Supplementary Information

Urolithin and reduced urolithin derivatives as potent inhibitors of tyrosinase and melanogenesis: importance of the 4-substituted resorcinol moiety

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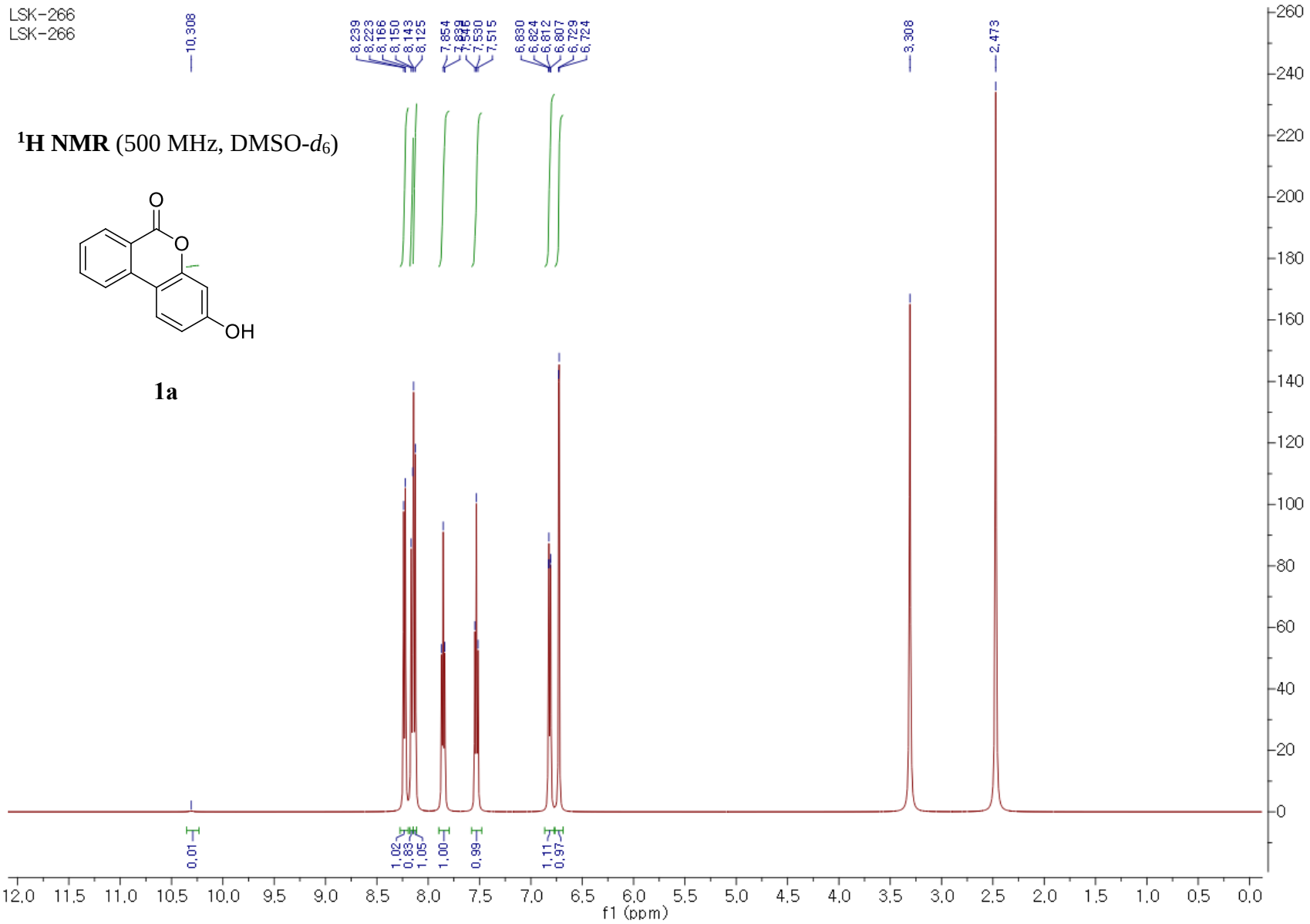
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^{13}C NMR spectrum of compound **1j** 32

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^{1}H NMR spectrum of compound **2a** 34

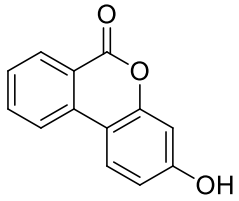
^{13}C NMR spectrum of compound **2a** 35
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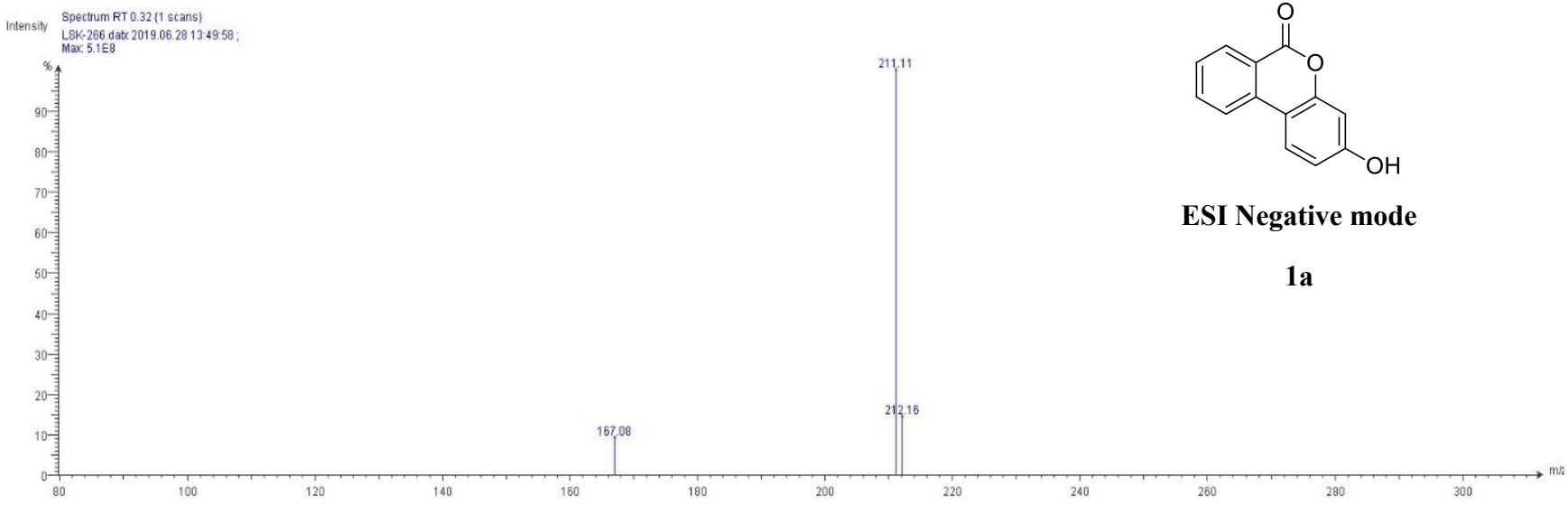
^{1}H NMR (500 MHz, DMSO-d_6)

1a

^{13}C NMR (100 MHz, DMSO-d_6)



1a

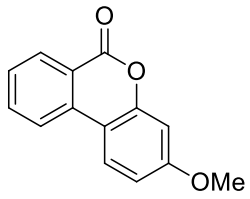


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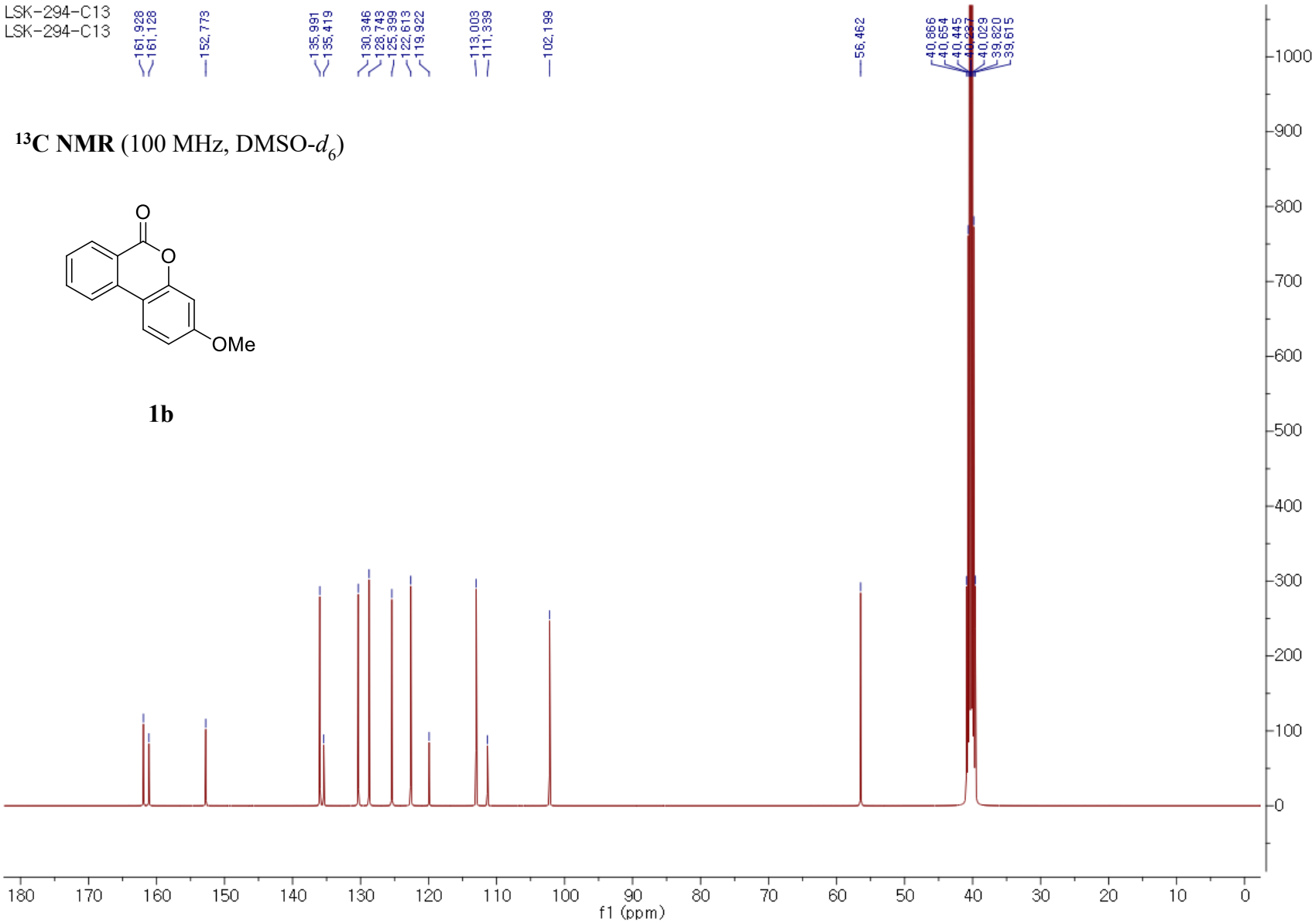
1a

LSK-294
LSK-294

^{1}H NMR (500 MHz, DMSO-d_6)

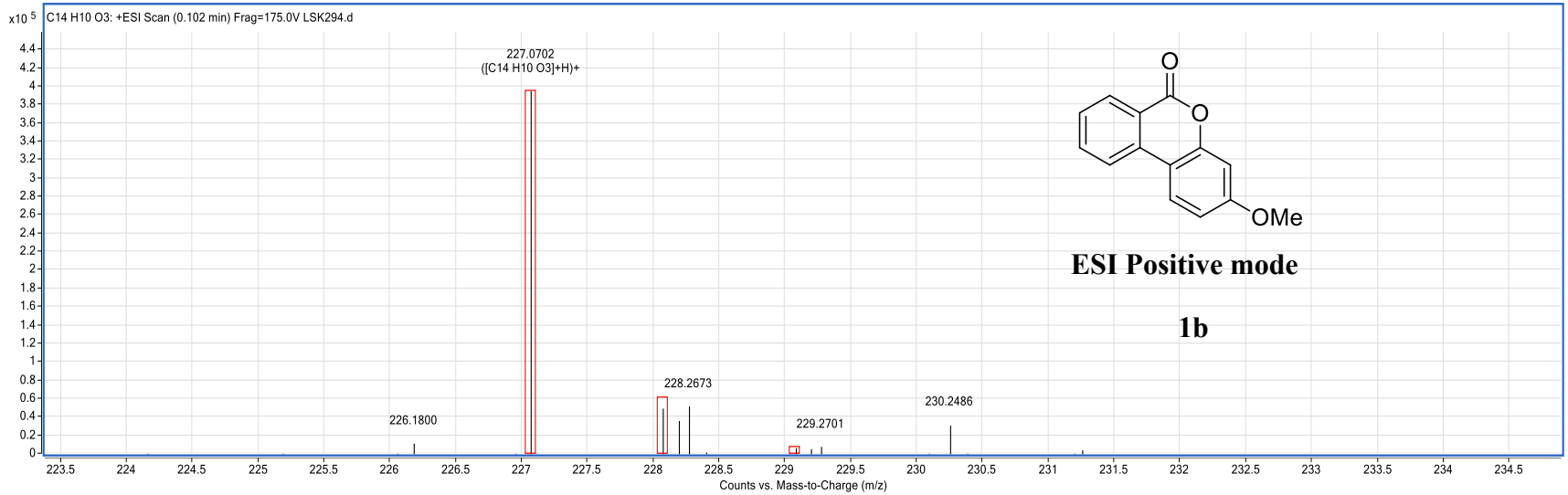


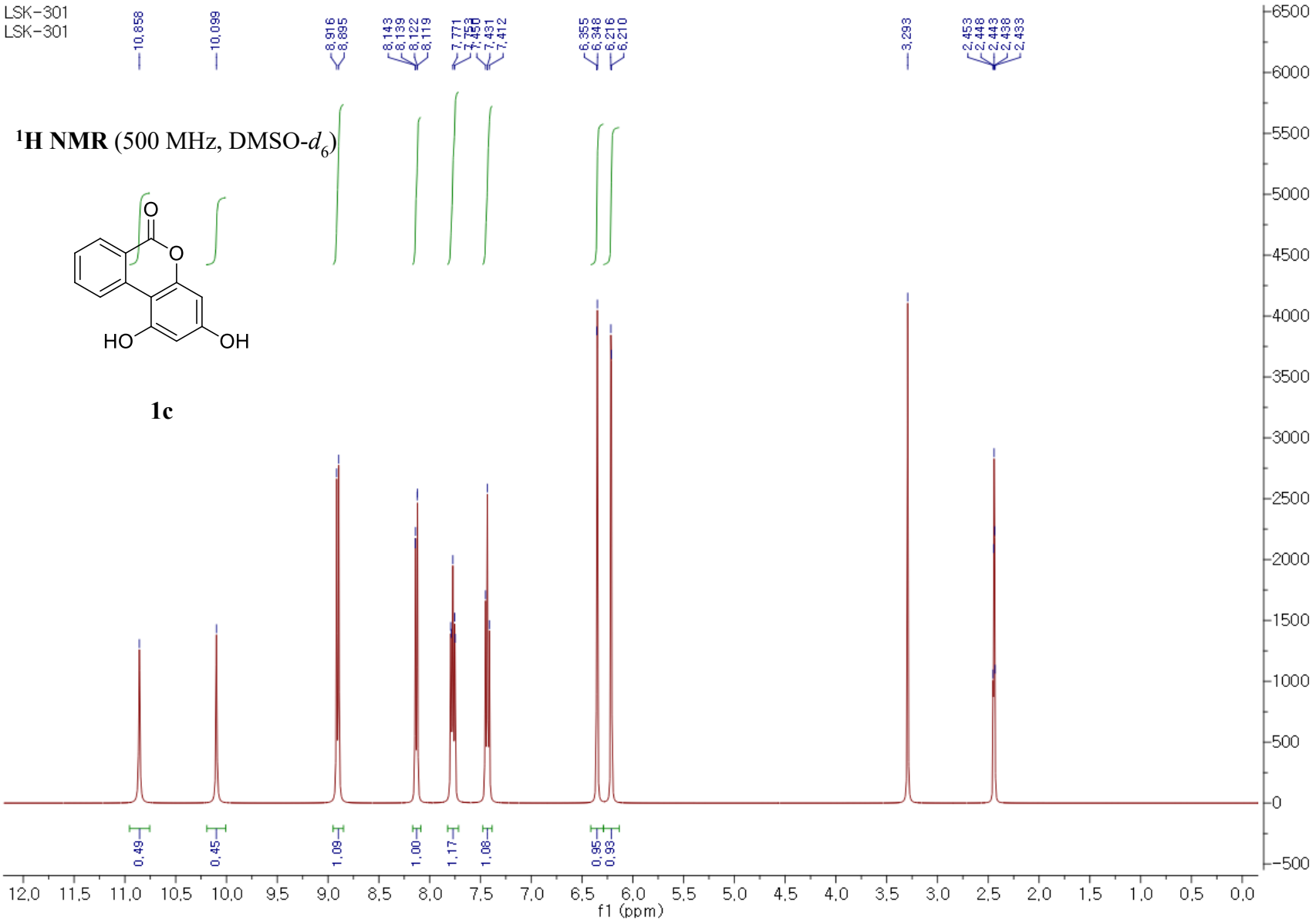
1b



^{13}C NMR (100 MHz, DMSO-d_6)

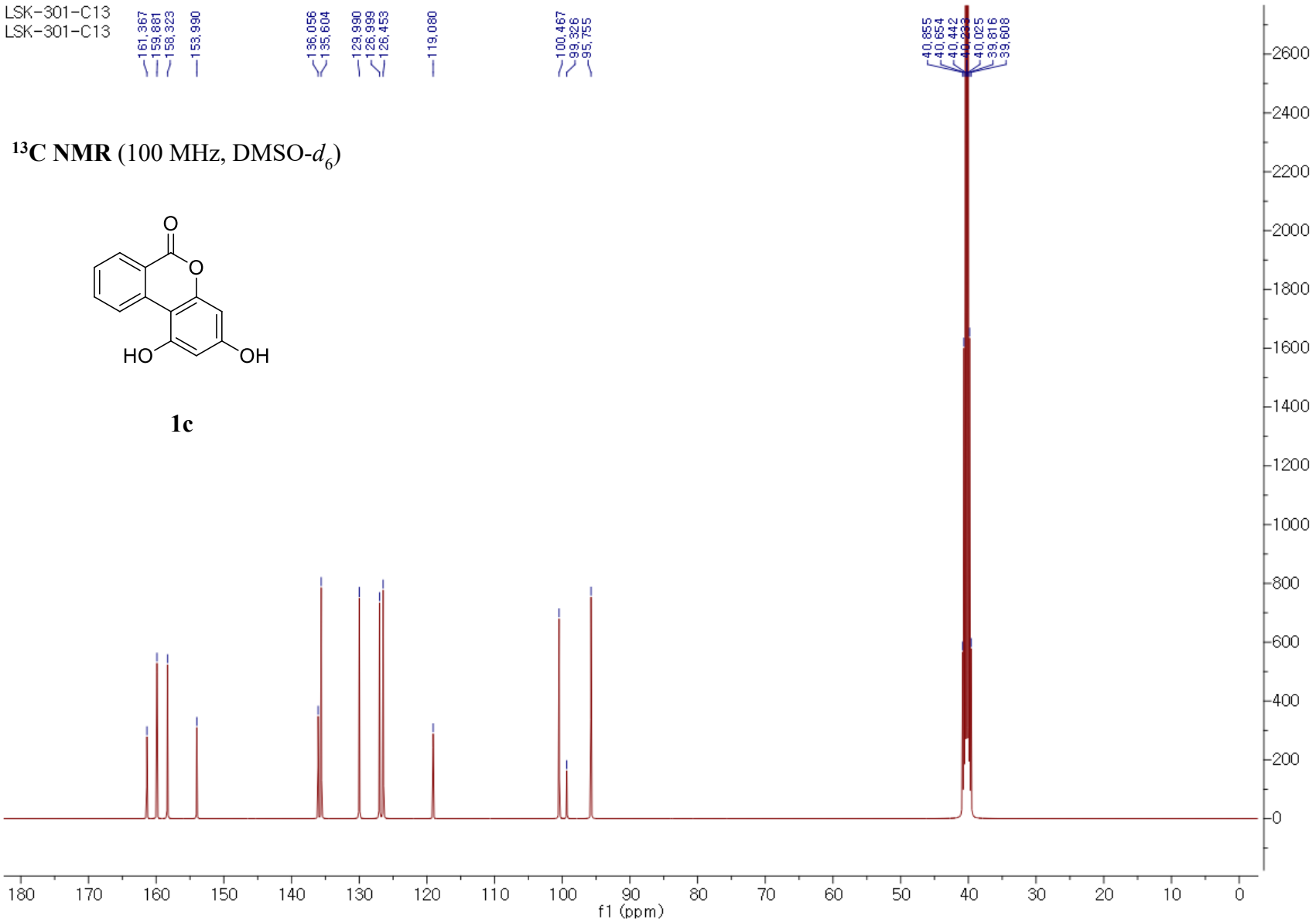
1b


x10 5
C14 H10 O3: +ESI Scan (0.102 min) Frag=175.0V LSK294.d
227.0702
([C14 H10 O3]+H)+
228.2673
226.1800
229.2701
230.2486
Counts vs. Mass-to-Charge (m/z)
O
O
OMe
ESI Positive mode
1b



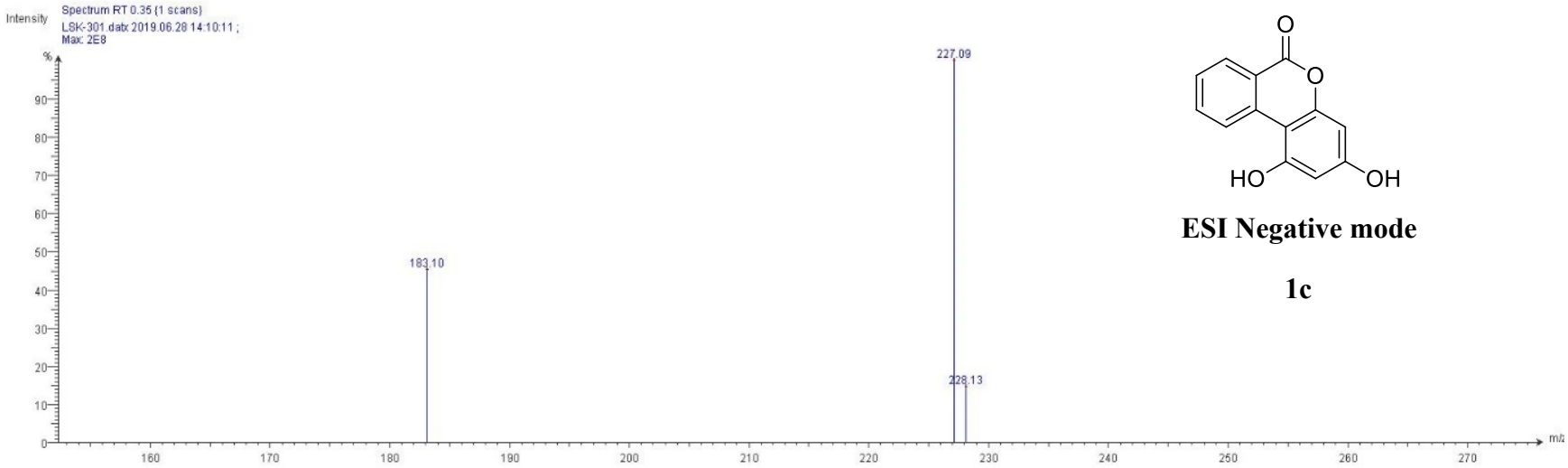
^{1}H NMR (500 MHz, DMSO-d_6)

1c



^{13}C NMR (100 MHz, DMSO-d_6)

1c

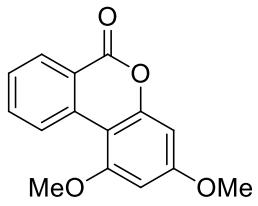


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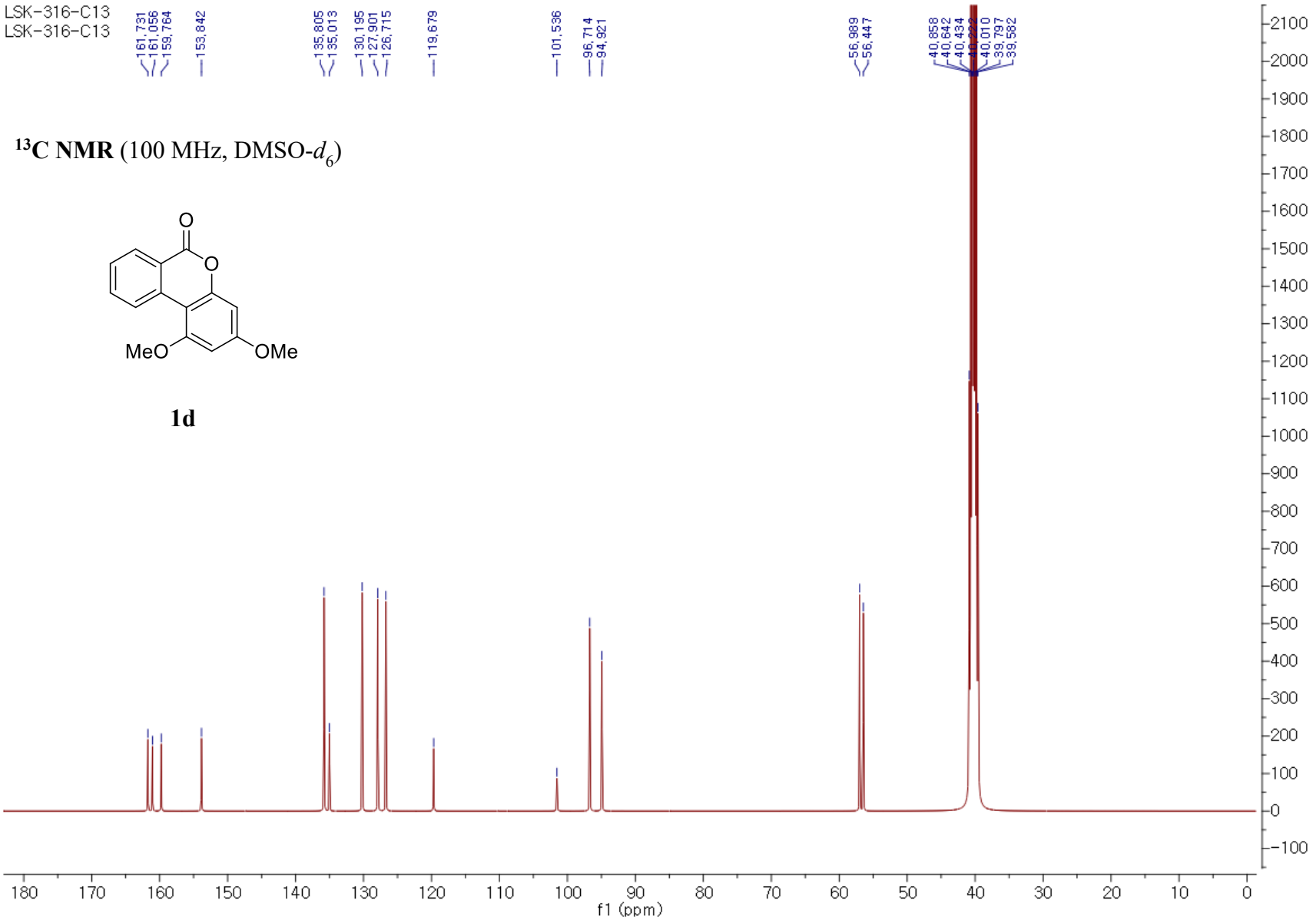
1c

LSK-316-500
LSK-316

^{1}H NMR (500 MHz, DMSO-d_6)

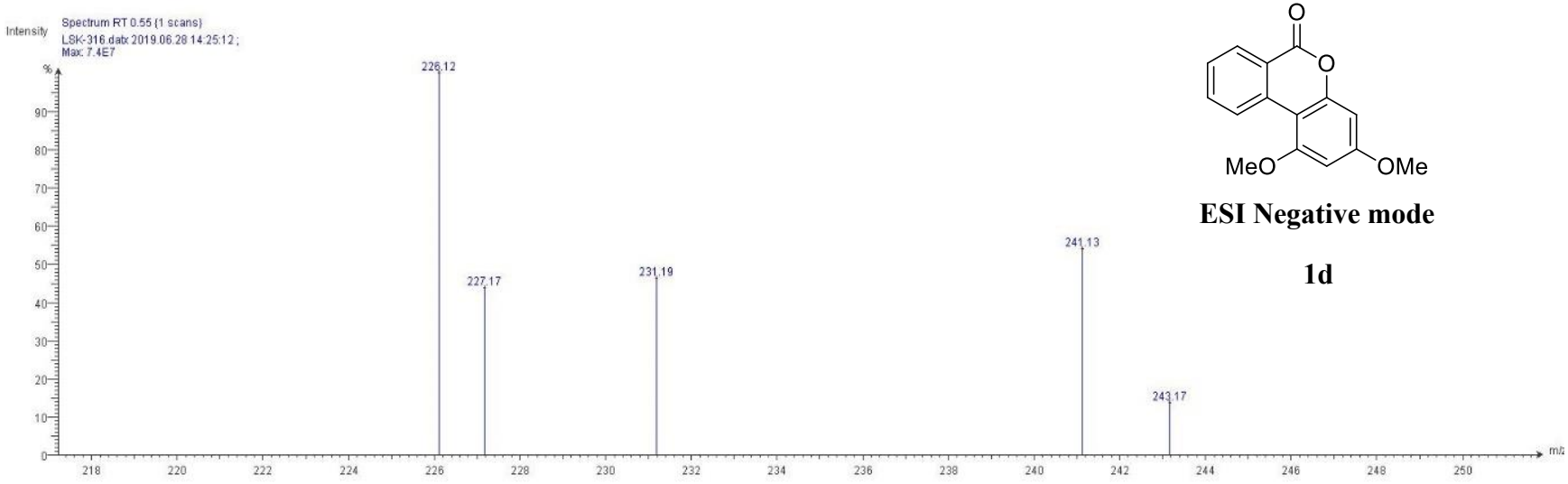


1d



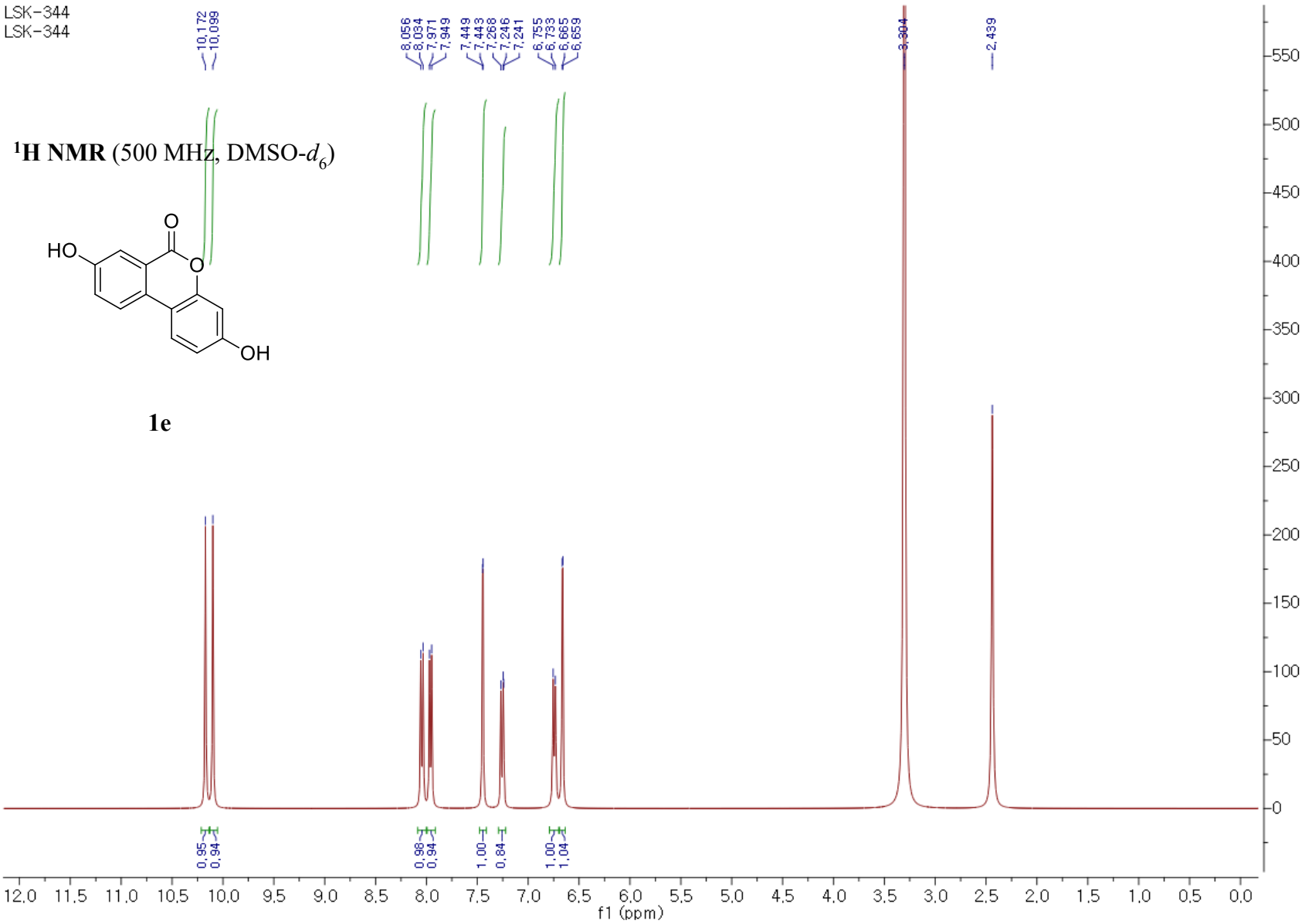
^{13}C NMR (100 MHz, DMSO-d_6)

1d



ESI Negative mode

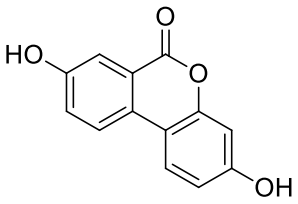
1d



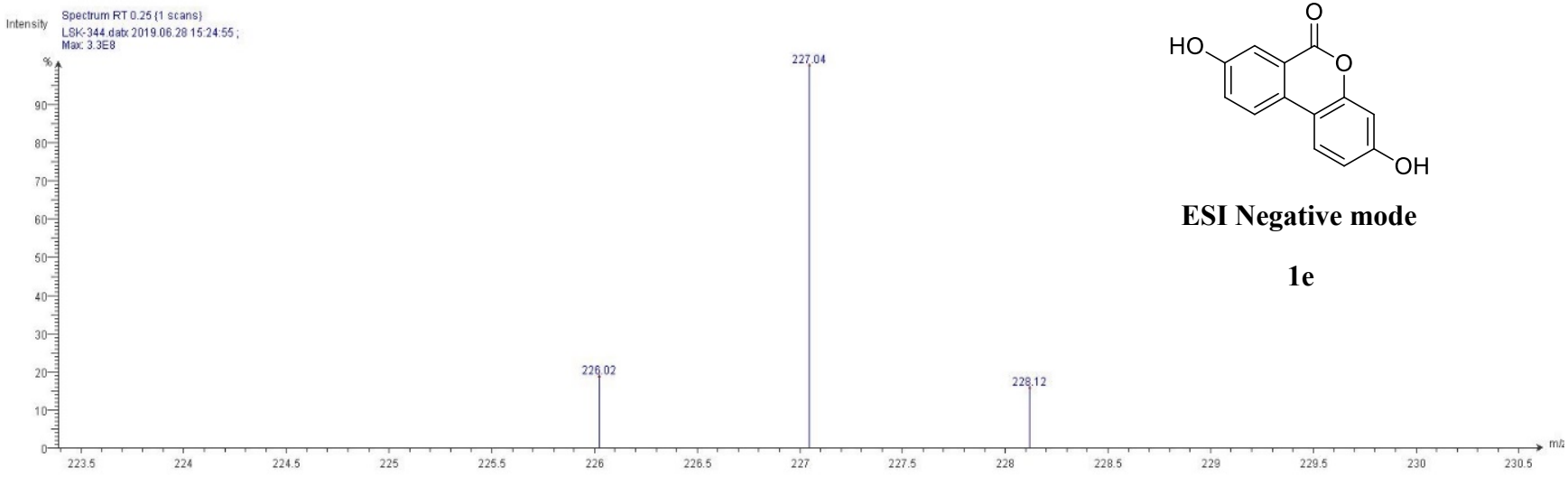
^{1}H NMR (500 MHz, DMSO-d_6)

1e

^{13}C NMR (100 MHz, DMSO-d_6)

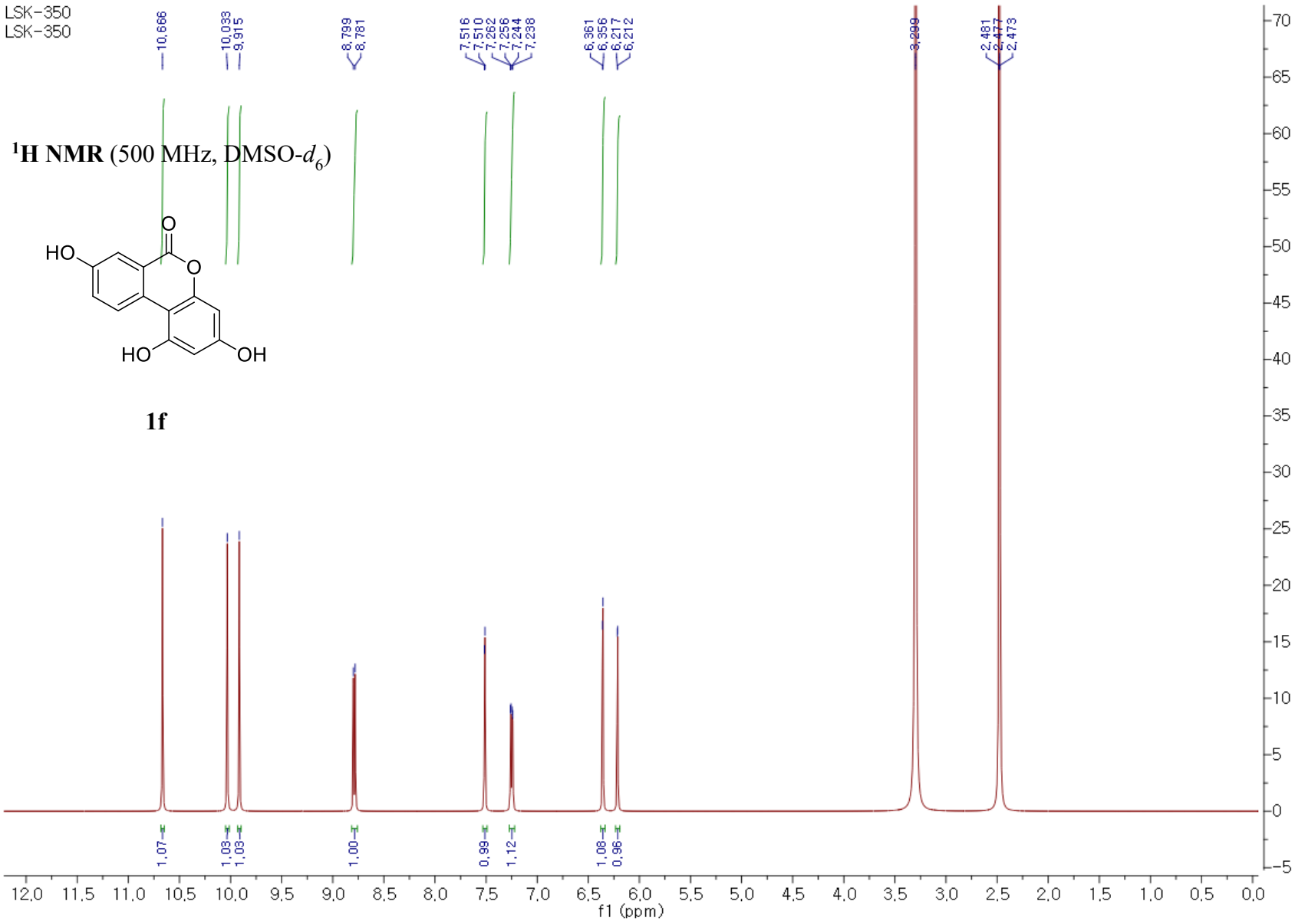


1e



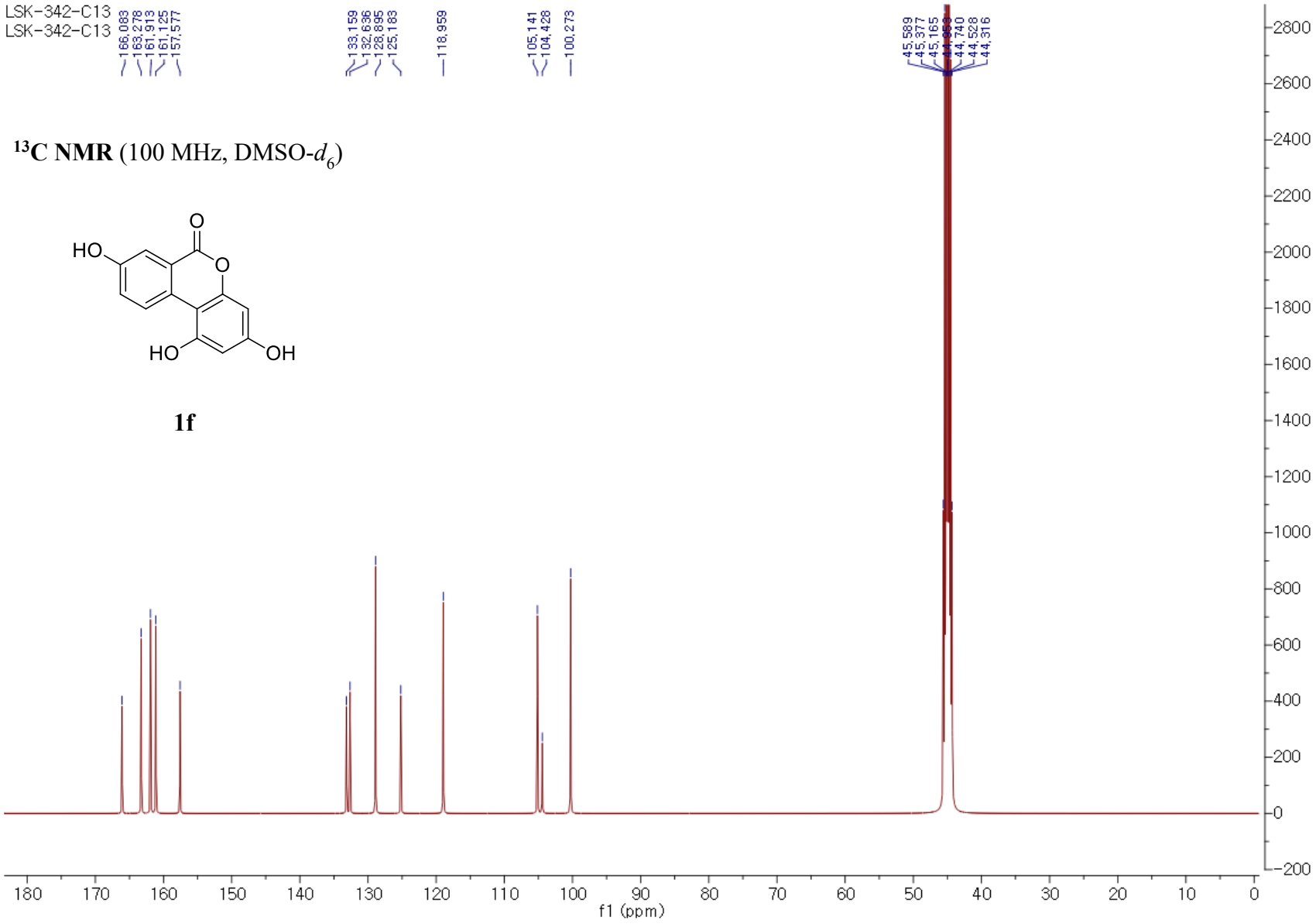
ESI Negative mode

1e



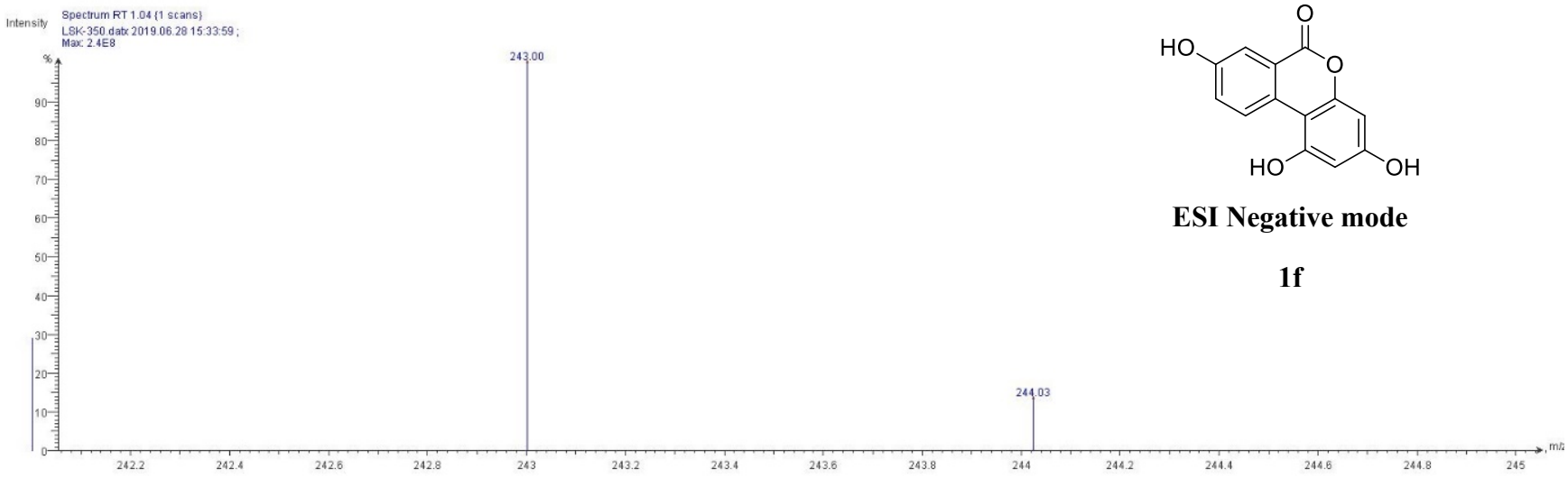
^{1}H NMR (500 MHz, DMSO-d_6)

1f



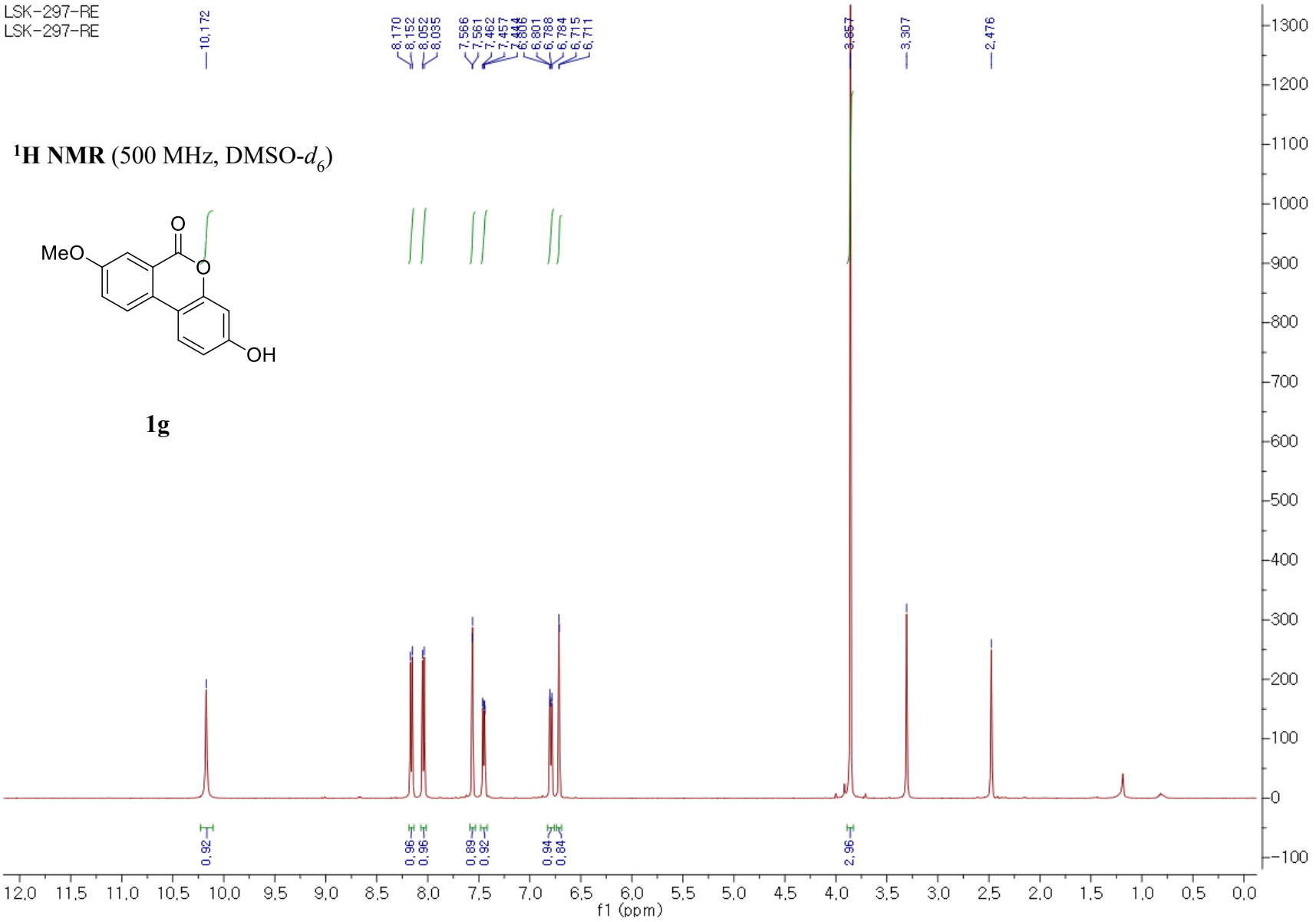
^{13}C NMR (100 MHz, DMSO-d_6)

1f



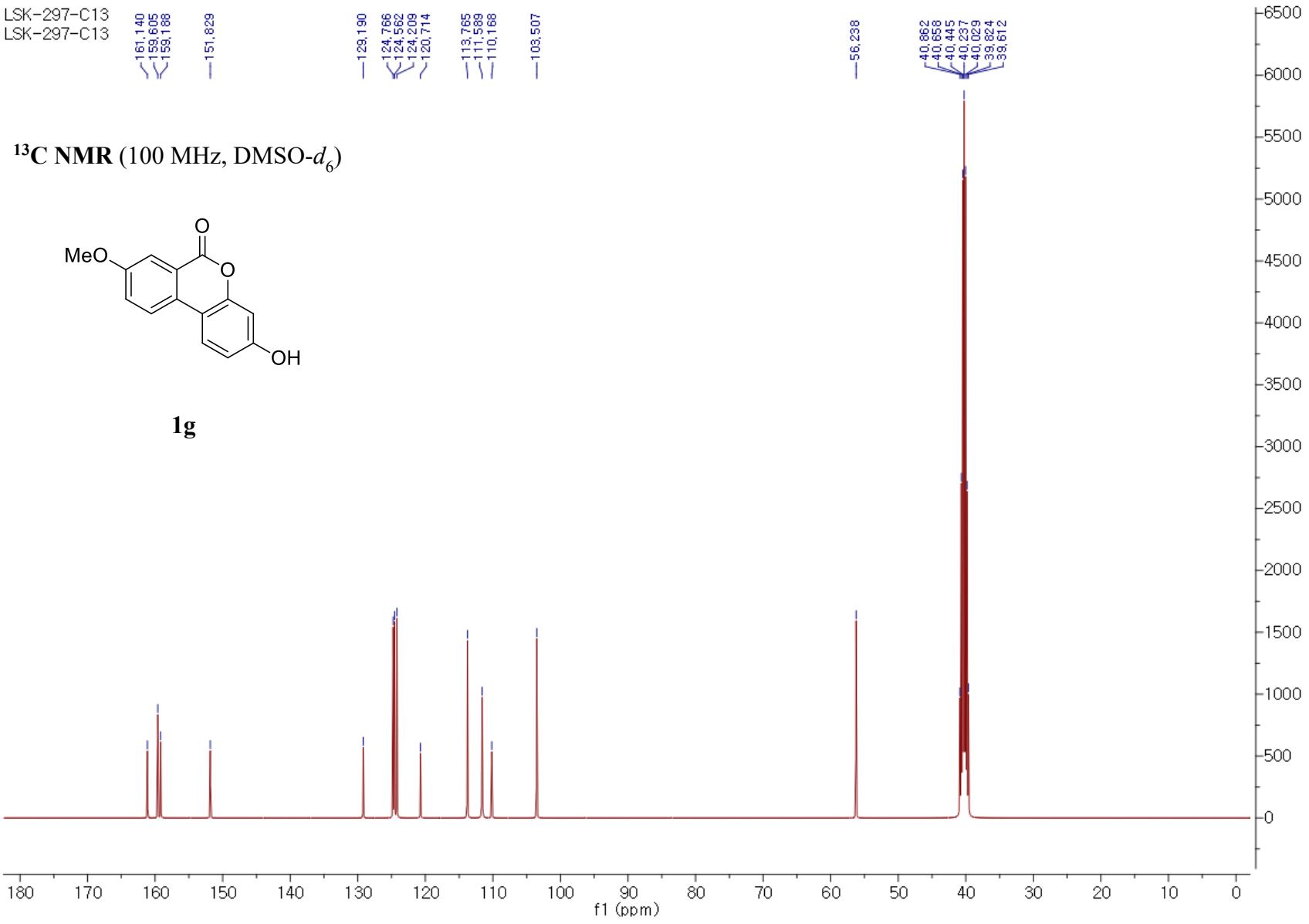
ESI Negative mode

1f



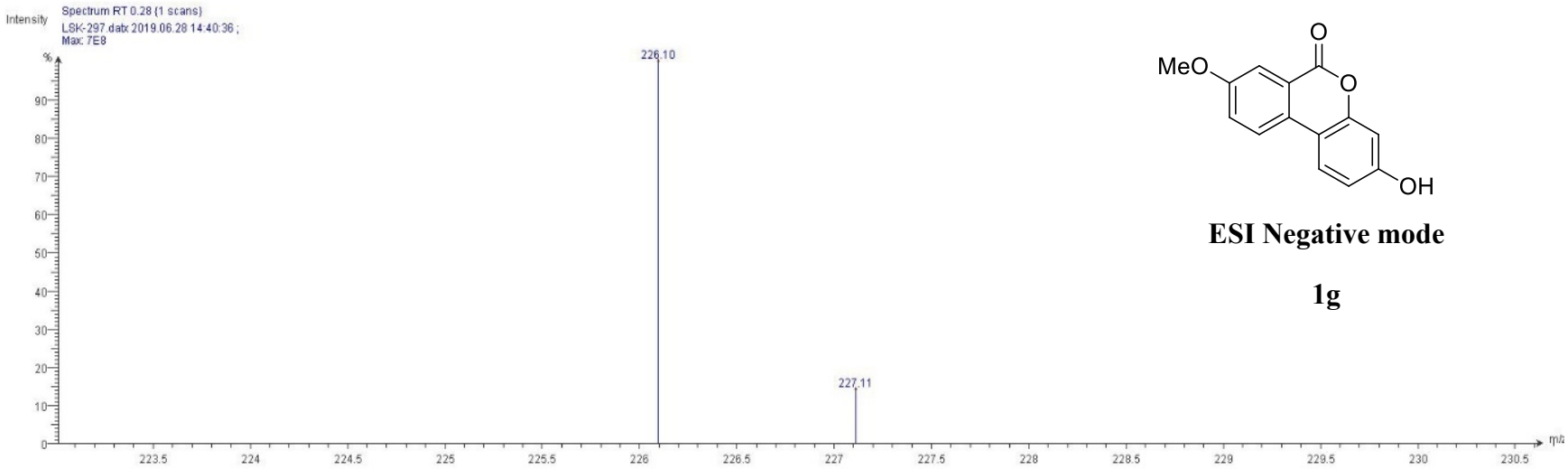
^{1}H NMR (500 MHz, DMSO-d_6)

1g



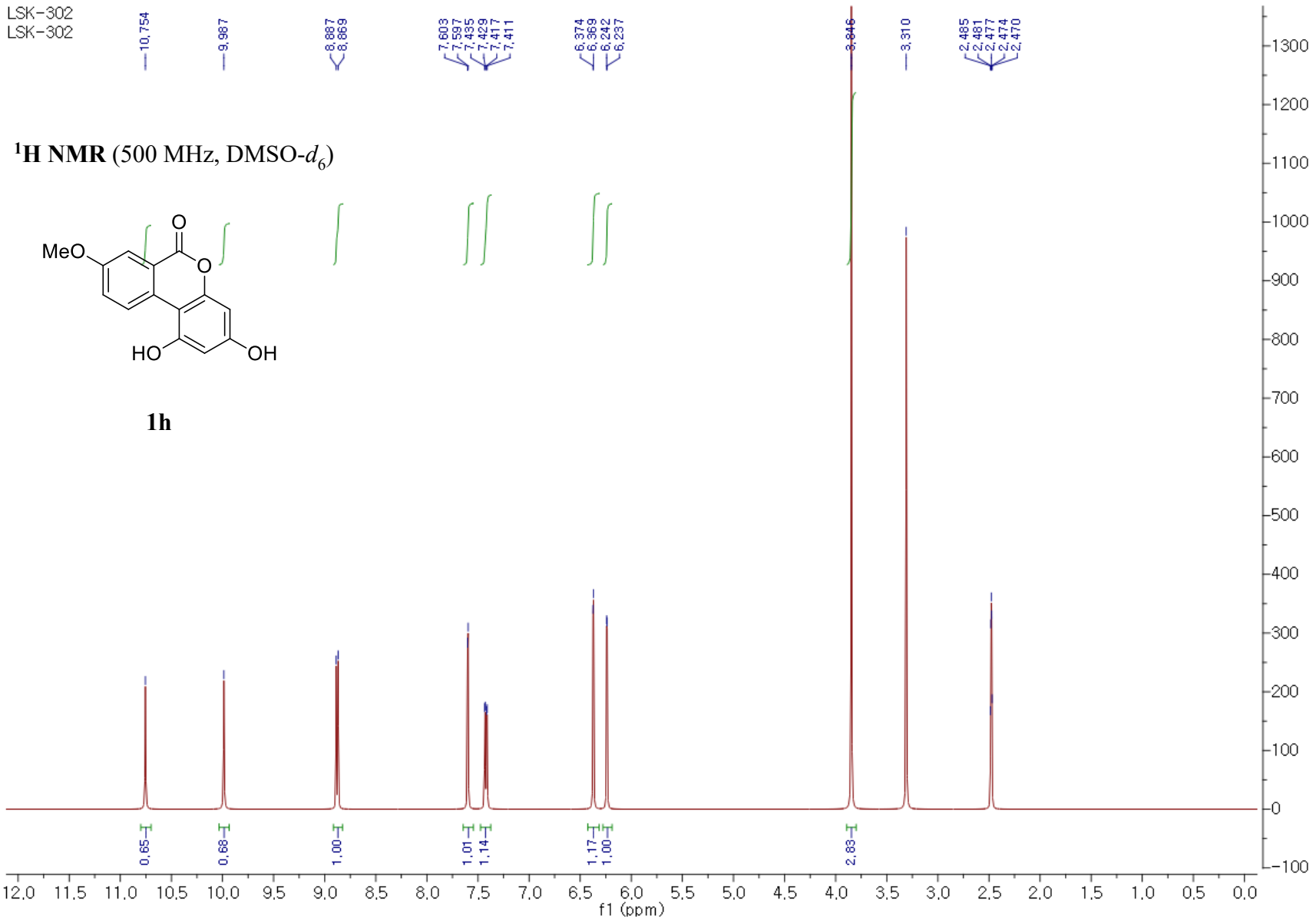
^{13}C NMR (100 MHz, DMSO-d_6)

1g



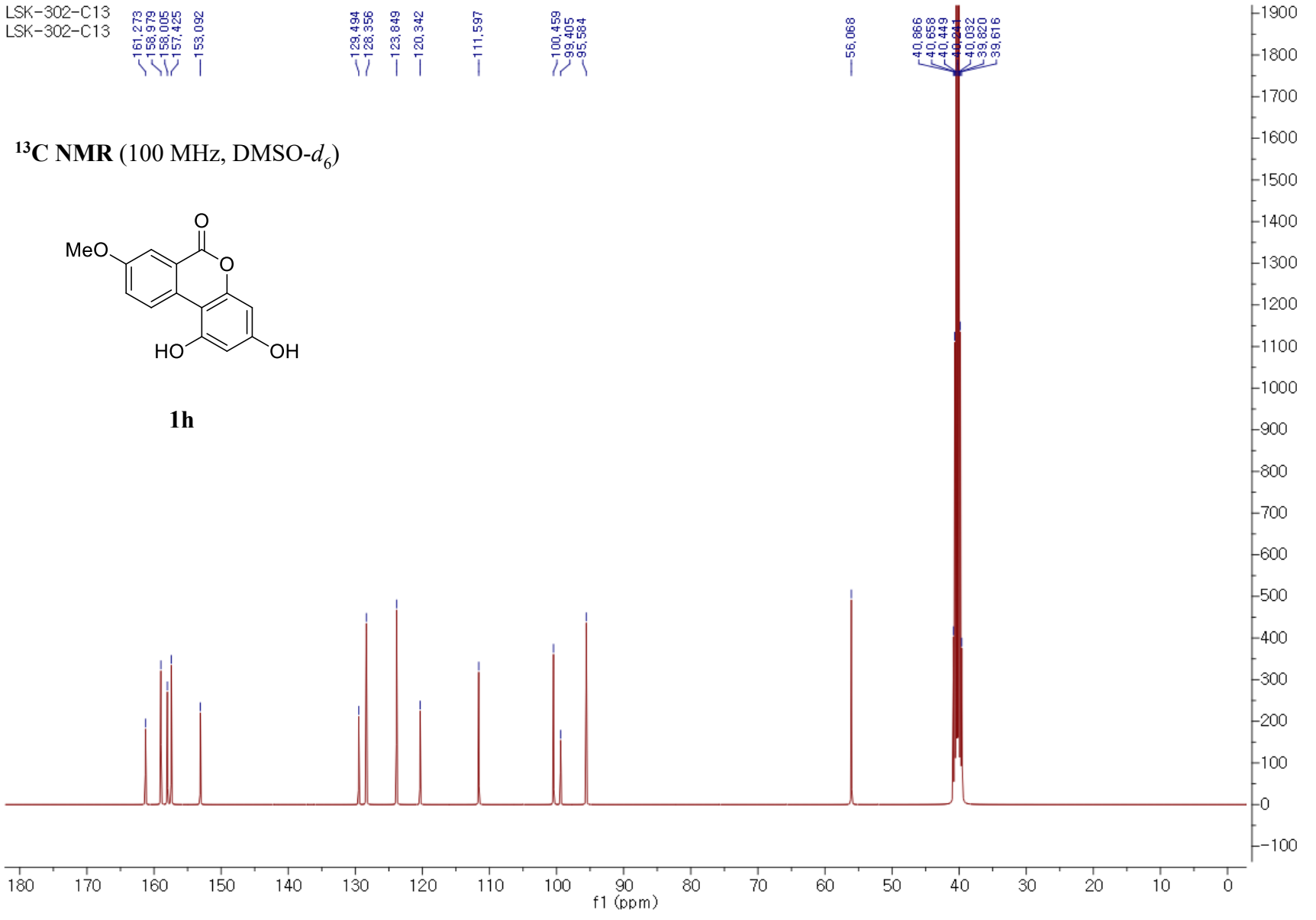
ESI Negative mode

1g



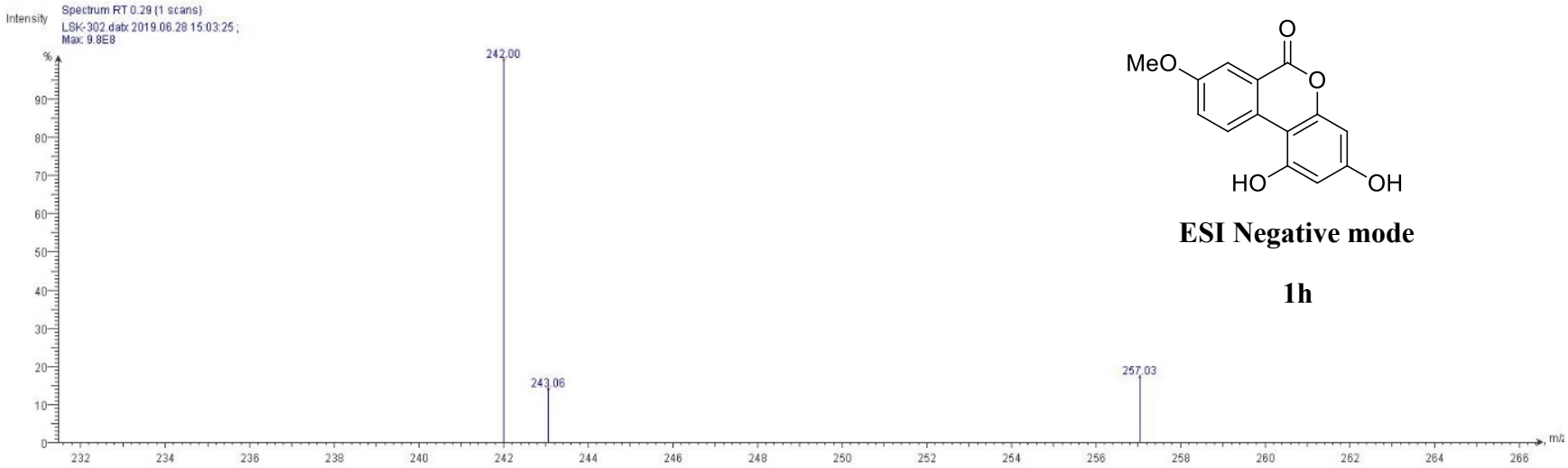
^{1}H NMR (500 MHz, DMSO-d_6)

1h



^{13}C NMR (100 MHz, DMSO-d_6)

1h

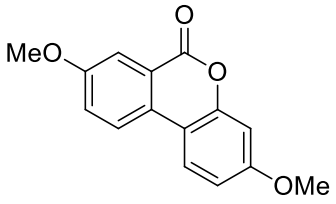


ESI Negative mode

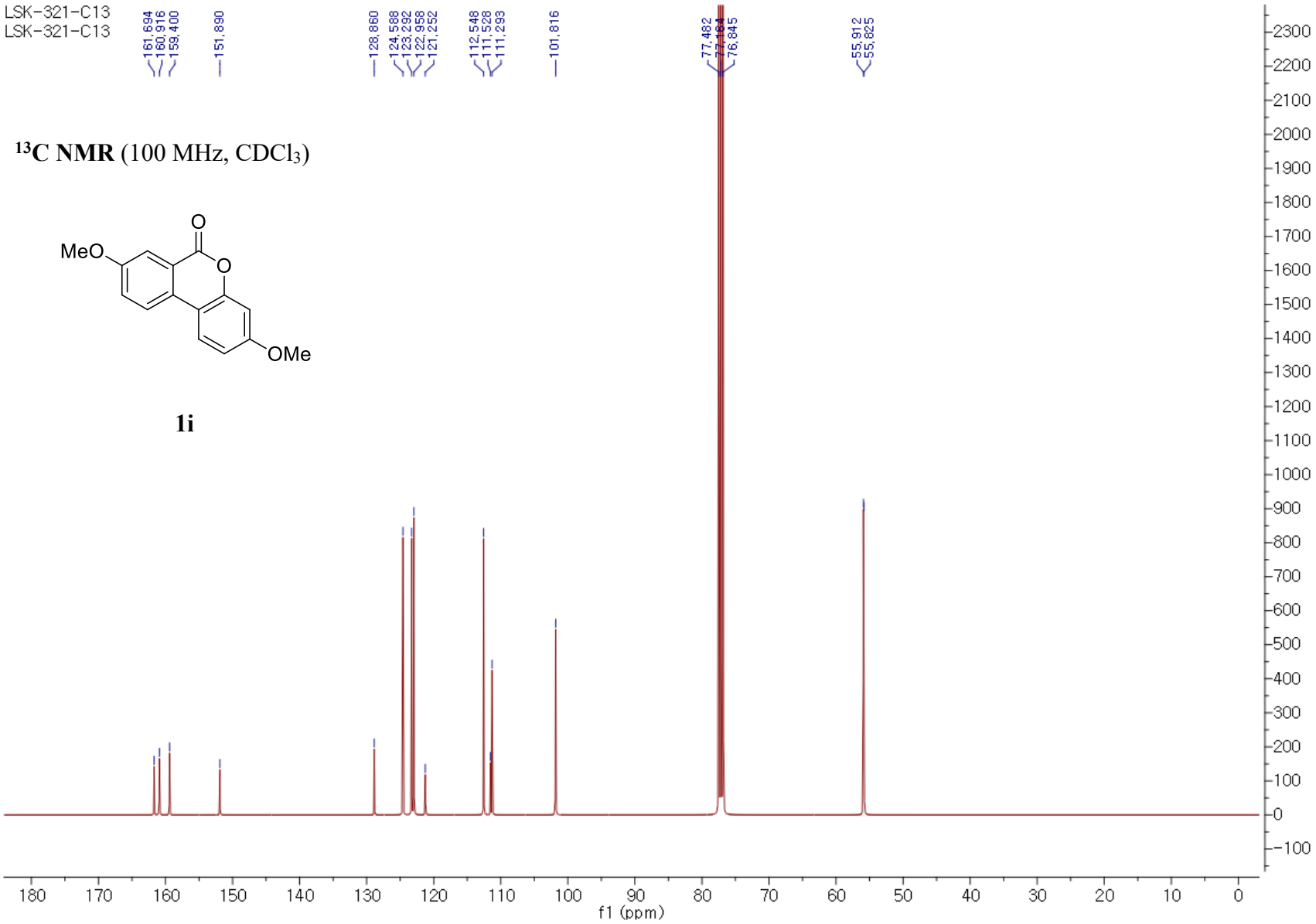
1h

LSK-321
LSK-321

^{1}H NMR (500 MHz, $CDCl_3$)

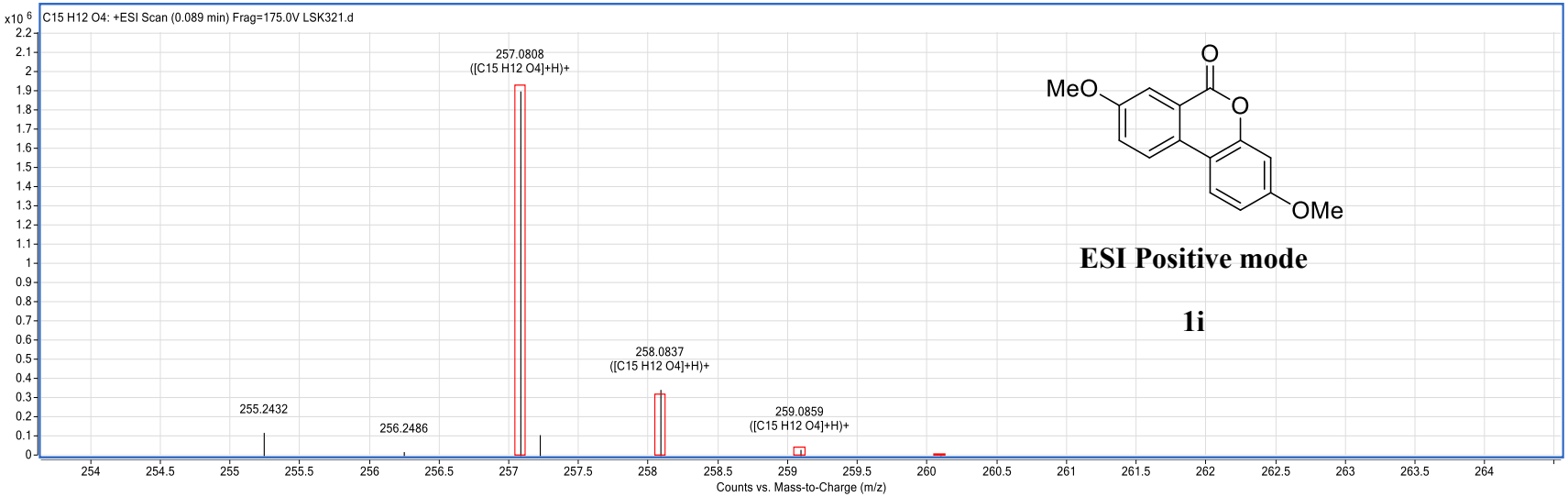


1i



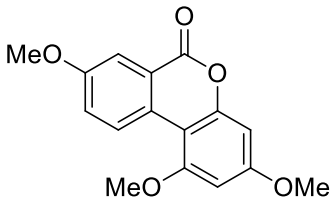
^{13}C NMR (100 MHz, $CDCl_3$)

1i


x10 6
C15 H12 O4: +ESI Scan (0.089 min) Frag=175.0V LSK321.d
257.0808
([C15 H12 O4]+H)+
258.0837
([C15 H12 O4]+H)+
255.2432
256.2486
259.0859
([C15 H12 O4]+H)+
Counts vs. Mass-to-Charge (m/z)
MeO
O
O
OMe
ESI Positive mode
1i

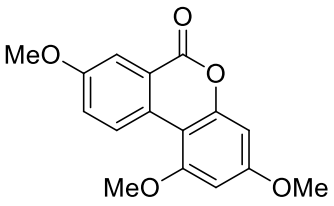
LSK-317
LSK-317

^{1}H NMR (500 MHz, DMSO-d_6)

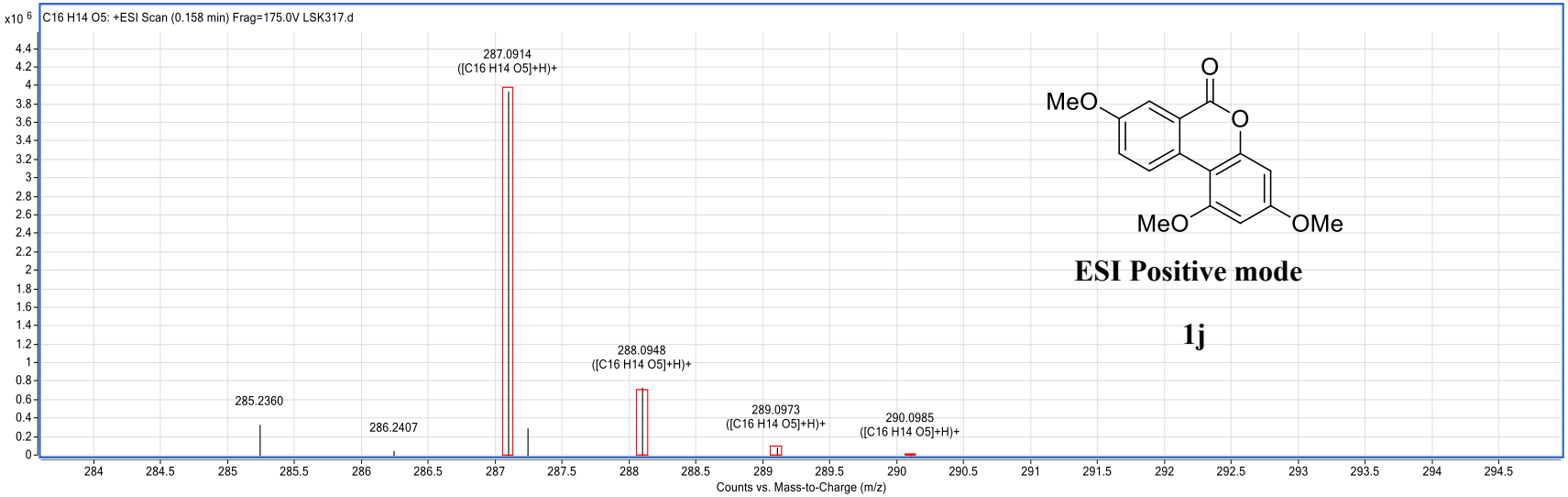


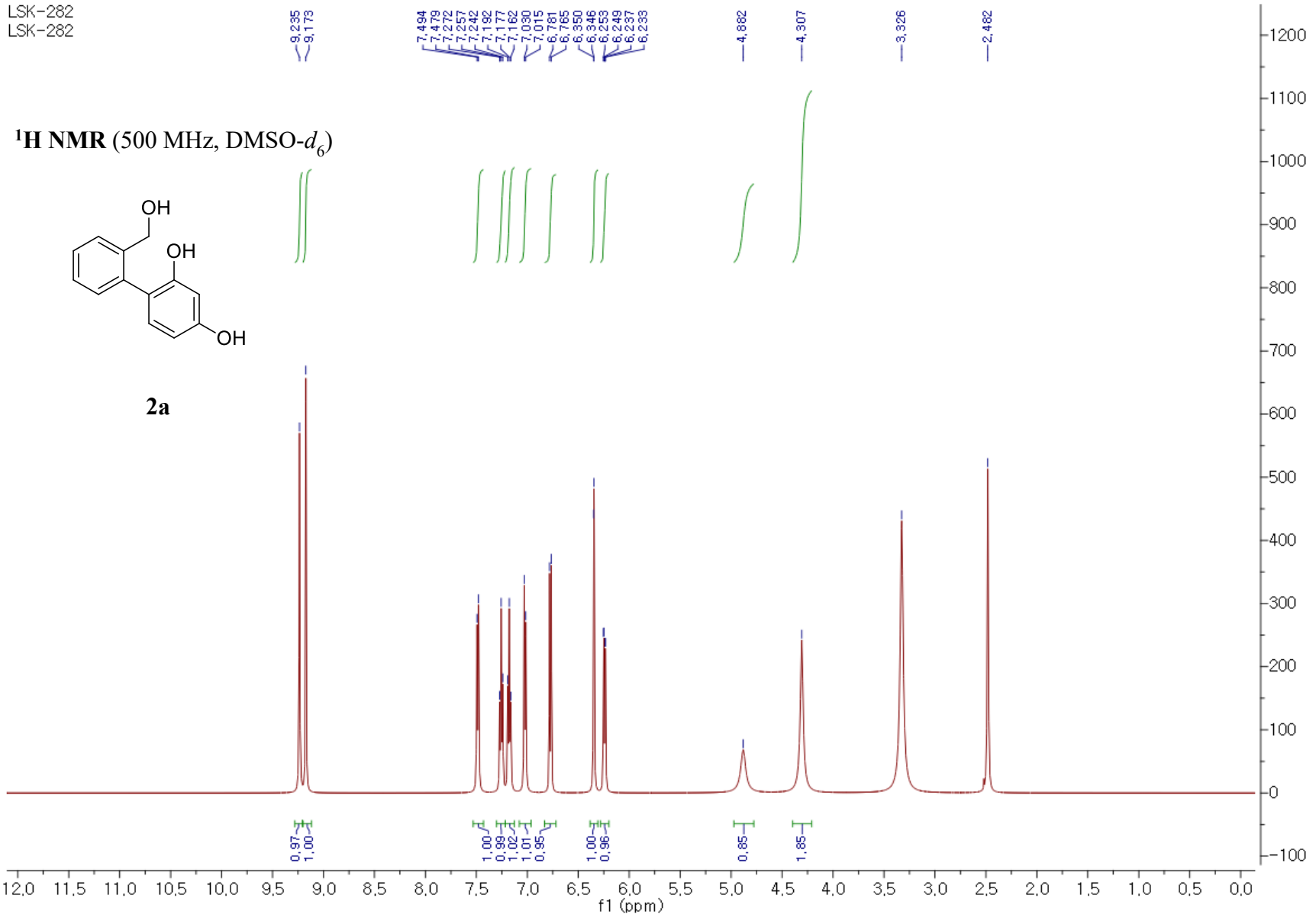
1j

^{13}C NMR (100 MHz, DMSO-d_6)



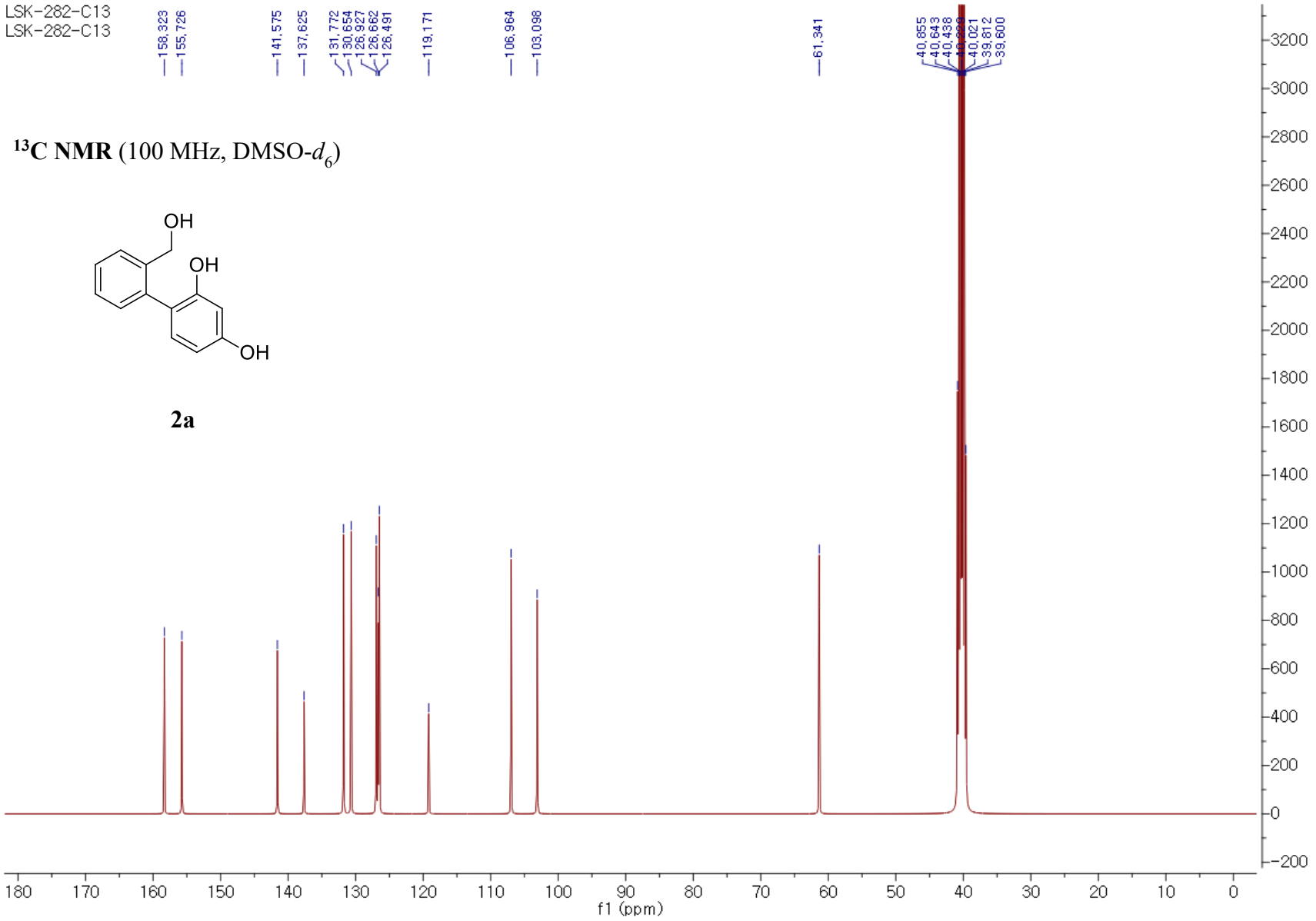
1j


x10 6
C16 H14 O5: +ESI Scan (0.158 min) Frag=175.0V LSK317.d
287.0914
([C16 H14 O5]+H)+
288.0948
([C16 H14 O5]+H)+
285.2360
286.2407
289.0973
([C16 H14 O5]+H)+
290.0985
([C16 H14 O5]+H)+
Counts vs. Mass-to-Charge (m/z)
MeO
O
O
MeO
OMe
ESI Positive mode
1j



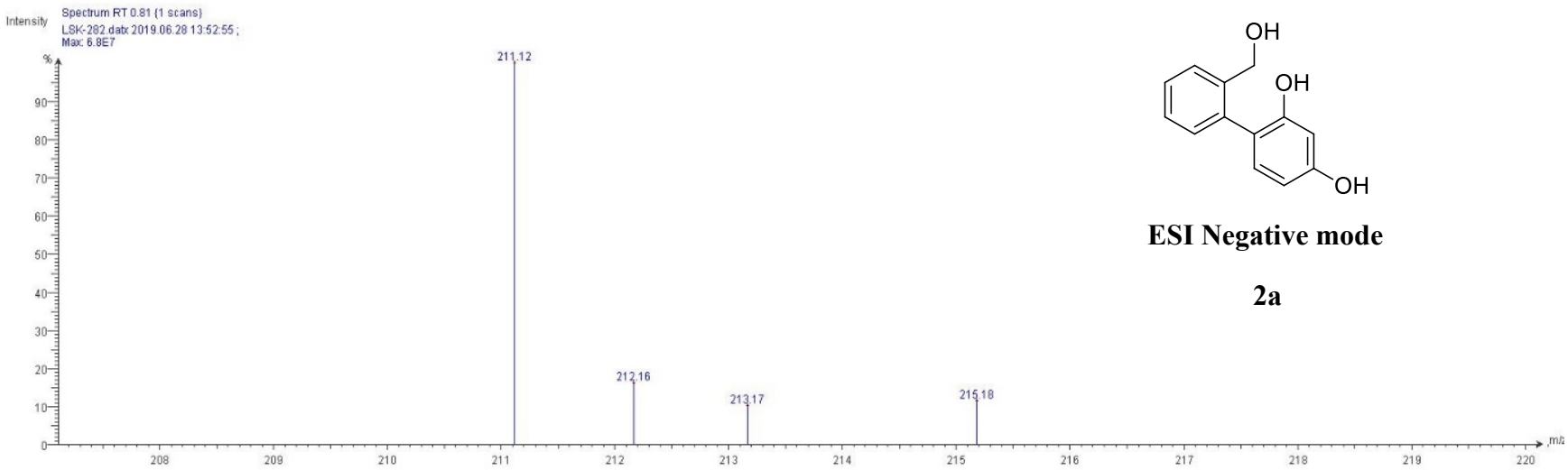
^{1}H NMR (500 MHz, DMSO-d_6)

2a



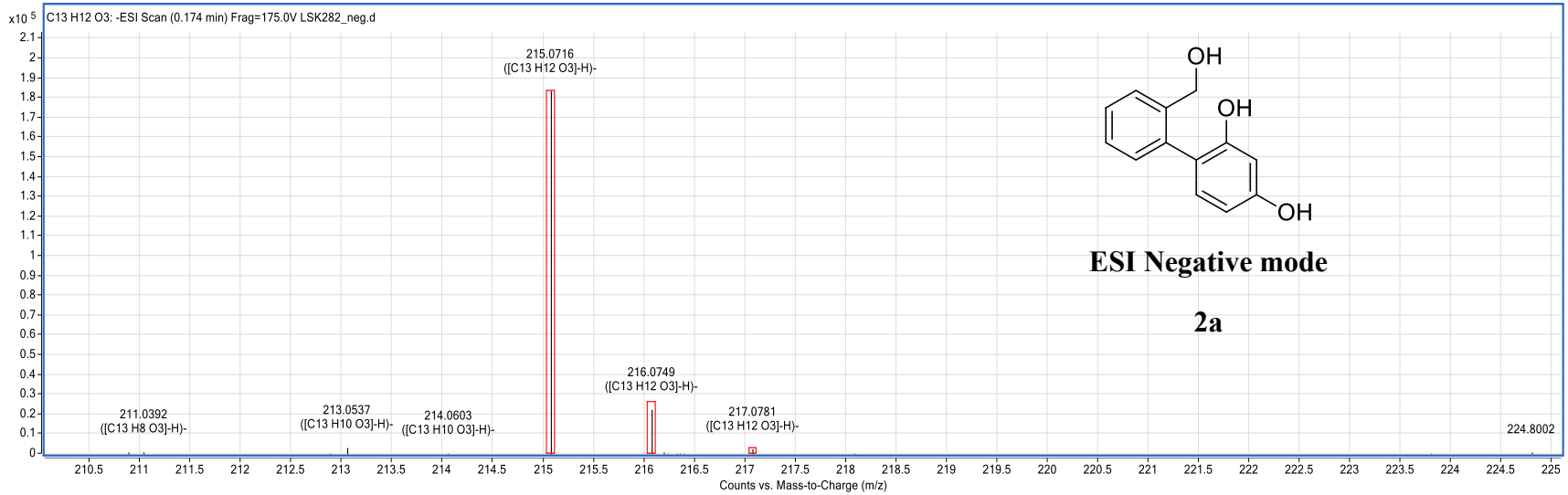
^{13}C NMR (100 MHz, DMSO-d_6)

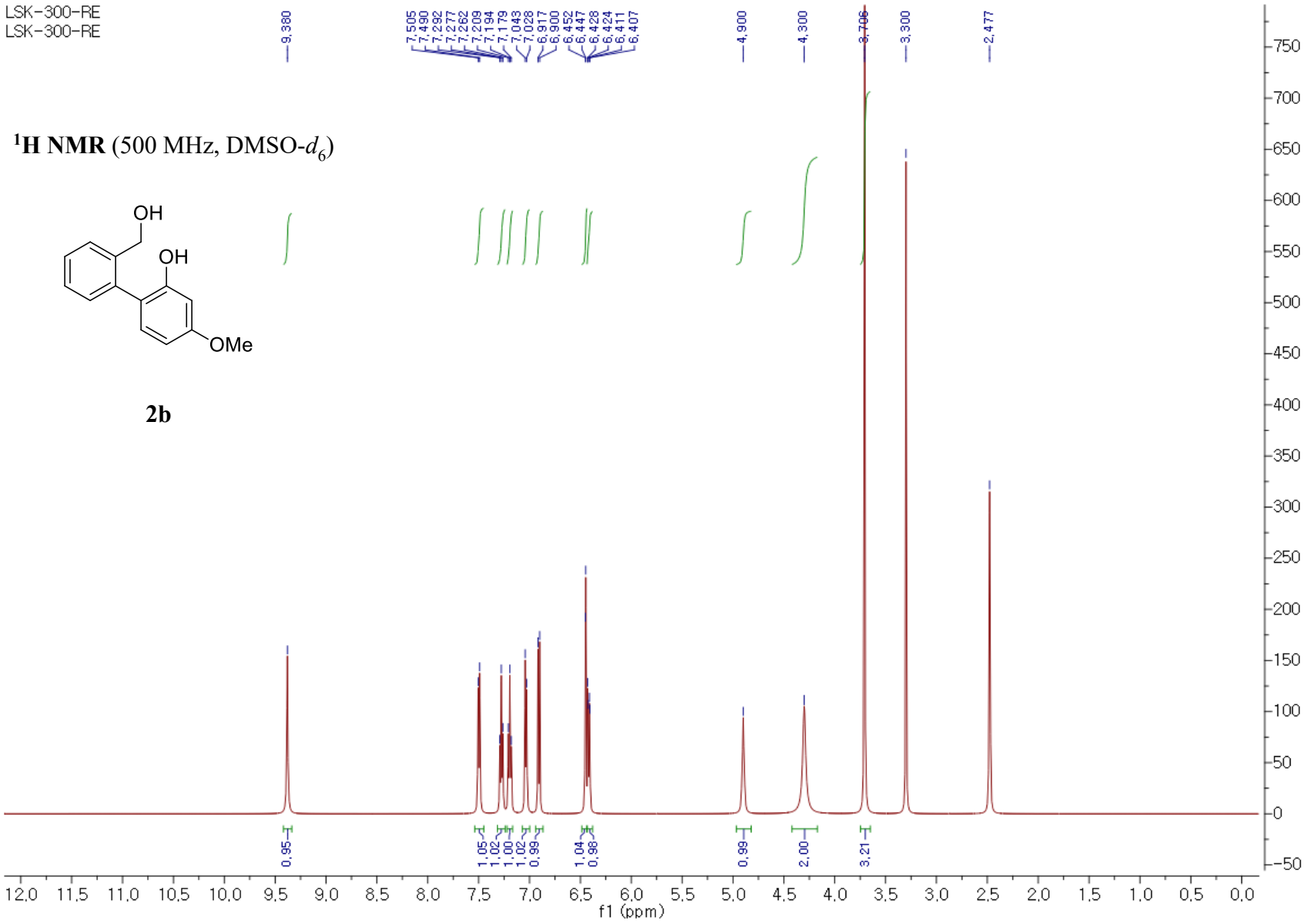
2a



ESI Negative mode

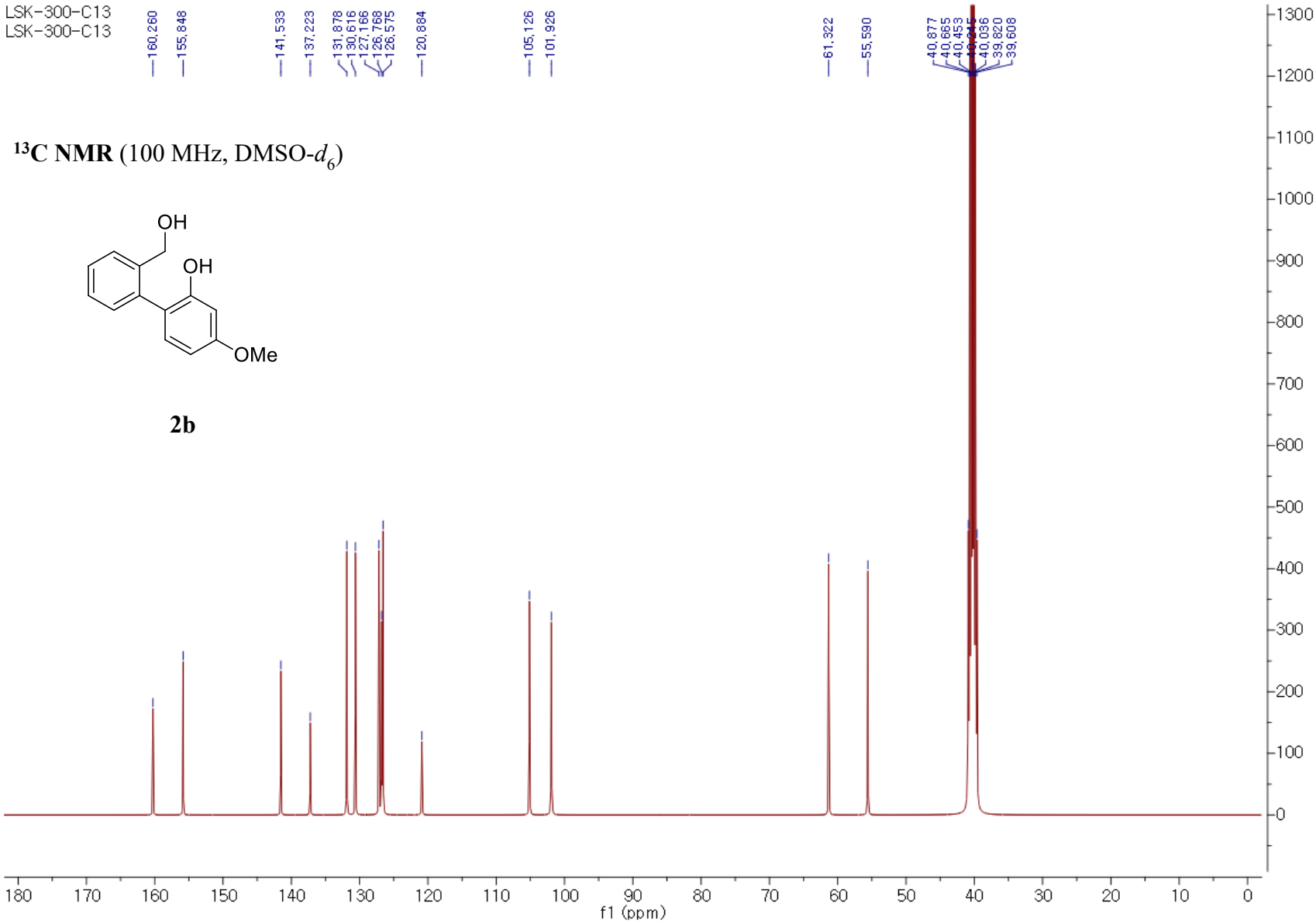
2a


x10 5
C13 H12 O3: -ESI Scan (0.174 min) Frag=175.0V LSK282_neg.d
215.0716
([C13 H12 O3]-H)-
216.0749
([C13 H12 O3]-H)-
211.0392
([C13 H8 O3]-H)-
213.0537
([C13 H10 O3]-H)-
214.0603
([C13 H10 O3]-H)-
217.0781
([C13 H12 O3]-H)-
224.8002
Counts vs. Mass-to-Charge (m/z)
OH
OH
OH
ESI Negative mode
2a



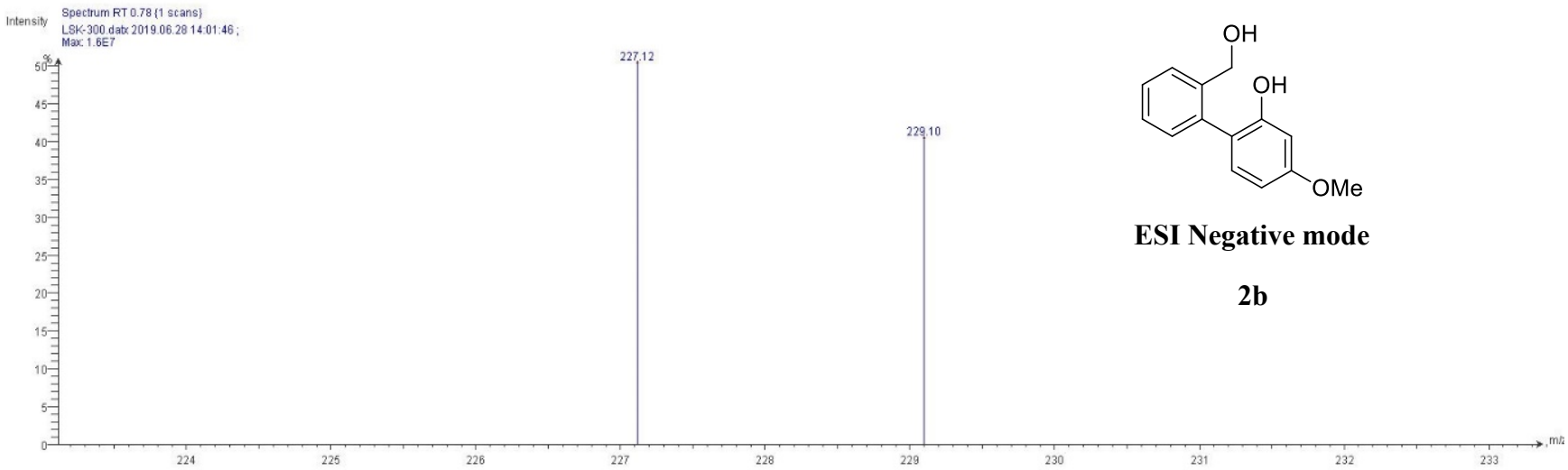
^{1}H NMR (500 MHz, DMSO-d_6)

2b



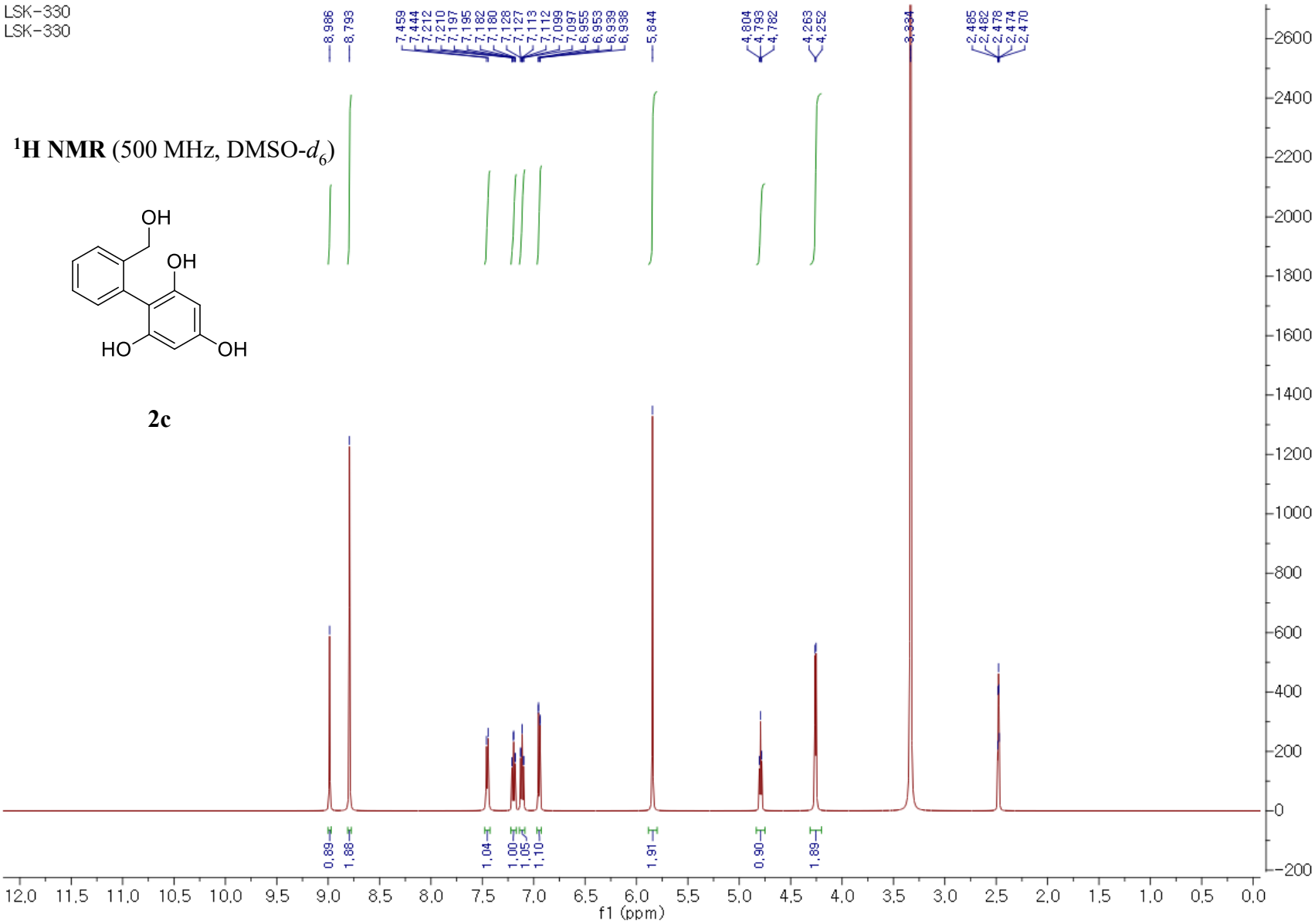
^{13}C NMR (100 MHz, DMSO-d_6)

2b



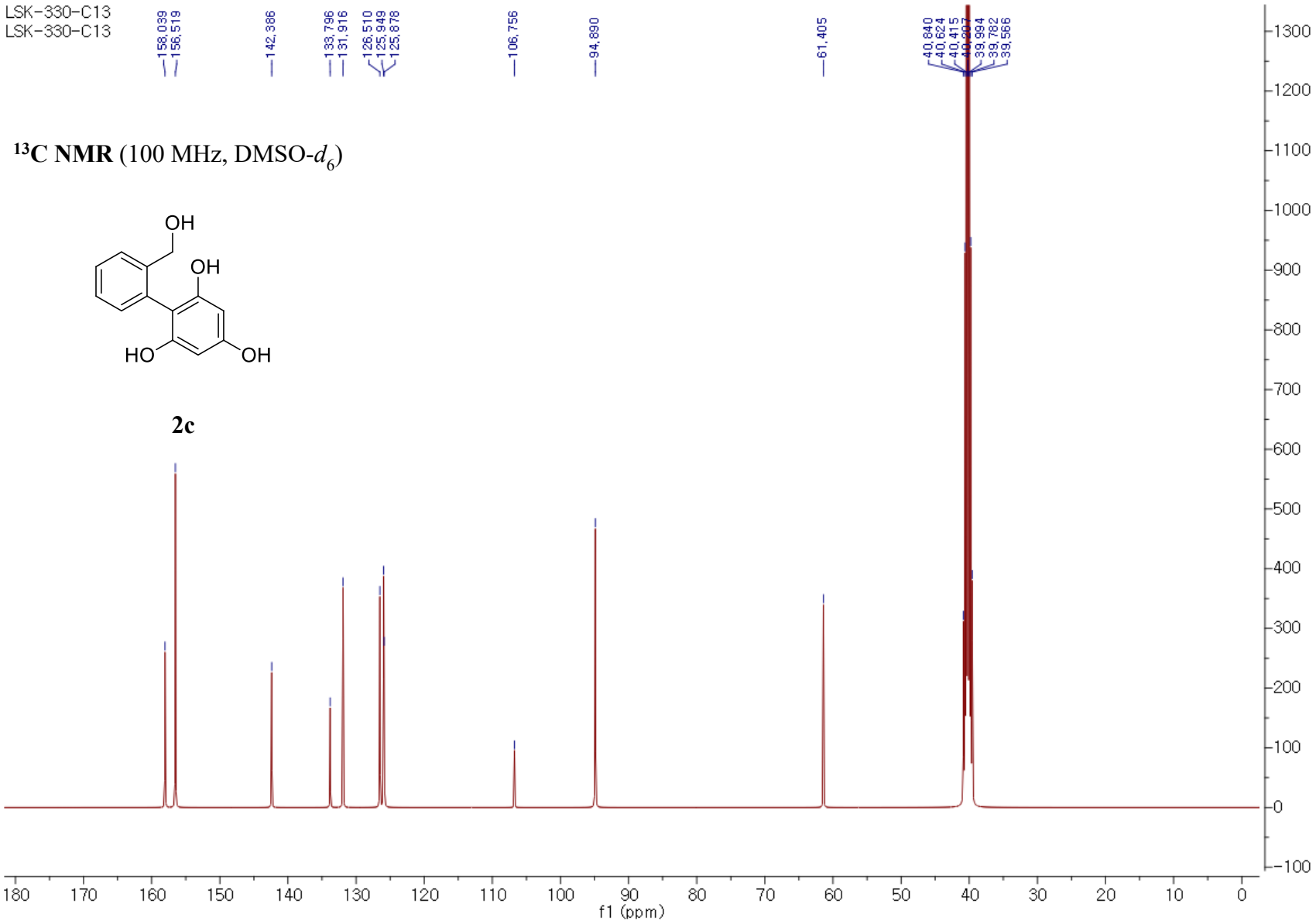
ESI Negative mode

2b



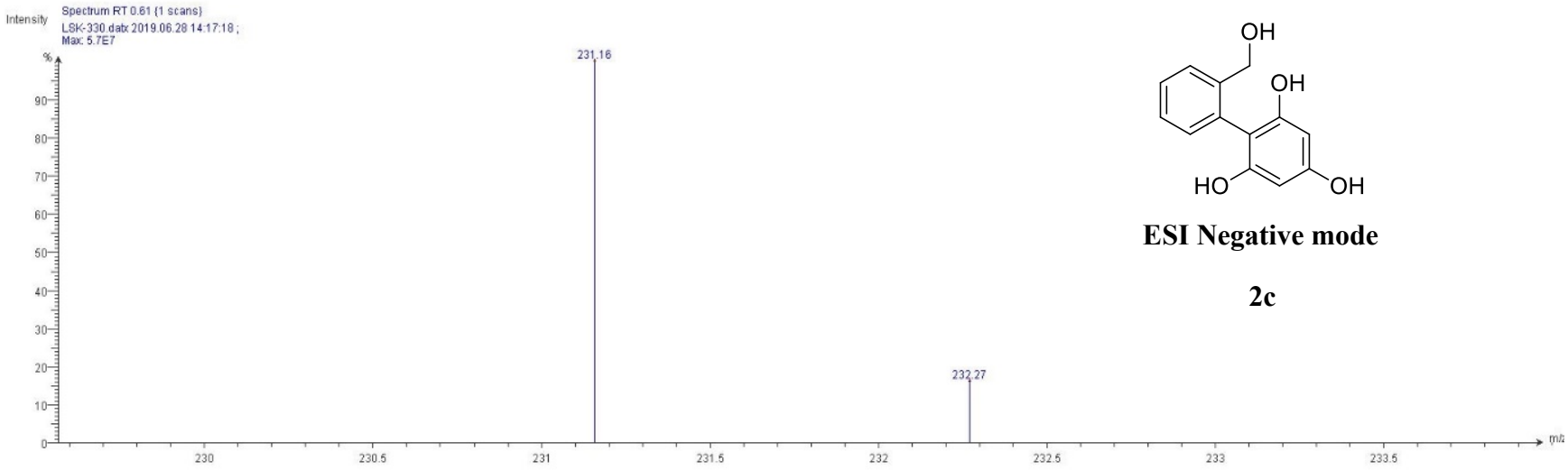
^{1}H NMR (500 MHz, DMSO-d_6)

2c



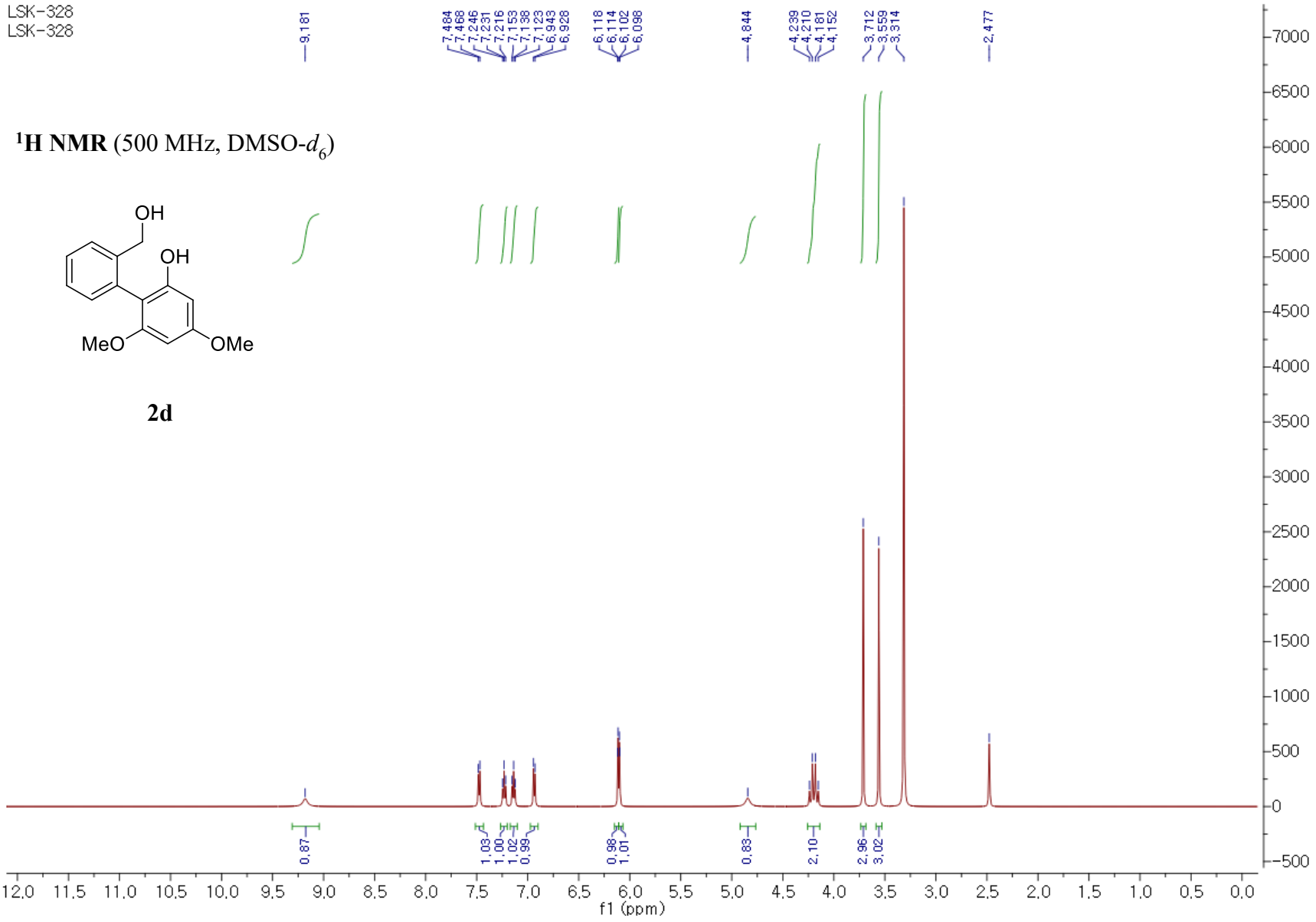
^{13}C NMR (100 MHz, DMSO-d_6)

2c



ESI Negative mode

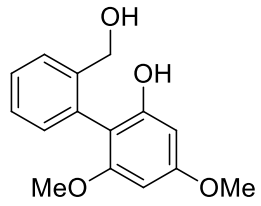
2c



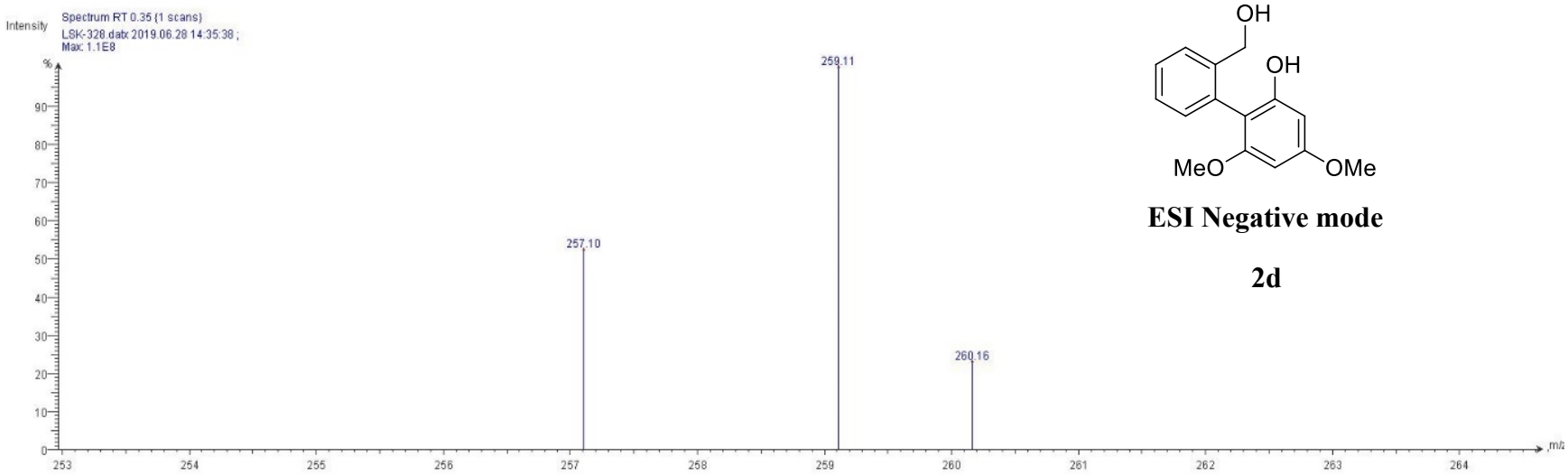
^{1}H NMR (500 MHz, DMSO-d_6)

2d

^{13}C NMR (100 MHz, DMSO-d_6)

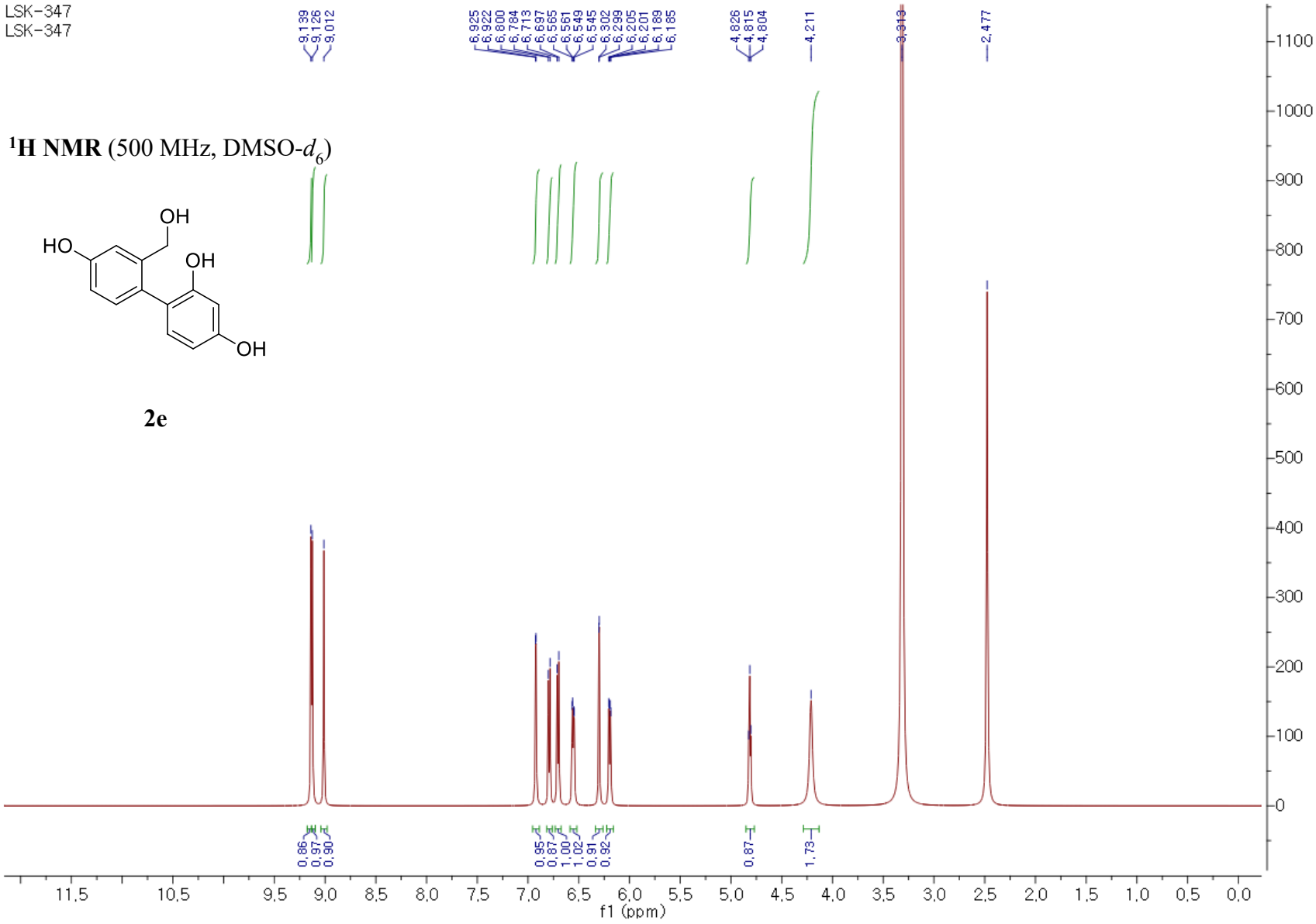


2d



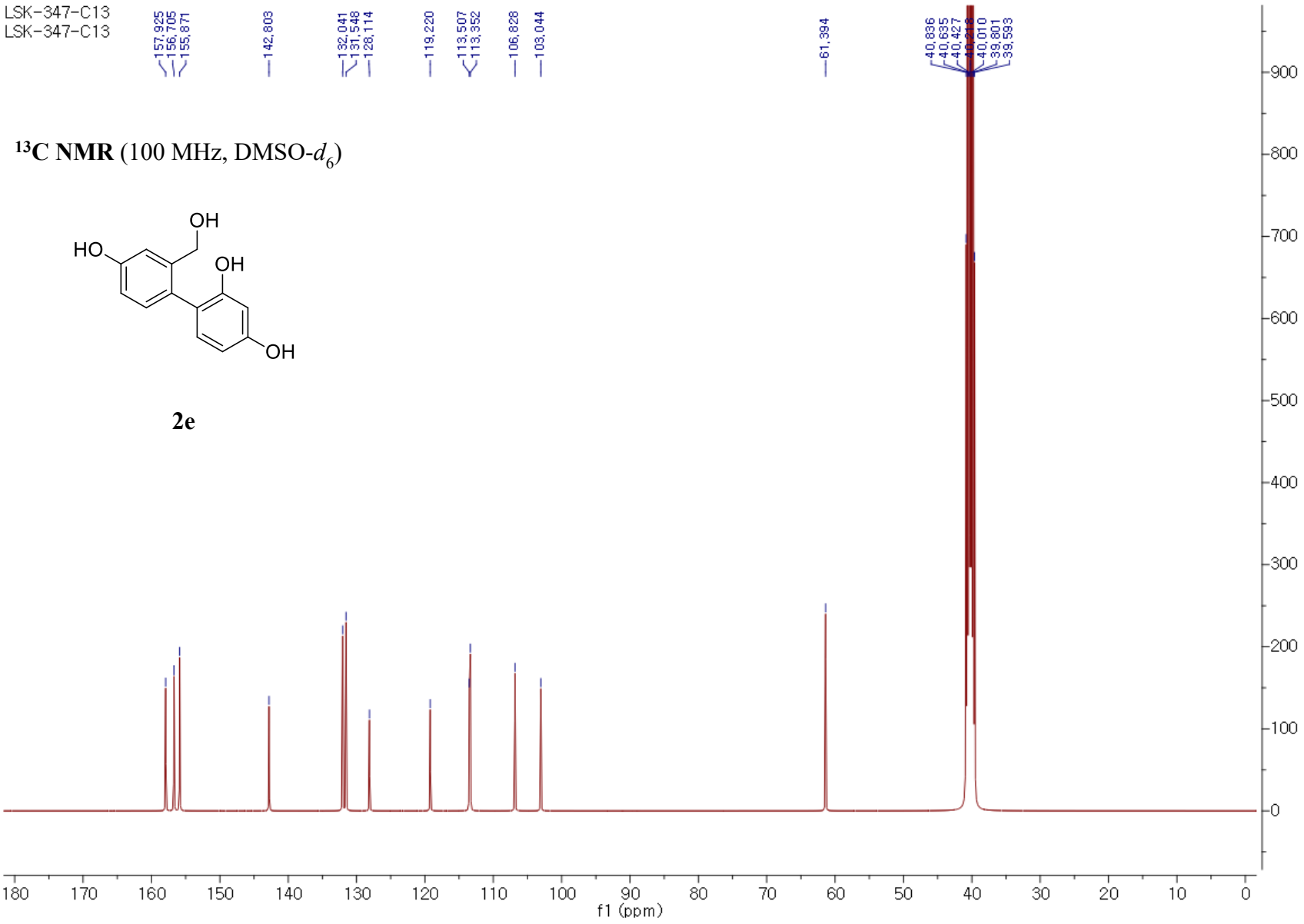
ESI Negative mode

2d



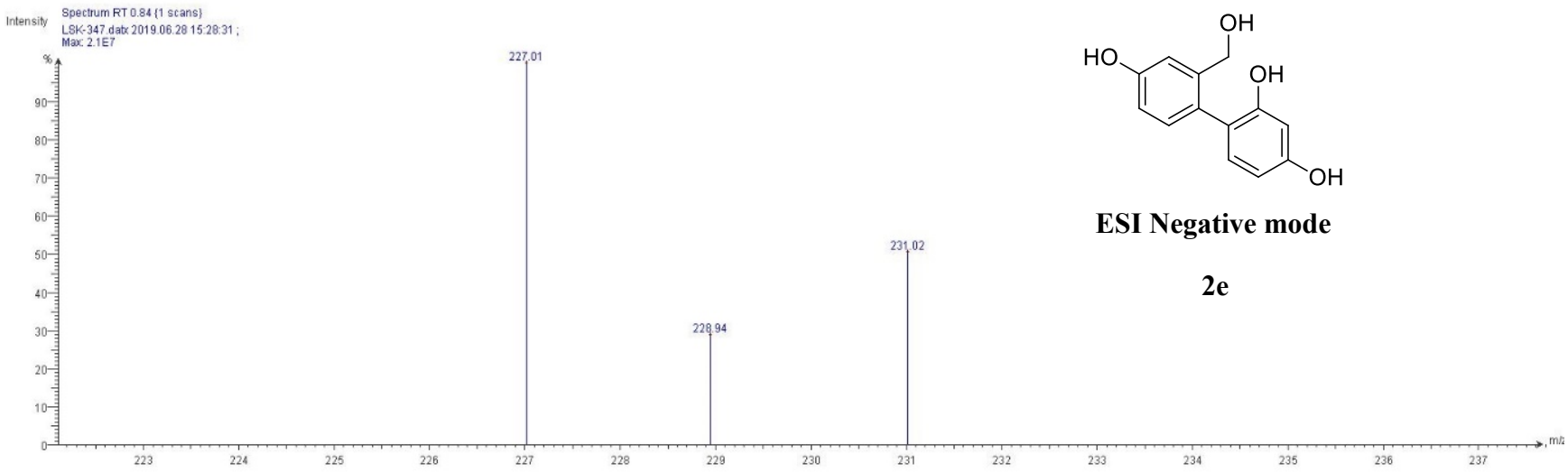
^{1}H NMR (500 MHz, DMSO-d_6)

2e



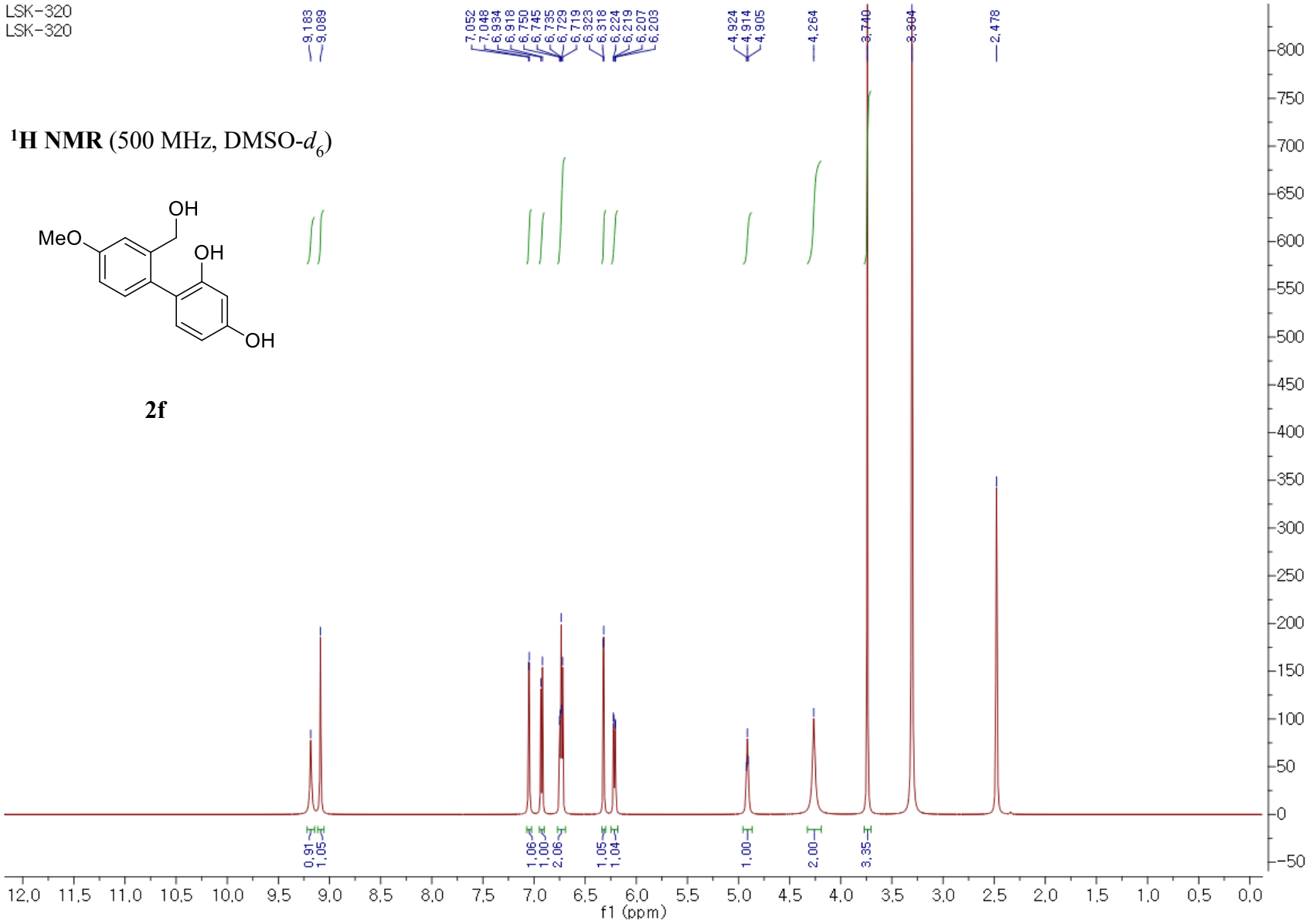
^{13}C NMR (100 MHz, DMSO-d_6)

2e



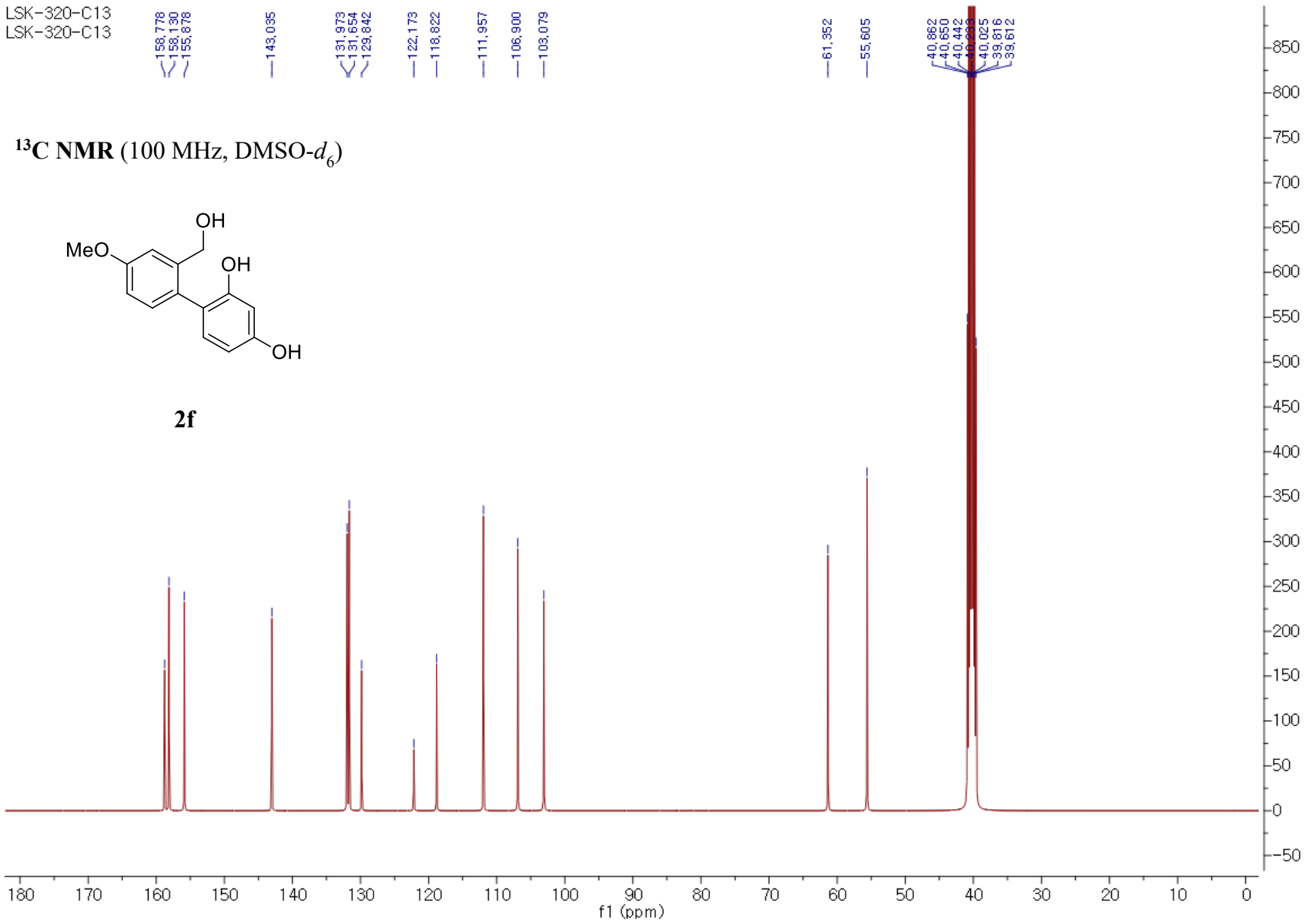
ESI Negative mode

2e



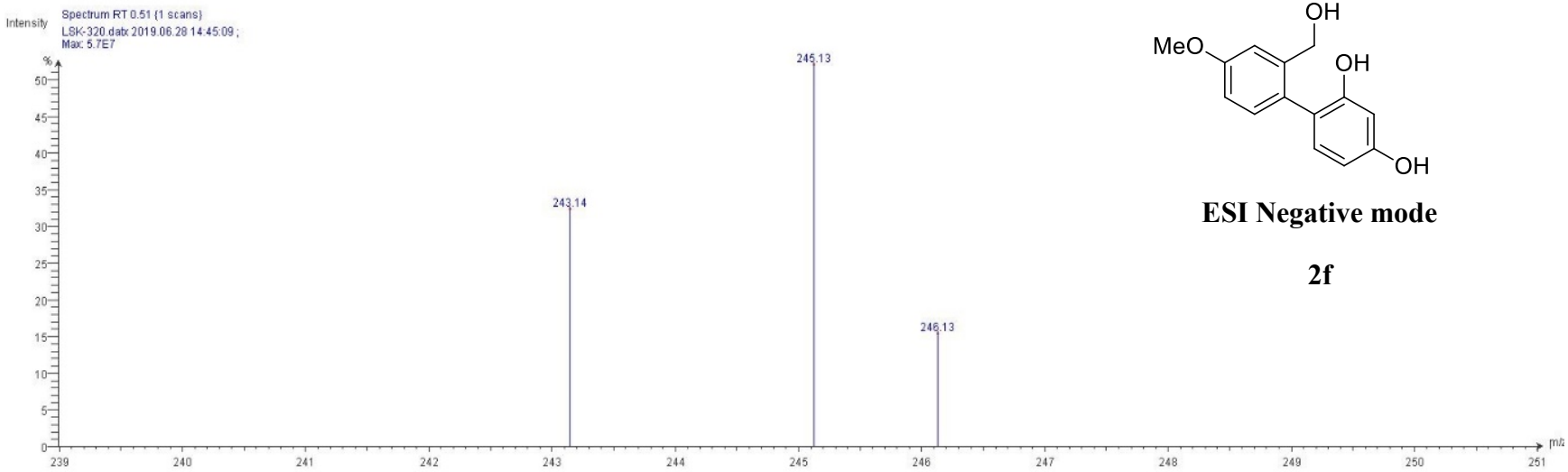
^{1}H NMR (500 MHz, DMSO-d_6)

2f



^{13}C NMR (100 MHz, DMSO-d_6)

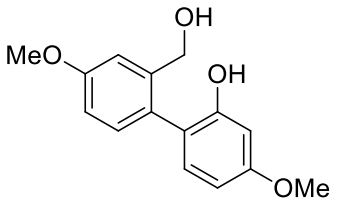
2f



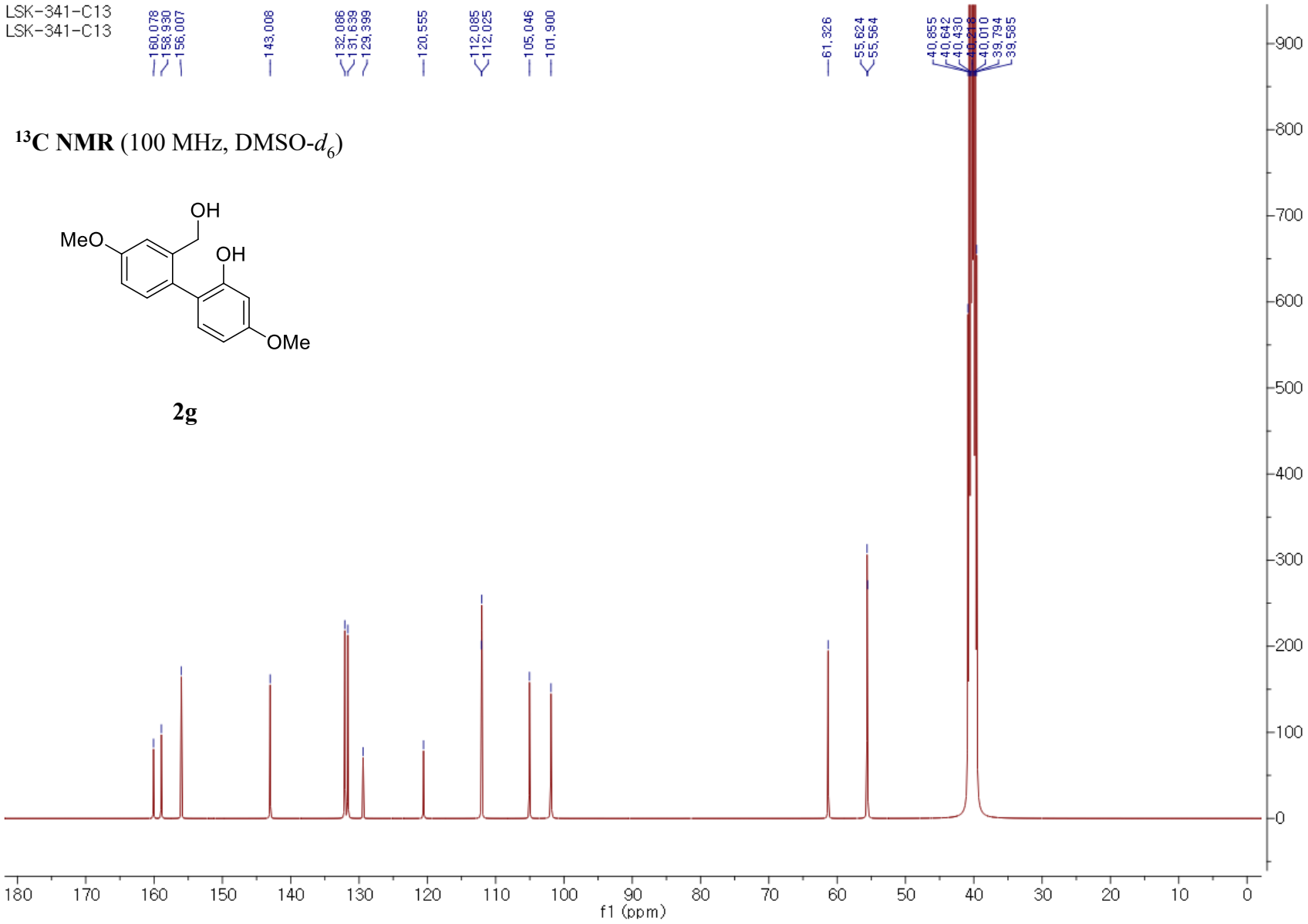
ESI Negative mode

2f

^{1}H NMR (500 MHz, DMSO-d_6)

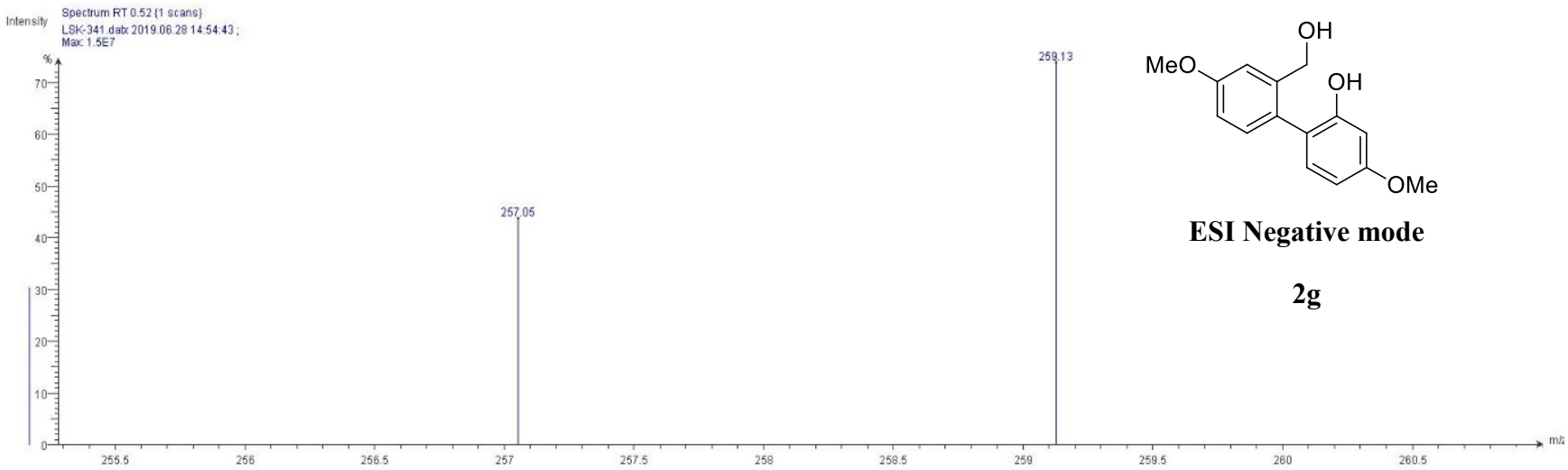


2g



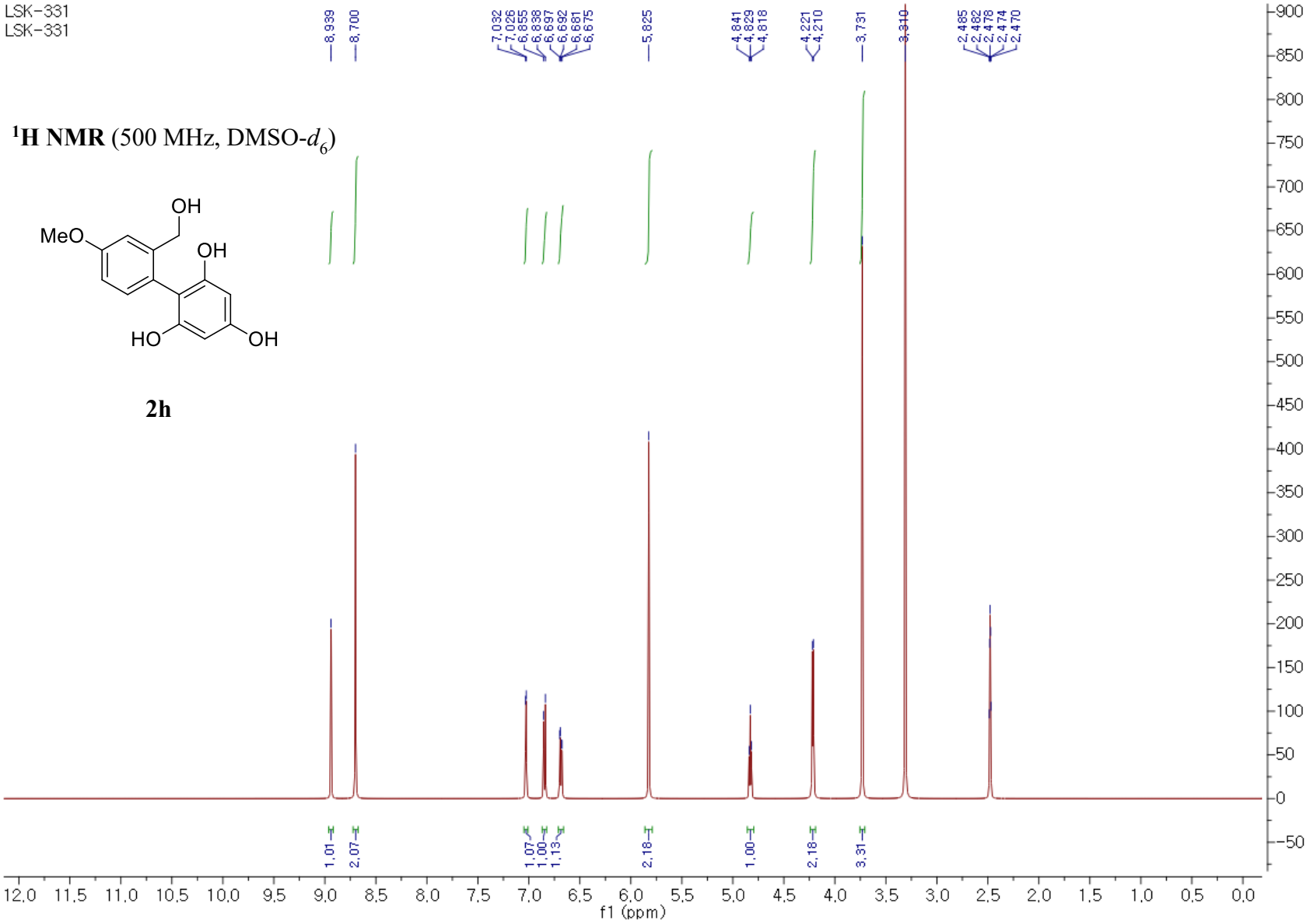
^{13}C NMR (100 MHz, DMSO-d_6)

2g

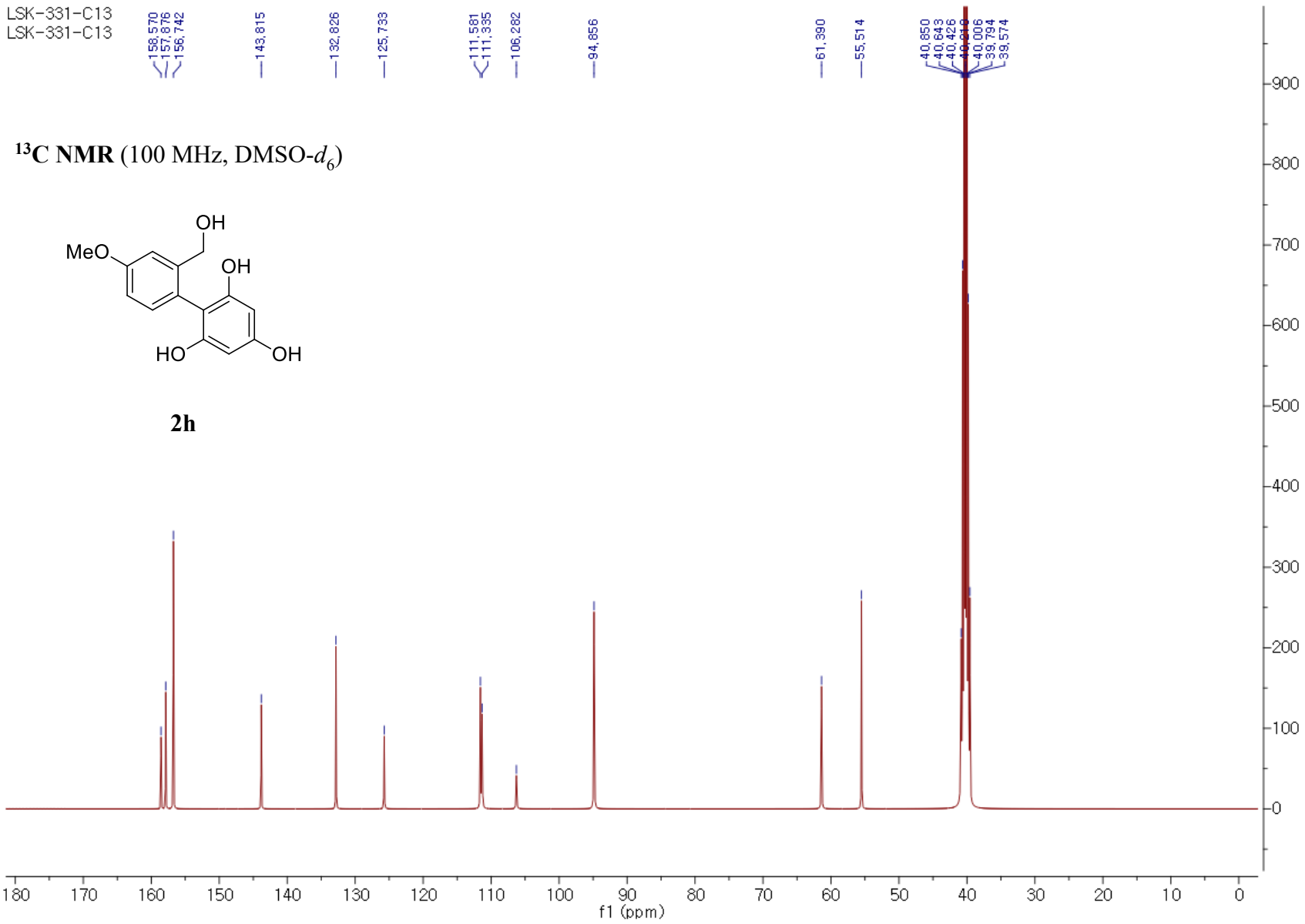


ESI Negative mode

2g

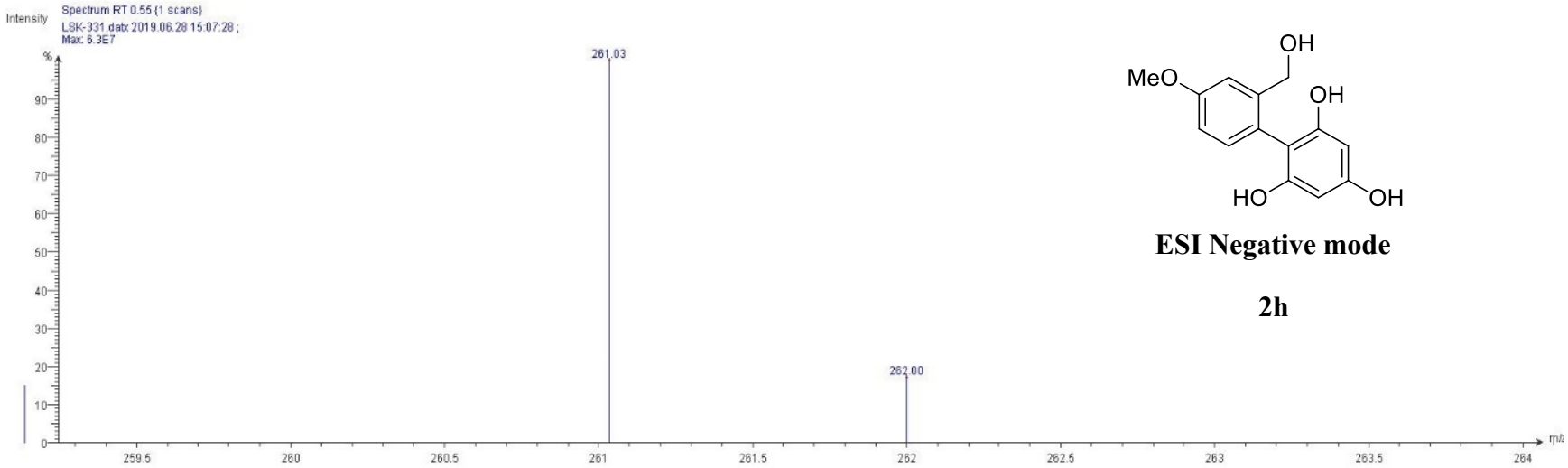


^{1}H NMR (500 MHz, DMSO-d_6)



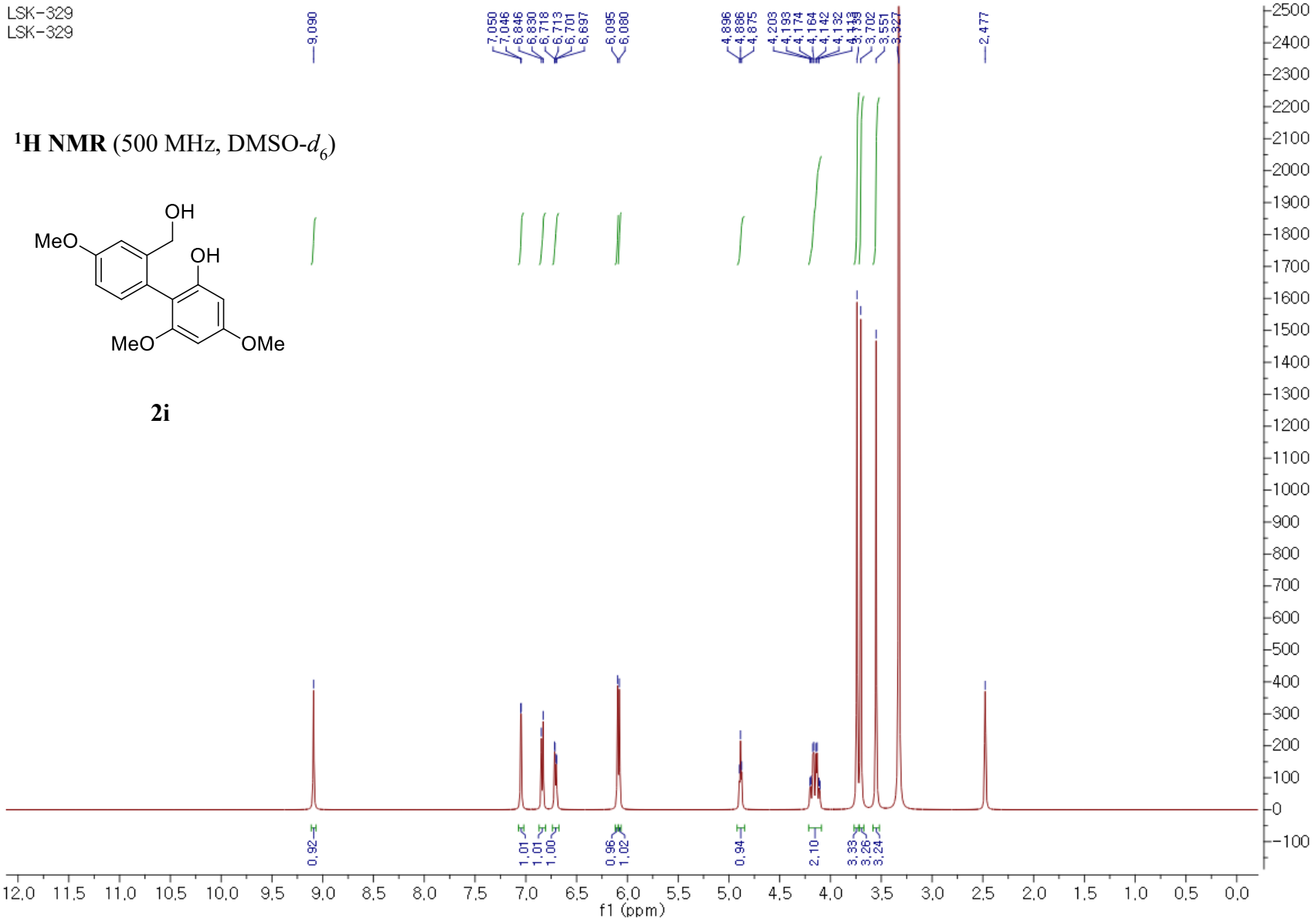
^{13}C NMR (100 MHz, DMSO-d_6)

2h



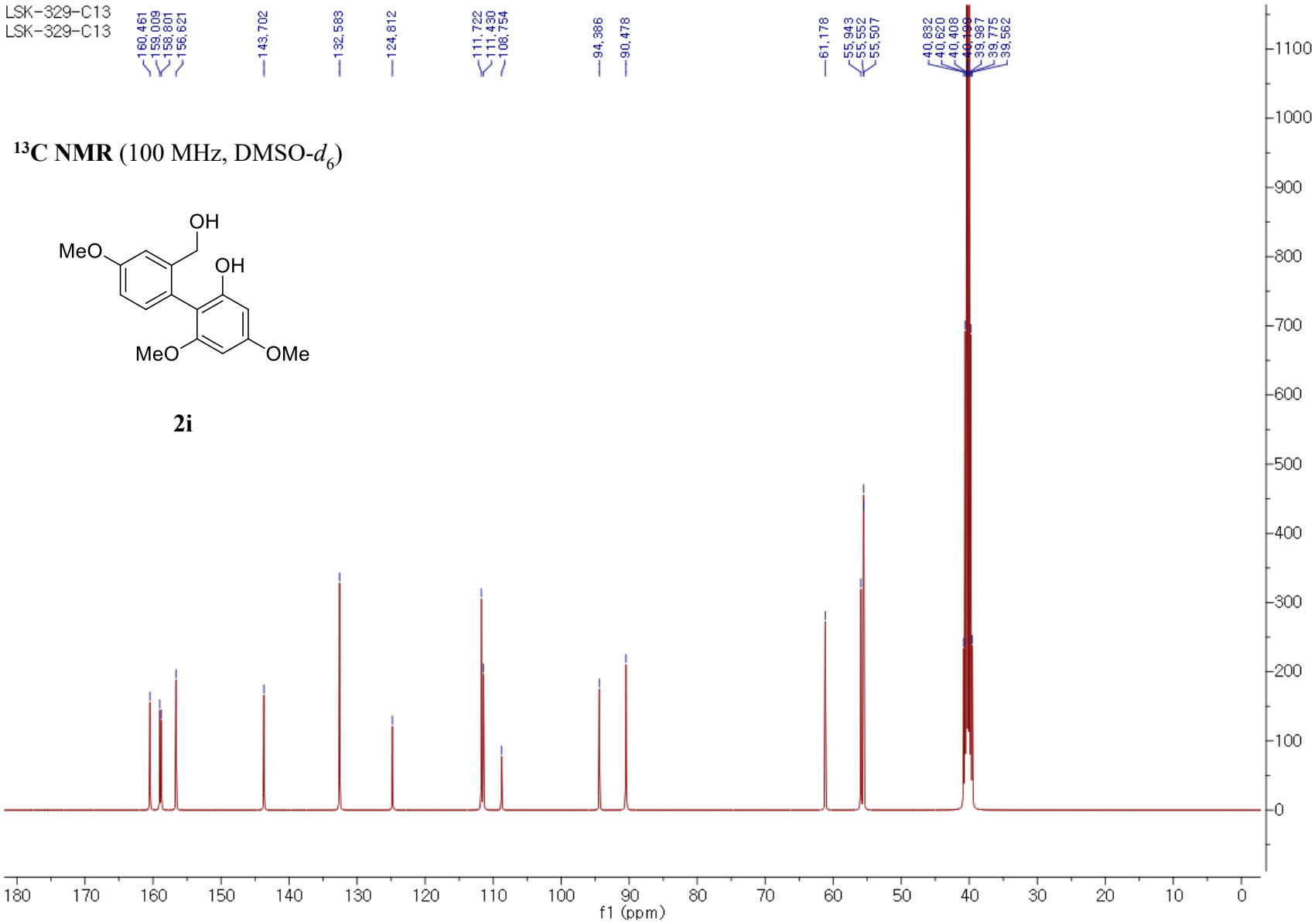
ESI Negative mode

2h



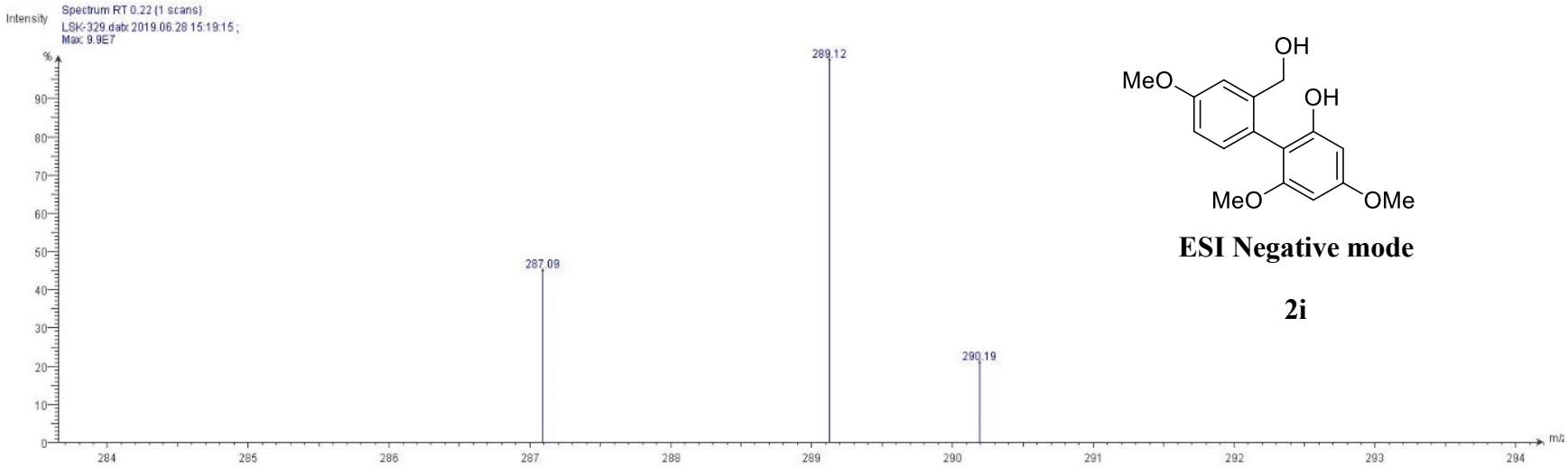
^{1}H NMR (500 MHz, DMSO-d_6)

2i



^{13}C NMR (100 MHz, DMSO-d_6)

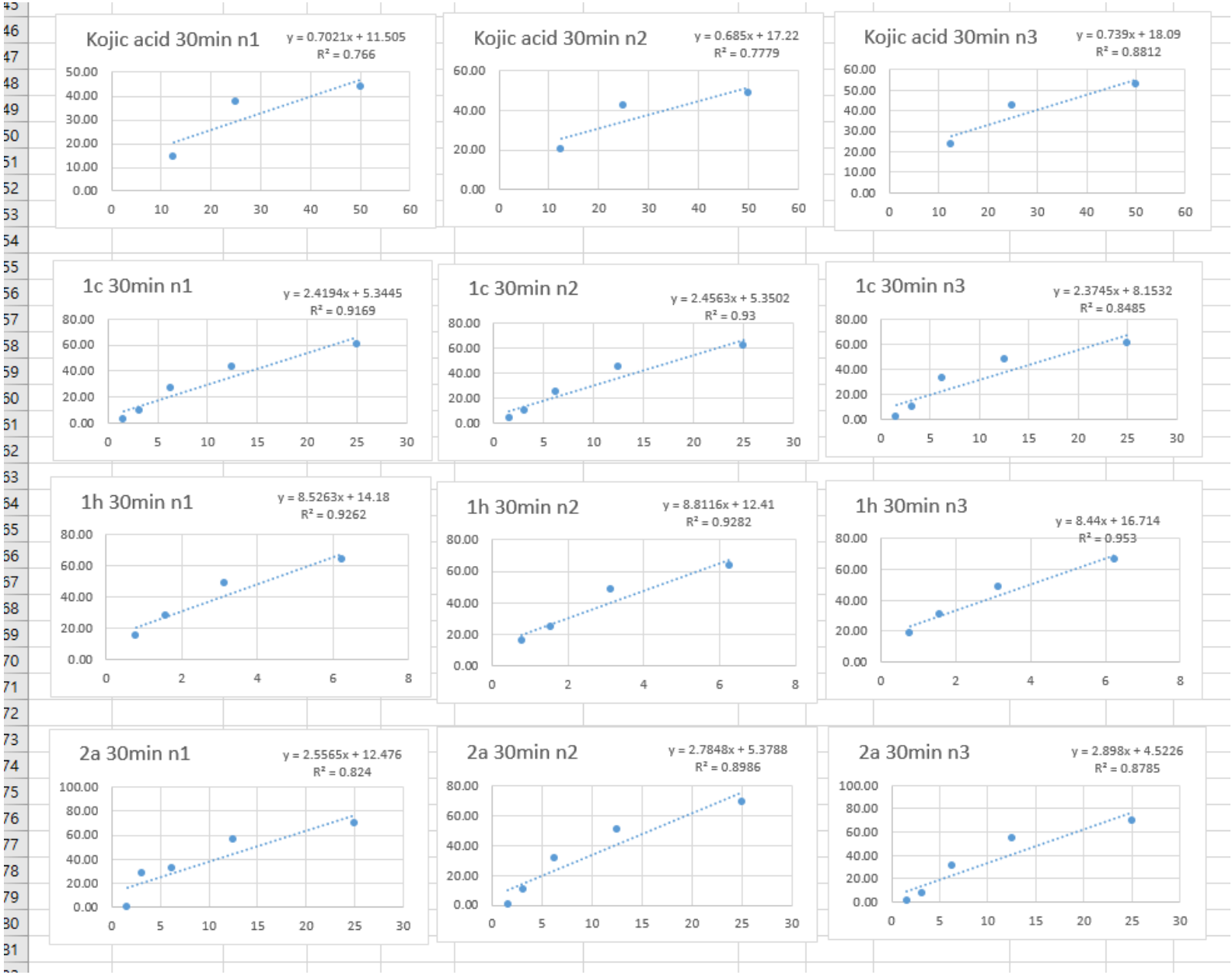
2i



ESI Negative mode

2i

	A	B	C	D	E	F	G	H	I	J	K	L	M	N	O	P
1	f.c (μM)		n1	n2	n3	Blank sample	②S-(SB F4)			③control average	④ activity(%) (②/③F4 *100)			activity aver.	stdev.	stdev/sqrt(count())
2	control		0.33	0.33	0.33	0.04	0.29	0.29	0.29	0.29	100.38	99.52	100.10	100.00	0.44	0.25
3	K.a	50	0.21	0.20	0.18	0.04	0.17	0.15	0.14		57.63	52.49	48.13	52.75	4.76	2.75
4		25	0.23	0.21	0.21	0.04	0.19	0.17	0.17		64.15	59.21	59.04	60.80	2.90	1.68
5		12.5	0.30	0.28	0.27	0.04	0.26	0.24	0.23		87.51	81.54	78.56	82.54	4.56	2.63
6	1c	25	0.15	0.15	0.15	0.04	0.11	0.11	0.11		39.11	38.15	39.11	38.79	0.55	0.32
7		12.5	0.21	0.20	0.19	0.04	0.16	0.16	0.15		56.26	54.82	51.63	54.24	2.37	1.37
8		6.25	0.25	0.26	0.24	0.04	0.21	0.22	0.20		72.69	74.92	66.90	71.50	4.14	2.39
9		3.125	0.30	0.30	0.30	0.04	0.26	0.26	0.26		90.63	90.39	89.16	90.06	0.79	0.46
10		1.5625	0.33	0.32	0.33	0.04	0.28	0.28	0.28		97.39	95.99	97.43	96.94	0.82	0.47
11	1h	6.25	0.15	0.15	0.14	0.04	0.11	0.11	0.10		36.02	36.05	33.21	35.09	1.63	0.94
12		3.125	0.19	0.19	0.19	0.04	0.15	0.15	0.15		51.29	51.29	51.08	51.22	0.12	0.07
13		1.5625	0.25	0.26	0.24	0.04	0.21	0.22	0.20		71.73	75.37	68.89	72.00	3.25	1.88
14		0.78125	0.29	0.29	0.28	0.04	0.25	0.25	0.24		84.32	84.39	81.06	83.26	1.90	1.10
15	2a	25	0.13	0.13	0.13	0.04	0.09	0.09	0.09		30.19	31.29	30.63	30.70	0.55	0.32
16		12.5	0.17	0.18	0.17	0.04	0.13	0.14	0.13		44.19	49.61	45.69	46.50	2.80	1.62
17		6.25	0.24	0.24	0.24	0.04	0.20	0.20	0.20		67.75	68.34	68.78	68.29	0.52	0.30
18		3.125	0.25	0.30	0.31	0.04	0.21	0.26	0.27		71.94	89.71	92.97	84.87	11.32	6.53
19		1.5625	0.33	0.33	0.33	0.04	0.29	0.29	0.29		99.73	99.28	98.94	99.31	0.40	0.23
20																
21			f.c (μM)	Inhibition (%)			inhibition (aver.)	IC50			IC50(aver)	stdev.	ev/sqrt(count())			
22		K.a	50	43.81	48.83	53.08	48.57	54.82	47.86	43.19	48.62	5.85	3.38			
23			25	37.46	42.27	42.44	40.72									
24			12.5	14.68	20.50	23.41	19.53									
25		1c	25	60.89	61.85	60.89	61.21	18.46	18.18	17.62	18.09	0.42	0.25			
26			12.5	43.74	45.18	48.37	45.76									
27			6.25	27.31	25.08	33.10	28.50									
28			3.125	9.37	9.61	10.84	9.94									
29			1.5625	2.61	4.01	2.57	3.06									
30		1h	6.25	63.98	63.95	66.79	64.91	4.20	4.27	3.94	4.14	0.17	0.10			
31			3.125	48.71	48.71	48.92	48.78									
32			1.5625	28.27	24.63	31.11										
33			0.78125	15.68	15.61	18.94	16.74									
34		2a	25	69.81	68.71	69.37	69.30	14.68	16.02	15.69	15.46	0.70	0.40			
35			12.5	55.81	50.39	54.31	53.50									
36			6.25	32.25	31.66	31.22	31.71									
37			3.125	28.06	10.29	7.03	15.13									
38			1.5625	0.27	0.72	1.06	0.69									
39																


Kojic acid 30min n1
y = 0.7021x + 11.505
R² = 0.766
Kojic acid 30min n2
y = 0.685x + 17.22
R² = 0.7779
Kojic acid 30min n3
y = 0.739x + 18.09
R² = 0.8812
1c 30min n1
y = 2.4194x + 5.3445
R² = 0.9169
1c 30min n2
y = 2.4563x + 5.3502
R² = 0.93
1c 30min n3
y = 2.3745x + 8.1532
R² = 0.8485
1h 30min n1
y = 8.5263x + 14.18
R² = 0.9262
1h 30min n2
y = 8.8116x + 12.41
R² = 0.9282
1h 30min n3
y = 8.44x + 16.714
R² = 0.953
2a 30min n1
y = 2.5565x + 12.476
R² = 0.824
2a 30min n2
y = 2.7848x + 5.3788
R² = 0.8986
2a 30min n3
y = 2.898x + 4.5226
R² = 0.8785