Bioactivity-Guided Discovery of Human Carboxylesterase Inhibitors from the Roots of *Paeonia lactiflora*

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Supplementary Information

The List of Contents

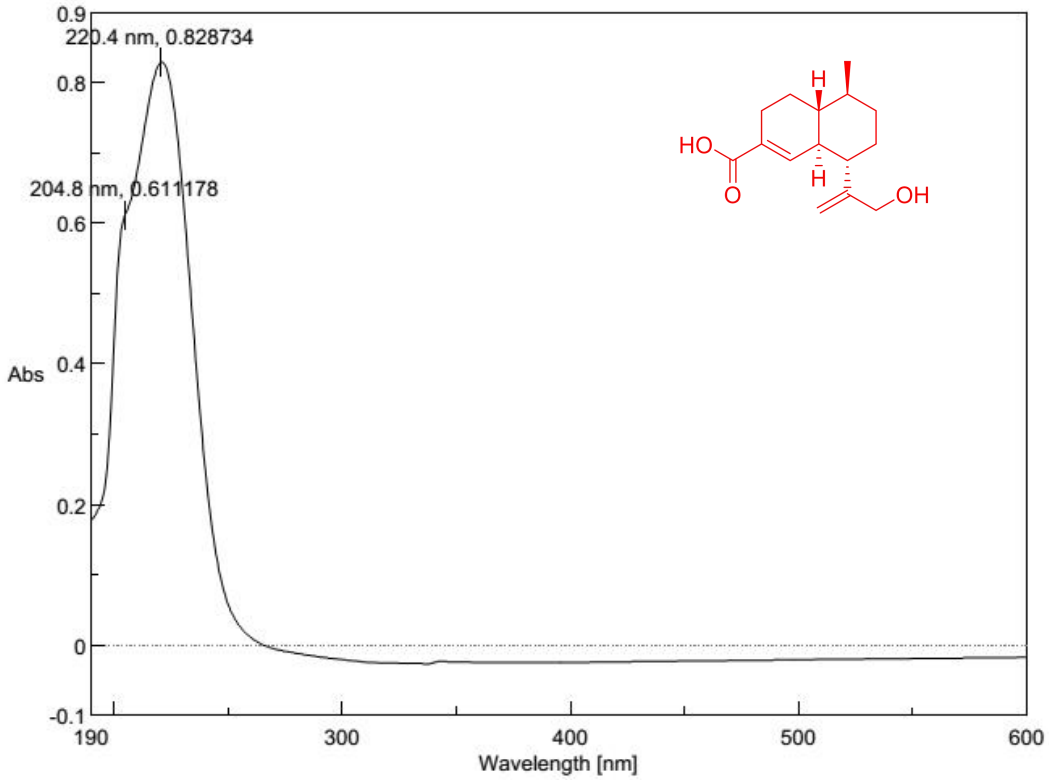


Figure S1. The UV Spectrum of Compound 1 in MeOH

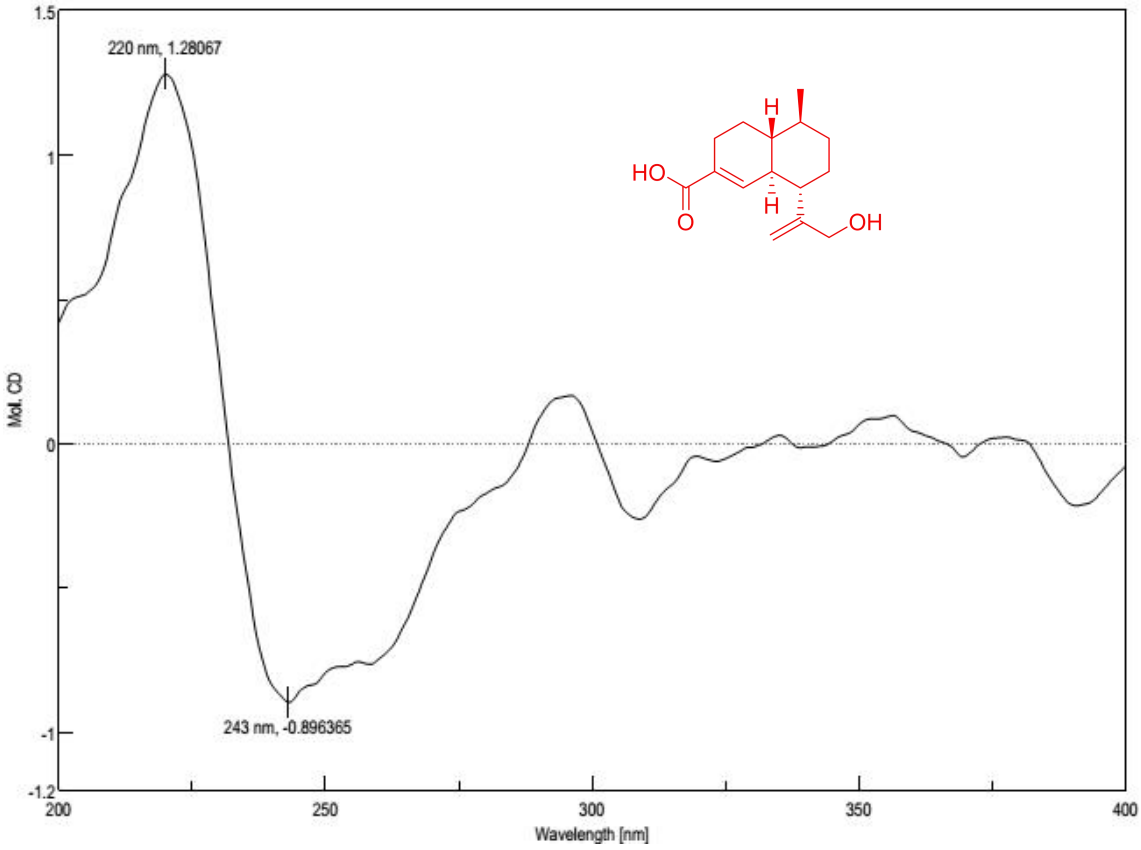
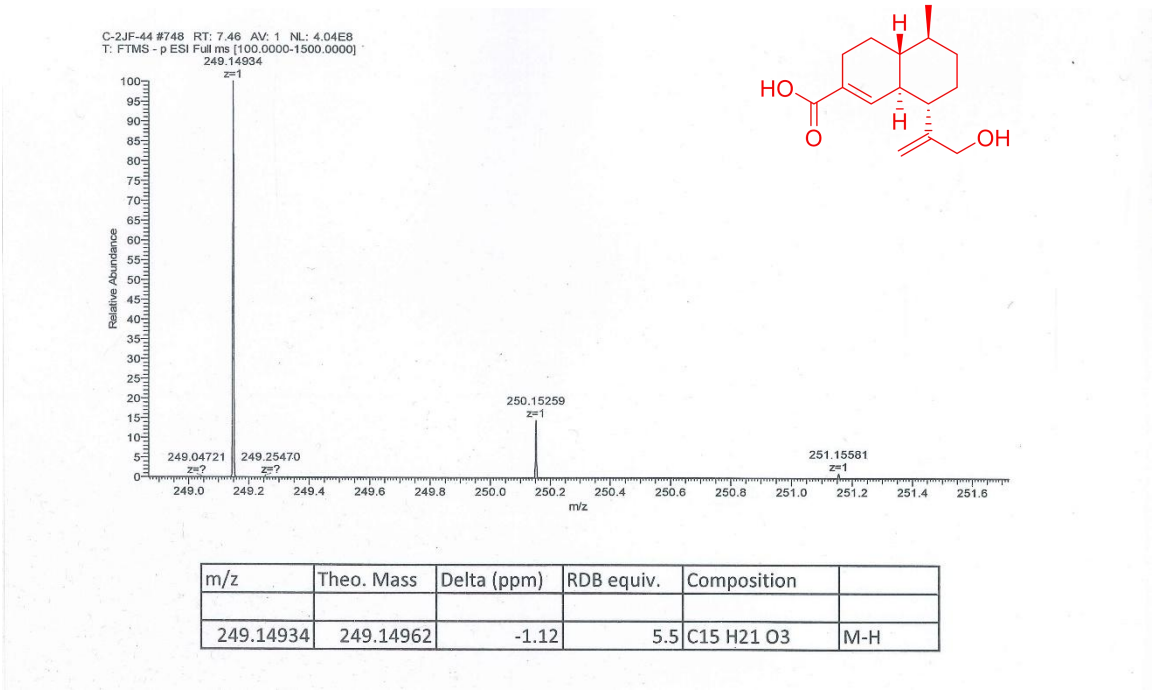


Figure S2. The CD Spectrum of Compound 1 in MeOH



m/z	Theo. Mass	Delta (ppm)	RDB equiv.	Composition	
249.14934	249.14962	-1.12	5.5	C15 H21 O3	M-H

Figure S3. The HR-mass Spectrum of Compound 1 in MeOH

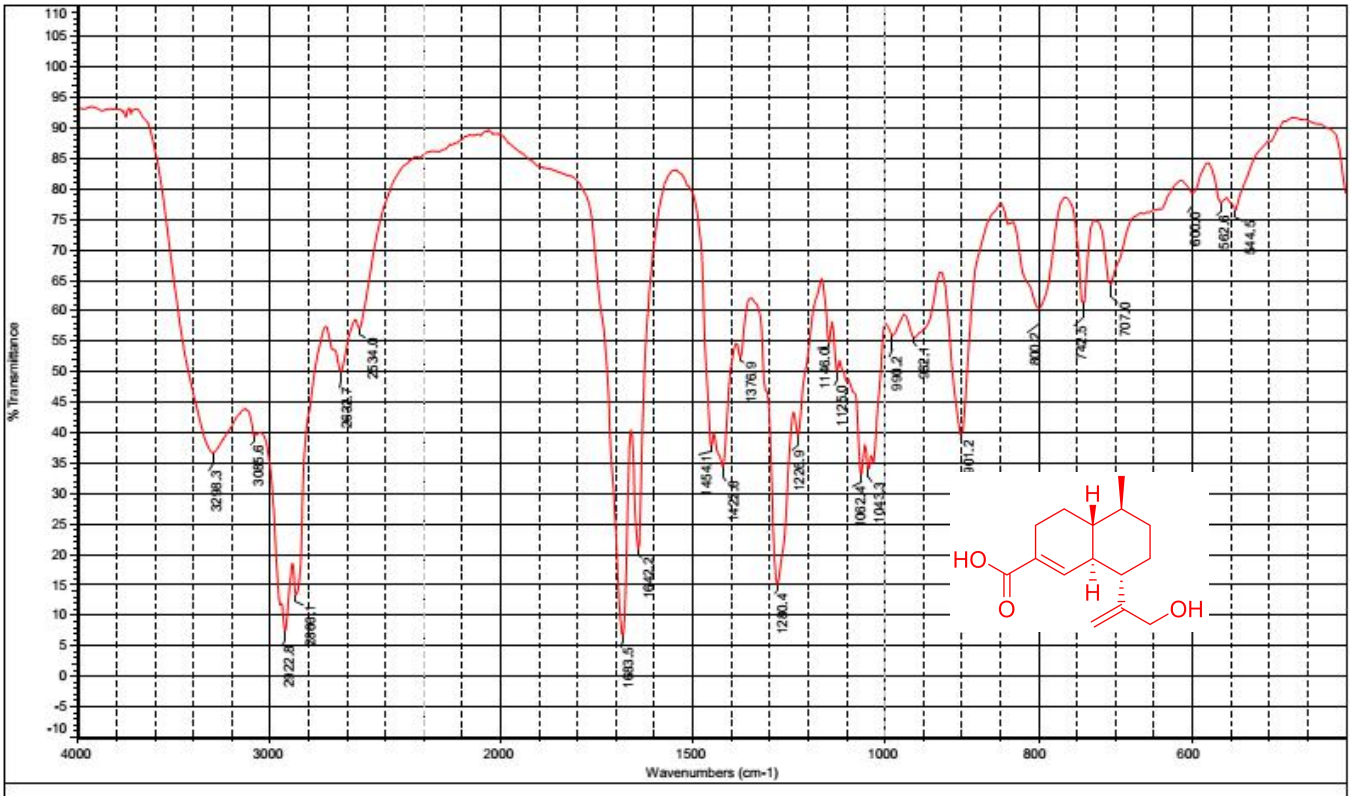


Figure S4. The IR Spectrum of Compound 1

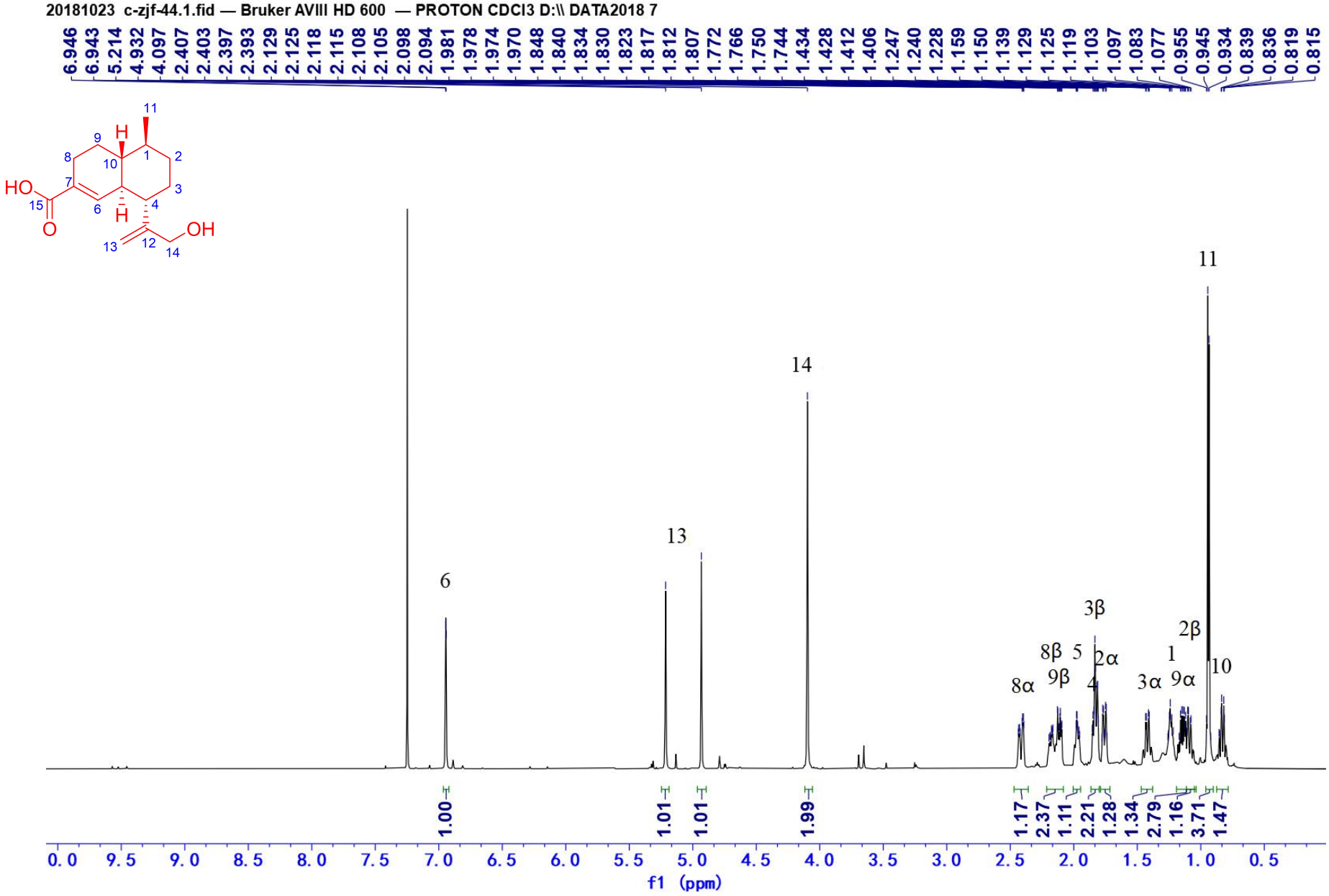


Figure S5. The ^{1}H NMR Spectrum of Compound 1 in $CDCl_3$ (600MHz)

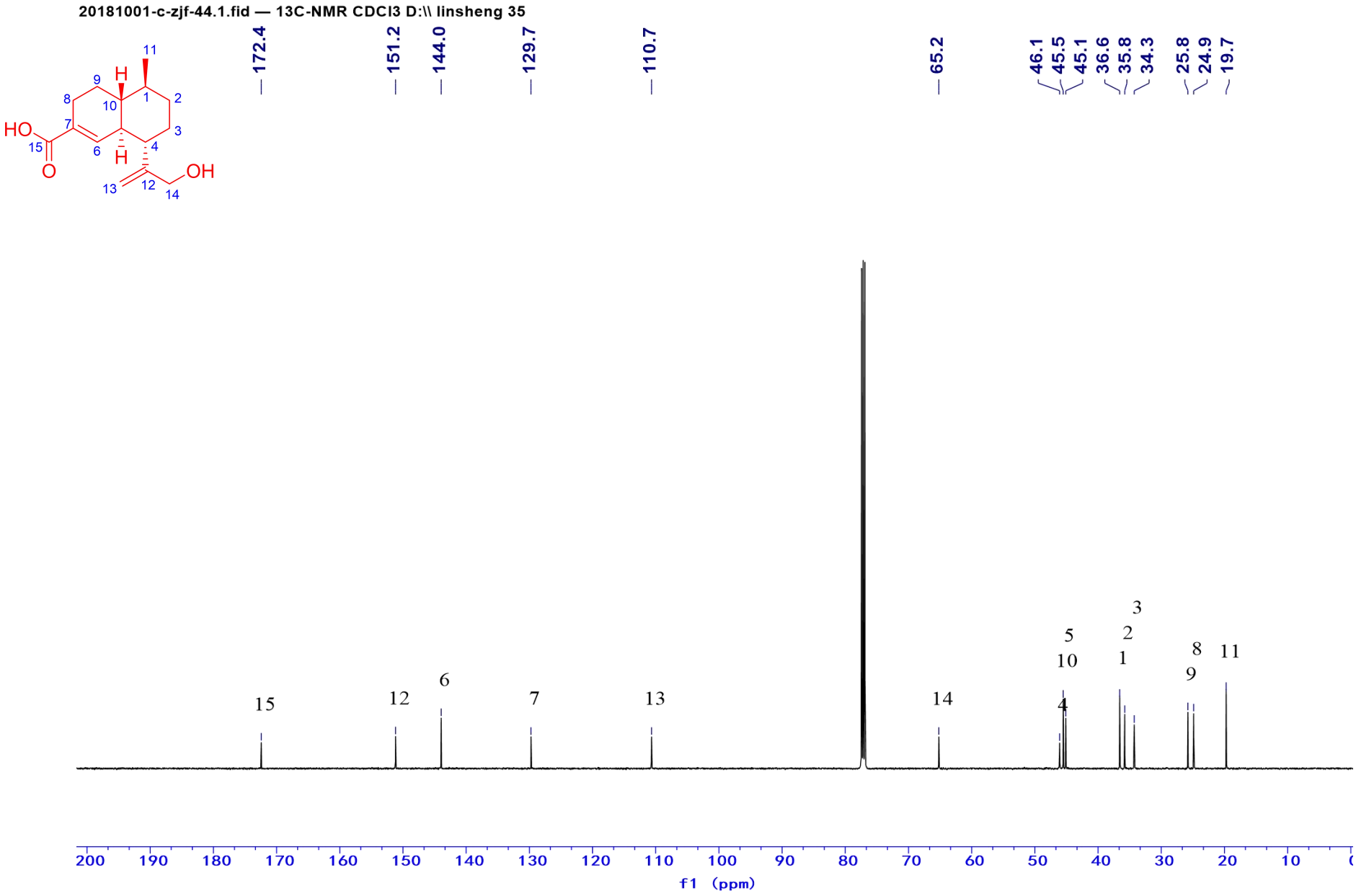


Figure S6. The ^{13}C NMR Spectrum of Compound 1 in $CDCl_3$ (150MHz)

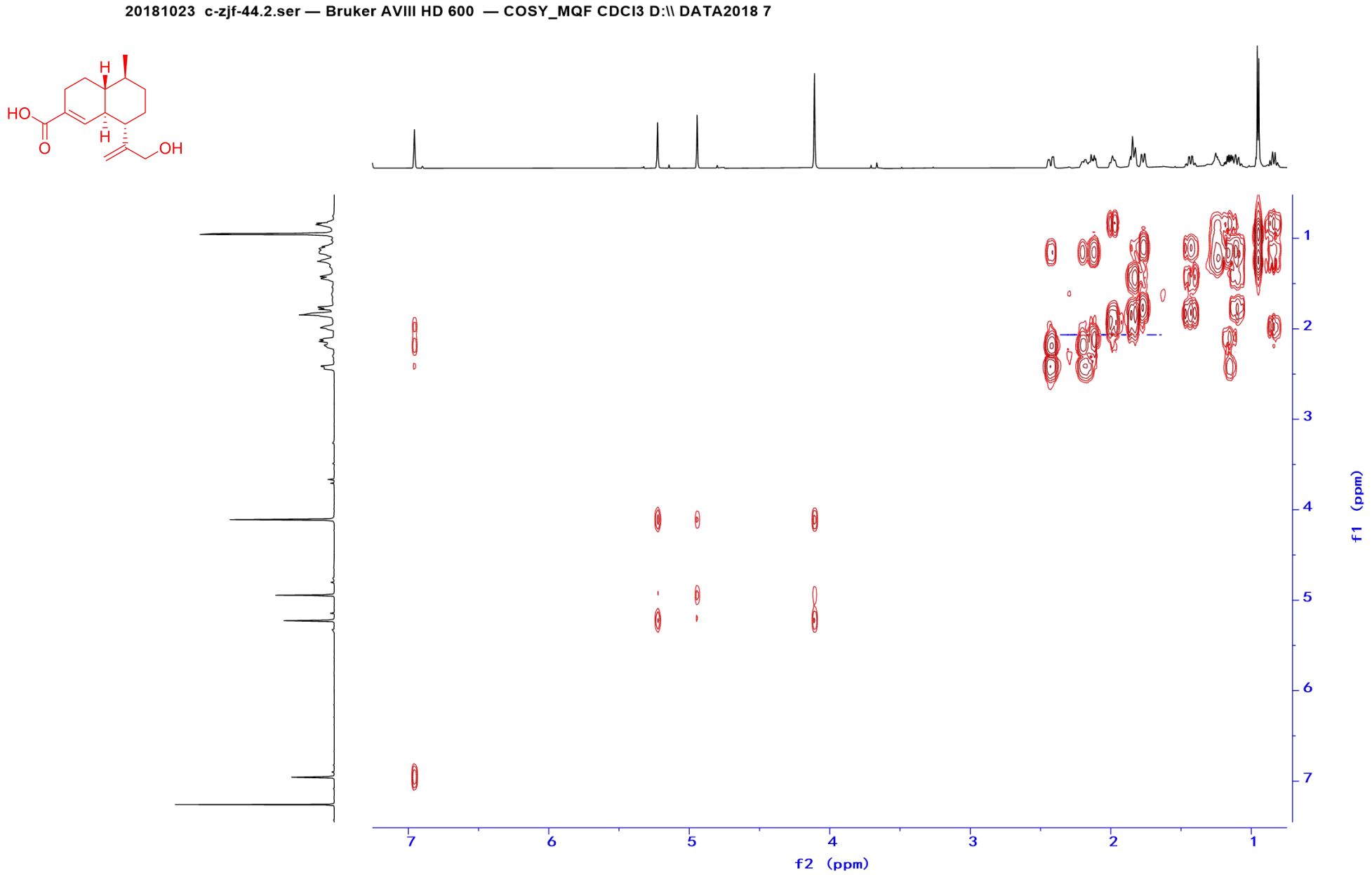


Figure S7. The ^{1}H-^{1}H COSY Spectrum of Compound 1 in $CDCl_3$ (600MHz)

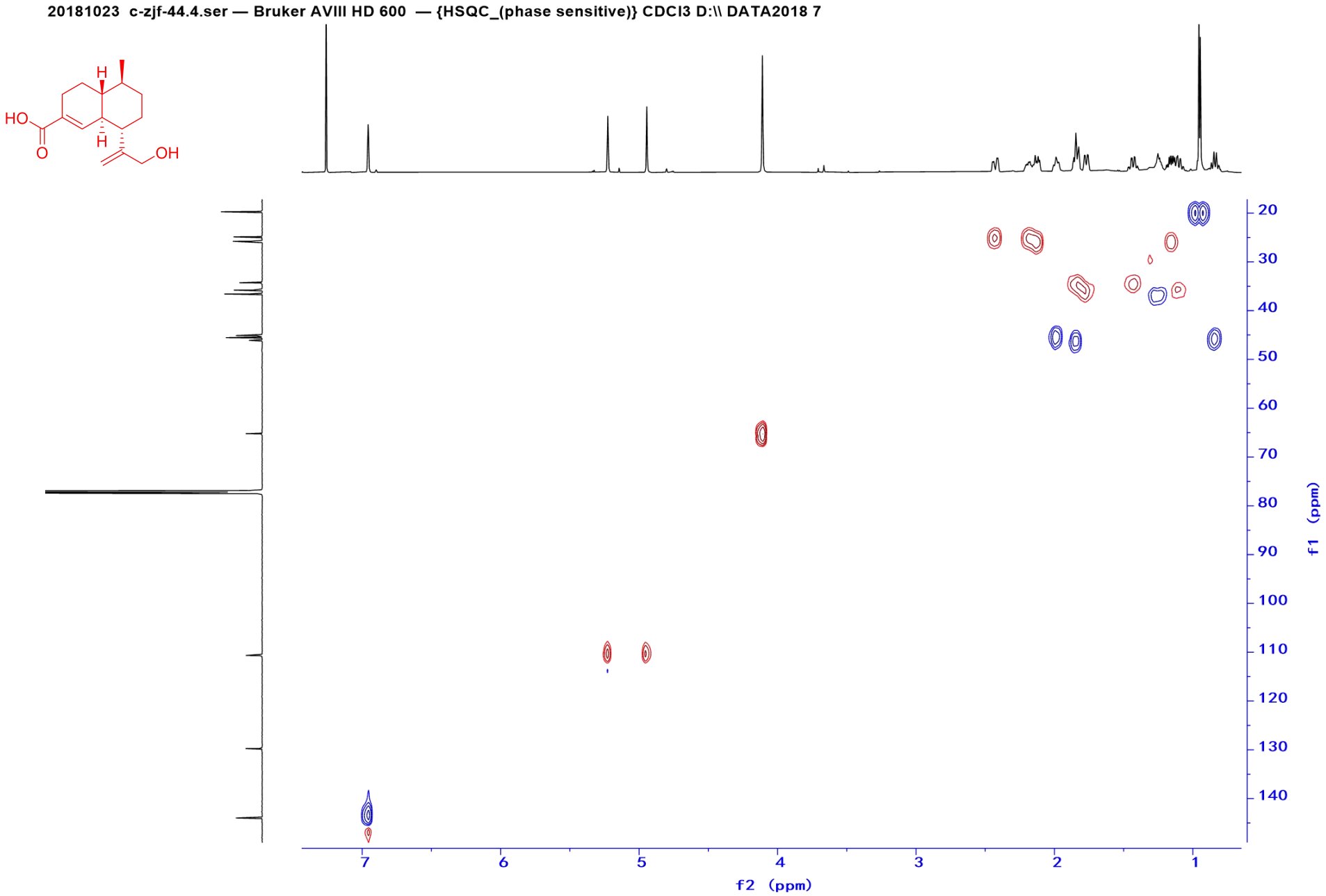


Figure S8. The HSQC Spectrum of Compound 1 in $CDCl_3$ (600MHz)

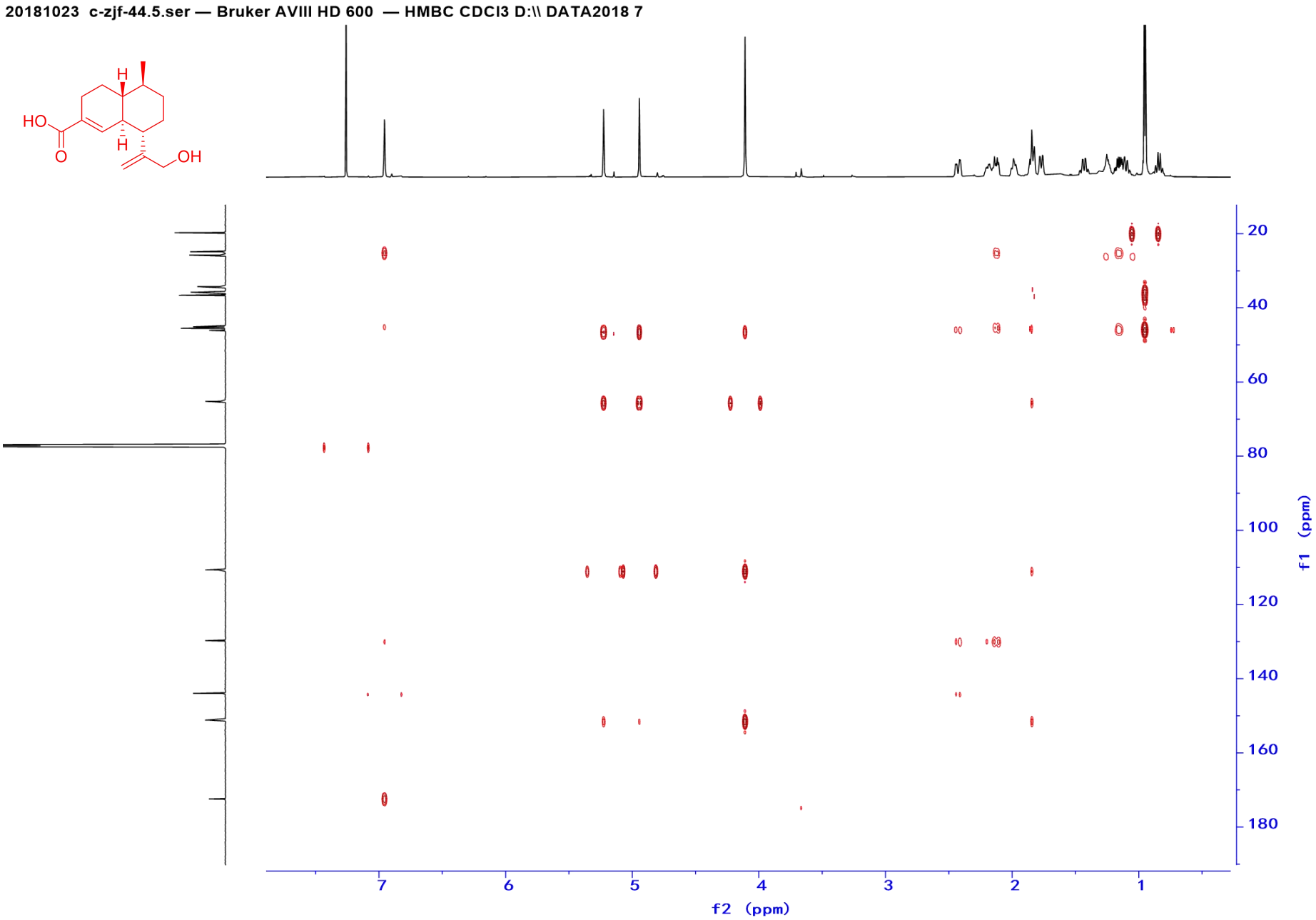


Figure S9. The HMBC Spectrum of Compound 1 in $CDCl_3$ (600MHz)

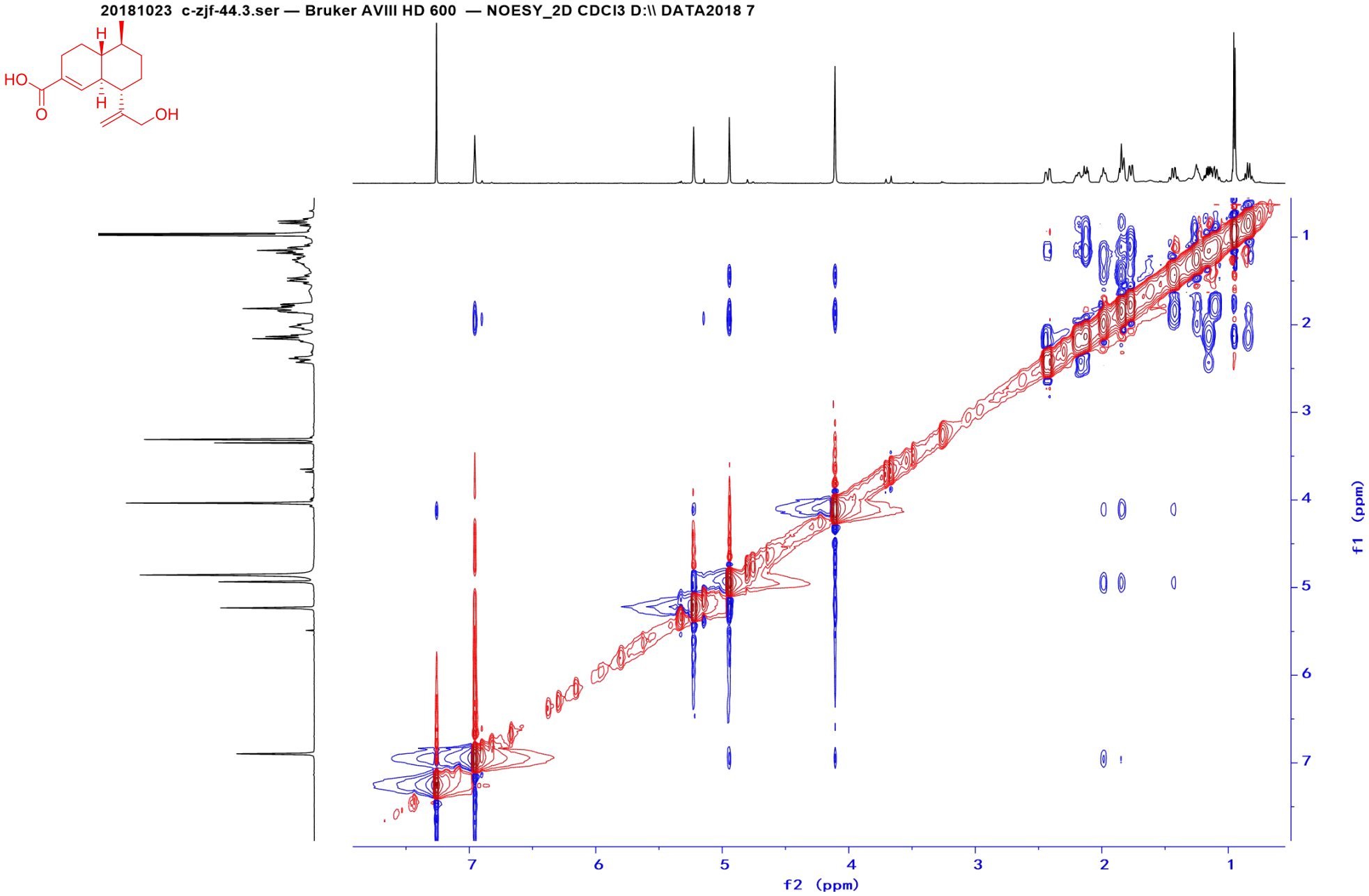


Figure S10. The NOESY Spectrum of Compound 1 in $CDCl_3$ (600MHz)

Table 1. Crystal data and structure refinement for mj19144.

Identification code	mj19144	
Empirical formula	C15 H22 O3	
Formula weight	250.32	
Temperature	170.02 K	
Wavelength	1.34139 Å	
Crystal system	Triclinic	
Space group	P1	
Unit cell dimensions	a = 8.6358(13) Å	α= 74.596(6)°.
	b = 9.3834(15) Å	β= 86.938(9)°.
	c = 9.8633(15) Å	γ = 68.597(9)°.
Volume	716.6(2) $Å^3$	
Z	2	
Density (calculated)	1.160 Mg/m^3	
Absorption coefficient	0.408 mm^{-1}	
F(000)	272	
Crystal size	0.12 x 0.03 x 0.02 mm^3	
Theta range for data collection	4.049 to 55.232°.	
Index ranges	-10<=h<=10, -11<=k<=11, -12<=l<=11	
Reflections collected	16803	
Independent reflections	5215 [R(int) = 0.0529]	
Completeness to theta = 53.594°	99.6 %	
Absorption correction	Semi-empirical from equivalents	
Max. and min. transmission	0.7508 and 0.5594	
Refinement method	Full-matrix-block least-squares on F^2	
Data / restraints / parameters	5215 / 7 / 339	
Goodness-of-fit on F^2	1.053	
Final R indices [I>2sigma(I)]	R1 = 0.0666, wR2 = 0.1808	
R indices (all data)	R1 = 0.0724, wR2 = 0.1881	
Absolute structure parameter	0.00(19)	
Extinction coefficient	n/a	
Largest diff. peak and hole	0.444 and -0.296 $e.Å^{-3}$	

Table 2. Atomic coordinates (x 10^4) and equivalent isotropic displacement parameters ($Å^2$x 10^3) for mj19144. U(eq) is defined as one third of the trace of the orthogonalized U^{ij} tensor.

	x	y	z	U(eq)
O(1)	16079(5)	-7715(4)	1634(3)	66
O(2)	15370(5)	-6265(4)	3165(3)	64
O(3)	16252(4)	-6109(3)	8946(3)	56
C(1)	19051(5)	-13240(5)	7439(5)	49
C(2)	19727(6)	-12802(5)	8607(5)	50
C(3)	18424(5)	-11425(5)	9057(4)	48
C(4)	17770(5)	-9955(4)	7811(4)	39
C(5)	17066(4)	-10367(4)	6627(4)	38
C(6)	16405(4)	-8962(4)	5361(4)	38
C(7)	16485(5)	-9065(5)	4035(4)	39
C(8)	17218(5)	-10621(5)	3655(4)	46
C(9)	17621(5)	-12048(5)	4944(5)	47
C(10)	18384(5)	-11772(5)	6187(4)	41
C(11)	20398(7)	-14634(6)	7036(6)	66
C(12)	16543(5)	-8552(5)	8283(4)	41
C(13)	15017(5)	-8430(6)	8619(5)	52
C(14)	17287(6)	-7363(5)	8386(4)	48
C(15)	15949(5)	-7631(5)	2834(4)	45
O(1A)	14046(4)	-2171(4)	8369(3)	53
O(2A)	14427(4)	-3727(4)	6940(3)	55
O(3A)	15198(4)	-3777(3)	1074(3)	52
C(1A)	10045(5)	2977(5)	2583(4)	44
C(2A)	10753(6)	2860(5)	1141(4)	51
C(3A)	11268(5)	1206(5)	949(4)	46
C(4A)	12498(5)	-63(4)	2128(4)	38
C(5A)	11697(4)	65(4)	3554(4)	37
C(6A)	12697(5)	-1229(4)	4793(4)	38
C(7A)	12851(5)	-1003(4)	6042(4)	39
C(8A)	12058(5)	585(5)	6352(4)	44
C(9A)	10710(5)	1741(4)	5248(4)	41
C(10A)	11302(4)	1721(4)	3750(4)	37
C(11A)	9548(7)	4661(5)	2733(6)	62
C(12A)	12988(5)	-1693(5)	1869(4)	43
C(11A)	9548(7)	4661(5)	2733(6)	62
C(12A)	12988(5)	-1693(5)	1869(4)	43
C(13A)	11938(6)	-2408(6)	1861(5)	56
C(14A)	14786(5)	-2382(5)	1544(4)	47
C(15A)	13843(5)	-2363(5)	7223(4)	40

Figure S11. X-ray single crystal diffraction data of compound 1

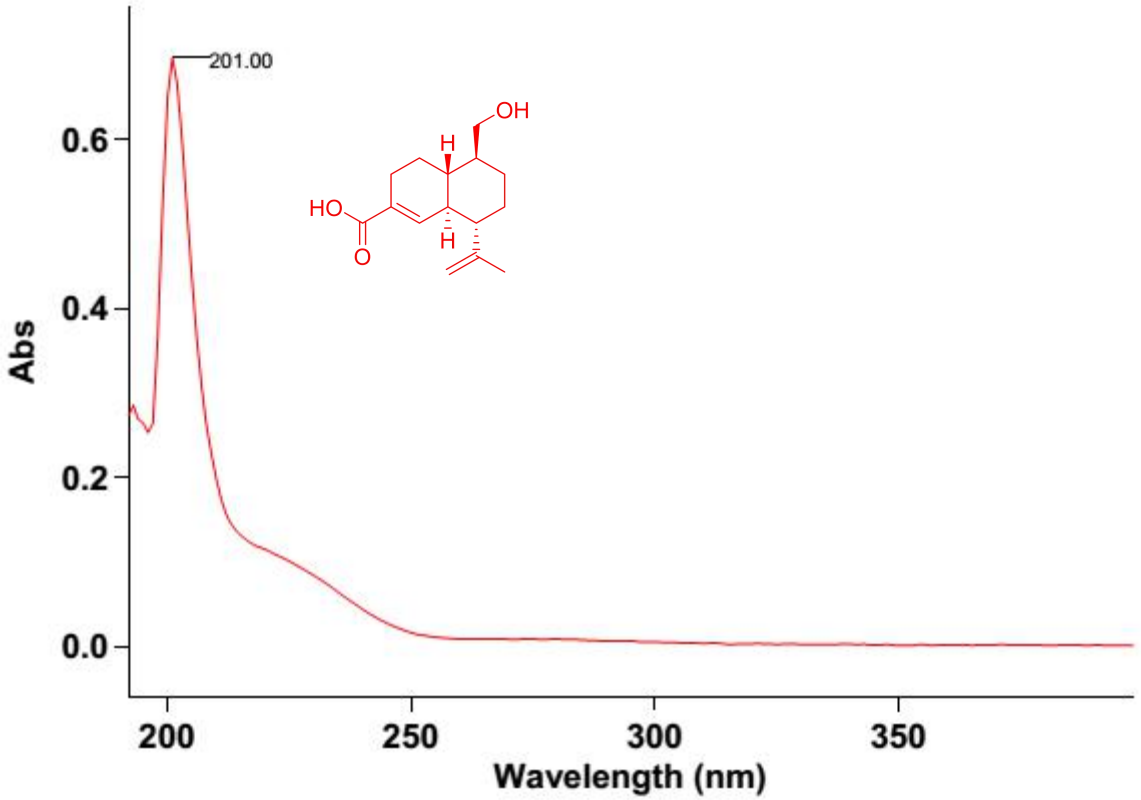


Figure S12. The UV Spectrum of compound 2 in MeOH

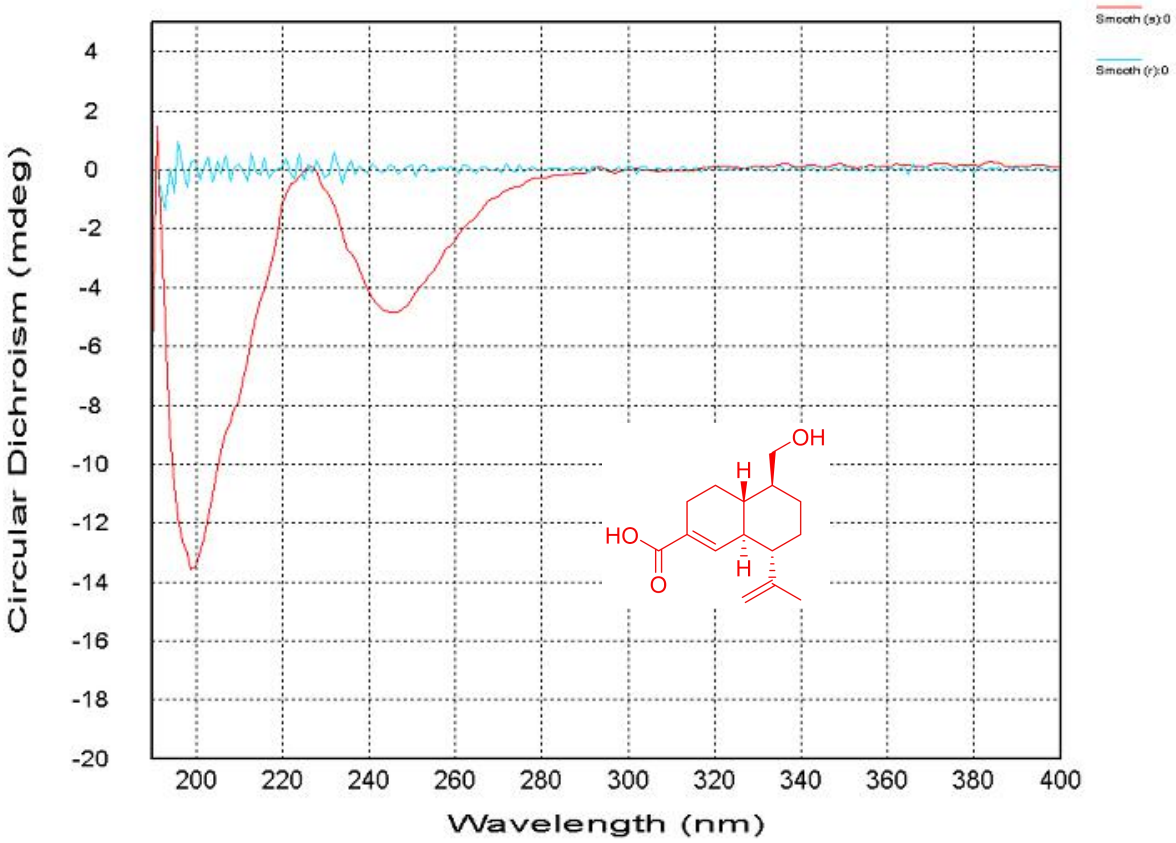
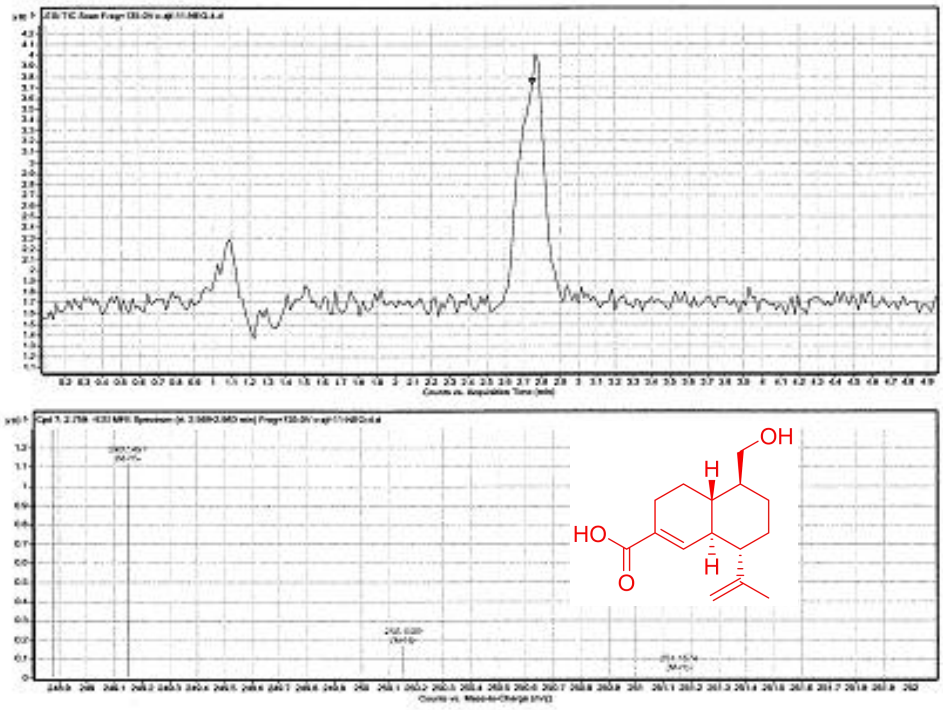


Figure S13. The CD Spectrum of compound 2 in

High resoltion compound report

Compound NO:C-ZJF-11

Method:20190108-ZJF-NEG



Formula (M)	Ion Formula	Mass (MFG)	m/z (Calc)	Diff (ppm)
C15 H22 O3	C15 H21 O3	250.1569	249.1496	2.07

MeOH

Figure S14. The HR-mass Spectrum of Compound 2 in MeOH

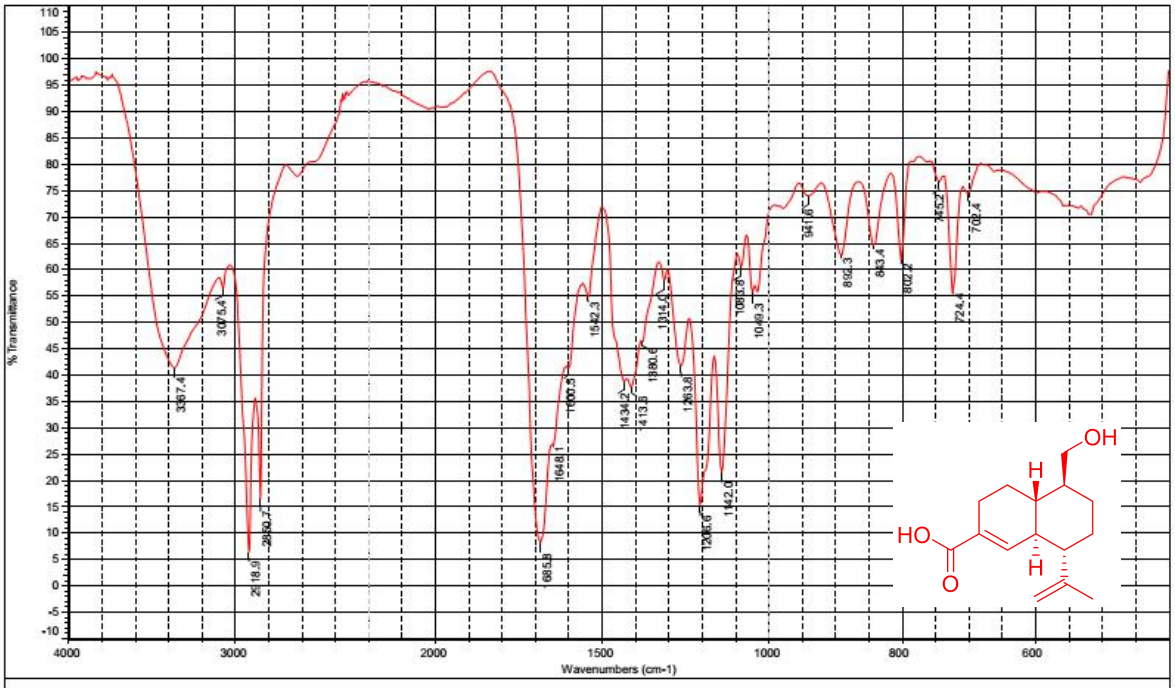


Figure S15. The IR Spectrum of Compound 2

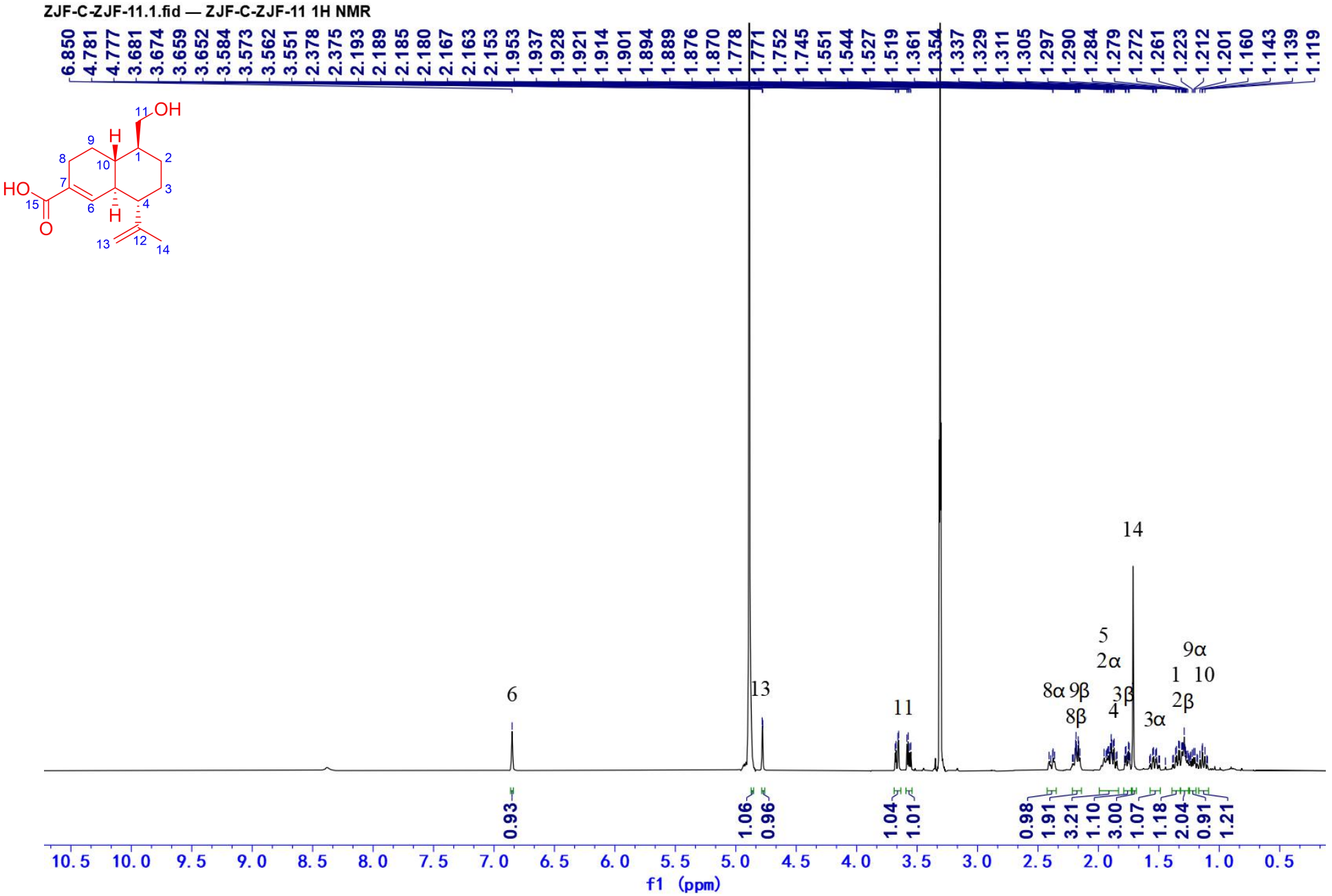


Figure S16. The ^{1}H NMR Spectrum of Compound 2 in MeOH-d_4 (500MHz)

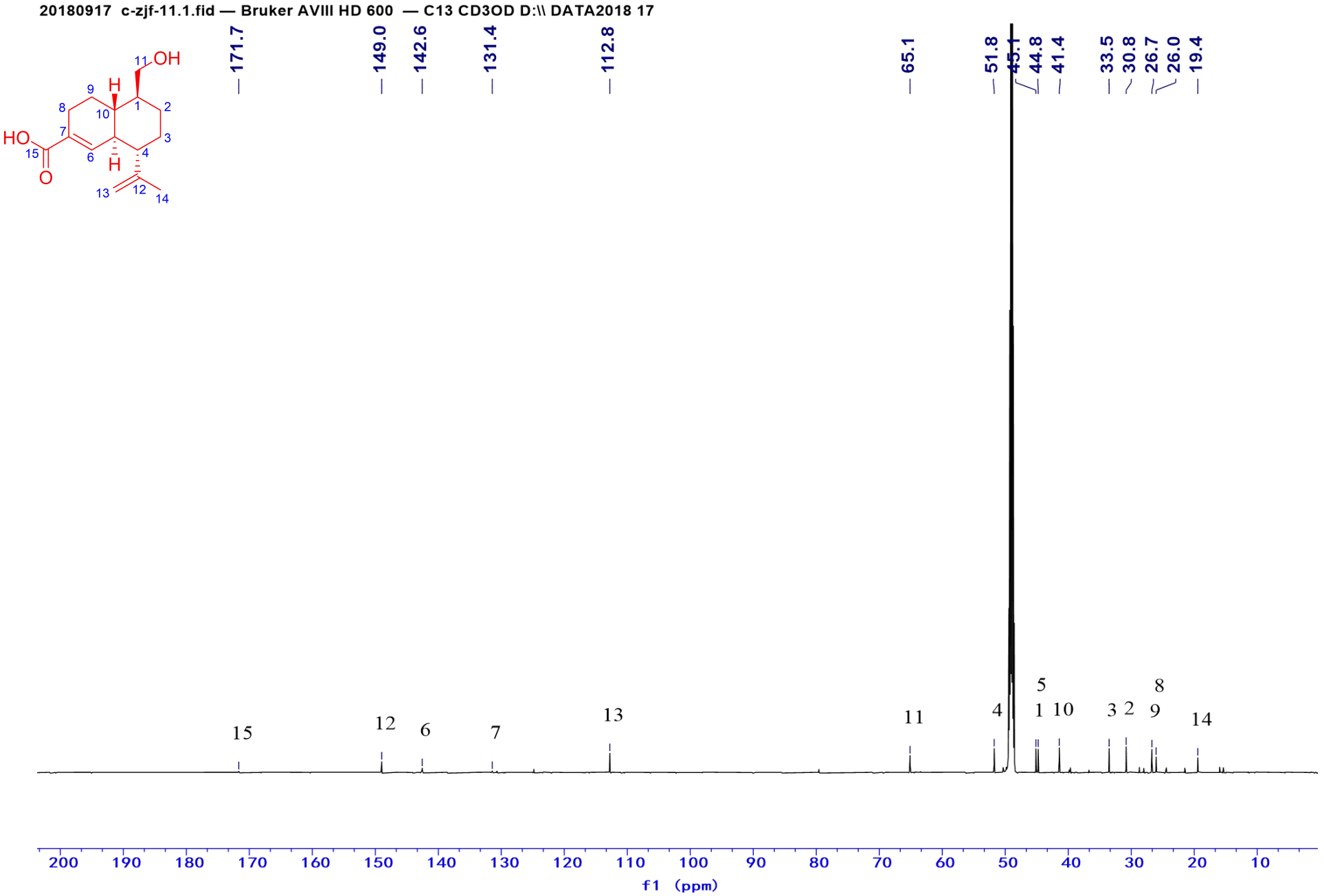


Figure S17. The ^{13}C NMR Spectrum of Compound 2 in MeOH-d_4 (125MHz)

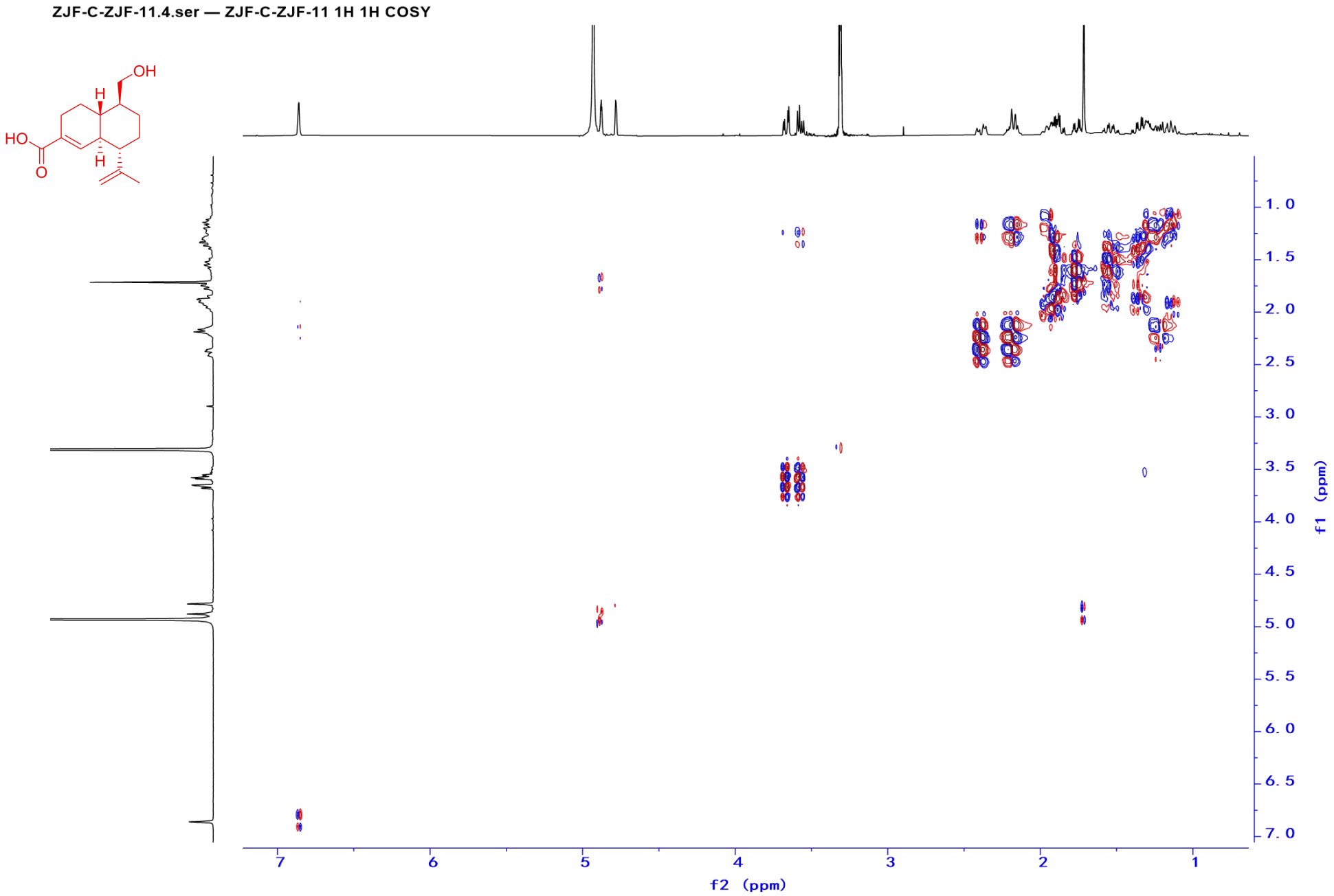


Figure S18. The ^{1}H-^{1}H COSY Spectrum of Compound 2 in MeOH-d_4 (500MHz)

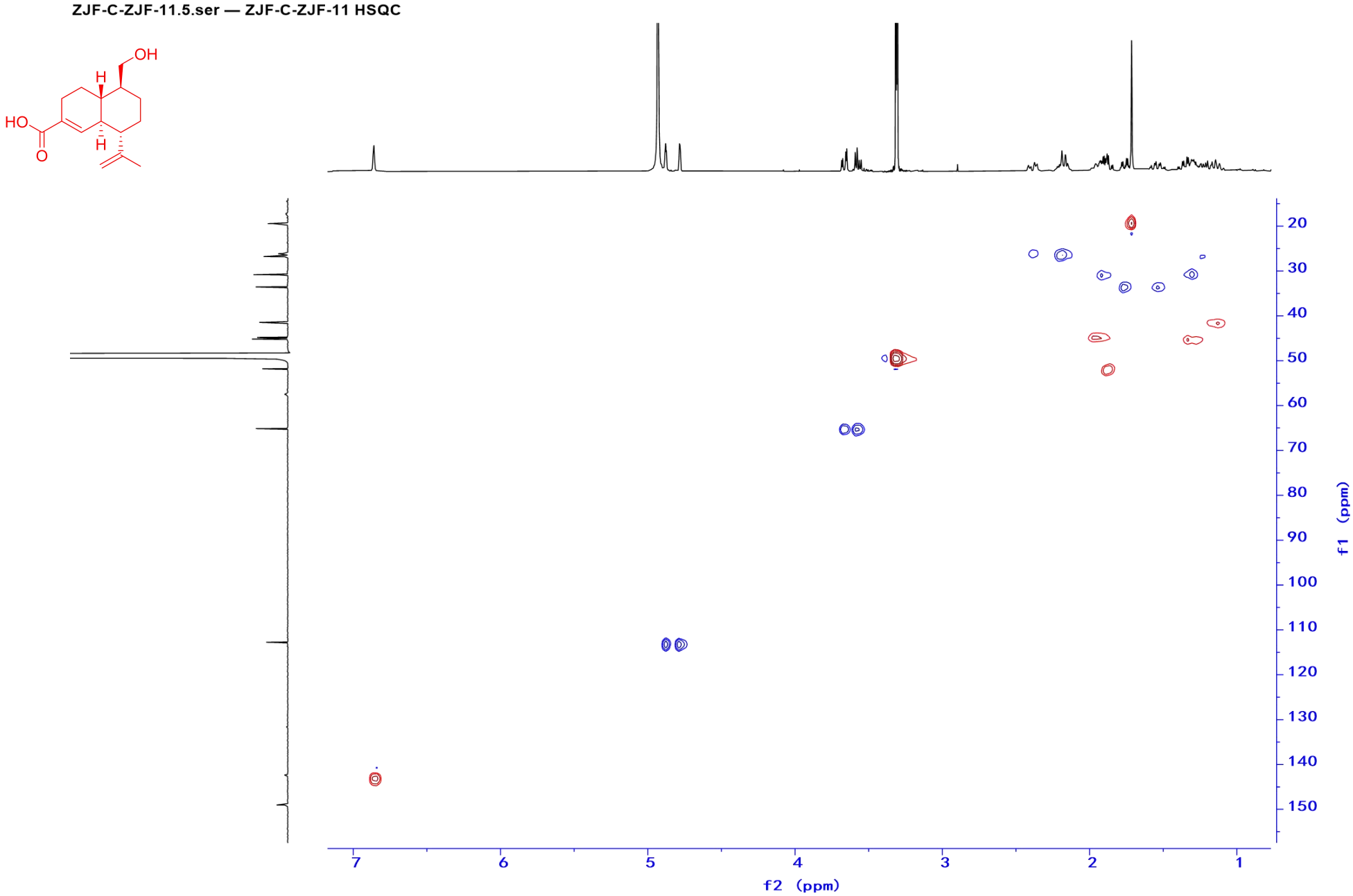


Figure S19. The HSQC Spectrum of Compound 2 in MeOH-d_4 (500MHz)

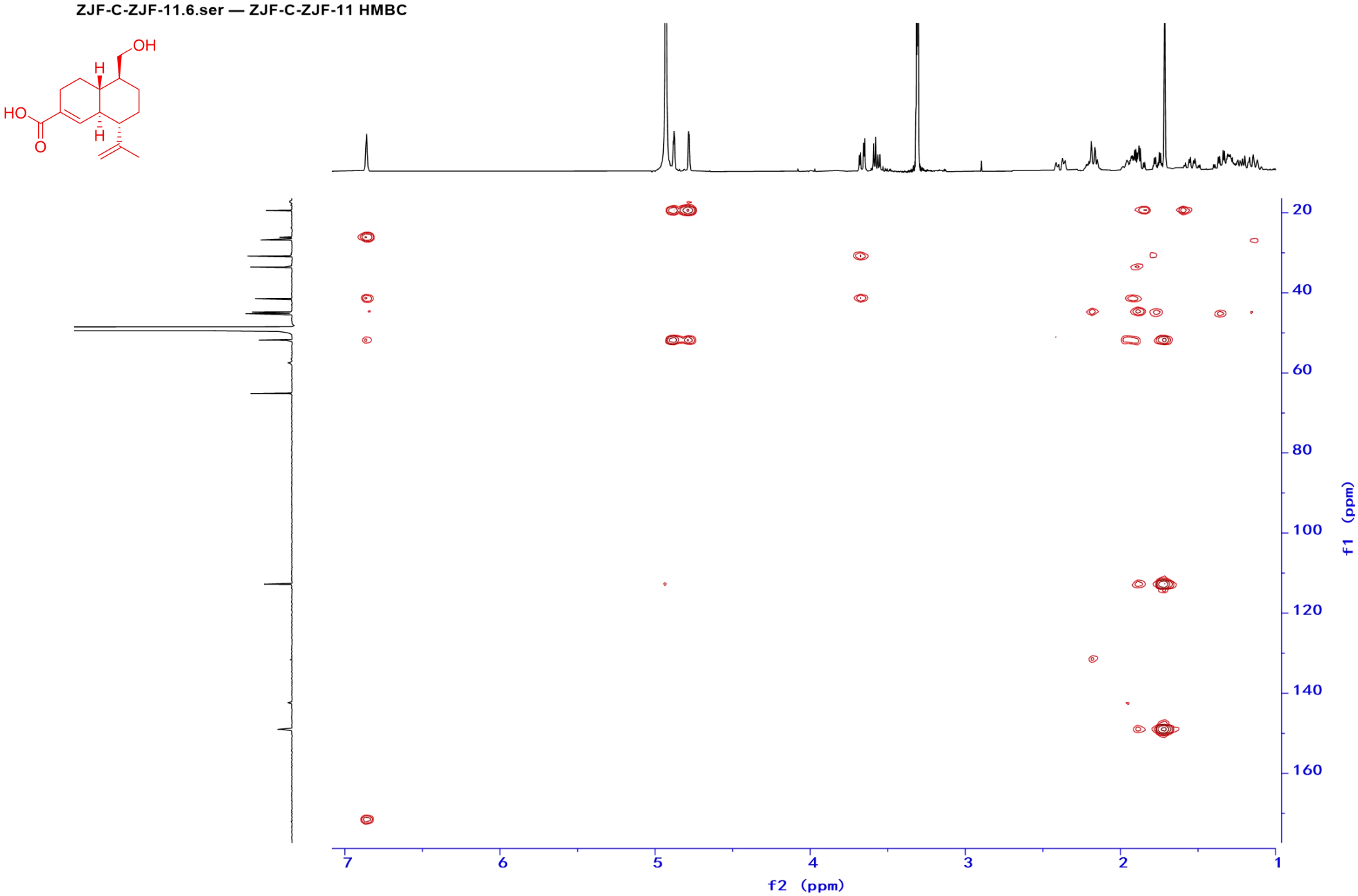


Figure S20. The HMBC Spectrum of Compound 2 in MeOH-d_4 (500MHz)

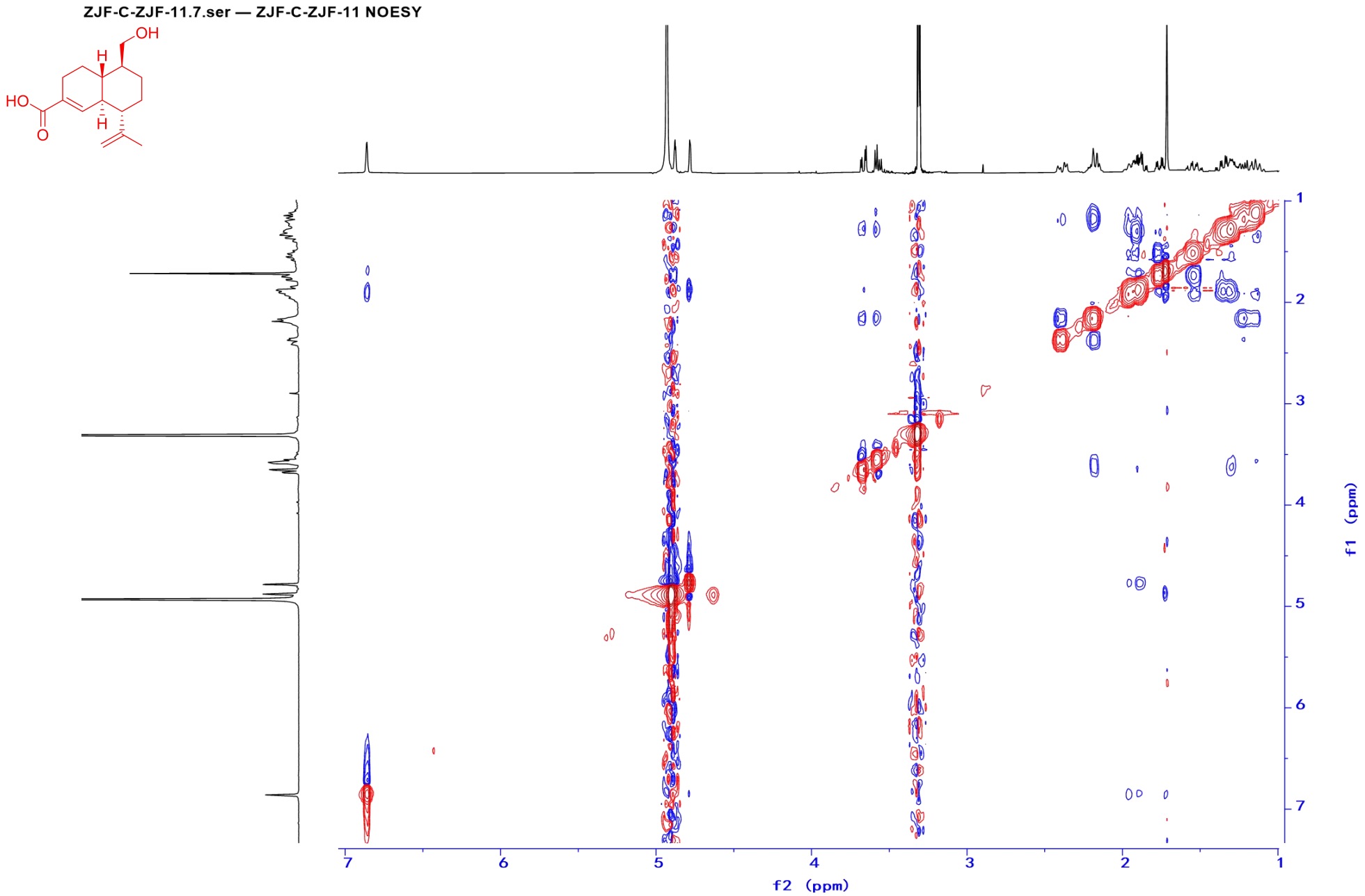


Figure S21. The NOESY Spectrum of Compound 2 in MeOH-d_4 (500MHz)

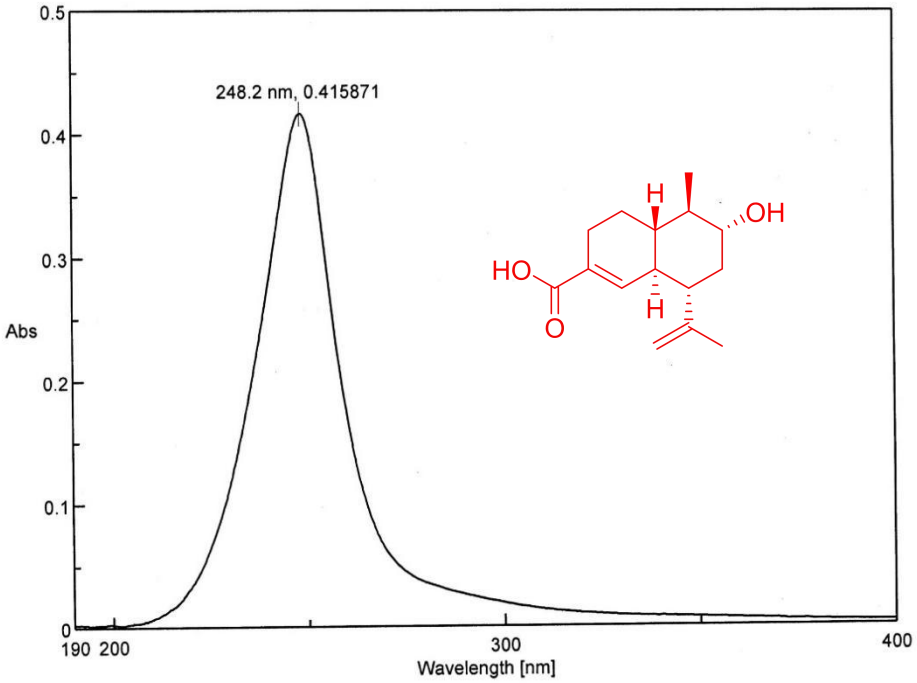


Figure S22. The UV Spectrum of Compound 3 in MeOH

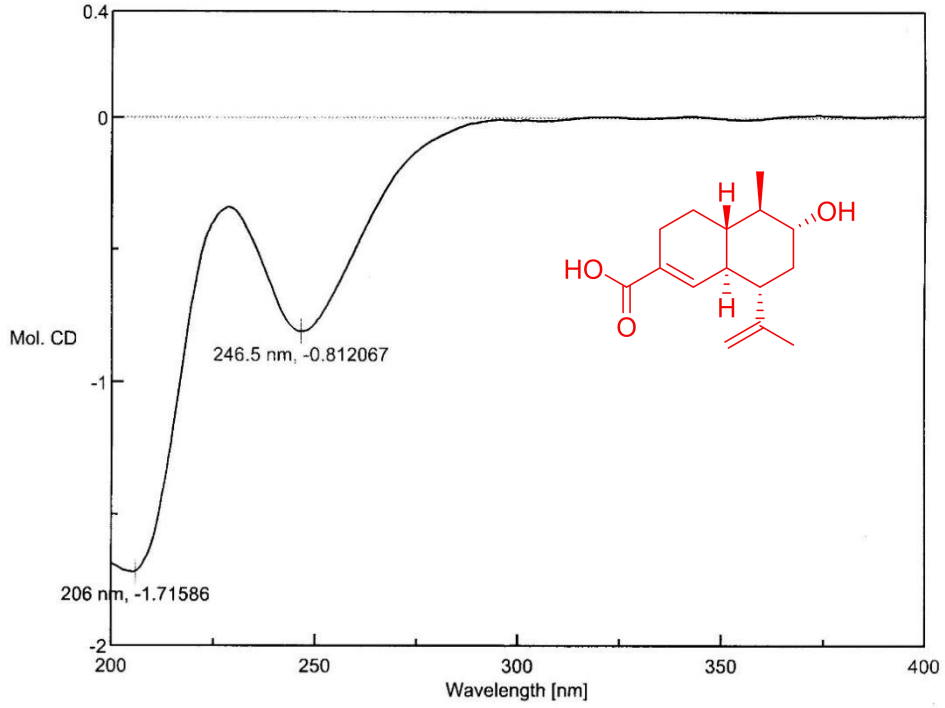


Figure S23. The CD Spectrum of Compound 3 in MeOH

MS Formula Results: + Scan (6.441 min) Sub (2016052001.d)

m/z	Ion	Formula	Abundance
251.1645	(M+H)+	C15 H23 O3	294250.3

Best	Formula (M)	Ion Formula	Score	Cross Sco	Mass	Calc Mass	Calc m/z	Diff (ppm)	Abs Diff (ppm)	Mass Match	Abund Match	Spacing Match	DBE
✔	C15 H22 O3	C15 H23 O3	99.86		250.1573	250.1569	251.1642	-1.47	1.47	99.94	99.73	99.86	5

Figure S24. The HR-mass Spectrum of Compound 3 in MeOH

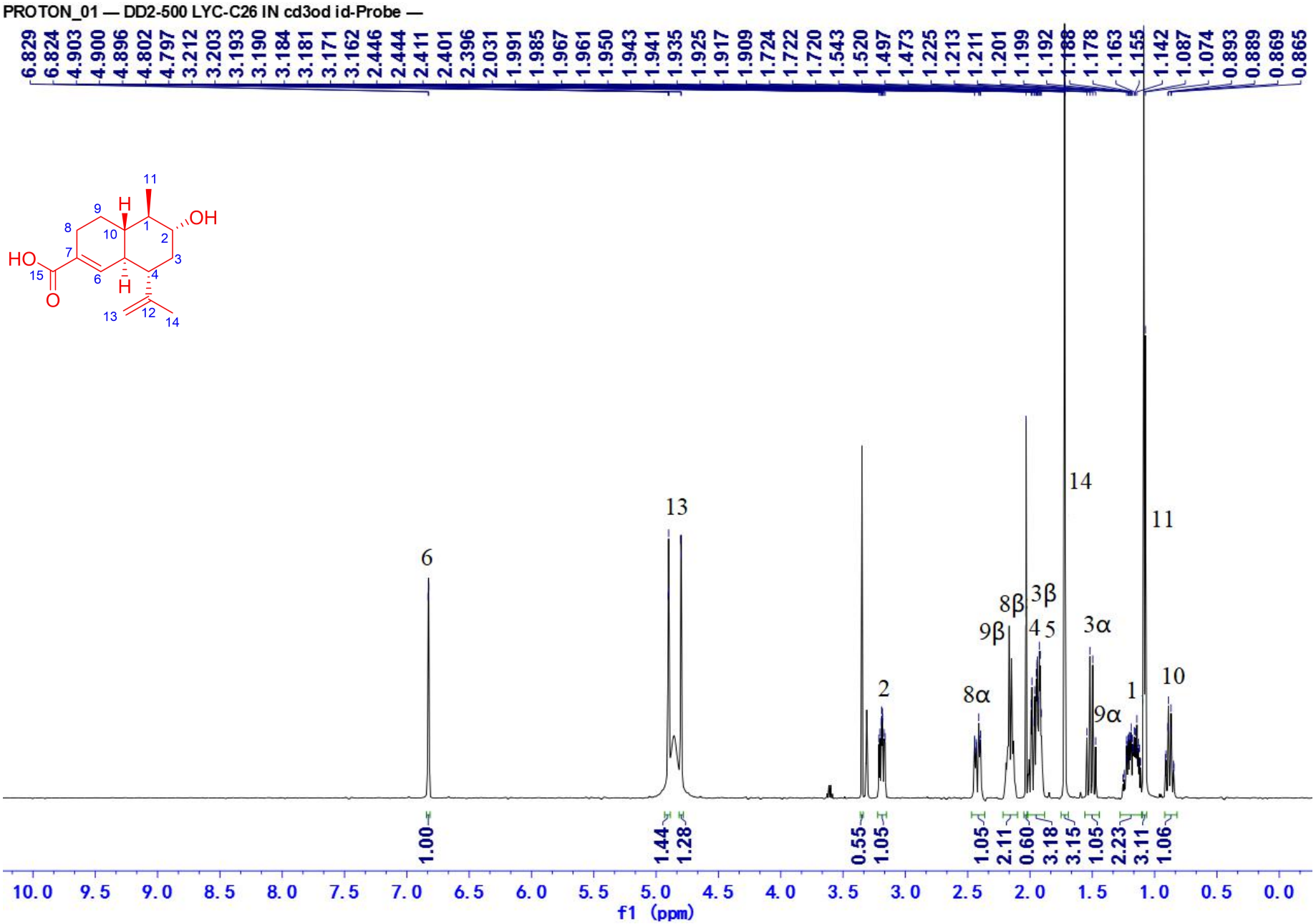


Figure S25. The ^{1}H NMR Spectrum of Compound 3 in MeOH-d_4 (500MHz)

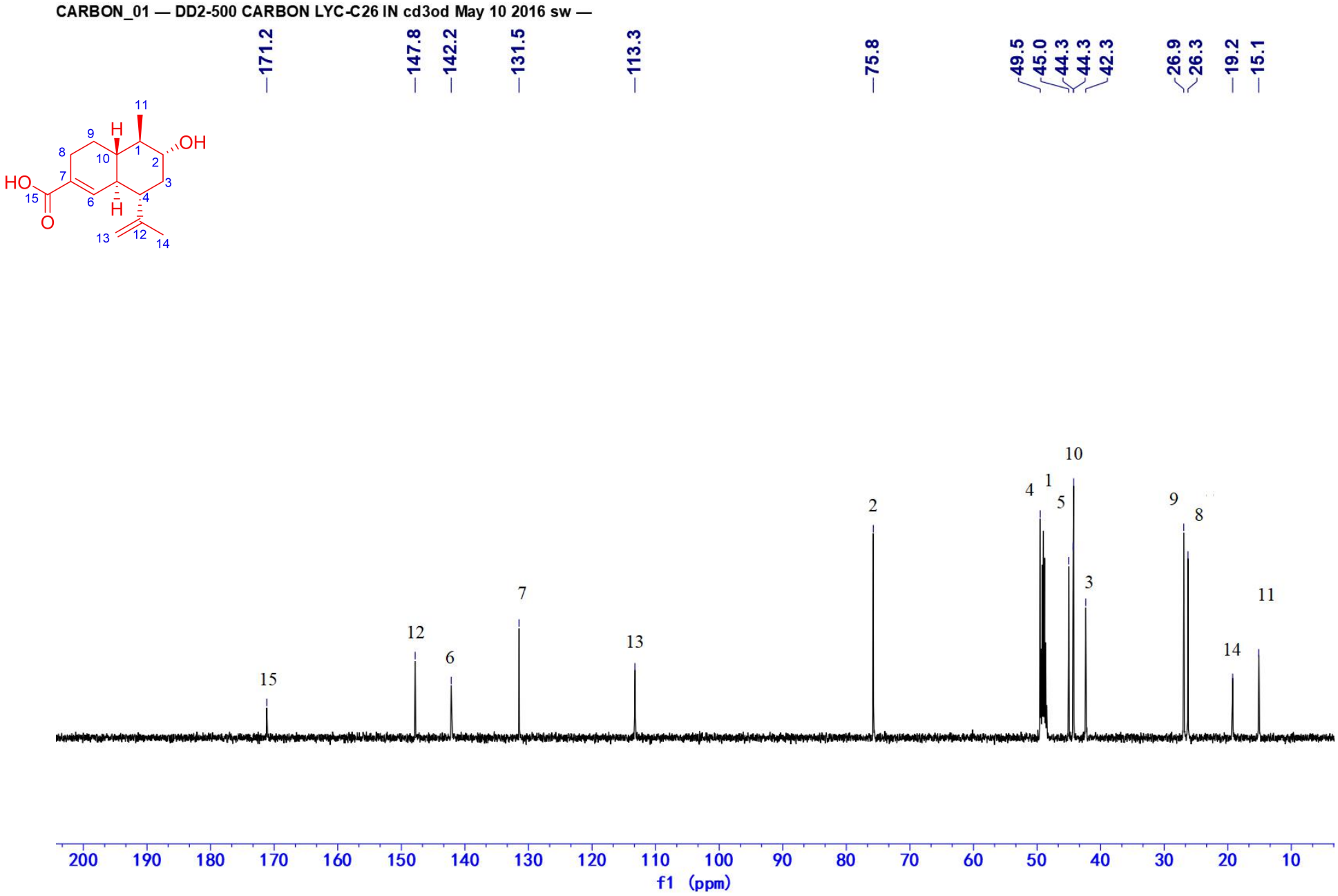


Figure S26. The ^{13}C NMR Spectrum of Compound 3 in MeOH-d_4 (125MHz)

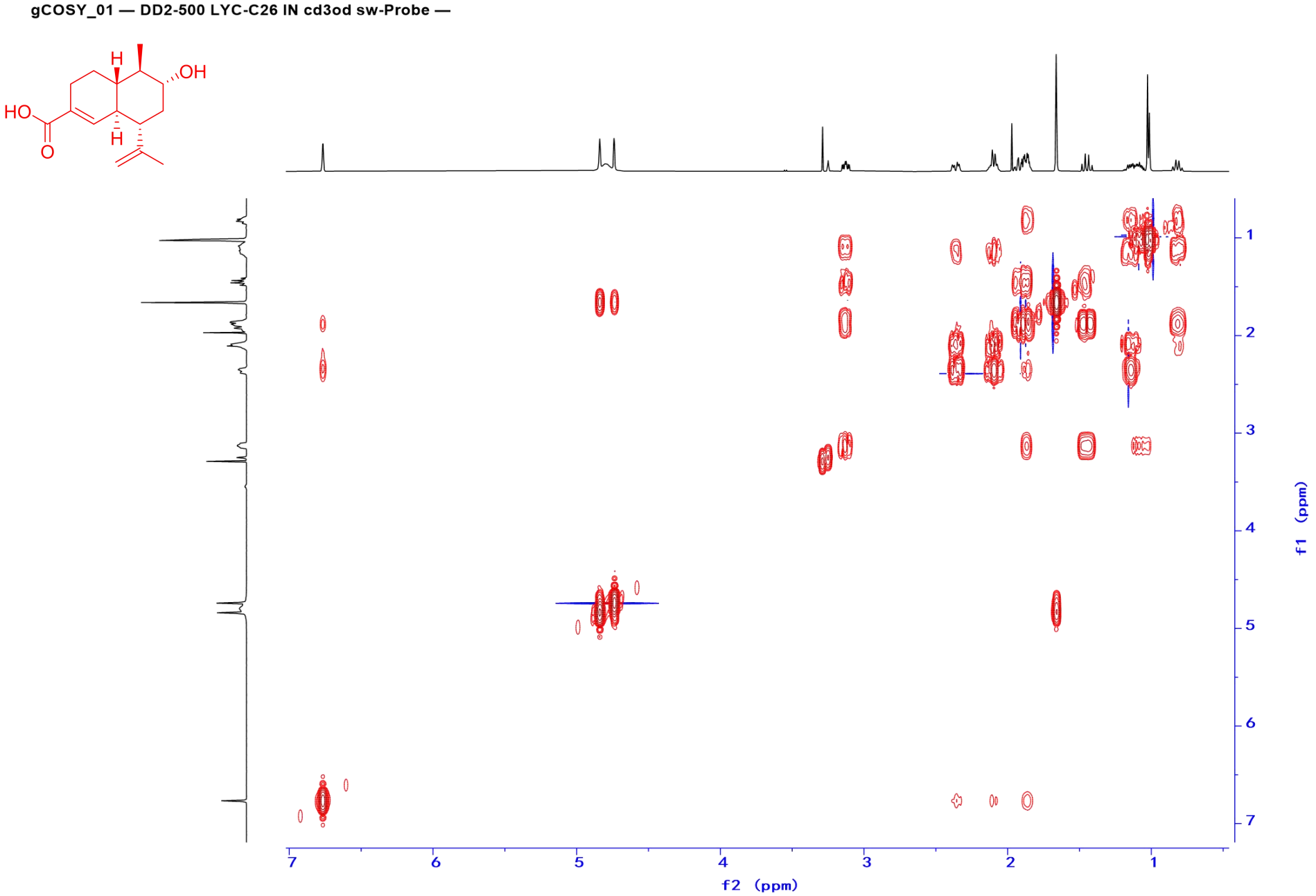


Figure27. The ^{1}H-^{1}H COSY Spectrum of Compound 3 in MeOH-d_4 (500MHz)

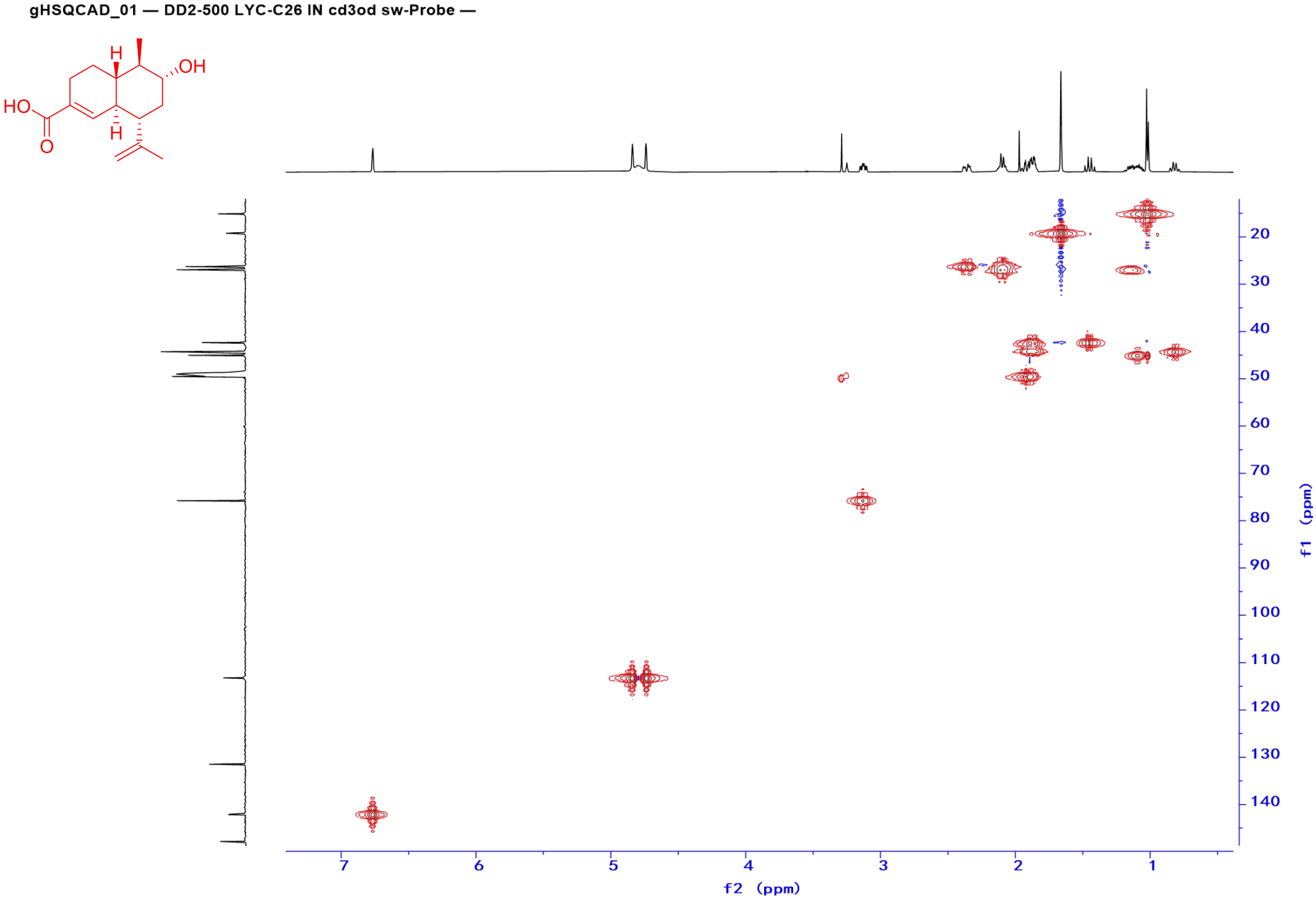


Figure S28. The HSQC Spectrum of Compound 3 in MeOH-d_4 (500MHz)

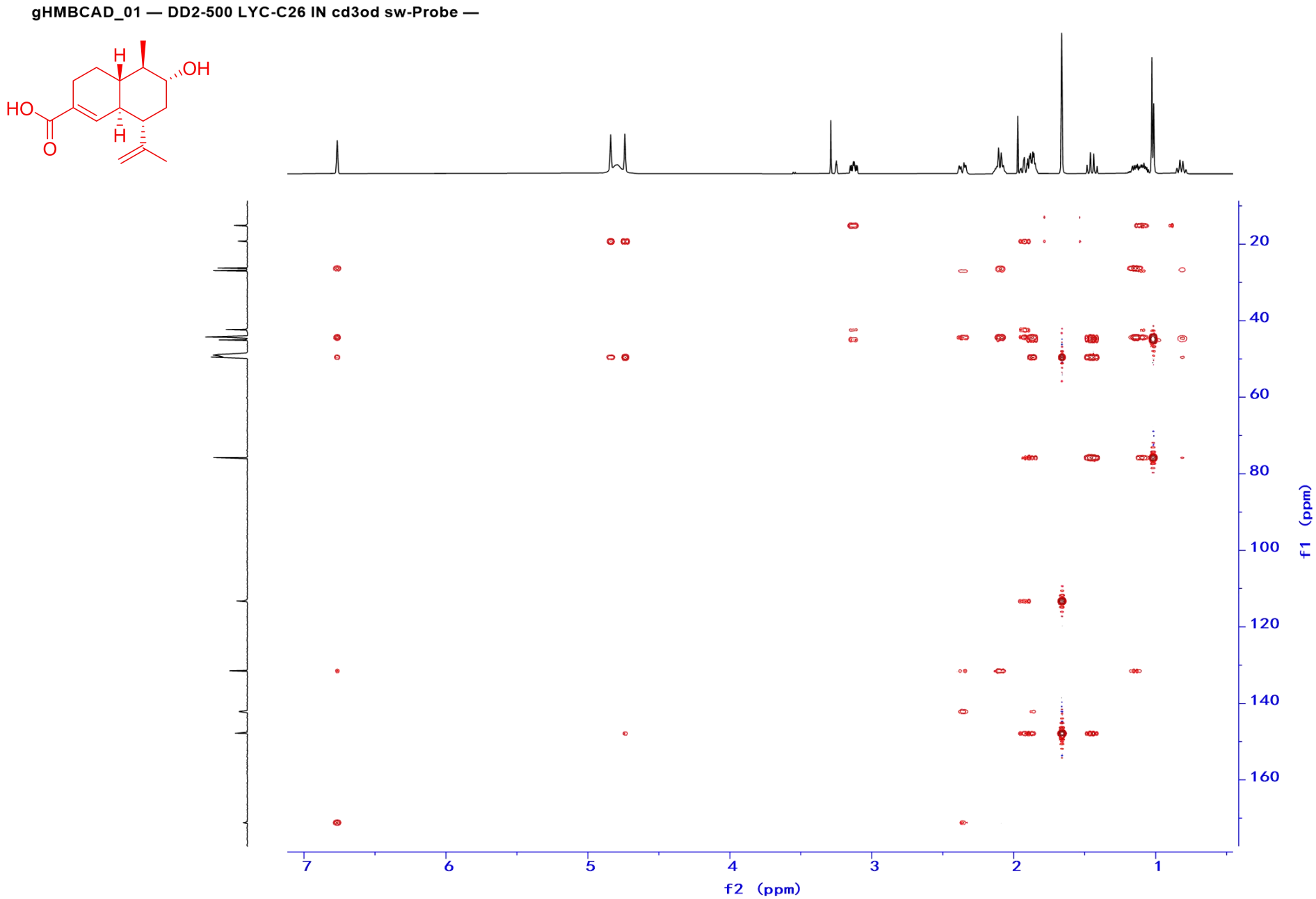


Figure S29. The HMBC Spectrum of Compound 3 in MeOH-d_4 (500MHz)

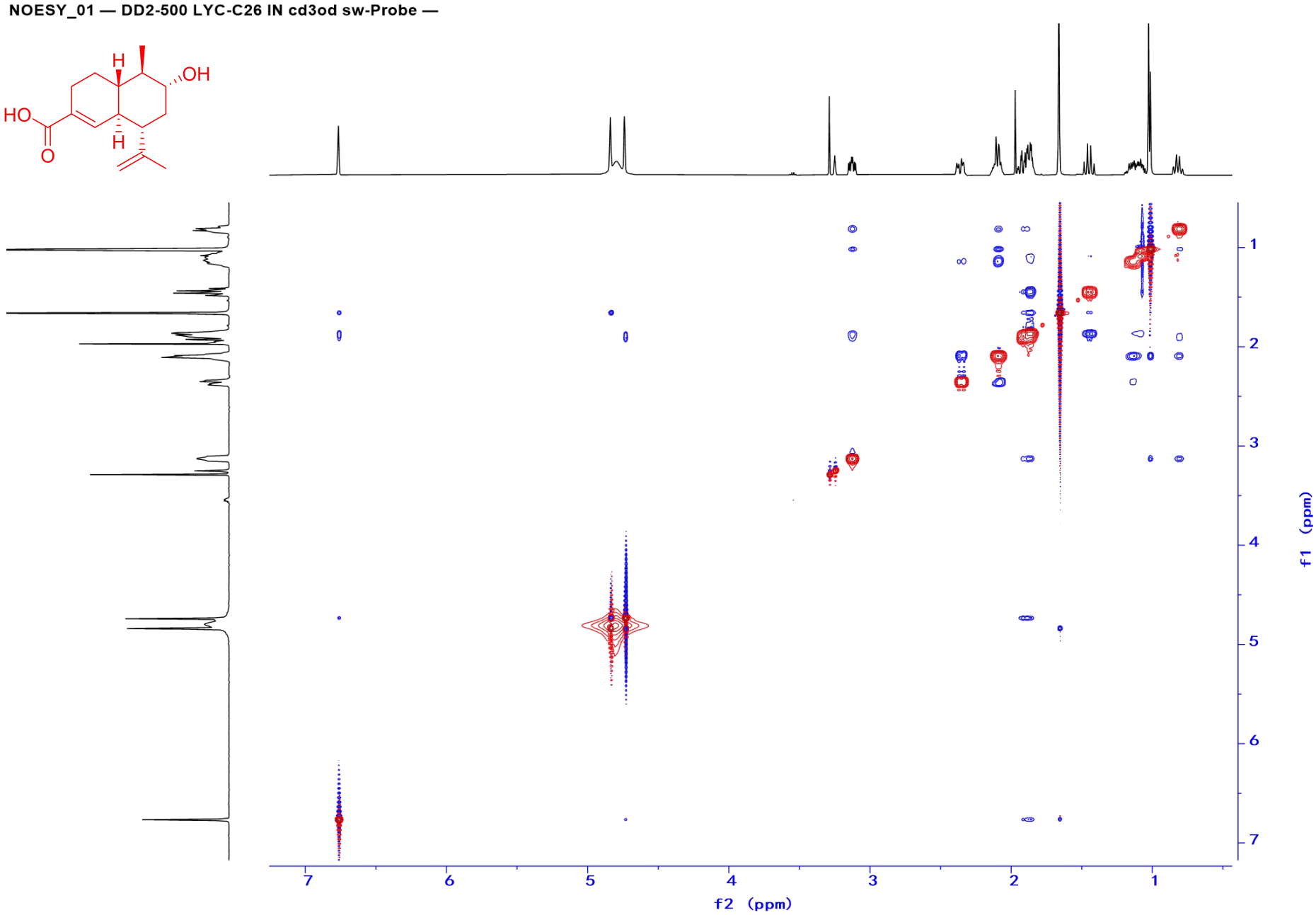


Figure S30. The NOESY Spectrum of Compound 3 in MeOH-d_4 (500MHz)

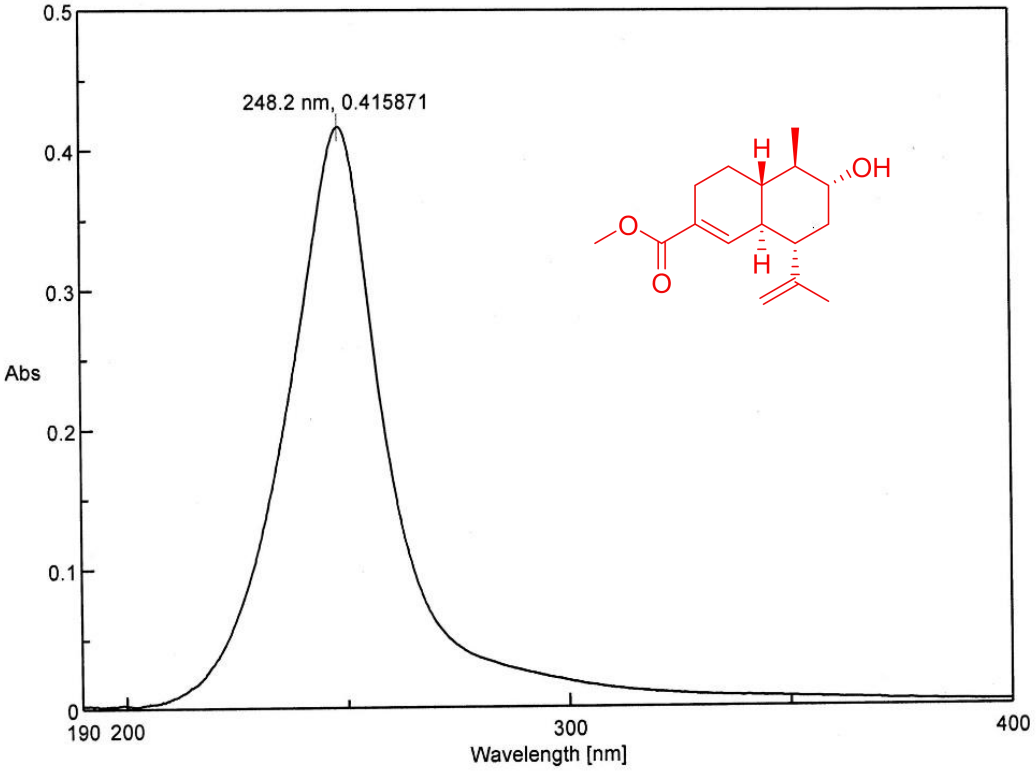


Figure S31. The UV Spectrum of Compound 4 in MeOH

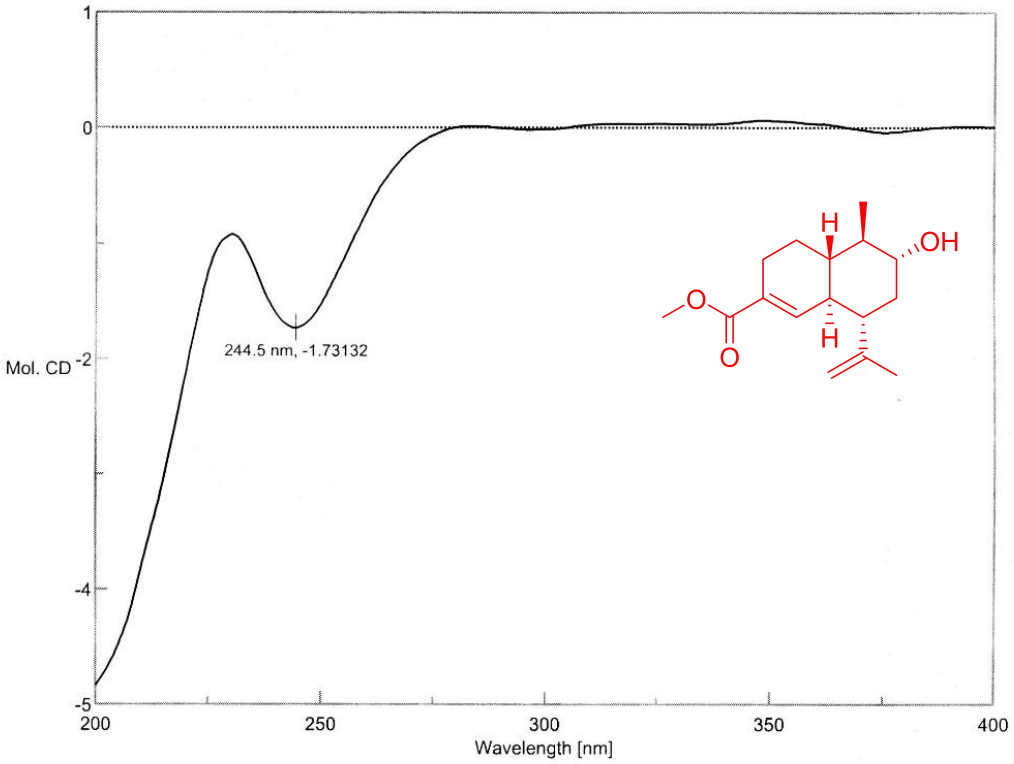


Figure S32. The CD Spectrum of Compound 4 in MeOH

MS Formula Results: + Scan (7.367 min) Sub (2016031002.d)

m/z	Ion	Formula	Abundance
265.1804	(M+H)+	C16 H25 O3	393274.3

Best	Formula (M)	Ion Formula	Score	Cross Sco	Mass	Calc Mass	Calc m/z	Diff (ppm)	Abs Diff (ppm)	Mass Match	Abund Match	Spacing Match	DBE
☑	C16 H24 O3	C16 H25 O3	99.68		264.1731	264.1725	265.1798	-2.18	2.18	99.86	99.72	99.28	5
☐	C11 H24 N2 O5	C11 H25 N2 O5	94.43		264.1731	264.1685	265.1758	-17.41	17.41	91.31	95.38	99.51	1
☐	C18 H20 N2	C18 H21 N2	81.84		264.1731	264.1626	265.1699	-39.64	39.64	62.43	99.65	99.3	10
☐	C15 H24 N2 O2	C15 H25 N2 O2	81.34		264.1731	264.1838	265.1911	40.34	40.34	61.4	99.53	99.39	5
☐	C20 H24	C20 H25	70.77		264.1731	264.1878	265.1951	55.57	55.57	39.63	99.02	99.16	9

Figure S33. The HR-mass Spectrum of Compound 4 in MeOH

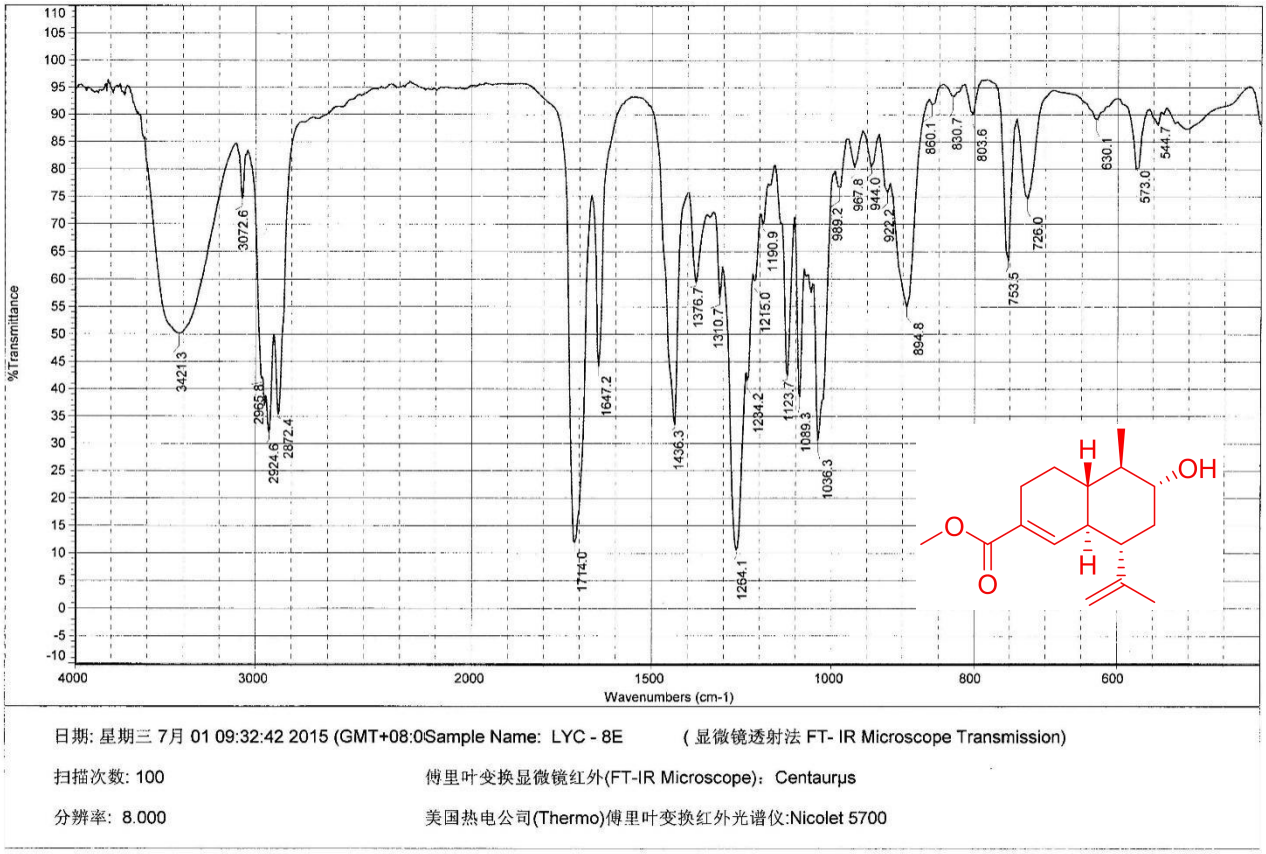


Figure S34. The IR Spectrum of Compound 4

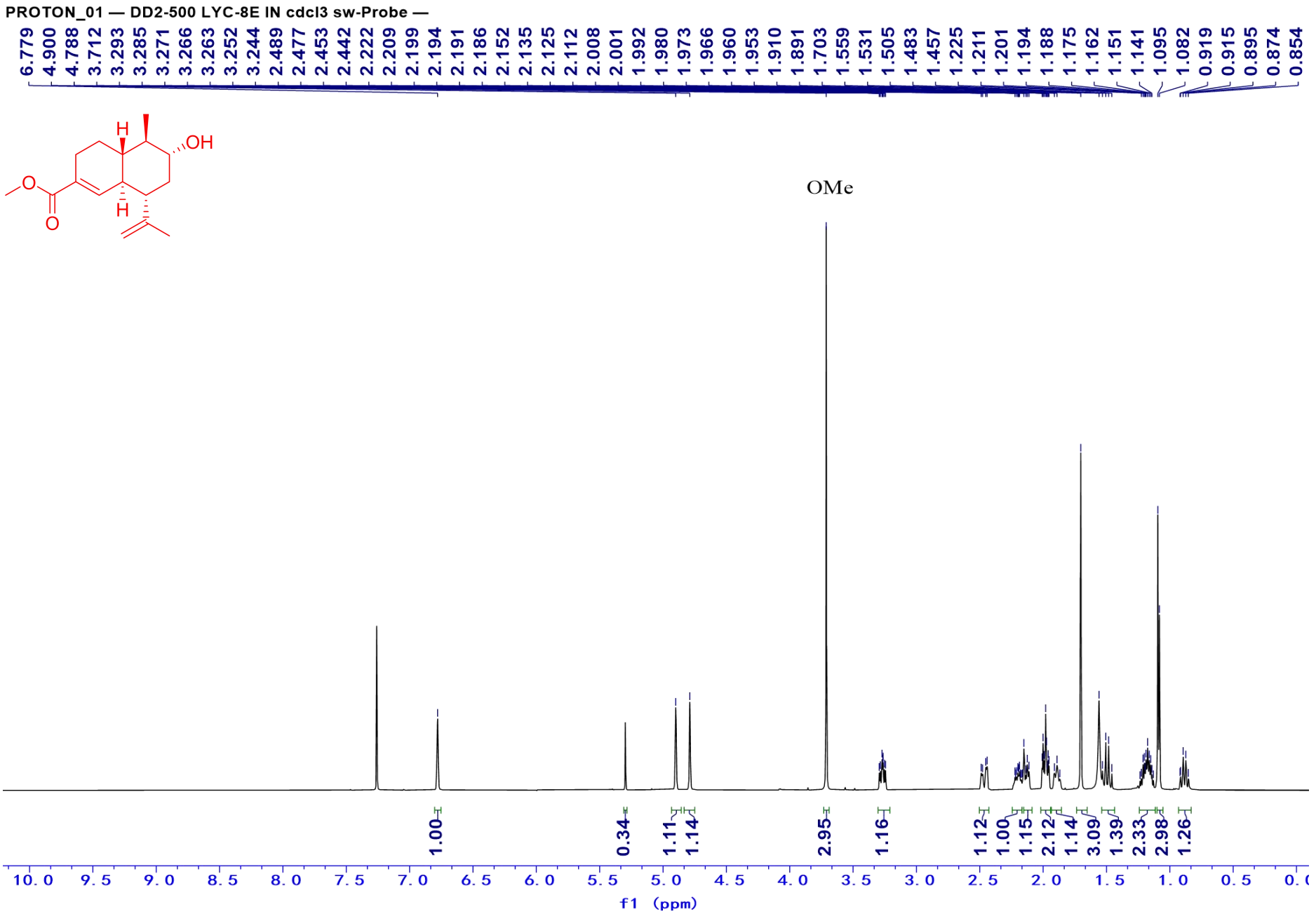


Figure S35. The 1H NMR Spectrum of Compound 4 in $CDCl_3$ (500MHz)

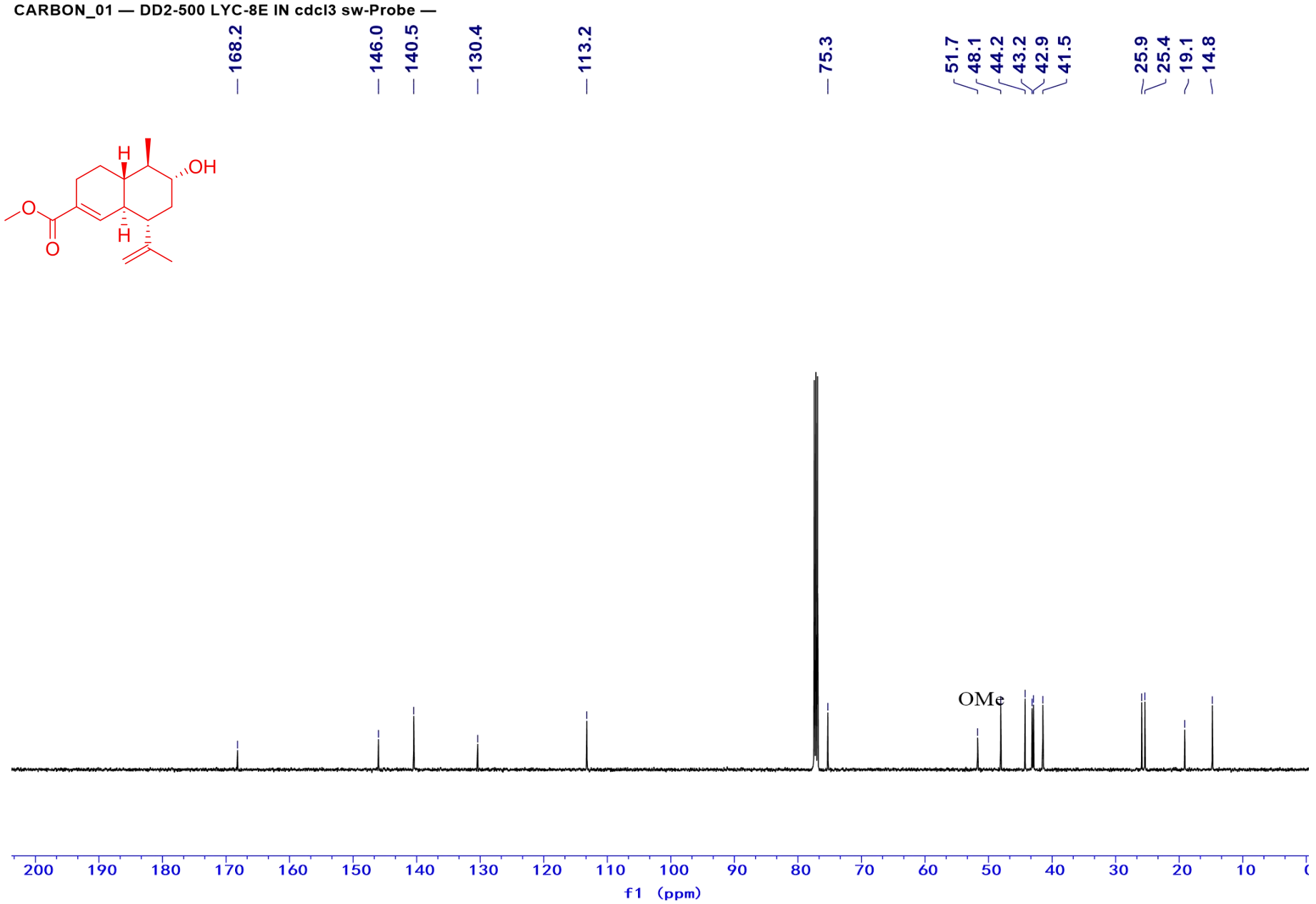


Figure S36. The ^{13}C NMR Spectrum of Compound 4 in $CDCl_3$ (125MHz)

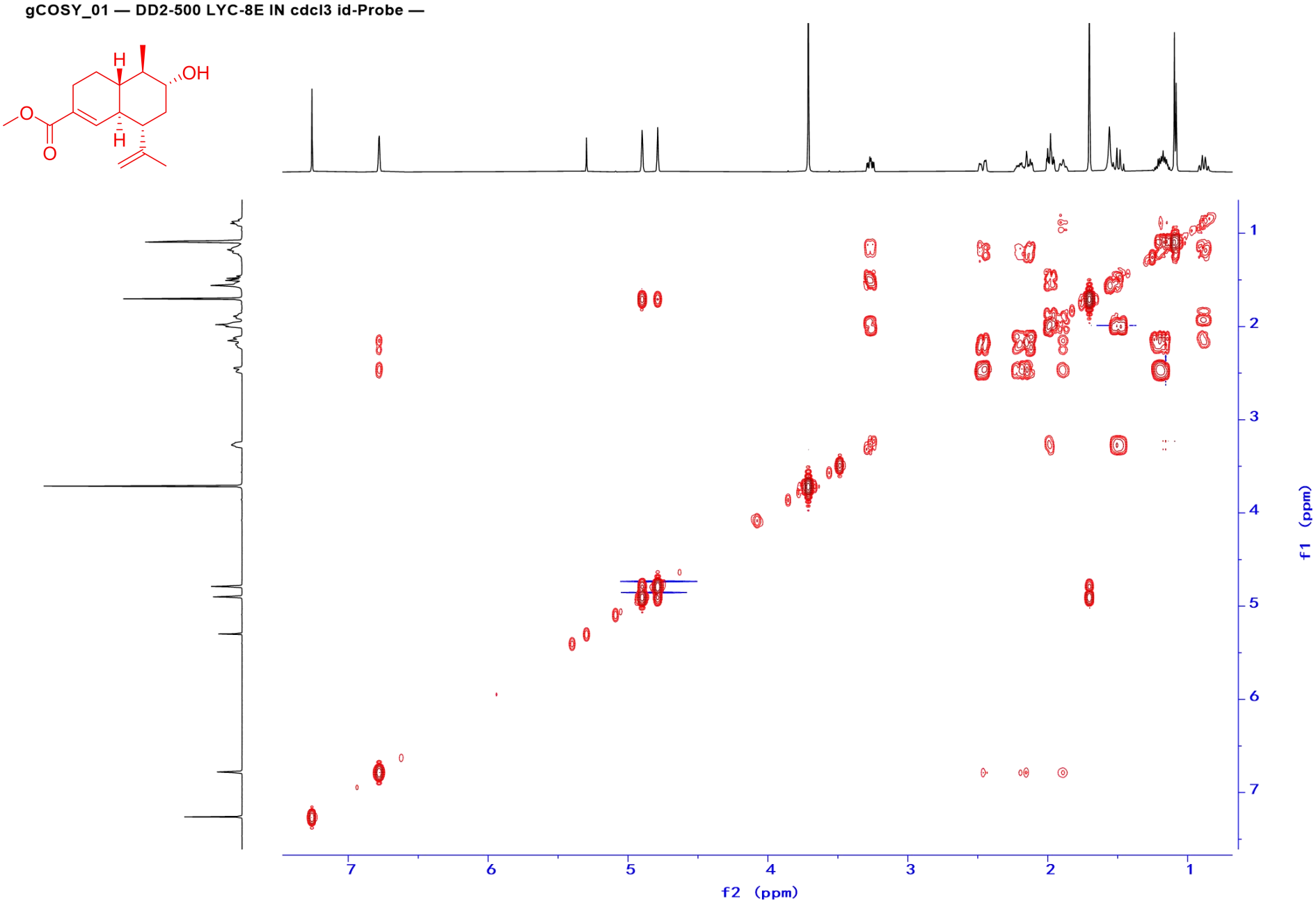


Figure S37. The ^{1}H-^{1}H COSY Spectrum of Compound 4 in $CDCl_3$ (500MHz)

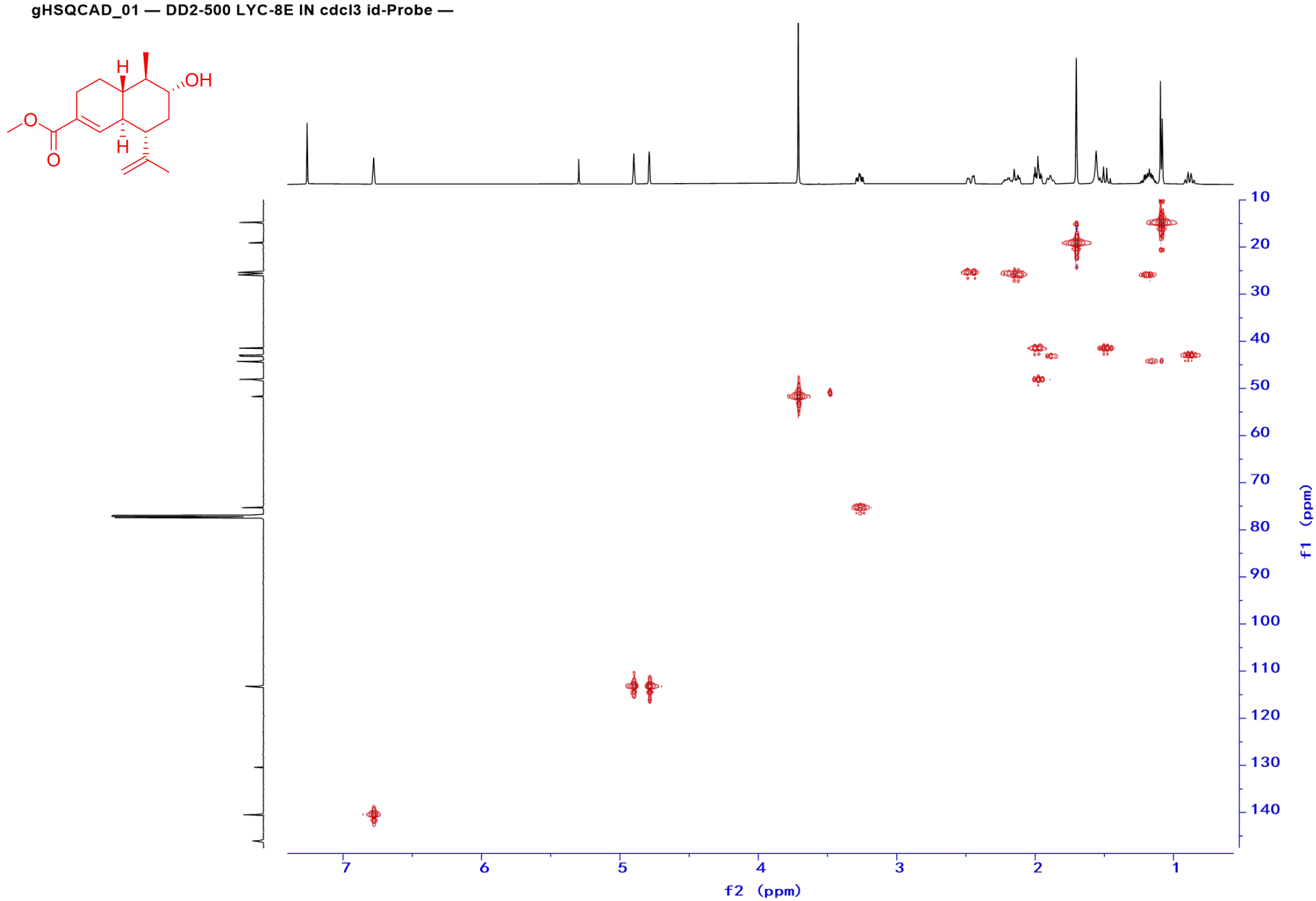


Figure S38. The HSQC Spectrum of Compound 4 in $CDCl_3$ (500MHz)

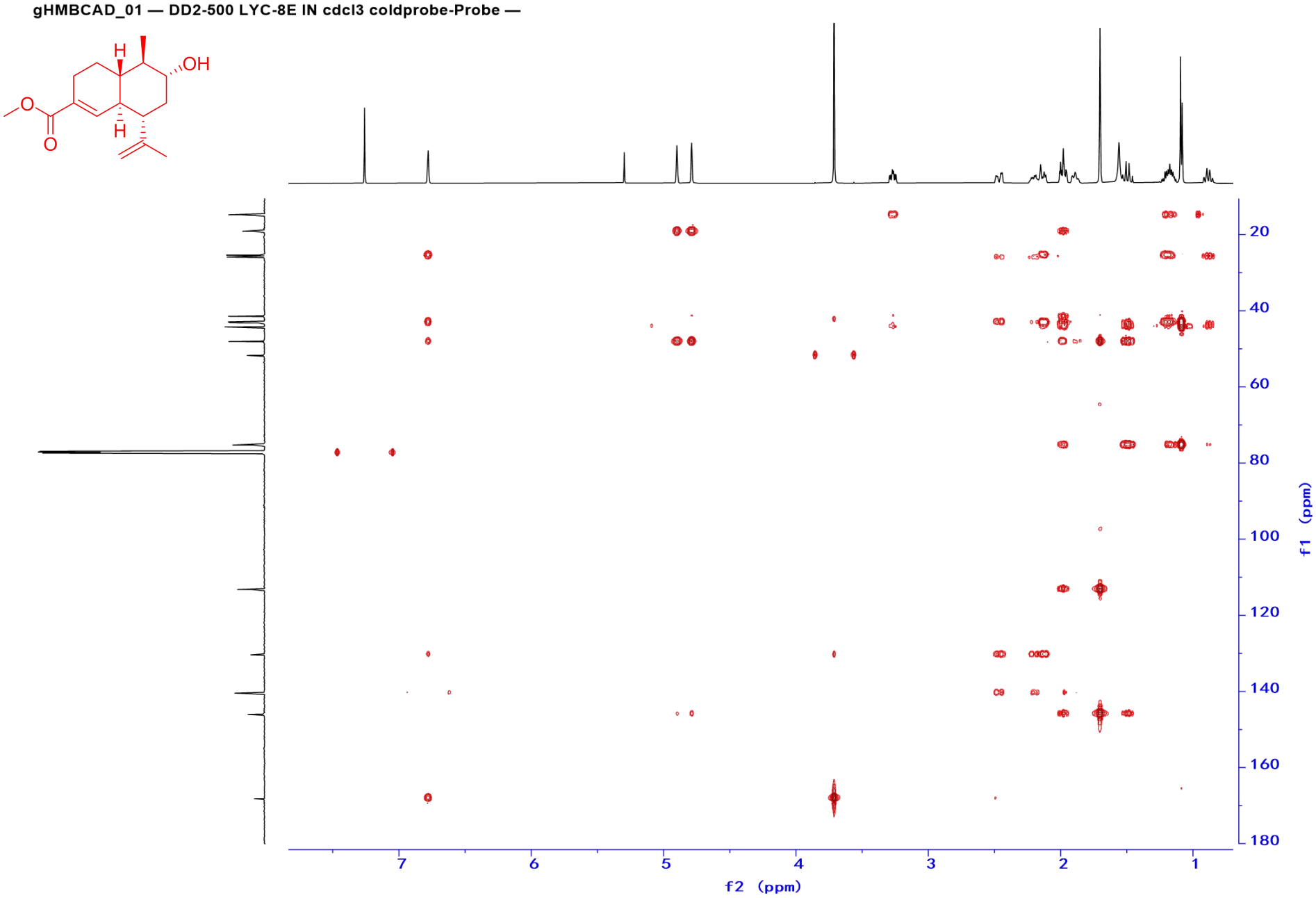


Figure S39. The HMBC Spectrum of Compound 4 in $CDCl_3$ (500MHz)

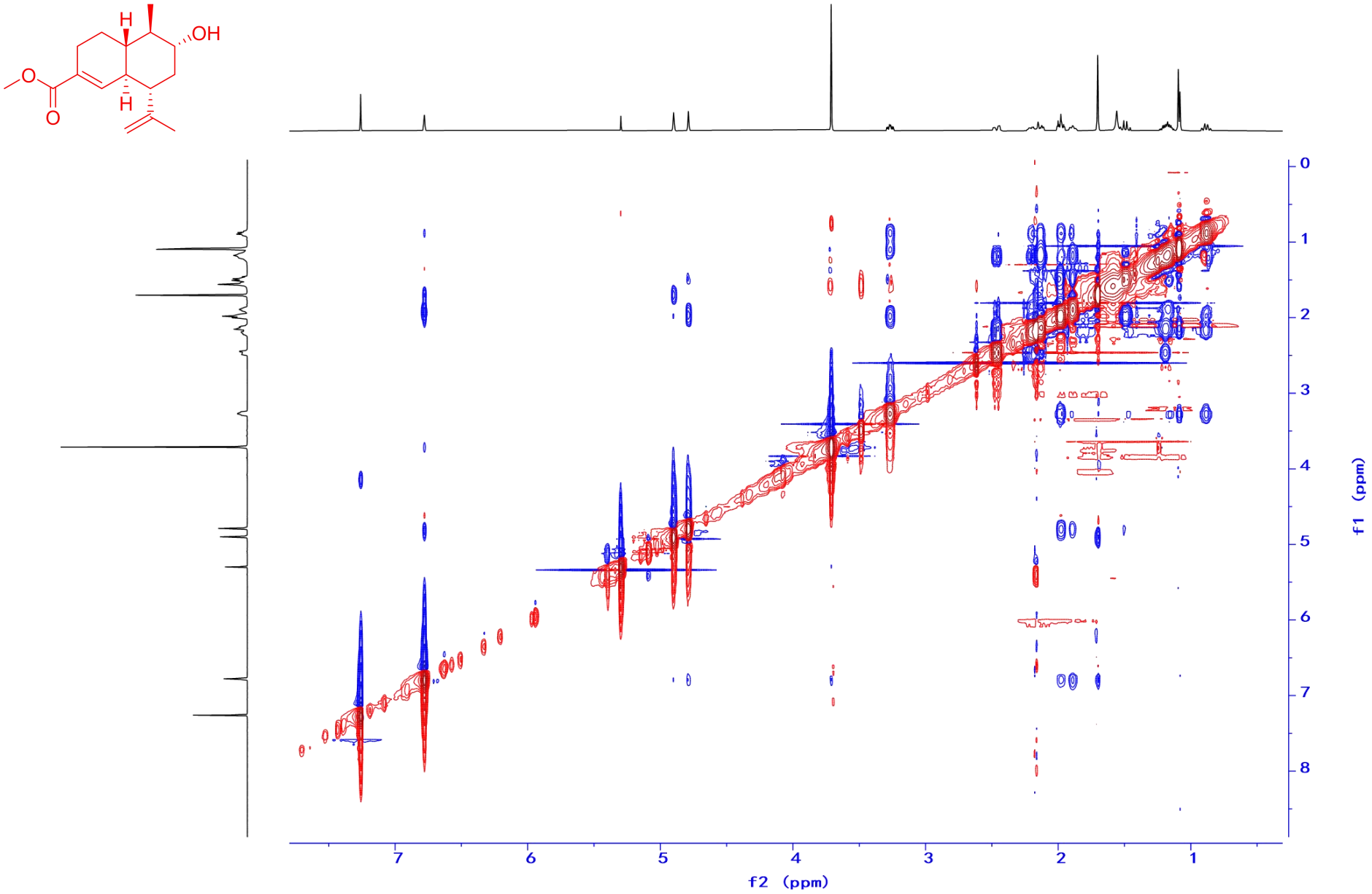


Figure S40. The NOESY Spectrum of Compound 4 in $CDCl_3$ (500MHz)

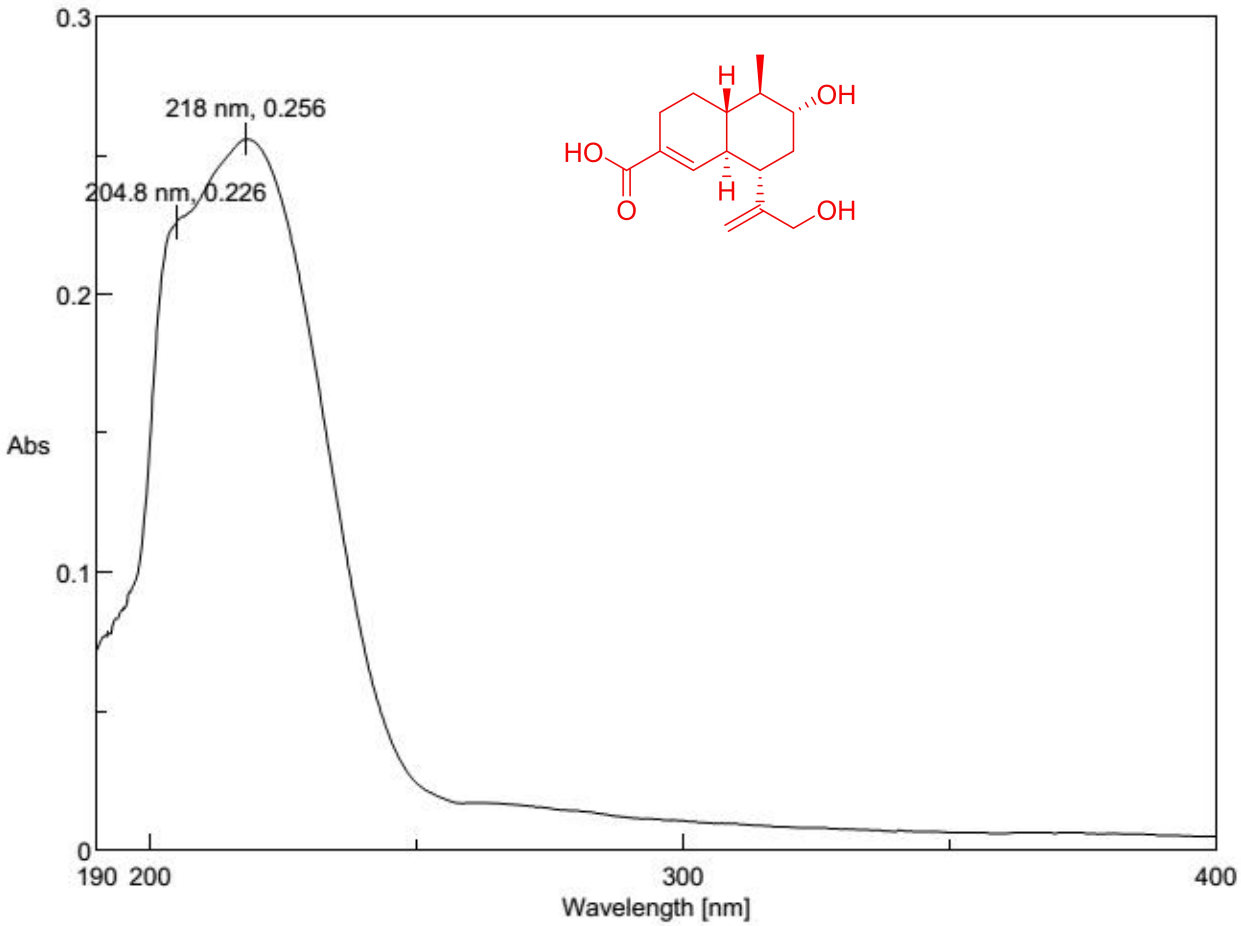


Figure S41. The UV Spectrum of Compound 5 in MeOH

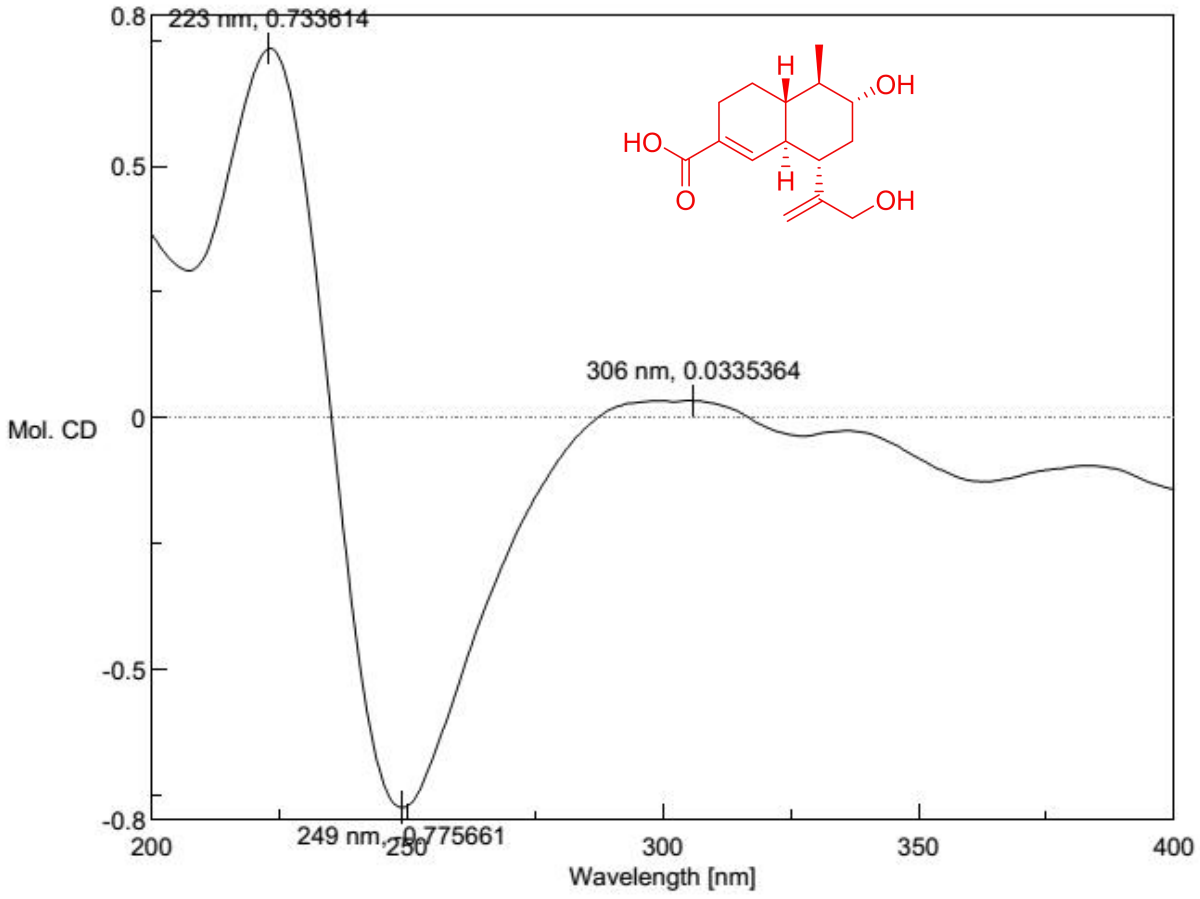
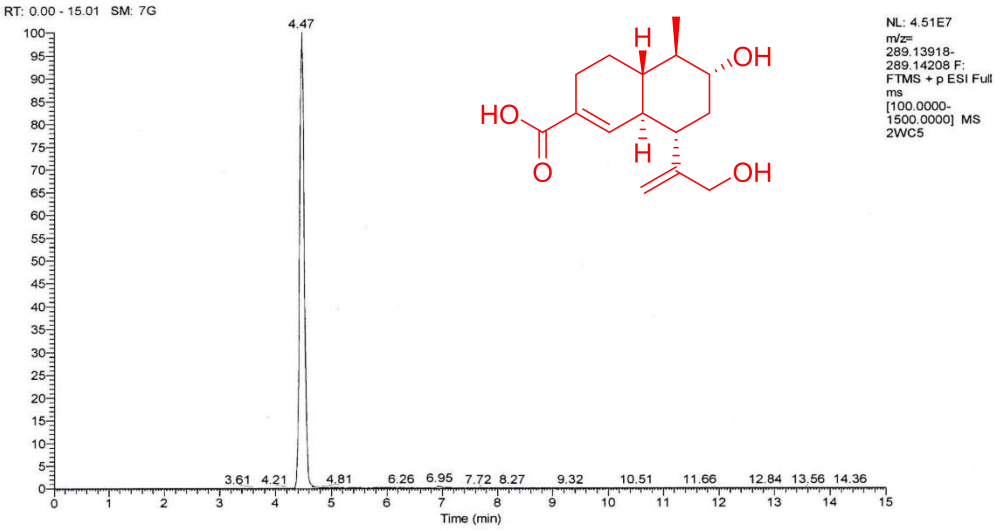


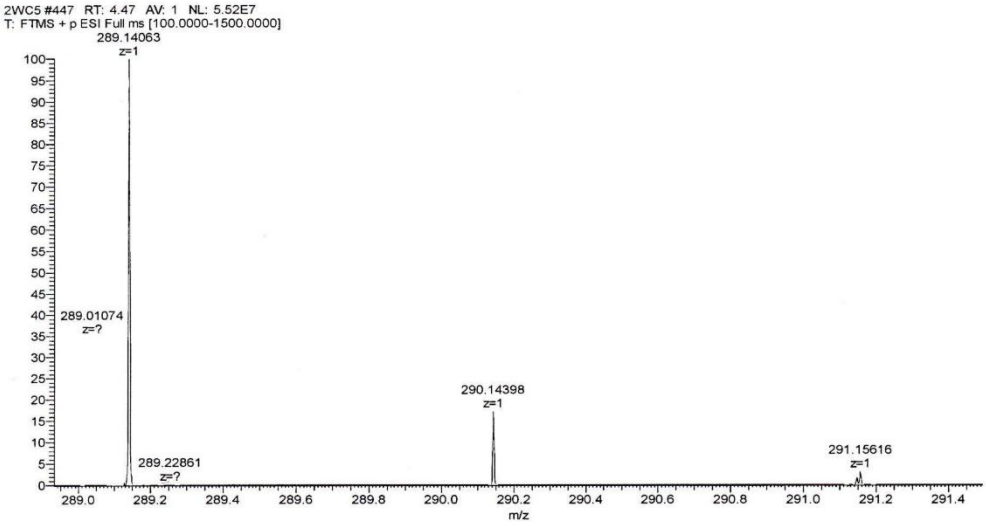
Figure S42. The CD Spectrum of Compound 5 in MeOH

Thermo Qexactive Focus Report

compound NO. : 2WC5

Method : LCMS(compound)-low





m/z	Theo. Mass	Delta (ppm)	RDB equiv.	Composition	
289.14063	289.14103	-1.38	4.5	C15 H22 O4 Na	M+Na

Figure S43. The HR-mass Spectrum of Compound 5 in MeOH

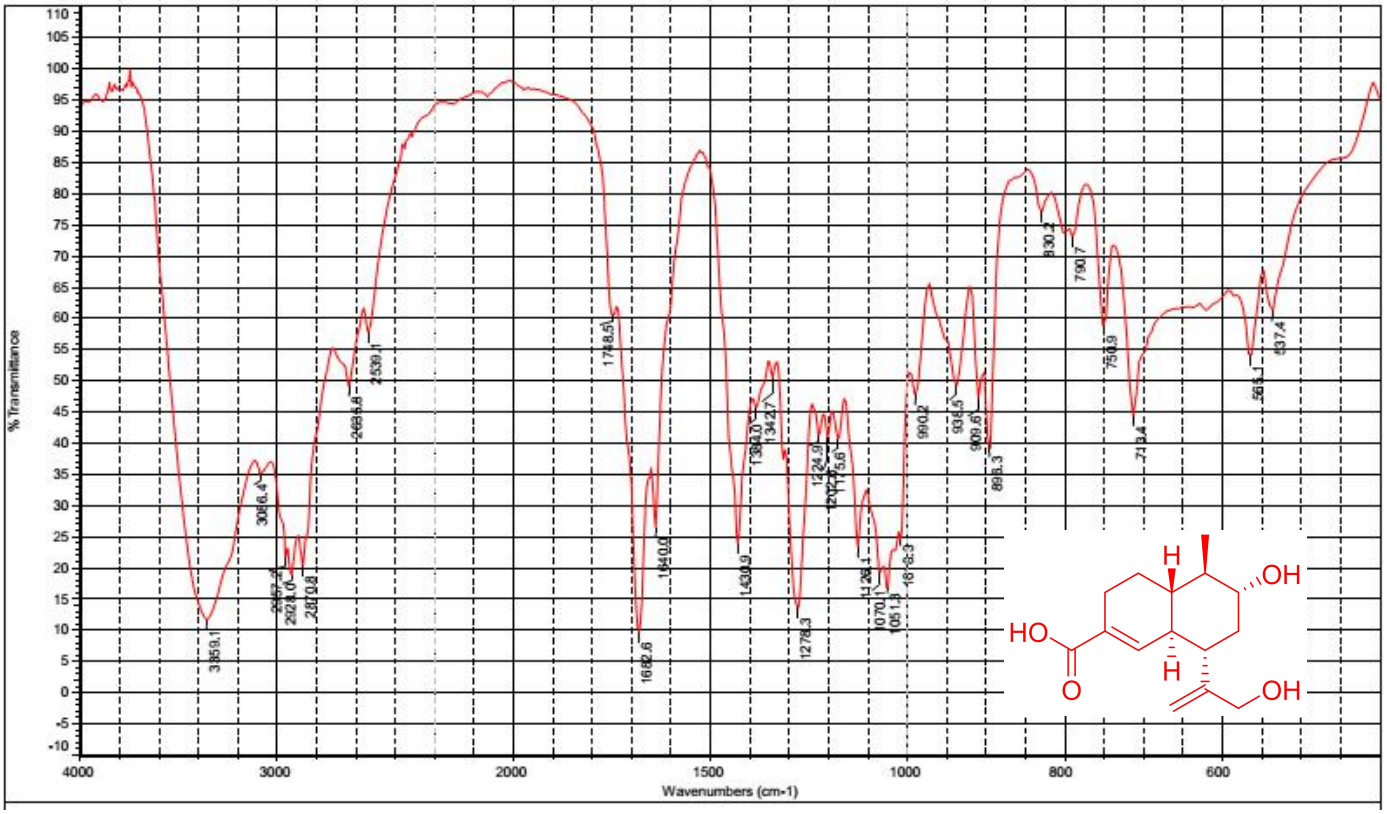


Figure S44. The IR Spectrum of Compound 5

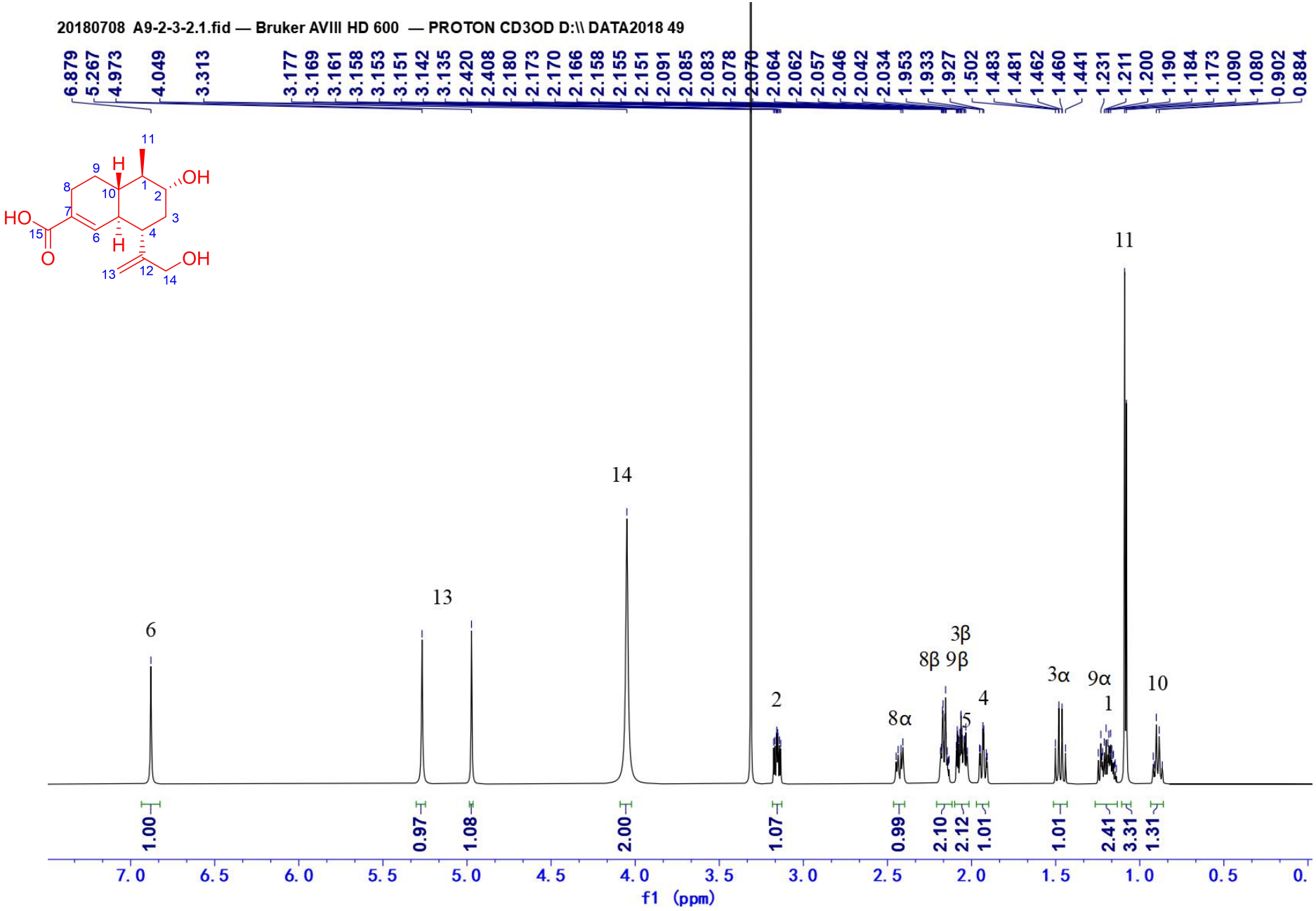


Figure S45. The ^{1}H NMR Spectrum of Compound 5 in MeOH-d_4 (600MHz)

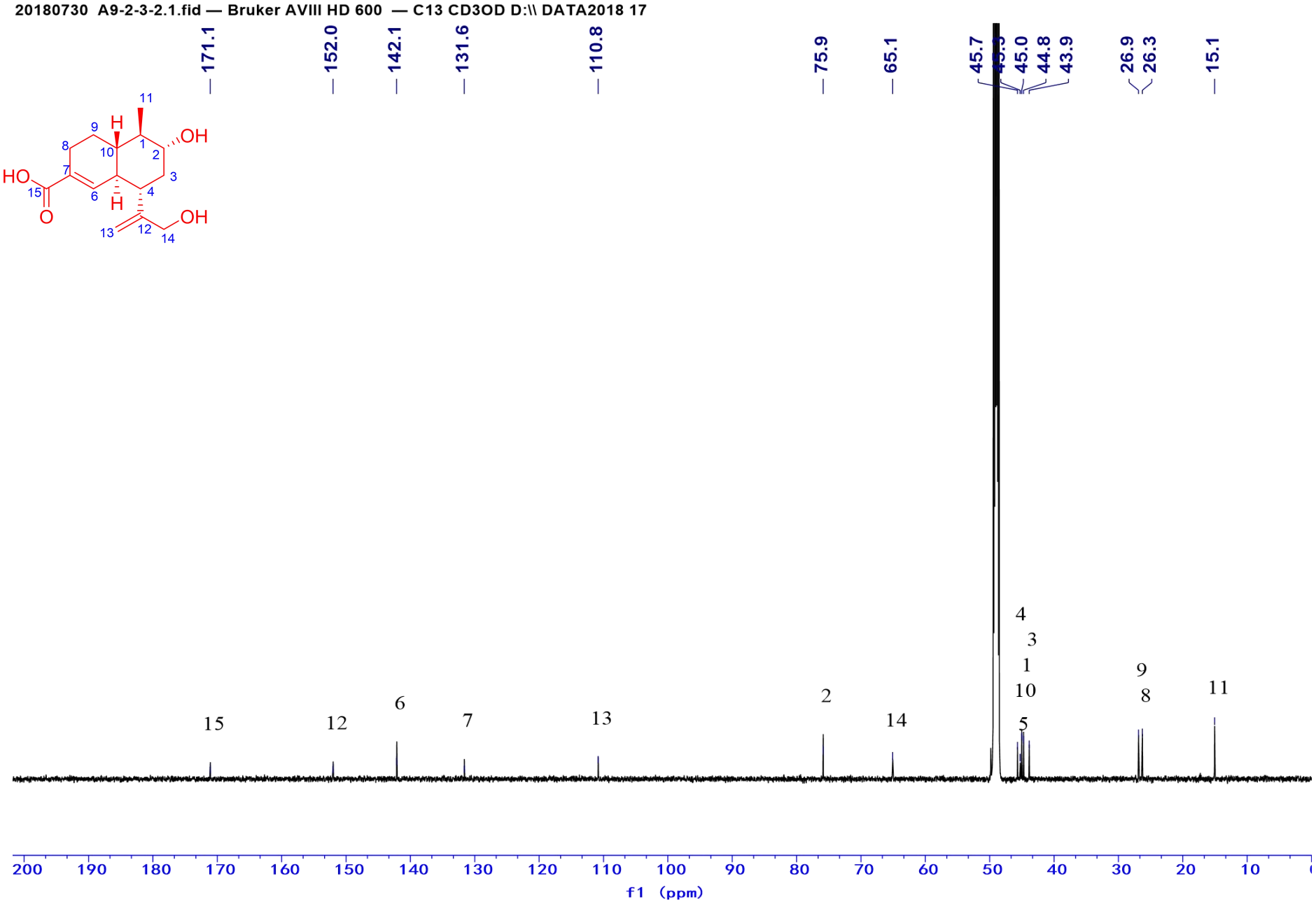


Figure S46. The ^{13}C NMR Spectrum of Compound 5 in MeOH-d_4 (150MHz)

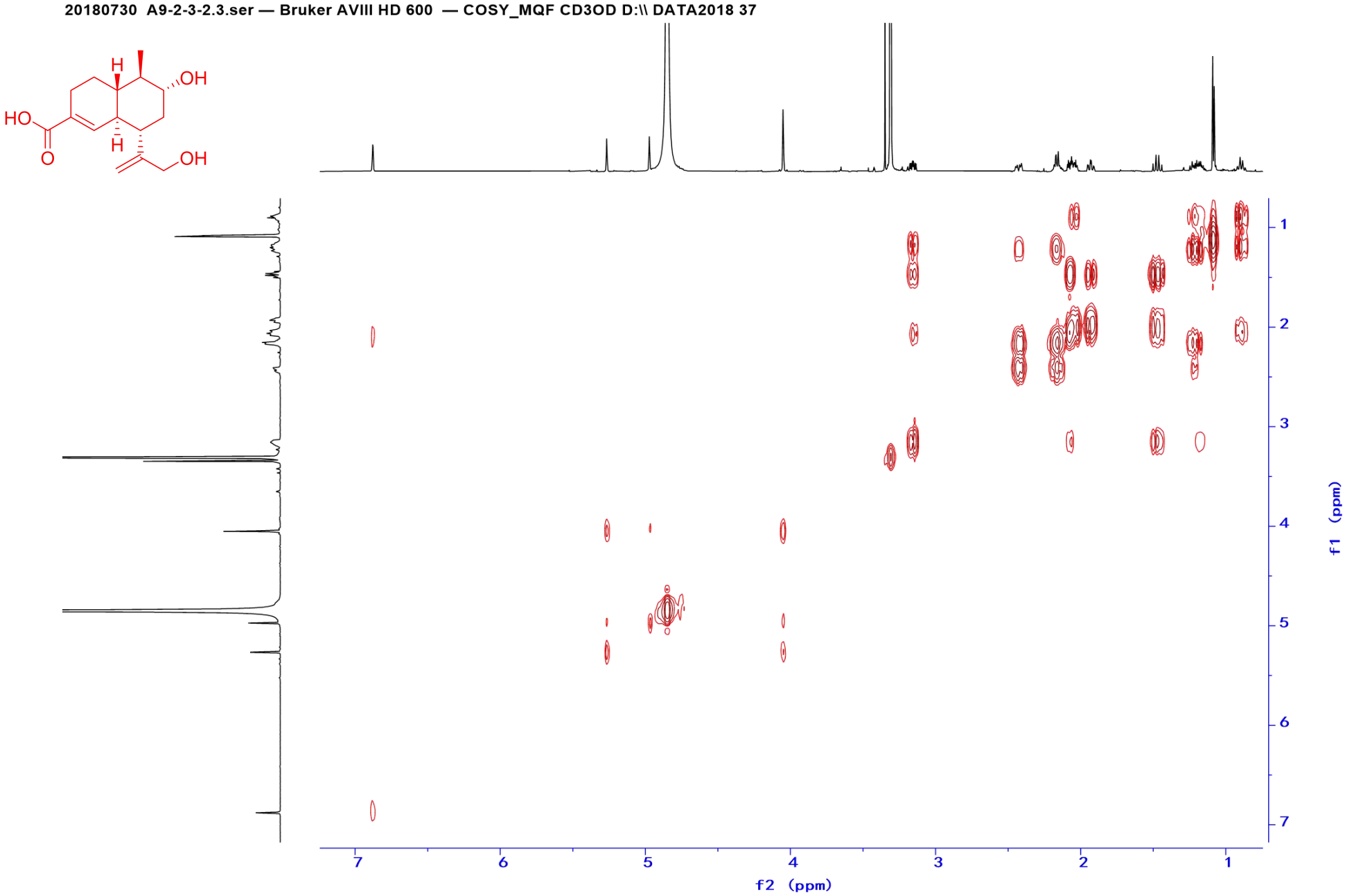


Figure S47. The ^{1}H-^{1}H COSY Spectrum of Compound 5 in MeOH-d_4 (600MHz)

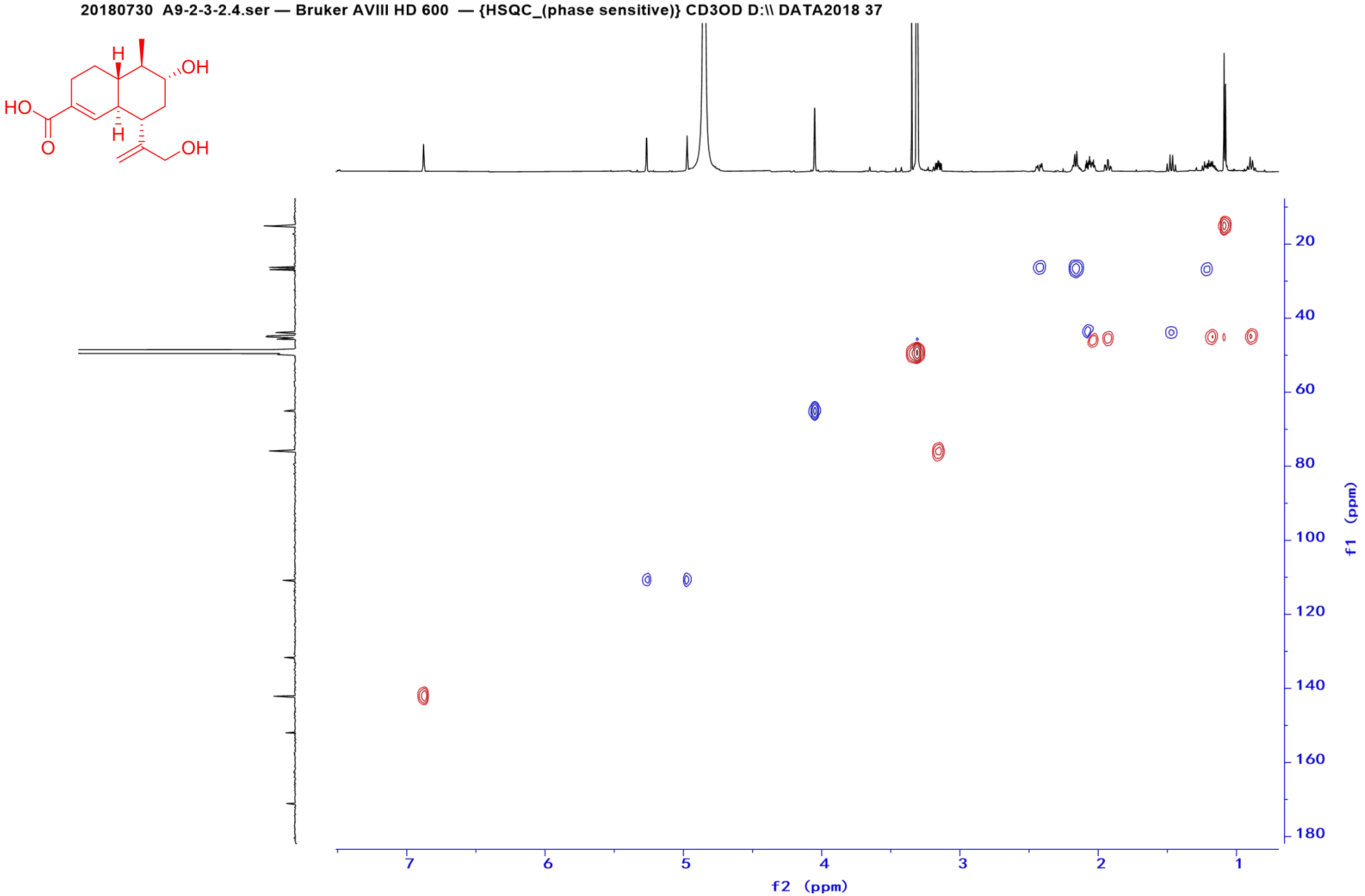


Figure S48. The HSQC Spectrum of Compound 5 in MeOH-d_4 (600MHz)

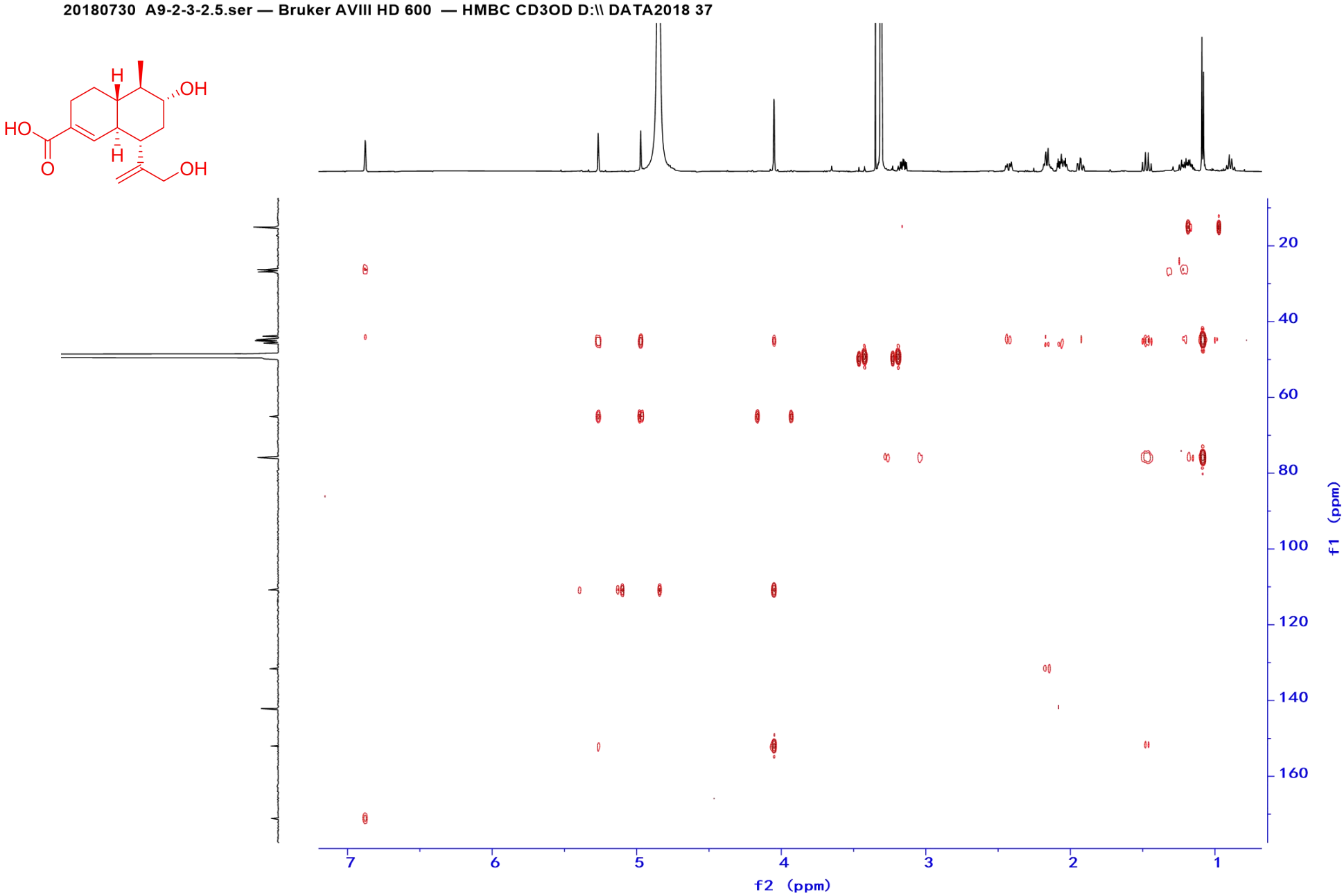


Figure S49. The HMBC Spectrum of Compound 5 in MeOH-d_4 (600MHz)

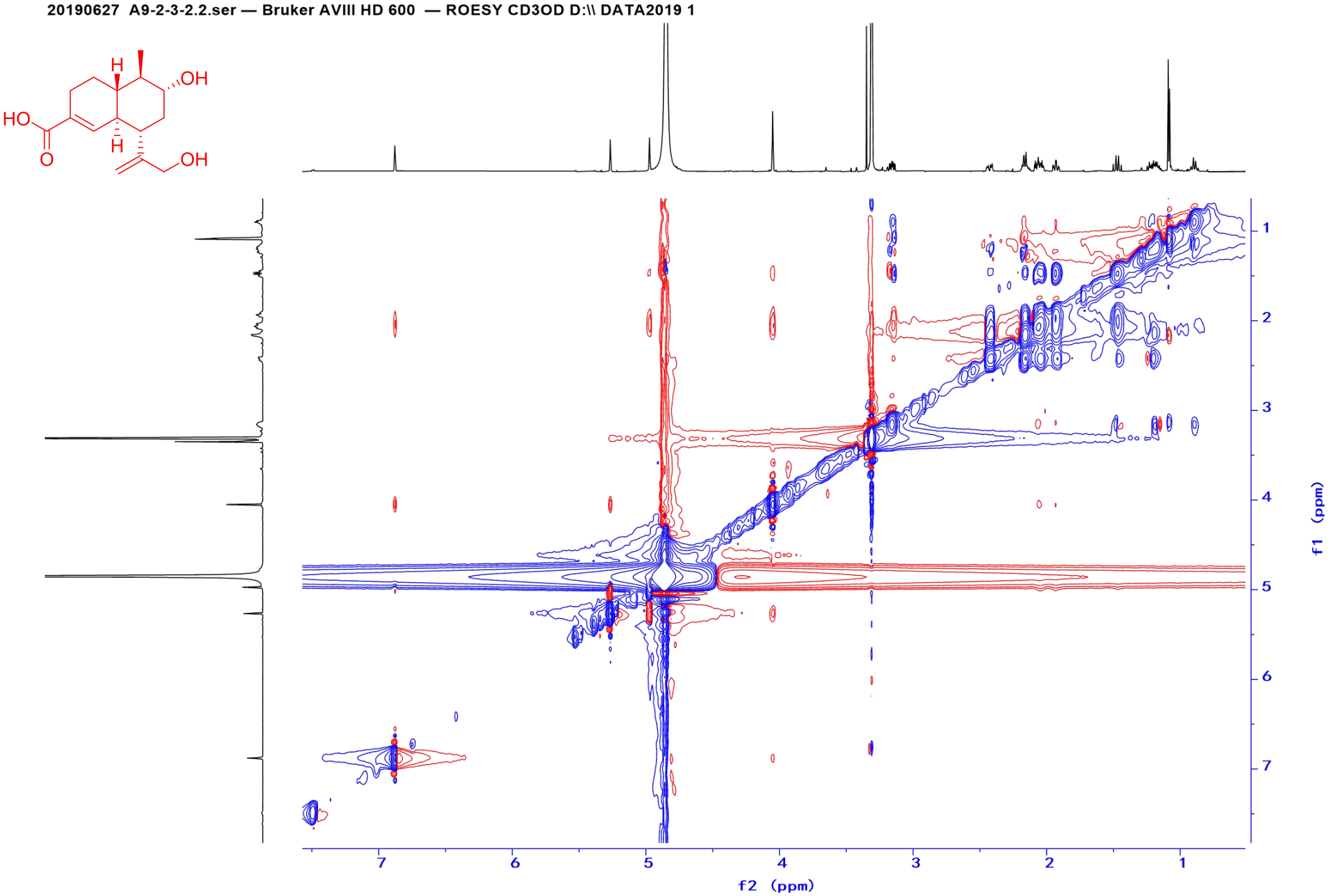


Figure S50. The NOESY Spectrum of Compound 5 in MeOH-d_4 (600MHz)

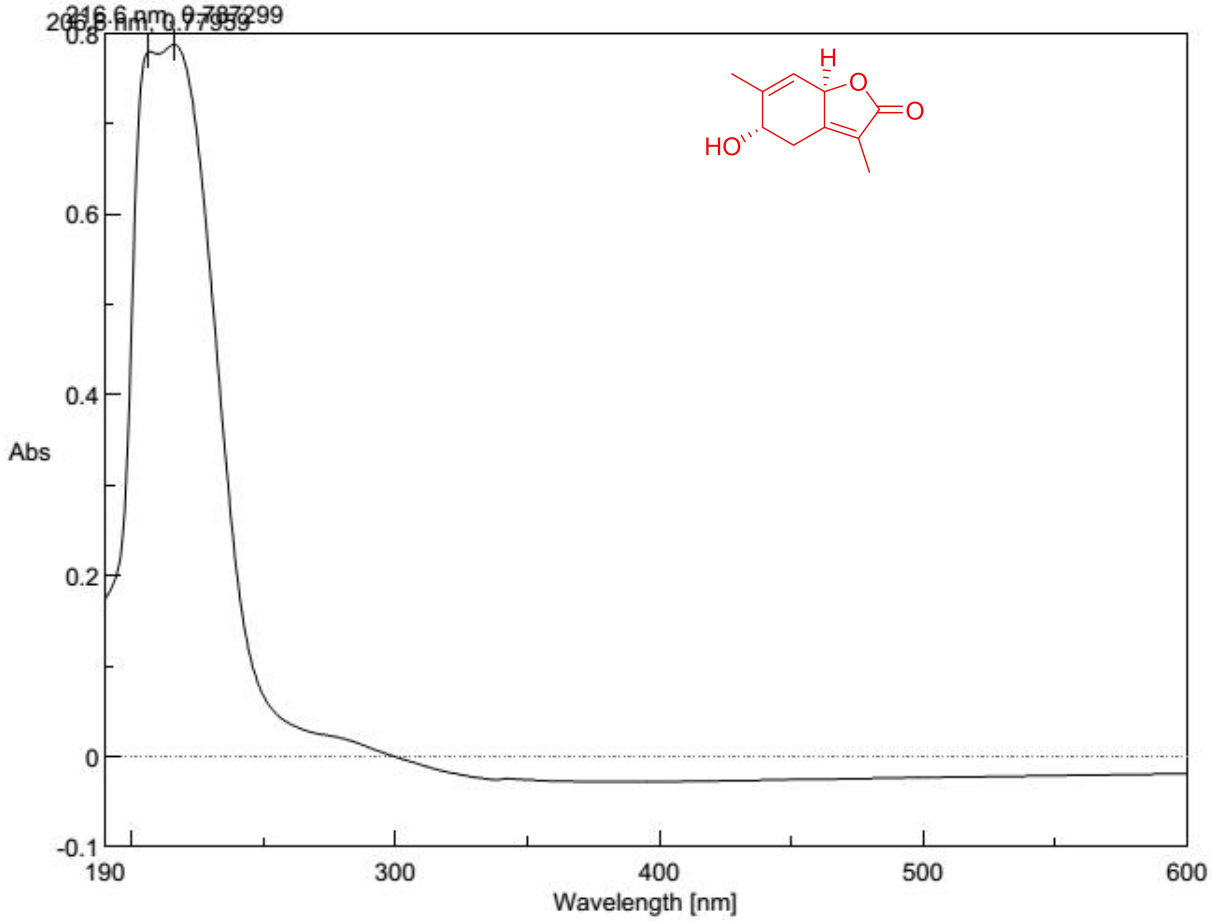


Figure S51. The UV Spectrum of Compound 7 in MeOH

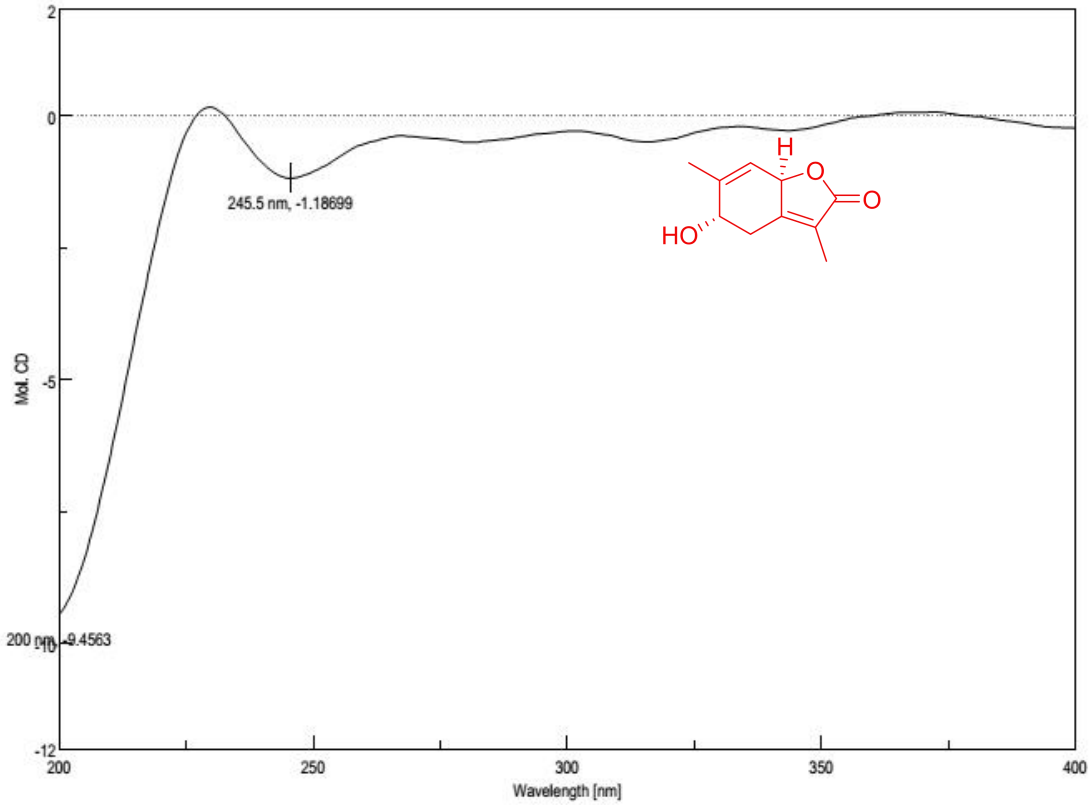
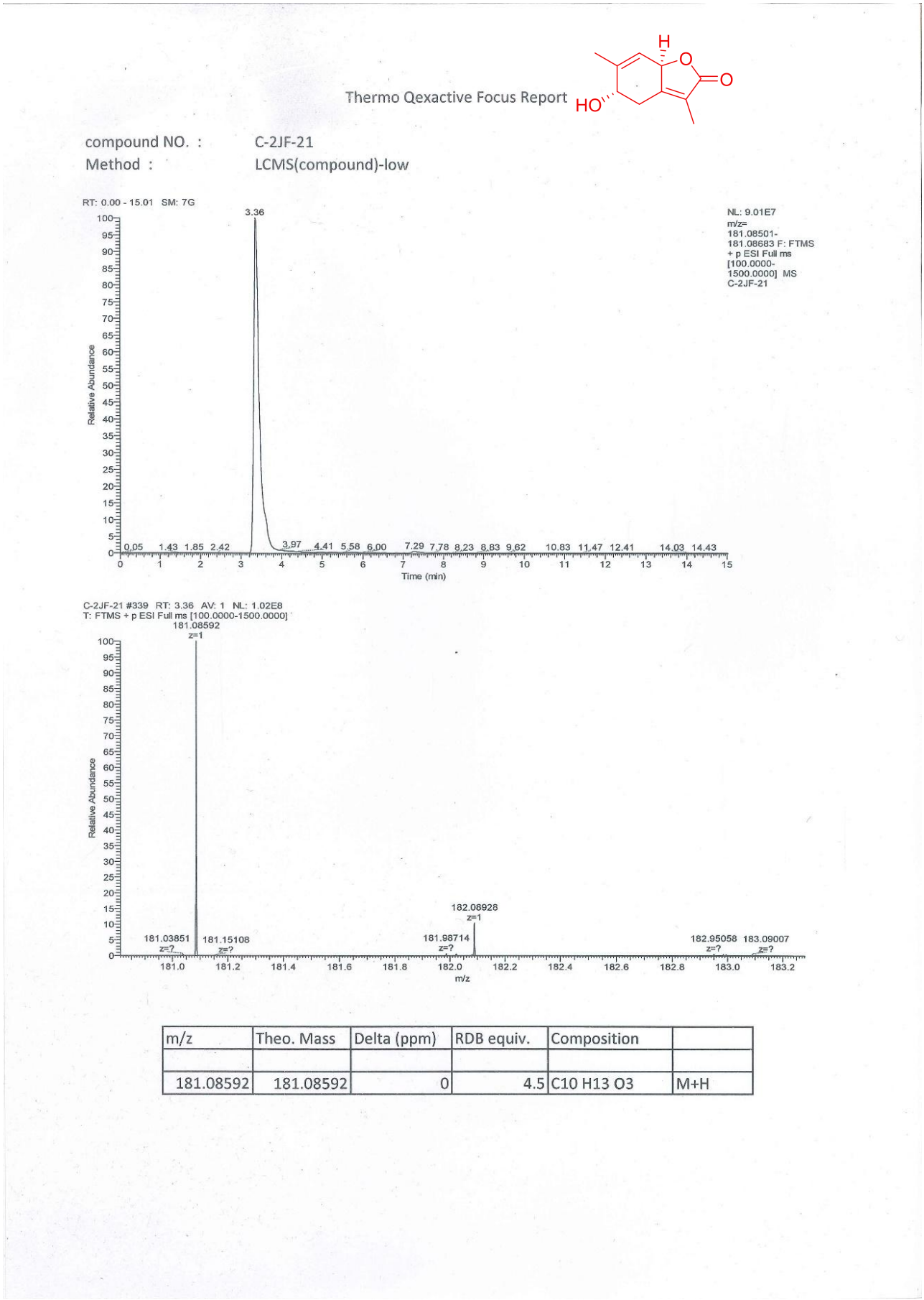


Figure S52. The CD Spectrum of Compound 7 in MeOH



m/z	Theo. Mass	Delta (ppm)	RDB equiv.	Composition	
181.08592	181.08592	0	4.5	C10 H13 O3	M+H

Figure S53. The HR-mass Spectrum of Compound 7 in MeOH

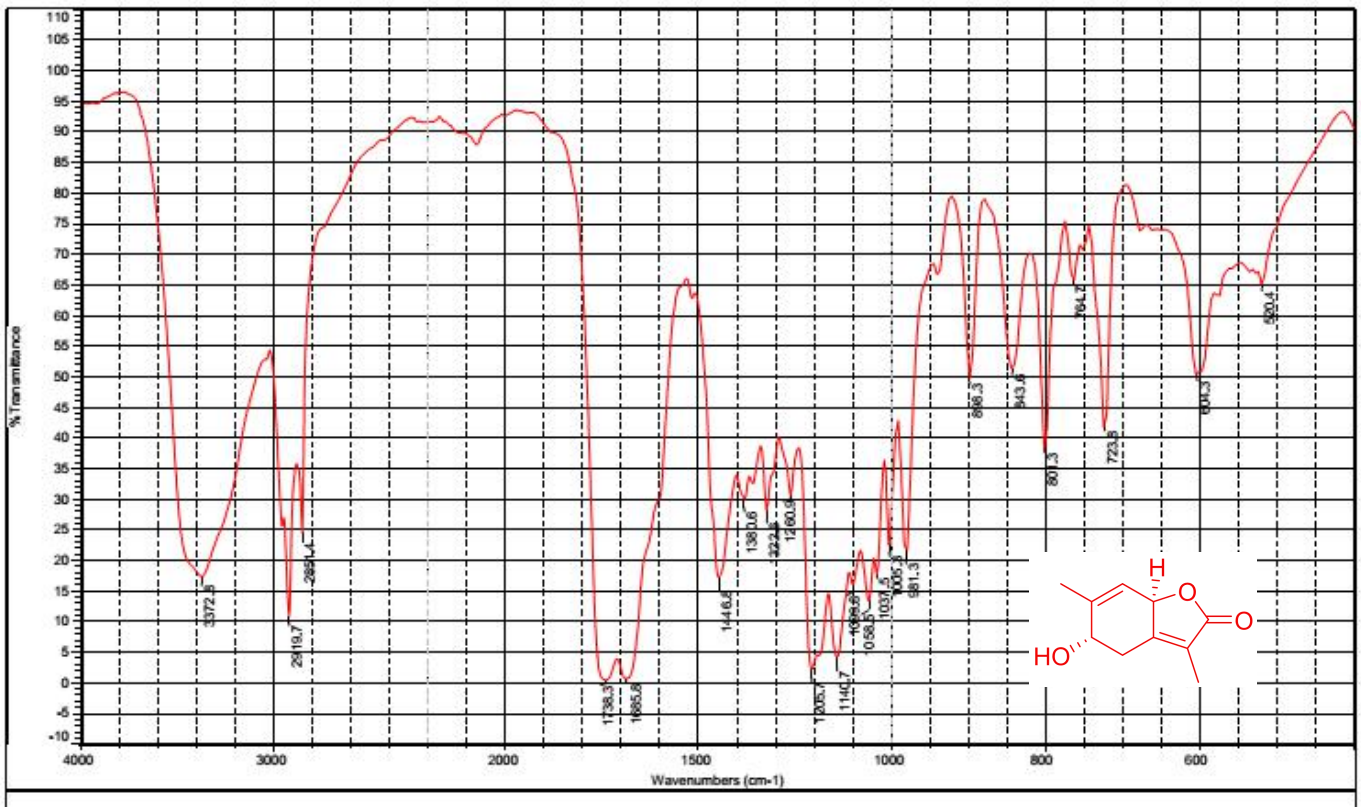


Figure S54. The IR Spectrum of Compound 7

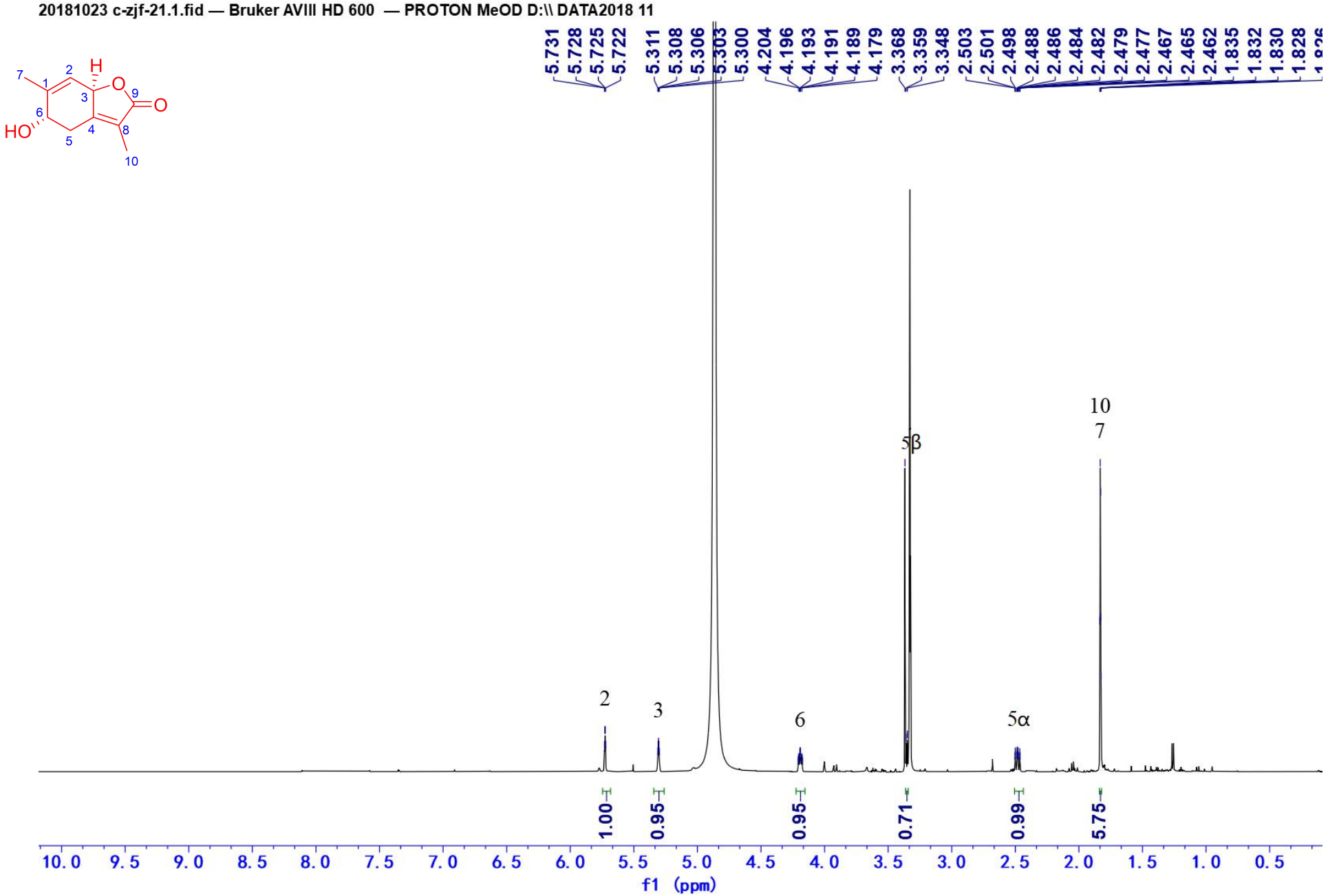


Figure S55. The ^{1}H NMR Spectrum of Compound 7 in MeOH-d_4 (600MHz)

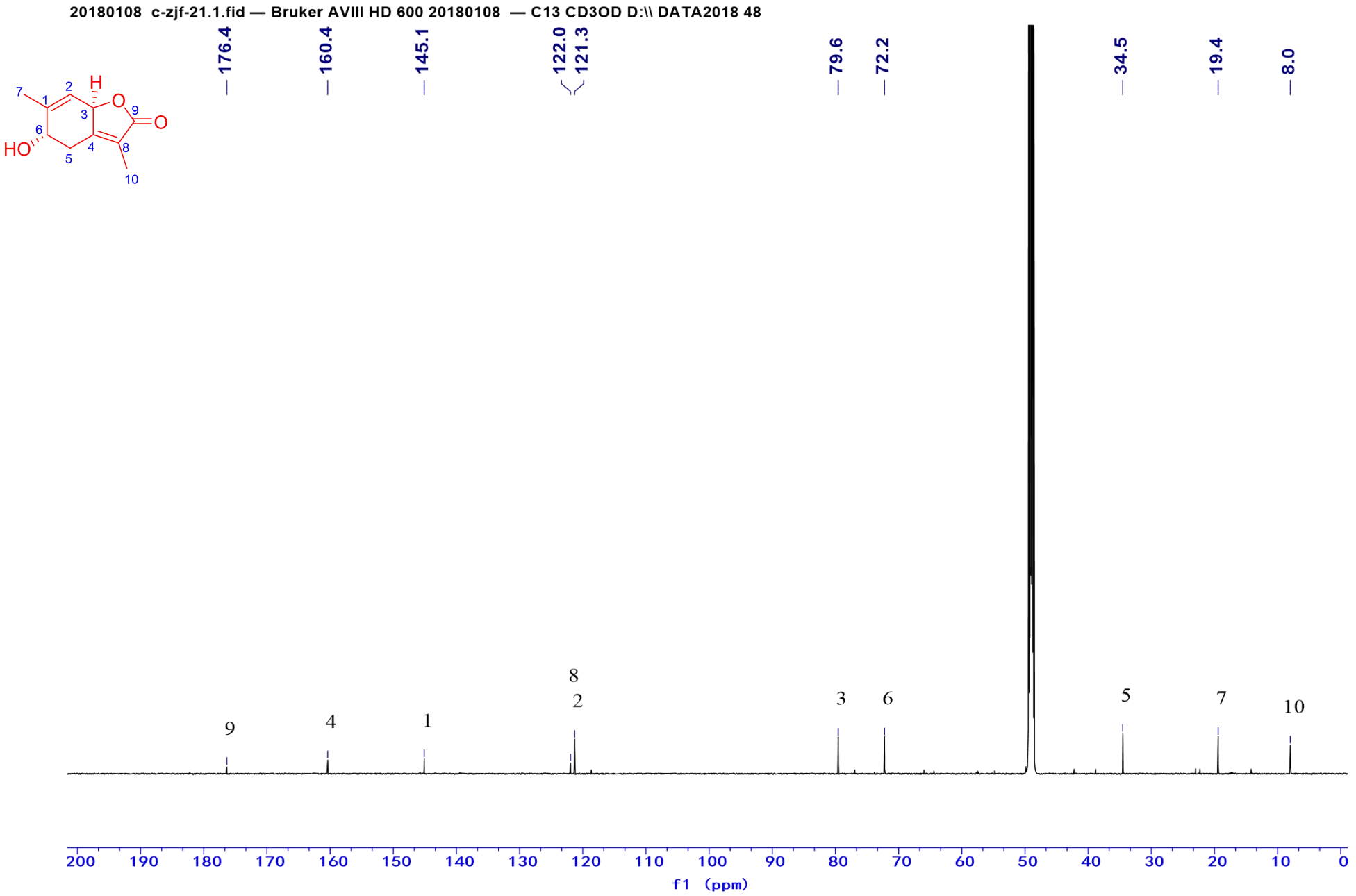


Figure S56. The ^{13}C NMR Spectrum of Compound 7 in MeOH-d_4 (150MHz)

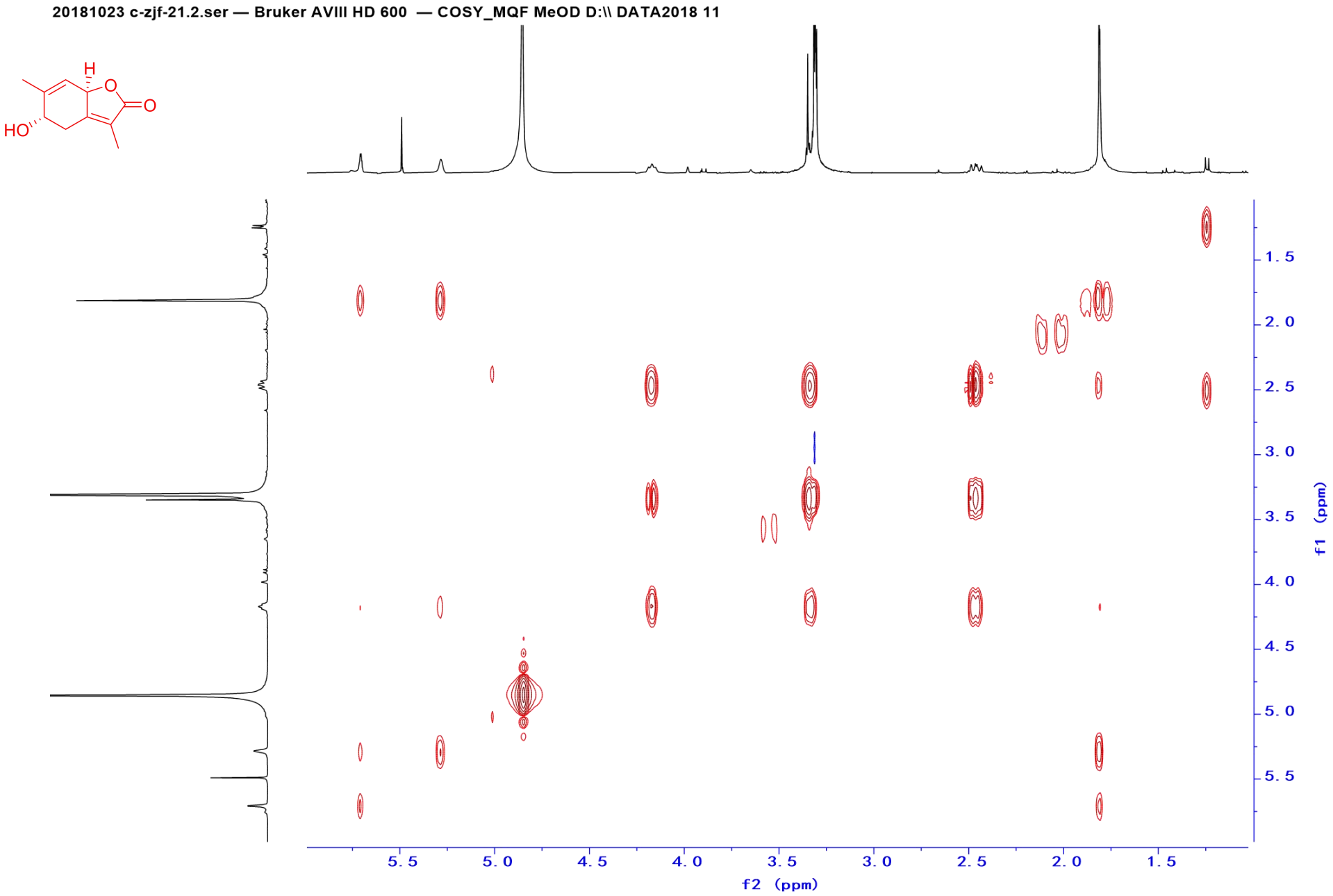


Figure S57. The ^{1}H-^{1}H COSY Spectrum of Compound 7 in MeOH-d_4 (600MHz)

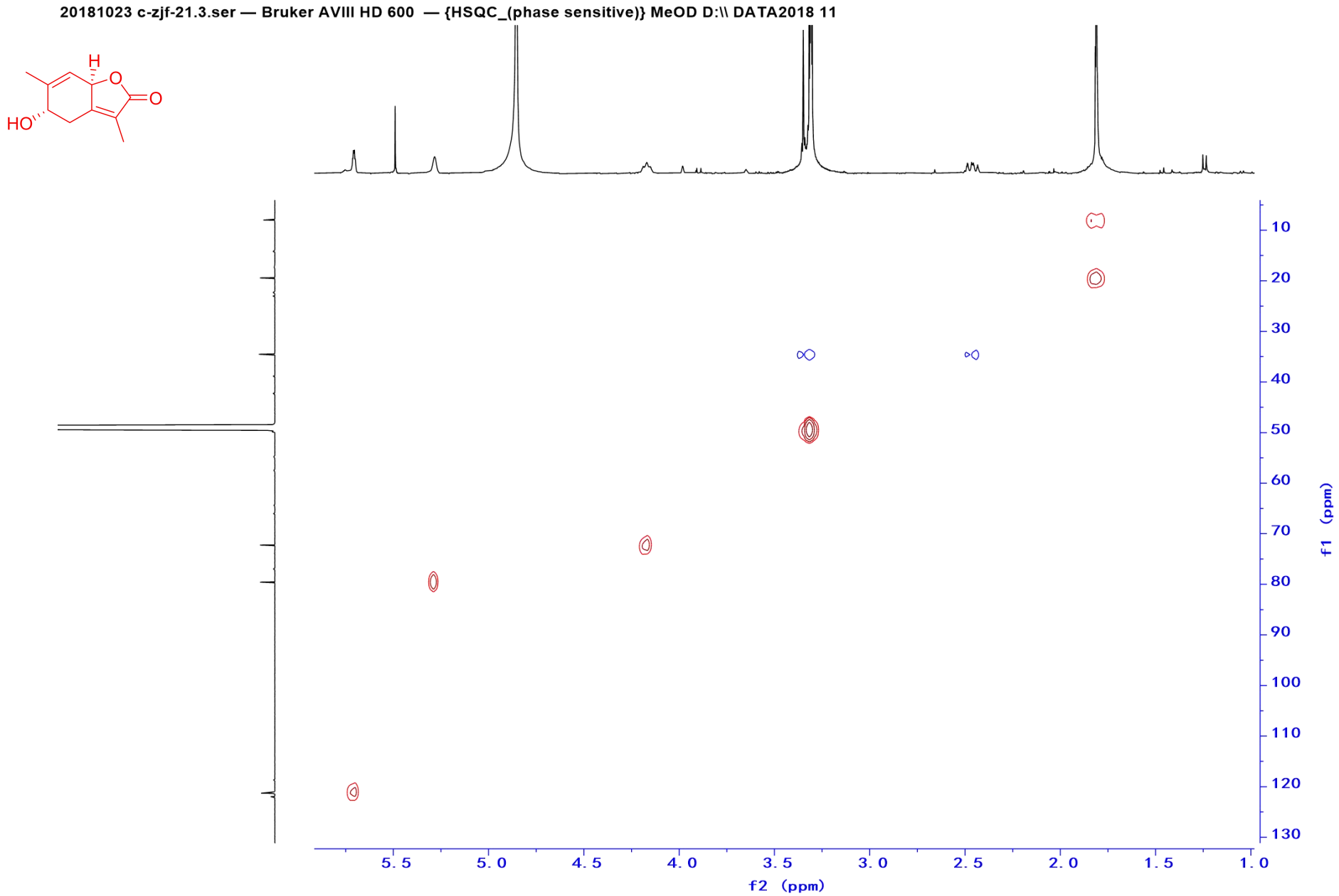


Figure S58. The HSQC Spectrum of Compound 7 in MeOH-d_4 (600MHz)

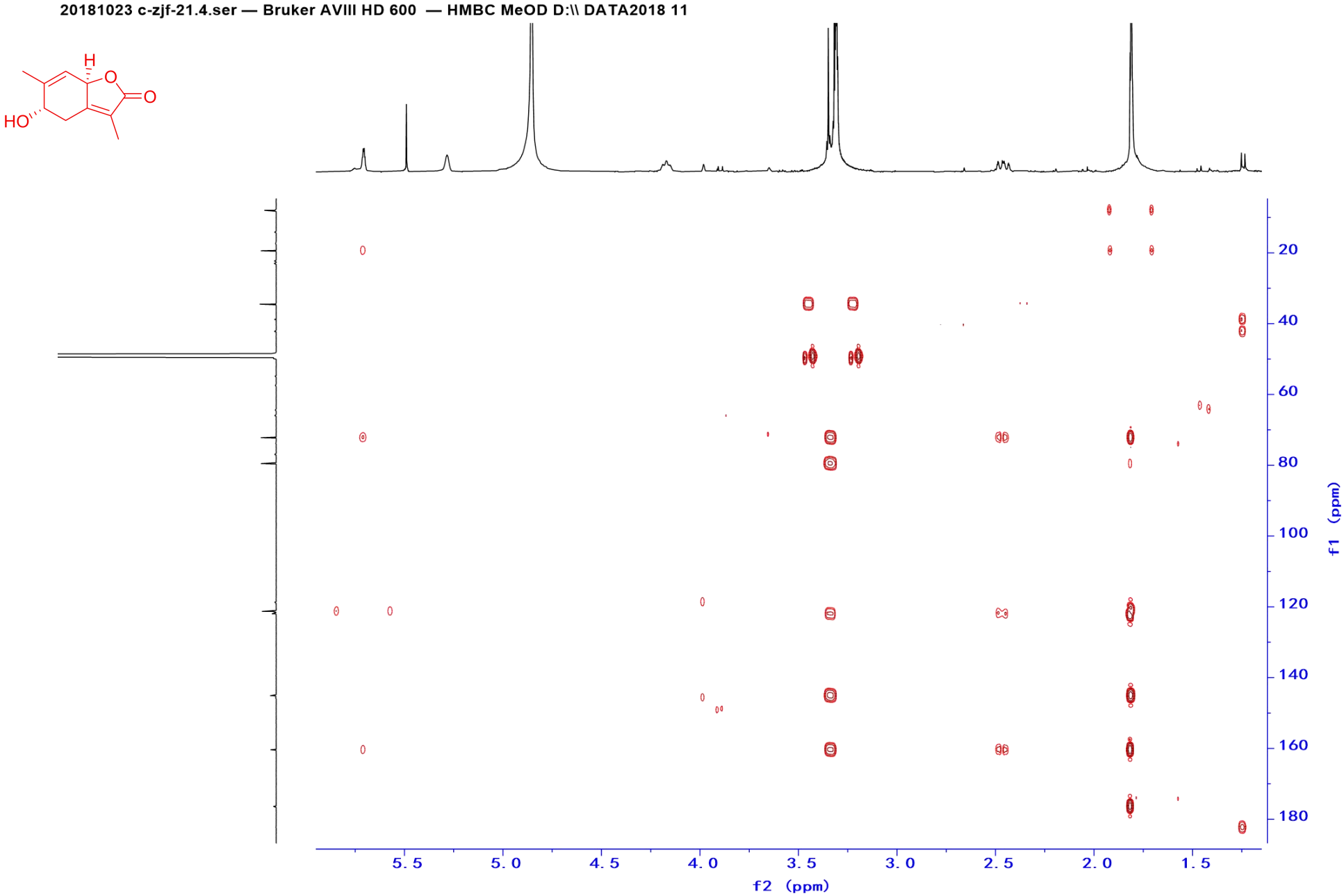


Figure S59. The HMBC Spectrum of Compound 7 in MeOH-d_4 (600MHz)

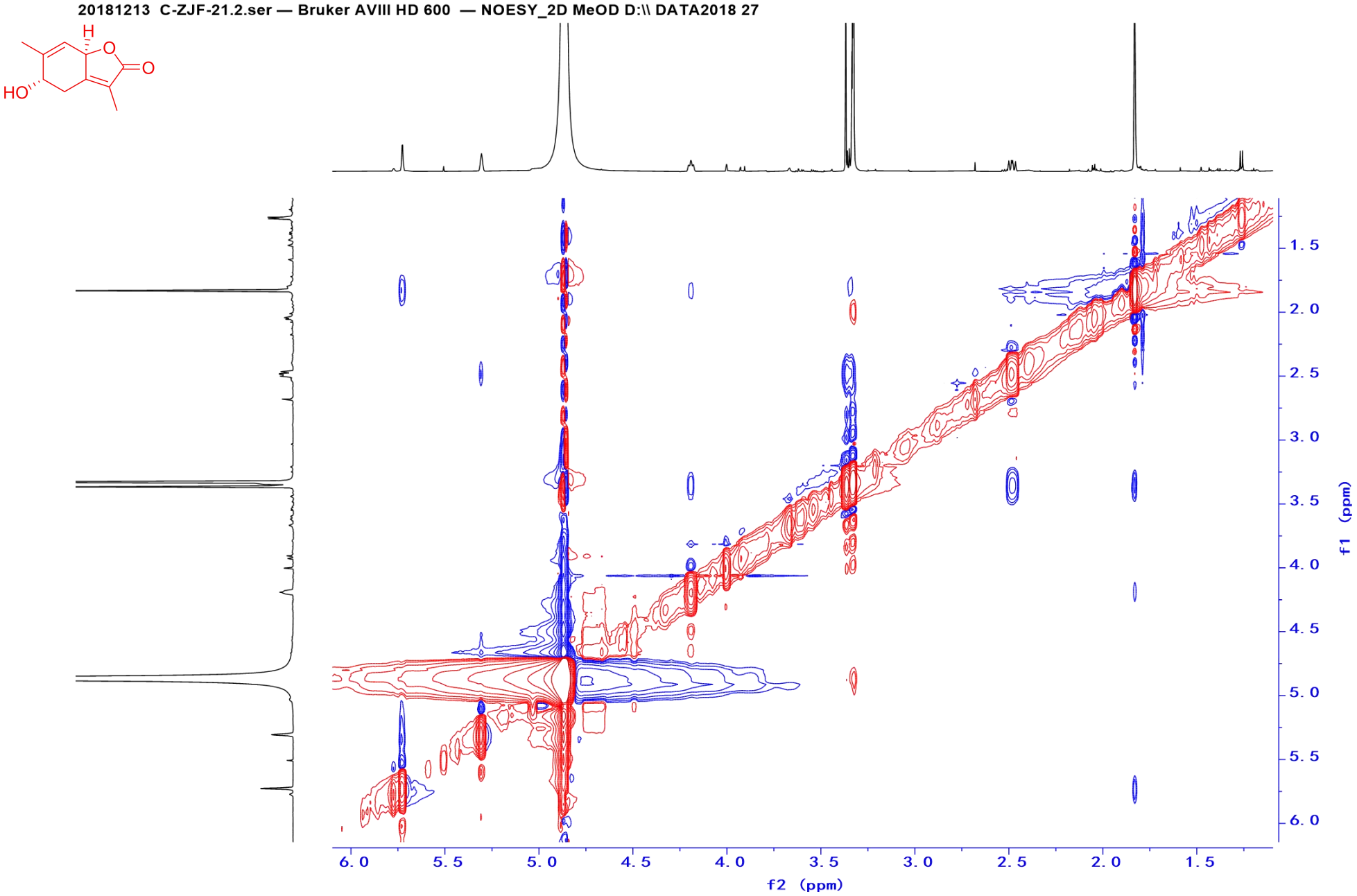


Figure S60. The NOESY Spectrum of Compound 7 in MeOH-d_4 (600MHz)

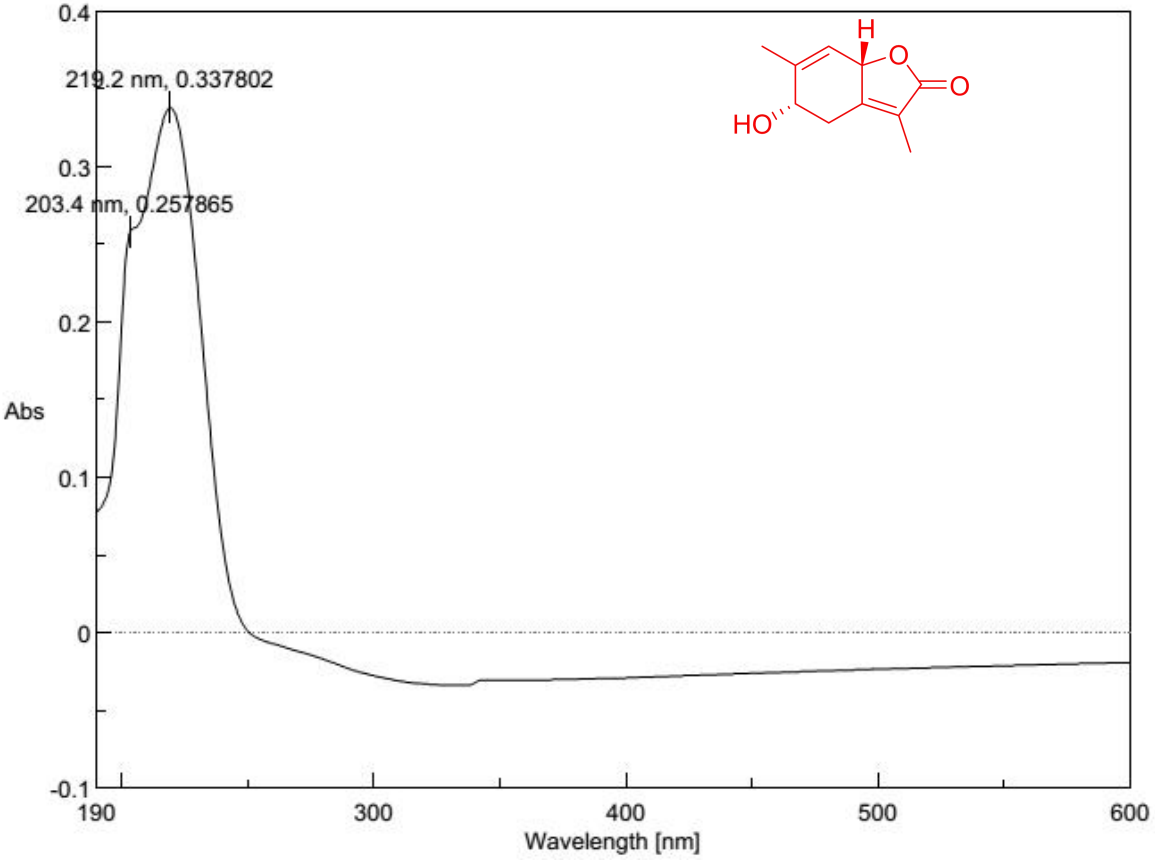


Figure S61. The UV Spectrum of Compound 8 in MeOH

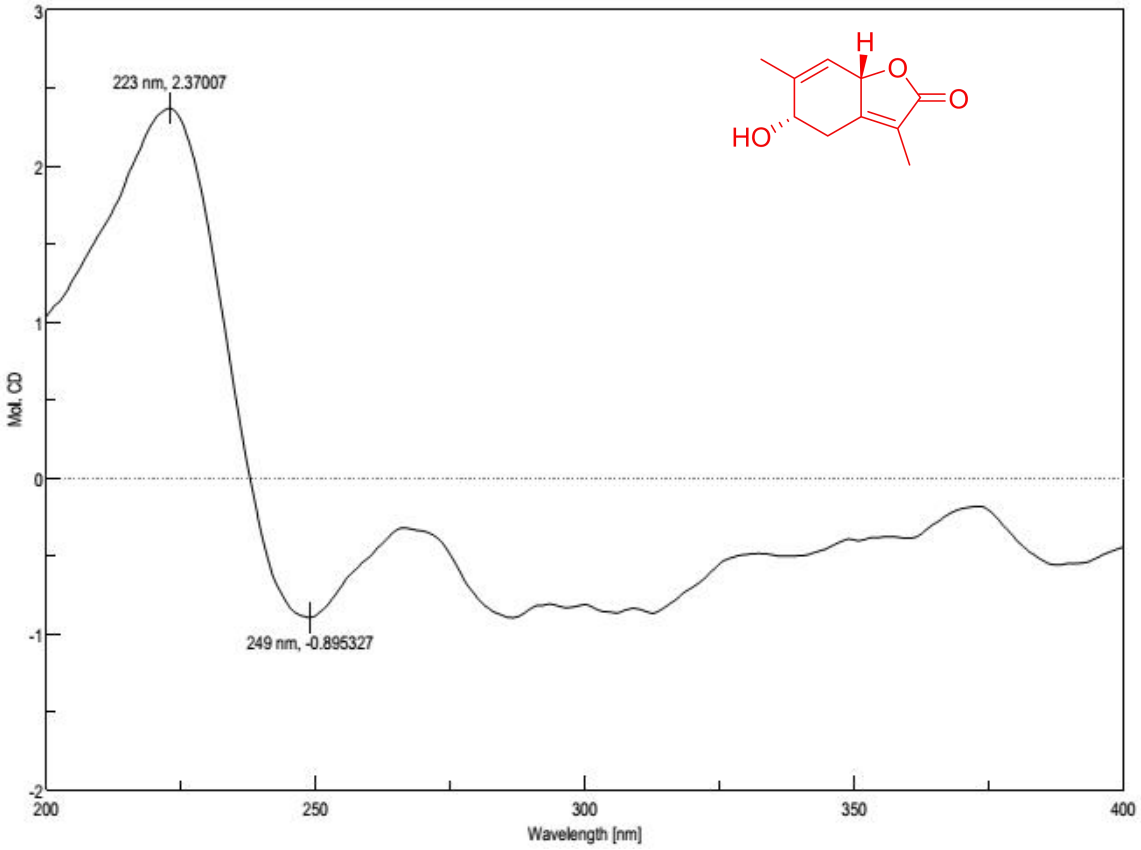
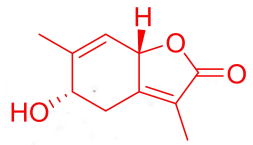


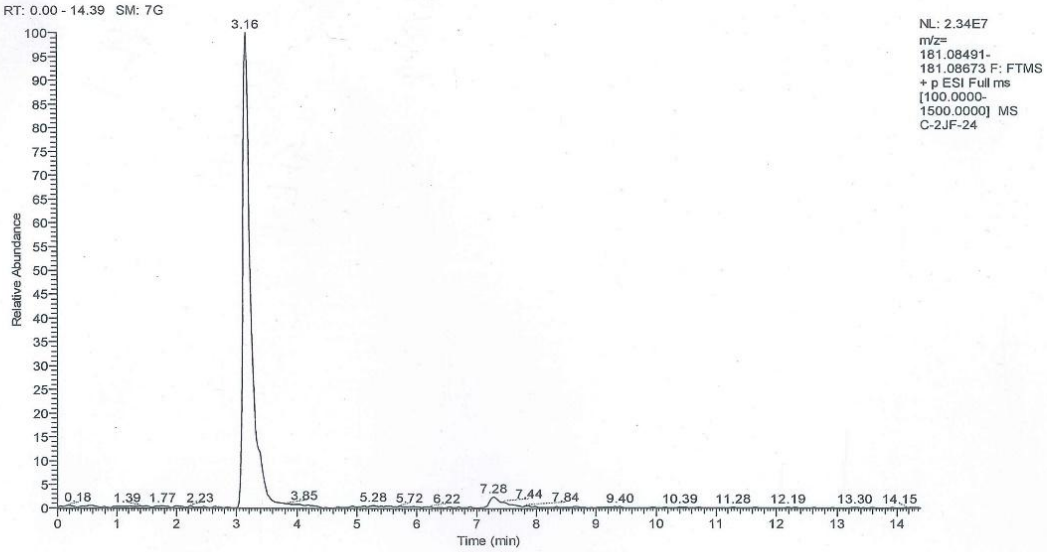
Figure S62. The CD spectrum of Compound 8 in MeOH

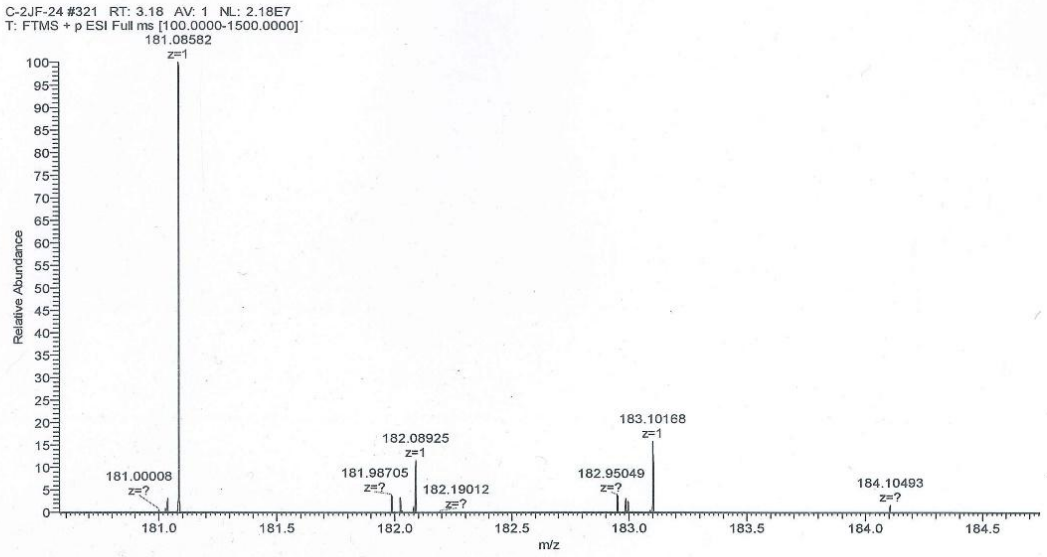


Thermo Qexactive Focus Report

compound NO. : C-2JF-24

Method : LCMS(compound)-low





m/z	Theo. Mass	Delta (ppm)	RDB equiv.	Composition	
181.08582	181.08592	-0.56	4.5	C10 H13 O3	M+H

Figure S63. The HR-mass Spectrum of Compound 8 in MeOH

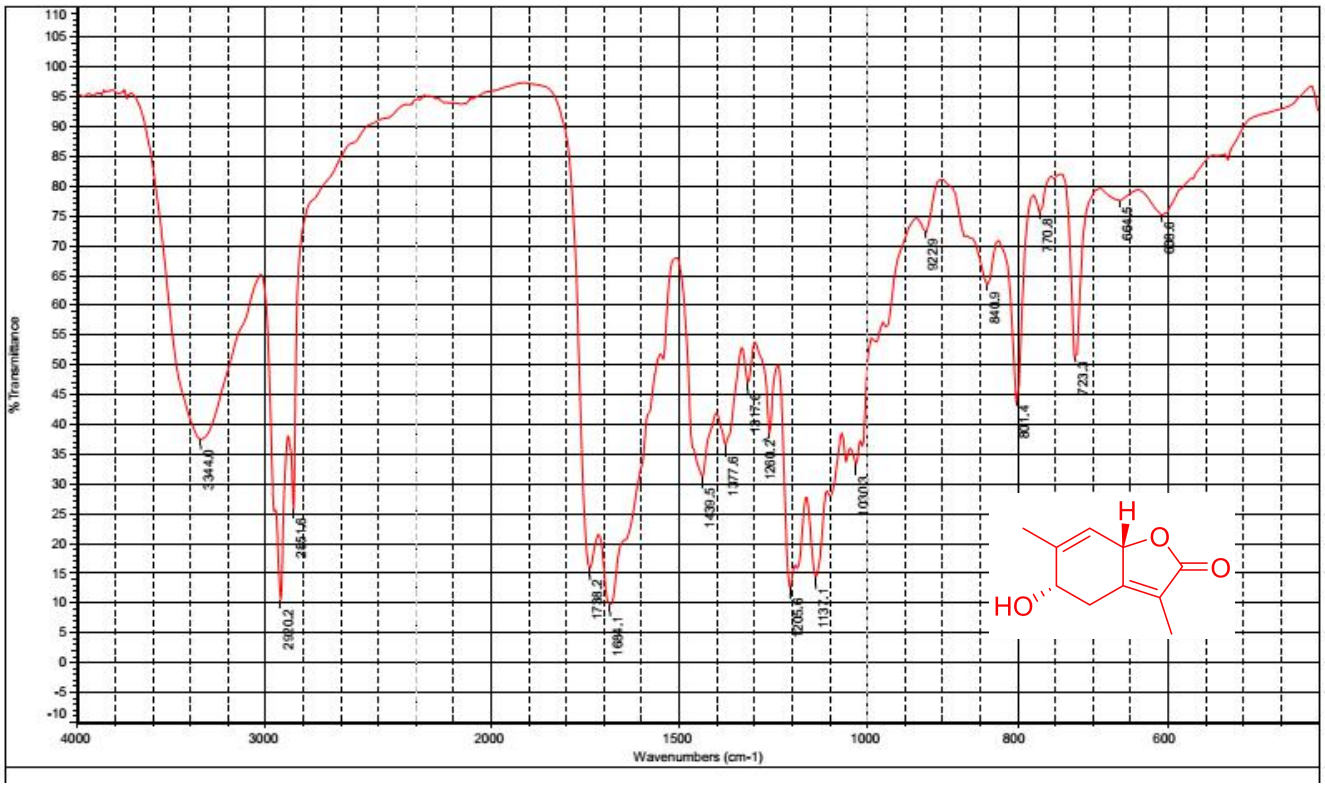


Figure S64. The IR Spectrum of Compound 8

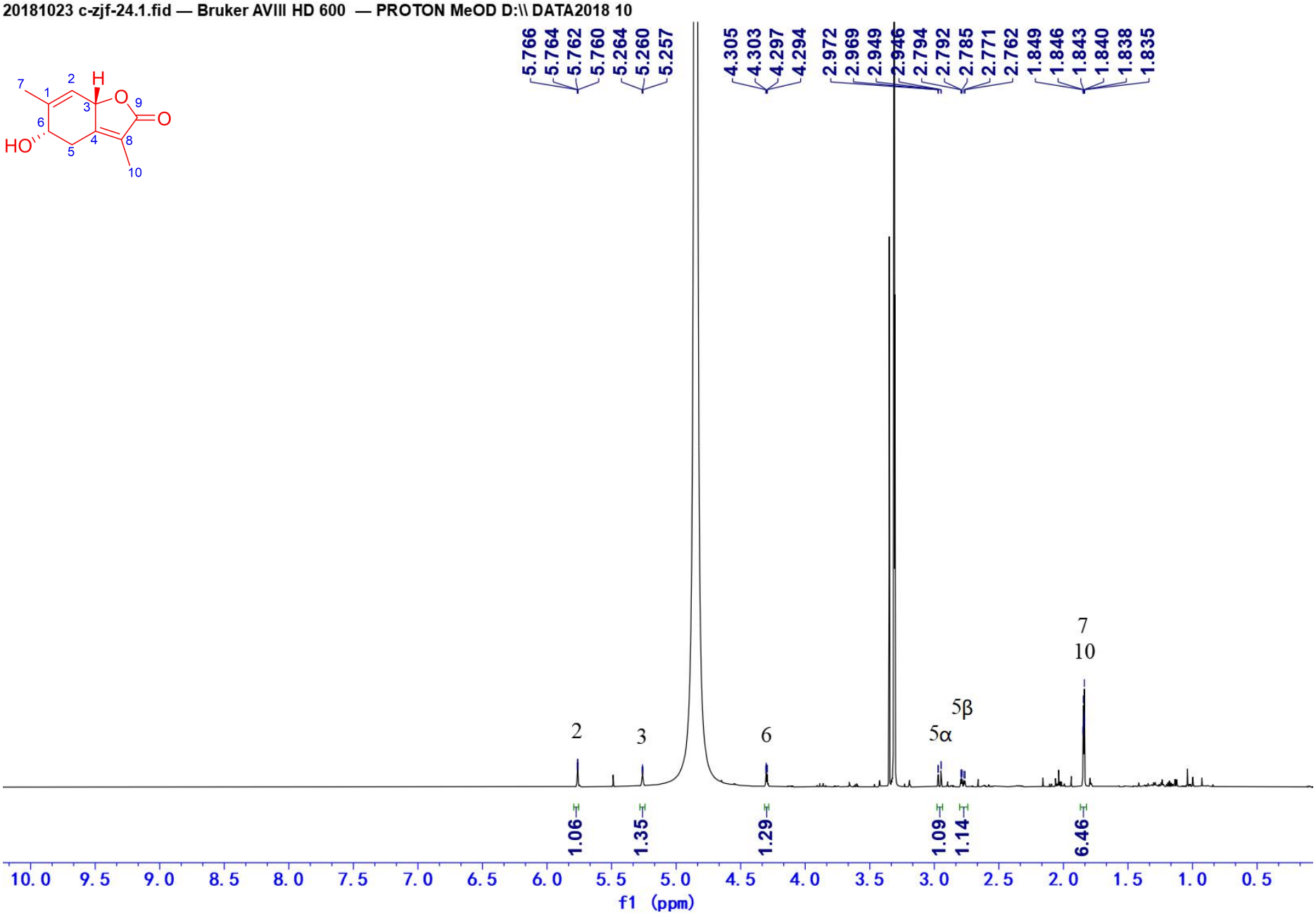


Figure S65. The ^{1}H NMR Spectrum of Compound 8 in MeOH-d_4 (600MHz)

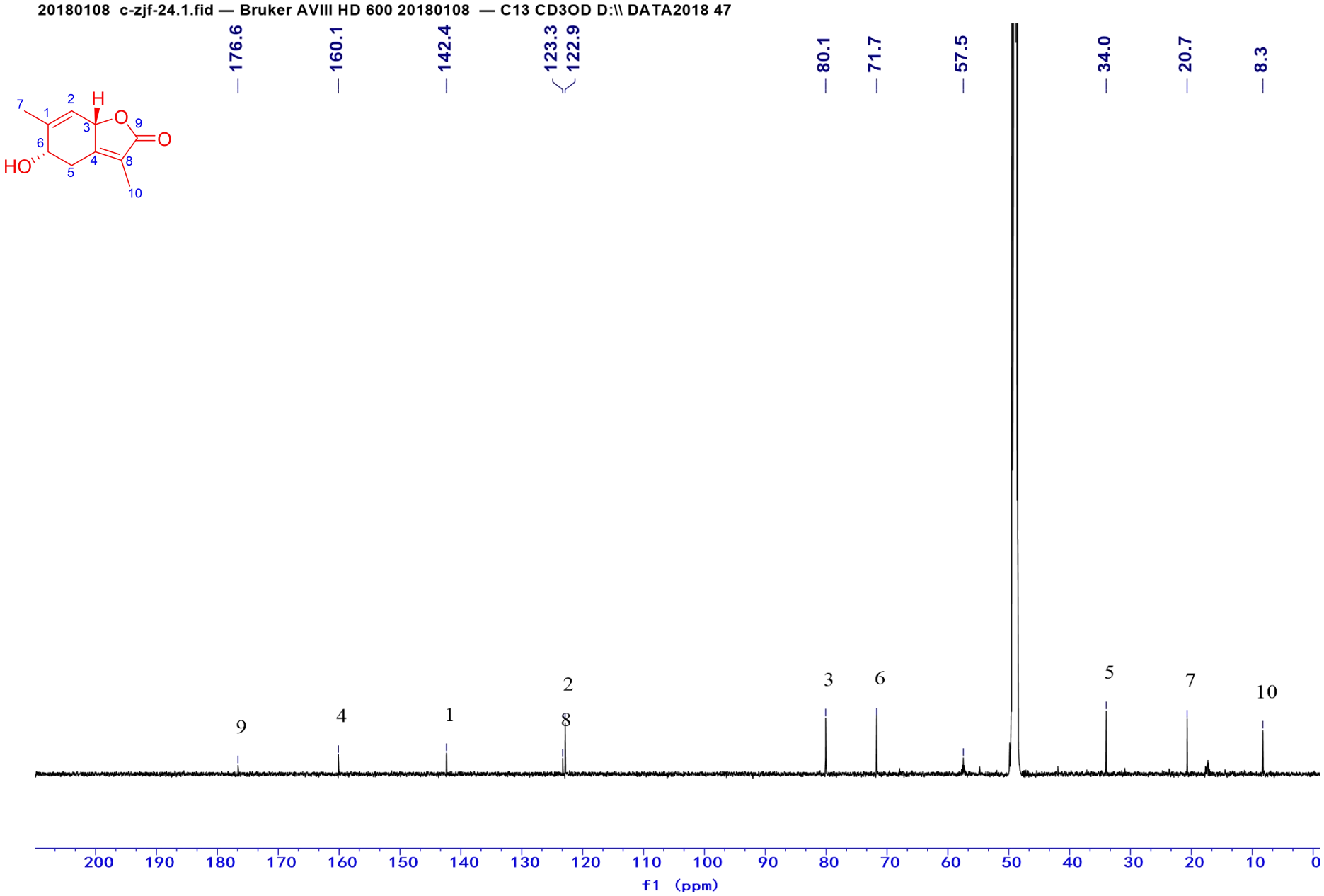


Figure S66. The ^{13}C NMR Spectrum of Compound 8 in MeOH-d_4 (150MHz)

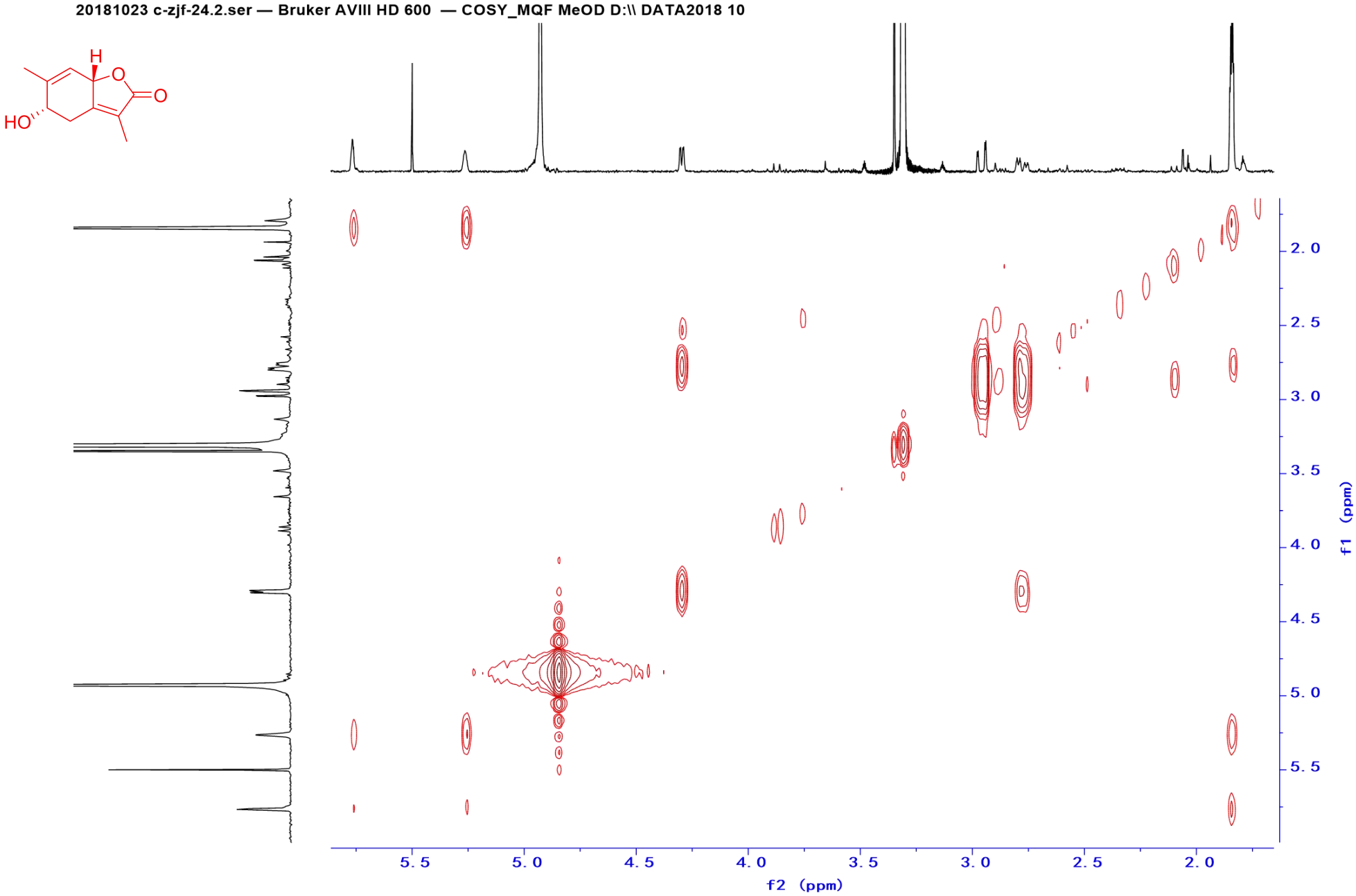


Figure S67. The ^{1}H-^{1}H COSY Spectrum of Compound 8 in MeOH-d_4 (600MHz)

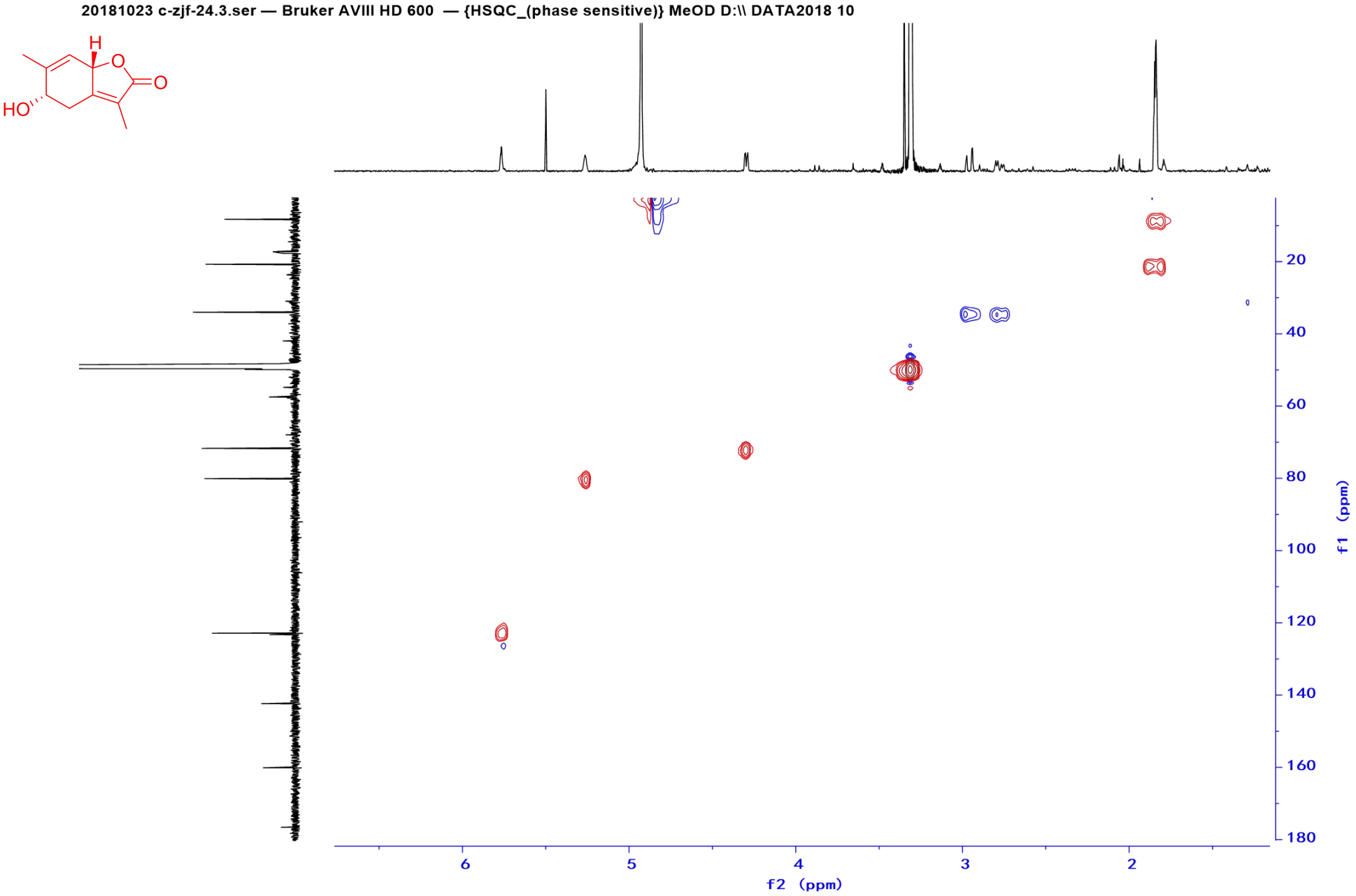


Figure S68. The HSQC Spectrum of Compound 8 in MeOH-d_4 (600MHz)

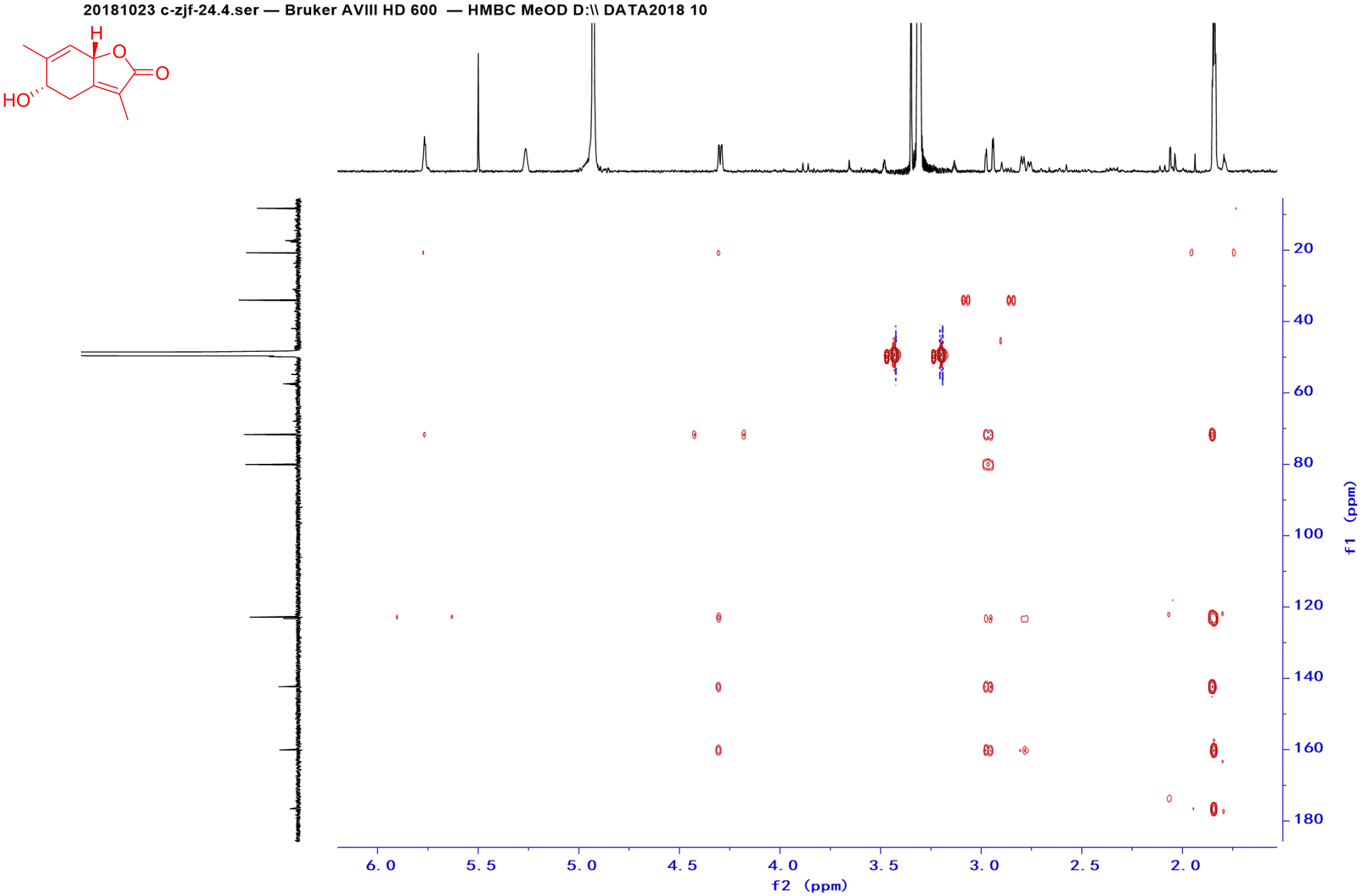


Figure S69. The HMBC Spectrum of Compound 8 in MeOH-d_4 (600MHz)

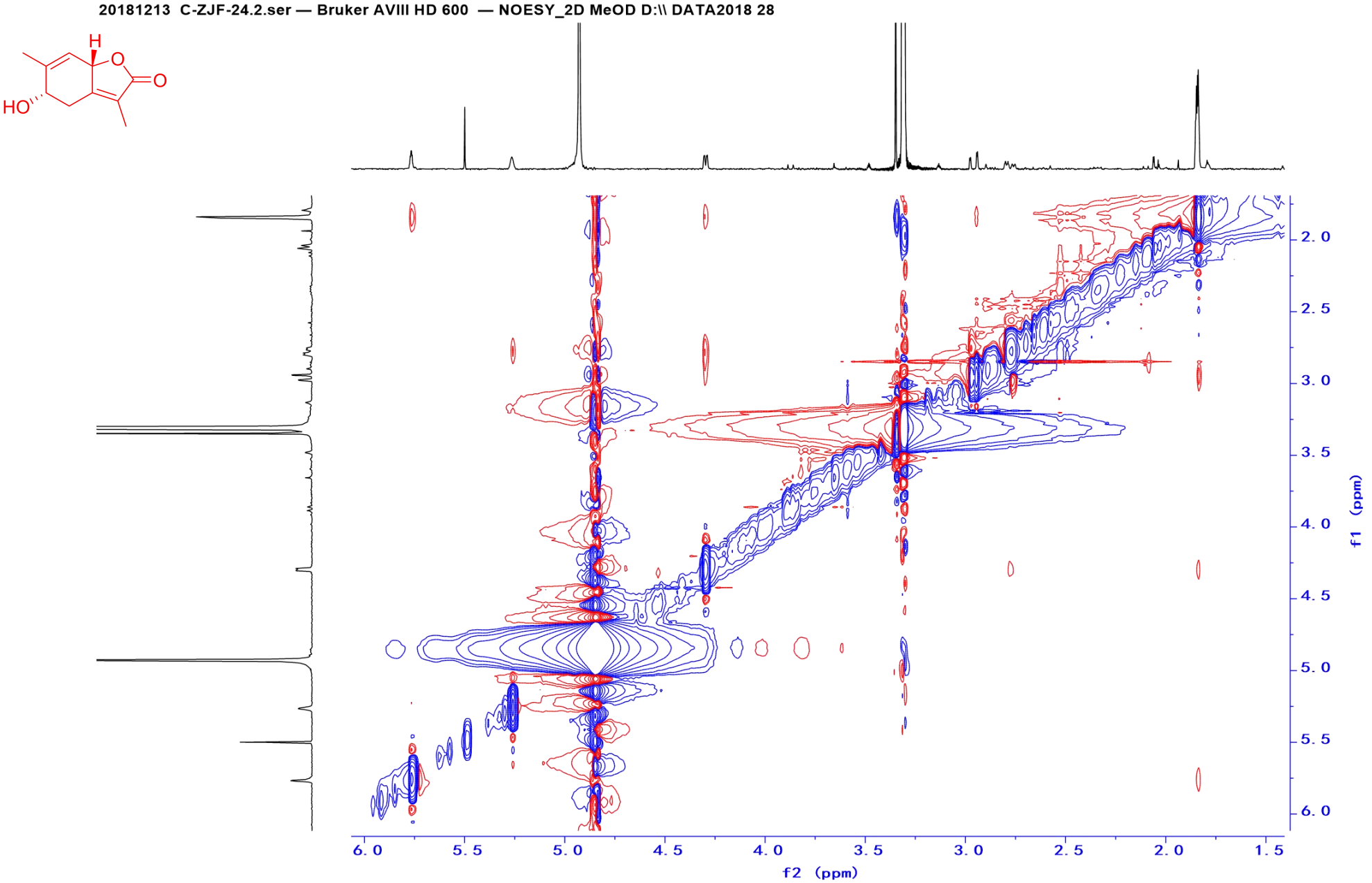


Figure S70. The NOESY Spectrum of Compound 8 in MeOH-d_4 (600MHz)

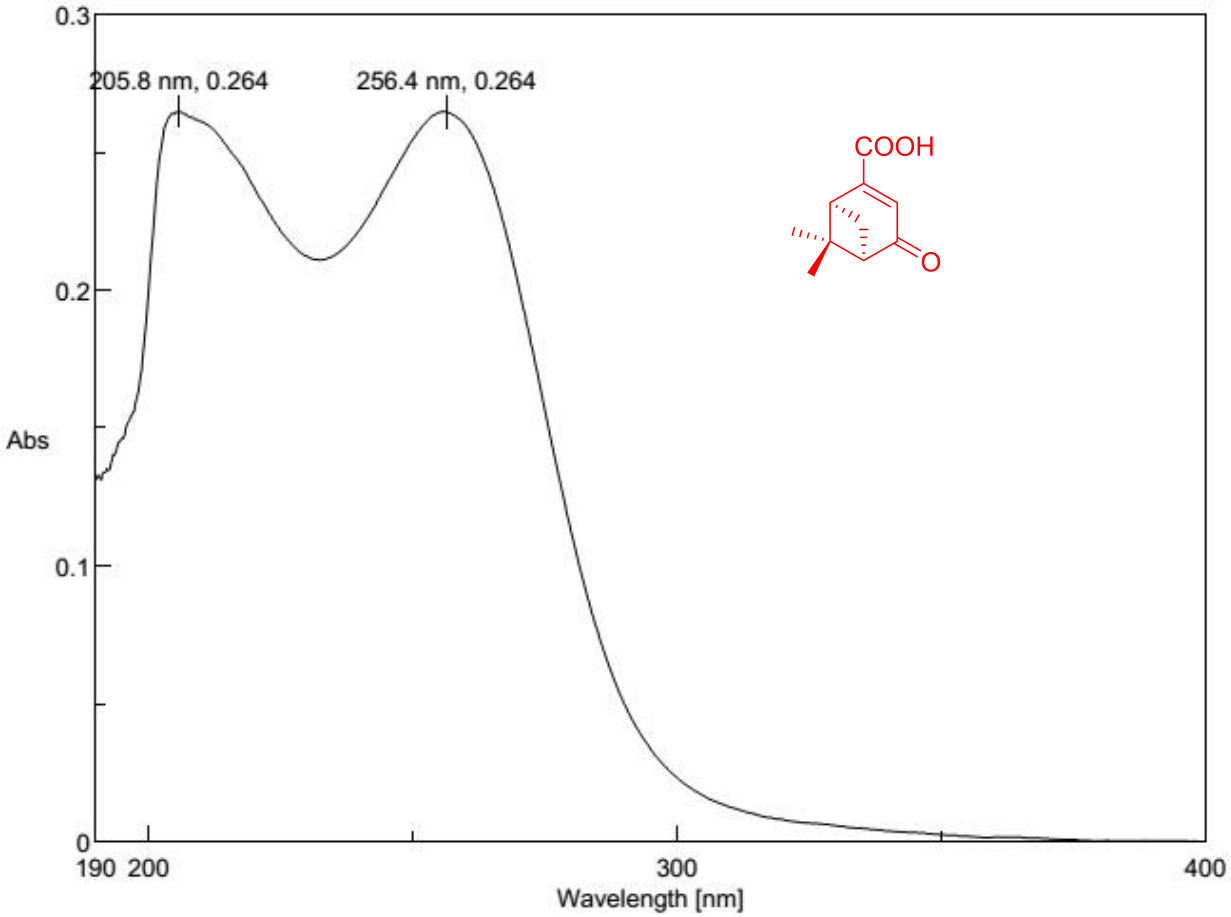


Figure S71. The UV Spectrum of Compound 9 in MeOH

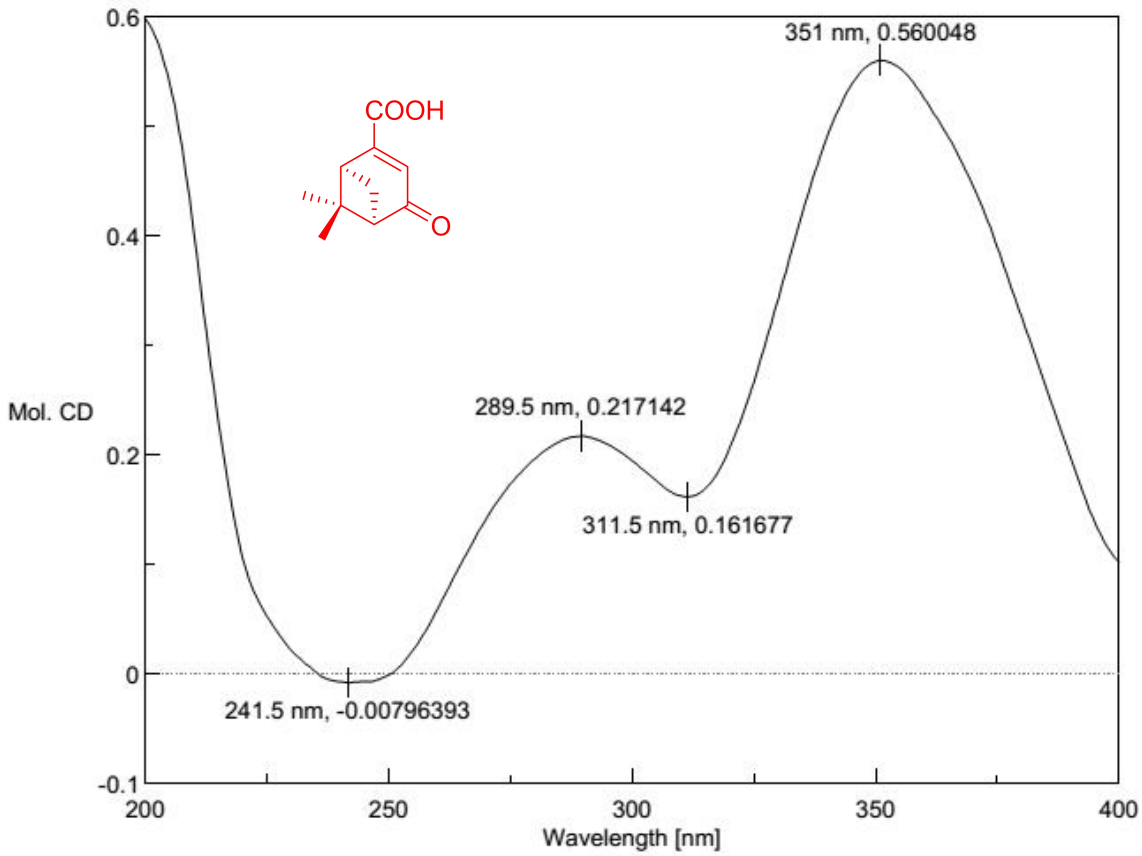
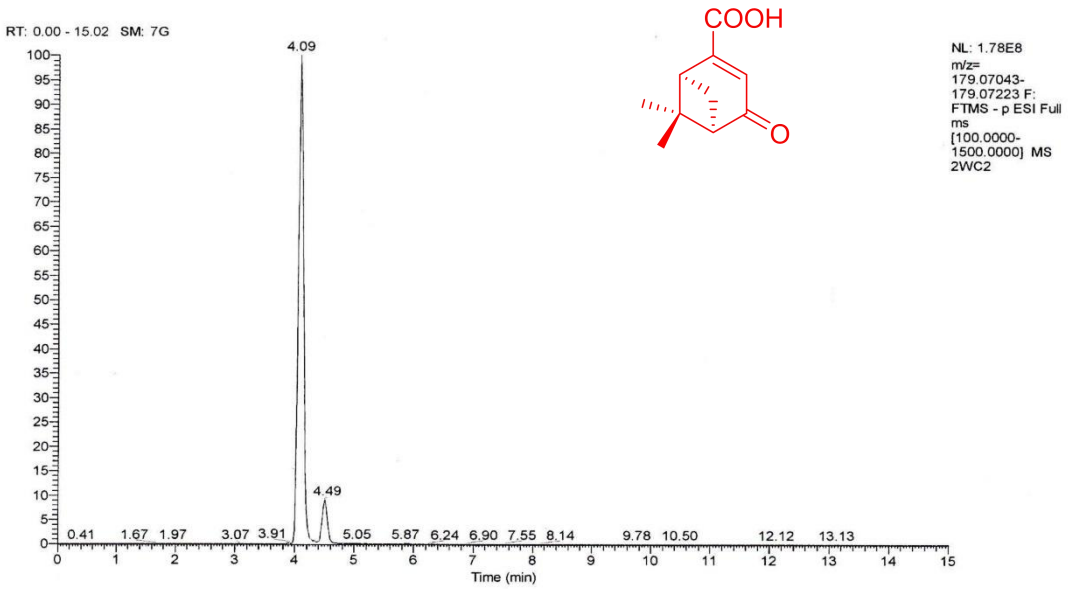


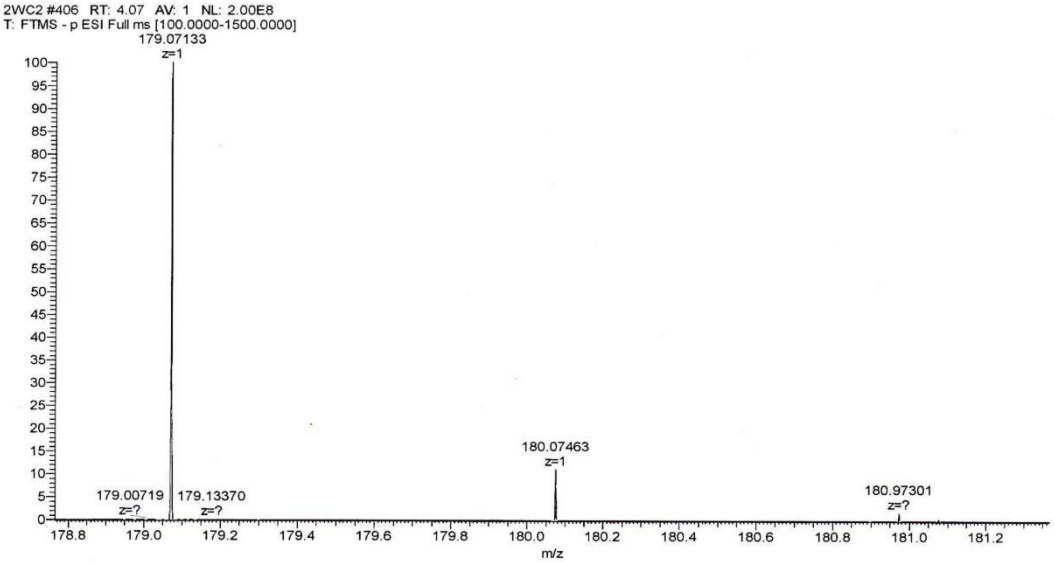
Figure S72. The CD Spectrum of Compound 9 in MeOH

Thermo Qexactive Focus Report

compound NO. : 2WC2

Method : LCMS(compound)-low





m/z	Theo. Mass	Delta (ppm)	RDB equiv.	Composition	
179.07133	179.07137	-0.21	5.5	C10 H11 O3	M-H

Figure S73. The HR-mass Spectrum of Compound 9 in MeOH

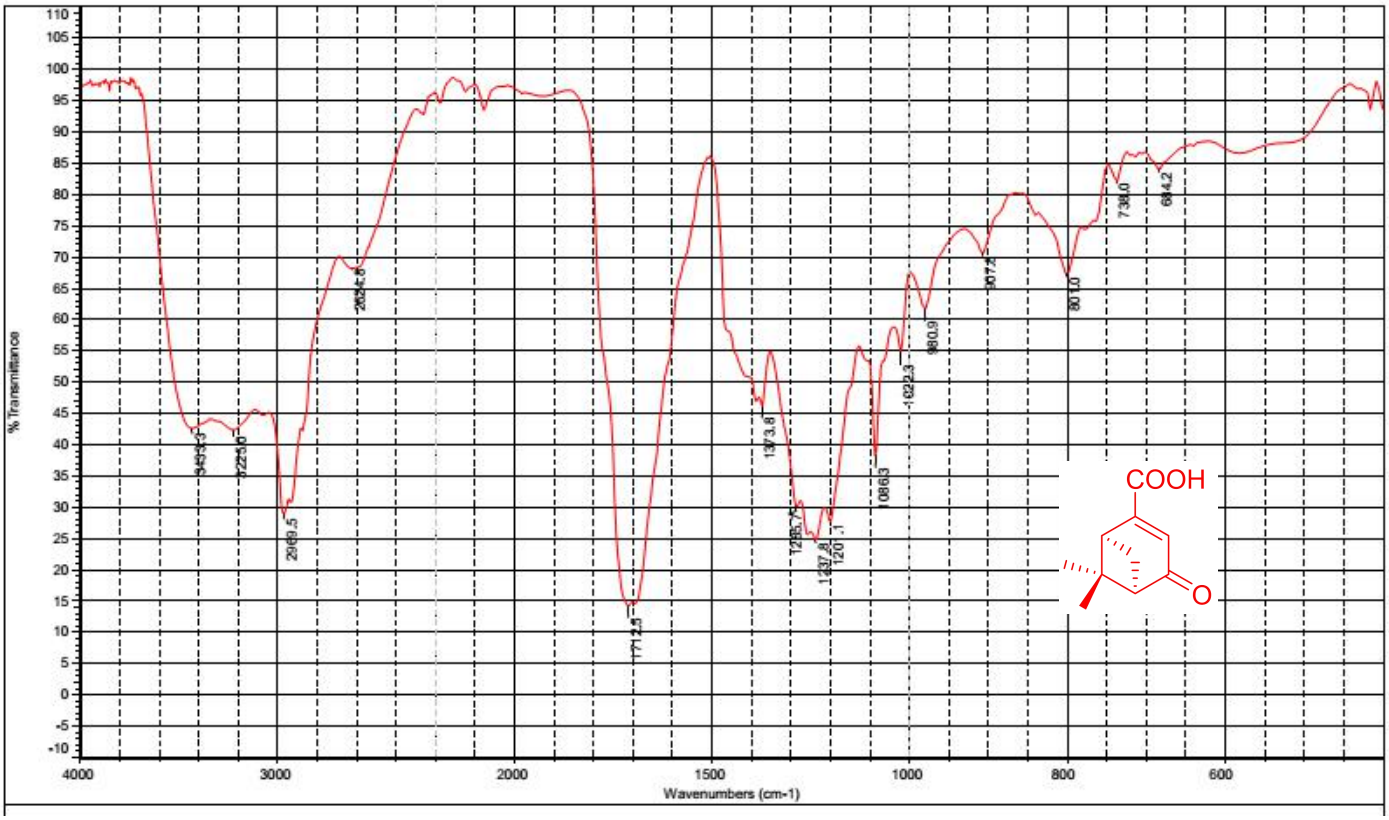


Figure S74. The IR Spectrum of Compound 9

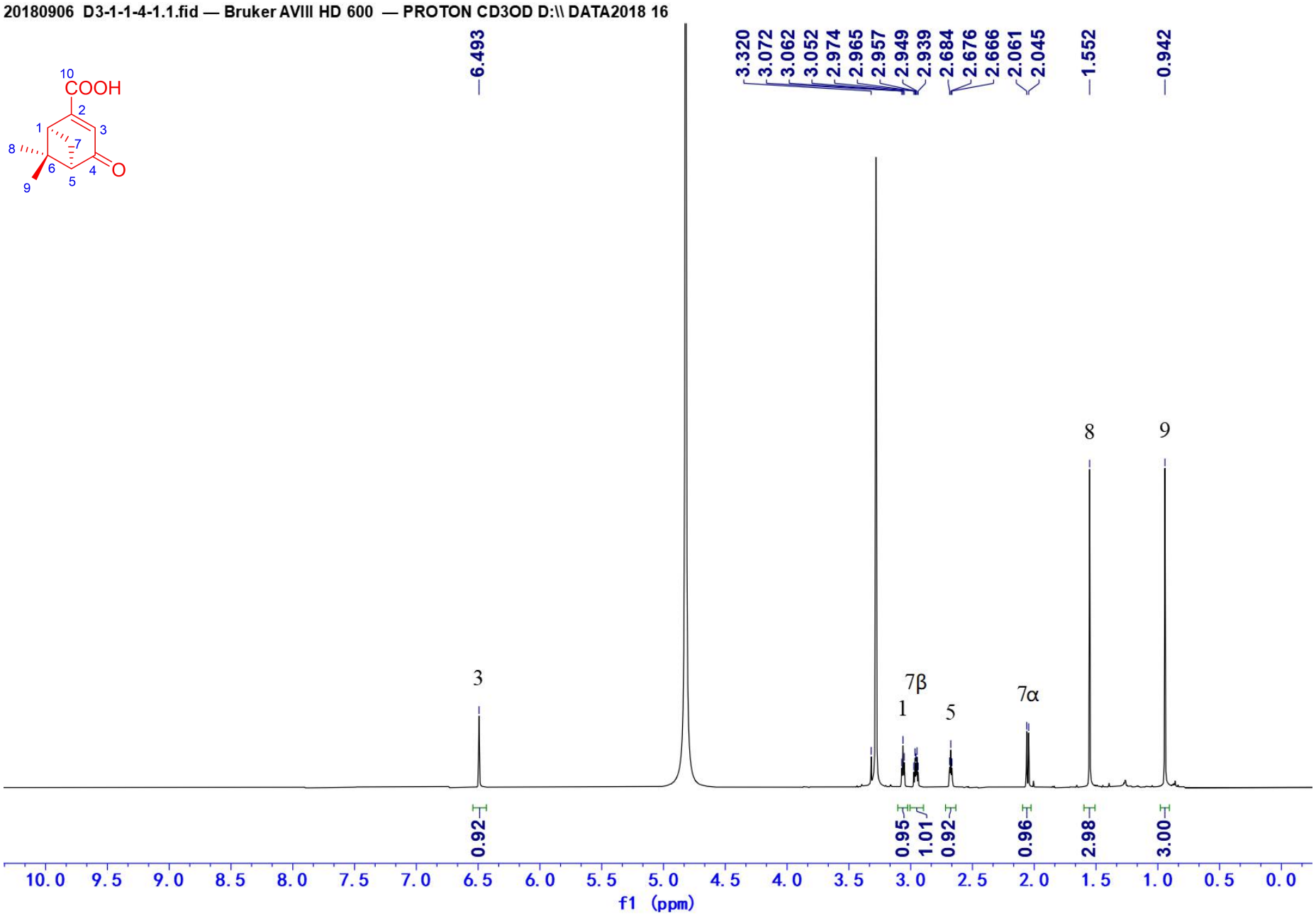


Figure S75. The ^{1}H NMR Spectrum of Compound 9 in MeOH-d_4 (600MHz)

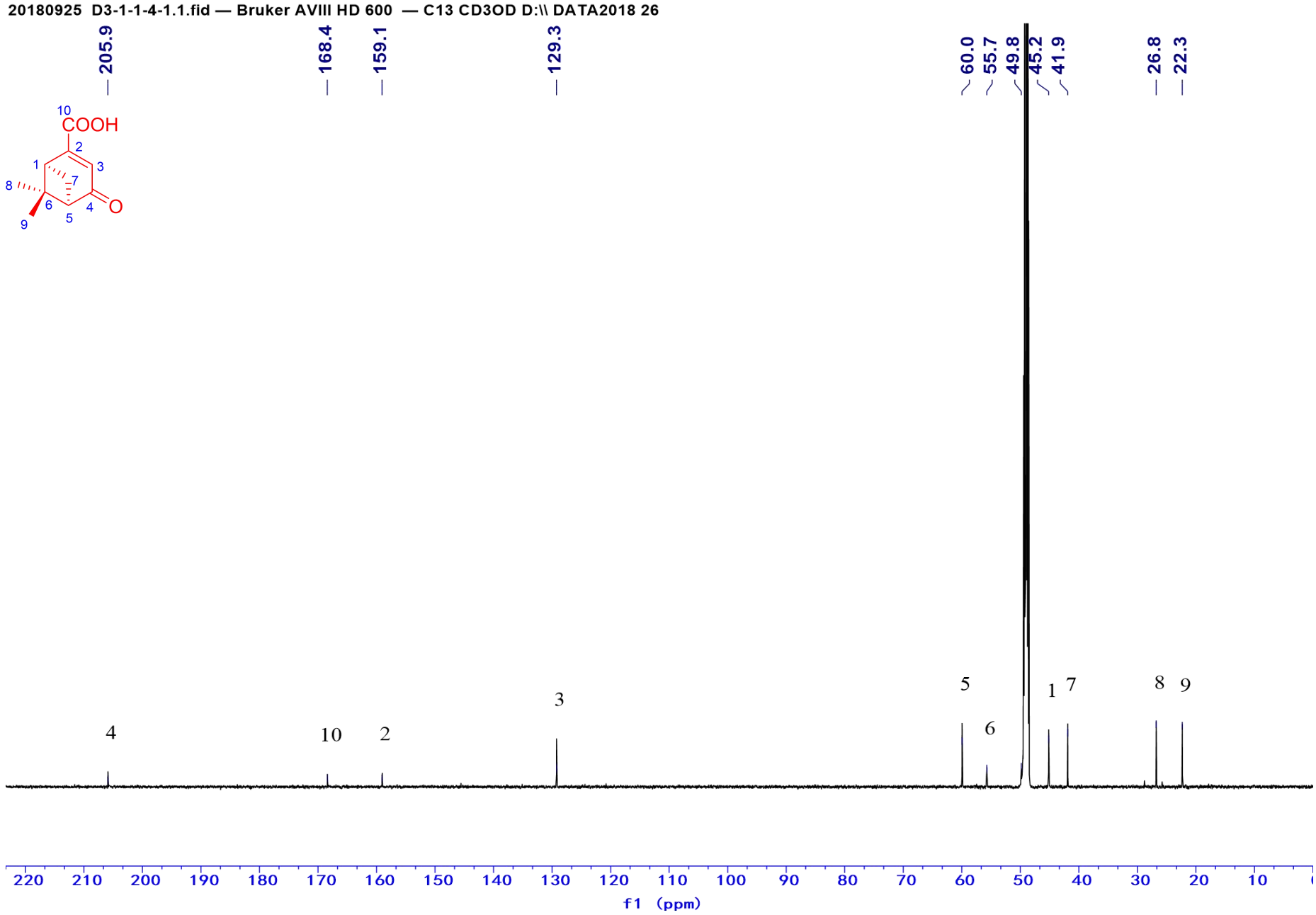


Figure S76. The ^{13}C NMR Spectrum of Compound 9 in MeOH-d_4 (150MHz)

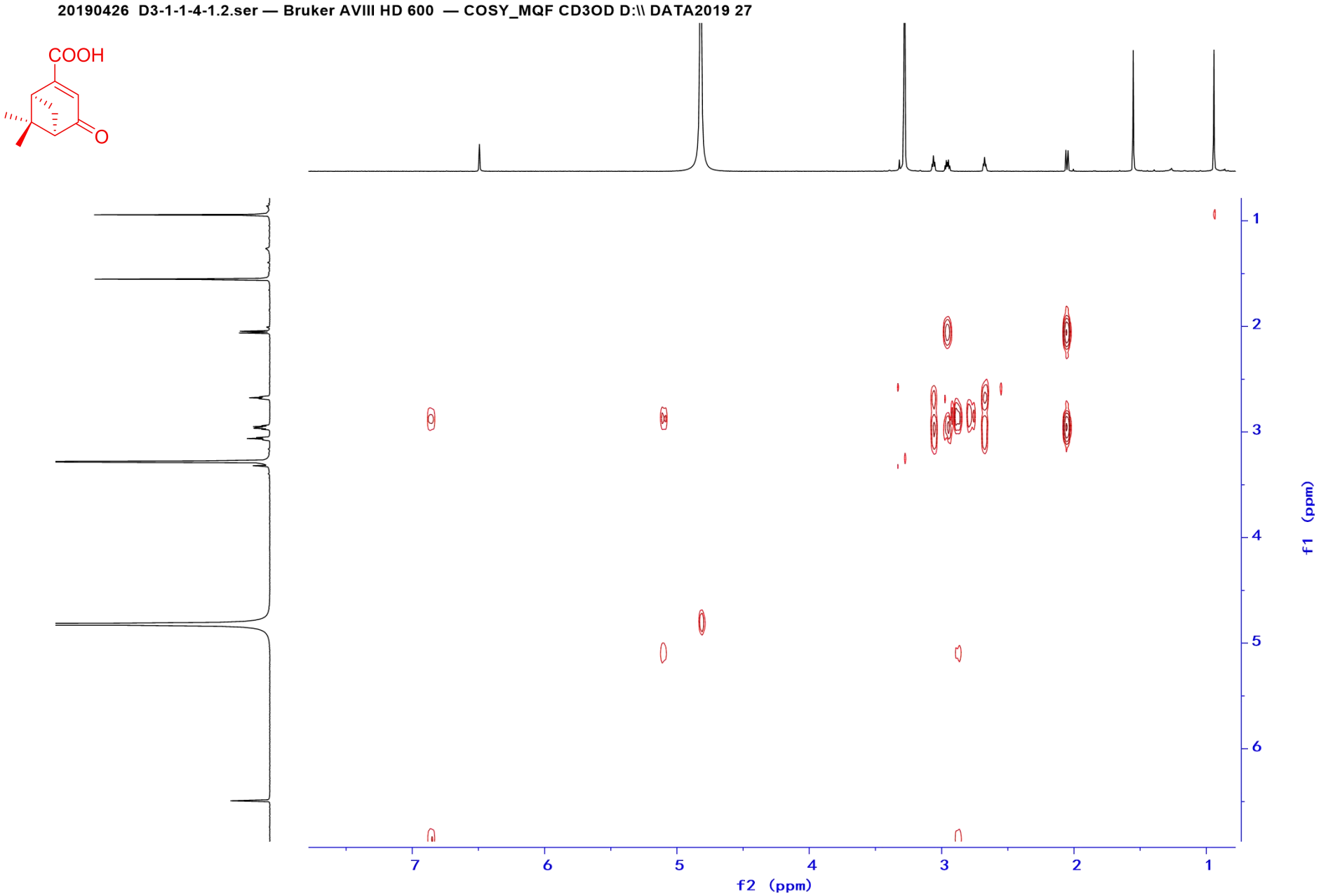


Figure S77. The ^{1}H-^{1}H COSY Spectrum of Compound 9 in MeOH-d_4 (600MHz)

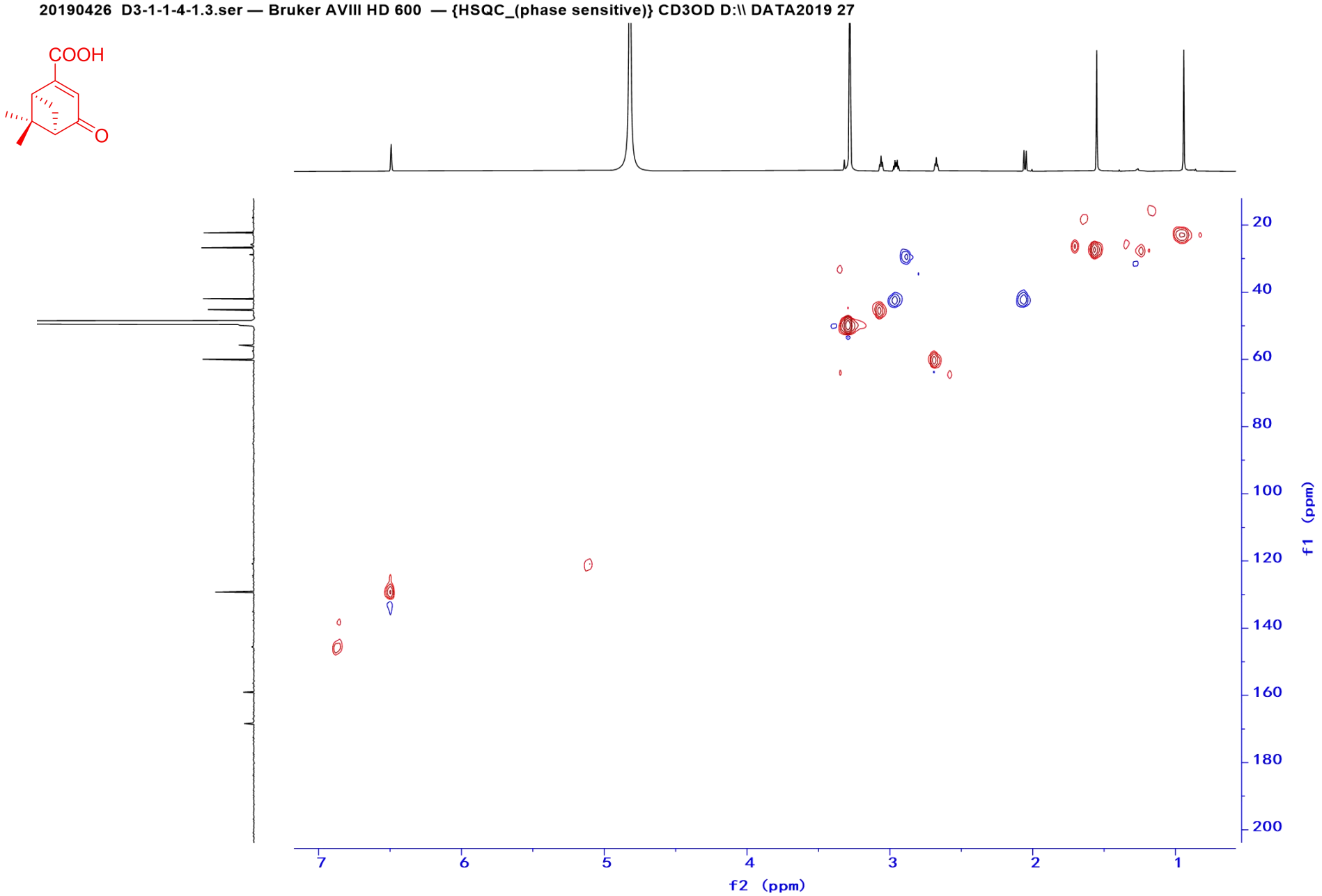


Figure S78. The HSQC Spectrum of Compound 9 in MeOH-d_4 (600MHz)

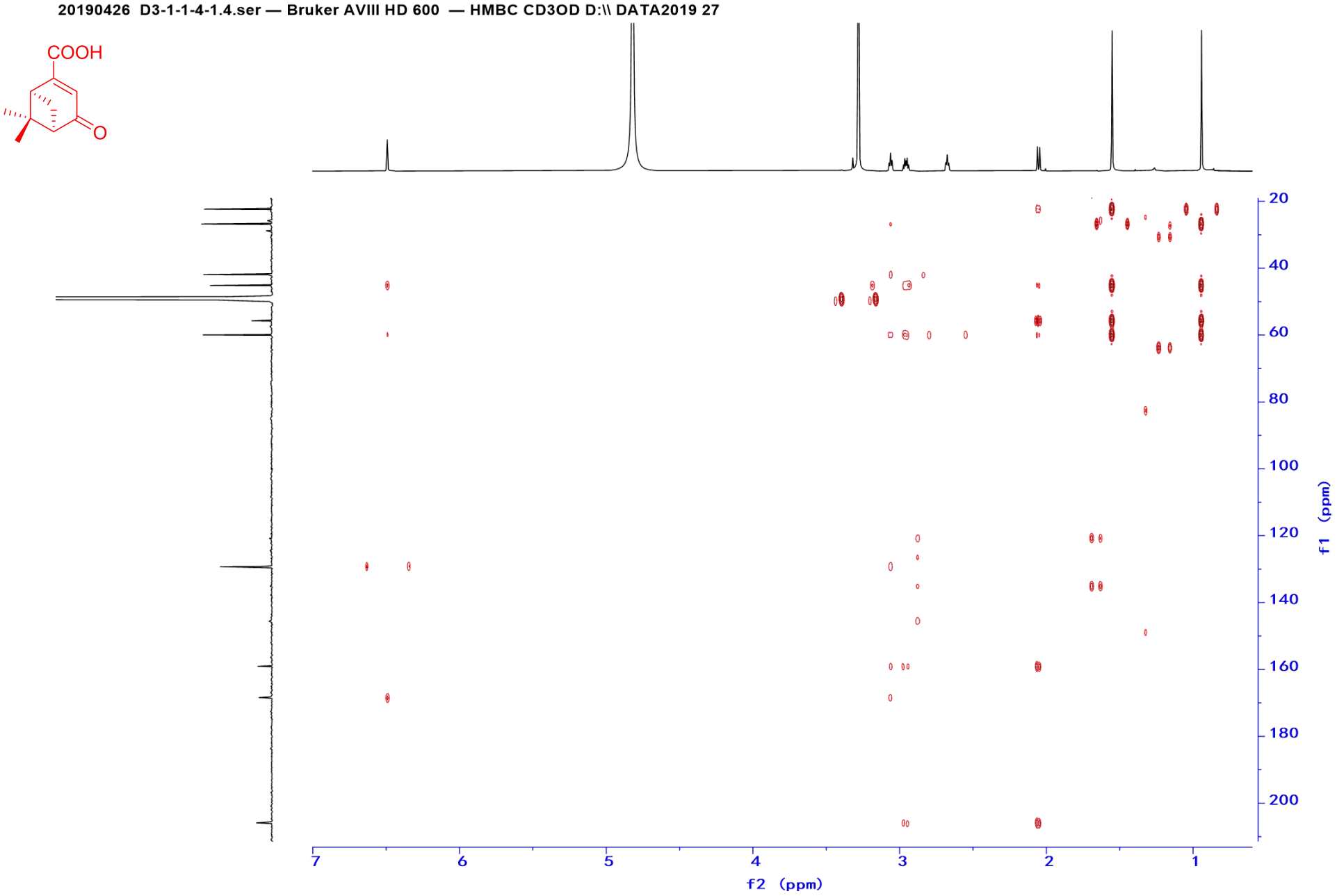


Figure S79. The HMBC Spectrum of Compound 9 in MeOH-d_4 (600MHz)

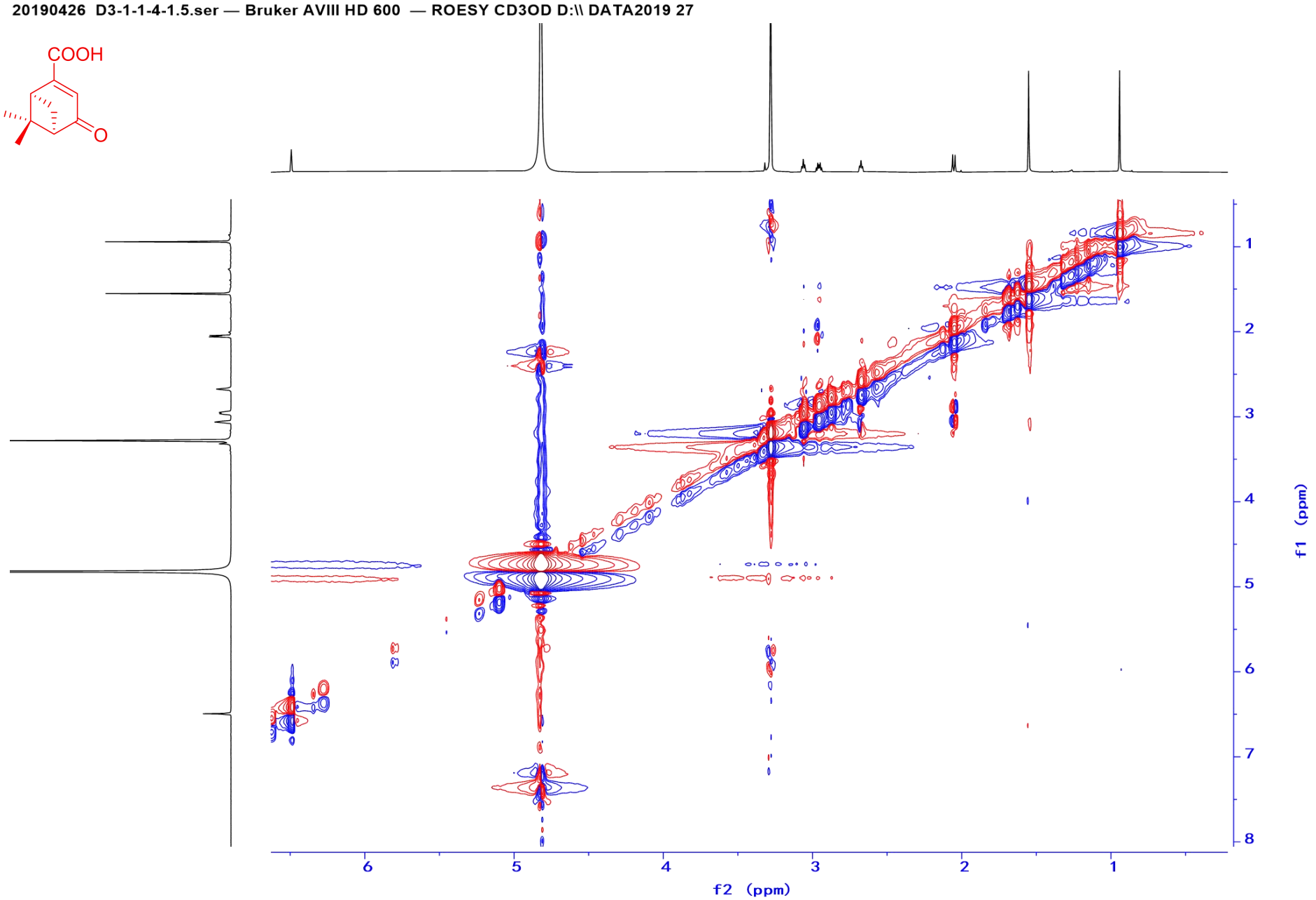


Figure S80. The NOESY Spectrum of Compound 9 in MeOH-d_4 (600MHz)

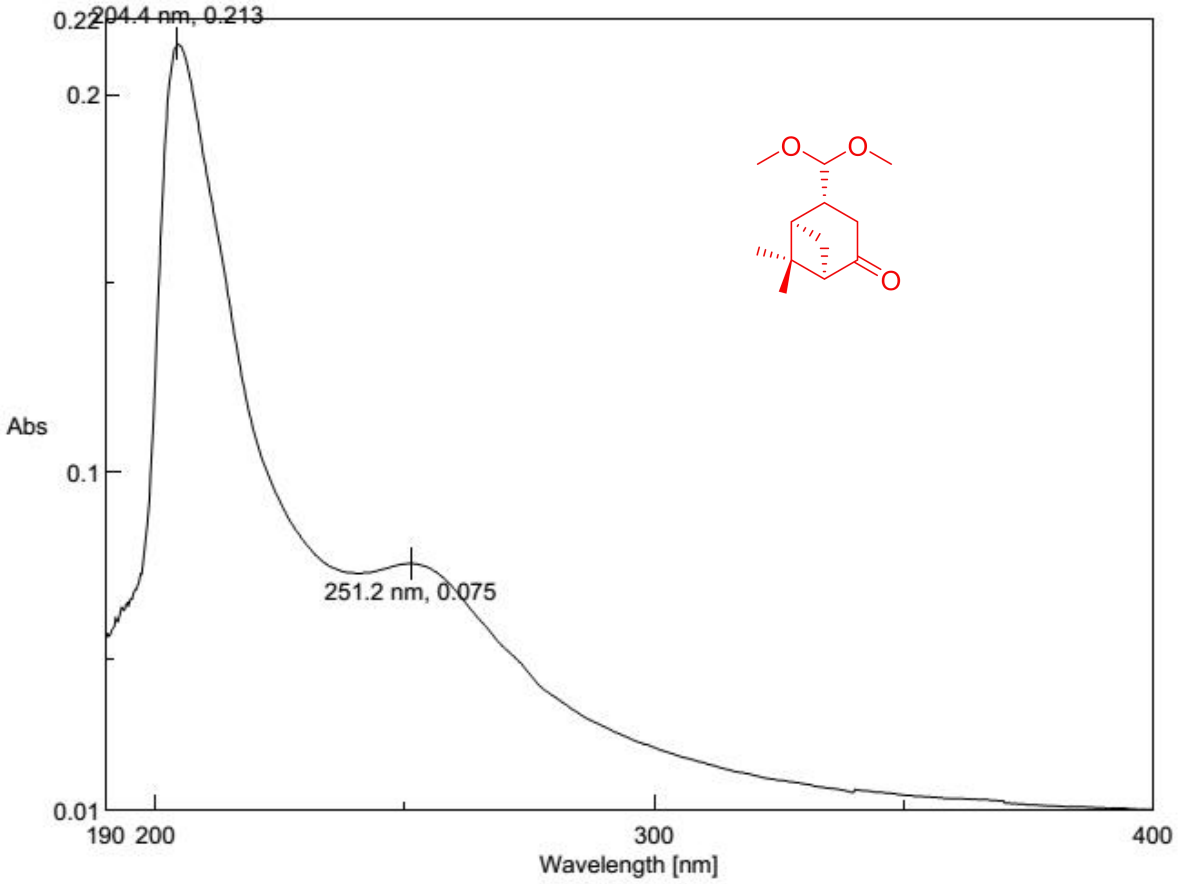


Figure S81. The UV Spectrum of Compound 10 in MeOH

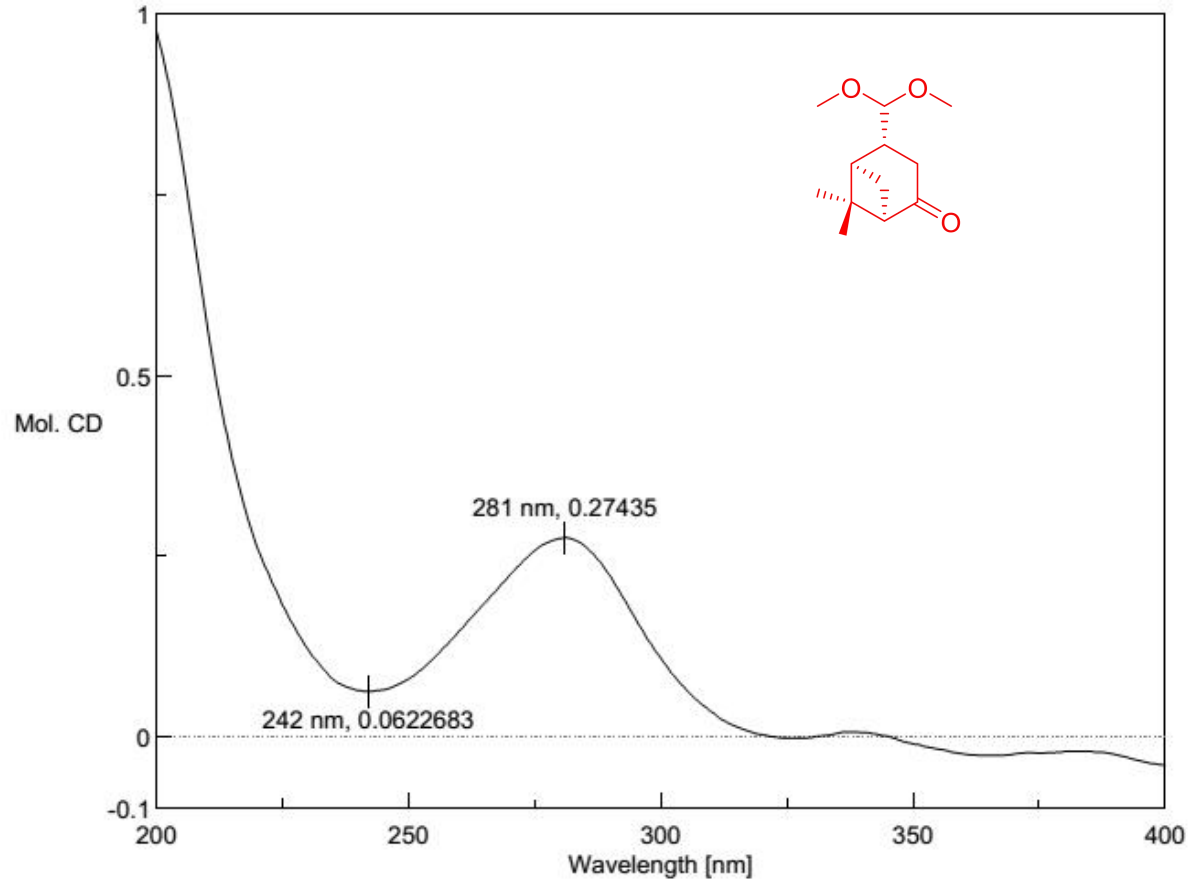
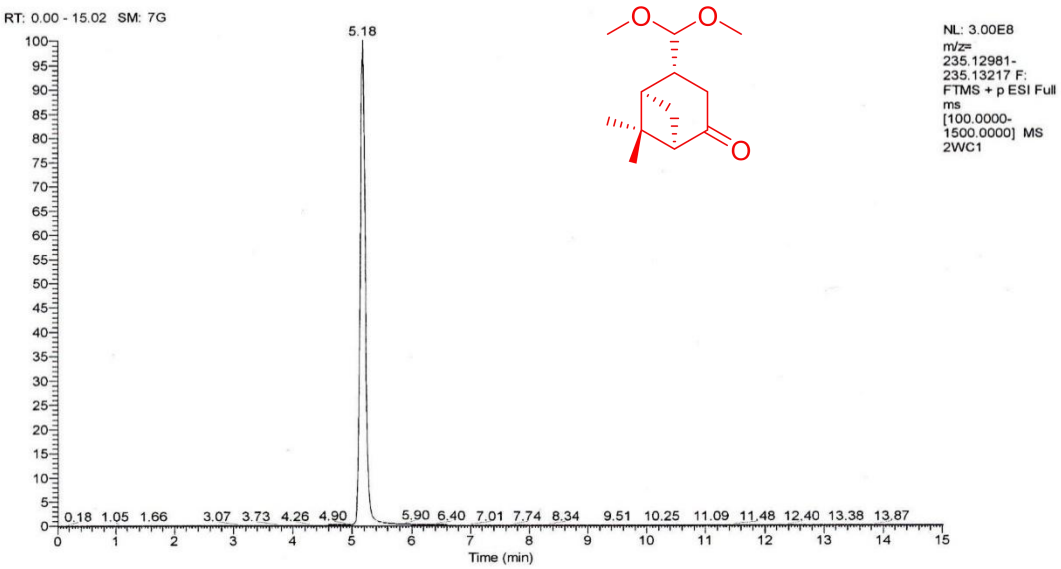


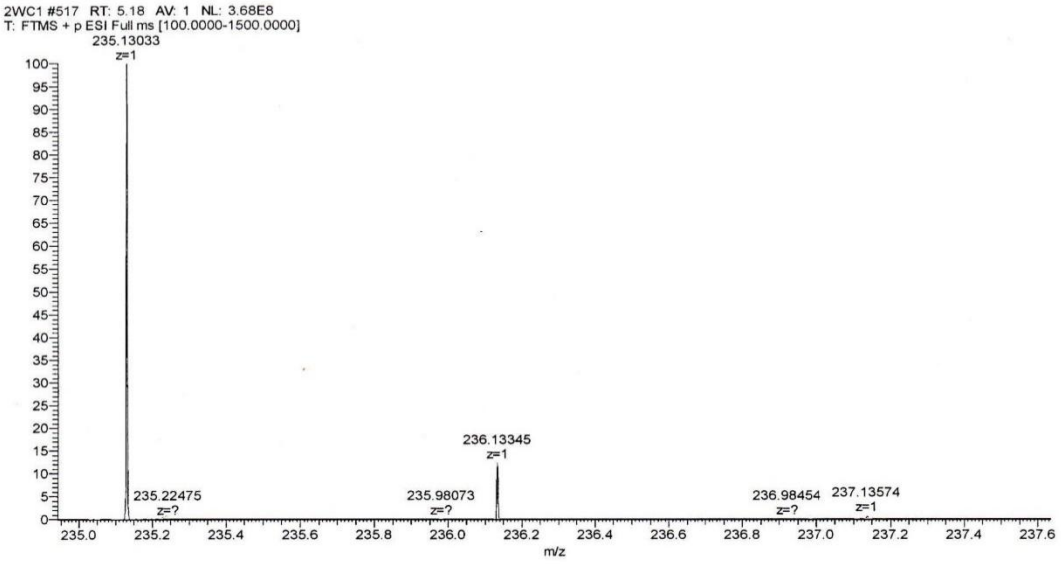
Figure S82. The CD spectrum of Compound 10 in MeOH

Thermo Qexactive Focus Report

compound NO. : 2WC1

Method : LCMS(compound)-low





m/z	Theo. Mass	Delta (ppm)	RDB equiv.	Composition	
235.13033	235.13047	-0.58	2.5	C12 H20 O3 Na	M+Na

Figure S83. The HR-mass Spectrum of Compound 10 in MeOH

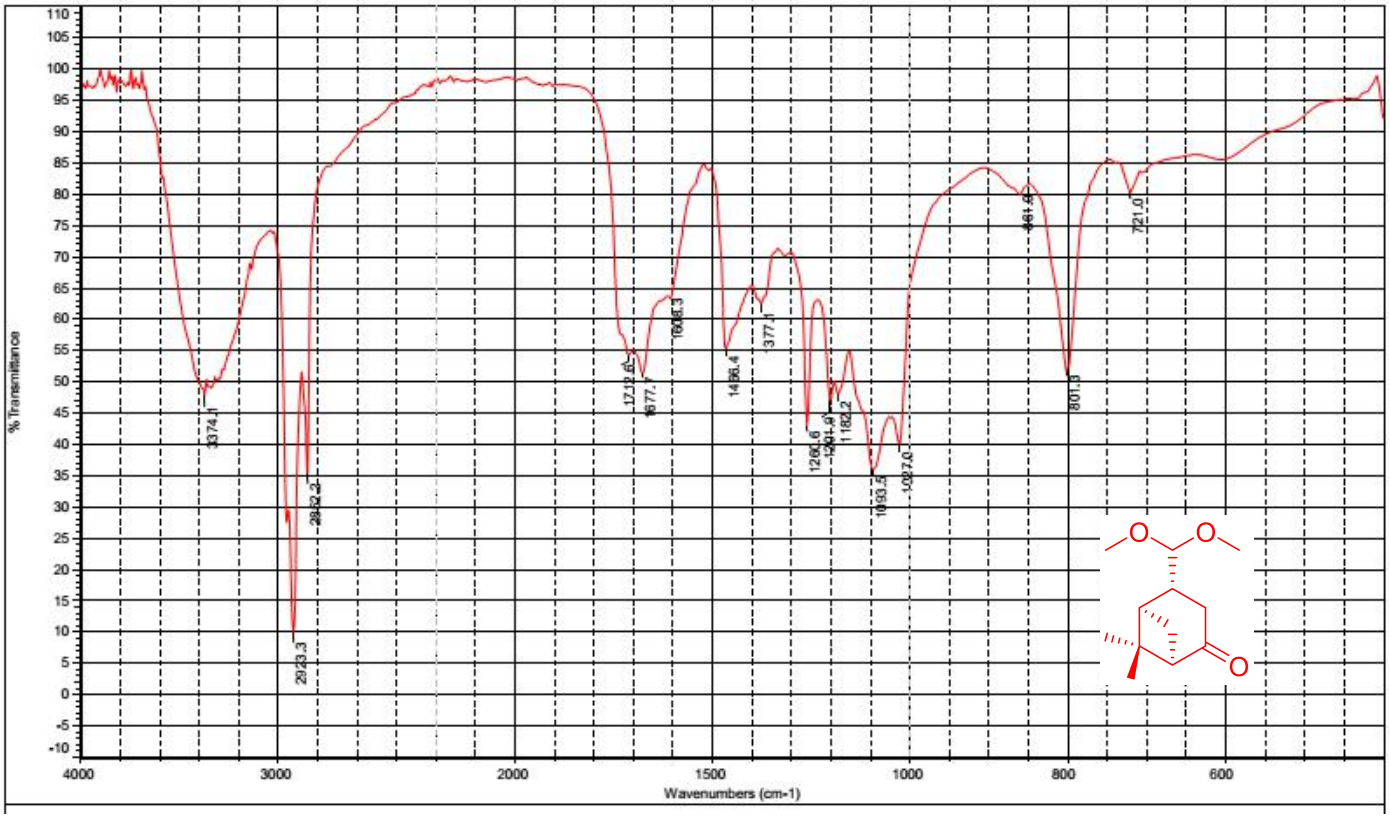


Figure S84. The IR Spectrum of Compound 10

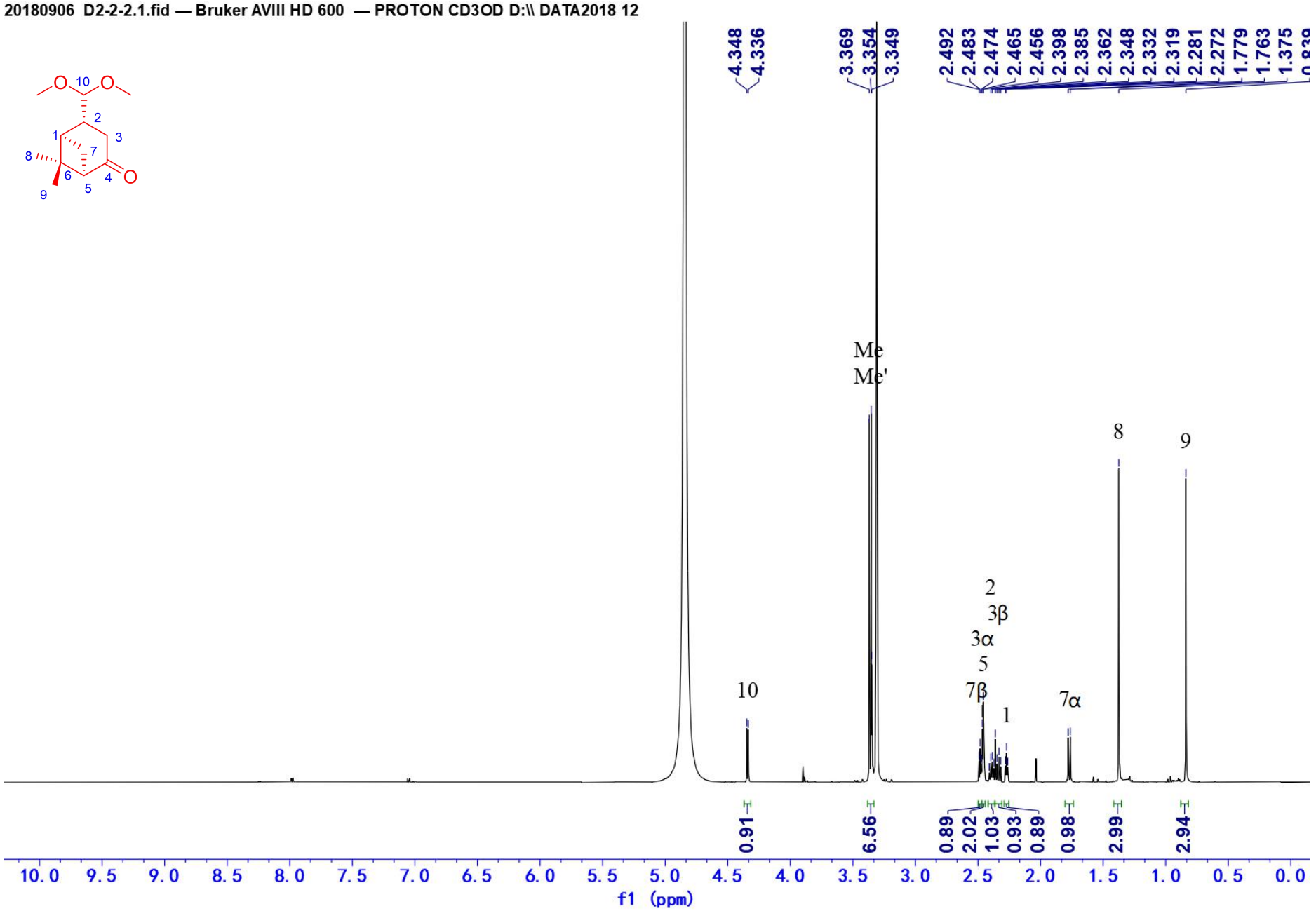


Figure S85. The ^{1}H NMR Spectrum of Compound 10 in MeOH-d_4 (600MHz)

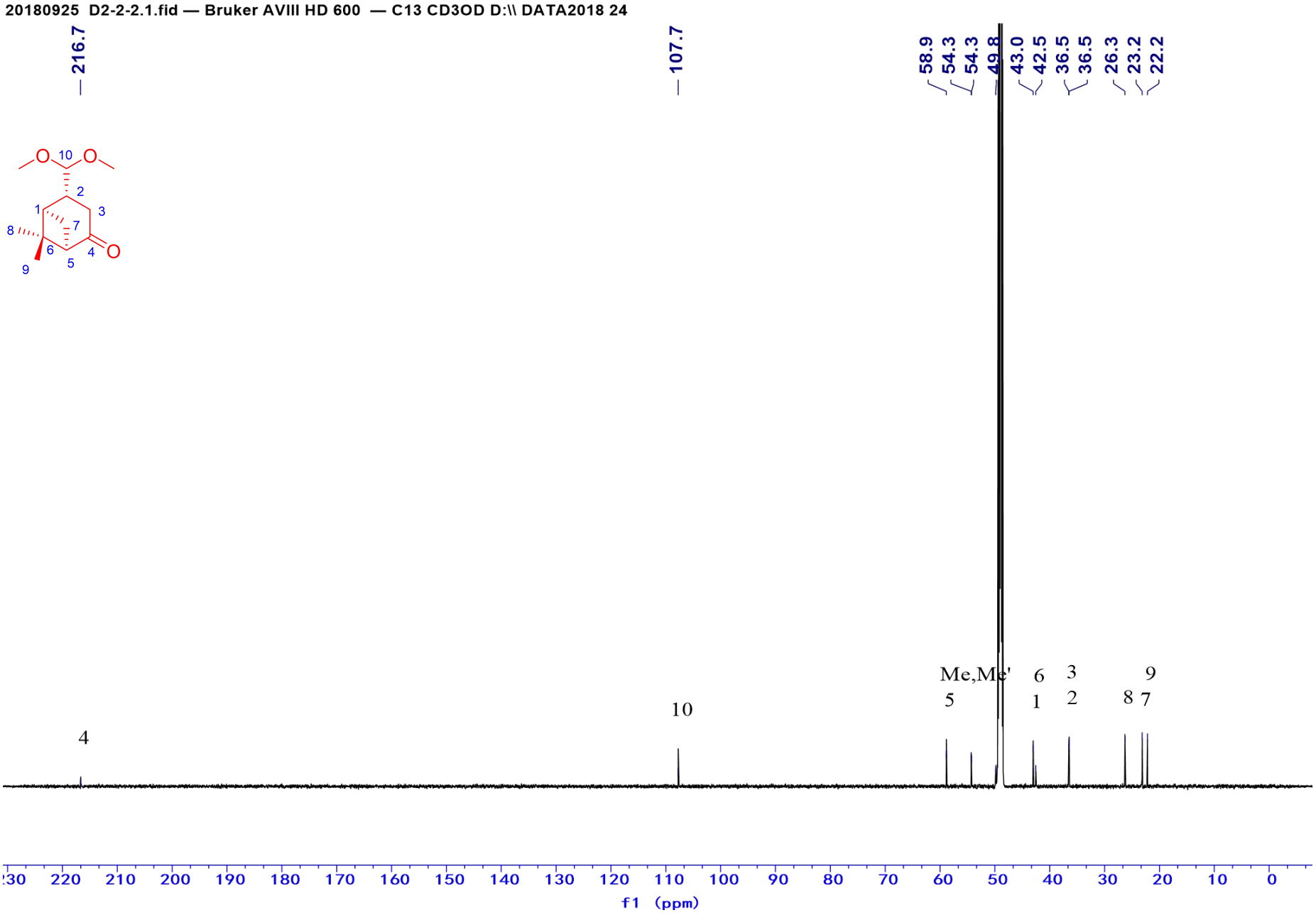


Figure S86. The ^{13}C NMR Spectrum of Compound 10 in MeOH-d_4 (150MHz)

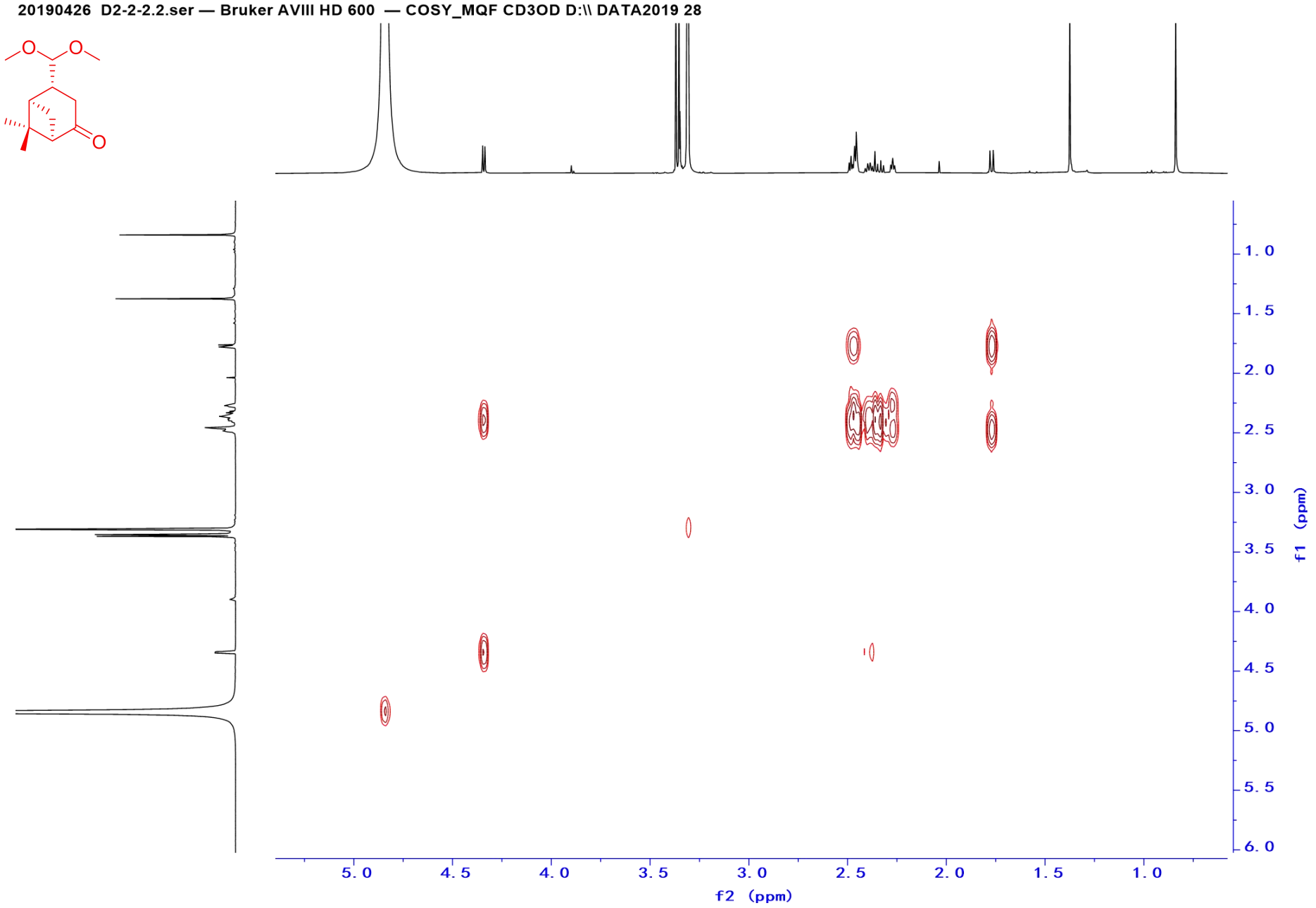


Figure S87. The ^{1}H-^{1}H COSY Spectrum of Compound 10 in MeOH-d_4 (600MHz)

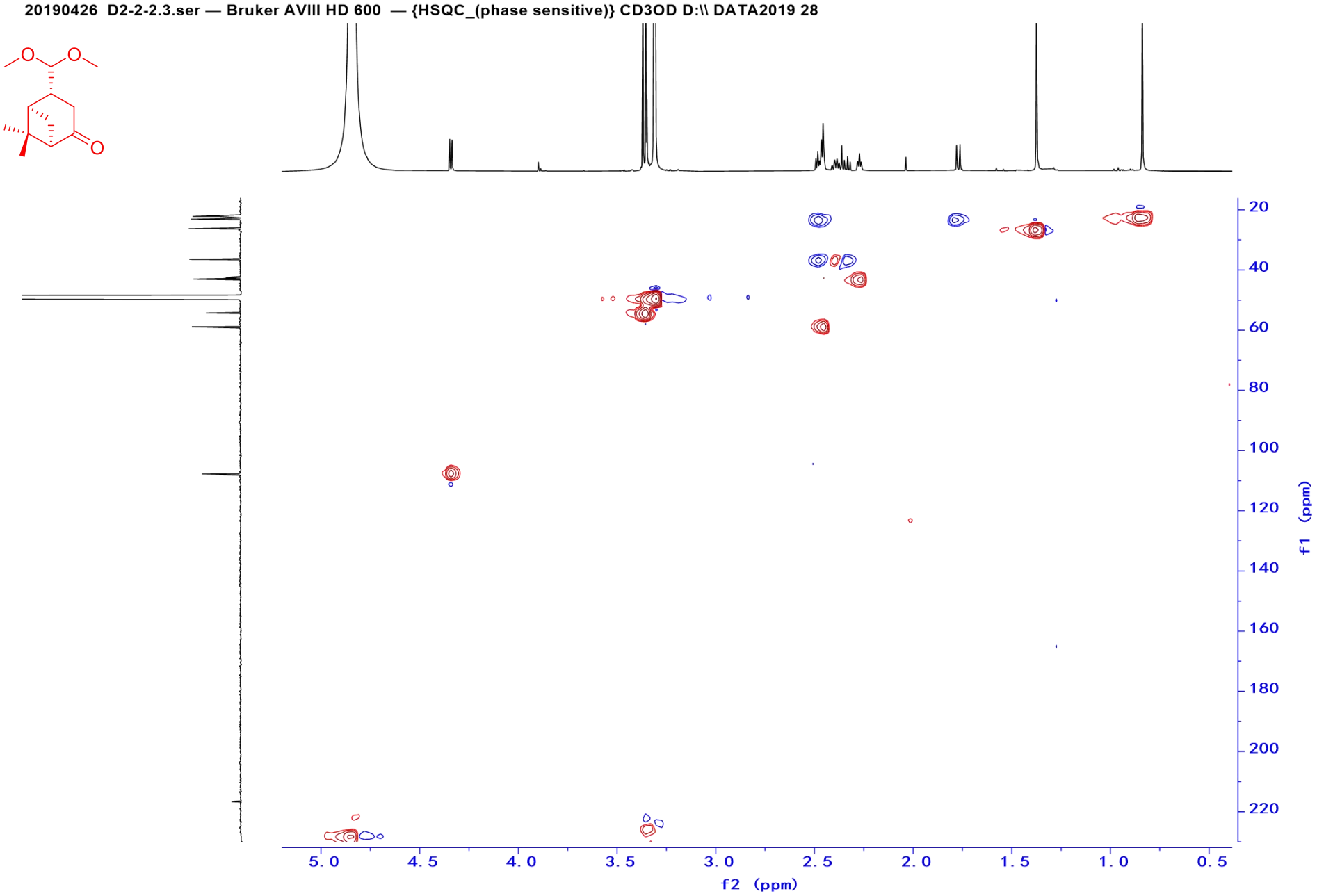


Figure S88. The HSQC Spectrum of Compound 10 in MeOH-d_4 (600MHz)

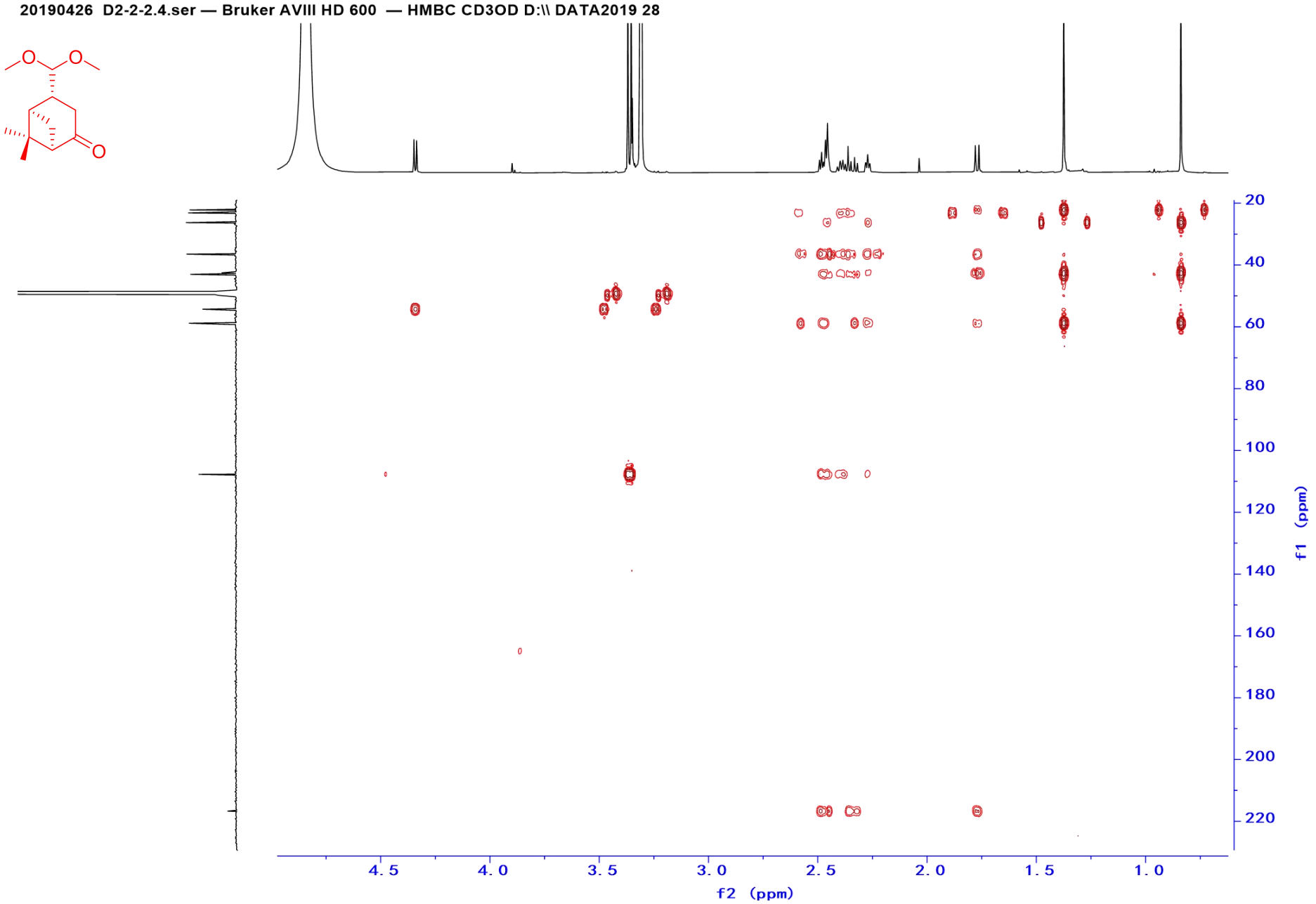


Figure S89. The HMBC Spectrum of Compound 10 in MeOH-d_4 (600MHz)

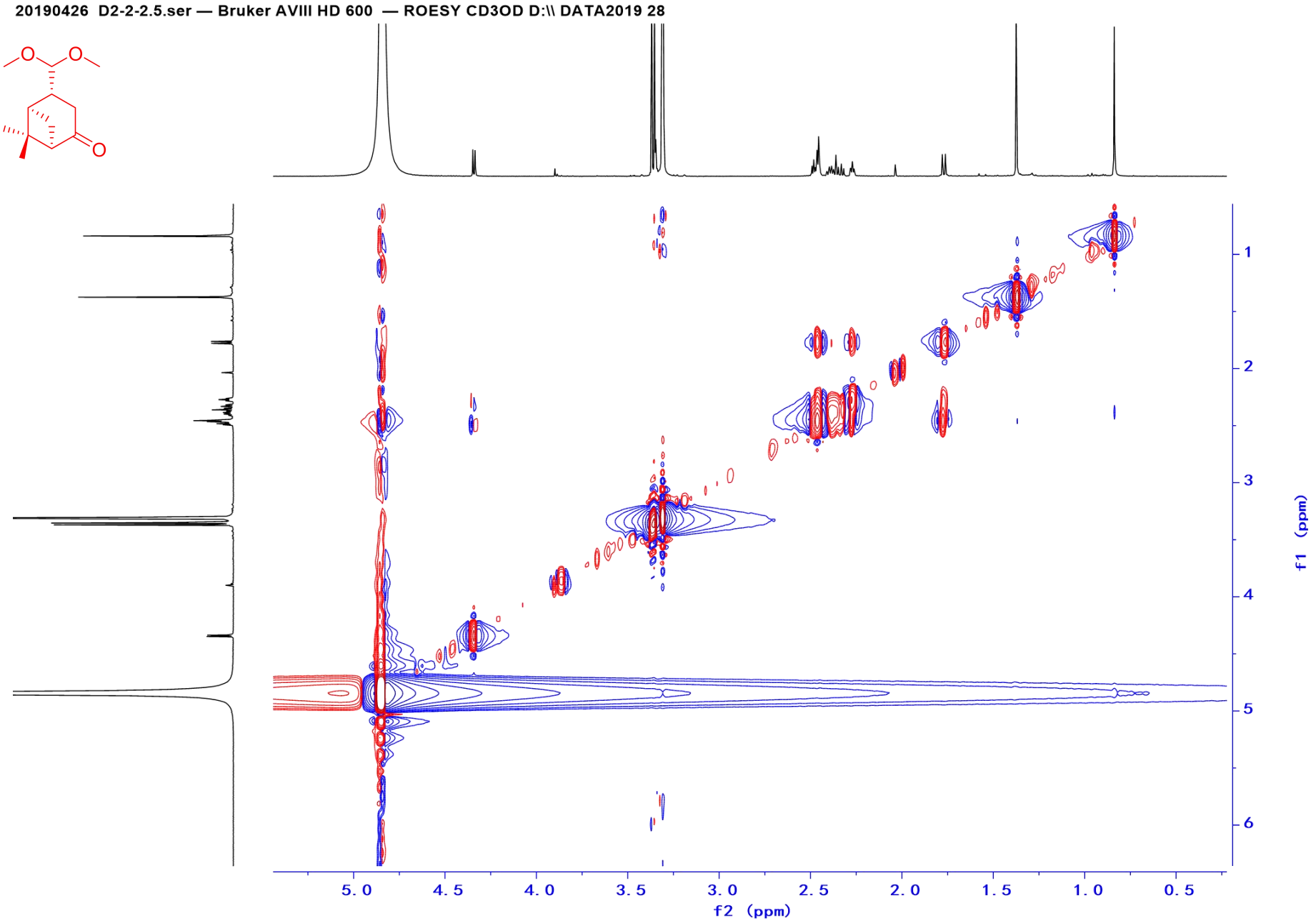


Figure S90. The NOESY Spectrum of Compound 10 in MeOH-d_4 (600MHz)

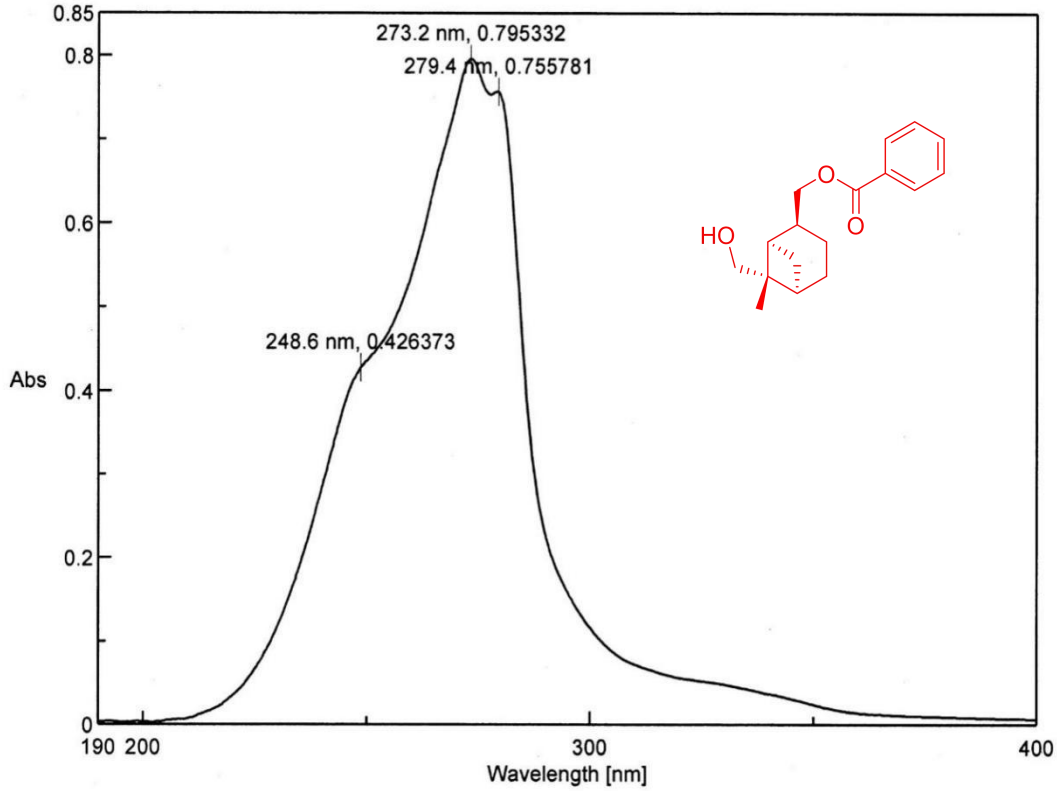


Figure S91. The UV Spectrum of Compound 11 in MeOH

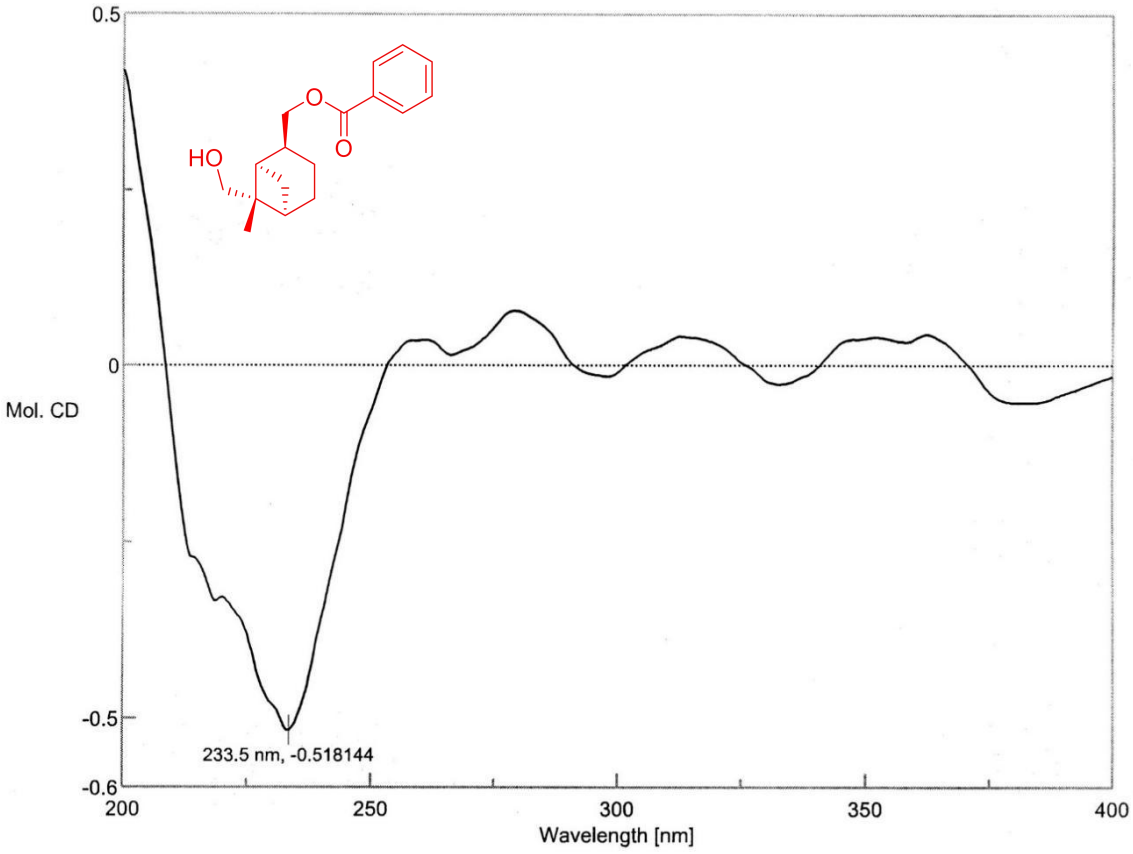


Figure S92. The CD Spectrum of Compound 11 in MeOH

MS Formula Results: + Scan (7.853 min) Sub (2016031005.d)

m/z	Ion	Formula	Abundance
297.1467	(M+Na)+	C17 H22 Na O3	570455.5

Best	Formula (M)	Ion Formula	Score	Cross Sco	Mass	Calc Mass	Calc m/z	Diff (ppm)	Abs Diff (ppm)	Mass Match	Abund Match	Spacing Match	DBE
☑	C17 H22 O3	C17 H22 Na O3	99.67		274.1575	274.1569	297.1461	-2.29	2.29	99.86	99.81	99.11	7
☐	C12 H22 N2 O5	C12 H22 N2 Na O5	95.15		274.1575	274.1529	297.1421	-16.98	16.98	92.66	96.21	98.86	3
☐	C19 H18 N2	C19 H18 N2 Na	84.24		274.1575	274.147	297.1362	-38.4	38.4	67.71	99.39	99.12	12
☐	C16 H22 N2 O2	C16 H22 N2 Na O2	84.11		274.1575	274.1681	297.1573	38.67	38.67	67.33	99.65	99.02	7
☐	C21 H22	C21 H22 Na	74.24		274.1575	274.1722	297.1614	53.35	53.35	47.1	98.63	99.24	11

Figure S93. The HR-mass Spectrum of Compound 11 in MeOH

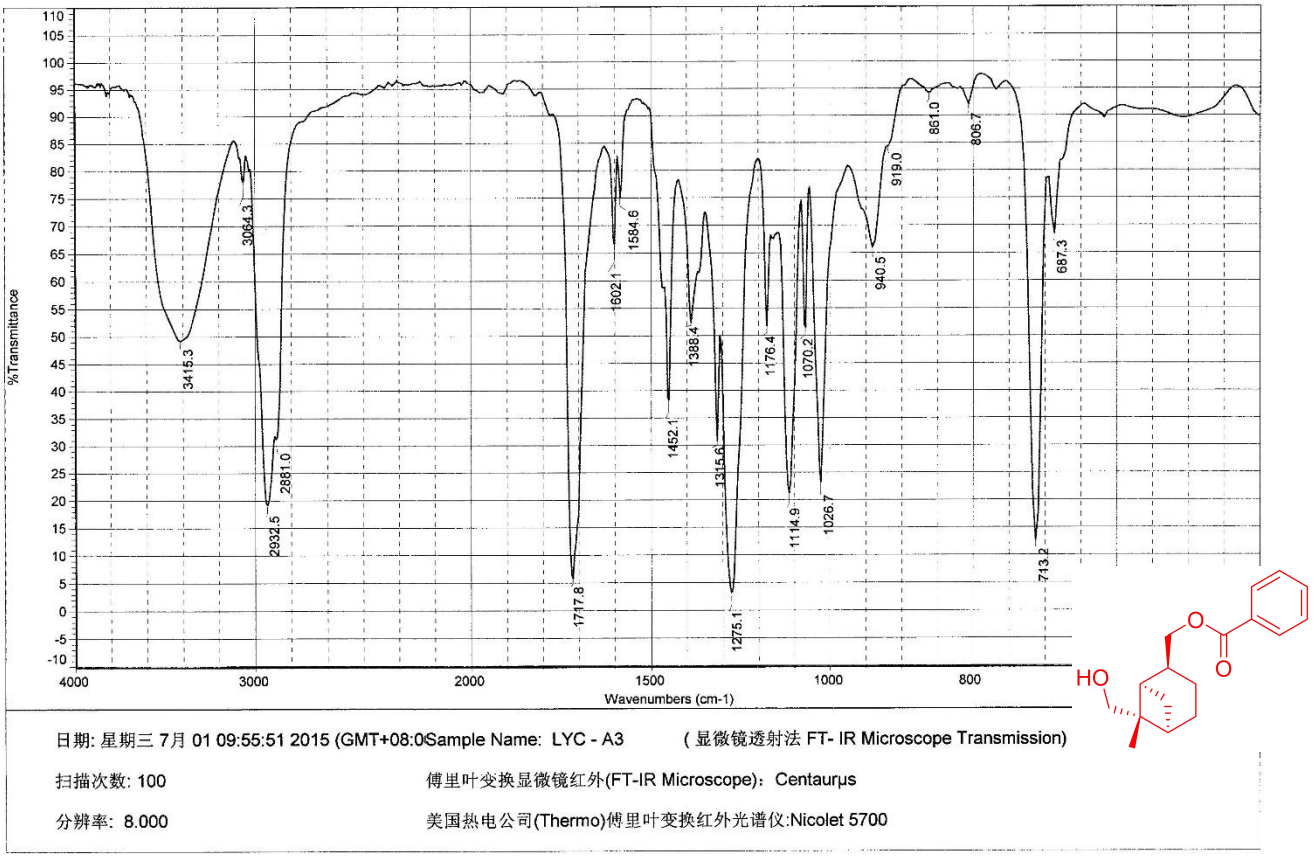


Figure S94. The IR Spectrum of Compound 11

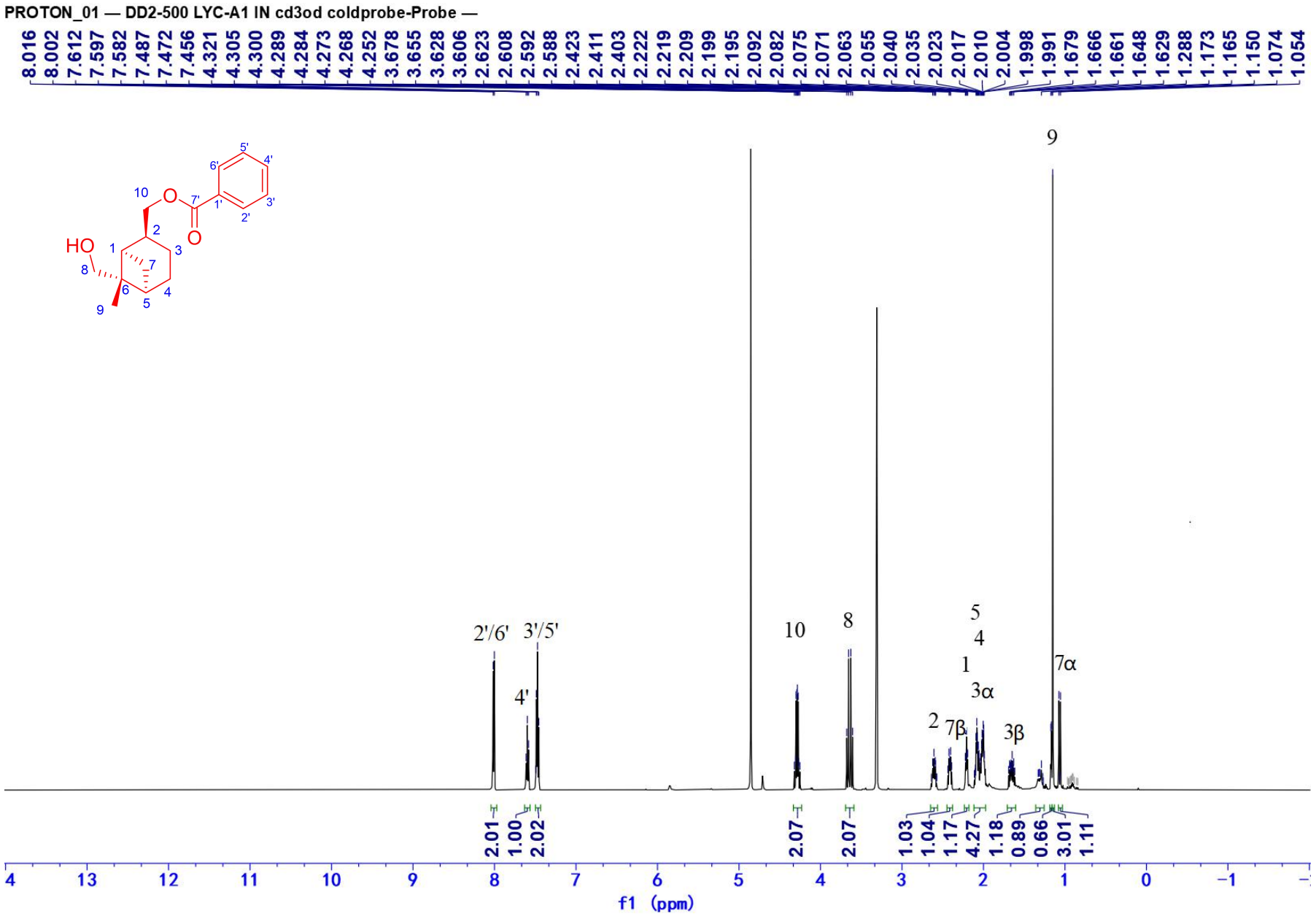


Figure S95. The ^{1}H NMR Spectrum of Compound 11 in MeOH-d_4 (500MHz)

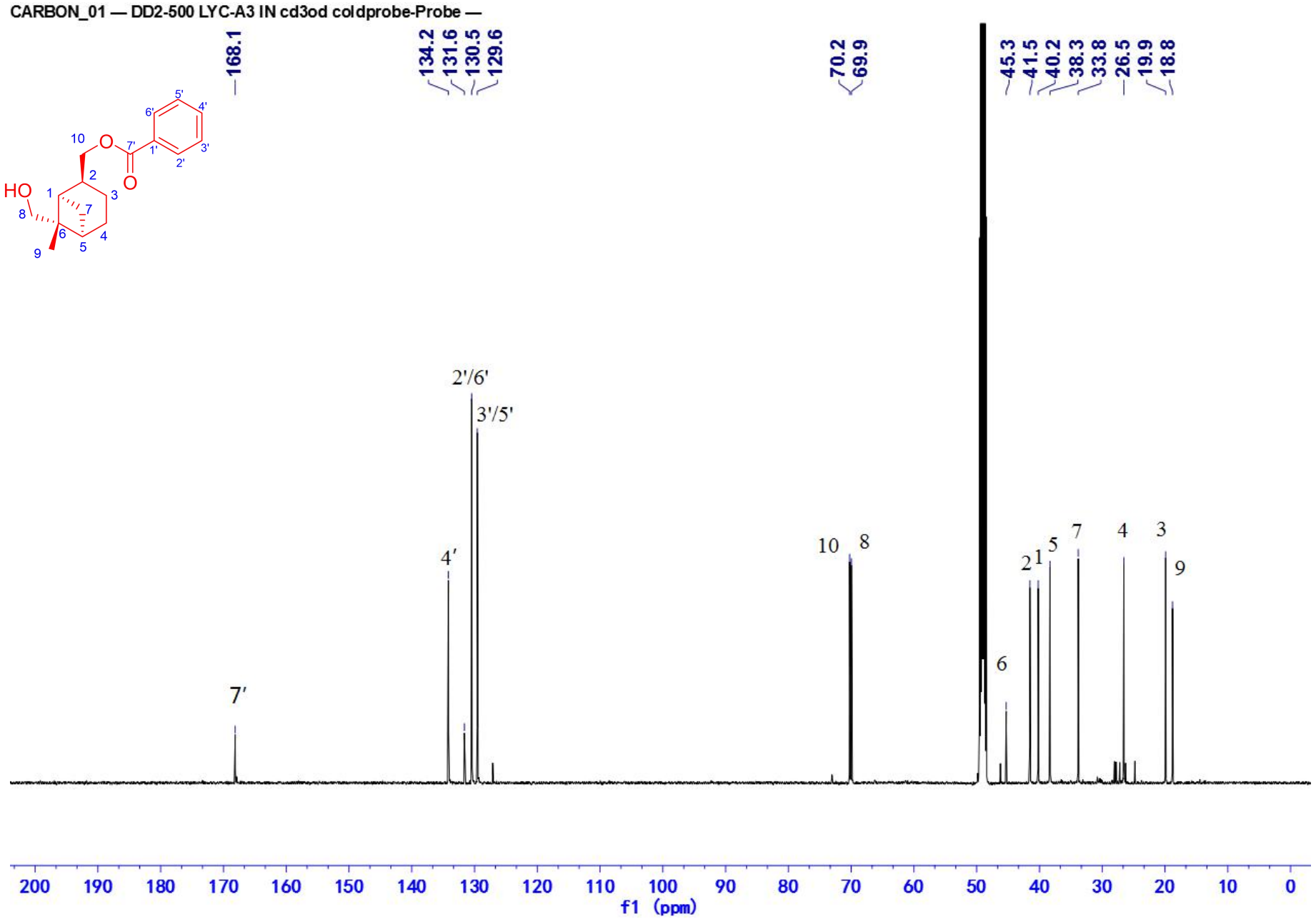


Figure S96. The ^{13}C NMR Spectrum of Compound 11 in MeOH-d_4 (125MHz)

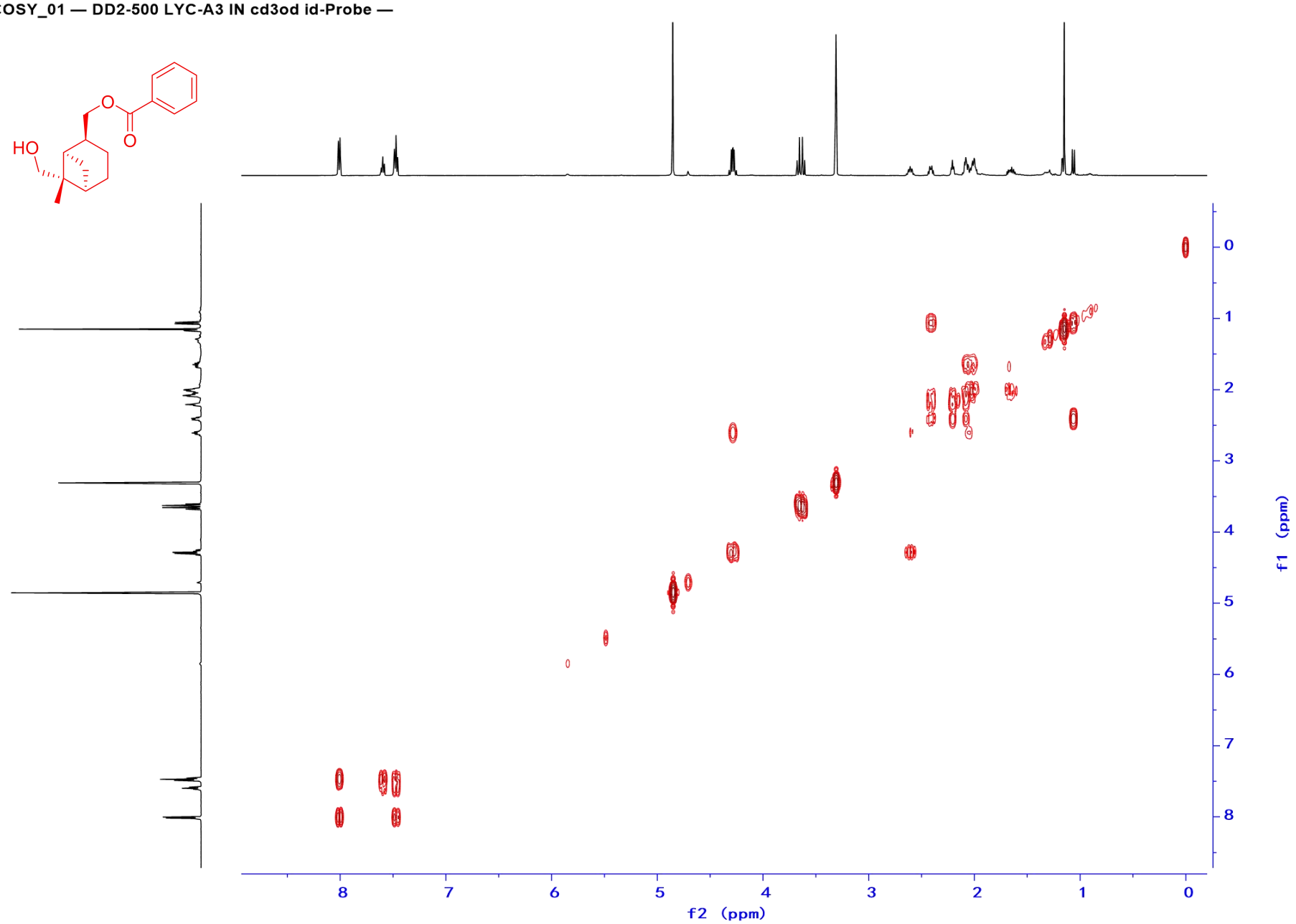


Figure S97. The ^{1}H-^{1}H COSY Spectrum of Compound 11 in MeOH-d_4 (500MHz)

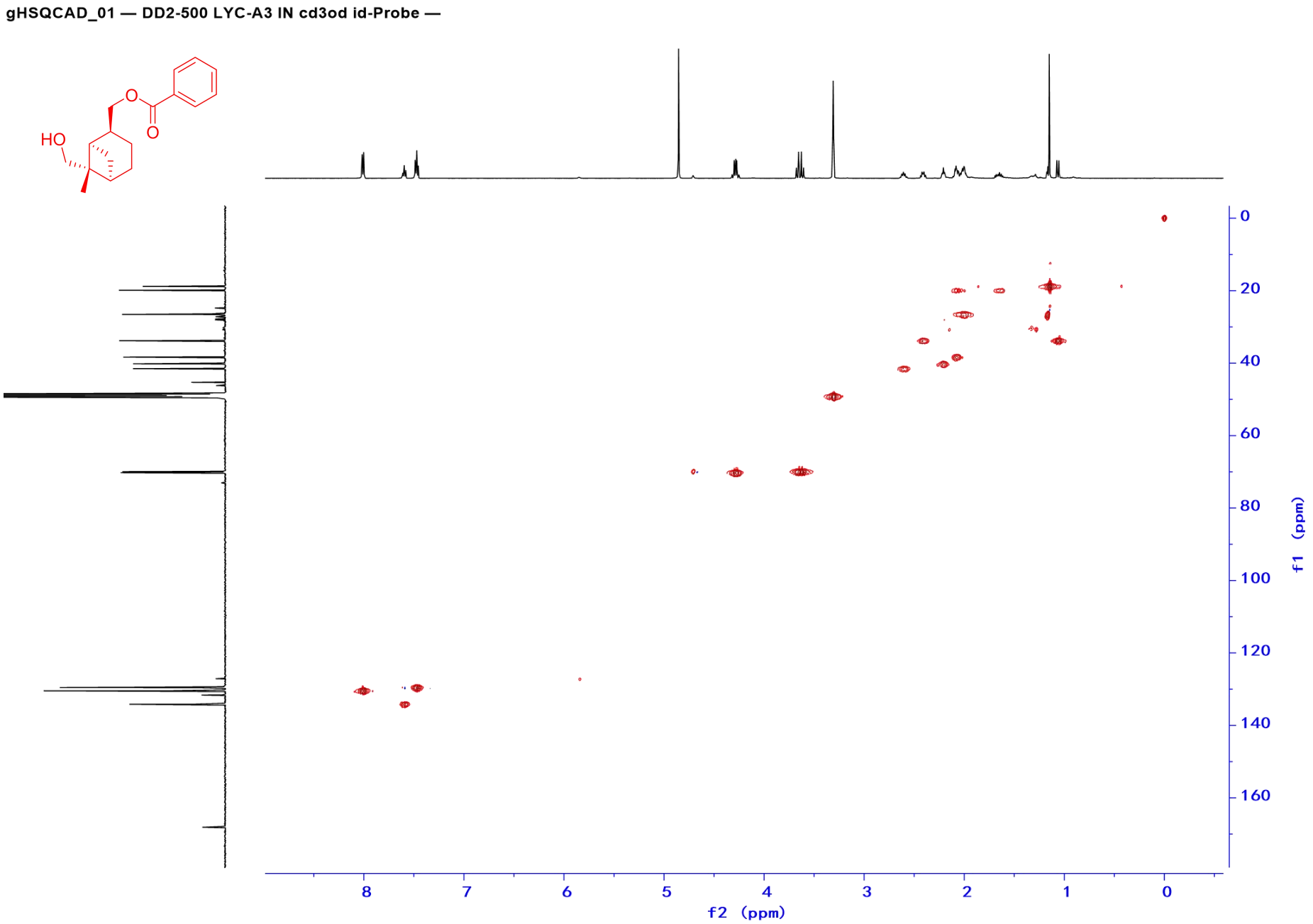


Figure S98. The HSQC Spectrum of Compound 11 in MeOH-d_4 (500MHz)

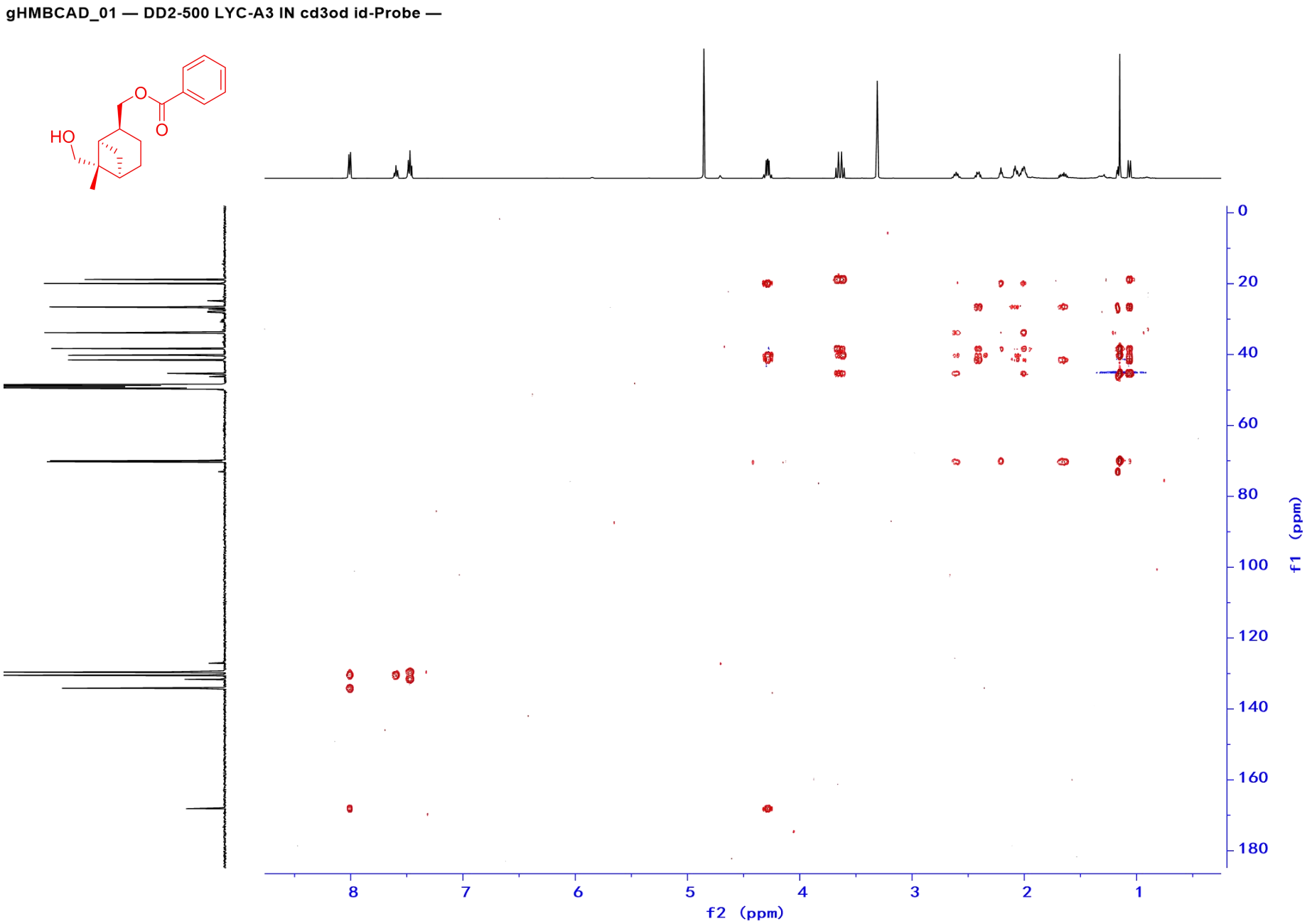


Figure S99. The HMBC Spectrum of Compound 11 in MeOH-d_4 (500MHz)

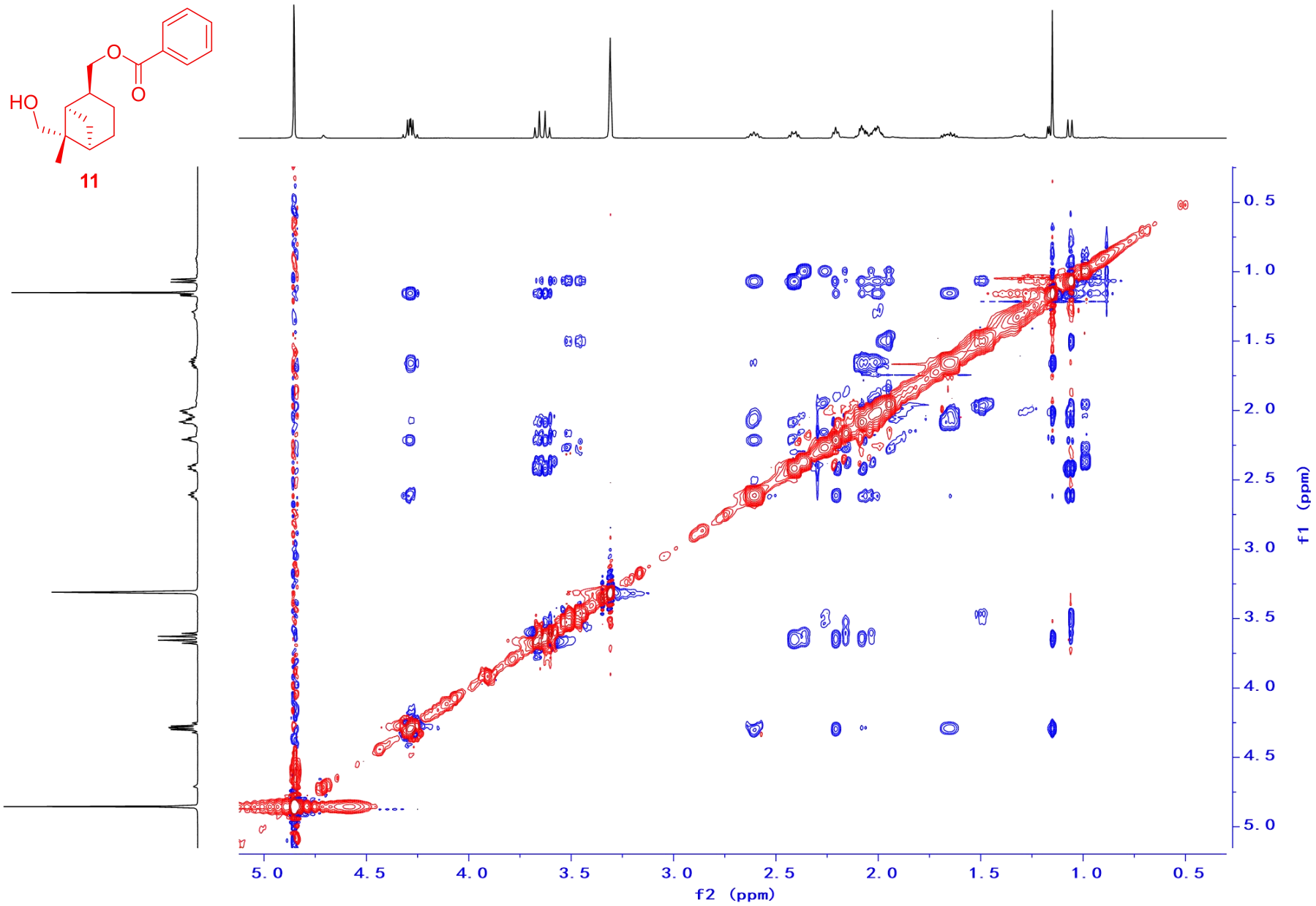


Figure S100. The NOESY Spectrum of Compound 11 in MeOH-d_4 (500MHz)

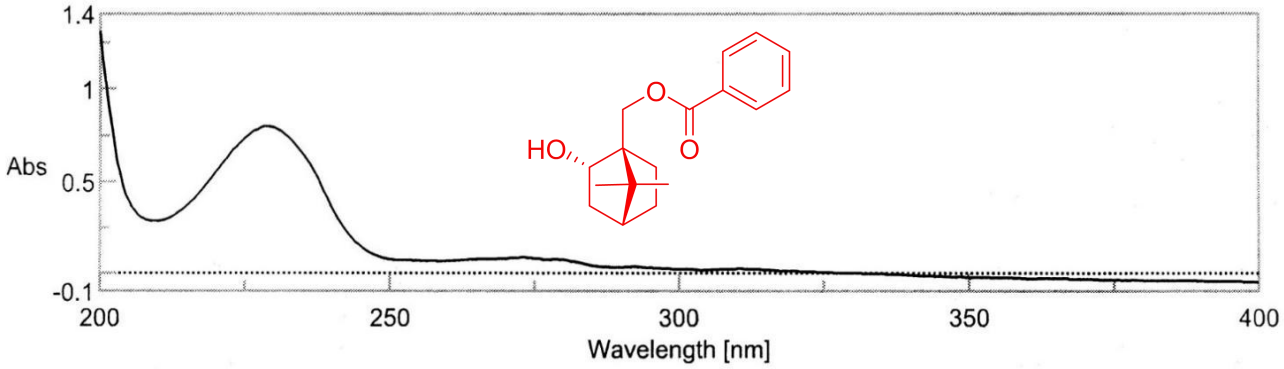


Figure S101. The UV Spectrum of Compound 12 in MeOH

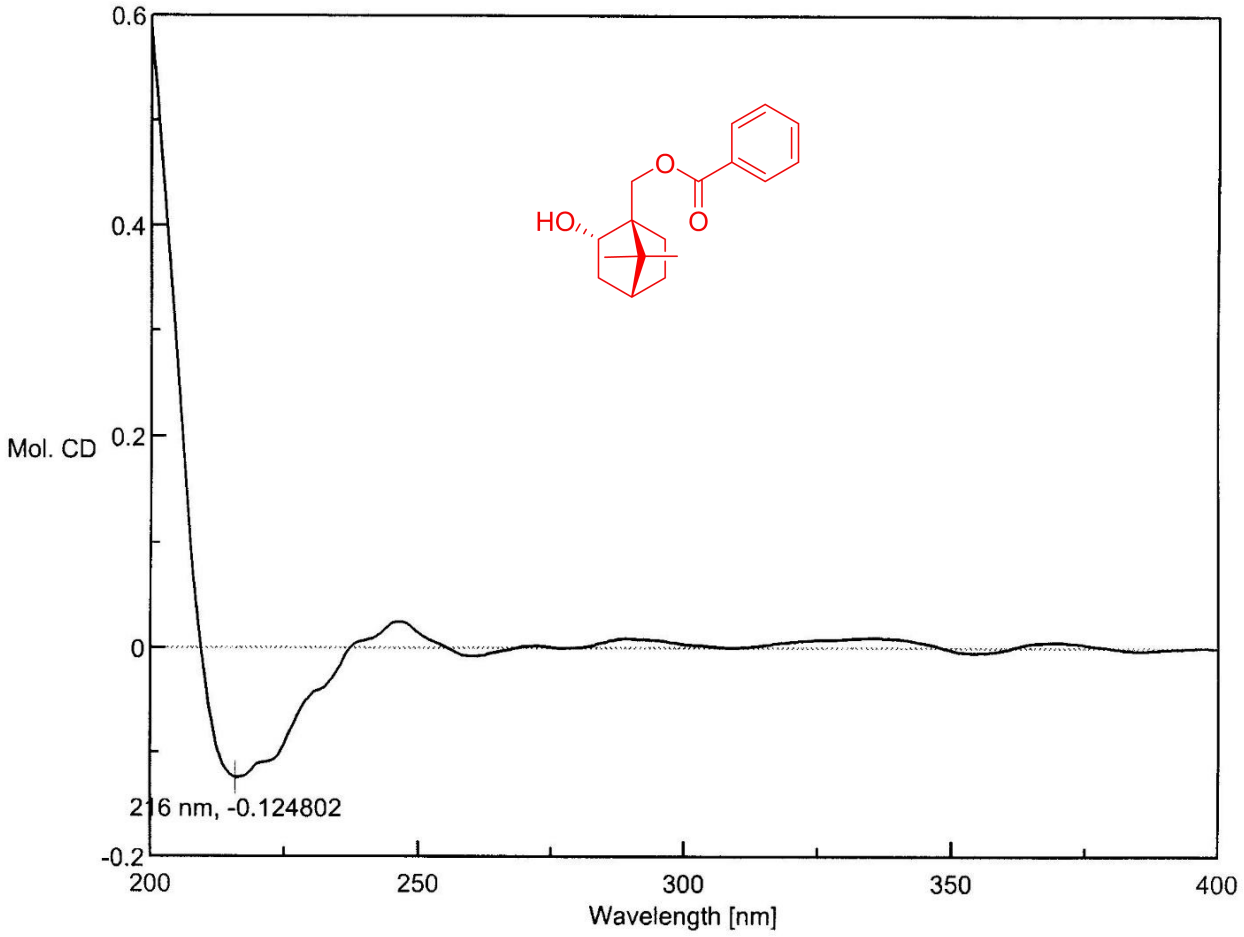


Figure S102. The CD Spectrum of Compound 12 in MeOH

MS Formula Results: + Scan (7.805-8.192 min) Sub (2016031001.d)

m/z	Ion	Formula	Abundance
297.147	(M+Na)+	C17 H22 Na O3	116016.4

Best	Formula (M)	Ion Formula	Score	Cross Sco	Mass	Calc Mass	Calc m/z	Diff (ppm)	Abs Diff (ppm)	Mass Match	Abund Match	Spacing Match	DBE
☑	C17 H22 O3	C17 H22 Na O3	99.66		274.1578	274.1569	297.1461	-3.33	3.33	99.71	99.32	99.99	7
☐	C12 H22 N2 O5	C12 H22 N2 Na O5	95.84		274.1578	274.1529	297.1421	-18.01	18.01	91.78	99.18	99.95	3
☐	C16 H22 N2 O2	C16 H22 N2 Na O2	84.98		274.1578	274.1681	297.1573	37.64	37.64	68.75	99.54	99.97	7
☐	C19 H18 N2	C19 H18 N2 Na	83.1		274.1578	274.147	297.1362	-39.43	39.43	66.28	97.06	99.98	12
☐	C21 H22	C21 H22 Na	74.12		274.1578	274.1722	297.1614	52.31	52.31	48.49	95.27	99.99	11

Figure S103. The HR-mass Spectrum of Compound 12 in MeOH

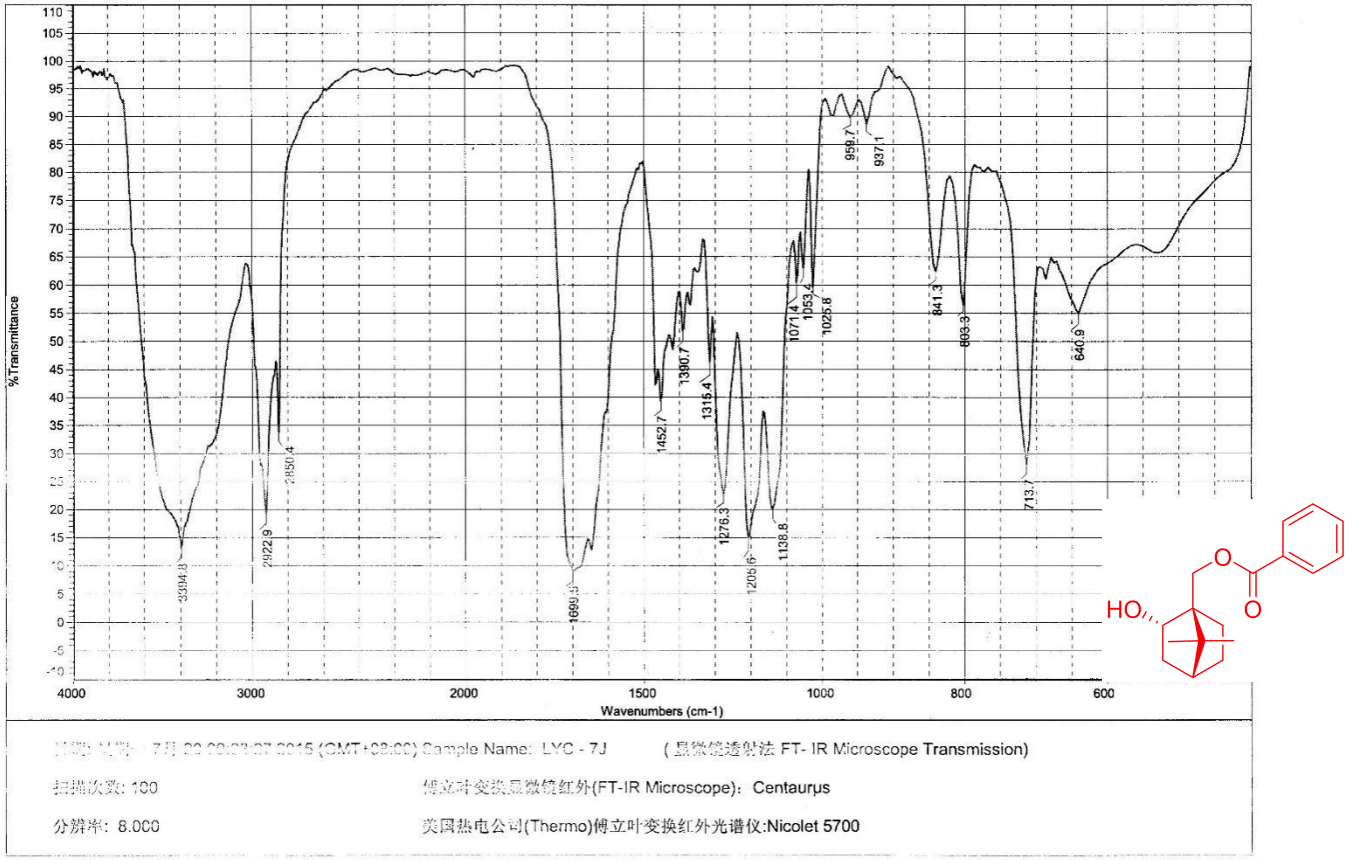


Figure S104. The IR Spectrum of Compound 12

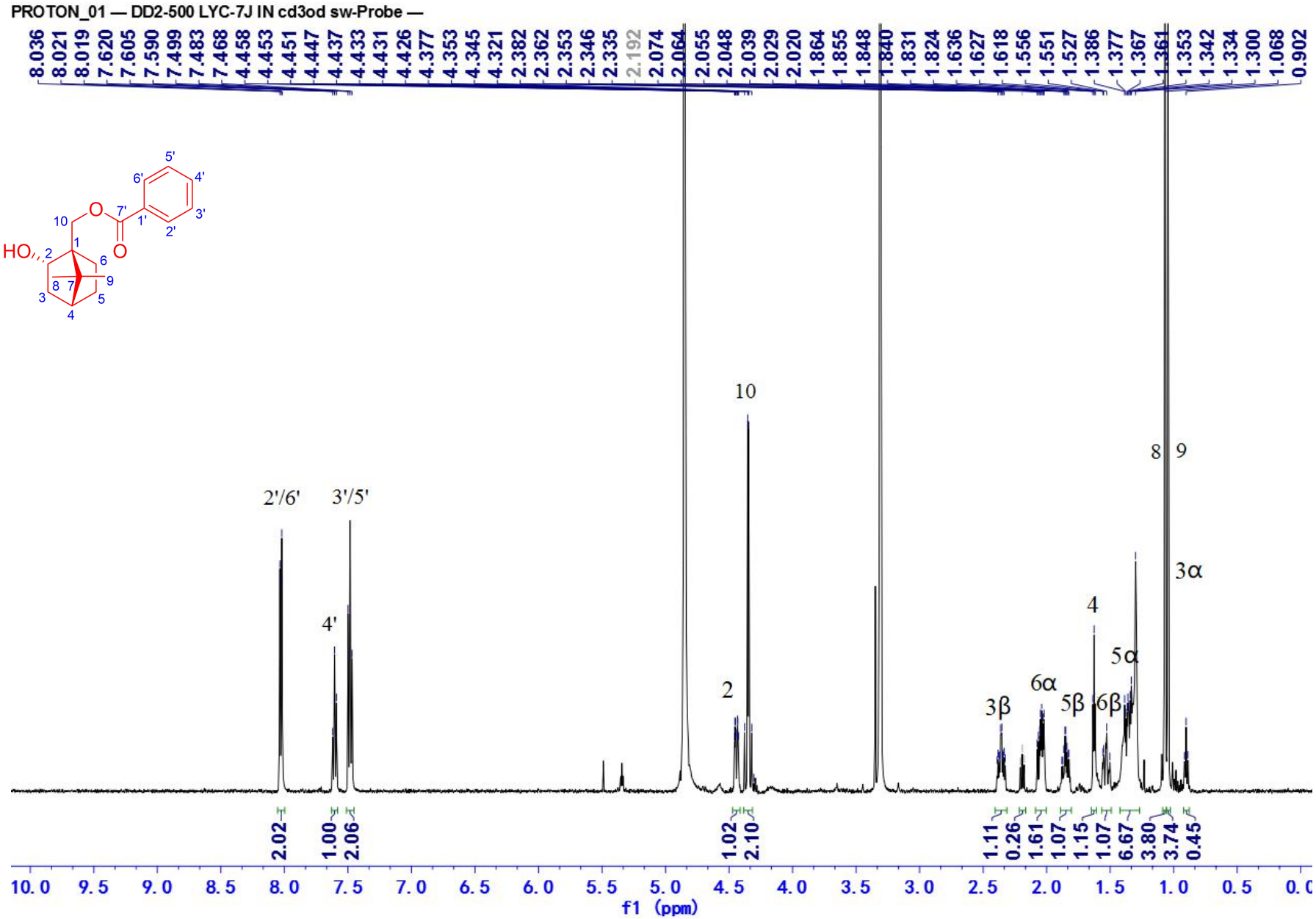


Figure S105. The ^{1}H NMR Spectrum of Compound 12 in MeOH-d_4 (500MHz)

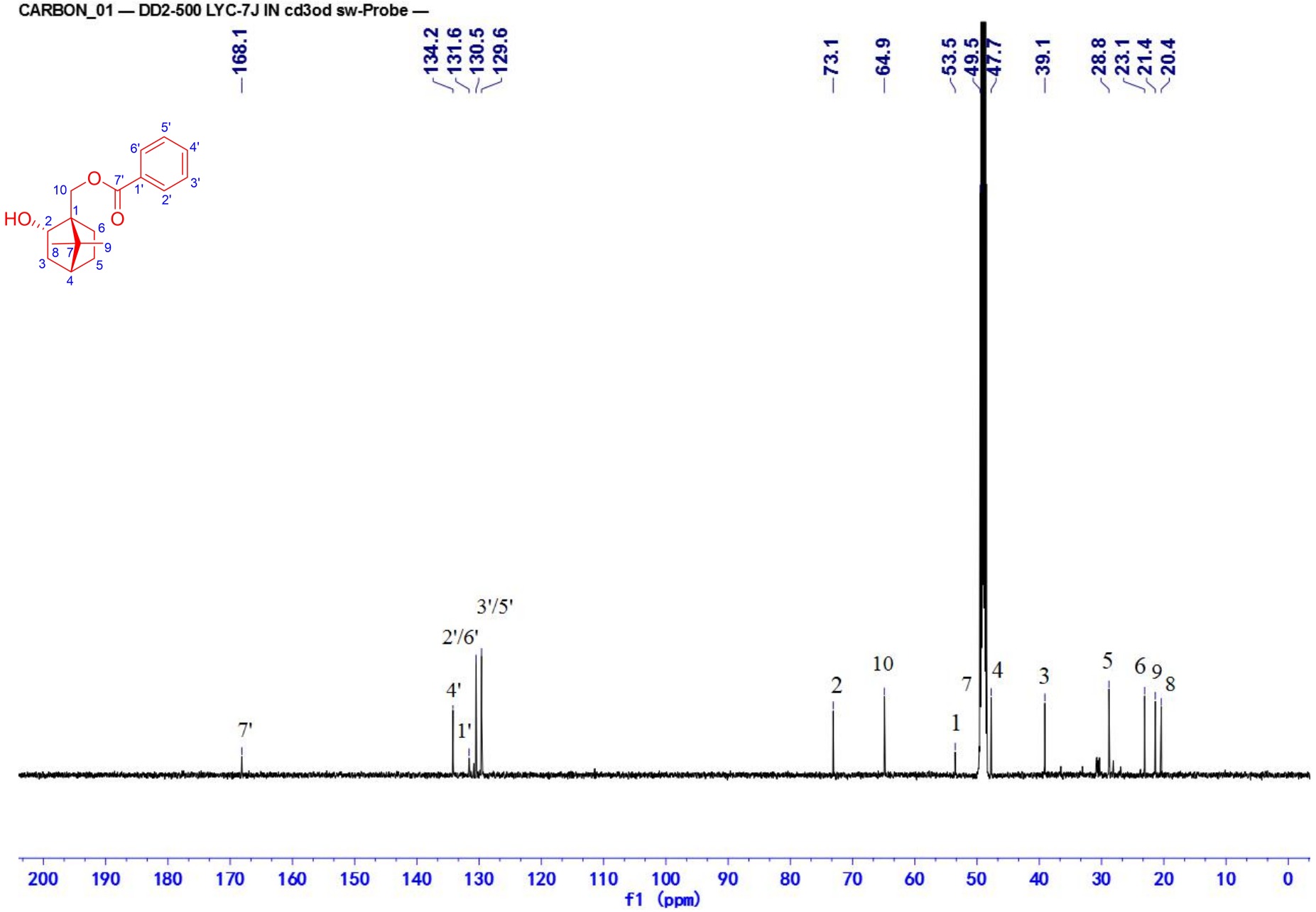


Figure S106. The ^{13}C NMR Spectrum of Compound 12 in MeOH-d_4 (125MHz)

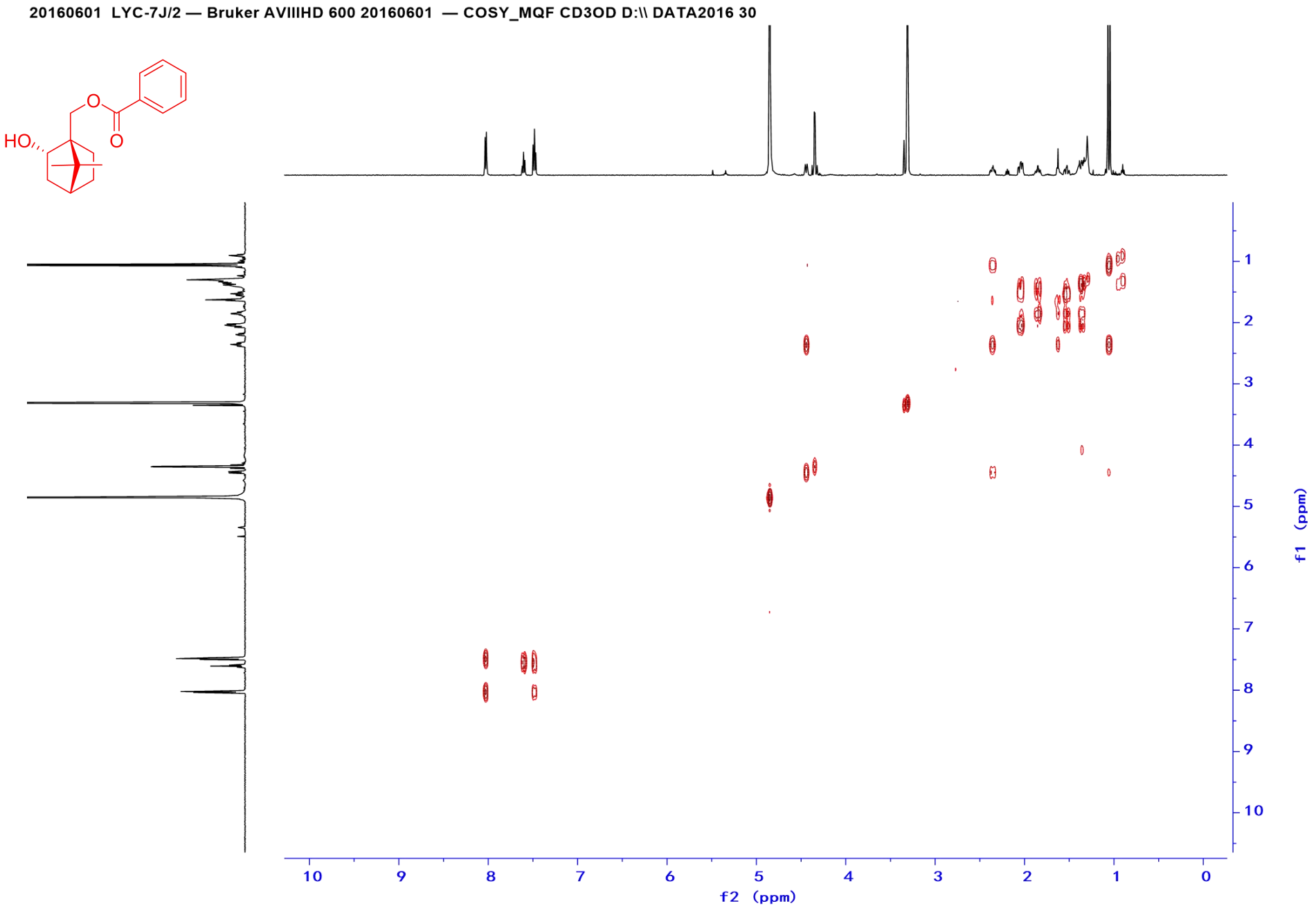


Figure S107. The ^{1}H-^{1}H COSY Spectrum of Compound 12 in MeOH-d_4 (500MHz)

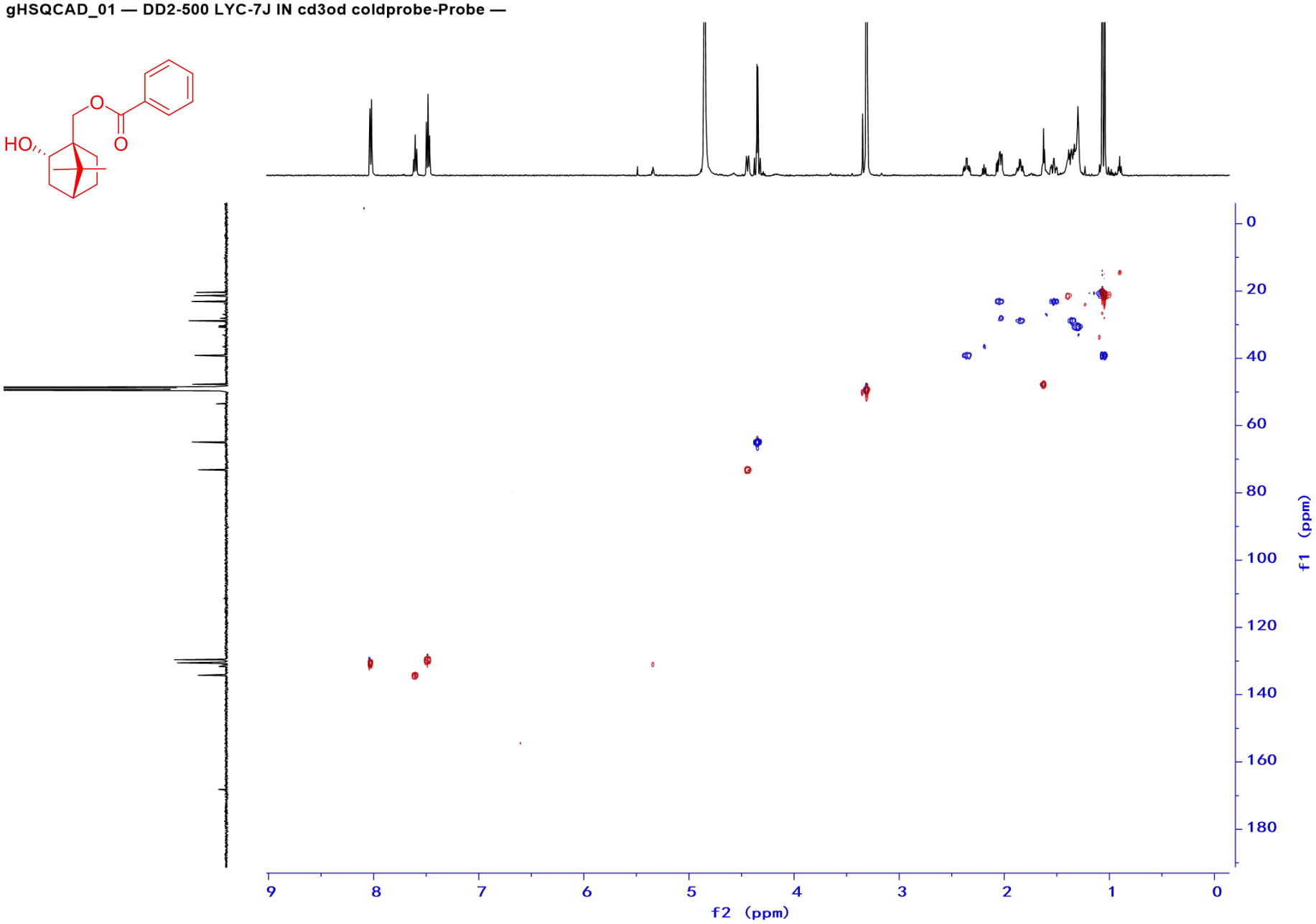


Figure S108. The HSQC Spectrum of Compound 12 in MeOH-d_4 (500MHz)

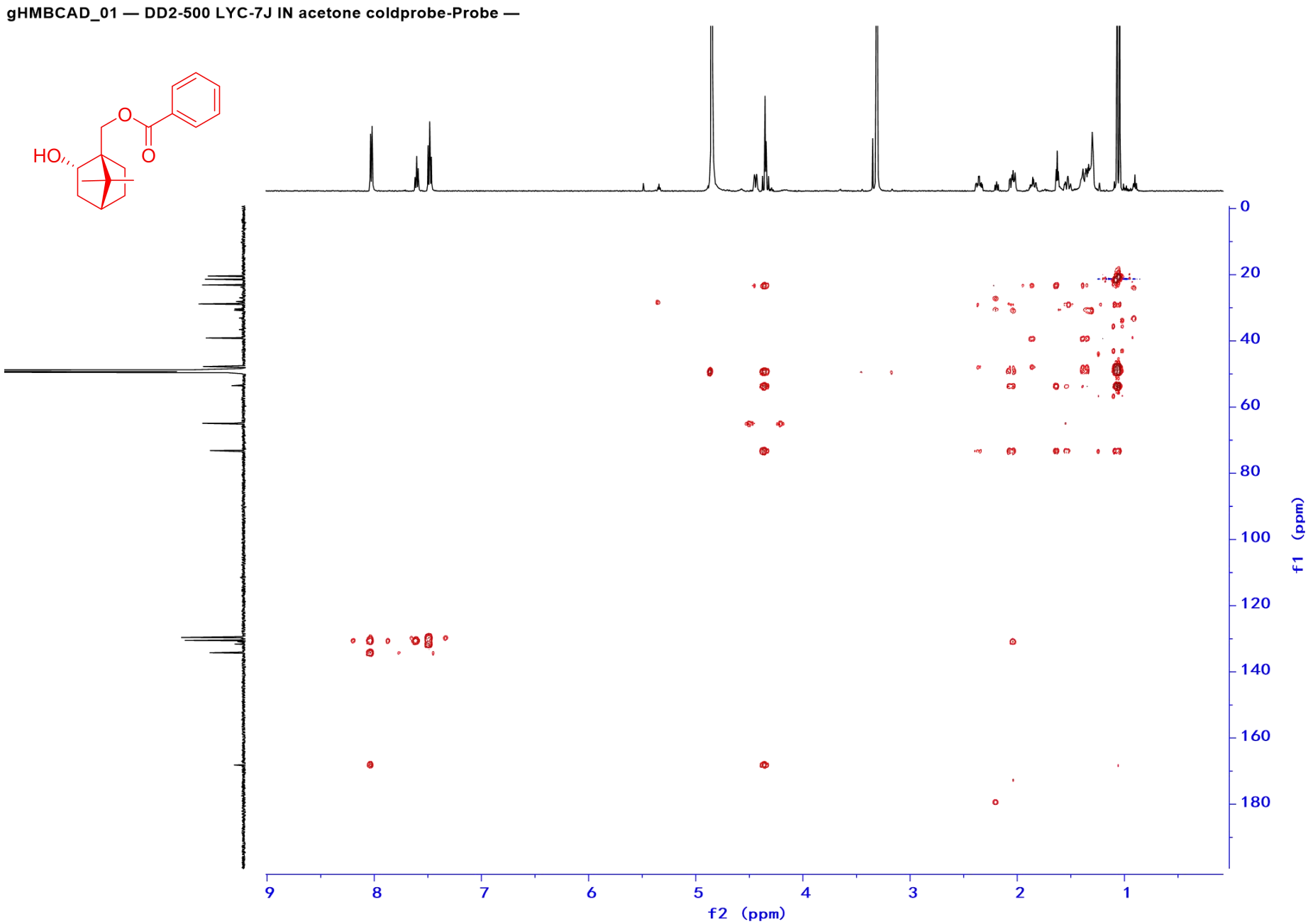


Figure S109. The HMBC Spectrum of Compound 12 in MeOH-d_4 (500MHz)

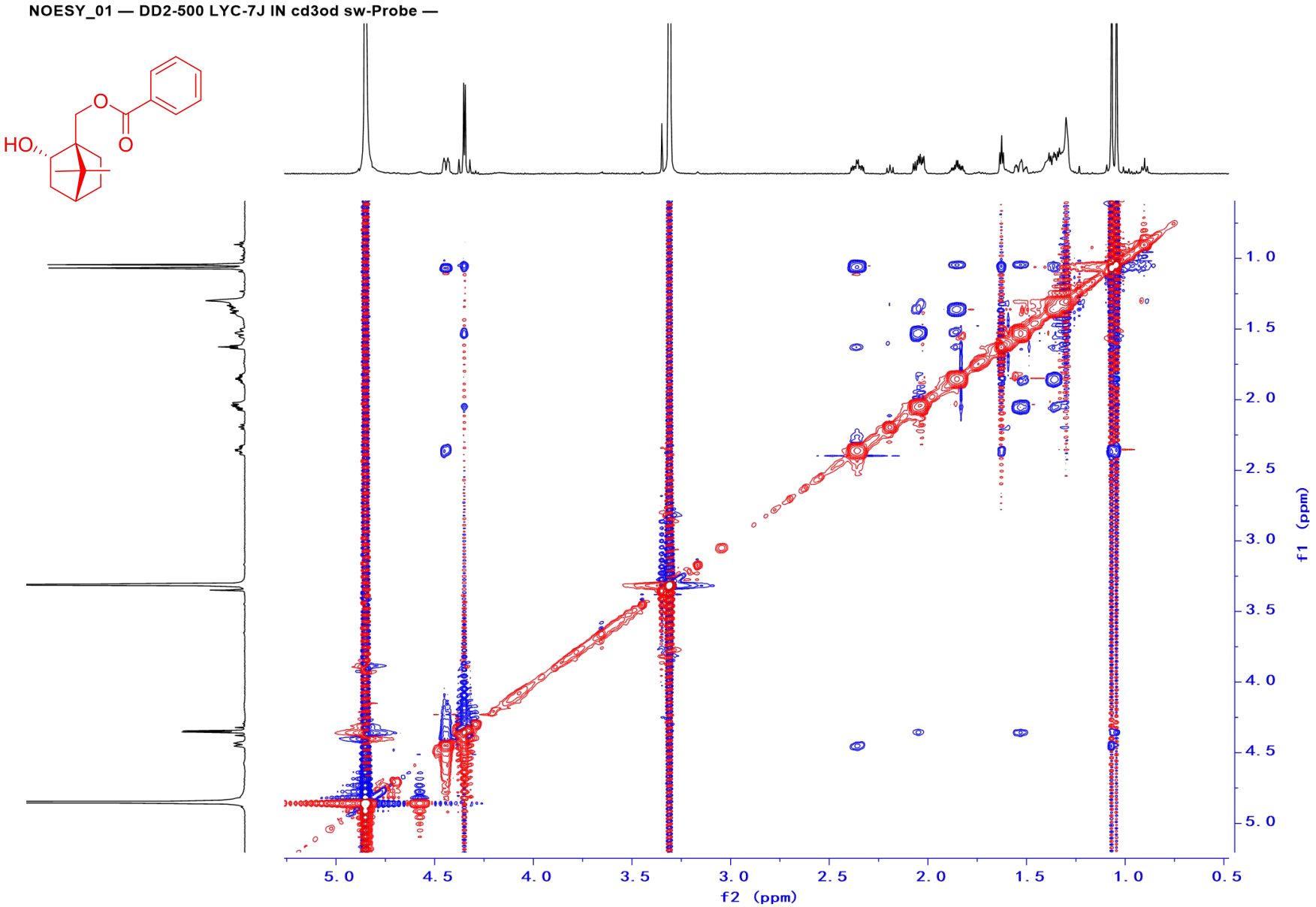


Figure S110. The NOESY Spectrum of Compound 12 in MeOH-d_4 (500MHz)

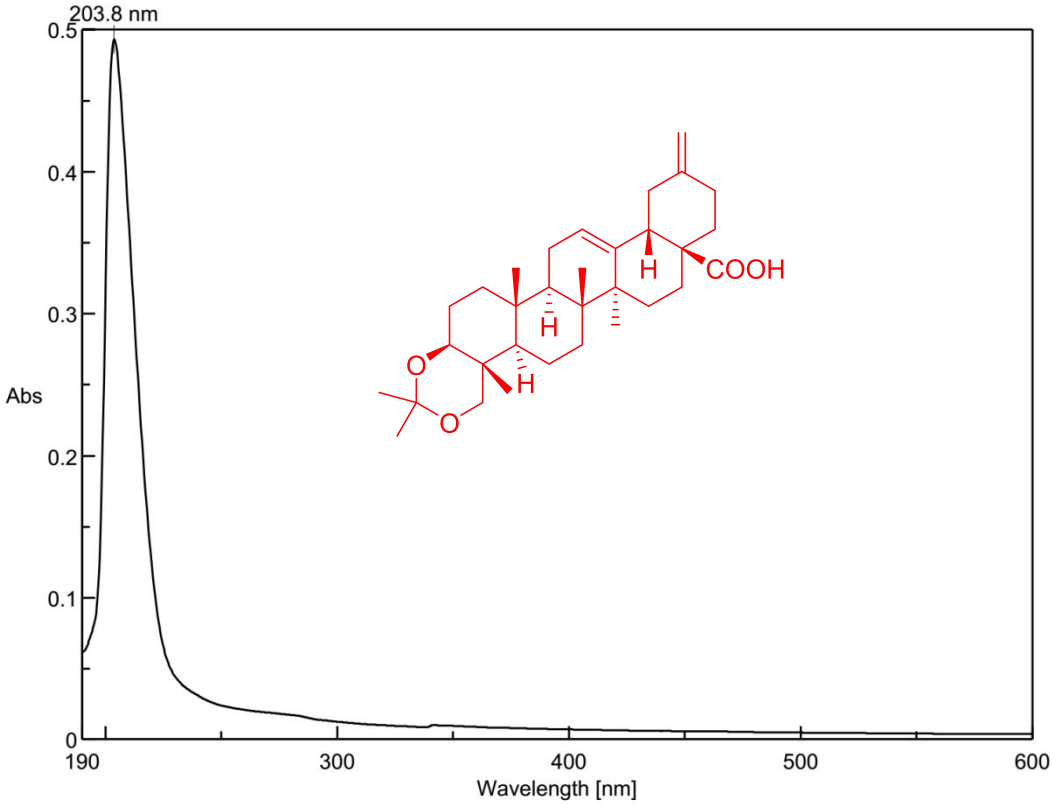


Figure S111. The UV Spectrum of Compound 26 in MeOH

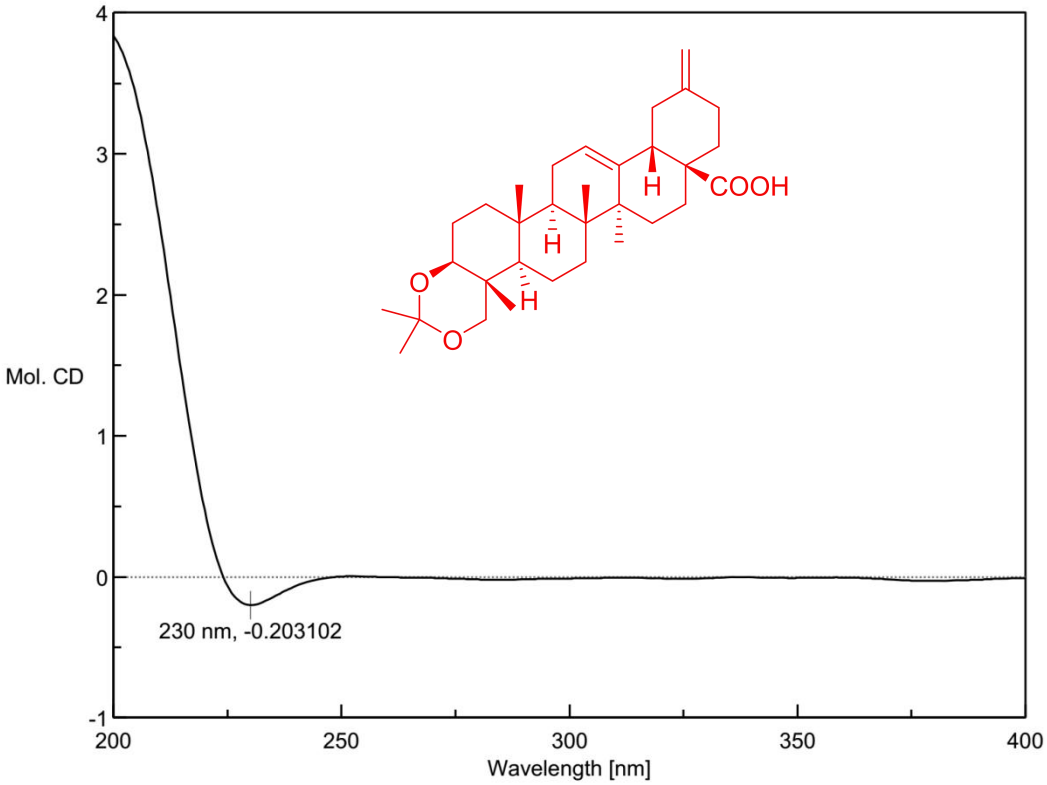
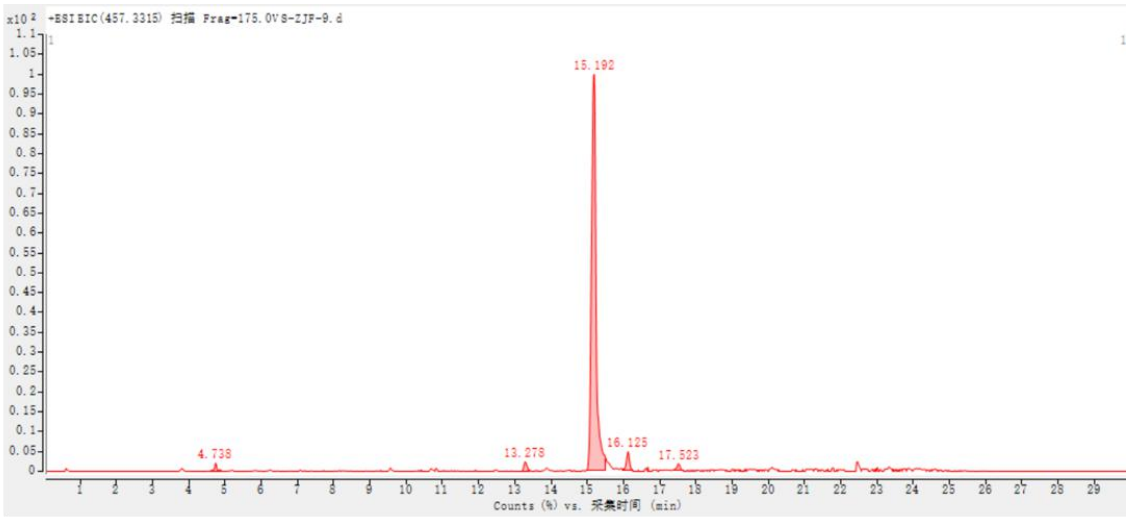


Figure S112. The CD Spectrum of Compound 26 in MeOH



最佳	ID 来源	名称	分子式	种类	m/z	分数	分数 (RT)	保留时间差	Diff (ppm)
▸ ○	MFG		C29 H44 O4	(M+H)+	457.3315	96.01			0.08

Figure S113. The HR-mass Spectrum of Compound 26 in MeOH

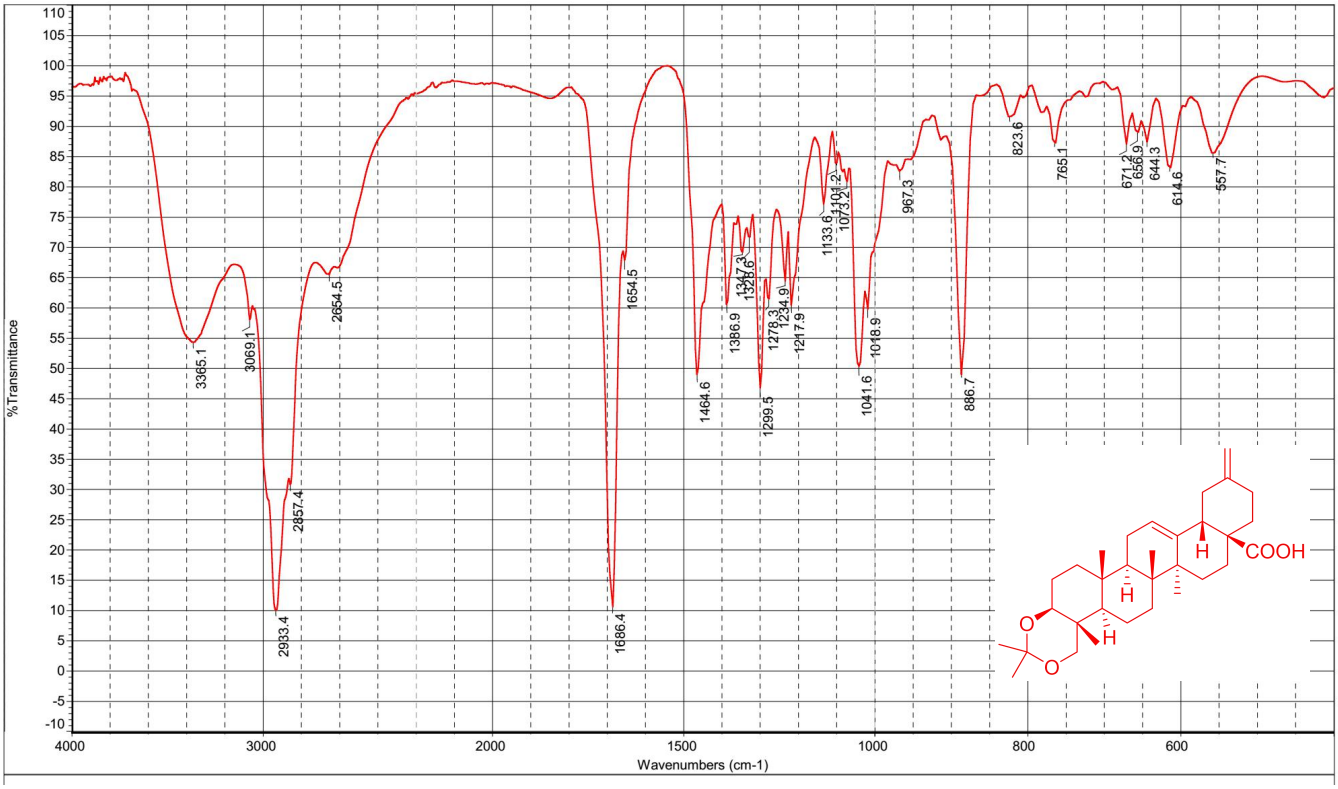


Figure S114. The IR Spectrum of Compound 26

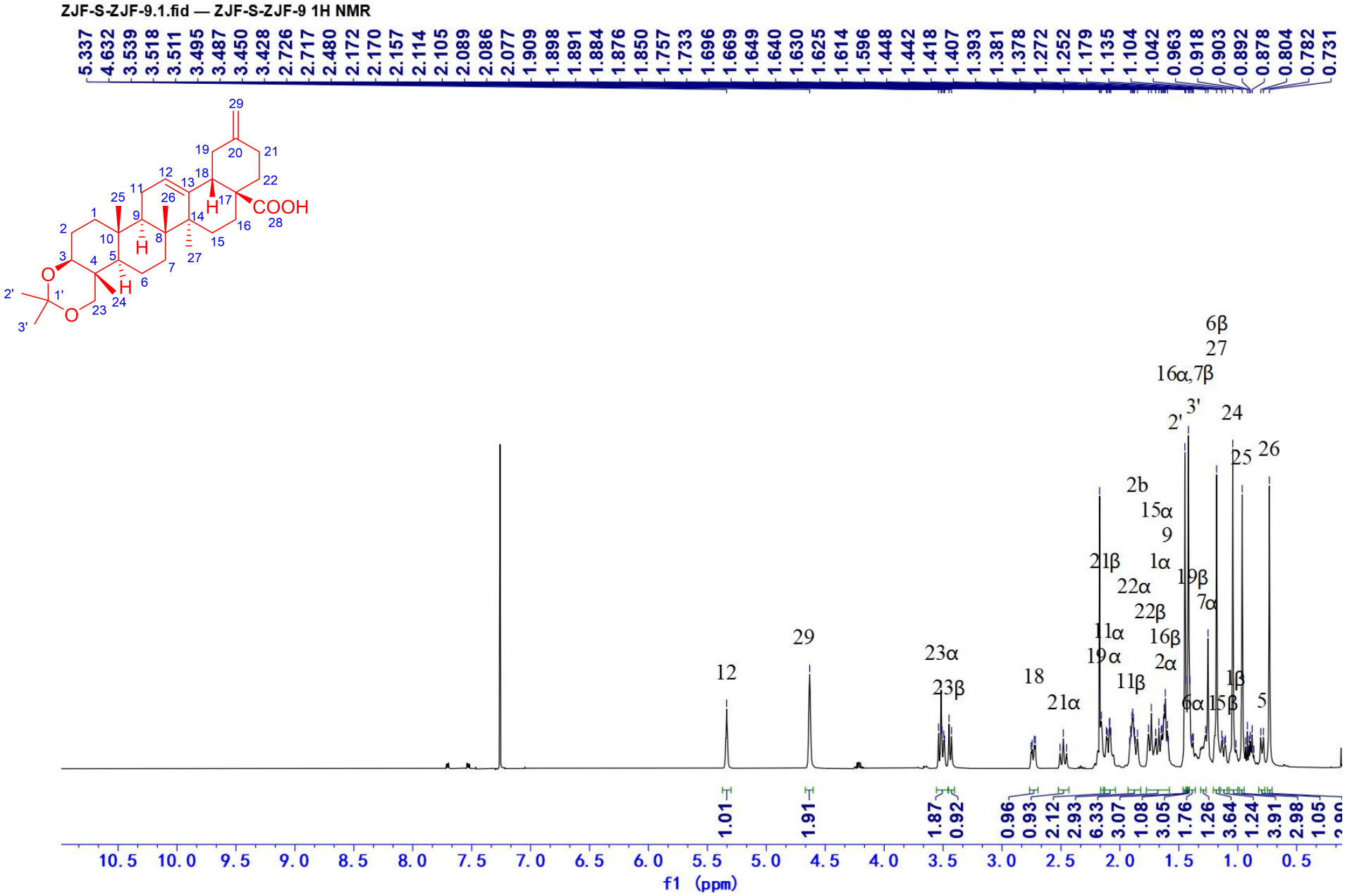


Figure S115. The ^{1}H NMR Spectrum of Compound 26 in CD_3Cl (500MHz)

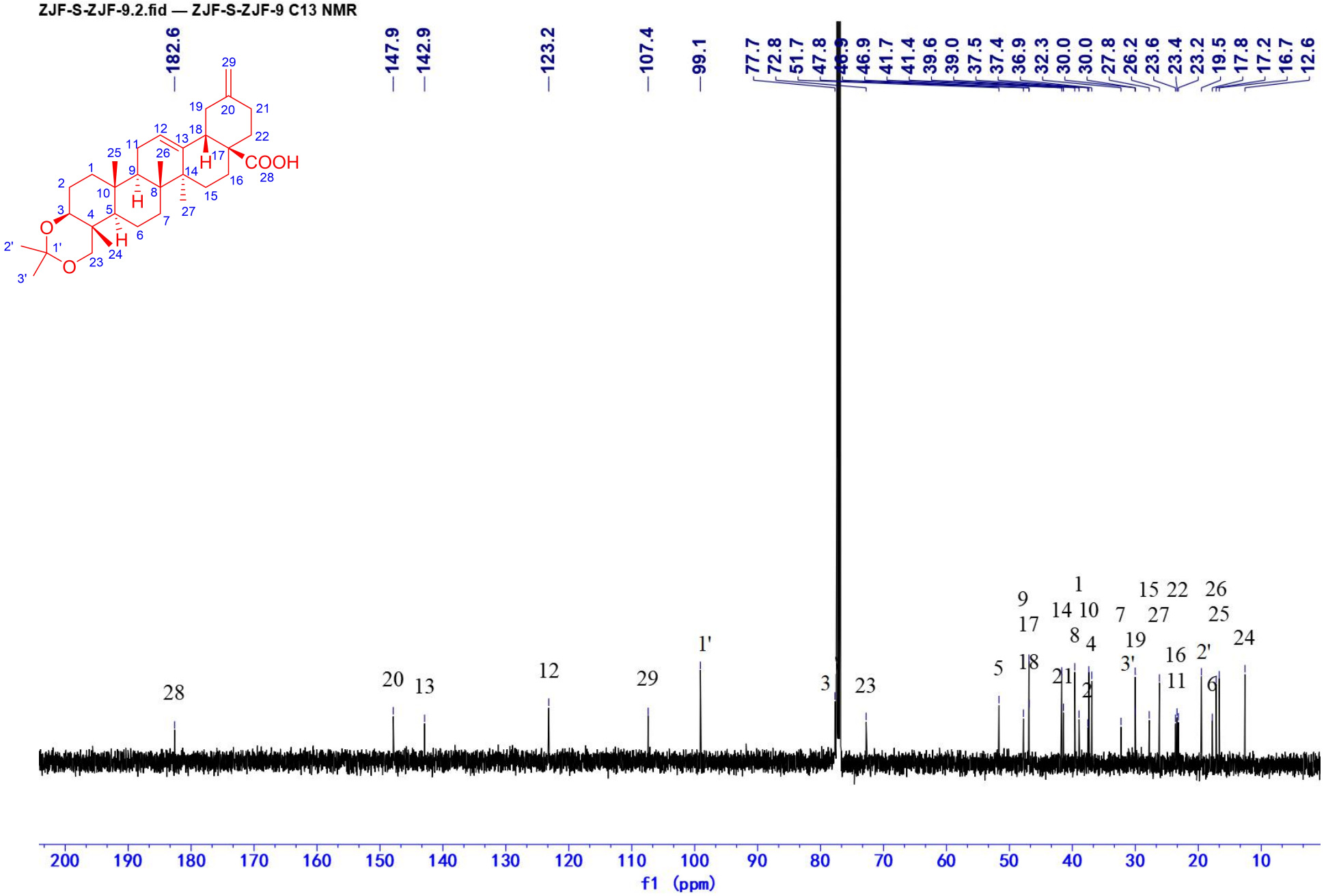


Figure S116. The ^{13}C NMR Spectrum of Compound 26 in CD_3Cl (125MHz)

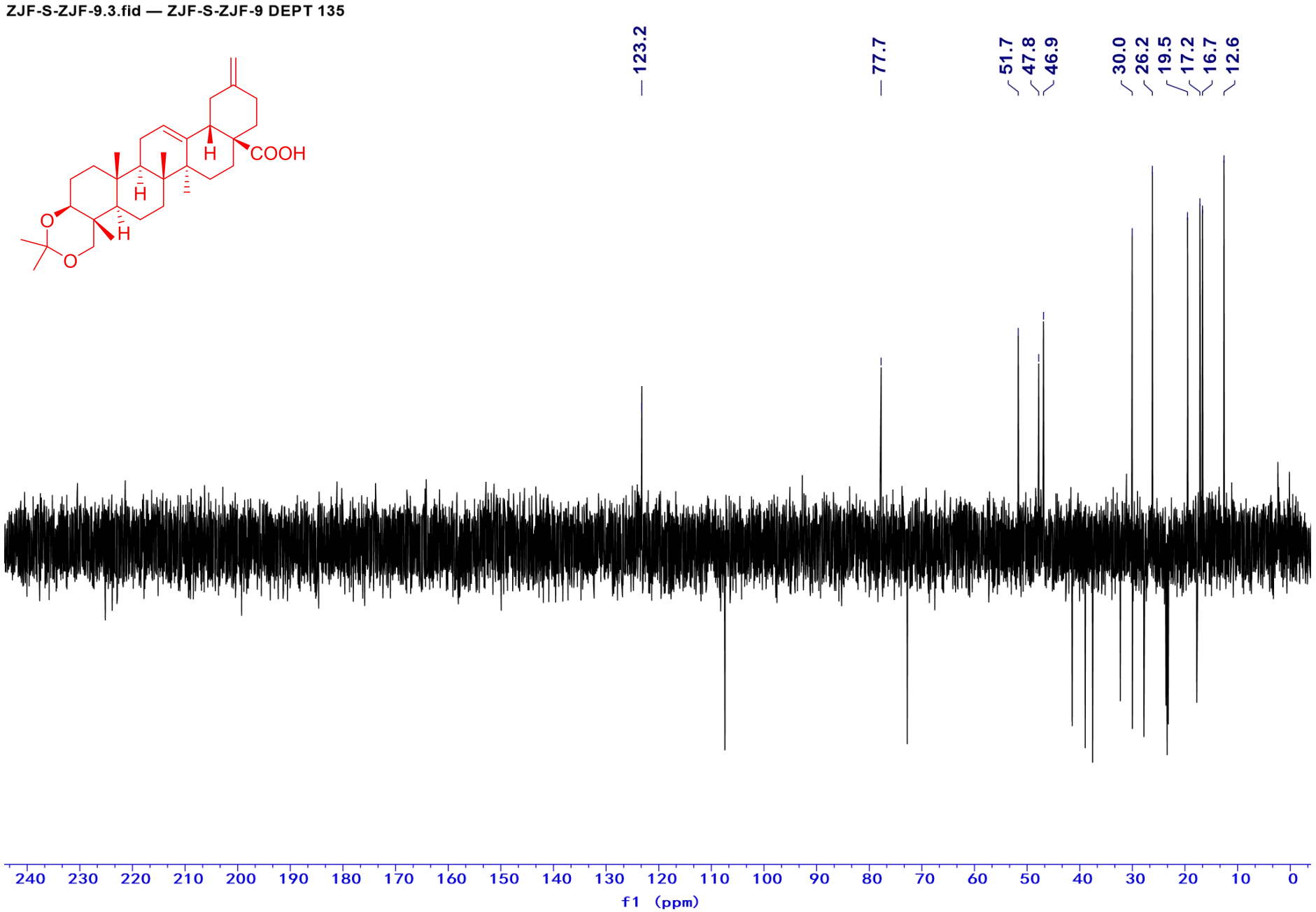


Figure S117. The DEPT Spectrum of Compound 26 in CD_3Cl (125MHz)

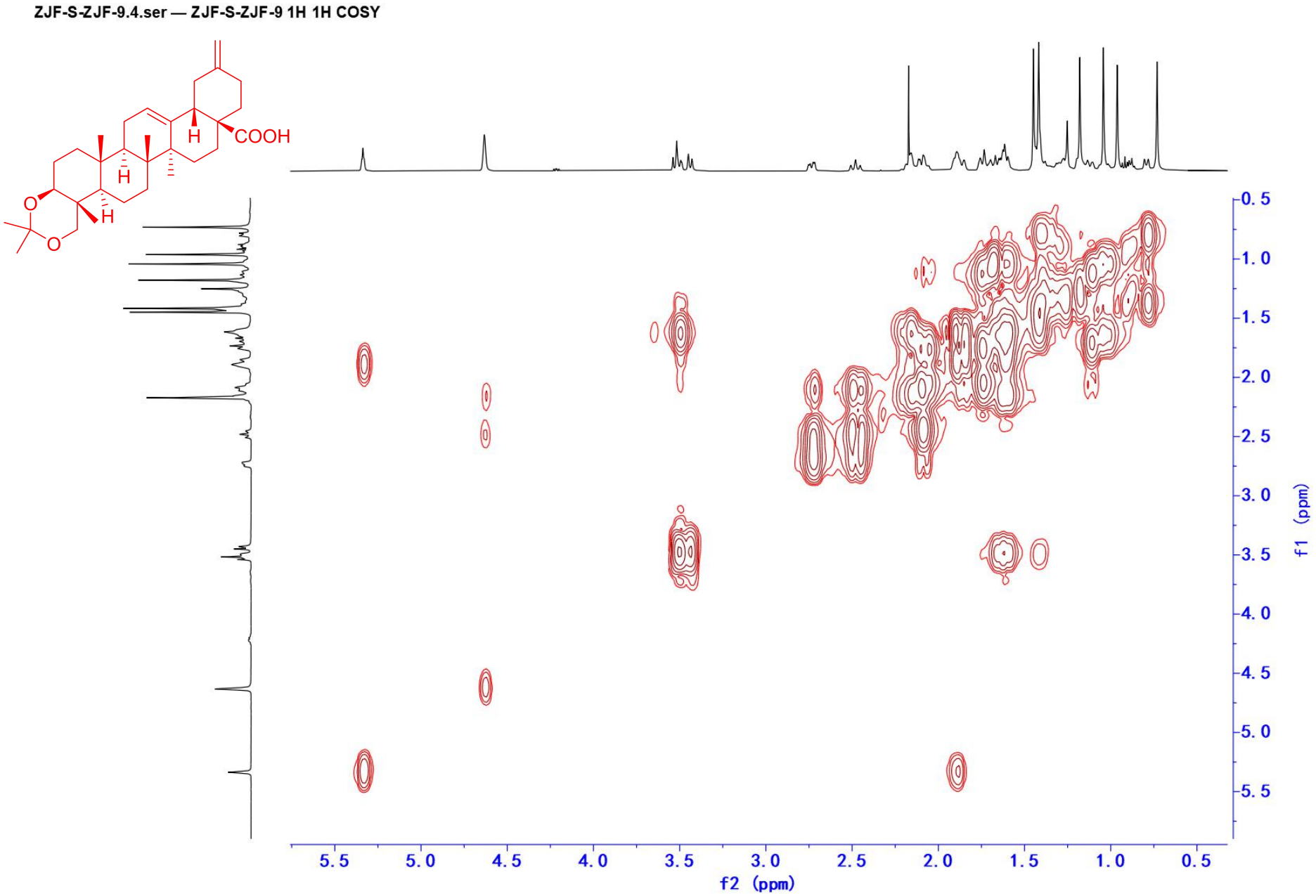


Figure S118. The ^{1}H-^{1}H COSY Spectrum of Compound 26 in CD_3Cl (500MHz)

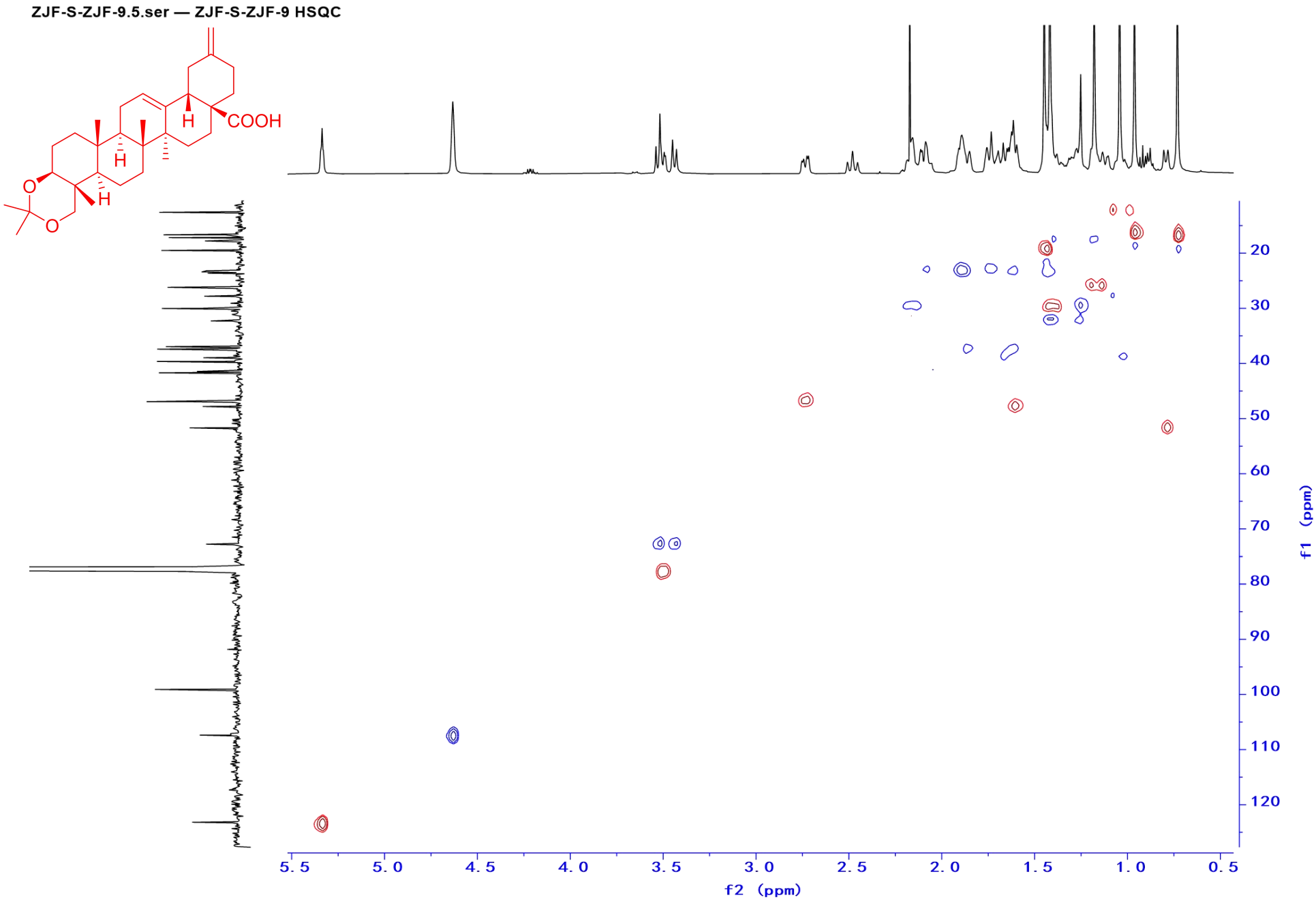


Figure S119. The HSQC Spectrum of Compound 26 in CD_3Cl (500MHz)

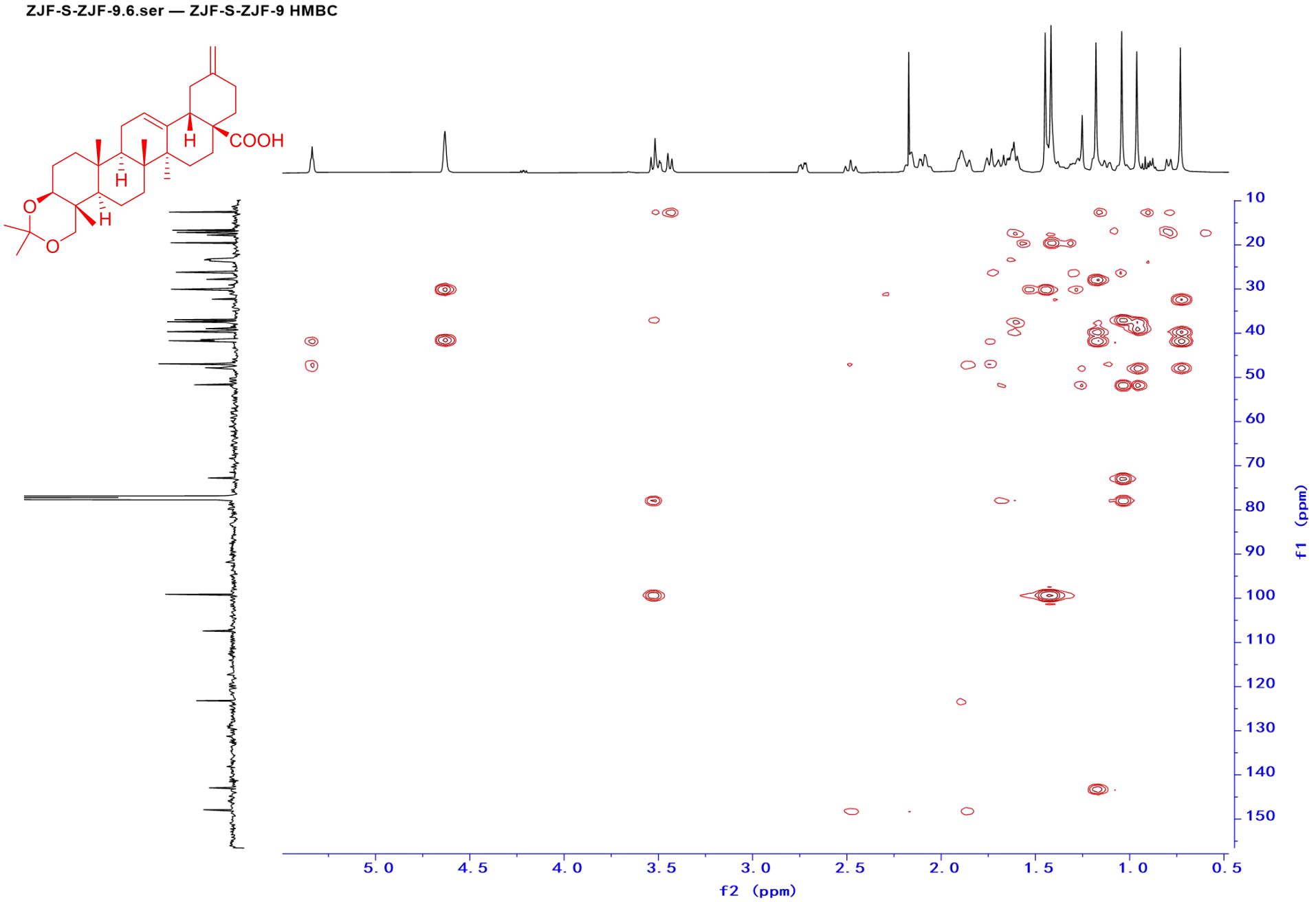


Figure S120. The HMBC Spectrum of Compound 26 in CD_3Cl (500MHz)

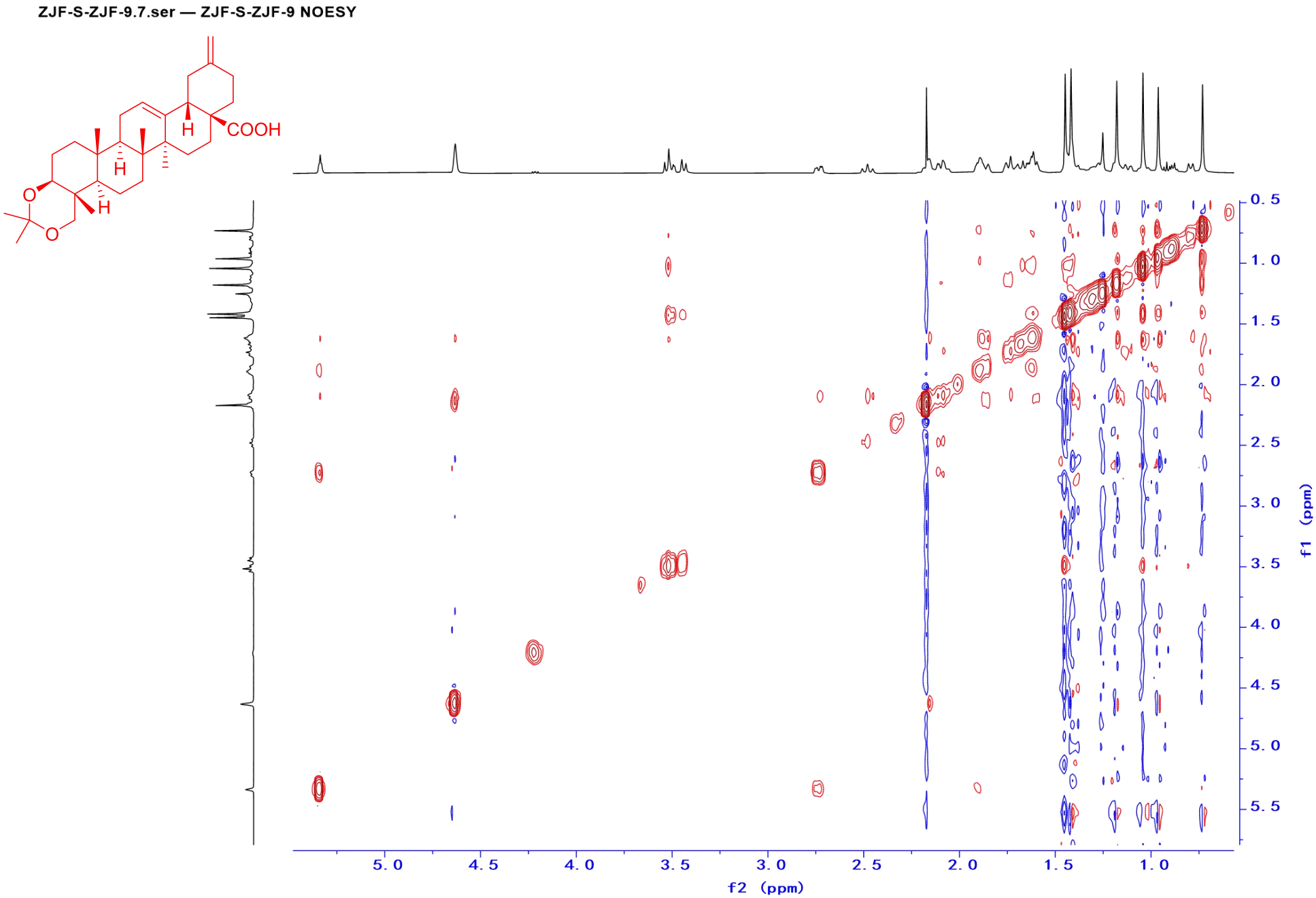


Figure S121. The NOESY Spectrum of Compound 26 in CD_3Cl (500MHz)

In silico prediction of ECD spectrum

All calculations were performed using Gaussian 16. [1] Conformation search using molecular mechanics calculations was performed in MOE (Molecular Operating Environment) 2015 with MMFF94s force field with 20 kcal mol^{-1} upper energy limit at best level. The conformers performed with the MOE 2015 software package were further optimized by using the TDDFT method at the B3LYP/6-31G (d, p) level, and the frequency was calculated at the same level of theory. For all optimized structures, vibrational spectra were calculated to ensure that no imaginary frequencies for energy minimum were obtained. The average values were obtained by the Boltzmann distributions, using the relative Gibbs free energies as weighting factors. The stable conformers were subjected to ECD calculation by the TDDFT method at the B3LYP/6-311G+ (d, p) level with the CPCM model in MeOH. ECD spectra of different conformers were simulated using SpecDis 1.71with a half-bandwidth of 0.3 eV, [2] and the final calculated ECD spectra were obtained according to the Boltzmann-calculated contribution of each con-former. The calculated ECD spectra were compared with the experimental data.

Refferences.

1. Gaussian 16, Revision A.03, M. J. Frisch, G. W. Trucks, H. B. Schlegel, G. E. Scuseria, M. A. Robb, J. R. Cheeseman, G. Scalmani, V. Barone, G. A. Petersson, H. Nakatsuji, X. Li, M. Caricato, A. V. Marenich, J. Bloino, B. G. Janesko, R. Gomperts, B. Mennucci, H. P. Hratchian, J. V. Ortiz, A. F. Izmaylov, J. L. Sonnenberg, D. Williams-Young, F. Ding, F. Lipparini, F. Egidi, J. Goings, B. Peng, A. Petrone, T. Henderson, D. Ranasinghe, V. G. Zakrzewski, J. Gao, N. Rega, G. Zheng, W. Liang, M. Hada, M. Ehara, K. Toyota, R. Fukuda, J. Hasegawa, M. Ishida, T. Nakajima, Y. Honda, O. Kitao, H. Nakai, T. Vreven, K. Throssell, J. A. Montgomery, Jr., J. E. Peralta, F. Ogliaro, M. J. Bearpark, J. J. Heyd, E. N. Brothers, K. N. Kudin, V. N. Staroverov, T. A. Keith, R. Kobayashi, J. Normand, K. Raghavachari, A. P. Rendell, J. C. Burant, S. S. Iyengar, J. Tomasi, M. Cossi, J. M. Millam, M. Klene, C. Adamo, R. Cammi, J. W. Ochterski, R. L. Martin, K. Morokuma, O. Farkas, J. B. Foresman, and D. J. Fox, Gaussian, Inc., Wallingford CT, **2016**.

2. T. Bruhn, A. Schaumlöffel, Y. Hemberger, G. Pescitelli, SpecDis version 1.71, Berlin, Germany, **2017**, http:/specdis-software.jimdo.com.

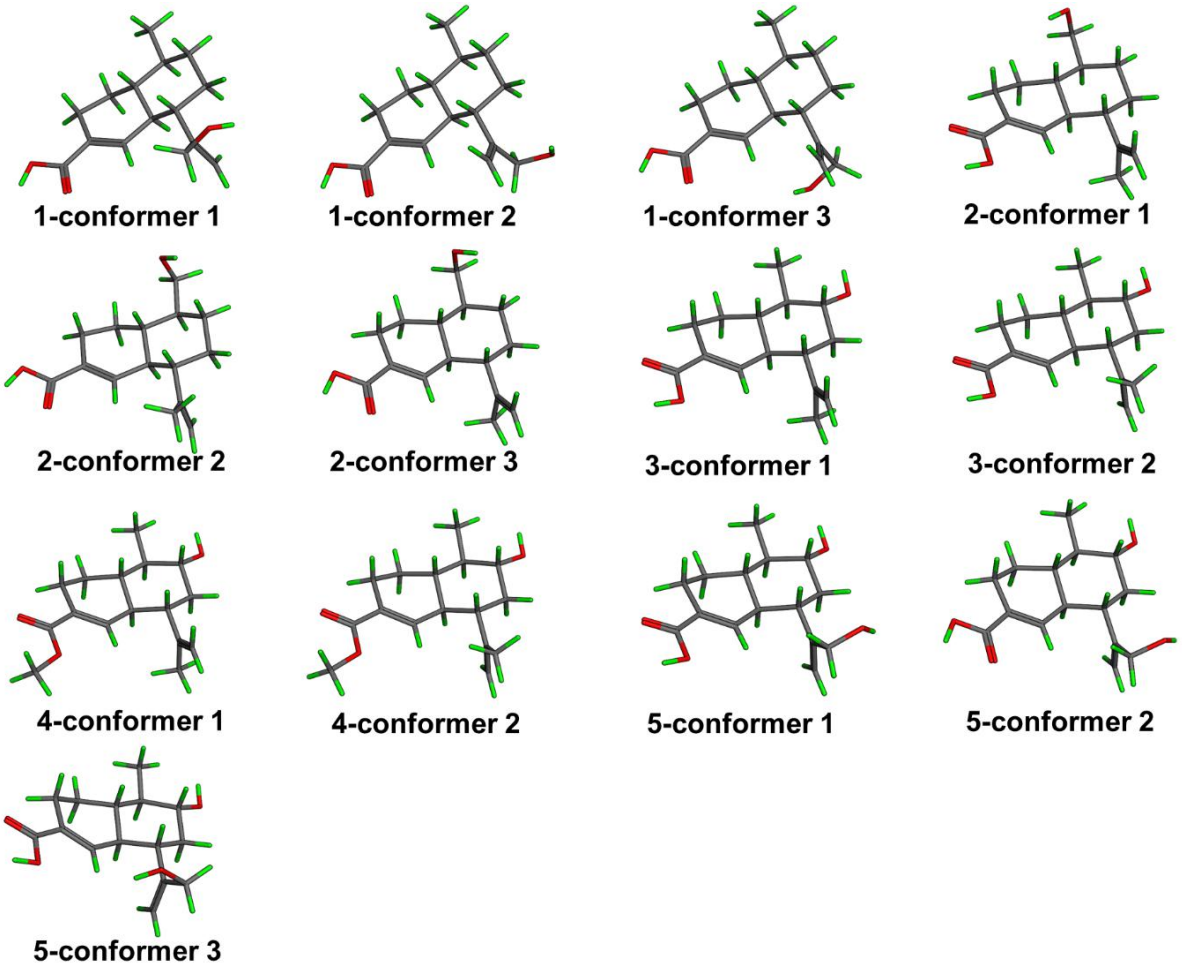


Figure S122. Low-energy Conformers of 1-5 in MeOH

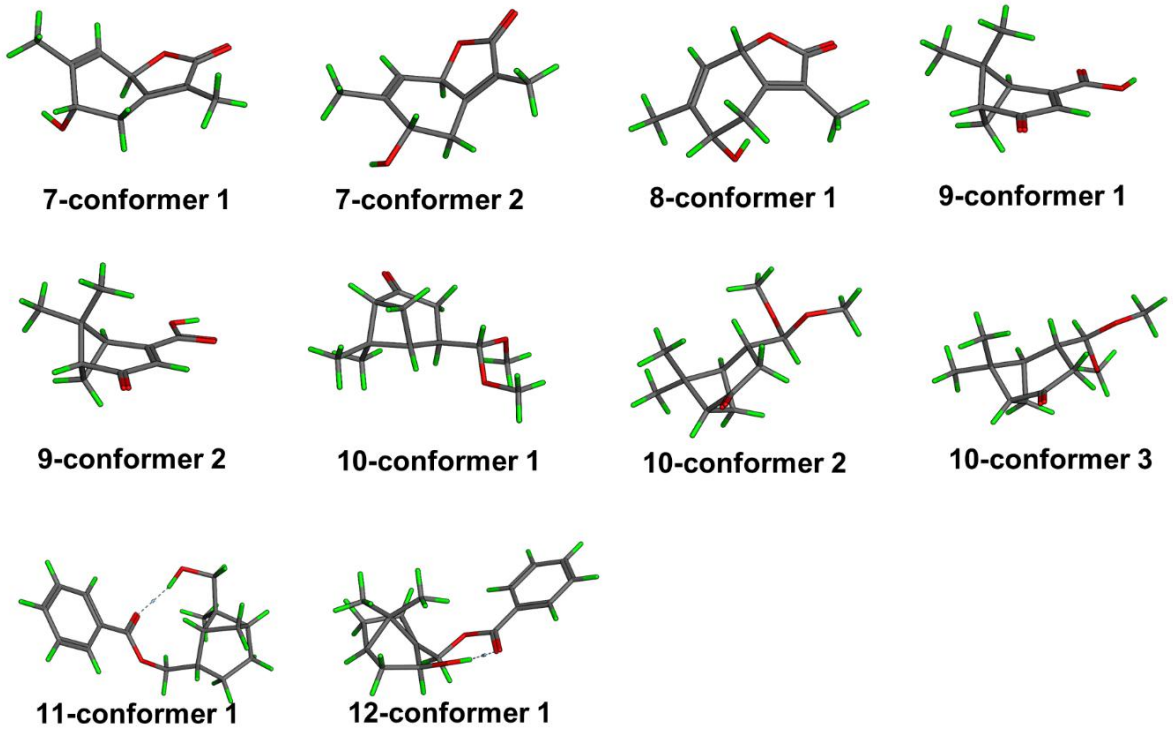


Figure S123. Low-energy Conformers of 7-12 in MeOH

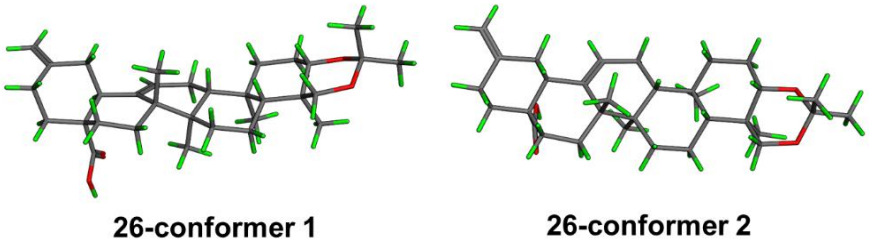


Figure S124. Low-energy Conformers of 26 in MeOH

Table S1. Relative Energies, Equilibrium Populations, Extracted heats and weighting factors of the optimized conformers of 1-5, 7-12 and 26 at B3LYP/6-311+G(d,p) level in MeOH with PCM

	Conformer	Relative Energies (kcal/mol)	Equilibrium Populations	Extracted heats (kcal/mol)	Boltzmann-calculated contribution(%)
1	1	0	0.566488367	-810.7540875	0
	2	0.40124696	0.287661470	-810.7538160	64.68
	3	0.83766931	0.137648574	-810.7522632	35.32
2	1	0	0.317138599	-810.7551857	48.72
	2	0.05453676	0.289232517	-810.7533952	15.64
	3	0.22636622	0.216377698	-810.7540376	35.64
3	1	0	0.563825898	-810.7600376	79.72
	2	0.16441619	0.427118060	-810.7587003	20.28
4	1	0	0.416040206	-850.0683802	81.28
	2	0.045812536	0.385063557	-850.0670320	18.72
5	1	0	0.299089009	-886.0000824	34.65
	2	0.18405204	0.219179905	-885.9995412	20.42
	3	0.34520575	0.166953925	-886.0003855	44.93
7	1	0	0.567562022	-614.1338724	0.9
	2	0.16099747	0.432437978	-614.1383070	99.1
8	1	0	0.999986637	-614.1384280	100
9	1	0	0.608080616	-614.1207607	70.27
	2	0.26007891	0.391919384	-614.1198746	29.73
10	1	0	0.377160690	-695.1496450	43.11
	2	0.16968693	0.283180483	-695.1497852	50.16
	3	0.47312698	0.169626650	-695.1479860	6.73
11	1	0	0.789955155	-886.9608809	100
12	1	0	0.940813546	-886.9765052	100
26	1	0	0.580513415	-1549.6159635	58.54
	2	0.197291	0.416009598	-1549.6156148	41.46

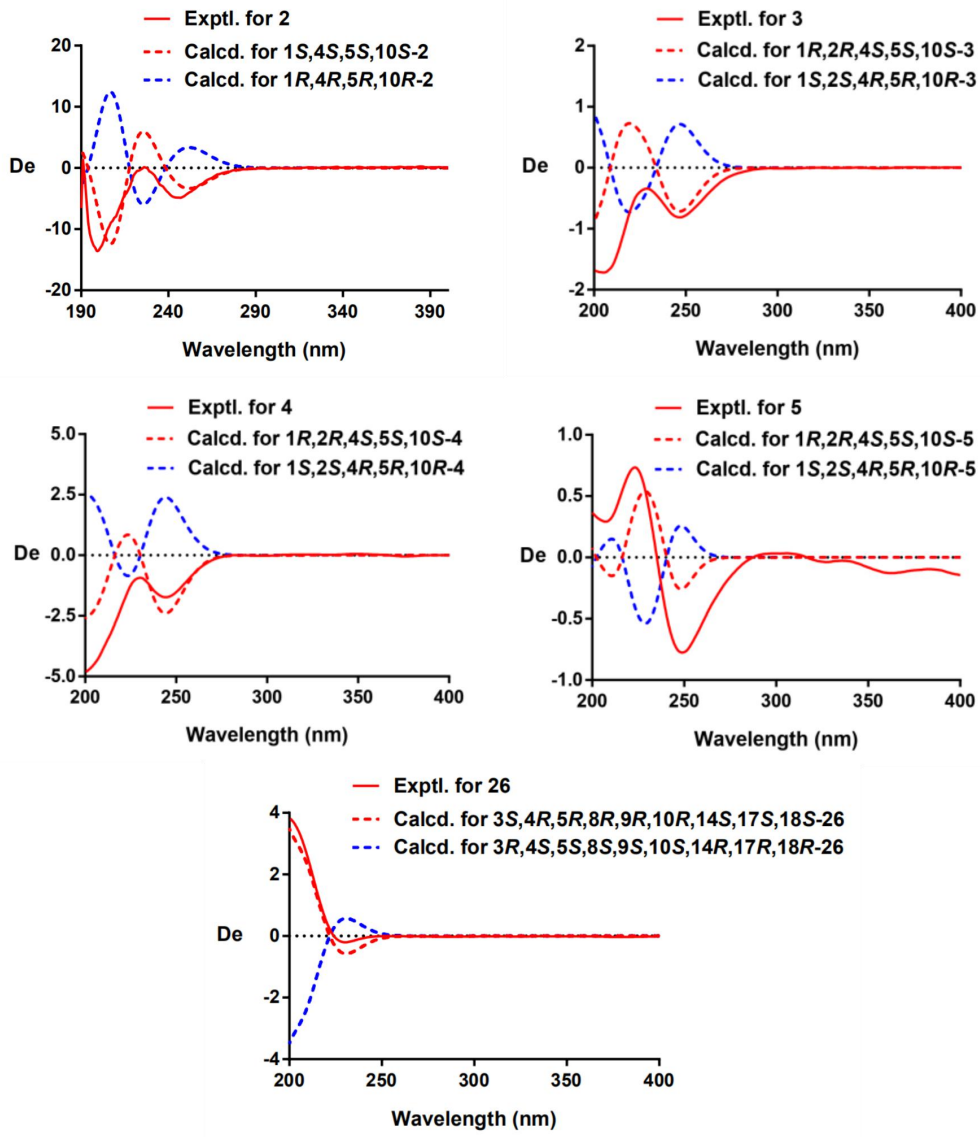


Figure S125. Experimental and calculated ECD data of compounds 2-5 and 26

General Experimental Procedures

Melting points were obtained on a Boetius Micro Melting Point Apparatus. Optical rotations were measured on a Rudolph Research Autopol III automatic polarimeter. UV spectra were measured on a Cary 300 spectrometer. ECD spectra were recorded on a JASCO J-815 spectrometer. IR spectra were obtained on a Nicolet Impact 400 FT-IR Spectrophotometer. The NMR experiments were conducted on a Bruker spectrometer (600 MHz for ^{1}H or 150 MHz for ^{13}C) or a Varian INOVA spectrometer (500 MHz for ^{1}H or 125 MHz for ^{13}C) equipped with an inverse detection probe. HR-ESIMS data were acquired on an Agilent 6520 Accurate-Mass Q-TOFL CMS spectrometers (Agilent Technologies, Ltd., Santa Clara, CA, USA). Column chromatography (CC) was run using MCI gel (CHP20P), silica gel (100-200 or 200-300 mesh, Qingdao Marine Chemical Inc., China), and Sephadex LH-20 (Pharmacia Biotech AB, Uppsala Sweden). Analytical HPLC was performed with an Agilent HP 1260 using a Titank column (Guangzhou FLM Scientific Instrument Co., Ltd.) packed with C_{18} (250 × 4.6 mm, 5 μm). HPLC separation was conducted on Waters HPLC equipment, namely, a Waters 600 pump, a Waters 600 controller, and Waters 2487 dual λ absorbance detector, using the following columns: Shiseido Capcell Pak MGIII C_{18} (250 × 4.6 mm, 5 μm), Waters XBridge^{TM} Prep Shield RP_{18} (250 × 10 mm, 5 μm), Welch Ultimate® XB-Phenyl (250 × 10 mm, 5 μm) and Welch Ultimate® XB-C8 (250 × 10 mm, 5 μm). All fluorescence-based assays were performed on a SpectraMax® iD3 Molecular Device.

Table S2. The Inhibitory Activity of Fractions A-J Against hCEs

Fractions	Inhibition (%) 10 μg/mL	
	hCES1A1	hCES2A1
A	**67.19**	**59.79**
B	**74.03**	**78.27**
C	**64.64**	**92.02**
D	**52.86**	**78.14**
E	**37.11**	**71.95**
F	**15.21**	**52.70**
G	**2.99**	**58.88**
H	**20.71**	**64.62**
I	**13.28**	**53.31**
J	**-0.29**	**45.08**

Table S3. IC_{50} Values of 1, 6, 10, 11, 13–15, 18–20, 22, and 24–26 on hCES2A1

compounds	IC_{50} (μM)	compounds	IC_{50} (μM)
1	5.1 ± 0.44	**18**	14.5 ± 2.84
6	3.8 ± 0.53	**19**	1.9 ± 0.26
10	6.3 ± 0.58	**20**	4.6 ± 0.59
11	8.2 ± 0.91	**22**	5.0 ± 0.98
13	10.2 ± 1.39	**24**	2.2 ± 0.23
14	16.8 ± 2.79	**25**	5.3 ± 0.66
15	5.8 ± 1.10	**26**	4.6 ± 0.27
LPA	1.20±0.10		

Table S4. IC_{50} Values of 18–26 on hCES1A1

compounds	IC_{50} (μM)
18	0.14±0.01
19	2.12±0.12
20	0.13±0.02
21	0.26±0.04
22	0.57±0.03
23	0.37±0.04
24	1.1±0.10
25	2.3±0.21
26	4.1±0.57