Supplementary Material

Heteroannelation of cyclic ketones: Synthesis, characterization and antitumor evaluation of some condensed azine derivatives

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Running Title: Heteroannelation of cyclic ketones.

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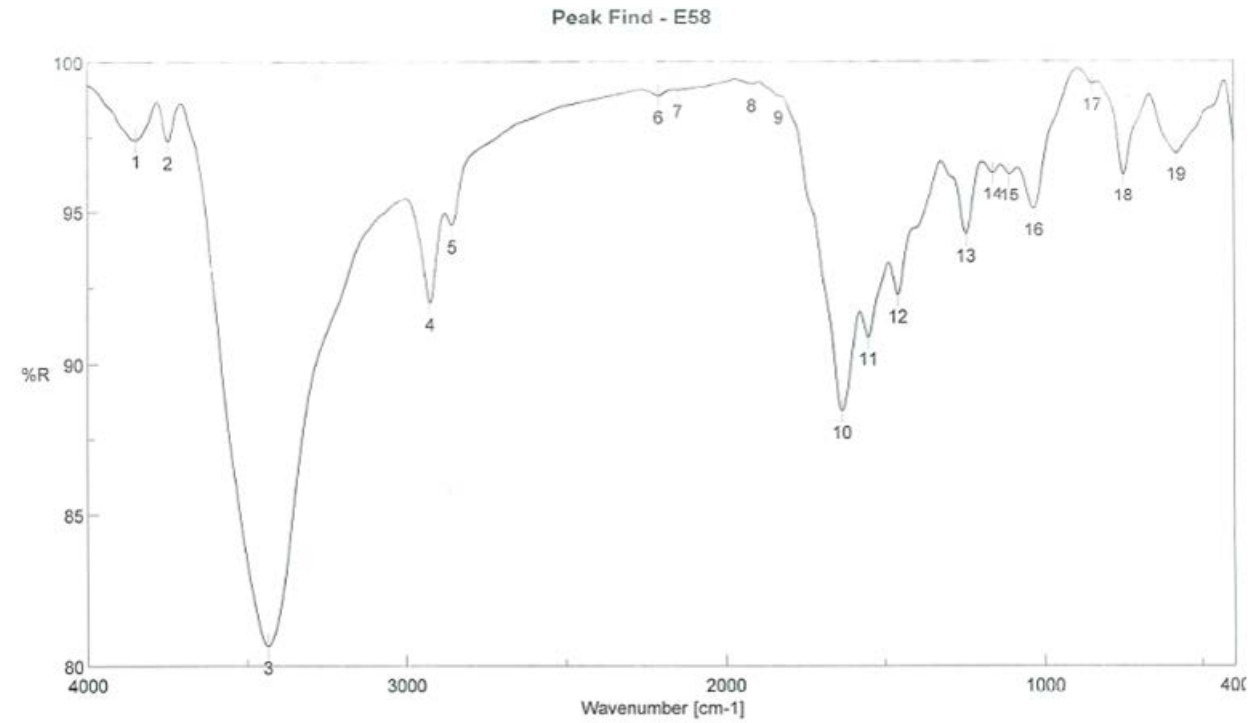
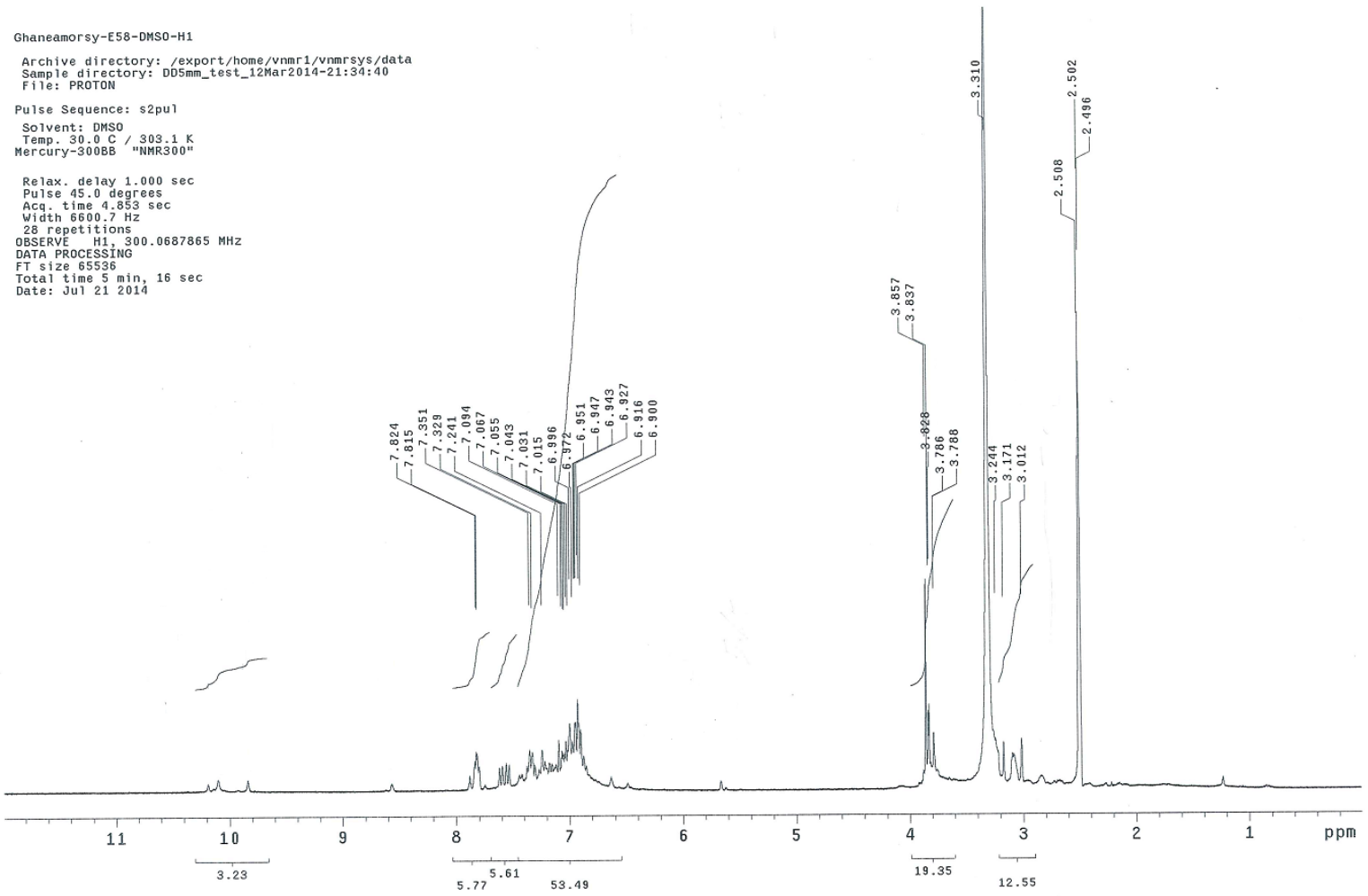


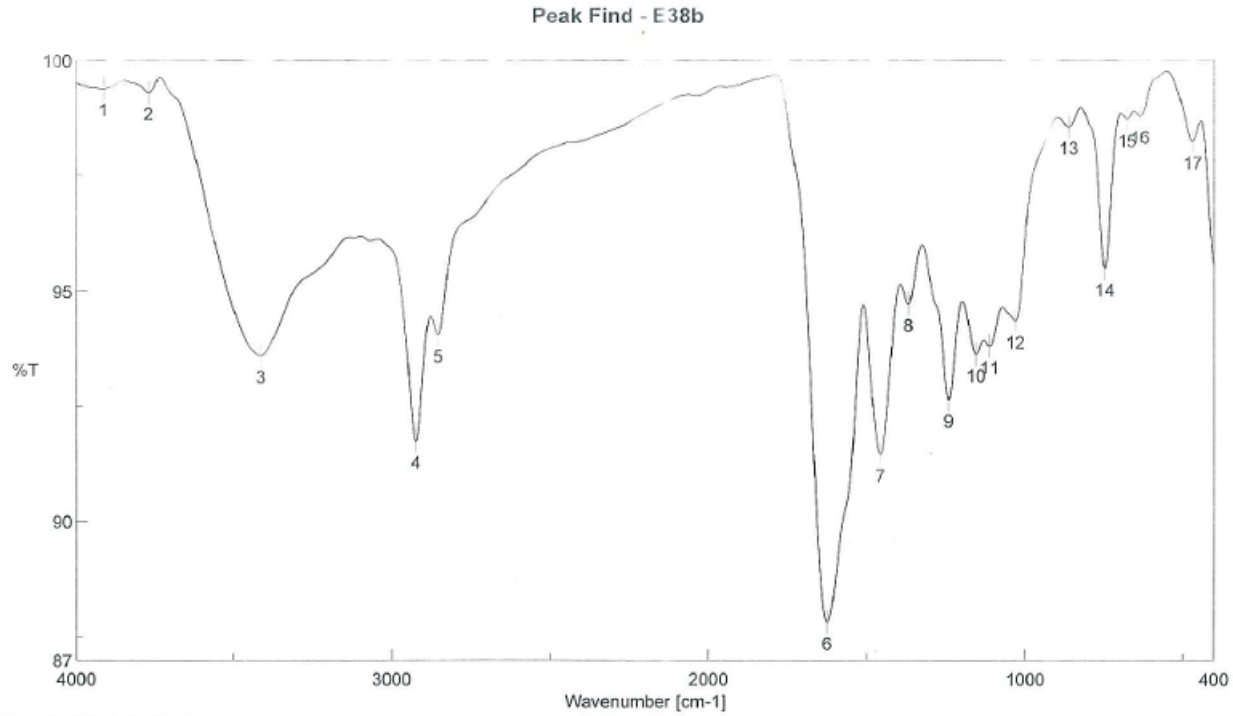
[Result of Peak Picking]

No.	Position	Intensity	No.	Position	Intensity	No.	Position	Intensity	No.	Position	Intensity
1	3847.29	97.4132	2	3747.01	97.36	3	3434.6	80.6656	4	2925.48	92.0129
5	2856.06	94.5459	6	2208.09	98.8739	7	2147.35	99.0681	8	1915.93	99.2567
9	1832.04	98.8647	10	1635.34	88.4186	11	1552.42	90.8622	12	1458.89	92.258
13	1245.79	94.2393	14	1160.94	96.308	15	1108.87	96.2701	16	1032.69	95.092
17	848.525	99.2763	18	751.138	96.2474	19	585.29	96.9564			

S1. IR spectrum (KBr, cm^{-1}) of compound 1



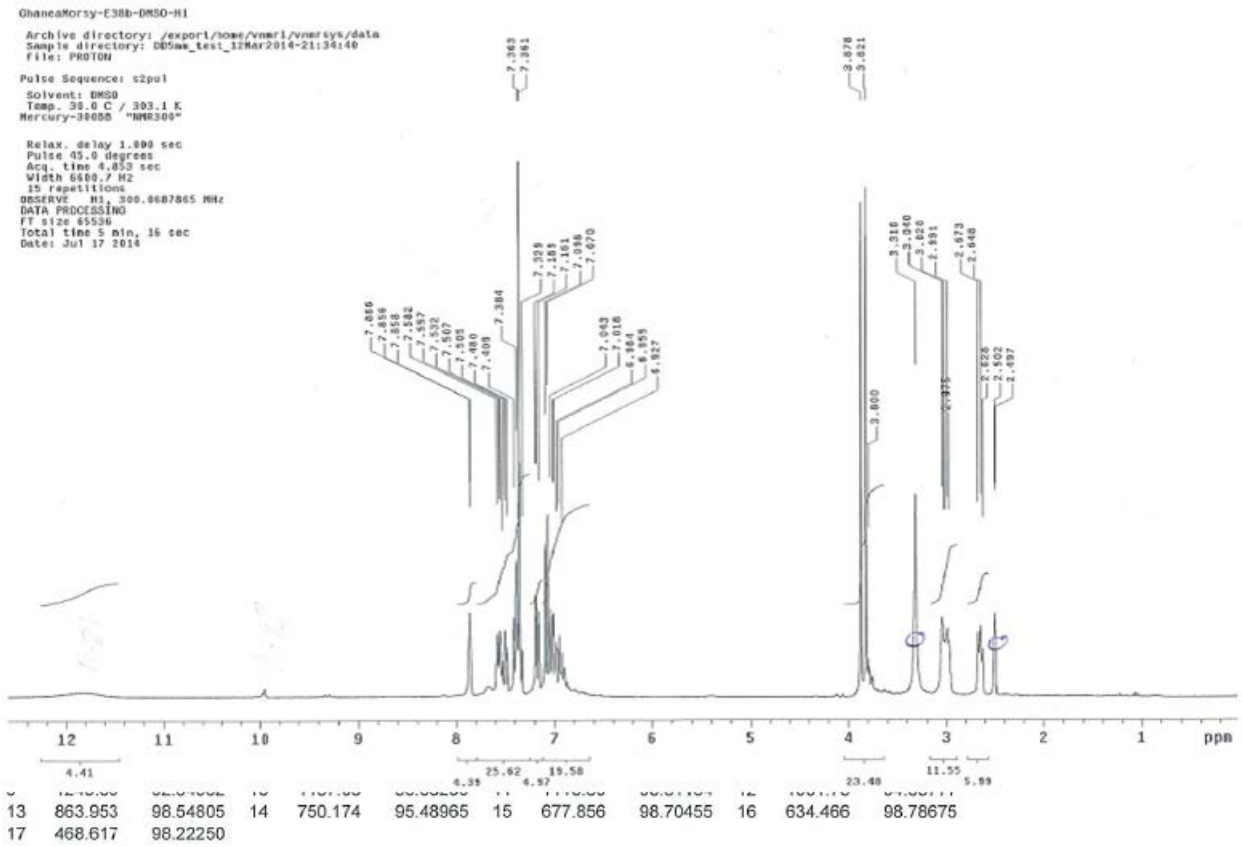
S1. ^{1}H NMR spectrum (300 MHz, DMSO-d_6) of compound 1



[Result of Peak Picking]

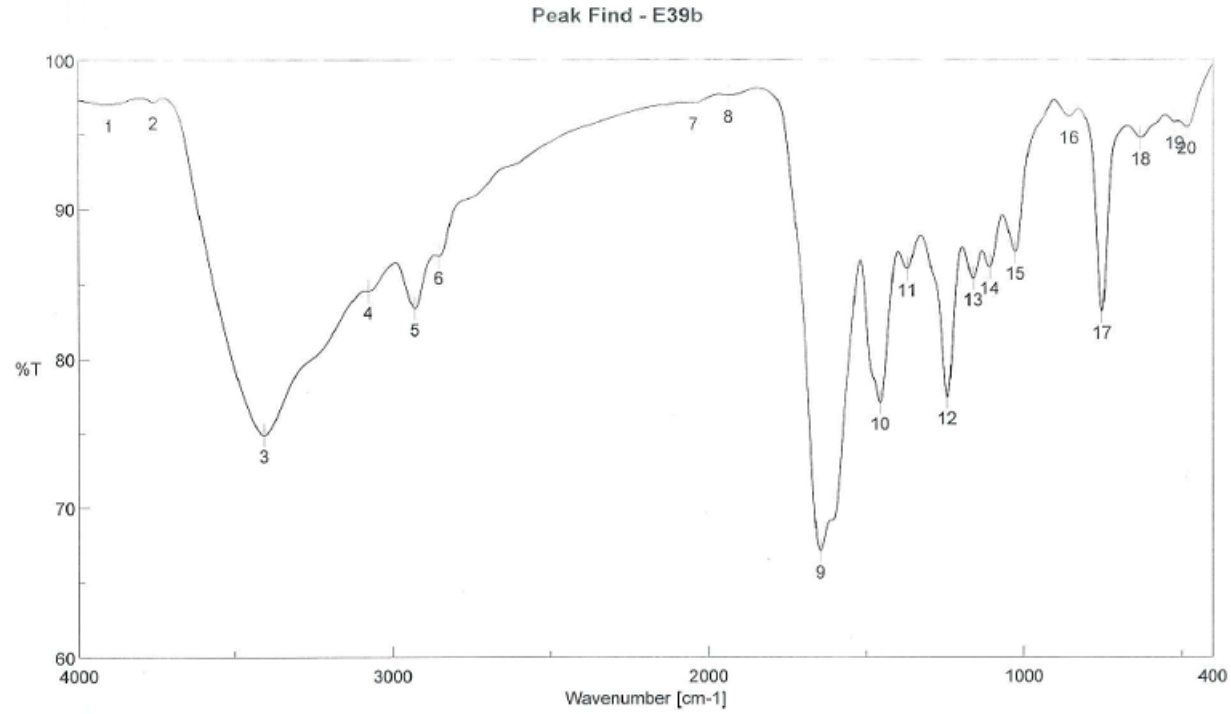
No.	Position	Intensity	No.	Position	Intensity	No.	Position	Intensity	No.	Position	Intensity
1	3913.82	99.38125	2	3768.22	99.29530	3	3414.35	93.59983	4	2924.52	91.74218
5	2854.13	94.05332	6	1626.66	87.82288	7	1458.89	91.45398	8	1371.14	94.72494
9	1243.86	92.64562	10	1157.08	93.63259	11	1113.69	93.81184	12	1031.73	94.35777
13	863.953	98.54805	14	750.174	95.48965	15	677.856	98.70455	16	634.466	98.78675
17	468.617	98.22250									

S2. IR spectrum (KBr, cm^{-1}) of compound 2



13	863.953	98.54805	14	750.174	95.48965	15	677.856	98.70455	16	634.466	98.78675
17	468.617	98.22250									

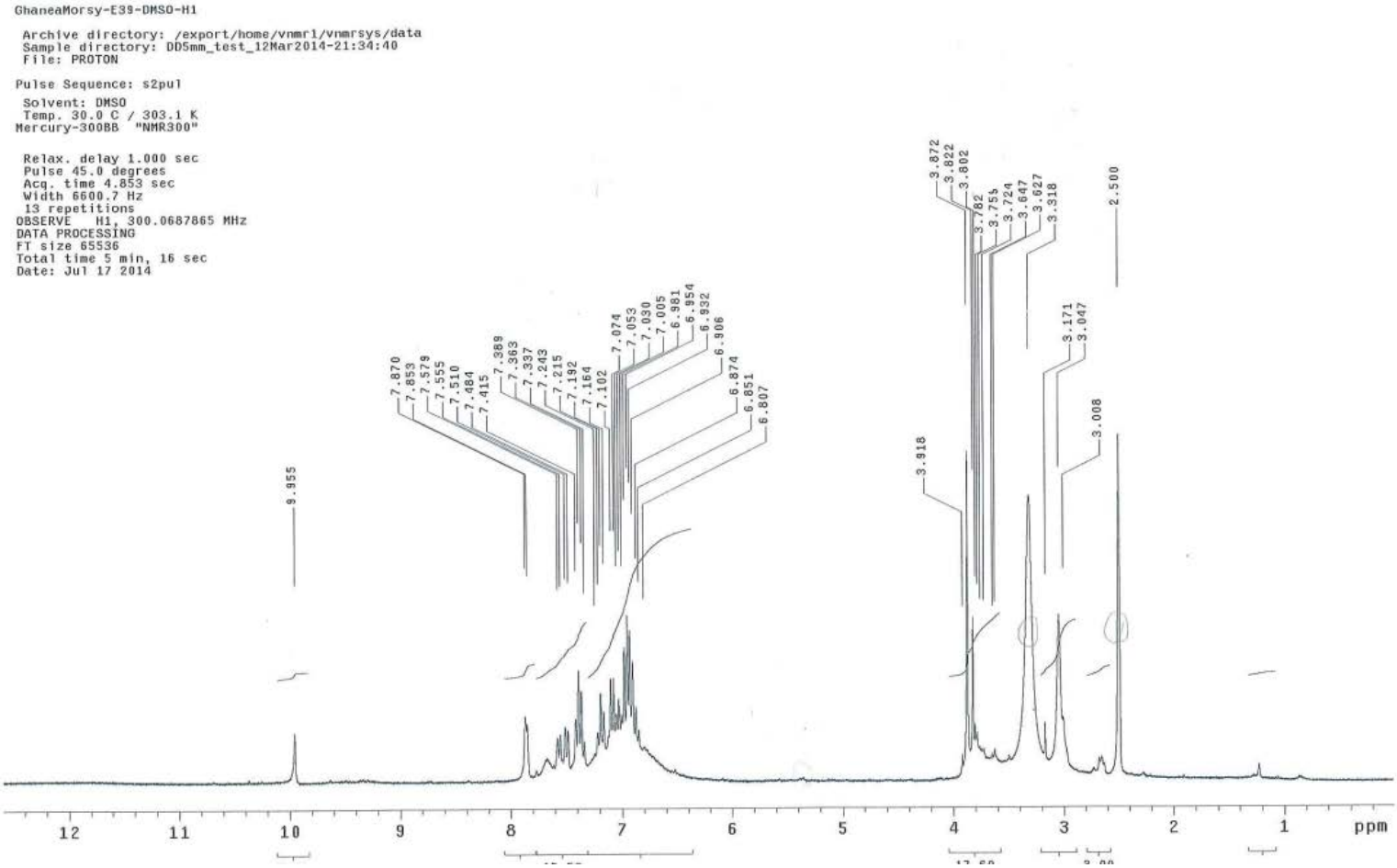
S2. ^{1}H NMR spectrum (300 MHz, DMSO-d_6) of compound 2



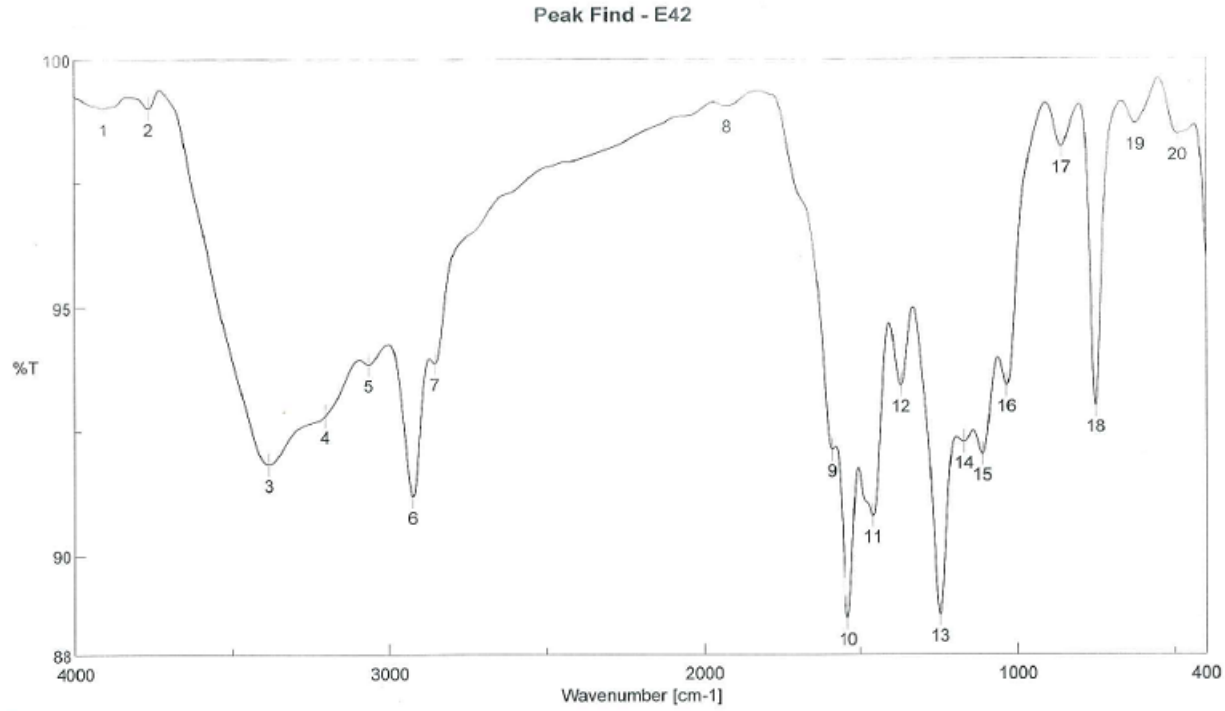
[Result of Peak Picking]

No.	Position	Intensity	No.	Position	Intensity	No.	Position	Intensity	No.	Position	Intensity
1	3902.25	97.00059	2	3756.65	97.18465	3	3408.57	74.87576	4	3076.87	84.51416
5	2930.31	83.37090	6	2854.13	86.81596	7	2048.03	97.10632	8	1938.11	97.59274
9	1646.91	67.07902	10	1457.92	77.05126	11	1372.1	85.98828	12	1244.83	77.40685
13	1162.87	85.35078	14	1110.8	86.12634	15	1028.84	87.11177	16	857.204	96.16417
17	754.995	83.16129	18	632.537	94.72434	19	521.65	95.79539	20	482.117	95.46081

S3. IR spectrum (KBr, cm^{-1}) of compound 3



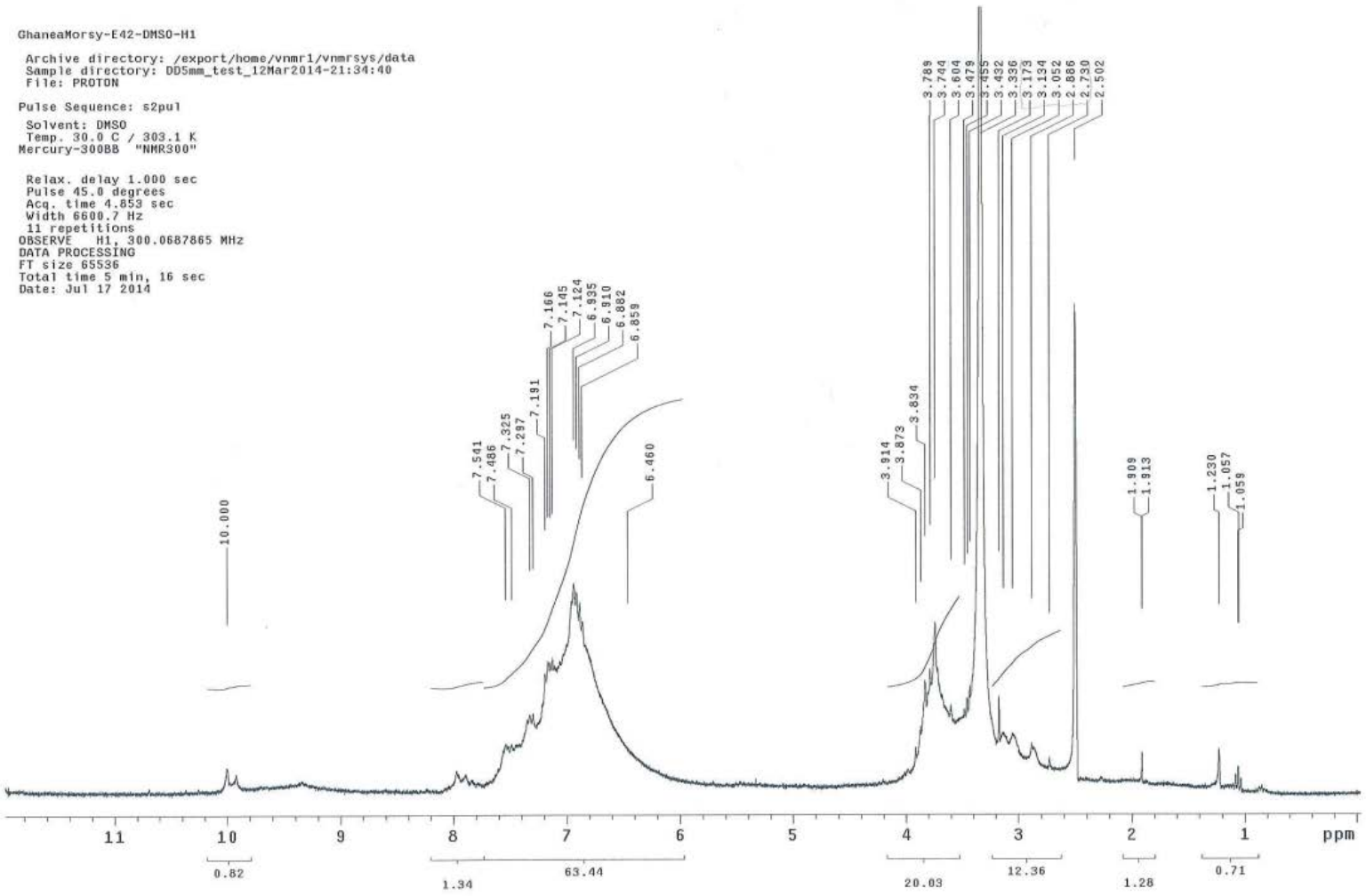
S3. ^{1}H NMR spectrum (300 MHz, DMSO-d_6) of compound 3



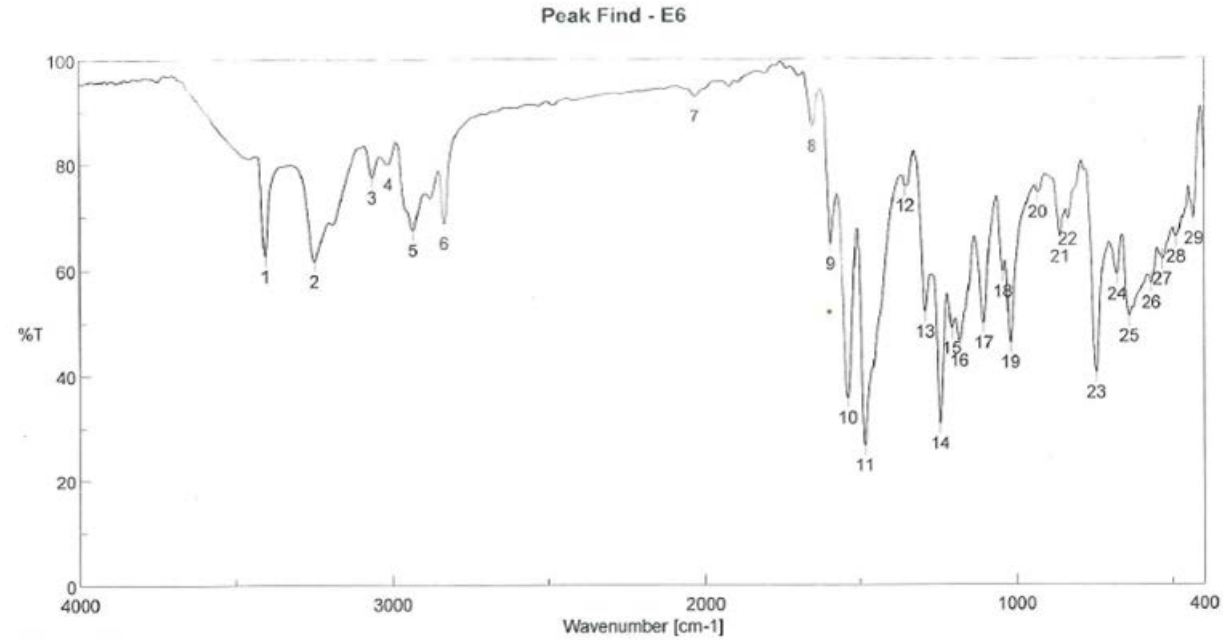
[Result of Peak Picking]

No.	Position	Intensity	No.	Position	Intensity	No.	Position	Intensity	No.	Position	Intensity
1	3907.07	99.01012	2	3764.37	99.01149	3	3383.5	91.82668	4	3205.11	92.81360
5	3066.26	93.84957	6	2925.48	91.17941	7	2857.02	93.87572	8	1928.47	99.04805
9	1592.91	92.11518	10	1541.81	88.72799	11	1459.85	90.78204	12	1371.14	93.42548
13	1244.83	88.80092	14	1170.58	92.28146	15	1112.73	92.03979	16	1035.59	93.43228
17	862.025	98.22542	18	752.102	93.02040	19	626.752	98.69072	20	491.759	98.47909

S4. IR spectrum (KBr, cm^{-1}) of compound 4



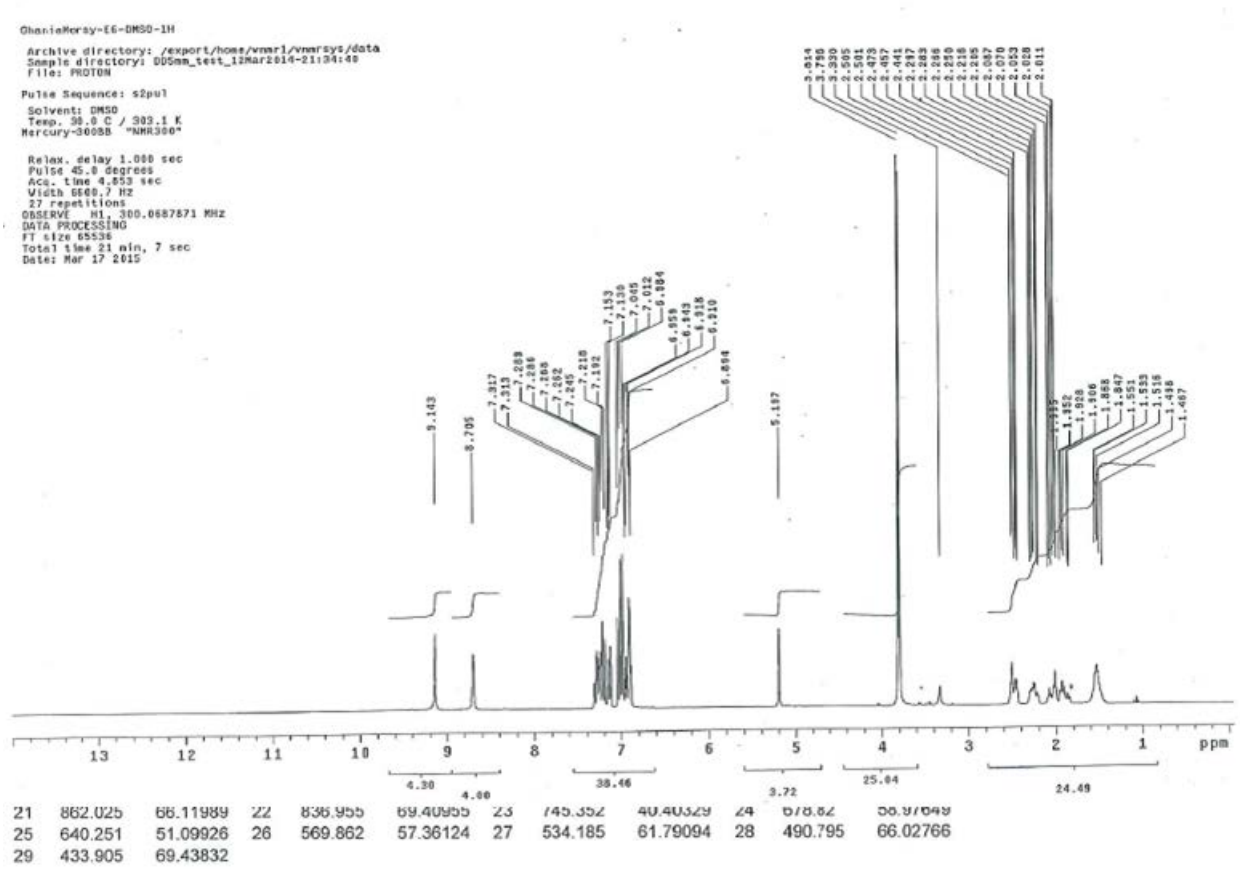
S4. ^{1}H NMR spectrum (300 MHz, DMSO-d_6) of compound 4



[Result of Peak Picking]

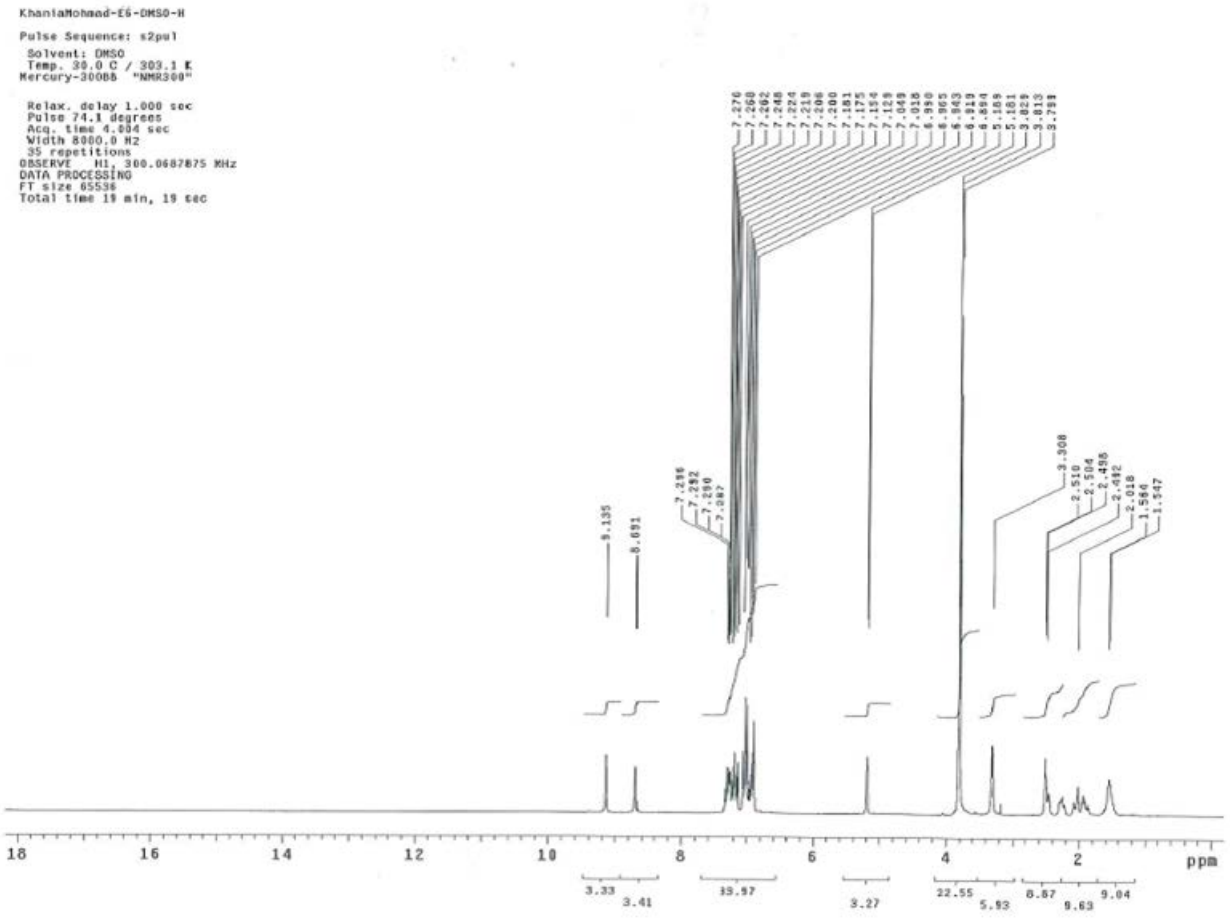
No.	Position	Intensity	No.	Position	Intensity	No.	Position	Intensity	No.	Position	Intensity
1	3404.71	62.67013	2	3247.54	61.69103	3	3063.37	77.45731	4	3011.3	79.95409
5	2933.2	67.45030	6	2832.92	68.73915	7	2032.6	92.86889	8	1655.59	87.04922
9	1594.84	64.79197	10	1539.88	35.57441	11	1484.92	26.51409	12	1356.68	75.76156
13	1292.07	51.98334	14	1243.86	30.68615	15	1207.22	48.85115	16	1183.11	46.48273
17	1105.01	49.83741	18	1044.26	59.55933	19	1020.16	46.14609	20	932.414	74.50311
21	862.025	66.11989	22	836.955	69.40955	23	745.352	40.40329	24	678.82	58.97649
25	640.251	51.09926	26	569.862	57.36124	27	534.185	61.79094	28	490.795	66.02766
29	433.905	69.43832									

S5$_a$. IR spectrum (KBr, cm^{-1}) of compound 7

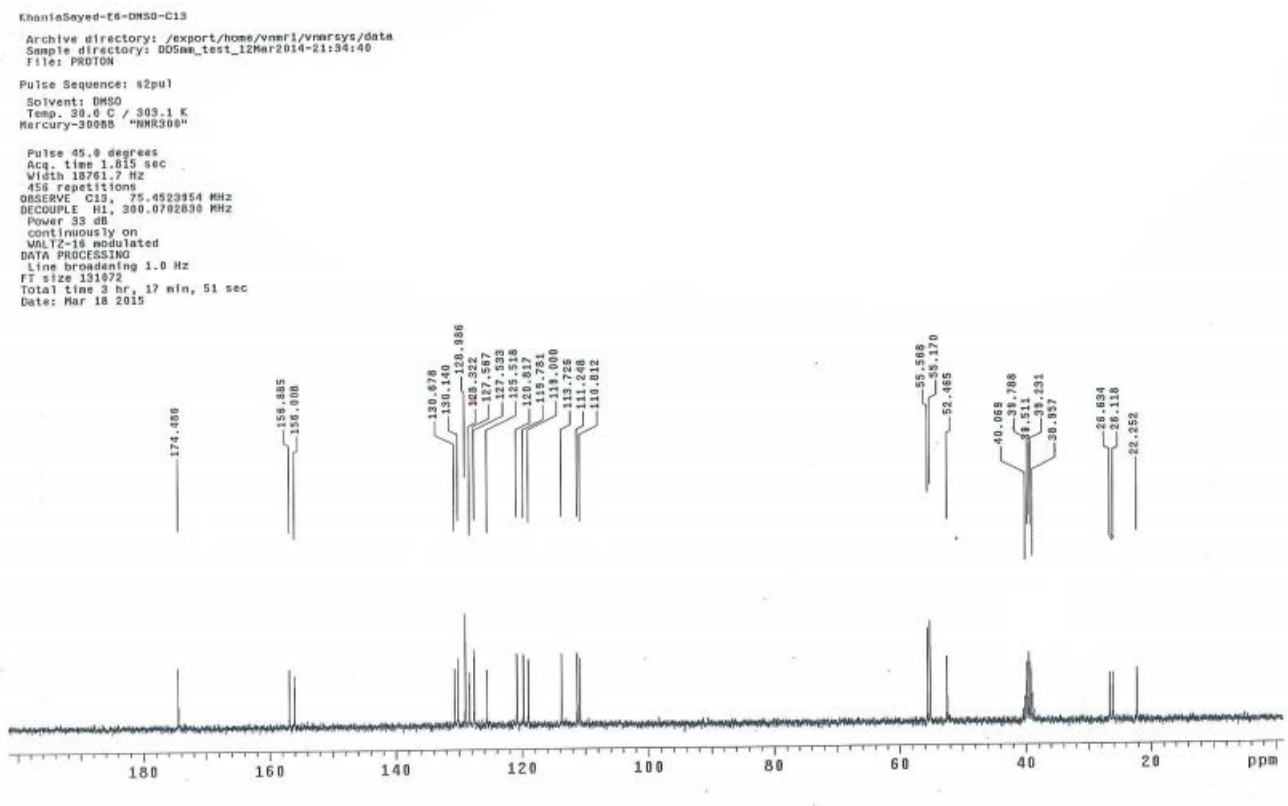


21	862.025	66.11989	22	836.955	59.40955	23	745.352	40.40329	24	678.82	56.97649
25	640.251	51.09926	26	569.862	57.36124	27	534.185	61.79094	28	490.795	66.02766
29	433.905	69.43832									

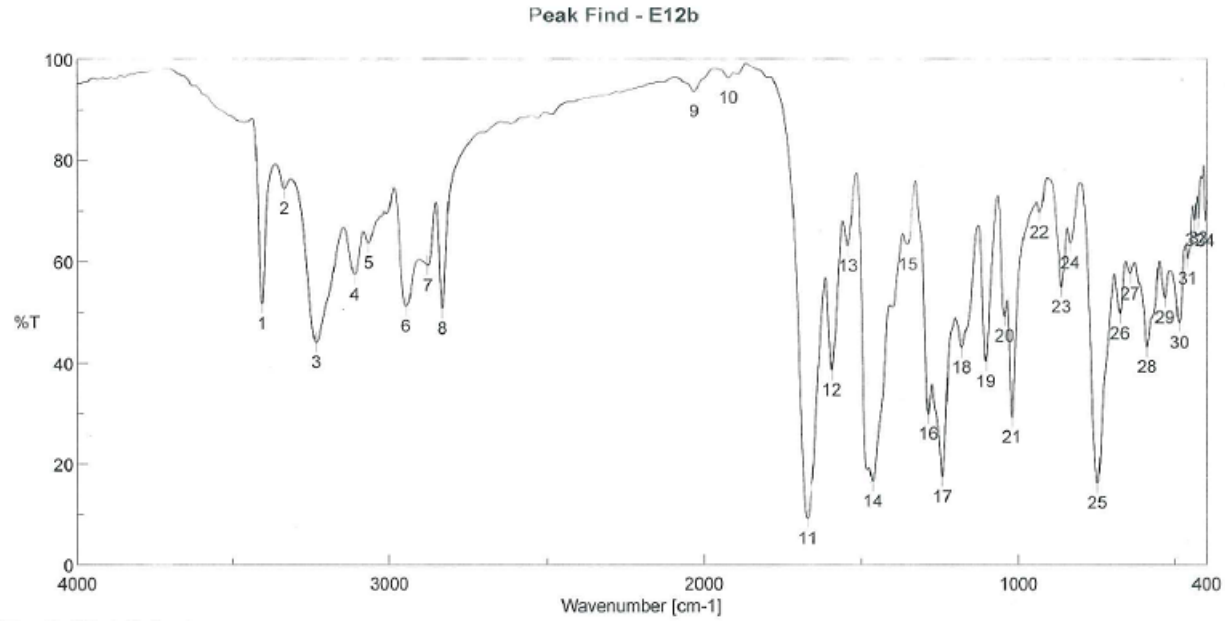
S5b. ^{1}H NMR spectrum (300 MHz, DMSO-d_6) of compound 7



S5$_b$. ^{1}H NMR spectrum (300 MHz, DMSO-d_6) of compound 7 (recrystallized)



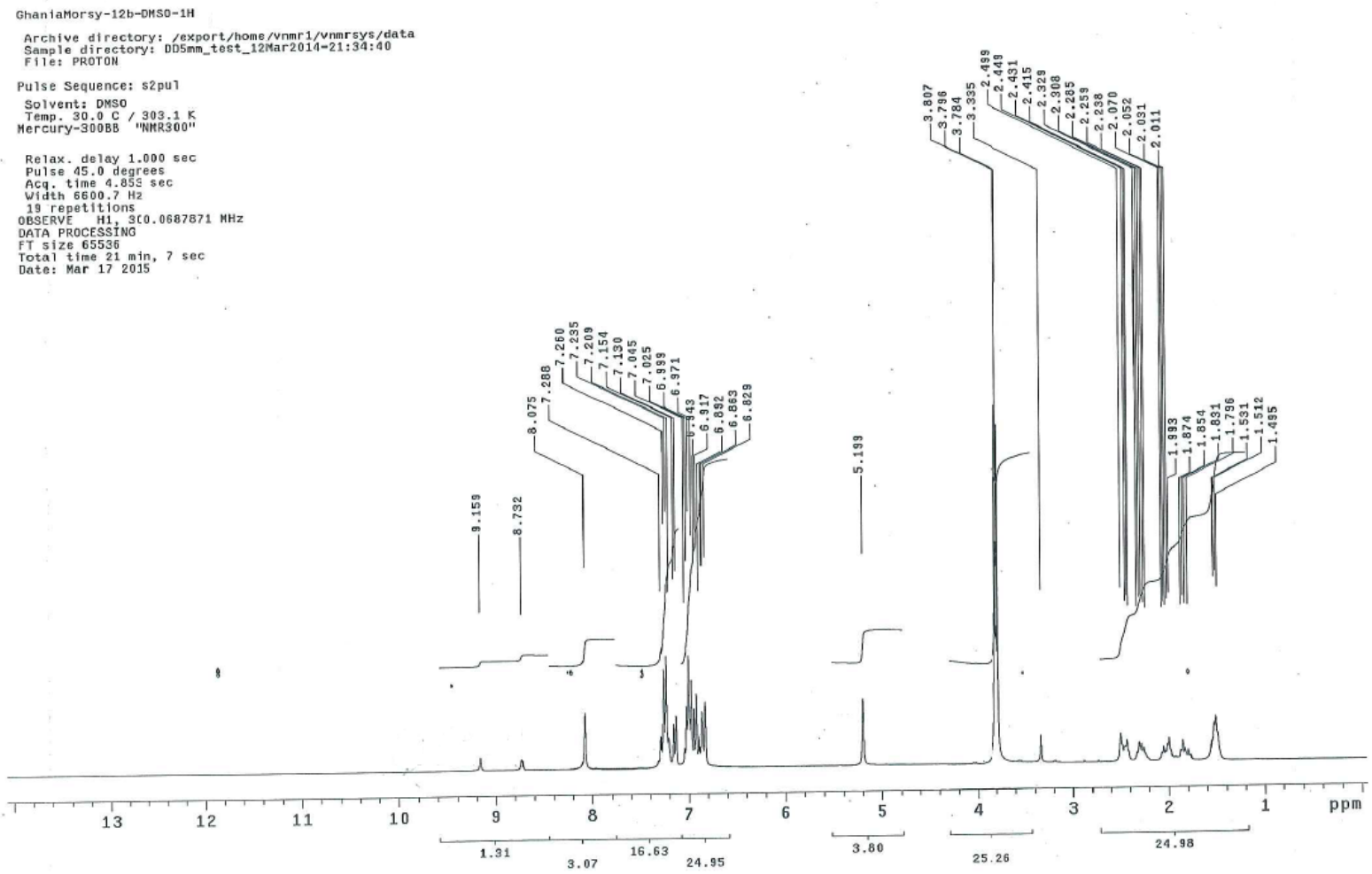
S5$_c$. ^{13}C NMR spectrum (75 MHz, DMSO-d_6) of compound 7



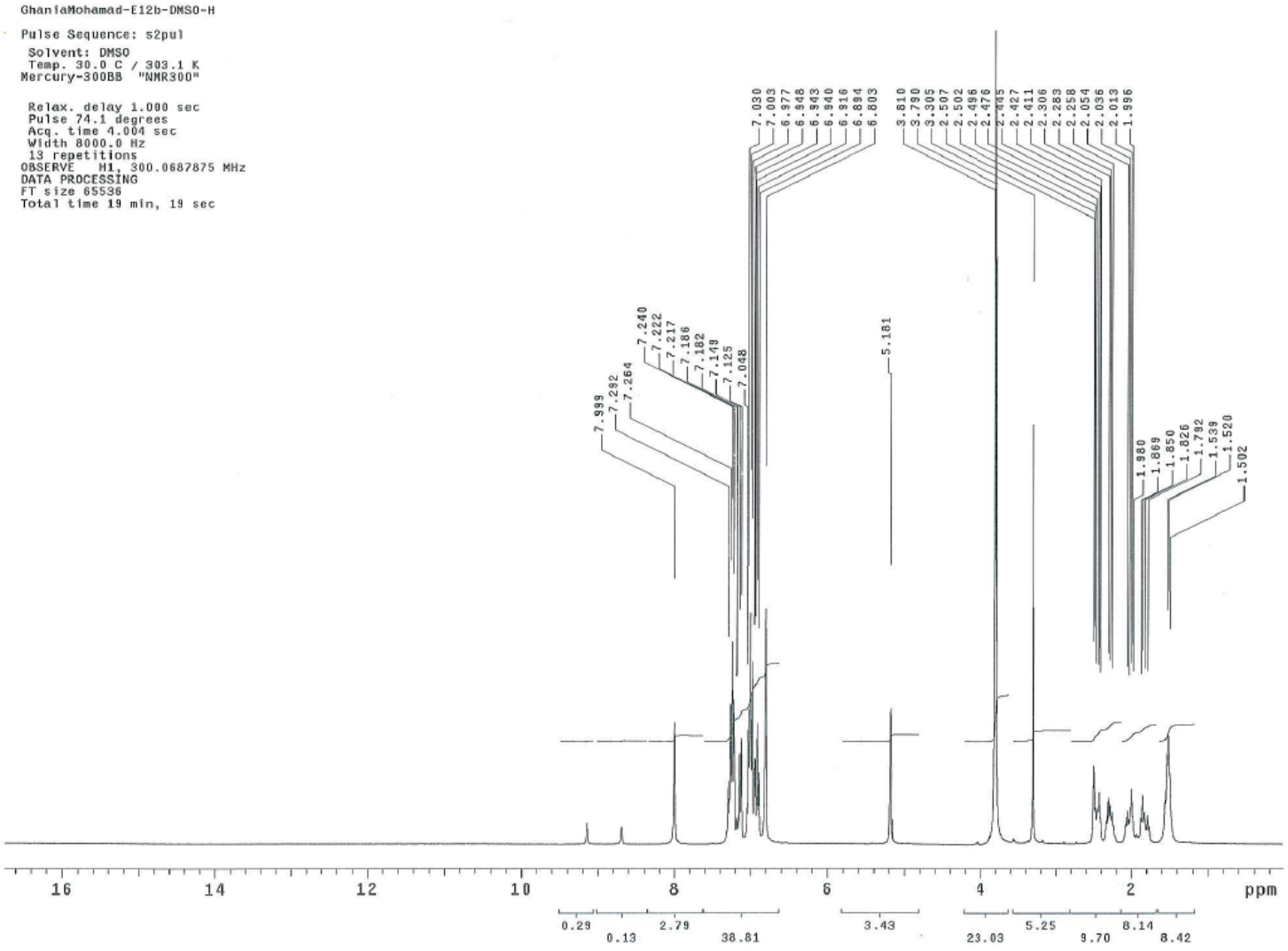
[Result of Peak Picking]

No.	Position	Intensity	No.	Position	Intensity	No.	Position	Intensity	No.	Position	Intensity
1	3407.6	51.76382	2	3336.25	74.30941	3	3235	44.13831	4	3111.58	57.42469
5	3067.23	63.67796	6	2947.66	51.23463	7	2878.24	59.23565	8	2831.95	50.76416
9	2033.57	93.54477	10	1923.65	96.25835	11	1671.02	9.11932	12	1594.84	38.61280
13	1542.77	63.09124	14	1463.71	16.50786	15	1352.82	63.37659	16	1287.25	29.93531
17	1242.9	17.45550	18	1182.15	43.08918	19	1105.01	40.31755	20	1045.23	49.34721
21	1021.12	29.28344	22	932.414	69.67442	23	862.989	55.02960	24	835.026	63.65382
25	747.281	16.18227	26	676.892	49.78593	27	645.072	57.61539	28	590.111	43.21335
29	534.185	52.92119	30	486.938	48.03564	31	460.904	60.61478	32	437.762	68.10007
33	427.155	68.51730	34	404.014	68.03063						

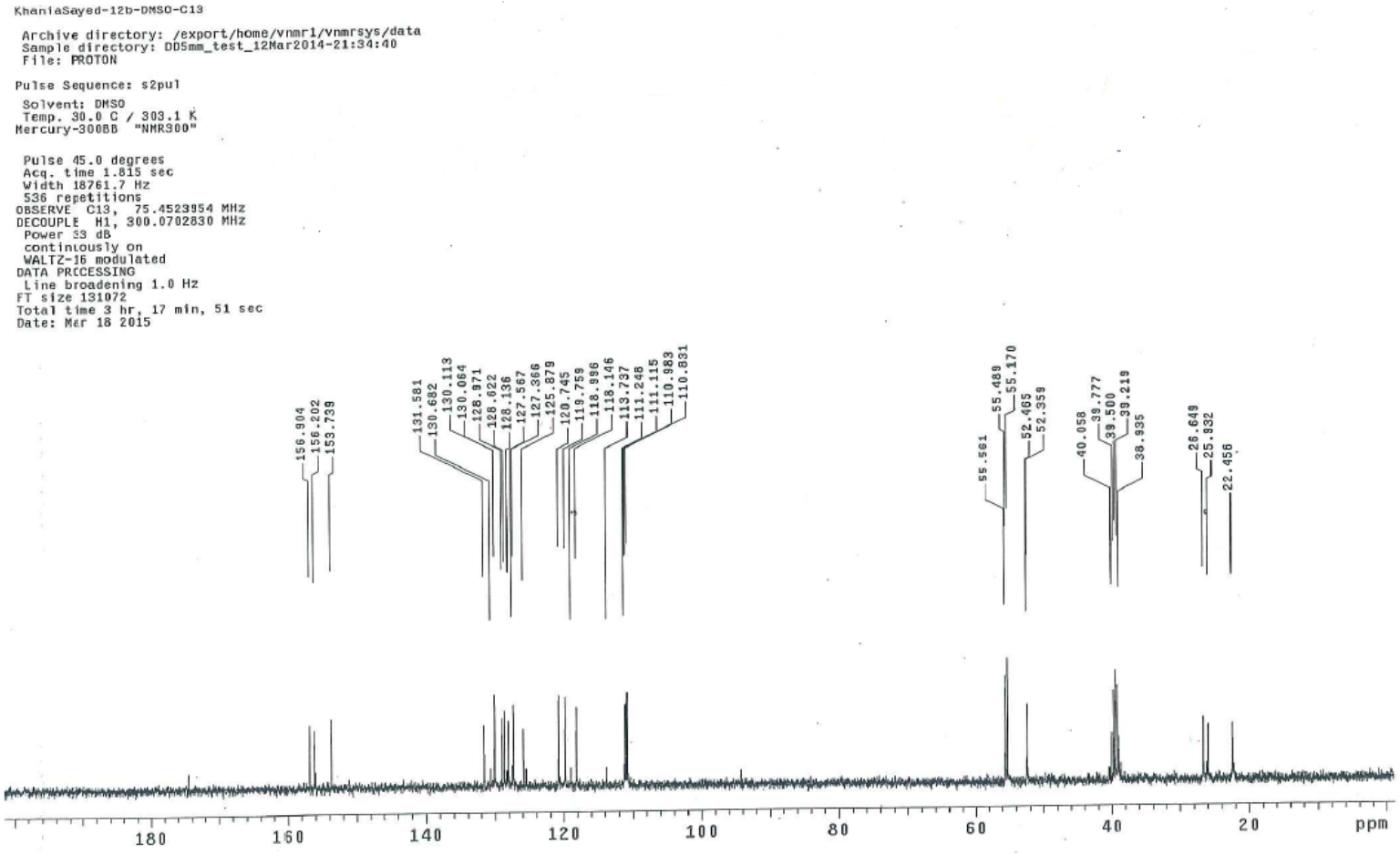
S6$_a$.IR spectrum (KBr, cm^{-1}) of compound 8



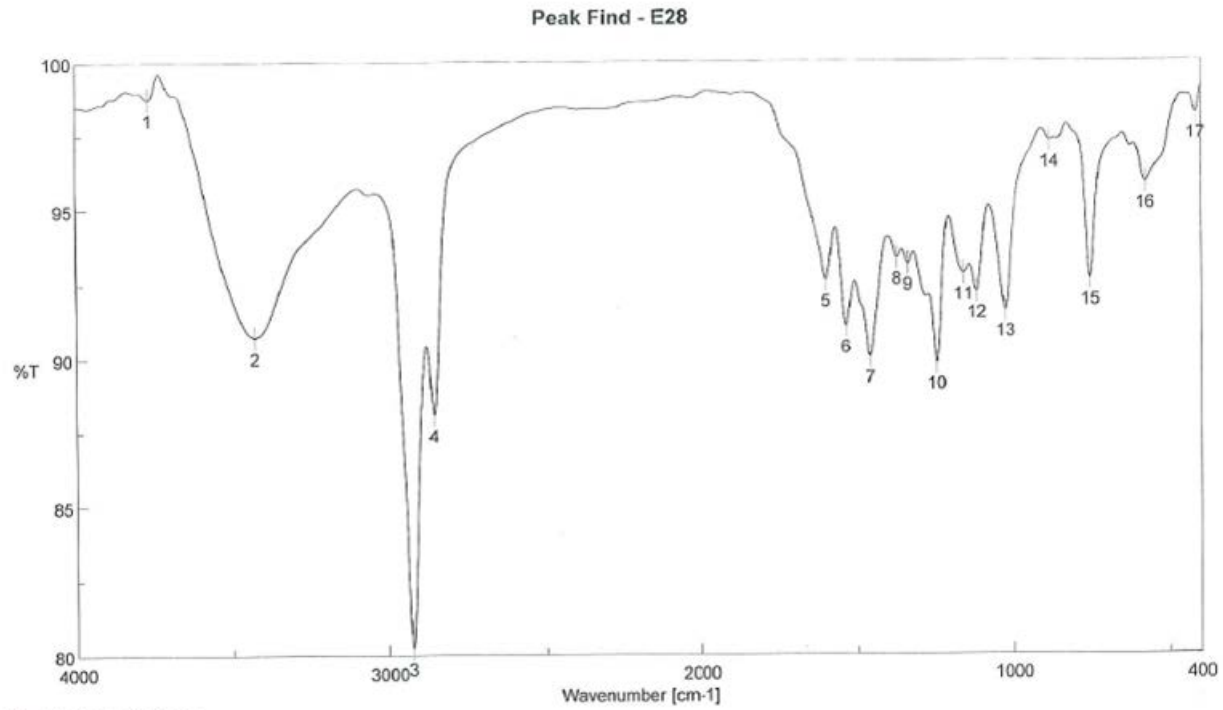
S6$_b$. ^{1}H NMR spectrum (300 MHz, DMSO-d_6) of compound 8



S6$_b$. ^{1}H NMR spectrum (300 MHz, DMSO-d_6) of compound 8 (recrystallized)



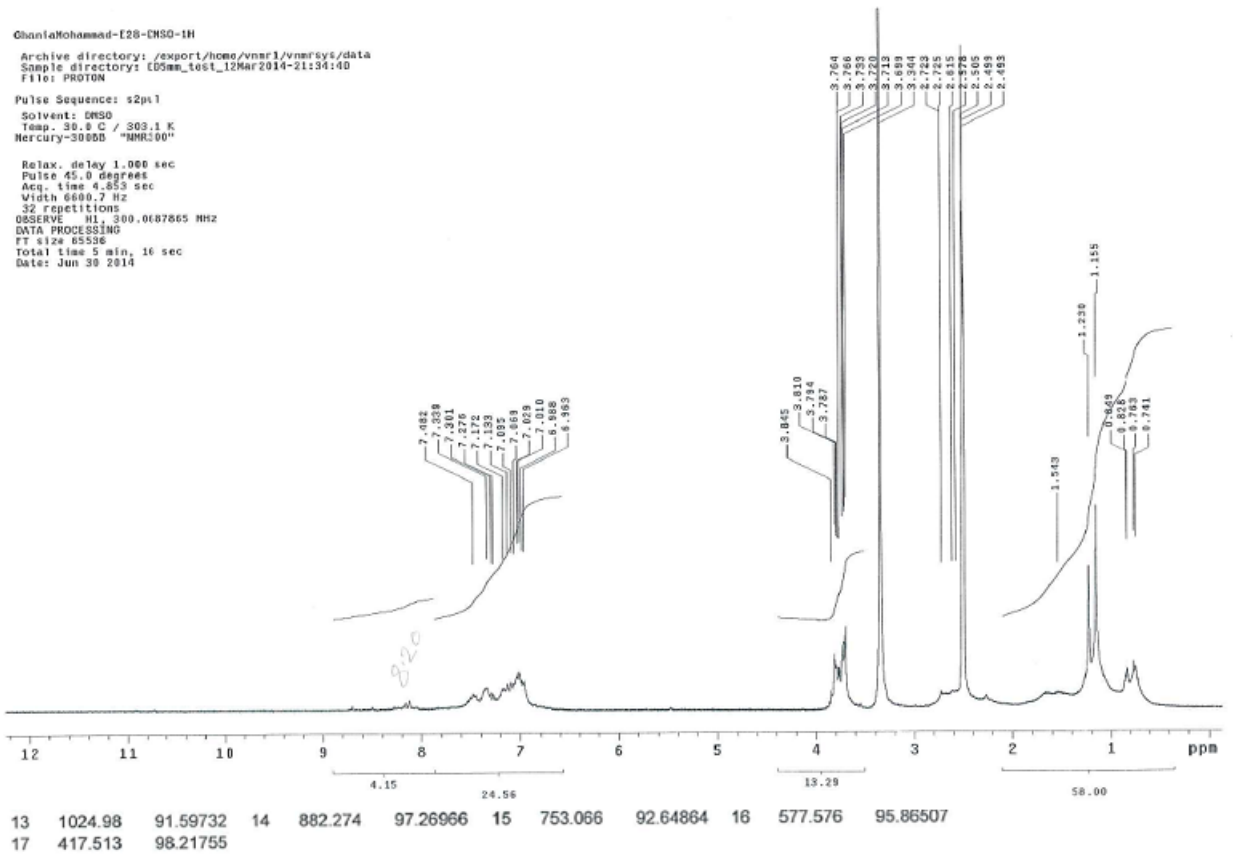
S6$_c$. ^{13}C NMR spectrum (75 MHz, DMSO-d_6) of compound 8



[Result of Peak Picking]

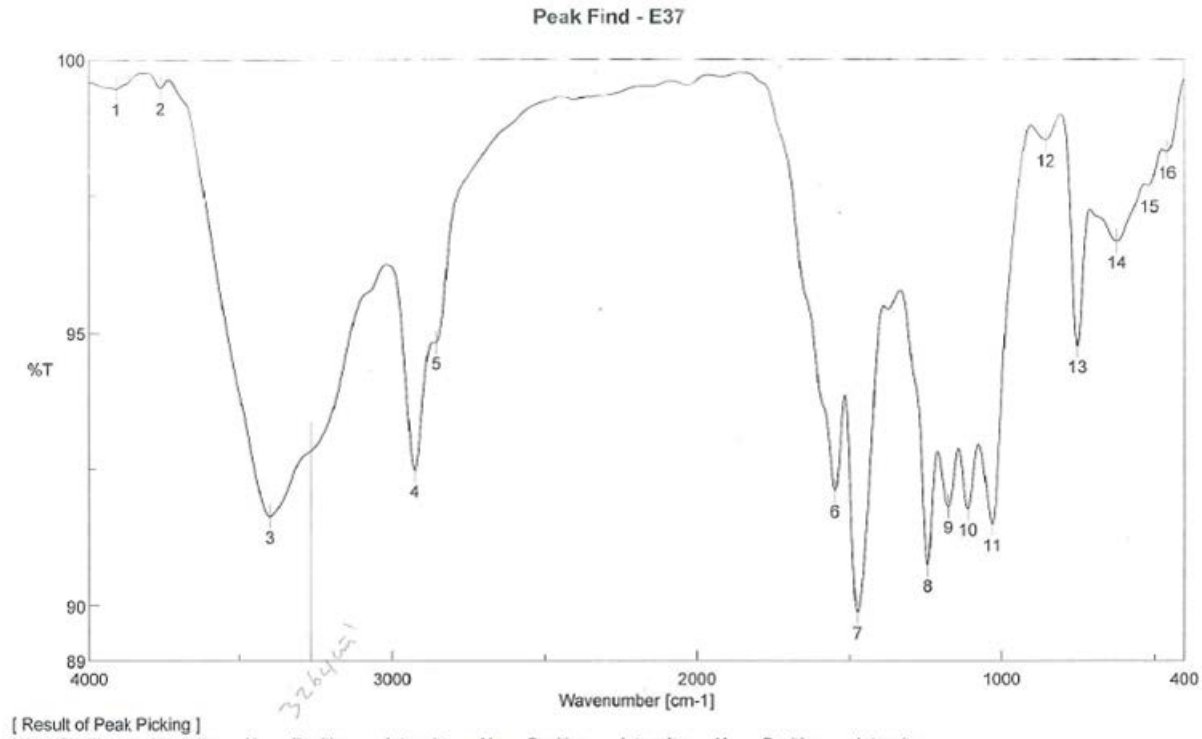
No.	Position	Intensity	No.	Position	Intensity	No.	Position	Intensity	No.	Position	Intensity
1	3770.15	98.76314	2	3427.85	90.73800	(3)	2924.52	80.24010	(4)	2856.06	88.10795
(5)	1600.63	92.61578	6	1536.02	91.08023	7	1458.89	90.04934	8	1374.03	93.35133
9	1338.36	93.15968	10	1245.79	89.82976	11	1159.97	92.83221	12	1117.55	92.21955
13	1024.98	91.59732	14	882.274	97.26966	15	753.066	92.64864	16	577.576	95.86507
17	417.513	98.21755									

S7$_a$. IR spectrum (KBr, cm^{-1}) of compound 9



13 1024.98 91.59732 14 882.274 97.26966 15 753.066 92.64864 16 577.576 95.86507
17 417.513 98.21755

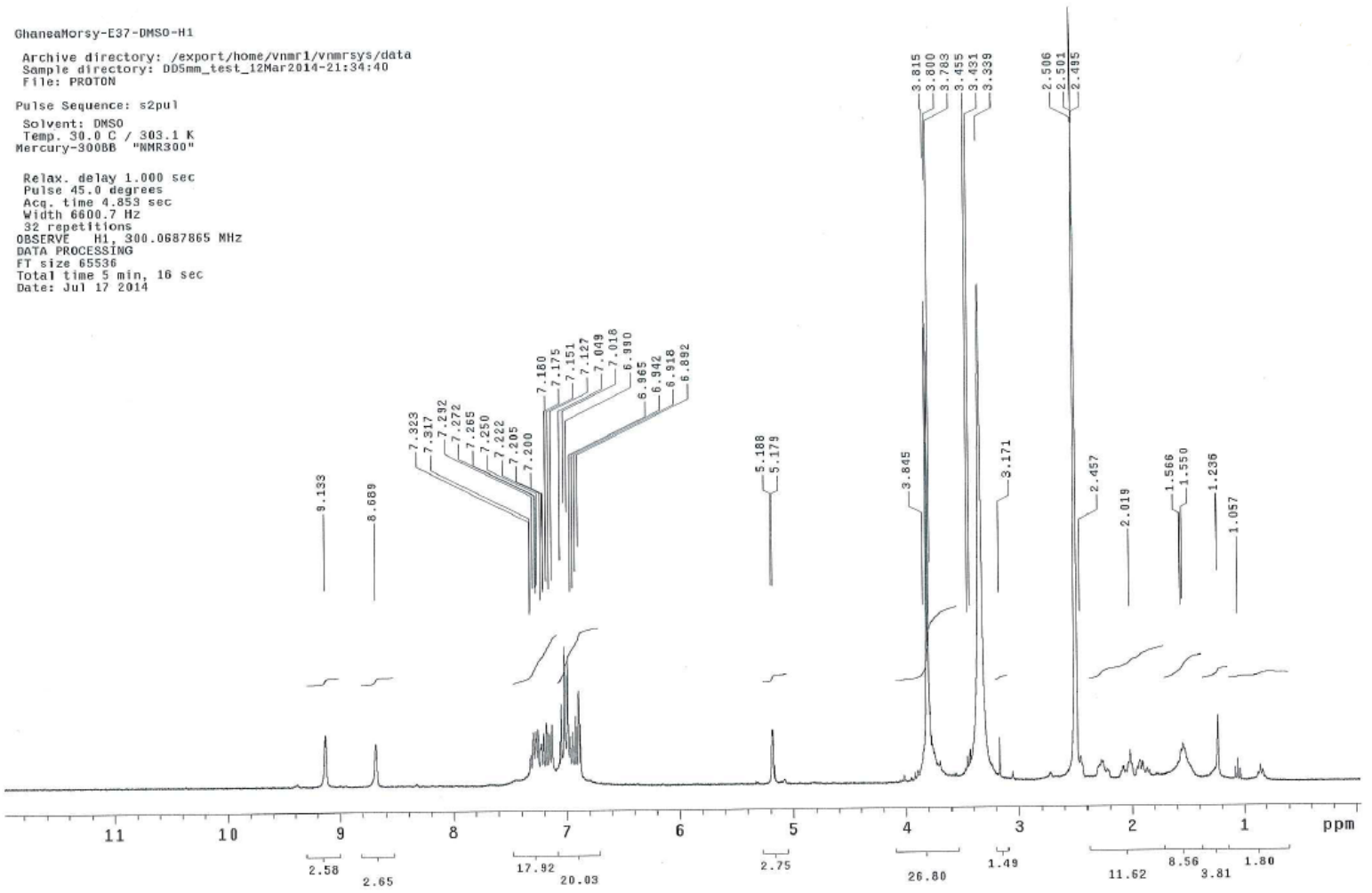
S7$_b$. ^{1}H NMR spectrum (300 MHz, DMSO-d_6) of compound 9



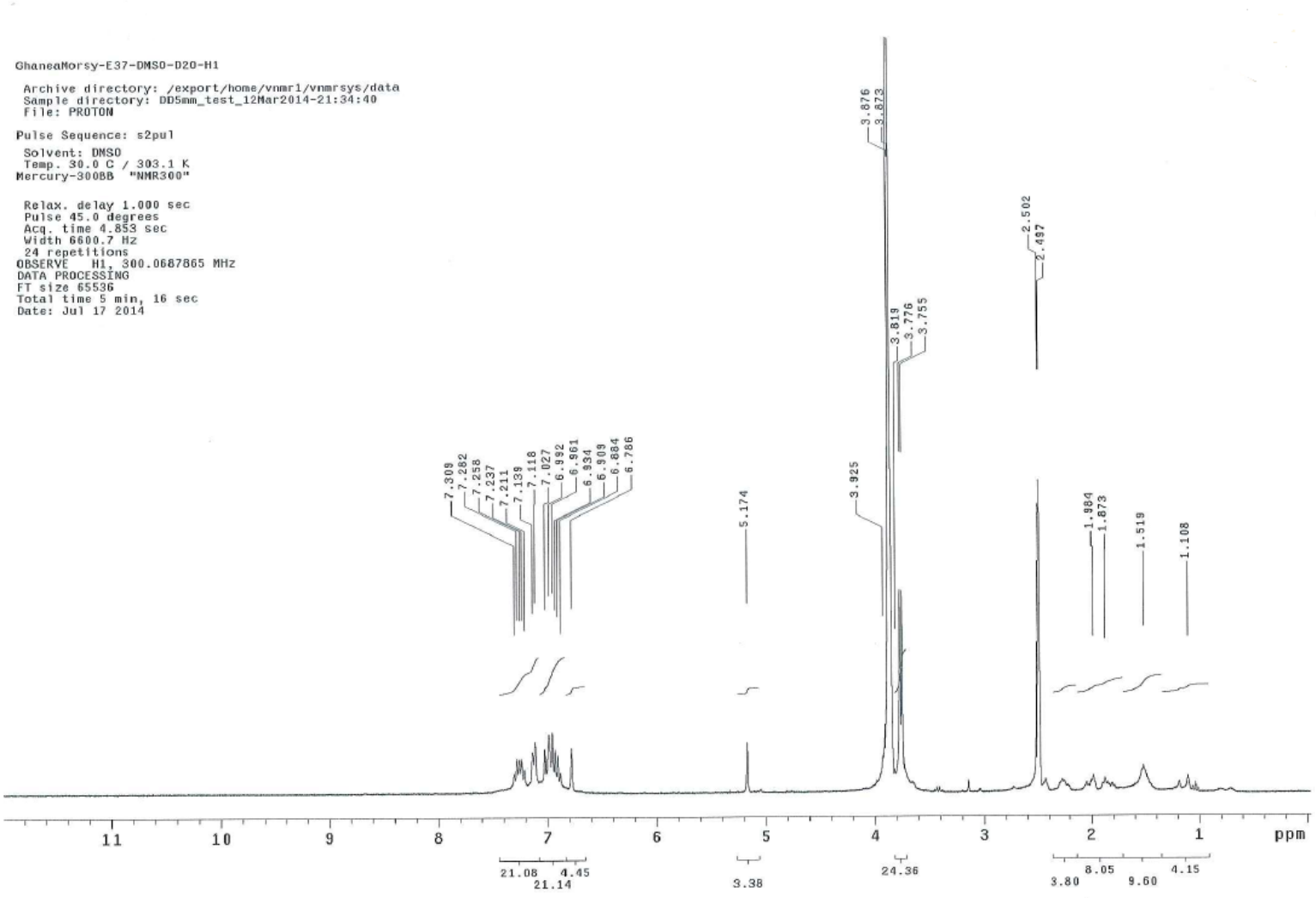
[Result of Peak Picking]

No.	Position	Intensity	No.	Position	Intensity	No.	Position	Intensity	No.	Position	Intensity
1	3910.93	99.45952	2	3759.55	99.47710	3	3400.85	91.63222	4	2926.45	92.47583
5	2856.06	94.83048	6	1548.56	92.10450	7	1475.28	89.88573	8	1243.86	90.74583
9	1176.36	91.81547	10	1110.8	91.77113	11	1030.77	91.48547	12	857.204	98.52319
13	753.066	94.76404	14	624.823	96.66809	15	517.793	97.68883	16	457.047	98.29981

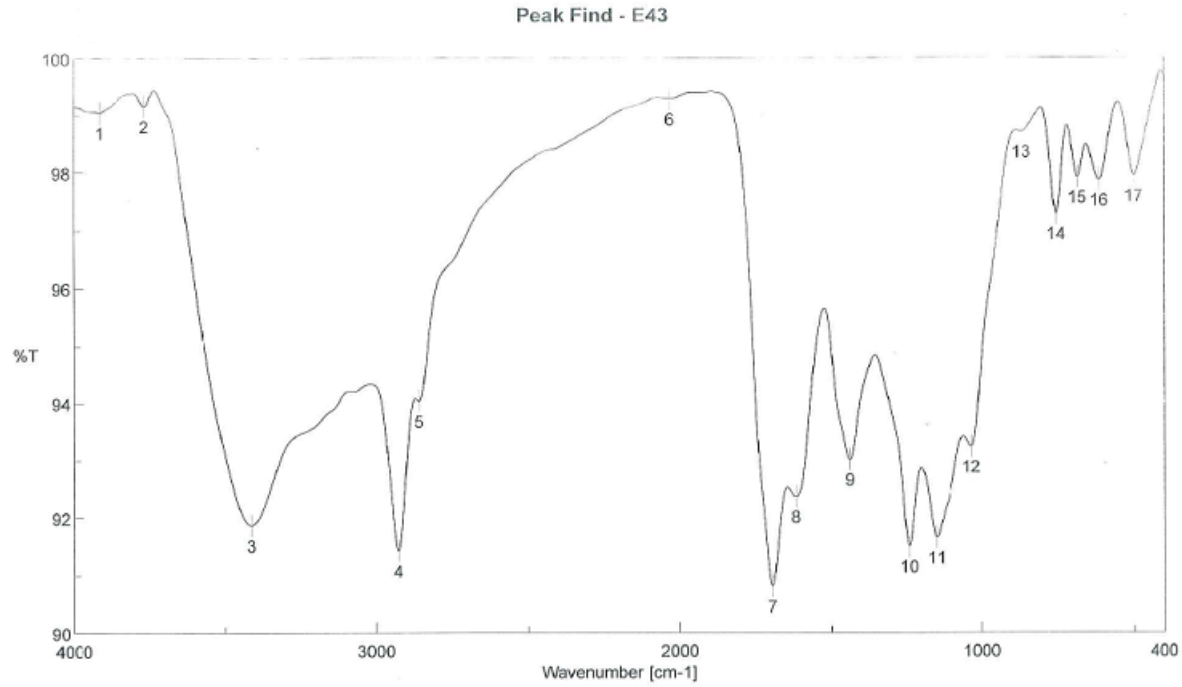
S8$_a$. IR spectrum (KBr, cm^{-1}) of compound 10



S8b. ^{1}H NMR spectrum (300 MHz, DMSO-d_6) of compound 10



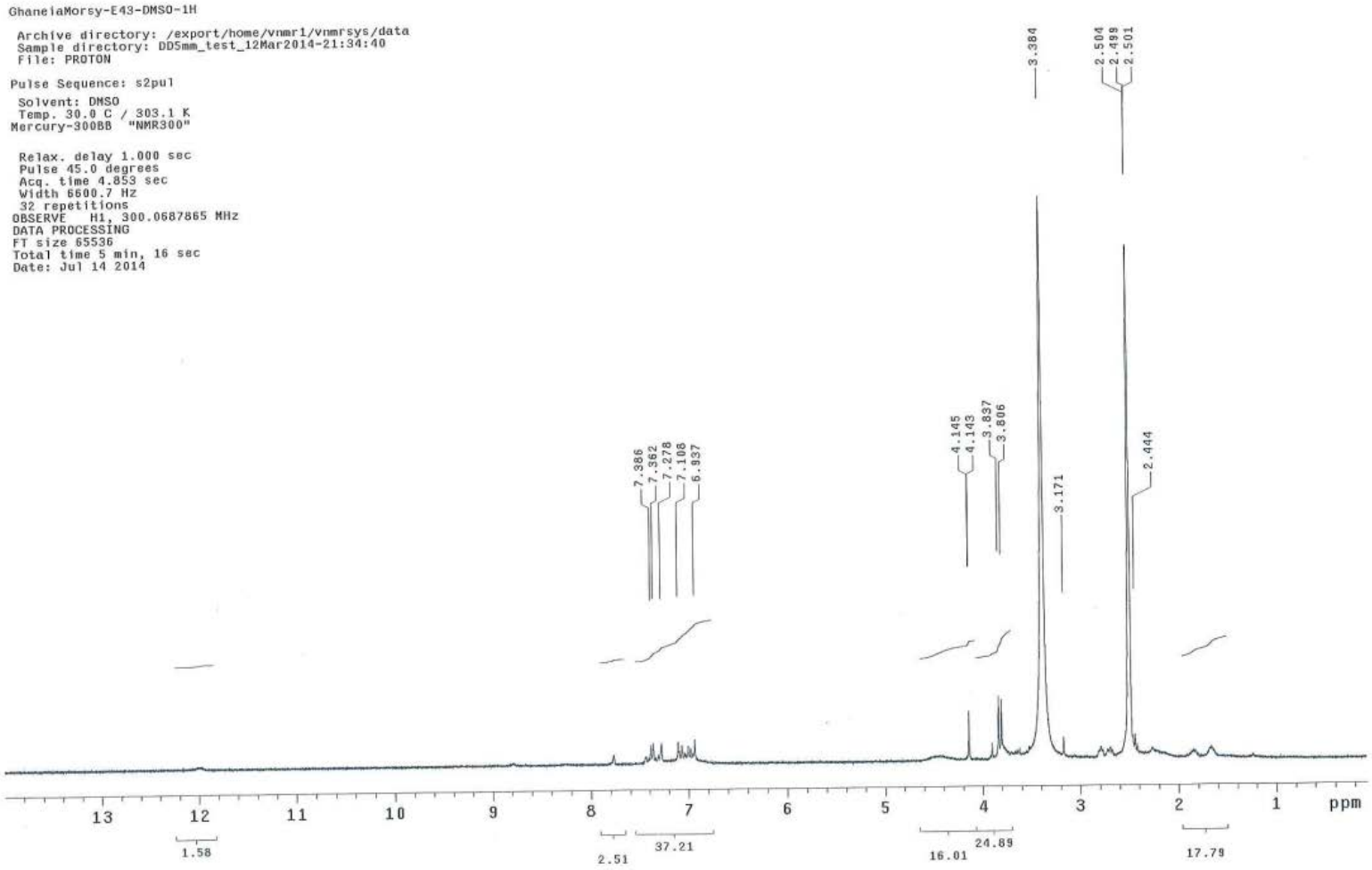
S8$_b$. ^{1}H NMR spectrum (300 MHz, DMSO-D$_2$O) of compound 10



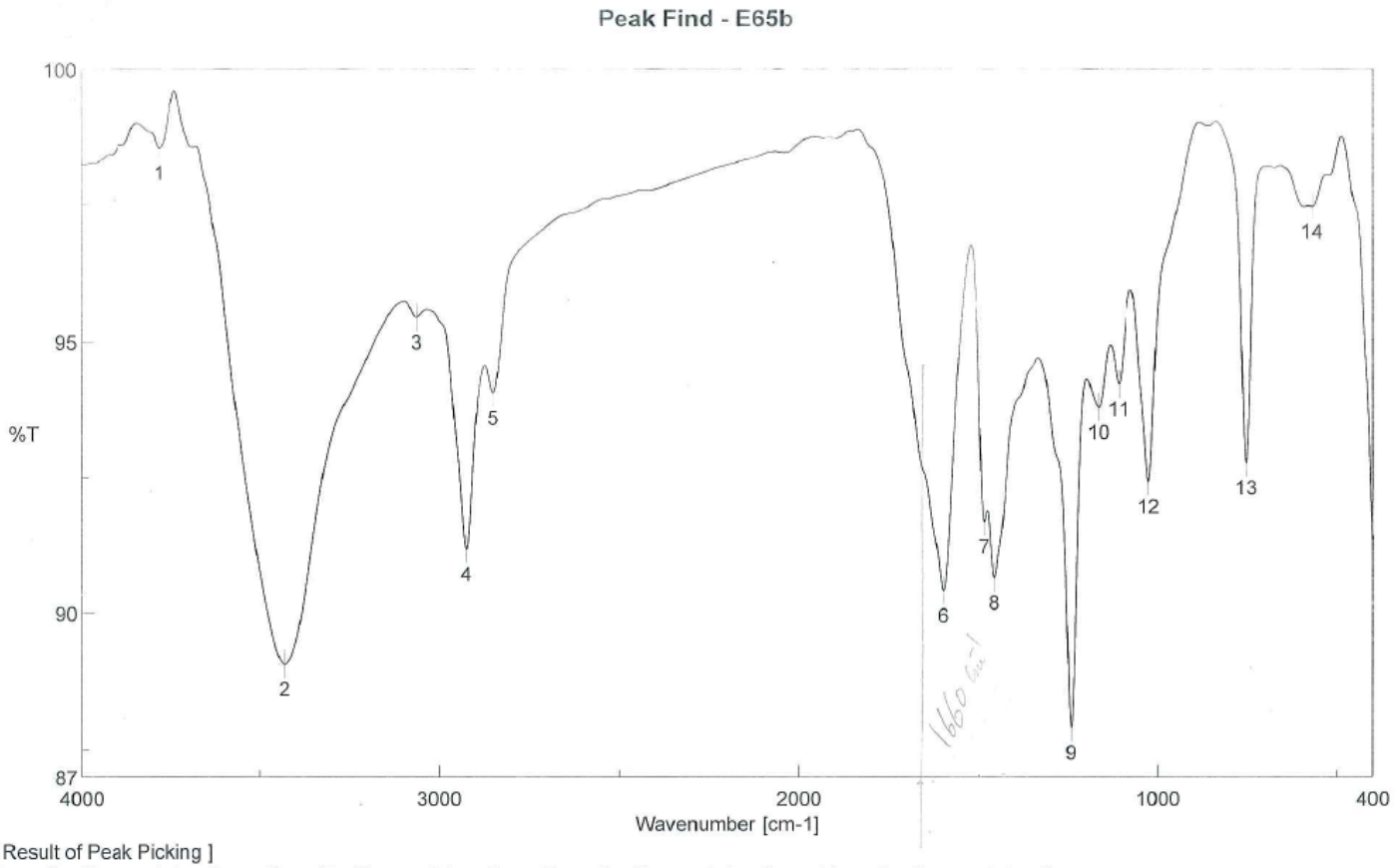
[Result of Peak Picking]

No.	Position	Intensity	No.	Position	Intensity	No.	Position	Intensity	No.	Position	Intensity
1	3911.9	99.04807	2	3763.4	99.15662	3	3411.46	91.86352	4	2927.41	91.42448
5	2859.92	94.03410	6	2034.53	99.27702	7	1696.09	90.80791	8	1618.95	92.35915
9	1440.56	93.00827	10	1243.86	91.49924	11	1152.26	91.65218	12	1036.55	93.23637
13	871.667	98.71235	14	757.888	97.29163	15	688.463	97.91861	16	617.109	97.86836
17	503.33	97.94212									

S9$_a$. IR spectrum (KBr, cm^{-1}) of compound 11



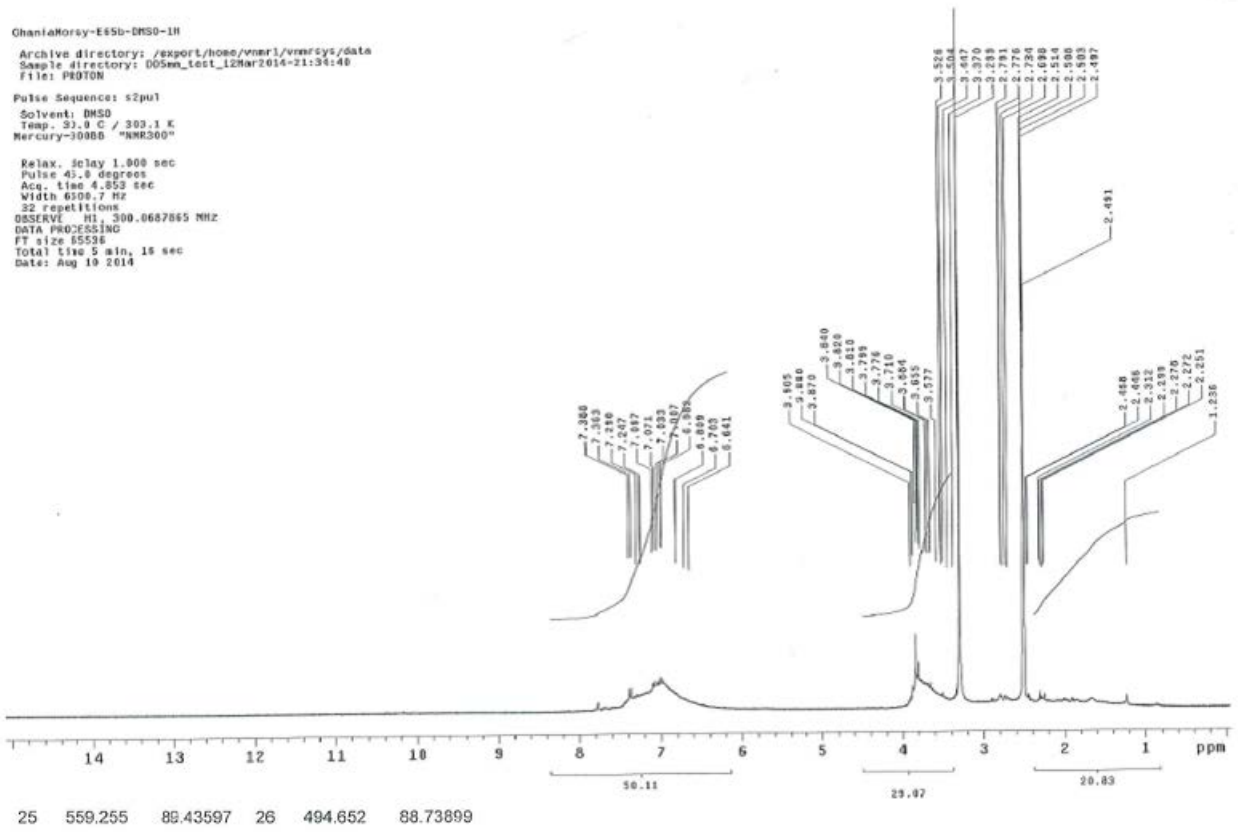
S9b. ^{1}H NMR spectrum (300 MHz, DMSO-d_6) of compound 11



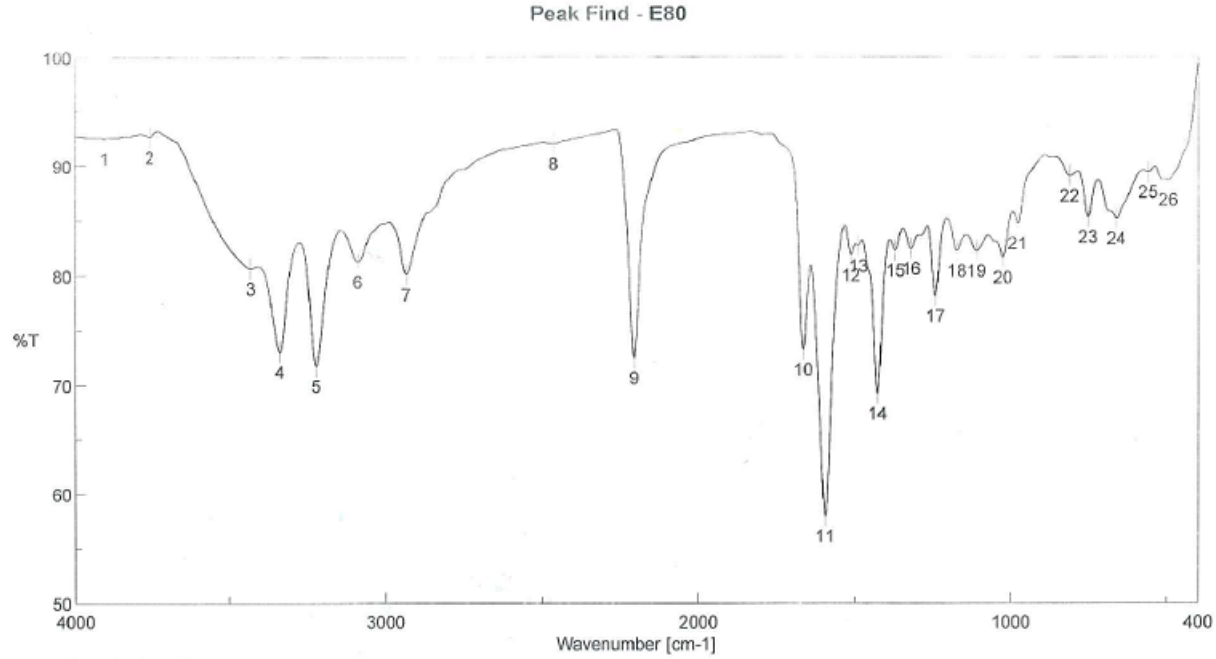
[Result of Peak Picking]

No.	Position	Intensity	No.	Position	Intensity	No.	Position	Intensity	No.	Position	Intensity
1	3778.83	98.54137	2	3429.78	89.06640	3	3064.33	95.44338	4	2925.48	91.17744
5	2851.24	94.06120	6	1600.63	90.41415	7	1486.85	91.68355	8	1458.89	90.64905
9	1244.83	87.90830	10	1168.65	93.79612	11	1111.76	94.21937	12	1026.91	92.42641
13	753.066	92.76951	14	570.826	97.46294						

S10$_a$. IR spectrum (KBr, cm^{-1}) of compound 13



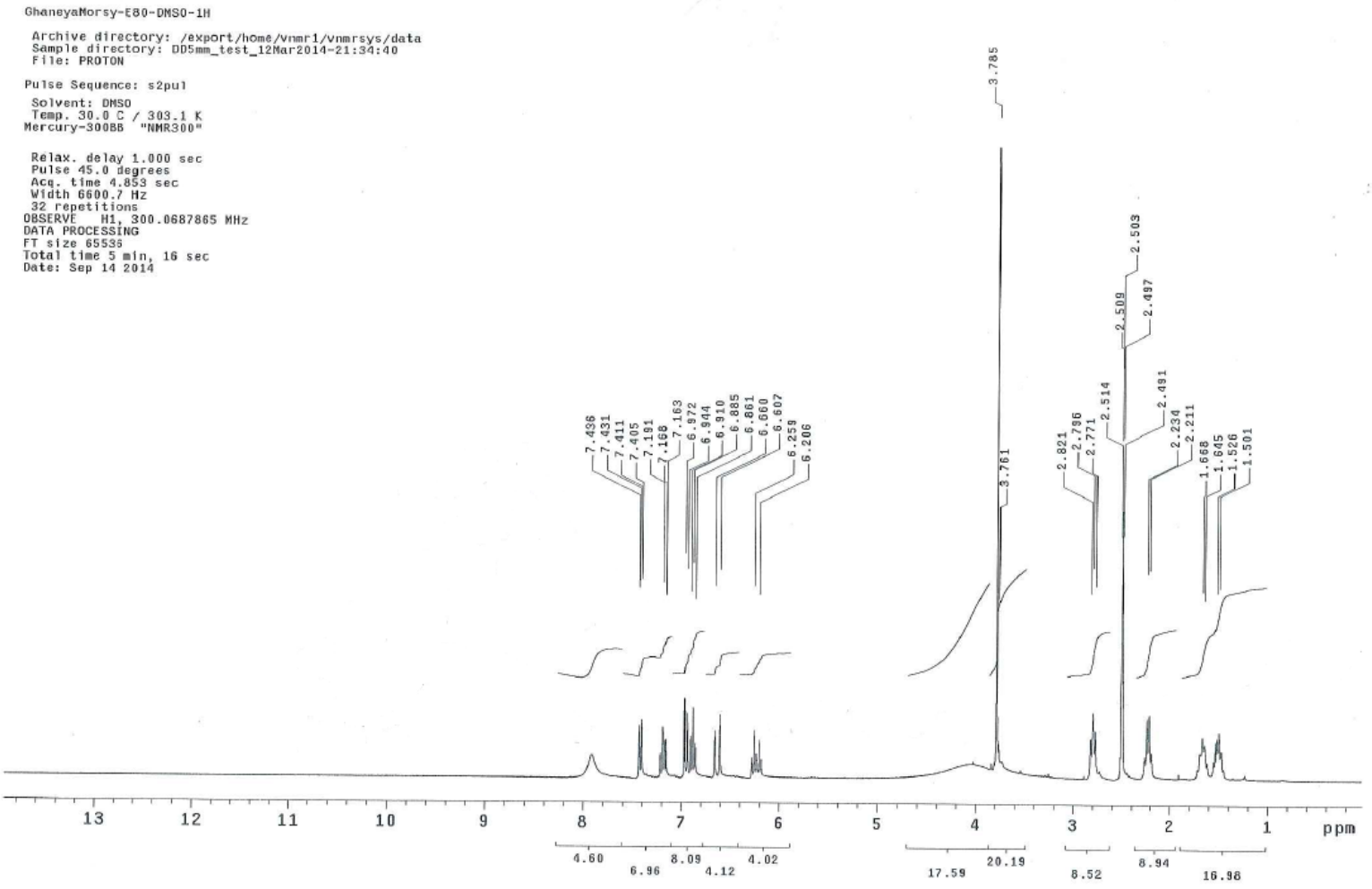
S10$_b$. ^{1}H NMR spectrum (300 MHz, DMSO-d_6) of compound 13



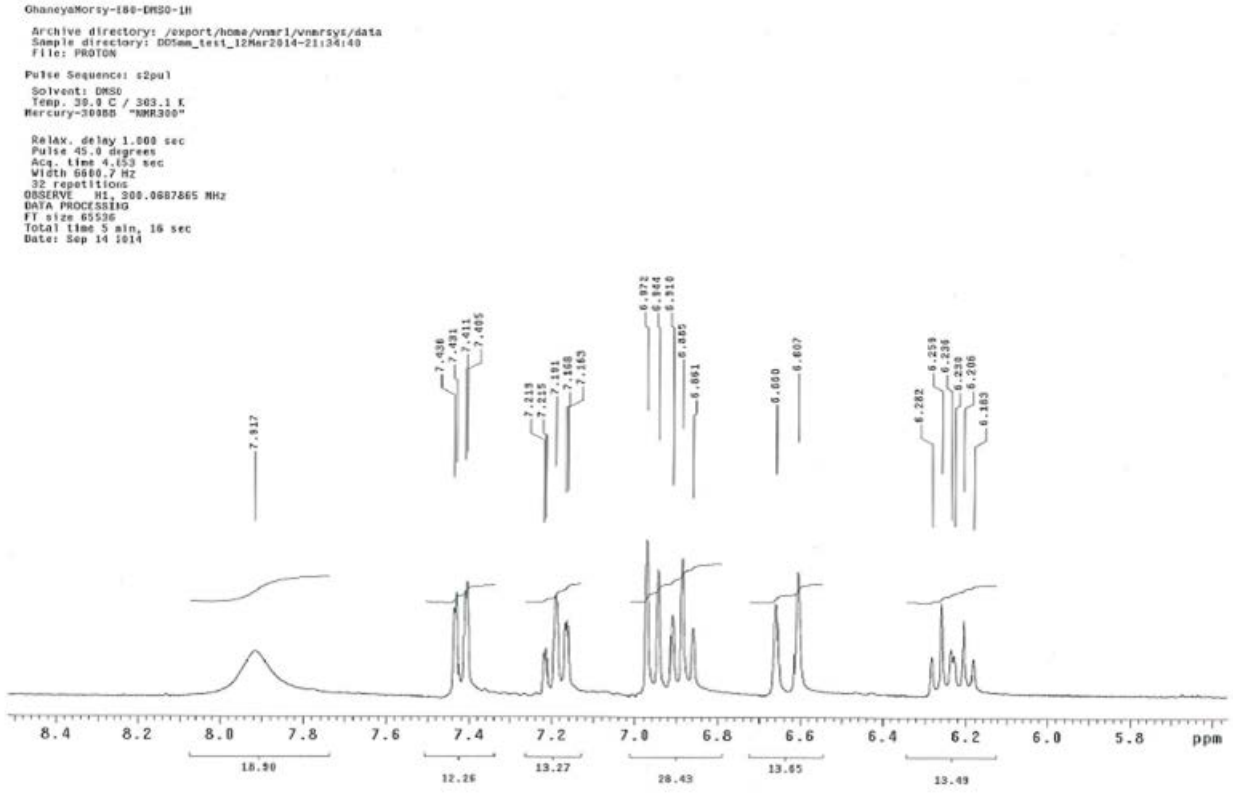
[Result of Peak Picking]

No.	Position	Intensity	No.	Position	Intensity	No.	Position	Intensity	No.	Position	Intensity
1	3907.07	92.46972	2	3758.58	92.61684	3	3433.64	80.64453	4	3340.1	73.03141
5	3223.43	71.73652	6	3089.4	81.26193	7	2935.13	80.11257	8	2464.58	92.02169
9	2205.2	72.52130	10	1664.27	73.26752	11	1593.88	57.95969	12	1511.92	81.89087
13	1488.78	82.72935	14	1427.07	69.23699	15	1370.18	82.33361	16	1320.04	82.45583
17	1241.93	78.17953	18	1172.51	82.28985	19	1109.83	82.27370	20	1024.98	81.66831
21	977.733	84.76556	22	811.885	89.08572	23	753.066	85.34871	24	661.464	85.21179
25	559.255	89.43597	26	494.652	88.73899						

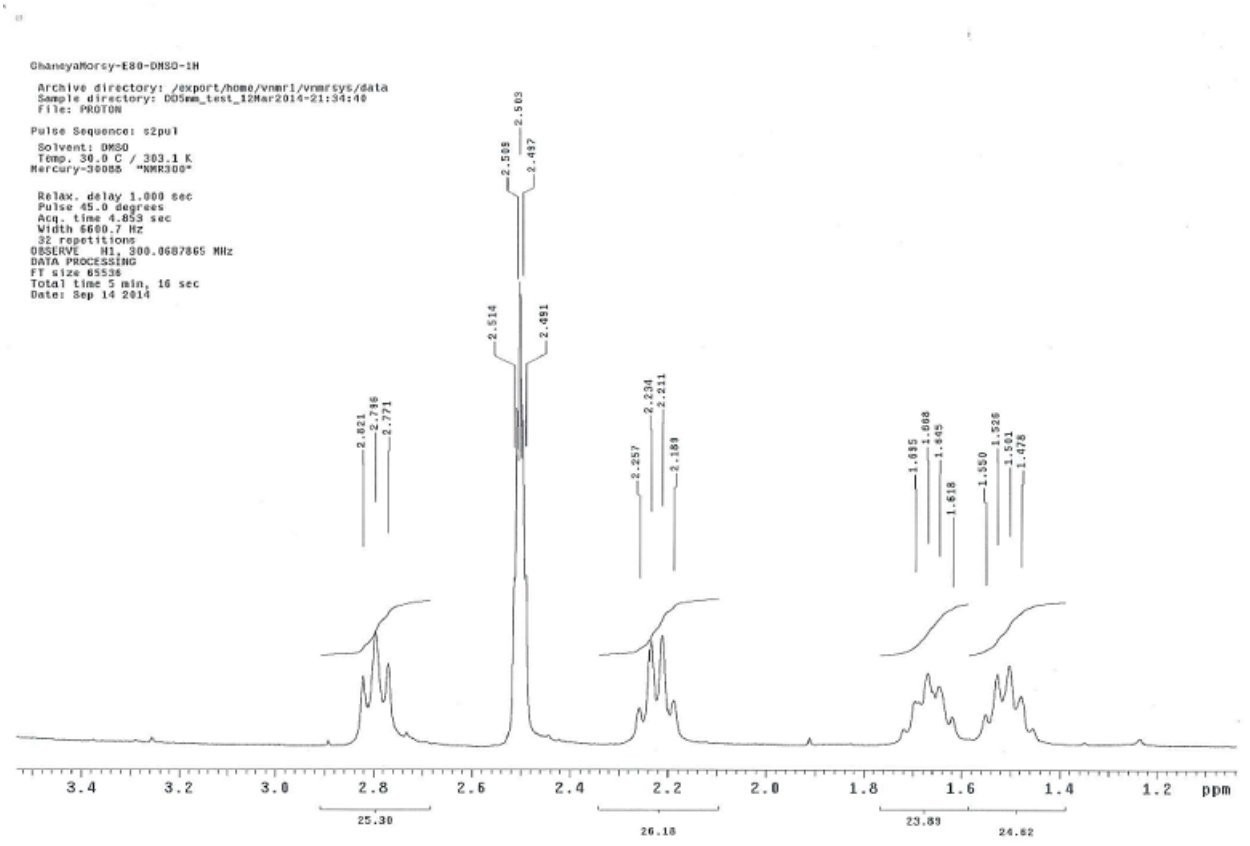
S11$_a$. IR spectrum (KBr, cm^{-1}) of compound 16



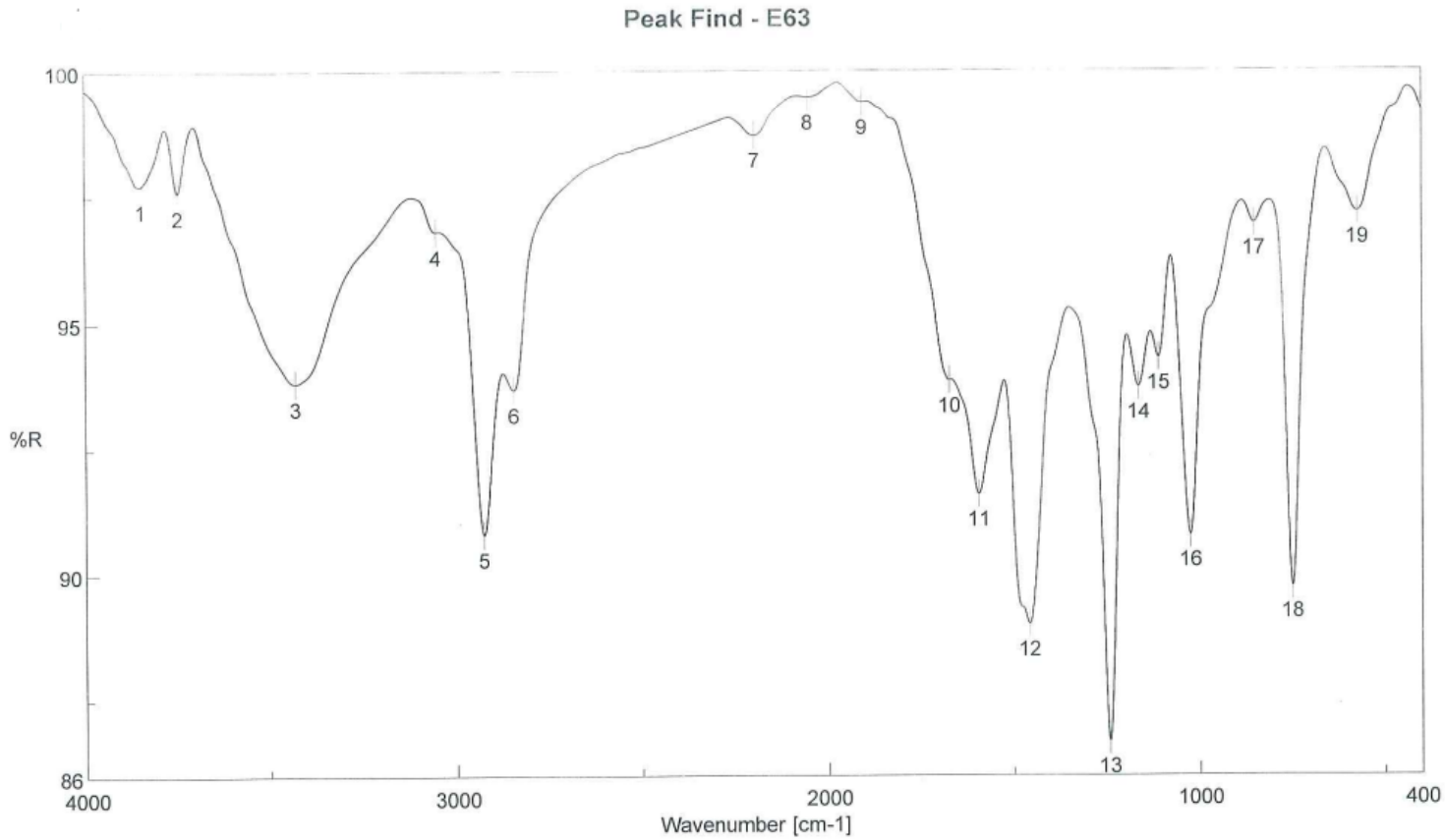
S11$_b$. ^{1}H NMR spectrum (300 MHz, DMSO-d_6) of compound 16



S11$_b$. ^{1}H NMR spectrum (300 MHz, DMSO-d_6) of compound 16 *(Magnified area)*



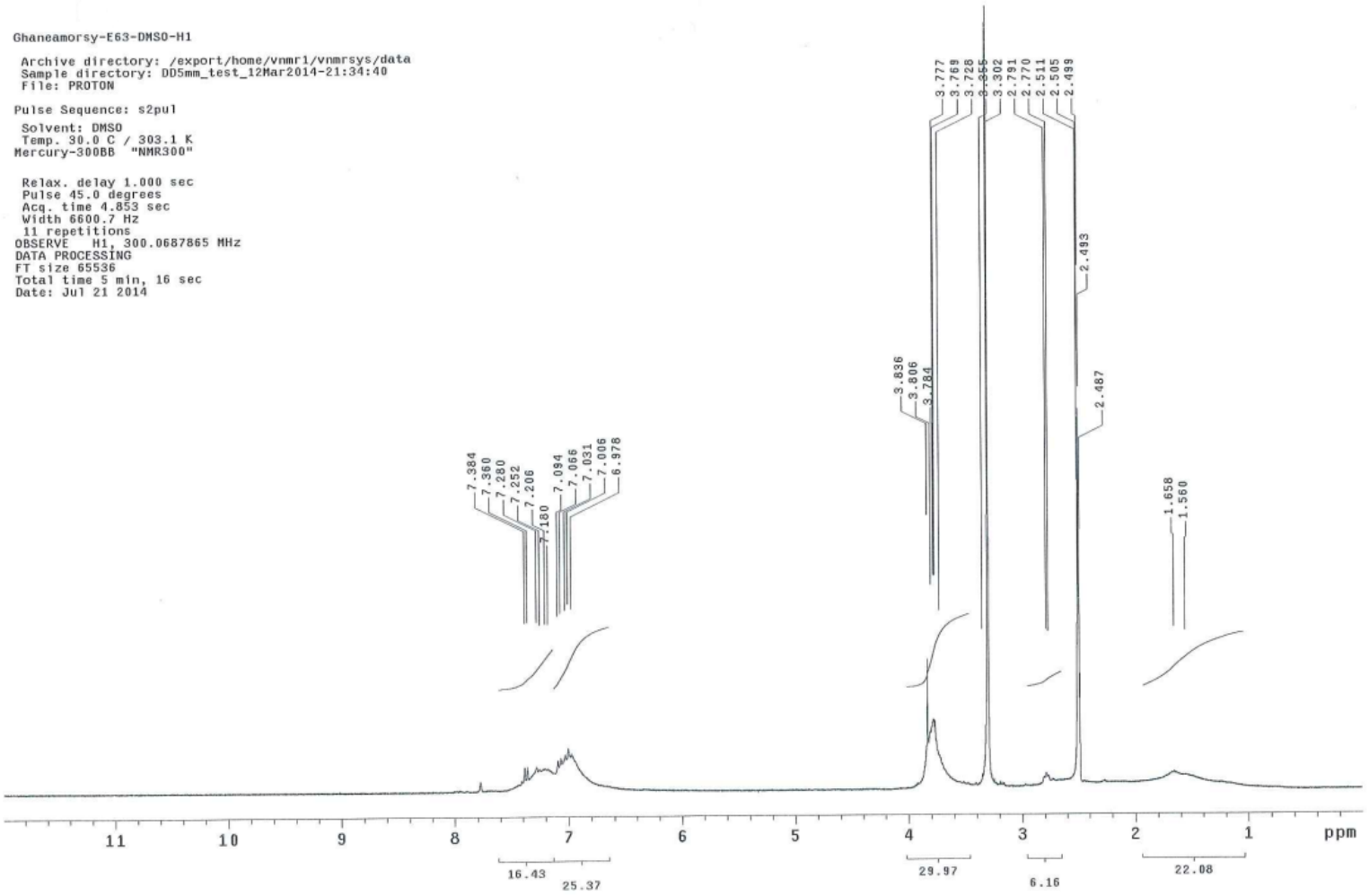
S11$_b$. ^{1}H NMR spectrum (300 MHz, DMSO-d_6) of compound 16 *(Magnified area)*



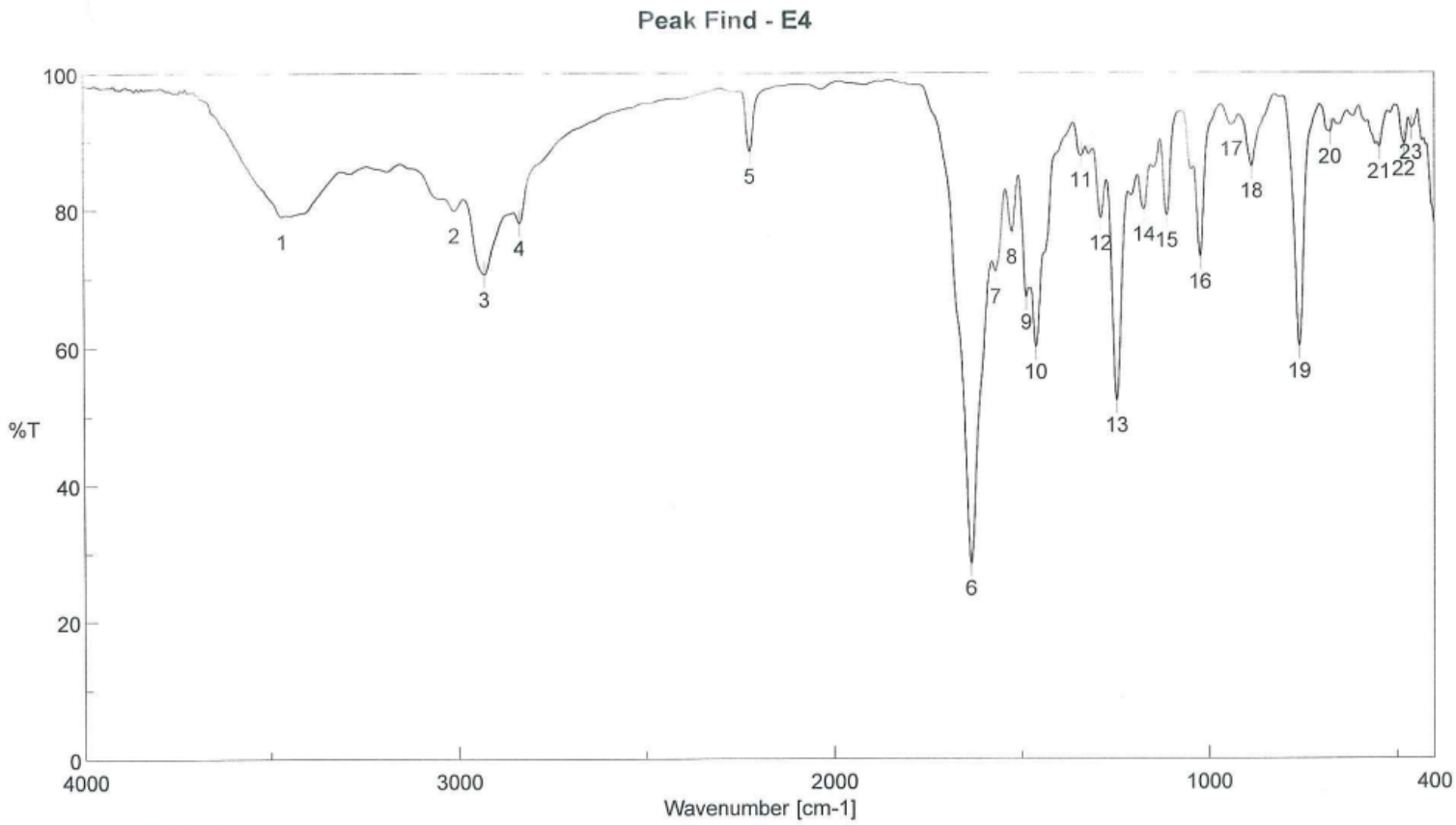
[Result of Peak Picking]

No.	Position	Intensity	No.	Position	Intensity	No.	Position	Intensity	No.	Position	Intensity
1	3848.26	97.7177	2	3747.01	97.5879	3	3432.67	93.8097	4	3055.66	96.7941
5	2927.41	90.7926	6	2846.42	93.6721	7	2197.49	98.7054	8	2053.82	99.4617
9	1908.22	99.3585	10	1674.87	93.8485	11	1594.84	91.5844	12	1458.89	88.994
13	1242.9	86.6773	14	1164.79	93.7204	15	1111.76	94.2983	16	1025.94	90.7722
17	853.347	96.9477	18	751.138	89.7399	19	575.647	97.1617			

S12$_a$. IR spectrum (KBr, cm^{-1}) of compound 17



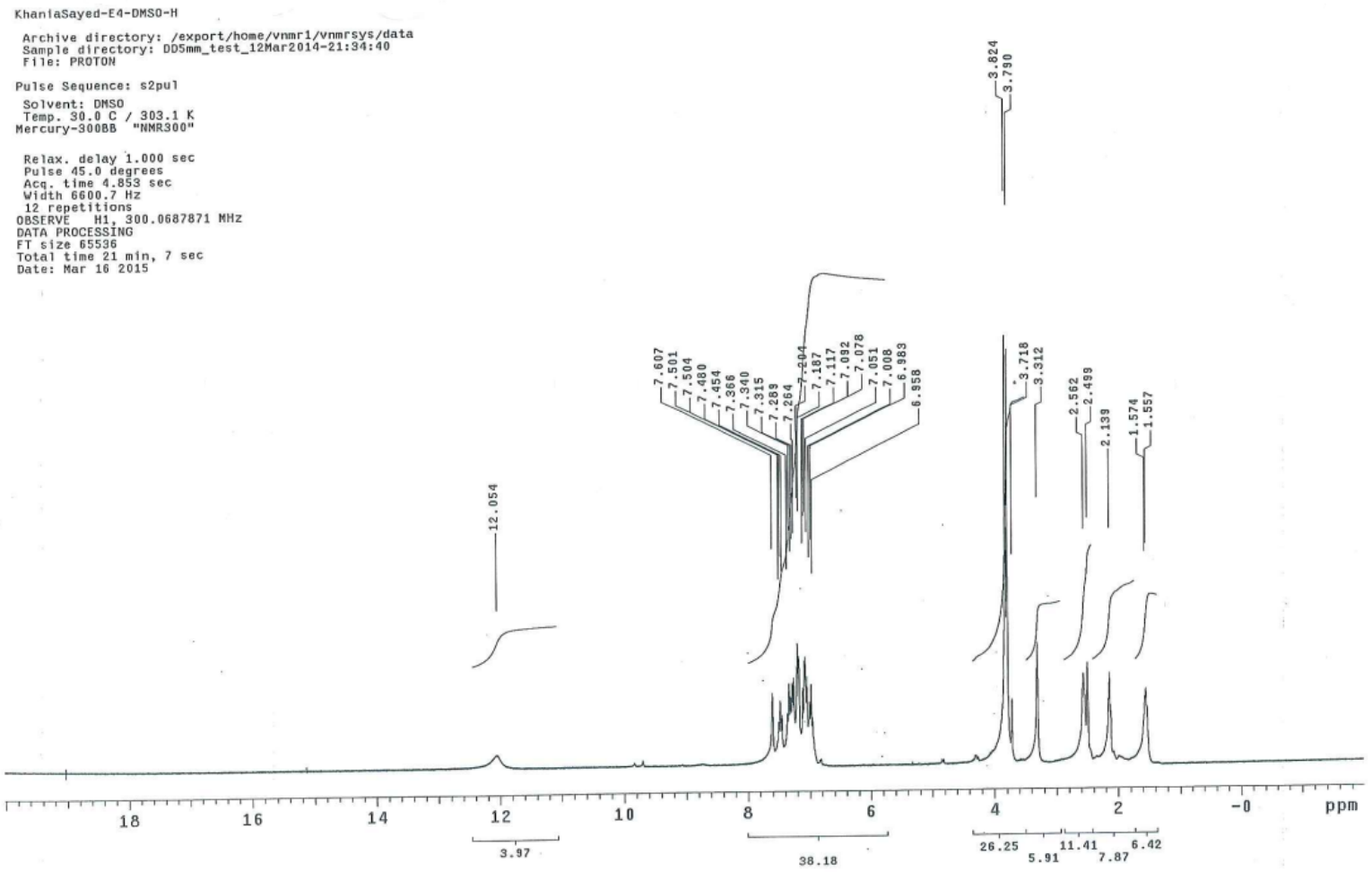
S12ᵦ.^{1}H NMR spectrum (300 MHz, DMSO-d_6) of compound 17



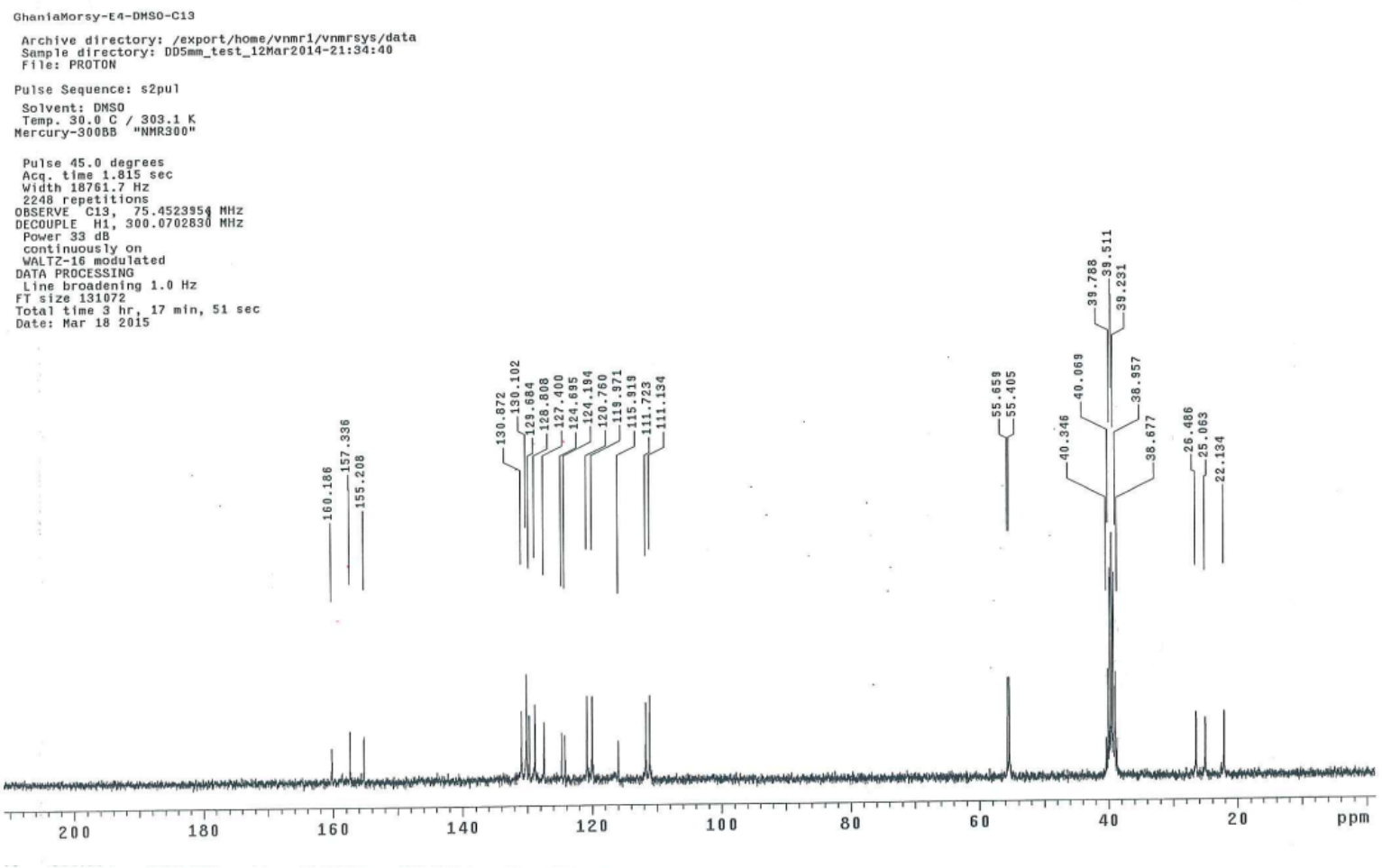
[Result of Peak Picking]

No.	Position	Intensity	No.	Position	Intensity	No.	Position	Intensity	No.	Position	Intensity
1	3468.35	78.96292	2	3011.3	79.83396	3	2932.23	70.56142	4	2837.74	78.02757
5	2223.52	88.42147	6	1635.34	28.43761	7	1569.77	70.95975	8	1526.38	76.68094
9	1487.81	67.21743	10	1462.74	60.03839	11	1341.25	87.82886	12	1288.22	78.63858
13	1246.75	52.29260	14	1173.47	79.96577	15	1112.73	79.08384	16	1023.05	73.09677
17	939.163	92.36802	18	886.131	86.25280	19	759.816	60.17382	20	676.892	91.25376
21	546.72	89.05956	22	481.153	89.44514	23	461.868	91.85877			

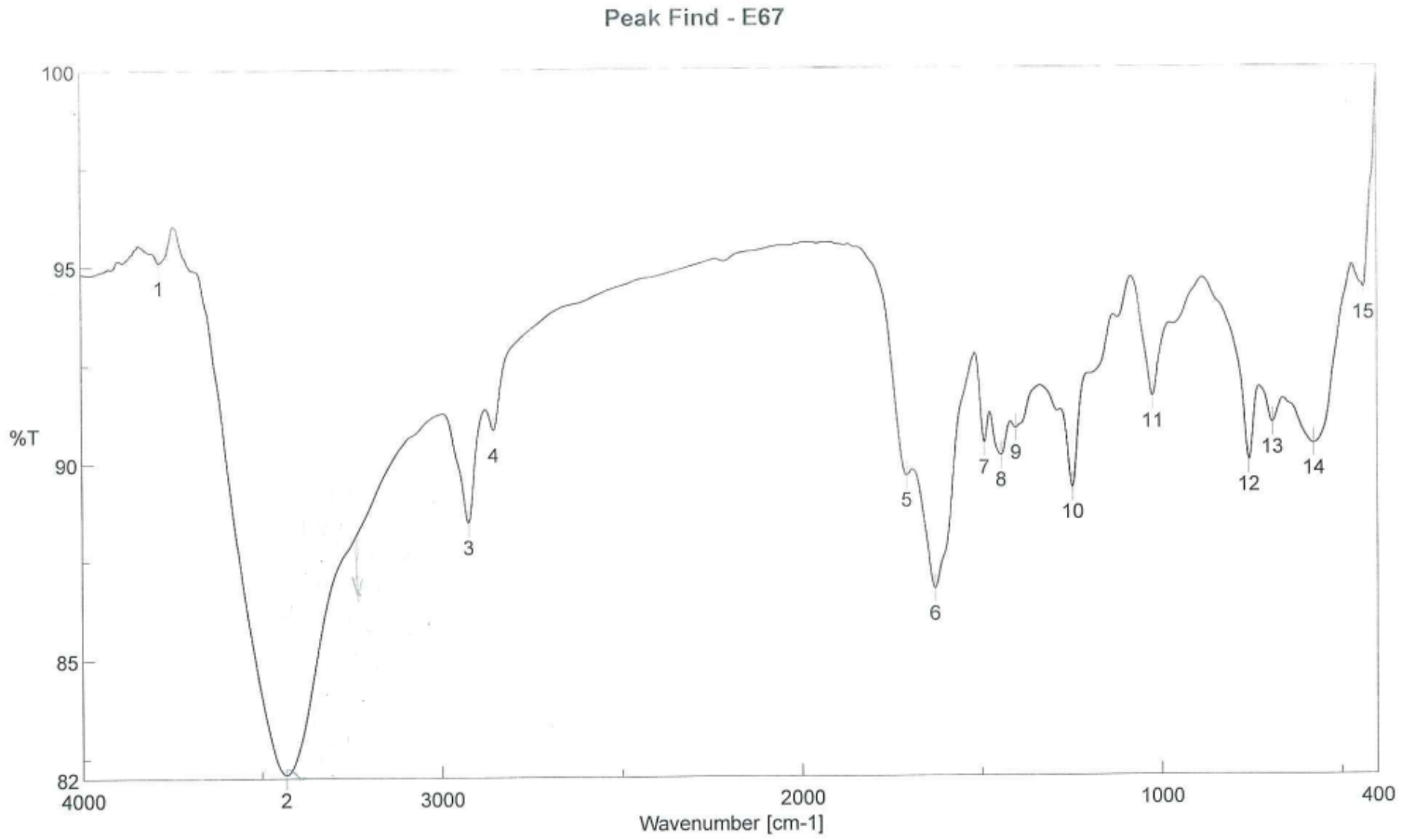
S13$_a$. IR spectrum (KBr, cm^{-1}) of compound 21



S13$_b$. ^{1}H NMR spectrum (300 MHz, DMSO-d_6) of compound 21



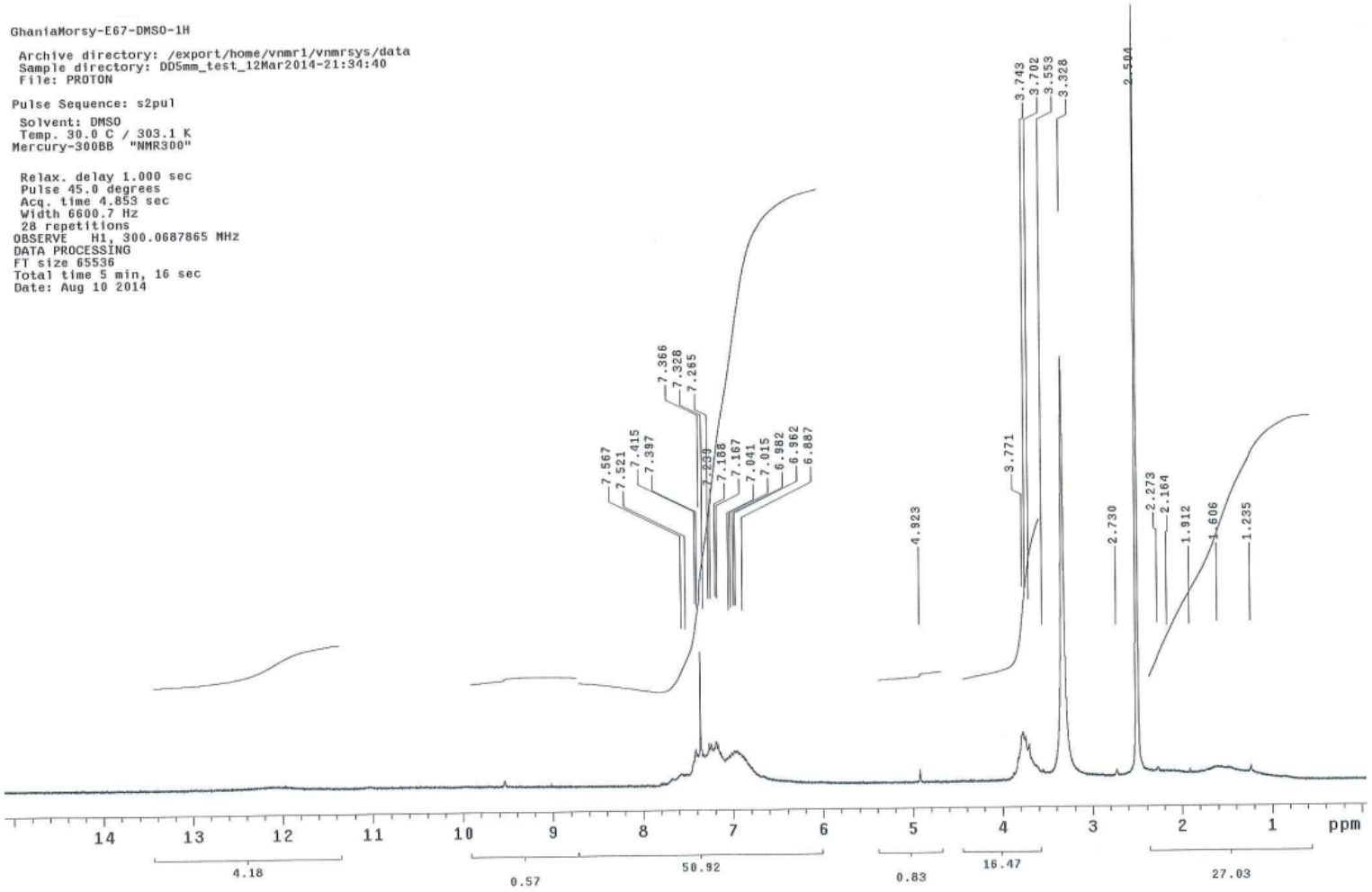
S13$_c$. ^{13}H NMR spectrum (75 MHz, DMSO-d_6) of compound 21



[Result of Peak Picking]

No.	Position	Intensity	No.	Position	Intensity	No.	Position	Intensity	No.	Position	Intensity
1	3781.72	95.09843	2	3432.67	82.08977	3	2924.52	88.46484	4	2854.13	90.83206
5	1707.66	89.62933	6	1628.59	86.73815	7	1491.67	90.45927	8	1445.39	90.14161
9	1403.92	90.83438	10	1246.75	89.31385	11	1024.02	91.62869	12	755.959	89.99448
13	690.391	90.94867	14	576.612	90.41011	15	437.762	94.35038			

S14$_a$. IR spectrum (KBr, cm^{-1}) of compound 23



S14$_b$. ^{1}H NMR spectrum (300 MHz, DMSO-d_6) of compound 23

Antitumor evaluation S1

Table S1 *Effect of compounds **1, 13, 16, 17** and **21** on the growth of three human tumor cell lines*

Sample ID	Compound	GI_{50} (μg L^{-1})(% Growth)		
		MCF-7	NCI-H460	SF-268
E53	**1**	20.23 ± 4.50	18.28 ± 4.21	42.62 ± 4.80
E65b	**13**	14.27 ± 6.07	18.15 ± 4.05	20.27 ± 2.40
E80	**16**	4.16 ± 1.09	7.25 ± 1.30	12.80 ± 3.90
E63	**17**	13.48 ± 4.22	6.09 ± 1.88	4.62 ± 1.12
E4	**21**	22.31 ± 3.40	18.29 ±2.40	28.11 ± 10.30
	Doxorubicin	0.04 ± 0.008	0.09 ± 0.008	0.09 ± 0.007

Table 1 Effect of compounds ----- *on the growth of three human tumor cell lines*

Compound	GI_{50} (μ g L^{-1})(% Growth)		
	MCF-7	NCI-H460	SF-268
E53	20.23 ± 4.50	**18.28 ± 4.21**	**42.62 ± 4.80**
E80	**4.16 ± 1.09**	**7.25 ± 1.30**	**12.80 ± 3.90**
E4	**22.31 ± 3.40**	**18.29 ± 2.40**	**28.11 ± 10.30**
E65b	**14.27 ± 6.07**	**18.15 ±** 4.05	**20.27 ± 2.40**
E63	**13.48 ± 4.22**	**6.09 ± 1.88**	**4.62 ± 1.12**
E60	**60.34 ± 12.36**	**58.20 ± 6.58**	**18.60 ± 2.09**
Doxorubicin	0.04 ± 0.008	0.09±0.008	0.09±0.007

Results are given in cconcentrations that were able to cause 50 % of cell growth inhibition (GI_{50}) after a continuous exposure of 48 h and show means ± SEM of three-independent experiments performed in duplicate.

Against MCF-7

Compound	Viability rate (%)			IC_{50} (mg/ml)
	0.1µg/ml	1 µg/ml	10 µg/ml	
E53	55.81 ± 9.12	50.39 ± 6.88	44.21 ± 8.92	20.22±2.02
E80	90.22 ± 6.47	88.87 ± 5.41	80.42 ± 6.80	6.80± 2.93
E4	70.41 ± 12.46	68.20 ± 9.34	66.13 ±10.68	20.50 ± 5.50
E65b	64.55 ± 2.53	62.40 ± 2.59	58.40 ± 6.31	11.01± 3.24

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E36	80.41 ± 4.49	76.21 ± 6.39	70.18 ± 5.63	8.44 ± 1.29
E60	78.54 ± 2.19	68.38 ± 8.39	62.31 ± 5.32	12.12± 3.37

Against NCI-H460

Compound	Viability rate (%)			IC_{50} (µg/ml)
	0.1µg/ml	1 µg/ml	10 µg/ml	
E53	68.21 ± 6.80	58.63 ± 2.90	52.08 ± 6.72	18.29±1.89
E80	87.28 ± 6.52	76.64 ± 5.83	70.93 ± 4.09	6.78± 2.61
E4	72.57 ± 3.60	65.28 ± 6.84	58.74 ± 6.03	18.22 ± 2.64
E65b	48.26 ± 4.53	40.56 ± 3.28	36.41 ± 4.68	30.42± 4.84
E36	92.58 ± 5.82	86.09 ± 5.93	80.51 ± 6.83	5.59 ± 1.25
E60	68.28 ± 3.05	59.41 ± 3.29	55.93 ± 6.82	19.26± 5.62

Results are given in cconcentrations that were able to cause 50 % of cell growth inhibition (GI_{50}) after a continuous exposure of 48 h and show means ± SEM of three-independent experiments performed in duplicate.

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Against SF-268

Compound	Viability rate (%)			IC_{50} (□g/ml)
	0.1µg/ml	1 µg/ml	10 µg/ml	
E53	78.23 ± 4.46	72.30 ± 4.27	68.21 ± 4.53	42.30±3.40
E80	80.42 ± 8.73	72.20 ± 4.80	63.44 ± 3.26	8.32± 1.90
E4	68.22 ± 5.31	60.19 ± 3.59	55.52 ± 2.49	12.33 ± 1.30
E65b	73.46 ± 8.20	66.39 ± 2.09	58.73 ± 5.90	27.52± 1.63
E36	84.77 ± 2.40	75.21 ± 3.49	66.42 ± 5.70	6.73 ± 1.69
E60	52.40 ± 4.63	46.27 ± 2.89	42.72 ± 3.62	58.48± 3.09

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