Electronic Supplementary Material (ESI) for Organic Chemistry Frontiers.

Supporting Information

Cunlanceloic acids A-D: unprecedented labdane diterpenoid dimers with AChE inhibitory and cytotoxic activities from *Cunninghamia lanceolata*

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Contents

X-ray Crystallographic Analysis of Compounds 1-3

Crystals of **1-3** were obtained by using the solvent vapor diffusion in methanol at room tempetature. Crystallographic data for **1-3** were collected on a Bruker APEX DUO diffractometer with graphite monochromater Cu Kα radiation. Crystal structures were solved by direct methods with SHELXS-97, expanded using difference Fourier technique, and refined with full-matrix least-squares on F^2 using SHELXS-97. Non-hydrogen atoms were refined anisotropically. Hydrogen atom were placed in idealized positions and refined using a riding model. Crystallographic data for compounds **1-3** have been deposited in the Cambridge Crystallographic Data Centre (deposition numbers: CCDC 2051450, 2051451, and 2051453, respectively). Copies of these data can be obtained free of charge via www.ccdc.cam.ac.uk (or from the Cambridge Crystallographic Data Centre, 12, Union Road, CAMBRIDGE CB2 1EZ, UK.; fax: (+44) 1223-336-033; or deposit@ccdc.cam.ac.uk).

Table S1. Crystallographic data of compound **1**.

Identification code	cu_fwf202_2_0m
Empirical formula	$1/2(C_{40}H_{56}O_6)$
Formula weight	316.42
Temperature	100(2) K
Wavelength	1.54178 Å
Crystal system	Orthorhombic
Space group	$C222_1$
Unit cell dimensions	a = 8.8961(3) Å a = 90°
	b = 10.7470(4) Å b = 90°
	c = 36.9444(14) Å g = 90°
Volume	3532.1(2) $Å^3$
Z	8
Calculated density	1.190 Mg/m^3
Absorption coefficient	0.618 mm^{-1}
F(000)	1376
Crystal size	0.585 x 0.570 x 0.230 mm^3
Theta range for data collection	4.788 to 69.086°
Indices ranges	$-9\leq h\leq 10$, $-12\leq k\leq 11$, $-42\leq l\leq 38$
Reflections collected	10155
Independent reflections	3084 [R(int) = 0.0253]
Completeness to theta = 67.679°	97.2 %
Absorption correction	Semi-empirical from equivalents
Refinement method	Full-matrix least-squares on F^2
Data/restraints/parameters	3084/0/211
Goodness-of-fit on F^2	1.047
Final R indices [$I > 2\sigma(I)$]	R_1 = 0.0310, wR_2 = 0.0776
R indices (all data)	R_1 = 0.0314, wR_2 = 0.0779
Absolute structure parameter	0.08(5)
Largest diff. peak and hole	0.168 and -0.196 $e.Å^{-3}$

Table S2. Crystallographic data of compound **2**.

Identification code	cu_fwf200_0m
Empirical formula	$2(C_{40}H_{60}O_3)\bullet H_2O$
Formula weight	1195.77
Temperature	100(2) K
Wavelength	1.54178 Å
Crystal system	Monoclinic
Space group	$P2_1$
Unit cell dimensions	a = 17.6987(3) Å α = 90°
	b = 7.57510(10) Å β = 105.9950(10)°
	c = 27.9558(5) Å γ = 90°
Volume	3602.92(10) $Å^3$
Z	2
Calculated density	1.102 Mg/m^3
Absorption coefficient	0.522 mm^{-1}
F(000)	1316
Crystal size	1.120 x 0.160 x 0.070 mm^3
Theta range for data collection	2.597 to 69.625°
Indices ranges	$-20\leq h\leq 20$, $-8\leq k\leq 7$, $-33\leq l\leq 32$
Reflections collected	34015
Independent reflections	10348 [R(int) = 0.0533]
Completeness to theta = 67.679°	95.3 %
Absorption correction	Semi-empirical from equivalents
Refinement method	Full-matrix least-squares on F^2
Data/restraints/parameters	10348 / 1 / 798
Goodness-of-fit on F^2	1.109
Final R indices [$I > 2\sigma(I)$]	R_1 = 0.0591, wR_2 = 0.1822
R indices (all data)	R_1 = 0.0636, wR_2 = 0.1928
Absolute structure parameter	0.04(11)
Largest diff. peak and hole	0.325 and -0.356 $e.Å^{-3}$

Table S3. Crystallographic data of compound **3**.

Identification code	cu_fwf199a_0m
Empirical formula	$3(C_{40}H_{60}O_3)\bullet 2(H_2O)$
Formula weight	1802.66
Temperature	100(2) K
Wavelength	1.54178 Å
Crystal system	Triclinic
Space group	P1
Unit cell dimensions	a = 7.3306(3) Å α = 79.290(2)°
	b = 13.0551(5) Å β = 89.420(2)°
	c = 29.0818(10) Å γ = 75.423(2)°
Volume	2644.70(18) Å^3
Z	1
Calculated density	1.132 Mg/m^3
Absorption coefficient	0.539 mm^{-1}
F(000)	992
Crystal size	0.880 x 0.250 x 0.030 mm^3
Theta range for data collection	3.095 to 69.052°
Indices ranges	-8≤h≤8, -14≤k≤15, -34≤l≤35
Reflections collected	36317
Independent reflections	14387 [R(int) = 0.0526]
Completeness to theta = 67.679°	93.6 %
Absorption correction	Semi-empirical from equivalents
Refinement method	Full-matrix least-squares on F^2
Data/restraints/parameters	14387 / 3 / 1200
Goodness-of-fit on F^2	1.028
Final R indices [$I > 2\sigma(I)$]	R_1 = 0.0724, wR_2 = 0.1806
R indices (all data)	R_1 = 0.0808, wR_2 = 0.1883
Absolute structure parameter	-0.04(16)
Largest diff. peak and hole	0.690 and -0.427 e.Å^{-3}

Figure S1. ^{1}H NMR (800 MHz) spectrum of cunlanceloic acid A (**1**) in pyridine-d_5.

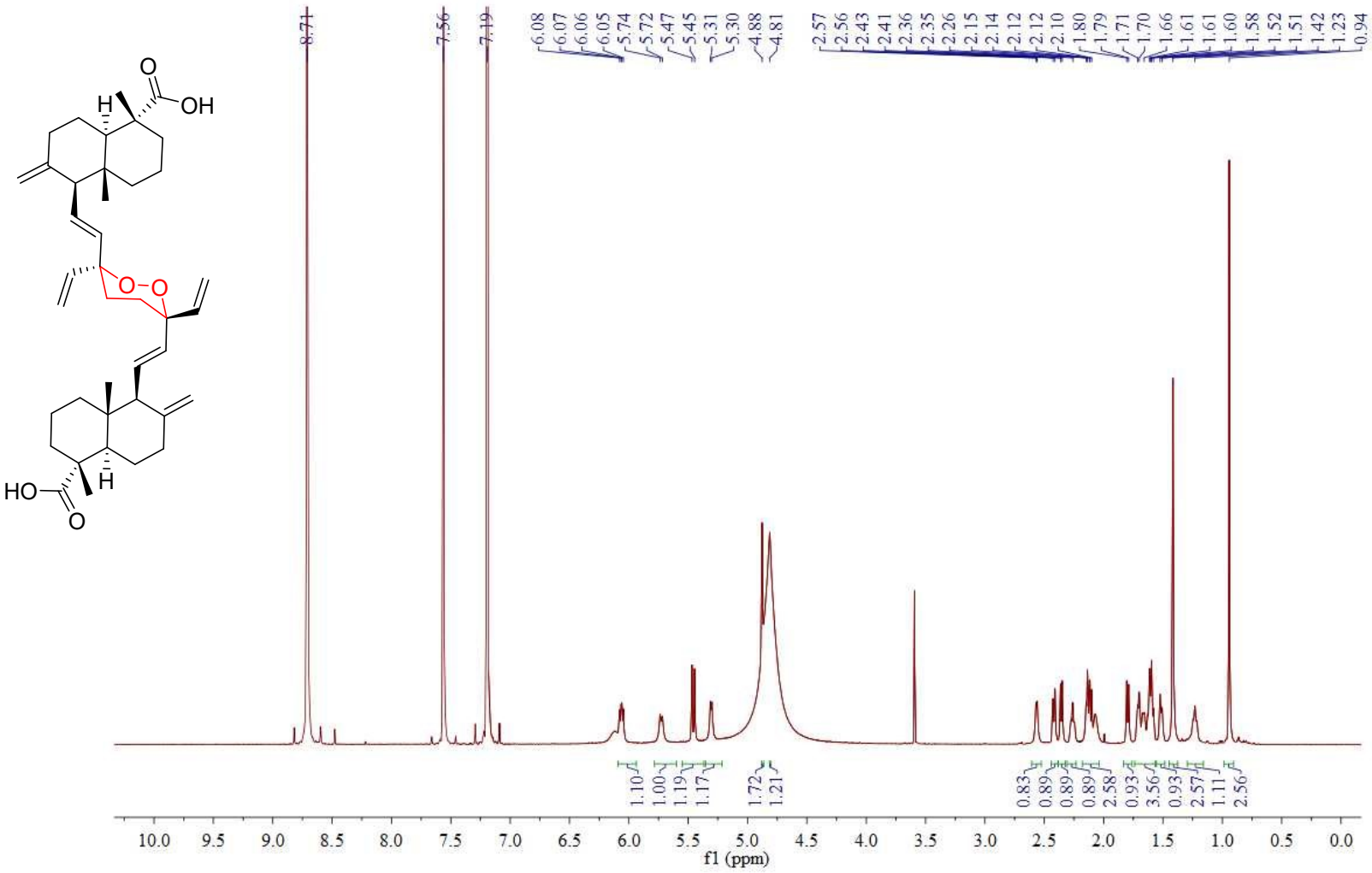


Figure S2. Expanded ^{1}H NMR spectrum of cunlanceloic acid A (**1**).

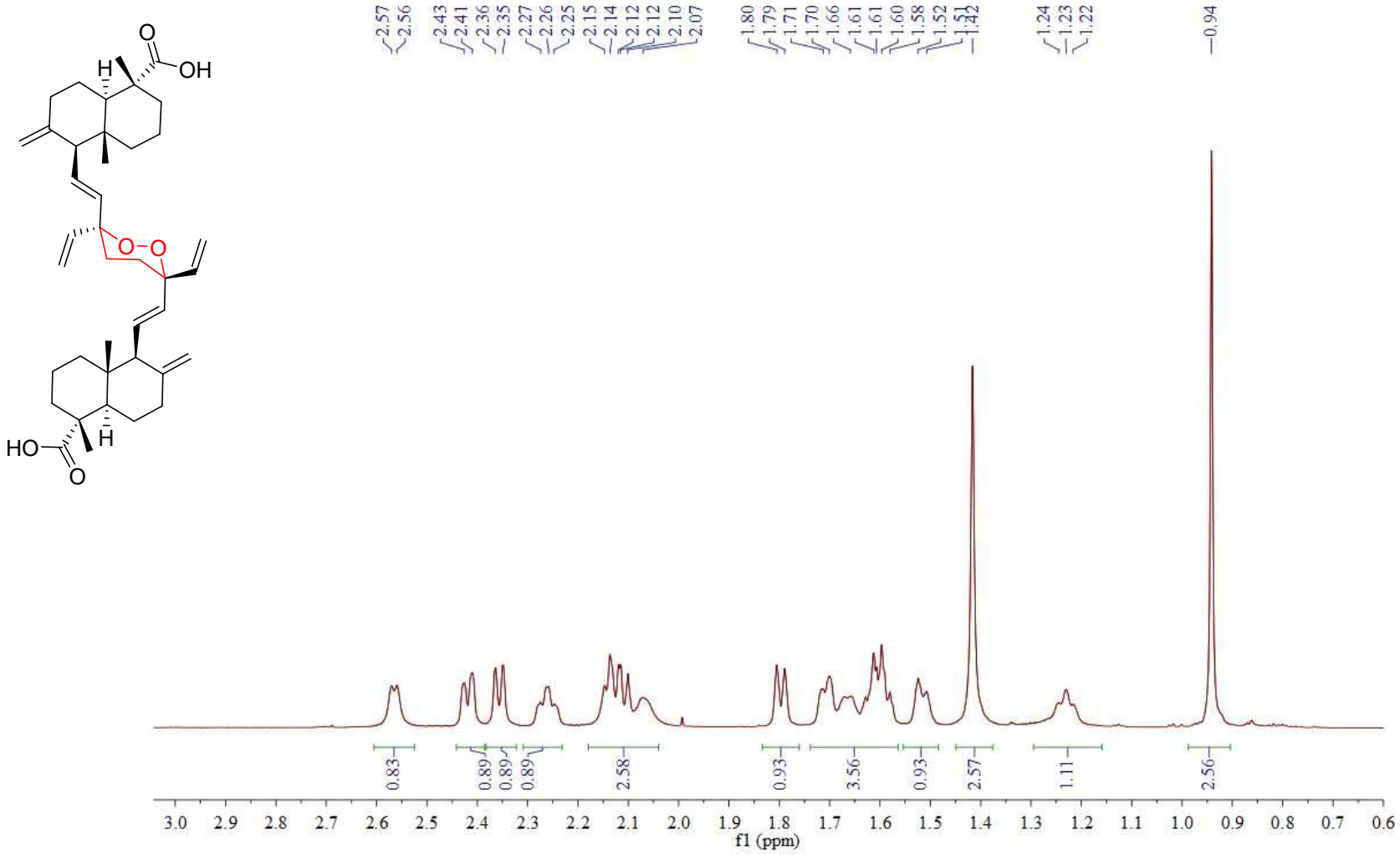


Figure S3. ^{13}C NMR and DEPT (200 MHz) spectra of cunlanceloic acid A (**1**) in pyridine-d_5.

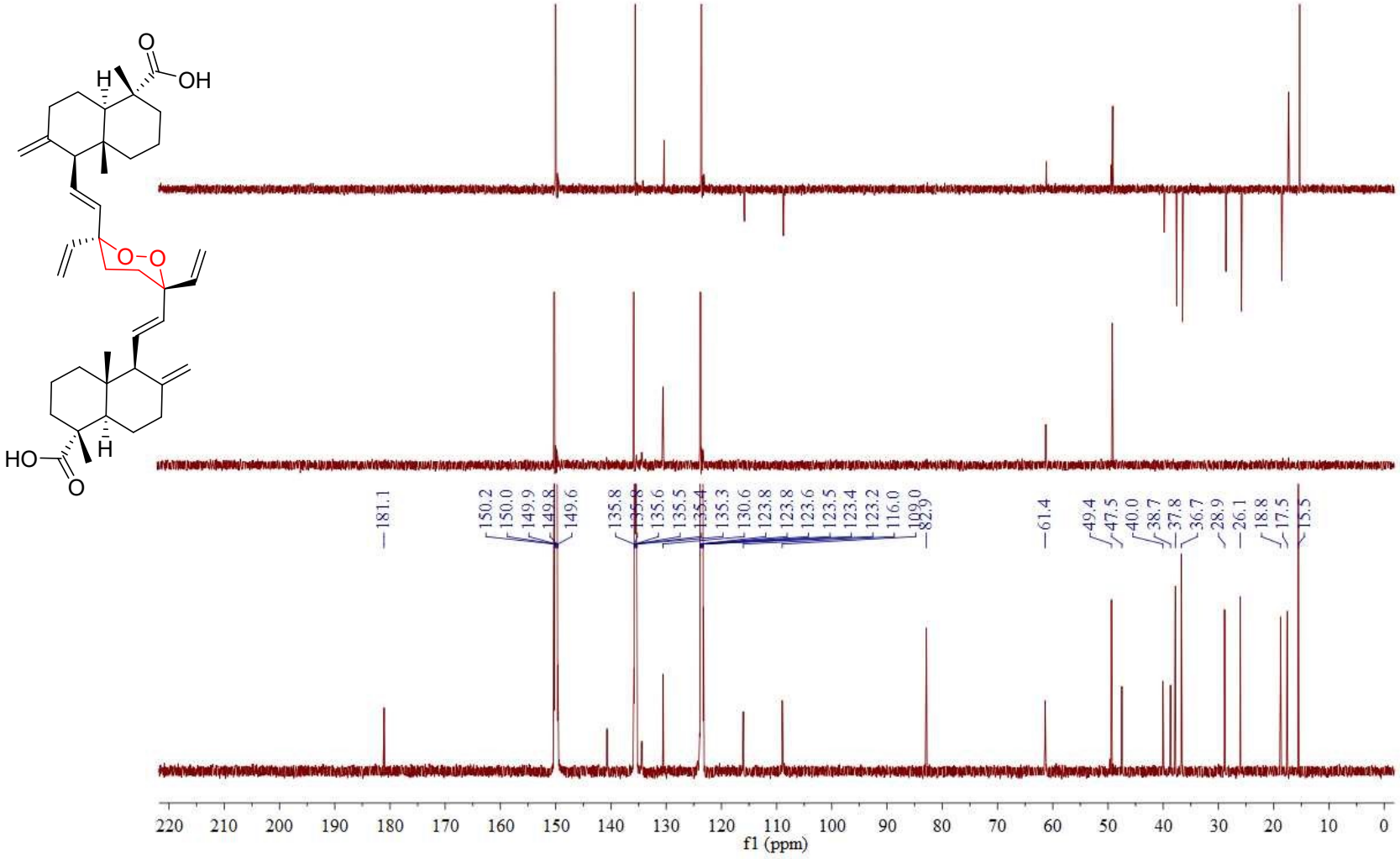


Figure S4. HSQC spectrum of cunlanceloic acid A (**1**).

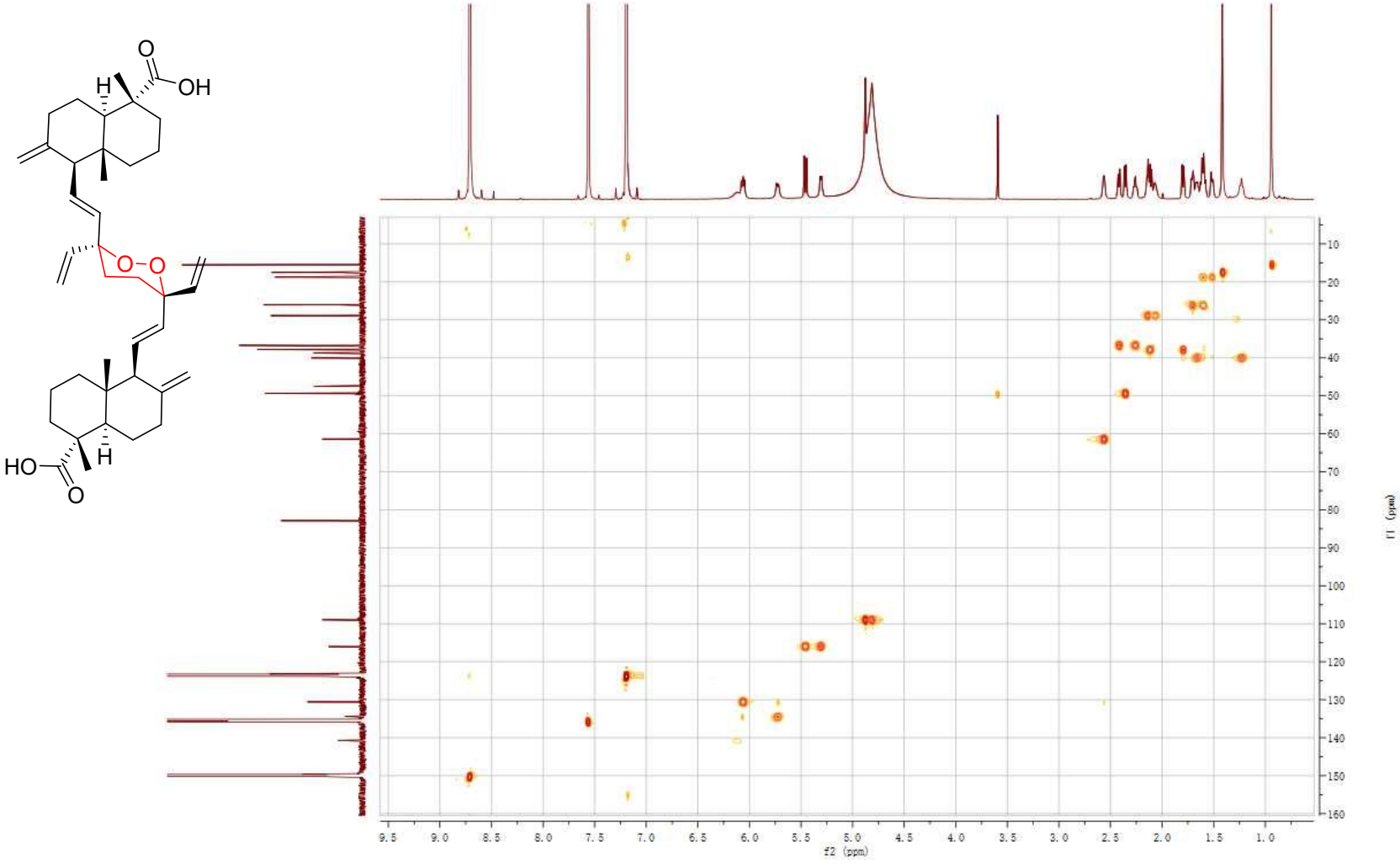


Figure S5. Expanded HSQC spectrum of cunlanceloic acid A (**1**).

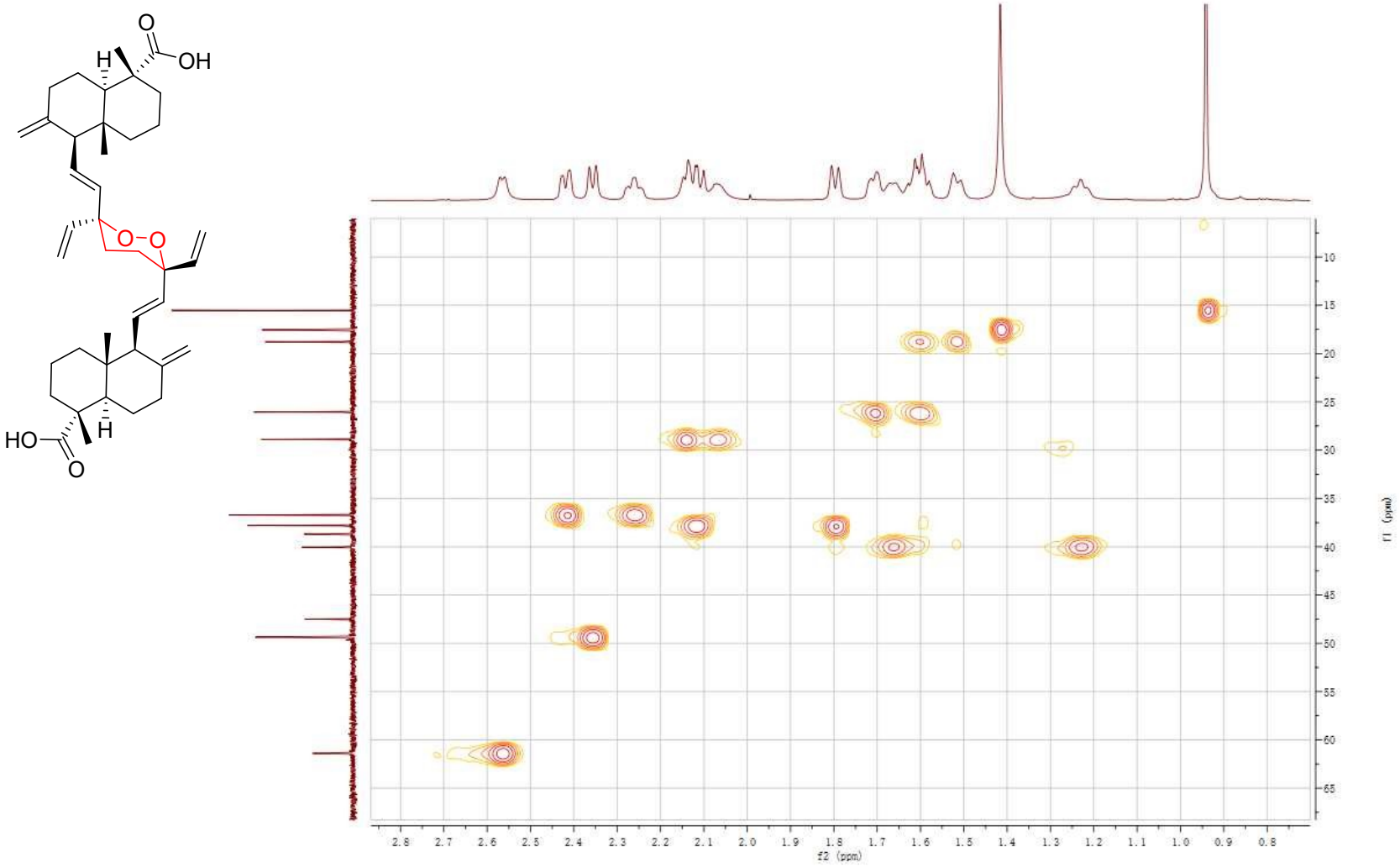


Figure S6. ^{1}H-^{1}H COSY spectrum of cunlanceloic acid A (**1**).

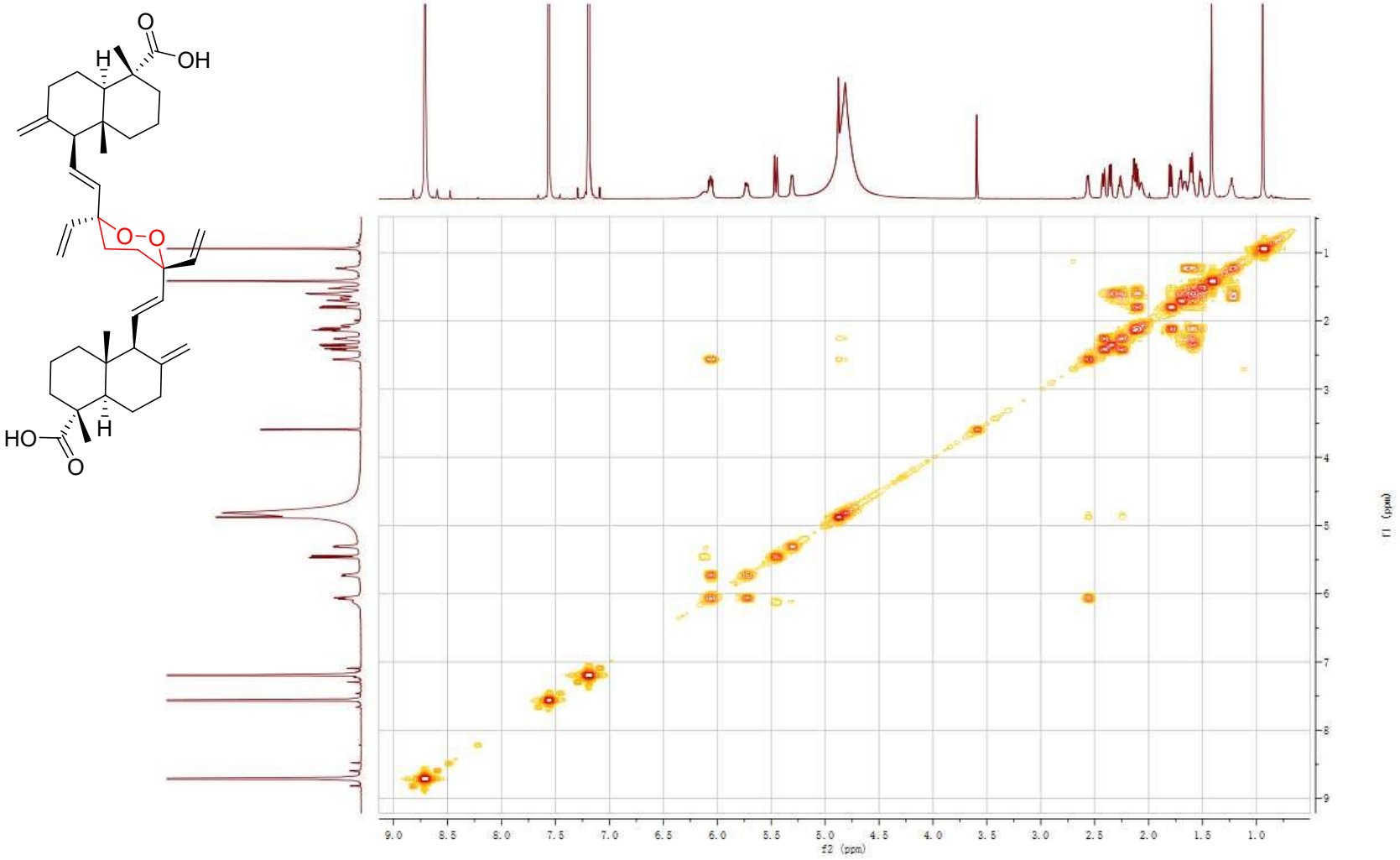


Figure S7. Expanded ^{1}H-^{1}H COSY spectrum of cunlanceloic acid A (**1**).

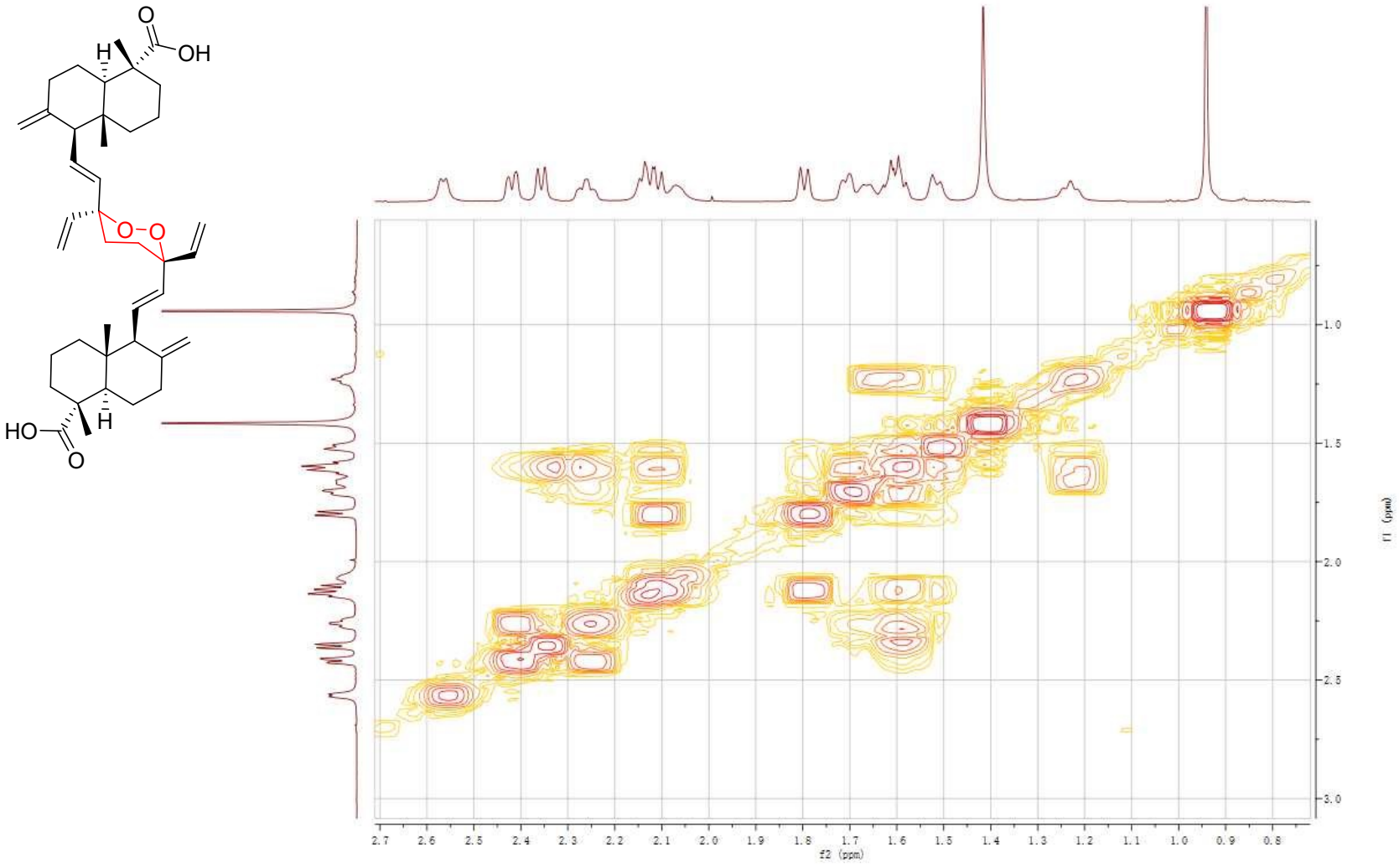


Figure S8. HMBC spectrum of cunlanceloic acid A (**1**).

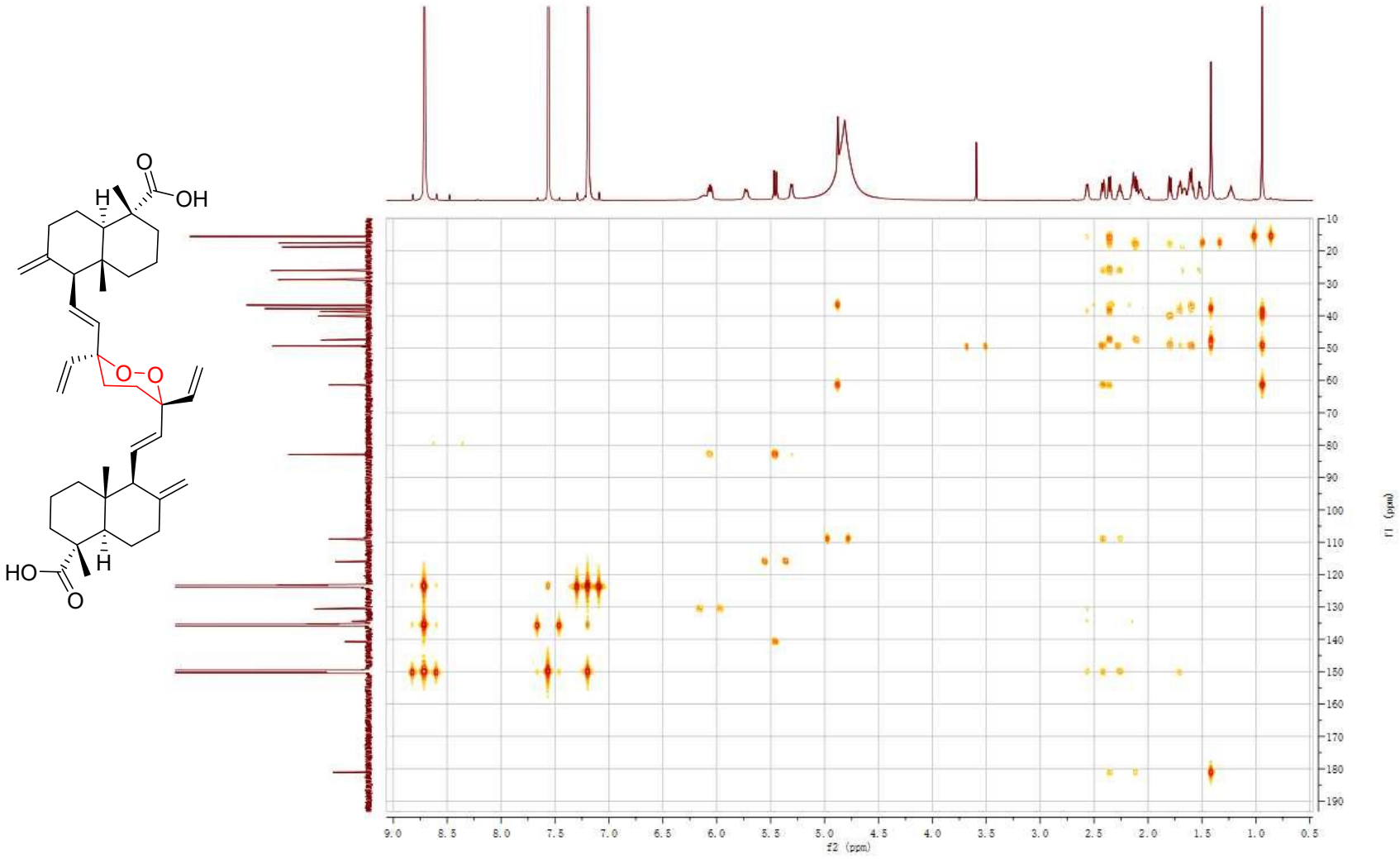


Figure S9. Expanded HMBC spectrum of cunlanceloic acid A (**1**).

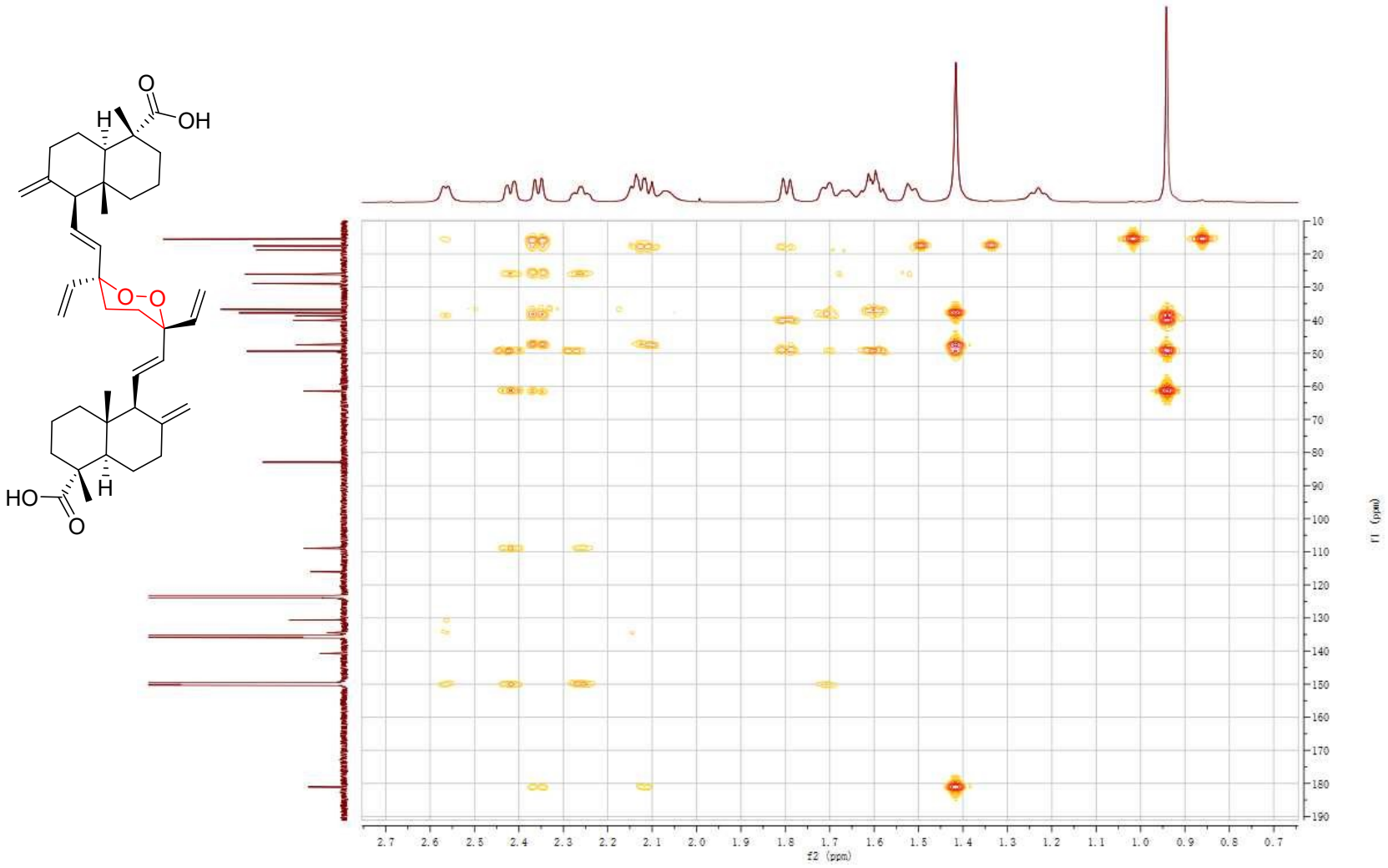


Figure S10. ROESY spectrum of cunlanceloic acid A (**1**).

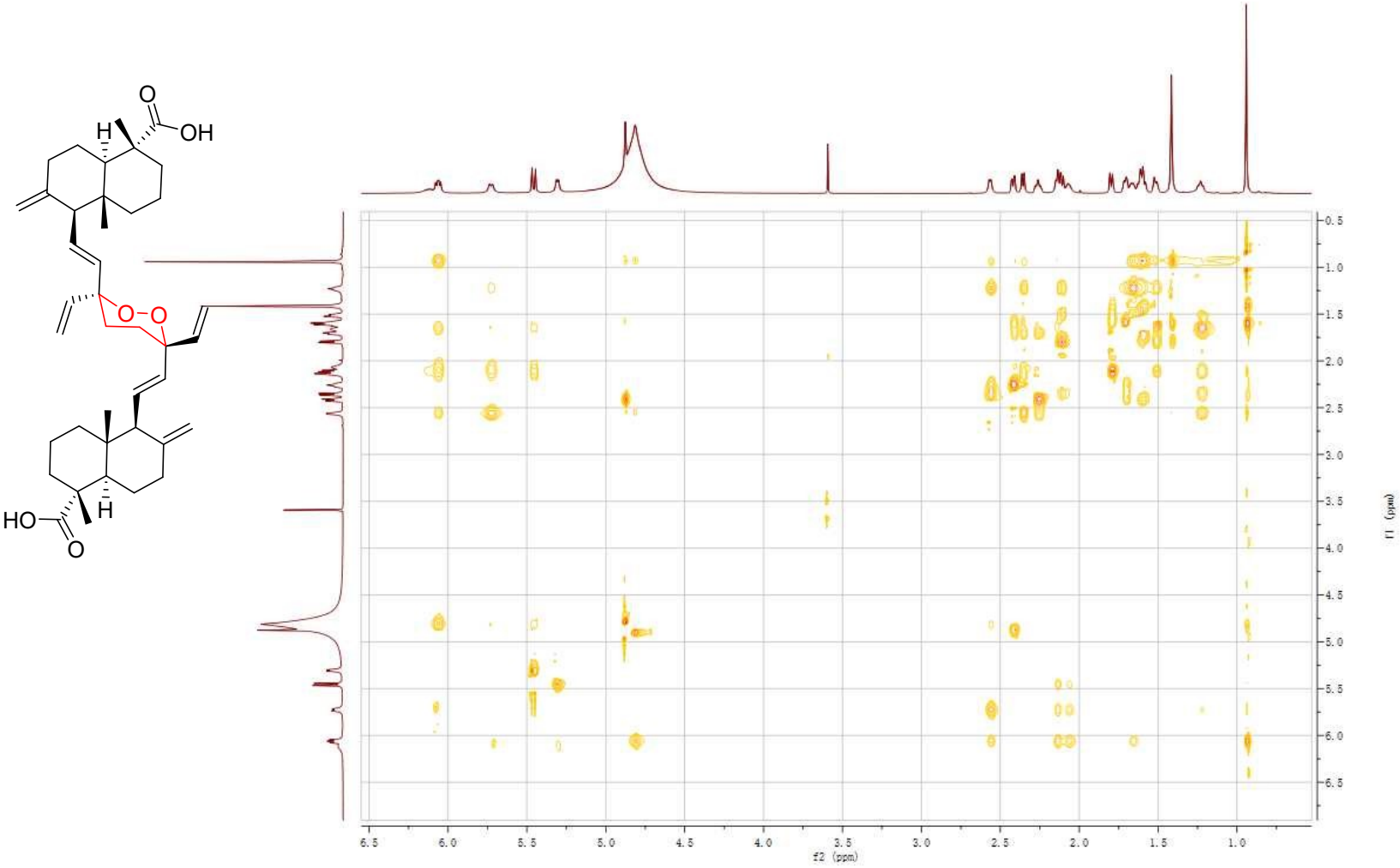


Figure S11. Expanded ROESY spectrum of cunlanceloic acid A (**1**).

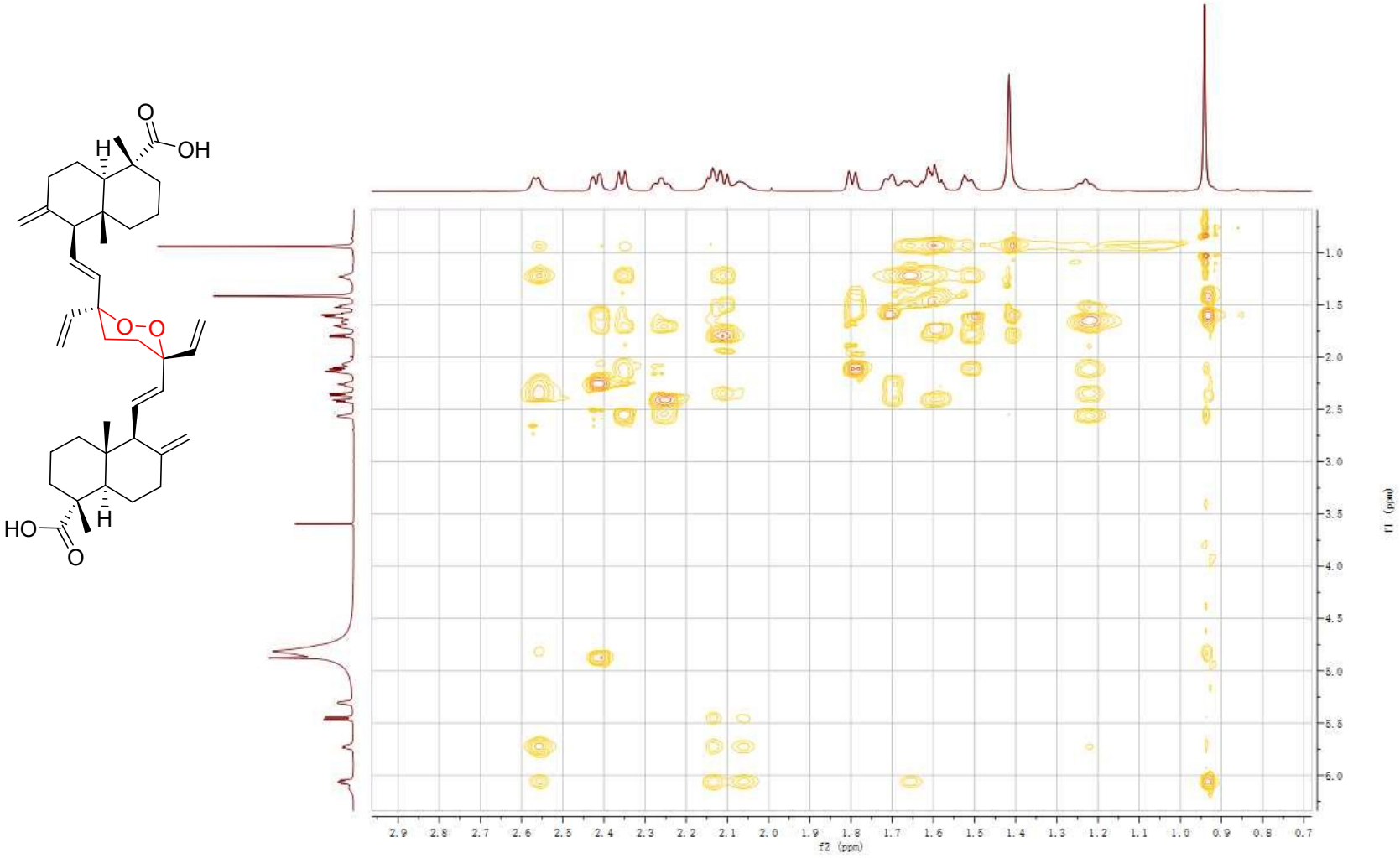


Figure S12. ESIMS spectrum of cunlanceloic acid A (**1**).

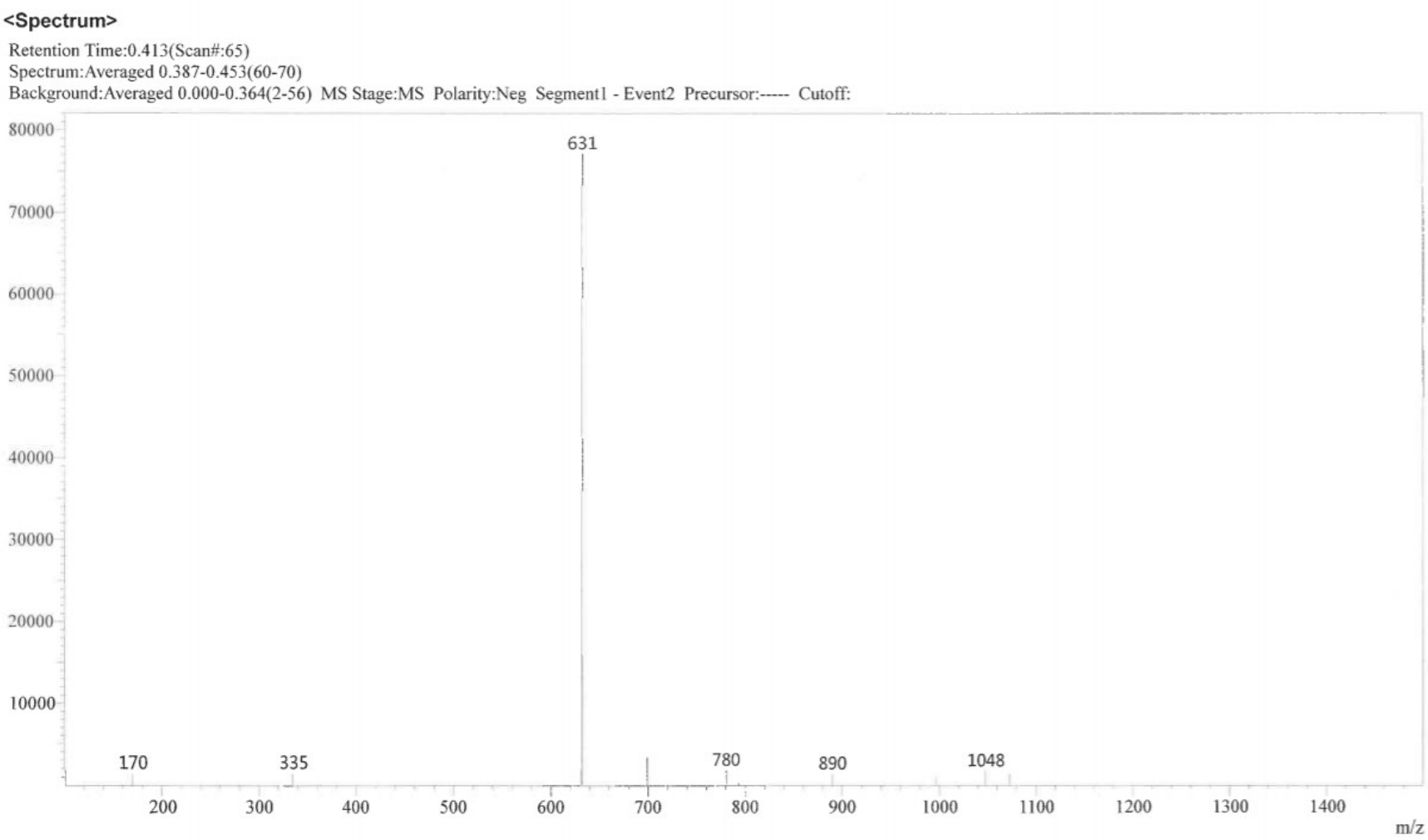


Figure S13. HRES

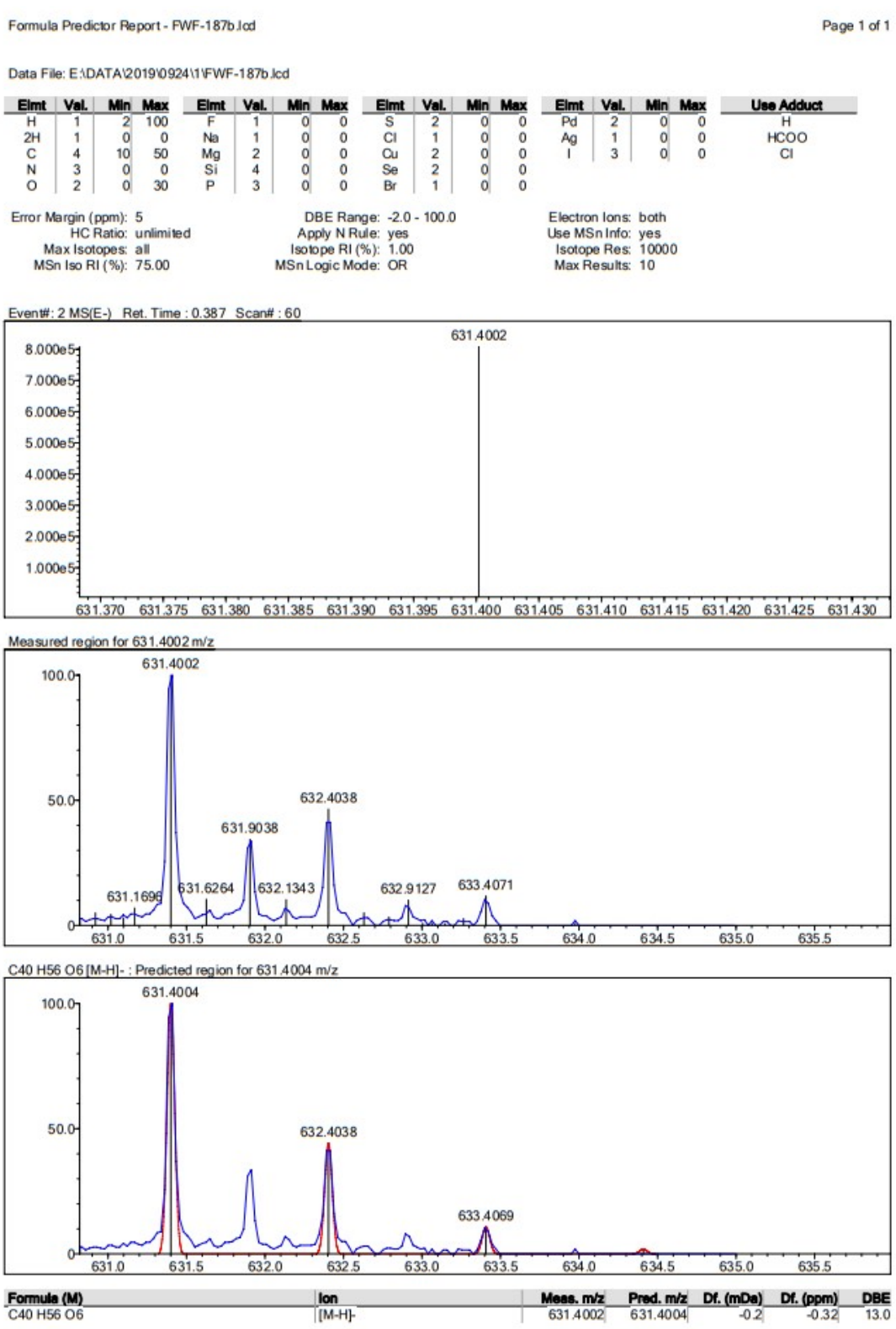


Figure S14. IR spectrum of cunlanceloic acid A (**1**).

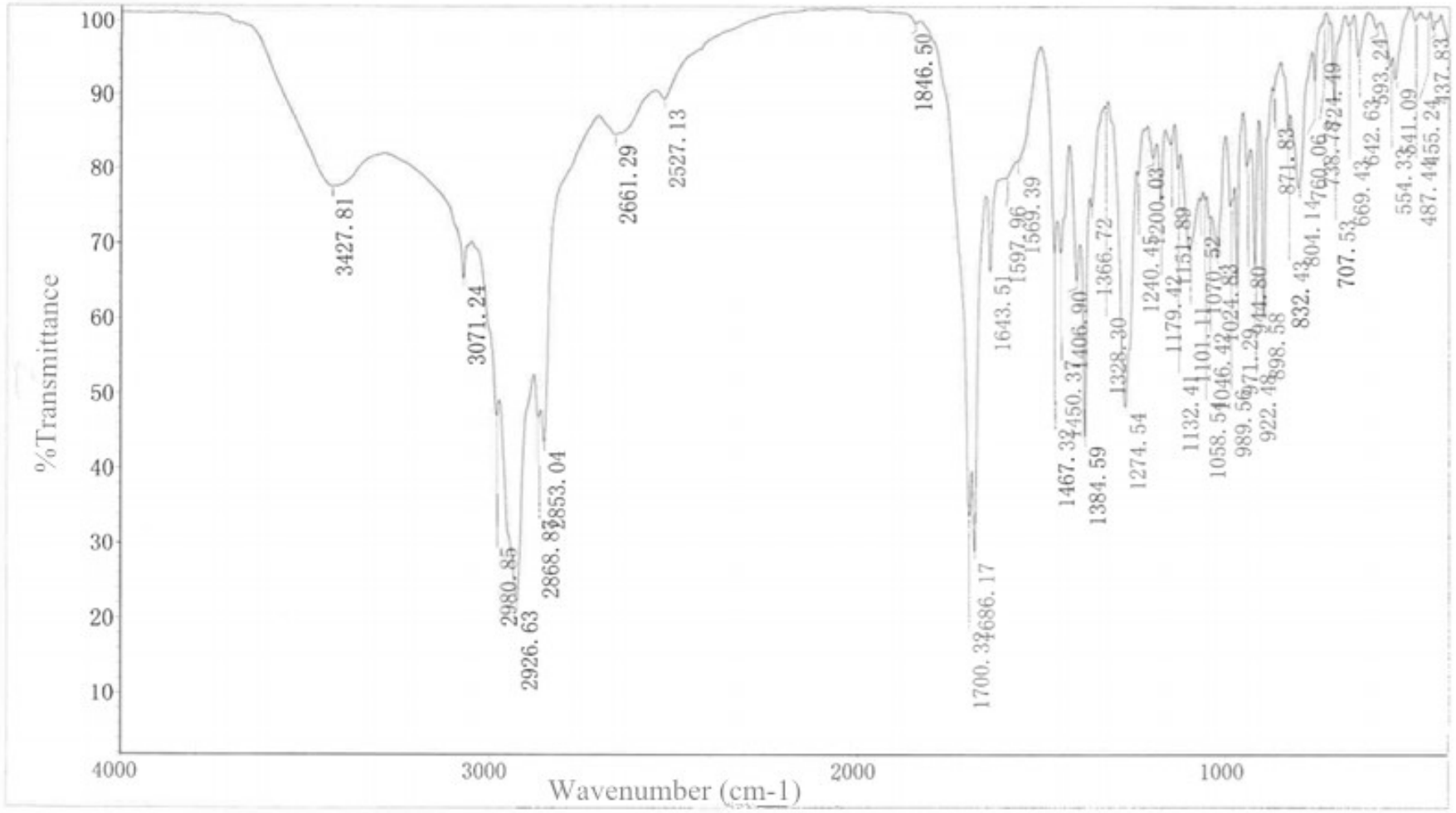


Figure S15. ^{1}H NMR (800 MHz) spectrum of cunlanceloic acid B (**2**) in pyridine-d_5.

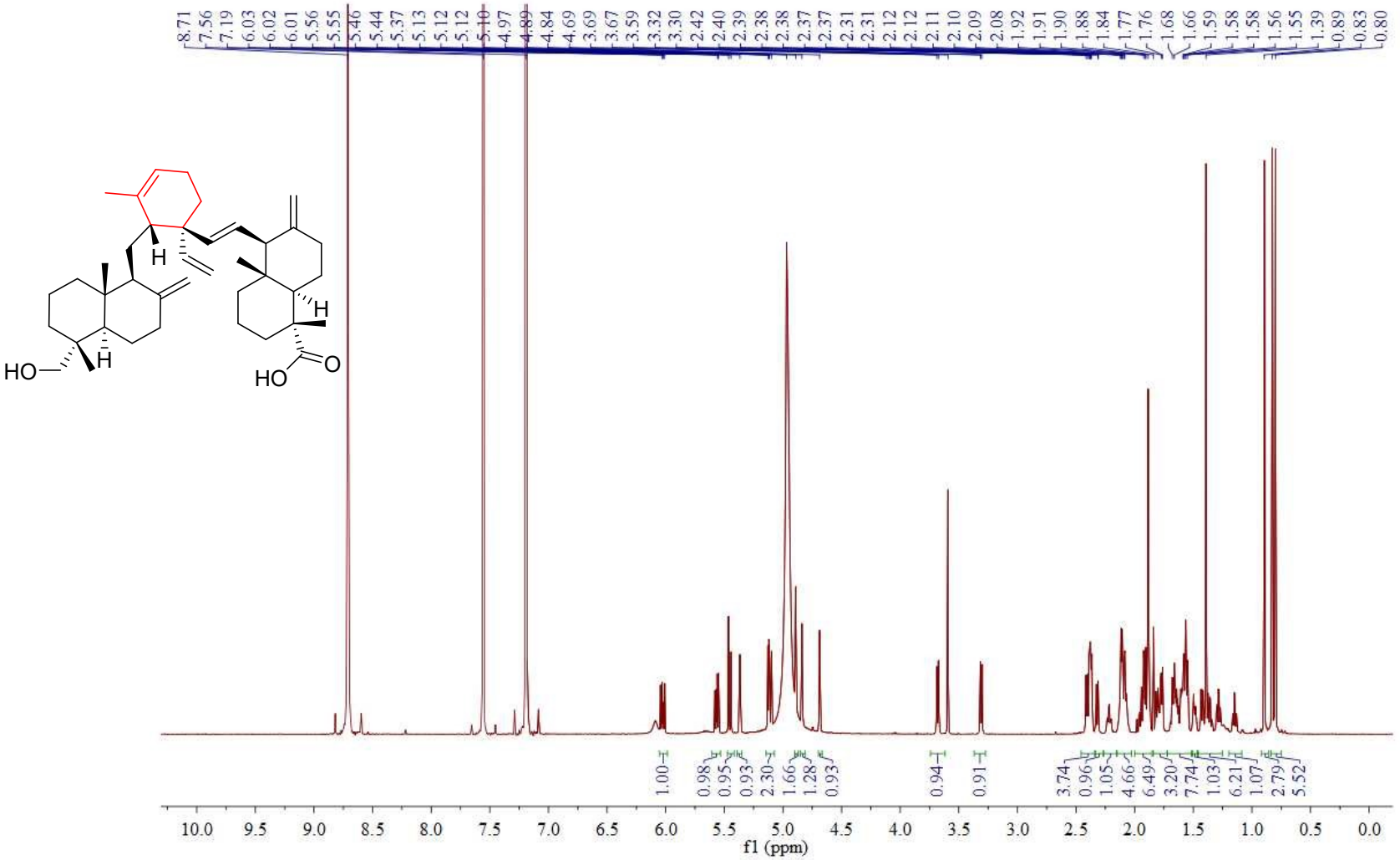


Figure S16. Expanded ^{1}H NMR spectrum of cunlanceloic acid B (**2**).

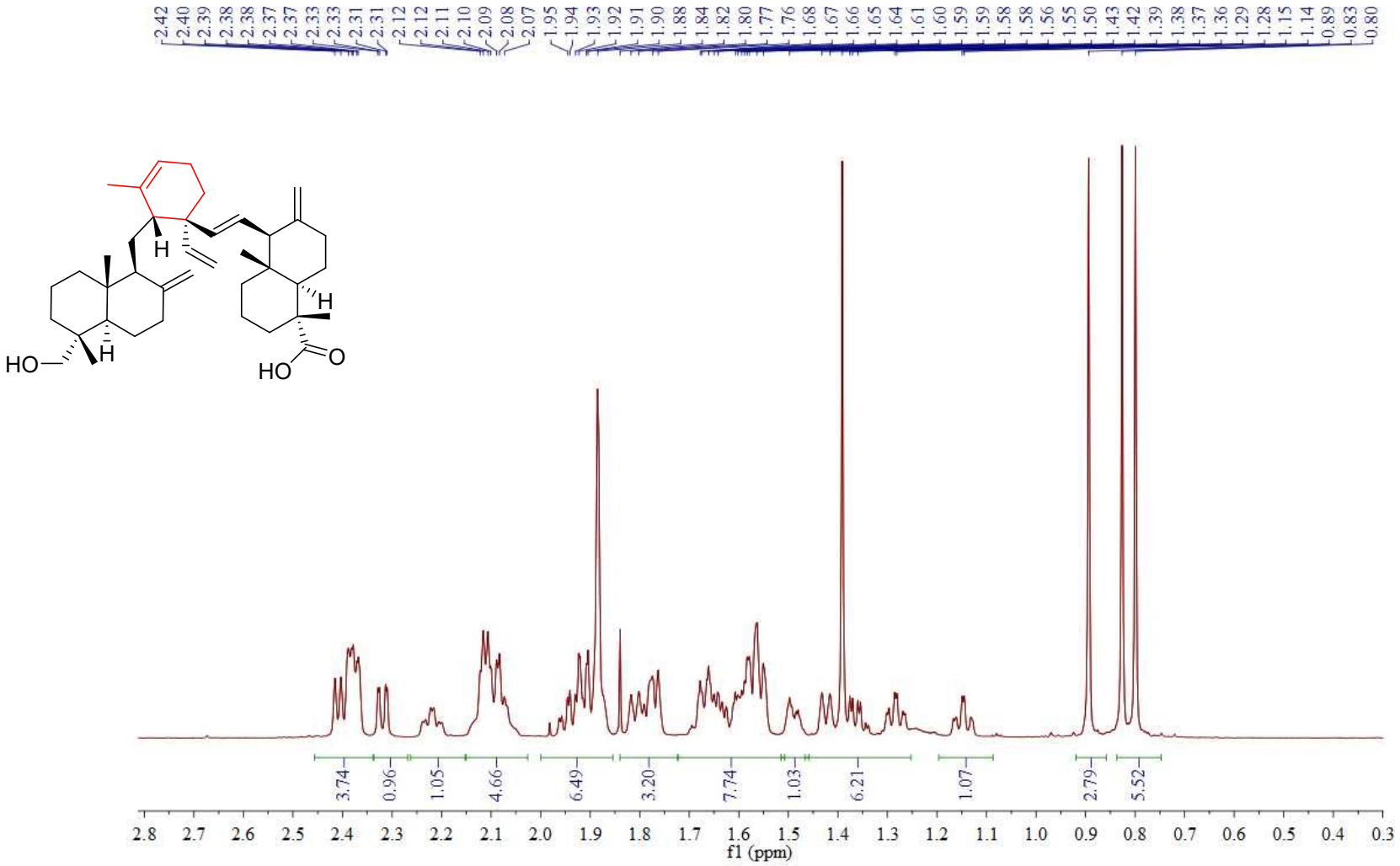


Figure S17. ^{13}C NMR and DEPT (200 MHz) spectra of cunlanceloic acid B (**2**) in pyridine-d_5.

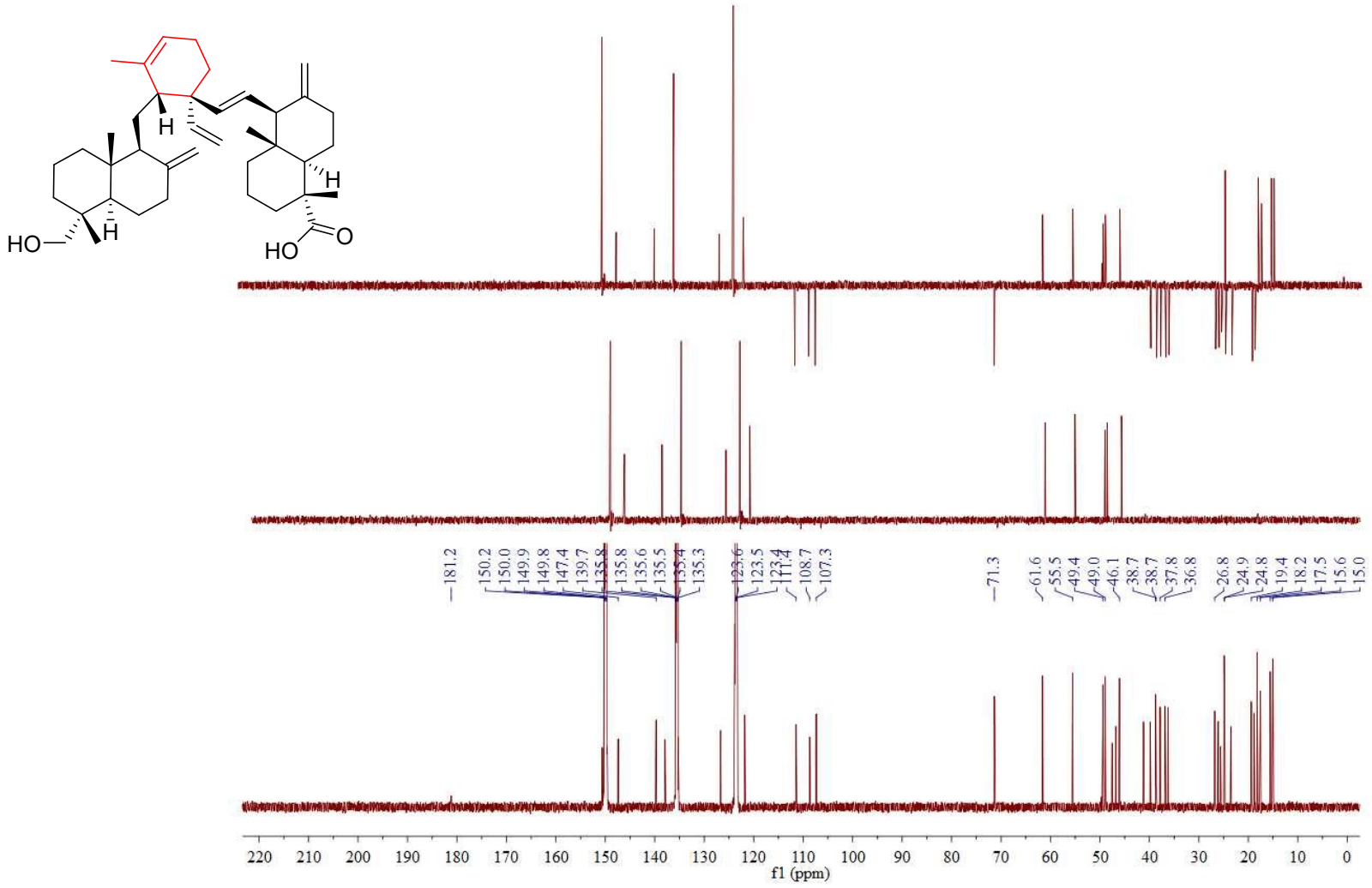


Figure S18. HSQC spectrum of cunlanceloic acid B (**2**).

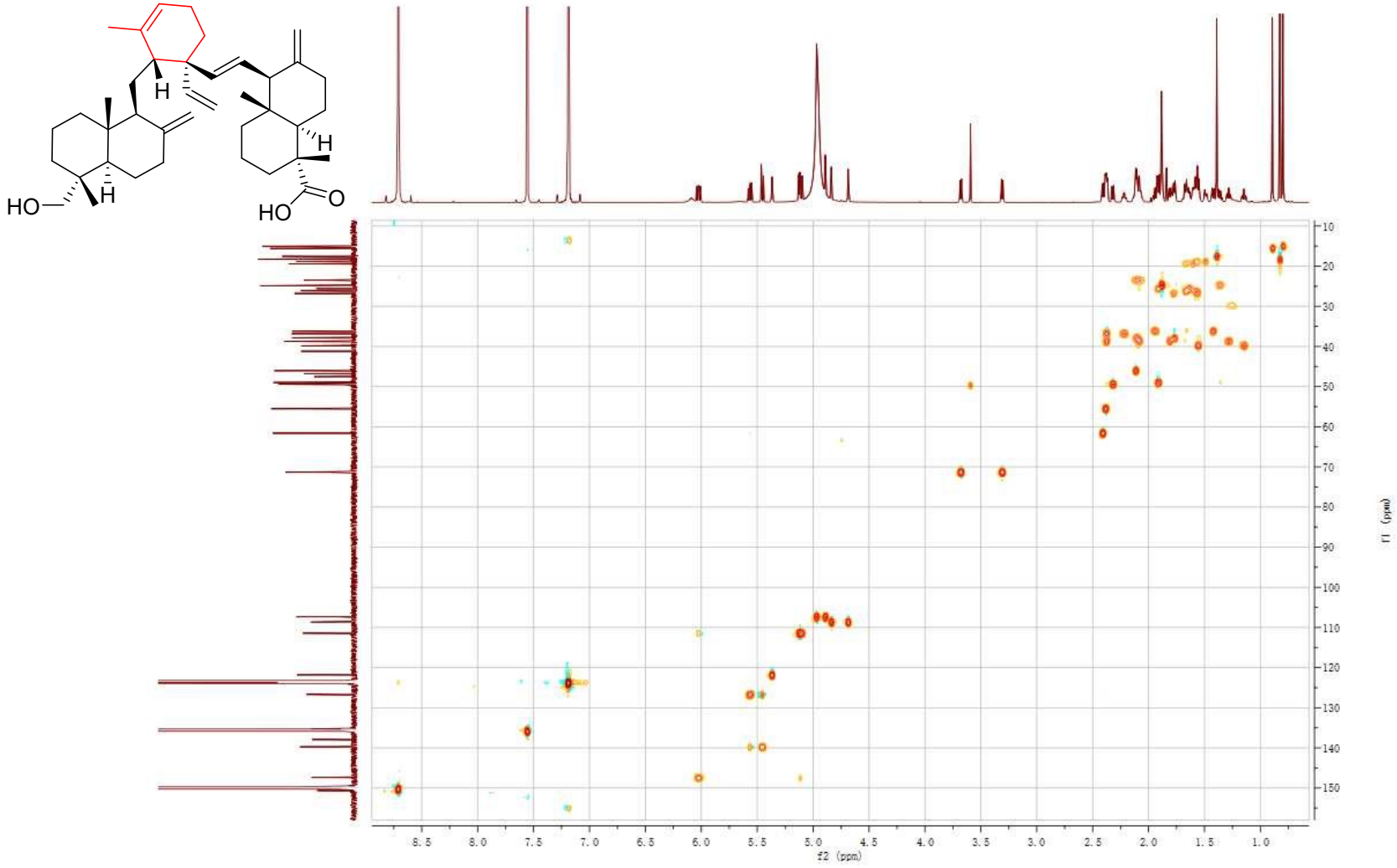


Figure S19. Expanded HSQC spectrum of cunlanceloic acid B (**2**).

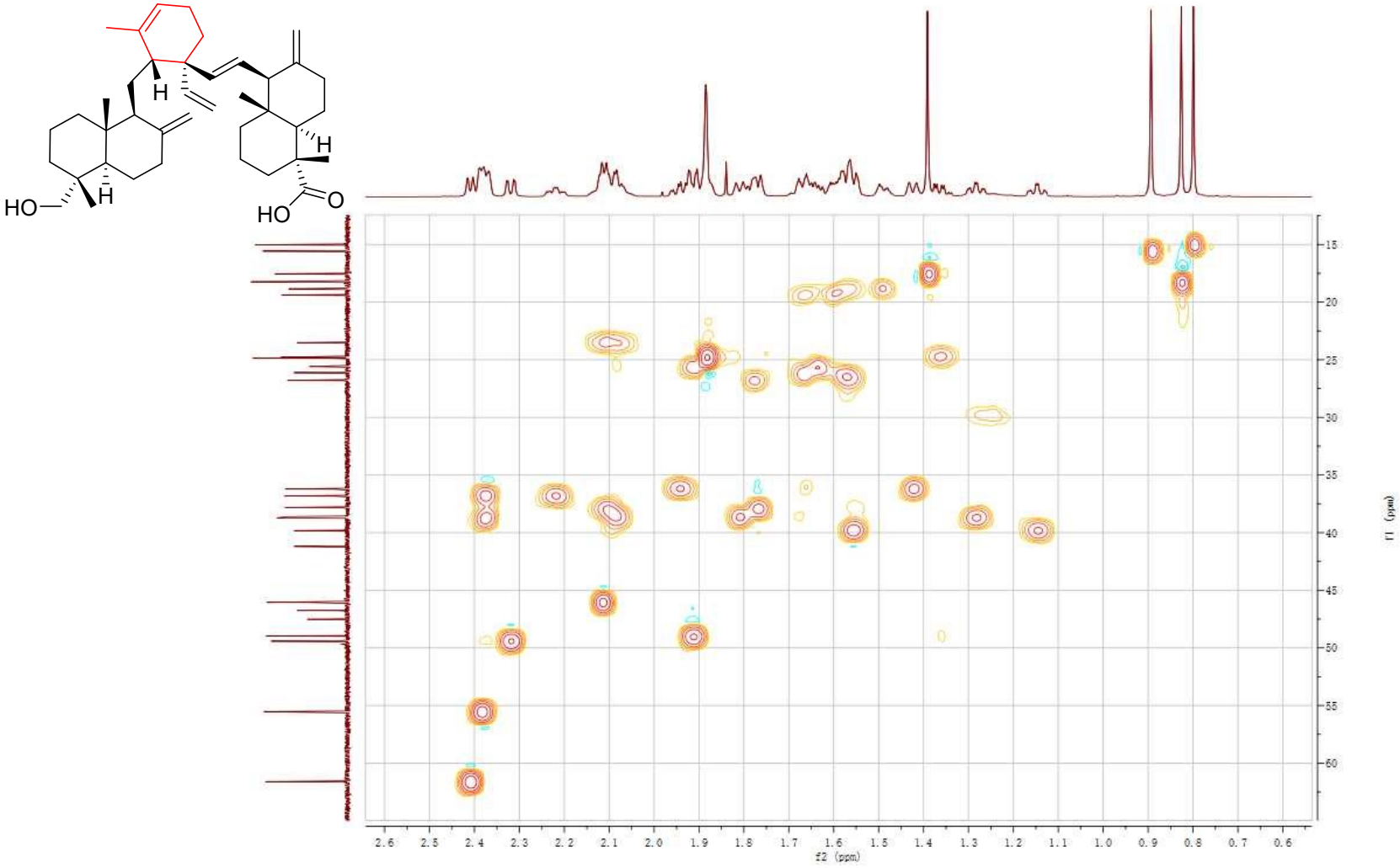


Figure S20. ^{1}H-^{1}H COSY spectrum of cunlanceloic acid B (**2**).

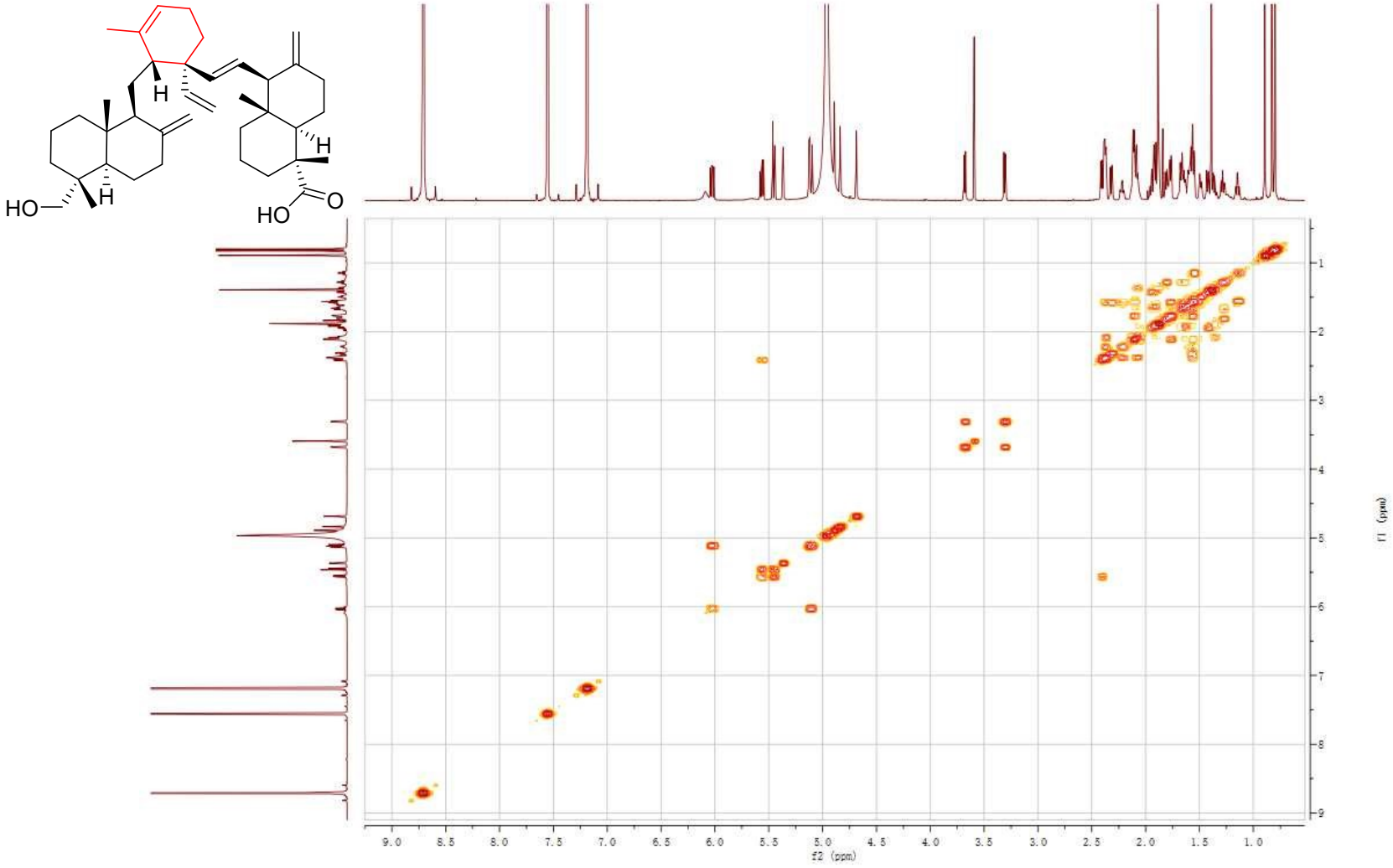


Figure S21. Expanded ^{1}H-^{1}H COSY spectrum of cunlanceloic acid B (**2**).

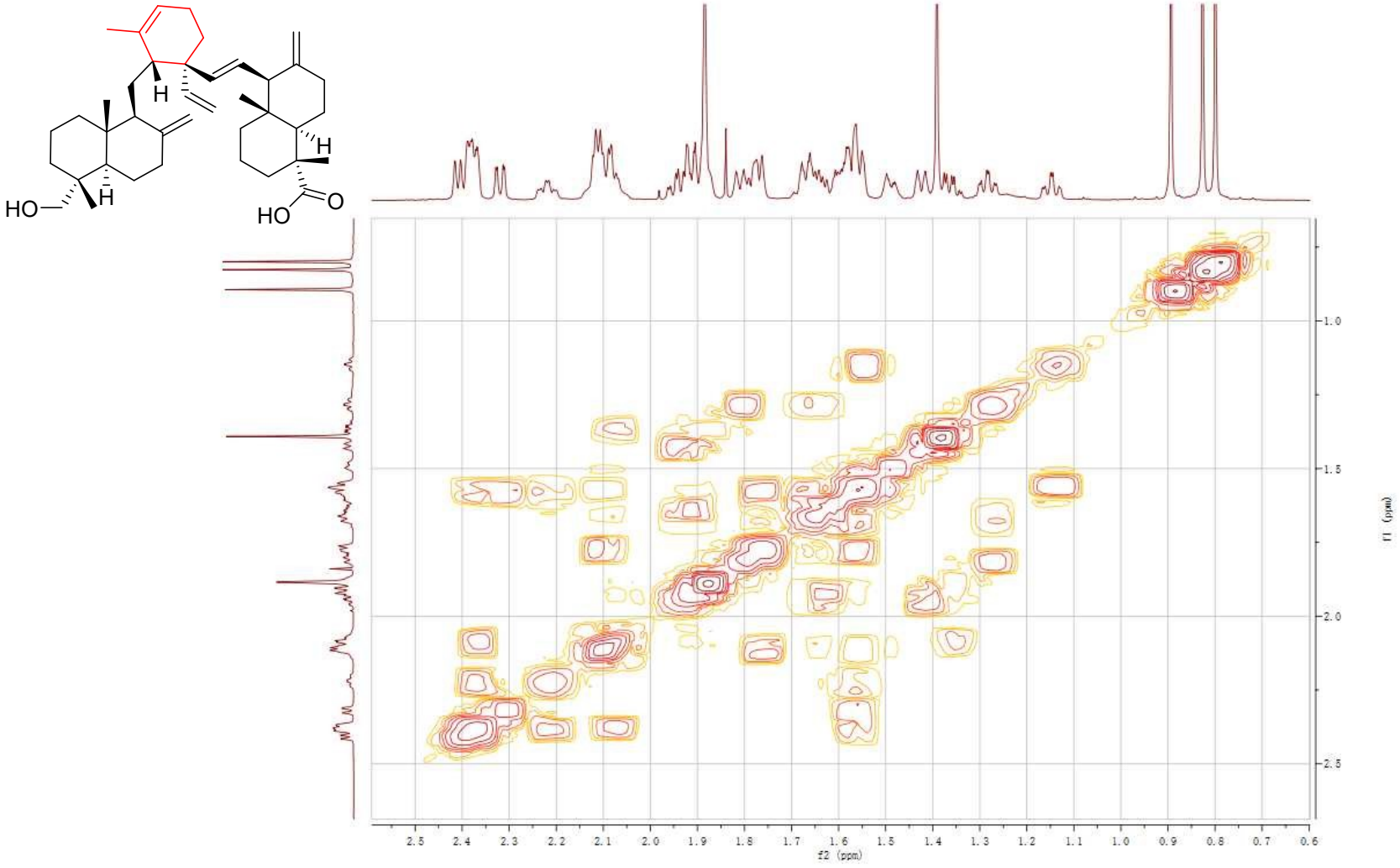


Figure S22. HMBC spectrum of cunlanceloic acid B (**2**).

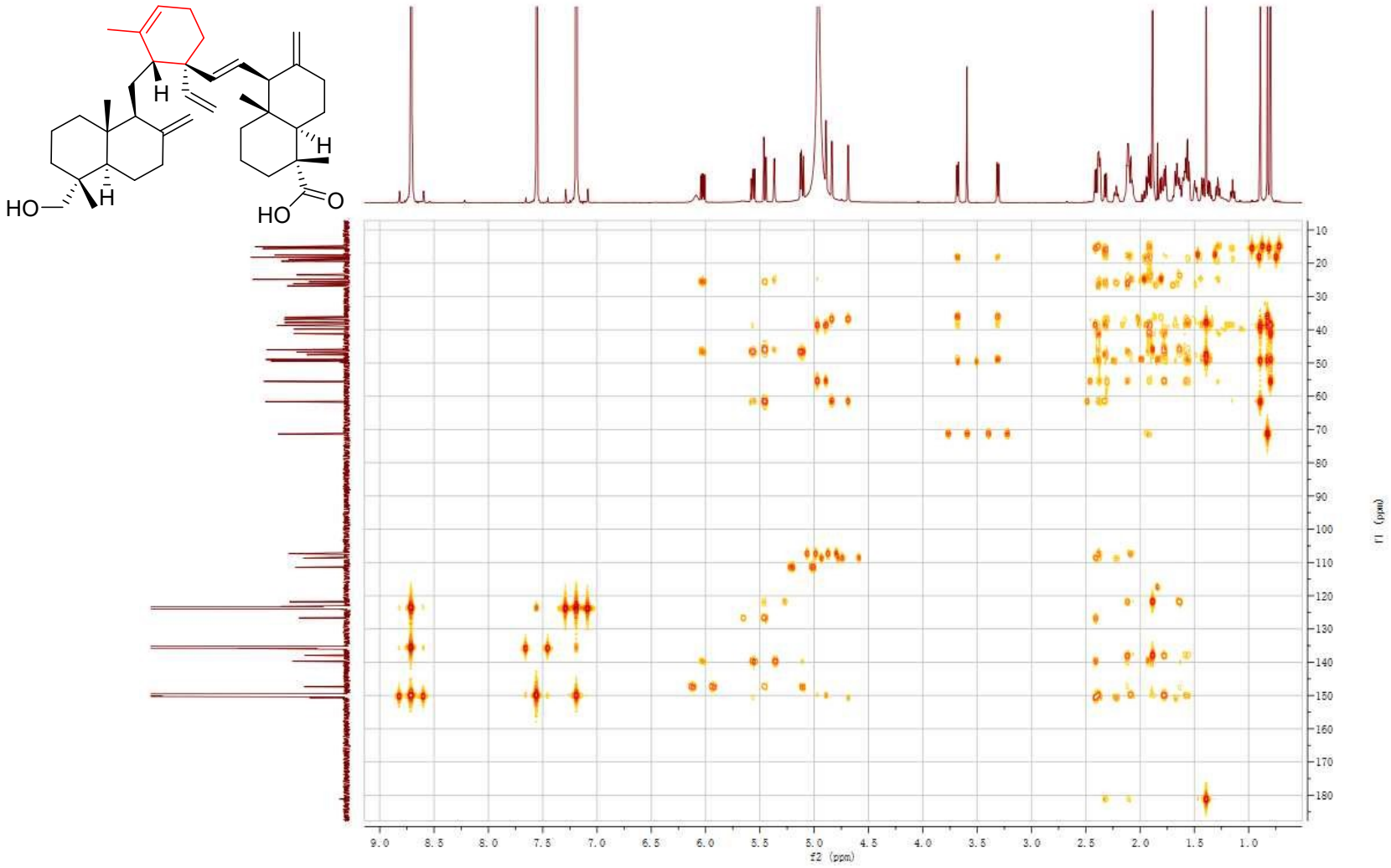


Figure S23. Expanded HMBC spectrum of cunlanceloic acid B (**2**).

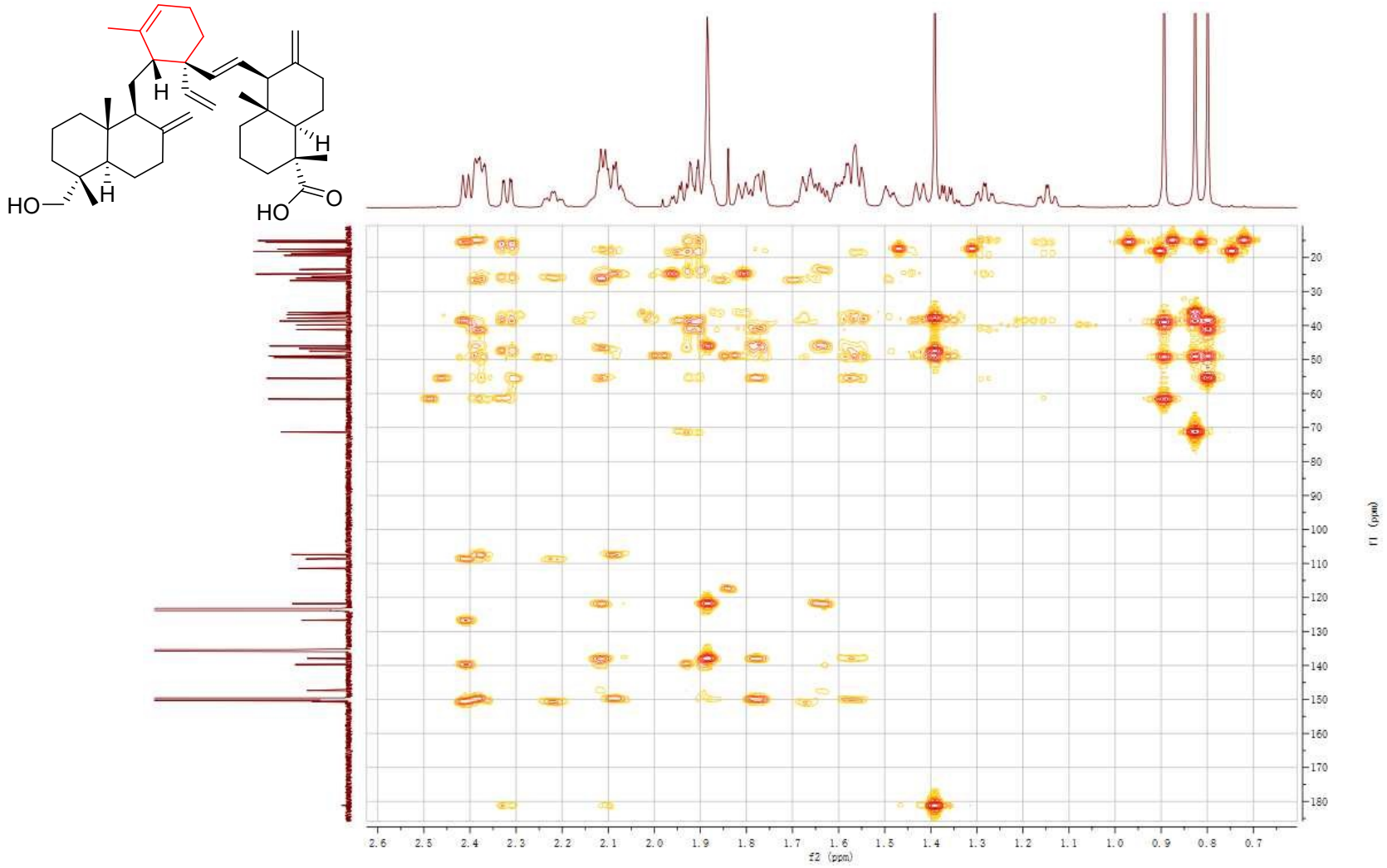


Figure S24. ROESY spectrum of cunlanceloic acid B (**2**).

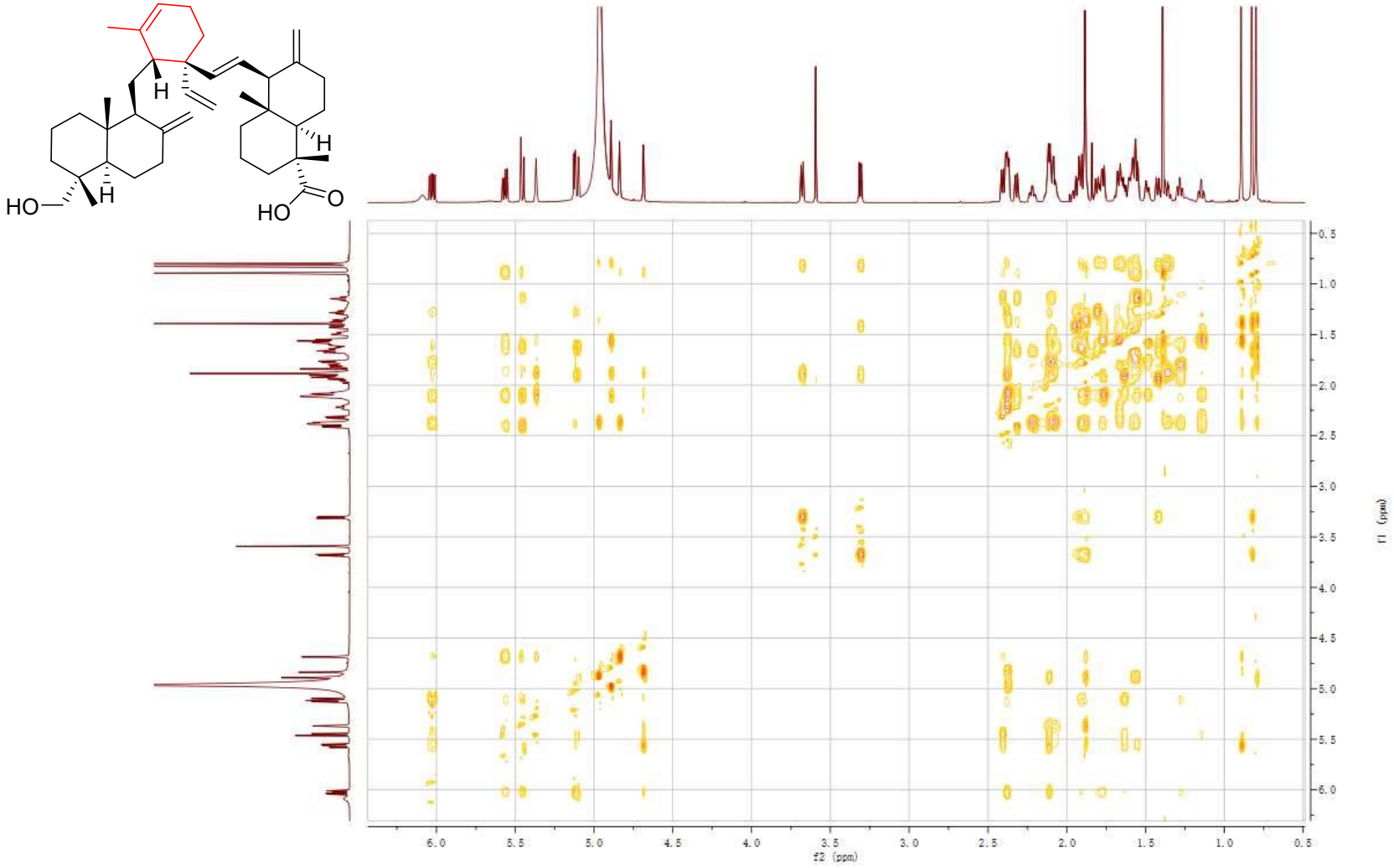


Figure S25. Expanded ROESY spectrum of cunlanceloic acid B (**2**).

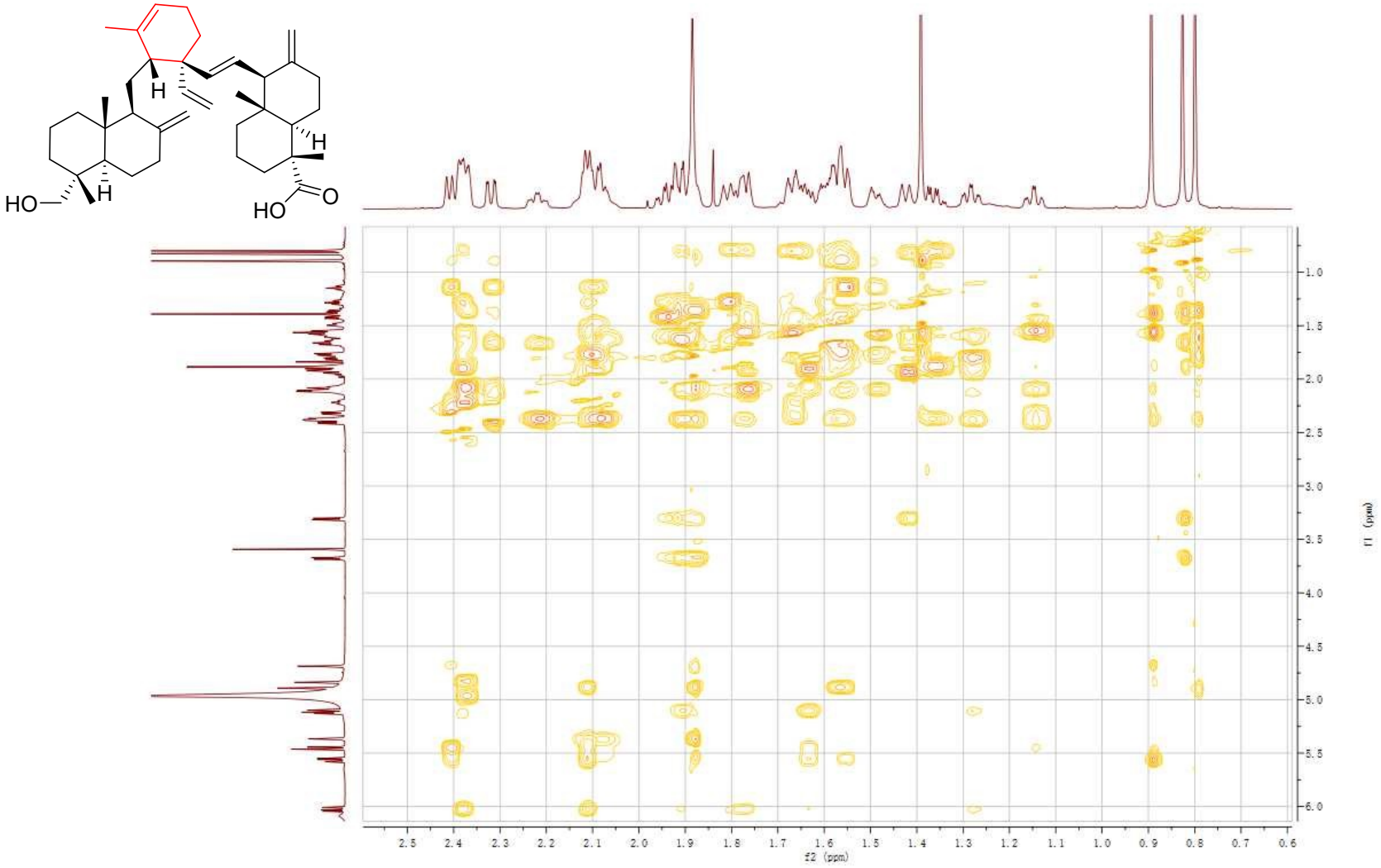


Figure S26. ESIMS spectrum of cunlanceloic acid B (**2**).

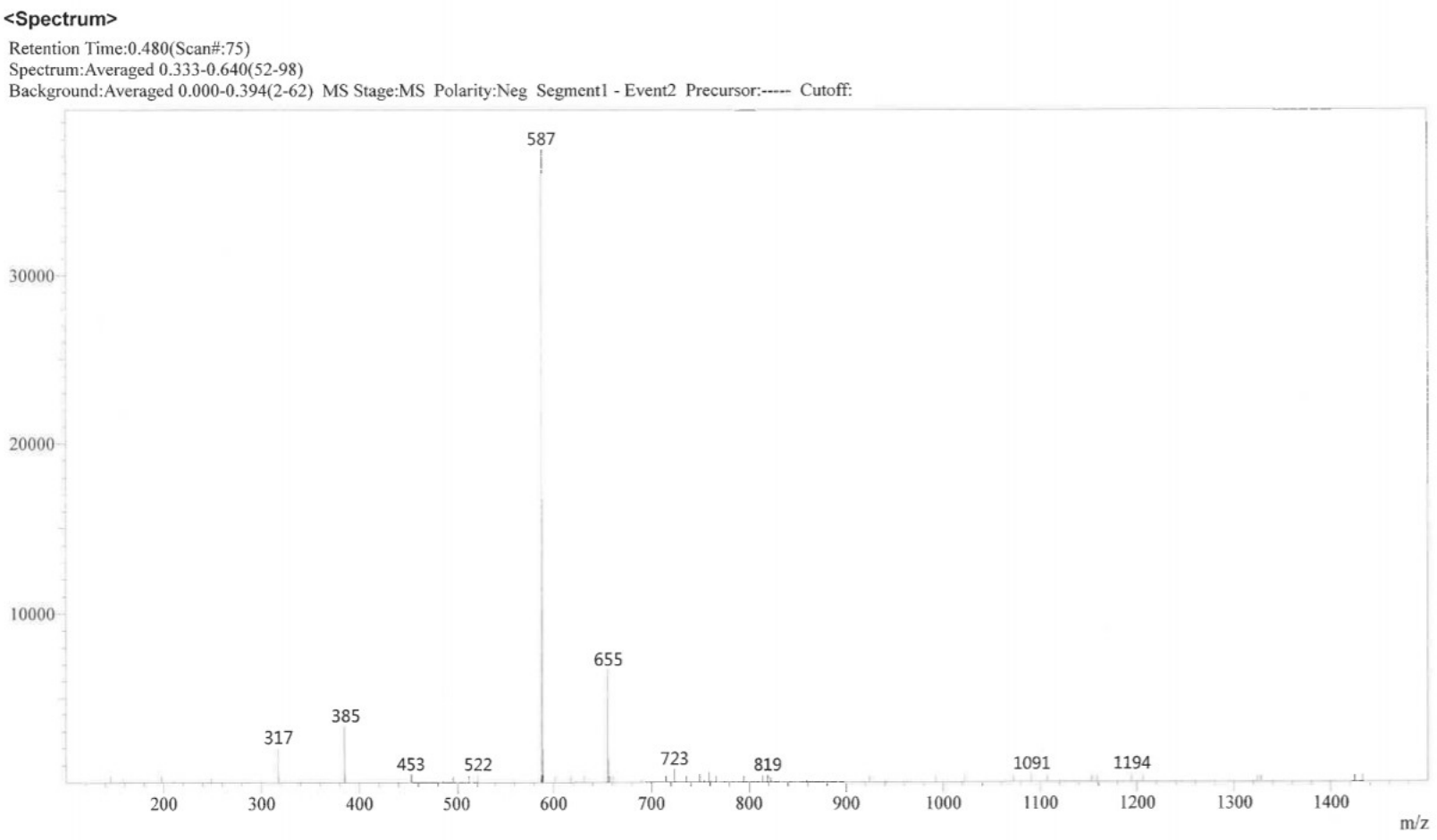


Figure S27. HRE

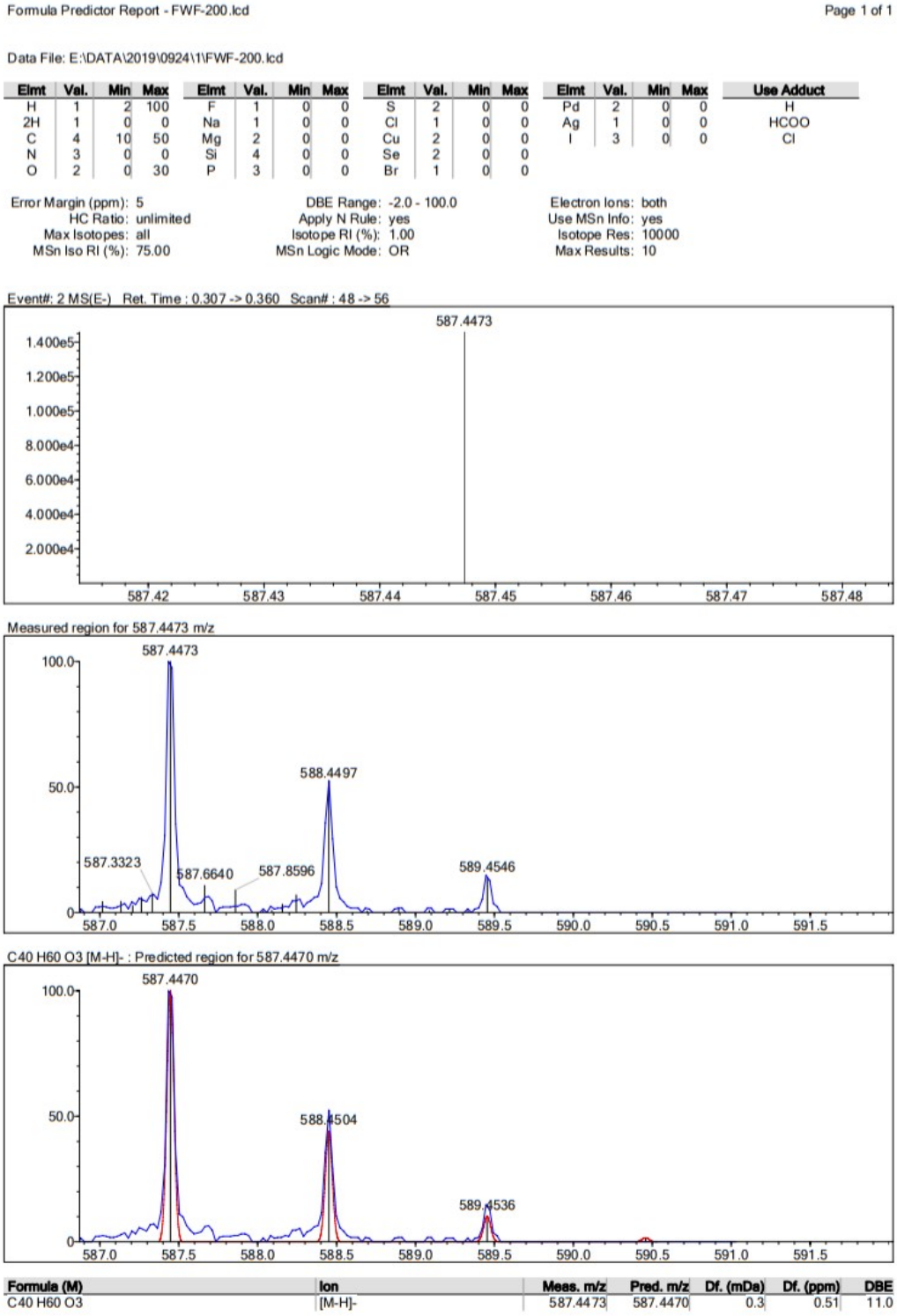


Figure S28. IR spectrum of cunlanceloic acid B (**2**).

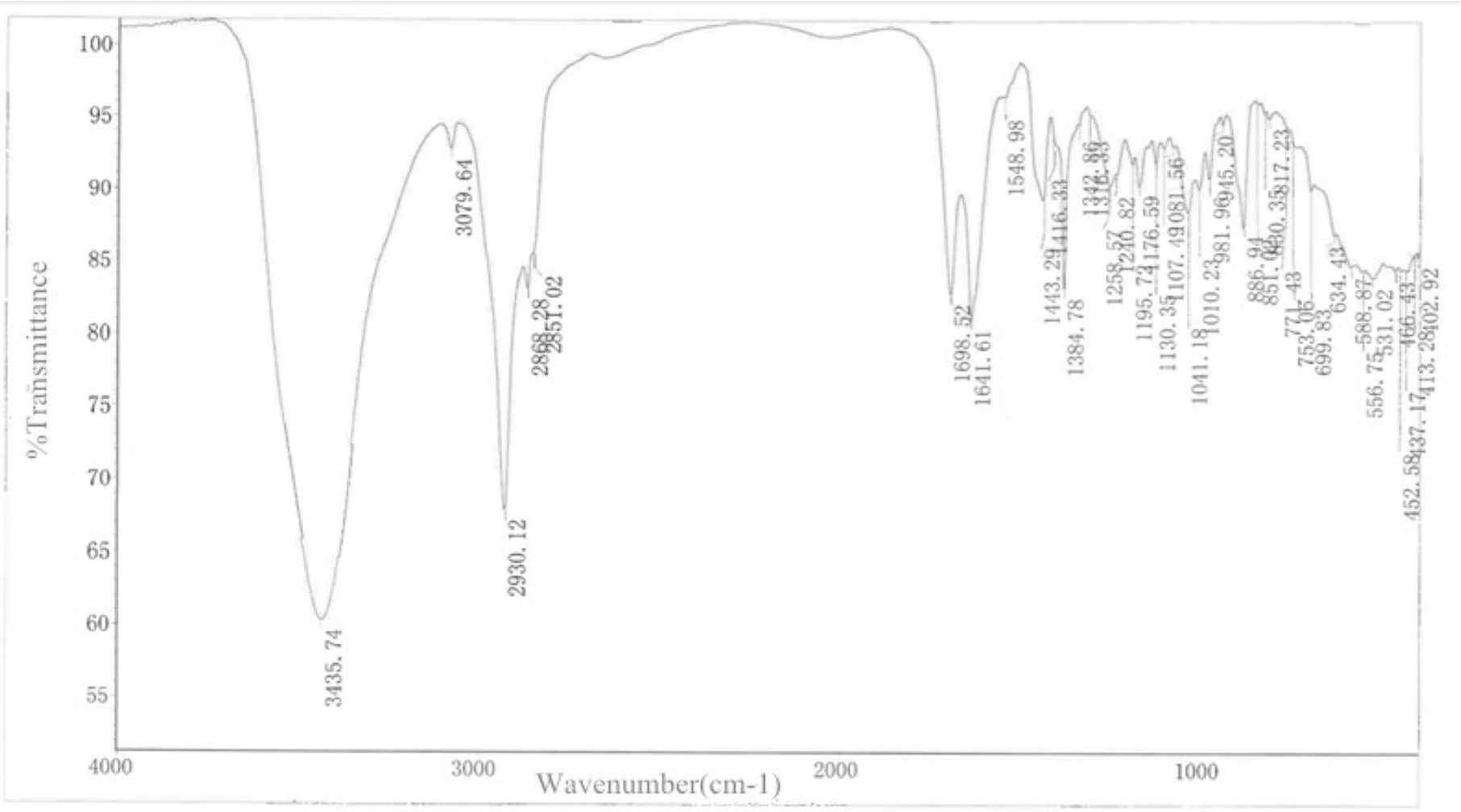


Figure S29. ^{1}H NMR (800 MHz) spectrum of cunlanceloic acid C (**3**) in pyridine-d_5.

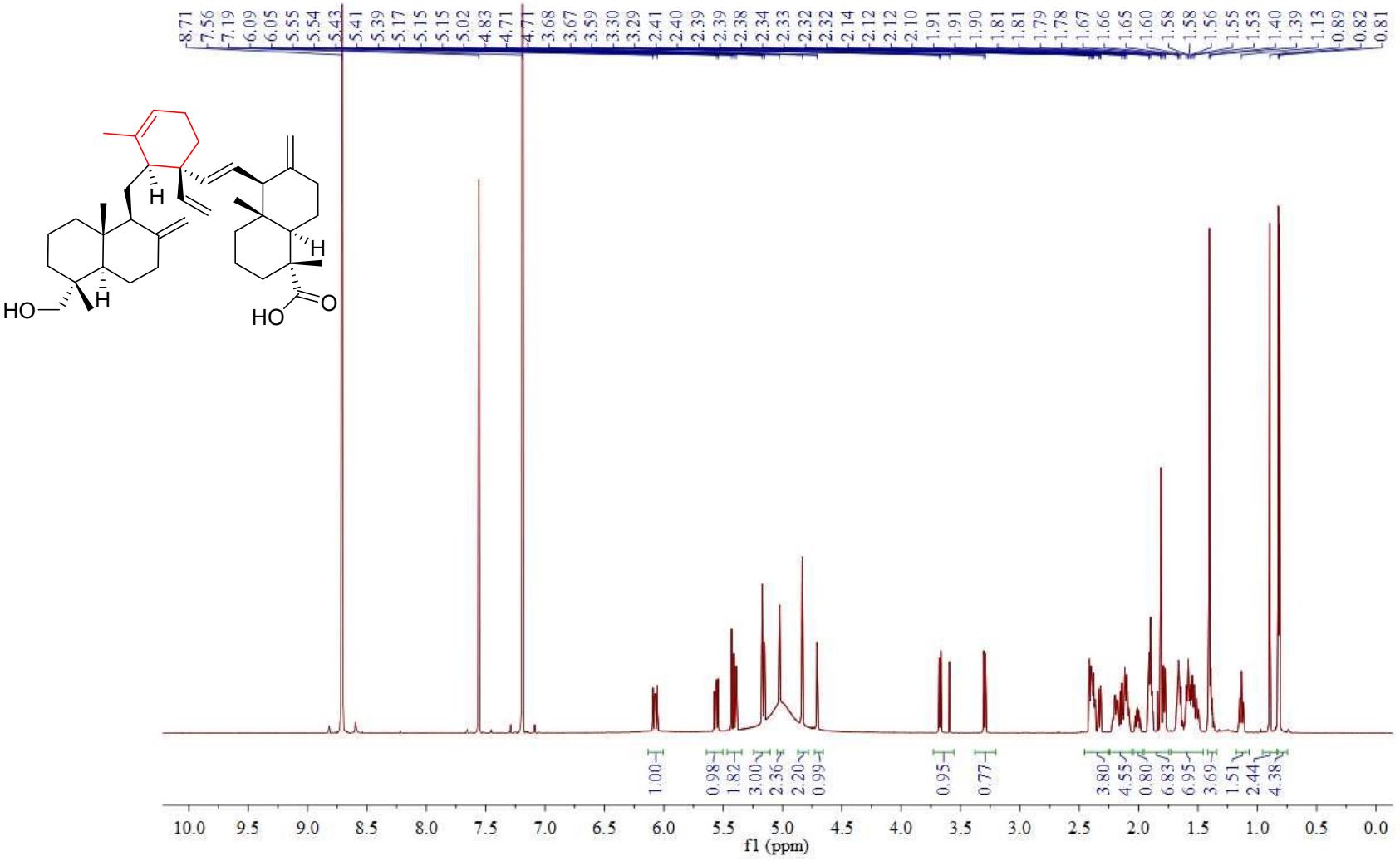


Figure S30. Expanded ^{1}H NMR spectrum of cunlanceloic acid C (**3**).

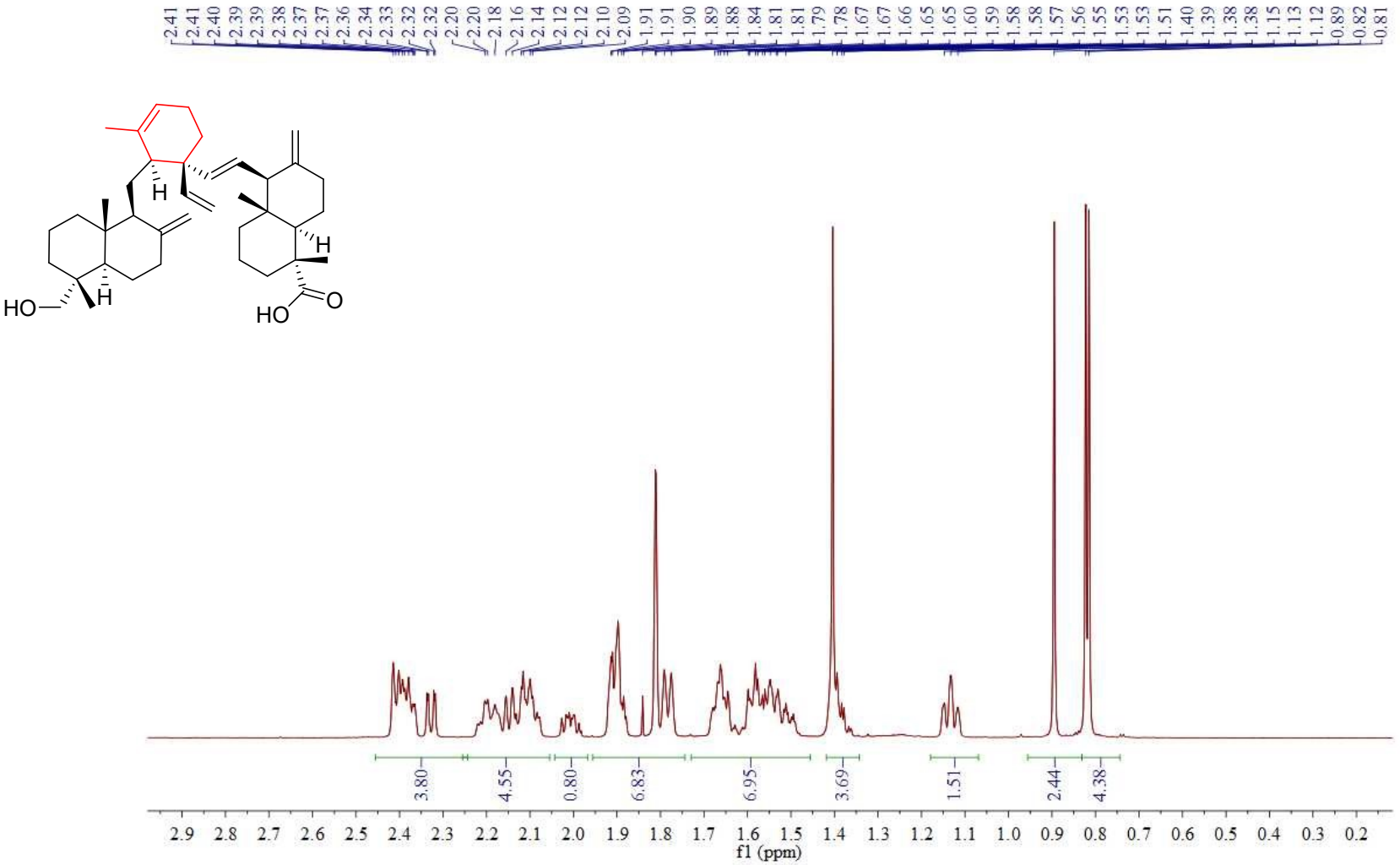


Figure S31. ^{13}C NMR and DEPT (200 MHz) spectra of cunlanceloic acid C (**3**) in pyridine-d_5.

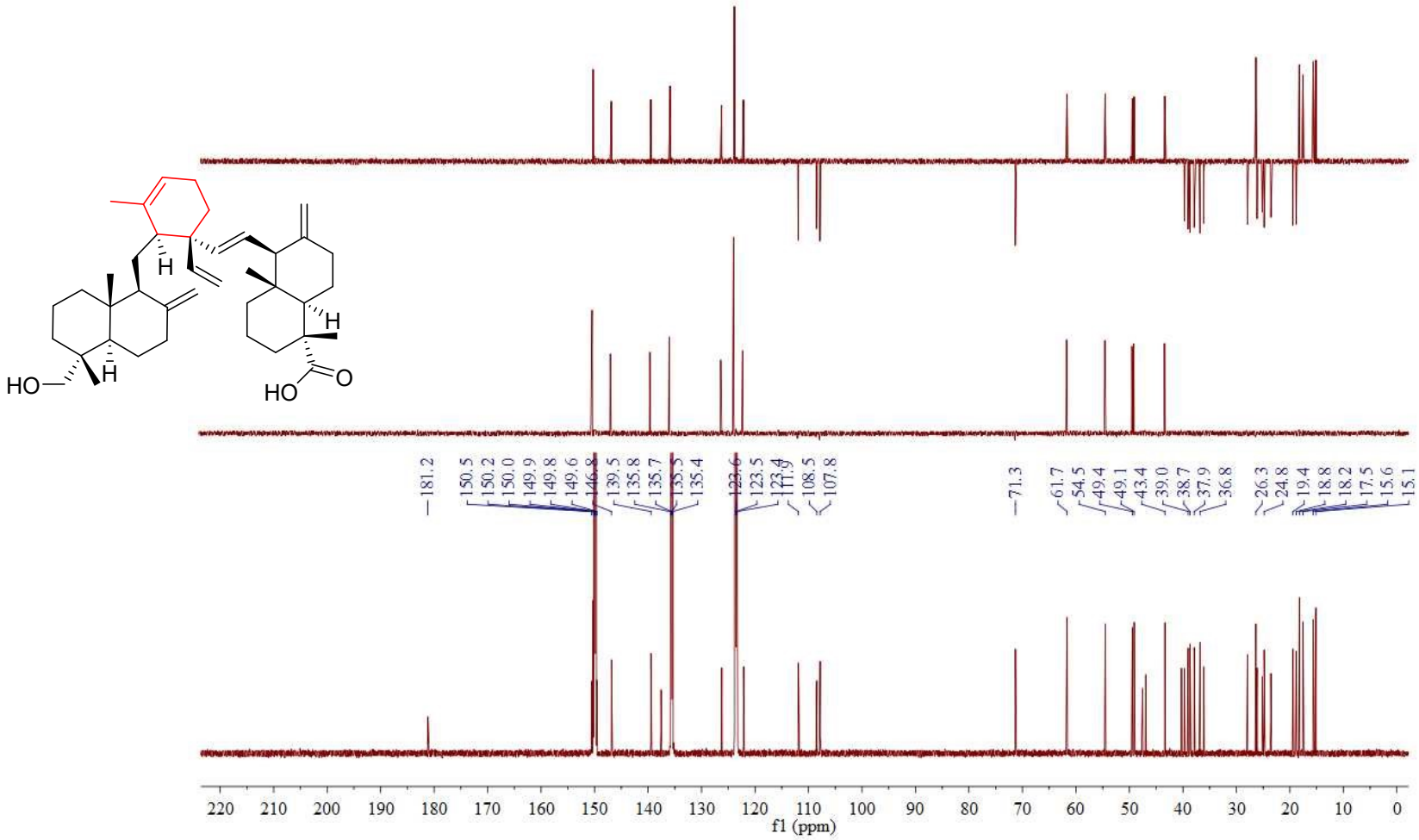


Figure S32. HSQC spectrum of cunlanceloic acid C (**3**).

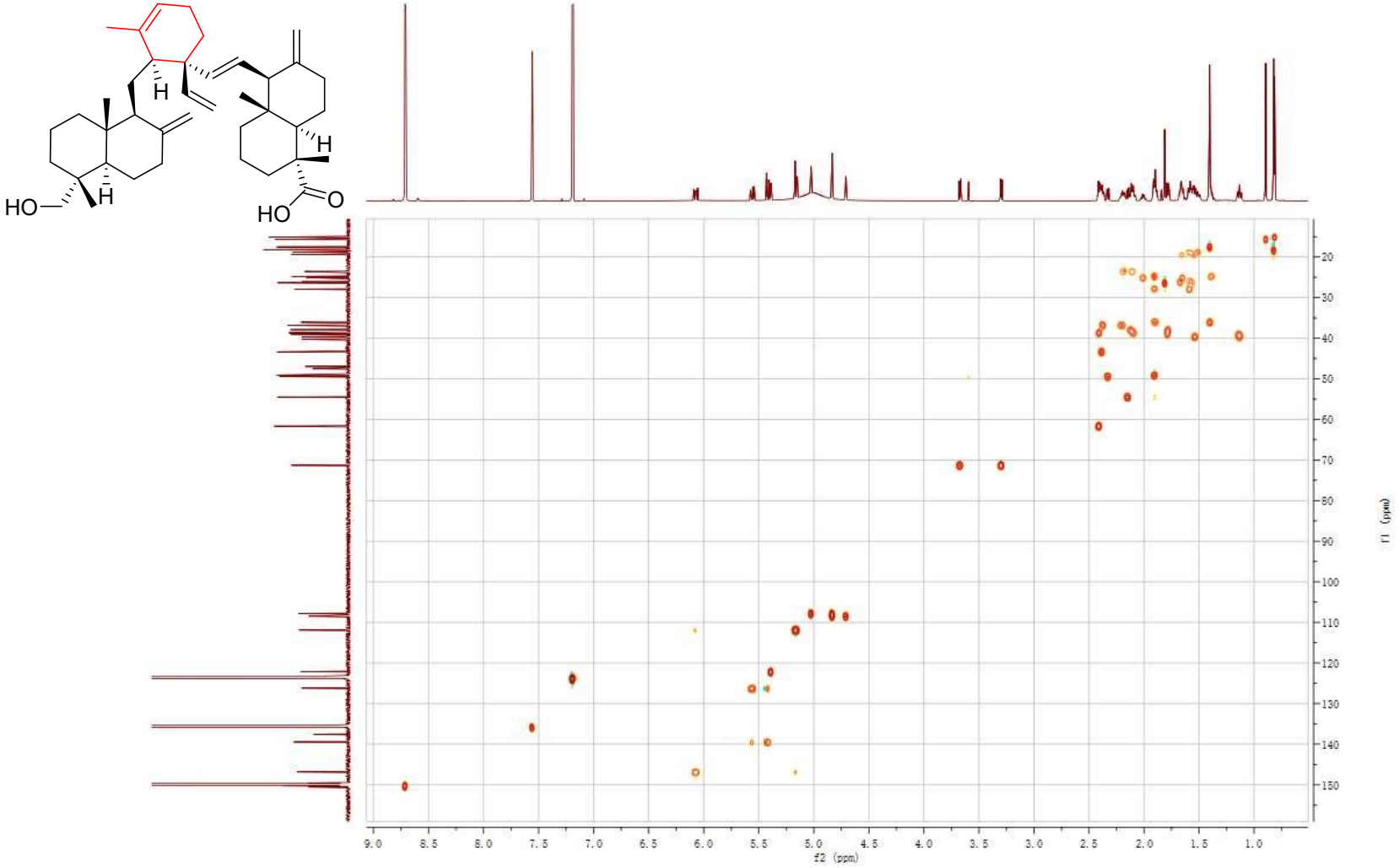


Figure S33. Expanded HSQC spectrum of cunlanceloic acid C (**3**).

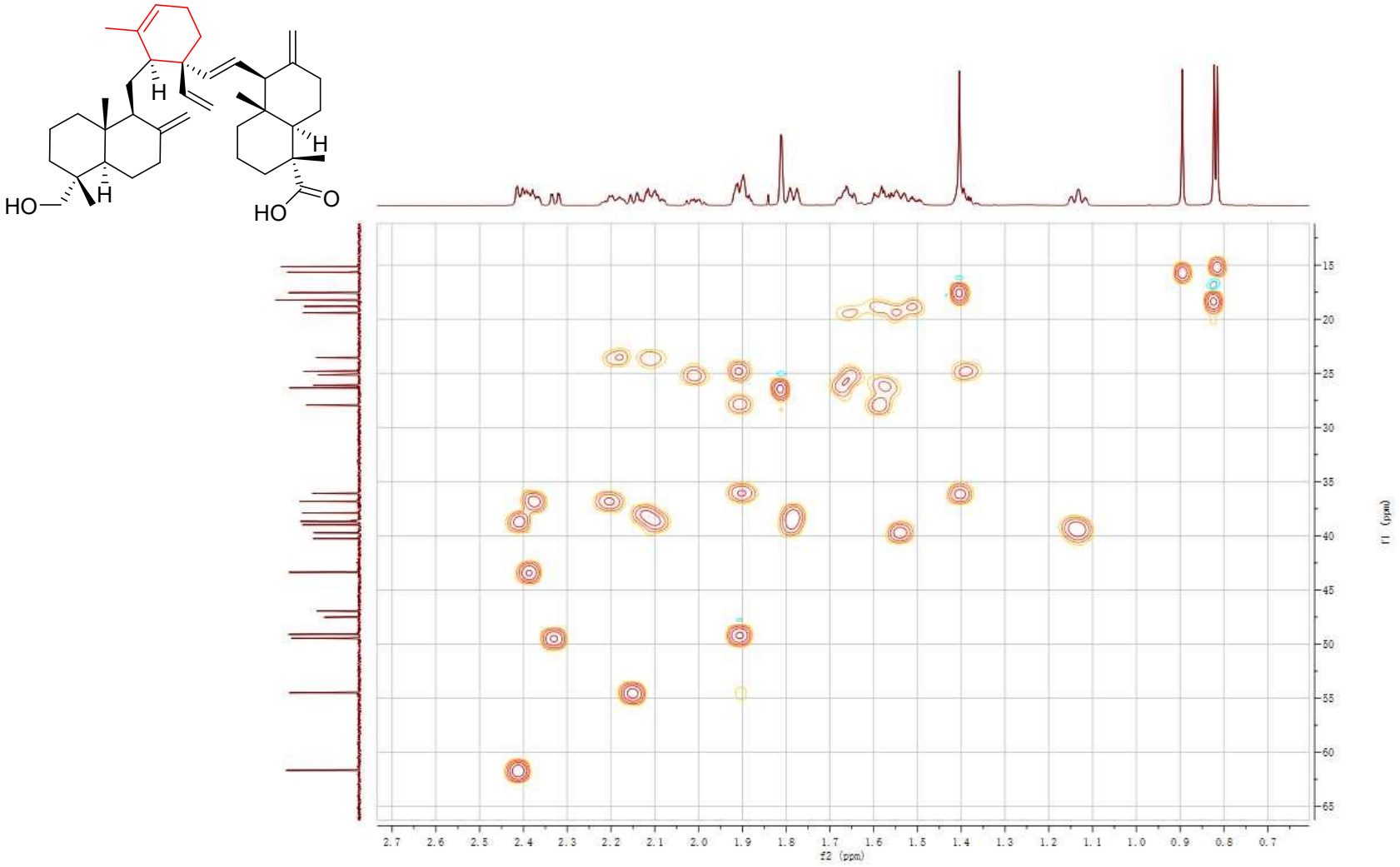


Figure S34. ^{1}H-^{1}H COSY spectrum of cunlanceloic acid C (**3**).

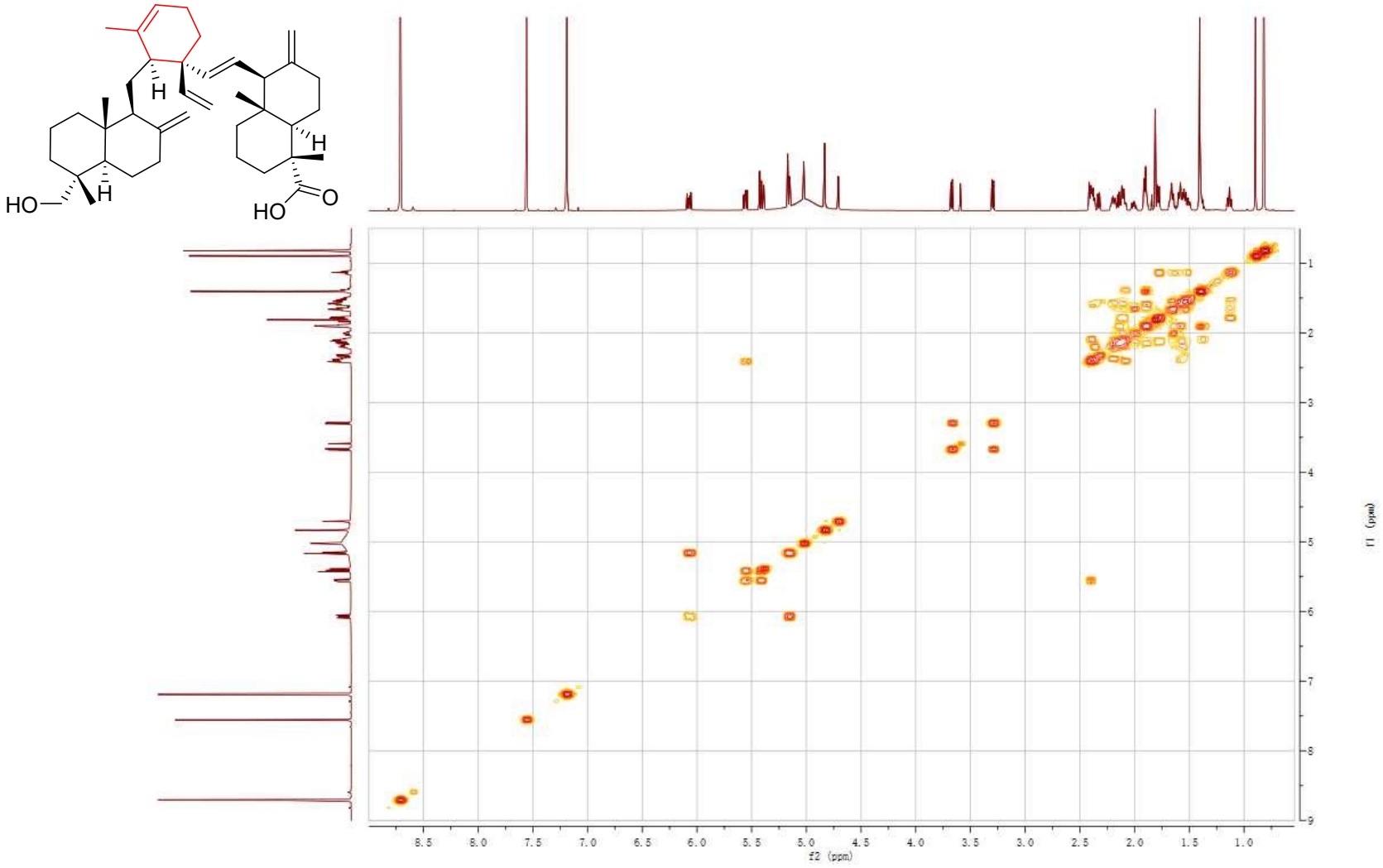


Figure S35. Expanded ^{1}H-^{1}H COSY spectrum of cunlanceloic acid C (**3**).

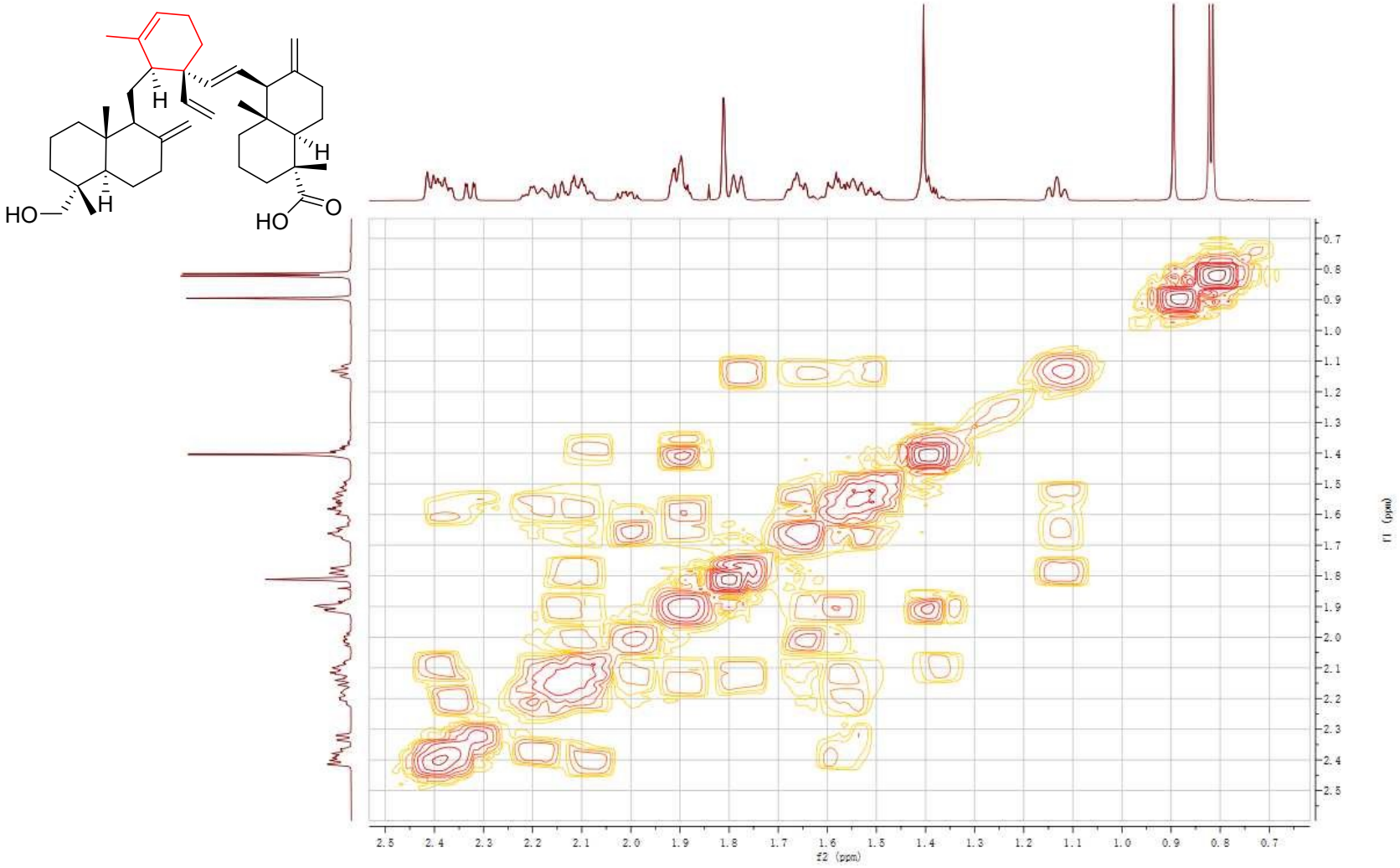


Figure S36. HMBC spectrum of cunlanceloic acid C (**3**).

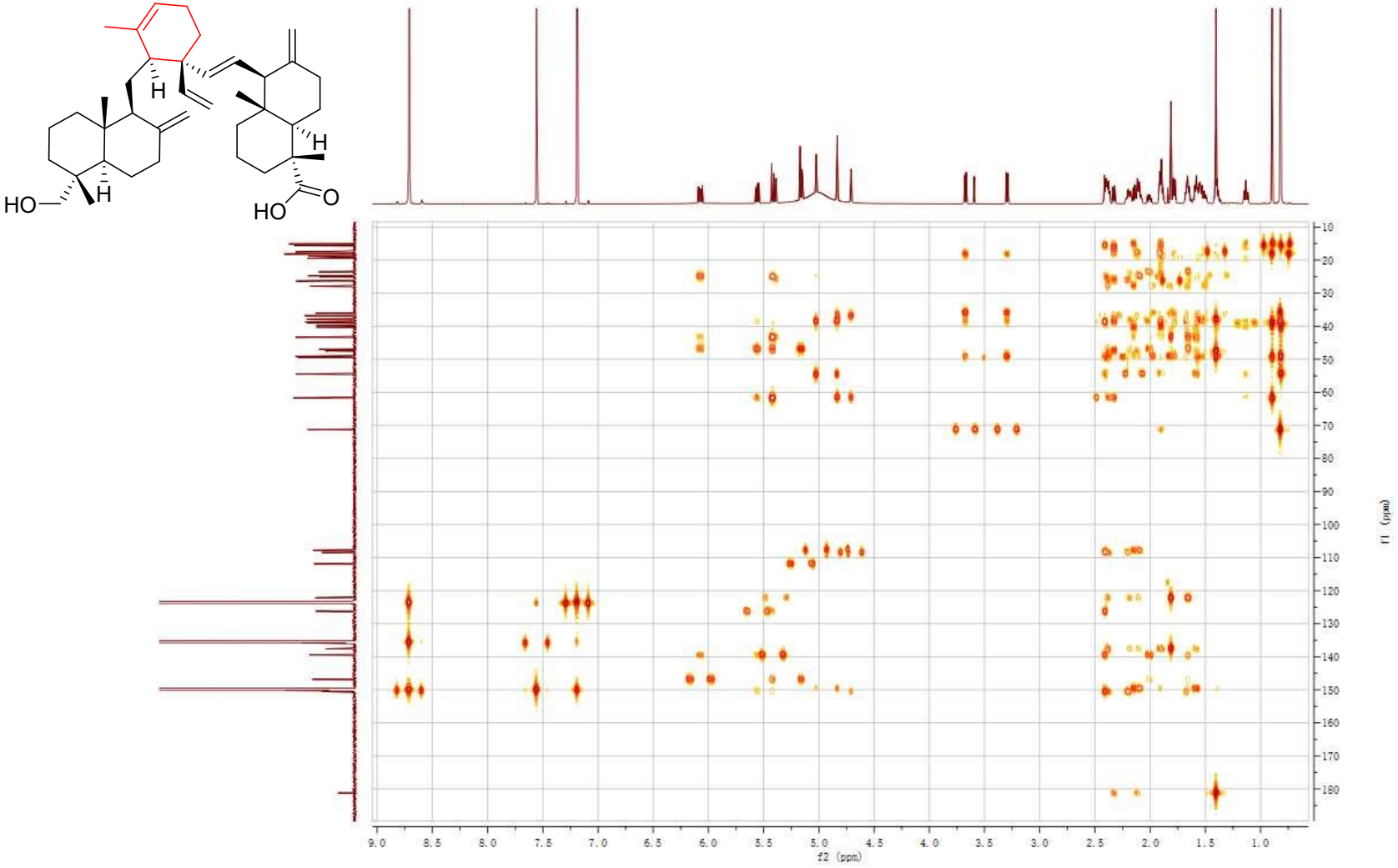


Figure S37. Expanded HMBC spectrum of cunlanceloic acid C (**3**).

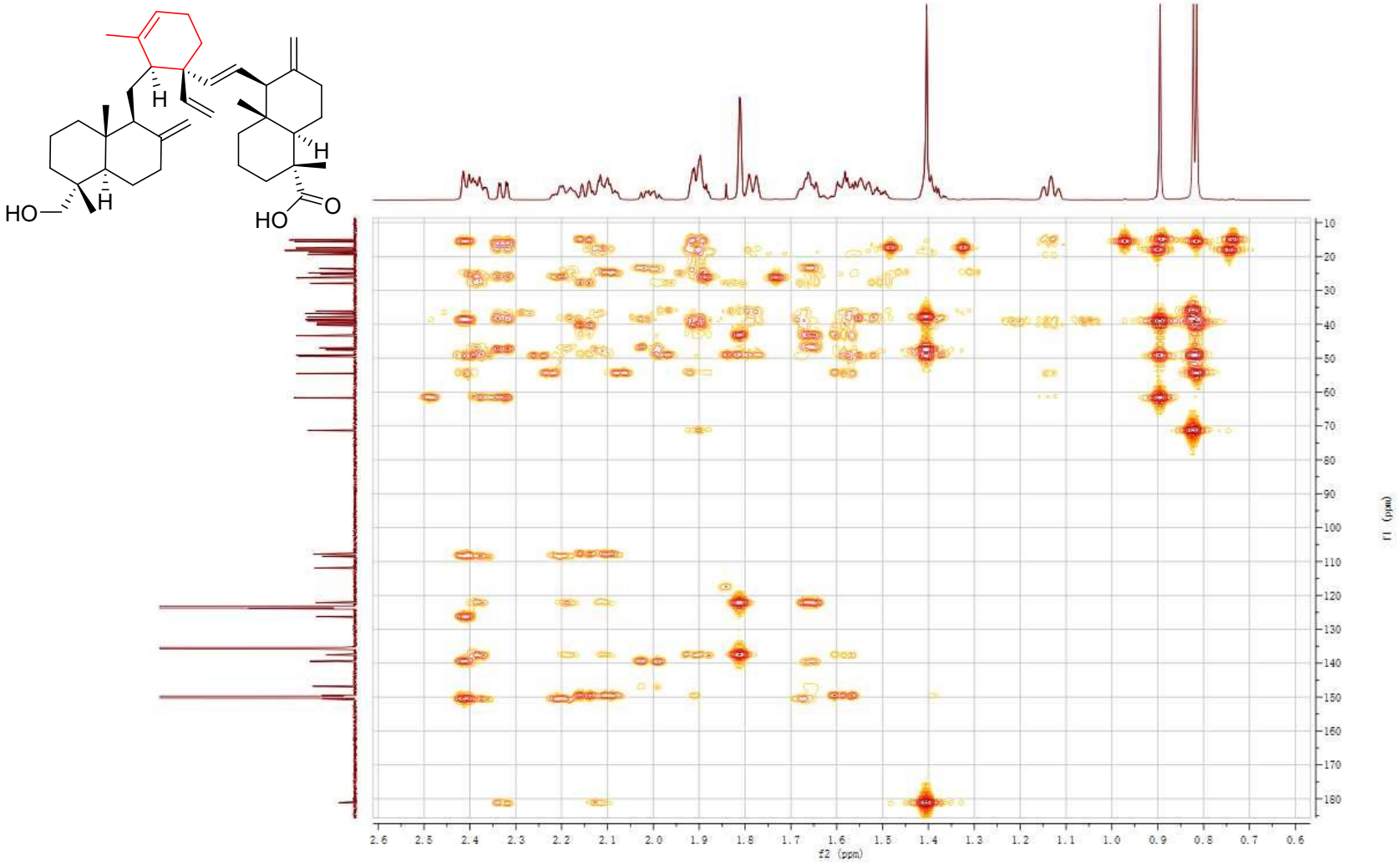


Figure S38. ROESY spectrum of cunlanceloic acid C (**3**).

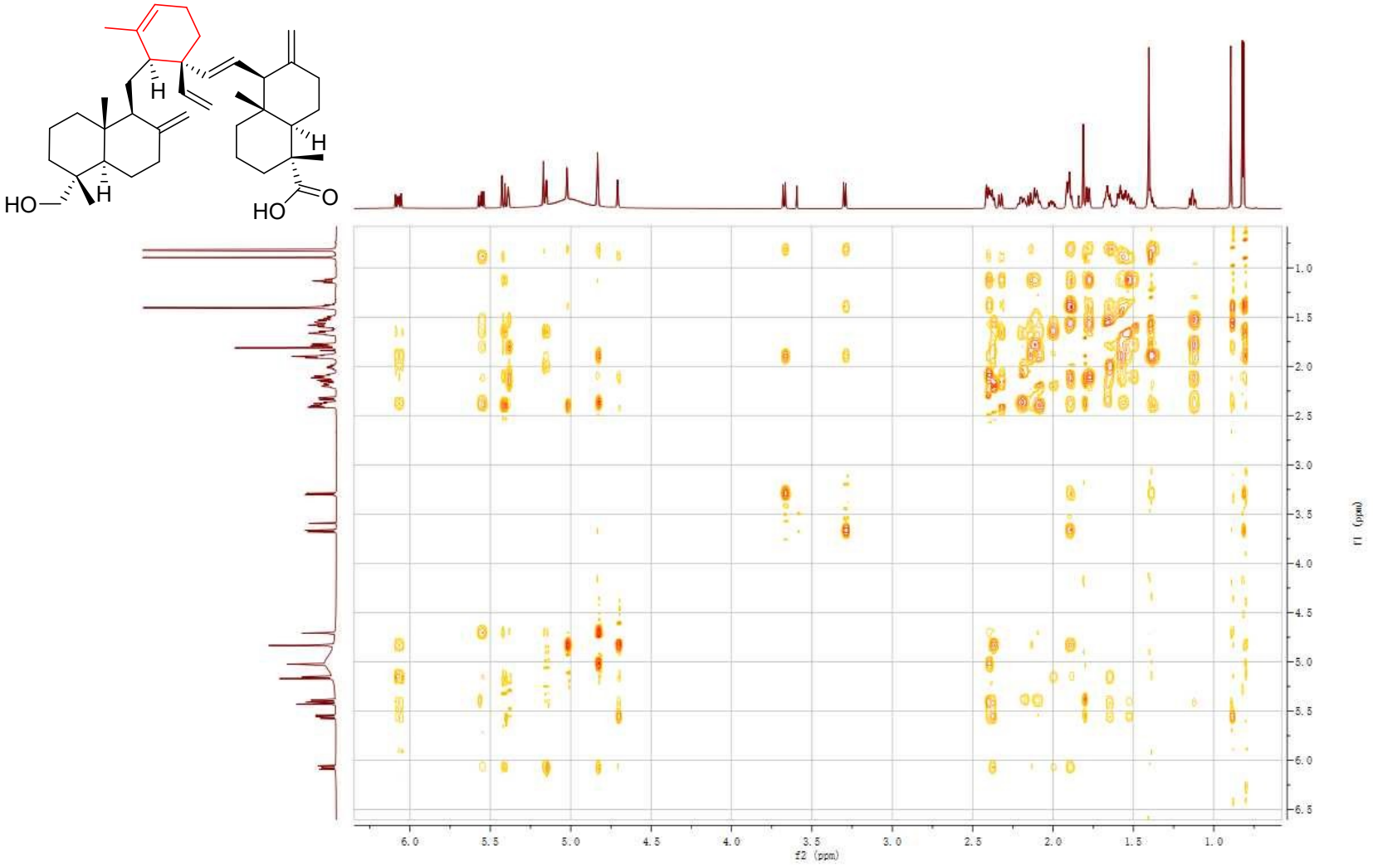


Figure S39. Expanded ROESY spectrum of cunlanceloic acid C (**3**).

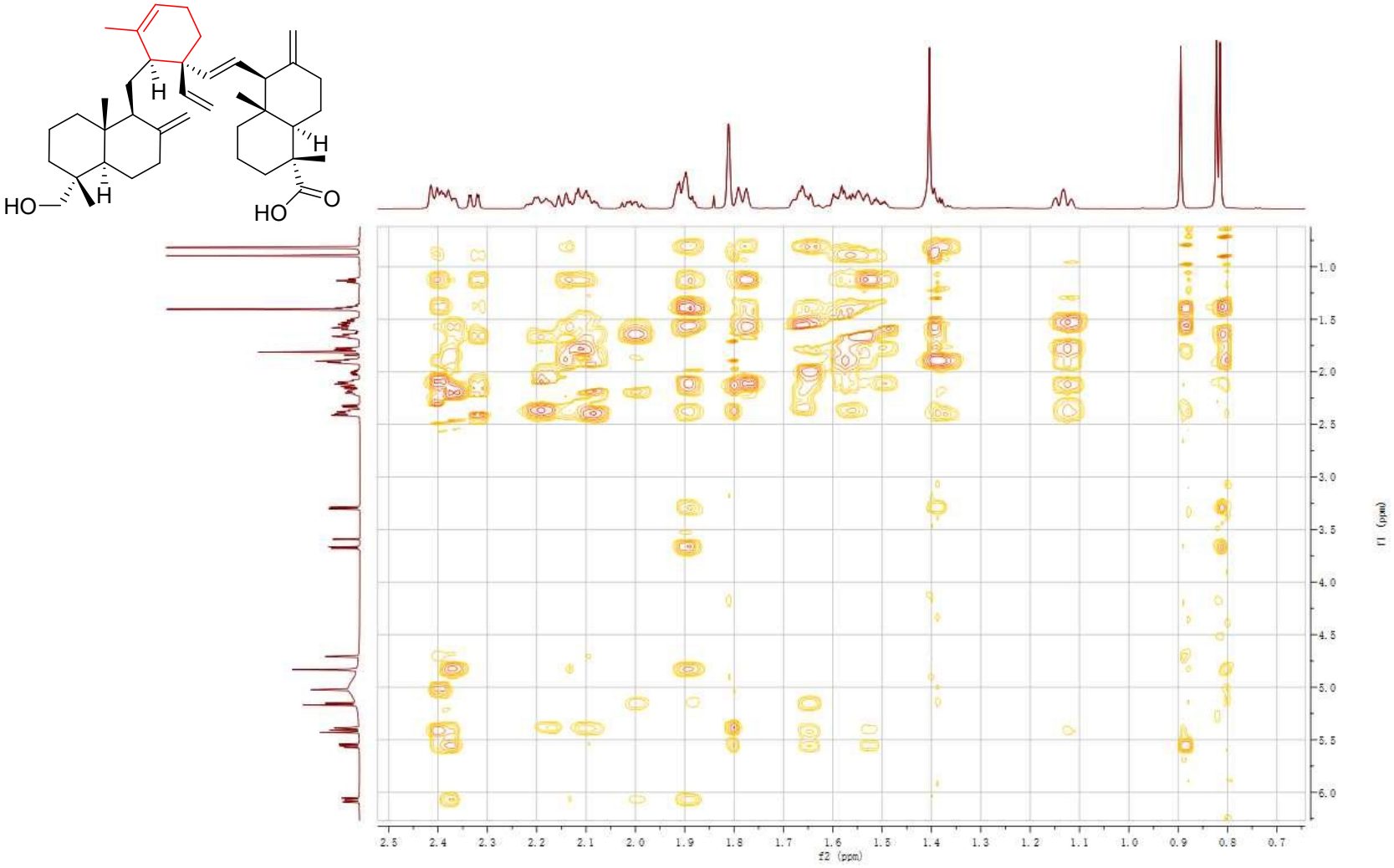


Figure S40. ESIMS spectrum of cunlanceloic acid C (**3**).

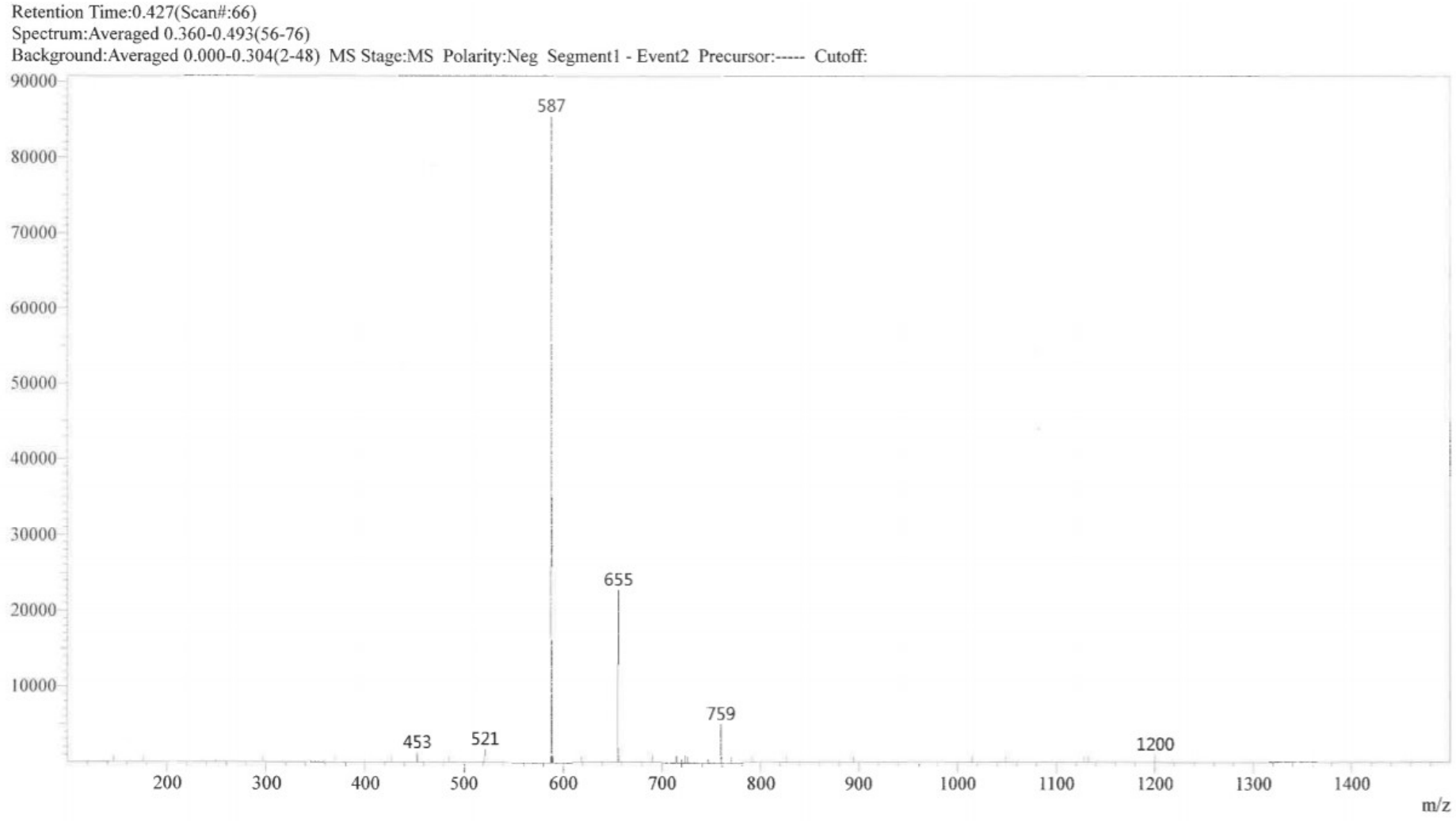


Figure S41. HRES

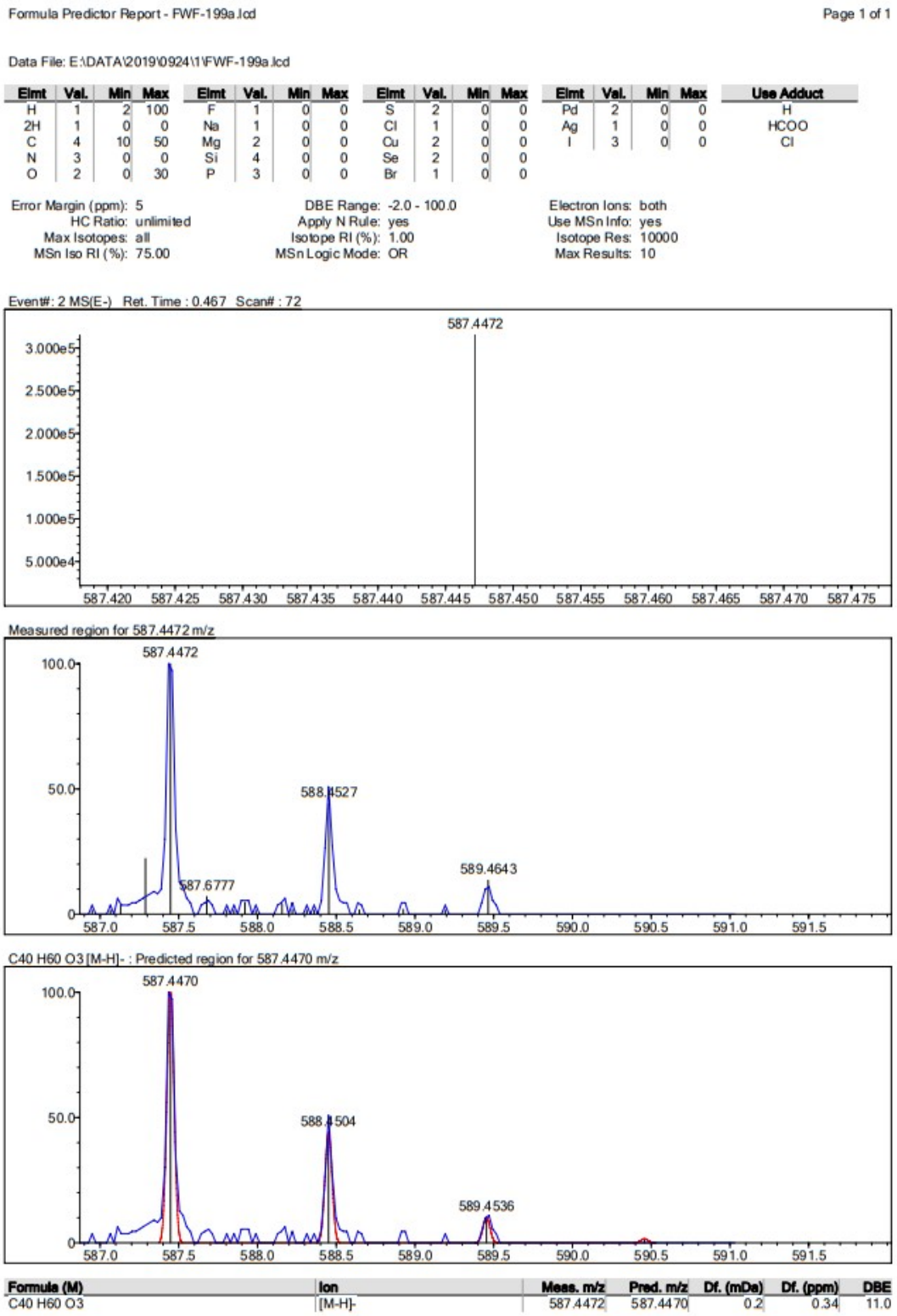


Figure S42. IR spectrum of cunlanceloic acid C (**3**).

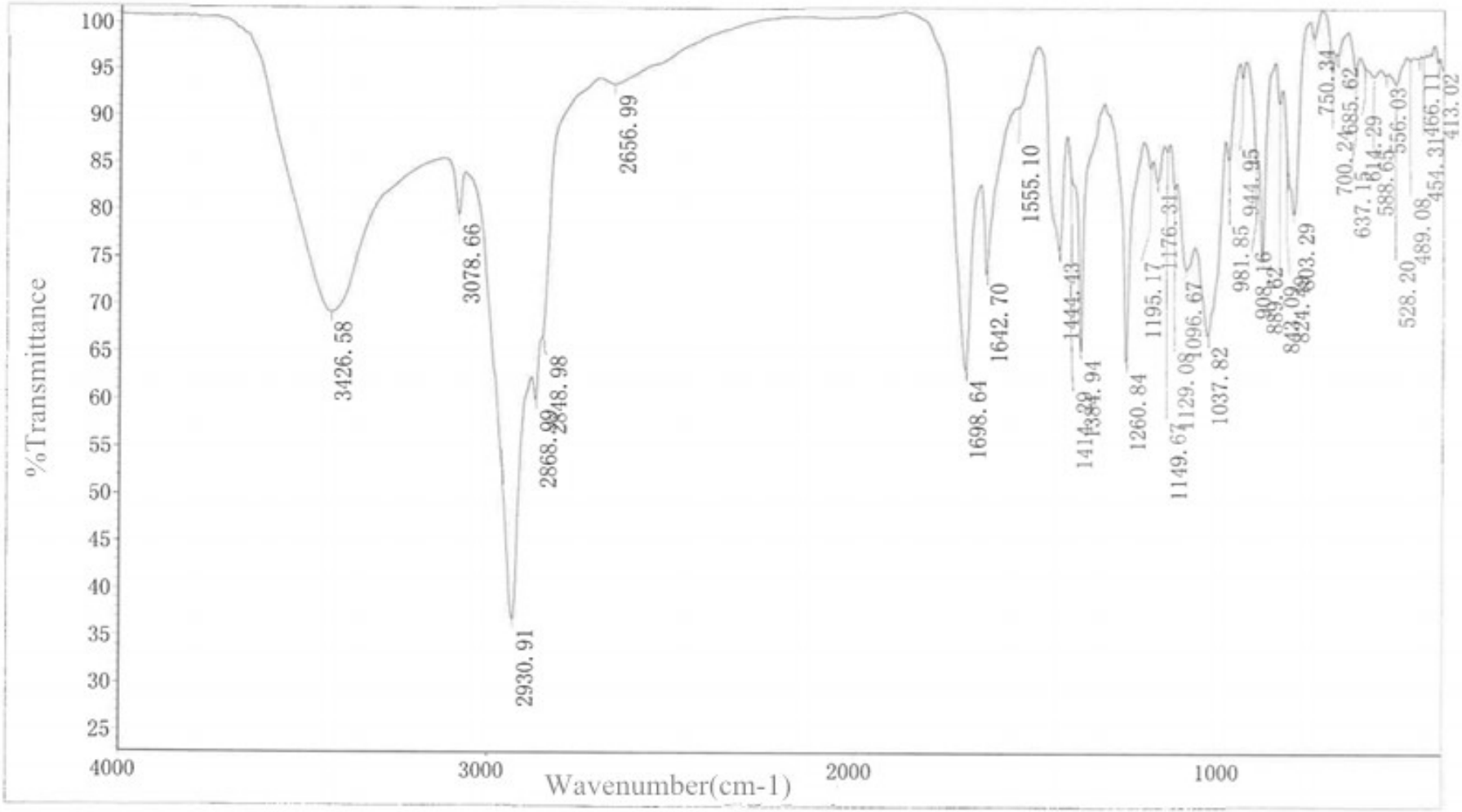


Figure S43. [1]H NMR (800 MHz) spectrum of cunlanceloic acid D (**4**) in pyridine-d_5.

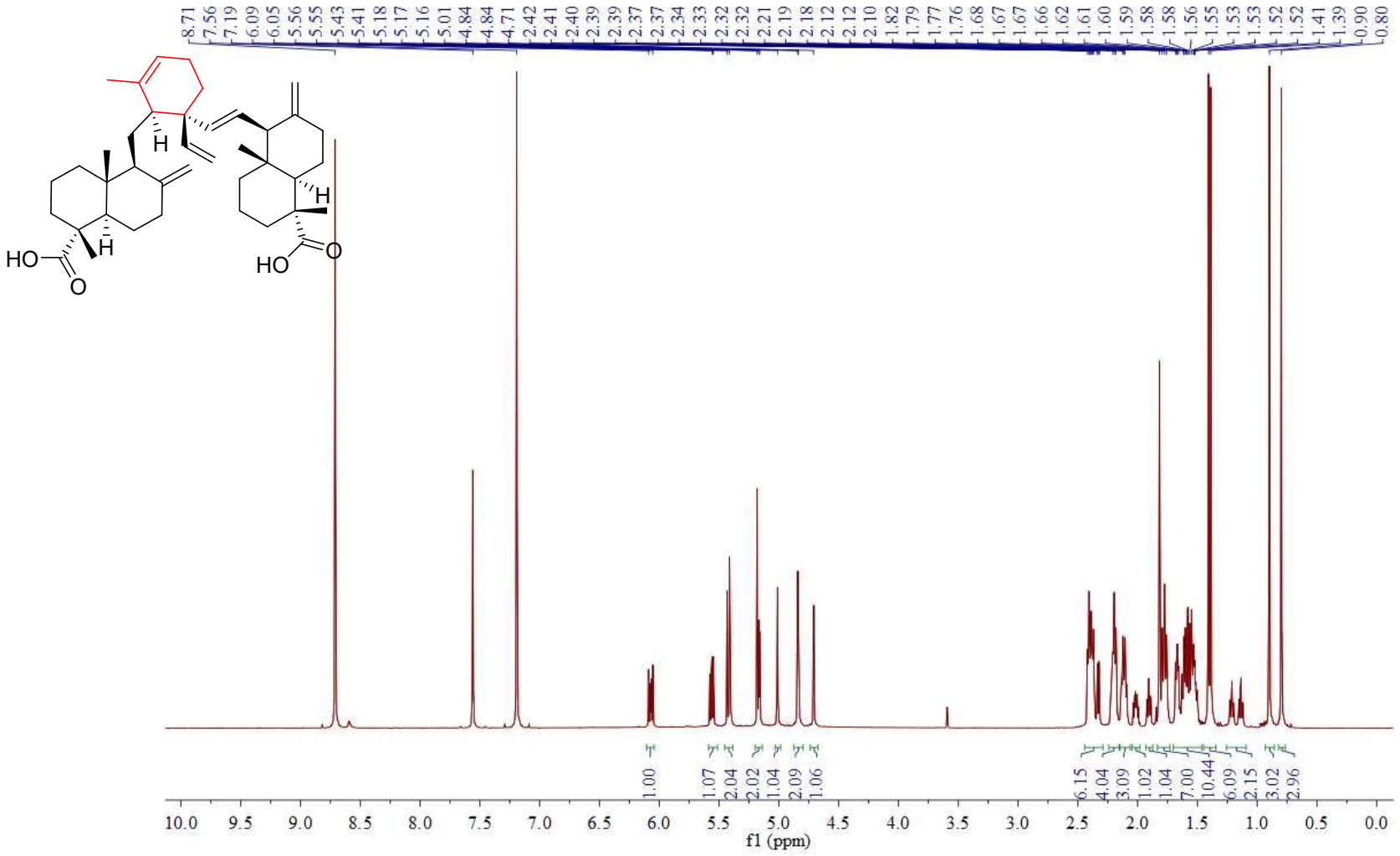


Figure S44. Expanded ^{1}H NMR spectrum of cunlanceloic acid D (**4**).

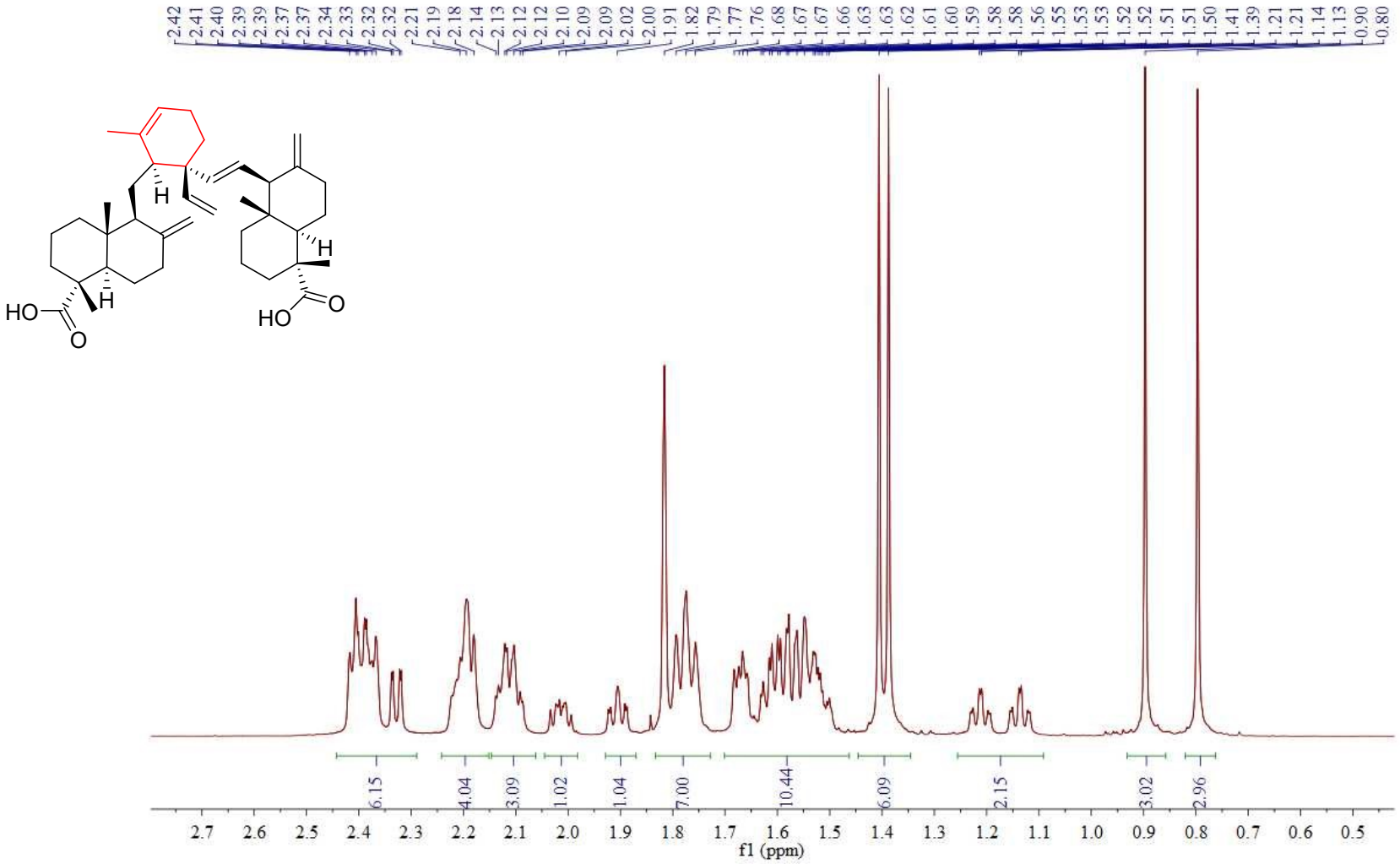


Figure S45. ^{13}C NMR and DEPT (200 MHz) spectra of cunlanceloic acid D (**4**) in pyridine-d_5.

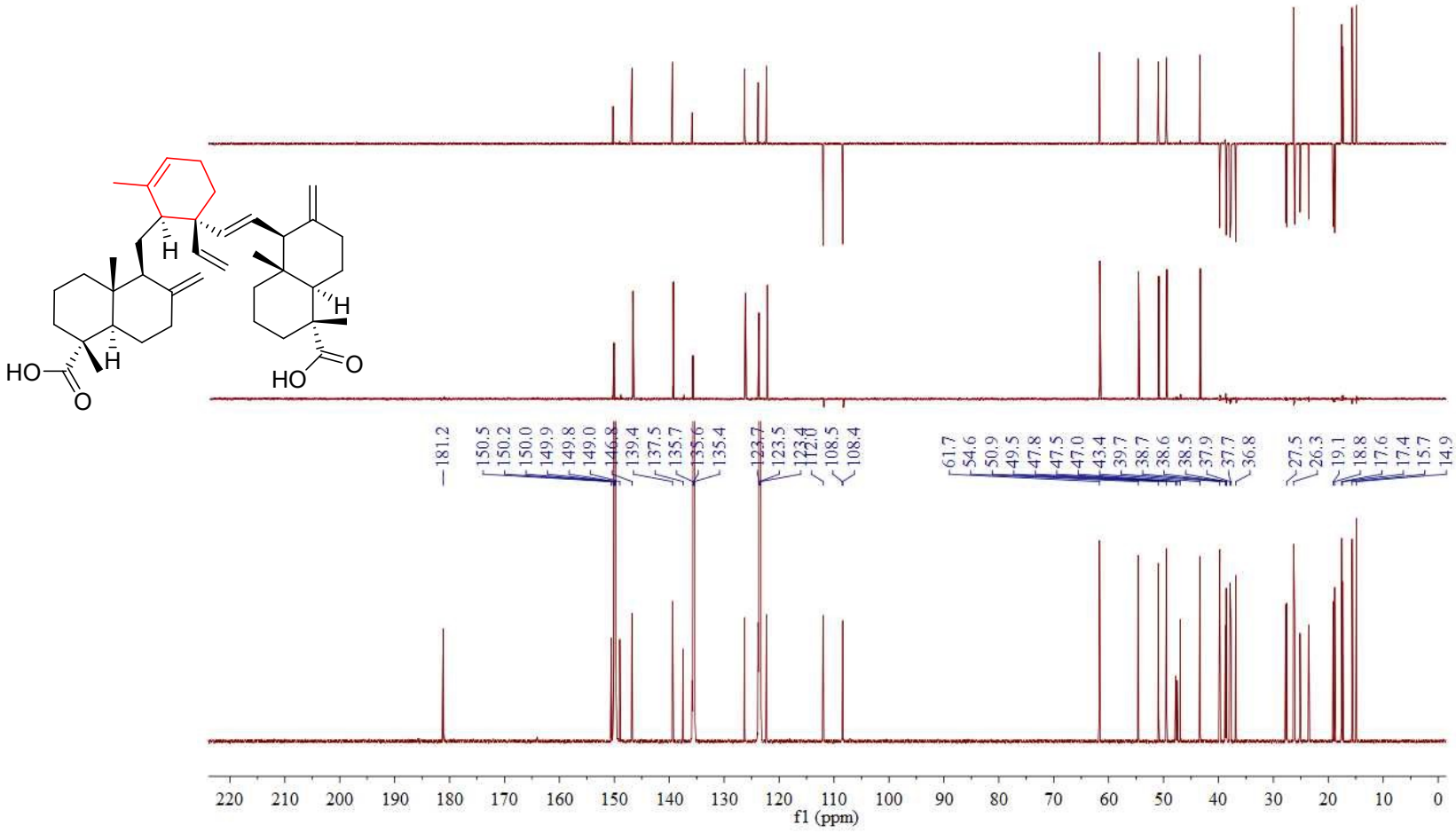


Figure S46. HSQC spectrum of cunlanceloic acid D (**4**).

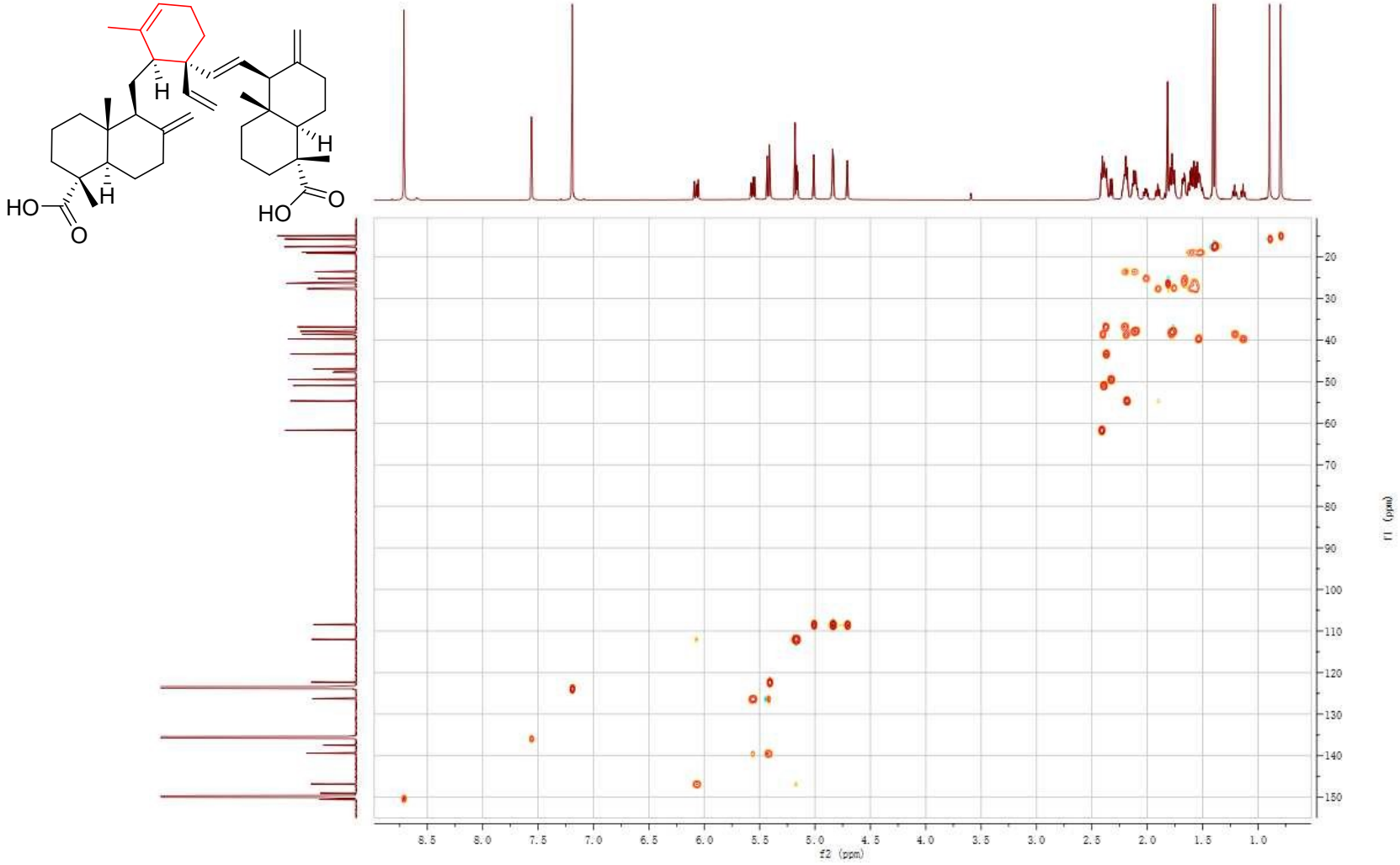


Figure S47. Expanded HSQC spectrum of cunlanceloic acid D (**4**).

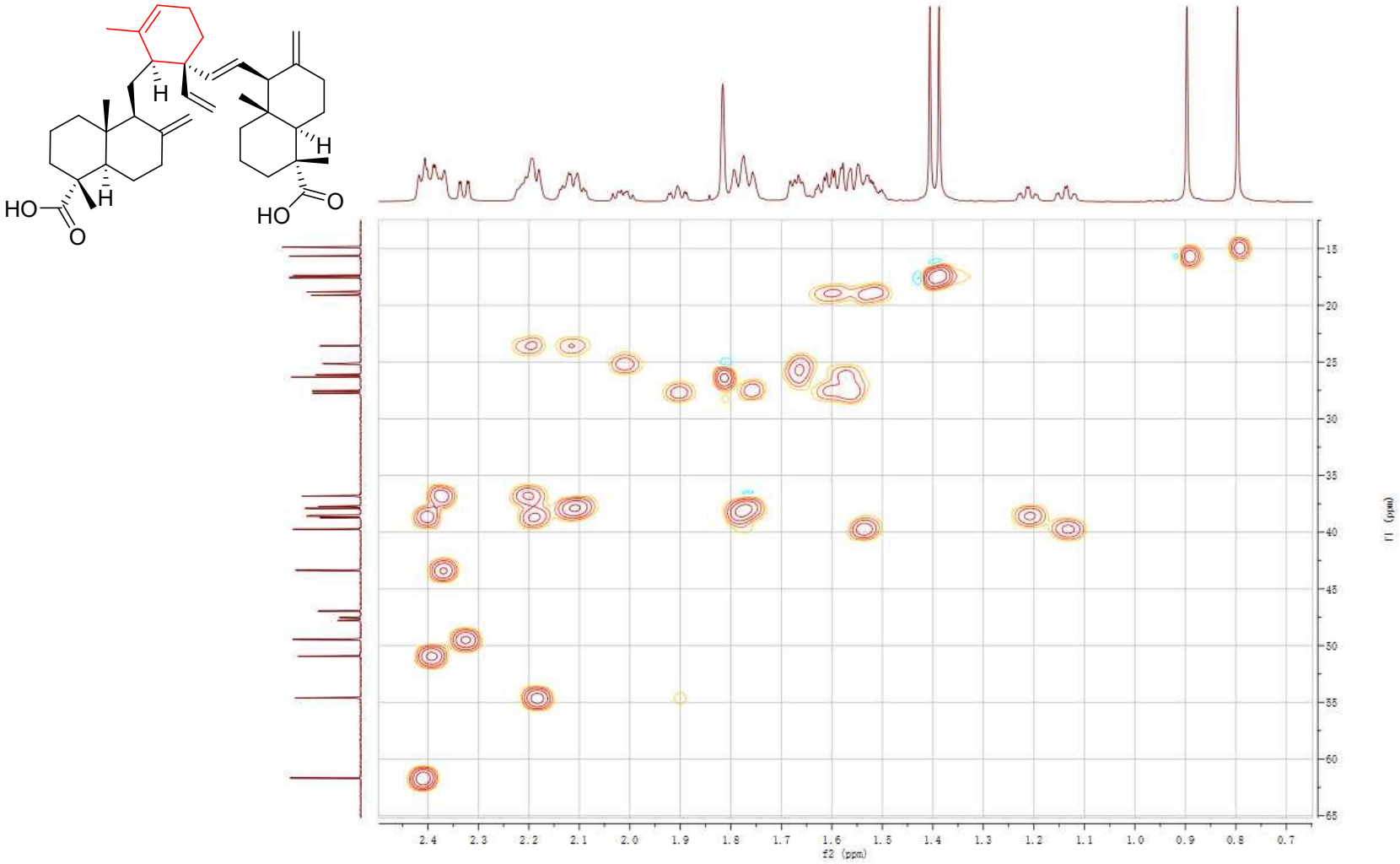


Figure S48. ^{1}H-^{1}H COSY spectrum of cunlanceloic acid D (**4**).

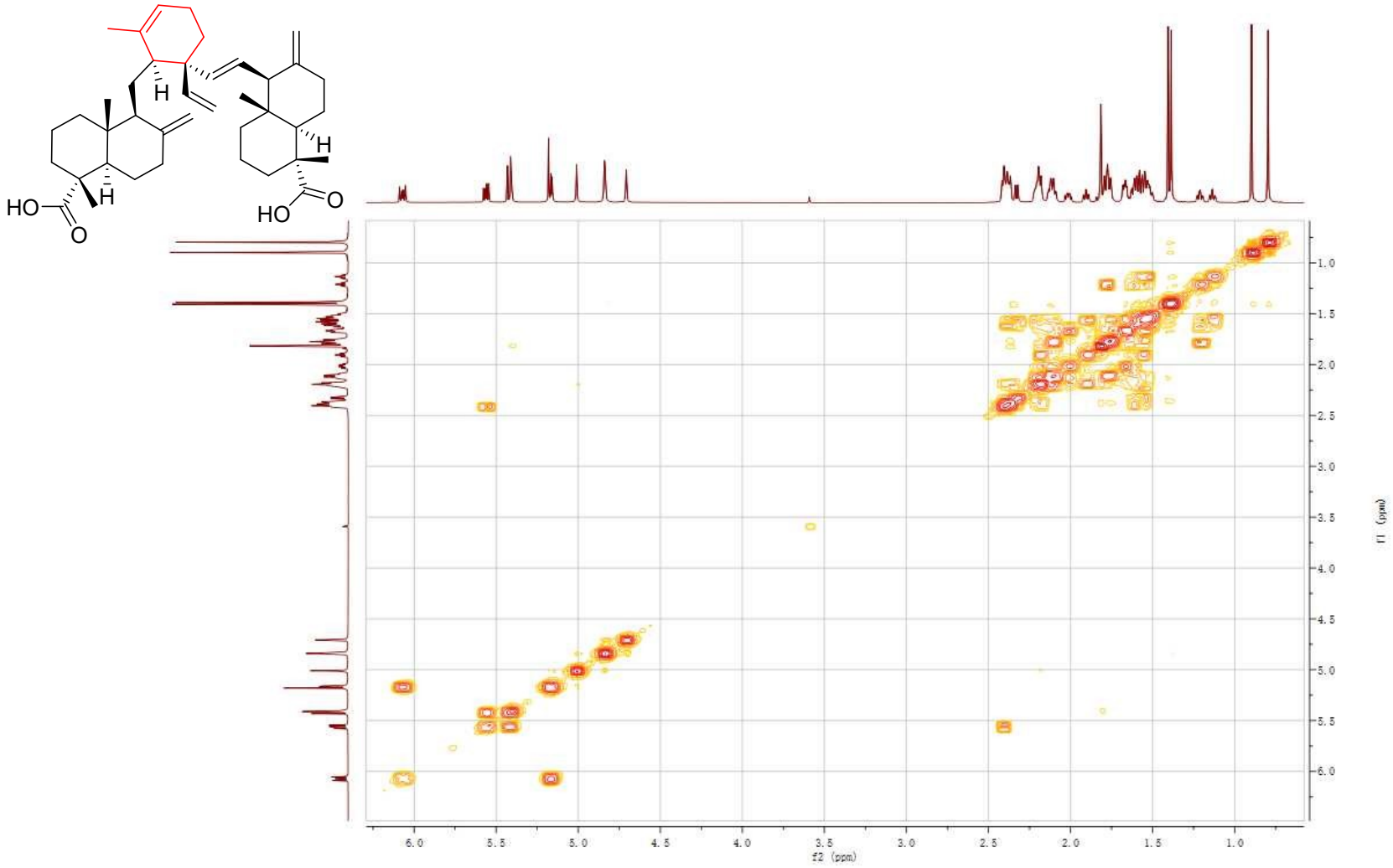


Figure S49. Expanded ^{1}H-^{1}H COSY spectrum of cunlanceloic acid D (**4**).

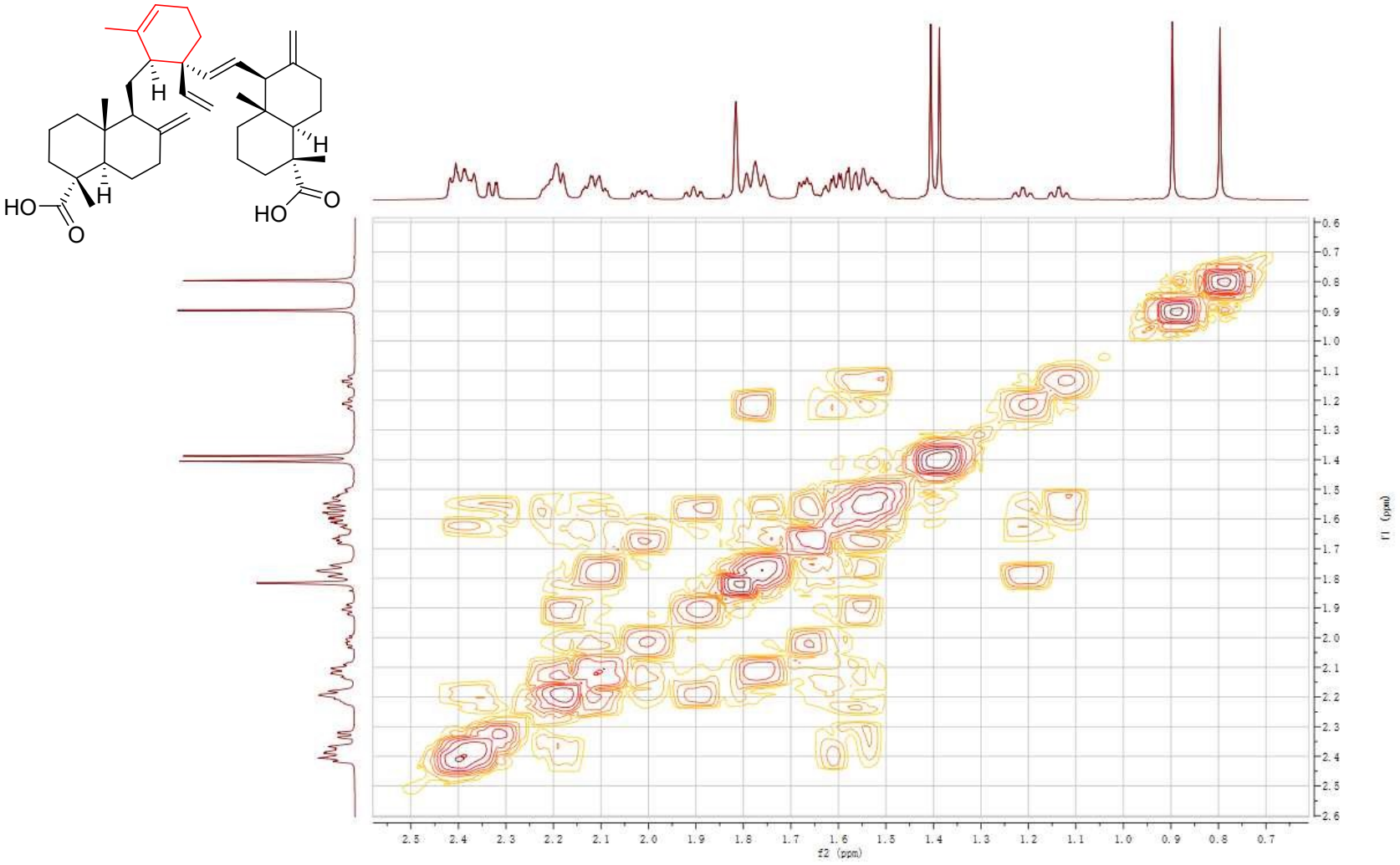


Figure S50. HMBC spectrum of cunlanceloic acid D (**4**).

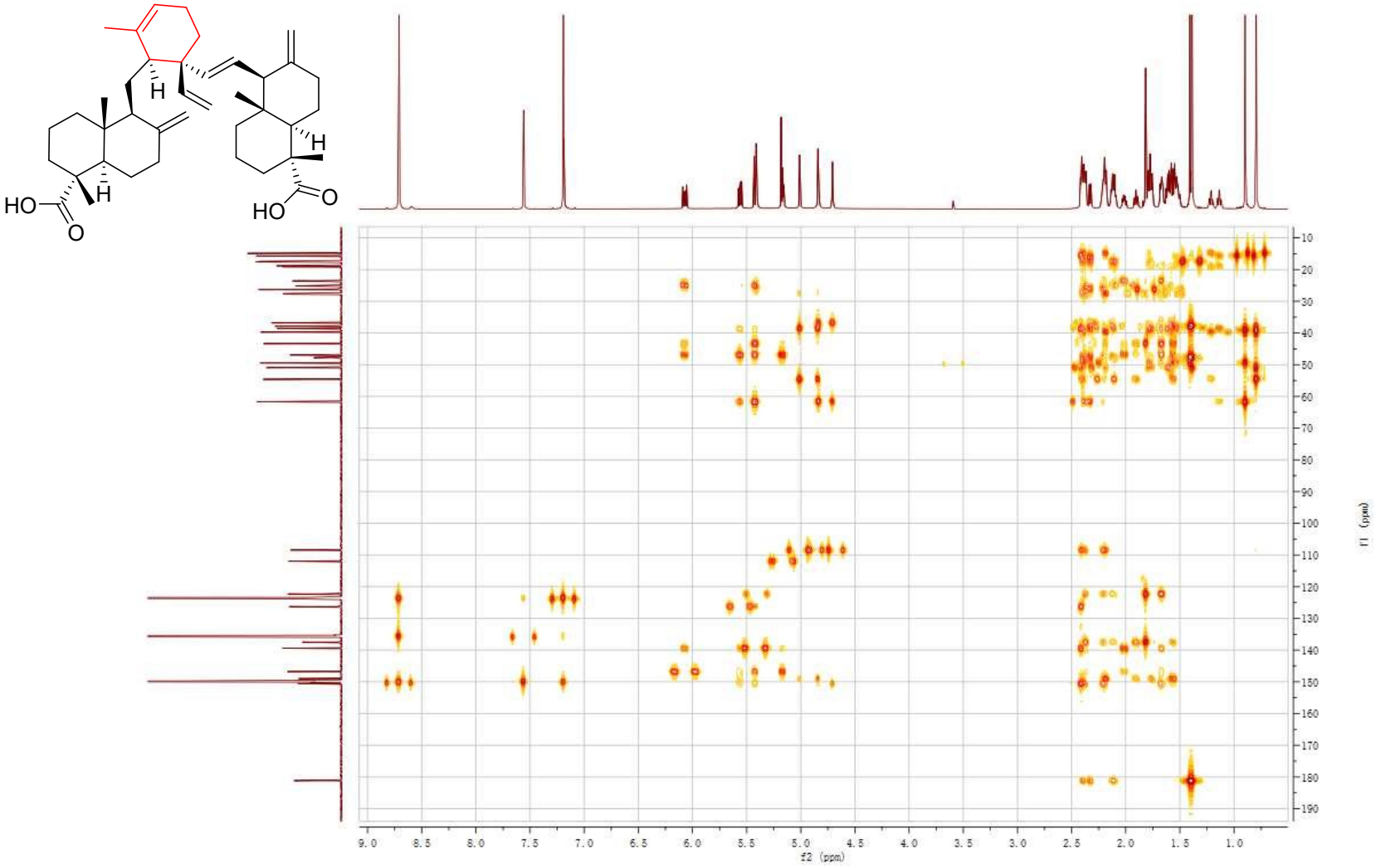


Figure S51. Expanded HMBC spectrum of cunlanceloic acid D (**4**).

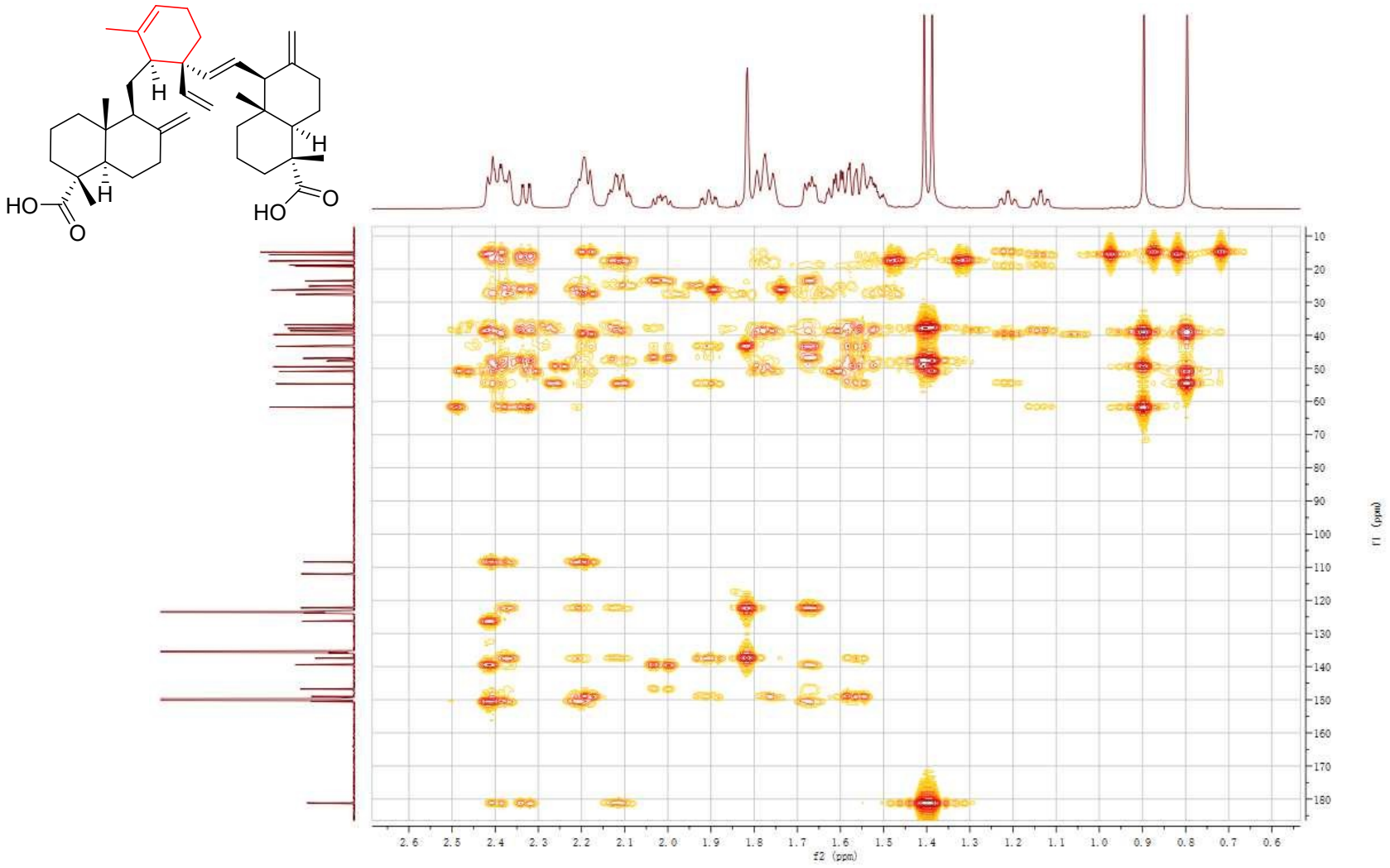


Figure S52. ROESY spectrum of cunlanceloic acid D (**4**).

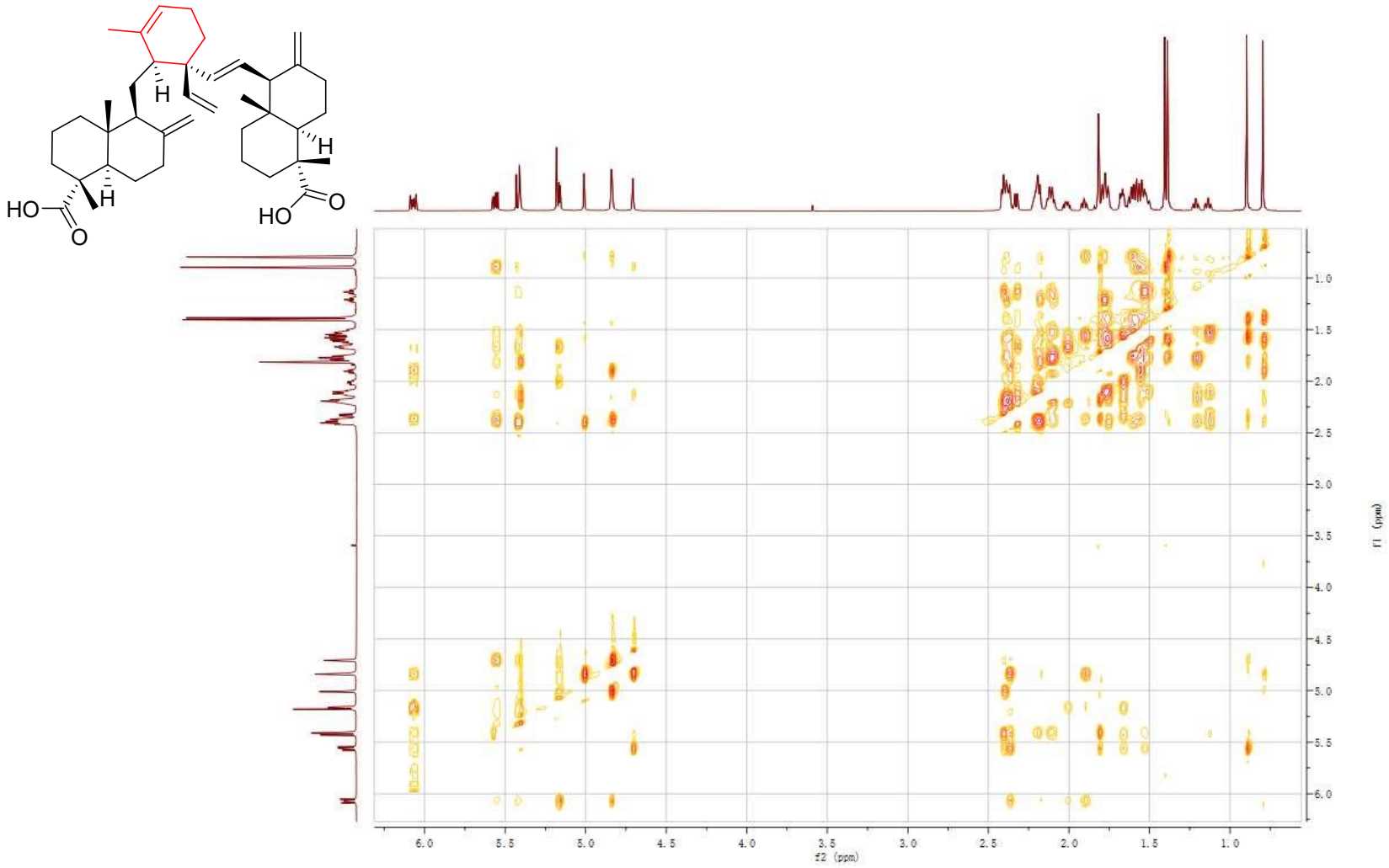


Figure S53. Expanded ROESY spectrum of cunlanceloic acid D (**4**).

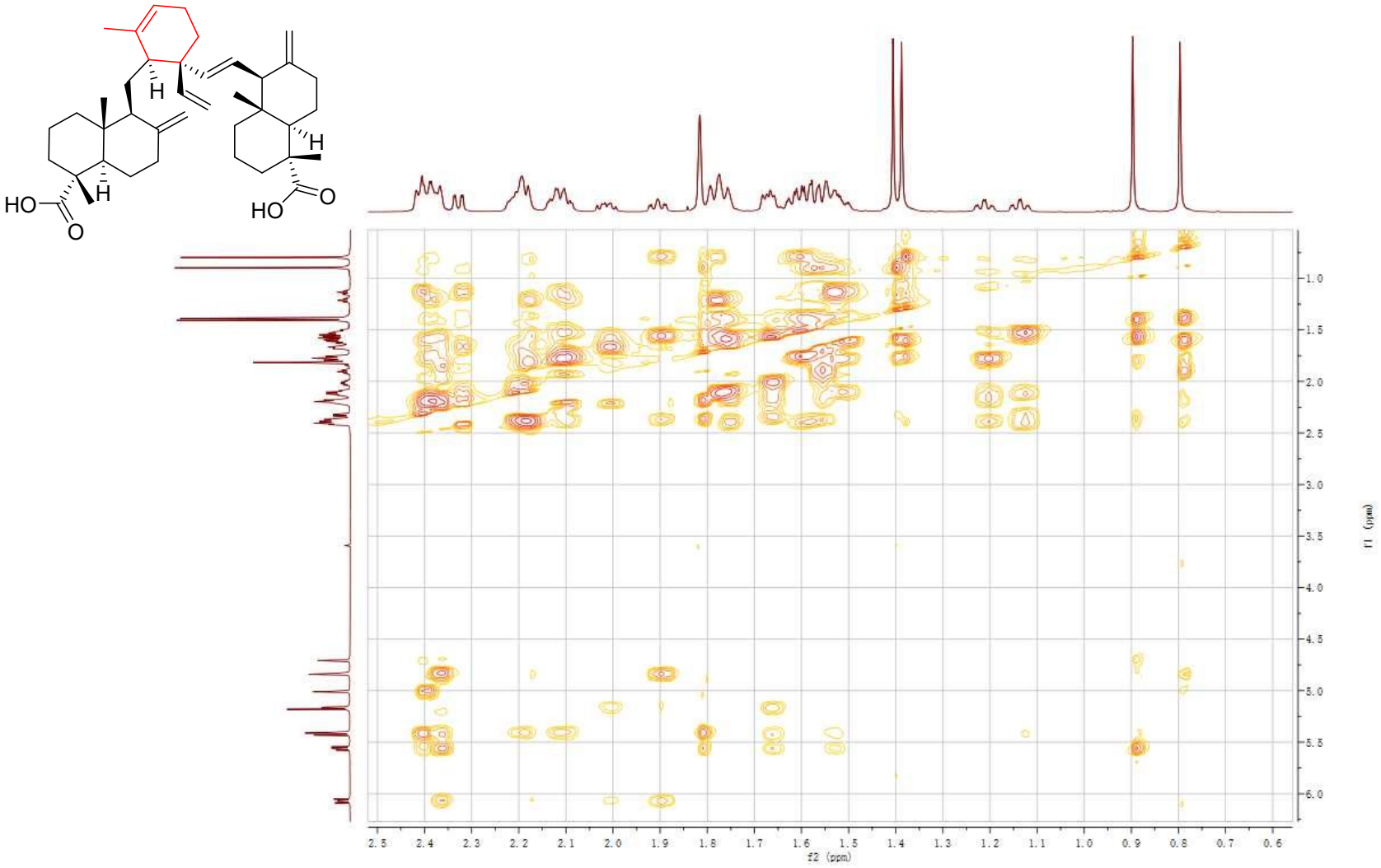


Figure S54. ESIMS spectrum of cunlanceloic acid D (**4**).

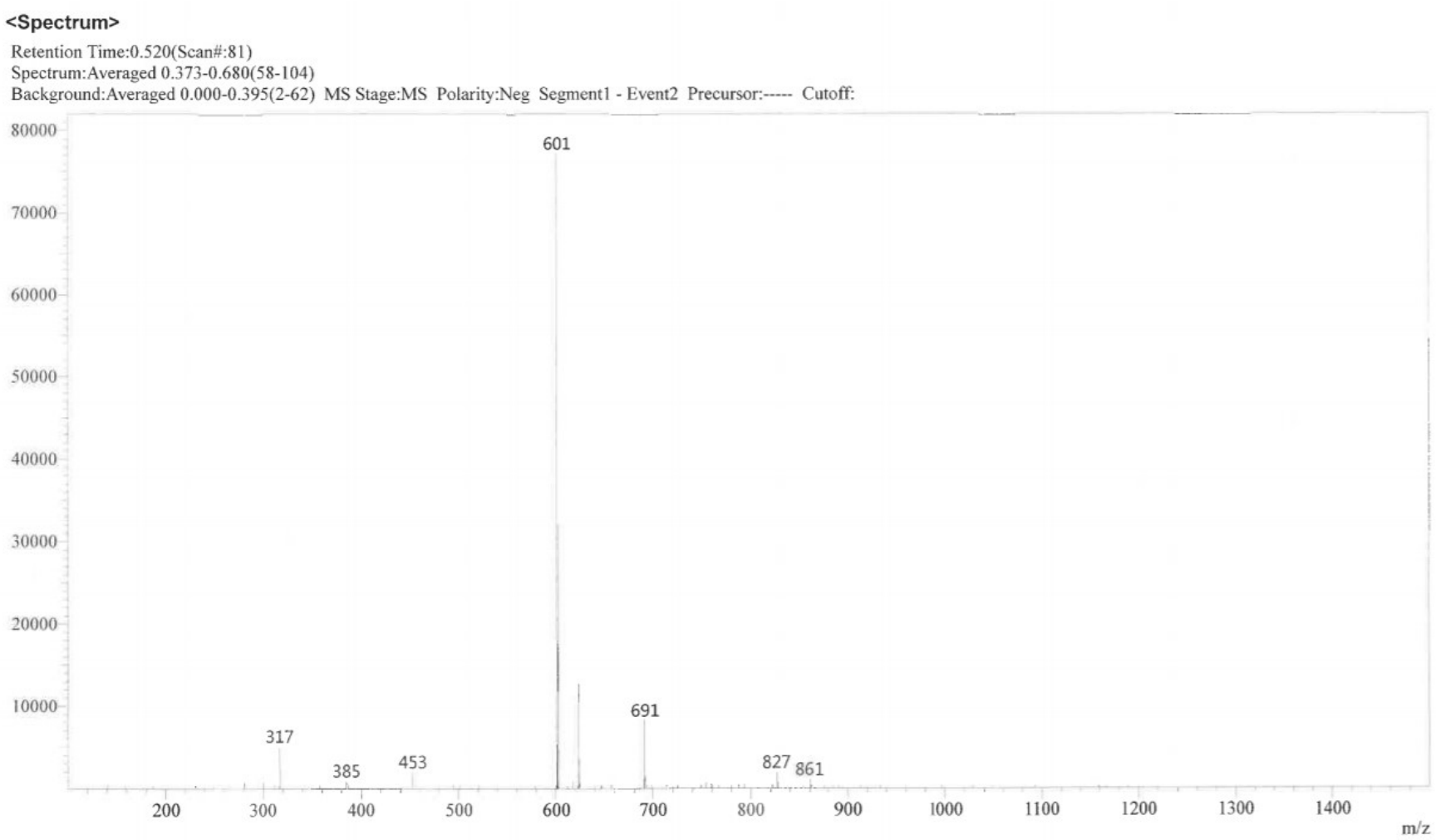


Figure S55. HRES

Formula Predictor Report - FWF-197.lcd

Data File: E:\DATA\2019\0924\1\FWF-197.lcd

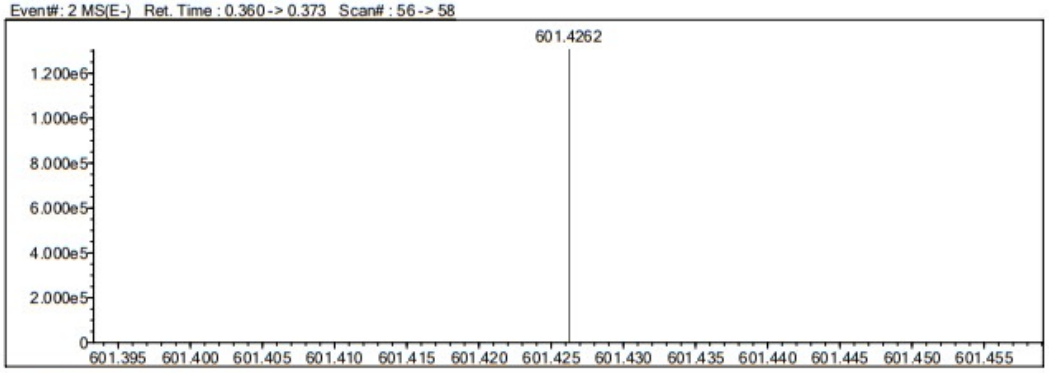
Elmt	Val.	Min	Max	Elmt	Val.	Min	Max	Elmt	Val.	Min	Max	Elmt	Val.	Min	Max	Use Adduct
H	1	2	100	F	1	0	0	S	2	0	0	Pd	2	0	0	H
2H	1	0	0	Na	1	0	0	Cl	1	0	0	Ag	1	0	0	HCOO
C	4	10	50	Mg	2	0	0	Cu	2	0	0	I	3	0	0	Cl
N	3	0	0	Si	4	0	0	Se	2	0	0					
O	2	0	30	P	3	0	0	Br	1	0	0					

Error Margin (ppm): 5
HC Ratio: unlimited
Max Isotopes: all
MSn Iso RI (%): 75.00

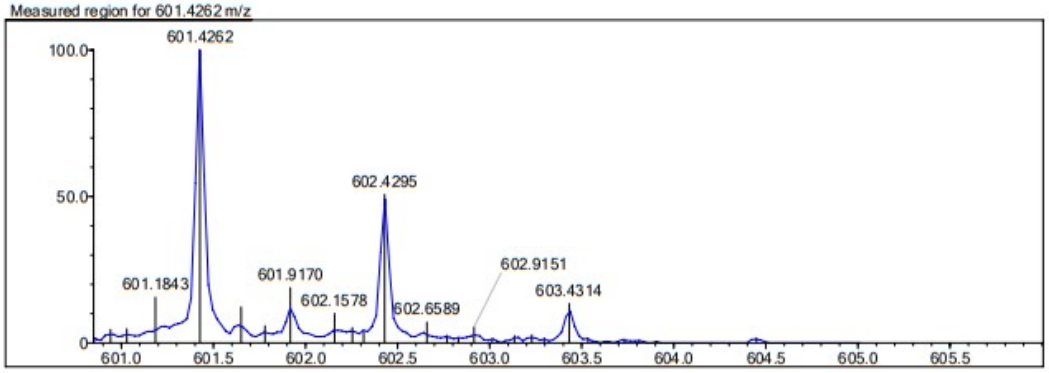
DBE Range: -2.0 - 100.0
Apply N Rule: yes
Isotope RI (%): 1.00
MSn Logic Mode: OR

Electron Ions: both
Use MSn Info: yes
Isotope Res: 10000
Max Results: 10

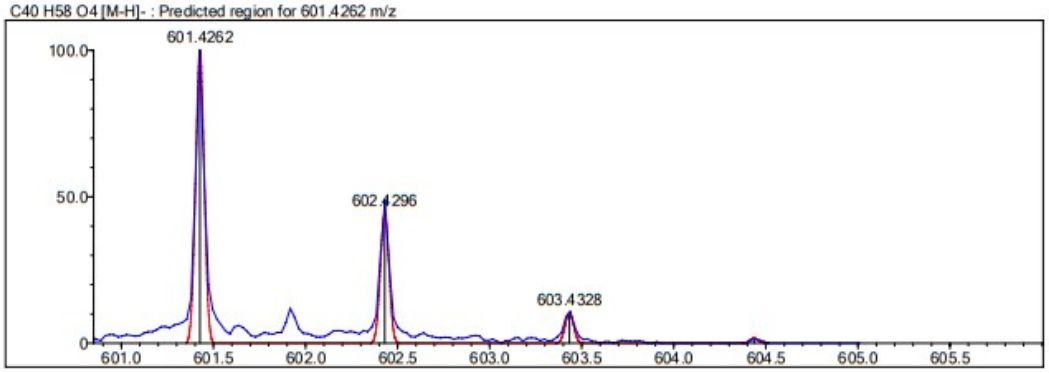
Event#: 2 MS(E-) Ret. Time : 0.360 -> 0.373 Scan# : 56 -> 58



Measured region for 601.4262 m/z



C40 H58 O4 [M-H]- : Predicted region for 601.4262 m/z



Formula (M)	Ion	Meas. m/z	Pred. m/z	Df. (mDa)	Df. (ppm)	DBE
C40 H58 O4	[M-H]-	601.4262	601.4262	-0.0	0.00	12.0

Figure S56. IR spectrum of cunlanceloic acid D (**4**).