Supplementary Information for

Spirocyclic Iridoid Alkaloids from *Plumeria rubra*

Xin-Hua Gao,[a] Bin Zhou,[a,b] Flavia M. Zimbres,[c] Zai-Yong Zhang,[a] Maria B. Cassera,[c] Jin-Xin Zhao,*[,a,b] and Jian-Min Yue*[,a,b]

[a] State Key Laboratory of Drug Research, Shanghai Institute of Materia Medica, Chinese Academy of Sciences, 555 Zuchongzhi Road, Shanghai 201203, People's Republic of China

[b] Shandong Laboratory of Yantai Drug Discovery, Bohai Rim Advanced Research Institute for Drug Discovery, 198 East Binhai Road, Yantai, Shandong 264117, People's Republic of China

[c] Department of Biochemistry and Molecular Biology, Center for Tropical and Emerging Global Diseases (CTEGD), University of Georgia, Athens, Georgia 30602, United States

*Corresponding authors

E-mail addresses: jxzhao@simm.ac.cn, jmyue@simm.ac.cn; Tel.: +86 21 68077967.

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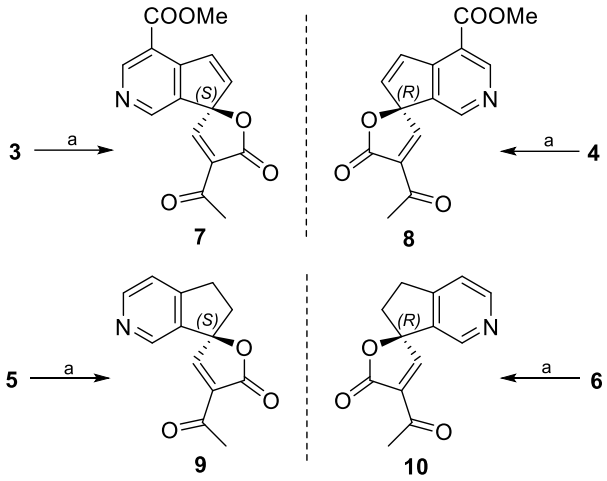
General procedure for Dess–Martin oxidation of compounds 3–6



Reaction and condition: (a) DMP (1.5 equiv), DCM, rt, 30 min (87%–93%)

Experimental: To a solution of the reactant (**3**, **4**, **5**, or **6**) in DCM (0.5 mL) was added Dess–Martin periodinane (DMP, 1.5 equiv) at room temperature. After being stirred for 30 min, the mixture was filtered through Celite, and the filtrate was concentrated in vacuo to give the corresponding oxidative product.

Entry	Reactant	DMP	Product	Yield
1	**3**, 1.5 mg	3.3 mg	**7**, 1.3 mg	87%
2	**4**, 1.9 mg	4.2 mg	**8**, 1.7 mg	90%
3	**5**, 2.4 mg	6.6 mg	**9**, 2.1 mg	88%
4	**6**, 1.3 mg	3.6 mg	**10**, 1.2 mg	93%

Table S1. Crystal data and structure refinement for compound **1**.

Identification code	cu_d8v18303_0m	
Empirical formula	$C_{15}H_{15}NO_5$	
Formula weight	289.28	
Temperature	296(2) K	
Wavelength	1.54178 Å	
Crystal system	Monoclinic	
Space group	P 21	
Unit cell dimensions	a = 6.14340(10) Å	= 90°.
	b = 10.1986(2) Å	= 94.6270(10)°.
	c = 11.1002(2) Å	= 90°.
Volume	693.21(2) $Å^3$	
Z	2	
Density (calculated)	1.386 Mg/m^3	
Absorption coefficient	0.880 mm^{-1}	
F(000)	304	
Crystal size	0.180 x 0.150 x 0.120 mm^3	
Theta range for data collection	7.983 to 70.152°.	
Index ranges	-6<=h<=7, -12<=k<=12, -13<=l<=13	
Reflections collected	8372	
Independent reflections	2531 [R(int) = 0.0318]	
Completeness to theta = 67.679°	96.2 %	
Absorption correction	Semi-empirical from equivalents	
Max. and min. transmission	0.7456 and 0.5096	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	2531 / 1 / 194	
Goodness-of-fit on F^2	1.053	
Final R indices [I>2sigma(I)]	R1 = 0.0294, wR2 = 0.0740	
R indices (all data)	R1 = 0.0298, wR2 = 0.0745	
Absolute structure parameter	0.09(6)	
Extinction coefficient	0.074(11)	
Largest diff. peak and hole	0.131 and -0.109 $e.Å^{-3}$	

Table S2. Crystal data and structure refinement for compound **2**.

Identification code	cu_22020101_0m	
Empirical formula	$C_{15}H_{15}NO_5$	
Formula weight	289.28	
Temperature	240.0 K	
Wavelength	1.54178 Å	
Crystal system	orthorhombic	
Space group	$P2_12_12_1$	
Unit cell dimensions	a = 8.3810(4) Å	= 90°.
	b = 16.4425(7) Å	= 94.6270(10)°.
	c = 20.4203(8) Å	= 90°.
Volume	2814.0(2) $Å^3$	
Z	8	
Density (calculated)	1.361 Mg/m^3	
Absorption coefficient	0.867 mm^{-1}	
F(000)	1208.0	
Crystal size	0.08 x 0.06 x 0.05 mm^3	
Theta range for data collection	6.902 to 149.514°.	
Index ranges	-8<=h<=10, -20<=k<=18, -25<=l<=25	
Reflections collected	19899	
Independent reflections	5732 [R(int) = 0.0366]	
Data / restraints / parameters	5732 / 0 / 385	
Goodness-of-fit on F^2	1.079	
Final R indices [I>2sigma(I)]	R1 = 0.0454, wR2 = 0.1250	
R indices (all data)	R1 = 0.0523, wR2 = 0.1335	
Flack parameter	0.00(6)	
Largest diff. peak and hole	0.37 and -0.29 e.$Å^{-3}$	

Table S3. Crystal data and structure refinement for compound **4**.

Identification code	mjl18230_0m	
Empirical formula	C15 H13 N O5	
Formula weight	287.26	
Temperature	170.0 K	
Wavelength	1.34139 Å	
Crystal system	Monoclinic	
Space group	P 1 21 1	
Unit cell dimensions	a = 6.9407(4) Å	= 90°.
	b = 23.6776(12) Å	= 91.765(2)°.
	c = 8.0529(5) Å	= 90°.
Volume	1322.78(13) $Å^3$	
Z	4	
Density (calculated)	1.442 mg/m^3	
Absorption coefficient	0.591 mm^{-1}	
F(000)	600	
Crystal size	0.12 x 0.1 x 0.08 mm^3	
Theta range for data collection	5.783 to 54.900°.	
Index ranges	-8<=h<=8, -28<=k<=28, -9<=l<=9	
Reflections collected	15931	
Independent reflections	4889 [R(int) = 0.0316]	
Completeness to theta = 53.594°	97.7 %	
Absorption correction	Semi-empirical from equivalents	
Max. and min. transmission	0.7508 and 0.6270	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	4889 / 1 / 385	
Goodness-of-fit on F^2	1.031	
Final R indices [I>2sigma(I)]	R1 = 0.0268, wR2 = 0.0742	
R indices (all data)	R1 = 0.0270, wR2 = 0.0744	
Absolute structure parameter	-0.04(4)	
Extinction coefficient	n/a	
Largest diff. peak and hole	0.165 and -0.138 $e.Å^{-3}$	

Table S4. Crystal data and structure refinement for compound **6**.

Identification code	cu_22020060_0m	
Empirical formula	C13H13NO3	
Formula weight	231.24	
Temperature	170.0 K	
Wavelength	1.54178 Å	
Crystal system	Orthorhombic	
Space group	$P2_12_12_1$	
Unit cell dimensions	a = 8.4661(2) Å	= 90°.
	b = 8.8867(2) Å	= 90°.
	c = 15.5541(4) Å	= 90°.
Volume	1170.22(5) $Å^3$	
Z	4	
Density (calculated)	1.313 mg/m^3	
F(000)	488.0	
Crystal size	0.15 x 0.12 x 0.08 mm^3	
Theta range for data collection	11.378 to 149.814°.	
Index ranges	-10<=h<=9, -11<=k<=11, -19<=l<=19	
Reflections collected	13255	
Independent reflections	2397 [R(int) = 0.0376, R(sigma) = 0.0245]	
Data / restraints / parameters	2397 / 0 / 156	
Goodness-of-fit on F^2	1.095	
Final R indices [I>2sigma(I)]	R1 = 0.0290, wR2 = 0.0781	
R indices (all data)	R1 = 0.0298, wR2 = 0.0790	
Flack parameter	0.11(6)	
Largest diff. peak and hole	0.17 and -0.15 $e.Å^{-3}$	

Table S5. The ^{13}C NMR data of **5**, **6**, plumerianine, and plumericidine.

			plumerianine[1]		
	5	**6**	major	minor	plumericidine[2]
no.	δ_C[a]	δ_C[a]	δ_C[a]	δ_C[a]	δ_C[b]
1	145.80	145.64	145.65	145.83	145.0
3	150.81	150.85	150.85	150.89	150.2
4	122.44	122.49	122.44	122.44	120.9
5	157.00	157.03	157.03	157.03	154.2
6	31.11	31.09	31.09	31.12	29.8
7	36.74	36.75	36.76	36.76	35.3
8	94.93	94.86	94.90	94.88	93.1
9	137.89	137.85	137.84	137.91	136.0
10	150.10	150.09	150.15	150.15	149.1
11	139.89	139.89	139.88	139.90	138.3
12	172.82	172.78	172.85	172.91	170.9
13	63.59	63.72	63.73	63.61	61.6
14	22.27	22.45	22.44	22.26	22.4

[a]Measured in CD_3OD. [b]Measured in DMSO-D_6.

Table S6. The specific rotation values of **5**, **6**, plumerianine, and plumericidine

5	**6**	plumerianine[1]	plumericidine[2]
−72 ($CHCl_3$), −47 (CH_3OH)	+25 ($CHCl_3$), +19 (CH_3OH)	+18 ($CHCl_3$)	+17 (CH_3OH)

The reported 1D NMR data of plumerianine showed a set of two signals for each carbon of rotamers in reference 1.[1] The minor rotamer of plumerianine was very likely to be compound **5** in our current isolation by careful and prudent NMR data comparison. The absolute configuration of plumericidine[2] can't be verified by the X-ray crystallography study without the Flack parameter and identification of radiation source in reference 2.

References

1. E. M. Hassan, A. A. Shahat, N. A. Ibrahim, A. J. Vlietinck, S. Apers and L. Pieters, *Planta Med.*, 2008, **74**, 1749–1750.

2. G. Ye, Z. X. Li, G. X. Xia, H. Peng, Z. L. Sun and C. G. Huang, *Helv. Chim. Acta*, 2009, **92**, 2790–2794.

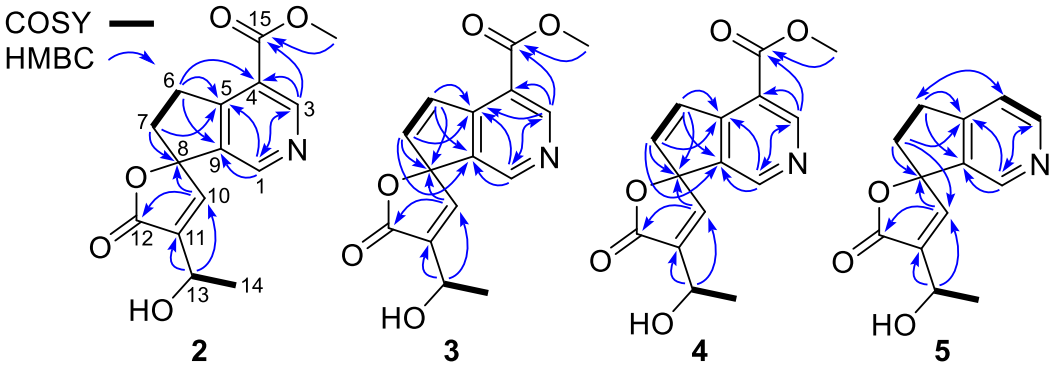


Figure S1. Key HMBC and COSY correlations of **2**–**5**.

Figure S2. ^{1}H NMR spectrum of plumerianoid A (**1**) in CD_3OD.

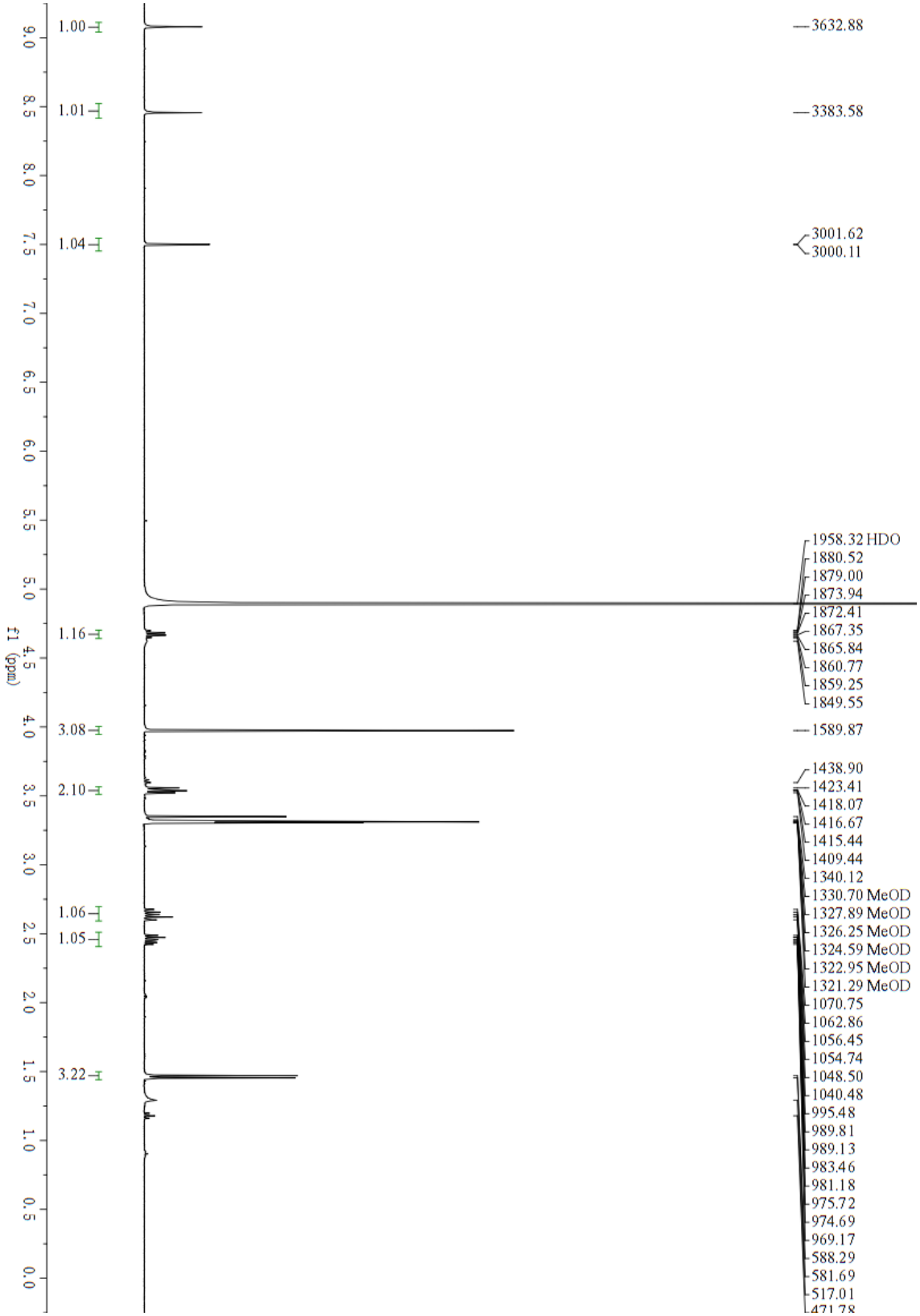


Figure S3. ^{13}C NMR Spectrum of plumerianoid A (**1**) in CD_3OD.

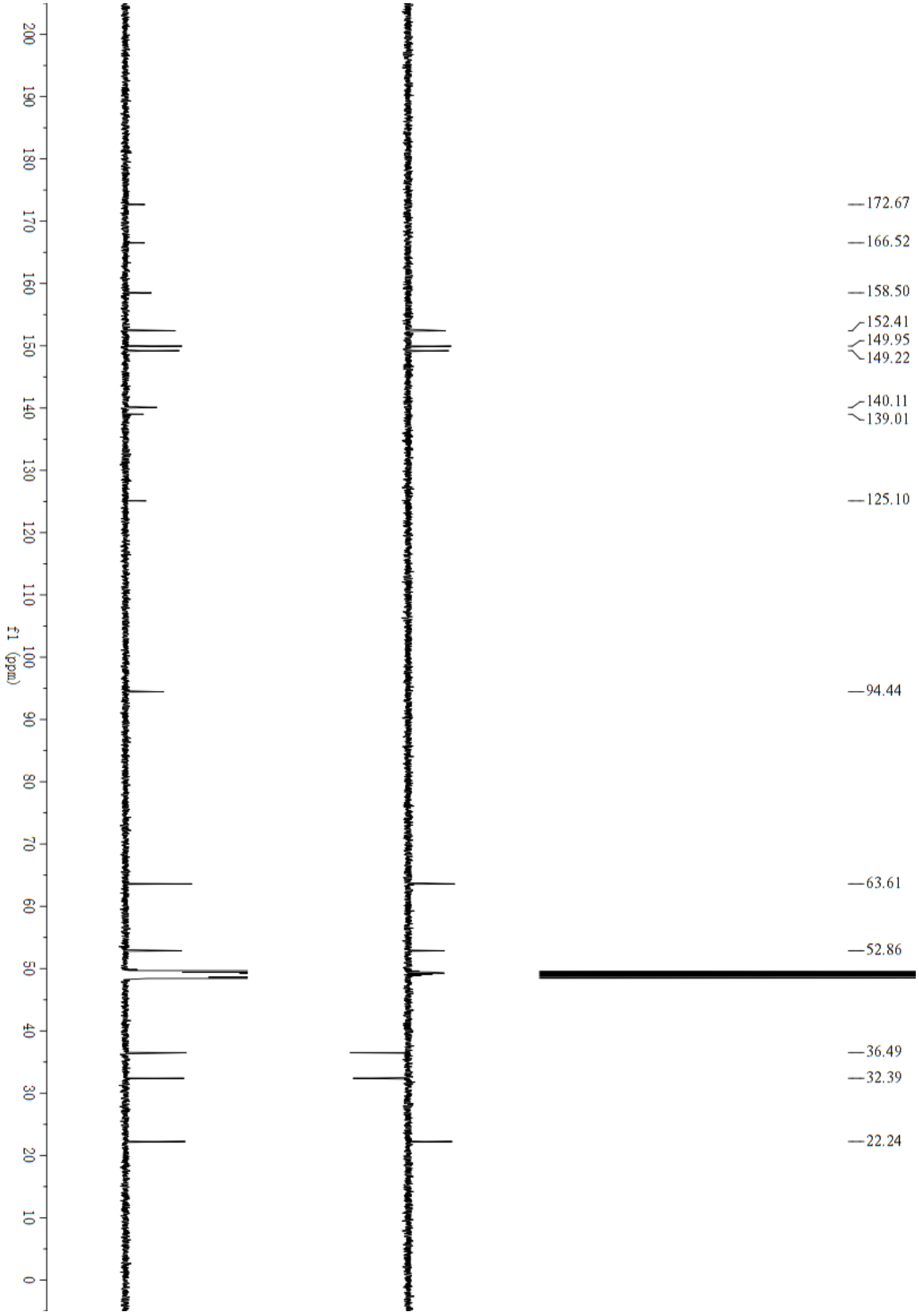


Figure S4. HSQC Spectrum of plumerianoid A (**1**) in CD_3OD.

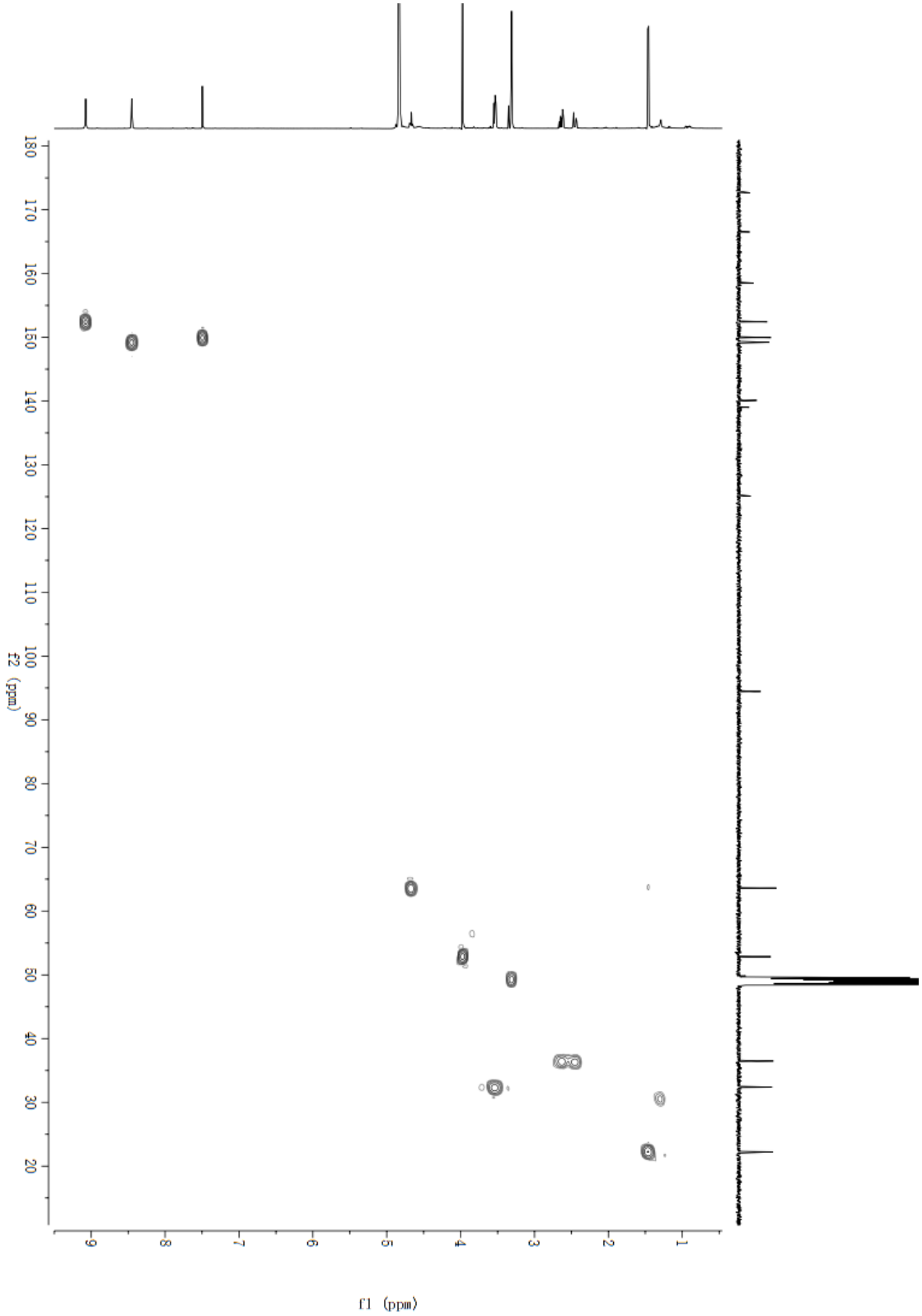


Figure S5. ^{1}H–^{1}H COSY Spectrum of plumerianoid A (**1**) in CD_3OD.

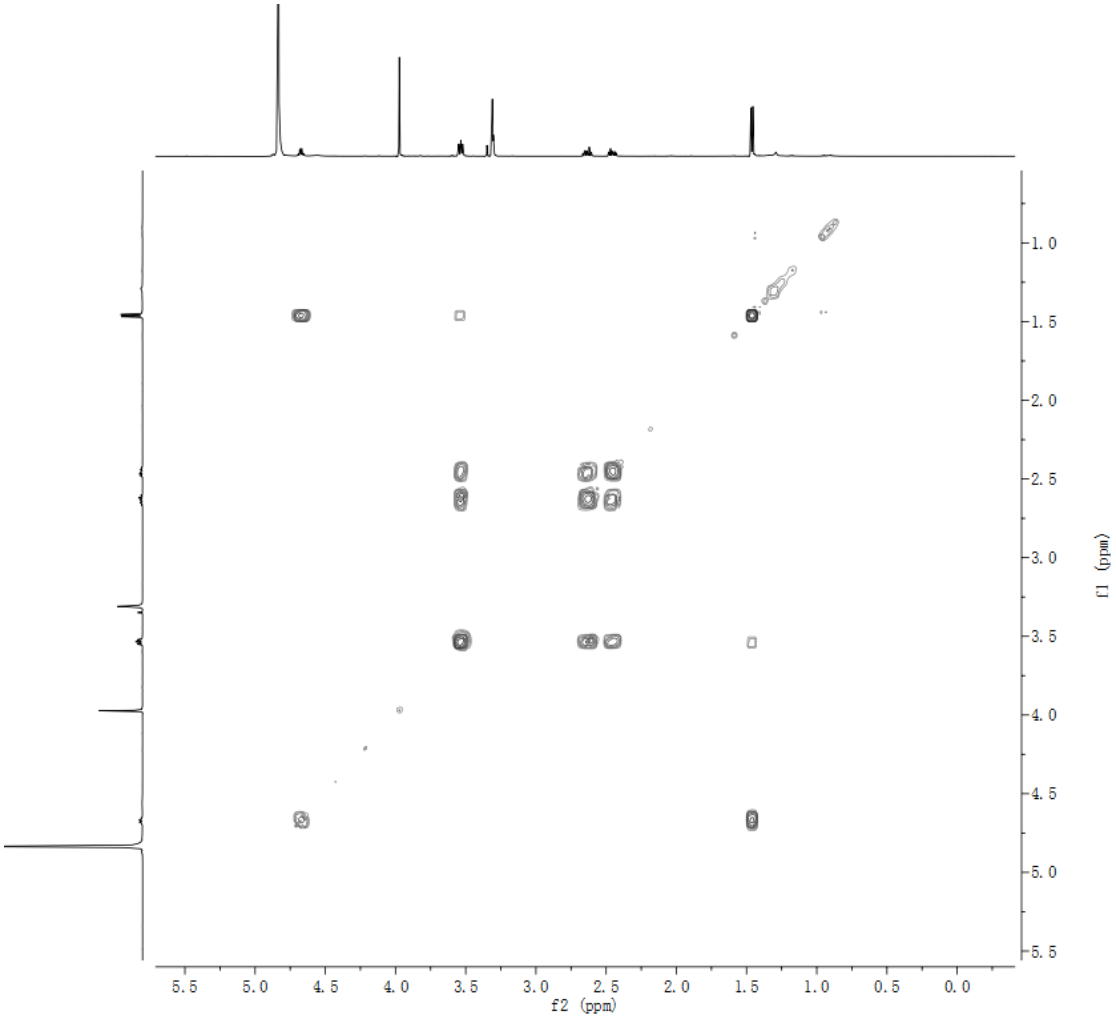


Figure S6. HMBC Spectrum of plumerianoid A (**1**) in CD_3OD.

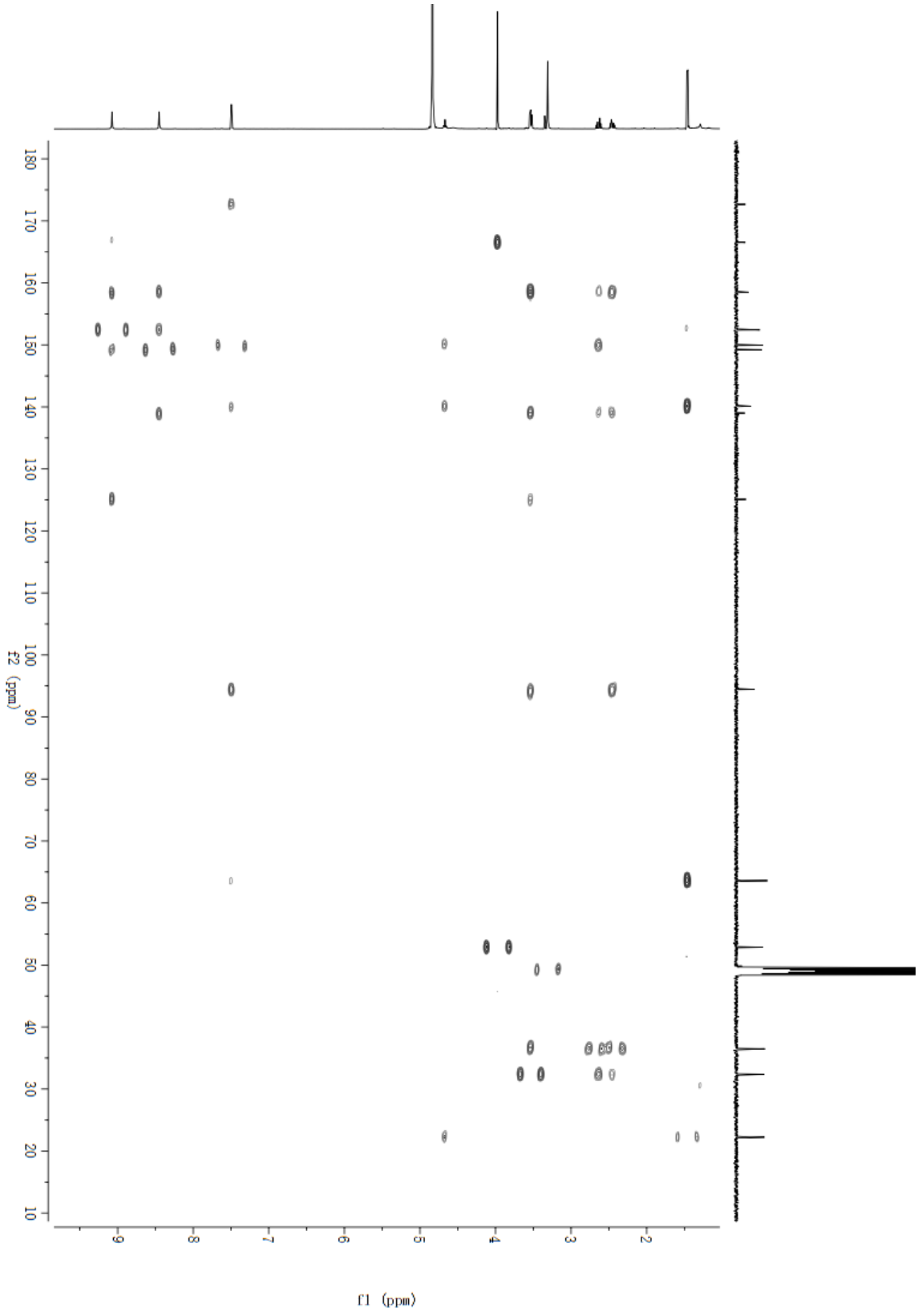


Figure S7. LR(+)ESIMS data of plumerianoid A (**1**).

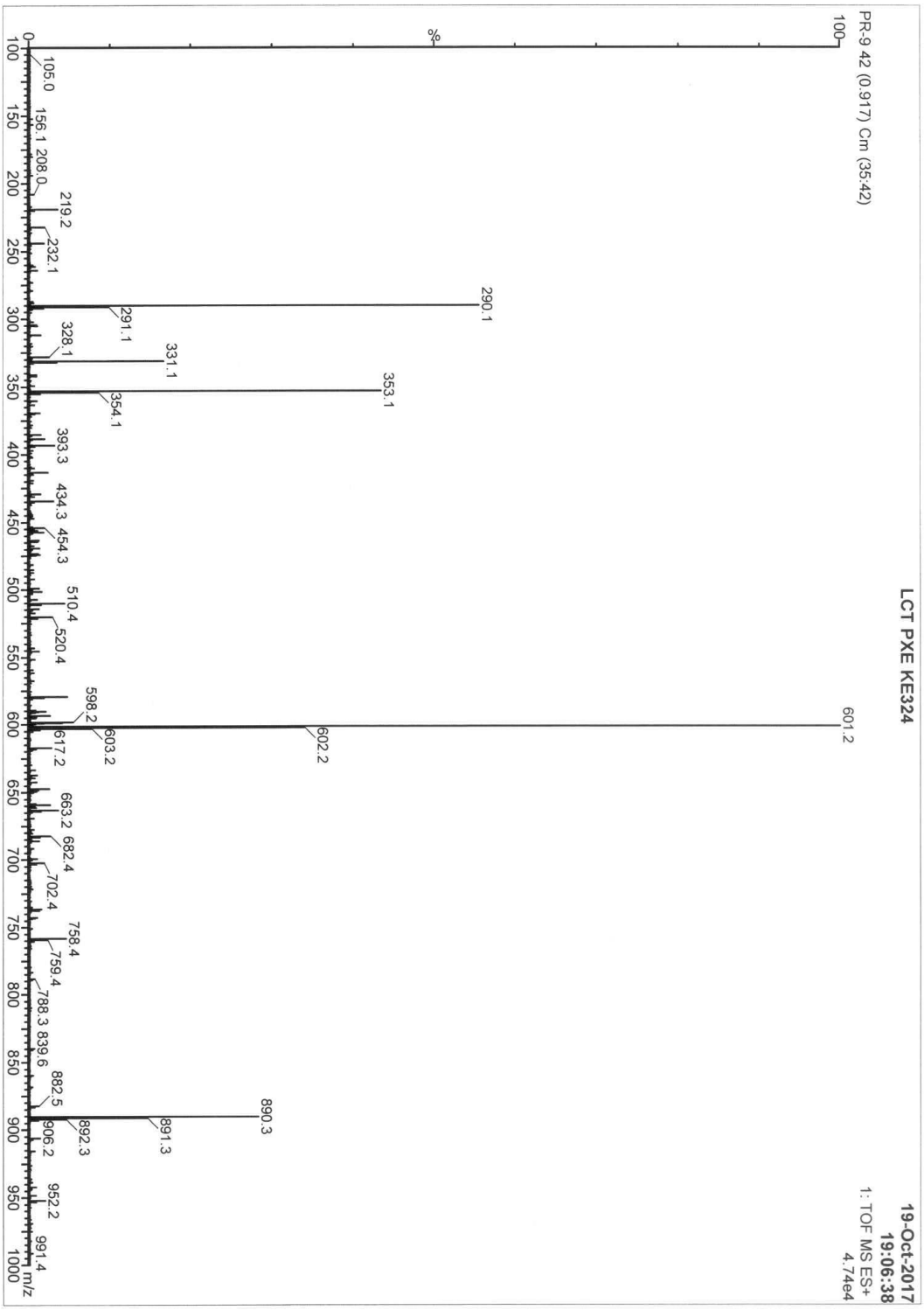
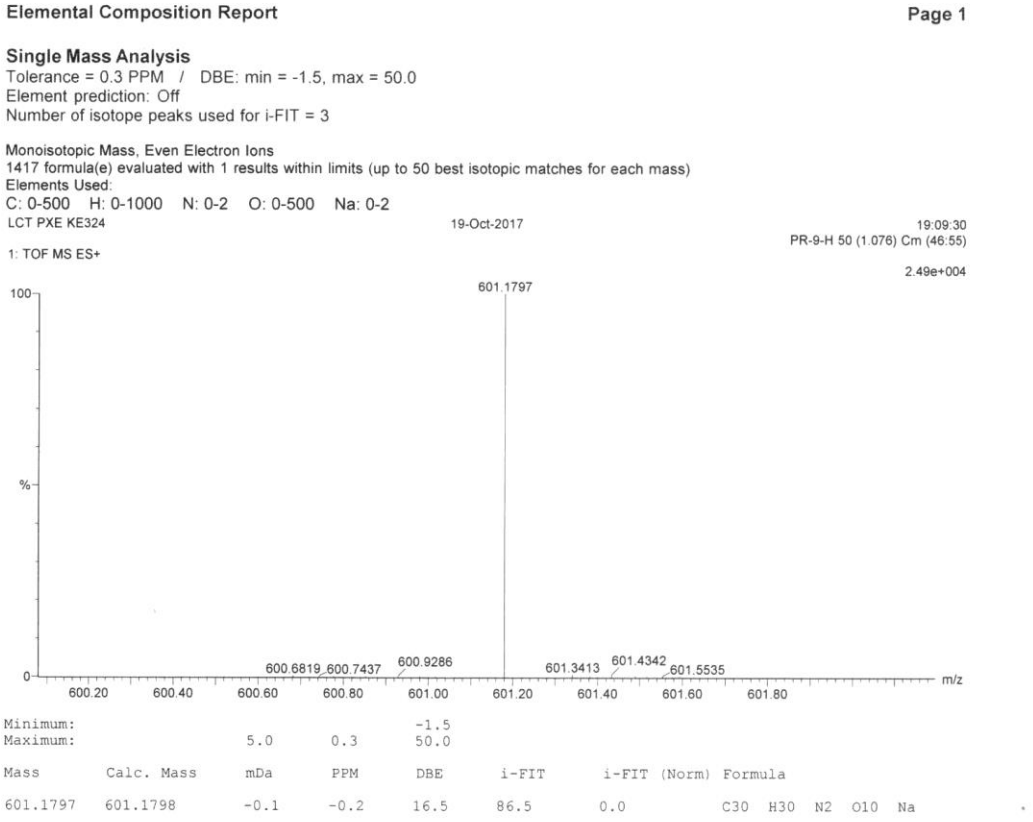


Figure S8. HR(+)ESIMS data of plumerianoid A (**1**).



Elemental Composition Report Page 1

Single Mass Analysis
Tolerance = 0.3 PPM / DBE: min = -1.5, max = 50.0
Element prediction: Off
Number of isotope peaks used for i-FIT = 3

Monoisotopic Mass, Even Electron Ions
1417 formula(e) evaluated with 1 results within limits (up to 50 best isotopic matches for each mass)
Elements Used:
C: 0-500 H: 0-1000 N: 0-2 O: 0-500 Na: 0-2

LCT PXE KE324 19-Oct-2017 19:09:30
PR-9-H 50 (1.076) Cm (46:55)
1: TOF MS ES+ 2.49e+004

Minimum:				-1.5			
Maximum:		5.0	0.3	50.0			
Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	i-FIT (Norm)	Formula
601.1797	601.1798	-0.1	-0.2	16.5	86.5	0.0	C30 H30 N2 O10 Na

Figure S9. IR spectrum of plumerianoid A (**1**).

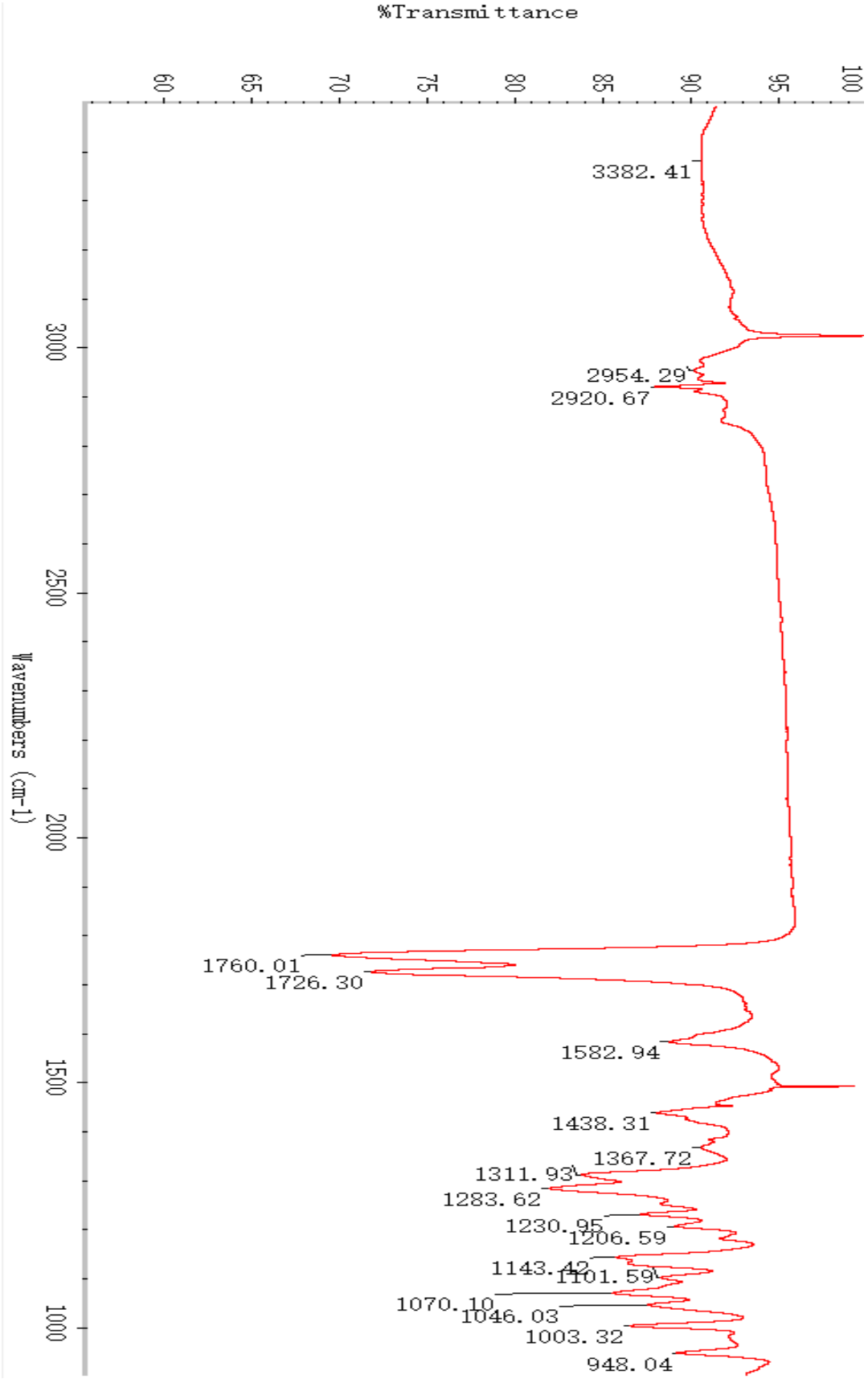


Figure S10. ^{1}H NMR spectrum of plumerianoid B (**2**) in CD_3OD.

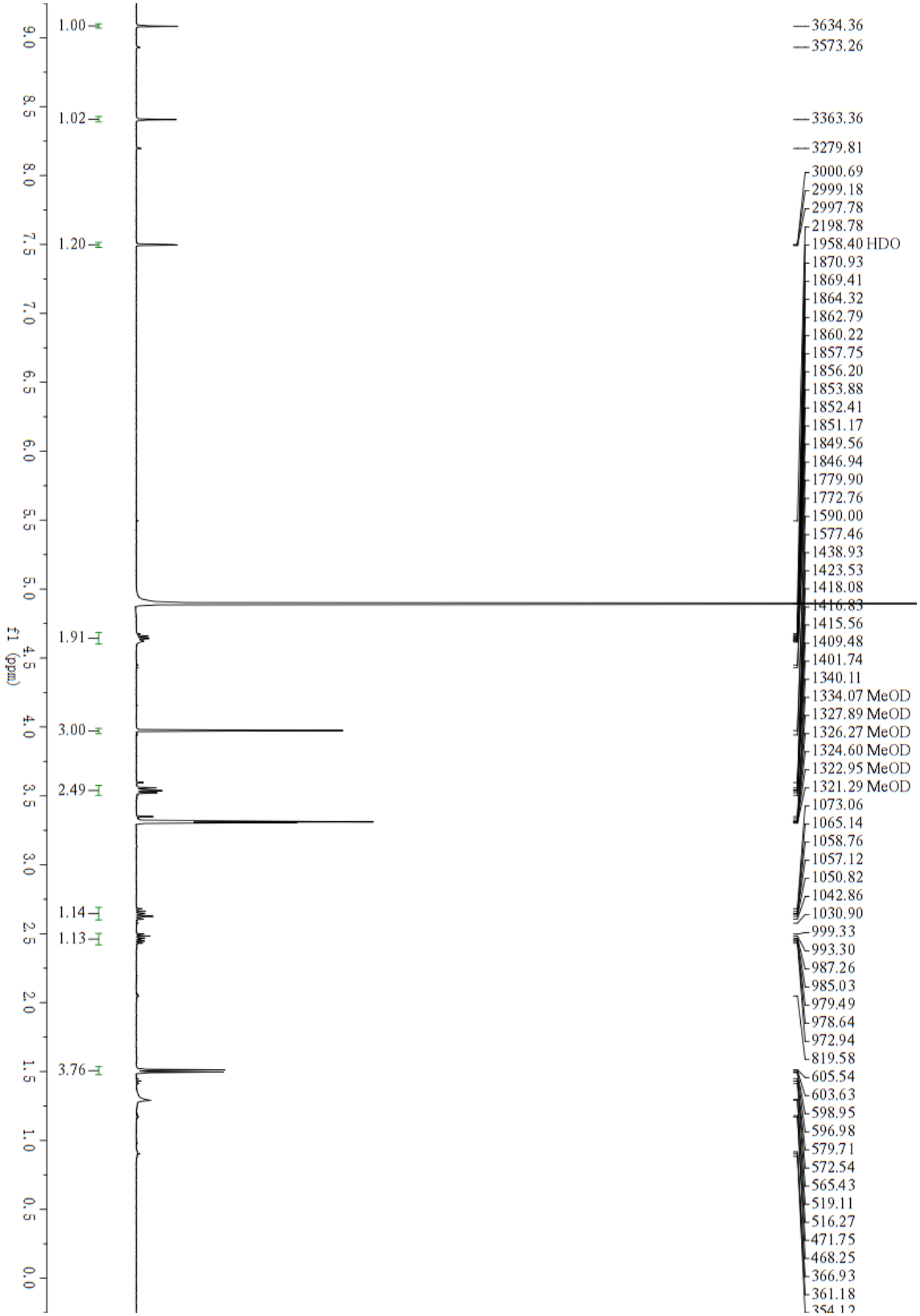


Figure S11. ^{13}C NMR spectrum of plumerianoid B (**2**) in CD_3OD.

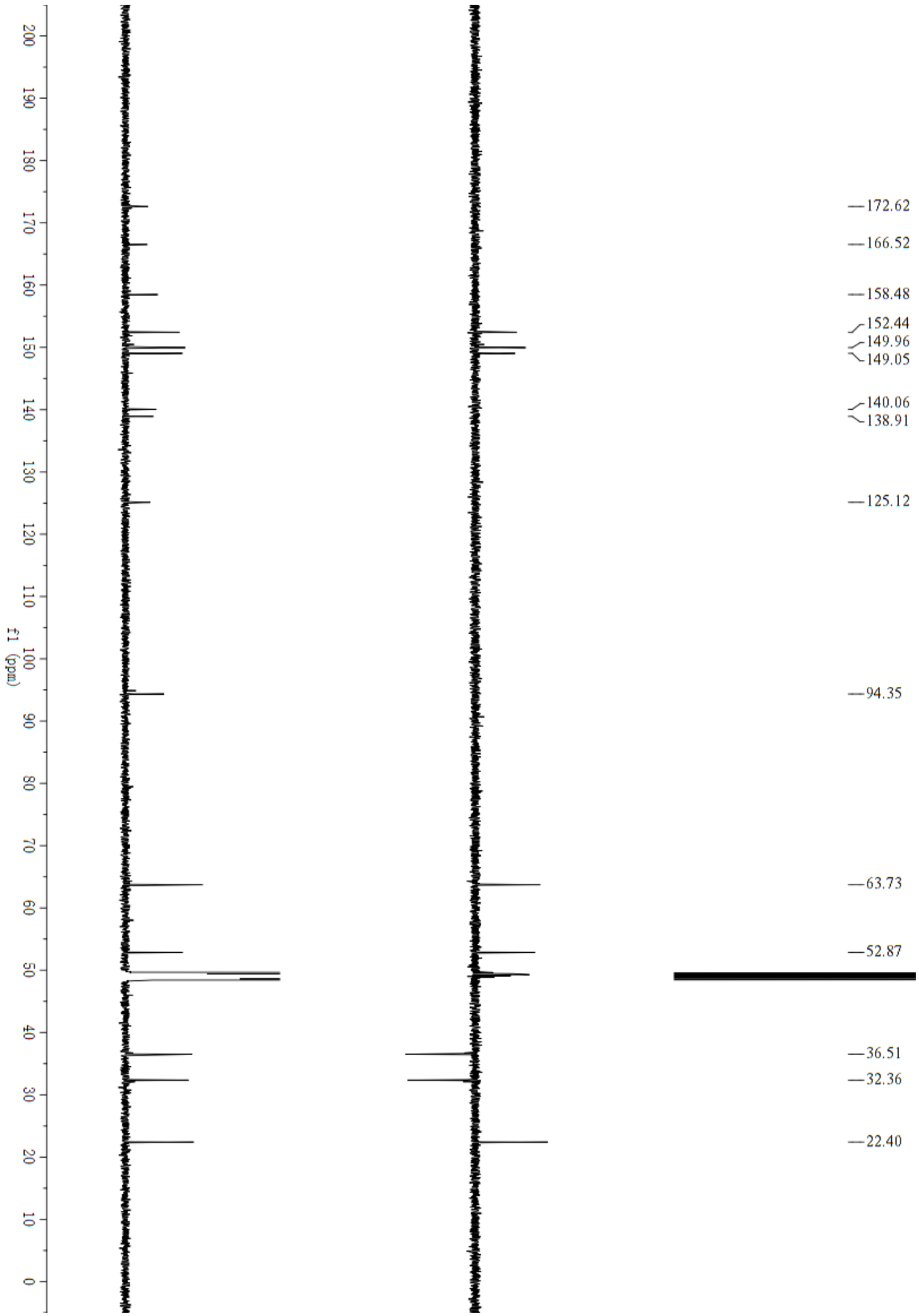


Figure S12. HSQC spectrum of plumerianoid B (**2**) in CD_3OD.

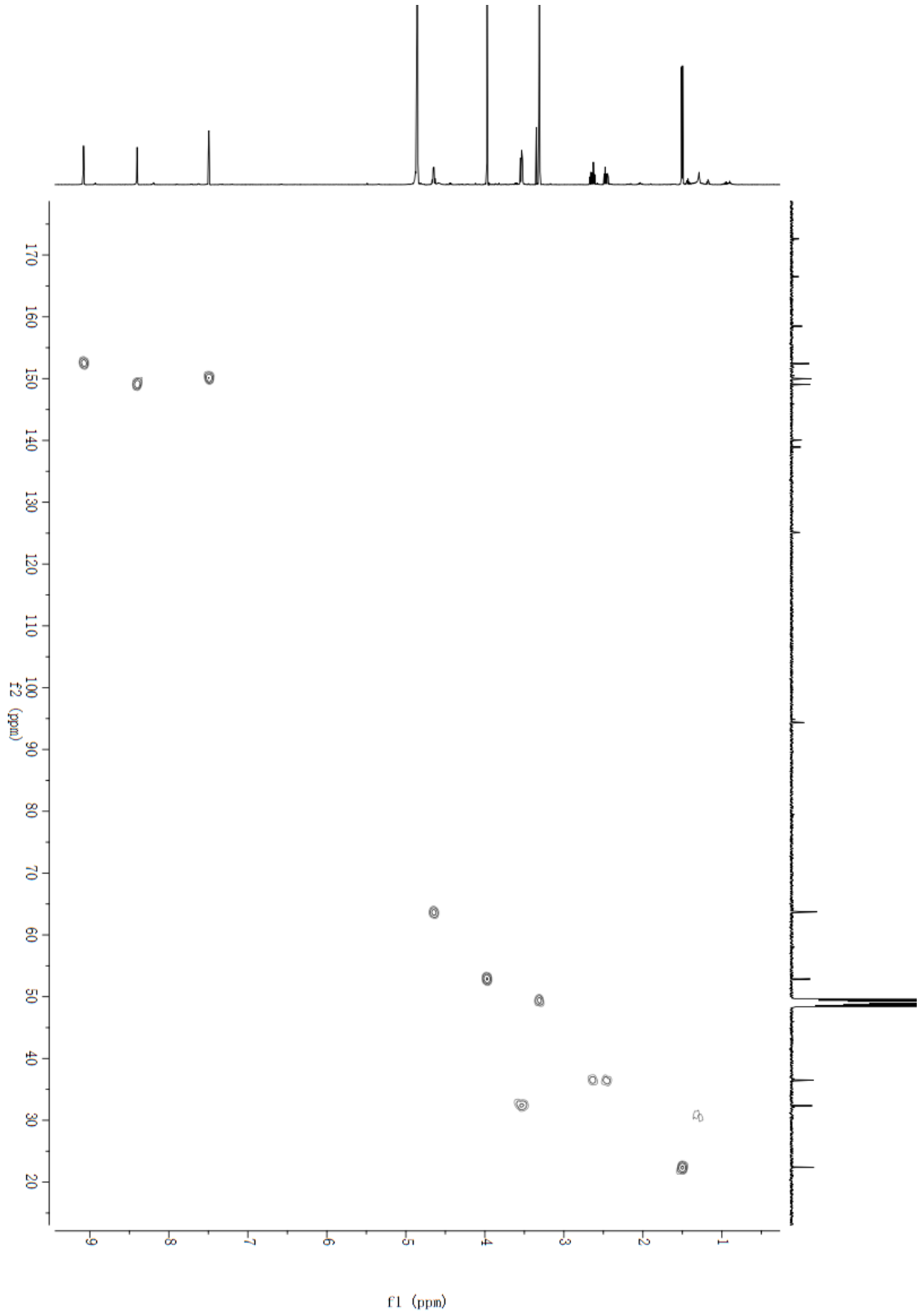


Figure S13. ^{1}H–^{1}H COSY spectrum of plumerianoid B (**2**) in CD_3OD.

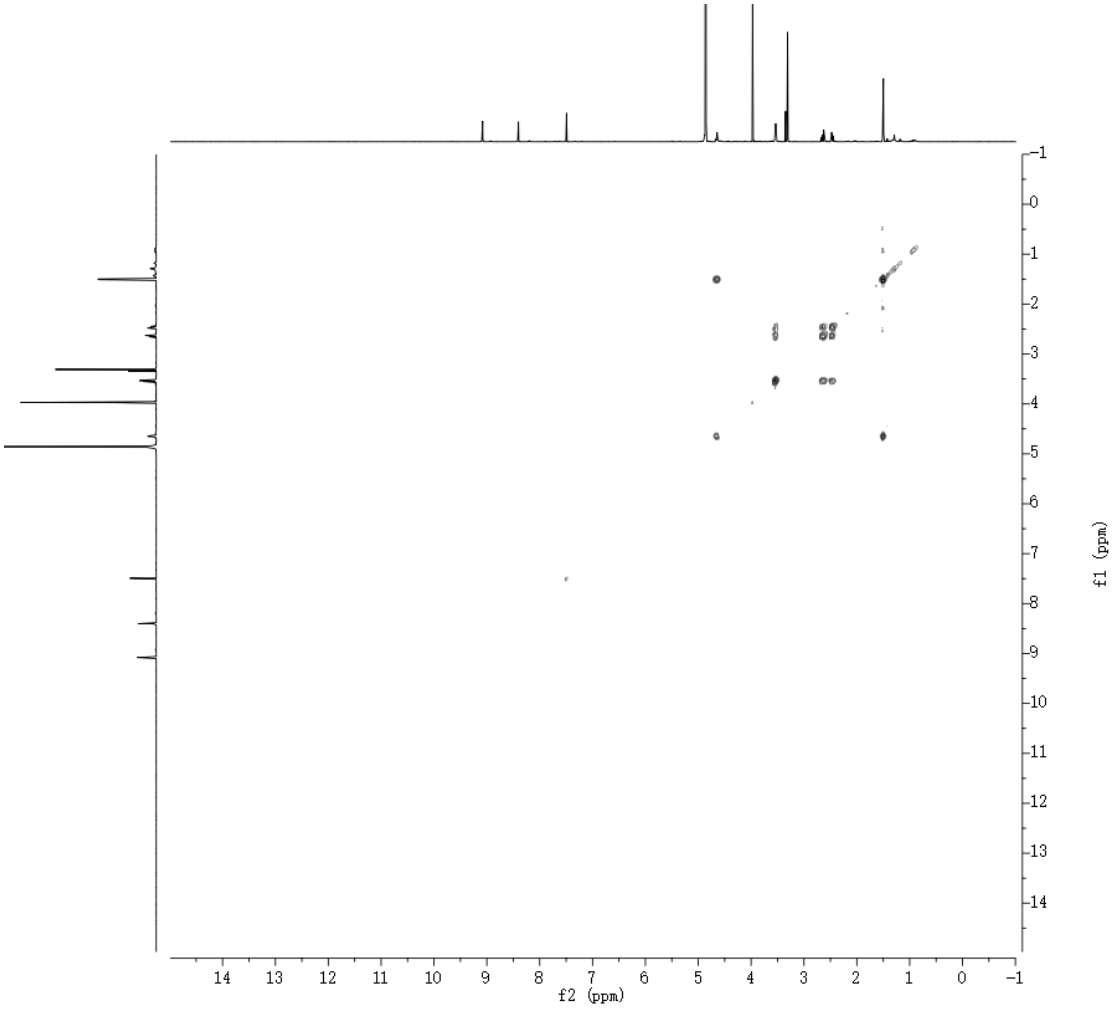


Figure S14. HMBC spectrum of plumerianoid B (**2**) in CD_3OD.

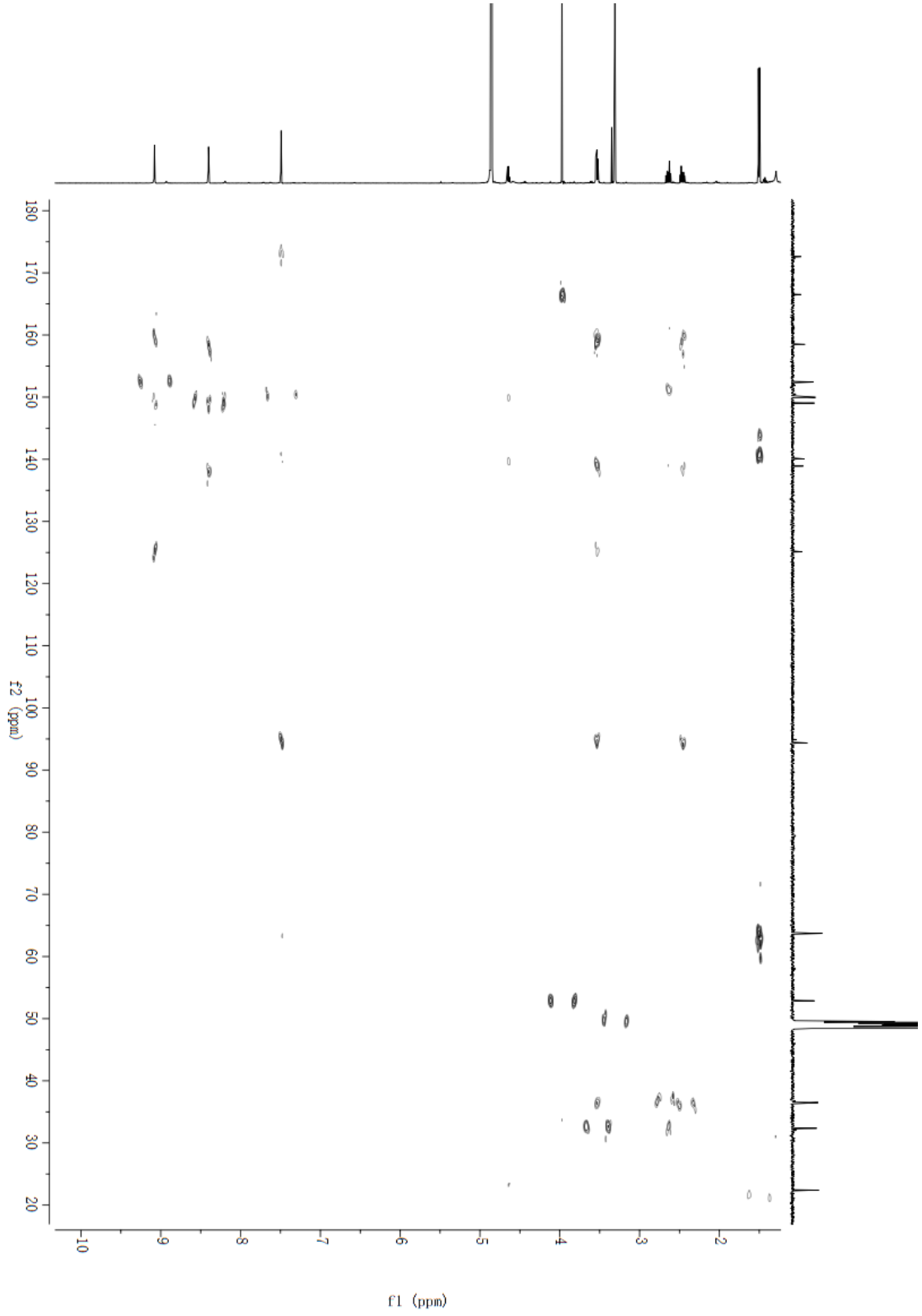


Figure S15. LR(+)ESIMS data of plumerianoid B (**2**).

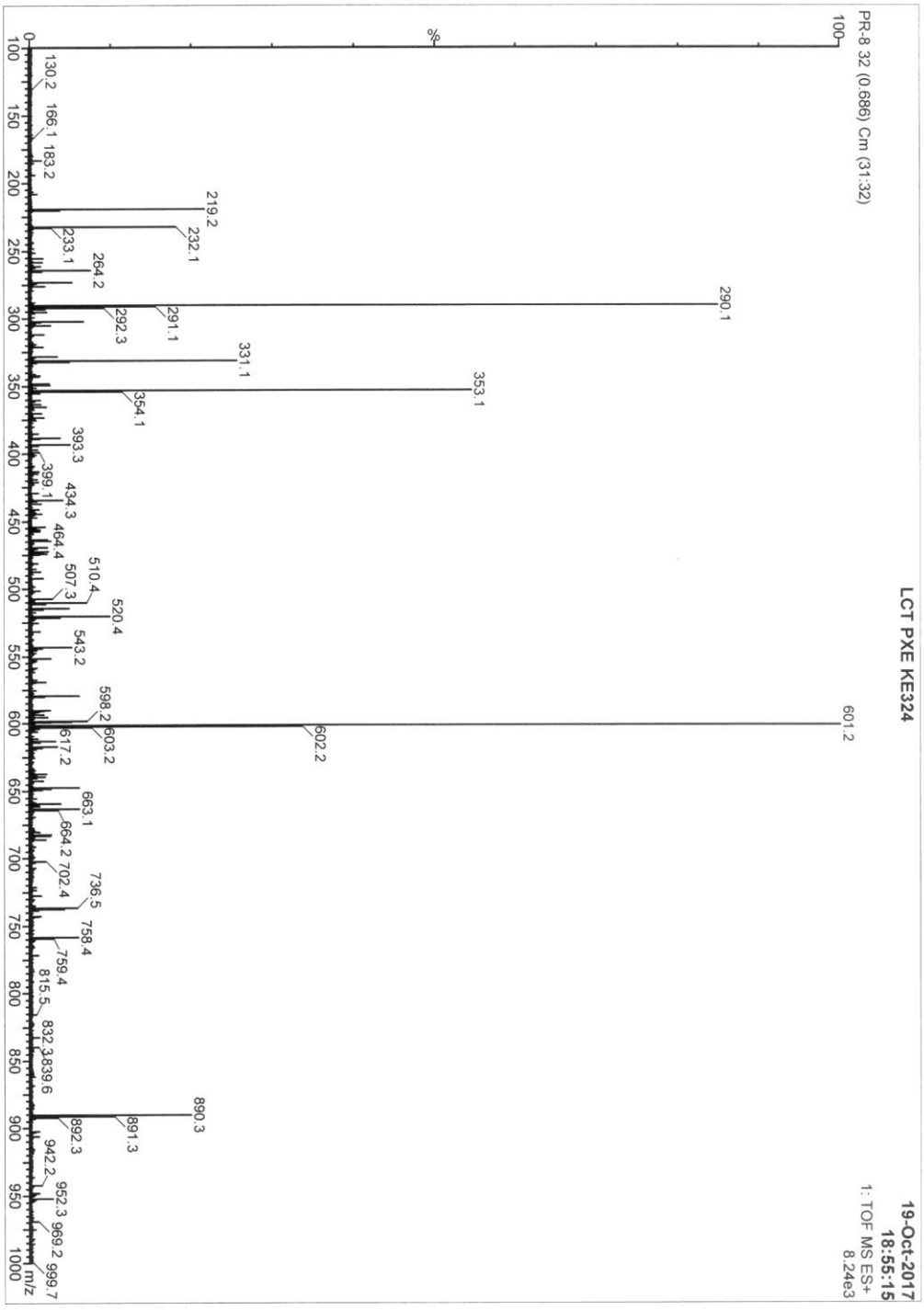


Figure S16. HR(+)ESIMS data of plumerianoid B (**2**).

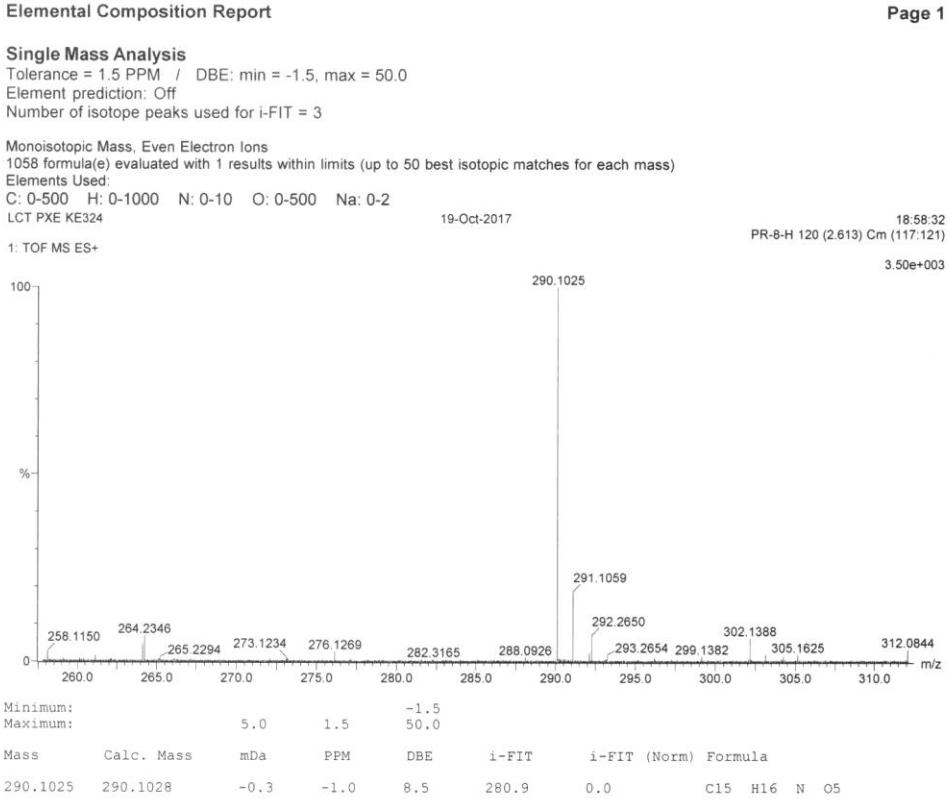


Figure S17. IR spectrum of plumerianoid B (**2**).

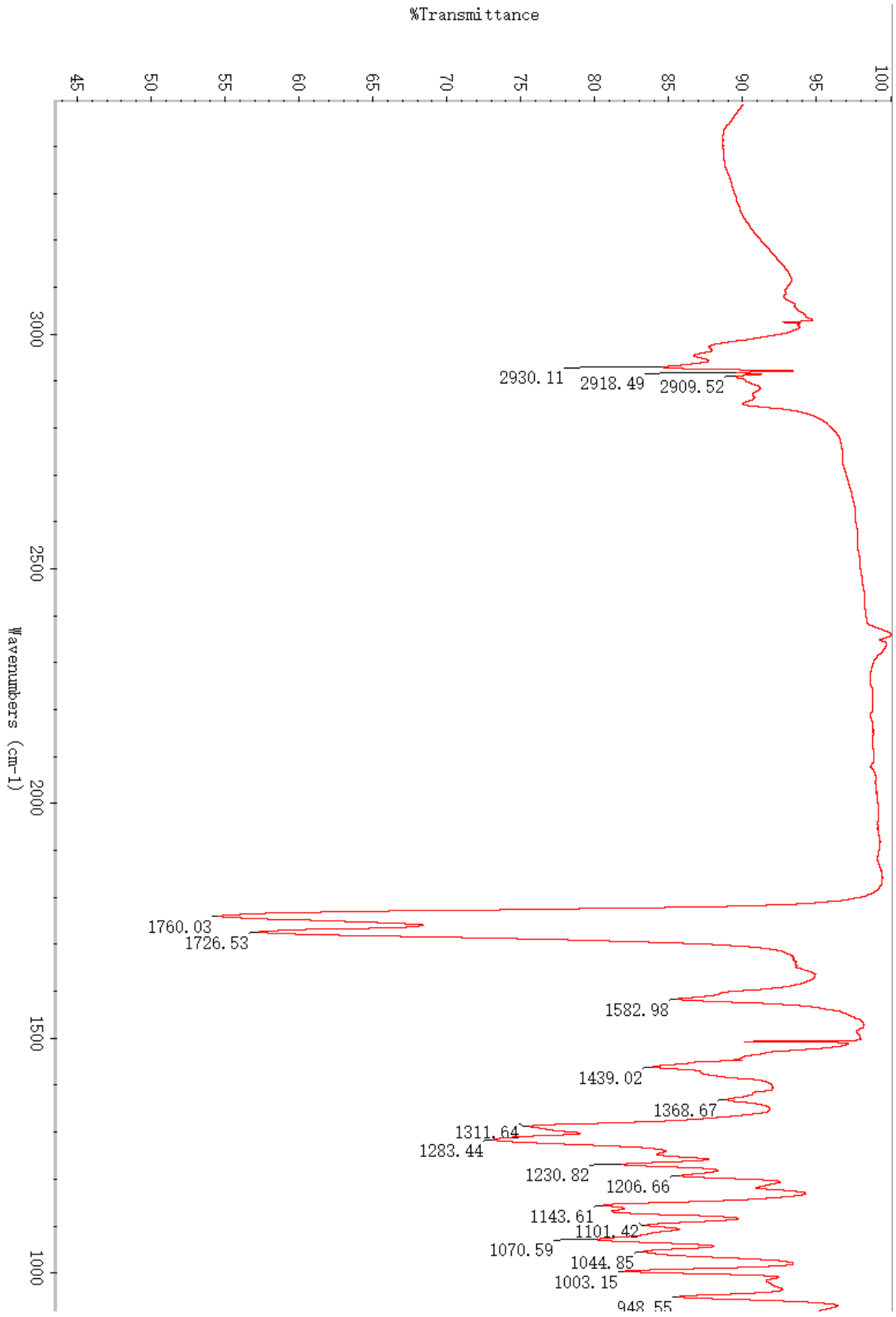


Figure S18. ^{1}H NMR spectrum of plumerianoid C (**3**) in CD_3OD.

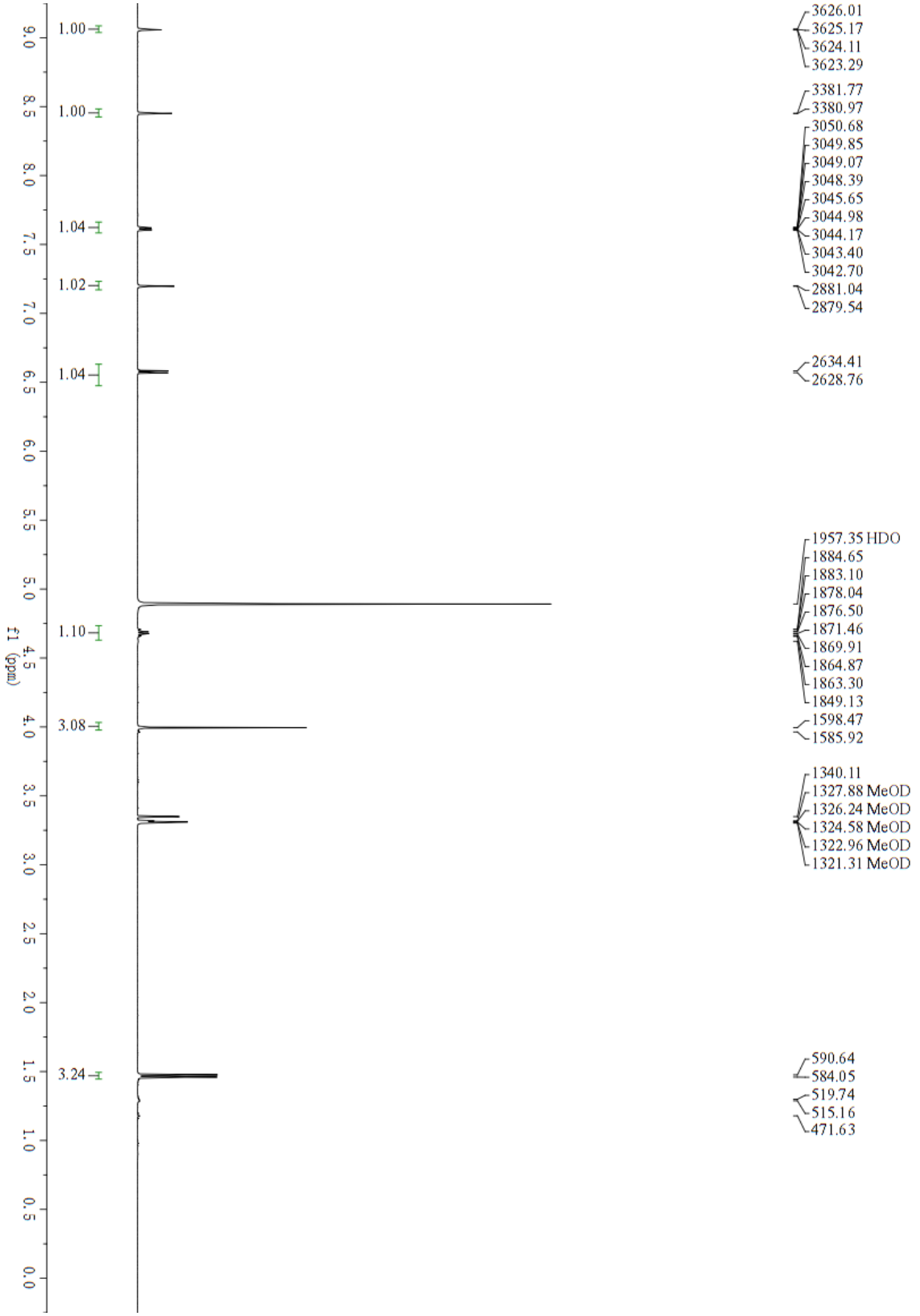


Figure S19. ^{13}C NMR spectrum of plumerianoid C (**3**) in CD_3OD.

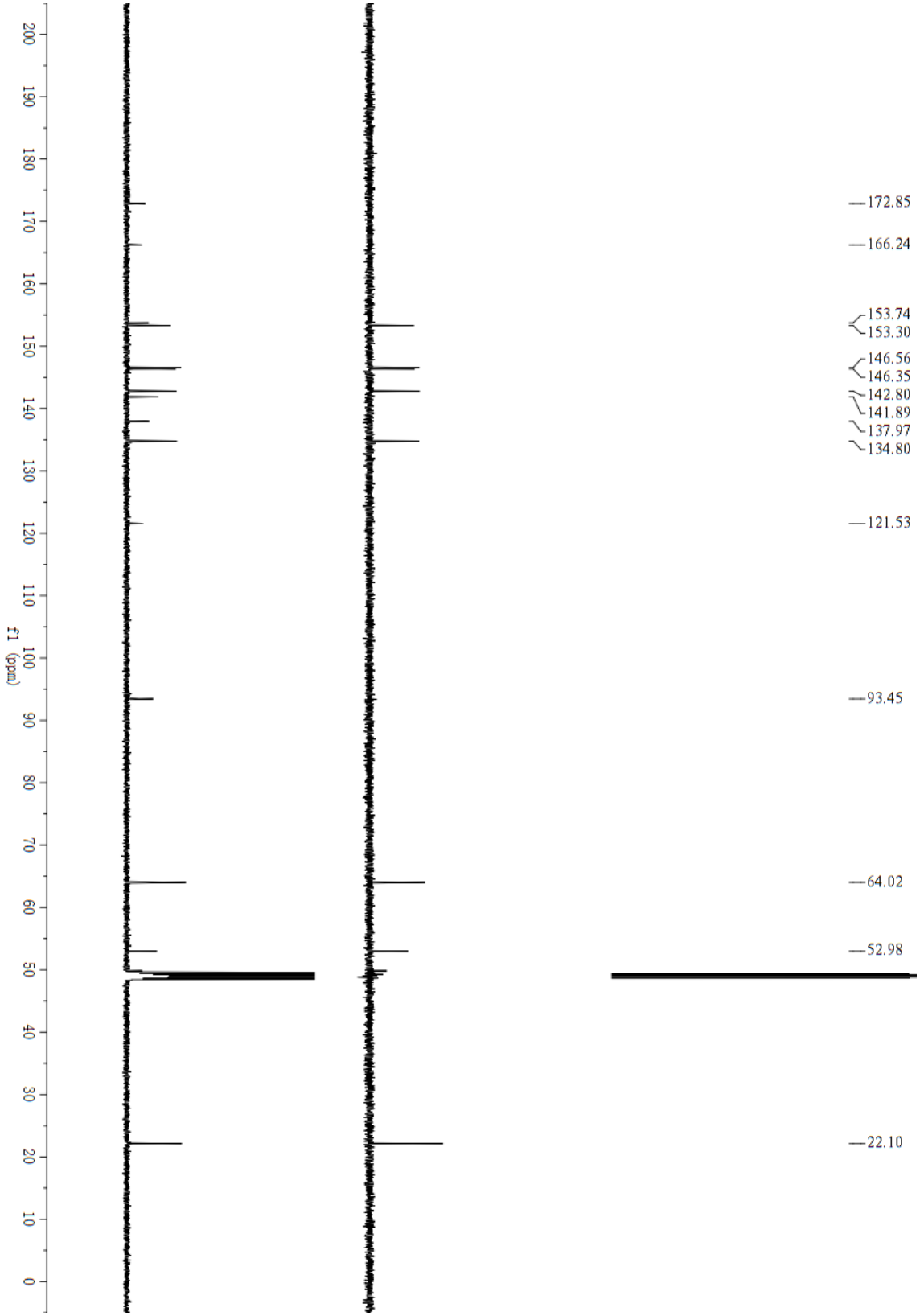


Figure S20. HSQC spectrum of plumerianoid C (**3**) in CD_3OD.

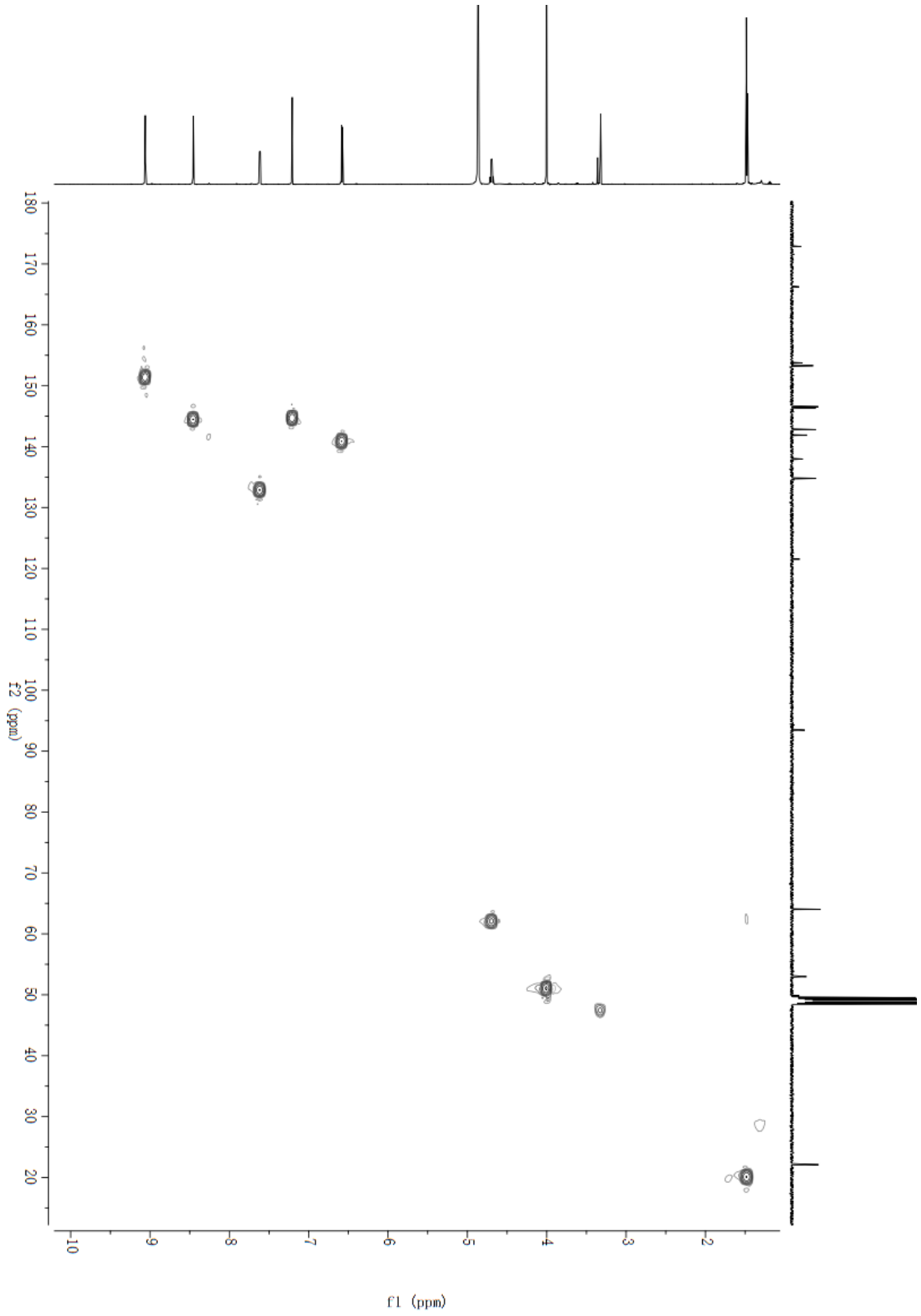


Figure S21. ^{1}H–^{1}H COSY spectrum of plumerianoid C (**3**) in CD_3OD.

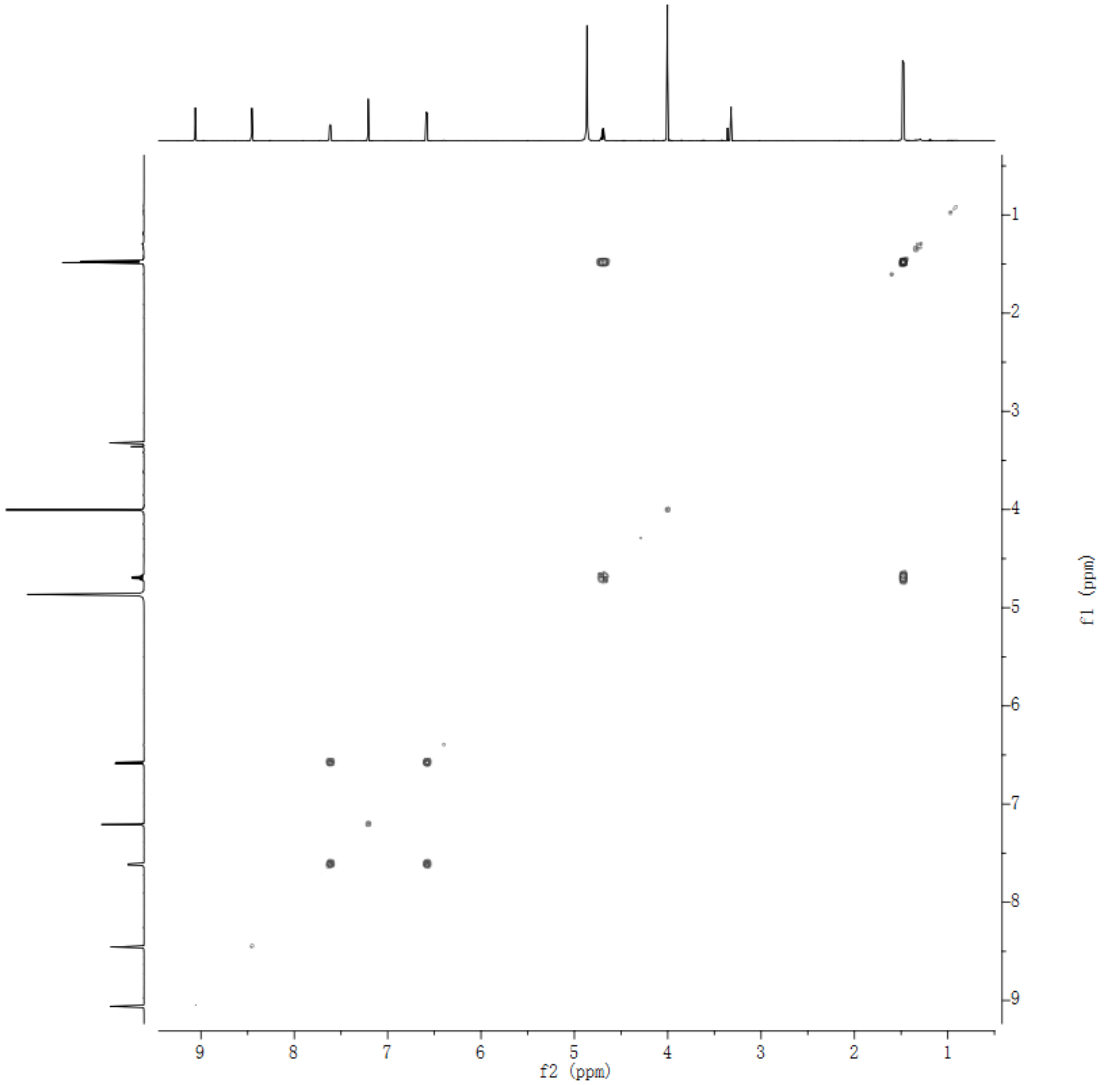


Figure S22. HMBC spectrum of plumerianoid C (**3**) in CD_3OD.

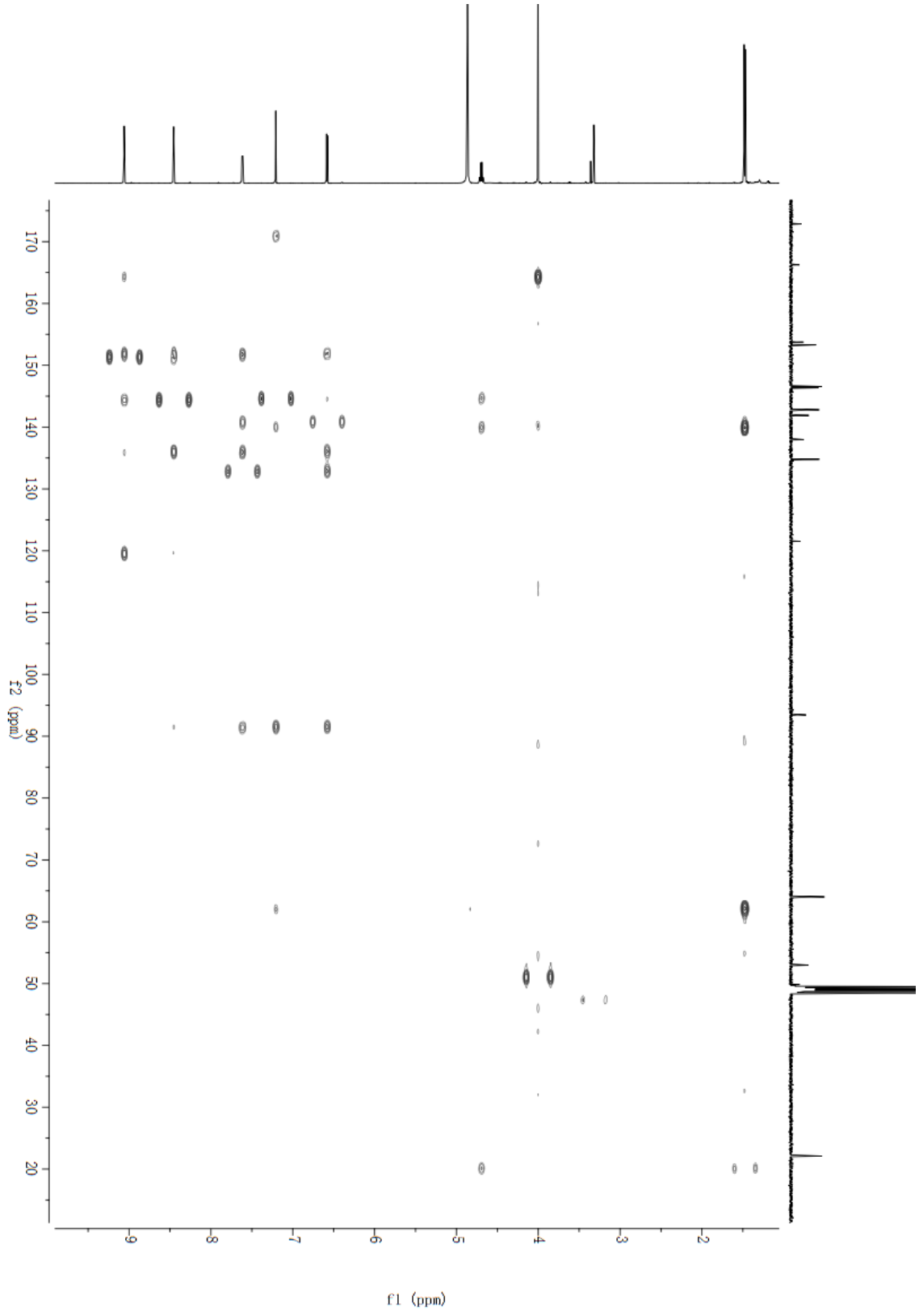


Figure S23. LR(+)ESIMS data of plumerianoid C (**3**).

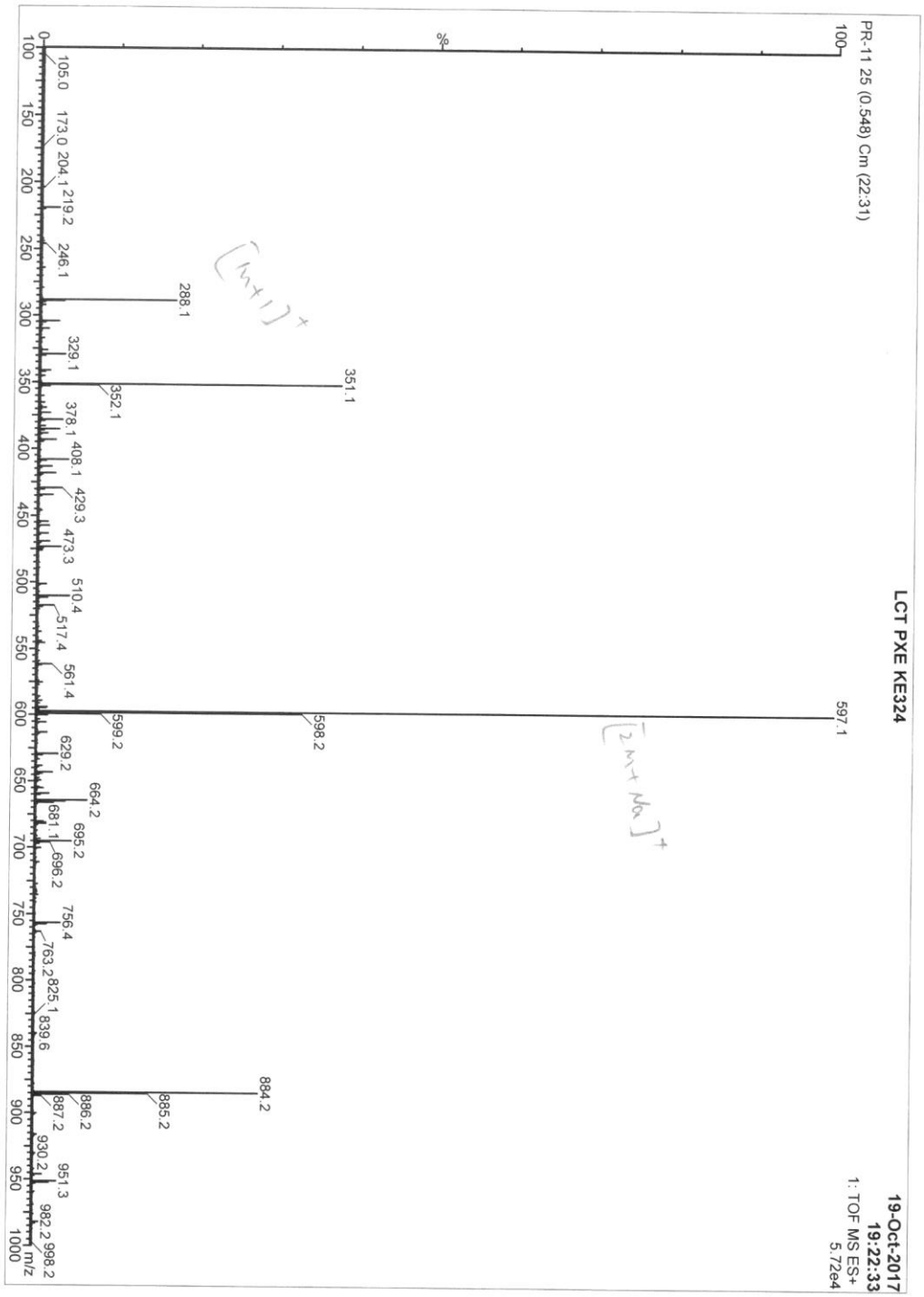


Figure S24. HR(+)ESIMS data of plumerianoid C (**3**).

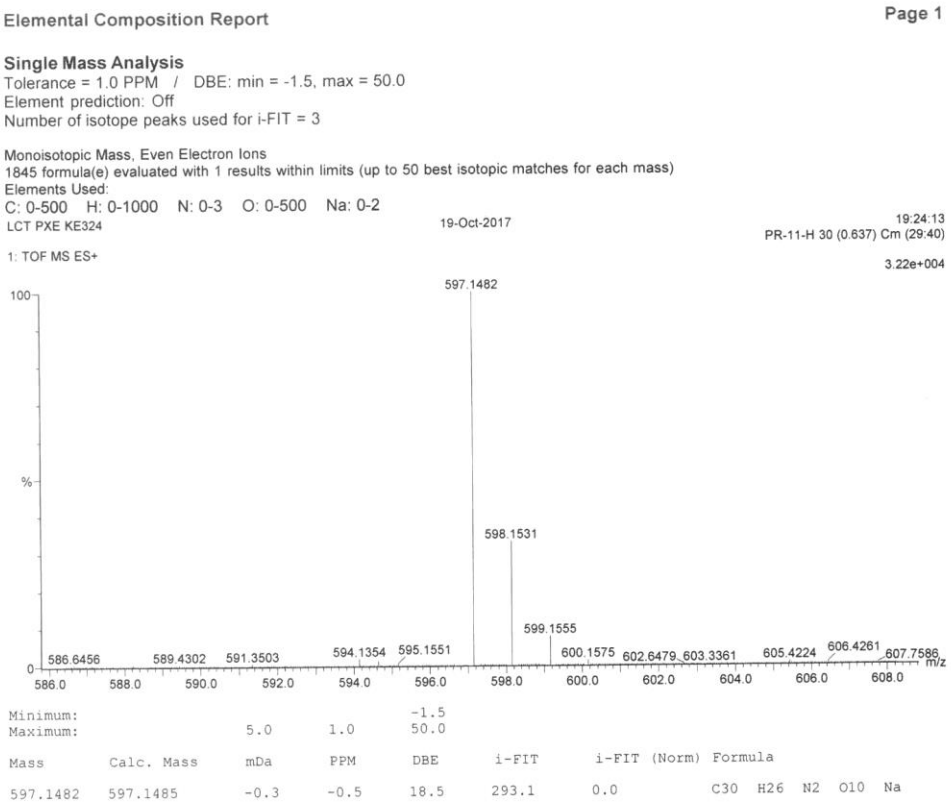


Figure S25. IR Spectrum of plumerianoid C (**3**).

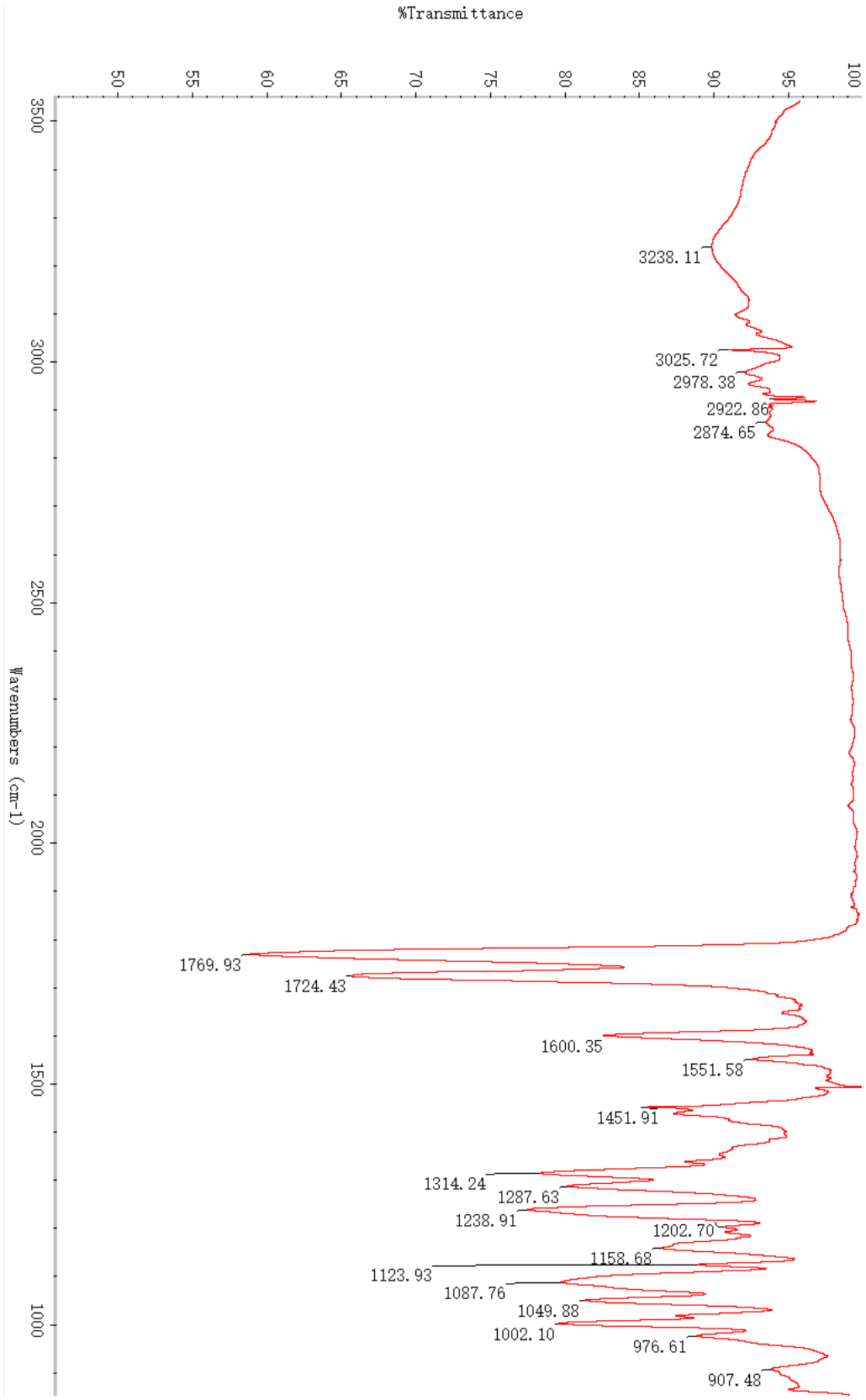


Figure S26. ^{1}H NMR spectrum of plumerianoid D (**4**) in CD_3OD.

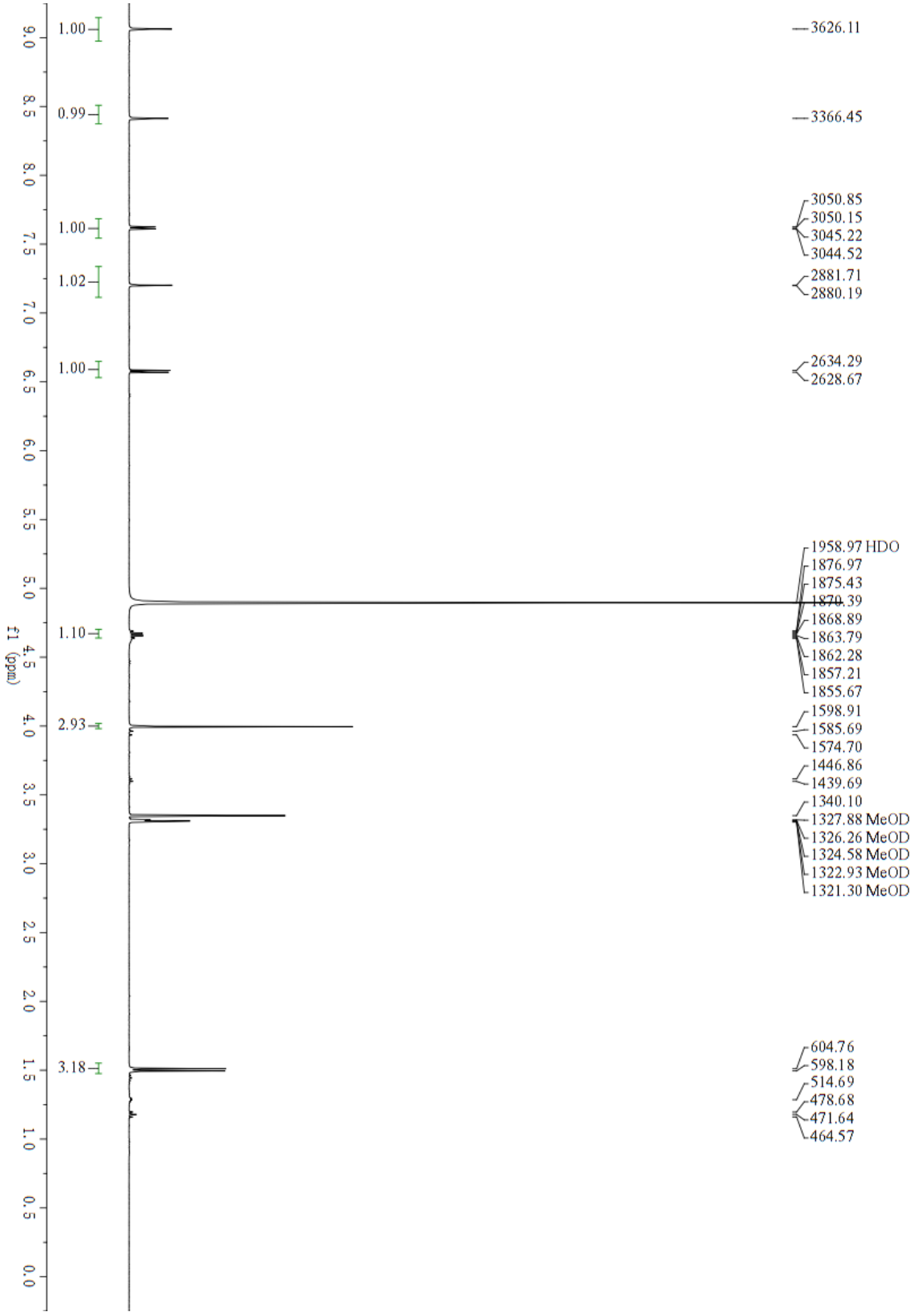


Figure S27. ^{13}C NMR spectrum of plumerianoid D (**4**) in CD_3OD.

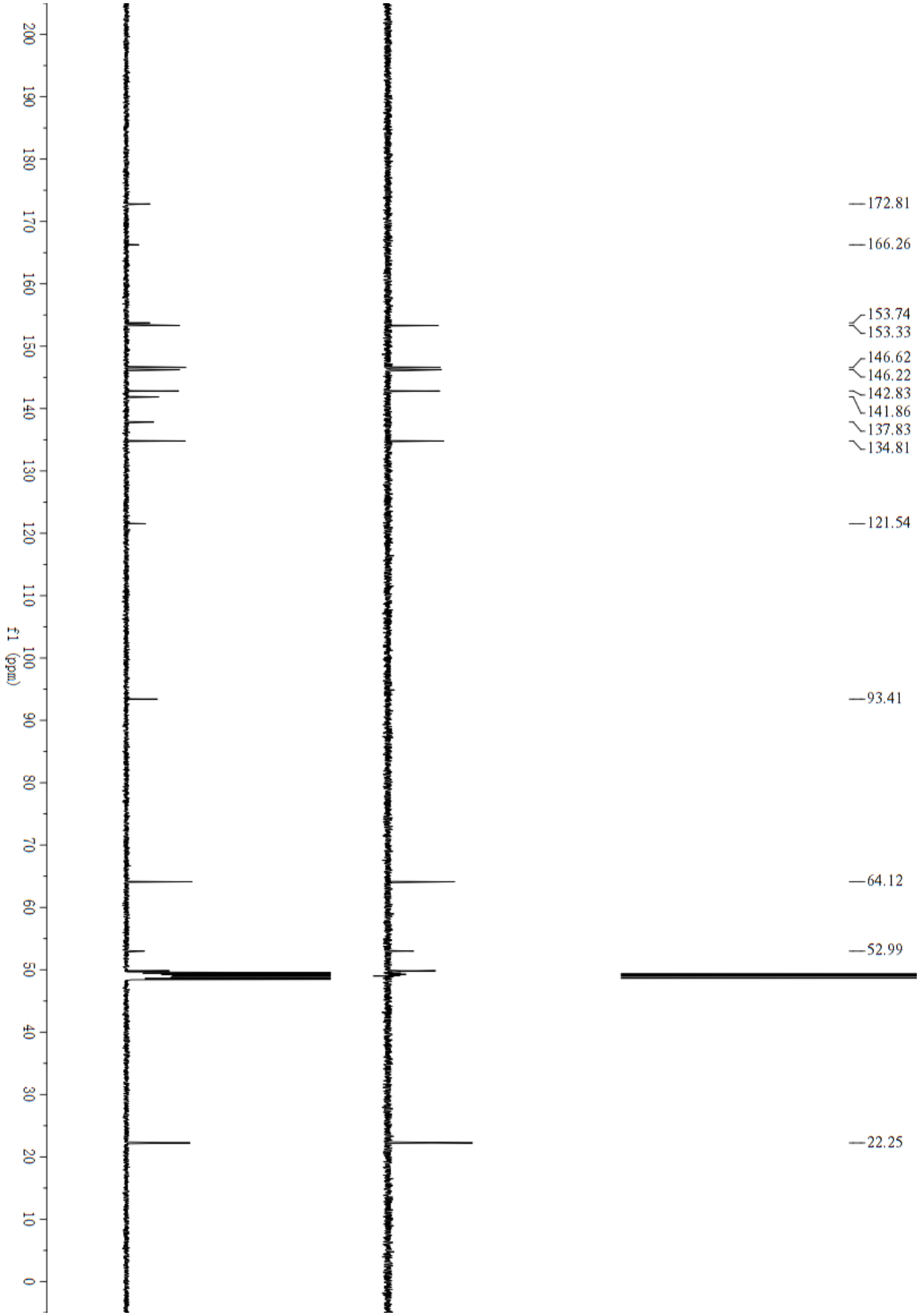


Figure S28. HSQC spectrum of plumerianoid D (**4**) in CD_3OD.

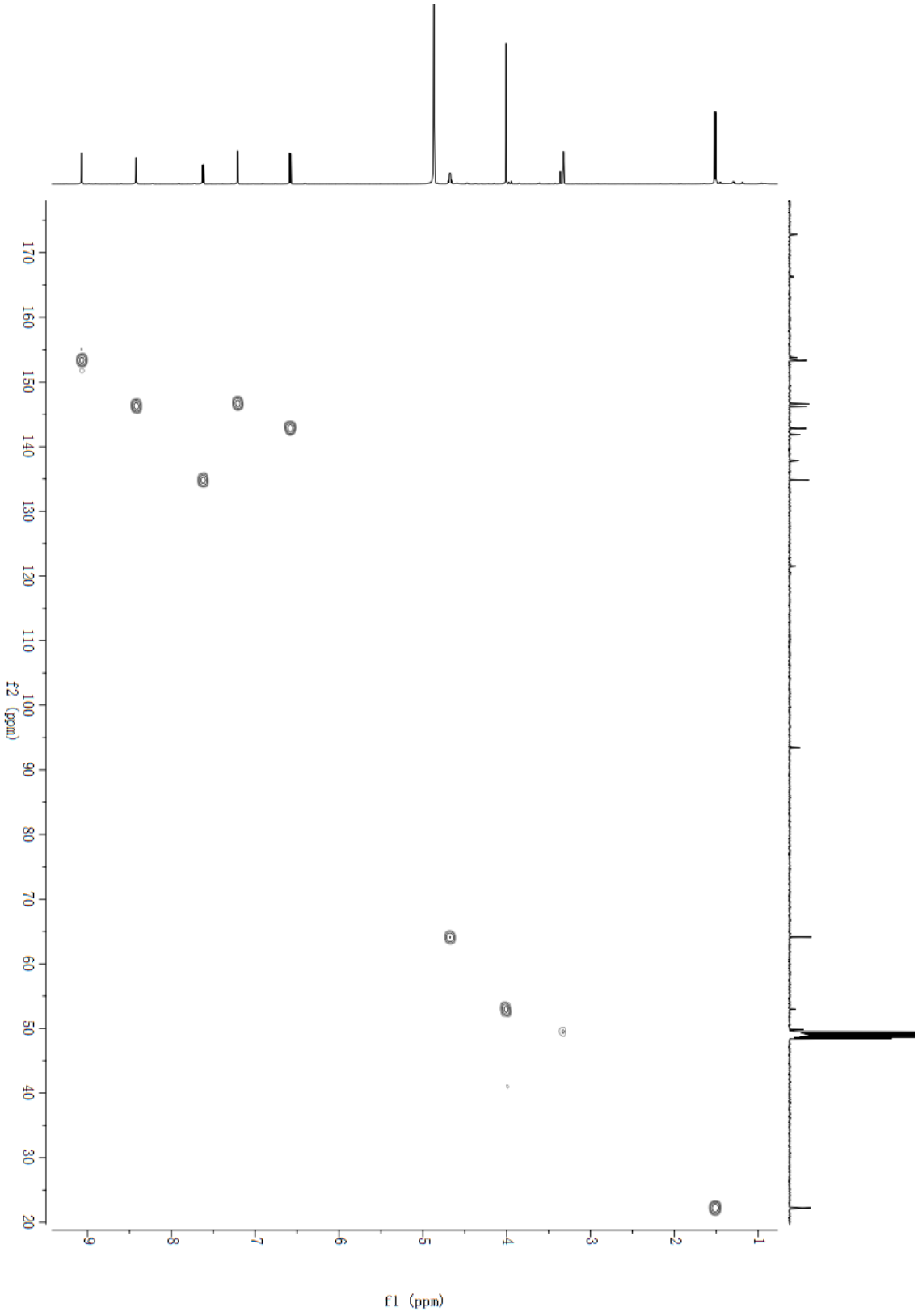


Figure S29. ^{1}H–^{1}H COSY spectrum of plumerianoid D (**4**) in CD_3OD.

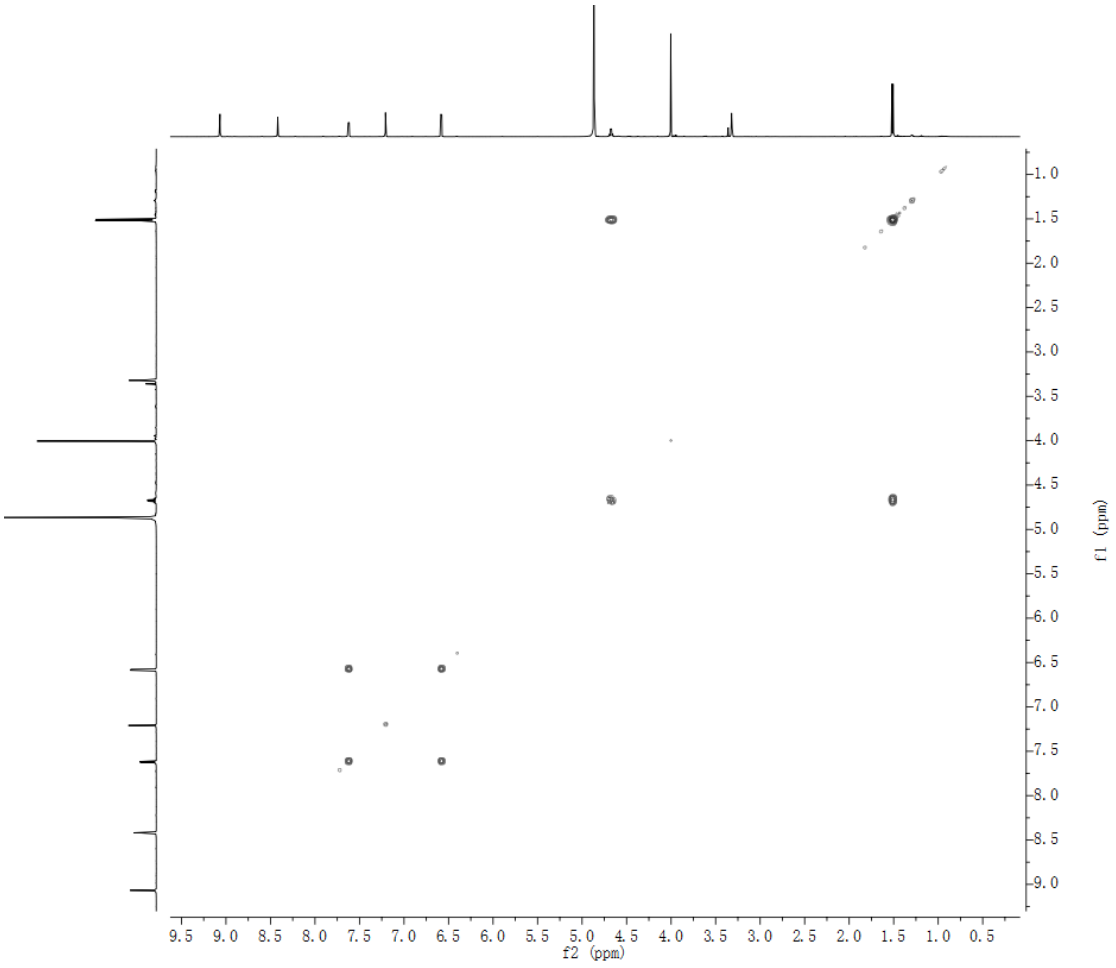


Figure S30. HMBC spectrum of plumerianoid D (**4**) in CD_3OD.

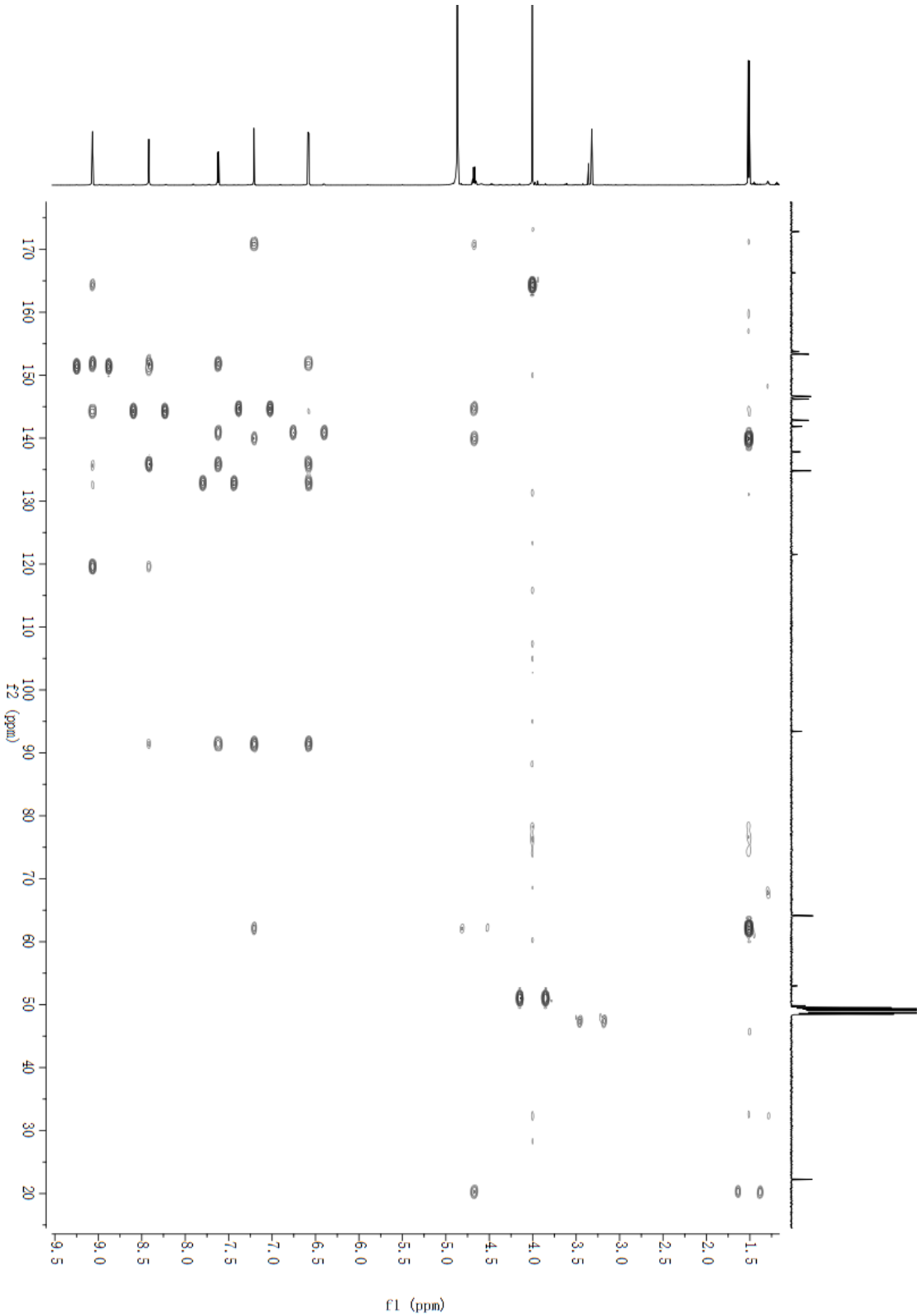


Figure S31. LR(+)ESIMS data of plumerianoid D (**4**).

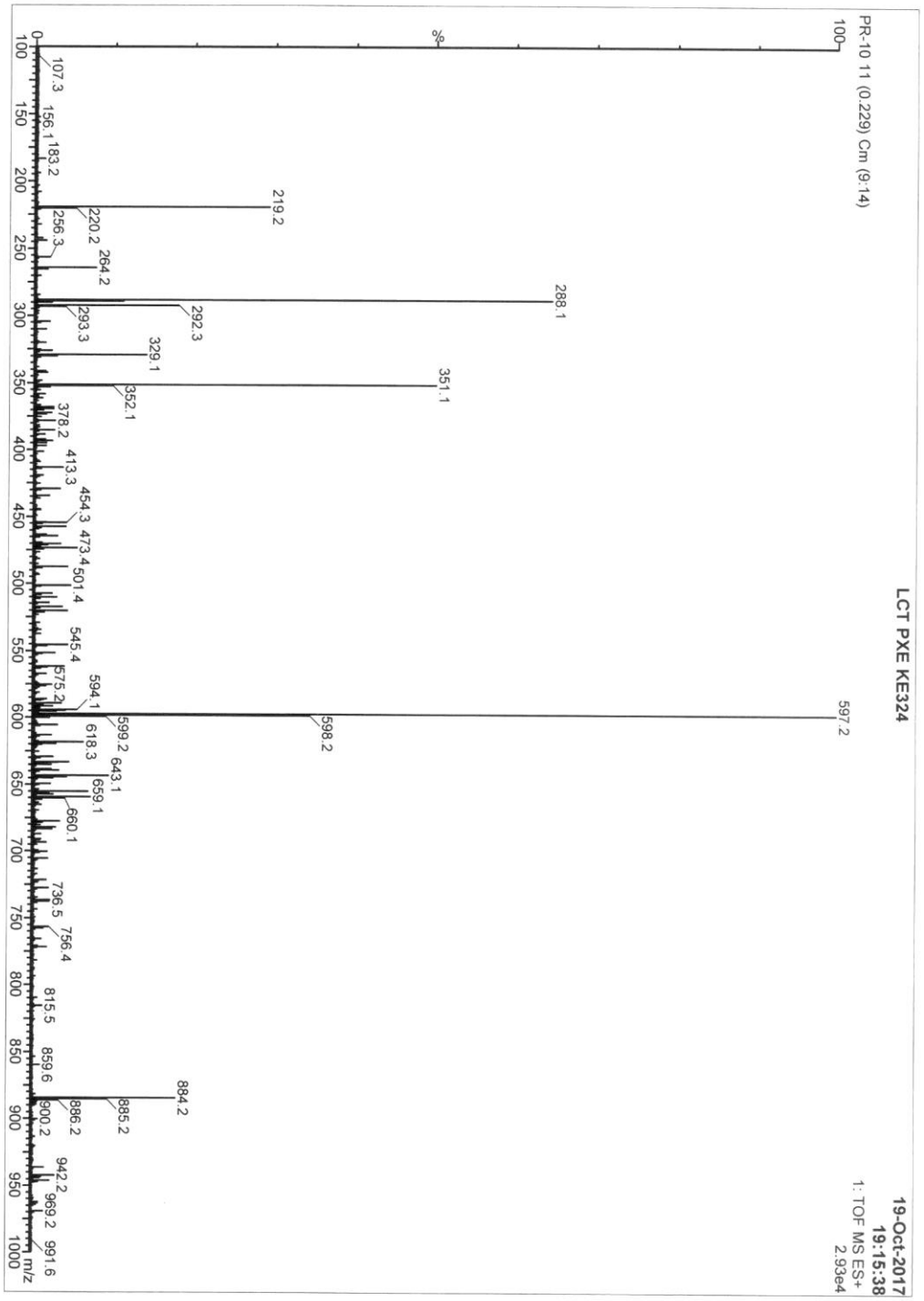
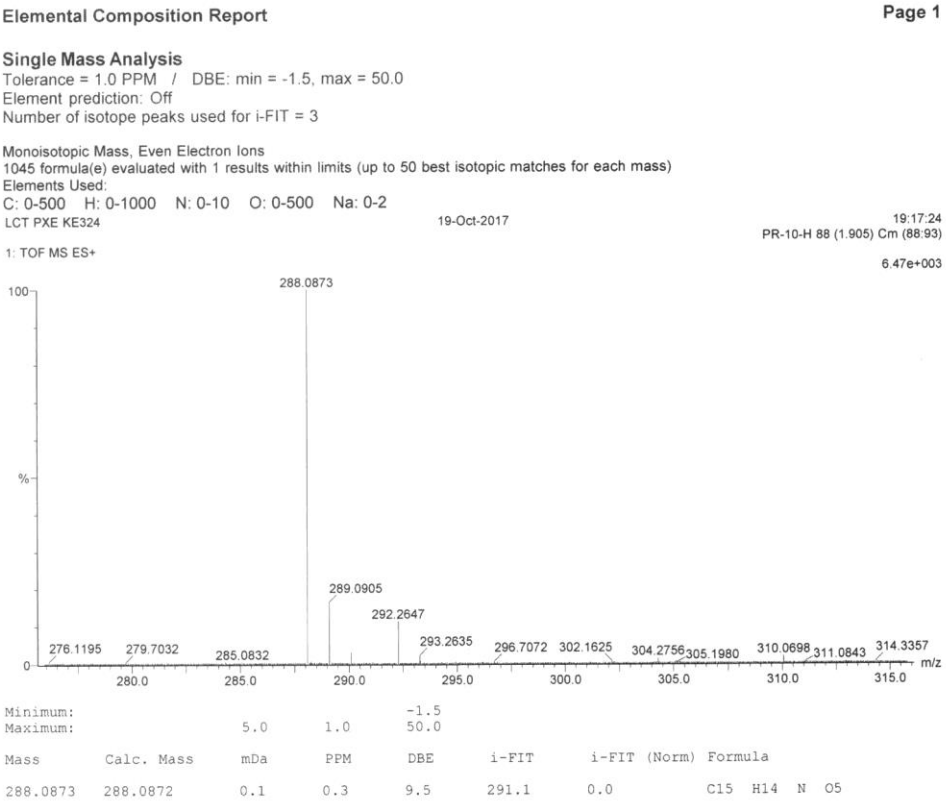


Figure S32. HR(+)ESIMS data of plumerianoid D (**4**).



Elemental Composition Report Page 1

Single Mass Analysis
Tolerance = 1.0 PPM / DBE: min = -1.5, max = 50.0
Element prediction: Off
Number of isotope peaks used for i-FIT = 3

Monoisotopic Mass, Even Electron Ions
1045 formula(e) evaluated with 1 results within limits (up to 50 best isotopic matches for each mass)
Elements Used:
C: 0-500 H: 0-1000 N: 0-10 O: 0-500 Na: 0-2

LCT PXE KE324 19-Oct-2017 19:17:24
PR-10-H 88 (1.905) Cm (88:93)
1: TOF MS ES+ 6.47e+003

Minimum:				-1.5			
Maximum:		5.0	1.0	50.0			
Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	i-FIT (Norm)	Formula
288.0873	288.0872	0.1	0.3	9.5	291.1	0.0	C15 H14 N O5

Figure S33. IR spectrum of plumerianoid D (**4**).

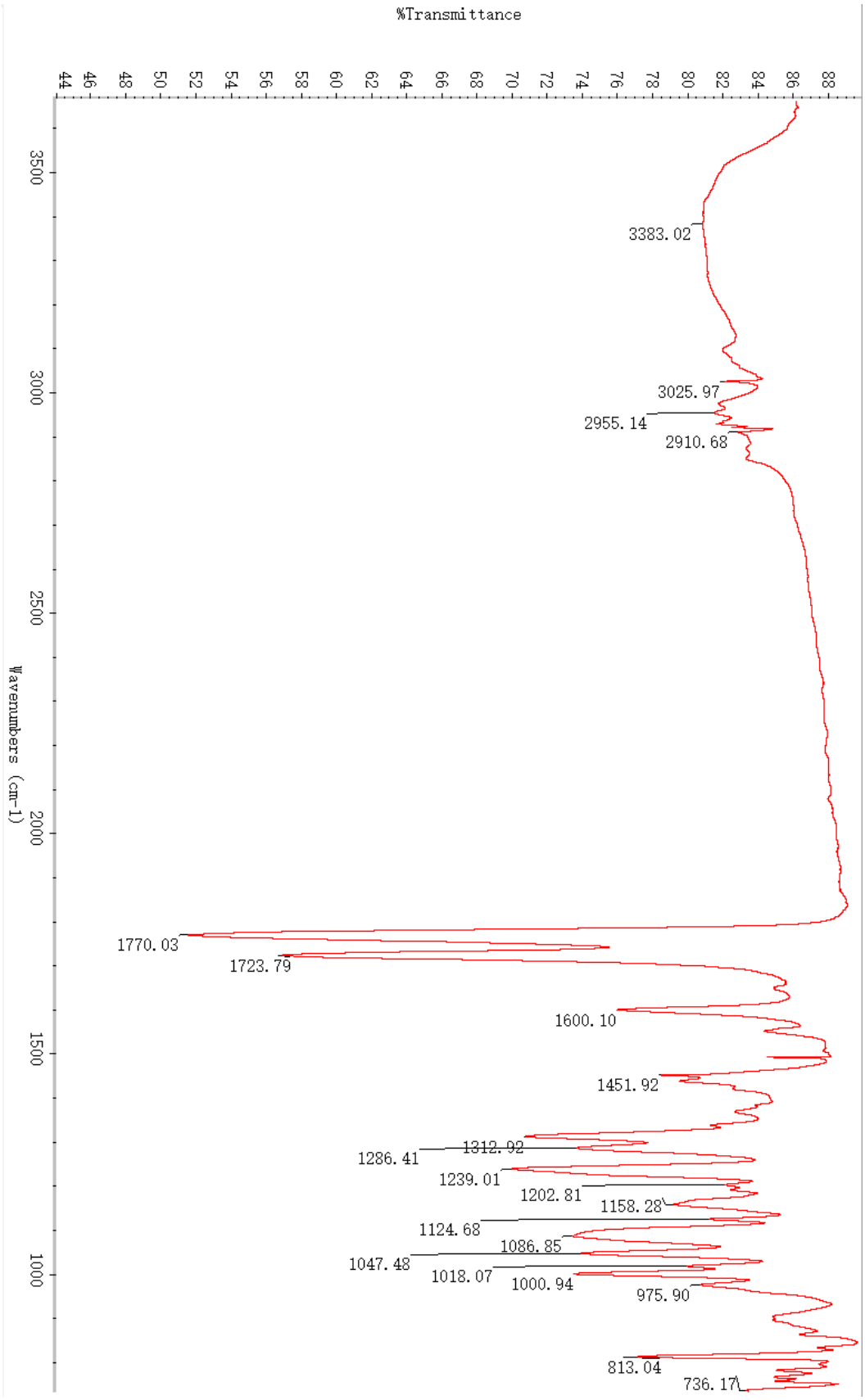


Figure S34. ^{1}H NMR spectrum of 8-*epi*-plumerianine (**5**) in CD_3OD.

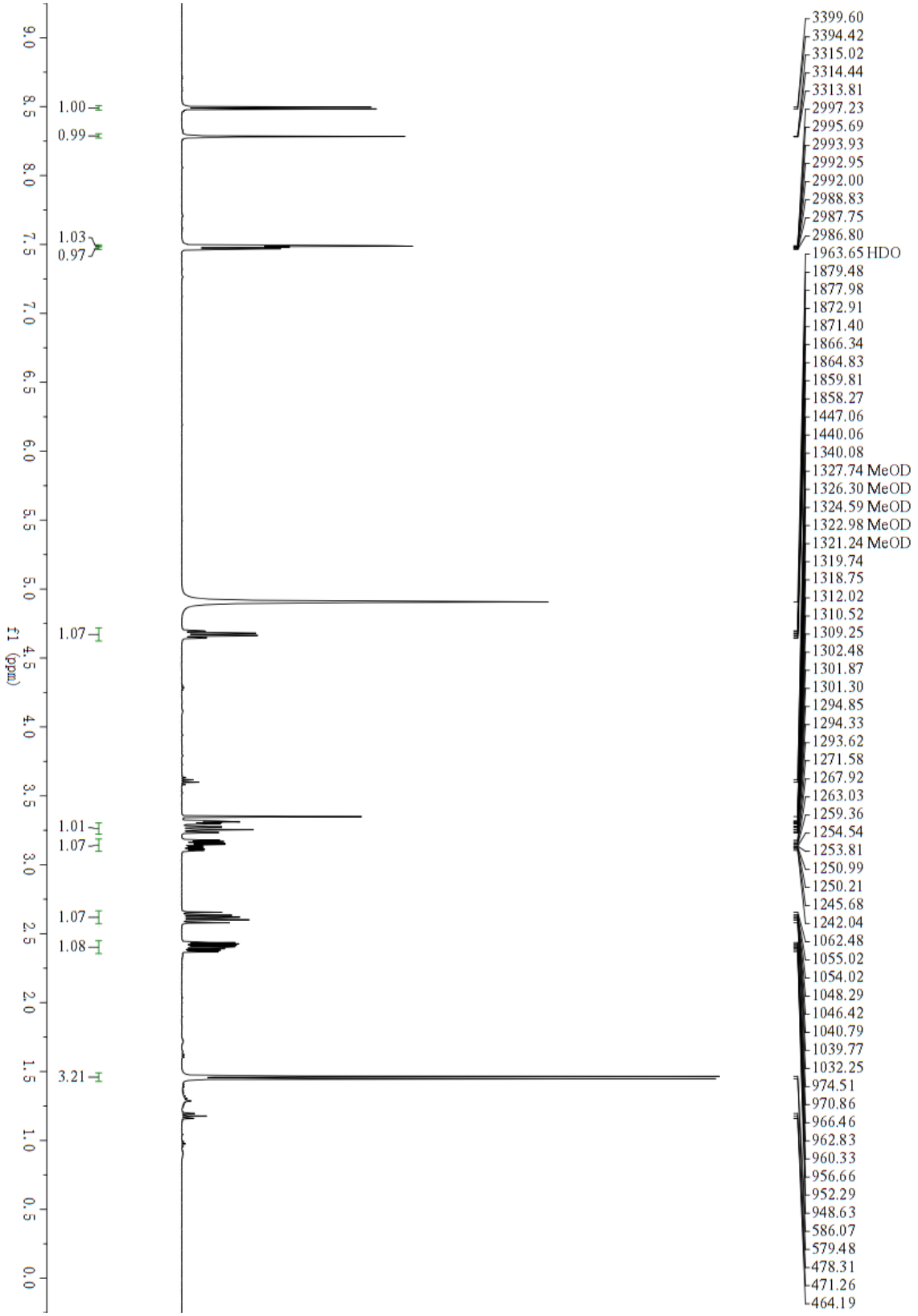


Figure S35. ^{13}C NMR spectrum of 8-*epi*-plumerianine (**5**) in CD_3OD.

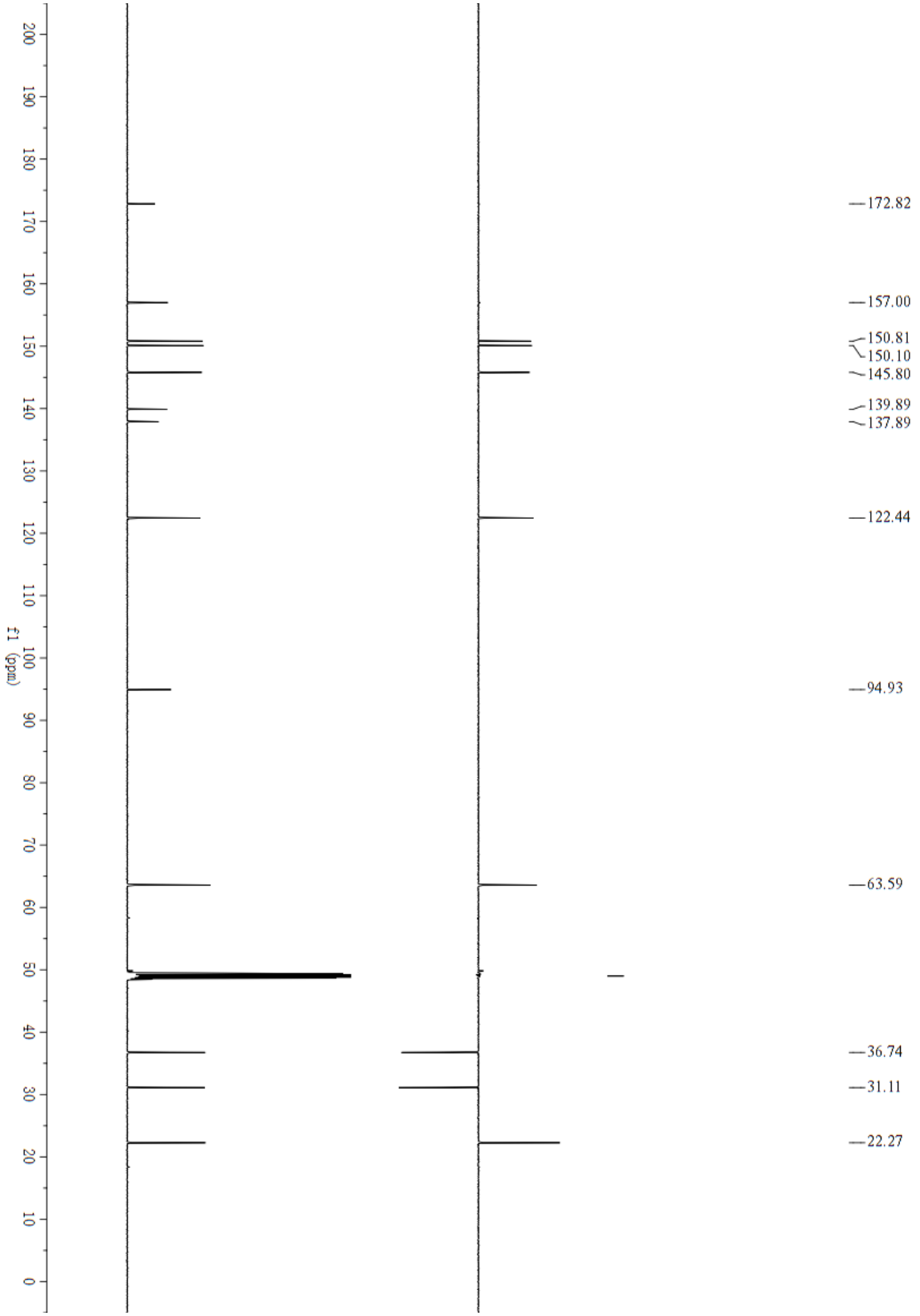


Figure S36. HSQC spectrum of 8-*epi*-plumerianine (**5**) in CD_3OD.

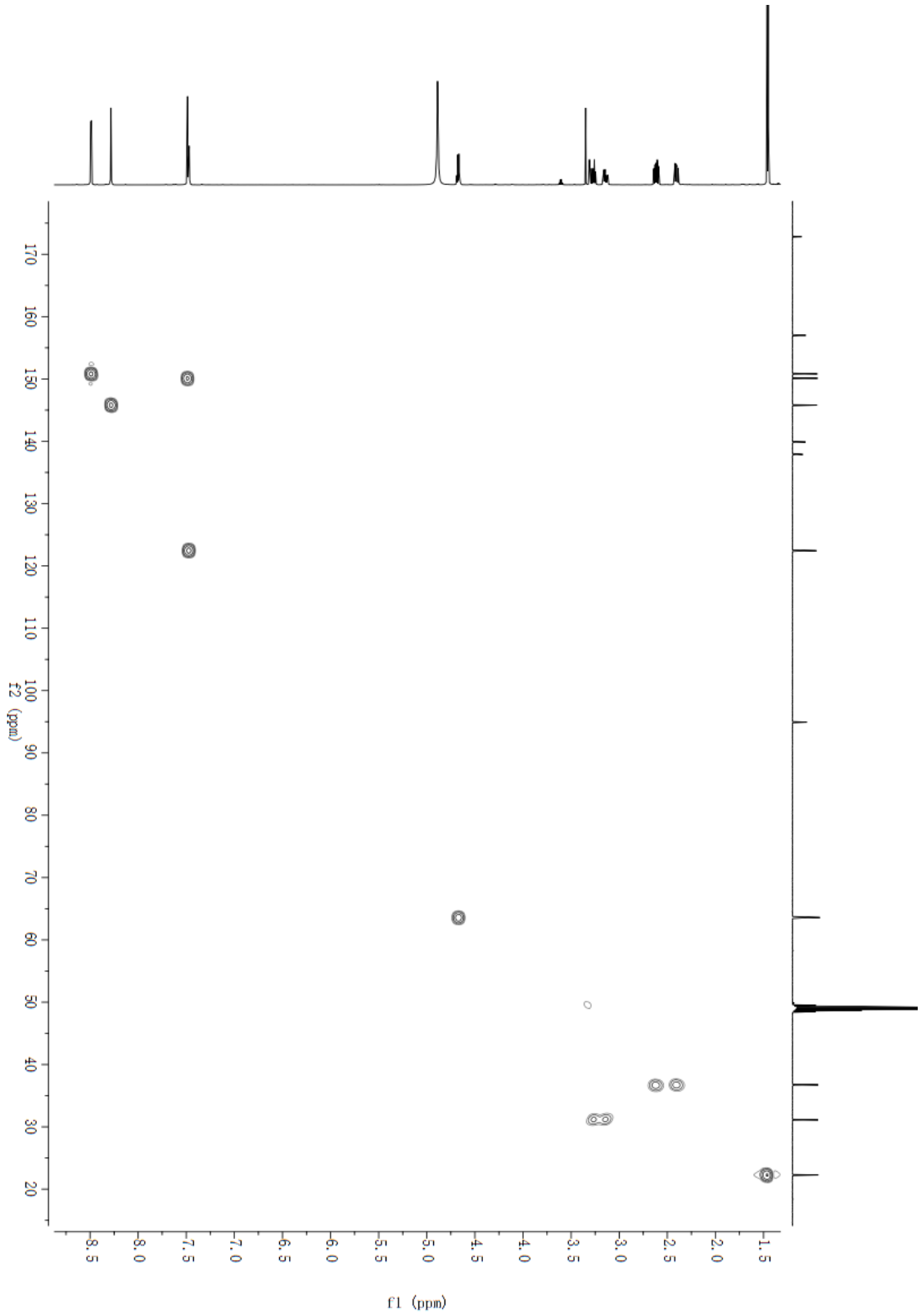


Figure S37. ^{1}H–^{1}H COSY spectrum of 8-*epi*-plumerianine (**5**) in CD_3OD.

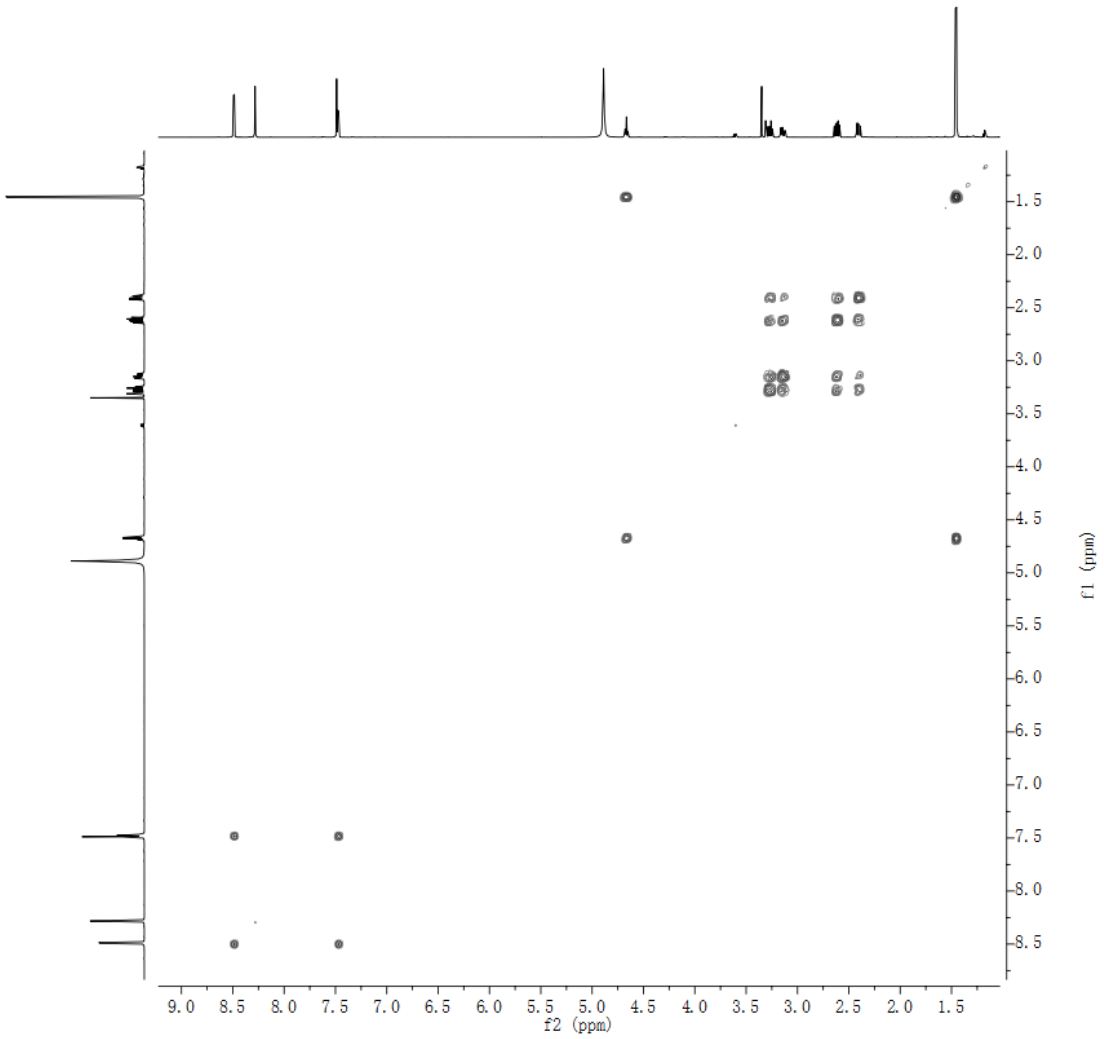


Figure S38. HMBC spectrum of 8-*epi*-plumerianine (**5**) in CD_3OD.

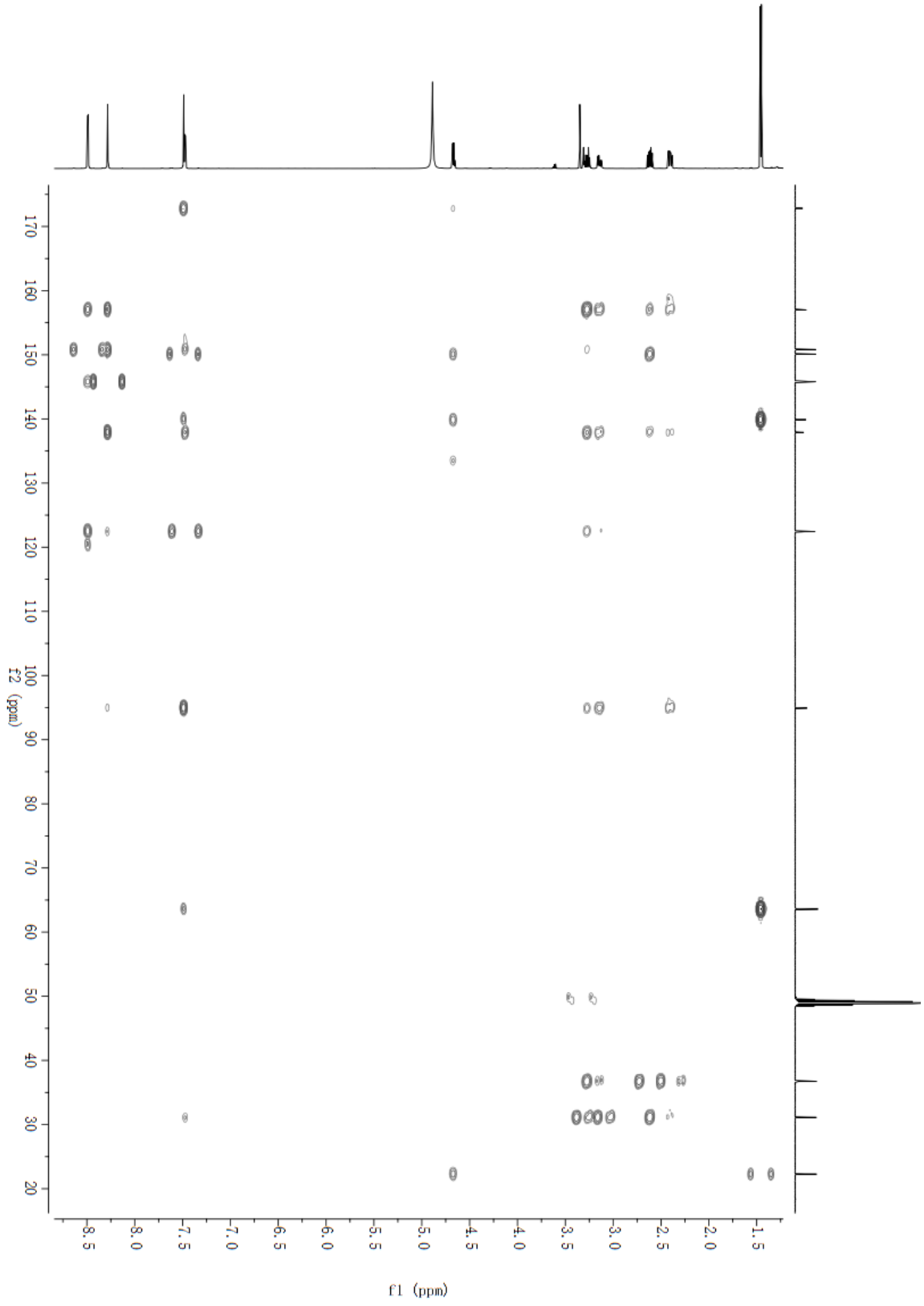


Figure S39. LR(+)ESIMS data of 8-*epi*-plumerianine (**5**).

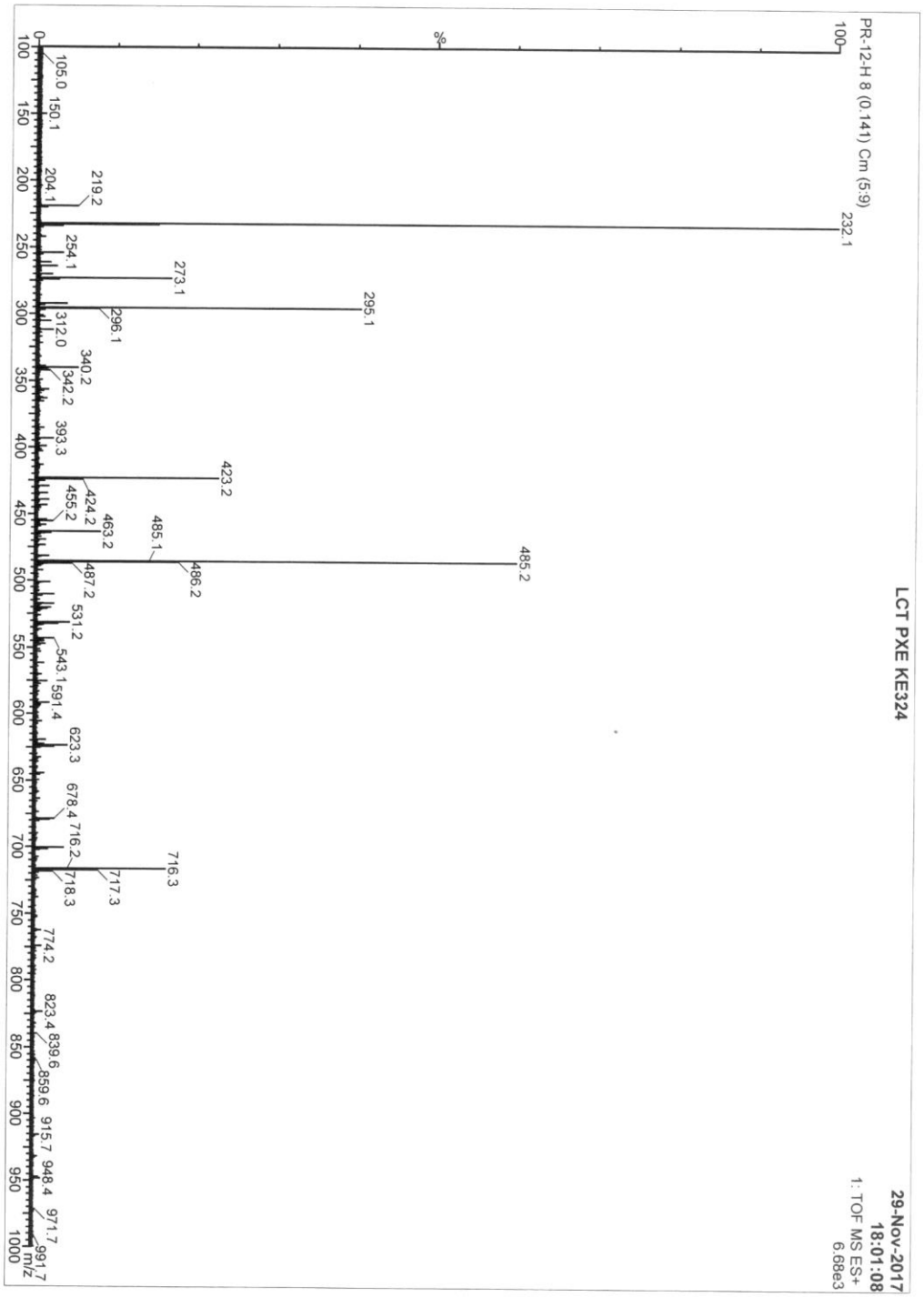


Figure S40. HR(+)ESIMS data of 8-*epi*-plumerianine (**5**).

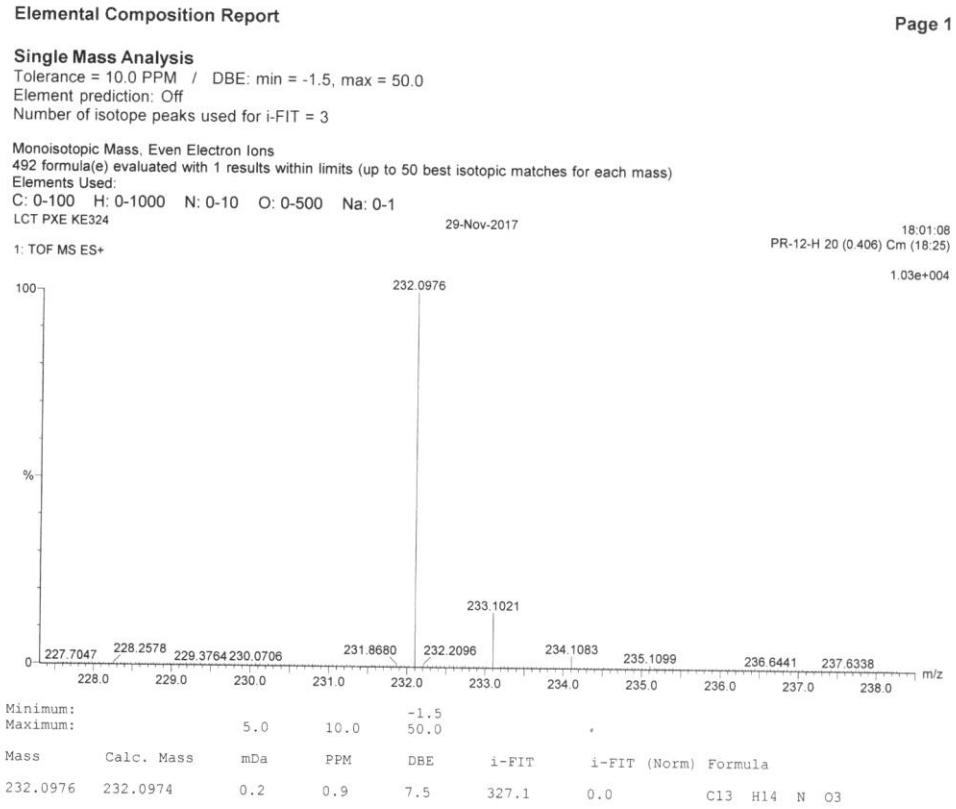


Figure S41. IR spectrum of 8-*epi*-plumerianine (**5**).

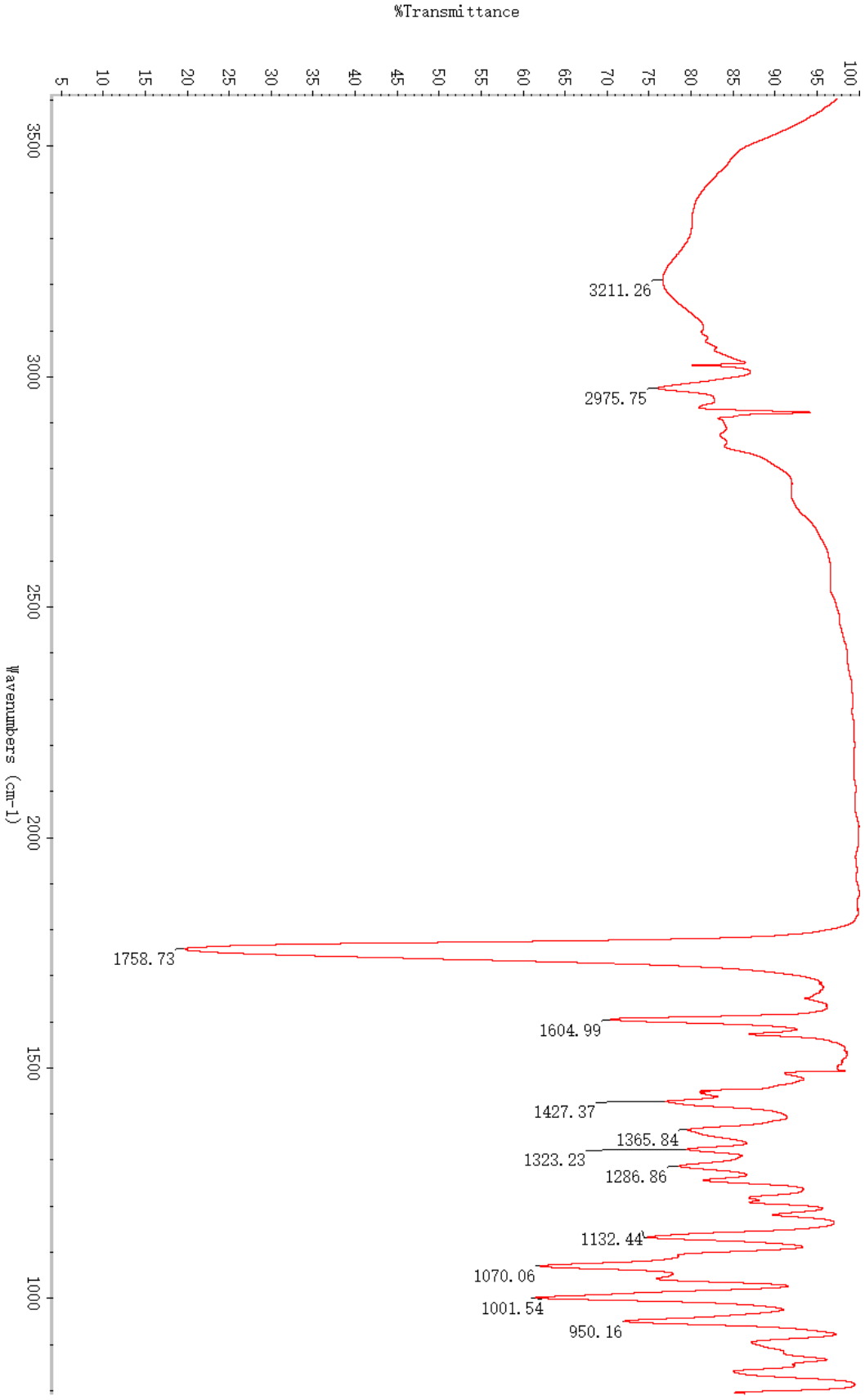


Figure S42. ^{1}H NMR spectrum of (8*R*,13*S*)-plumerianine (**6**) in CD_3OD.

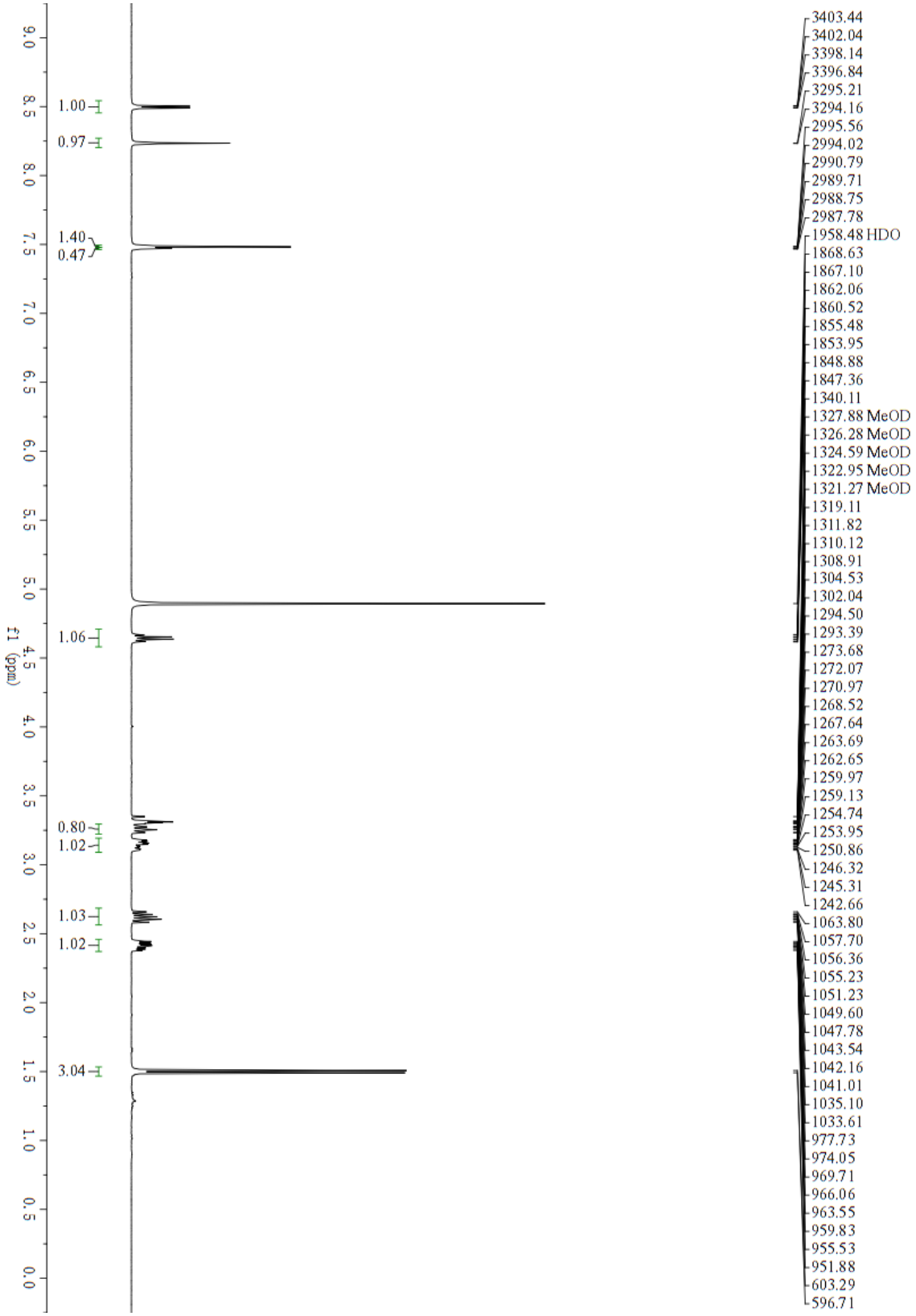


Figure S43. ^{13}C NMR spectrum of (8*R*,13*S*)-plumerianine (**6**) in CD_3OD.

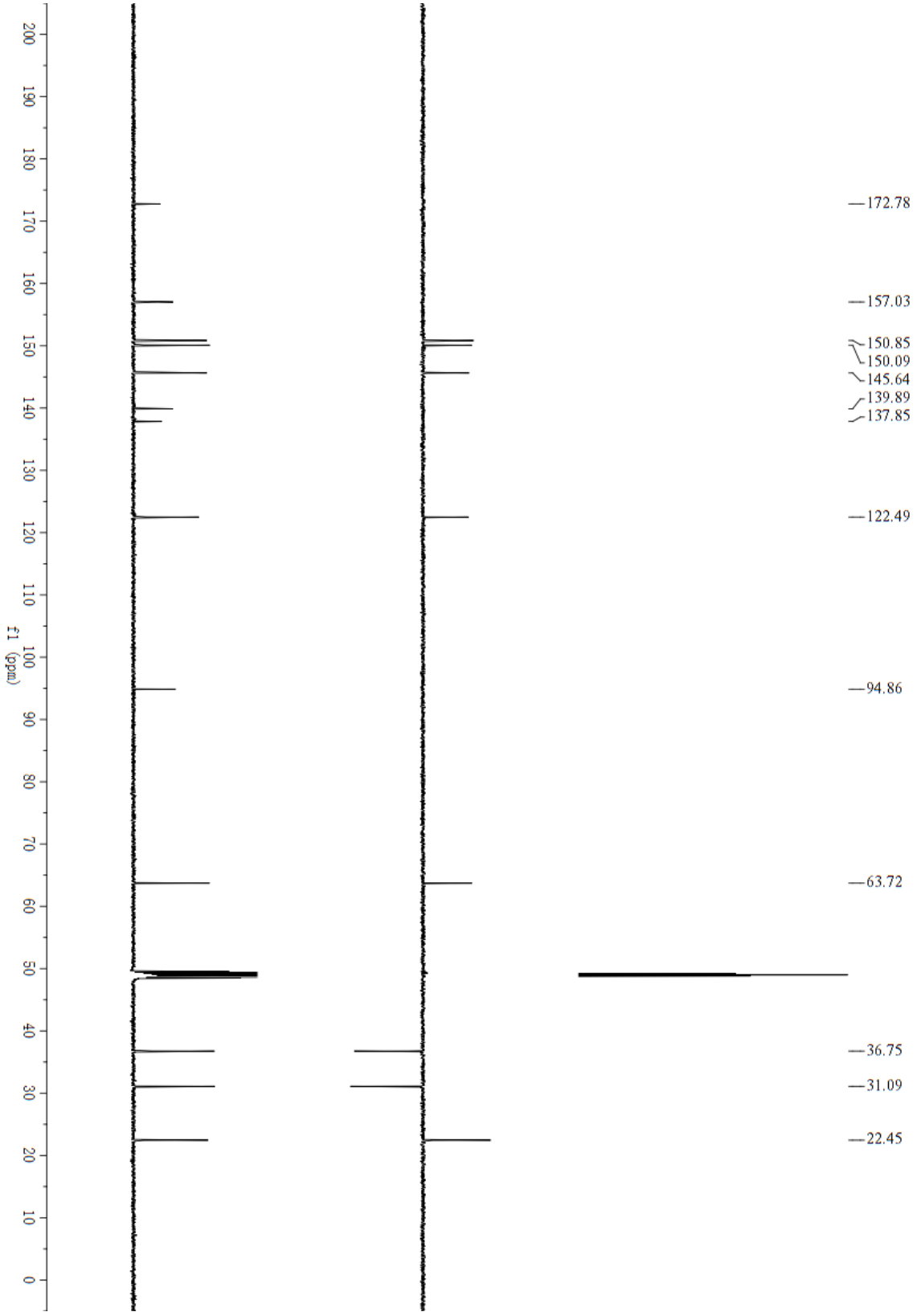


Figure S44. LR(+)ESIMS data of (8*R*,13*S*)-plumerianine (**6**).

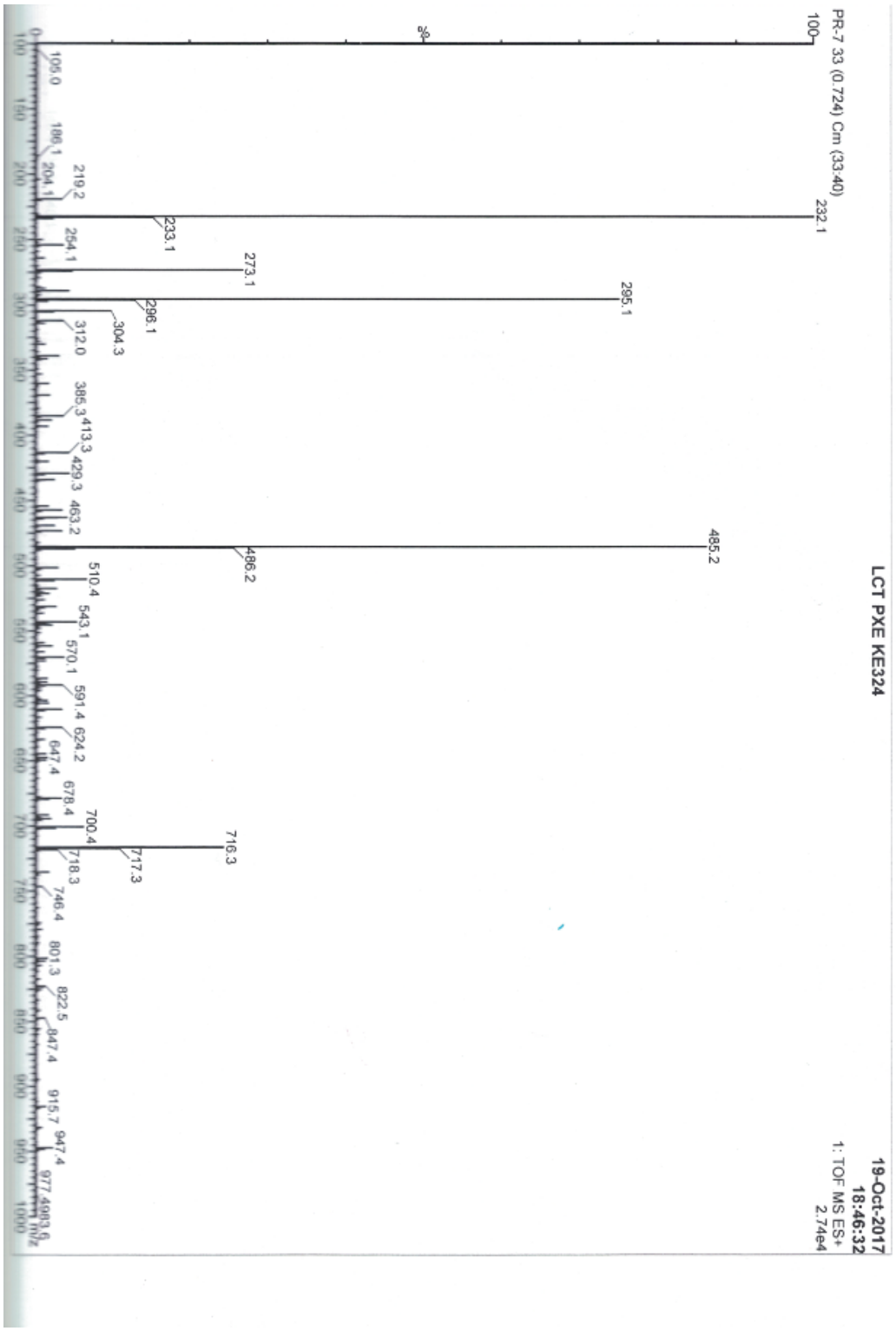
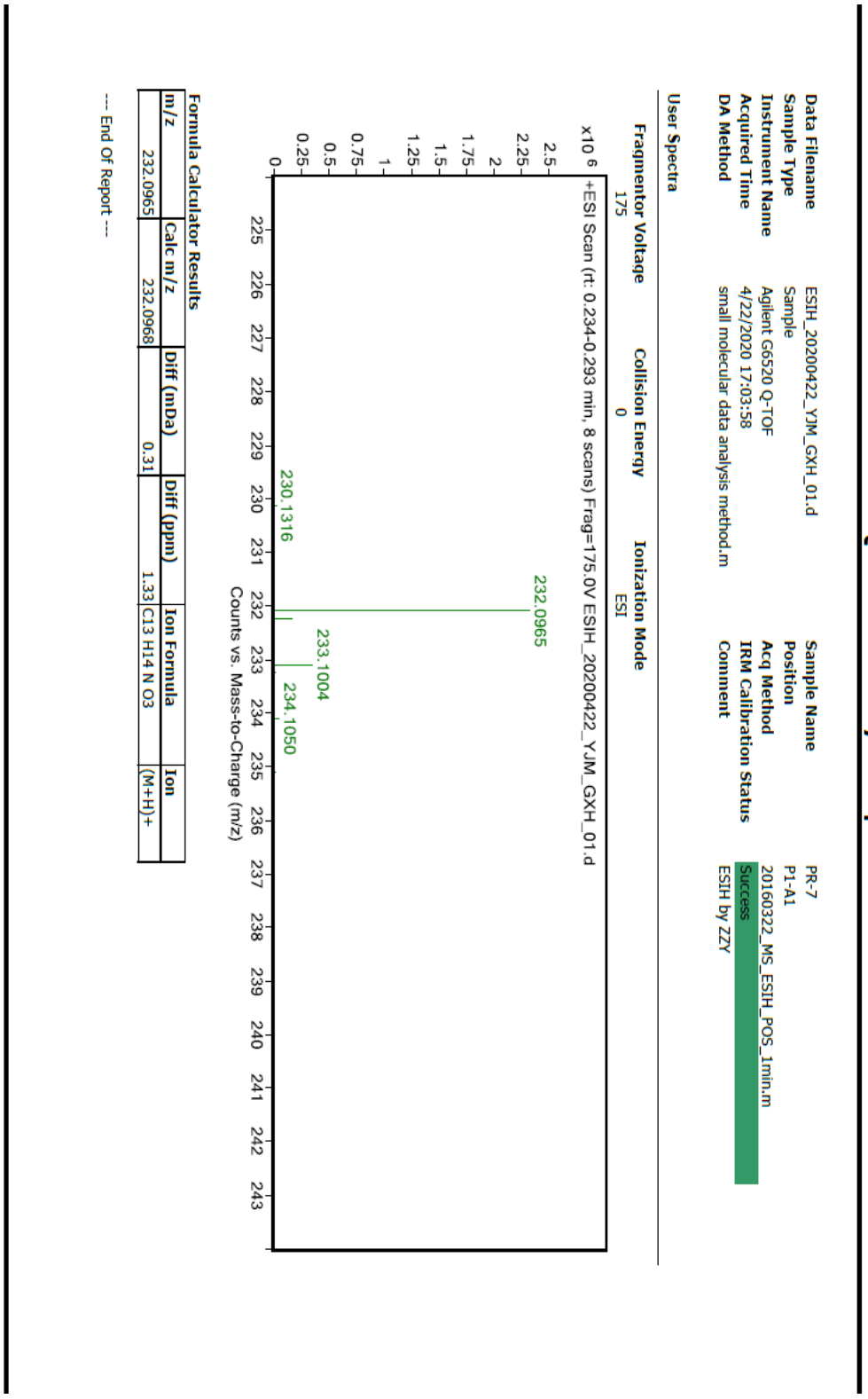


Figure S45. HR(+)ESIMS data of (8*R*,13*S*)-plumerianine (**6**).



Qualitative Analysis Report

Data Filename	ESIH_20200422_YJM_GXH_01.d	Sample Name	PR-7
Sample Type	Sample	Position	P1-A1
Instrument Name	Agilent G6520 Q-TOF	Acq Method	20160322_MS_ESIH_POS_1min.m
Acquired Time	4/22/2020 17:03:58	IRM Calibration Status	Success
DA Method	small molecular data analysis method.m	Comment	ESIH by ZZY

User Spectra

Fragmentor Voltage	Collision Energy	Ionization Mode
175	0	ESI

Formula Calculator Results

m/z	Calc m/z	Diff (mDa)	Diff (ppm)	Ion Formula	Ion
232.0965	232.0968	0.31	1.33	C13 H14 N O3	(M+H)+

--- End Of Report ---

Figure S46. ^{1}H NMR spectrum of **7**/**8** in CD_3OD.

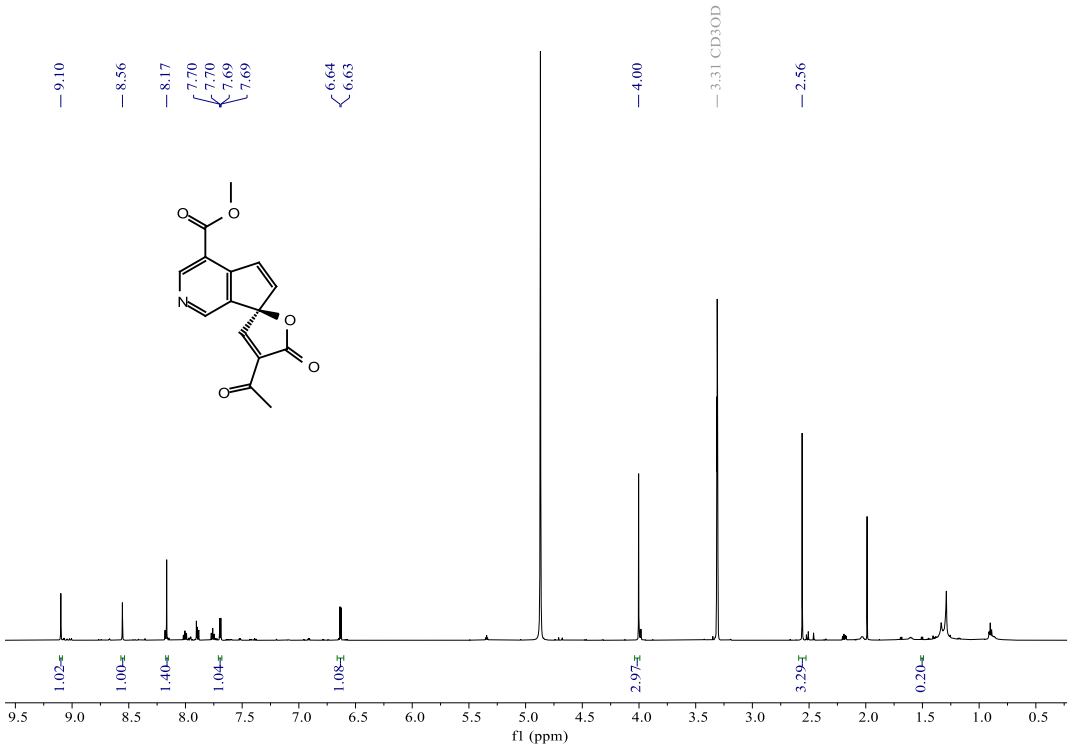


Figure S47. ^{13}C NMR spectrum of **7**/**8** in CD_3OD.

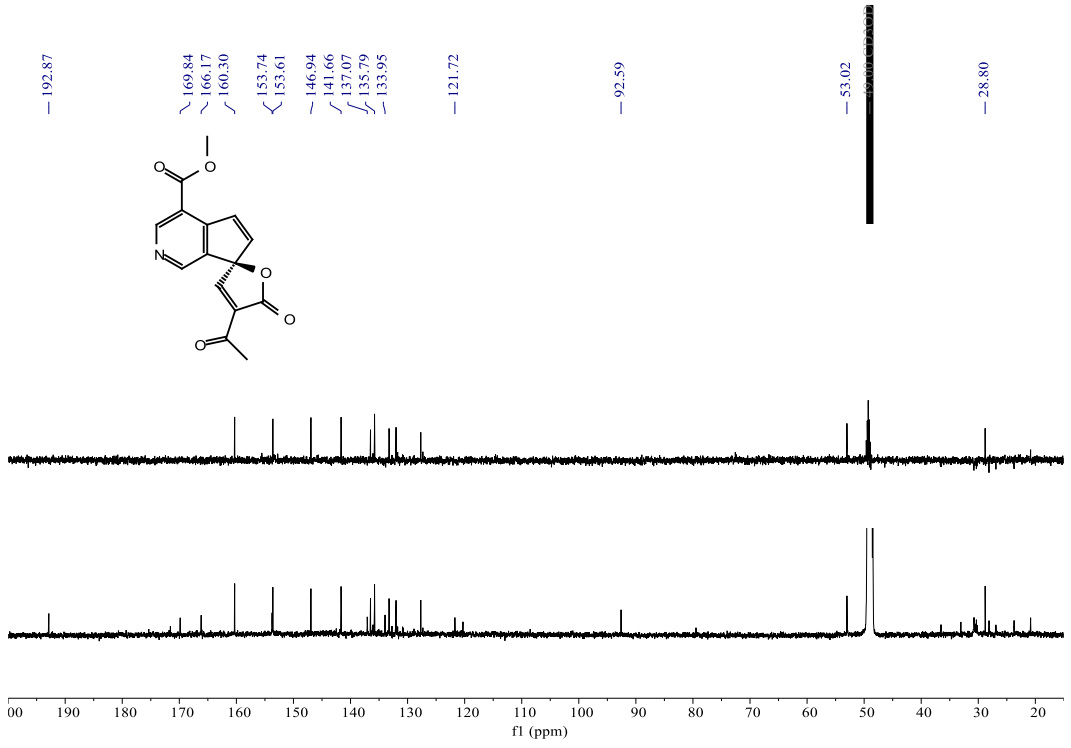


Figure S48. ^{1}H NMR spectrum of **9/10** in CD_3OD.

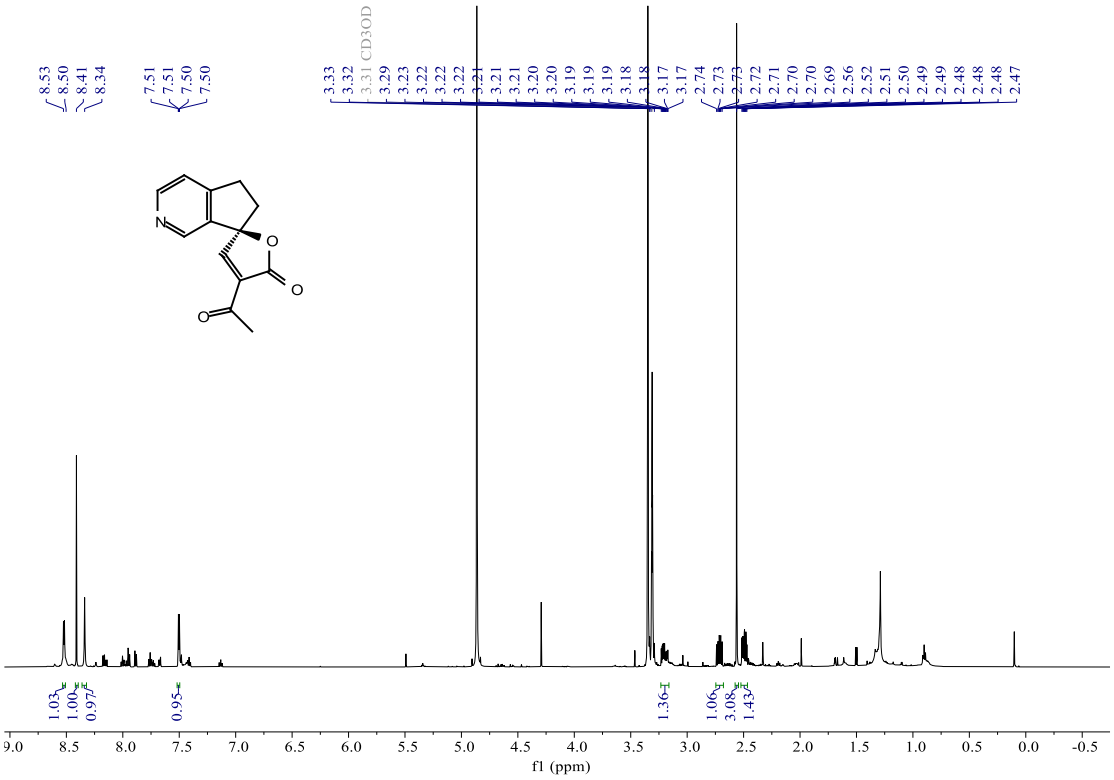


Figure S49. ^{13}C NMR spectrum of **9/10** in CD_3OD.