Guaianolides and a seco-eudesmane from the resinous exudates of cushion bush (Leucophyta brownii) and evaluation of their cytostatic and anti-inflammatory activity

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Supporting Information

Guaianolides and a seco-Eudesmane from the Resinous Exudates of Cushion Bush (*Leucophyta brownii*) and Evaluation of Their Cytostatic and Anti-inflammatory Activity

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Supporting Information Contents

Supporting information contains an analytical HPLC chromatogram of the dichloromethane extract of fresh aerial parts of *Leucophyta brownii* at 210 nm showing the separation and t_R of the isolated compounds **1**–**10**, ^{1}H, ^{13}C, DEPT, and 2D NMR (^{1}H–^{1}H COSY, NOESY, HSQC, and HMBC) spectra of compounds **1**–**10,** crystal structures (ORTEP diagrams) of the sesquiterpene lactones **2**–**4**, **7**, and **8** with displacement ellipsoids at 50% probability for non-H atoms, and a description of physical (melting point, optical activity), spectroscopic (UV, IR) and spectrometric (APCIMS, HRESIMS) data of compounds **1**–**4** and **7**–**9** (page 5 to 92).

Supporting Information Contents

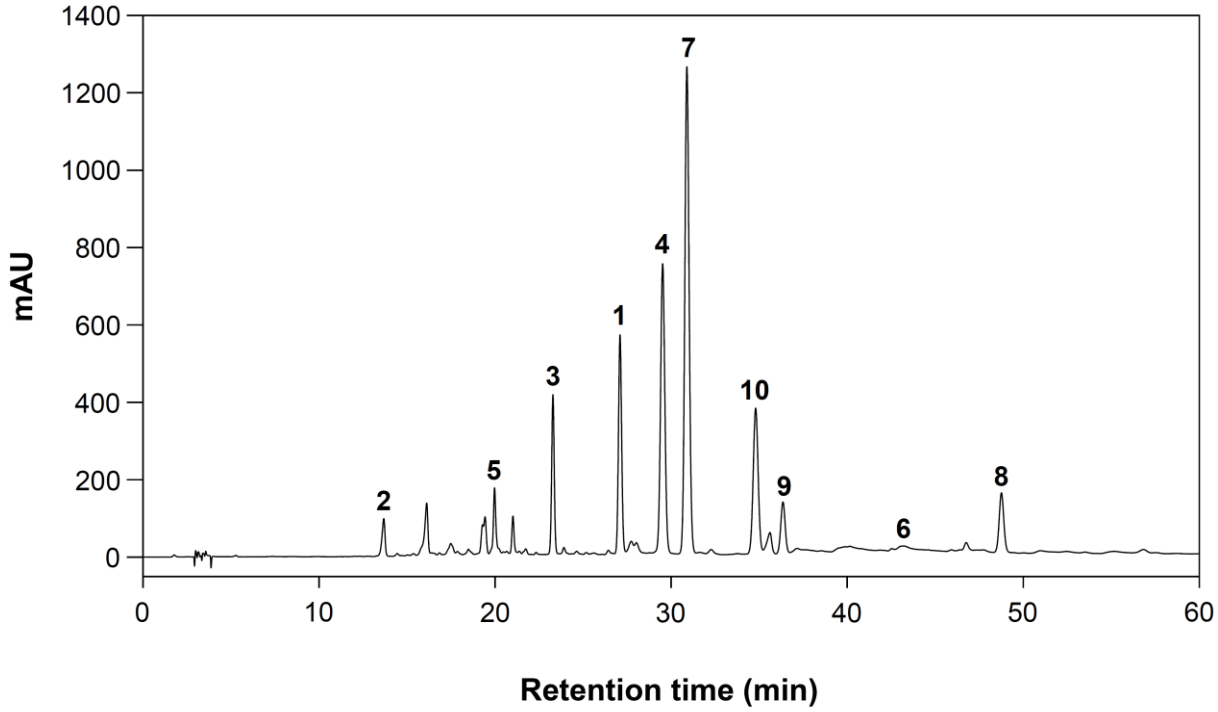
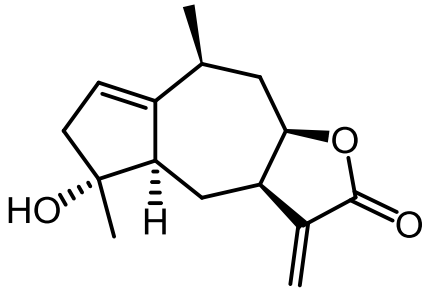


Fig. S1. Analytical HPLC chromatogram of the dichloromethane extract of fresh aerial parts of *Leucophyta brownii* at 210 nm (Peak numbers **1**–**10** in the HPLC chromatogram refer to compound numbers).

*4α-Hydroxy-5αH,10αH-1,11(13)-guaidien-8β,12-olide (**1**)*

Colorless resin-like oil; $[\alpha]_D^{25}$ +153 (*c* 0.4, MeOH); UV (MeOH) λ_{max} (log ε) 205 (3.66) nm; IR (KBr) ν_{max} 3338, 2926, 1771, 1660, 1110 cm^{-1} APCIMS: *m/z* 249 $[M + H]^+$ (14), 231 $[M + H - H_2O]^+$ (100); HRESIMS *m/z* 249.1489 (calcd for $C_{15}H_{21}O_3$, 249.1491).



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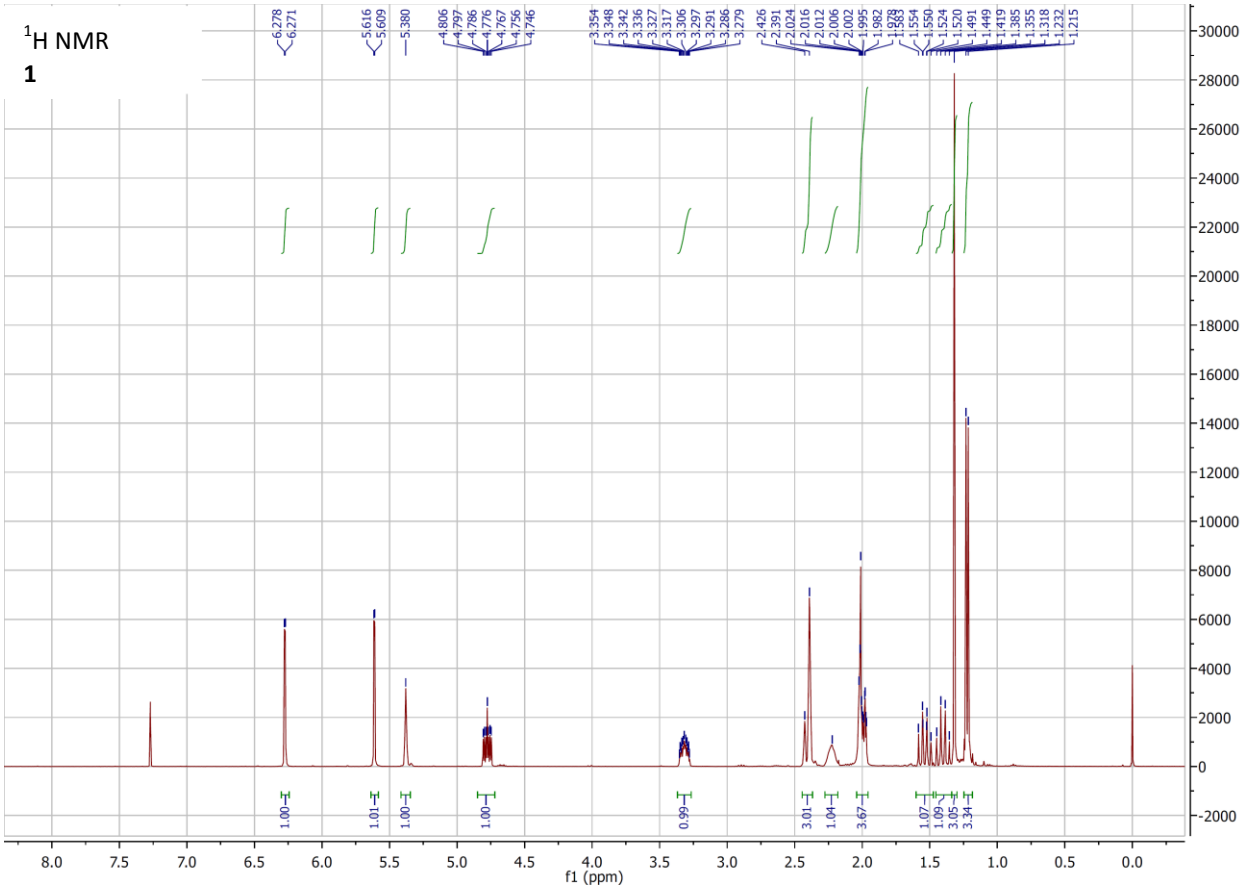


Fig. S2. ^{1}H NMR (400 MHz, $CDCl_3$) spectrum of compound **1**.

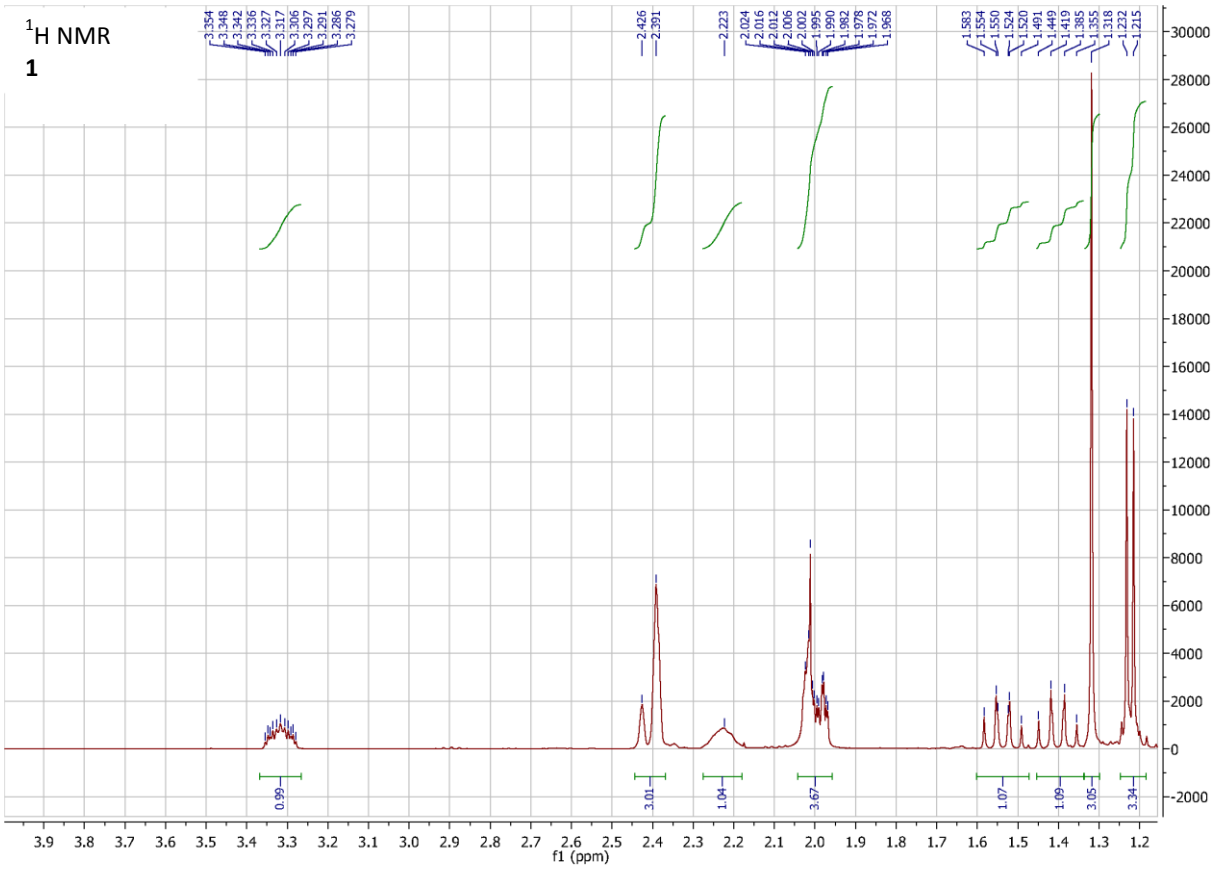


Fig. S3. ^{1}H NMR (400 MHz, $CDCl_3$) spectrum of compound **1** expanded in the region 1.1–4.0 ppm.

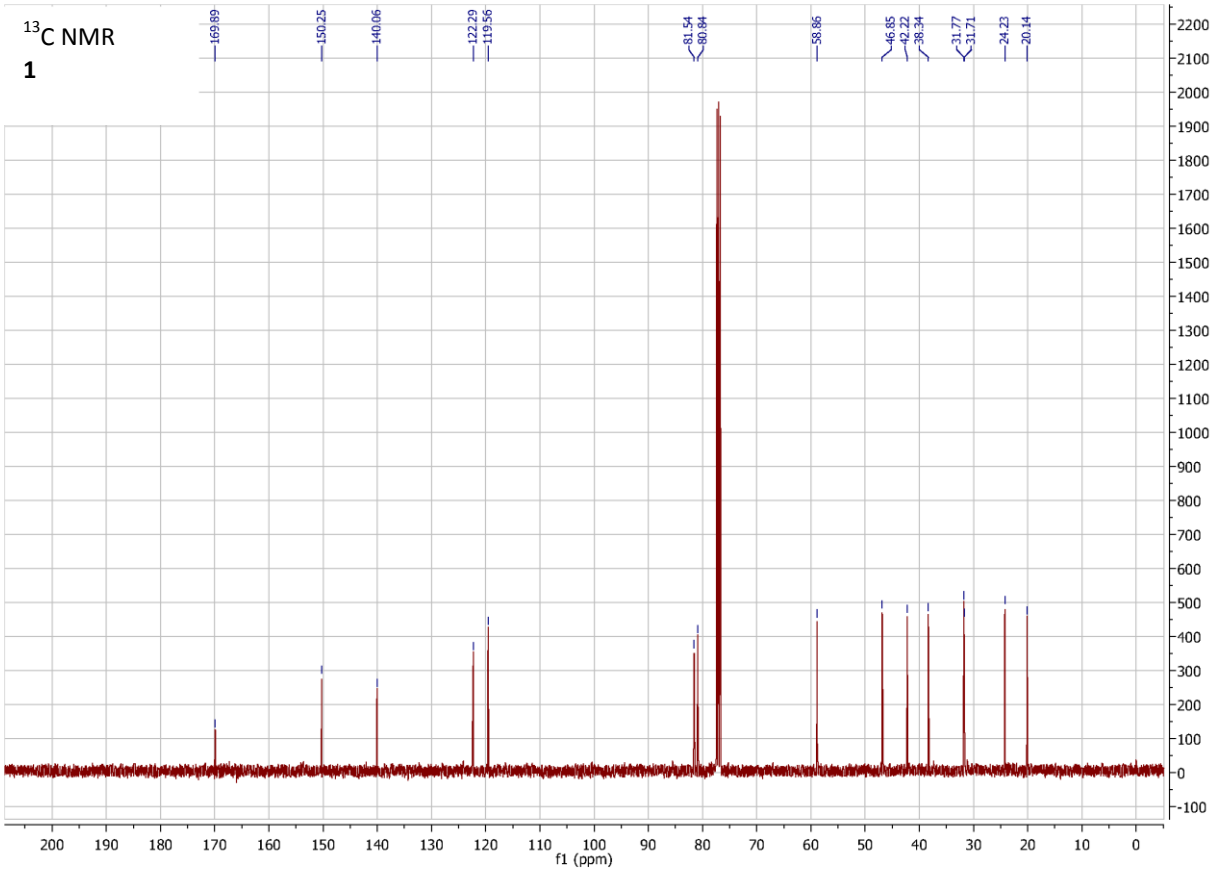


Fig. S4. ^{13}C NMR (100 MHz, $CDCl_3$) spectrum of compound **1**.

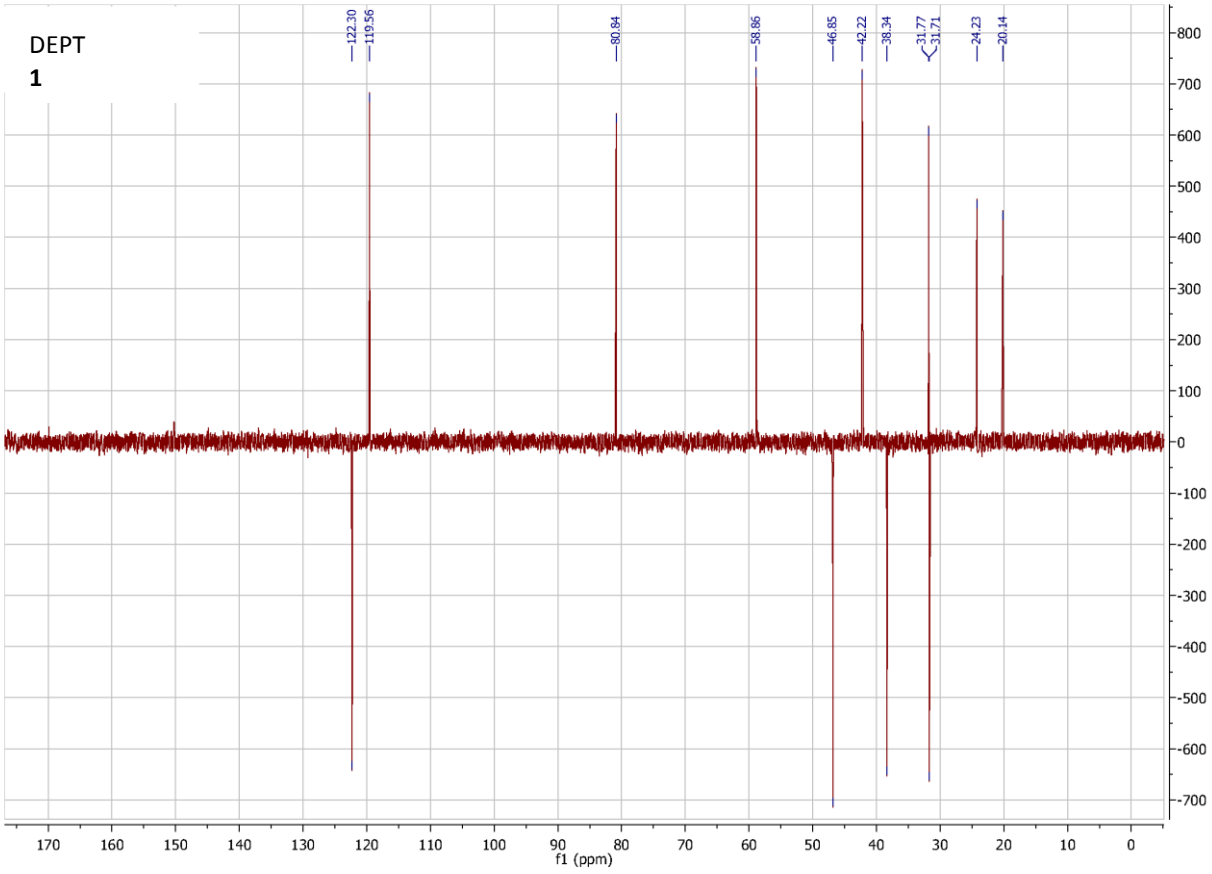


Fig. S5. DEPT spectrum of compound **1**.

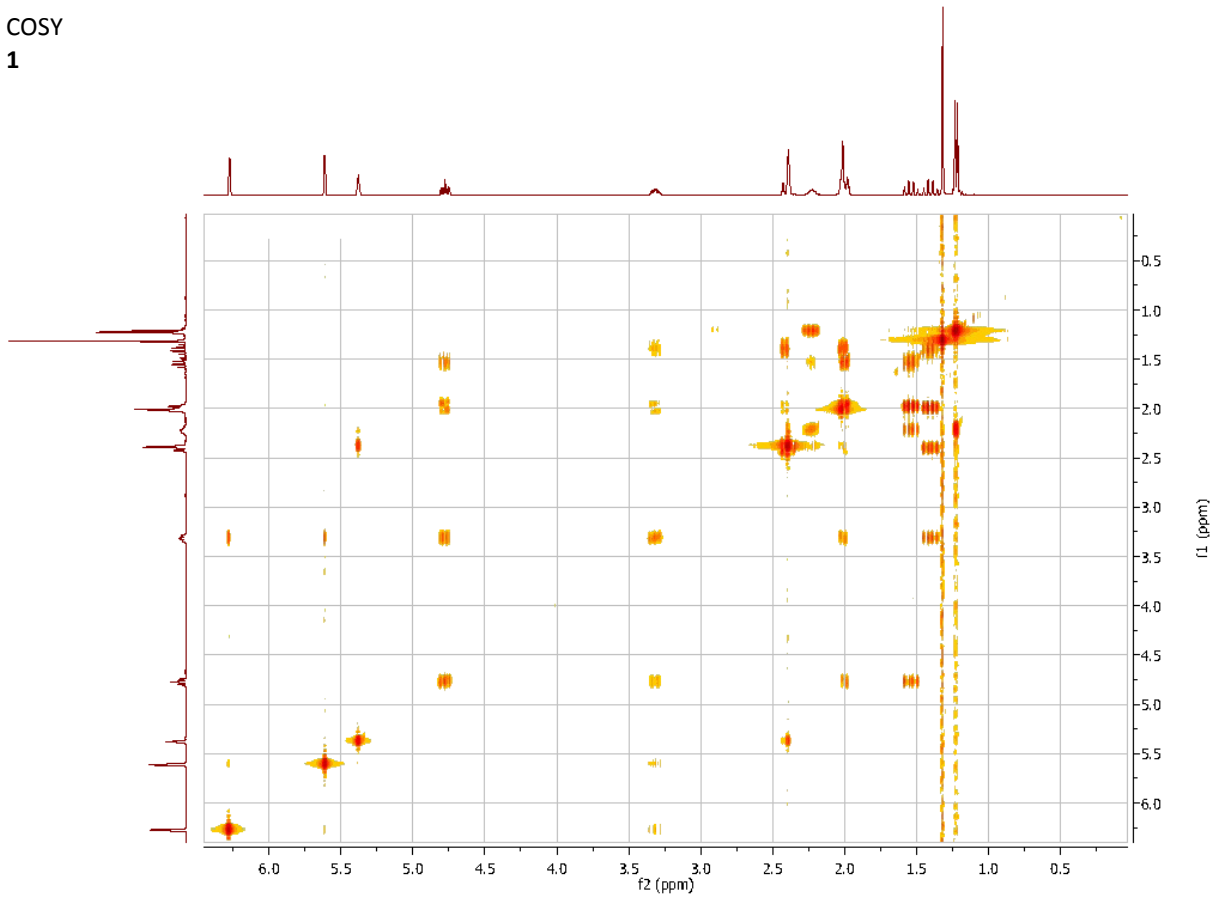


Fig. S6. $^{1}H–^{1}H$ COSY spectrum of compound **1**.

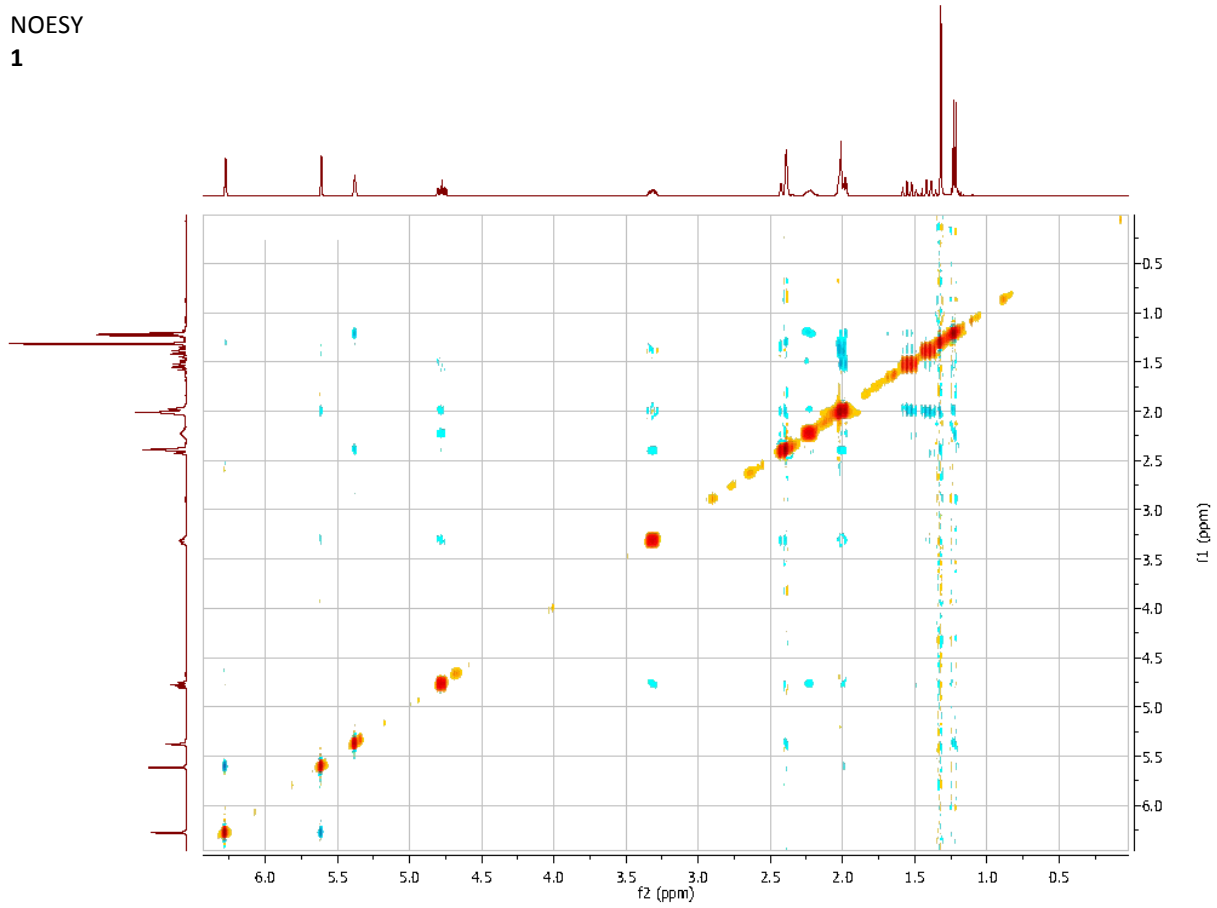


Fig. S7. NOESY spectrum of compound **1**.

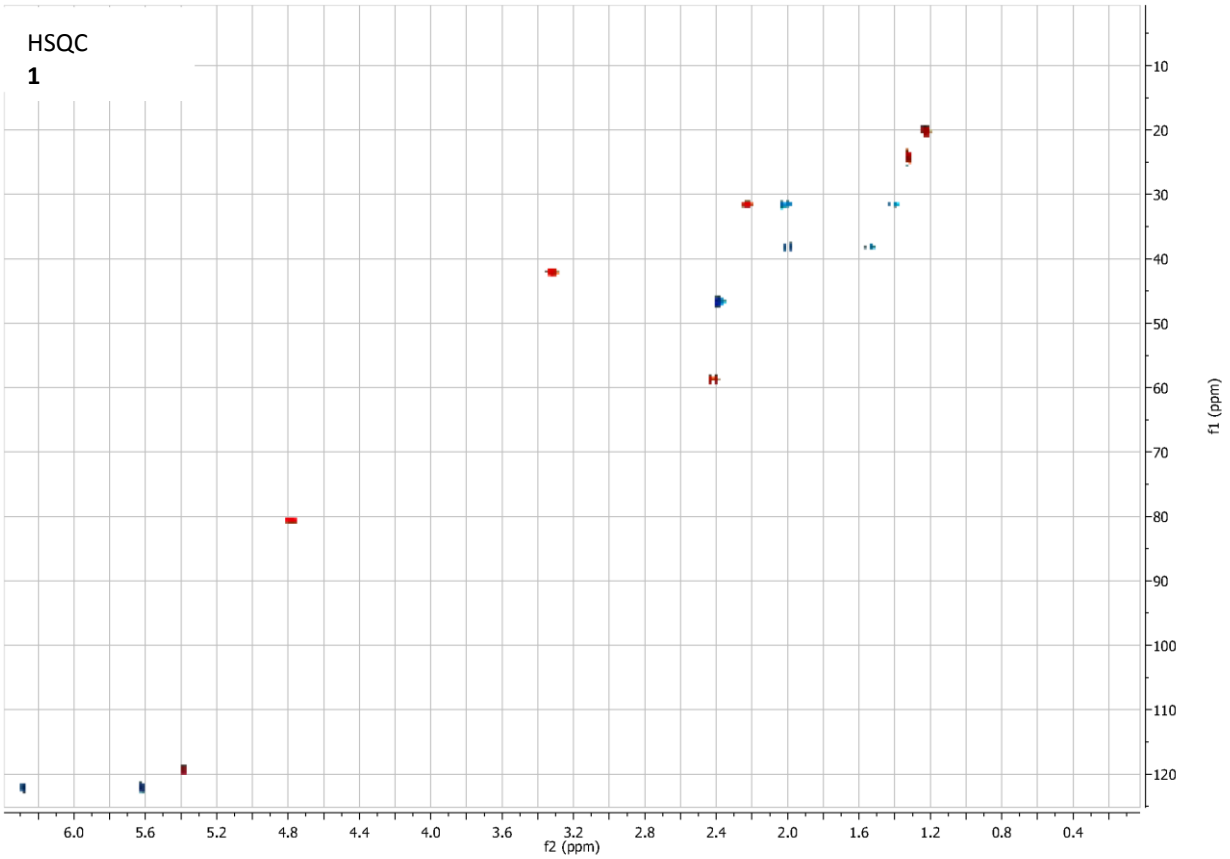


Fig. S8. HSQC spectrum of compound **1**.

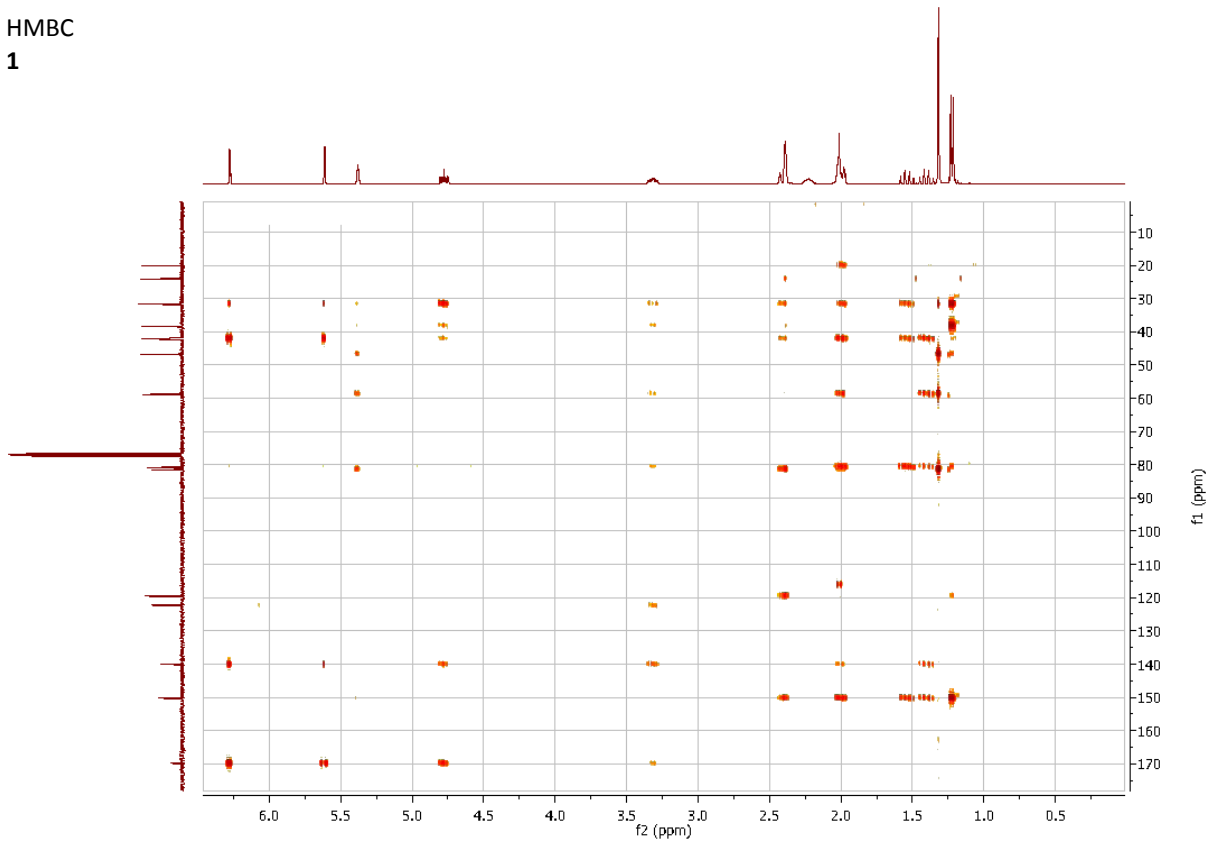
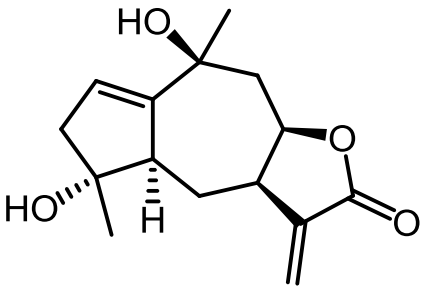


Fig. S9. HMBC spectrum of compound **1**.

*4α,10β-Dihydroxy-5αH-1,11(13)-guaidien-8β,12-olide (**2**)*

Colorless needle-like crystals; mp 169–170 °C; $[\alpha]_D^{25}$ +34 (*c* 0.4, MeOH); UV (MeOH) λ_{max} (log ε) 209 (3.84) nm; IR (KBr) ν_{max} 3338, 2941, 1758, 1655, 1380, 1273, 1169 cm^{-1}. APCIMS: *m/z* 265 $[M + H]^+$ (8), 247 $[M - H_2O + H]^+$ (51), 229 $[M - 2\ H_2O + H]^+$ (100); HRESIMS *m/z* 265.1441 (calcd for $C_{15}H_{21}O_4$, 265.1440).



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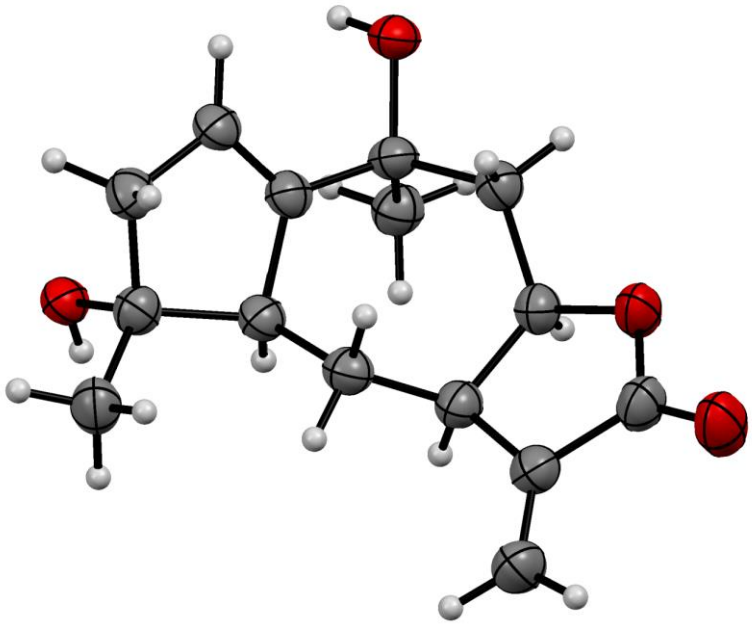


Fig. S10. Crystal structure of compound **2** (ORTEP diagram) with displacement ellipsoids at 50% probability for non-H atoms.

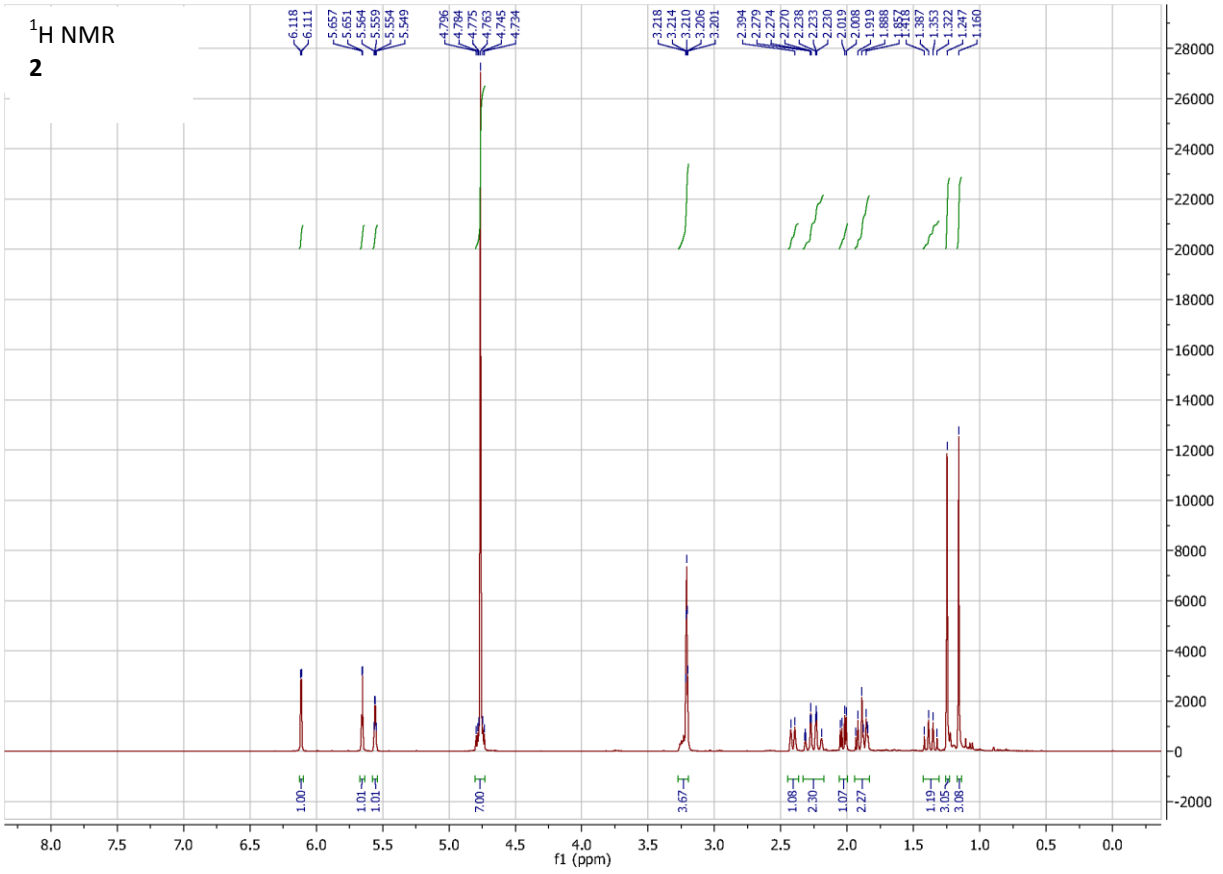


Fig. S11. ^{1}H NMR (400 MHz, methanol-d_4) spectrum of compound **2**.

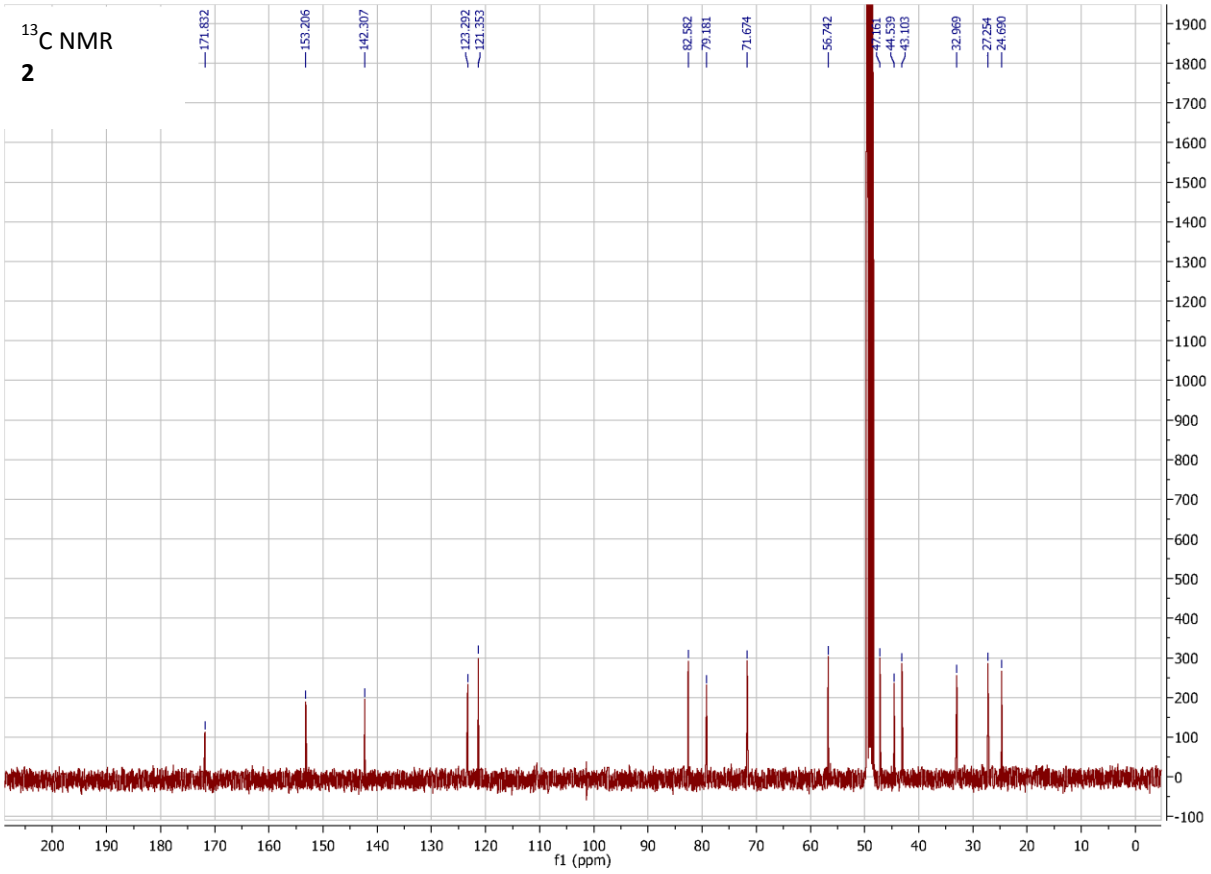


Fig. S12. ^{13}C NMR (100 MHz, methanol-d_4) spectrum of compound **2**.

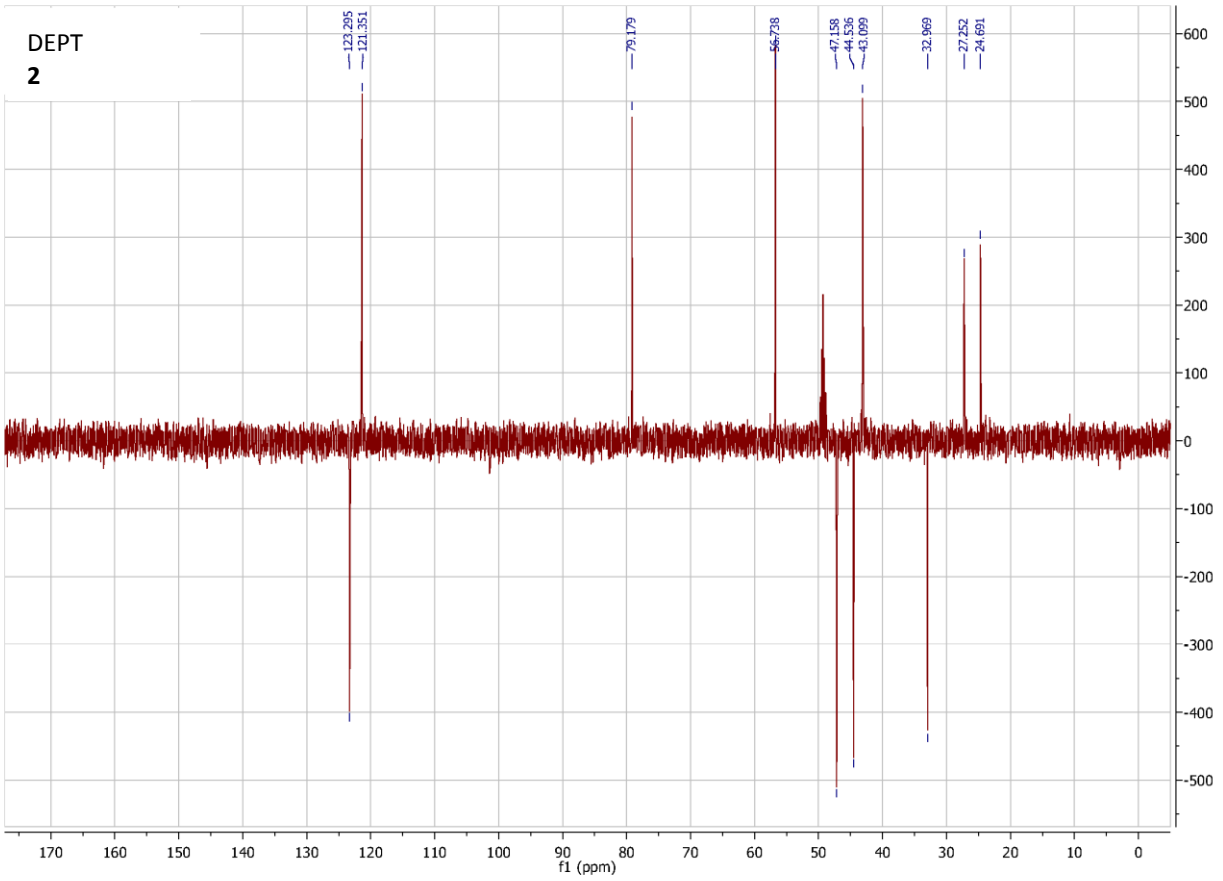


Fig. S13. DEPT spectrum of compound **2**.

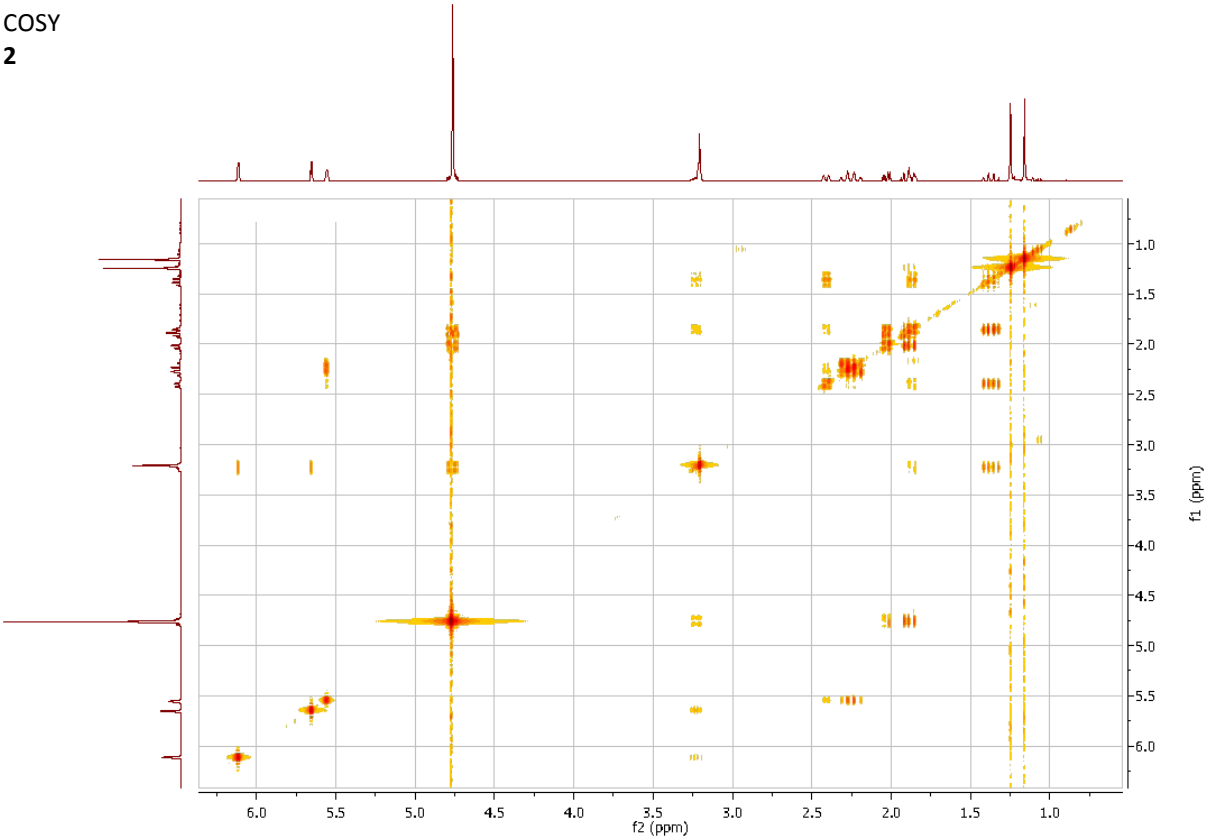


Fig. S14. $^{1}H–^{1}H$ COSY spectrum of compound **2**.

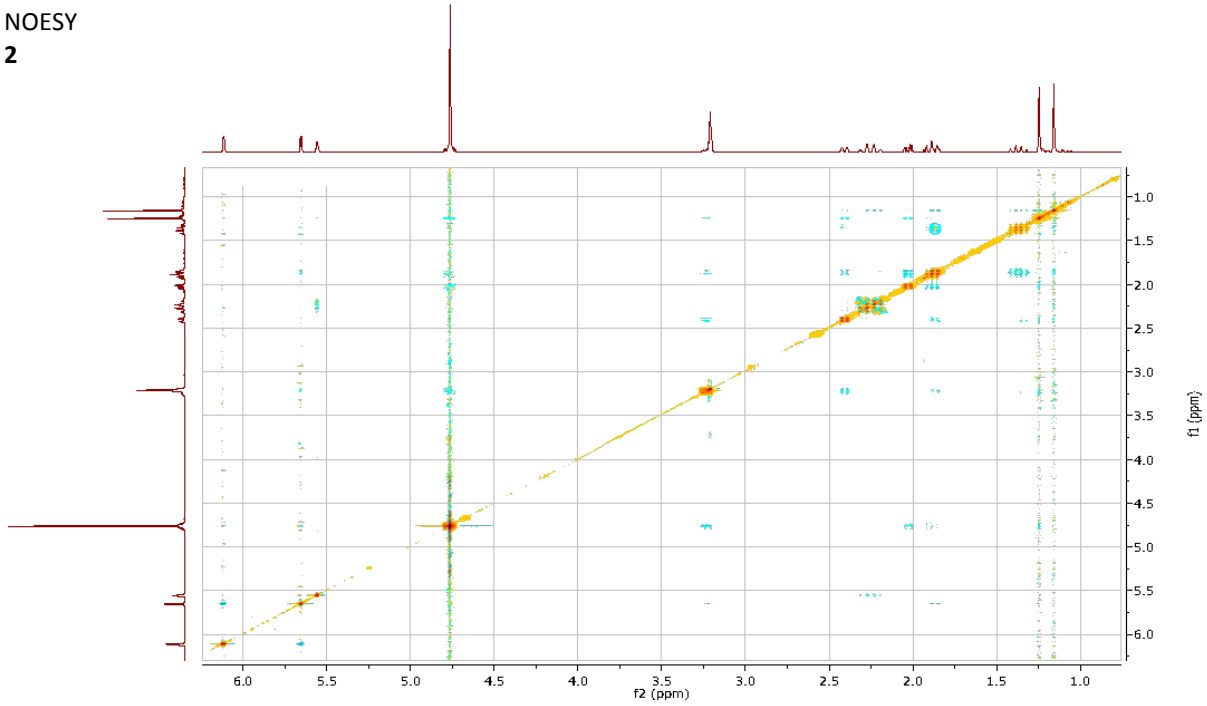


Fig. S15. NOESY spectrum of compound **2**.

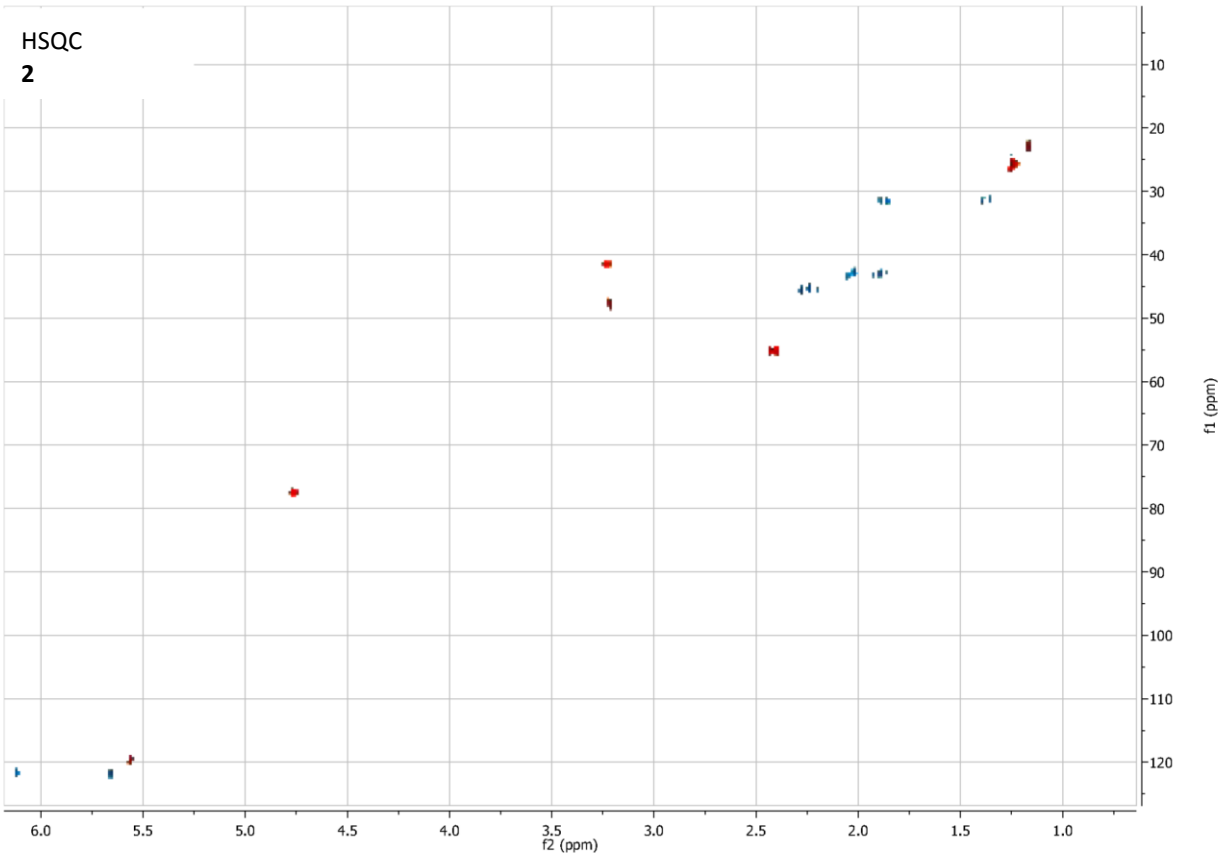


Fig. S16. HSQC spectrum of compound **2**.

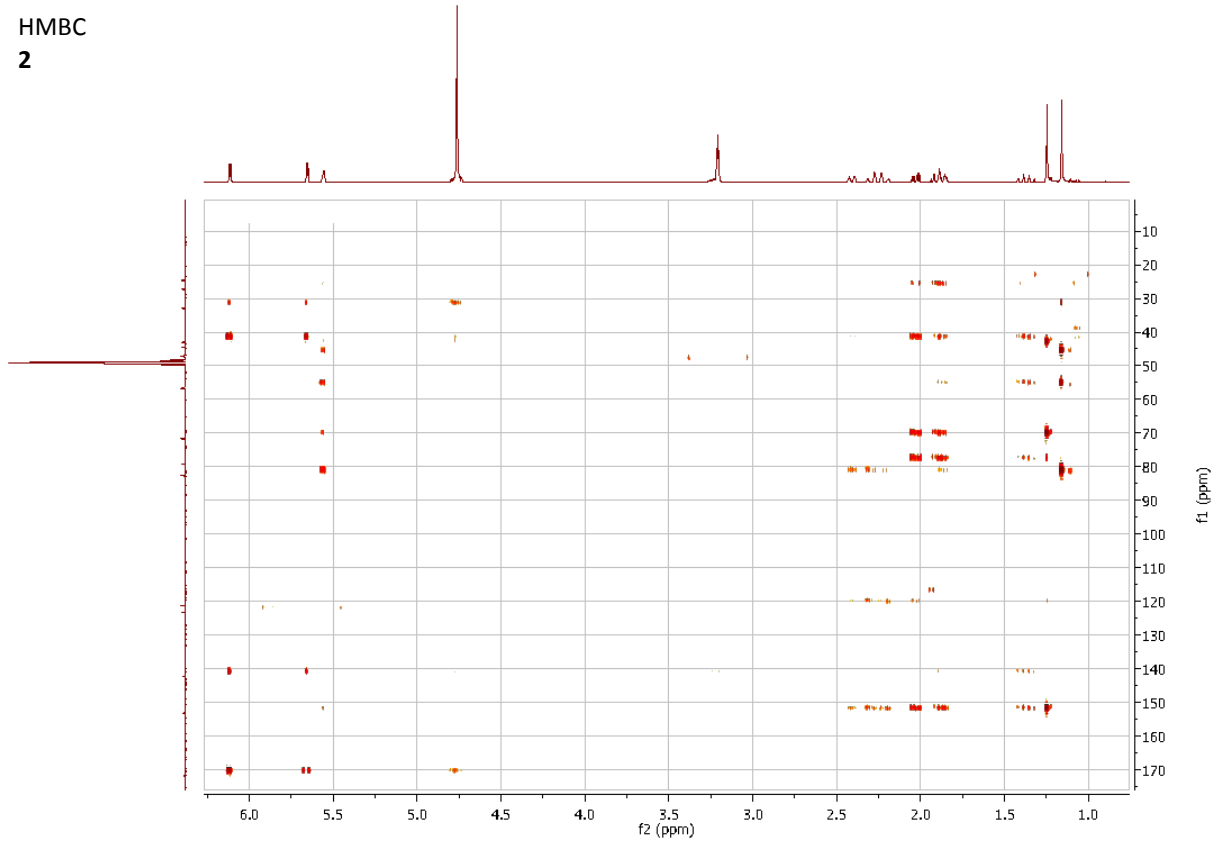
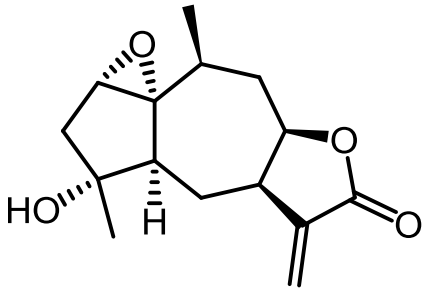


Fig. S17. HMBC spectrum of compound **2**.

*4α-Hydroxy-1α,2α-epoxy-5αH,10αH-11(13)-guaien-8β,12-olide (**3**)*

Colorless crystals; mp 168–169 °C; $[\alpha]_D^{25}$ +31 (*c* 0.4, $CHCl_3$); UV (MeOH) λ_{max} (log ε) 210 (4.11) nm; IR (KBr) ν_{max} 3497, 2949, 1757, 1658, 1398, 1271, 1131 cm^{-1}; APCIMS: *m/z* 265 $[M + H]^+$ (13), 247 $[M - H_2O + H]^+$ (39), 229 $[M - 2\ H_2O + H]^+$ (100); HRESIMS *m/z* 265.1440 (calcd for $C_{15}H_{21}O_4$, 265.1440).



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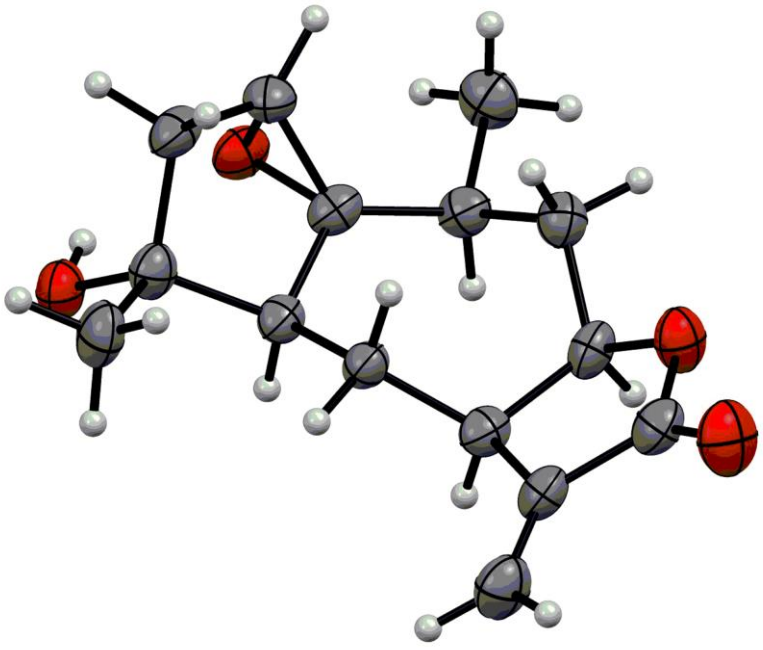


Fig. S18. Crystal structure of compound **3** (ORTEP diagram) with displacement ellipsoids at 50% probability for non-H atoms.

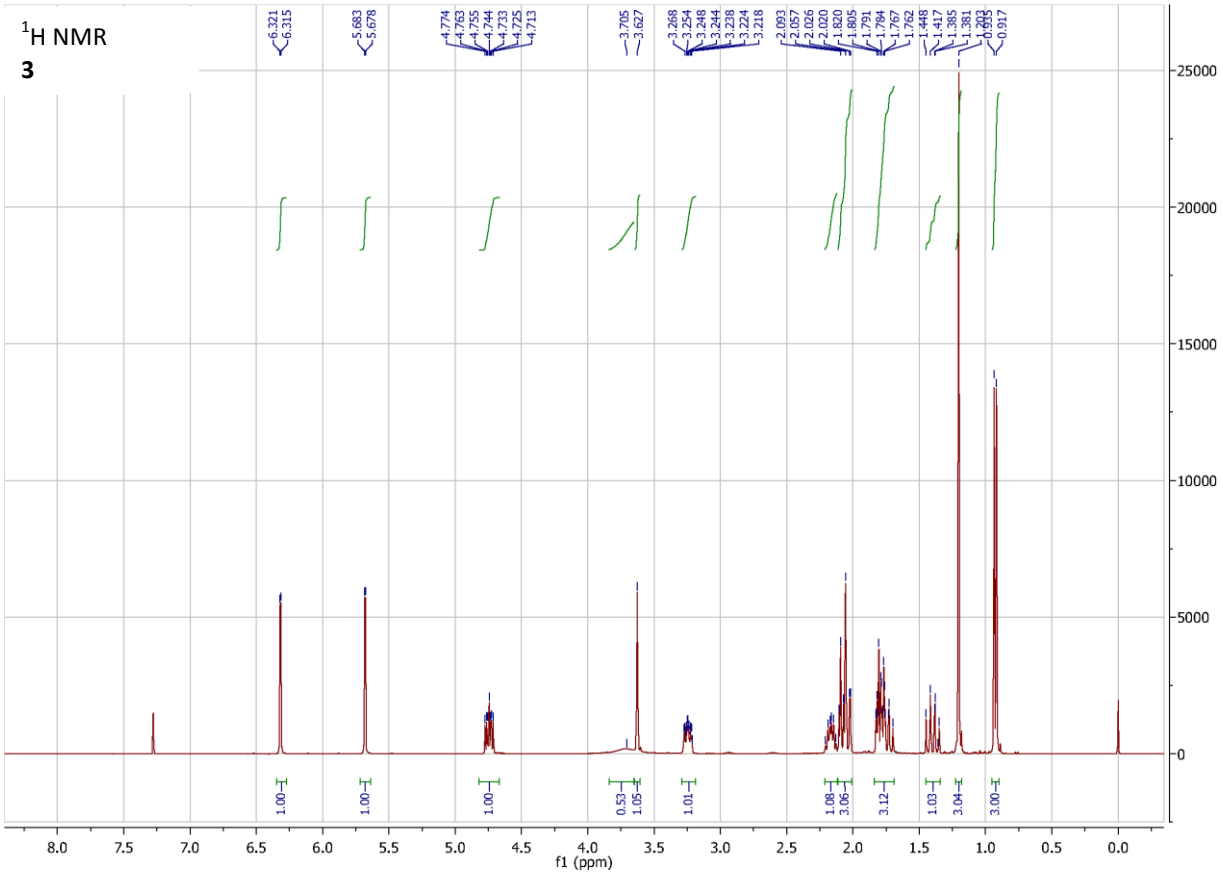


Fig. S19. ^{1}H NMR (400 MHz, $CDCl_3$) spectrum of compound **3**.

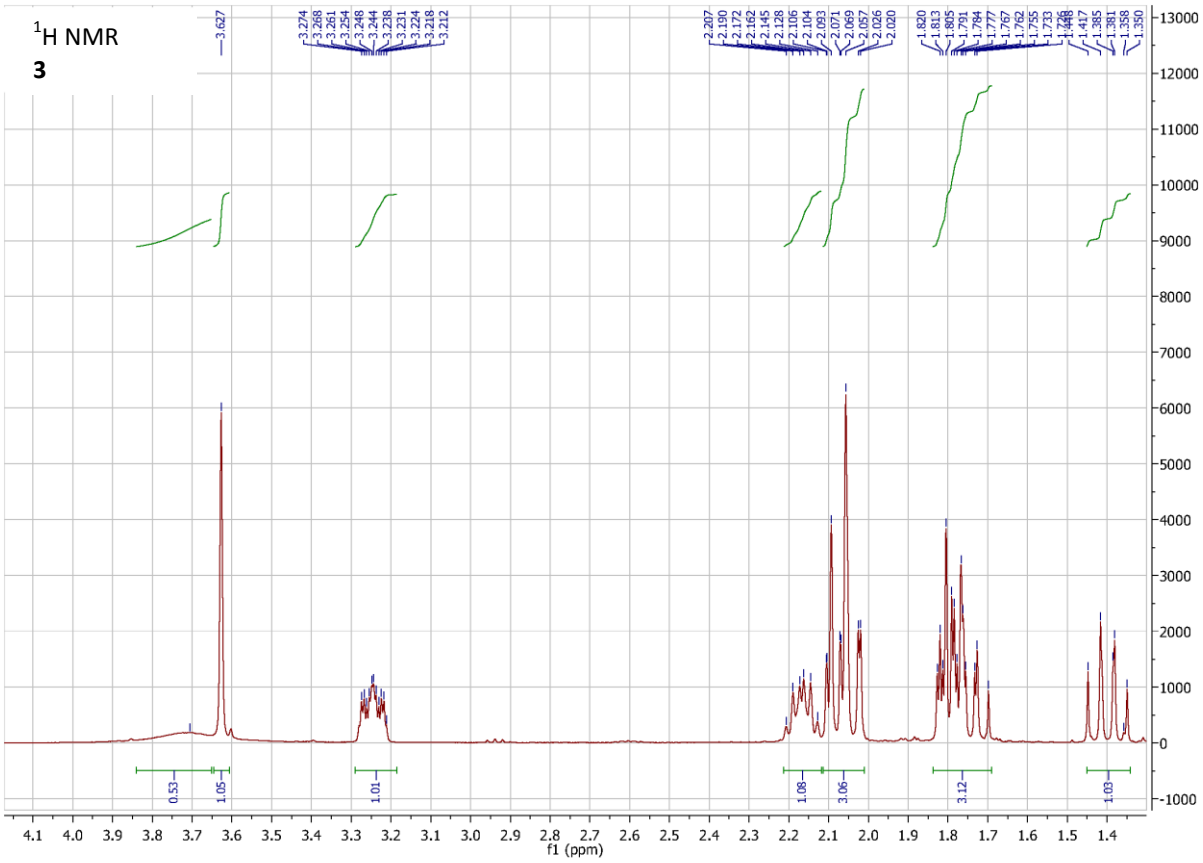


Fig. S20. ^{1}H NMR (400 MHz, $CDCl_3$) spectrum of compound **3** expanded in the region 1.3–4.2 ppm.

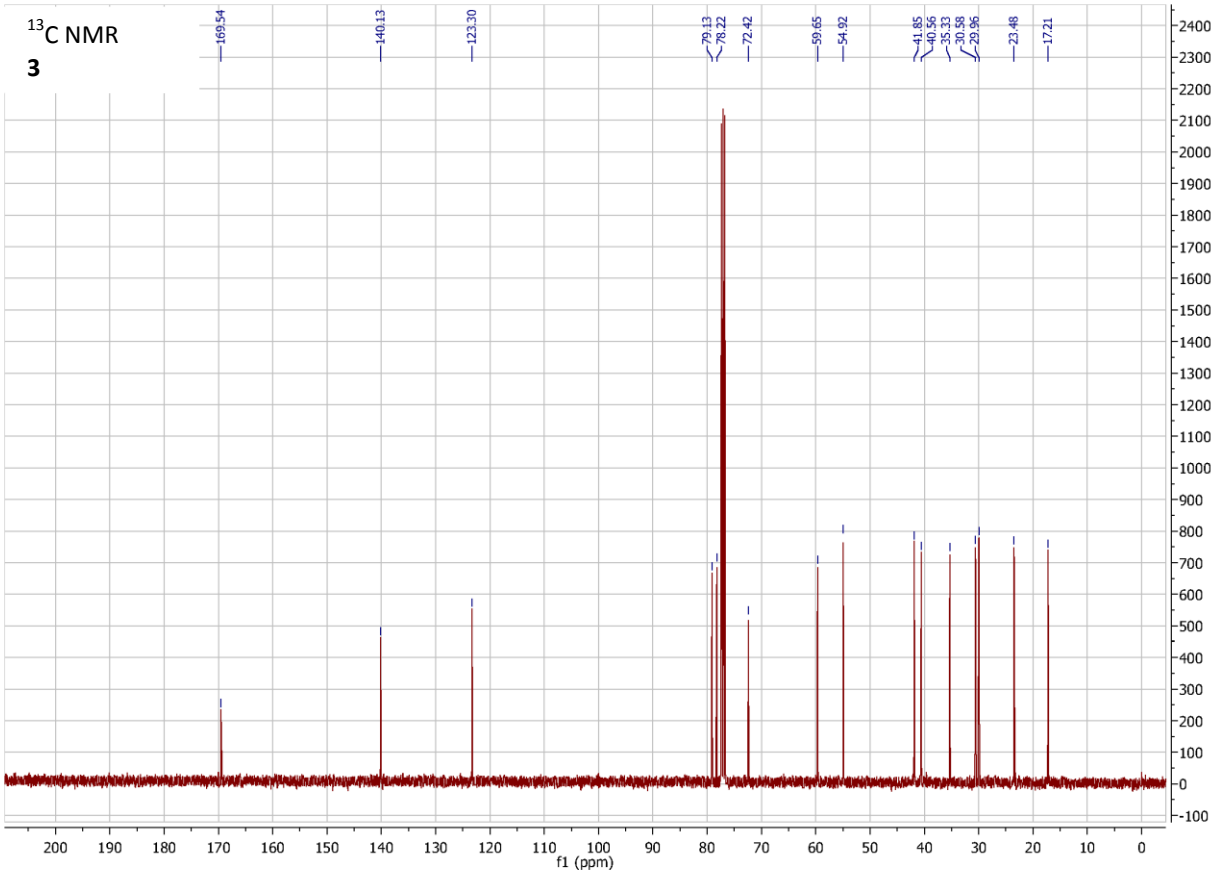


Fig. S21. ^{13}C NMR (100 MHz, $CDCl_3$) spectrum of compound **3**.

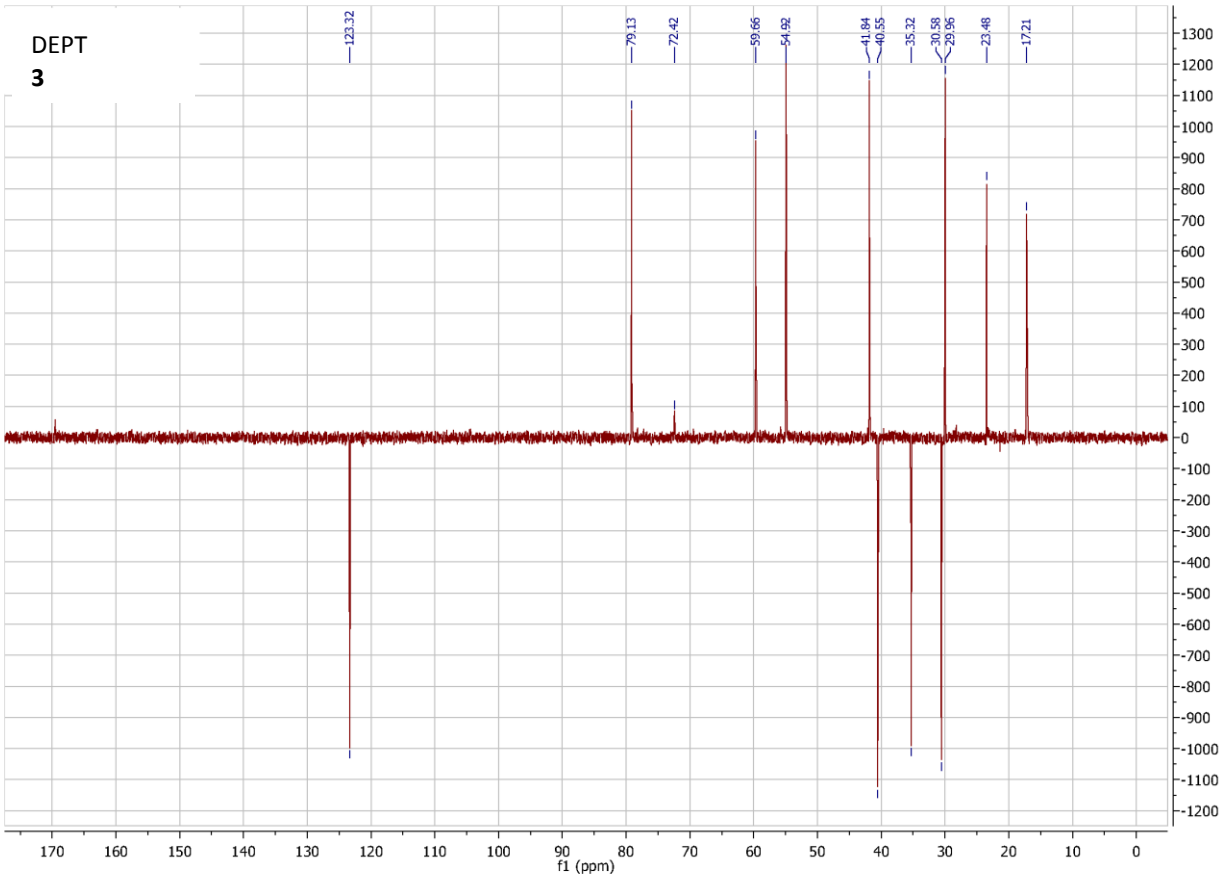


Fig. S22. DEPT spectrum of compound **3**.

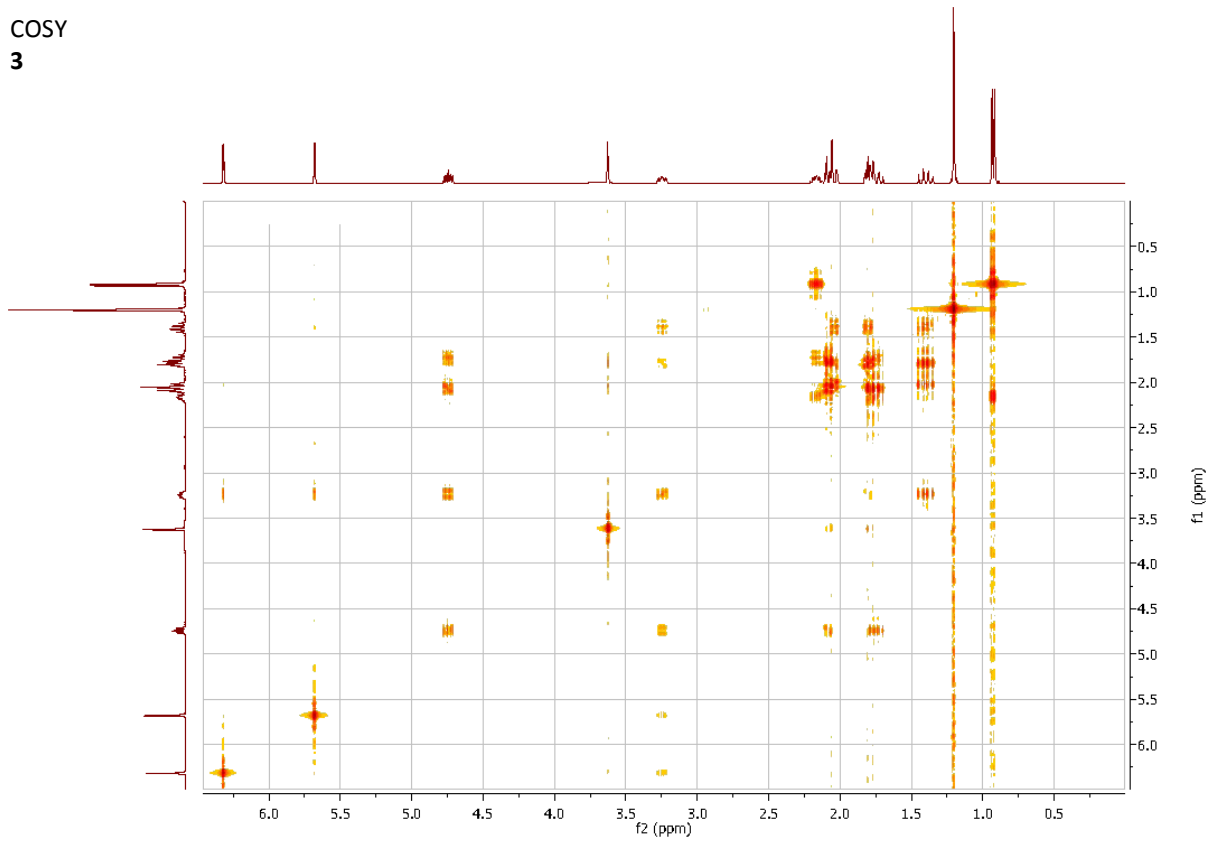


Fig. S23. $^{1}H–^{1}H$ COSY spectrum of compound **3**.

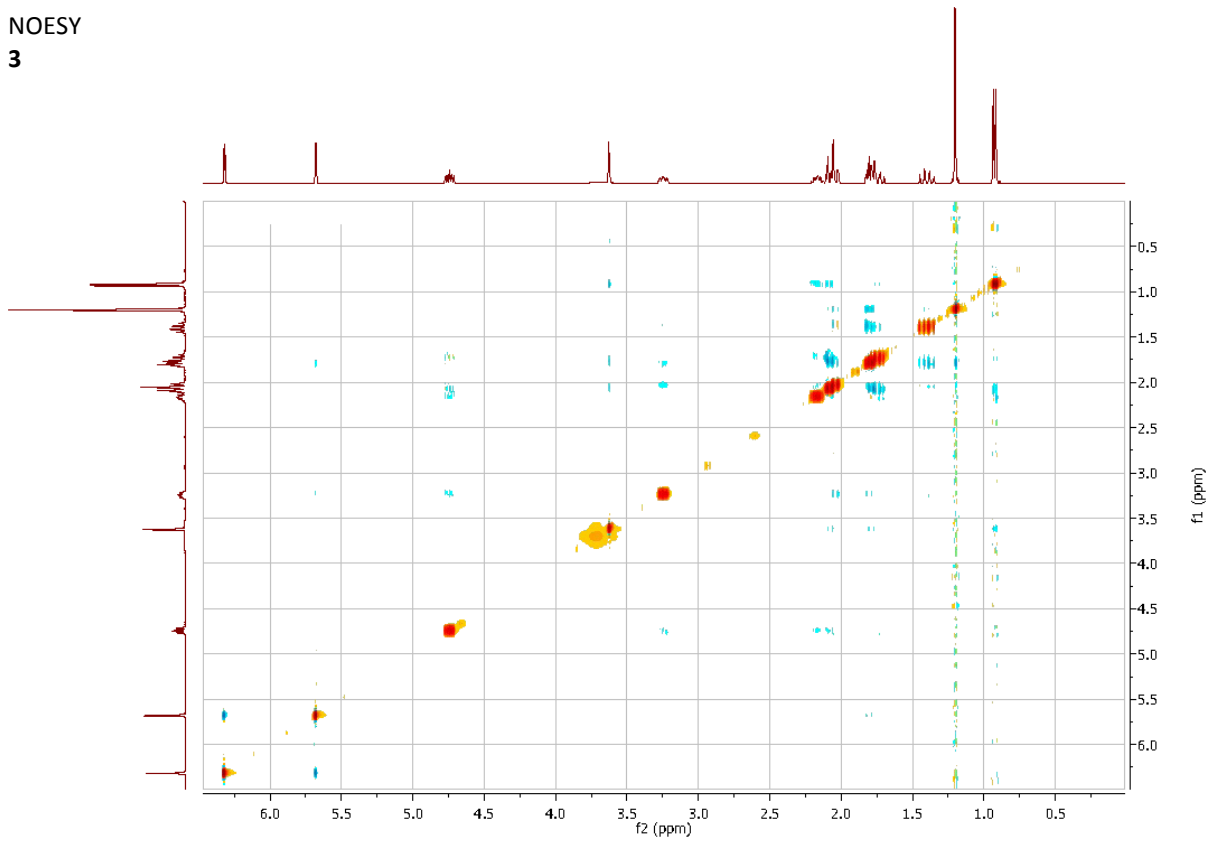


Fig. S24. NOESY spectrum of compound **3**.

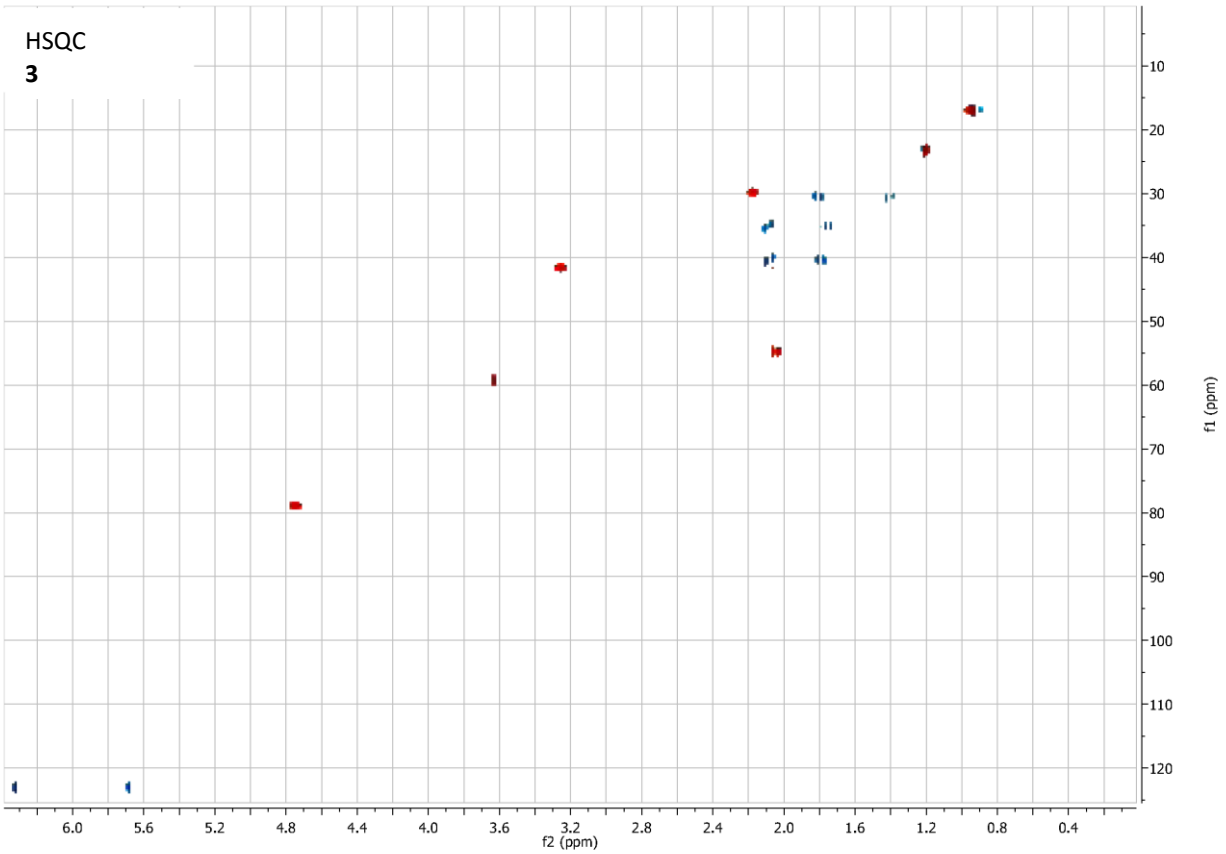


Fig. S25. HSQC spectrum of compound **3**.

HMBC
3

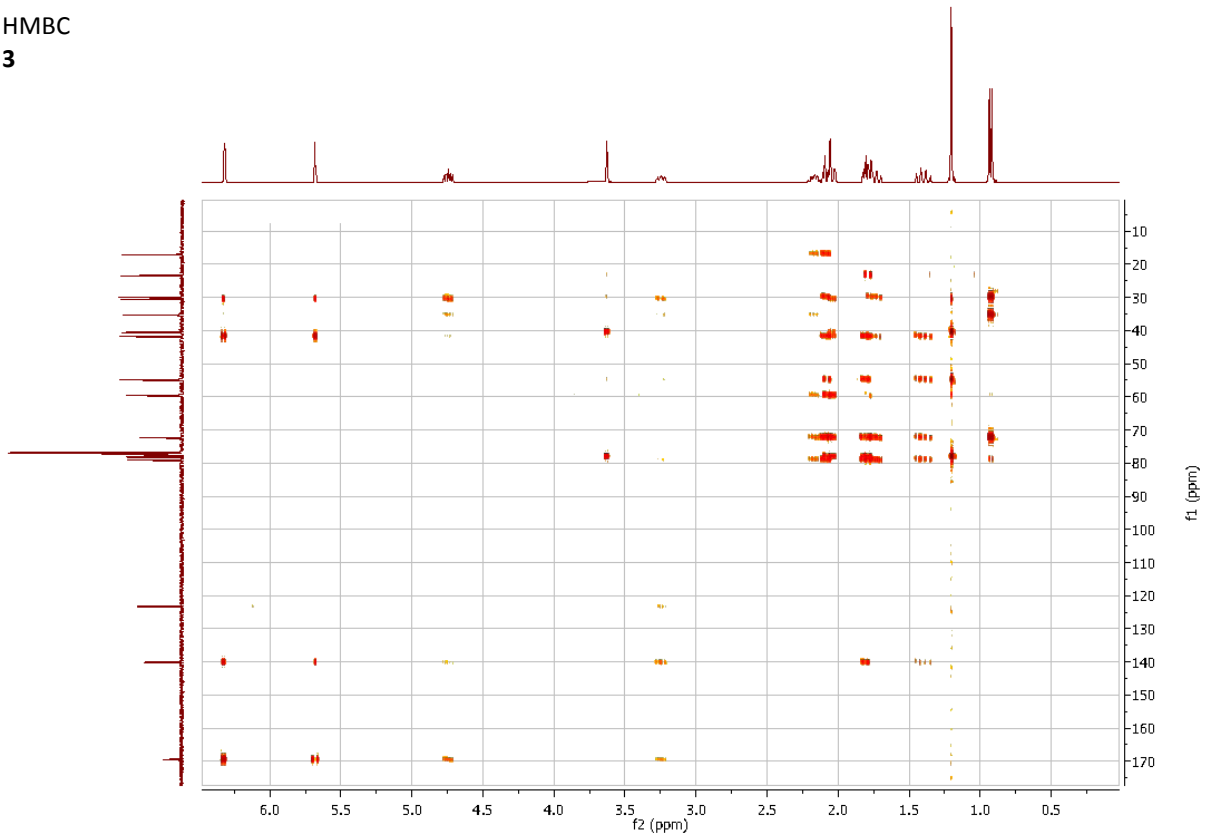
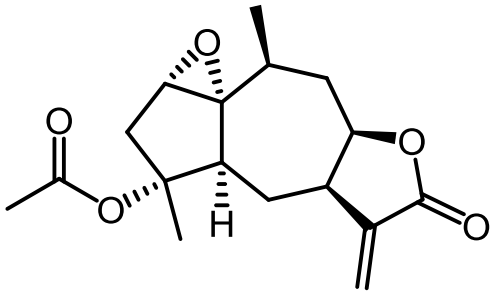


Fig. S26. HMBC spectrum of compound **3**.

*Calocephalin [4α-acetoxy-1α,2α-epoxy-5αH,10αH-11(13)-guaien-8β,12-olide] (**4**)*

Colorless crystals; mp 125–126 °C; $[\alpha]_D^{25}$ +14 (*c* 0.4, $CHCl_3$); UV (MeOH) (log ε) 212 (4.12) nm; IR (KBr) ν_{max} 3425, 2920, 1746, 1716, 1657, 1459, 1370, 1263, 1115, 1007 cm^{-1}; APCIMS: *m/z* 307 $[M + H]^+$ (23), 264 $[M + H - Ac]^+$ (16), 247 $[M + H - HOAc]^+$ (100), 229 $[M + H - HOAc - H_2O]^+$ (93); HRESIMS *m/z* 307.1540 (calcd for $C_{17}H_{23}O_5$, 307.1546).



Calocephalin (**4**)

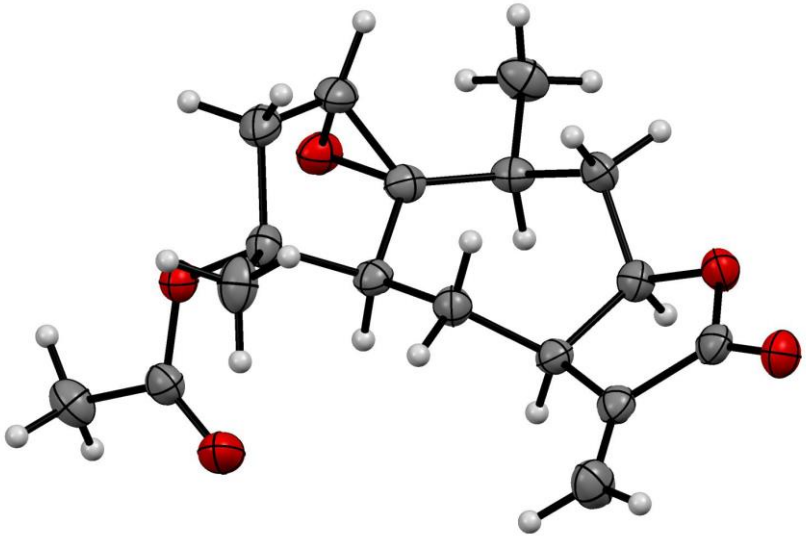


Fig. S27. Crystal structure of calocephalin (**4**) [ORTEP diagram] with displacement ellipsoids at 50% probability for non-H atoms.

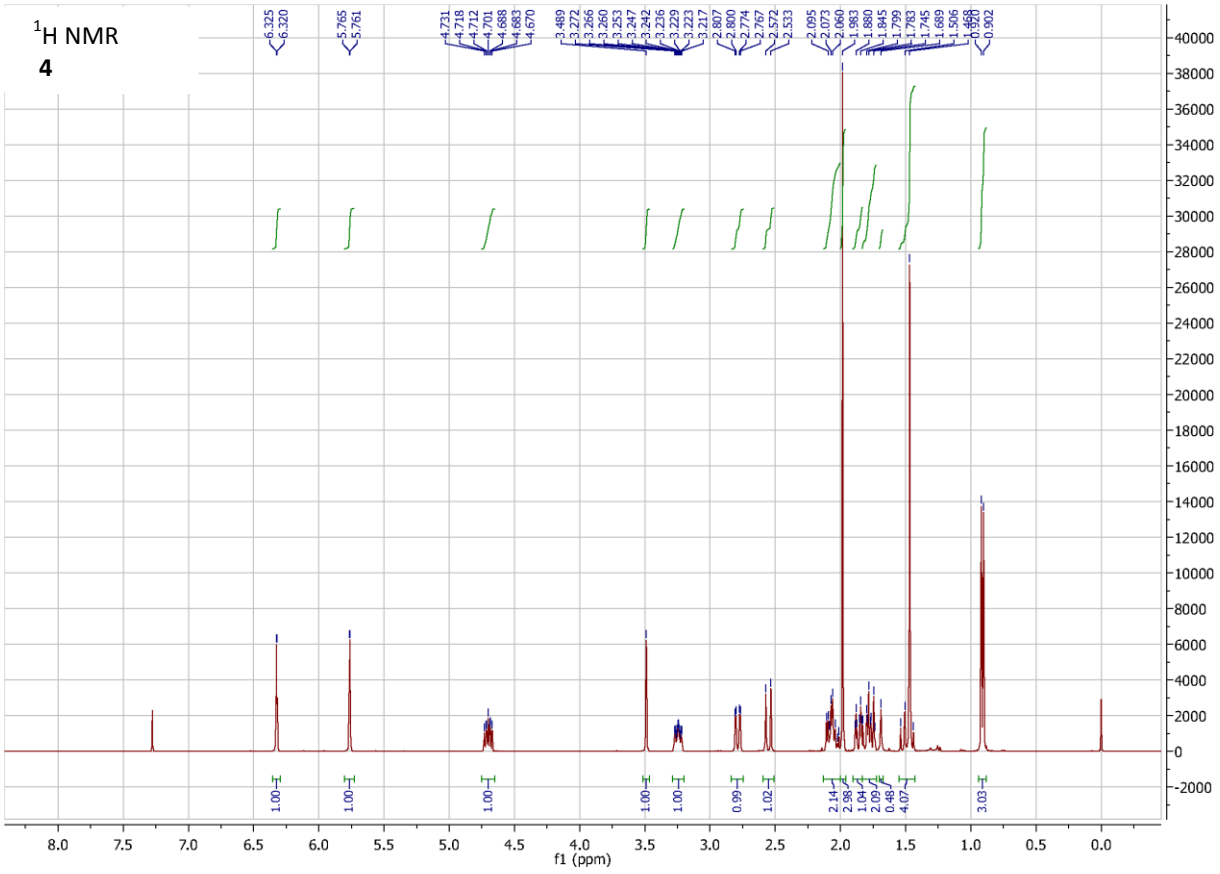


Fig. S28. ^{1}H NMR (400 MHz, $CDCl_3$) spectrum of calocephalin (**4**).

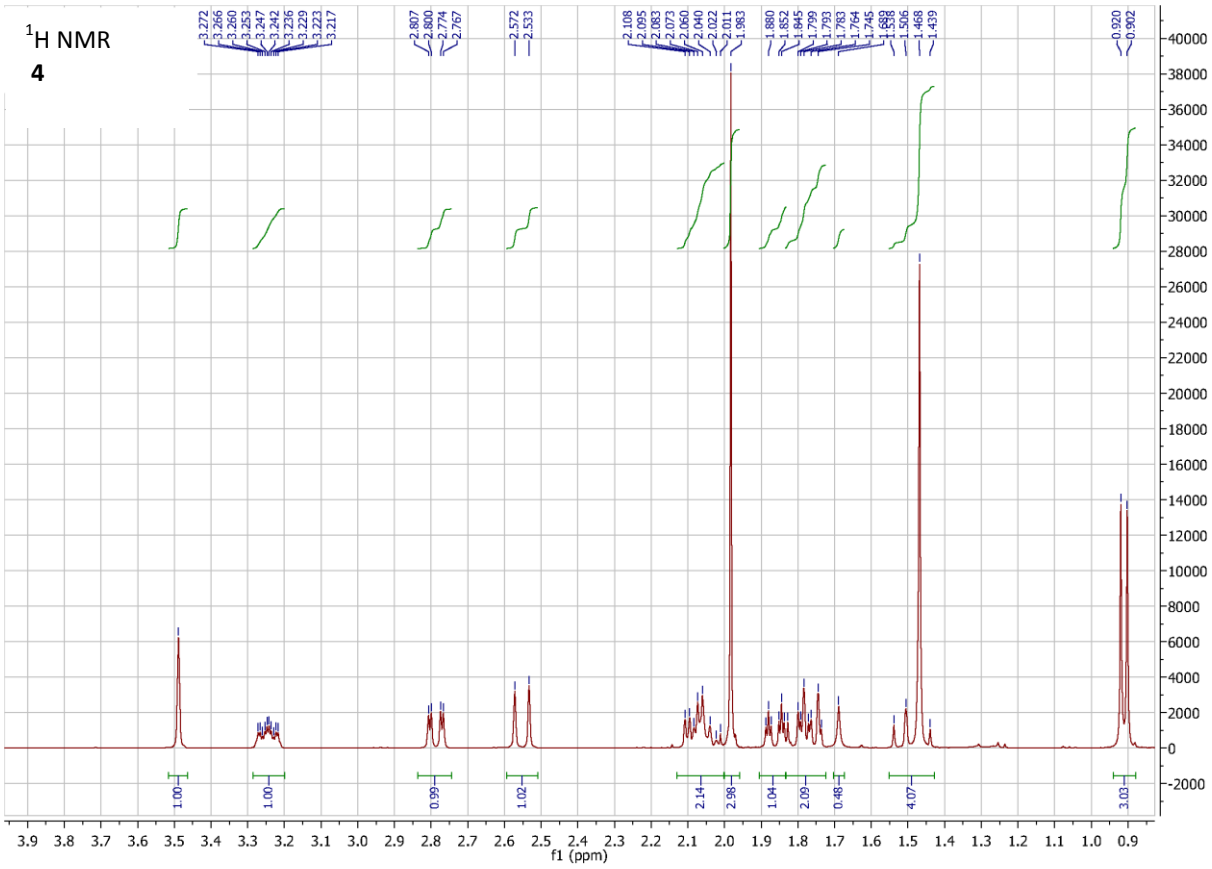


Fig. S29. ^{1}H NMR (400 MHz, $CDCl_3$) spectrum of calocephalin (**4**) expanded in the region 0.83–3.97 ppm.

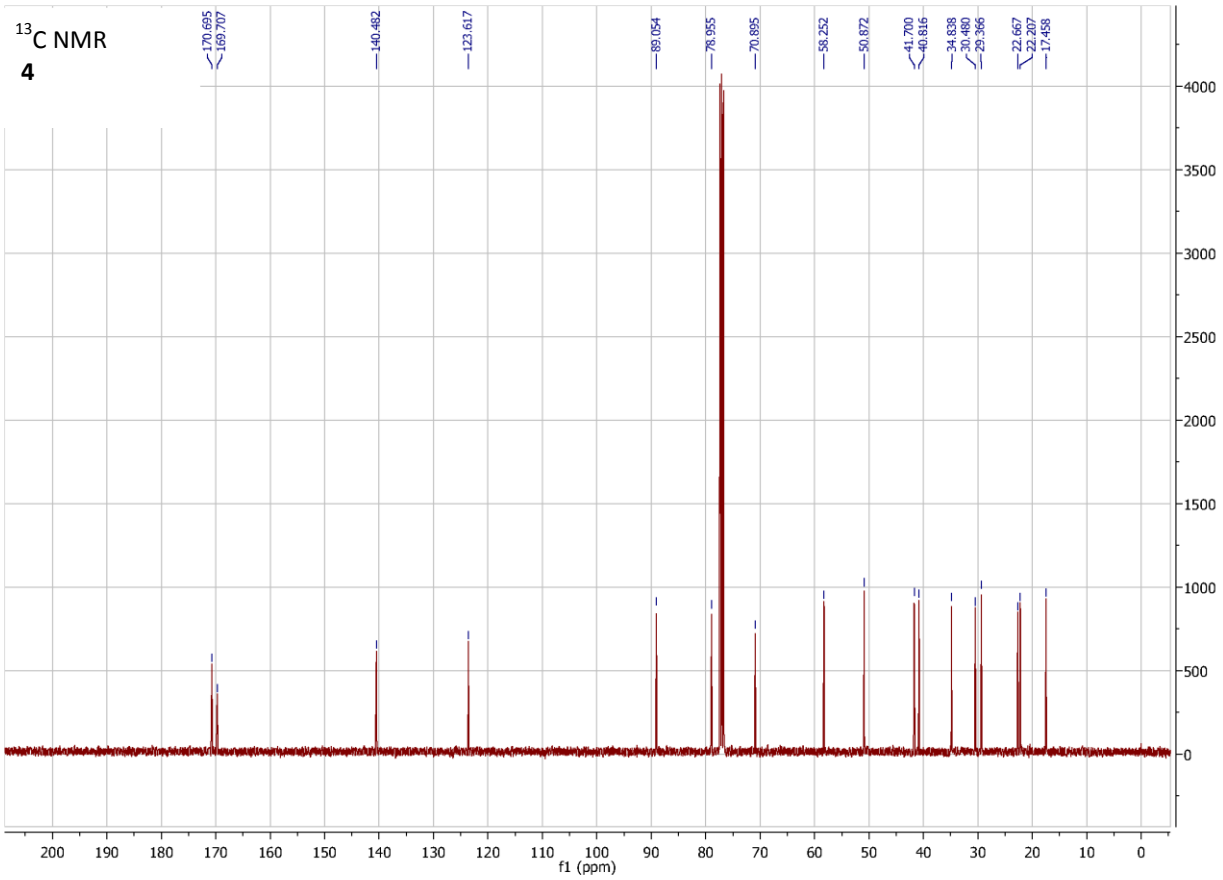


Fig. S30. ^{13}C NMR (100 MHz, $CDCl_3$) spectrum of calocephalin (**4**).

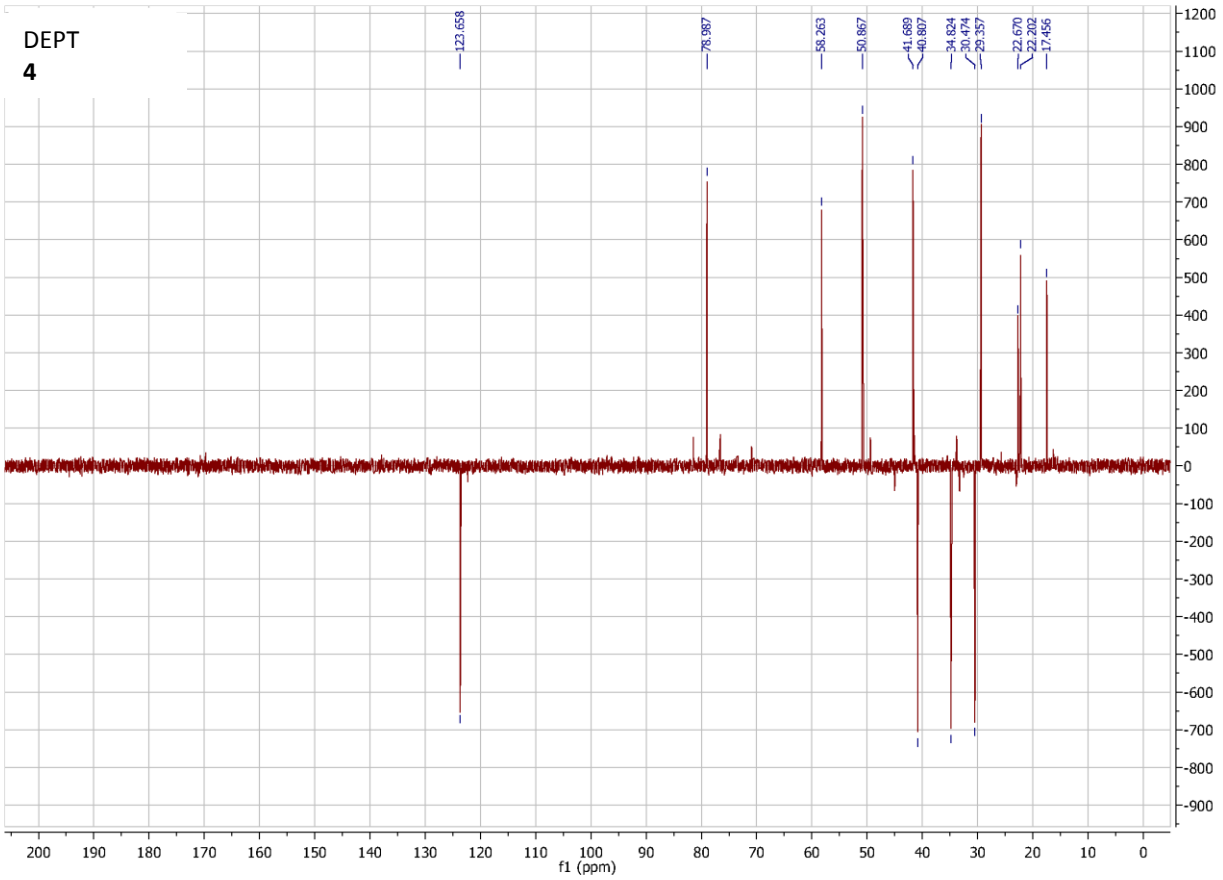


Fig. S31. DEPT spectrum of calocephalin (**4**).

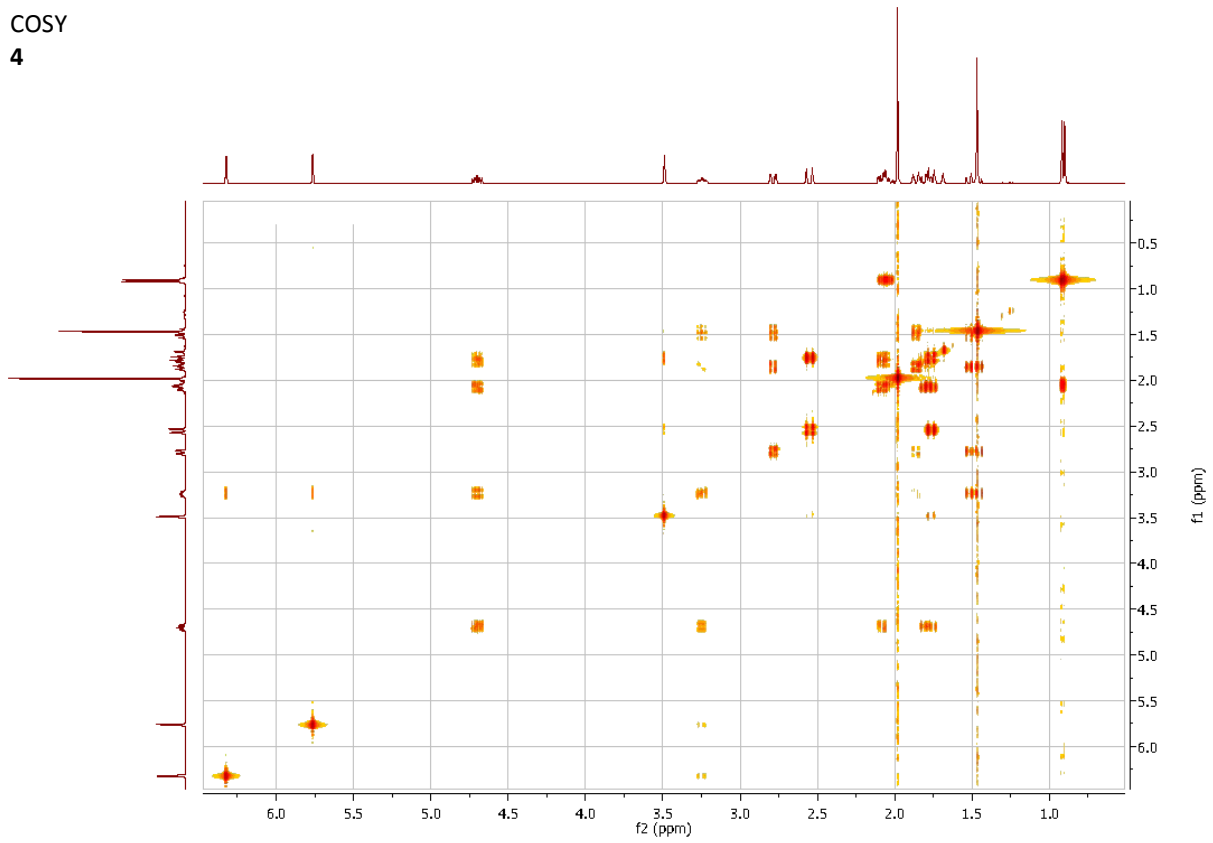


Fig. S32. $^{1}H–^{1}H$ COSY spectrum of calocephalin (**4**).

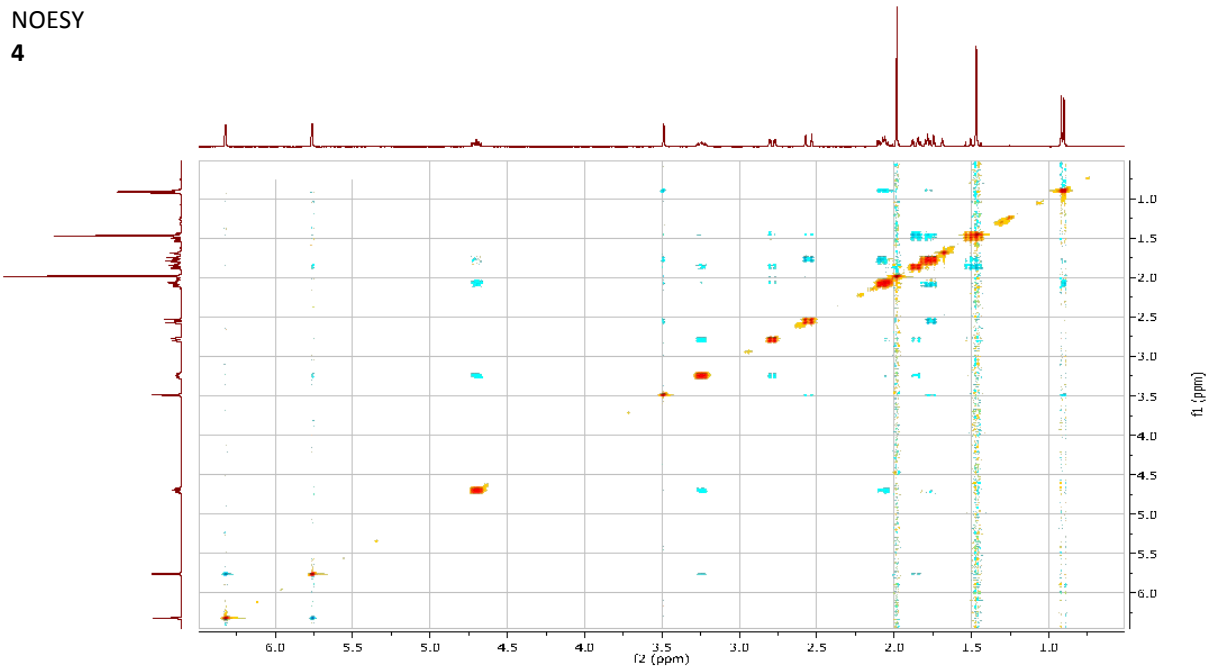


Fig. S33. NOESY spectrum of calocephalin (**4**).

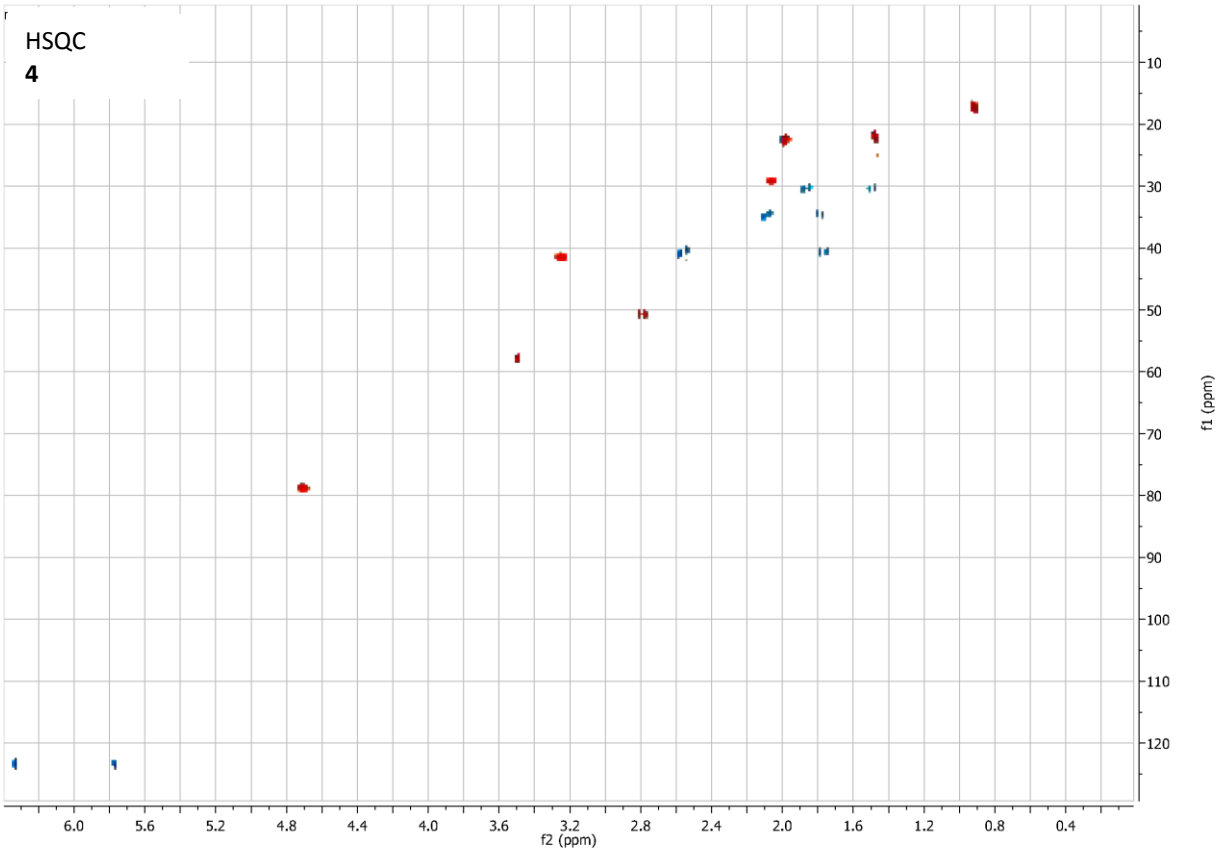


Fig. S34. HSQC spectrum of calocephalin (**4**).

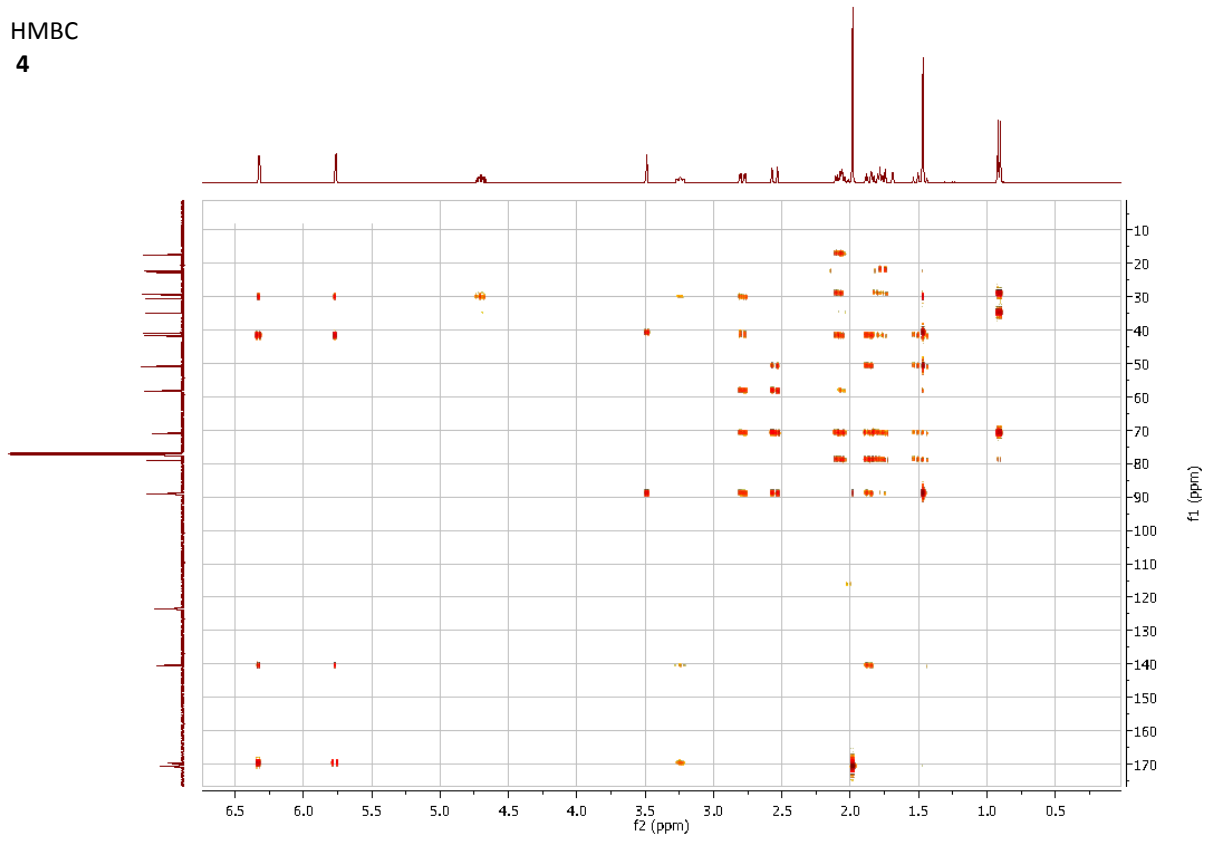


Fig. S35. HMBC spectrum of calocephalin (**4**).

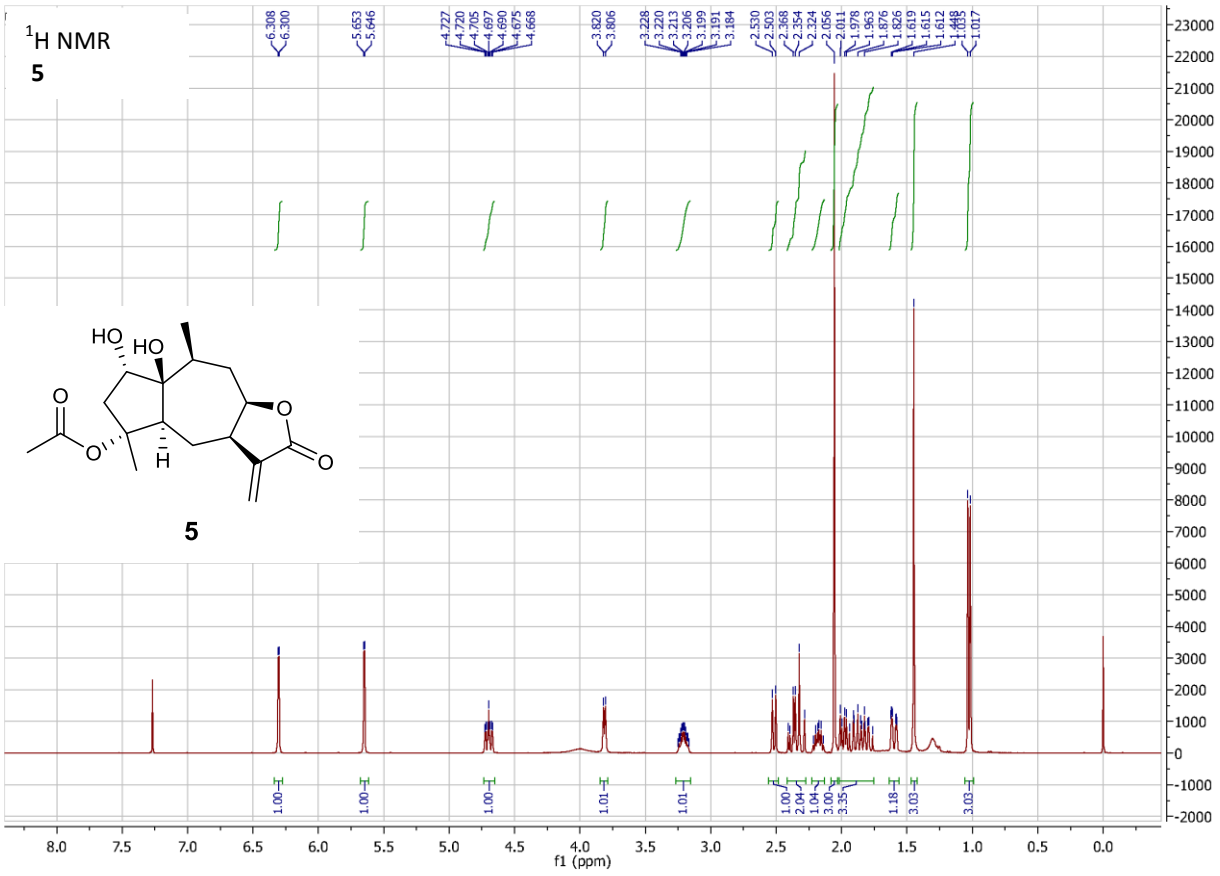


Fig. S36. ^{1}H NMR (400 MHz, $CDCl_3$) spectrum of the new compound **5.**

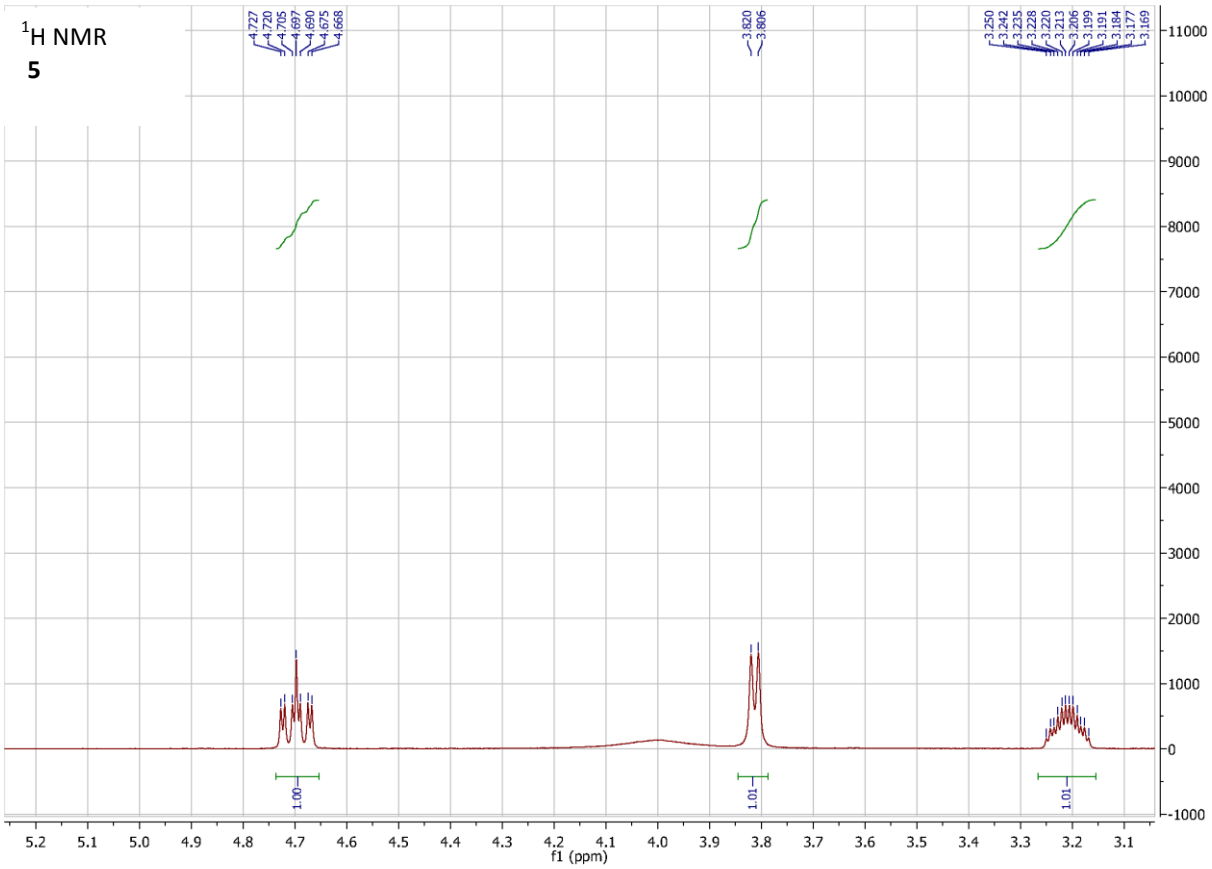


Fig. S37. ^{1}H NMR (400 MHz, $CDCl_3$) spectrum of the new compound **5** expanded in the region 3.04–5.26 ppm.

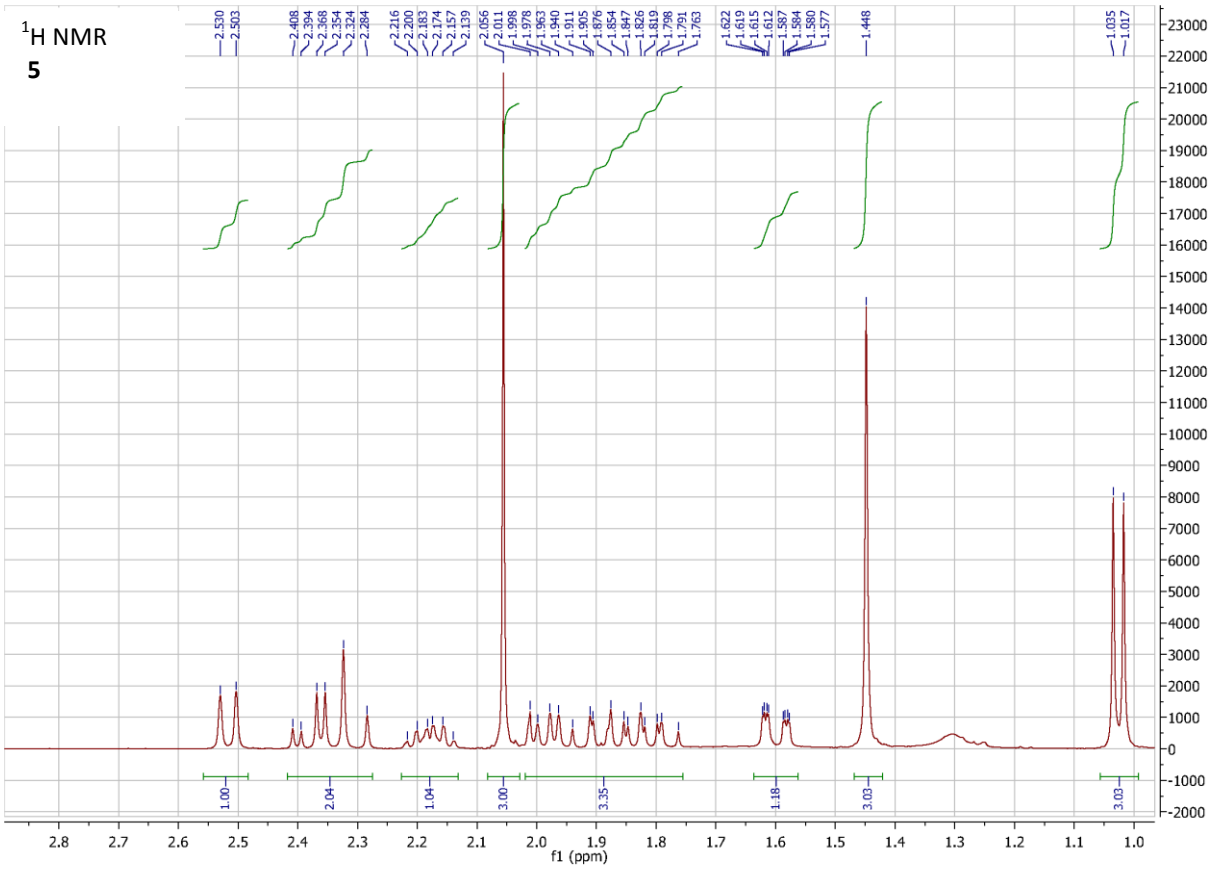


Fig. S38. ^{1}H NMR (400 MHz, $CDCl_3$) spectrum of the new compound **5** expanded in the region 0.9–3.0 ppm.

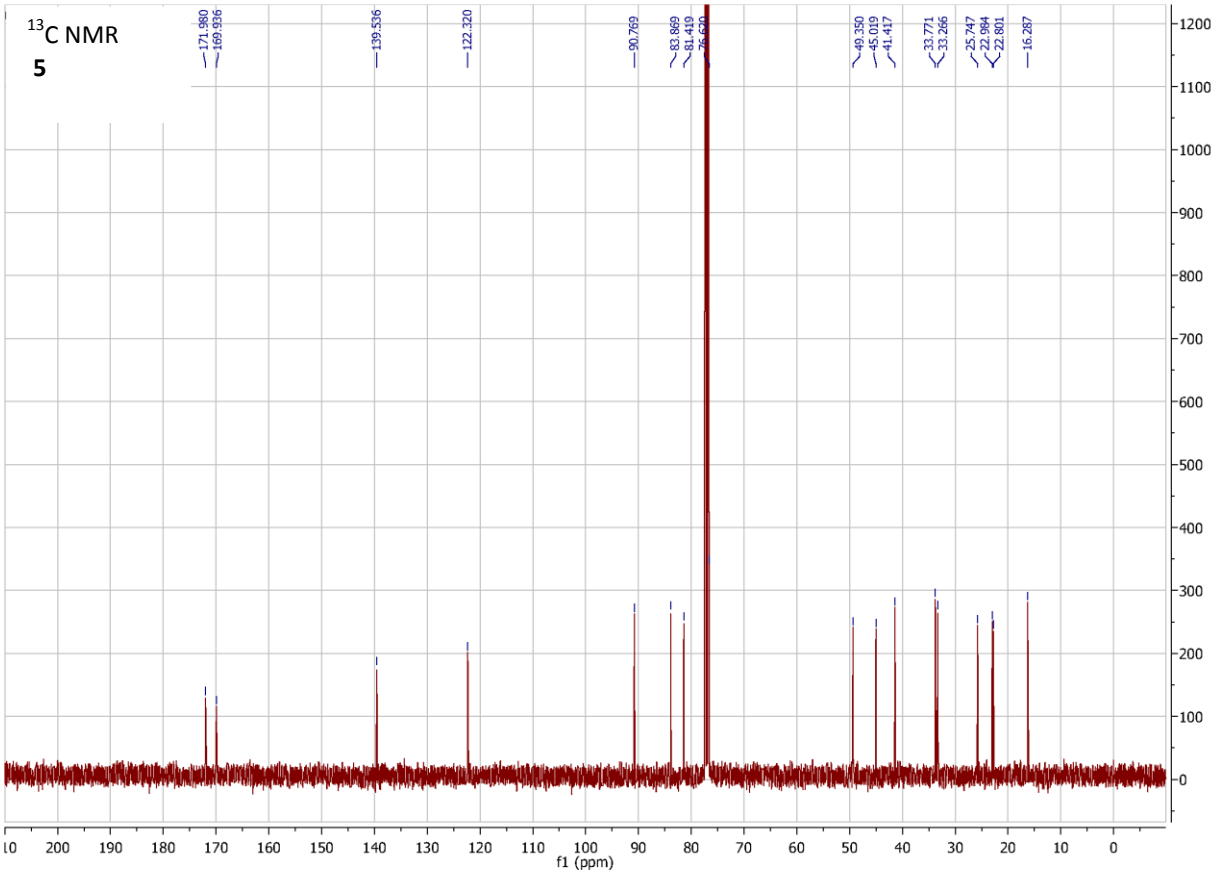


Fig. S39. ^{13}C NMR (100 MHz, $CDCl_3$) spectrum of the new compound **5**.

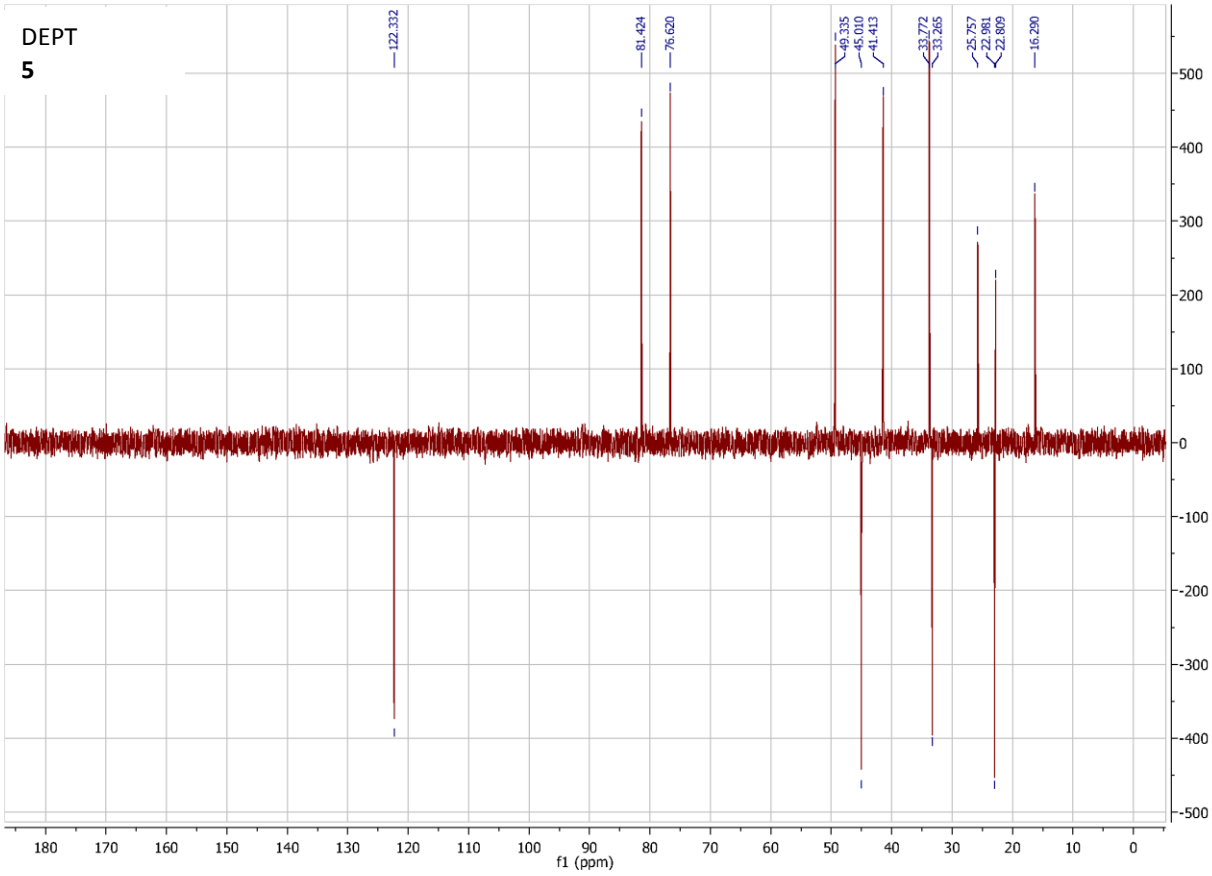


Fig. S40. DEPT spectrum of the new compound **5**.

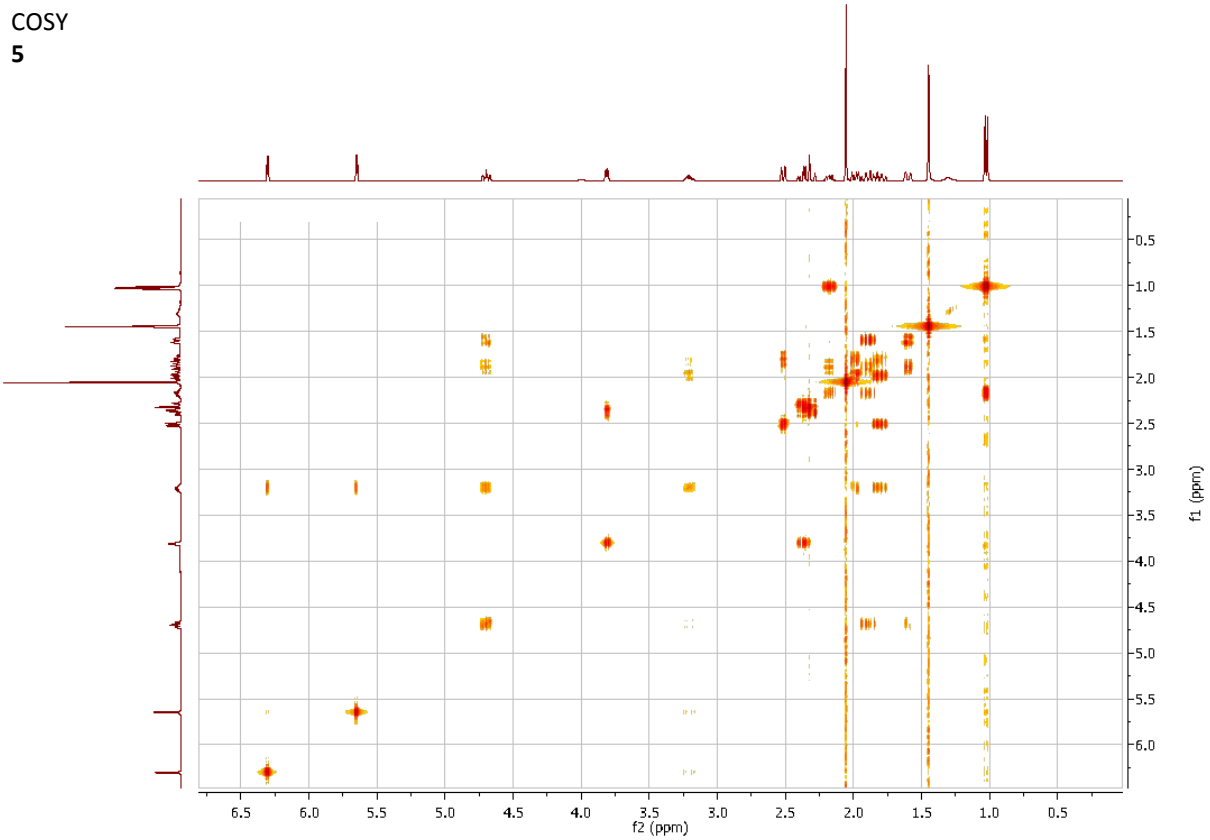


Fig. S41. $^{1}H–^{1}H$ COSY spectrum of the new compound **5**.

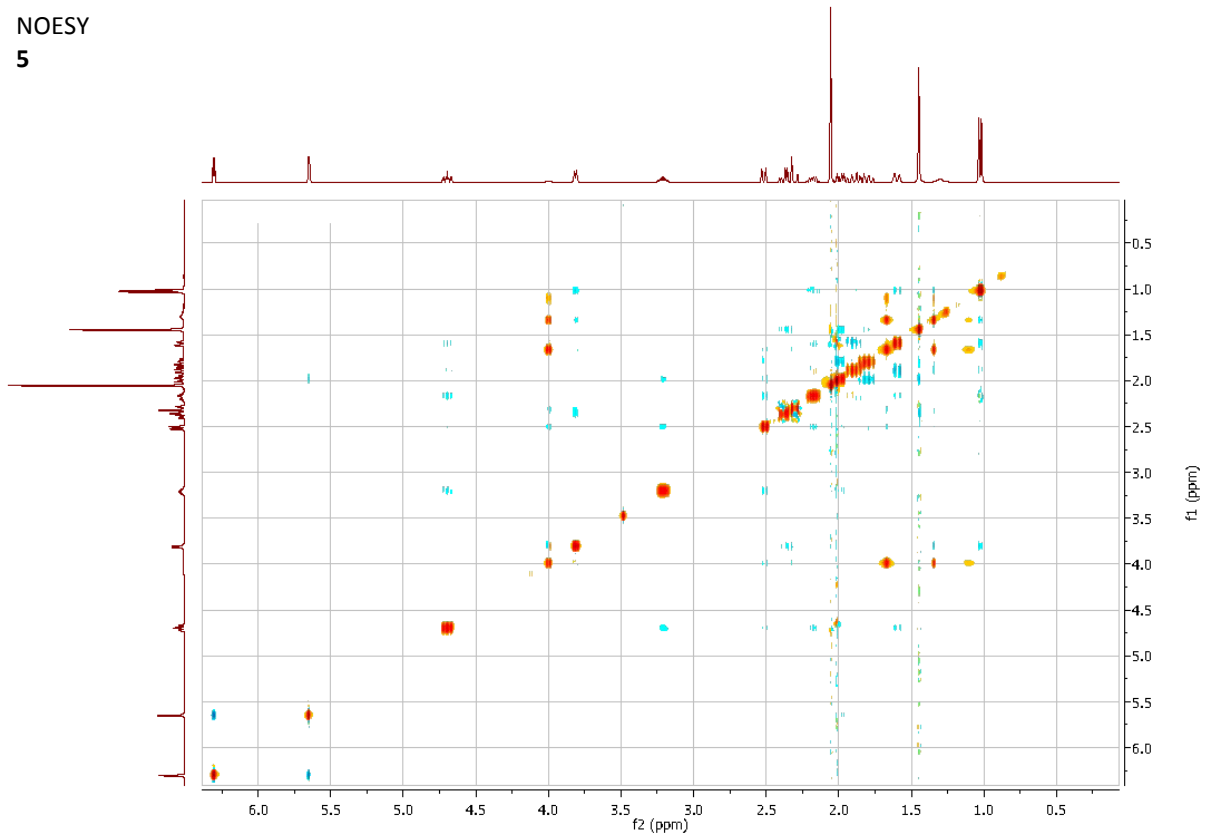


Fig. S42. NOESY spectrum of the new compound **5**.

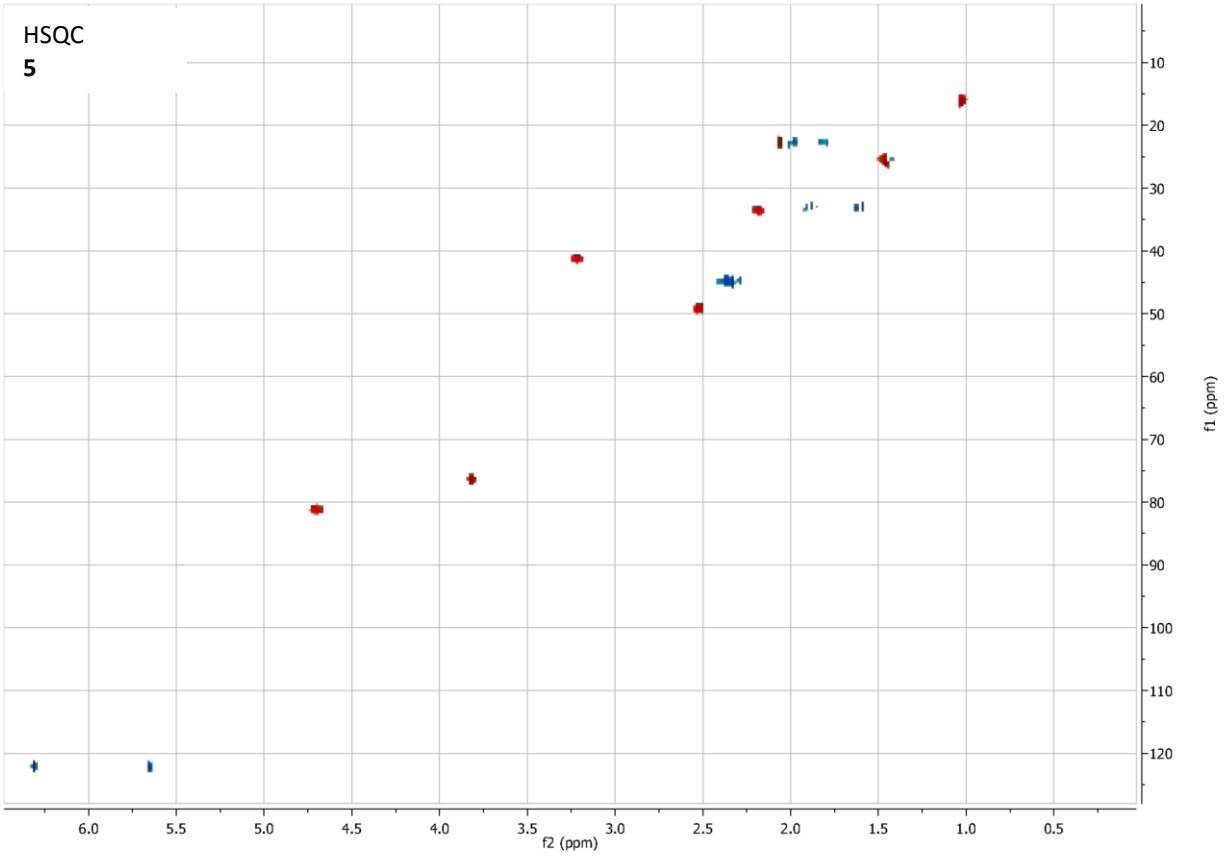


Fig. S43. HSQC spectrum of the new compound **5**.

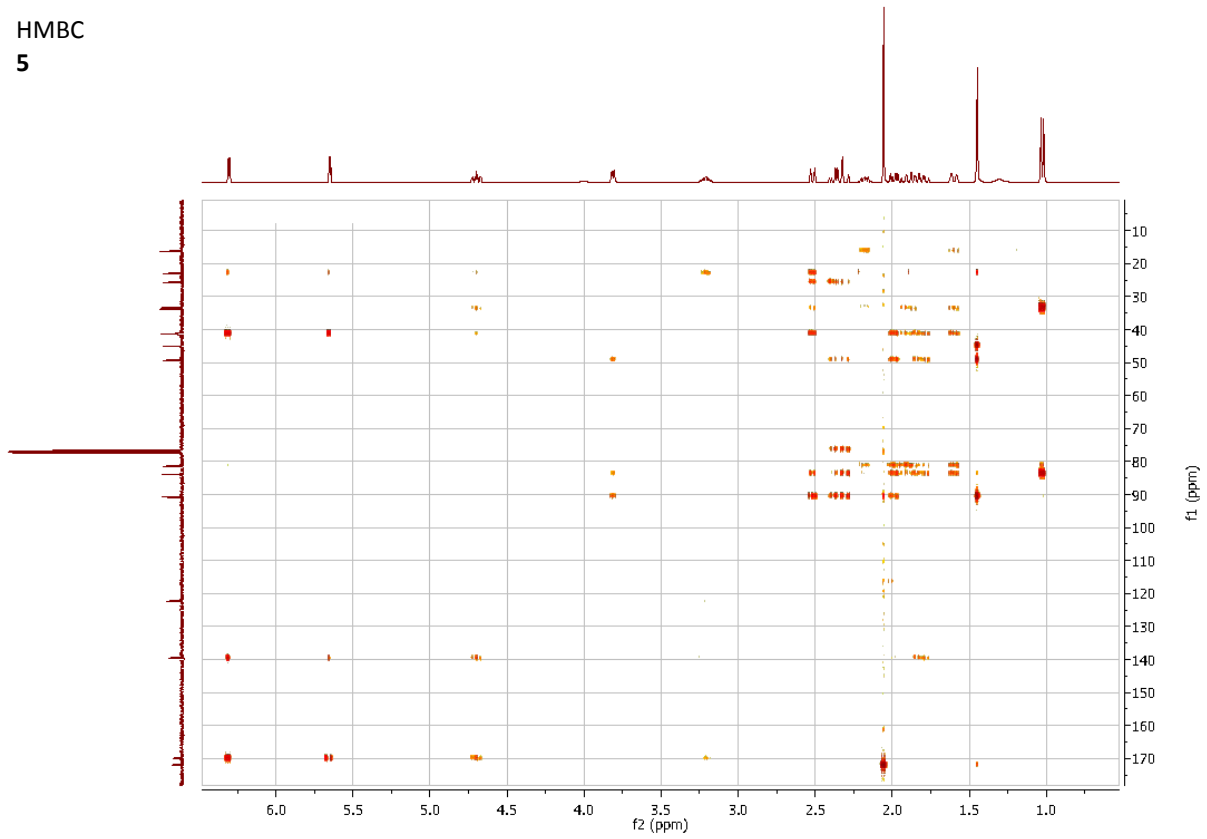


Fig. S44. HMBC spectrum of the new compound **5**.

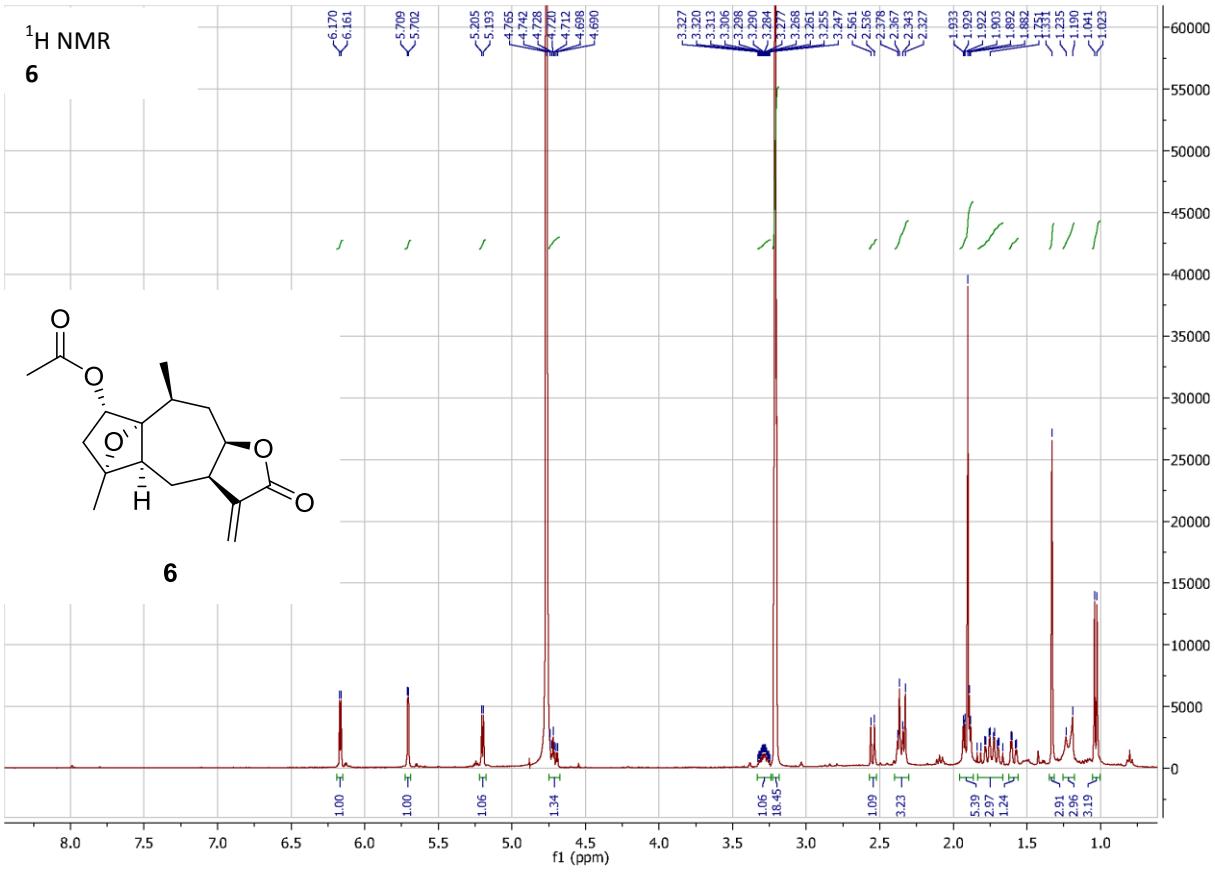


Fig. S45. ^{1}H NMR (400 MHz, methanol-d_4) spectrum of the new compound **6**.

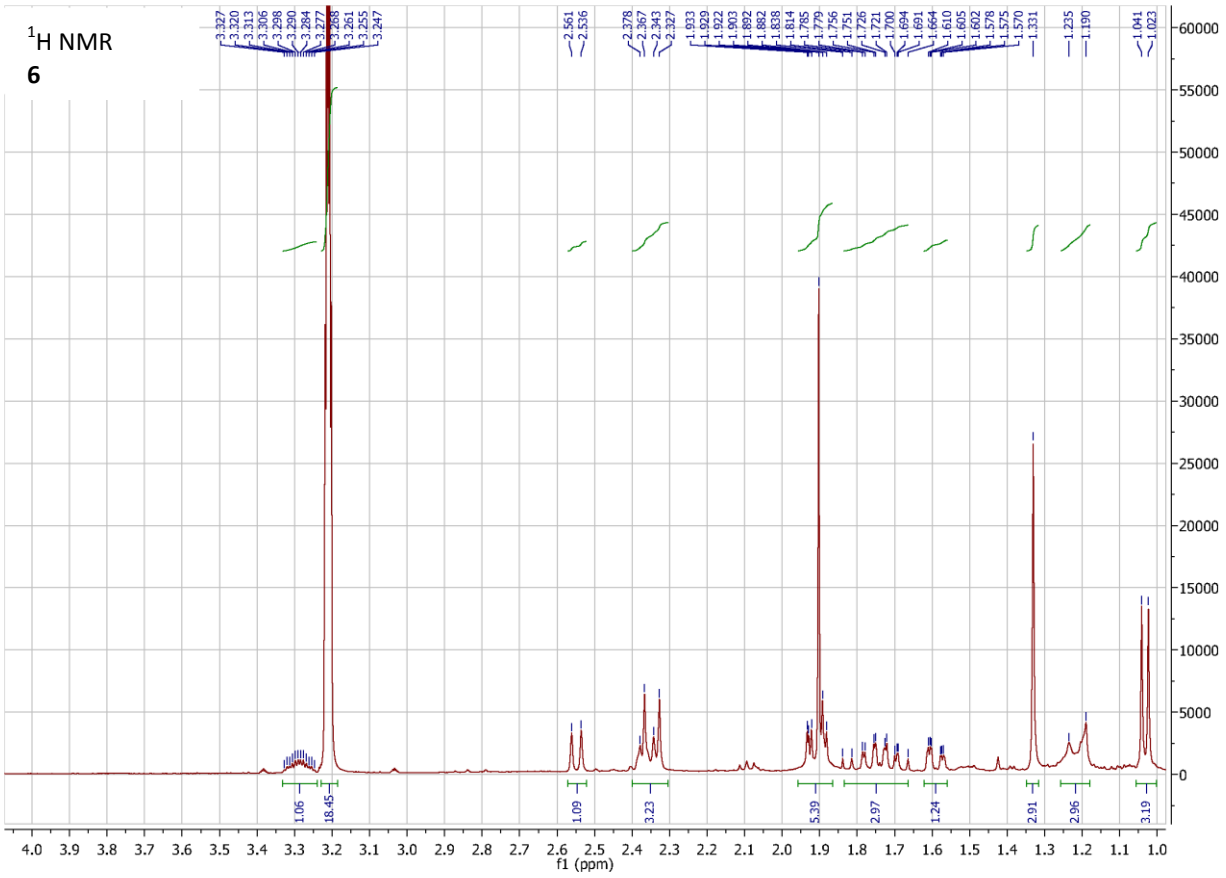


Fig. S46. ^{1}H NMR (400 MHz, methanol-d_4) spectrum of the new compound **6** expanded in the region 0.95–4.15 ppm.

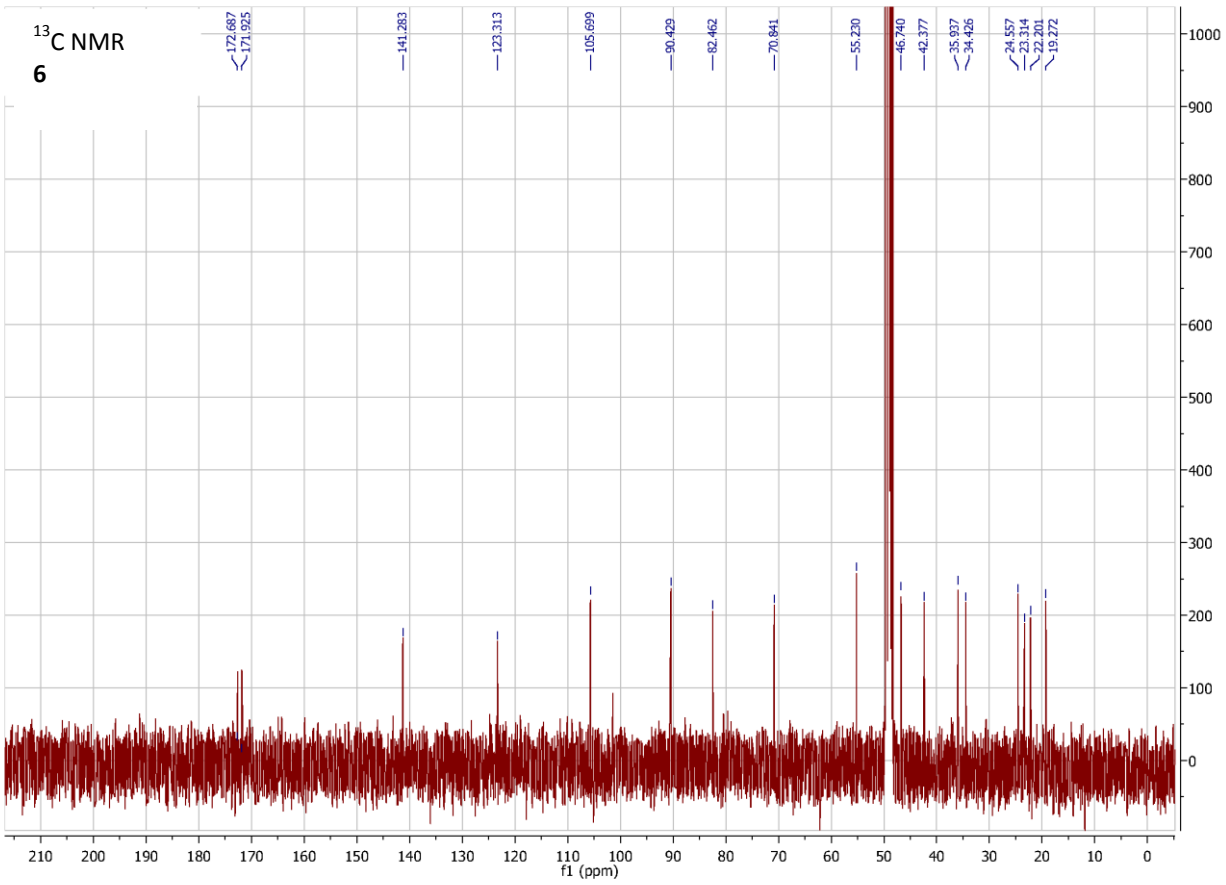


Fig. S47. ^{13}C NMR (100 MHz, methanol-d_4) spectrum of the new compound **6**.

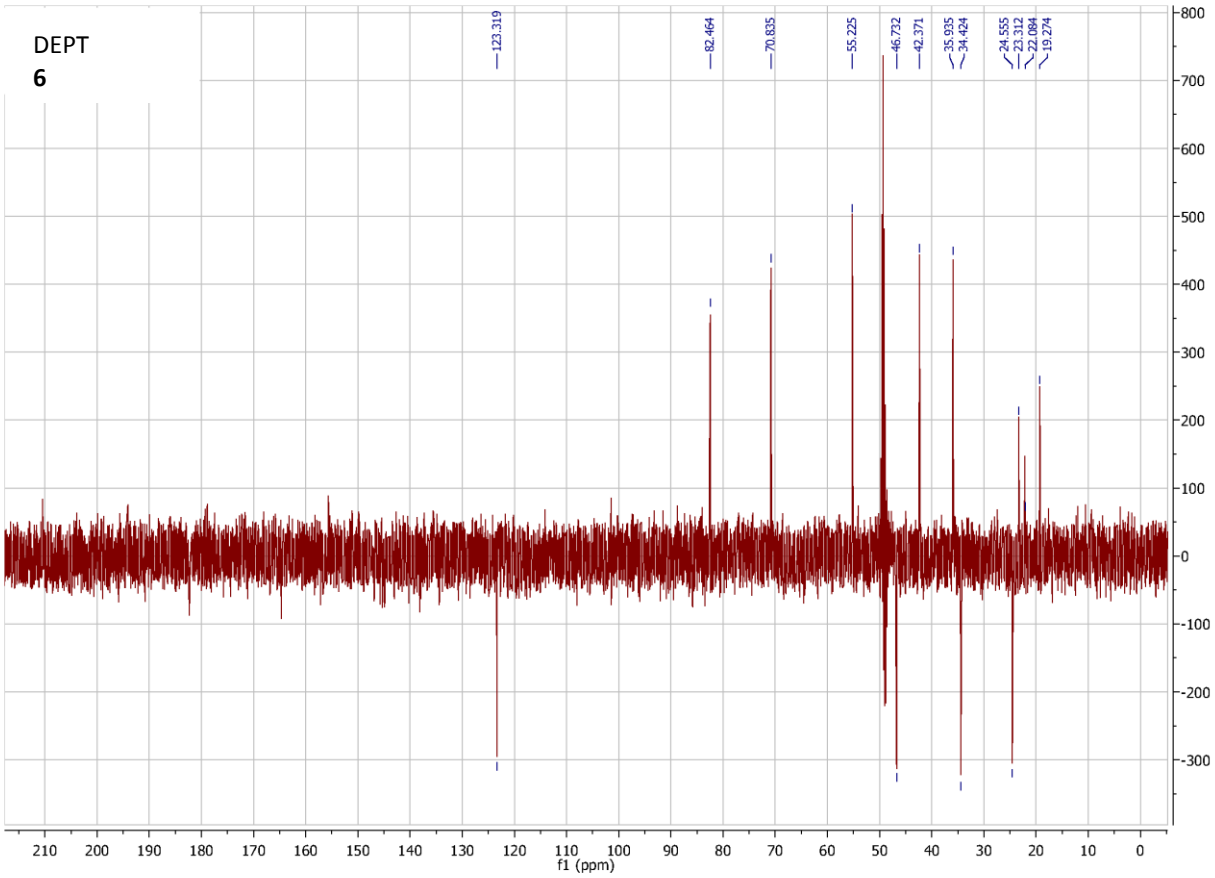


Fig. S48. DEPT spectrum of the new compound **6**.

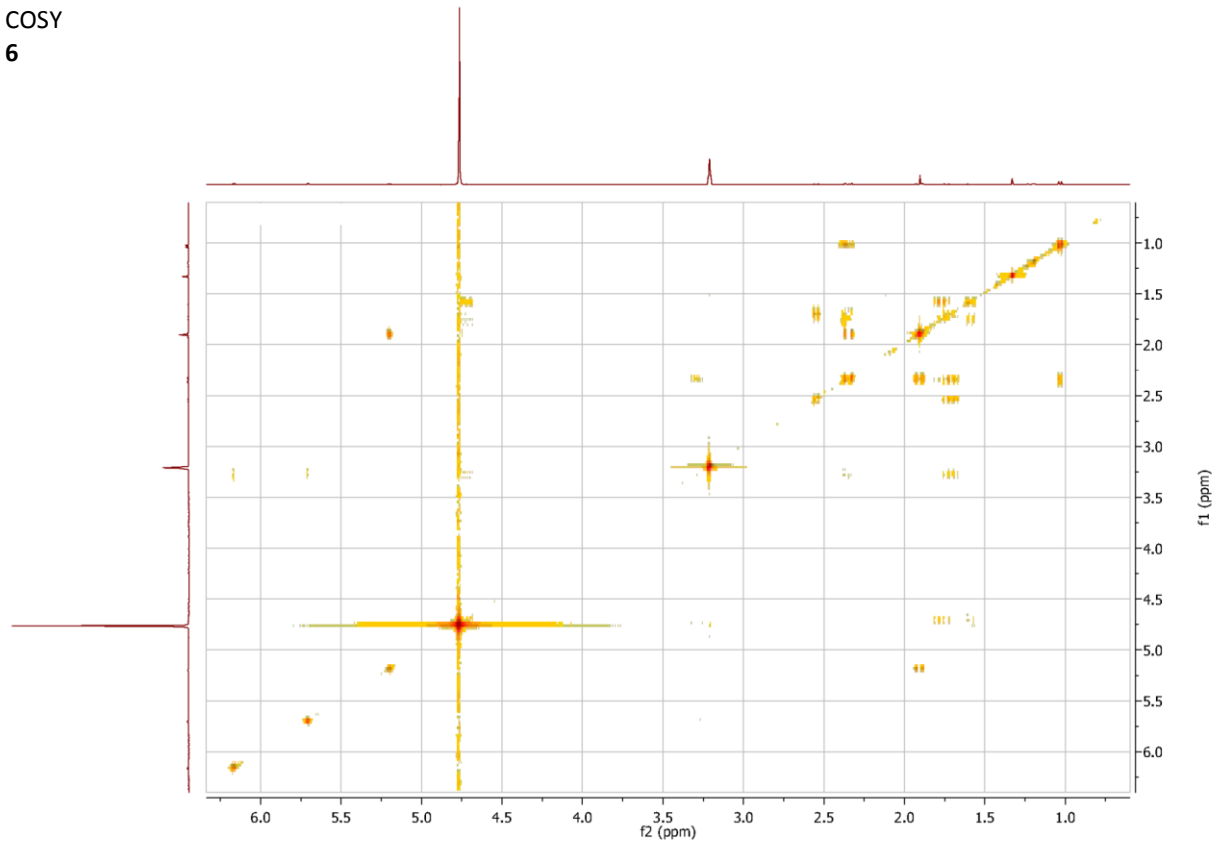


Fig. S49. $^{1}H–^{1}H$ COSY spectrum of the new compound **6**.

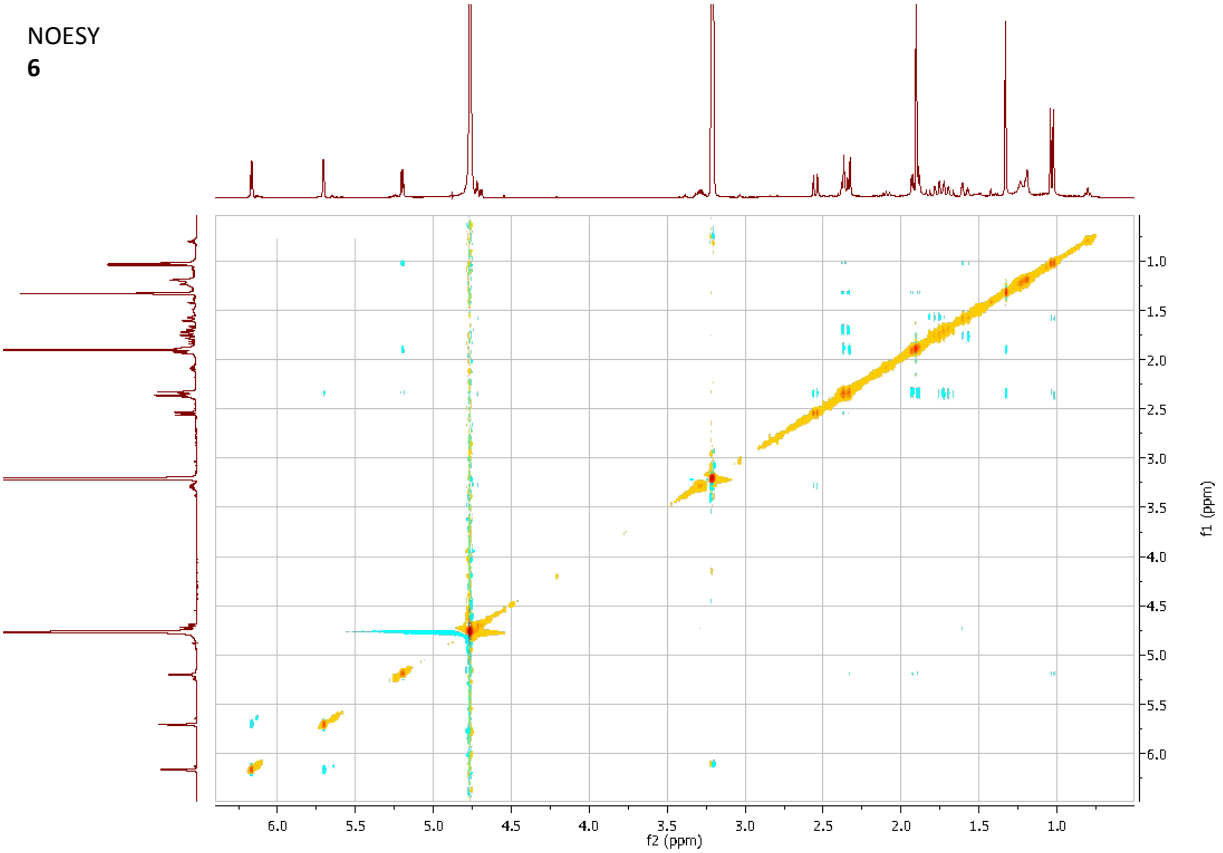


Fig. S50. NOESY spectrum of the new compound **6**.

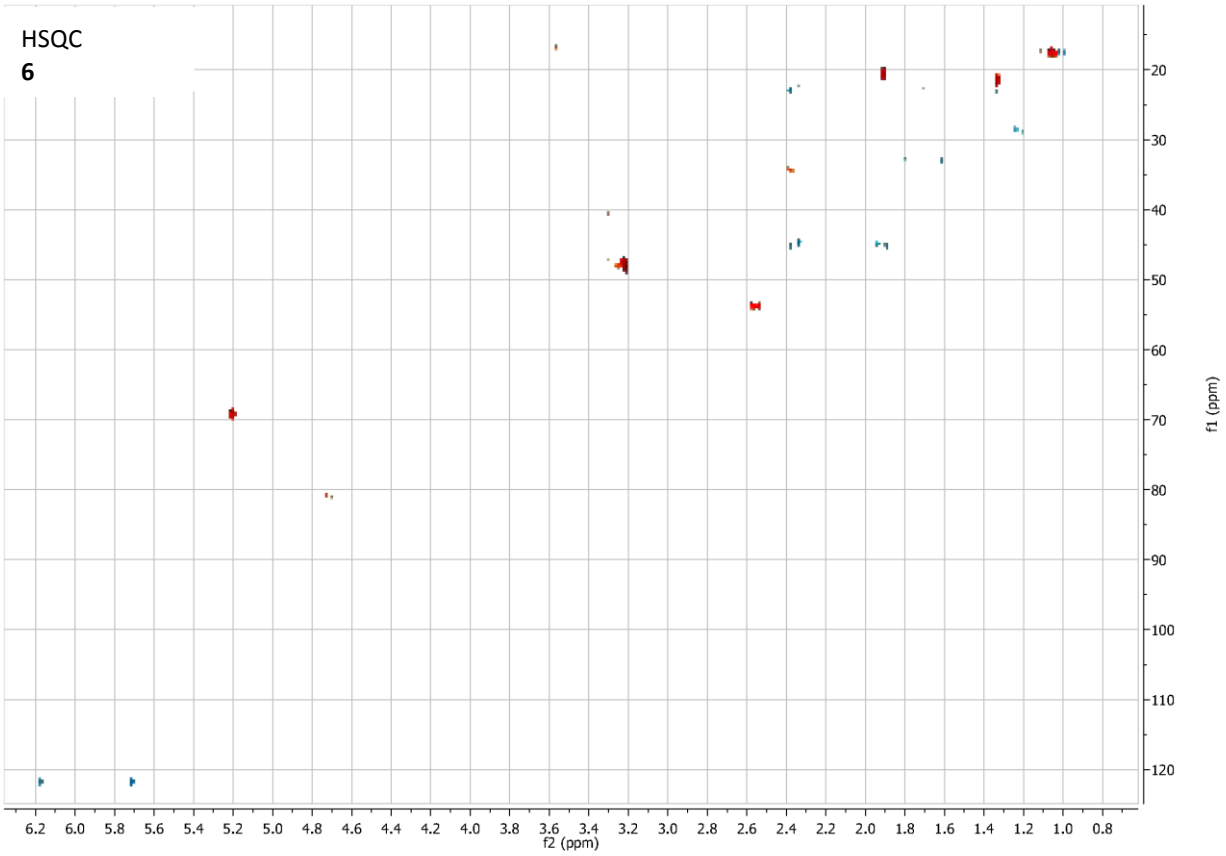


Fig. S51. HSQC spectrum of the new compound **6**.

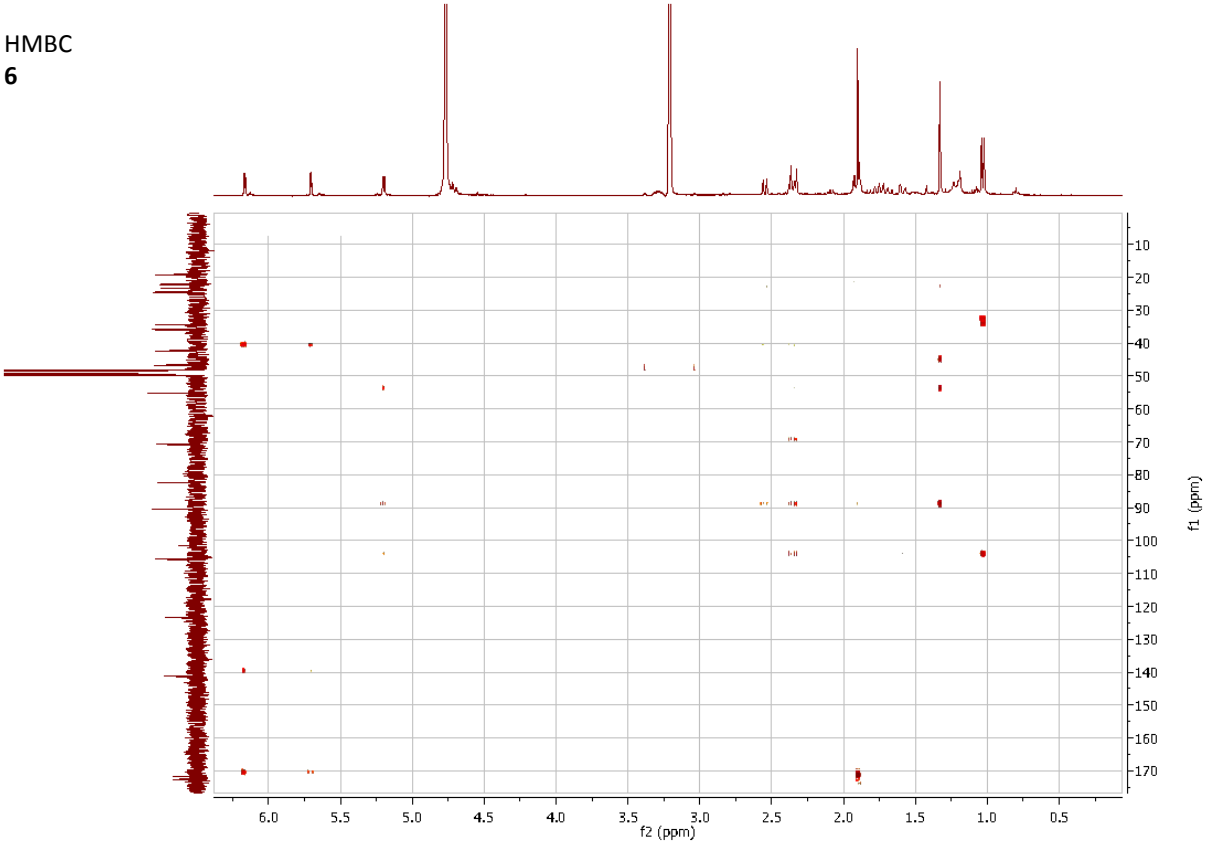
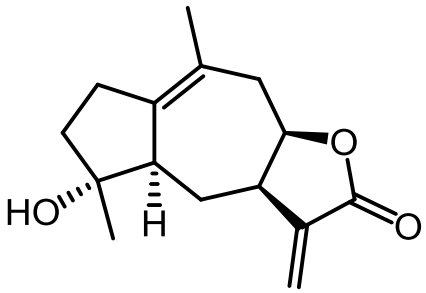


Fig. S52. HMBC spectrum of the new compound **6**.

*Pseudoivalin [4α-hydroxy-5αH-10,11(13)-guaidien-8β,12-olide] (**7**)*

Colorless crystals; mp 121–122 °C; $[\alpha]_D^{25}$ –146 (*c* 0.4, $CHCl_3$); UV (MeOH) λ_{max} (log ε) 214 (4.15) nm; IR (KBr) ν_{max} 3578, 3342, 2971, 1772, 1754, 1640, 1308, 1105 cm^{-1}; APCIMS: *m/z* 249 $[M + H]^+$ (21), 231 $[M + H - H_2O]^+$ (100); HRESIMS *m/z* 249.1487 (calcd for $C_{15}H_{21}O_3$, 249.1491).



Pseudoivalin (**7**)

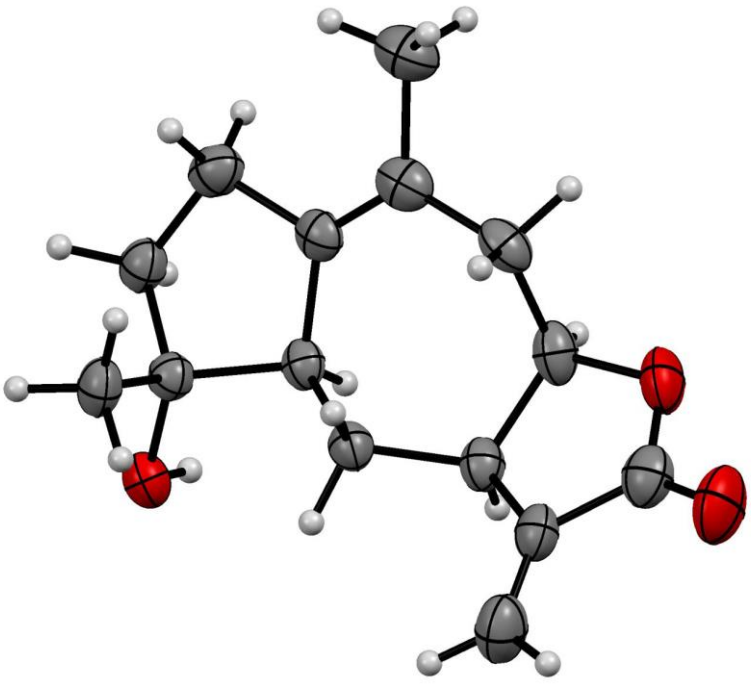


Fig. S53. Crystal structure of pseudoivalin (**7**) [ORTEP diagram] with displacement ellipsoids at 50% probability for non-H atoms.

Fig. S54. ^{1}H NMR (400 MHz, $CDCl_3$) spectrum of pseudoivalin (**7**).

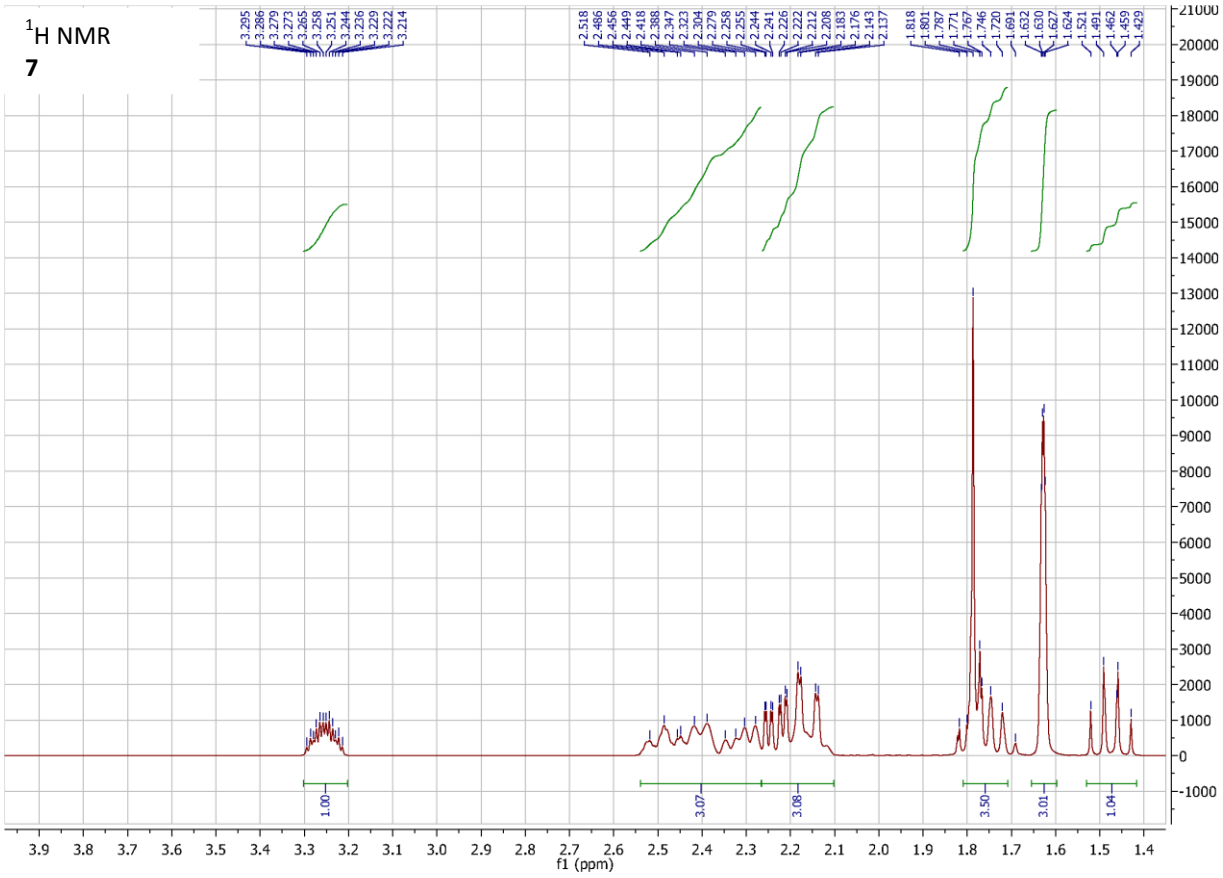


Fig. S55. ^{1}H NMR (400 MHz, $CDCl_3$) spectrum of pseudoivalin (**7**) expanded in the region 1.35–3.98 ppm.

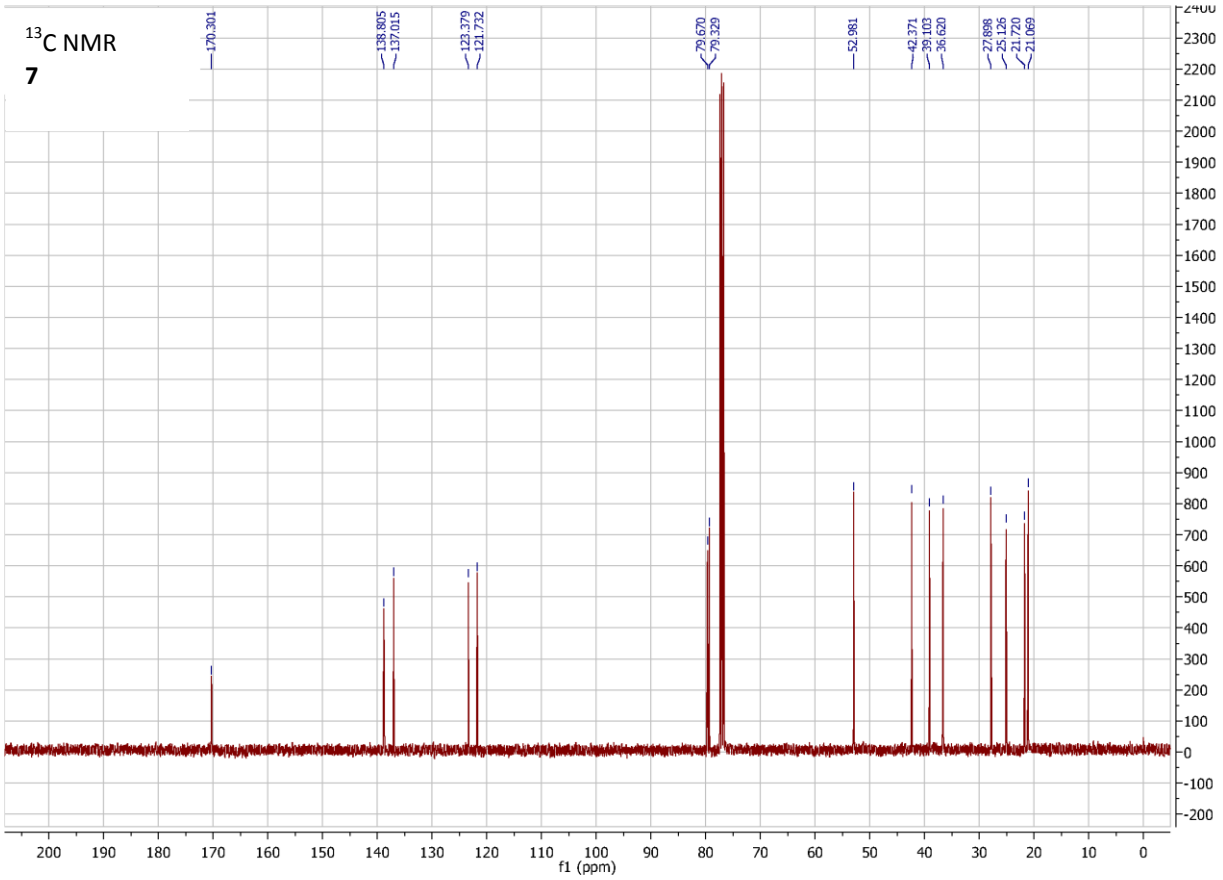


Fig. S56. ^{13}C NMR (100 MHz, $CDCl_3$) spectrum of pseudoivalin (**7**).

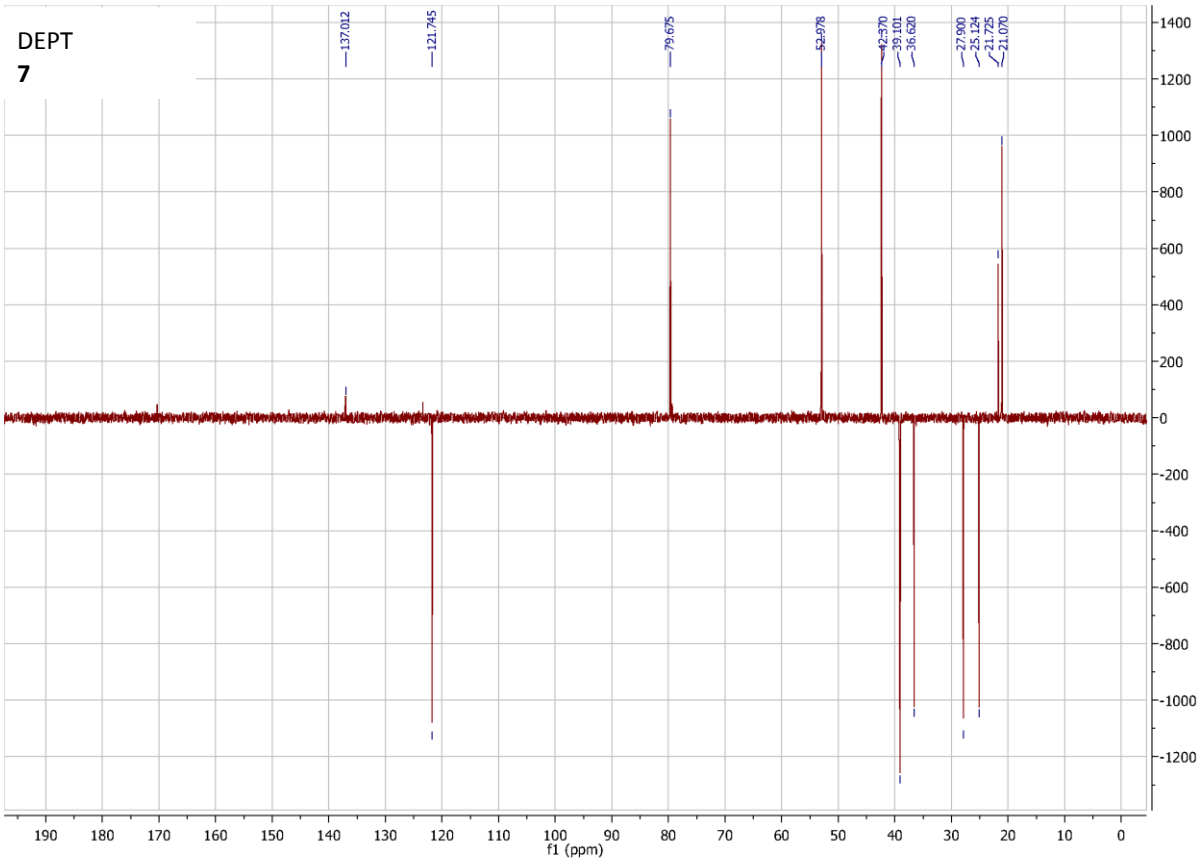


Fig. S57. DEPT spectrum of pseudoivalin (**7**).

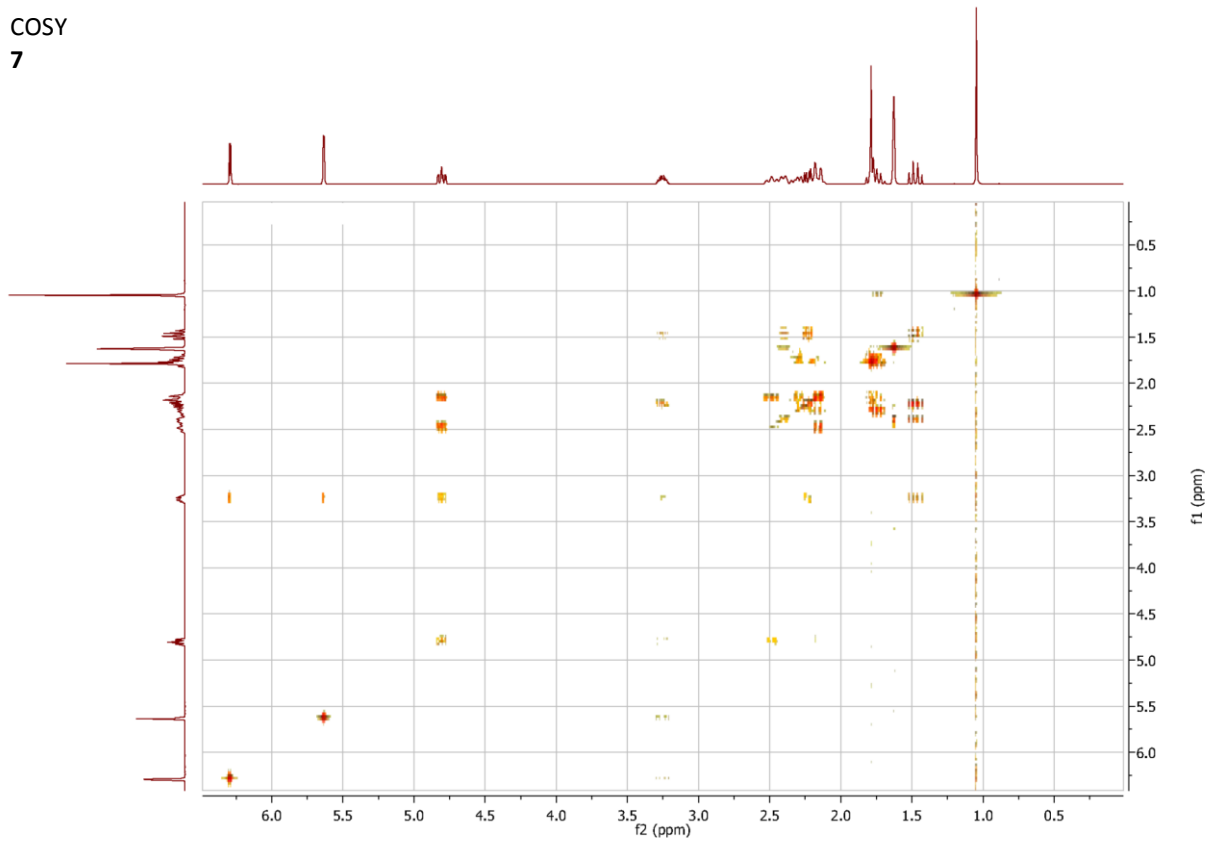


Fig. S58. $^{1}H–^{1}H$ COSY spectrum of pseudoivalin (**7**).

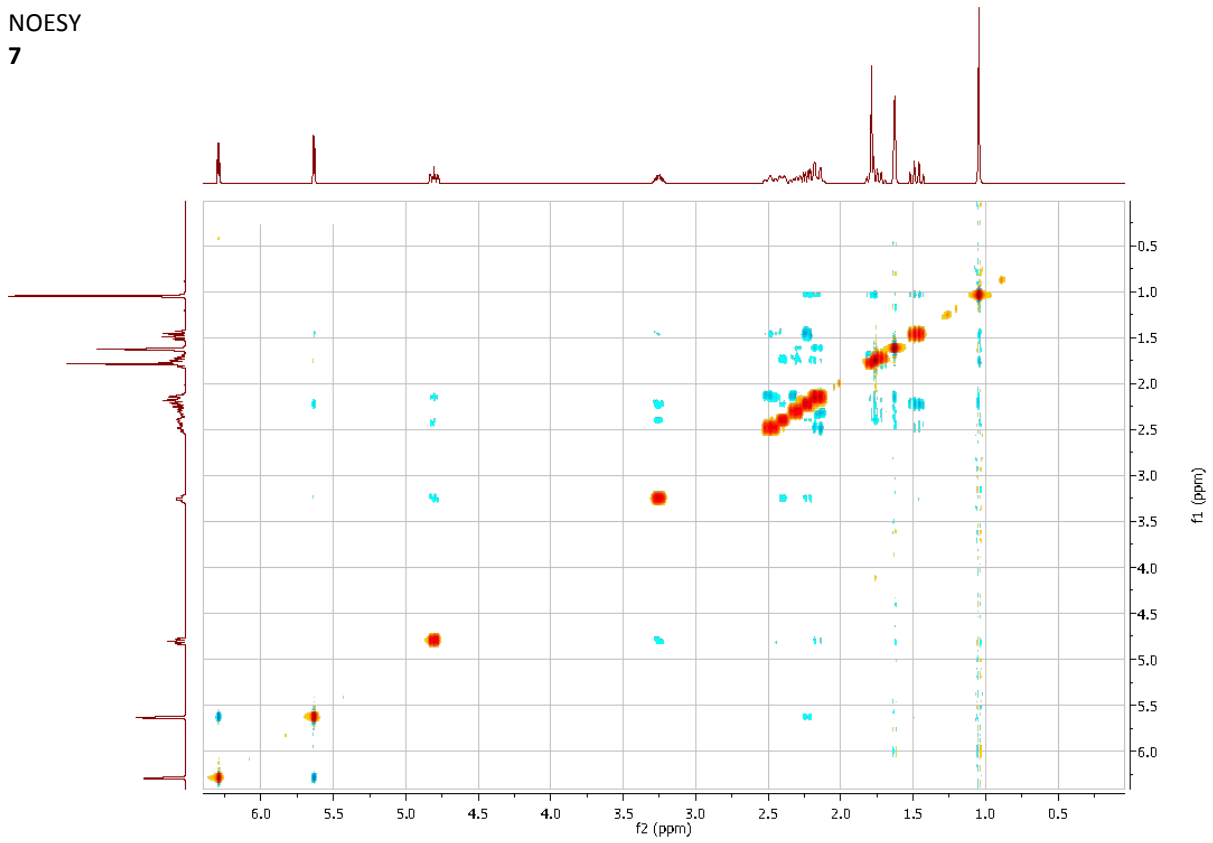


Fig. S59. NOESY spectrum of pseudoivalin (**7**).

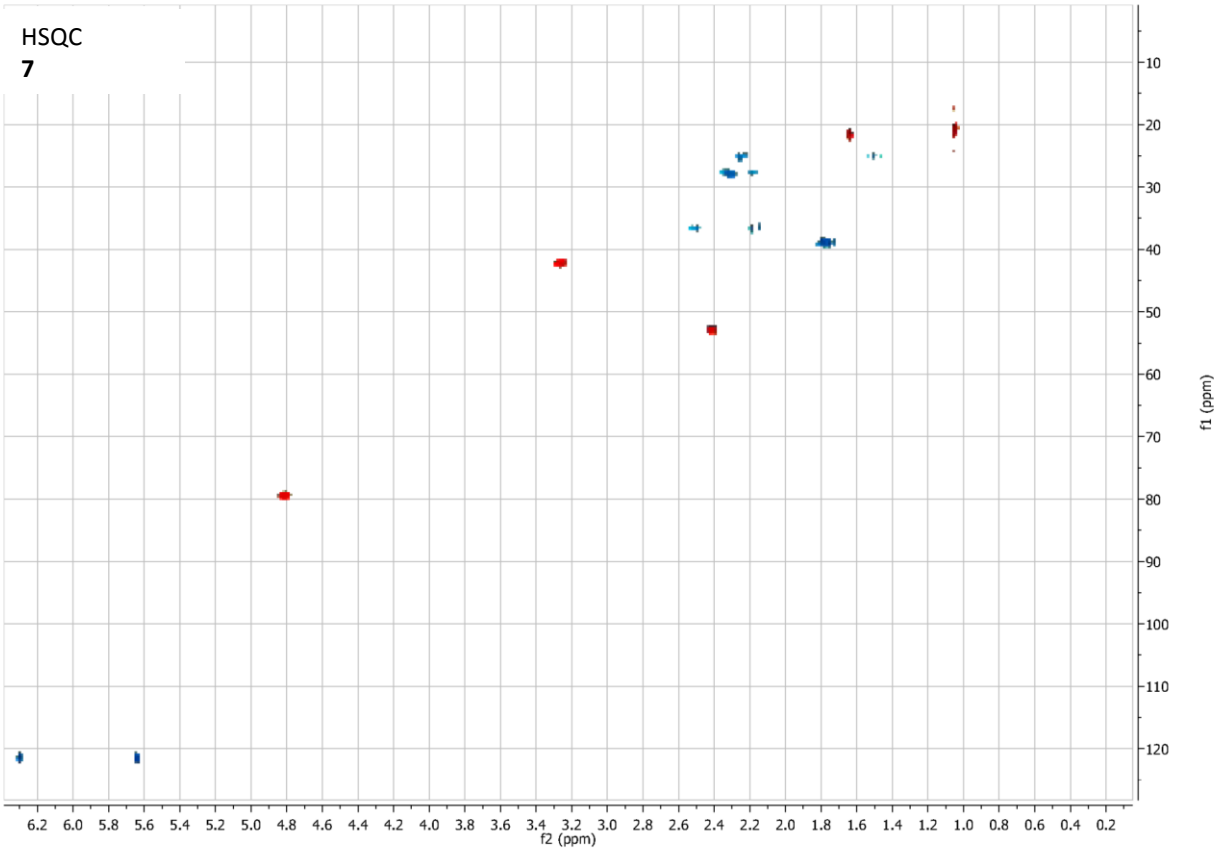


Fig. S60. HSQC spectrum of pseudoivalin (**7**).

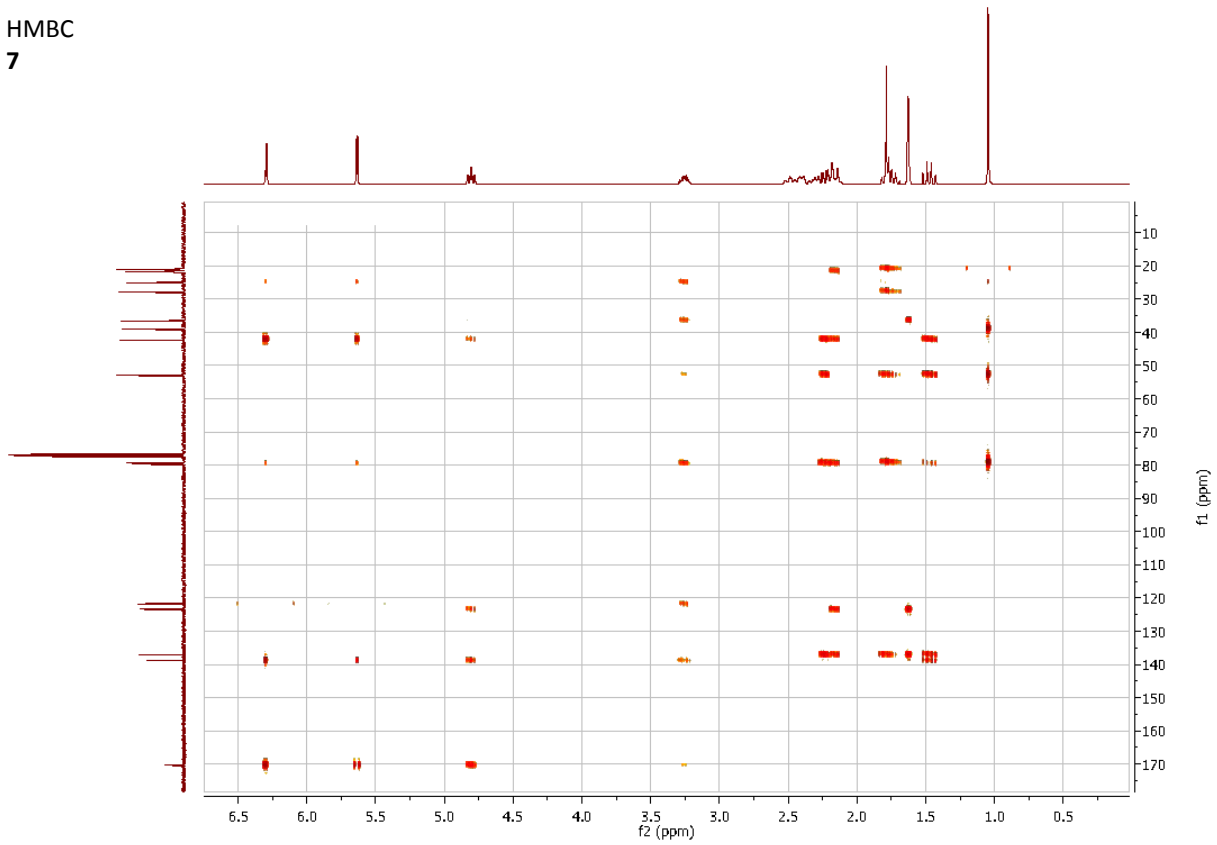
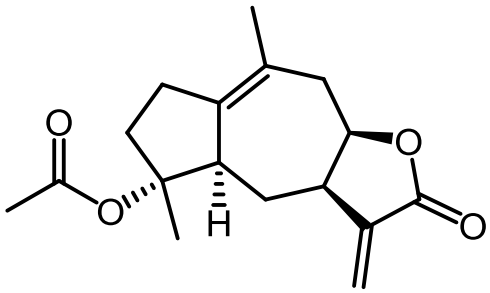


Fig. S61. HMBC spectrum of pseudoivalin (**7**).

*Pseudoivalin acetate [4α-acetoxy-5αH-10,11(13)-guaidien-8β,12-olide] (**8**)*

Colorless crystals; mp 160–161 °C; $[\alpha]_D^{25}$ –164 (*c* 0.4, $CHCl_3$); UV (MeOH) λ_{max} (log ε) 207 (4.05) nm; IR (KBr) ν_{max} 3430, 2942, 1766, 1725, 1664, 1373, 1260, 1117, 1060 cm^{-1}; APCIMS: *m/z* 248 $[M + H - Ac]^+$ (21), 231 $[M + H - HOAc]^+$ (100); HRESIMS *m/z* 313.1408 (calcd for $C_{17}H_{22}O_4Na$, 313.1416).



Pseudoivalin acetate (**8**)

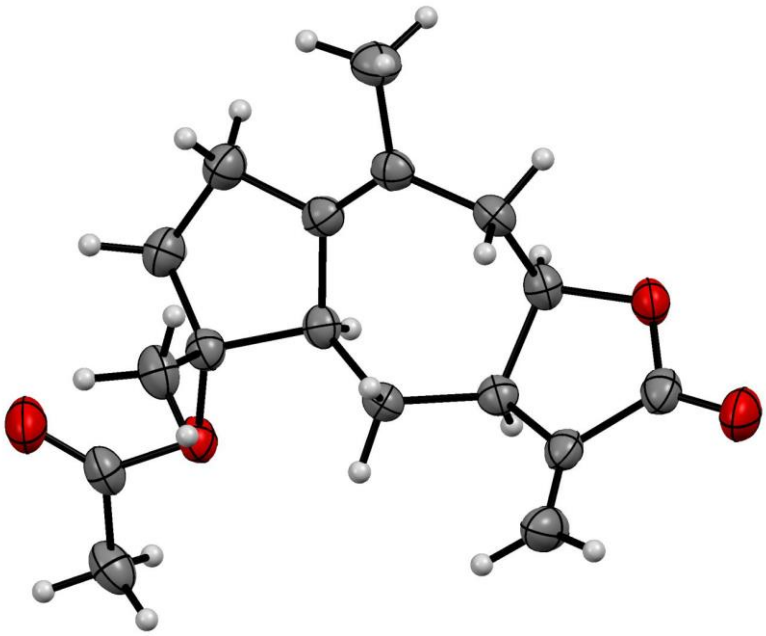


Fig. S62. Crystal structure of pseudoivalin acetate (**8**) [ORTEP diagram] with displacement ellipsoids at 50% probability for non-H atoms.

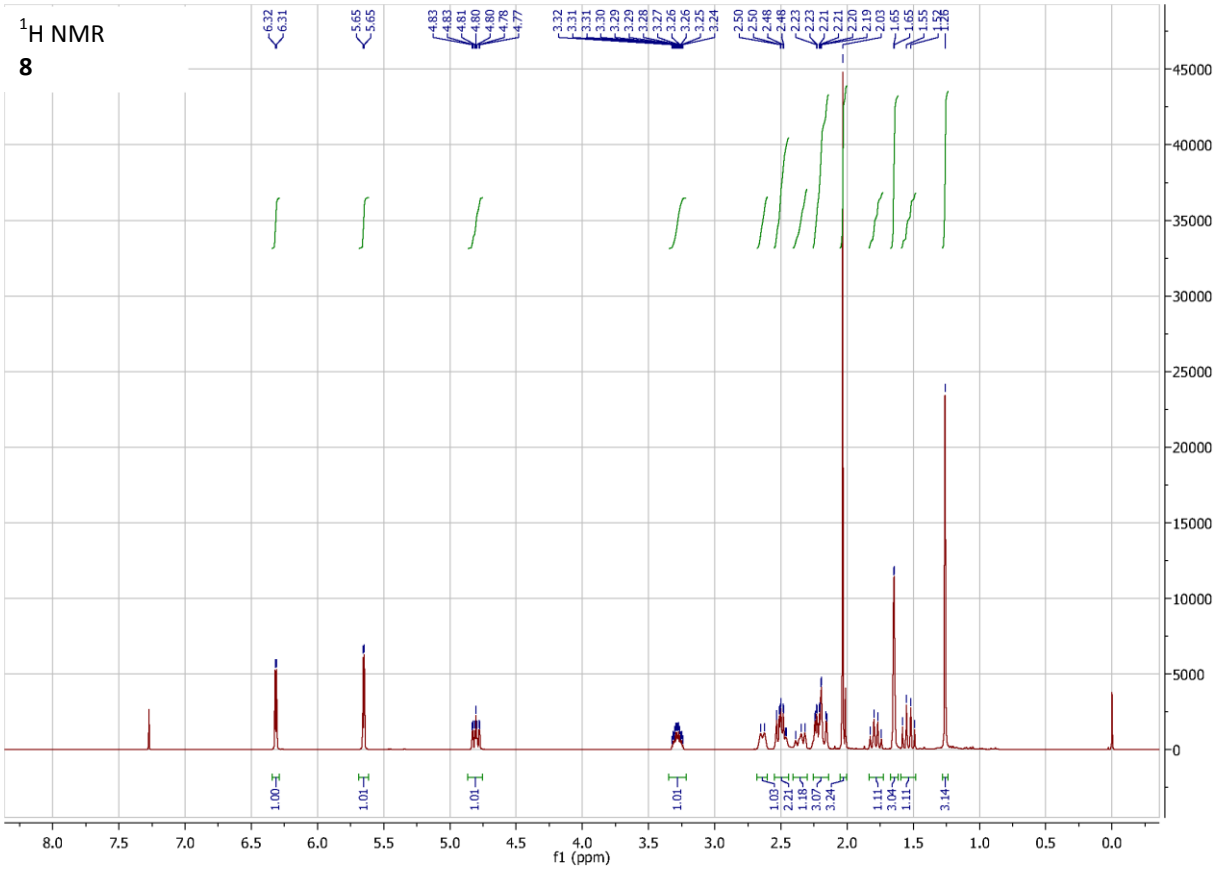


Fig. S63. ^{1}H NMR (400 MHz, $CDCl_3$) spectrum of pseudoivalin acetate (**8**).

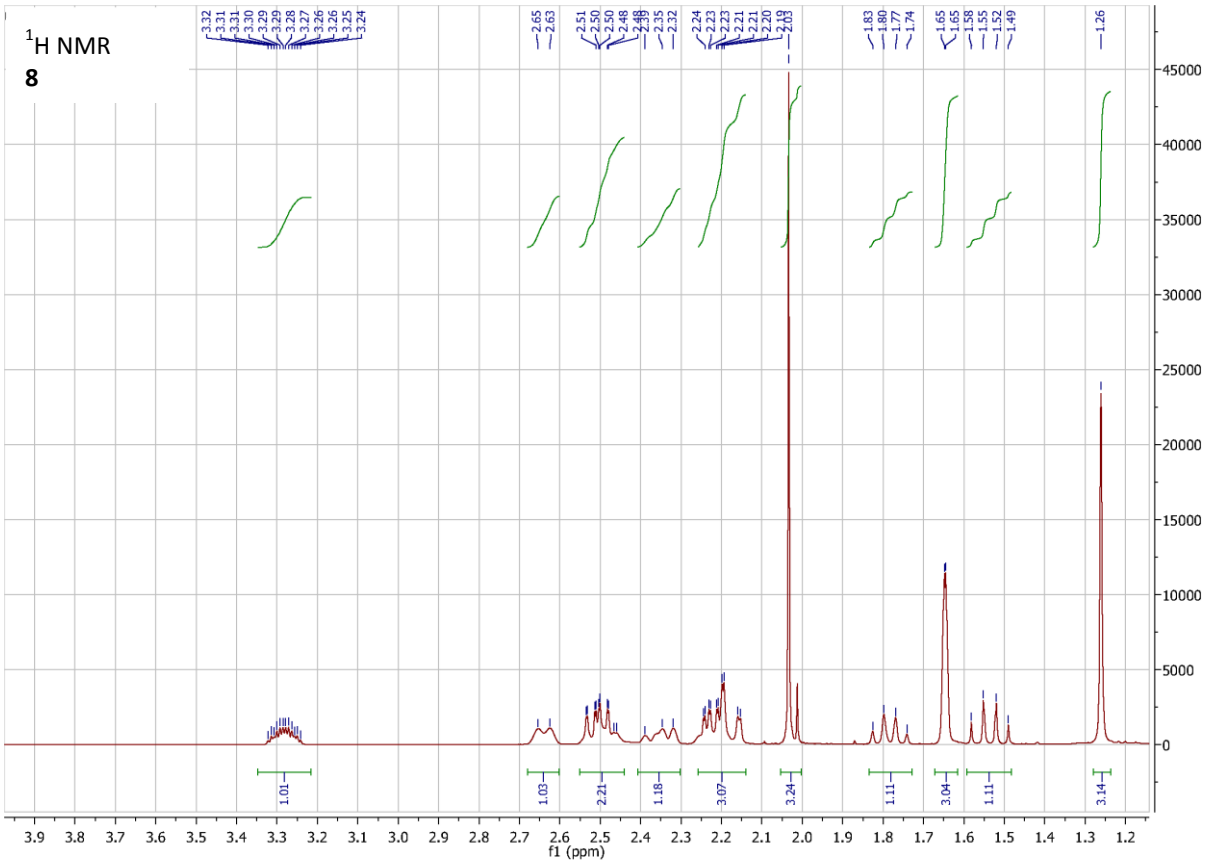


Fig. S64. ^{1}H NMR (400 MHz, $CDCl_3$) spectrum of pseudoivalin acetate (**8**) expanded in the region 1.03–3.98 ppm.

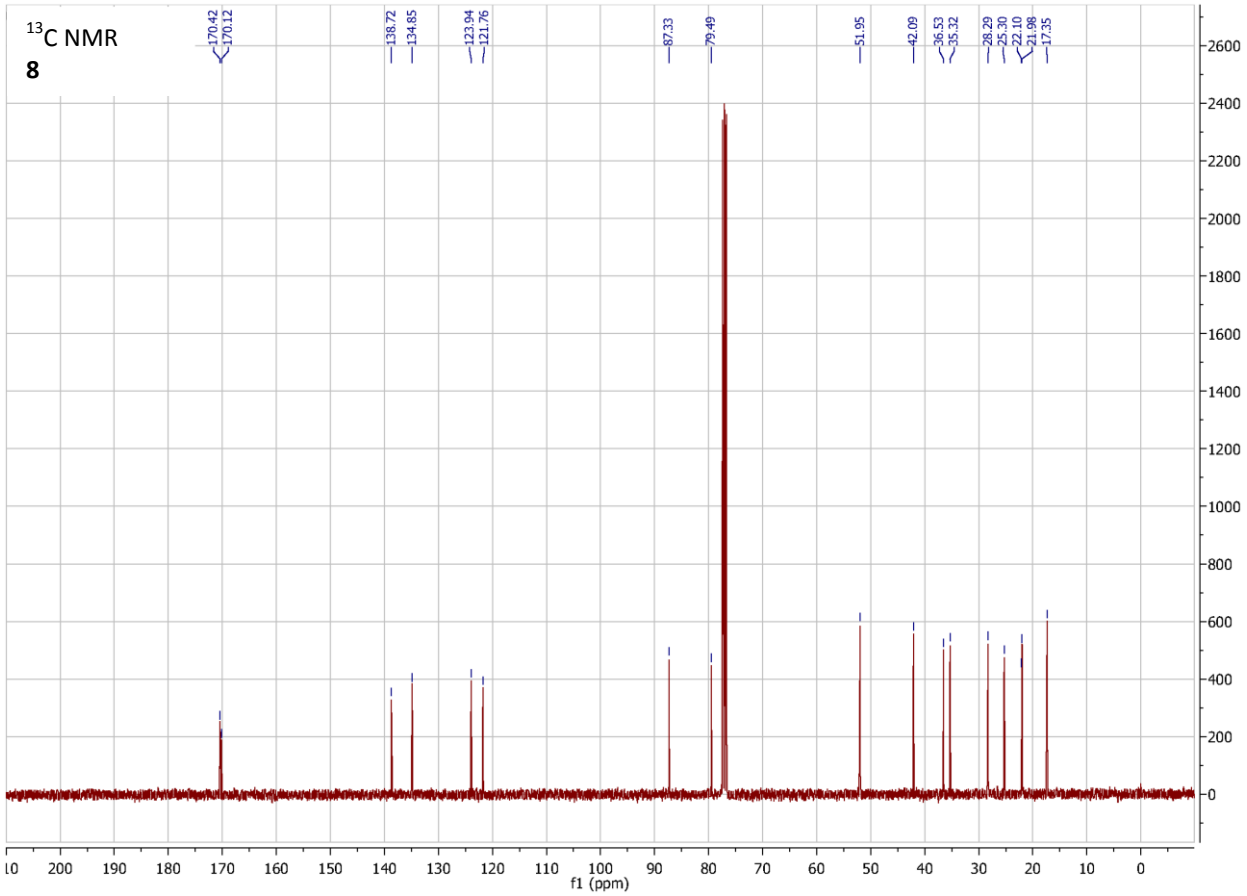


Fig. S65. ^{13}C NMR (100 MHz, $CDCl_3$) spectrum of pseudoivalin acetate (**8**).

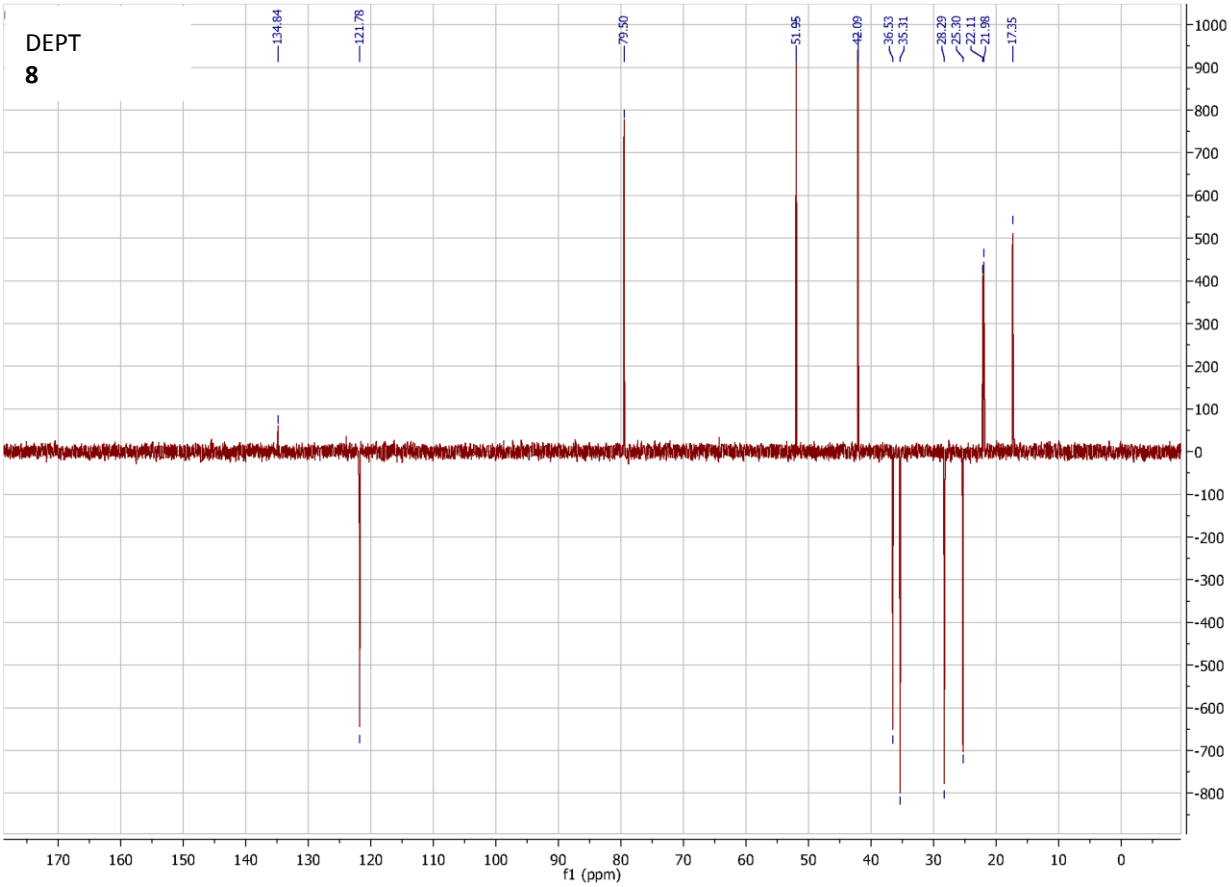


Fig. S66. DEPT spectrum of pseudoivalin acetate (**8**).

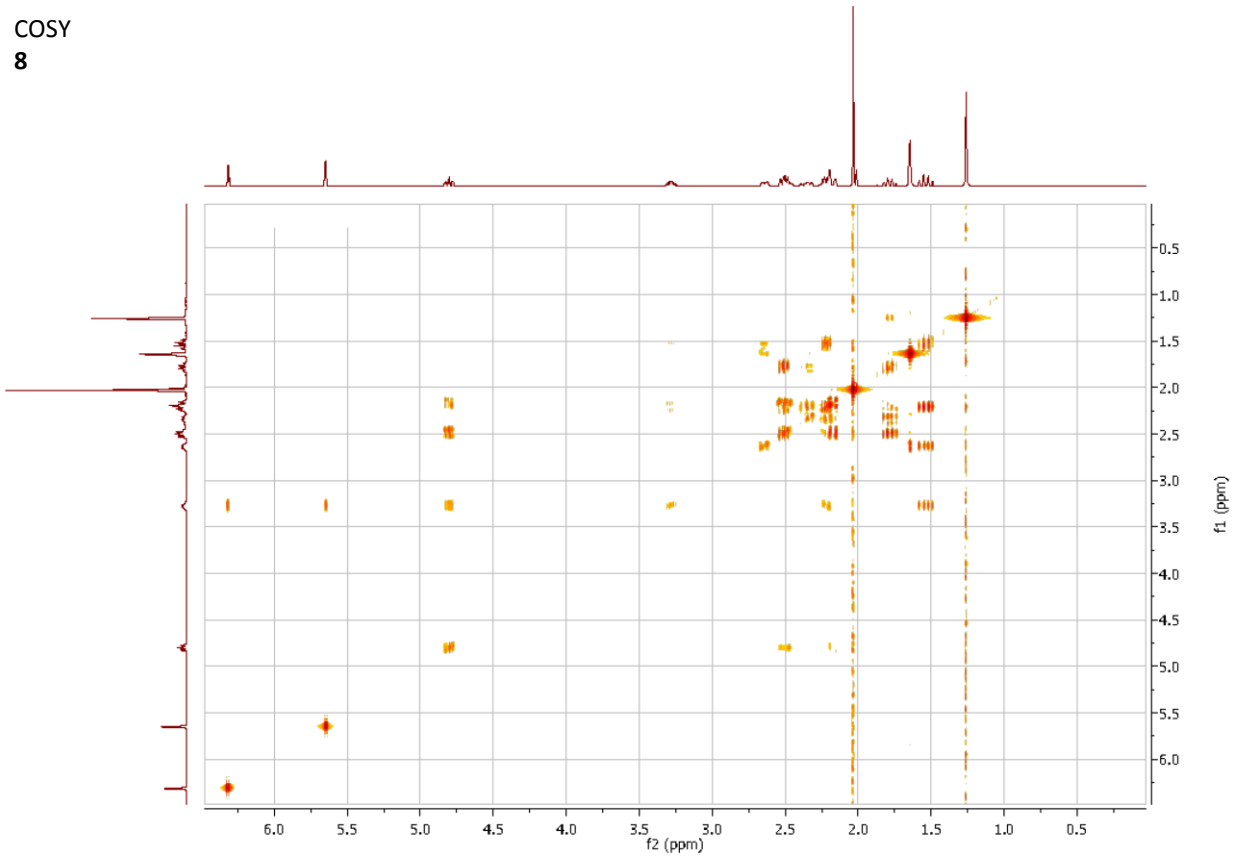


Fig. S67. $^{1}H–^{1}H$ COSY spectrum of pseudoivalin acetate (**8**).

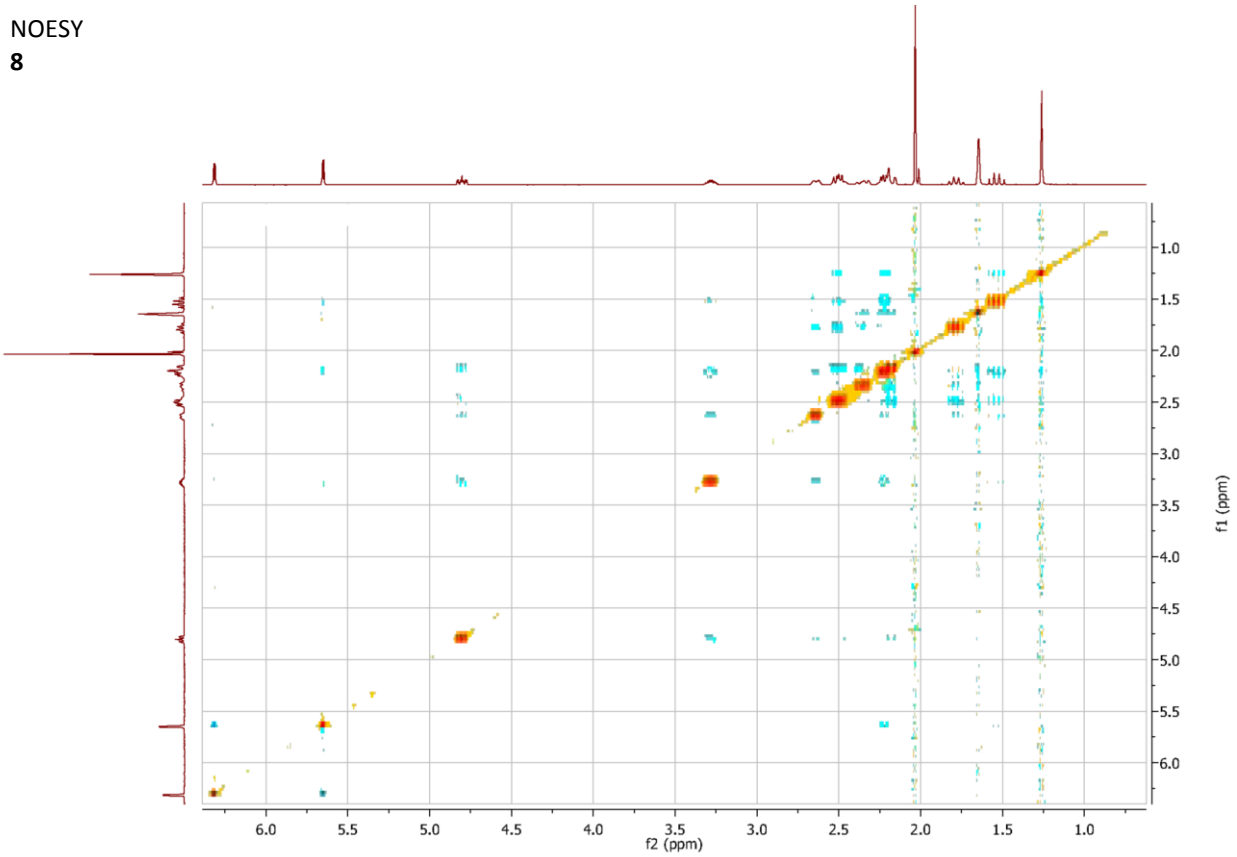


Fig. S68. NOESY spectrum of pseudoivalin acetate (**8**).

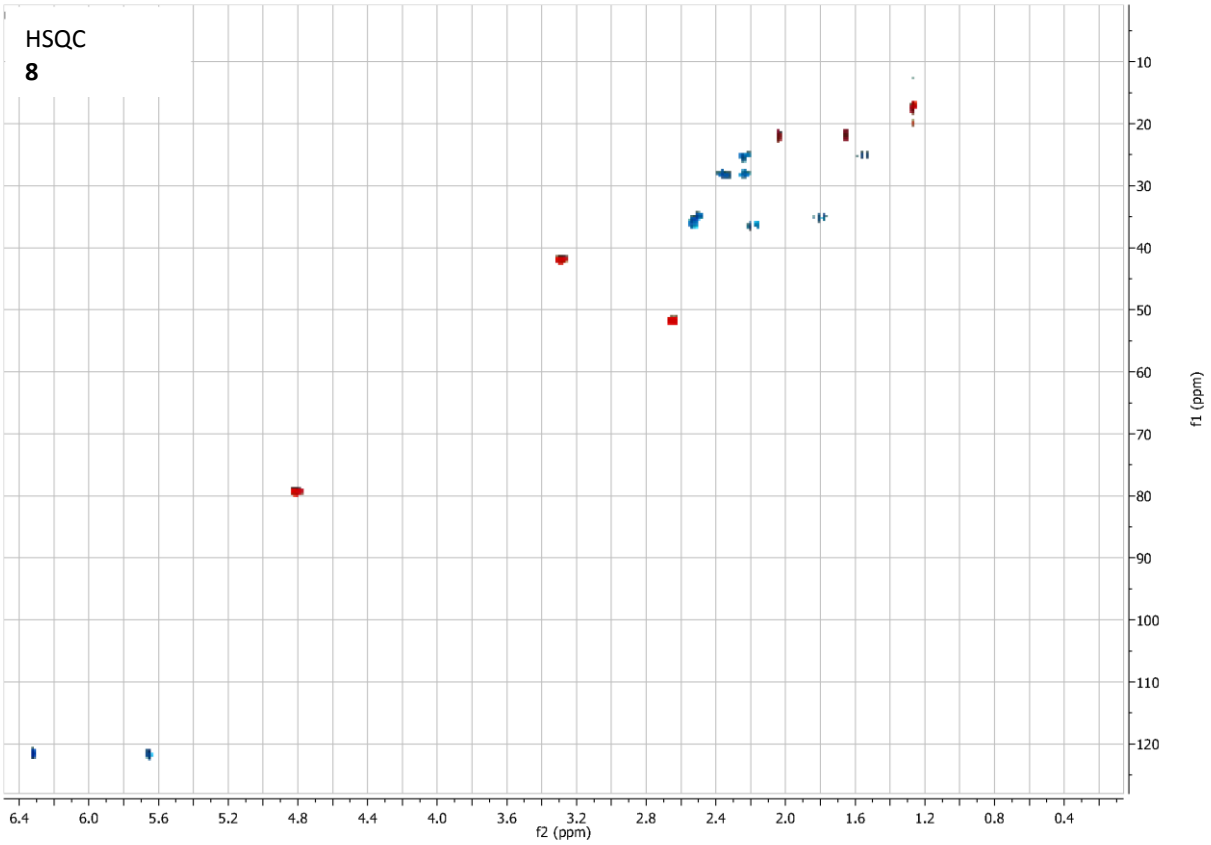


Fig. S69. HSQC spectrum of pseudoivalin acetate (**8**).

HMBC
8

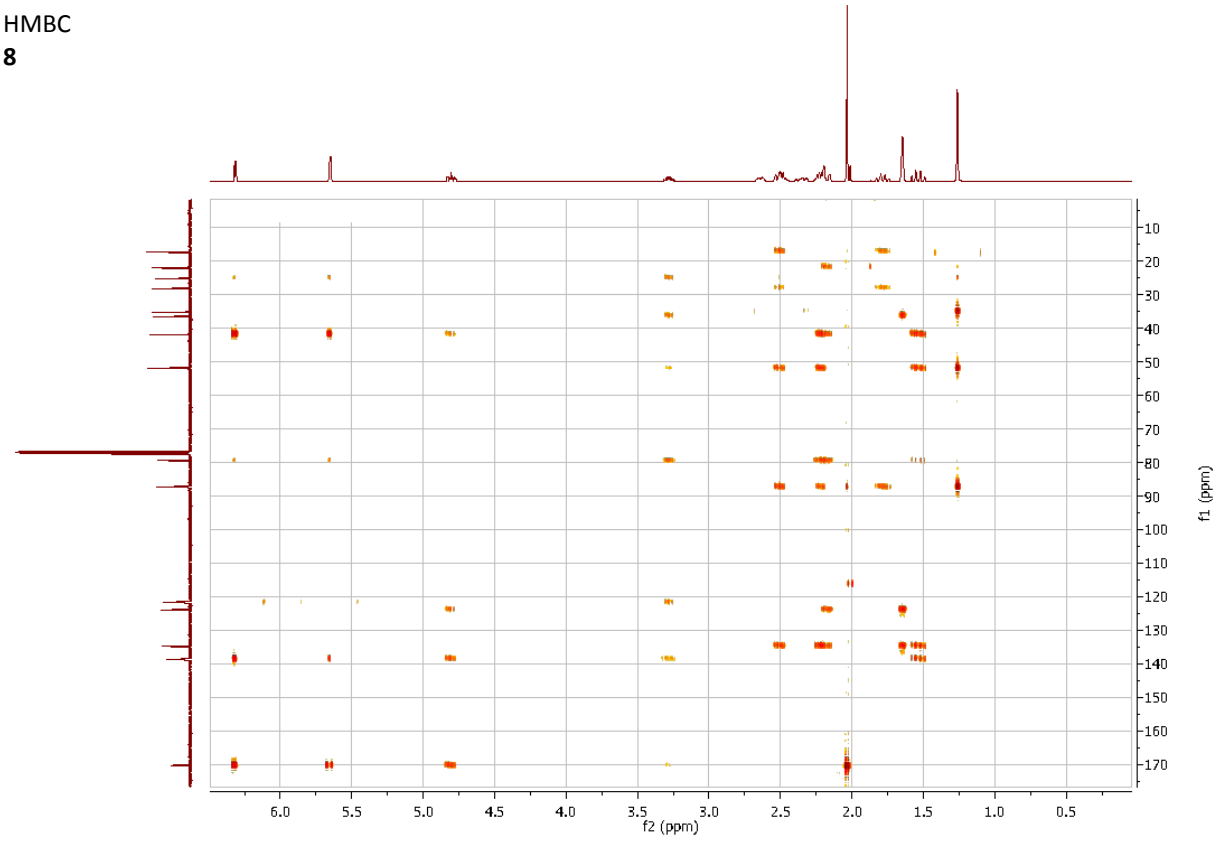
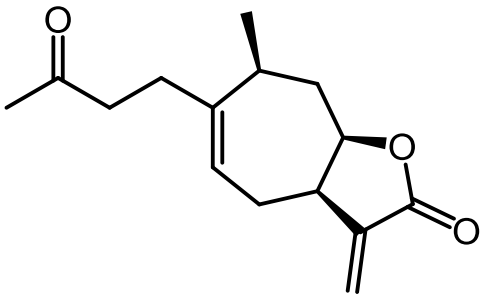


Fig. S70. HMBC spectrum of pseudoivalin acetate (**8**).

*Tomentosin (**9**)*

Colorless oil; $[\alpha]_D^{25}$ +8 (*c* 0.4, $CHCl_3$); UV (MeOH) λ_{max} (log ε) 215 (4.12) nm; APCIMS: *m/z* 249 $[M + H]^+$ (100), 231 $[M + H - H_2O]^+$ (65); HRESIMS *m/z* 249.1490 (calcd for $C_{15}H_{21}O_3$, 249.1491).



Tomentosin (**9**)

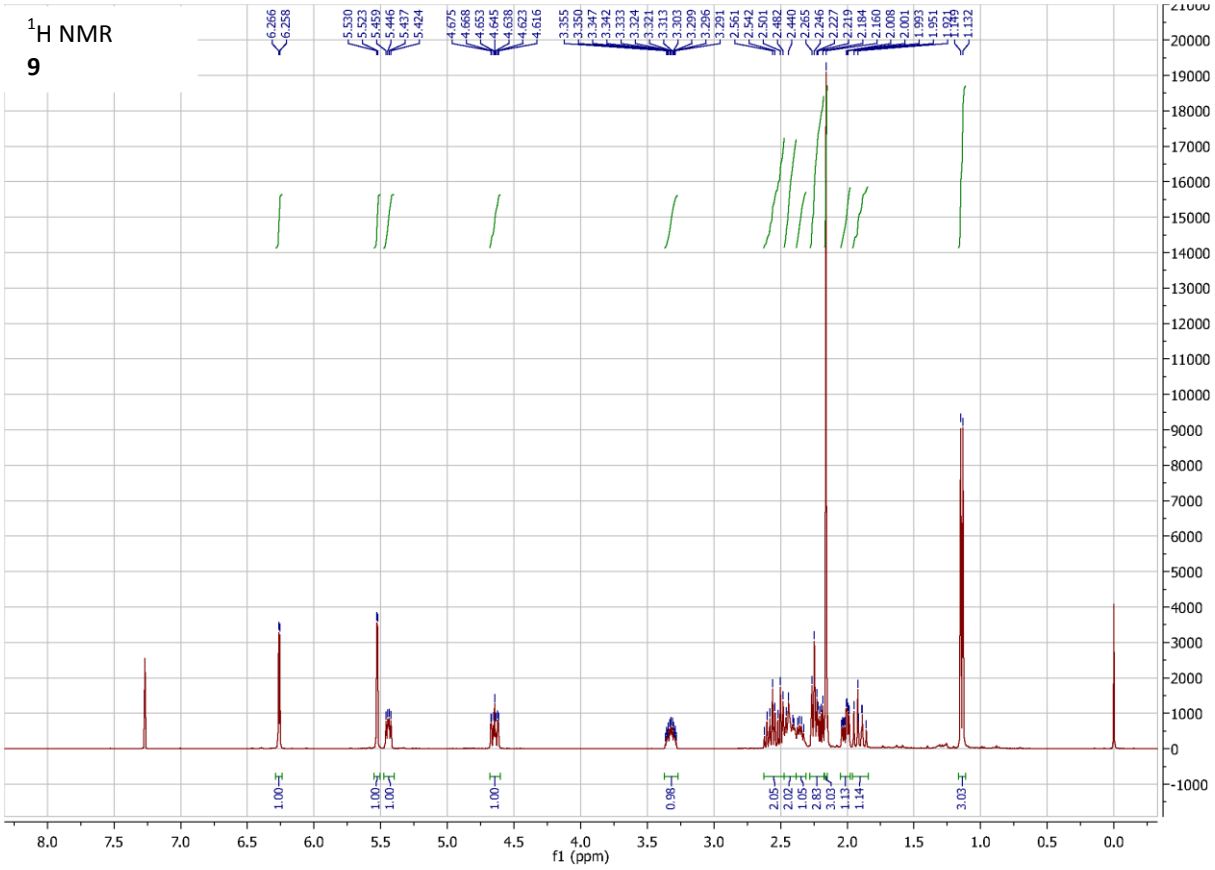


Fig. S71. ^{1}H NMR (400 MHz, $CDCl_3$) spectrum of tomentosin (**9**).

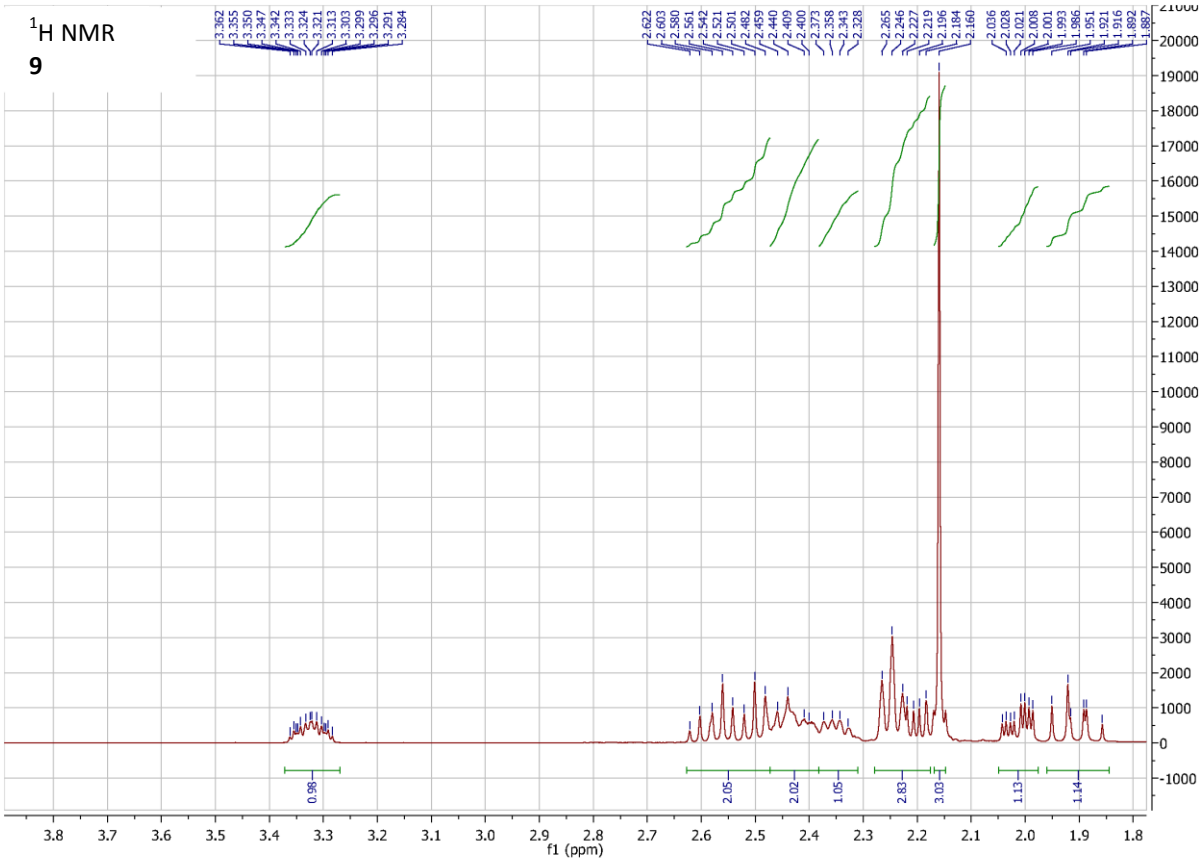


Fig. S72. ^{1}H NMR (400 MHz, $CDCl_3$) spectrum of tomentosin (**9**) expanded in the region 1.78–3.98 ppm.

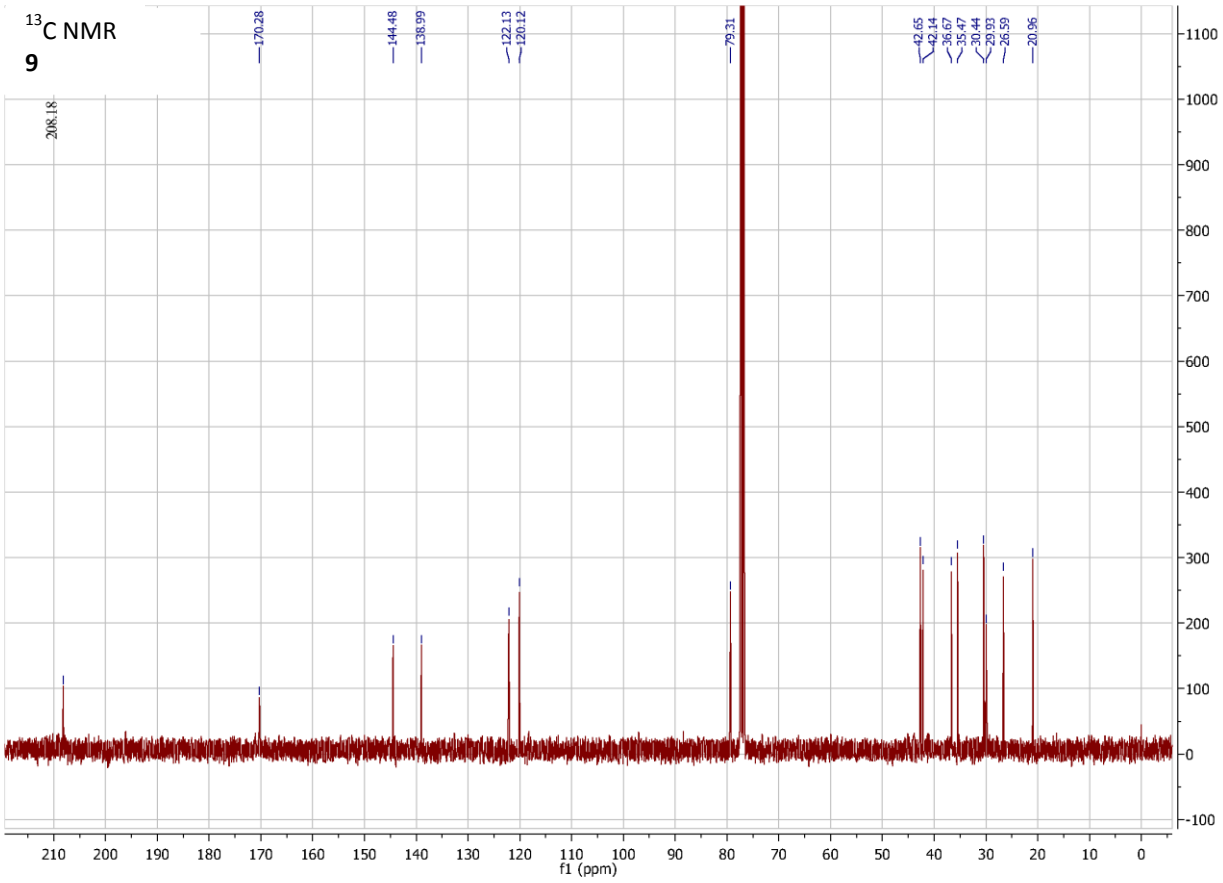


Fig. S73. ^{13}C NMR (100 MHz, $CDCl_3$) spectrum of tomentosin (**9**).

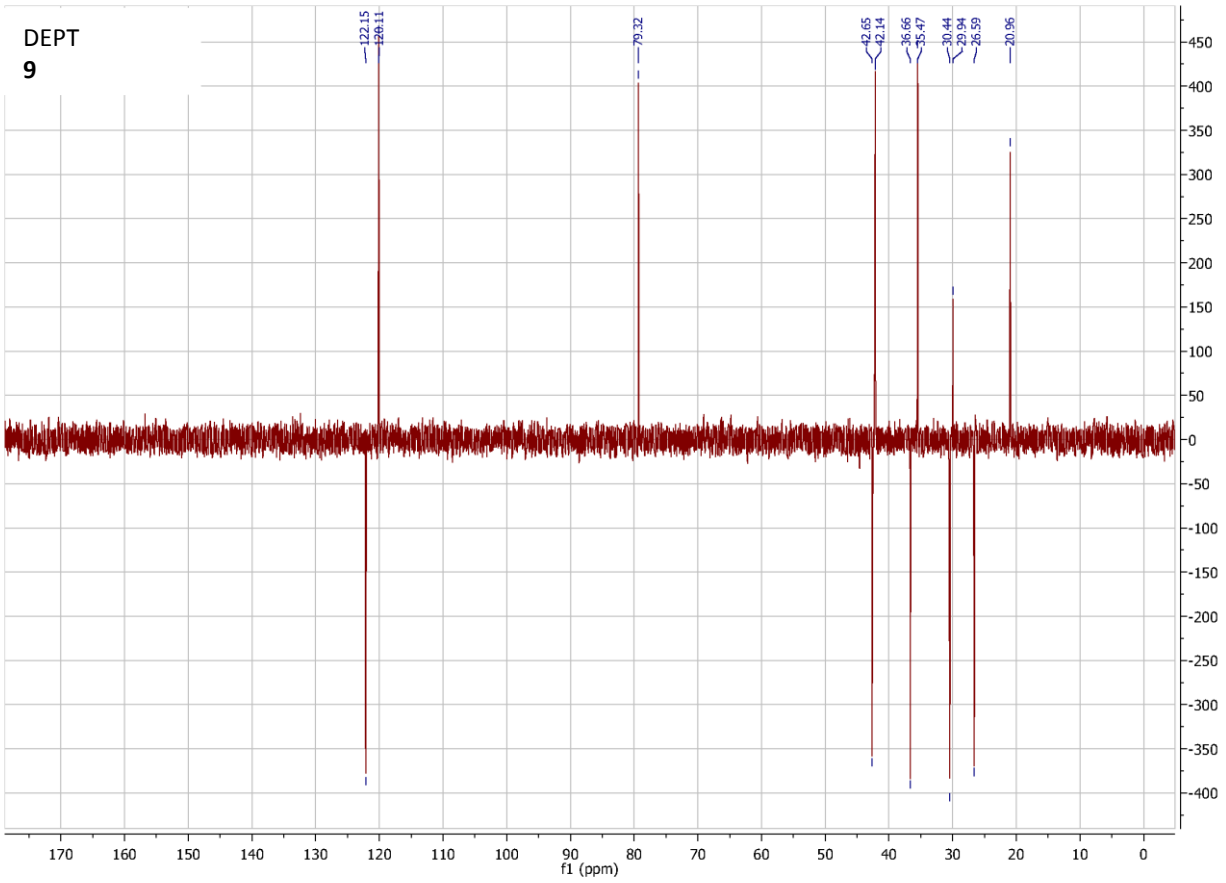


Fig. S74. DEPT spectrum of tomentosin (**9**).

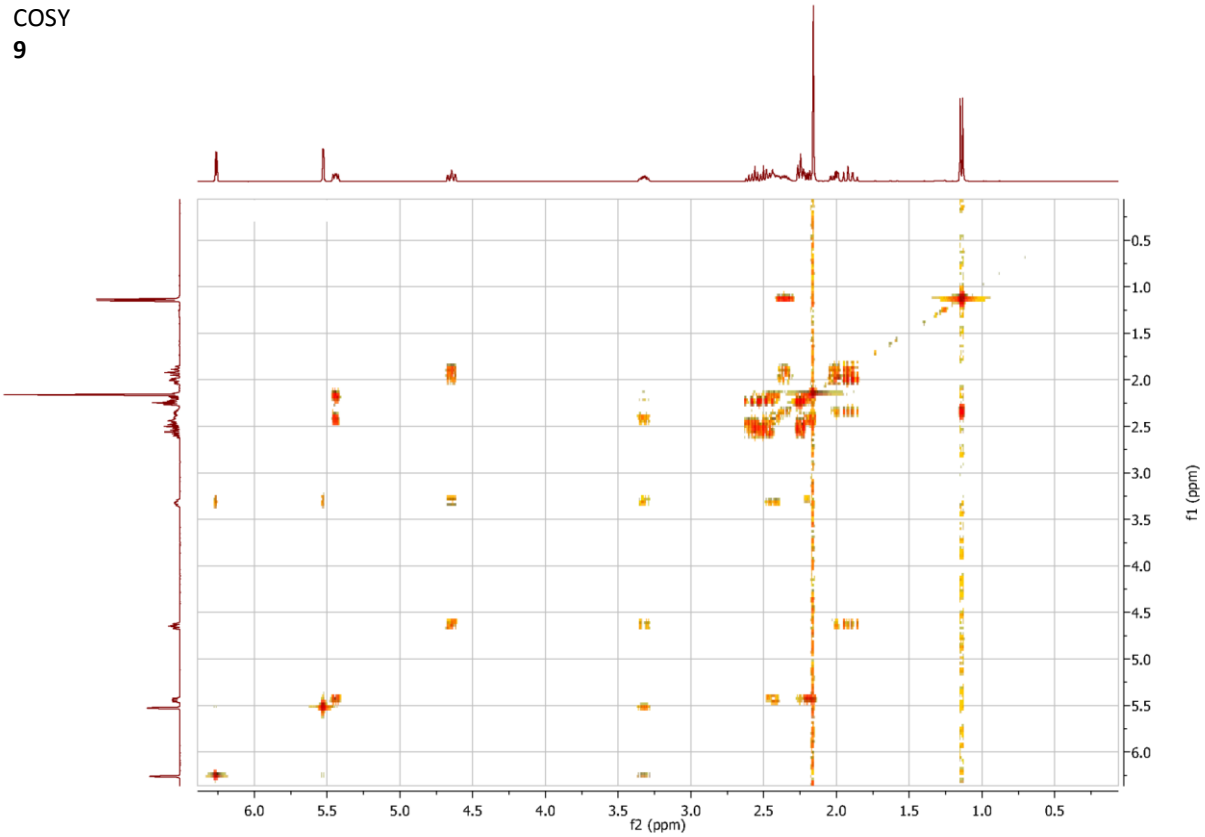


Fig. S75. $^{1}H–^{1}H$ COSY spectrum of tomentosin (**9**).

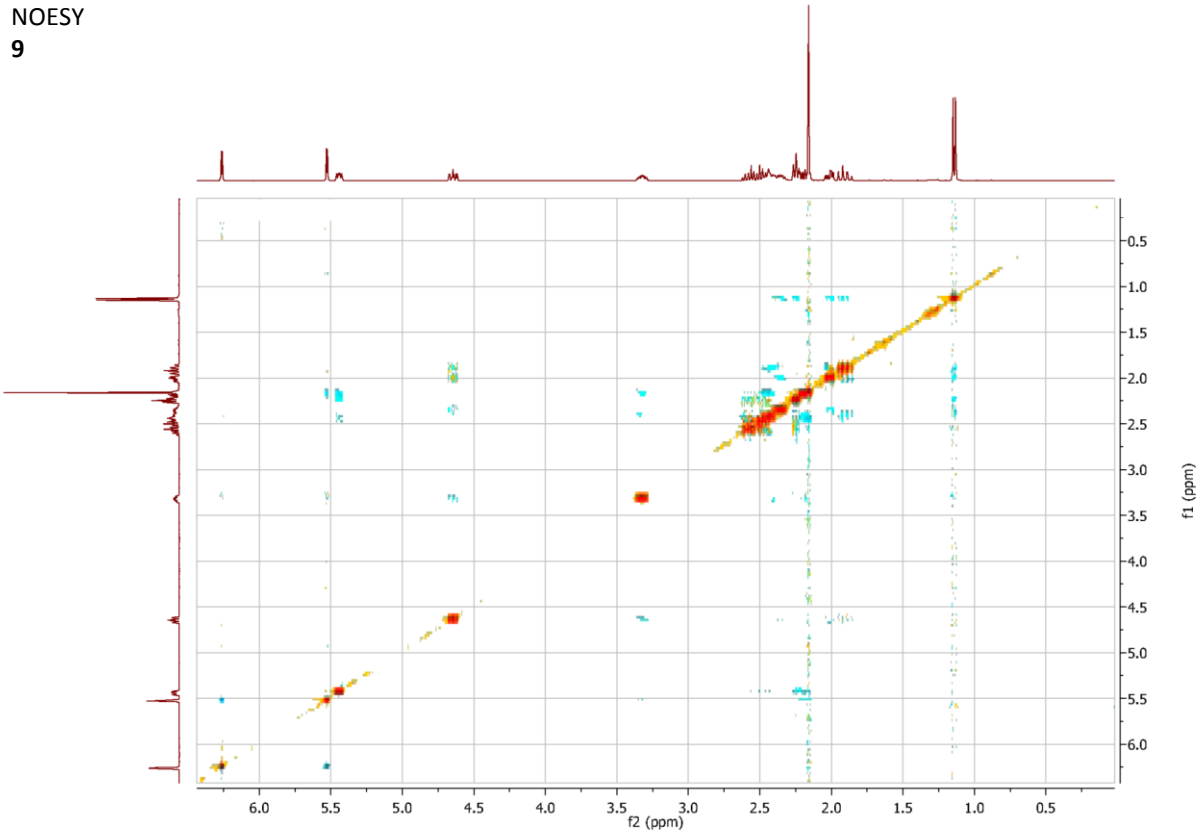


Fig. S76. NOESY spectrum of tomentosin (**9**).

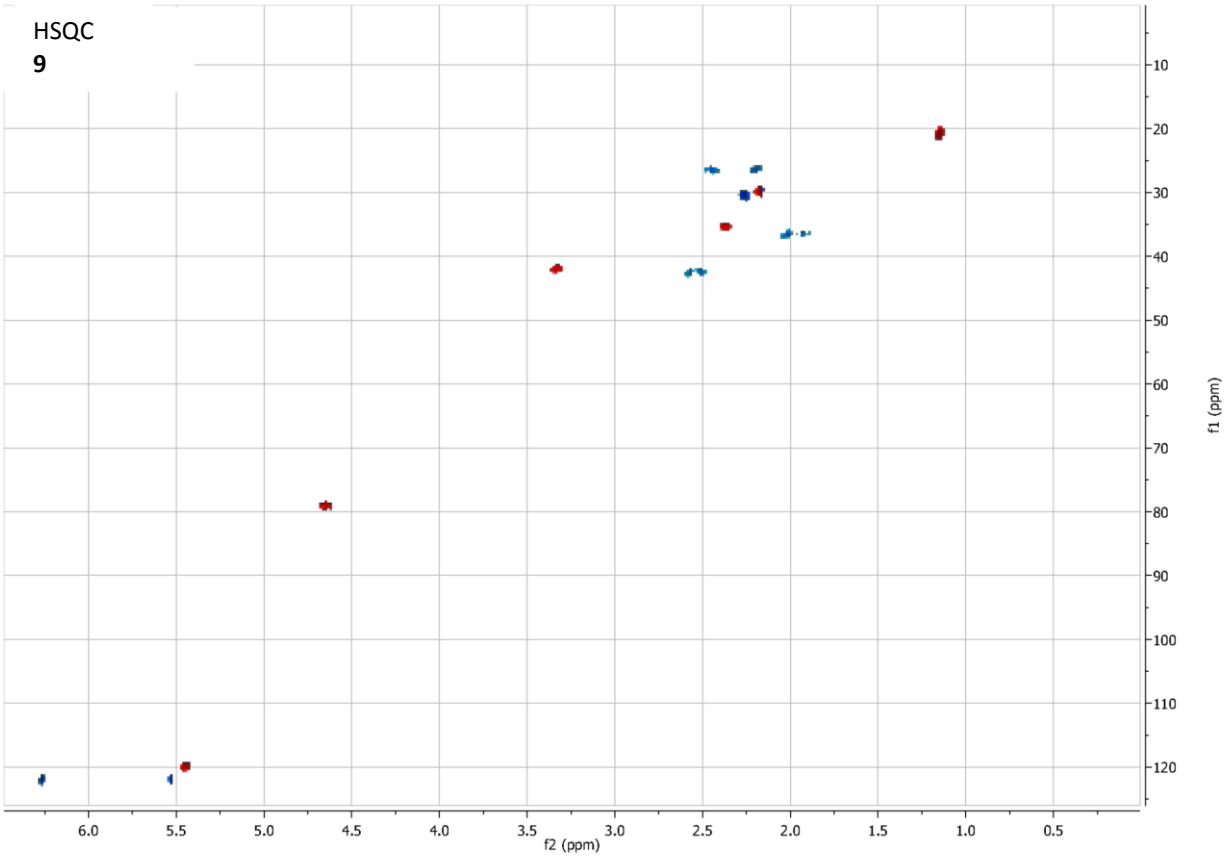


Fig. S77. HSQC spectrum of tomentosin (**9**).

HMBC
9

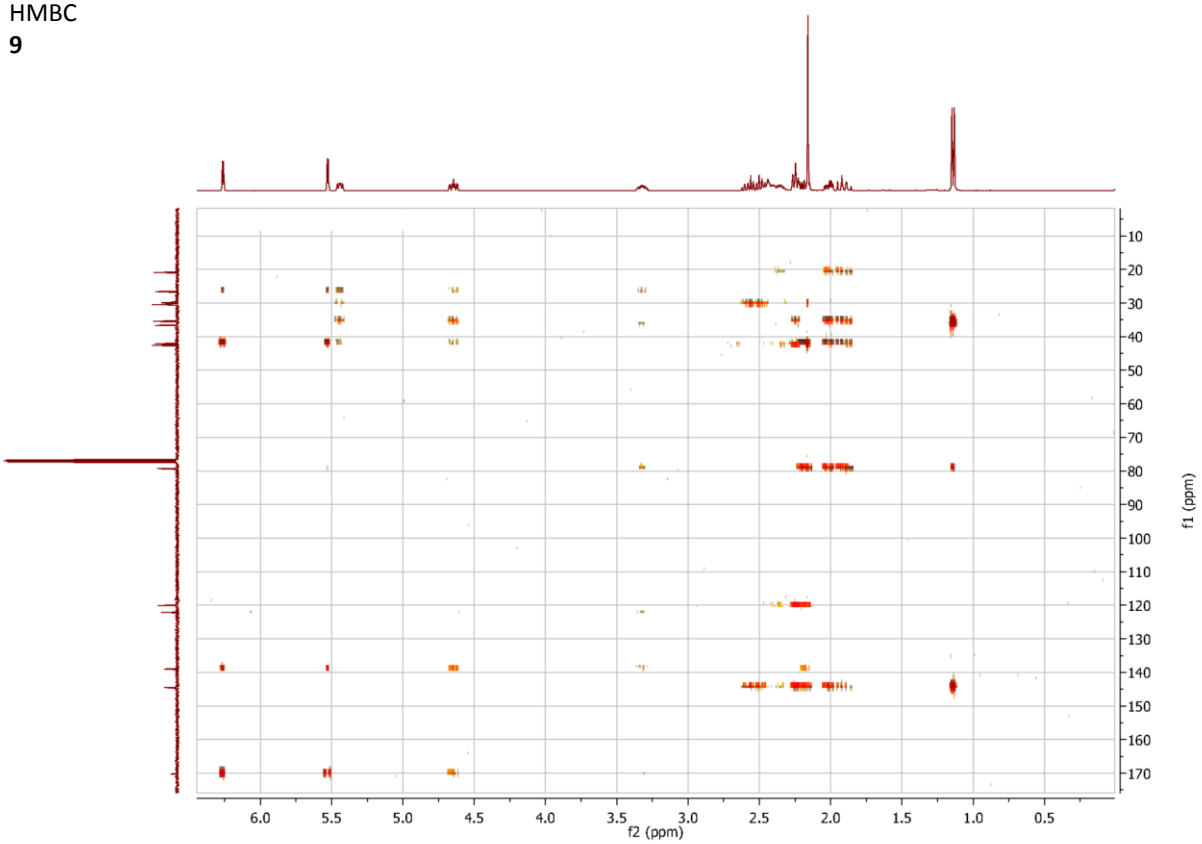


Fig. S78. HMBC spectrum of tomentosin (**9**).

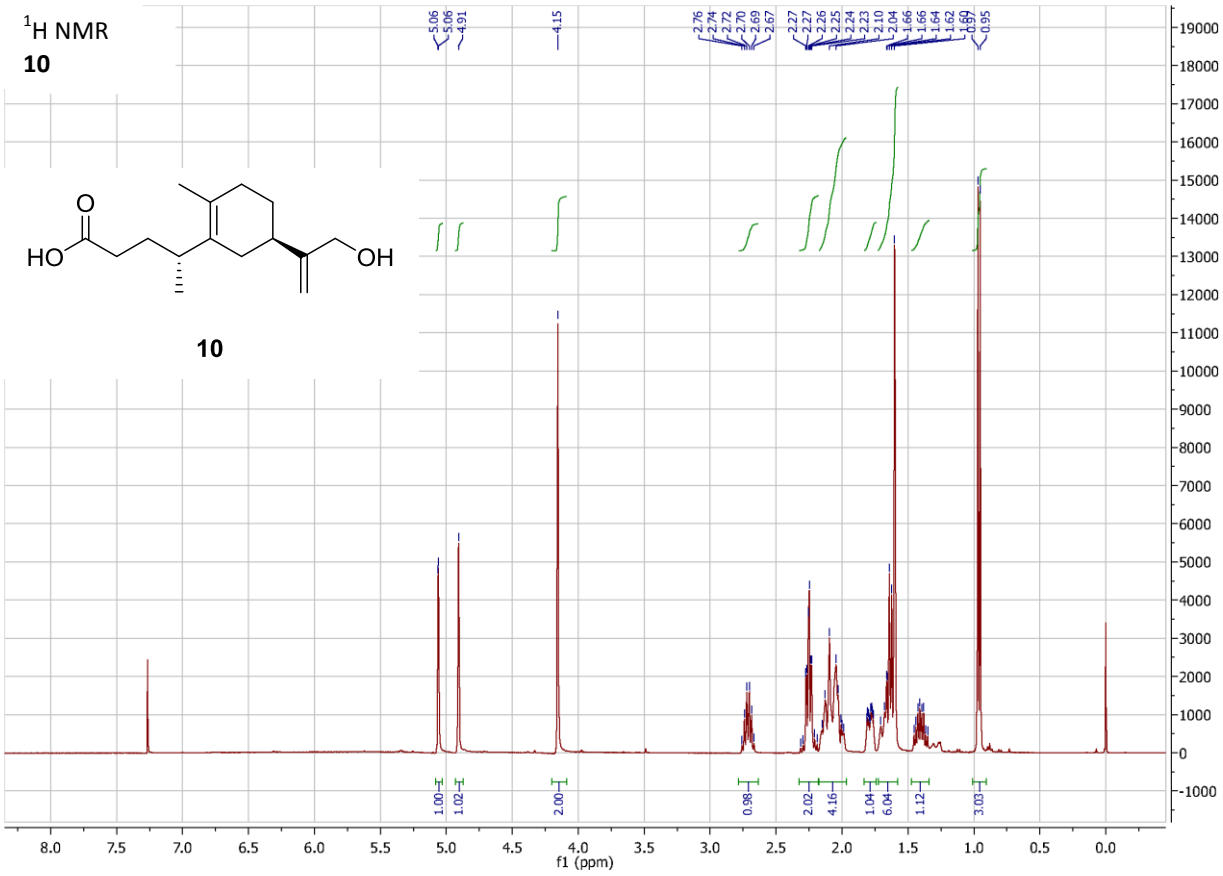


Fig. S79. ^{1}H NMR (400 MHz, $CDCl_3$) spectrum of the new compound **10.**

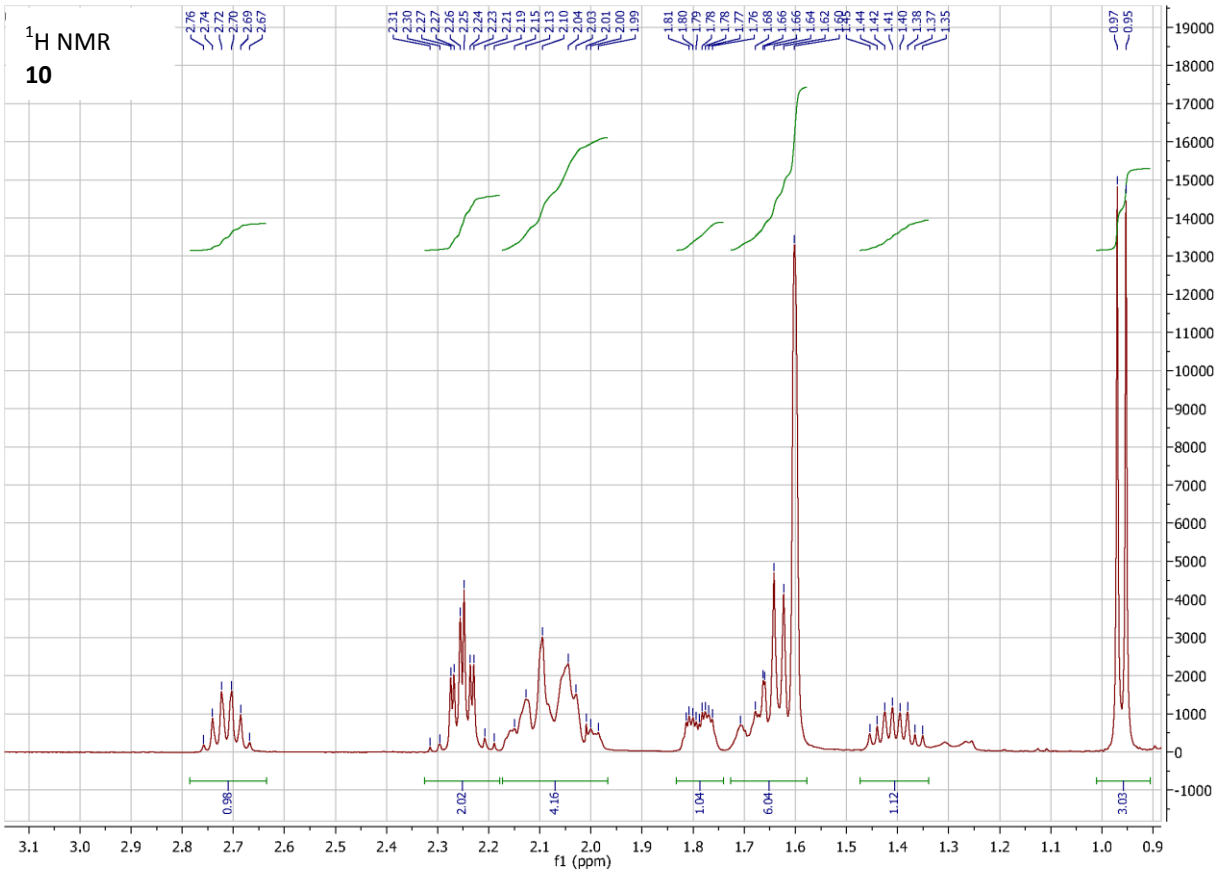


Fig. S80. ^{1}H NMR (400 MHz, $CDCl_3$) spectrum of the new compound **10** expanded in the region 0.88–3.15 ppm.

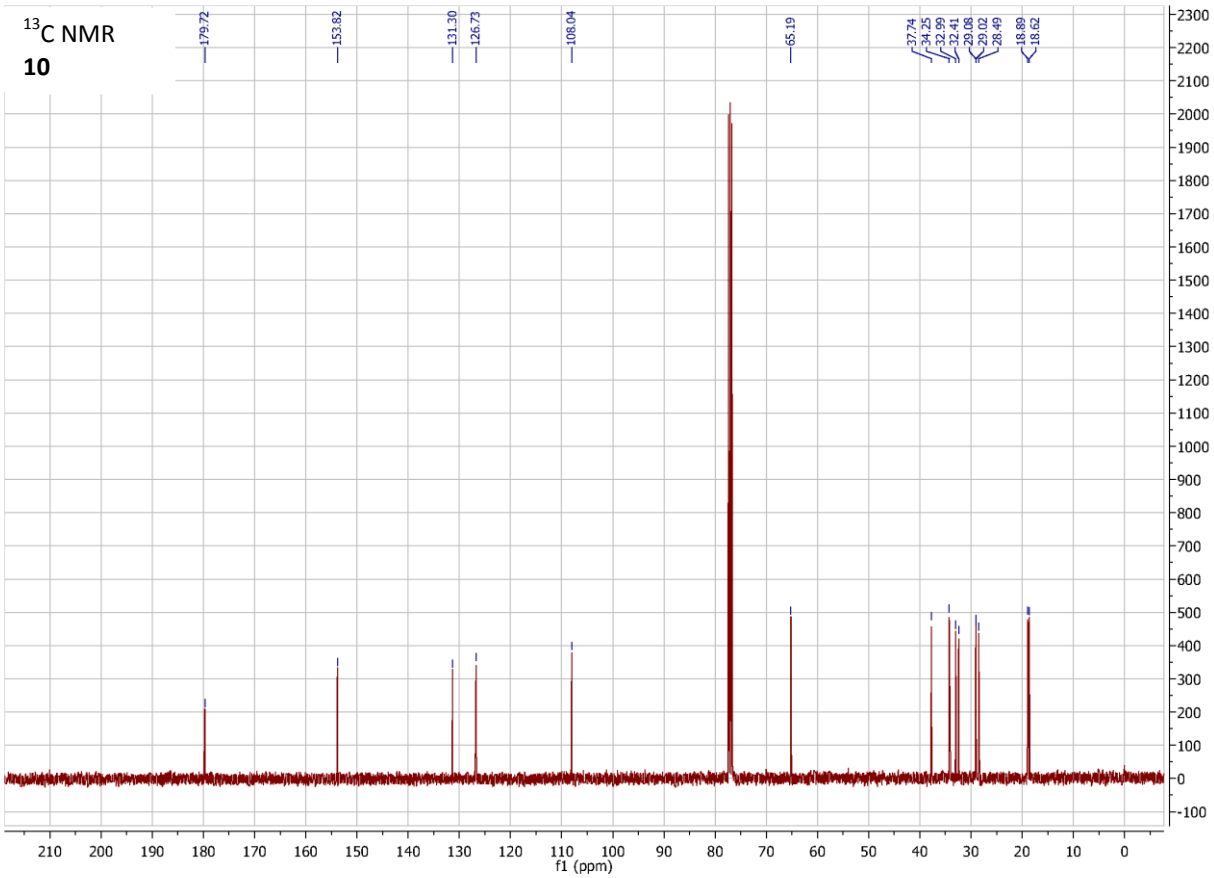


Fig. S81. ^{13}C NMR (100 MHz, $CDCl_3$) spectrum of the new compound **10**.

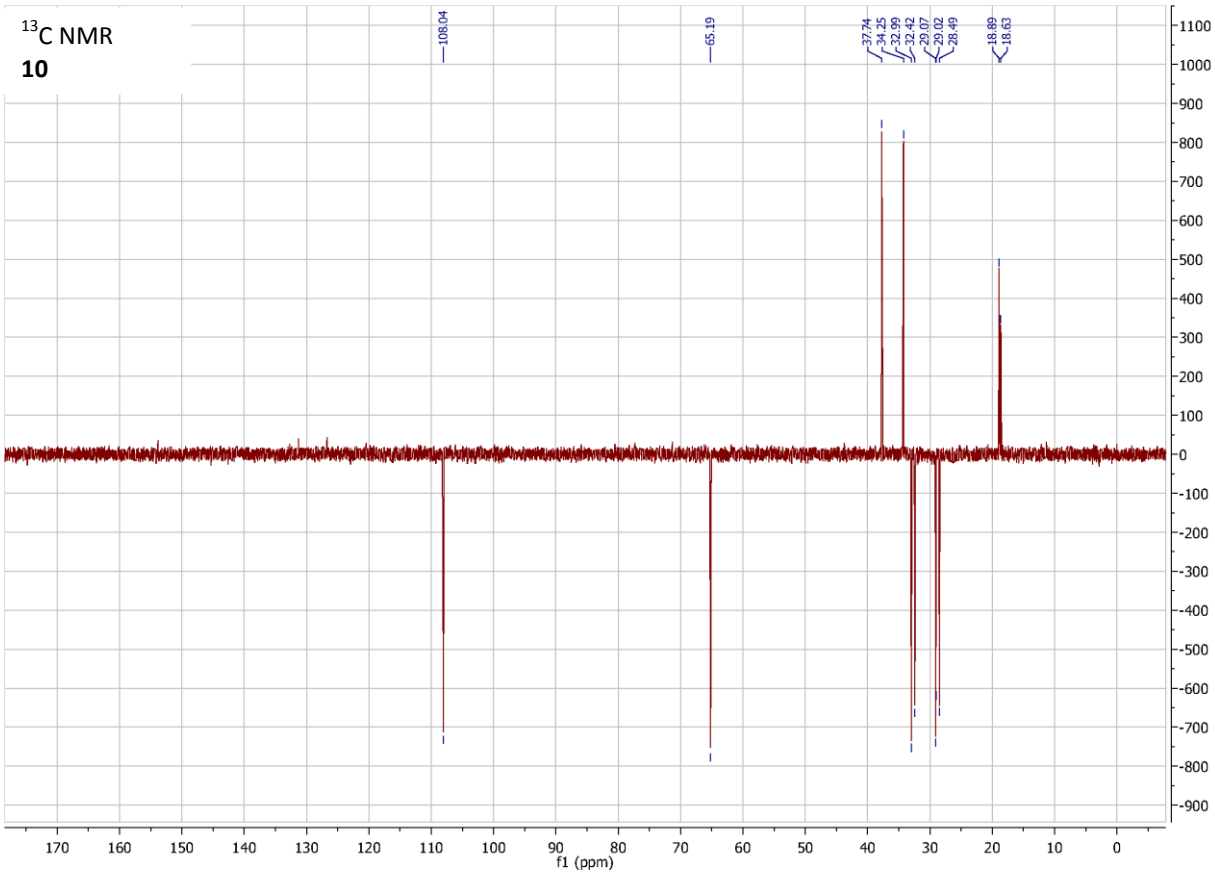


Fig. S82. DEPT spectrum of the new compound **10**.

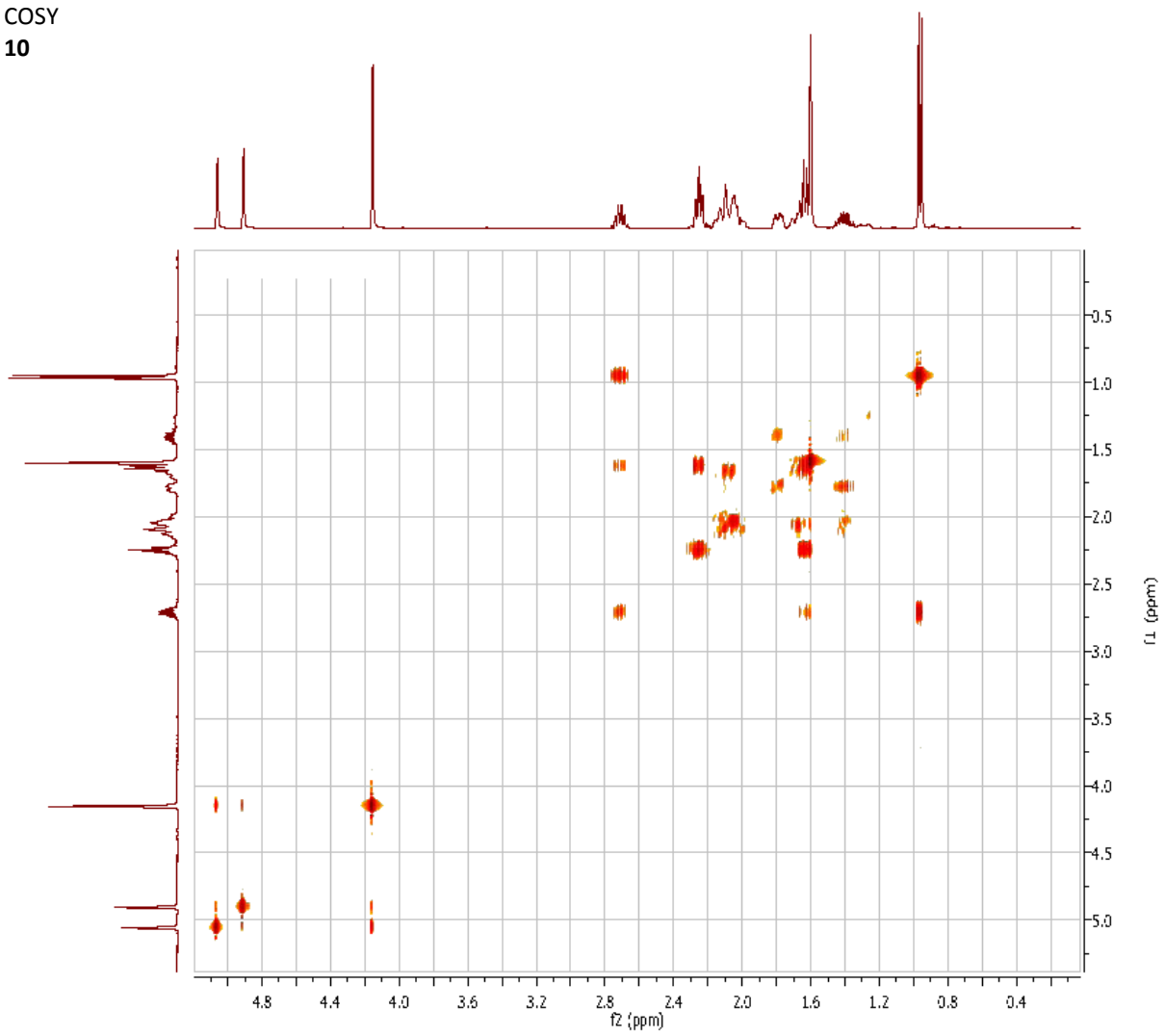


Fig. S83. $^{1}H–^{1}H$ COSY spectrum of the new compound **10**.

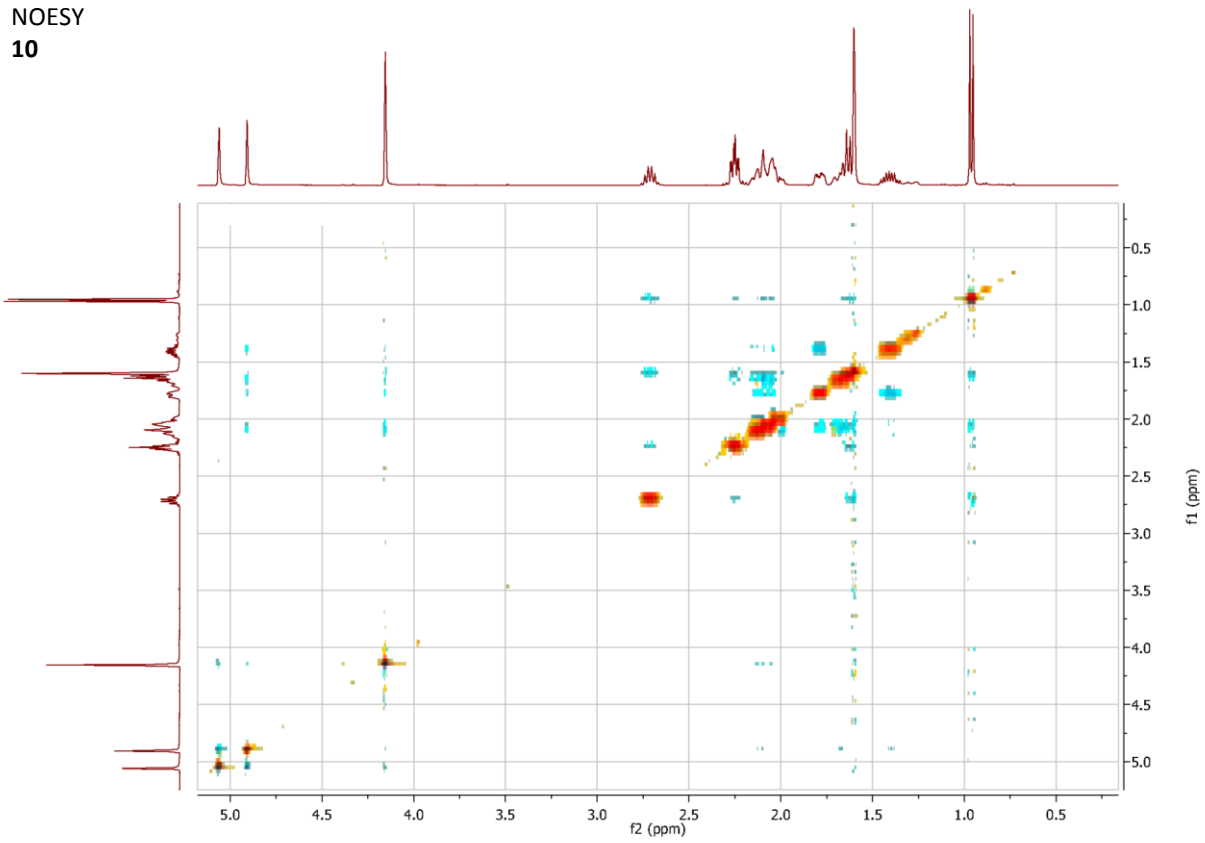


Fig. S84. NOESY spectrum of the new compound **10**.

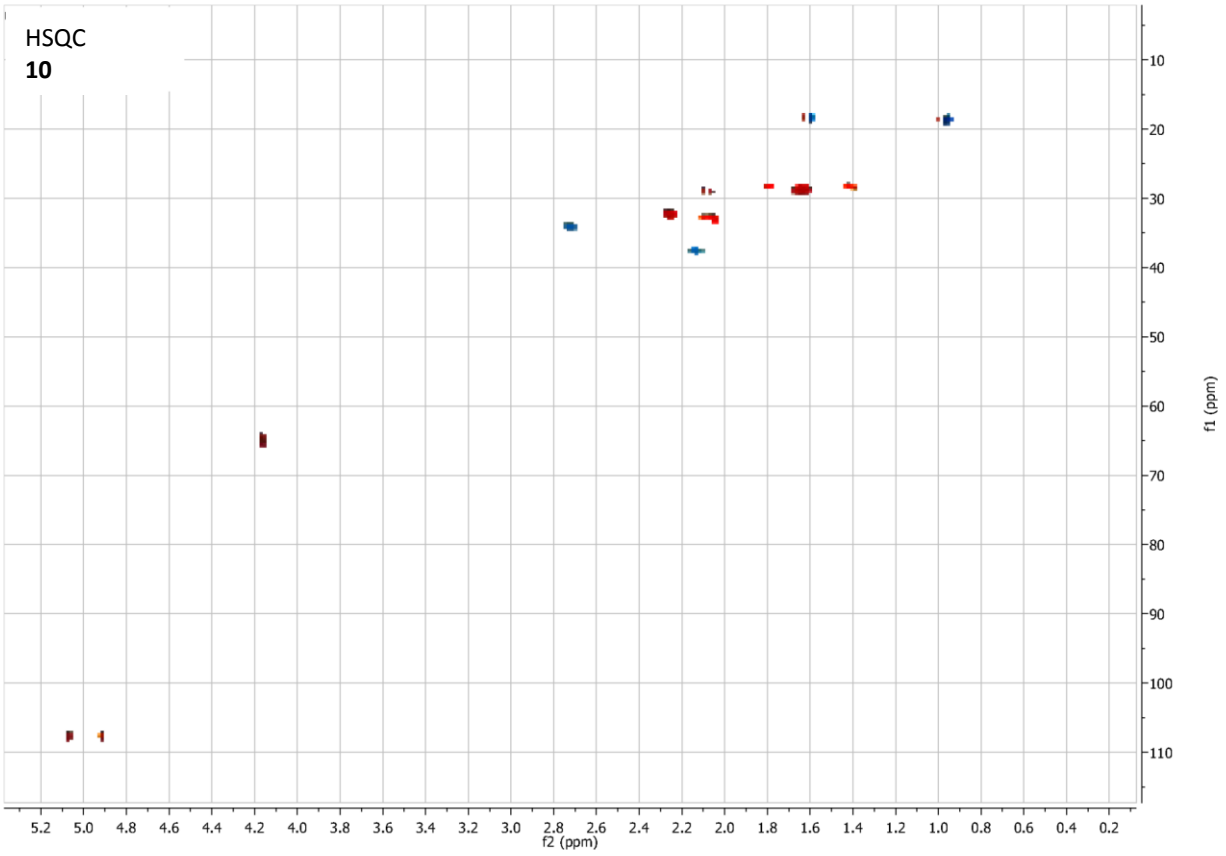


Fig. S85. HSQC spectrum of the new compound **10**.

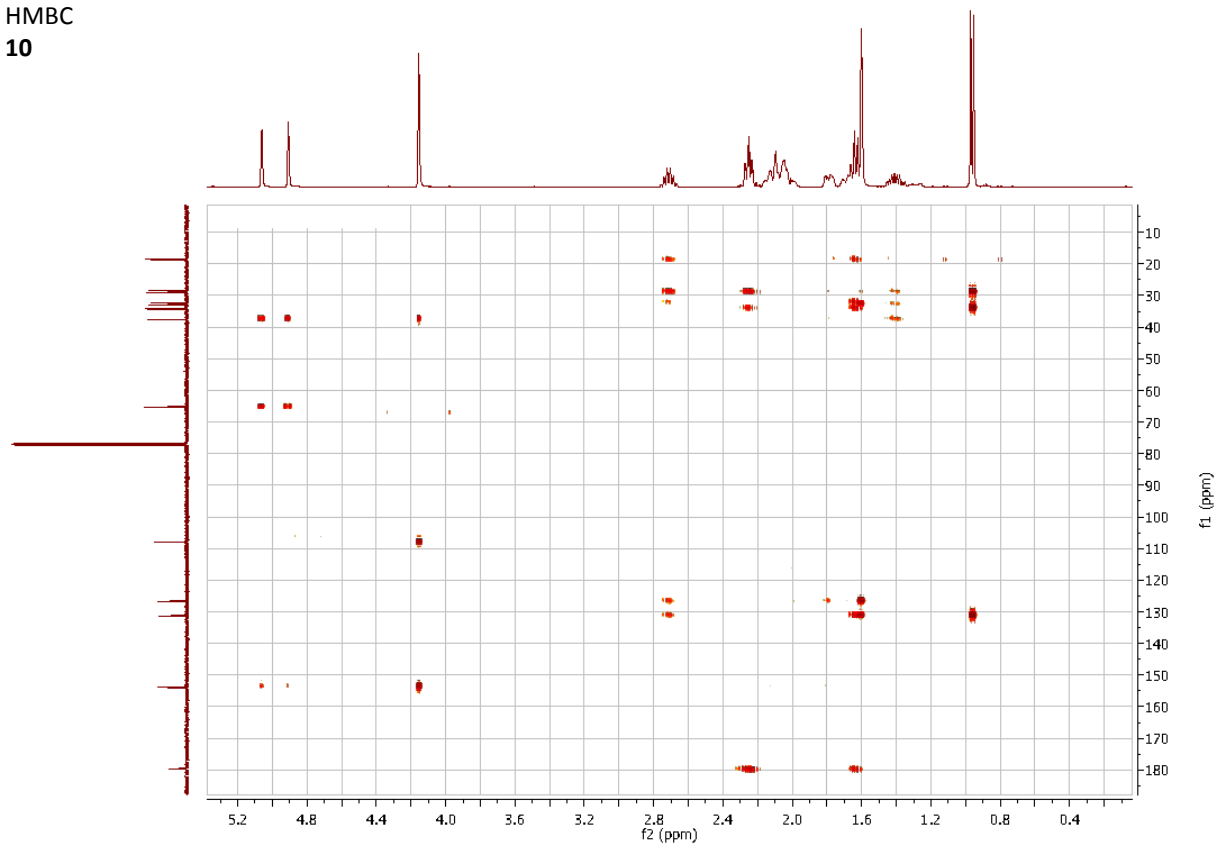


Fig. S86. HMBC spectrum of the new compound **10**.