Electronic Supplementary Material (ESI) for Organic Chemistry Frontiers.

Miharadienes A–D with Unique Cyclic Skeletons from a Marine-Derived *Streptomyces miharaensis*

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Supporting Information

List of Contents

Mass	Calc. Mass	mDa	PPM	DBE	Formula
345.1702	345.1702	0.0	0.0	8.5	C20 H25 O5
367.1522	367.1521	0.1	0.3	8.5	C20 H24 O5 Na

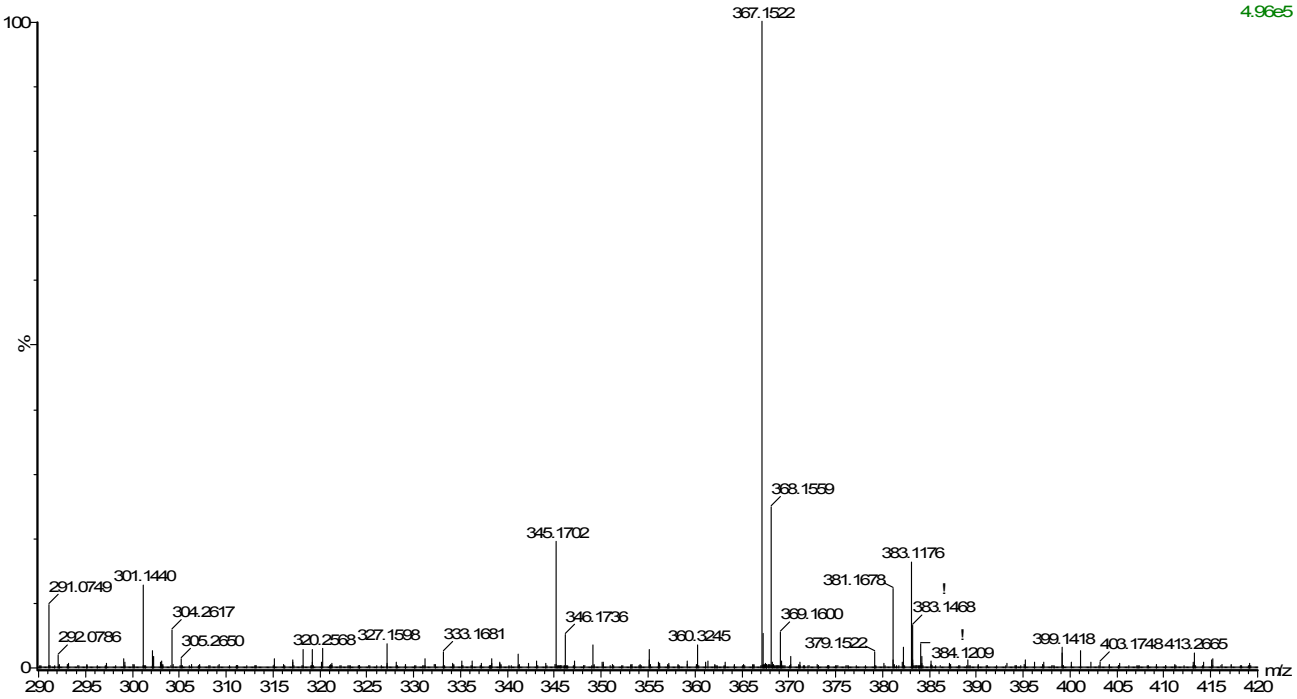


Figure S1. HRESIMS data of **1**.

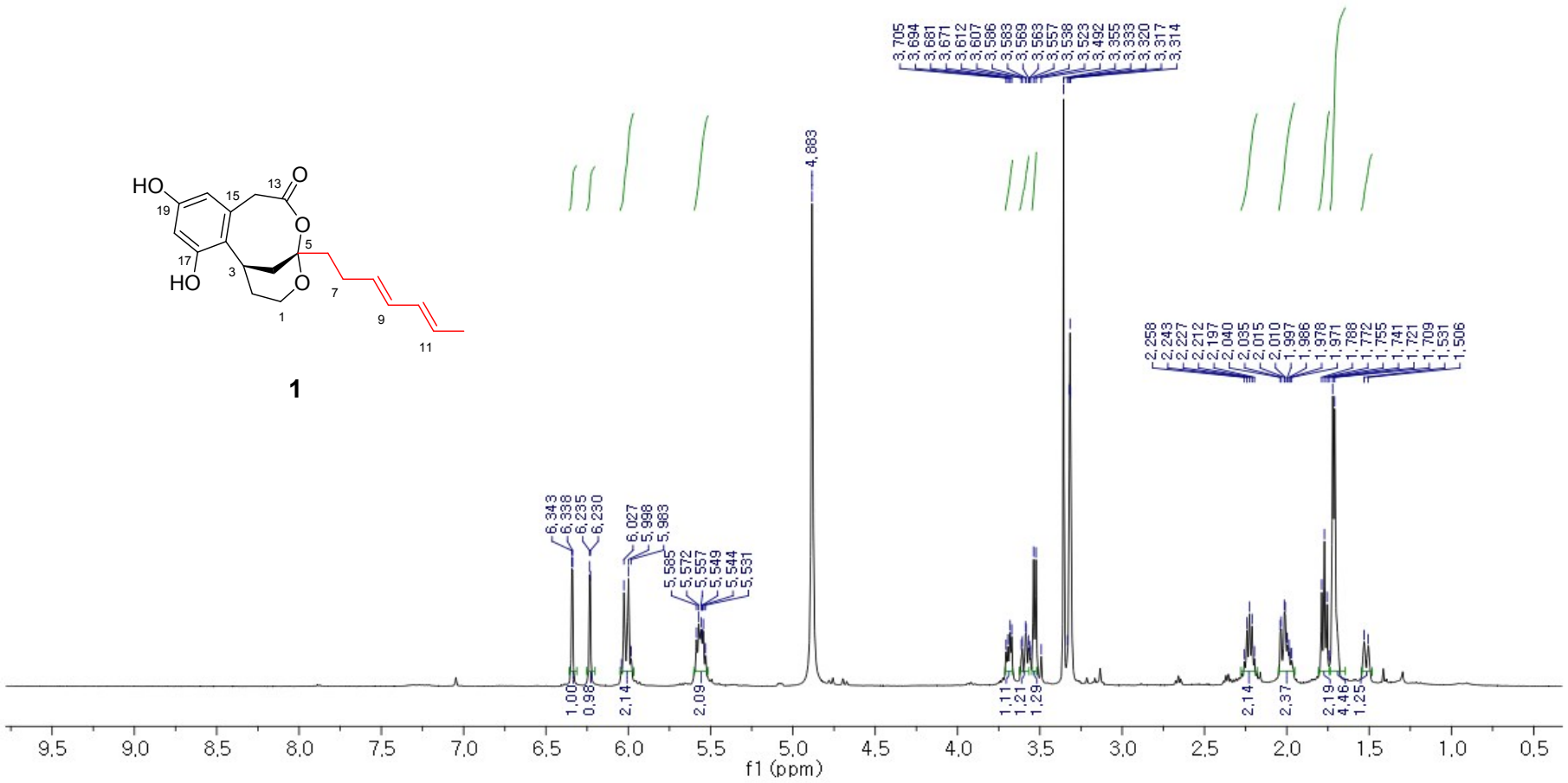


Figure S2. ^{1}H NMR spectrum of miharadiene (**1**) in CD_3OD.

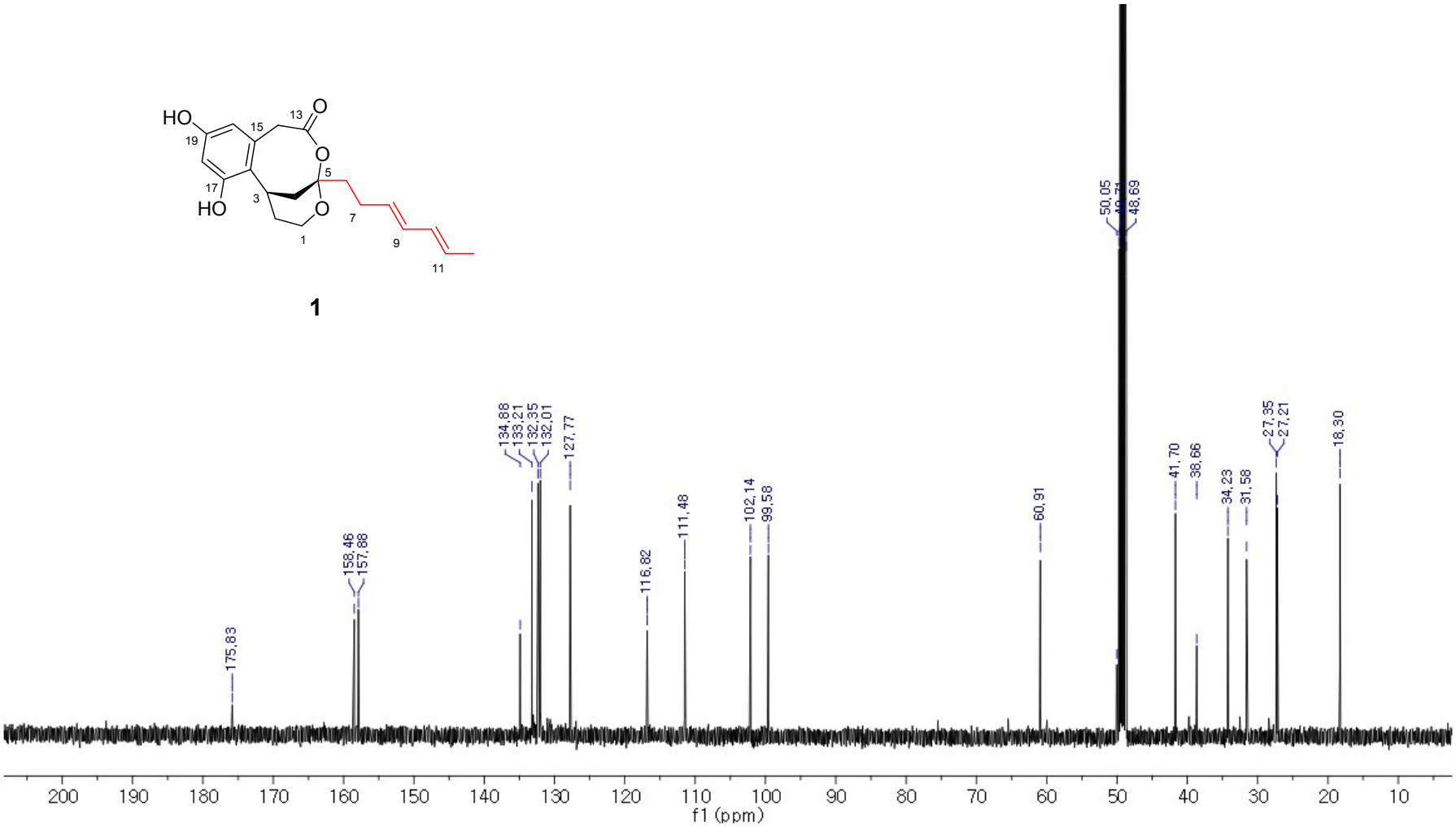


Figure S3. ^{13}C NMR spectrum of miharadiene A (**1**) in CD_3OD.

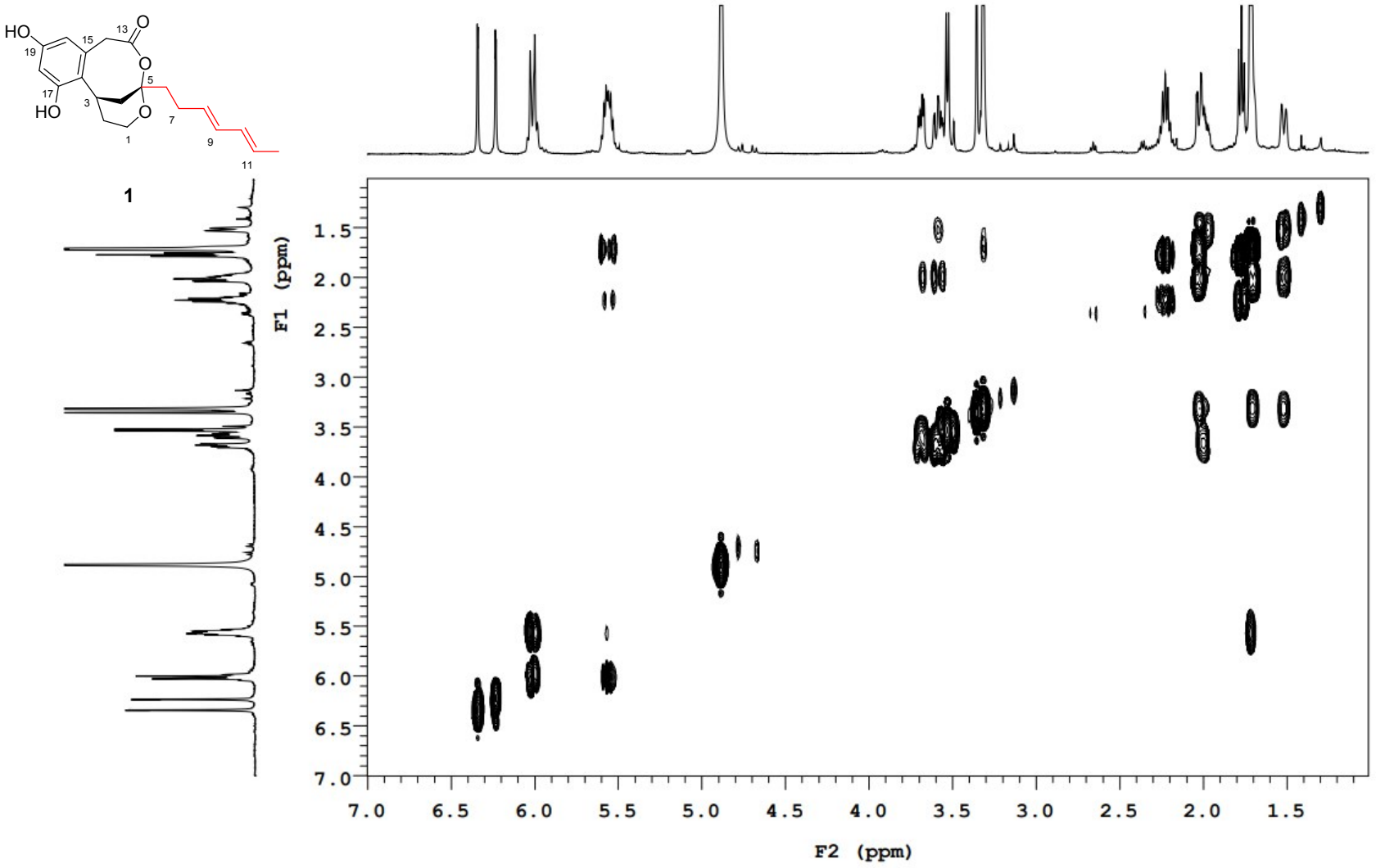


Figure S4. ^{1}H-^{1}H COSY spectrum of miharadiene A (**1**) in CD_3OD.

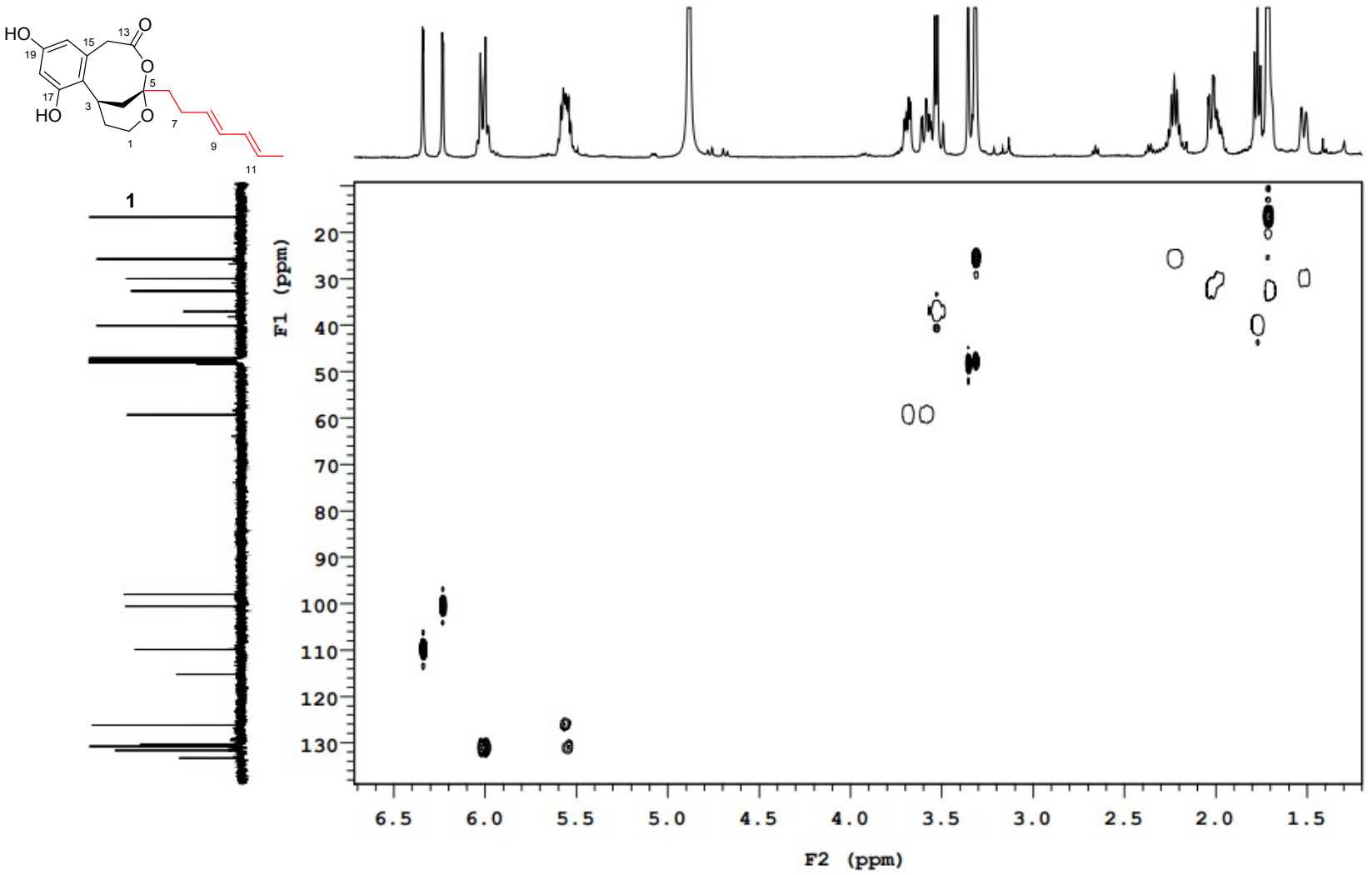


Figure S5. HSQC spectrum of miharadiene A (**1**) in CD_3OD.

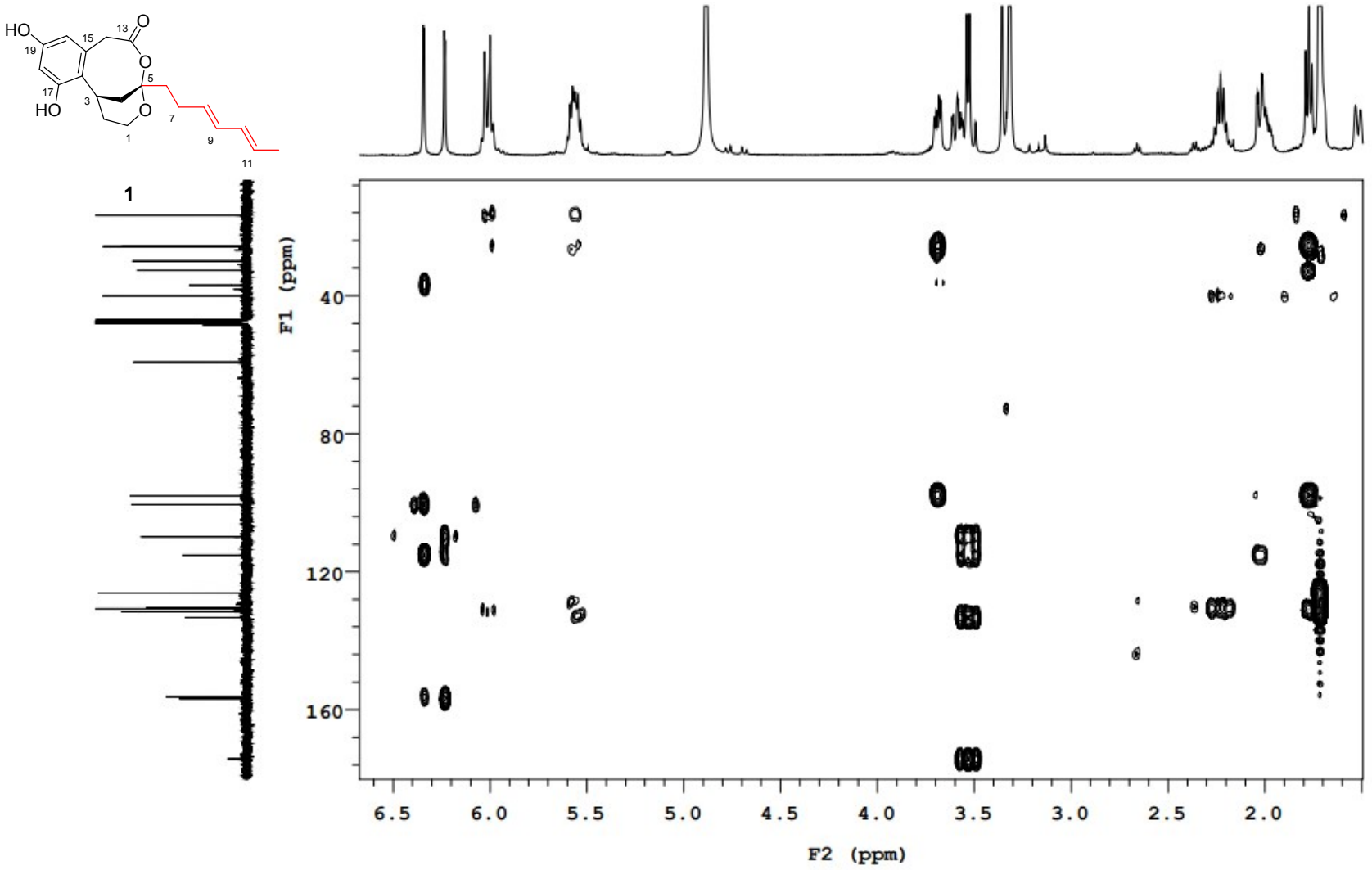


Figure S6. HMBC spectrum of miharadiene A (**1**) in CD_3OD.

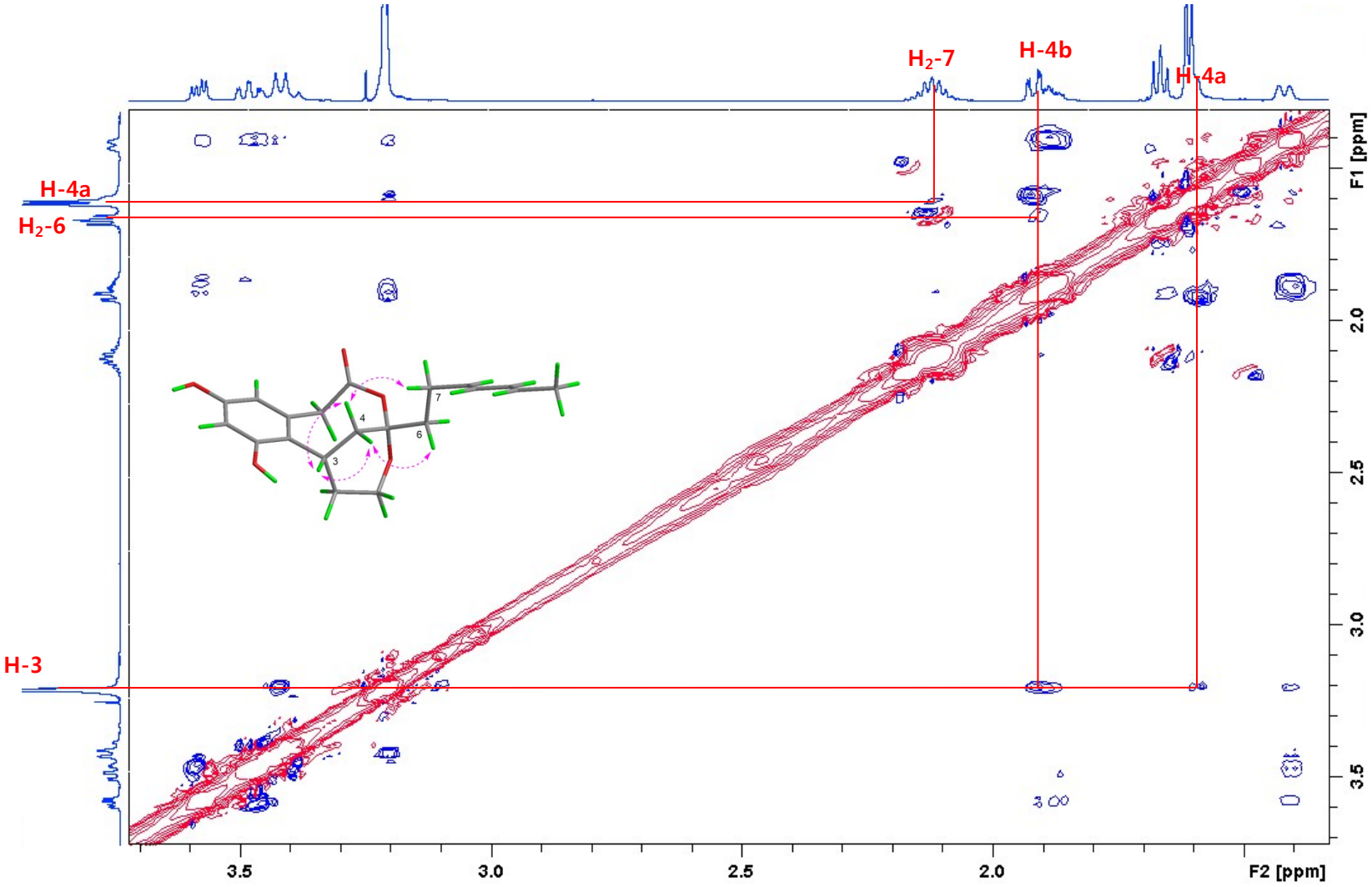


Figure S7. NOESY spectrum of miharadiene A (**1**) in CD_3OD.

Mass	Calc. Mass	mDa	PPM	DBE	Formula
367.1886	367.1885	0.1	0.3	7.5	C21 H28 O4 Na

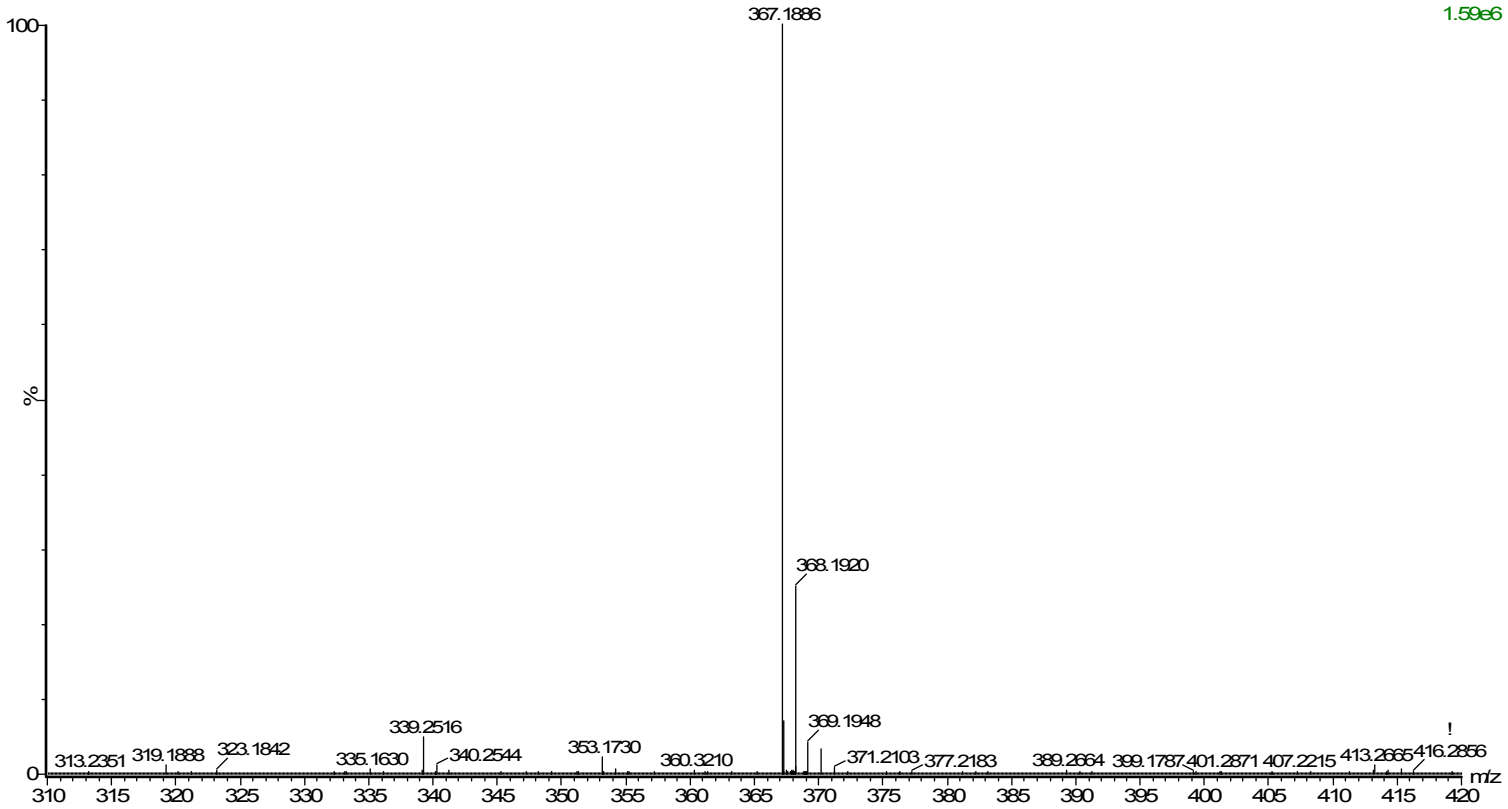


Figure S8. HRESIMS spectrum of miharadiene B (**2**).

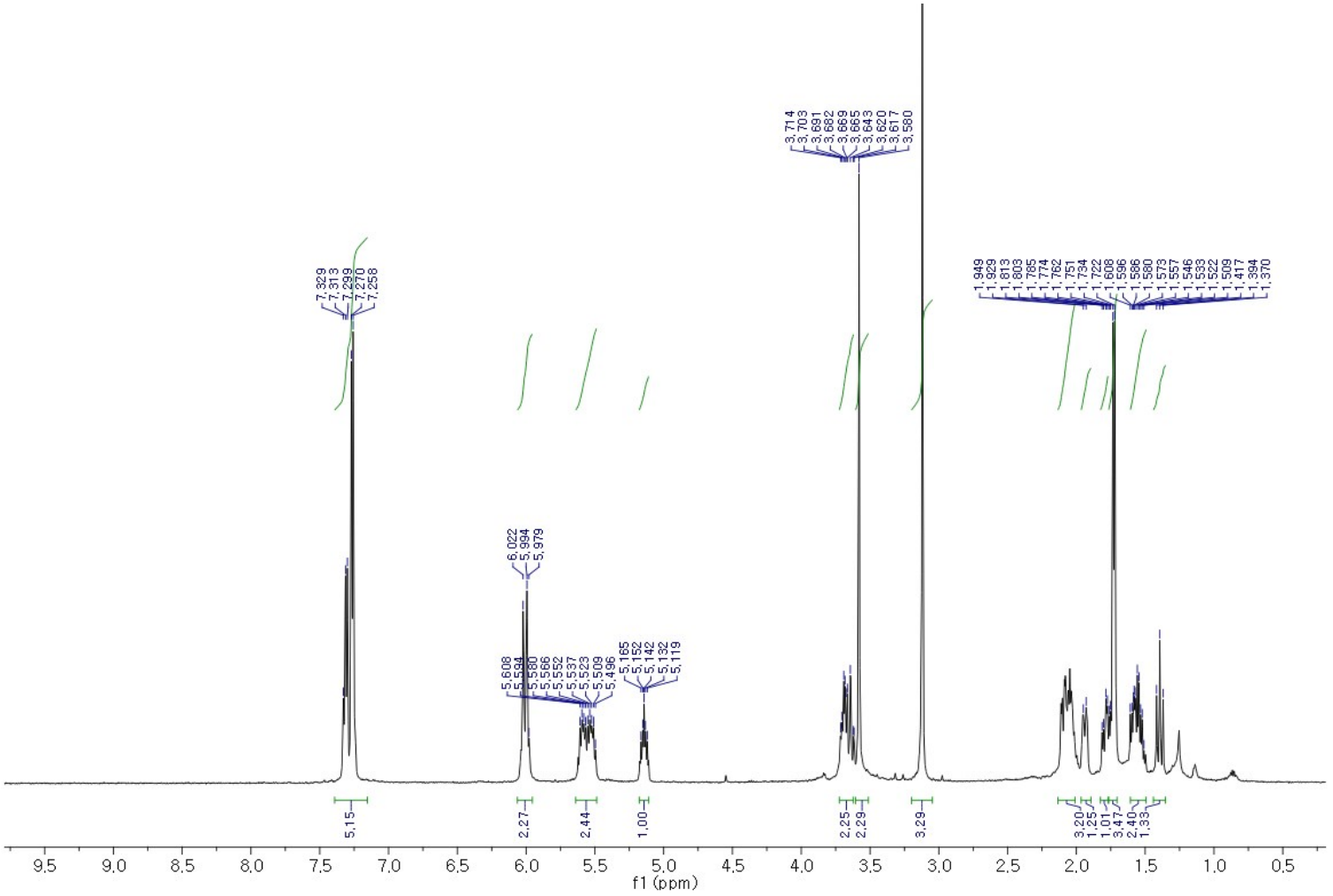


Figure S9. ^{1}H NMR spectrum of miharadiene B (**2**) in $CDCl_3$.

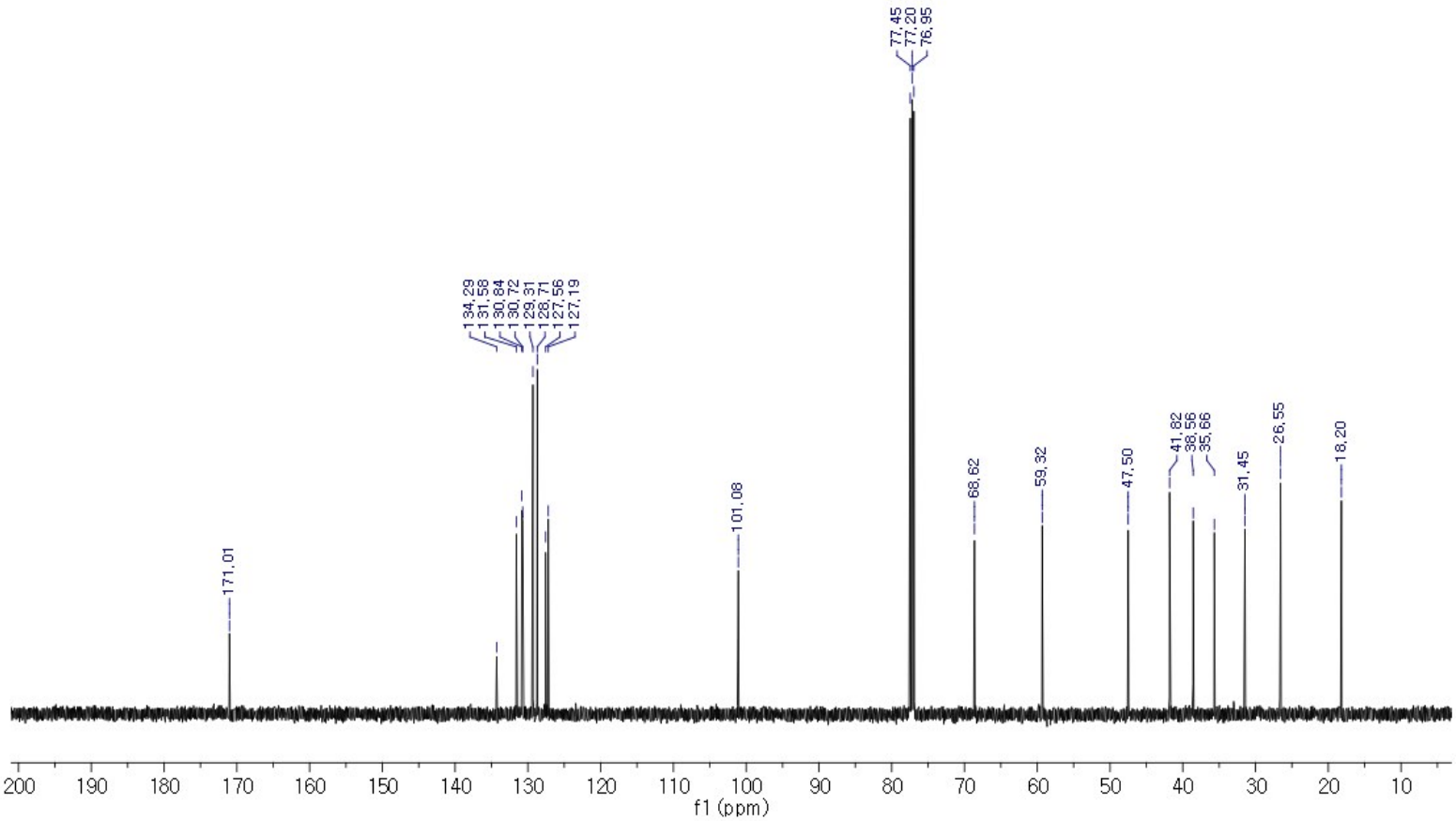


Figure S10. ^{13}C NMR spectrum of miharadiene B (**2**) in $CDCl_3$.

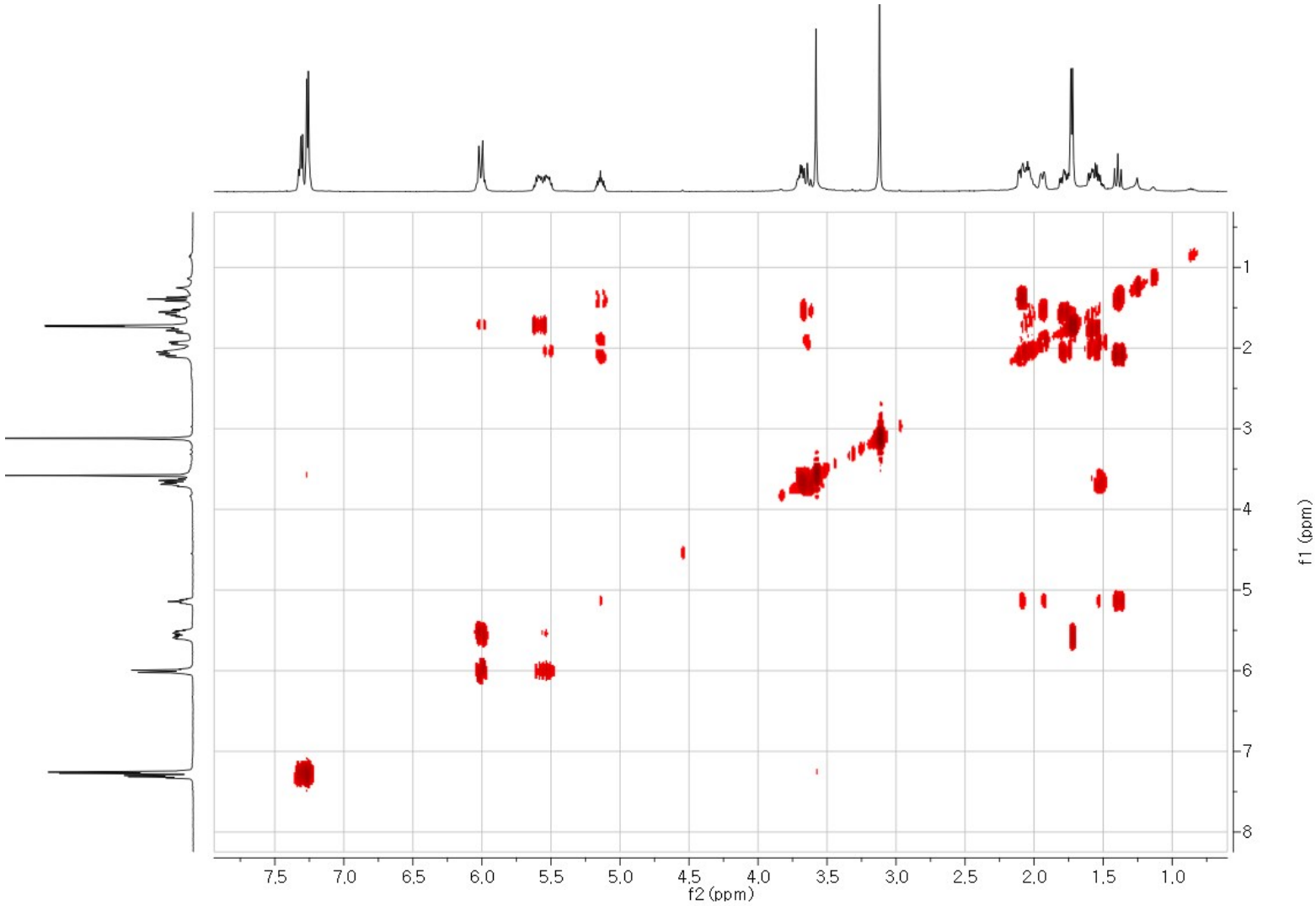


Figure S11. ^{1}H-^{1}H COSY spectrum of miharadiene B (**2**) in $CDCl_3$.

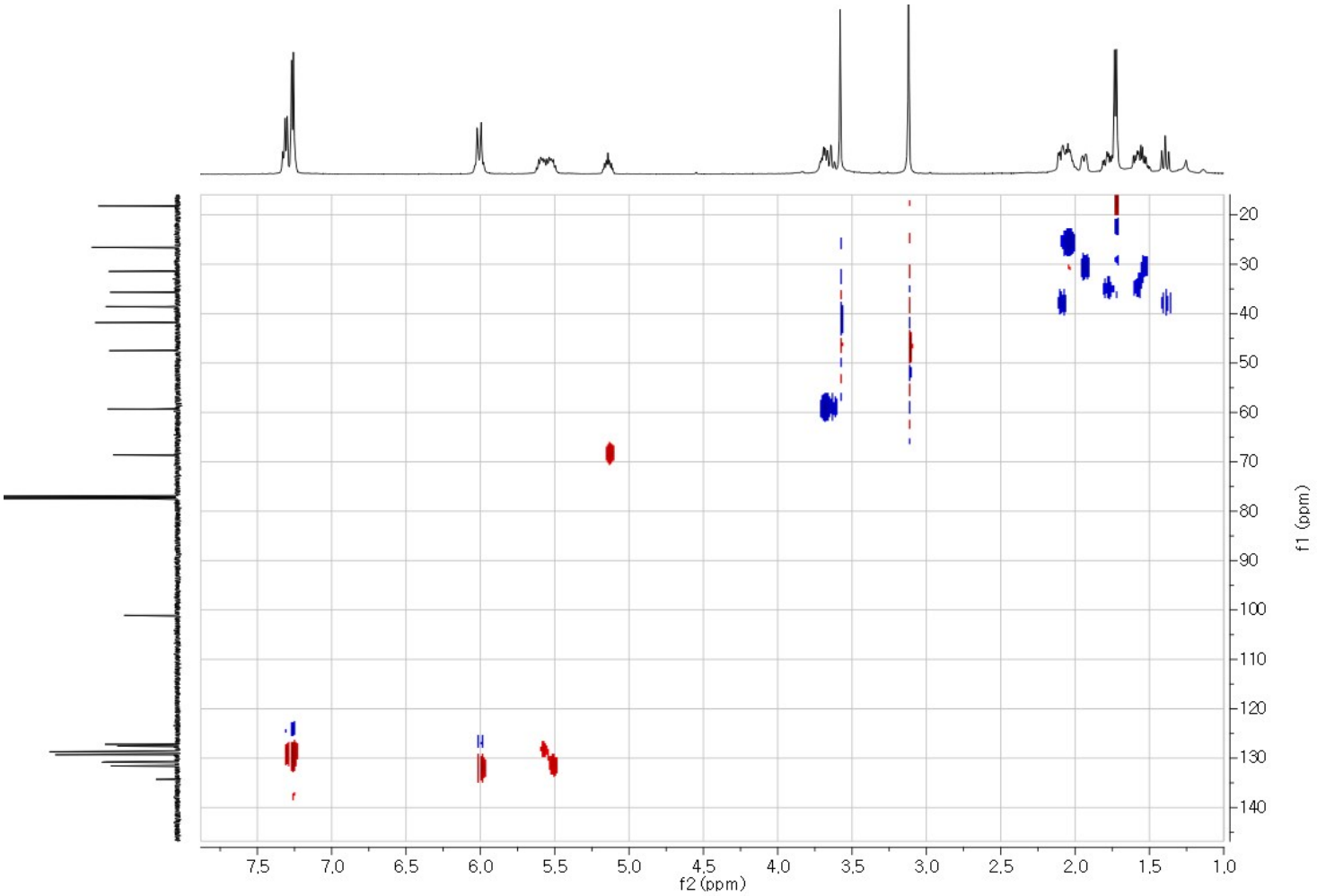


Figure S12. HSQC spectrum of miharadiene B (**2**) in $CDCl_3$.

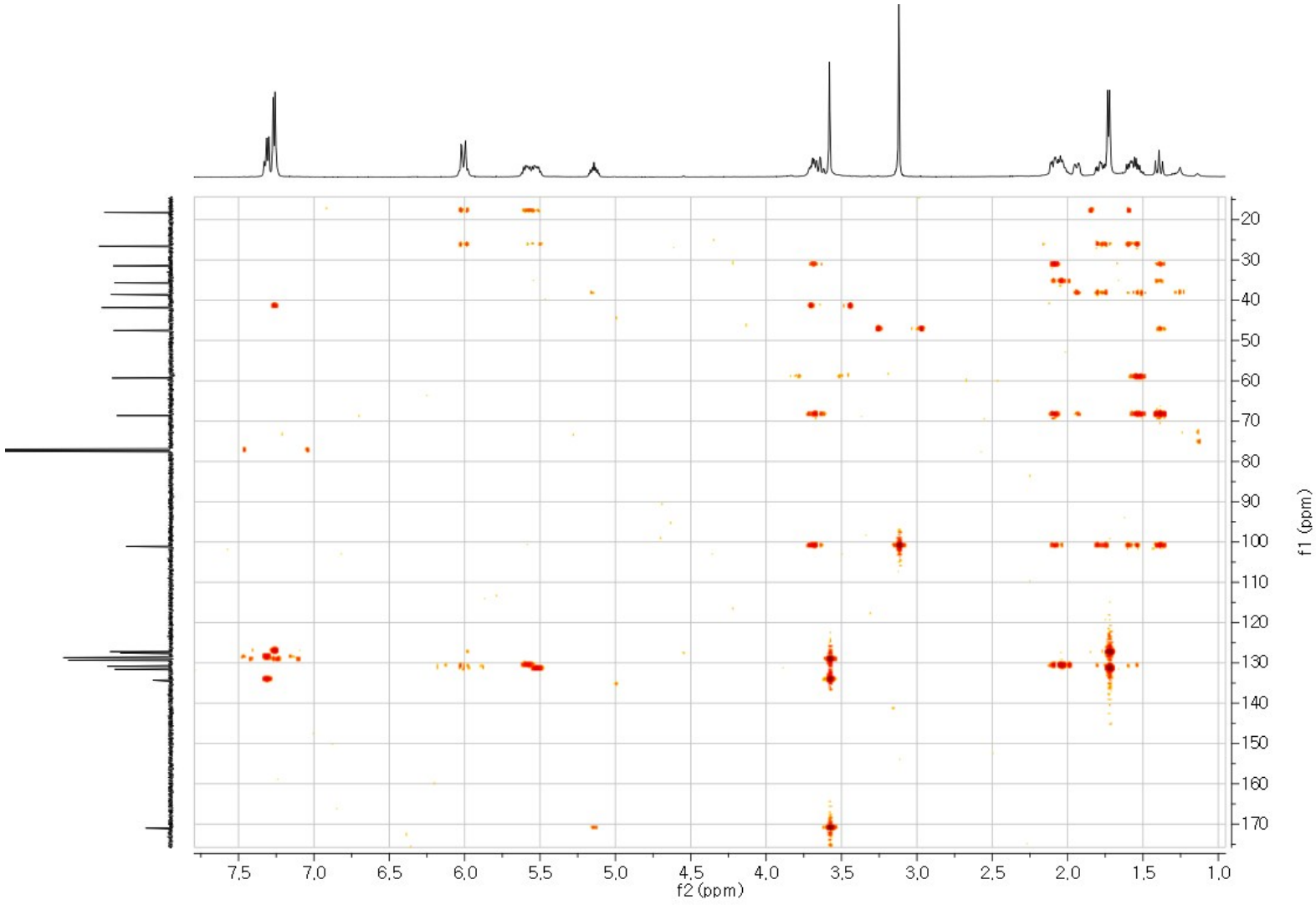
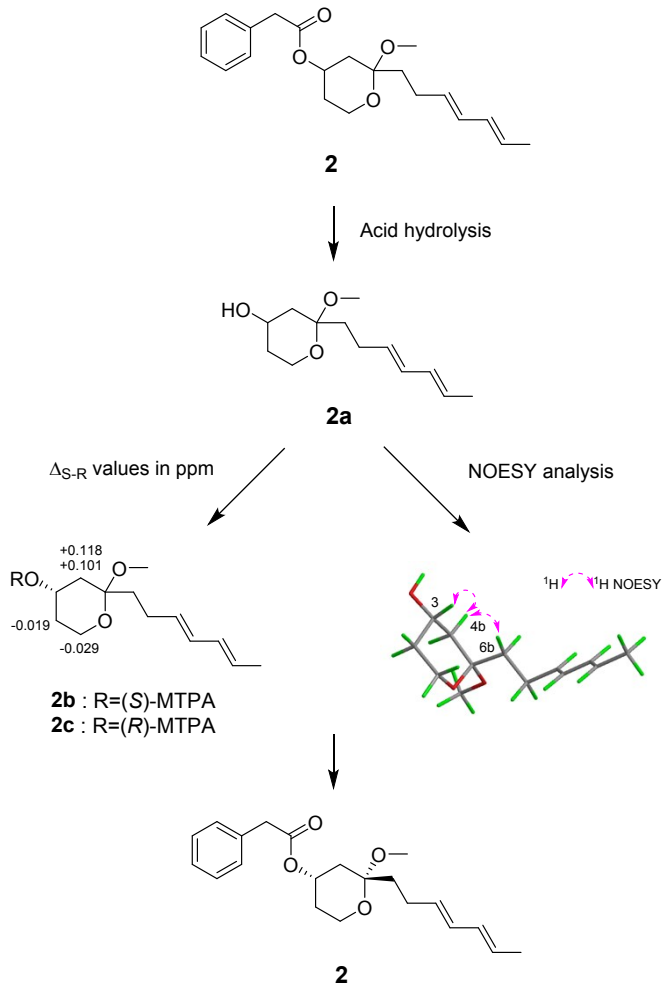


Figure S13. HMBC spectrum of miharadiene B (**2**) in $CDCl_3$.

Scheme S1. Determination of absolute configuration for **2**.



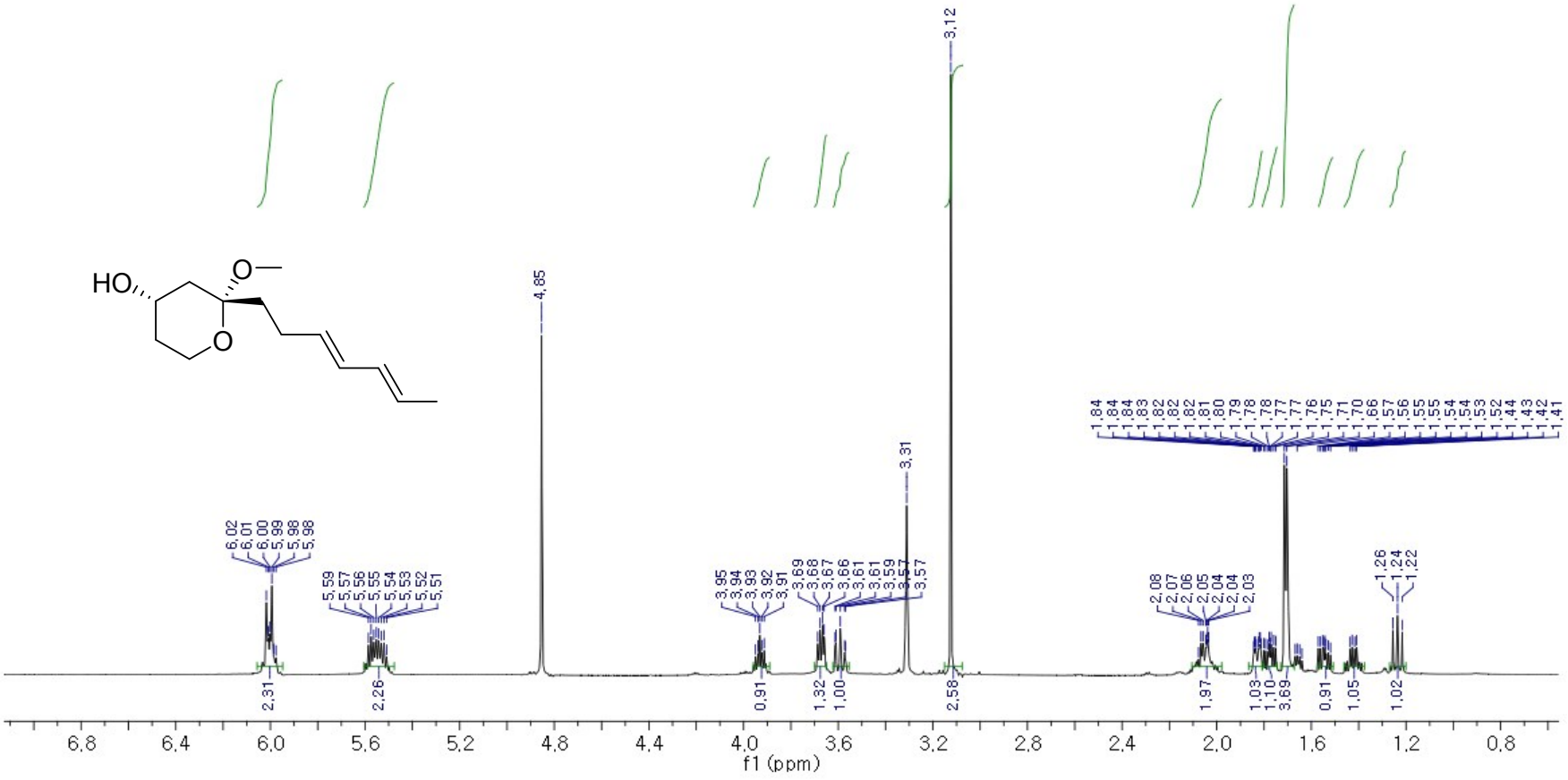


Figure S14. ^{1}H NMR spectrum of compound **2a** in CD_3OD.

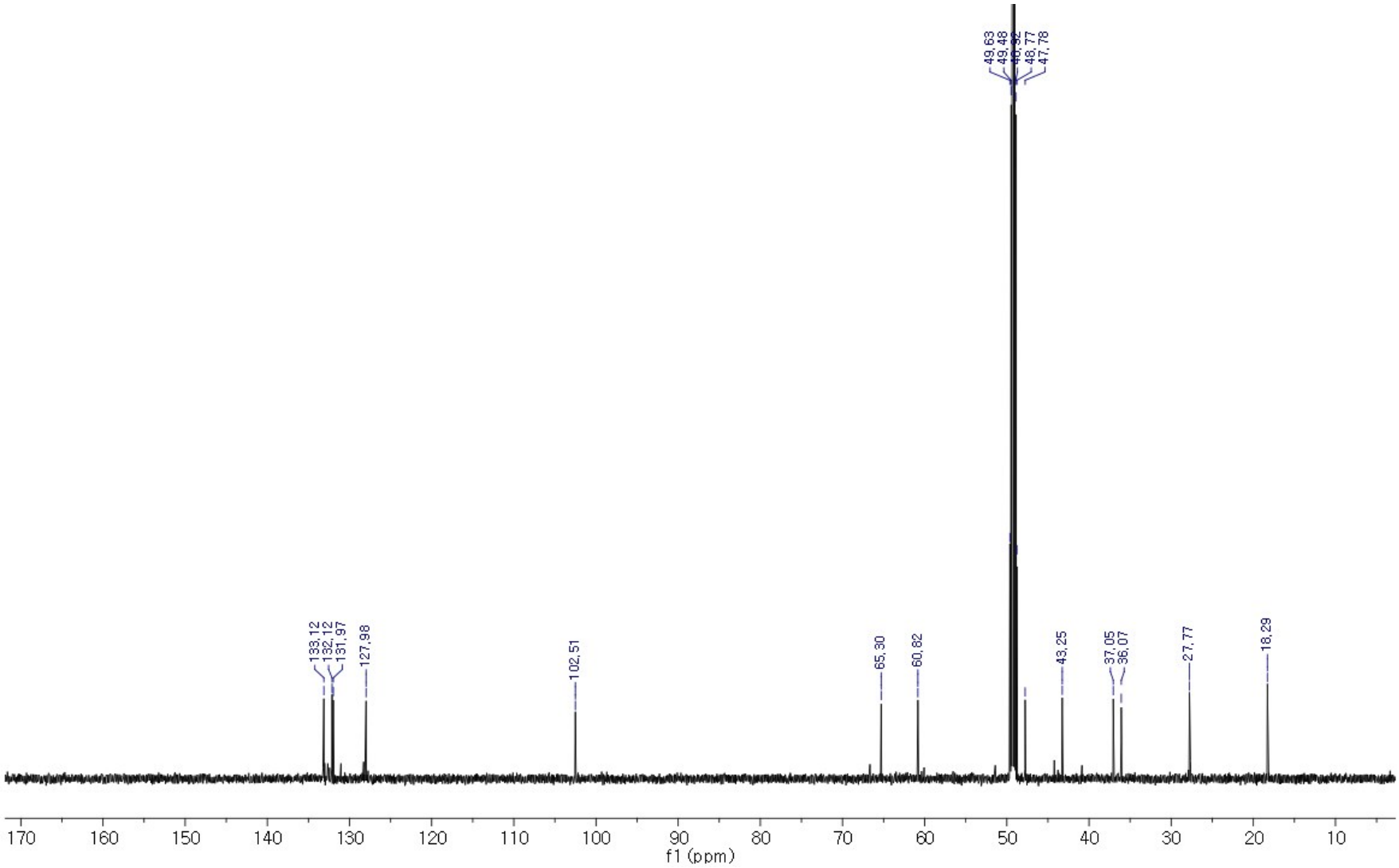


Figure S15. ^{13}C NMR spectrum of compound **2a** in CD_3OD.

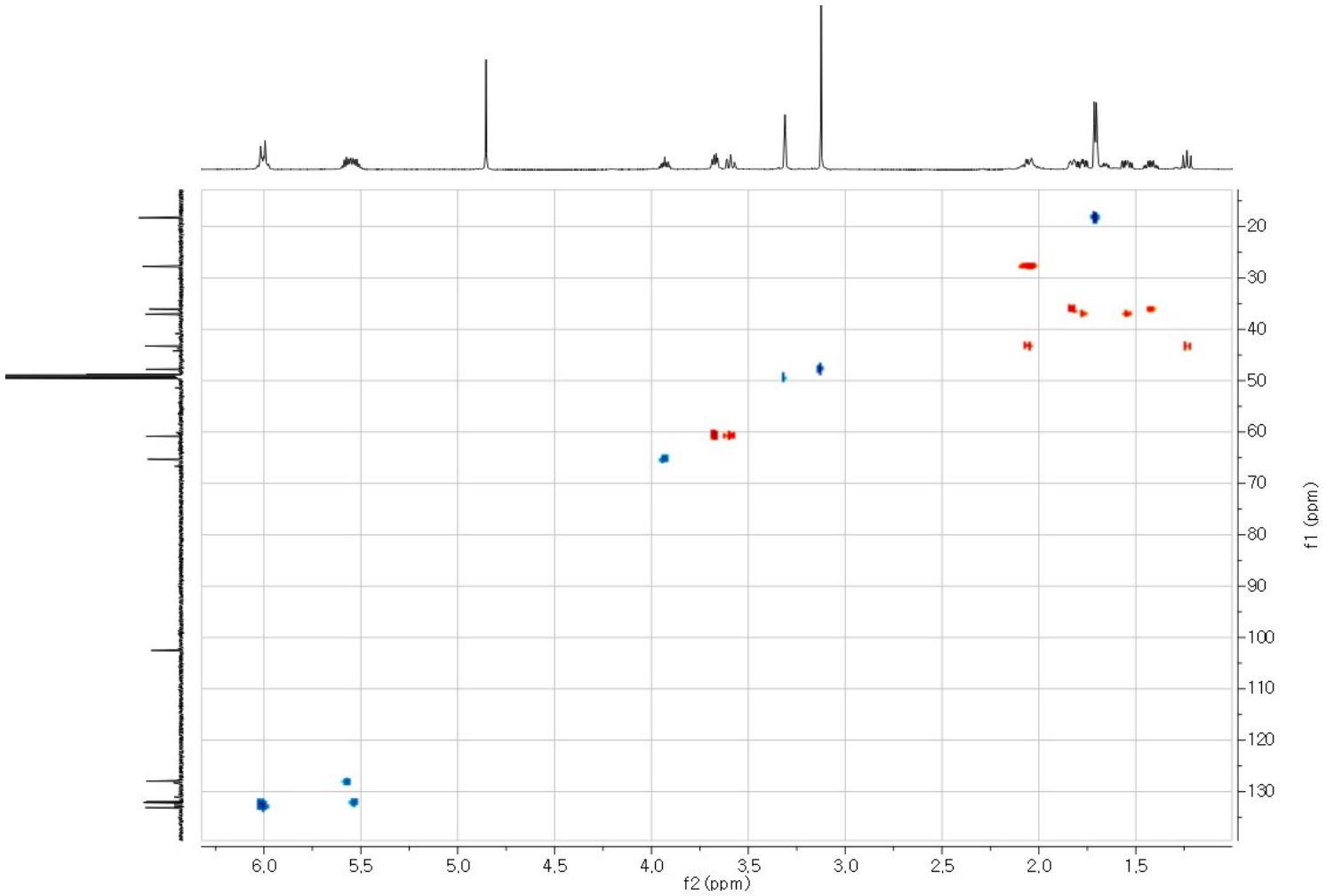


Figure S16. HSQC spectrum of compound **2a** in CD_3OD.

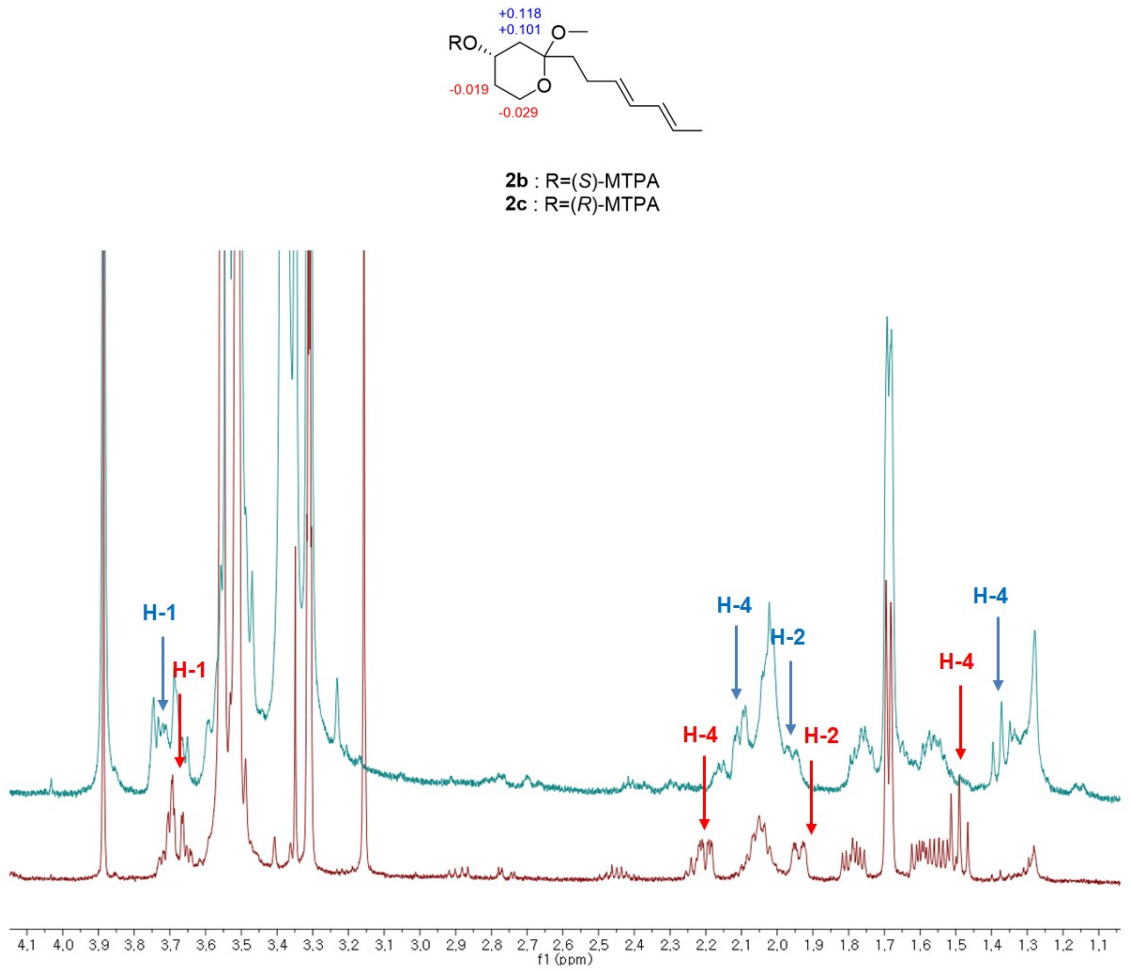


Figure S17. Selected regions of ^{1}H spectrum of Mosher's ester analysis of hydrolysate of **2a**.

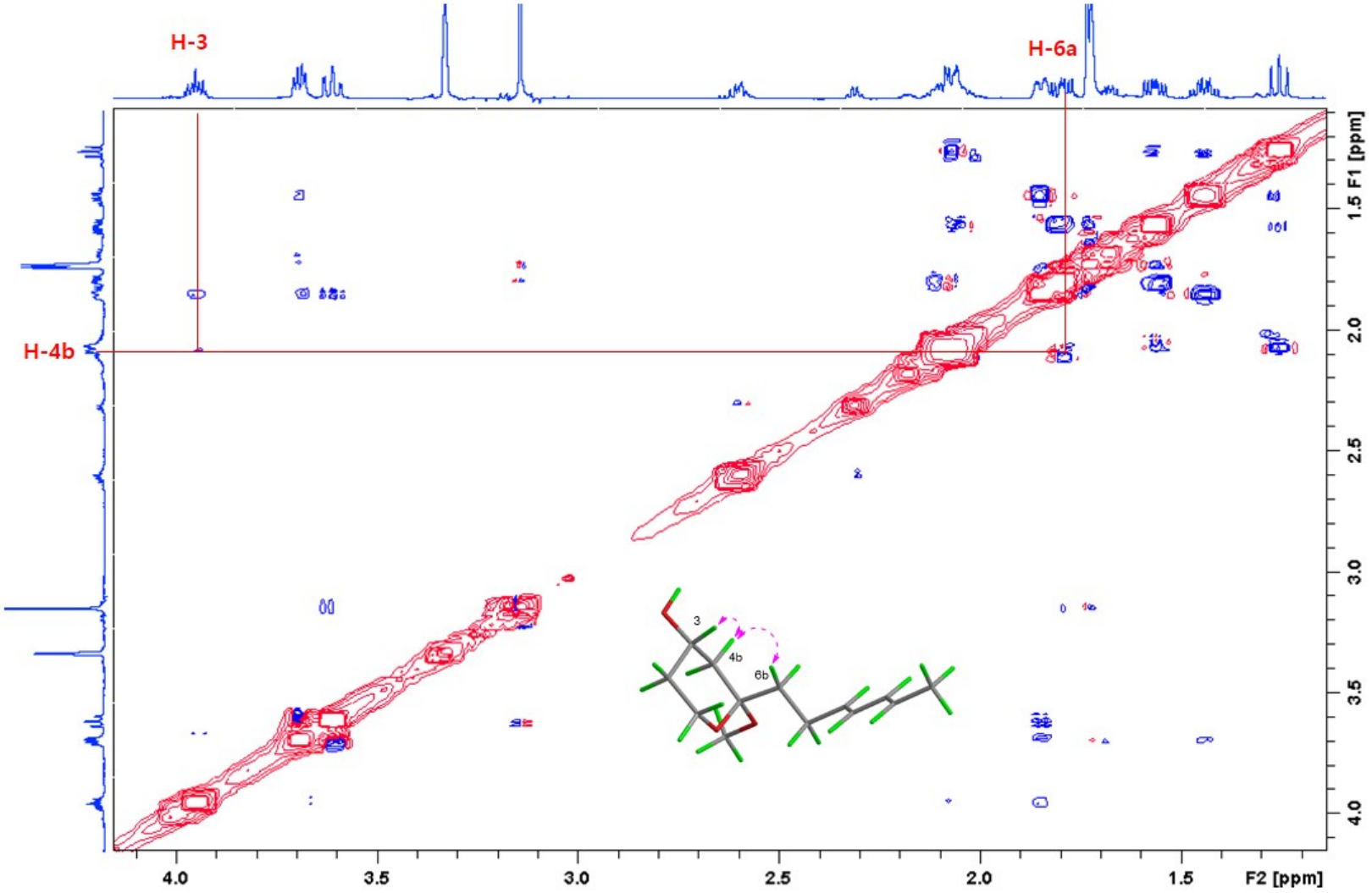


Figure S18. NOESY spectrum of compound **2a** in CD_3OD.

Mass	Calc. Mass	mDa	PPM	DBE	Formula
368.1837	368.1838	-0.1	-0.3	7.5	C20 H27 N O4 Na

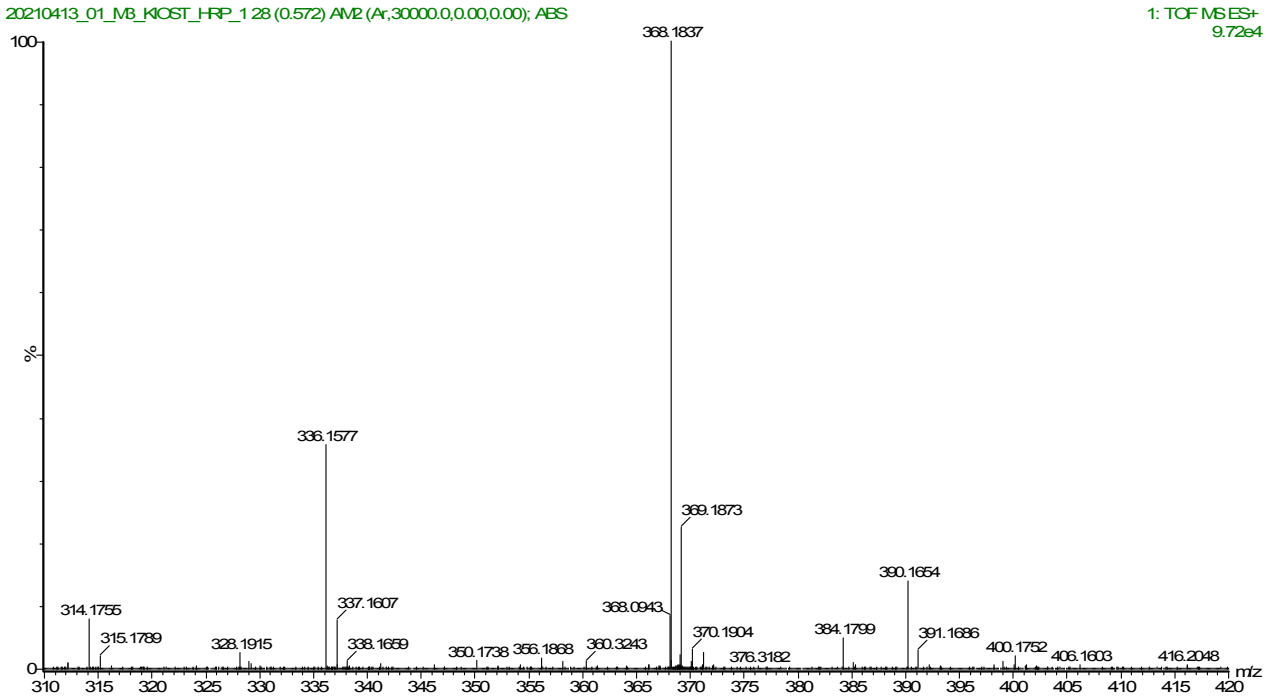


Figure S19. HRESIMS spectrum of miharadiene C (**3**).

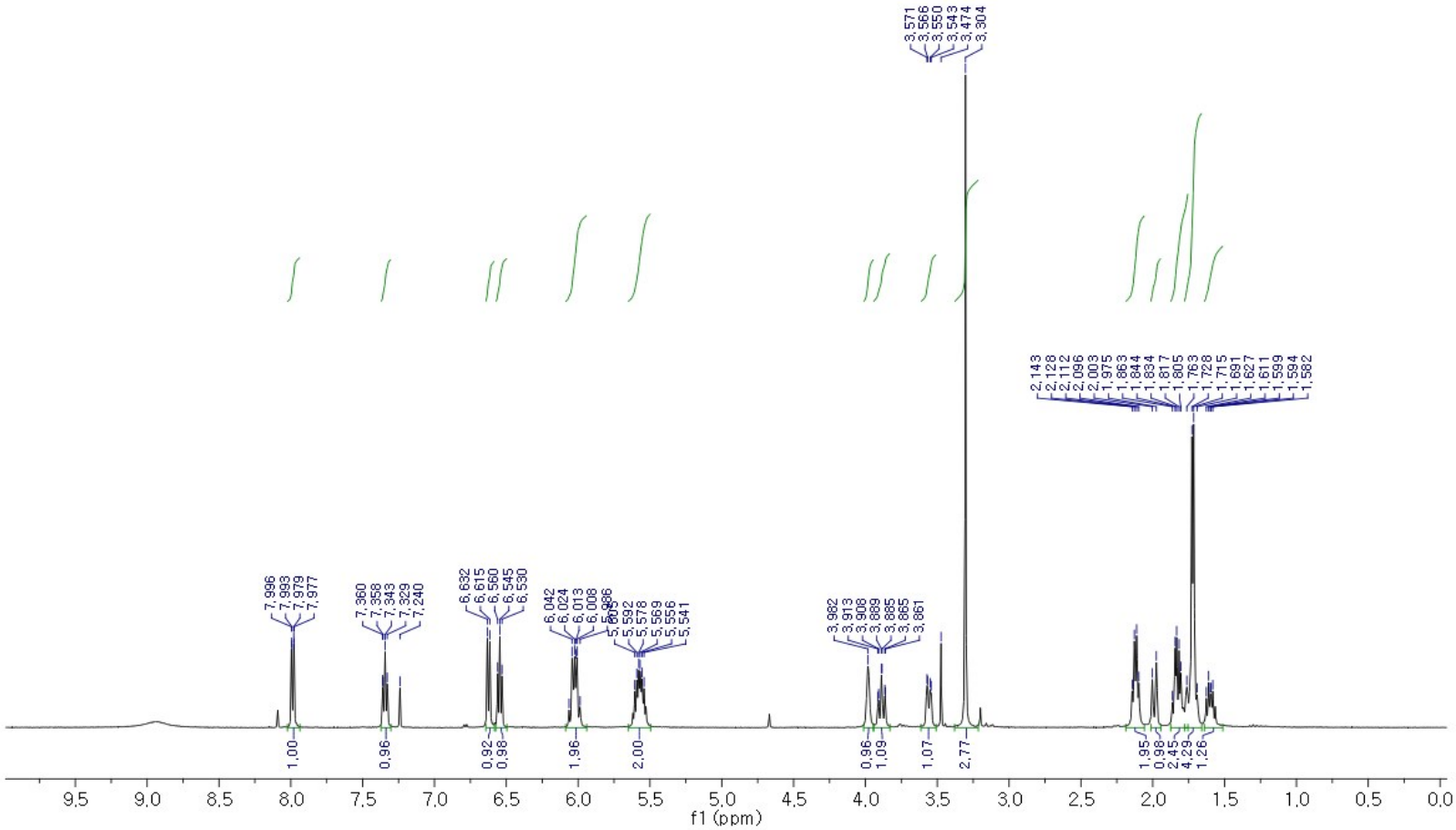


Figure S20. ^{1}H NMR spectrum of miharadiene C (**3**) in $CDCl_3$.

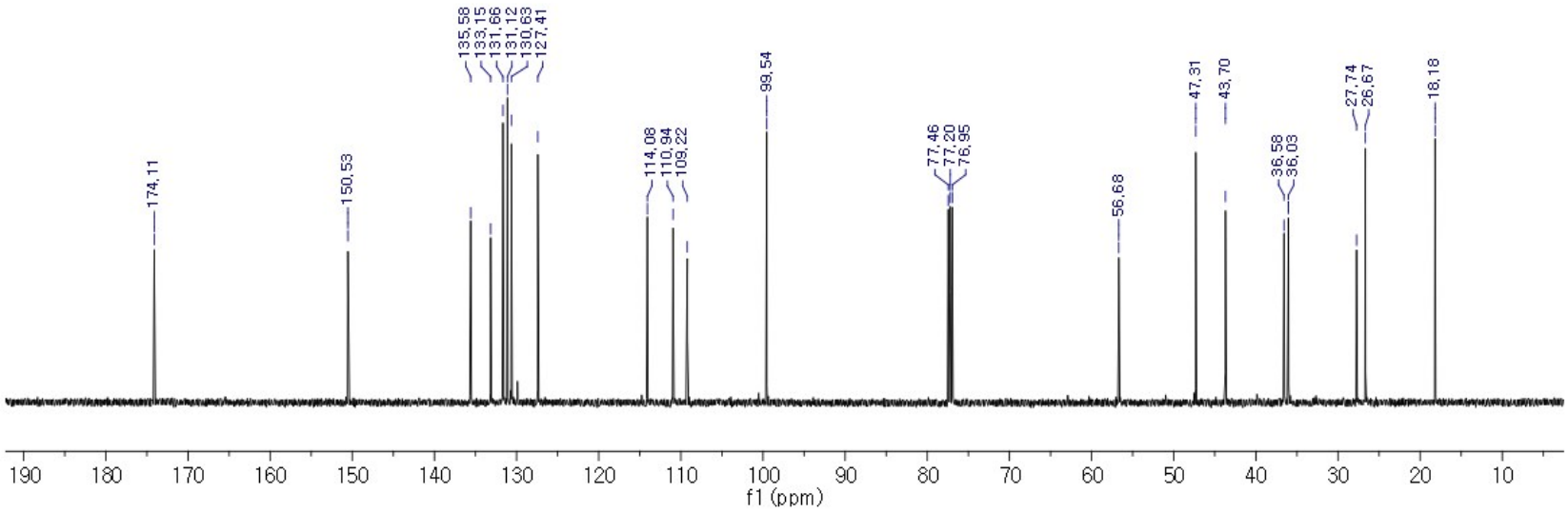


Figure S21. ^{13}C NMR spectrum of miharadiene C (**3**) in $CDCl_3$.

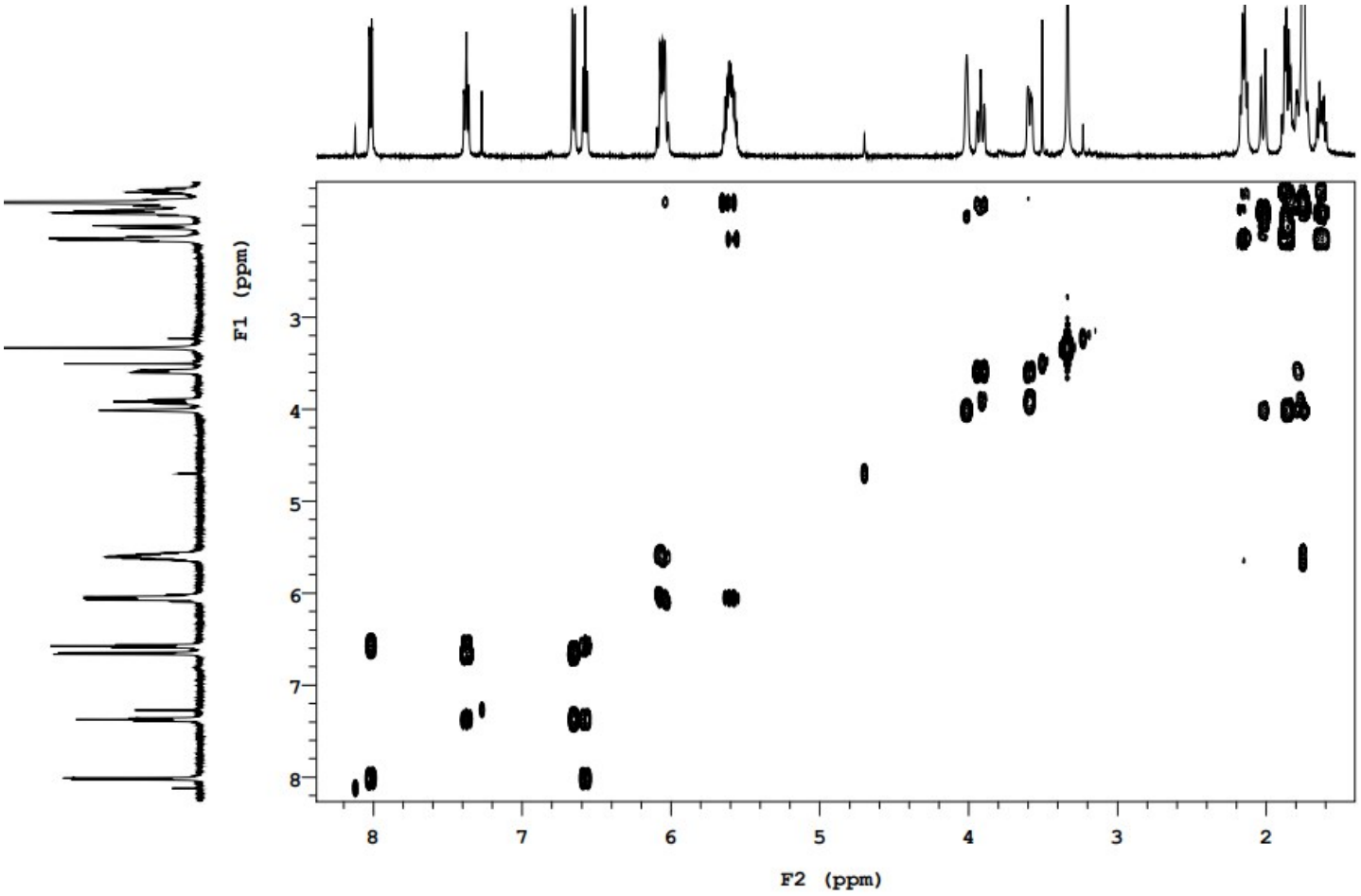


Figure S22. ^{1}H-^{1}H COSY spectrum of miharadiene C (**3**) in $CDCl_3$.

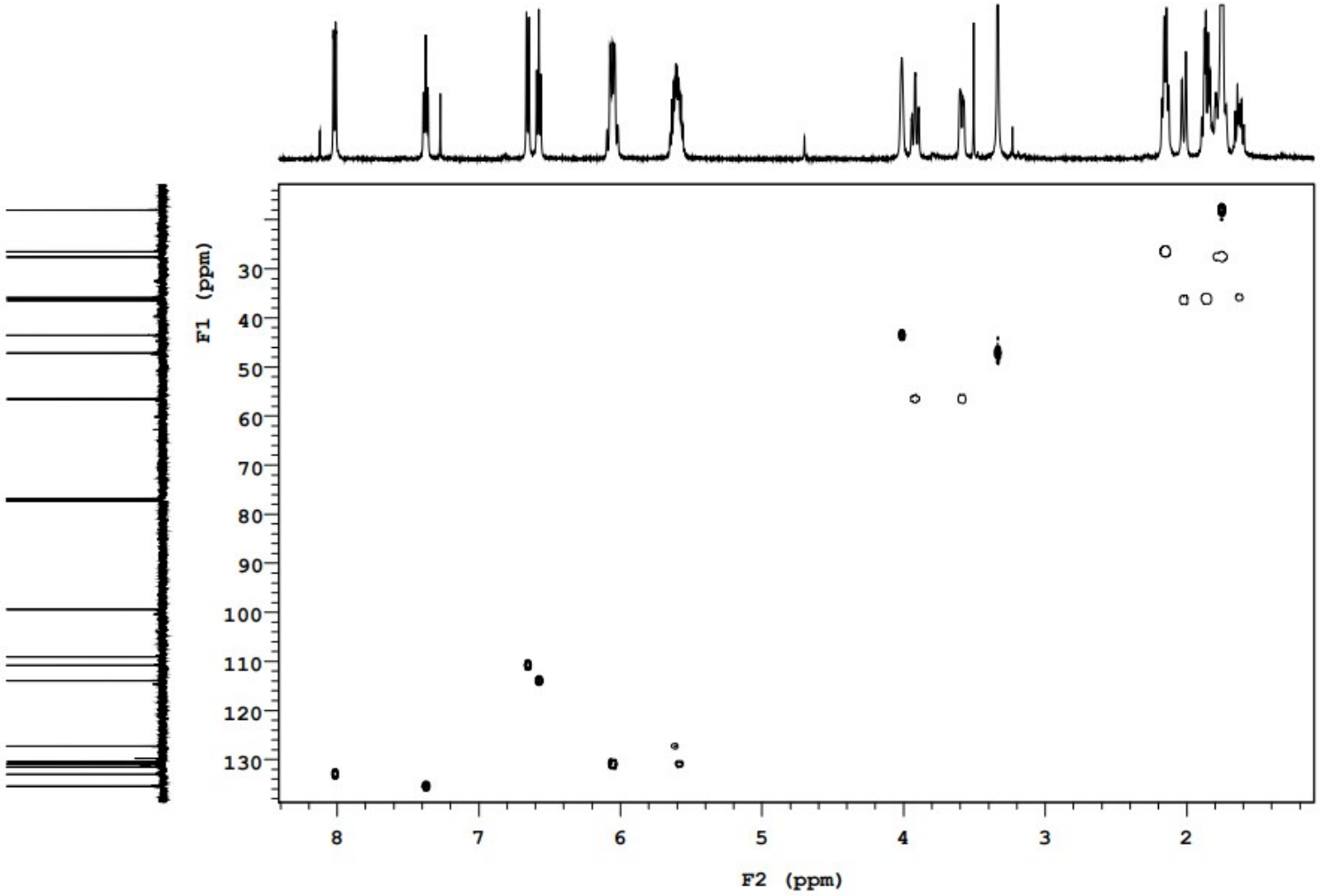


Figure S23. HSQC spectrum of miharadiene C (**3**) in $CDCl_3$.

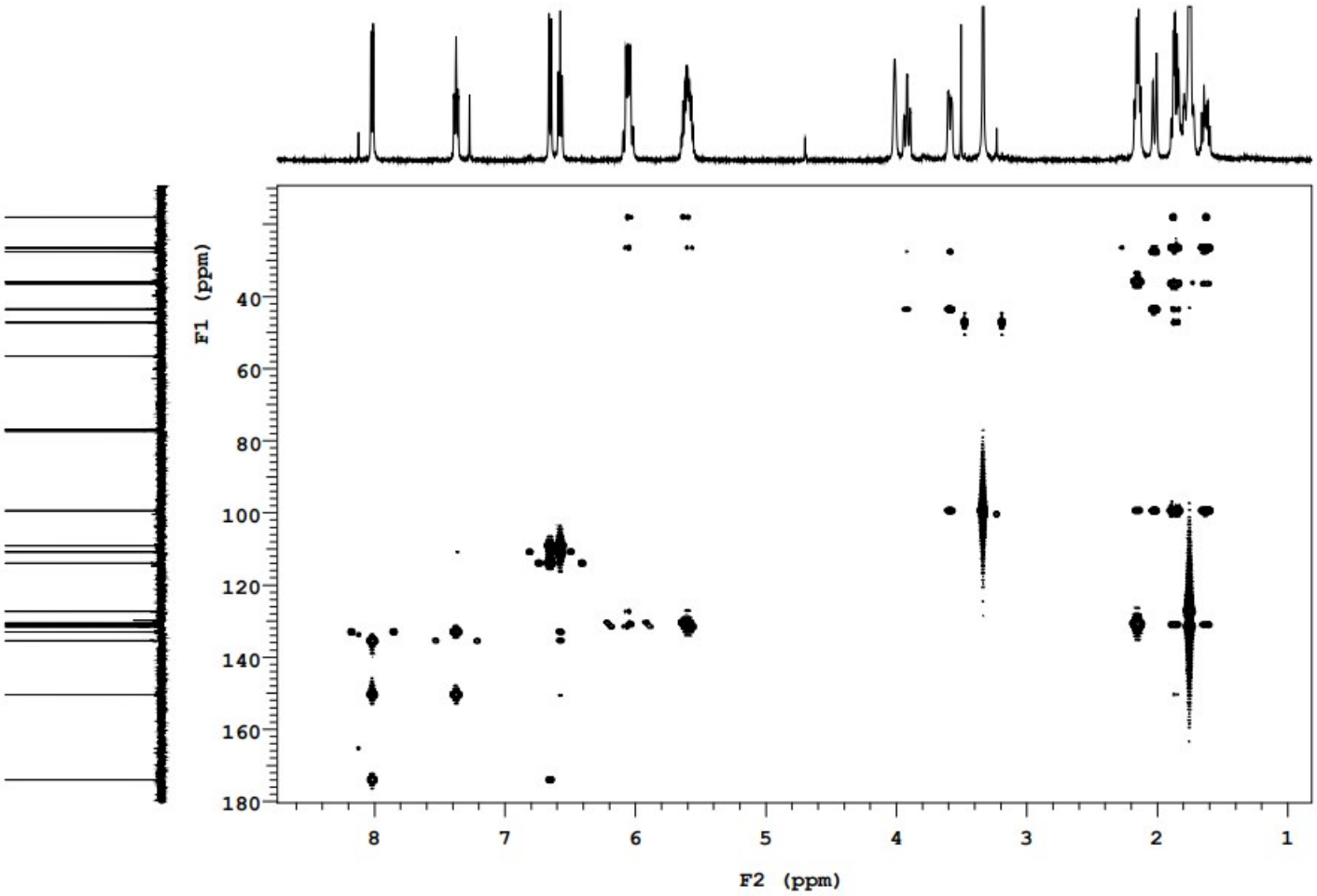


Figure S24. HMBC spectrum of miharadiene C (**3**) in $CDCl_3$.

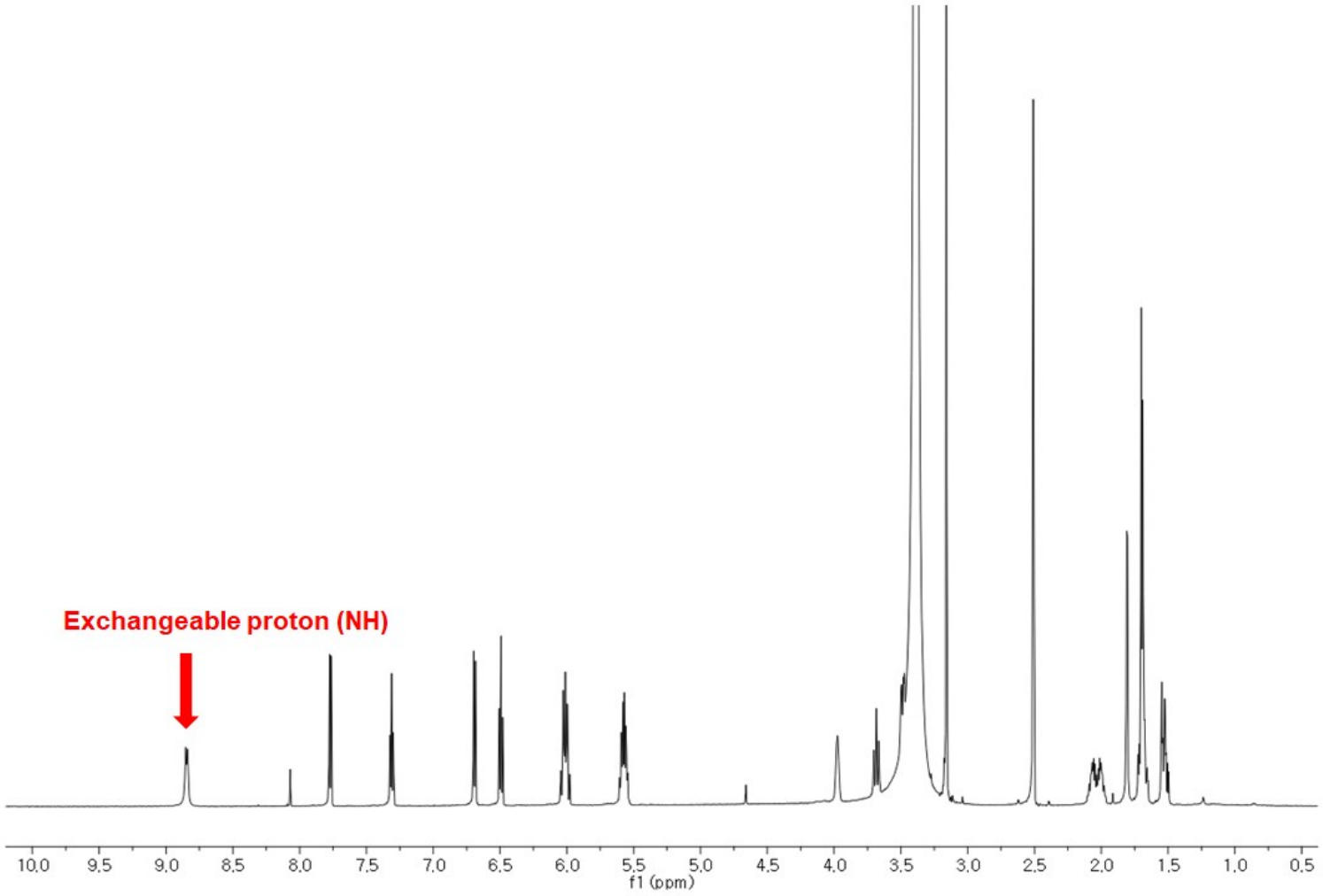


Figure S25. ^{1}H NMR spectrum of miharadiene C (**3**) in DMSO-d_6.

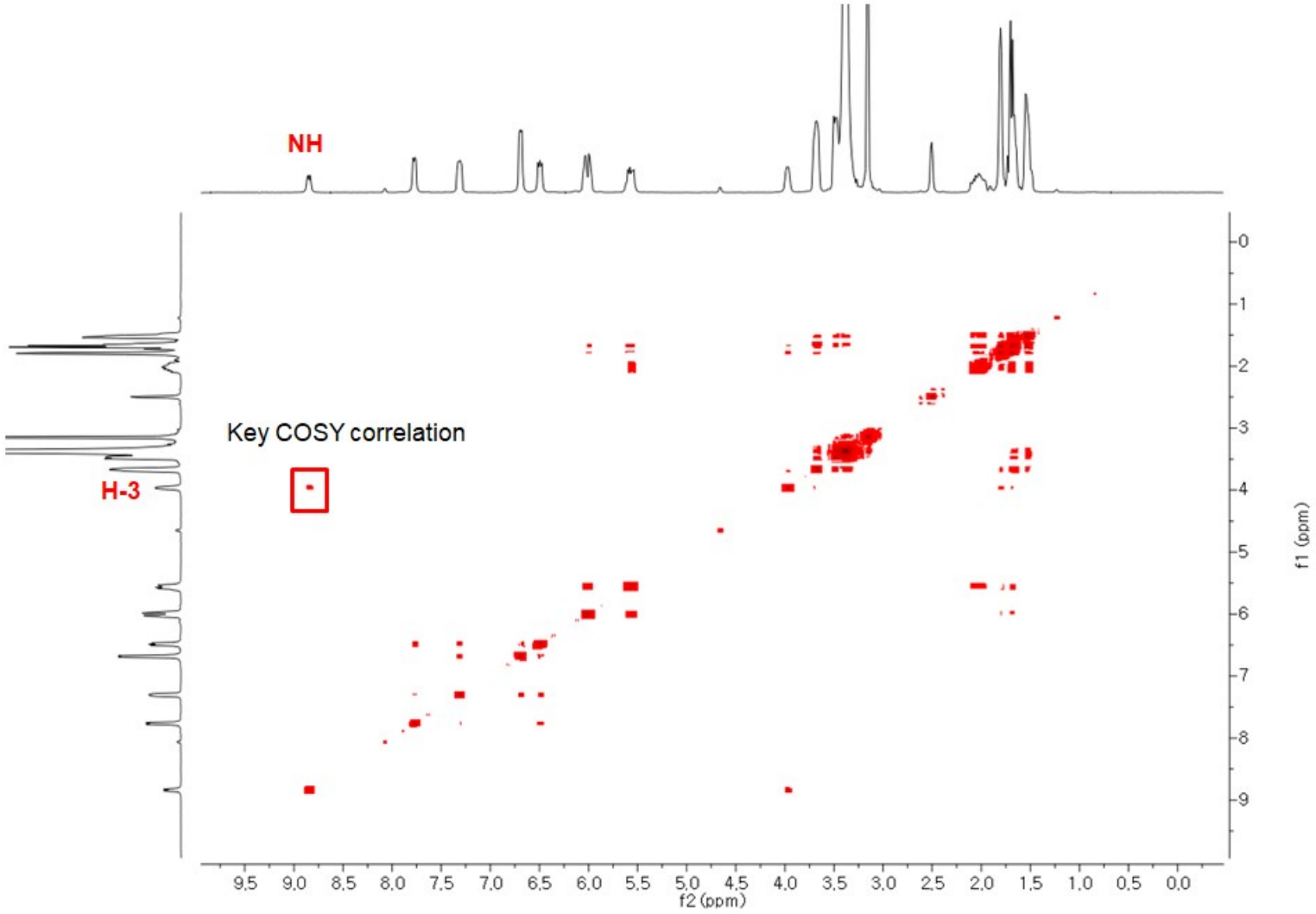


Figure S26. ^{1}H-^{1}H COSY spectrum of miharadiene C (**3**) in DMSO-d_6.

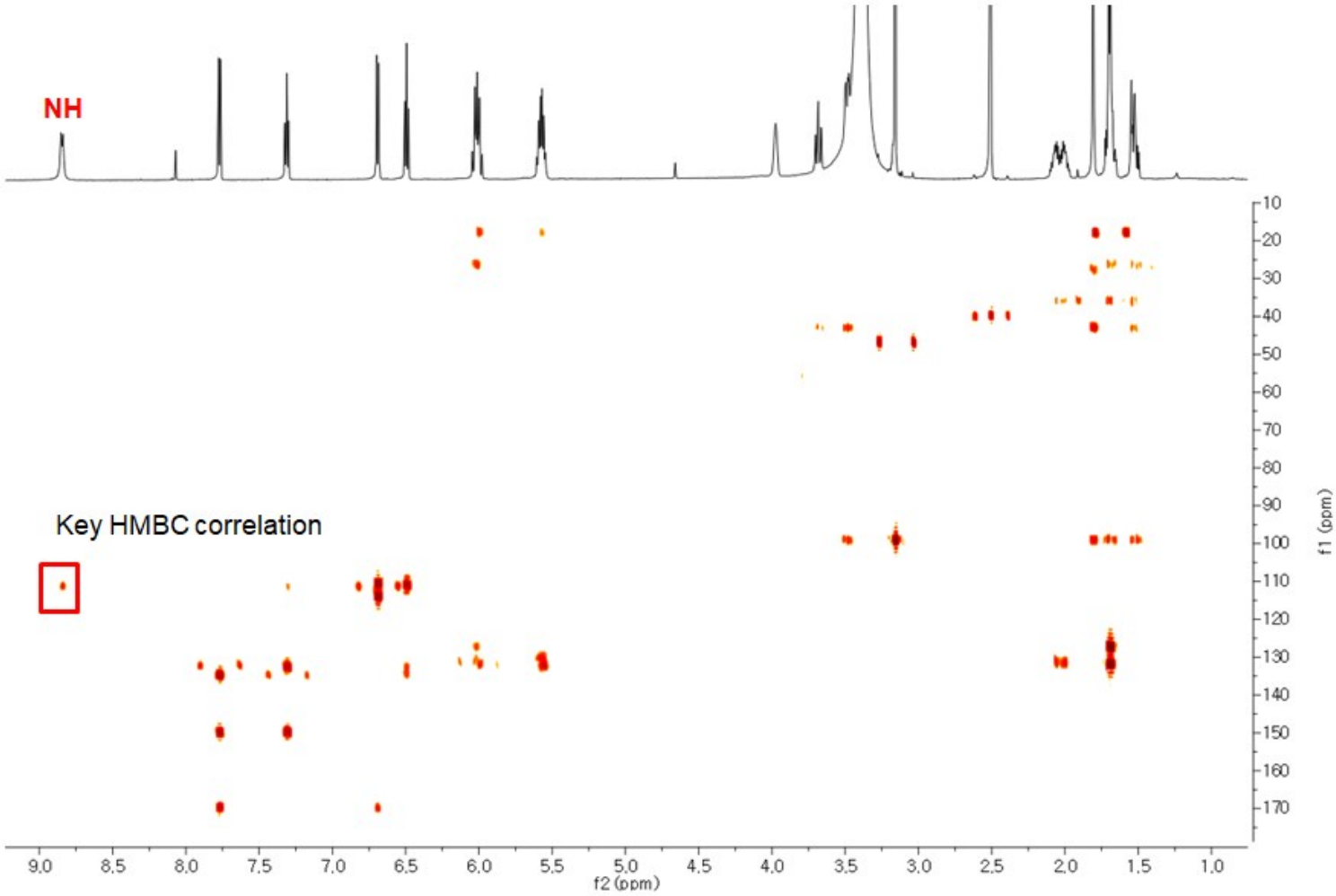


Figure S27. HMBC spectrum of miharadiene C (**3**) in DMSO-d_6.

Mass	Calc. Mass	mDa	PPM	DBE	Formula
271.1305	271.1310	-0.5	0.1	5.5	C15 H20 O3 Na

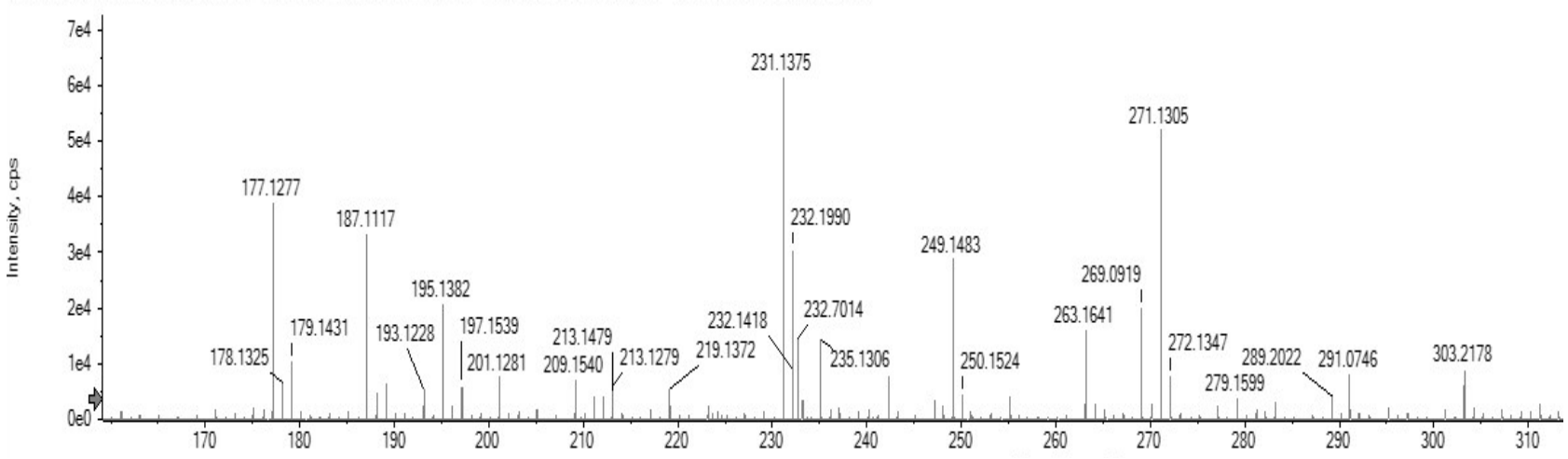


Figure S28. HRESIMS spectrum of miharadiene D (**4**).

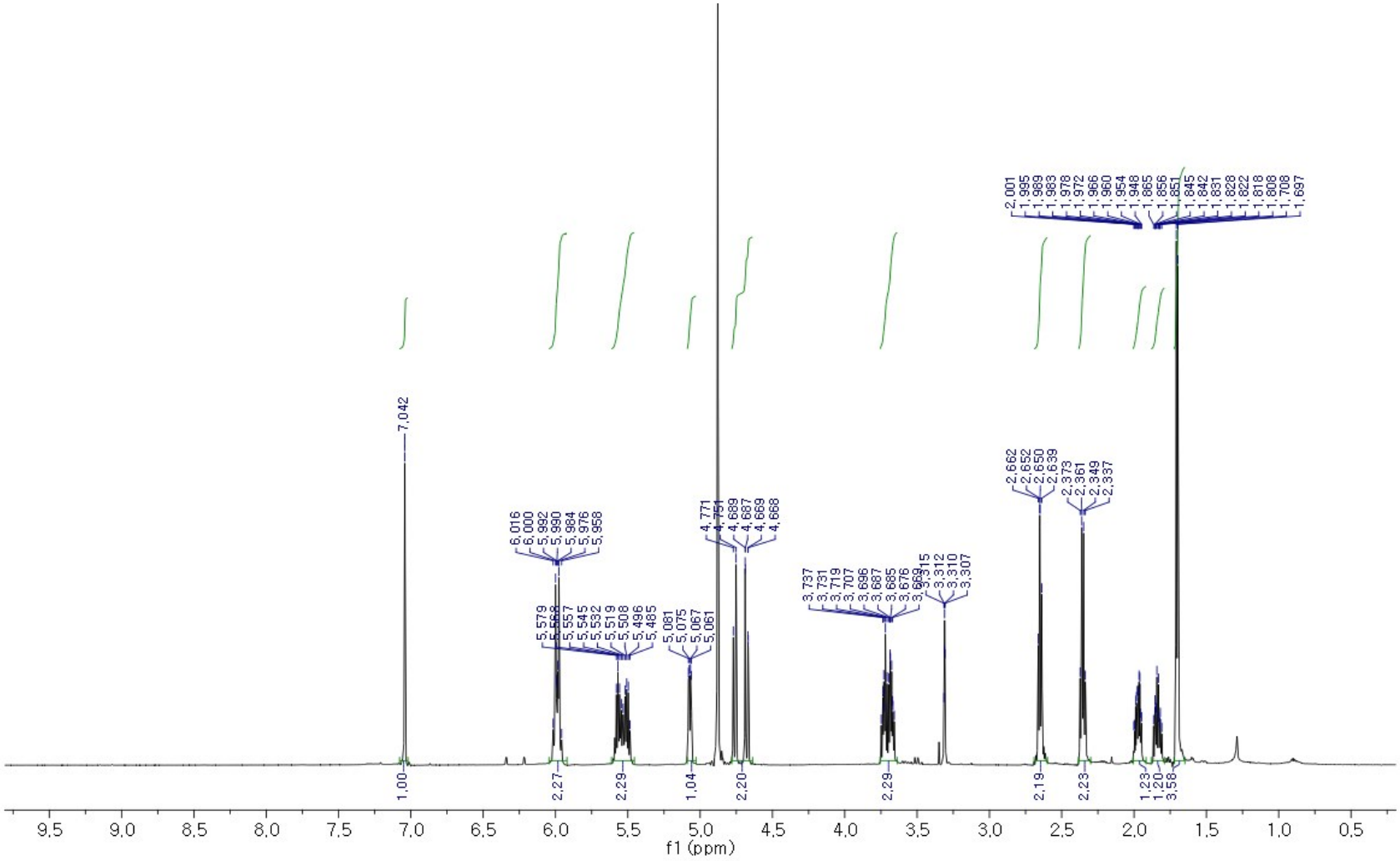


Figure S29. ^{1}H NMR spectrum of miharadiene D (**4**) in CD_3OD.

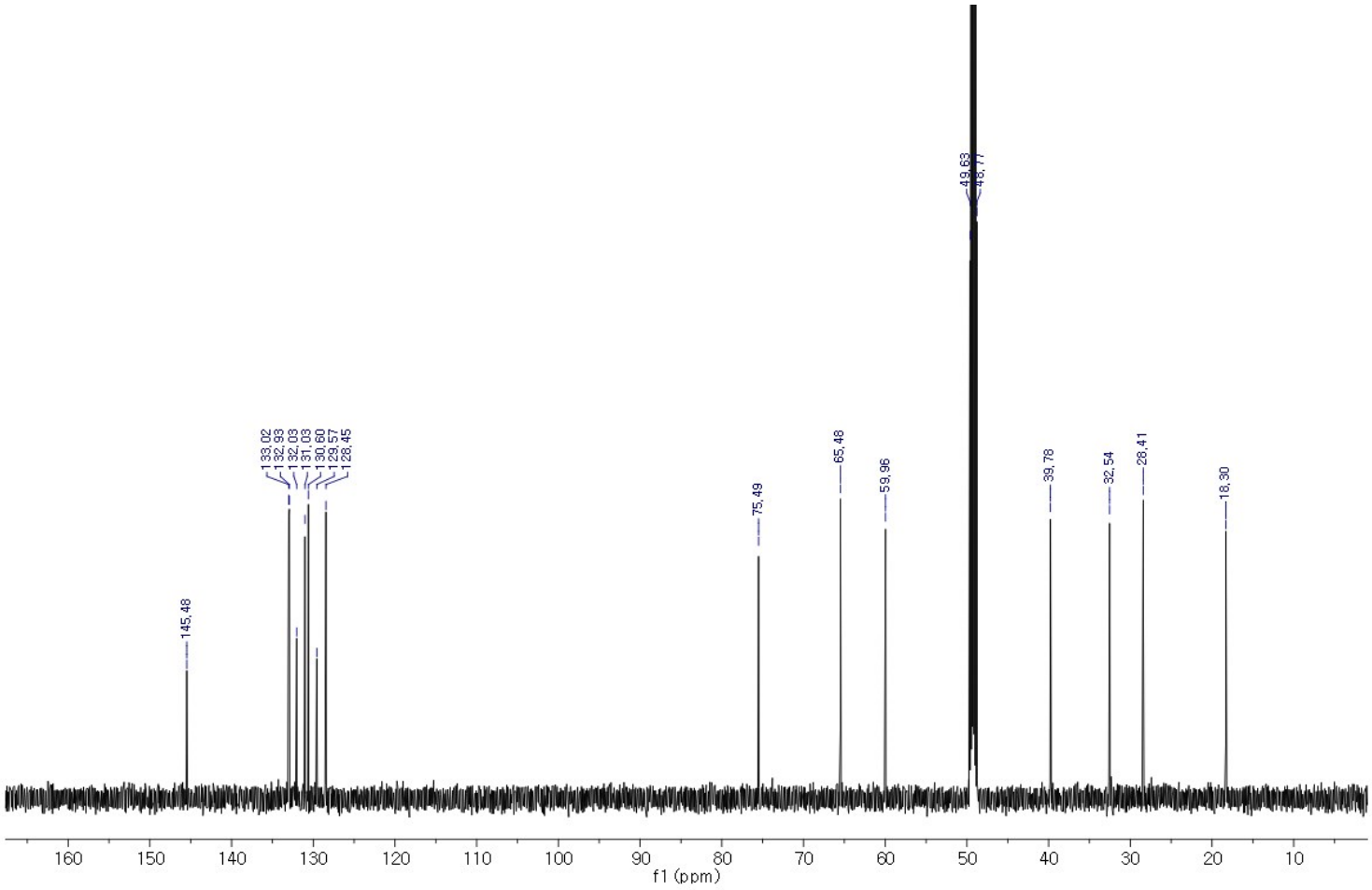


Figure S30. ^{13}C NMR spectrum of miharadiene D (**4**) in CD_3OD.

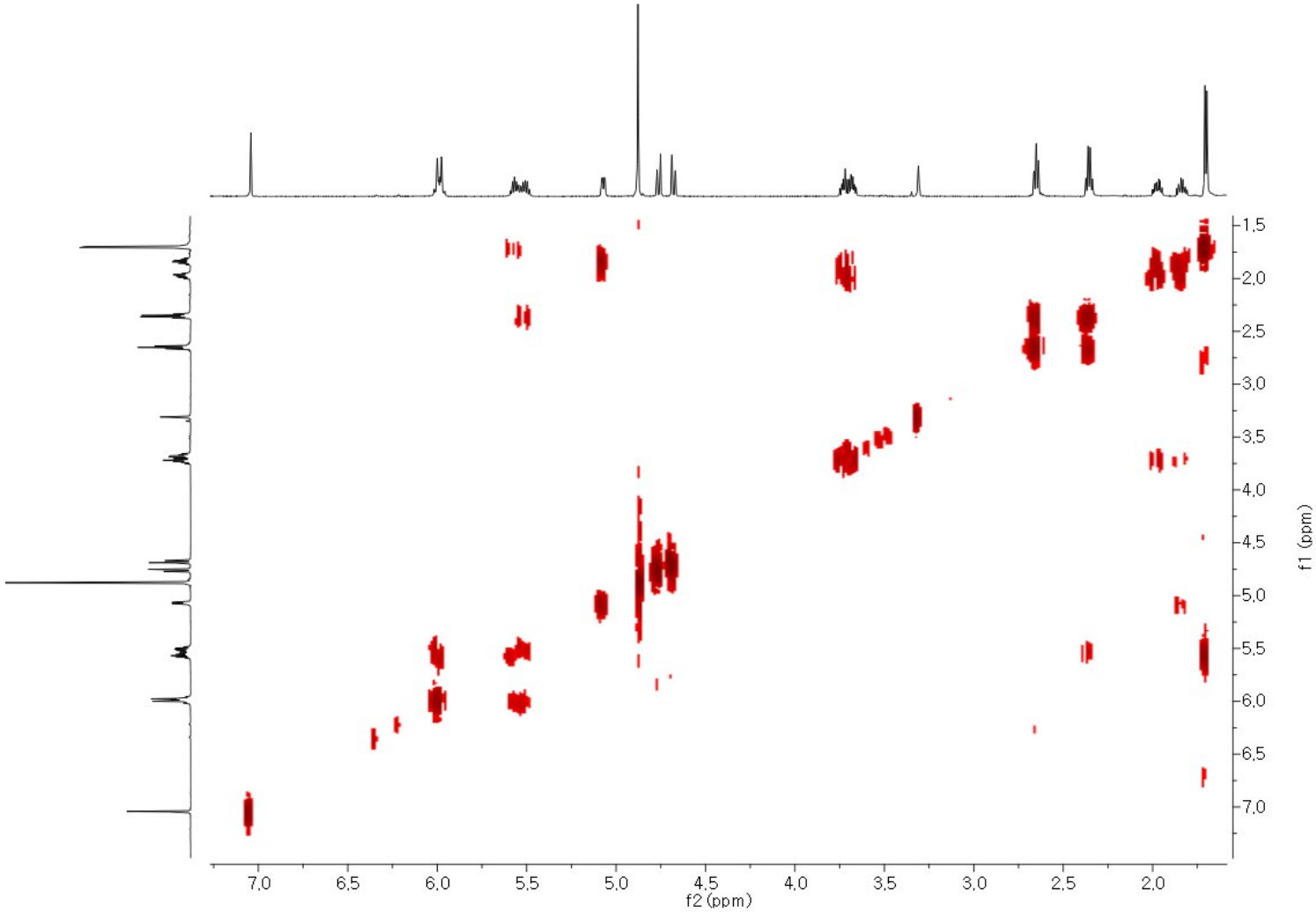


Figure S31. ^{1}H-^{1}H COSY spectrum of miharadiene D (**4**) in CD_3OD.

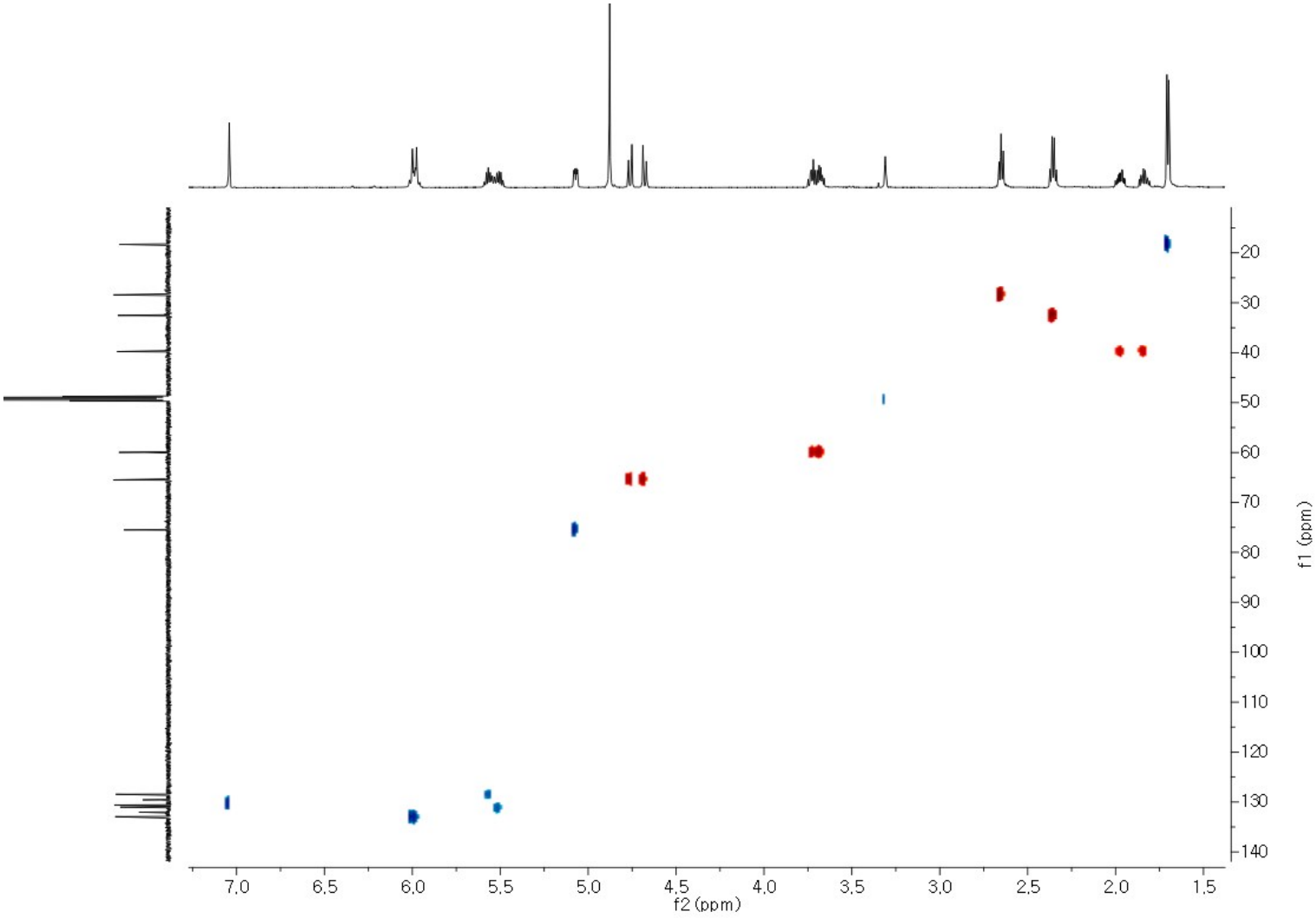


Figure S32. HSQC spectrum of miharadiene D (**4**) in CD_3OD.

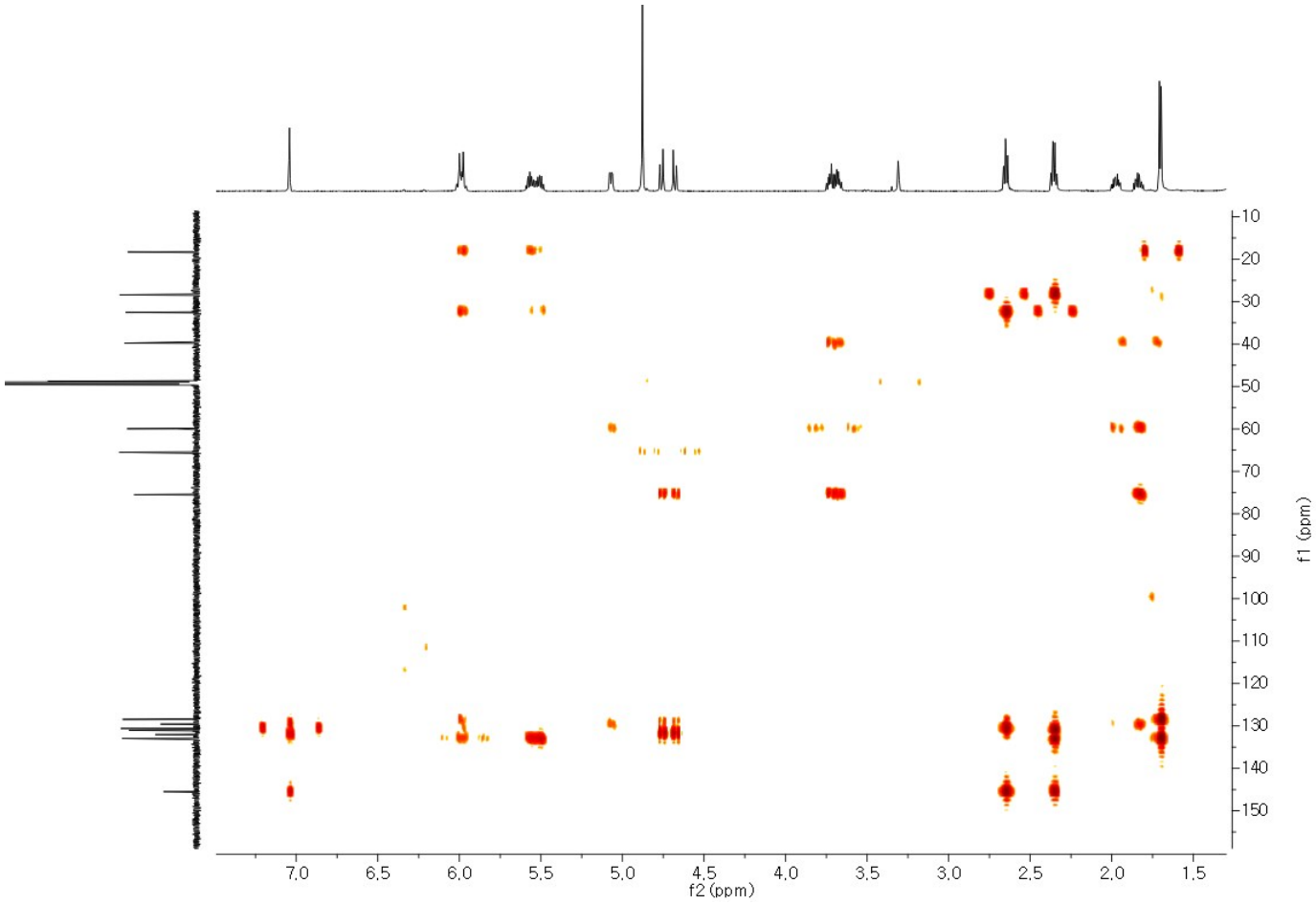
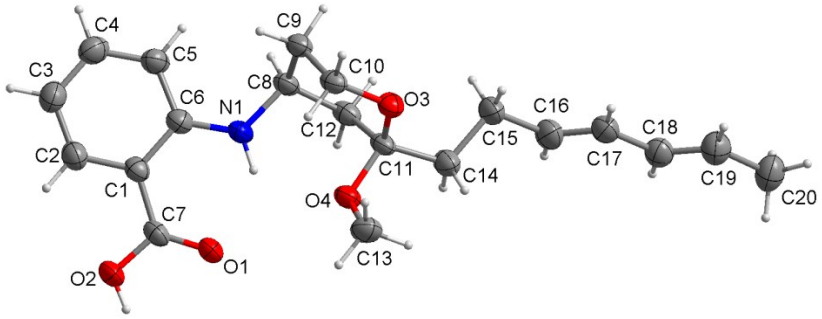


Figure S33. HMBC spectrum of miharadiene D (**4**) in CD_3OD.

X-ray Crystallographic analysis. Single-crystal X-ray diffraction data were collected using an Bruker SMART APEX2 ULTRA and a APEX II CCD area detector with a multilayer-monochromated Mo Kα radiation (λ = 0.71073 Å) generated by a rotating anode. Data collection, data reduction, and semiempirical absorption correction were carried out using the software package APEX2.(1) All of the calculations for the structure determination were carried out using the SHELXTL package. (2) All non-H atoms were refined anisotropically. All hydrogen atoms were included in calculated positions with isotropic thermal parameters 1.2 times those of attached atoms.

(1) APEX2 (Version 2009.1−0) Data Collection and Processing Software; Bruker AXS Inc.: Madison, Wisconsin, U.S.A., 2008.
(2) SHELXTL-PC (Version 6.22) Program for Solution and Refinement of Crystal Structures; Bruker AXS Inc.: Madison, Wisconsin, U.S.A., 2001.



Crystal data for **3.** Formula= $C_{22}H_{39}CuN_5O_6$, crystal size = 0.30 × 0.24 × 0.13 mm, Monoclinic, space group $P2_1/n$, a = 16.5612(2) Å, b = 9.2100(1) Å, c = 16.7191(2) Å, β = 115.463(1)°, V = 2303.4(1) Å^3, Z = 4, D_c = 1.538 g cm^{-3}, μ = 0.669 mm^{-1}, T = 173(2) K, $F(000)$ = 1132, T_{max}/T_{min} = 0.89/0.80, $2\theta_{max}$ = 27.54°; 5297 reflections collected, 307 independent reflections, R_{int} = 0.0317, R1 = 0.03 and R2 = 0.08 for I ≥ 2σ(I), R1 = 0.39 and R2 = 0.08 for all data, GoF = 1.044.

Table S1. Crystal data and structural refinement

	3
Formula	$C_{13}H_{12}BrCuN_4S_2$
M	431.84
T/K	173(2)
Crystal system	Triclinic
Space group	P-1
a/Å	8.6303(13)
b/Å	9.8063(12)
c/Å	9.9415(14)
α/°	69.229(8)
β/°	71.497(6)
γ/°	81.910(8)
V/Å^3	745.6(2)
Z	2
μ(Mo-Kα)/mm^{-1}	4.420
Crystal size/mm	0.08 × 0.05 × 0.02
Absorption correction	Multi-scan SADABS
Reflections collected	11391
Independent reflections	2898
Goodness-of-fit on F^2	1.064
Final $R1$, $wR2$ [$I > 2\sigma(I)$]	0.1134, 0.3054
(all data)	0.1456, 0.3367

Figure S34. DFT optimized conformers and populations of miharadiene A (3*S*, 5*S*) above 5% population.

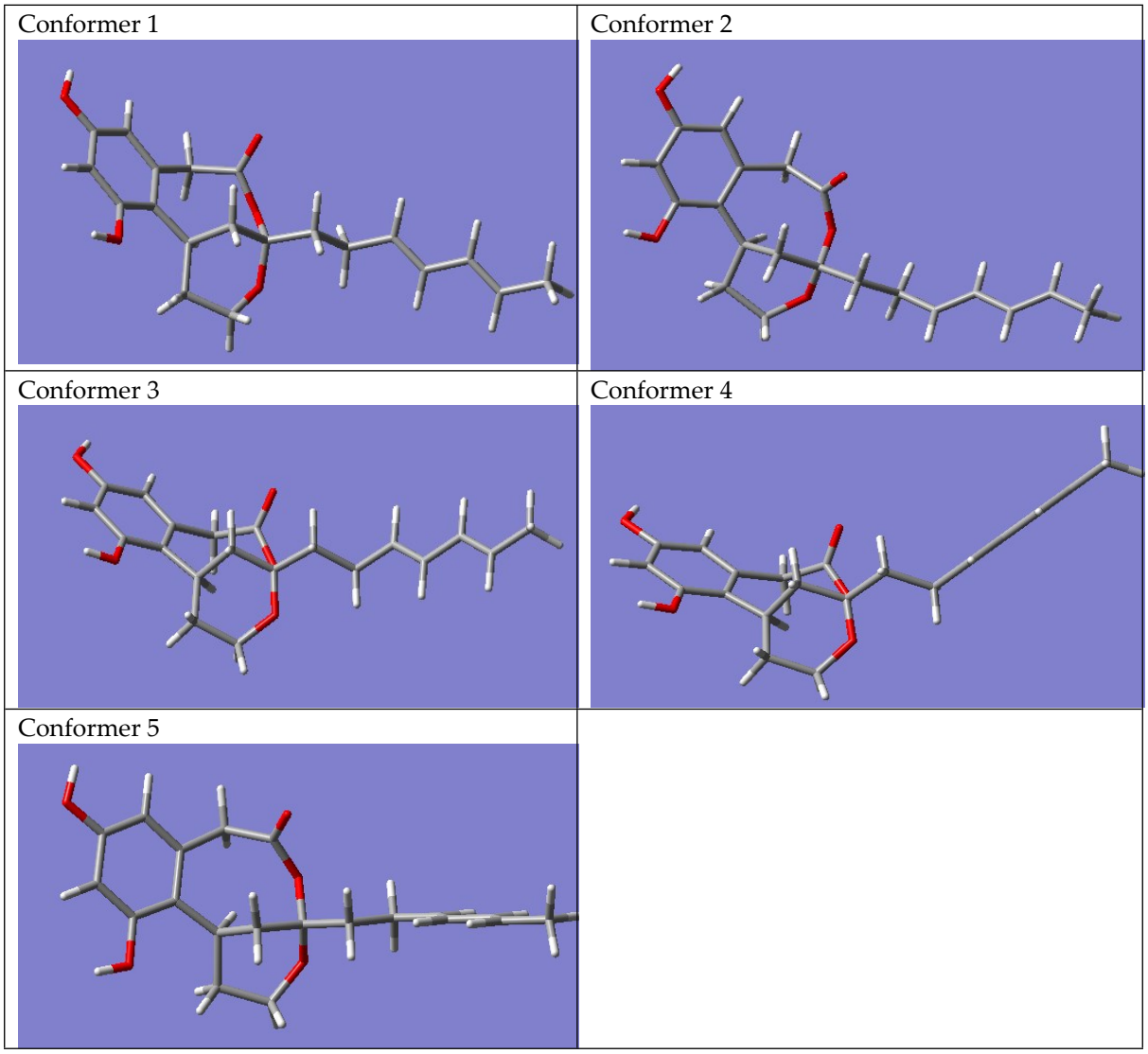


Figure S35. DFT optimized conformers and populations of miharadiene D (3*R*) above 2% population.

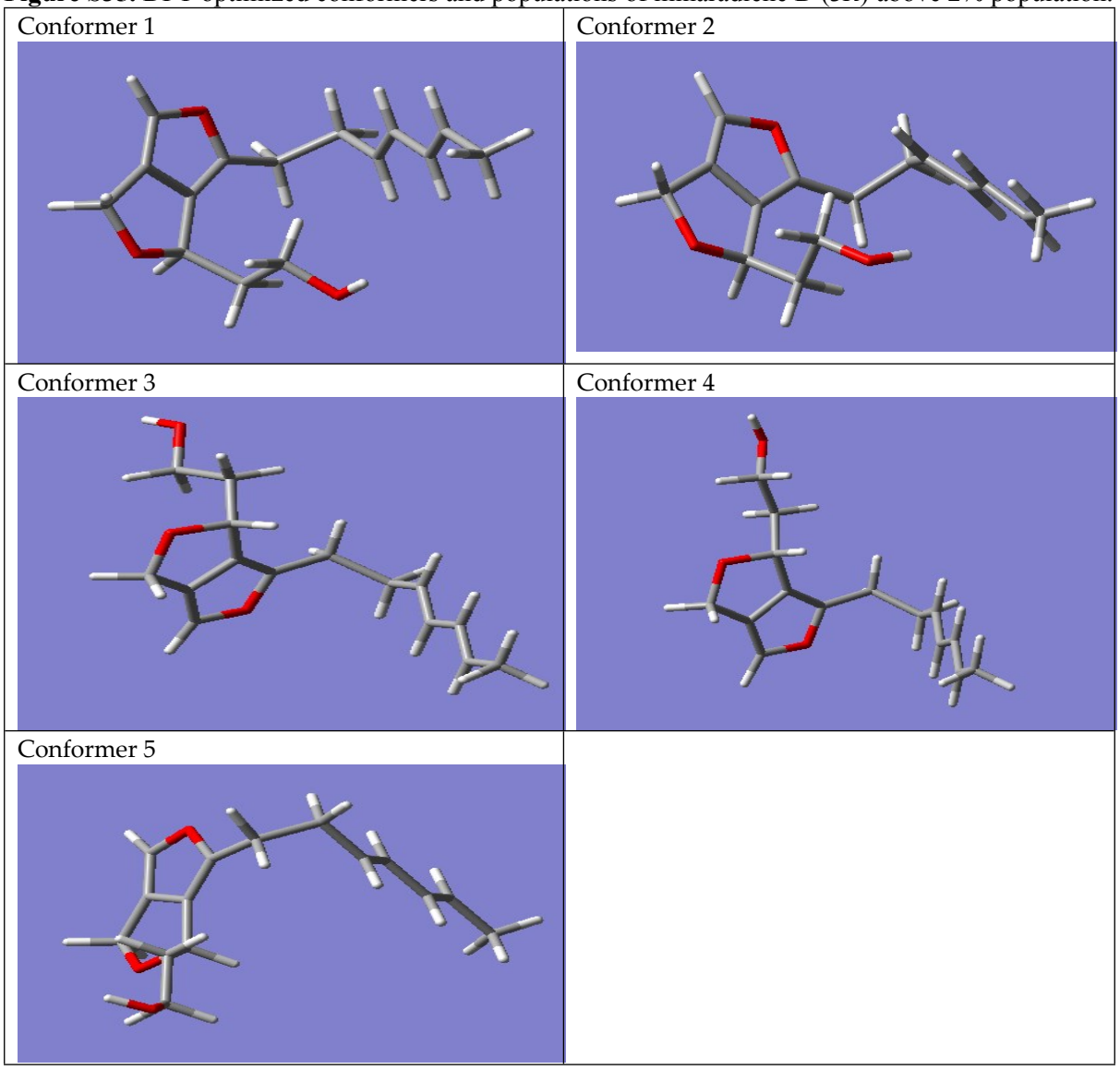


Table S2. Gibbs free energies and Boltzmann distribution of conformers of **1**

B3LYP/6-311+G(d,p) Gibbs free energy (298.15K)		
	G (Hartree)	Population (%)
Conformer 1	-1152.483640	20.77
Conformer 2	-1152.486823	13.53
Conformer 3	-1152.487408	13.17
Conformer 4	-1152.487148	9.44
Conformer 5	-1152.485161	6.21

Table S3. Gibbs free energies and Boltzmann distribution of conformers of **4**

B3LYP/6-311+G(d,p) Gibbs free energy (298.15K)		
	G (Hartree)	Population (%)
Conformer 1	-808.849283	8.17
Conformer 2	-808.850206	5.50
Conformer 3	-808.848945	4.01
Conformer 4	-808.849516	3.85
Conformer 5	-809.274794	3.17