

## Electronic Supplementary Information

### **Bioactive compounds from the seeds of *Amomum tsaoko* Crevost et Lemaire, a Chinese spice as inhibitors of sphingosine kinases, SPHK1/2**

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Figure S1. HR-ESIMS data of 1

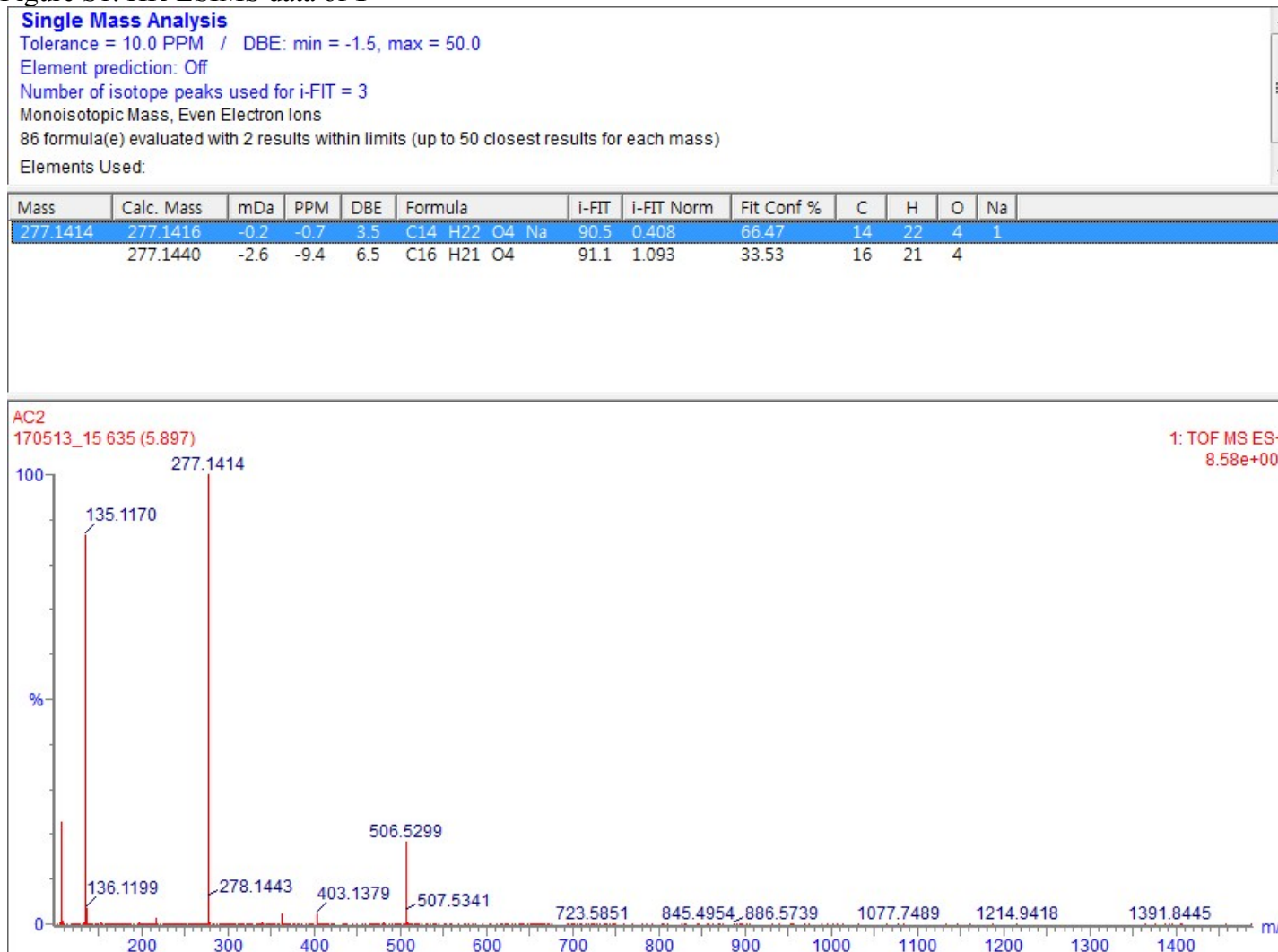


Figure S2.  $^1\text{H}$  NMR spectrum of **1** ( $\text{CDCl}_3$ , 700 MHz)

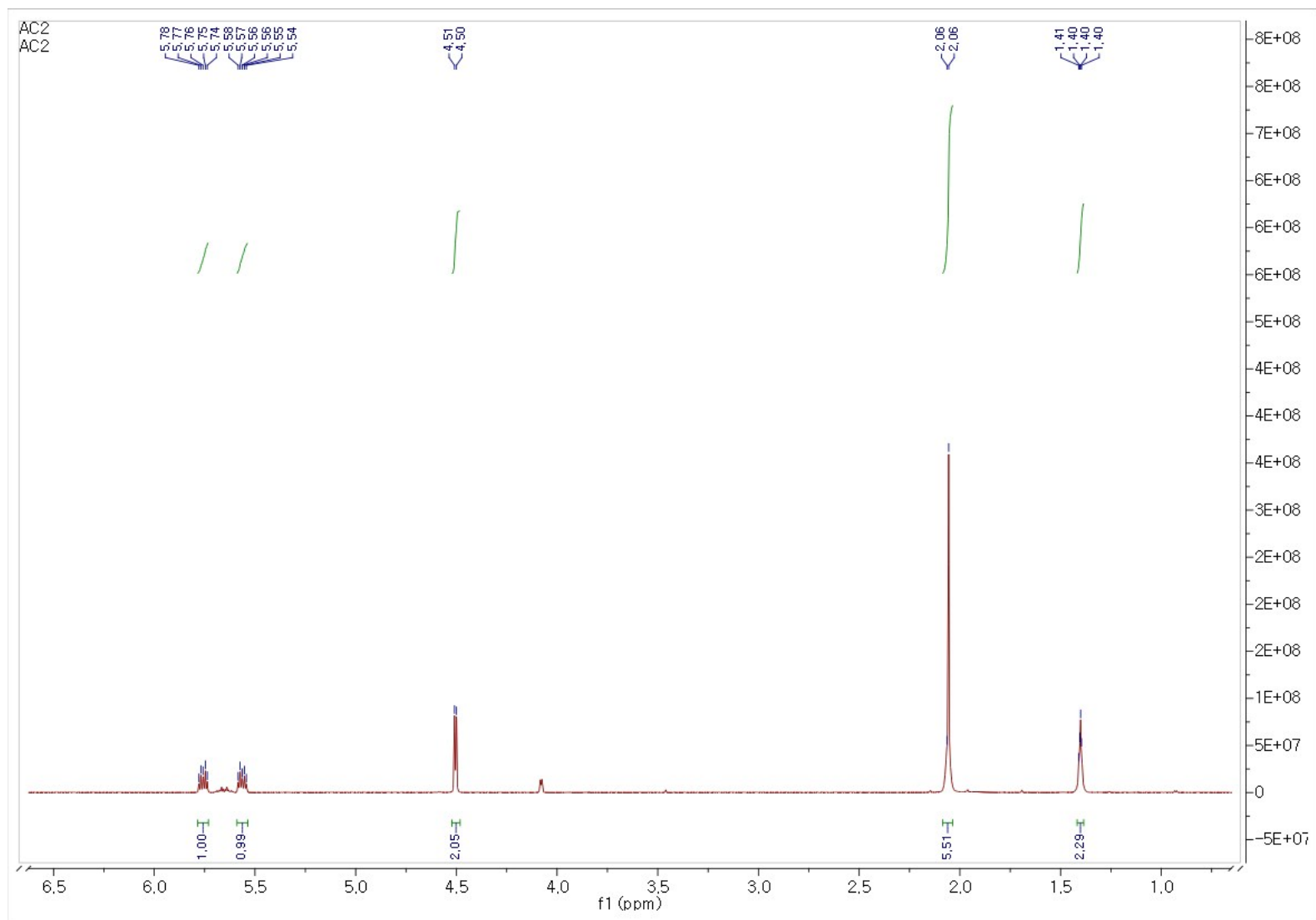


Figure S3.  $^{13}\text{C}$  NMR spectrum of **1** ( $\text{CDCl}_3$ , 175 Hz)

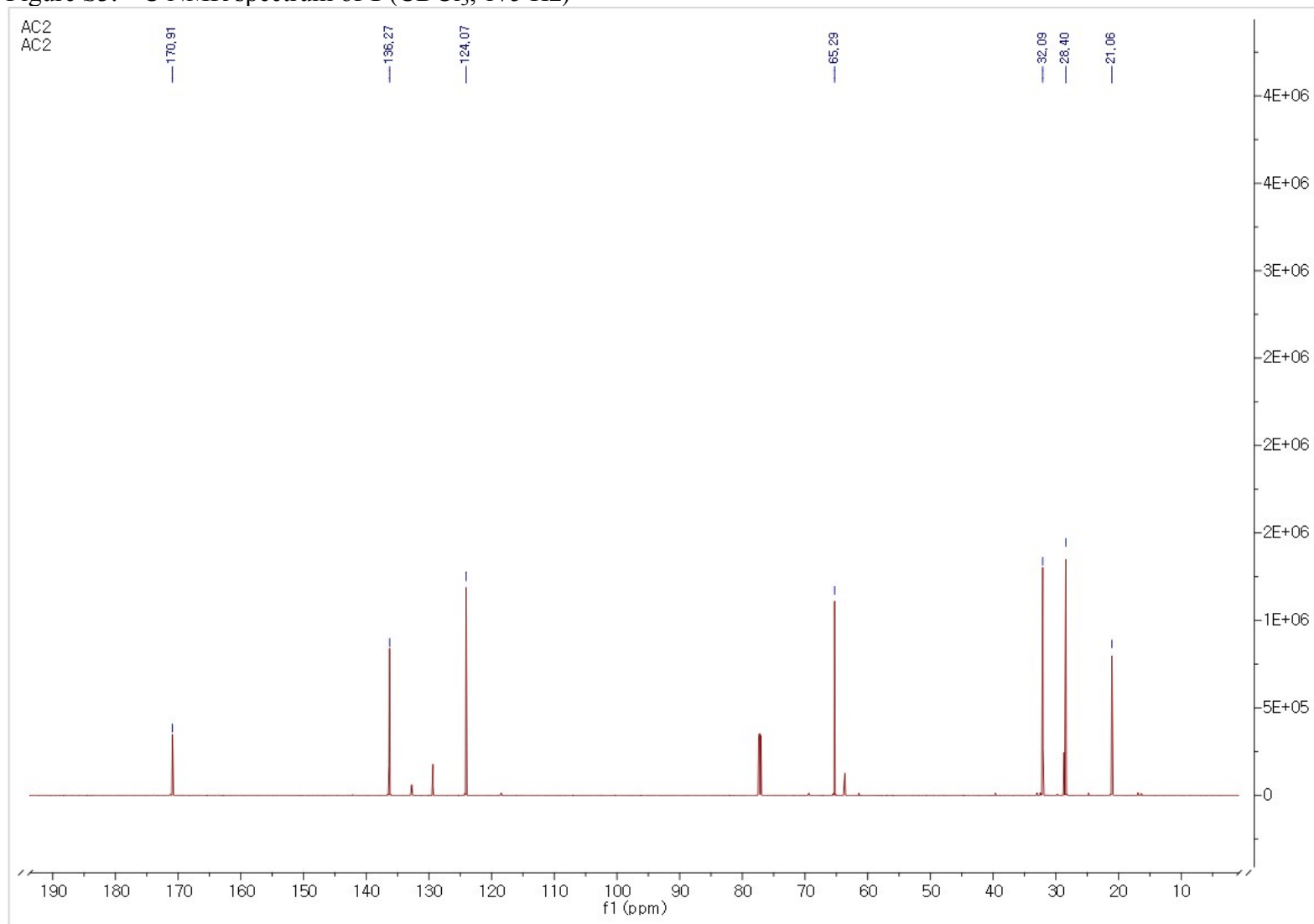


Figure S4.  $^1\text{H}$ - $^1\text{H}$  COSY spectrum of **1** ( $\text{CDCl}_3$ )

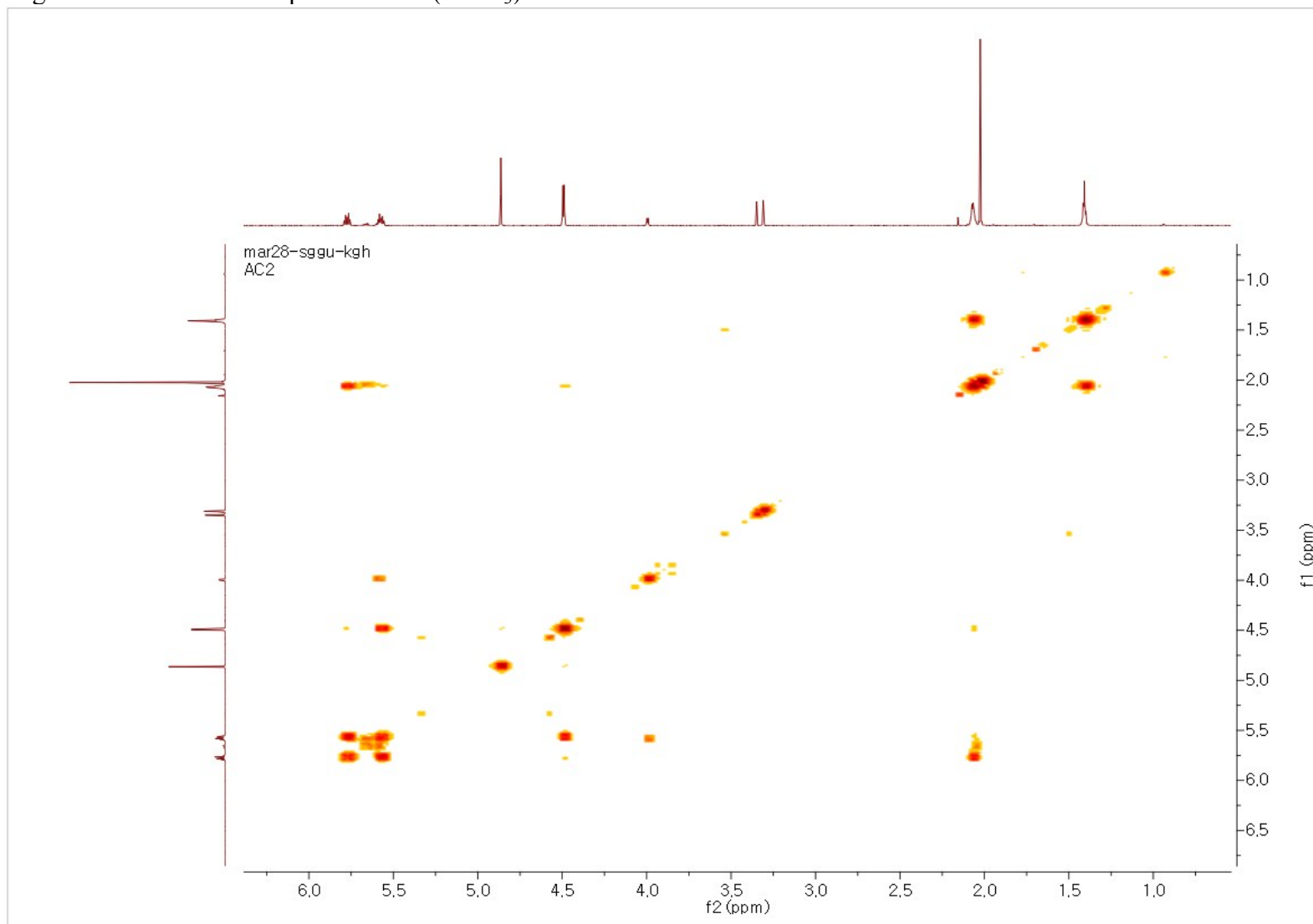


Figure S5. HSQC spectrum of **1** (CDCl<sub>3</sub>)

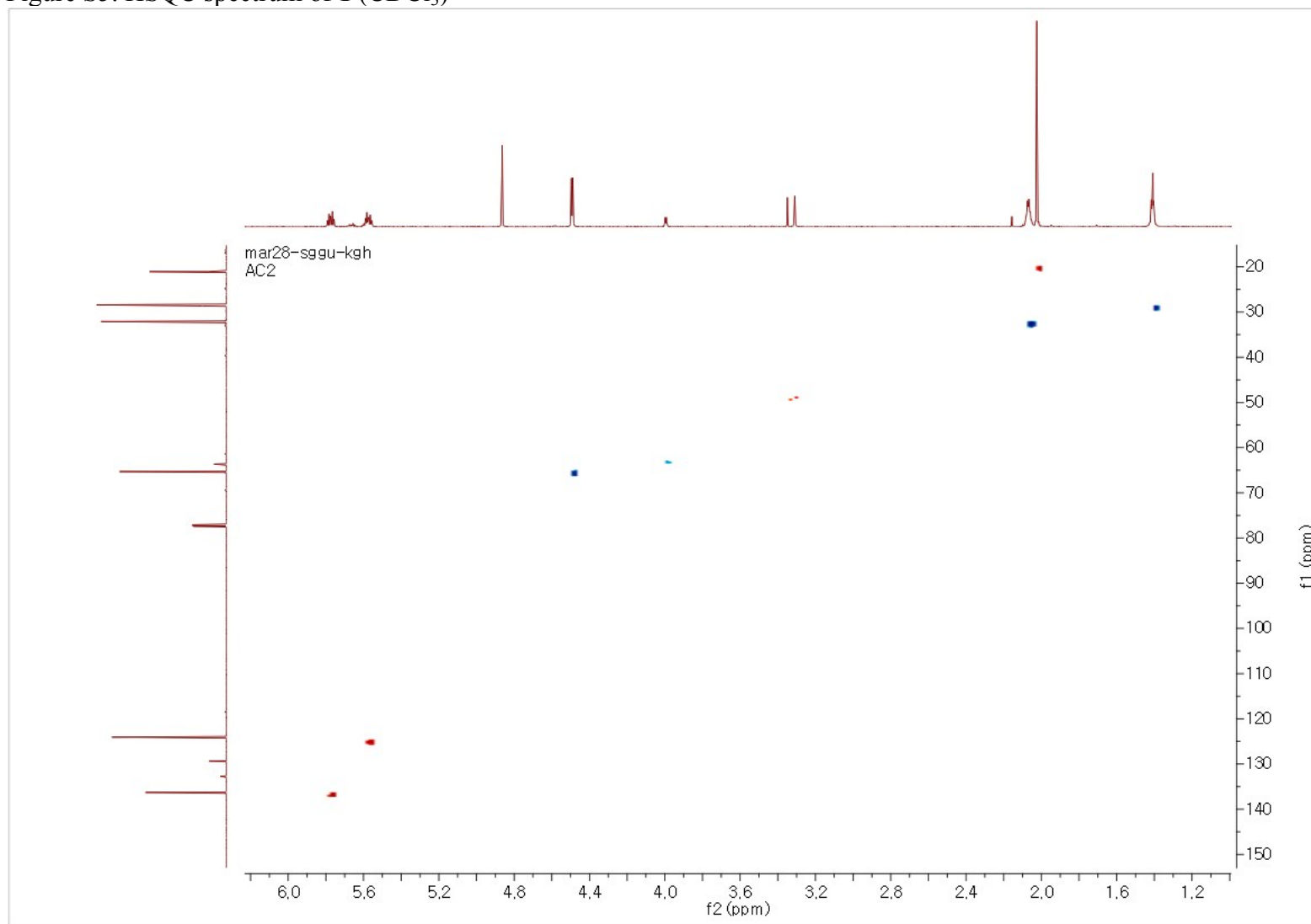




Figure S6. HMBC spectrum of **1** (CDCl<sub>3</sub>)

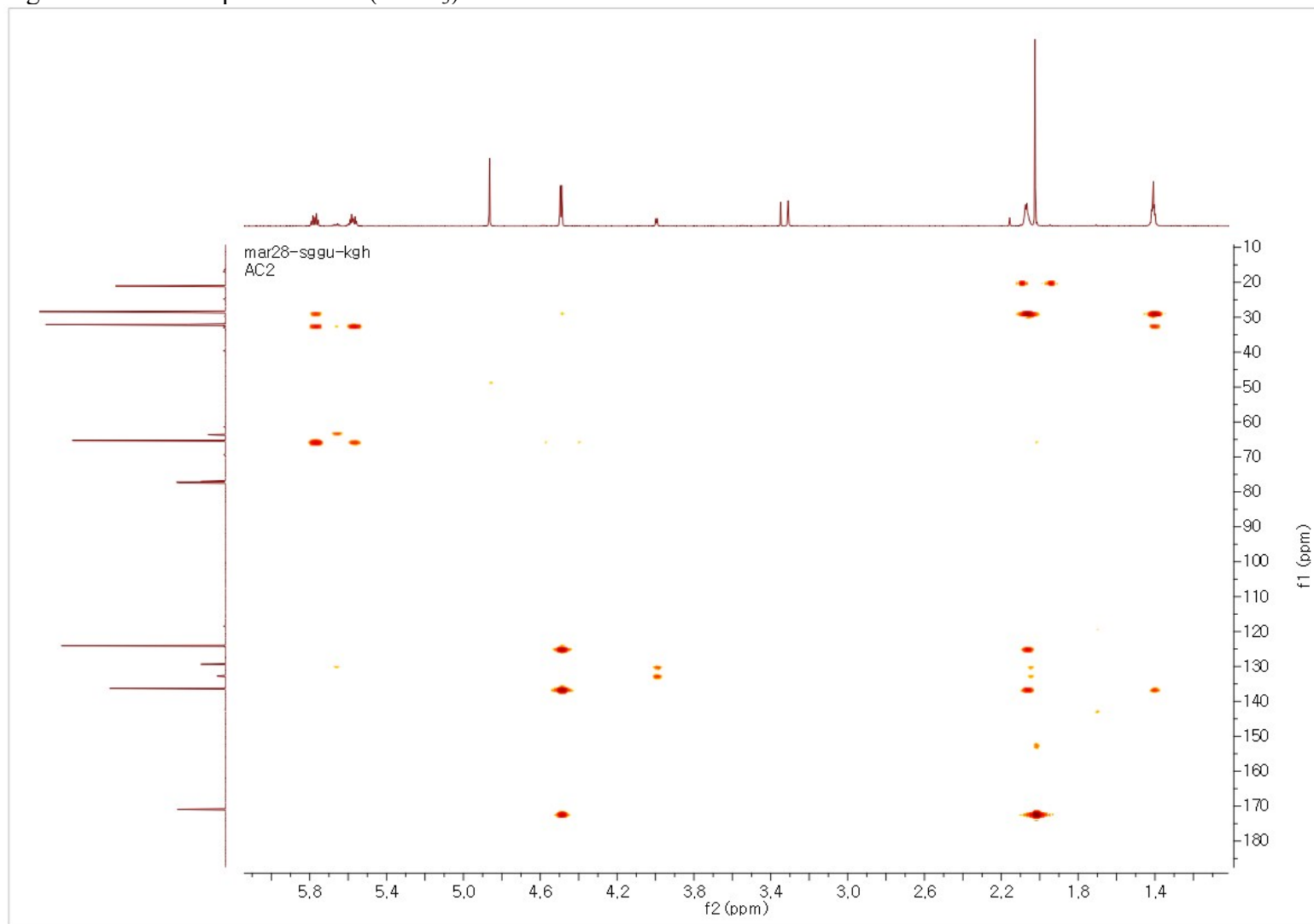


Figure S7. HR-ESIMS data of **2**

**Single Mass Analysis**

Tolerance = 10.0 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

70 formula(e) evaluated with 1 results within limits (up to 50 closest results for each mass)

Elements Used:

Mass	Calc. Mass	mDa	PPM	DBE	Formula	i-FIT	i-FIT Norm	Fit Conf %	C	H	O	Na
235.1310	235.1310	0.0	0.0	2.5	C <sub>12</sub> H <sub>20</sub> O <sub>3</sub> Na	35.9	n/a	n/a	12	20	3	1

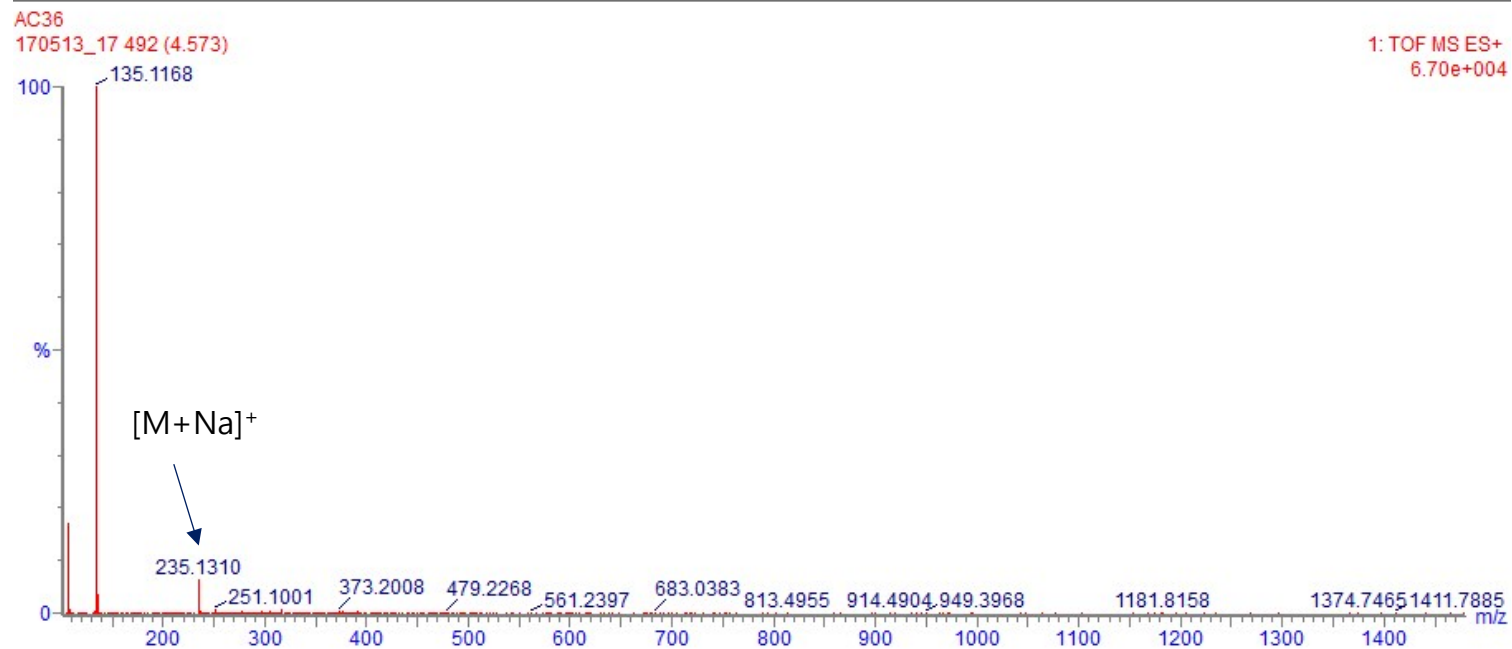


Figure S8.  $^1\text{H}$  NMR spectrum of **2** ( $\text{CDCl}_3$ , 700 MHz)

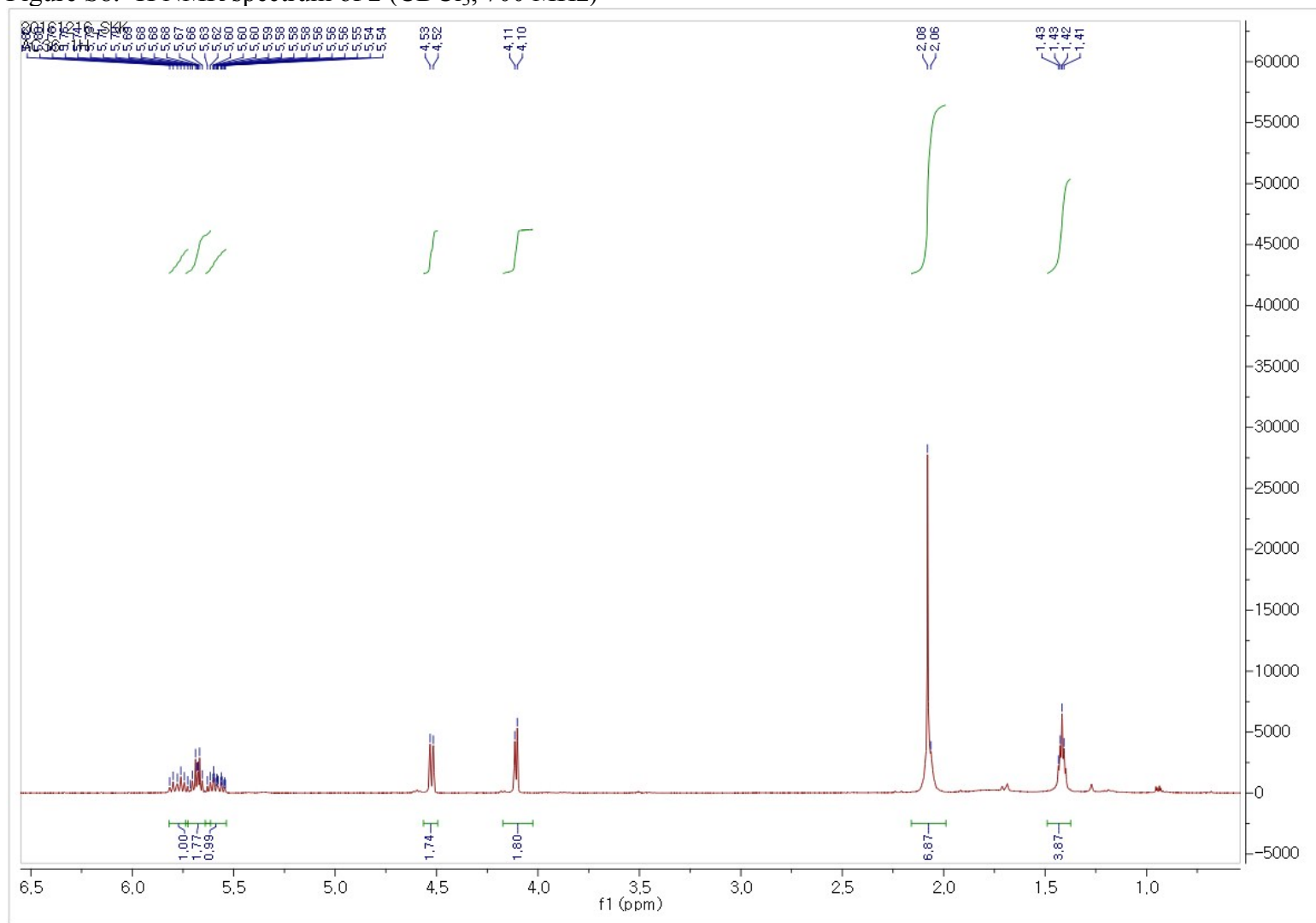


Figure S9.  $^{13}\text{C}$  NMR spectrum of **2** ( $\text{CDCl}_3$ , 175 MHz)

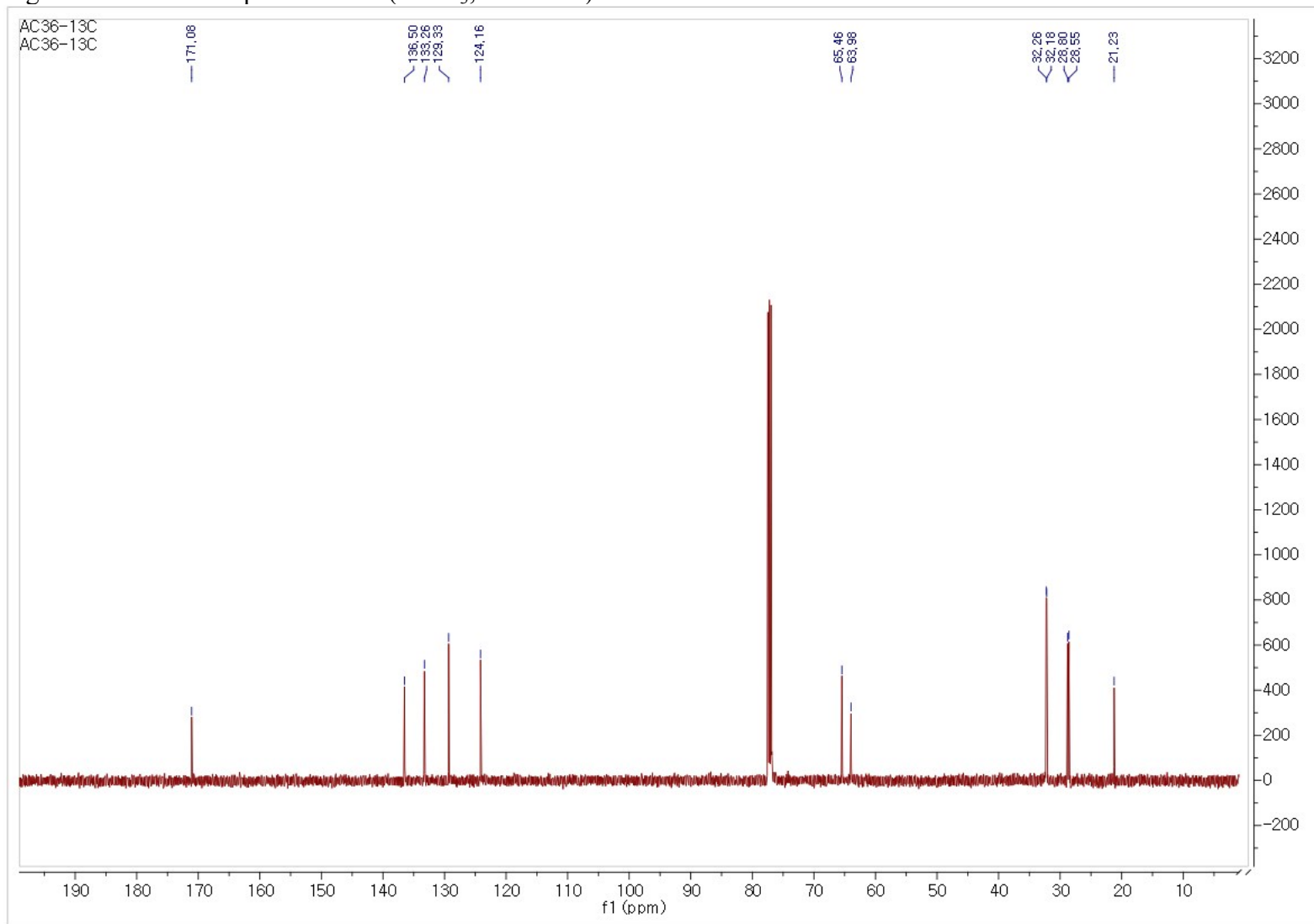


Figure S10. TOCSY spectrum of **2** (CDCl<sub>3</sub>)

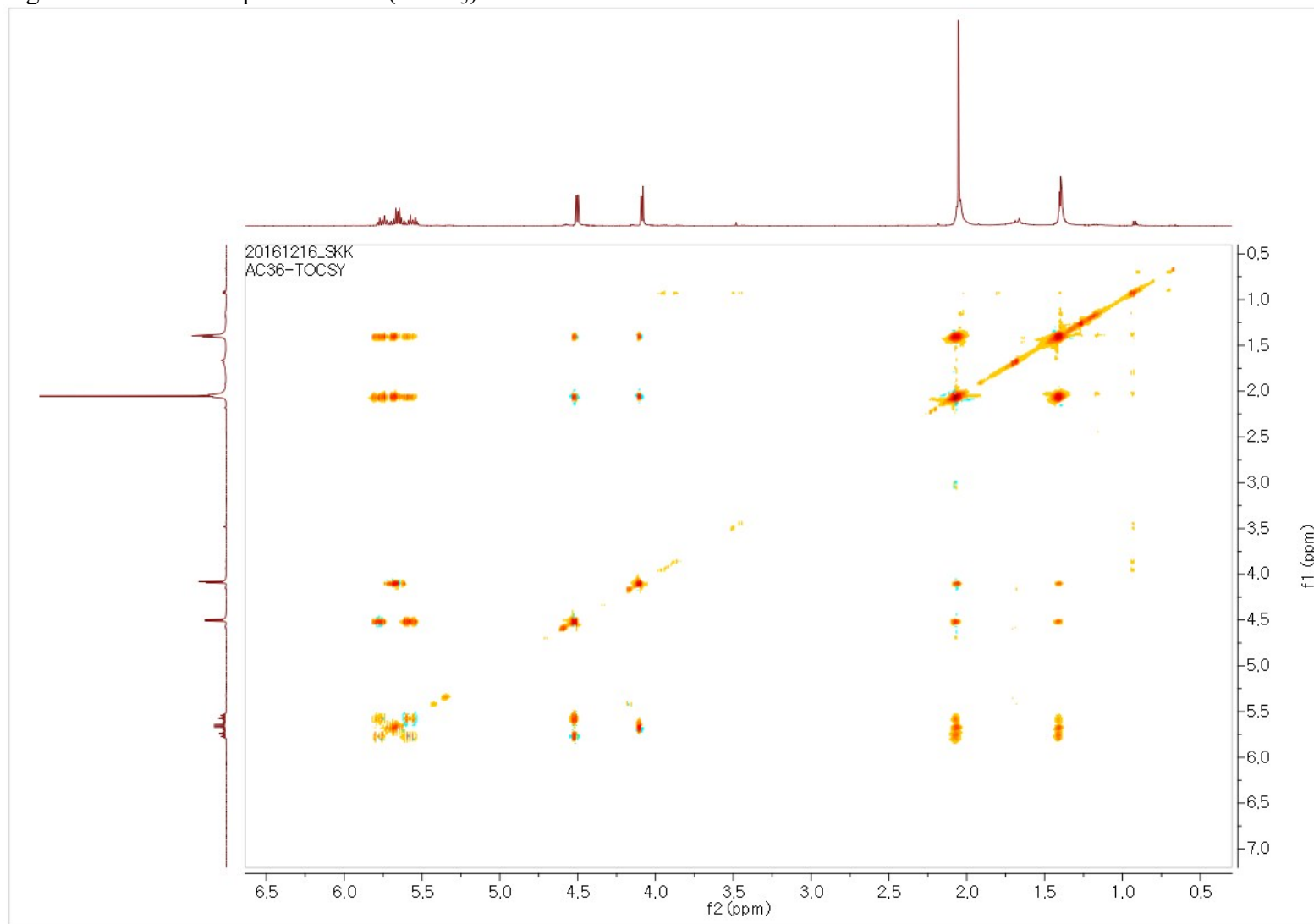


Figure S11. HSQC spectrum of **2** (CDCl<sub>3</sub>)

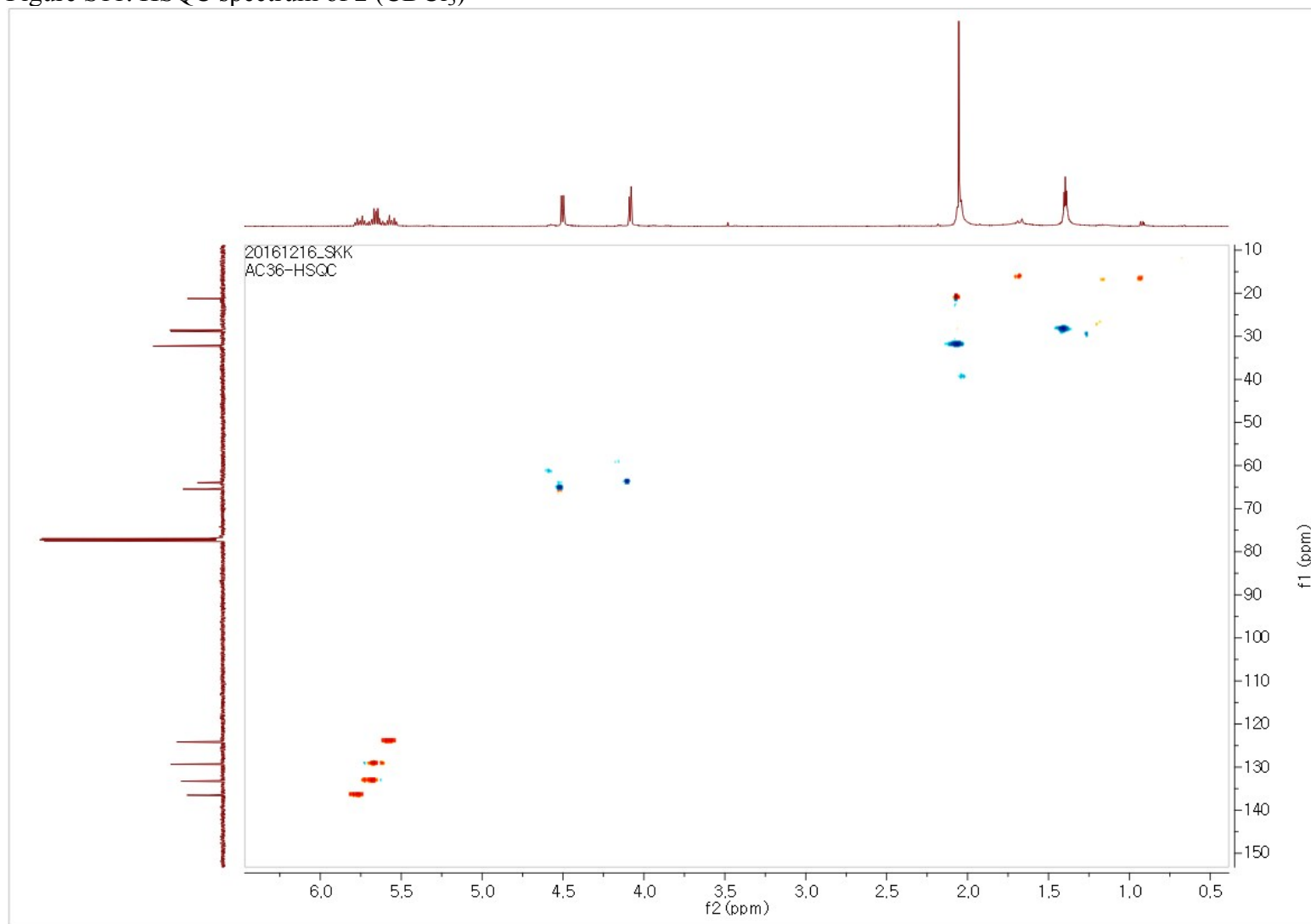


Figure S12. HMBC spectrum of **2** (CDCl<sub>3</sub>)

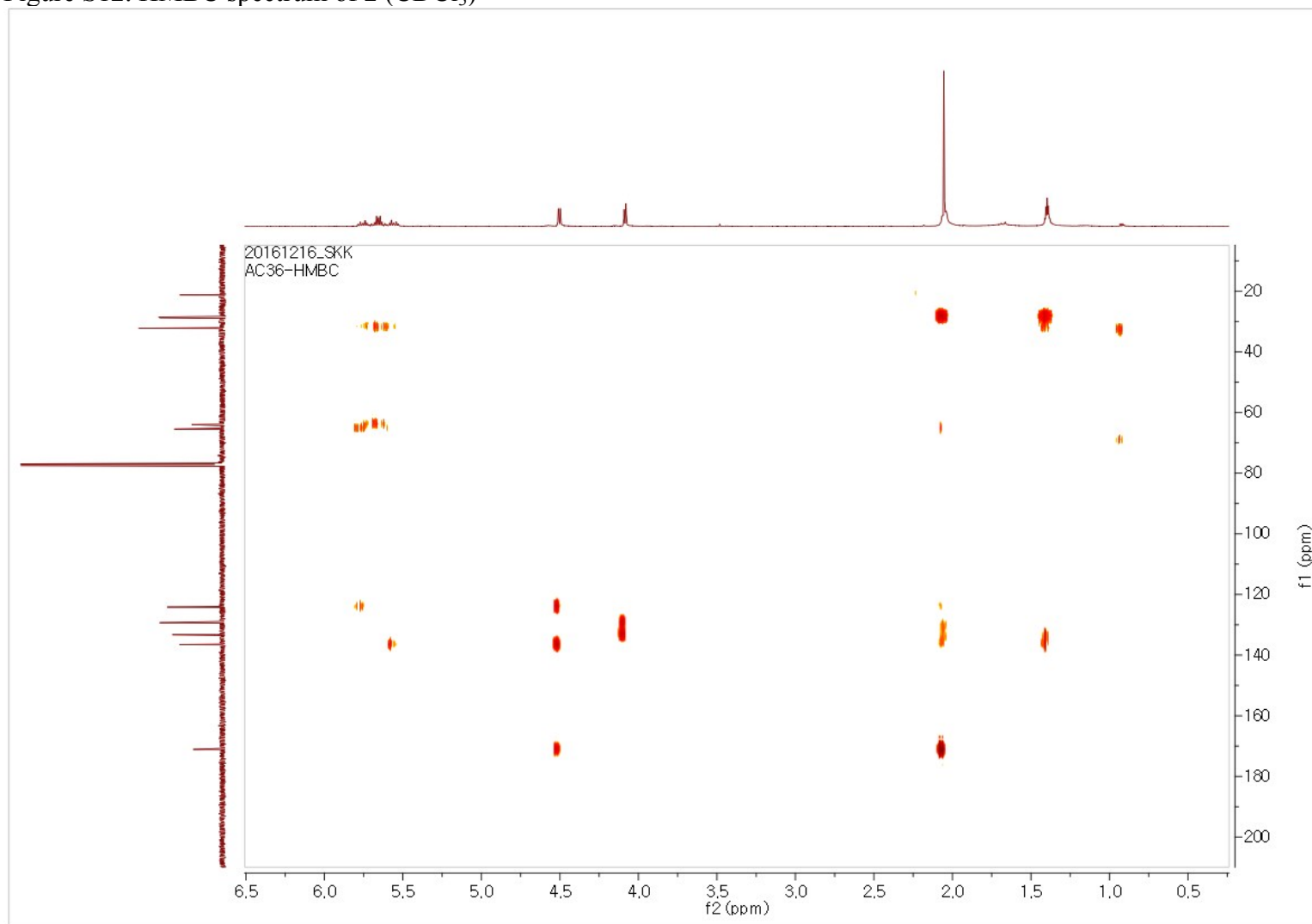


Figure S13. HR-ESIMS data of **5**

**Single Mass Analysis**

Tolerance = 10.0 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

80 formula(e) evaluated with 2 results within limits (up to 50 closest results for each mass)

Elements Used:

Mass	Calc. Mass	mDa	PPM	DBE	Formula	i-FIT	i-FIT Norm	Fit Conf %	C	H	O	Na
265.1795	265.1804	-0.9	-3.4	4.5	C16 H25 O3	354.4	0.022	97.81	16	25	3	
	265.1780	1.5	5.7	1.5	C14 H26 O3 Na	358.2	3.823	2.19	14	26	3	1

AC16

170513\_2 604 (5.608)

1: TOF MS ES-  
2.59e+005

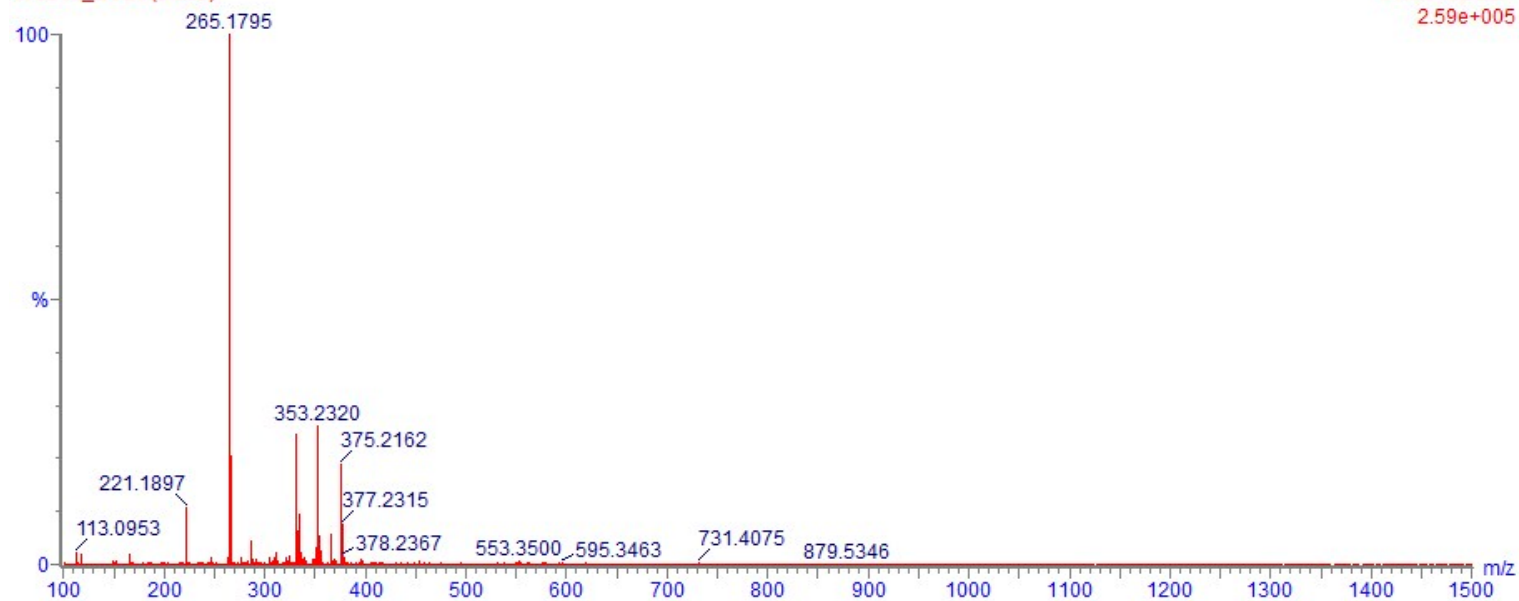




Figure S14.  $^1\text{H}$  NMR spectrum of **5** ( $\text{CDCl}_3$ , 600 MHz)

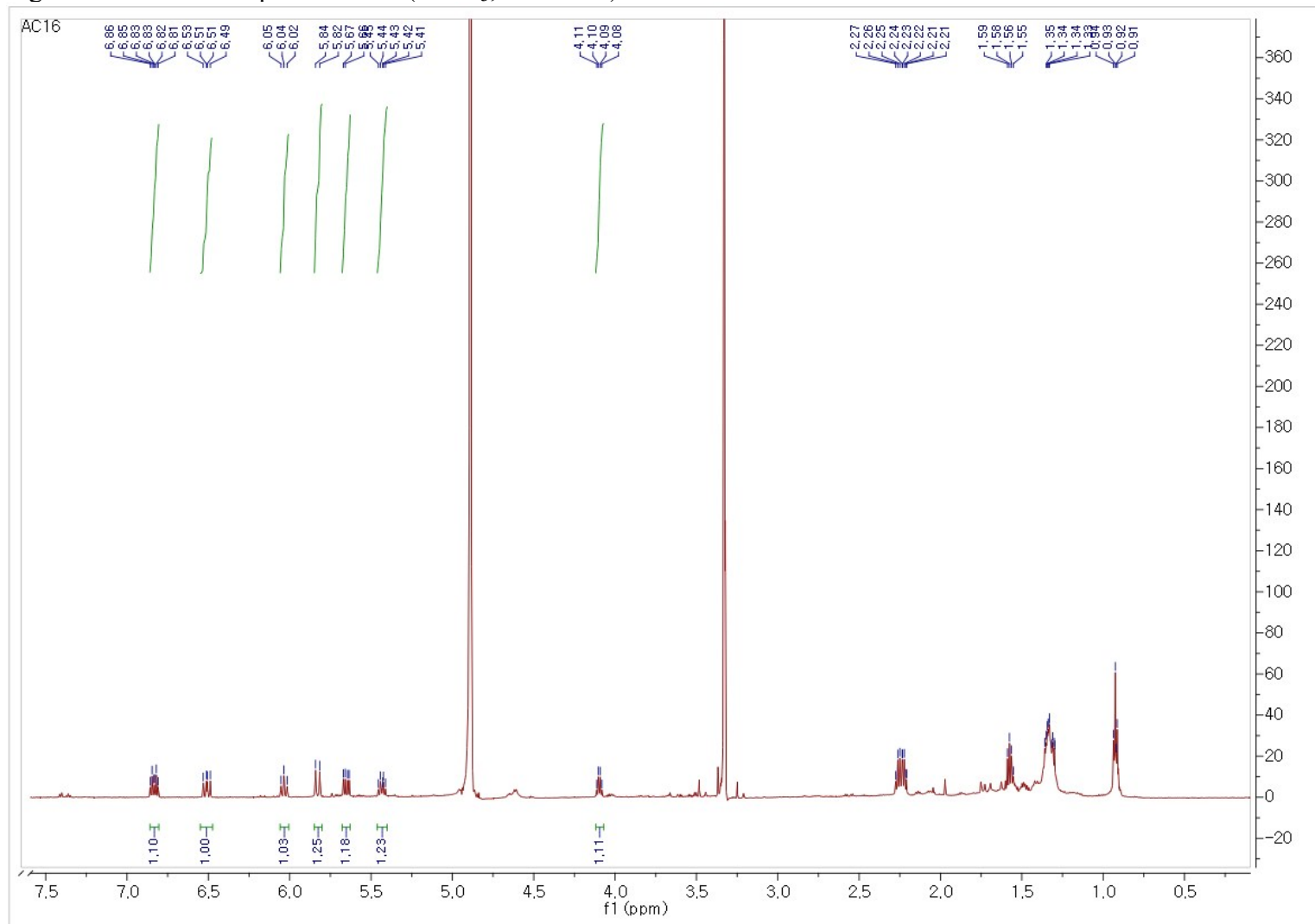


Figure S15.  $^{13}\text{C}$  NMR spectrum of **5** ( $\text{CDCl}_3$ , 150 MHz)

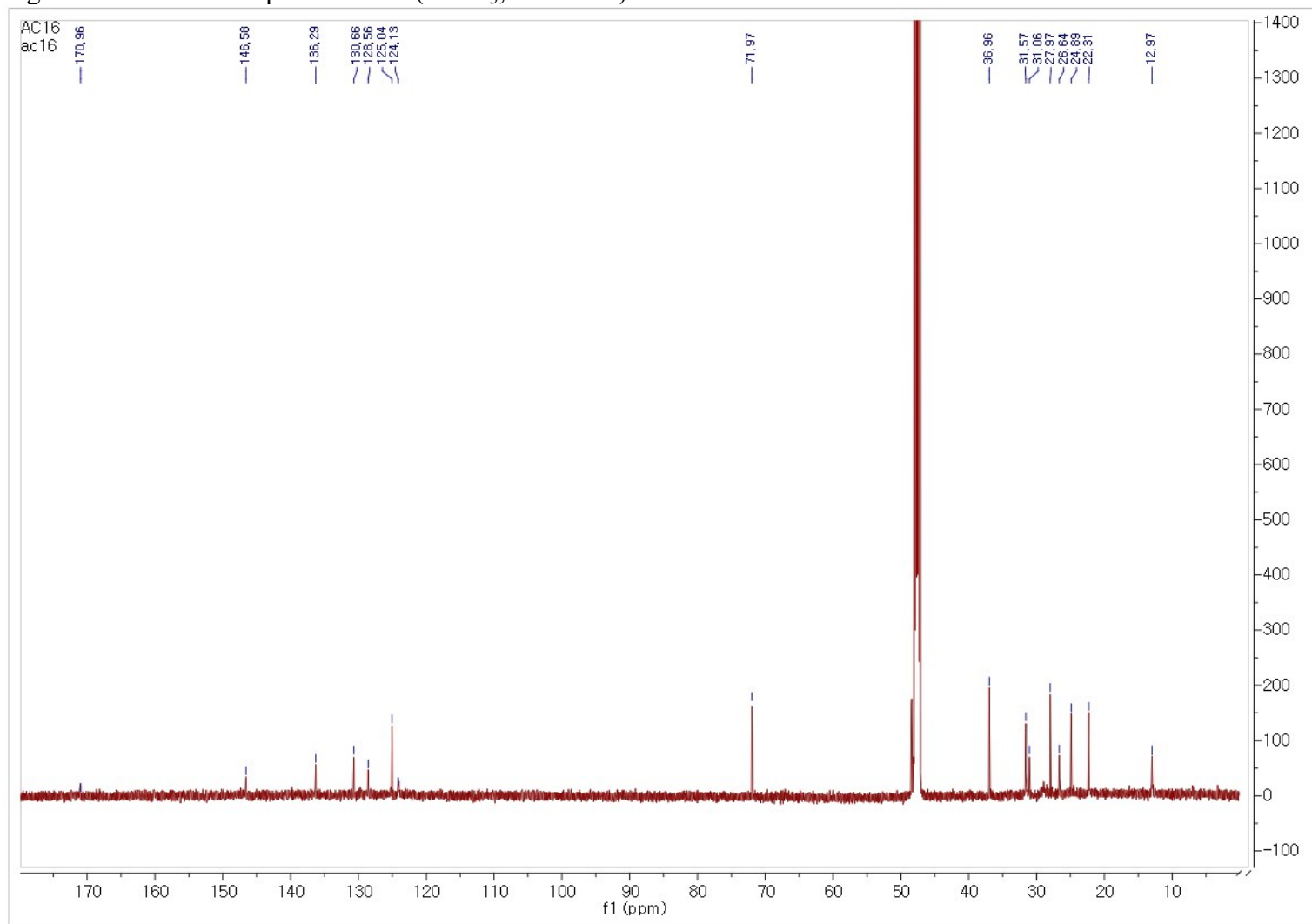


Figure S16.  $^1\text{H}$ - $^1\text{H}$  COSY spectrum of **5** ( $\text{CDCl}_3$ )

20170308 AC16-HMBC\_COSY.013.esp

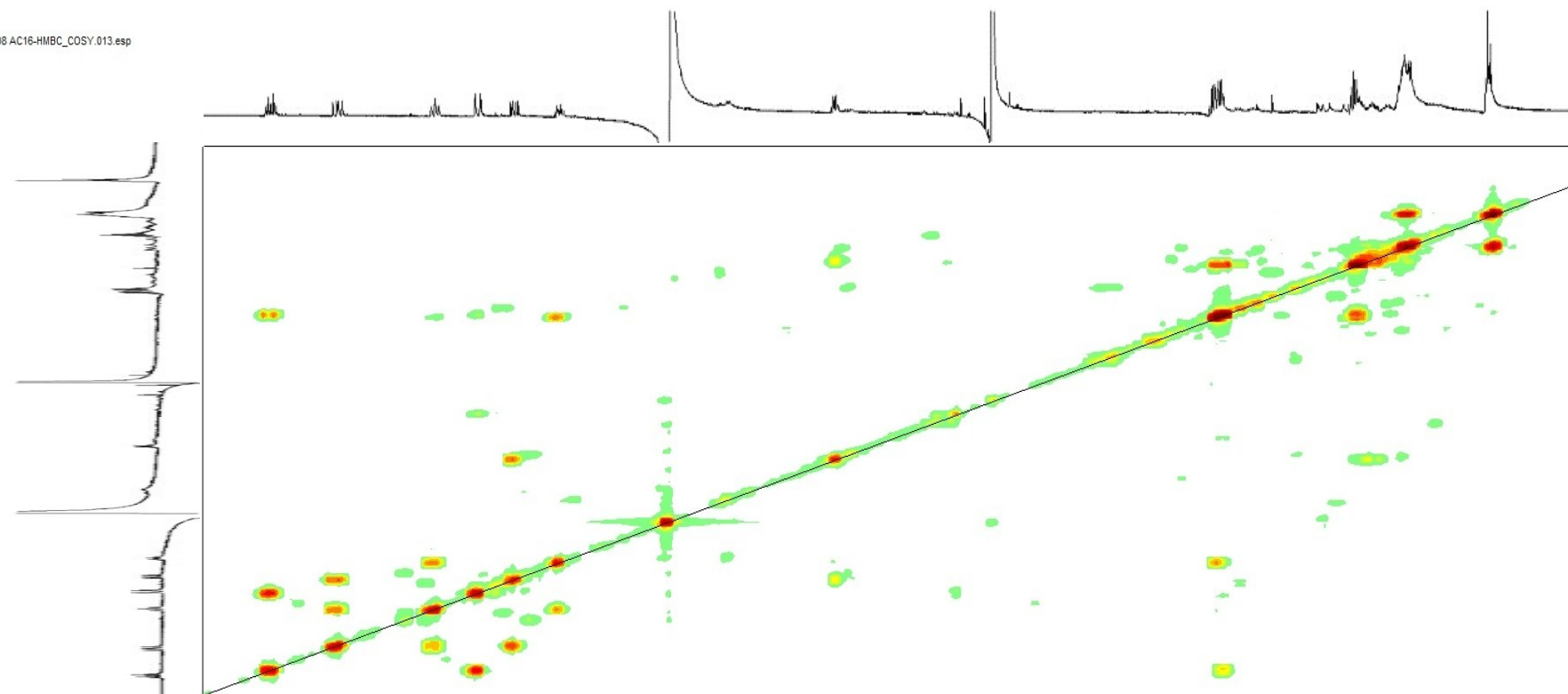


Figure S17. HSQC spectrum of **5** (CDCl<sub>3</sub>)

2D NMR ac16-hsqc (1).011.esp

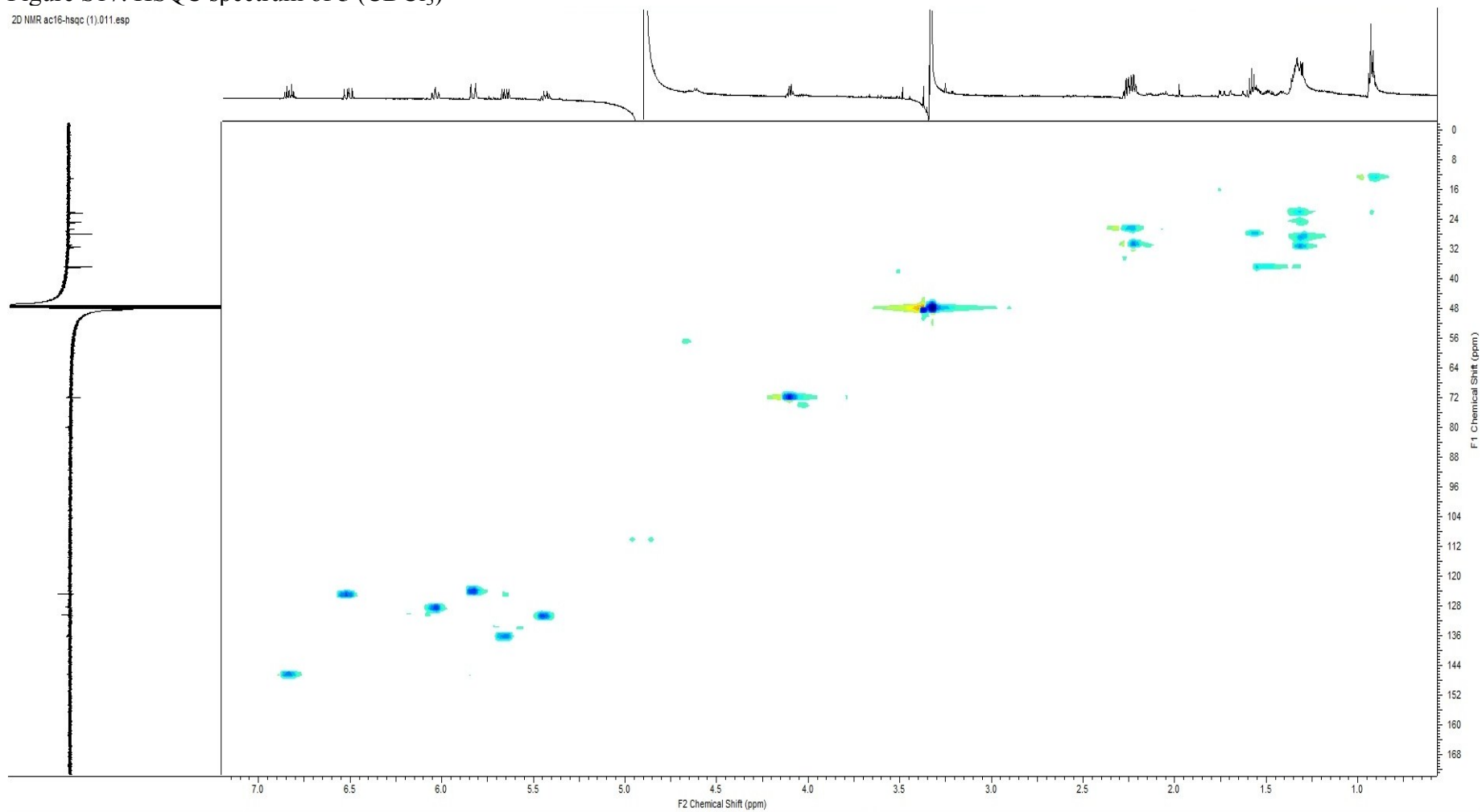


Figure S18. HMBC spectrum of **5** (CDCl<sub>3</sub>)

20170308 AC16-HMBC\_COSY.012.esp

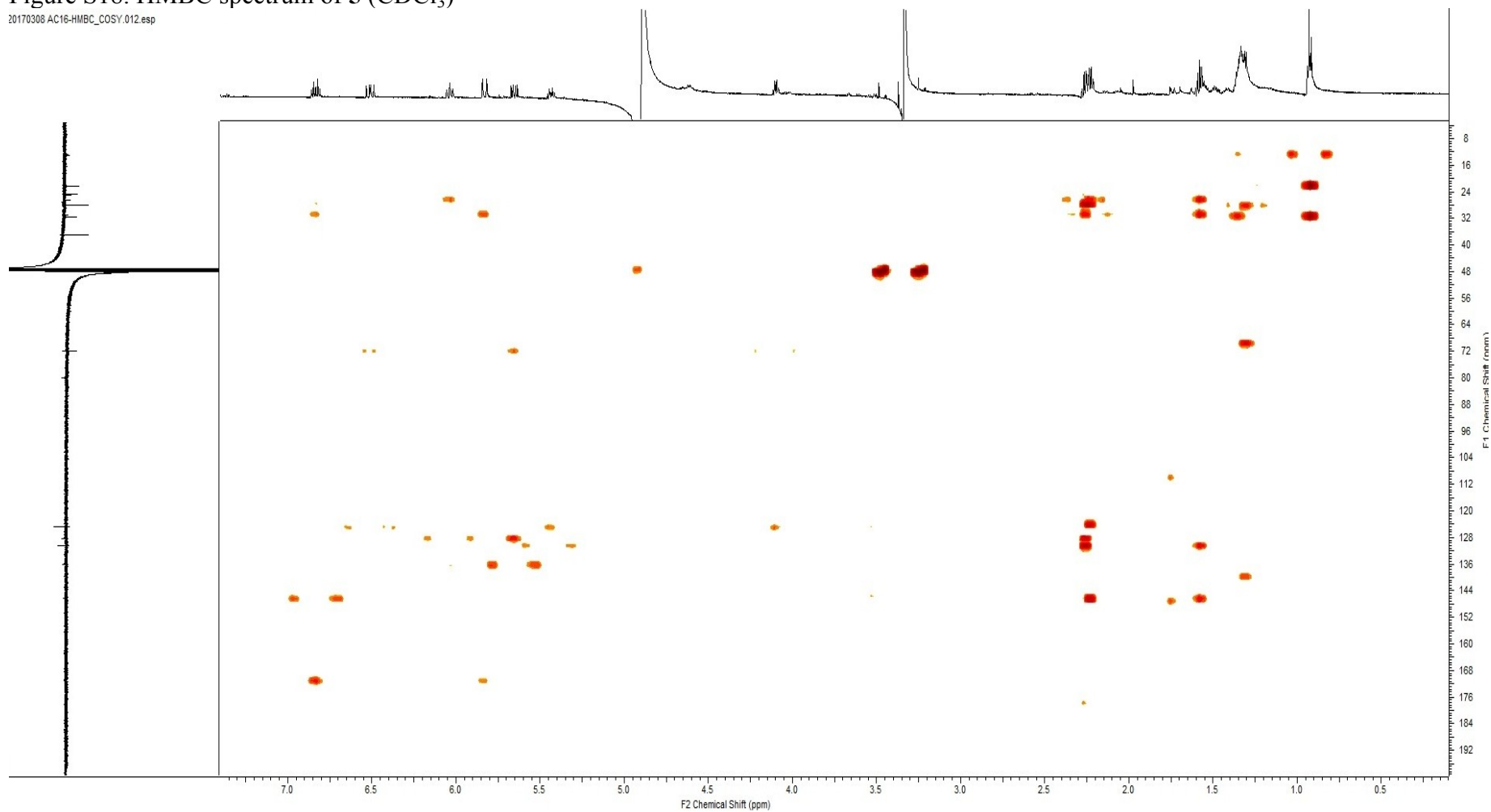


Figure S19. MS/MS analysis of **5** (MS<sup>2</sup> 265 → full-scan)

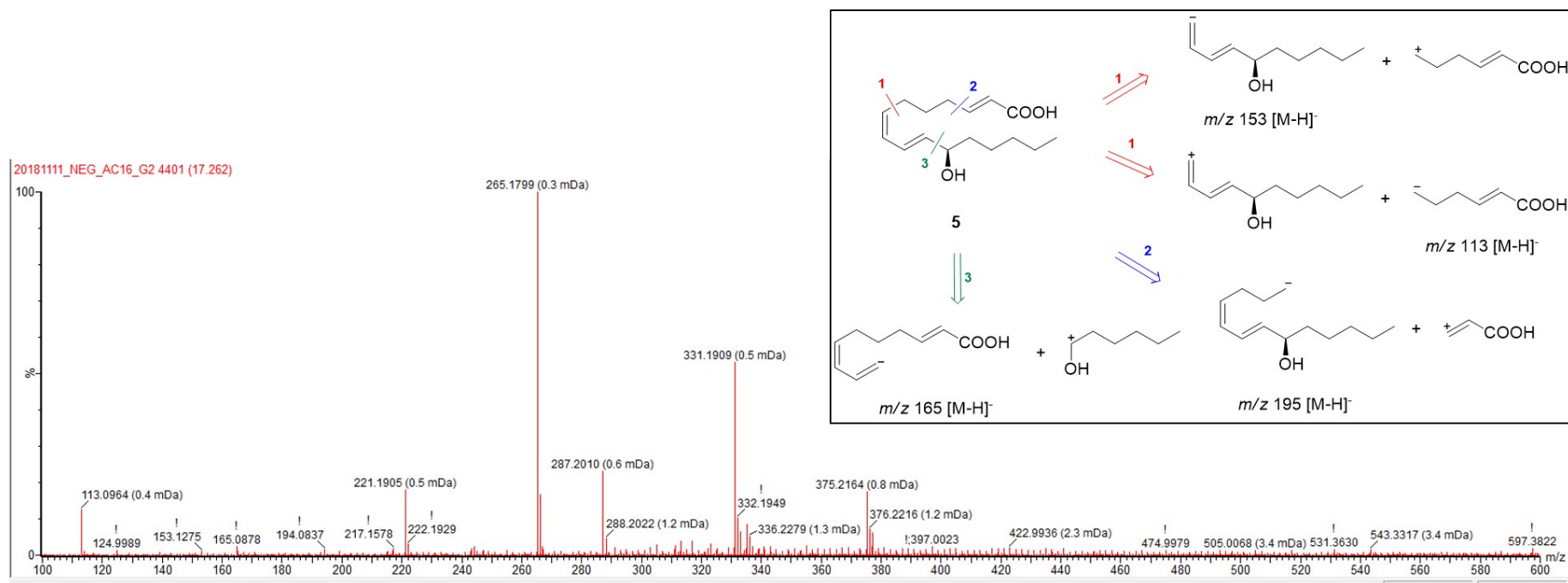
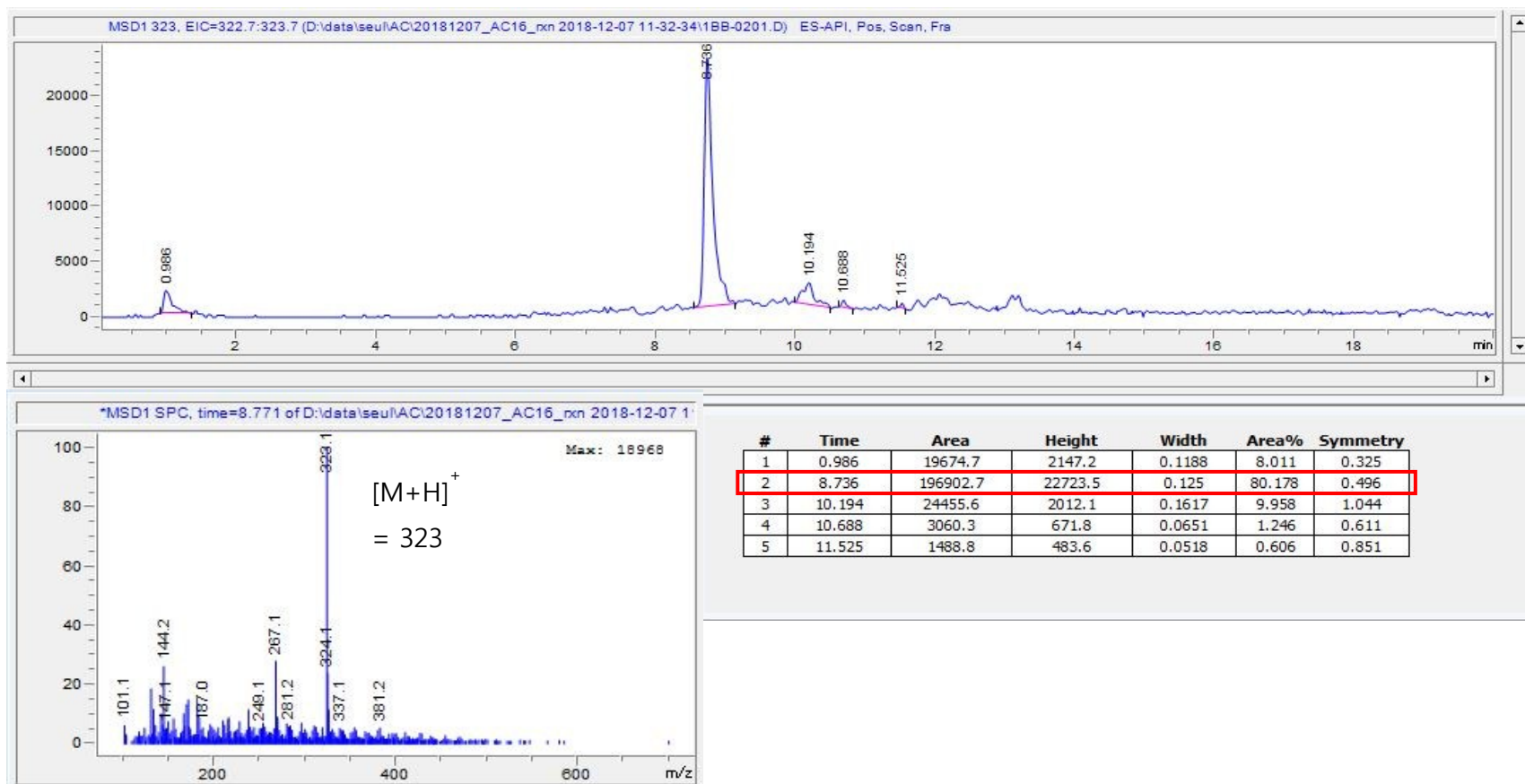


Figure S20. LC/MS data of acylated derivative from CEA reaction of **5**: (a) An acylated derivative of compound **5** in *R*-HBTM catalyzed acylation reaction at 10 min; (b) An acylated derivative of compound **5** in *S*-HBTM catalyzed acylation reaction at 10 min

a) An acylated derivative of compound **5** in *R*-HBTM catalyzed acylation reaction at 10 min



b) An acylated derivative of compound **5** in *S*-HBTM catalyzed acylation reaction at 10 min

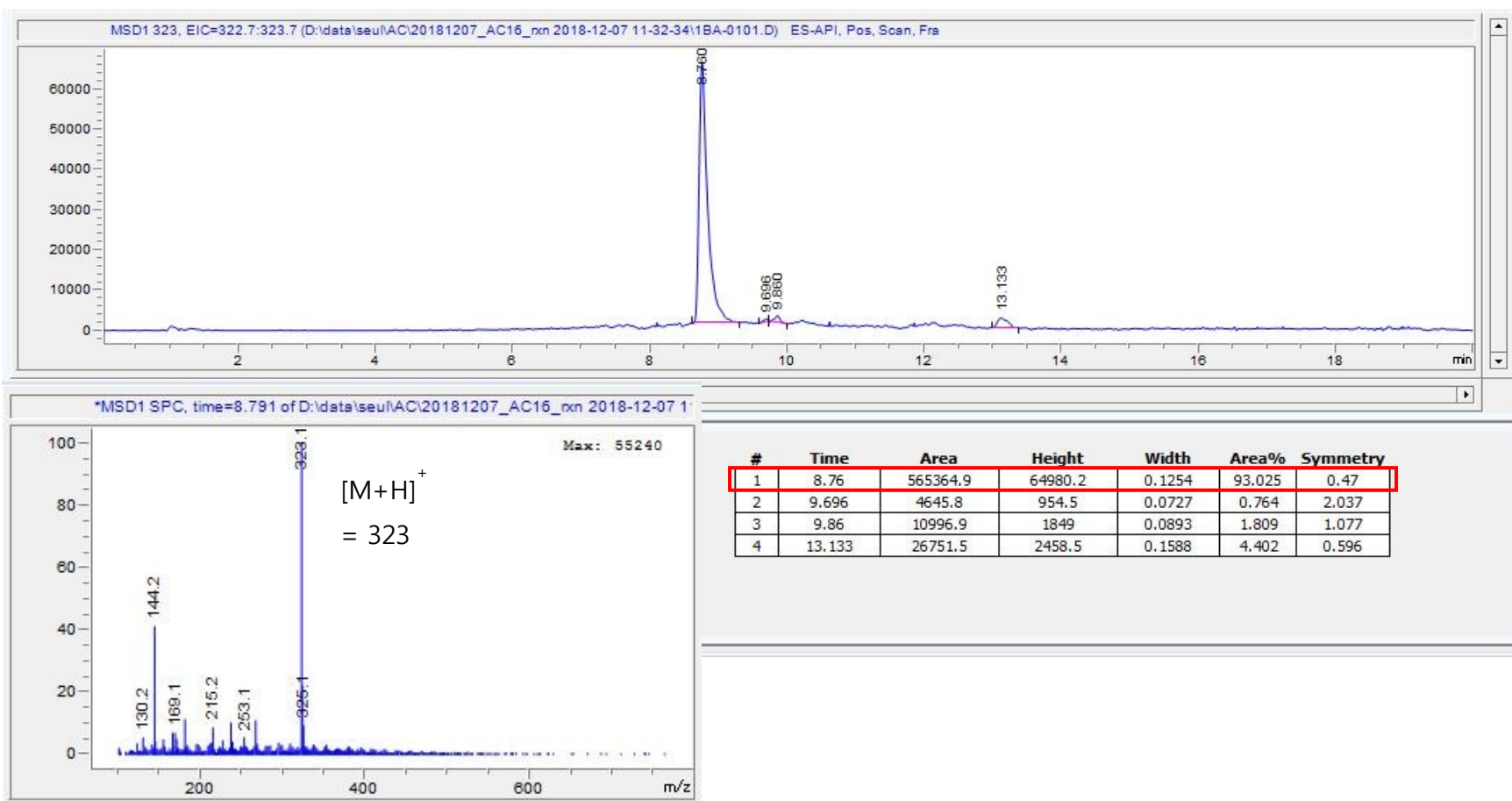




Figure S21. HR-ESIMS data of **10**

**Single Mass Analysis**  
Tolerance = 10.0 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  
58 formula(e) evaluated with 2 results within limits (up to 50 closest results for each mass)  
Elements Used:

Mass	Calc. Mass	mDa	PPM	DBE	Formula	i-FIT	i-FIT Norm	Fit Conf %	C	H	O	Na
211.0962	211.0970	-0.8	-3.8	4.5	C11 H15 O4	100.2	0.710	49.15	11	15	4	
	211.0946	1.6	7.6	1.5	C9 H16 O4 Na	100.2	0.676	50.85	9	16	4	1

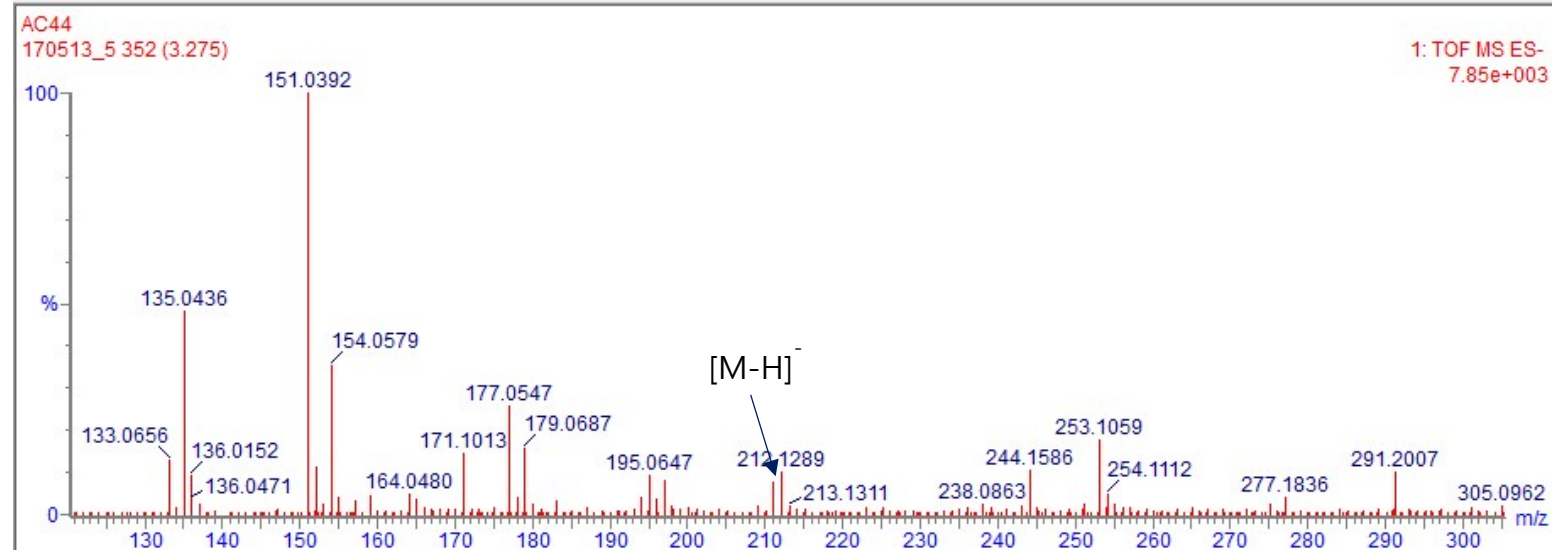


Figure S22.  $^1\text{H}$  NMR spectrum of **10** ( $\text{CD}_3\text{OD}$ , 850 MHz)

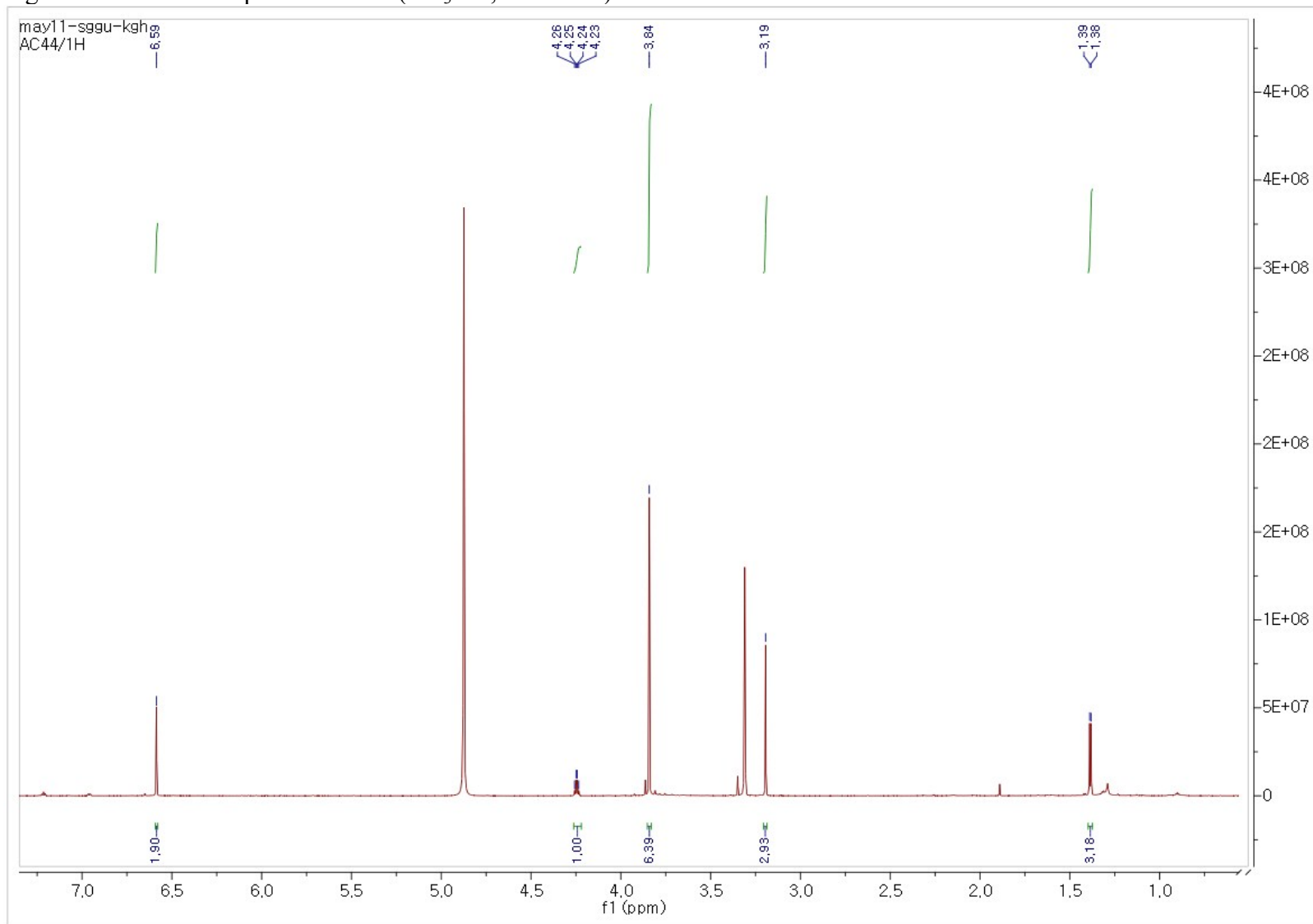


Figure S23.  $^1\text{H}$ - $^1\text{H}$  COSY spectrum of **10** ( $\text{CD}_3\text{OD}$ )

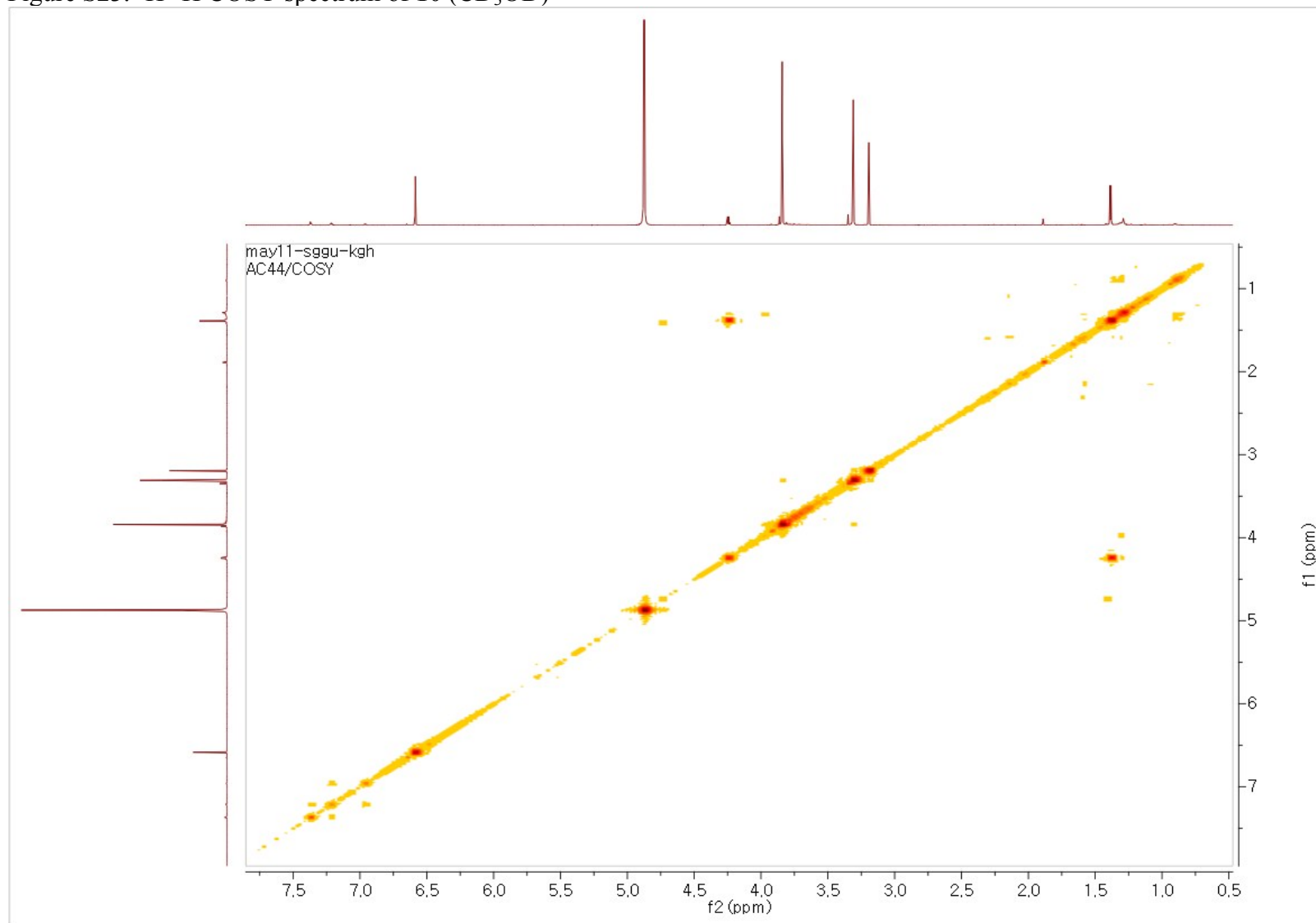


Figure S24. HSQC spectrum of **10** (CD<sub>3</sub>OD)

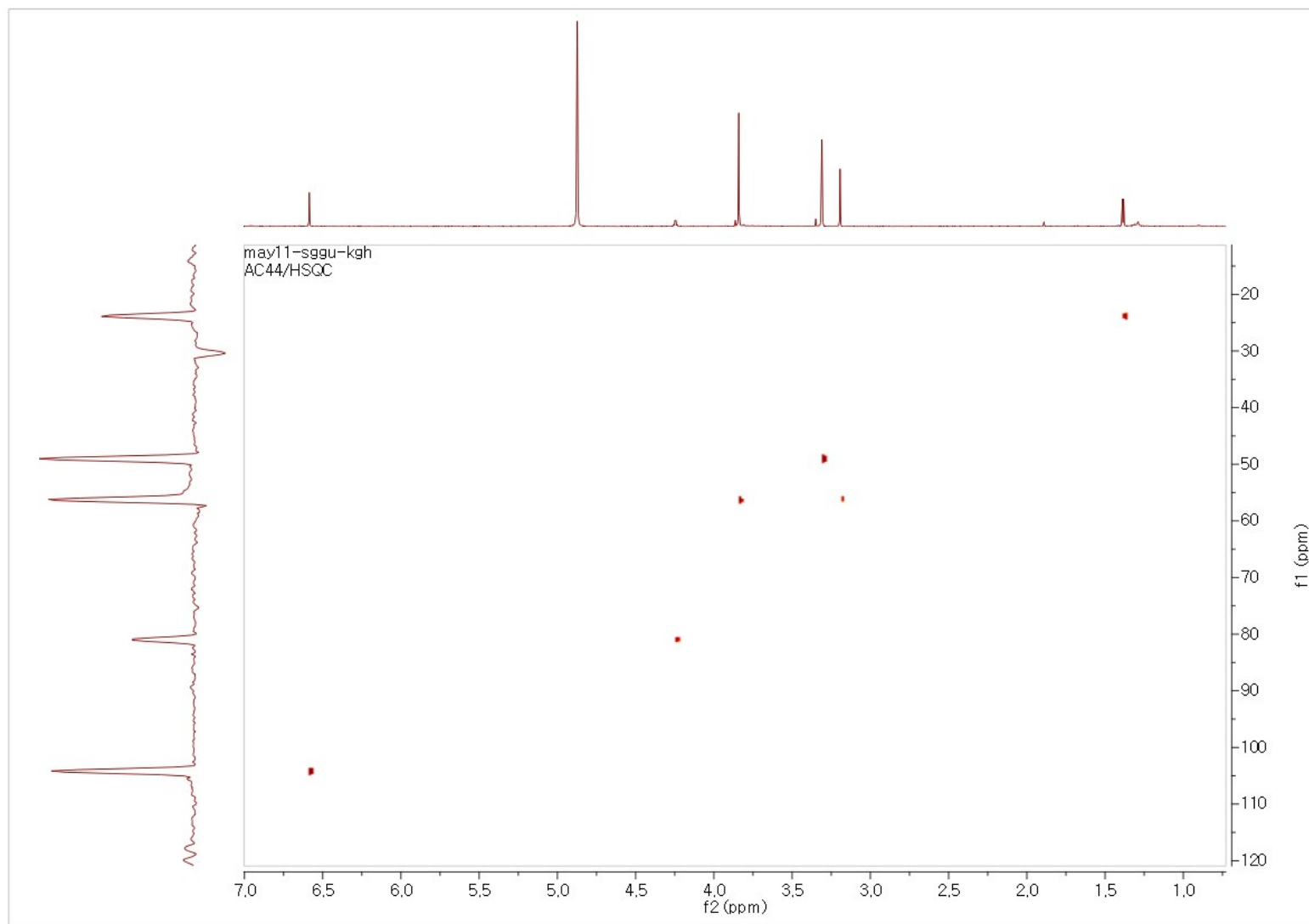


Figure S25. HMBC spectrum of **10** (CD<sub>3</sub>OD)

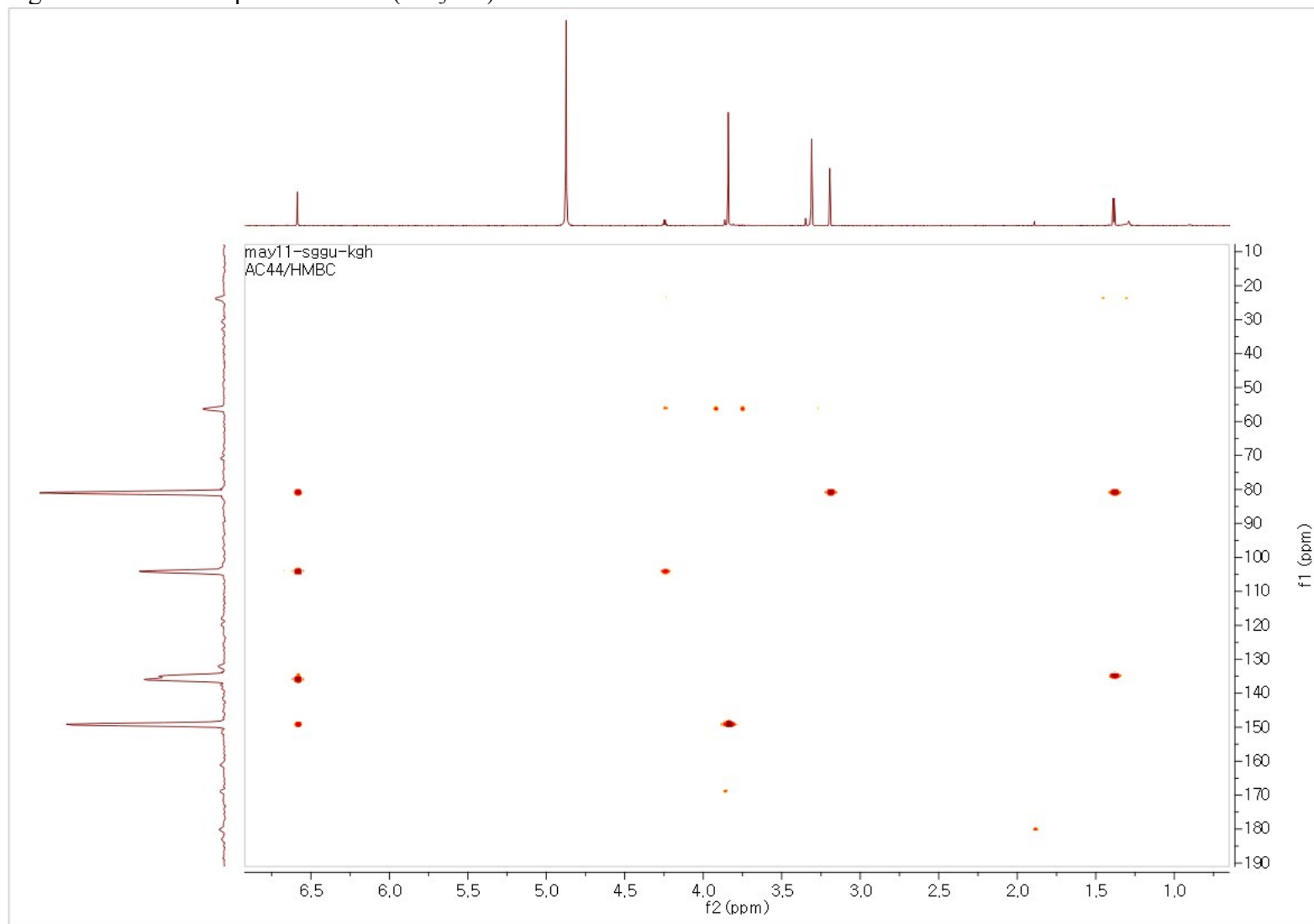


Figure S26. HR-ESIMS data of **11**

**Single Mass Analysis**

Tolerance = 10.0 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

72 formula(e) evaluated with 2 results within limits (up to 50 closest results for each mass)

Elements Used:

Mass	Calc. Mass	mDa	PPM	DBE	Formula	i-FIT	i-FIT Norm	Fit Conf %	C	H	O	Na
249.1102	249.1103	-0.1	-0.4	3.5	C12 H18 O4 Na	64.2	0.496	60.91	12	18	4	1
	249.1127	-2.5	-10.0	6.5	C14 H17 O4	64.6	0.939	39.09	14	17	4	

AC28

170513\_16 430 (3.994)

1: TOF MS ES+  
7.24e+004

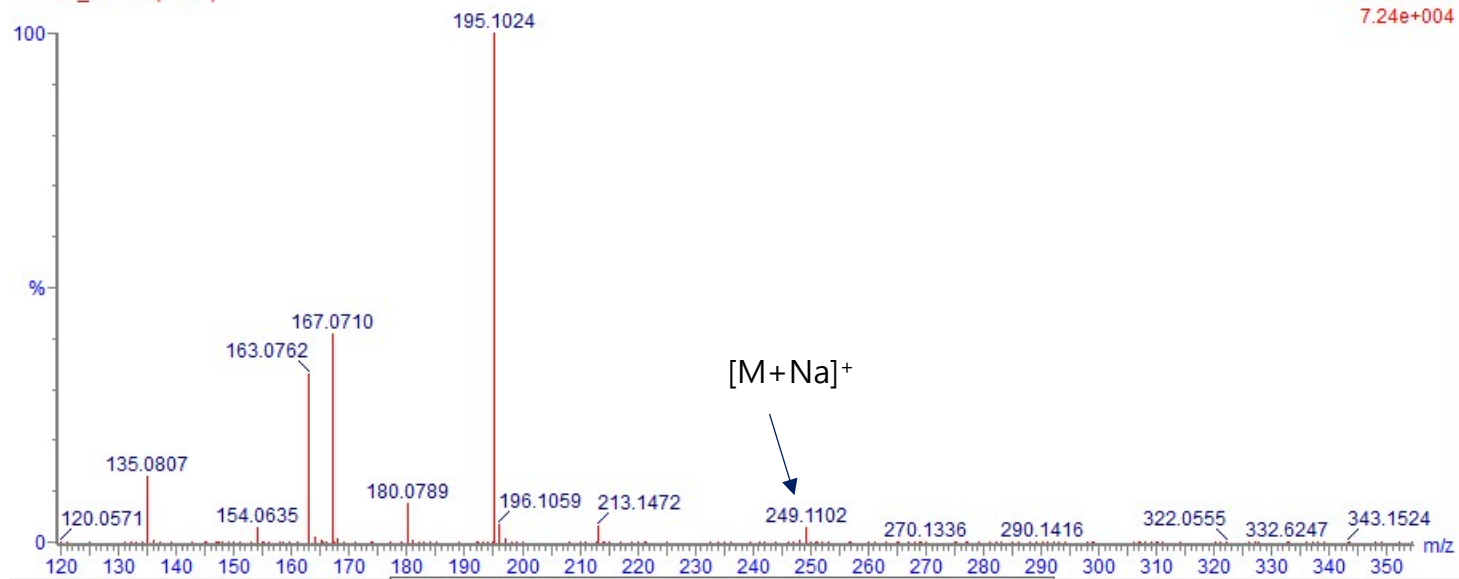


Figure S27.  $^1\text{H}$  NMR spectrum of **11** ( $\text{CD}_3\text{OD}$ , 800 MHz)

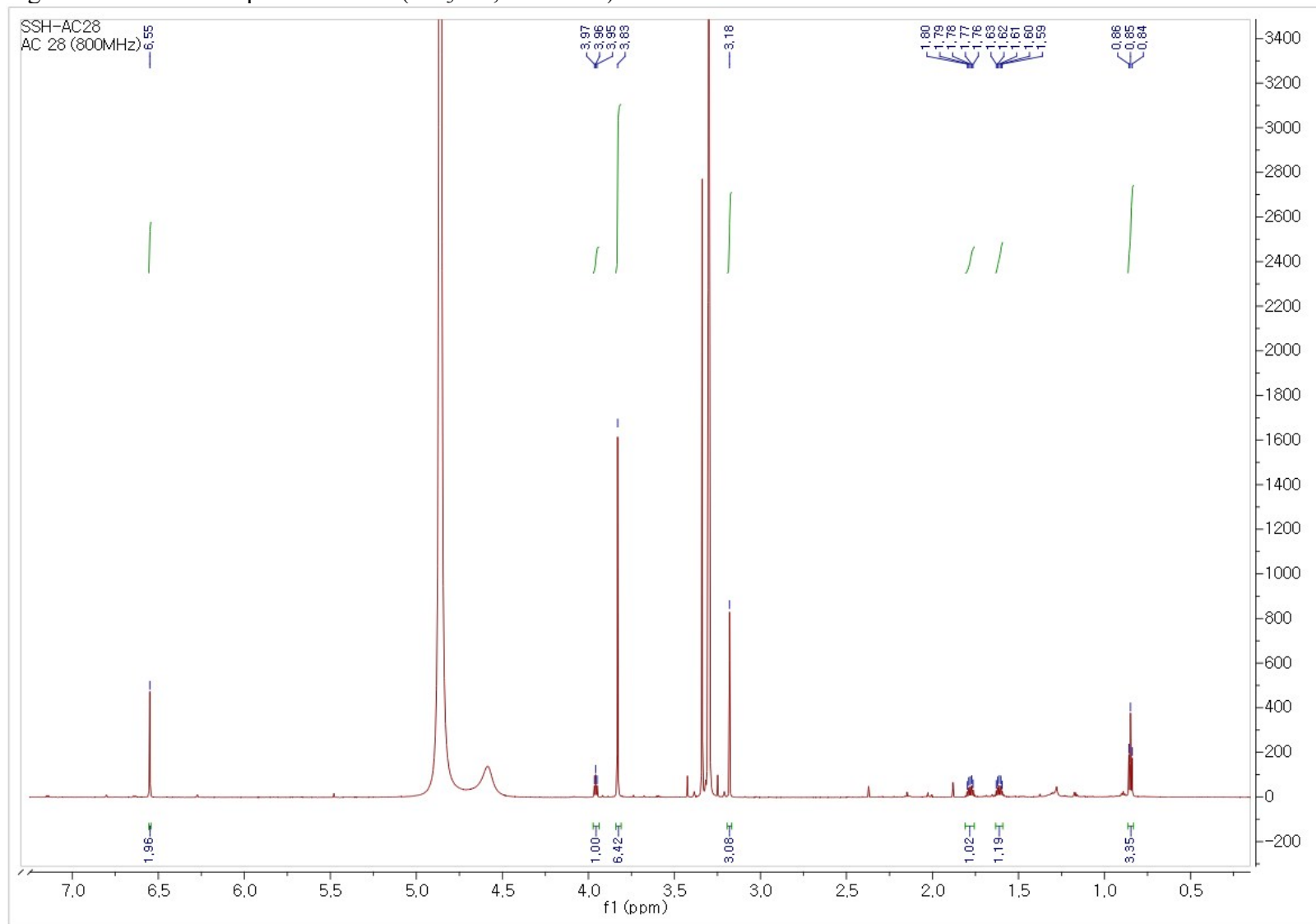


Figure S28.  $^1\text{H}$ - $^1\text{H}$  COSY spectrum of **11** ( $\text{CD}_3\text{OD}$ )

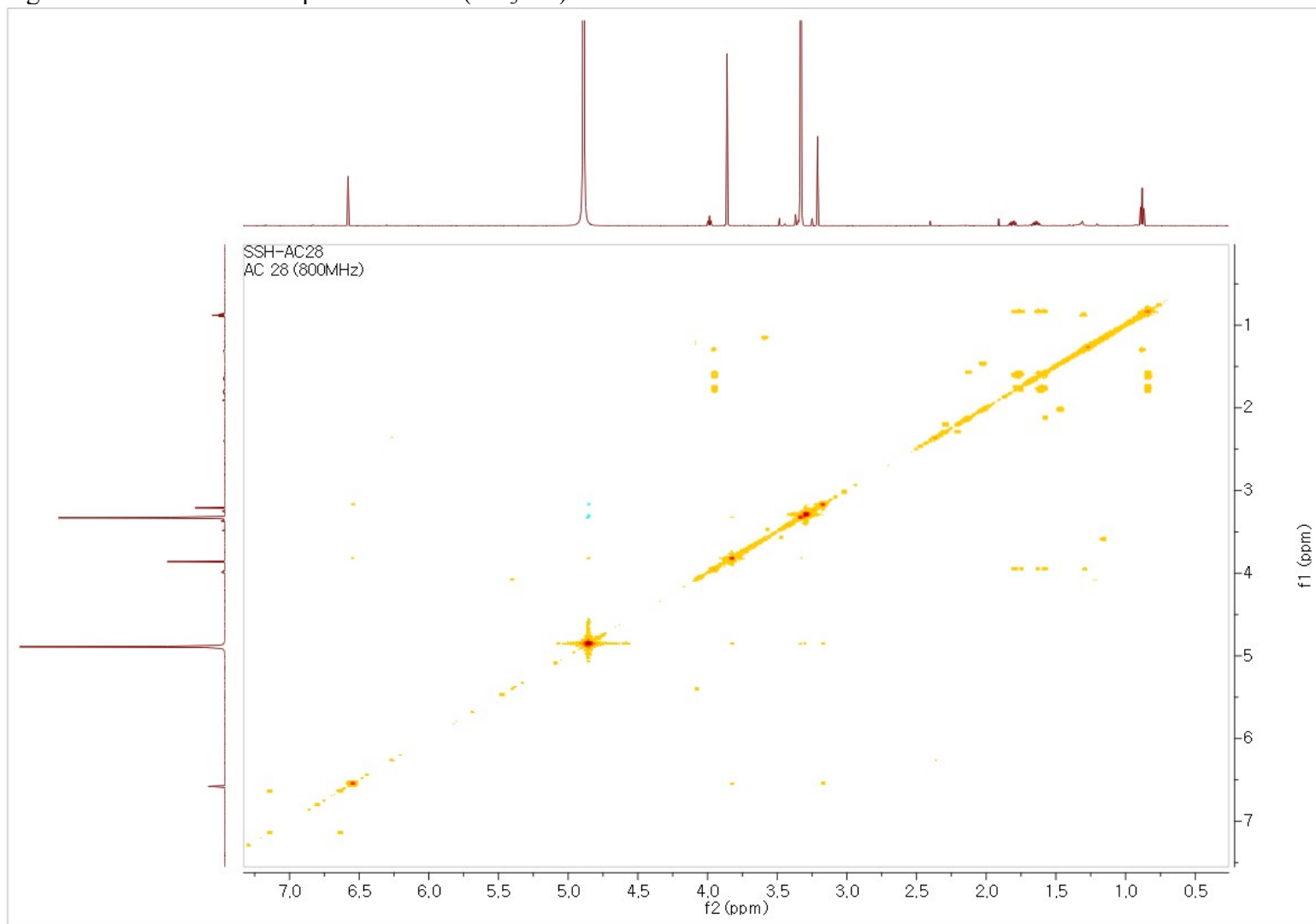




Figure S29. HSQC spectrum of **11** (CD<sub>3</sub>OD)

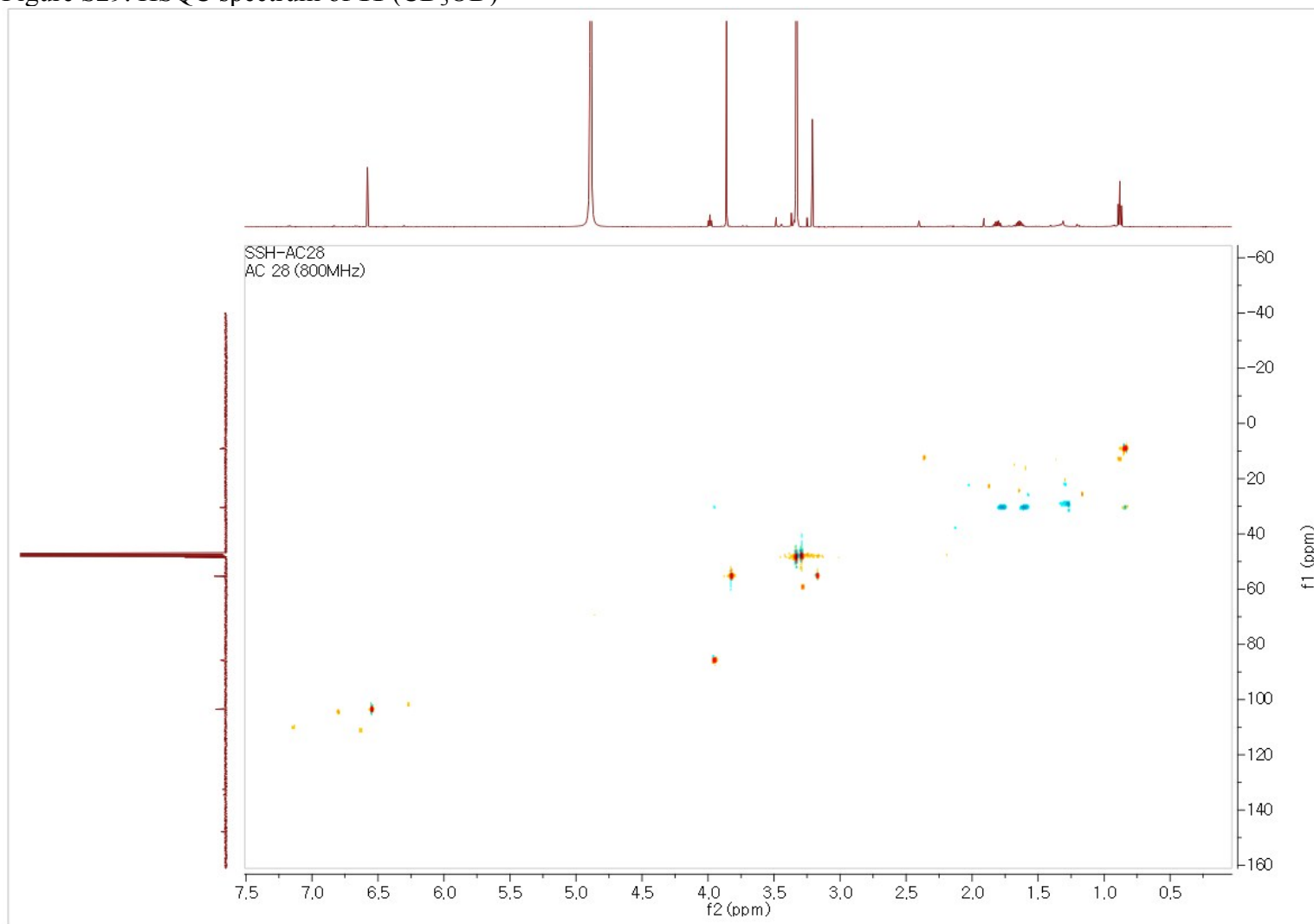


Figure S30. HMBC spectrum of **11** (CD<sub>3</sub>OD)

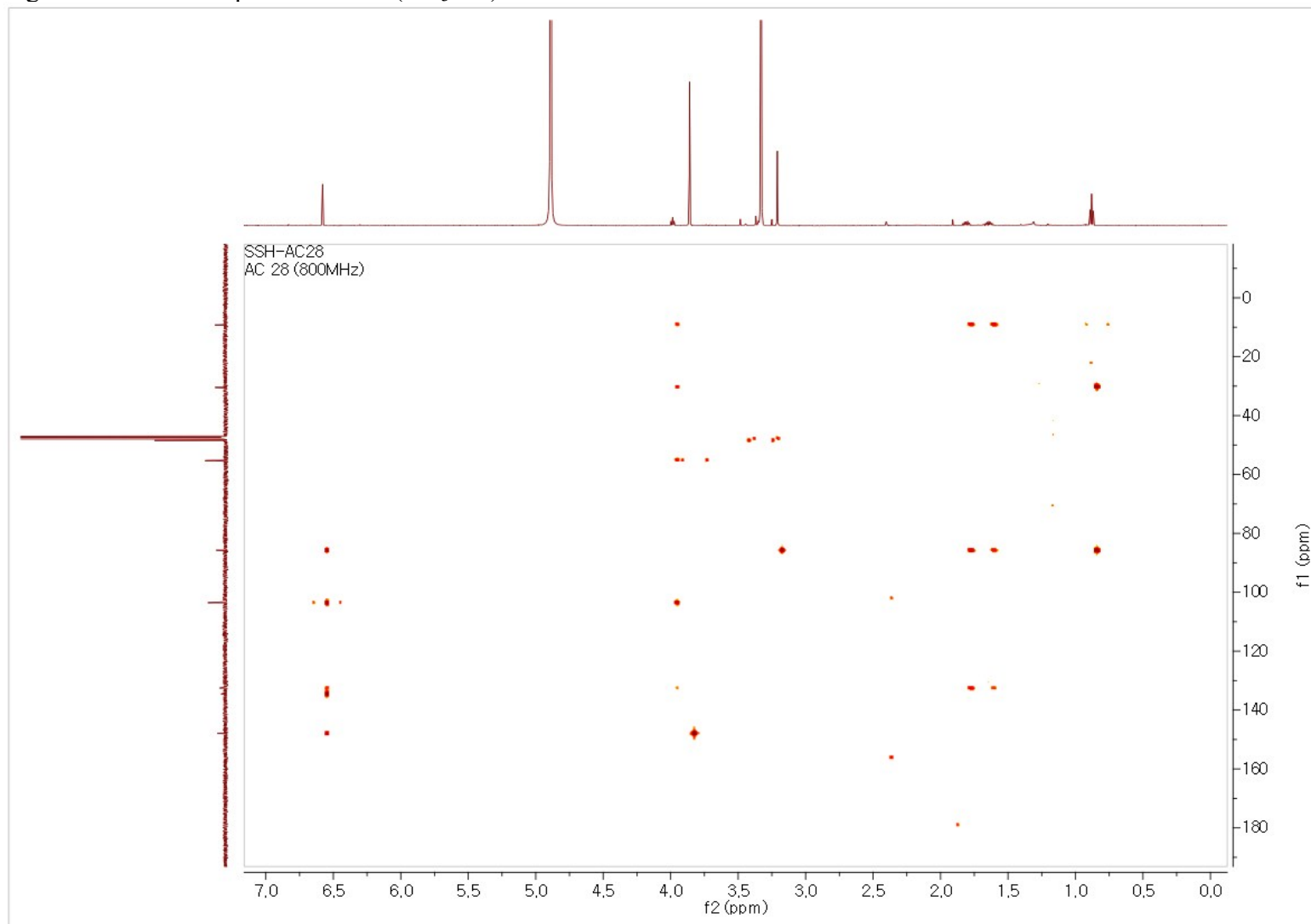


Figure S31. Amino acid sequence alignment of human SPHK1(PDB id : 3VZD) and human SPHK2 using the homology modeling module embedded in the Schrodinger Maestro 11.6 software.

```

AAH10671_1  MAPPPLAASTPLLHGEGSYVARGPRFALTLTSQALHIQRLRPKPEARPRGGLVPLAE 60
3VZD_C      -----0

AAH10671_1  VSGCCTLRSRSPSDSAAYFCIVTYPRGRRGARRRATRTFRADGAATVEENRAEAQRWATA 120
3VZD_C      -----0

AAH10671_1  LTCLLRGLPLPGDGEITPDLLPRPPRLLLVNPFGGRGLAWQWCKNHVLPIMSEAGLSFN 180
3VZD_C      -----47
                -----GAMGSGVLRPCRVLYLLNPRGGKQKALQLFRSHVQPLLAEEISFT
                * : .:***** *:!:*** **!* * * :,** *::** !**

AAH10671_1  LIQTERQNHARELYQGLSLSEWDGIVTYSGDGLLHEVLNGLLDRPDWEEAVKMPVGI LPC 240
3VZD_C      LMLTERRNHARELYRSEELGRWDALVYMSGDGLMHEVYVNGLMERPDWETAIQKPLCSLPA 107
                *! ***:*****:, ,*,**,*:,*****:***:***:***** *:: *! **,

AAH10671_1  GSGNALAGAVNQHGGEFEPALGLDLLNCSLLLCRGGGHPDLLSVTLASGSRCSFSLVA 300
3VZD_C      GSGNALAASLNHYAGVEQVTNEDLLTNCTLLLCRRLSPMNLSSLHTASGLRFLFSVLSLA 167
                *****,:!::,* * , , *** **!***** *!****: *** * **,**!

AAH10671_1  WGFVSDYDIQSERFRALGSARFTLGTVLGLATLHTYRGRLSYLPATVEPASPTPAHSLPR 360
3VZD_C      WGFADVLESEKYRRLGEMRFTLGTFLRLAALRTYRGRLAYLPVG-----213
                ***:***:***:!* **, *****,* **!******:***,

AAH10671_1  AKSELTLPDPAPMAHSPHRSVSDLPPLPQPALASPGSPEPLPILSLNGGGPELAGD 420
3VZD_C      -----213

AAH10671_1  WGGAGDAPLSPDLLSSPPGSPKAALHSPVSEGAPVIPPSSGLPLPTDARVGAStCGPP 480
3VZD_C      -----RVGSKTPASPVVVR-----QGPPV 231
                ,* * ,* **

AAH10671_1  DHLLPPLGTPLPDWV-TLEGDFVLMIAISPSHLGADLYAAPHARFDDGLVHLCWVRSGL 539
3VZD_C      DAHLVPLEEPVPSHWTVVPOEDFVVLALLHSHLGSEMFAAPMGRCAAGVMHLFVYRAGV 291
                * * ** *!* ,* , : *****! : *****:*** ,* *!*** !**!

AAH10671_1  SRAALLRLFLAMERGSFSLGCPQLGYAAARAFRLEPLTPRGVLTVDGEQVEYGPLQAQM 599
3VZD_C      SRAMLLRLFLAMEKGRHMEVECPVLYVYVVAFRLEPKDGKGVFAVDGELMVSEAVQGQV 351
                *** *****!* *!, ** * * , ***** !**!***** : !*,:

AAH10671_1  HPGIGTLLTGPPGCPGREP 618
3VZD_C      HPNVFWMVSG-----361
                **, :!:*

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