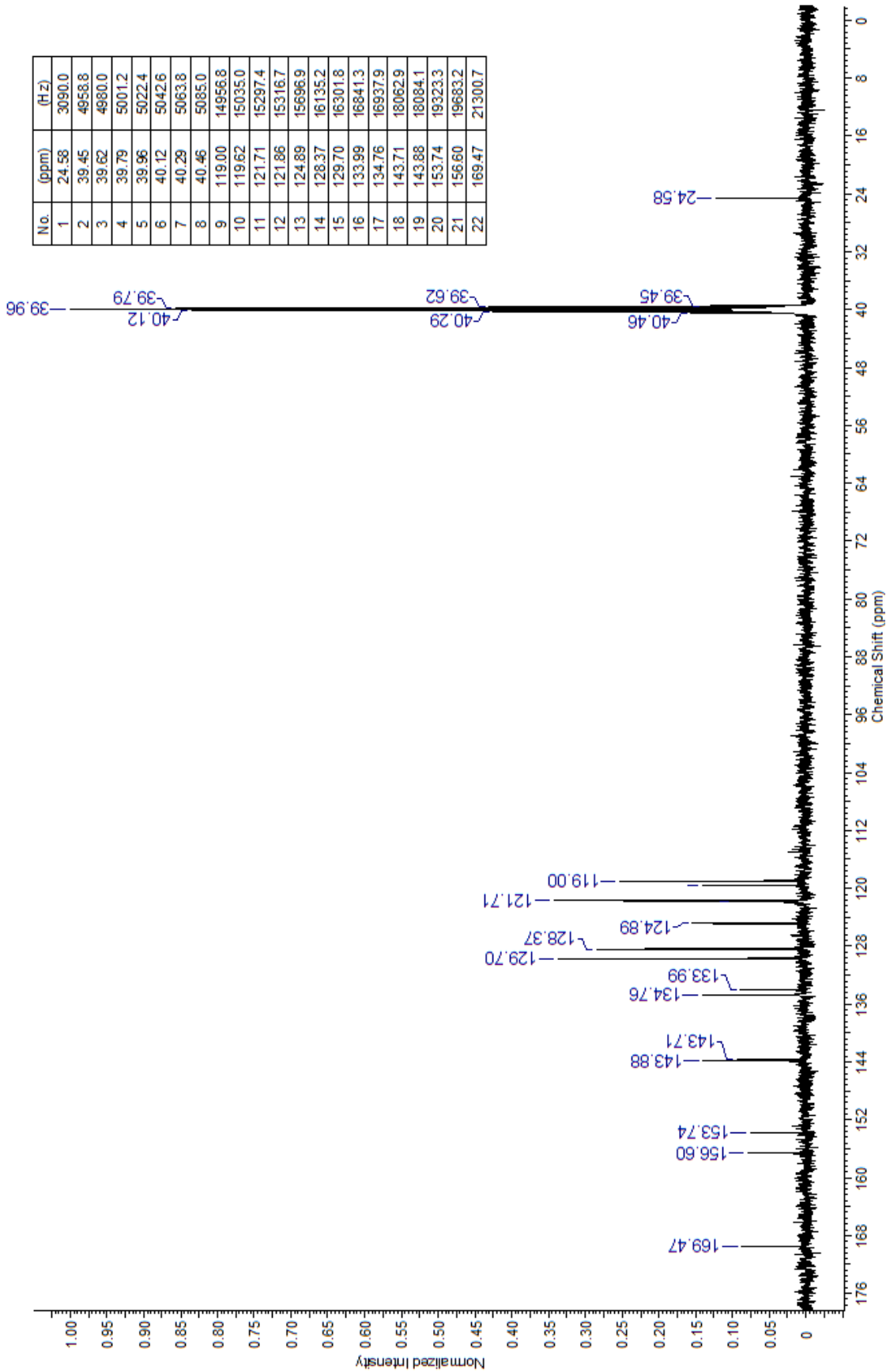


Spectrum 4. ^{13}C NMR of compd **4** (125 MHz, DMSO-d_6).

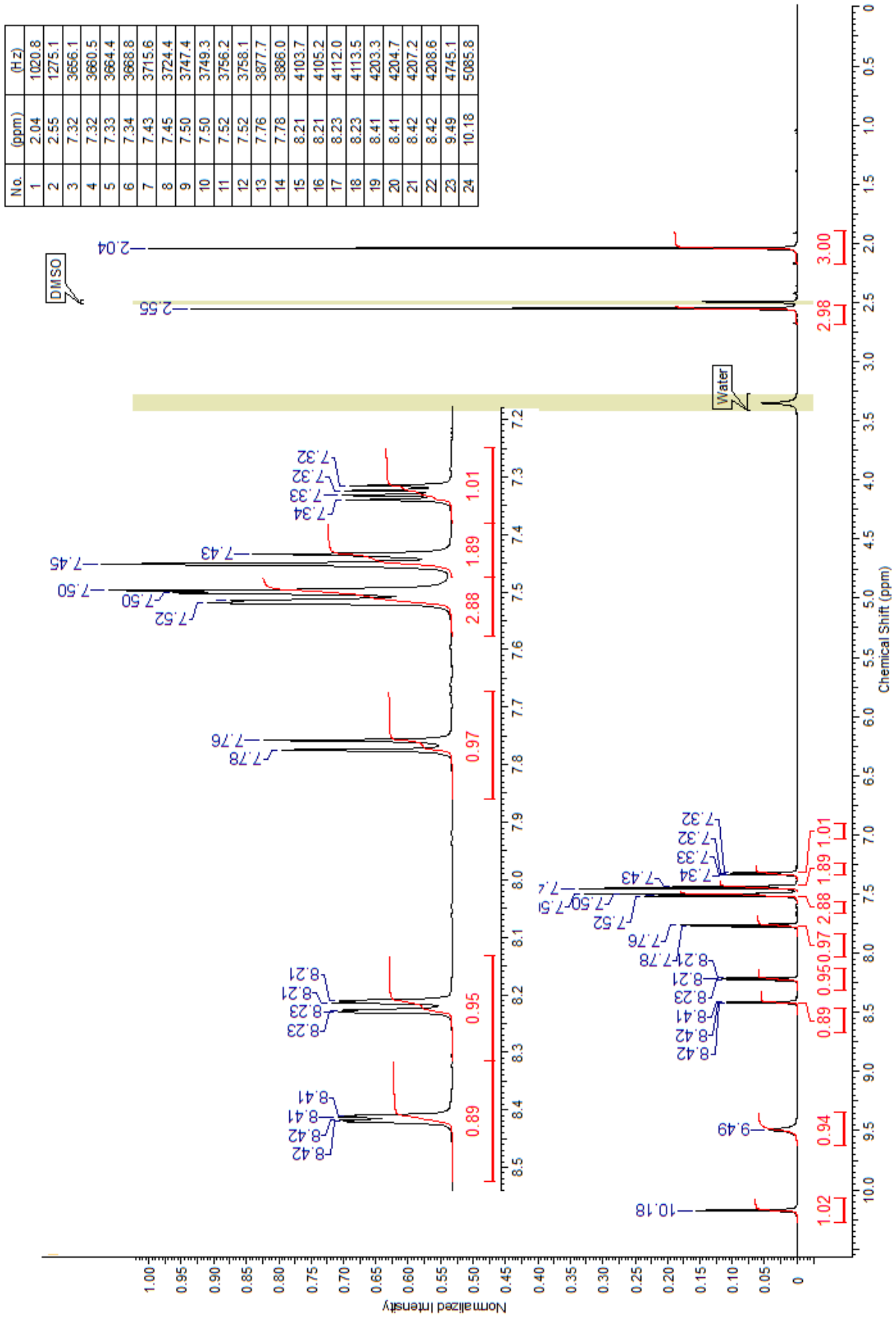


No.	(ppm)	(Hz)
1	2.08	1040.8
2	6.73	3363.2
3	6.74	3371.0
4	7.07	3532.6
5	7.08	3537.5
6	7.08	3540.4
7	7.09	3545.3
8	7.13	3563.8
9	7.15	3571.2
10	7.16	3578.5
11	7.28	3640.0
12	7.30	3648.3
13	7.31	3655.6
14	7.66	3826.4
15	7.67	3835.2
16	7.68	3838.2
17	7.70	3847.4
18	7.72	3859.1
19	7.72	3860.6
20	7.74	3867.0
21	7.74	3868.4
22	7.83	3913.3
23	7.83	3914.8
24	7.84	3918.2
25	7.84	3919.7
26	10.06	5029.6
27	10.32	5157.0

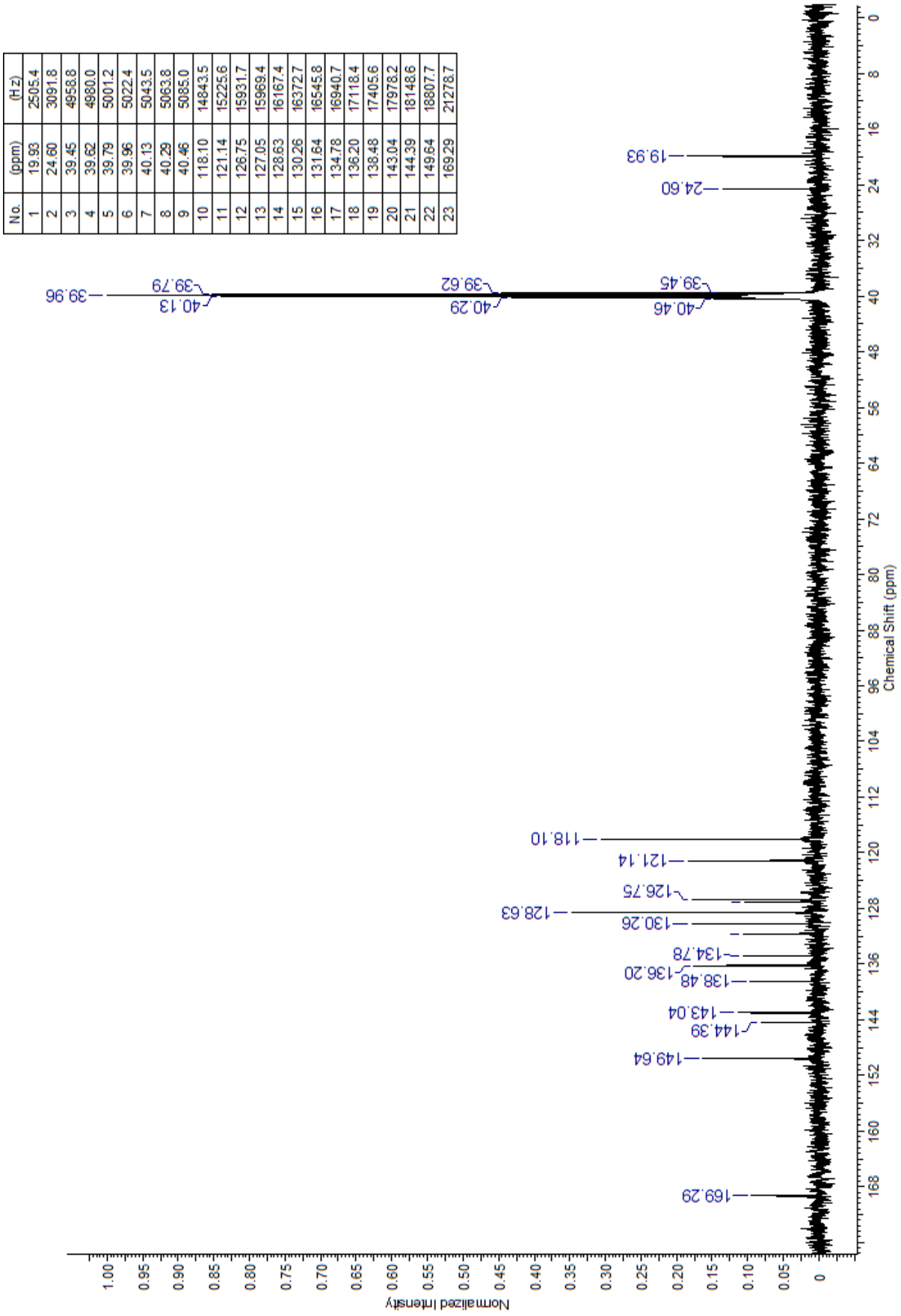
Spectrum 5. ^{1}H NMR of compd **5** (500 MHz, DMSO-d_6).



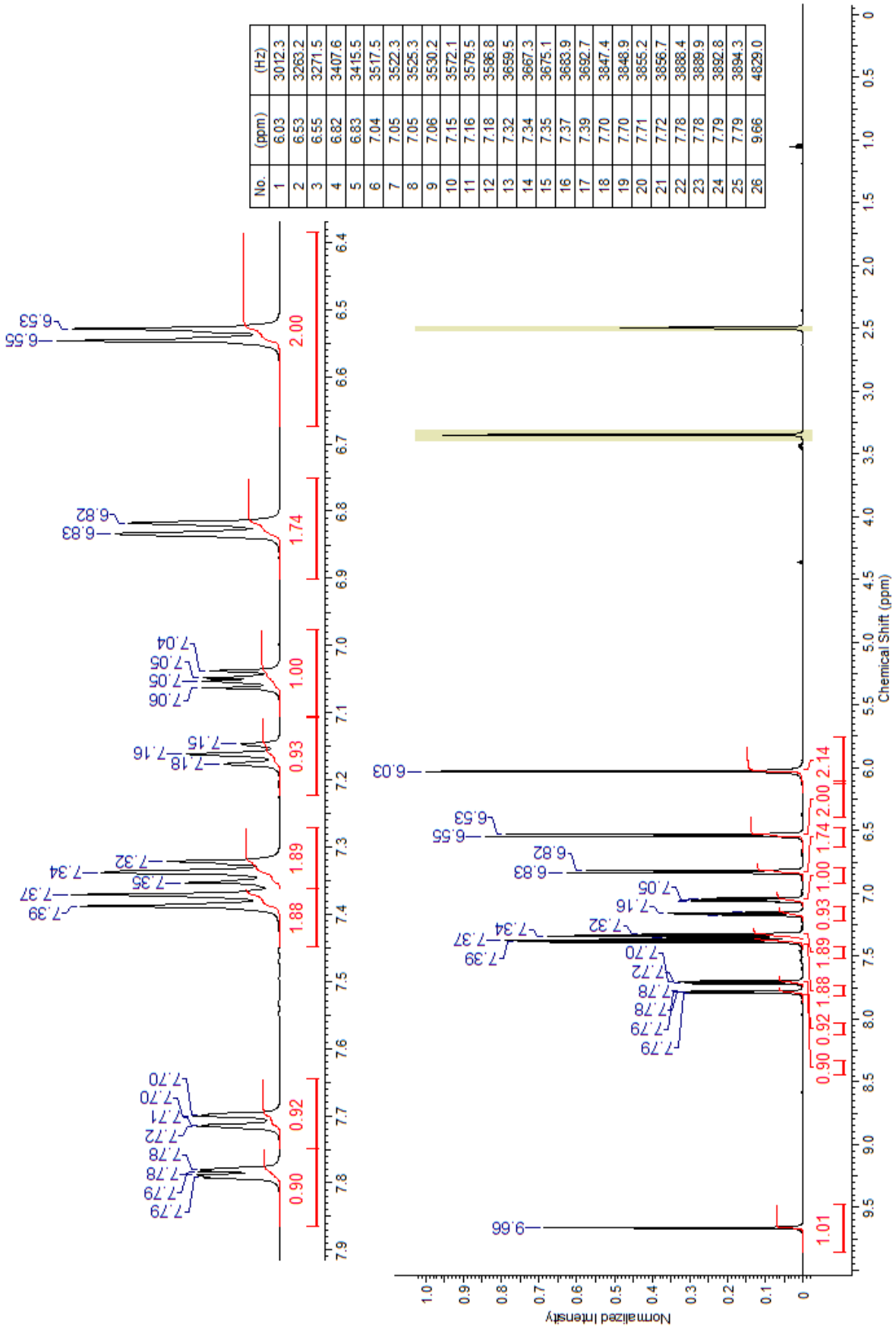
Spectrum 6. ^{13}C NMR of compd **5** (125 MHz, DMSO-d_6).



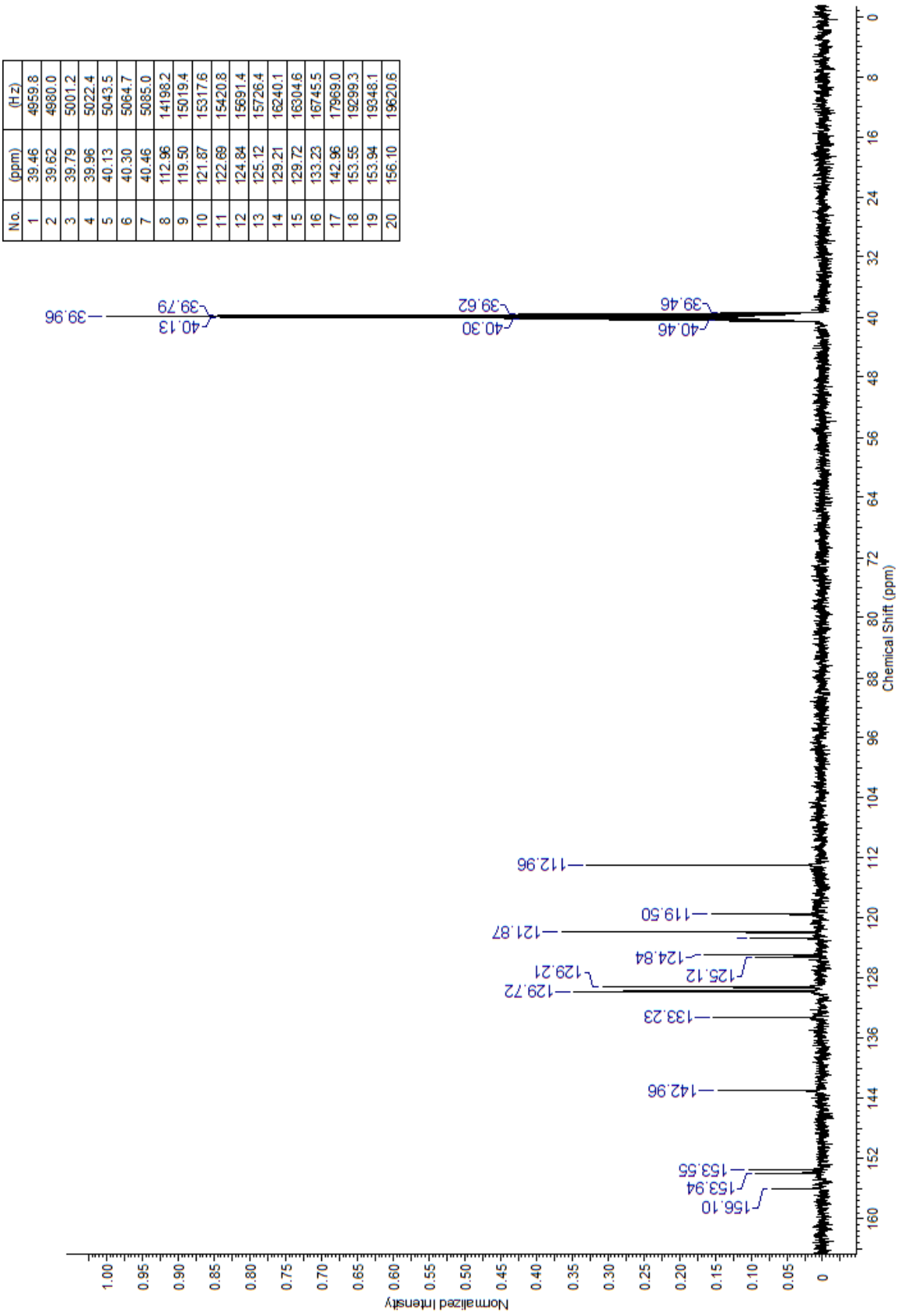
Spectrum 7. ^{1}H NMR of compd **8** (500 MHz, DMSO-d_6).



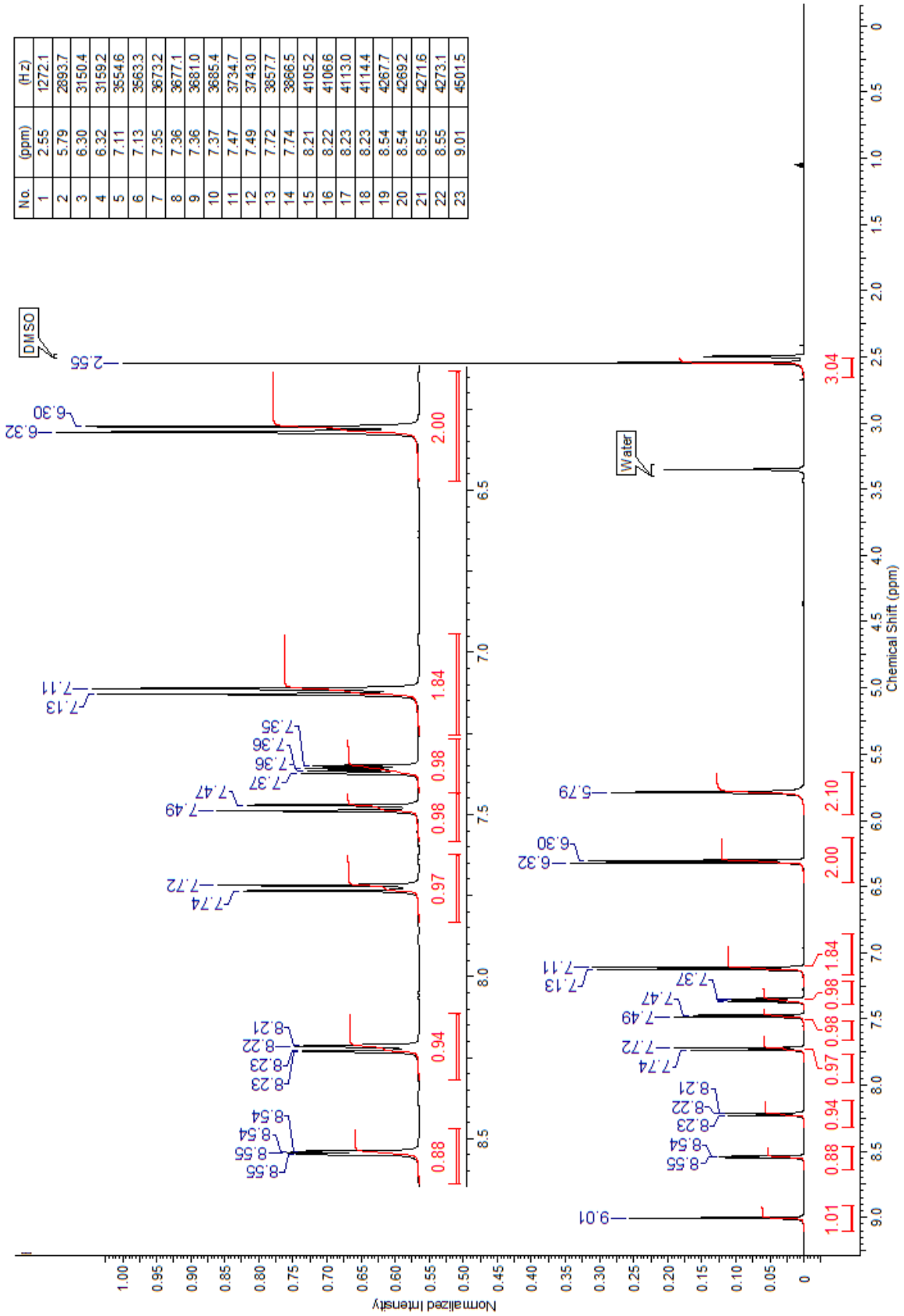
Spectrum 8. ^{13}C NMR of compd **8** (125 MHz, DMSO-d_6).



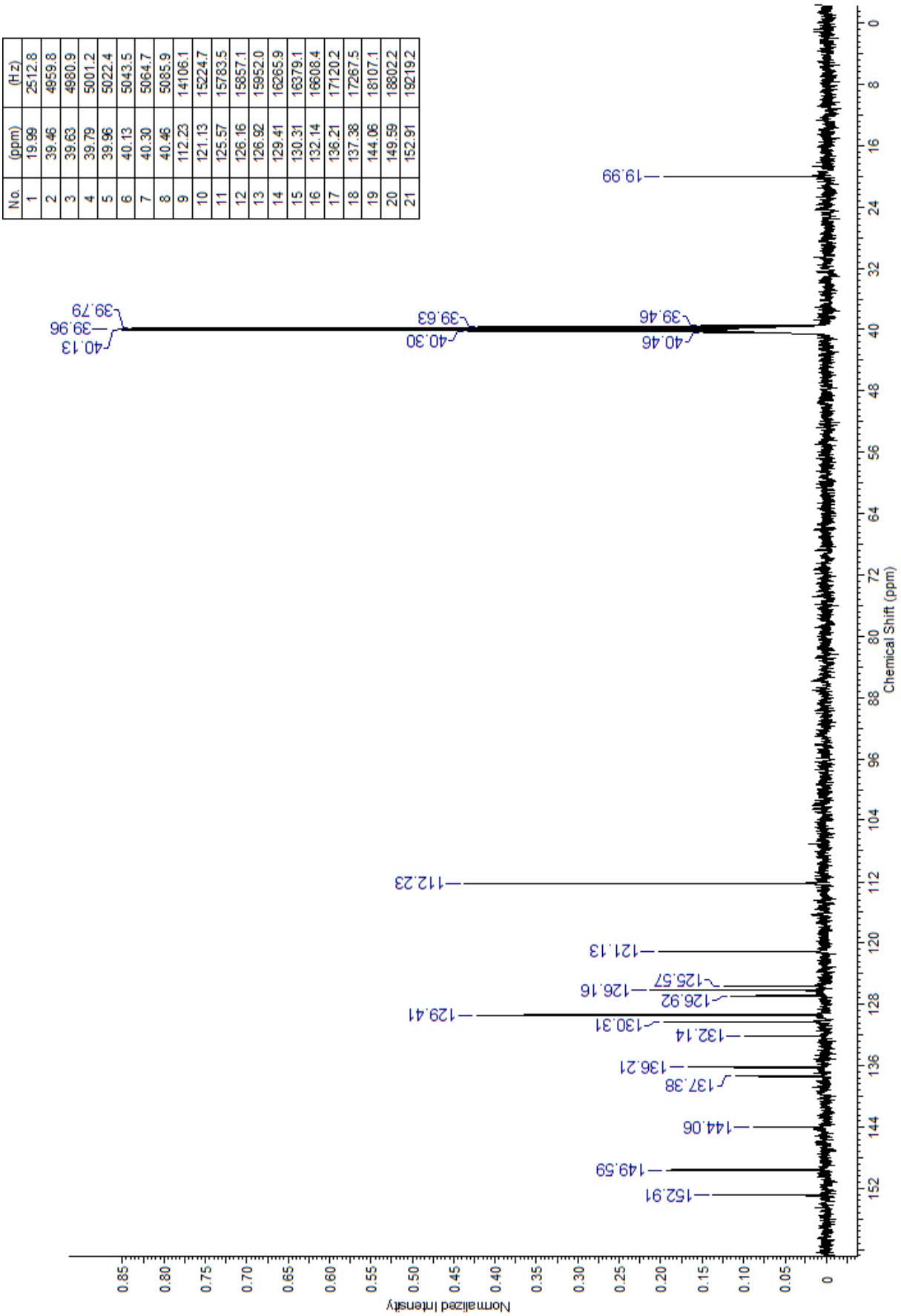
Spectrum 9. ^{1}H NMR of compd **16** (500 MHz, DMSO-d_6).



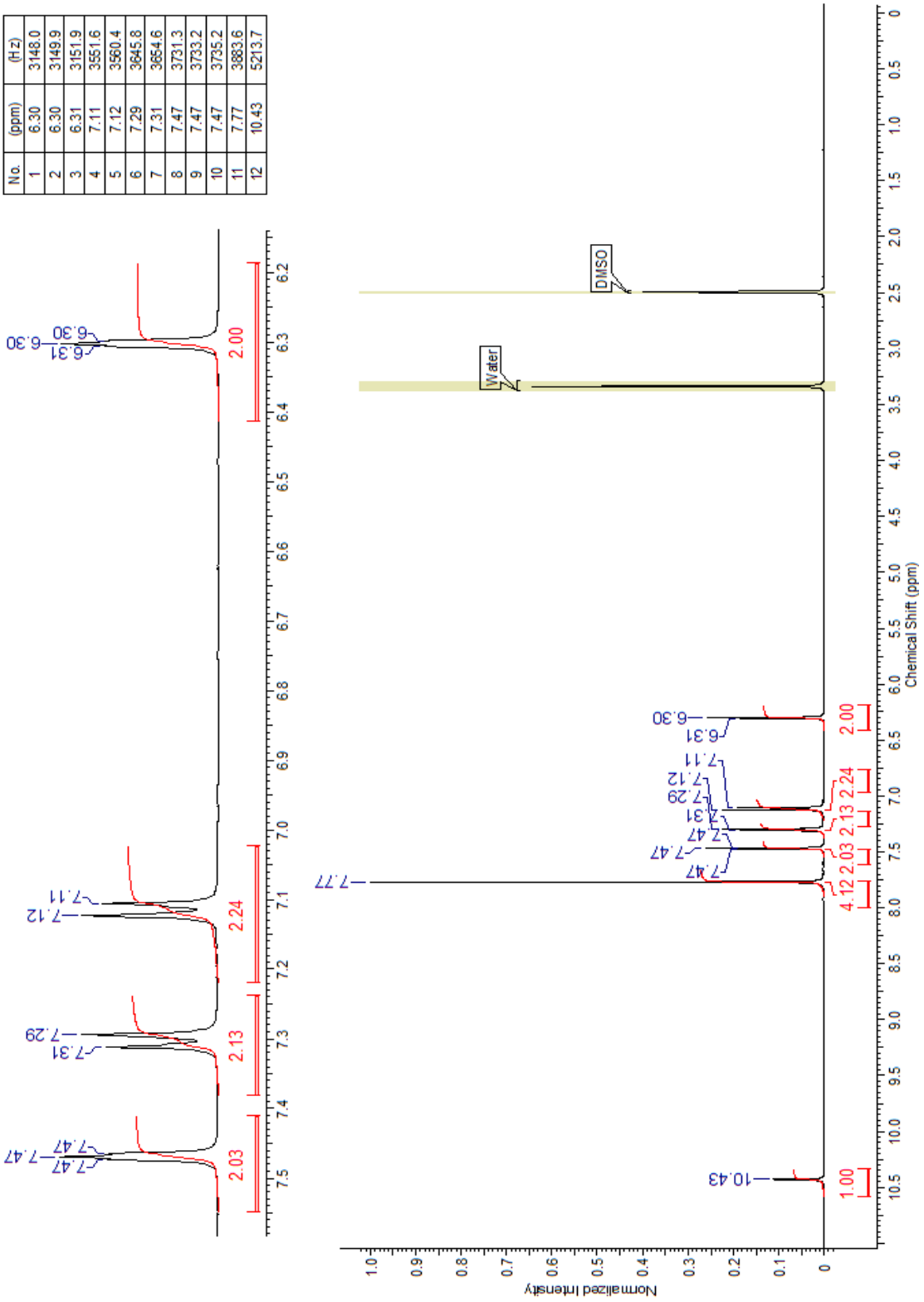
Spectrum 10. ^{13}C NMR of compd **16** (125 MHz, DMSO-d_6).



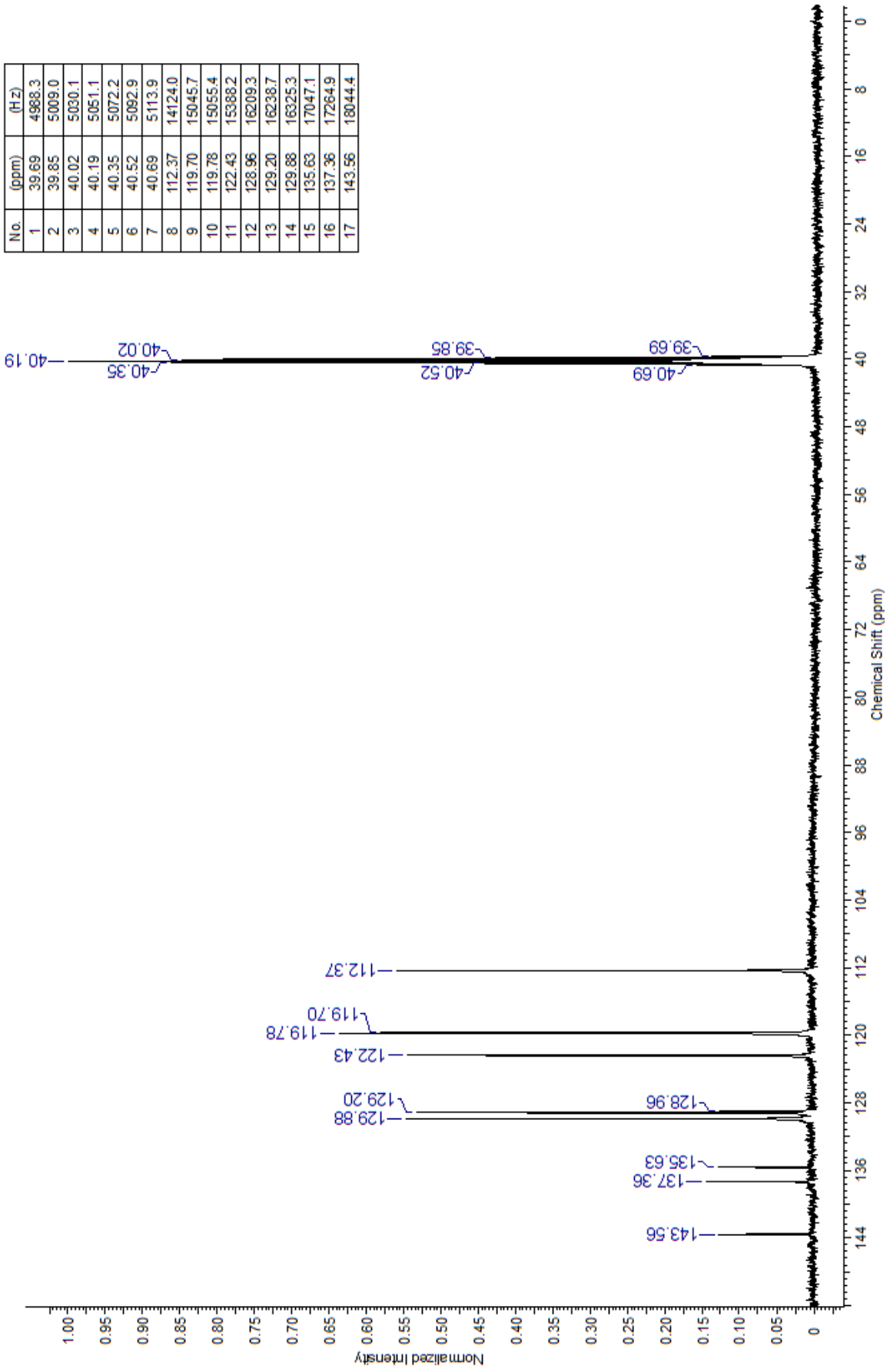
Spectrum 11. ^{1}H NMR of compd **19** (500 MHz, DMSO-d_6).



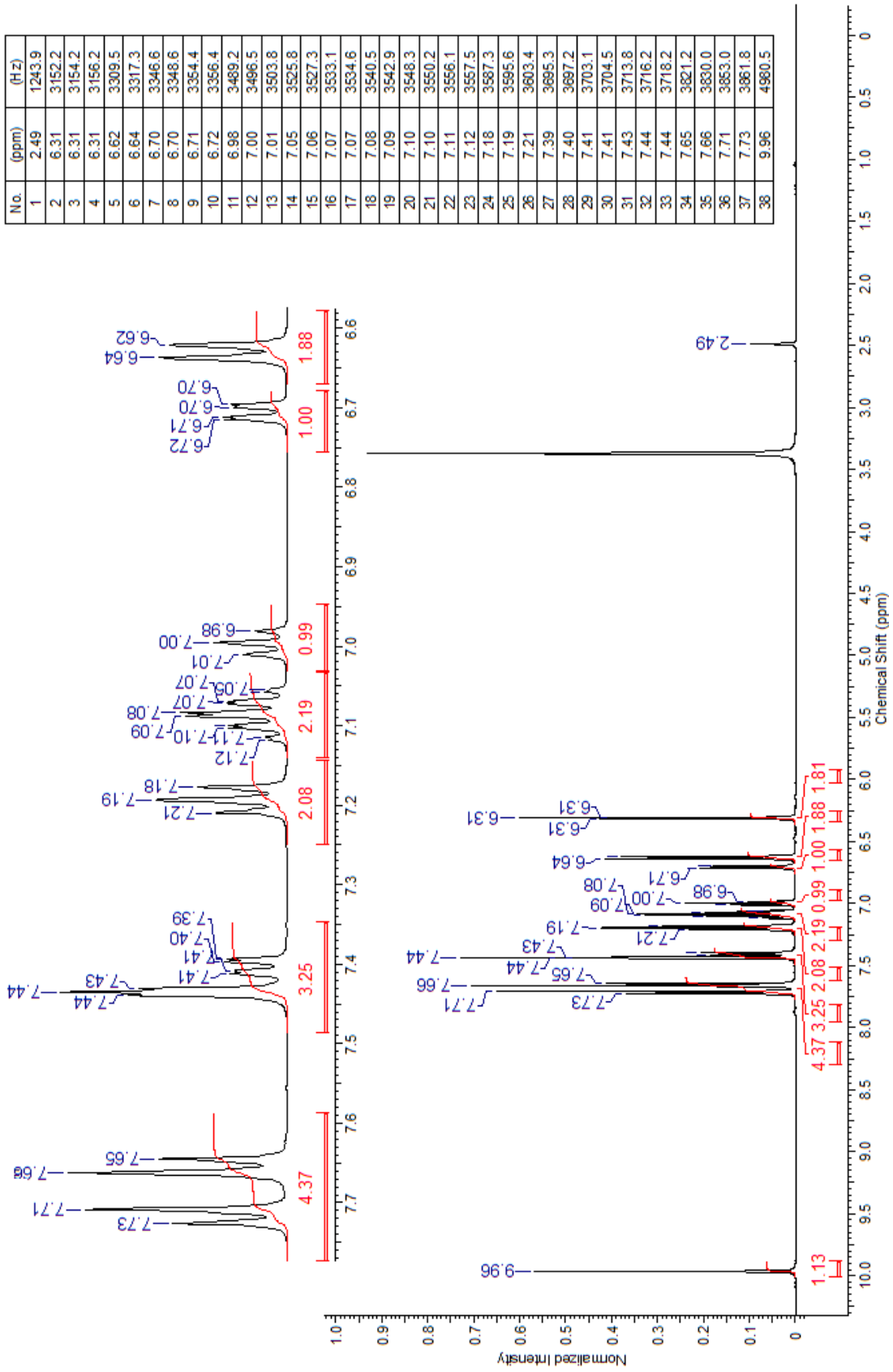
Spectrum 12. ^{13}C NMR of compd **19** (125 MHz, DMSO-d_6).



Spectrum 13. ^{1}H NMR of compd **23** (500 MHz, DMSO-d_6).

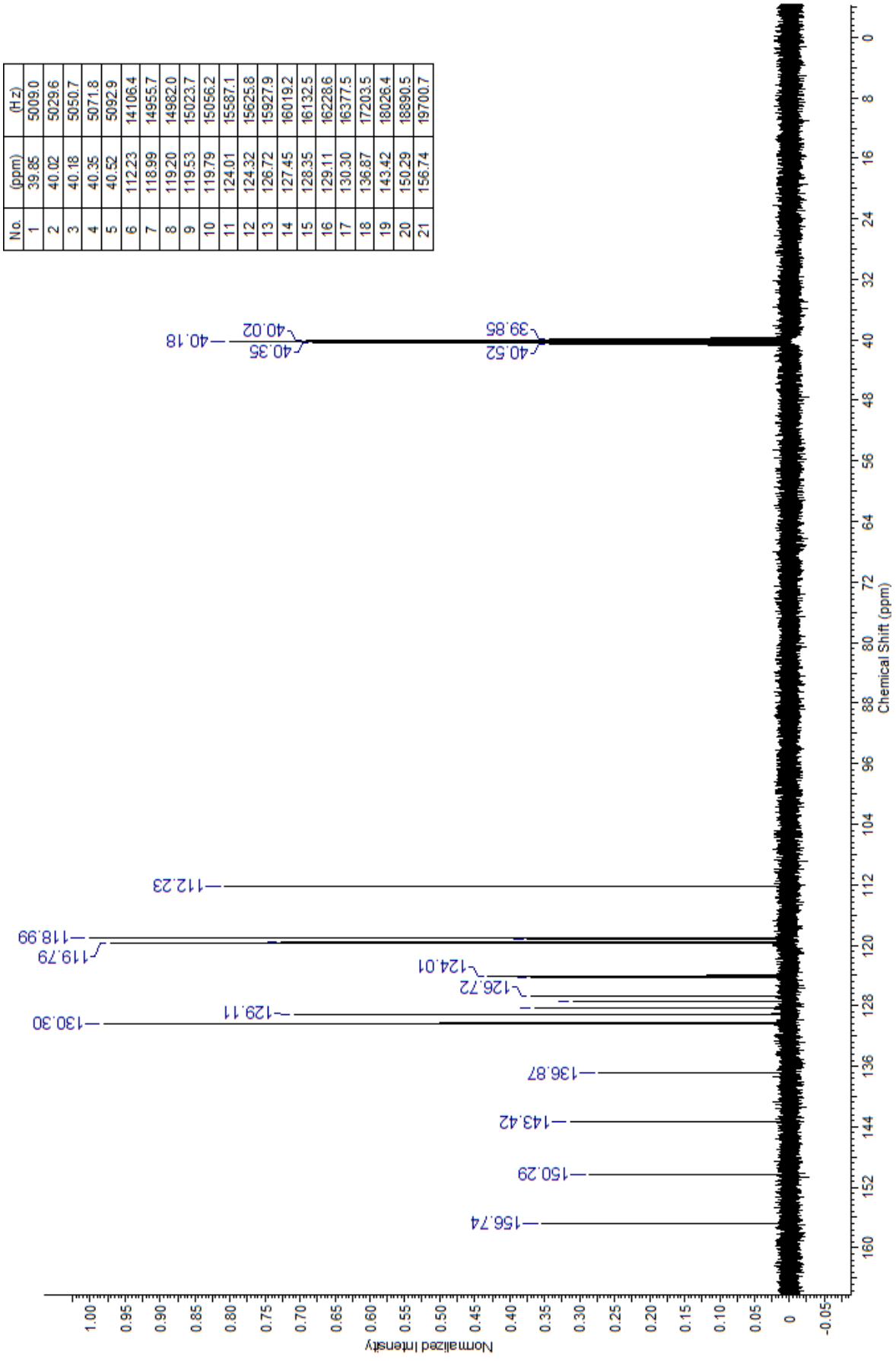


Spectrum 14. ^{13}C NMR of compd **23** (125 MHz, DMSO-d_6).

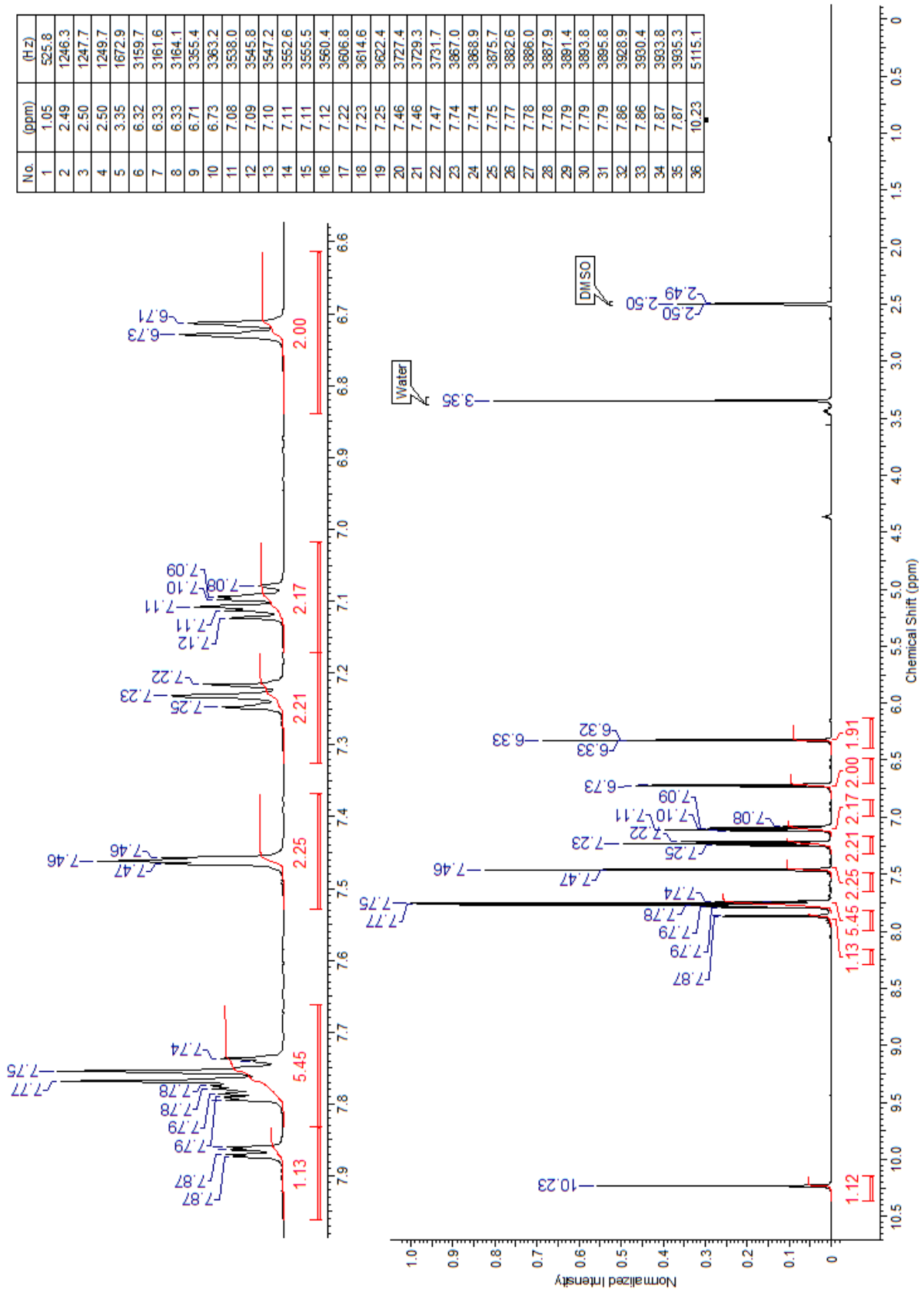


No.	(ppm)	(Hz)
1	2.49	1243.9
2	6.31	3152.2
3	6.31	3154.2
4	6.31	3156.2
5	6.62	3309.5
6	6.64	3317.3
7	6.70	3346.6
8	6.70	3348.6
9	6.71	3354.4
10	6.72	3356.4
11	6.98	3489.2
12	7.00	3496.5
13	7.01	3503.8
14	7.05	3525.8
15	7.06	3527.3
16	7.07	3533.1
17	7.07	3534.6
18	7.08	3540.5
19	7.09	3542.9
20	7.10	3548.3
21	7.10	3550.2
22	7.11	3556.1
23	7.12	3557.5
24	7.18	3587.3
25	7.19	3595.6
26	7.21	3603.4
27	7.39	3695.3
28	7.40	3697.2
29	7.41	3703.1
30	7.41	3704.5
31	7.43	3713.8
32	7.44	3716.2
33	7.44	3718.2
34	7.65	3821.2
35	7.66	3830.0
36	7.71	3853.0
37	7.73	3861.8
38	9.96	4980.5

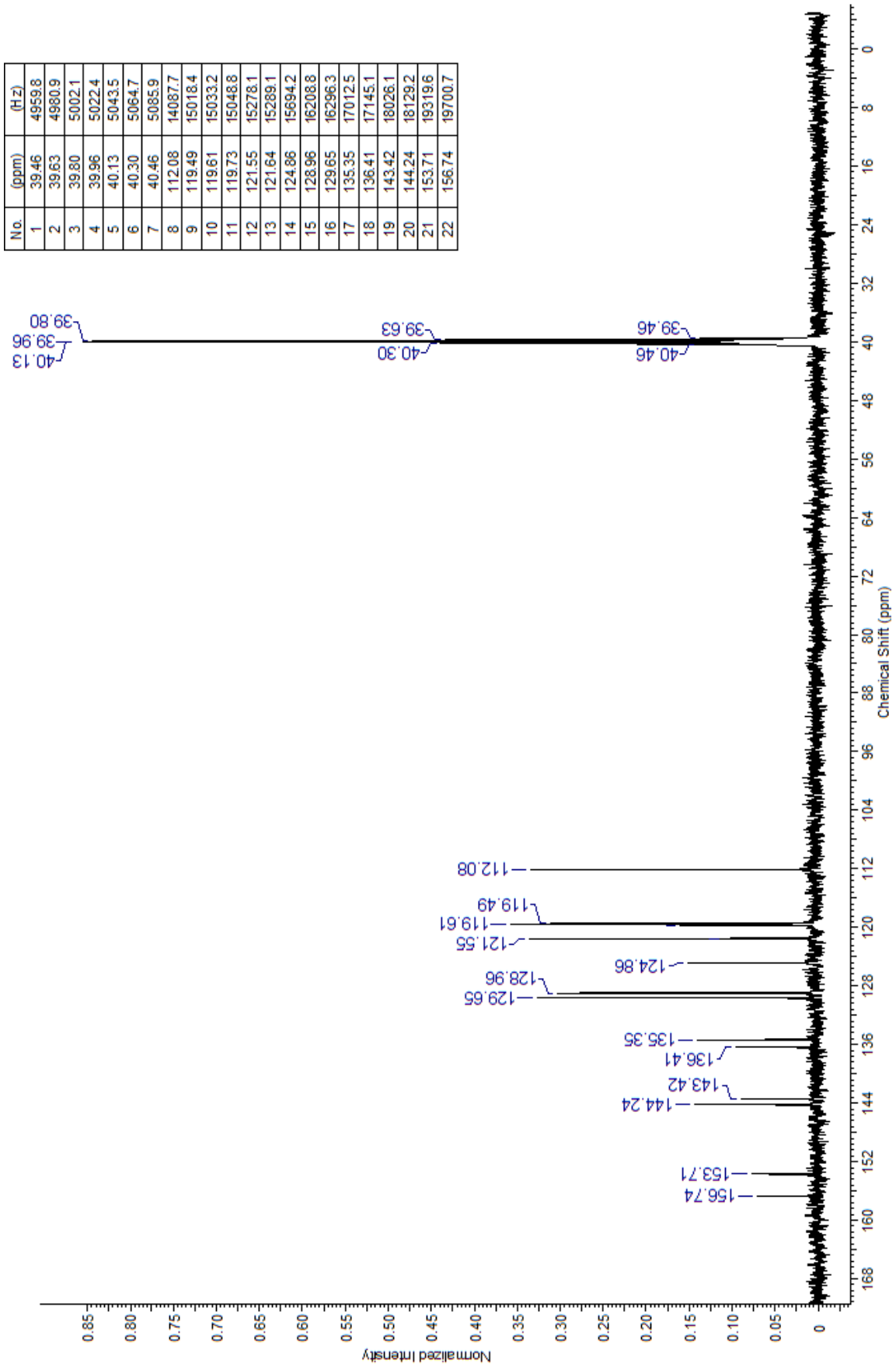
Spectrum 15. ^{1}H NMR of compd **25** (500 MHz, DMSO-d_6).



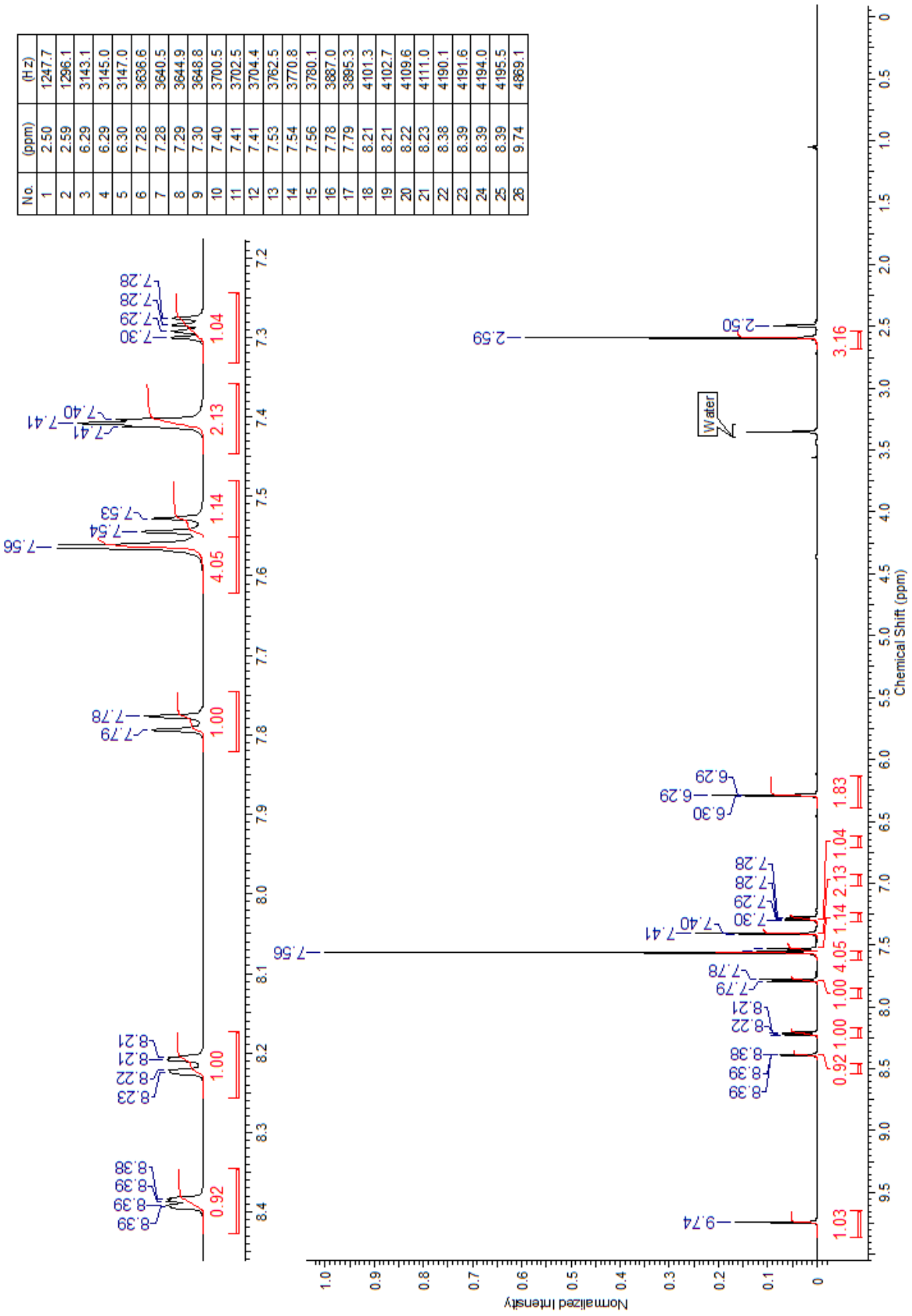
Spectrum 16. ^{13}C NMR of compd **25** (125 MHz, DMSO-d_6).



Spectrum 17. ^{1}H NMR of compd **27** (500 MHz, DMSO-d_6).

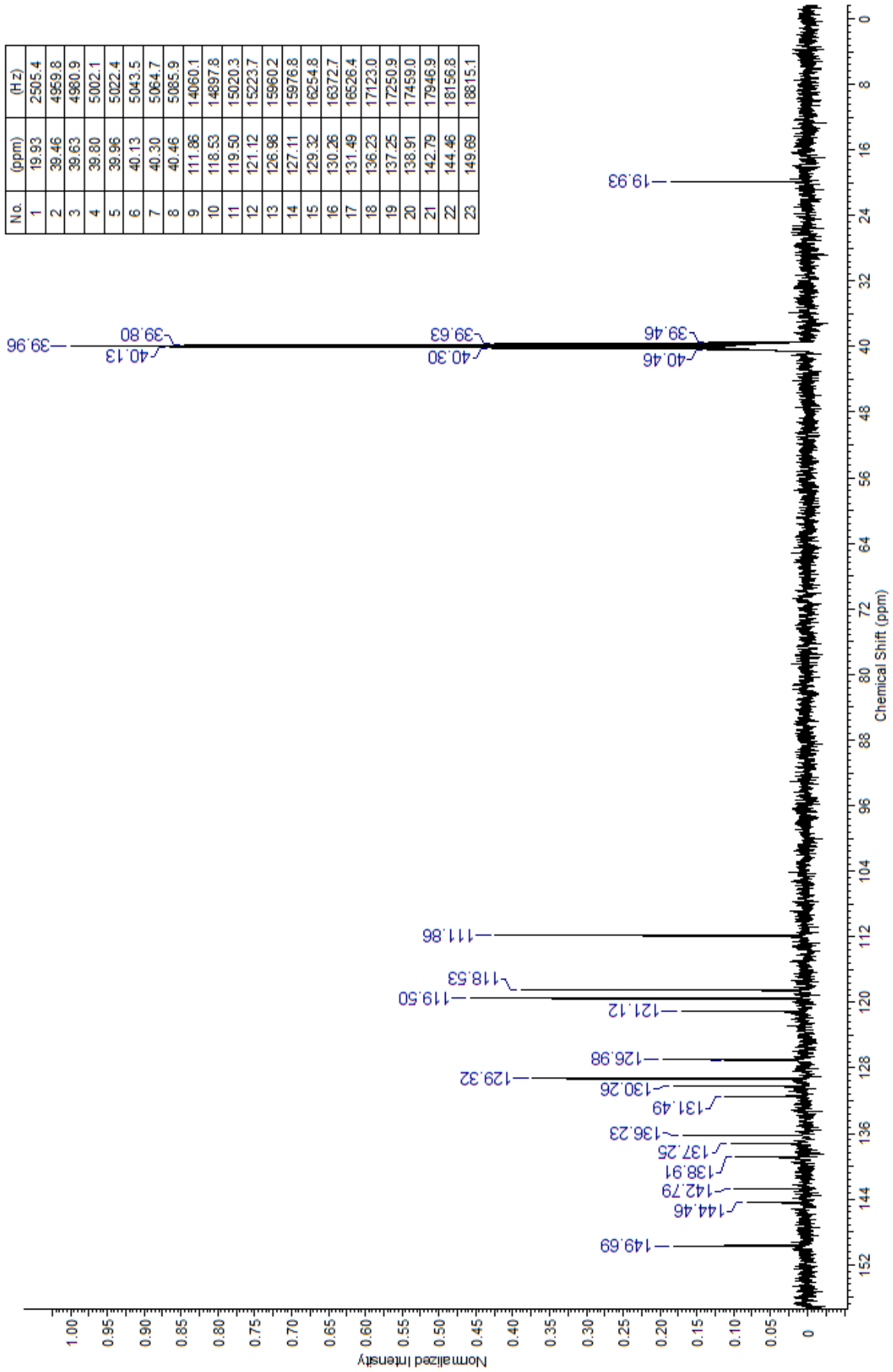


Spectrum 18. ^{13}C NMR of compd **27** (125 MHz, DMSO-d_6).



No.	(ppm)	(Hz)
1	2.50	1247.7
2	2.59	1296.1
3	6.29	3143.1
4	6.29	3145.0
5	6.30	3147.0
6	7.28	3636.6
7	7.28	3640.5
8	7.29	3644.9
9	7.30	3648.8
10	7.40	3700.5
11	7.41	3702.5
12	7.41	3704.4
13	7.53	3762.5
14	7.54	3770.8
15	7.56	3780.1
16	7.78	3887.0
17	7.79	3895.3
18	8.21	4101.3
19	8.21	4102.7
20	8.22	4109.6
21	8.23	4111.0
22	8.38	4190.1
23	8.39	4191.6
24	8.39	4194.0
25	8.39	4195.5
26	9.74	4869.1

Spectrum 19. ^{1}H NMR of compd **30** (500 MHz, DMSO-d_6).



Spectrum 20. ^{13}C NMR of compd **30** (125 MHz, DMSO-d_6).