Supporting Information

Biologically active drimane derivatives isolated from submerged cultures of the wood-inhabiting basidiomycete *Dentipellis fragilis*

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(1) Antimicrobial assays

Table S1: Antibacterial activities of compounds **1**–**6**.

Microorganism	MIC (µg/mL)						
	1	**2**	**3**	**4**	**5**	**6**	Ref.
Bacillus subtilis (DSM 10)	n.i.	ND	n.i.	n.i.	n.i.	ND	4.2[a]
Mycolicibacterium smegmatis (ATCC 700084)	n.i.	ND	n.i.	n.i.	n.i.	ND	1.7[b]
Staphylococcus aureus (DSM 346)	n.i.	ND	66.7	n.i.	n.i.	ND	0.20[a]
Actinobacter baumannii (DSM 30008)	n.i.	ND	n.i.	n.i.	n.i.	ND	0.26[c]
Chromobacterium violaceum (DSM 30191)	n.i.	ND	n.i.	n.i.	n.i.	ND	0.83[a]
Escherichia coli (DSM 1116)	n.i.	ND	n.i.	n.i.	n.i.	ND	3.3[a]
Pseudomonas aeruginosa (DSM PA14)	n.i.	ND	n.i.	n.i.	n.i.	ND	0.42[d]

n.i..: no inhibition, ND: not tested, Ref.: reference ([a]: oxytetracycline, 2 mg/mL; [b]: kanamycin 2 mg/mL; [c]: ciprofloxacin, 2.5 mg/mL; [d]: gentamycin, 2 mg/mL).

Table S2: Antifungal activities of compounds **1**–**6**.

Microorganism	MIC (µg/mL)						
	1	**2**	**3**	**4**	**5**	**6**	Ref.
Candida albicans (DSM 1665)	n.i.	ND	n.i.	n.i.	n.i.	n.i.	8.3
Pichia anomala (DSM 6766)	n.i.	ND	n.i.	n.i.	n.i.	n.i.	8.3
Rhodotorula glutinis (DSM 10134)	n.i.	ND	n.i.	n.i.	n.i.	n.i.	2.1
Schizosaccharomyces pombe (DSM 70572)	n.i.	ND	n.i.	n.i.	n.i.	n.i.	4.2
Mucor hiemalis (DSM 2656)	n.i.	ND	66.7	n.i.	n.i.	n.i.	4.2

n.i..: no inhibition, ND: not tested, Ref.: reference (nystatin, 20 mg/mL).

(2) Cytotoxicity assays

Table S3: Cytotoxic activities of compounds **1**–**6**.

Cell line	IC_{50} (µM)						
	1	**2**	**3**	**4**	**5**	**6**	Ref.
L929 (ACC2)	n.c.	ND	93.5	n.c.	n.c.	n.c.	4.7×10^{-5}
KB3.1 (ACC158)	n.c.	121.0	21.2	n.c.	n.c.	n.c.	3.3×10^{-5}

n.c.: no cytotoxicity, ND: not tested, Ref.: reference (epothilon B).

(3) Neurite outgrowth assays

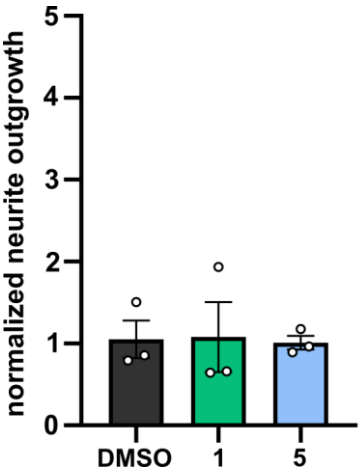


Figure S1: Bar chart displaying the normalized neurite outgrowth of PC-12 cells that were solely treated with either DMSO (5 µg/mL), compound **1** (5 µg/mL) or compound **5** (5 µg/mL) for 24 h. Neurite outgrowths were normalized with respect to the neurite outgrowths detected after 0 h (t_0) and are given in fold changes ± S.E.M. Data originates from three independent experiments.

Table S4: Normalized values of the individual neurite outgrowth assays as well as their mean and S.E.M. used for the illustrations in Figure 5 and Figure S1.

Neurite outgrowth assays supplemented with NGF (5 ng/mL) as displayed in Figure 5			
Experiment	DMSO + NGF (5 ng/mL)	compound **1** + NGF	compound **5** + NGF
1	1.09	3.69	4.25
2	1.26	3.64	3.31
3	2.02	3.95	2.87
Mean	1.46	3.76	3.48
S.E.M.	0.29	0.10	0.41
Neurite outgrowth assays not supplemented with NGF as displayed in Figure S1			
Experiment	DMSO	compound **1**	compound **5**
1	0.86	0.66	1.18
2	1.51	1.93	0.97
3	0.79	0.64	0.89
Mean	1.05	1.08	1.01
S.E.M.	0.23	0.43	0.08

(4) RT-qPCR assays

Table S5: Normalized values for NGF and BDNF mRNA levels as determined by RT-qPCR as well as their respective mean and S.E.M. used for the illustration in Figure 6.

	DMSO	compound **1**		compound **5**	
Experiment	BDNF/NGF expression	BDNF expression	NGF expression	BDNF expression	NGF expression
1	1.00	3.29	1.20	3.16	1.67
2	1.00	2.19	7.35	1.30	2.06
2	1.00	4.25	3.29	3.27	1.09
Mean	1.00	3.24	3.95	2.58	1.61
S.E.M.	0.00	0.60	1.81	0.64	0.28

(5) Analytical data of compound 1

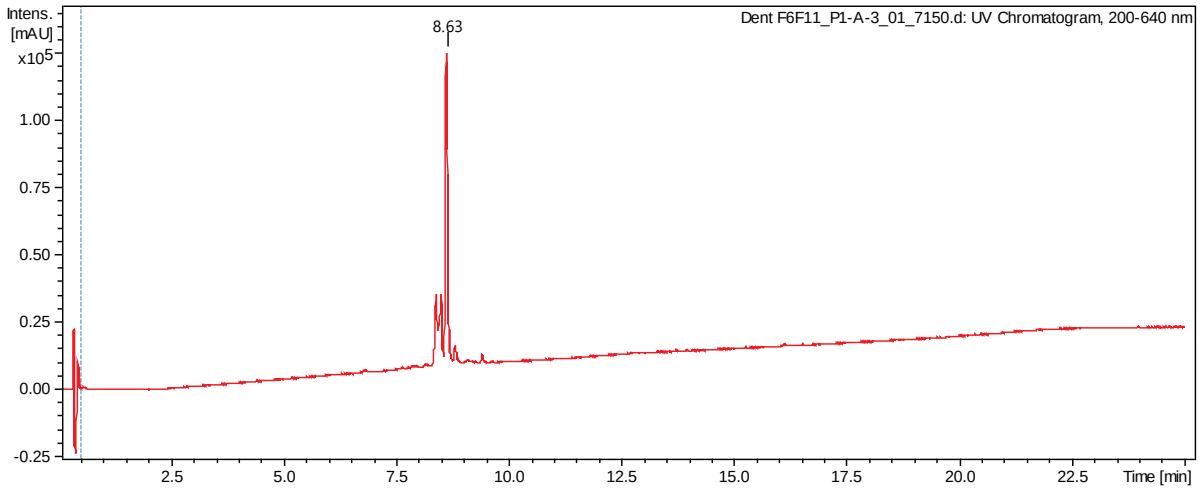


Figure S1: HPLC-DAD chromatogram of compound **1**.

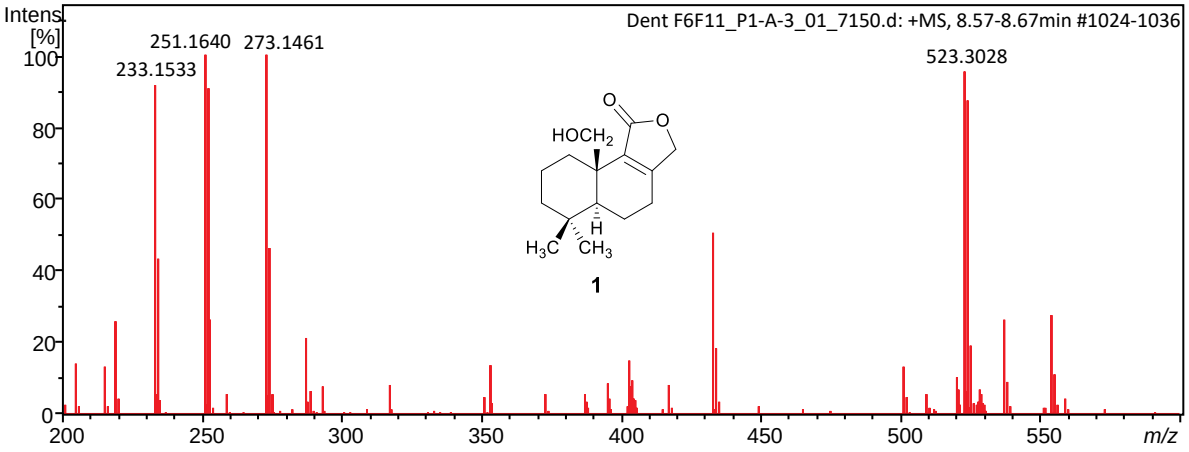


Figure S2: HR-(+)ESIMS spectrum of compound **1**.

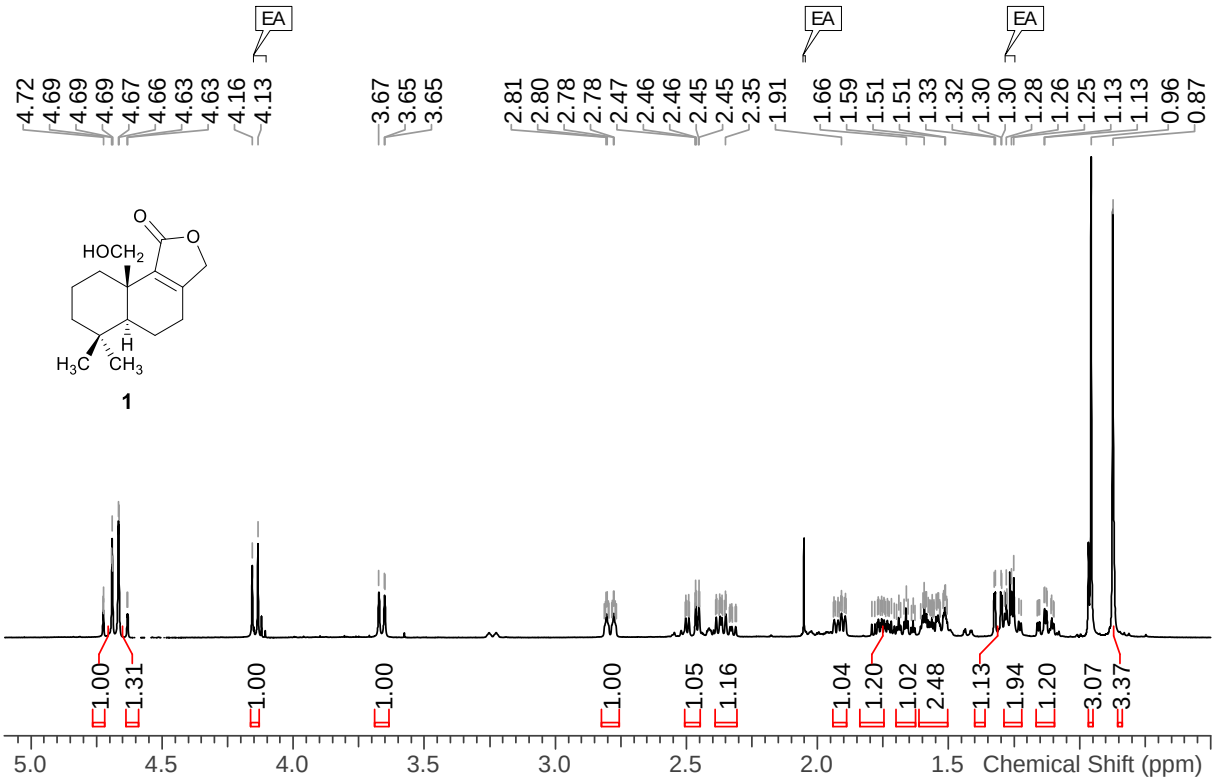


Figure S3: ^{1}H NMR spectrum (500 MHz, $CDCl_3$, 298 K) of the purified compound **1**. EA: ethyl acetate.

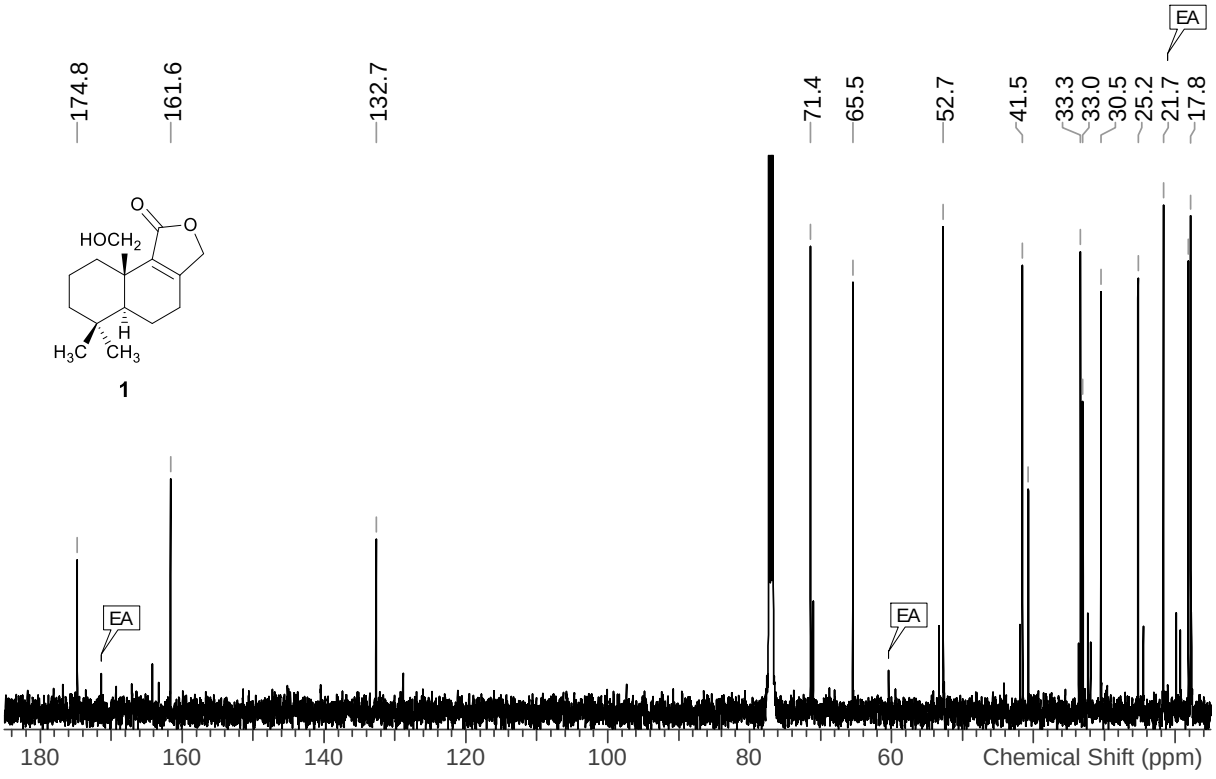


Figure S4: ^{13}C NMR spectrum (125 MHz, $CDCl_3$, 298 K) of the purified compound **1**. EA: ethyl acetate.

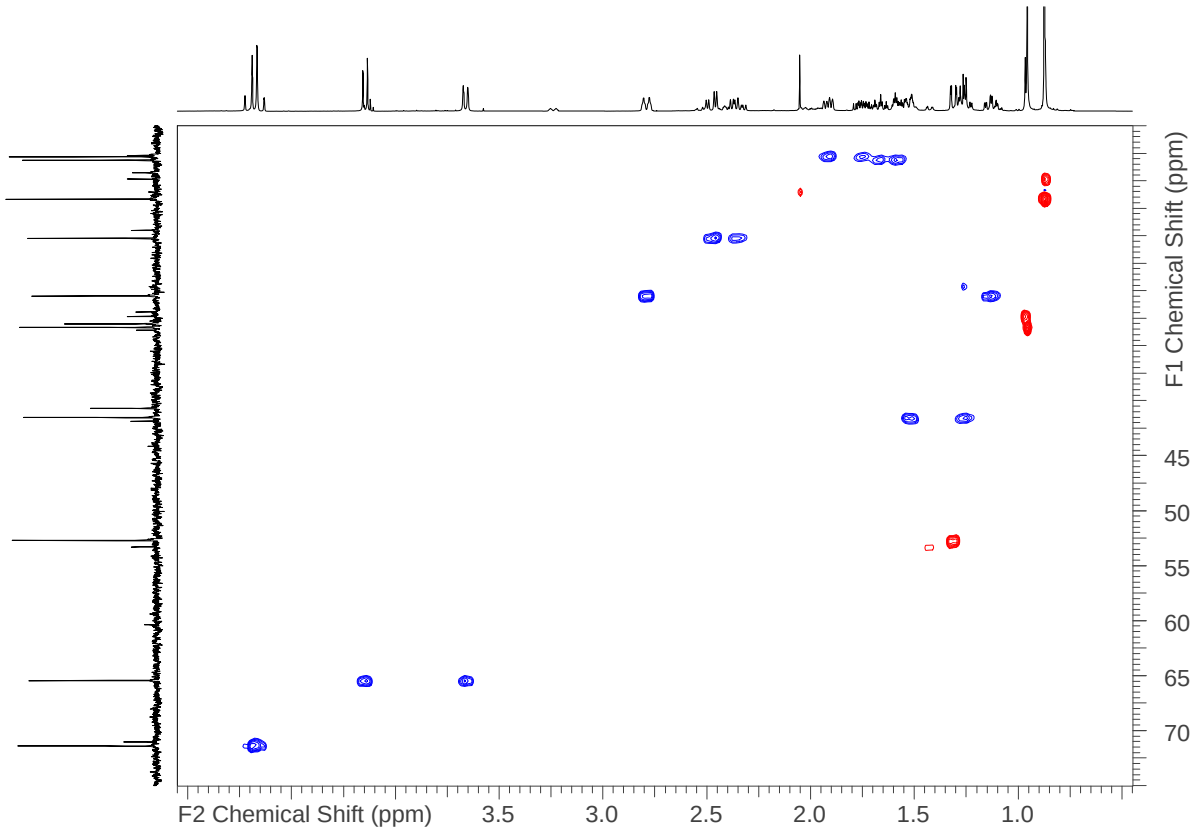


Figure S5: $^{1}H,^{13}C$ DEPT-HSQC spectrum (500 MHz, $CDCl_3$, 298 K) of the purified compound **1**.

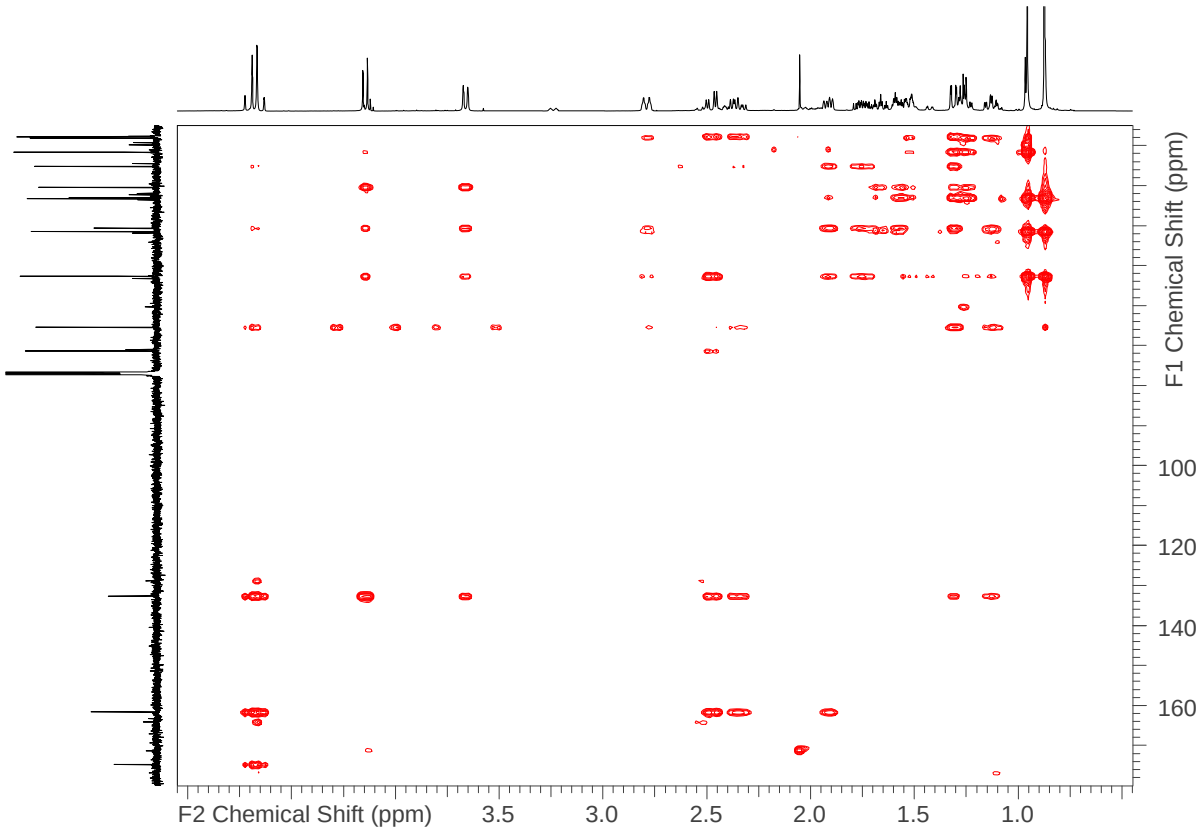


Figure S6: $^{1}H,^{13}C$ HMBC spectrum (500 MHz, $CDCl_3$, 298 K) of the purified compound **1**.

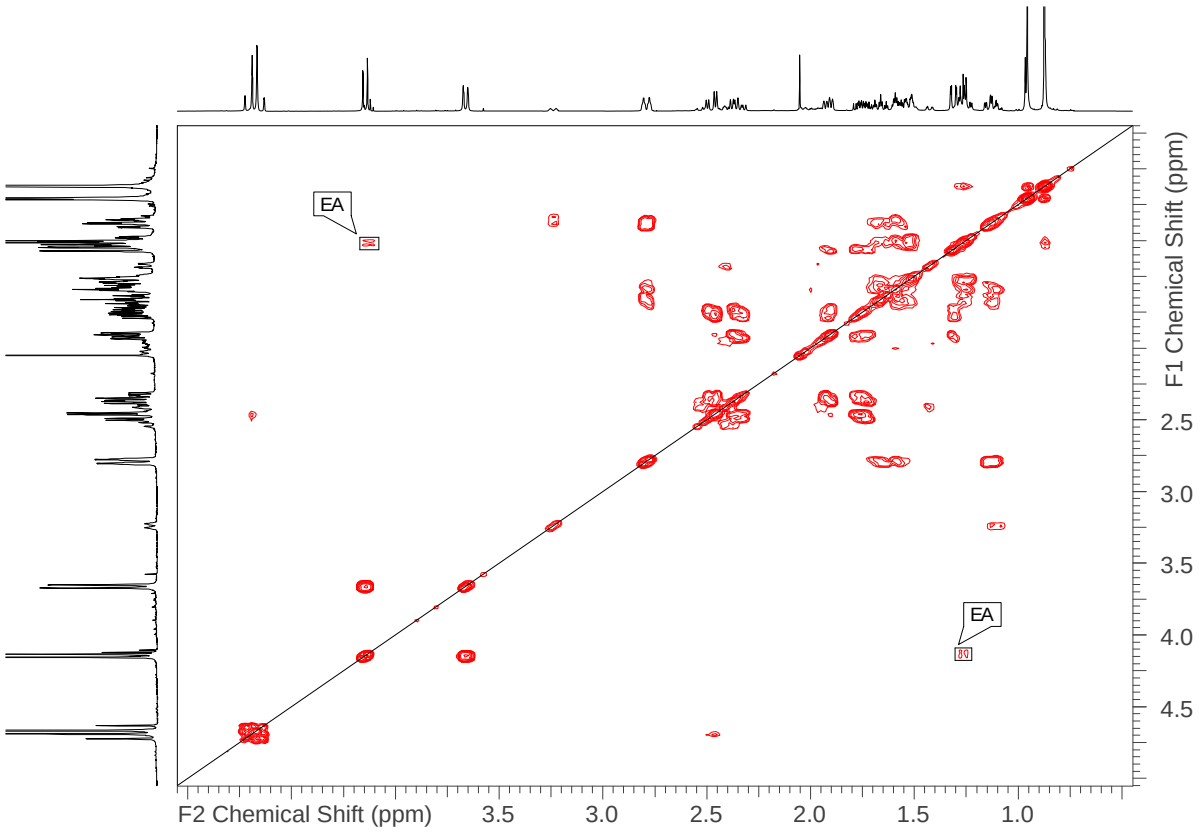


Figure S7: $^{1}H,^{1}H$ COSY spectrum (500 MHz, $CDCl_3$, 298 K) of the purified compound **1**. EA: ethyl acetate.

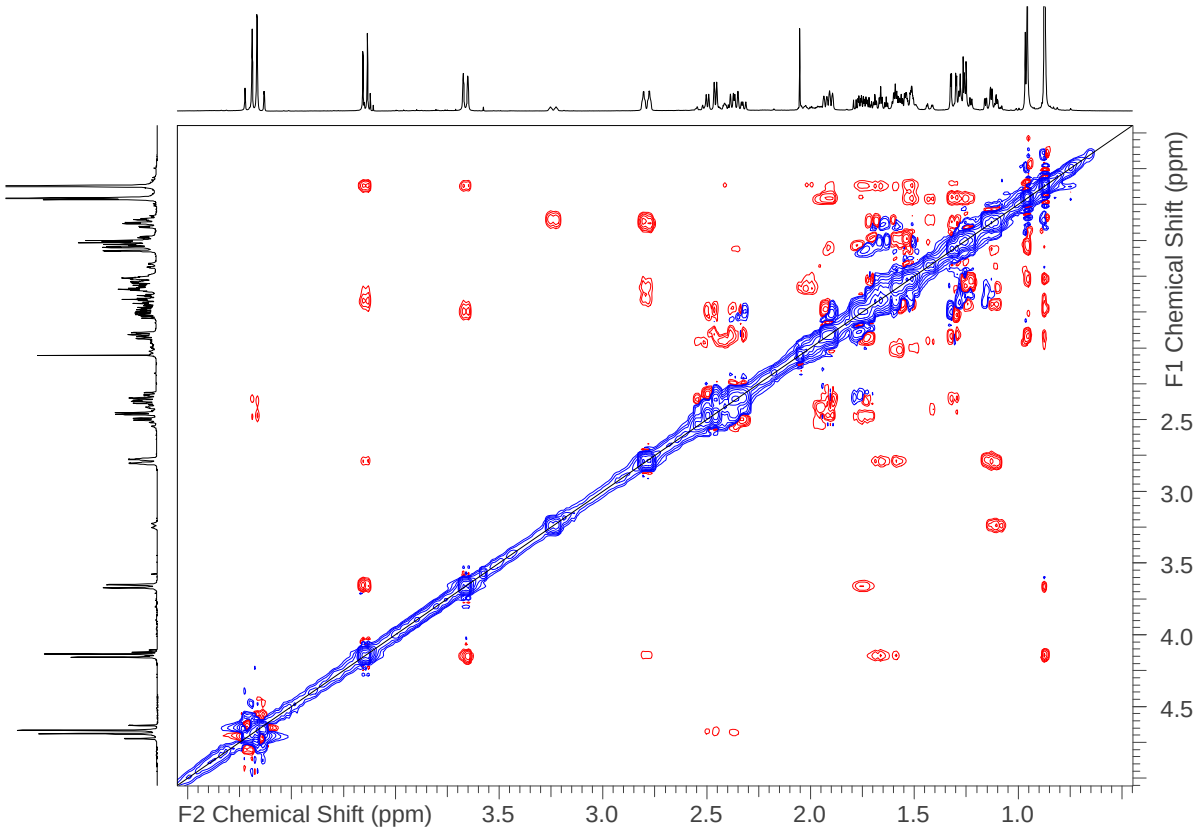


Figure S8: $^{1}H,^{1}H$ ROESY spectrum (500 MHz, $CDCl_3$, 298 K) of the purified compound **1**.

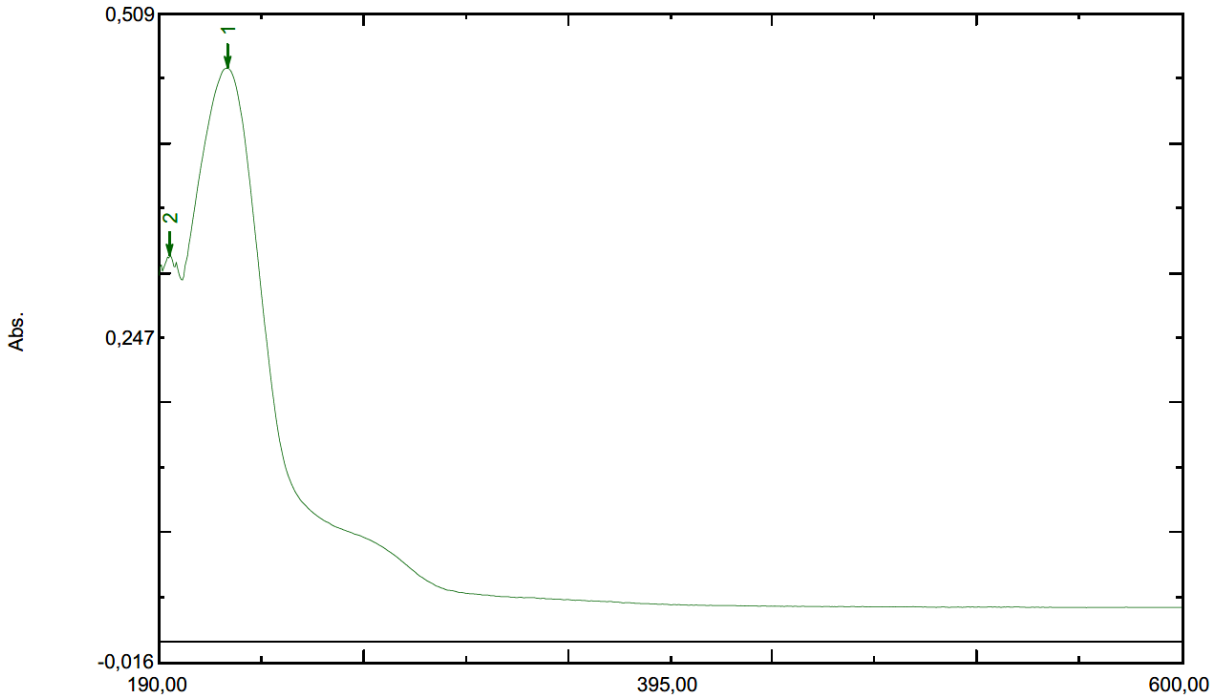


Figure S9: UV/Vis spectrum of compound **1** in MeOH.

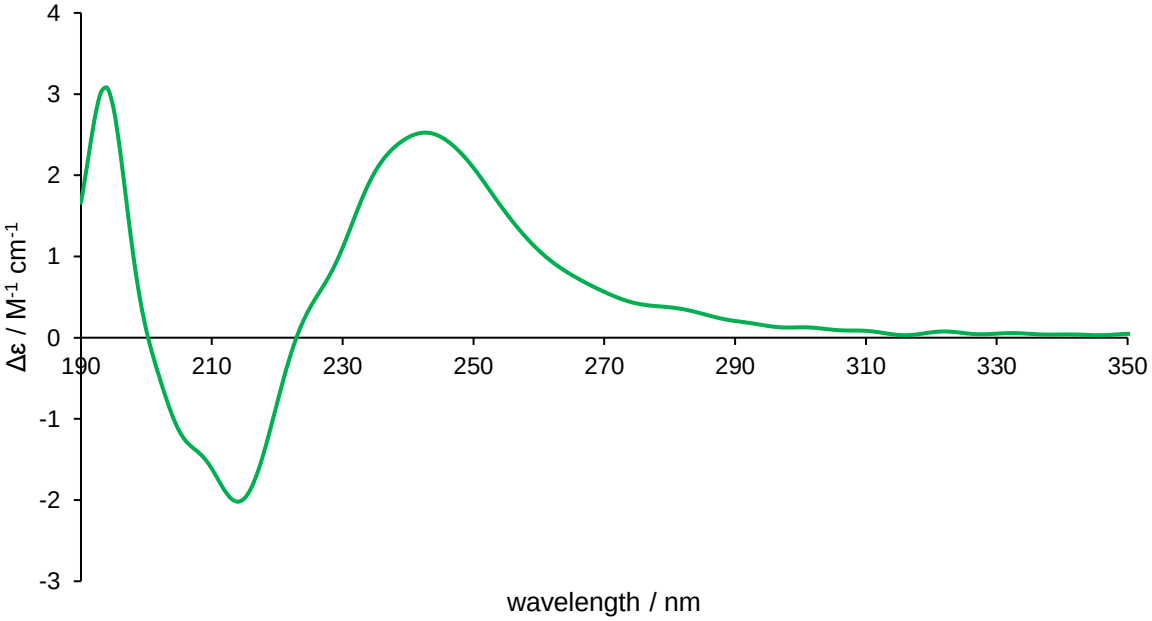


Figure S10: ECD spectrum of compound **1** in MeOH.

(6) Analytical data of compound 2

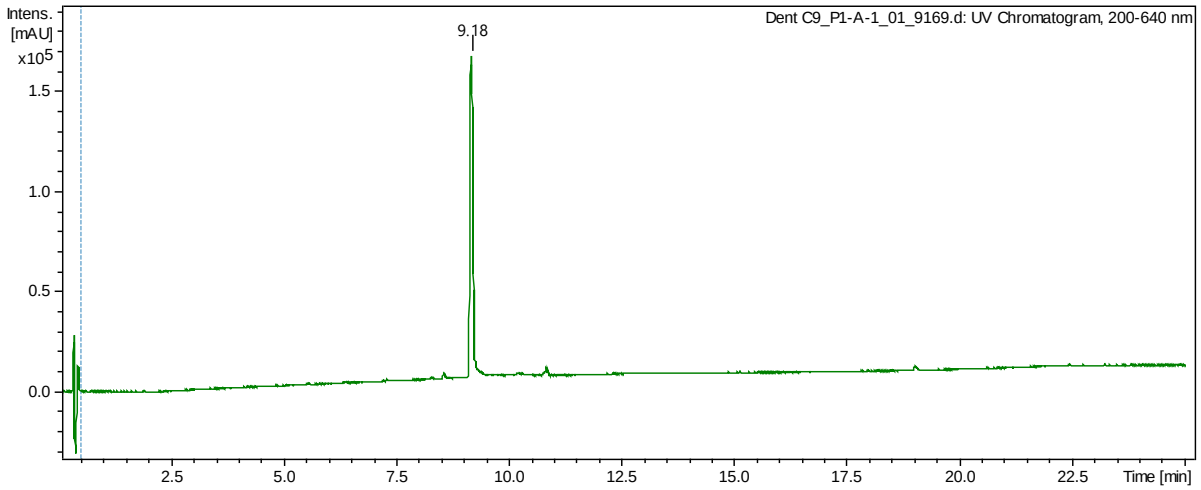


Figure S11: HPLC-DAD chromatogram of compound **2**.

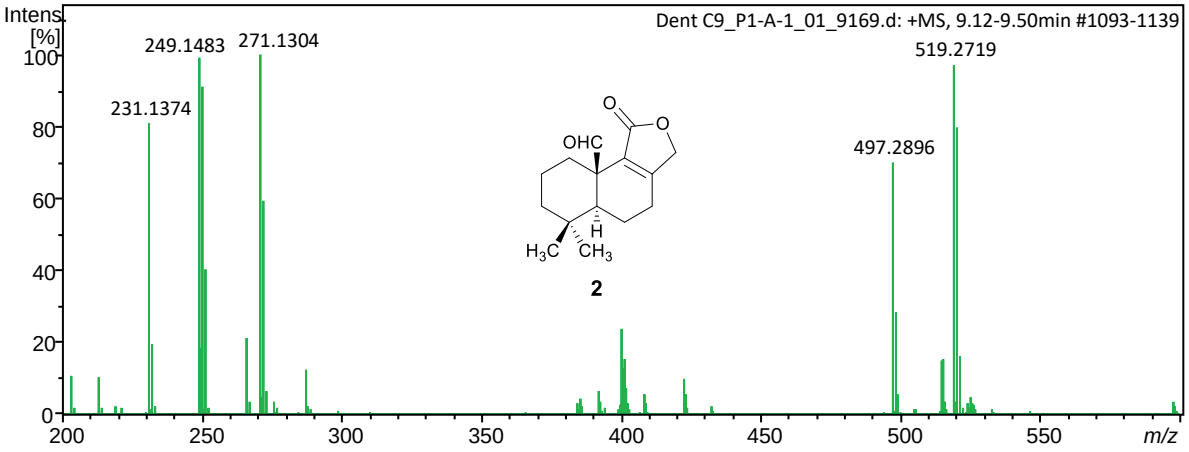


Figure S12: HR-(+)ESIMS spectrum of compound **2**.

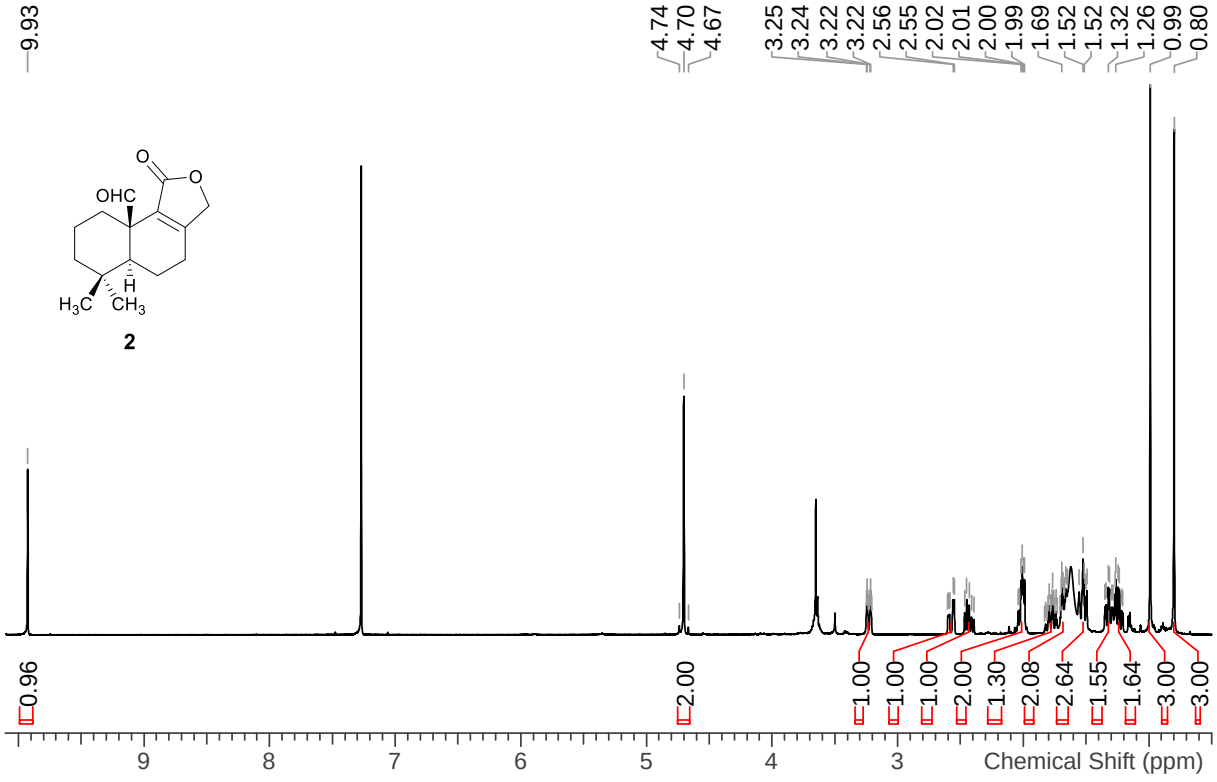


Figure S13: ^{1}H NMR spectrum (500 MHz, $CDCl_3$, 298 K) of the purified compound **2**.

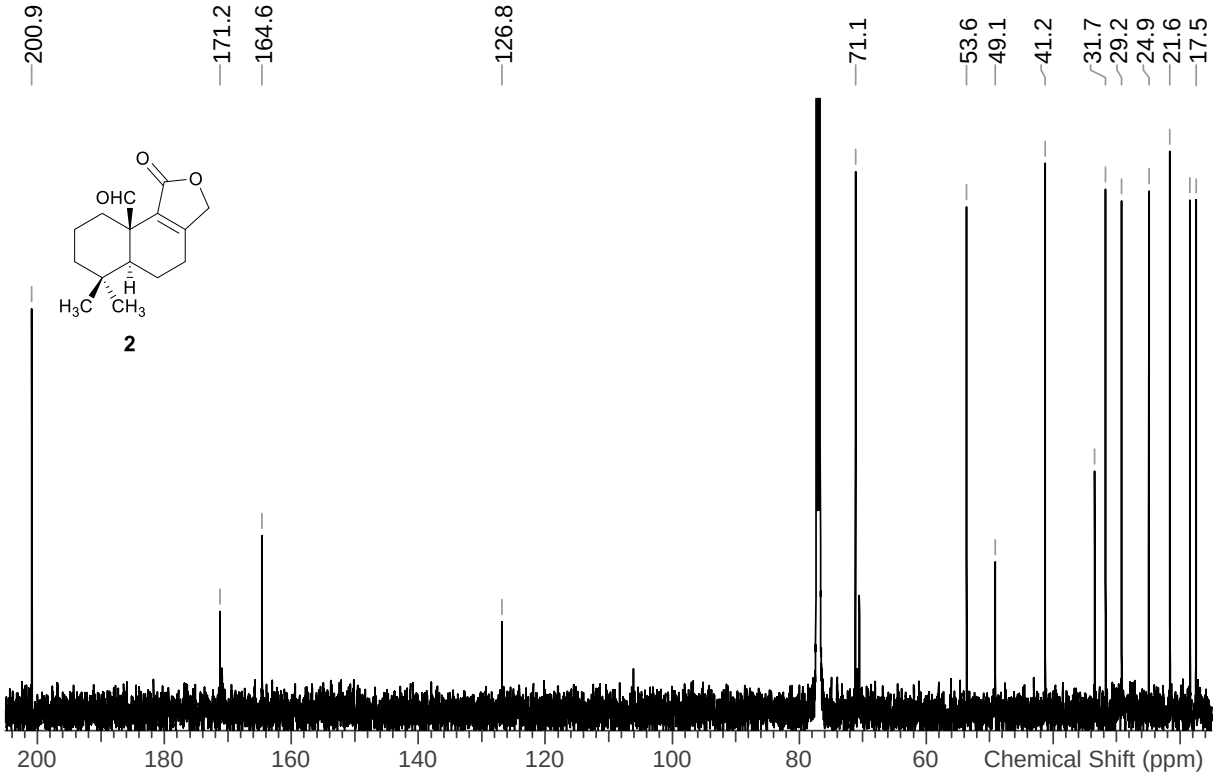


Figure S14: ^{13}C NMR spectrum (125 MHz, $CDCl_3$, 298 K) of the purified compound **2**.

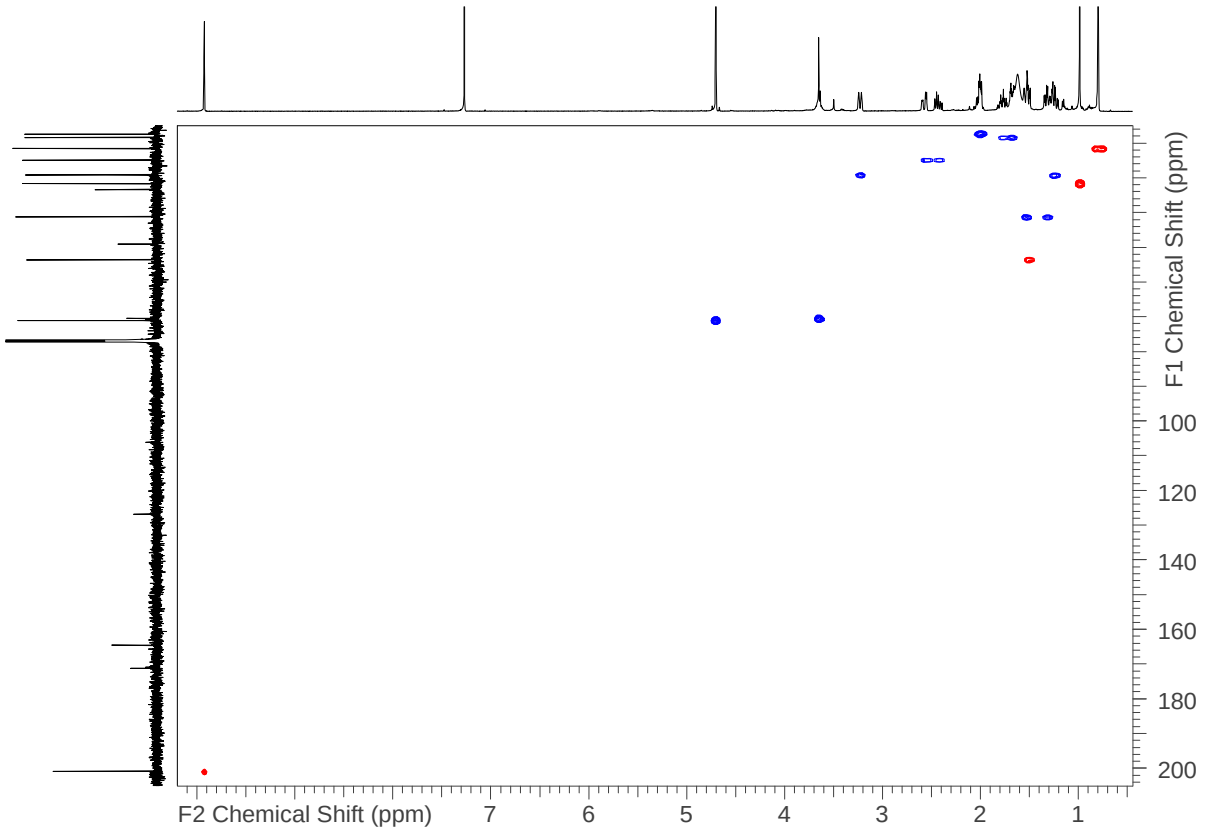


Figure S15: $^{1}H,^{13}C$ DEPT-HSQC spectrum (500 MHz, $CDCl_3$, 298 K) of the purified compound **2**.

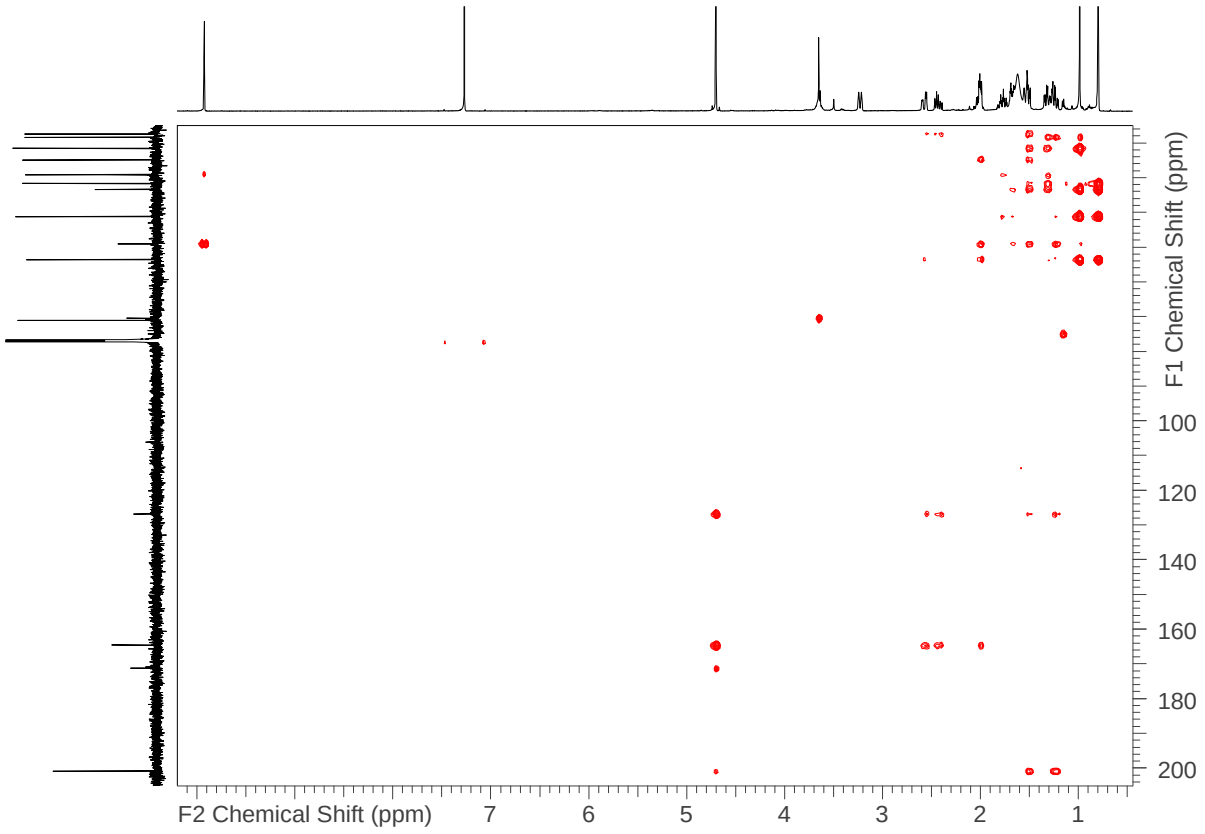


Figure S16: $^{1}H,^{13}C$ HMBC spectrum (500 MHz, $CDCl_3$, 298 K) of the purified compound **2**.

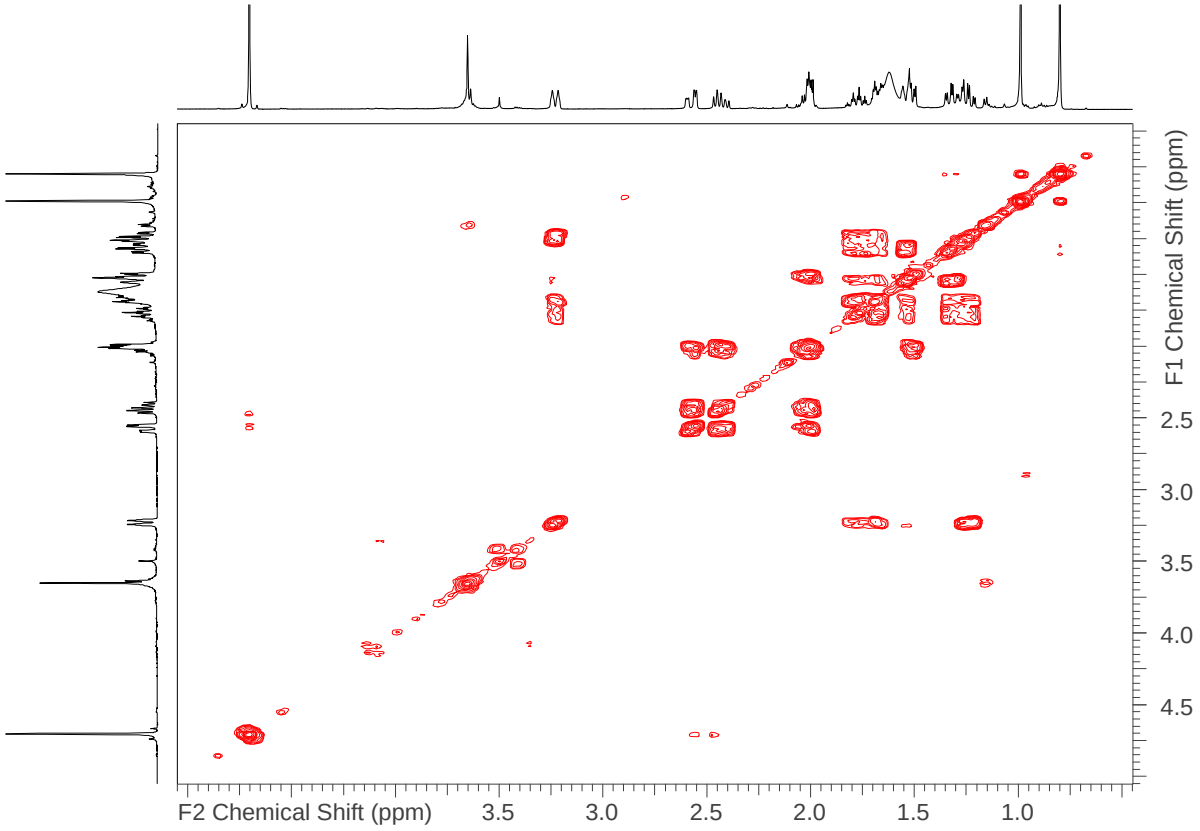


Figure S17: $^{1}H,^{1}H$ COSY spectrum (500 MHz, $CDCl_3$, 298 K) of the purified compound **2**.

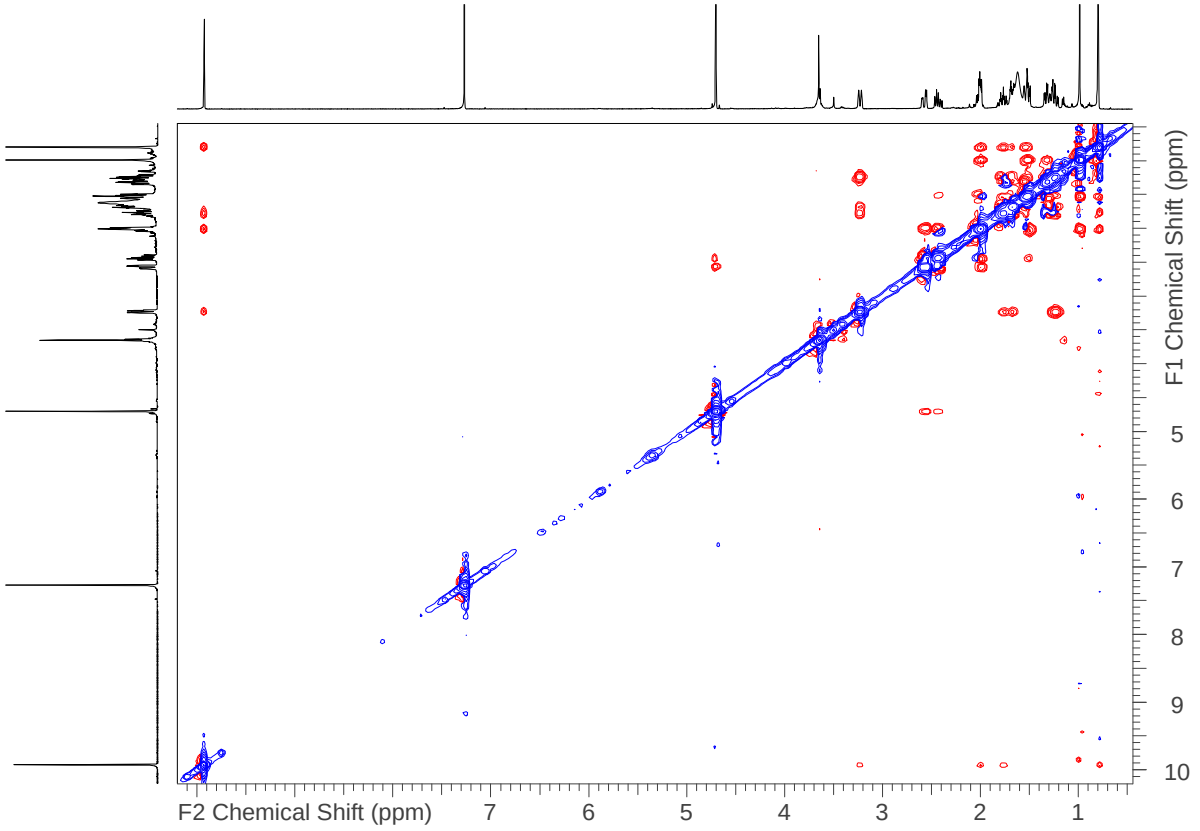


Figure S18: $^{1}H,^{1}H$ ROESY spectrum (500 MHz, $CDCl_3$, 298 K) of the purified compound **2**.

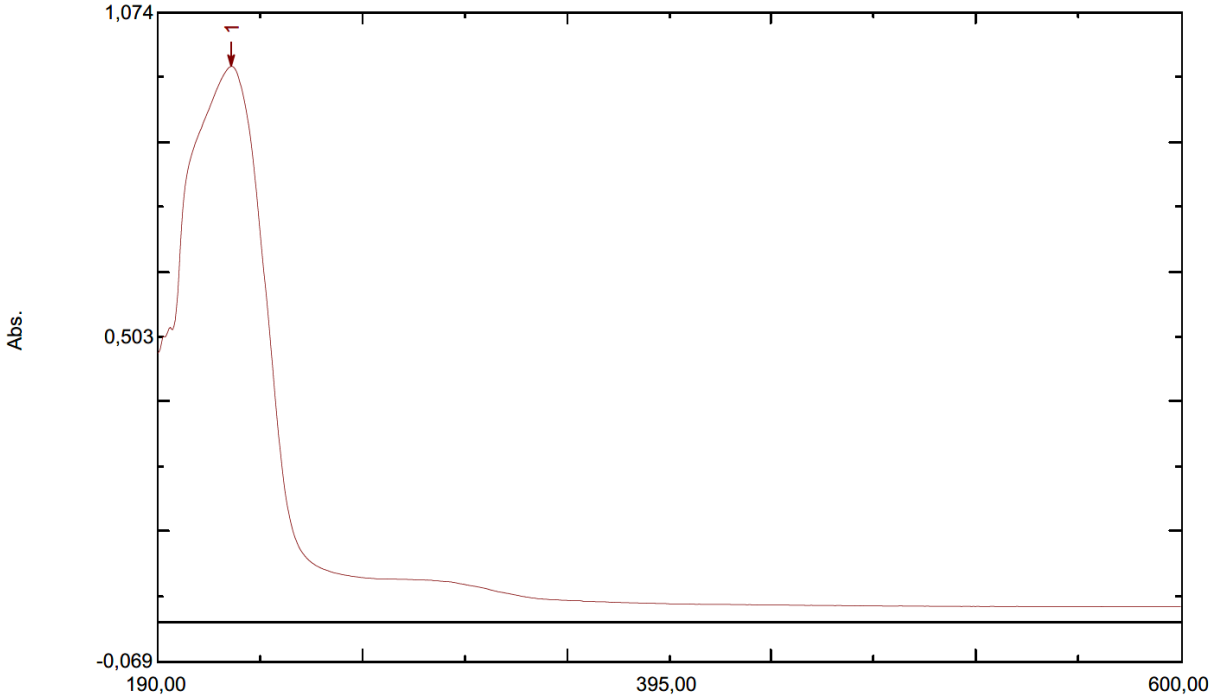


Figure S19: UV/Vis spectrum of compound **2** in MeOH.

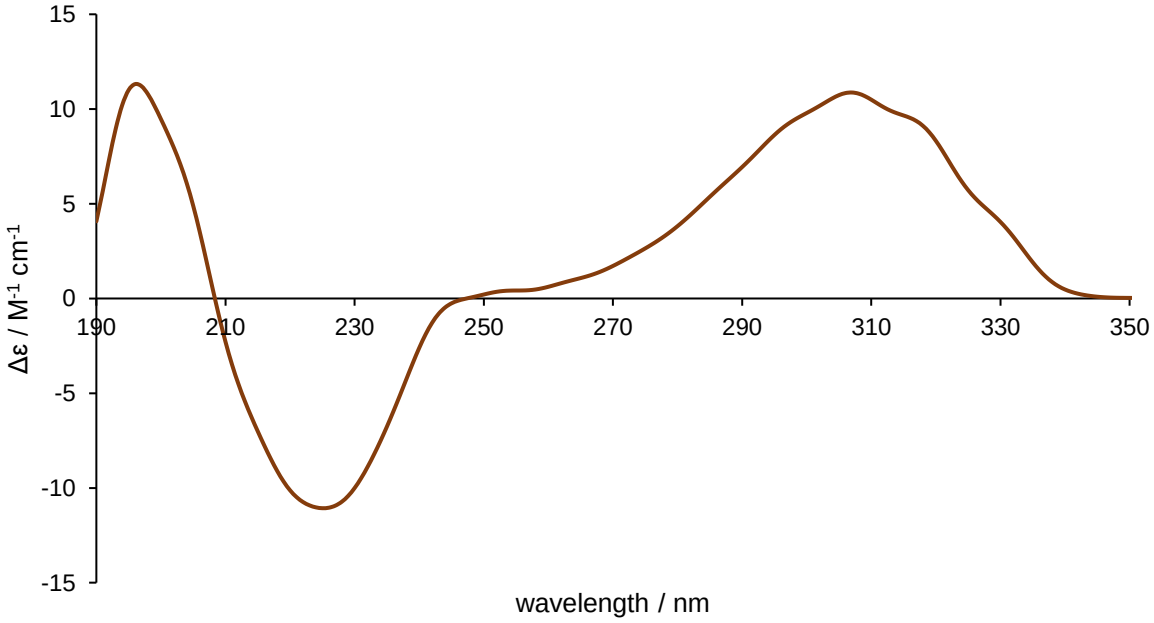


Figure S20: ECD spectrum of compound **2** in MeOH

(7) Analytical data of compound 3

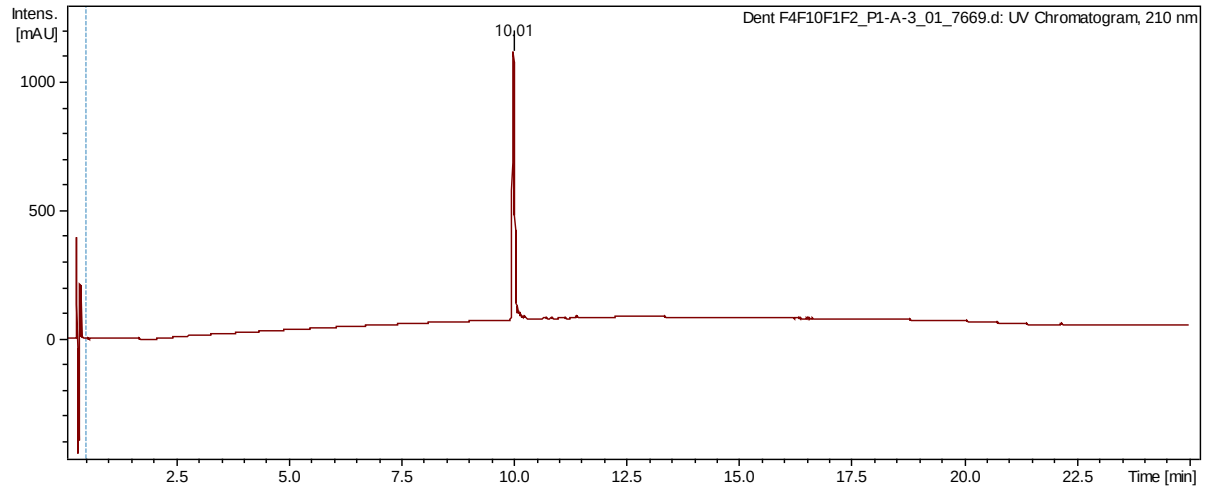


Figure S21: HPLC-DAD chromatogram of compound **3**.

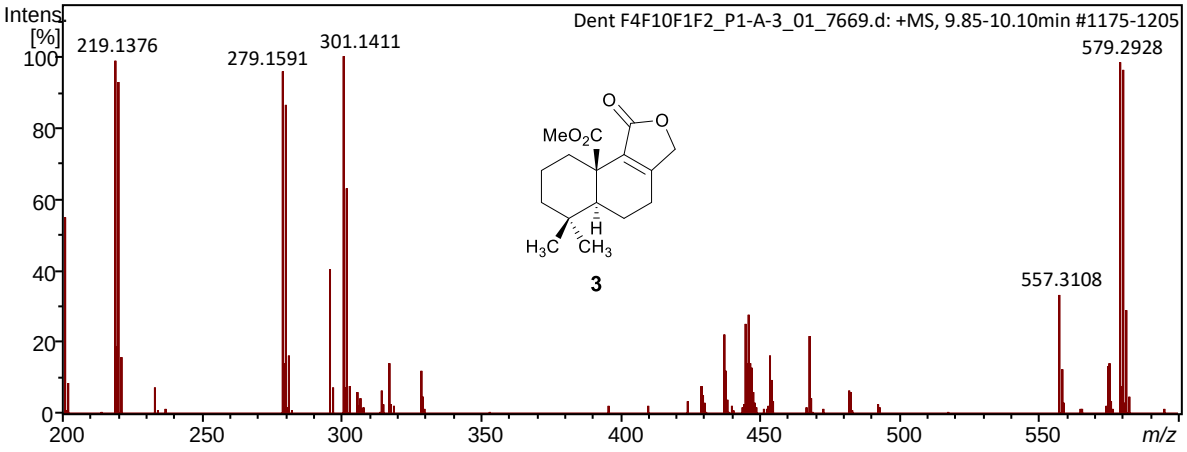


Figure S22: HR-(+)ESIMS spectrum of compound **3**.

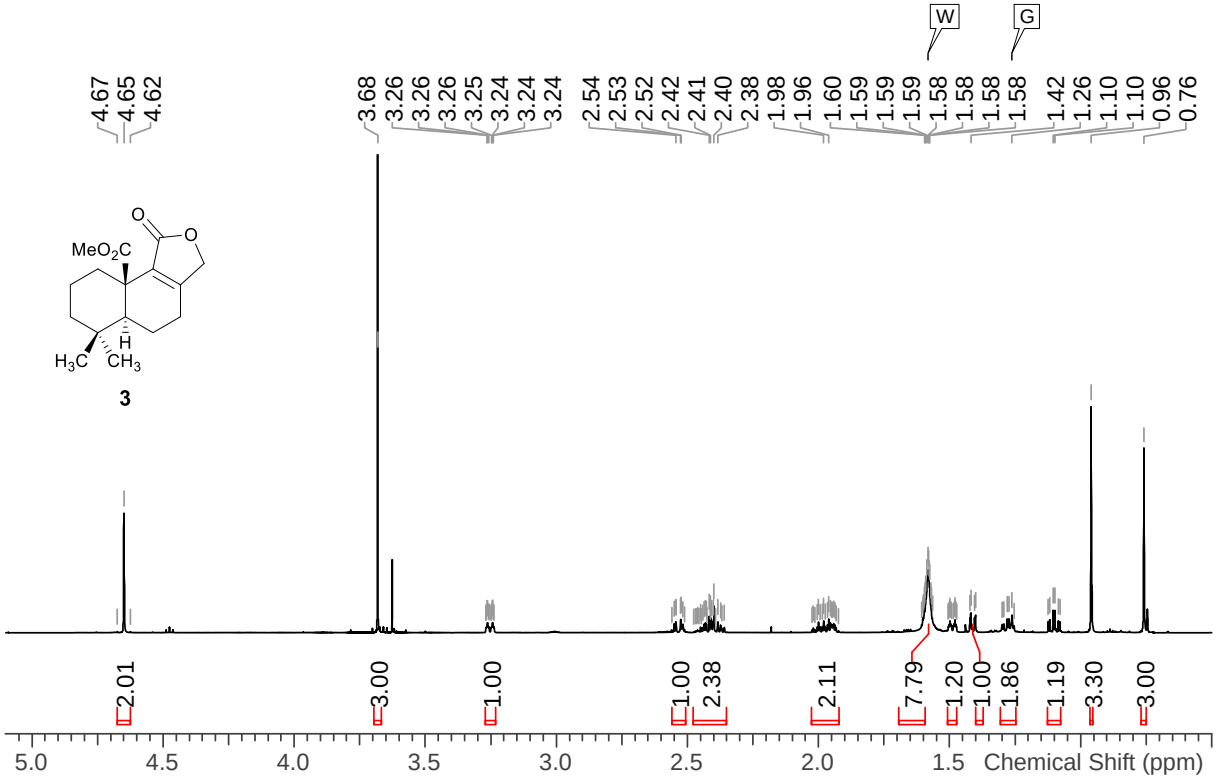


Figure S23: ^{1}H NMR spectrum (700 MHz, $CDCl_3$, 298 K) of the purified compound **3**. EA: ethyl acetate.

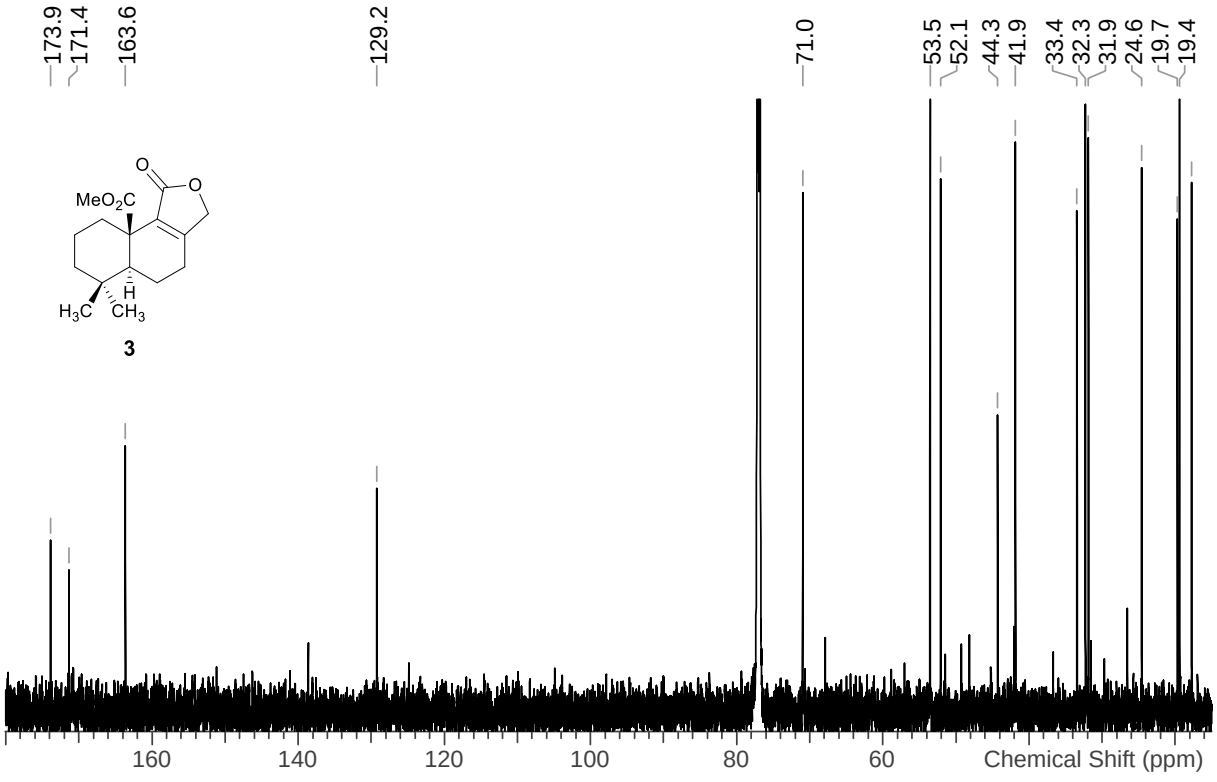


Figure S24: ^{13}C NMR spectrum (175 MHz, $CDCl_3$, 298 K) of the purified compound **3**.

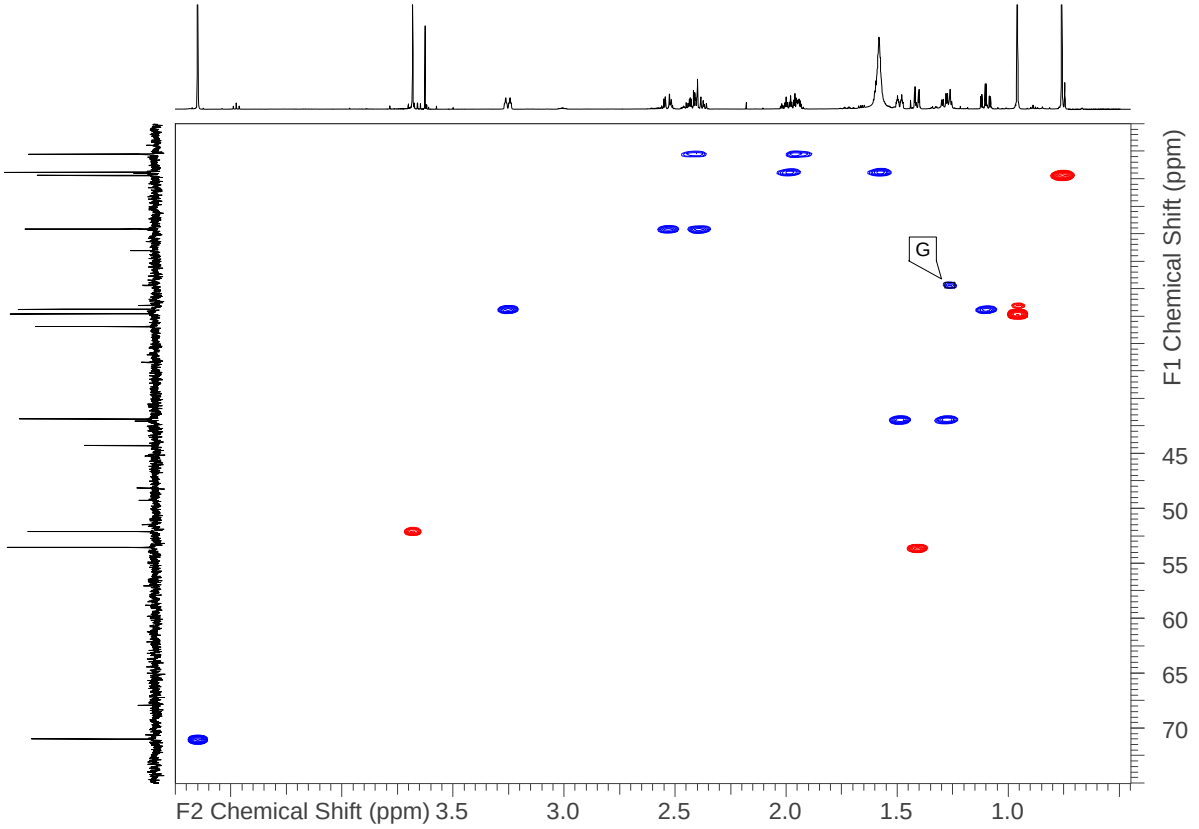


Figure S25: $^{1}H,^{13}C$ DEPT-HSQC spectrum (700 MHz, $CDCl_3$, 298 K) of the purified compound **3**. G: grease.

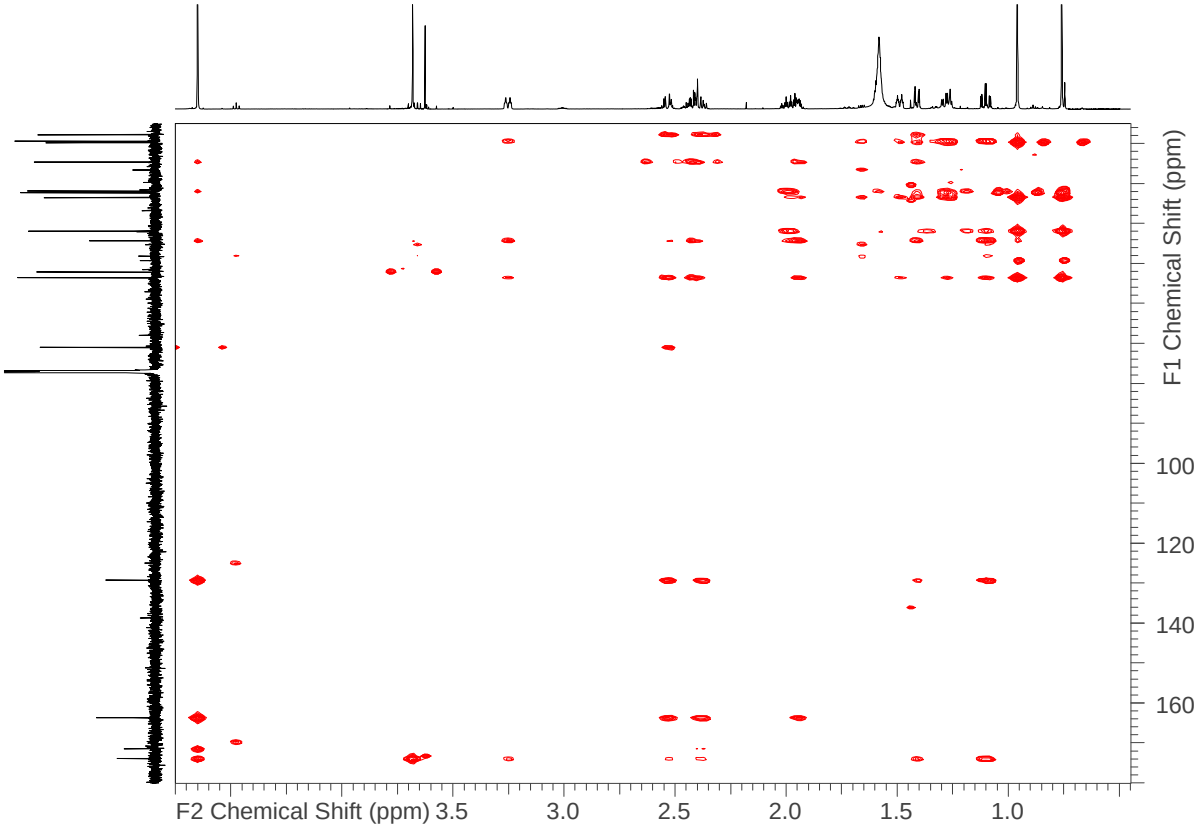


Figure S26: $^{1}H,^{13}C$ HMBC spectrum (700 MHz, $CDCl_3$, 298 K) of the purified compound **3**.

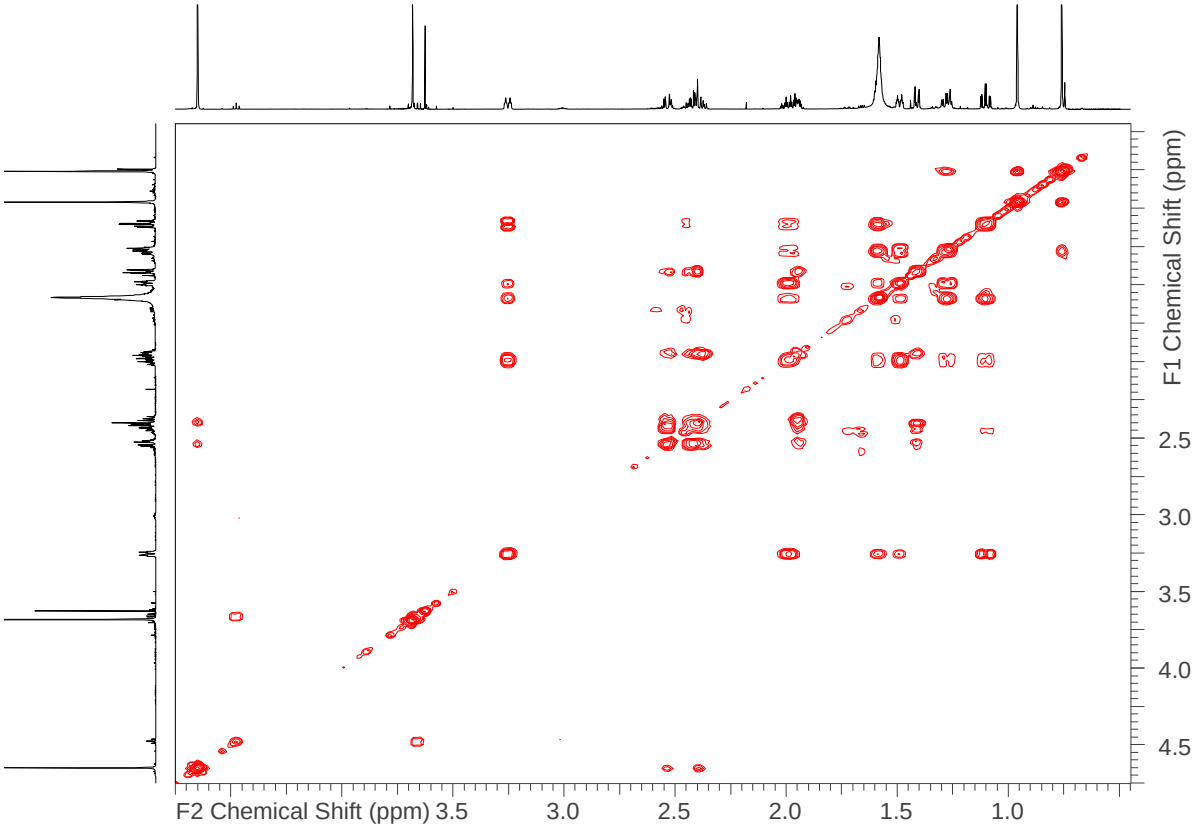


Figure S27: $^{1}H,^{1}H$ COSY spectrum (700 MHz, $CDCl_3$, 298 K) of the purified compound **3**.

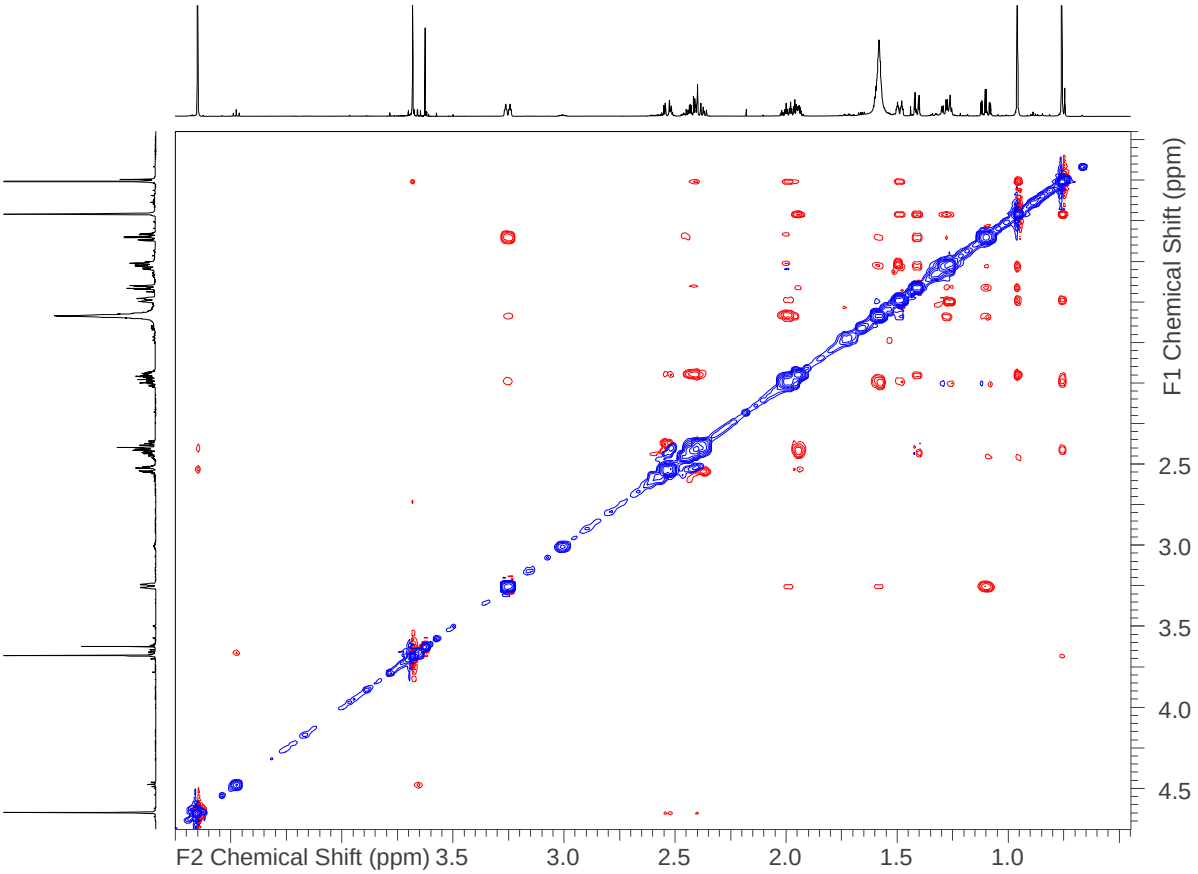


Figure S28: $^{1}H,^{1}H$ ROESY spectrum (700 MHz, $CDCl_3$, 298 K) of the purified compound **3**.

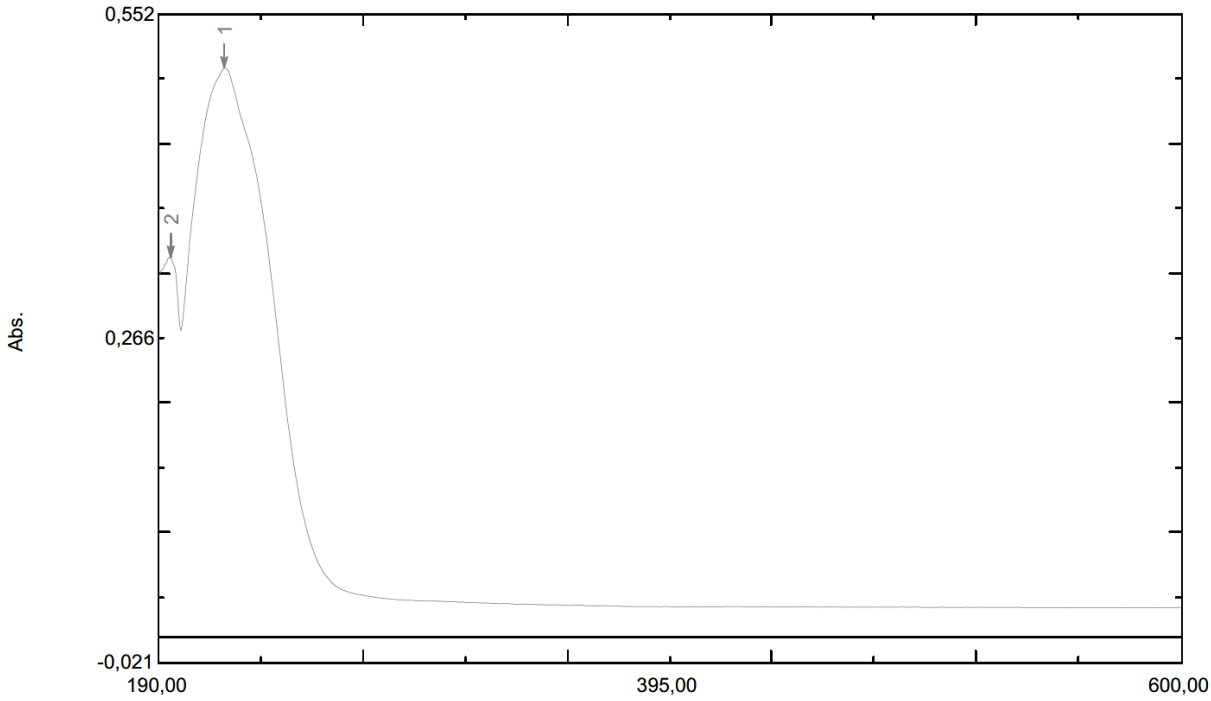


Figure S29: UV/Vis spectrum of compound **3** in MeOH.

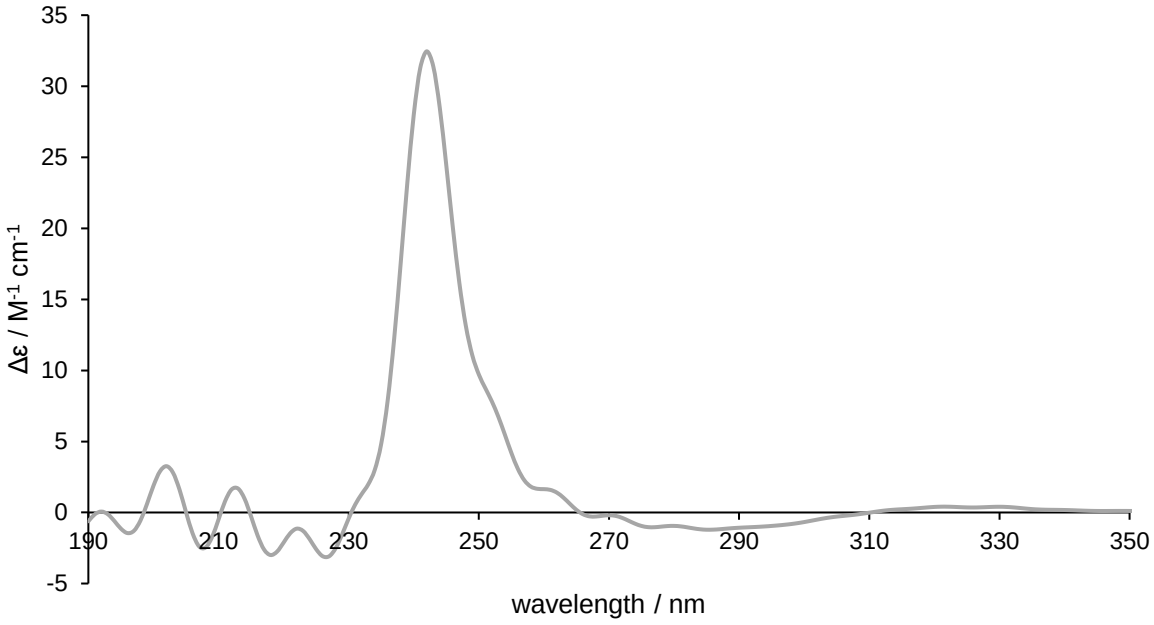


Figure S30: ECD spectrum of compound **3** in MeOH.

(8) Analytical data of compound 4

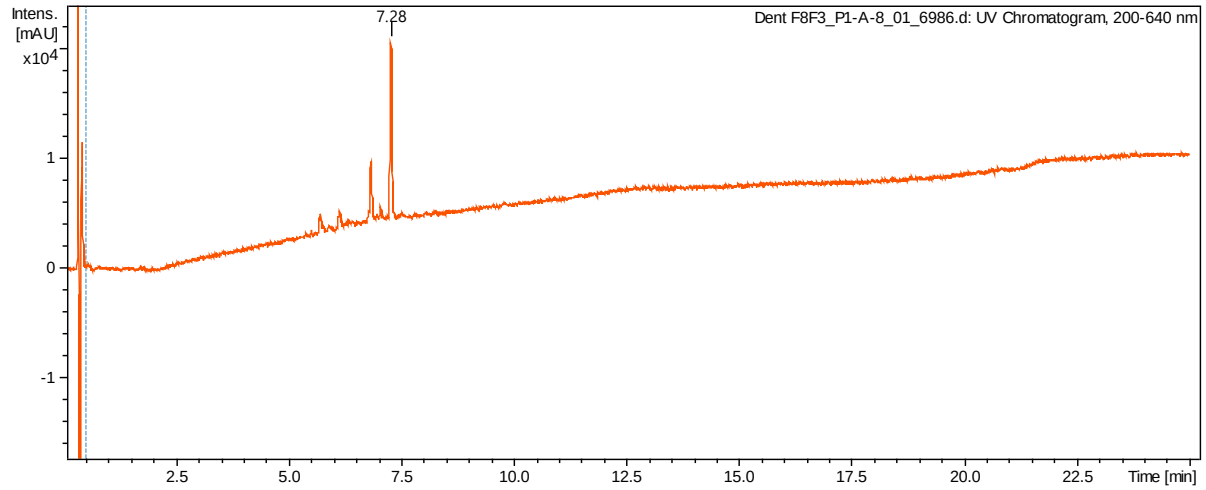


Figure S31: HPLC-DAD chromatogram of compound **4**.

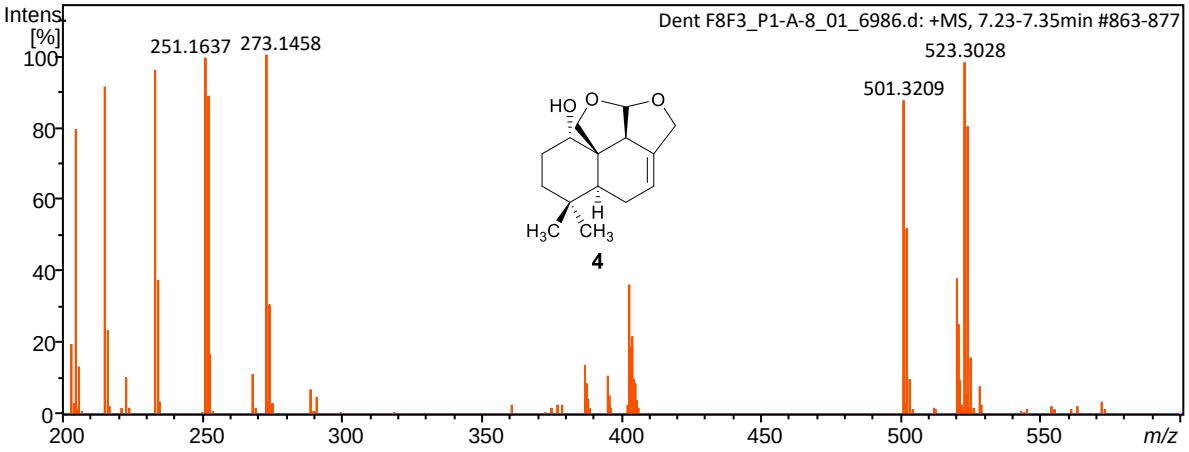


Figure S32: HR-(+)ESIMS spectrum of compound **4**.

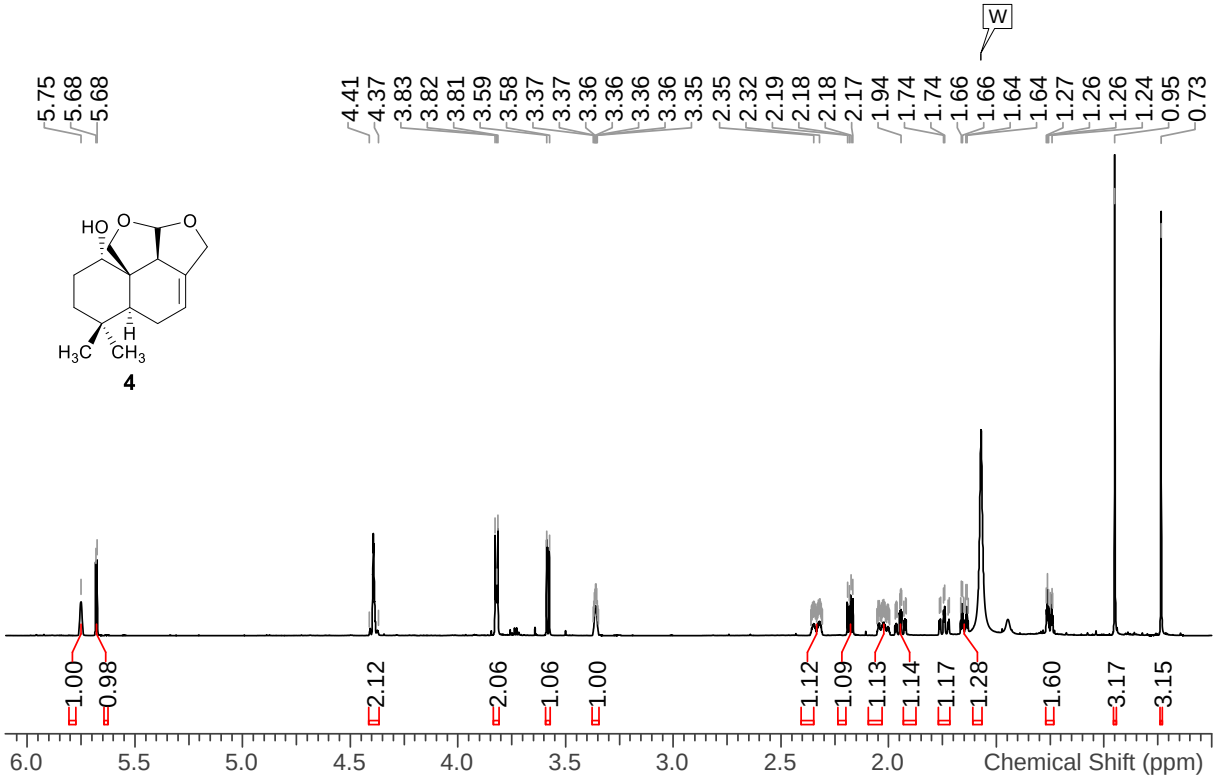


Figure S33: ^{1}H NMR spectrum (700 MHz, $CDCl_3$, 298 K) of the purified compound **4**. W: H_2O, A: acetone, M: methanol.

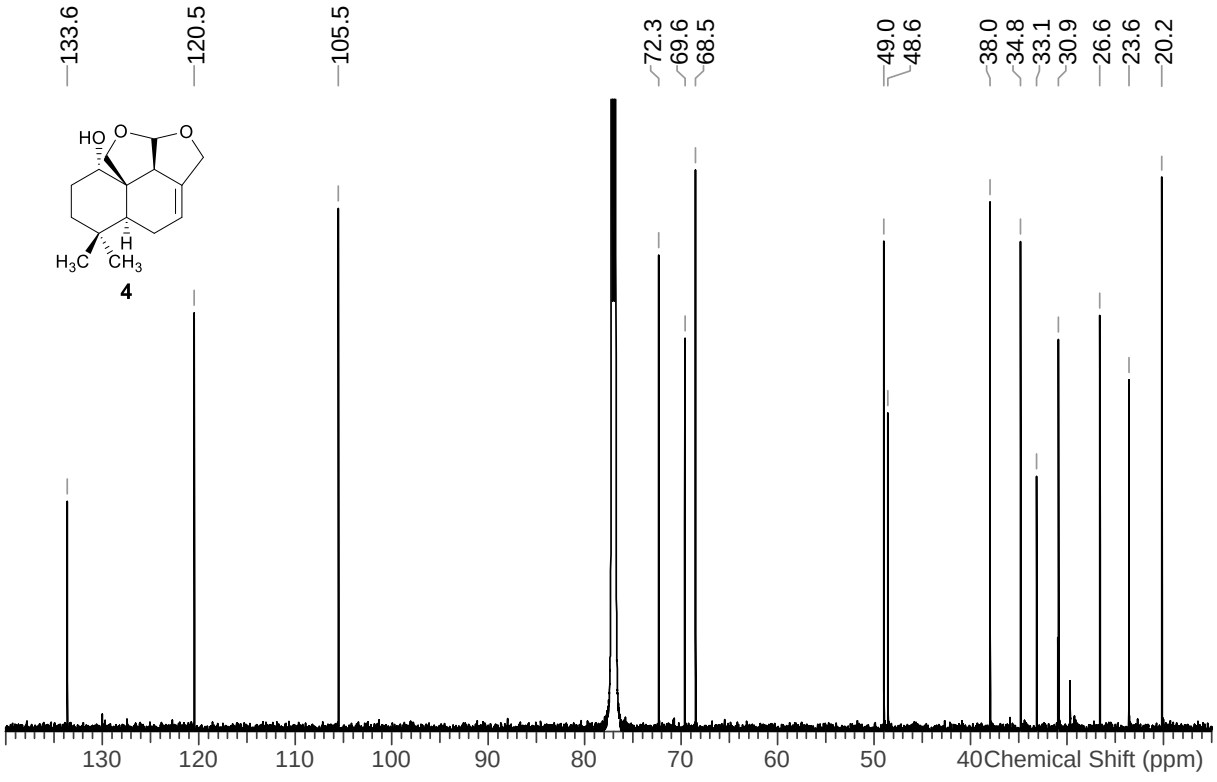


Figure S34: ^{13}C NMR spectrum (175 MHz, $CDCl_3$, 298 K) of the purified compound **4**.

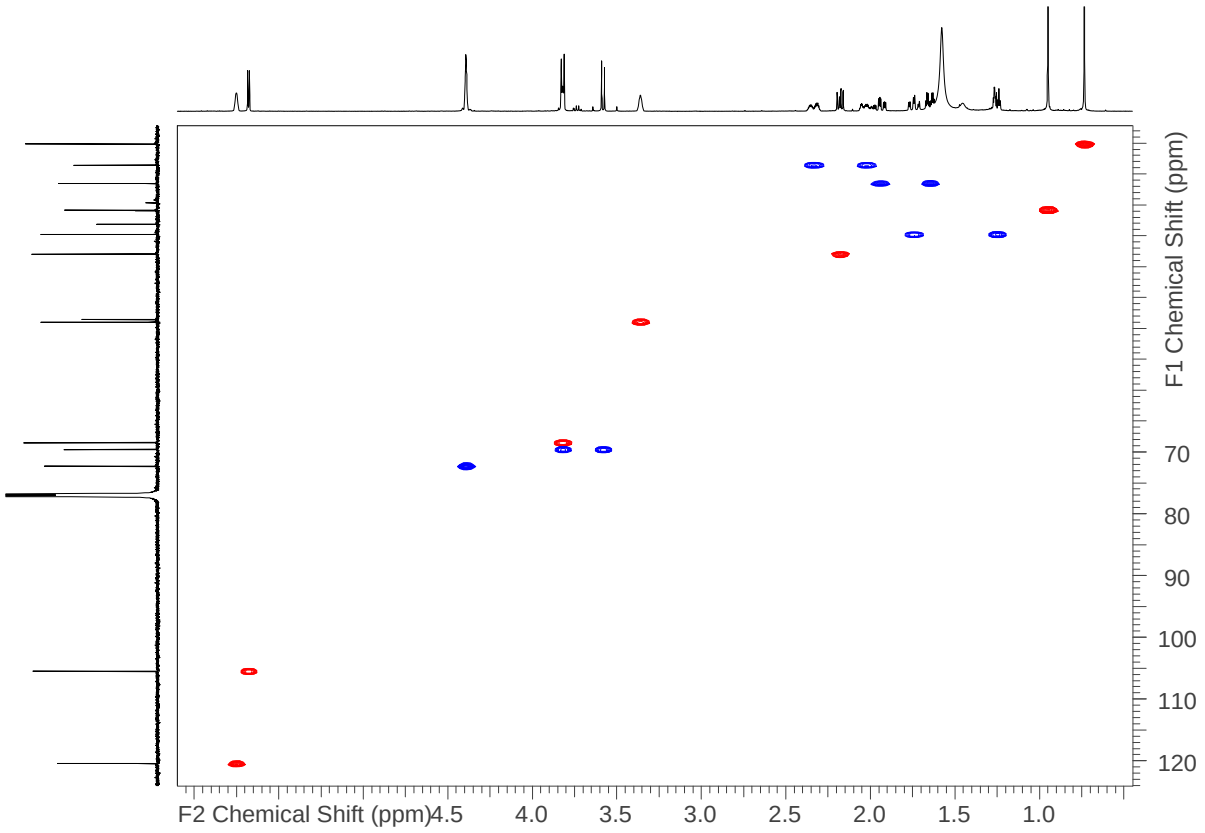


Figure S35: $^{1}H,^{13}C$ DEPT-HSQC spectrum (700 MHz, $CDCl_3$, 298 K) of the purified compound **4**.

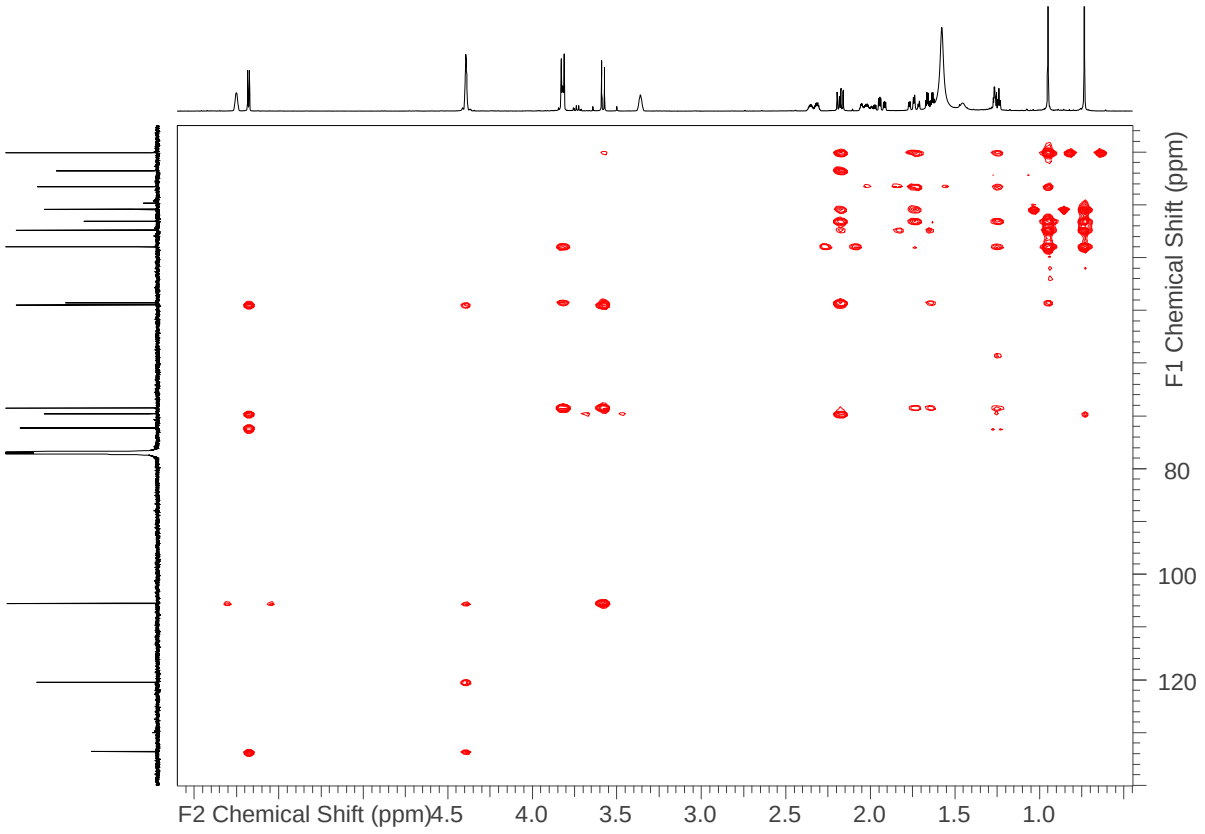


Figure S36: $^{1}H,^{13}C$ HMBC spectrum (700 MHz, $CDCl_3$, 298 K) of the purified compound **4**.

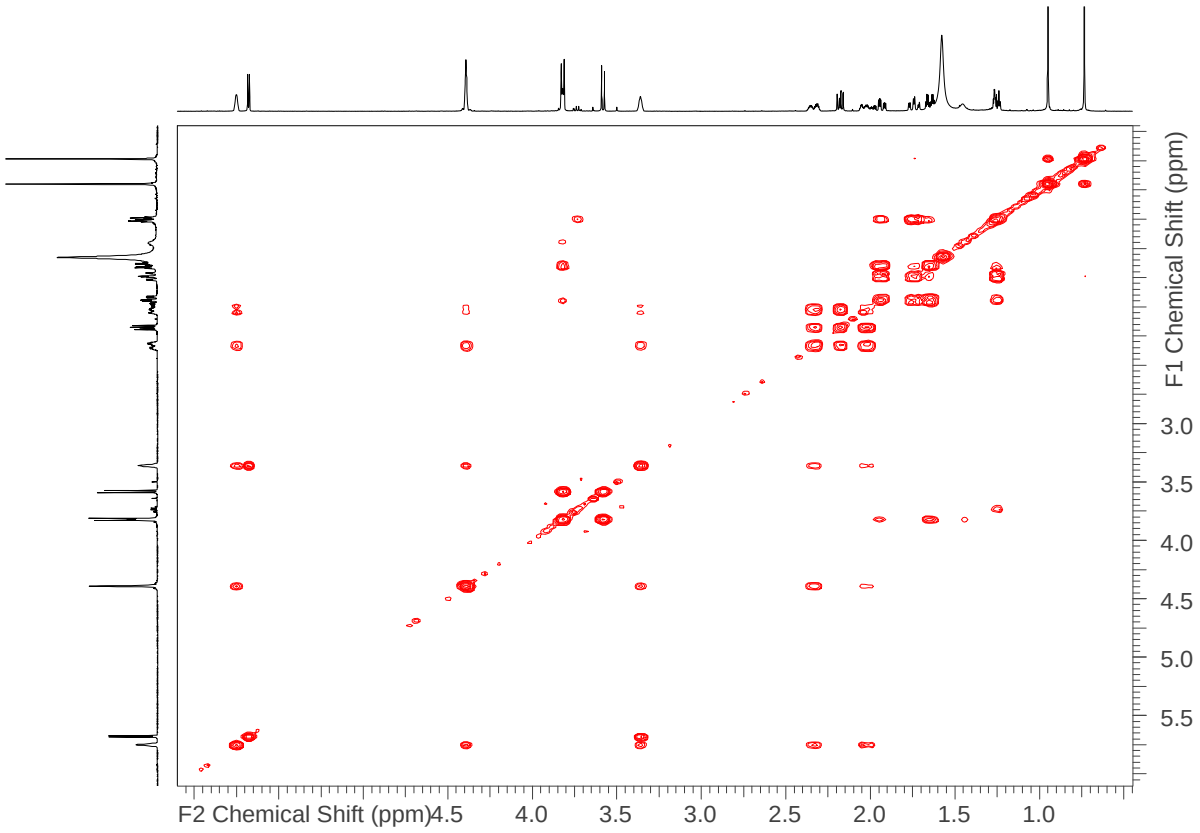


Figure S37: $^{1}H,^{1}H$ COSY spectrum (700 MHz, $CDCl_3$, 298 K) of the purified compound **4**.

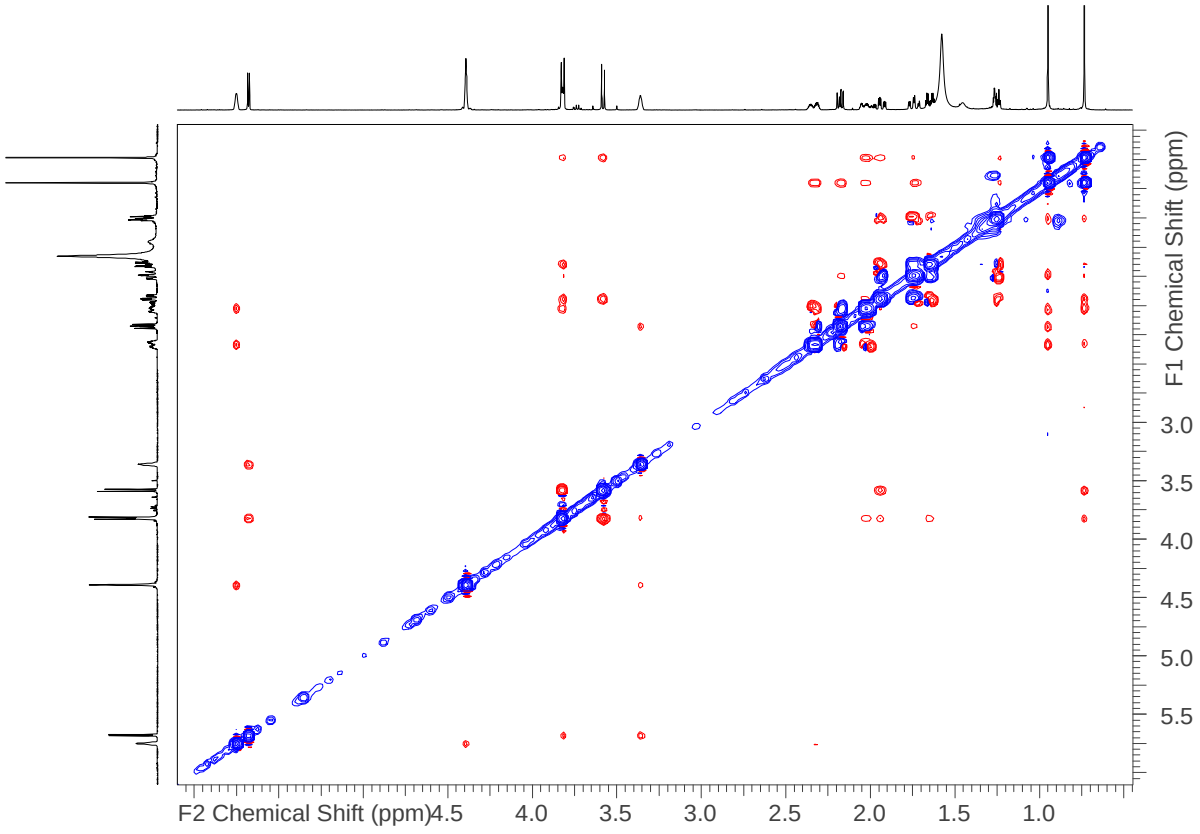


Figure S38: $^{1}H,^{1}H$ ROESY spectrum (700 MHz, $CDCl_3$, 298 K) of the purified compound **4**.

Table S6: NMR data of compound **4**, recorded at 700 MHz (^{1}H) or 175 MHz (^{13}C) in CD_3OD at 298 K. δ_H and δ_C are given in ppm.

	δ_C	δ_H (mult., *J* in Hz)
1	69.2, CH	3.67 (t, *J*2.9 Hz)
2	27.2, CH_2	1.64 (dq, 14.4, 3.3 Hz, 1H, α)
		1.92 (dddd, 14.4, 14.1, 3.8, 2.6 Hz, 1H, β)
3	36.2, CH_2	1.19 (dddd, 13.3, 3.8, 2.9, 0.8 Hz, 1H, β)
		1.80 (ddd, 14.1, 13.3, 3.7 Hz, 1H, α)
4	34.2, Cq	
5	39.4, CH	2.18 (dd, 11.2, 6.9 Hz, 1H, α)
6	24.8, CH_2	2.06 (m, 1H, β)
		2.32 (m, 1H, α)
7	122.0, CH	5.78 (m, 1H)
8	134.9, Cq	
9	50.4, CH	3.29 (m, 1H, α)
10	50.2, Cq	
11	107.0, CH	5.58 (d, 4.3, 1H)
12	73.2, CH_2	4.33 (m, 2H)
13	20.7, CH_3	0.74 (s, 3H, β)
14	31.6, CH_3	0.93 (s, 3H, α)
15	70.8, CH_2	3.58 (d, 8.4 Hz, 1H, α)
		3.78 (d, 8.4 Hz, 1H, β)

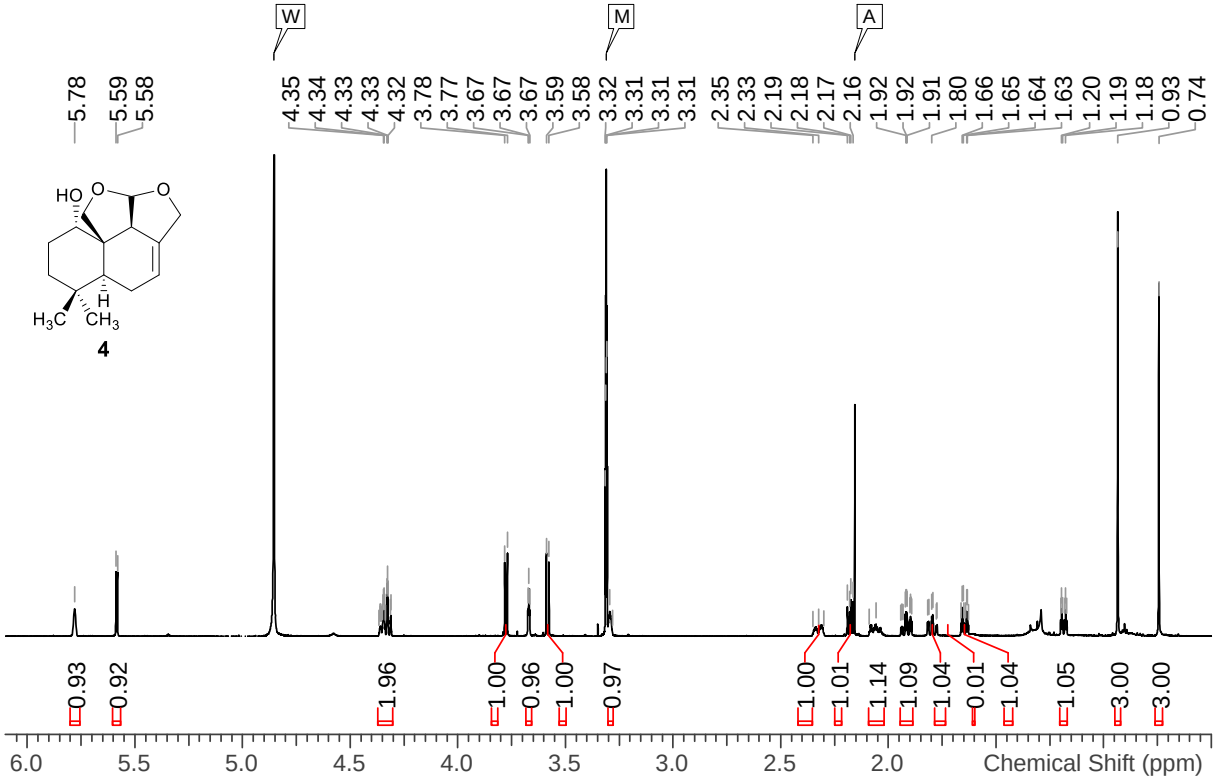


Figure S39: ^{1}H NMR spectrum (700 MHz, CD_3OD, 298 K) of the purified compound **4**. W: H_2O, M: methanol, A: acetone.

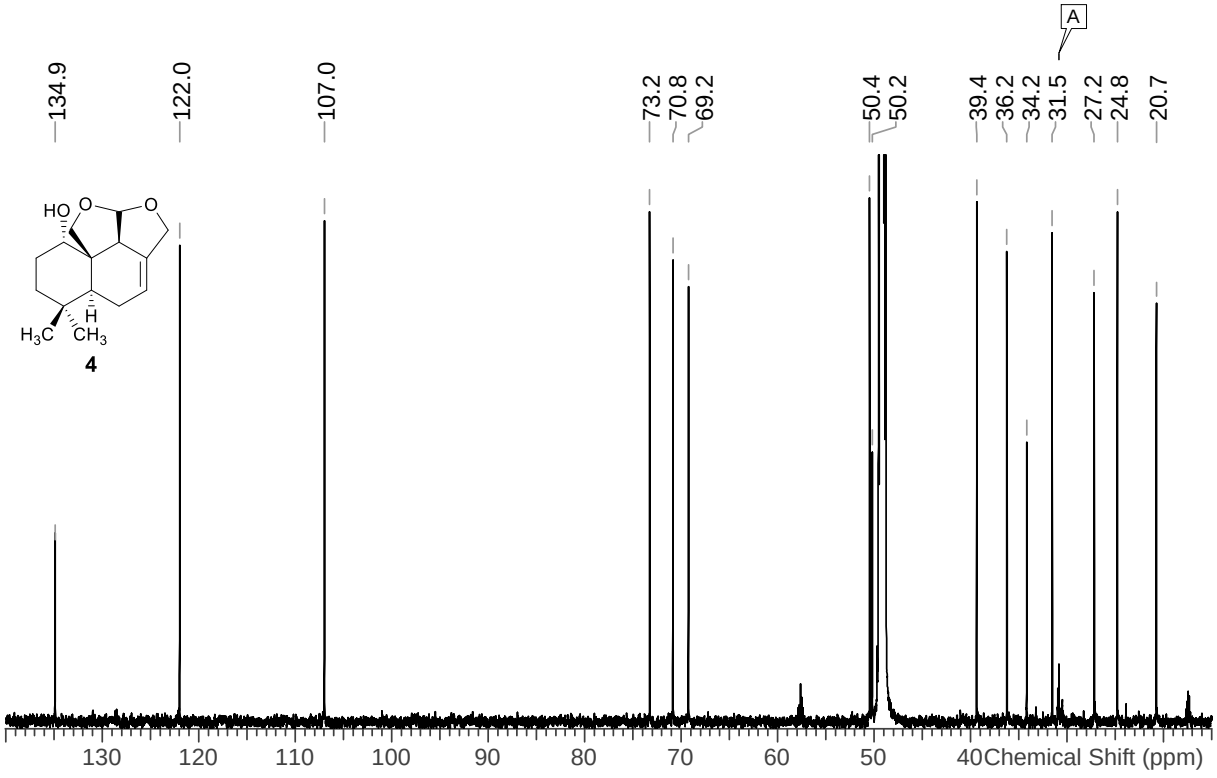


Figure S40: ^{13}C NMR spectrum (175 MHz, CD_3OD, 298 K) of the purified compound **4**. A: acetone.

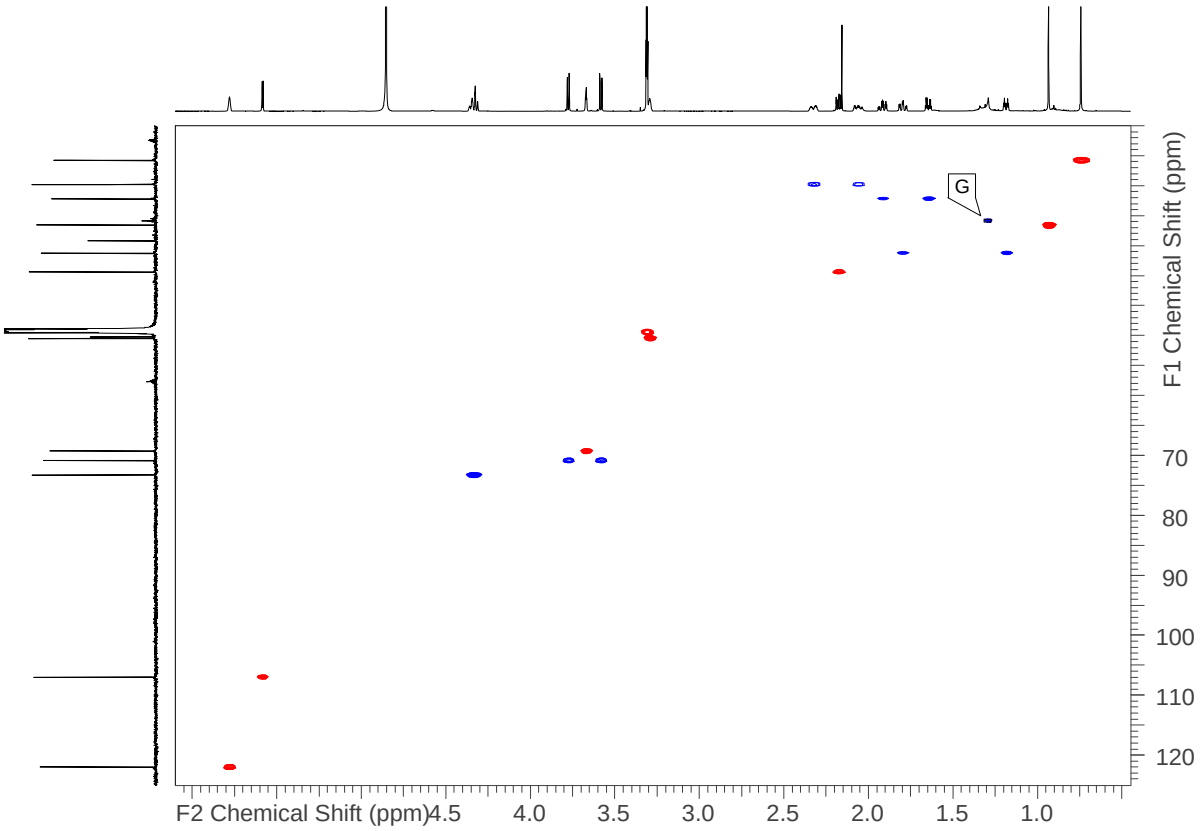


Figure S41: $^{1}H,^{13}C$ DEPT-HSQC spectrum (700 MHz, CD_3OD, 298 K) of the purified compound **4**.

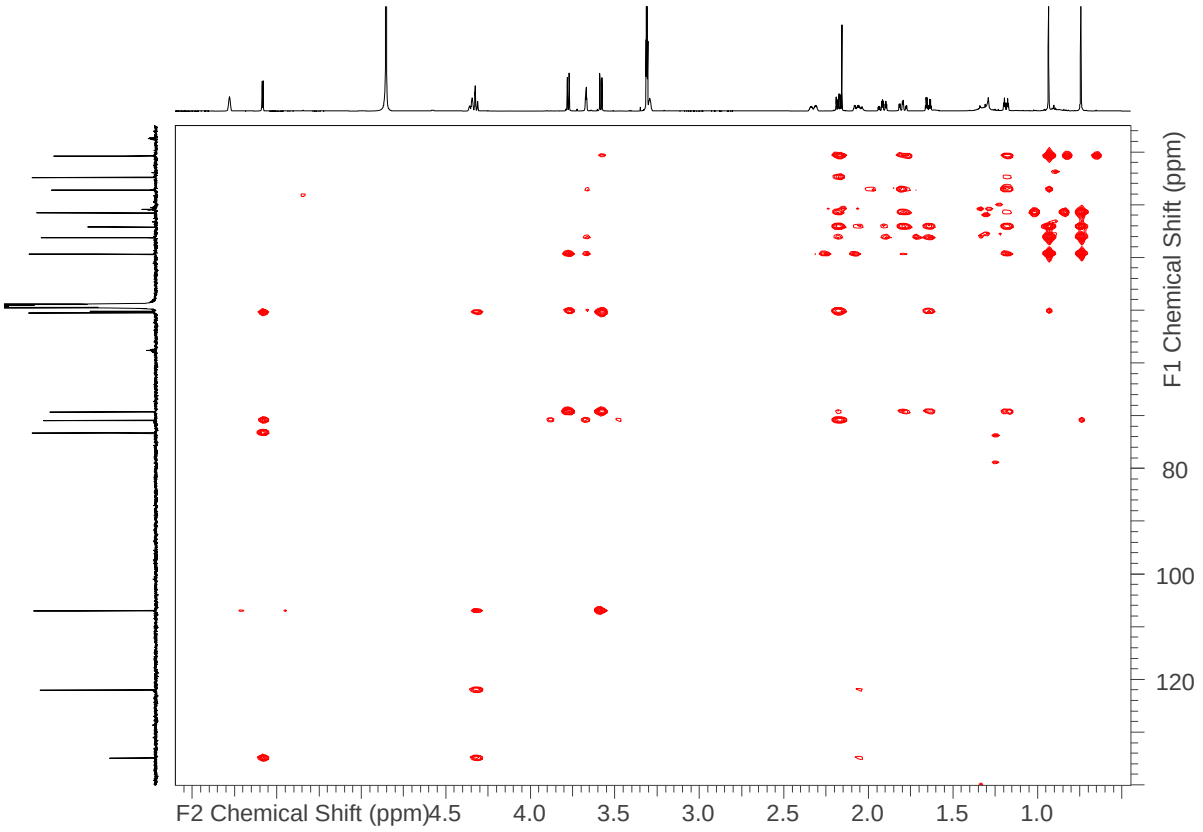


Figure S42: $^{1}H,^{13}C$ HMBC spectrum (700 MHz, CD_3OD, 298 K) of the purified compound **4**.

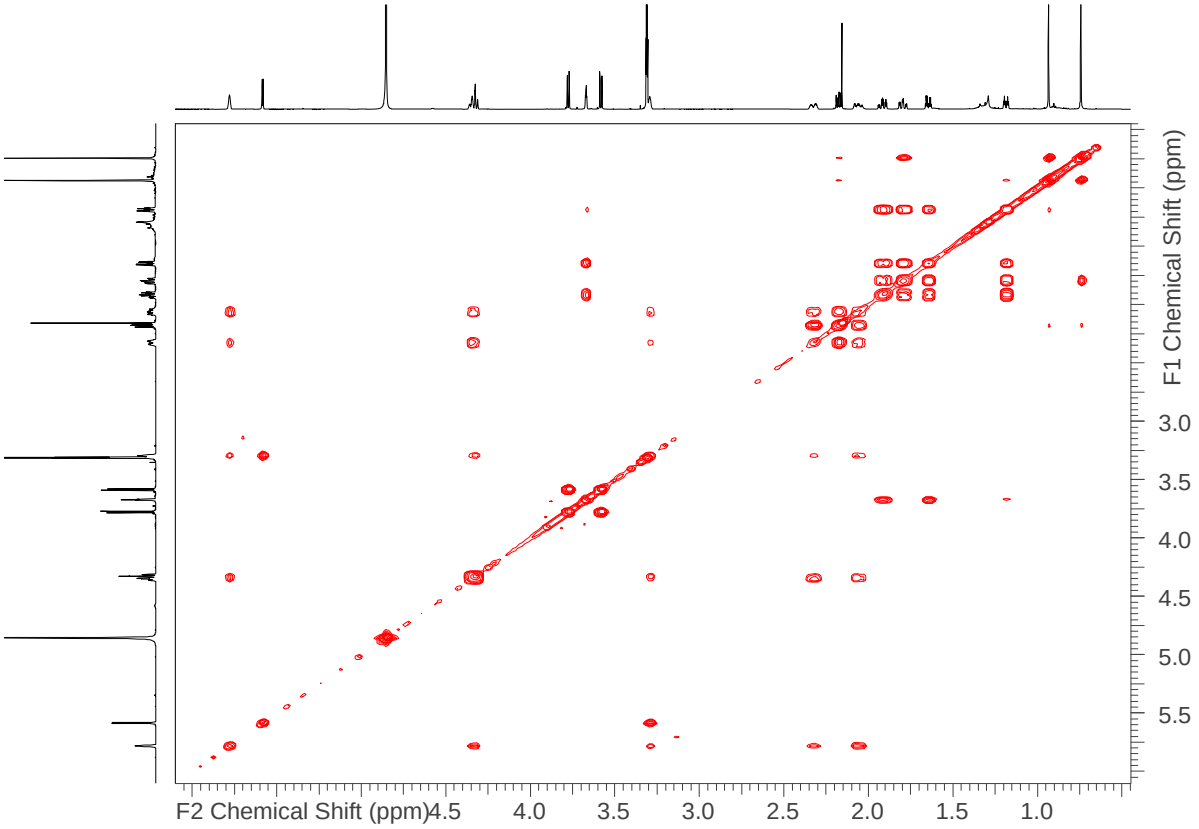


Figure S43: $^{1}H,^{1}H$ COSY spectrum (700 MHz, CD_3OD, 298 K) of the purified compound **4**.

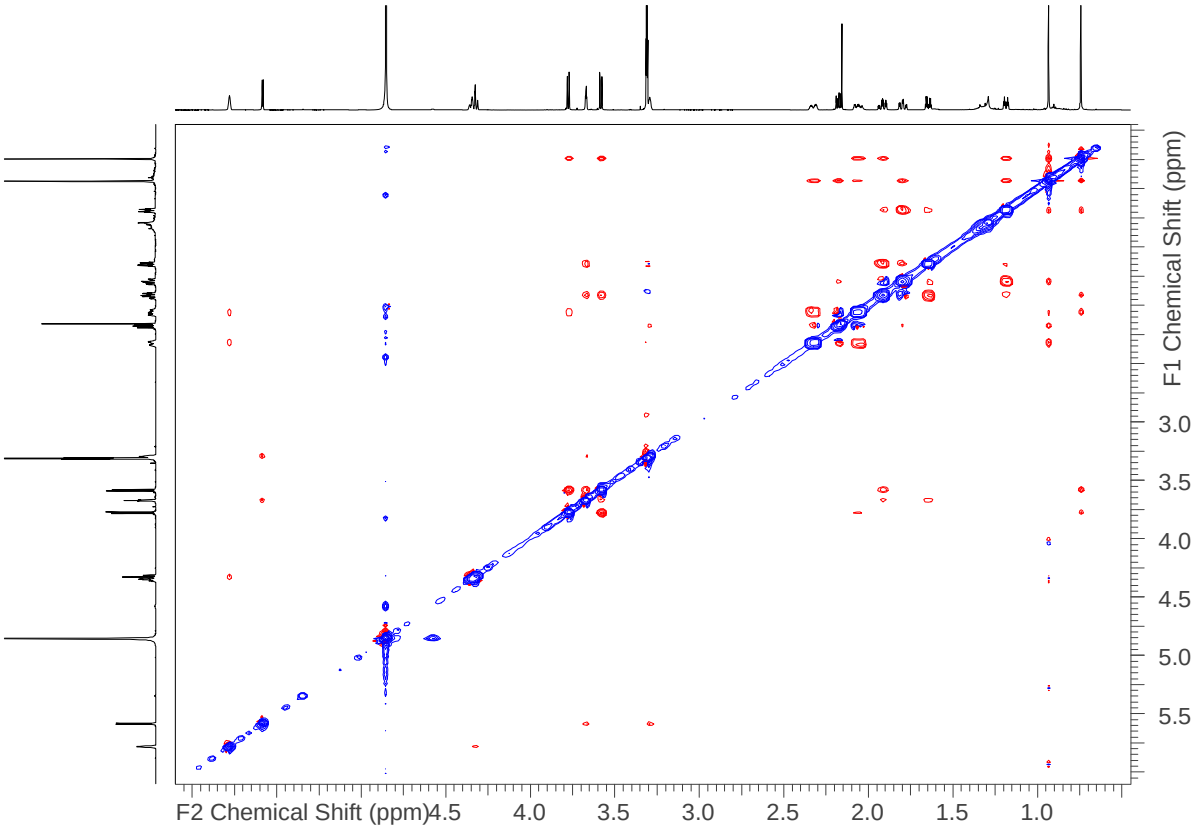


Figure S44: $^{1}H,^{1}H$ ROESY spectrum (700 MHz, CD_3OD, 298 K) of the purified compound **4**.

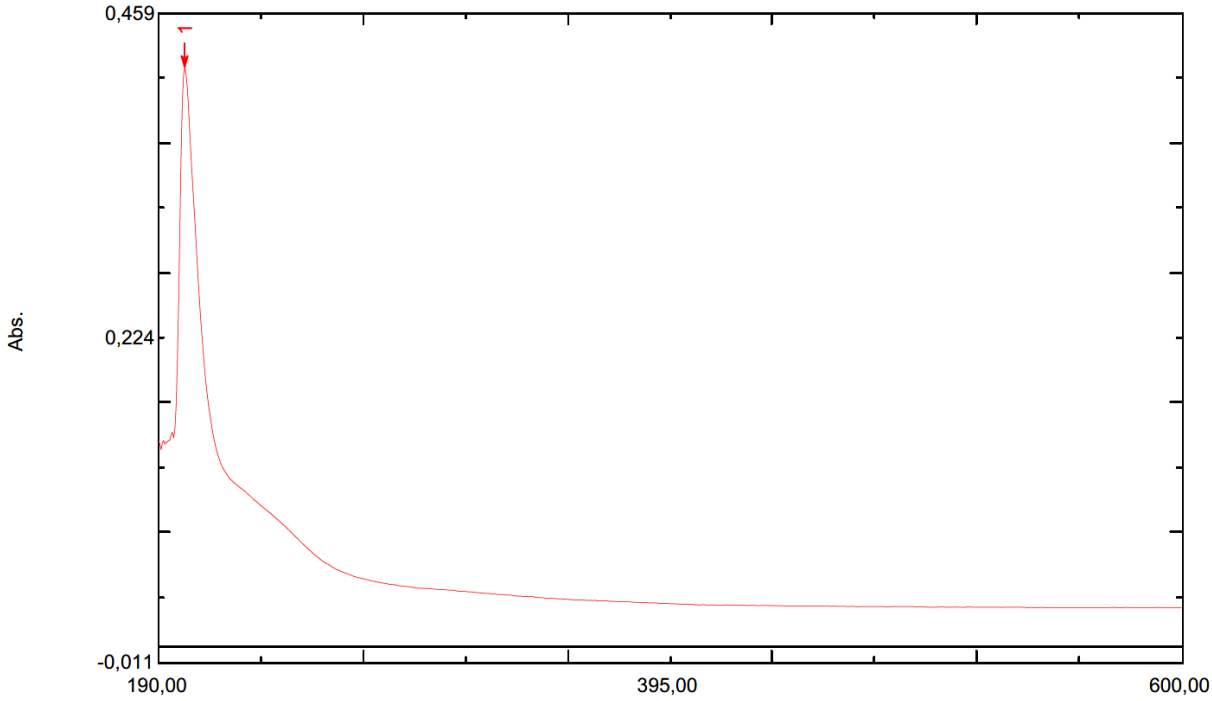


Figure S45: UV/Vis spectrum of compound **4** in MeOH.

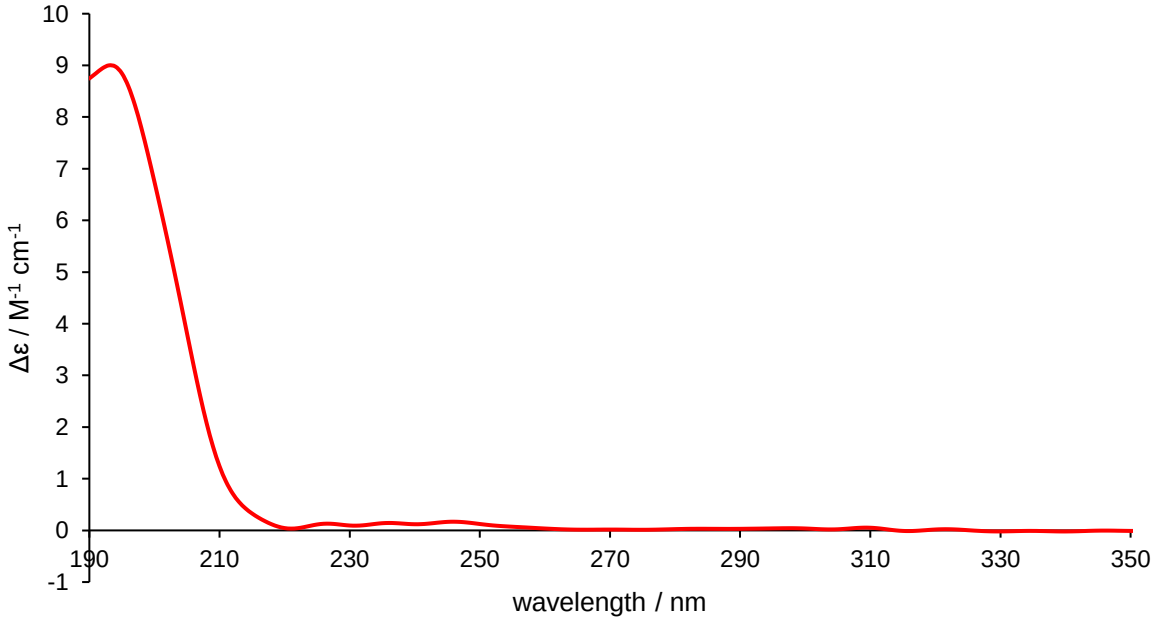


Figure S46: ECD spectrum of compound **4** in MeOH.

(9) Analytical data of compound 5

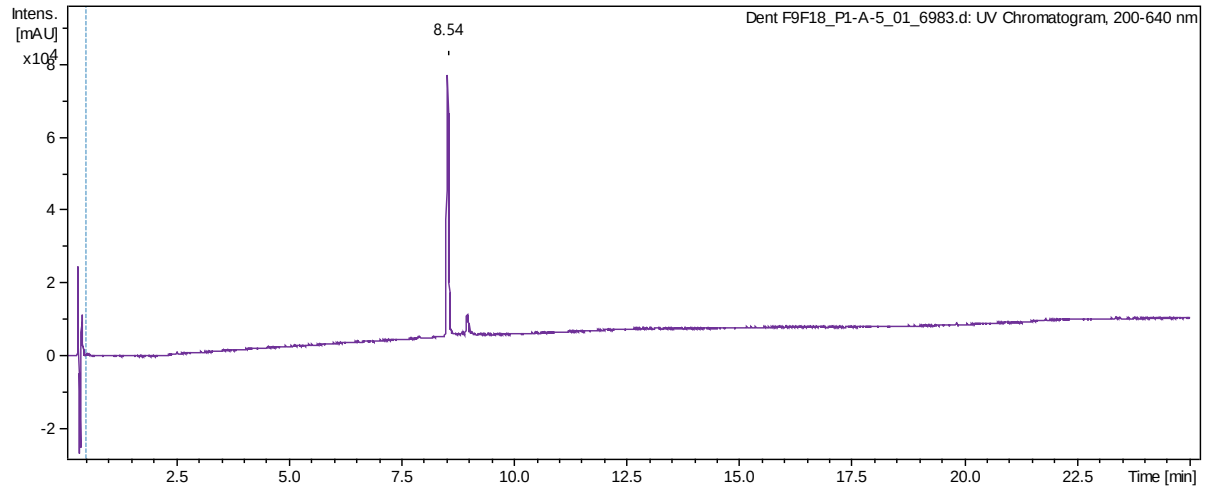


Figure S47: HPLC-DAD chromatogram of compound **5**.

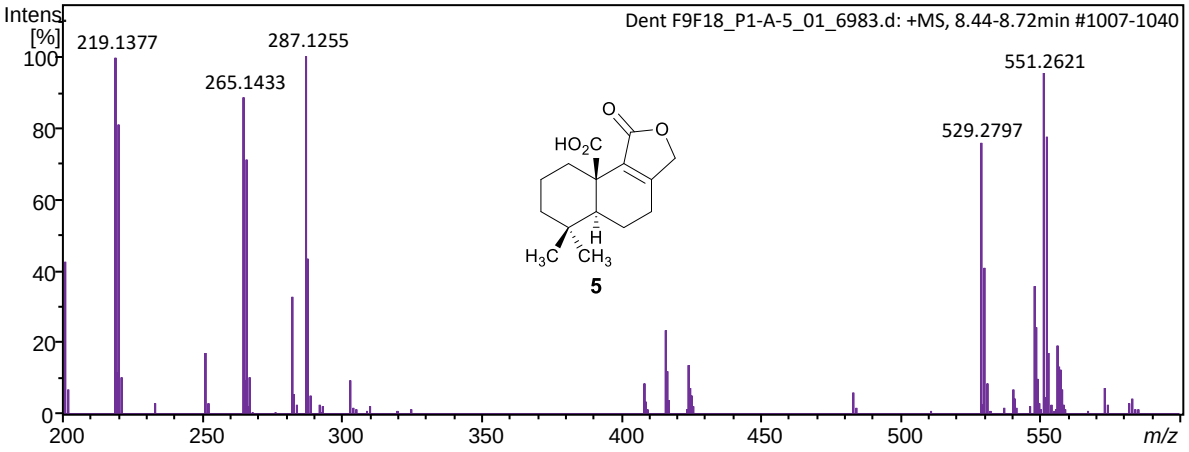


Figure S48: HR-(+)ESIMS spectrum of compound **5**.

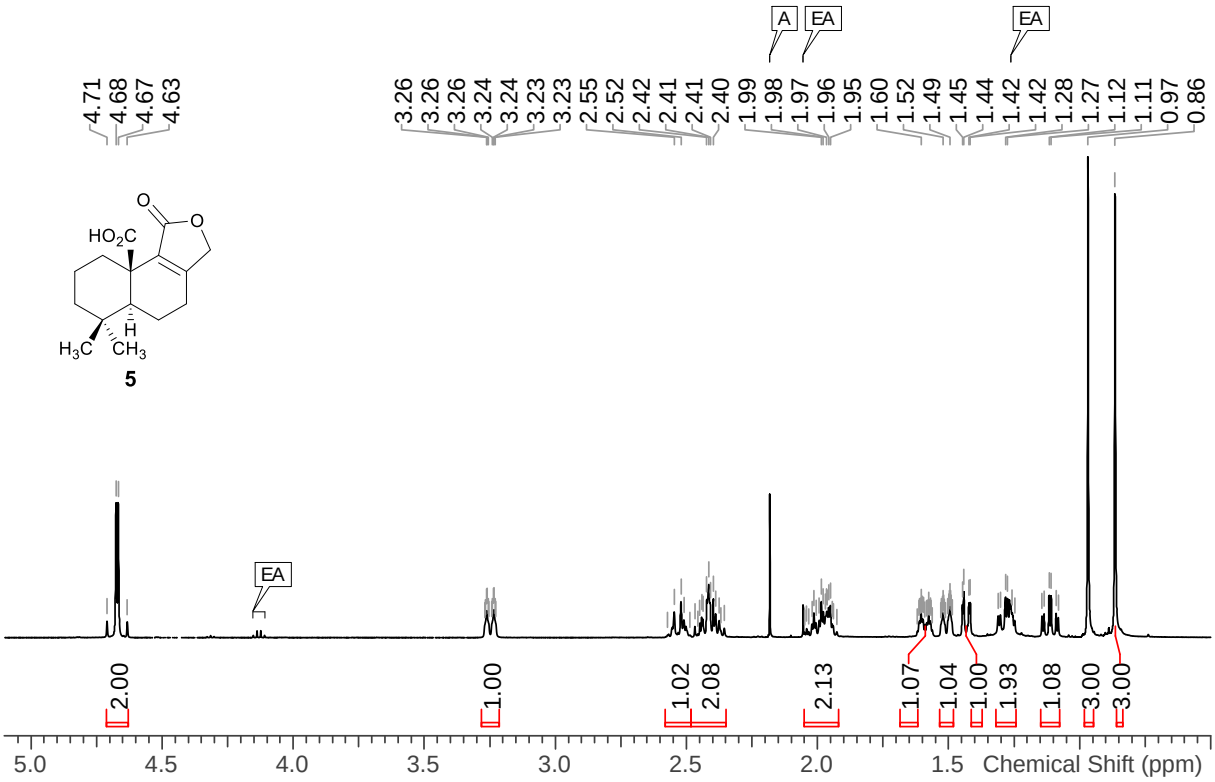


Figure S49: ^{1}H NMR spectrum (500 MHz, $CDCl_3$, 298 K) of the purified compound **5**. EA: ethyl acetate, A: acetone.

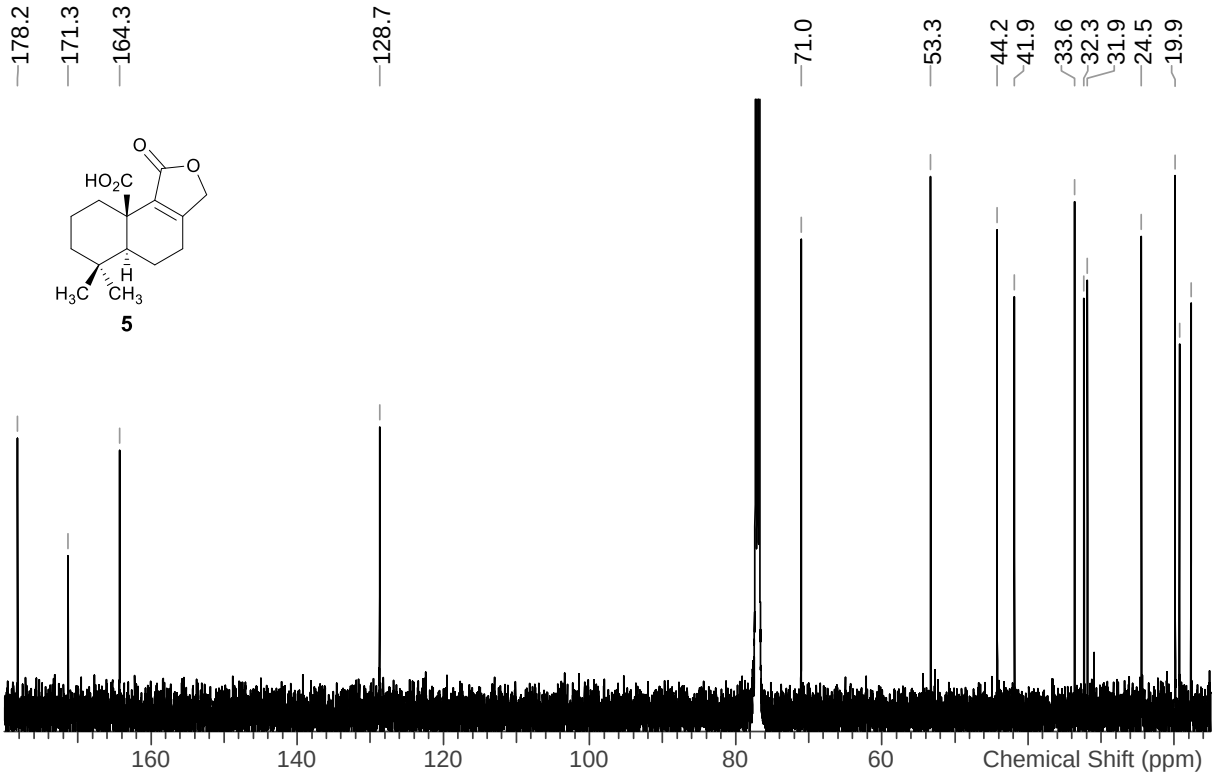


Figure S50: ^{13}C NMR spectrum (125 MHz, $CDCl_3$, 298 K) of the purified compound **5**. EA: ethyl acetate, A: acetone.

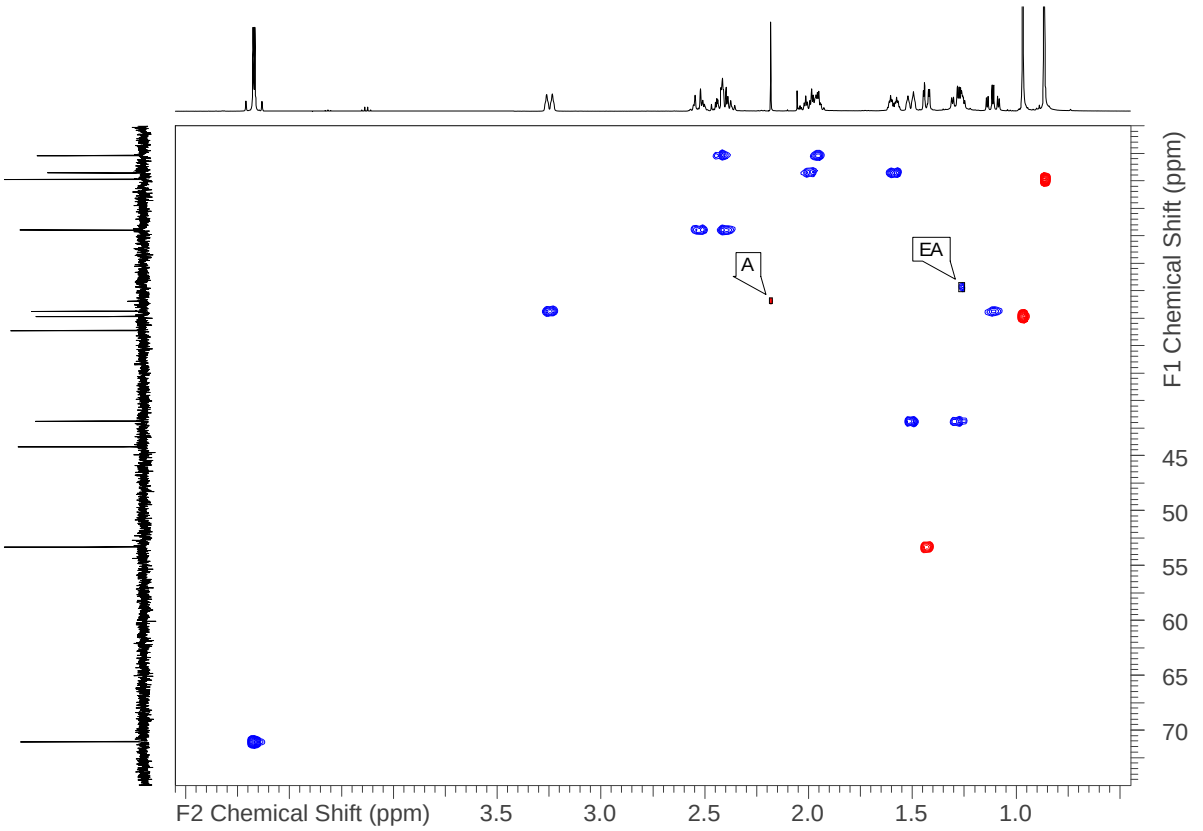


Figure S51: $^{1}H,^{13}C$ DEPT-HSQC spectrum (500 MHz, $CDCl_3$, 298 K) of the purified compound **5**.

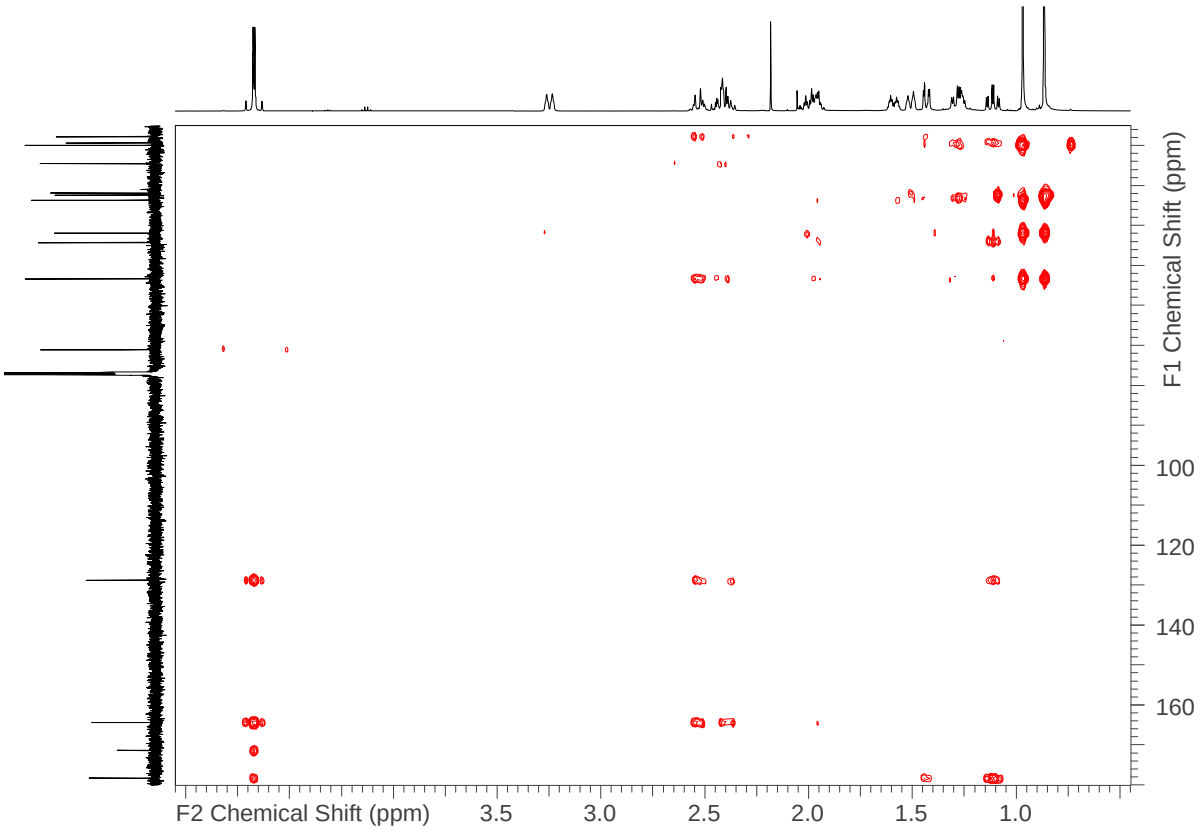


Figure S52: $^{1}H,^{13}C$ HMBC spectrum (500 MHz, $CDCl_3$, 298 K) of the purified compound **5**.

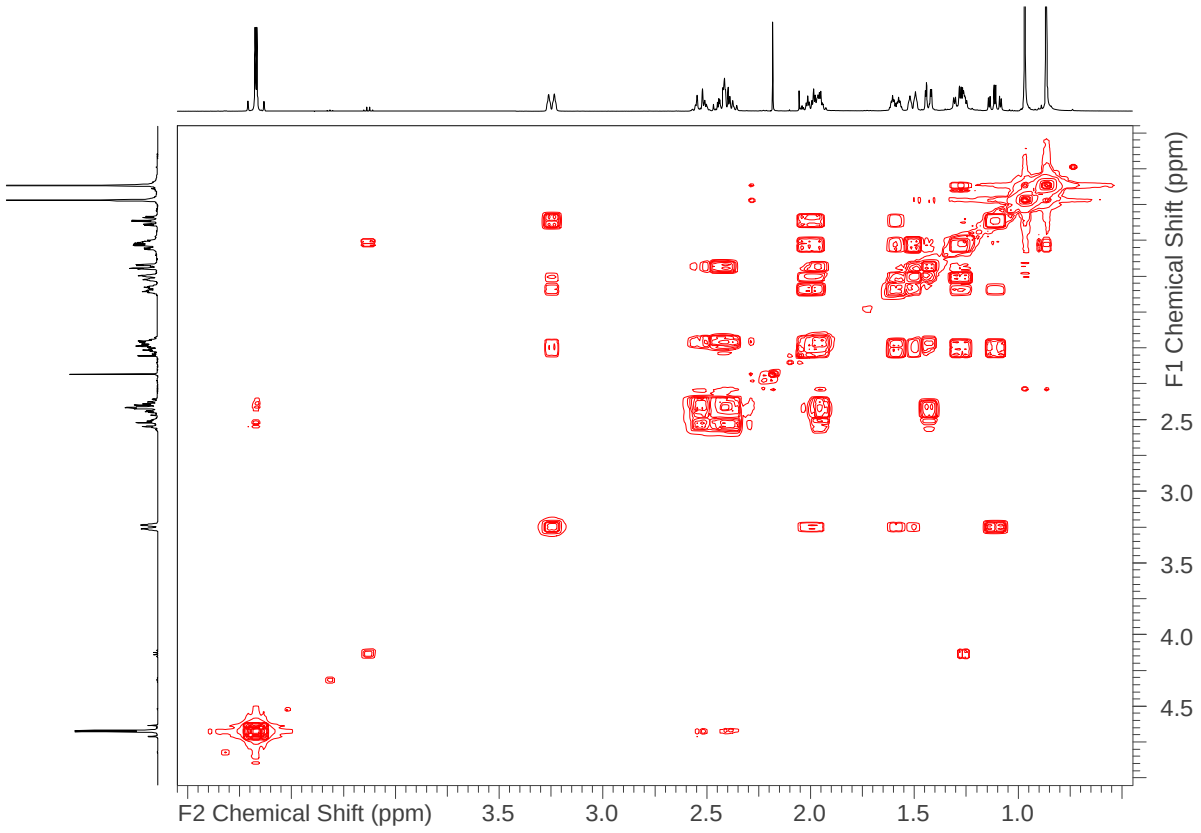


Figure S53: $^{1}H,^{1}H$ COSY spectrum (500 MHz, $CDCl_3$, 298 K) of the purified compound **5**.

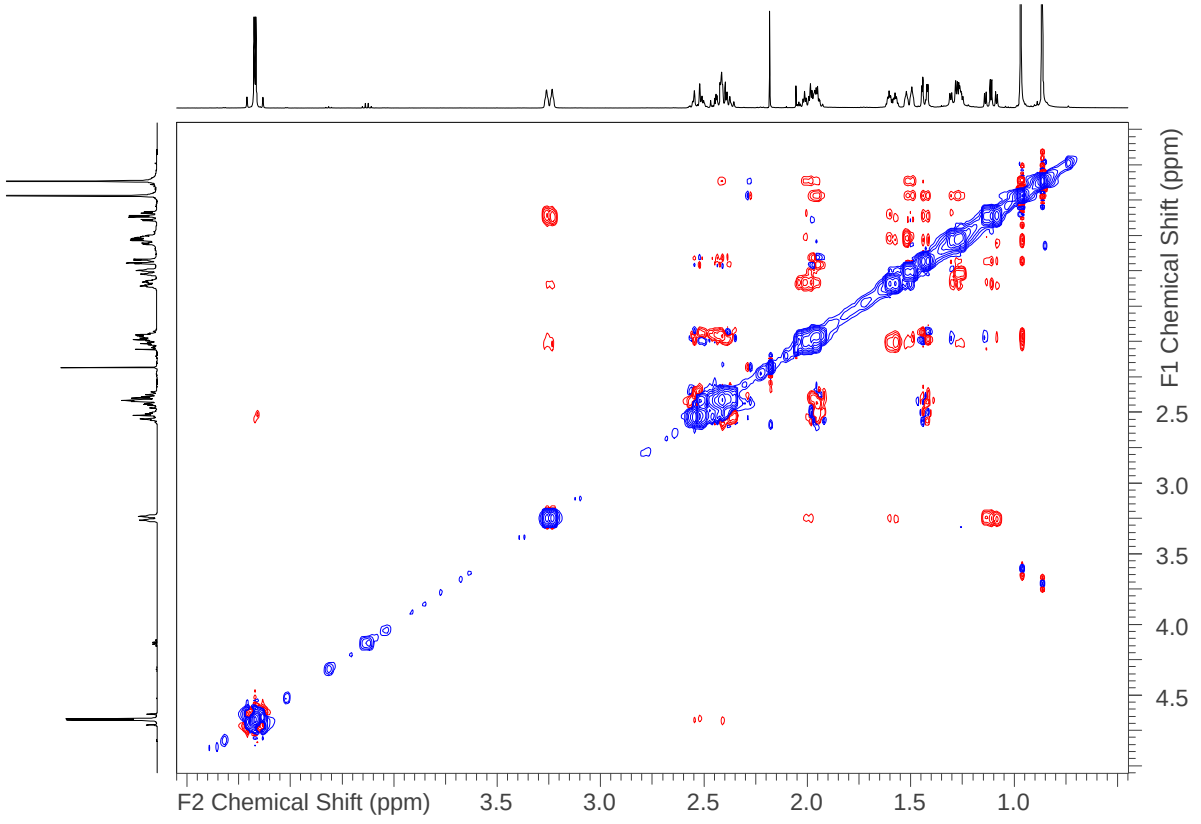


Figure S54: $^{1}H,^{1}H$ ROESY spectrum (500 MHz, $CDCl_3$, 298 K) of the purified compound **5**.

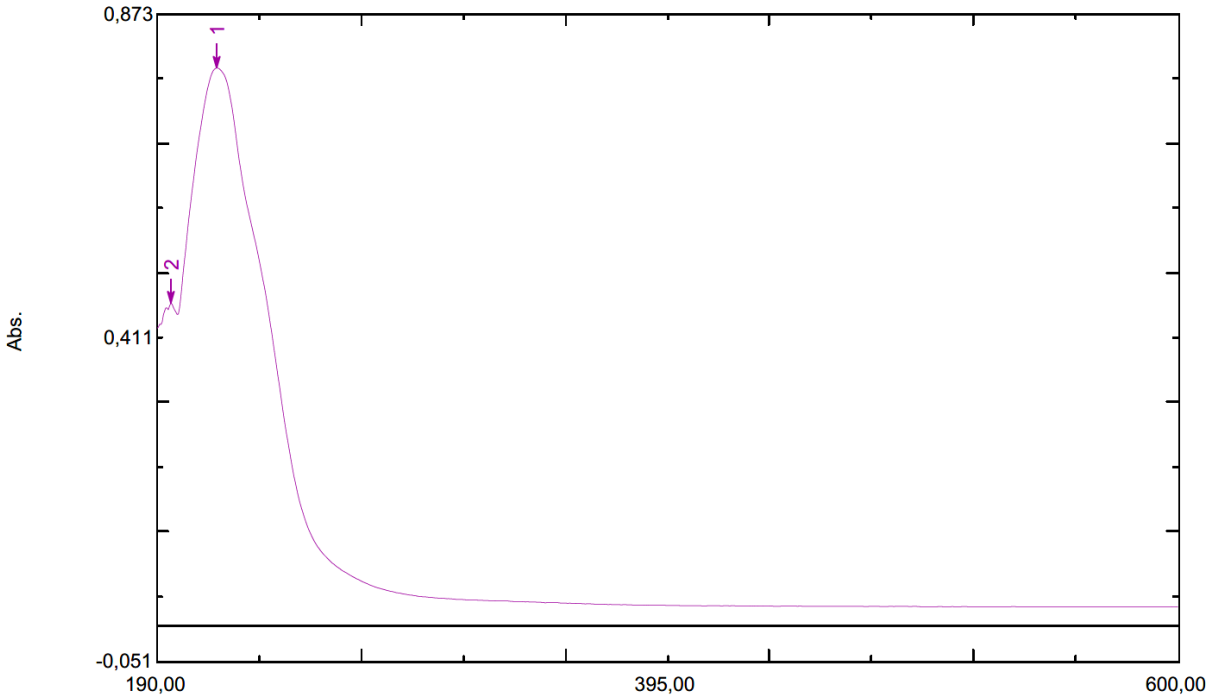


Figure S55: UV/Vis spectrum of compound **5** in MeOH.

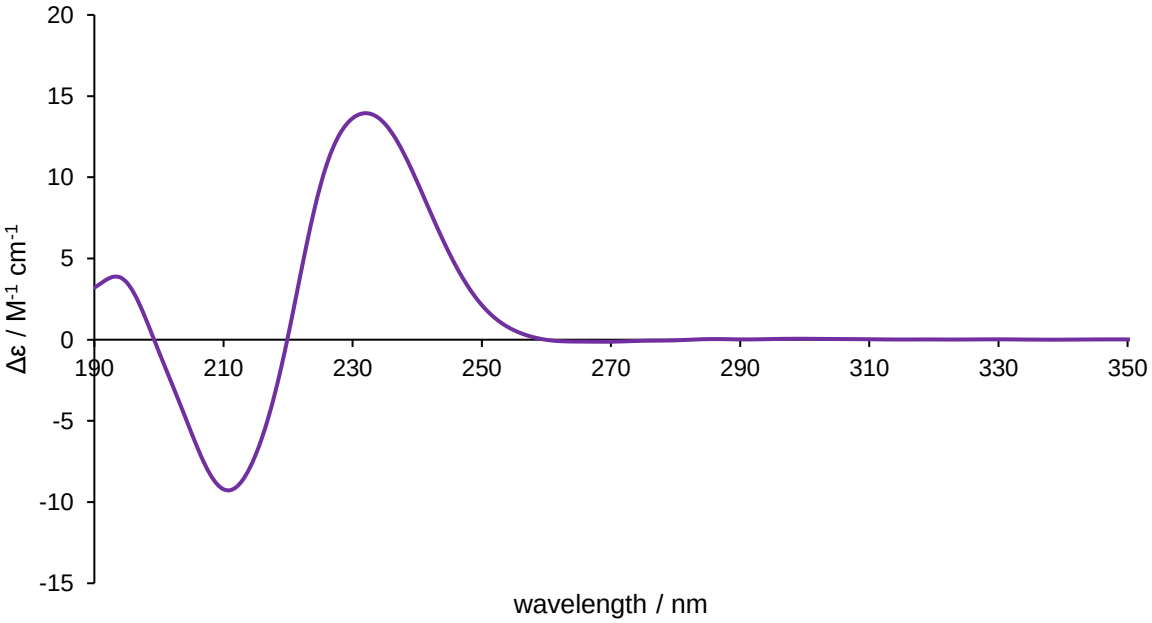


Figure S56: ECD spectrum of compound **5** in MeOH.

(10) Analytical data of compound 6

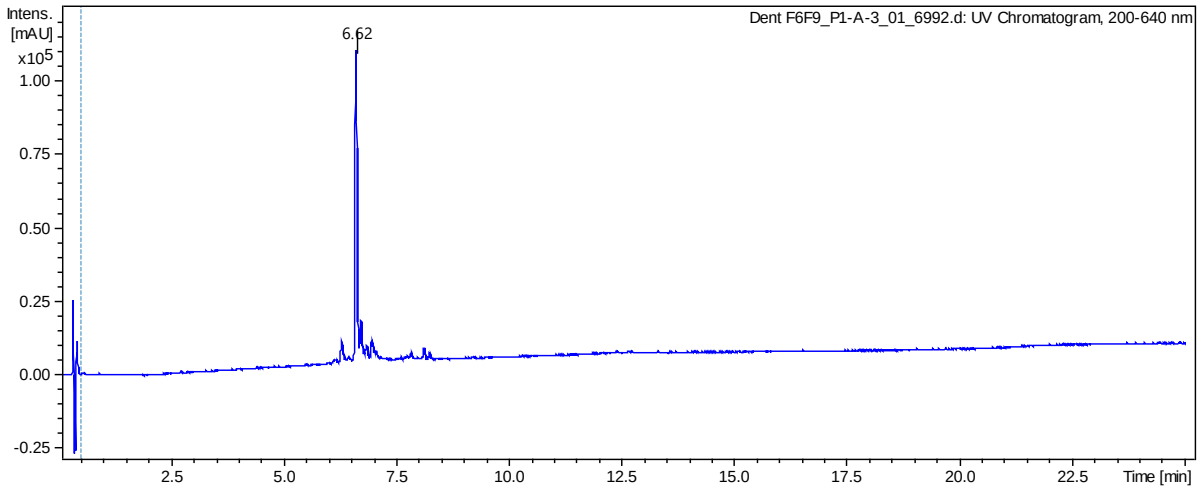


Figure S57: HPLC-DAD chromatogram of compound **6**.

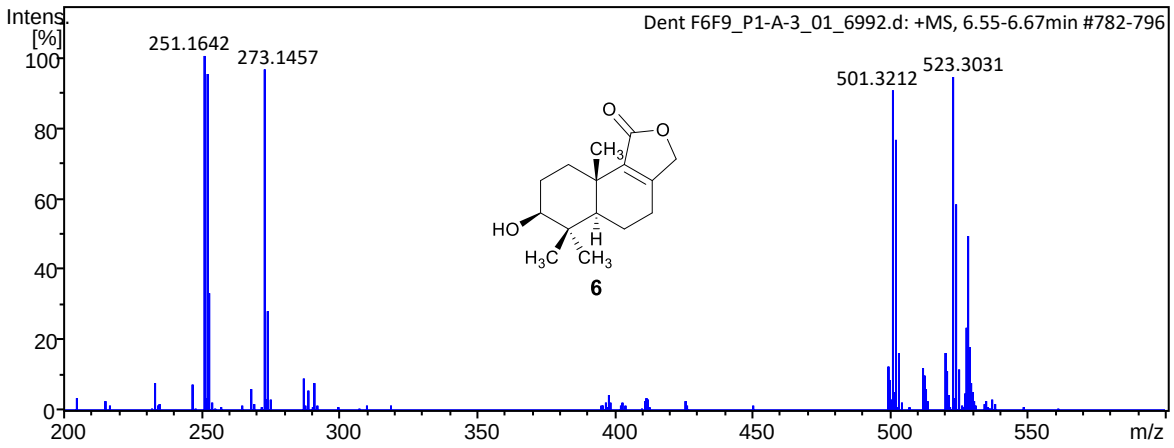
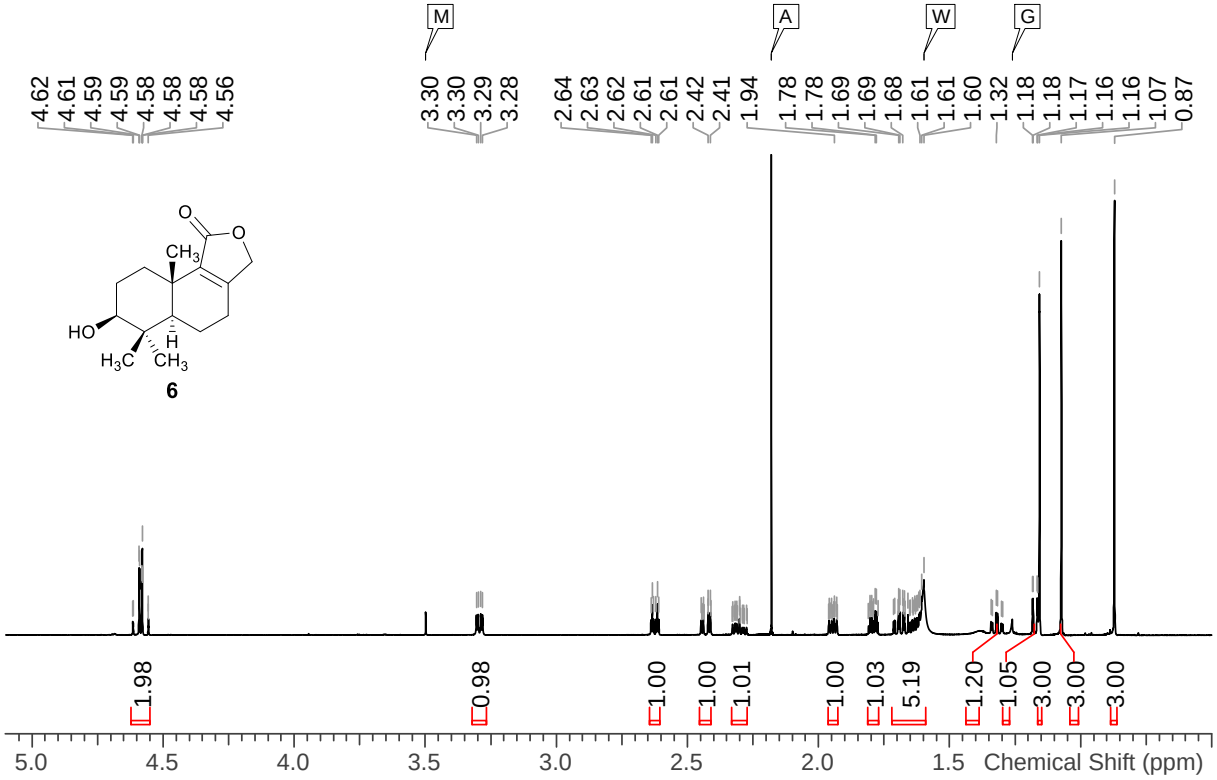
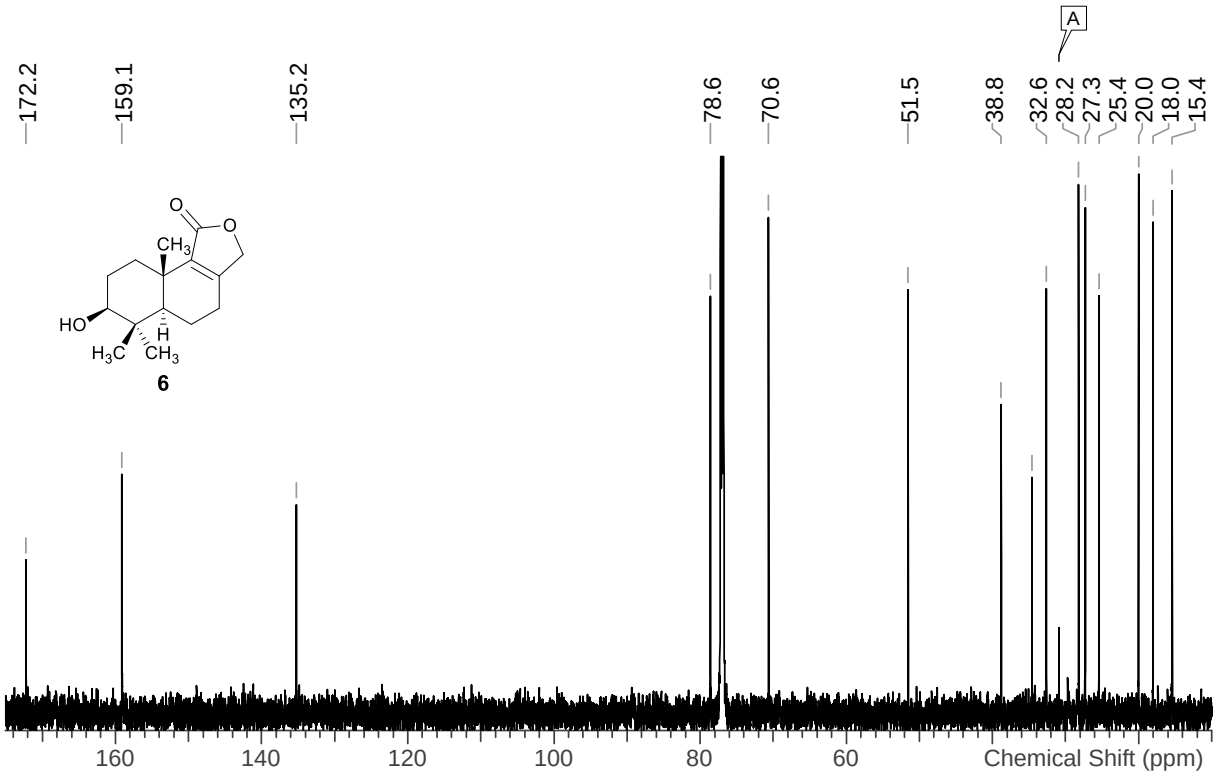


Figure S58: HR-(+)ESIMS spectrum of compound **6**.



6

Figure S59: ^{1}H NMR spectrum (700 MHz, $CDCl_3$, 298 K) of the purified compound **6**. W: H_2O, A: acetone, M: methanol, G: grease.



6

Figure S60: ^{13}C NMR spectrum (175 MHz, $CDCl_3$, 298 K) of the purified compound **6**. A: acetone.

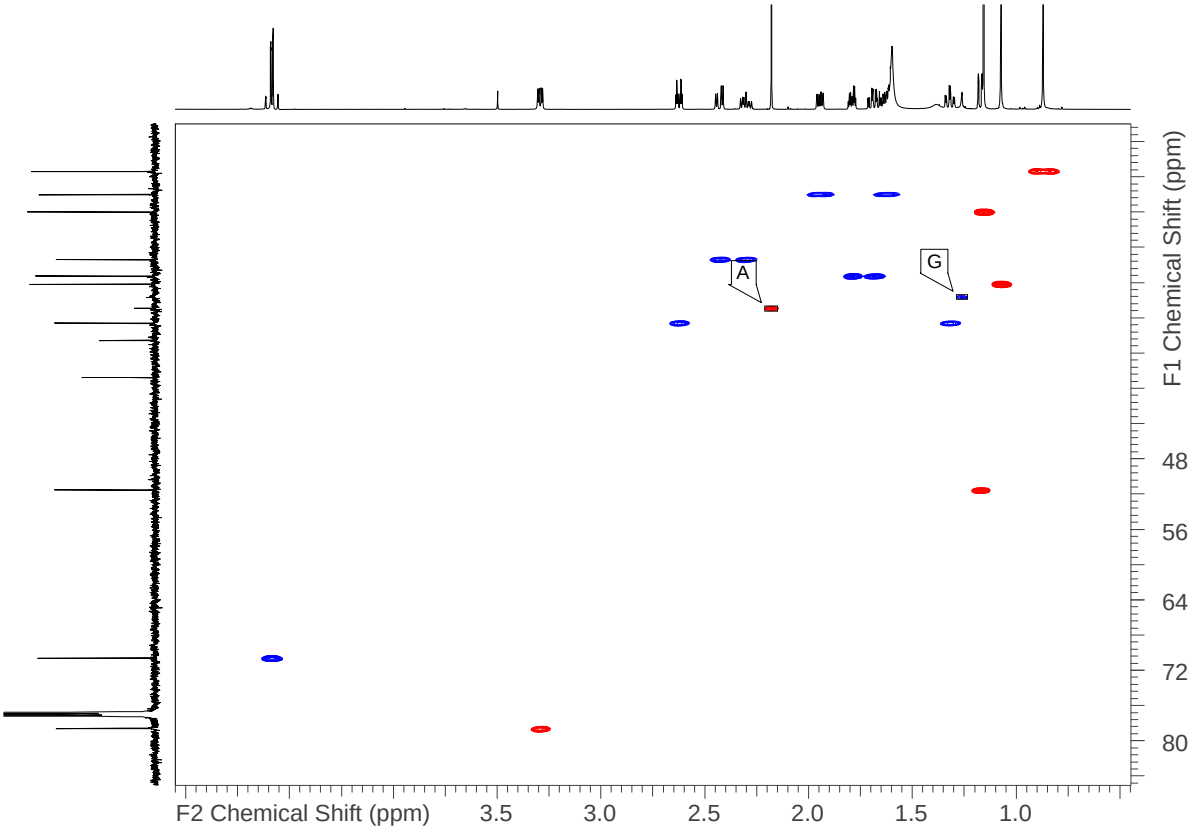


Figure S61: $^{1}H,^{13}C$ DEPT-HSQC spectrum (700 MHz, $CDCl_3$, 298 K) of the purified compound **6**.

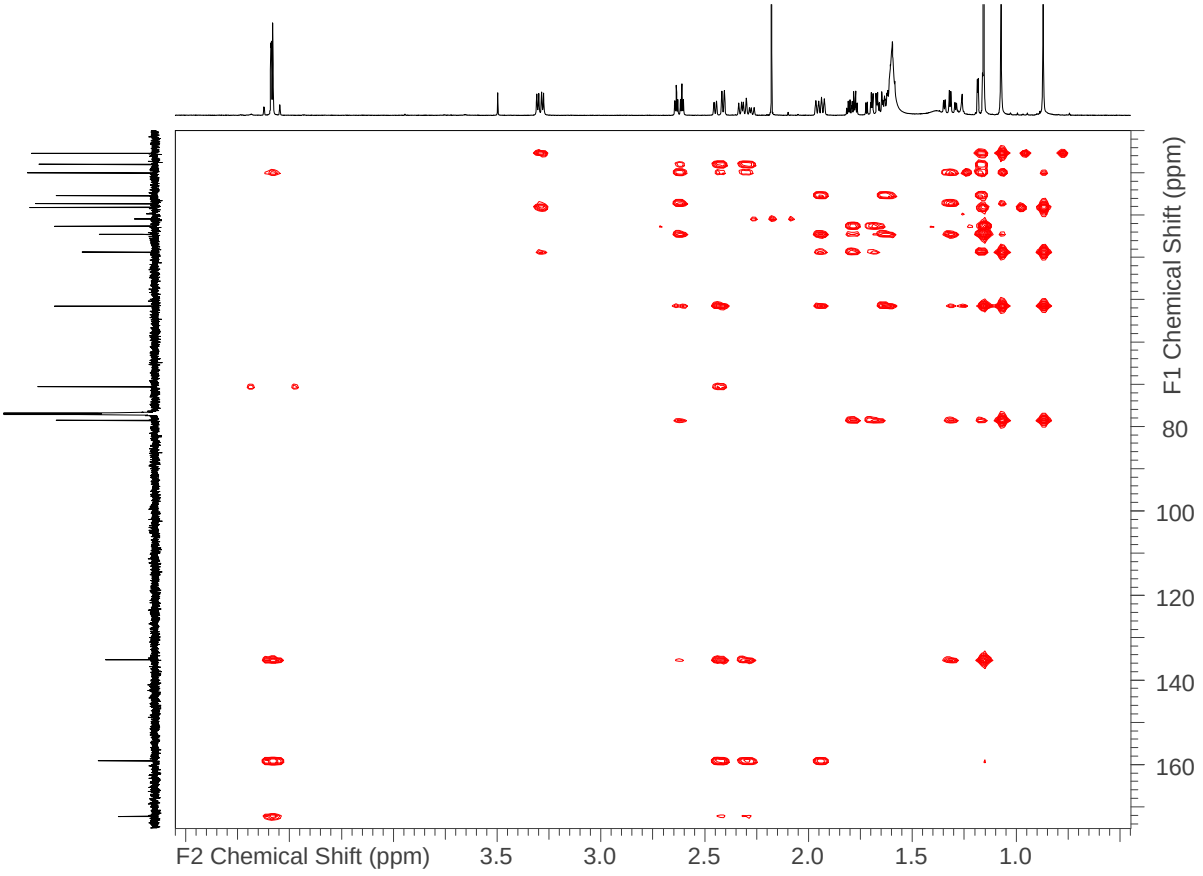


Figure S62: $^{1}H,^{13}C$ HMBC spectrum (700 MHz, $CDCl_3$, 298 K) of the purified compound **6**.

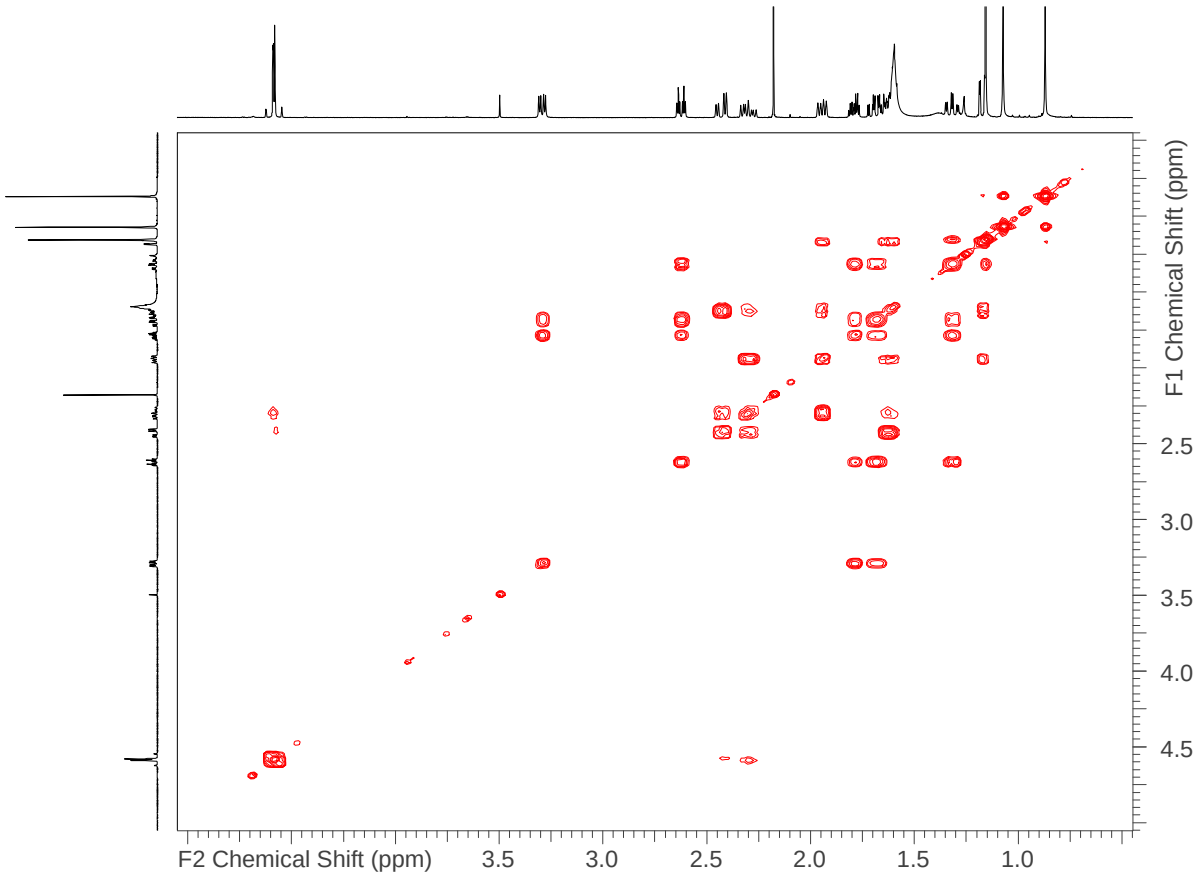


Figure S63: $^{1}H,^{1}H$ COSY spectrum (700 MHz, $CDCl_3$, 298 K) of the purified compound **6**.

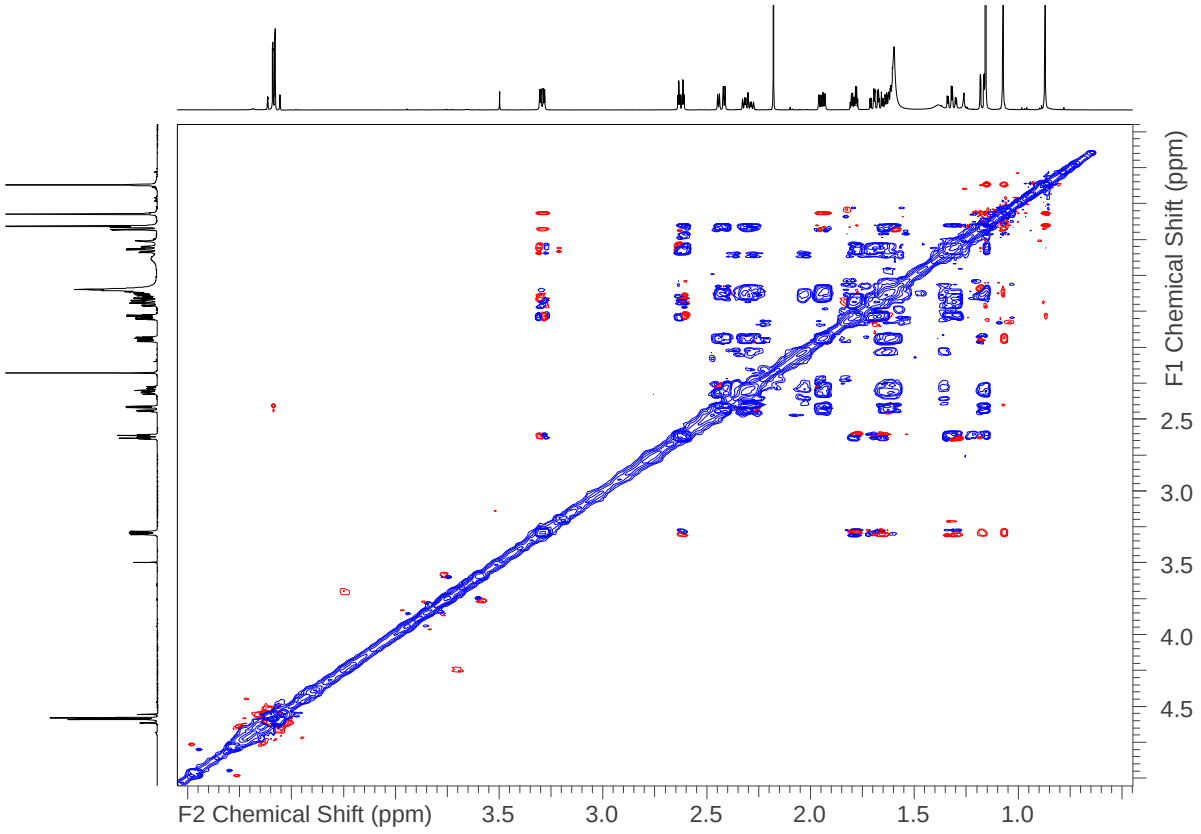


Figure S64: $^{1}H,^{1}H$ ROESY spectrum (500 MHz, $CDCl_3$, 298 K) of the purified compound **6**.

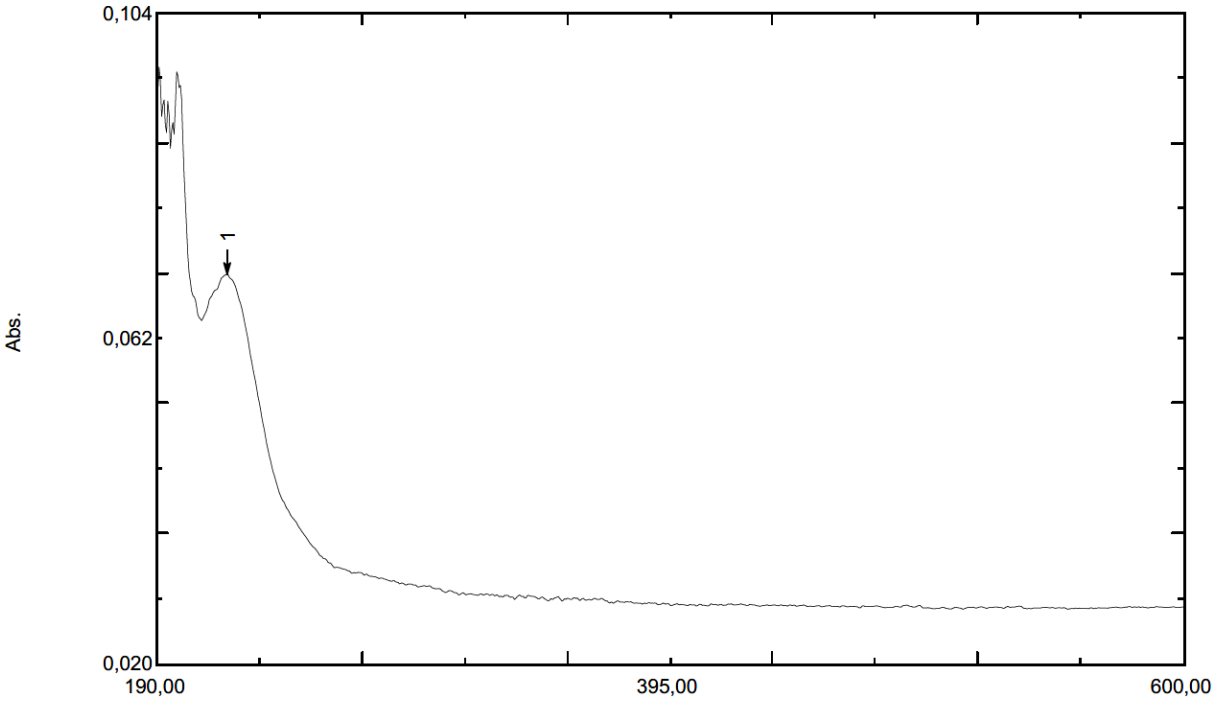


Figure S65: UV/Vis spectrum of compound **6** in MeOH.

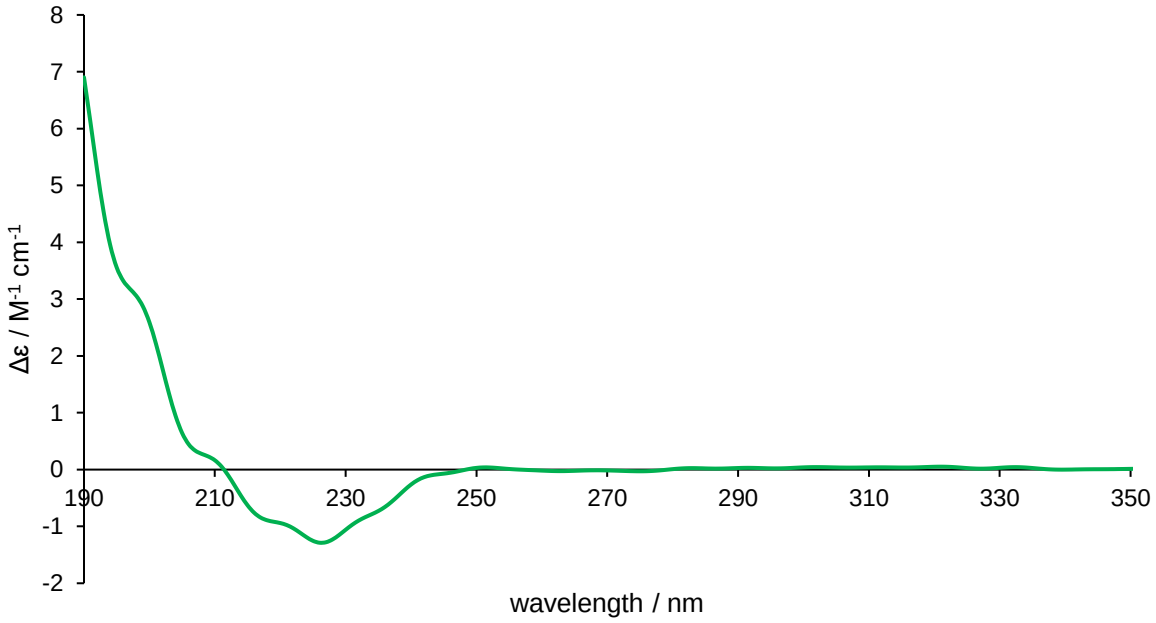


Figure S66: ECD spectrum of compound **6** in MeOH.