

Supporting Information

A Series of new Pyrrole Alkaloids with ALR2 Inhibitory Activities from the Sponge

Styliissa massa

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Table S1. ^{13}C (125 MHz) NMR Data for **1–5** and **13–14** acquired in DMSO-*d*₆.

no.	1	2	3	4	5	13	14
	δ_{C} , type						
2	104.3, C	122.7, CH	122.0, CH	122.6, CH	122.4, CH	122.6, CH	120.4, CH
3	108.5, CH	110.0, CH	110.2, CH	107.2, CH	110.4, CH	109.6, CH	112.6, CH
4	123.3, C	117.8, C	118.7, C	121.9, C	120.4, C	120.4, C	118.6, C
5	127.9, C	126.5, C	125.3, C	123.6, C	126.6, C	126.6, C	126.1, C
6	162.1, C	162.9, C	163.3, C	163.4, C	163.0, C	163.0, C	163.9, C
8	37.4, CH ₂	45.4, CH ₂	45.6, CH ₂	39.9, CH ₂	39.0, CH ₂	39.1, CH ₂	38.3, CH ₂
9	125.0, CH	62.8, CH	63.4, CH	126.7, CH	31.5, CH ₂	31.4, CH ₂	36.6, CH ₂
10	133.6, C	132.0, C	125.7, C	105.8, C	132.0, C	129.6, C	130.5, C
11	57.2, CH	122.4, C	124.7, C	53.3, CH	122.4, C	121.0, C	122.3, C
12	170.5, C	163.9, C	165.2, C	171.2, C	163.0, C	164.4, C	161.2, C
14	156.4, C	155.4, C	154.4, C	152.3, C	154.7, C	154.9, C	153.4, C

Table S2. ^1H (500 MHz) NMR Data for **1–5** and **13–14** acquired in DMSO-*d*₆.

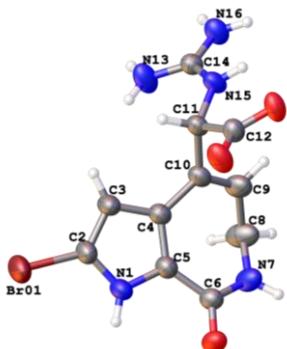
no.	1	2	3	4	5	13	14
	δ_{H} (<i>J</i> in Hz)						
1-NH	12.71, brs	12.05, brs	11.75, brs	11.79, s	12.05, brs	12.10, brs	11.90, brs
2		7.09, t (2.8)	6.96, t (2.8)	7.00, t (3.5)	7.09, t (2.3)	7.13, t (2.4)	6.91, t (2.3)
3	6.36, d (2.3)	6.45, t (2.4)	6.43, t (2.5)	6.44, t (3.1)	6.71, m	6.50, t (2.4)	6.79, t (2.2)
4							
5							
6							
7-NH	7.79, t (4.7)	7.75, dd (5.5, 3.9)	7.59, t (4.3)	7.83, t (5.0)	8.03, t (4.5)	8.05, t (4.3)	7.98, t (4.3)
8	3.42, m	3.29, m; 3.24, dq (14.3, 2.1)	3.26, m; 3.19, m	3.69, 3.60, dd (15.5, 5.0)	3.28, m	3.28, m	3.26, q (4.5)
9	6.04, t (6.8)	5.80, dd (7.4, 2.0)	5.83, d (6.6)		3.34, m	3.28, m	2.85, q (4.5)
10							
11	5.21, d (8.5)			4.97, d (3.6)			
12							
13-NH			11.16, s				
14							
15-NH	7.80, d (8.3)		9.45, s	8.90, brs			
16-NH				8.12, brs			9.23, brs
13-NMe					3.11, s		
9-OH			4.99, brs	10.89, brs			

Table S3. ^{13}C (125 MHz) NMR Data for **6-12** acquired in DMSO- d_6 .

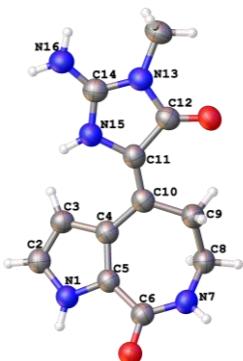
no.	6	7	8	9	10	11	12
	δ_{C} , type						
2	89.7, C	121.5, CH	103.6, C	104.0, C	167.0, C	166.0, C	167.0, C
3	144.2, CH	110.0, CH	112.1, CH	111.2, CH	121.2, C	120.5, C	121.4, C
4	120.3, C	122.6, C	123.7, C	121.3, C	144.5, CH	145.9, CH	144.4, CH
5	163.1, C	122.7, C	124.9, C	127.9, C	92.0, C	91.9, C	91.9, C
6	63.9, CH	163.1, C	162.0, C	162.2, C	167.5, C	74.1, CH ₂	165.5, C
8	156.4, C	38.6, CH ₂	38.4, CH ₂	37.4, CH ₂			35.3, CH ₂
9		30.4, CH ₂	30.3, CH ₂	134.3, CH			33.2, CH ₂
10	81.3, C	43.8, CH	43.4, CH	130.3, CH			171.6, C
11	39.5, CH ₂	175.0, C	173.6, C	166.0, C			
12	19.7, CH ₂						
13	45.0, CH ₂						
15	161.9, C						
2-OMe	50.6, CH ₃						
5-OMe					51.1, CH ₃	49.7, CH ₃	51.0, CH ₃
6-OMe						59.1, CH ₃	
10-OMe							51.4, CH ₃
11-OMe			52.0, CH ₃	52.1, CH ₃			

Table S4. ^1H (500 MHz) NMR Data for **6-12** acquired in DMSO- d_6 .

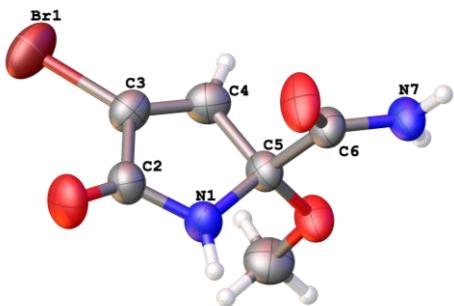
no.	6	7	8	9	10	11	12
	δ_{H} (<i>J</i> in Hz)						
1-NH		11.17, brs	12.05, brs		9.07, brs	8.81, brs	9.13, brs
2		6.83, t (2.7)					
3	7.79, s	6.06, t (2.4)	6.06, s	6.54, s			
4					7.35, s	7.32, d (1.6)	7.31, d (0.9)
5							
6	5.80, s					3.56, 3.42, d (10.0)	
7-NH	9.53, brs	7.65, brs	7.80, t (4.5)	7.83, t (4.9)	7.64, d (15.8)		8.31, t (5.9)
8		3.27, m;	3.22, m; 3.14, m	3.50, dd (6.8, 5.3)			3.33, m
9	9.88, brs	2.08, q (6.0)	2.08, q (6.2)	6.91, t (7.0)			2.51, m
10		3.79, t (6.3)	3.92, t (6.6)				
11	2.25, m						
12	1.98, m						
13	3.47, tt (8.0, 2.7);						
14							
15							
16-NH	8.23, brs						
2-OMe	3.15, s						
5-OMe					3.17, s	3.07, s	3.18, s
6-OMe						3.27, s	
10-OMe							3.59, s
11-OMe			3.64, s	3.75, s			

Table S5. X-ray diffraction analysis of compound **1**.

Empirical formula	C ₁₃ H ₁₈ BrN ₅ O ₄
Formula weight	388.23
Temperature/K	298
Crystal system	monoclinic
Space group	P21/n
a/Å	9.0283(3)
b/Å	15.5478(3)
c/Å	11.7424(3)
α/°	90
β/°	90.939(2)
γ/°	90
Volume/Å ³	1648.06(8)
Z	4
ρ _{calcg/cm³}	1.565
μ/mm ⁻¹	3.656
F(000)	792.0
Crystal size/mm ³	0.2 × 0.1 × 0.1
Radiation	CuKα ($\lambda = 1.54184$)
2Θ range for data collection/°	9.44 to 152.61
Index ranges	-11 ≤ h ≤ 9, -19 ≤ k ≤ 18, -14 ≤ l ≤ 14
Reflections collected	11402
Independent reflections	3322 [R _{int} = 0.0858, R _{sigma} = 0.0906]
Data/restraints/parameters	3322/0/210
Goodness-of-fit on F ²	1.077
Final R indexes [I>=2σ(I)]	R1 = 0.0556, wR2 = 0.1518
Final R indexes [all data]	R1 = 0.0886, wR2 = 0.1736
Largest diff. peak/hole / e Å ⁻³	0.55/-0.79

Table S6. X-ray diffraction analysis of compound **5**.

Empirical formula	C ₁₄ H ₁₆ F ₃ N ₅ O ₅
Formula weight	391.32
Temperature/K	150.0
Crystal system	monoclinic
Space group	P21/n
a/Å	20.7232(6)
b/Å	8.2740(2)
c/Å	20.9101(6)
α/°	90
β/°	117.162(2)
γ/°	90
Volume/Å ³	3189.93(16)
Z	8
ρ _{calcg} /cm ³	1.630
μ/mm ⁻¹	1.291
F(000)	1616.0
Crystal size/mm ³	0.2 × 0.15 × 0.1
Radiation	CuKα (λ = 1.54178)
2Θ range for data collection/°	4.974 to 144.002
Index ranges	-25 ≤ h ≤ 25, -10 ≤ k ≤ 9, -25 ≤ l ≤ 25
Reflections collected	26228
Independent reflections	6243 [R _{int} = 0.0421, R _{sigma} = 0.0301]
Data/restraints/parameters	6243/2/495
Goodness-of-fit on F ²	1.049
Final R indexes [I>=2σ (I)]	R1 = 0.0781, wR2 = 0.2177
Final R indexes [all data]	R1 = 0.0866, wR2 = 0.2296
Largest diff. peak/hole / e Å ⁻³	0.80/-0.51

Table S7. X-ray diffraction analysis of compound **10**.

Empirical formula	C ₆ H ₇ BrN ₂ O ₃
Formula weight	235.05
Temperature/K	293(2)
Crystal system	monoclinic
Space group	P21/c
a/Å	9.8547(3)
b/Å	8.4945(2)
c/Å	10.1134(3)
α/°	90
β/°	92.843(3)
γ/°	90
Volume/Å ³	845.56(4)
Z	4
ρ _{calcg} /cm ³	1.846
μ/mm ⁻¹	6.435
F(000)	464.0
Crystal size/mm ³	0.31 × 0.25 × 0.17
Radiation	CuKα ($\lambda = 1.54184$)
2Θ range for data collection/°	8.984 to 156.222
Index ranges	-12 ≤ h ≤ 11, -4 ≤ k ≤ 10, -12 ≤ l ≤ 10
Reflections collected	5155
Independent reflections	1706 [R _{int} = 0.0967, R _{sigma} = 0.0604]
Data/restraints/parameters	1706/0/110
Goodness-of-fit on F ²	1.026
Final R indexes [I>=2σ(I)]	R1 = 0.0928, wR2 = 0.2292
Final R indexes [all data]	R1 = 0.0961, wR2 = 0.2374
Largest diff. peak/hole / e Å ⁻³	1.24/-1.86

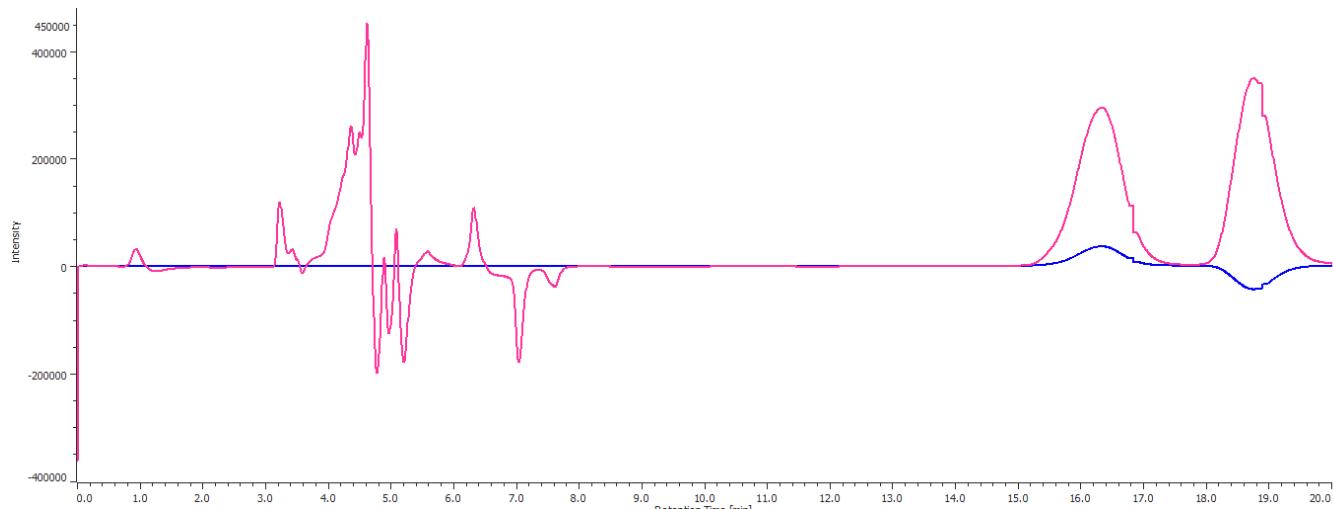


Figure S1. The LC-CD analysis figure of compounds **1a** ($R_f=16.2$ min), **1b** ($R_f=18.8$ min) on chiral Daicel Chiralpack AD-H column (250 × 4.6 mm, 5 μm) under the HPLC condition of n-hexane/ isopropanol (75:25) solution.

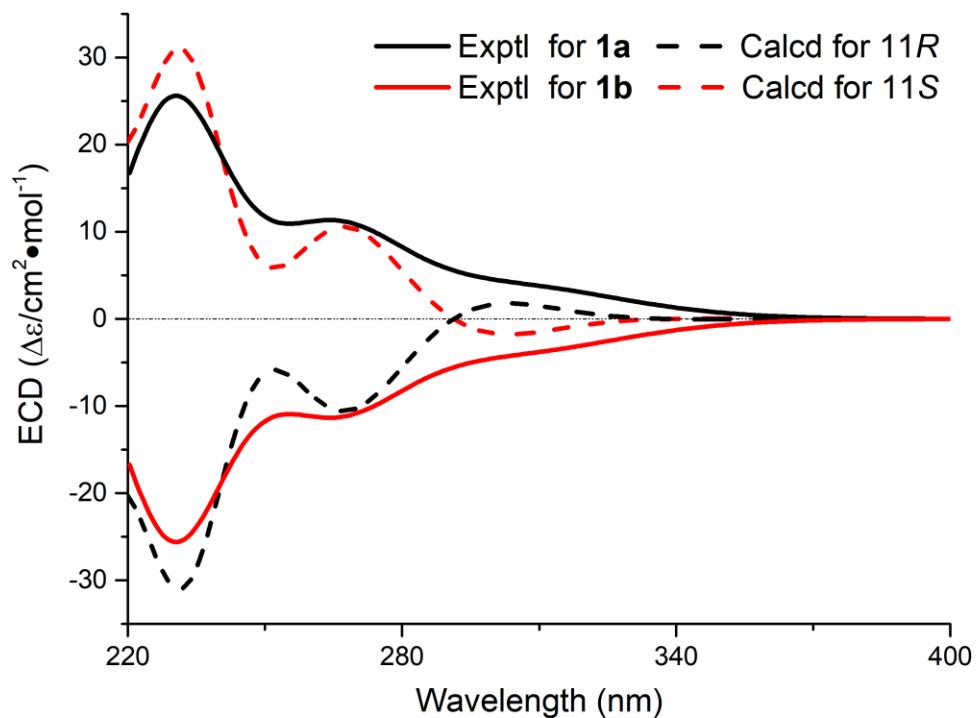


Figure S2. Calculated and experimental ECD spectra of compounds **1a** and **1b**.

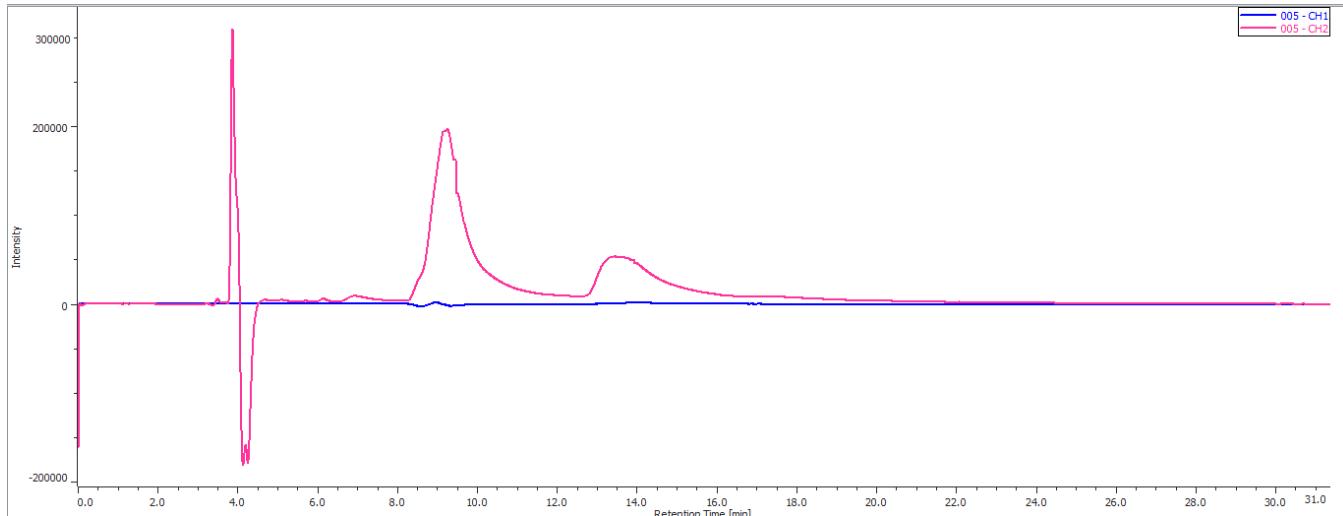


Figure S3. The LC-CD analysis figure of compounds **2a** ($R_f=9.2$ min), **2b** ($R_f=13.5$ min) on chiral Daicel Chiralpack AD-H column (250 × 4.6 mm, 5 μm) under the HPLC condition of n-hexane/ isopropanol (65:35) solution.

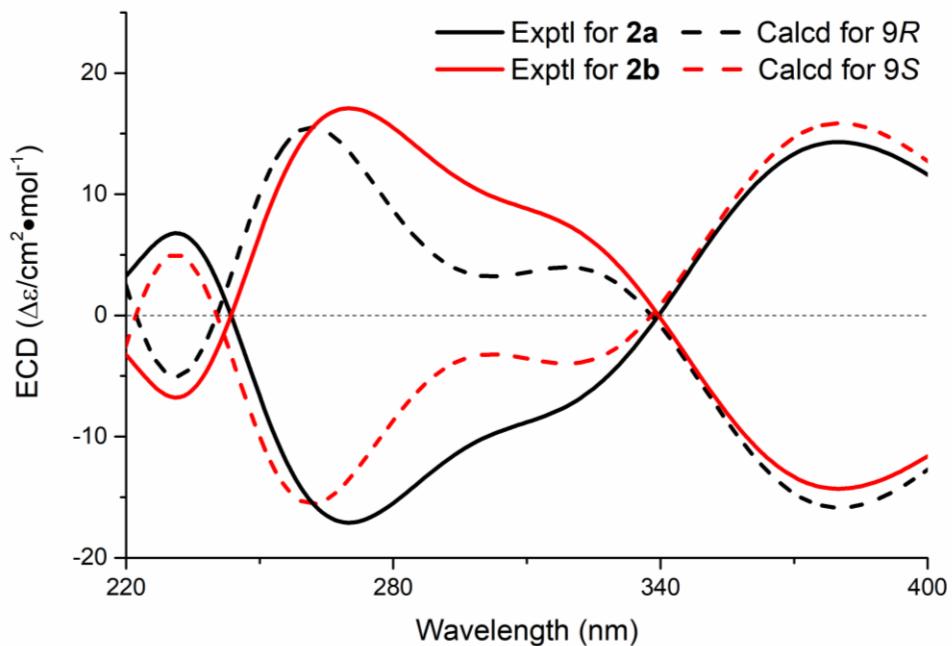


Figure S4. Calculated and experimental ECD spectra of compounds **2a** and **2b**.

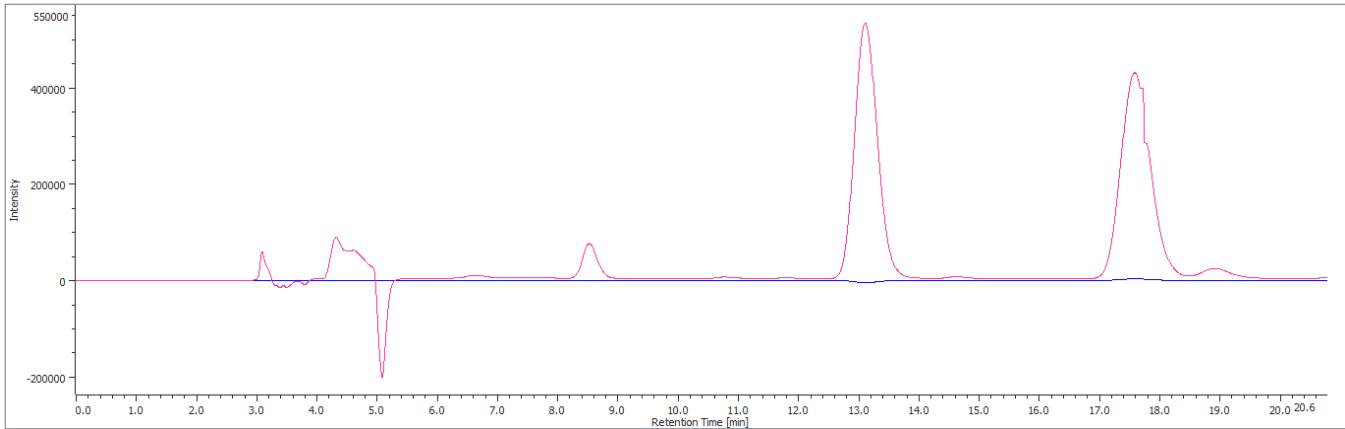


Figure S5. The LC-CD analysis figure of compounds **3a** ($R_f=13.1$ min), **3b** ($R_f=17.6$ min) on chiral Daicel Chiralpack AD-H column (250 × 4.6 mm, 5 μm) under the HPLC condition of n-hexane/ isopropanol (90:10) solution.

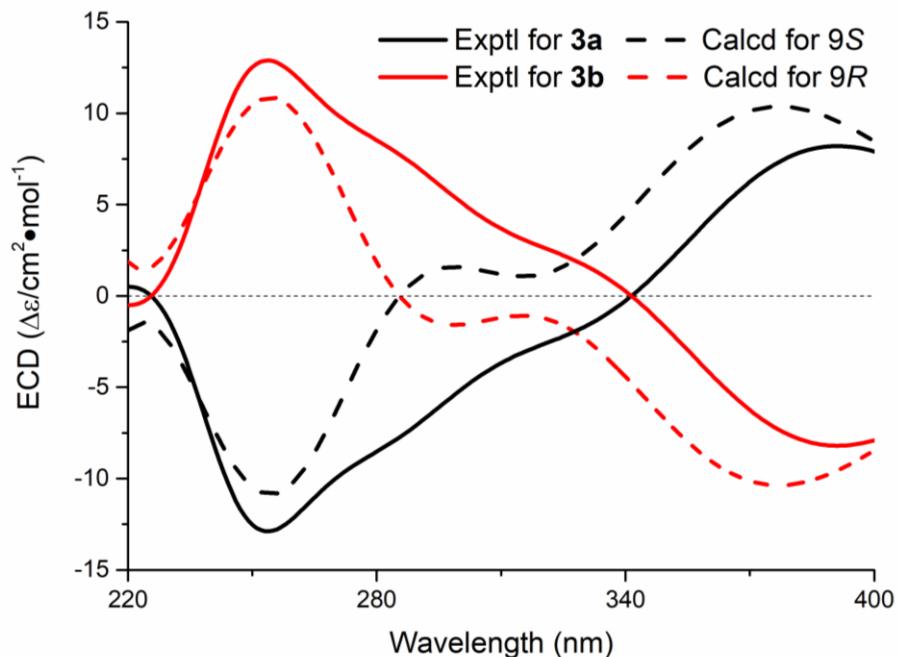


Figure S6. Calculated and experimental ECD spectra of compounds **3a** and **3b**.

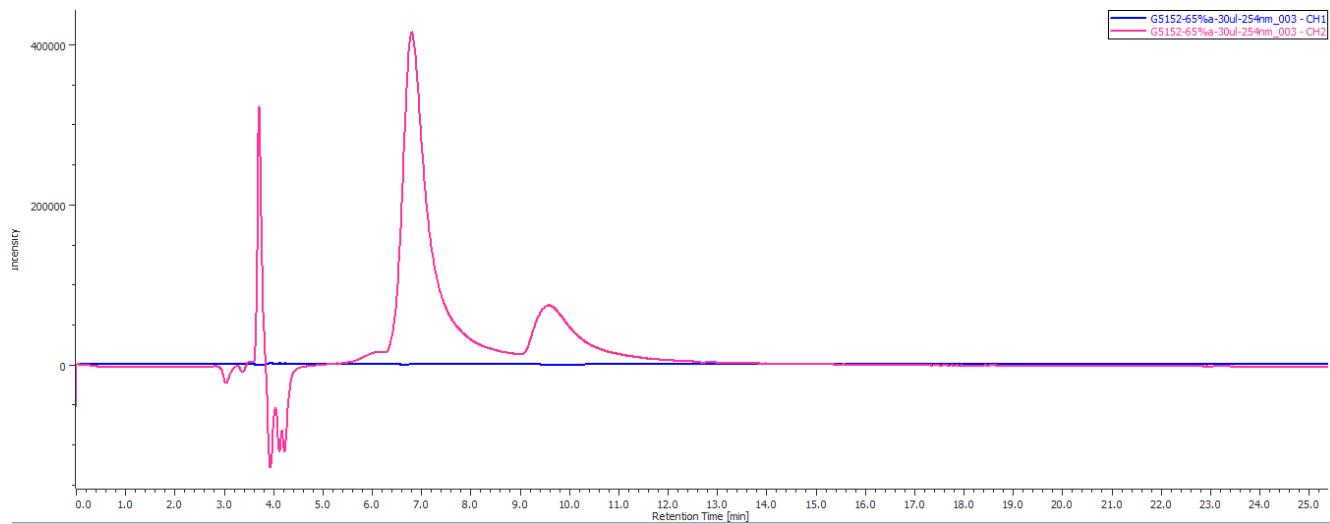


Figure S7. The LC-CD analysis figure of compounds **4a** ($R_f=6.8$ min), **4b** ($R_f=9.6$ min) on chiral Daicel Chiralpack AD-H column (250×4.6 mm, $5 \mu\text{m}$) under the HPLC condition of n-hexane/ isopropanol (65:35) solution.

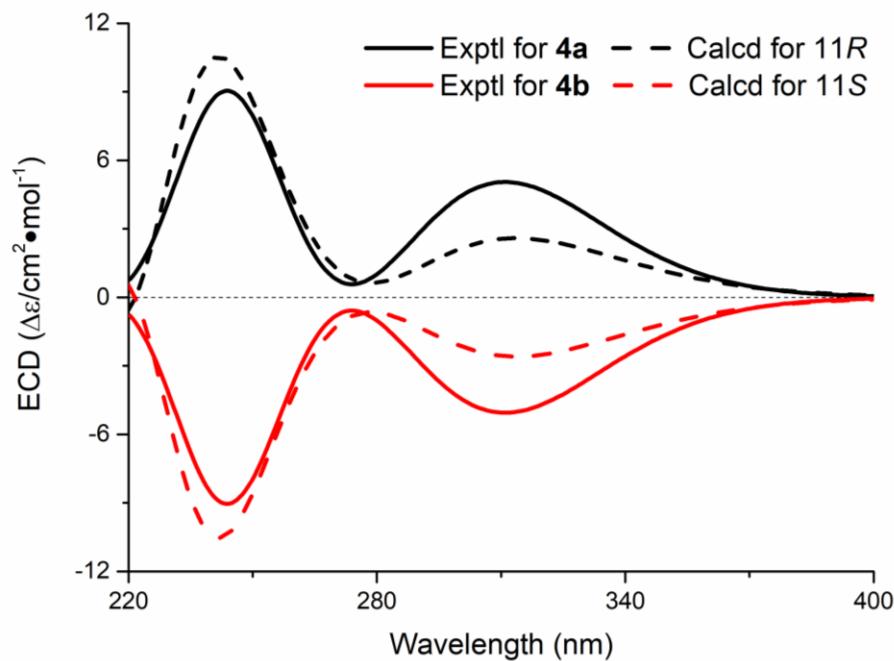


Figure S8. Calculated and experimental ECD spectra of compounds **4a** and **4b**.

Functional		Solvent?		Basis Set		Type of Data	
B3LYP		PCM		6-311+G(d,p)		Unscaled Shifts	
		DP4+		0.00%		100.00%	
Nuclei	sp2?	xperimenta	Isomer 1	Isomer 2	Isomer 3	Isomer 4	Isomer 5
C			19.7	27.59	25.50	26.09	25.66
C			39.5	35.56	47.03	42.95	37.60
C			45	51.41	49.54	48.60	47.91
C			50.6	51.91	53.95	56.95	53.91
C			63.9	79.12	70.24	78.50	77.12
C			81.3	96.07	100.50	101.41	98.46
C			89.7	99.07	95.95	94.28	100.98
C	x		120.3	146.74	146.56	149.06	149.78
C	x		144.2	162.61	157.12	154.44	157.88
C	x		156.4	170.28	168.51	168.75	171.22
C	x		161.9	185.46	172.47	173.68	173.31
C	x		163.1	178.53	170.58	167.35	176.91
H			1.98	2.48	1.96	1.95	0.99
H			1.98	1.51	2.12	1.95	1.54
H			2.25	2.12	2.01	2.09	1.95
H			2.25	2.21	2.38	2.30	2.09
H			3.15	3.57	3.61	3.51	3.35
H			3.35	3.99	3.53	3.85	4.24
H			5.8	4.69	5.78	5.31	5.31
H	x		7.79	7.68	7.55	7.82	7.58
H			3.15	3.39	3.42	3.60	3.44
A	B	C	D	E	F	G	H
1	Functional	Solvent?	Basis Set		Type of Data		
2	B3LYP	PCM	6-311+G(d,p)		Unscaled Shifts		
3							
4			Isomer 1	Isomer 2	Isomer 3	Isomer 4	Isomer 5
5	sDP4+ (H data)		0.00%	99.93%	0.07%	0.00%	-
6	sDP4+ (C data)		0.70%	98.75%	0.00%	0.54%	-
7	sDP4+ (all data)		0.00%	100.00%	0.00%	0.00%	-
8	uDp4+ (H data)		0.00%	83.90%	16.10%	0.00%	-
9	uDp4+ (C data)		0.00%	100.00%	0.00%	0.00%	-
10	uDp4+ (all data)		0.00%	100.00%	0.00%	0.00%	-
11	DP4+ (H data)		0.00%	99.99%	0.01%	0.00%	-
12	DP4+ (C data)		0.00%	100.00%	0.00%	0.00%	-
13	DP4+ (all data)		0.00%	100.00%	0.00%	0.00%	-

Figure S9. Detailed DP4+ probability (calculated at PCM/b3lyp/6-311+G(d,p) level) for compounds **6** and **16** (Isomer 1: 2R6R10R, Isomer 2: 2R6R10S, Isomer 3: 2R6S10R, Isomer 4: 2R6S10S).

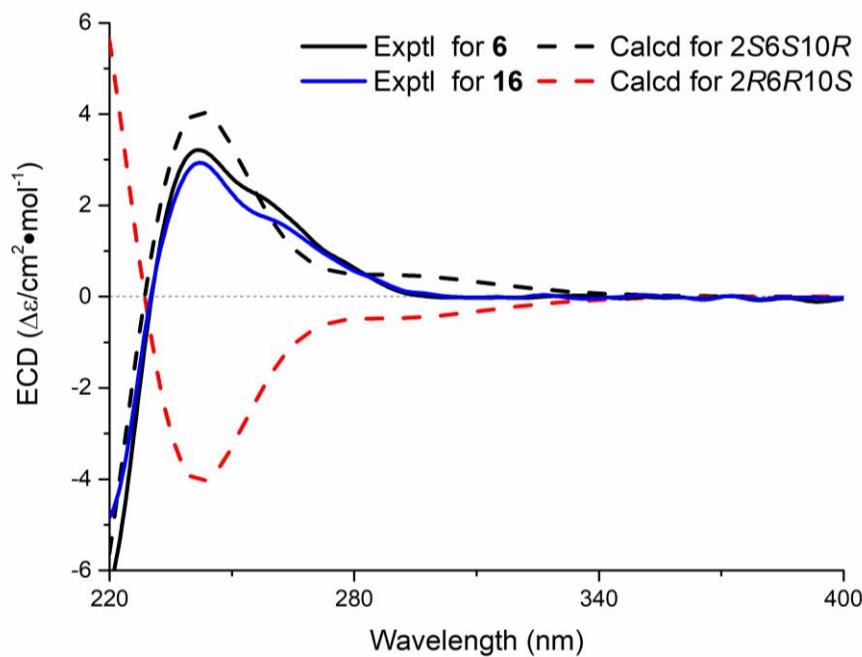


Figure S10. Calculated and experimental ECD spectra of compounds **6** and **16**.

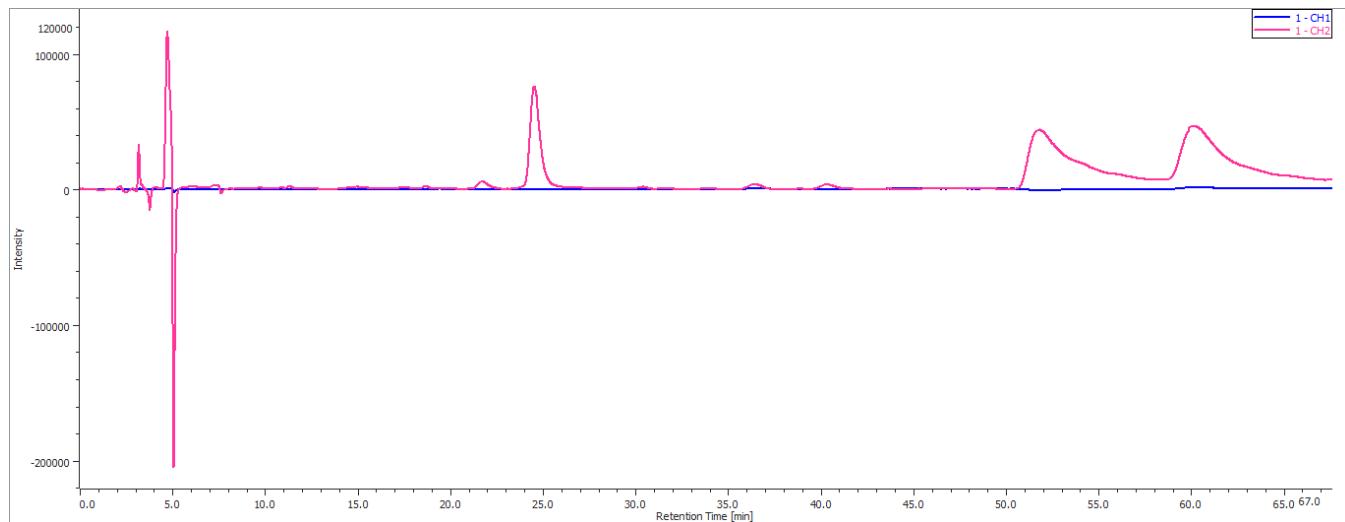


Figure S11. The LC-CD analysis figure of compounds **7a** ($R_f=52.2$ min), **7b** ($R_f=60.5$ min) on chiral Daicel Chiralpack AD-H column (250 × 4.6 mm, 5 μm) under the HPLC condition of n-hexane/isopropanol (90:10) solution.

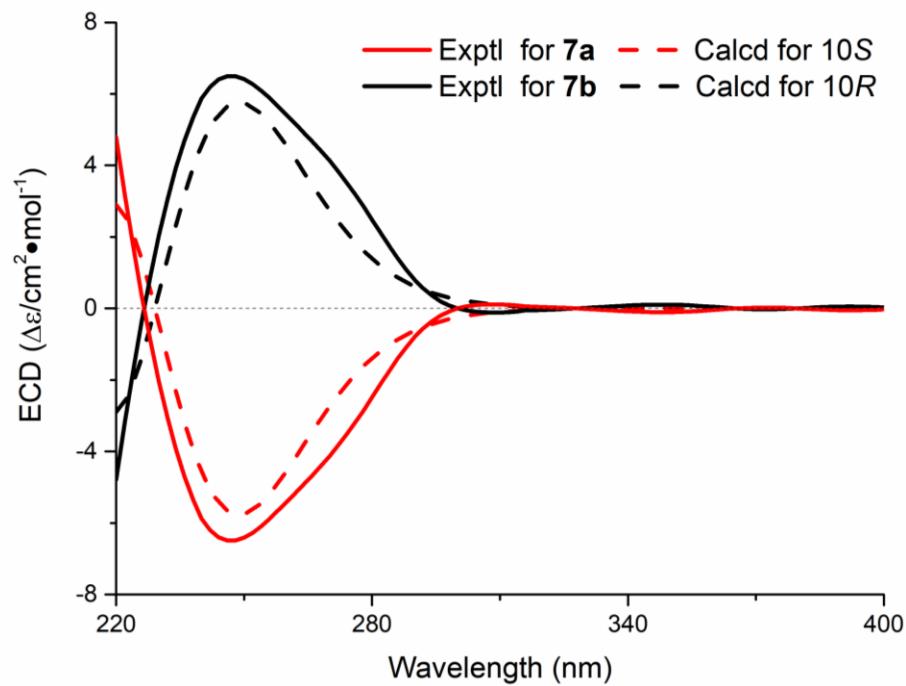


Figure S12. Calculated and experimental ECD spectra of compounds **7a** and **7b**.

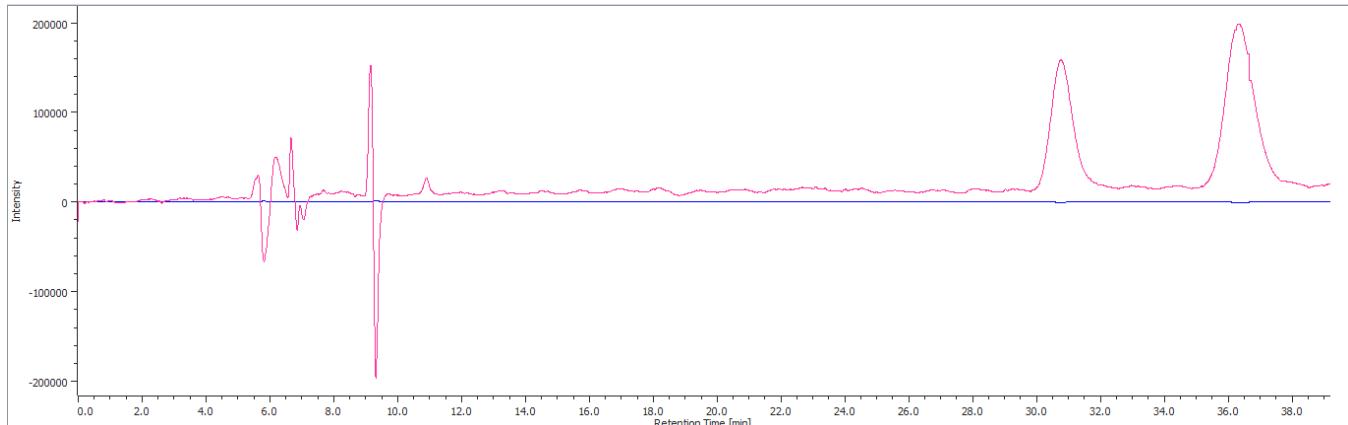


Figure S13. The LC-CD analysis figure of compounds **8a** ($R_f=30.6$ min), **8b** ($R_f=36.2$ min) on chiral Daicel Chiralpack AD-H column (250 × 4.6 mm, 5 μm) under the HPLC condition of n-hexane/isopropanol (90:10) solution.

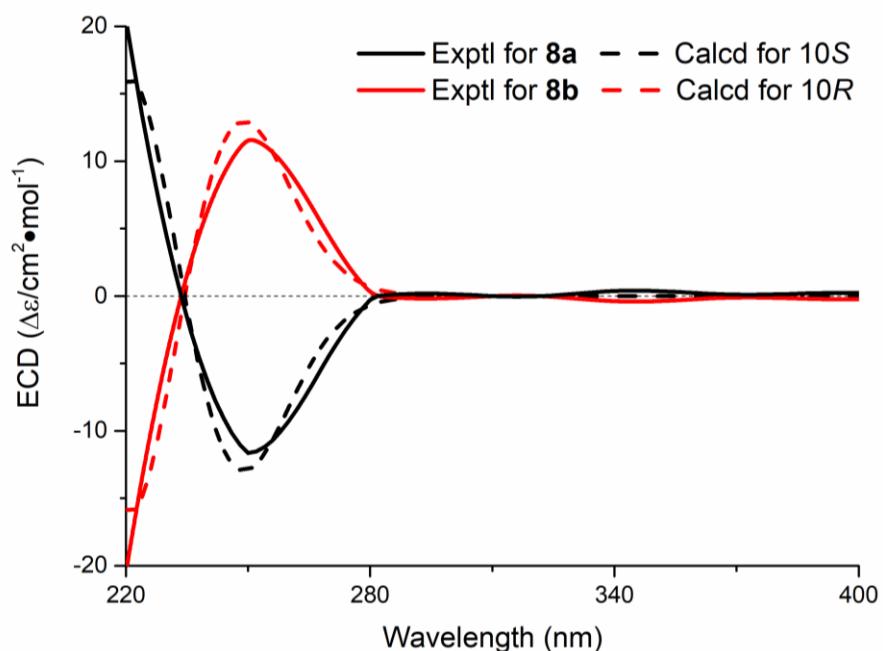


Figure S14. Calculated and experimental ECD spectra of compounds **8a** and **8b**.

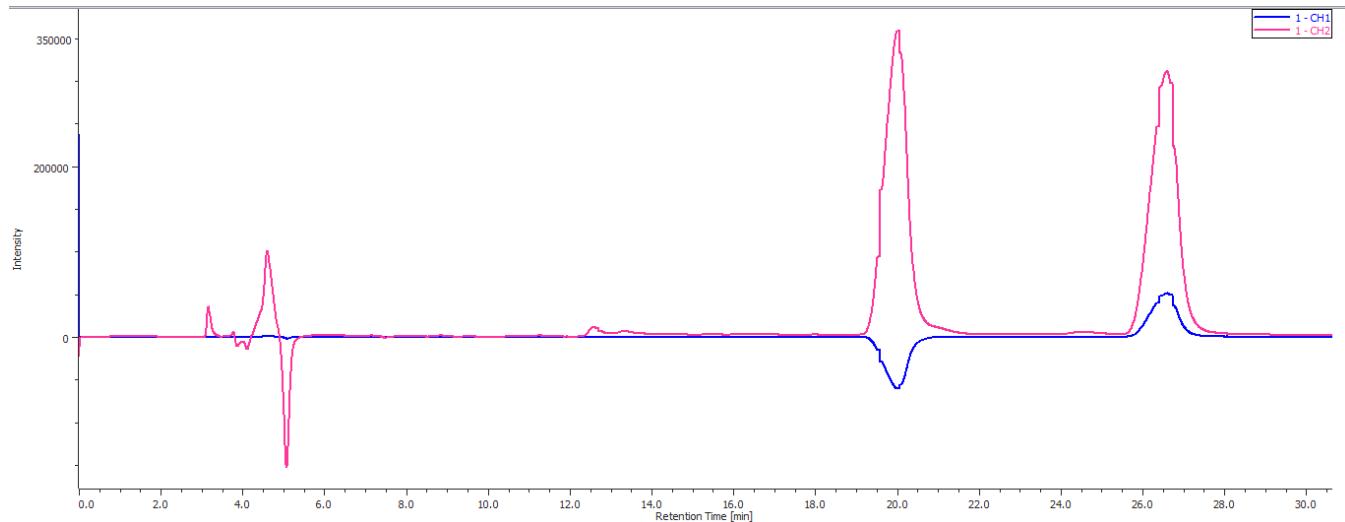


Figure S15. The LC-CD analysis figure of compounds **10a** ($R_f=19.8$ min), **10b** ($R_f=26.6$ min) on chiral Daicel Chiralpack AD-H column (250 × 4.6 mm, 5 μm) under the HPLC condition of n-hexane/isopropanol (90:10) solution.

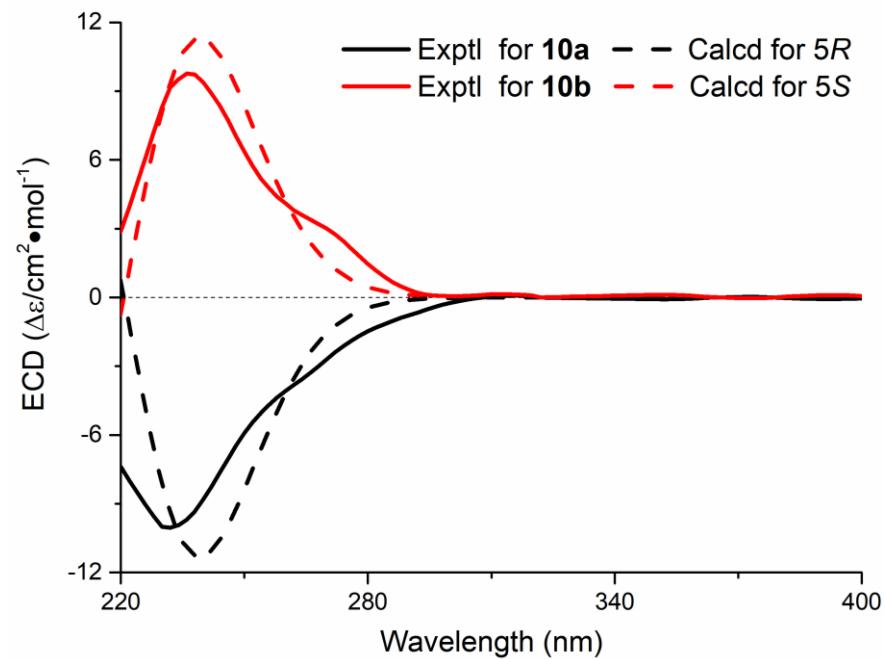


Figure S16. Calculated and experimental ECD spectra of compounds **10a** and **10b**.

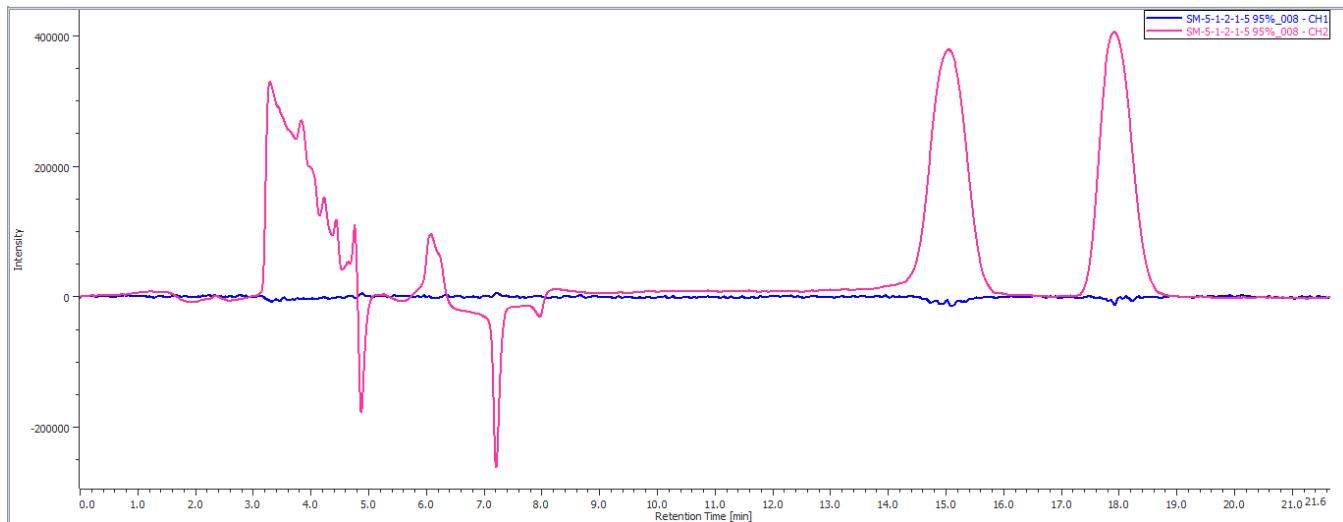


Figure S17. The LC-CD analysis figure of compounds **11a** ($R_f=14.9$ min), **11b** ($R_f=17.8$ min) on chiral Daicel Chiralpack AD-H column (250 × 4.6 mm, 5 μ m) under the HPLC condition of n-hexane/isopropanol (90:10) solution.

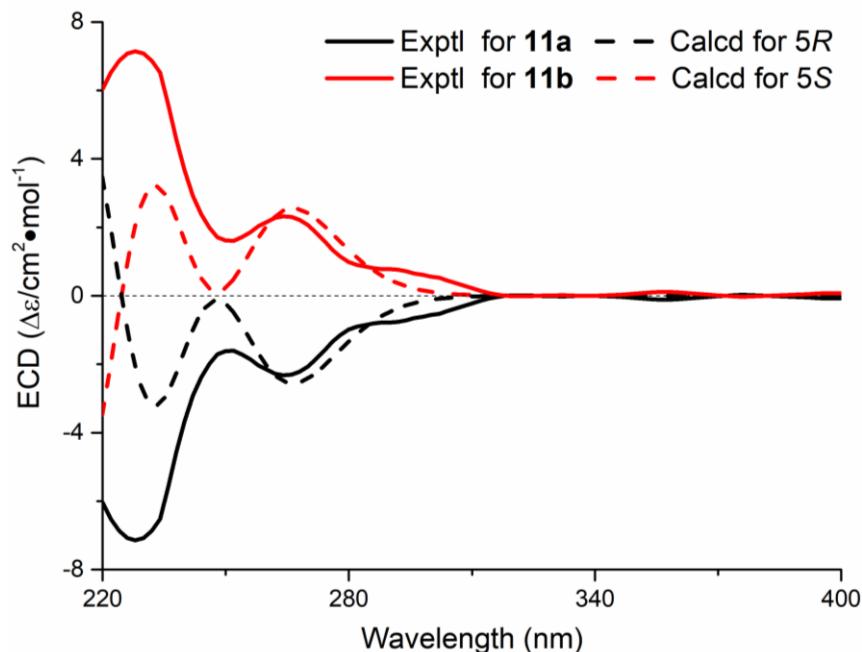


Figure S18. Calculated and experimental ECD spectra of compounds **11a** and **11b**.

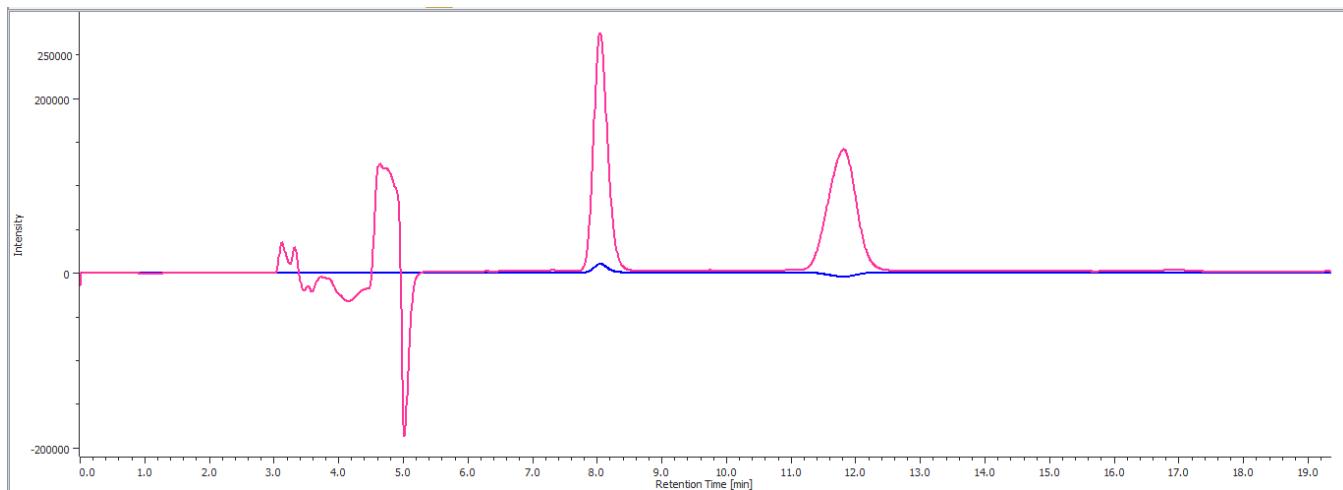


Figure S19. The LC-CD analysis figure of compounds **12a** ($R_f=8.1$ min), **12b** ($R_f=11.8$ min) on chiral Daicel Chiralpack AD-H column (250 × 4.6 mm, 5 μm) under the HPLC condition of n-hexane/isopropanol (80:20) solution.

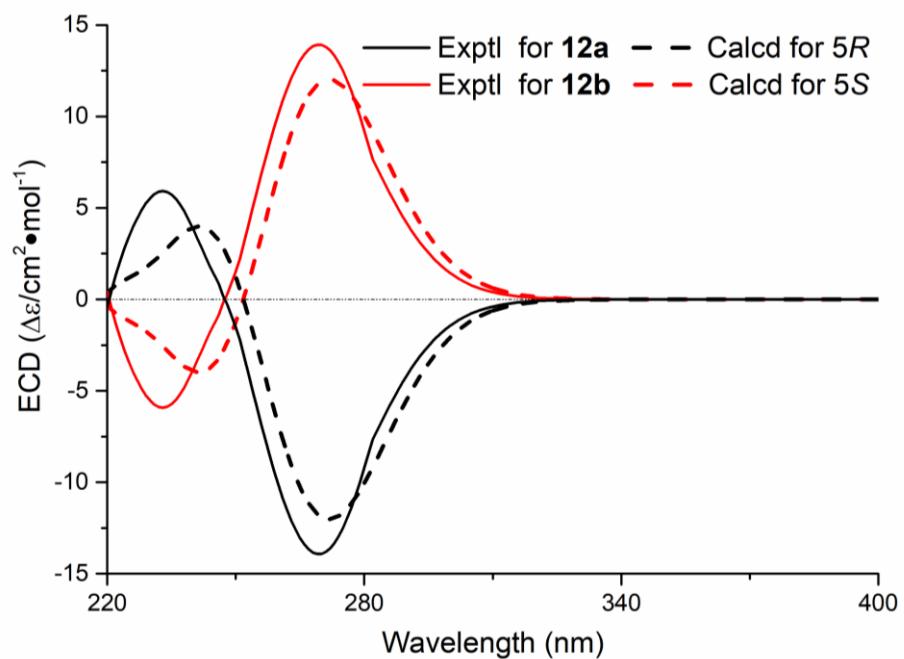


Figure S20. Calculated and experimental ECD spectra of compounds **12a** and **12b**.

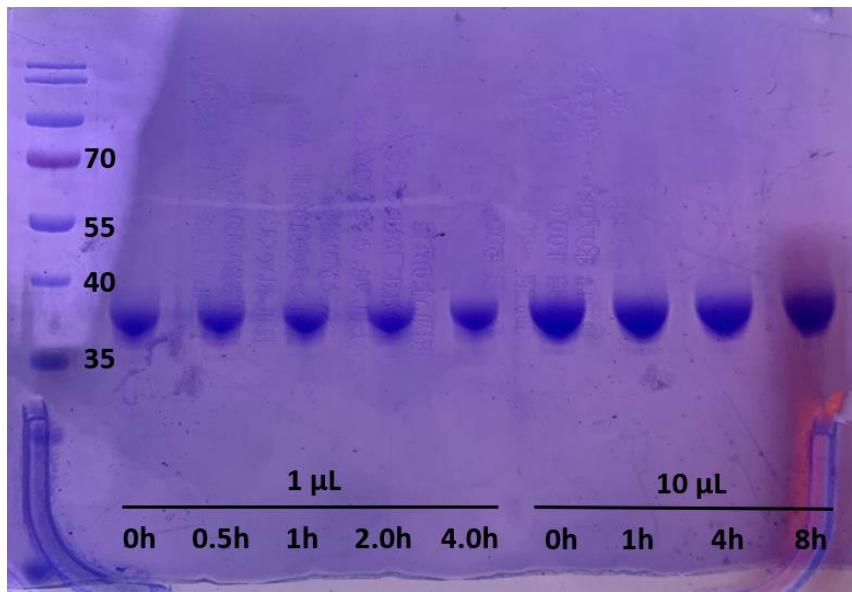


Figure S21. SDS PAGE of the ALR2 stability investigation for surface plasmon resonance (SPR) experiment during 0-8h at room temperature.

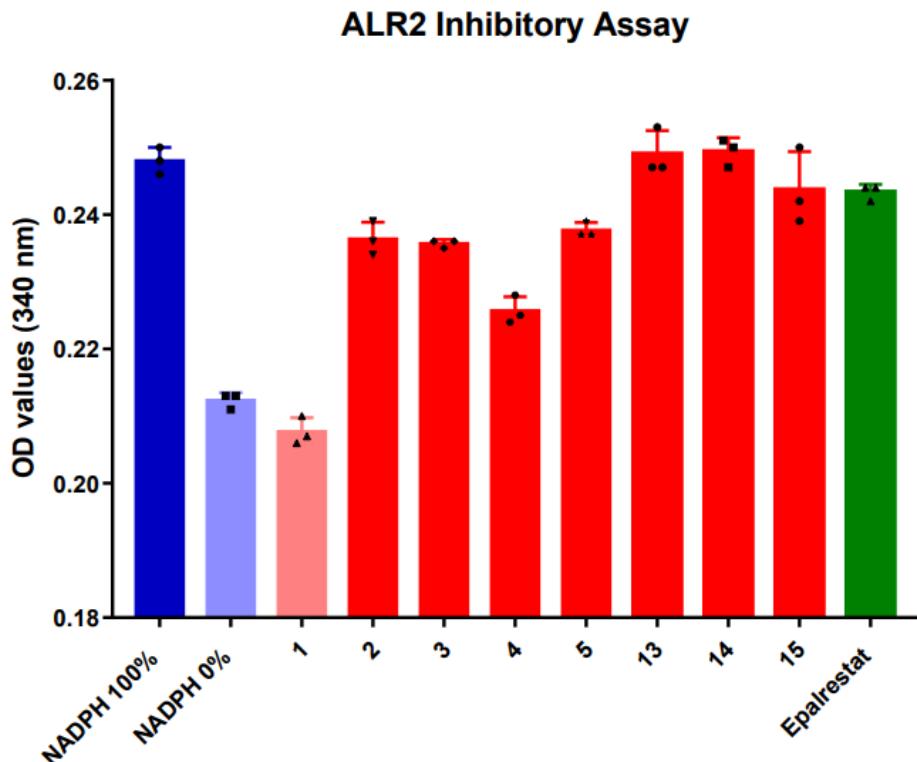


Figure S22. Compounds **2-5** and **13-15**, representative of 5/7/5 tricyclic spogiacidin-type PIA compounds, displayed the superior activities (>50% inhibition rate) at 20 μ M.

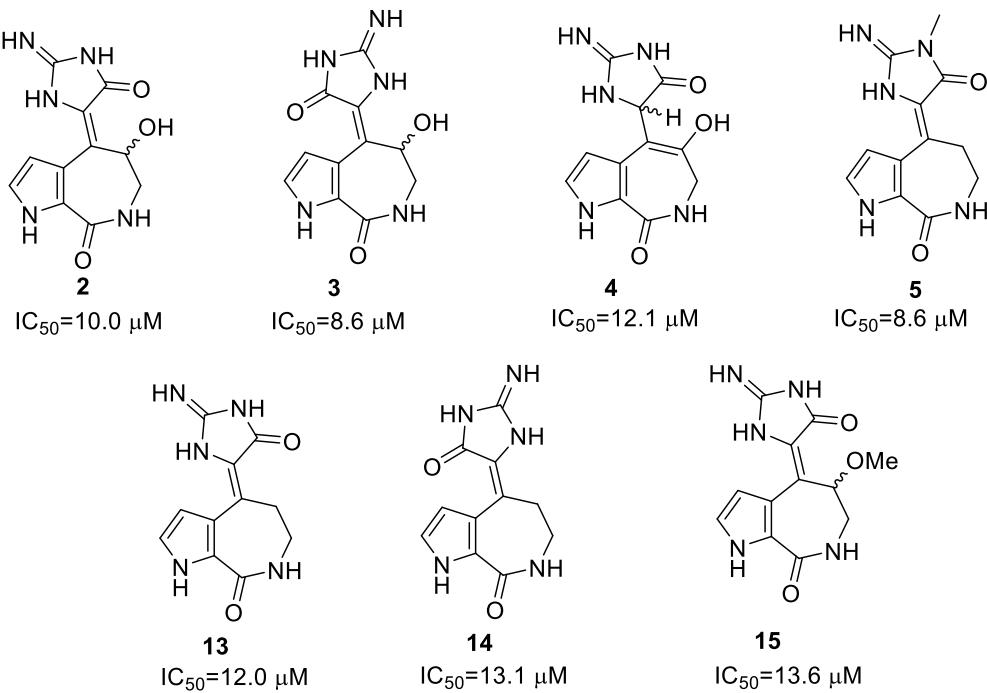


Figure S23. IC_{50} values of ALR2 inhibitory activities for spongiacidin-type PIAs (compounds **2-5** and **13-15**).

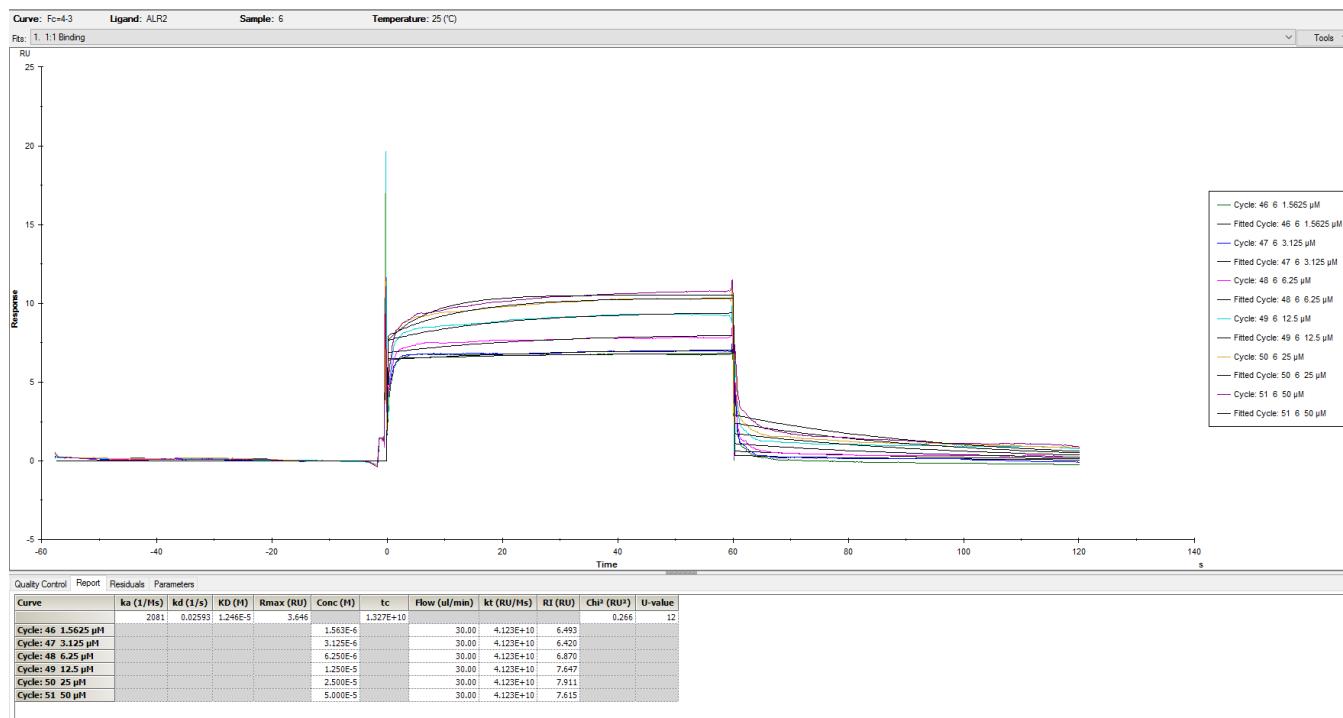


Figure S24. SPR experiment of compound **13** using the Biacore T200 instrument.

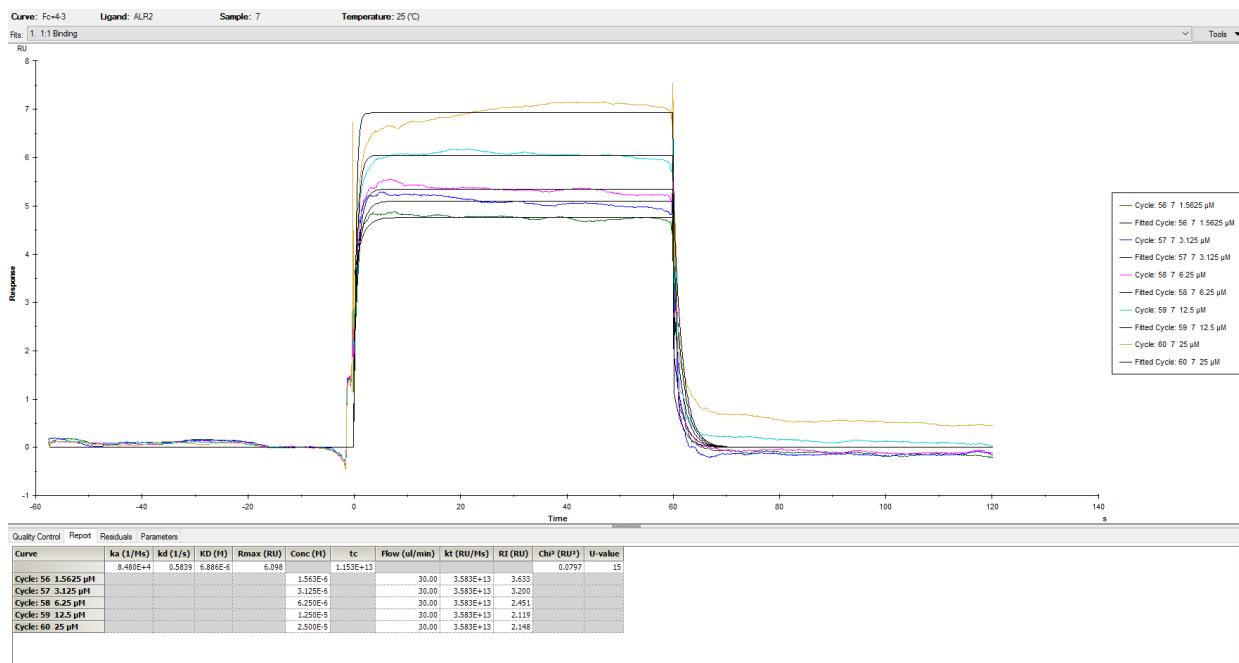


Figure S25. SPR experiment of compound **14** using the Biacore T200 instrument.

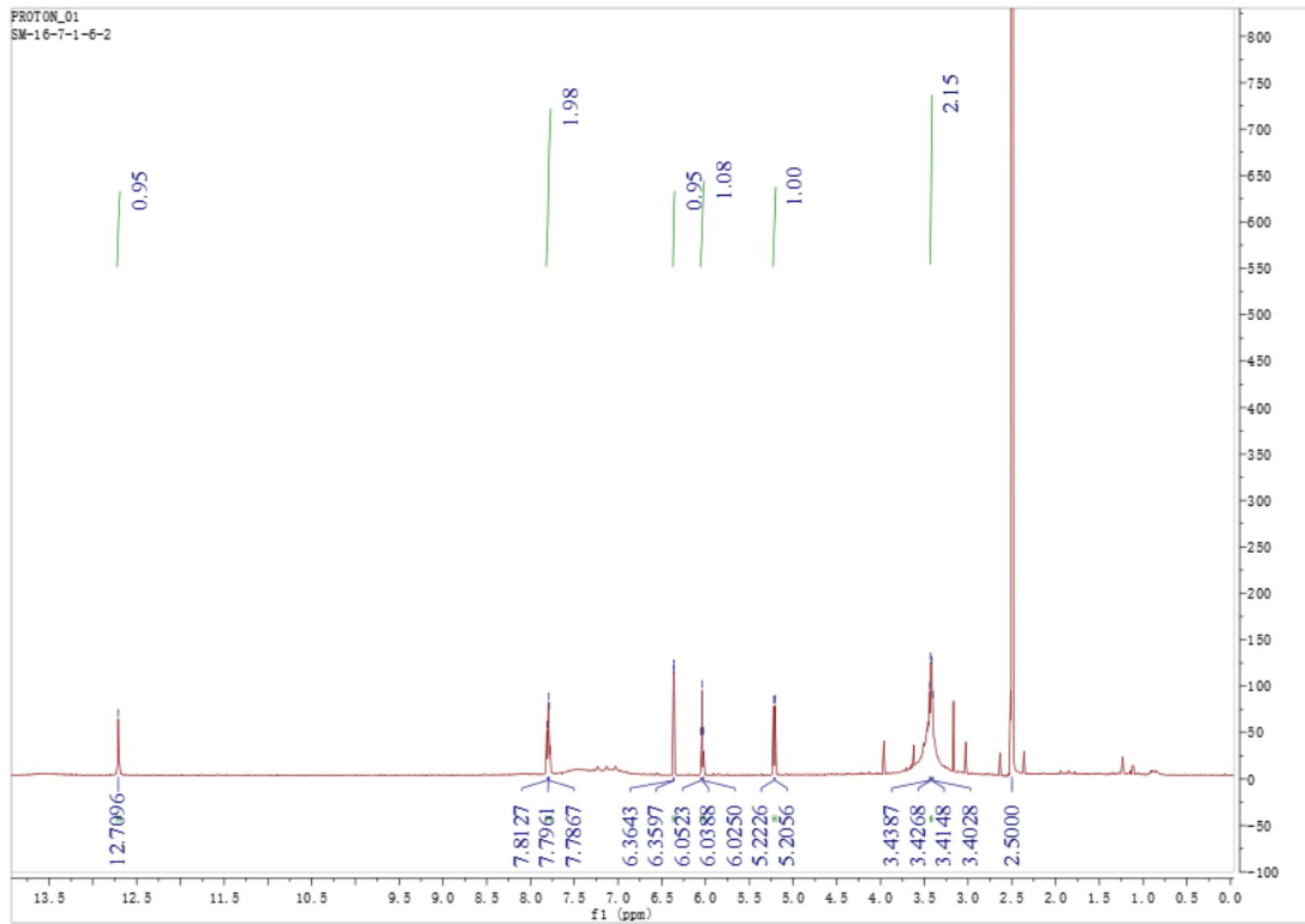


Figure S26. ^1H NMR spectrum of compound **1** in $\text{DMSO}-d_6$ (500 MHz).

CARBON_01
SM-16-7-1-6-2

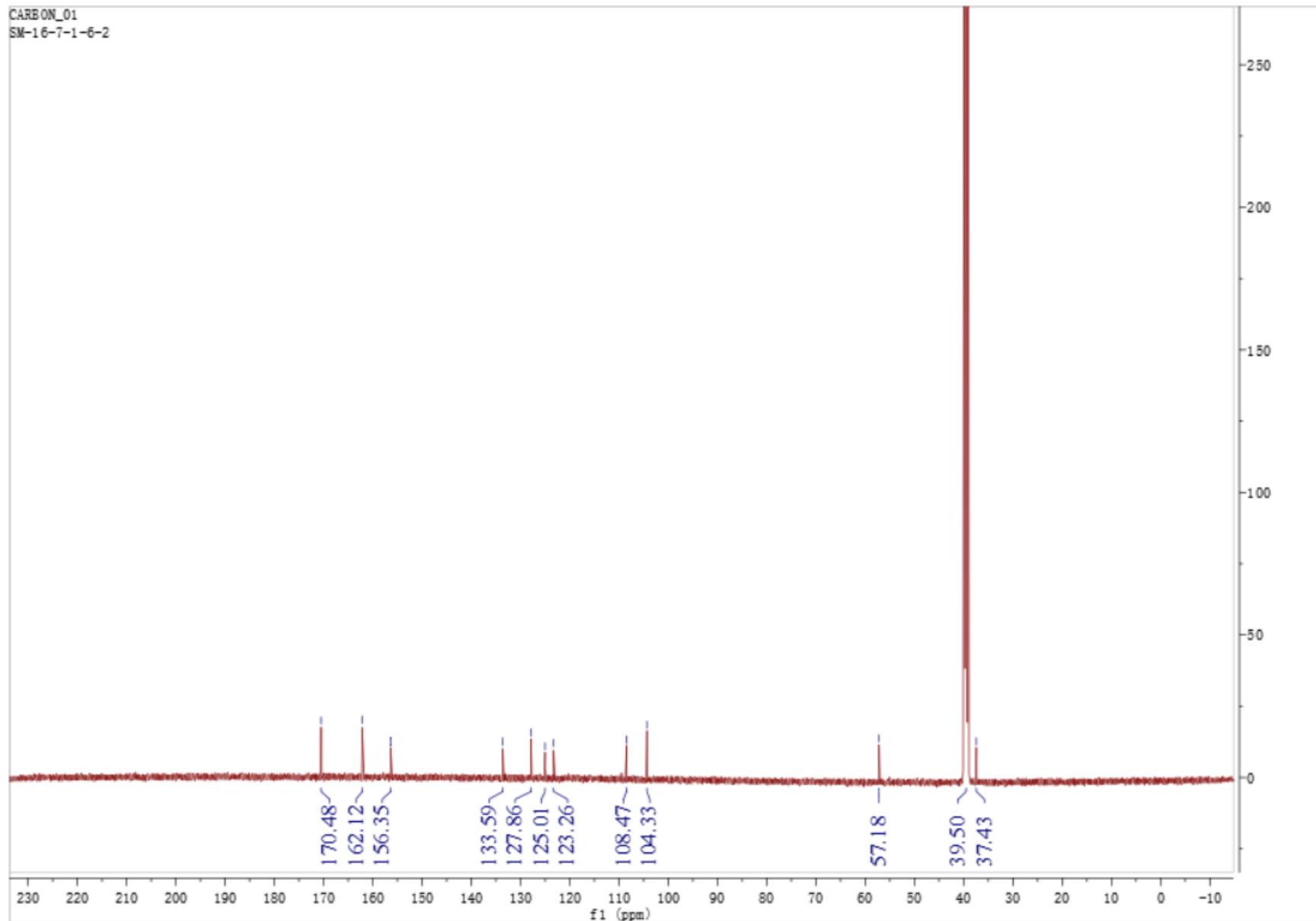


Figure S27. ¹³C NMR spectrum of compound **1** in DMSO-*d*₆ (125 MHz).

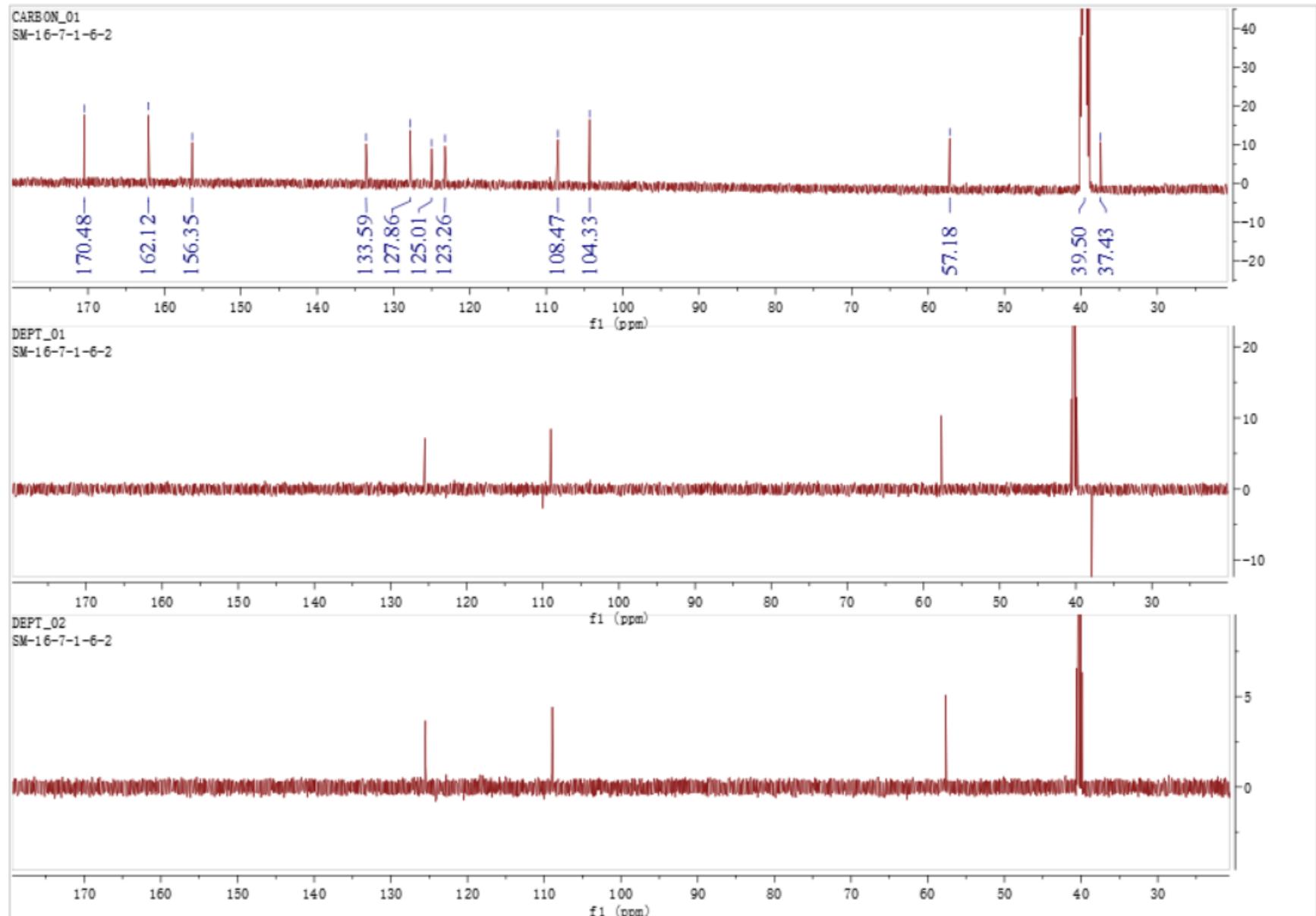


Figure S28. ^{13}C NMR and DEPT spectrum of compound **1** in $\text{DMSO}-d_6$ (125 MHz).

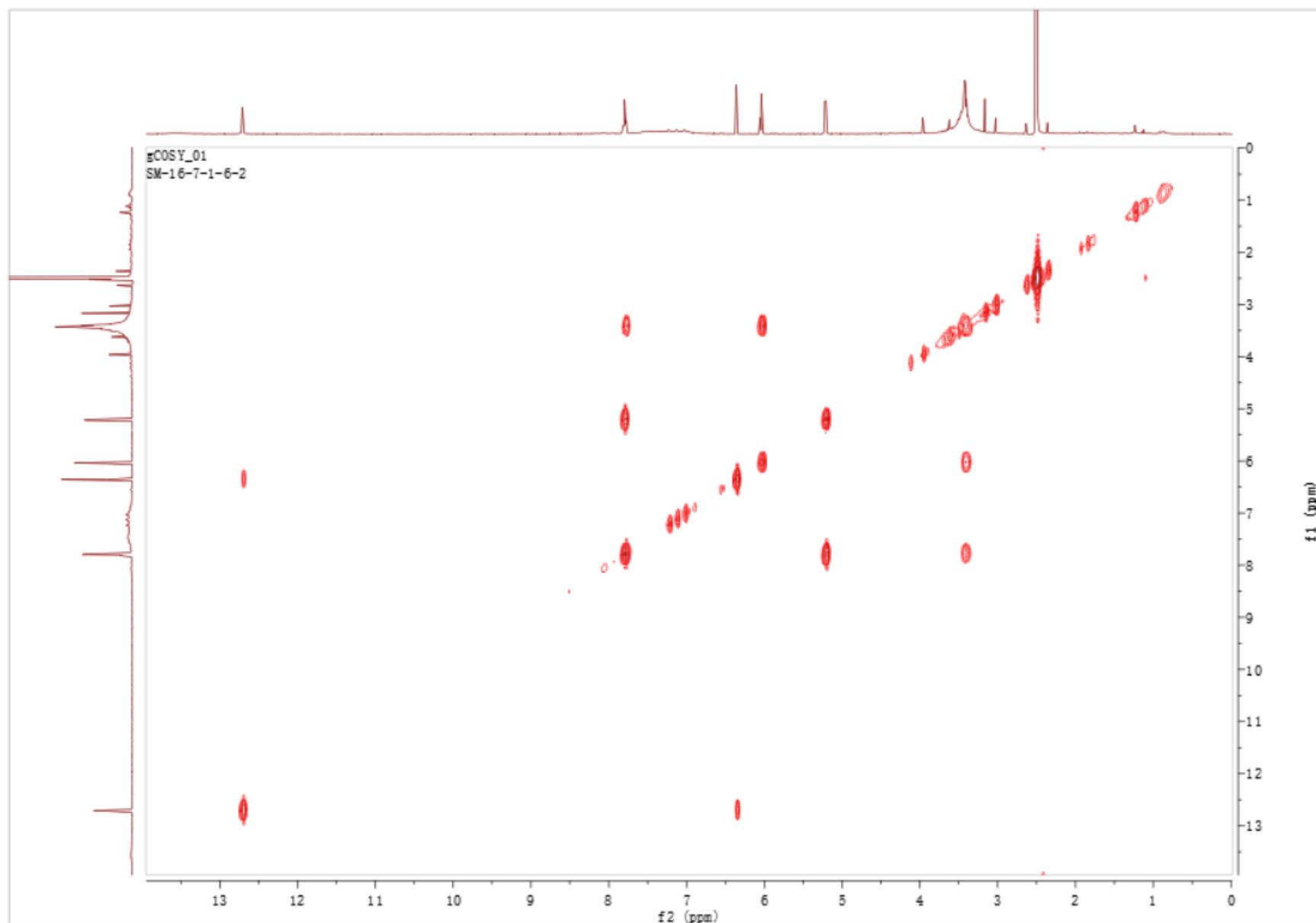


Figure S29. ^1H - ^1H COSY spectrum of compound **1** in $\text{DMSO}-d_6$ (500 MHz).

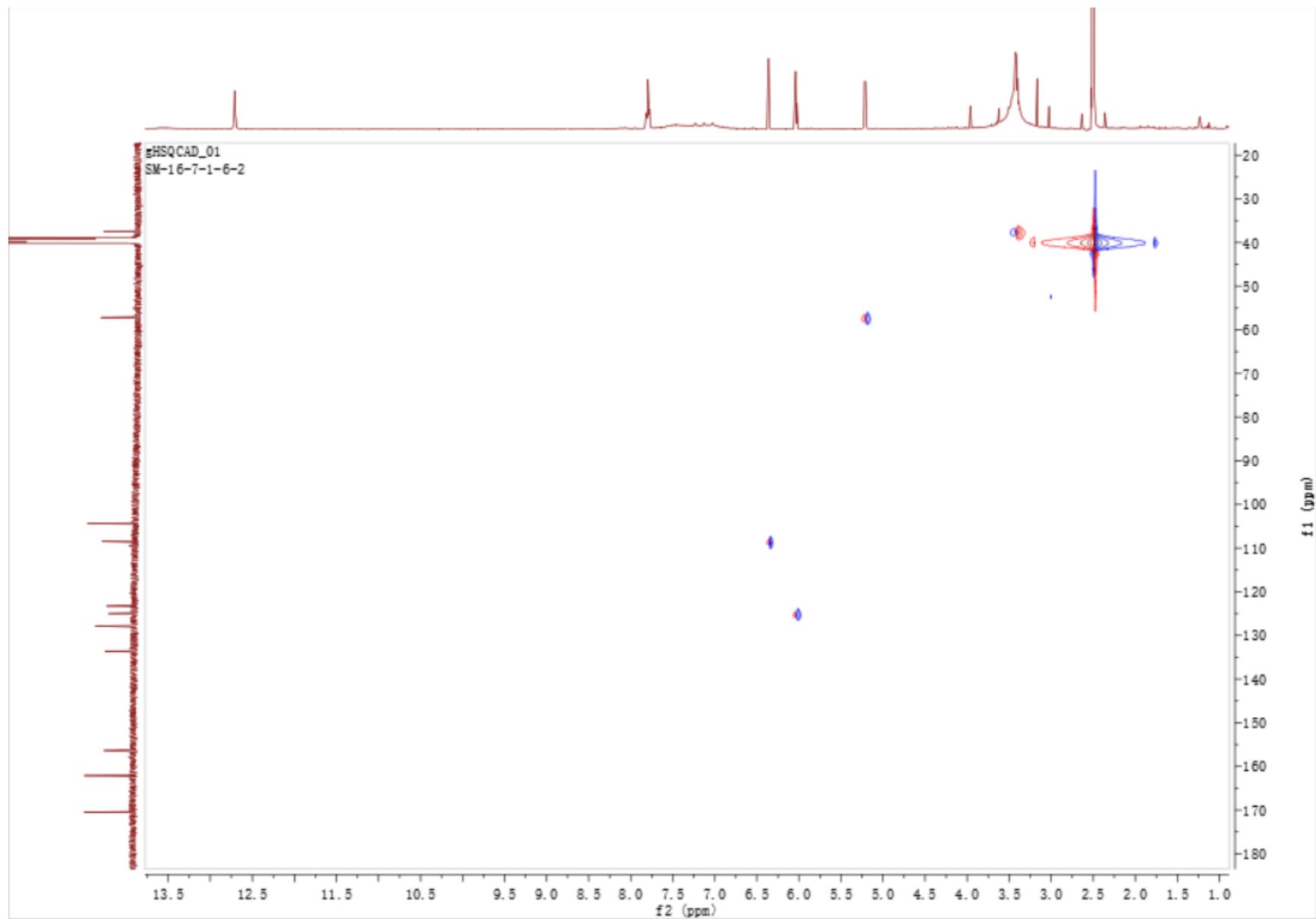


Figure S30. HSQC spectrum of compound **1** in $\text{DMSO}-d_6$ (500 MHz).

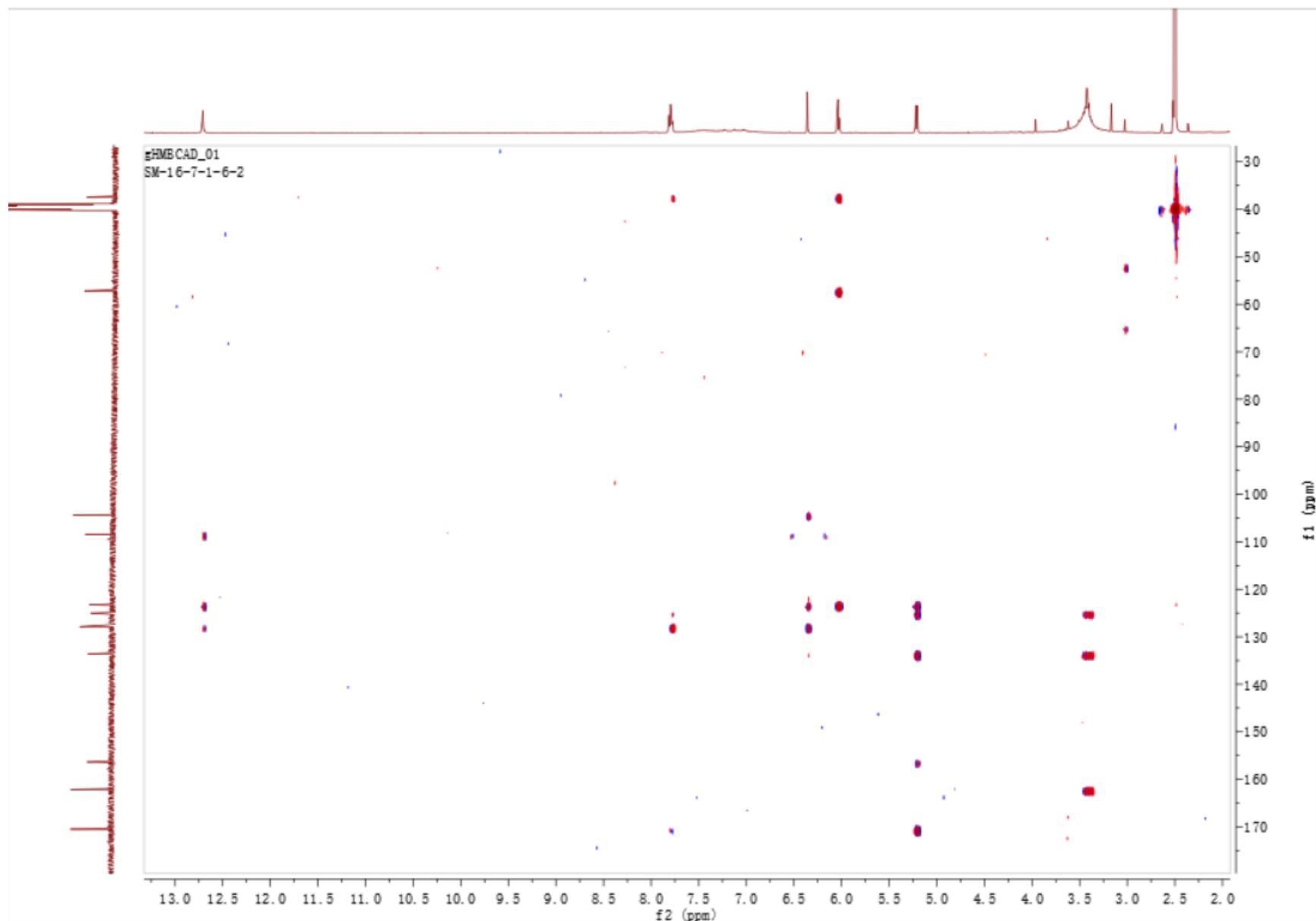


Figure S31. HMBC spectrum of compound **1** in $\text{DMSO}-d_6$ (500 MHz).

SM-16-7-1-6-2 #42 RT: 0.10 AV: 1 NL: 2.67E9
T: FTMS + p ESI Full ms [200.0000-500.0000]

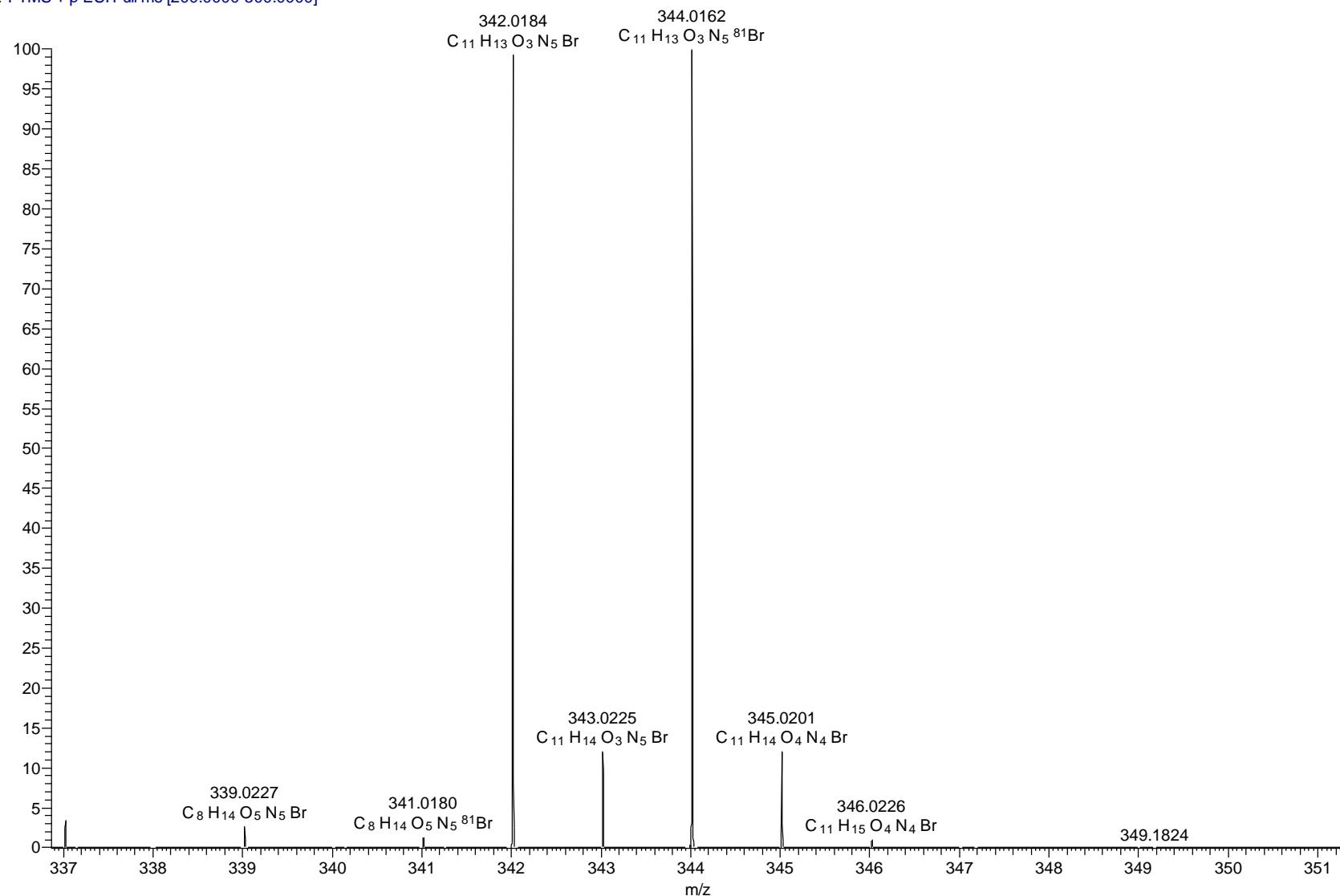


Figure S32. HRESIMS data of compound 1.

SM-15-2-4-1
single_pulse

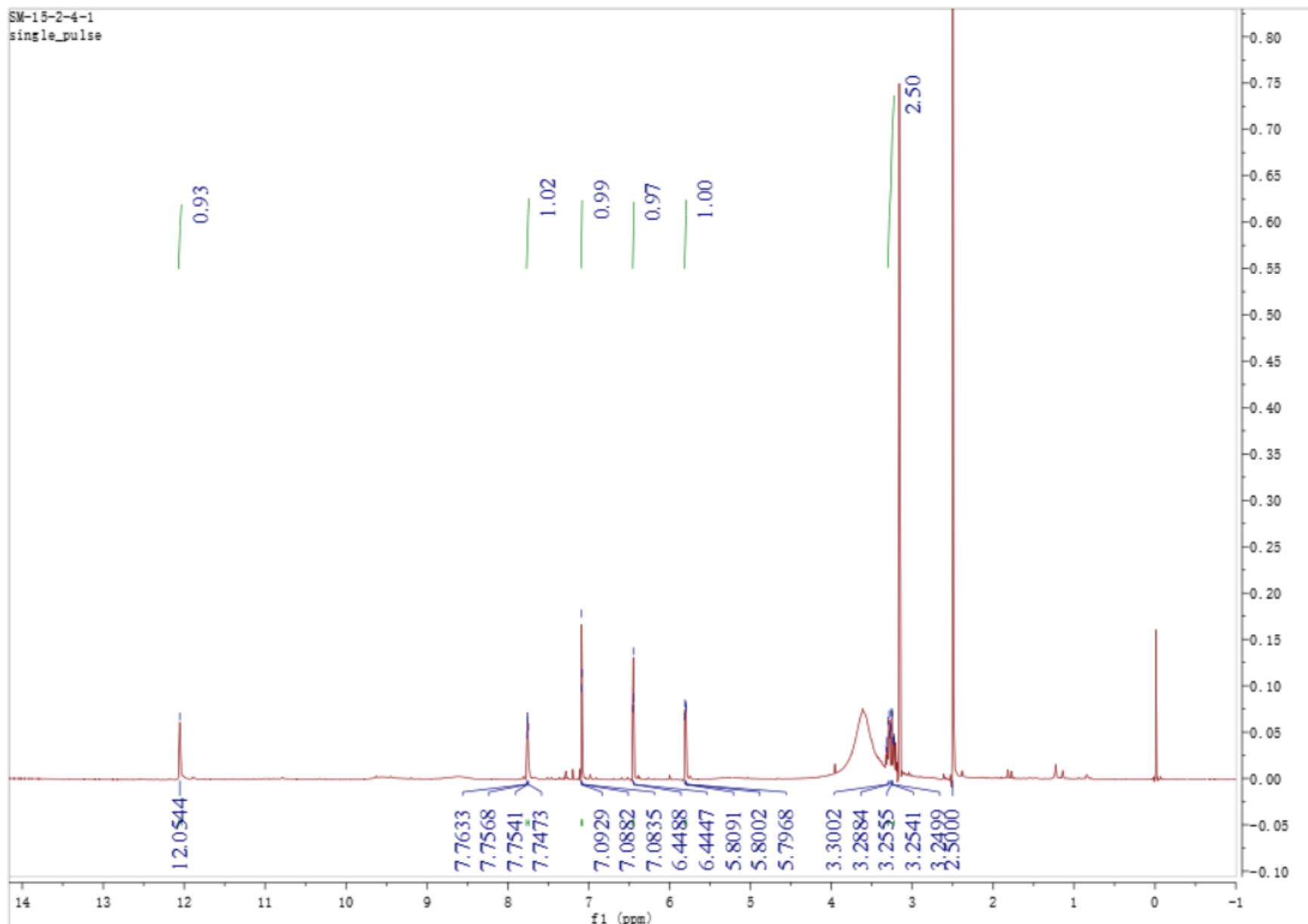


Figure S33. ¹H NMR spectrum of compound 2 in DMSO-*d*₆ (500 MHz).

SM-15-2-4-1
single pulse decoupled gated NOE

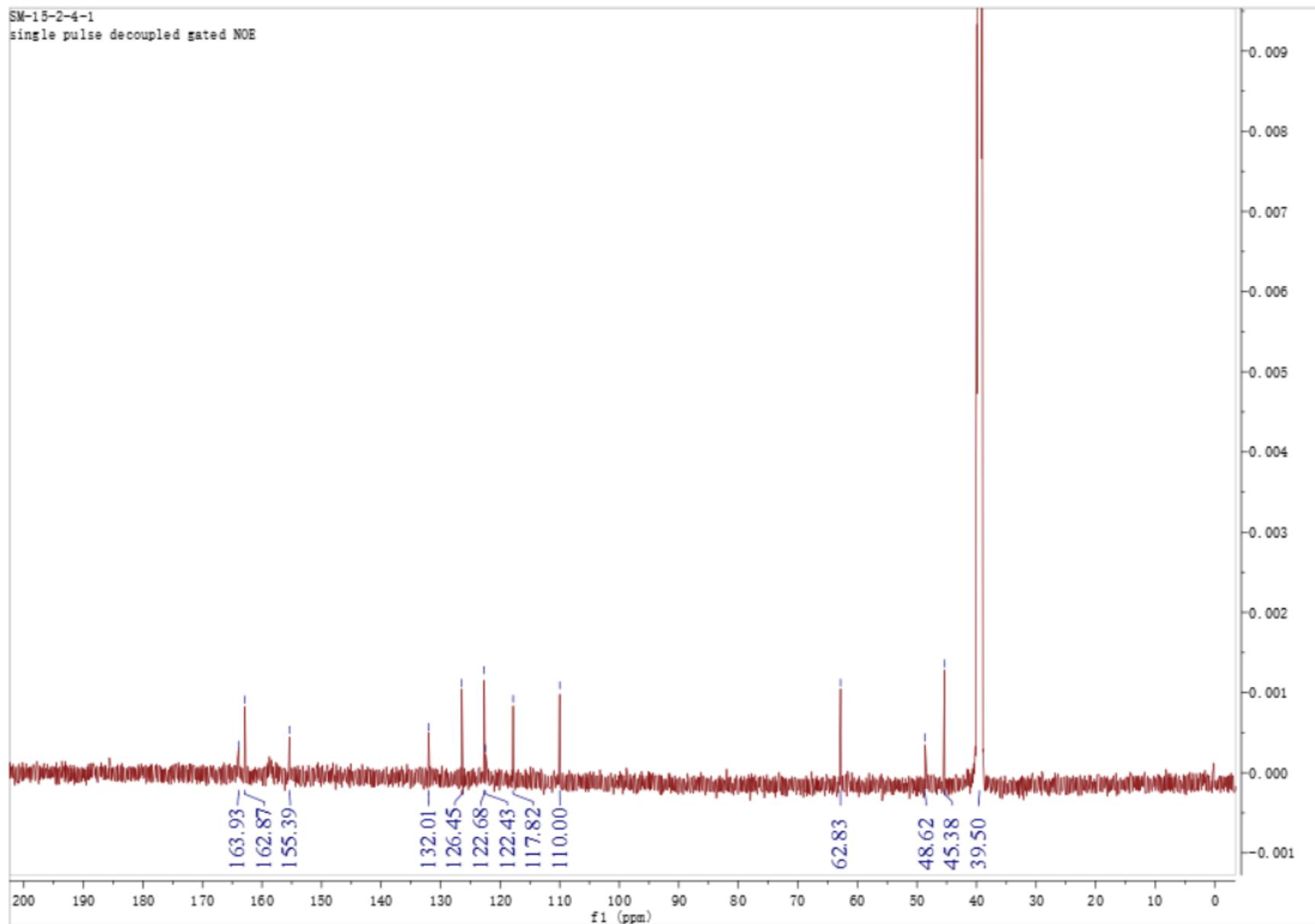


Figure S34. ¹³C NMR spectrum of compound 2 in DMSO-*d*₆ (125 MHz).

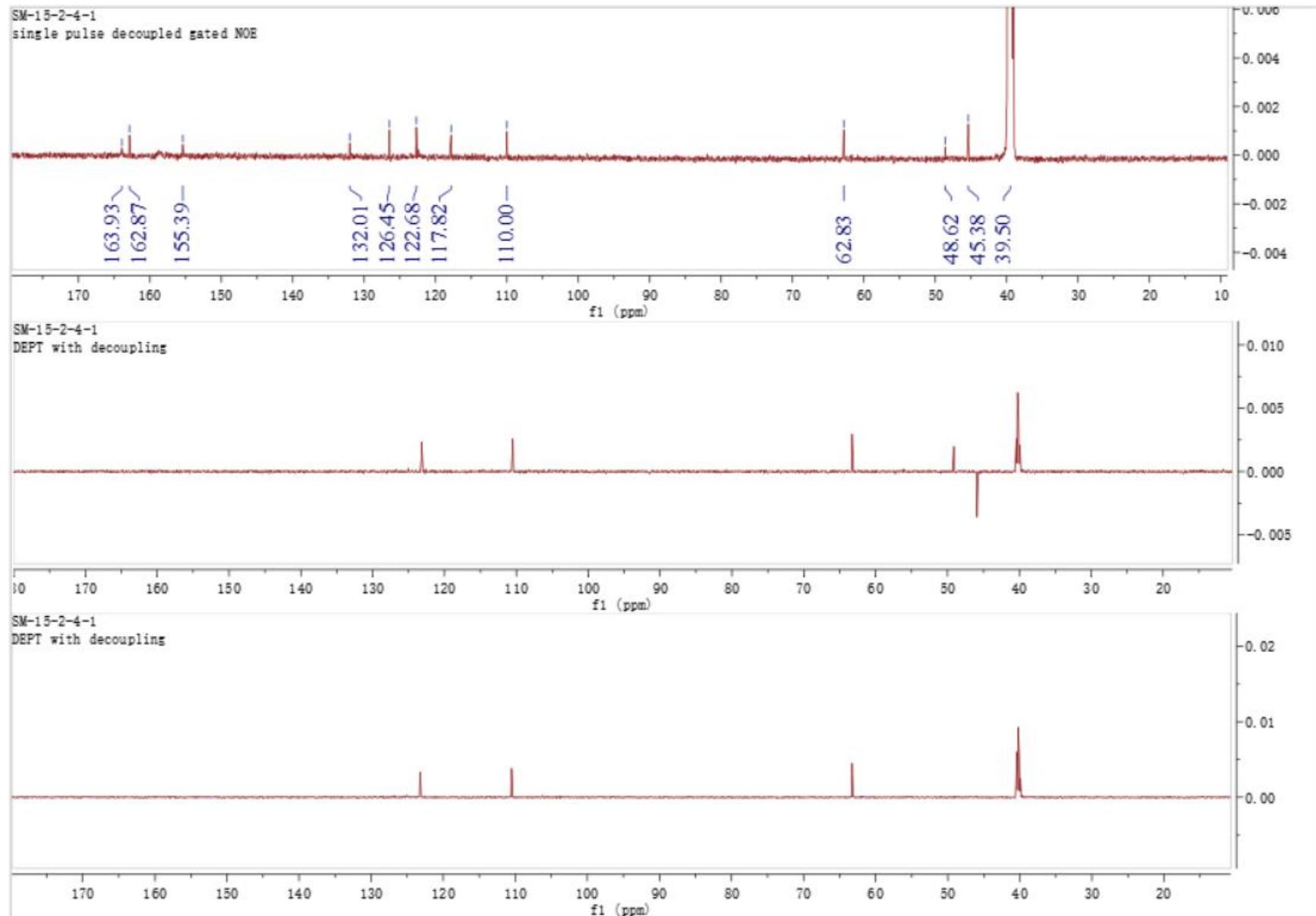


Figure S35. ^{13}C NMR and DEPT spectrum of compound 2 in $\text{DMSO}-d_6$ (125 MHz).

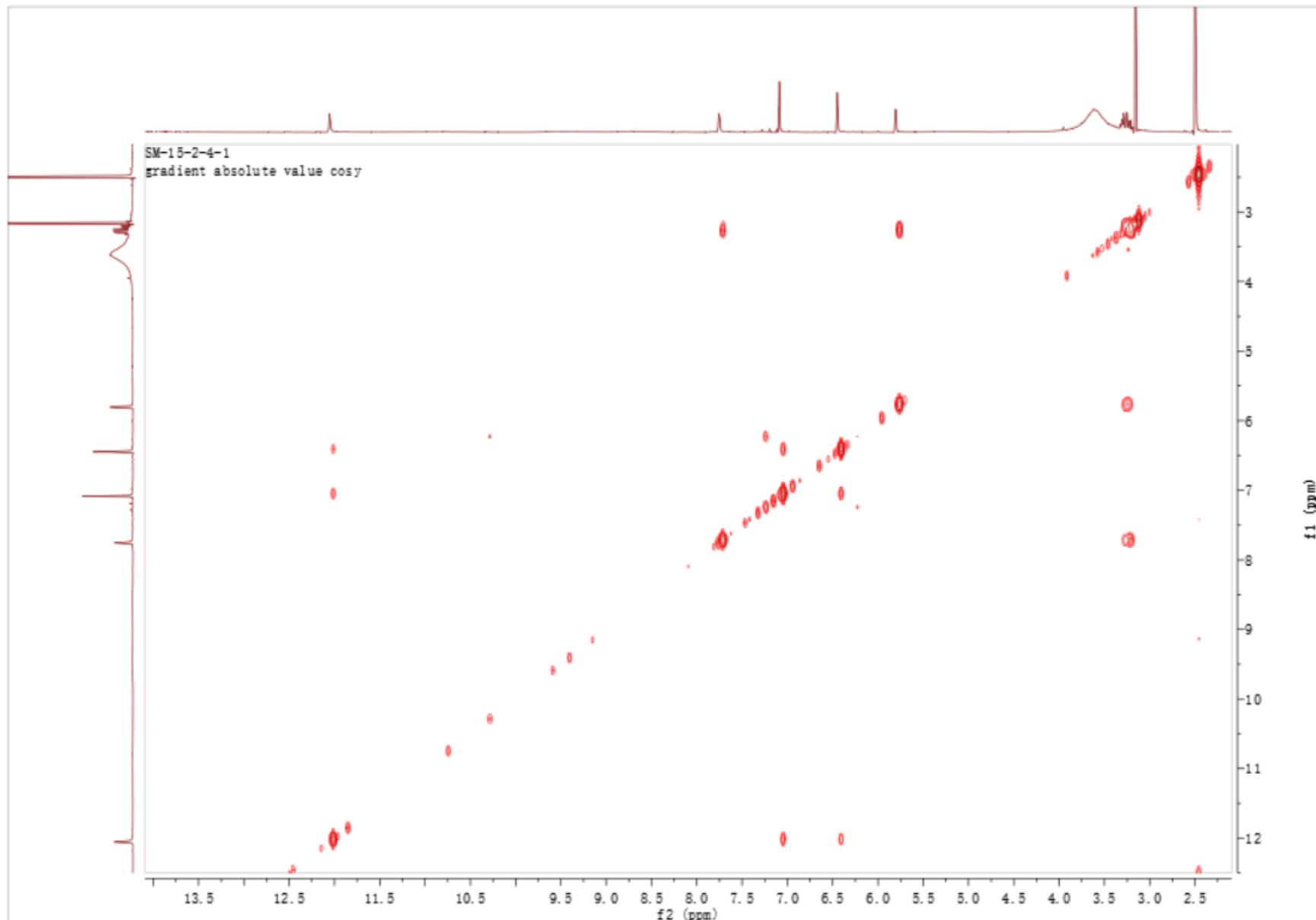


Figure S36. ^1H - ^1H COSY spectrum of compound 2 in $\text{DMSO}-d_6$ (500 MHz).

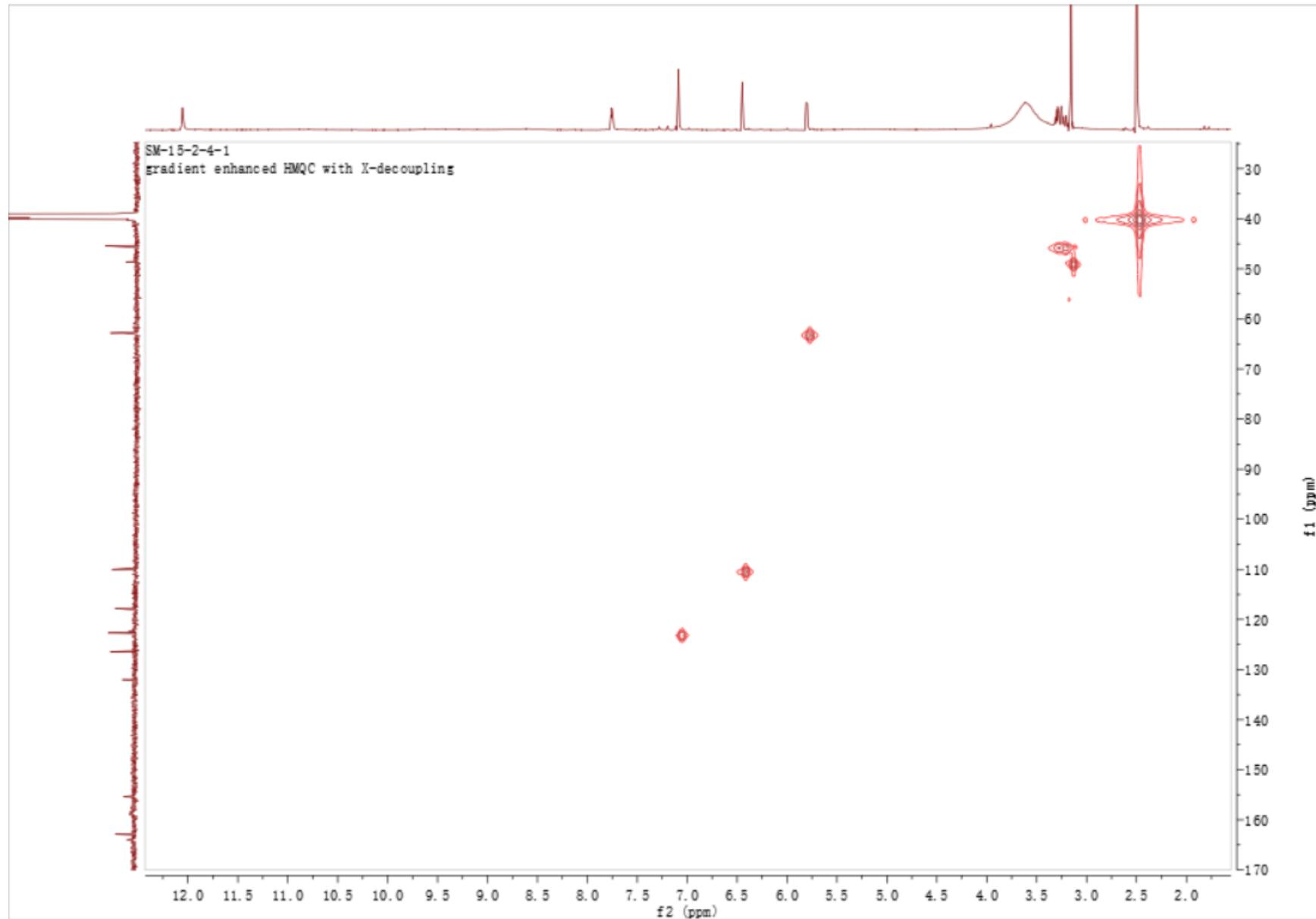


Figure S37. HSQC spectrum of compound **2** in $\text{DMSO}-d_6$ (500 MHz).

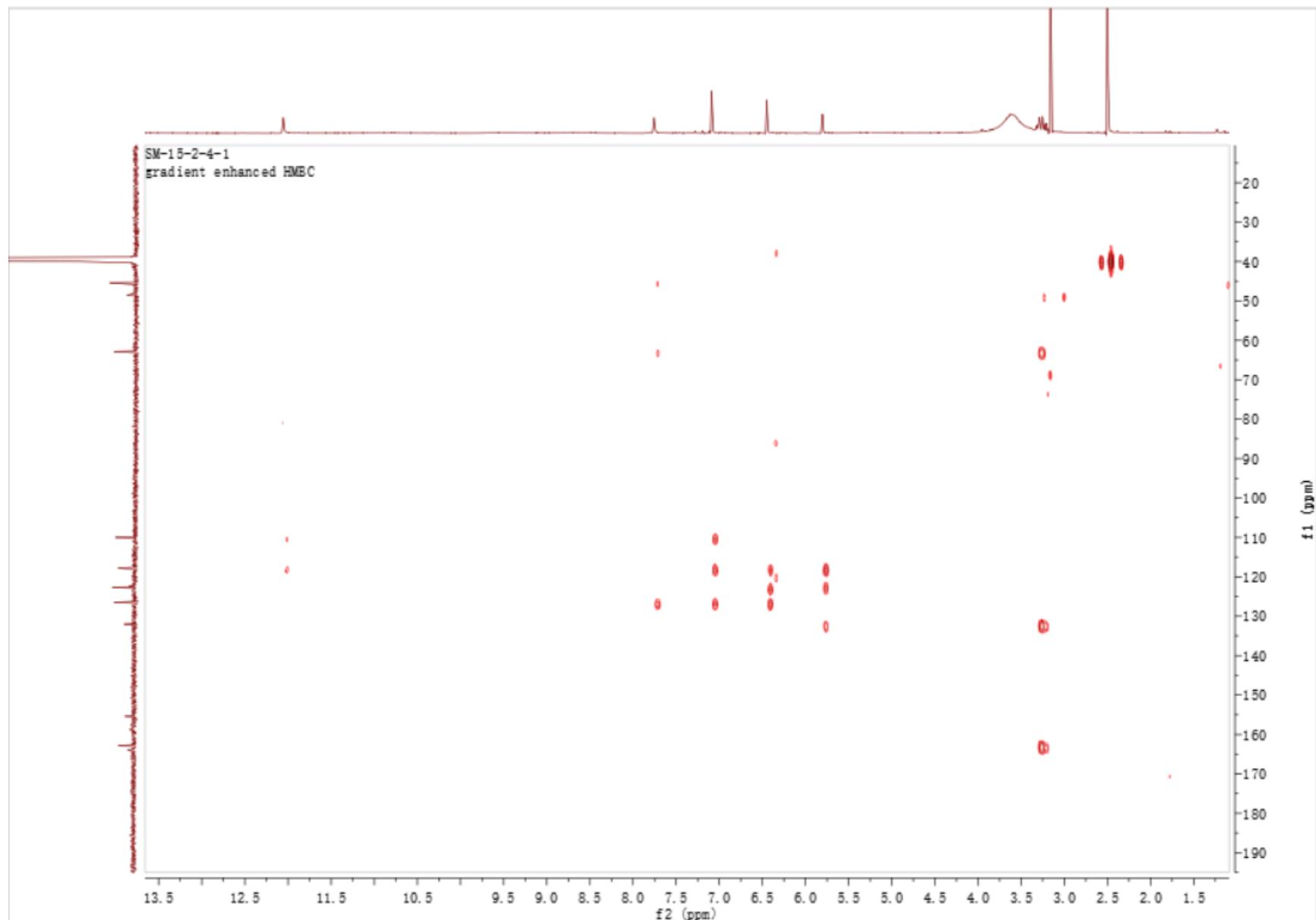


Figure S38. HMBC spectrum of compound **2** in $\text{DMSO}-d_6$ (500 MHz).

20211008-SM-15-2-4-1_211008084545 #75 RT: 0.59 AV: 1 SB: 16 0.24-0.36 NL: 9.92E7
T: FTMS + p ESI Full ms [150.00-1000.00]

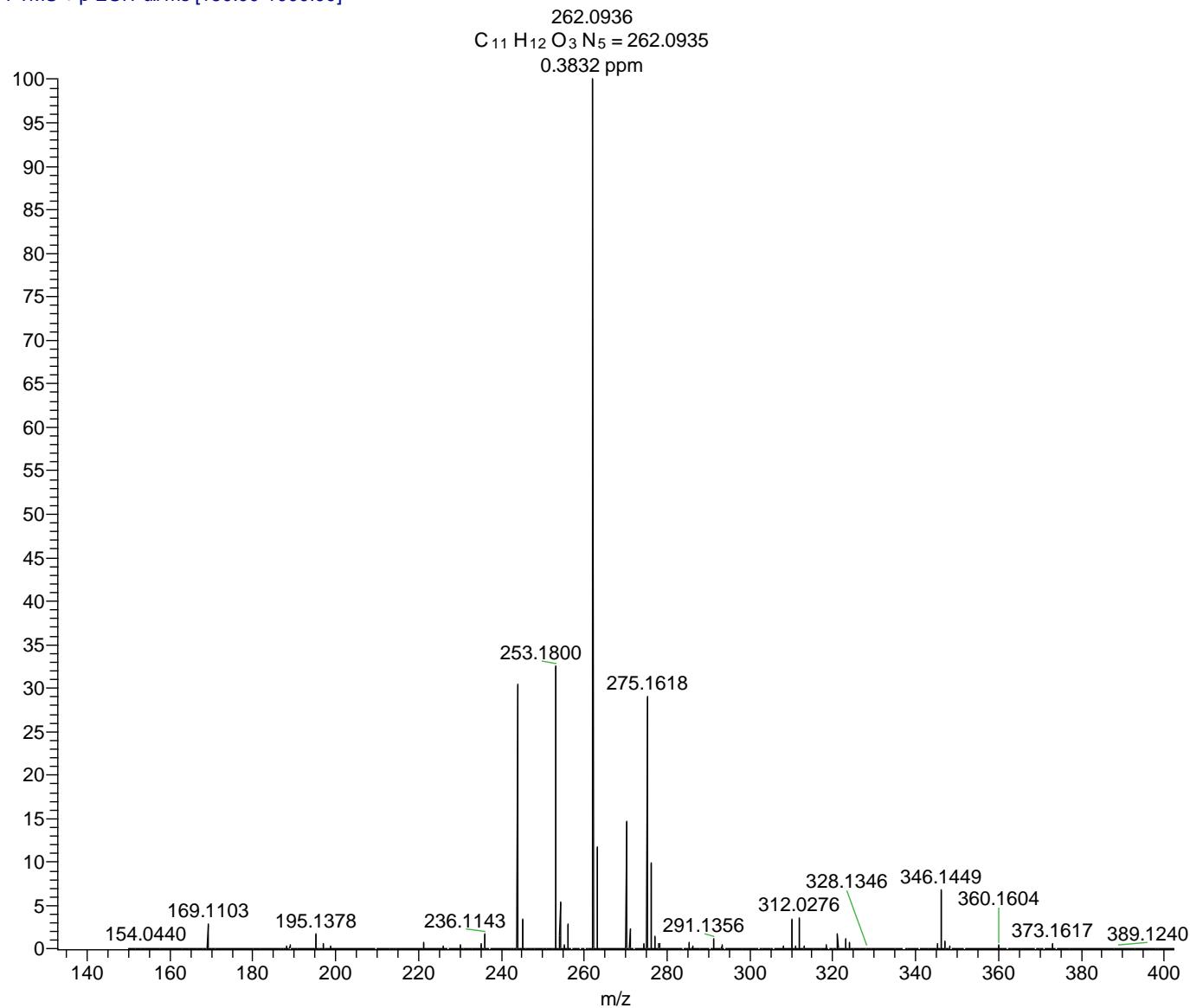


Figure S39. HRESIMS data of compound 2.

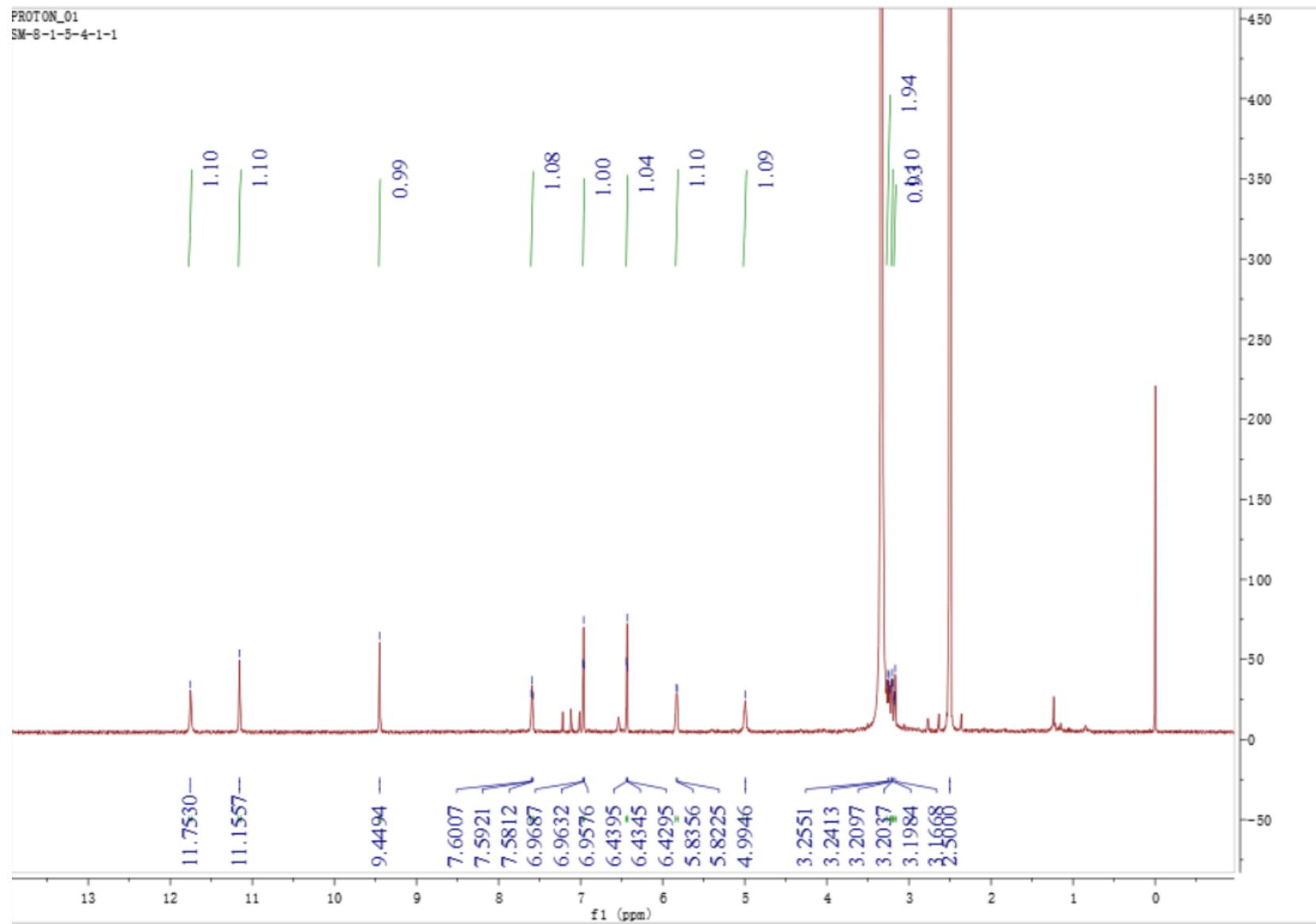


Figure S40. ^1H NMR spectrum of compound 3 in $\text{DMSO}-d_6$ (500 MHz).

CARBON_01
SM-8-1-5-4-1-1

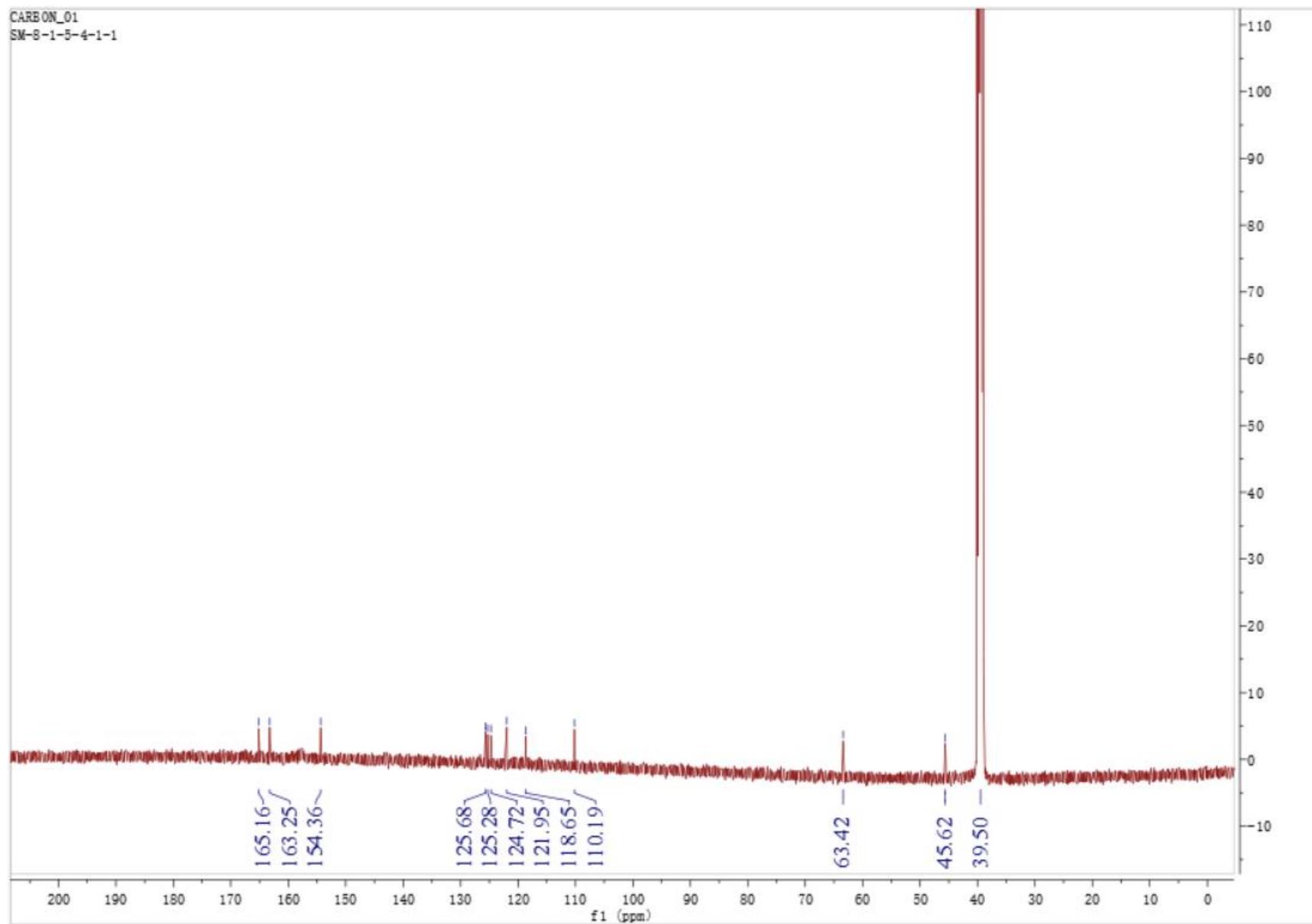
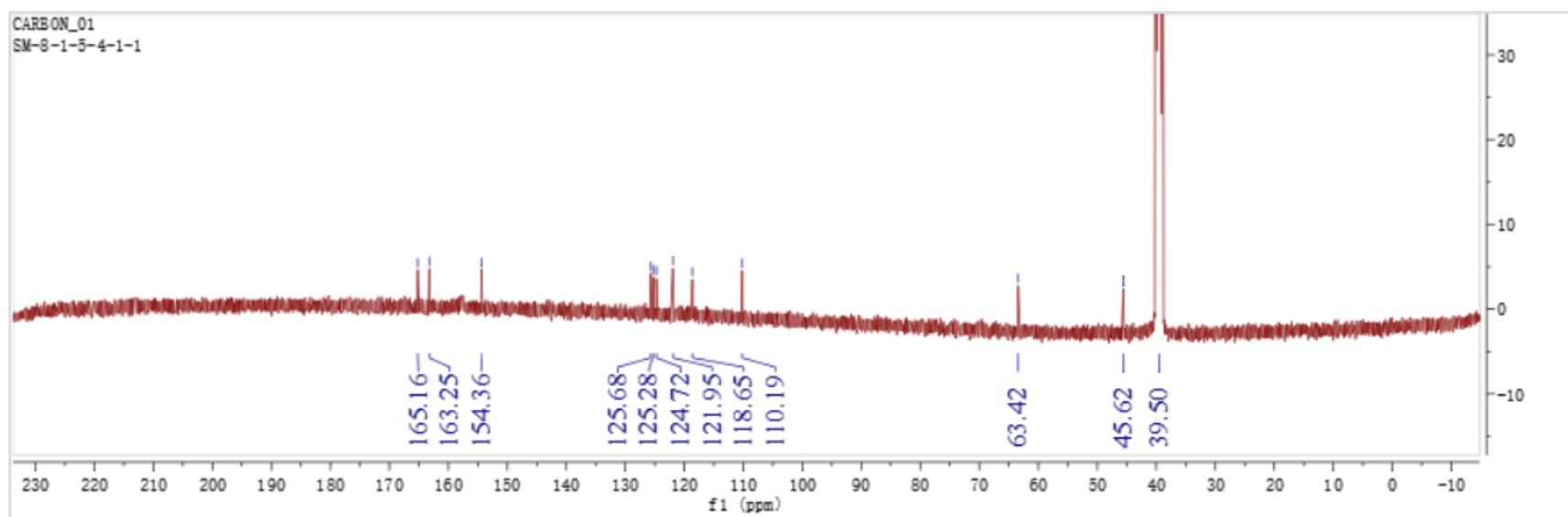


Figure S41. ¹³C NMR spectrum of compound 3 in DMSO-*d*₆ (125 MHz).

CARBON_01
SM-8-1-5-4-1-1



DEPT_01
SM-8-1-5-4-1-1

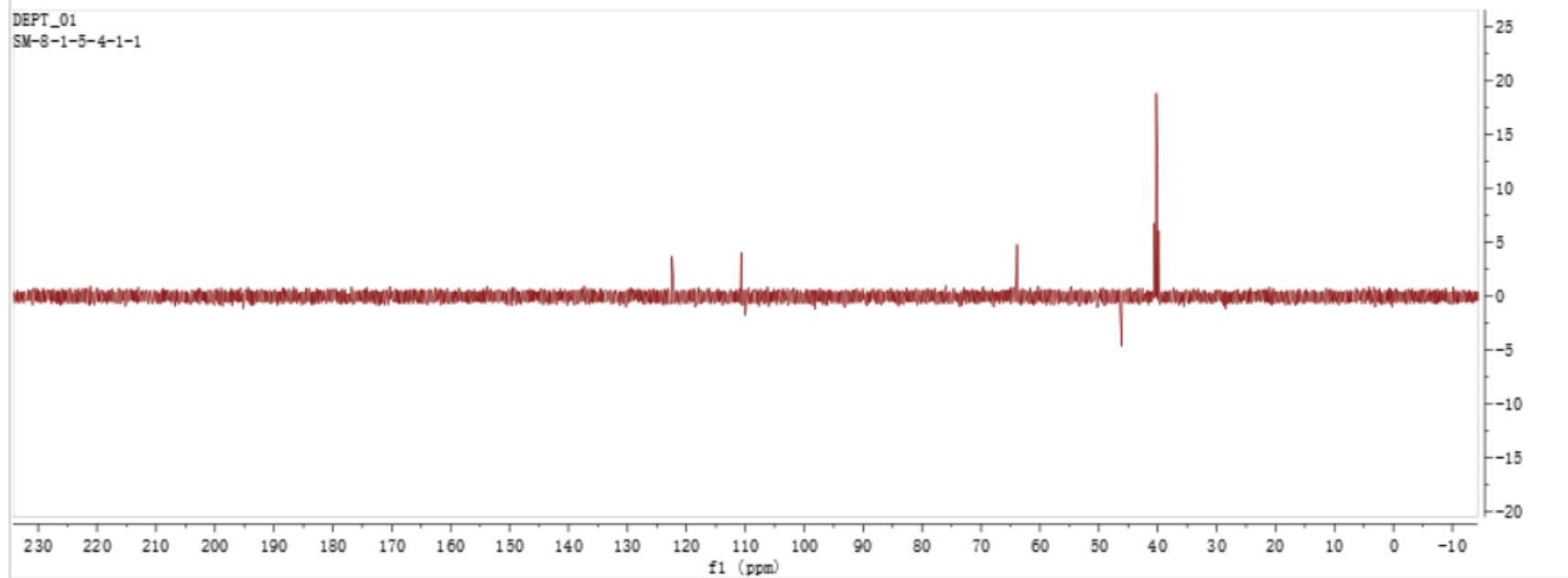


Figure S42. ¹³C NMR and DEPT spectrum of compound 3 in DMSO-*d*₆ (125 MHz).

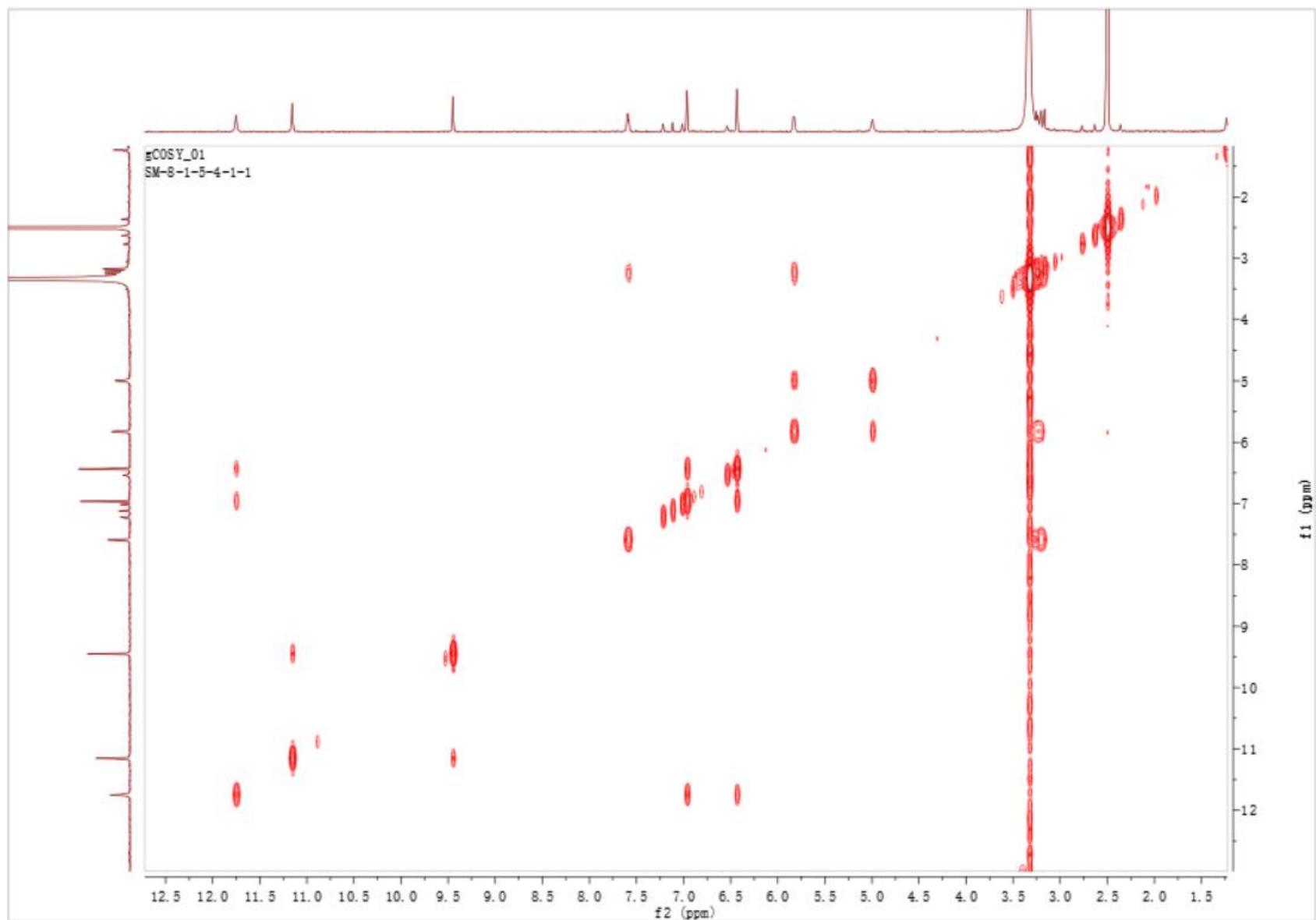


Figure S43. ^1H - ^1H COSY spectrum of compound **3** in $\text{DMSO}-d_6$ (500 MHz)

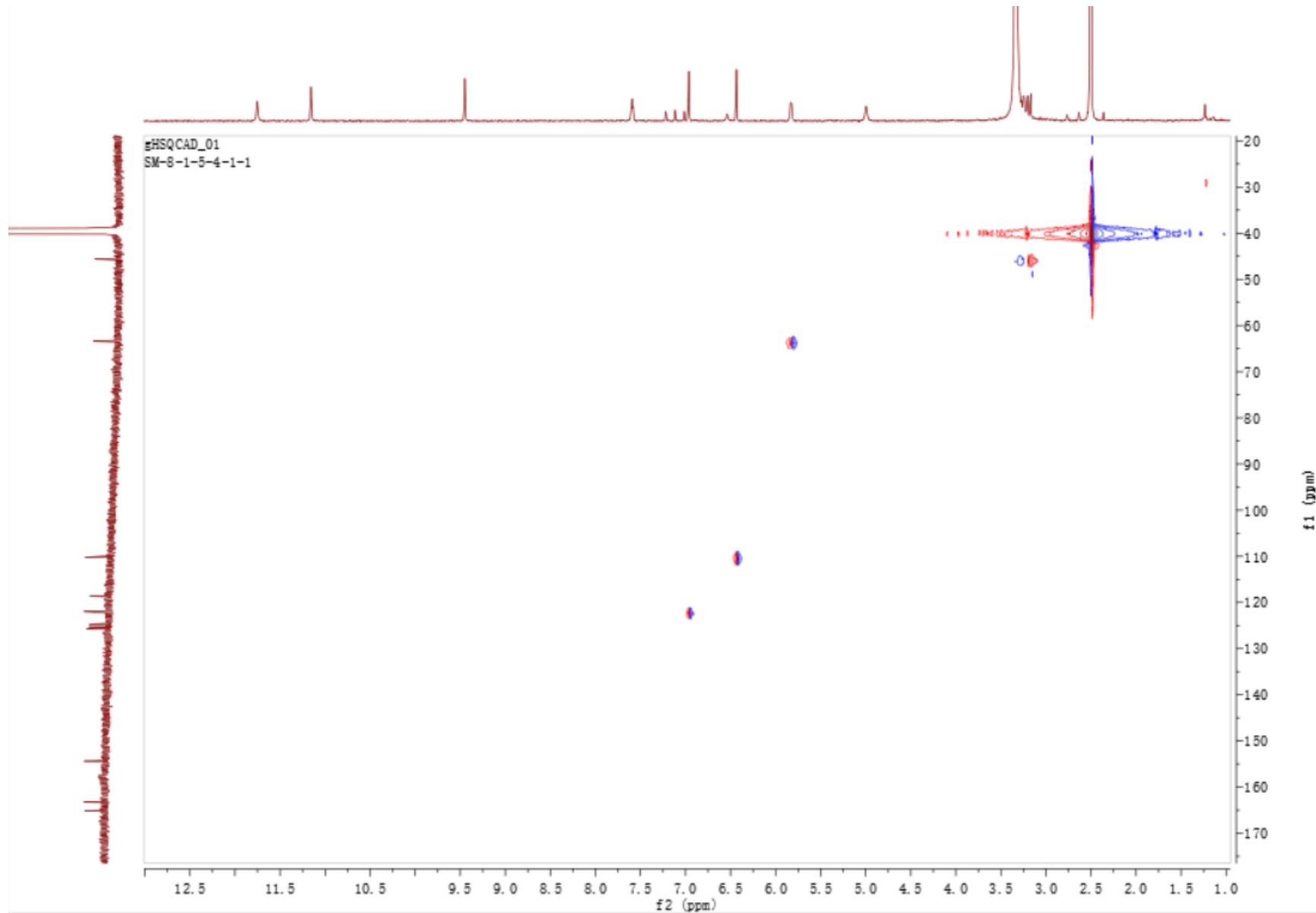


Figure S44. HSQC spectrum of compound **3** in $\text{DMSO}-d_6$ (500 MHz).

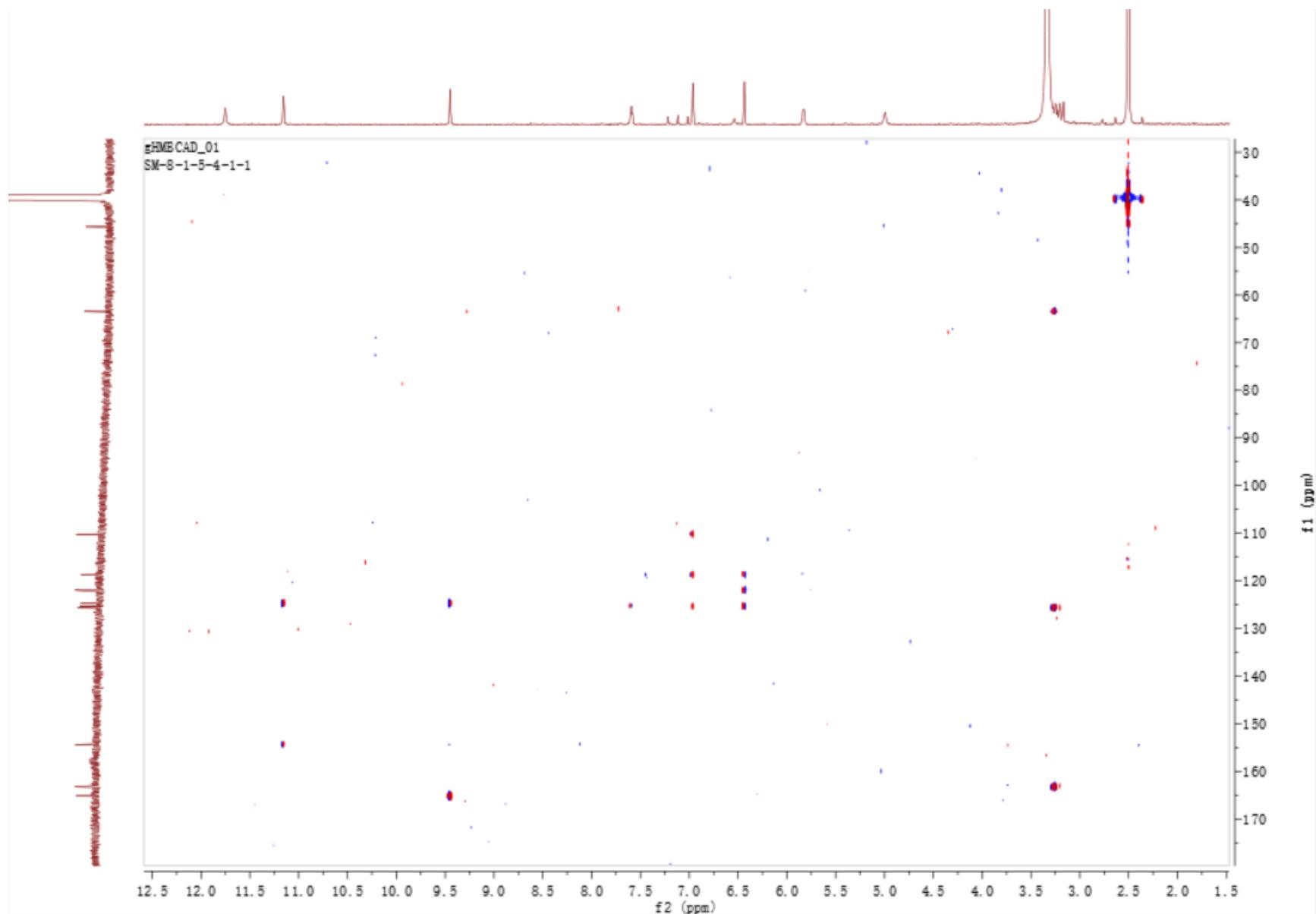


Figure S45. HMBC spectrum of compound **2** in DMSO-*d*₆ (500 MHz).

SM_815411 #356 RT: 0.25 AV: 1 NL: 1.97E7
T: FTMS + p ESI Full ms [200.0000-800.0000]

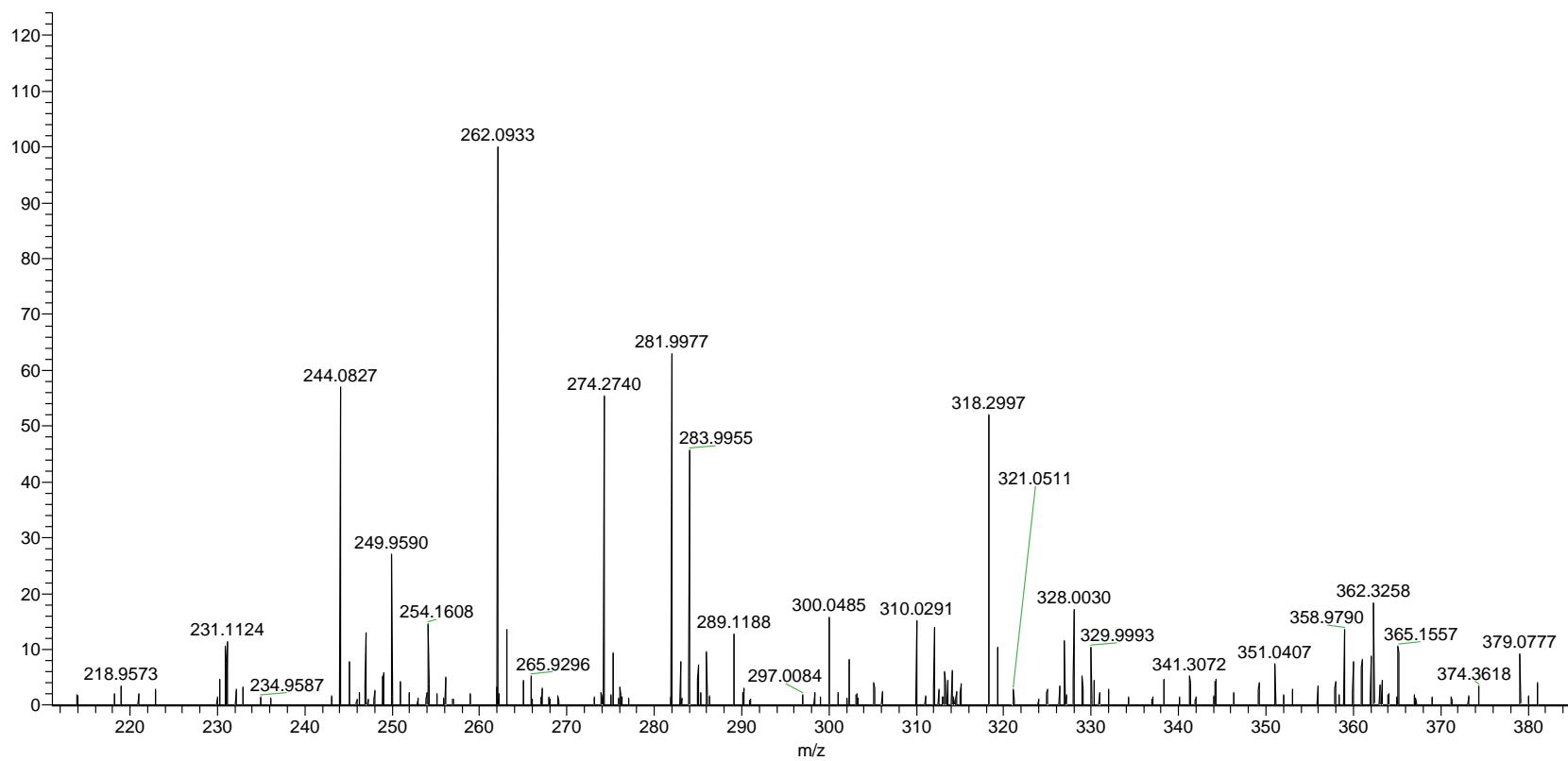


Figure S46. HRESIMS data of compound 3.

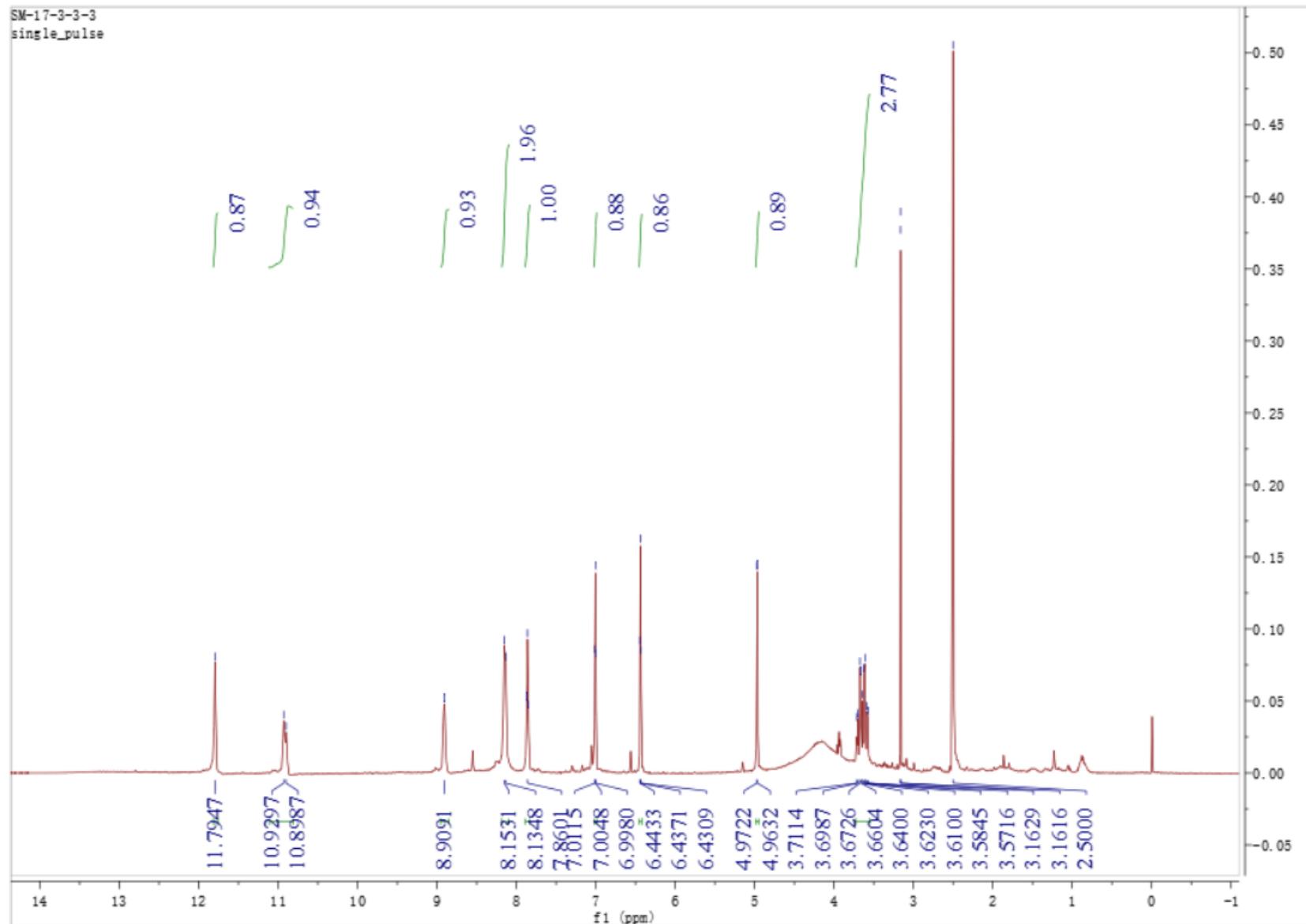


Figure S47. ^1H NMR spectrum of compound 4 in $\text{DMSO}-d_6$ (500 MHz)

CARBON_02
SM-17-3-3-3

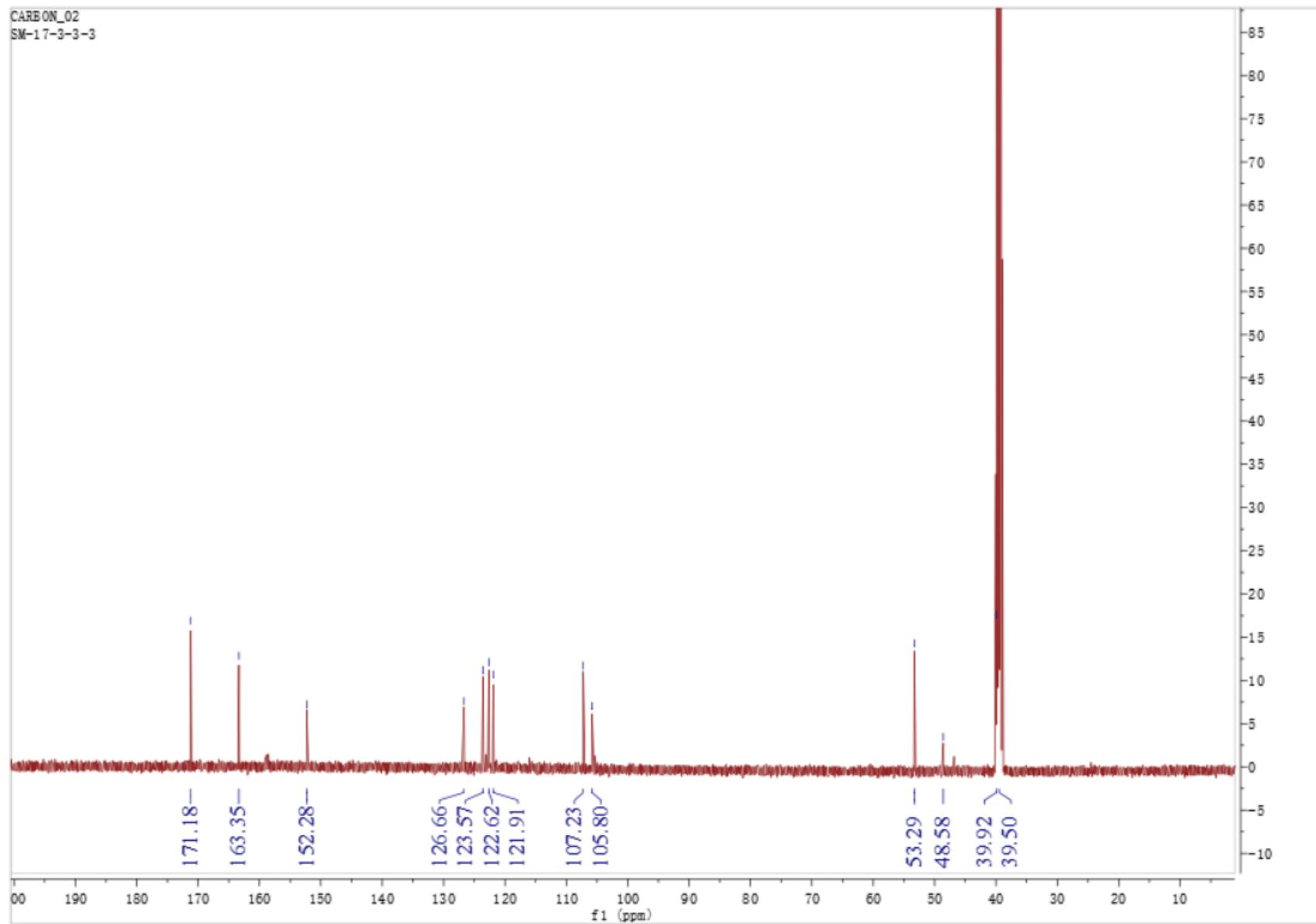


Figure S48. ¹³C NMR spectrum of compound 4 in DMSO-*d*₆ (125 MHz).

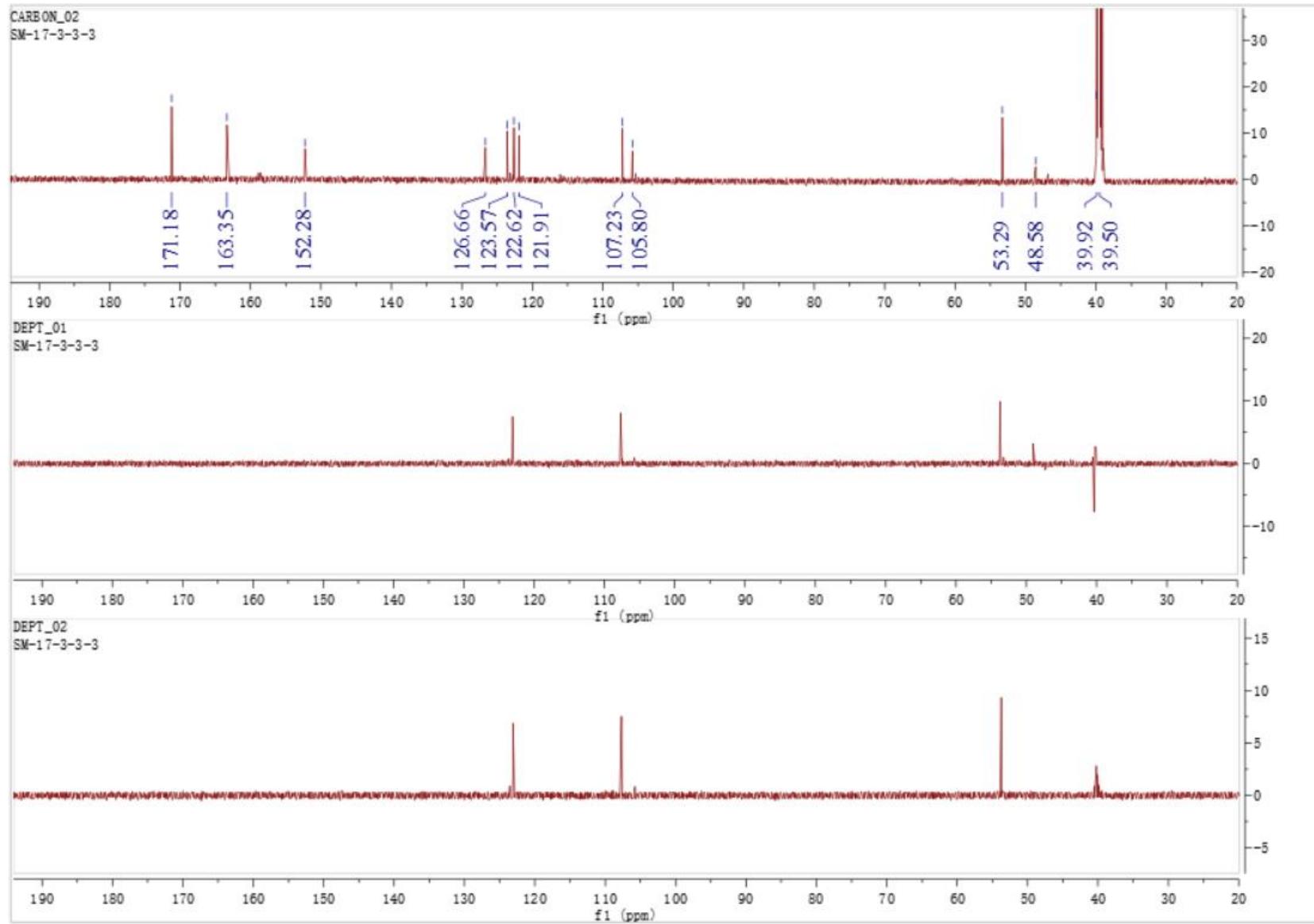


Figure S49. ^{13}C NMR and DEPT spectrum of compound 4 in $\text{DMSO}-d_6$ (125 MHz)

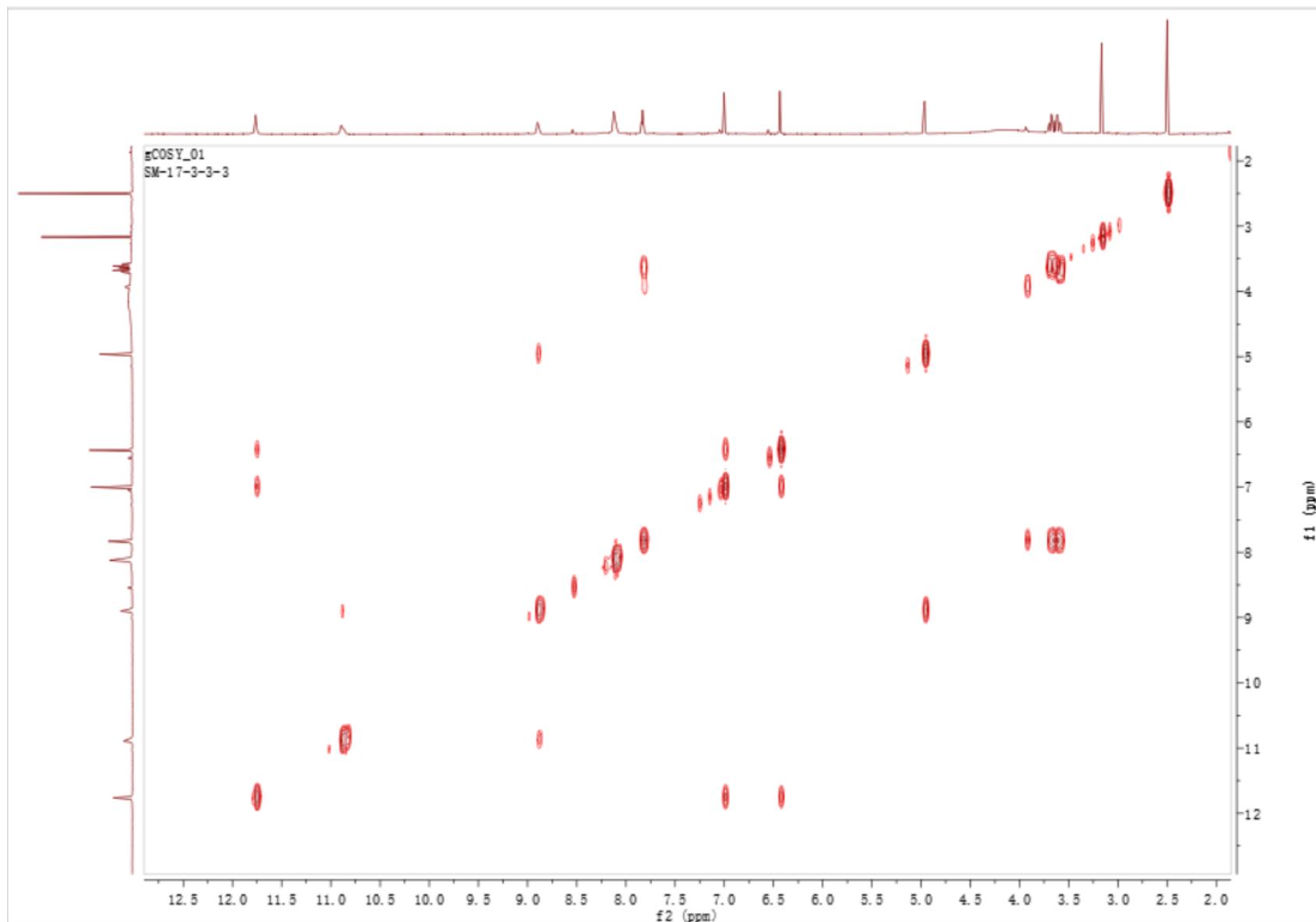
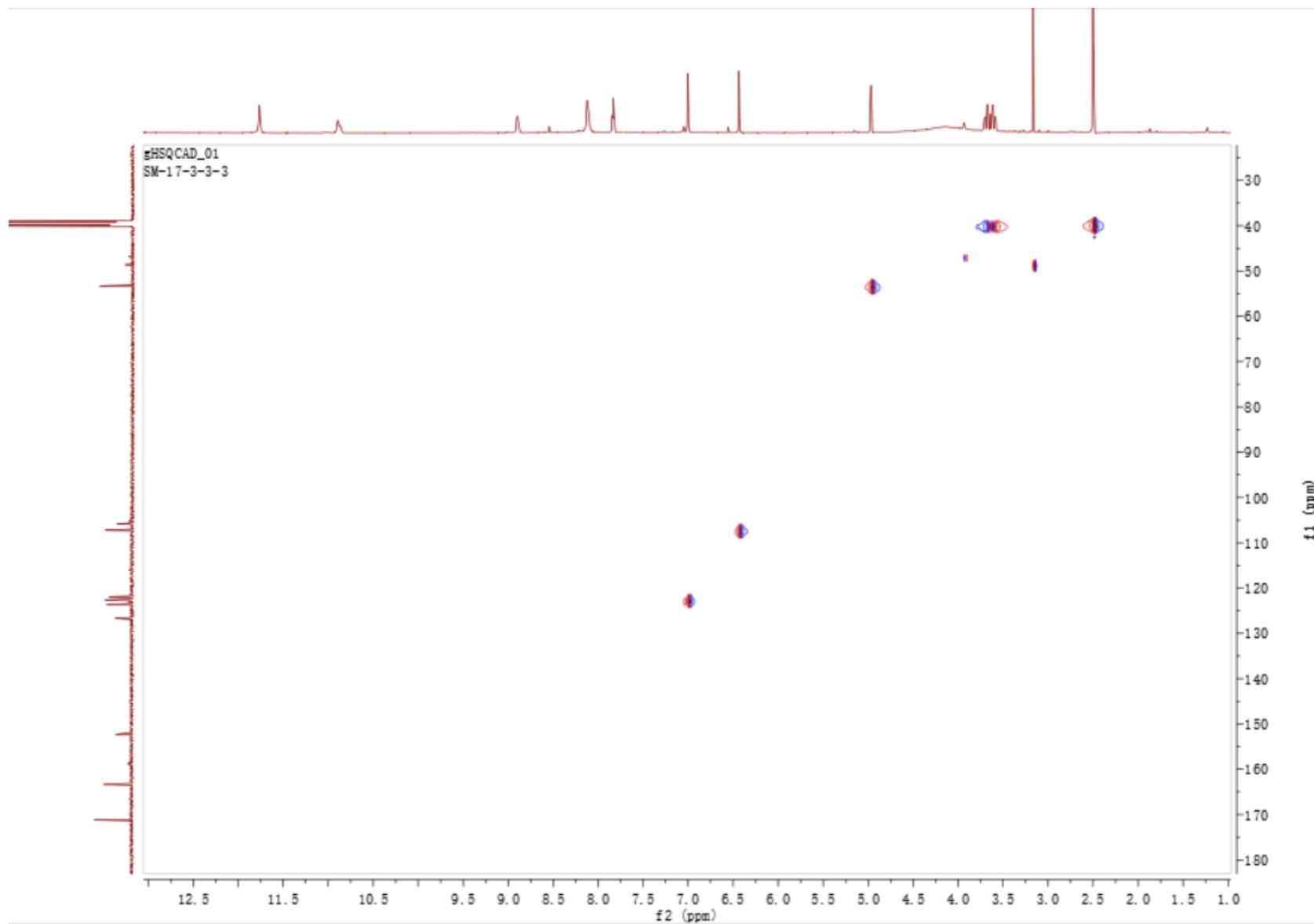


Figure S50. ^1H - ^1H COSY spectrum of compound 4 in $\text{DMSO}-d_6$ (500 MHz).



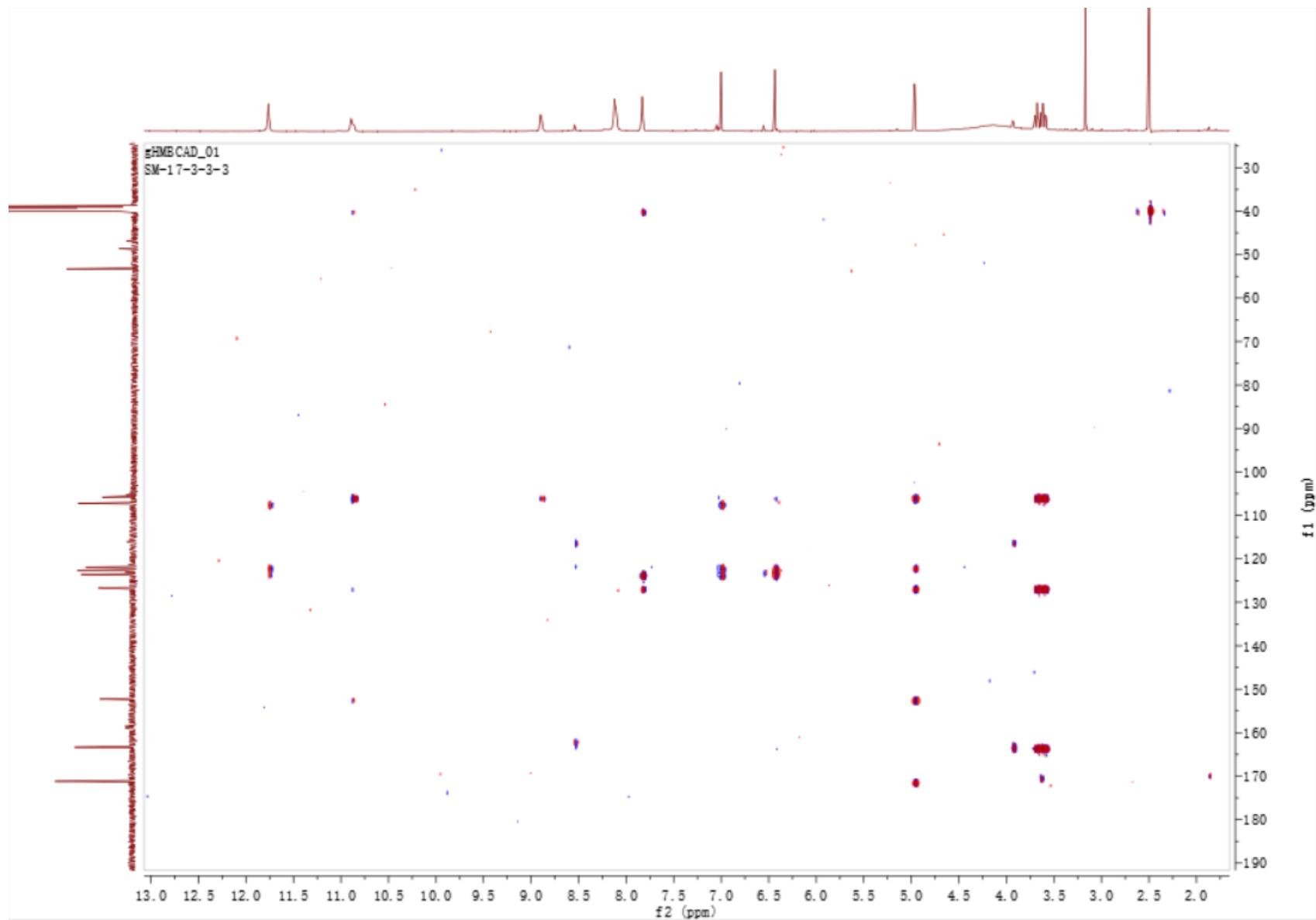


Figure S52. HMBC spectrum of compound 4 in $\text{DMSO}-d_6$ (500 MHz).

SM_17_333 #481 RT: 0.35 AV: 1 NL: 1.06E8
T: FTMS + p ESI Full ms [250.0000-800.0000]

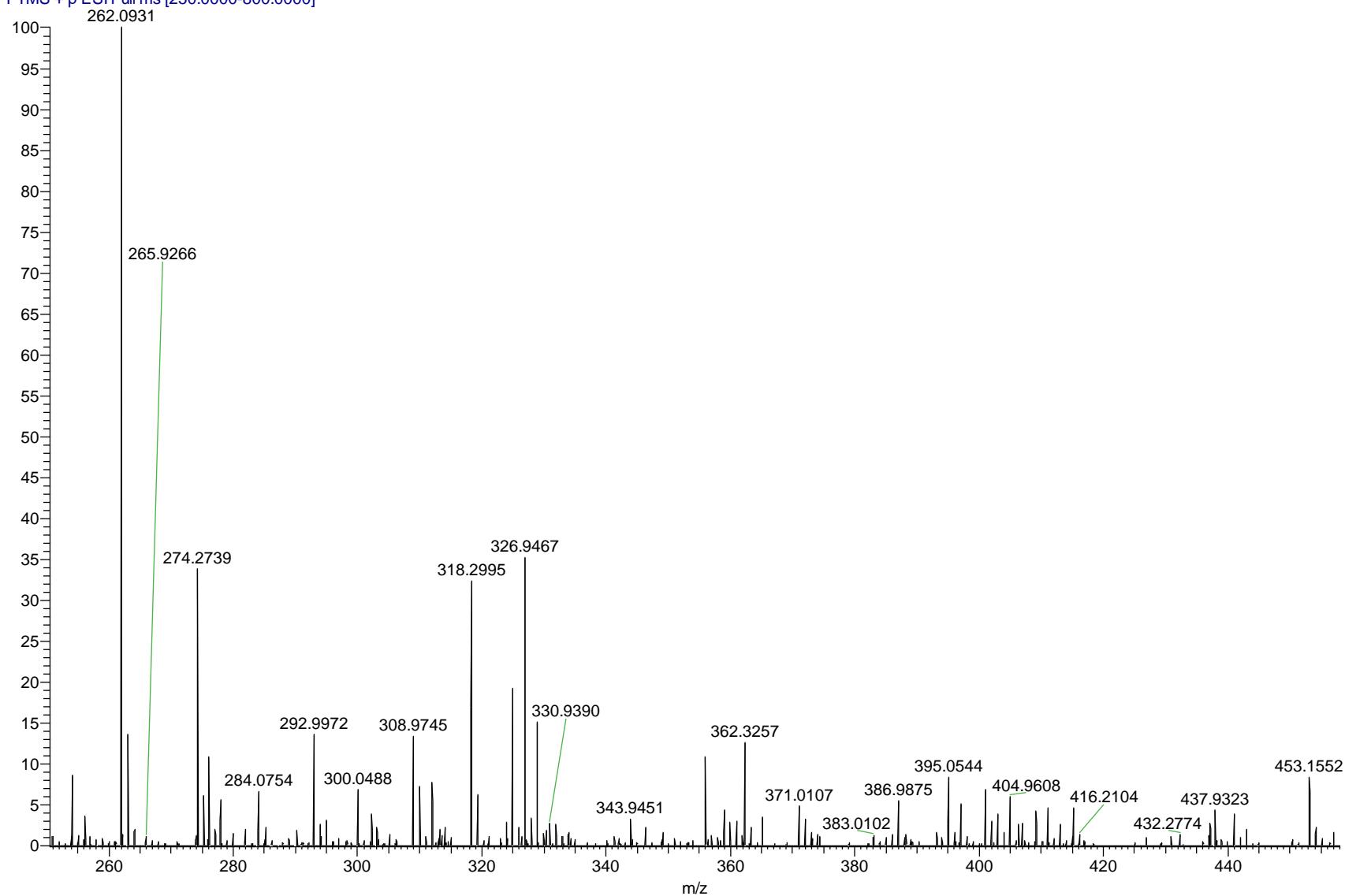


Figure S53. HRESIMS data of compound 4.

PROTON_01
SM-8-1-5-4-4

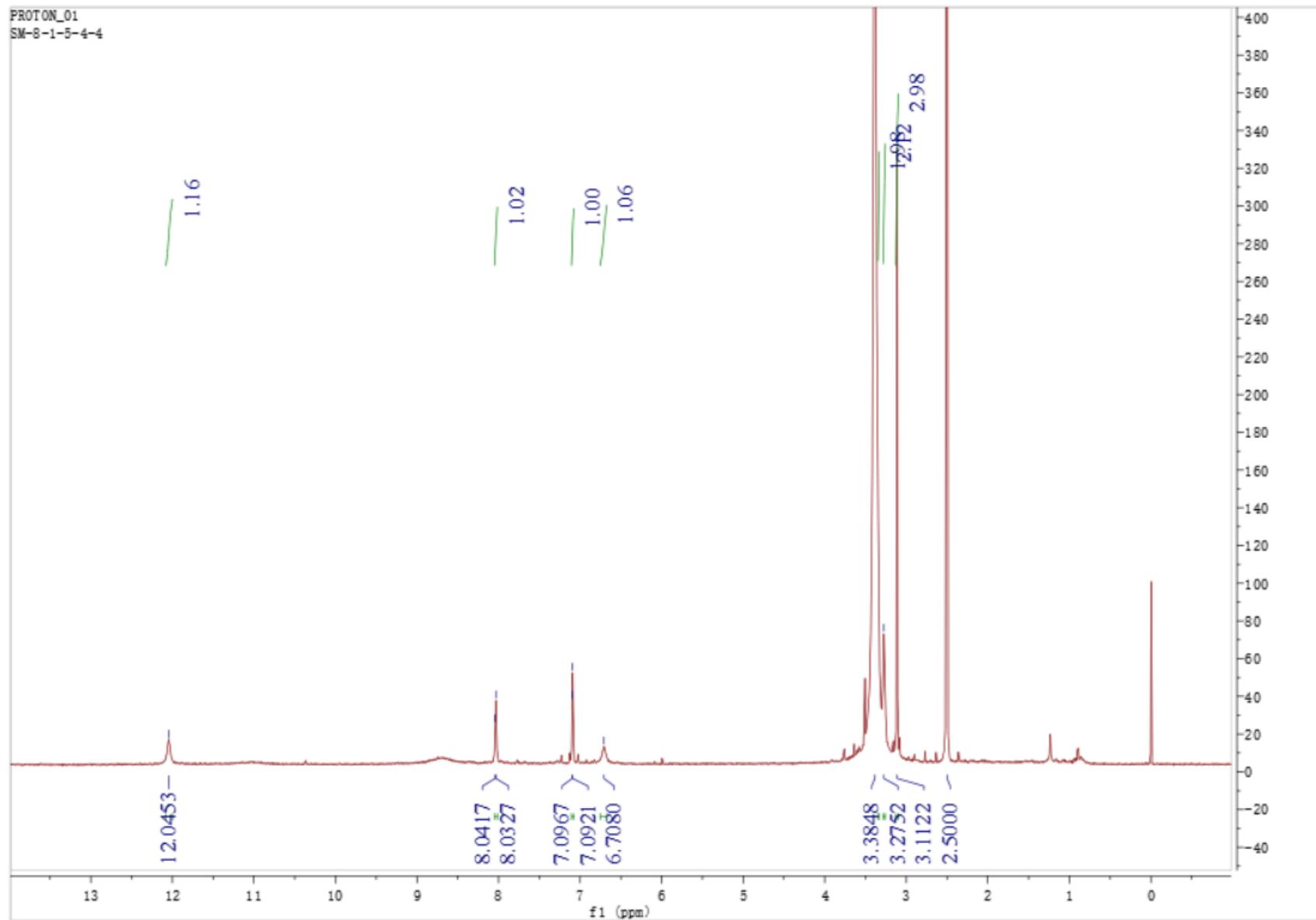


Figure S54. ^1H NMR spectrum of compound 5 in $\text{DMSO}-d_6$ (500 MHz).

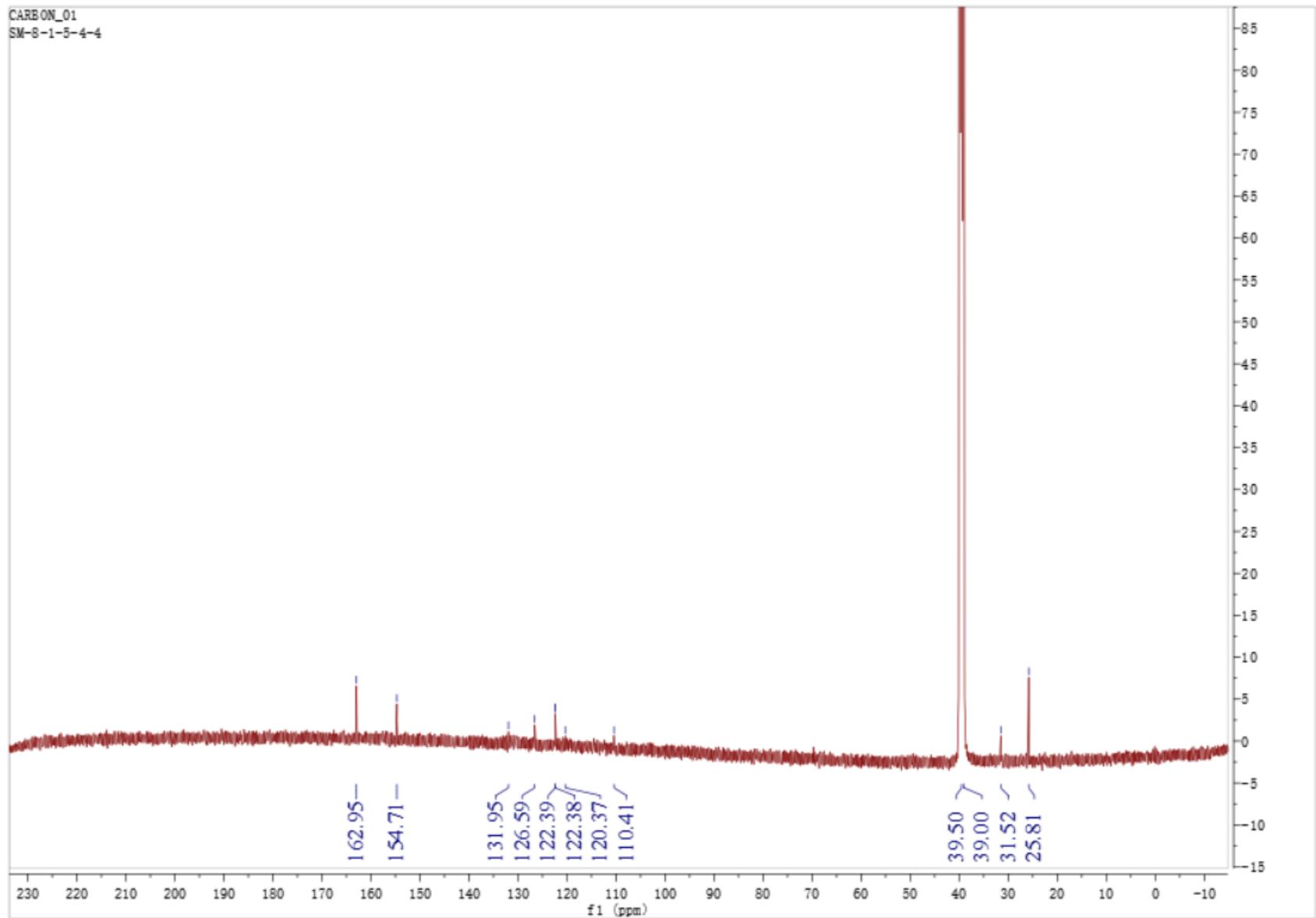


Figure S55. ¹³C NMR spectrum of compound 5 in DMSO-*d*₆ (125 MHz).

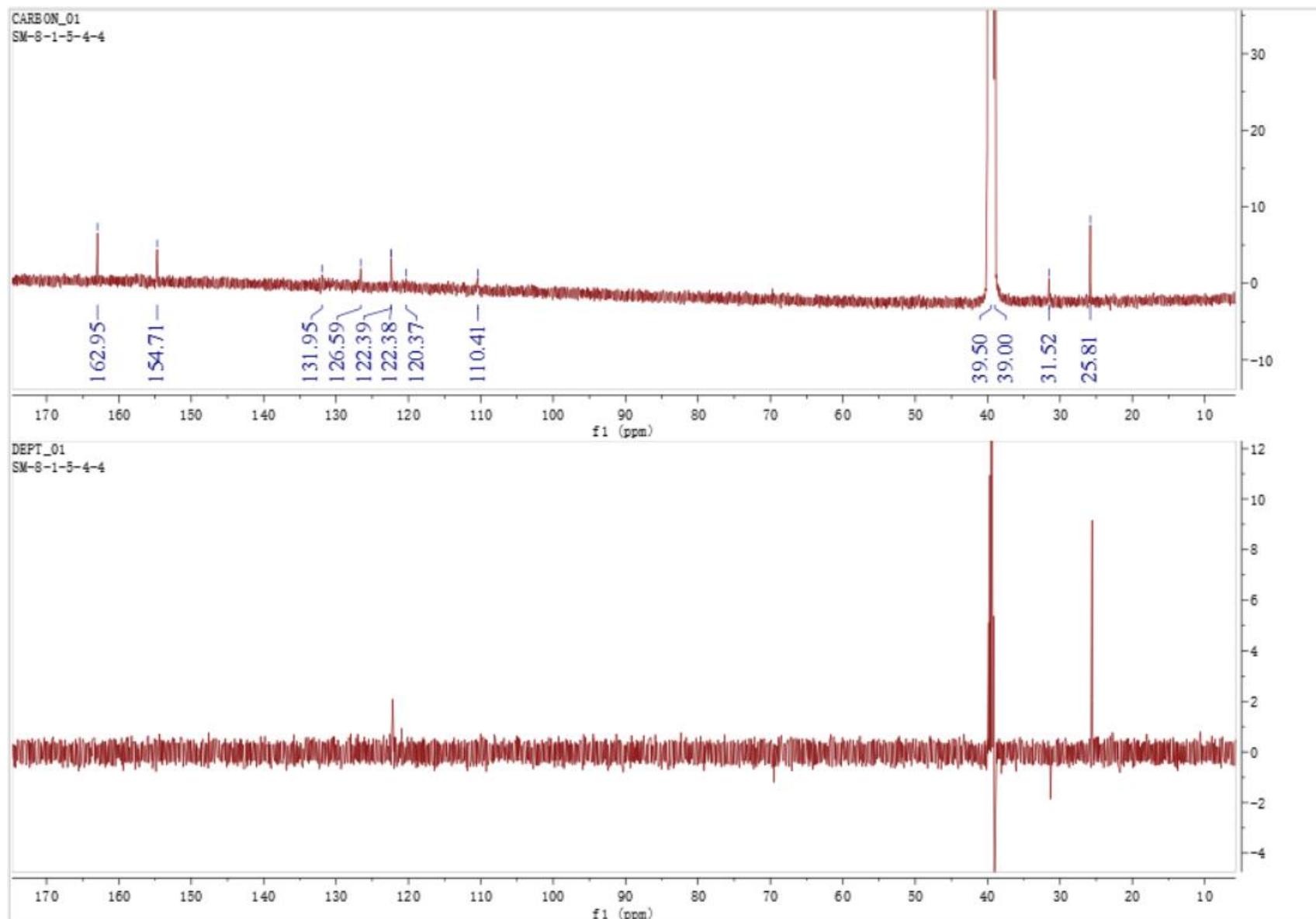


Figure S56. ^{13}C NMR and DEPT spectrum of compound **5** in $\text{DMSO}-d_6$ (125 MHz).

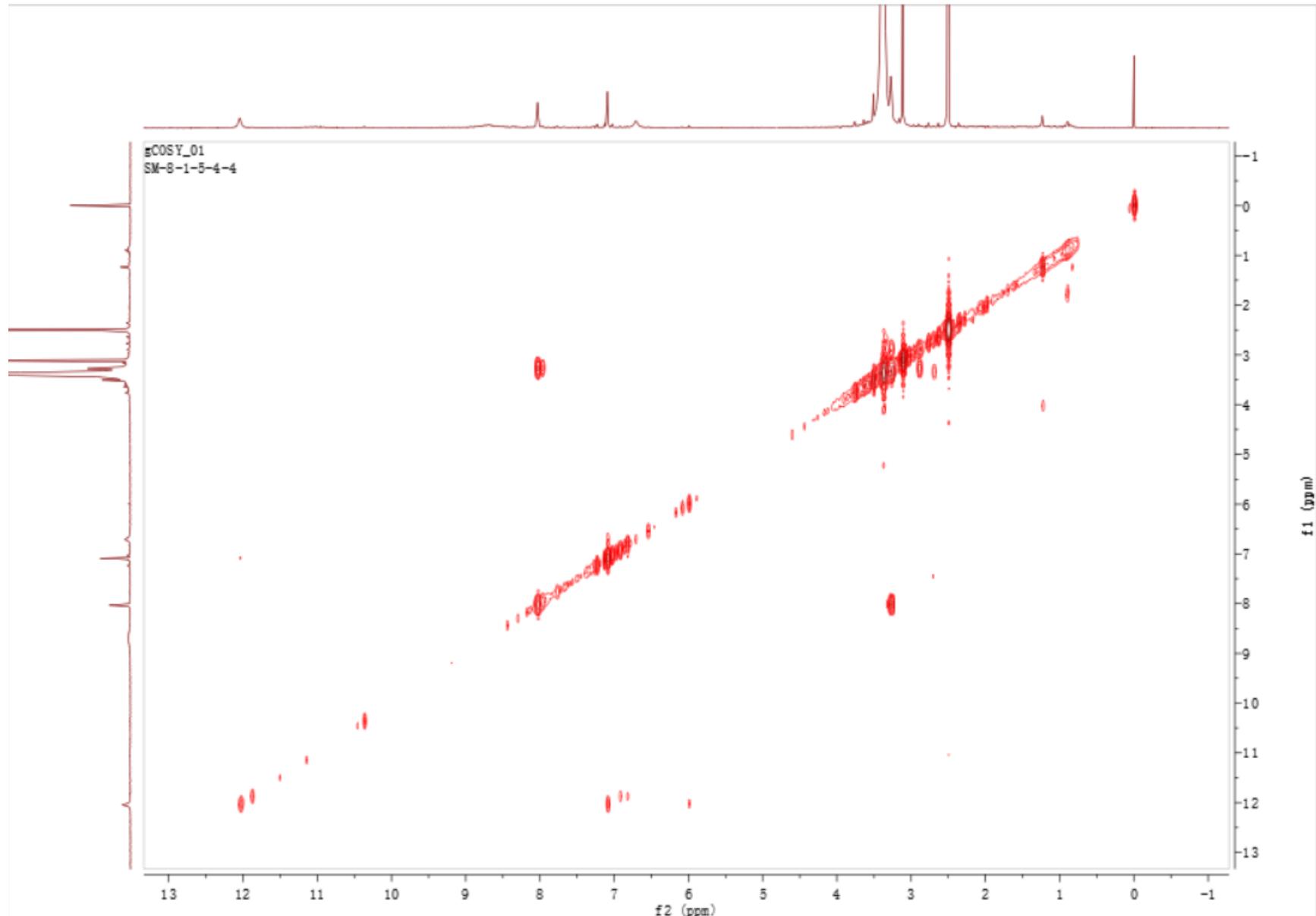


Figure S57. ^1H - ^1H COSY spectrum of compound **5** in $\text{DMSO}-d_6$ (500 MHz).

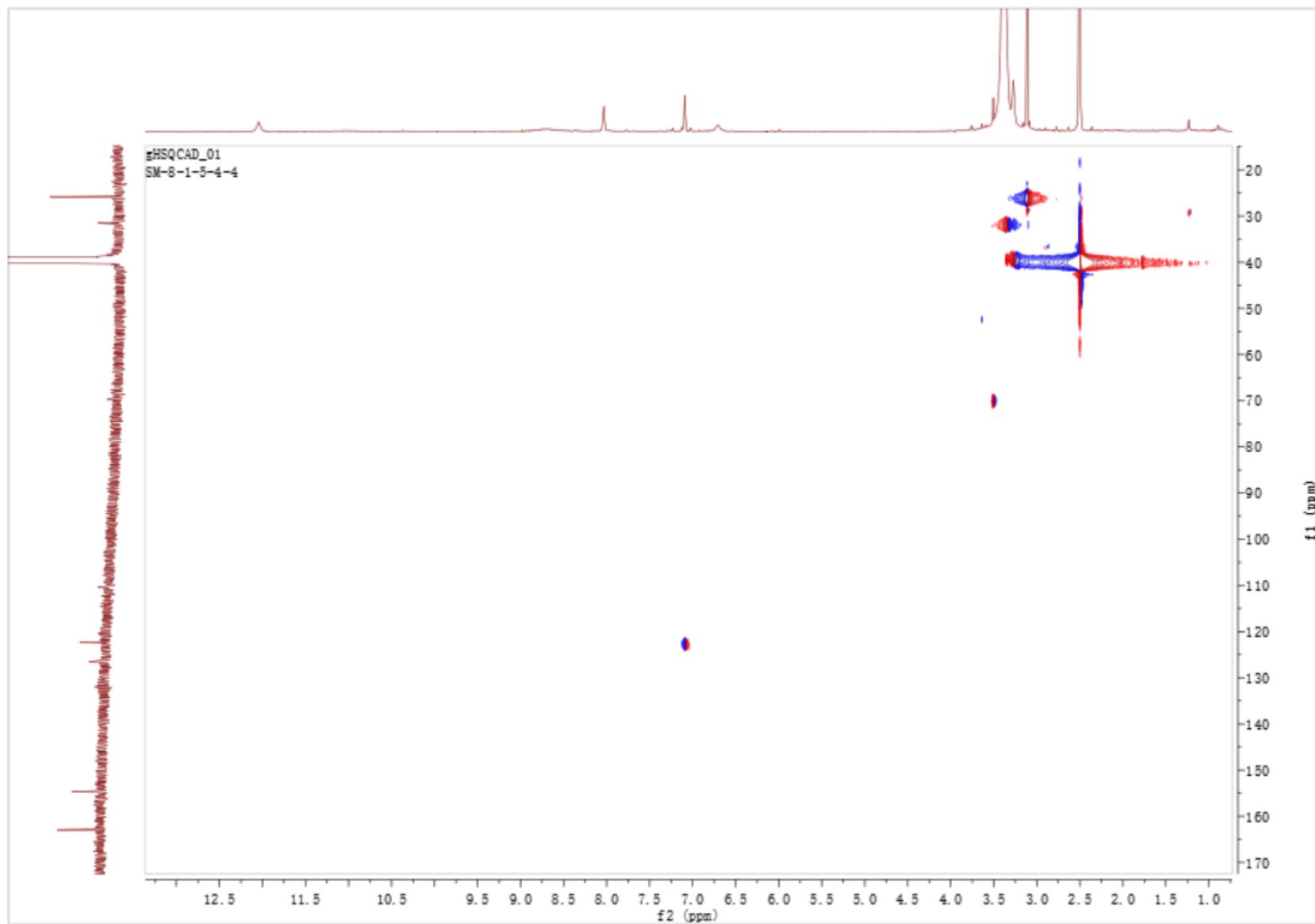


Figure S58. HSQC spectrum of compound 5 in $\text{DMSO}-d_6$ (500 MHz)

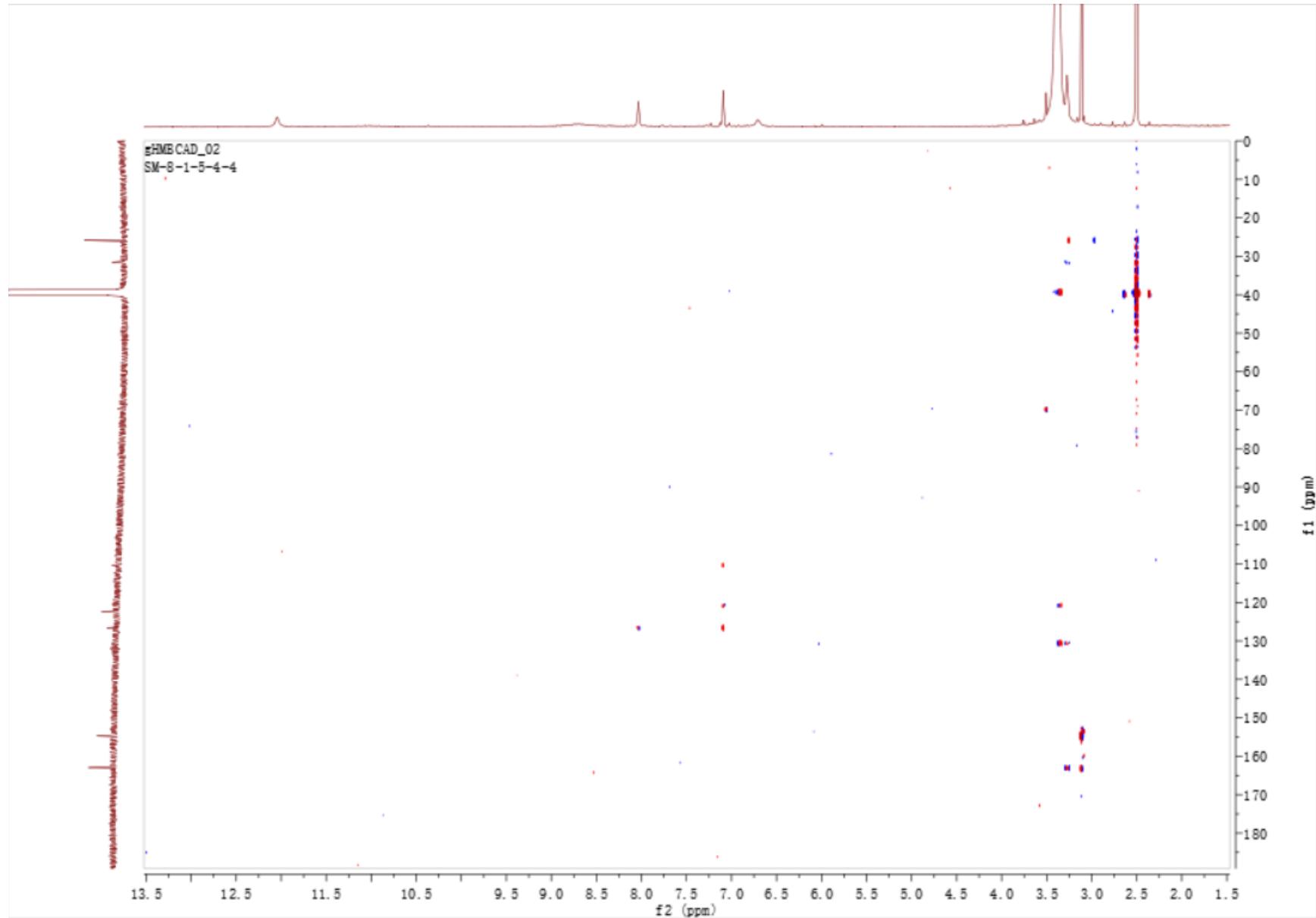


Figure S59. HMBC spectrum of compound **5** in $\text{DMSO}-d_6$ (500 MHz)

20210702-sm-8-1-5-4-4_210702084852 #18-19 RT: 0.14-0.15 AV: 2 NL: 2.37E7
T: FTMS + c ESI Full ms [150.00-2000.00]

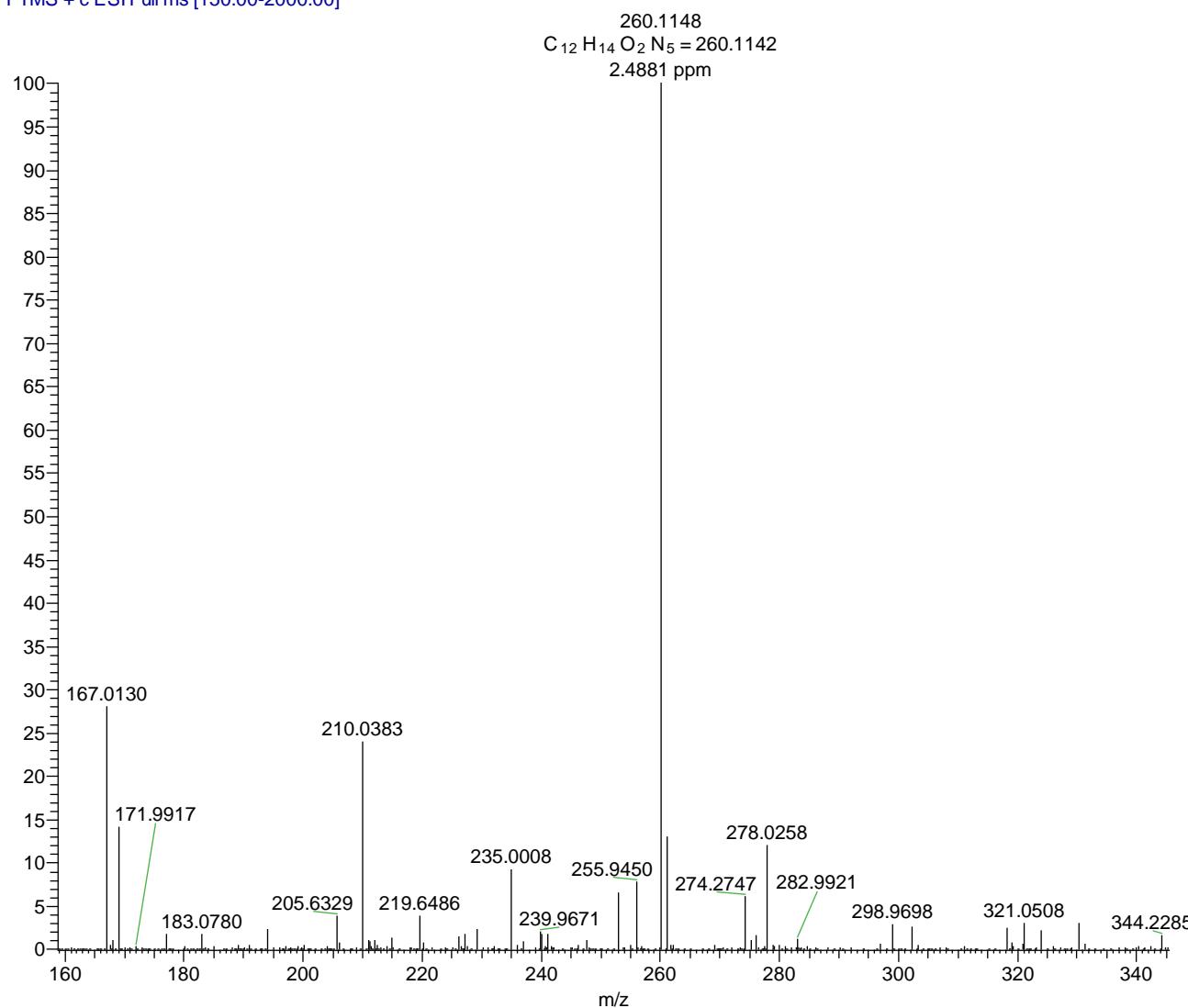


Figure S60. HRESIMS data of compound 5.

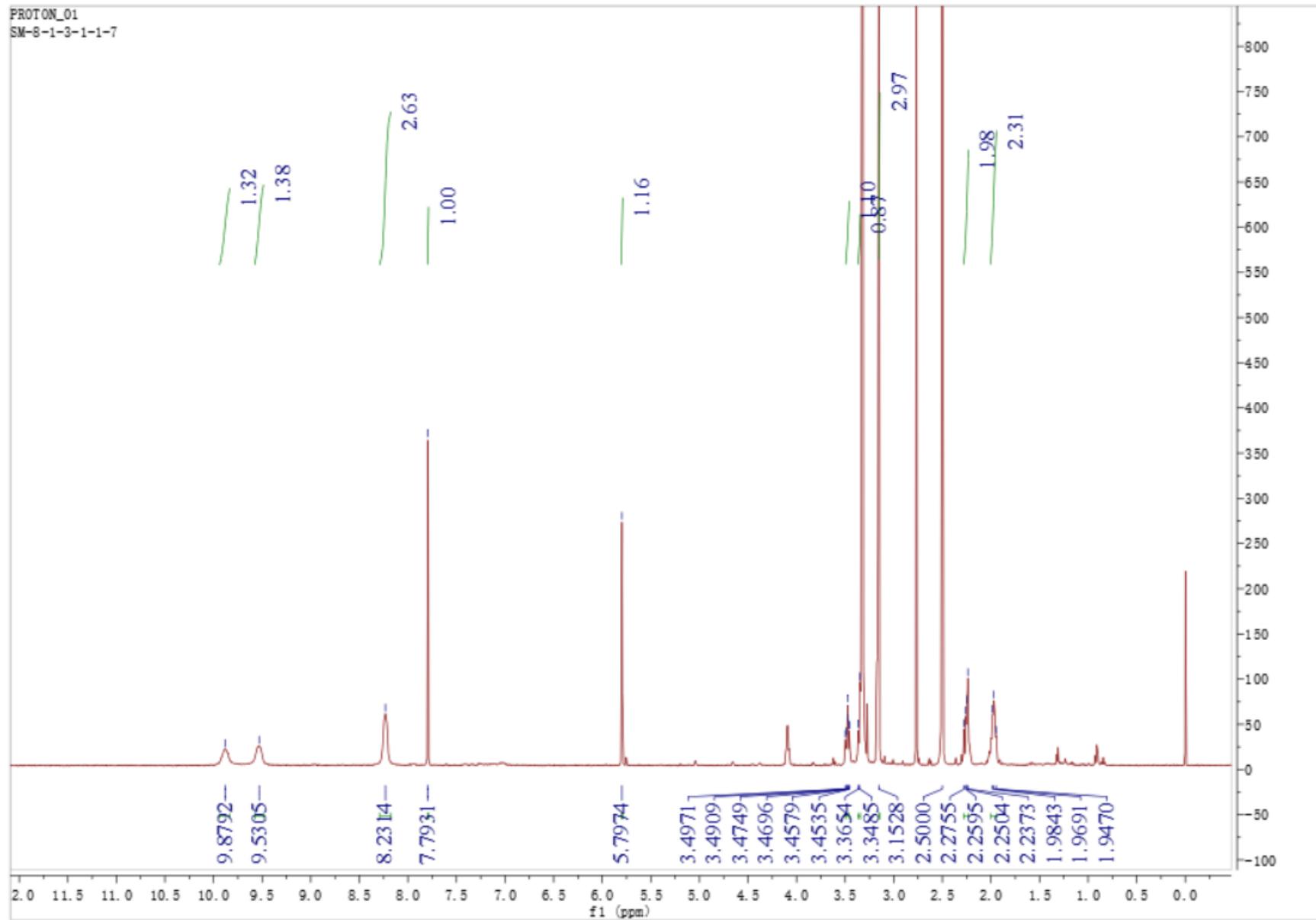


Figure S61. ^1H NMR spectrum of compound **6** in $\text{DMSO}-d_6$ (500 MHz).

CARBON_01
SM-8-1-3-1-1-7

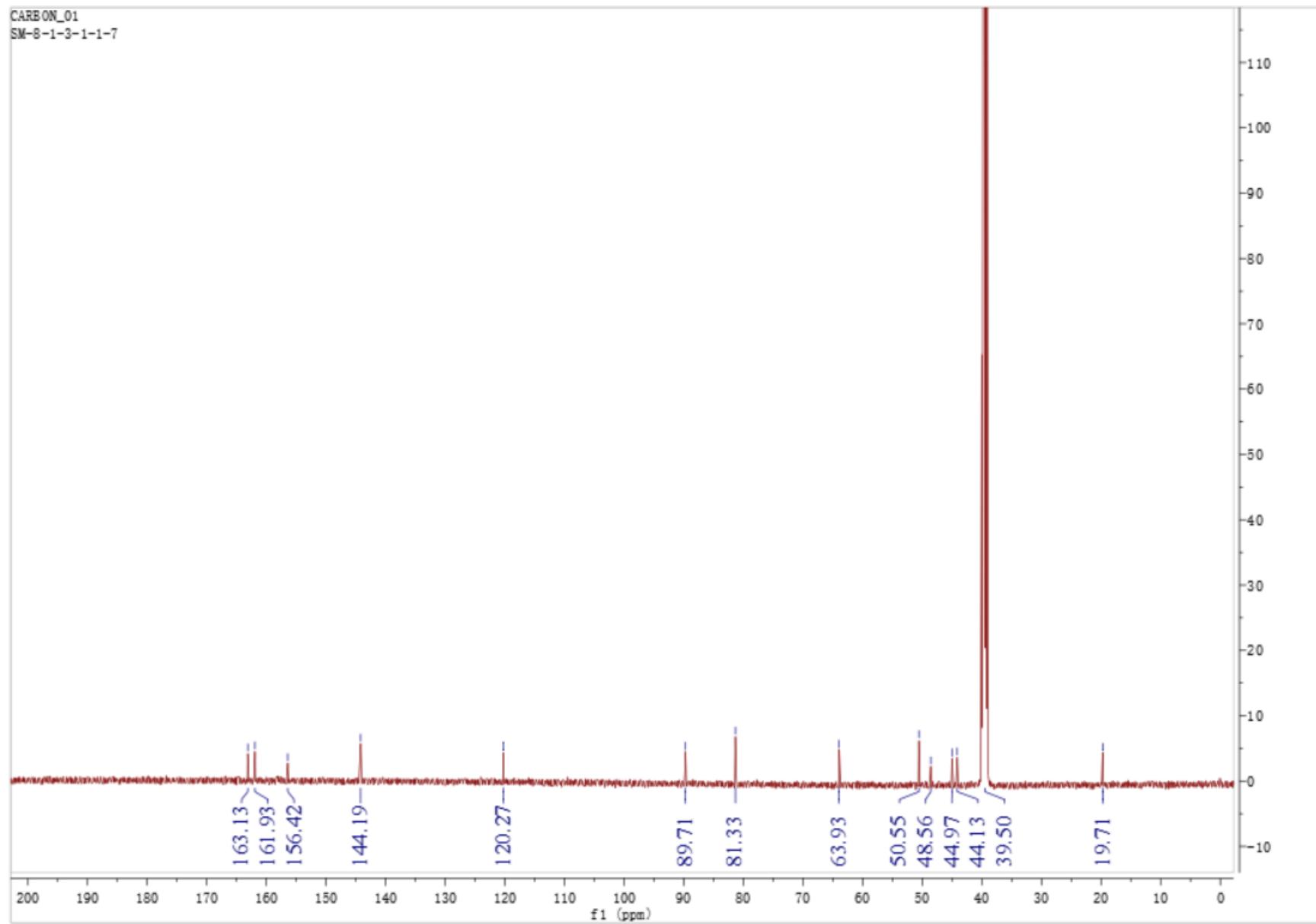


Figure S62. ¹³C NMR spectrum of compound 6 in DMSO-*d*₆ (125 MHz).

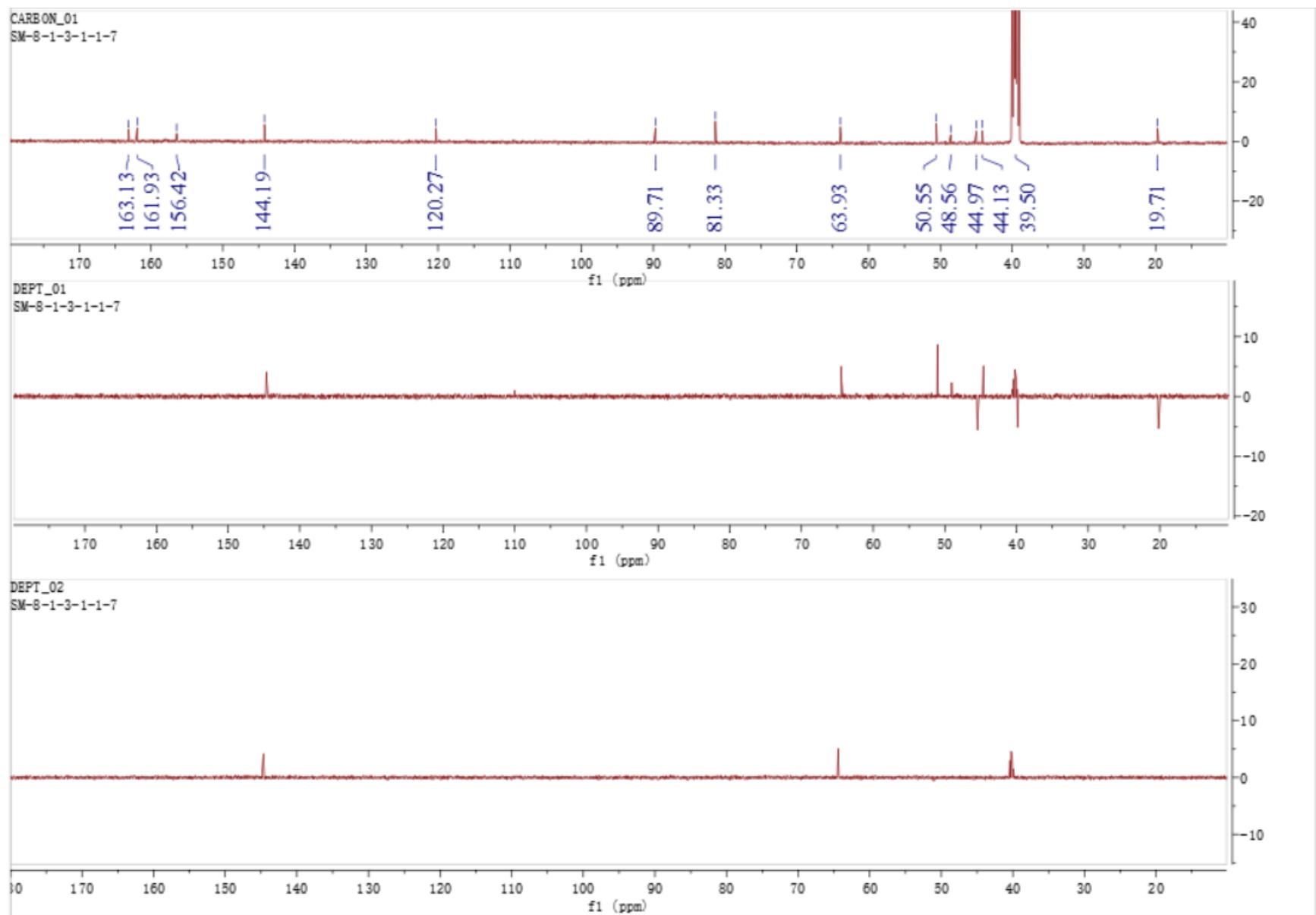


Figure S63. ^{13}C NMR and DEPT spectrum of compound **6** in $\text{DMSO}-d_6$ (125 MHz).

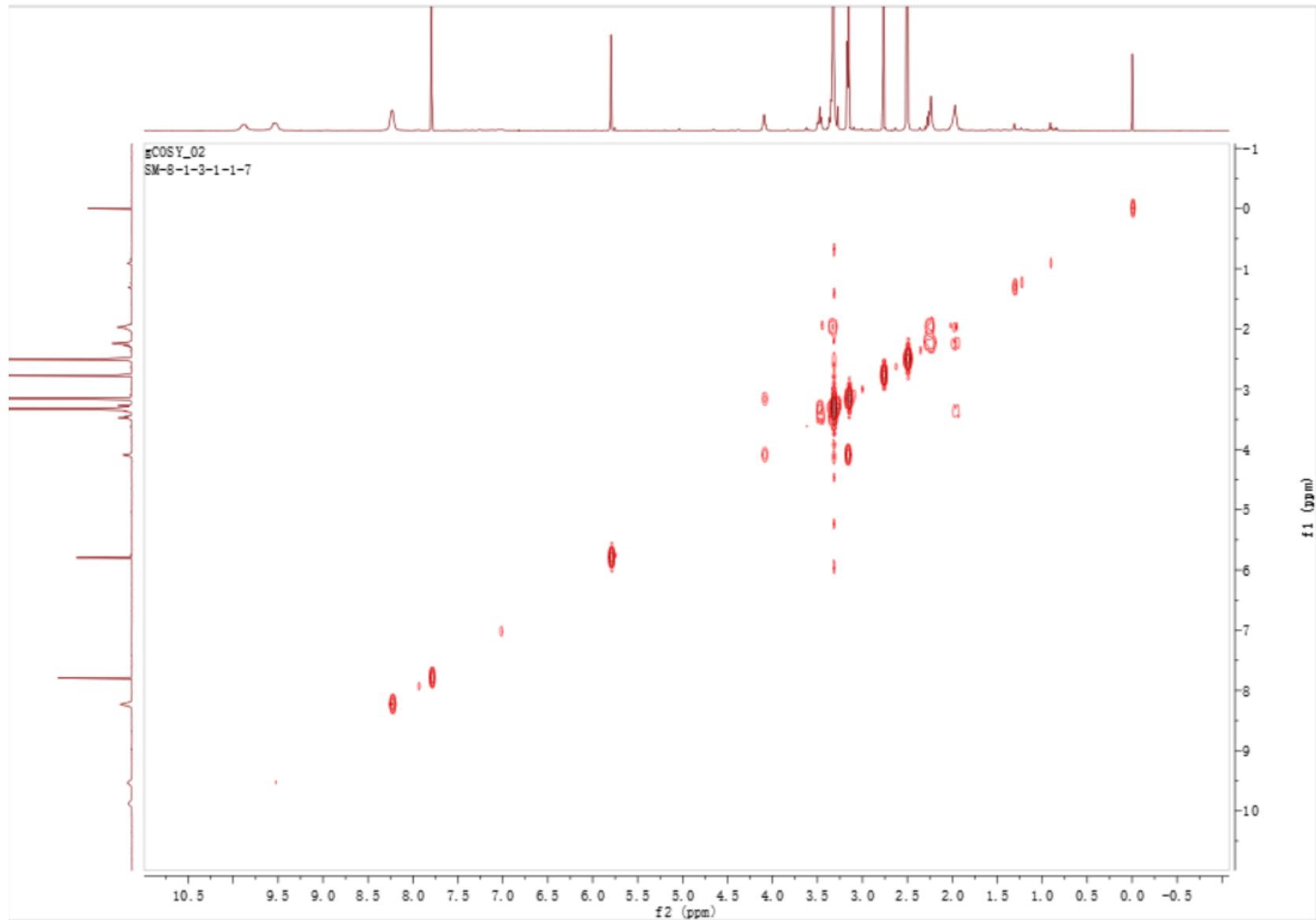


Figure S64. ^1H - ^1H COSY spectrum of compound **6** in $\text{DMSO}-d_6$ (500 MHz).

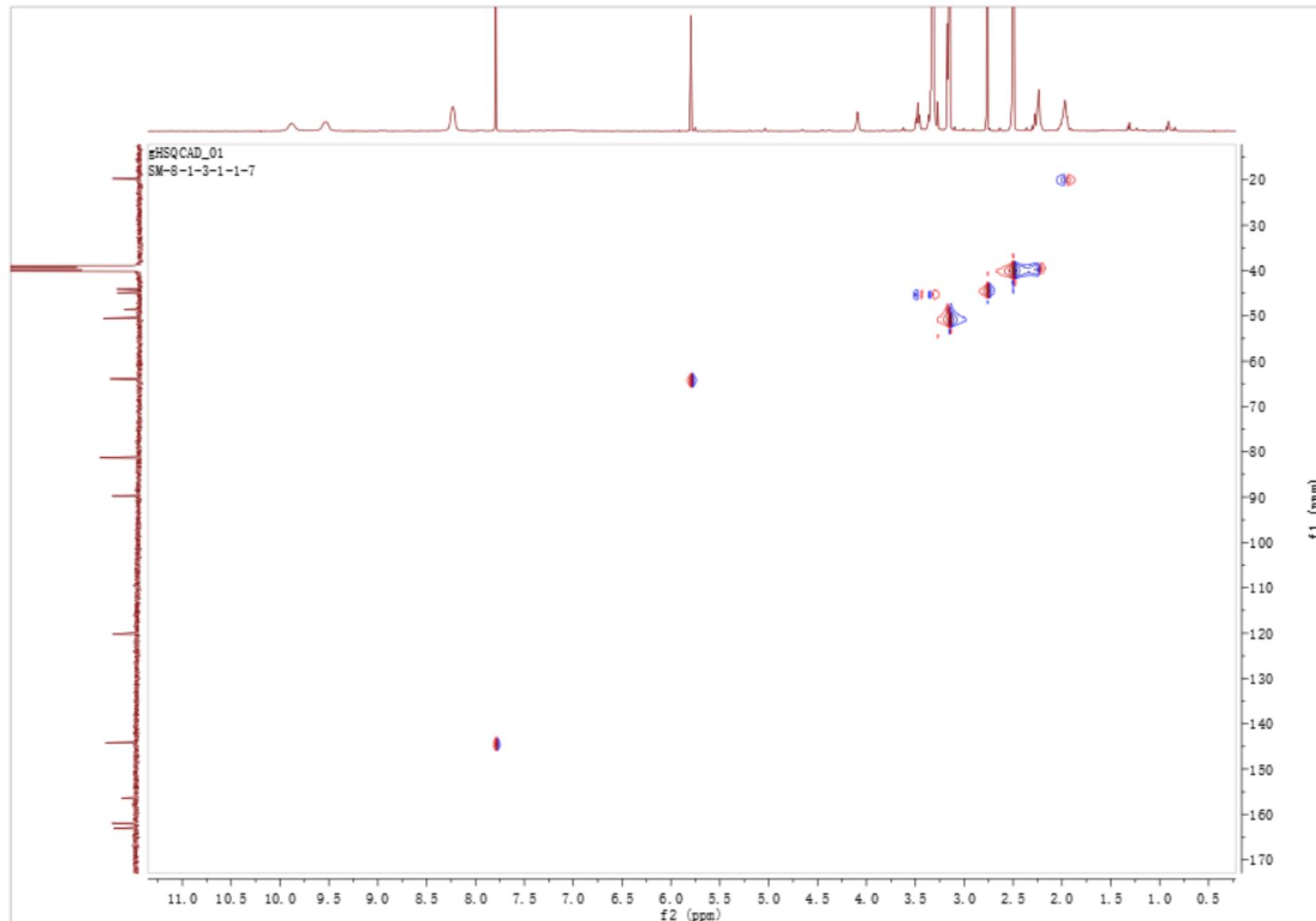


Figure S65. HSQC spectrum of compound **6** in $\text{DMSO}-d_6$ (500 MHz).

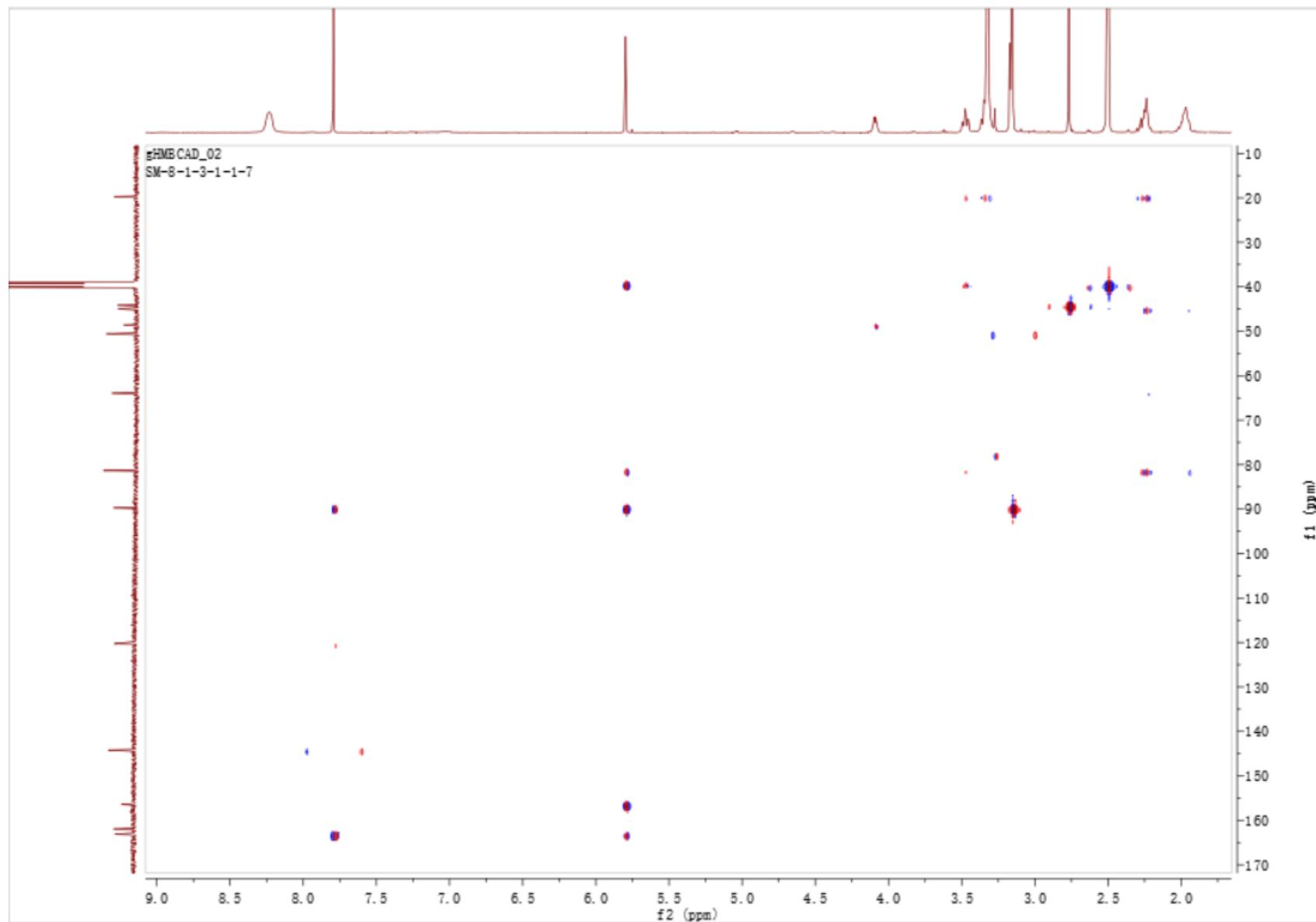


Figure S66. HMBC spectrum of compound **6** in $\text{DMSO}-d_6$ (500 MHz)

20210520-SM-813117_210520105231 #29 RT: 0.27 AV: 1 NL: 9.34E7

T: FTMS + p ESI sid=35.00 Full ms [120.00-1000.00]

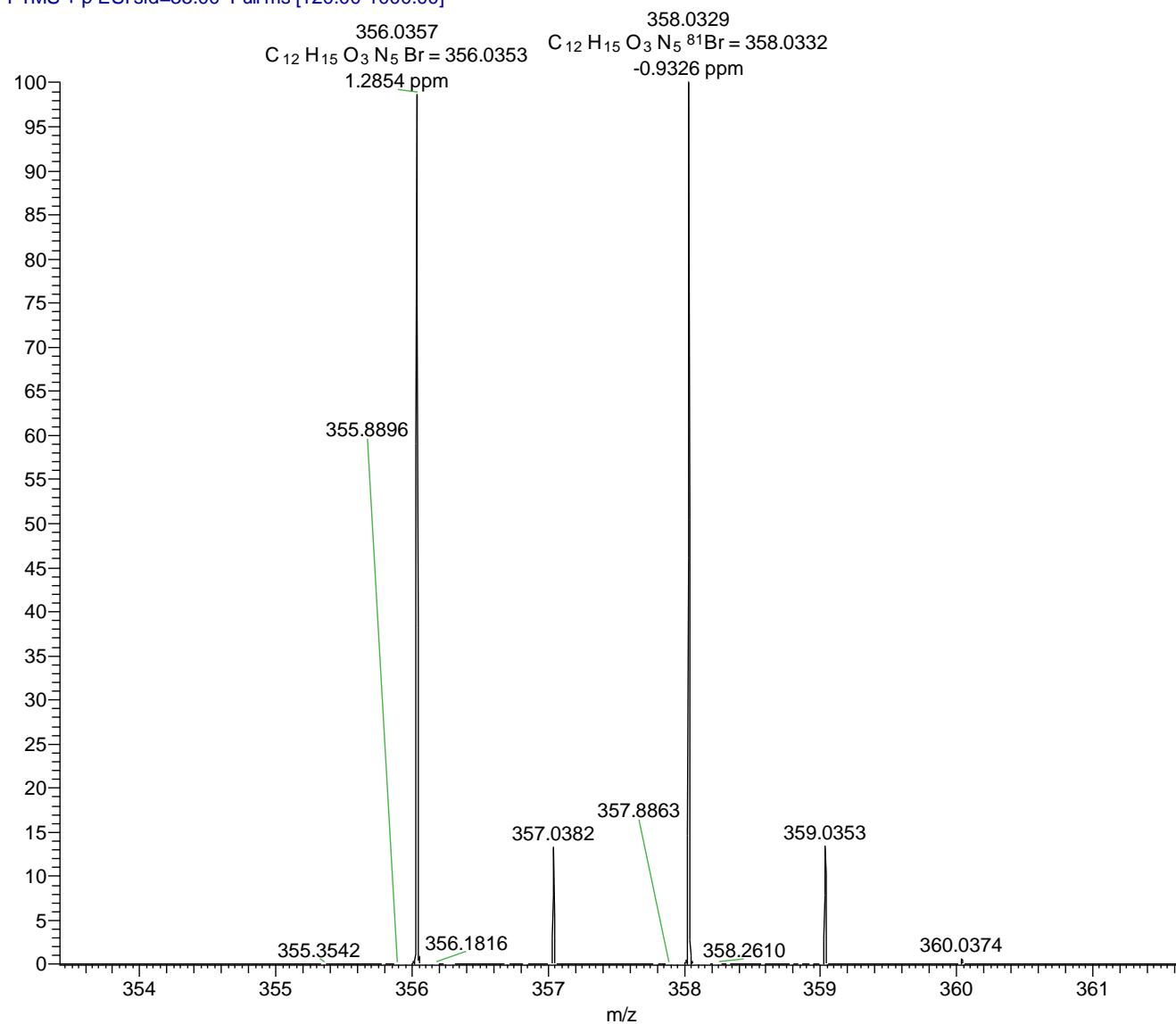


Figure S67. HRESIMS data of compound **6**.

PROTON_01
SM-8-1-3-1-3-3

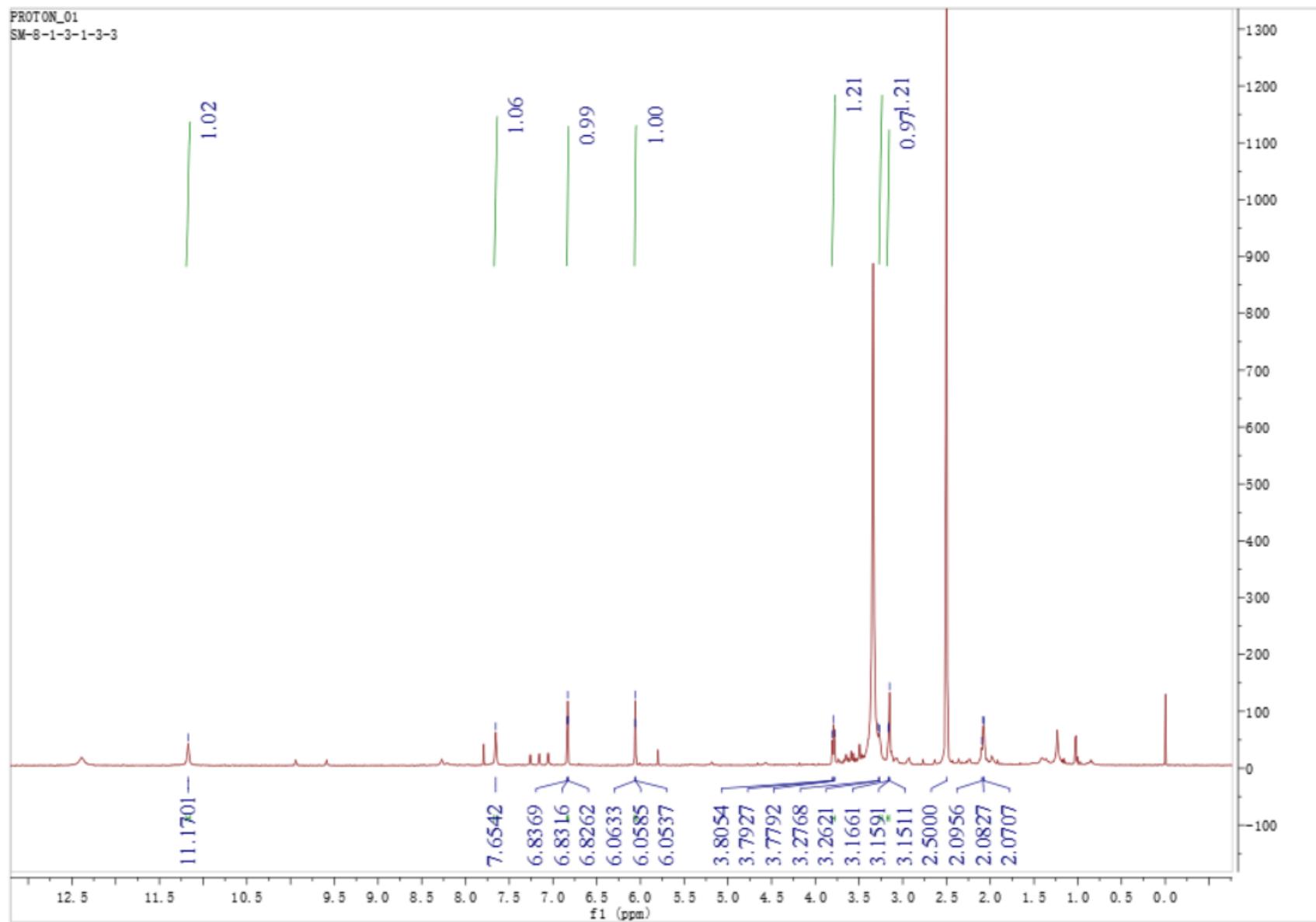


Figure S68. ¹H NMR spectrum of compound 7 in DMSO-*d*₆ (500 MHz).

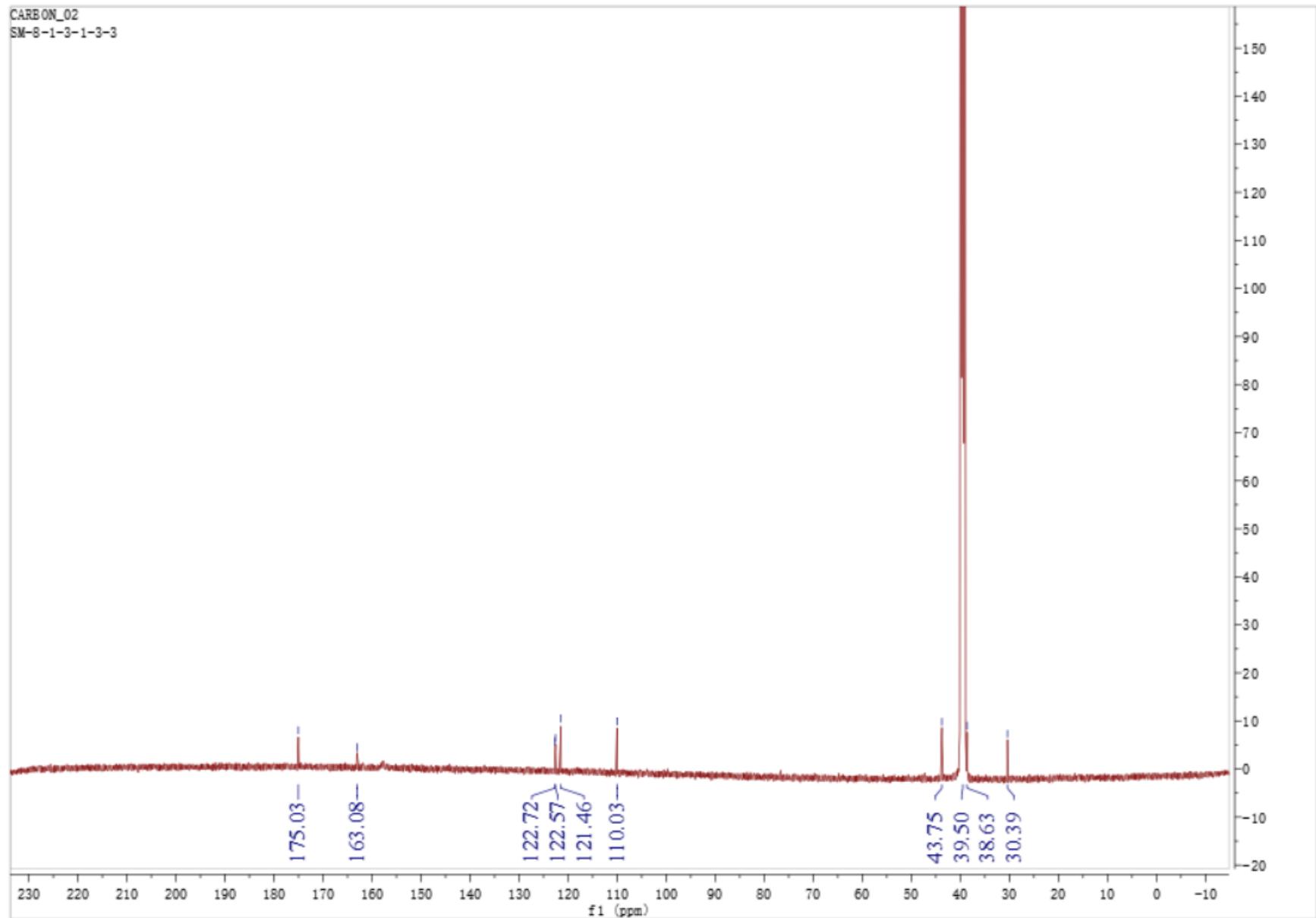


Figure S69. ^{13}C NMR spectrum of compound 7 in $\text{DMSO}-d_6$ (125 MHz).

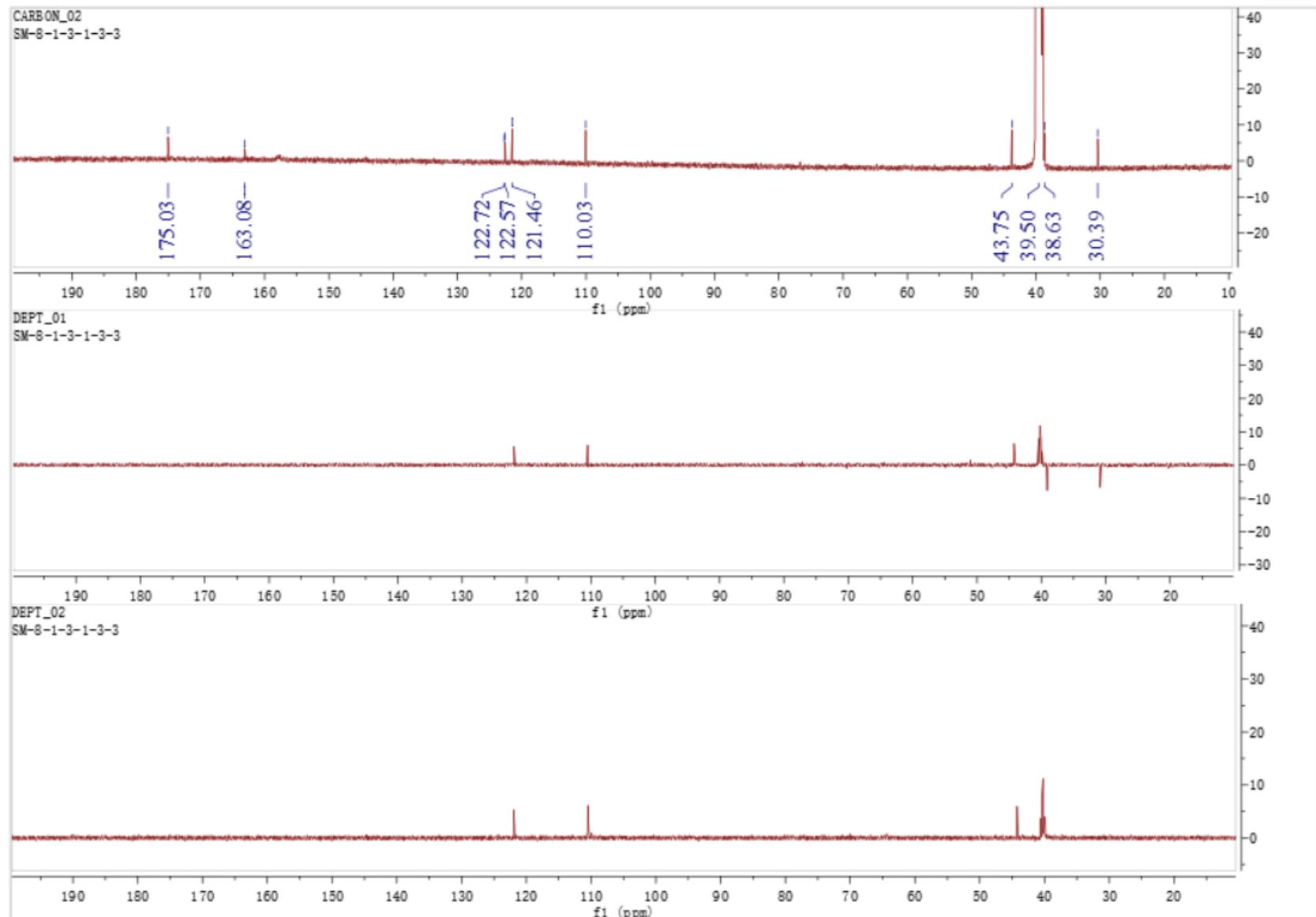


Figure S70. ^{13}C NMR and DEPT spectrum of compound 7 in $\text{DMSO}-d_6$ (125 MHz).

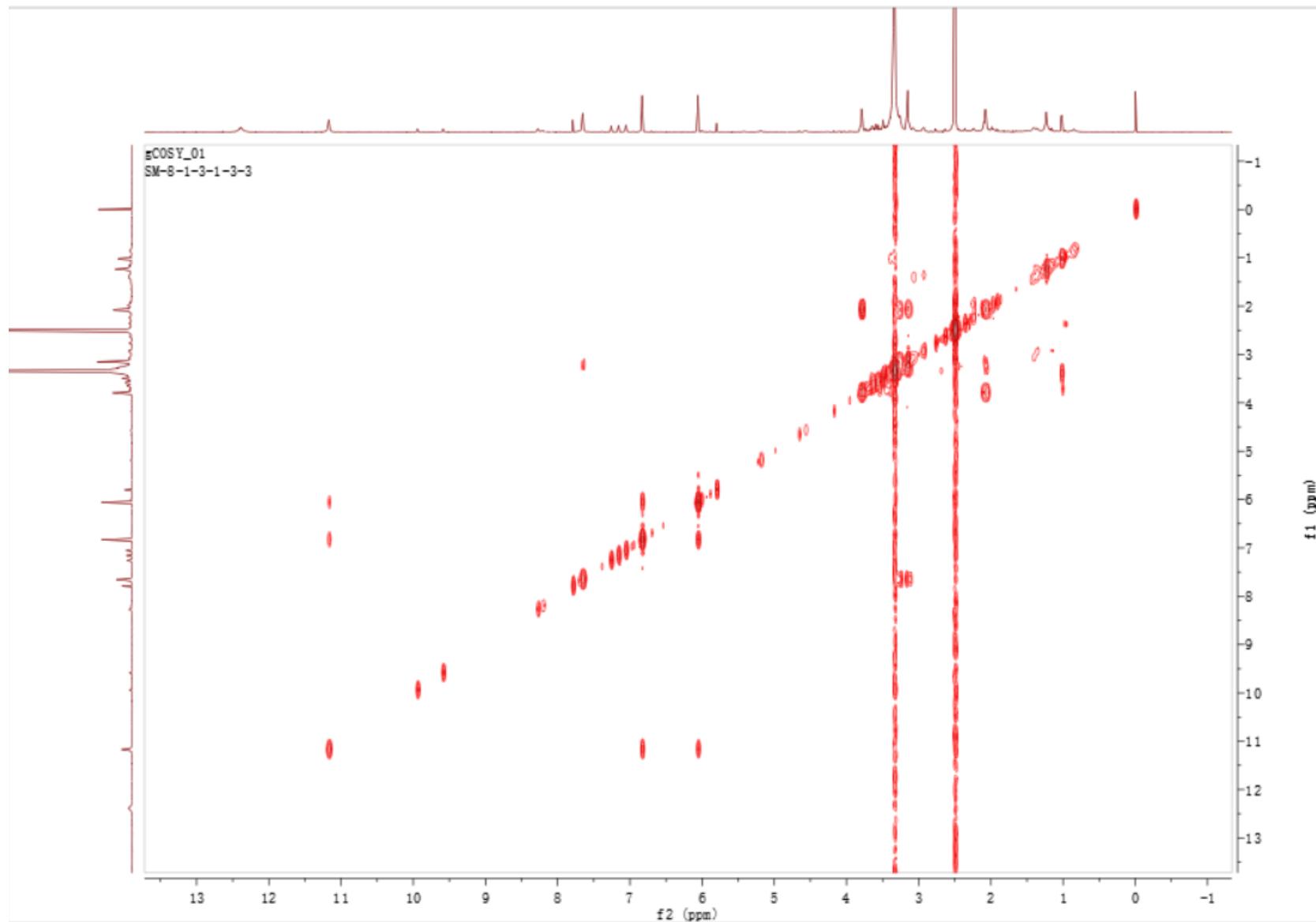


Figure S71. ^1H - ^1H COSY spectrum of compound 7 in $\text{DMSO}-d_6$ (500 MHz)

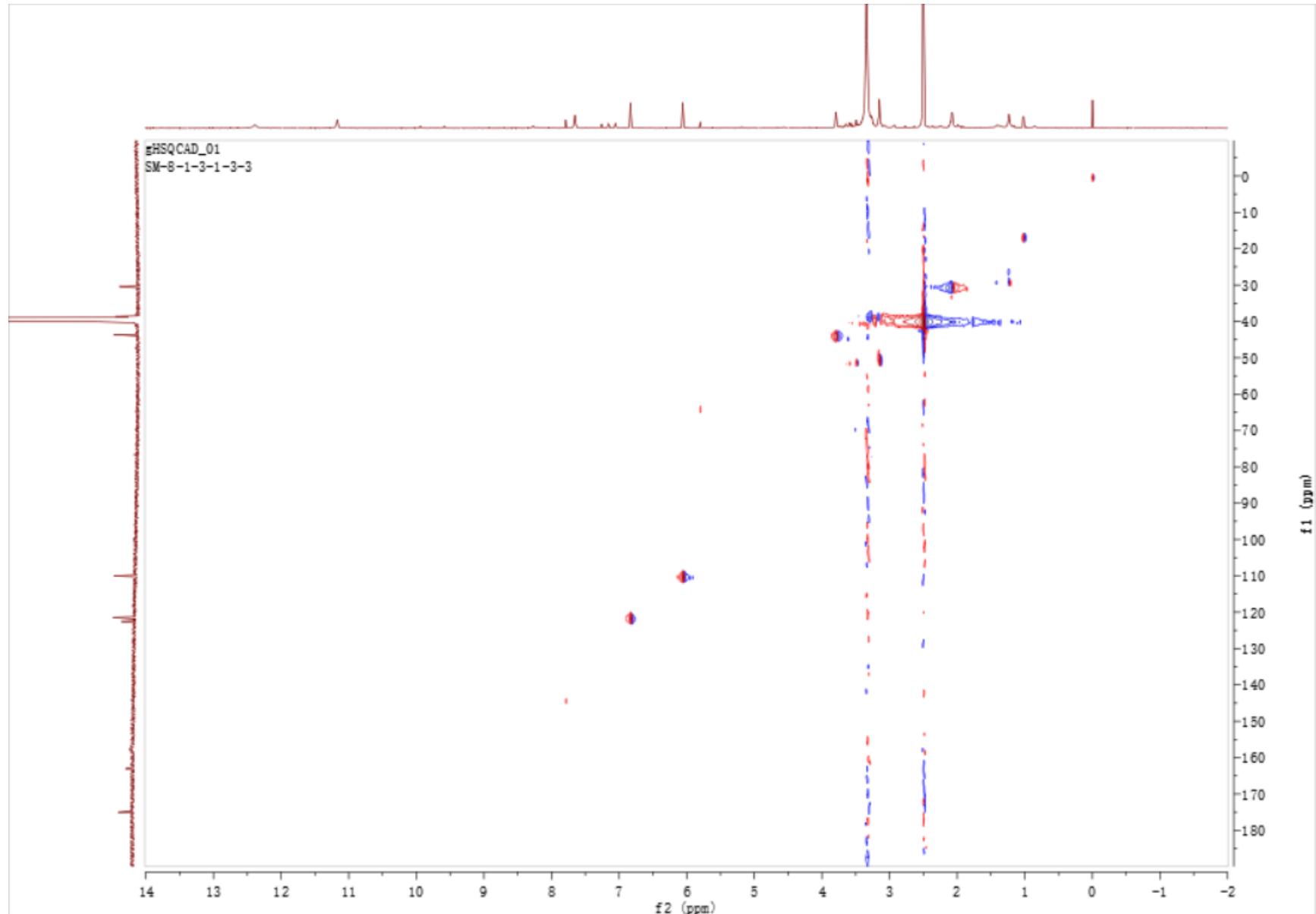


Figure S72. HSQC spectrum of compound 7 in DMSO-*d*₆ (500 MHz).

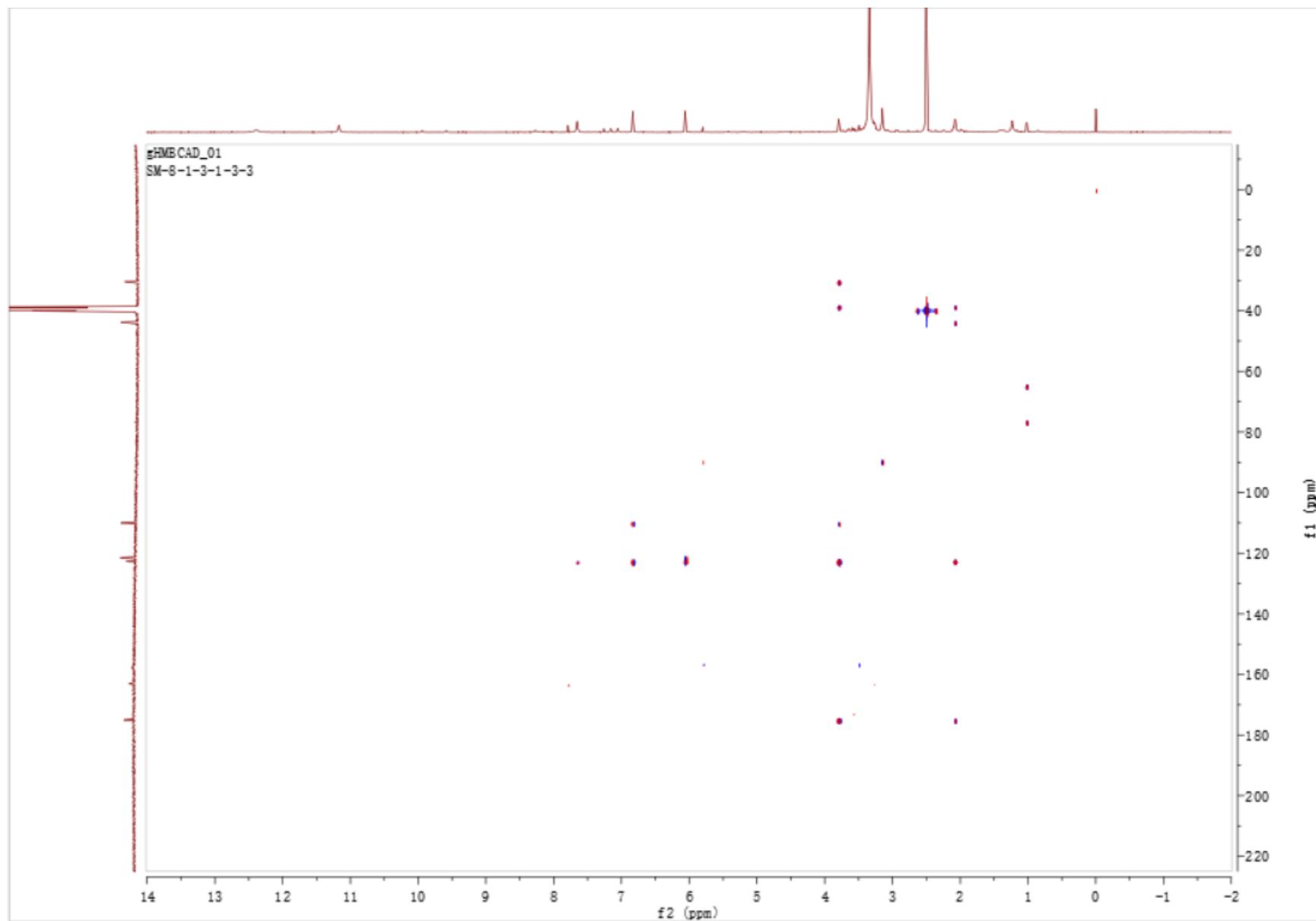


Figure S73. HMBC spectrum of compound 7 in $\text{DMSO}-d_6$ (500 MHz).

20210611-sm-8-1-3-1-3-3_210611132610 #13 RT: 0.10 AV: 1 NL: 5.79E6
T: FTMS + p ESI Full ms [170.00-2000.00]

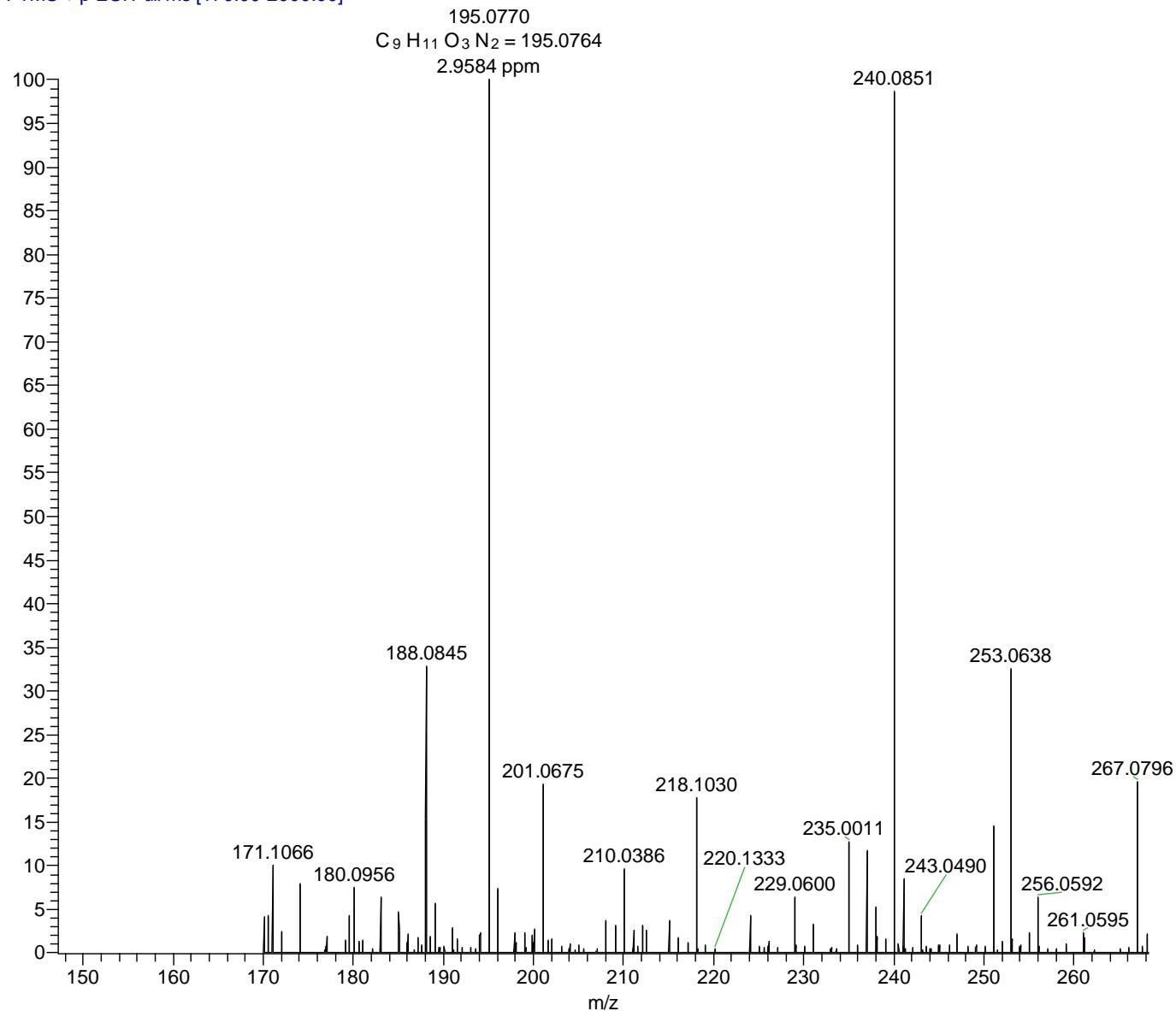


Figure S74. HRESIMS data of compound 7.

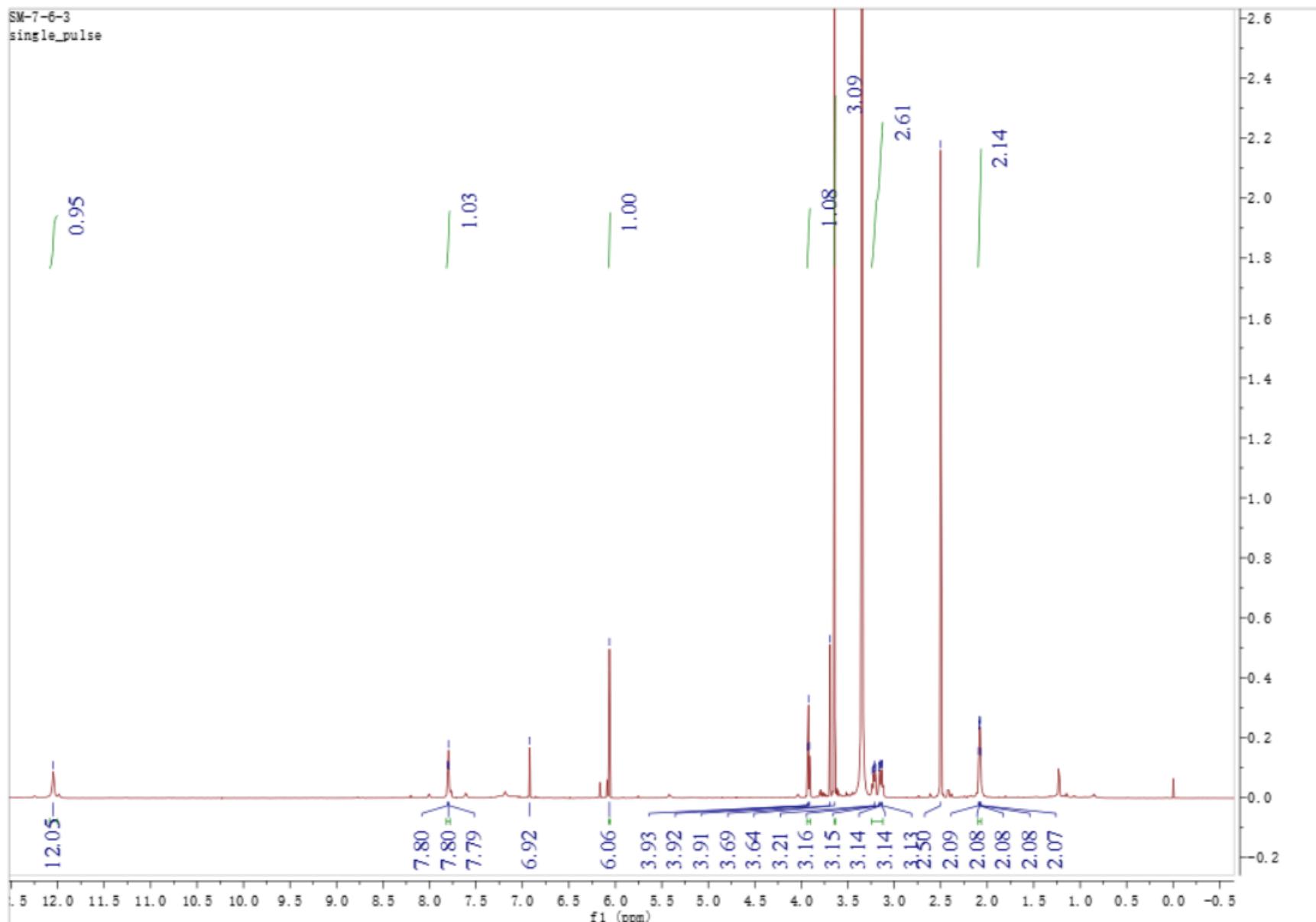


Figure S75. ^1H NMR spectrum of compound **8** in $\text{DMSO}-d_6$ (500 MHz).

SM-7-6-3
single pulse decoupled gated NOE

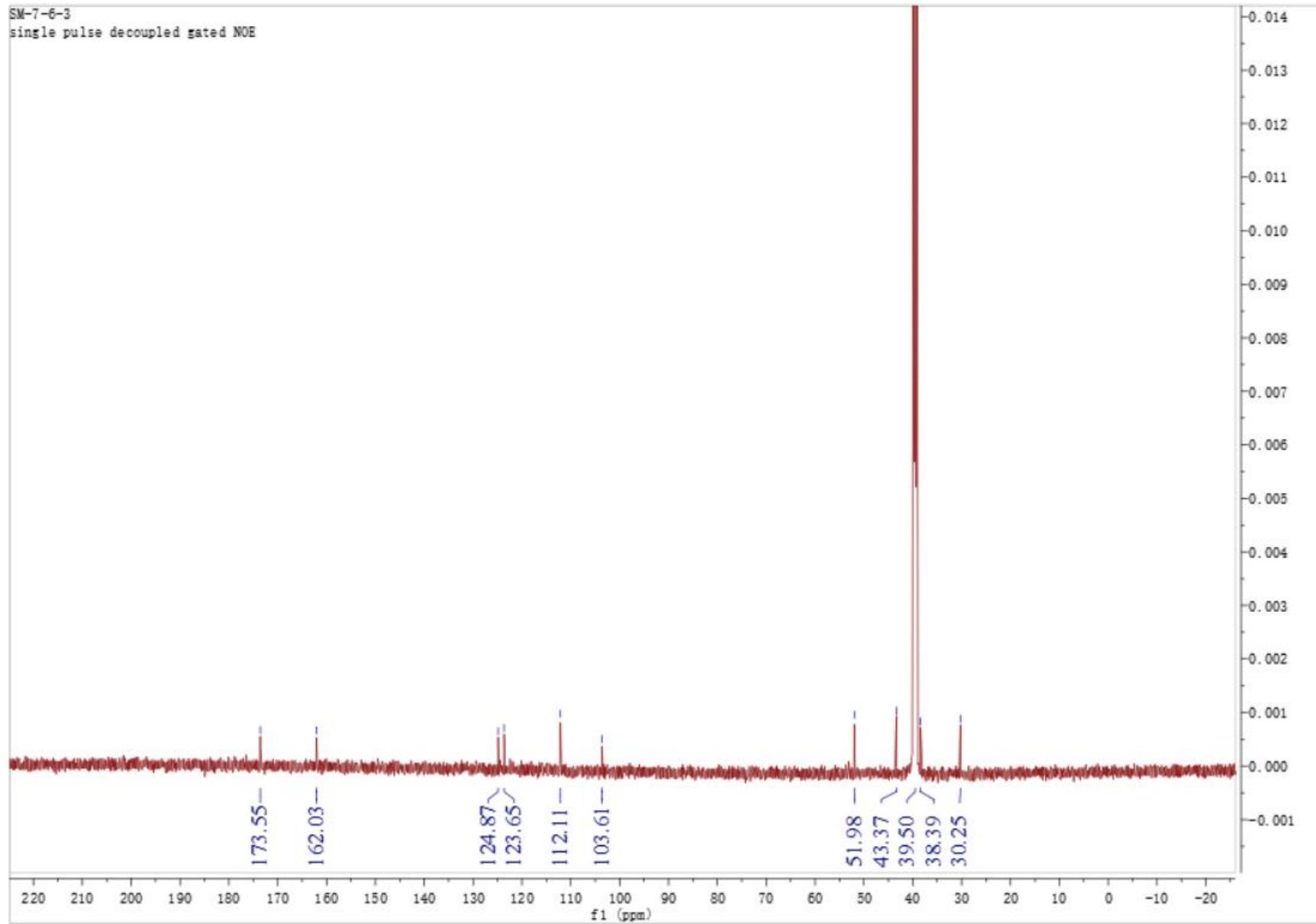


Figure S76. ¹³C NMR spectrum of compound 8 in DMSO-*d*₆ (125 MHz).

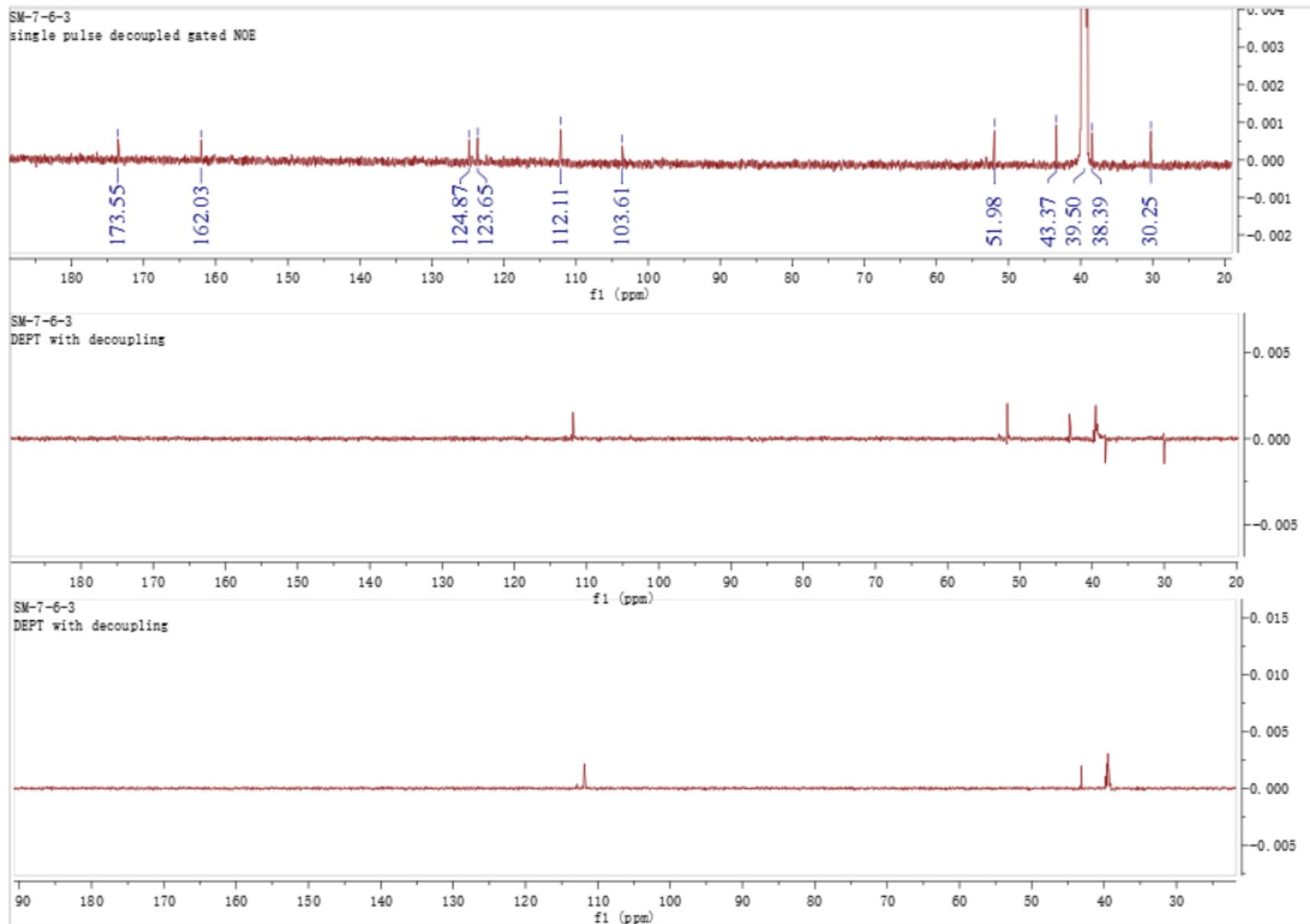


Figure S77. ^{13}C NMR and DEPT spectrum of compound **8** in $\text{DMSO}-d_6$ (125 MHz)

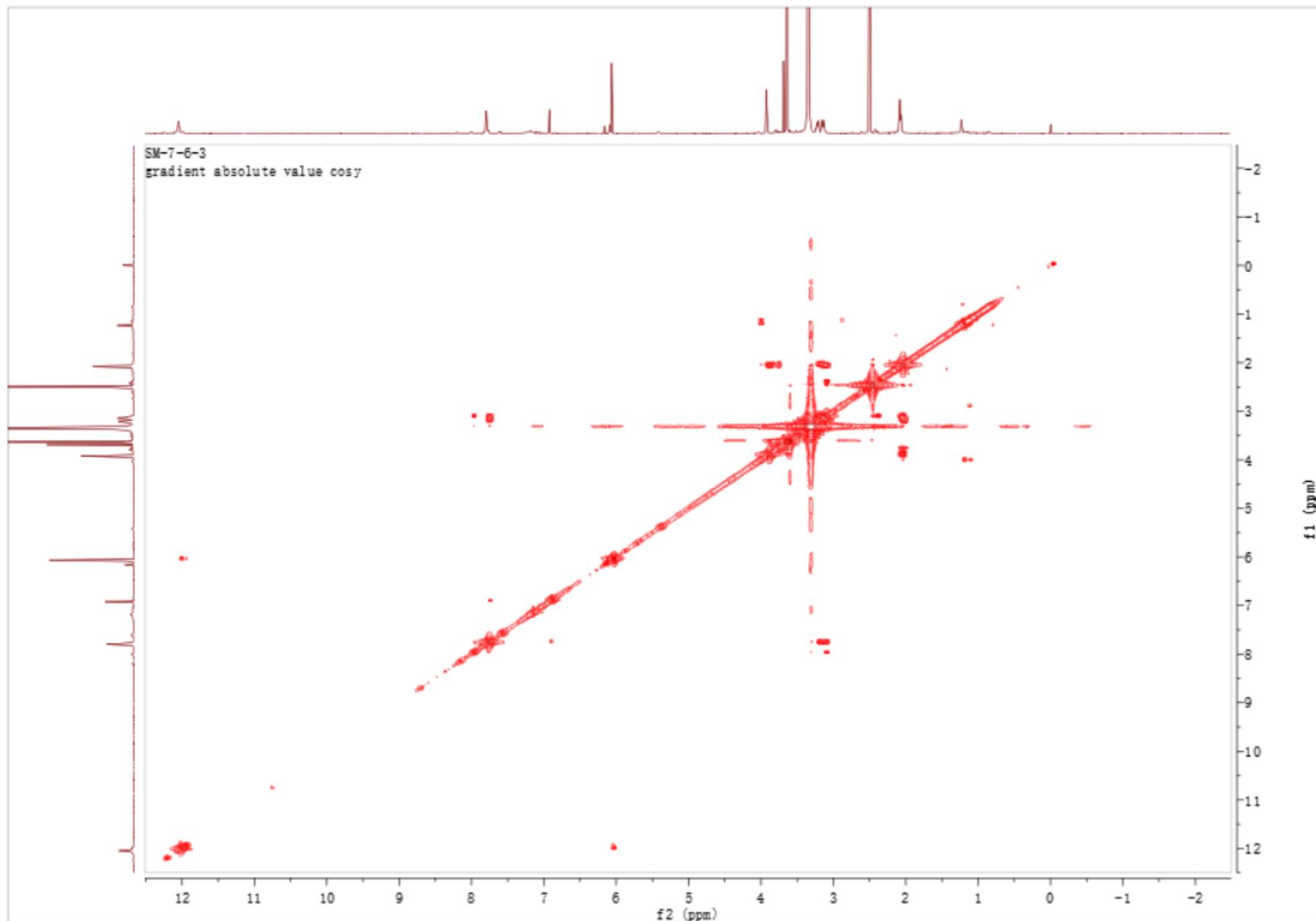


Figure S78. ^1H - ^1H COSY spectrum of compound **8** in $\text{DMSO}-d_6$ (500 MHz).

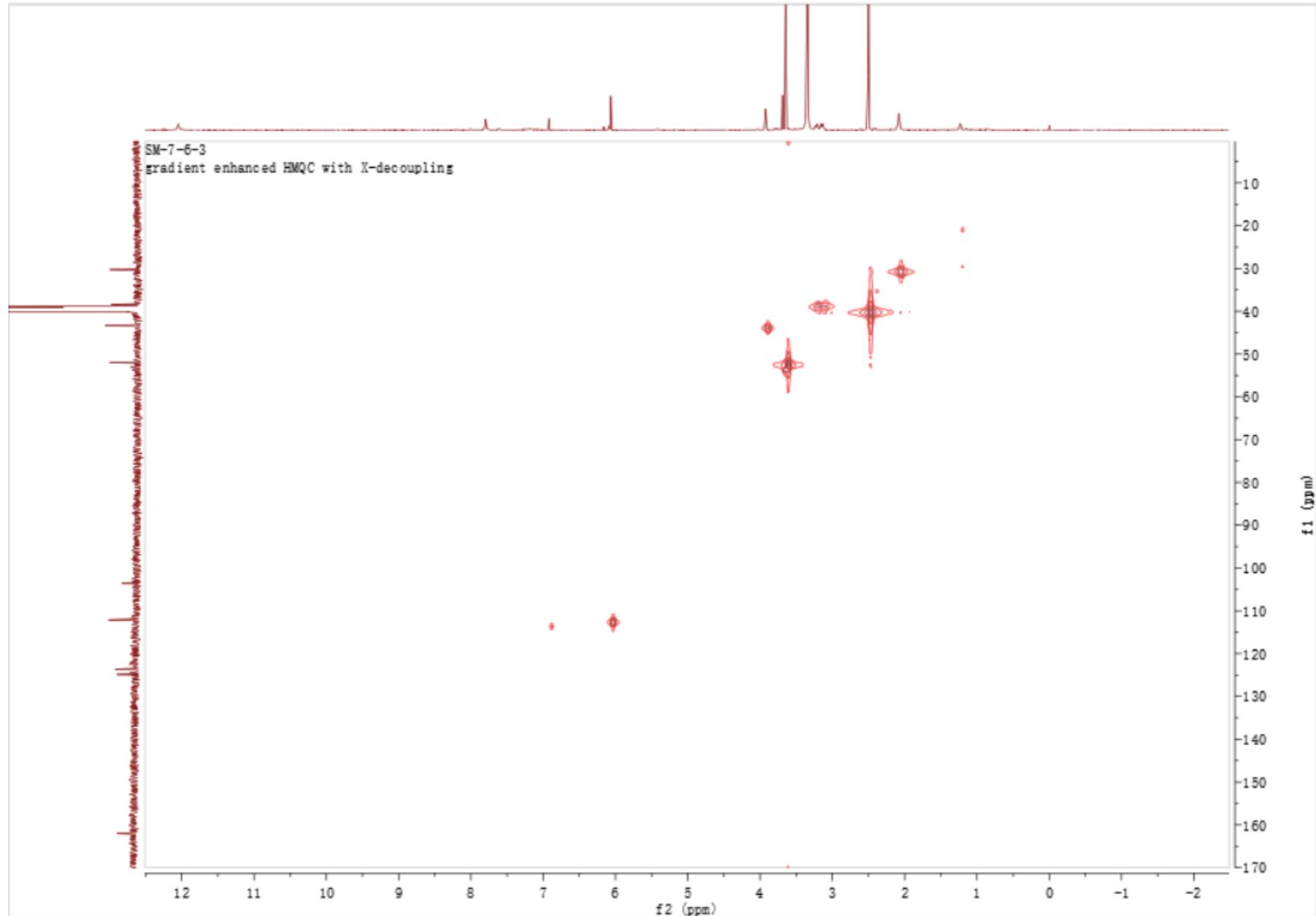


Figure S79. HSQC spectrum of compound **8** in $\text{DMSO}-d_6$ (500 MHz).

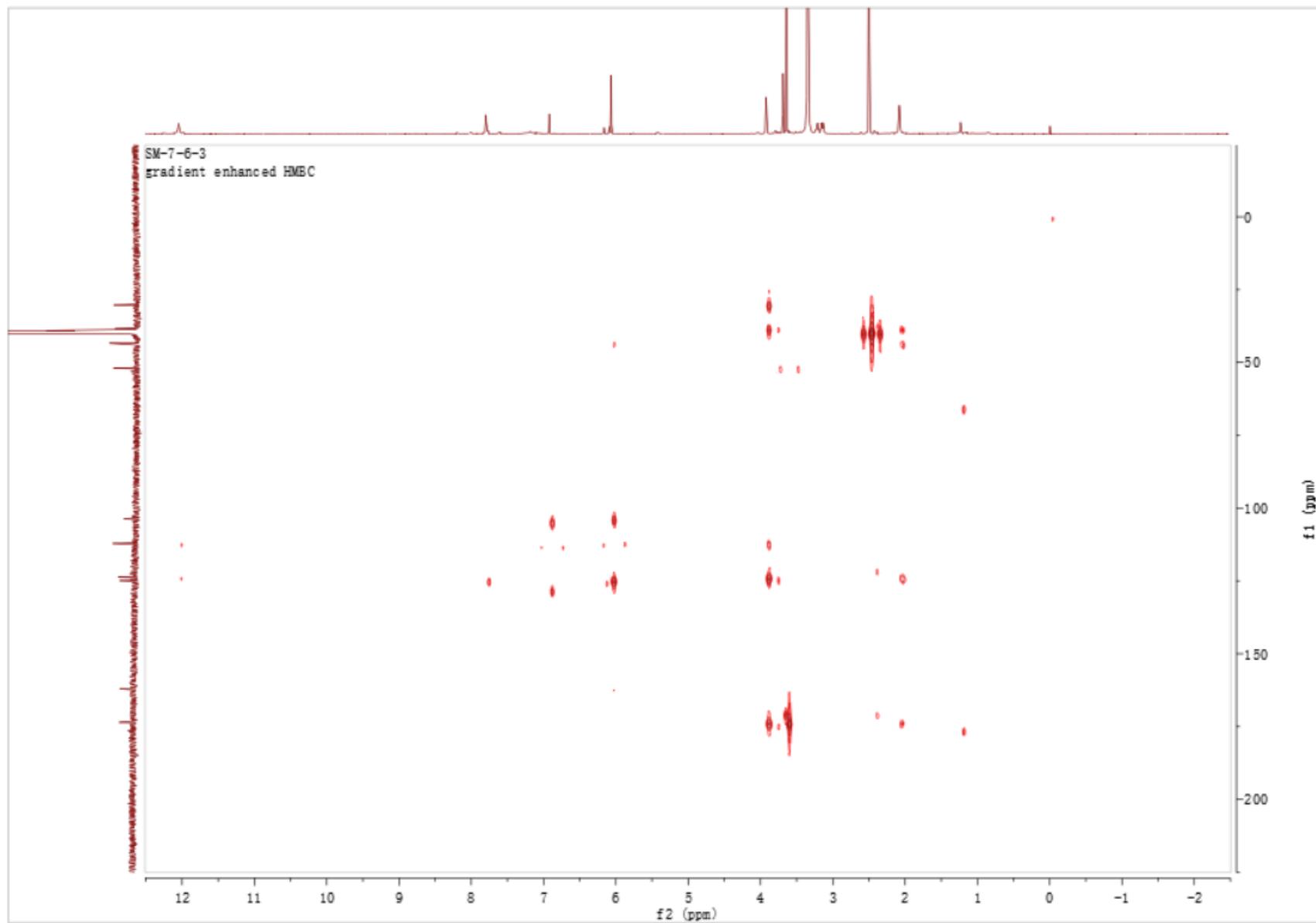


Figure S80. HMBC spectrum of compound **8** in $\text{DMSO}-d_6$ (500 MHz).

20210831-SM-7-6-3_210831093738 #37 RT: 0.38 AV: 1 SB: 10 0.10-0.20 NL: 3.45E6
T: FTMS + p ESI Full ms [150.00-1000.00]

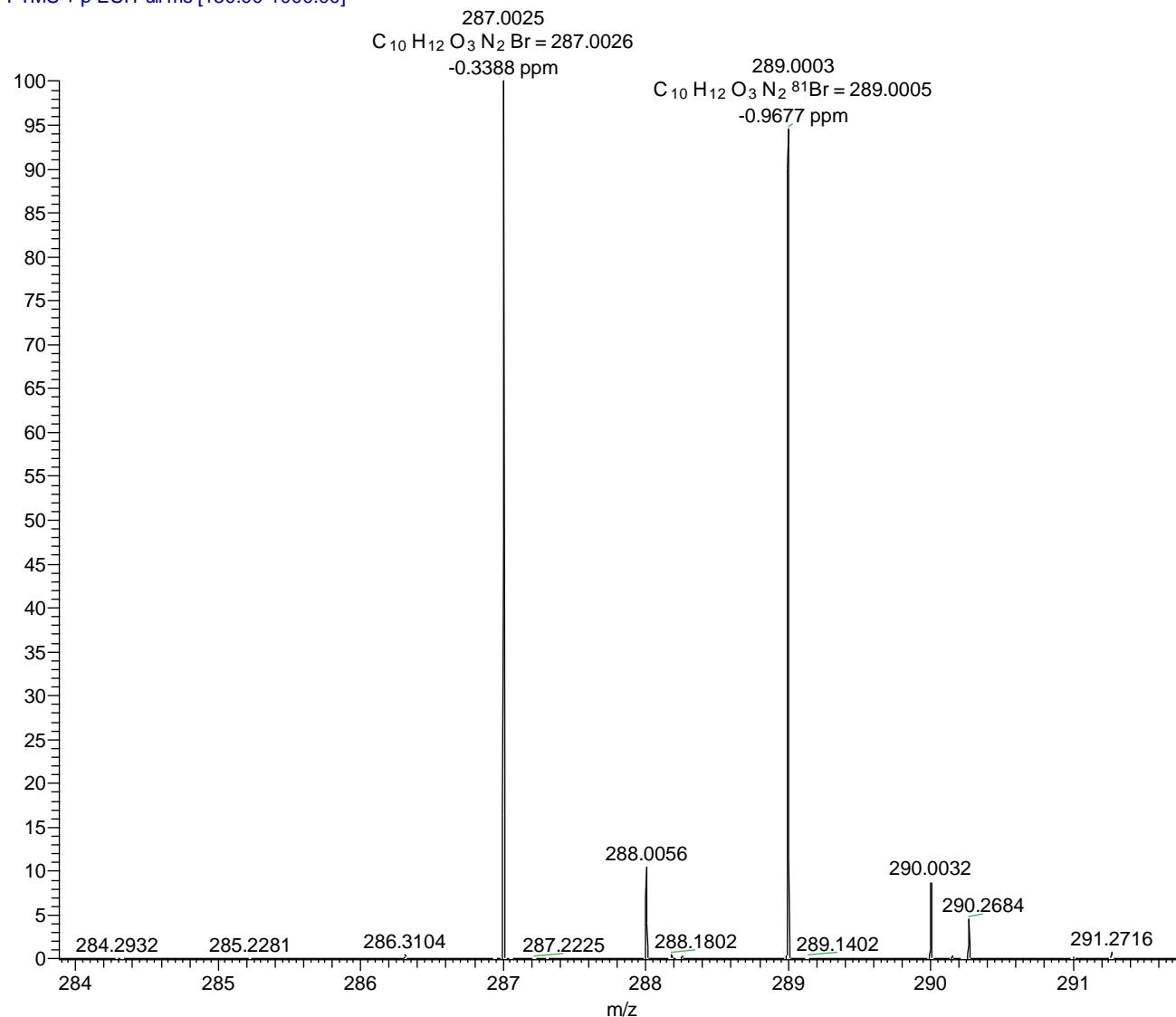


Figure S81. HRESIMS data of compound 8.

SM-7-6-7
single_pulse

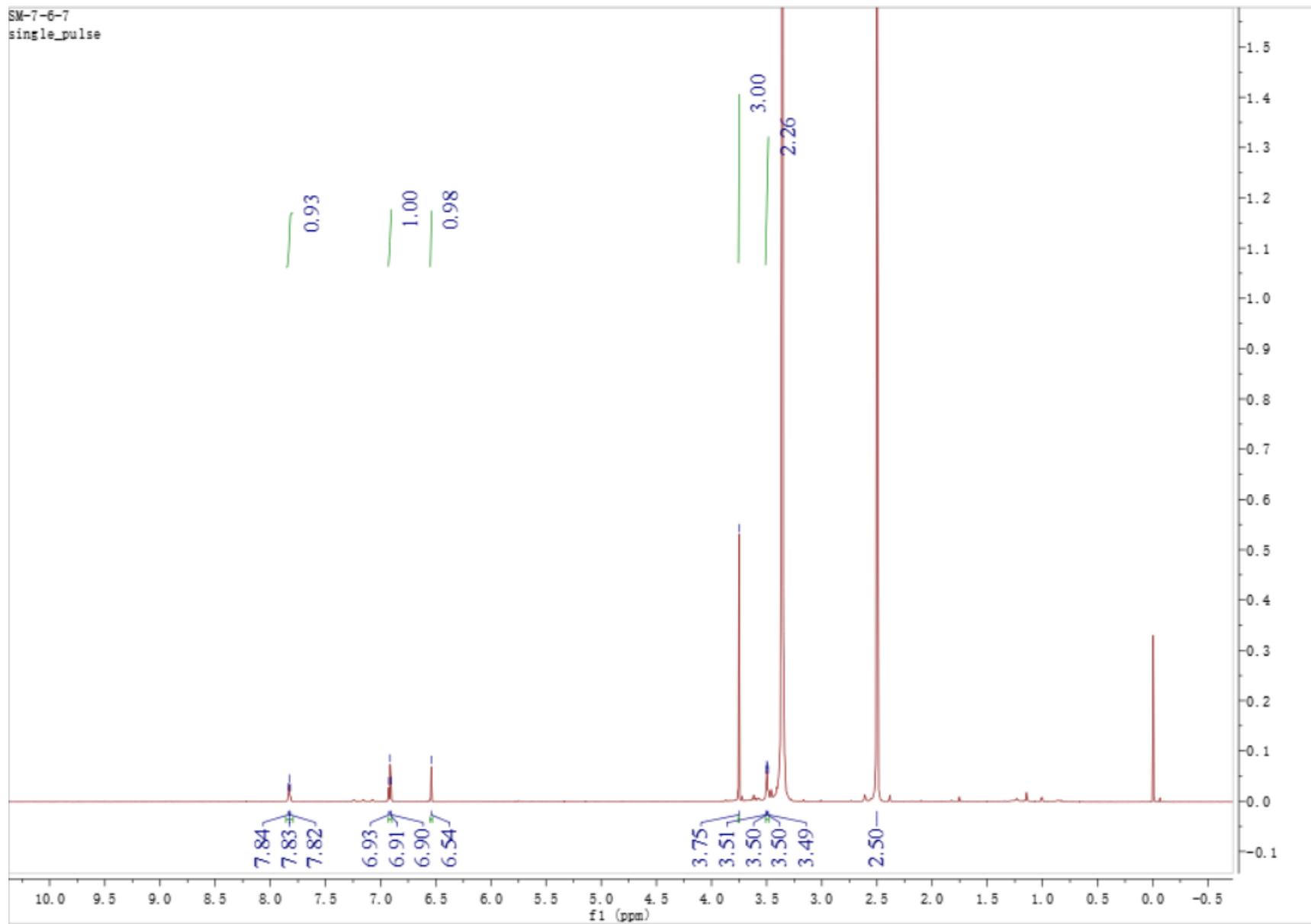


Figure S82. ¹H NMR spectrum of compound 9 in DMSO-*d*₆ (500 MHz).

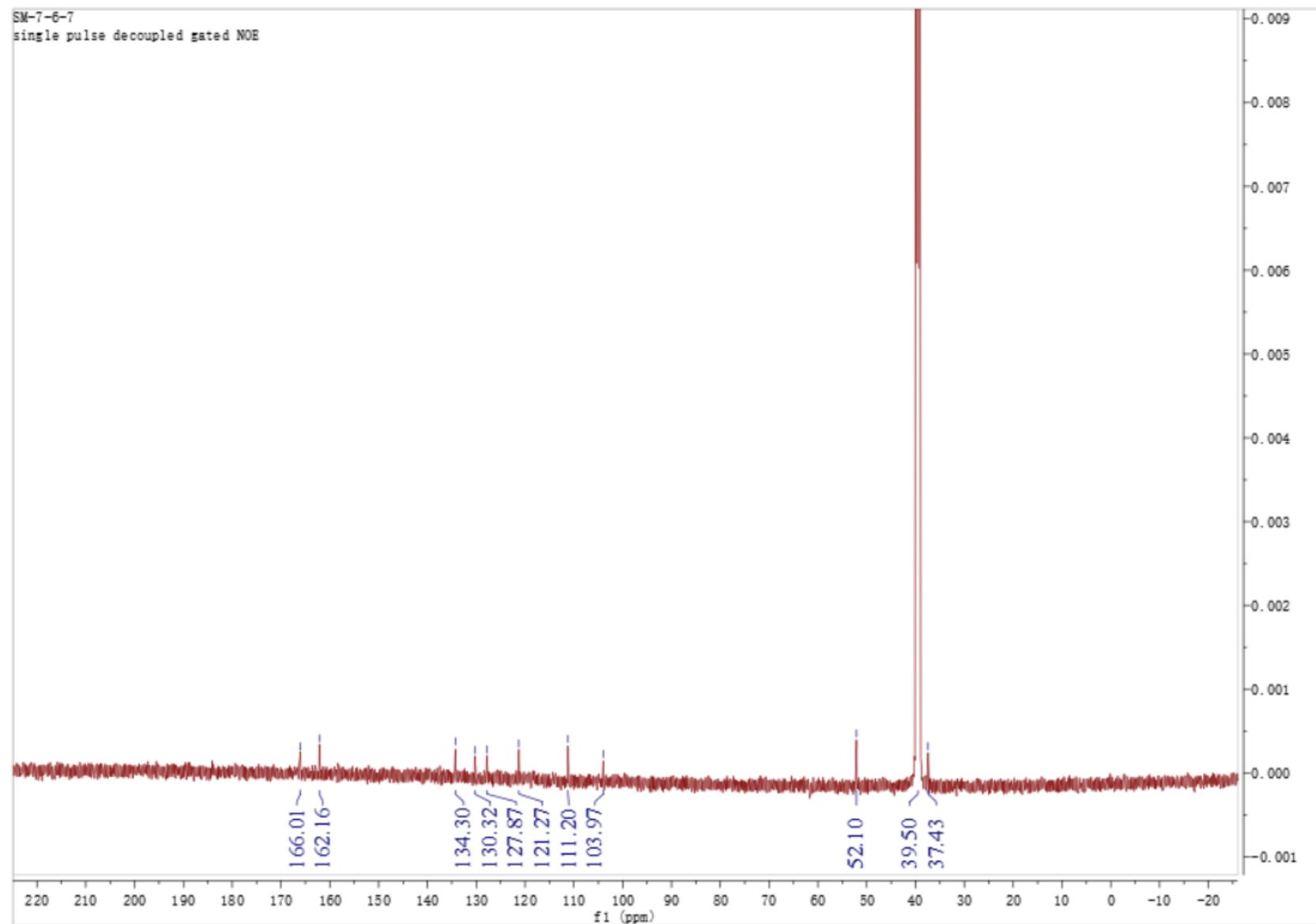


Figure S83. ^{13}C NMR spectrum of compound **9** in $\text{DMSO}-d_6$ (125 MHz).

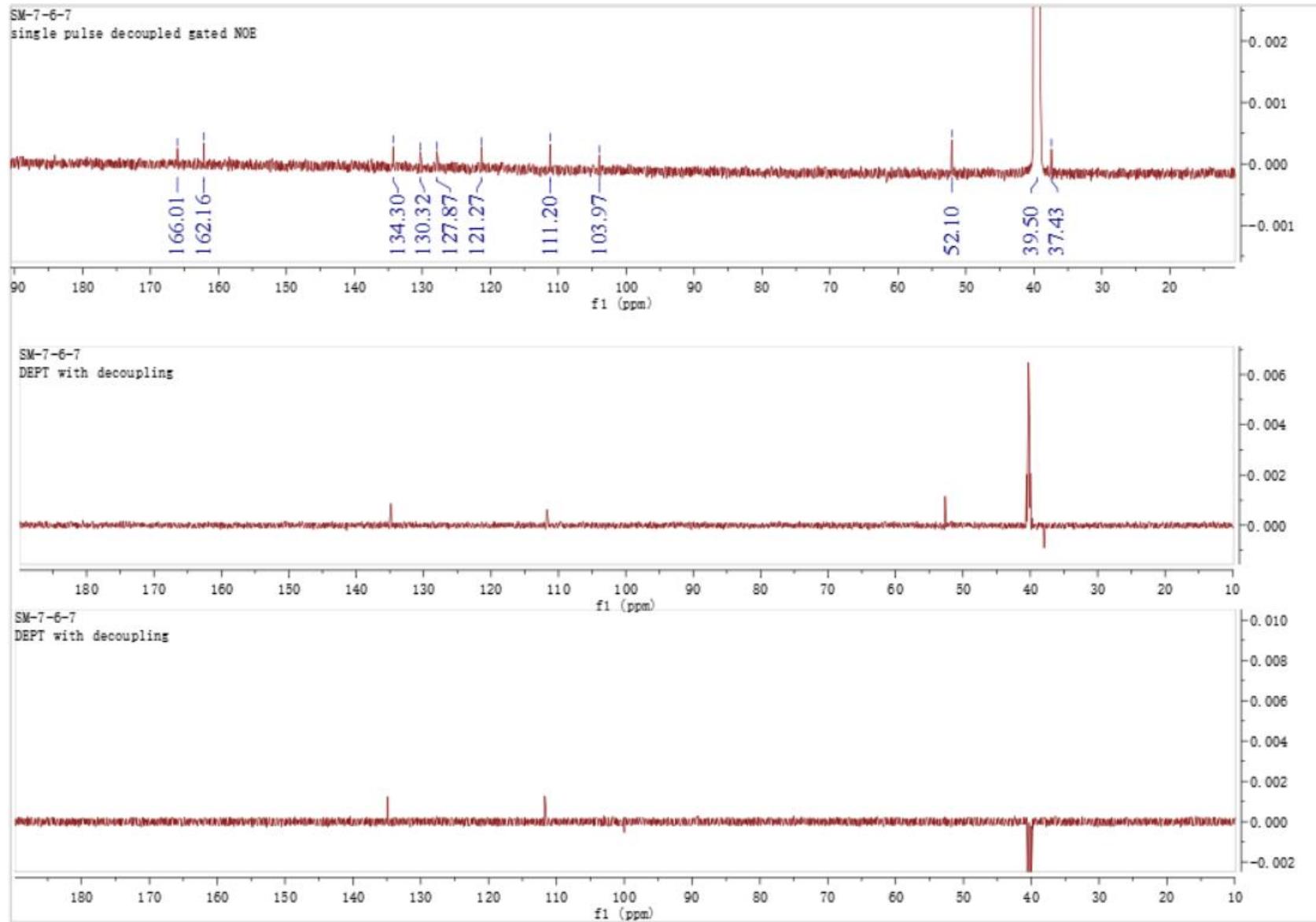


Figure S84. ^{13}C NMR and DEPT spectrum of compound **9** in $\text{DMSO}-d_6$ (125 MHz).

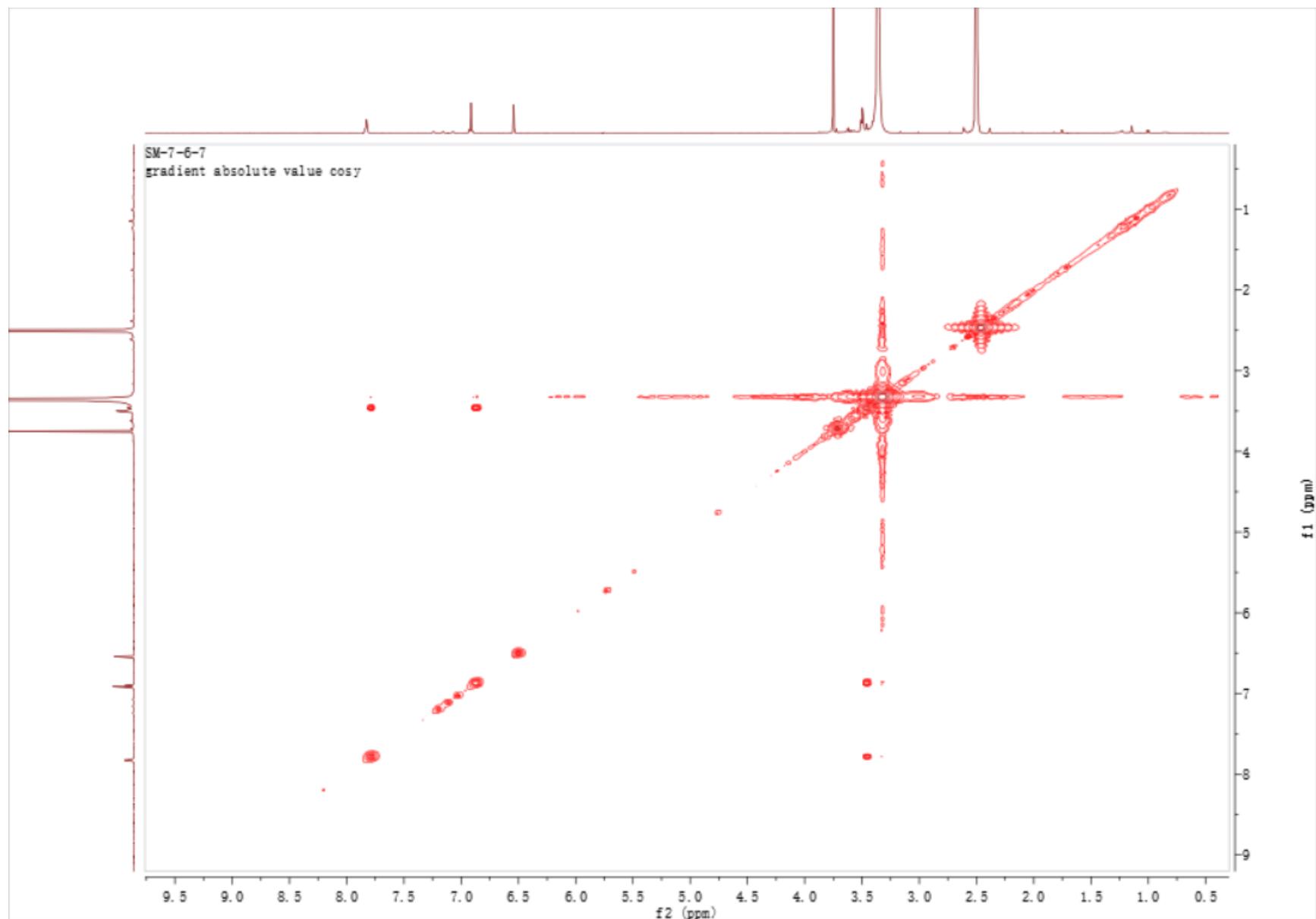


Figure S85. ^1H - ^1H COSY spectrum of compound 9 in $\text{DMSO}-d_6$ (500 MHz).

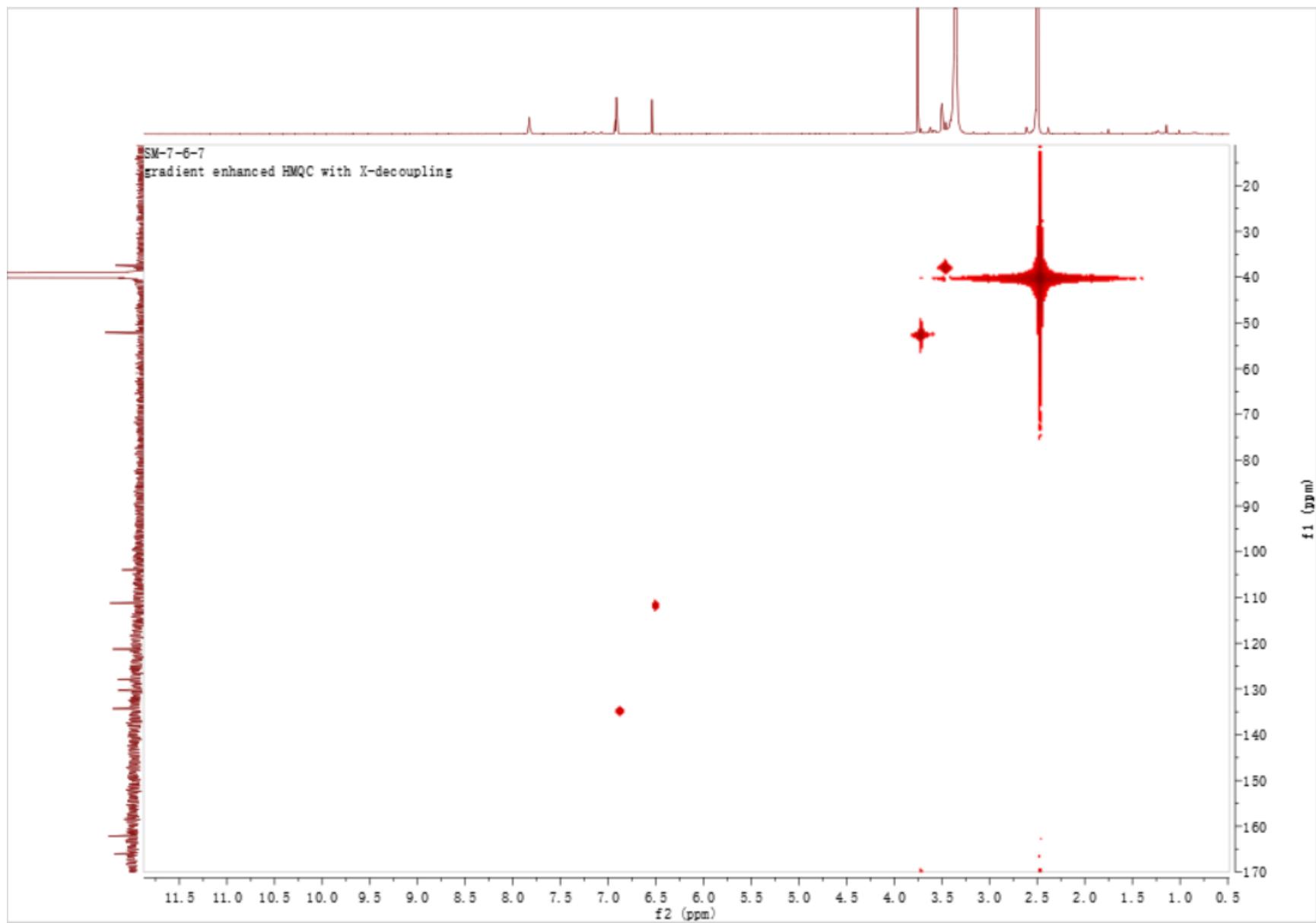


Figure S86. HSQC spectrum of compound **9** in $\text{DMSO}-d_6$ (500 MHz).

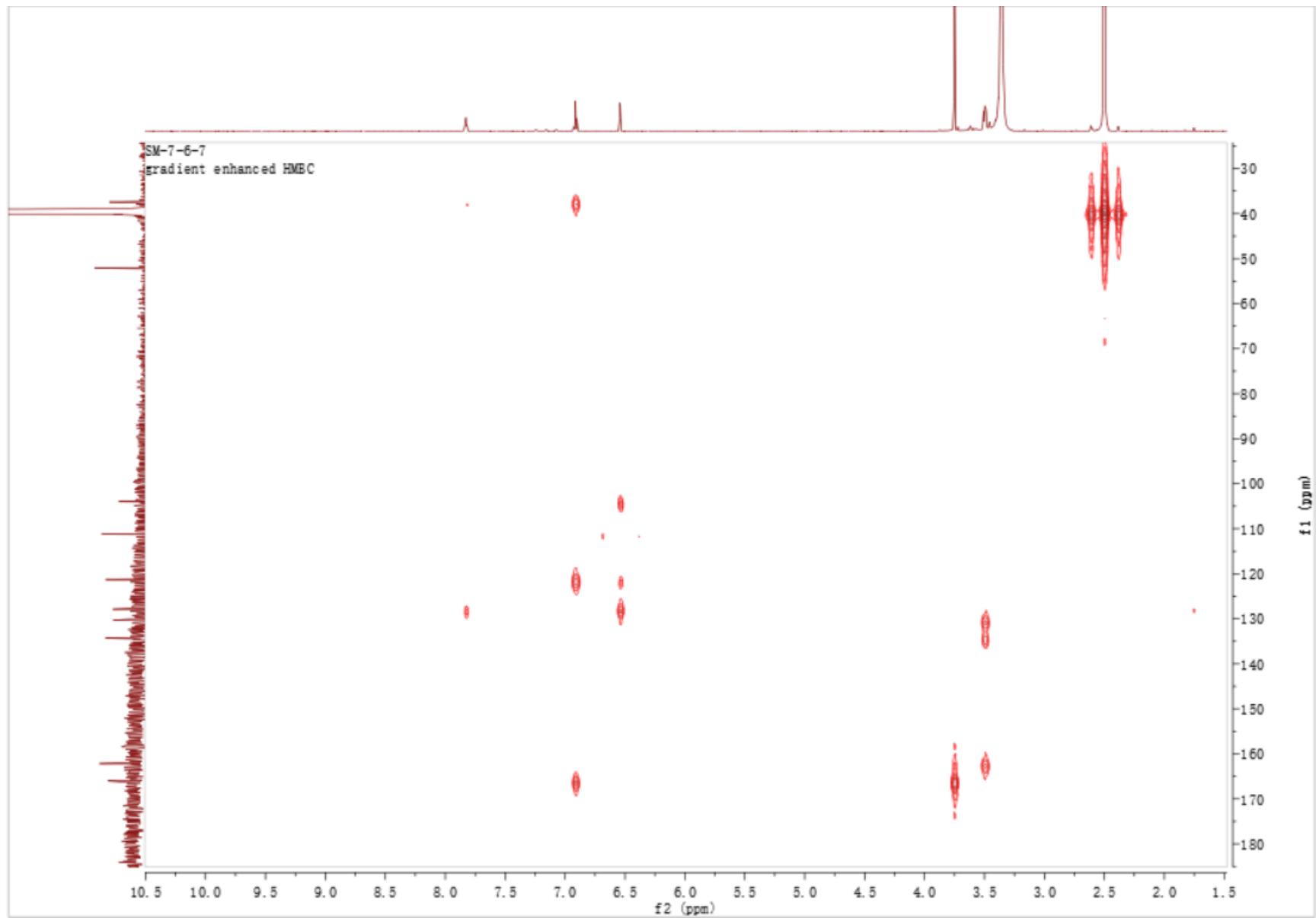


Figure S87. HMBC spectrum of compound **9** in $\text{DMSO}-d_6$ (500 MHz).

20210831-SM-7-6-7_210831093738 #4 RT: 0.03 AV: 1 NL: 2.12E5
T: FTMS + p ESI Full ms [150.00-1000.00]

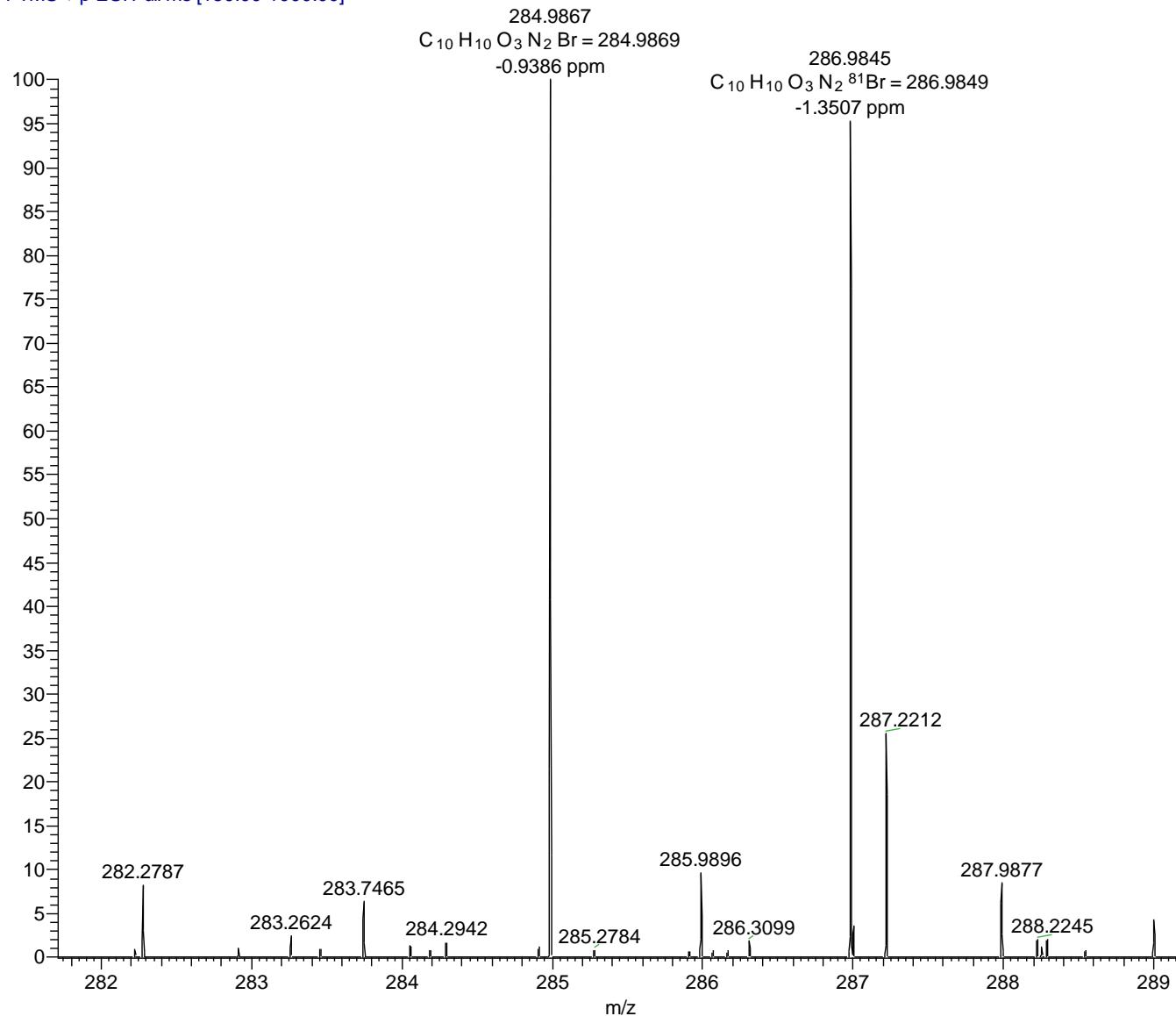


Figure S88. HRESIMS data of compound 9.

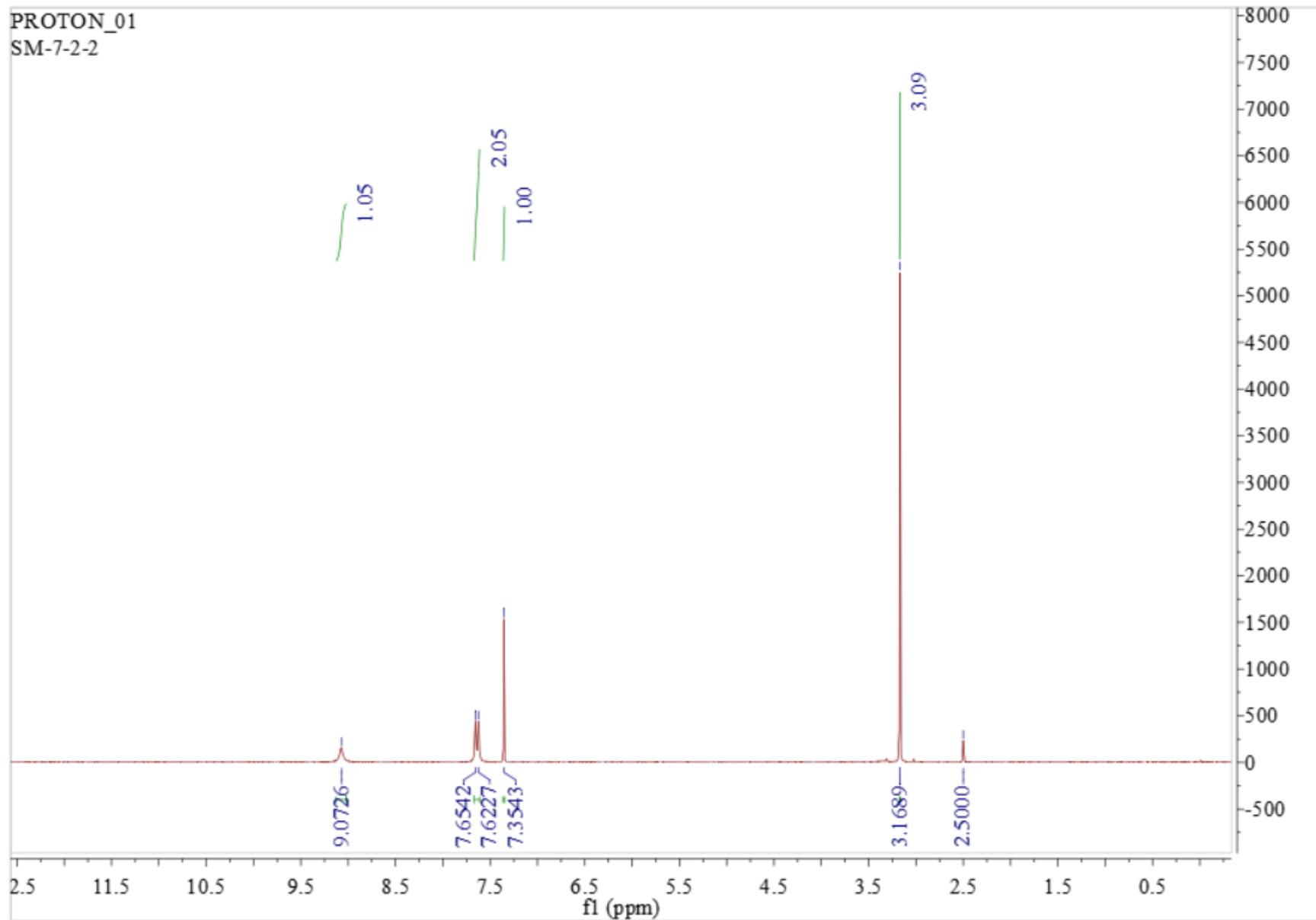


Figure S89. ^1H NMR spectrum of compound **10** in $\text{DMSO}-d_6$ (500 MHz).

CARBON_01
SM-7-2-2

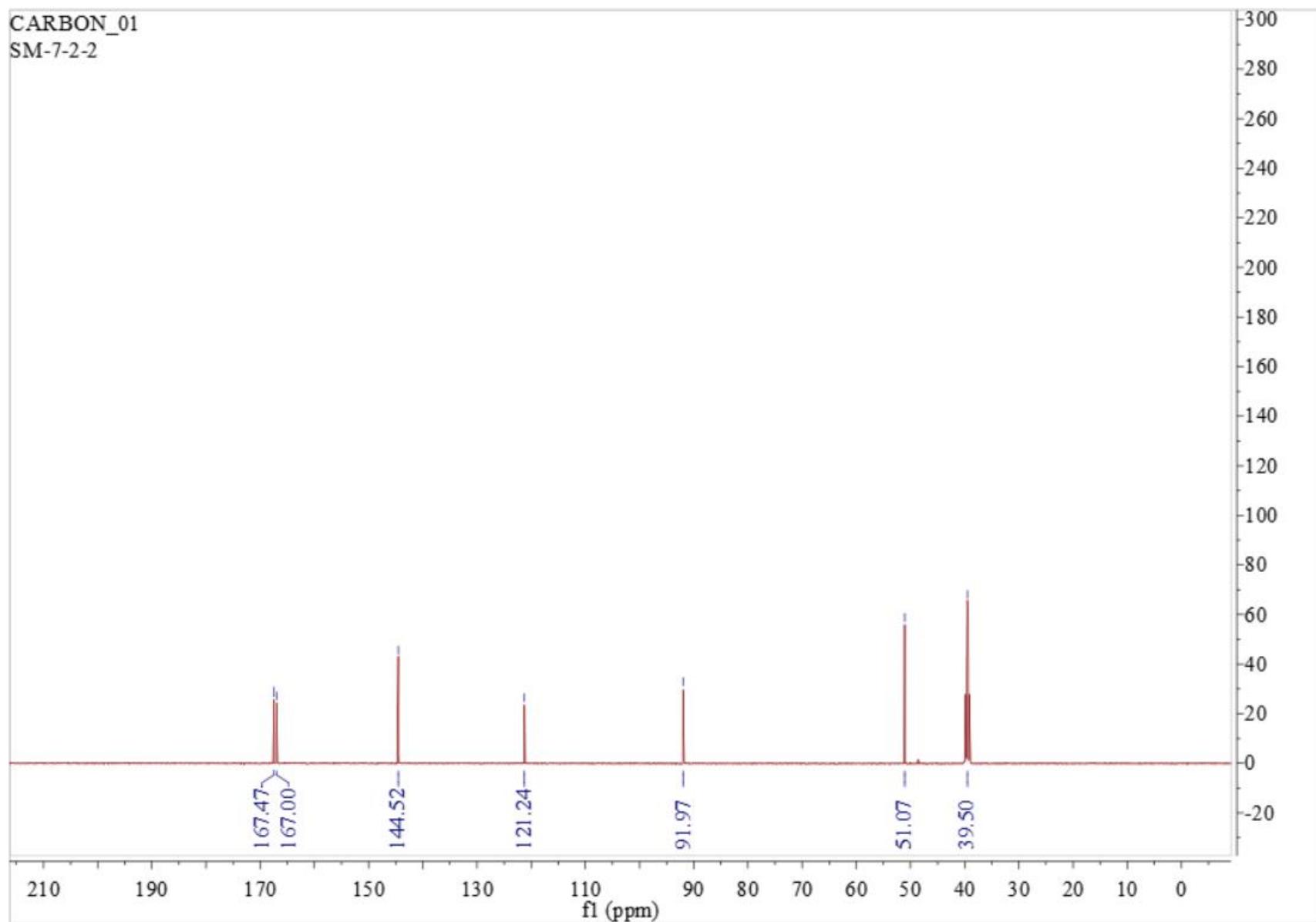


Figure S90. ¹³C NMR spectrum of compound **10** in DMSO-*d*₆ (125 MHz).

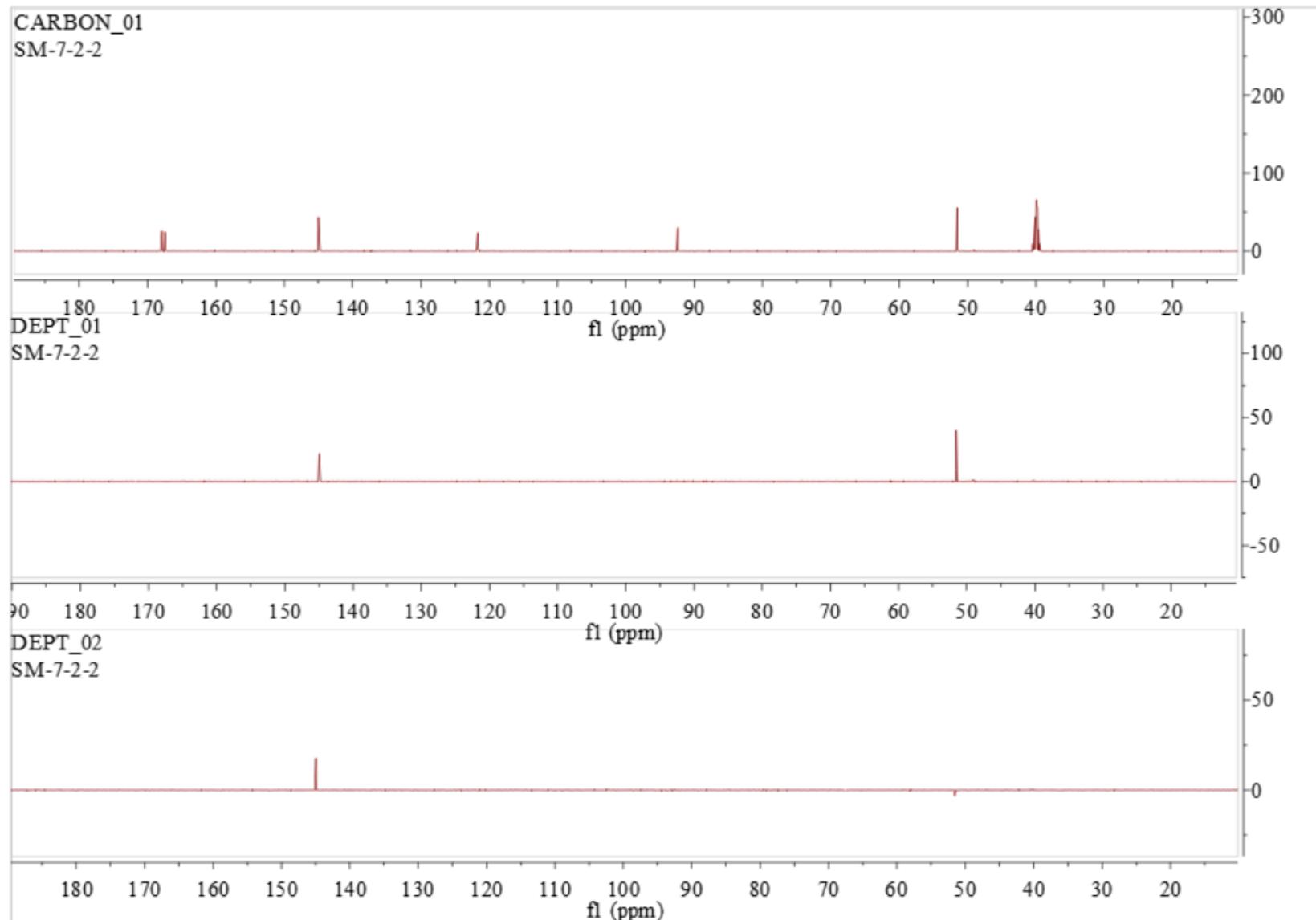


Figure S91. ^{13}C NMR and DEPT spectrum of compound **10** in $\text{DMSO}-d_6$ (125 MHz).

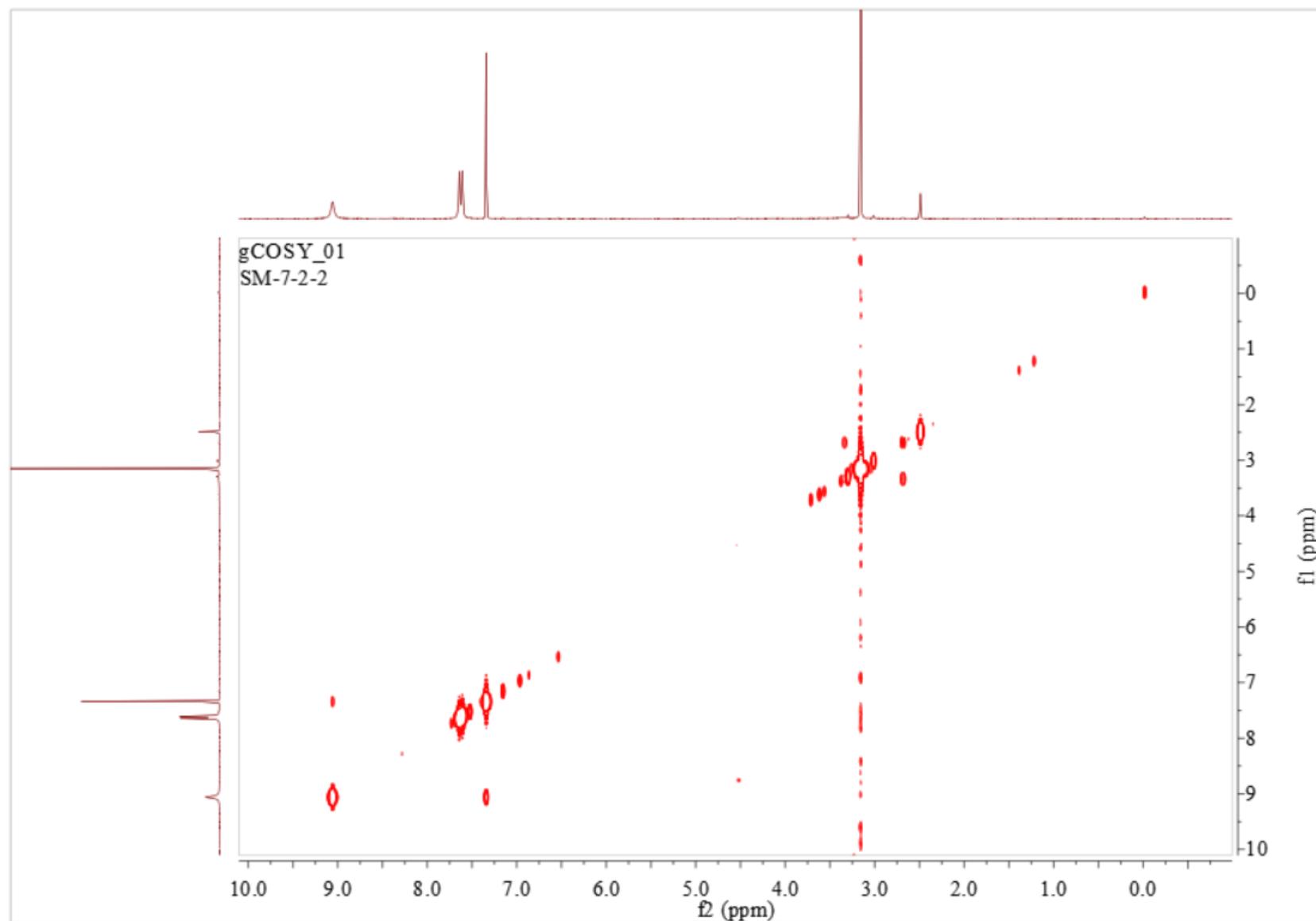


Figure S92. ^1H - ^1H COSY spectrum of compound **10** in $\text{DMSO}-d_6$ (500 MHz).

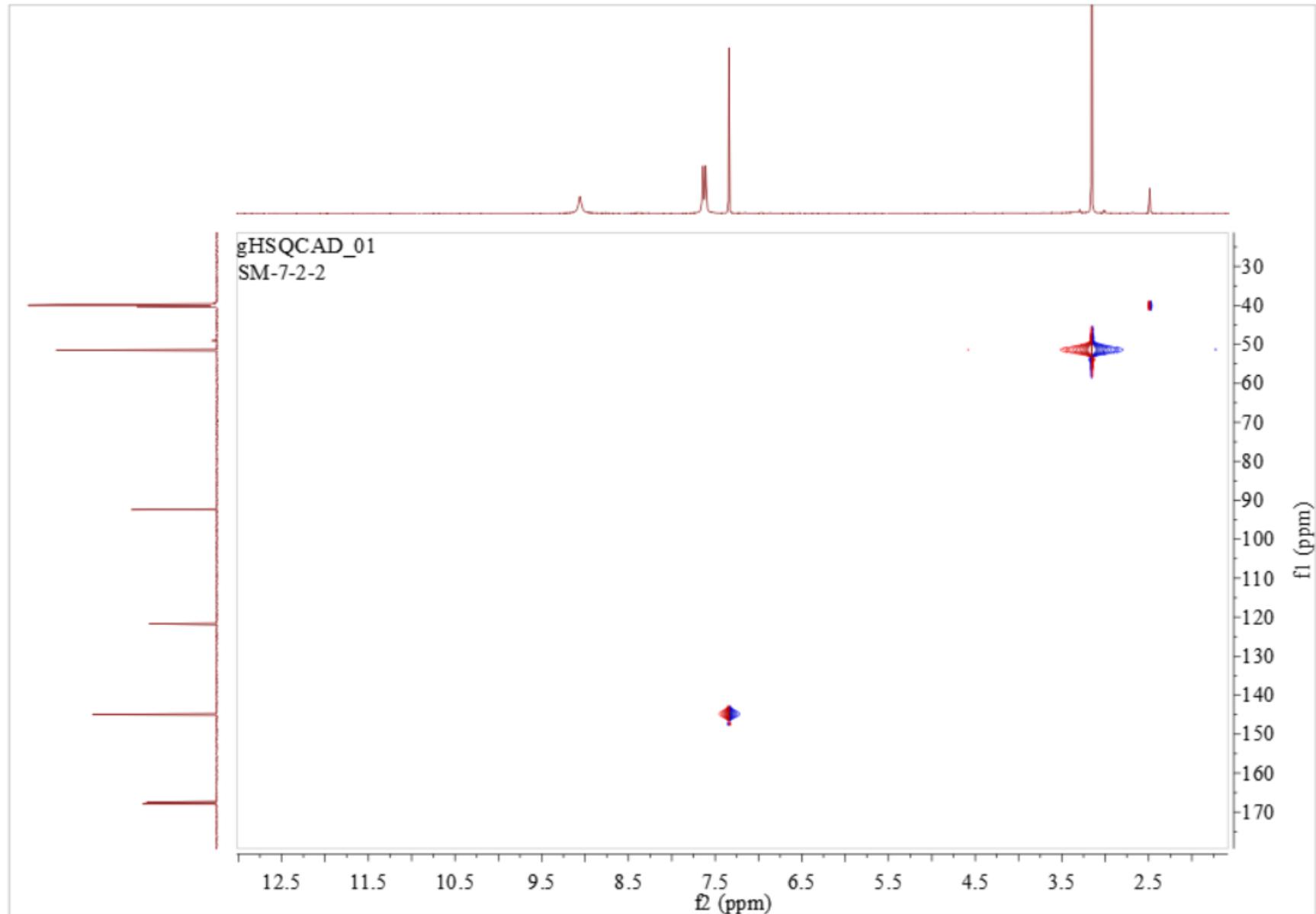


Figure S93. HSQC spectrum of compound **10** in $\text{DMSO}-d_6$ (500 MHz).

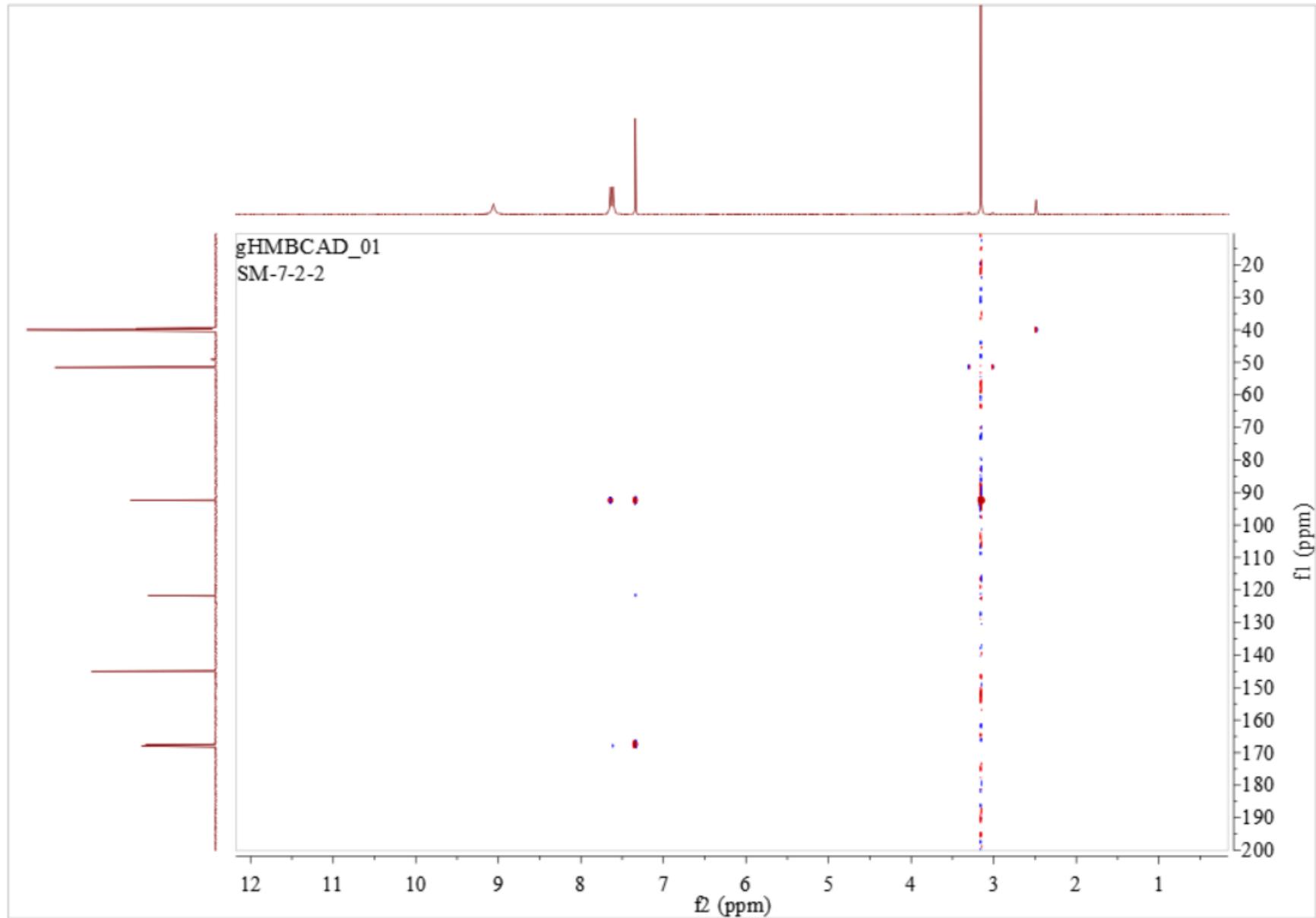


Figure S94. HMBC spectrum of compound **10** in $\text{DMSO}-d_6$ (500 MHz).

20210520-SM-7-2-2_210520105231 #31 RT: 0.27 AV: 1 NL: 1.37E6

T: FTMS + p ESI sid=35.00 Full ms [120.00-1000.00]

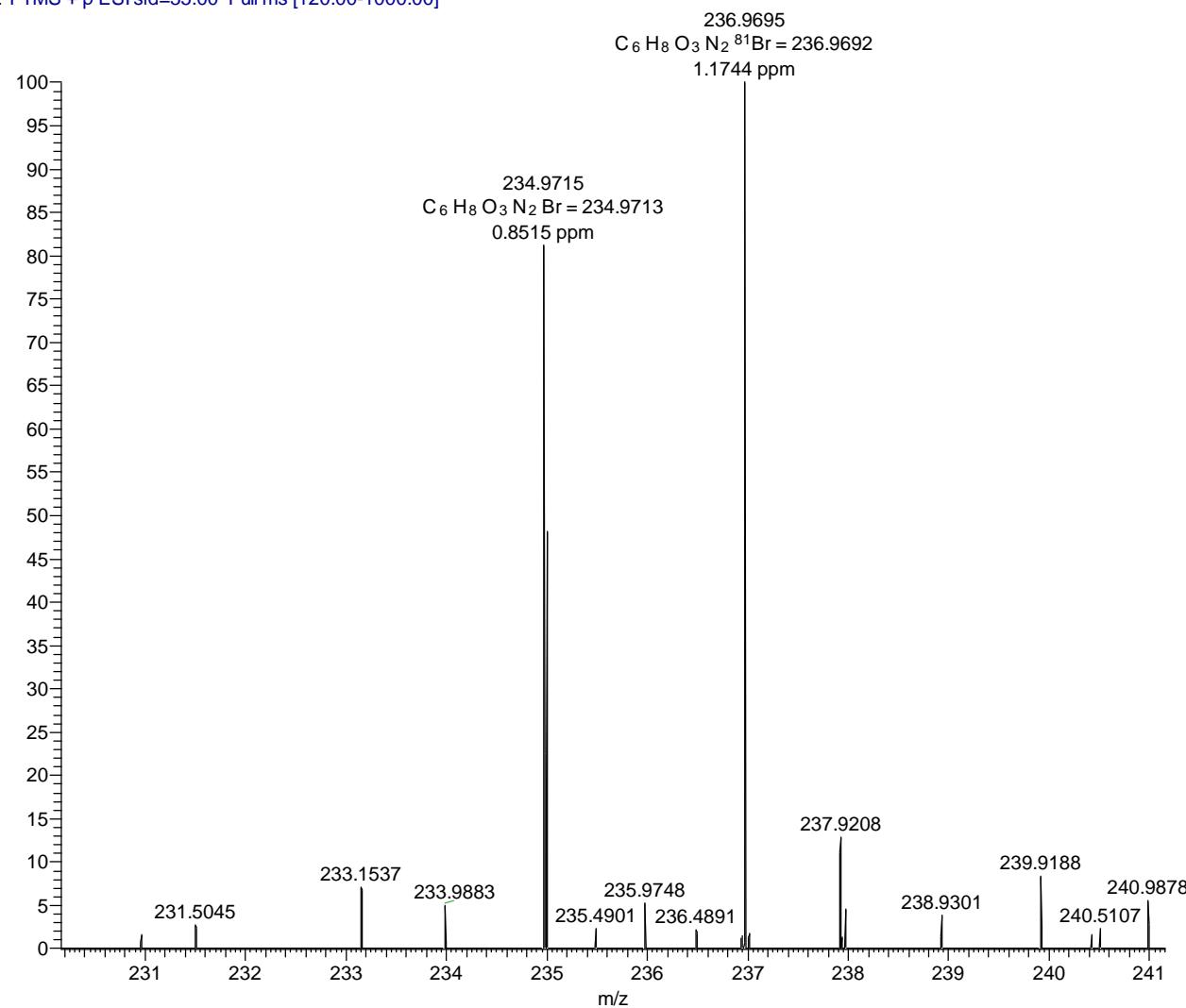


Figure S95. HRESIMS data of compound **10**.

PROTON_01
SM-5-1-2-1-5

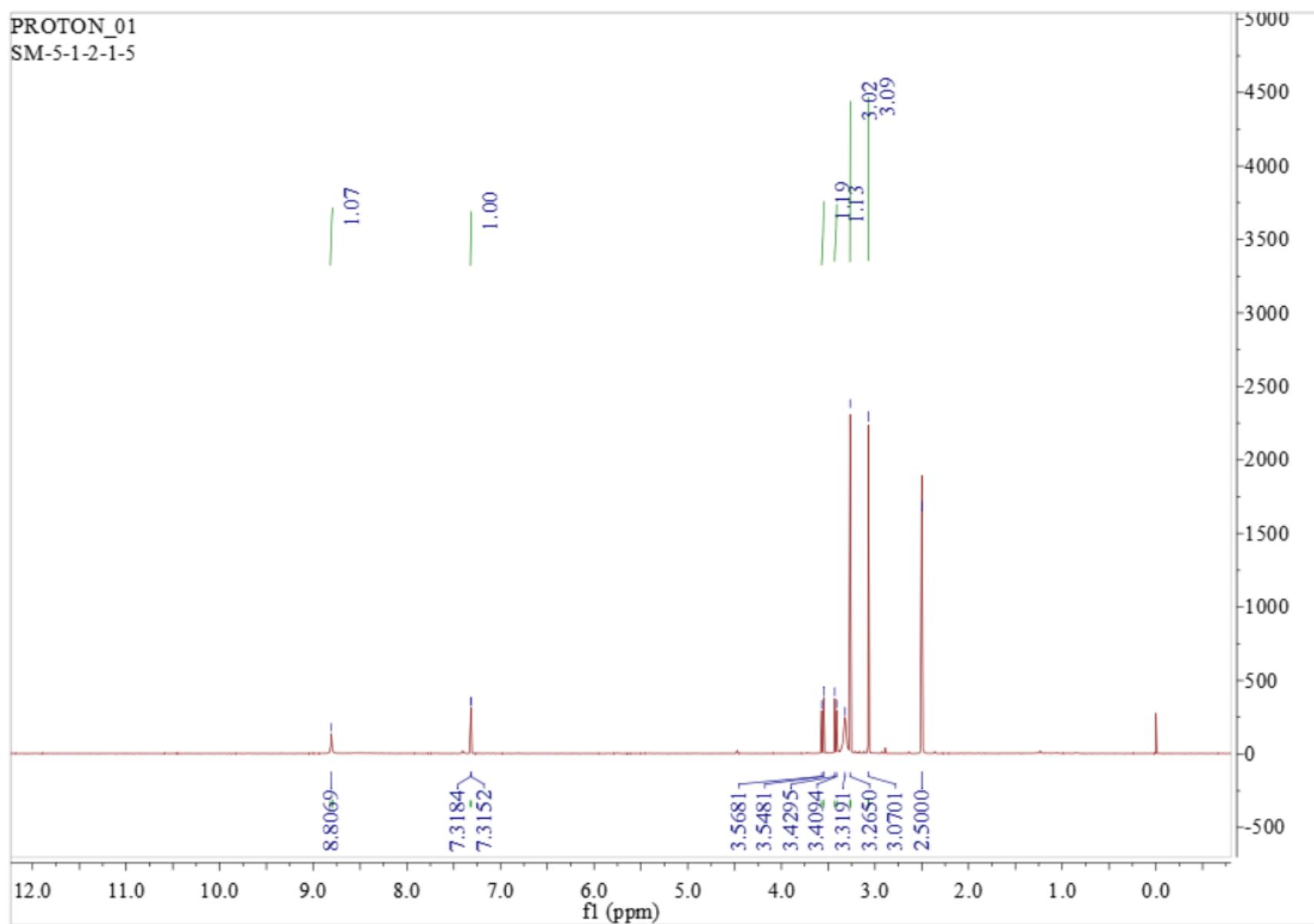


Figure S96. ¹H NMR spectrum of compound 11 in DMSO-*d*₆ (500 MHz).

CARBON_01
SM-5-1-2-1-5

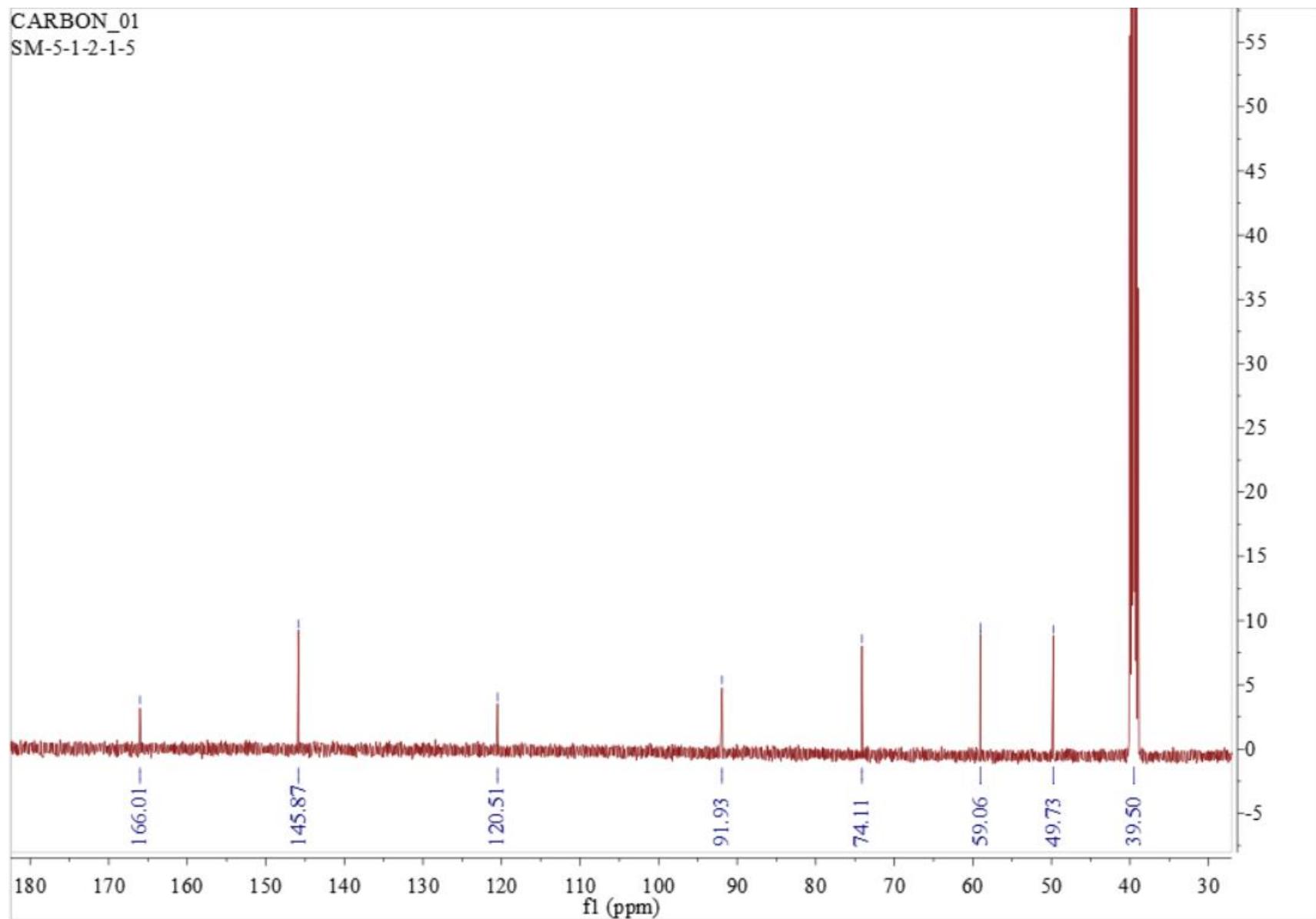


Figure S97. ¹³C NMR spectrum of compound **11** in DMSO-*d*₆ (125 MHz).

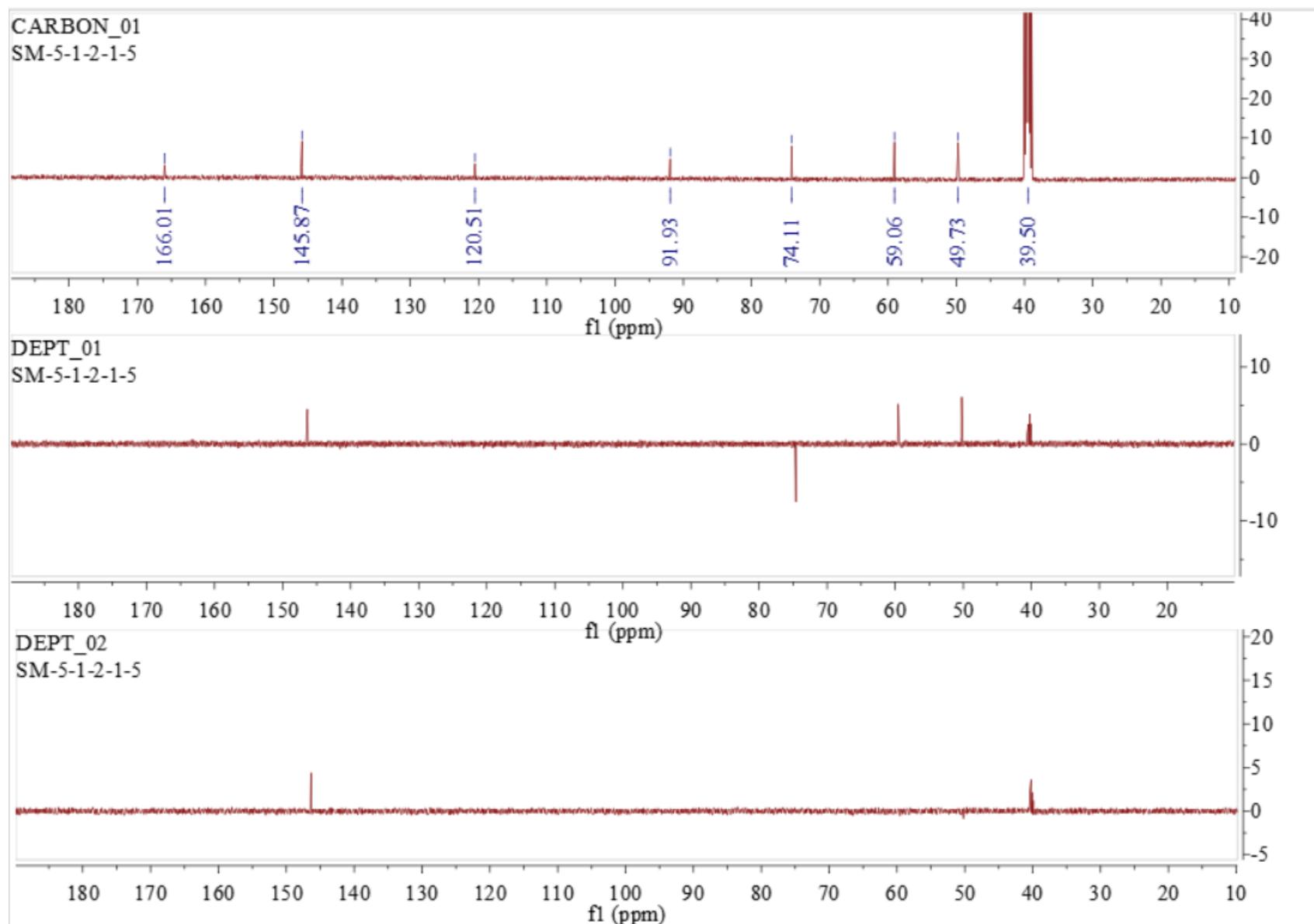


Figure S98. ¹³C NMR and DEPT spectrum of compound **11** in DMSO-*d*₆ (125 MHz).

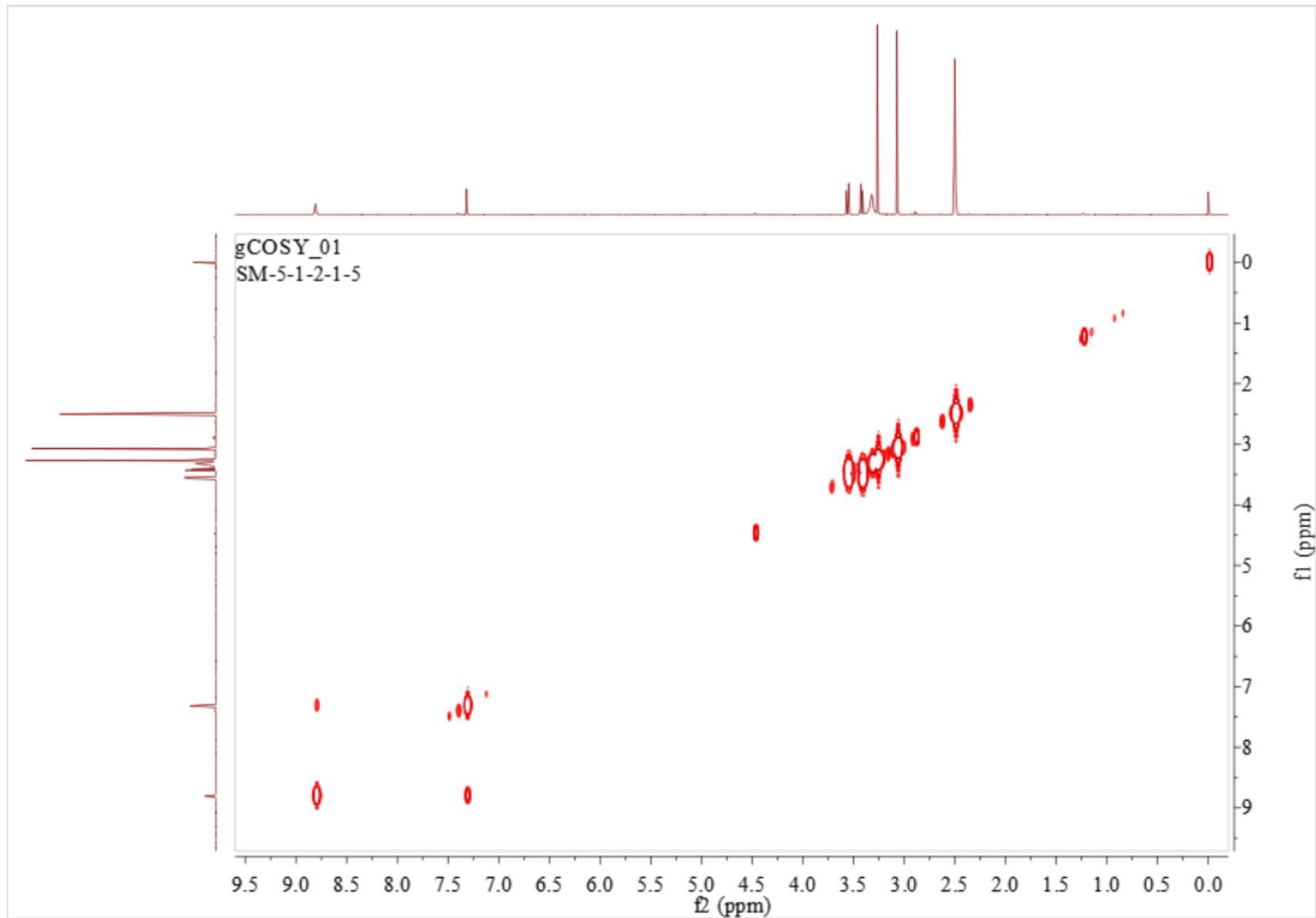


Figure S99. ^1H - ^1H COSY spectrum of compound **11** in $\text{DMSO}-d_6$ (500 MHz).

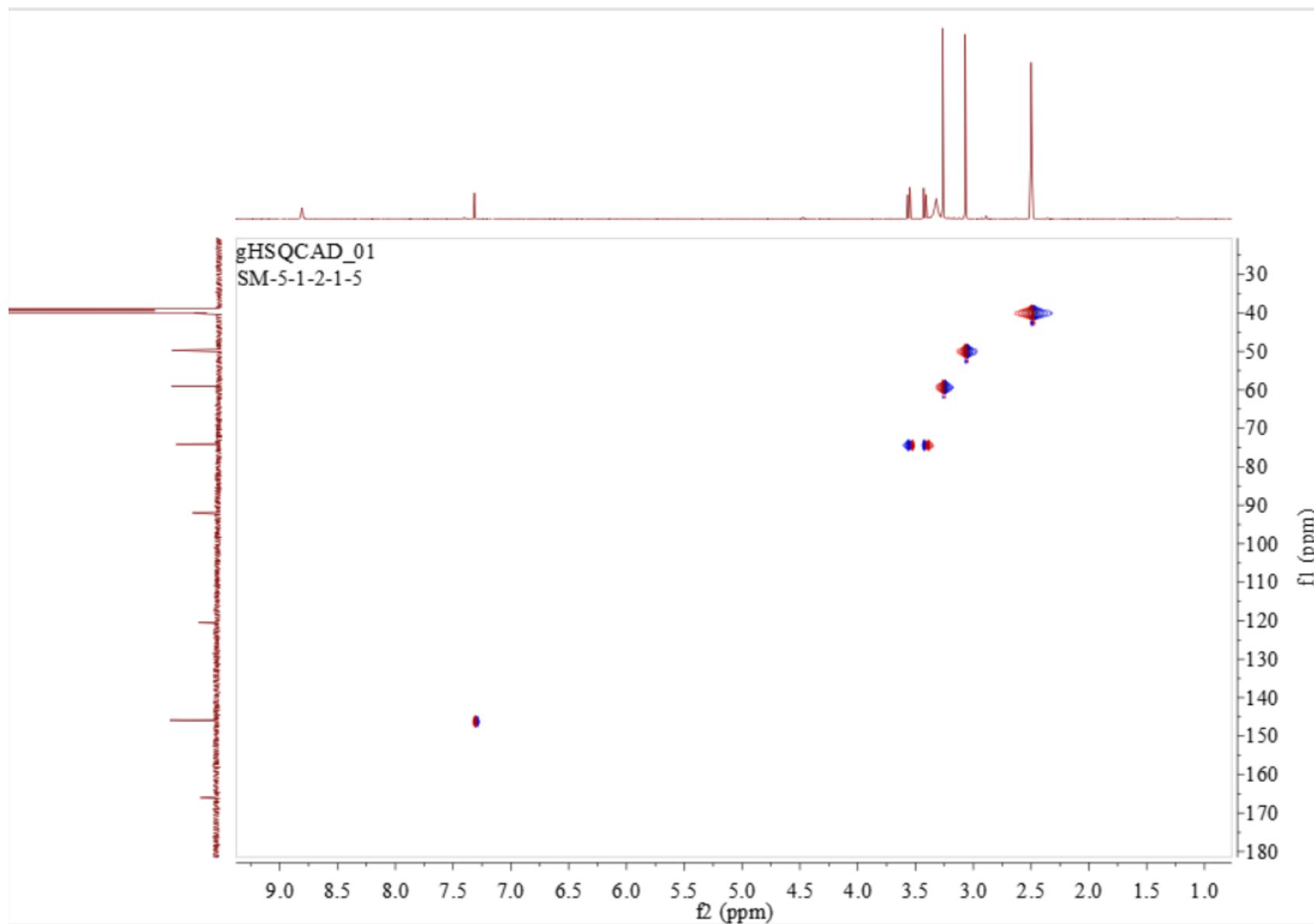


Figure S100. HSQC spectrum of compound **11** in $\text{DMSO}-d_6$ (500 MHz).

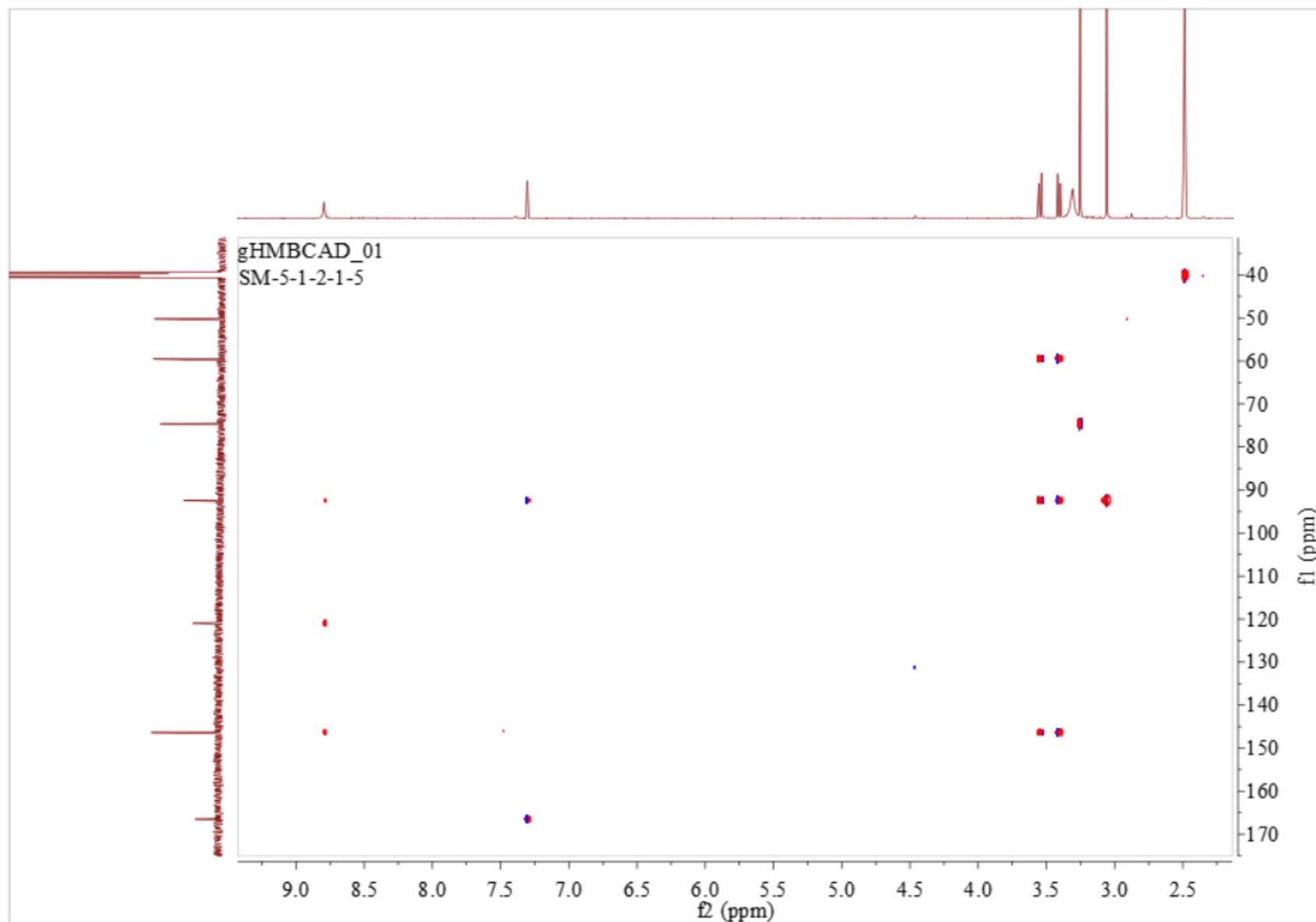


Figure S101. HMBC spectrum of compound **11** in $\text{DMSO}-d_6$ (500 MHz).

D:\MS-DATA\20210119-HG-5_210118123729

1/19/2021 8:30:36 AM

HG-5

20210119-HG-5_210118123729 #59-60 RT: 0.53-0.54 AV: 2 SB: 18 0.05-0.22 NL: 1.87E6
T: FTMS + p ESI Full ms [100.00-1500.00]

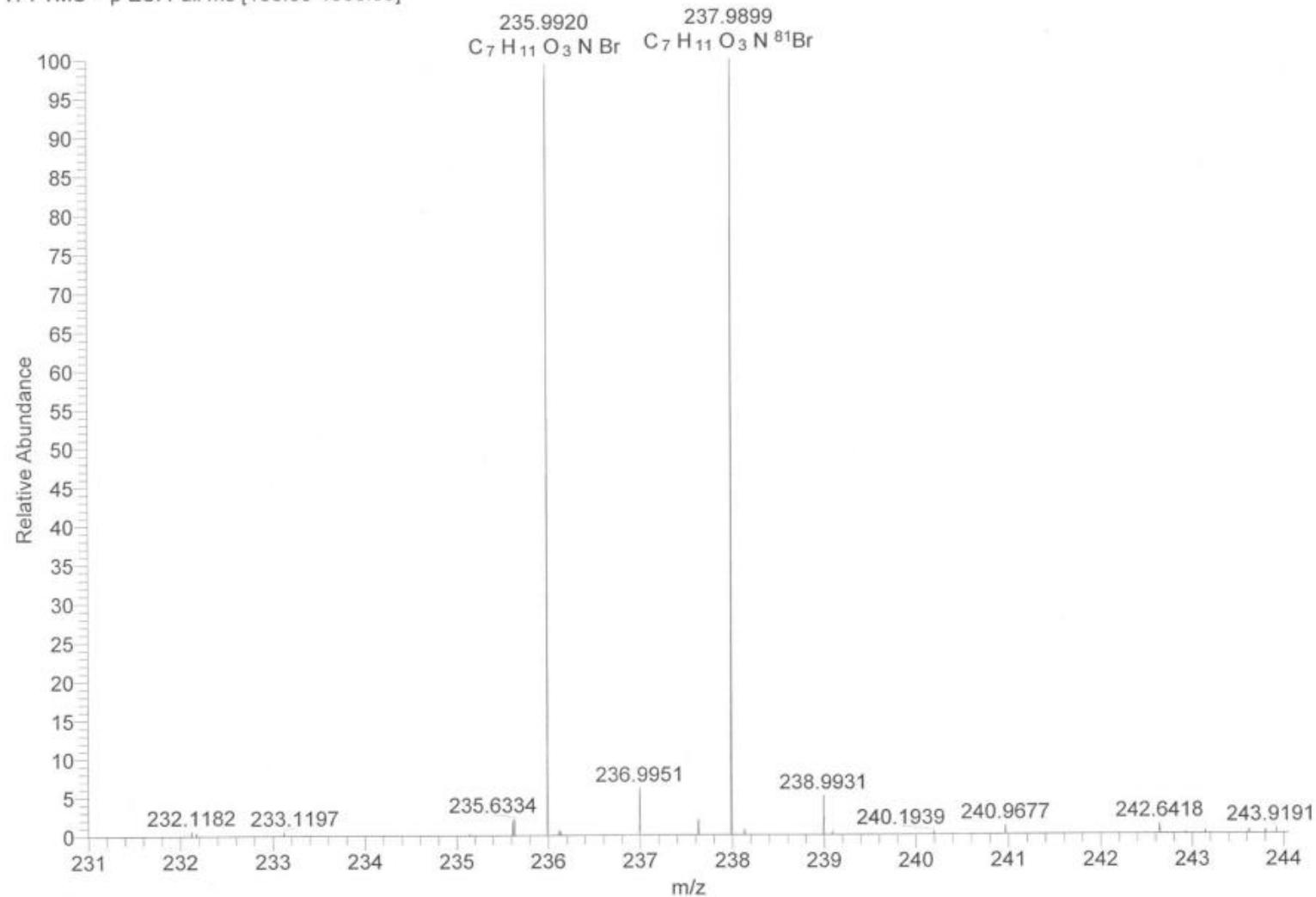


Figure S102. HRESIMS data of compound 11.

PROTON_01
SM-5-1-2-1-4

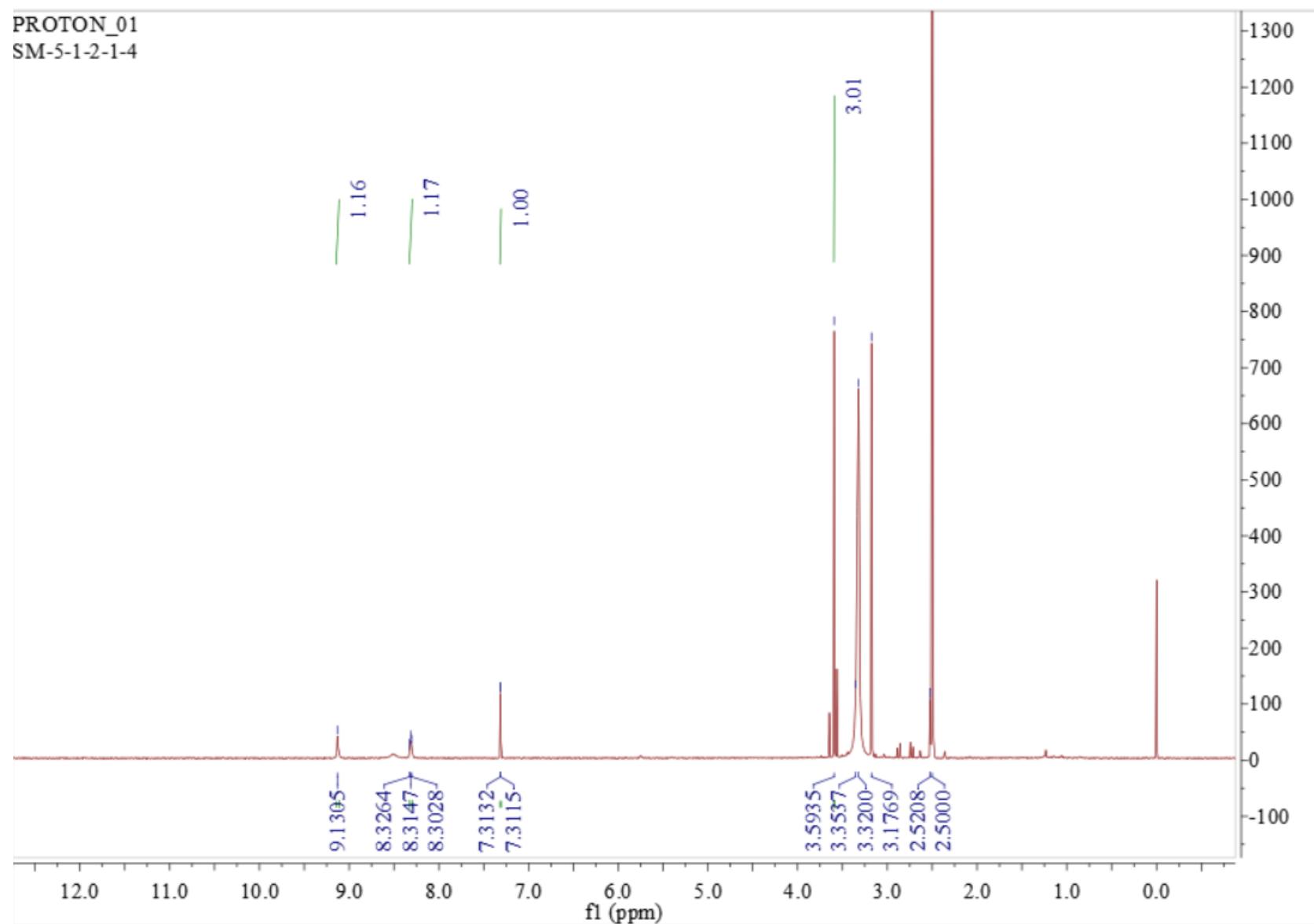


Figure S103. ^1H NMR spectrum of compound **12** in $\text{DMSO}-d_6$ (500 MHz).

101

CARBON_02
SM-5-1-2-1-4

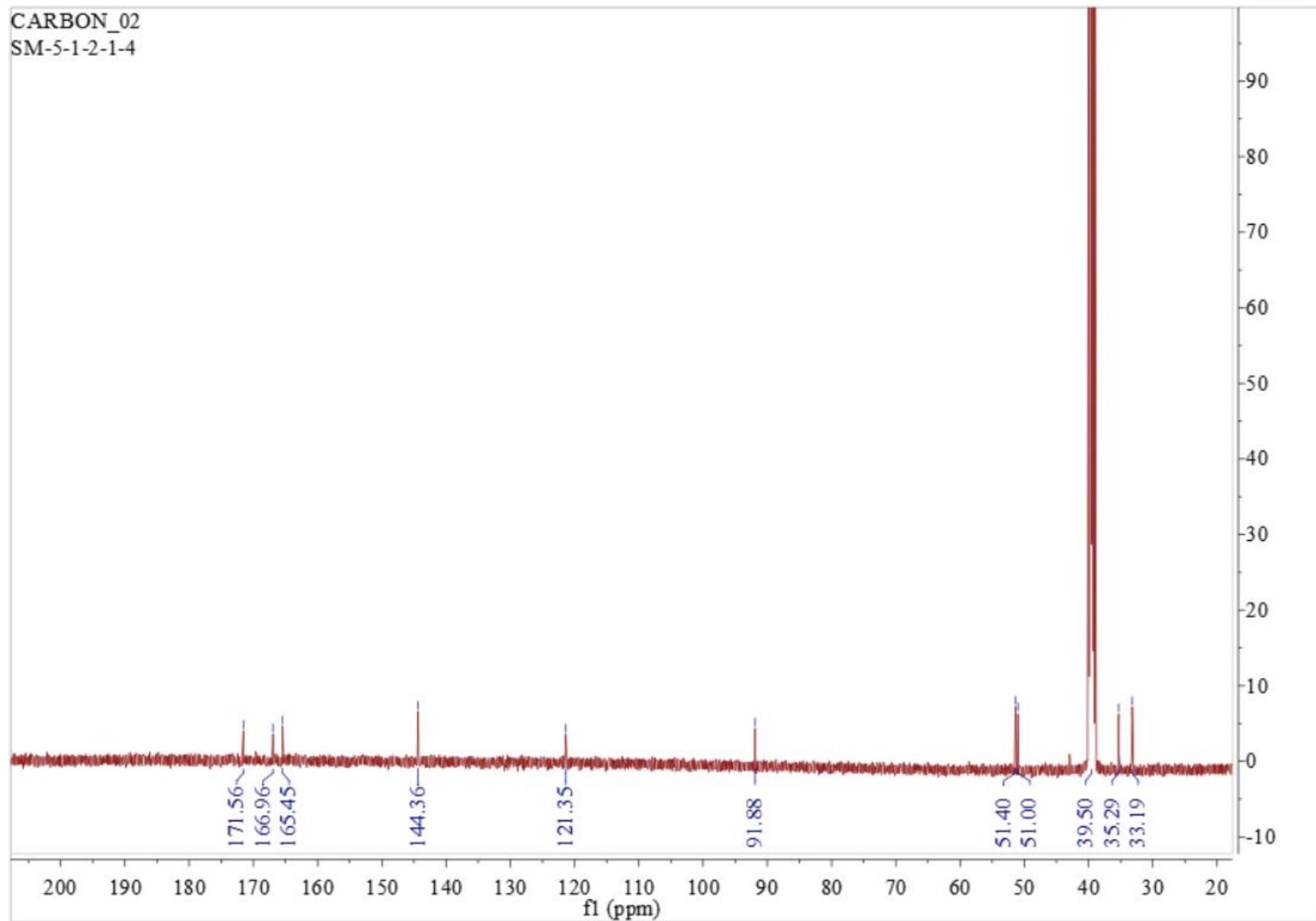


Figure S104. ¹³C NMR spectrum of compound **12** in DMSO-*d*₆ (125 MHz).

102

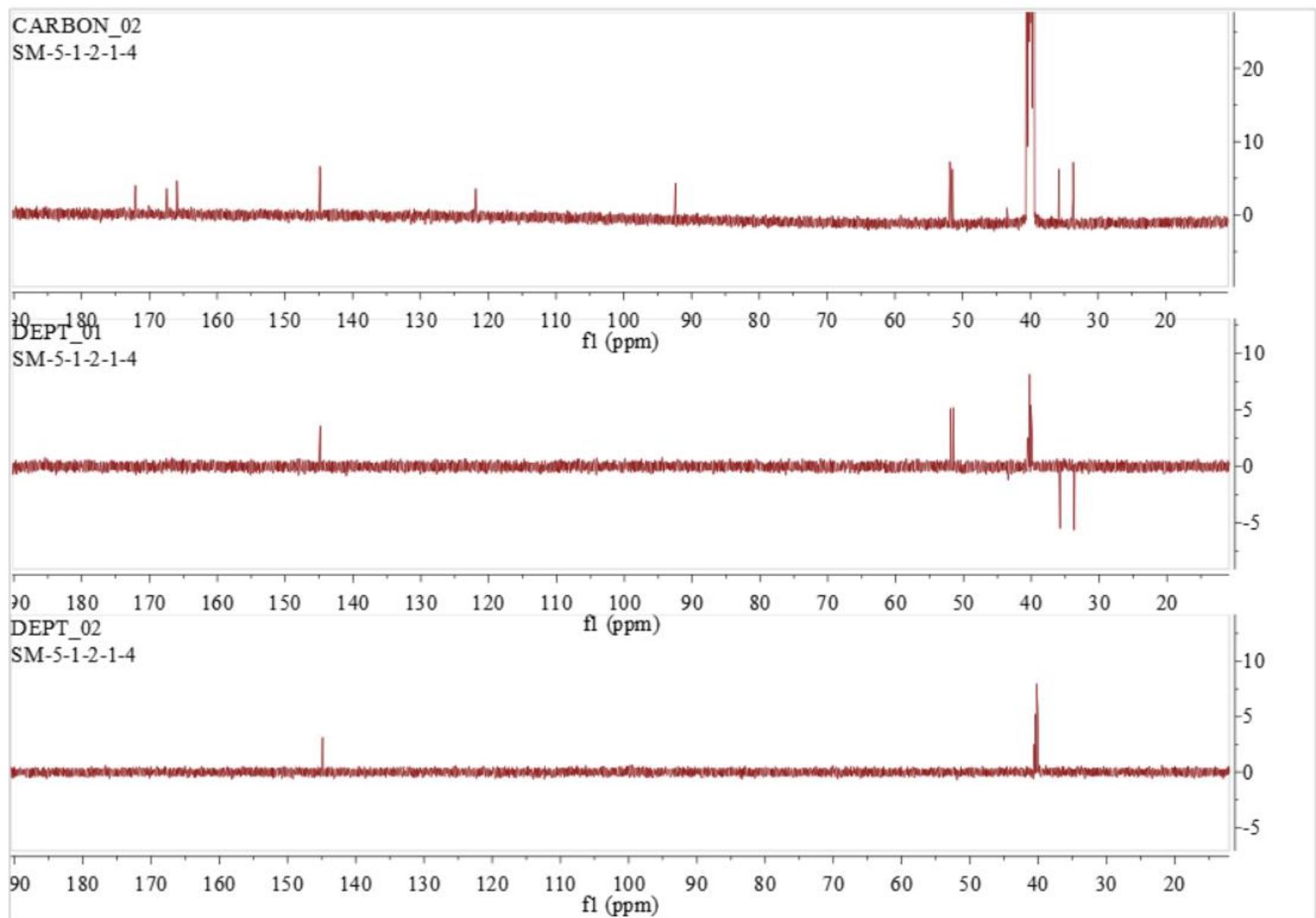


Figure S105. ^{13}C NMR and DEPT spectrum of compound **12** in $\text{DMSO}-d_6$ (125 MHz).

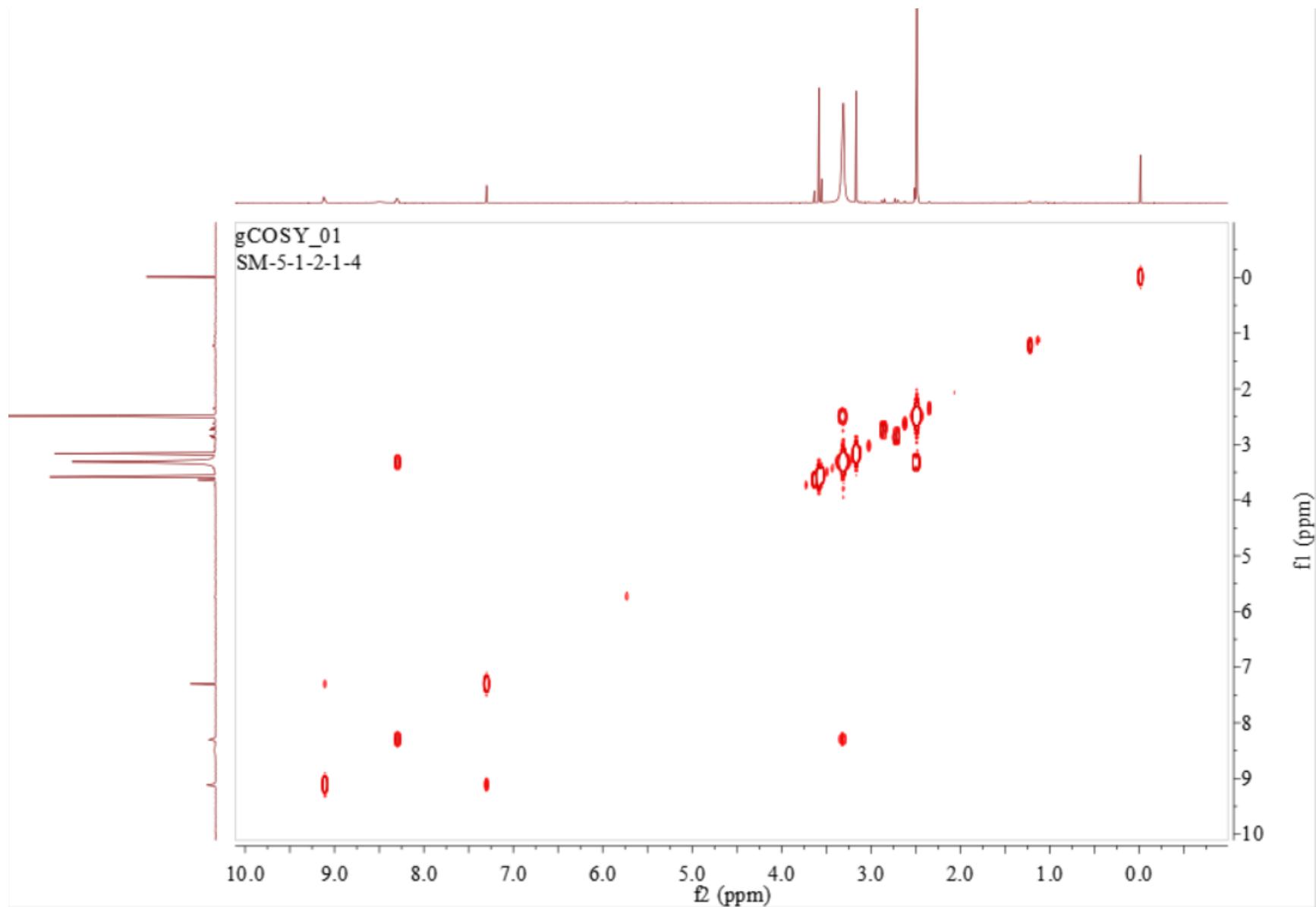


Figure S106. ^1H - ^1H COSY spectrum of compound **12** in $\text{DMSO}-d_6$ (500 MHz).

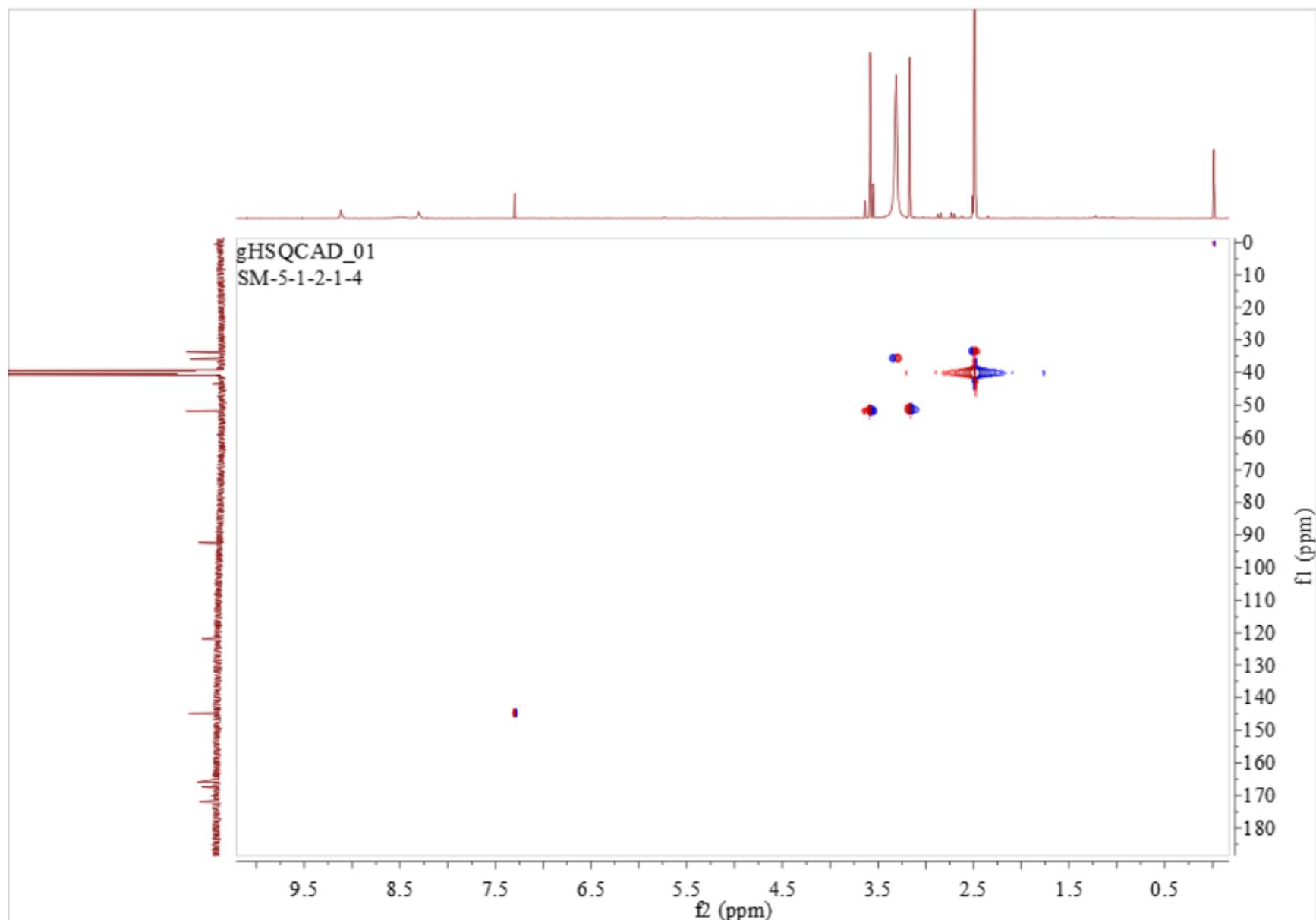


Figure S107. HSQC spectrum of compound **12** in $\text{DMSO}-d_6$ (500 MHz).

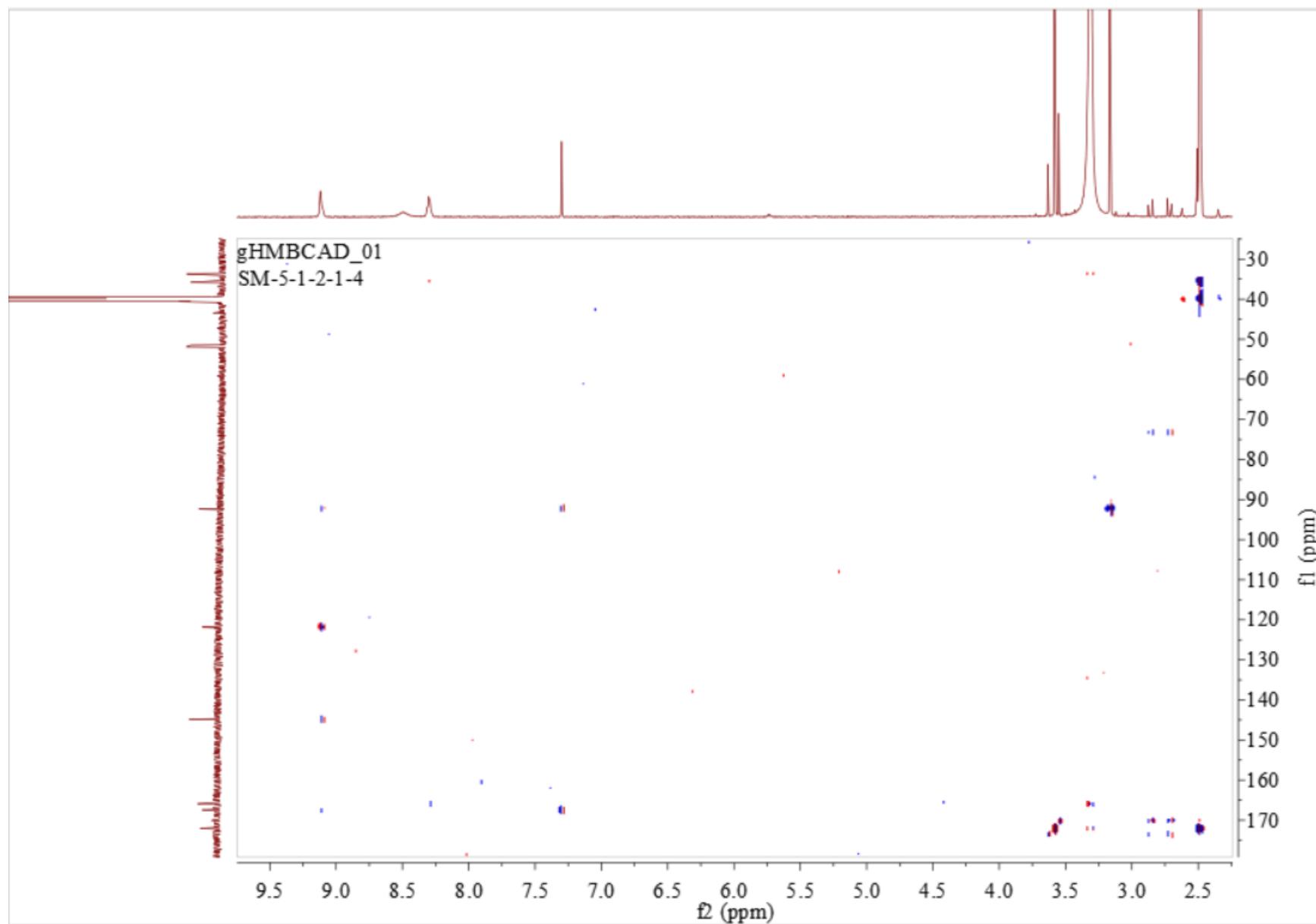


Figure S108. HMBC spectrum of compound **12** in $\text{DMSO}-d_6$ (500 MHz).

20201223-SM-5-1-2-1-4_201224100207 #52-53 RT: 0.52-0.53 AV: 2 NL: 1.16E5
T: FTMS + p ESI Full ms [180.00-1000.00]

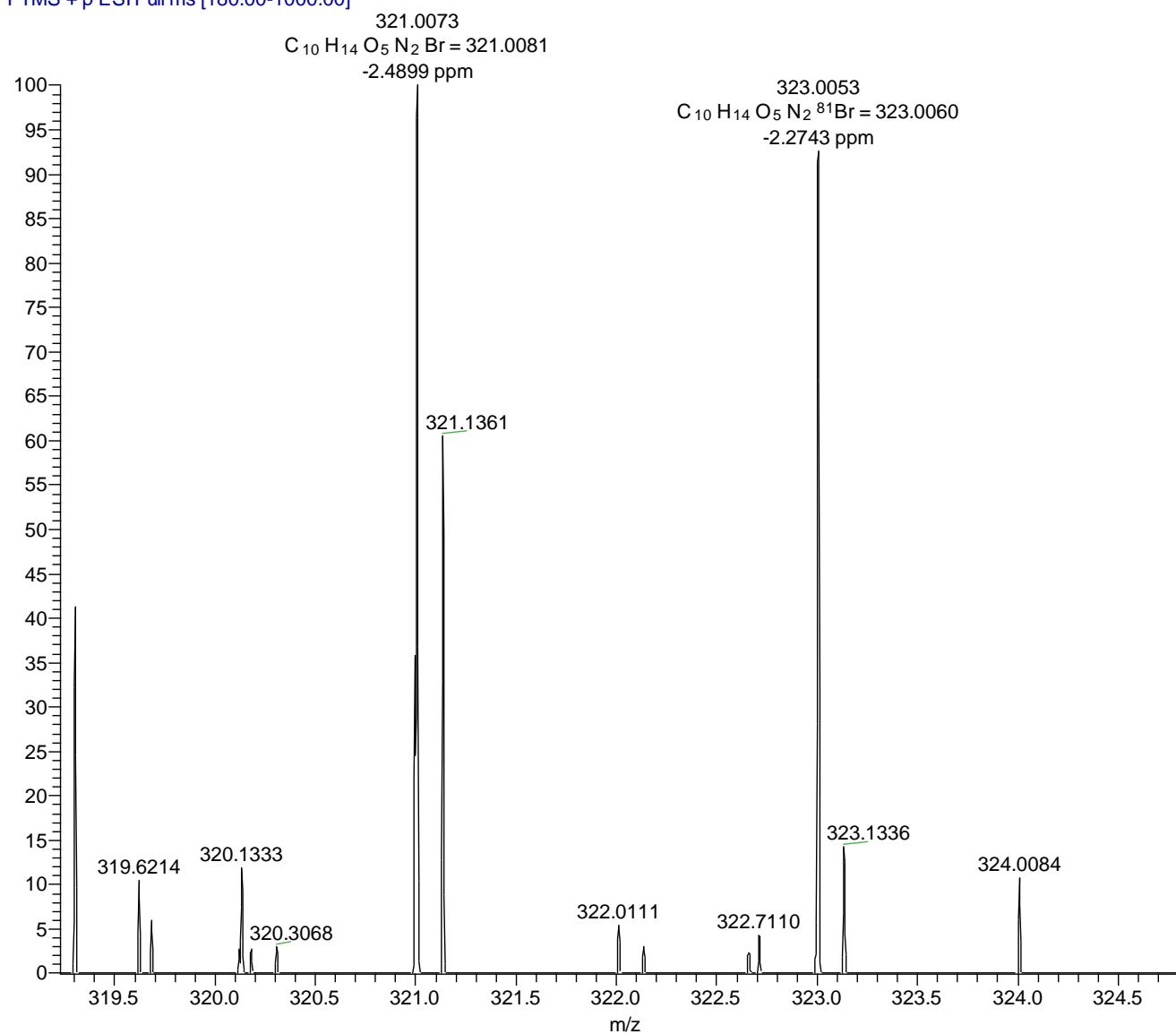


Figure S109. HRESIMS data of compound 12.

PROTON_01
SM-8-2-2-1

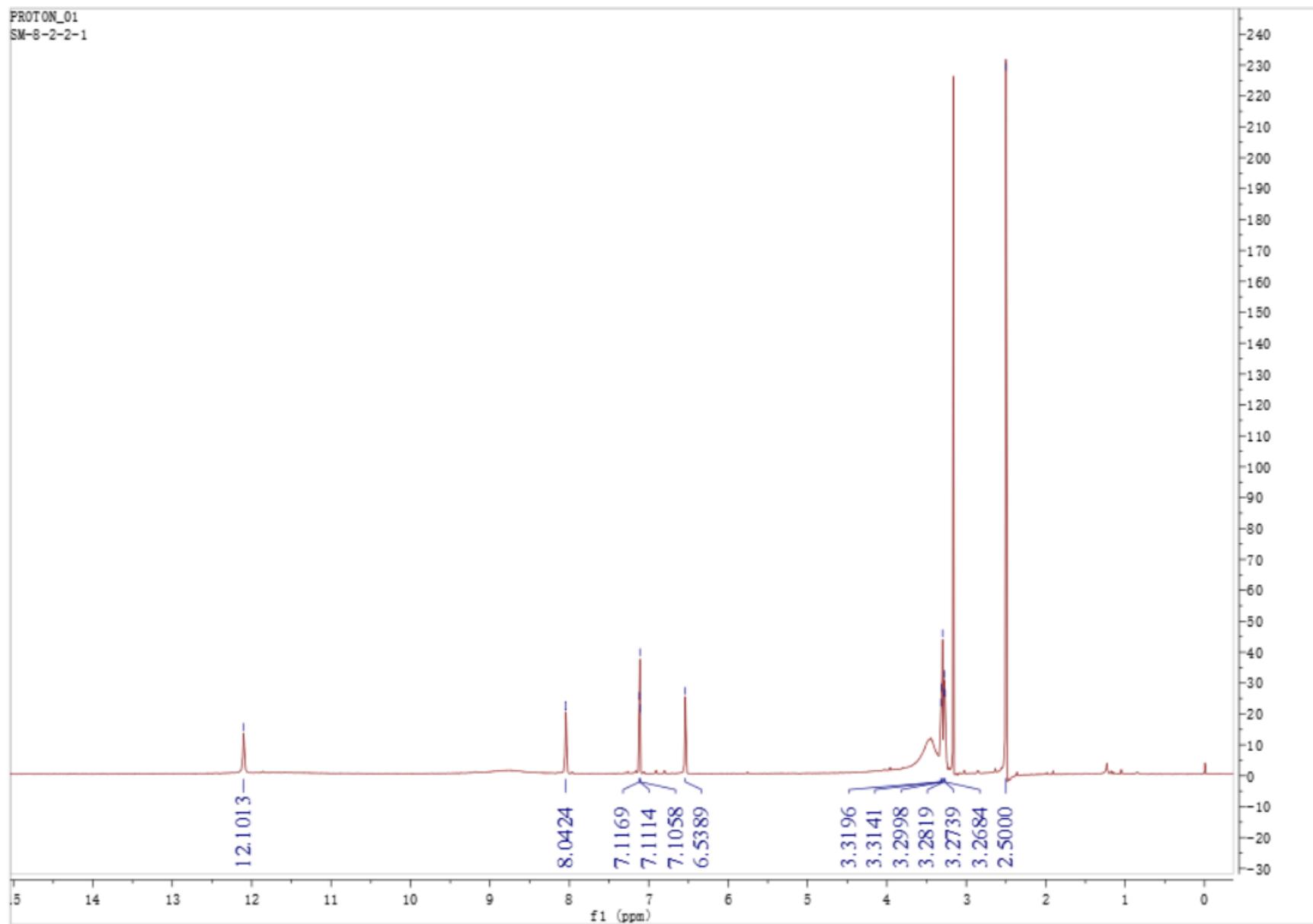


Figure S110. ¹H NMR spectrum of compound 13 in DMSO-*d*₆ (500 MHz).

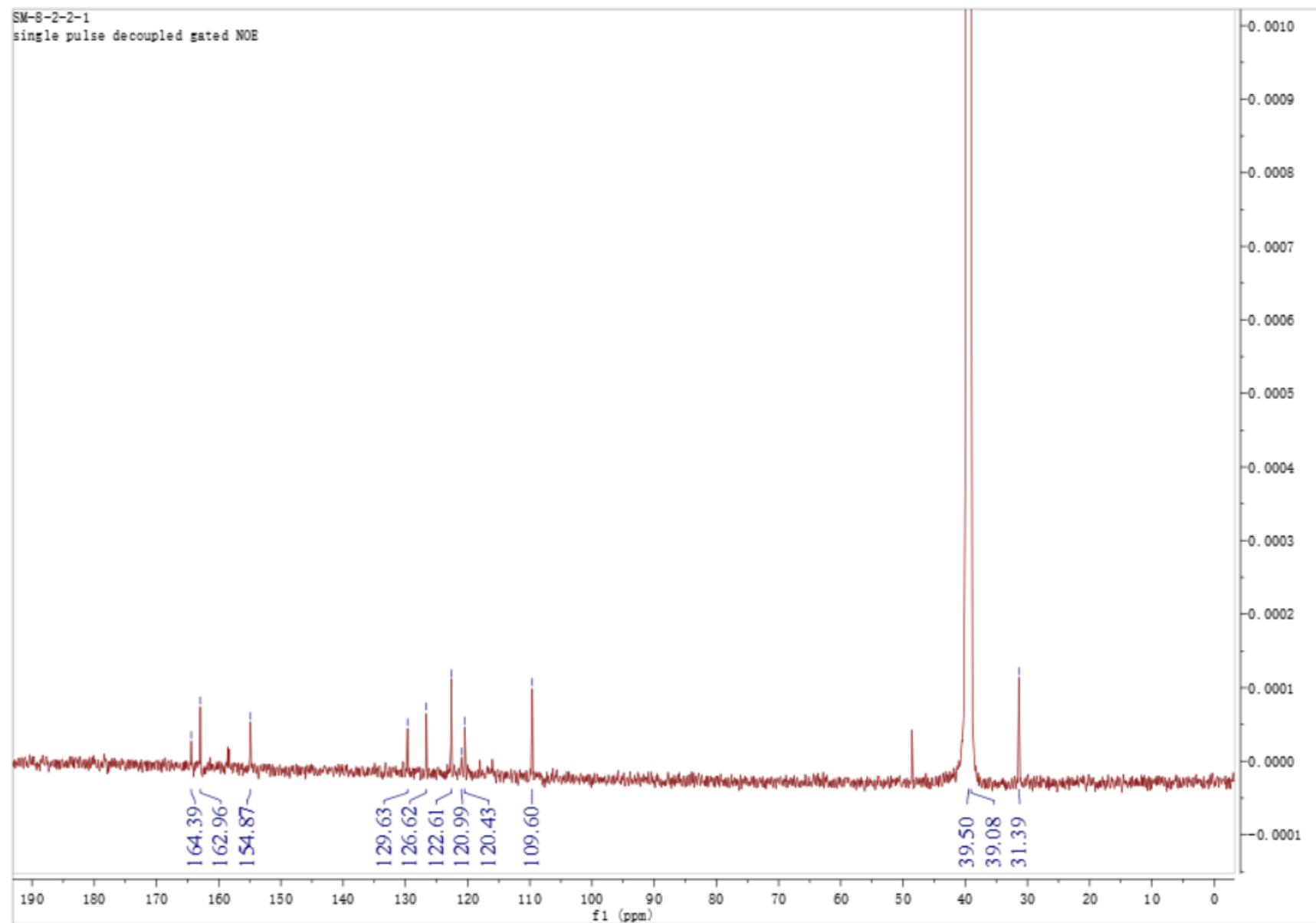


Figure S111. ^{13}C NMR spectrum of compound **13** in $\text{DMSO}-d_6$ (125 MHz).

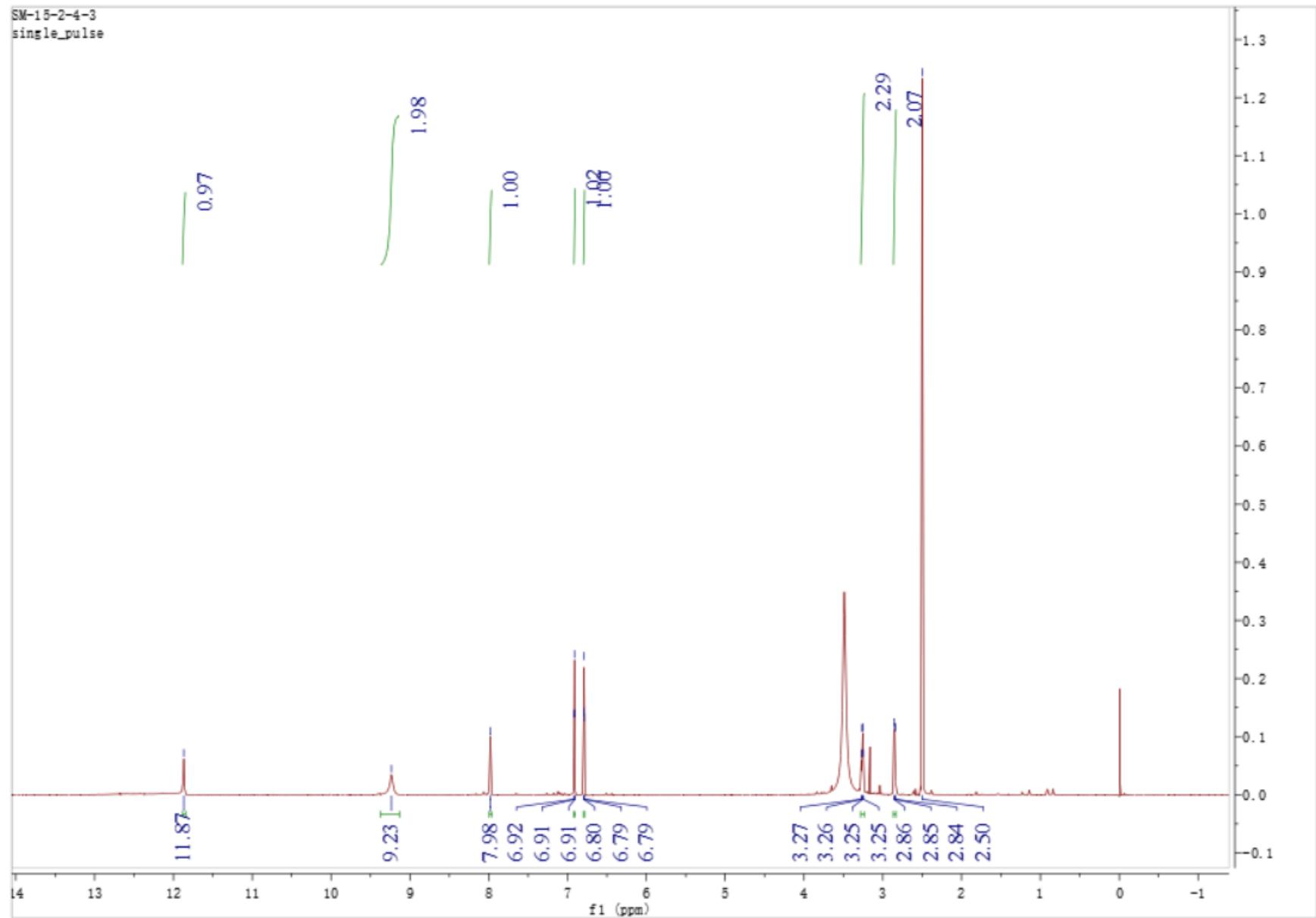


Figure S112. ^1H NMR spectrum of compound **14** in $\text{DMSO}-d_6$ (500 MHz).

110

SM-15-2-4-3
single pulse decoupled gated NOE

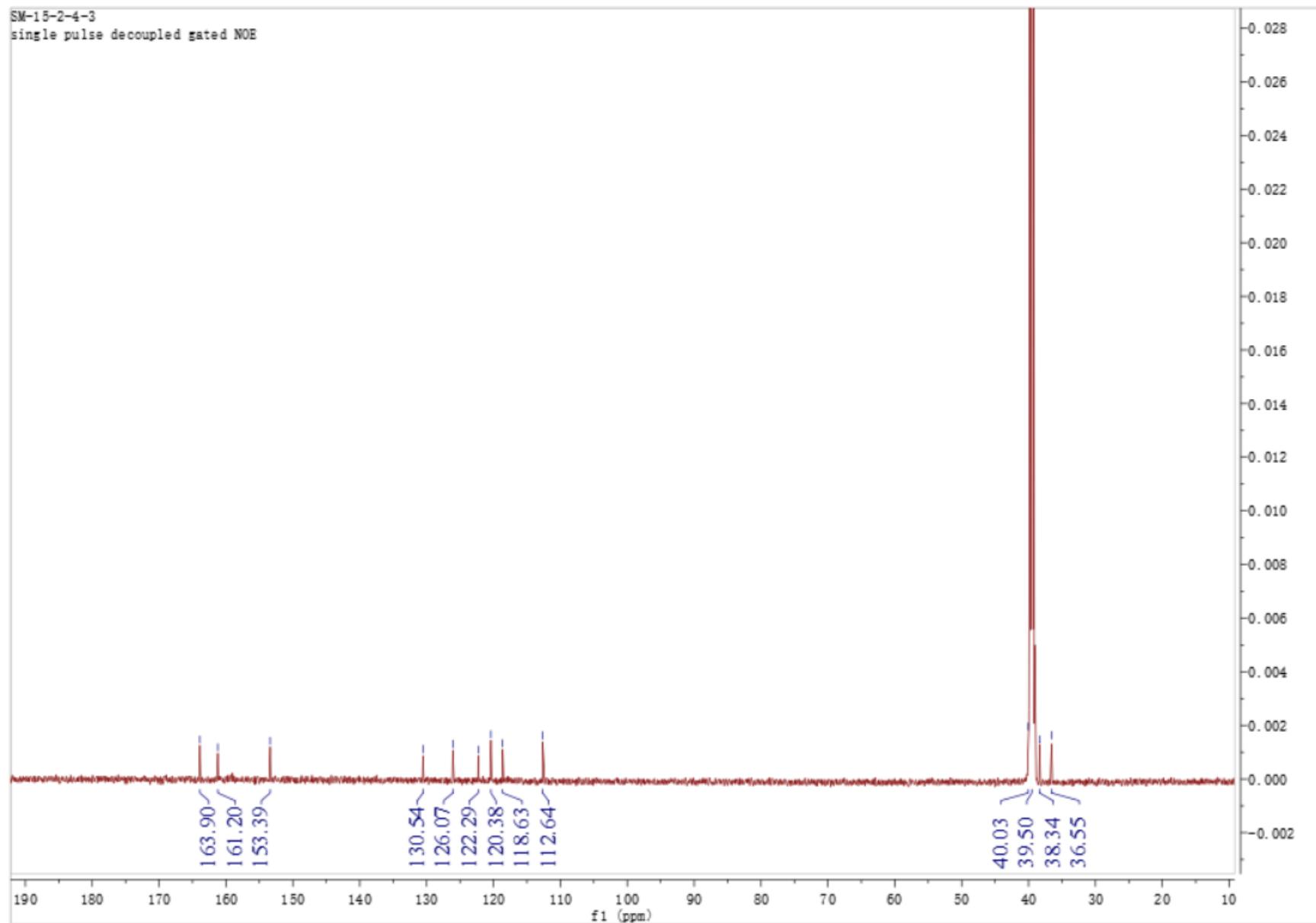


Figure S113. ¹³C NMR spectrum of compound **14** in $\text{DMSO}-d_6$ (125 MHz).

SM-15-2-4-2
single_pulse

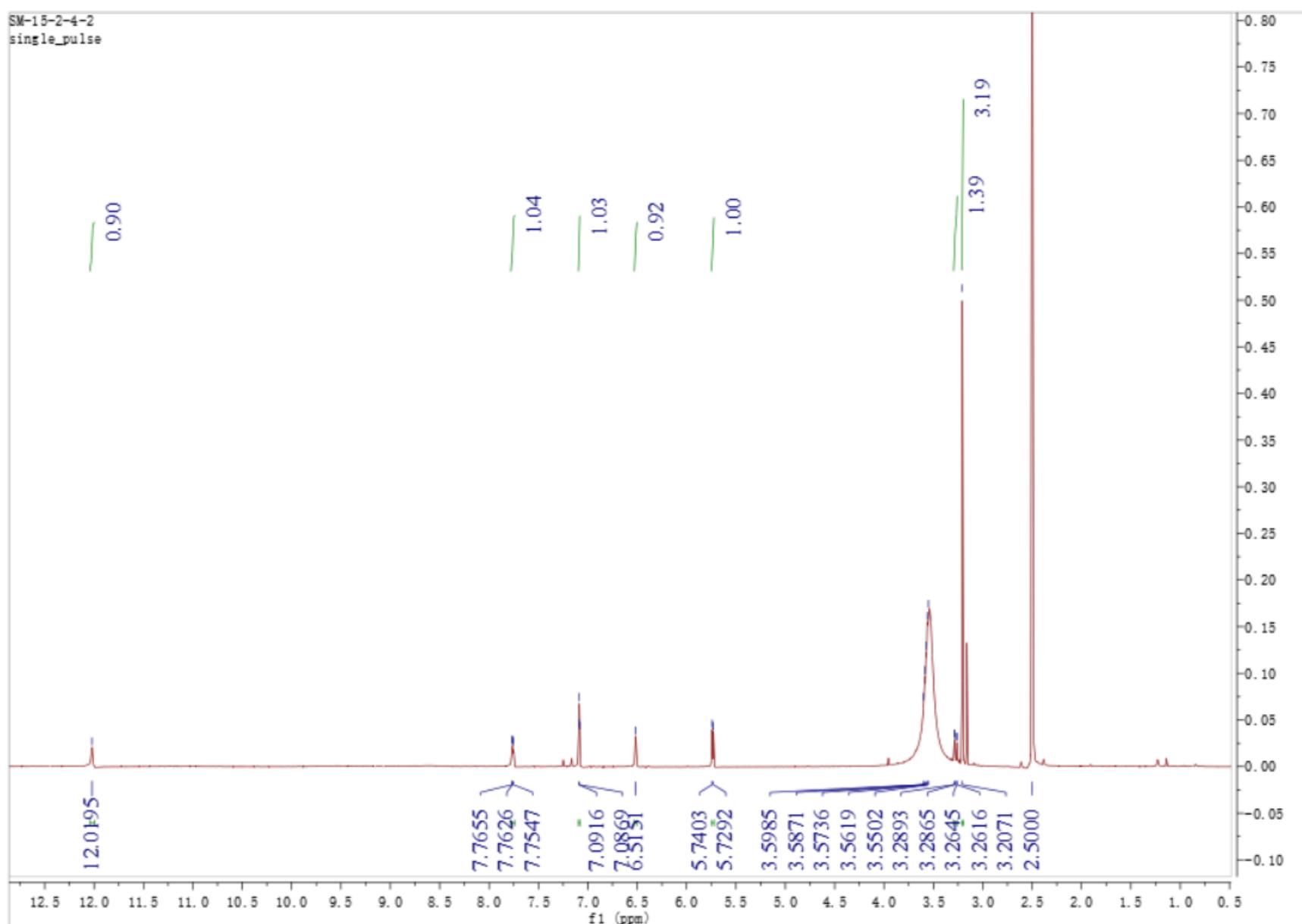


Figure S114. ^1H NMR spectrum of compound **15** in $\text{DMSO}-d_6$ (500 MHz).

SM-15-2-4-2
single pulse decoupled gated NOE

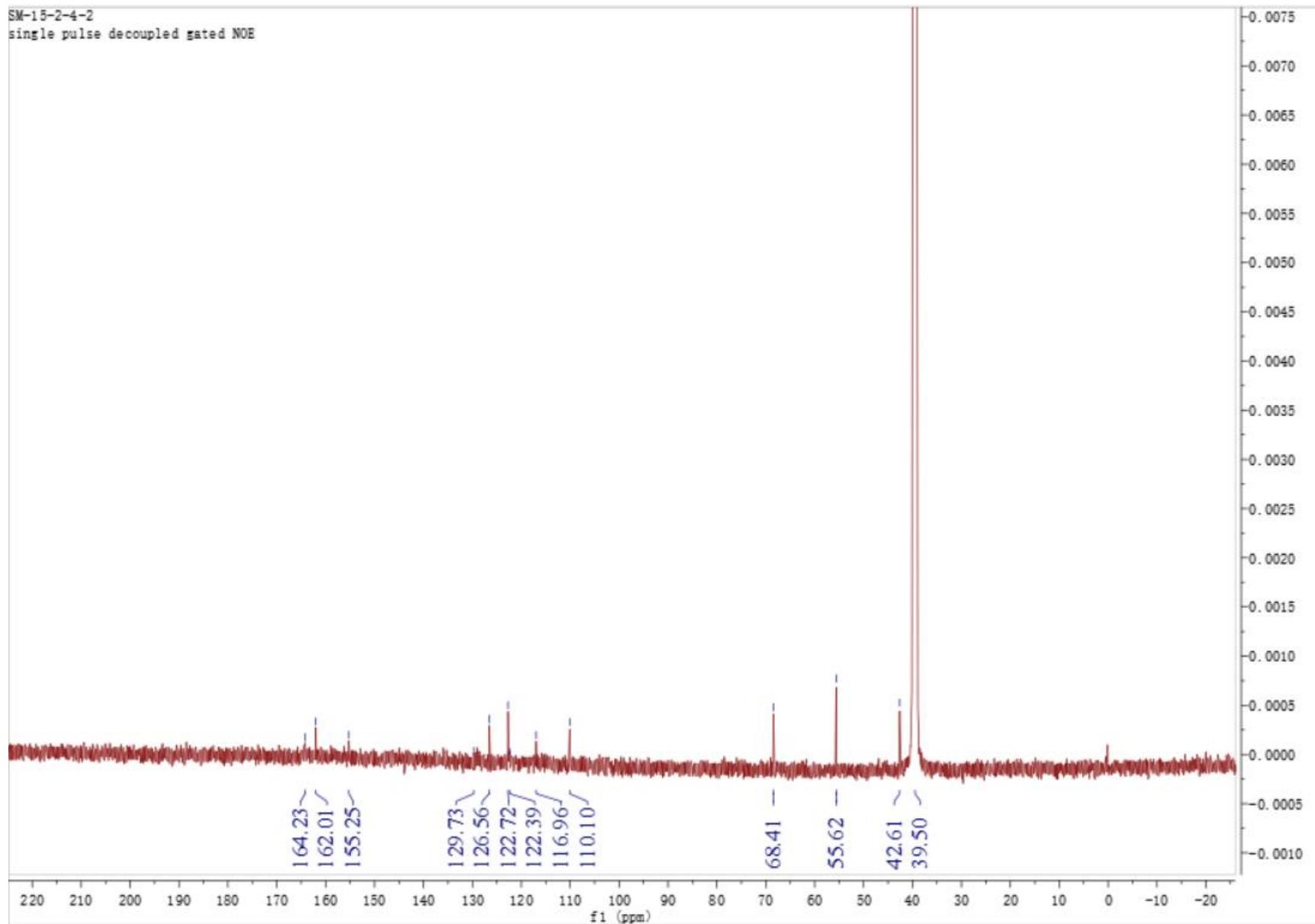


Figure S115. ¹³C NMR spectrum of compound **15** in *DMSO-d*₆ (125 MHz).

PROTON_01
SM-8-1-3-1-1-5

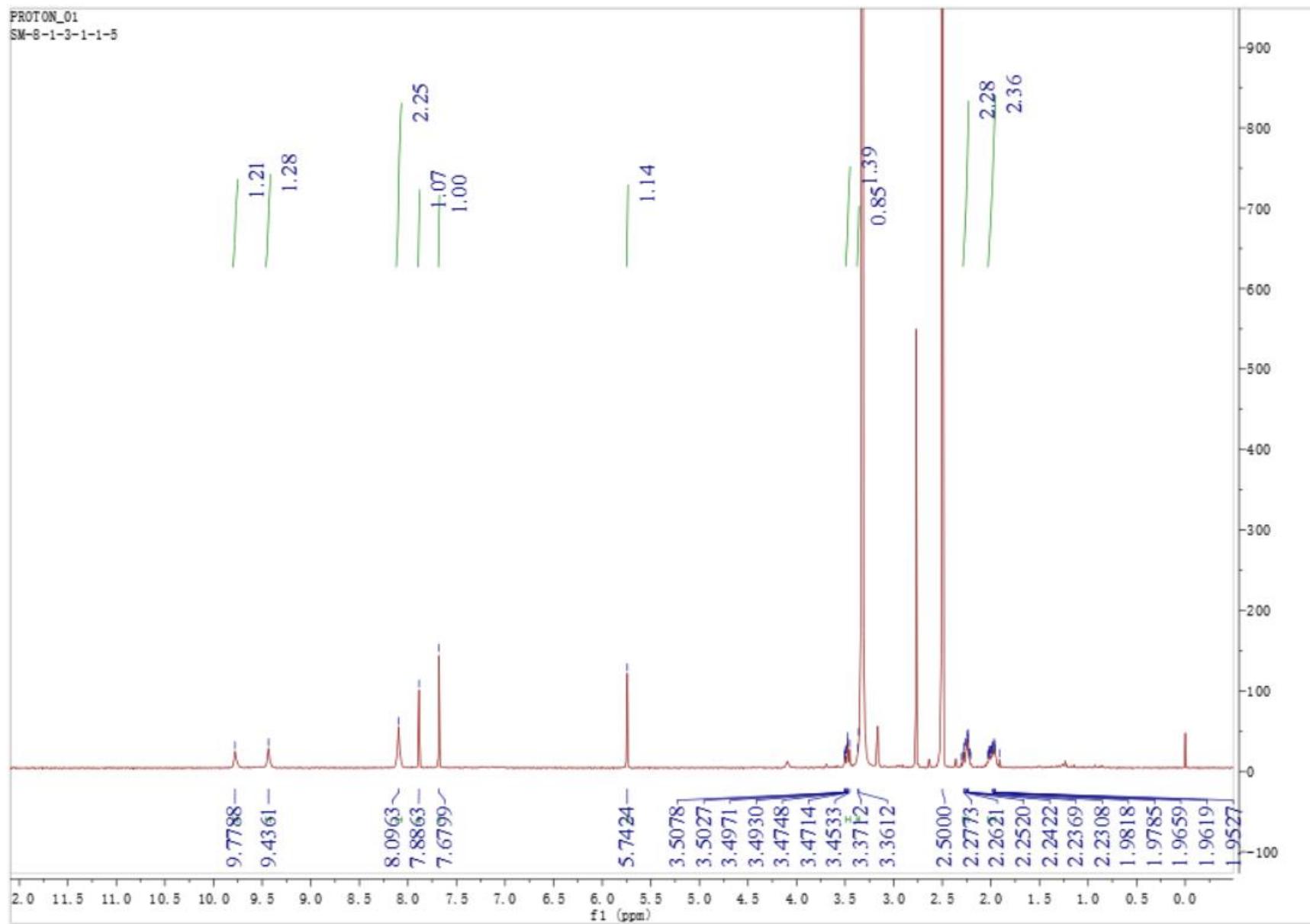


Figure S116. ¹H NMR spectrum of compound **16** in DMSO-*d*₆ (500 MHz).

CARBON_02
SM-8-1-3-1-1-5

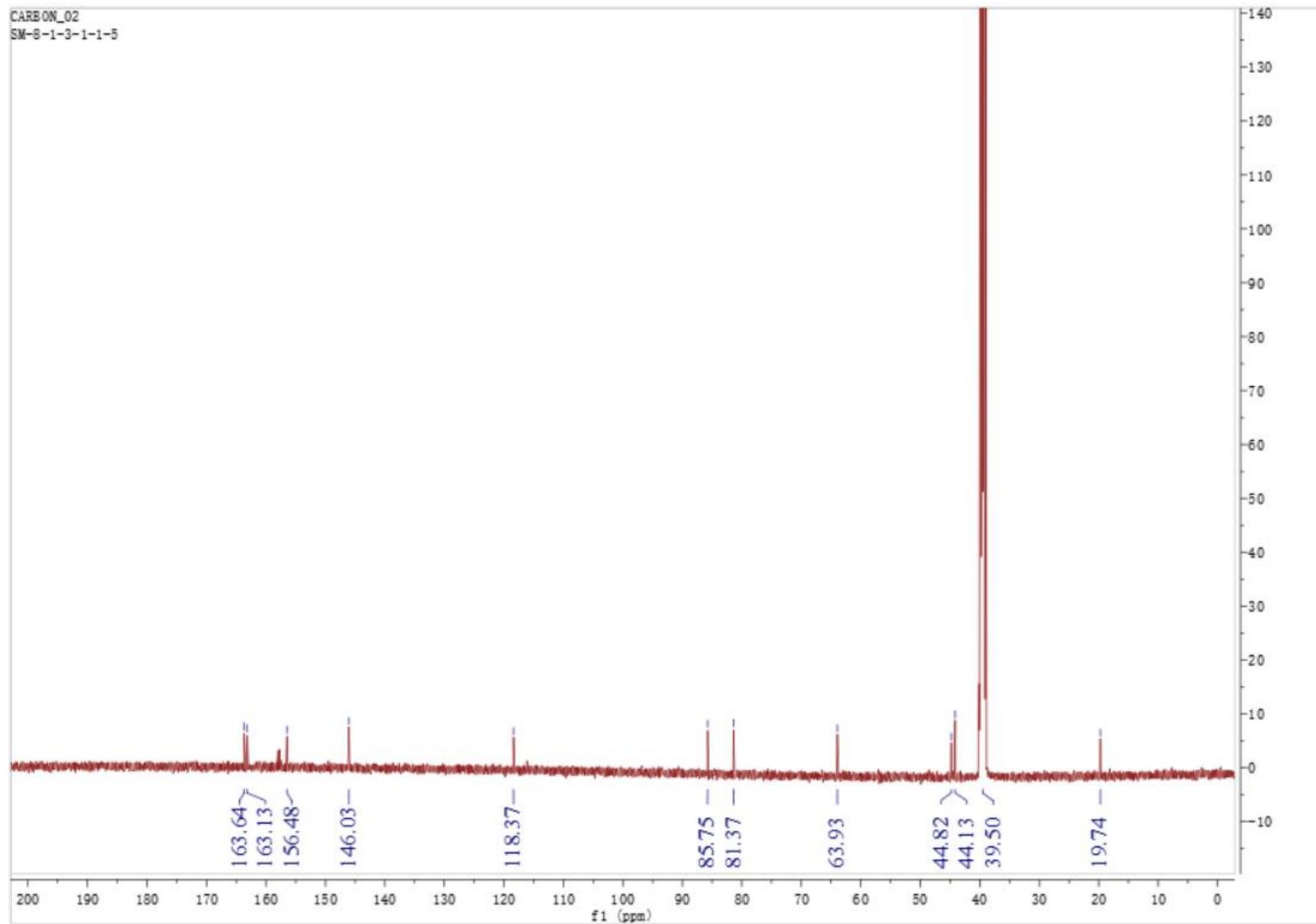


Figure S117. ¹³C NMR spectrum of compound **16** in DMSO-*d*₆ (125 MHz).