Electronic Supplementary Material (ESI) for MedChemComm.

Supplementary information for:

Stereoselective semi-synthesis of the neuroprotective natural product, serofendic acid

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Table S1: Summary of the molecules that have a name that differs from the IUPAC convention

Molecule #	Name in article	IUPAC name
1A	**Serofendic acid A**	***ent*-(15S,16R,S)-15-hydroxy-17-methylsulfinylatisan-19-oic acid**
1B	**Serofendic acid B**	***ent*-(15S,16R,R)-15-hydroxy-17-methylsulfinylatisan-19-oic acid**
S2	**Methyl (15S)-15-hydroxy-*ent*-atis-16-en-19-oate**	**Methyl *ent*-(15R)-15-hydroxyatis-16-en-19-oate**
S3	**Methyl (15S,16R)-15,17-dihydroxy-*ent*-atisan-19-oate**	**Methyl *ent*-(15R,16S)-15,17-dihydroxyatisan-19-oate**
S4	**Methyl (16R)-17-hydroxy-15-oxo-*ent*-atisan-19-oate**	**Methyl *ent*-(16S)-17-hydroxy-15-oxoatisan-19-oate**
3	**Methyl (15R,16R)-15,17-dihydroxy-*ent*-atisan-19-oate**	**Methyl *ent*-(15S,16S)-15,17-dihydroxyatisan-19-oate**
S8	**Methyl (16S)-17-methylsulfenyl-15-oxo-*ent*-atisan-19-oate**	**Methyl *ent*-(16R)-17-methylsulfenyl-15-oxoatisan-19-oate**
S9	**Methyl (16R)-17-methylsulfenyl-15-oxo-*ent*-atisan-19-oate**	**Methyl *ent*-(16S)-17-methylsulfenyl-15-oxoatisan-19-oate**
4	**Methyl (15R,16S)-15-hydroxy-17-methylsulfenyl-*ent*-atisan-19-oate**	**Methyl *ent*-(15S,16R)-15-hydroxy-17-methylsulfenylatisan-19-oate**
S10	**Methyl (15S,16R)-15-hydroxy-17-methylsulfenyl-*ent*-atisan-19-oate**	**Methyl *ent*-(15R,16S)-15-hydroxy-17-methylsulfenylatisan-19-oate**
S11	**Methyl (15S,16S)-15-hydroxy-17-methylsulfenyl-*ent*-atisan-19-oate**	**Methyl *ent*-(15R,16R)-15-hydroxy-17-methylsulfenylatisan-19-oate**
S12	**Methyl (15R,16R)-15-hydroxy-17-methylsulfenyl-*ent*-atisan-19-oate**	**Methyl *ent*-(15S,16S)-15-hydroxy-17-methylsulfenylatisan-19-oate**
7	**(16S)-17-methylsulfenyl-15-oxo-*ent*-atisan-19-oic acid**	***ent*-(16R)-17-methylsulfenyl-15-oxo-atisan-19-oic acid**
8	**(16R)-17-methylsulfenyl-15-oxo-*ent*-atisan-19-oic acid**	***ent*-(16S)-17-methylsulfenyl-15-oxo-atisan-19-oic acid**

9	**(15R,16S)-15-hydroxy-17-methylsulfenyl-*ent*-atisan-19-oic acid**	***ent*-(15S,16R)-15-hydroxy-17-methylsulfenylatisan-19-oic acid**
10	**(15S,16S)-15-hydroxy-17-methylsulfenyl-*ent*-atisan-19-oic acid**	***ent*-(15R,16R)-15-hydroxy-17-methylsulfenylatisan-19-oic acid**
11	**(15S,16R)-15-hydroxy-17-methylsulfenyl-*ent*-atisan-19-oic acid**	***ent*-(15R,16S)-methyl-15-hydroxy-17-methylsulfenylatisan-19-oic acid**
12	**(15R,16R)-15-hydroxy-17-methylsulfenyl-*ent*-atisan-19-oic acid**	***ent*-(15S,16S)-15-hydroxy-17-methylsulfenylatisan-19-oic acid**
13A	**(16S,R)-17-methylsulfinyl-15-oxo-*ent*-atisan-19-oic acid**	***ent*-(16R,S)-17-methylsulfinyl-15-oxo-atisan-19-oic acid**
13B	**(16S,S)-17-methylsulfinyl-15-oxo-*ent*-atisan-19-oic acid**	***ent*-(16R,R)-17-methylsulfinyl-15-oxo-atisan-19-oic acid**
14A	**(16R,R)-17-methylsulfinyl-15-oxo-*ent*-atisan-19-oic acid**	***ent*-(16S,S)-17-methylsulfinyl-15-oxo-atisan-19-oic acid**
14B	**(16R,S)-17-methylsulfinyl-15-oxo-*ent*-atisan-19-oic acid**	***ent*-(16S,R)-17-methylsulfinyl-15-oxo-atisan-19-oic acid**
15A	**(15S,16S,R)-15-hydroxy-17-methylsulfinyl-*ent*-atisan-19-oic acid**	***ent*-(15R,16R,S)-15-hydroxy-17-methylsulfinylatisan-19-oic acid**
15B	**(15S,16S,S)-15-hydroxy-17-methylsulfinyl-*ent*-atisan-19-oic acid**	***ent*-(15R,16R,R)-15-hydroxy-17-methylsulfinylatisan-19-oic acid**
16A	**(15R,16R,R)-15-hydroxy-17-methylsulfinyl-*ent*-atisan-19-oic acid**	***ent*-(15S,16S,S)-15-hydroxy-17-methylsulfinylatisan-19-oic acid**
16B	**(15R,16R,S)-15-hydroxy-17-methylsulfinyl-*ent*-atisan-19-oic acid**	***ent*-(15S,16S,R)-15-hydroxy-17-methylsulfinylatisan-19-oic acid**
17A	**(15S,16R,R)-15-hydroxy-17-methylsulfinyl-*ent*-atisan-19-oic acid**	***ent*-(15R,16S,S)-15-hydroxy-17-methylsulfinylatisan-19-oic acid**
17B	**(15S,16R,S)-15-hydroxy-17-methylsulfinyl-*ent*-atisan-19-oic acid**	***ent*-(15R,16S,R)-15-hydroxy-17-methylsulfinylatisan-19-oic acid**

Material and Methods

All chemicals and reagents were purchased from commercial sources and used directly without further purification. All non-aqueous reactions were performed under an atmosphere of argon in flame-dried glassware. Reaction progress was monitored by thin-layer chromatography (TLC) using silica gel plates (silica gel 60 F254). Eluted TLC plates were visualized with UV light (254 nm) and dyed using ethanol acidified with sulfuric acid (5% v/v). Compounds were purified either by flash silica gel (230-400 mesh) column chromatography or by Büchi C-700 chromatograph apparatus with 4 g or 25 g Büchi FlashPure EcoFlex cartridges. NMR experiments were performed on Bruker Advance III 500 MHz (Broadband Observe SmartProbe) or Bruker Advance 700 MHz (5-mm triple resonance cryoprobe) spectrometers. Chemical shifts were reported as ppm relative to either chloroform-d (7.26 ppm for ^{1}H, 77.16 ppm for ^{13}C) or methanol-d$_4$ (3.31 ppm for ^{1}H and 49.00 ppm for ^{13}C). ^{1}H constant coupling (*J*) are expressed in hertz (Hz), and multiplicity is described as follows: s = singlet, d = doublet, d$_{app}$ = appearing doublet, t = triplet, br = broad, m = multiplet. Compounds were analyzed by HR-ESI-MS (ThermoScientific, Q Exactive, Quadrupole, Orbitrap, Heated-Electrospray Ionization probe source (HESI-II)).

Trace elements solution preparation

A mixture of zinc (II) chloride (40 mg), iron (III) chloride hexahydrate (200 mg), copper (II) chloride dihydrate (10 mg), manganese (II) chloride tetrahydrate (10 mg), sodium tetraborate decahydrate (10 mg) and ammonium molybdate tetrahydrate (10 mg) were dissolved in Milli-Q water (up to 1L). The solution was autoclaved at 120°C for 30 min.

R2YE medium preparation

A first solution was prepared. For that, a mixture of sucrose (103 g), potassium sulfate (0.25 g), magnesium chloride hexahydrate (10.12 g), glucose (10 g), casamino acids (0.1 g), yeast extract (5 g) and TES buffer (5.73 g) were diluted in Milli-Q water (up to 950 mL). This solution was autoclaved at 120°C for 30 min.

To 4.75 mL of this sterile solution, once cooled down to room temperature, were added trace elements solution (10 µL), sodium hydroxide 1 M (25 µL), a solution of monopotassium phosphate 0.5% (m/v) (50 µL), a solution of proline 20% (m/v) (75 µL) and calcium chloride 1M (100 µL).

ISM3 medium preparation

A mixture of yeast extract (7.5 g), malt extract (5 g), magnesium sulfate heptahydrate (0.5 g), iron (III) chloride hexahydrate (0.15g) and glucose (10 g) were dissolved in Milli-Q water (up to 500 mL). The mixture was autoclaved at 120°C for 30 min.

Synthesis of 15-hydroxy-17-methylsulfenyl-*ent*-atisan-19-oic acids (9-12) using different reducing reagents

Procedure for sodium borohydride (Hsu, et al.)

The synthesis of **9**-**12** was performed as reported in literature (Hsu, et al., in revision). Briefly, to a solution of sodium borohydride (185.2 mg, 4.90 mmol) in ethanol (200 proof, 15 mL) cooled down to 0° C was added dropwise an epimeric mixture of **7** and **8** (178.5 mg, 0.49 mmol) in ethanol (200 proof, 5.0 mL). After 25 min of stirring at 0° C, hydrochloric acid 1M was added to mixture until the bubbling stop. The solution was then evaporated and the residue was dissolved in ethyl acetate (20 mL), washed with brine (10 mL), dried over anhydrous magnesium sulfate and concentrated. Column chromatography using an *n*-hexane to *n*-hexane/ethyl acetate (7:3 v/v) gradient allowed the isolation of a mixture composed of **9** and **10**, **11** (19.5 mg, white powder, 11%) and **12** (69.8 mg, white powder, 39%). Semi preparative HPLC purification on the latter mixture using the gradient 0 – 1 min, 95 % solvent A; 1 – 3 min, 95% solvent B; 3 – 7 min, 95% solvent B; 7 – 9 min, 95% solvent A; 9 – 18 min, 95% solvent A, allowed the separation of **9** (17.8 mg, white powder, 10%) from **10** (53.0 mg, white powder, 30%). For ^{1}H and ^{13}C NMR data of **9**-**12**, see **Supplementary Fig. S28-39**. HRESIMS: *m/z* calculated for $C_{21}H_{29}O_{3}S^{-}$ $[M-H]^{-}$ 365.2156 (100%), $[M+2-H]^{-}$ 367.2114 (4%), **9**: found 365.2155 (100%), 367.2113 (4%), **10:** found 365.2155 (100%), 367.2113 (4%), **11**: found 365.2155 (100%), 367.2113 (4%), **12:** found 365.2155 (100%), 367.2113 (4%).

Procedure for borane-THF complex in THF 1 M, L-selectride in THF 1M and disiamylborane in THF 0.5 M

To an epimeric mixture of sulfides **7** and **8** (2.0 mg, 5.5 µmol) in THF (50 µL) cooled down to 0°C was added a solution of reducing reagent (10 eq, 54.9 µmol). The reaction medium was stirring at 0°C for 1 h. The medium was then quenched with the addition of methanol (40 µL) followed by a solution of HCl 10% (20 µL). 10 µL of medium was collected, diluted with methanol (up to 1 mL) and then injected in LCMS for analysis.

Procedure for sodium triacetoxyborohydride with acetic acid [1,2]

To a solution of sodium triacetoxyborohydride (5.8 mg, 27.4 µmol) in acetonitrile (800 µL) was added acetic acid (2.0 µL, 54.9 µmol). The mixture was cooled down to 0°C and then an epimeric mixture of sulfides **7** and **8** (2.0 mg, 5.5 µmol) in acetonitrile (800 µL) was added. The mixture was stirred at 0°C for 4 h and then was quenched by adding methanol (40 µL) and a solution of HCl 10% (20 µL). 10 µL of medium was collected, diluted with methanol (up to 1 mL) and then injected in LCMS for analysis.

Procedure for sodium triacetoxyborohydride without acetic acid

To a solution of sodium triacetoxyborohydride (5.8 mg, 27.4 µL, 5eq. or 11.6 mg, 54.9 µmol, 10 eq.) cooled down to 0°C an epimeric mixture of sulfides **7** and **8** (2.0 mg, 5.5 µmol) in acetonitrile (800 µL) was added. The mixture was stirred at 0°C for 4 h and then was quenched by adding methanol (40 µL) and a solution of HCl 10% (20 µL). 10 µL of medium was collected, diluted with methanol (up to 1 mL) and then injected in LCMS for analysis.

Procedure for pinacolborane activated by alkoxide

To a solution of pinacolborane (7.0 mg, 54.9 µmol) in THF (100 µL) was added a solution of potassium *tert*-butoxide (6.2 mg, 54.9 µmol) in THF (100 µL). After stirring at room temperature for 10 min, an epimeric mixture of sulfides **7** and **8** (4.0 mg, 11.0 µmol) in solution in THF (100 µL) was added to the medium. The reaction medium was stirred at room temperature for 24 h. The medium was then quenched with the addition of methanol (40 µL) followed by a solution of HCl 10% (20 µL). The mixture was concentrated and then diluted in a mixture of ethyl acetate and water. Once the layers separated, the organic phase was dried out. The residue was dissolved in chloroform-d for ^{1}H NMR analysis.

Procedure for pinacolborane activated by alkoxide with cerium

To a solution of pinacolborane (7.0 mg, 54.9 µmol) in THF (50 µL) were added a solution of potassium *tert*-butoxide (6.2 mg, 54.9 µmol) in THF (100 µL) and a solution of cerium (III) chloride (1.4 mg, 5.49 µmol) in THF (50 µL). After stirring at room temperature for 10 min, an epimeric mixture of sulfides **7** and **8** (4.0 mg, 11.0 µmol) in solution in THF (100 µL) was added to the medium. The reaction medium was stirred at room temperature for 24 h. The medium was then quenched with the addition of methanol (40 µL) followed by a solution of HCl 10% (20 µL). The mixture was concentrated and then diluted in a mixture of ethyl acetate and water. Once the layers separated, the organic phase was dried out. The residue was dissolved in chloroform-d for ^{1}H NMR analysis.

Procedure for (+) and (-)-2-methyl-CBS-oxazoboroline with borane in THF

To a solution of CBS reagent (15.2 mg, 54.9 µmol) in THF (150 µL) was added a solution of borane-THF complex (1 M, 54.9 µmol). After stirring at room temperature for 10 min, an epimeric mixture of sulfides **7** and **8** (4.0 mg, 11.0 µmol) in solution in THF (150 µL) was added to the medium. The reaction medium was stirred at room temperature for 24 h. The medium was then quenched with the addition of methanol (40 µL) followed by a solution of HCl 10% (20 µL). The mixture was concentrated and then diluted in a mixture of ethyl acetate and water. Once the layers separated, the organic phase was dried out. The residue was dissolved in chloroform-d for ^{1}H NMR analysis.

Synthesis of 15-hydroxy-17-methylsulfinyl-*ent*-atisan-19-oic acids (1, 15-17) using different reducing reagents

Procedure for neutral reducing reagents (diisobutylaluminum hydride, pinacolborane, borane in tetrahydrofuran)

To a solution of **13** and **14** (2.0 mg, 5.26 µmol) in THF (300 µL) cooled down to 0°C was added reducing reagent (5 eq.). The reaction was stirred at cold temperature for 1h. The reaction was quenched by adding methanol (40 µL) and a solution of HCl 10% (20 µL). The mixture was concentrated and then diluted in a mixture of ethyl acetate and water. Once the layers separated, the organic phase was dried out. The residue was dissolved in methanol-d_4 for ^{1}H NMR analysis. For ^{1}H and ^{13}C NMR data of **1**, **15** and **16**, see **Supplementary Fig. S50-68.**

Procedure for neutral reducing reagents (pinacolborane, borane in tetrahydrofuran) with Lewis acid (cerium chloride)

To a solution of **13** and **14** (4.0 mg, 10.5 µmol) in THF (300 µL) was added a solution of Lewis acid (1.1 eq.) in THF (300 µL) and stirred at room temperature for 1 h. After, the mixture was cooled down to 0°C and reducing reagent (5 eq.) was added. The reaction was stirred at cold temperature for 1h. The reaction was quenched by adding methanol (80 µL) and a solution of HCl 10% (40 µL). The mixture was concentrated and then diluted in a mixture of ethyl acetate and water. Once the layers separated, the organic phase was dried out. The residue was dissolved in methanol-d_4 for ^{1}H NMR analysis.

Procedure for ionic reducing reagents (sodium borohydride)

To a solution of **13** and **14** (4.0 mg, 10.5 µmol) in 200 proof ethanol (300 µL) cooled down to 0°C was added a solution of sodium borohydride (4.0 mg, 105.1 µmol) in 200 proof ethanol (300 µL). The reaction was stirred at cold temperature for 45 min. The reaction was quenched by adding methanol (80 µL) and a solution of HCl 10% (80 µL). The mixture was concentrated and then diluted in a mixture of ethyl acetate and water. Once the layers separated, the organic phase was dried out. The residue was dissolved in methanol-d_4 for ^{1}H NMR analysis.

Procedure for ionic reducing reagents (sodium borohydride) with Lewis acid (cerium chloride)

To a solution of **13** and **14** (4.0 mg, 10.5 µmol) in 200 proof ethanol (300 µL) was added a solution of cerium chloride (2.9 mg, 11.6 µmol) in 200 proof ethanol (150 µL) and stirred at room temperature for 1 h. After, the mixture was cooled down to 0°C and sodium borohydride was added (4.0 mg, 105.1 µmol). The reaction was stirred at cold temperature for 45 min. The reaction was quenched by adding methanol (80 µL) and a solution of HCl 10% (40 µL). The mixture was concentrated and then diluted in a mixture of ethyl acetate and water. Once the layers separated, the organic phase was dried out. The residue was dissolved in methanol-d_4 for ^{1}H NMR analysis.

Fig. S1

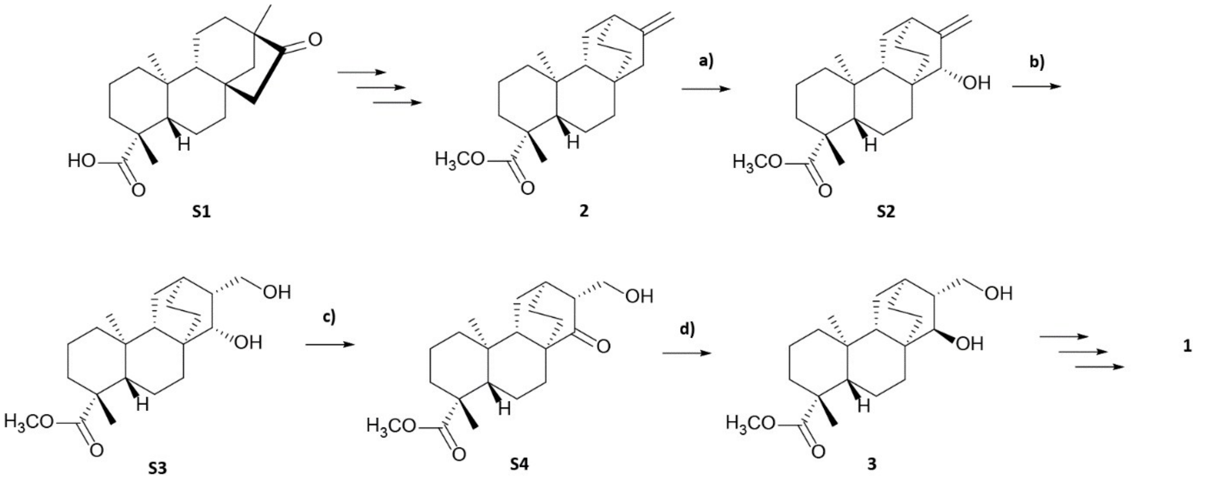


Fig. S1. Chemical synthesis of serofendic acids **1** from (-)-isosteviol **S1** from Terauchi et al.[1,2] Reagents and conditions: **S1** to **2**, 8 steps, 13.4%; a) SeO_2, ^tBuOOH, CH_2Cl_2, r.t., 15 h, 28%; b) i. BH_3-THF, THF, r.t., 4 h, ii. NaOH aq., H_2O_2 aq., r.t., 2 h, 91%; c) $NaBrO_3$, $NaHSO_3$, CH_3CN, H_2O, r.t., 3 h, 80%; d) $NaB(OAc)_3H$, AcOH, CH_3CN, rt, 4 h, 73%; **3** to **1**, 3 steps, 50.9%.

Fig. S2

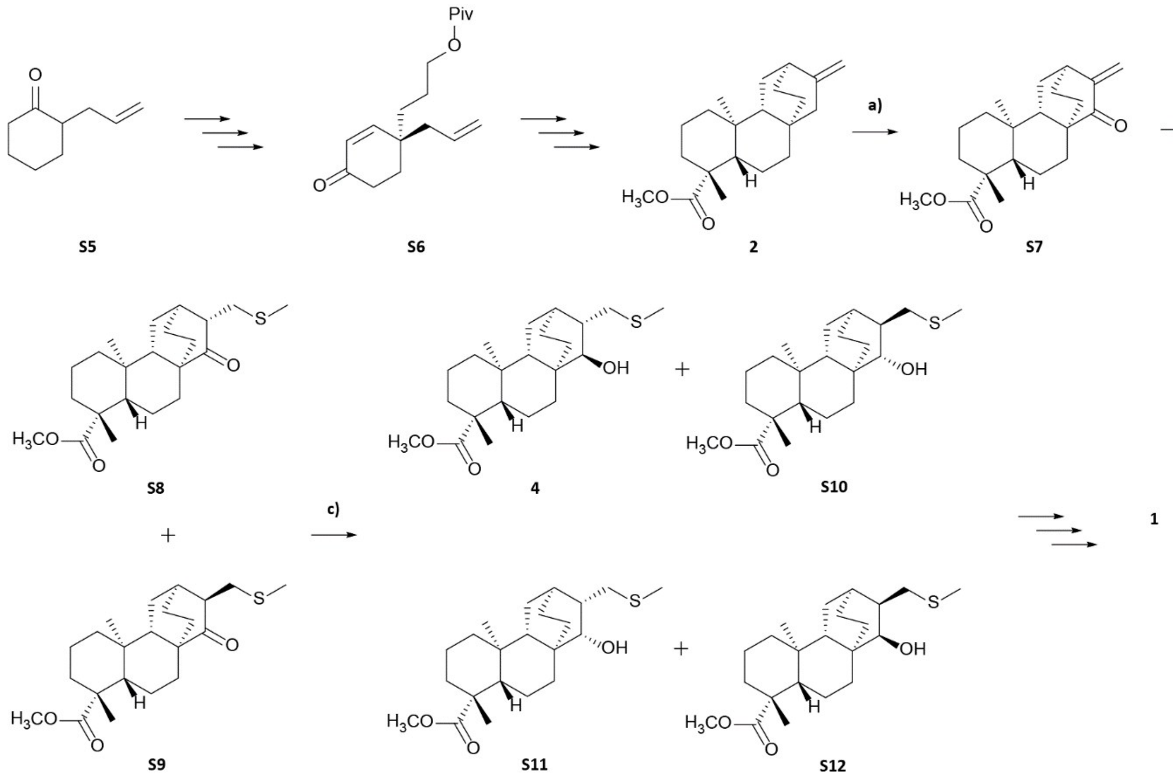


Fig. S2. Chemical synthesis of serofendic acids **1** from 2-allylcyclohexanone **S5** from Toyota, et al.[3,4] Reagents and conditions: **S5** to **S6**, 4 steps, 33.9%;[3] **S6** to **2**, 8 steps, 15.4%; a) $(PhSeO)_2O$, benzene, reflux, 4 h, 80%; b) NaSMe aq., THF, r.t., 1 h; c) BH_3-THF, THF, 0°C; 1 h, 27% **4**, 27% **S10**, 18% **S11**, 18% **S12**; **4** to **1**, 2 steps, 80%.[4]

Fig. S3

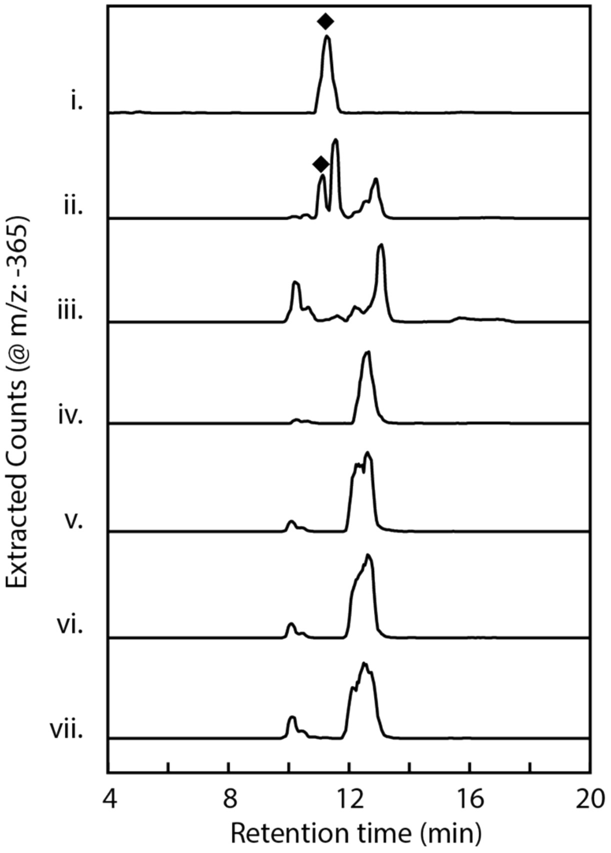


Fig. S3. LC-MS analysis of the reaction between an epimeric mixture of 17-methylsulfenyl-15-oxo-*ent*-atisan-19-oic acid **7** and **8** and different reducing reagents and different experimental conditions. Y-axis: i. (15R,16S)-15-hydroxy-17-methylsulfenyl-*ent*-atisan-19-oic acid **9** standard; ii. $NaBH_4$, EtOH, 0°C; iii. L-selectride, THF, 0°C; iv. $NaBH(OAc)_3$ (5 eq.), AcOH, CH_3CN, 0°C; v. $NaBH(OAc)_3$ (5 eq.), CH_3CN, 0°C; vi. $NaBH(OAc)_3$ (10 eq.), CH3CN, 0°C; vii. Disiamylborane, THF, 0°C.

Fig. S4

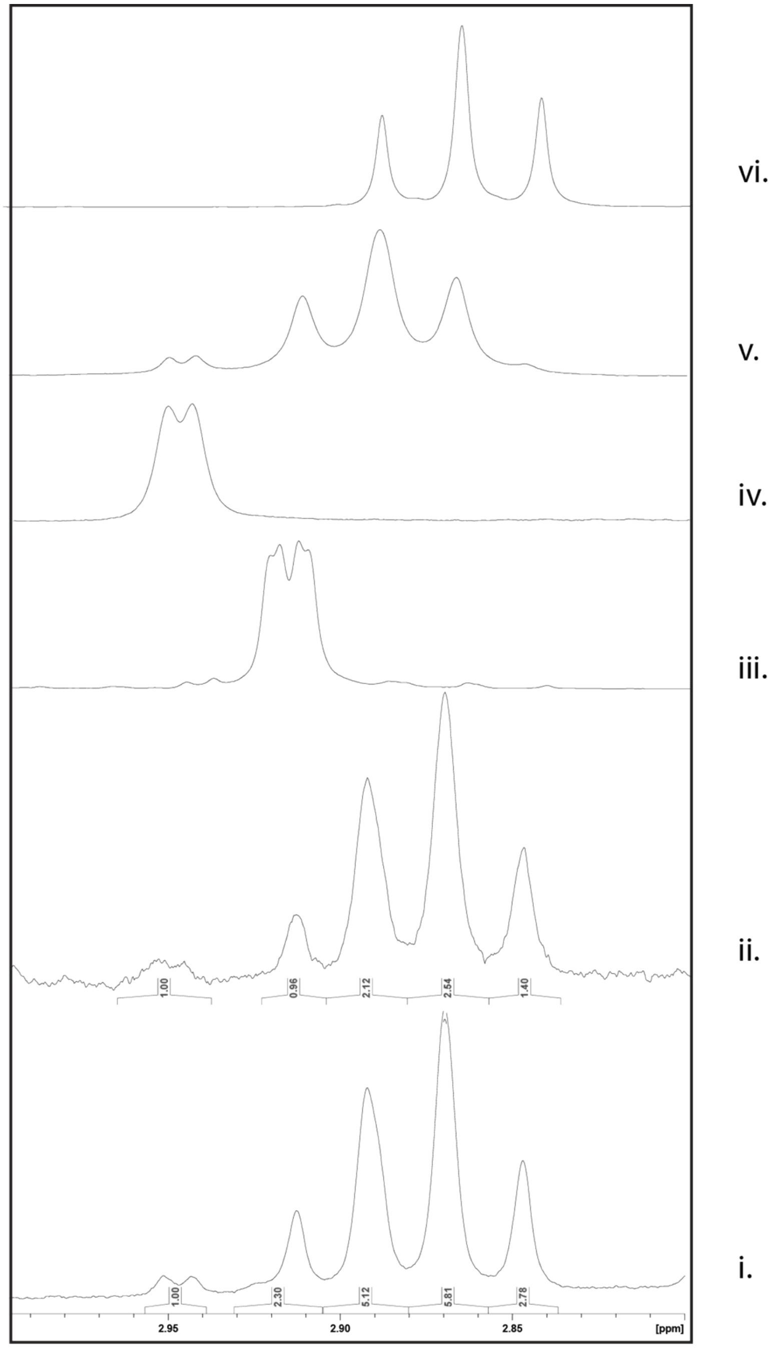


Fig. S4. ^{1}H NMR analysis chloroform-d of the reaction between 17-methylsulfenyl-15-oxo-*ent*-atisan-19-oic acids **7** and **8** and activated pinacolborane in the presence or not of cerium (III) chloride. i. Reaction of **7** and **8** with activated HBpin; ii. Reaction of **7** and **8** with activated HBpin plus $CeCl_3$; iii.-vi. 15-hydroxy-17-methylsulfenyl-*ent*-atisan-19-oic acids standards (iii. **9**; iv. **10**, v. **11**, vi. **12**).

Fig. S5

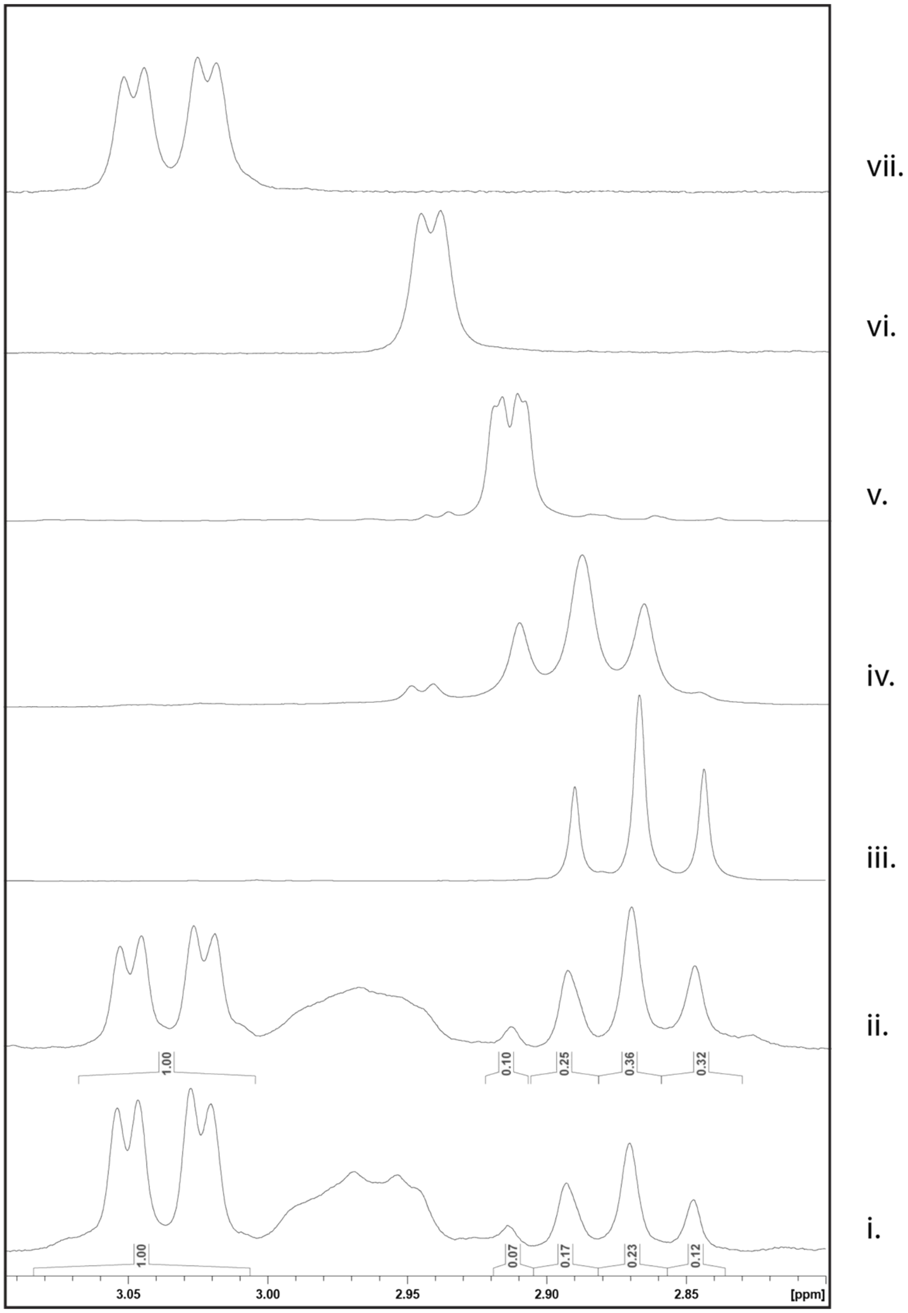


Fig. S5. ^{1}H NMR analysis in chloroform-d of the reaction between 17-methylsulfenyl-15-oxo-*ent*-atisan-19-oic acids **7** and **8** and 2-methyl-CBS-oxazaborolidines. i. Reaction of **7** and **8** with (+)-2- methyl-CBS-oxazaborolidine; ii. Reaction of **7** and **8** with (-)-2- methyl-CBS-oxazaborolidine; iii.-vi. 15-hydroxy-17-methylsulfenyl-*ent*-atisan-19-oic acids standards (iii. **12**; iv. **10**, v. **11**, vi. **9**); vii. **7** and **8**.

Fig. S6

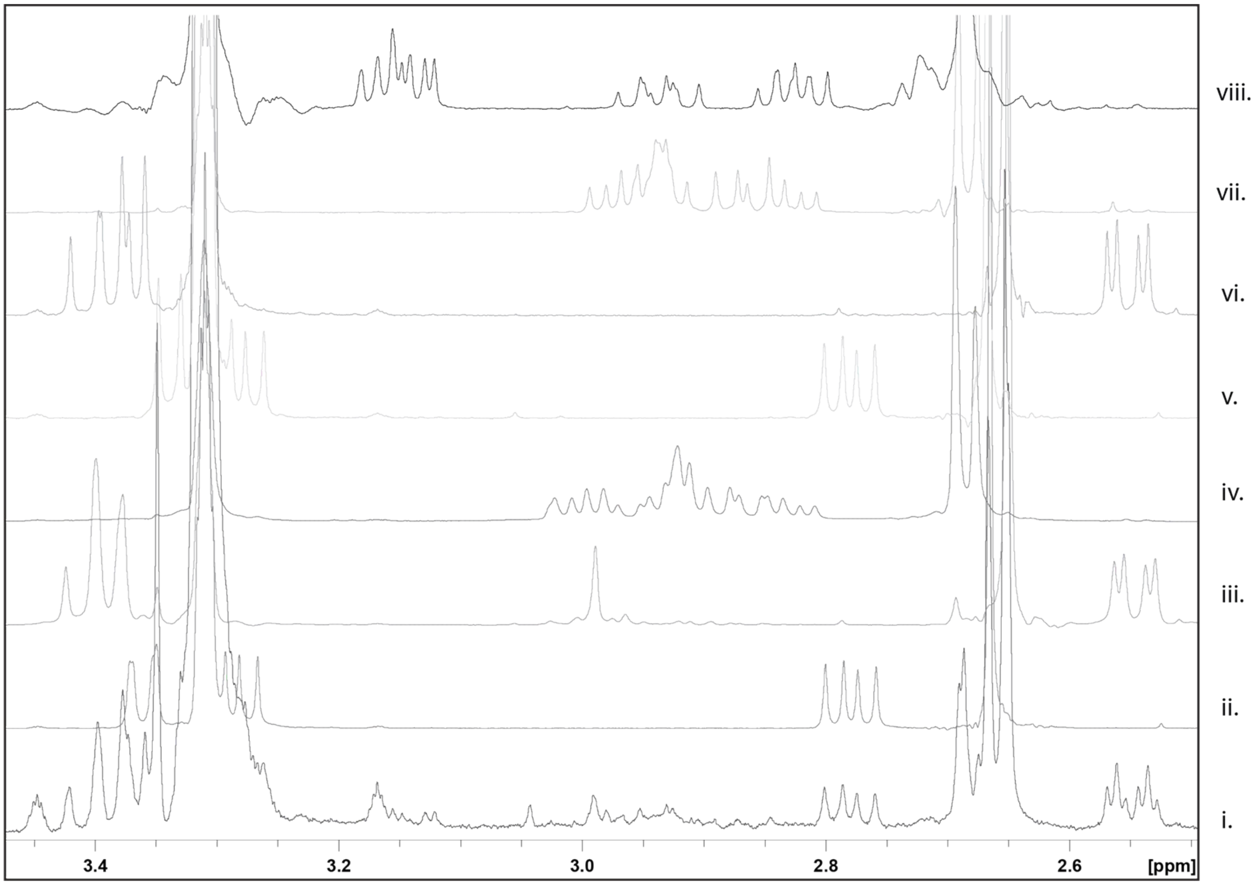


Fig. S6. ^{1}H NMR analysis in methanol-d$_4$ of the reaction between 17-methylsulfinyl-15-oxo-*ent*-atisan-19-oic acids **13** and **14** and DiBAl-H. i. Reaction of **13** and **14** with DiBAl-H; ii.-vii. 15-hydroxy-17-methylsulfinyl-*ent*-atisan-19-oic acid standards (ii. **15B**; iii. **15A**; iv. mixture of **1A** and **1B**; v. **16B**; vi. **16A**; vii. mixture of **17A** and **17B**); viii. **13** and **14**.

Fig. S7

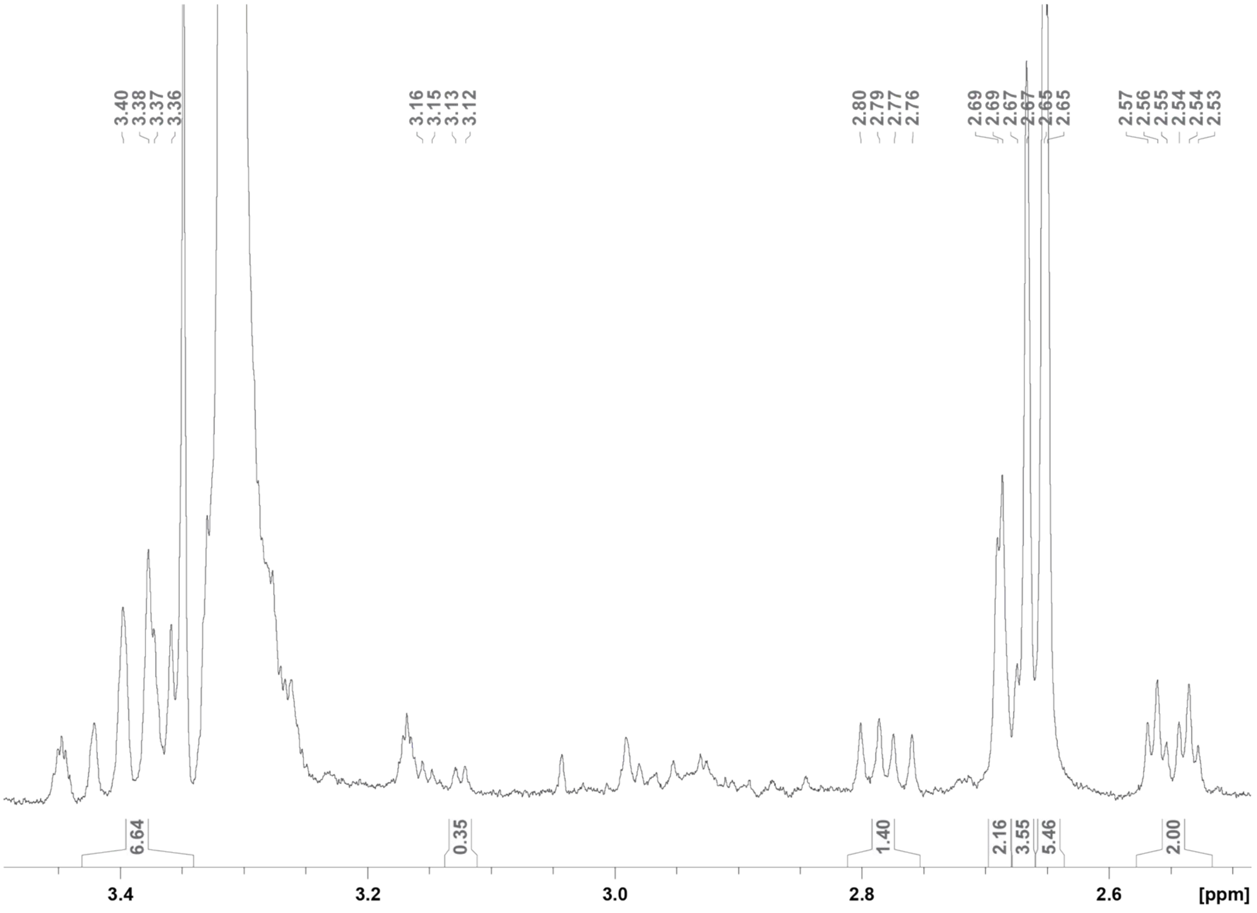


Fig. S7. ^{1}H NMR spectrum in methanol-d$_4$ of the reaction between 17-methylsulfinyl-15-oxo-*ent*-atisan-19-oic acids **13** and **14** and DiBAl-H. The molar ratio between the reactants and the products was determined by using the integration of the peaks corresponding to the methylsulfoxide group (chemical shifts: 2.654 ppm = *cis* **15A** and **16A**; 2.668 ppm = *cis* **15B** and **16B**; 2.676 ppm = *trans* **1A** and **17A**, 2.685 ppm = **13** and **14**and 2.692 ppm = *trans* **1B** and **17B**) of the different compounds in the sample. Assuming that all the starting material would be converted into products, we used the following formulas:

$$\%\ of\ cis\ = 100 * \frac{integration\ of\ all\ cis\ methylsulfoxide\ peaks}{integration\ of\ all\ methylsulfoxide\ peaks}$$

$$\%\ of\ trans\ = 100 * \frac{integration\ of\ all\ trans\ methylsulfoxide\ peaks}{integration\ of\ all\ methylsulfoxide\ peaks}$$

$$\%\ of\ starting\ material = 100 * \frac{integration\ of\ starting\ material\ methylsulfoxide\ peak}{integration\ of\ all\ methylsulfoxide\ peaks}$$

Fig. S8

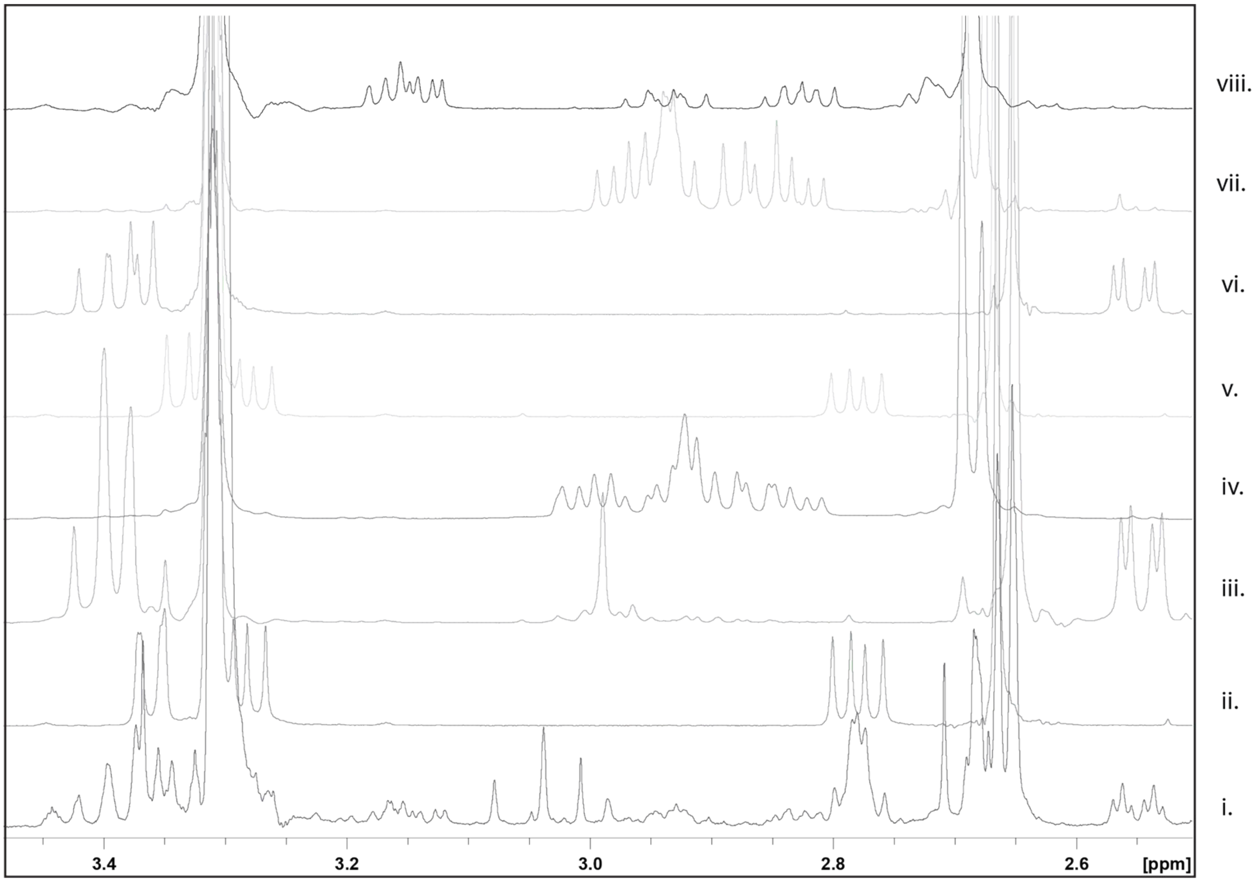


Fig. S8. ^{1}H NMR analysis in methanol-d$_4$ of the reaction between 17-methylsulfinyl-15-oxo-*ent*-atisan-19-oic acids **13** and **14** and DiBAl-H/CeCl$_3$. i. Reaction of **13** and **14** with DiBAl-H/CeCl$_3$; ii.-vii. 15-hydroxy-17-methylsulfinyl-*ent*-atisan-19-oic acid standards (ii. **15B**; iii. **15A**; iv. mixture of **1A** and **1B**; v. **16B**; vi. **16A**; vii. mixture of **17A** and **17B**); viii. **13** and **14**.

Fig. S9

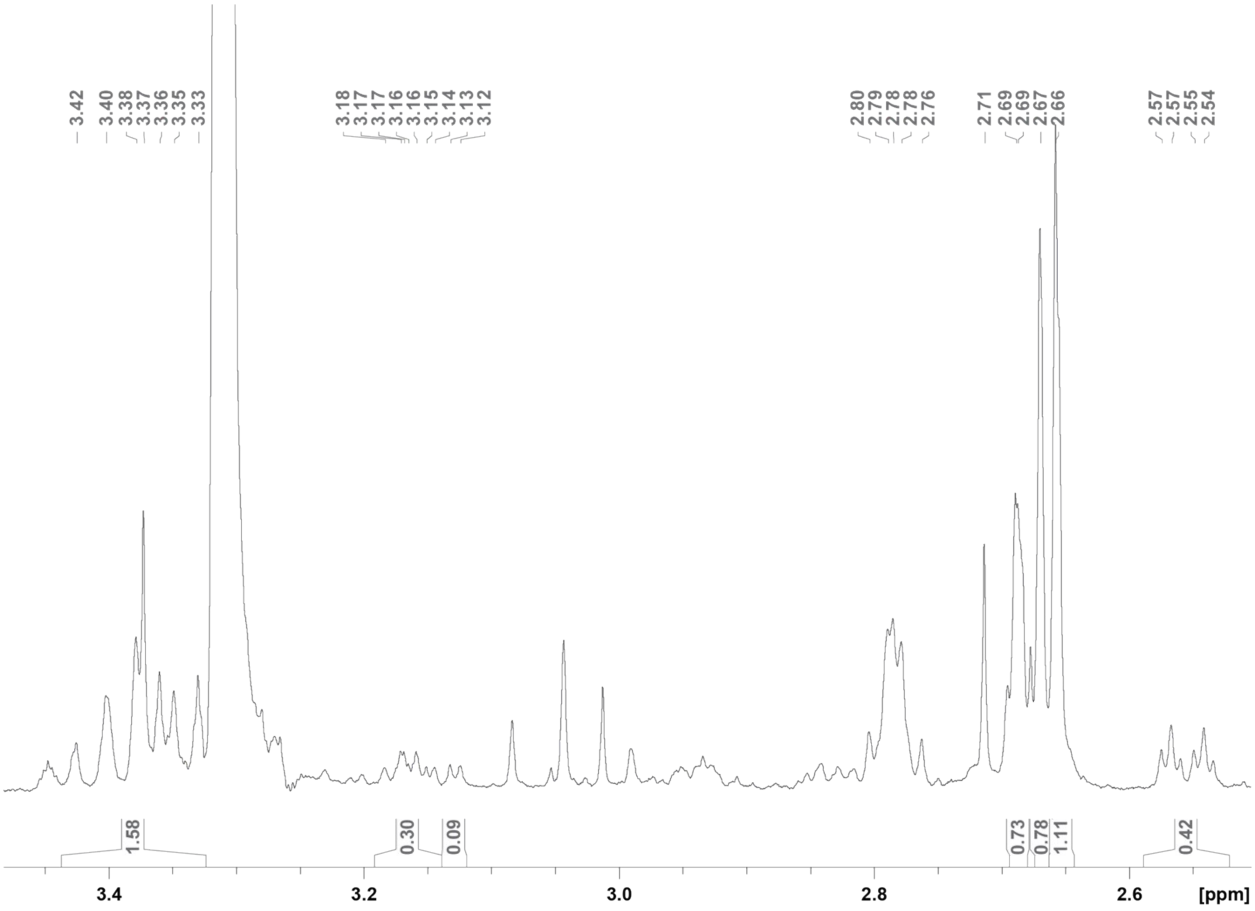


Fig. S9. ^{1}H NMR spectrum in methanol-d$_4$ of the reaction between 17-methylsulfinyl-15-oxo-*ent*-atisan-19-oic acids **13** and **14** and DiBAl-H/CeCl$_3$. The molar ratio between the reactants and the products was determined by using the integration of the peaks corresponding to the methylsulfoxide group (chemical shifts: 2.654 ppm = *cis* **15A** and **16A**; 2.668 ppm = *cis* **15B** and **16B**; 2.676 ppm = *trans* **1A** and **17A**, 2.685 ppm = **13** and **14**and 2.692 ppm = *trans* **1B** and **17B**) of the different compounds in the sample. Assuming that all the starting material would be converted into products, we used the following formulas:

$$\%\ of\ cis\ = 100 * \frac{integration\ of\ all\ cis\ methylsulfoxide\ peaks}{integration\ of\ all\ methylsulfoxide\ peaks}$$

$$\%\ of\ trans\ = 100 * \frac{integration\ of\ all\ trans\ methylsulfoxide\ peaks}{integration\ of\ all\ methylsulfoxide\ peaks}$$

$$\%\ of\ starting\ material = 100 * \frac{integration\ of\ starting\ material\ methylsulfoxide\ peak}{integration\ of\ all\ methylsulfoxide\ peaks}$$

Fig. S10

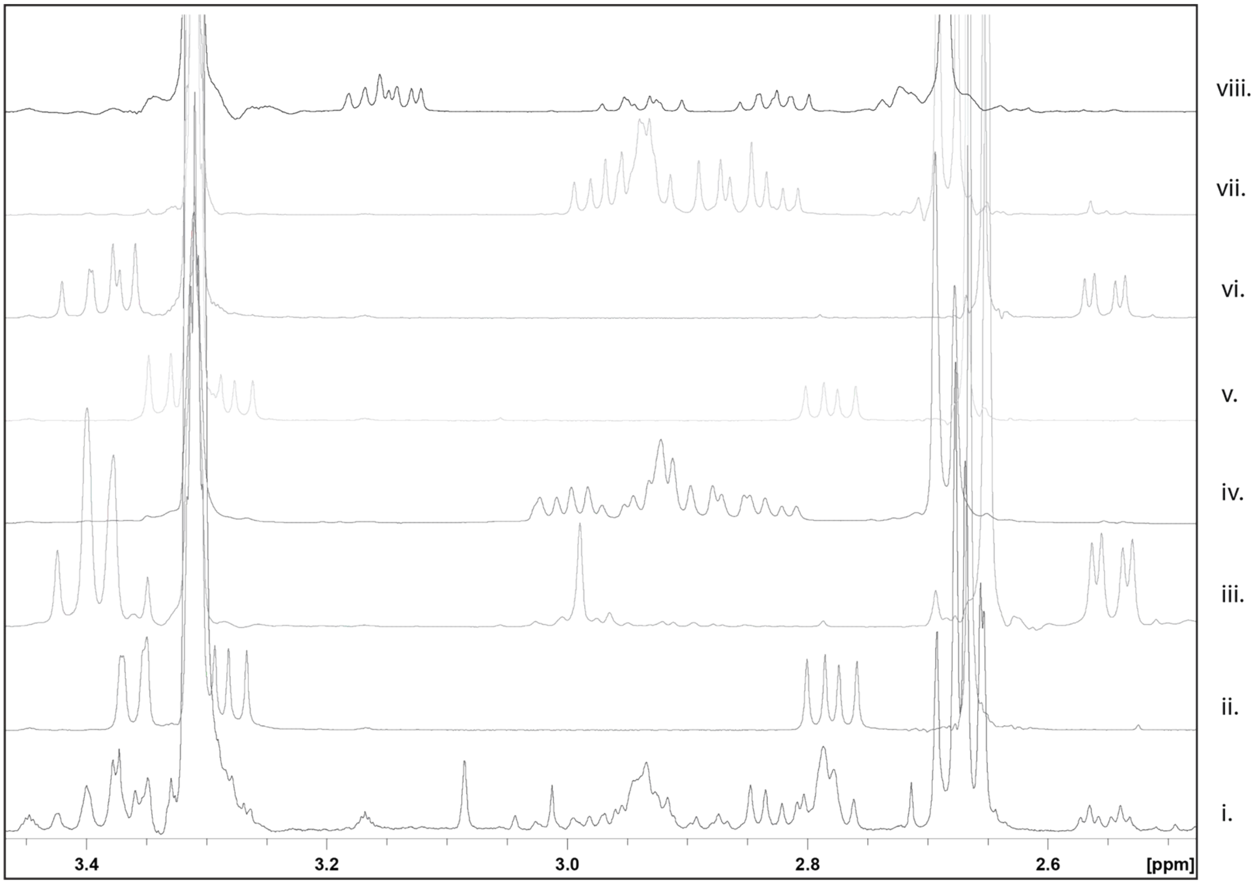


Fig. S10. ^{1}H NMR analysis in methanol-d$_4$ of the reaction between 17-methylsulfinyl-15-oxo-*ent*-atisan-19-oic acids **13** and **14** and DiBAl-H/ZnCl$_2$. i. Reaction of **13** and **14** with DiBAl-H/ZnCl$_2$; ii.-vii. 15-hydroxy-17-methylsulfinyl-*ent*-atisan-19-oic acid standards (ii. **15B**; iii. **15A**; iv. mixture of **1A** and **1B**; v. **16B**; vi. **16A**; vii. mixture of **17A** and **17B**); viii. **13** and **14**.

Fig. S11

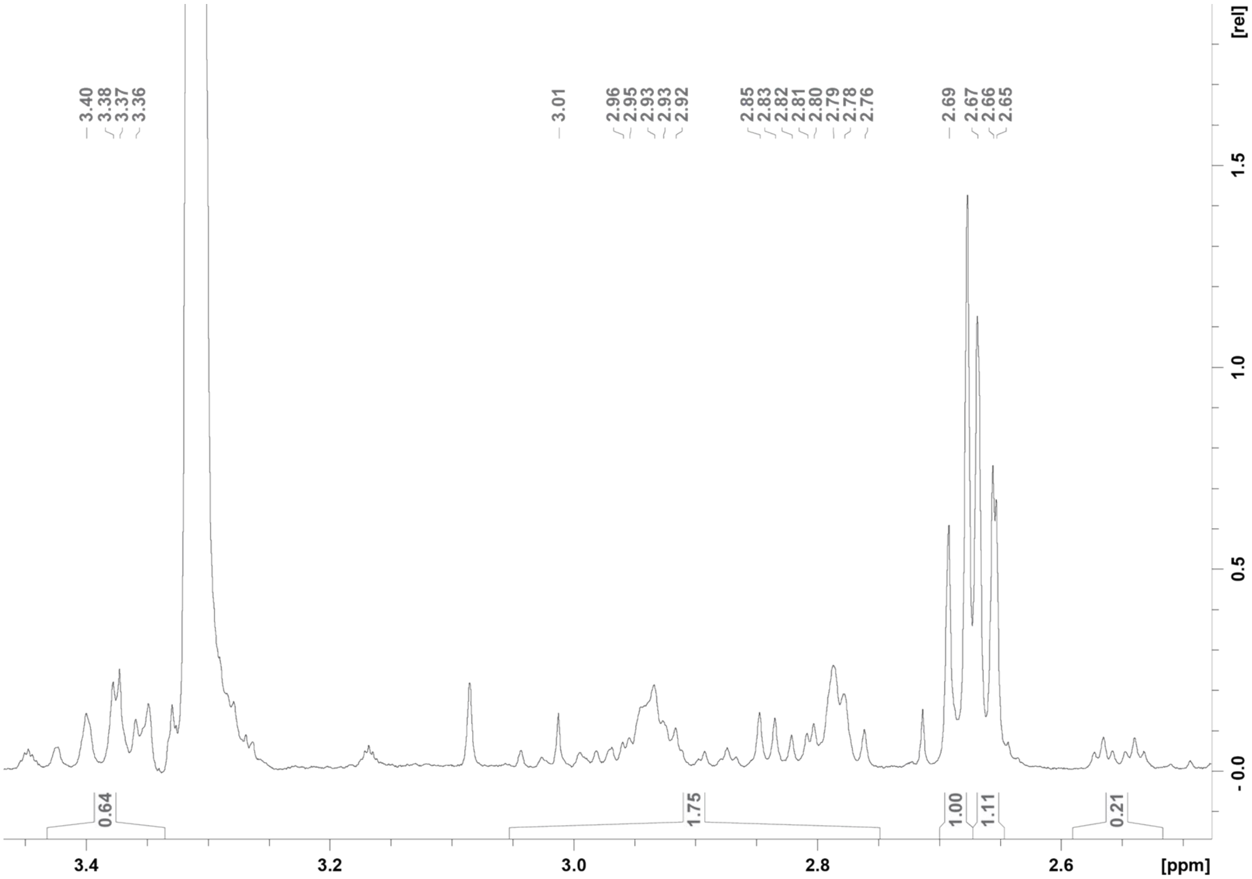


Fig. S11. ^{1}H NMR spectrum in methanol-d_4 of the reaction between 17-methylsulfinyl-15-oxo-*ent*-atisan-19-oic acids **13** and **14** and DiBAl-H/ZnCl$_2$. The molar ratio between the reactants and the products was determined by using the integration of the peaks corresponding to the methylsulfoxide group (chemical shifts: 2.654 ppm = *cis* **15A** and **16A**; 2.668 ppm = *cis* **15B** and **16B**; 2.676 ppm = *trans* **1A** and **17A**, 2.685 ppm = **13** and **14**and 2.692 ppm = *trans* **1B** and **17B**) of the different compounds in the sample. Assuming that all the starting material would be converted into products, we used the following formulas:

$$\%\ of\ cis\ = 100 * \frac{integration\ of\ all\ cis\ methylsulfoxide\ peaks}{integration\ of\ all\ methylsulfoxide\ peaks}$$

$$\%\ of\ trans\ = 100 * \frac{integration\ of\ all\ trans\ methylsulfoxide\ peaks}{integration\ of\ all\ methylsulfoxide\ peaks}$$

$$\%\ of\ starting\ material = 100 * \frac{integration\ of\ starting\ material\ methylsulfoxide\ peak}{integration\ of\ all\ methylsulfoxide\ peaks}$$

Fig. S12

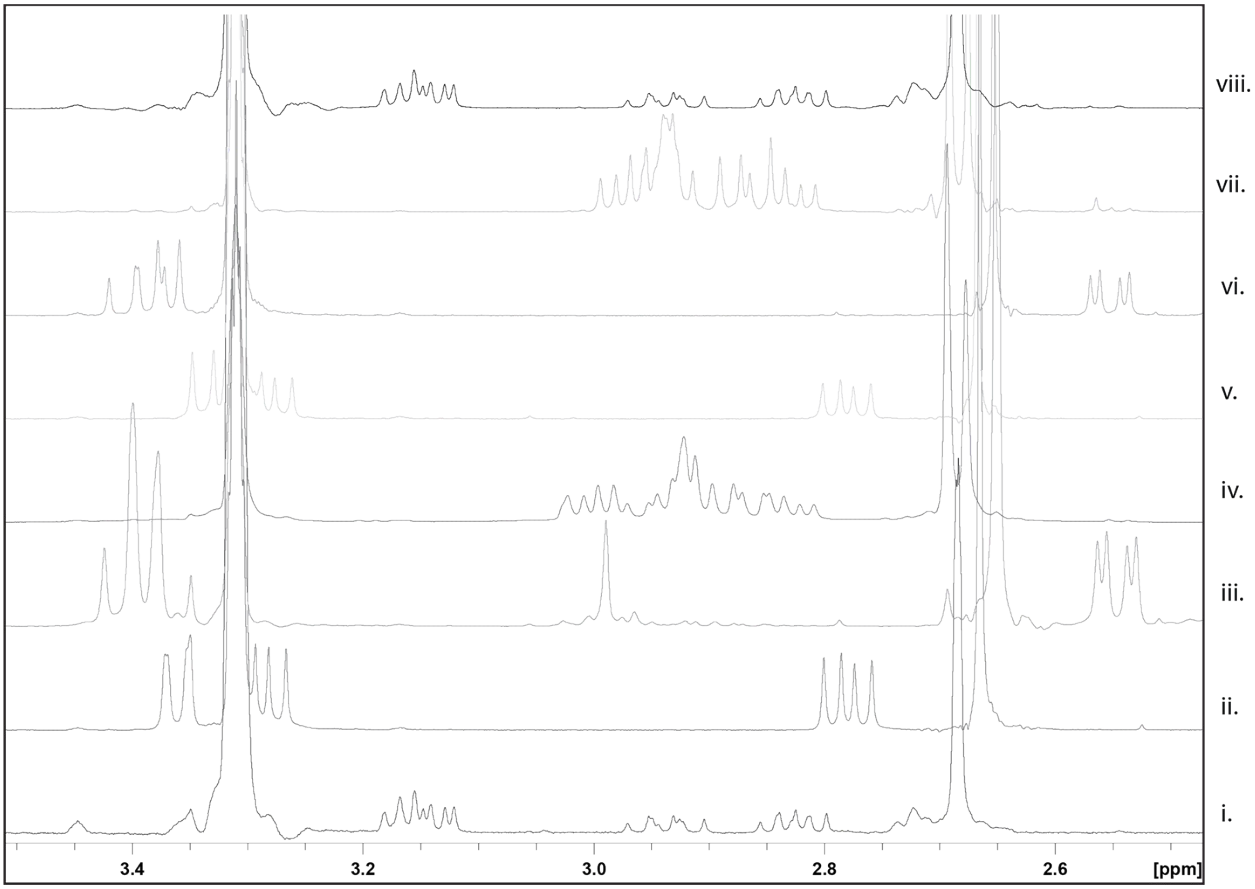


Fig. S12. ^{1}H NMR analysis in methanol-d$_4$ of the reaction between 17-methylsulfinyl-15-oxo-*ent*-atisan-19-oic acids **13** and **14** and HBpin. i. Reaction of **13** and **14** with HBpin; ii.-vii. 15-hydroxy-17-methylsulfinyl-*ent*-atisan-19-oic acid standards (ii. **15B**; iii. **15A**; iv. mixture of **1A** and **1B**; v. **16B**; vi. **16A**; vii. mixture of **17A** and **17B**); viii. **13** and **14**.

Fig. S13

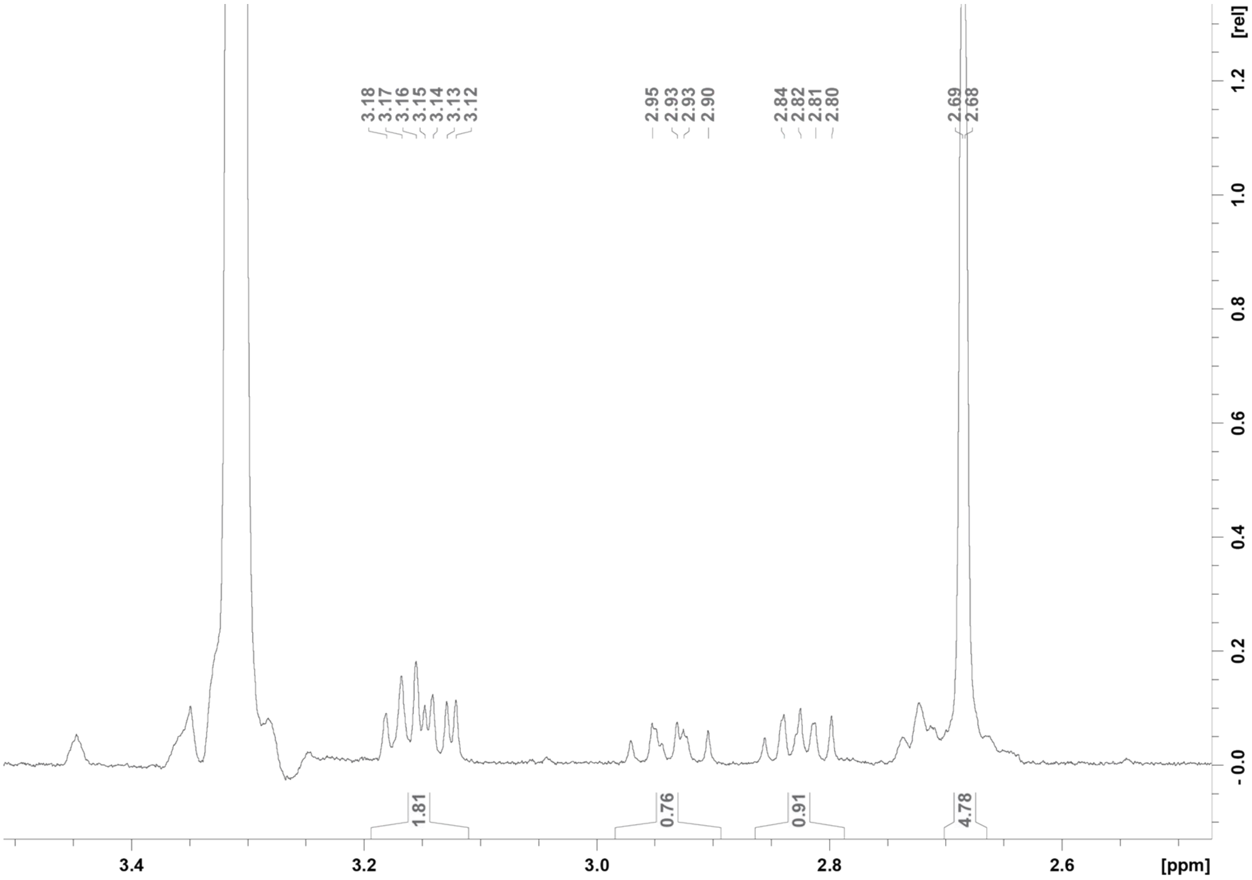


Fig. S13. ^{1}H NMR spectrum in methanol-d$_4$ of the reaction between 17-methylsulfinyl-15-oxo-*ent*-atisan-19-oic acids **13** and **14** and HBpin. The molar ratio between the reactants and the products was determined by using the integration of the peaks corresponding to the methylsulfoxide group (chemical shifts: 2.654 ppm = *cis* **15A** and **16A**; 2.668 ppm = *cis* **15B** and **16B**; 2.676 ppm = *trans* **1A** and **17A**, 2.685 ppm = **13** and **14**and 2.692 ppm = *trans* **1B** and **17B**) of the different compounds in the sample. Assuming that all the starting material would be converted into products, we used the following formulas:

$$\%\ of\ cis\ = 100 * \frac{integration\ of\ all\ cis\ methylsulfoxide\ peaks}{integration\ of\ all\ methylsulfoxide\ peaks}$$

$$\%\ of\ trans\ = 100 * \frac{integration\ of\ all\ trans\ methylsulfoxide\ peaks}{integration\ of\ all\ methylsulfoxide\ peaks}$$

$$\%\ of\ starting\ material = 100 * \frac{integration\ of\ starting\ material\ methylsulfoxide\ peak}{integration\ of\ all\ methylsulfoxide\ peaks}$$

Fig. S14

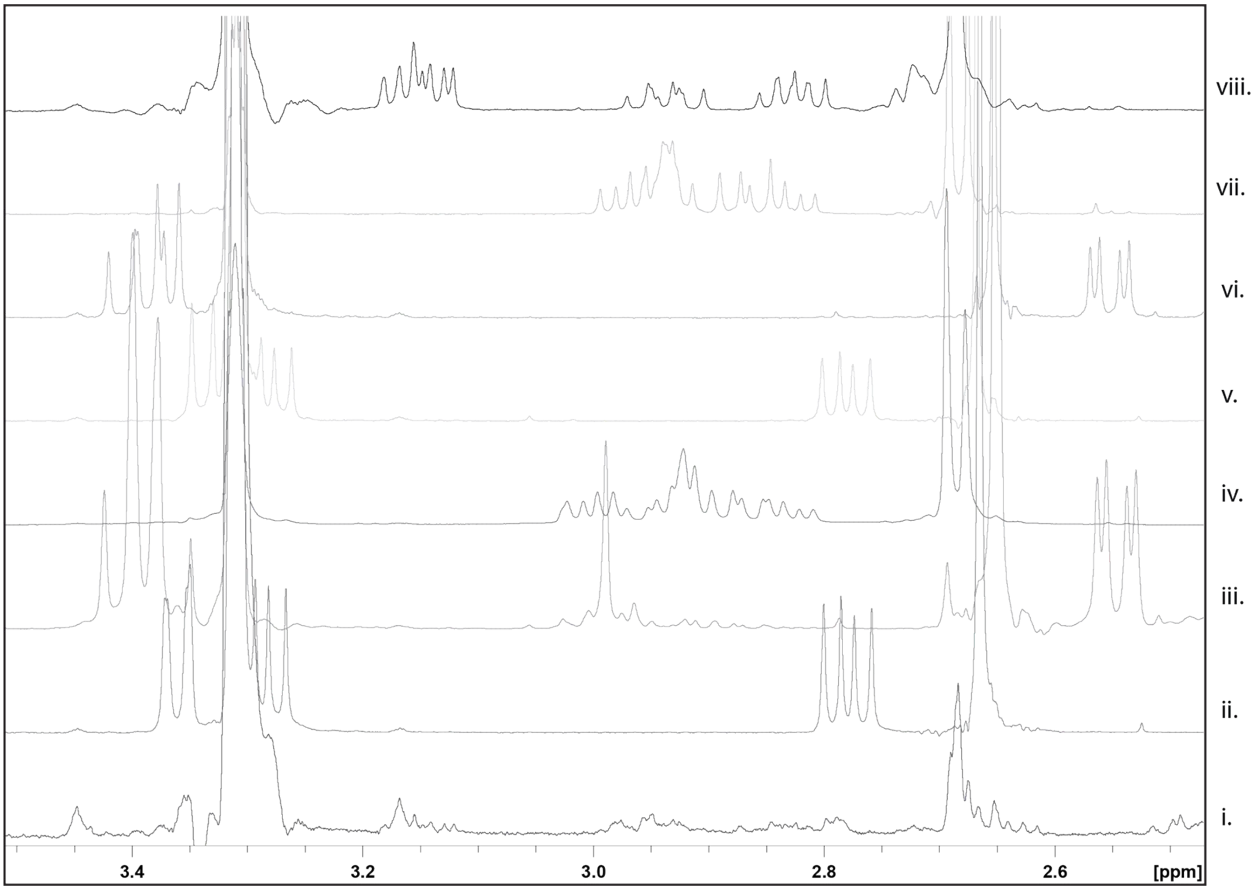


Fig. S14. ^{1}H NMR analysis in methanol-d_4 of the reaction between 17-methylsulfinyl-15-oxo-*ent*-atisan-19-oic acids **13** and **14** and BH_3-THF. i. Reaction of **13** and **14** with BH_3-THF; ii.-vii. 15-hydroxy-17-methylsulfinyl-*ent*-atisan-19-oic acid standards (ii. **15B**; iii. **15A**; iv. mixture of **1A** and **1B**; v. **16B**; vi. **16A**; vii. mixture of **17A** and **17B**); viii. **13** and **14**.

Fig. S15

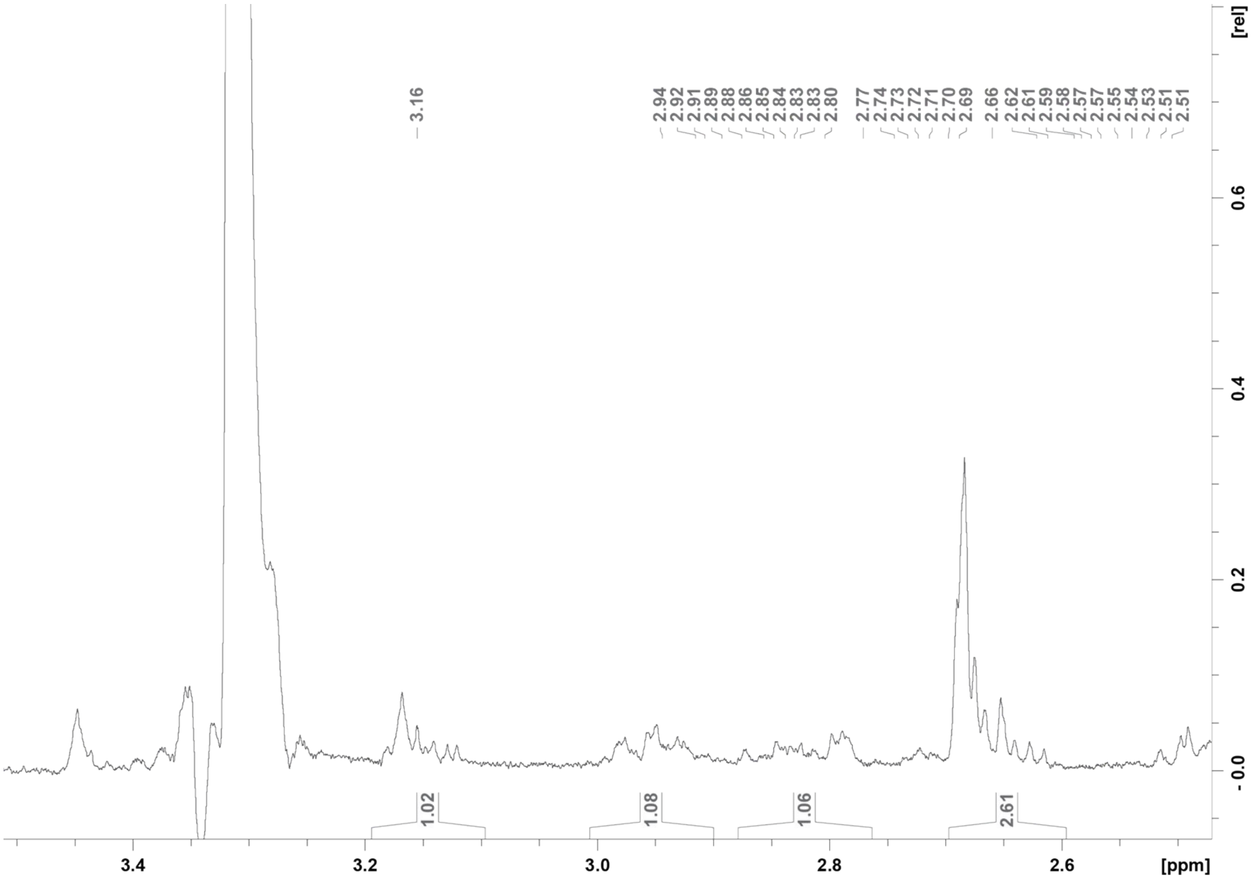


Fig. S15. ^{1}H NMR spectrum in methanol-d_4 of the reaction between 17-methylsulfinyl-15-oxo-*ent*-atisan-19-oic acids **13** and **14** and BH_3-THF. The molar ratio between the reactants and the products was determined by using the integration of the peaks corresponding to the methylsulfoxide group (chemical shifts: 2.654 ppm = *cis* **15A** and **16A**; 2.668 ppm = *cis* **15B** and **16B**; 2.676 ppm = *trans* **1A** and **17A**, 2.685 ppm = **13** and **14**and 2.692 ppm = *trans* **1B** and **17B**) of the different compounds in the sample. Assuming that all the starting material would be converted into products, we used the following formulas:

$$\% \, of \, cis \; = 100 * \frac{integration \, of \, all \, cis \, methylsulfoxide \, peaks}{integration \, of \, all \, methylsulfoxide \, peaks}$$

$$\% \, of \, trans \; = 100 * \frac{integration \, of \, all \, trans \, methylsulfoxide \, peaks}{integration \, of \, all \, methylsulfoxide \, peaks}$$

$$\% \, of \, starting \, material = 100 * \frac{integration \, of \, starting \, material \, methylsulfoxide \, peak}{integration \, of \, all \, methylsulfoxide \, peaks}$$

Fig. S16

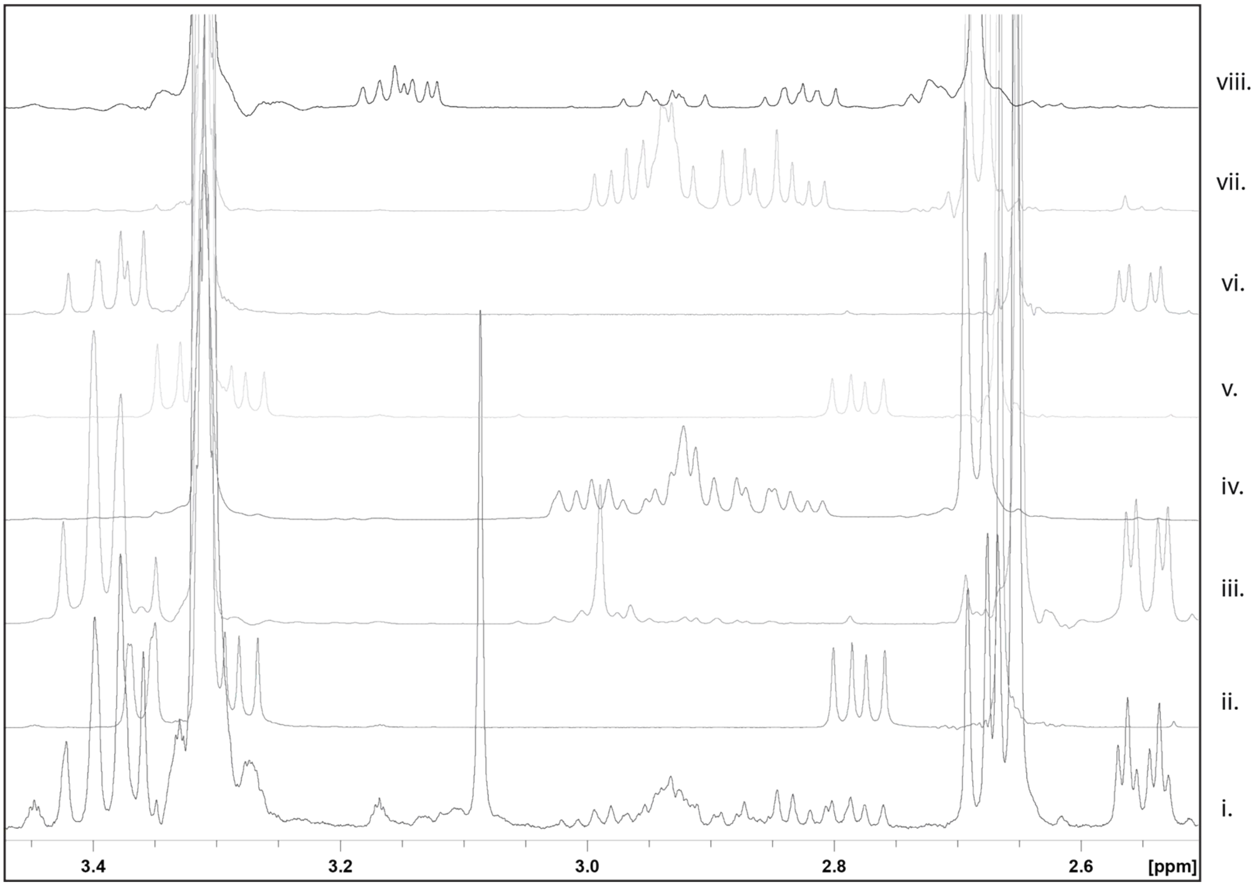


Fig. S16. ^{1}H NMR analysis in methanol-d_4 of the reaction between 17-methylsulfinyl-15-oxo-*ent*-atisan-19-oic acids **13** and **14** and NaBH$_4$. i. Reaction of **13** and **14** with NaBH$_4$; ii.-vii. 15-hydroxy-17-methylsulfinyl-*ent*-atisan-19-oic acid standards (ii. **15B**; iii. **15A**; iv. mixture of **1A** and **1B**; v. **16B**; vi. **16A**; vii. mixture of **17A** and **17B**); viii. **13** and **14**.

Fig. S17

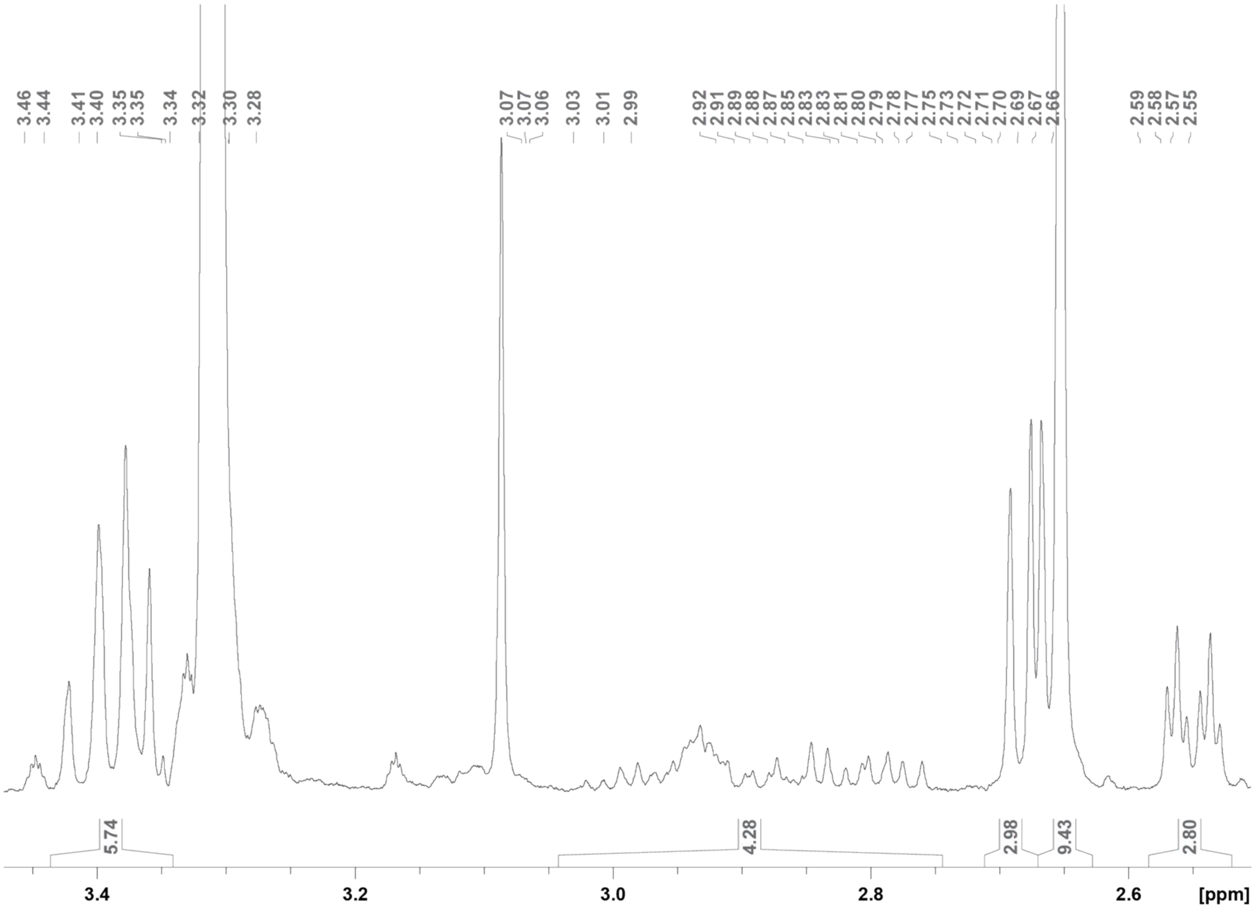


Fig. S17. ^{1}H NMR spectrum in methanol-d$_4$ of the reaction between 17-methylsulfinyl-15-oxo-*ent*-atisan-19-oic acids **13** and **14** and NaBH$_4$. The molar ratio between the reactants and the products was determined by using the integration of the peaks corresponding to the methylsulfoxide group (chemical shifts: 2.654 ppm = *cis* **15A** and **16A**; 2.668 ppm = *cis* **15B** and **16B**; 2.676 ppm = *trans* **1A** and **17A**, 2.685 ppm = **13** and **14**and 2.692 ppm = *trans* **1B** and **17B**) of the different compounds in the sample. Assuming that all the starting material would be converted into products, we used the following formulas:

$$\%\ of\ cis\ = 100 * \frac{integration\ of\ all\ cis\ methylsulfoxide\ peaks}{integration\ of\ all\ methylsulfoxide\ peaks}$$

$$\%\ of\ trans\ = 100 * \frac{integration\ of\ all\ trans\ methylsulfoxide\ peaks}{integration\ of\ all\ methylsulfoxide\ peaks}$$

$$\%\ of\ starting\ material = 100 * \frac{integration\ of\ starting\ material\ methylsulfoxide\ peak}{integration\ of\ all\ methylsulfoxide\ peaks}$$

Fig. S18

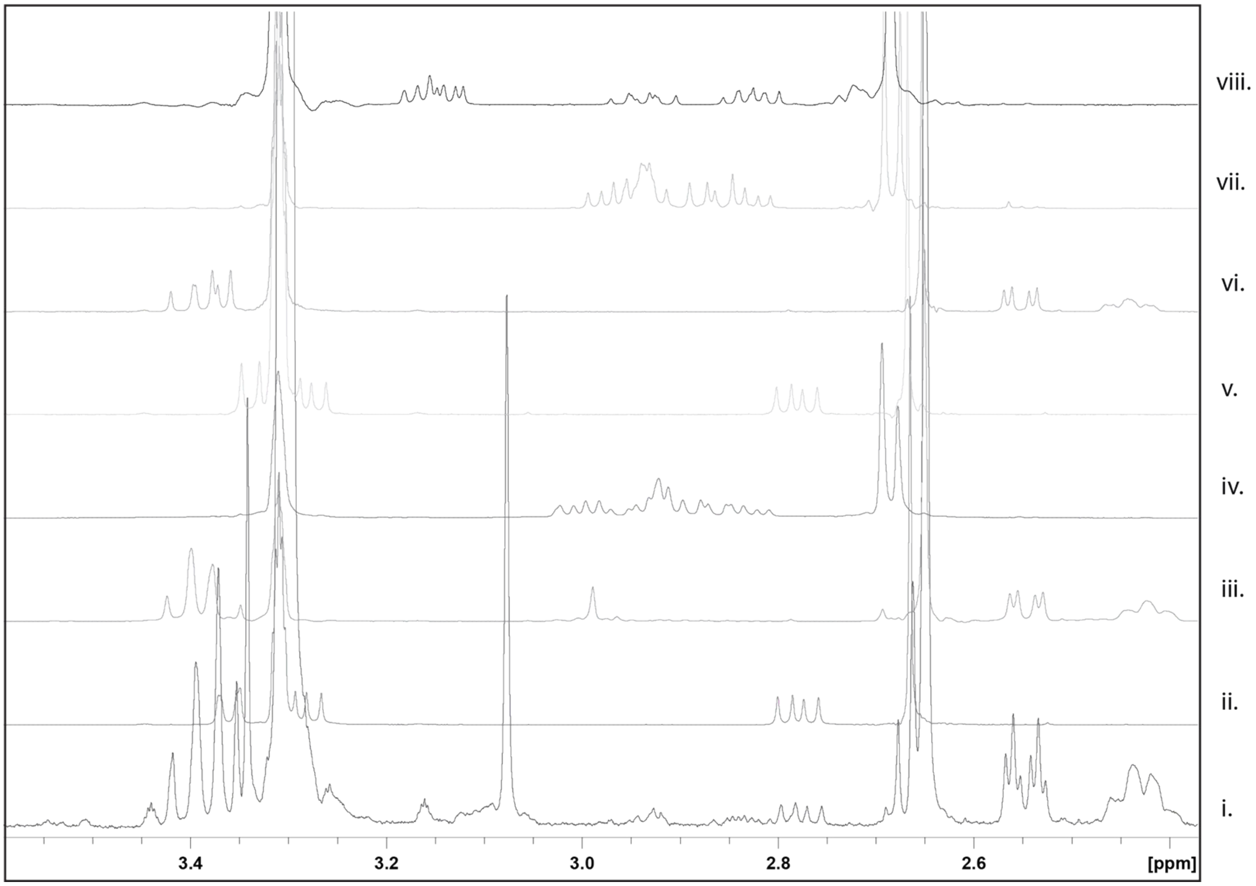


Fig. S18. ^{1}H NMR analysis in methanol-d_4 of the reaction between 17-methylsulfinyl-15-oxo-*ent*-atisan-19-oic acids **13** and **14** and $NaBH_4/CeCl_3$. i. Reaction of **13** and **14** with $NaBH_4/CeCl_3$; ii.-vii. 15-hydroxy-17-methylsulfinyl-*ent*-atisan-19-oic acid standards (ii. **15B**; iii. **15A**; iv. mixture of **1A** and **1B**; v. **16B**; vi. **16A**; vii. mixture of **17A** and **17B**); viii. **13** and **14**.

Fig. S19

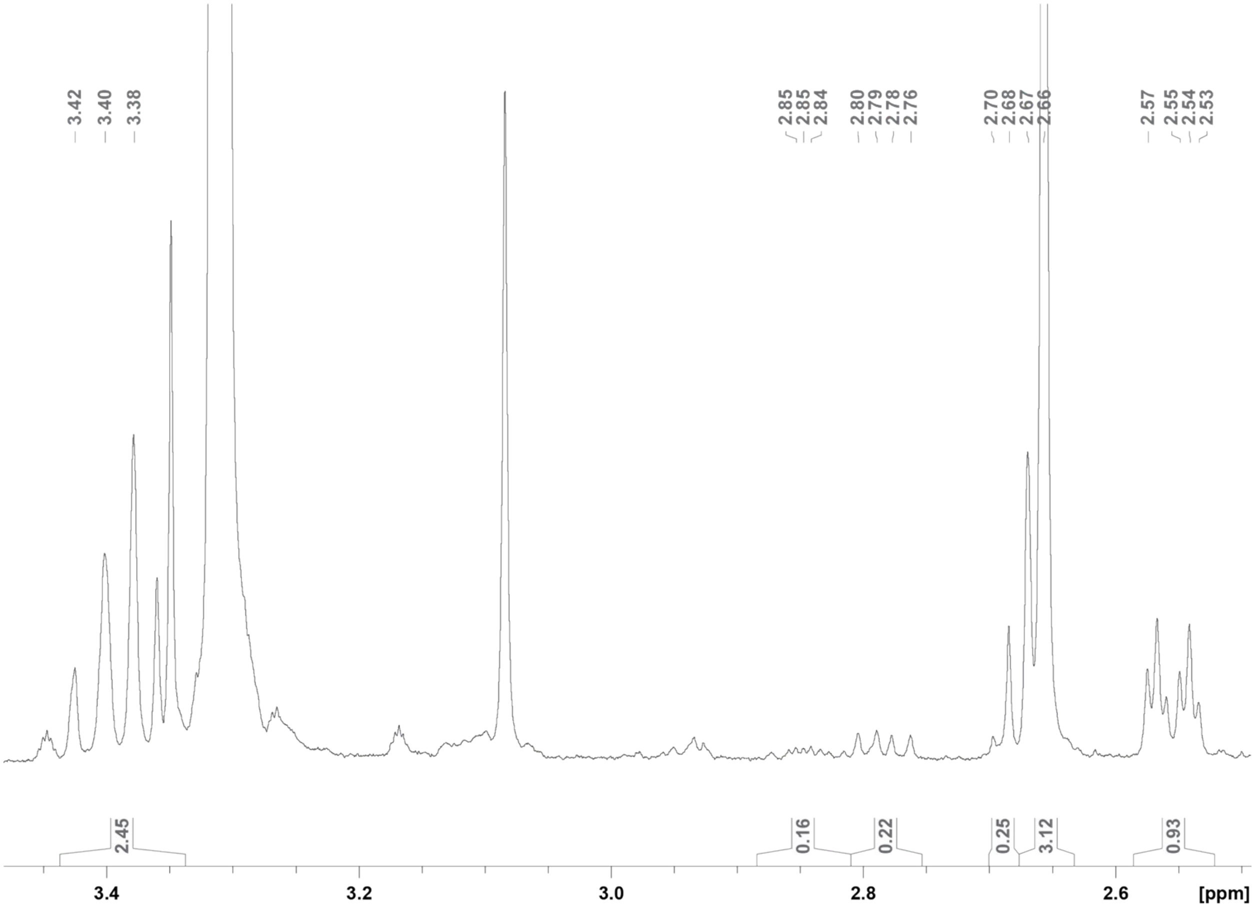


Fig. S19. ^{1}H NMR spectrum in methanol-d$_4$ of the reaction between 17-methylsulfinyl-15-oxo-*ent*-atisan-19-oic acids **13** and **14** and NaBH$_4$/CeCl$_3$. The molar ratio between the reactants and the products was determined by using the integration of the peaks corresponding to the methylsulfoxide group (chemical shifts: 2.654 ppm = *cis* **15A** and **16A**; 2.668 ppm = *cis* **15B** and **16B**; 2.676 ppm = *trans* **1A** and **17A**, 2.685 ppm = **13** and **14**and 2.692 ppm = *trans* **1B** and **17B**) of the different compounds in the sample. Assuming that all the starting material would be converted into products, we used the following formulas:

$$\%\ of\ cis\ = 100 * \frac{integration\ of\ all\ cis\ methylsulfoxide\ peaks}{integration\ of\ all\ methylsulfoxide\ peaks}$$

$$\%\ of\ trans\ = 100 * \frac{integration\ of\ all\ trans\ methylsulfoxide\ peaks}{integration\ of\ all\ methylsulfoxide\ peaks}$$

$$\%\ of\ starting\ material = 100 * \frac{integration\ of\ starting\ material\ methylsulfoxide\ peak}{integration\ of\ all\ methylsulfoxide\ peaks}$$

Fig. S20

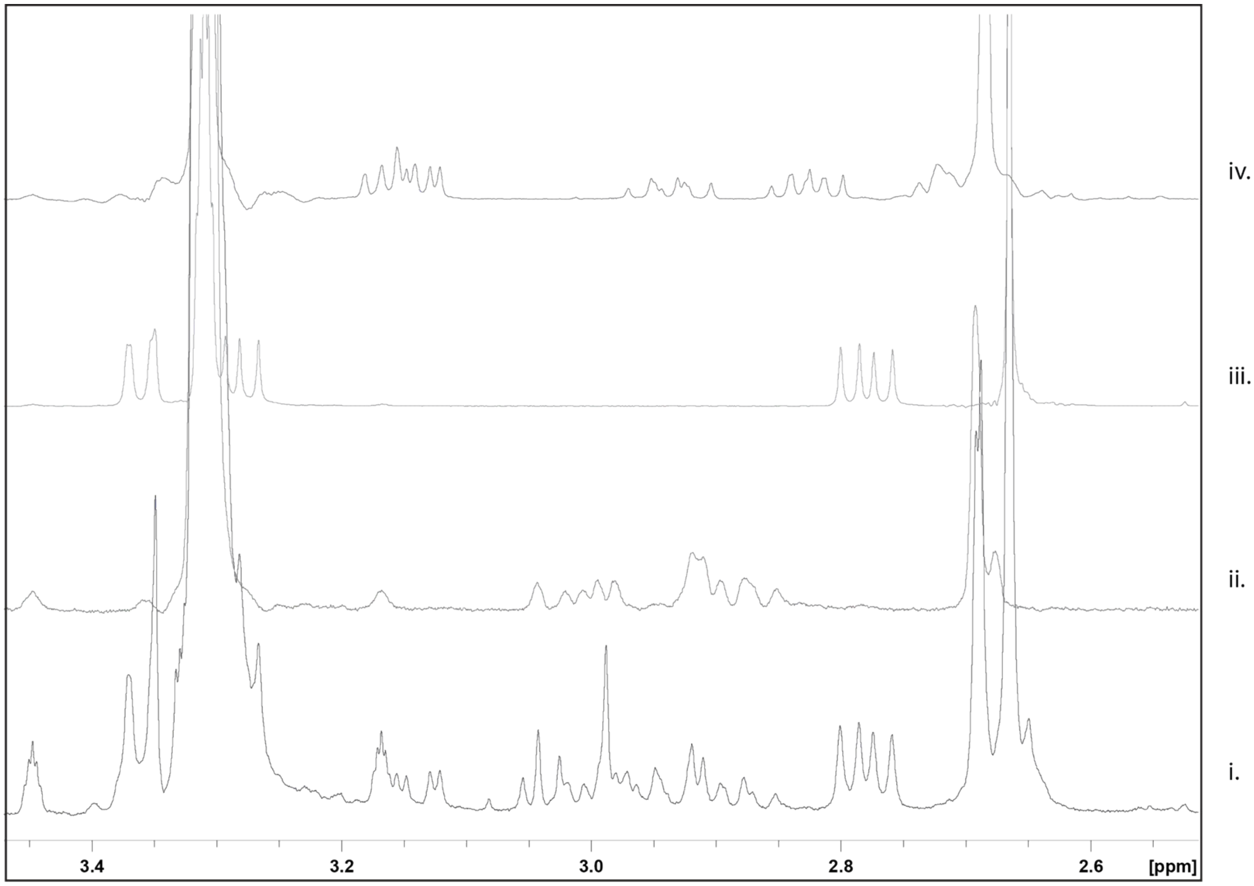


Fig. S20. ^{1}H NMR analysis in methanol-d_4 of the reaction between (16S,S)-17-methylsulfinyl-15-oxo-*ent*-atisan-19-oic acid **13B** and DiBAl-H/ZnCl$_2$. i. Reaction of **13B** with DiBAl-H/ZnCl$_2$; ii.-iii. 15-hydroxy-17-methylsulfinyl-*ent*-atisan-19-oic acid standards (ii. **1B**; iii. **15B**); vi. **13** and **14**.

Fig. S21

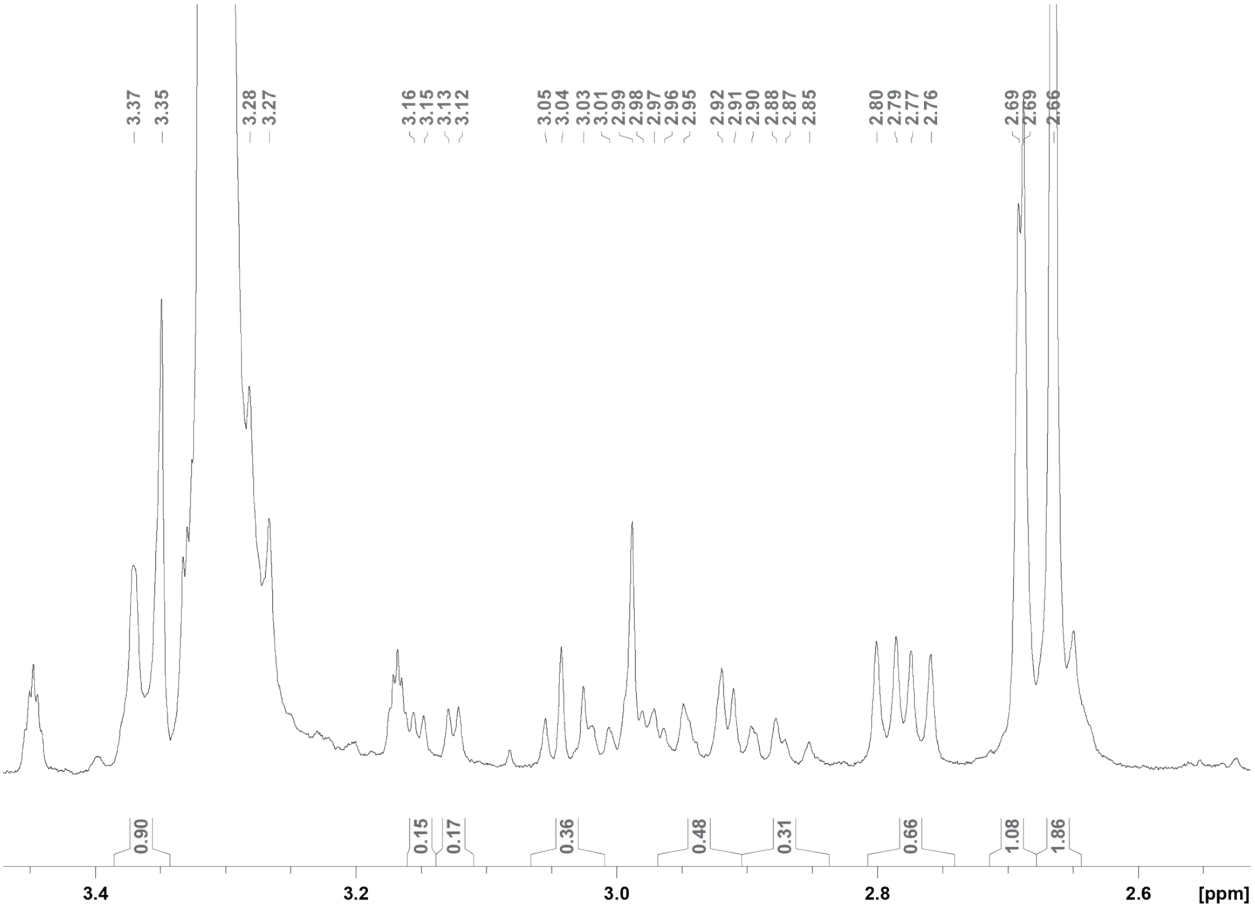


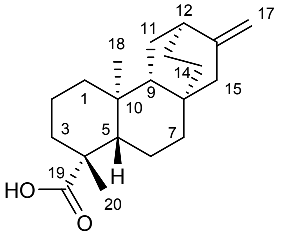
Fig. S21. ^{1}H NMR spectrum in methanol-d$_4$ of the reaction between (16S,S)-17-methyl-sulfinyl-15-oxo-*ent*-atisan-19-oic acid **13B** and DiBAl-H/ZnCl$_2$. The molar ratio between the reactants and the products was determined by using the integration of the peaks corresponding to the one of the protons of the C17-methylene group (chemical shifts: 2.78 ppm = **15B**, 2.88 ppm = **1B** and 3.14 ppm =**13B**) of the different compounds in the sample. For the methylene of **13B**, as one part of the doublet of doublets is overlapping another peak (on the right in the spectrum), we doubled the value of the integration of the left part the doublet of doublet (0.17 x 2= 0.34). Assuming that all the starting material would be converted into products, we used the following formulas:

$$\%\ of\ cis\ = 100 * \frac{integration\ of\ methylene\ peak\ of\ 15B}{integration\ of\ all\ methylene\ peaks}$$

$$\%\ of\ trans\ = 100 * \frac{integration\ of\ methylene\ peak\ of\ 1B}{iintegration\ of\ all\ methylene\ peaks}$$

$$\%\ of\ starting\ material = 100 * \frac{integration\ of\ methylene\ peak\ of\ 13B}{ntegration\ of\ all\ methylene\ peaks}$$

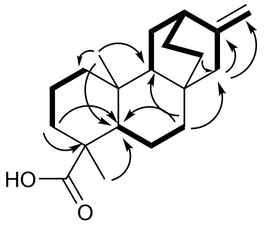
Fig. S22



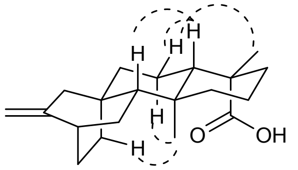
***ent*-atis-16-en-19-oic acid (5)**

Annotated NMR data for **5** in chloroform-*d*.

No.	δ_H (#H, mult., *J*(Hz))	δ_C
1	0.85 (1H, td, 3.3, 13.2) 1.59 (1H, m)	39.6
2	1.40 (1H, m) 1.87 (1H, m)	18.8
3	1.01 (1H, m) 2.15 (1H, d, 14.0)	38.3
4	-	43.9
5	1.05 (1H, dd, 1.5, 12.1)	57.2
6	1.75 (1H, m) 1.82 (1H, m)	20.2
7	1.11 (1H, m) 1.47 (1H, td, 2.9, 13.2)	39.6
8	-	33.6
9	1.13 (1H, m)	52.2
10	-	38.5
11	1.40 (1H, m) 1.59 (1H, m)	28.7
12	2.22 (1H, m)	36.6
13	1.54 (1H, m) 1.60 (1H, m)	27.3
14	1.00 (1H, m) 1.97 (1H, m)	28.3
15	1.88 (1H, d, 16.6) 2.04 (1H, d, 16.6)	48.3
16	-	152.6
17	4.56 (1H, d, 1.9) 4.73 (1H, d, 1.9)	104.7
18	0.90 (3H, s)	12.1
19	-	185.0
20	1.24 (3H, s)	29.0



Key COSY (bold) and HMBC (arrows) correlations



Key NOESY correlations

Fig. S23

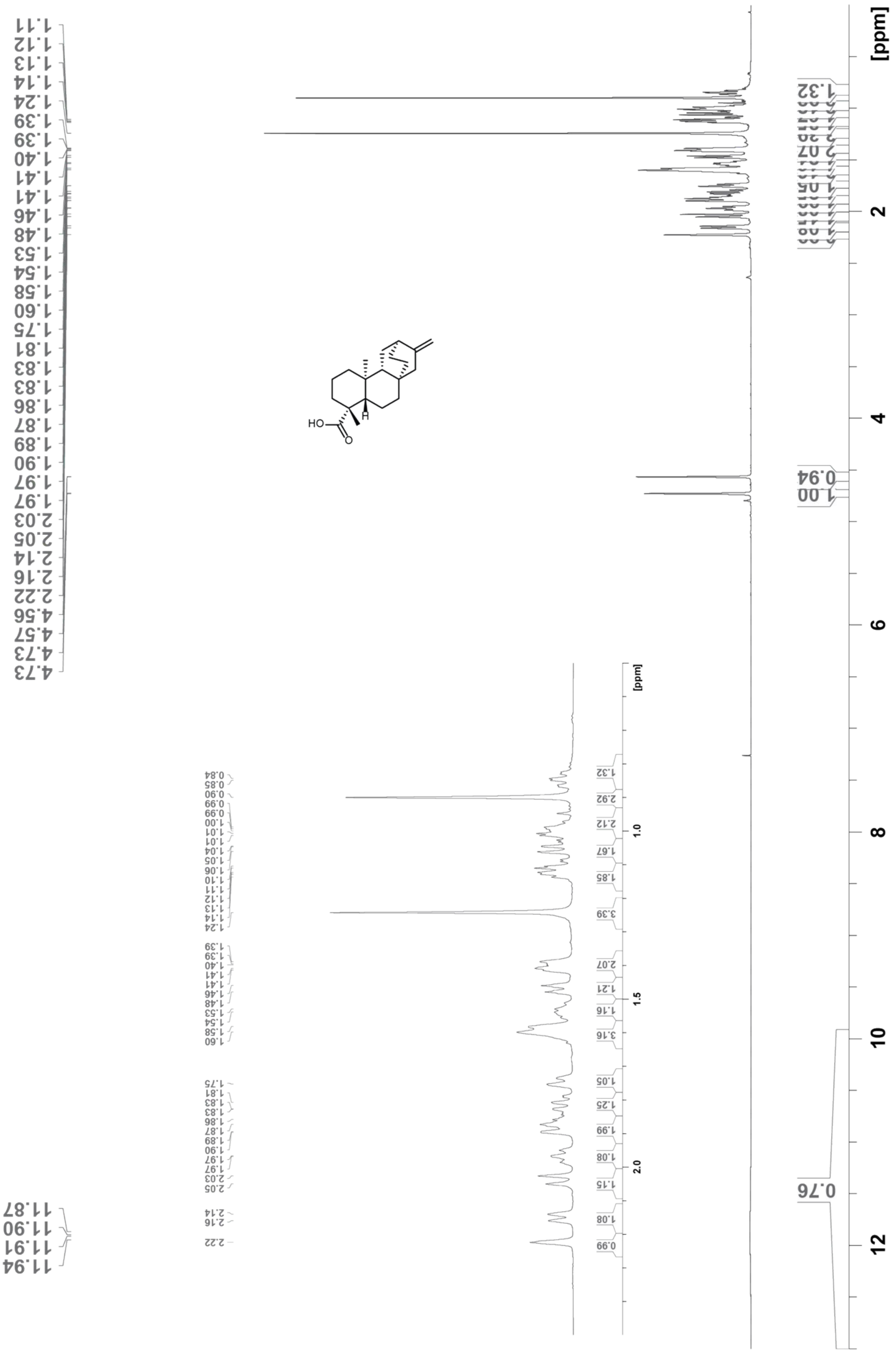


Fig. S23. ^{1}H spectrum of **5**.

Fig. S24.

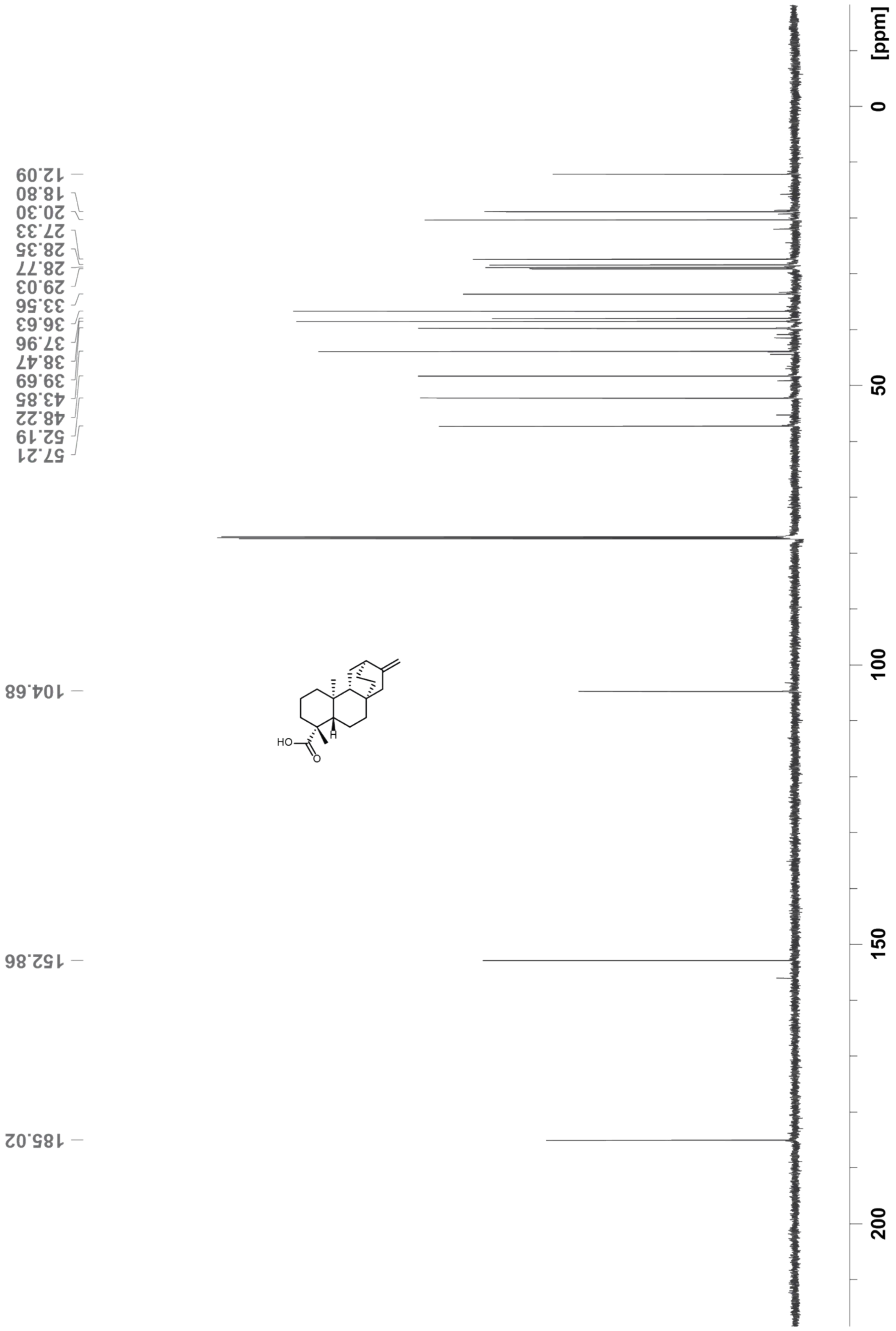
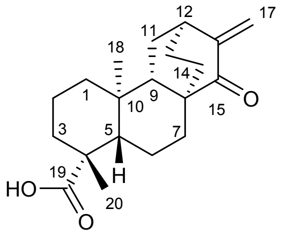


Fig. S24. ^{13}C spectrum of **5**.

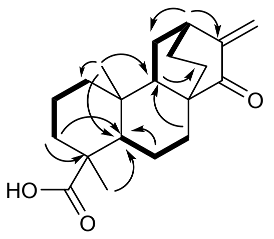
Fig. S25.



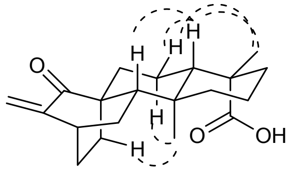
***ent*-15-oxoatis-16-en-19-oic acid (6)**

Annotated NMR data for **6** in chloroform-*d*

No.	δ_H (#H, mult., *J*(Hz))	δ_C
1	0.85 (1H, dd, 4.0, 13.5) 1.62 (1H, m)	39.8
2	1.42 (1H, m) 1.86 (1H, m)	18.7
3	1.02 (1H, m) 2.17 (1H, d, 13.5)	37.8
4	-	45.5
5	1.05 (1H, m)	56.3
6	1.84(1H, m) 1.92 (1H, m)	19.6
7	1.50 (1H, m) 1.83 (1H, m)	30.1
8	-	60.6
9	1.32 (1H, m)	46.7
10	-	39.3
11	1.57 (1H, m) 1.71 (1H, m)	28.2
12	2.76 (1H, m)	36.2
13	1.25 (1H, m) 2.23 (1H, ddd, 3.2, 11.2, 14.3)	24.8
14	1.72 (2H, m)	26.2
15	-	203.9
16	-	147.3
17	5.20 (1H, d, 1.3) 5.94 (1H, d, 1.3)	117.0
18	1.01 (3H, s)	12.8
19	-	182.6
20	1.27 (3H, s)	29.0



Key COSY (bold) and HMBC (arrows) correlations



Key NOESY correlations

Fig. S26.

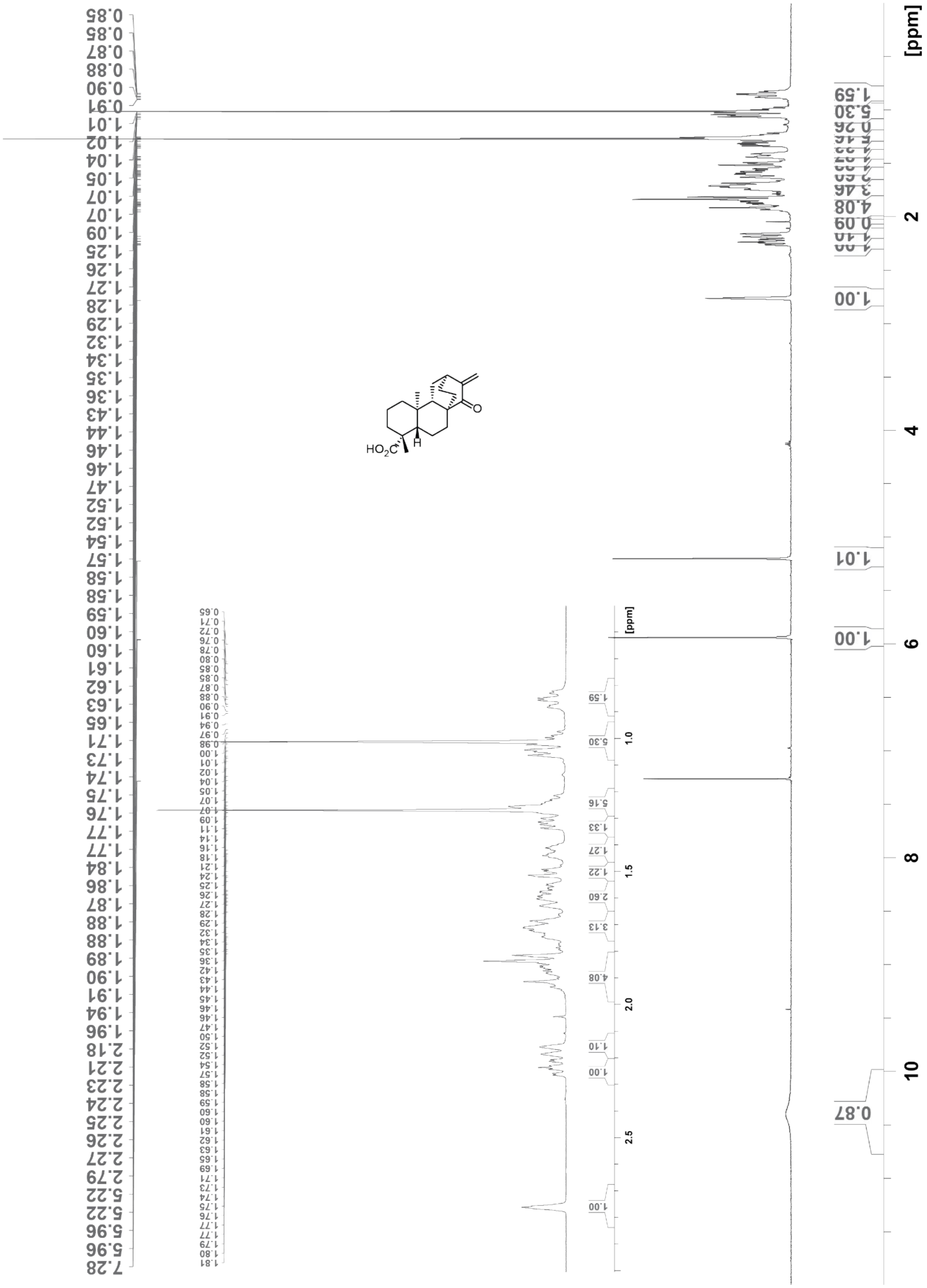


Fig. S26. ^{1}H spectrum of **6**.

Fig. S27.

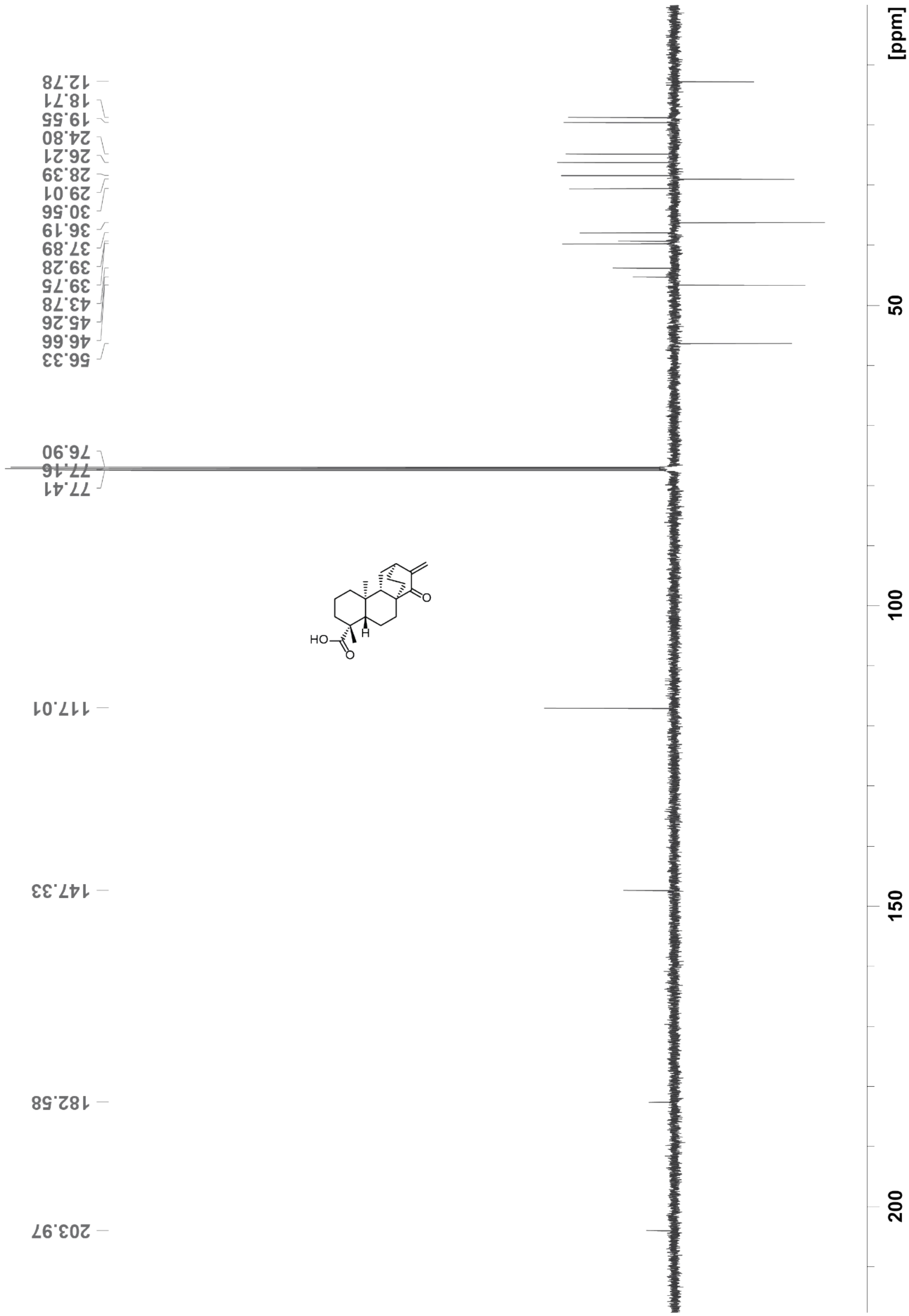
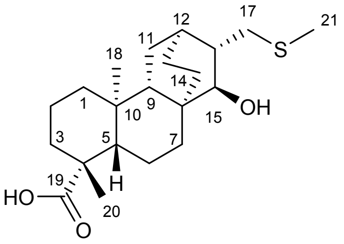


Fig. S27.^{13}C spectrum of **6**.

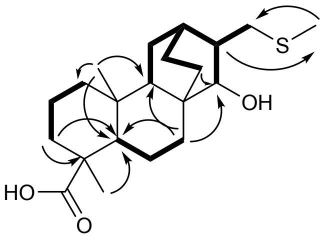
Fig. S28.



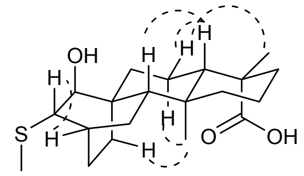
***ent*-(15S,16R)-15-hydroxy-17-methylsulfenylatisan-19-oic acid (9)**

Annotated NMR data for **9** in chloroform-*d.*

No.	δ_H (#H, mult., *J*(Hz))	δ_C
1	0.88 (1H, m)	39.9
	1.63 (1H, m)	
2	1.42 (1H, m)	18.9
	1.85 (1H, m)	
3	1.03 (1H, m)	37.6
	2.15 (1H, m)	
4	-	43.8
5	1.08 (1H, m)	56.6
6	1.80 (2H, m)	19.7
7	1.12 (1H, dt, 2.7, 13.1)	33.2
	1.69 (1H, m)	
8	-	36.5
9	1.61 (1H, m)	47.4
10	-	38.1
11	1.48 (1H, m)	29.3
	1.53 (1H, m)	
12	1.66 (1H, m)	30.0
13	1.30 (1H, m)	21.3
	1.53 (1H, m)	
14	0.74 (1H, td, 6.5, 13.1)	27.5
	1.97 (1H, m)	
15	2.95 (1H, d, 3.7)	81.1
16	1.54 (1H, m)	42.1
17	2.53 (2H, d, 7.8)	39.3
18	0.91 (3H, s)	13.0
19	-	182.5
20	1.25 (3H, s)	29.0
21	2.14 (3H, s)	15.7



Key COSY (bold) and HMBC (arrows) correlations



Key NOESY correlations

Fig. S29.

Fig. S29. ^1H spectrum of **9**.

Fig. S30.

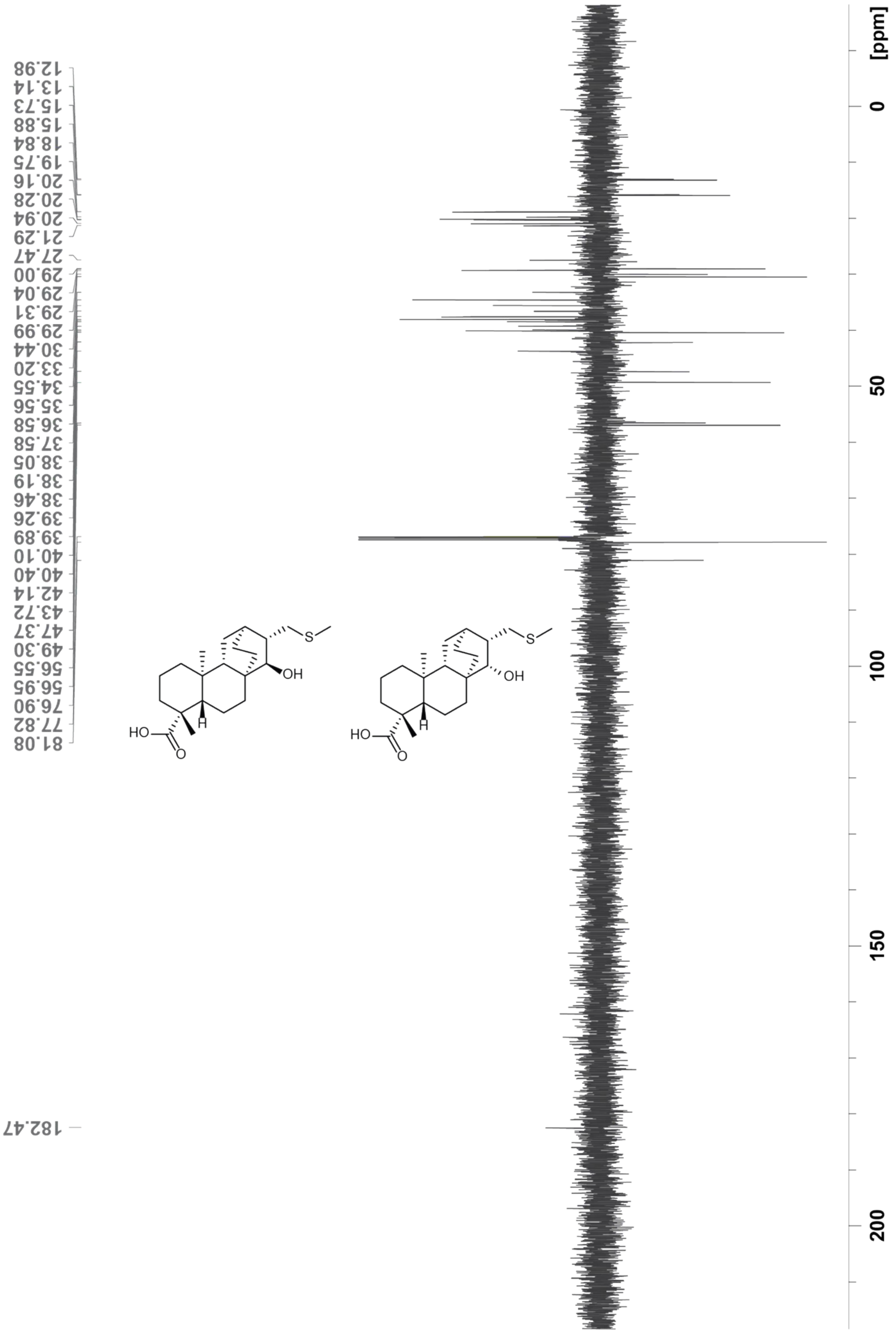
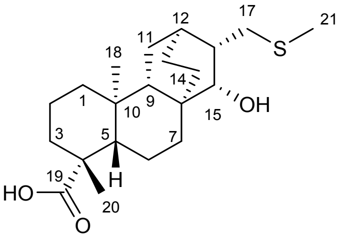


Fig. S30.^{13}C spectrum of **9** and **10**.

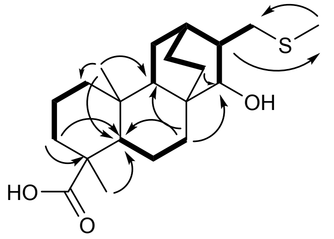
Fig. S31.



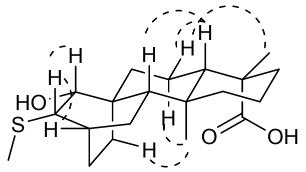
***ent*-(15R,16R)-15-hydroxy-17-methylsulfenylatisan-19-oic acid (10)**

Annotated NMR data for **10** in chloroform-*d*.

No.	δ_H (#H, mult., *J*(Hz))	δ_C
1	0.88 (1H, m)	40.1
	1.63 (1H, m)	
2	1.41 (1H, m)	18.8
	1.87 (1H, m)	
3	1.02 (1H, m)	38.0
	2.15 (1H, m)	
4	-	43.8
5	1.02 (1H, m)	57.0
6	1.72 (1H, m)	20.1
	1.78 (1H, m)	
7	1.06 (1H, m)	37.6
	1.80	
8	-	35.6
9	0.99 (1H, m)	49.3
10	-	38.5
11	1.37 (1H, m)	29.3
	1.48 (1H, m)	
12	1.54 (1H, m)	30.4
13	1.27 (1H, m)	20.9
	1.64 (1H, m)	
14	1.47 (1H, m)	20.3
	1.64 (1H, m)	
15	3.45 (1H, d, 8.8)	77.8
16	1.97 (1H, m)	40.4
17	2.51 (1H, dd, 5.3, 12.2)	34.4
	2.89 (1H, m)	
18	0.94 (3H, s)	13.1
19	-	182.5
20	1.25 (3H, s)	29.0
21	2.14 (3H, s)	15.9



Key COSY (bold) and HMBC (arrows) correlations



Key NOESY correlations

Fig. S32.

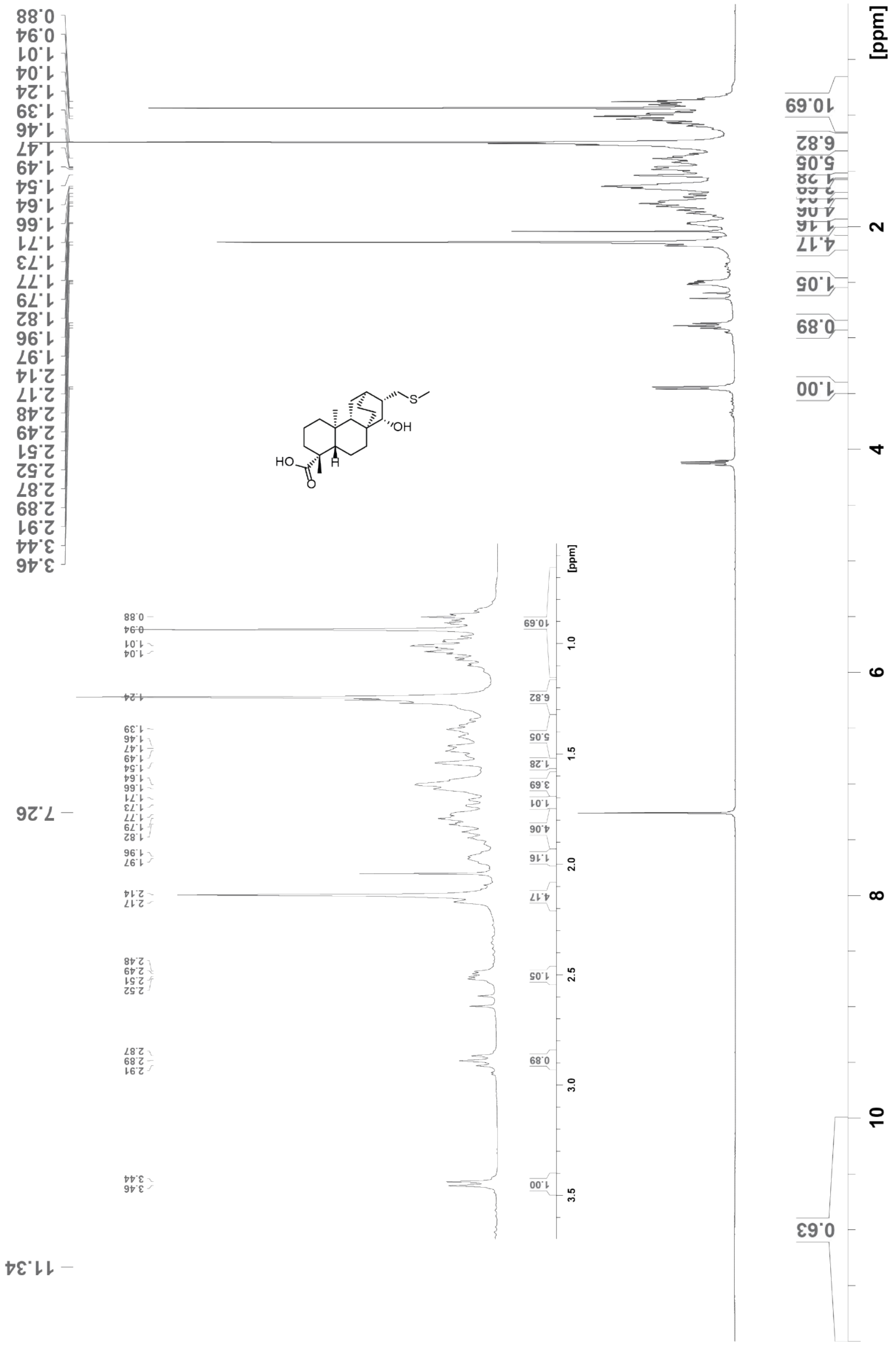


Fig. S32. ^{1}H spectrum of **10**.

Fig. S33.

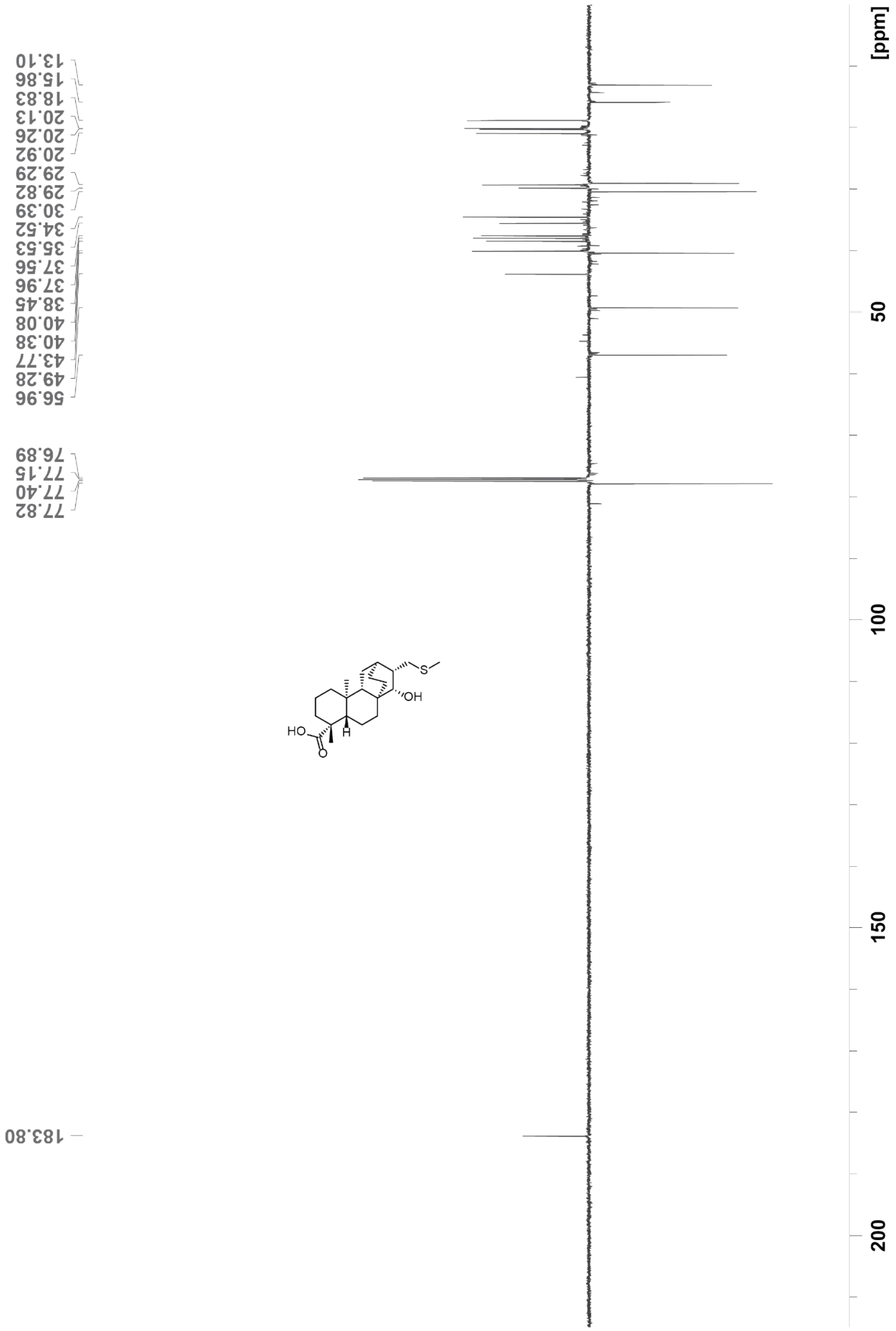
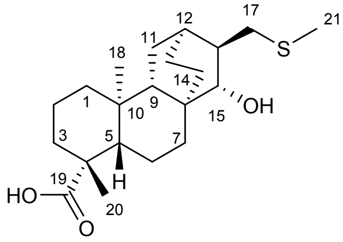


Fig. S33.^{13}C spectrum of **10**.

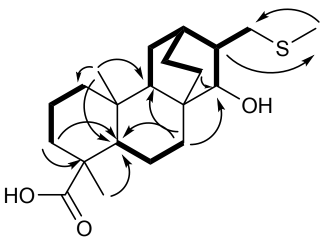
Fig. S34.



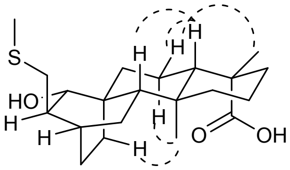
***ent*-(15R,16S)-15-hydroxy-17-methylsulfenylatisan-19-oic acid (11)**

Annotated NMR data for **11** in chloroform-*d.*

No.	δ_H (#H, mult., *J*(Hz))	δ_C
1	0.84 (1H, m)	39.9
	1.62 (1H, m)	
2	1.41 (1H, m)	18.8
	1.87 (1H, m)	
3	1.01 (1H, m)	38.0
	2.16 (1H, m)	
4	-	43.8
5	1.02 (1H, m)	57.1
6	1.77 (2H, m)	20.0
7	1.03 (1H, m)	35.5
	1.70 (1H, m)	
8	-	36.2
9	0.86 (1H, m)	50.8
10	-	38.5
11	1.16 (1H, dd, 6.4,13.9)	22.8
	1.51 (1H, m)	
12	1.65 (1H, m)	29.3
13	1.47 (1H, m)	20.2
	1.66 (1H, m)	
14	1.47 (1H, m)	27.6
	1.58 (1H, m)	
15	2.92 (1H, dd, 1.7, 4.4)	84.4
16	1.61 (1H, m)	46.7
17	2.53 (2H, m)	39.1
18	0.92 (3H, s)	12.5
19	-	183.9
20	1.24 (3H, s)	29.0
21	2.13 (3H, s)	15.7



Key COSY (bold) and HMBC (arrows) correlations



Key NOESY correlations

Fig. S35.

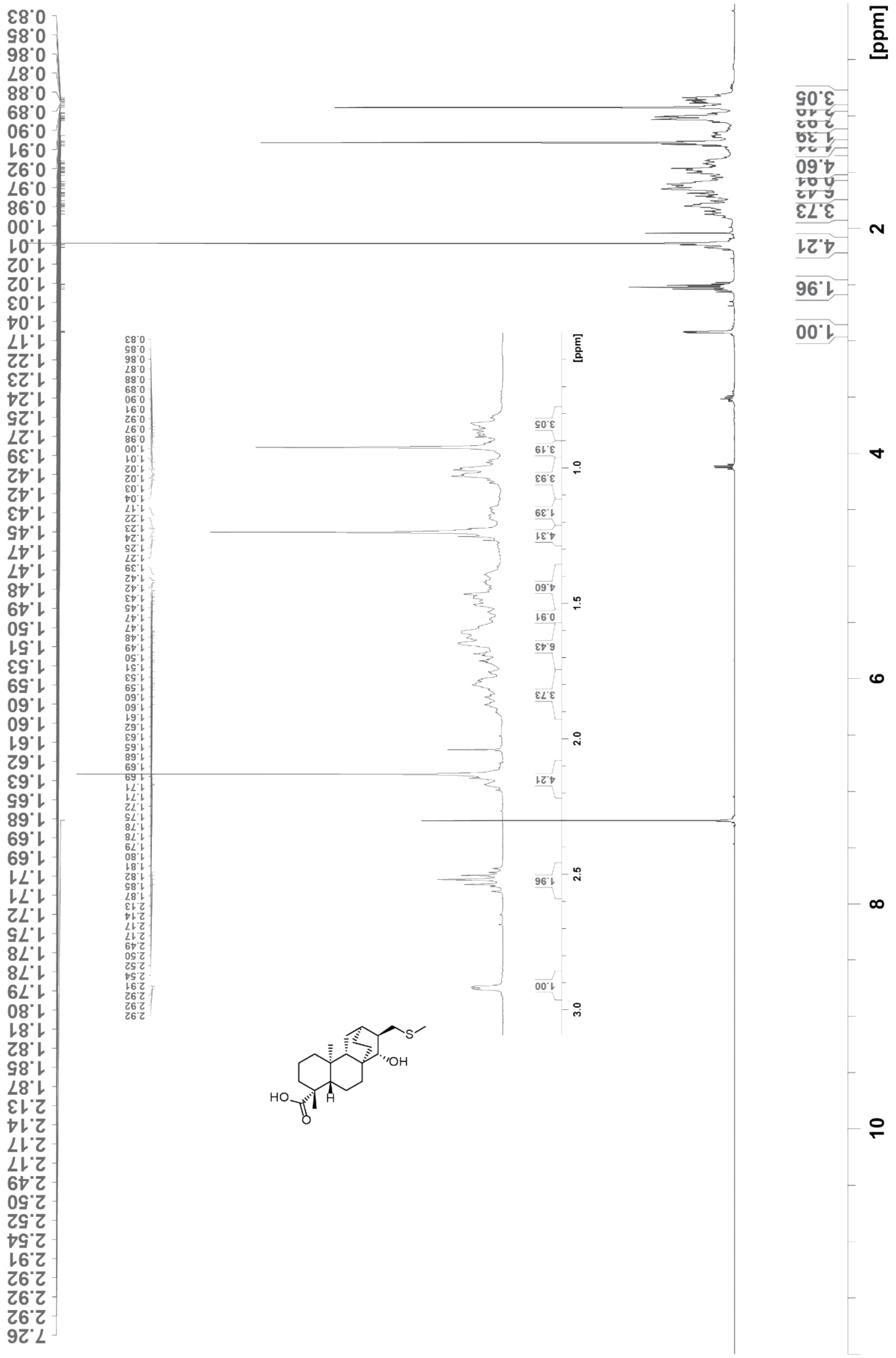


Fig. S35. ^{1}H spectrum of **11**.

Fig. S36.

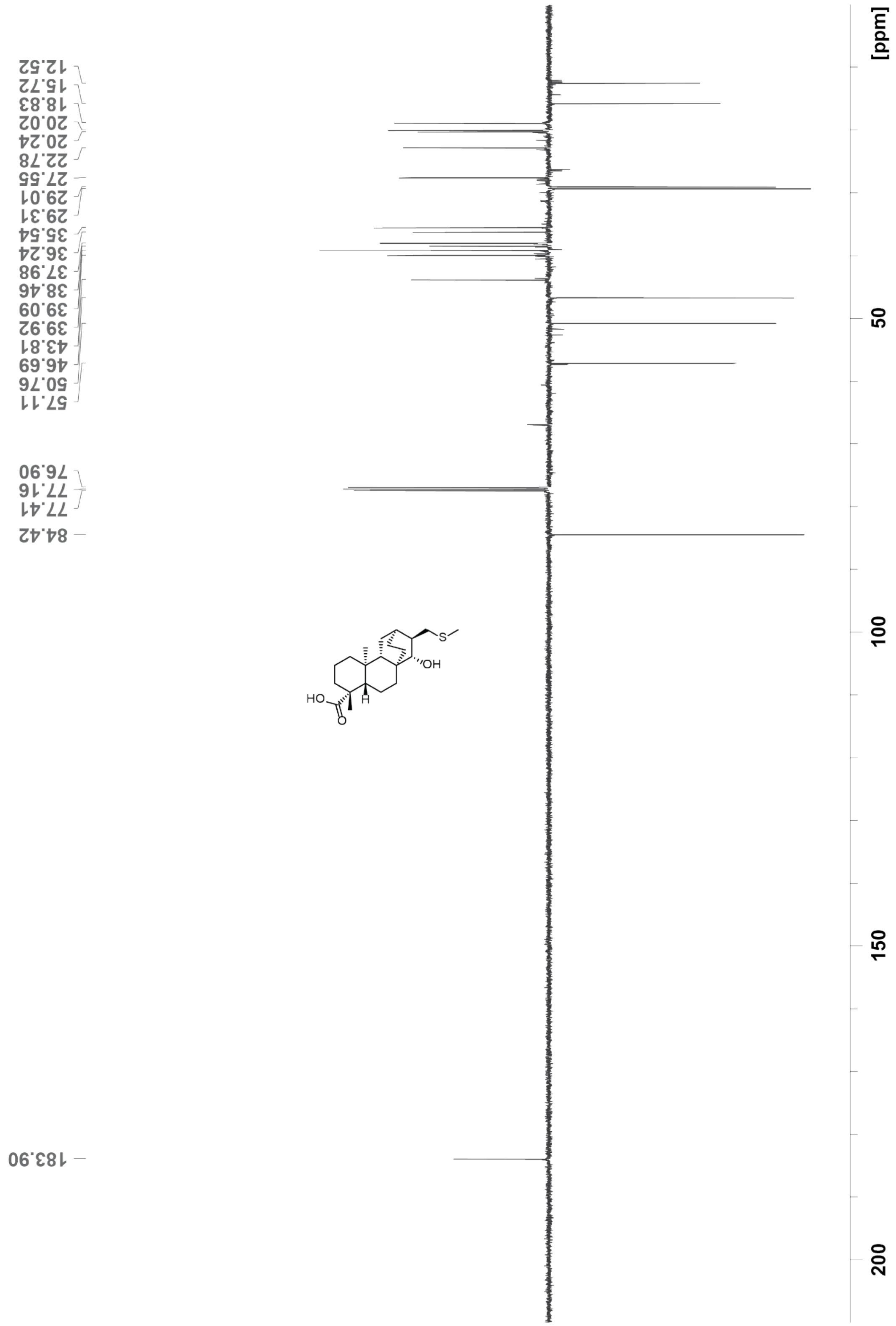
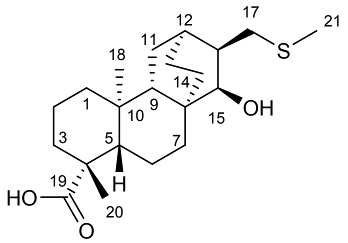


Fig. S36. ^{13}C spectrum of **11**.

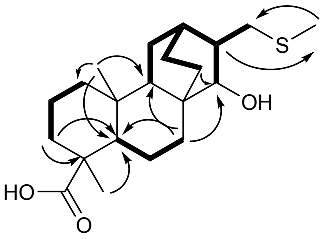
Fig. S37.



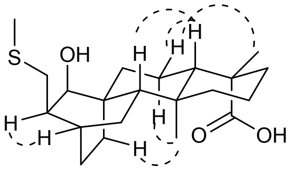
***ent*-(15S,16S)-15-hydroxy-17-methylsulfenylatisan-19-oic acid (12)**

Annotated NMR data for **12** in chloroform-*d.*

No.	δ_H (#H, mult., *J*(Hz))	δ_C
1	0.92 (1H, m) 1.58 (1H, m)	40.1
2	1.40 (1H, m) 1.80 (1H, m)	18.7
3	1.01 (td, 4.2, 13.5, 17.6) 2.14 (1H, m)	38.0
4	-	43.9
5	1.10 (1H, m)	56.7
6	1.70 (1H, m) 1.78 (1H, m)	20.0
7	1.11 (1H, m) 1.70 (1H, m)	34.0
8	-	35.8
9	1.63 (1H, m)	41.7
10	-	38.2
11	1.1 (1H, m) 1.63 (1H, m)	22.5
12	1. 51 (1H, m)	31.3
13	1.47 (2H, m)	27.8
14	0.89 (1H, m) 1.95 (1H, m)	26.9
15	3.46 (1H, d, 8.8)	74.6
16	1.97 (1H, m)	40.1
17	2.51 (1H, dd, 4.8, 12.1) 2.87 (t, 11.8)	34.9
18	0.90 (3H, s)	12.7
19	-	184.4
20	1.23 (3H, s)	29.0
21	2.15 (3H, s)	15.8



Key COSY (bold) and HMBC (arrows) correlations



Key NOESY correlations

Fig. S38.

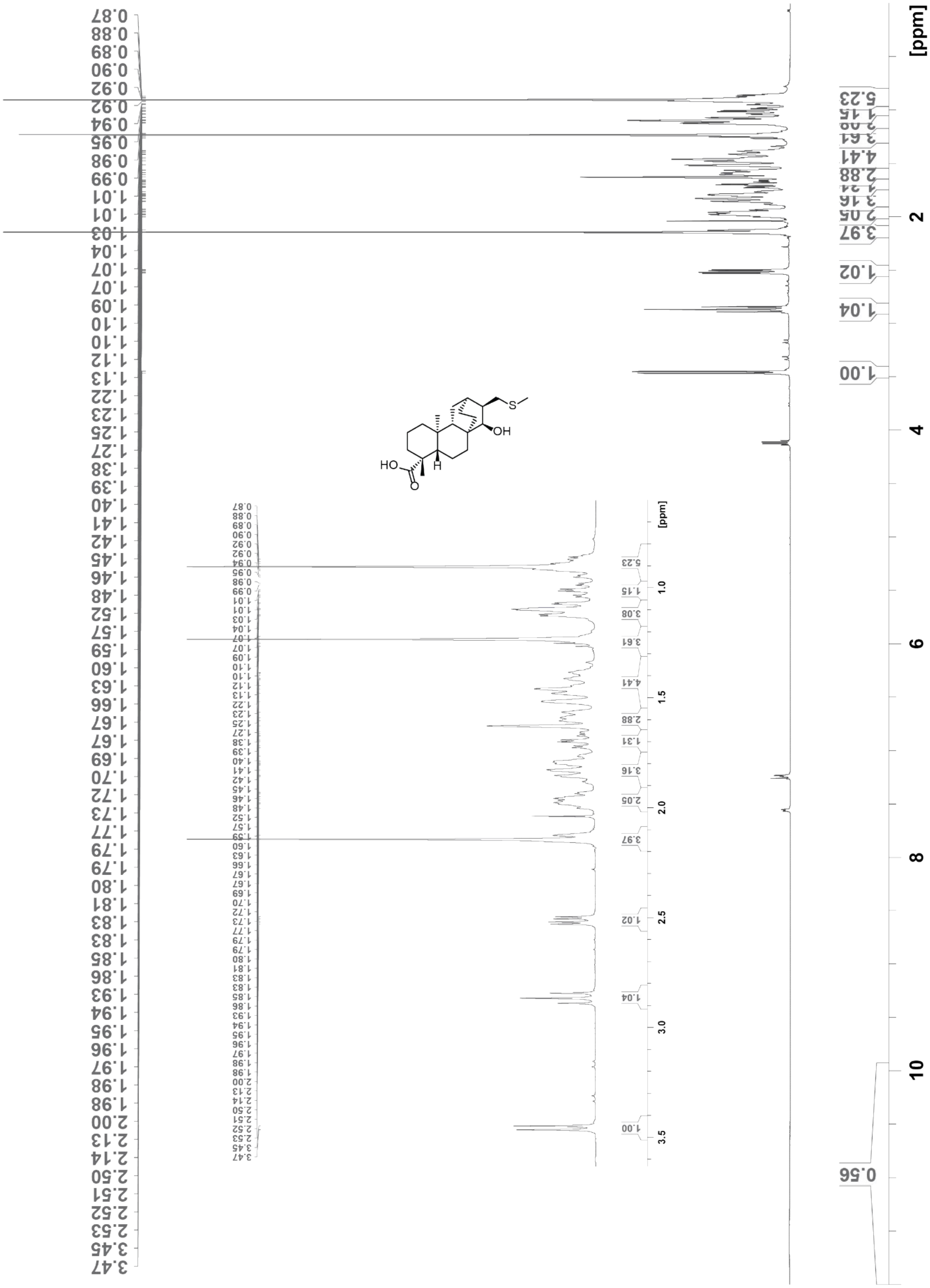


Fig. S38. ^{1}H spectrum of **12**.

Fig. S39.

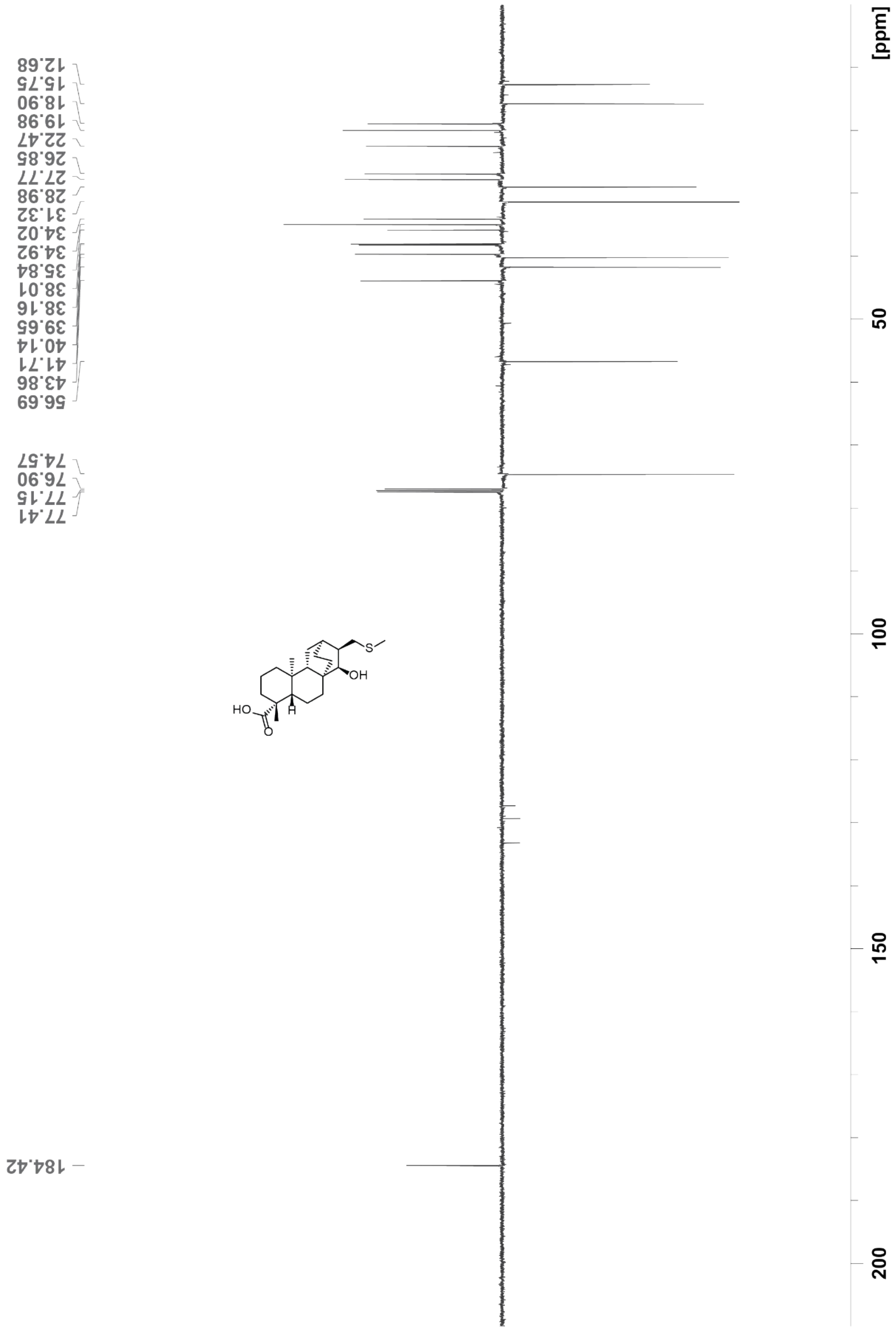
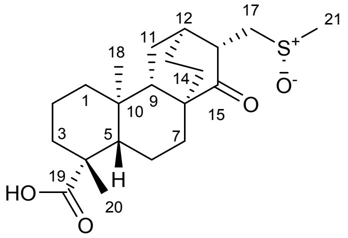


Fig. S39. ^{13}C spectrum of **12**.

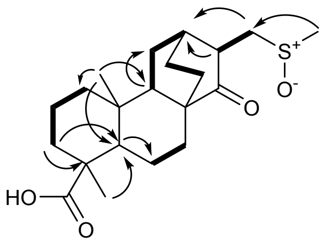
Fig. S40.



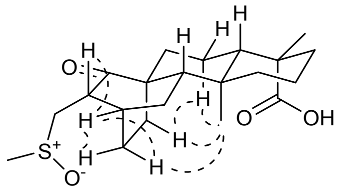
ent-(16R,R)-17-methylsulfinyl-15-oxoatisan-19-oic acid (13B)

Annotated NMR data for **13B** in chloroform-*d*.

No.	δ_H (#H, mult., J(Hz))	δ_C
1	0.88 (1H, m)	39.7
	1.66 (1H, m)	
2	1.44 (1H, m)	18.7
	1.85 (1H, m)	
3	1.03 (1H, m)	37.8
	2.18 (1H, d_{app}, 13.3)	
4	-	43.7
5	1.02 (1H, m)	56.2
6	1.63 (1H, m)	21.1
	1.74 (1H, m)	
7	1.13 (1H, m)	25.9
	2.30 (1H, m)	
8	-	45.3
9	1.39 (1H, dd, 7.2, 11.0)	45.3
10	-	39.2
11	1.63 (1H, m)	28.2
	1.84 (1H, m)	
12	2.35 (1H, m)	30.9
13	1.73 (1H, m)	19.5
	1.84 (1H, m)	
14	1.50 (1H, m)	31.1
	1.68 (1H, m)	
15	-	216.9
16	2.78 (1H, m)	44.7
17	2.68 (1H, dd, 10.3, 13.0)	53.0
	3.18 (1H, dd, 3.6, 13.0)	
18	1.02 (3H, s)	13.0
19	-	182.4
20	1.25 (3H, s)	29.0
21	2.63 (3H, s)	38.8



Key COSY (bold) and HMBC (arrows) correlations



Key NOESY correlations

Fig. S41.

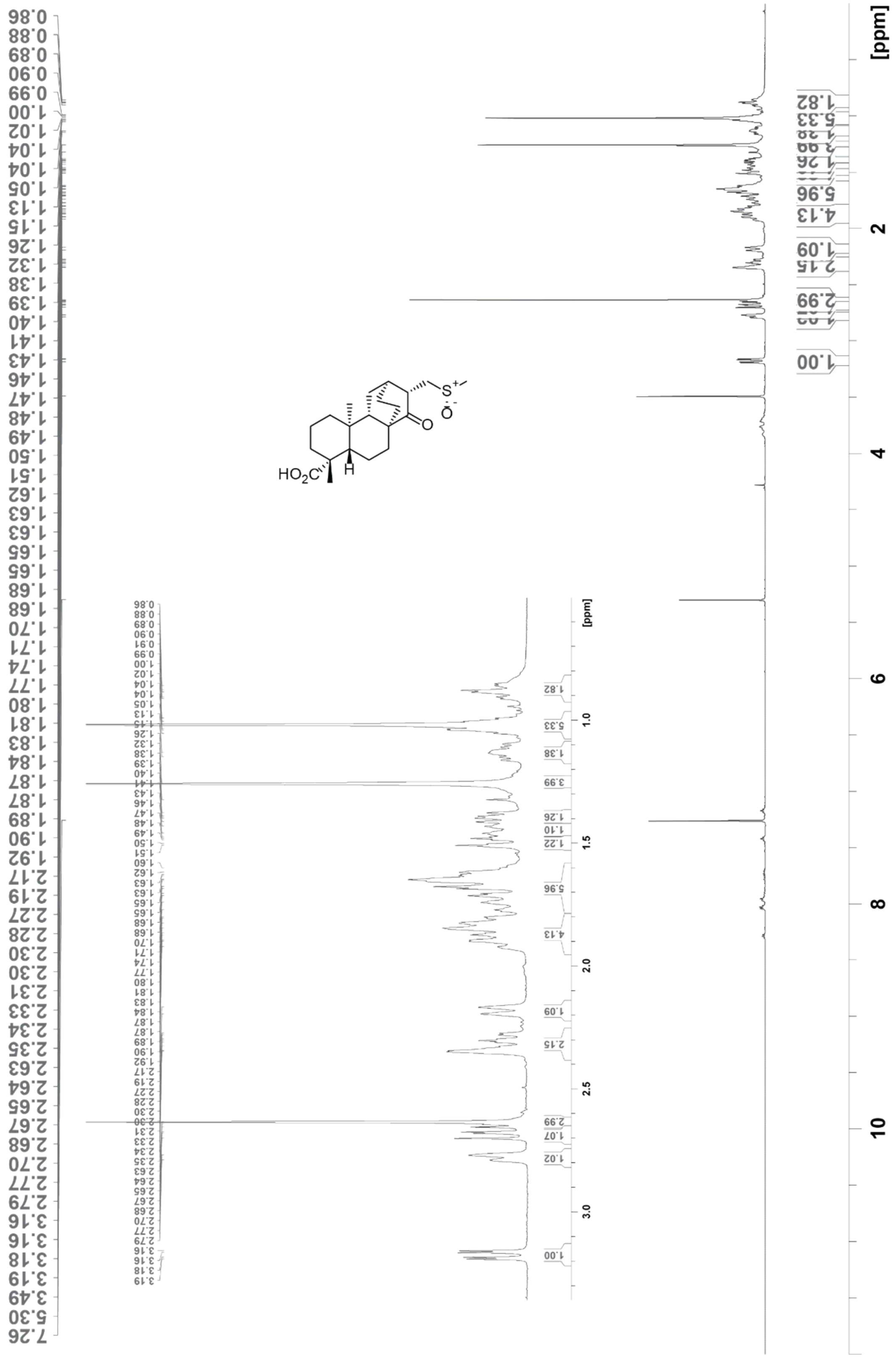


Fig. S41. ^{1}H spectrum of **13B**.

Fig. S42.

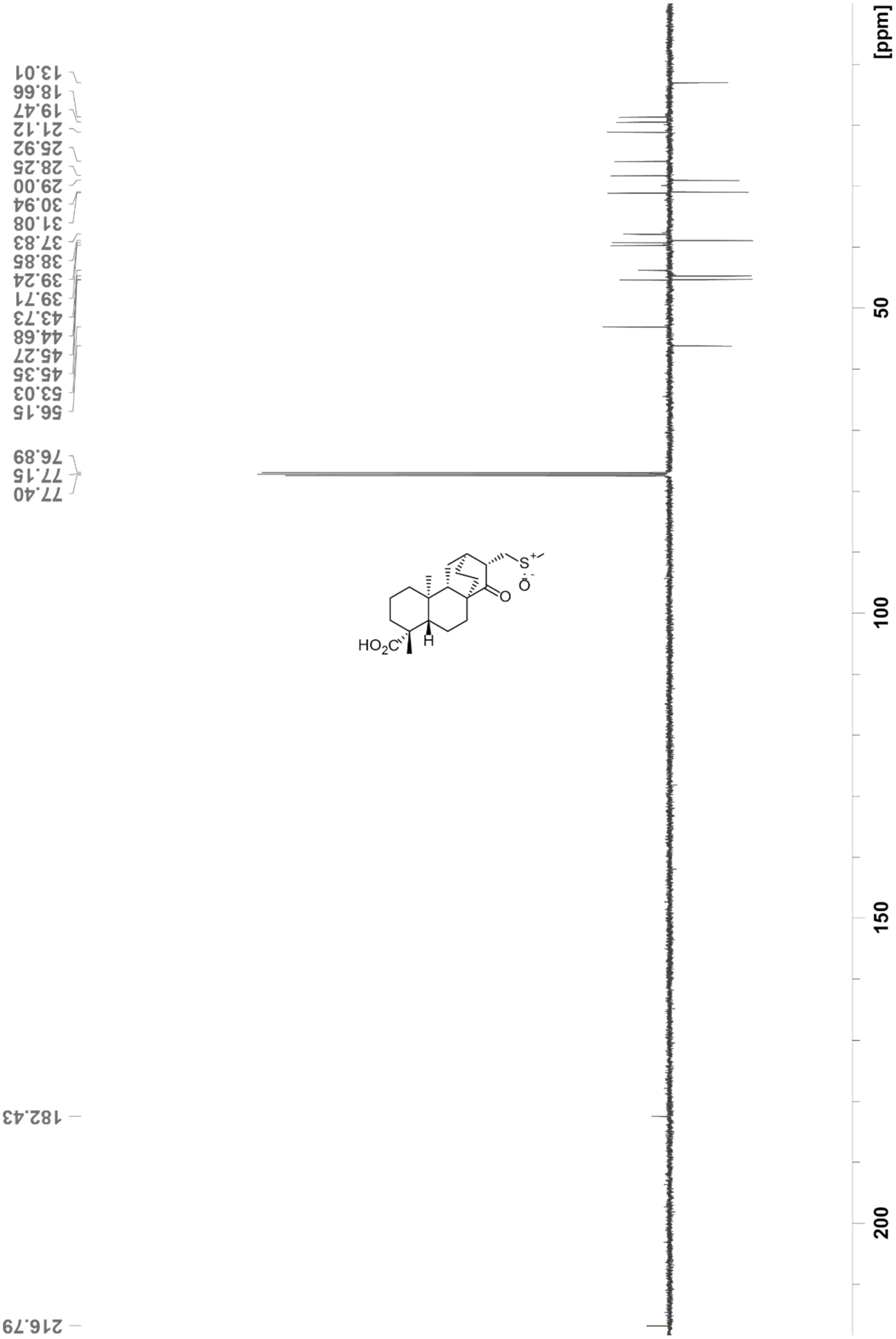
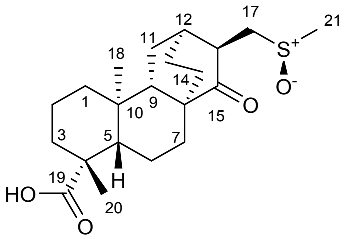


Fig. S42. ^{13}C spectrum of **13B**.

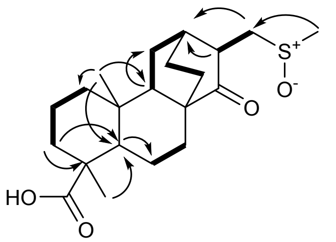
Fig. S43.



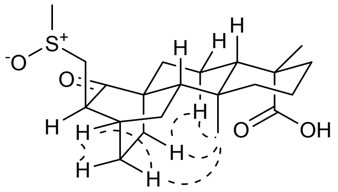
***ent*-(16S,S)-17-methylsulfinyl-15-oxoatisan-19-oic acid (14A)**

Annotated NMR data for **14A** in chloroform-*d*.

No.	δ_H (#H, mult., *J*(Hz))	δ_C
1	0.82 (1H, td, 3.6, 13.1, 16.9) 1.61 (1H, m)	40.0
2	1.43 (1H, m) 1.87 (1H, m)	18.8
3	1.00 (1H, m) 2.18 (1H, $d_{app.}$, 13.6)	38.0
4	-	43.8
5	1.02 (1H, m)	56.3
6	1.76 (1H, m) 1.88 (1H, m)	26.0
7	1.36 (1H, m) 2.24 (1H, m)	23.6
8	-	45.3
9	1.17 (1H, dd, 6.8, 11.7)	47.9
10	-	39.6
11	1.49 (1H, m) 1.72 (1H, m)	23.0
12	2.33 (1H, m)	31.0
13	1.87 (2H, m)	19.4
14	1.40 (1H, m) 1.82 (1H, m)	30.3
15	-	216.8
16	2.82 (1H, m)	44.5
17	2.66 (1H, m) 3.18 (1H, m)	53.0
18	1.02 (3H, s)	12.7
19	-	182.3
20	1.25 (3H, s)	29.0
21	2.64 (3H, s)	38.9



Key COSY (bold) and HMBC (arrows) correlations



Key NOESY correlations

Fig. S44.

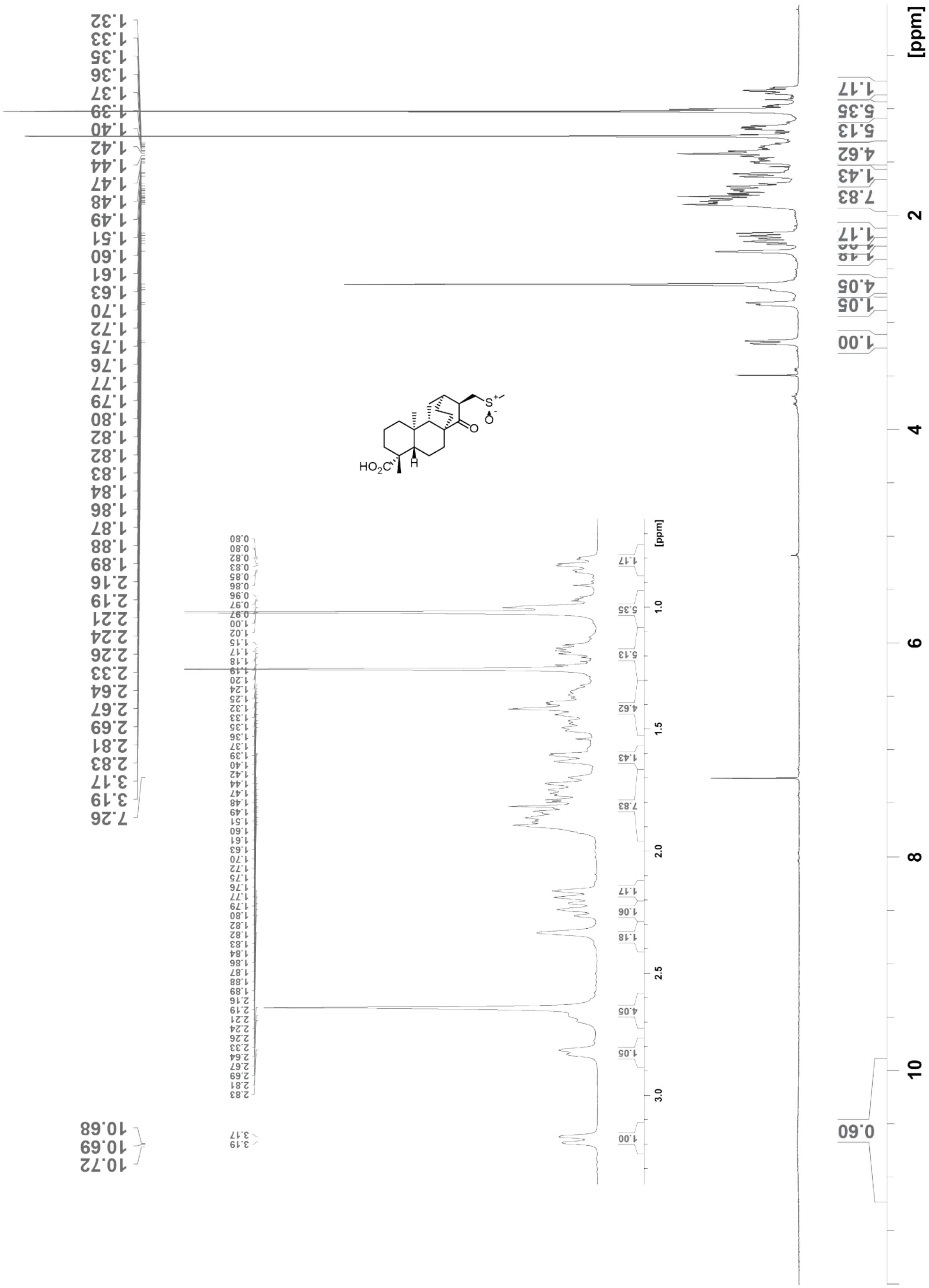


Fig. S44. ^{1}H spectrum of **14A**.

Fig. S45.

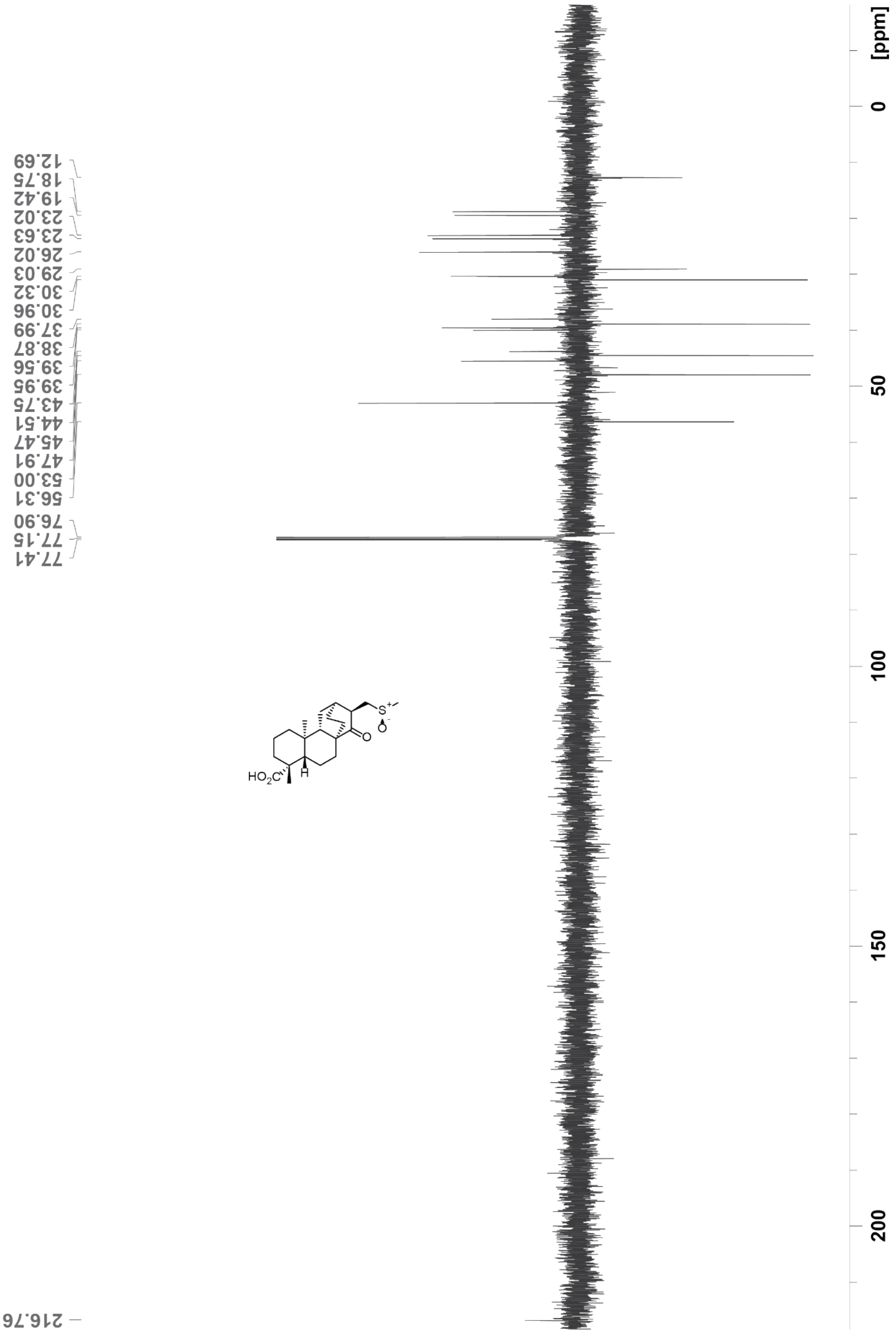


Fig. S45. ^{13}C spectrum of **14A**.

Fig. S46.

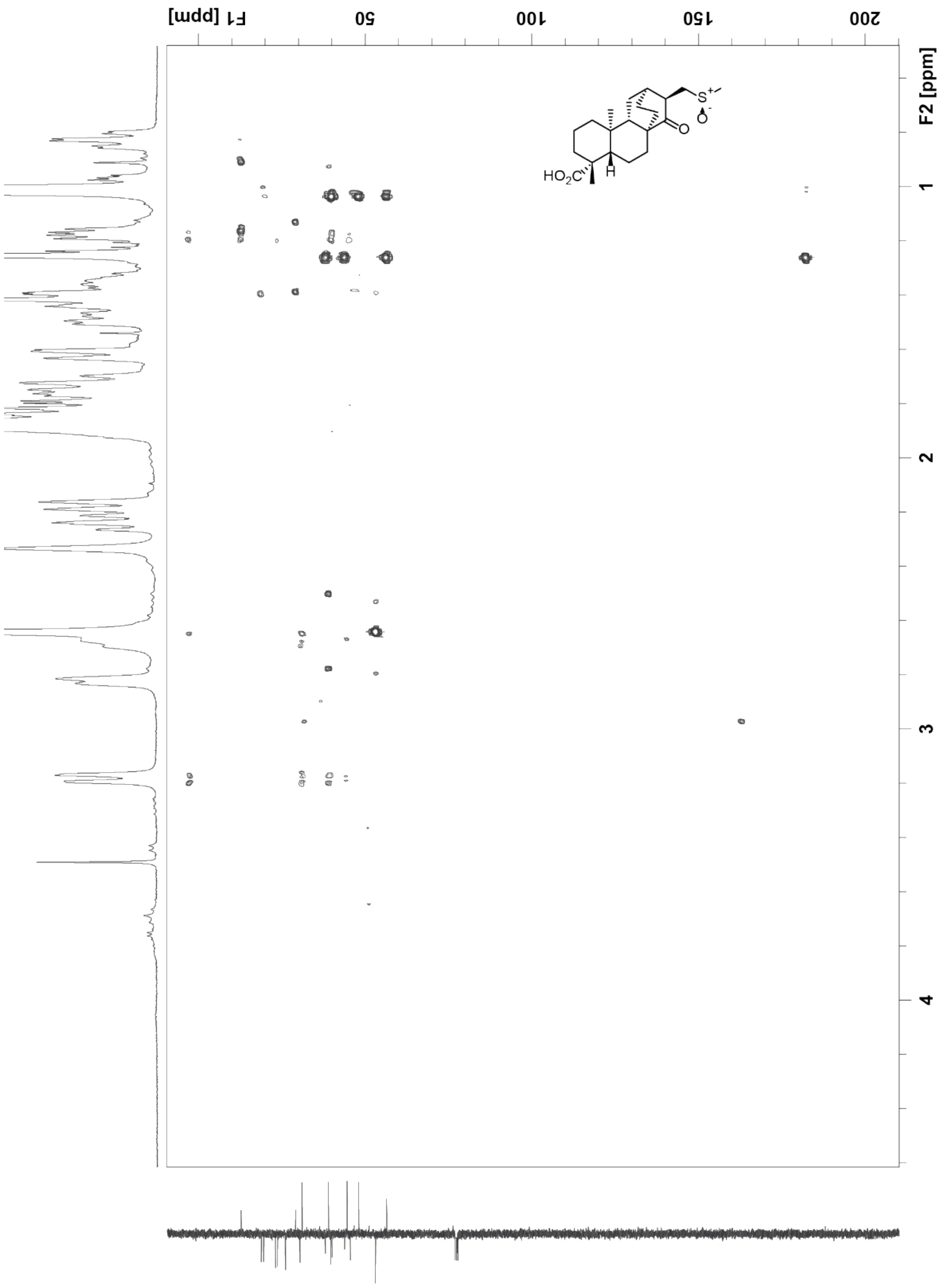
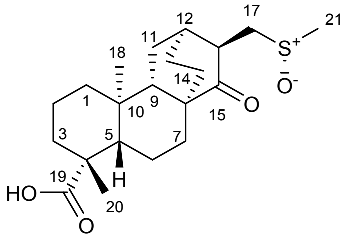


Fig. S46. ^{1}H-^{13}C HMBC spectrum of **14A**

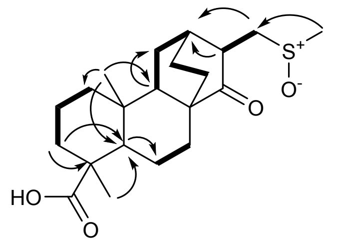
Fig. S47.



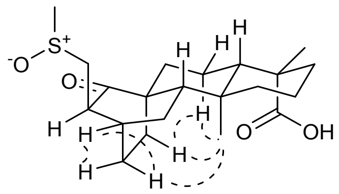
ent-(16S,R)-17-methylsulfinyl-15-oxoatisan-19-oic acid (14B)

Annotated NMR data for **14B** in chloroform-*d*.

No.	δ_H (#H, mult., *J*(Hz))	δ_C
1	0.83 (1H, td, 4.1, 13.6, 17.3) 1.61 (1H, m)	39.9
2	1.42 (1H, m) 1.83 (1H, m)	18.7
3	1.00 (1H, m) 2.17 (1H, d_{app}, 13.6)	37.9
4	-	43.7
5	1.01 (1H, m)	56.3
6	1.39 (1H, m) 1.83 (1H, m)	26.2
7	1.33 (1H, m) 2.23 (1H, m)	23.5
8	-	45.3
9	1.17 (1H, dd, 6.5, 11.4)	47.8
10	-	39.6
11	1.46 (1H, m) 1.80 (1H, m)	23.0
12	2.34 (1H, m)	32.1
13	1.89 (2H, m)	19.4
14	1.75 (1H, m) 1.80 (1H, m)	30.2
15	-	216.9
16	2.68 (1H, m)	47.1
17	2.78 (1H, dd, 8.0, 13.3) 3.06 (1H, dd, 4.8, 12.9)	54.9
18	1.01 (3H, s)	12.7
19	-	181.4
20	1.24 (3H, s)	29.0
21	2.67 (3H, s)	40.0



Key COSY (bold) and HMBC (arrows) correlations



Key NOESY correlations

Fig. S48.

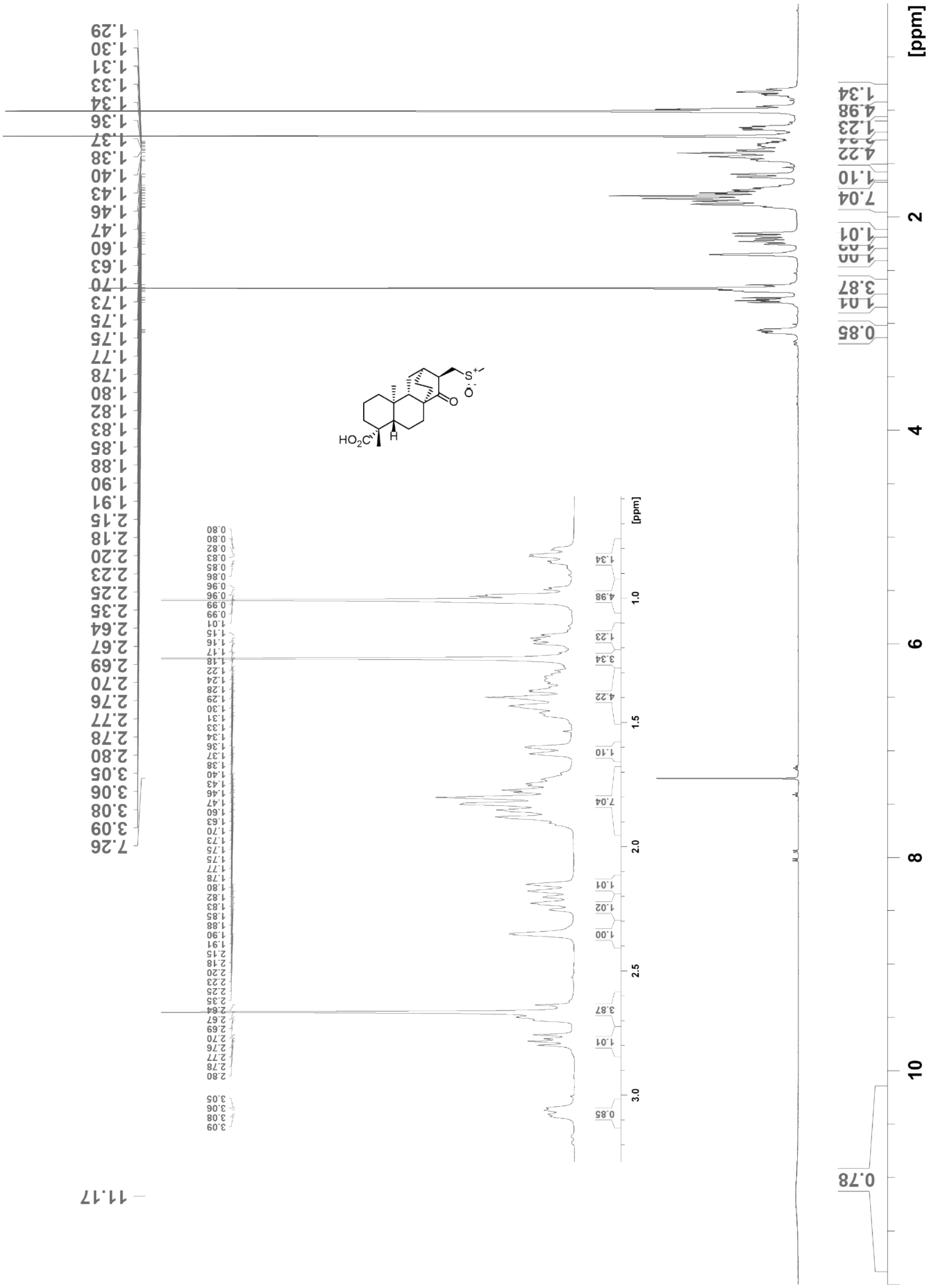


Fig. S48. ^{1}H spectrum of **14B**.

Fig. S49.

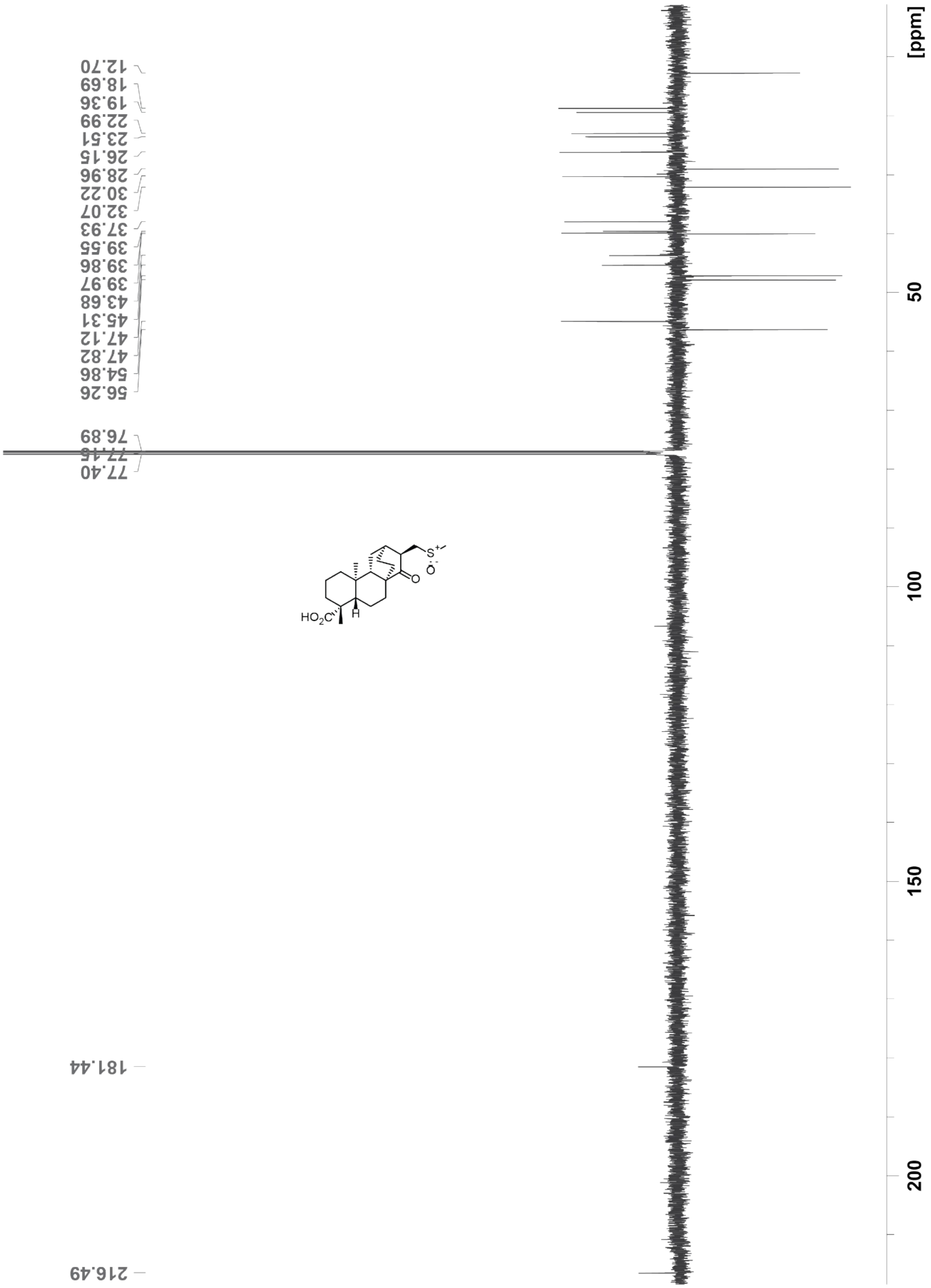
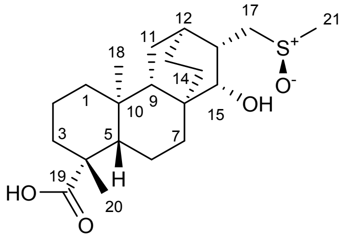


Fig. S49. ^{13}C spectrum of **14B**.

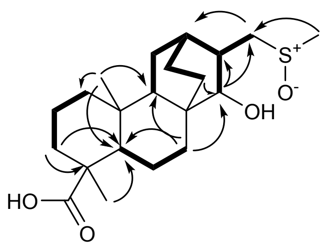
Fig. S50



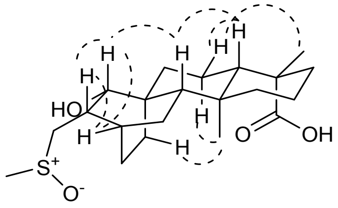
***ent*-(15R,16R,S)-15-hydroxy-17-methylsulfinylatisan-19-oic acid (15A)**

Annotated NMR data for **15A** in methanol-d_4

No.	δ_H (#H, mult., *J*(Hz))	δ_C
1	0.93 (1H, m)	41.3
	1.67 (1H, m)	
2	1.38 (1H, m)	20.0
	1.94 (1H, m)	
3	1.01 (1H, m)	39.2
	2.14 (1H, br. d, 13.2)	
4	-	44.6
5	1.00 (1H, m)	58.1
6	1.80 (2H, m)	21.2
7	1.03 (1H, m)	38.3
	1.71 (1H, m)	
8	-	36.7
9	1.06 (1H, m)	50.7
10	-	39.5
11	1.45 (1H, m)	30.1
	1.58 (1H, m)	
12	1.56 (1H, m)	32.6
13	1.34 (1H, m)	21.9
	1.67 (1H, m)	
14	1.48 (1H, m)	21.0
	1.67 (1H, m)	
15	3.39 (1H, m)	77.3
16	2.42 (1H, m)	37.7
17	2.54 (1H, dd, 4.0, 12.7)	57.1
	3.40 (1H, m)	
18	0.99 (3H, s)	13.6
19	-	181.5
20	1.17 (3H, s)	29.5
21	2.65 (3H, s)	38.7



Key COSY (bold) and HMBC (arrows) correlations



Key NOESY correlations

Fig. S51.

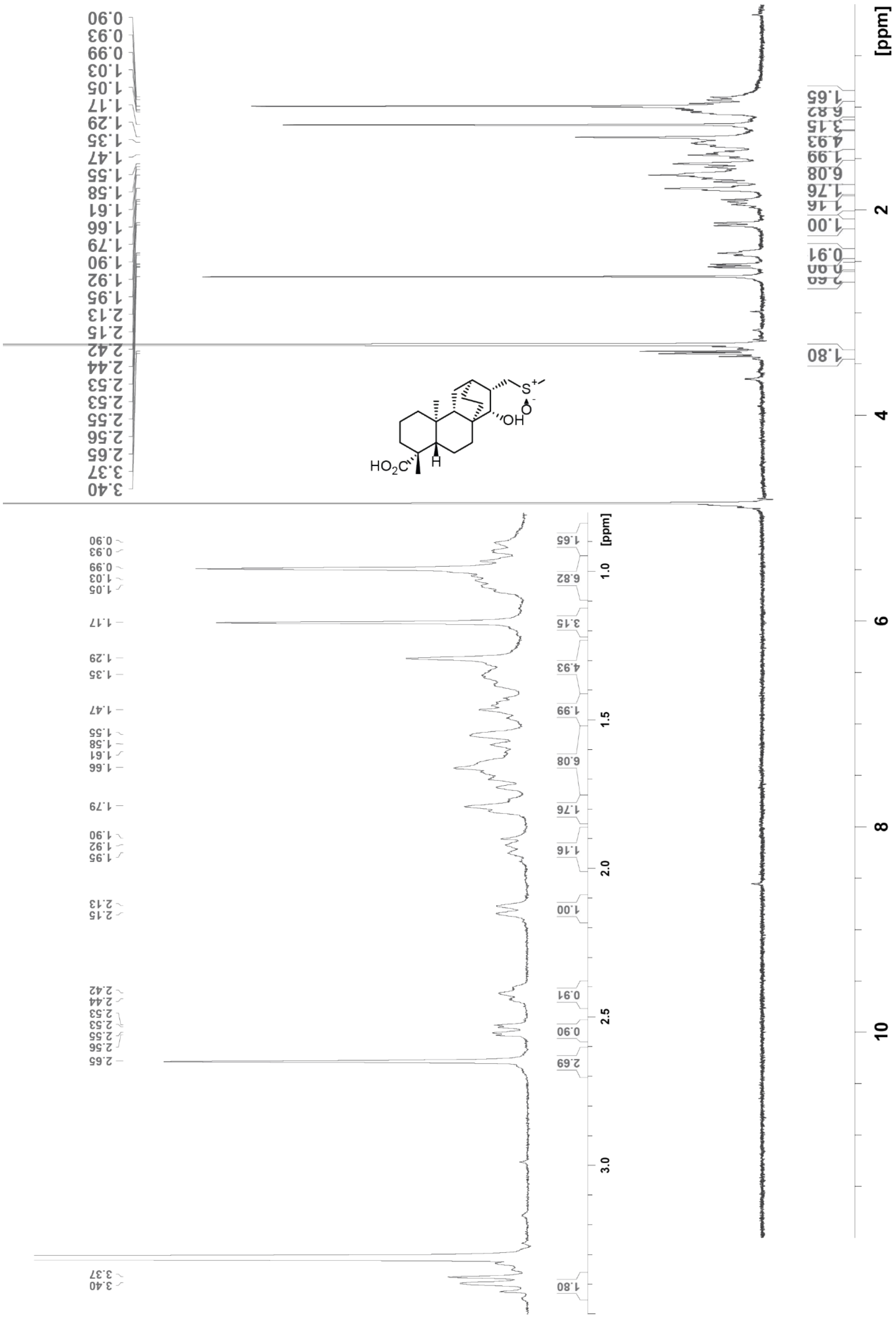


Fig. S51. ^{1}H spectrum of **15A**.

Fig. S52.

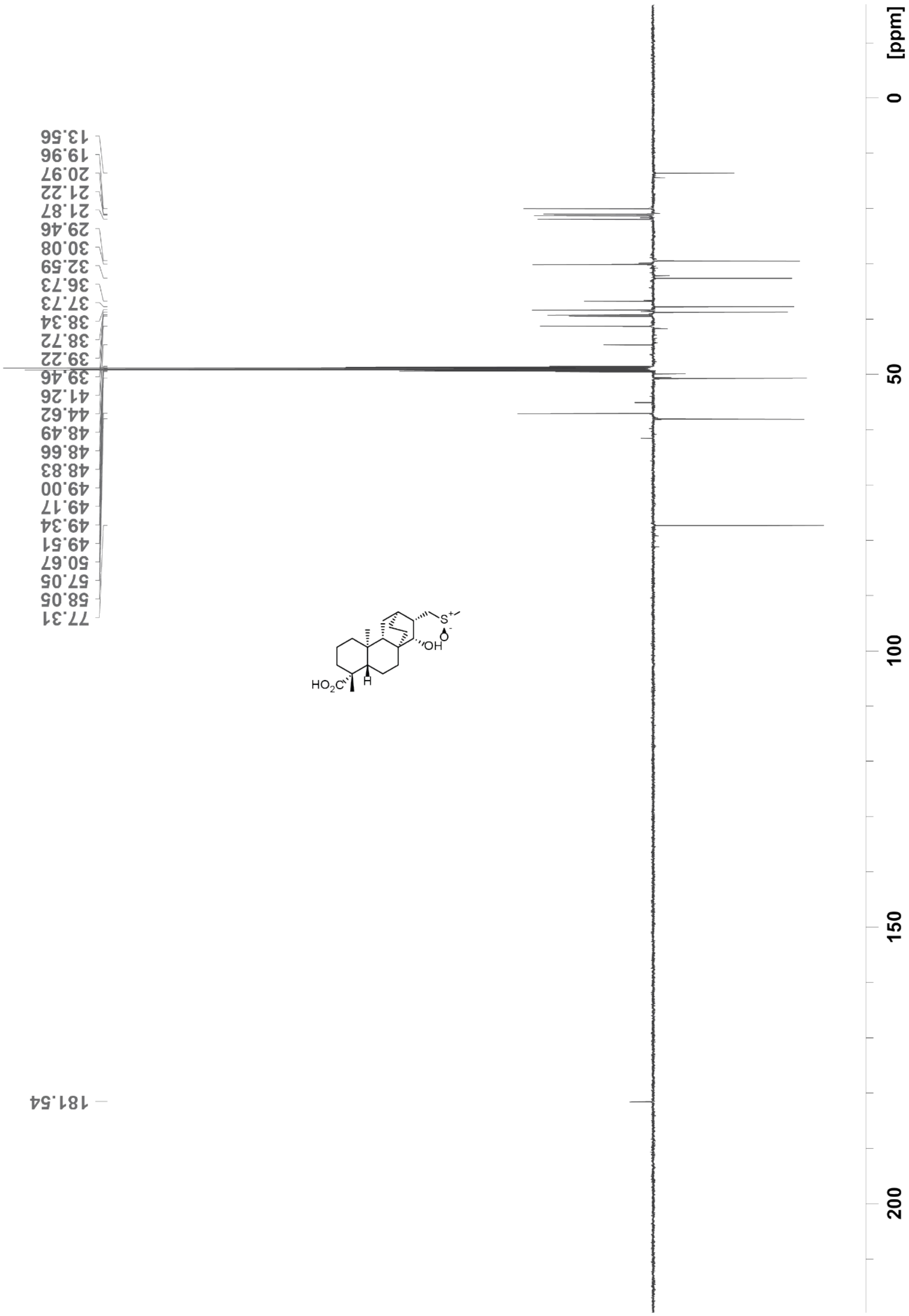
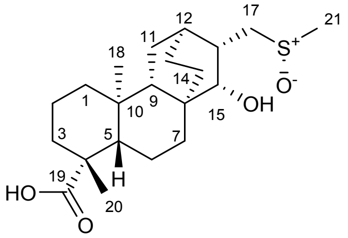


Fig. S52. ^{13}C spectrum of **15A**.

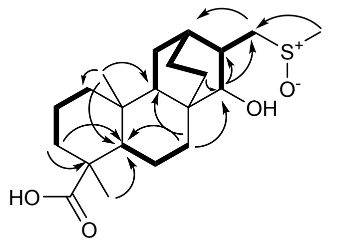
Fig. S53.



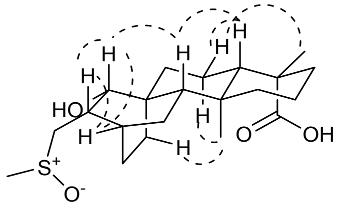
***ent*-(15R,16R,R)-15-hydroxy-17-methylsulfinylatisan-19-oic acid (15B)**

Annotated NMR data for **15B** in methanol-*d*$_4$.

No.	δ_H (#H, mult., *J*(Hz))	δ_C
1	0.95 (1H, m)	41.3
	1.67 (1H, m)	
2	1.39 (1H, m)	20.0
	1.91 (1H, m)	
3	1.05 (1H, m)	39.1
	2.13 (1H, d, 13.1)	
4	-	44.6
5	1.05 (1H, m)	58.0
6	1.74-1.78 (2H, m)	21.3
7	1.08 (1H, m)	38.5
	1.75 (1H, m)	
8	-	36.7
9	1.08 (1H, m)	50.7
10	-	39.5
11	1.46 (1H, m)	29.9
	1.57 (1H, m)	
12	1.69 (1H, m)	31.1
13	1.34 (1H, m)	21.6
	1.68 (1H, m)	
14	1.49 (1H, m)	21.0
	1.66 (1H, m)	
15	3.36 (1H, d, 9.2)	78.1
16	2.33 (1H, m)	38.9
17	2.78 (1H, dd, 7.6, 13.2)	55.3
	3.29 (1H, dd, 7.6, 13.2)	
18	0.98 (3H, s)	13.6
19	-	181.6
20	1.20 (3H, s)	29.4
21	2.67 (3H, s)	38.5



Key COSY (bold) and HMBC (arrows) correlations



Key NOESY correlations

Fig. S54.

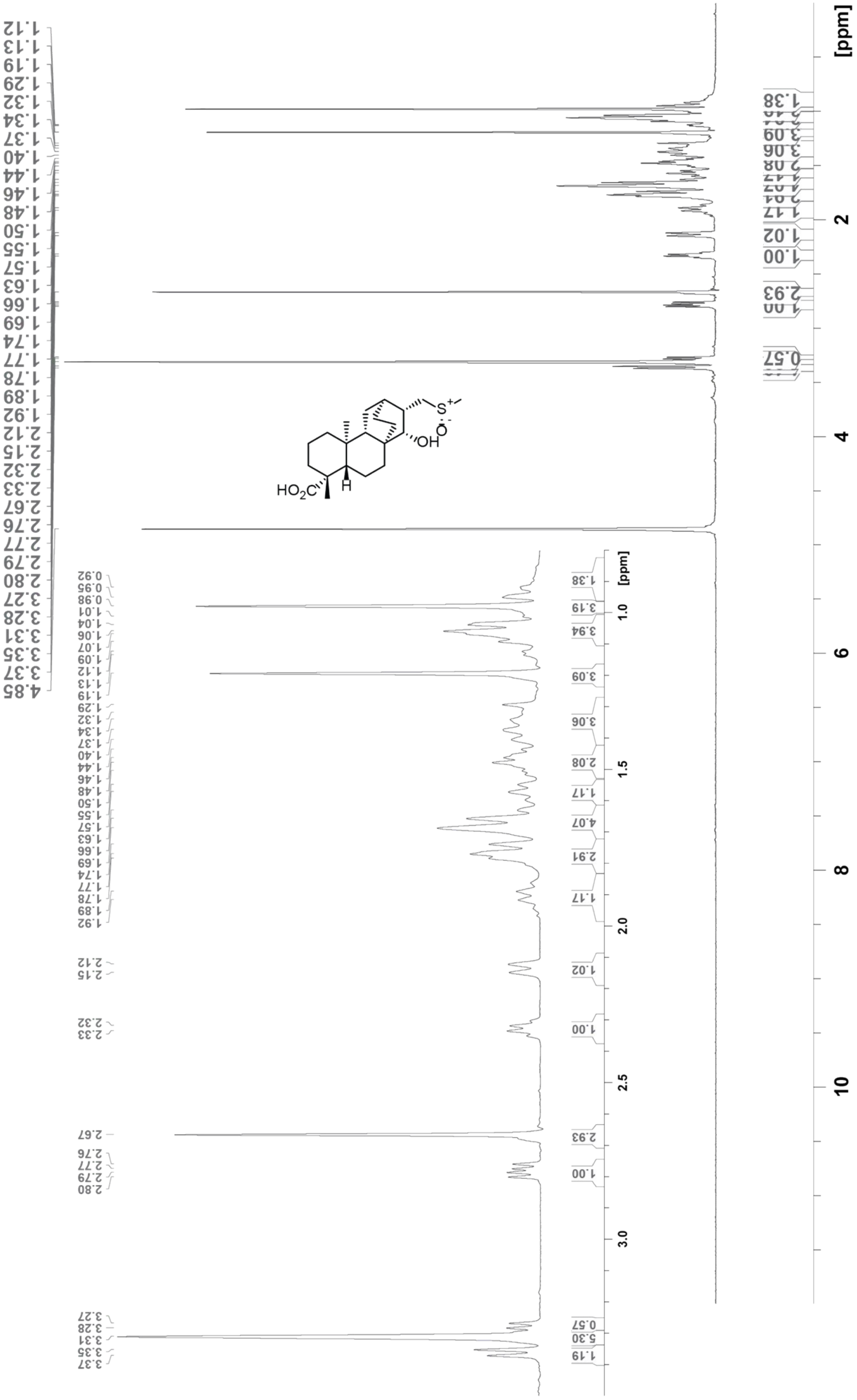


Fig. S54. ^{1}H spectrum of **15B**.

Fig. S55.

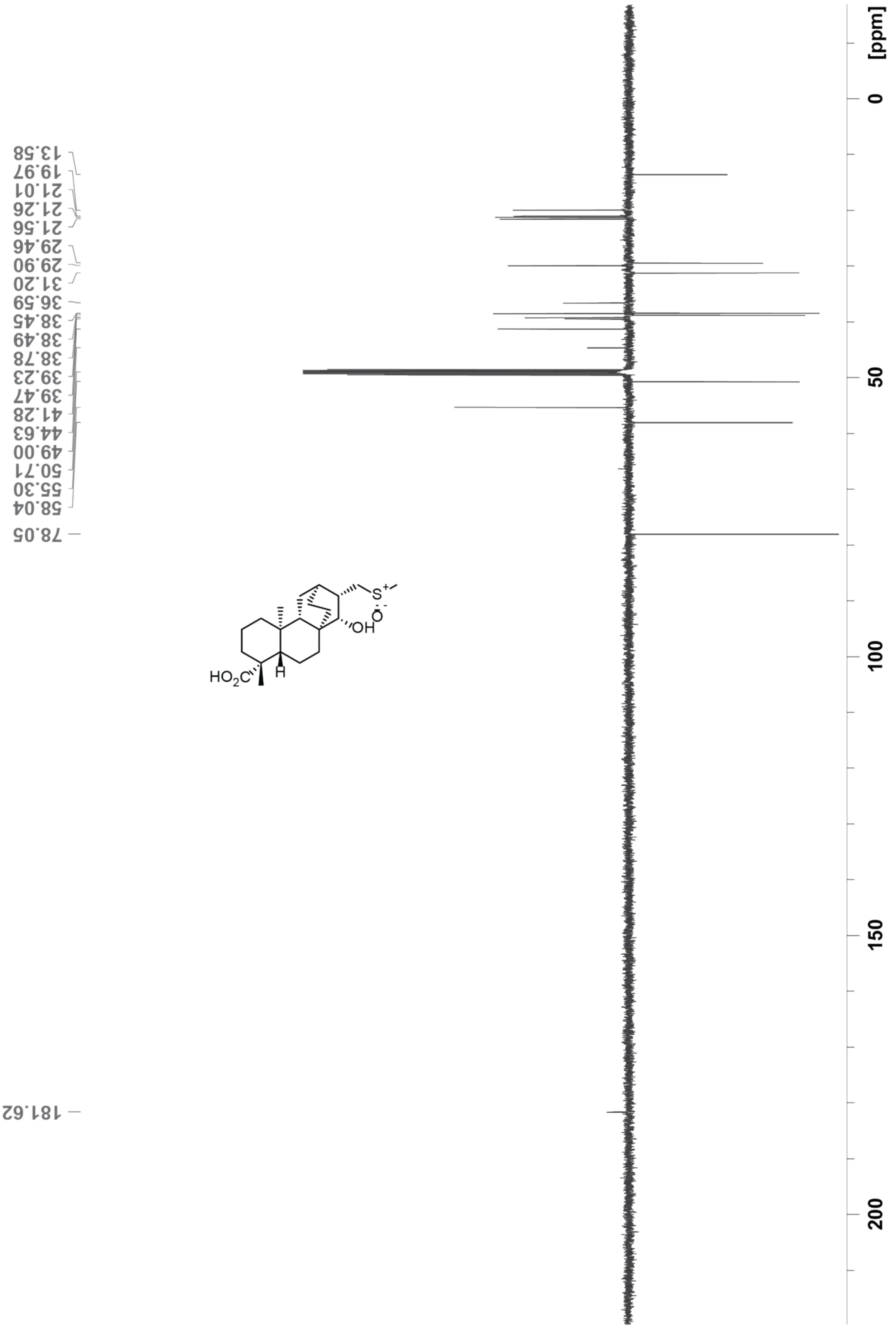
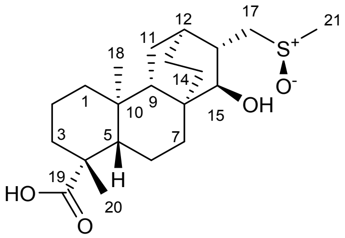


Fig. S55. ^{13}C spectrum of **15B**.

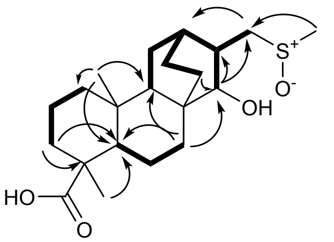
Fig. S56.



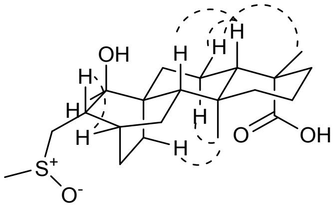
Serofendic acid A (1A)

Annotated NMR data for **1A** in methanol-*d_4*.

No.	δ_H (#H, mult., *J*(Hz))	δ_C
1	0.88 (1H, m)	41.2
	1.62 (1H, m)	
2	1.38 (1H, m)	20.0
	1.89 (1H, m)	
3	1.03 (1H, m)	39.2
	2.13 (1H, d, 13.0)	
4	-	44.7
5	1.04 (1H, m)	57.9
6	1.79 (1H, m)	20.9
	1.86 (1H, m)	
7	1.07 (1H, m)	34.3
	1.71 (1H, m)	
8	-	37.7
9	1.57 (1H, m)	42.8
10	-	39.2
11	1.41 (1H, m)	30.0
	1.59 (1H, m)	
12	1.77 (1H, m)	32.2
13	1.38 (1H, m)	22.2
	1.64 (1H, m)	
14	0.83 (1H, m)	28.2
	2.02 (1H, ddd, 2.8, 11.8, 14.1)	
15	2.93 (1H, d, 4.4)	81.3
16	1.92 (1H, m)	44.4
17	2.83 (1H, dd, 6.1, 13.1)	60.9
	2.95 (1H, dd, 9.3, 13.1)	
18	0.95 (3H, s)	13.4
19	-	181.7
20	1.20 (3H, s)	29.6
21	2.68 (3H, s)	38.7



Key COSY (bold) and HMBC (arrows) correlations



Key NOESY correlations

Fig. S57.

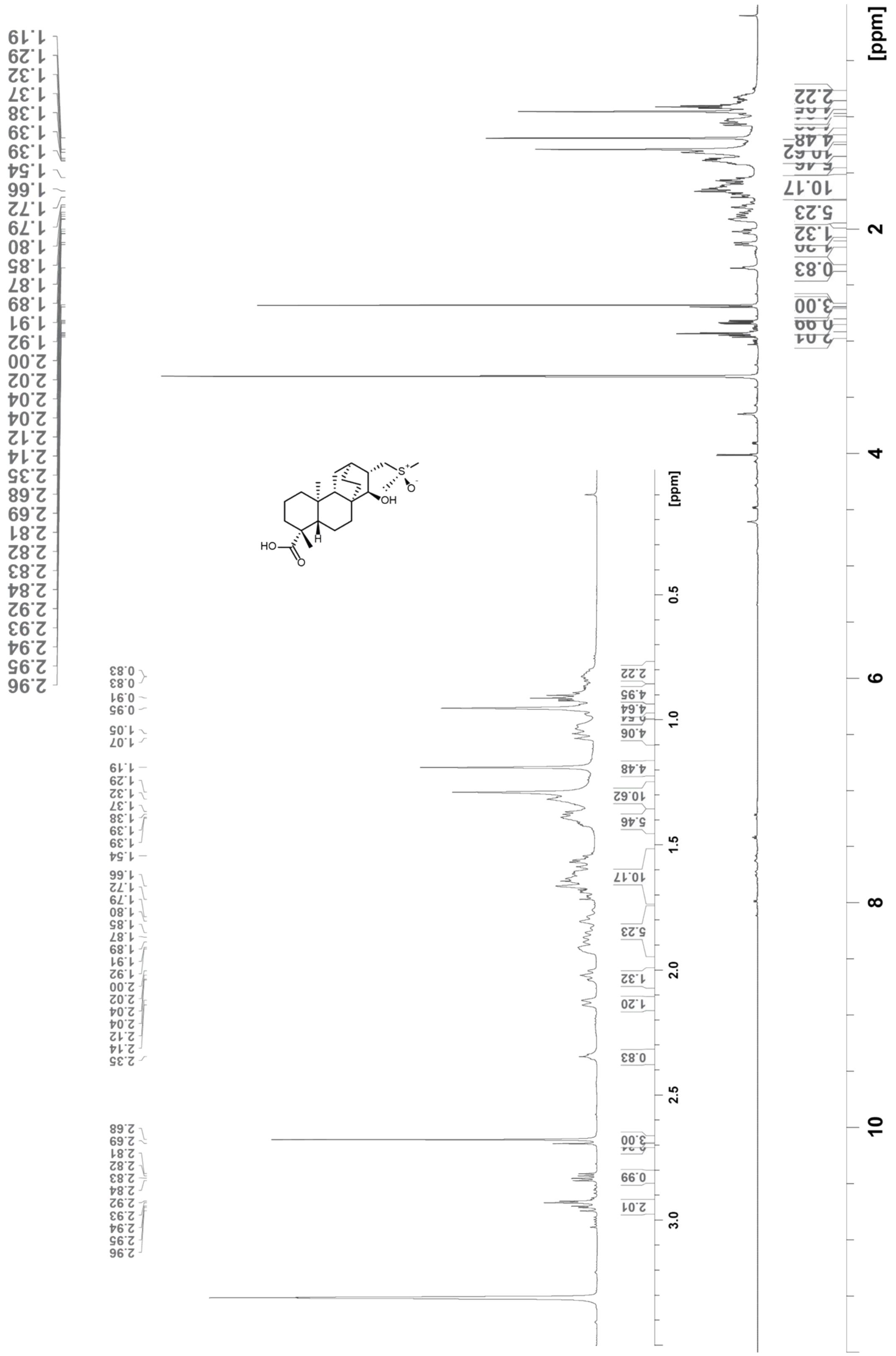


Fig. S57. ^{1}H spectrum of **1A**.

Fig. S58.

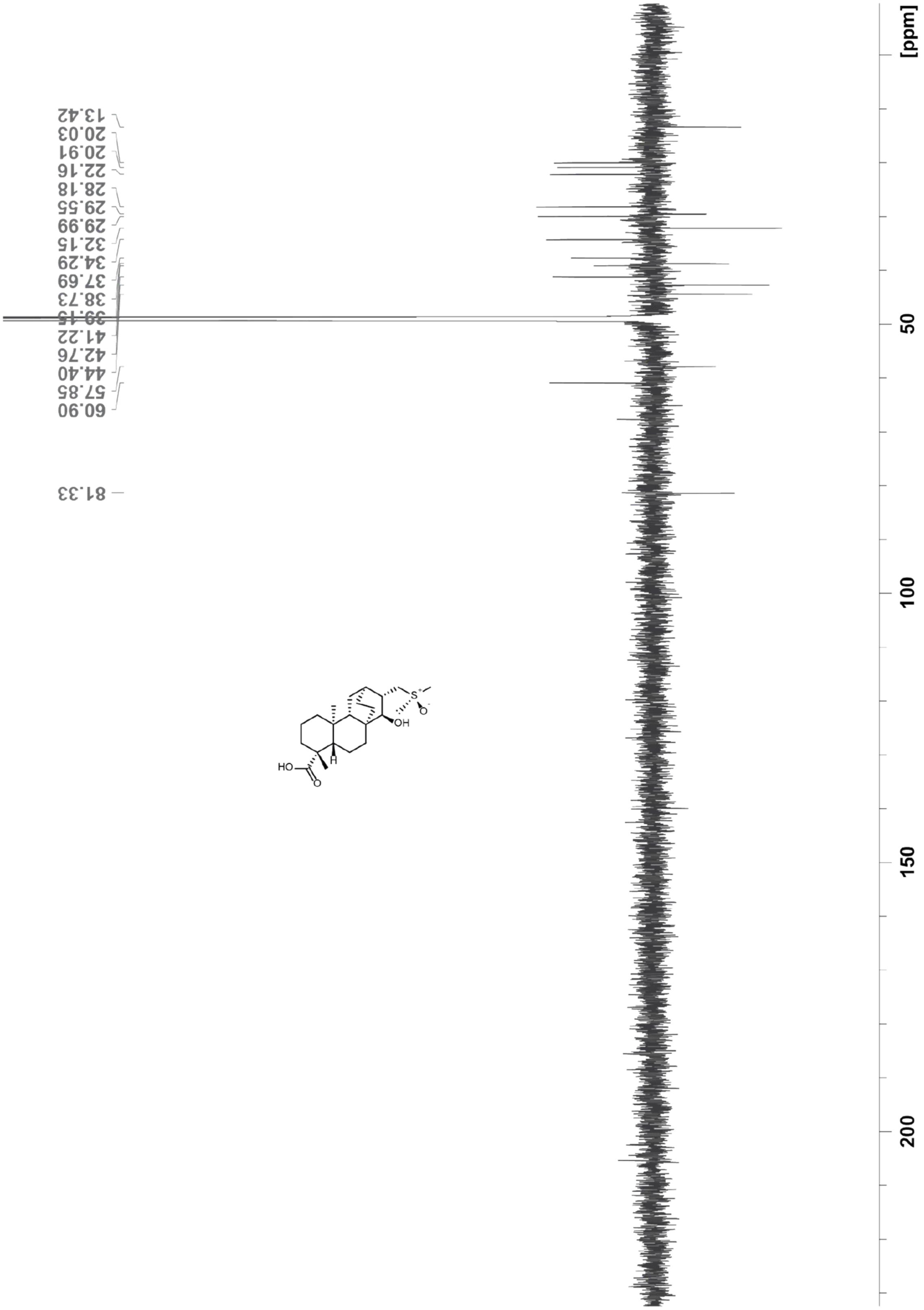
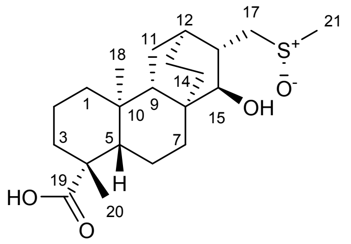


Fig. S58. ^{13}C spectrum of **1A**.

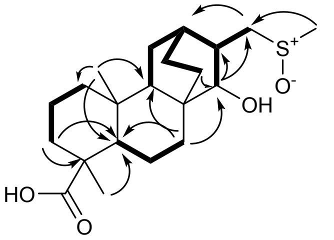
Fig. S59.



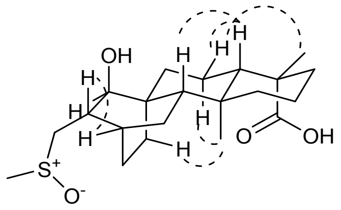
Serofendic acid B (1B)

Annotated NMR data for **1B** in methanol-*d*$_4$.

No.	δ_H (#H, mult., *J*(Hz))	δ_C
1	0.96 (1H, m)	41.3
	1.62 (1H, m)	
2	1.38 (1H, m)	20.1
	1.92 (1H, m)	
3	1.04 (1H, m)	39.4
	2.13 (1H, br. d, 13.2)	
4	-	44.3
5	1.04 (1H, m)	57.9
6	1.79 (1H, m)	21.0
	1.86 (1H, m)	
7	1.06 (1H, m)	34.3
	1.69 (1H, m)	
8	-	37.7
9	1.58 (1H, m)	42.9
10	-	39.2
11	1.42 (1H, m)	29.9
	1.59 (1H, m)	
12	1.75 (1H, m)	30.8
13	1.40 (1H, m)	21.9
	1.62 (1H, m)	
14	0.82 (1H, ddd, 6.2, 12.2, 14.0)	28.4
	2.04 (1H, ddd, 3.0, 11.7, 14.0)	
15	2.91 (1H, d, 4.4)	81.2
16	1.88 (1H, m)	44.3
17	2.88 (1H, dd, 9.3, 13.1)	59.8
	3.00 (1H, dd, 6.8,13.1)	
18	0.95 (3H, s)	13.5
19	-	181.0
20	1.19 (3H, s)	29.6
21	2.69 (3H, s)	38.3



Key COSY (bold) and HMBC (arrows) correlations



Key NOESY correlations

Fig. S60.

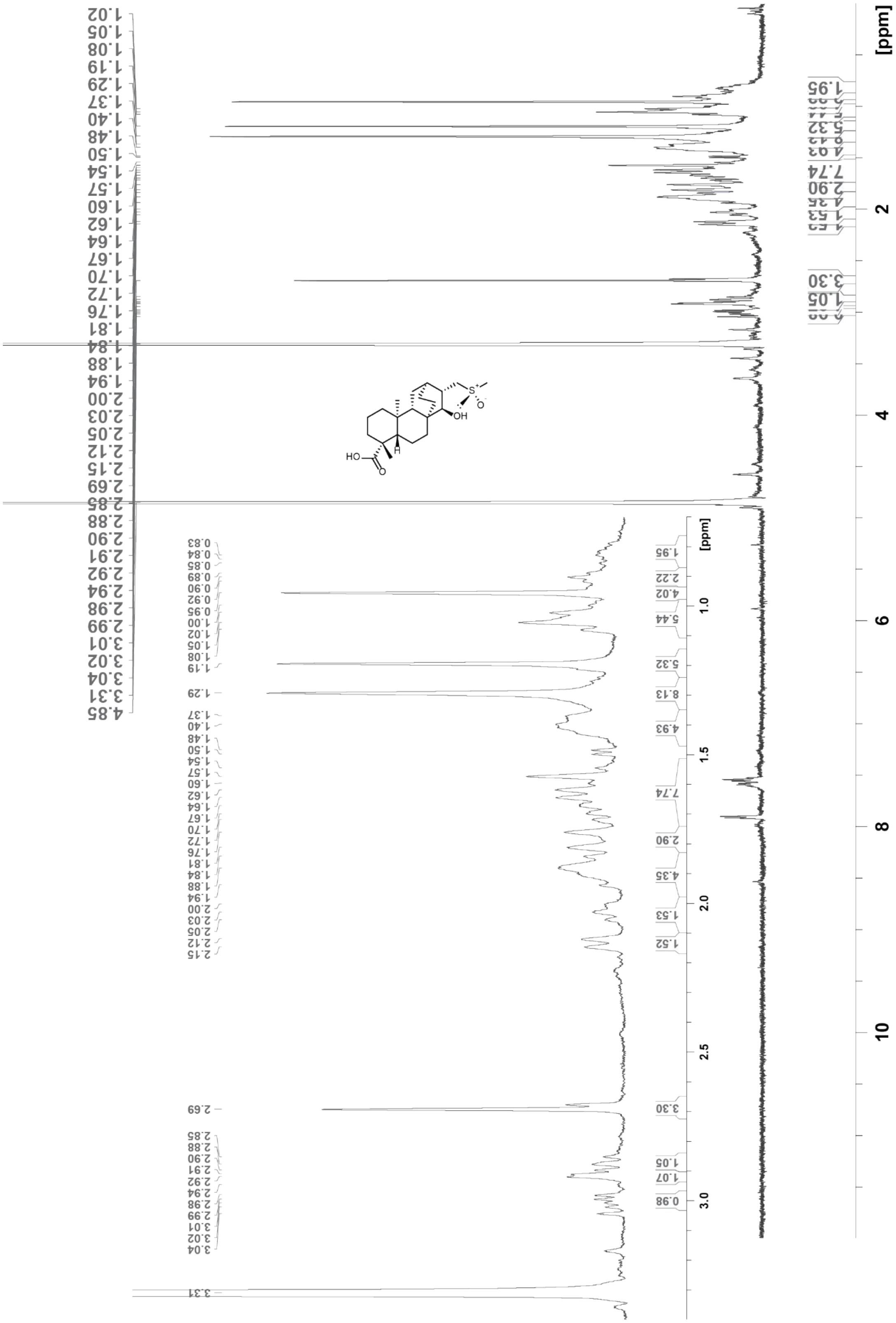


Fig. S60. ^{1}H spectrum of **1B**.

Fig. S61.

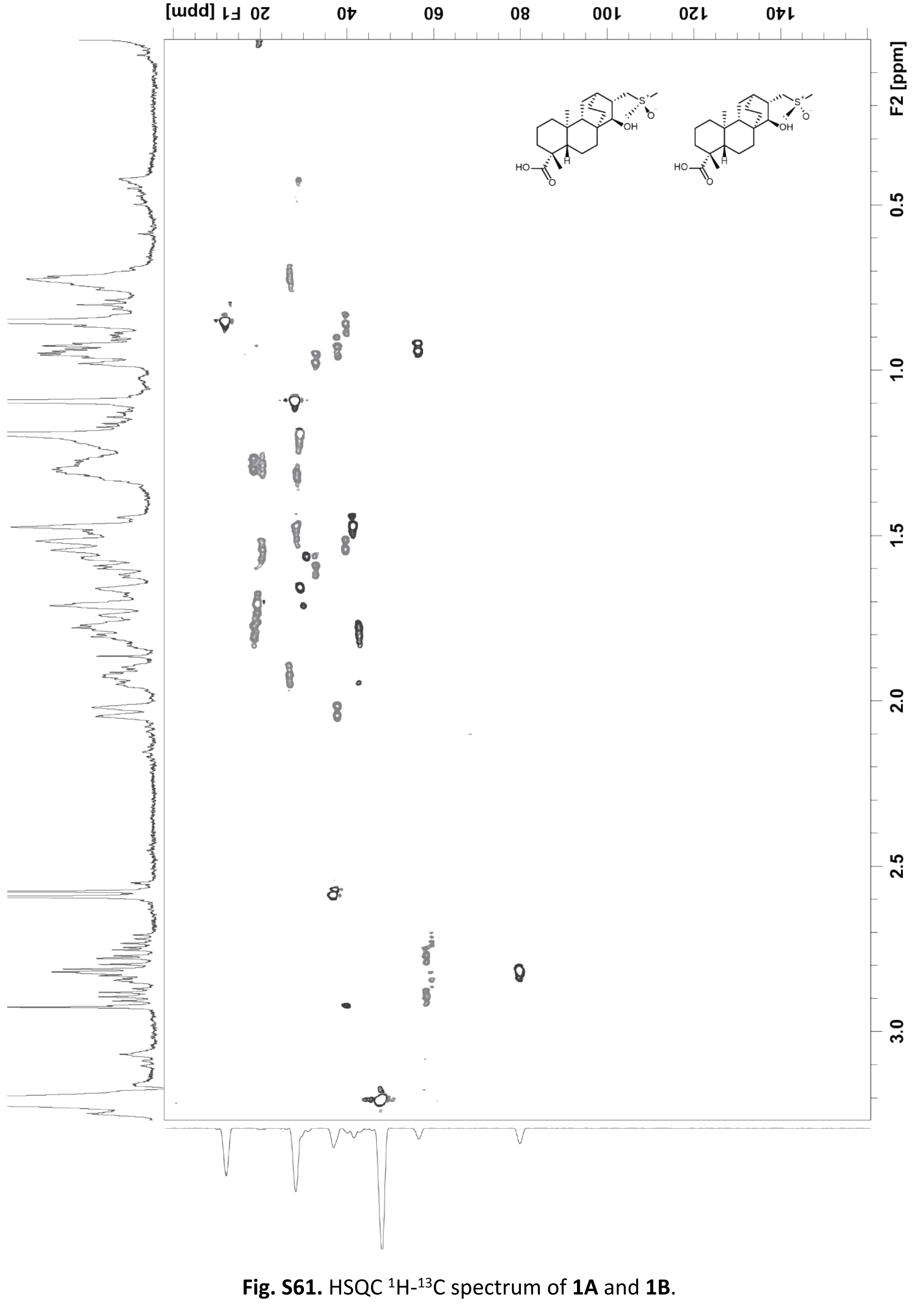


Fig. S61. HSQC ^{1}H-^{13}C spectrum of **1A** and **1B**.

Fig. S62.

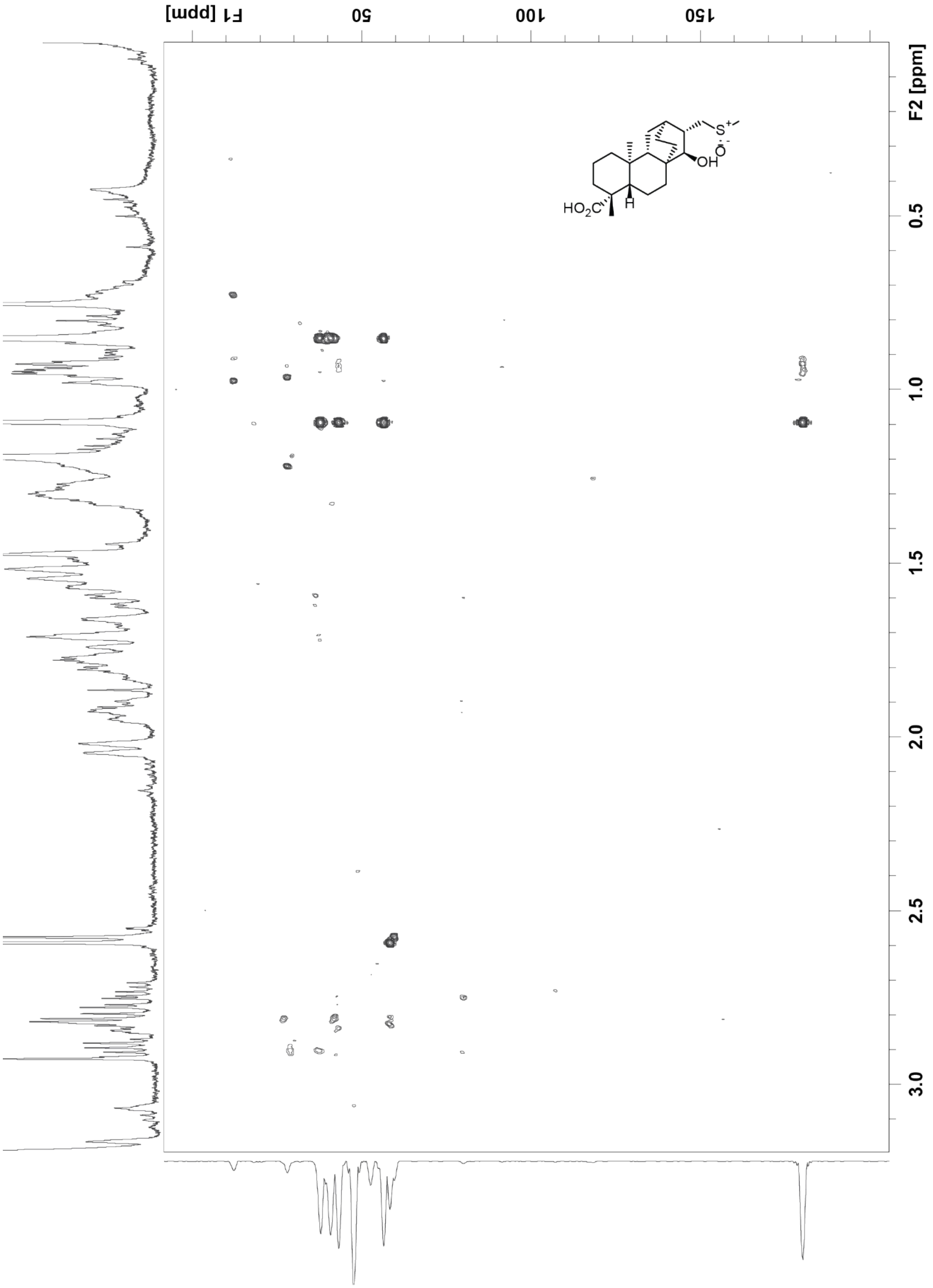
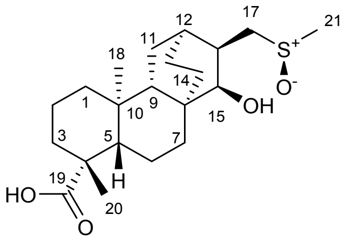


Fig. S62. HMBC ^{1}H-^{13}C spectrum of **1B**.

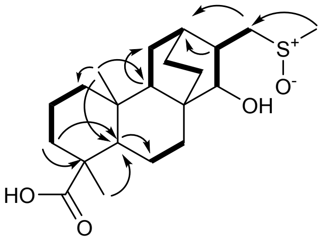
Fig. S63.



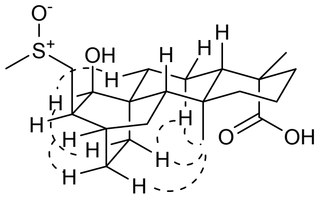
***ent*-(15S,16S,S)-15-hydroxy-17-methylsulfinylatisan-19-oic acid (16A)**

Annotated NMR data for **16A** in methanol-d_4.

No.	δ_H (#H, mult., *J*(Hz))	δ_C
1	0.91 (1H, m)	41.0
	1.61 (1H, m)	
2	1.38 (1H, m)	20.0
	1.86 (1H, m)	
3	1.02 (1H, m)	39.4
	2.14 (1H, d_{app}, 13.5)	
4	-	44.7
5	1.03 (1H, m)	58.0
6	1.79 (1H, m)	21.1
	1.86 (1H, m)	
7	1.08 (1H, td, 2.9, 6.5, 12.9)	35.0
	1.62 (1H, m)	
8	-	37.2
9	1.63 (1H, m)	42.6
10	-	39.2
11	1.20 (1H, m)	23.3
	1.62 (1H, m)	
12	1.57 (1H, m)	33.3
13	1.52 (1H, m)	28.5
	1.58 (1H, m)	
14	0.96 (1H, m)	27.8
	2.00 (1H, m)	
15	3.37 (1H, d, 9.4)	74.4
16	2.44 (1H, m)	37.6
17	2.55 (1H, dd, 4.1, 12.8)	57.4
	3.40 (1H, dd, 11.4, 12.8)	
18	1.19 (3H, s)	29.5
19	-	181.0
20	0.94 (3H, s)	13.2
21	2.65 (3H, s)	38.7



Key COSY (bold) and HMBC (arrows) correlations



Key NOESY correlations

Fig. S64.

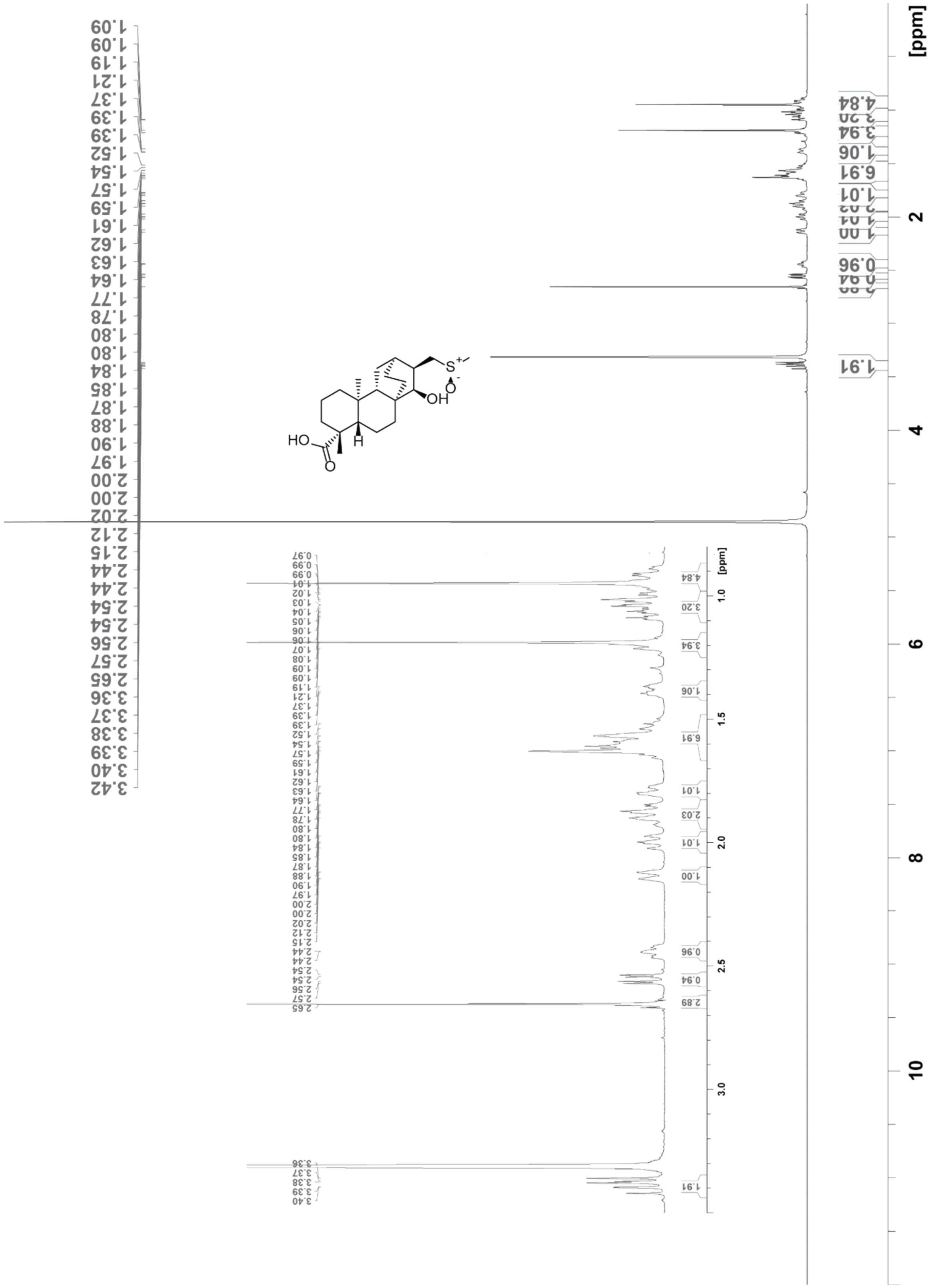


Fig. S64. ^{1}H spectrum of **16A**.

Fig. S65.

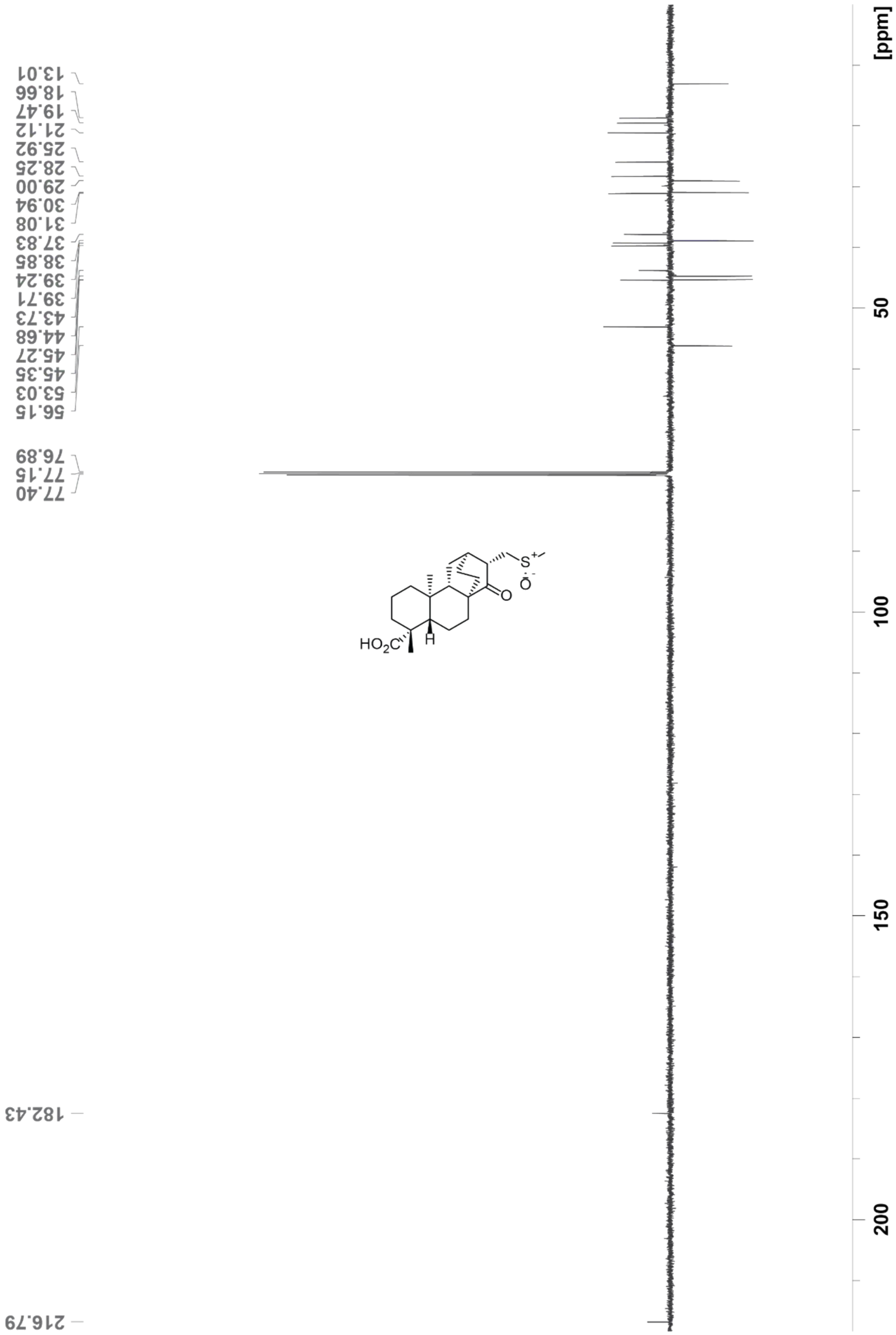
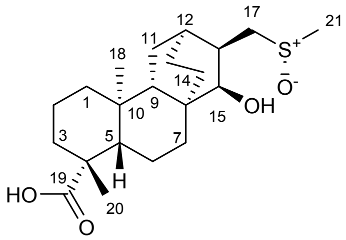


Fig. S65. ^{13}C spectrum of **16A**.

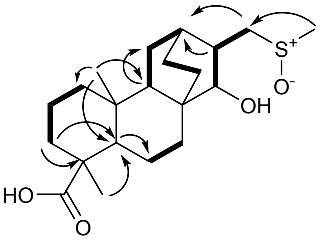
Fig. S66.



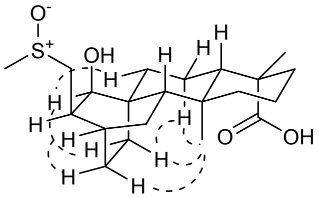
ent-(15S,16S,R)-15-hydroxy-17-methylsulfinylatisan-19-oic acid (16B)

Annotated NMR data for **16B** in methanol-d_4.

No.	δ_H (#H, mult., J(Hz))	δ_C
1	0.92 (1H, m)	41.0
	1.61 (1H, m)	
2	1.38 (1H, m)	20.0
	1.89 (1H, m)	
3	1.02 (1H, m)	39.2
	2.13 (1H, d_{app}, 13.3)	
4	-	44.7
5	1.05 (1H, m)	57.9
6	1.78 (1H, m)	21.1
	1.88 (1H, m)	
7	1.08 (1H, m)	35.0
	1.67 (1H, m)	
8	-	37.0
9	1.65 (1H, m)	42.6
10	-	39.4
11	1.56 (2H, m)	28.3
12	1.70 (1H, m)	31.9
13	1.20 (1H, m)	23.0
	1.64 (1H, m)	
14	0.96 (1H, m)	27.9
	2.00 (1H, m)	
15	3.34 (1H, d, 9.2)	75.1
16	2.34 (1H, m)	38.7
17	2.78 (1H, dd, 7.7, 13.3)	55.6
	3.28 (1H, dd, 7.6, 13.3)	
18	0.95 (3H, s)	13.2
19	-	181.7
20	1.19 (3H, s)	29.5
21	2.67 (3H, s)	38.5



Key COSY (bold) and HMBC (arrows) correlations



Key NOESY correlations

Fig. S67.

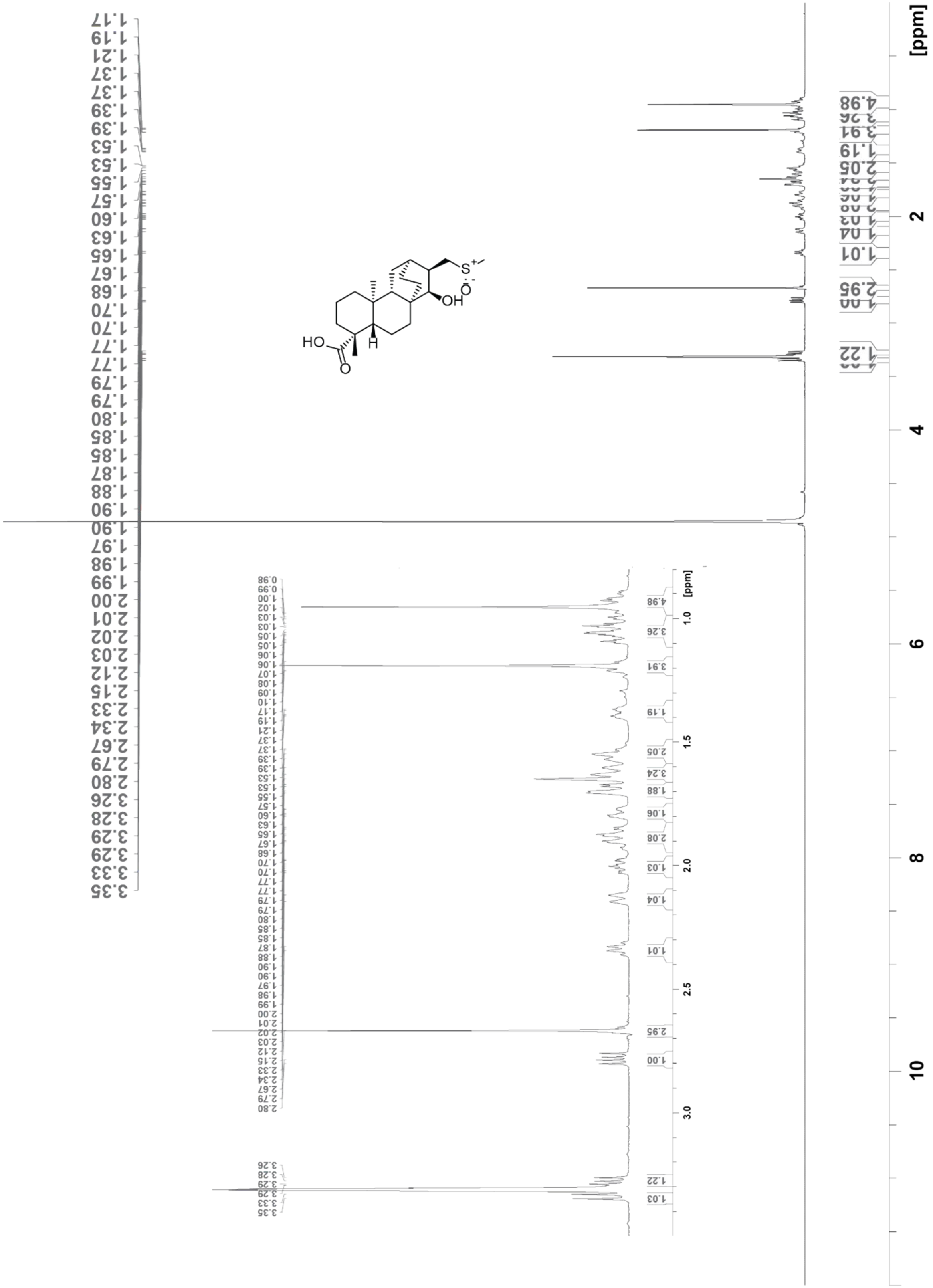


Fig. S67. ^{1}H spectrum of **16B**.

Fig. S68.

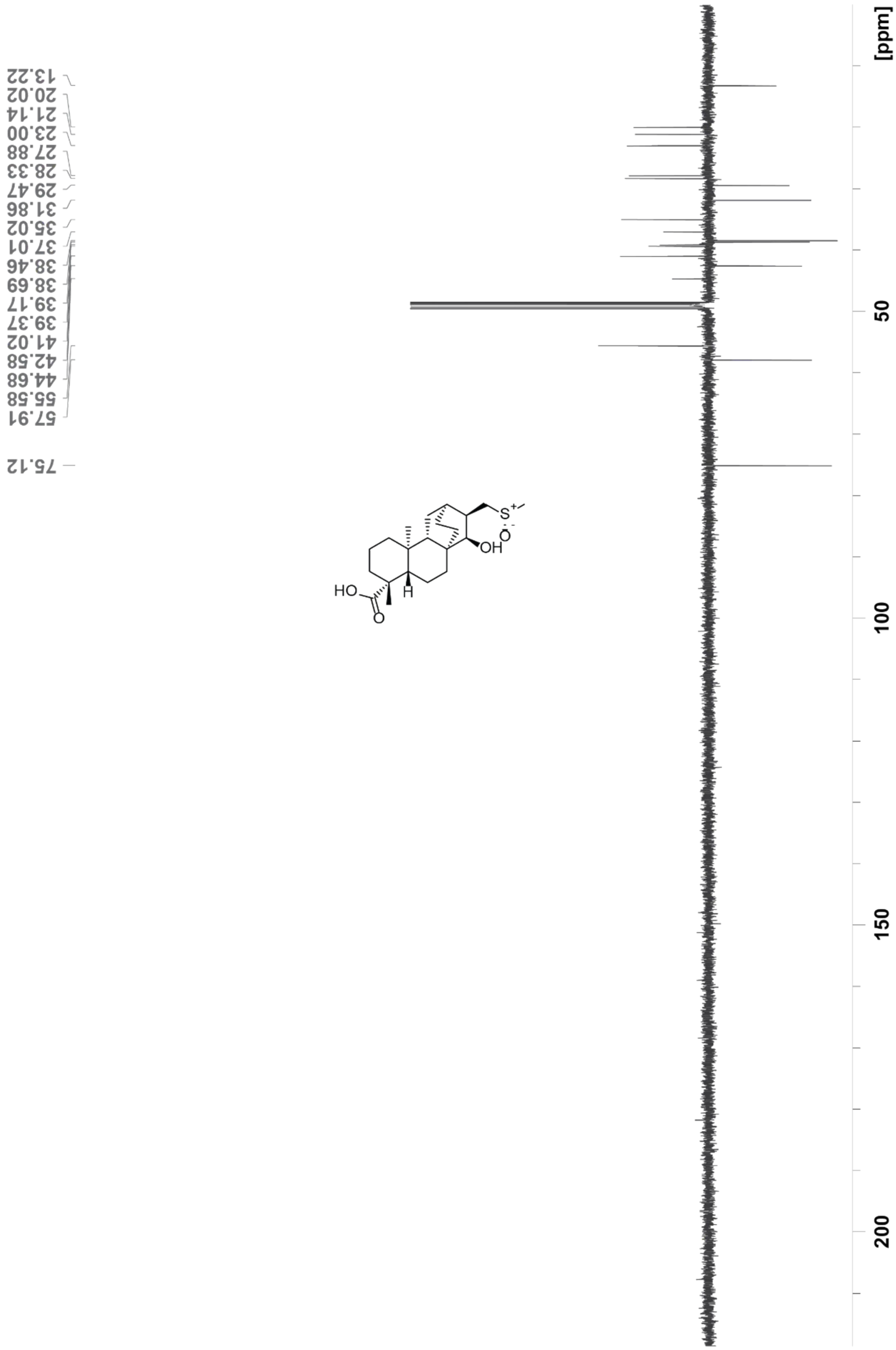


Fig. S68. ^{13}C spectrum of **16B**.

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2 T. Terauchi, N. Asai, T. Doko, R. Taguchi, O. Takenaka, H. Sakurai, M. Yonaga, T. Kimura, A. Kajiwara, T. Niidome, T. Kume, A. Akaike and H. Sugimoto, *Bioorg. Med. Chem.*, 2007, **15**, 7098–7107.

3 M. Toyota, T. Wada and M. Ihara, *J. Org. Chem.*, 2000, **65**, 4565–4570.

4 M. Toyota, Takeshi Asano and M. Ihara, *Org. Lett.*, 2005, **7**, 3929–3932.