

***Albatrellus confluens* (Alb. & Schwein.) Kotl. & Pouz. : natural fungal compounds and synthetic derivatives with anthelmintic and anticancer activities**

Mthandazo Dube¹, Dayma Llanes¹, Mohamad Saoud¹, Robert Rennert¹, Peter Imming², Cécile Häberli^{3,4}, Jennifer Keiser^{3,4} and Norbert Arnold^{1*}

¹ Department of Bioorganic Chemistry, Leibniz Institute of Plant Biochemistry, Weinberg 3, D-06120 Halle (Saale), Germany; Mthandazo.Dube@ipb-halle.de (M.D.); Dayma.LlanesMartinez@ipb-halle.de (D.L); Mohamad.Saoud@ipb-halle.de (M.S.); Robert.Rennert@ipb-halle.de (R.R.); Norbert.Arnold@ipb-halle.de (N.A.)

² Institute of Pharmacy, Faculty of Natural Sciences, Martin-Luther-University Halle-Wittenberg, D-06120 Halle (Saale), Germany; peter.imming@pharmazie.uni-halle.de (P.I.)

³ Swiss Tropical and Public Health Institute, Kreuzstr.2, CH-4123 Allschwil, Switzerland; cecile.haeberli@swisstph.ch (C.H.), jennifer.keiser@swisstph.ch (J.K.)

⁴ University of Basel, CH-4051 Basel, Switzerland

* Correspondence: Norbert.Arnold@ipb-halle.de (N.A.); Tel.: +49-345-5582-1310 (N.A.)¹

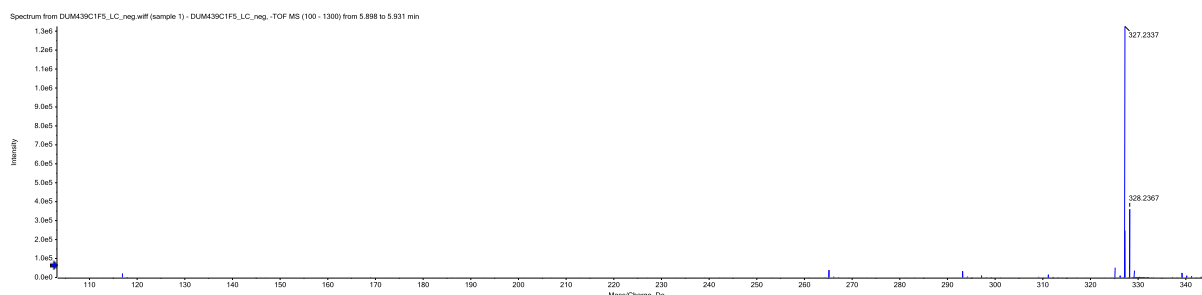


Figure S1: ESI-HRMS (neg. ion mode) spectrum of grifolin (**1**).

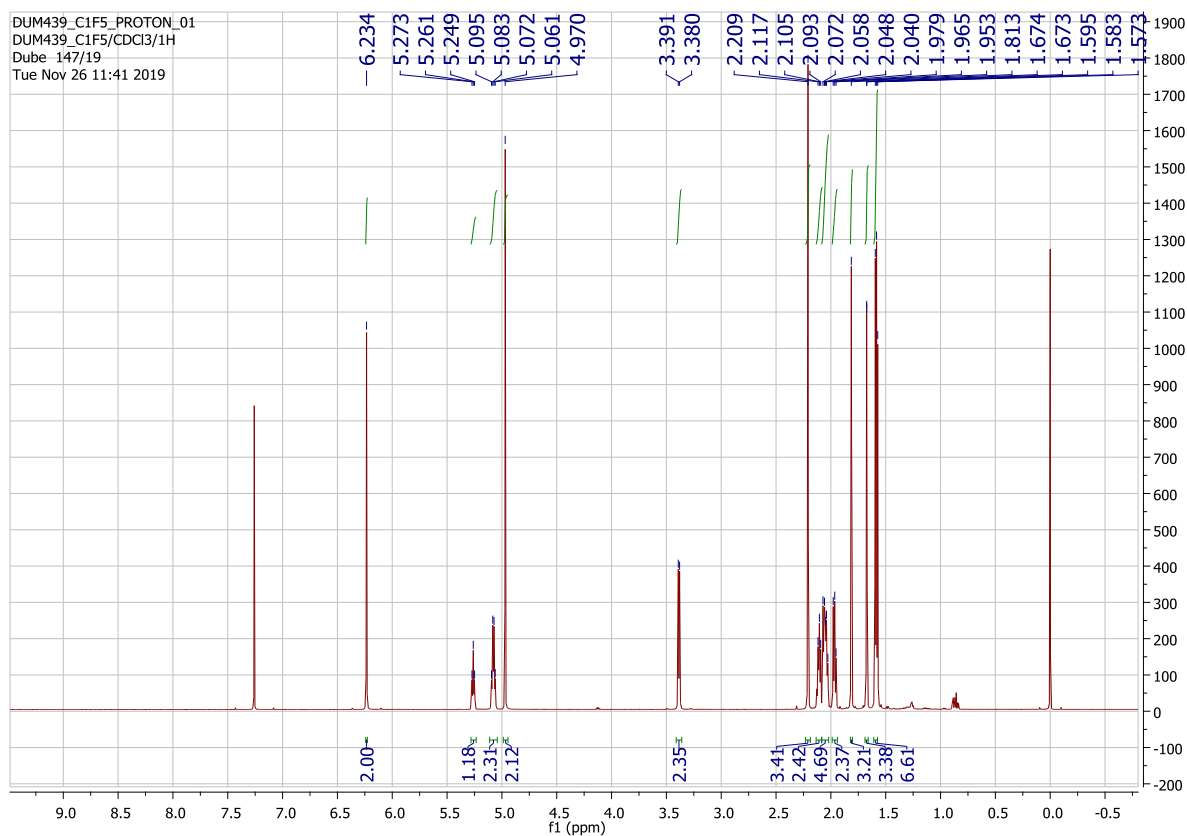


Figure S2: ^1H NMR spectrum of grifolin (**1**) in CDCl_3 (400 MHz, δ in ppm).

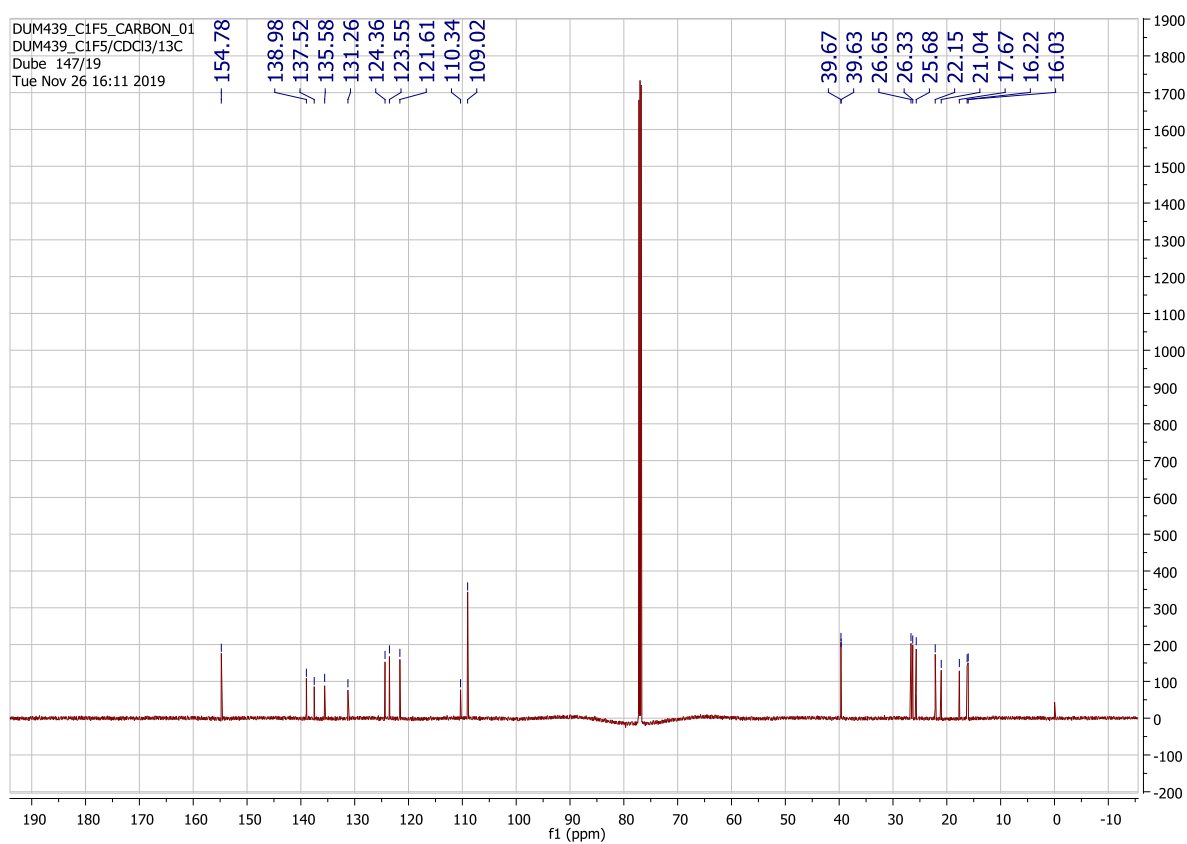


Figure S3: ^{13}C NMR spectrum of grifolin (**1**) in CDCl_3 (400 MHz, δ in ppm).

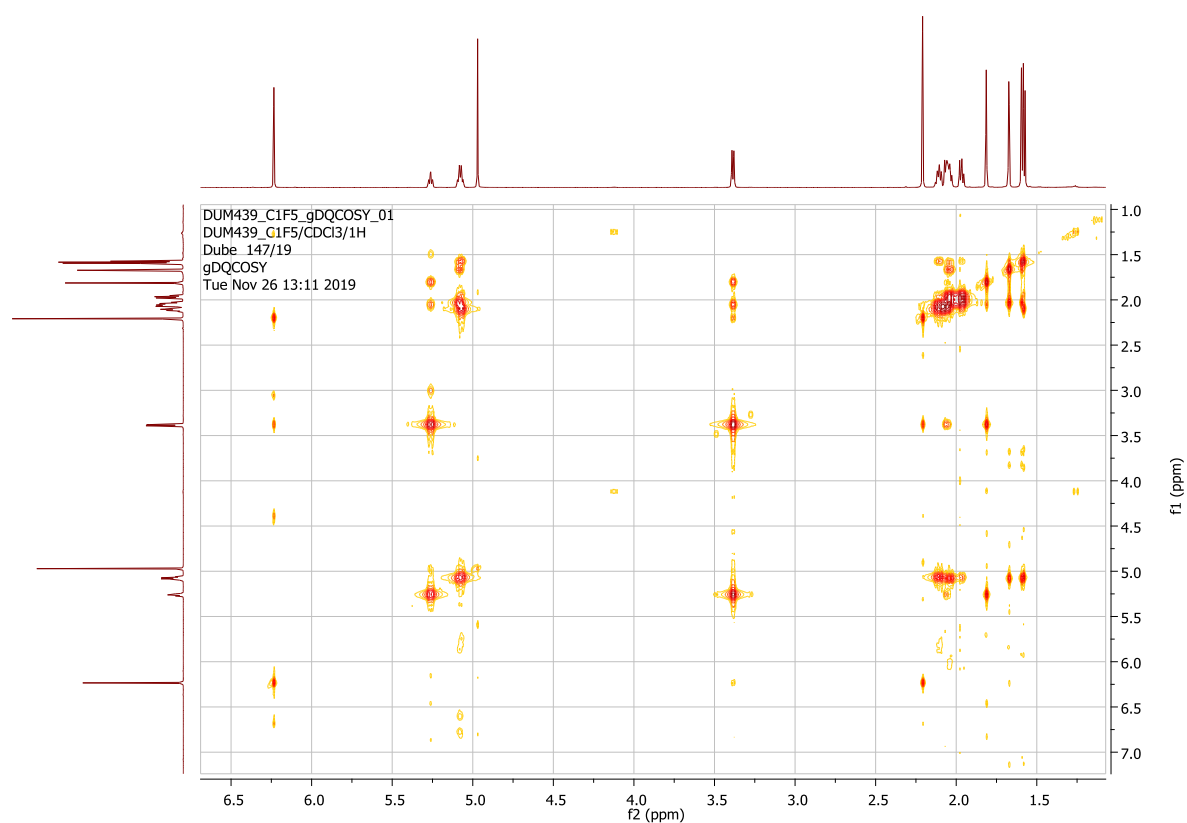


Figure S4: gDQCOSY spectrum of grifolin (**1**) in CDCl₃ (400 MHz, δ in ppm).

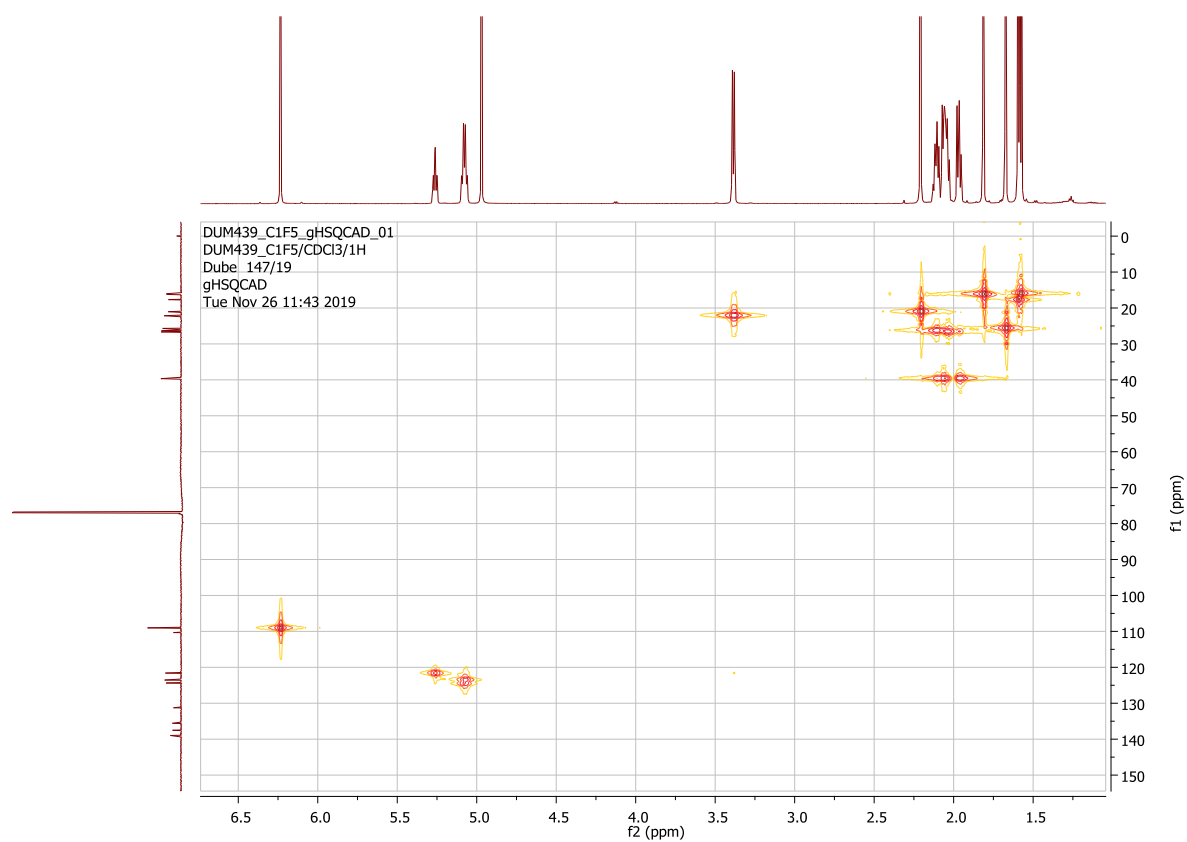


Figure S5: gHSQC spectrum of grifolin (**1**) in CDCl₃ (400 MHz, δ in ppm).

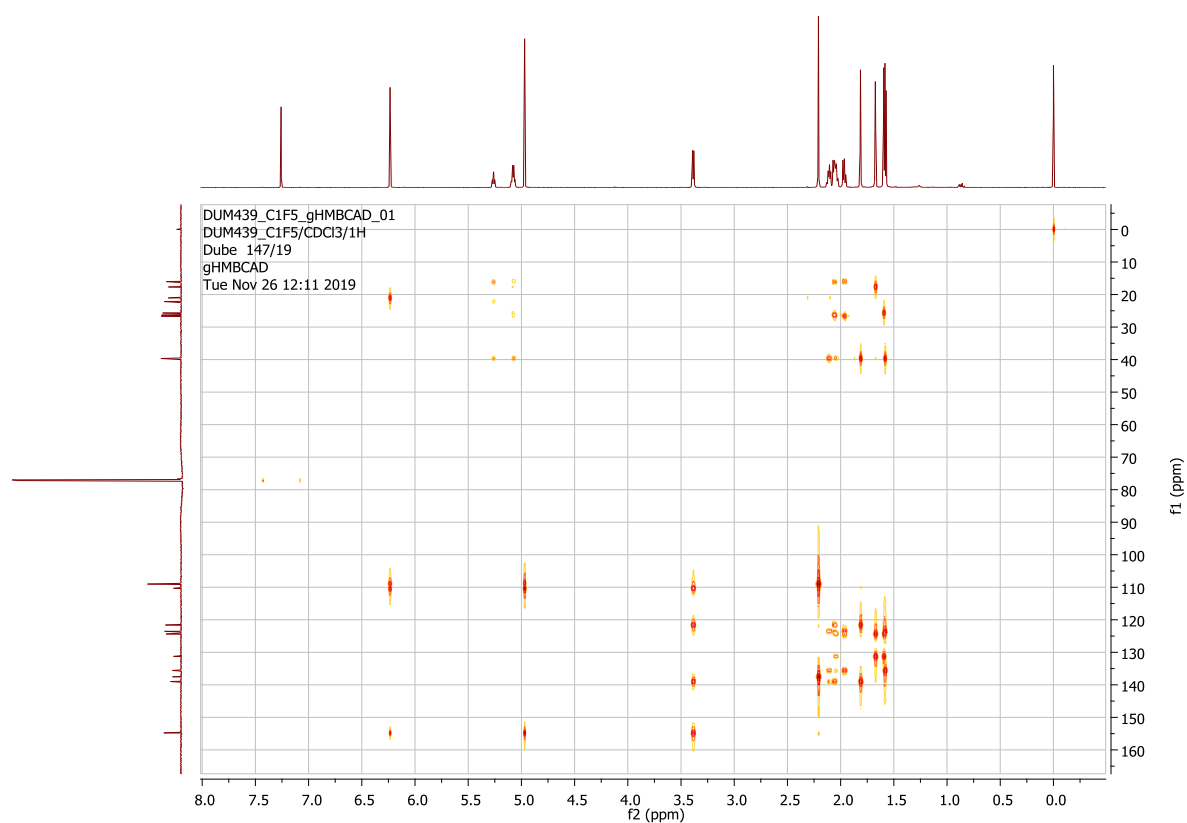


Figure S6: gHMBC spectrum of grifolin (**1**) in CDCl_3 (400 MHz, δ in ppm).

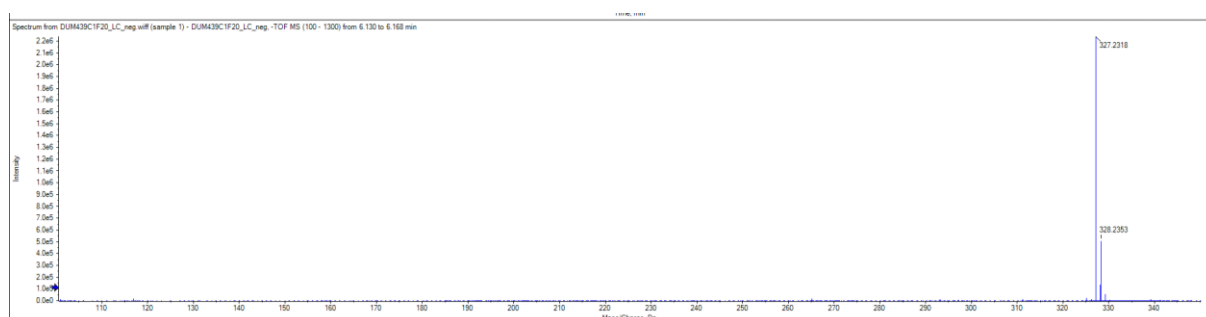


Figure S7: ESI-HRMS (neg. ion mode) of neogrifolin (**2**).

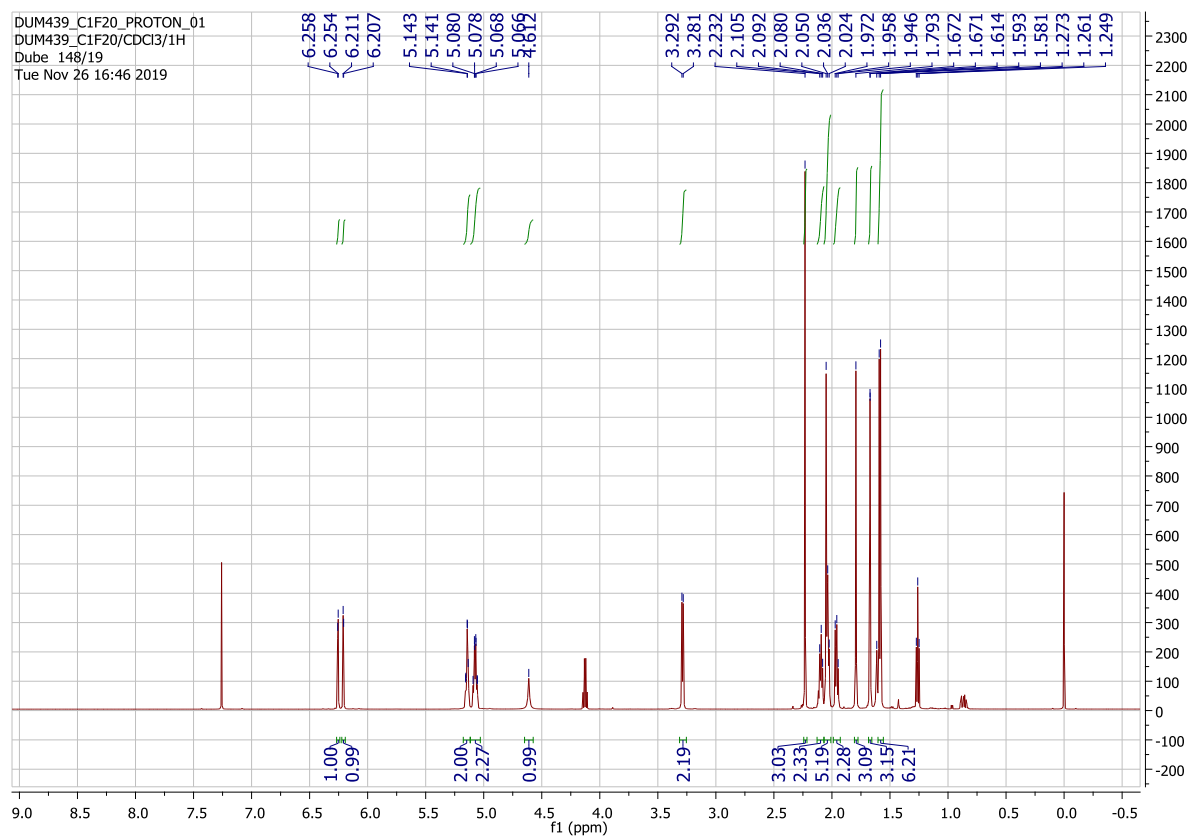


Figure S8: ^1H NMR spectrum of neogrifolin (**2**) in CDCl_3 (400 MHz, δ in ppm).

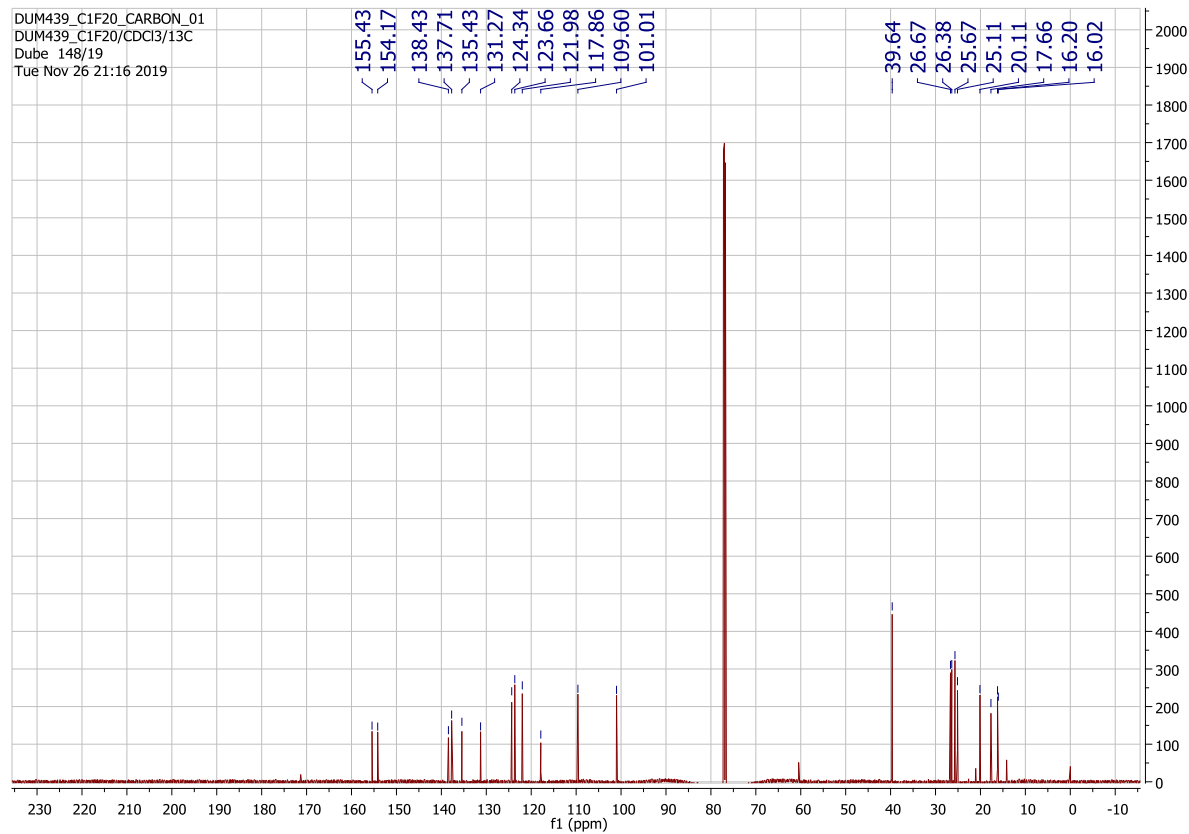


Figure S9: ^{13}C NMR spectrum of neogrifolin (**2**) in CDCl_3 (400 MHz, δ in ppm).

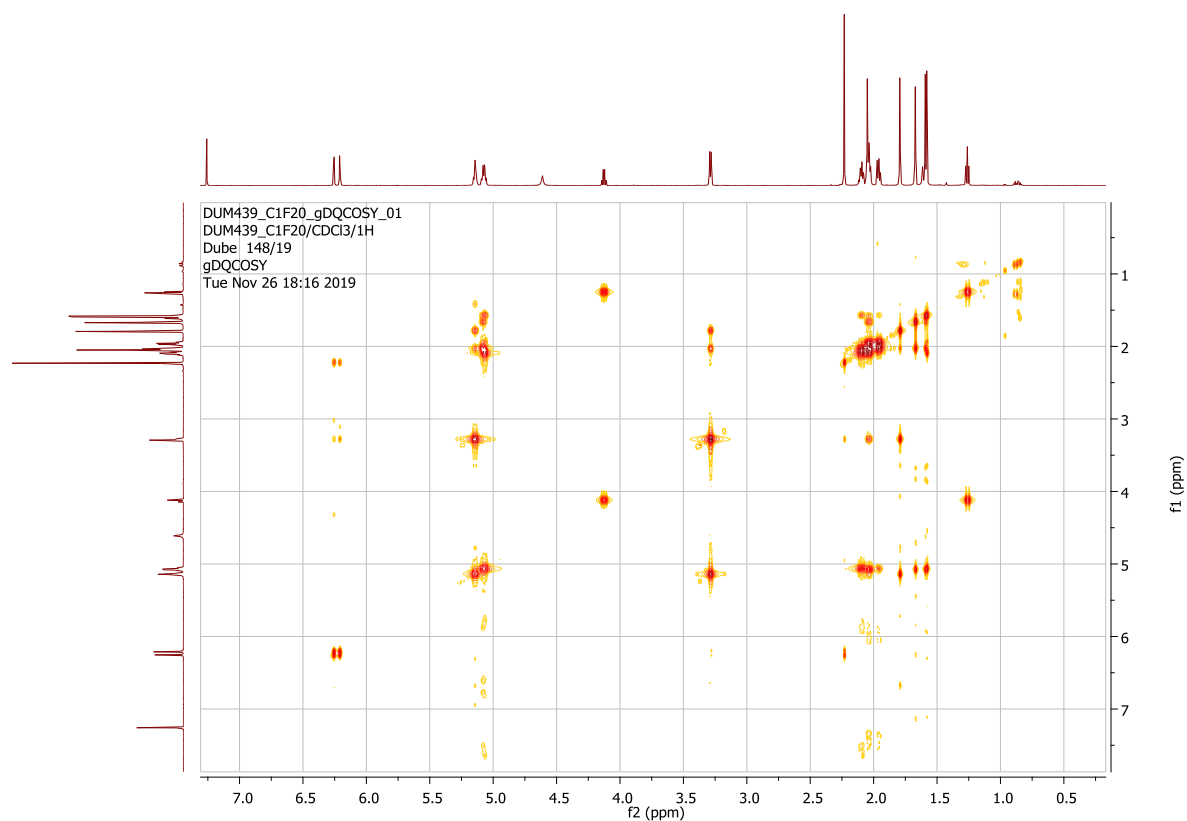


Figure S10: gDQCOSY spectrum of neogrifolin (**2**) in CDCl₃ (400 MHz, δ in ppm).

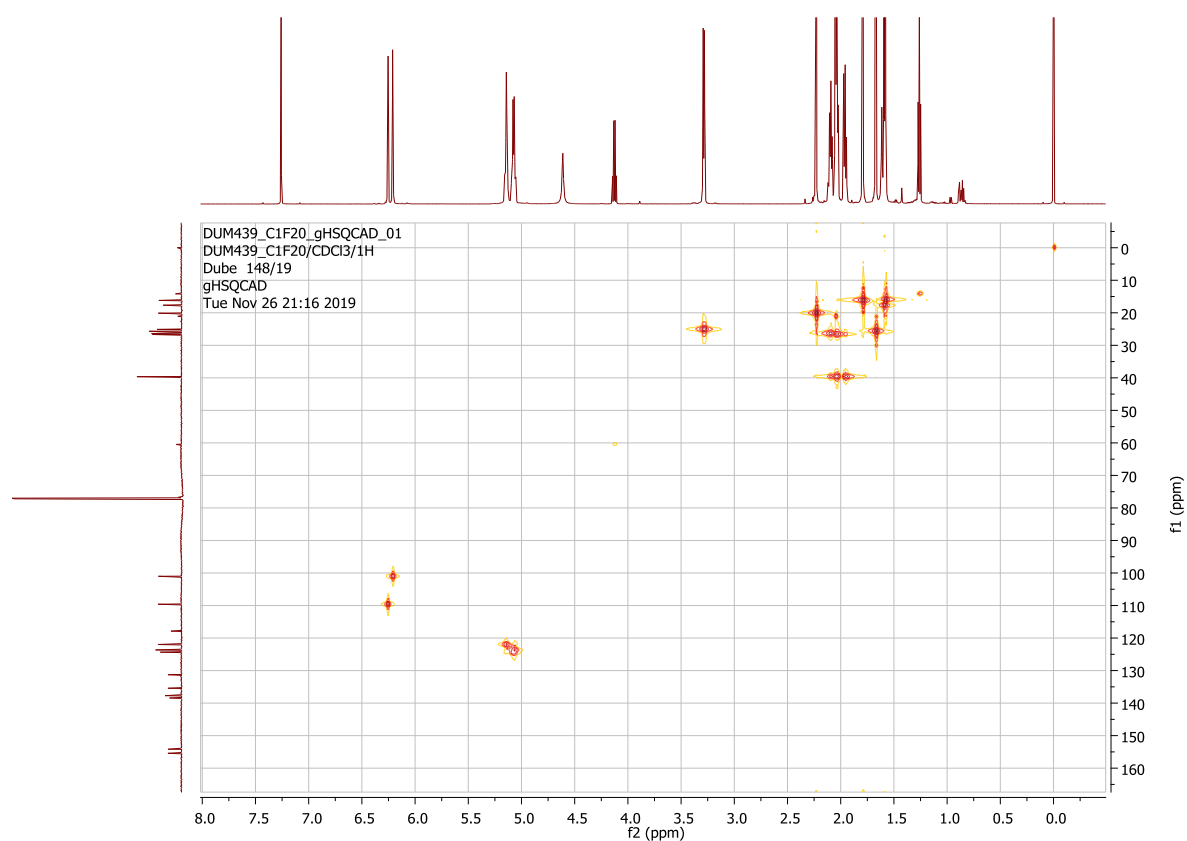


Figure S11: gHSQC spectrum of neogrifolin (**2**) in CDCl₃ (400 MHz, δ in ppm).

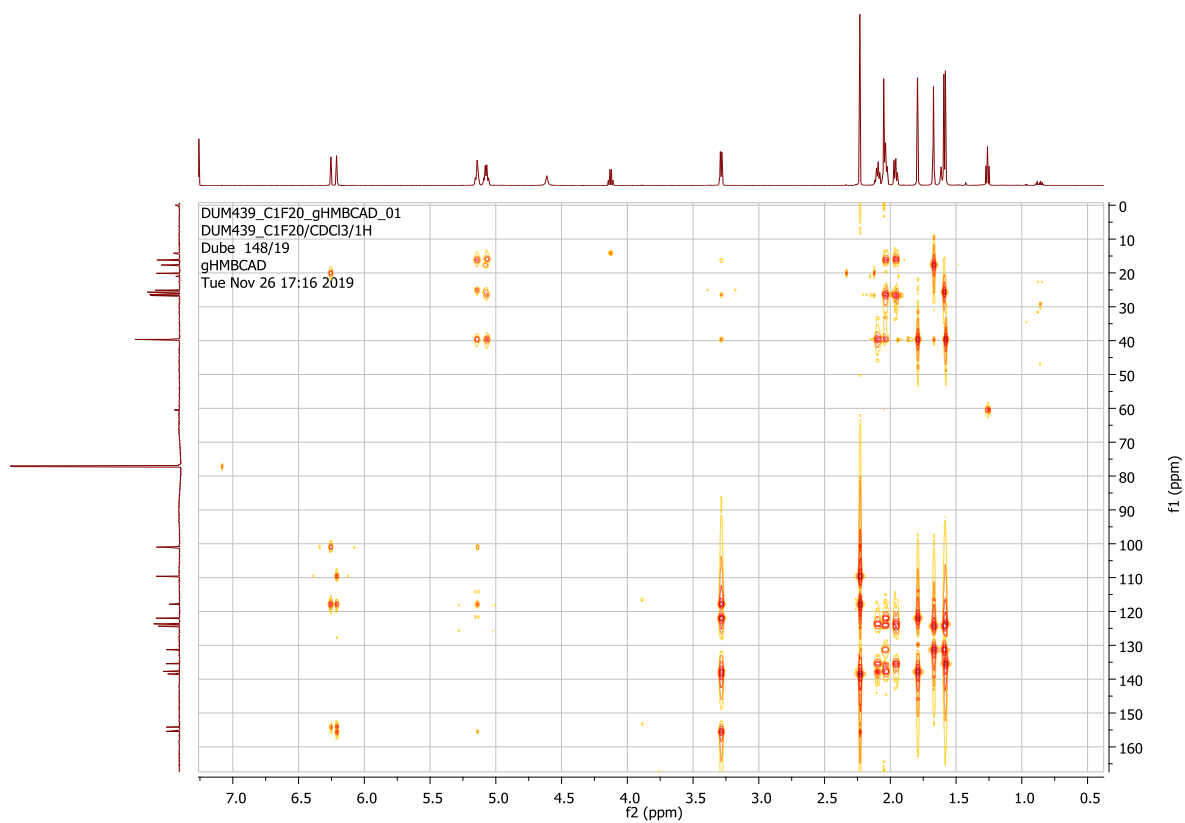


Figure S12: gHMBC spectrum of neogrifolin (2) in CDCl₃ (400 MHz, δ in ppm).

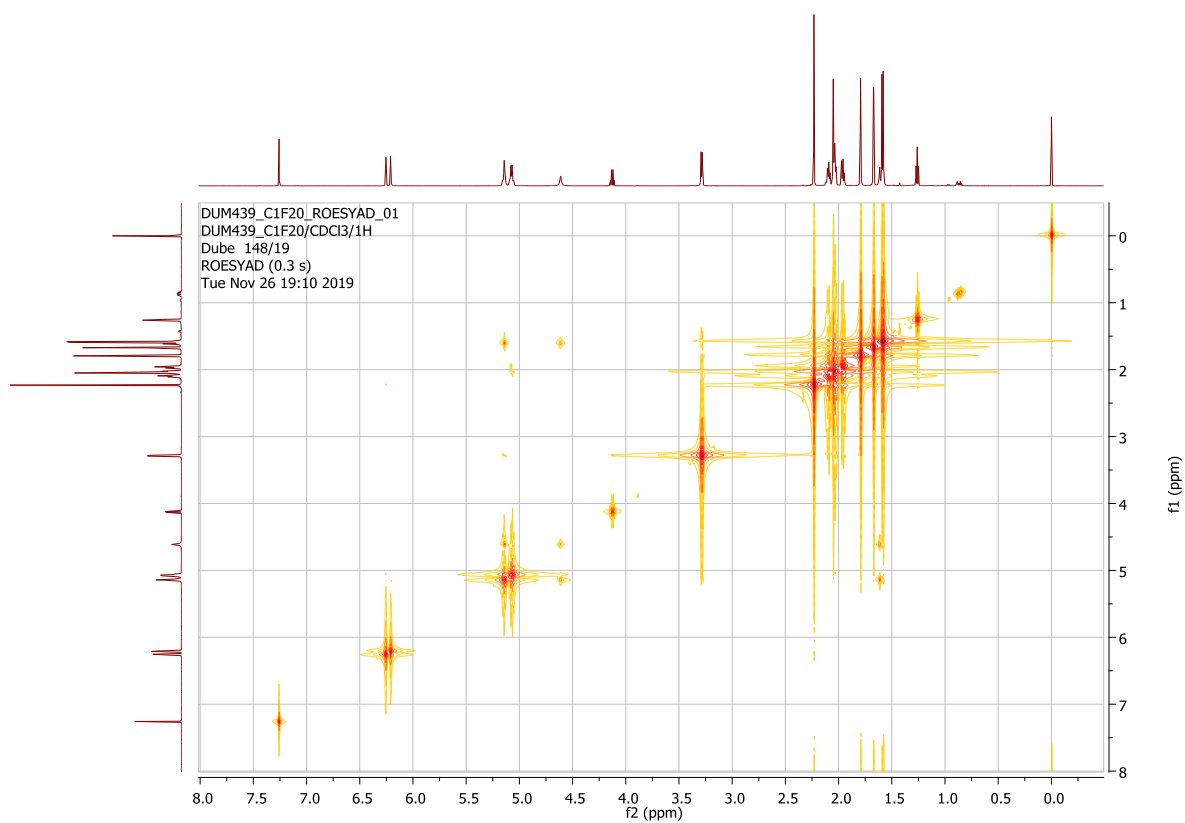


Figure S13: NOESY spectrum of neogrifolin (2) in CDCl₃ (400 MHz, δ in ppm).

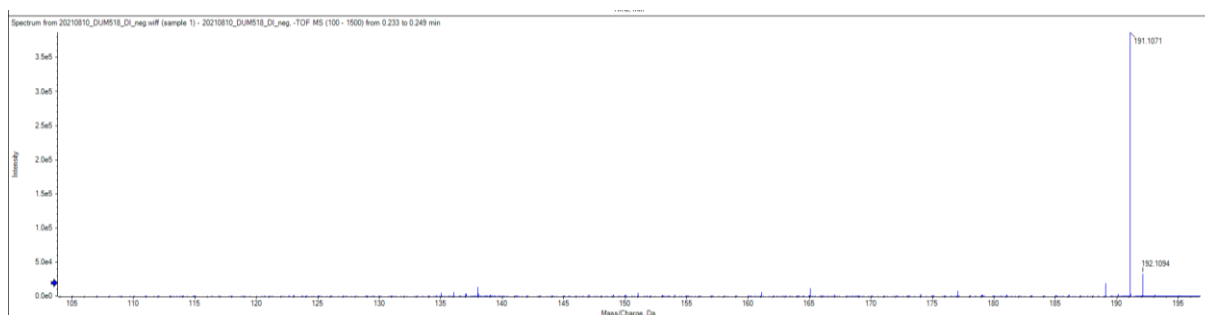


Figure S14: ESI-HRMS (neg. ion mode) of prenyl-2-orcinol (**4**).

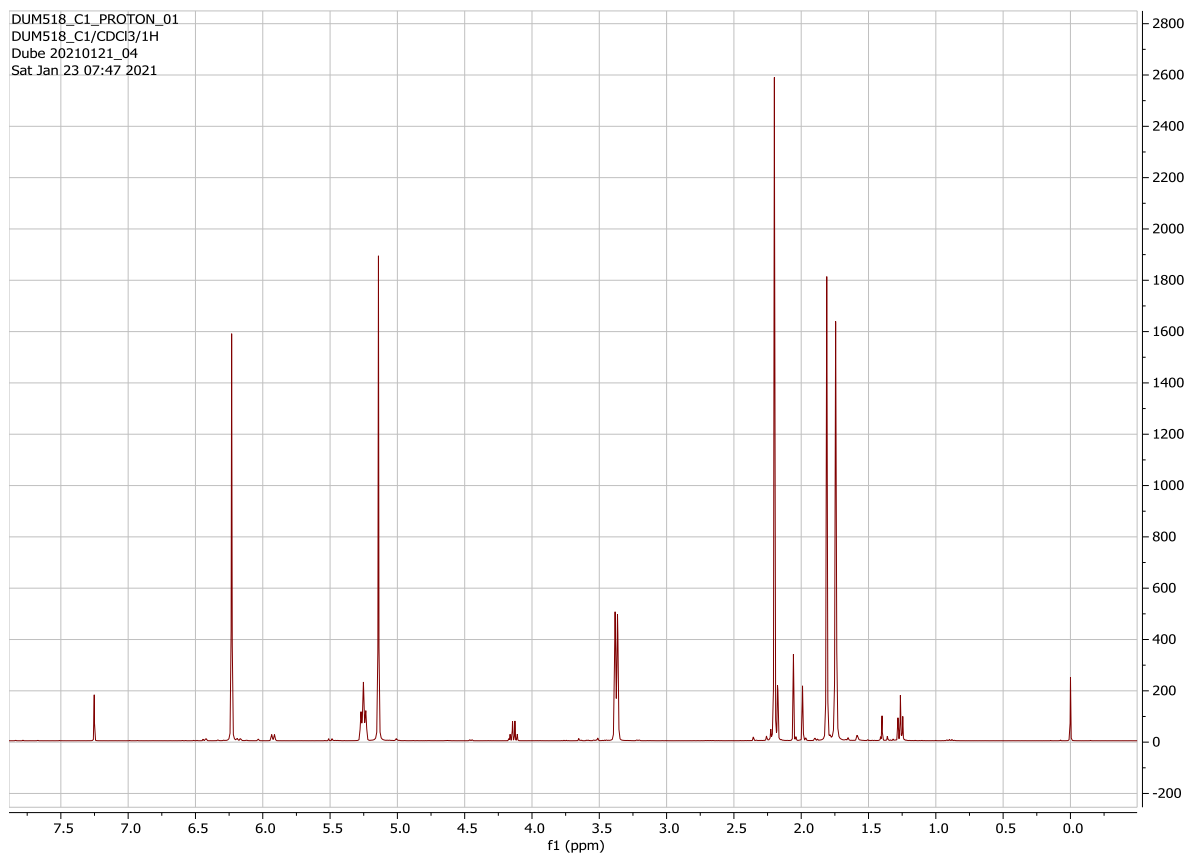


Figure S15: ^1H NMR spectrum of prenyl-2-orcinol (**4**) in CDCl_3 (400 MHz, δ in ppm) without integration.

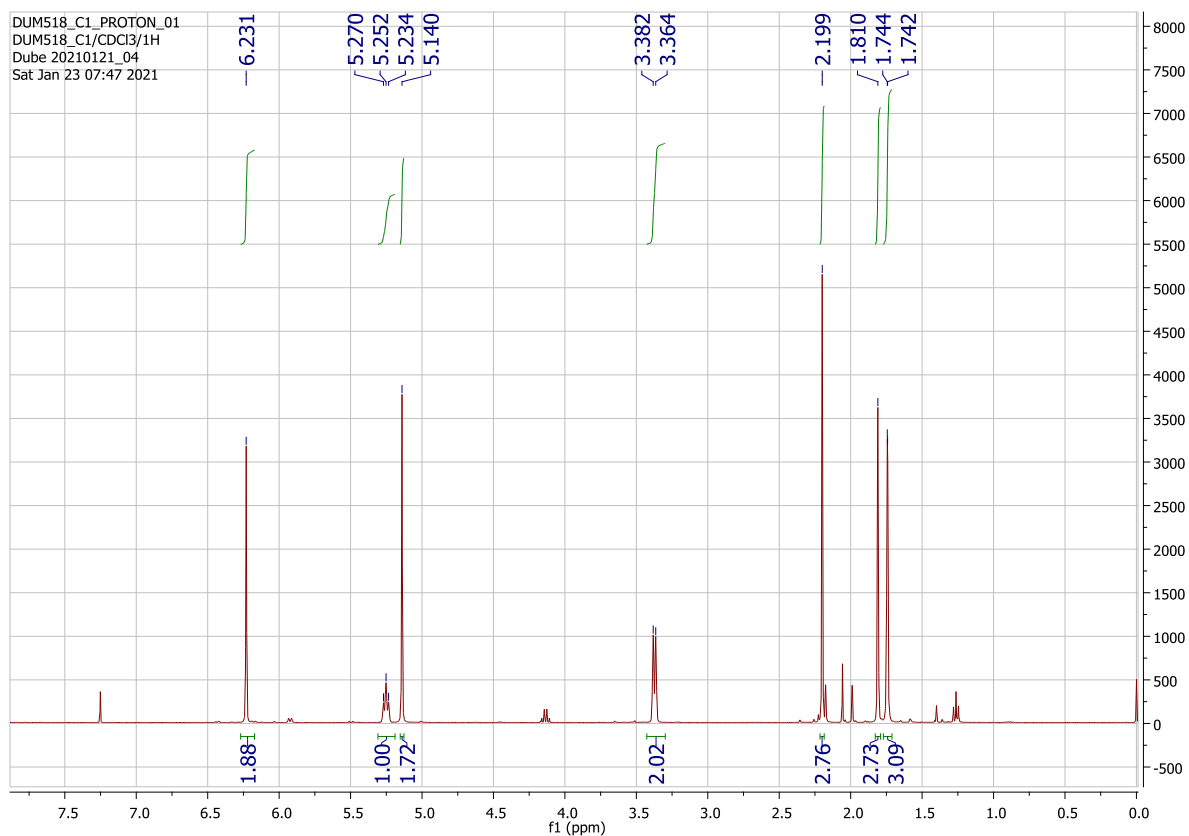


Figure S16: ^1H NMR spectrum of prenyl-2-orninol (**4**) in CDCl_3 (400 MHz, δ in ppm).

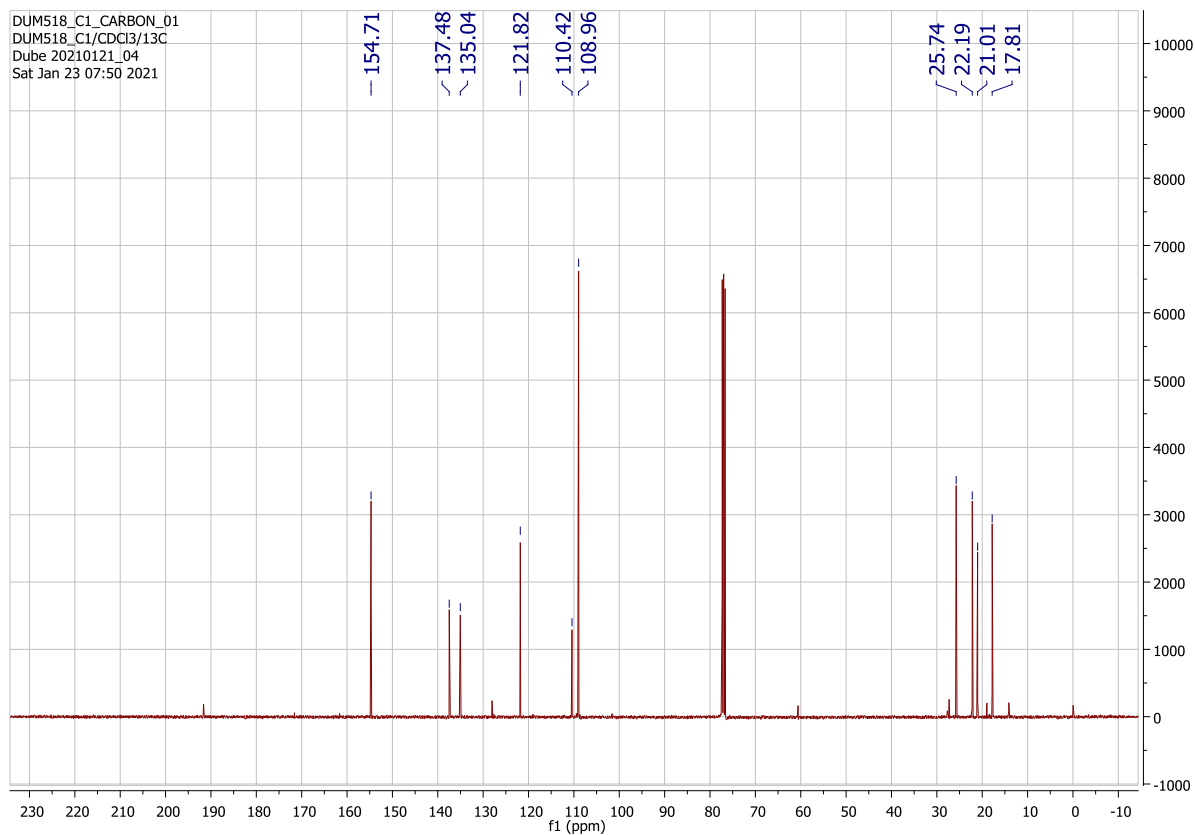


Figure S17: ^{13}C NMR spectrum of prenyl-2-orninol (**4**) in CDCl_3 (400 MHz, δ in ppm).

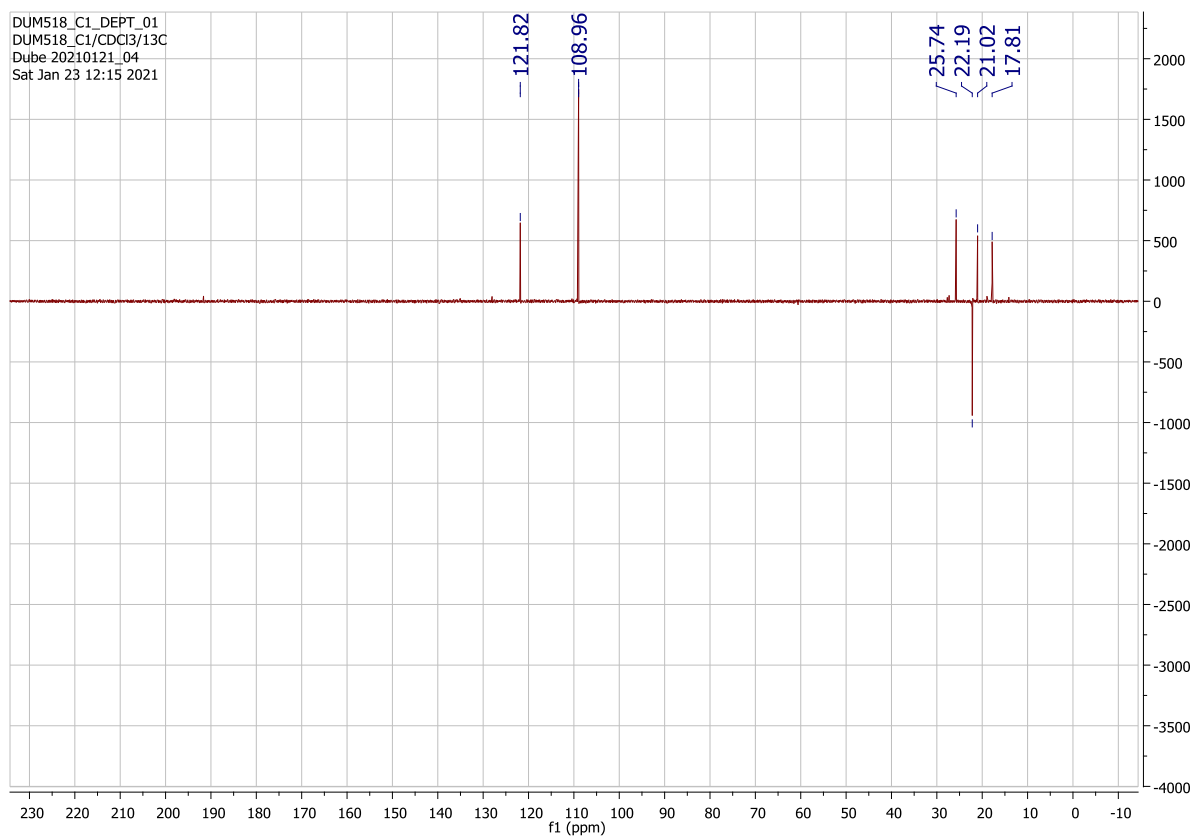


Figure S18: DEPT 135 spectrum of prenyl-2-orninol (**4**) in CDCl₃ (400 MHz, δ in ppm).

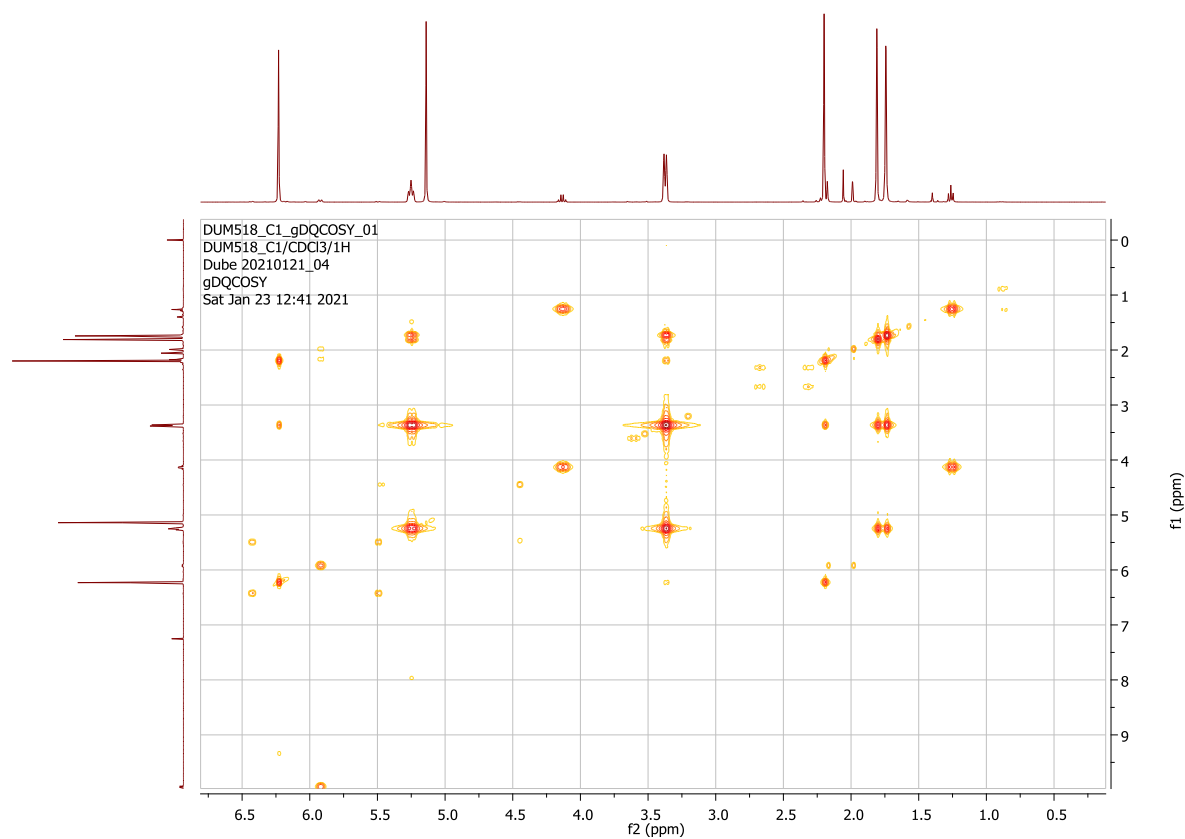


Figure S19: gDQCOSY spectrum of prenyl-2-orninol (**4**) in CDCl₃ (400 MHz, δ in ppm).

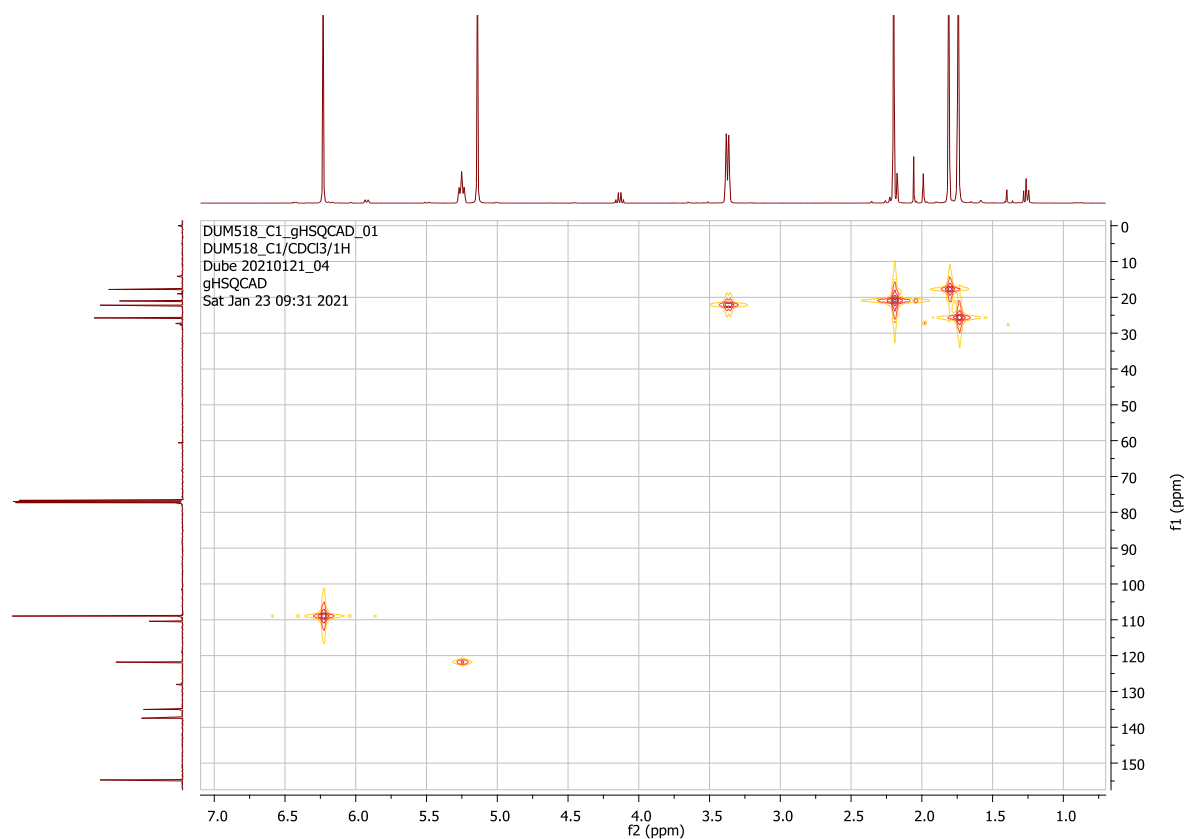


Figure S20: gHSQC spectrum of prenyl-2-orchinol (4) in CDCl₃ (400 MHz, δ in ppm).

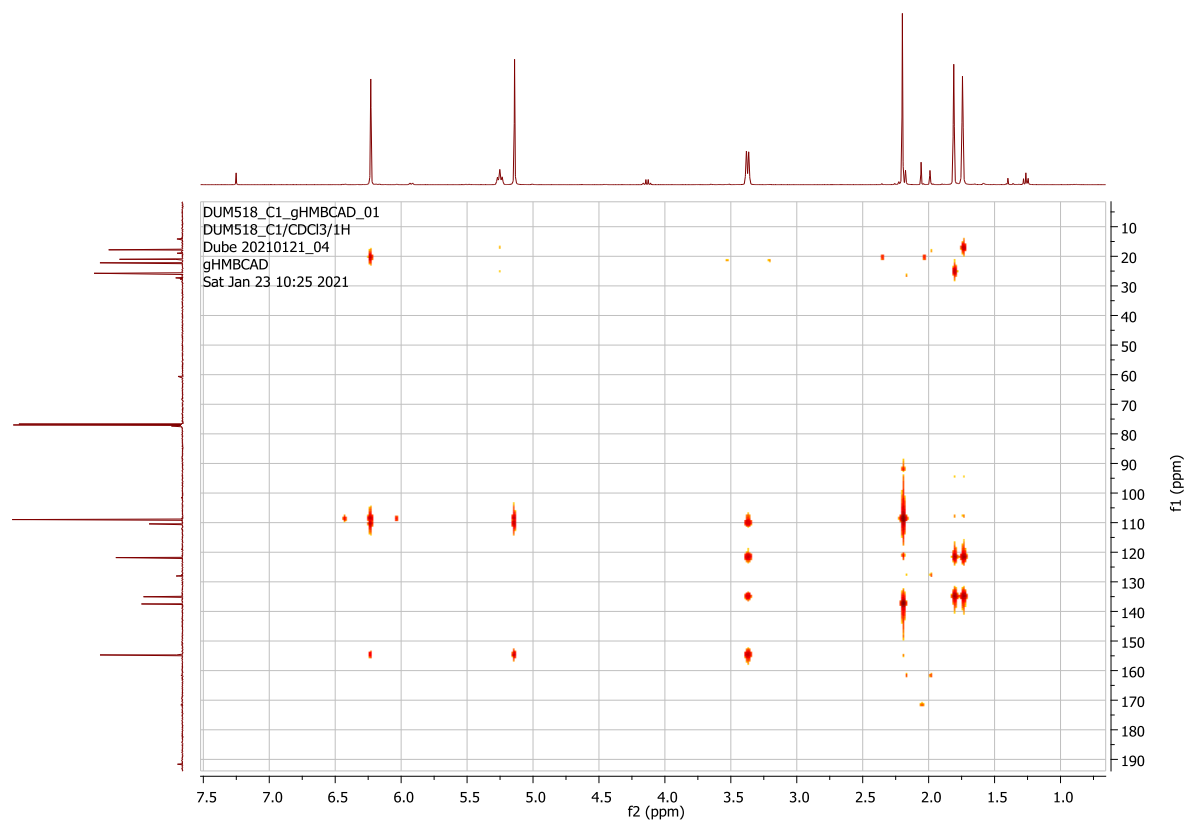


Figure S21: gHMBC spectrum of prenyl-2-orchinol (4) in CDCl₃ (400 MHz, δ in ppm).

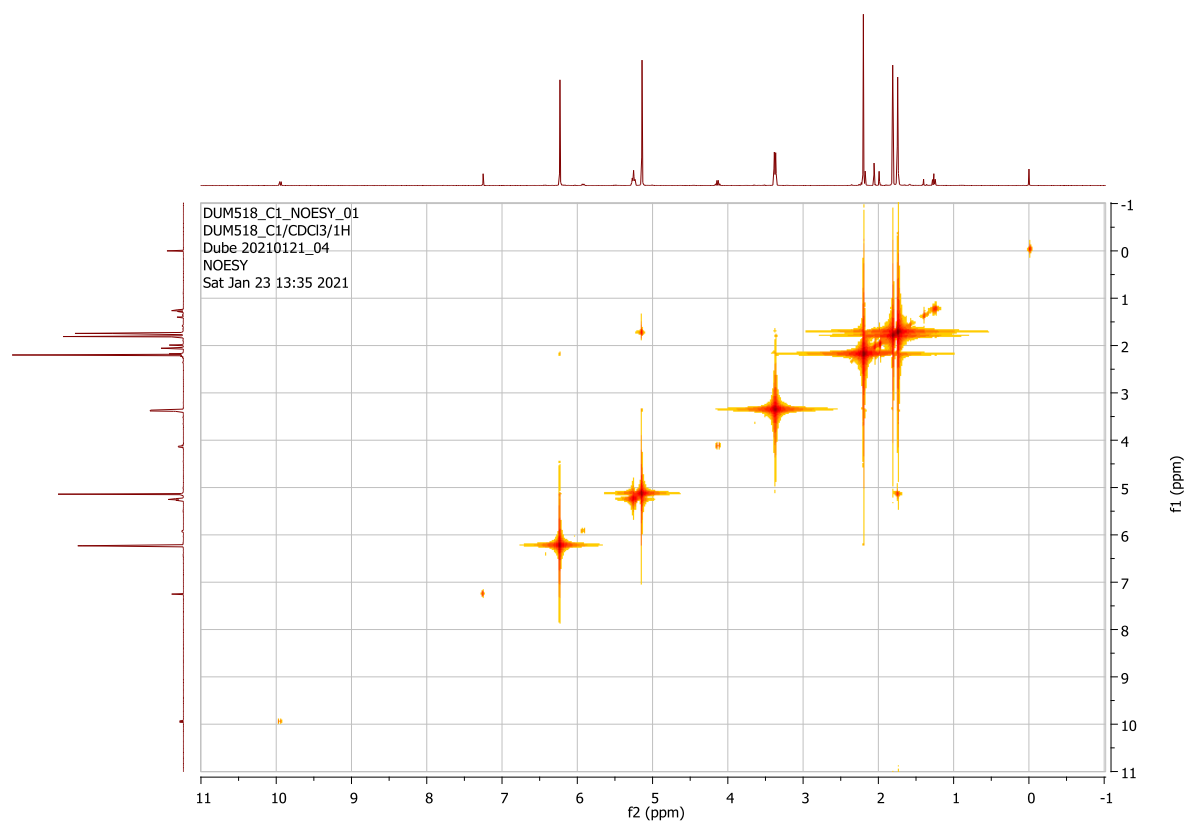


Figure S22: NOESY spectrum of prenyl-2-orkinol (4) in CDCl₃ (400 MHz, δ in ppm).

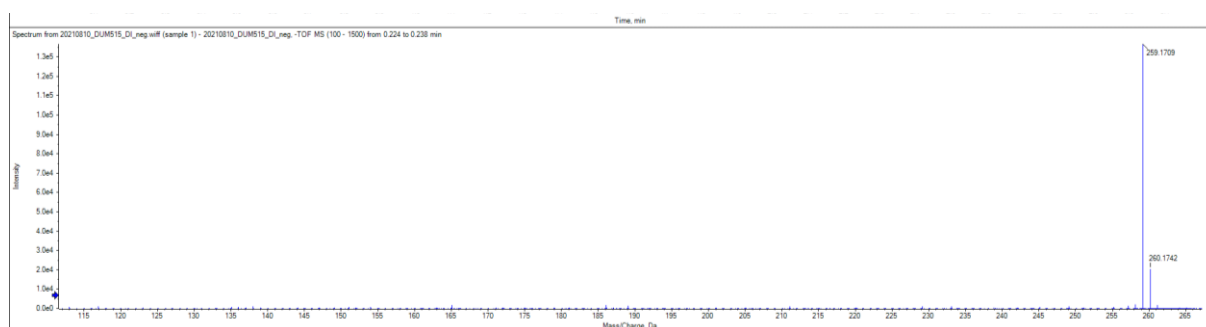


Figure S23: ESI-HRMS (neg. ion mode) spectrum of geranyl-2-orkinol (5).

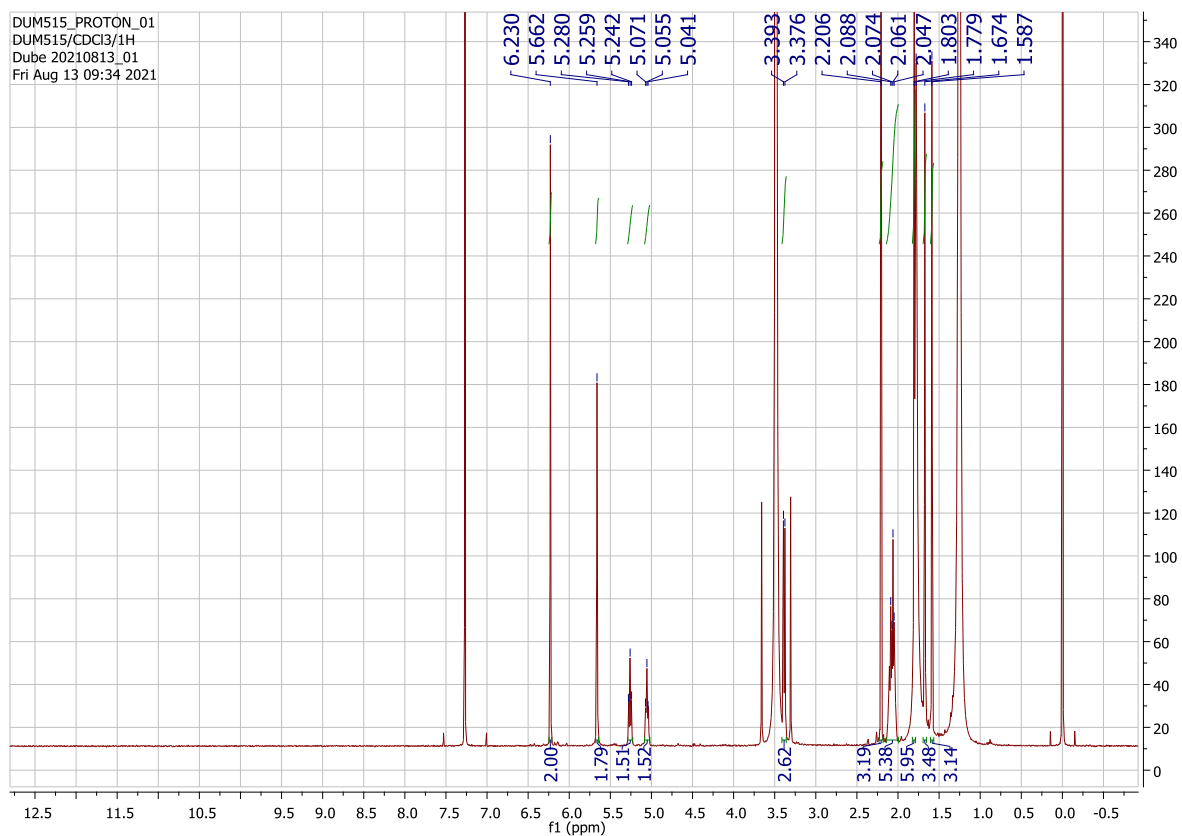


Figure S24: ^1H NMR spectrum of geranyl-2-orninol (**5**) in CDCl_3 (400 MHz, δ in ppm).

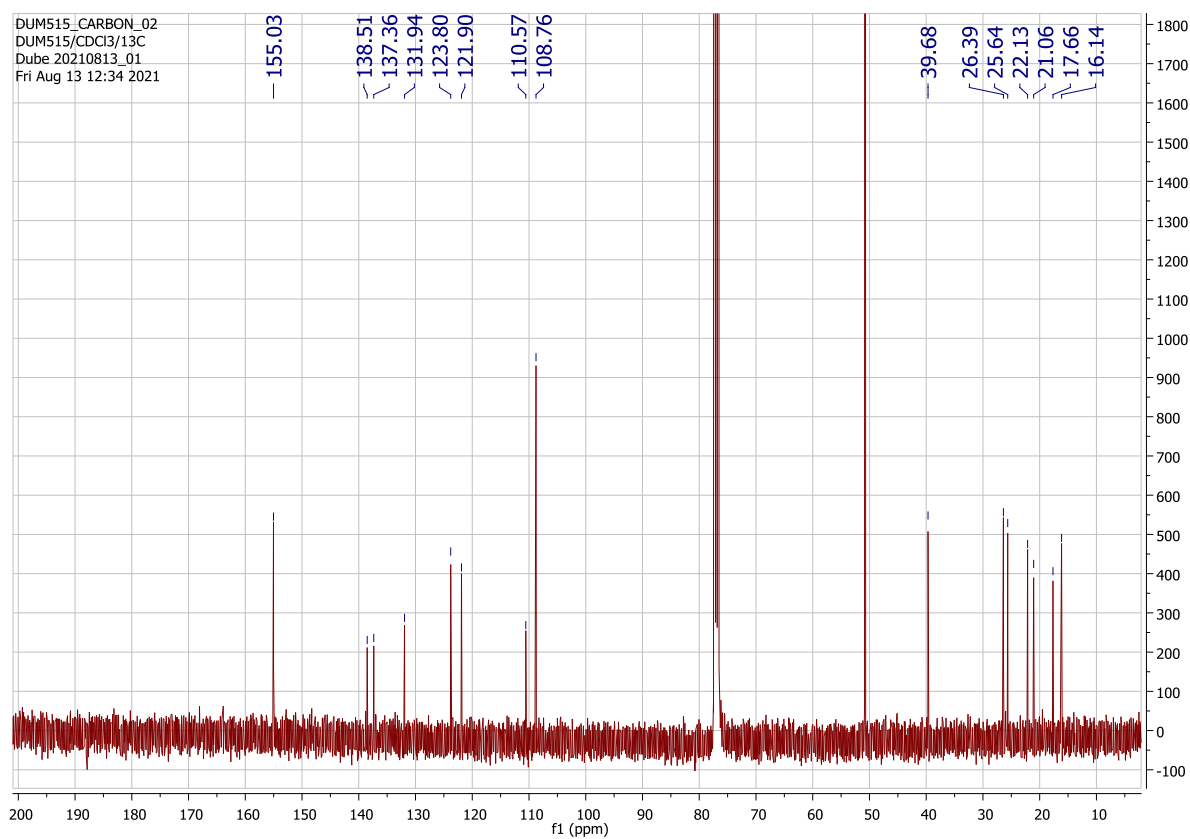


Figure S25: ^{13}C NMR spectrum of geranyl-2-orninol (**5**) in CDCl_3 (400 MHz, δ in ppm).

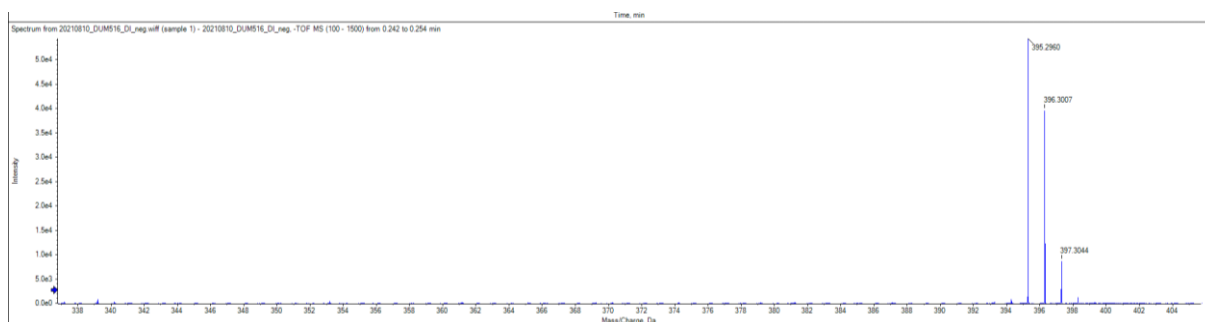


Figure S26: ESI-HRMS (neg. ion mode) spectrum of geranylgeranyl-2-orninol (**6**).

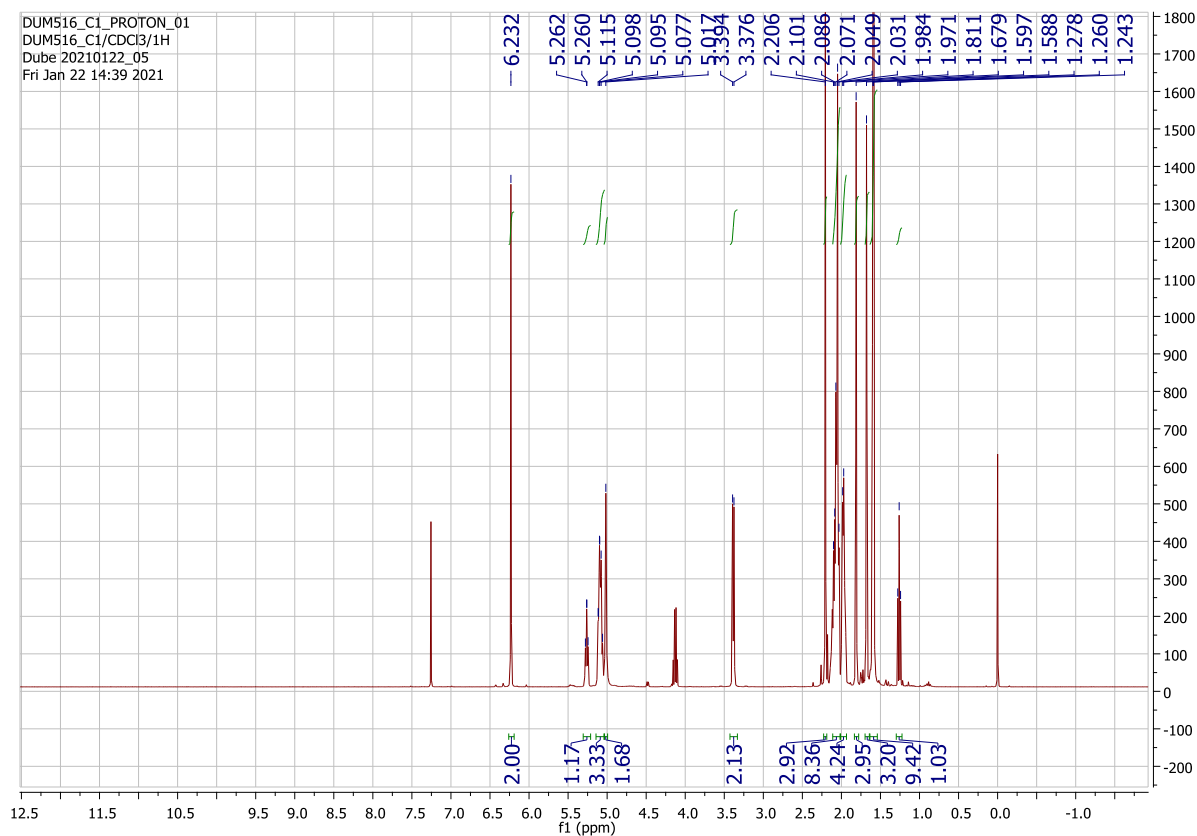


Figure S27: ^1H NMR spectrum of geranylgeranyl-2-orninol (**6**) in CDCl_3 (400 MHz, δ in ppm).

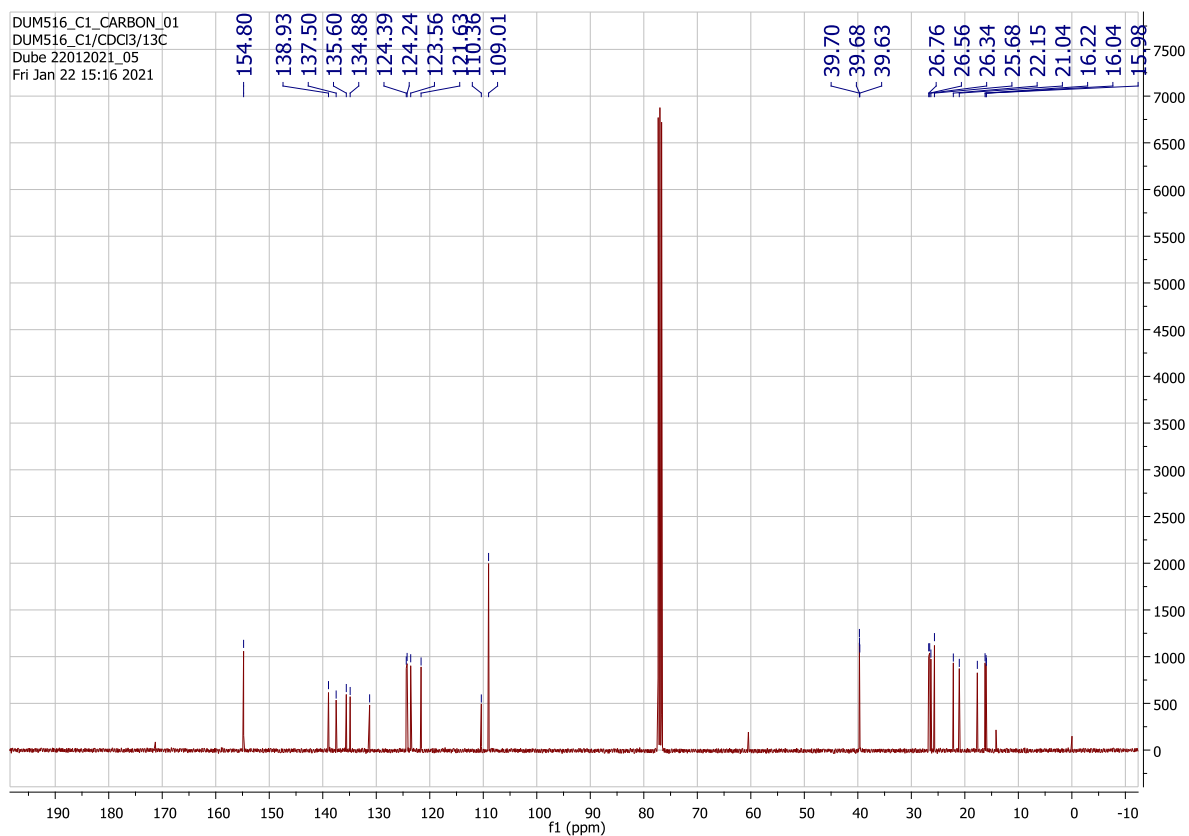


Figure S28: ^{13}C NMR spectrum of geranylgeranyl-2-orninol (**6**) in CDCl_3 (400 MHz, δ in ppm).

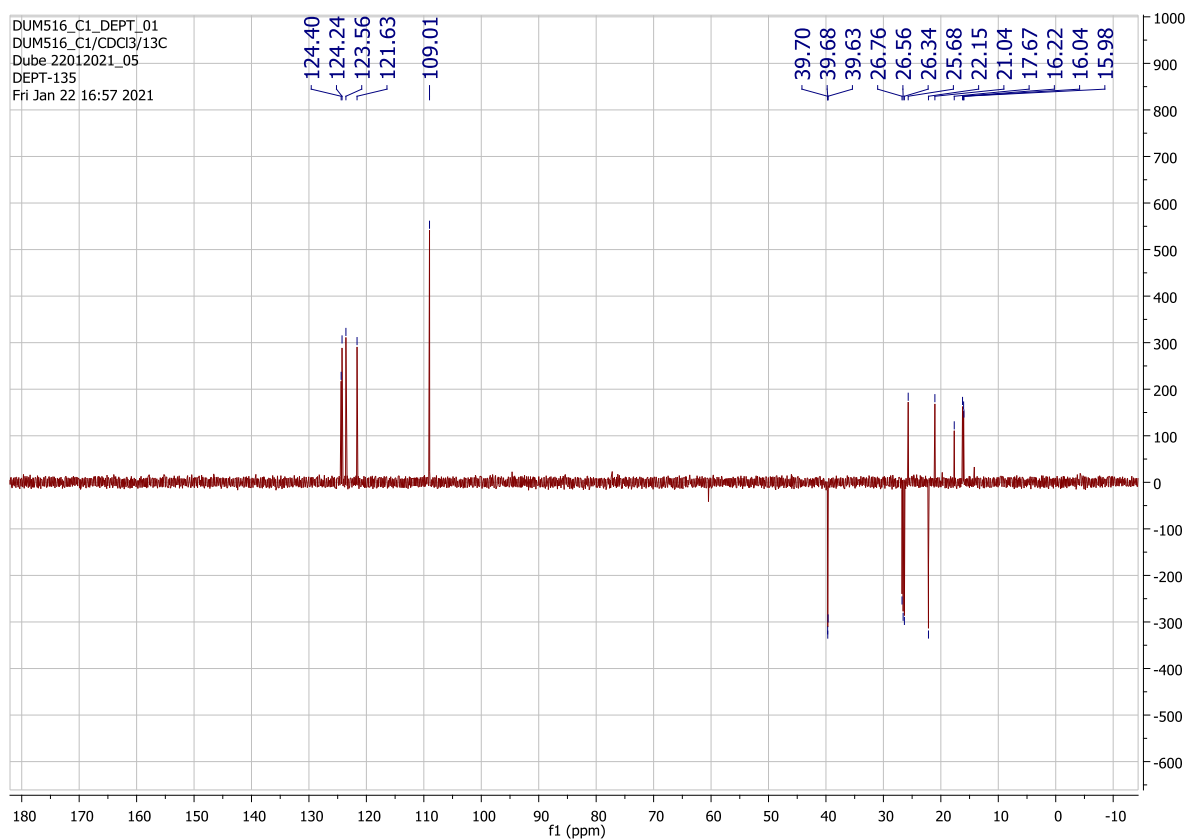


Figure S29: DEPT 135 spectrum of geranylgeranyl-2-orninol (**6**) in CDCl_3 (400 MHz, δ in ppm).

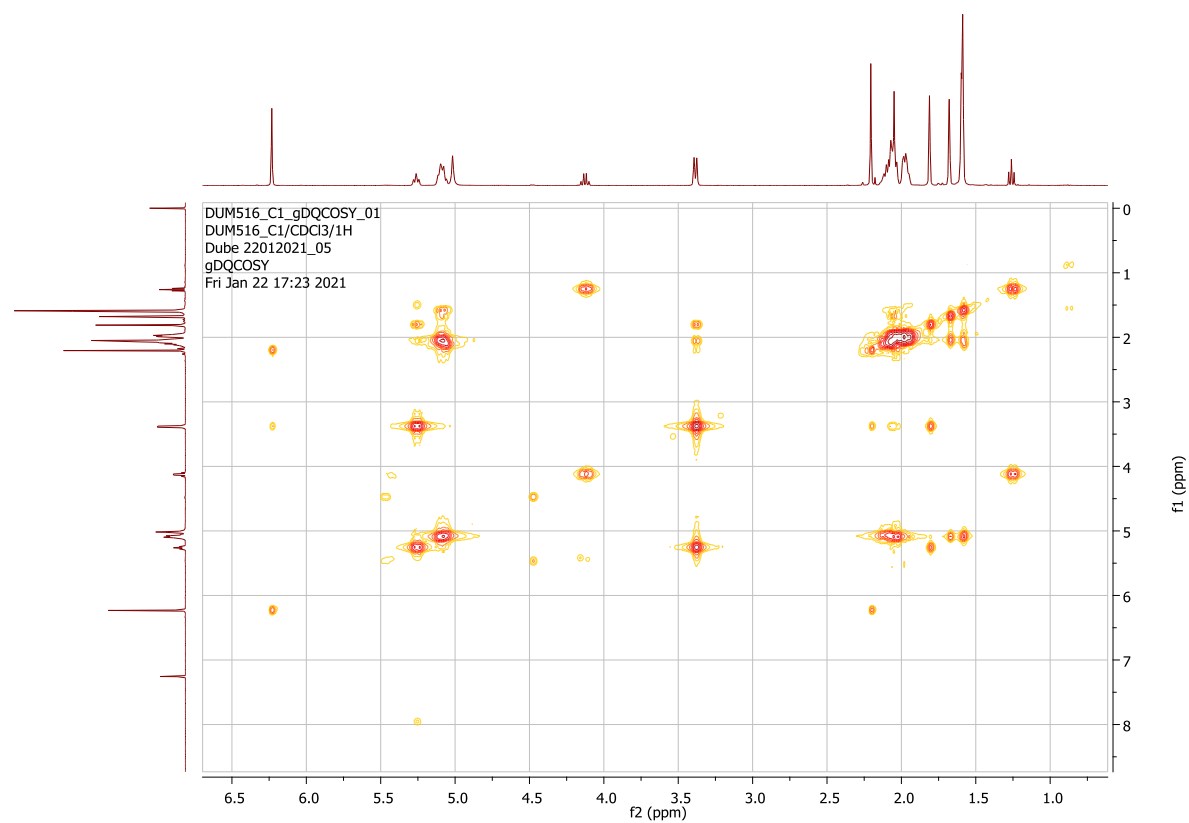


Figure S30: gDQCOSY spectrum of geranylgeranyl-2-ornicins (**6**) in CDCl₃ (400 MHz, δ in ppm).

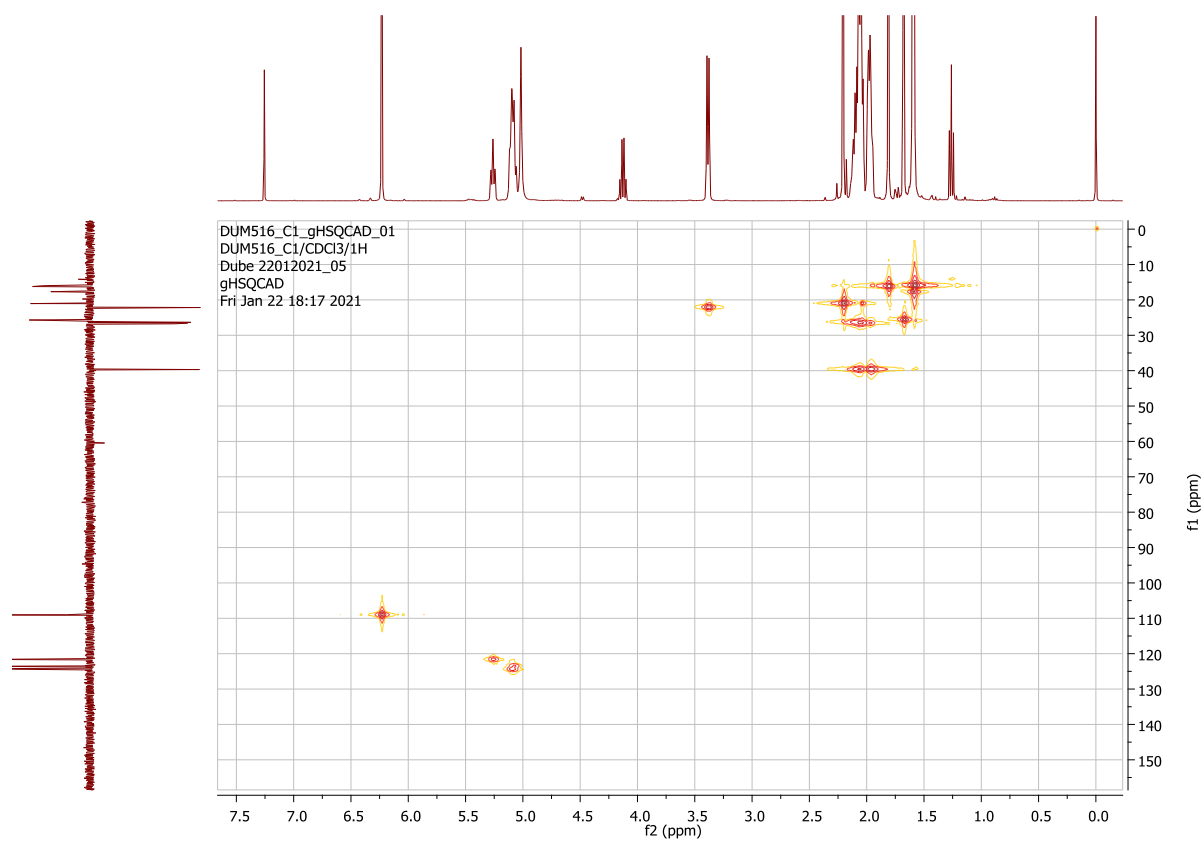


Figure S31: gHSQC spectrum of geranylgeranyl-2-ornicins (**6**) in CDCl₃ (400 MHz, δ in ppm).

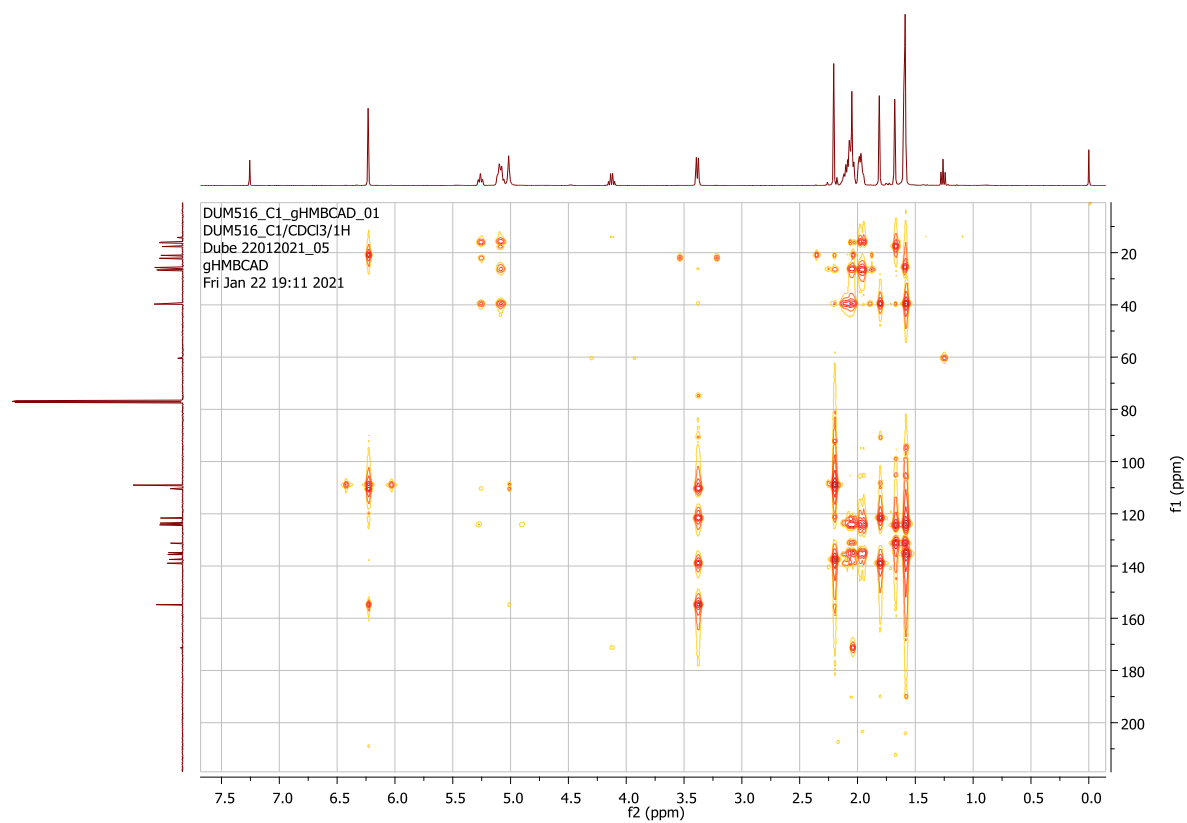


Figure S32: gHMBC spectrum of geranylgeranyl-2-orninol (**6**) in CDCl₃ (400 MHz, δ in ppm).

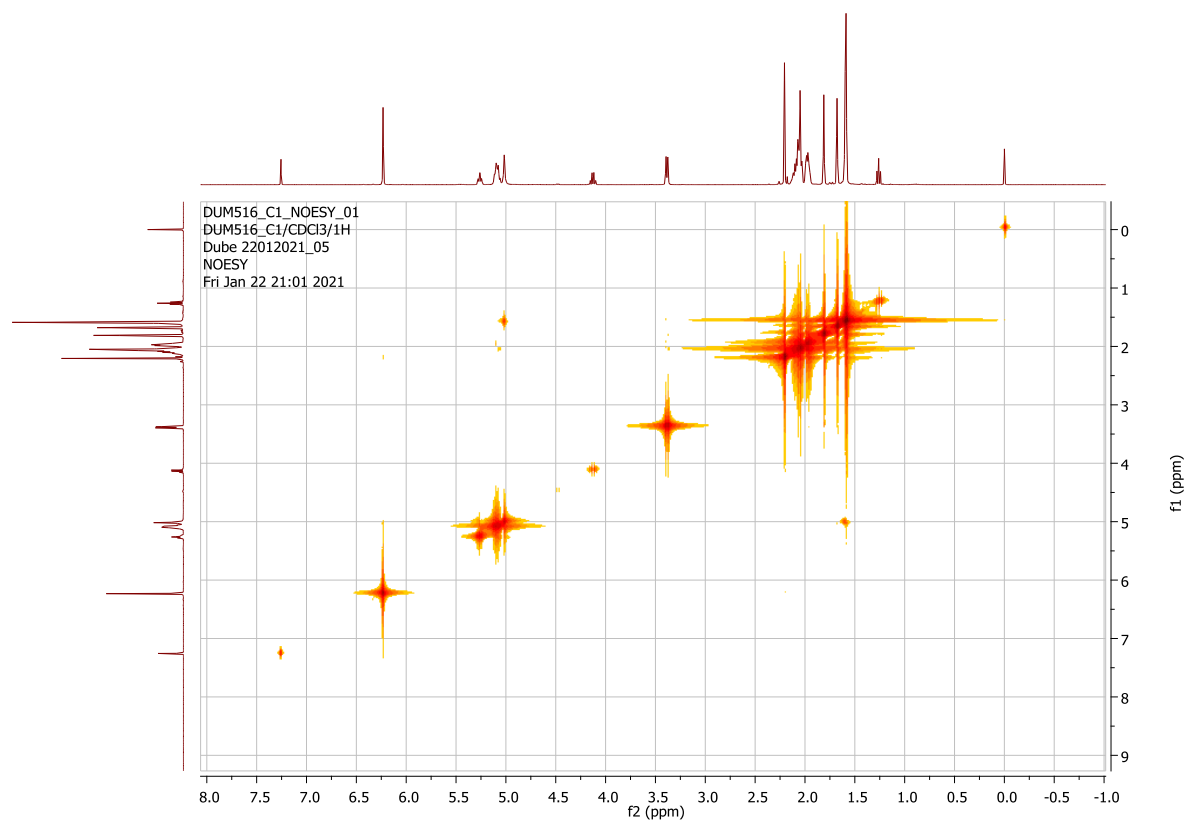
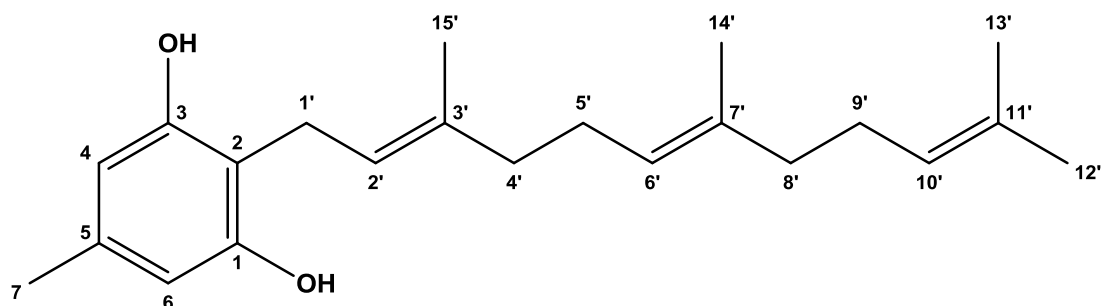


Figure S33: NOESY spectrum of geranylgeranyl-2-orninol (**6**) in CDCl₃ (400 MHz, δ in ppm).

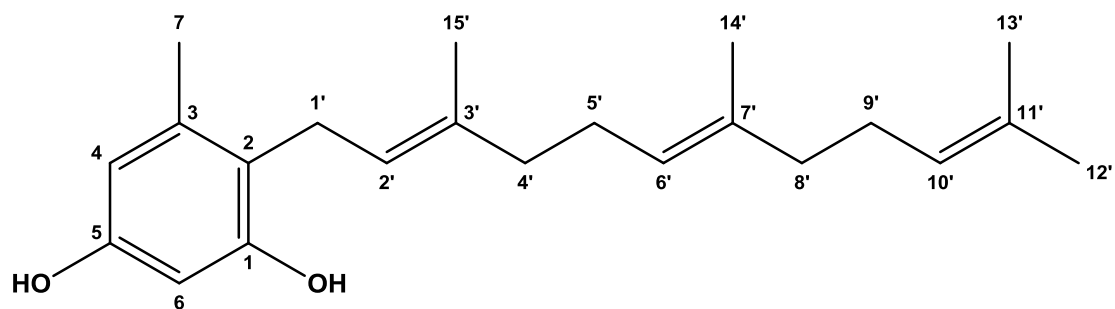
Table S1. ^1H (400 MHz, δ in ppm) and ^{13}C (100 MHz, δ in ppm) NMR data of grifolin (**1**) in CDCl_3 .



Position	δ_{H} (m)	δ_{C} (m)
1	-	154.8 (s)
2	-	110.3 (s)
3	-	154.8 (s)
4	6.23 (1H, s)	109.0 (d)
5	-	137.5 (s)
6	6.23 (1H, s))	109.0 (d)
7	2.21 (3H,s)	21.0 (q)
OH-1 ^a OH-3 ^a	4.97 (2H, s)	-
1'	3.39 (2H, d, 7.1)	22.2 (t)
2'	5.26 (1H, t, 7.1)	121.6 (d)
3'	-	138.9 (s)
4'	2.08 – 2.13 (2H, m)	39.7 (t)
5'	2.01 – 2.08 (2H, m)	26.7 (t)
6'	5.08 (1H, m)	123.6 (d)
7'	-	135.6 (s)
8'	2.01 – 2.08 (2H, m)	39.6 (t)
9'	1.93-2.00 (2H, m)	26.3 (t)
10'	5.08 (1H, m)	124.4 (d)
11'	-	131.3 (s)
12'	1.67 (3H, s)	25.7 (q)
13'	1.60 (3H, s)-	17.7 (q)
14'	1.58 (3H, s)	16.2 (q)
15'	1.81 (3H, s)	16.0 (q)

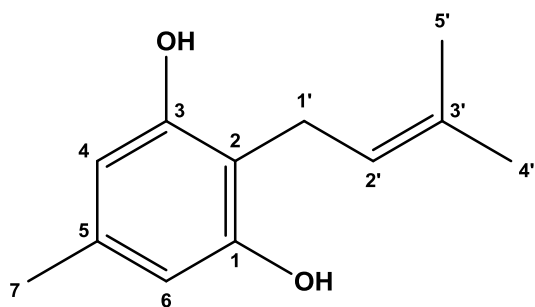
^aSignals may be interchanged.

Table S2. ^1H (400 MHz, δ in ppm) and ^{13}C (100 MHz, δ in ppm) NMR data of compound **2** in CDCl_3 .



Position	δ_{H} (m)	δ_{C} (m)
1	-	155.4 (s)
2	-	117.9 (s)
3	-	138.4 (s)
4	6.26 (1H, d, 2.4)	109.6 (d)
5	-	154.2 (s)
6	6.21 (1H, d, 2.5)	101.0 (d)
7	2.23 (3H,s)	21.0 (q)
OH-1	5.14 (1H,s)	-
OH-5	4.61 (1H, s)	-
1'	3.29 (2H, d, 6.8)	25.1 (t)
2'	5.15 (1H, t, 7.1)	122.0 (d)
3'	-	137.7 (s)
4'	2.09 (2H, t, 7.5)	39.6 (t)
5'	2.01 – 2.06 (2H, m)	26.7 (t)
6'	5.07 (1H, m)	123.7 (d)
7'	-	135.4 (s)
8'	2.01 – 2.06 (2H, m)	39.6 (t)
9'	1.93-1.98 (2H, m)	26.4 (t)
10'	5.07 (1H, m)	124.4 (d)
11'	-	131.3 (s)
12'	1.67 (3H, s)	25.7 (q)
15'	1.79 (3H, s)	16.0 (q)
14'	1.58 (3H, s)	16.2 (q)
13'	1.59 (3H, s)-	17.7 (q)

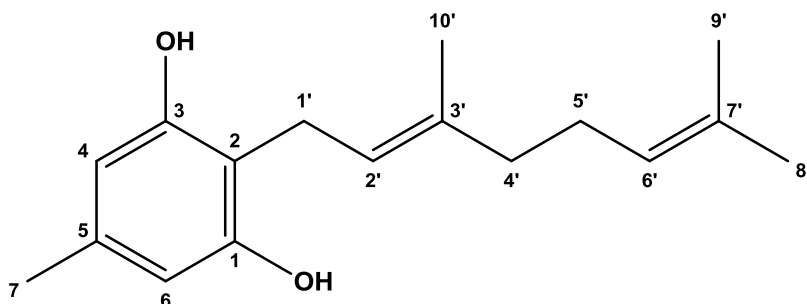
Table S3. ^1H (400 MHz, δ in ppm) and ^{13}C (100 MHz, δ in ppm) NMR data of prenyl-2-oricinol (**4**) in CDCl_3 .



Position	δ_{H} (m)	δ_{C} (m)
1	-	154.7 (s)
2	-	110.4 (s)
3	-	154.7 (s)
4	6.23 (1H, s)	109.0 (d)
5		137.5 (s)
6	6.23 (1H, s))	109.0 (d)
7	2.20 (3H,s)	21.0 (q)
OH-1 ^a OH-3 ^a	5.14 (2H, s)	-
1'	3.37 (2H, d, 7.1)	22.2 (t)
2'	5.25 (1H, t, 7.1)	121.8 (d)
3'	-	135.0 (s)
4'	1.74 (3H, s)	25.7 (q)
5'	1.81 (3H, s)	17.8 (q)

^aSignals may be interchanged.

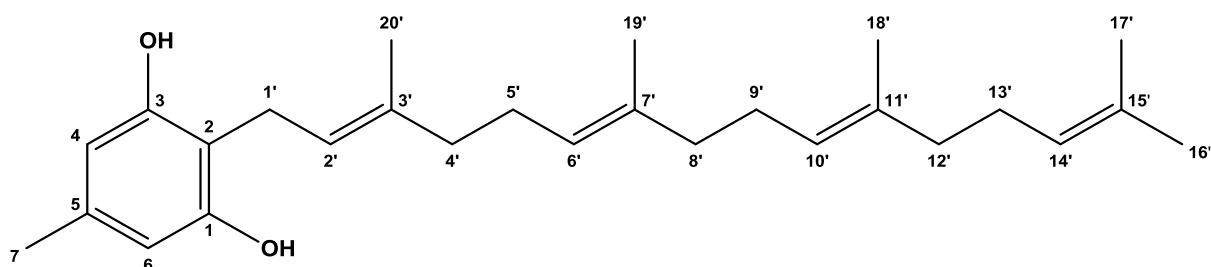
Table S4. ^1H (400 MHz, δ in ppm) and ^{13}C (100 MHz, δ in ppm) NMR data of geranyl-2-orycinol (**5**) in CDCl_3 .



Position	δ_{H} (m) _H	δ_{C} (m)
1	-	155.0 (s)
2	-	110.6 (s)
3	-	155.0 (s)
4	6.23 (1H, s)	108.8 (d)
5	-	137.4 (s)
6	6.23 (1H, s))	108.8 (d)
7	2.21 (3H,s)	21.0 (q)
OH-1 ^a OH-3 ^a	5.66 (2H, s)	-
1'	3.38 (2H, d, 7.1)	22.1 (t)
2'	5.26 (1H, t, 7.6)	121.9 (d)
3'	-	138.5 (s)
4'	2.07 (2H, m)	39.7 (t)
5'	2.07 (2H, m)	26.4 (t)
6'	5.06 (1H, t, 6.0)	123.8 (d)
7'	-	131.9 (s)
8'	1.67 (3H, s)	25.6 (q)
9'	1.59 (3H, s)	17.7 (q)
10'	1.80 (3H, s)	16.1 (q)

^a Signals may be interchanged.

Table S5. ^1H (400 MHz, δ in ppm) and ^{13}C (100 MHz, δ in ppm) NMR data of geranylgeranyl-2-ornicoll (**6**) in CDCl_3 .



Position	δ_{H} (m) _H	δ_{C} (m)
1	-	154.8 (s)
2	-	110.4 (s)
3	-	154.8 (s)
4	6.23 (1H, s)	109.0 (d)
5	-	137.5 (s)
6	6.23 (1H, s))	109.0 (d)
7	2.21 (3H,s)	21.0 (q)
OH-1 ^a OH-3 ^a	5.02 (2H, s)	-
1'	3.38 (2H, d, 7.1)	22.2 (t)
2'	5.26 (1H, dd, 7.1; 6.4)	121.6 (d)
3'	-	138.9 (s)
4'	1.98-2.07 (2H, m)	39.7 (t)
5'	1.98-2.07 (2H, m)	26.8 (t)
6'	5.09 (1H, m)	124.4 (d)
7'	-	135.6 (s)
8'	1.98-2.07 (2H, m)	39.7 (t)
9'	1.98-2.07 (2H, m)	26.6 (t)
10'	5.09 (1H, m)	123.6 (d)
11'	-	134.8 (s)
12'	1.98-2.07 (2H, m)	39.6 (t)
13'	1.98-2.07 (2H, m)	26.3 (t)
14'	5.09 (1H, m)	124.2 (d)
15'	-	131.2 (s)
16'	1.68 (3H, s)	25.7 (q)
17'	1.59 (3H, s)	17.7 (q)
18	1.59 (3H, s)	16.0 (q)
19'	1.59 (3H, s)	16.2 (q)
20'	1.81 (3H, s)	16.0 (q)

^a Signals may be interchanged.

Compound **2** (LC₅₀ 410.6 µg/mL)

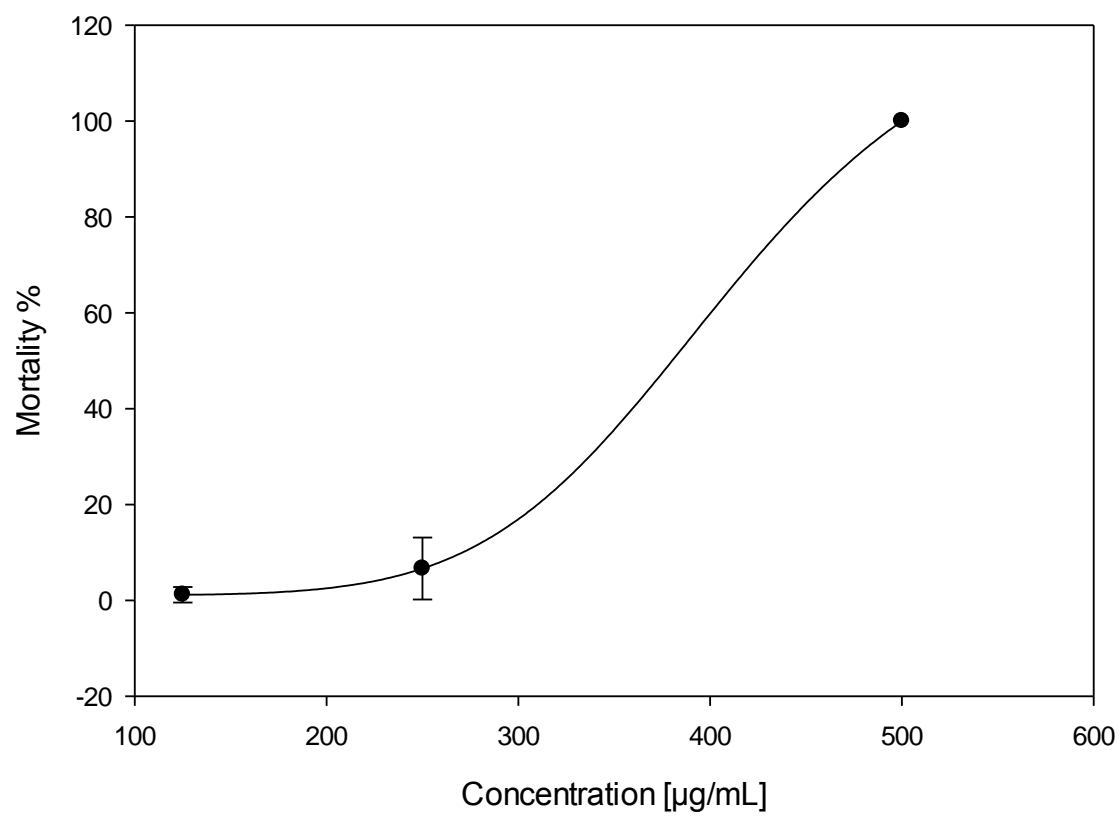


Figure S34: LC₅₀ curve for in vitro anthelmintic activity of Compound **2** against *C. elegans*.