Supplementary Information

Aromatic Polyketides and Macrolides from *Microsphaeropsis arundinis*

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Spectral data for compounds **2**-**7**

(*R*)-1-(2,5-Dihydroxyphenyl)-3-hydroxybutanone (**2**)

Yellow, amorphous solid; $[\alpha]_D^{20}$ –23.0 (*c* 0.1, MeOH); UV (MeOH) λ_{max} / nm 225, 258, 360; ^{1}H NMR (600 MHz, CD_3OD) δ 1.27 (d, 3H, *J* 6.2, CH_3), 3.03 (dd, 1H, *J* 4.9, 16.1, CH_2), 3.17 (dd, 1H, *J* 7.6, 16.1, CH_2), 4.37 (dqd, 1H, *J* 4.9, 6.2, 7.6, CH), 6.79 (d, 1H, *J* 8.9, CH), 7.01 (dd, 1H, *J* 2.9, 8.9, CH), 7.24 (d, 1H, *J* 2.9, CH); ^{13}C NMR (150 MHz, CD_3OD) δ 23.5, 48.4, 65.3, 115.9, 119.7, 120.8, 125.9, 150.6, 156.7, 206.2; (+)-QTOF HRMS *m/z*, calculated for $C_{10}H_{12}O_4$ $[M + Na]^+$: 219.0628, found: 219.0629 (mass error: 0.46 ppm).

1-(2,5-Dihydroxyphenyl)-2-buten-1-one (**3**)

Yellow, amorphous solid; UV (MeOH) λ_{max} / nm 220.5, 257.2, 362.2; ^{1}H NMR (600 MHz, CD_3OD) δ 1.34 (d, 3H, *J* 6.3, CH_3), 1.97 (s, 3H, CH_3), 3.16 (dd, 1H, *J* 5.0, 16.7, CH_2), 3.40 (dd, 1H, *J* 7.6, 16.7, CH_2), 5.43 (dqd, 1H, *J* 5.0, 6.3, 7.6, CH), 6.80 (d, 1H, J 8.9, CH), 7.02 (dd, 1H, *J* 2.9, 8.9, CH), 7.23 (d, 1H, *J* 2.9, CH); ^{13}C NMR (150 MHz, CD_3OD) δ 20.3, 21.1, 45.3, 68.6, 115.7, 119.7, 120.7, 126.0, 150.7, 156.6, 172.3, 204.5; (+)-QTOF HRMS *m/z*, calculated for $C_{10}H_{10}O_3$ $[M + Na]^+$: 179.0703, found: 179.0705 (mass error: 1.11 ppm).

Modiolide D (**4**)

White, amorphous solid; $[\alpha]_D^{25}$ +94.0 (*c* 0.1, MeOH); ^{1}H NMR (600 MHz, CD_3OD) δ 1.24 (d, 3H, *J* 6.4, CH_3), 1.74 (dt, 1H, *J* 11.1, 14.0, CH_2), 1.90 (ddd, 1H, *J* 1.7, 3.4, 14.0, CH_2), 2.05 (s, 3H, CH_3), 4.13 (ddd, 1H, *J* 3.4, 7.2, 11.1, CH), 5.28 (tdd, 1H, *J* 1.7, 6.4, 12.5, CH), 5.60 (dd, 1H, *J* 8.1, 16.0, CH), 5.71 (dd, 1H, *J* 8.1, 16.0, CH), 5.79 (dd, 1H, *J* 3.6, 12.2, CH), 5.81 (m, 1H, CH), 6.03 (dd, 1H, *J* 1.7, 12.2, CH); ^{13}C NMR (150 MHz, CD_3OD) δ 20.9, 21.6, 43.8, 70.2, 72.7, 73.9, 125.6, 126.6, 133.3, 140.9, 169.9, 171.8; (+)-QTOF HRMS *m/z*, calculated for $C_{12}H_{16}O_5$ $[M + Na]^+$: 263.0890, found: 263.0891 (mass error: 0.38 ppm).

Modiolide E (**5**)

White, amorphous solid; $[\alpha]_D^{25}$ +5.0 (*c* 0.1, MeOH); ^{1}H NMR (600 MHz, CD_3OD) δ 1.24 (d, 3H, *J* 6.4, CH_3), 1.85 (dt, 1H, *J* 11.2, 13.9, CH_2), 1.94 (ddd, 1H, *J* 1.9, 3.2, 13.9, CH_2), 2.00 (s, 3H, CH_3), 4.69 (m, 1H, CH), 5.22 (m, 1H, CH), 5.31 (tdd, 1H, *J* 1.9, 6.3, 12.5, CH), 5.60 (dd, 1H, *J* 9.5, 15.9, CH), 5.76 (dd, 1H, *J* 8.4, 15.9, CH), 5.83 (dd, 1H, *J* 3.3, 12.6, CH), 5.89 (dd, 1H, *J* 1.8, 12.6, CH); ^{13}C NMR (150 MHz, CD_3OD) δ 21.1, 21.5, 40.7, 69.7, 72.0, 75.2, 122.9, 133.9, 134.0, 137.7, 170.0, 171.7; (+)-QTOF HRMS *m/z*, calculated for $C_{12}H_{16}O_5$ $[M + Na]^+$: 263.0890, found: 263.0899 (mass error: 3.42 ppm).

Modiolide A (**6**)

White, amorphous solid; $[\alpha]_D^{25}$ +38.0 (*c* 0.1, MeOH); ^{1}H NMR (600 MHz, CD_3OD) δ 1.23 (d, 3H, *J* 6.4, CH_3), 1.72 (ddt, 1H, *J* 11.3, 13.4, 14.0, CH_2), 1.88 (ddd, 1H, *J* 1.8, 3.3, 14.0, CH_2), 4.13 (ddd, 1H, *J* 3.3, 8.8, 11.3, CH), 4.69 (ddd, 1H, *J* 1.7, 3.2, 8.0, CH), 5.26 (dqd, 1H, *J* 1.8, 6.4, 13.4, CH), 5.56 (dd, 1H, *J* 8.8, 15.9, CH), 5.63 (dd, 1H, *J* 8.0, 15.9, CH), 5.83 (dd, 1H, *J* 3.2, 12.5, CH), 5.88 (dd, 1H, *J* 1.7, 12.5, CH); ^{13}C NMR (150 MHz, CD_3OD) δ 21.6, 43.9, 70.1, 72.2, 72.8, 122.9, 131.0, 137.8, 138.7, 170.2; (+)-QTOF HRMS *m/z*, calculated for $C_{10}H_{14}O4$ $[M + Na]^+$: 221.0784, found: 221.0785 (mass error: 0.45 ppm).

(*R*)-6-Hydroxy-2-methyl-4-chromanone (**7**)

White, amorphous solid; UV (MeOH) λ_{max} / nm 228.0, 255.9, 355.4; ^{1}H NMR (600 MHz, CD_3OD) δ 1.46 (d, 3H, *J* 6.3, CH_3), 2.63 (d, 2H, *J* 4.3, CH_2), 4.51 (qt, 1H, *J* 4.3, 6.3, CH), 6.85 (d, 1H, *J* 8.9, CH), 7.01 (dd, 1H, *J* 3.1, 8.9, CH), 7.16 (d, 1H, *J* 3.1, CH); ^{13}C NMR (150 MHz, CD_3OD) δ 21.2, 45.4, 75.7, 111.2, 120.0, 122.0, 125.8, 152.7, 157.1, 195.1; (+)-QTOF HRMS *m/z*, calculated for $C_{10}H_{10}O_3$ $[M + Na]^+$: 179.0703, found: 179.0706 (mass error: 1.67 ppm).

Table S1. IC_{50} values of compounds **1-7** against three tumor cell lines

Compound	IC_{50} ± SD / (μg mL^{-1})		
	LM3	LP07	MCF-7
1	78.43 ± 12.45	> 125	64.42 ± 6.02
2	36.83 ± 4.86	80.78 ± 5.06	54.37 ± 6.05
3	58.37 ± 6.40	91.09 ± 4.38	33.95 ± 3.62
4	76.84 ± 13.43	> 125	70.22 ± 3.47
5	66.69 ± 2.63	> 125	88.05 ± 3.61
6	292.40 ± 7.08	> 125	61.41 ± 6.62
7	101.54 ± 15.38	> 125	68.54 ± 5.29
Doxorubicin	0.012 ± 0.0010	0.037 ± 0.0031	0.04 ± 0.003

IC_{50}: half-maximal inhibitory concentration; SD: standard deviation.

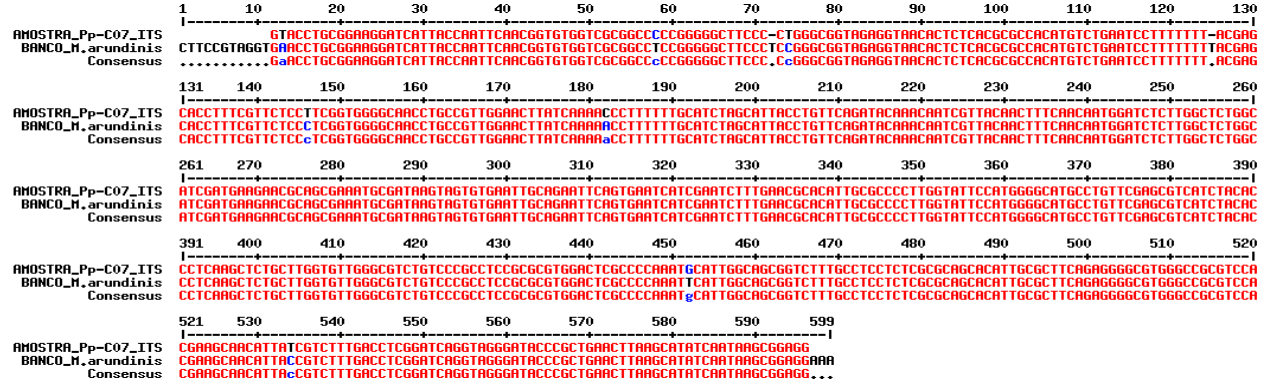

Figure S1. Alignment of the target strain (C-07) with database in the internal transcribed spacer (ITS) region, resulting in the identification of the endophyte *M. arundinis*.

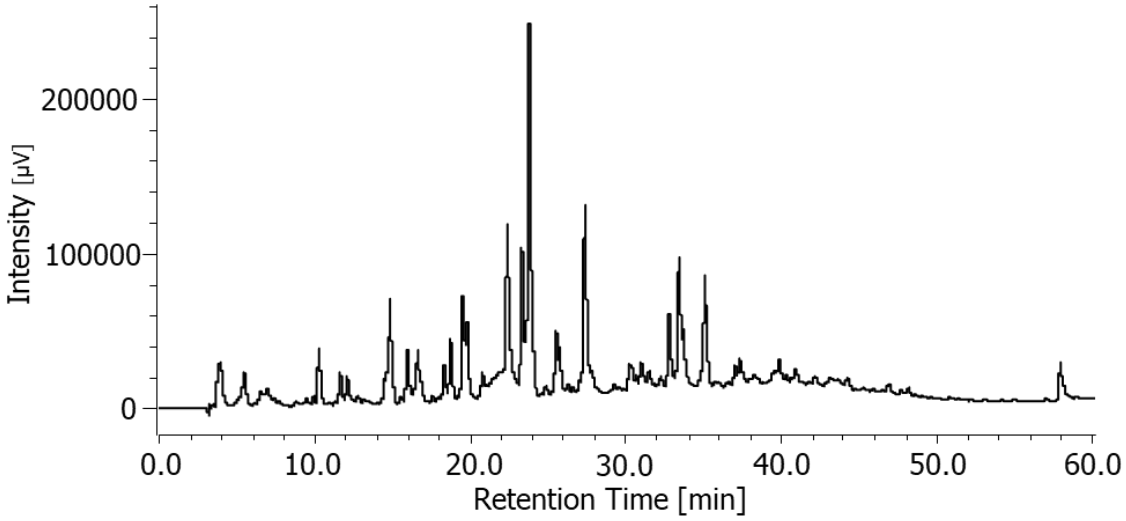

Figure S2. Chromatographic profile of the extract cultivated in potato dextrose broth.

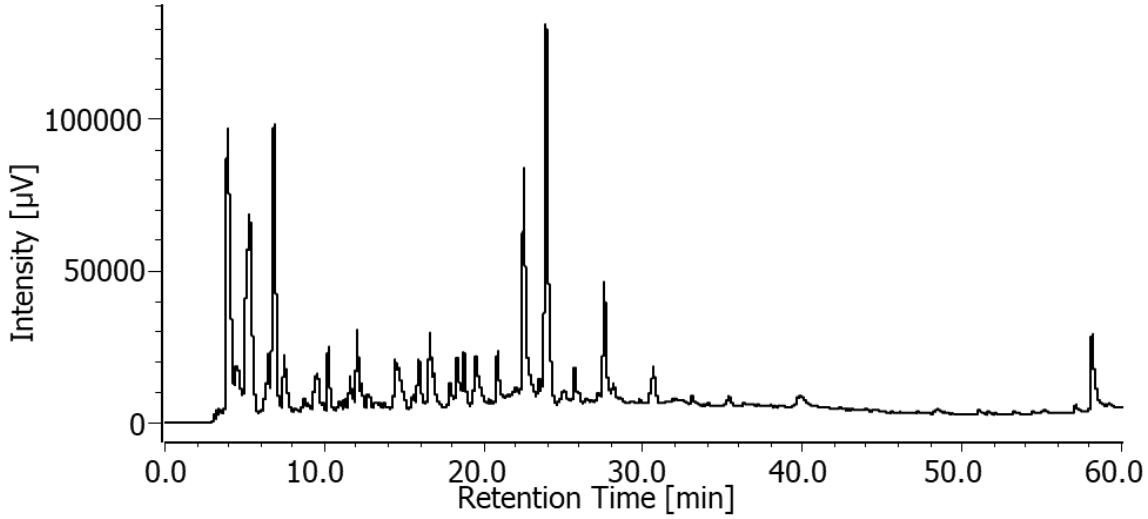

Figure S3. Chromatographic profile of the extract cultivated in yeast malt (YM) broth.

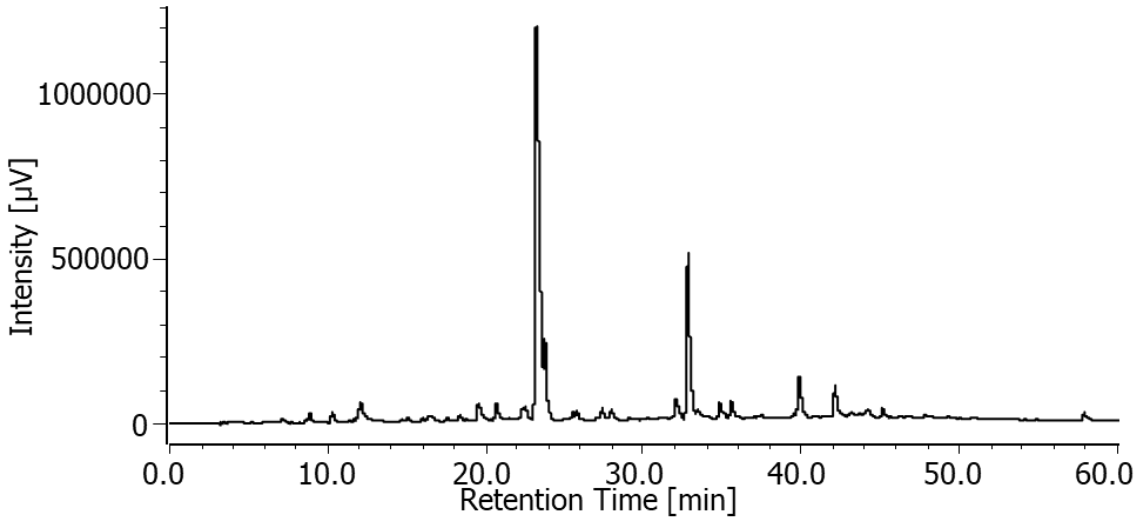

Figure S4. Chromatographic profile of the extract cultivated in malt extract.

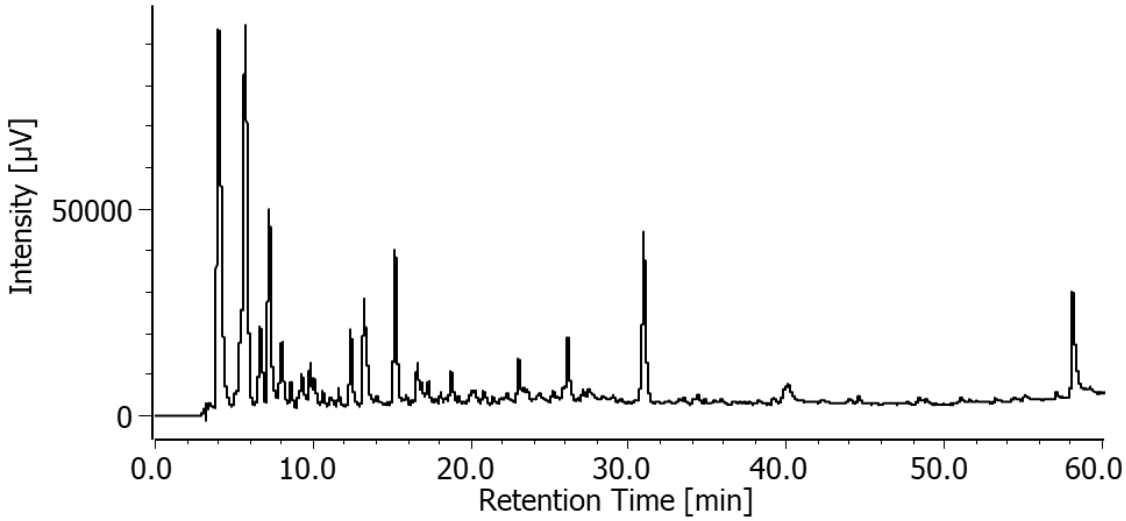

Figure S5. Chromatographic profile of the extract cultivated in nutrient broth.

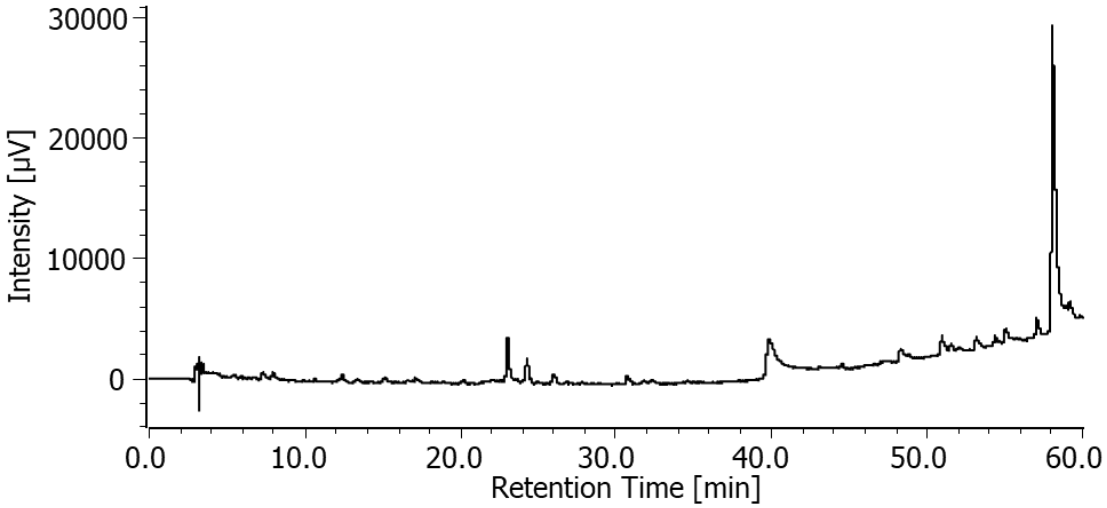

Figure S6. Chromatographic profile of the extract cultivated in Czapek-Dox broth.

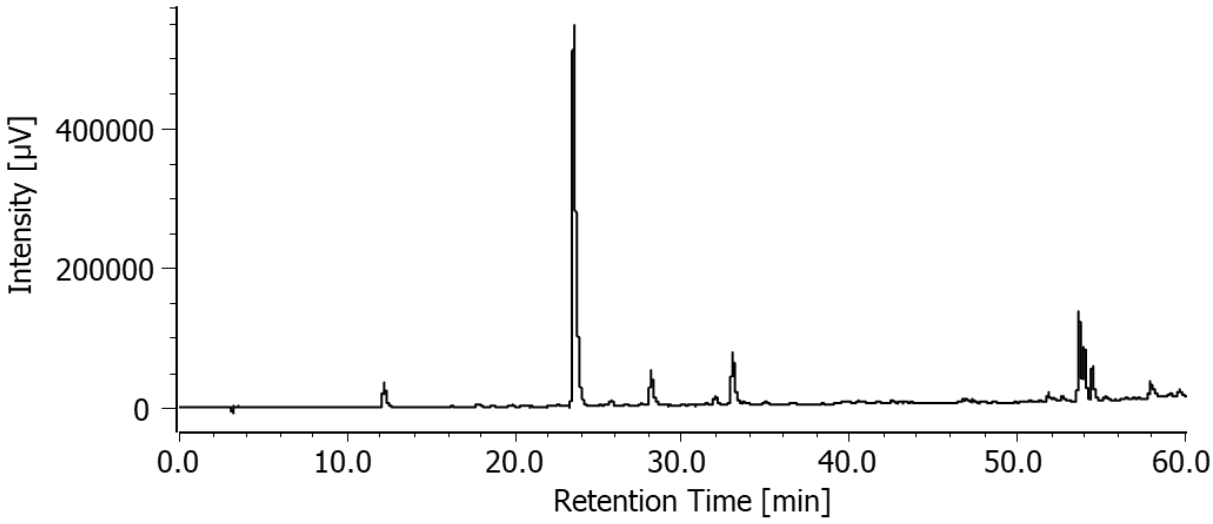

Figure S7. Chromatographic profile of the extract cultivated in parboiled rice.

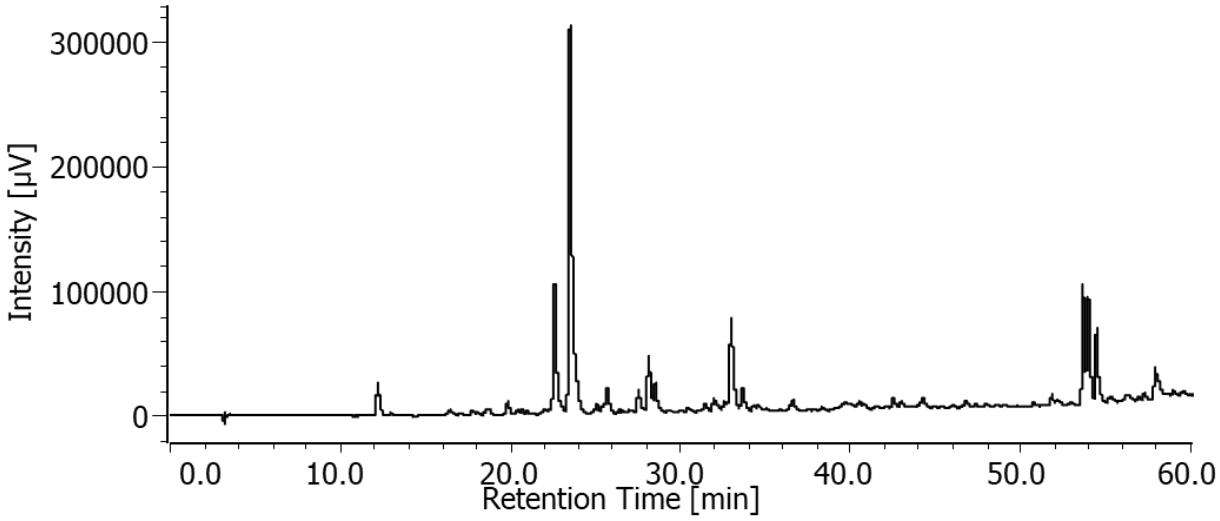

Figure S8. Chromatographic profile of the extract cultivated in corn.

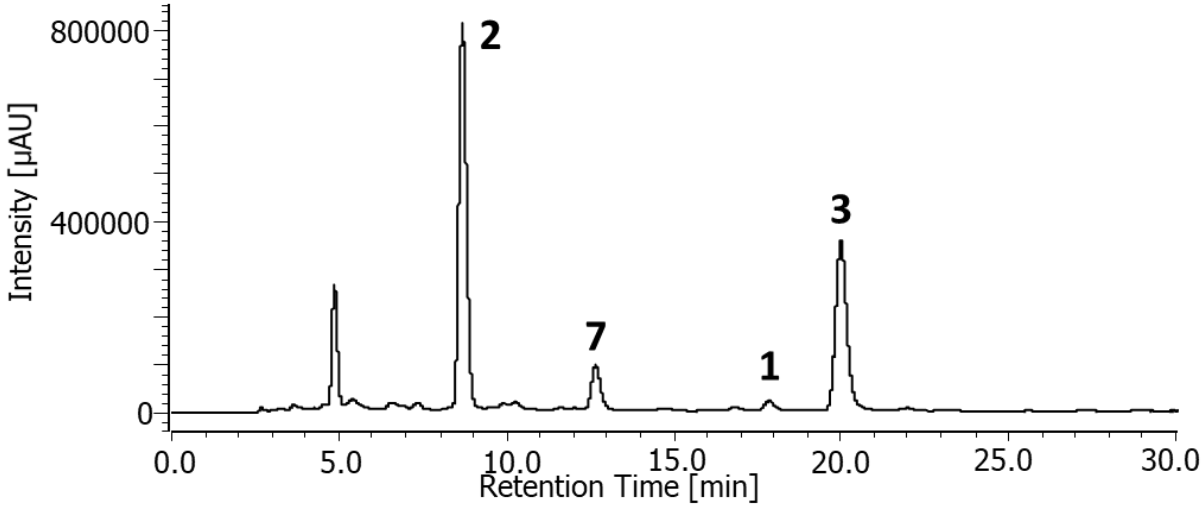

Figure S9. Chromatogram of rice extract after optimization used for the purification of compounds **1**-**3** and **7** using high performance liquid chromatography coupled to a photodiode array detector (HPLC-PDA).

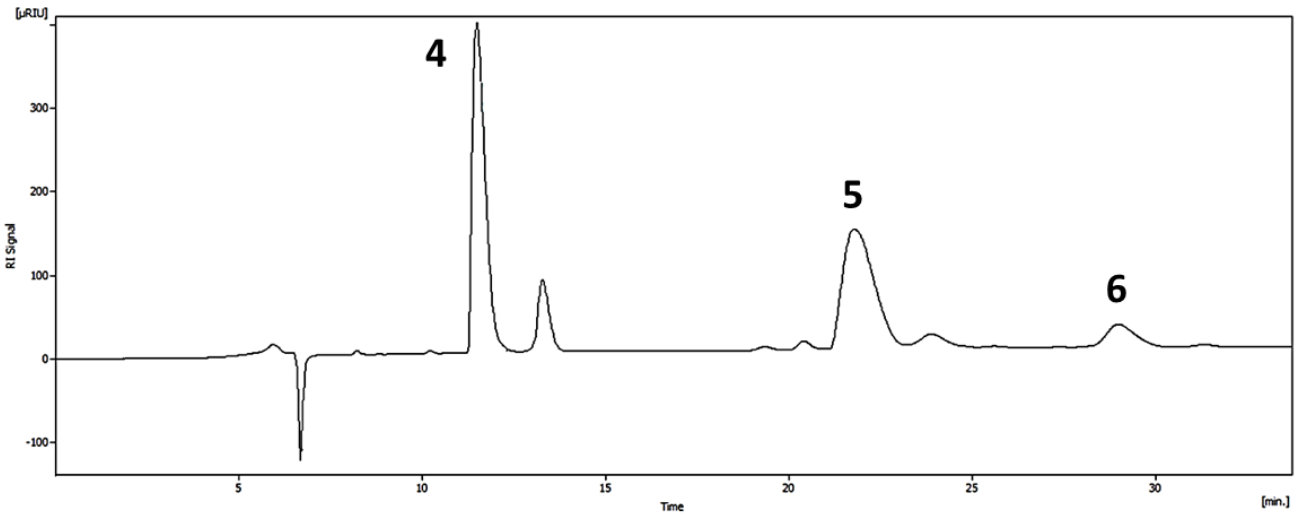

Figure S10. Chromatogram of rice extract optimized for the purification of compounds **4**-**6** using high performance liquid chromatography coupled to a refractive index detector (HPLC-RI).

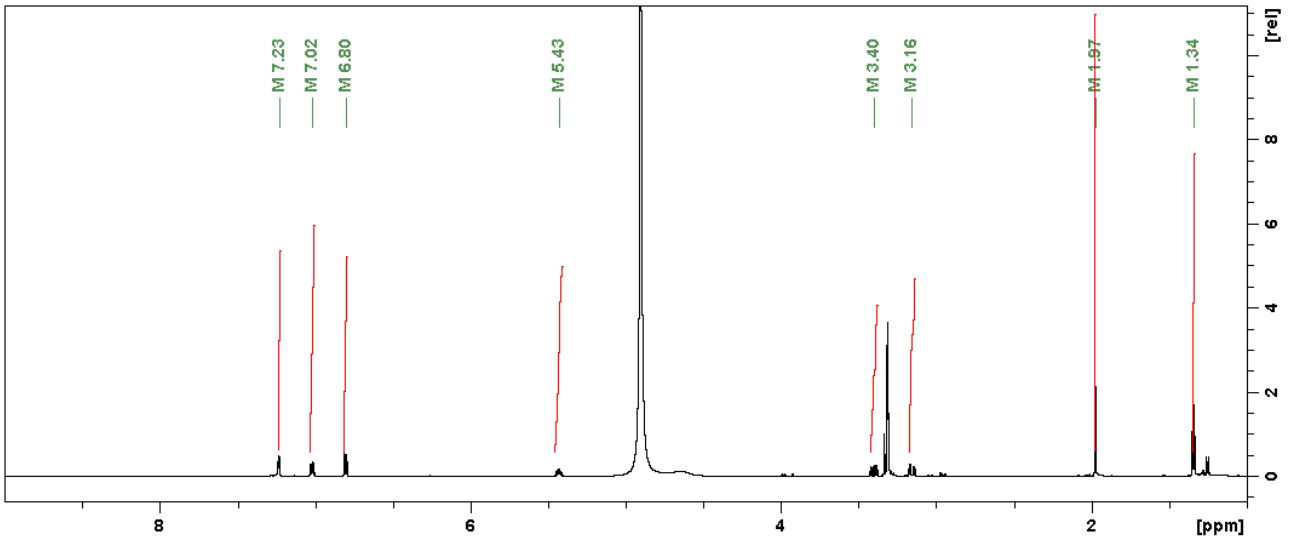

Figure S11. ^{1}H nuclear magnetic resonance (NMR) spectrum (600 MHz, CD_3OD) of the new compound **1**.

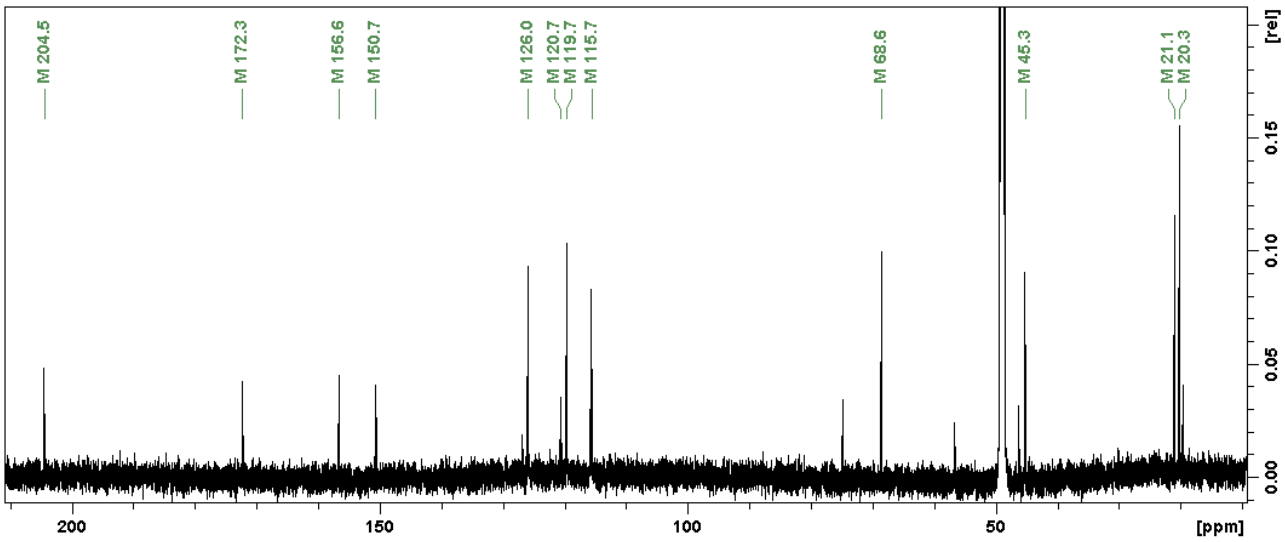

Figure S12. ^{13}C NMR spectrum (150 MHz, CD_3OD) of the new compound **1**.

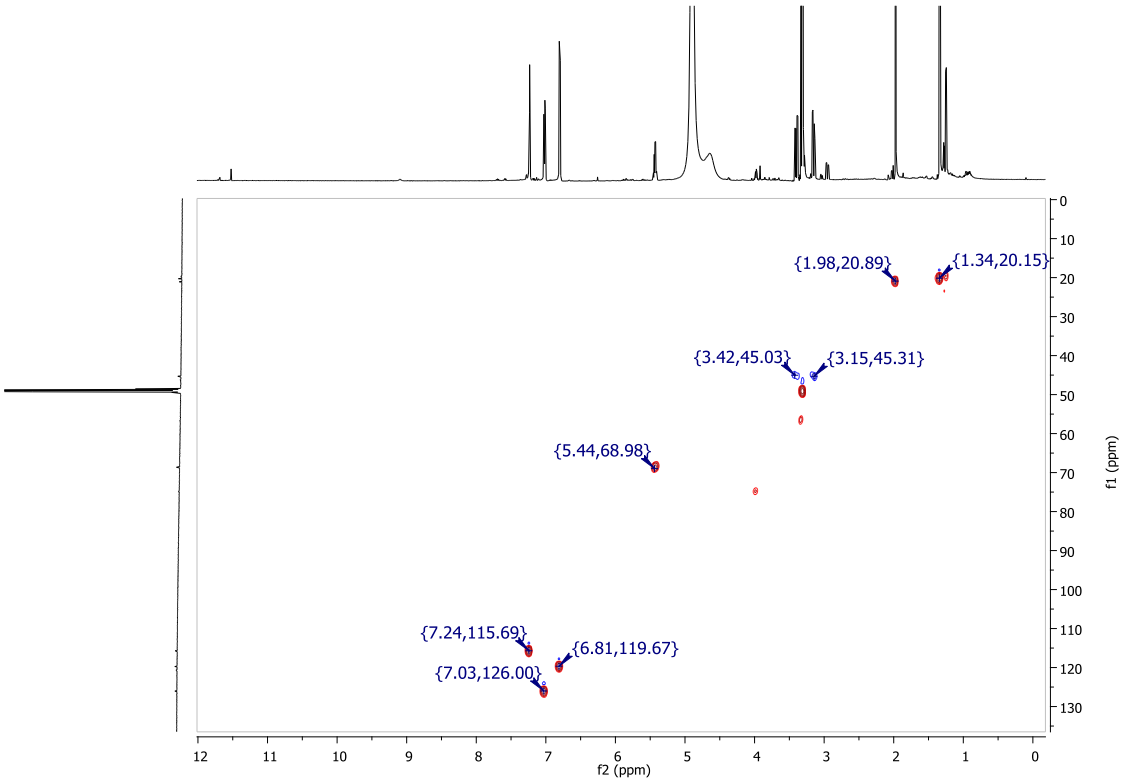

Figure S13. Heteronuclear single-quantum correlation (HSQC) spectrum (CD_3OD) of the new compound **1**.

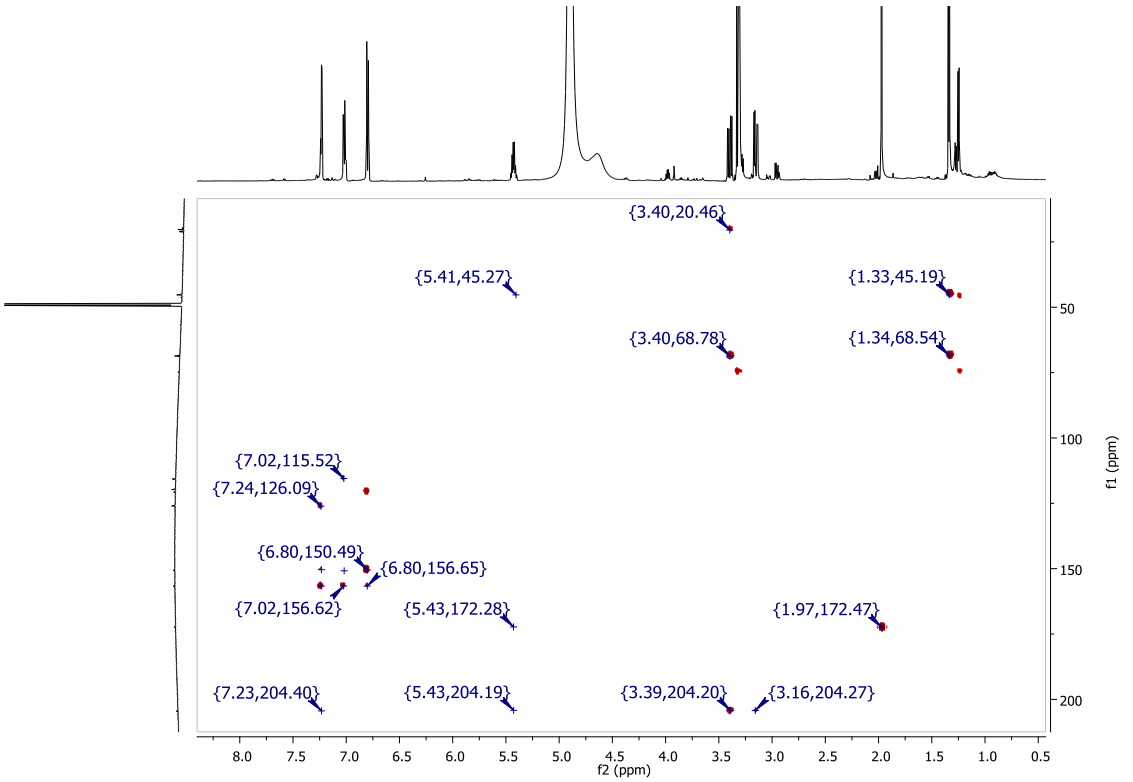

Figure S14. Heteronuclear multiple bond correlation (HMBC) spectrum (CD_3OD) of the new compound **1**.

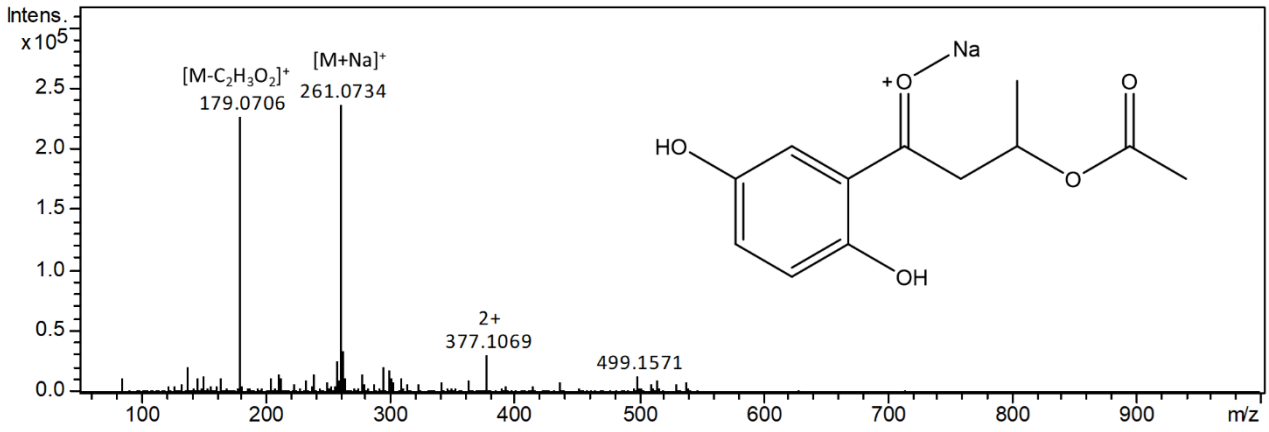

Figure S15. High resolution mass spectrometry (HRMS) spectrum of the new compound **1**.

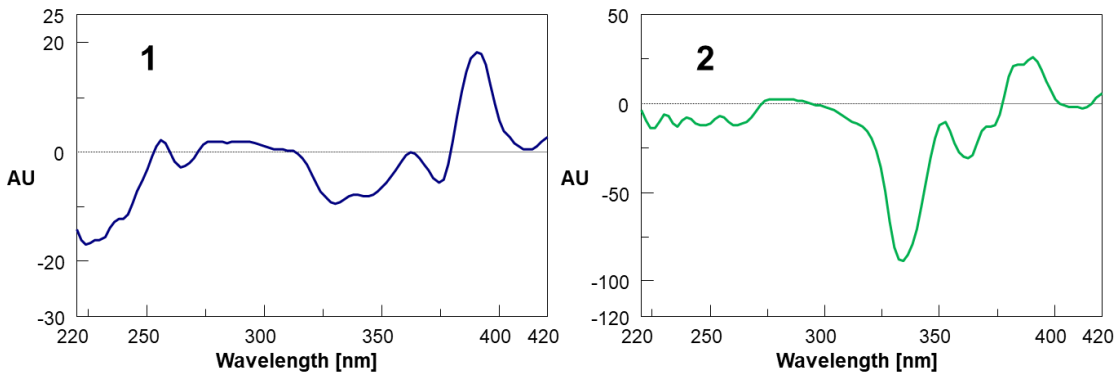

Figure S16. Comparison of the electronic circular dichroism (ECD) spectrum (CH_3OH) for compounds **1** and **2**.

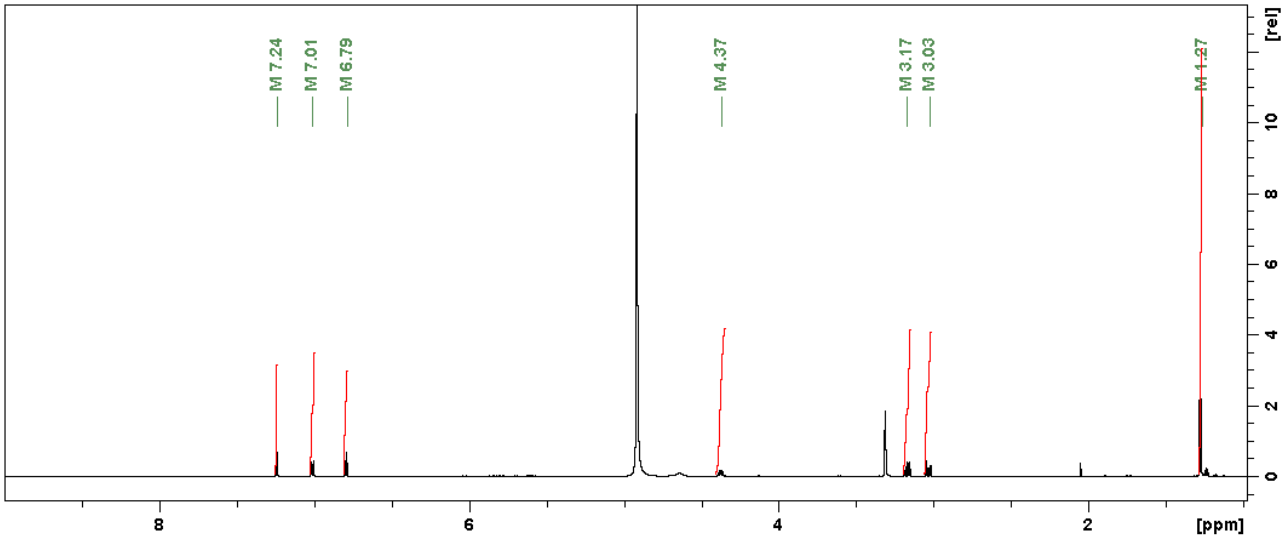

Figure S17. ^{1}H NMR spectrum (600 MHz, CD_3OD) of compound **2**.

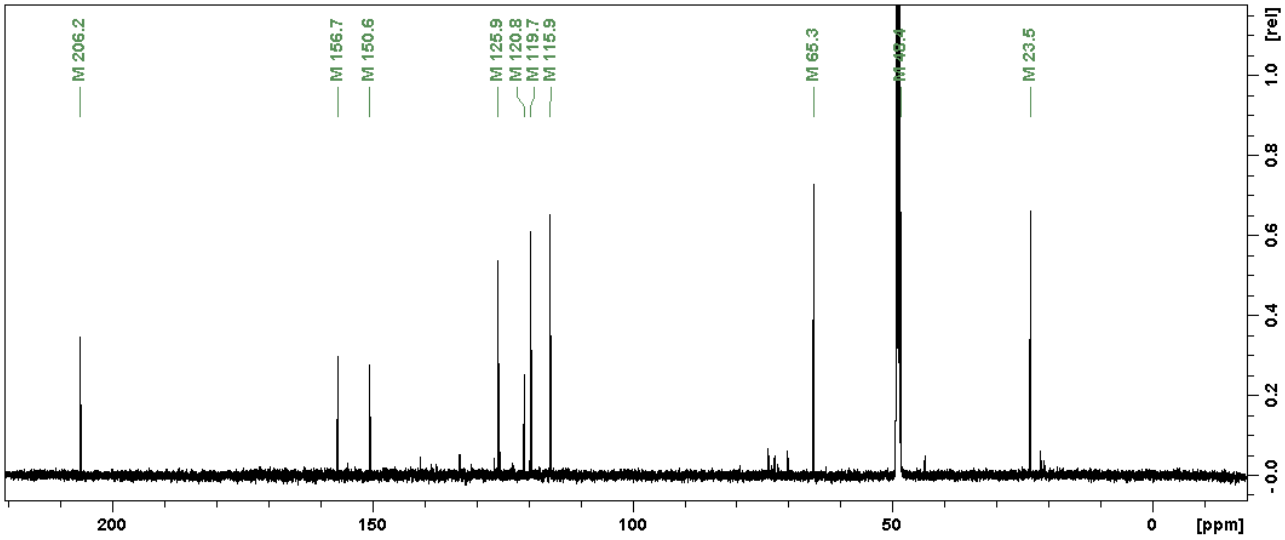

Figure S18. ^{13}C NMR spectrum (150 MHz, CD_3OD) of compound **2**.

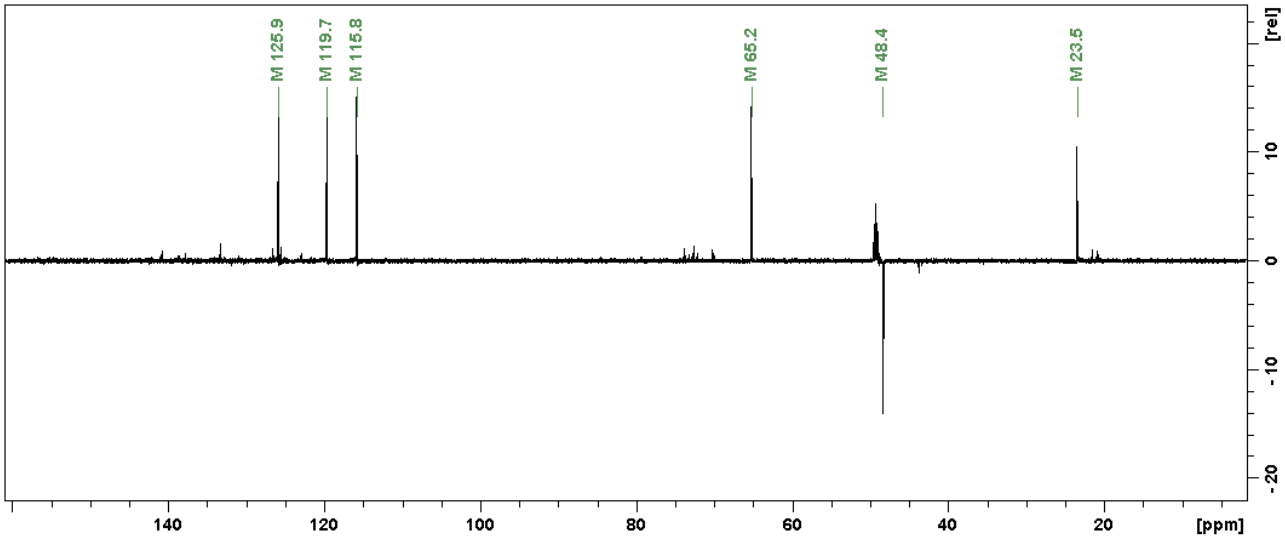

Figure S19. Distortionless enhancement by polarization (DEPT-135) NMR spectrum (150 MHz, CD_3OD) of compound **2**.

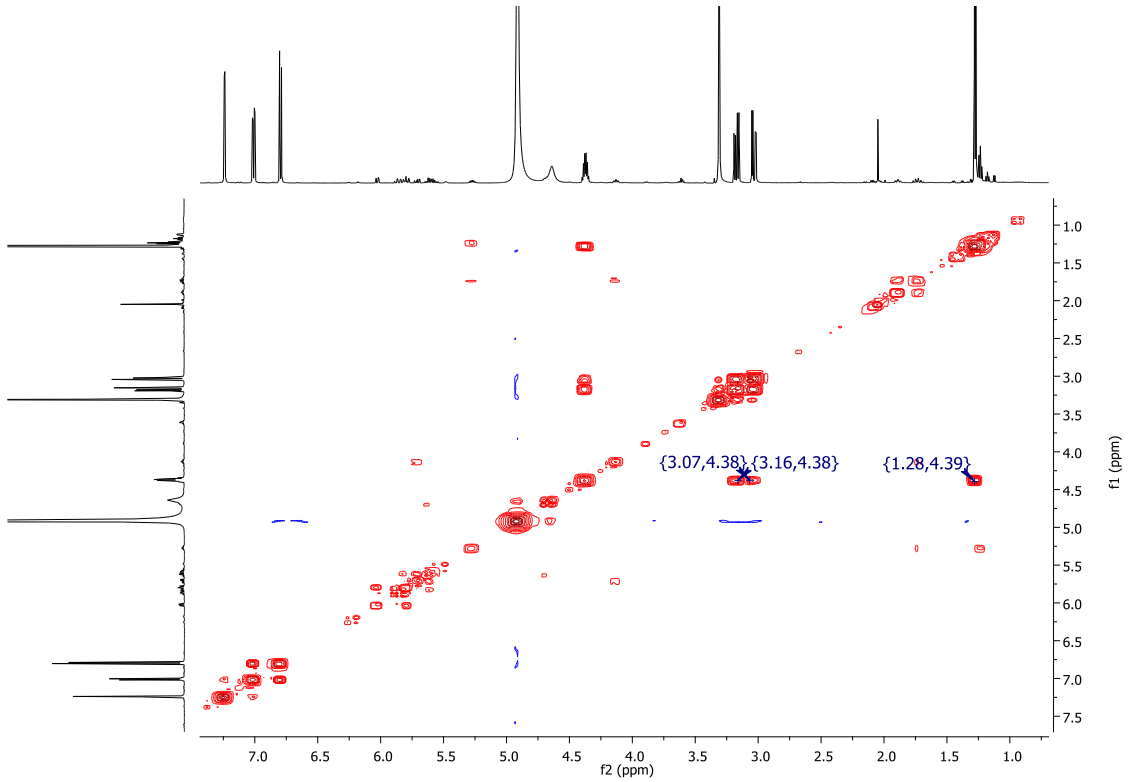

Figure S20. Correlation spectroscopy (COSY) spectrum (600 MHz, CD_3OD) of compound **2**.

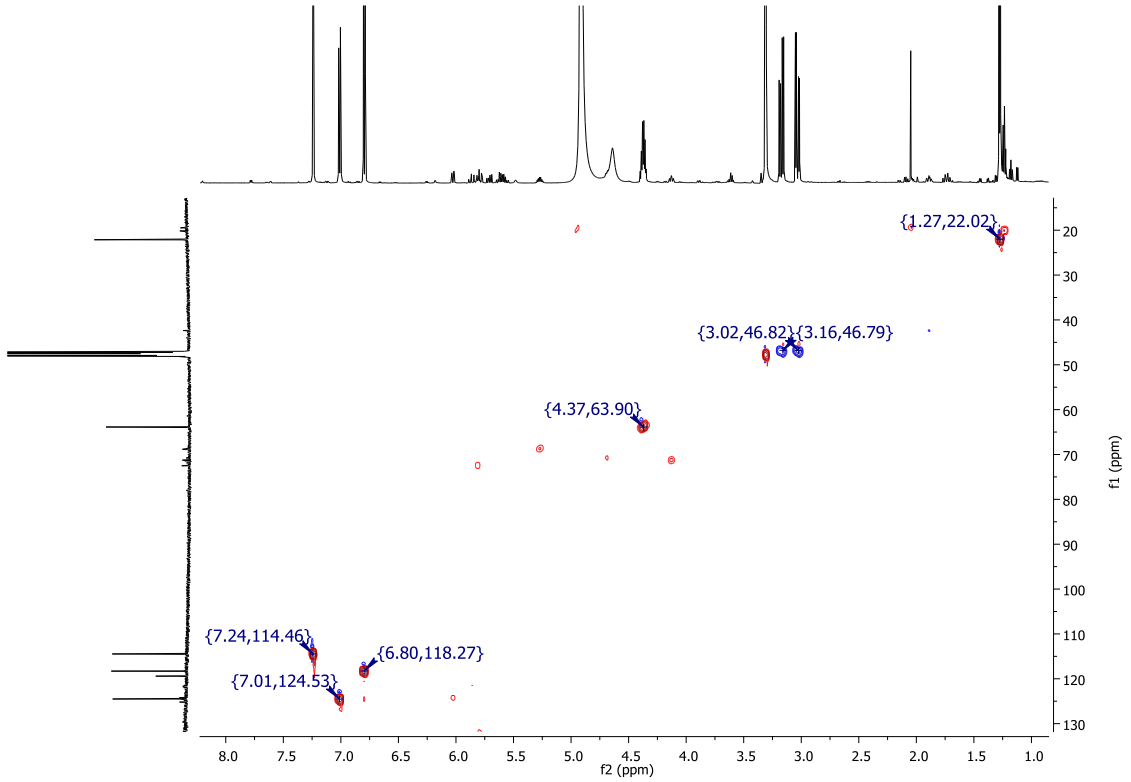

Figure S21. HSQC spectrum (CD_3OD) of compound **2**.

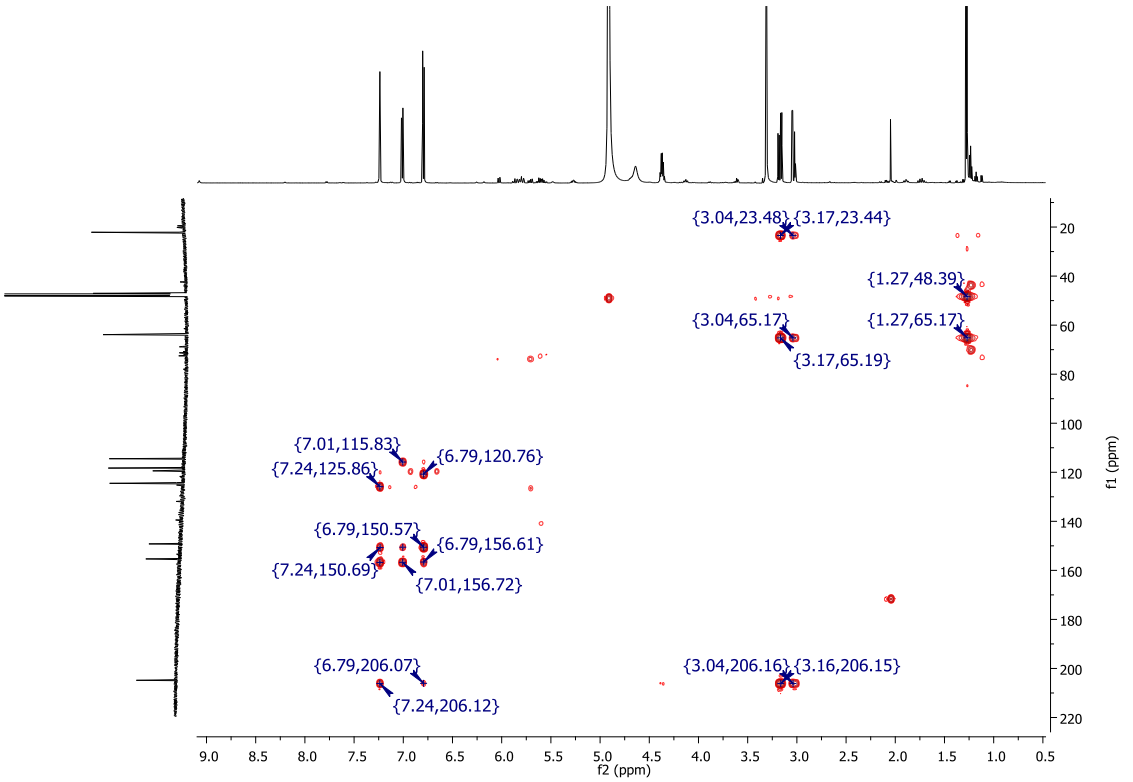

Figure S22. HMBC spectrum (CD_3OD) of compound **2**.

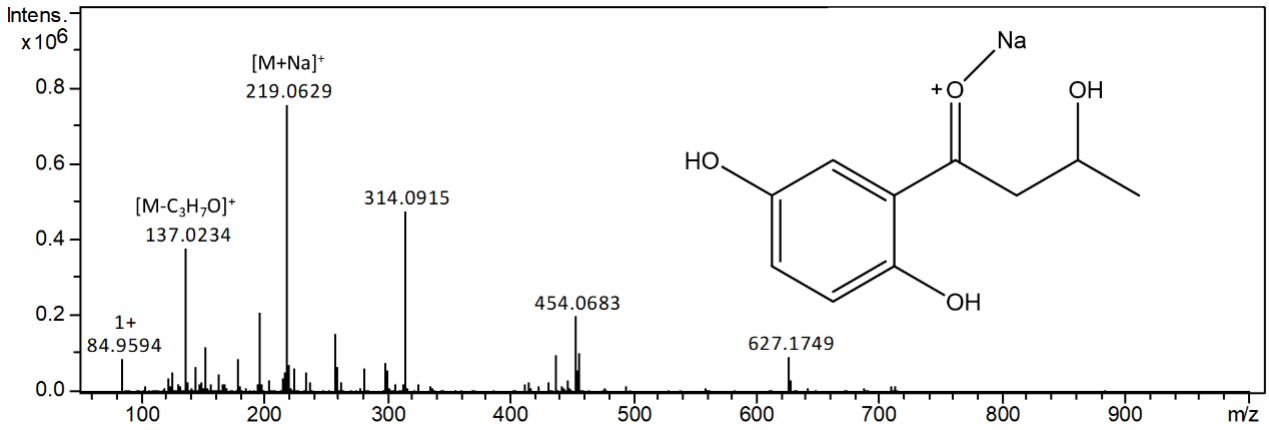

Figure S23. HRMS spectrum of compound **2**.

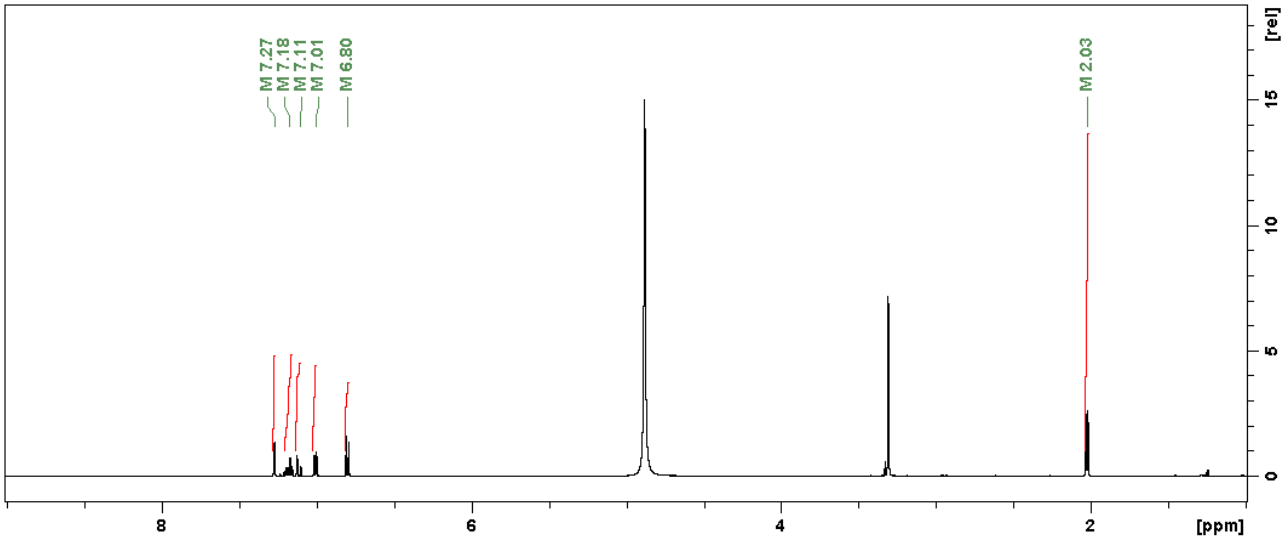

Figure S24. ^{1}H NMR spectrum (600 MHz, CD_3OD) of compound **3**.

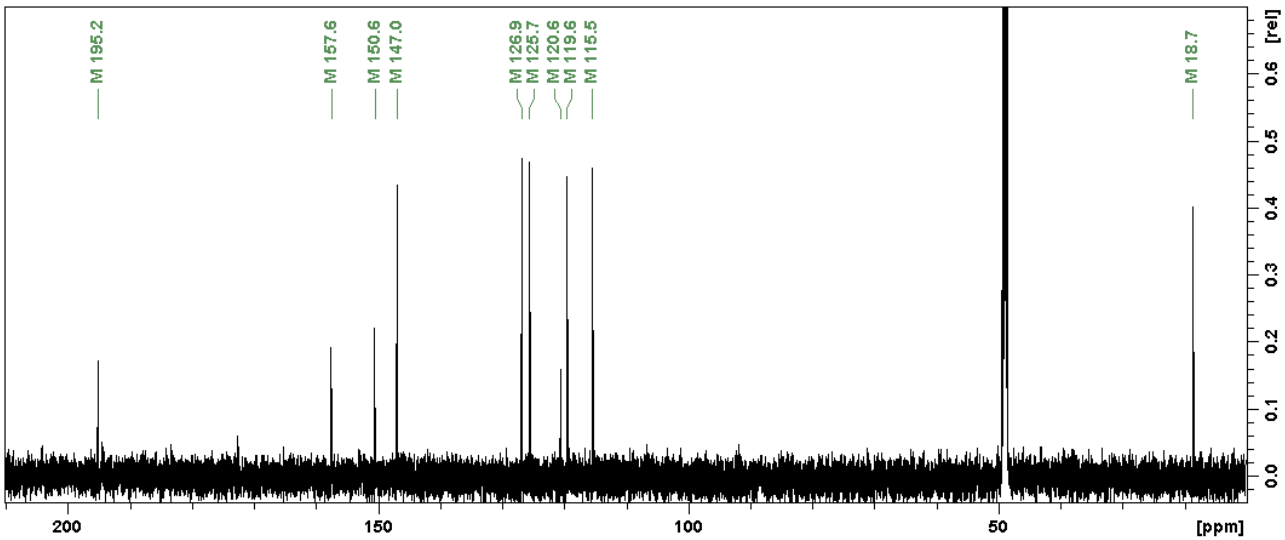

Figure S25. ^{13}C NMR spectrum (150 MHz, CD_3OD) of compound **3**.

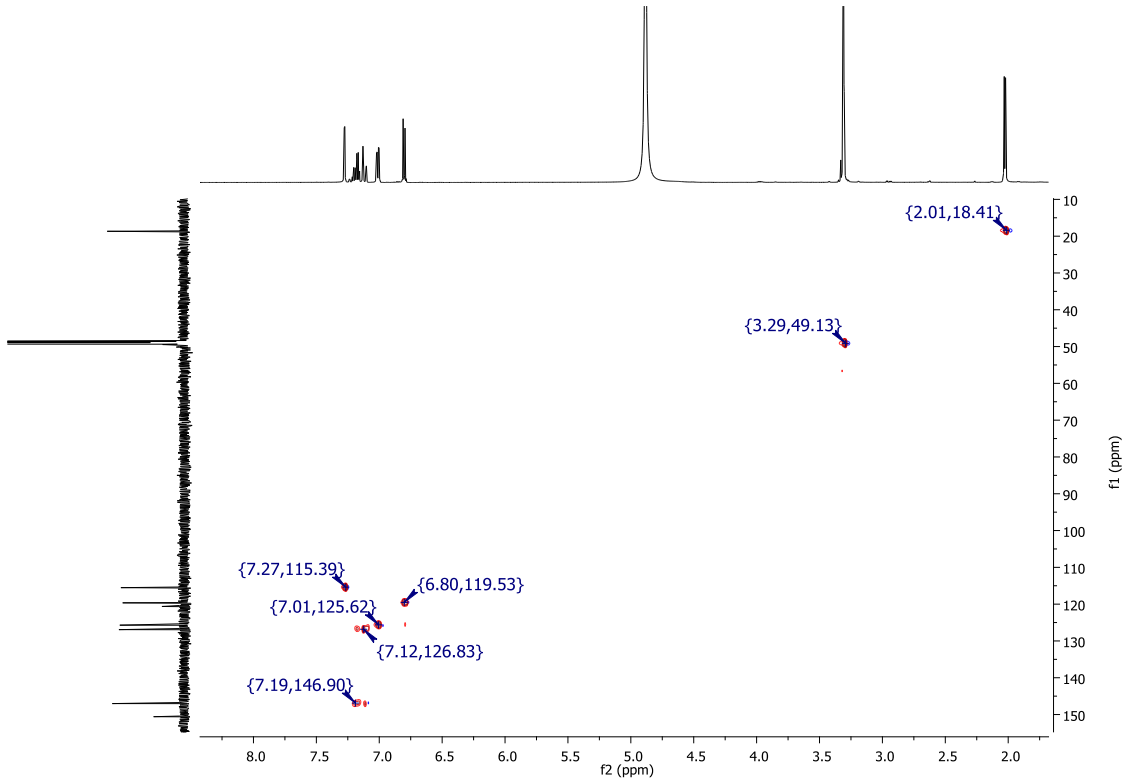

Figure S26. HSQC spectrum (CD_3OD) of compound **3**.

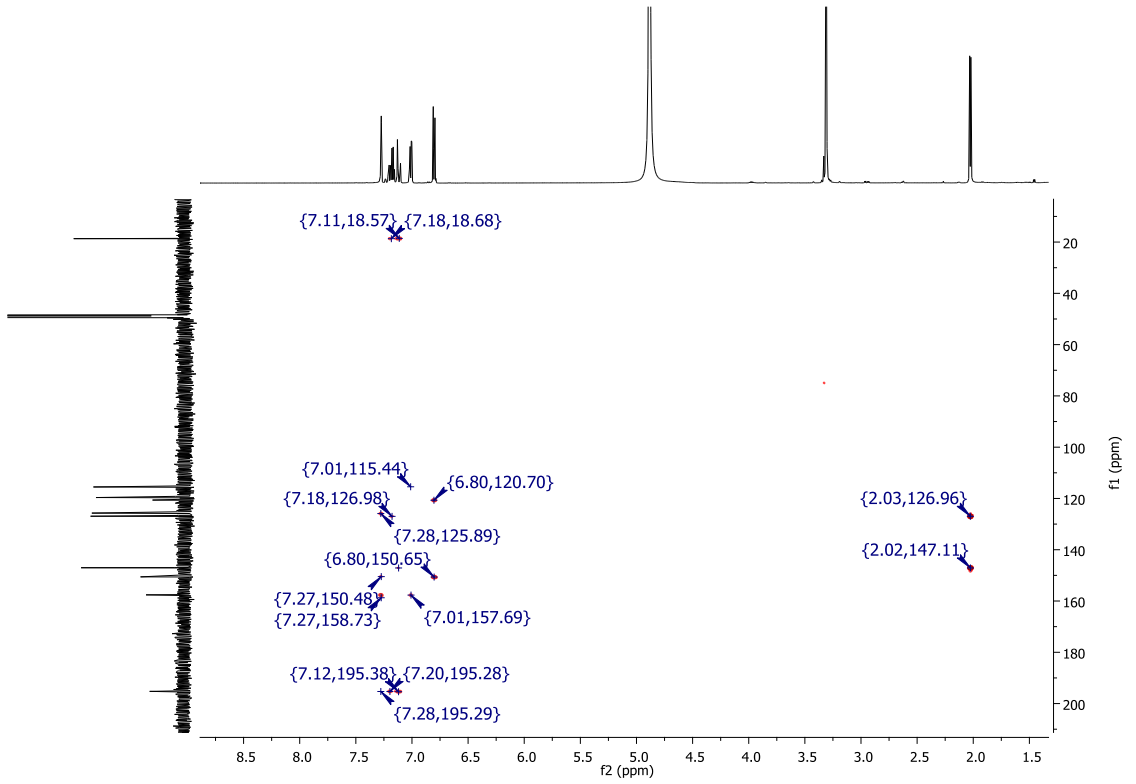

Figure S27. HMBC spectrum (CD_3OD) of compound **3**.

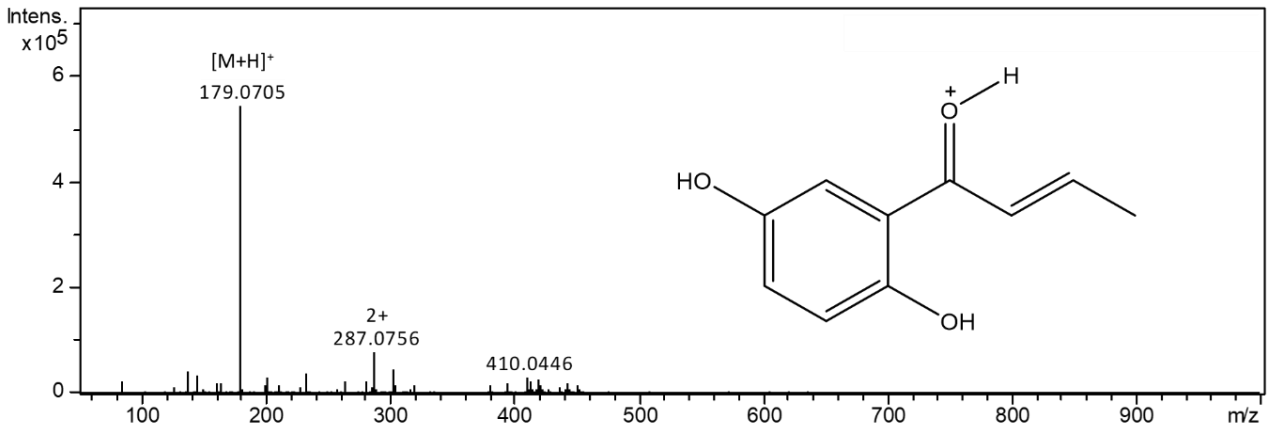

Figure S28. HRMS spectrum of compound **3**.

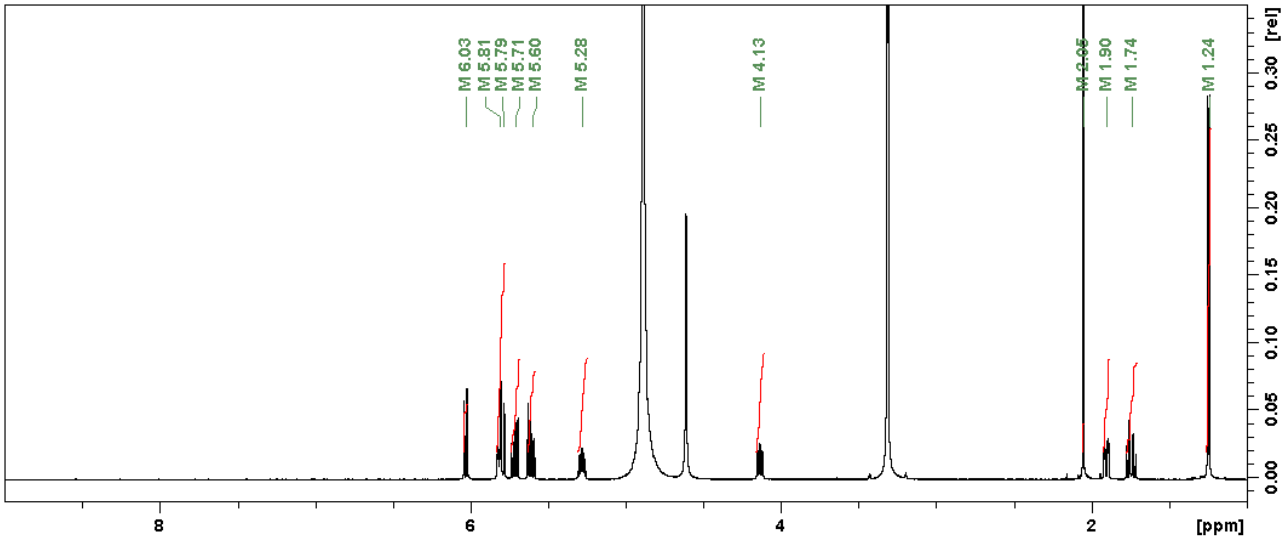

Figure S29. ^{1}H NMR spectrum (600 MHz, CD_3OD) of compound **4**.

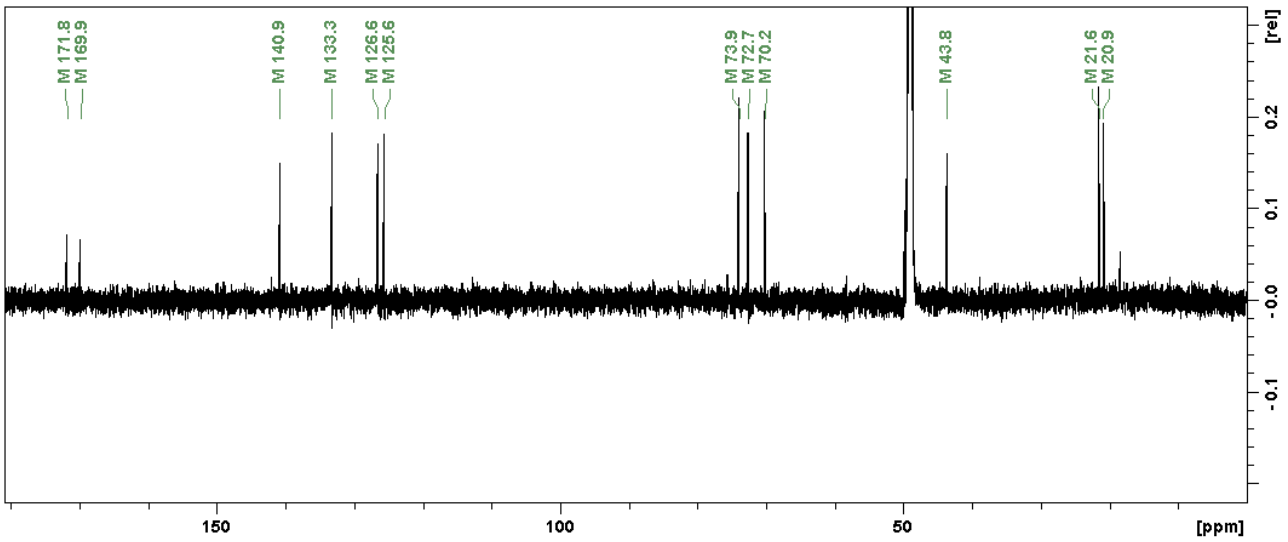

Figure S30. ^{13}C NMR spectrum (150 MHz, CD_3OD) of compound **4**.

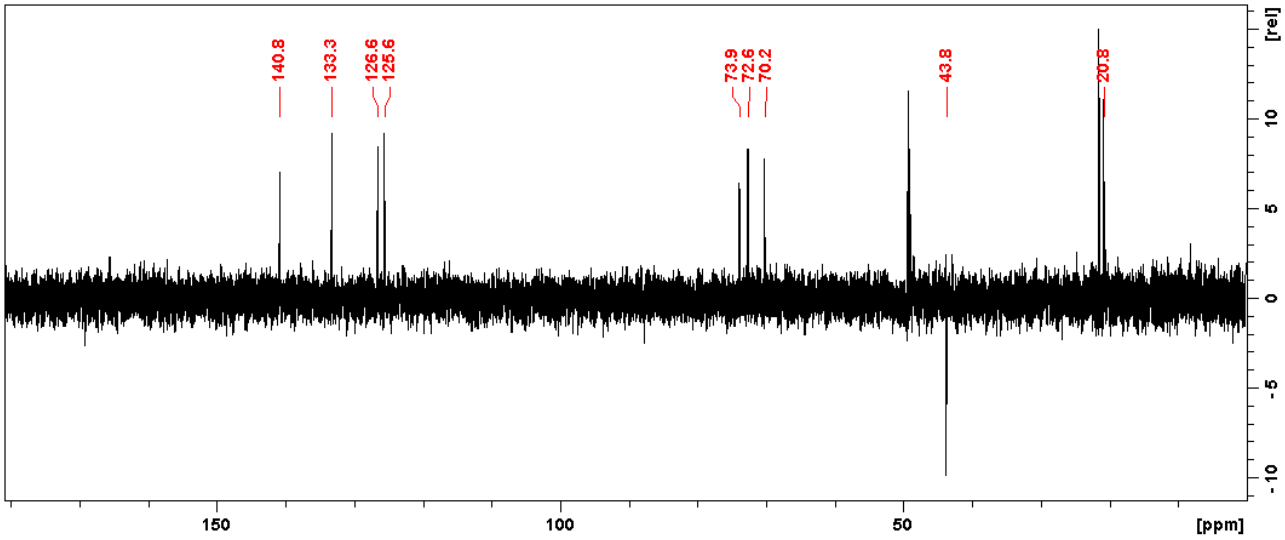

Figure S31. DEPT-135 NMR spectrum (150 MHz, CD_3OD) of compound **4**.

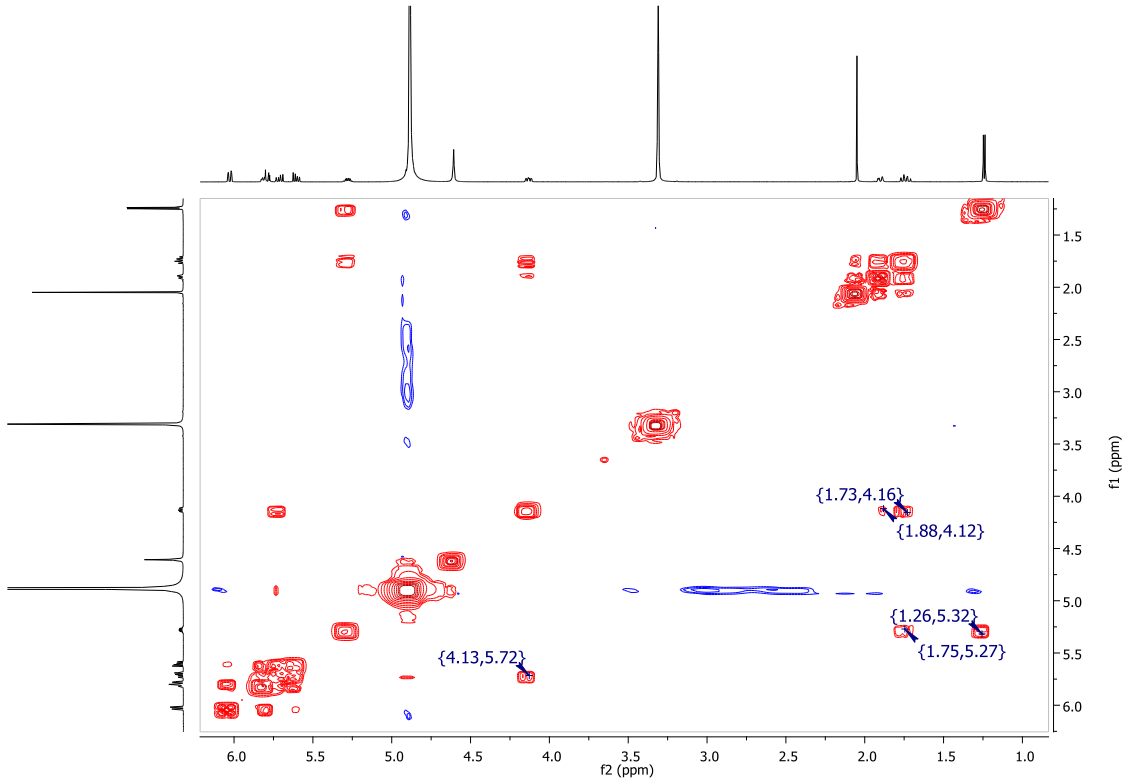

Figure S32. COSY spectrum (600 MHz, CD_3OD) of compound **4**.

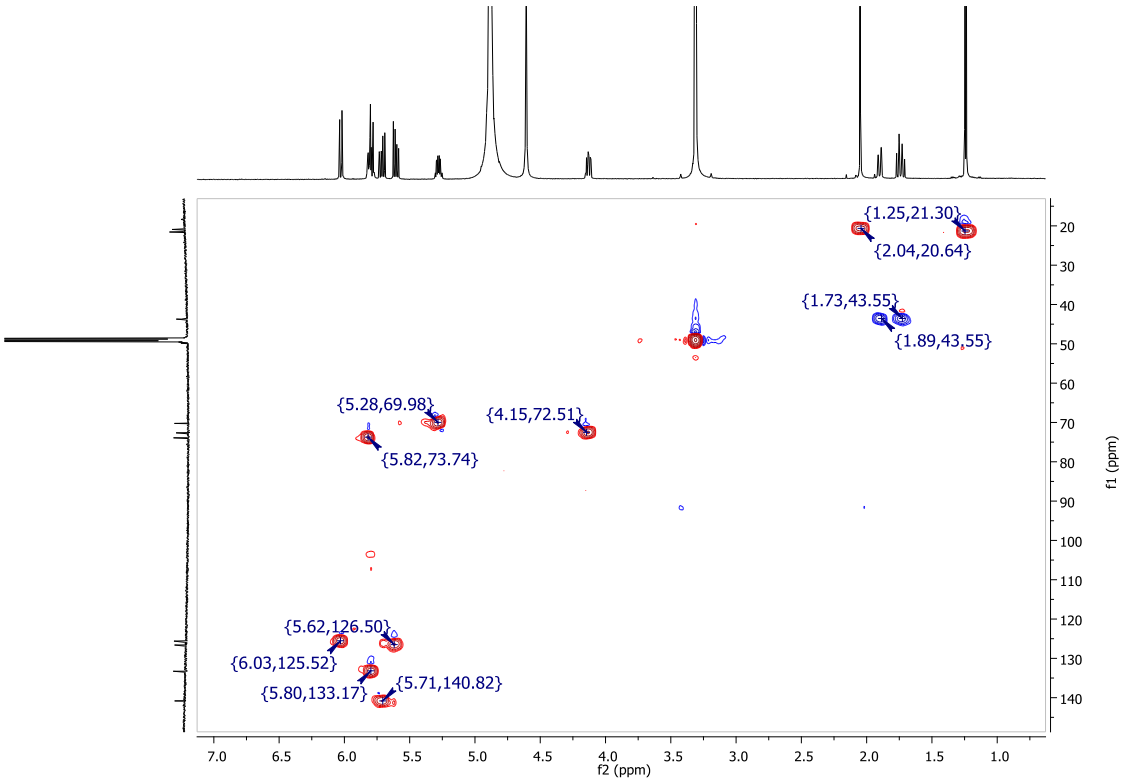

Figure S33. HSQC spectrum (CD_3OD) of compound **4**.

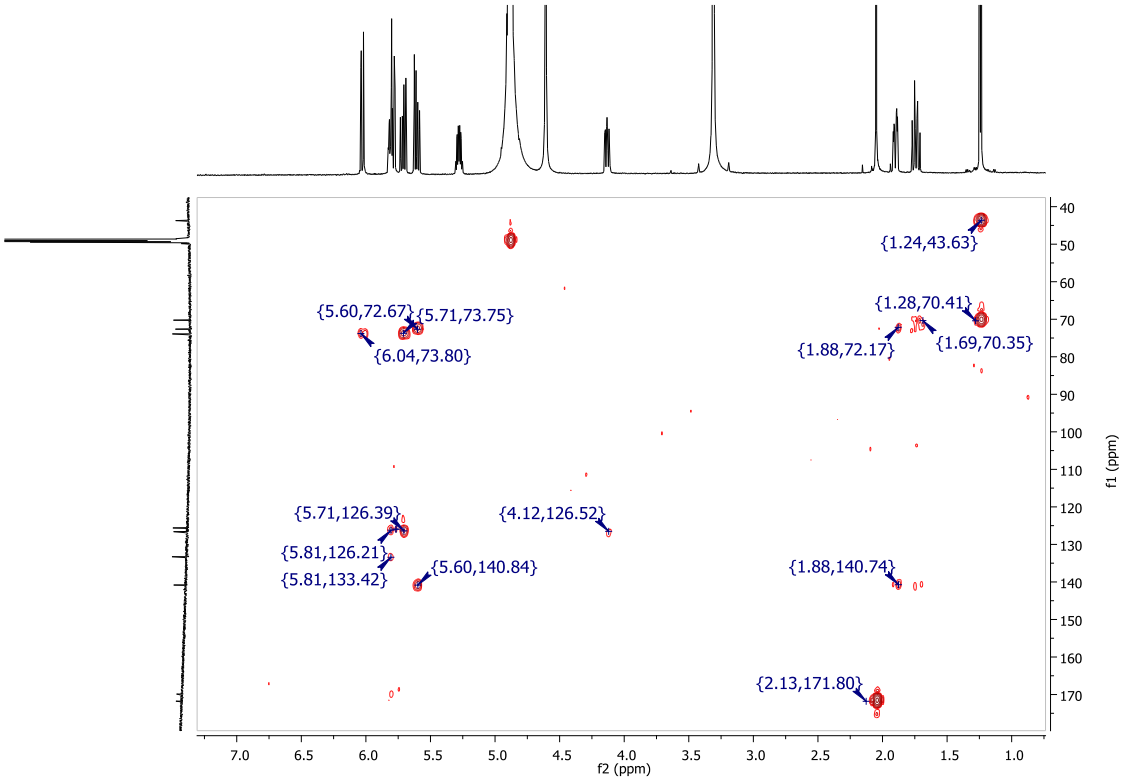

Figure S34. HMBC spectrum (CD_3OD) of compound **4**.

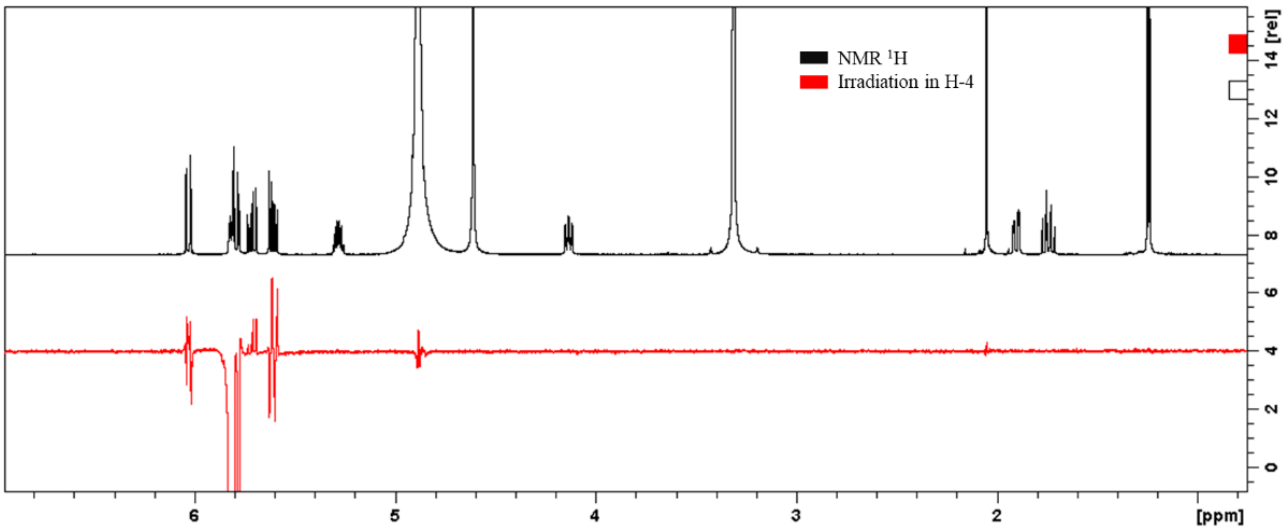

Figure S35. Nuclear Overhauser effect spectroscopy (NOESY) 1D spectrum of H-4 (δ_H 5.81, CD_3OD) for compound **4**.

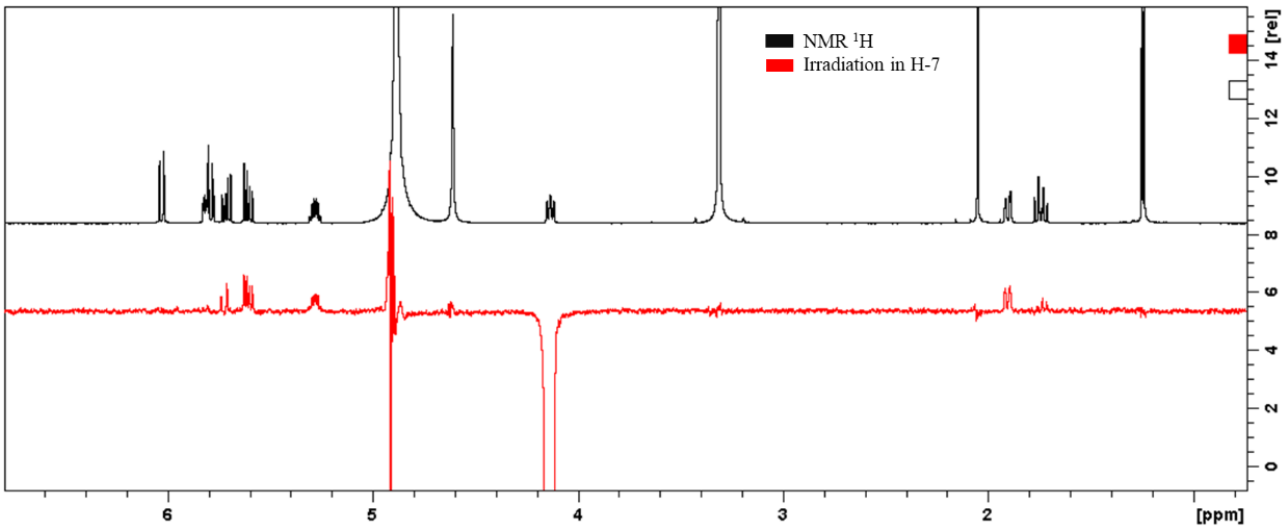

Figure S36. NOESY 1D spectrum of H-7 (δ_H 4.13, CD_3OD) for compound **4**.

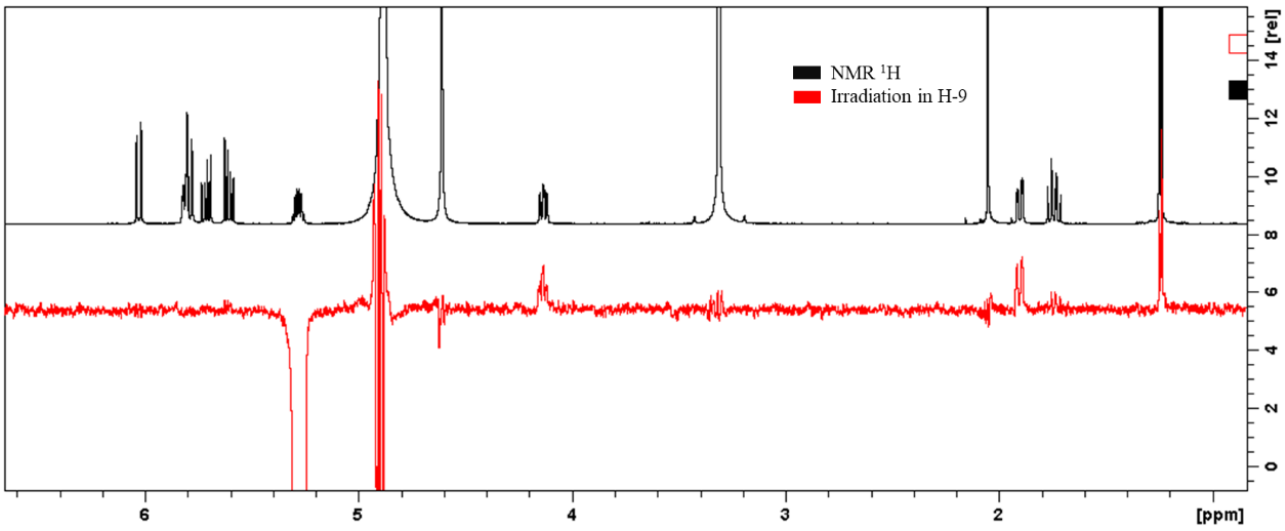

Figure S37. NOESY 1D spectrum of H-9 (δ_H 5.28, CD_3OD) for compound **4**.

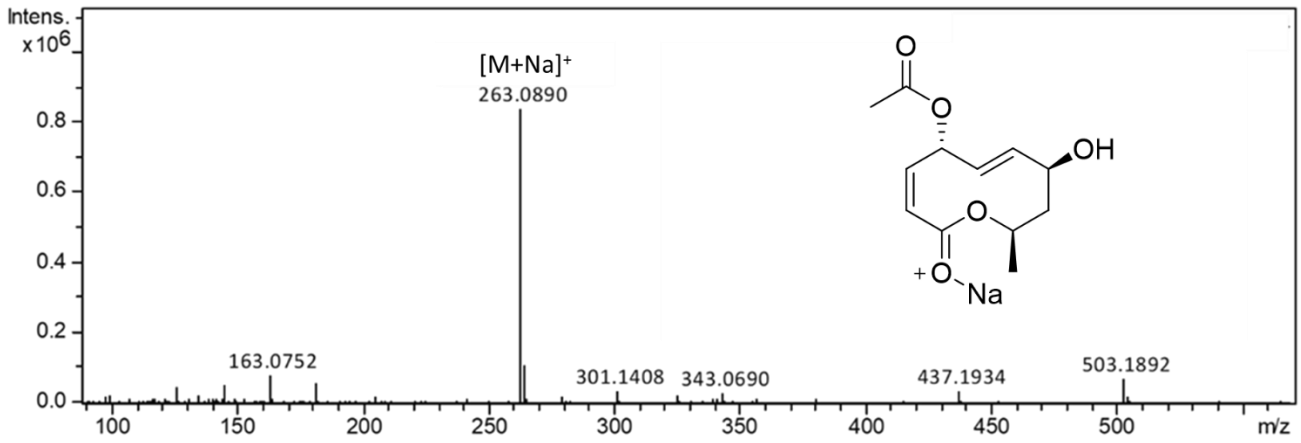

Figure S38. HRMS spectrum of compound **4**.

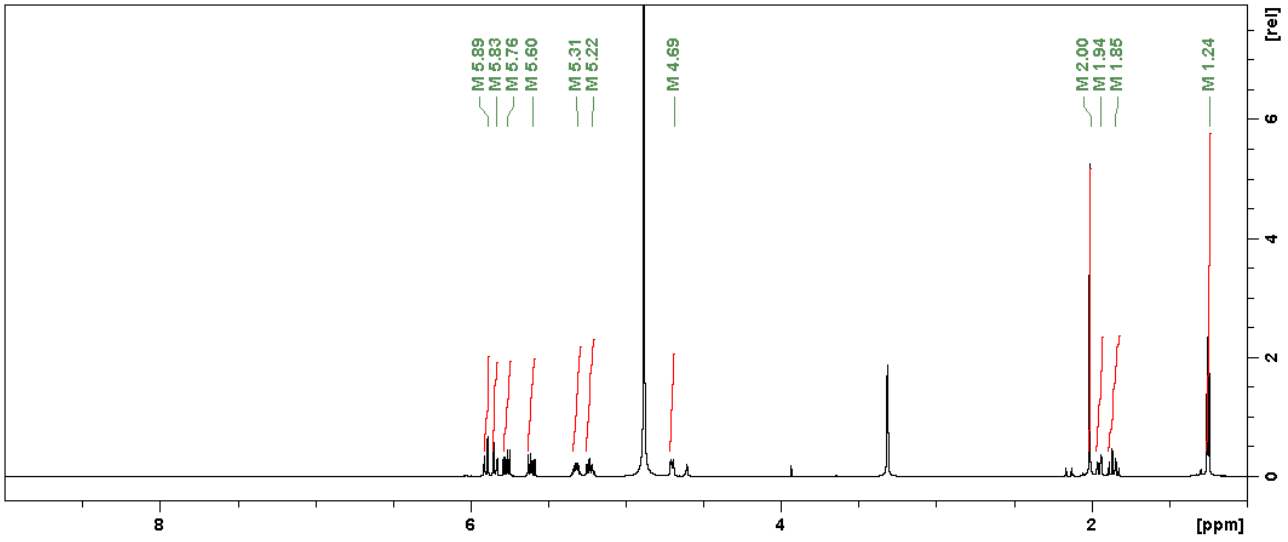

Figure S39. ^{1}H NMR spectrum (600 MHz, CD_3OD) of compound **5**.

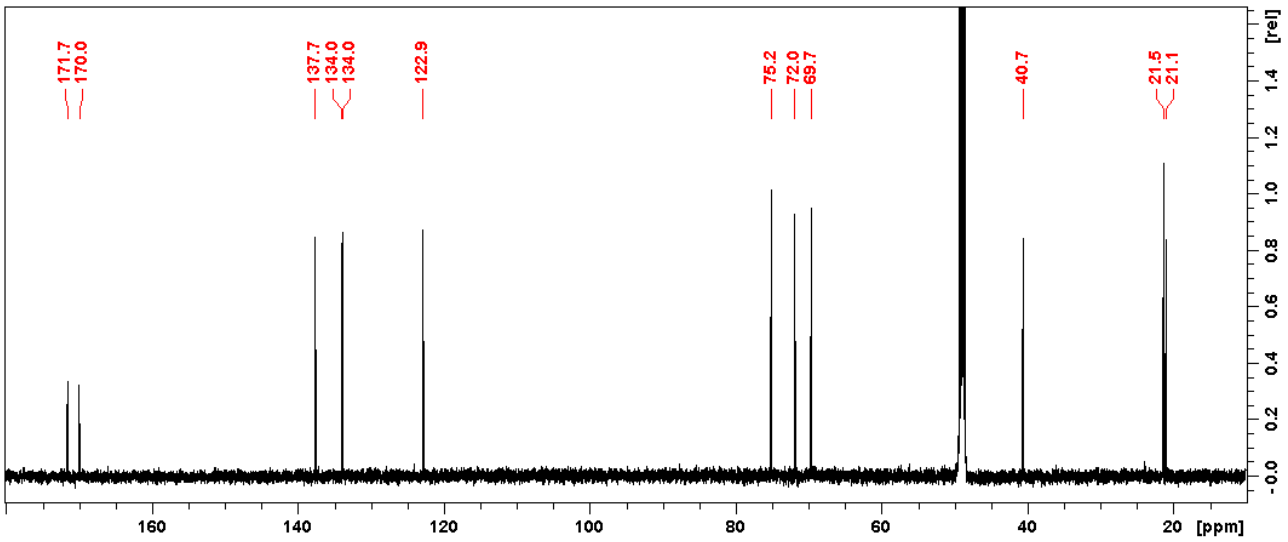

Figure S40. ^{13}C NMR spectrum (150 MHz, CD_3OD) of compound **5**.

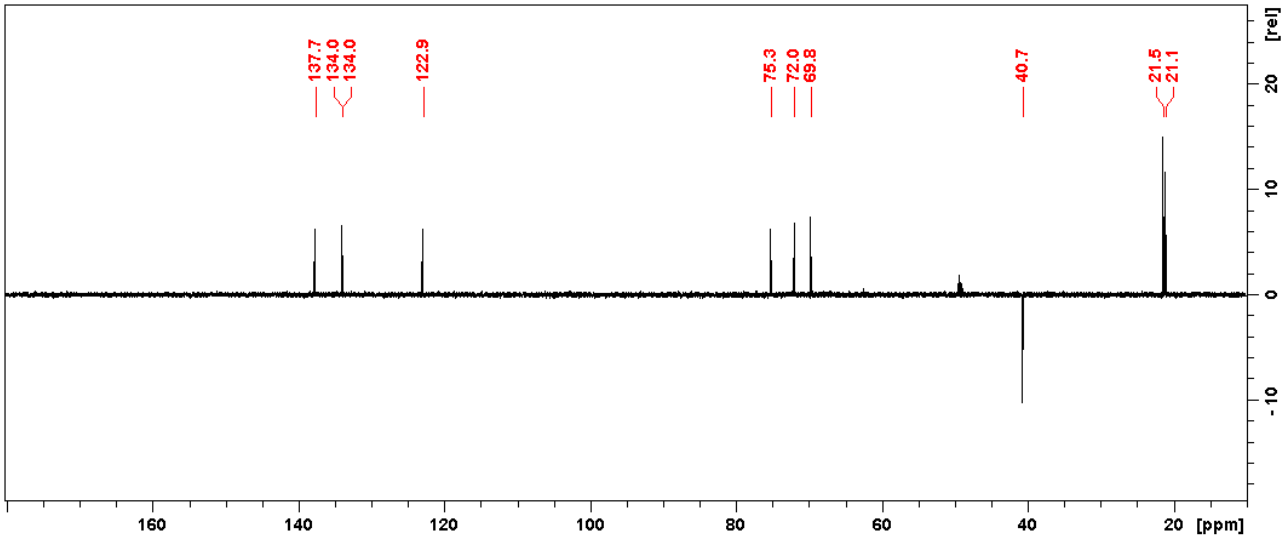

Figure S41. DEPT-135 NMR spectrum (150 MHz, CD_3OD) of compound **5**.

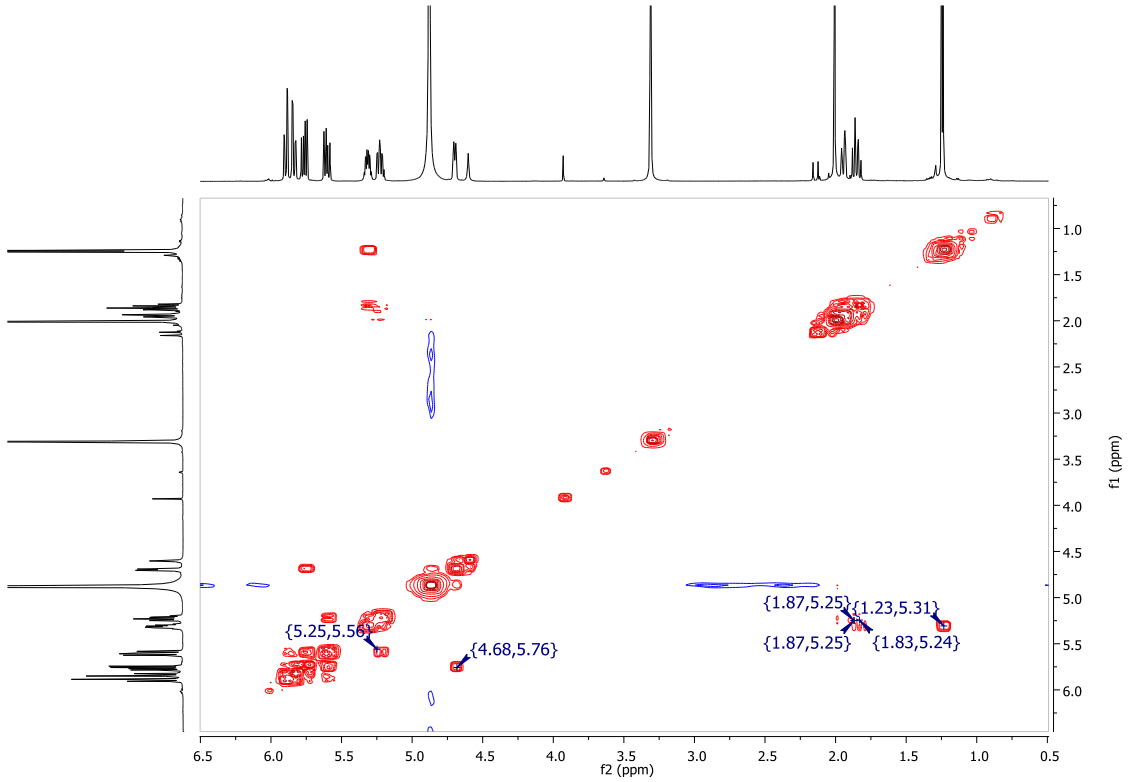

Figure S42. COSY spectrum (600 MHz, CD_3OD) of compound **5**.

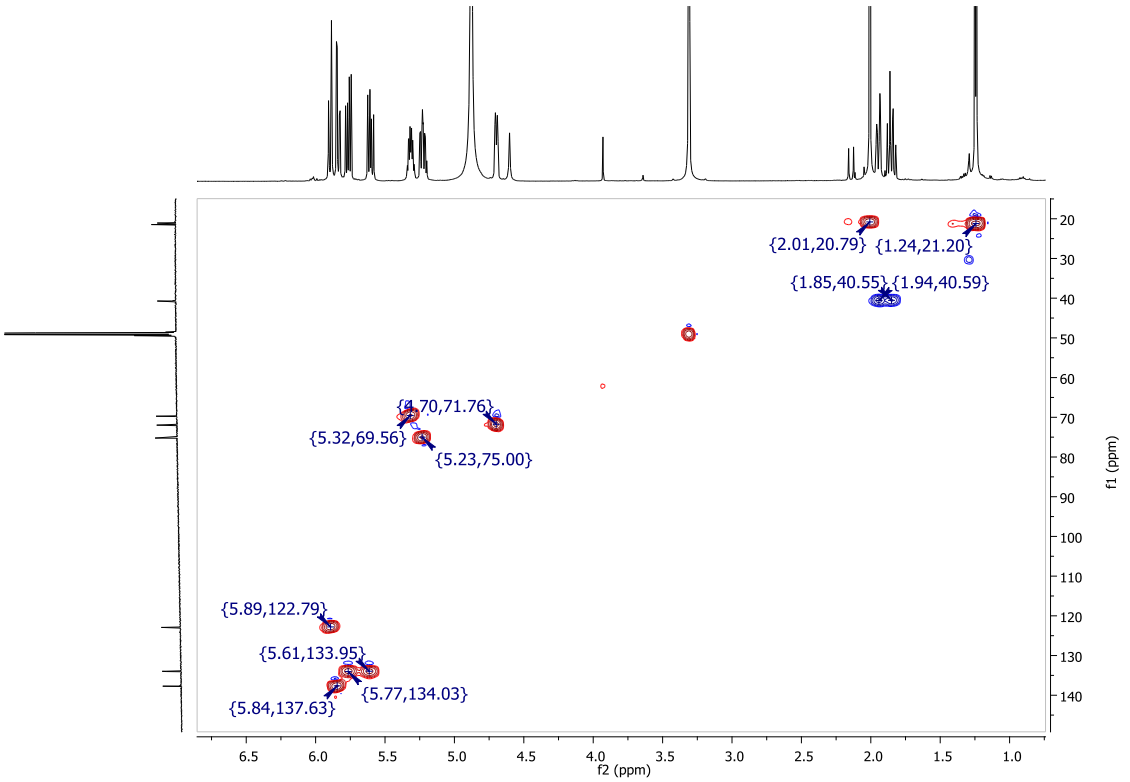

Figure S43. HSQC spectrum (CD_3OD) of compound **5**.

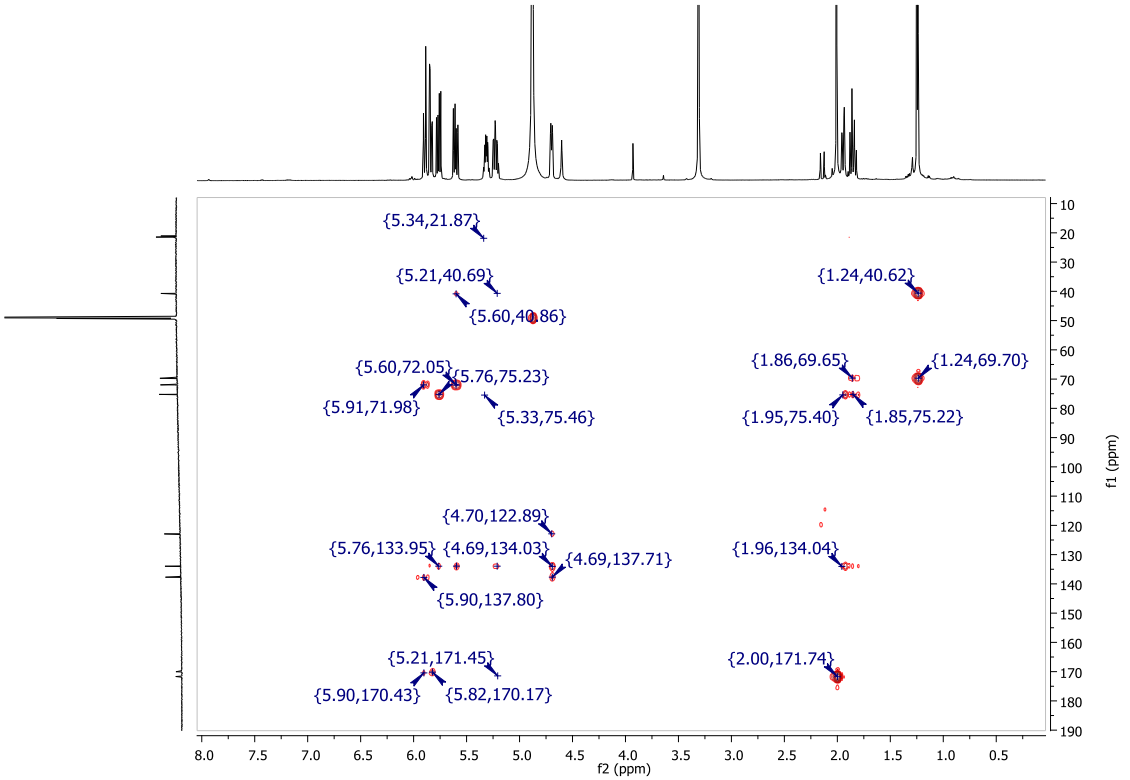

Figure S44. HMBC spectrum (CD_3OD) of compound **5**.

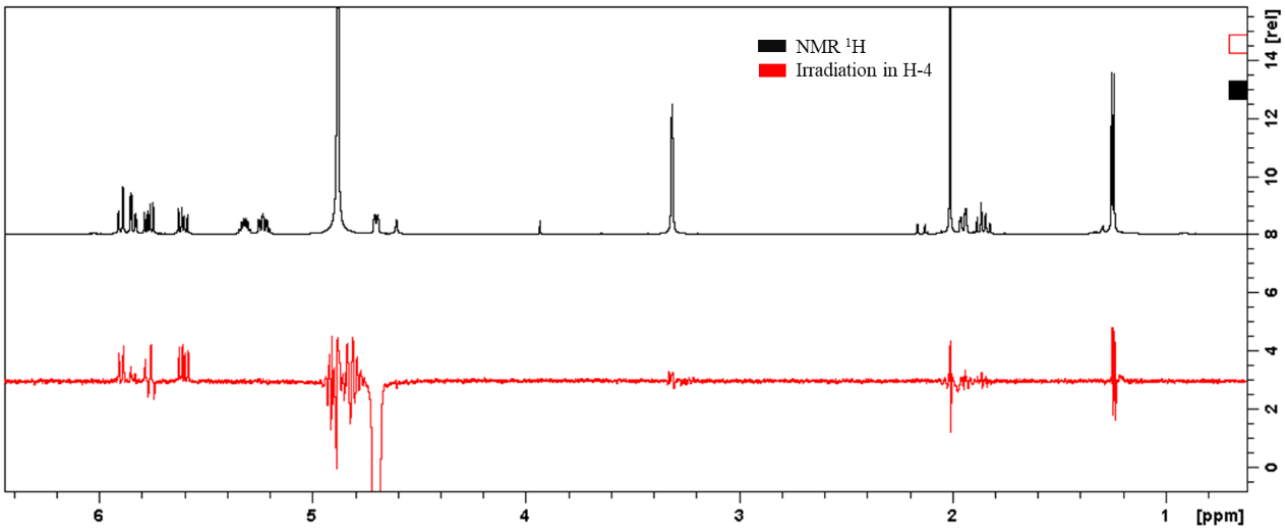

Figure S45. NOESY 1D spectrum of H-4 (δ_H 4.69, CD_3OD) for compound **5**.

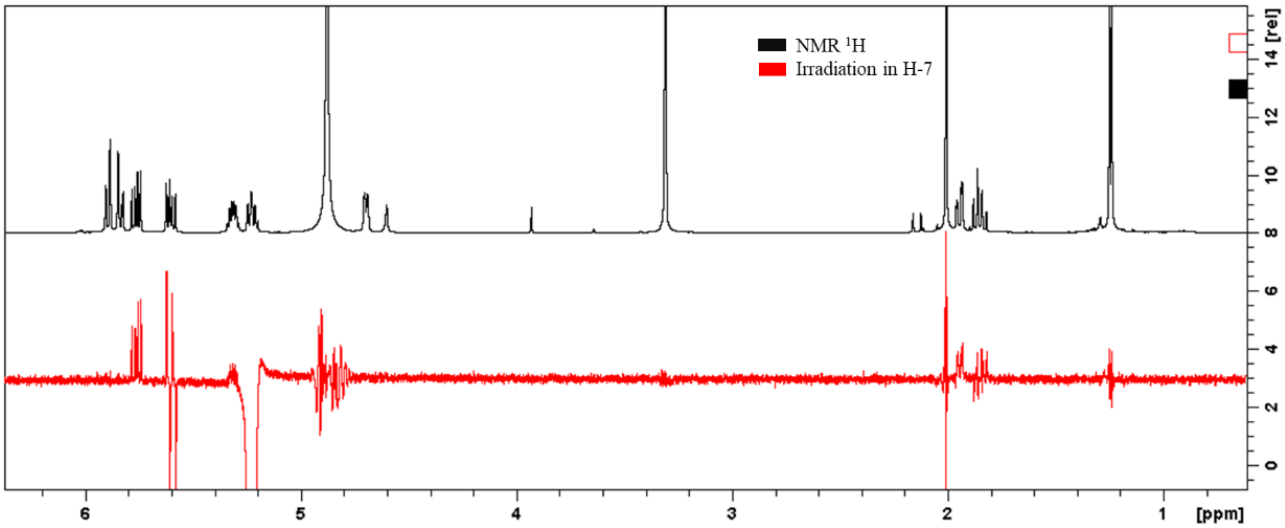

Figure S46. NOESY 1D spectrum of H-7 (δ_H 5.22, CD_3OD) for compound **5**.

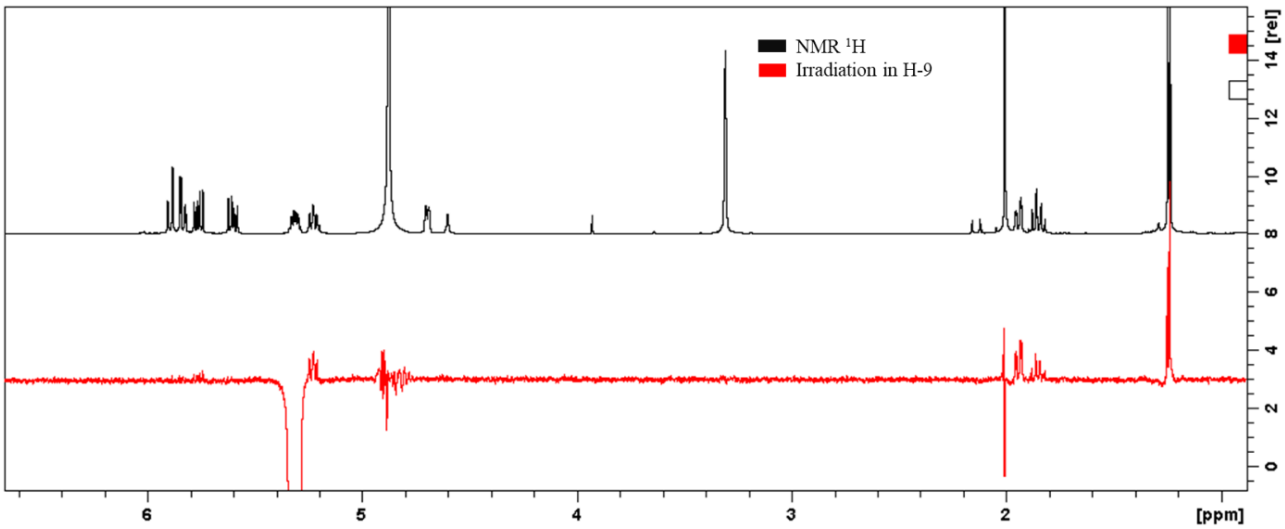

Figure S47. NOESY 1D spectrum of H-9 (δ_H 5.31, CD_3OD) for compound **5**.

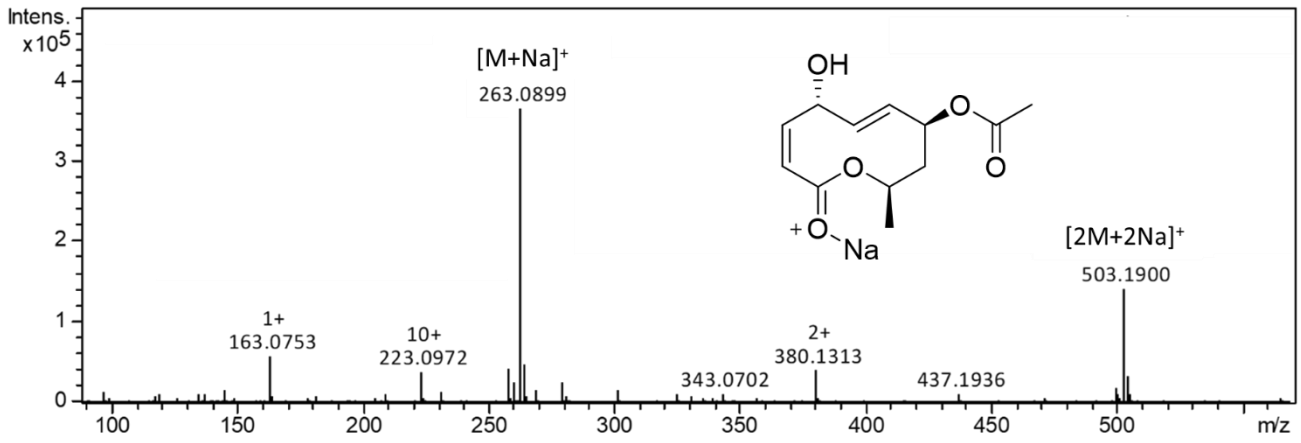

Figure S48. HRMS spectrum of compound **5**.

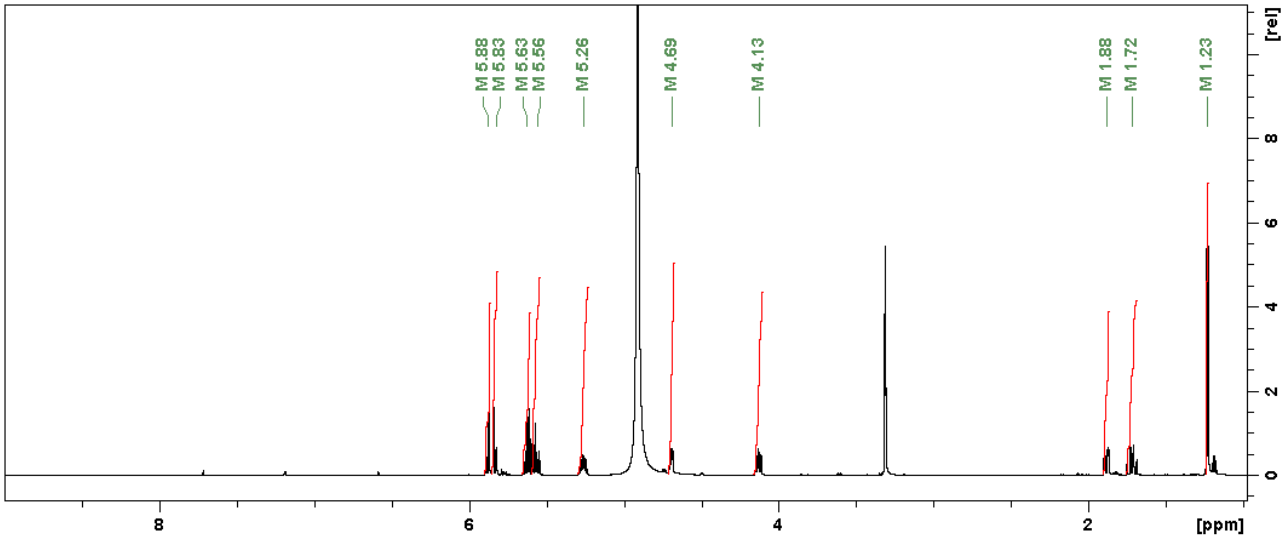

Figure S49. ^{1}H NMR spectrum (600 MHz, CD_3OD) of compound **6**.

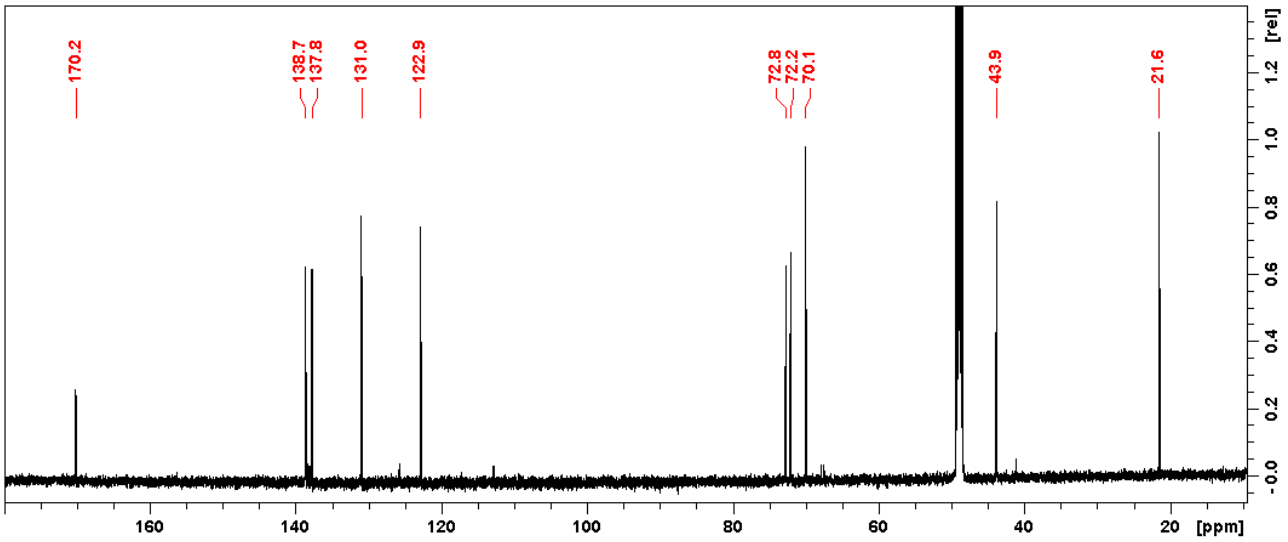

Figure S50. ^{13}C NMR spectrum (150 MHz, CD_3OD) of compound **6**.

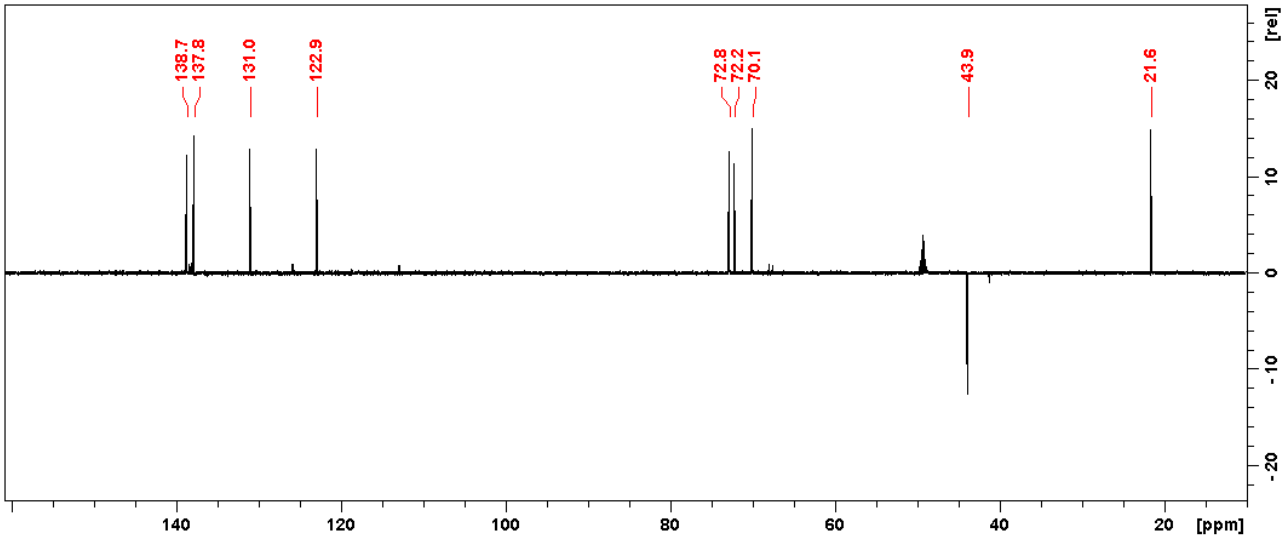

Figure S51. DEPT-135 NMR spectrum (150 MHz, CD_3OD) of compound **6**.

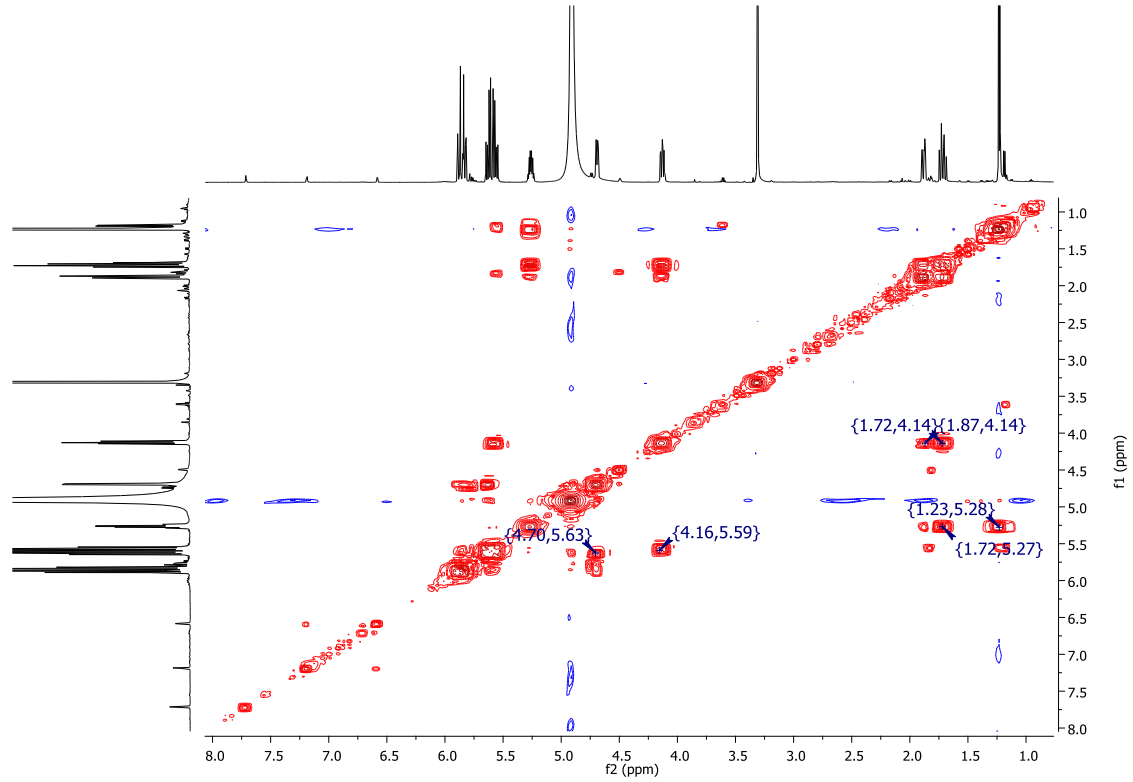

Figure S52. COSY spectrum (600 MHz, CD_3OD) of compound **6**.

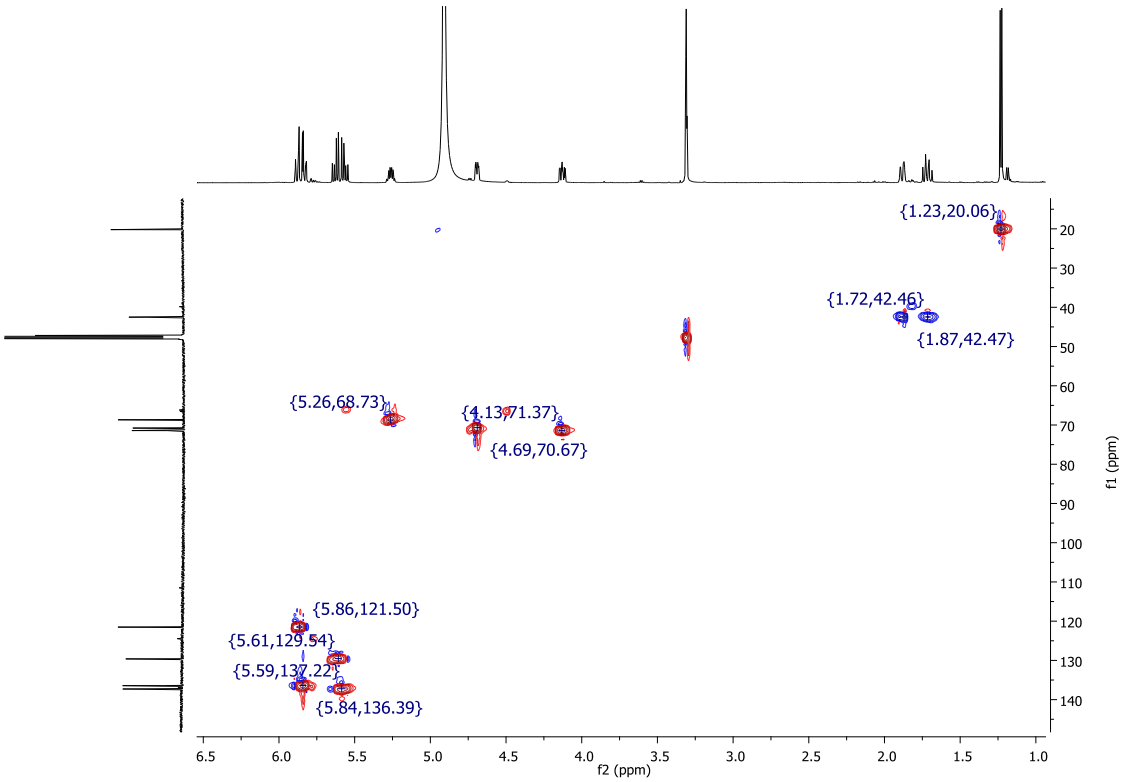

Figure S53. HSQC spectrum (CD_3OD) of compound **6**.

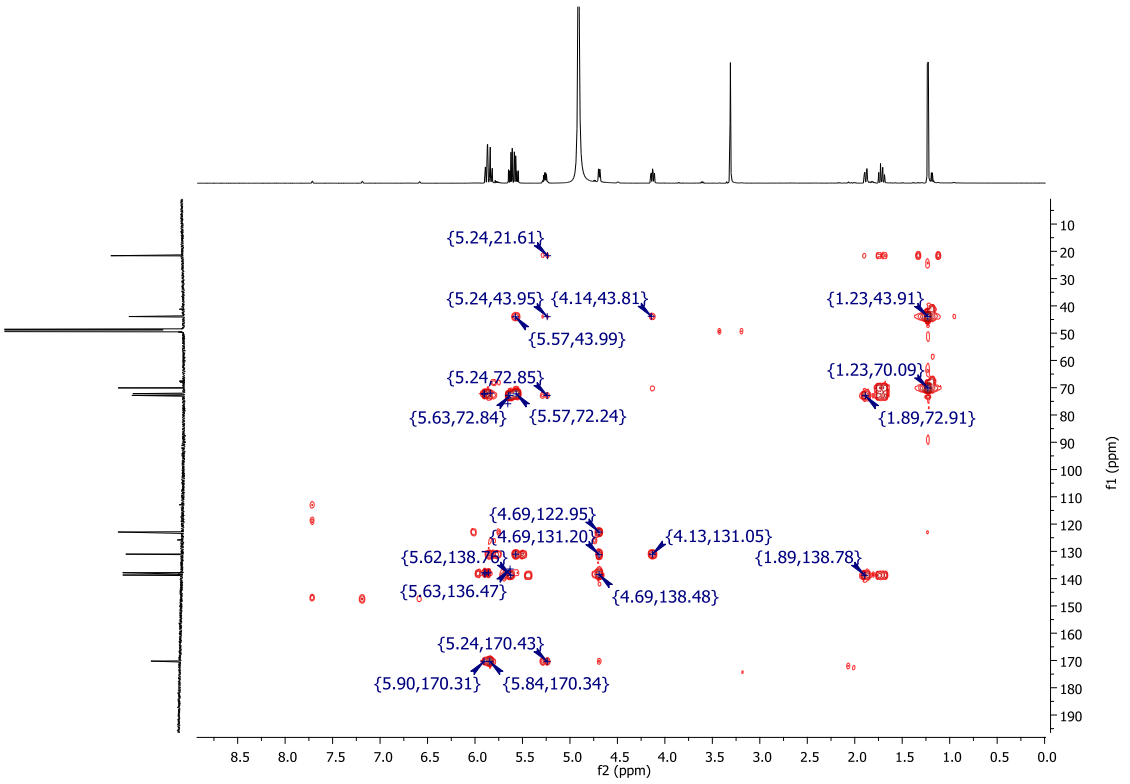

Figure S54. HMBC spectrum (CD_3OD) of compound **6.**

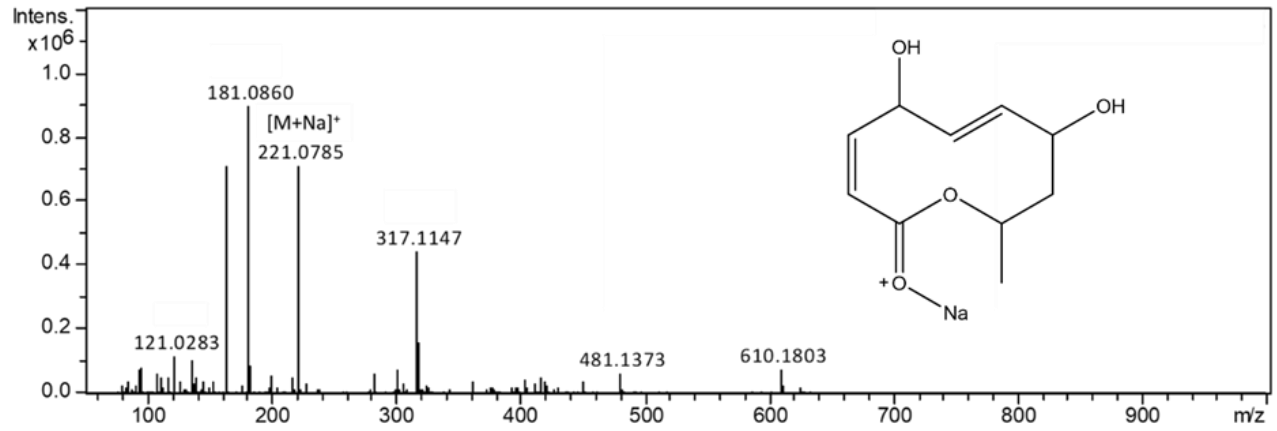

Figure S55. HRMS spectrum of compound **6**.

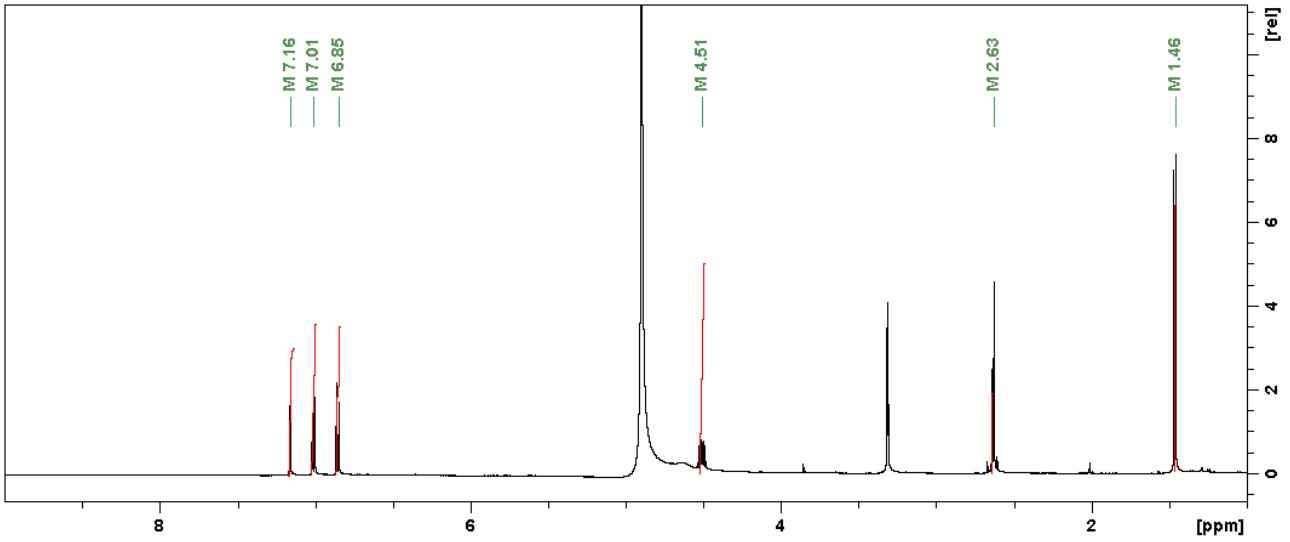

Figure S56. ^{1}H NMR spectrum (600 MHz, CD_3OD) of compound **7**.

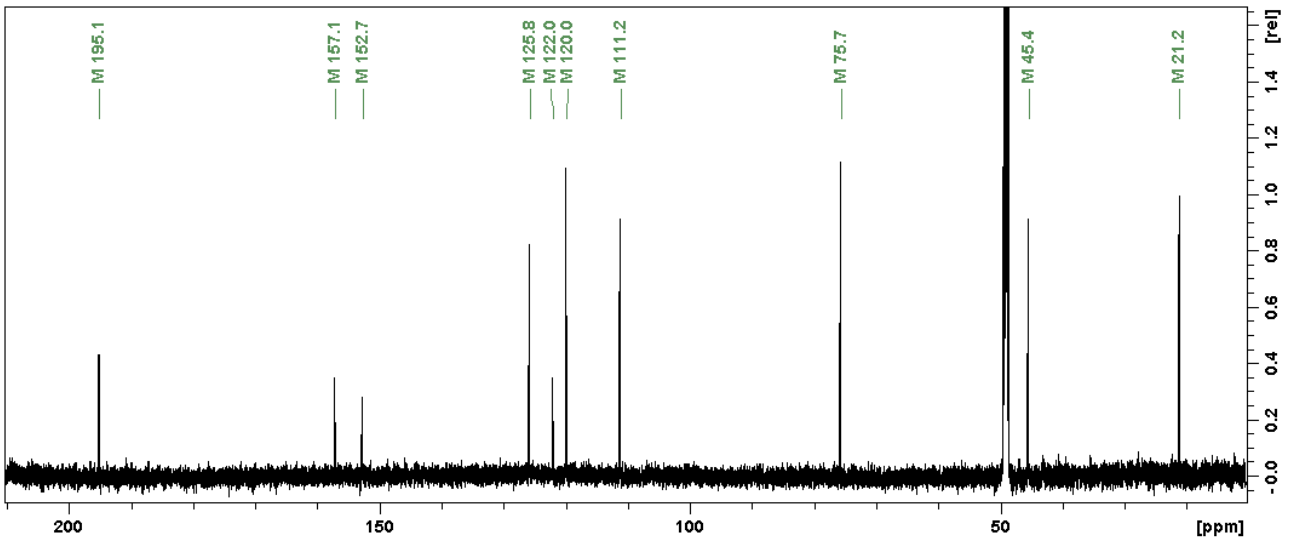

Figure S57. ^{13}C NMR spectrum (150 MHz, CD_3OD) of compound **7**.

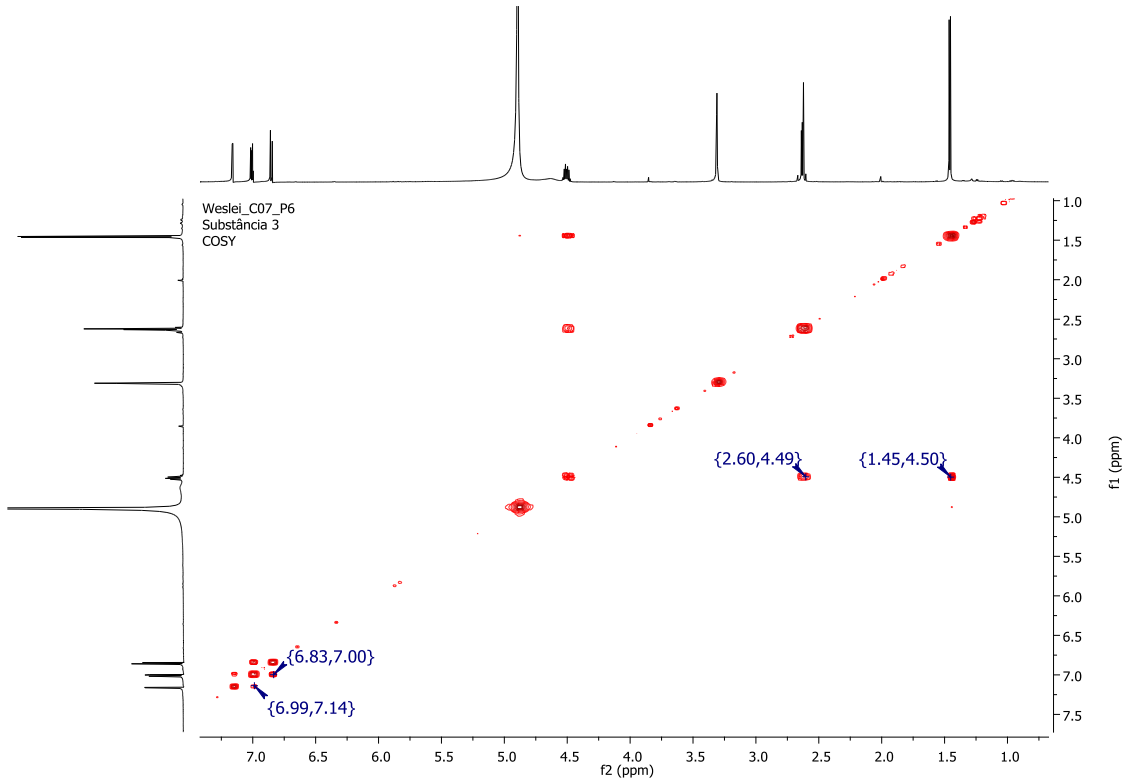

Figure S58. COSY spectrum (600 MHz, CD_3OD) of compound **7**.

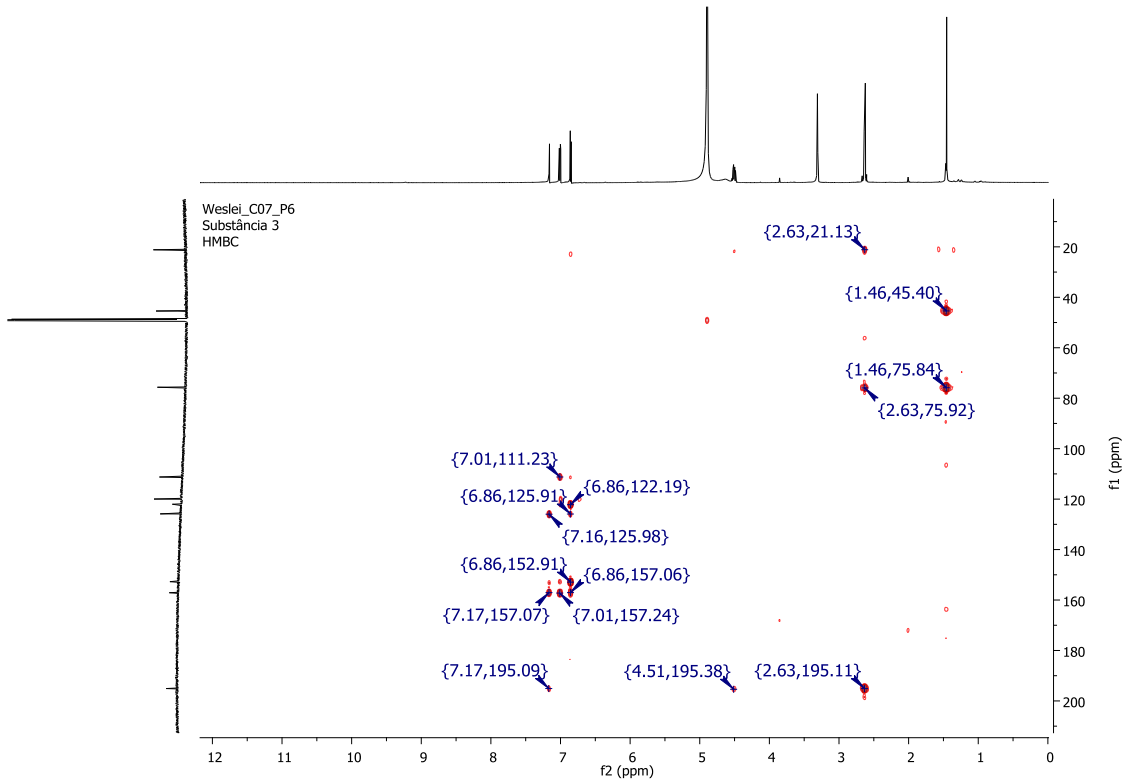

Figure S59. HSQC spectrum (CD_3OD) of compound **7**.

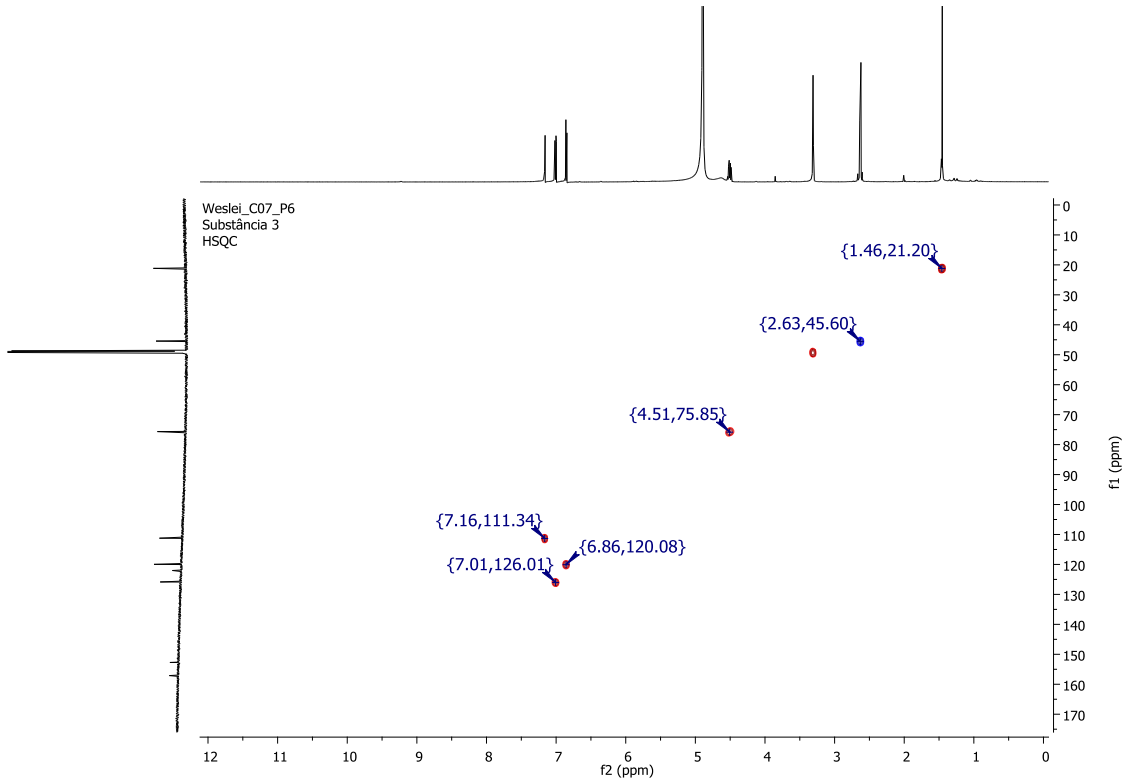

Figure S60. HMBC spectrum (CD_3OD) of compound **7**.

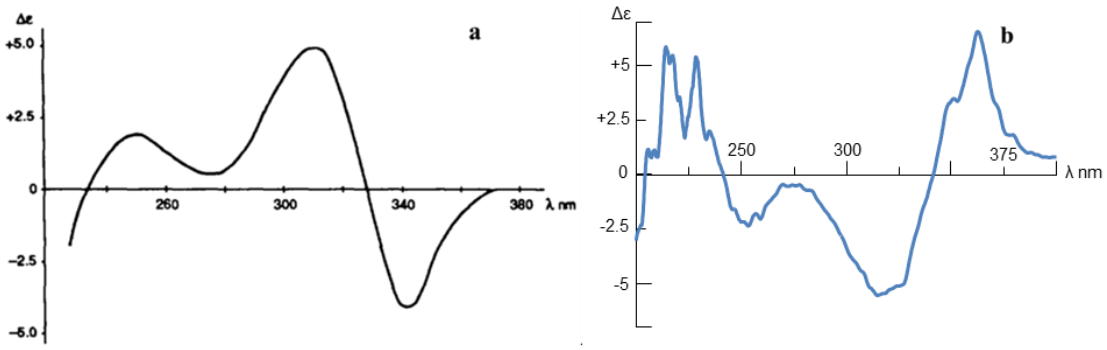

Figure S61. Comparison of the ECD spectrum (CH_3OH) of (a) *S*-6-hydroxy-2-methyl-4-chromanone and (b) compound **7**.

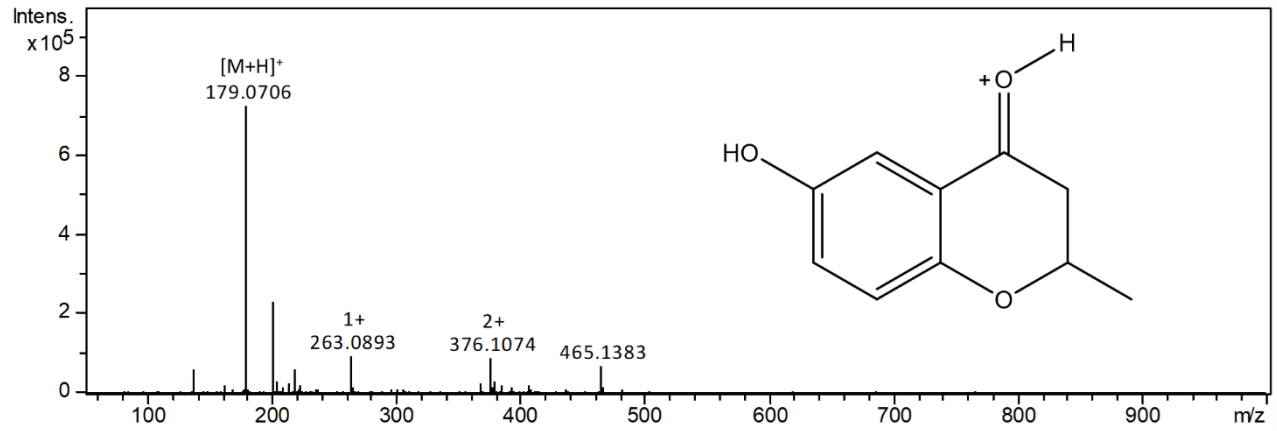

Figure S62. HRMS spectrum of compound **7**.

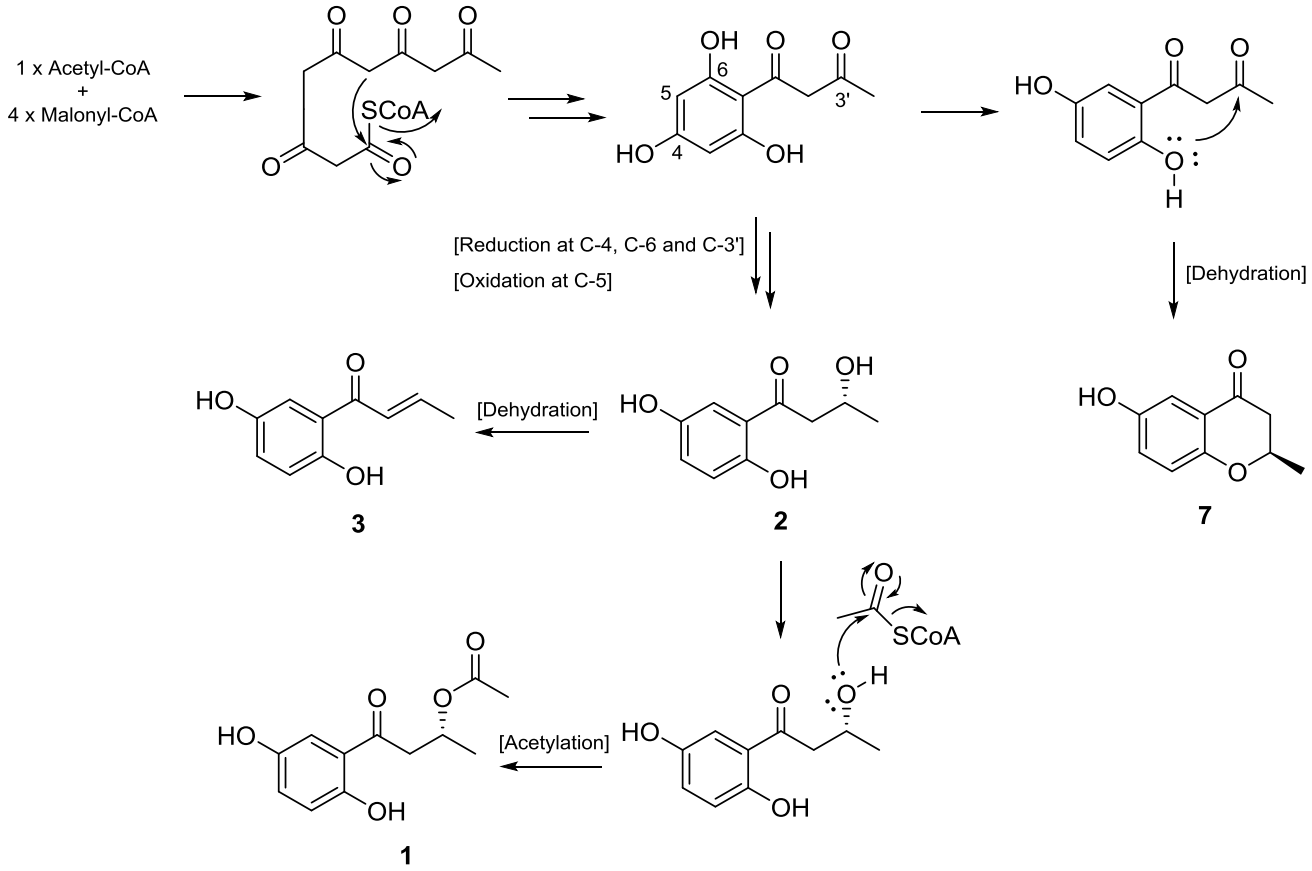

Figure S63. Proposed biosynthetic pathway for the production of compounds **1**-**3** and **7** (adapted from reference 1).

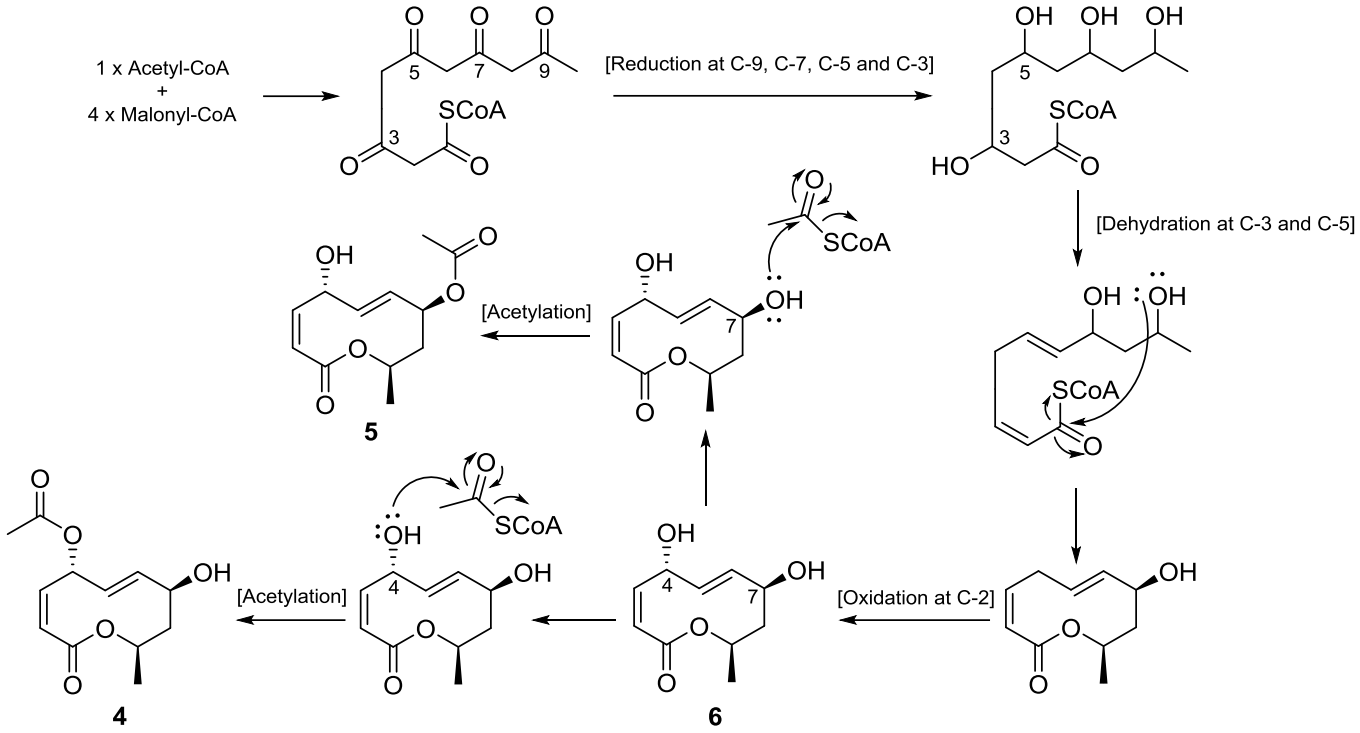

Figure S64. Proposed biosynthetic pathway for the production of compounds **4**-**6** (adapted from reference 1).

References

1. Dewick, P. M; *Medicinal Natural Products: A Biosynthetic Approach*, 3rd ed.; Wiley: Nottingham, United Kingdom, 2012.