ChemistryOPEN

Supporting Information

© 2016 The Authors. Published by Wiley-VCH Verlag GmbH & Co. KGaA, Weinheim

Novel Natural Oximes and Oxime Esters with a Vibralactone Backbone from the Basidiomycete *Boreostereum vibrans*

He-Ping Chen,[a, c] Zhen-Zhu Zhao,[a, c] Zheng-Hui Li,[a, b] Ze-Jun Dong,[a] Kun Wei,[a] Xue Bai,[a] Ling Zhang,[a] Chun-Nan Wen,[a, c] Tao Feng,*[a, b] and Ji-Kai Liu*[a, b]

open_201500198_sm_miscellaneous_information.pdf

Supporting Information

Table of Contents

1. Bioassays 6

1.1 Assessment of the inhibitory activity against pancreatic lipase. 6

1.2 Results of the inhibitory activity against pancreatic lipase of compounds **1-16**. 7

1.3 Cytotoxicity assay. 8

2. Semisynthesis of compound **1** from vibralactone..... 9

2.1 From vibralactone to (1*R*,5*S*)-1-(3-methylbut-2-en-1-yl)-7-oxo-6-oxabicyclo[3.2.0]hept-2-ene-3-carbaldehyde (**17**) 9

2.2 From (1*R*,5*S*)-1-(3-methylbut-2-en-1-yl)-7-oxo-6-oxabicyclo[3.2.0]hept-2-ene-3-carbaldehyde (17) to vibralactoxime A (**1a**)..... 9

Figure A. ^{1}H NMR spectrum of **17** (600 MHz, acetone-d6). 10

Figure B. ^{1}H NMR spectrum of **1a** (600 MHz, acetone-d_6) 10

Figure C. The CD and UV spectra of vibralactone (solvent: MeCN). 11

Figure D. The CD and UV spectra of **1** (solvent: MeCN)..... 12

Figure E. The CD and UV spectra of synthesized 1a (solvent: MeCN)..... 13

3. Representative HPLC spectra of some final compounds. 14

Figure F. HPLC spectra of compound **1** (t_R = 8.71 min)..... 14

Figure G. HPLC spectra of compound **2** (t_R = 8.07 min). 14

Figure H. HPLC spectra of compound **4** (t_R = 9.82 min). 15

Figure I. HPLC spectra of compound **6** (t_R = 8.92 min)..... 15

Figure J. HPLC spectra of compound **8** (t_R = 9.19 min)..... 16

Figure K. HPLC spectra of compound **13** (t_R = 8.73 min). 16

Table 1S. ^{1}H (600 MHz) and ^{13}C NMR (150 MHz) spectral data of **1** and **2** in acetone-d_6. 17

Table 2S. ^{1}H (600 MHz) and ^{13}C NMR (150 MHz) spectral data of **3** in acetone-d_6..... 18

Table 3S. ^{1}H (600 MHz) and ^{13}C NMR (150 MHz) spectral data of **4** and **5** in acetone-d_6. 19

Table 4S. ^{1}H (600 MHz) and ^{13}C NMR (150 MHz) spectral data of **6** and **7** in acetone-d_6. 20

Table 5S. ^{1}H (600 MHz) and ^{13}C NMR (150 MHz) spectral data of **8** and **13** in acetone-d_6. 21

Table 6S. ^{1}H (600 MHz) and ^{13}C NMR (150 MHz) spectral data of **9** and **14** in acetone-d_6. 22

Table 7S. ^{1}H (600 MHz) and ^{13}C NMR (150 MHz) spectral data of **10** in acetone-d_6..... 24

Table 8S. Characteristic ^{1}H NMR (600 MHz) spectral data of **11**, **12**, **15** and **16** in acetone-d_6. 25

4. Supplementary NMR spectra. 26

Figure 1S: ^{1}H NMR spectrum of **1** (acetone-d_6, 600MHz)..... 26

Figure 2S: ^{13}C NMR and DEPT spectra of **1** (acetone-d_6, 150MHz) 27

Figure 3S: HSQC spectrum of **1**..... 28

Figure 4S: ^{1}H-^{1}H COSYspectrum of **1**. 29

Figure 5S: HMBC spectrum of **1**..... 30

Figure 6S: ROESYspectrum of **1**. 31

Figure 7S: HREIMSspectrum of **1**. 32

Figure 8S: Optical rotation of compound **1**. 33

Figure 9S: 1H NMR spectrum of **2** (acetone-d6, 600MHz) 34

Figure 10S: 13C NMR and DEPT spectra of **2** (acetone-d6, 150MHz) 35

Figure 11S: HSQC spectrum of **2**..... 36

Figure 12S: 1H-1H COSY spectrum of **2**..... 37

Figure 13S: HMBC spectrum of **2**..... 38

Figure 14S: ROESYspectrum of **2**. 39

Figure 15S: HREIMSspectrum of **2**. 40

Figure 16S: ^{1}H NMR spectrum of **3** (acetone-d_6, 600MHz)..... 41

Figure 17S: Enlarged view of ^{1}H NMR spectra of **3** (acetone-d_6, 600MHz) 42

Figure 18S: ^{13}C NMR and DEPT spectra of **3** (acetone-d_6, 150MHz) 43

Figure 19S: Enlarged view of ^{13}C NMR spectrum of **3** (acetone-d_6, 150MHz) 44

Figure 20S: HSQC spectrum of **3**..... 45

Figure 21S: ^{1}H-^{1}H COSYspectrum of **3**. 46

Figure 22S: HMBC spectrum of **3**..... 47

Figure 23S: Enlarged view of HMBC spectrum of **3**. 48

Figure 24S: ROESYspectrum of **3**. 49

Figure 25S: HRESIMS spectrum of **3**. 50

Figure 26S: ^{1}H NMR spectrum of **4** (acetone-d_6, 600MHz)..... 51
Figure 27S: ^{13}C NMR and DEPT spectra of **4** (acetone-d_6, 150MHz)..... 52
Figure 28S: Enlarged view of ^{13}C NMR spectrum of **4** (acetone-d_6, 150MHz)..... 53
Figure 29S: HSQC spectrum of **4**..... 54
Figure 30S: ^{1}H-^{1}H COSYspectrum of **4**..... 55
Figure 31S: HMBC spectrum of **4**..... 56
Figure 32S: Enlarged view of HMBC spectra of **4**. 57
Figure 33S: ROESYspectrum of **4**. 58
Figure 34S: HREIMSspectrum of **4**. 59
Figure 35S: IR spectrum of **4**. 60
Figure 36S: ^{1}H NMR spectrum of **5** (acetone-d_6, 600MHz)..... 61
Figure 37S: ^{13}C NMR and DEPT spectra of **5** (acetone-d_6, 150MHz)..... 62
Figure 38S: Enlarged view of ^{13}C NMR spectrum of **5** (acetone-d_6, 150MHz)..... 63
Figure 39S: HSQC spectrum of **5**..... 64
Figure 40S: ^{1}H-^{1}H COSYspectrum of **5**..... 65
Figure 41S: HMBC spectrum of **5**..... 66
Figure 42S: Enlarged view of HMBC spectra of **5**. 67
Figure 43S: ROESYspectrum of **5**. 68
Figure 44S: IR spectrum of **5**. 69
Figure 45S: HRESIMS spectrum of **5**..... 70
Figure 46S: ^{1}H NMR spectrum of **6** (acetone-d_6, 600MHz)..... 71
Figure 47S: ^{13}C NMR and DEPT spectra of **6** (acetone-d_6, 150MHz)..... 72
Figure 48S: HSQC spectrum of **6**..... 73
Figure 49S: ^{1}H-^{1}H COSYspectrum of **6**..... 74
Figure 50S: HMBC spectrum of **6**..... 75
Figure 51S: Enlarged view of HMBC spectra of **6**. 76
Figure 52S: ROESYspectrum of **6**. 77
Figure 53S: HRESIMSspectrum of **6**..... 78
Figure 54S: ^{1}H NMR spectrum of **7** (acetone-d_6, 600MHz)..... 80
Figure 55S: ^{13}C NMR and DEPT spectra of **7** (acetone-d_6, 150MHz)..... 81
Figure 56S: HSQC spectrum of 7..... 82

Figure 57S: ^{1}H-^{1}H COSYspectrum of **7**. 83
Figure 58S: Enlarged view of ^{1}H-^{1}H COSY spectrum. 84
Figure 59S: HMBC spectrum of **7**. 85
Figure 60S: ROESYspectrum of **7**. 86
Figure 61S: HRESIMSspectrum of **7**. 87
Figure 62S: ^{1}H NMR spectrum of **8** (acetone-d_6, 600MHz). 88
Figure 63S: ^{13}C NMR and DEPT spectra of **8** (acetone-d_6, 150MHz) 89
Figure 64S: HSQC spectrum of **8**. 90
Figure 65S: ^{1}H-^{1}H COSYspectrum of **8**. 91
Figure 66S: HMBC spectrum of **8**. 92
Figure 67S: ROESYspectrum of **8**. 93
Figure 68S: HREIMSspectrum of **8**. 94
Figure 69S: ^{1}H NMR spectrum of **9** (acetone-d_6, 600MHz). 95
Figure 70S: ^{13}C NMR and DEPT spectra of **9** (acetone-d_6, 150MHz) 96
Figure 71S: HSQC spectrum of **9**. 97
Figure 72S: ^{1}H-^{1}H COSYspectrum of **9**. 98
Figure 73S: HMBC spectrum of **9**. 99
Figure 74S: ROESYspectrum of **9**. 100
Figure 75S: HREIMSspectrum of **9**. 101
Figure 76S: ^{1}H NMR spectrum of **10** (acetone-d_6, 600MHz). 102
Figure 77S: Enlarged view of ^{1}H NMR spectra of **10** (acetone-d_6, 600MHz) 103
Figure 78S: ^{13}C NMR and DEPT spectra of **10** (acetone-d_6, 150MHz) 104
Figure 79S: Enlarged view of ^{13}C NMR and DEPT spectra of **10** (acetone-d_6, 150MHz) 105
Figure 80S: HSQC spectrum of **10**. 106
Figure 81S: Enlarged view of HSQC spectrum of **10**. 107
Figure 82S: ^{1}H-^{1}H COSYspectrum of **10**. 108
Figure 83S: HMBC spectrum of **10**. 109
Figure 84S: Enlarged view of HMBC spectrum of **10**. 110
Figure 85S: ROESYspectrum of **10**. 111
Figure 86S: HRESIMSspectrum of **10**. 112
Figure 87S: ^{1}H NMR spectrum of **11** (acetone-d_6, 600MHz). 113

Figure 88S: Enlarged view of ^{1}H NMR spectrum of **11** (acetone-d_6, 600MHz) 114
Figure 89S: HRESIMSspectrum of **11**. 115
Figure 90S: ^{1}H NMR spectrum of **12** (acetone-d_6, 600MHz)..... 116
Figure 91S: Enlarged view of ^{1}H NMR spectrum of **12** (acetone-d_6, 600MHz) 117
Figure 92S: HRESIMSspectrum of **12**. 118
Figure 93S: ^{1}H NMR spectrum of **13** (acetone-d_6, 600MHz)..... 119
Figure 94S: ^{13}C NMR and DEPT spectra of **13** (acetone-d_6, 150MHz) 120
Figure 95S: Enlarged view of ^{13}C NMR and DEPT spectra of **13** (acetone-d_6, 150MHz) 121
Figure 96S: HSQC spectrum of **13**. 122
Figure 97S: ^{1}H-^{1}H COSY spectrum of **13**. 123
Figure 98S: HMBC spectrum of **13**..... 124
Figure 99S: ROESY spectrum of **13**. 125
Figure 100S: HREIMS spectrum of **13**. 126
Figure 101S: ^{1}H NMR spectrum of **14** (acetone-d_6, 600MHz)..... 127
Figure 102S: ^{13}C NMR and DEPT spectra of **14** (acetone-d_6, 150MHz) 128
Figure 103S: HSQC spectrum of **14**. 129
Figure 104S: ^{1}H-^{1}H COSYspectrum of **14**. 130
Figure 105S: HMBC spectrum of **14**..... 131
Figure 106S: Enlarged view of HMBC spectrum of **14**. 132
Figure 107S: ROESYspectrum of **14**. 133
Figure 108S: HRESIMSspectrum of **14**. 134
Figure 109S: ^{1}H NMR spectrum of **15** (acetone-d_6, 600MHz)..... 135
Figure 110S: Enlarged view of ^{1}H NMR spectra of **15** (acetone-d_6, 600MHz) 136
Figure 111S: HRESIMSspectrum of **15**. 137
Figure 112S: ^{1}H NMR spectrum of **16** (acetone-d_6, 600MHz)..... 138
Figure 113S: Enlarged view of ^{1}H NMR spectrum of **16** (acetone-d_6, 600MHz) 139
Figure 114S: HRESIMSspectrum of **16**. 140

1. Bioassays

1.1 Assessment of the inhibitory activity against pancreatic lipase.

Porcine pancreatic lipase was used to evaluate the inhibitory activity of the monascus pigment derivatives. *p*-Nitrophenyl butyrate (*p*-NPS) was used as the substrate. Firstly, an enzyme-buffer solution was prepared by adding 30μL of lipase solution (in 10 mM morpholine propane sulfonic acid (MOPS) and 1 mM EDTA, pH 6.8) to 850 μL of Tris buffer (100 mM Tris–HCl and 5 mM $CaCl_2$, pH 7.0). Pigment solutions were prepared by dissolving each pigment in a mixture (1:1) of ethanol and distilled water. Subsequently, 100 μL of the pigment solution was mixed with 880 μL of the enzyme-buffer solution. Following incubation of the enzyme-pigment mixture for 15 min at37 ℃, 20 μL of the substrate solution (10 mM *p*-NPB in dimethyl formamide) was added. Enzymatic reactions were conducted for 15 min at 37 ℃. The hydrolysis of *p*-NPB to*p*-nitrophenol was monitored at 400 nm using a spectrophotometer. One unit of the enzyme was defined as the amount required to liberate 1 mol of *p*-nitrophenol under standard assay conditions.

Reference: K. Wei, G. Q. Wang, X. Bai, Y. F. Niu, H. P. Chen, C. N. Wen, Z. H. Li, Z. J. Dong, Z. L. Zuo, W. Y. Xiong, J. K. Liu, *Nat. Prod. Bioprospect.* **2015**, *5*, 129-157

1.2 Results of the inhibitory activity against pancreatic lipase of compounds 1-16.

Compound	Concentration (μM)	PPL inhibitory rate (%)	IC_{50} (μM)
Orlistat	0.005	86.024	0.0018
	0.002	51.526	
	0.001	28.284	
Vibralactone	10000	91.800	48.668
	1000	87.038	
	100	57.678	
	10	33.130	
1	50	71.318	23.061
	10	26.847	
	2	5.197	
2	50	-13.600	
3	50	-14.573	
4	50	84.188	20.580
	10	22.026	
	2	-27.792	
5	50	78.439	28.619
	10	-3.936	
	2	-22.889	
6	50	19.483	
7	50	89.319	16.813
	10	31.203	
	2	-24.384	
8	50	45.843	
9	50	79.213	23.189
	10	17.979	
	2	-16.907	
10	50	67.824	19.812
	10	36.842	
	2	-35.413	
11	50	60.084	11.108
	10	49.160	
	2	8.359	
12	50	18.841	
13	50	-35.847	
14	50	-34.719	
15	50	-2.875	
16	50	-8.293	

Note: The compounds which PPL inhibitory rate less than 50% on the concentration 50 μM were not to test their IC_{50} values.

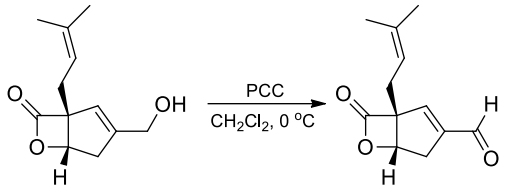
1.3 Cytotoxicity assay.

The following human tumor cell lines were used: HL-60, SMMC-7721, A-549, MCF-7, and SW-480. All cells were cultured in RPMI-1640 medium (Hyclone, Logan, UT, USA), supplemented with 10% fetal bovine serum (FBS, Hyclone) at 37 ºC in a humidified atmosphere with 5% CO_2. Cell viability was assessed by conducting colorimetric measurements of the amount of insoluble formazan formed in living cells based on the reduction of 3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide (MTT) (Sigma, St. Louis, MO, USA). Briefly, 100 μL of adherent cells was seeded into each well of a 96-well cell culture plate and allowed to adhere for 12 h before test compound addition, while suspended cells were seeded just before test compound addition, both with an initial density of 1×10^5 cells/mL in 100 μL of medium. Each tumor cell line was exposed to the test compound at various concentrations in triplicate for 48 h, with cis-platin and paclitaxel (Sigma) as positive control. After the incubation, MTT (100 μg) was added to each well, and the incubation continued for 4 h at 37 ºC. The cells were lysed with 100 μL of 20% SDS-50% DMF after removal of 100 μL of medium. The optical density of the lysate was measured at 595 nm in a 96-well microtiter plate reader (Bio-Rad 680). The IC_{50} value of each compound was calculated by Reed and Muench's method.

References: a) M. C. Alley, D. A. Scudiero, A. Monks, M. L. Hursey, M. J. Czerwinski, D. L. Fine, B. J. Abbott, J. G. Mayo, R. H. Shoemaker, M. R. Boyd, *Cancer Res*. **1988**, *48*, 589-601; b) J. J. Zhang, X. W. Yang, J. Z. Ma, X. Liu, L. X. Yang, S. C. Yang, G. Xu, *Nat. Prod. Bioprospect.* **2014**, *4*, 73-79.

2. Semisynthesis of compound 1 from vibralactone.

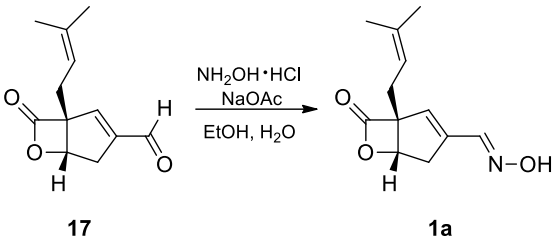
2.1 From vibralactone to (1*R*,5*S*)-1-(3-methylbut-2-en-1-yl)-7-oxo-6-oxabicyclo[3.2.0]hept-2-ene-3-carbaldehyde (17)



To a solution of vibralactone (16 mg, 0.077 mmol) in CH_2Cl_2 (1 mL) was added PCC (17.2 mg, 0.080 mmol). The mixture was stirred at 0 °C for 30 min, during which the progress of the reaction was monitored by TLC. The reaction mixture was passed through a short silica gel pad (eluent: ethyl acetate) and then purified by prep-HPLC [method: 30-50% (acetonitrile/water), 20 min, 8 mL/min, detected UV wavelength: 205 nm, 247 nm, t_R = 9.85 min] to afford **17** (12.4 mg, 78% yield): ^{1}H NMR (600 MHz, acetone-d_6): δ_H 6.93 (s, H-2), 2.88 (overlapped, H-4a), 2.94 (dd, *J* = 19.0, 13.0 Hz, H-4b), 5.08 (d, *J* = 5.5 Hz, H-5), 2.64 (dd, *J* = 15.0, 7.4 Hz, H-8a), 2.78 (dd, *J* = 15.0, 7.4 Hz, H-8b), 5.21 (br. t, *J* = 7.4 Hz, H-9), 1.68 (s, 3H, H-11), 1.71 (s, 3H, H-12), 9.86 (s, H-13).

Reference: M. Y. Jiang, F. Wang, X. L. Yang, L. Z. Fang, Z. J. Dong, H. J. Zhu, J. K. Liu, *Chem. Pharm. Bull.* **2008**, *56*, 1286-1288.

2.2 From (1*R*,5*S*)-1-(3-methylbut-2-en-1-yl)-7-oxo-6-oxabicyclo[3.2.0]hept-2-ene-3-carbaldehyde (17) to vibralactoxime A (1a)



A solution of $NH_2OH \cdot HCl$ (4.6 mg, 0.067 mmol) and sodium acetate (5.5 mg, 0.067 mmol) in EtOH/H_2O (1:1, 0.6 mL) was added dropwise to a solution aldehyde **17** (6.8 mg, 0.033 mmol) in EtOH (0.3 mL) at 0 °C. The mixture was stirred at 0 °C for 20 min, during which the progress of the reaction was monitored by TLC. The mixture was concentrated under reduced pressure then purified by prep-HPLC [method: 30-50% (acetonitrile/water), 20 min, 8 mL/min, detected UV wavelength: 247 nm, t_R = 15.6 min] to afford **1a** (6.56 mg, 90% yield).

Reference: R. A. Aungst, Jr, C. Chan, R. L. Funk, *Org. Lett.* **2001**, *3*, 2611-2613.

Figure A. ^{1}H NMR spectrum of **17** (600 MHz, acetone-d_6).

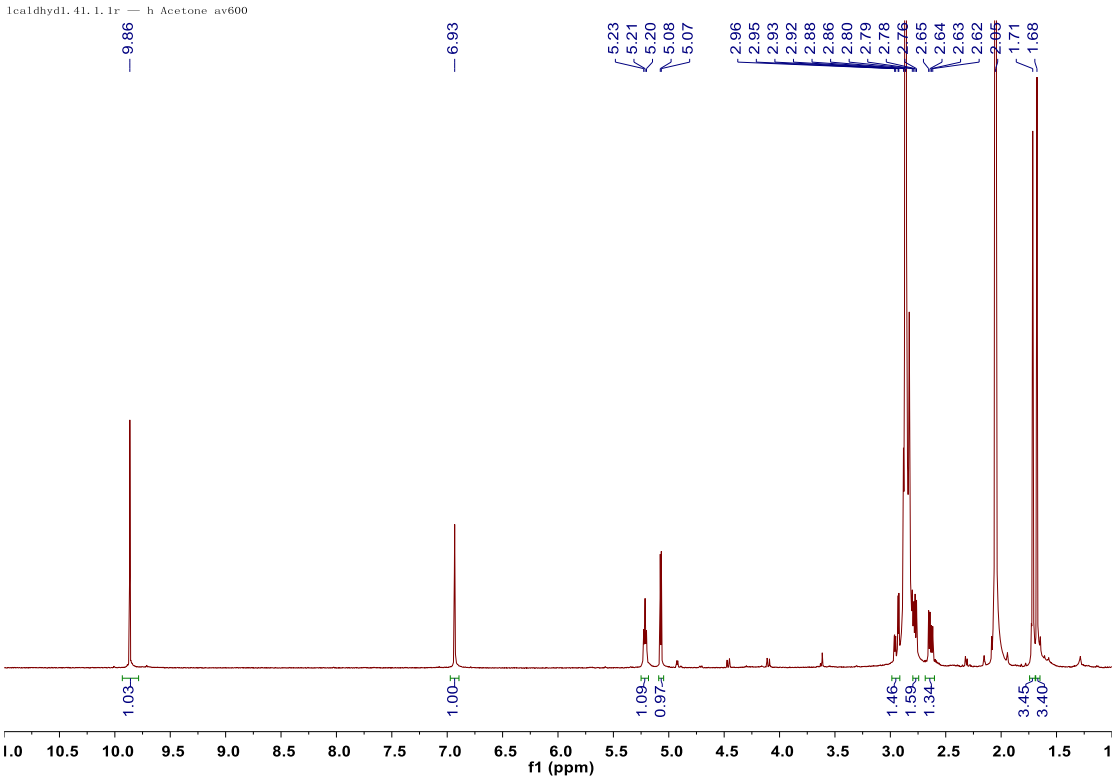


Figure B. ^{1}H NMR spectrum of **1a** (600 MHz, acetone-d_6)

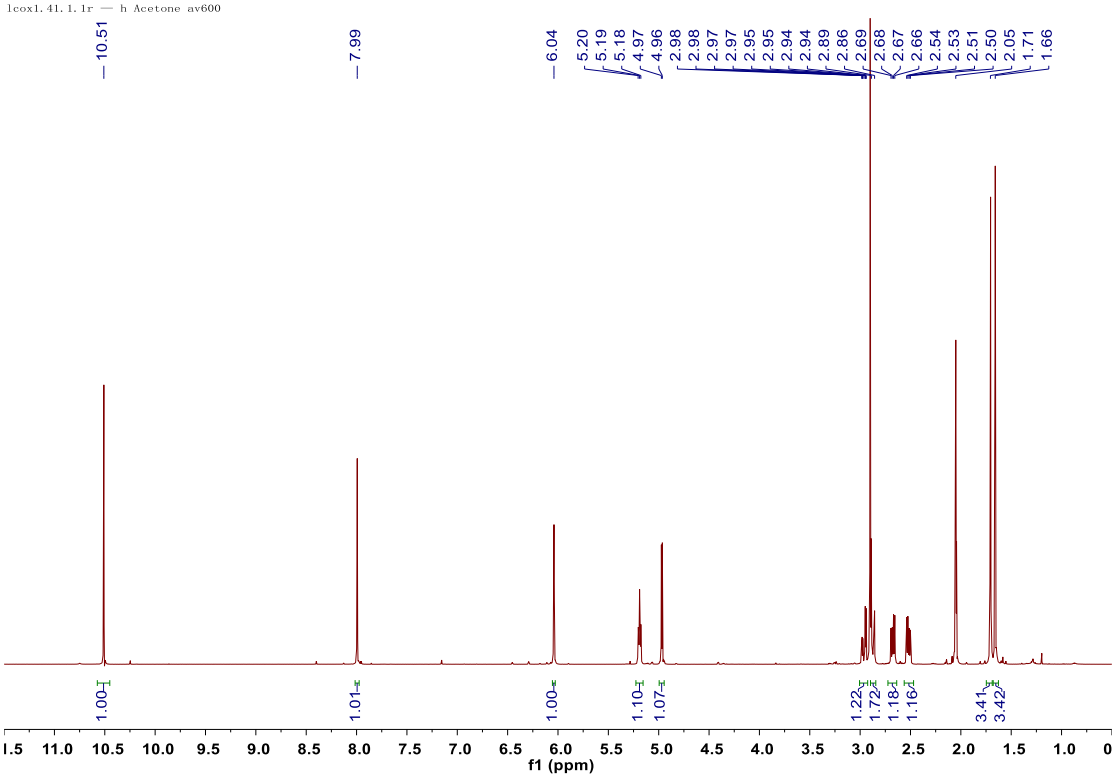
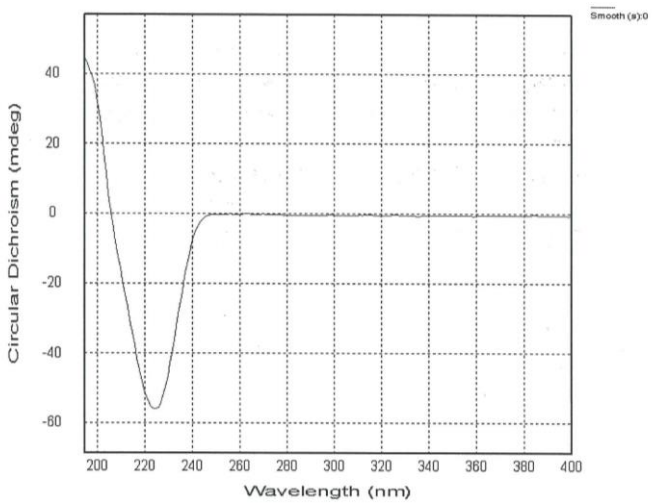
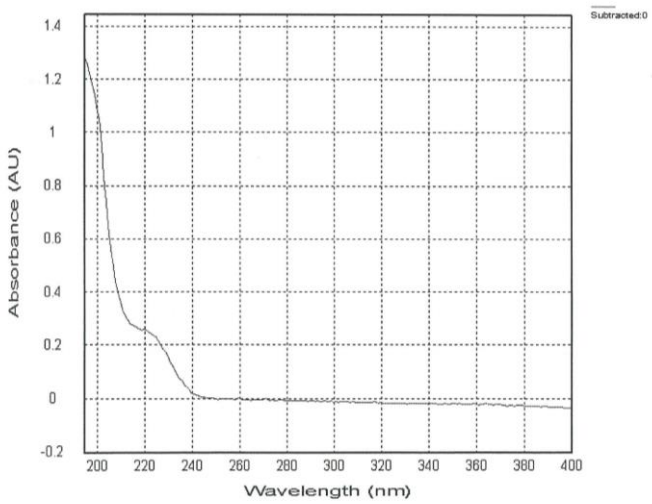


Figure C. The CD and UV spectra of vibralactone (solvent: MeCN).

LCVIB





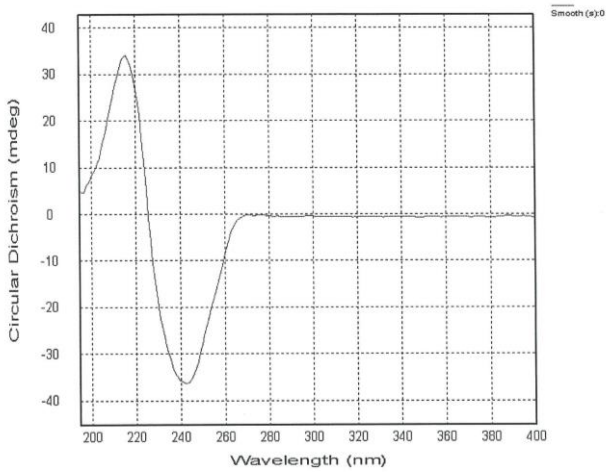
File: CD LCVIB-1mm(195-400)15112612.dsx
ProBinaryX
Attributes :
- Time Stamp :Thu Nov 26 17:09:58 2015

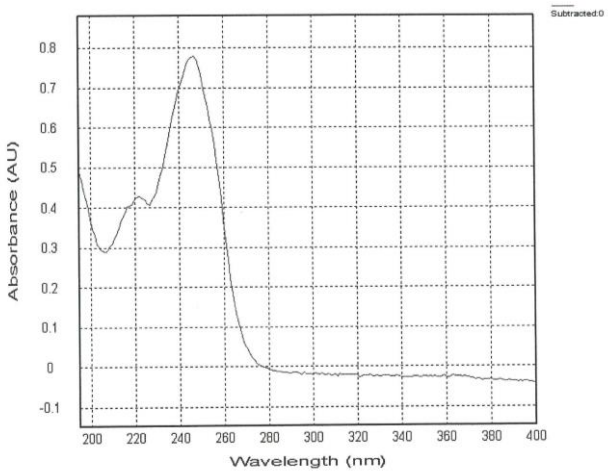
- File ID : {257931F1-1A3F-4bdb-9C09-1407AE93E278}
- Is CFR Compliant : false
- Original unaltered data
Remarks:
- HV (CDDC channel): 0 v
- Time per point: 1 s
- Description: Sample 1
- Concentration: 0.0960mg/mL Acetonitrile
- Pathlength: 1 mm

Settings:
- Time-per-point: 1s (25us x 40000)
- Wavelength: 195nm - 400nm
- Step Size: 1nm
- Bandwidth: 1nm

Figure D. The CD and UV spectra of 1 (solvent: MeCN).

LCBVB-3A1





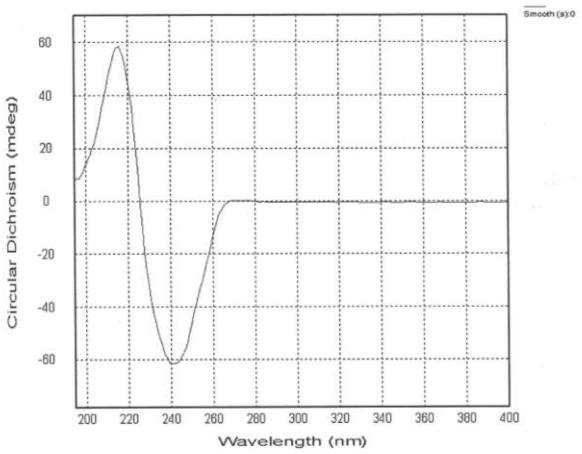
File: CD LCBVB-3A1-1mm(195-400)15112614.dsx
ProBinaryX
Attributes :
- Time Stamp :Thu Nov 26 17:42:25 2015

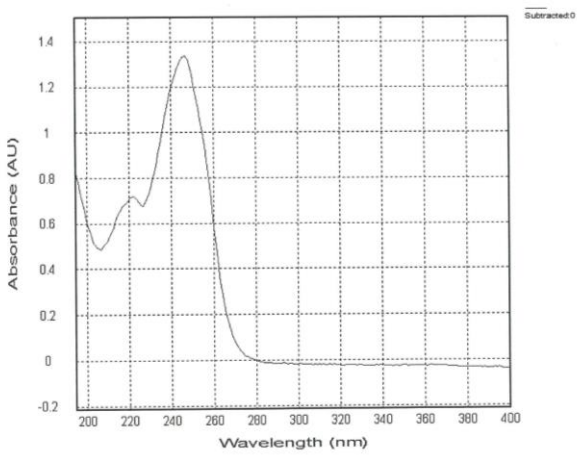
- File ID : {C095BDC9-0152-4636-892A-6F1935FC6F54}
- Is CFR Compliant : false
- Original unaltered data
Remarks:
  - HV (CDDC channel): 0 v
  - Time per point: 1 s
  - Description: Sample 1
  - Concentration: 0.0300mg/mL Acetonitrile
  - Pathlength: 1 mm

Settings:
  - Time-per-point: 1s (25us x 40000)
  - Wavelength: 195nm - 400nm
  - Step Size: 1nm
  - Bandwidth: 1nm

Figure E. The CD and UV spectra of synthesized 1a (solvent: MeCN).

LCOX-1





File: CD LCOX-1-1mm(195-400)15112613.dsx
ProBinaryX
Attributes :
- Time Stamp :Thu Nov 26 17:23:50 2015

- File ID : {6FFFC8A3-7792-4b78-A7CA-A33391B5F007}
- Is CFR Compliant : false
- Original unaltered data
Remarks:
  - HV (CDDC channel): 0 v
  - Time per point: 1 s
  - Description: Sample 1
  - Concentration: 0.1700mg/mL Acetonitrile
  - Pathlength: 1 mm

Settings:
  - Time-per-point: 1s (25us x 40000)
  - Wavelength: 195nm - 400nm
  - Step Size: 1nm
  - Bandwidth: 1nm

3. Representative HPLC spectra of some final compounds.

The HPLC profile were carried out on an agilent 1100 liquid chromatography system equipped with a Zorbax SB-C18 column (4.9 × 150 mm, particle size 5μm) and a DAD detector. Acetonitrile and water were used as the mobile phase. The method used to analyze these compounds was as follows:

Time	B% (Acetonitrile)	Flowrate (mL/min)
0	0	1
12	100	1
15	100	1
18	0	1

The detected wavelength of these compounds were at 247 and 205 nm.

Figure F. HPLC spectra of compound **1** (t_R = 8.71 min).

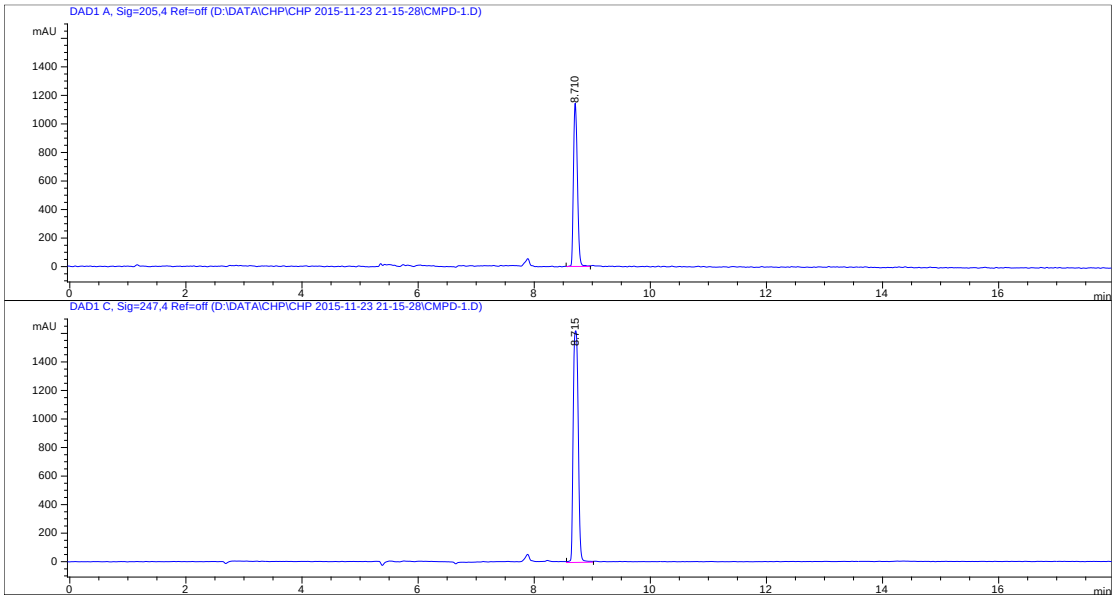


Figure G. HPLC spectra of compound **2** (t_R = 8.07 min).

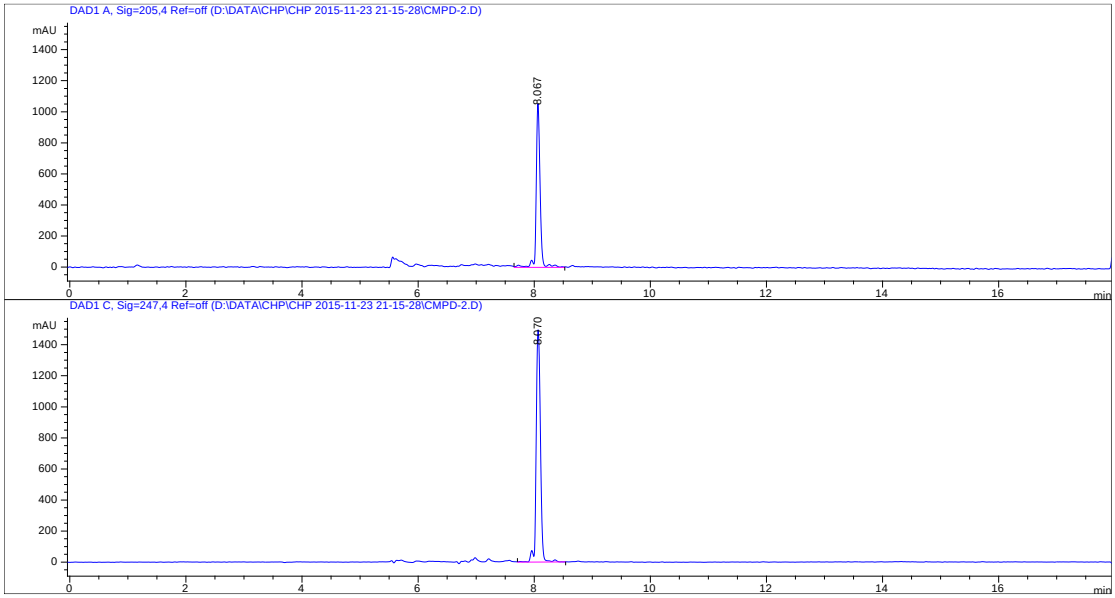


Figure H. HPLC spectra of compound **4** (t_R = 9.82 min).

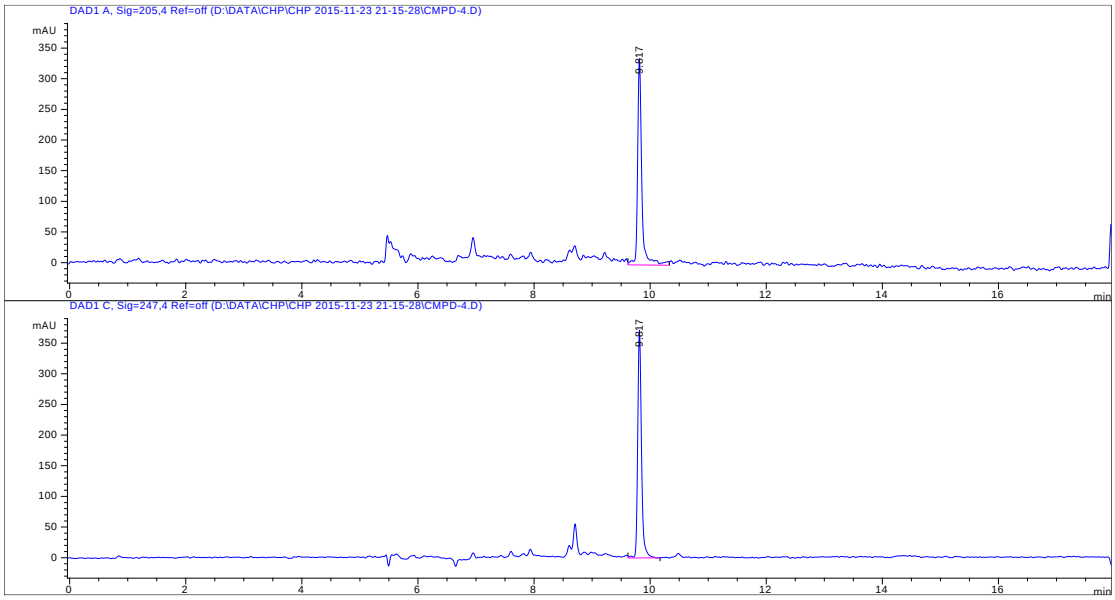


Figure I. HPLC spectra of compound **6** (t_R = 8.92 min).

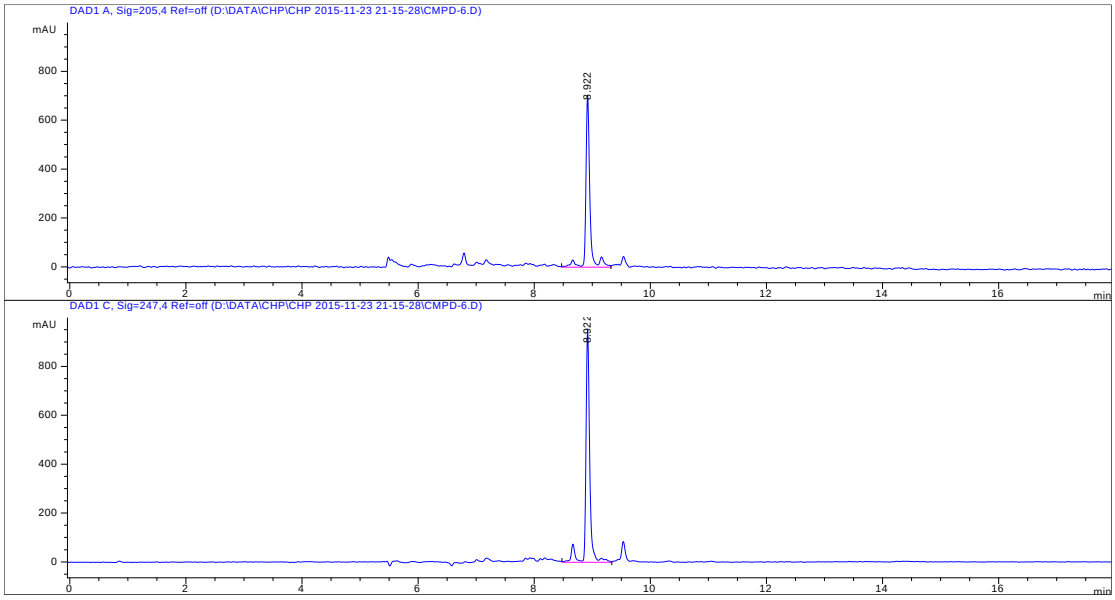


Figure J. HPLC spectra of compound **8** (t_R = 9.19 min).

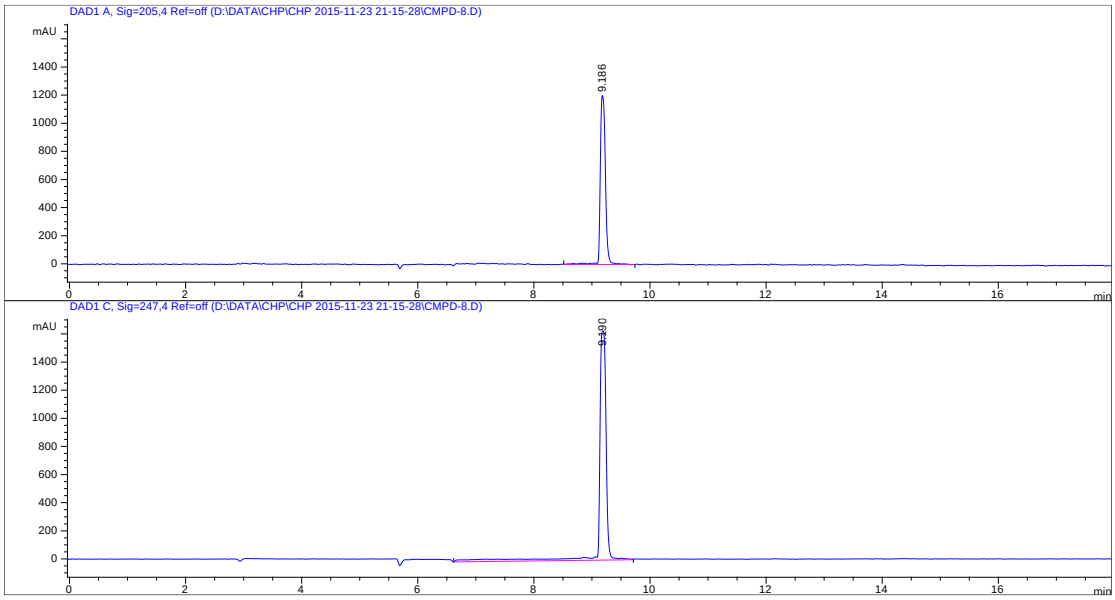
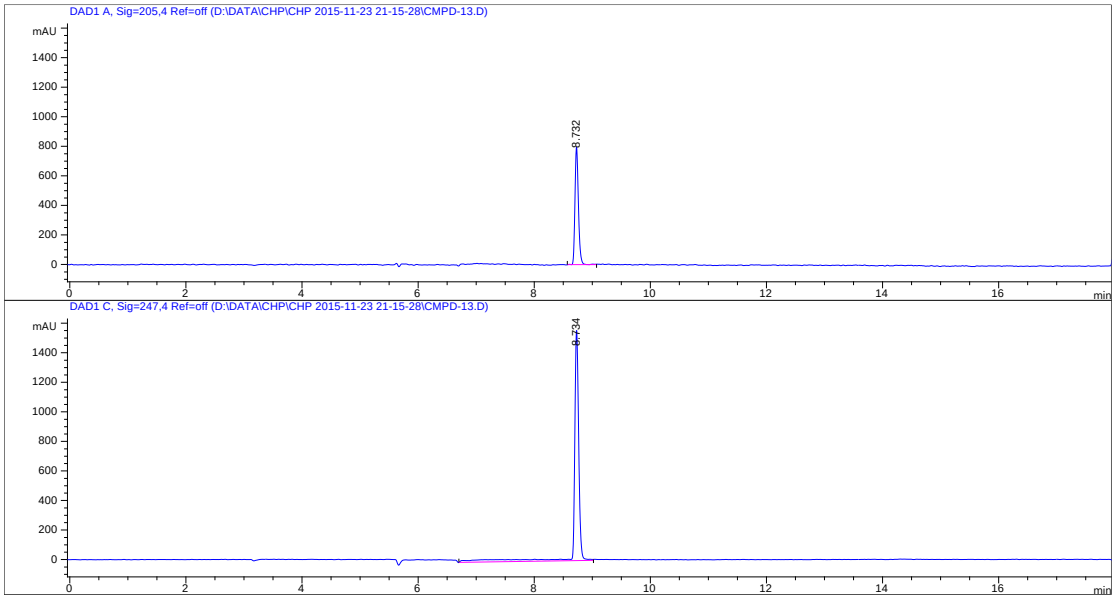
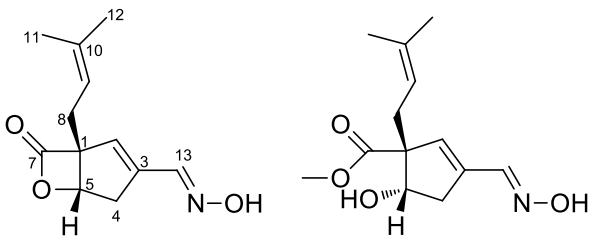


Figure K. HPLC spectra of compound **13** (t_R = 8.73 min).

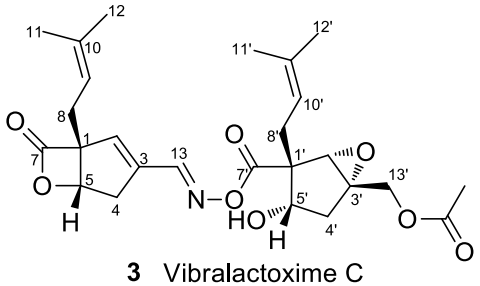




1 Vibralactoxime A **2** Vibralactoxime B

Table 1S. ^{1}H (600 MHz) and ^{13}C NMR (150 MHz) spectral data of **1** and **2** in acetone-d_6.

No.	**1**		**2**	
	δ_C, type	δ_H, multi.	δ_C, type	δ_H, multi.
1	76.5, s		66.7, s	
2	131.3, d	6.04, s	136.4, d	6.06, s
3	141.1, s		138.5, s	
4	36.7, t	2.88, d (19.2)	39.9, t	2.54, dd (17.0, 1.8)
		2.94, dd (19.2, 5.4)		2.84, overlapped
5	78.9, d	4.97, d (5.4)	78.5, d	4.27, ddd (6.0, 5.9, 1.8)
7	172.4, s		173.5, s	
8	28.0, t	2.52, dd (15.0, 7.4)	35.7, t	2.20, dd (13.9, 7.6)
		2.67, dd(15.0, 7.4)		2.62, dd (13.9, 7.6)
9	118.5, d	5.19, t (7.4)	120.4, d	5.06, t (7.6)
10	136.4, s		134.9, s	
11	18.0, q	1.66, s, 3H	17.9, q	1.57, s, 3H
12	25.9, q	1.70, s, 3H	26.0, q	1.66, s, 3H
13	146.5, d	7.99, s	147.3, d	7.93, s
7-OCH_3			51.6, s	3.63, s, 3H
N-OH		10.53, s,		10.20, s
5-OH				4.18, d (5.9)

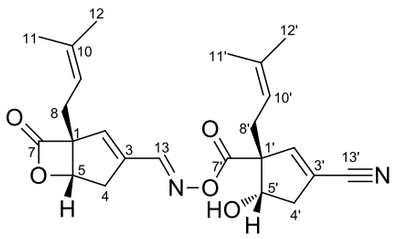


3 Vibralactoxime C

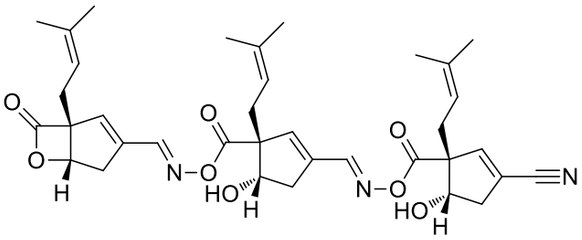
Table 2S. ^{1}H (600 MHz) and ^{13}C NMR (150 MHz) spectral data of **3** in acetone-d_6.

3					
No.	δ_C, type	δ_H, multi.	*No.*	δ_C, type	δ_H, multi.
1	77.1, s		1′	61.4, s	
2	138.9, d	6.48, s	2′	64.9, d	3.77, s
3	139.3, s		3′	65.3, s	
4	36.6, t	3.08, dd (18.4, 5.8) 2.99, d (18.4)	4′	37.2, t	2.44, dd (15.2, 6.1) 2.10, d (15.2)
5	79.1, d	5.08, d (5.8)	5′	76.8, d	3.95, dd (7.5, 6.1)
7	171.7, s		7′	168.7, s	
8	28.0, t	2.74, dd (14.8, 7.5) 2.60, overlapped	8′	32.8, t	2.60, overlapped 2.23, dd (14.3, 7.5)
9	118.4, d	5.20, br.t (7.5)	9′	118.8, d	5.16, br. t (7.5)
10	136.8, s		10′	136.4, s	
11	18.1, q	1.67, s, 3H	11′	18.1, q	1.63, s, 3H
12	26.1, q	1.71, s, 3H	12′	26.0, q	1.69, s, 3H
13	154.2, d	8.44, s	13′	64.0, t	4.49, d, (12.5) 4.20, d (12.5)
CH_3CO-	20.6, q	2.07, overlapped*			
CH_3CO-	170.8, s				
5′-OH		2.98, d (7.5)			

Note: * overlapped in solvent residual peaks.



4 Vibralactoxime D

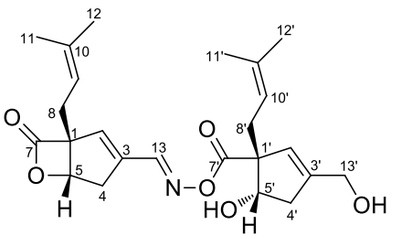


5 Vibralactoxime E

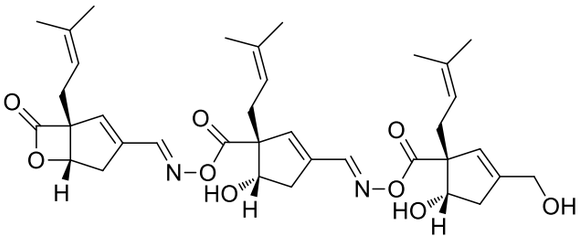
Table 3S. ^{1}H (600 MHz) and ^{13}C NMR (150 MHz) spectral data of **4** and **5** in acetone-d_6.

No.	**4**		**5**	
	δ_C, type	δ_H, multi.	δ_C, type	δ_H, multi.
1	77.0, s		77.0,s	
2	138.9, d	6.48, s	138.6,d	6.46,s
3	139.2, s		139.3,s	
4	36.5, t	3.08, dd (19.0, 5.7)	36.5,t	3.08,br.dd(18.7,5.8)
		2.97, d (19.0)		2.97,d (18.7)
5	79.0, d	5.07, d (5.6)	79.1,d	5.07,d (5.8)
7	171.6, s		171.6,s	
8	27.9, t	2.73, overlapped	27.9,t	2.72,overlapped
		2.59, overlapped		2.58,dd (15.5,7.5)
9	118.3, d	5.20, br. t (7.4)	118.3,d	5.20,br.t (7.5)
10	136.7, s		136.7,s	
11	18.0, q	1.67, s, 3H	18.1,q	1.67,s, 3H^a
12	25.9, q	1.71, s, 3H	25.9,q	1.71,s, 3H^b
13	154.3, d	8.45, s	154.0,d	8.42,s
1′	67.5, s		66.9,s	
2′	149.4, d	6.82, s	143.8,d	6.56,s
3′	115.0, s		137.2,s	
4′	43.3, t	3.11, dd (17.6, 5.8)	39.8,t	3.00,dd(17.0,6.0)
		2.61, dd (17.6, 1.7)		2.68,d(17.0)
5′	77.8, d	4.44, ddd (5.8, 5.7, 1.7)	78.6,d	4.45,br.t (6.0)
7′	168.2, s		168.3,s	
8′	34.8, t	2.74, overlapped	34.8,t	2.75,overlapped
		2.33, dd (14.2, 7.8)		2.34,dd (14.5, 7.5)
9′	119.0, d	5.11, br. t (7.8)	119.2,d	5.12,br.t (7.5)
10′	136.3, s		136.3,s	
11′	18.0, q	1.60, s, 3H	18.0,q	1.59,s, 3H^a
12′	26.0, q	1.68, s, 3H	26.0,q	1.69,s, 3H^b
13′	116.8, s		155.0,d	8.40,s
1″			67.4,s	
2″			149.5,d	6.83,s
3″			114.9,s	
4″			43.3,t	3.11,br.dd(16.4,6.0)
				2.62,d (16.4)
5″			77.9,d	4.43,br.t (6.0)
7″			169.1,s	
8″			35.3,t	2.76,dd(14.5,7.5)
				2.33,dd (14.5,7.5)
9″			119.7,d	5.12,br.t (7.5)
10″			135.7,s	
11″			18.0,q	1.61,s, 3H^a
12″			26.0,q	1.67,s, 3H^b
13″			116.8,s	
5′-OH		4.83, d (5.7)		4.61,d (6.0)
5″-OH				4.82,d (6.0)

Note: ^{a} Interchangable; ^{b} Interchangable



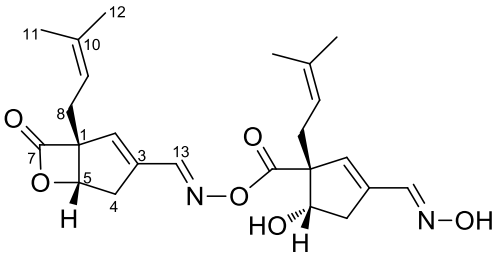
6 Vibralactoxime F



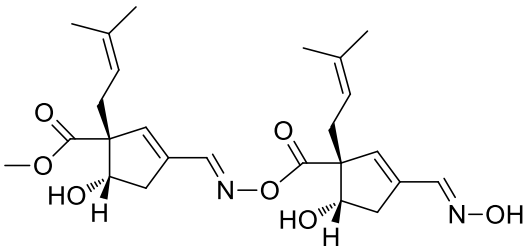
7 Vibralactoxime G

Table 4S. ^{1}H (600 MHz) and ^{13}C NMR (150 MHz) spectral data of **6** and **7** in acetone-d_6.

No.	**6**		**7**	
	δ_C, type	δ_H, multi.	δ_C, type	δ_H, multi.
1	77.0, s		77.0, s	
2	138.2, d	6.44, s	138.6, d	6.46, s
3	139.5, s		139.3, s	
4	36.5, t	3.07, br. dd (19.0, 5.6)	36.5, t	3.07, ddd (18.8, 5.5, 2.2)
		2.97, d (19.0)		2.97, d (18.2)
5	79.1, d	5.06, d (5.6)	79.1, d	5.07, d (5.6)
7	171.7, s		171.6, s	
8	27.9, t	2.72, overlapped	27.9, t	2.72,overlapped
		2.58, dd (15.0, 7.5)		2.58, dd (15.0, 7.3)
9	118.3, d	5.20, br. t (7.5)	118.3, d	5.20, br. t (7.5)
10	136.7, s		136.7, s	
11	18.0, q	1.66, s, 3H	18.1, q	1.67, s, 3H
12	25.9, q	1.71, s, 3H	26.1, q	1.71, s, 3H
13	153.7, d	8.38, s	154.0, d	8.42, s
1′	65.5, s		66.8, s	
2′	125.1, d	5.67, s	143.0, d	6.52, s
3′	146.1, s		137.5, s	
4′	41.6, t	2.72, overlapped	39.9, t	3.00, ddd (17.7, 6.5, 2.3)
		2.35, br. d (16.5)		2.68, d (17.7)
5′	79.1, d	4.29, br. t (6.5)	78.7, d	4.43, ddd (6.5, 6.0, 2.3)
7′	170.5, s		169.1, s	
8′	35.8, t	2.65, overlapped	35.3, t	2.75, dd (15.0, 7.2)
		2.21, dd (14.3, 8.0)		2.32, dd (15.0, 8.2)
9′	120.6, d	5.12, br. t (8.0)	119.8, d	5.15, br. t (7.5)
10′	134.7, s		134.6, s	
11′	18.1, q	1.58, s, 3H	18.1, q	1.59, s, 3H
12′	26.1, q	1.67, s, 3H	25.9, q	1.67, s, 3H
13′	61.7, t	4.14, dd (14.0, 5.5)	154.3, d	8.34, s
		4.10, dd (14.0, 5.5)		
1″			65.4, s	
2″			125.2, d	5.67, s
3″			146.0, s	
4″			41.6, t	2.72, overlapped
				2.37, d (16.0)
5″			79.2, d	4.29, ddd (6.2, 6.2, 3.0)
7″			170.6, s	
8″			35.7, t	2.65, dd (14.0, 7.0)
				2.22, dd (14.0, 8.0)
9″			120.7, d	5.14, br. t (7.5)
10″			135.6, s	
11″			18.0, q	1.59, s, 3H
12″			26.0, q	1.67, s, 3H
13″			61.7, t	4.12, dd (14.0, 5.5)
				4.13, dd (14.0, 5.5)
5′-OH		4.24, d (6.5)		4.59, d (6.0)
5″-OH				4.24, d (6.0)
13′-OH		3.91, t (5.5)		
13″-OH				3.91, t (5.5)



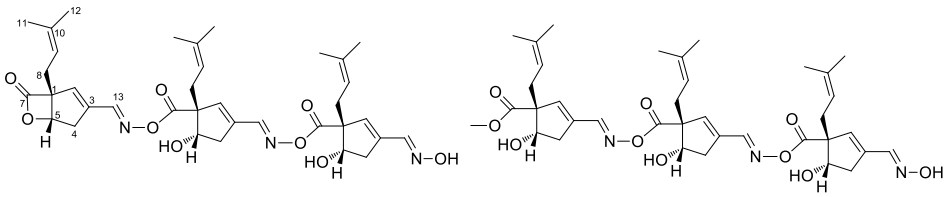
8 Vibralactoxime H



13 Vibralactoxime M

Table 5S. ^{1}H (600 MHz) and ^{13}C NMR (150 MHz) spectral data of **8** and **13** in acetone-d_6.

No.	**8**		**13**	
	δ_C, type	δ_H, multi.	δ_C, type	δ_H, multi.
1	77.0, s		67.2, s	
2	138.4, d	6.46, s	144.1, d	6.49, s
3	139.4, s		136.9, s	
4	36.5, t	3.07, br. dd (19.0, 5.6)	39.7, t	2.94, overlapped
		2.97, d (19.0)		2.61, overlapped
5	79.0, d	5.07, d (5.6)	78.5, d	4.34, overlapped
7	171.7, s		172.9, s	
8	27.9, t	2.72, overlapped	35.4, t	2.66,dd (14.0, 7.7)
		2.58, overlapped		2.25, dd (14.0, 7.7)
9	118.3, d	5.20, br. t (7.5)	120.0, d	5.06, br. t (7.5)
10	136.7, s		135.2, s	
11	18.1, q	1.67, s, 3H	18.1, q	1.58, s, 3H
12	26.0, q	1.71, s, 3H	26.0, q	1.66, s, 3H
13	153.8, d	8.40., s	154.6, d	8.33, s
1′	66.3, s		66.2, s	
2′	135.6, d	6.11, s	135.8, d	6.11, s
3′	139.1, s		139.0, s	
4′	40.1, t	2.90, overlapped	40.1, t	2.89, overlapped
		2.60, overlapped		2.61, overlapped
5′	78.7, d	4.36, ddd (6.0, 6.0, 2.7)	78.7, d	4.35, overlapped
7′	169.6, s		169.7, s	
8′	35.6, t	2.72, overlapped	35.6, t	2.71, dd (14.0, 7.6)
		2.27, dd (14.0, 8.0)		2.27, dd (14.0, 7.6)
9′	120.1, d	5.12, br. t (7.5)	120.2, d	5.13, br. t (7.6)
10′	135.3, s		135.2, s	
11′	18.0, q	1.58, s, 3H	17.9, q	1.59, s, 3H
12′	25.9, q	1.66, s, 3H	26.0, q	1.67, s, 3H
13′	147.2, d	7.95, s	147.2, d	7.96, s
N-OH		10.26, s		10.26, s
5-OH				4.36, overlapped
5′-OH		4.42, d (6.0)		4.41, d (6.0)
7-OCH_3			51.8, q	3.64, s 3H

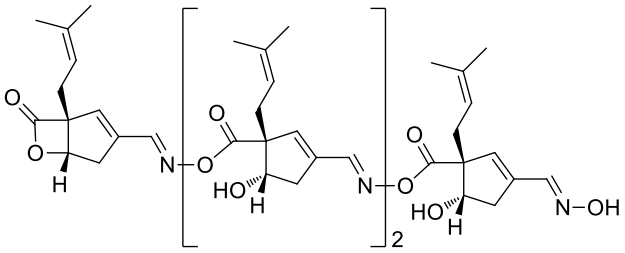


9 Vibralactoxime I **14** Vibralactoxime N

Table 6S. ^{1}H (600 MHz) and ^{13}C NMR (150 MHz) spectral data of **9** and **14** in acetone-d_6.

No.	**9**		**14**	
	δ_C, type	δ_H, multi.	δ_C, type	δ_H, multi.
1	77.0, s		67.3, s	
2	138.6, d	6.46, s	144.3, d	6.49, s
3	139.3, s		136.8, s	
4	36.5, t	3.07, dd (19.1, 5.6)	39.7, t	2.94, dd (17.0, 5.2)
		2.97, d (19.2)		2.62, d (17.0)
5	79.1, d	5.07, d (5.6)	78.4, d	4.34, overlapped
7	171.6, s		172.9, s	
8	27.9, t	2.58, overlapped	35.4, t	2.66, overlapped
		2.72, overlapped		2.25, dd (14, 8.0)
9	118.3, d	5.20, t (7.5)	120.0, d	5.06, t (7.5)
10	136.7, s		135.2, s	
11	18.1, q	1.66, s, 3H	18.0, q	1.57, s, 3H
12	26.0, q	1.71, s, 3H	26.1, q	1.65, s, 3H
13	154.0, d	8.42, s	154.6, d	8.35, s
1′	66.8, s		66.7, s	
2′	143.3, d	6.54, s	143.5, d	6.54, s
3′	137.4, s		137.3, s	
4′	39.8, t	3.00, dd (16.0, 6.0)	39.8, t,	2.99, dd (16.7, 6.0)
		2.68, overlapped		2.67, overlapped
5′	78.7, d	4.43, ddd (6.0, 6.0, 2.3)	78.6, d	4.42, overlapped
7′	169.1, s		169.2, s	
8′	35.3, t	2.75, overlapped	35.3, t	2.75, dd (14.0, 7.0)
		2.32, dd (14.2, 8.0)		2.30, overlapped
9′	119.8, d	5.12, t (7.5)	120.2, d	5.13, t (7.5)
10′	135.6, s		135.5, s	
11′	18.0, q	1.59, s, 3H	18.1, q	1.59, s, 3H
12′	26.0, q	1.67, s, 3H	26.1, q	1.67, s, 3H
13′	154.5, d	8.35, s	154.8, d	8.36, s
1″	66.2, s		66.2, s	
2″	135.7, d	6.12, s	135.7, d	6.12, s
3″	139.0, s		139.0, s	
4″	40.1, t	2.90, overlapped	40.1, t	2.91, overlapped
		2.61, overlapped		2.62, overlapped
5″	78.7, d	4.36, ddd (6.0, 6.0, 2.8)	78.7, d	4.35, overlapped

7″	169.7, s		169.7, s	
8″	35.6, t	2.72, overlapped	35.6, t	2.73, overlapped
		2.28, dd (14.2, 8.1)		2.27, overlapped
9″	120.2, d	5.13, t (7.5)	119.9, d	5.13, t (7.5)
10″	135.2, s		135.2, s	
11″	18.1, q	1.59, s, 3H	18.1, q	1.59, s, 3H
12″	25.9, q	1.66, s, 3H	26.0, q	1.67, s, 3H
13″	147.2, d	7.96, s	147.1, d	7.96, s
5-OH				4.42, d (6.0)
5′-OH		4.60, d (6.0)		4.57, d (6.0)
5″-OH		4.42, d (6.0)		unobserved
N-OH		10.25, s		10.26, s
$-OCH_3$			51.8, q	3.64, s, 3H



10 Vibralactoxime J

Table 7S. ^{1}H (600 MHz) and ^{13}C NMR (150 MHz) spectral data of **10** in acetone-d_6.

No.	δ_C, type	δ_H, multi.	No.	δ_C, type	δ_H, multi.
1	77.0, s		1″	66.7, s	
2	138.6, d	6.46, s	2″	143.5, d	6.54, s
3	139.3, s		3″	137.4, s	
4	36.5, t	3.07, dd (19.0, 6.0)	4″	39.8, t	3.00, overlapped
		2.97, d (19.0)			2.69, dd (17.0, 10.0)
5	79.0, d	5.07, d (5.6)	5″	78.7, d	4.43, overlapped
7	171.6, s		7″	169.2, s	
8	27.9, t	2.72, overlapped	8″	35.3, t	2.76, overlapped
		2.58, dd (15.0, 7.4)			2.33, dd (14.5, 7.8)
9	118.3, d	5.20, t (7.5)	9″	119.9, d	5.13, t (7.5)
10	136.7, s		10″	135.6, s	
11	18.0, q	1.59, s, 3H	11″	18.1, q	1.60, s, 3H
12	25.9, q	1.71, s, 3H	12″	26.1, q	1.66, s, 3H
13	154.0, d	8.42, s	13″	154.6, d	8.36, s
1′	66.8, s		1‴	66.2, s	
2′	143.4, d	6.54, s	2‴	135.7, d	6.12, s
3′	137.4, s		3‴	139.0, s	
4′	39.8, t	3.00, overlapped	4‴	40.1, t	2.90, overlapped
		2.69, dd (17.0, 10.0)			2.61, d (16.2)
5′	78.7, d	4.43, overlapped	5‴	78.6, d	4.36, ddd (6.0, 6.0, 2.5)
7′	169.1, s		7‴	169.7, s	
8′	35.3, t	2.76, overlapped	8‴	35.6, t	2.74, overlapped
		2.33, dd (14.5, 7.8)			2.28, dd (14.8, 8.2)
9′	119.8, d	5.13, t (7.5)	9‴	120.2, d	5.12, t (7.5)
10′	135.6, s		10‴	135.2, s	
11′	18.1, q	1.60, s, 3H	11‴	18.1, q	1.67, s, 3H
12′	26.1, q	26.1, s, 3H	12‴	26.1, q	1.67, s, 3H
13′	154.7, d	8.37, s	13‴	147.2, d	7.96, s
5′-OH		4.60, d (5.5)	5″-OH		4.60, d (5.5)
5‴-OH		4.43, overlapped	N-OH		10.27, s

Table 8S. Characteristic ^{1}H NMR (600 MHz) spectral data of **11**, **12**, **15** and **16** in acetone-d_6.

No.	**11**	**12**	**15**	**16**
H-2 of head unit	6.46, s	6.47, s	6.49, s	6.49, s
H-9 of head unit	5.20, t (7.5)	5.19, t (7.5)	5.06, t (7.5)	5.06, t (7.5)
H-13 of head unit	8.41, s	8.42, s	8.35, s	8.35, s
H-2 of tail unit	6.12, s	6.12, s	6.12, s	6.12, s
H-9 of tail unit	5.12, t (7.5)	5.12, t (7.5)	5.13, t (7.5)	5.12, t (7.5)
H-13 of tail unit	7.96, s	7.96, s	7.96, s	7.96, s
H-2 of the other unit	6.54, each s, totally 3H, overlapped	6.56, each s, totally 4H, overlapped	6.55, each s, totally 2H, overlapped	6.55, each s, totally 3H, overlapped
H-9 of the other unit	5.13, t (7.5), totally 3H, overlapped	5.13, t (7.5), totally 4H, overlapped	5.14, t (7.5), totally 2H, overlapped	5.13, t (7.5), totally 3H, overlapped
H-13 of the other unit	8.36, each s, totally 3H, overlapped	8.36, s 8.37, s 8.38, each s, totally 2H, overlapped	8.36, s 8.37, s	8.36, s 8.37, s 8.38, s
N-OH	10.23, s	10.28, s	10.23, s	10.27, s
OCH_3			3.85, s, 3H	3.84, s, 3H

4. Supplementary NMR spectra.

Figure 1S: ^{1}H NMR spectrum of **1** (acetone-d_6, 600MHz)

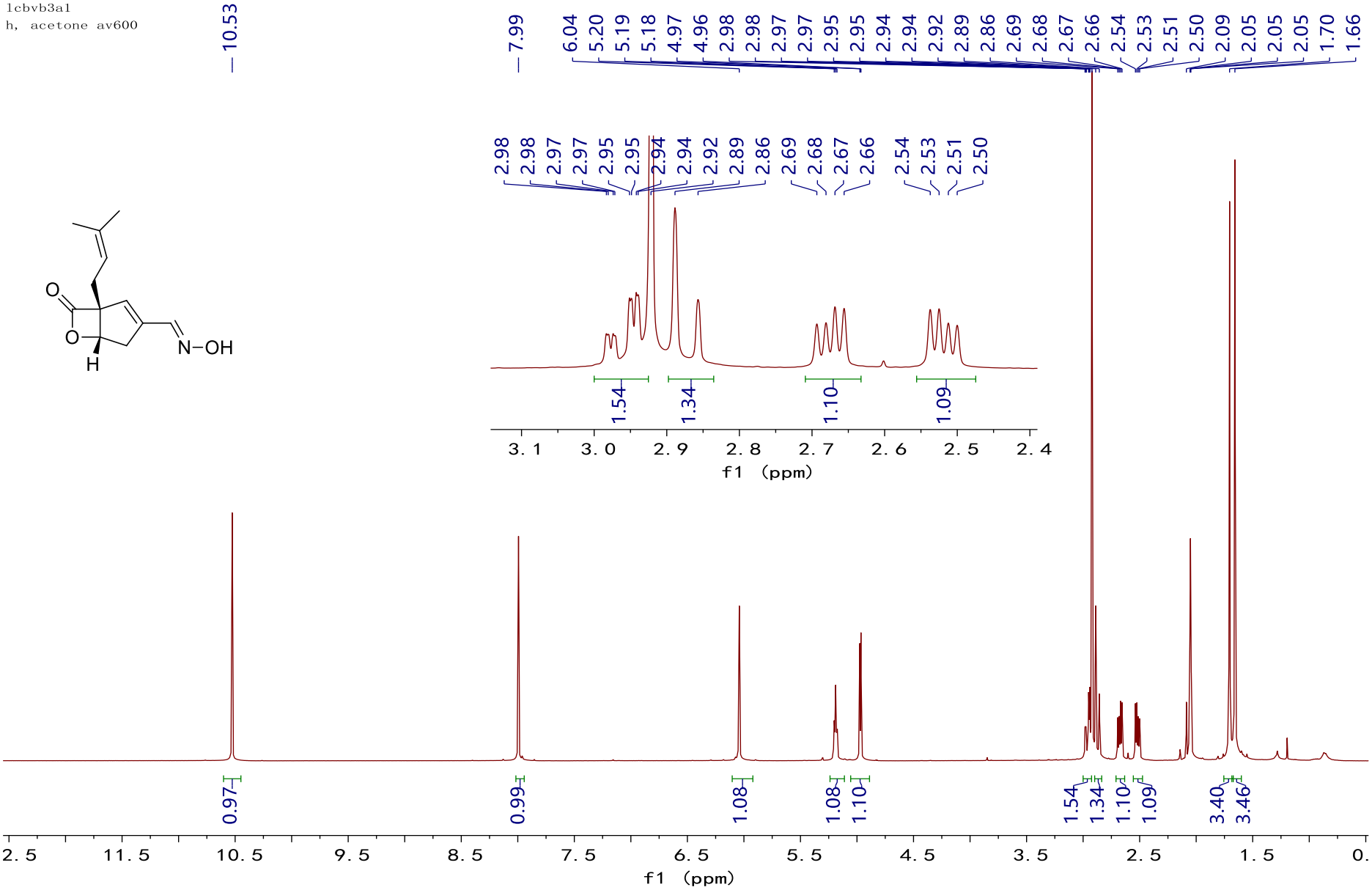


Figure 2S: ^{13}C NMR and DEPT spectra of **1** (acetone-d_6, 150MHz)

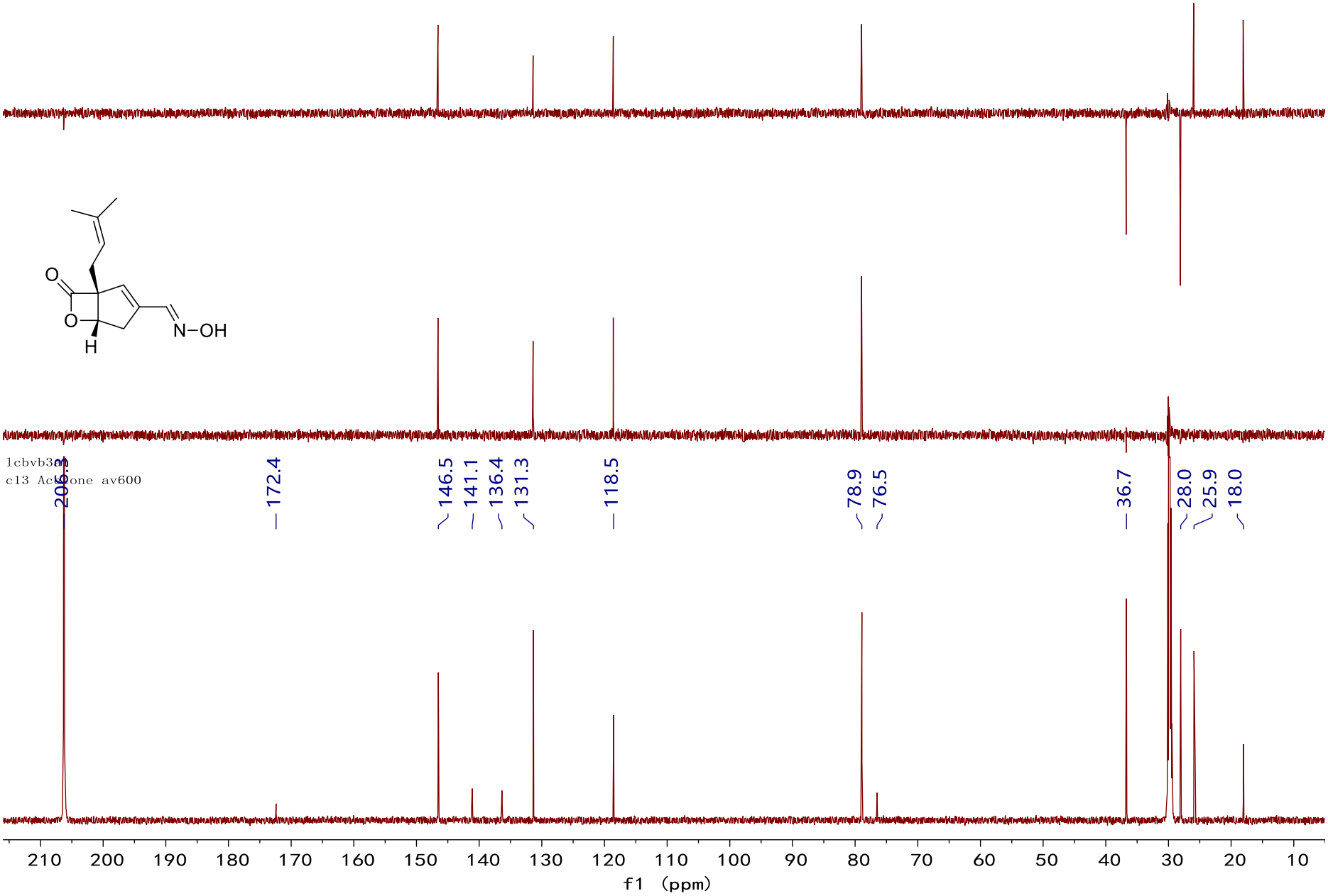


Figure 3S: HSQC spectrum of **1**.

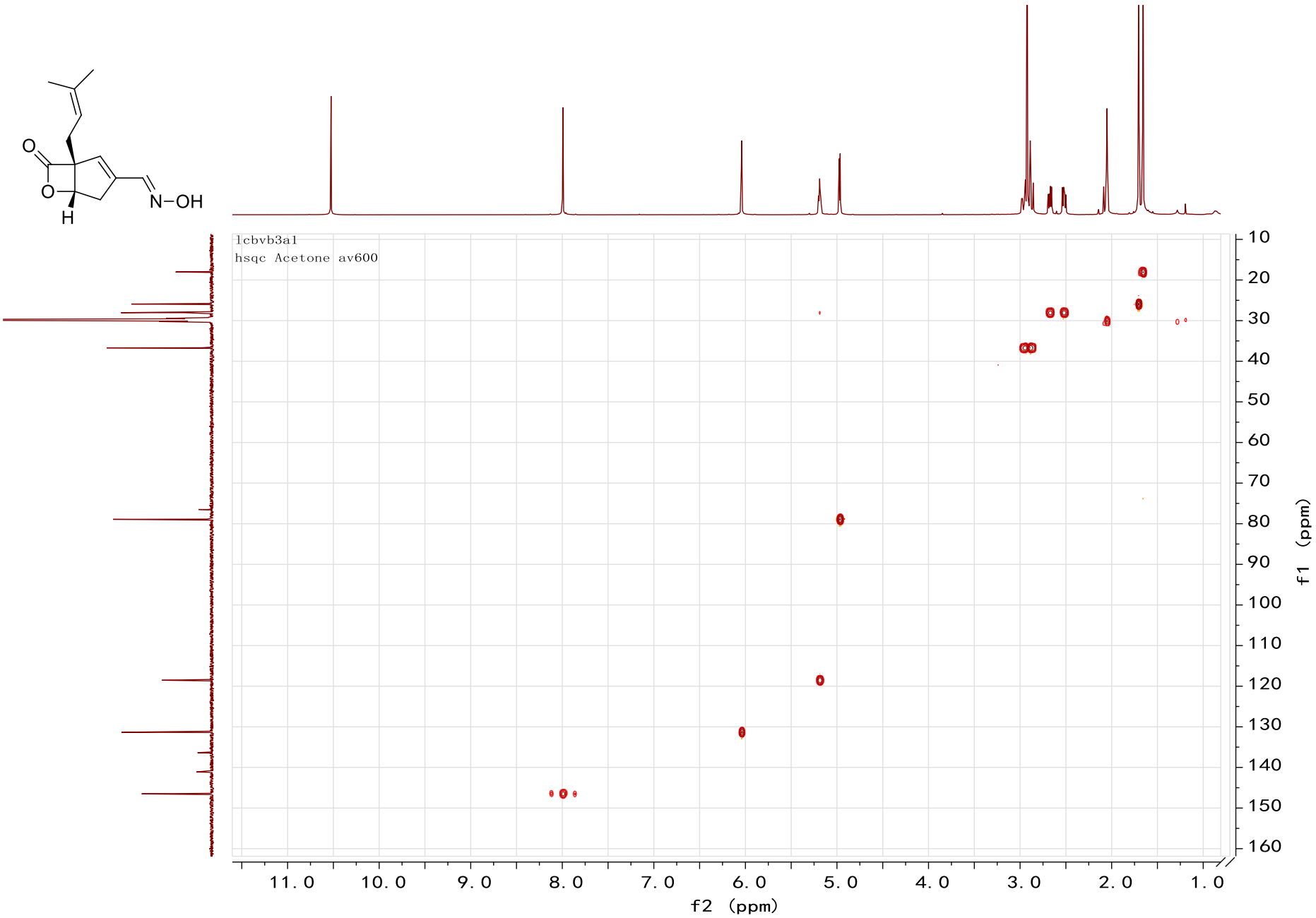


Figure 4S: ^{1}H-^{1}H COSYspectrum of **1**.

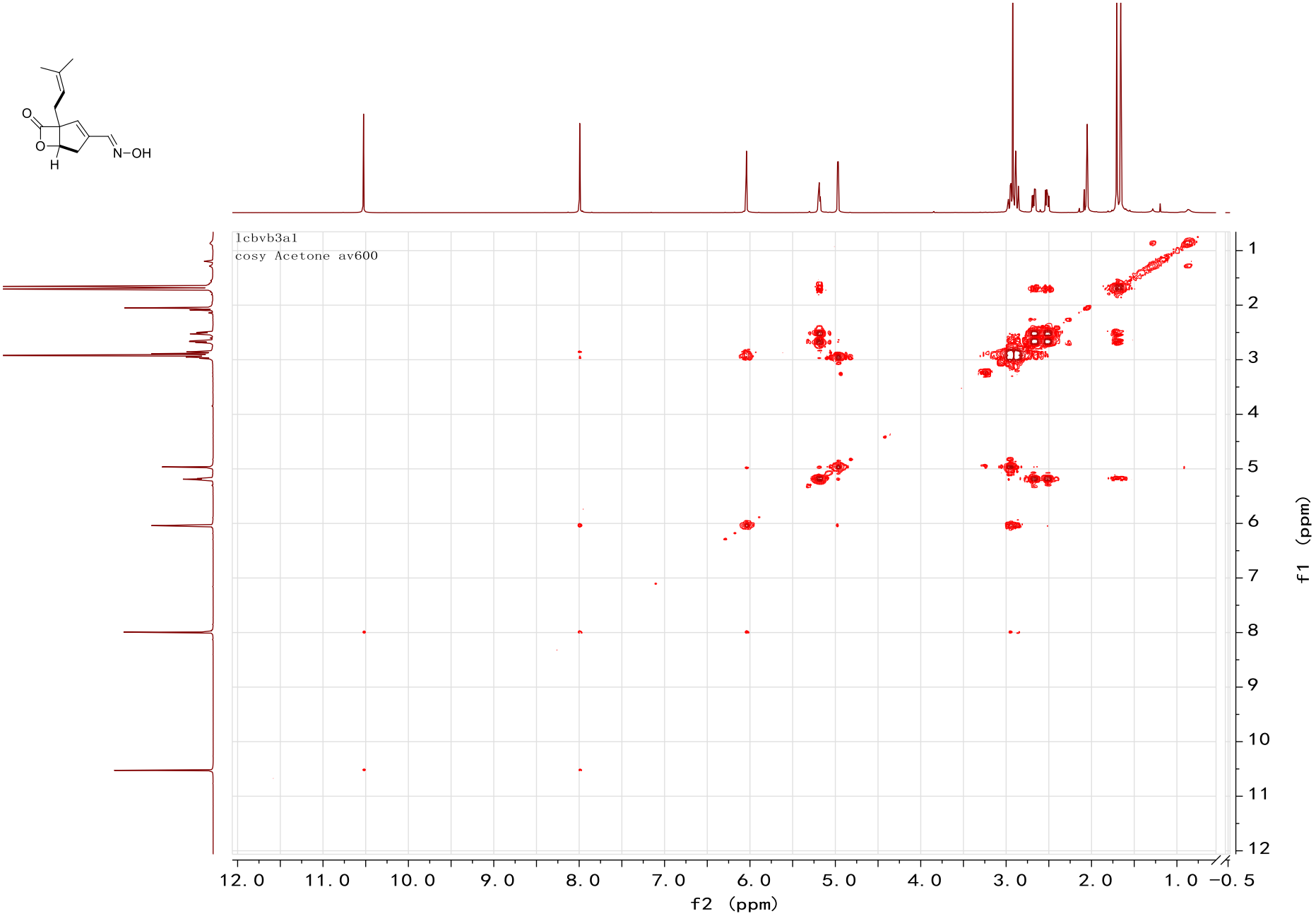


Figure 5S: HMBC spectrum of **1**.

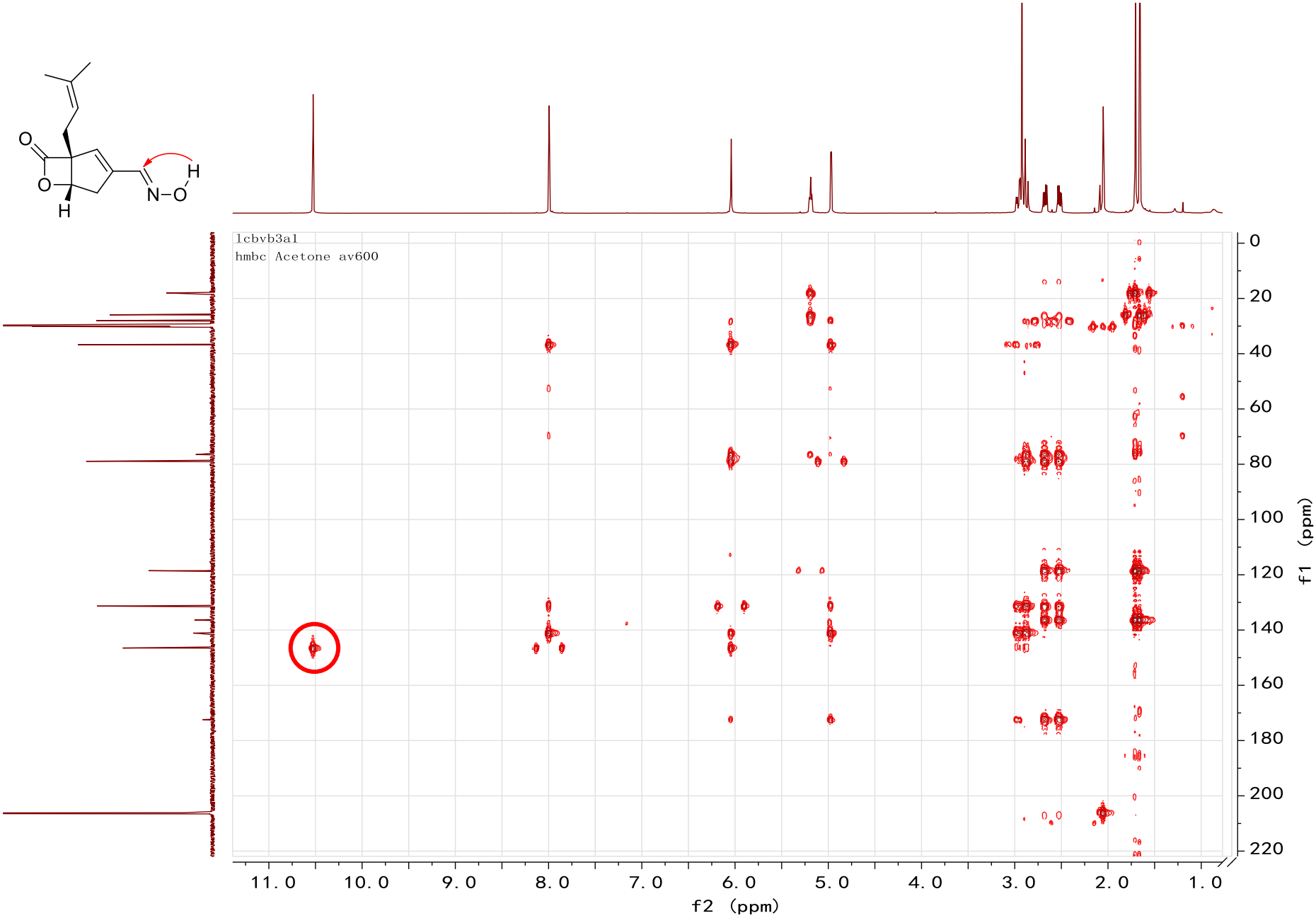


Figure 6S: ROESY spectrum of **1**.

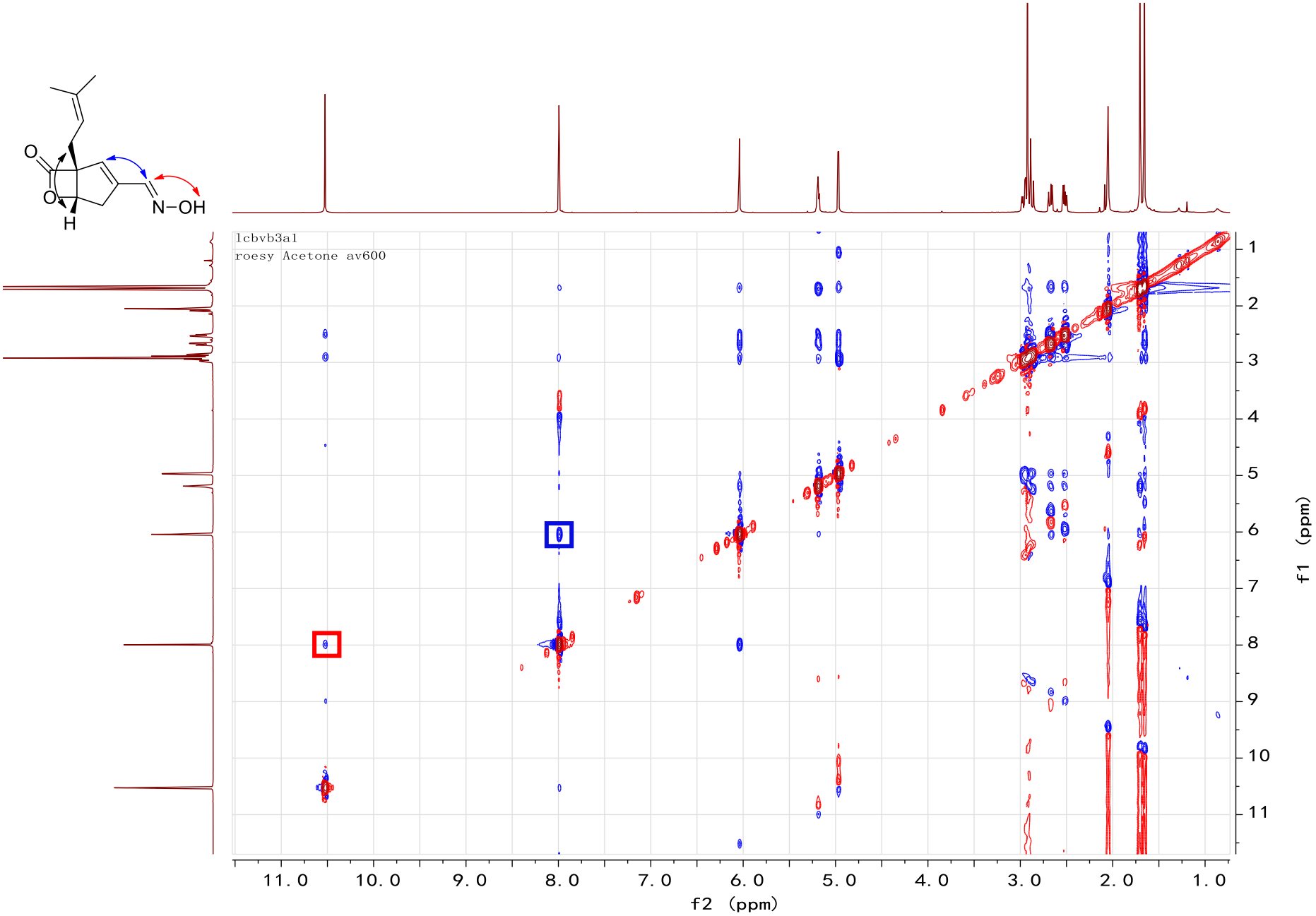


Figure 7S: HREIMS spectrum of **1**.

Elemental Composition Report

Page 1

Single Mass Analysis

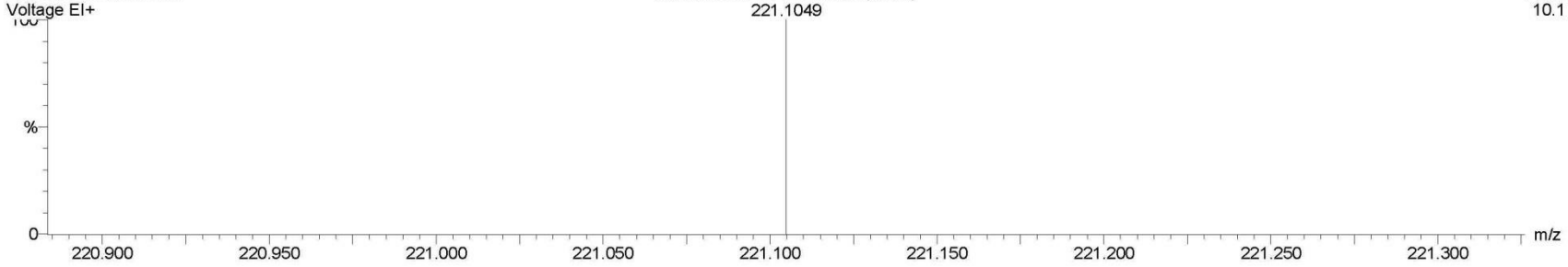
Tolerance = 10.0 PPM / DBE: min = -10.0, max = 120.0
Selected filters: None

Monoisotopic Mass, Odd and Even Electron Ions
12 formula(e) evaluated with 1 results within limits (up to 51 closest results for each mass)
Elements Used:
C: 0-200 H: 0-400 N: 1-1 O: 2-4

Icbvb-3a1
09:38:12 20-Nov-2013
Voltage EI+

KIB
M131120EA-03AFAMM 15 (1.378)
221.1049

Autospec Premier
P776
10.1



Minimum:				-10.0		
Maximum:		200.0	10.0	120.0		
Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	Formula
221.1049	221.1052	-0.3	-1.4	6.0	5546025.5	C12 H15 N O3

Figure 8S: Optical rotation of compound **1**.

Optical rotation measurement

Model : P-1020 (A060460638)

No.	Sample	Mode	Data	Monitor Blank	Temp. Cell Temp Point	Date Comment Sample Name	Light Filter Operator	Cycle Time Integ Time
No.1	2 (1/3)	Sp.Rot	-192.6320	-0.1830 0.0000	22.9 50.00 Cell	Thu Mar 12 14:38:40 2015 0.00190g/mL Acetonitrile LCBVB-3A1	Na 589nm	2 sec 10 sec
No.2	2 (2/3)	Sp.Rot	-193.3680	-0.1837 0.0000	22.8 50.00 Cell	Thu Mar 12 14:38:53 2015 0.00190g/mL Acetonitrile LCBVB-3A1	Na 589nm	2 sec 10 sec
No.3	2 (3/3)	Sp.Rot	-190.8420	-0.1813 0.0000	22.8 50.00 Cell	Thu Mar 12 14:39:07 2015 0.00190g/mL Acetonitrile LCBVB-3A1	Na 589nm	2 sec 10 sec

$-192.380)^{\circ}$

Figure 9S: ^{1}H NMR spectrum of **2** (acetone-d_6, 600MHz)

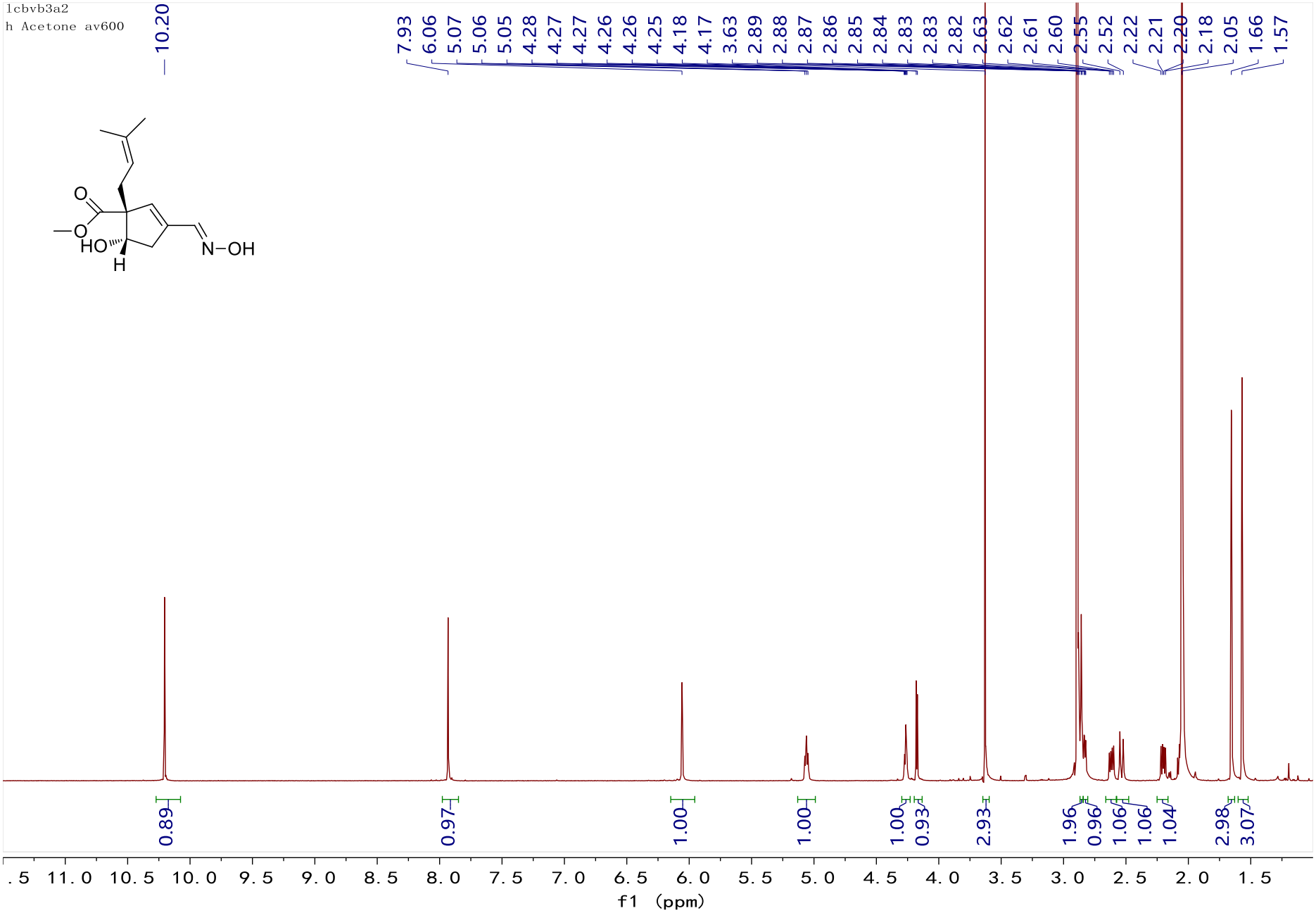


Figure 10S: ^{13}C NMR and DEPT spectra of **2** (acetone-d_6, 150MHz).

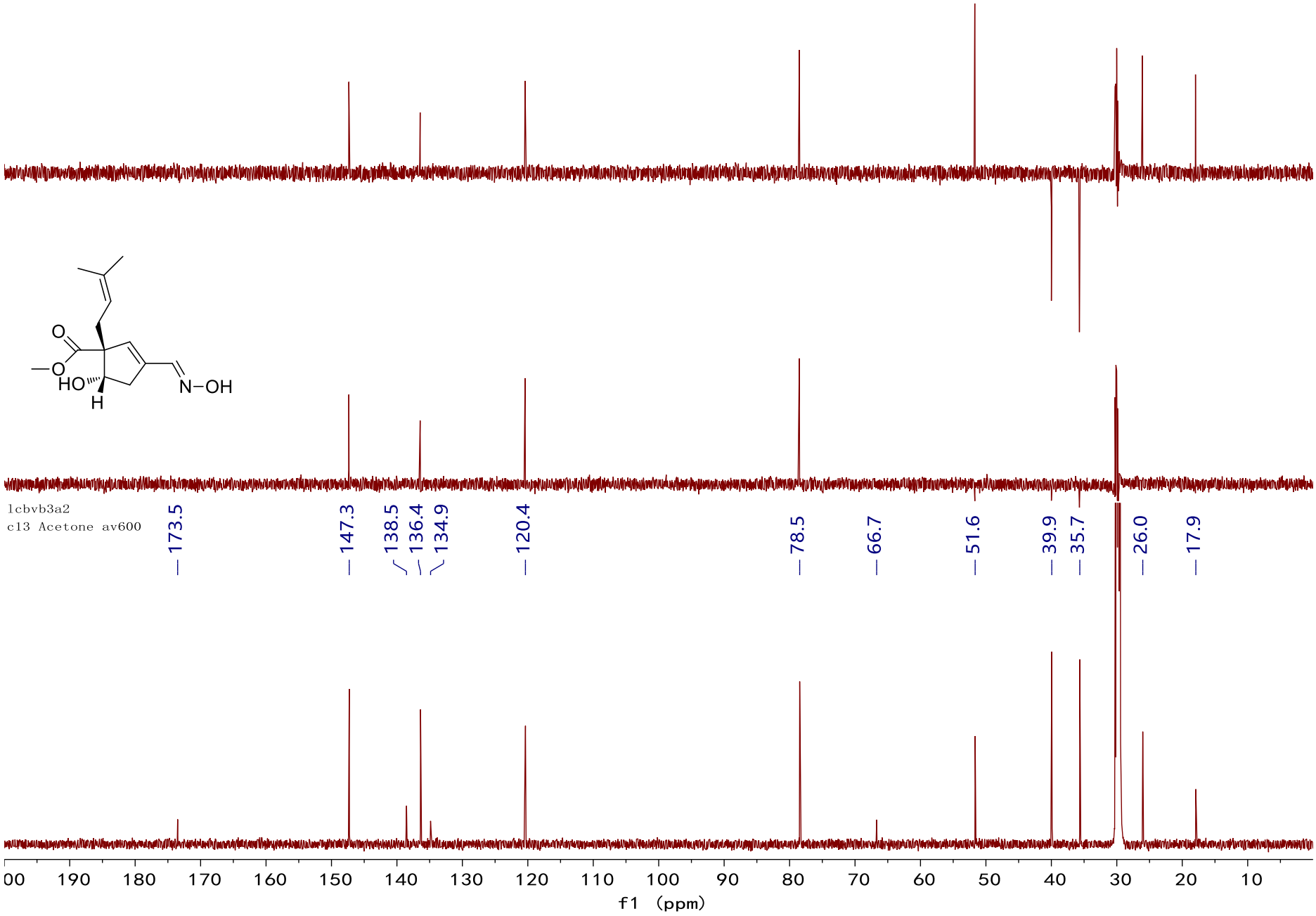


Figure 11S: HSQC spectrum of **2**.

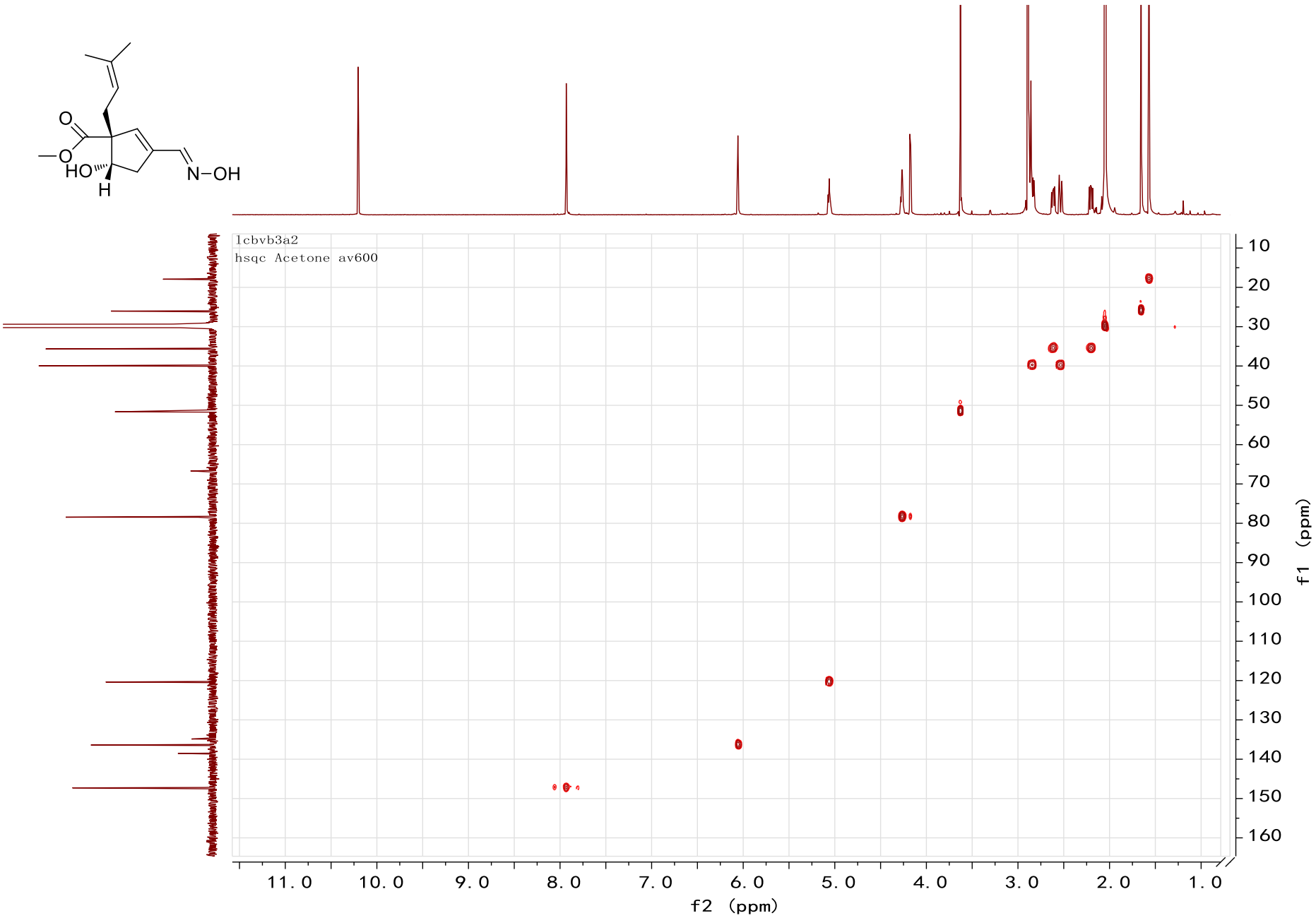


Figure 12S: ^{1}H-^{1}H COSY spectrum of **2**.

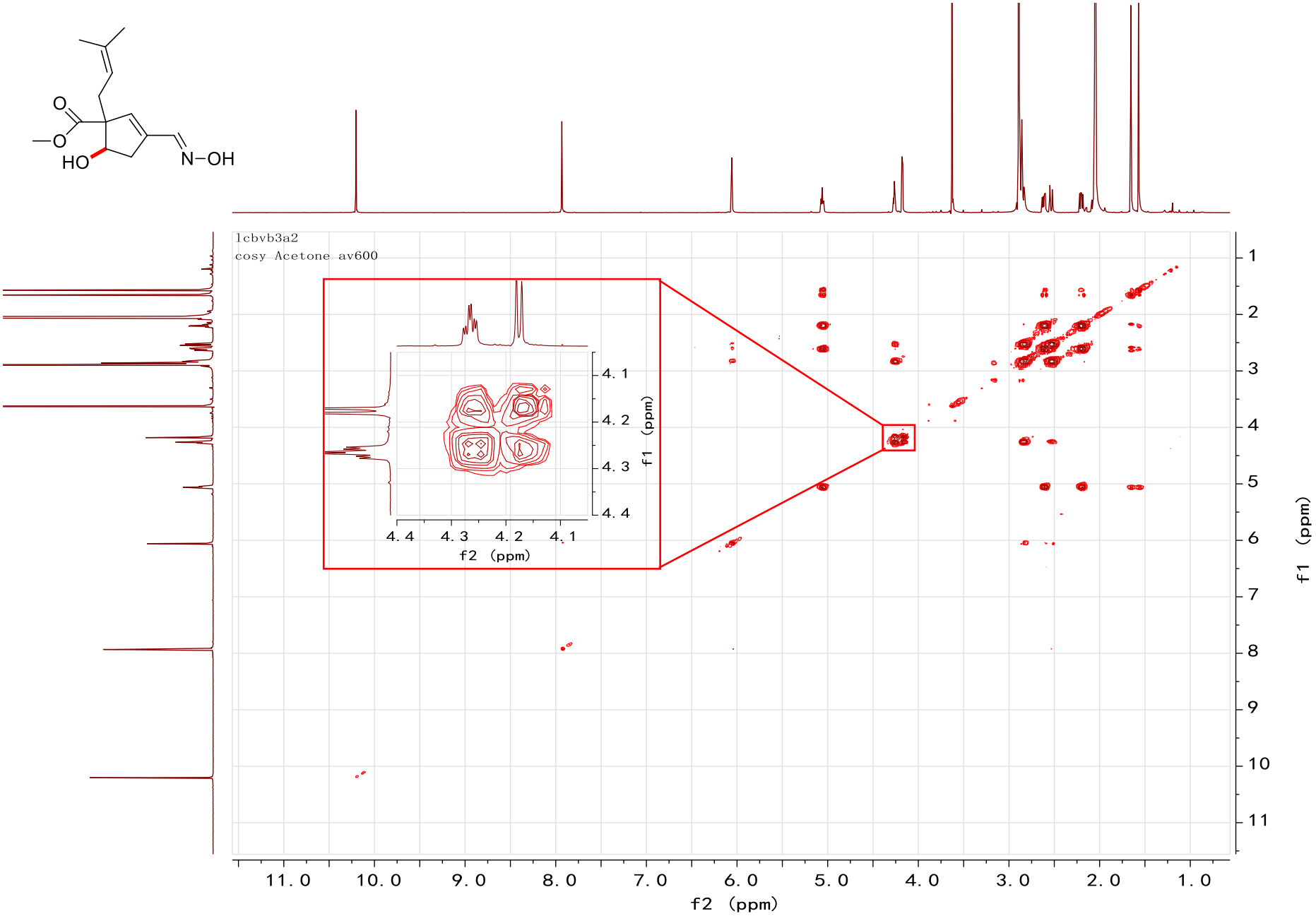


Figure 13S: HMBC spectrum of **2**.

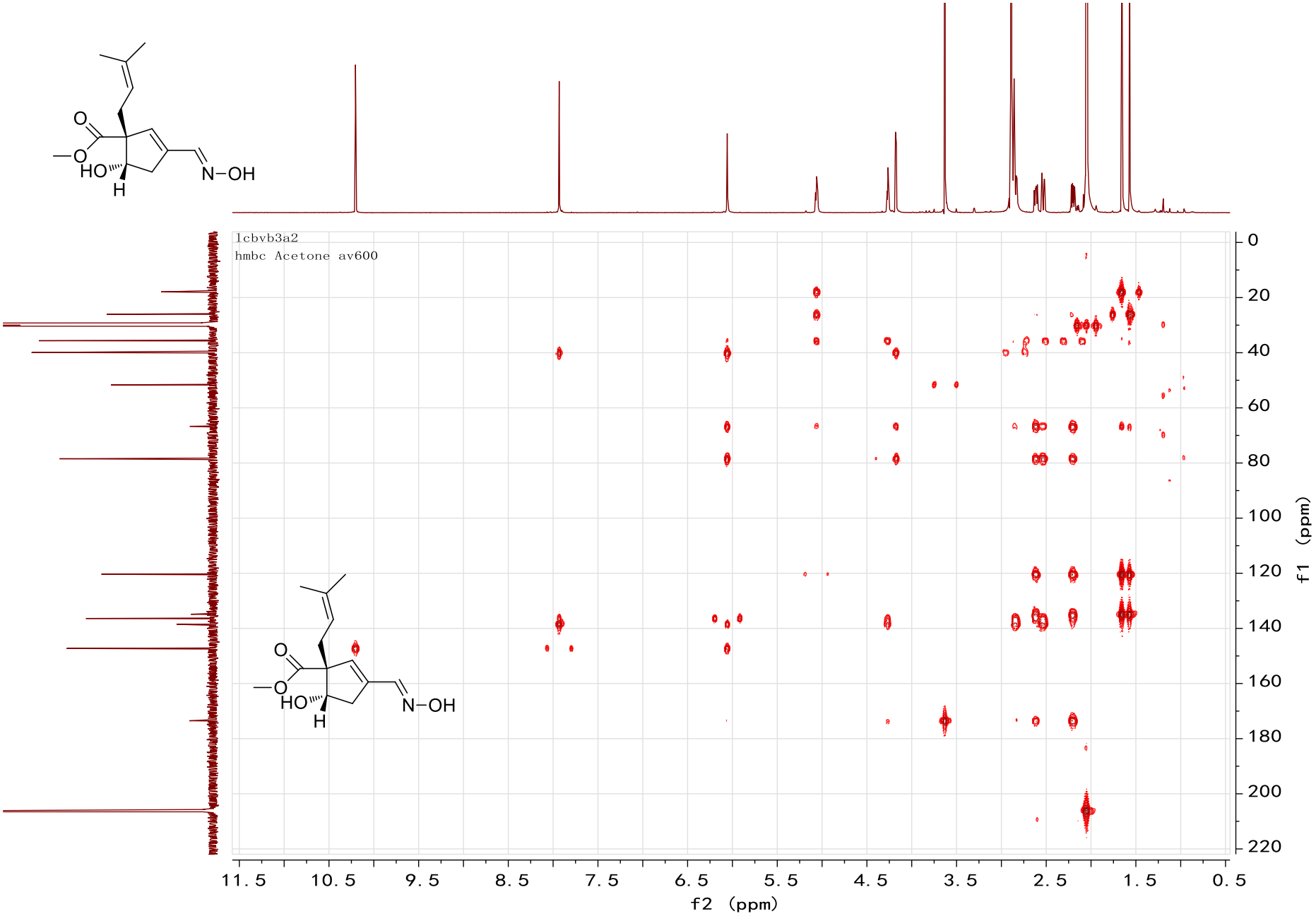


Figure 14S: ROESY spectrum of **2**.

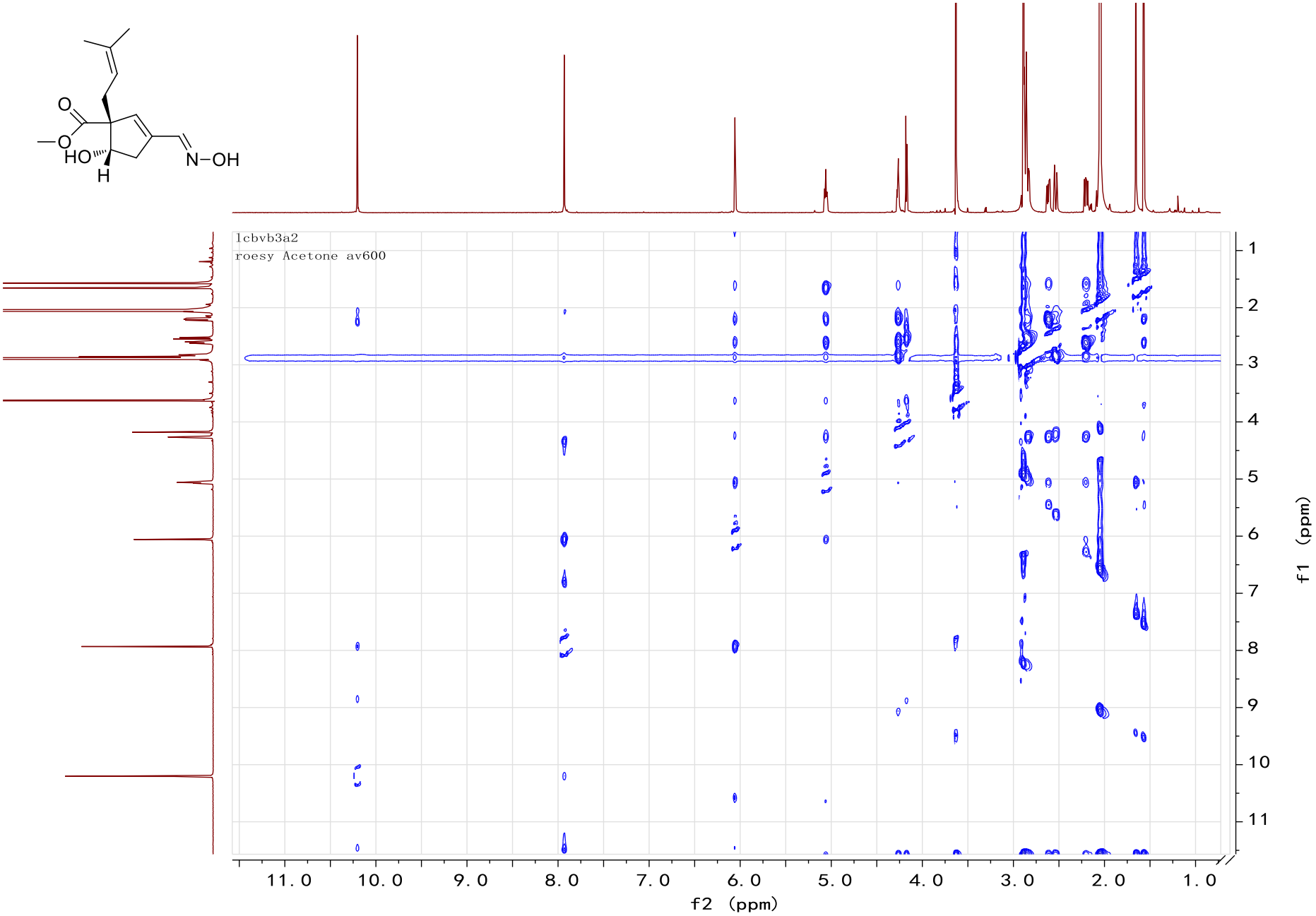


Figure 15S: HREIMS spectrum of **2**.

Elemental Composition Report

Page 1

Single Mass Analysis

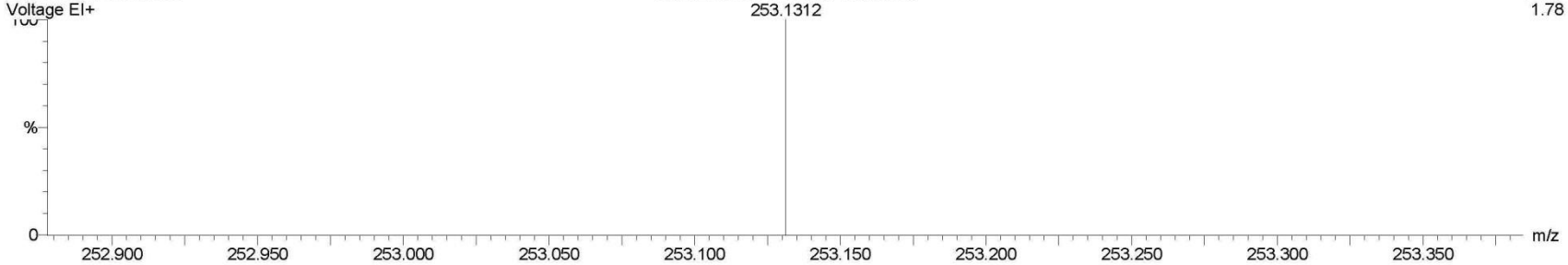
Tolerance = 10.0 PPM / DBE: min = -10.0, max = 120.0
Selected filters: None

Monoisotopic Mass, Odd and Even Electron Ions
13 formula(e) evaluated with 1 results within limits (up to 51 closest results for each mass)
Elements Used:
C: 0-200 H: 0-400 N: 1-1 O: 3-5

lcbvb-3a2
14:49:25 31-Dec-2013
Voltage EI+

KIB
M131231EA-02AFAMM 16 (1.470)
253.1312

Autospec Premier
P776
1.78



Minimum:				-10.0		
Maximum:		200.0	10.0	120.0		
Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	Formula
253.1312	253.1314	-0.2	-0.8	5.0	5546025.5	C13 H19 N O4

Figure 16S: ^{1}H NMR spectrum of **3** (acetone-d_6, 600MHz).

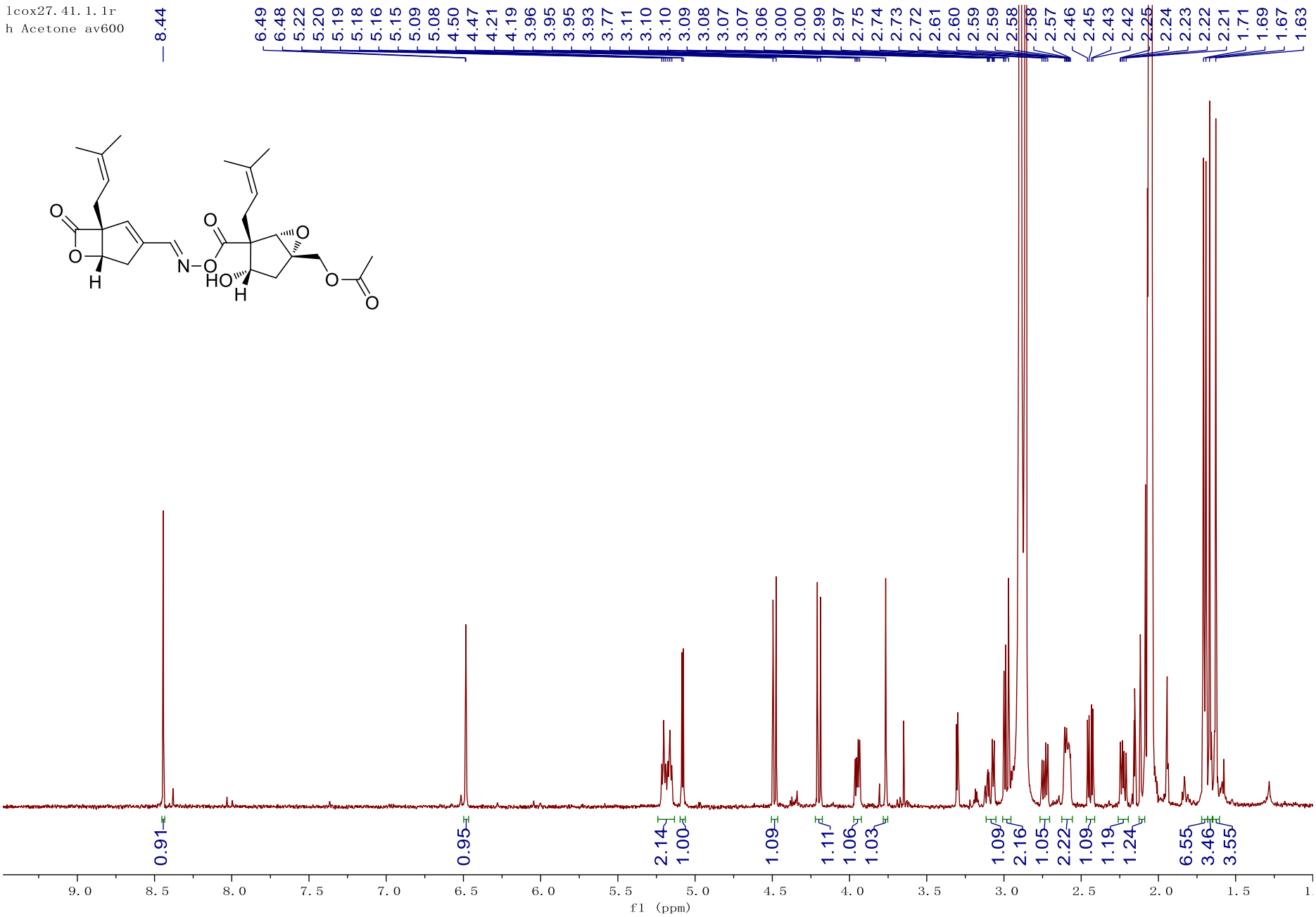
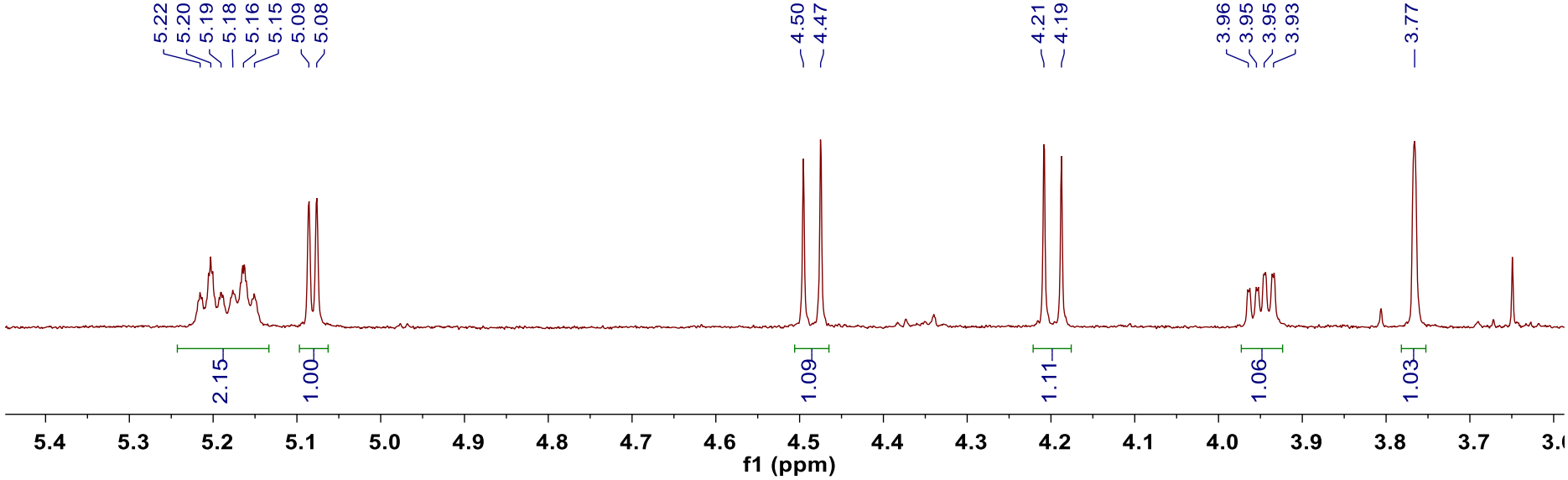


Figure 17S: Enlarged view of ^{1}H NMR spectra of **3** (acetone-d_6, 600MHz)



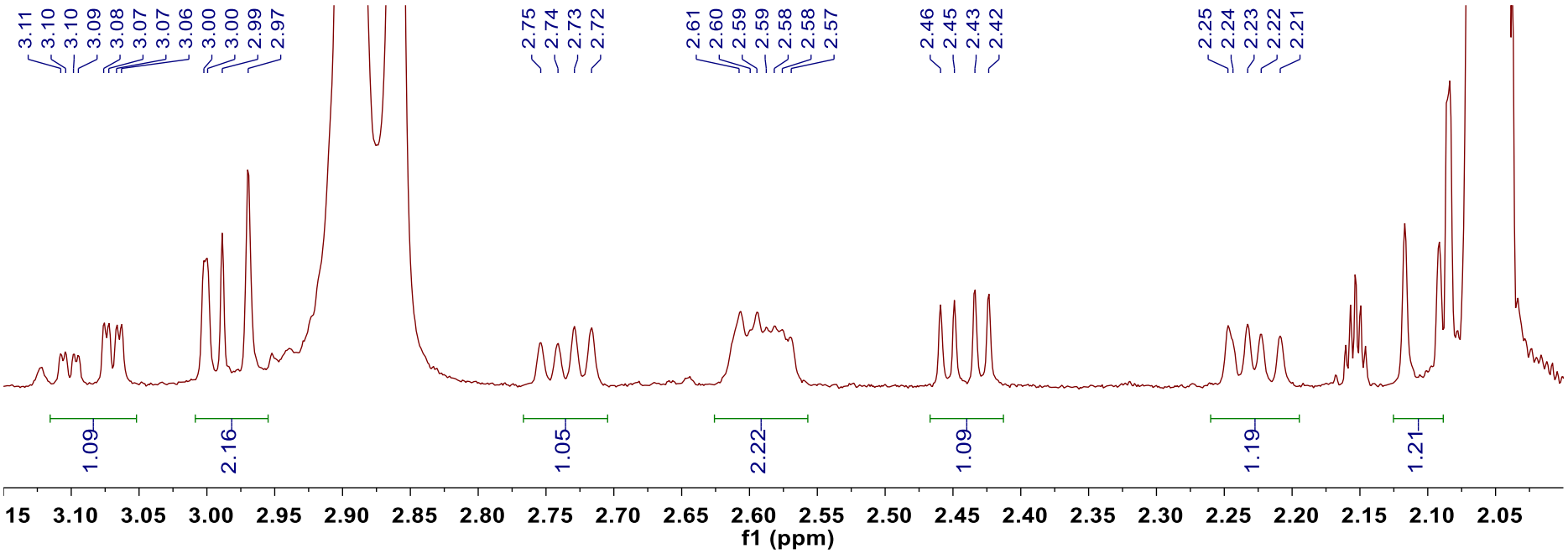


Figure 18S: ^{13}C NMR and DEPT spectra of **3** (acetone-d_6, 150MHz**)**

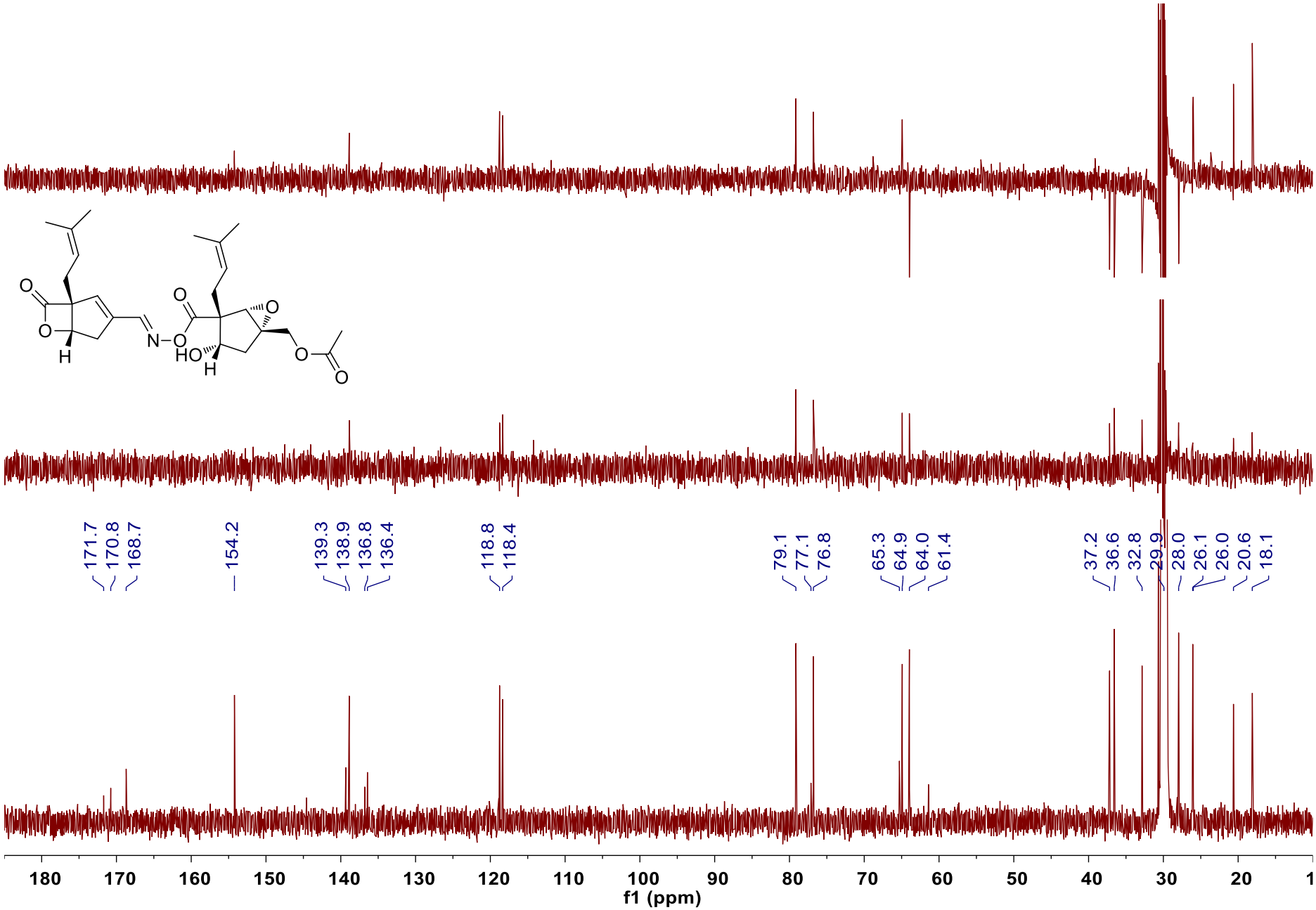


Figure 19S: Enlarged view of ^{13}C NMR spectrum of **3** (acetone-d_6, 150MHz)

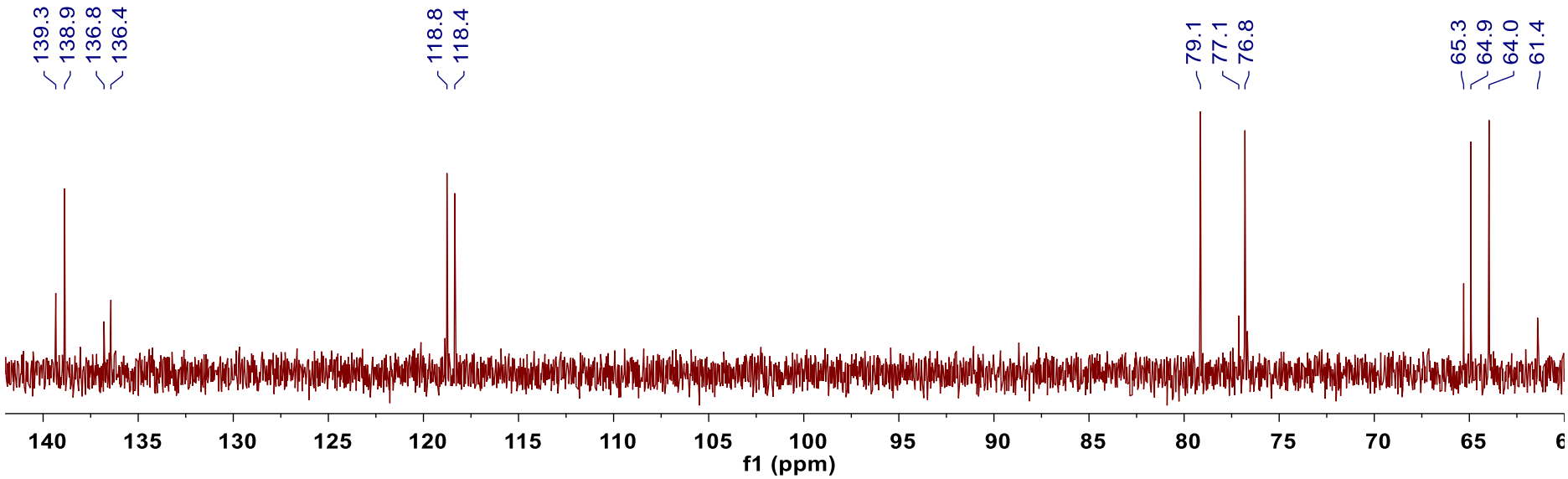


Figure 20S: HSQC spectrum of **3**.

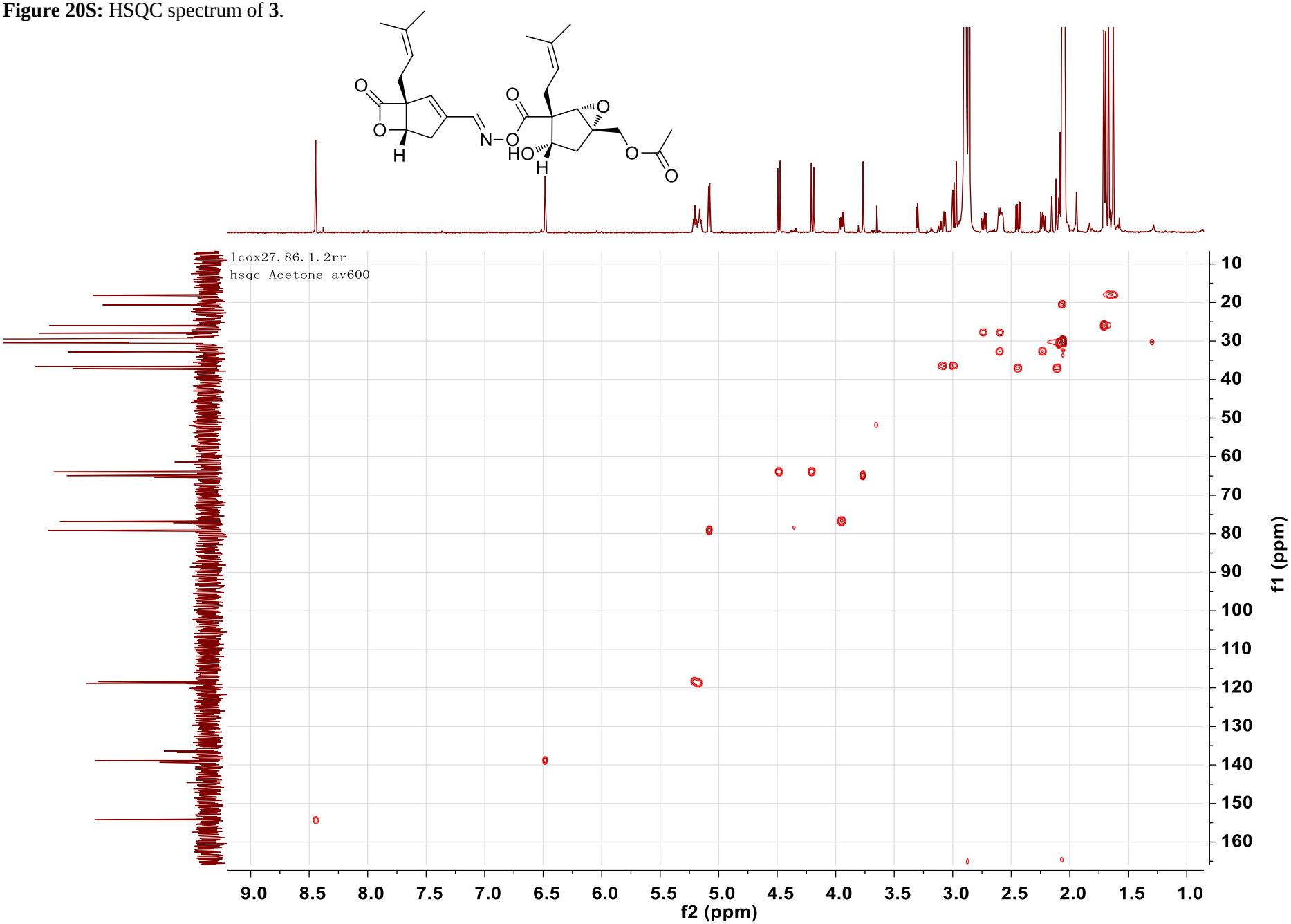


Figure 21S: ^{1}H-^{1}H COSYspectrum of **3**.

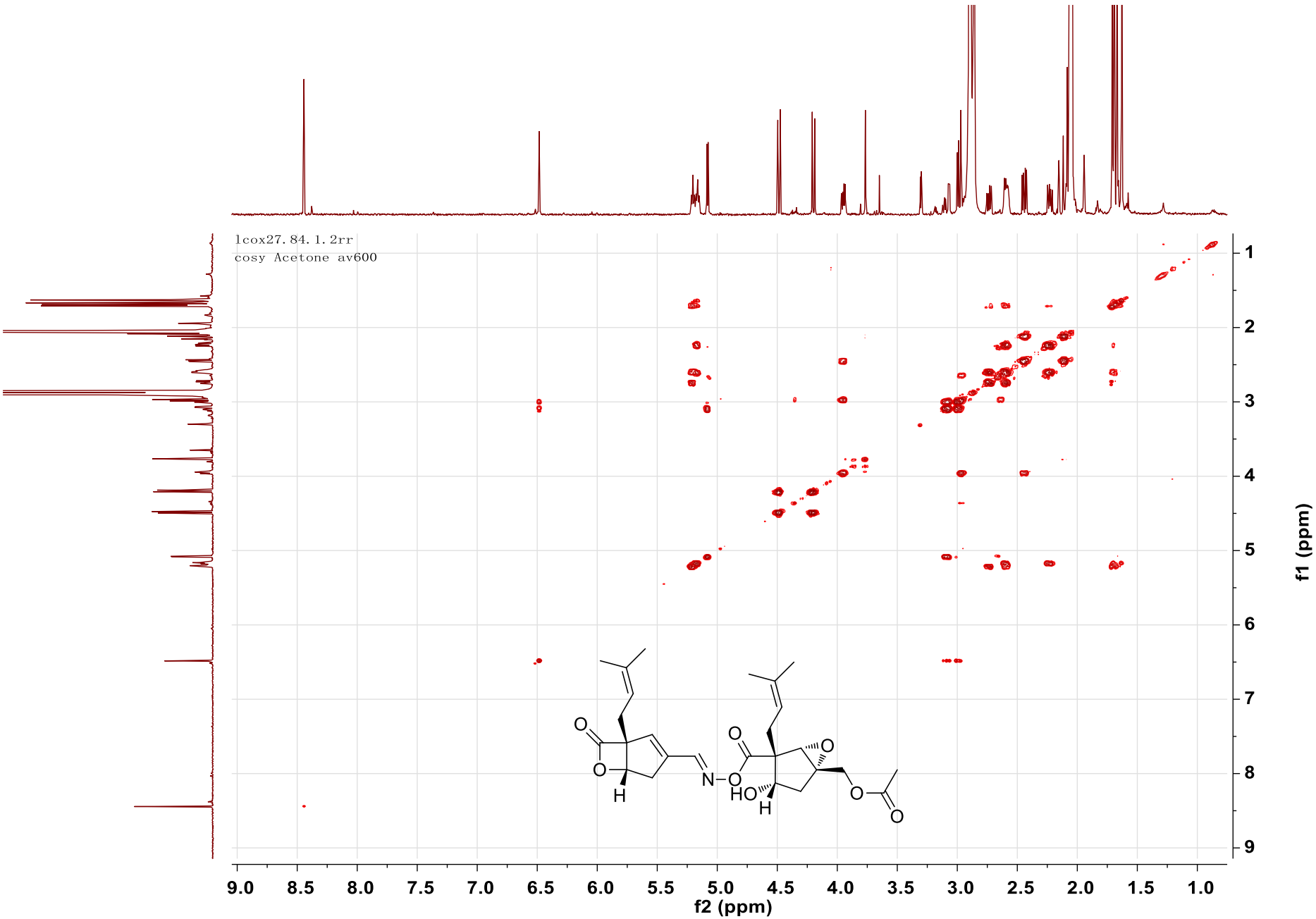


Figure 22S: HMBC spectrum of **3**.

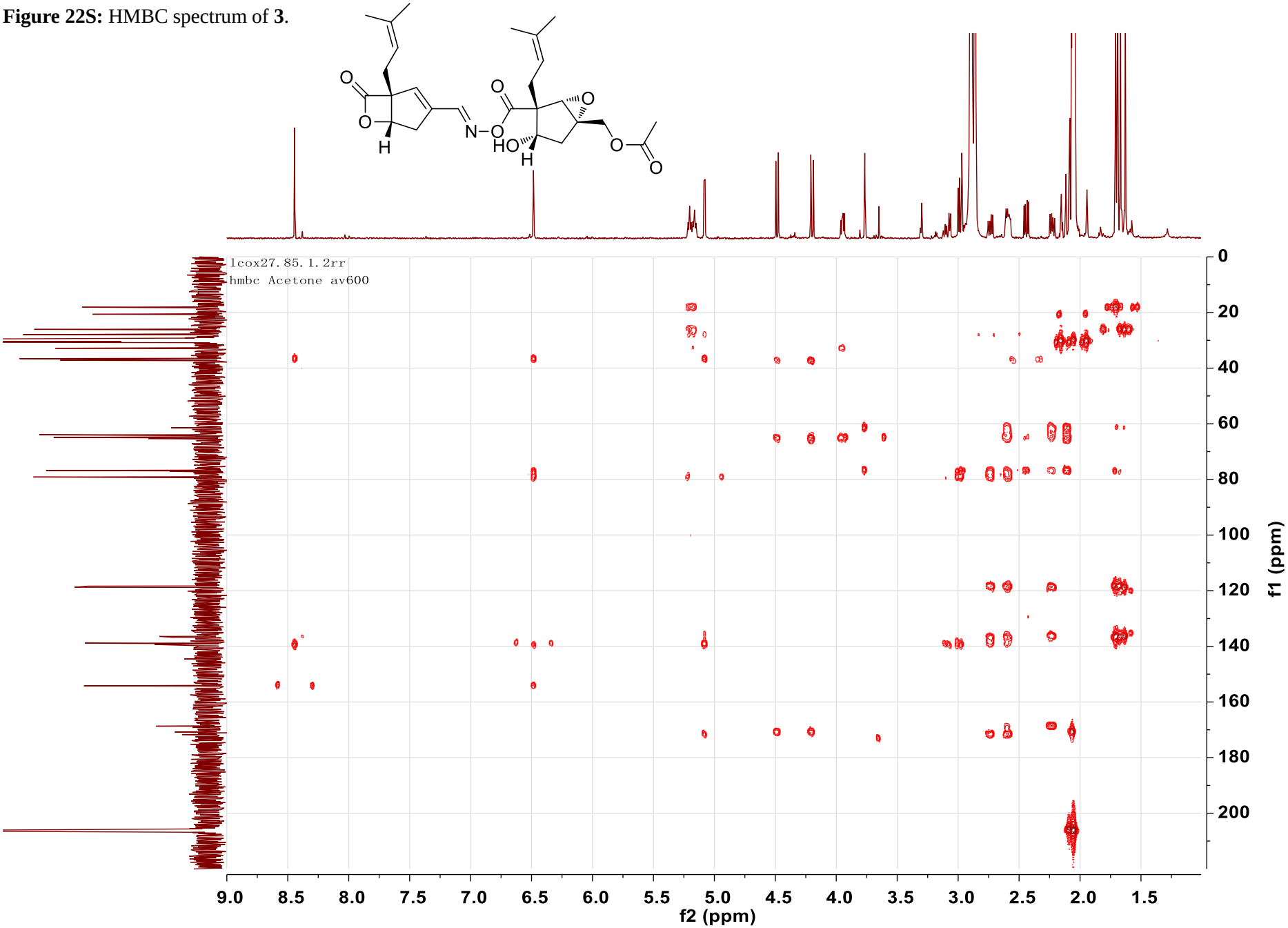
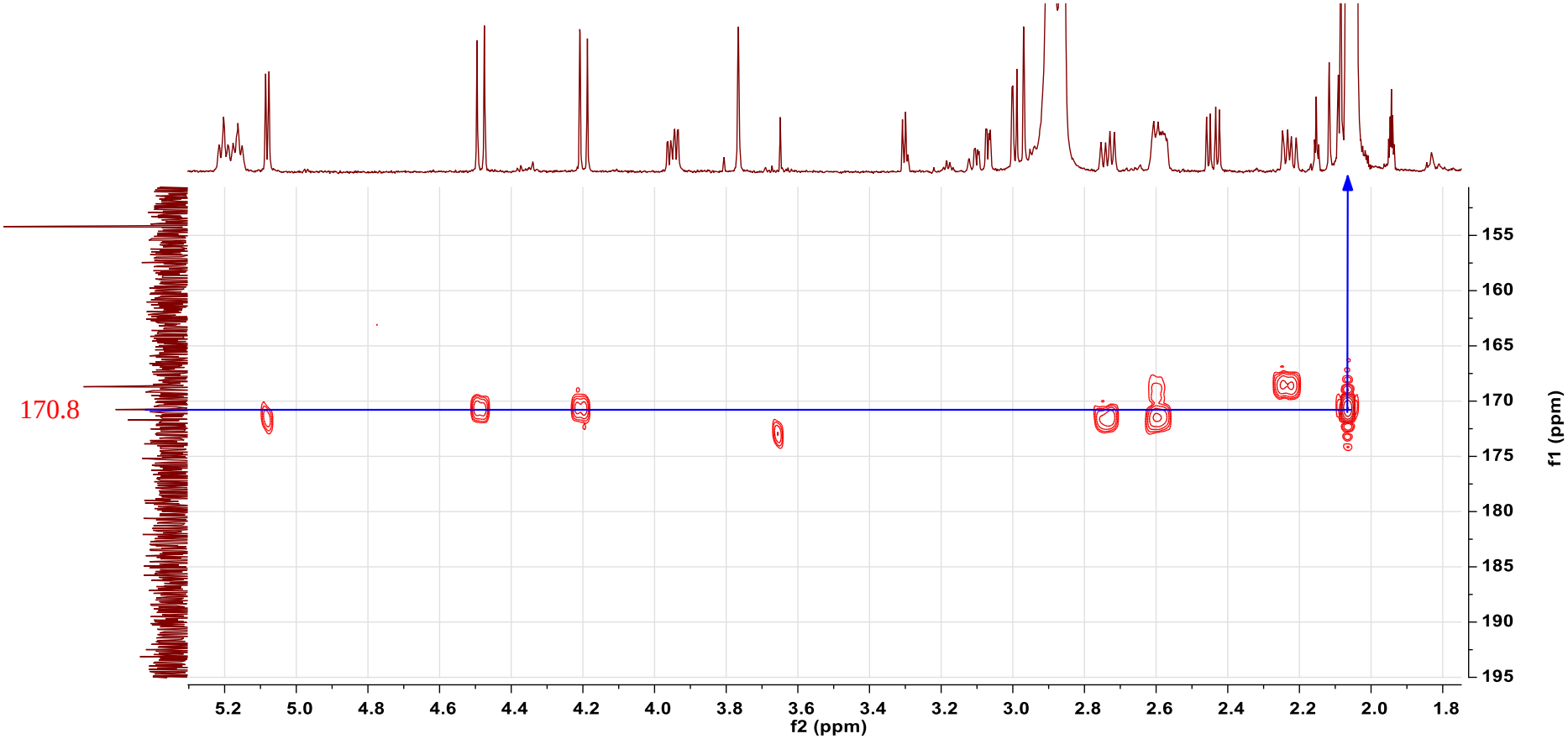


Figure 23S: Enlarged view of HMBC spectrum of **3**.



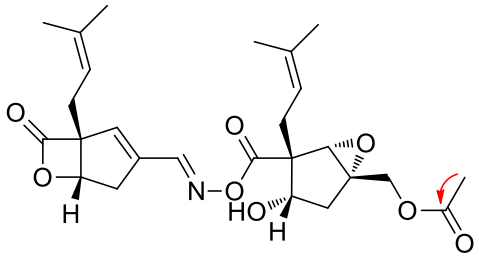


Figure 24S: ROESY spectrum of **3**.

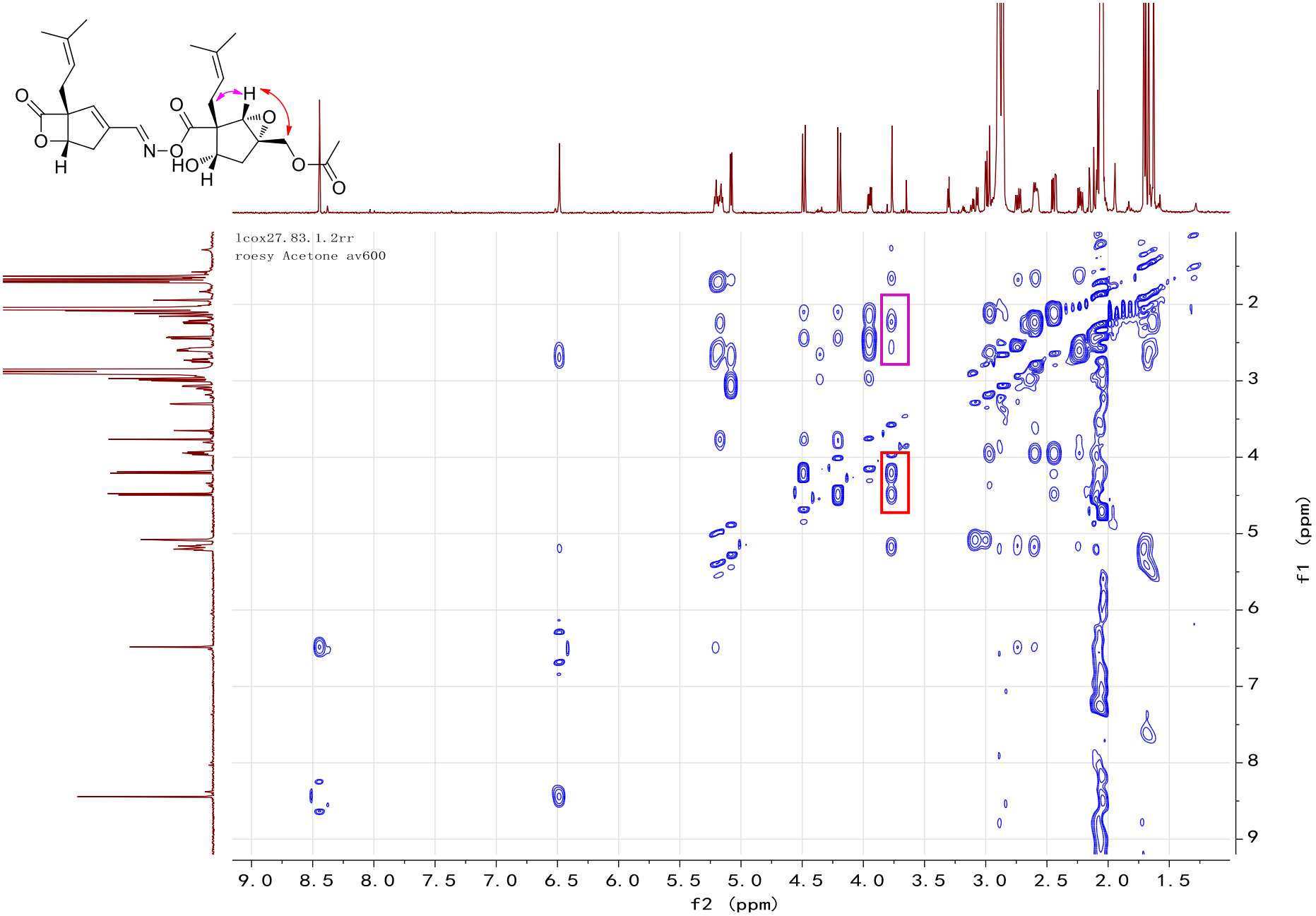


Figure 25S: HRESIMS spectrum of **3**.

Qualitative Analysis Report

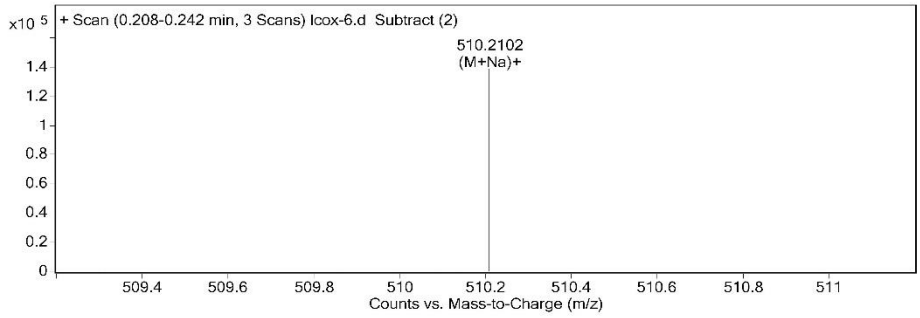
Data Filename	lcox-27.d	**Sample Name**	lcox-27
Sample Type	Sample	**Position**	P1-B3
Instrument Name	Instrument 1	**User Name**	
Acq Method	SIBU.m	**Acquired Time**	3/10/2015 3:53:53 PM
IRM Calibration Status	Success	**DA Method**	Default.m
Comment			

Sample Group **Info.**

Acquisition SW Version 6200 series TOF/6500 series Q-TOF B.05.01 (B5125.2)

User Spectra

Fragmentor Voltage	Collision Energy	Ionization Mode
135	0	ESI



Peak List

m/z	z	Abund	Formula	Ion
274.2741	1	32309.41		
318.3002	1	19627.41		
510.2102	1	138483.17	C26 H33 N O8	(M+Na)+
511.2137	1	38055.41	C26 H33 N O8	(M+Na)+
526.1843	1	230987.25		
527.1877	1	65481.15		
528.1861	1	24762.72		
542.2361	1	20034.74		
558.2104	1	43224.76		
997.4312	1	30187.51		

Formula Calculator Element Limits

Element	Min	Max
C	3	60
H	0	120
O	0	30
N	0	10

Formula Calculator Results

Formula	CalculatedMass	CalculatedMz	Mz	Diff. (mDa)	Diff. (ppm)	DBE
C26 H33 N O8	487.2206	510.2098	510.2102	-0.4	-0.8	11.0000

--- End Of Report ---

Agilent Technologies Page 1 of 1 Printed at: 4:22 PM on: 3/10/2015

Figure 26S: ^{1}H NMR spectrum of **4** (acetone-d_6, 600MHz).

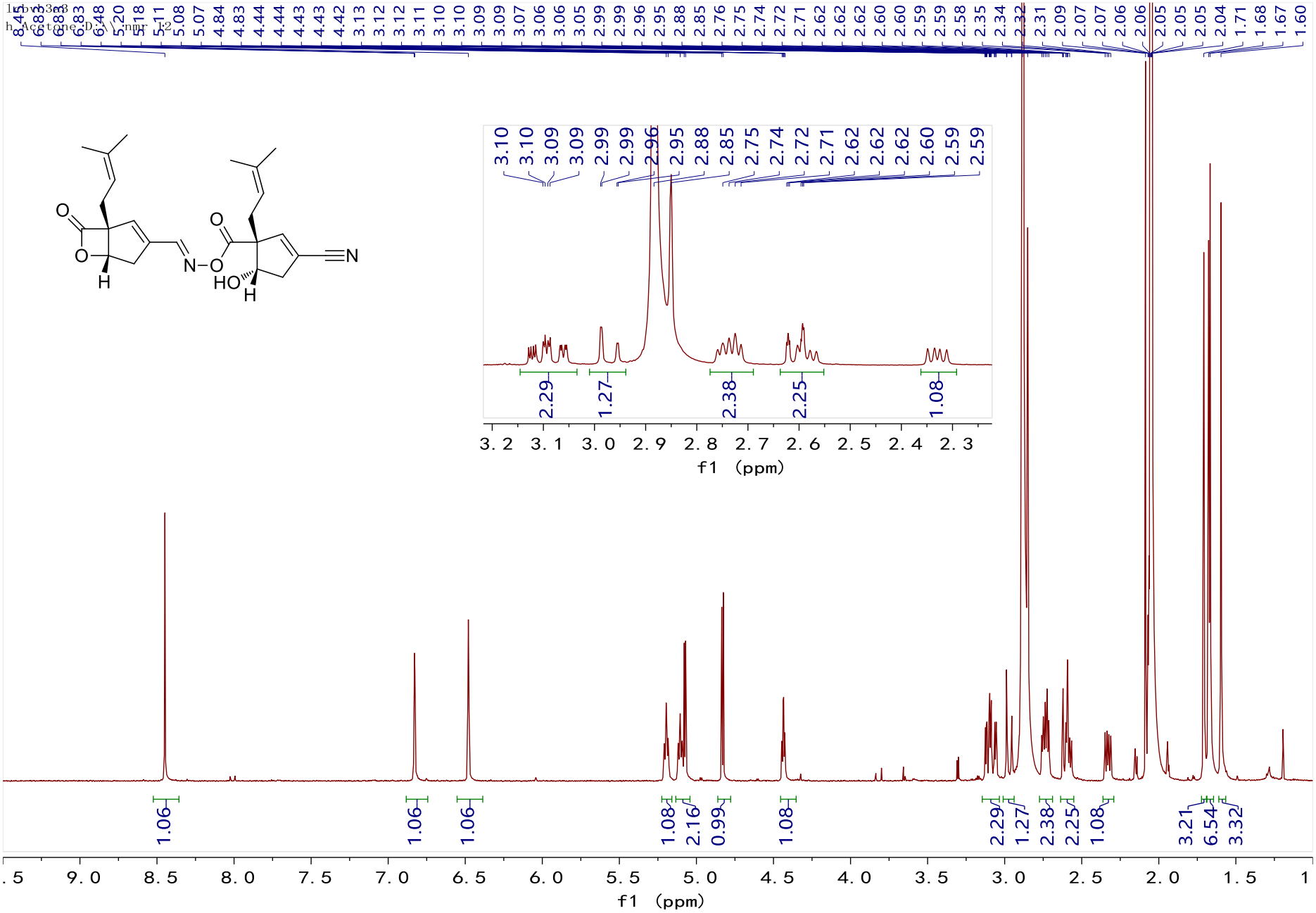


Figure 27S: ^{13}C NMR and DEPT spectra of **4** (acetone-d_6, 150MHz).

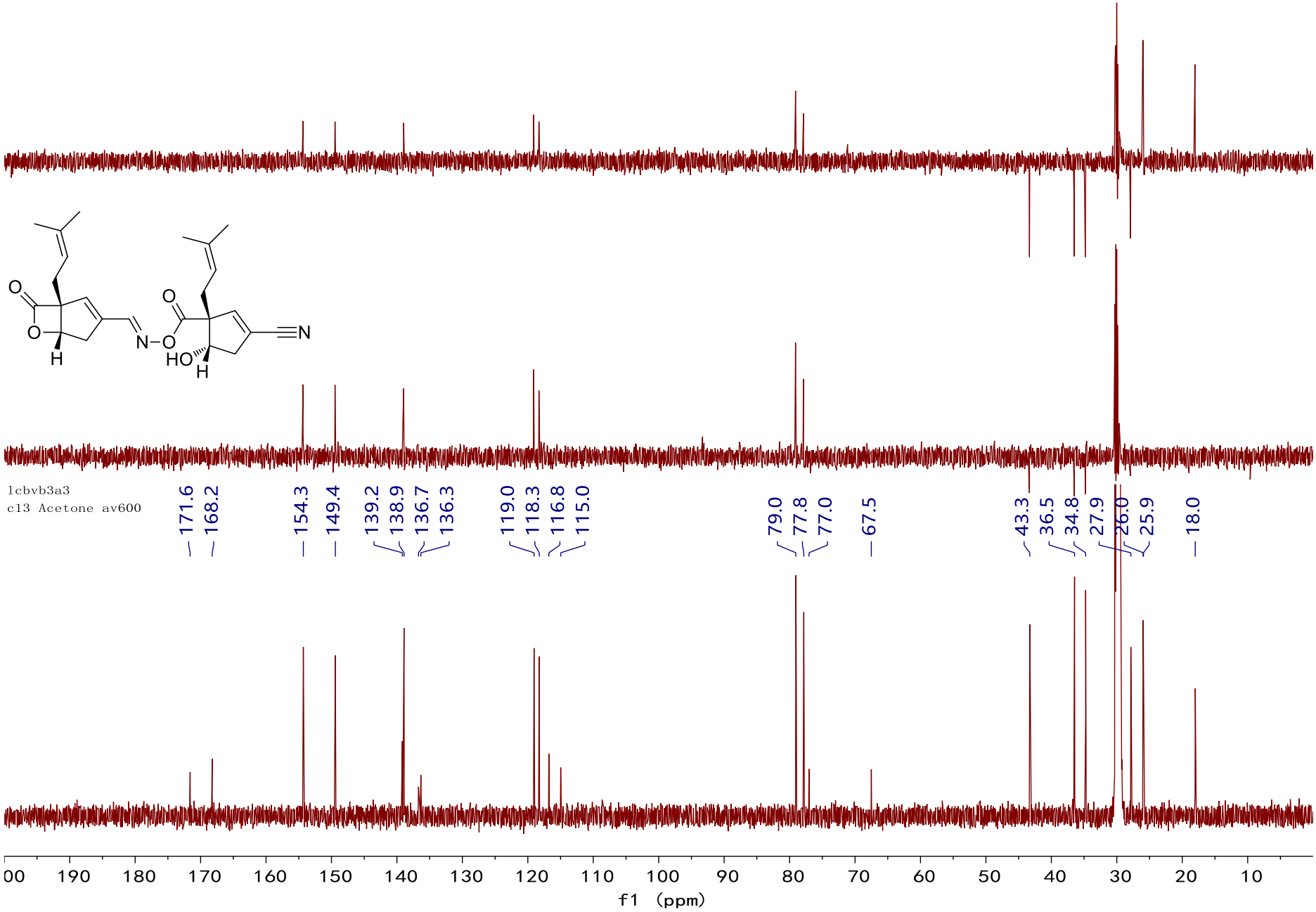


Figure 28S: Enlarged view of ^{13}C NMR spectrum of **4** (acetone-d_6, 150MHz).

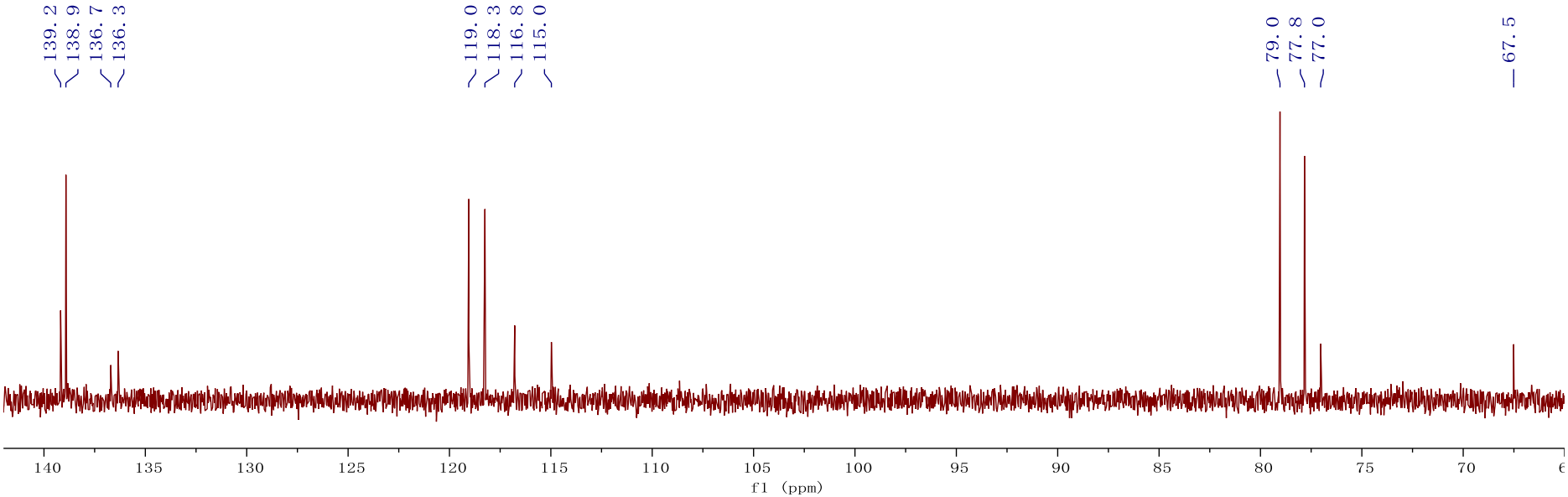


Figure 29S: HSQC spectrum of **4**.

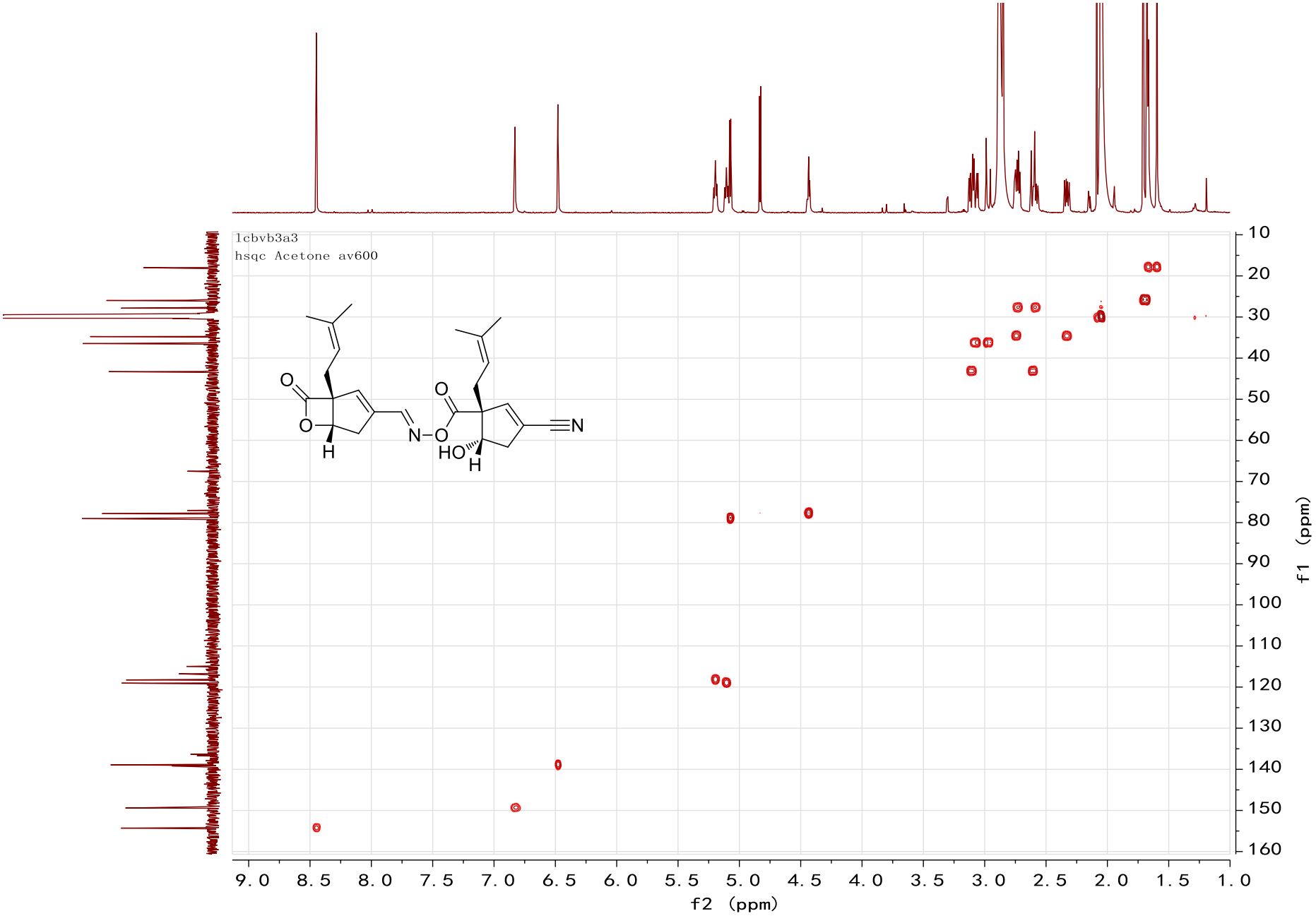


Figure 30S: ^{1}H-^{1}H COSY spectrum of **4**.

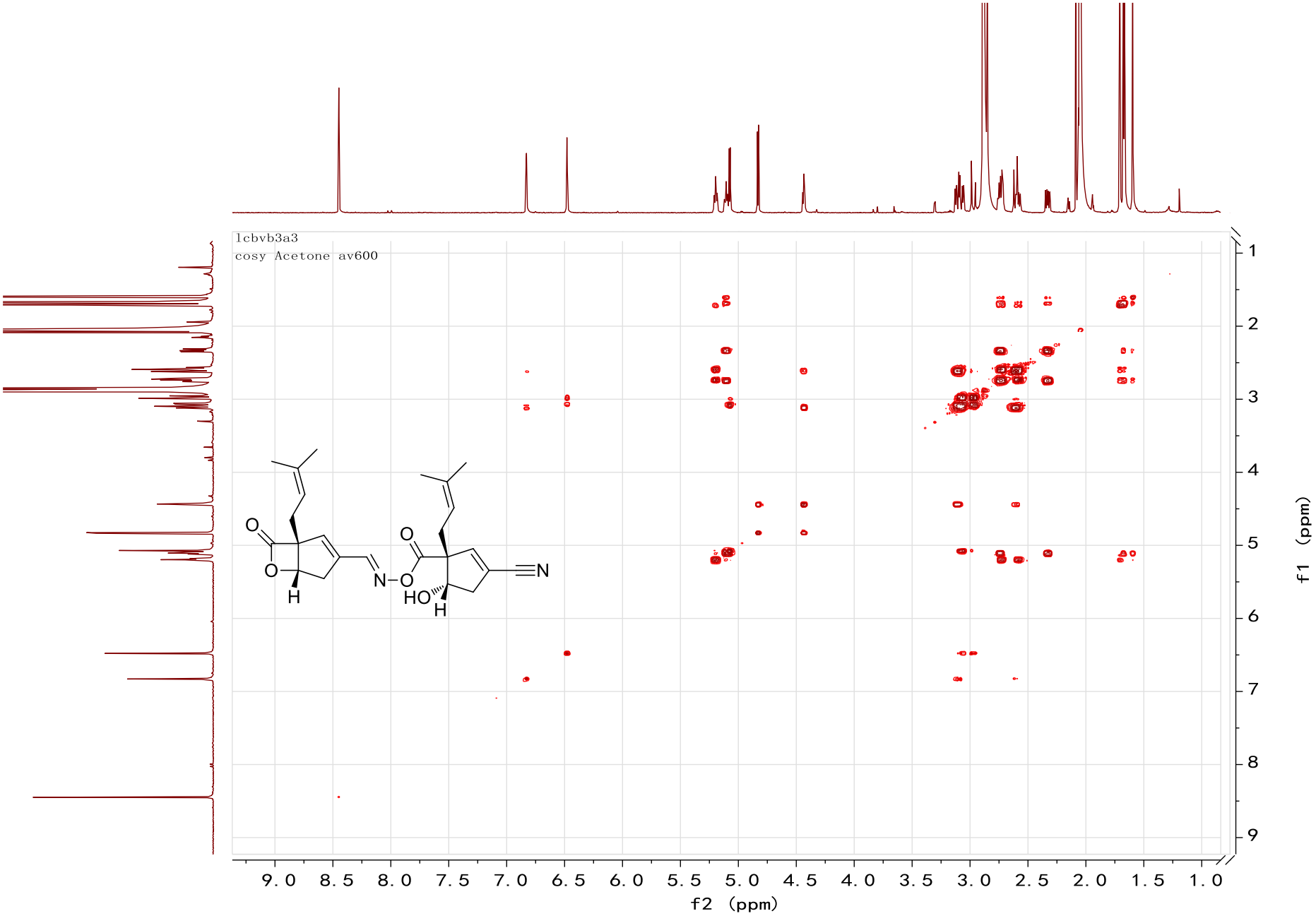


Figure 31S: HMBC spectrum of **4**.

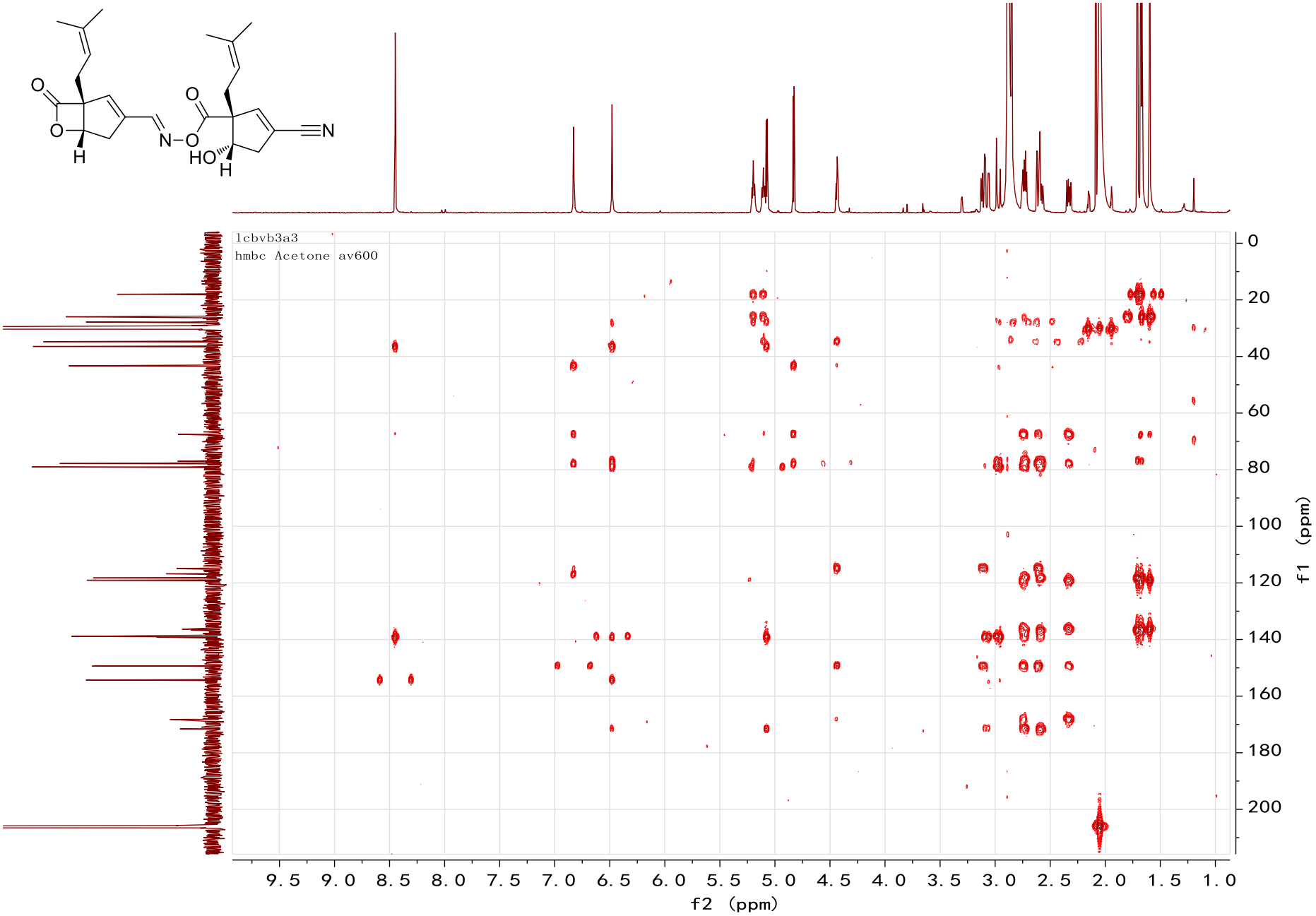


Figure 32S: Enlarged view of HMBC spectra of **4**.

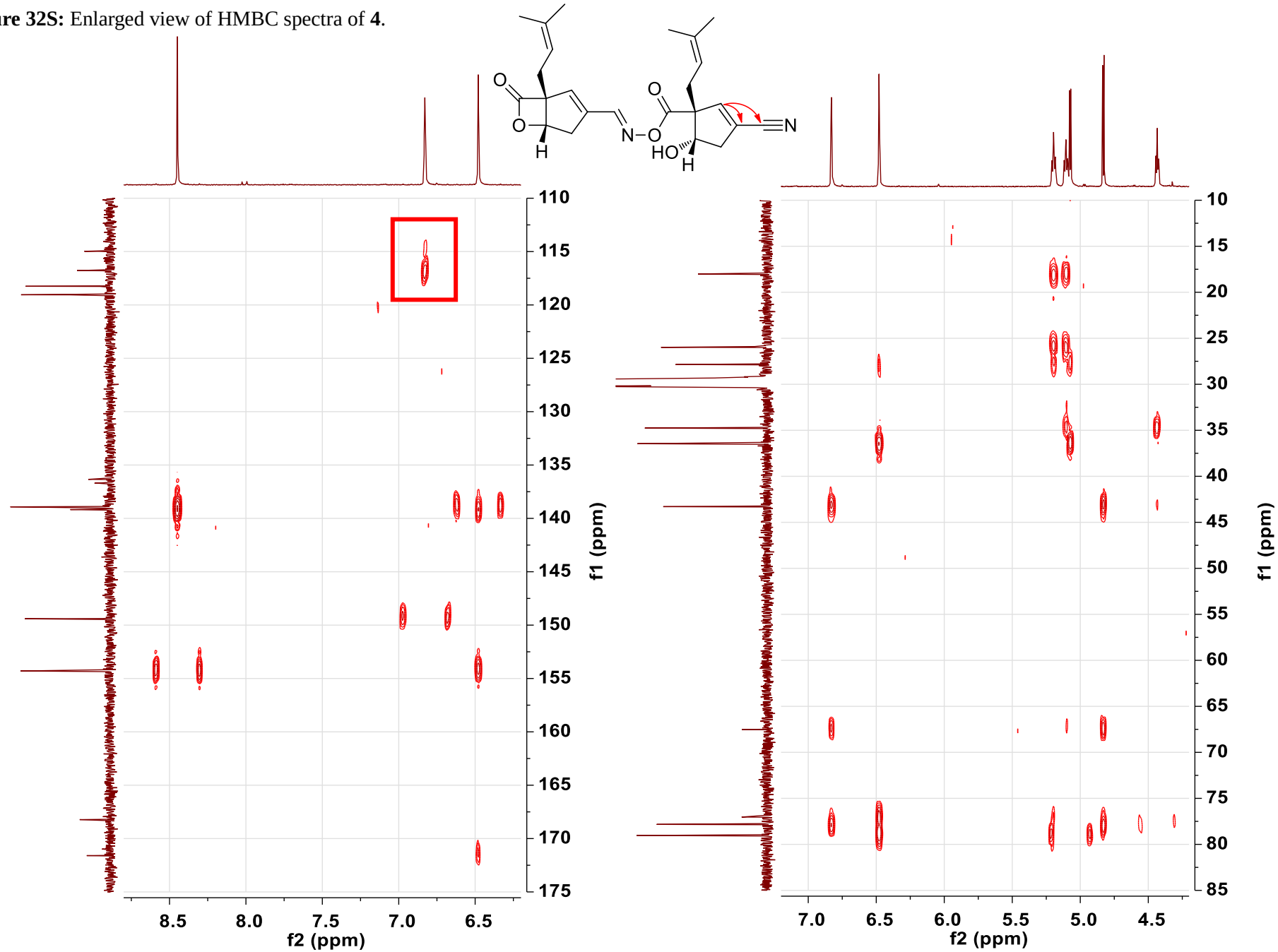


Figure 33S: ROESY spectrum of **4**.

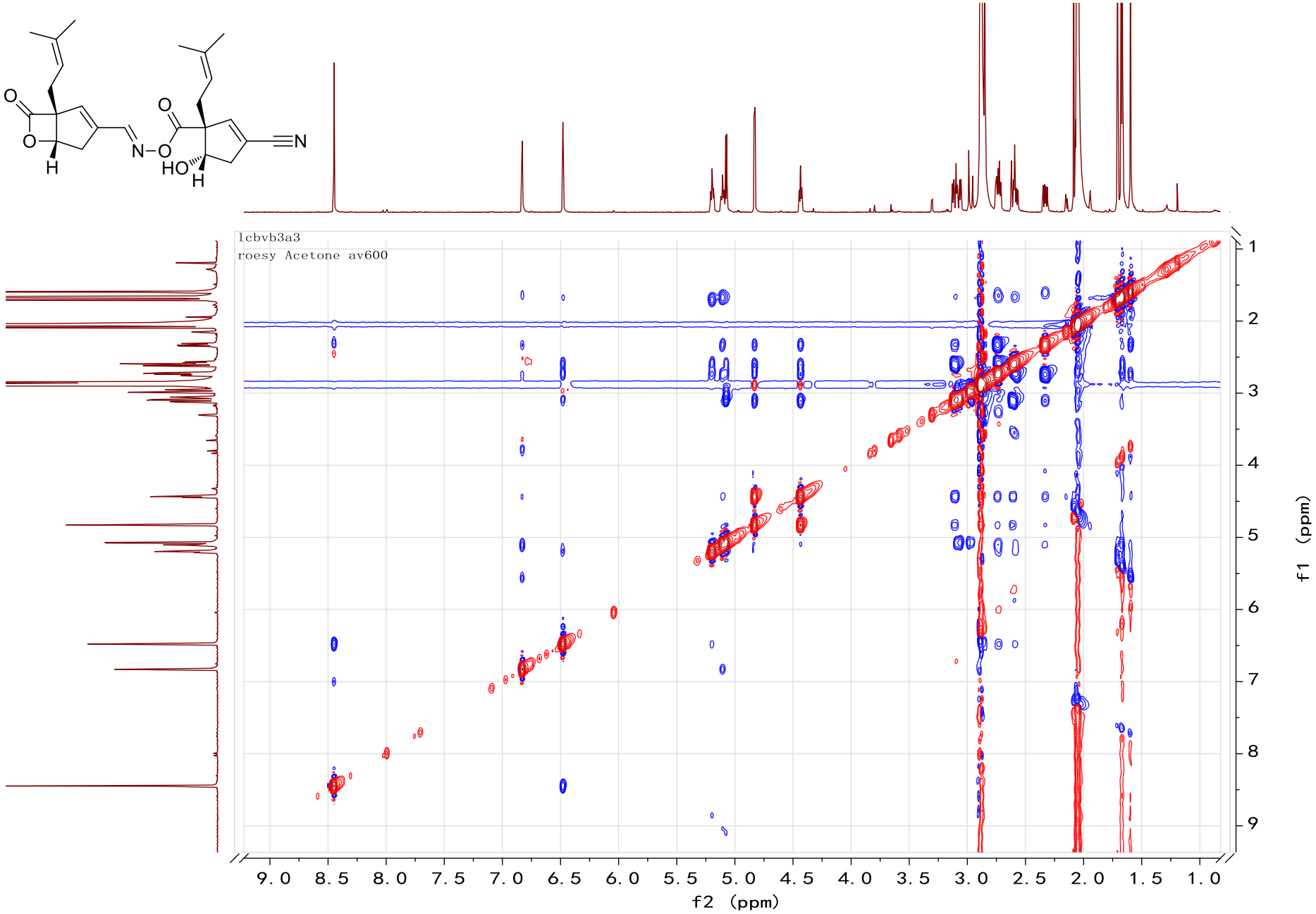


Figure 34S: HREIMS spectrum of **4**.

Elemental Composition Report

Page 1

Single Mass Analysis

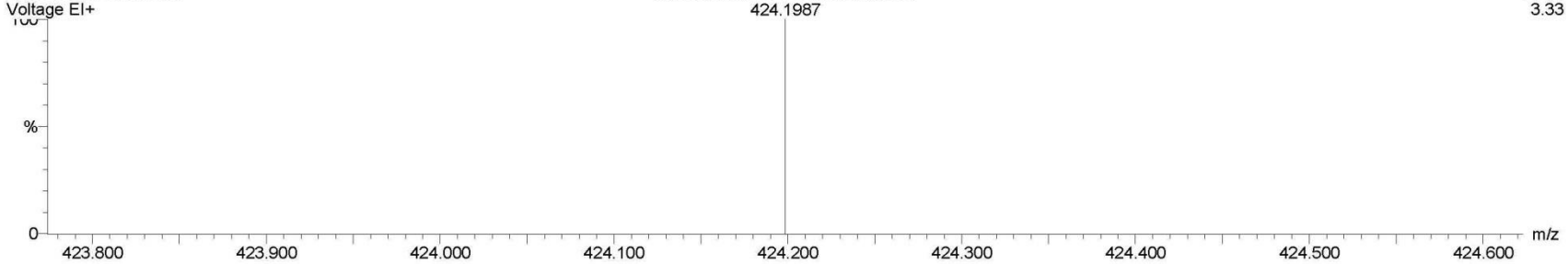
Tolerance = 10.0 PPM / DBE: min = -10.0, max = 120.0
Selected filters: None

Monoisotopic Mass, Odd and Even Electron Ions
18 formula(e) evaluated with 1 results within limits (up to 51 closest results for each mass)
Elements Used:
C: 0-200 H: 0-400 N: 2-2 O: 4-6

lcbvb-3a3
14:55:39 31-Dec-2013
Voltage EI+

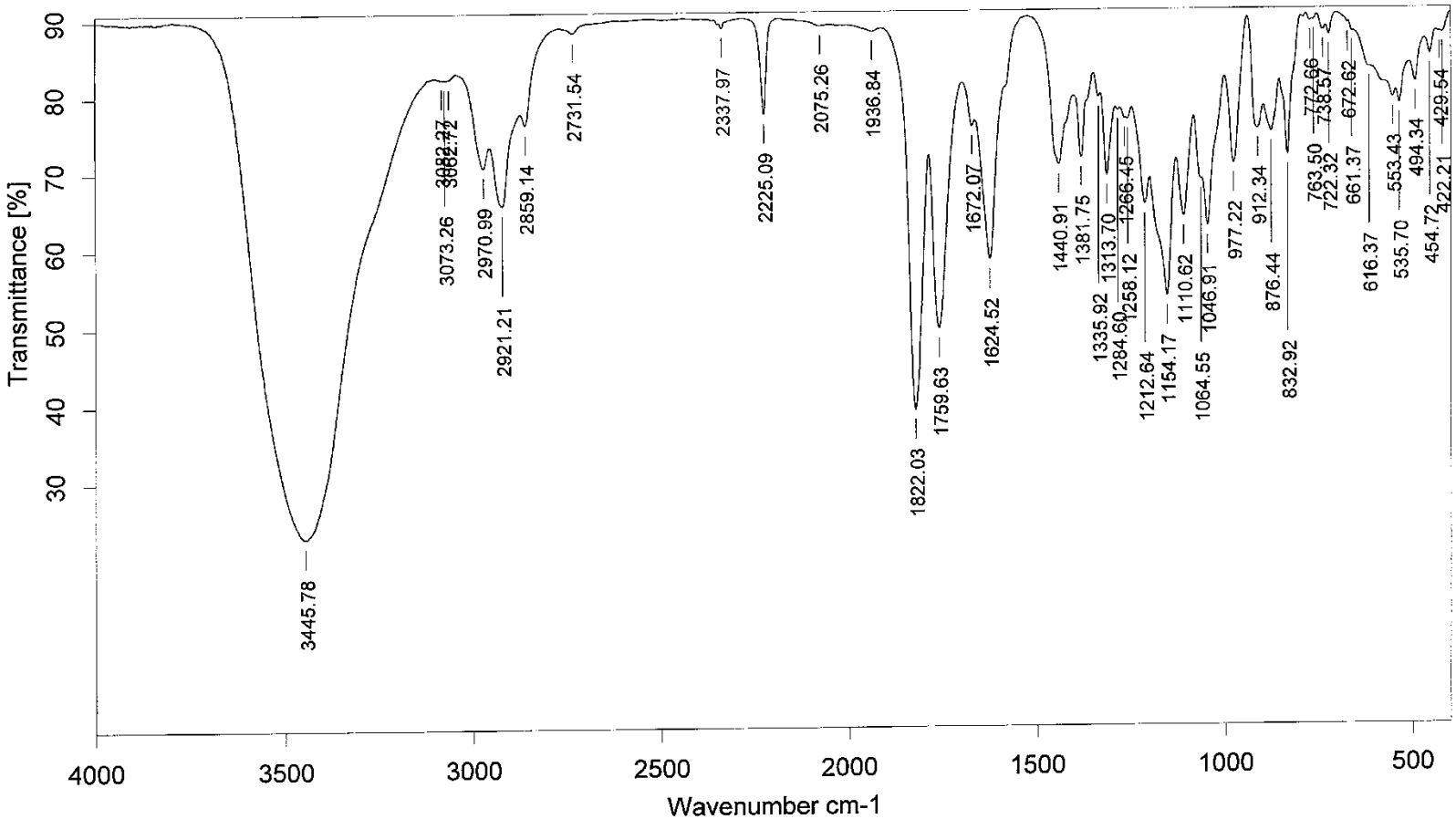
KIB
M131231EA-03AFAMM 14 (1.285)
424.1987

Autospec Premier
P776
3.33



Minimum:				-10.0		
Maximum:		200.0	10.0	120.0		
Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	Formula
424.1987	424.1998	-1.1	-2.6	12.0	5546025.5	C24 H28 N2 O5

Figure 35S: IR spectrum of 4.



Sample : Icbvb-3a3	Frequency Range : 399.246 - 3996.32	Measured on : 17/03/2015	
Technique : KBr压片	Resolution : 4	Instrument : Tensor27	Sample Scans : 16
Customer : 150317IR6	Zerofilling : 2	Acquisition : Double Sided,For	

Figure 36S: ^{1}H NMR spectrum of **5** (acetone-d_6, 600MHz).

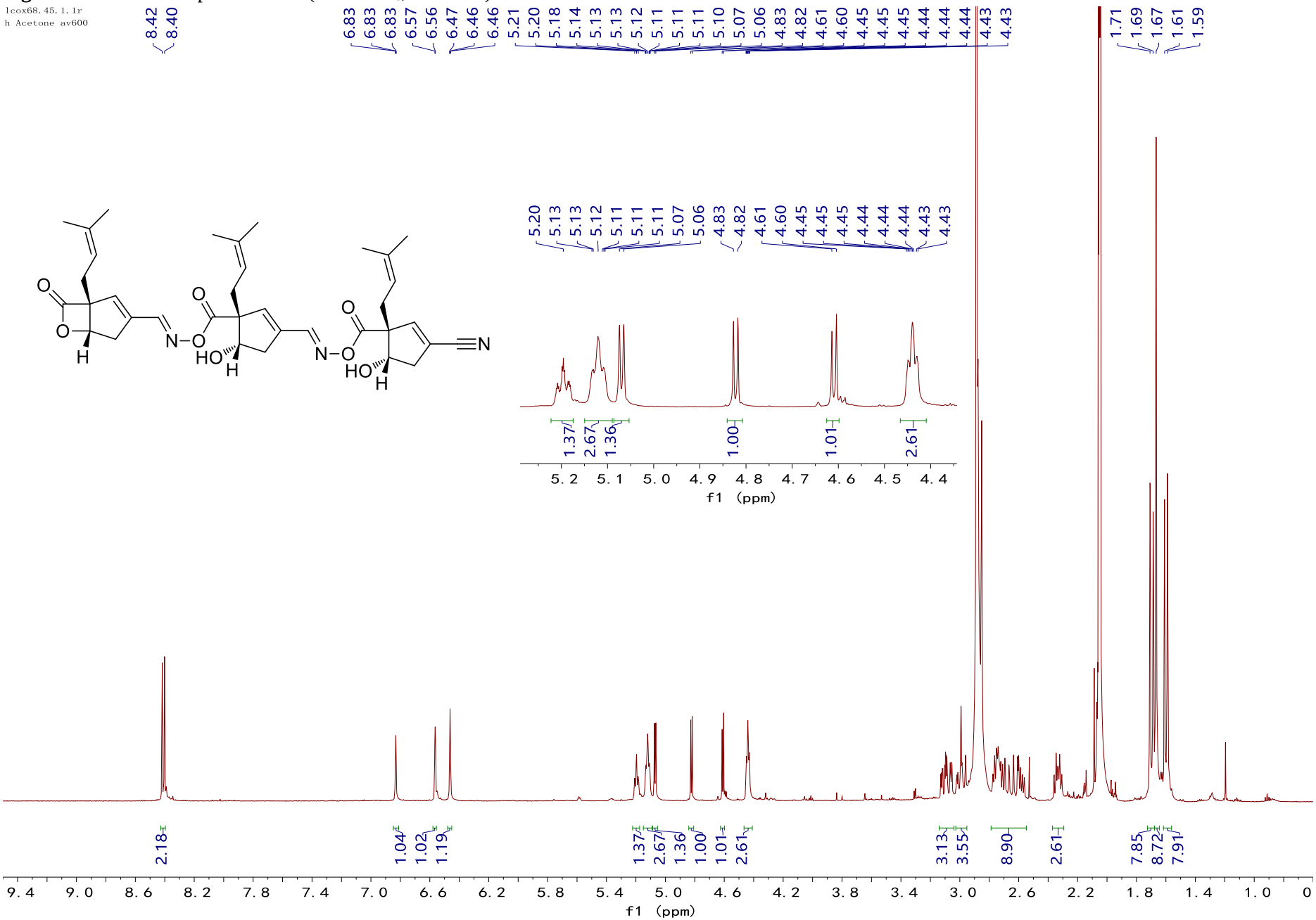


Figure 37S: ^{13}C NMR and DEPT spectra of **5** (acetone-d_6, 150MHz).

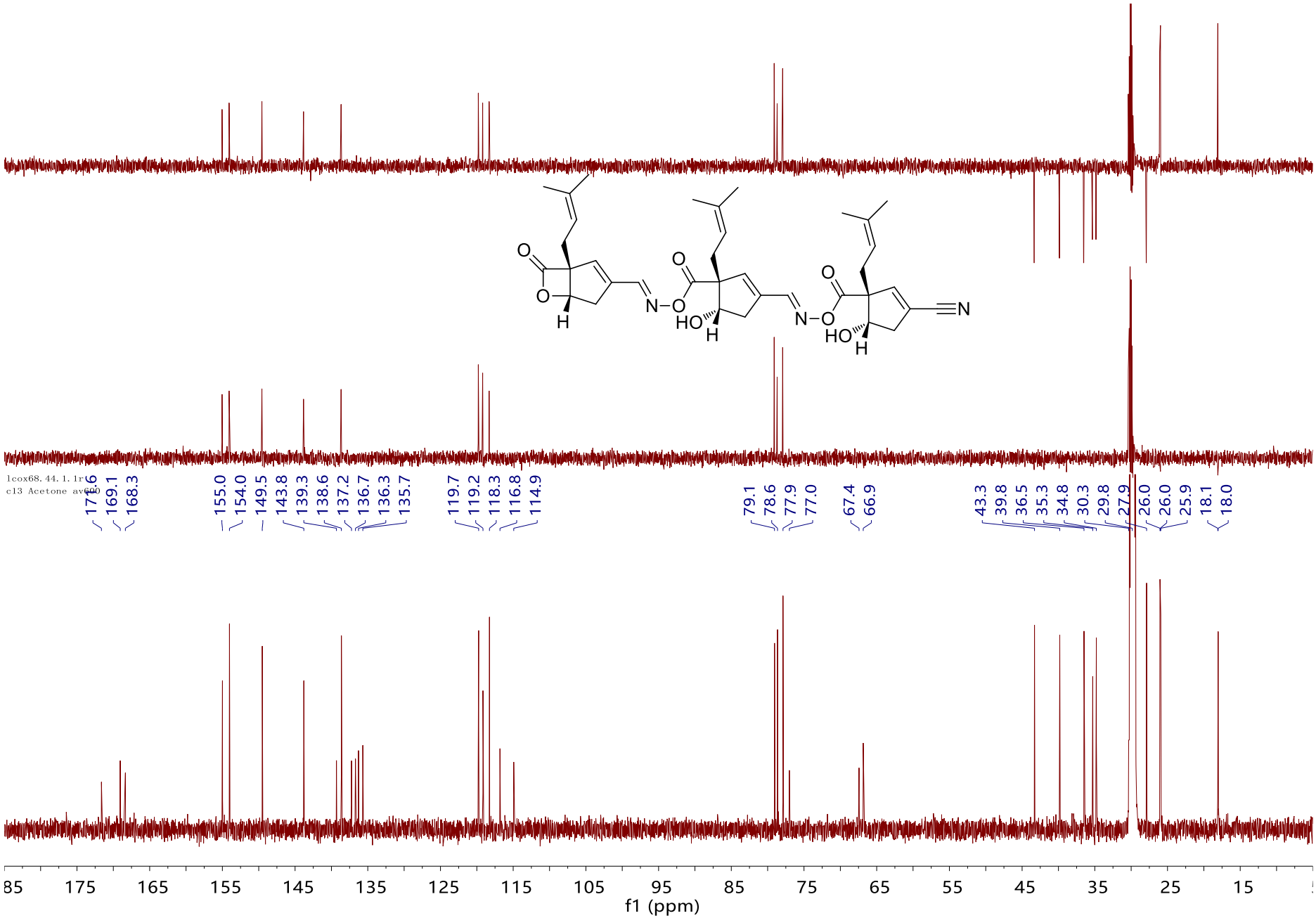


Figure 38S: Enlarged view of ^{13}C NMR spectrum of **5** (acetone-d_6, 150MHz).

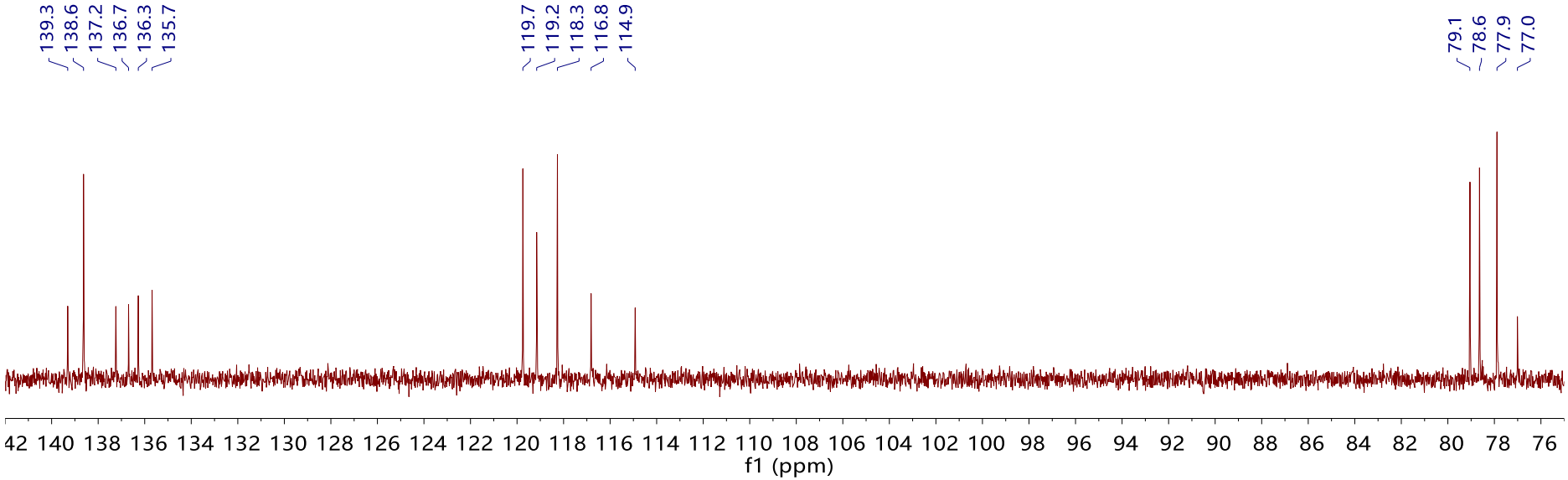


Figure 39S: HSQC spectrum of **5**.

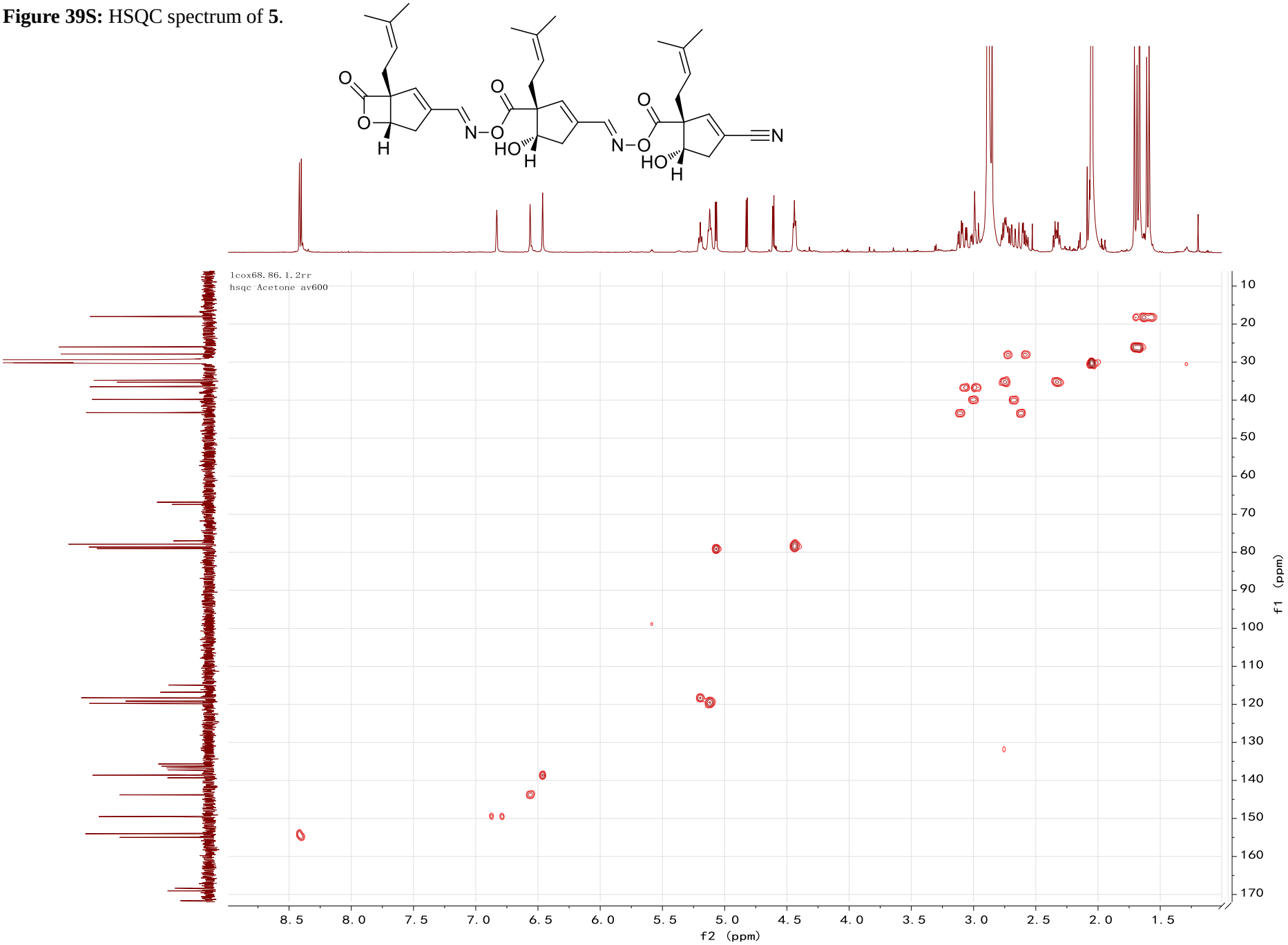


Figure 40S: ^{1}H-^{1}H COSYspectrum of **5**.

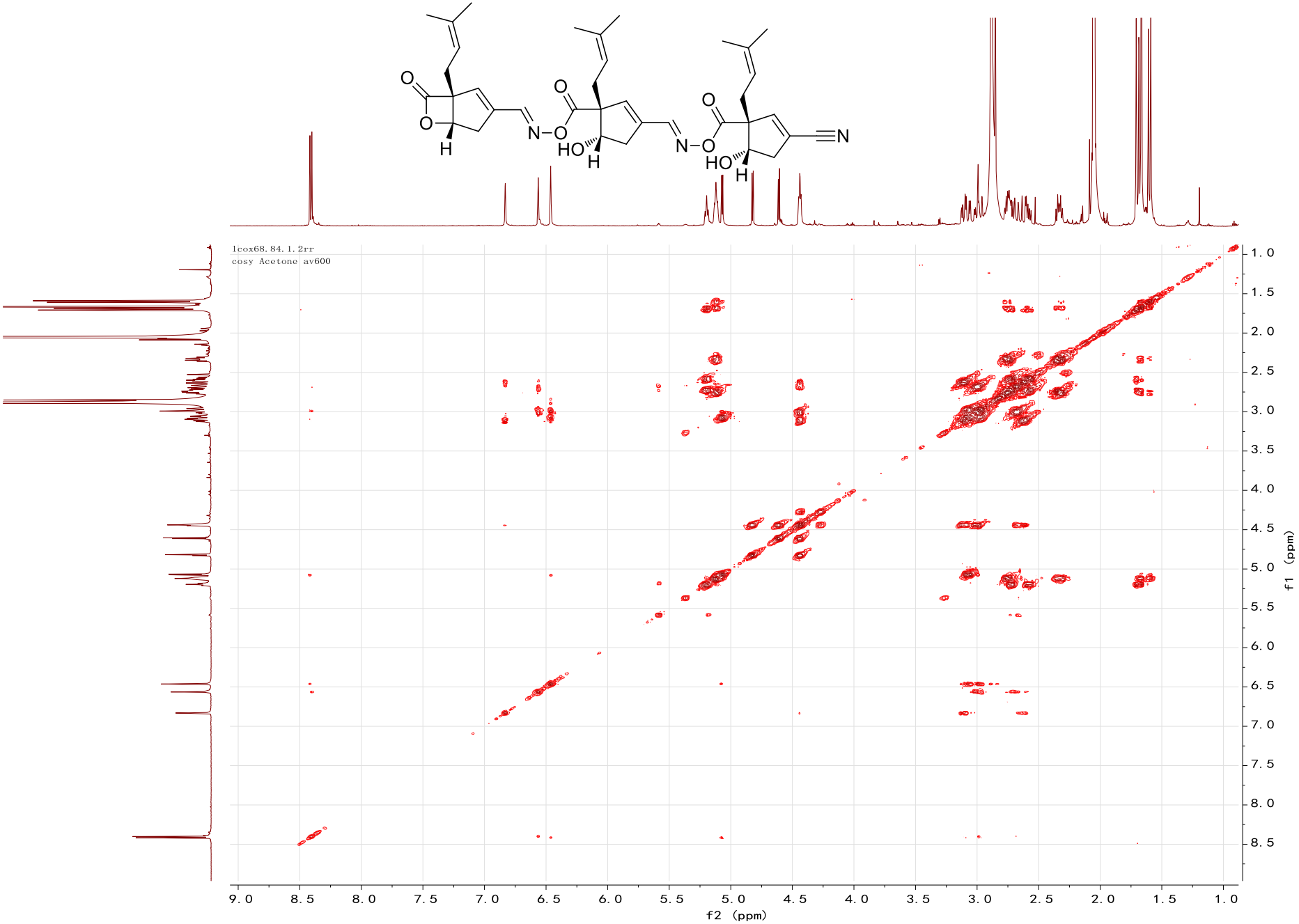


Figure 41S: HMBC spectrum of **5**.

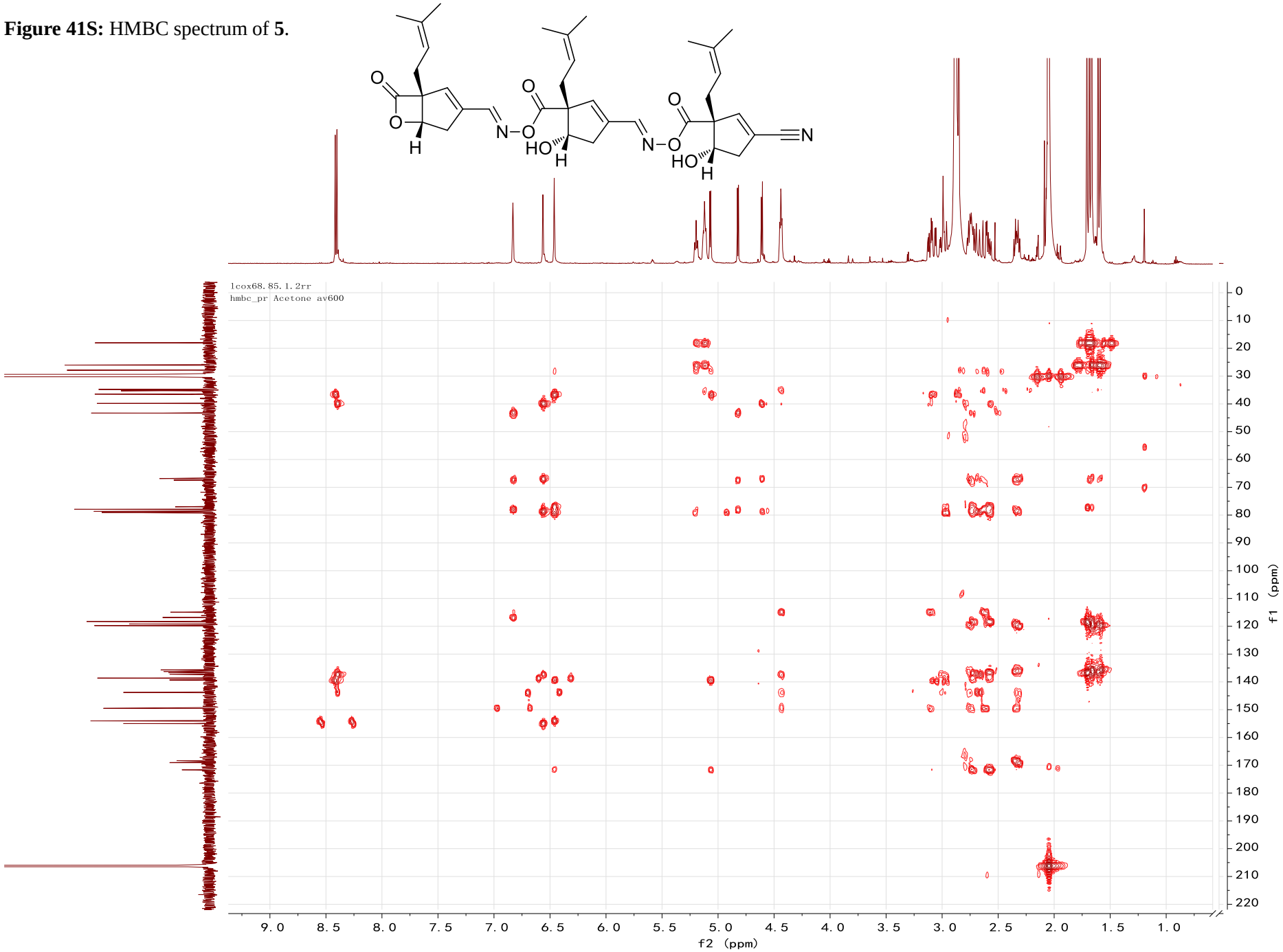


Figure 42S: Enlarged view of HMBC spectra of **5**.

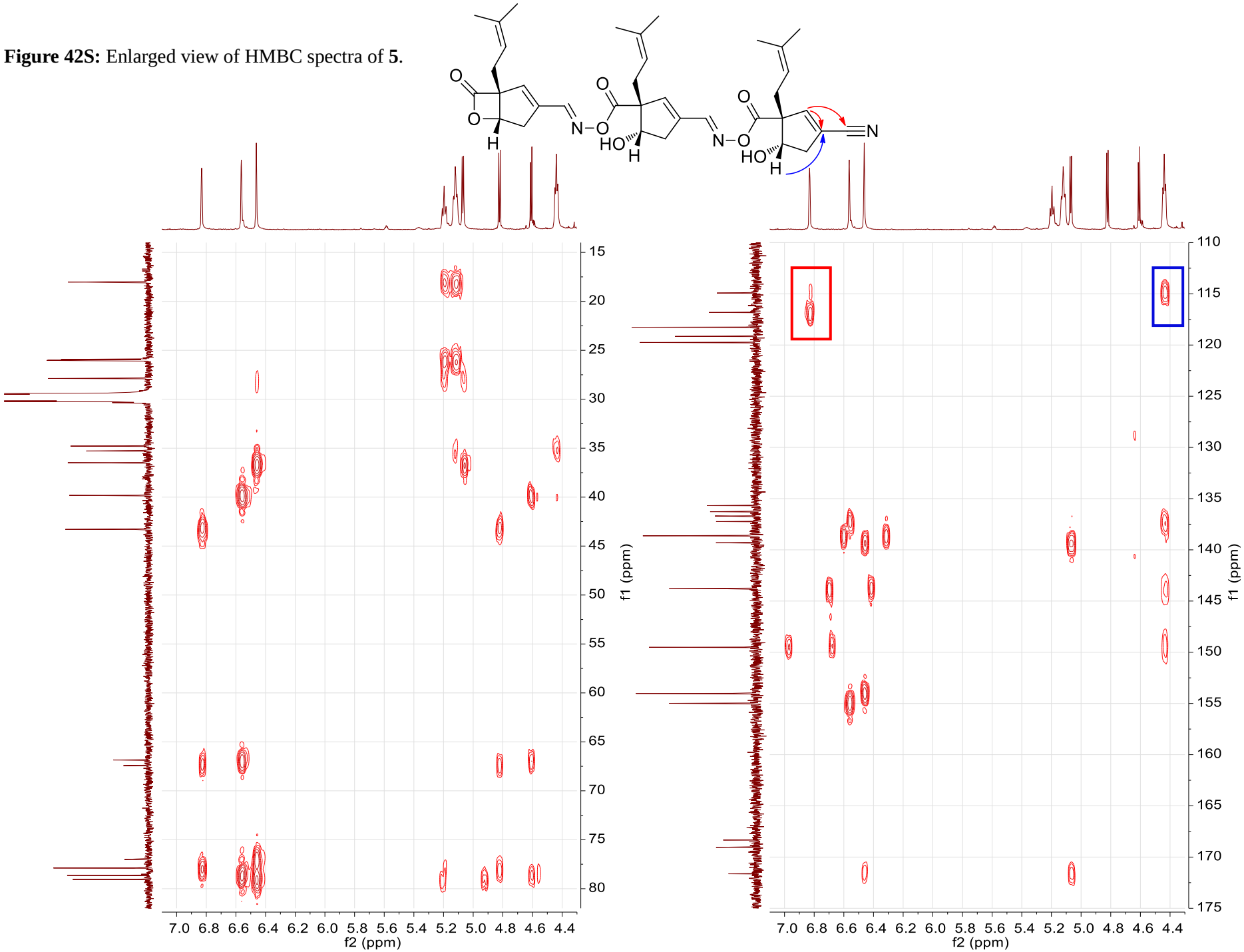


Figure 43S: ROESY spectrum of **5**.

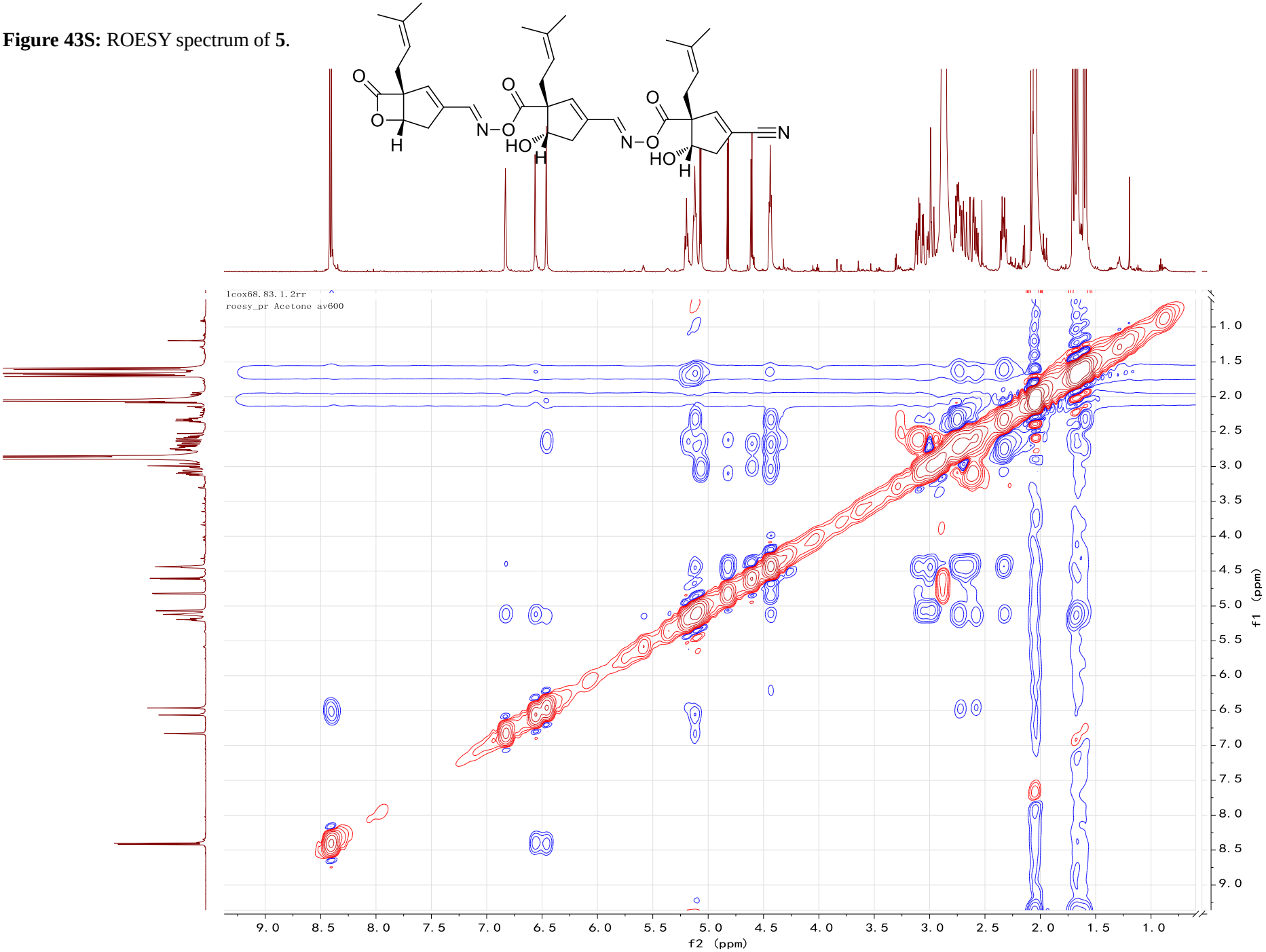


Figure 44S: IR spectrum of **5**.

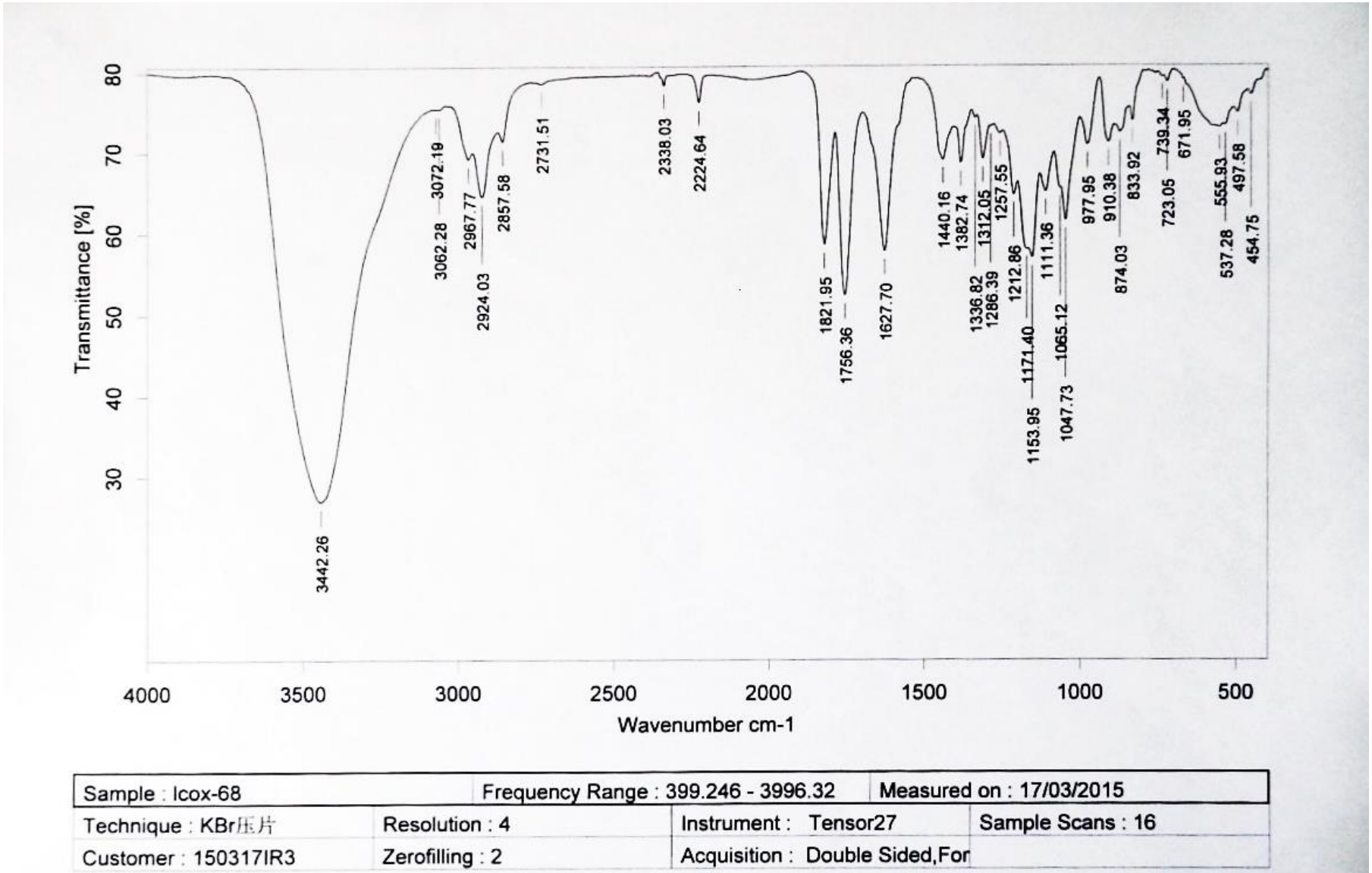


Figure 45S: HRESIMS spectrum of **5**.

Qualitative Analysis Report

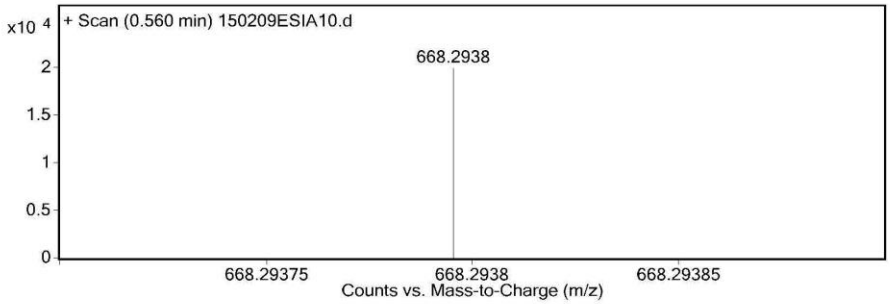
Data Filename	150209ESIA10.d	**Sample Name**	Icox-68
Sample Type	Sample	**Position**	
Instrument Name	Agilent G6230 TOF MS	**User Name**	KIB
Acq Method	ESI.m	**Acquired Time**	2/9/2015 4:40:06 PM
IRM Calibration Status	Success	**DA Method**	ESI.m
Comment			

Sample Group **Info.**

Acquisition SW Version 6200 series TOF/6500 series Q-TOF B.05.01 (B5125.2)

User Spectra

Fragmentor Voltage	Collision Energy	Ionization Mode
200	0	ESI



Peak List

m/z	z	Abund
121.0509	1	32167.5
230.2472	1	29344.04
274.2741	1	203815.23
275.2771	1	31088.2
318.3006	1	312160.5
319.3034	1	53387.34
352.1542	1	55843.86
362.3267	1	121212.16
406.3523	1	30843.82
922.0098	1	29313.56

Formula Calculator Element Limits

Element	Min	Max
C	0	200
H	0	400
O	5	10
Na	1	1
N	3	3

Formula Calculator Results

Formula	CalculatedMass	CalculatedMz	Mz	Diff. (mDa)	Diff. (ppm)	DBE
C36 H43 N3 Na O8	668.2948	668.2942	668.2938	0.4	0.5	16.5000

--- End Of Report ---

Agilent Technologies Page 1 of 1 Printed at: 4:43 PM on: 2/9/2015

Figure 46S: ^{1}H NMR spectrum of **6** (acetone-d_6, 600MHz).

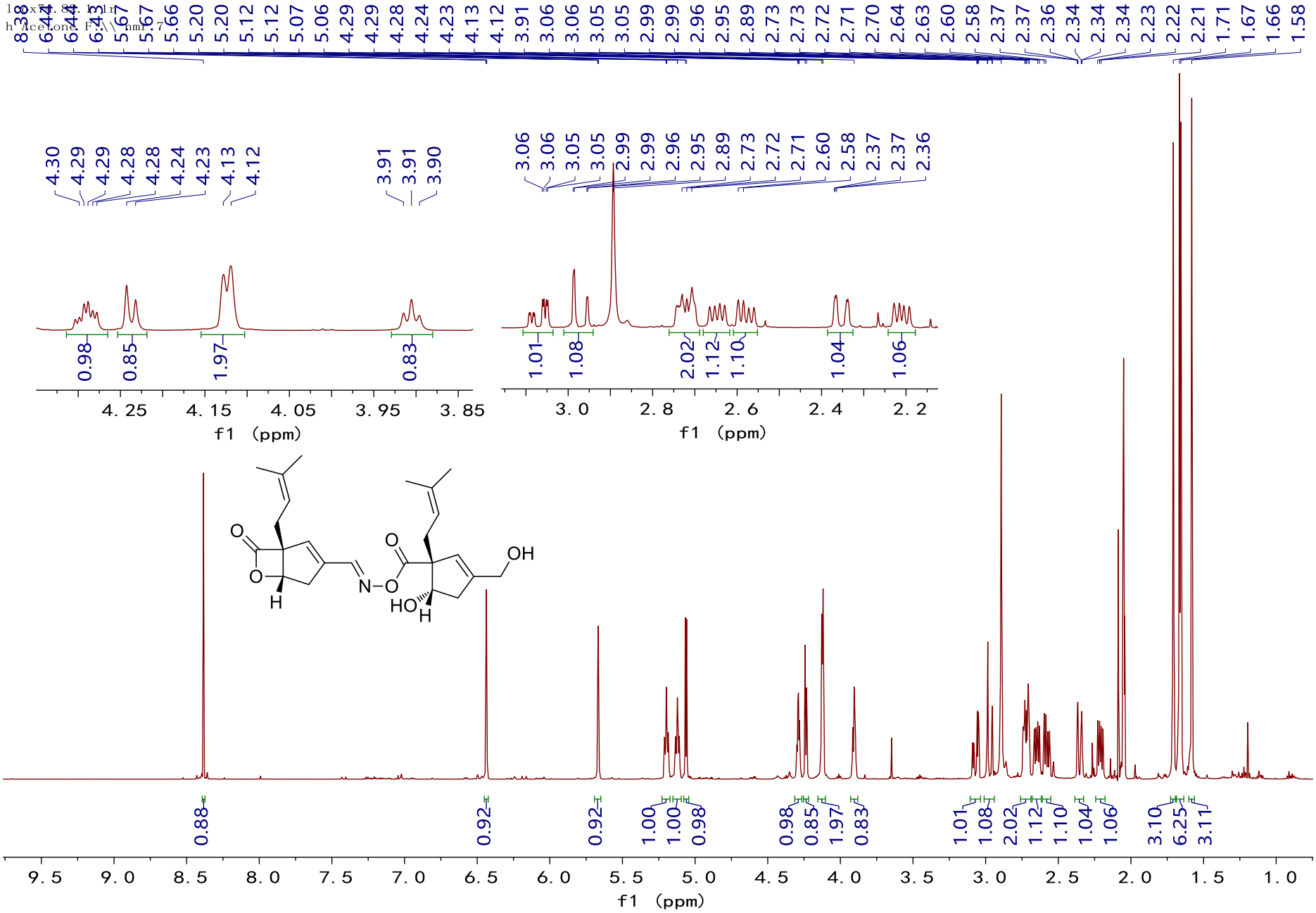


Figure 47S: ^{13}C NMR and DEPT spectra of **6** (acetone-d_6, 150MHz).

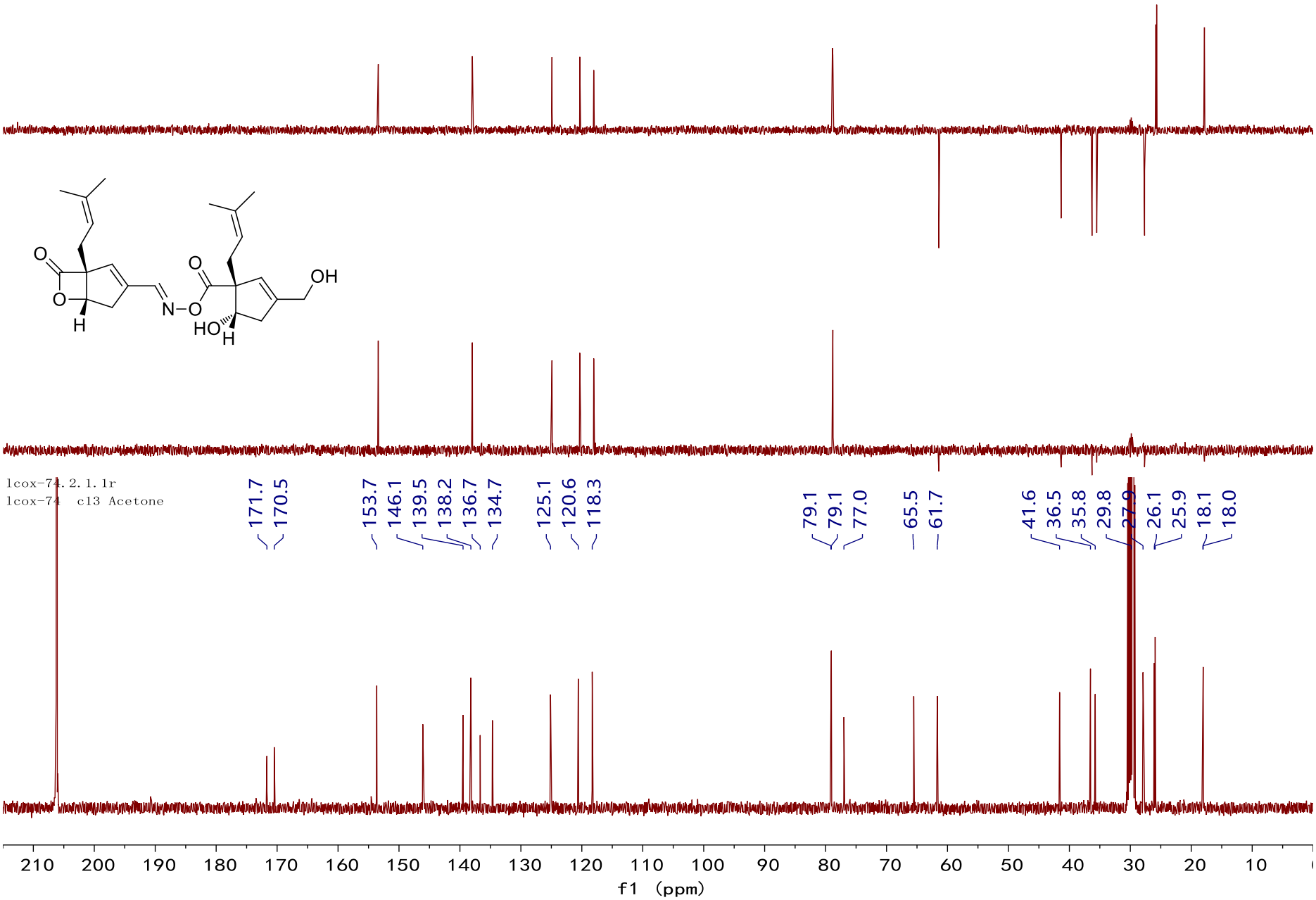


Figure 48S: HSQC spectrum of **6**.

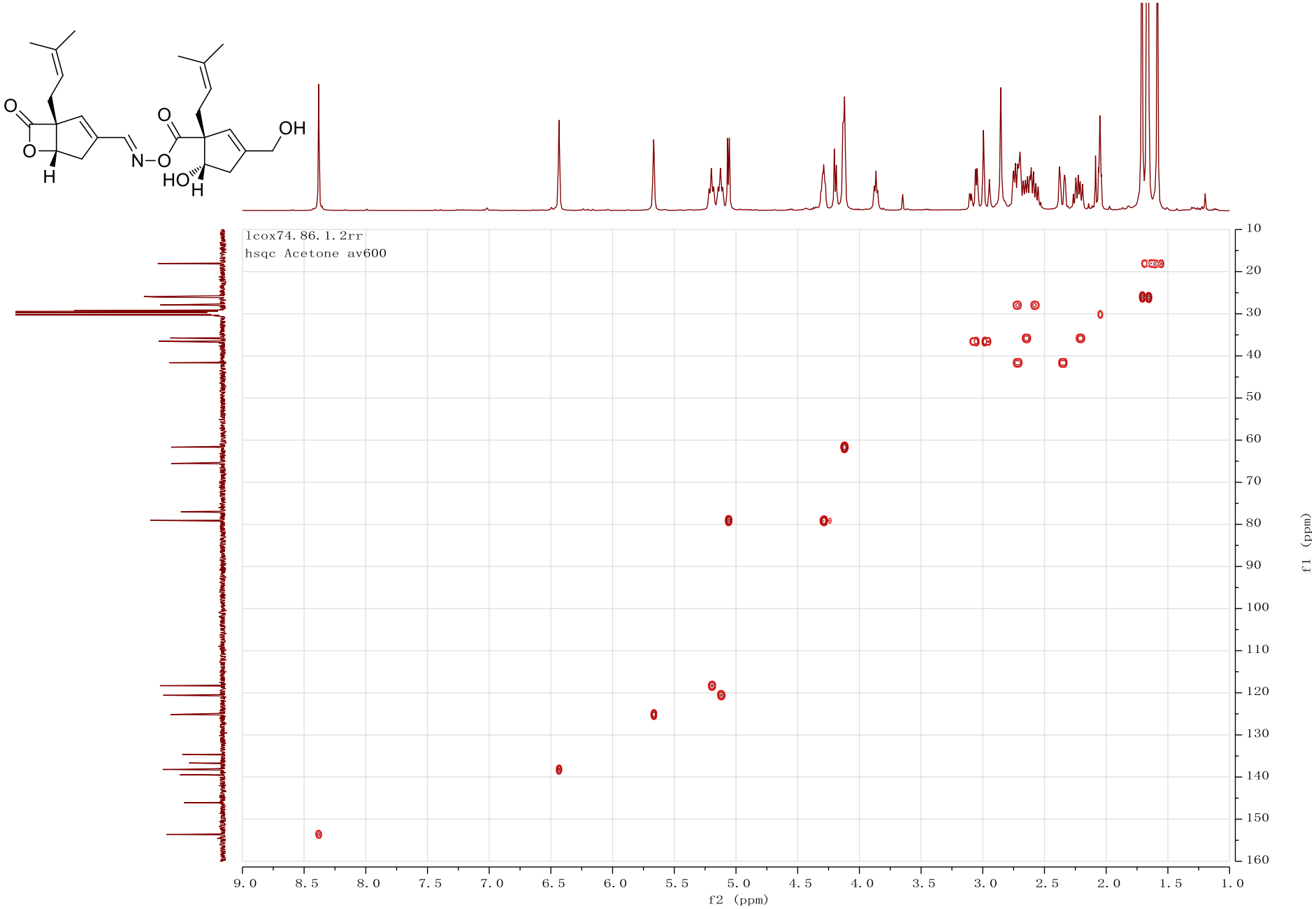


Figure 49S: ^{1}H-^{1}H COSYspectrum of **6**.

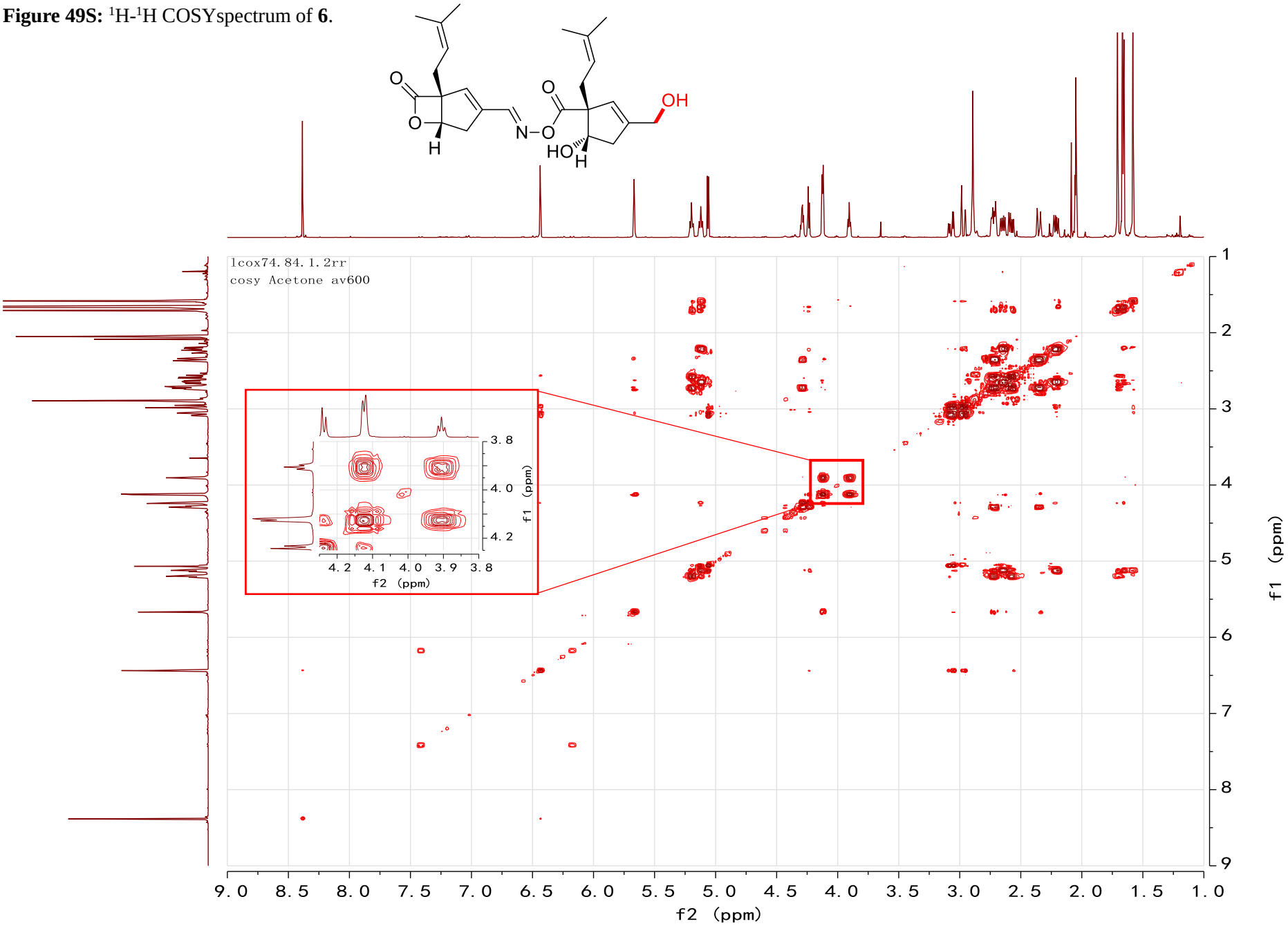


Figure 50S: HMBC spectrum of **6**.

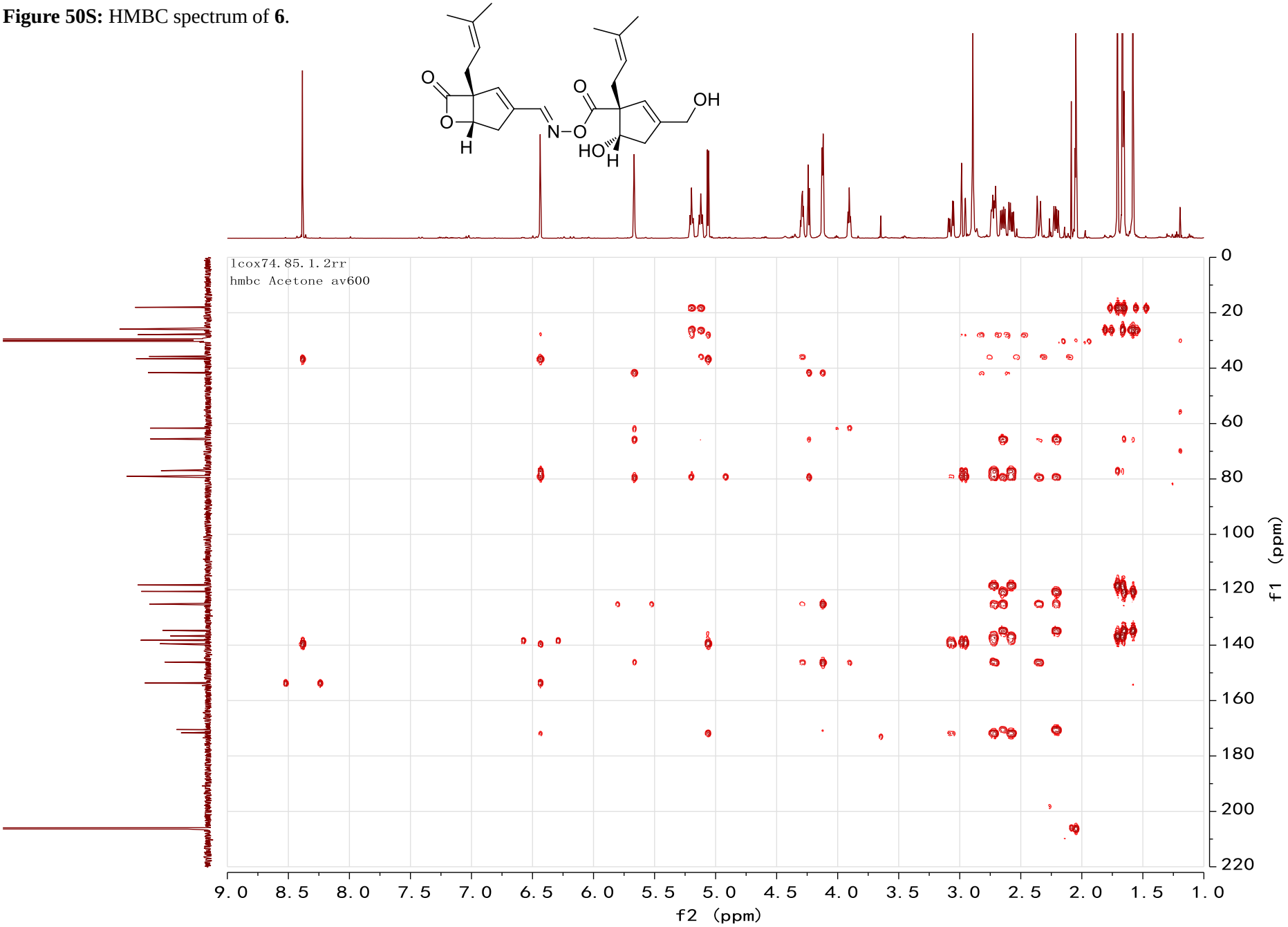


Figure 51S: Enlarged view of HMBC spectra of **6**.

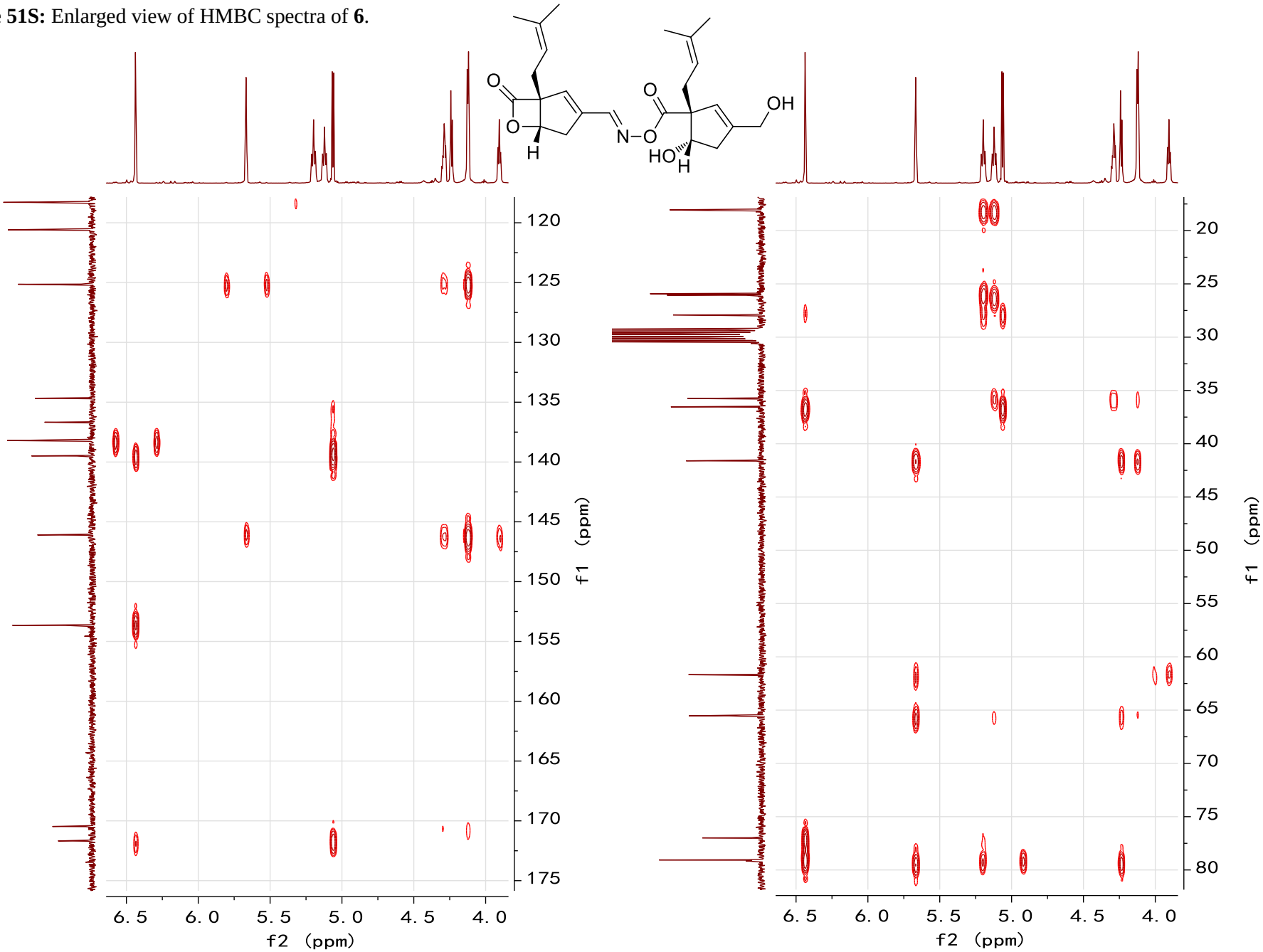


Figure 52S: ROESY spectrum of **6**.

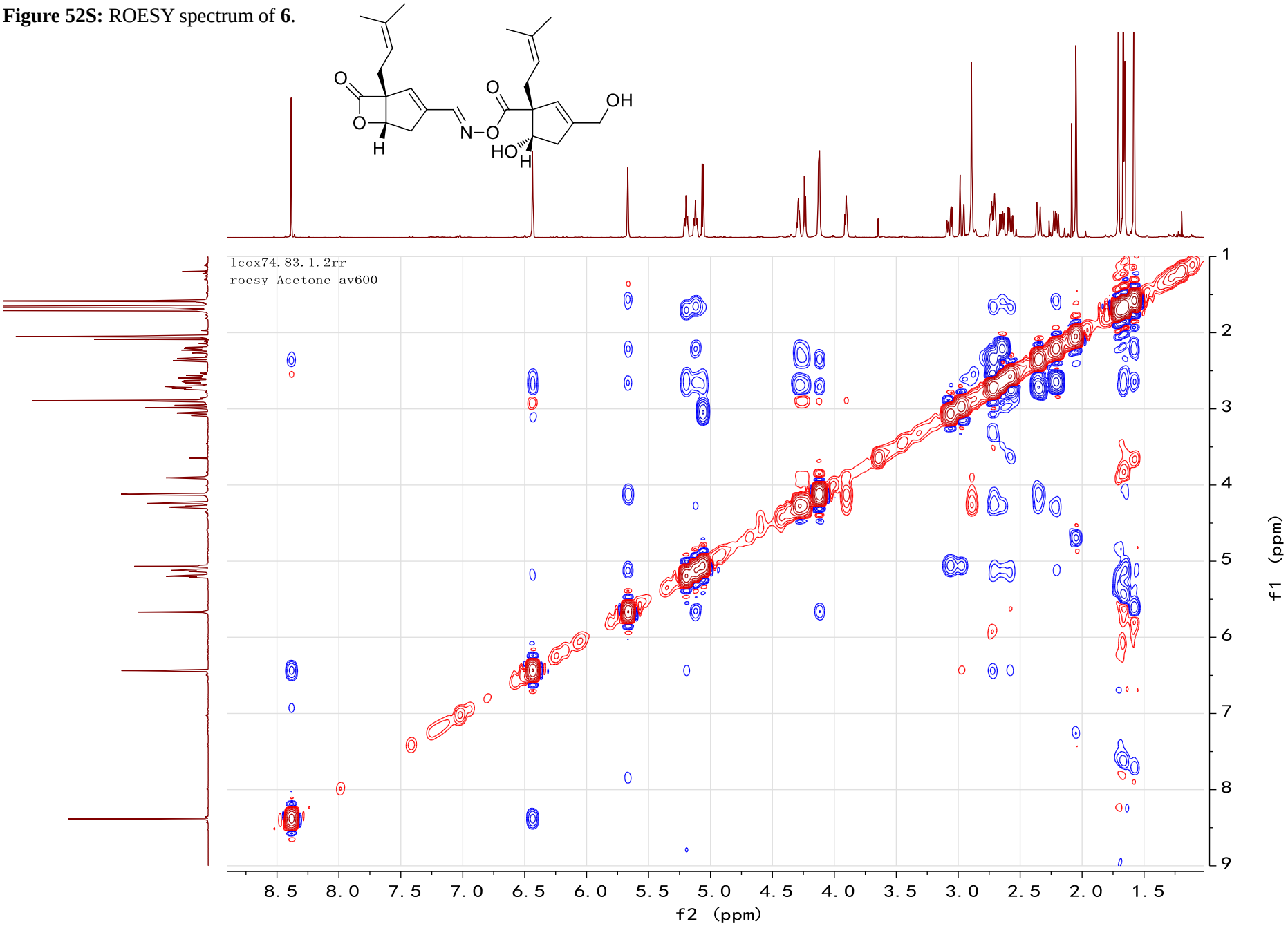


Figure 53S: HRESIMS spectrum of **6**.

Qualitative Analysis Report

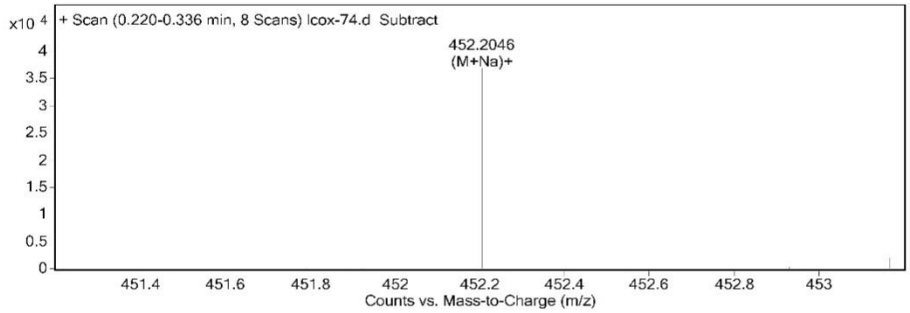
Data Filename	lcox-74.d	**Sample Name**	lcox-74
Sample Type	Sample	**Position**	P1-B7
Instrument Name	Instrument 1	**User Name**	
Acq Method	SIBU.m	**Acquired Time**	3/9/2015 10:34:24 AM
IRM Calibration Status	Success	**DA Method**	Default.m
Comment			

Sample Group **Info.**

Acquisition SW Version 6200 series TOF/6500 series Q-TOF B.05.01 (B5125.2)

User Spectra

Fragmentor Voltage	Collision Energy	Ionization Mode
135	0	ESI



Peak List

m/z	z	Abund	Formula	Ion
102.1279	1	93262.92		
103.1311	1	6175.42		
274.2742	1	15380.4		
301.1413	1	6937.4		
318.3003	1	21869.02		
340.2824	1	10073.84		
430.2231	1	11604.17		
452.2046	1	36882.11	C24 H31 N O6	(M+Na)+
453.2076	1	10524.28	C24 H31 N O6	(M+Na)+
468.1786	1	100357.7		
469.1818	1	28506.38		
470.1801	1	10598.65		
500.2042	1	18659.6		
881.4201	1	9003		
897.395	1	10103.26		

Formula Calculator Element Limits

Element	Min	Max
C	3	60
H	0	120
O	0	30
N	0	5

Formula Calculator Results

Formula	CalculatedMass	CalculatedMz	Mz	Diff. (mDa)	Diff. (ppm)	DBE
C24 H31 N O6	429.2151	452.2044	452.2046	-0.2	-0.4	10.0000

Agilent Technologies Page 1 of 2 Printed at: 8:19 AM on: 3/10/2015

--- End Of Report ---

Figure 54S: ^{1}H NMR spectrum of **7** (acetone-d_6, 600MHz).

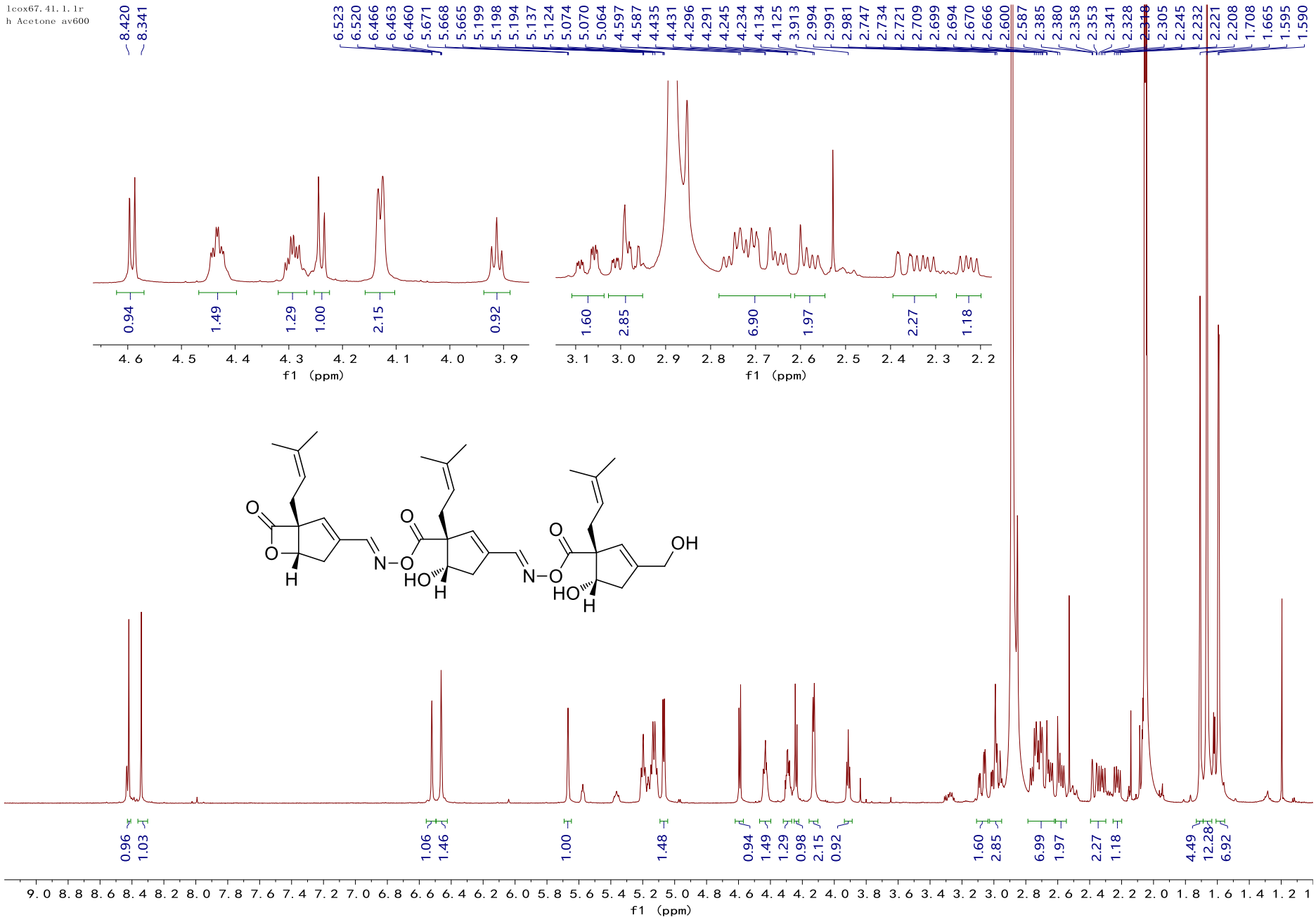


Figure 55S: ^{13}C NMR and DEPT spectra of **7** (acetone-d_6, 150MHz).

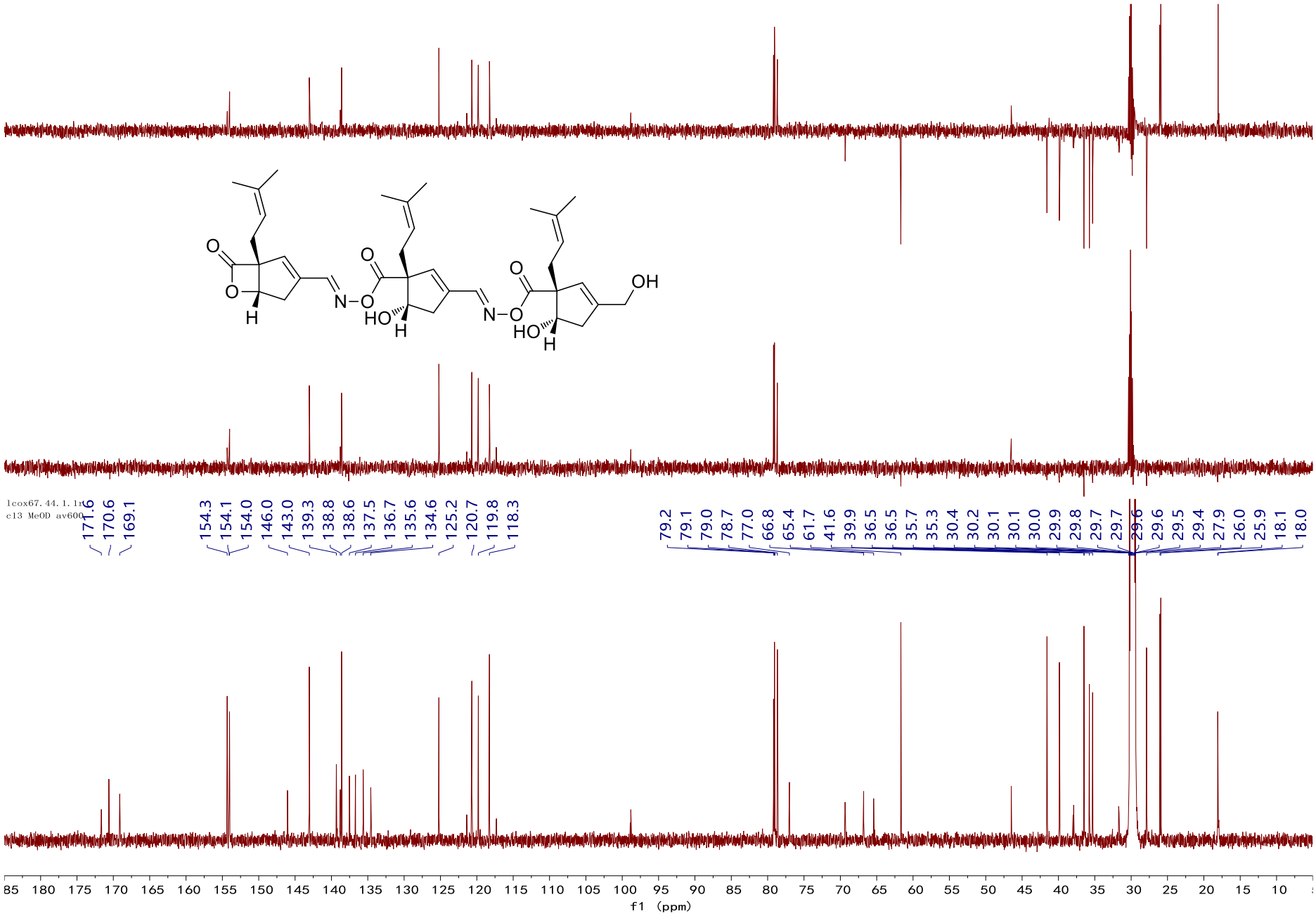


Figure 56S: HSQC spectrum of **7**.

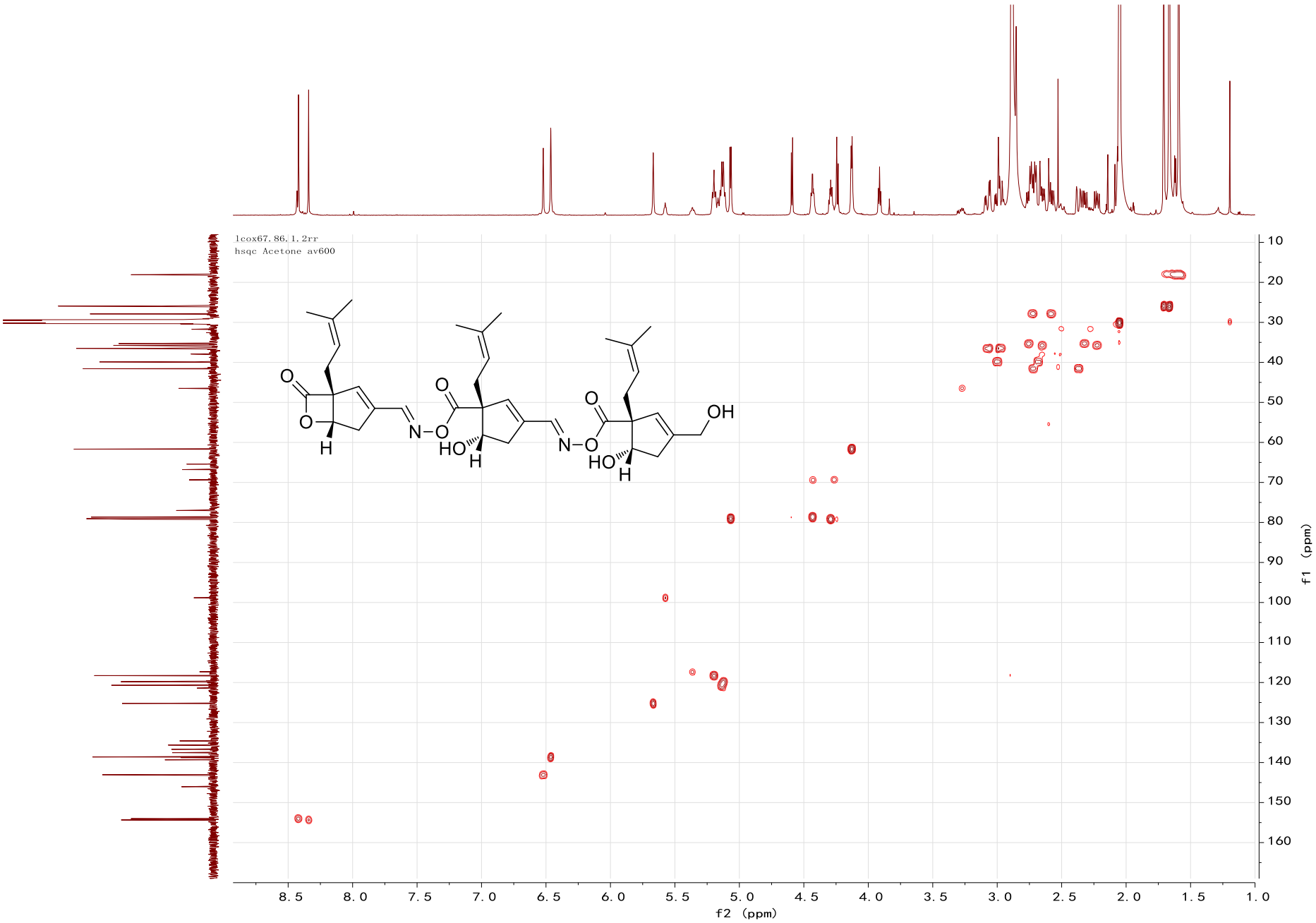


Figure 57S: ^{1}H-^{1}H COSY spectrum of **7**.

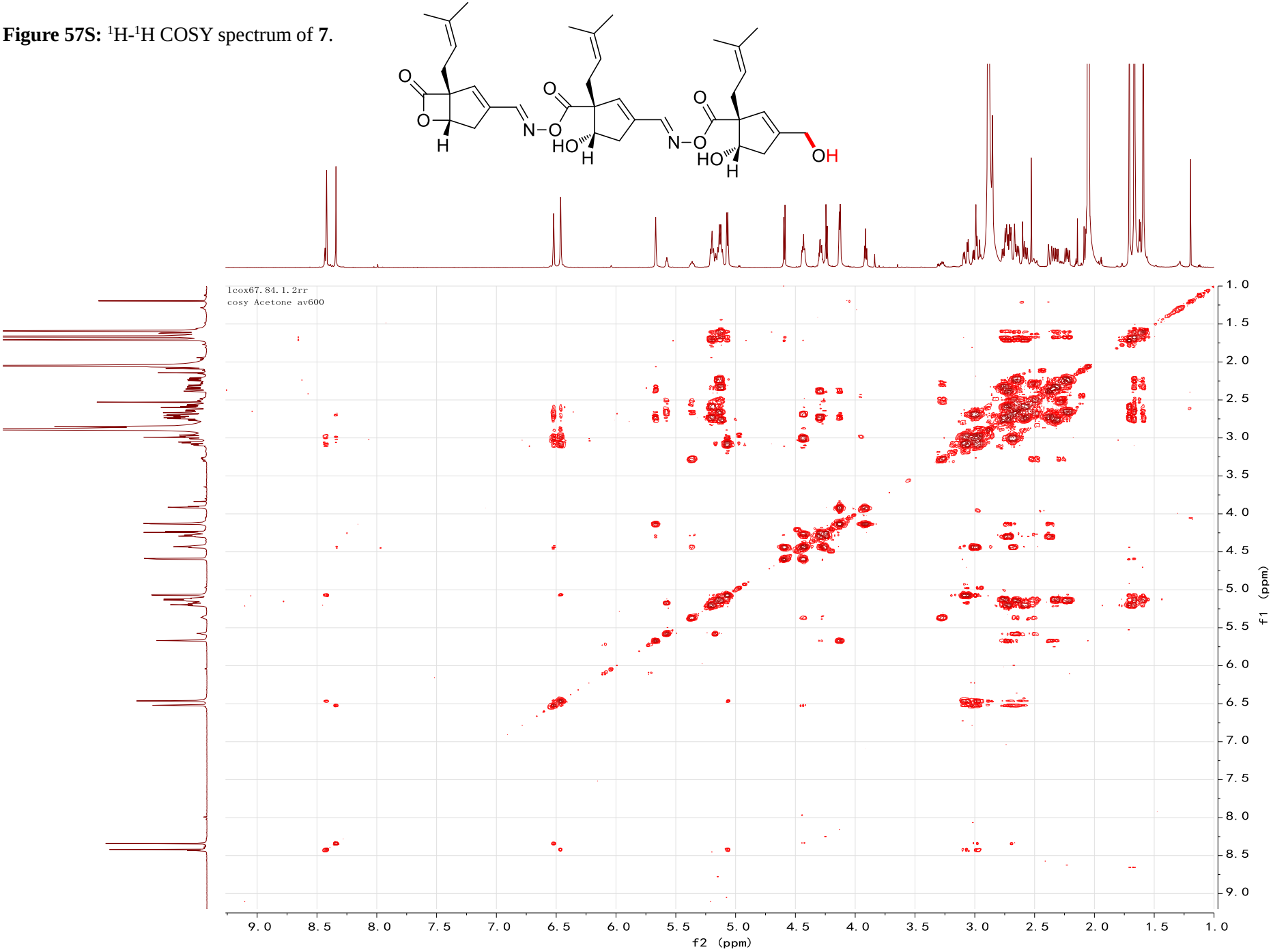


Figure 58S: Enlarged view of ^{1}H-^{1}H COSY spectrum.

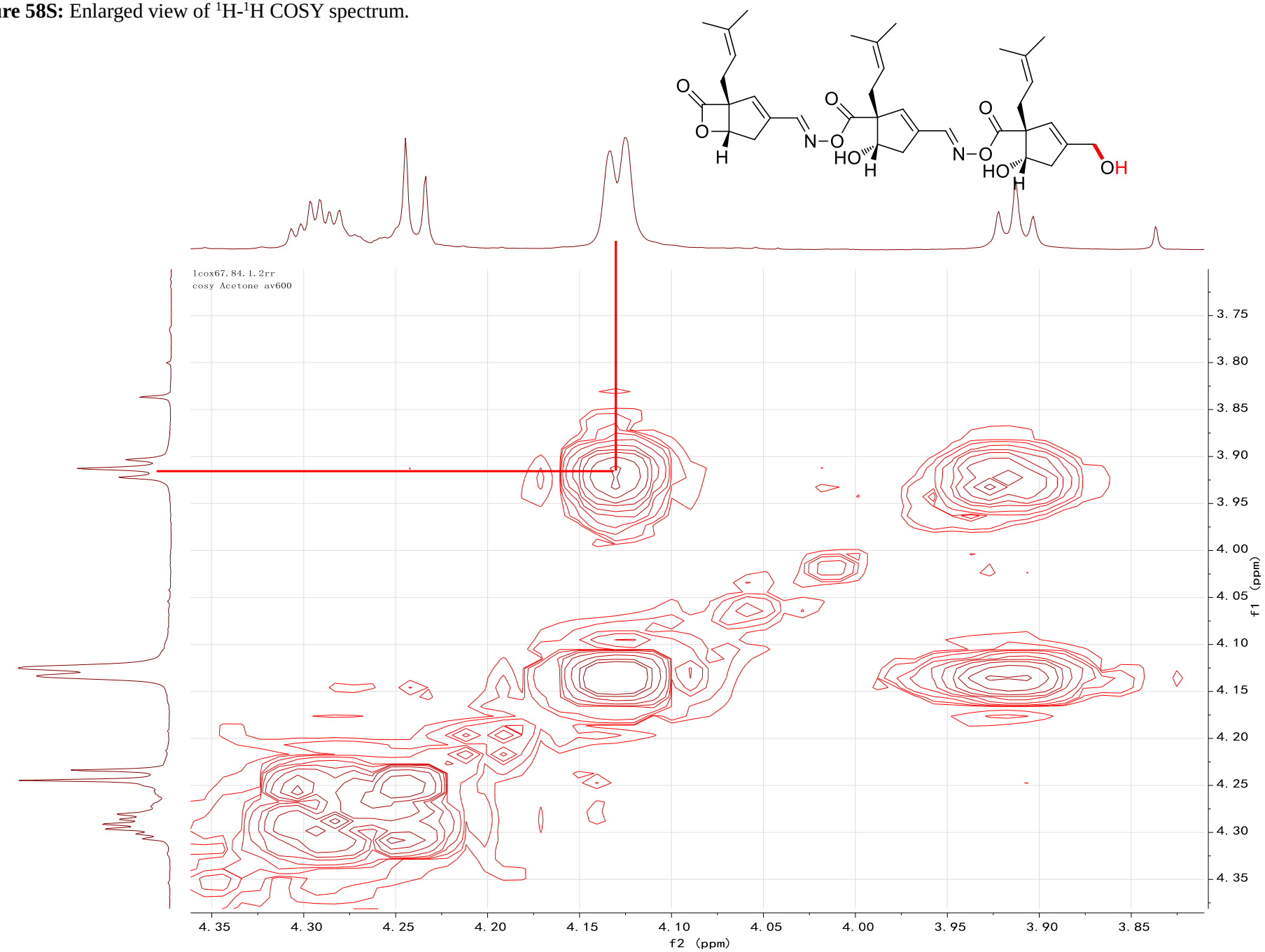


Figure 59S: HMBC spectrum of **7**.

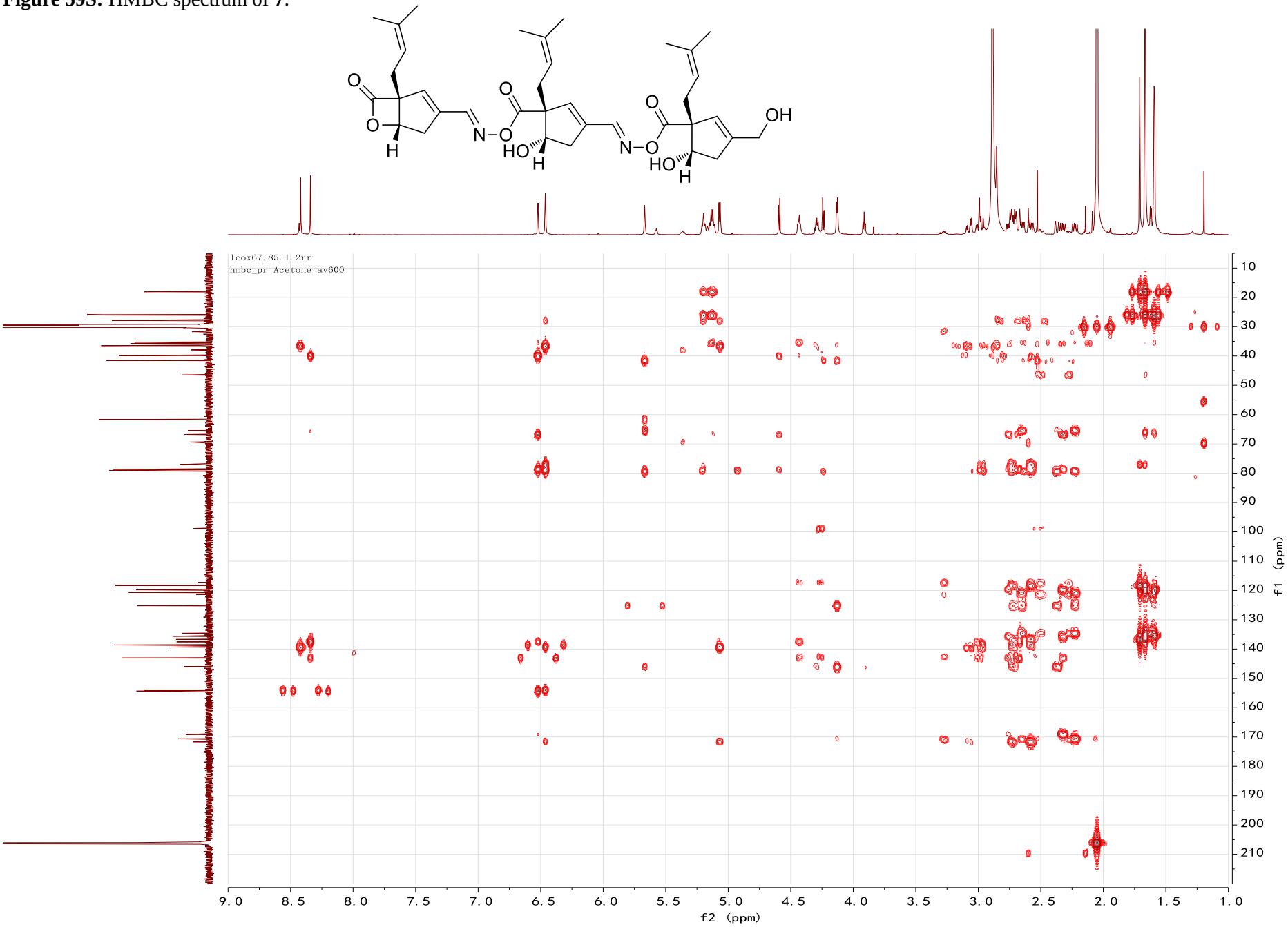


Figure 60S: ROESY spectrum of **7**.

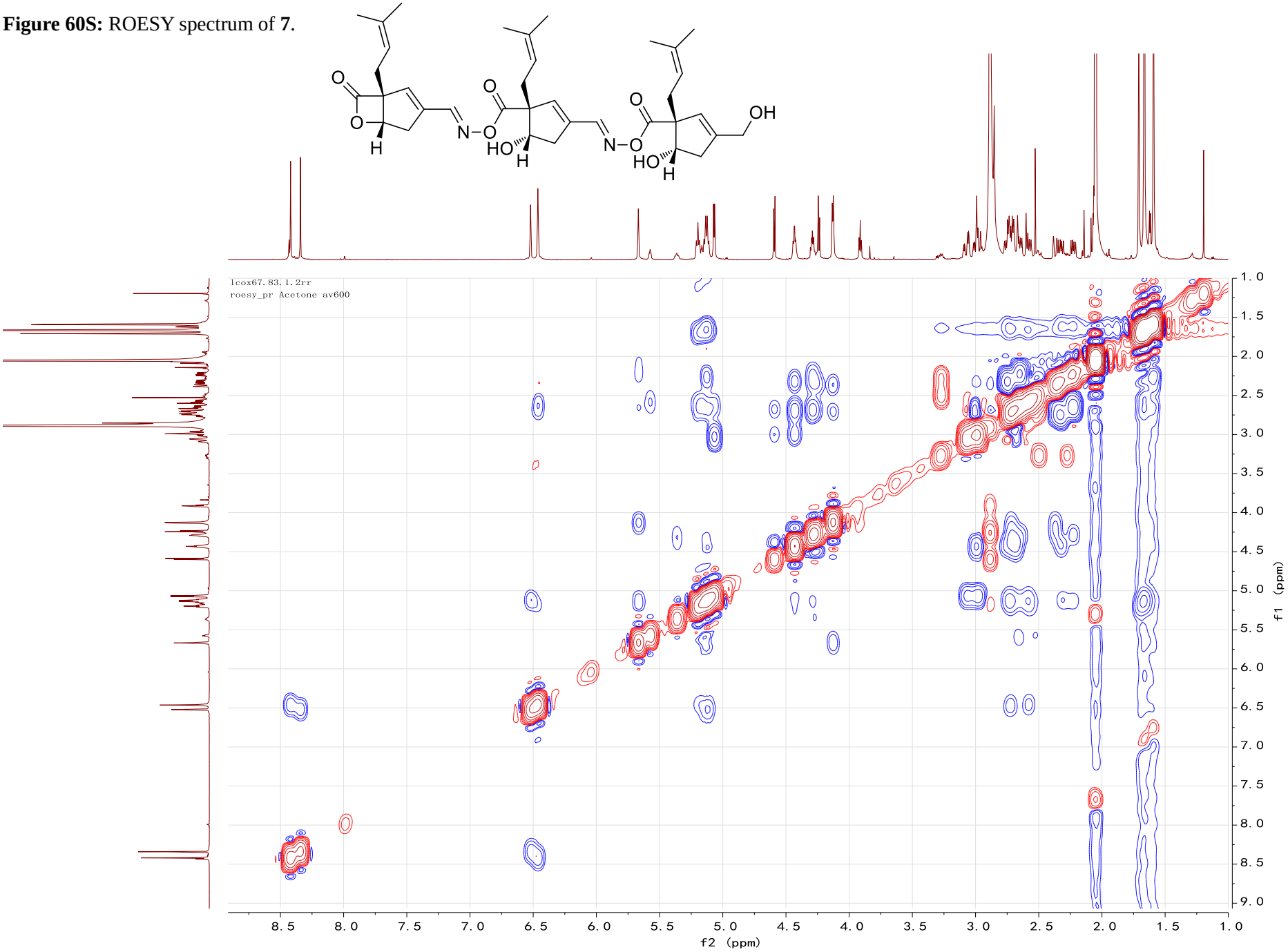


Figure 61S: HRESIMS spectrum of **7**.

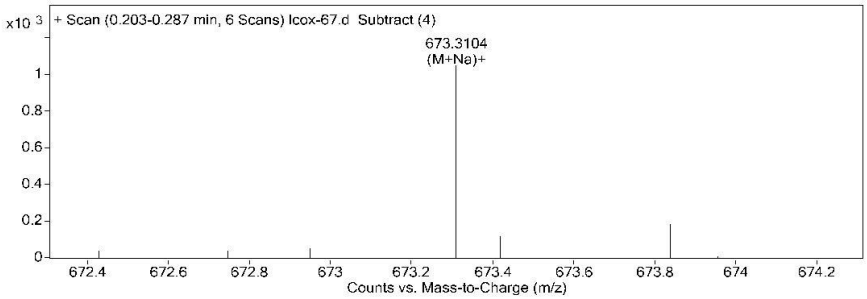
Qualitative Analysis Report

Data Filename	Icox-67.d	**Sample Name**	Icox-67
Sample Type	Sample	**Position**	P1-B5
Instrument Name	Instrument 1	**User Name**	
Acq Method	SIBU.m	**Acquired Time**	3/9/2015 10:29:39 AM
IRM Calibration Status	Success	**DA Method**	Default.m
Comment			

Sample Group		**Info.**
Acquisition SW Version	6200 series TOF/6500 series Q-TOF B.05.01 (B5125.2)	

User Spectra

Fragmentor Voltage	Collision Energy	Ionization Mode
135	0	ESI



Peak List

m/z	z	Abund	Formula	Ion
274.274	1	7256.5		
275.2774	1	1445.26		
296.2561		2391.28		
318.2999	1	6337.43		
319.3036	1	1533.73		
340.2821		2261.19		
384.3075		1078.58		
411.0943		1458.01		
427.0686	1	1445.7		
452.205		1404.92		
468.1782	1	5010.77		
469.1817	1	1631.39		
673.3104	1	1046.02	C36 H46 N2 O9	(M+Na)+
689.2841	1	2269.47		
690.2864	1	1062.86		

Formula Calculator Element Limits

Element	Min	Max
C	3	60
H	0	120
O	0	30
N	0	5

Formula Calculator Results

Formula	CalculatedMass	CalculatedMz	Mz	Diff. (mDa)	Diff. (ppm)	DBE
C36 H46 N2 O9	650.3203	673.3096	673.3104	-1.6	-2.4	15.0000

--- End Of Report ---

Agilent Technologies

Page 1 of 1

Printed at: 3:10 PM on: 3/9/2015

Figure 62S: ^{1}H NMR spectrum of **8** (acetone-d_6, 600MHz).

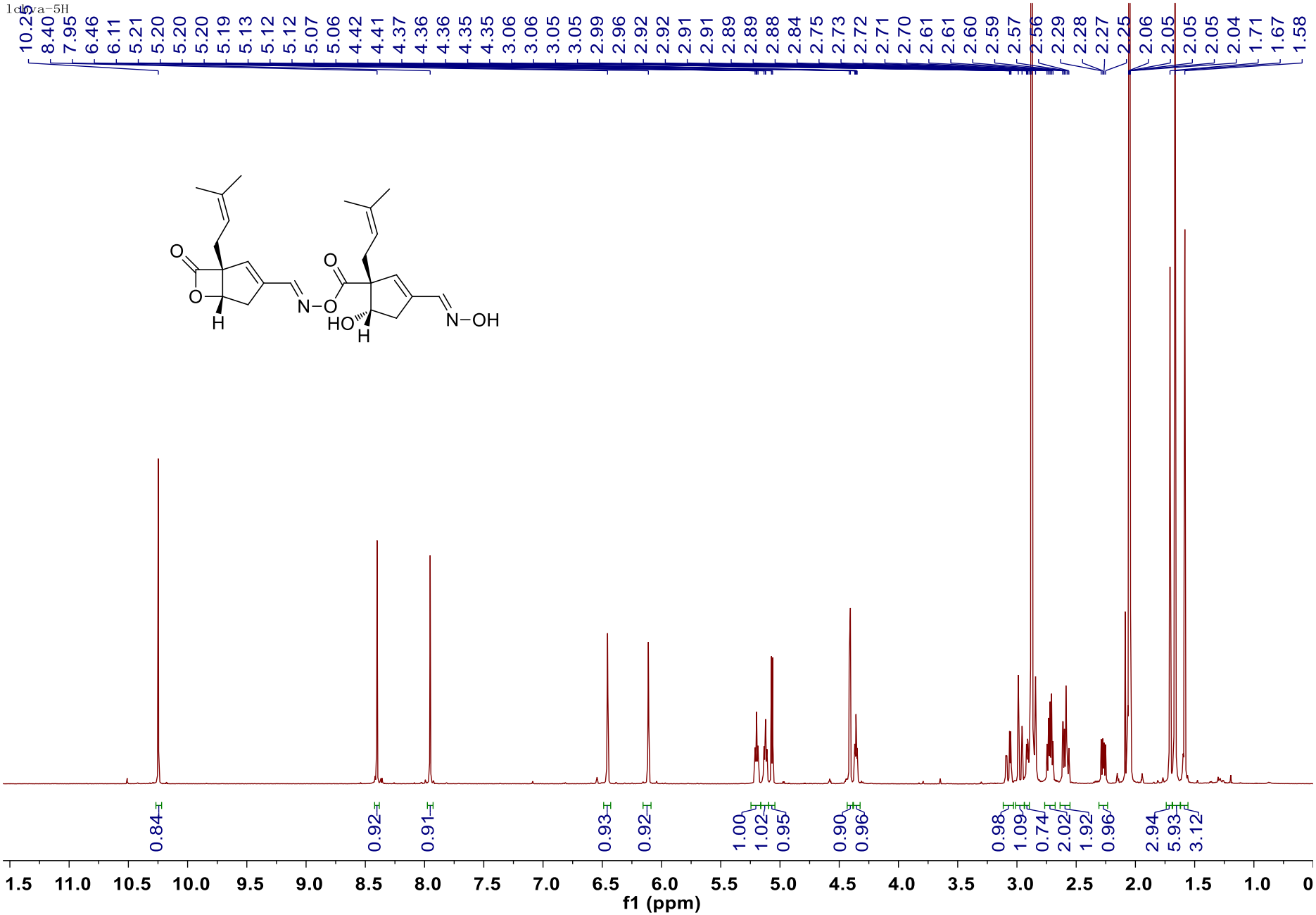


Figure 63S: ^{13}C NMR and DEPT spectra of **8** (acetone-d_6, 150MHz).

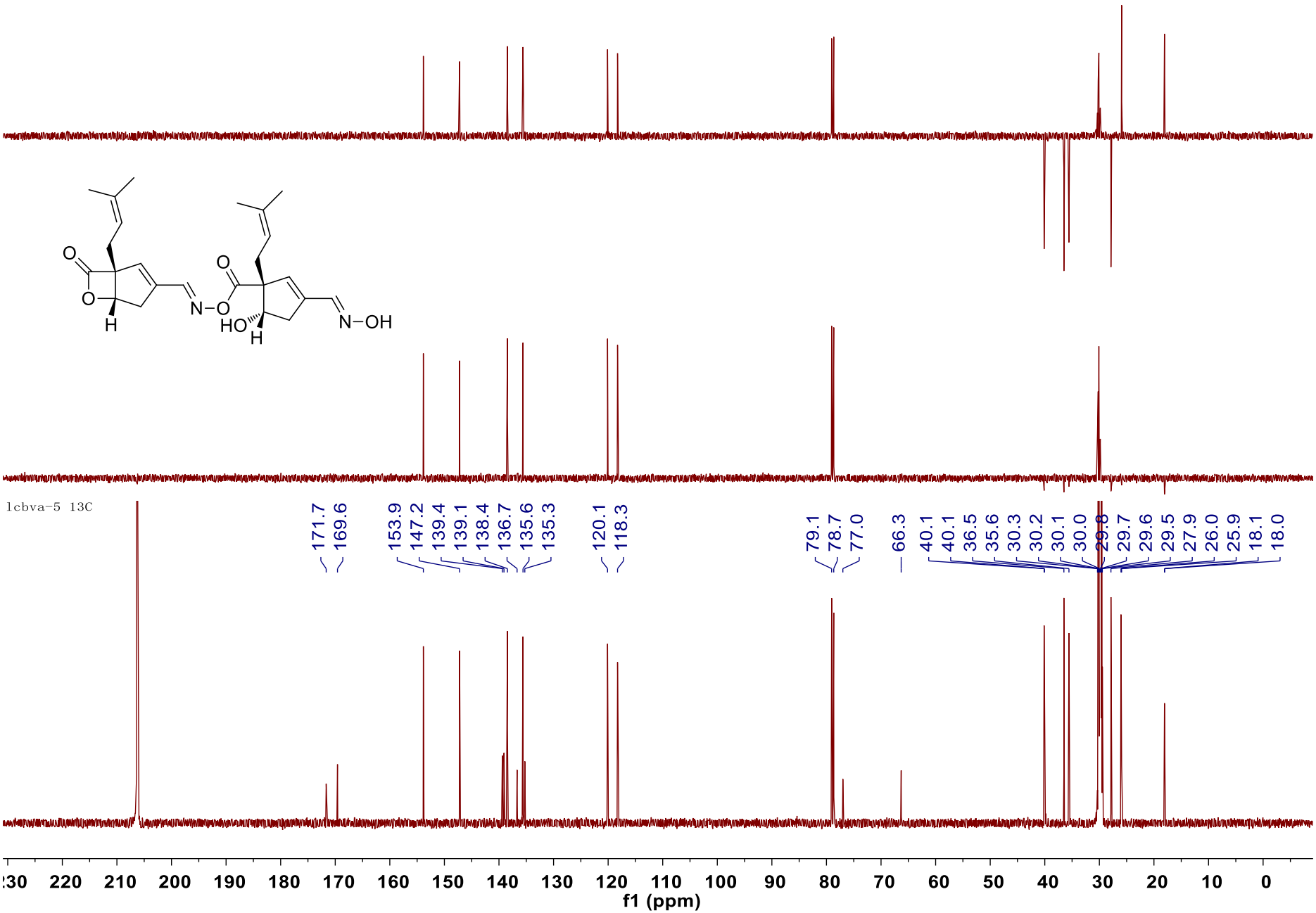


Figure 64S: HSQC spectrum of **8**.

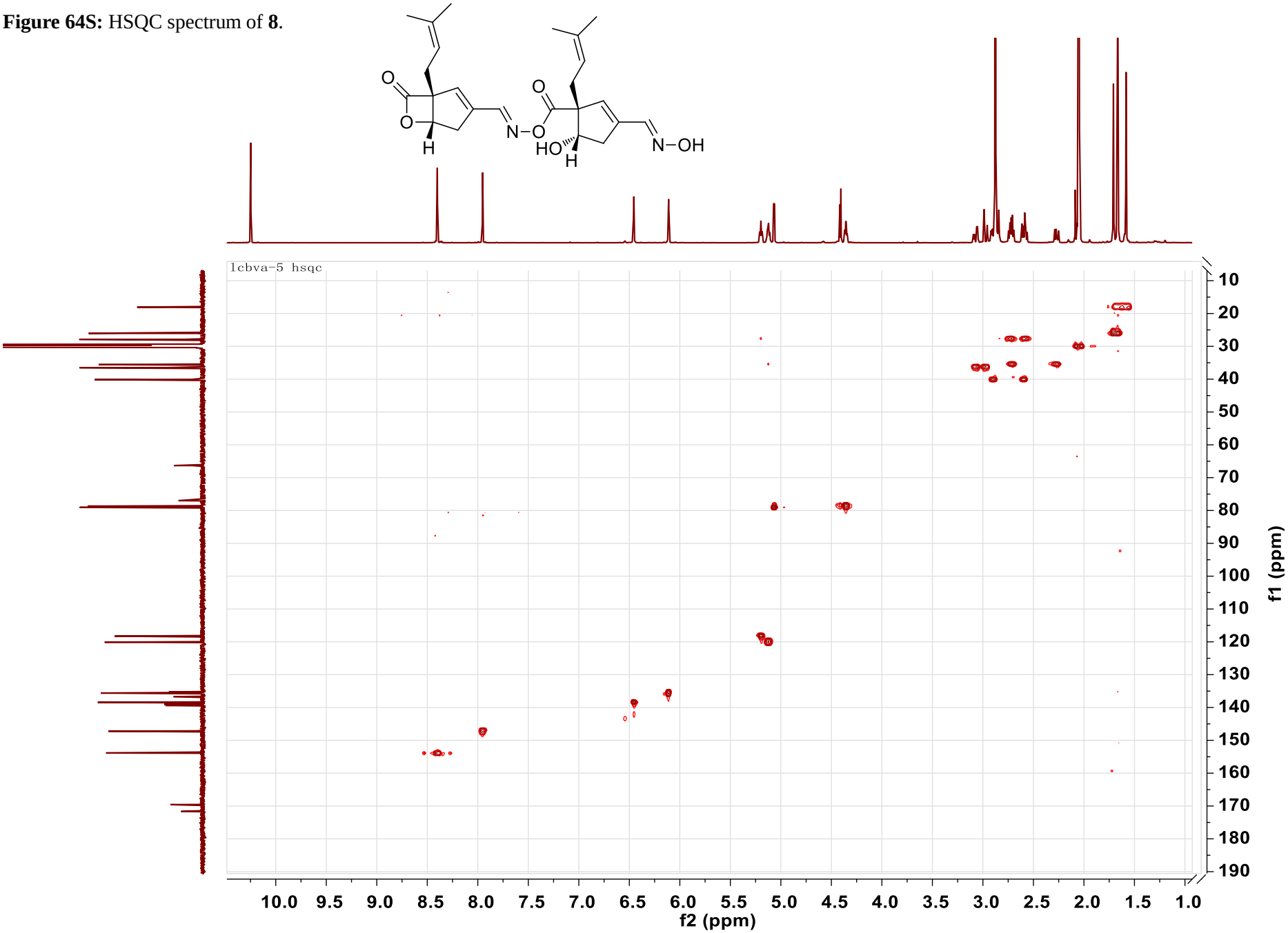


Figure 65S: ^{1}H-^{1}H COSYspectrum of **8**.

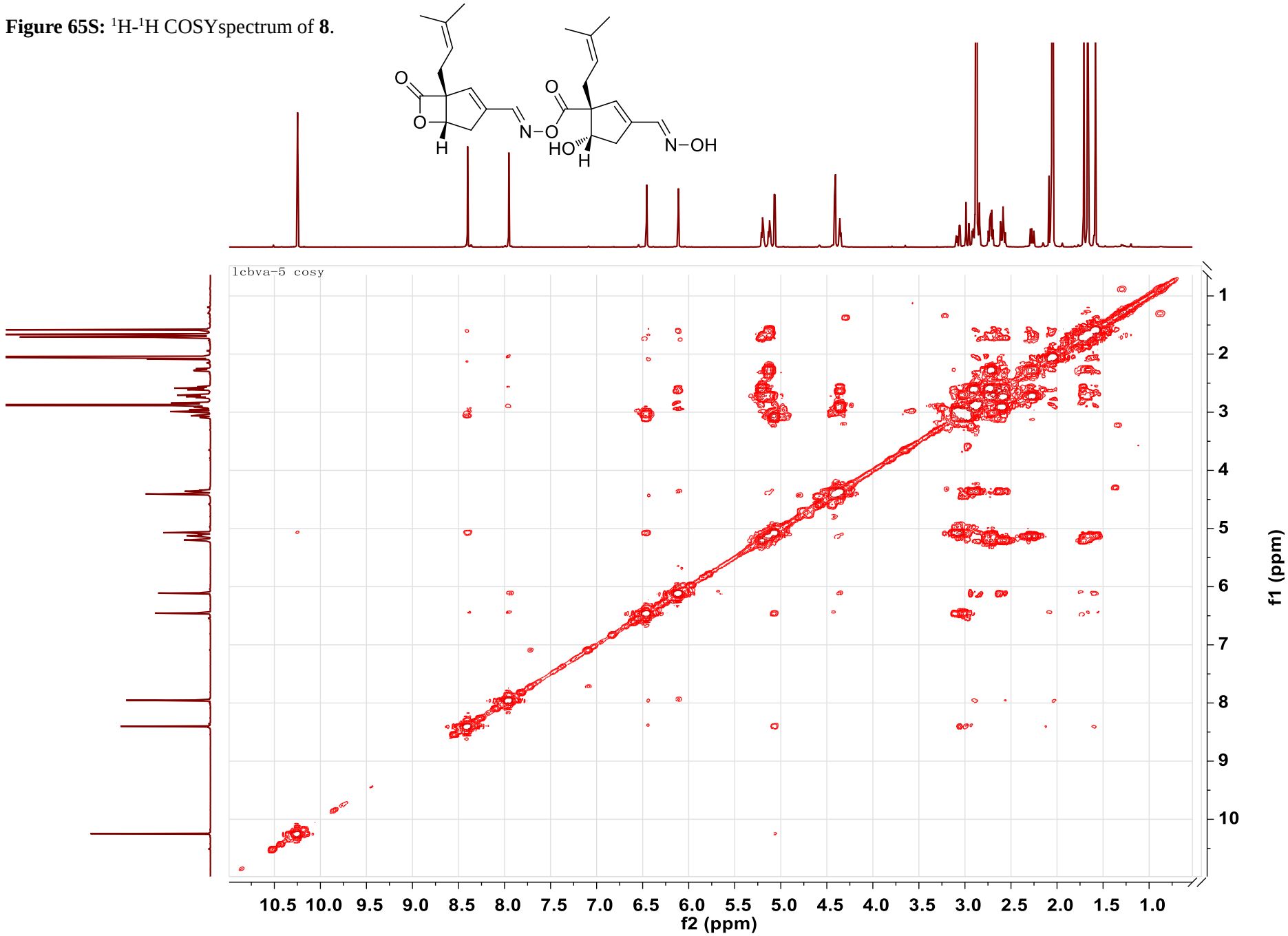


Figure 66S: HMBC spectrum of **8**.

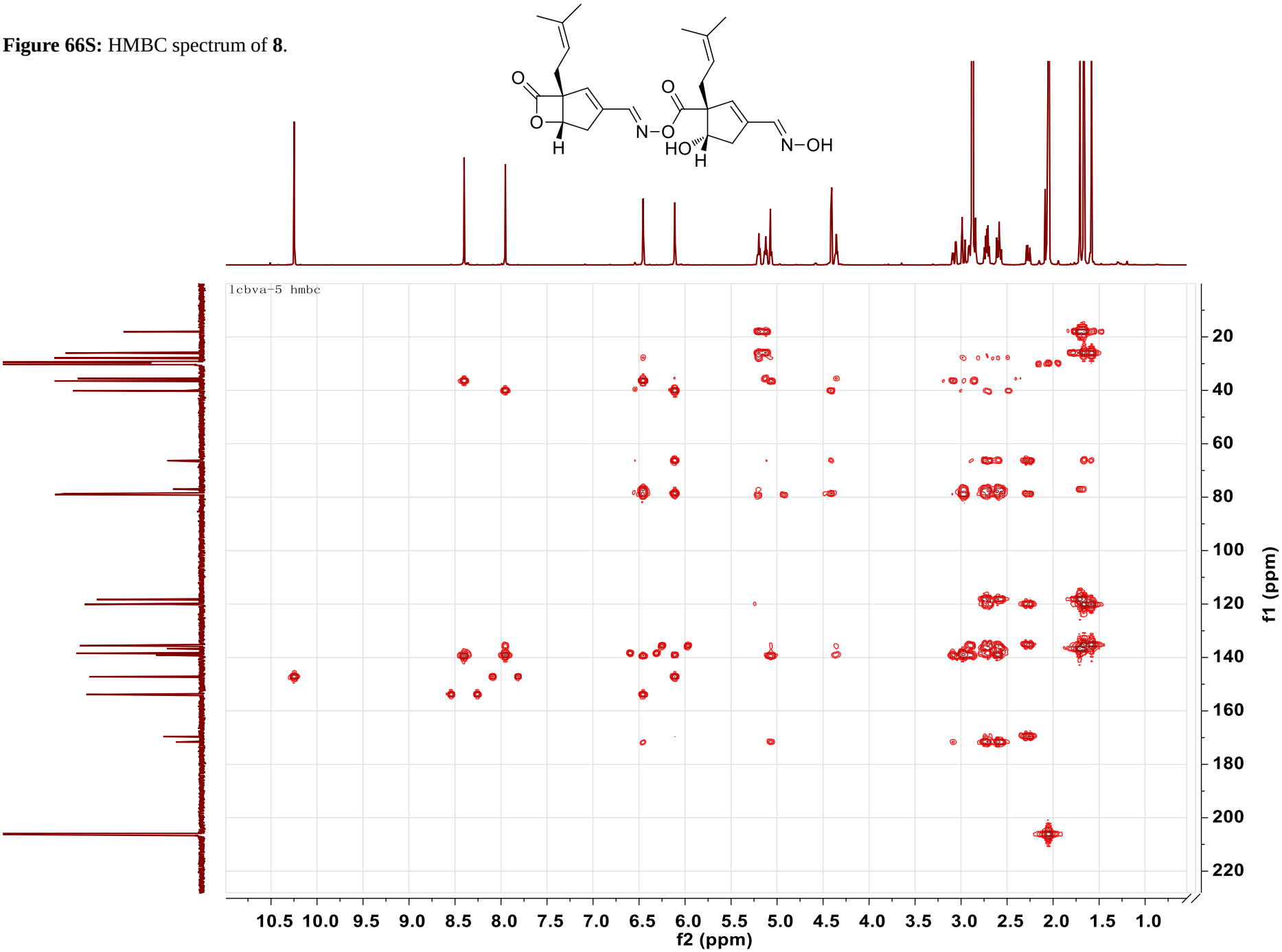


Figure 67S: ROESY spectrum of **8**.

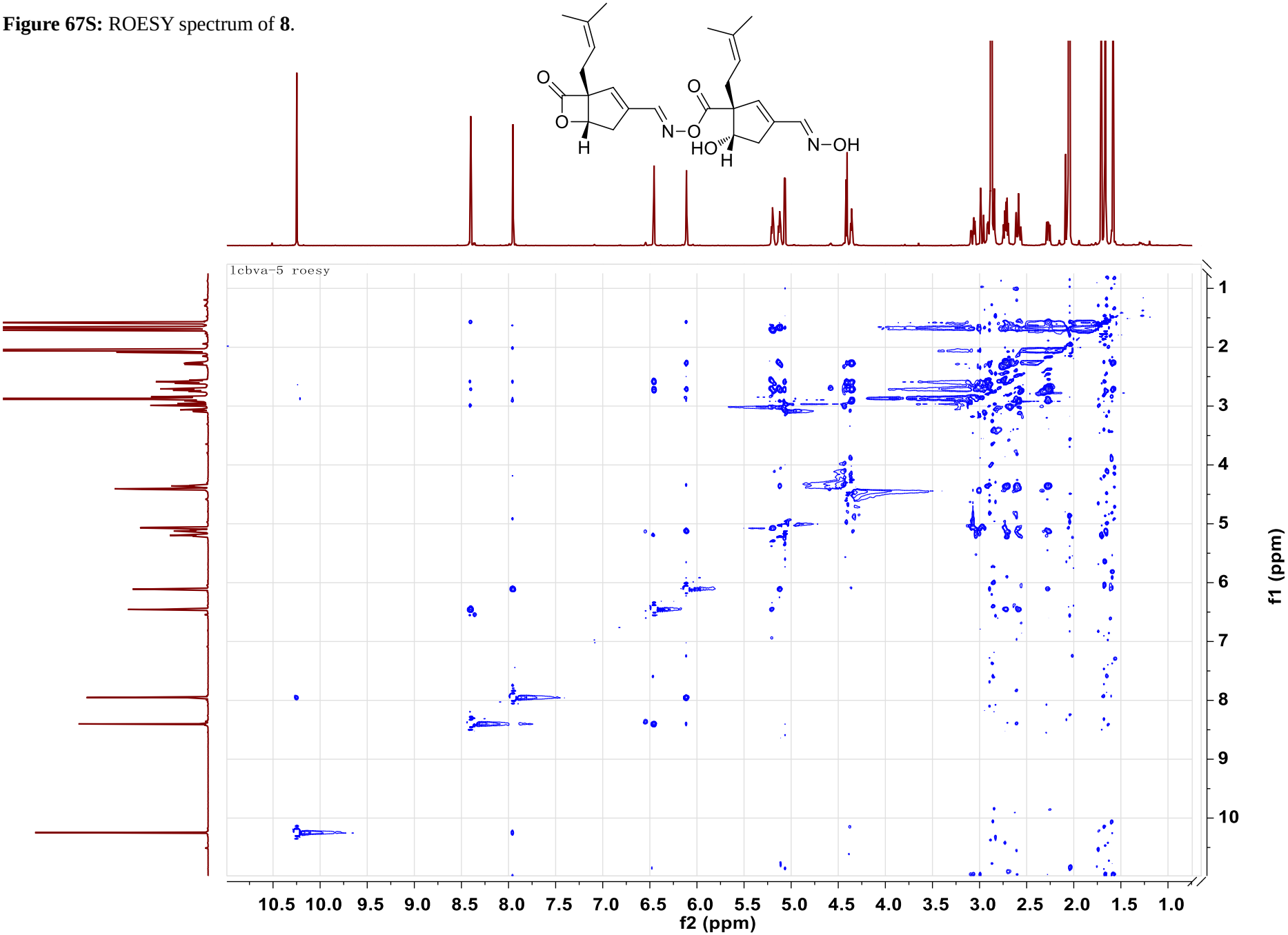


Figure 68S: HREIMS spectrum of **8**.

Elemental Composition Report **Page 1**

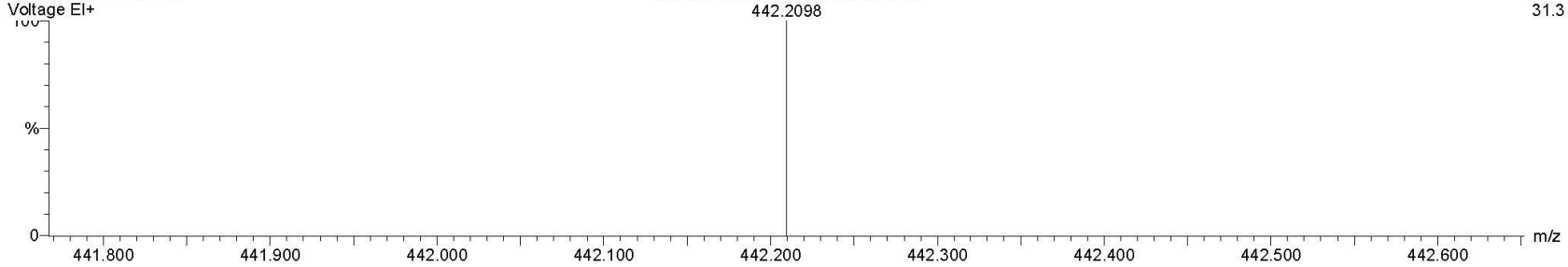
Single Mass Analysis
Tolerance = 10.0 PPM / DBE: min = -10.0, max = 120.0
Selected filters: None

Monoisotopic Mass, Odd and Even Electron Ions
18 formula(e) evaluated with 1 results within limits (up to 51 closest results for each mass)
Elements Used:
C: 0-200 H: 0-400 N: 2-2 O: 5-7

lcbva-5
15:17:29 31-Dec-2013
Voltage EI+

KIB
M131231EA-05AFAMM 27 (2.479)
442.2098

Autospec Premier
P776
31.3



Minimum:				-10.0		
Maximum:		200.0	10.0	120.0		
Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	Formula
442.2098	442.2104	-0.6	-1.4	11.0	5546034.0	C24 H30 N2 O6

Figure 69S: ^{1}H NMR spectrum of **9** (acetone-d_6, 600MHz).

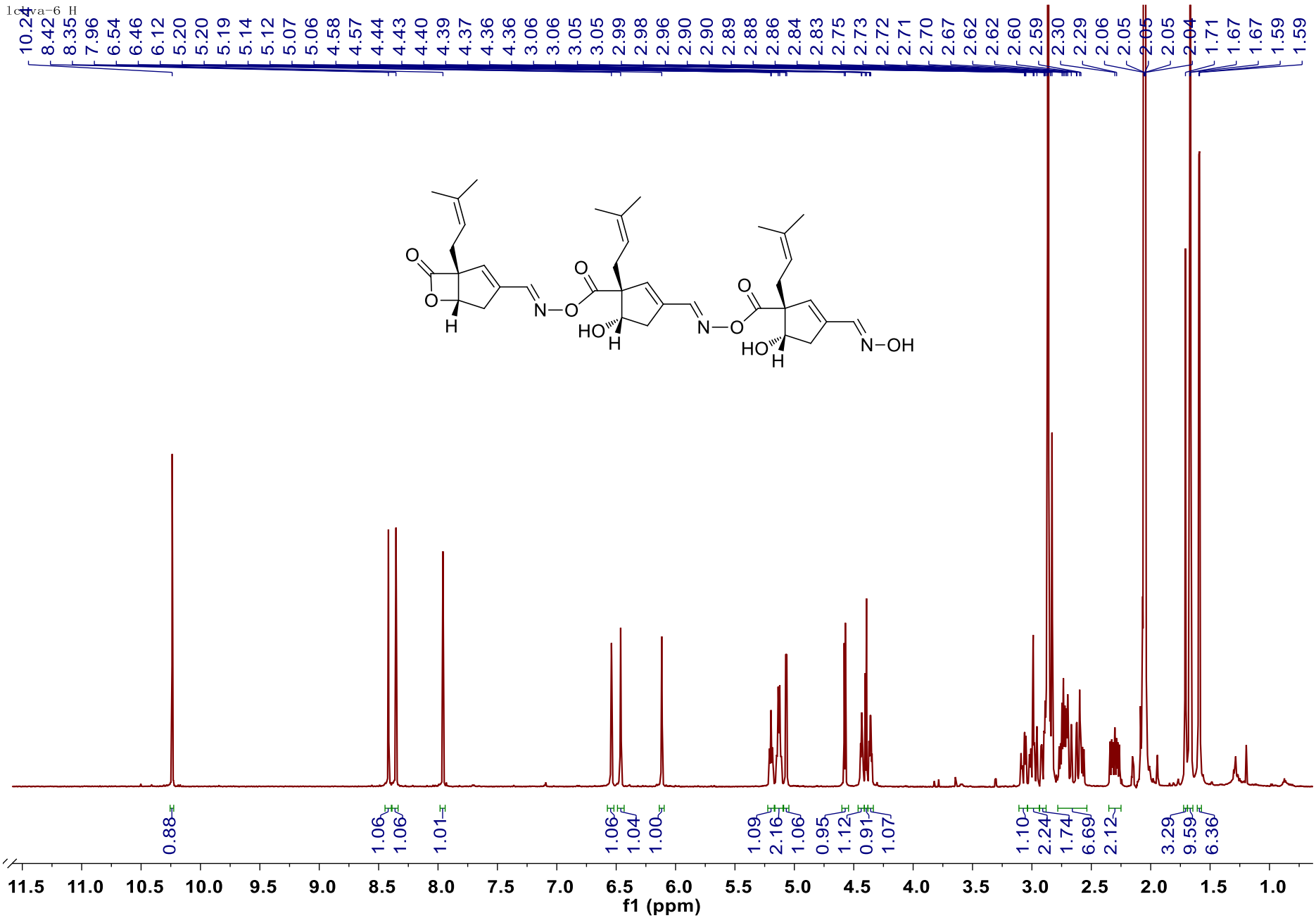


Figure 70S: ^{13}C NMR and DEPT spectra of **9** (acetone-d_6, 150MHz).

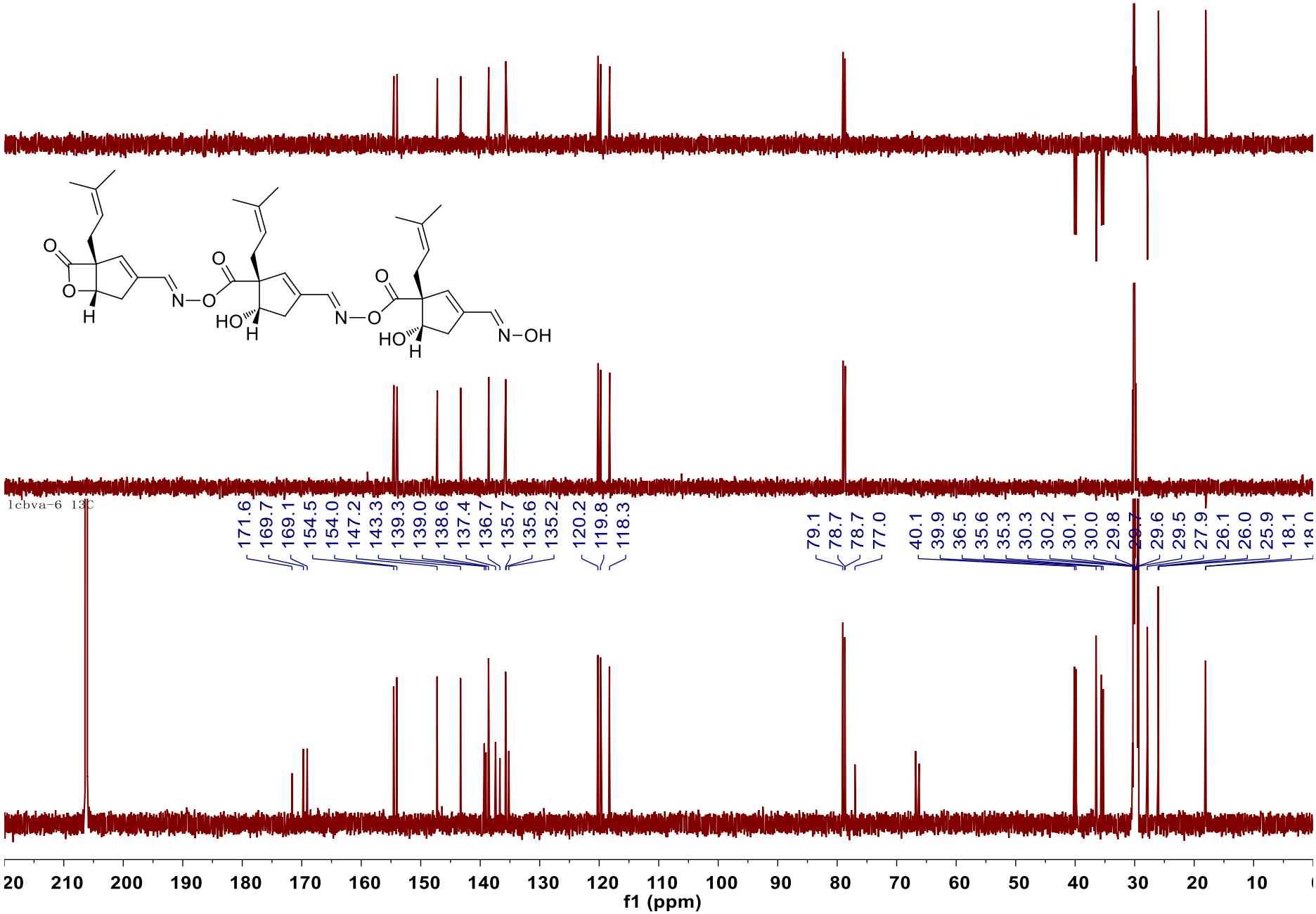


Figure 71S: HSQC spectrum of **9**.

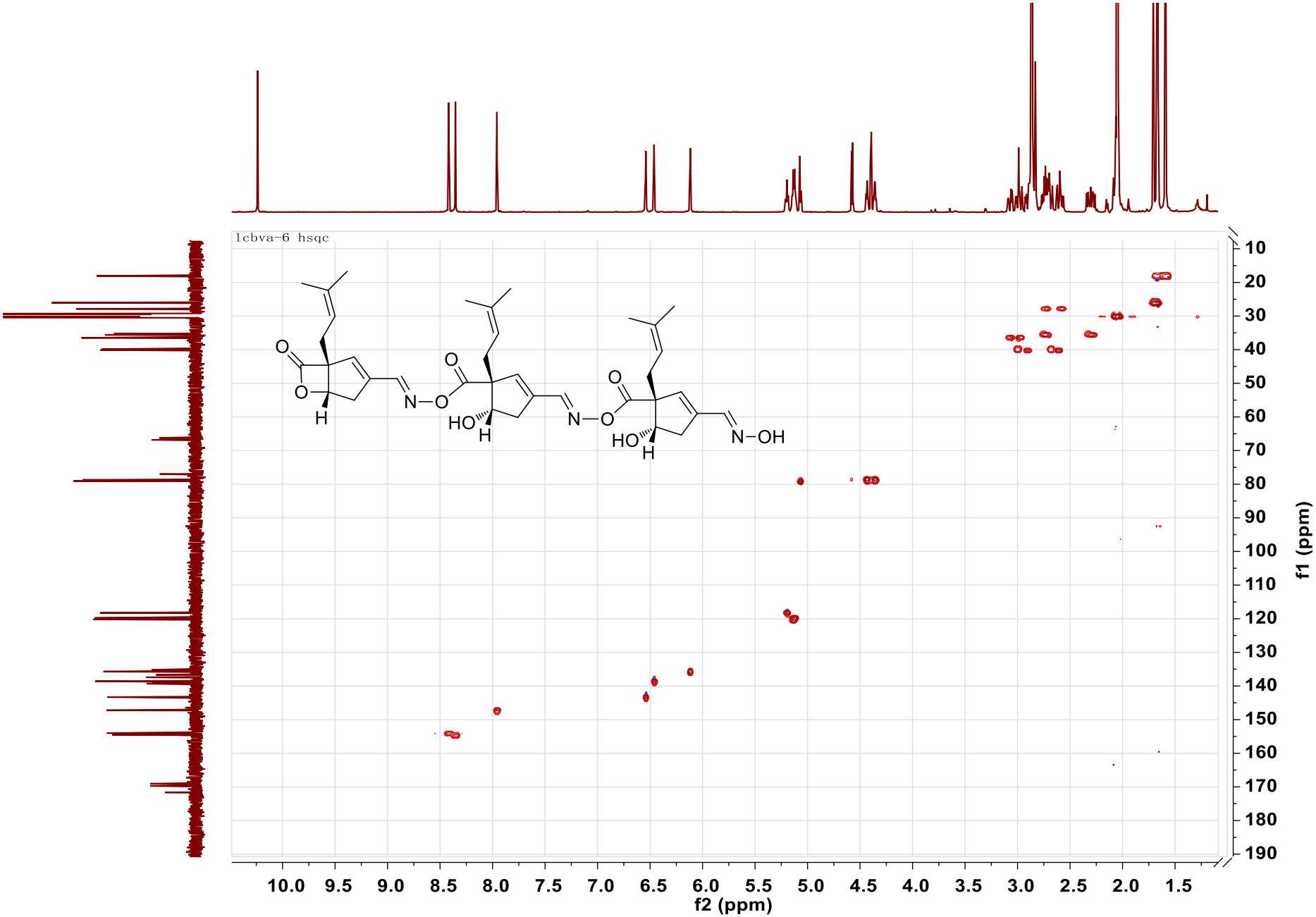


Figure 72S: ^{1}H-^{1}H COSY spectrum of **9**.

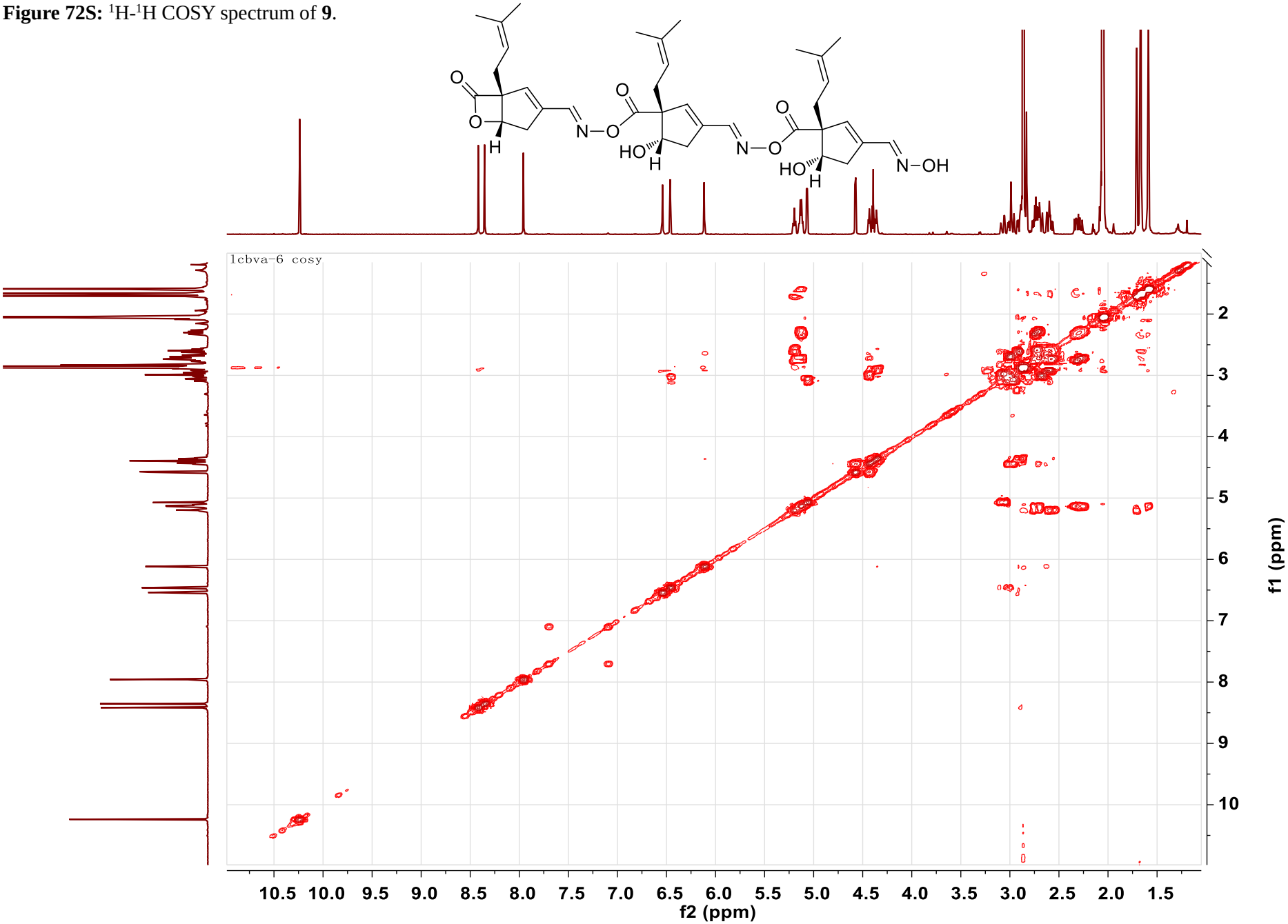


Figure 73S: HMBC spectrum of **9**.

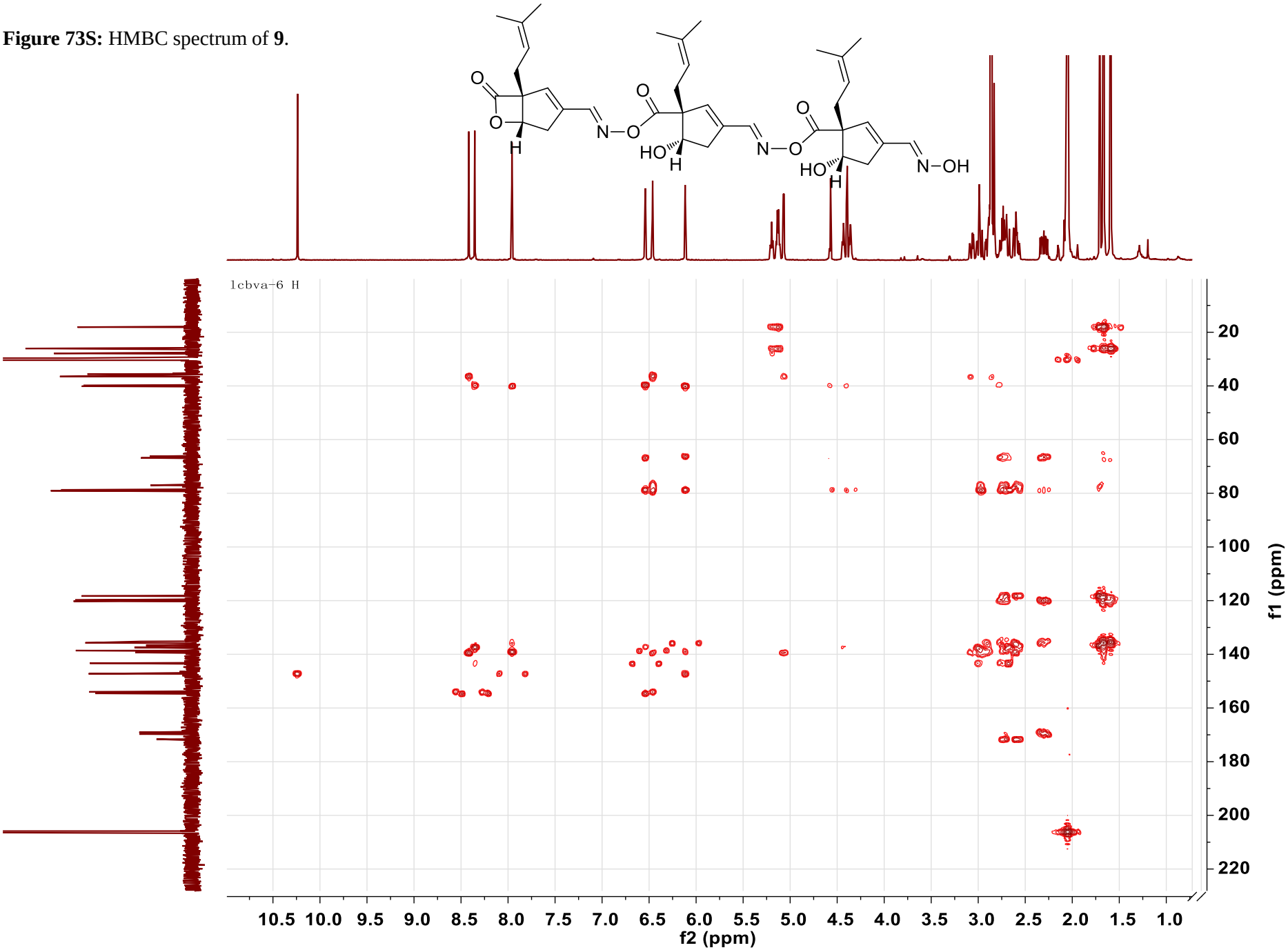


Figure 74S: ROESY spectrum of **9**.

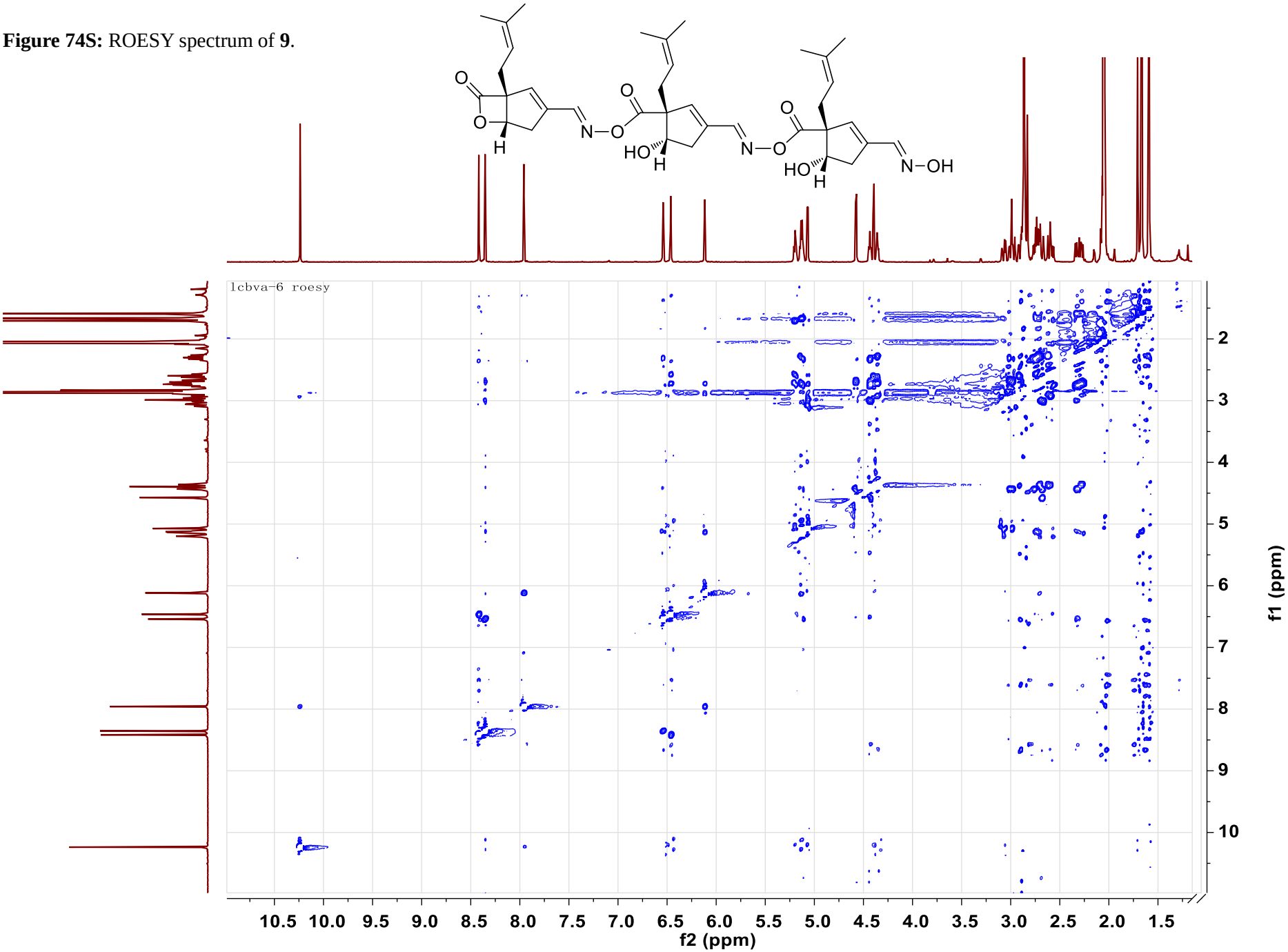


Figure 75S: HREIMS spectrum of **9**.

Elemental Composition Report

Page 1

Single Mass Analysis

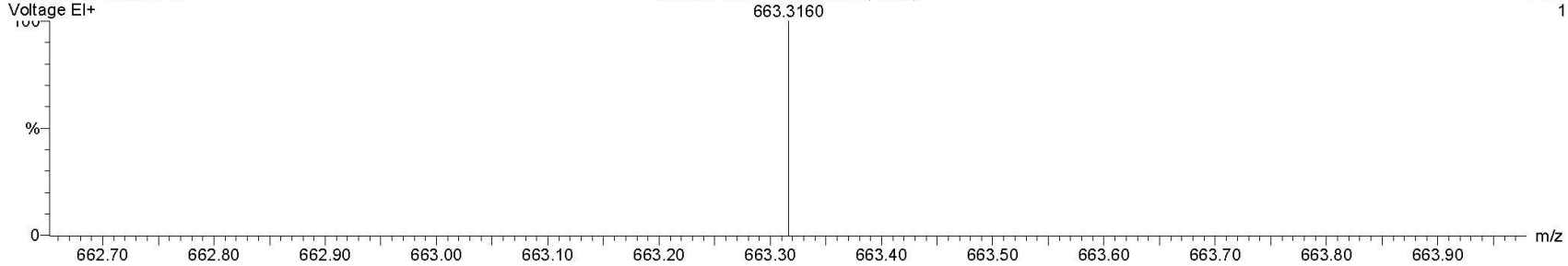
Tolerance = 10.0 PPM / DBE: min = -10.0, max = 120.0
Selected filters: None

Monoisotopic Mass, Odd and Even Electron Ions
25 formula(e) evaluated with 1 results within limits (up to 51 closest results for each mass)
Elements Used:
C: 0-200 H: 0-400 N: 3-3 O: 8-10

lcbva-6
15:43:23 31-Dec-2013
Voltage EI+

KIB
M131231EA-06AFAMM 82 (7.527)
663.3160

Autospec Premier
P776
1



Minimum:				-10.0		
Maximum:		200.0	10.0	120.0		
Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	Formula
663.3160	663.3156	0.4	0.6	16.0	5546025.5	C36 H45 N3 O9

Figure 76S: ^{1}H NMR spectrum of **10** (acetone-d_6, 600MHz).

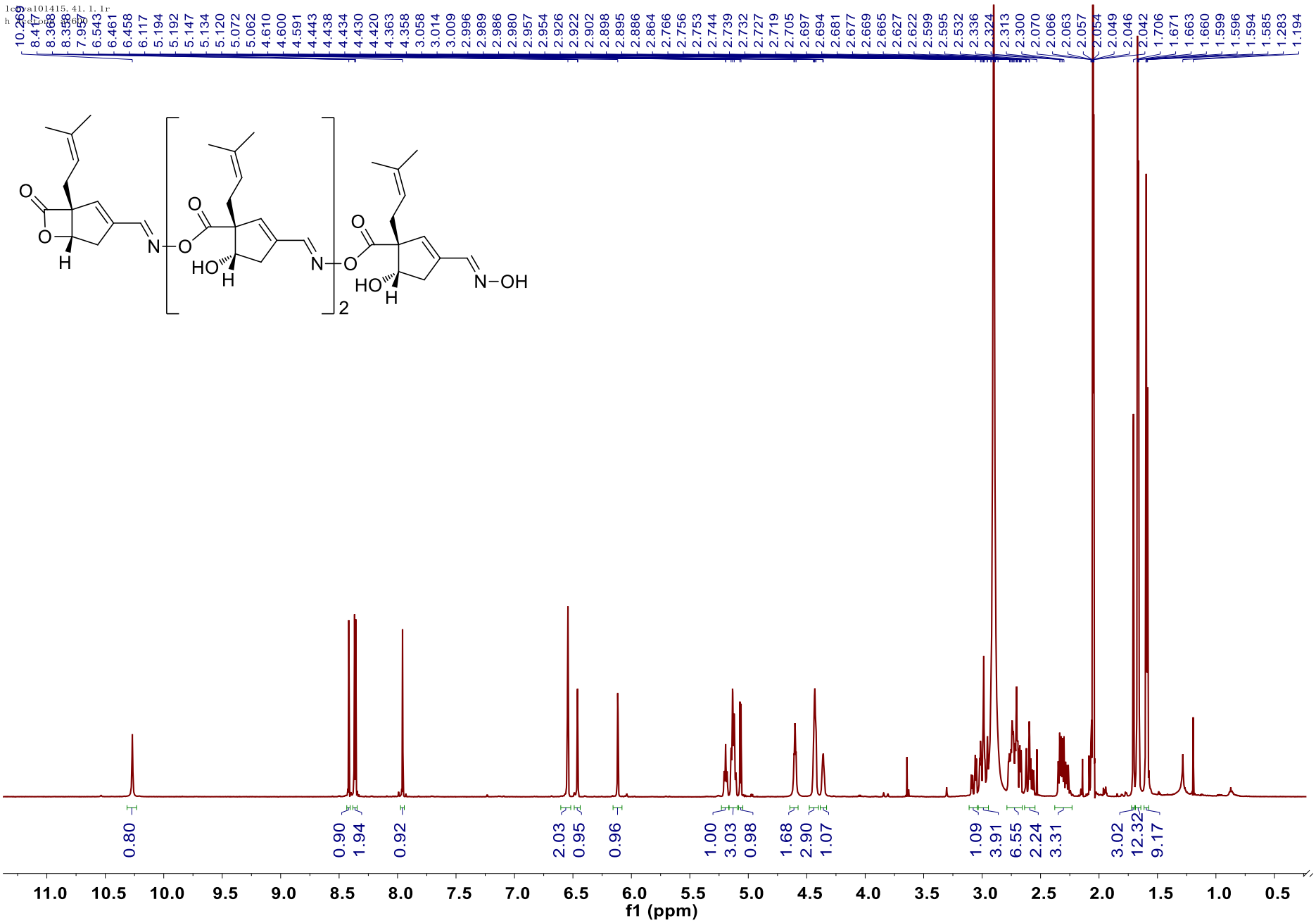


Figure 77S: Enlarged view of ^{1}H NMR spectra of **10** (acetone-d_6, 600MHz)

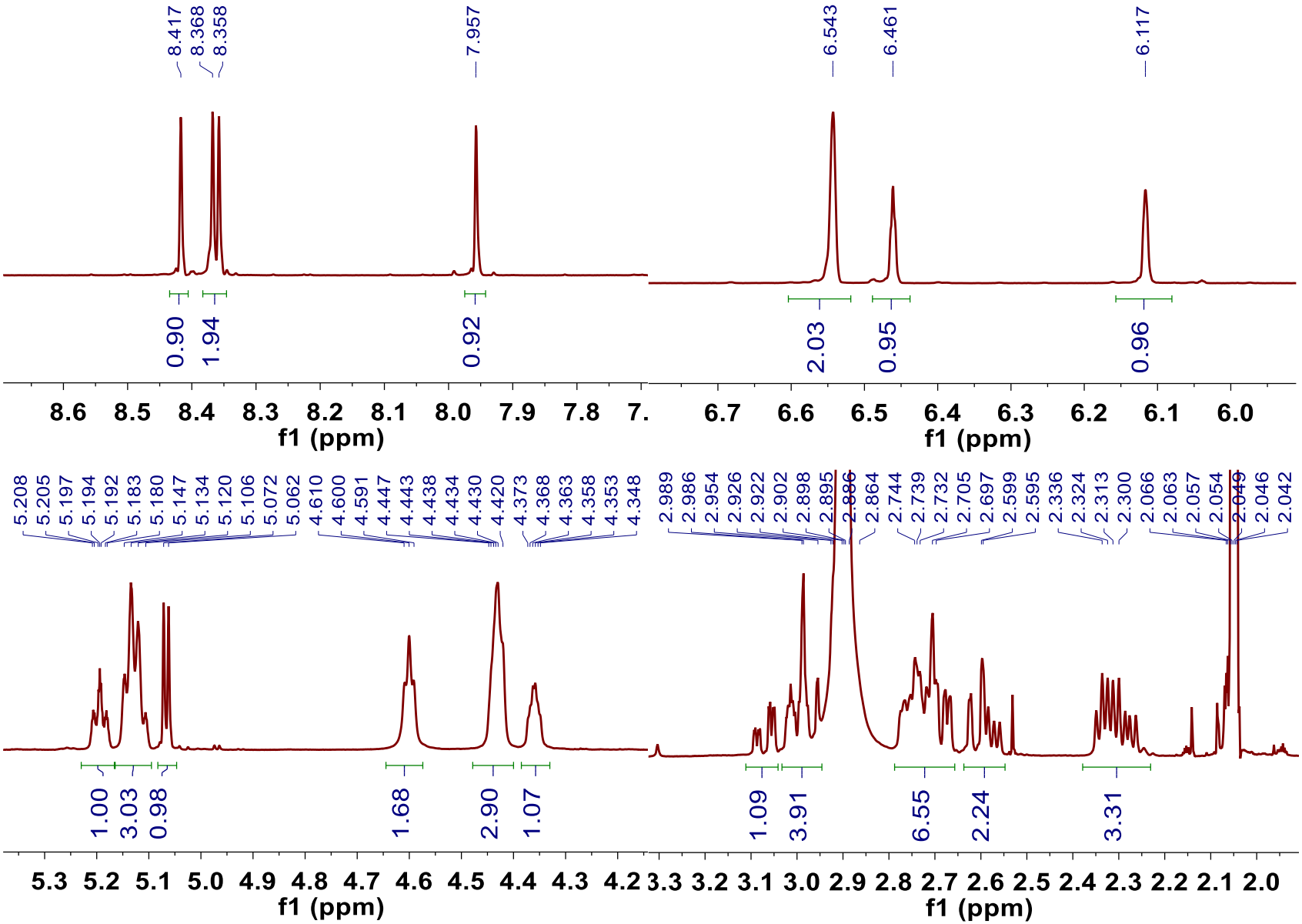


Figure 78S: ^{13}C NMR and DEPT spectra of **10** (acetone-d_6, 150MHz).

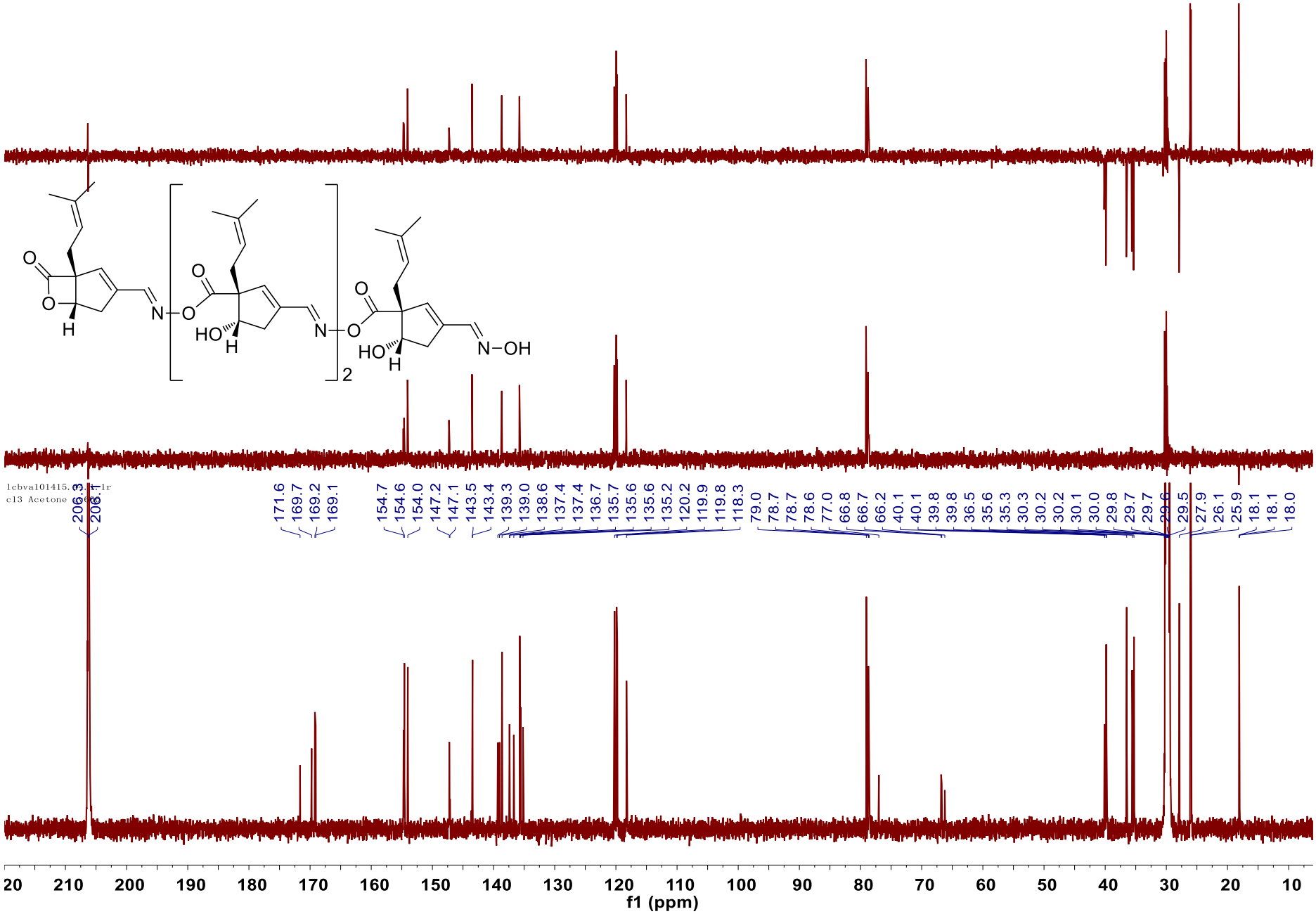


Figure 79S: Enlarged view of ^{13}C NMR and DEPT spectra of **10** (acetone-d_6, 150MHz).

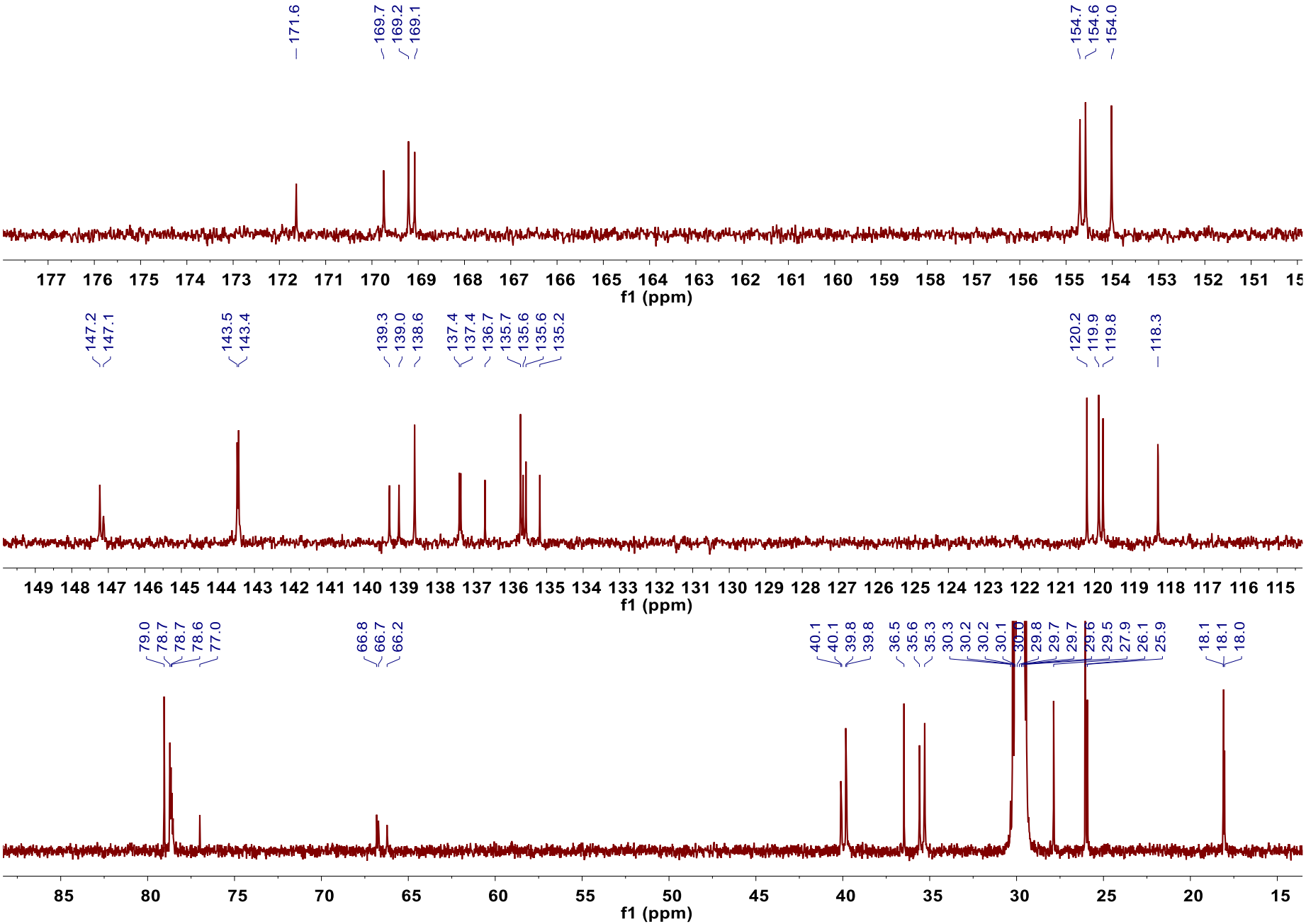


Figure 80S: HSQC spectrum of **10**.

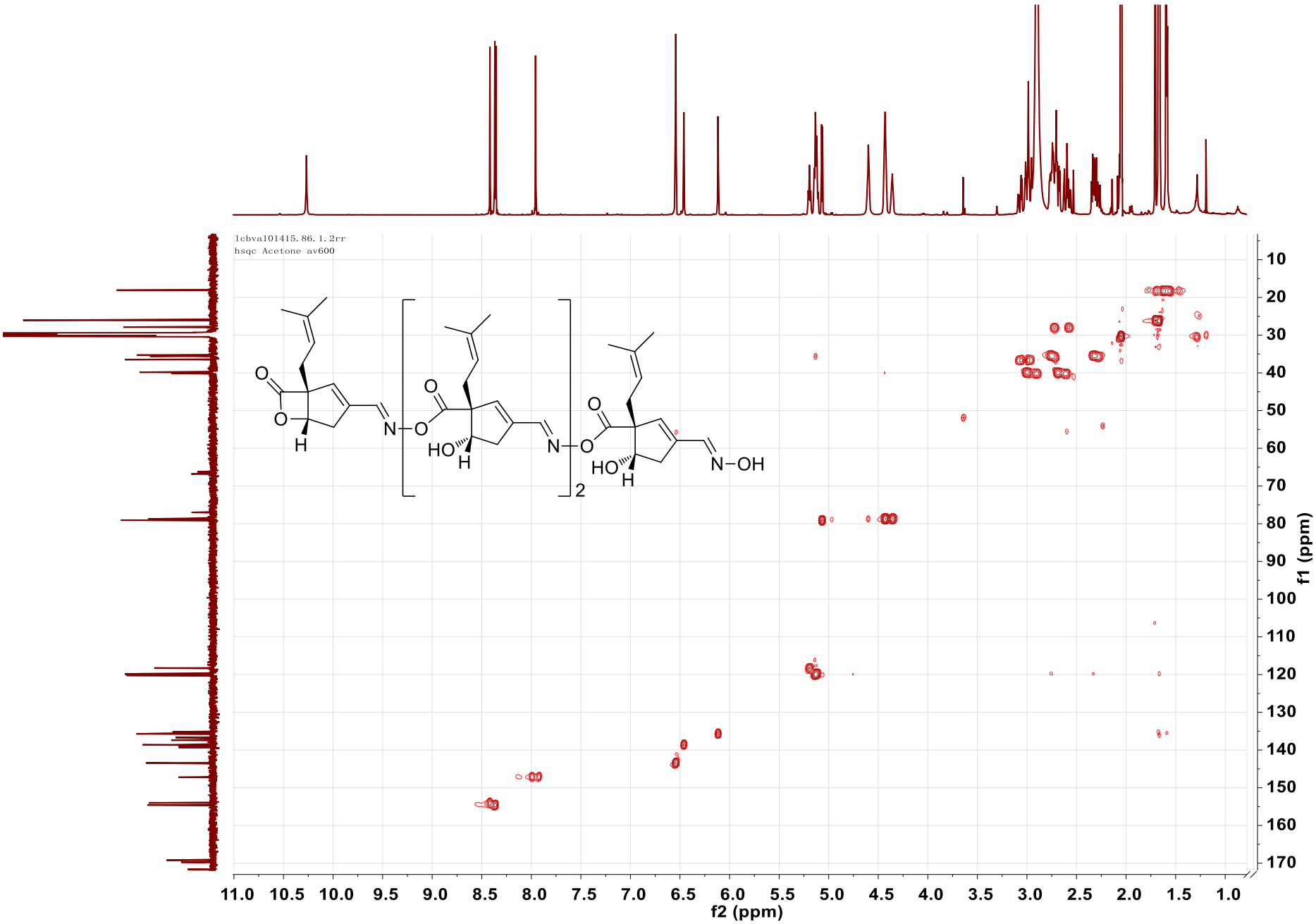


Figure 81S: Enlarged view of HSQC spectrum of **10**.

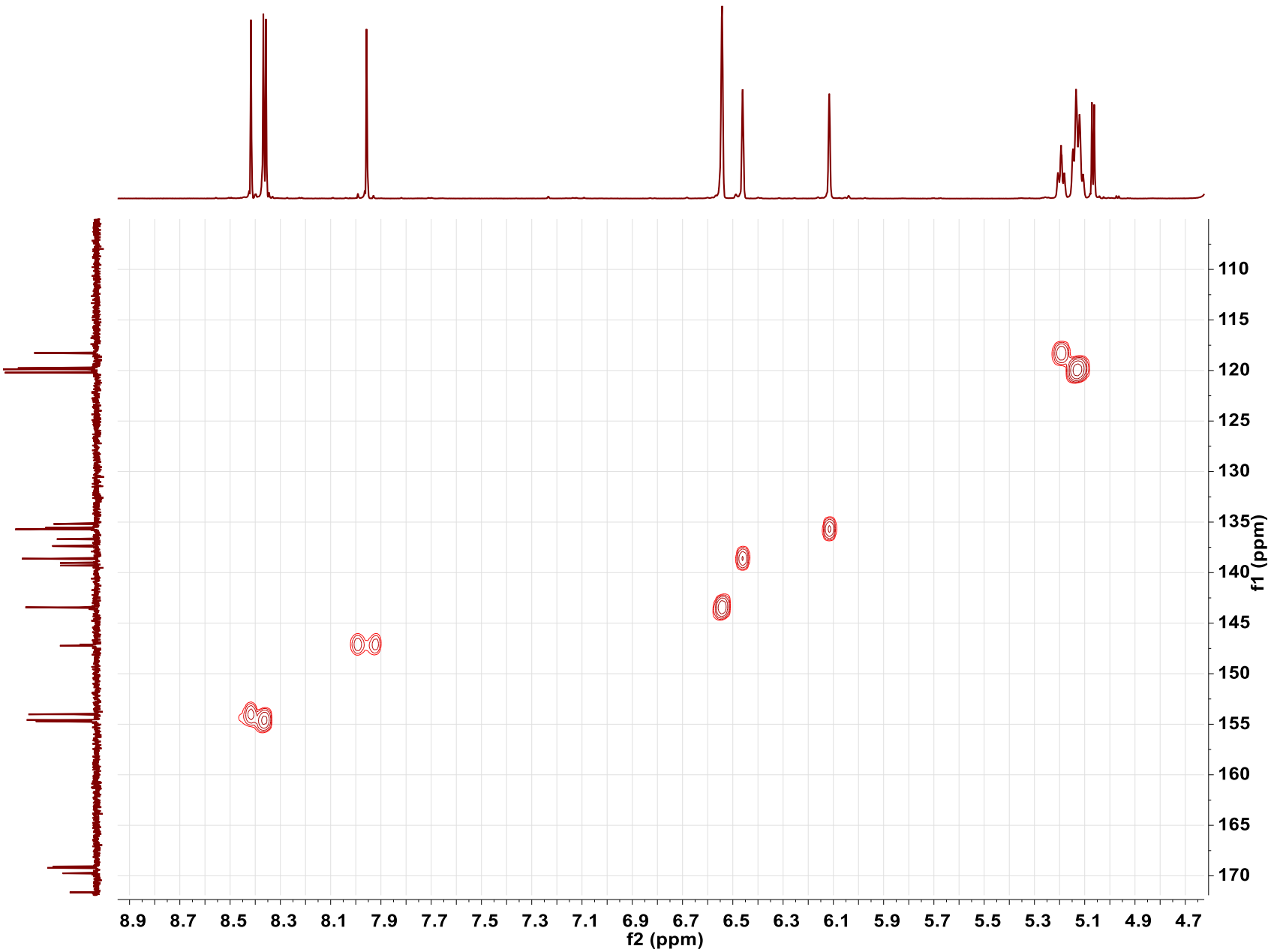


Figure 82S: ^{1}H-^{1}H COSYspectrum of **10**.

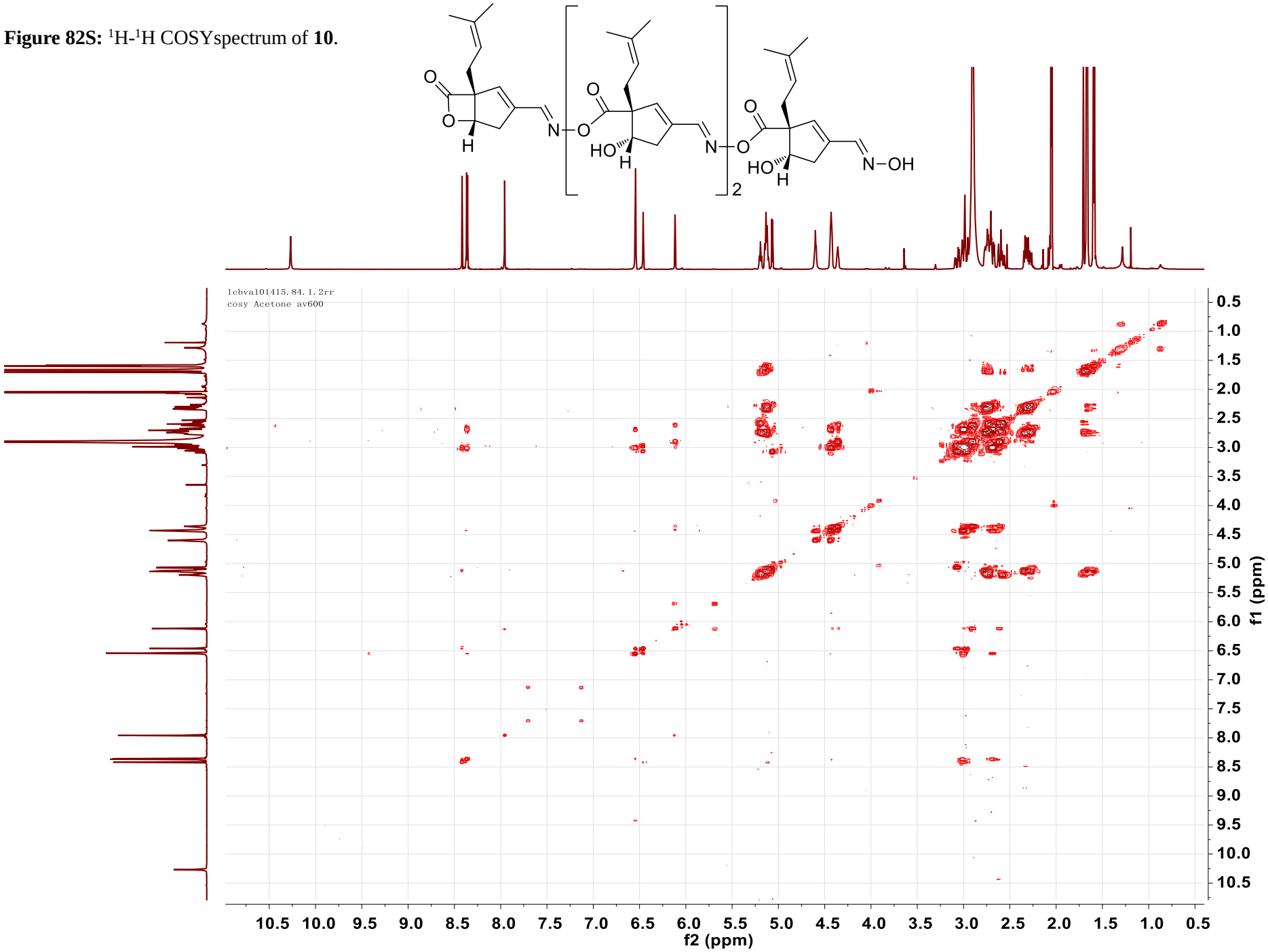


Figure 83S: HMBC spectrum of **10**.

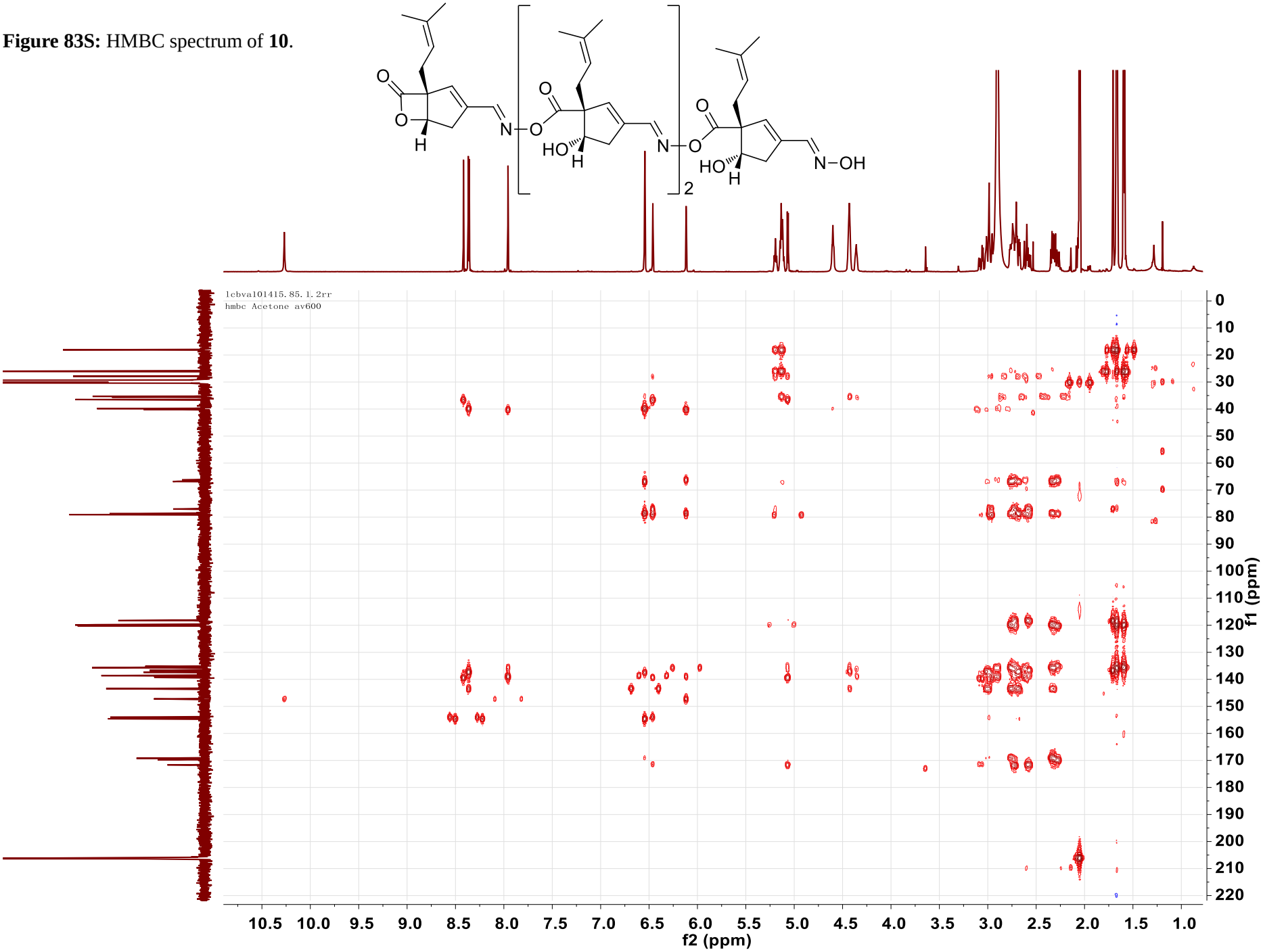


Figure 84S: Enlarged view of HMBC spectrum of **10**.

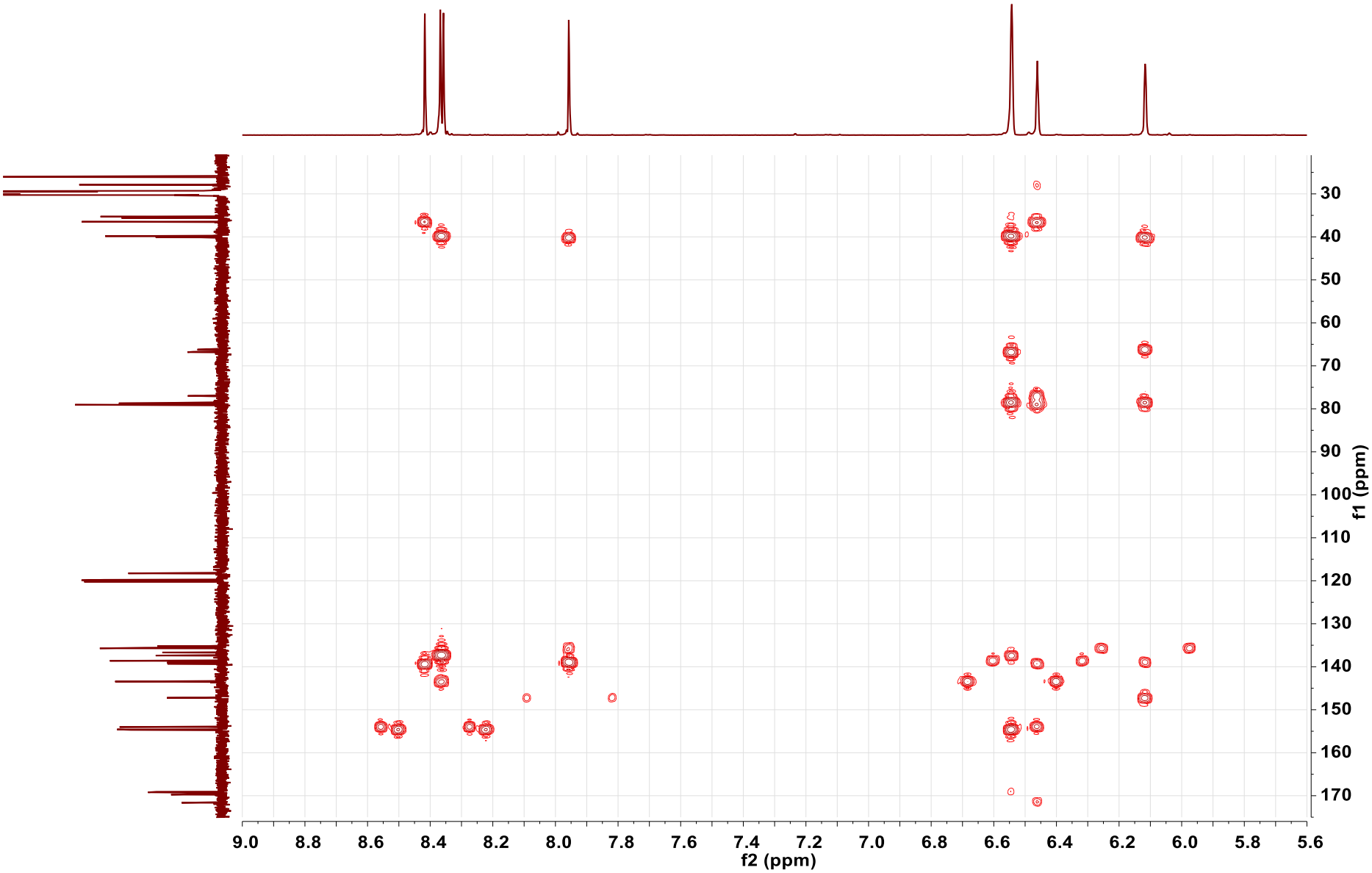


Figure 85S: ROESY spectrum of **10**.

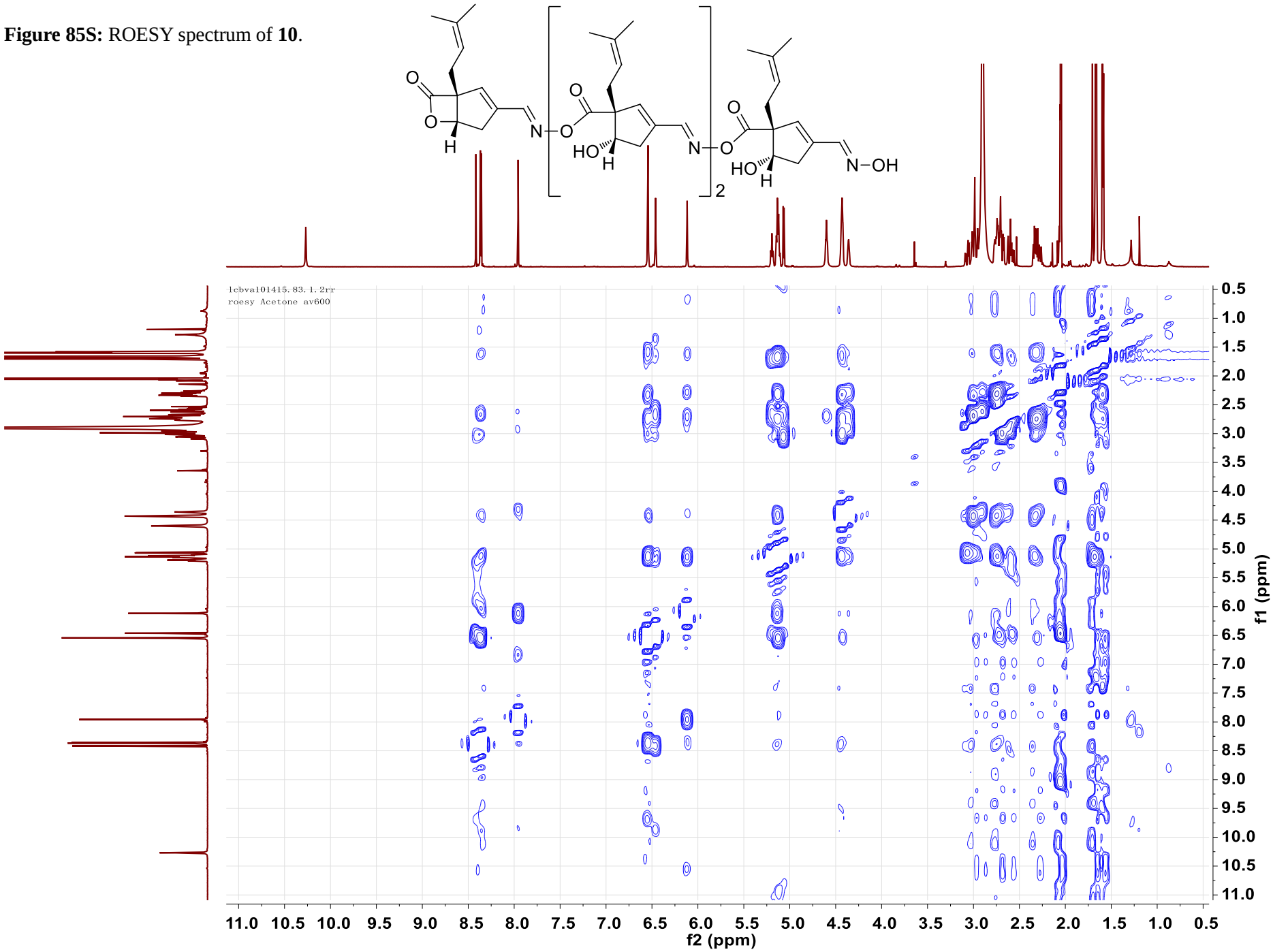


Figure 86S: HRESIMS spectrum of **10**.

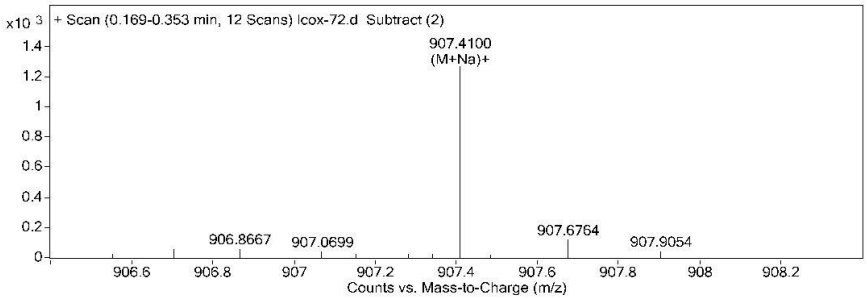
Qualitative Analysis Report

Data Filename	Icox-72.d	**Sample Name**	Icox-72
Sample Type	Sample	**Position**	P1-B6
Instrument Name	Instrument 1	**User Name**	
Acq Method	SIBU.m	**Acquired Time**	3/10/2015 8:42:51 AM
IRM Calibration Status	Success	**DA Method**	Default.m
Comment			

Sample Group		**Info.**	
Acquisition SW Version	6200 series TOF/6500 series Q-TOF B.05.01 (B5125.2)		

User Spectra

Fragmentor Voltage	Collision Energy	Ionization Mode
135	0	ESI



Peak List

m/z	z	Abund
102.1281	1	335324.28
103.1312	1	23138.34
163.1231	1	32261.13
274.2743	1	93798.95
318.3006	1	94393.51
319.3035	1	18947.31
362.3267	1	19927.98
432.2388	1	18251.21
437.1937	1	37663.06
453.1679	1	57979.79

Formula Calculator Element Limits

Element	Min	Max
C	3	60
H	0	120
O	0	30
N	0	10

Formula Calculator Results

Formula	CalculatedMass	CalculatedMz	Mz	Diff. (mDa)	Diff. (ppm)	DBE
C48 H60 N4 O12	884.4208	907.4100	907.4100	0.8	0.9	21.0000

--- End Of Report ---

Agilent Technologies Page 1 of 1 Printed at: 8:47 AM on: 3/10/2015

Figure 87S: ^{1}H NMR spectrum of **11** (acetone-d_6, 600MHz).

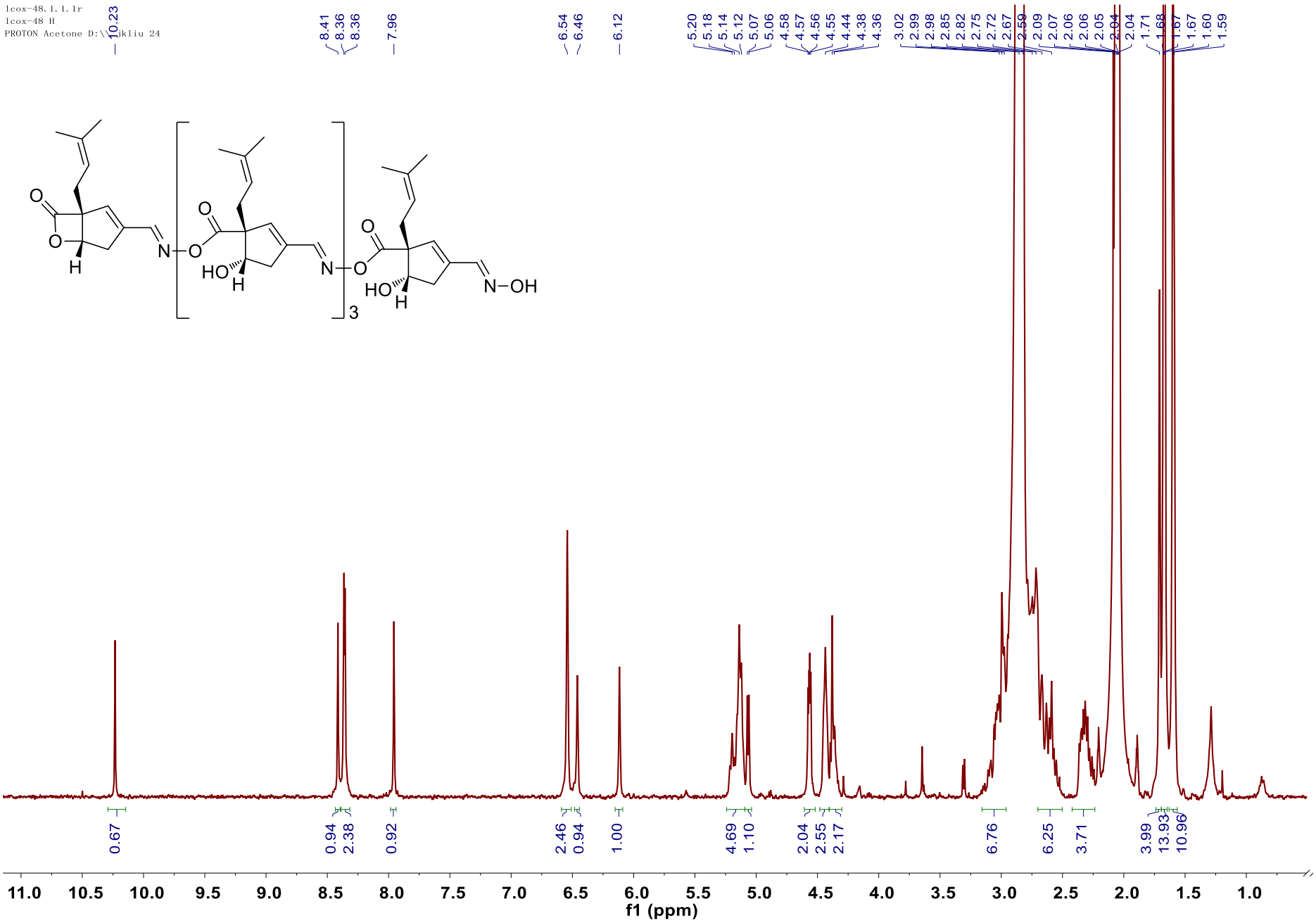


Figure 88S: Enlarged view of ^{1}H NMR spectrum of **11** (acetone-d_6, 600MHz)

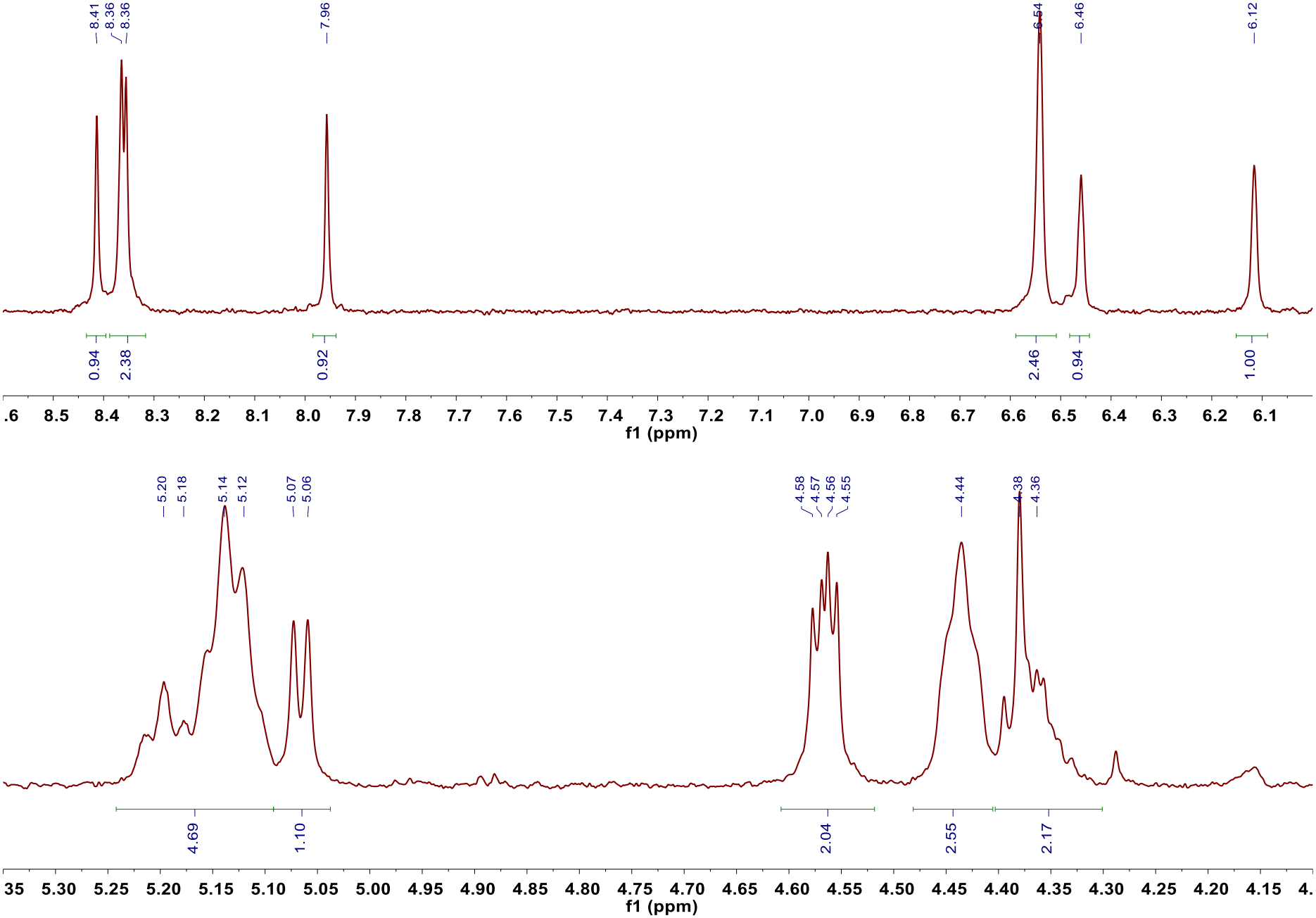


Figure 89S: HRESIMSspectrum of **11**.

Qualitative Analysis Report

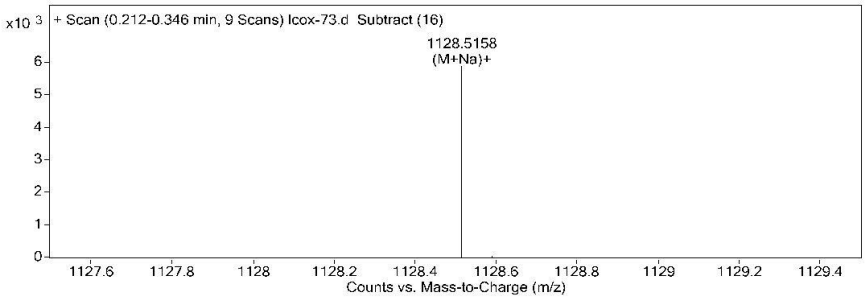
Data Filename	lcox-48.d	**Sample Name**	lcox-48
Sample Type	Sample	**Position**	P1-B1
Instrument Name	Instrument 1	**User Name**	
Acq Method	SIBU.m	**Acquired Time**	3/10/2015 3:49:12 PM
IRM Calibration Status	Success	**DA Method**	Default.m
Comment			

Sample Group **Info.**

Acquisition SW Version 6200 series TOF/6500 series Q-TOF B.05.01 (B5125.2)

User Spectra

Fragmentor Voltage	Collision Energy	Ionization Mode
135	0	ESI



Peak List

m/z	z	Abund	Formula	Ion
102.1277	1	101863.34		
103.1313	1	8485.26		
144.0805		10690.44		
187.1232		9680.63		
230.248		8409.56		
274.274	1	29855.7		
275.2776	1	6881.42		
318.3003	1	36899.34		
362.3268		10662.17		
1128.5158	1	5871.05	C60 H75 N5 O15	(M+Na)+

Formula Calculator Element Limits

Element	Min	Max
C	3	60
H	0	120
O	0	30
N	0	10

Formula Calculator Results

Formula	CalculatedMass	CalculatedMz	Mz	Diff. (mDa)	Diff. (ppm)	DBE
C60 H75 N5 O15	1105.5260	1128.5152	1128.5158	-0.2	-0.2	26.0000

--- End Of Report ---

Agilent Technologies Page 1 of 1 Printed at: 4:20 PM on: 3/10/2015

Figure 90S: ^{1}H NMR spectrum of **12** (acetone-d_6, 600MHz).

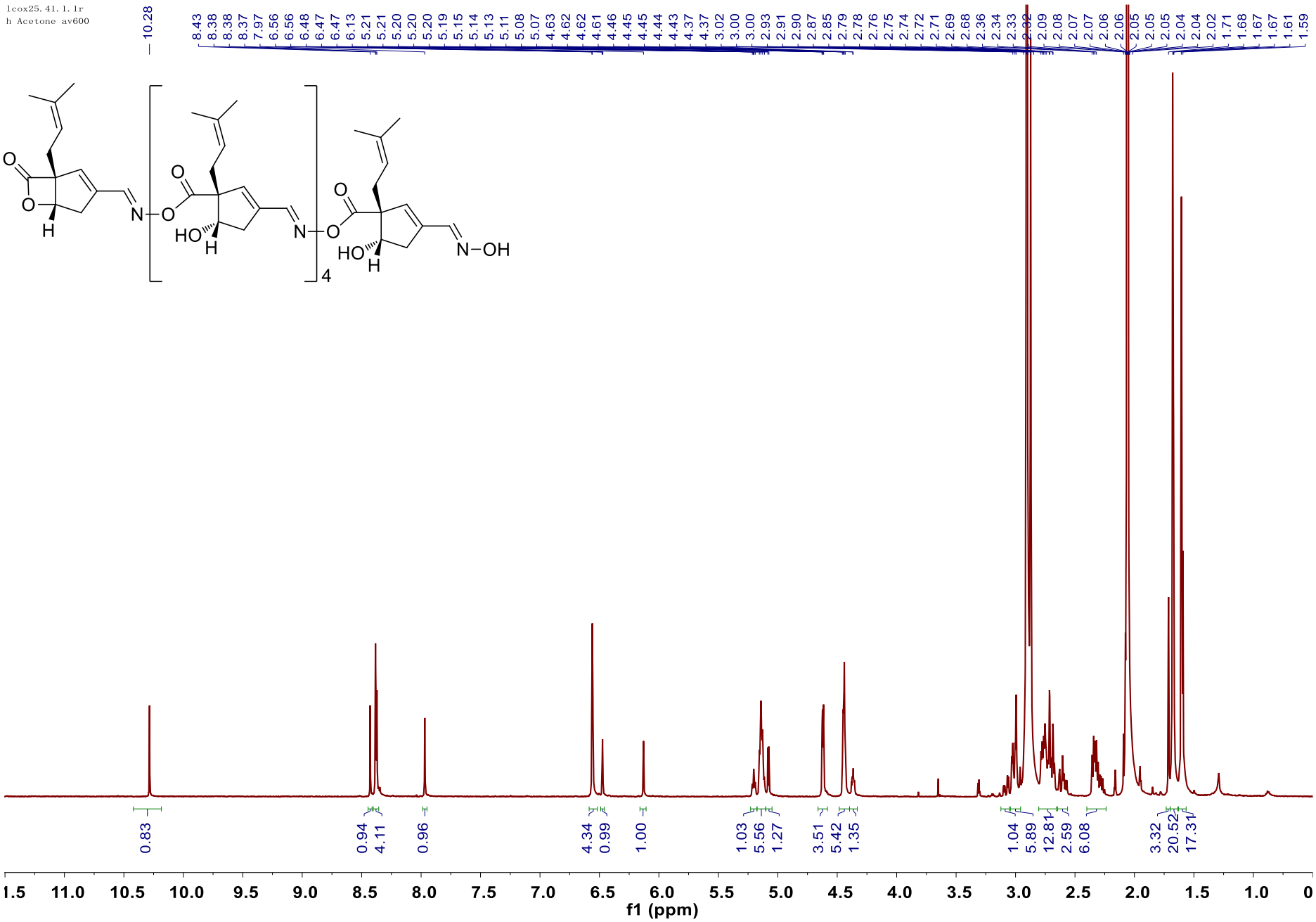
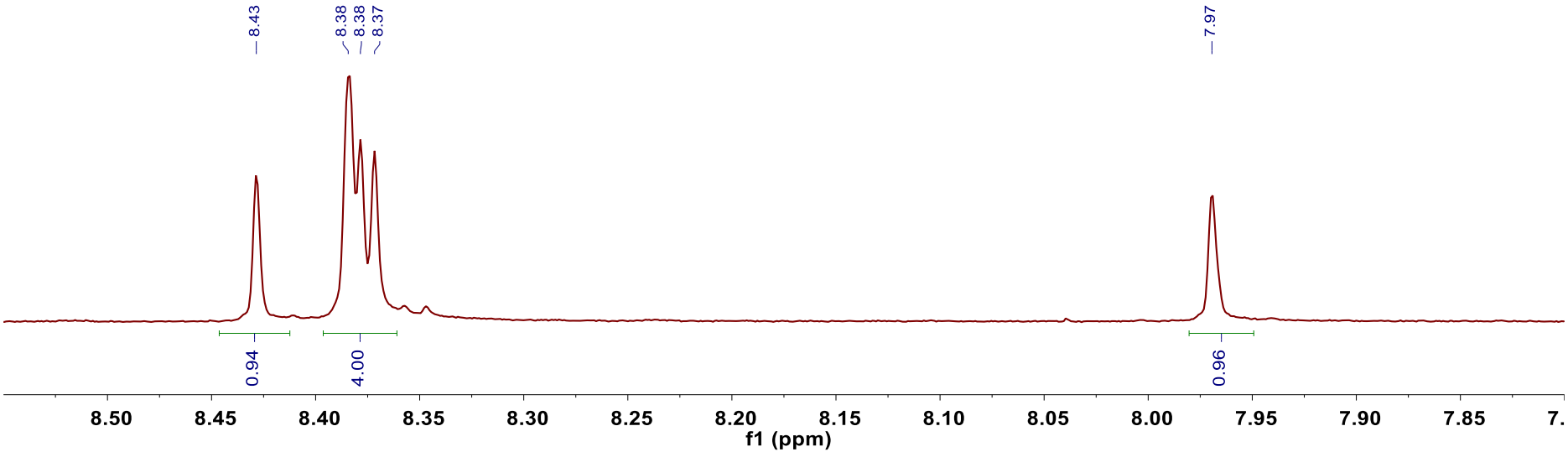


Figure 91S: Enlarged view of ^{1}H NMR spectrum of **12** (acetone-d_6, 600MHz)



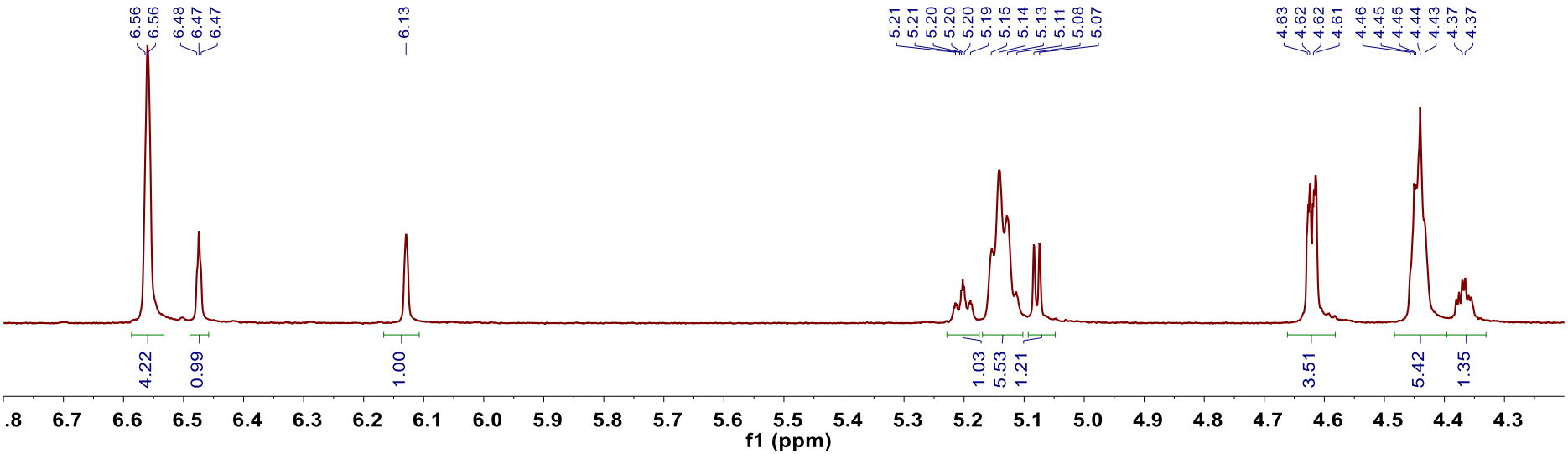


Figure 92S: HRESIMS spectrum of **12**.

Qualitative Analysis Report

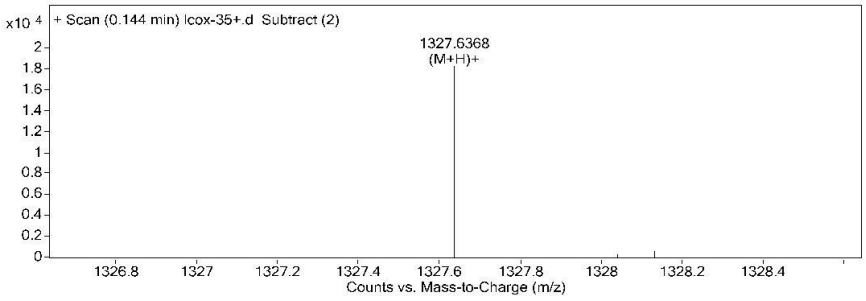
Data Filename	lcox-25.d	**Sample Name**	lcox-25
Sample Type	Sample	**Position**	P1-A6
Instrument Name	Instrument 1	**User Name**	
Acq Method	SIBU.m	**Acquired Time**	3/23/2015 4:30:40 PM
IRM Calibration Status	Success	**DA Method**	Default.m
Comment			

Sample Group **Info.**

Acquisition SW Version 6200 series TOF/6500 series Q-TOF B.05.01 (B5125.2)

User Spectra

Fragmentor Voltage	Collision Energy	Ionization Mode
135	0	ESI



Peak List

m/z	z	Abund	Formula	Ion
675.3102	2	13176.74		
675.8108	2	13227.66		
683.2972	2	39890.23		
683.7988	2	30519.08		
1327.6368	1	18248.74	C72 H90 N6 O18	(M+H)+
1328.6397	1	15092.47	C72 H90 N6 O18	(M+H)+

Formula Calculator Element Limits

Element	Min	Max
C	3	100
H	0	200
O	0	30
N	0	10

Formula Calculator Results

Formula	CalculatedMass	CalculatedMz	Mz	Diff. (mDa)	Diff. (ppm)	DBE
C72 H90 N6 O18	1326.6312	1327.6384	1327.6368	1.7	1.3	31.0000

--- End Of Report ---

Agilent Technologies Page 1 of 1 Printed at: 4:33 PM on: 3/23/2015

Figure 93S: ^{1}H NMR spectrum of **13** (acetone-d_6, 600MHz).

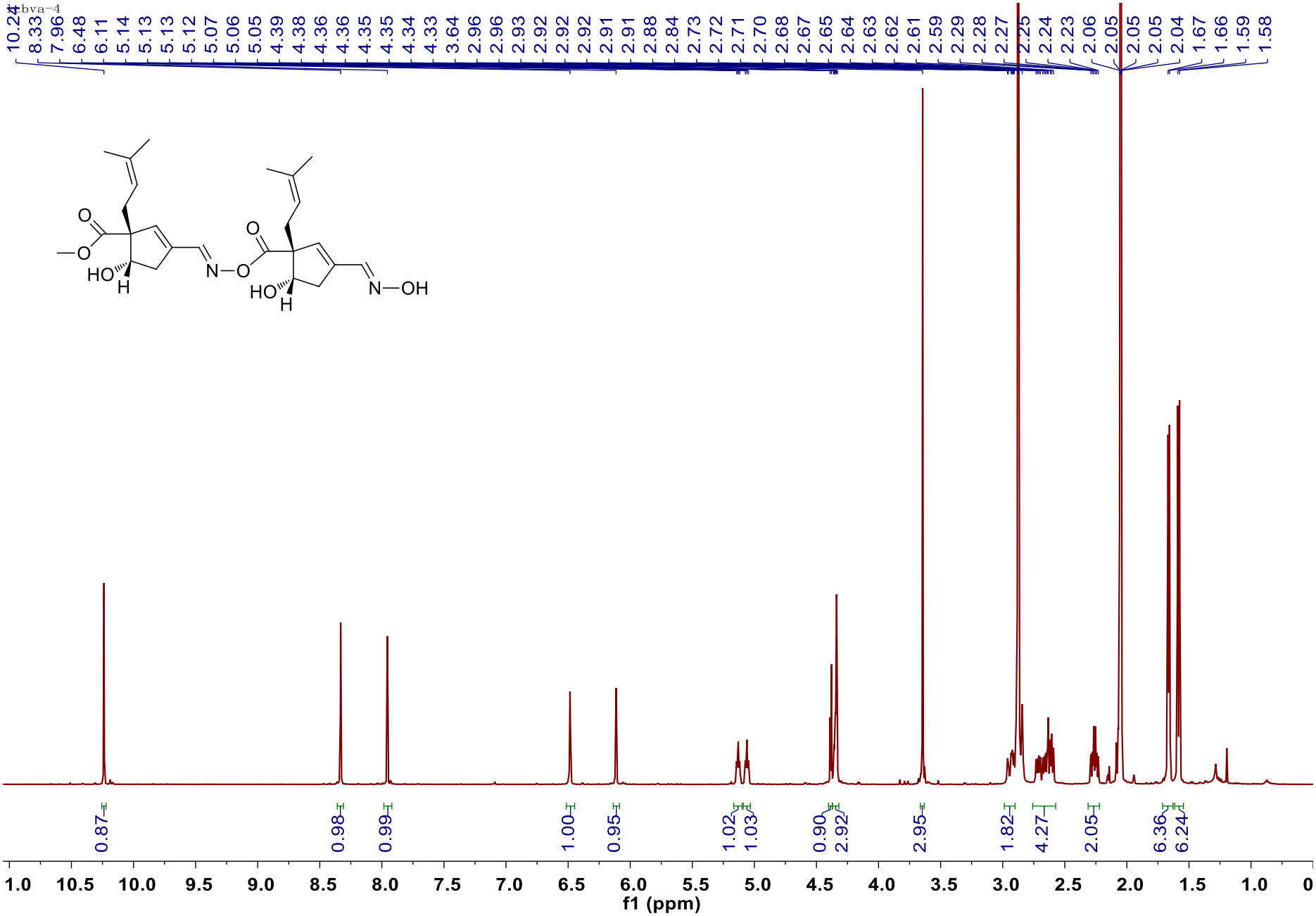


Figure 94S: ^{13}C NMR and DEPT spectra of **13** (acetone-d_6, 150MHz).

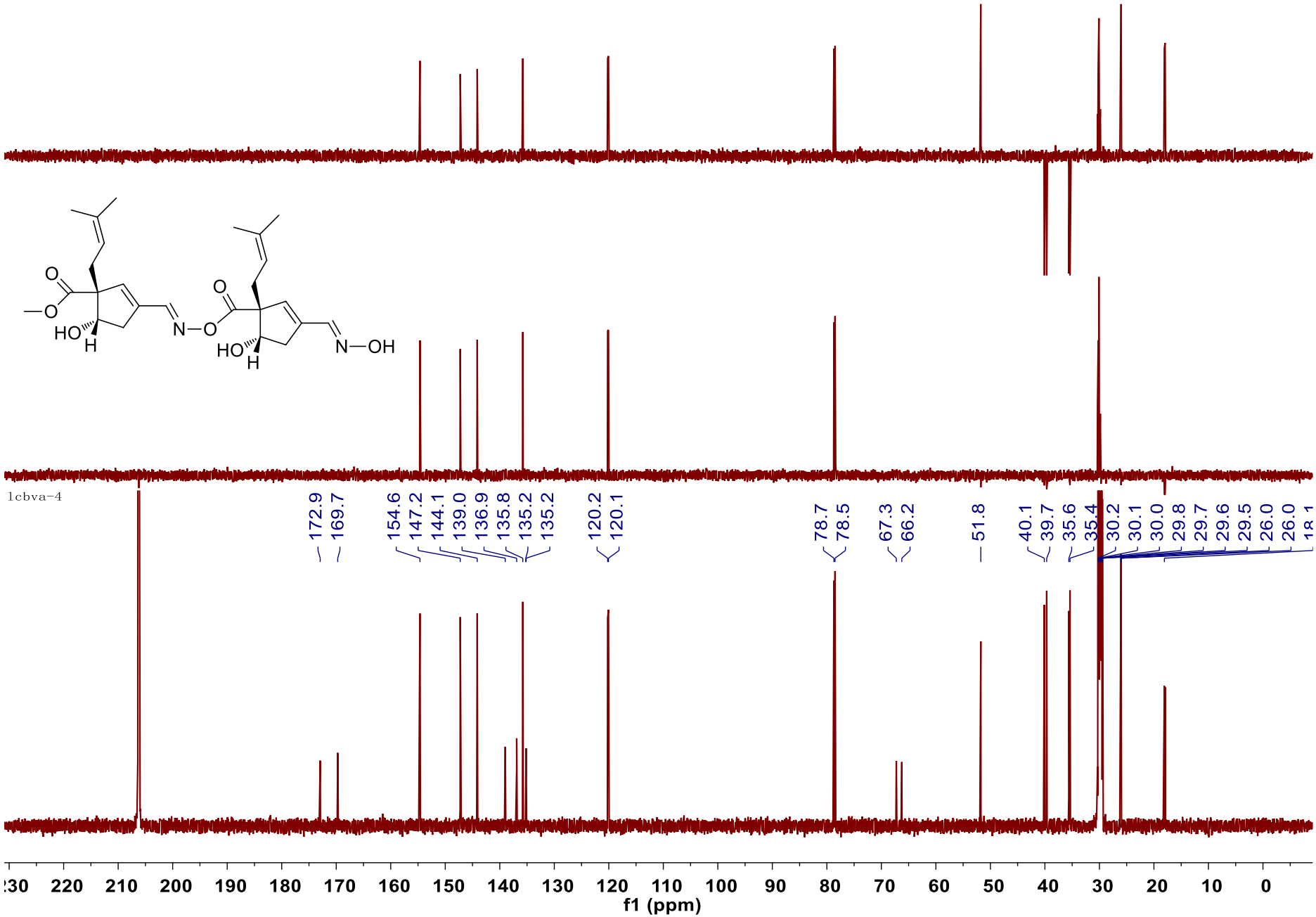


Figure 95S: Enlarged view of ^{13}C NMR and DEPT spectra of **13** (acetone-d_6, 150MHz).

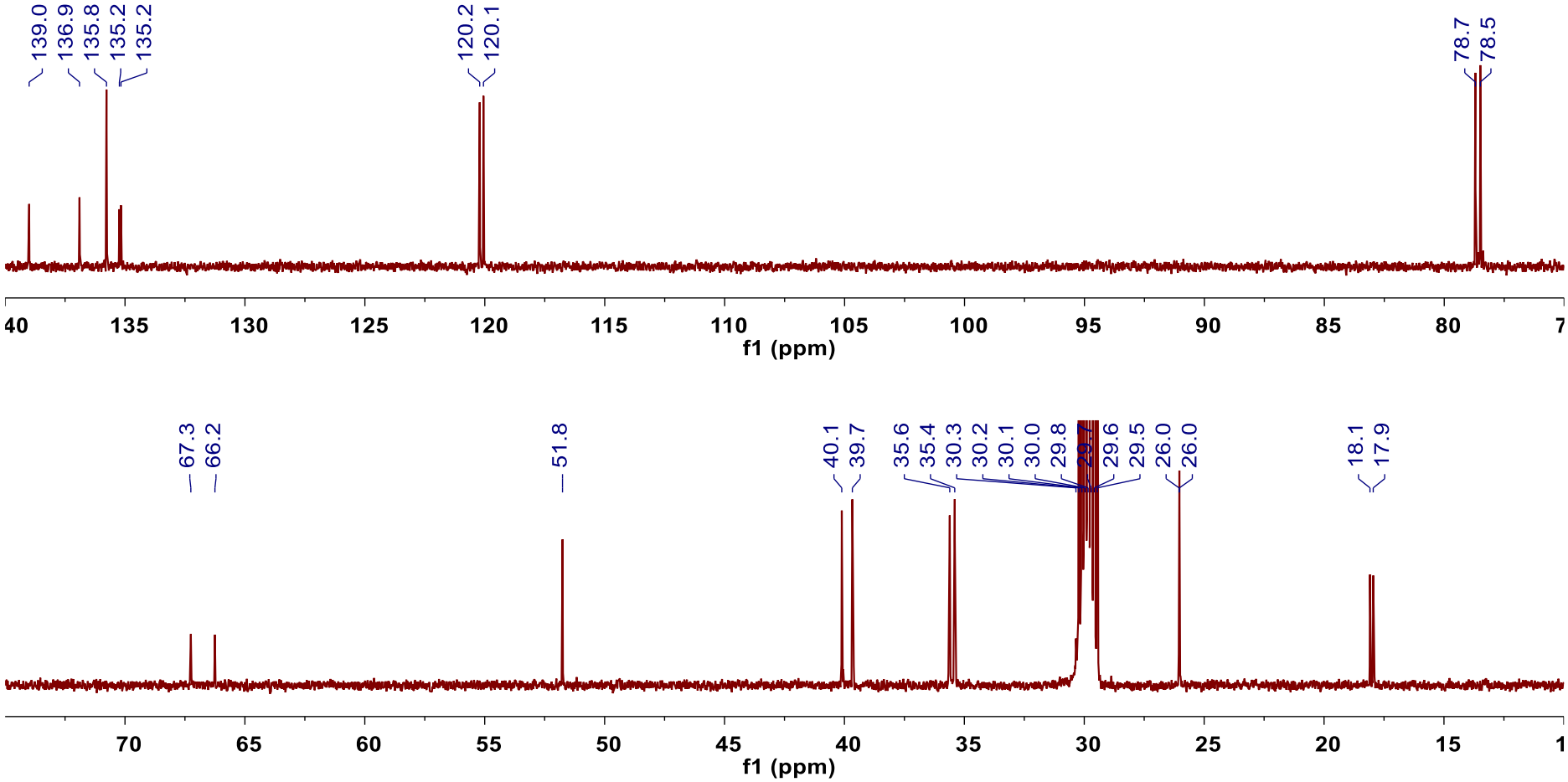


Figure 96S: HSQC spectrum of **13**.

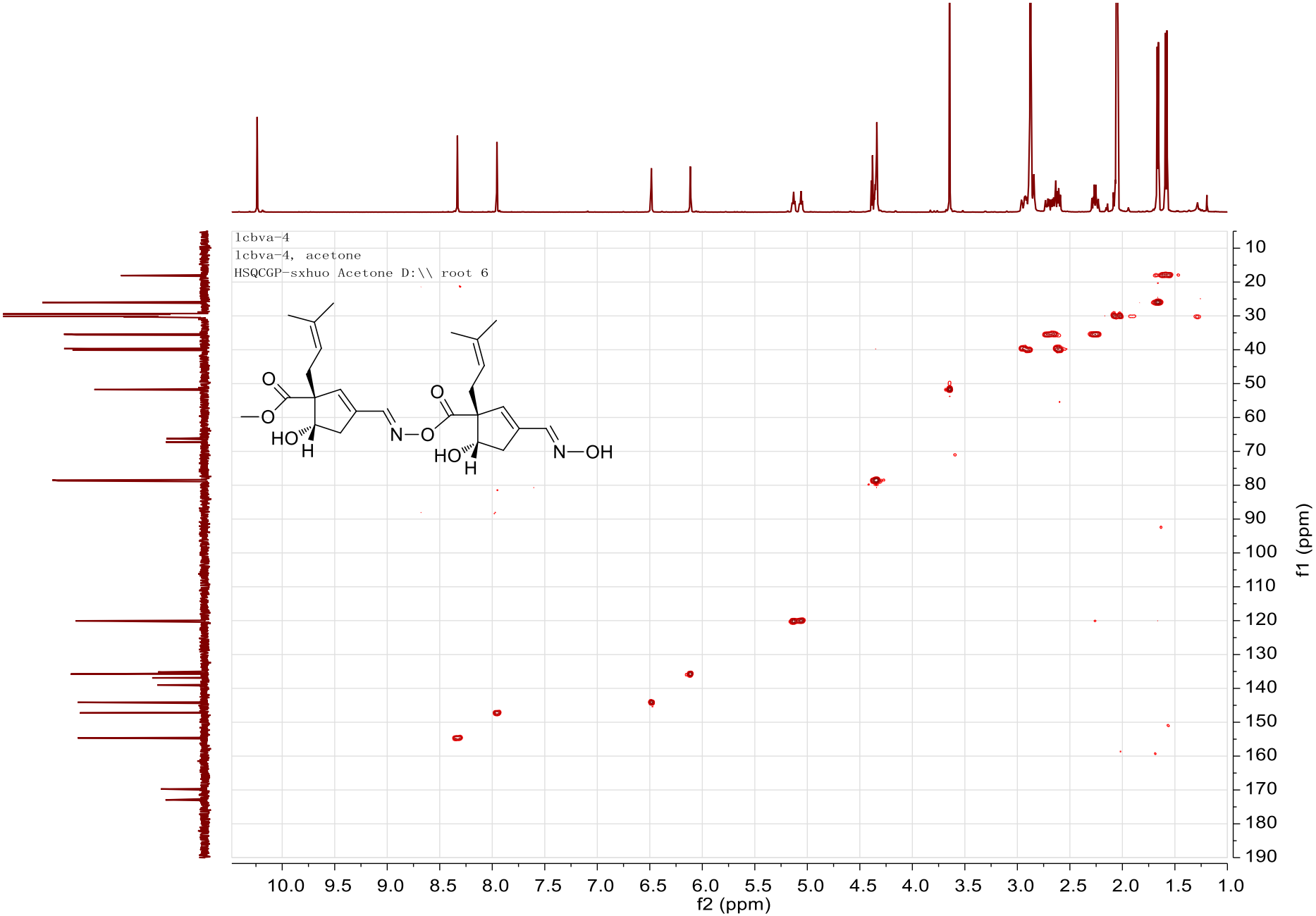


Figure 97S: ^{1}H-^{1}H COSY spectrum of **13**.

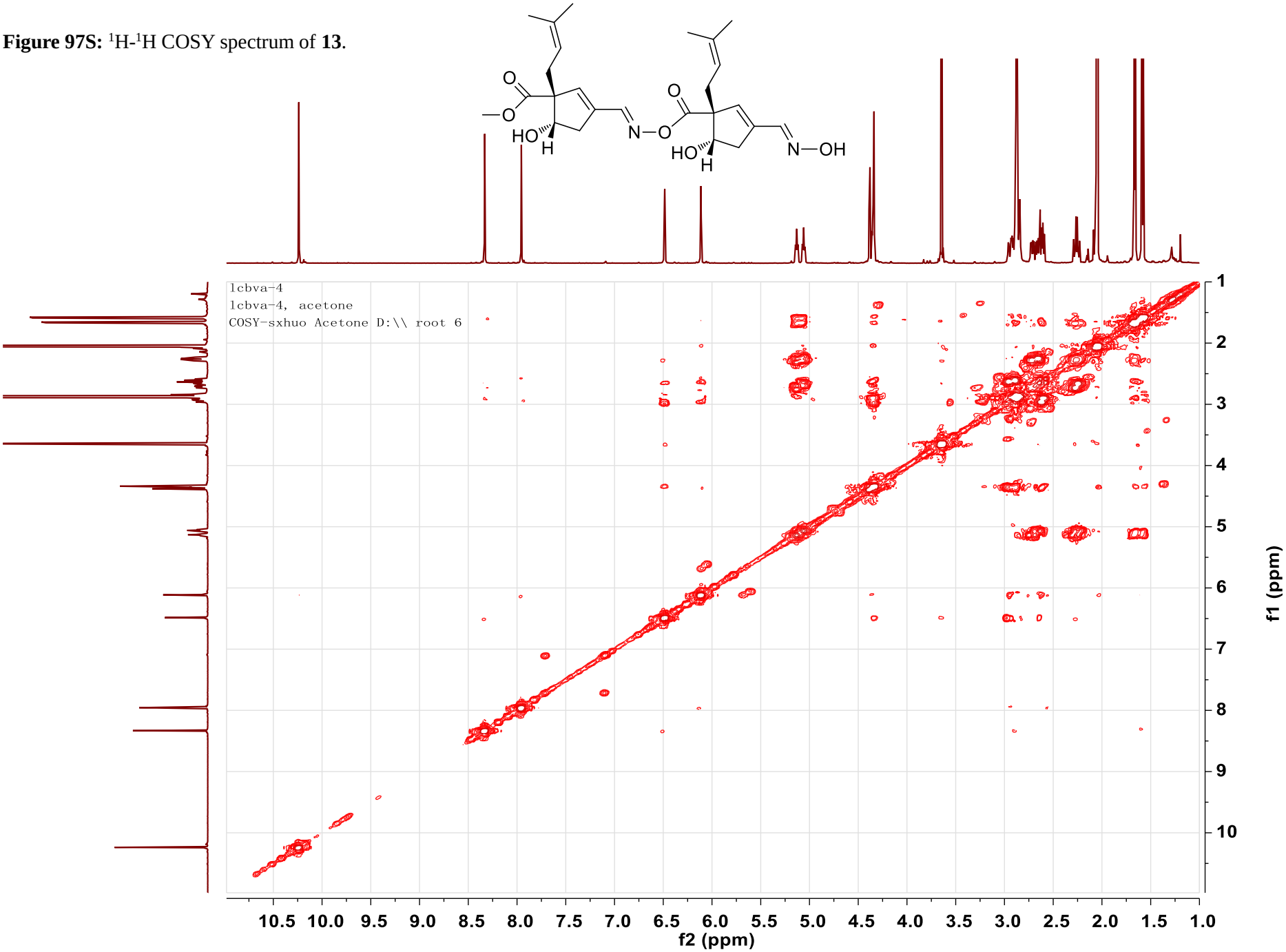


Figure 98S: HMBC spectrum of **13**.

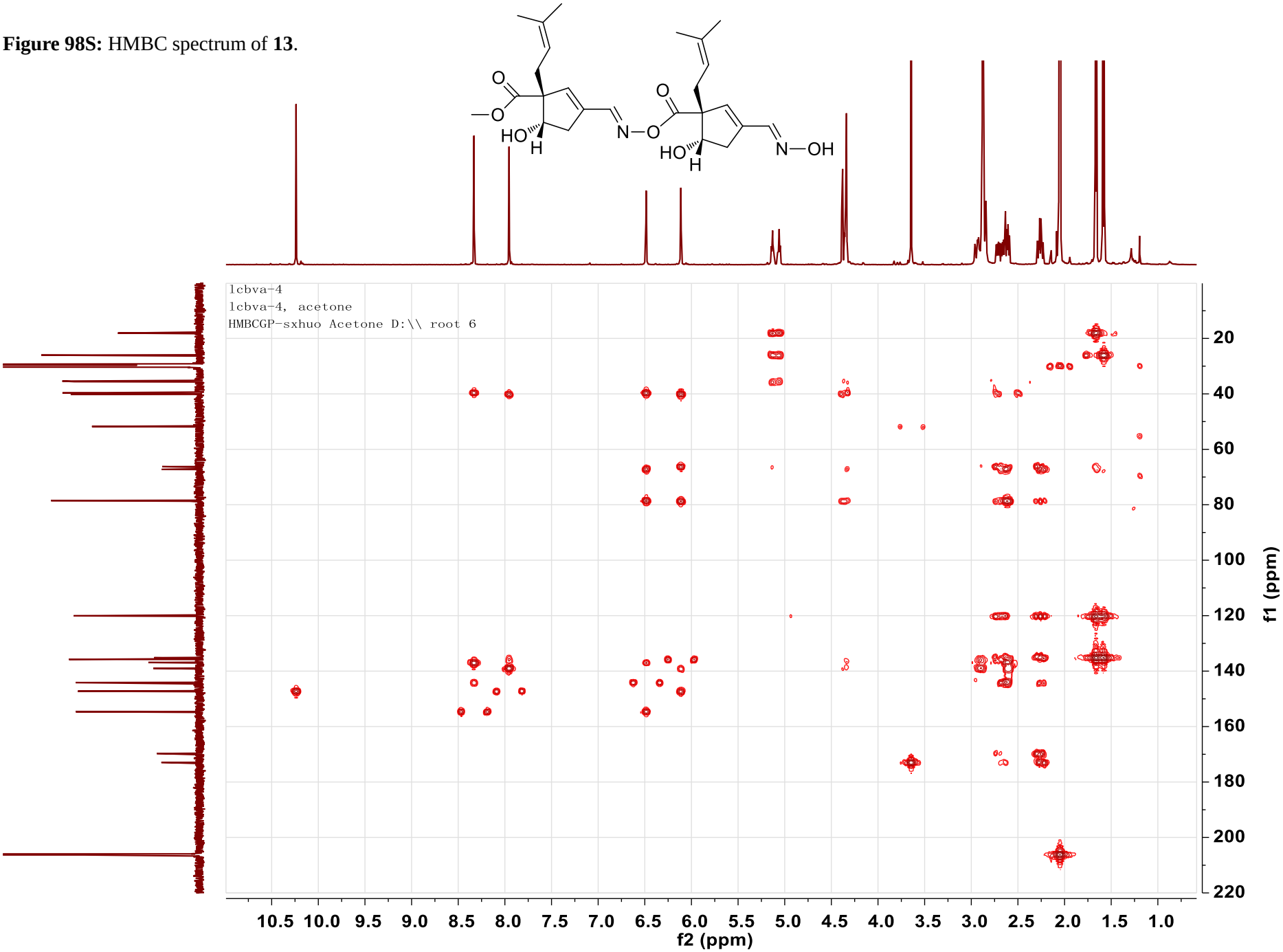


Figure 99S: ROESY spectrum of **13**.

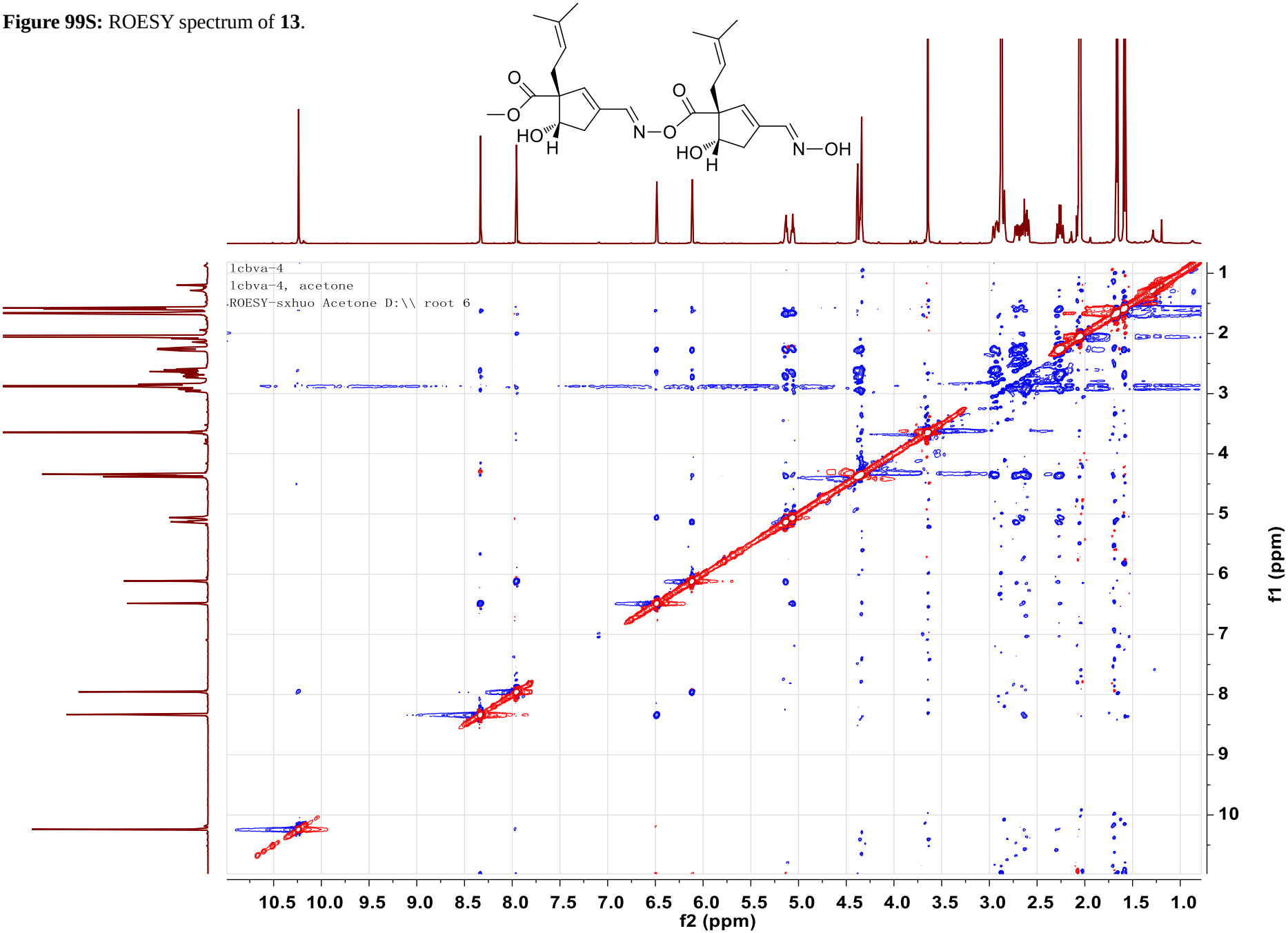


Figure 100S: HREIMS spectrum of **13**.

Elemental Composition Report

Page 1

Single Mass Analysis

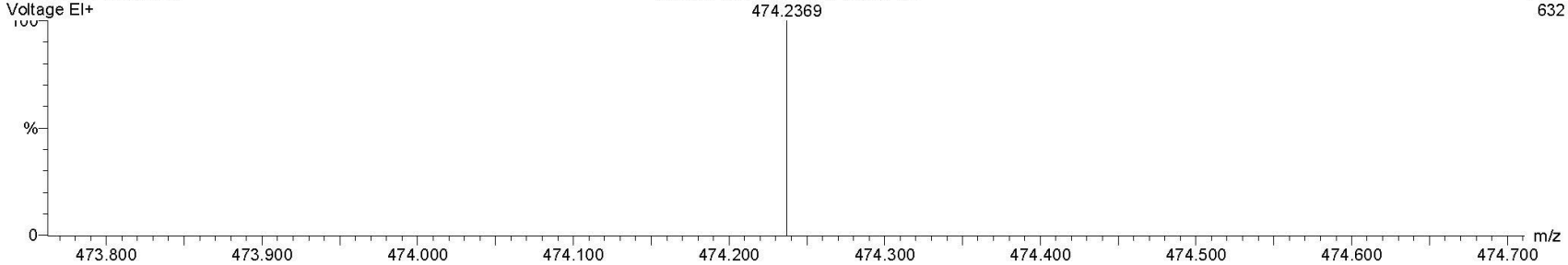
Tolerance = 10.0 PPM / DBE: min = -10.0, max = 120.0
Selected filters: None

Monoisotopic Mass, Odd and Even Electron Ions
19 formula(e) evaluated with 1 results within limits (up to 51 closest results for each mass)
Elements Used:
C: 0-200 H: 0-400 N: 2-2 O: 6-8

lcbva-4
15:07:59 31-Dec-2013
Voltage EI+

KIB
M131231EA-04AFAMM 43 (3.947)
474.2369

Autospec Premier
P776
632



Minimum:				-10.0		
Maximum:		200.0	10.0	120.0		
Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	Formula
474.2369	474.2366	0.3	0.6	10.0	5546332.0	C25 H34 N2 O7

Figure 101S: ^{1}H NMR spectrum of **14** (acetone-d_6, 600MHz).

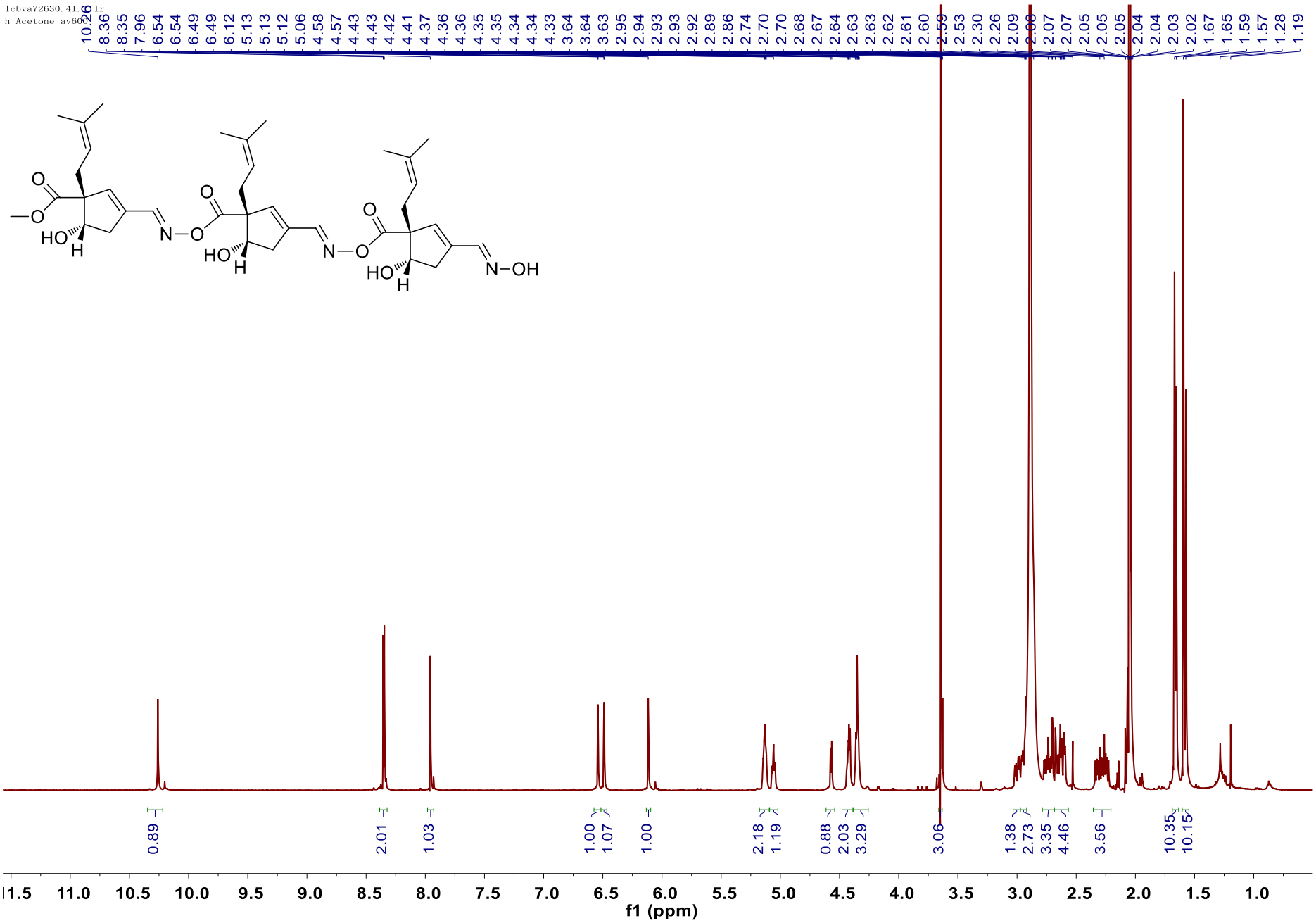


Figure 102S: ^{13}C NMR and DEPT spectra of **14** (acetone-d_6, 150MHz).

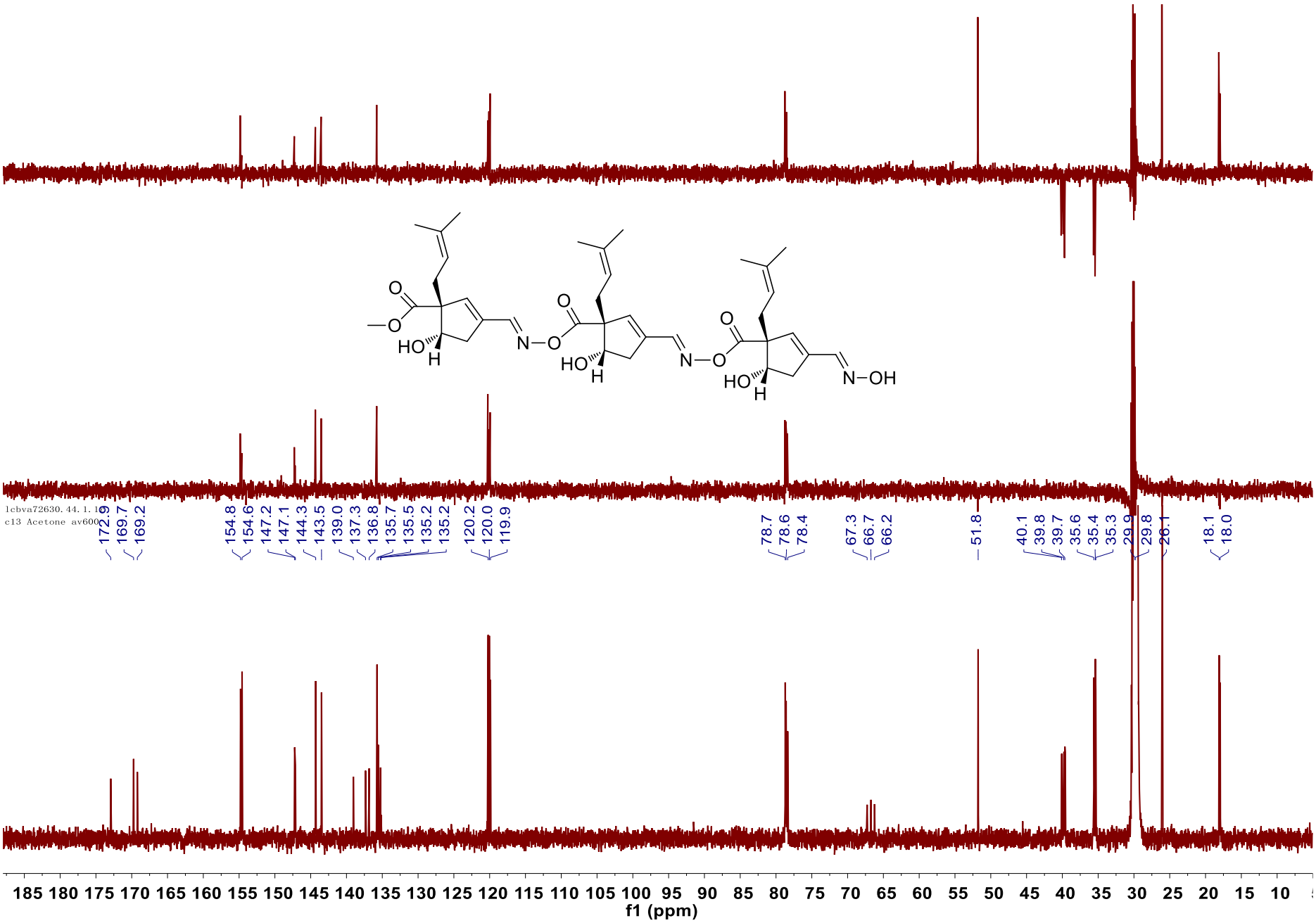


Figure 103S: HSQC spectrum of **14**.

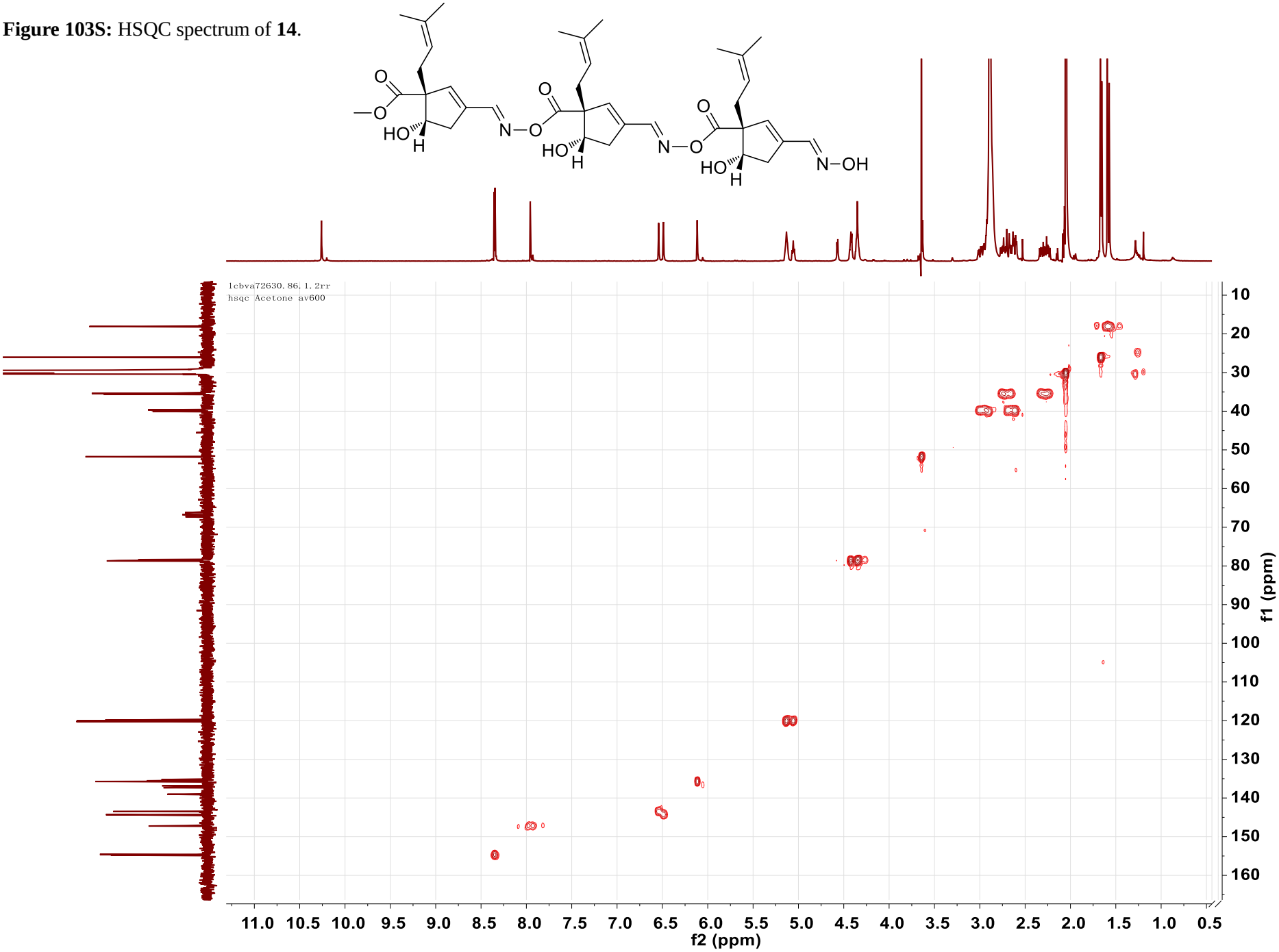


Figure 104S: ^{1}H-^{1}H COSYspectrum of **14**.

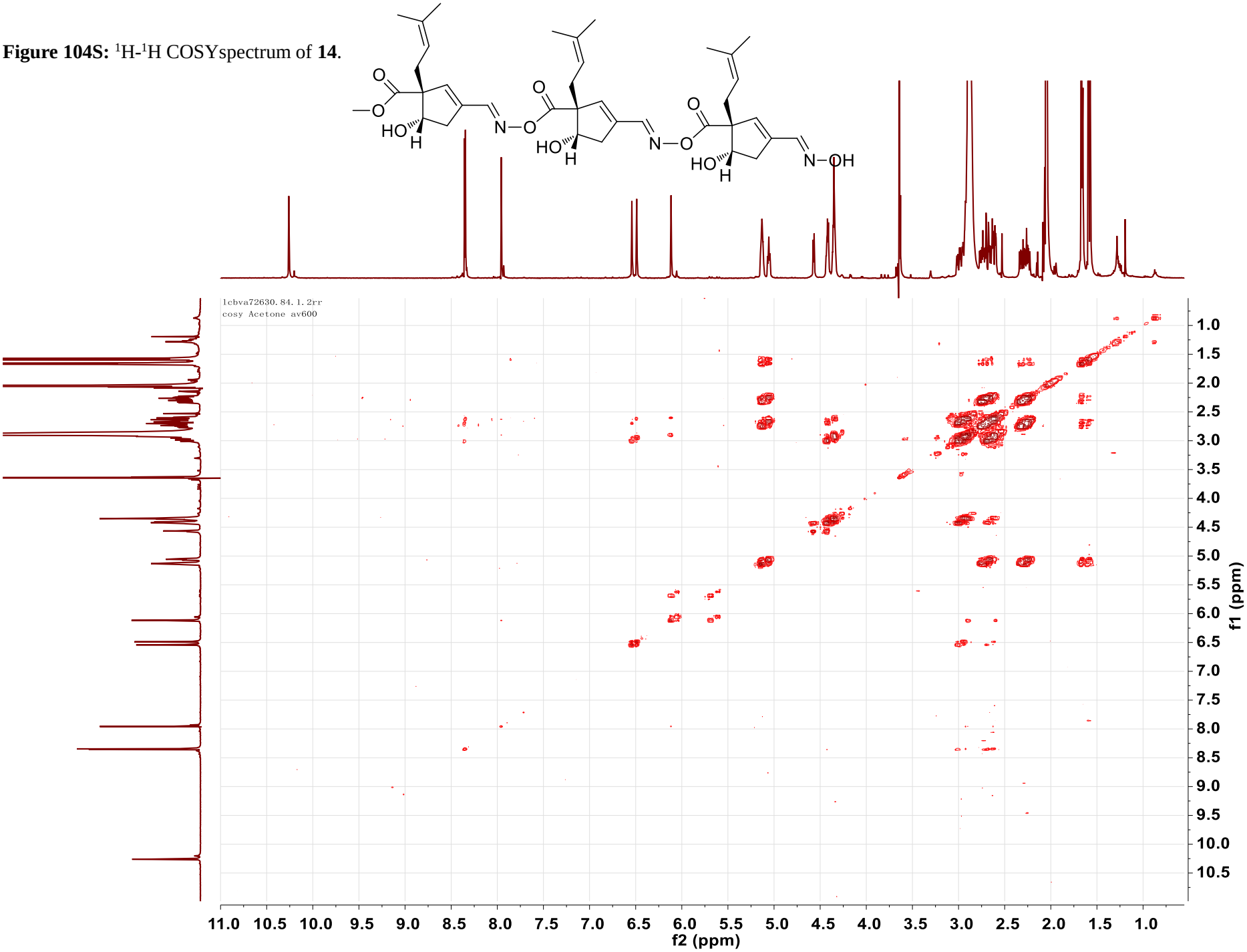


Figure 105S: HMBC spectrum of **14**.

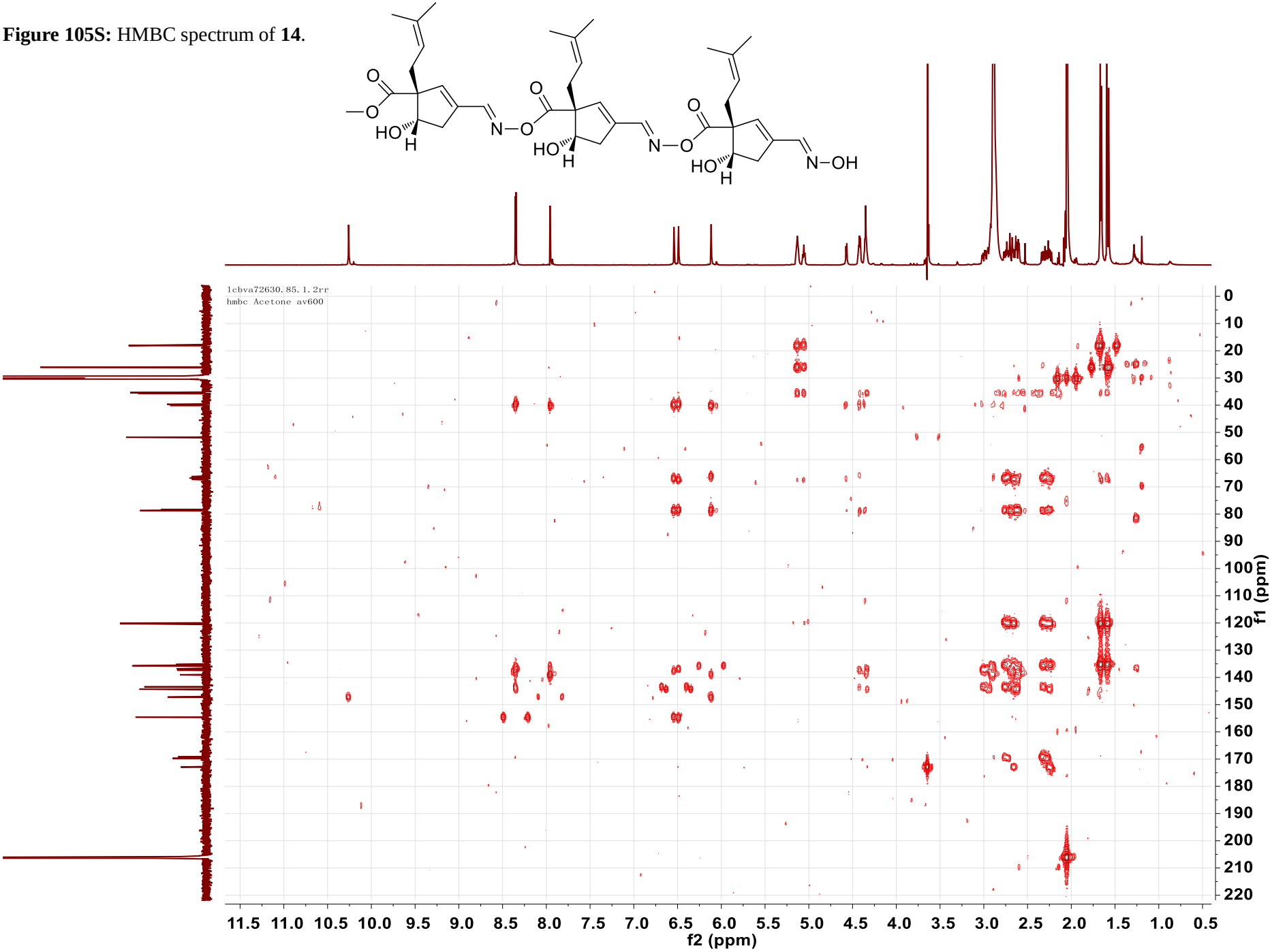


Figure 106S: Enlarged view of HMBC spectrum of **14**.

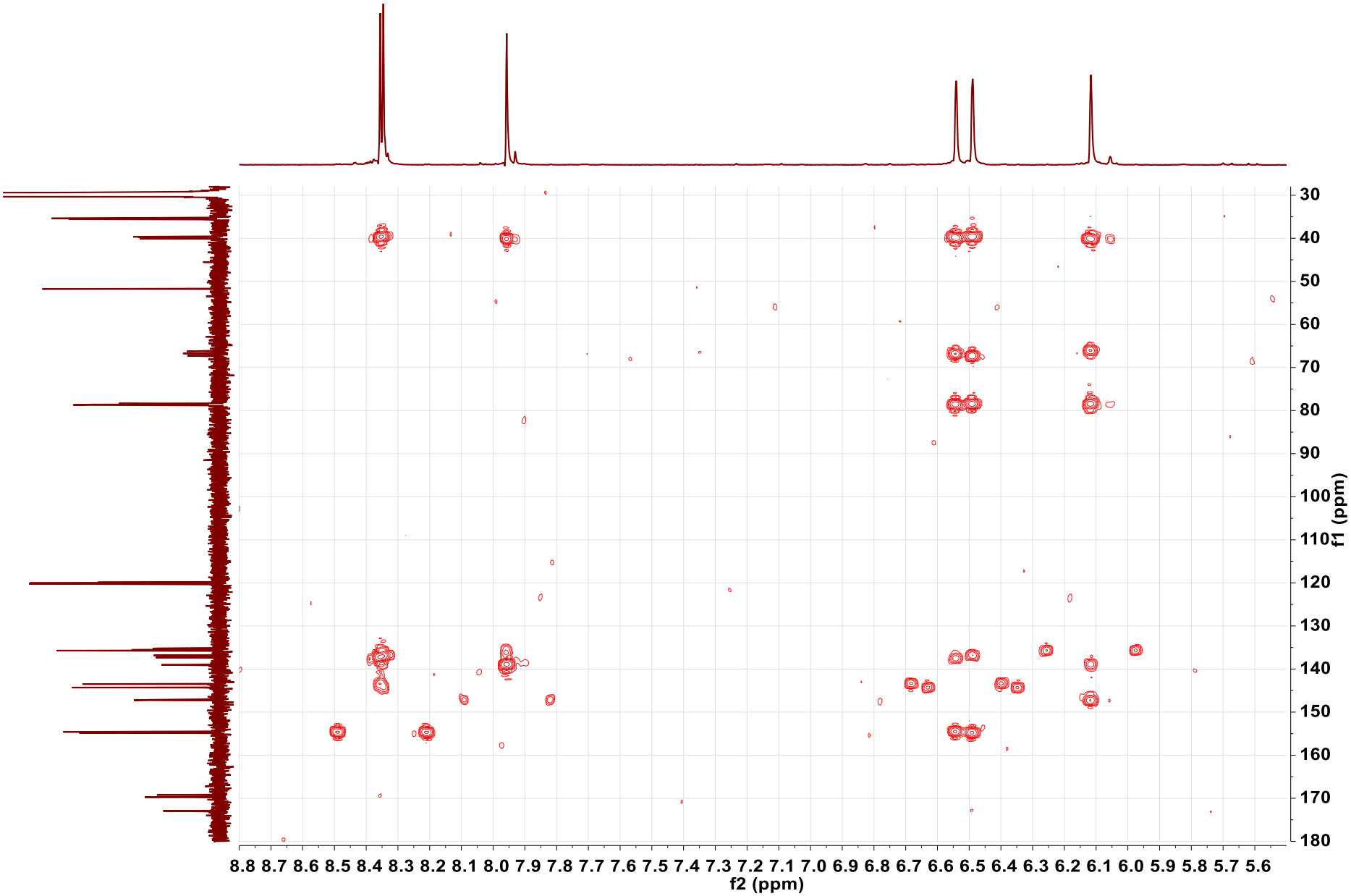


Figure 107S: ROESY spectrum of **14**.

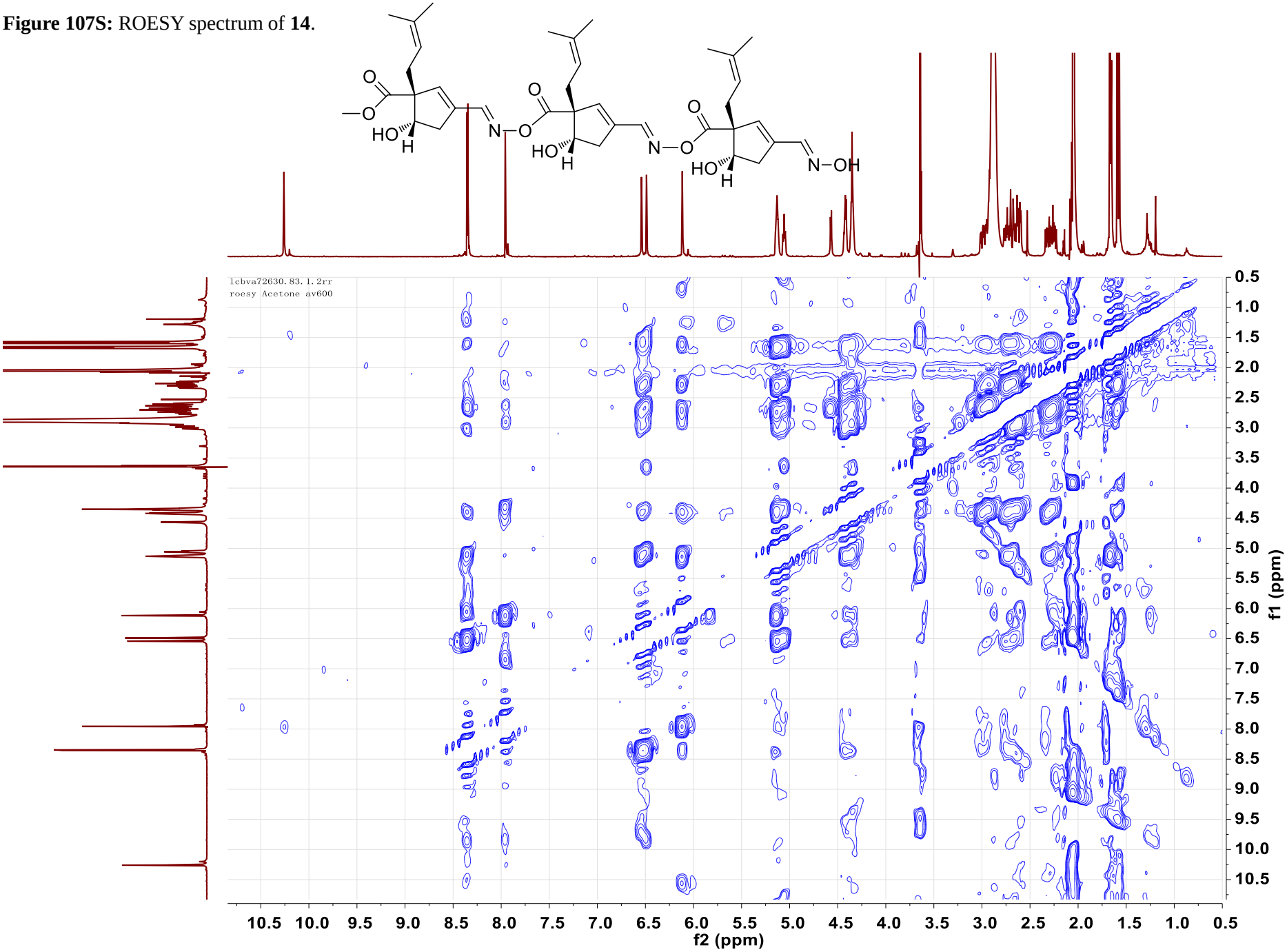


Figure 108S: HRESIMS spectrum of **14**.

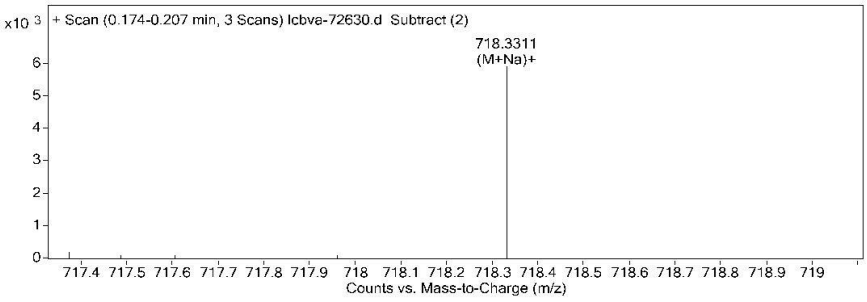
Qualitative Analysis Report

Data Filename	lcbva-72630.d	**Sample Name**	lcbva-72630
Sample Type	Sample	**Position**	P1-B8
Instrument Name	Instrument 1	**User Name**	
Acq Method	SIBU.m	**Acquired Time**	3/10/2015 8:57:06 AM
IRM Calibration Status	Success	**DA Method**	Default.m
Comment			

Sample Group		**Info.**	
Acquisition SW Version	6200 series TOF/6500 series Q-TOF B.05.01 (B5125.2)		

User Spectra

Fragmentor Voltage	Collision Energy	Ionization Mode
135	0	ESI



Peak List

m/z	z	Abund	Formula	Ion
102.128	1	37223.71		
163.1235	1	9297.78		
274.2742	1	17934.31		
318.3004	1	19673.47		
319.3035	1	4342.35		
340.2822	1	5525.16		
513.2003	1	12429.02		
718.3311	1	5901.76	C37 H49 N3 O10	(M+Na)+
734.3056	1	14048.74		
735.3088	1	5943.43		

Formula Calculator Element Limits

Element	Min	Max
C	3	60
H	0	120
O	0	30
N	0	10

Formula Calculator Results

Formula	CalculatedMass	CalculatedMz	Mz	Diff. (mDa)	Diff. (ppm)	DBE
C37 H49 N3 O10	695.3418	718.3310	718.3311	-1.1	-1.6	15.0000

--- End Of Report ---

Agilent Technologies Page 1 of 1 Printed at: 9:07 AM on: 3/10/2015

Figure 109S: ^{1}H NMR spectrum of **15** (acetone-d_6, 600MHz).

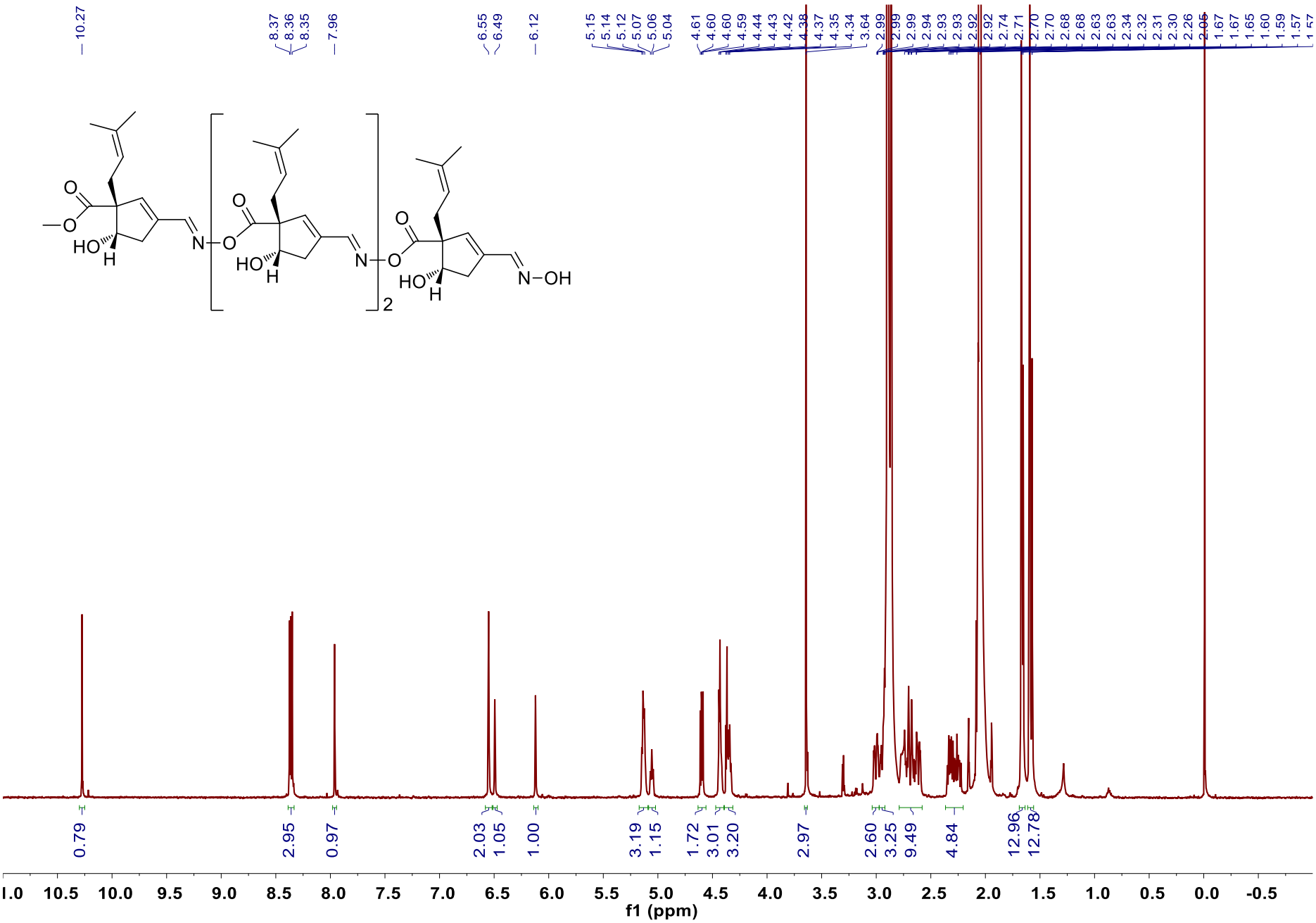


Figure 110S: Enlarged view of ^{1}H NMR spectra of **15** (acetone-d_6, 600MHz).

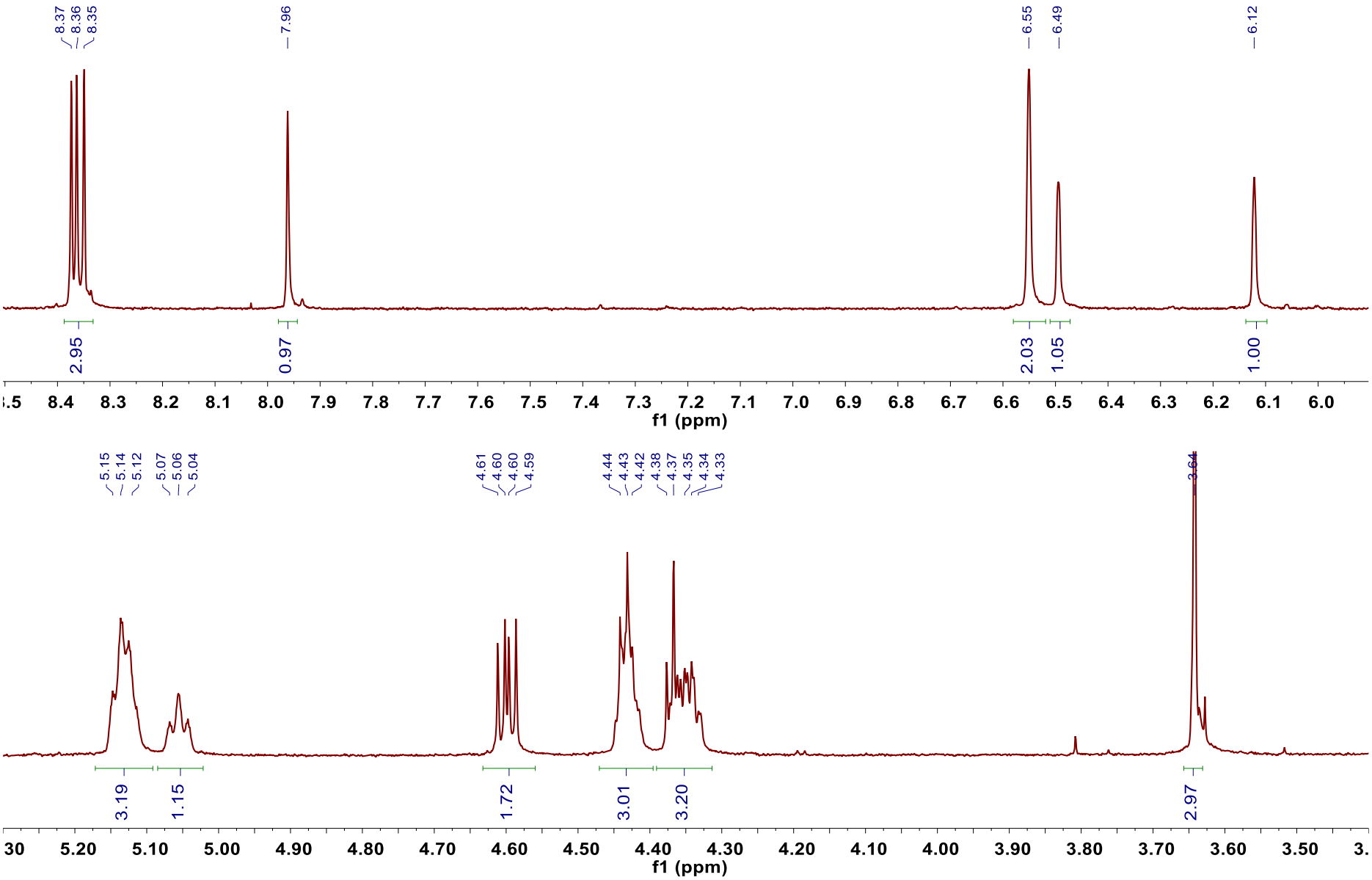


Figure 111S: HRESIMS spectrum of **15**.

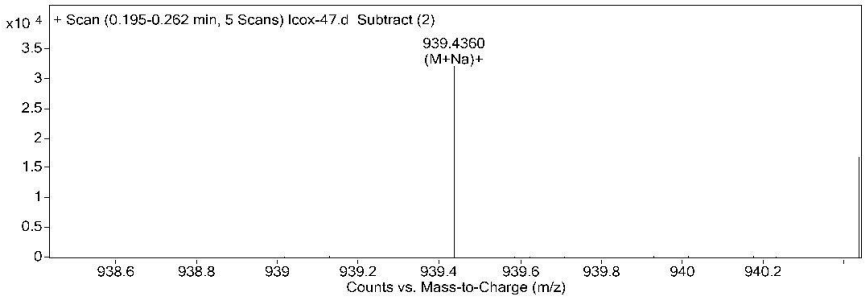
Qualitative Analysis Report

Data Filename	Icox-47.d	**Sample Name**	Icox-47
Sample Type	Sample	**Position**	P1-B2
Instrument Name	Instrument 1	**User Name**	
Acq Method	SIBU.m	**Acquired Time**	3/10/2015 3:51:32 PM
IRM Calibration Status	Success	**DA Method**	Default.m
Comment			

Sample Group		**Info.**	
Acquisition SW Version	6200 series TOF/6500 series Q-TOF B.05.01 (B5125.2)		

User Spectra

Fragmentor Voltage	Collision Energy	Ionization Mode
135	0	ESI



Peak List

m/z	z	Abund	Formula	Ion
274.2745	1	19914.81		
318.3001	1	22309.2		
479.2151	2	21511.53		
495.1891	1	37214		
513.1998	1	27252.69		
939.436	1	32073.08	C49 H64 N4 O13	(M+Na)+
940.438	1	16767.01	C49 H64 N4 O13	(M+Na)+
955.4105	1	79761.27		
956.4138	1	45534.26		
957.4137	1	19558.31		

Formula Calculator Element Limits

Element	Min	Max
C	3	60
H	0	120
O	0	30
N	0	10

Formula Calculator Results

Formula	CalculatedMass	CalculatedMz	Mz	Diff. (mDa)	Diff. (ppm)	DBE
C49 H64 N4 O13	916.4470	939.4362	939.4360	0.7	0.8	20.0000

--- End Of Report ---

Agilent Technologies Page 1 of 1 Printed at: 4:21 PM on: 3/10/2015

Figure 112S: ^{1}H NMR spectrum of **16** (acetone-d_6, 600MHz).

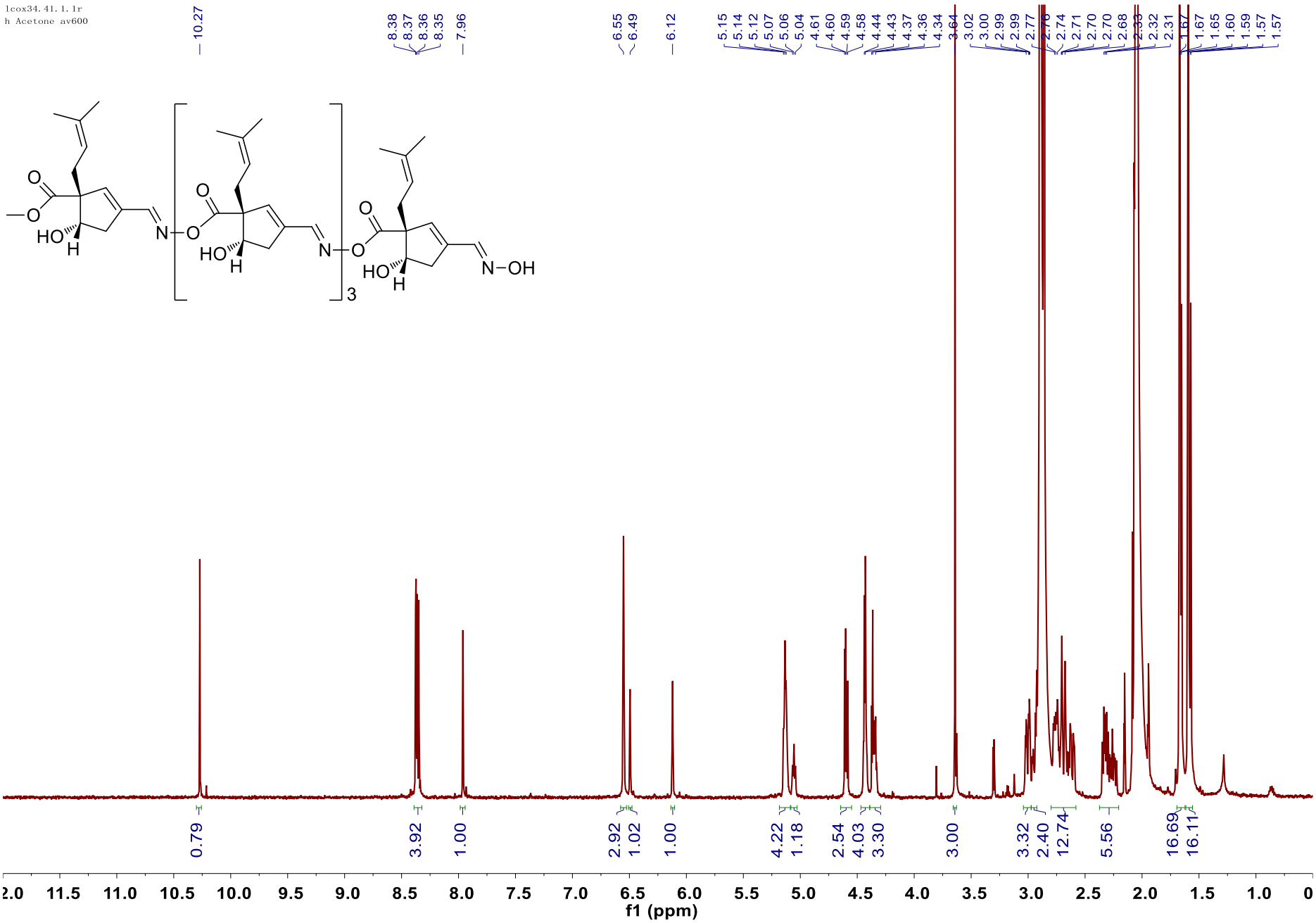


Figure 113S: Enlarged view of ^{1}H NMR spectrum of **16** (acetone-d_6, 600MHz).

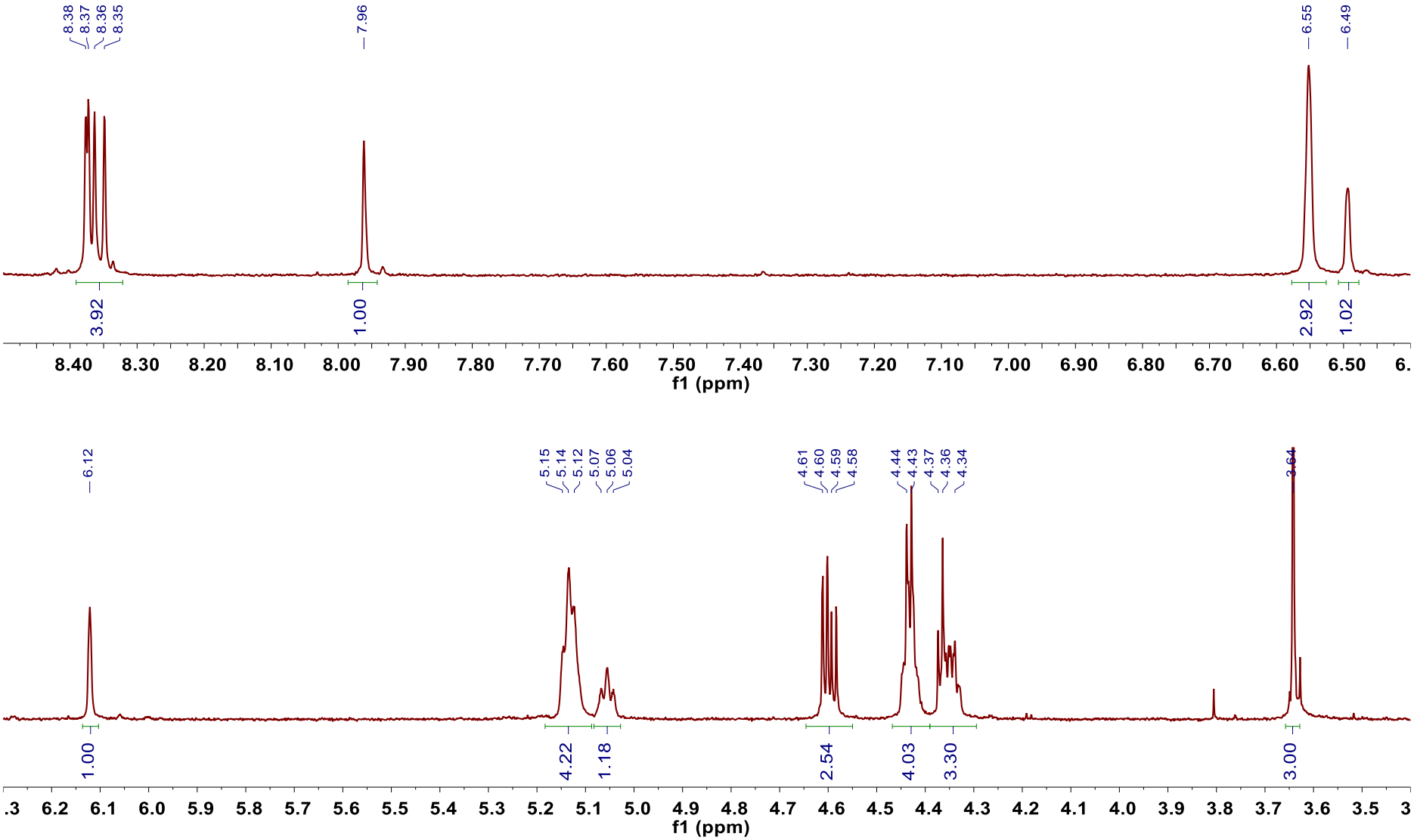


Figure 114S: HRESIMS spectrum of **16**.

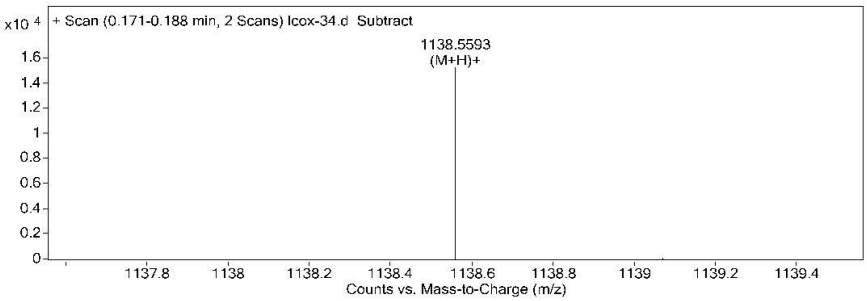
Qualitative Analysis Report

Data Filename	Icox-34.d	**Sample Name**	Icox-34
Sample Type	Sample	**Position**	P1-A5
Instrument Name	Instrument 1	**User Name**	
Acq Method	SIBU.m	**Acquired Time**	3/23/2015 4:13:22 PM
IRM Calibration Status	Success	**DA Method**	Default.m
Comment			

Sample Group		**Info.**	
Acquisition SW	6200 series TOF/6500 series		
Version	Q-TOF B.05.01 (B5125.2)		

User Spectra

Fragmentor Voltage	Collision Energy	Ionization Mode
135	0	ESI



Peak List

m/z	z	Abund	Formula	Ion
274.274	1	15805.6		
318.3006	1	15193.98		
588.7575	2	31665.42		
589.2593	2	26469.95		
1138.5593	1	15225.89	C61 H79 N5 O16	(M+H)+
1160.541	1	15176.26		

Formula Calculator Element Limits

Element	Min	Max
C	3	100
H	0	200
O	0	30
N	0	10

Formula Calculator Results

Formula	CalculatedMass	CalculatedMz	Mz	Diff. (mDa)	Diff. (ppm)	DBE
C61 H79 N5 O16	1137.5522	1138.5595	1138.5593	0.2	0.2	25.0000

--- End Of Report ---

Agilent Technologies Page 1 of 1 Printed at: 4:18 PM on: 3/23/2015