Supporting Information

Preparation of Antimalarial Endoperoxides By a Formal [2+2+2] Cycloaddition

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General Reactions were carried out using oven-dried glassware under an atmosphere of dry Ar or N_2 and magnetically stirred, unless noted otherwise. Air- and moisture-sensitive liquids and solutions were transferred *via* syringe or stainless steel canula.

Reagents were purchased from commercial suppliers (Acros, Sigma-Aldrich) and used without further purification, unless noted otherwise.

Solvents (methylene chloride, diethylether, tetrahydrofuran, acetonitrile, toluene) for reactions were purified by filtration and dried by passage over activated anhydrous neutral A-2 alumina (Innovative Technology solvent drying system) under an atmosphere of dry nitrogen. Methanol (analytical grade) was used as received. Analytical grade solvents were used as received for extractions and chromatographic purifications. Deuterated-solvents were purchased from Cambridge Isotope Laboratories, Inc. (Andover, MA, USA).

Thin Layer Chromatography were used for monitoring reactions and carried out using Merck silica gel 60 F_{254} plates, visualized with UV light or developed either with aqueous cerium ammonium molybdate (CAM) stain solution followed by heating.

Flash Chromatography was performed using Silicycle SiliaFlash® P60 (230-400 Mesh) at a pressure of *ca.* 0.3 bar. Eluents and R_f are indicated.

^{1}H-NMR spectra were recorded on Varian Gemini Bruker DPX 400 MHz spectrometer at 298K in the indicated deuterated solvent, unless otherwise stated. Data are reported as follow: chemical shift (δ, ppm), multiplicity (s, singulet; d, doublet; dd, doublet of doublets; dt, doublet of triplets; m, multiplet or not resolved signal), coupling constant (*J,* Hz) integration. All signals were referenced to the internal solvent signal as standard ($CDCl_3$, δ = 7.26).

^{13}C-NMR spectra were recorded with ^{1}H-decoupling on Varian Gemini 101 MHz spectrometer at 298K in the indicated deuterated solvent, unless otherwise stated. All signals were referenced to the internal solvent signal as standard ($CDCl_3$, δ = 77.16).

IR spectra were recorded on a Varian 800 FT-IR ATR spectrometer and data are reported in terms of frequency of absorption (ν, cm^{-1}).

Optical rotations $[\alpha]_D^T$ were measured at the sodium D line using a 1 mL cell with a 1 dm path length on a Jasco P-2000 digital polarimeter and the concentration *c* is given in g/100mL in the indicated solvent.

Mass spectra: All masses spectra were recorded at the University of Basel on a QTOF-ESI Spectrometer (bruker maXis 4G).

Melting points (Mp) were determined using a Büchi B-545 apparatus in open capillaries and are uncorrected.

X-ray analyses: Data collections for all crystal structures were performed at low temperature (123 K) using MoK_α or CuK_α radiation on a Bruker Kappa APEX diffractometer. Integration of the frames and data reduction was carried out using the APEX2 software [1]. The structures were solved by direct methods using SIR92 [2]. All non-hydrogen atoms were refined using anisotropically by full-matrix least-squares on F using CRYSTALS [3].

[1] Bruker Analytical X-ray Systems, Inc., 2006. *Apex2*, Version 2 User Manual, M86-E01078, Madison, WI.

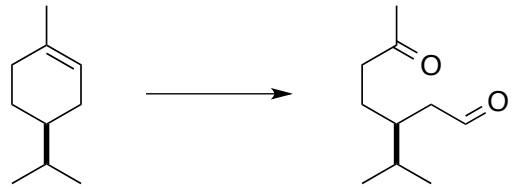
[2] A. Altomare, G. Cascarano, G. Giacovazzo, A. Guagliardi, M. C. Burla, G. Polidori and M. Camalli, *J. Appl. Cryst.* 1994, **27**, 435.

[3] Betteridge, P.W., Carruthers, J.R., Cooper, R.I., Prout, K. & Watkin, D.J. (2003). J. Appl. Cryst. 36, 1487.

Literature references refer to the citations in the communication.

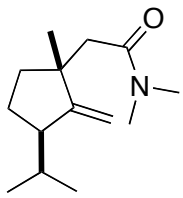
Synthesis of allylic alcohol **9** was performed according to the reported procedure with the exception of the ketoaldehyde intermediate presented below.[12]

(*S*)-3-Isopropyl-6-oxoheptanal:



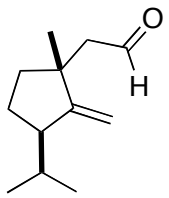
In an oven dried 100 ml flask, the olefin (1.85 g, 13.4 mmol, 1.0 eq) was dissolved in MeOH (7.0 ml) and DCM (35.0 ml). The colorless solution was cooled to -78 °C and ozone was bubbled trough the solution until it turned blue. The reaction was stirred for additional 5 min at -78 °C and oxygen was bubbled trough the blue solution until the color disappeared. Zn (1.75 g, 26.8 mmol, 2.0 eq) and AcOH (2.30 ml, 2.41 g, 40.1 mmol, 3.0 eq) were added at -78 °C and the mixture was allowed to warm up to rt for 1 h and stirred for additional 15 min at this temperature. The suspension was filtered over celite and washed with DCM (3 x 15 ml). The organic layer was extracted with sat. $NaHCO_3$ soln. (15 ml) and the aqueous layer was extracted with DCM (2 x 10 ml). The combined organic layers were dried over Na_2SO_4, filtered and evaporated to obtain pale yellow oil. The residue was purified by flash chromatography (pentane/Et_2O 4:1) to yield the ketoaldehyde as a pale yellow oil (1.85 g, 10.8 mmol, 81%). The analytical data were in good agreement with those reported.[12]

2-((1*R*,3*R*)-3-Isopropyl-1-methyl-2-methylenecyclopentyl)-*N*,*N*-dimethylacetamide (10): The allyl alcohol **9** (18 mg, 0.12 mmol, 1.0 eq) was added to a oven dried 10 ml Schlenk tube, dissolved in *p*-xylene (1.0 ml) and 1,1-dimethoxyethyl(dimethyl)amine (90% in MeOH, 173 mg, 1.17 mmol, 10 eq) was added. Argon was bubbled for 2 minutes through the yellow solution, and the reaction vessel was then sealed and heated to 150 °C behind a blast shield. After 16 h, the mixture was allowed to cool to rt and then completely evaporated to obtain an orange oil. The residue was purified by flash chromatography (pentane/EtOAc 4:1 to 3:1) to yield **10** as a slightly yellow oil (24.8 mg, 0.11 mmol, 95%, d.r. 24:1); R_f = 0.08 (pentane/Et_2O 4:1); $[\alpha]_D^{25.6}$ = +23.1 (*c* = 0.074 in $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ = 4.80 (d, *J* = 2.9 Hz, 1H), 4.77 (d, *J* = 2.5 Hz, 1H), 3.00 (s, 3H), 2.92 (s, 3H), 2.59 – 2.51 (m,



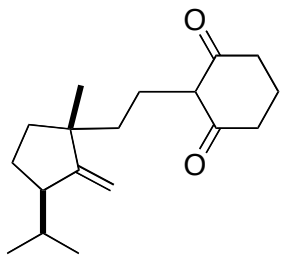
1H), 2.53 (d, *J* = 15.1, 1H), 2.37 (d, *J* = 15.1 1H), 2.01 – 1.93 (m, 1H), 1.87 – 1.79 (m, 1H), 1.67 – 1.59 (m, 2H), 1.45 – 1.35 (m, 1H), 1.09 (s, 3H), 0.97 (d, *J* = 6.9 Hz, 3H), 0.77 (d, *J* = 6.8 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ = 171.8, 163.4, 103.3, 50.9, 45.2, 43.8, 38.0, 37.5, 35.5, 28.9, 27.6, 23.3, 22.0, 16.6; IR (film) ν = 2955, 2870, 1642, 1466, 1394, 1264, 1126, 882 cm^{-1}; HRMS (ESI+, m/z): calcd for $C_{14}H_{26}N_1O_1$ $[M+H]^+$: 224.2009, found 224.2015.

2-((1*R*,3*R*)-3-Isopropyl-1-methyl-2-methylenecyclopentyl)acetaldehyde (11):



The amide **10** (4.3 mg, 19.3 µmol, 1.0 eq) was dissolved in dry THF (0.2 ml), 1,1,3,3-tetramethyldisiloxane (8.01 mg, 0.01 ml, 57.9 µmol, 3.0 eq) and titanium(IV)isopropoxide (16.7 mg, 0.02 ml, 57.9 µmol, 3.0 eq) were added, and the reaction mixture was stirred at rt for 18 h. Et_2O (1 ml) was added, the mixture was washed with HCl (1 M, 3 x 0.3 ml), and the combined aqueous layer were re-extracted with Et_2O (3 x 0.5 ml). The combined organic layers were washed with brine (0.5 ml), dried over Na_2SO_4 and the solvent was removed *in vacuo*. The residue was purified by flash chromatography (pentane/Et_2O 4:1) to yield **11** as a colorless oil (3.3 mg, 18.3 µmol, 95%). The analytical data were in good agreement with those reported.[12]

2-(2-((1*R*,3*R*)-3-Isopropyl-1-methyl-2-methylenecyclopentyl)ethyl)cyclohexane-1,3-dione (3):

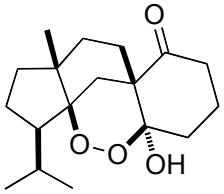


Aldehyde **11** (5.68 g, 31.5 mmol, 1.0 eq) was dissolved in dry CH_2Cl_2 (300 ml). Cyclohexan-1,3-dione (10.8 g, 94.4 mmol, 3.0 eq), Hantzsch ester (16.3 g, 63.0 mmol, 2.0 eq) and L-proline (370 mg, 3.15 mmol, 0.1 eq) were added to the reaction mixture. The yellow mixture was stirred at room temperature for 19 h and was subsequently washed with H_2O (20 ml), HCl (10%, 3 x 15 ml) and brine (15 ml). The combined aqueous layers was extracted with CH_2Cl_2 (20 ml) and the combined organic layers were dried over Na_2SO_4. The solvent was removed *in vacuo* and the residue was purified by flash chromatography (pentane/EtOAc 4:1 to 1:1) to yield **3** as an instable yellow solid (7.92 g, 28.7 mmol, 91%). HRMS (ESI+, m/z): calcd for $C_{18}H_{29}O_2$ $[M+H]^+$: 277.2162, found 277.2162.

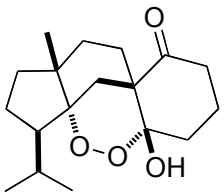
(3*R*,3*aS*,5*aR*,9*aR*,11*aR*)-5*a*-Hydroxy-3-isopropyl-11*a*-methyloctahydro-1*H*-3*a*,9*a*-methanobenzo[*c*]cyclopenta[*g*][1,2]dioxocin-9(10*H*)-one (4) and (3*R*,3*aR*,5*aS*,9*aS*,11*aR*)-5*a*-Hydroxy-3-isopropyl-11*a*-methyloctahydro-1*H*-3*a*,9*a*-methanobenzo[*c*]cyclopenta[*g*][1,2]dioxocin-9(10*H*)-one (12)

Method A: Diketone **3** (17.7 mg, 64.0 µmol, 1.0 eq) was allowed to react in an open-flask (or dissolved in EtOAc) exposed to sunlight and air. After 16 h, the yellow solid was dissolved in EtOAc and purified by flash column chromatography (pentane/EtOAc 12:1) to give the endoperoxides **4** (10.6 mg, 34.4 µmol, 54%) and **12** (2.20 mg, 7.13 µmol, 11%) as white solids.

Method B: Diketone **3** (3.66 mg, 13.2 µmol, 1.0 eq) was dissolved in AcOH (0.36 ml), $Mn(OAc)_3$ (0.53 mg, 1.99 µmol, 0.15 eq) was added, and the reaction flask was charged with a balloon containing O_2. The yellow solution was stirred at rt for 19 h and then quenched with H_2O (0.2 ml) and sat. $NaHCO_3$ solution (0.8 ml). The aqueous phase was extracted with EtOAc (4 x 1 ml) and the combined organic layers were washed with sat. $NaHCO_3$ solution (1 ml) and brine (0.5 ml), then dried over Na_2SO_4, filtered and the solvent removed *in vacuo*. The residue was purified by flash column chromatography (pentane/EtOAc 12:1) to obtain the desired endoperoxides **4** (3.16 mg, 10.2 µmol, 77%) and **12** (0.79 mg, 2.56 µmol, 19%) as white solids.



4: R_f = 0.63 (pentane/EtOAc 4:1); mp = 124.6 – 126.4 °C; $[\alpha]_D^{25.3}$ = –116.0 (*c* = 0.236 in $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ = 3.14 (s, 1H), 2.63 – 2.54 (m, 1H), 2.33 – 2.27 (m, 1H), 2.16 (d, *J* = 13.5 Hz, 1H), 2.08 – 2.01 (m, 3H), 1.93 – 1.91 (m, 1H), 1.75 – 1.72 (m, 2H), 1.70 – 1.67 (m, 2H), 1.65 – 1.64 (m, 2H), 1.57 – 1.50 (m, 5H), 1.19 (s, 3H), 1.04 (d, *J* = 6.4 Hz, 3H), 0.85 (d, *J* = 6.7 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ = 211.1, 103.4, 90.5, 60.5, 50.6, 45.7, 40.2, 35.8, 34.5, 30.8, 28.7, 28.5, 28.4, 27.3, 23.8, 22.2, 22.0, 19.4; IR (film) ν = 3452, 3395, 2952, 2927, 2867, 1696, 1470, 1260, 1179, 1163, 1068, 1012, 991, 891, 762 cm^{-1}; HRMS (ESI+, m/z): calcd for $C_{18}H_{28}O_4Na_1$ $[M+Na]^+$: 331.1880, found 331.1881.

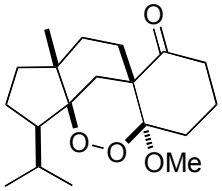


12: R_f = 0.50 (pentane/EtOAc 4:1); mp = 147.5 – 149.1 °C; $[\alpha]_D^{25.3}$ = +118.2 (*c* = 0.045 in $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ = 3.23 (s, 1H), 2.73 – 2.57 (m, 2H), 2.43 (dd, *J* = 13.9, 2.1 Hz, 1H), 2.32 (dd, *J* = 15.7, 4.0 Hz, 1H), 2.15 – 2.10 (m, 1H), 2.03 (d, *J* = 13.8, 1H), 1.99 – 1.96 (m, 1H), 1.91 – 1.79 (m, 2H), 1.76 – 1.70 (m, 1H), 1.68 – 1.62 (m, 2H), 1.59 – 1.55 (m, 2H), 1.47 – 1.38 (m, 2H), 1.32 – 1.25 (m, 2H), 1.06 (d, *J* = 6.3 Hz, 3H), 0.96 (s, 3H), 0.89 (d, *J* = 6.6 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ = 211.0, 103.4, 98.0, 52.8, 52.1, 45.9, 36.2, 35.7, 33.0, 30.5, 29.1, 28.4, 26.7, 24.9, 24.6, 23.4, 22.2, 19.6; IR (film) ν = 3501, 3428, 2965, 2923, 1456, 1377, 1313, 1261, 1250, 1160, 1068, 1160, 1068, 999, 961, 885, 799, 785, 619 cm^{-1}; HRMS (ESI+, m/z): calcd for $C_{18}H_{28}O_4Na_1$ $[M+Na]^+$: 331.1880, found 331.1880; for X-ray crystal structure analysis see page S-12.

General method for Ag_2O mediated *O*-alkylation of endoperoxides:

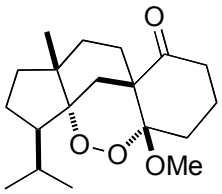
To a solution of the endoperoxide (**4** or **12**) (3.74 μmol, 1.0 eq) in MeCN (0.10 ml) MeI (131 μmol, 35 eq) and Ag_2O (14.2 μmol, 3.8 eq) were added, and the reaction mixture was stirred for 16 h at 40 °C. The mixture was allowed to cool to rt and was then filtered over celite and rinsed with EtOAc (3 x 0.3 ml). The solvent was removed *in vacuo* and the yellow solid was purified by flash column chromatography to yield the corresponding methylated endoperoxide.

(3*R*,3*aS*,5*aR*,9*aR*,11*aR*)-3-Isopropyl-5*a*-methoxy-11*a*-methyloctahydro-1*H*-3*a*,9*a*-methanobenzo[*c*]cyclopenta[*g*][1,2]dioxocin-9(10*H*)-one (19)



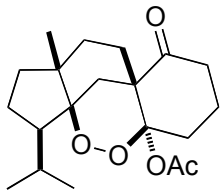
Flash column chromatography (pentane/Et_2O 12:1); white solid (10.8 mg, 0.033 mmol, 54%); R_f = 0.59 (pentane/Et_2O 5:1); mp = 84.7 – 85.9 °C; $[\alpha]_D^{25.4}$ = –59.5 (*c* = 0.043 in $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ = 3.32 (s, 3H), 2.65 – 2.49 (m, 2H), 2.39 – 2.33 (m, 1H), 2.21 – 2.13 (m, 2H), 2.03 – 1.96 (m, 1H), 1.93 – 1.86 (m, 2H), 1.84 – 1.75 (m, 2H), 1.67 – 1.58 (m, 4H), 1.55 – 1.48 (m, 1H), 1.46 – 1.40 (m, 2H), 1.37 – 1.32 (m, 1H), 1.13 (s, 3H), 1.03 (d, *J* = 6.3 Hz, 3H), 0.85 (d, *J* = 6.7 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ = 211.7, 106.7, 89.1, 57.4, 53.8, 49.8, 45.4, 42.4, 37.7, 36.8, 34.2, 29.3, 27.2, 24.1, 24.0, 22.5, 21.8, 21.5, 18.5; IR (film) ν = 2954, 2869, 1707, 1455, 1378, 1316, 1262, 1200, 1060, 1031, 993, 899, 662, 628 cm^{-1}; HRMS (ESI+, m/z): calcd for $C_{19}H_{30}O_4Na_1$ $[M+Na]^+$: 345.2036, found 345.2041; for X-ray crystal structure analysis see page S-13.

(3*R*,3*aR*,5*aS*,9*aS*,11*aR*)-3-Isopropyl-5*a*-methoxy-11*a*-methyloctahydro-1*H*-3*a*,9*a*-methanobenzo[*c*]cyclopenta[*g*][1,2]dioxocin-9(10*H*)-one (20)



Flash column chromatography (pentane/Et_2O 10:1); white solid (5.22 mg, 0.016 mmol, 88%); R_f = 0.55 (pentane/Et_2O 3:1); mp = 136.6 – 137.9 °C; $[\alpha]_D^{23.3}$ = +98.1 (*c* = 0.058 in $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ = 3.24 (s, 3H), 2.71 – 2.53 (m, 3H), 2.31 – 2.26 (m, 1H), 2.14 – 2.08 (m, 1H), 1.92 – 1.79 (m, 5H), 1.78 – 1.67 (m, 2H), 1.66 – 1.61 (m, 1H), 1.60 – 1.53 (m, 2H), 1.45 – 1.35 (m, 2H), 1.30 – 1.23 (m, 1H), 1.05 (d, *J* = 6.3 Hz, 3H), 0.94 (s, 3H), 0.87 (d, *J* = 6.7 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ = 211.1, 105.3, 97.5, 52.9, 51.9, 47.7, 45.9, 36.1, 35.8, 32.9, 30.4, 29.1, 26.7, 24.6, 23.9, 23.3, 22.3, 22.2, 19.3; IR (film) ν = 2954, 2924, 2863, 1711, 1460, 1263, 1181, 1092, 1066, 1035, 928, 784 cm^{-1}; HRMS (ESI+, m/z): calcd for $C_{19}H_{30}O_4Na_1$ $[M+Na]^+$: 345.2036, found 345.2040; for X-ray crystal structure analysis see page S-14.

(3*R*,3*aS*,5*aR*,9*aR*,11*aR*)-3-Isopropyl-11*a*-methyl-9-oxodecahydro-1*H*-3*a*,9*a*-methanobenzo[*c*]cyclopenta[*g*][1,2]dioxocin-5*a*-yl acetate (18)



A solution of endoperoxide (**4**) (4.47 mg, 14.5 µmol, 1.0 eq) in dry DCM (0.32 ml) was cooled to 0 °C. DMAP (1.08 mg, 8.7 µmol, 0.6 eq), 2-*tert*-butyl-1,1,3,3-tetramethylguanidine (Barton's Base, 0.06 ml, 0.29 mmol, 20 eq) and Ac_2O (0.028 ml, 0.29 mmol, 20 eq) were added. The mixture was allowed to warm up to rt and stirred for 18 h. Et_2O (1 ml) was added and washed with HCl (1 M, 2 x 0.3 ml) and sat. $NaHCO_3$ soln. (0.3 ml) and brine (0.3 ml). The organic layer was dried over Na_2SO_4, filtered and the solvent removed *in vacuo*. The residue was purified by flash column chromatography (pentane/Et_2O 6:1 to 4:1) to obtain the acetylated endoperoxide **18** as colorless sticky oil (3.88 mg, 11.1 µmol, 76%). R_f = 0.53 (pentane/Et_2O 2:1); $[\alpha]_D^{25.7}$ = –13.9 (*c* = 0.15 in $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ = 2.82 (dt, *J* = 14.7, 4.6 Hz, 1H), 2.59 – 2.42 (m, 3H), 2.17 – 2.10 (m, 1H), 2.07 (s, 3H), 2.04 – 1.93 (m, 3H), 1.90 – 1.83 (m, 1H), 1.77 – 1.70 (m, 1H), 1.68 – 1.65 (m, 2H), 1.62 – 1.58 (m, 2H), 1.55 – 1.51 (m, 1H), 1.45 – 1.40 (m, 2H), 1.38 – 1.33 (m, 1H), 1.06 (s, 3H), 1.03 (d, *J* = 6.4 Hz, 3H), 0.87 (d, *J* = 6.7 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ = 210.2, 168.8, 110.9, 90.2, 57.0, 53.3, 45.1, 40.0, 38.3, 36.6, 34.6, 28.8, 27.5, 26.6, 23.8, 21.9, 21.6, 21.5, 20.9, 18.6; IR (film) ν = 2951, 2927, 2869, 1762, 1709, 1459, 1369, 1259, 1209, 1170, 1013, 961, 630 cm^{-1}; HRMS (ESI+, m/z): calcd for $C_{20}H_{30}O_5Na_1$ $[M+Na]^+$: 373.1985, found 373.1992.

***In Vitro* Assay:**

Activity against *P. falciparum*:

In vitro activity against erythrocytic stages of *P. falciparum* was determined using a ^{3}H-hypoxanthine incorporation assay,[1, 2] using the drug sensitive NF54 strain (Schipol Airport, The Netherlands,)[3] and the standard drugs chloroquine (Sigma C6628) and artemisinin (Sigma 361593). Compounds were dissolved in DMSO at 10 mg/ml and added to parasite cultures incubated in RPMI 1640 medium without hypoxanthine, supplemented with HEPES (5.94 g/l), $NaHCO_3$ (2.1 g/l), neomycin (100 U/ml), Albumax (5 g/l) and washed human red cells A+ at 2.5% haematocrit (0.3% parasitaemia). Serial drug dilutions of eleven 3-fold dilution steps covering a range from 100 to 0.002 µg/ml were prepared. The 96-well plates were incubated in a humidified atmosphere at 37 °C; 4% CO_2, 3% O_2, 93% N_2. After 48 h 50 µl of ^{3}H - hypoxanthine (=0.5 µCi) was added to each well of the plate. The plates were incubated for a further 24 h under the same conditions. The plates were then harvested with a Betaplate™ cell harvester (Wallac, Zurich, Switzerland), and the red blood cells transferred onto a glass fibre filter and then washed with distilled water. The dried filters were inserted into a plastic foil with 10 ml of scintillation fluid, and counted in a Betaplate™ liquid scintillation counter (Wallac, Zurich, Switzerland). IC_{50} values were calculated from sigmoidal inhibition curves by linear regression[4] using Microsoft Excel.

In vitro cytotoxicity with L-6 cells:

Assays were performed in 96-well microtiter plates, each well containing 100 µl of RPMI 1640 medium supplemented with 1% L-glutamine (200 mM) and 10% fetal bovine serum, and 4000 L-6 cells (a primary cell line derived from rat skeletal myoblasts).[5, 6] Serial drug dilutions of eleven 3-fold dilution steps covering a range from 100 to 0.002 µg/ml were prepared. After 70 hours of incubation the plates were inspected under an inverted microscope to assure growth of the controls and sterile conditions. 10 µl of Alamar Blue was then added to each well and the plates incubated for another 2 hours. Then the plates were read with a Spectramax Gemini XS microplate fluorometer (Molecular Devices Cooperation, Sunnyvale, CA, USA) using an excitation wave length of 536 nm and an emission wave length of 588 nm. The IC_{50} values were calculated by linear regression[4] from the sigmoidal dose inhibition curves using SoftmaxPro software (Molecular Devices Cooperation, Sunnyvale, CA, USA). Podophyllotoxine (Sigma P4405) is used as control.

[1] R. E. Desjardins, C. J. Canfield, J. D. Haynes, J. D. Chulay, *Antimicrobial Agents and Chemotherapy* **1979**, *16*, 710.

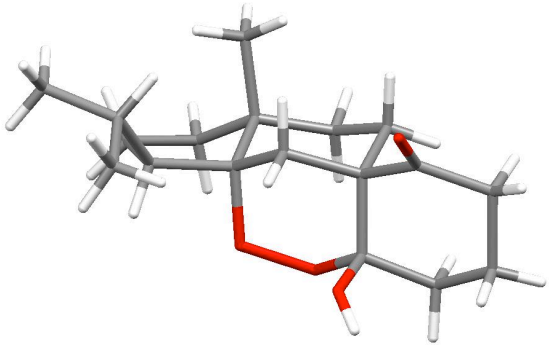
[2] H. Matile, J. R. L. Pink, in I. Lefkovits and B. Pernis (ed.), *ImmunologicalMethods*, Academic Press, San Diego **1990**.

[3] T. Ponnudurai, A. D. Leeuwenberg, J. H. Meuwissen, *Tropical and Geographical Medicine* **1981**, *33*, 50.

[4] W. Huber, J. C. Koella, *Acta Trop*. **1993**, *55*, 257.

[5] B. Page, M. Page, and C. Noel, *International Journal of Oncology* **1993**, *3*, 473.

[6] S. A. Ahmed, R. M. Gogal, J. E. Walsh, *The Journal of Immunological Methods* **1994**, *170*, 211.



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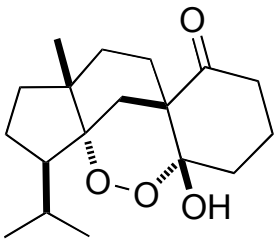


Table 1. Crystal data for **12**	CCDC 914565
formula	$C_{18}H_{28}O_4$
formula weight	308.42
Z, calculated density	8, 1.287 Mg · m^{-3}
F(000)	1344
description and size of crystal	colorless plate, 0.030 · 0.110 · 0.320 mm^3
absorption coefficient	0.089 mm^{-1}
min/max transmission	0.99 / 1.00
temperature	123K
radiation(wavelength)	Mo *K*α (λ = 0.71073 Å)
Crystal system, space group	tetragonal, P 4_1 2_1 2
a	7.3830(3) Å
b	7.3830(3) Å
c	58.407(3) Å
α	90°
β	90°
γ	90°
V	3183.7(3) $Å^3$
min/max Θ	1.395° / 27.484°
number of collected reflections	12591
number of independent reflections	2311 (merging r = 0.096)
number of observed reflections	1905 (I>2.0σ(I))
number of refined parameters	199
r	0.1061
rW	0.0784

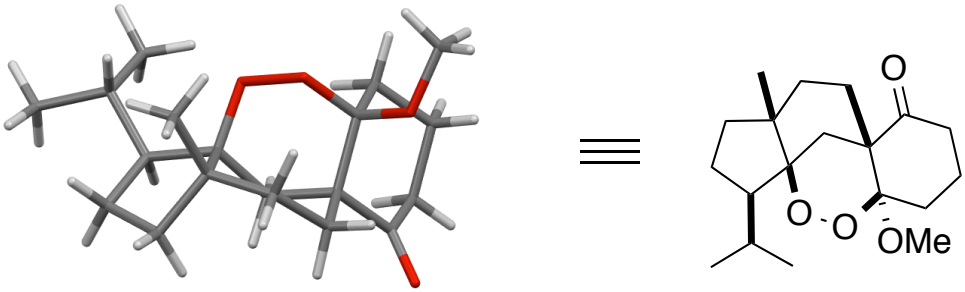
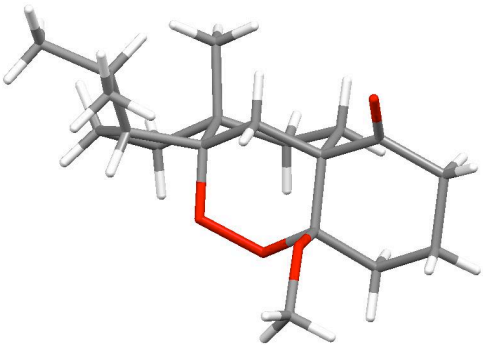


Table 2. Crystal data for **19**	CCDC 1054561
formula	$C_{19}H_{30}O_4$
formula weight	322.44
Z, calculated density	4, 1.221 Mg · m^{-3}
F(000)	703.994
description and size of crystal colourless needle	0.030 · 0.080 · 0.210 mm^3
absorption coefficient	0.671 mm^{-1}
min/max transmission	0.95 / 0.98
temperature	123K
radiation(wavelength)	Cu Kα (λ = 1.54178 Å)
Crystal system, space group	monoclinic, P c
a	14.9923(19) Å
b	9.5834(11) Å
c	12.5518(15) Å
α	90°
β	103.442(2)°
γ	90°
V	1754.0(2) $Å^3$
min/max Θ	3.030° / 69.128°
number of collected reflections	23344
number of independent reflections	6318 (merging r = 0.059)
number of observed reflections	6292 (I>2.0σ(I))
number of refined parameters	415
r	0.0372
rW	0.0409
goodness of fit	1.0900



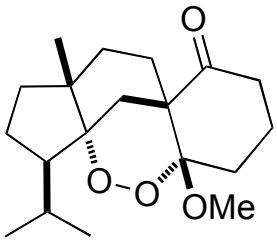
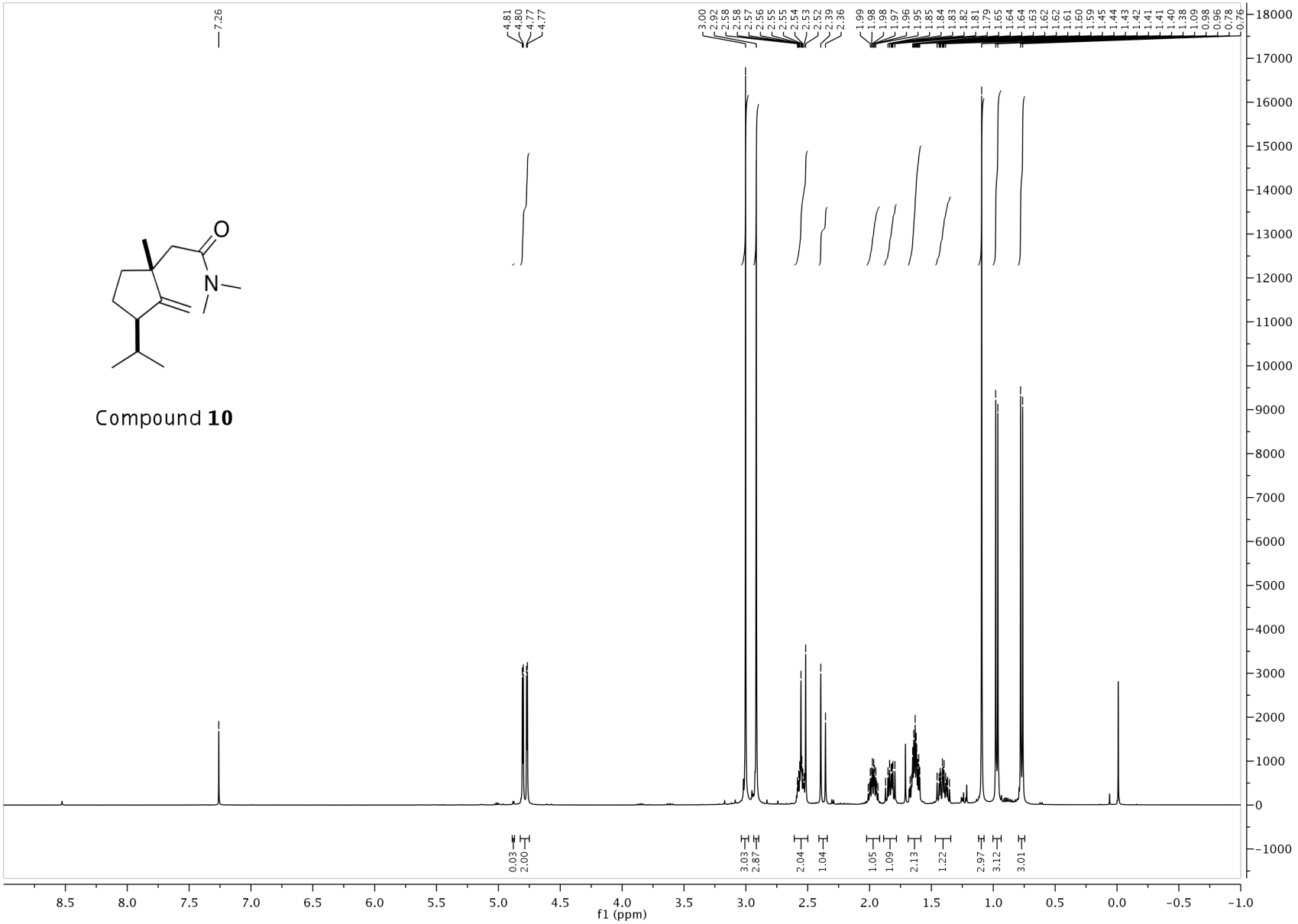
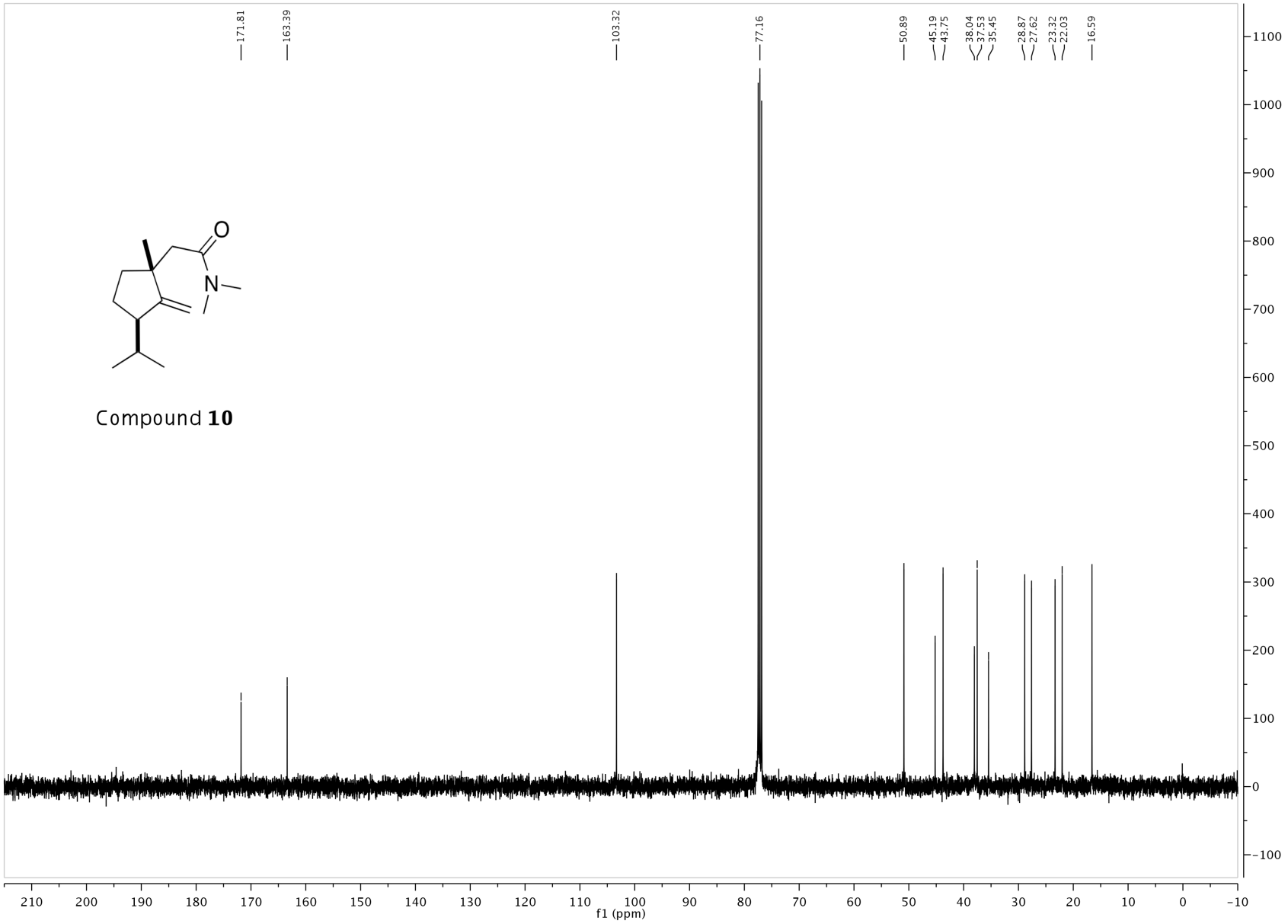
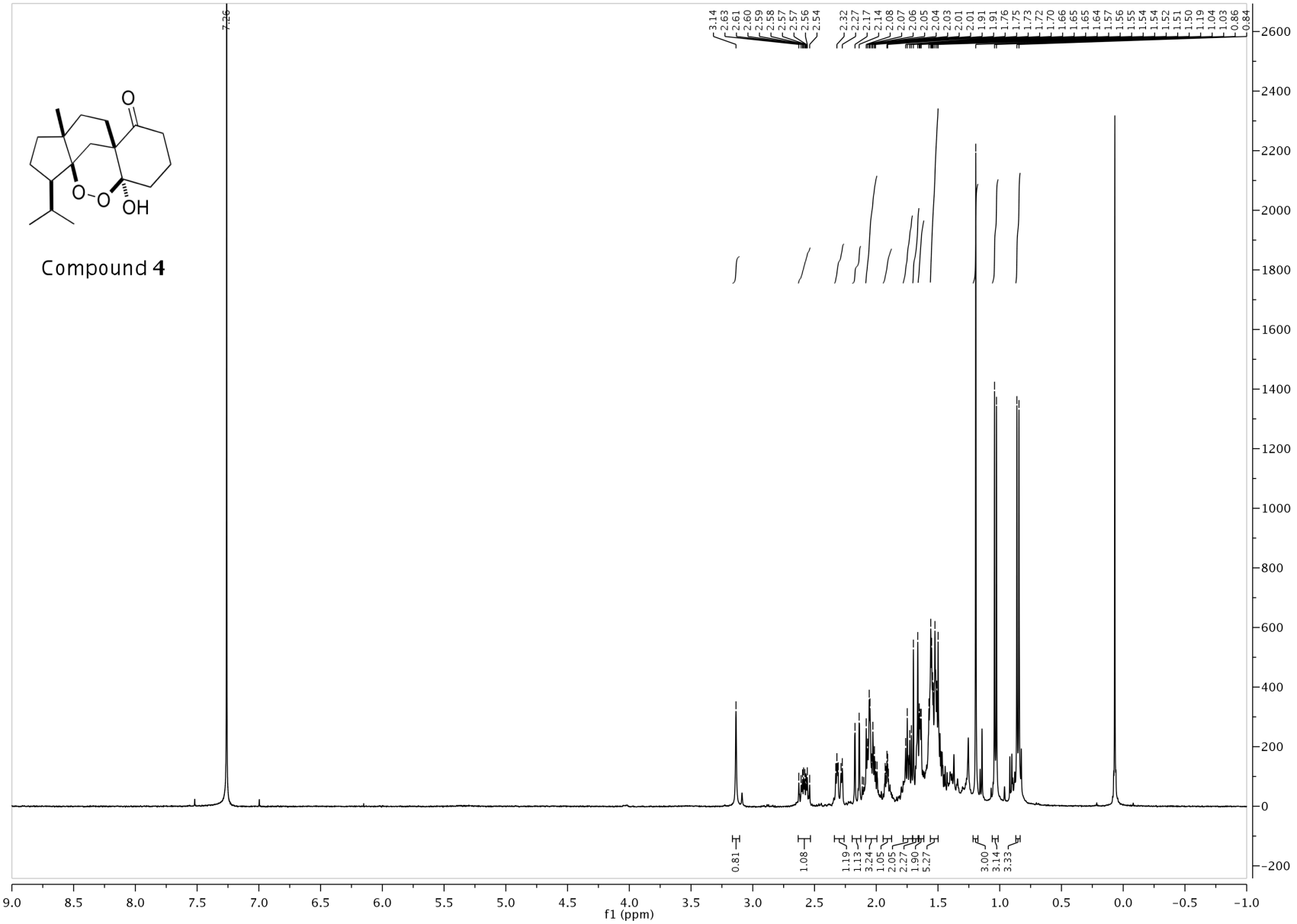
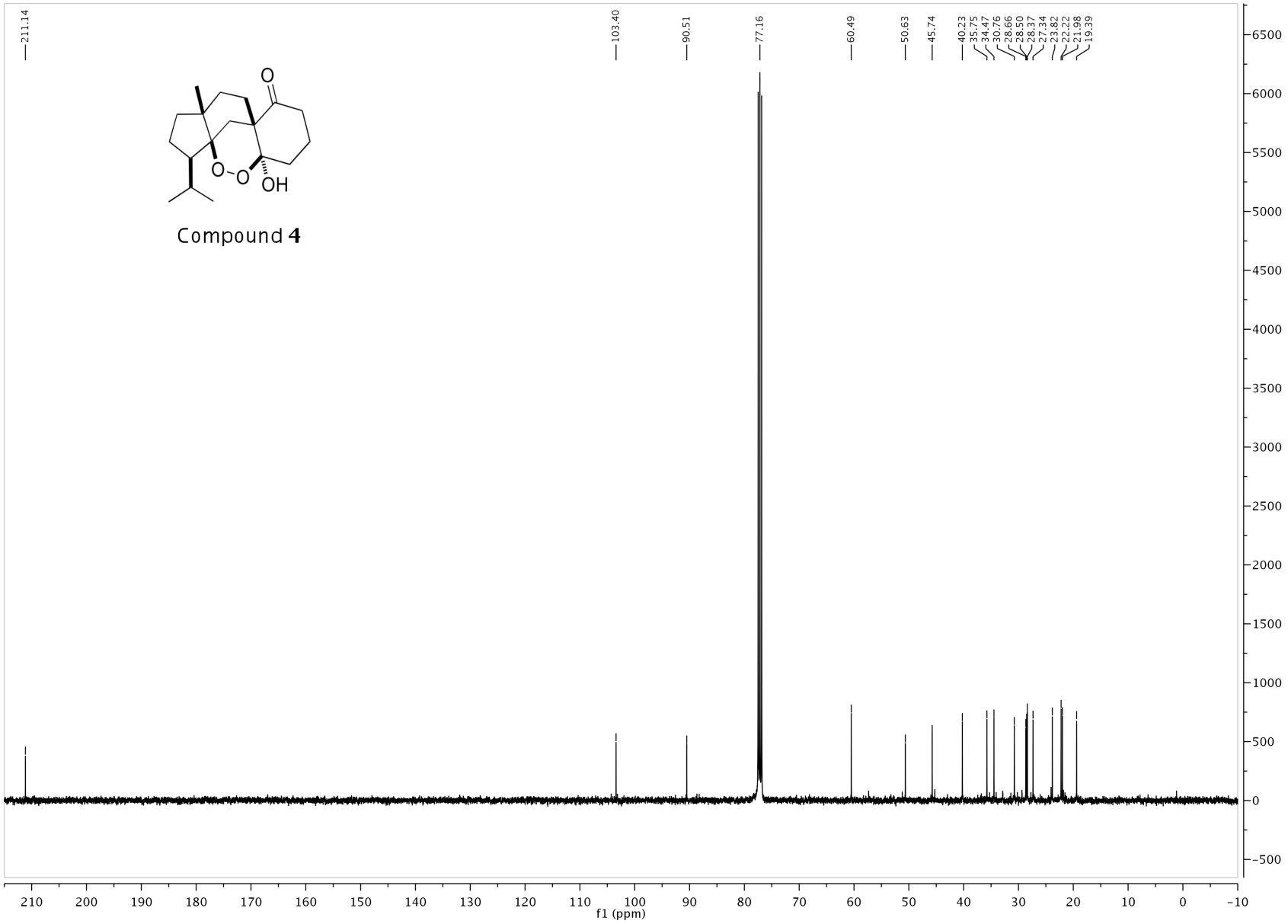


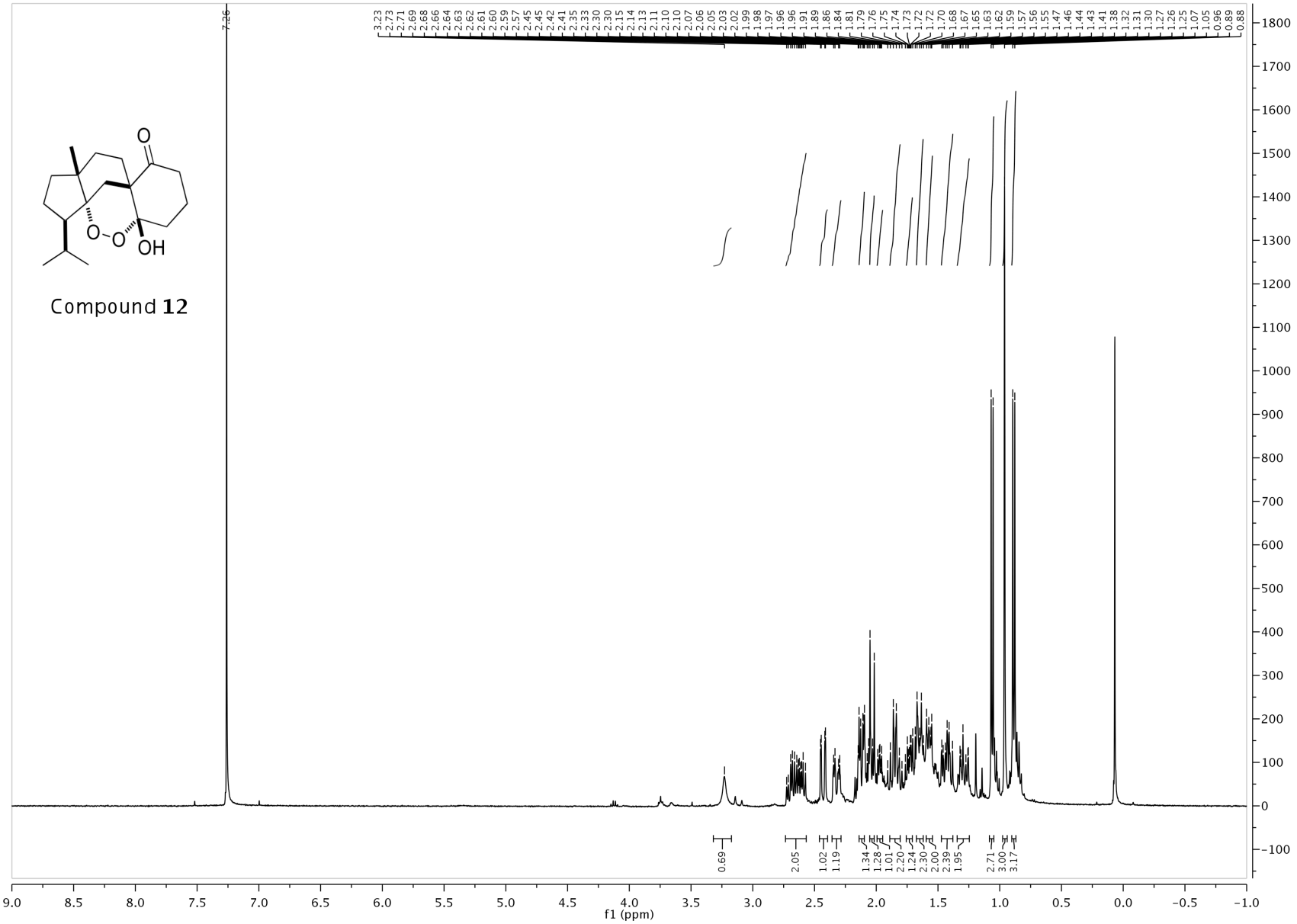
Table 3. Crystal data for **20**	CCDC 914569
formula	$C_{19}H_{30}O_4$
formula weight	322.44
Z, calculated density	2, 1.255 Mg · m^{-3}
F(000)	352
description and size of crystal	colorless plate, 0.010 · 0.170 · 0.260 mm^3
absorption coefficient	0.086 mm^{-1}
min/max transmission	0.99 / 1.00
temperature	123K
radiation(wavelength)	Mo *K*α (λ = 0.71073 Å)
Crystal system, space group	monoclinic, P 1 2_1 1
a	7.6255(11) Å
b	7.0963(11) Å
c	15.962(2) Å
α	90°
β	99.002(9)°
γ	90°
V	853.1(2) $Å^3$
min/max Θ	2.584° / 28.289°
number of collected reflections	9053
number of independent reflections	2233 (merging r = 0.094)
number of observed reflections	2223 (I>2.0σ(I))
number of refined parameters	208
r	0.0612
rW	0.1476
goodness of fit	0.9166

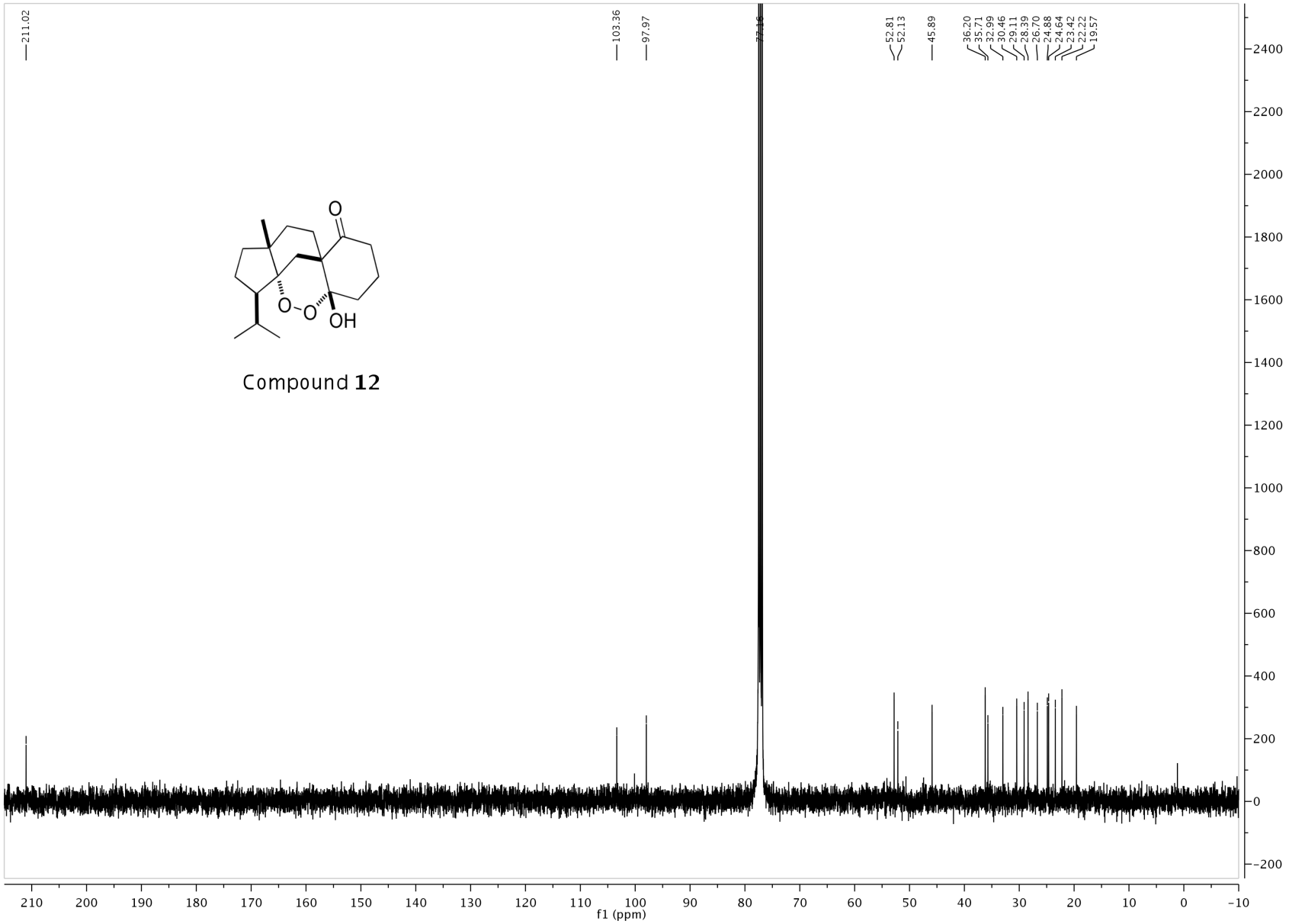

Compound **10**
f1 (ppm)

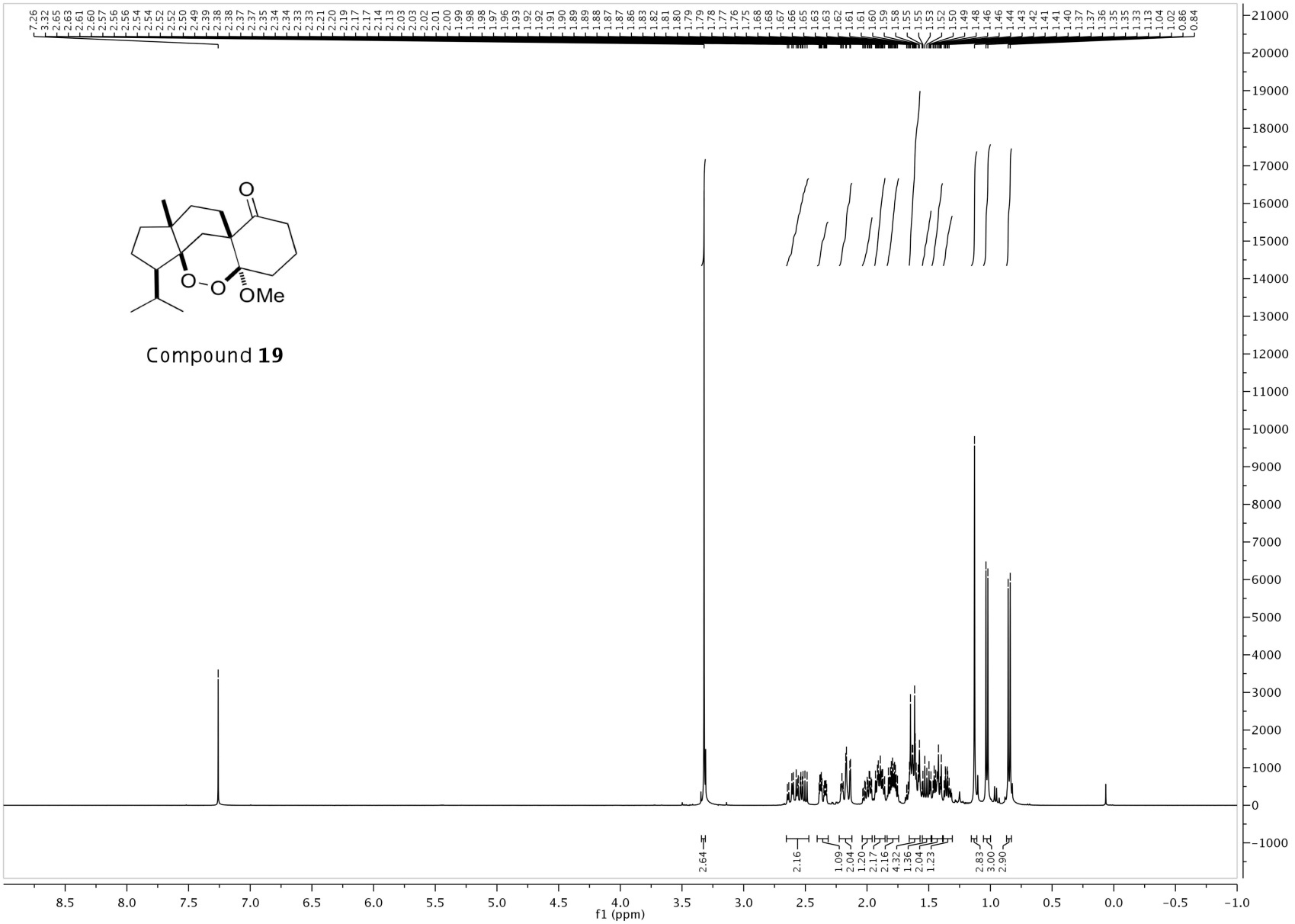

171.81
163.39
103.32
77.16
50.89
45.19
43.75
38.04
37.53
35.45
28.87
27.62
23.32
22.03
16.59
O
N
Compound **10**
f1 (ppm)


Compound 4
O
O
O
OH
f1 (ppm)

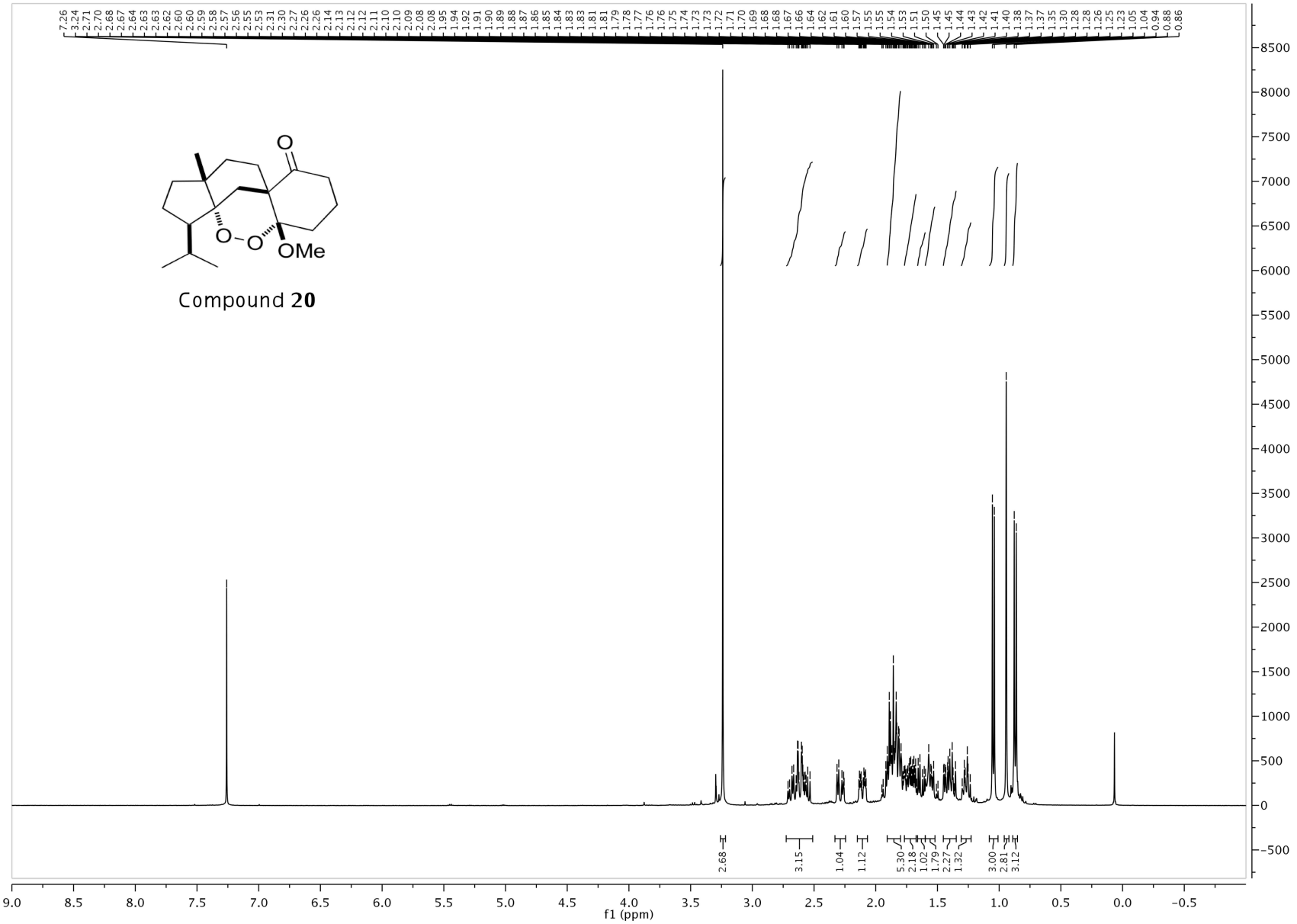

211.14
103.40
90.51
77.16
60.49
50.63
45.74
40.23
35.75
34.47
30.76
28.66
28.50
28.37
27.34
23.82
22.22
21.98
19.39
O
O
O
OH
Compound 4
f1 (ppm)

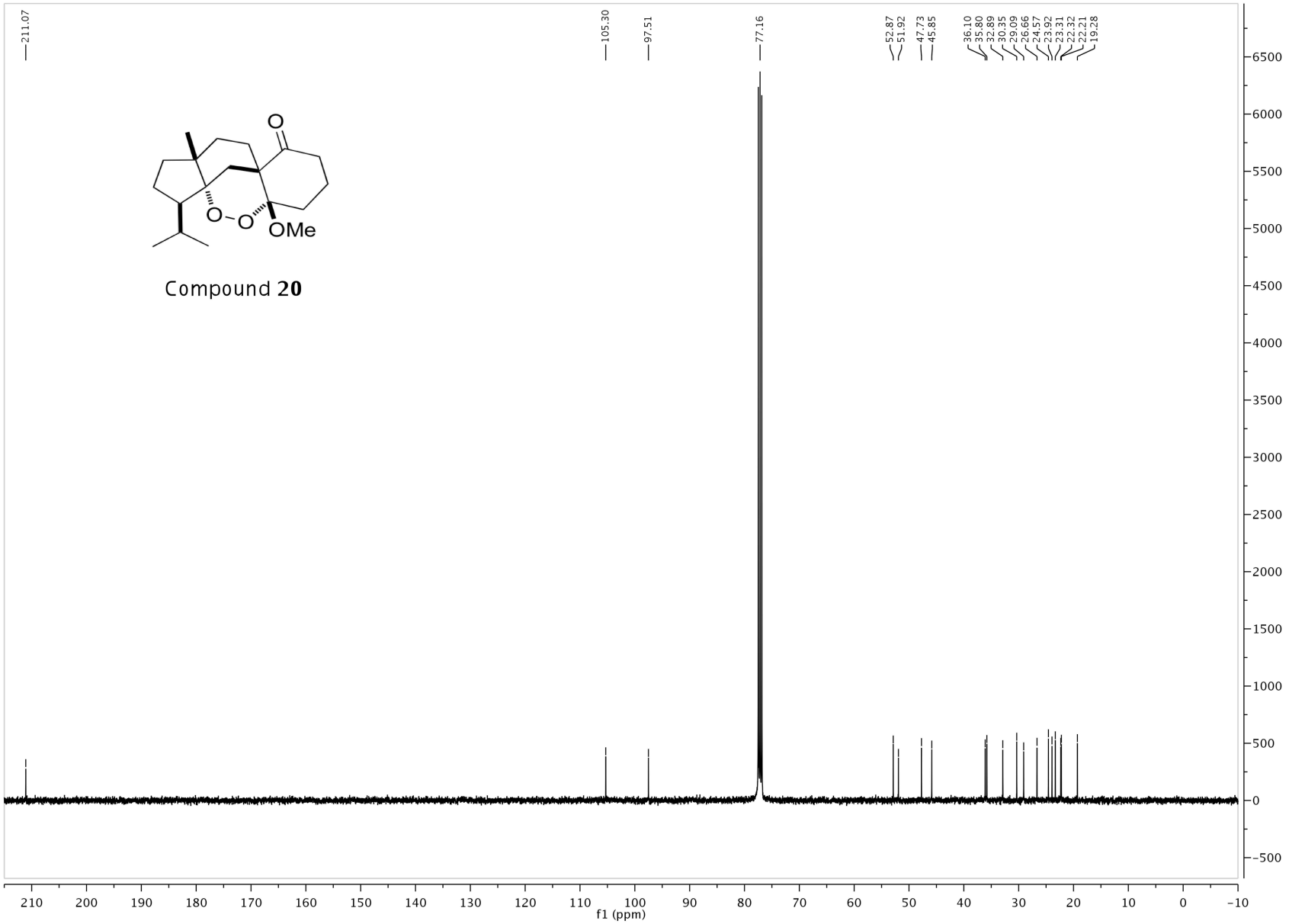

Compound 12
f1 (ppm)

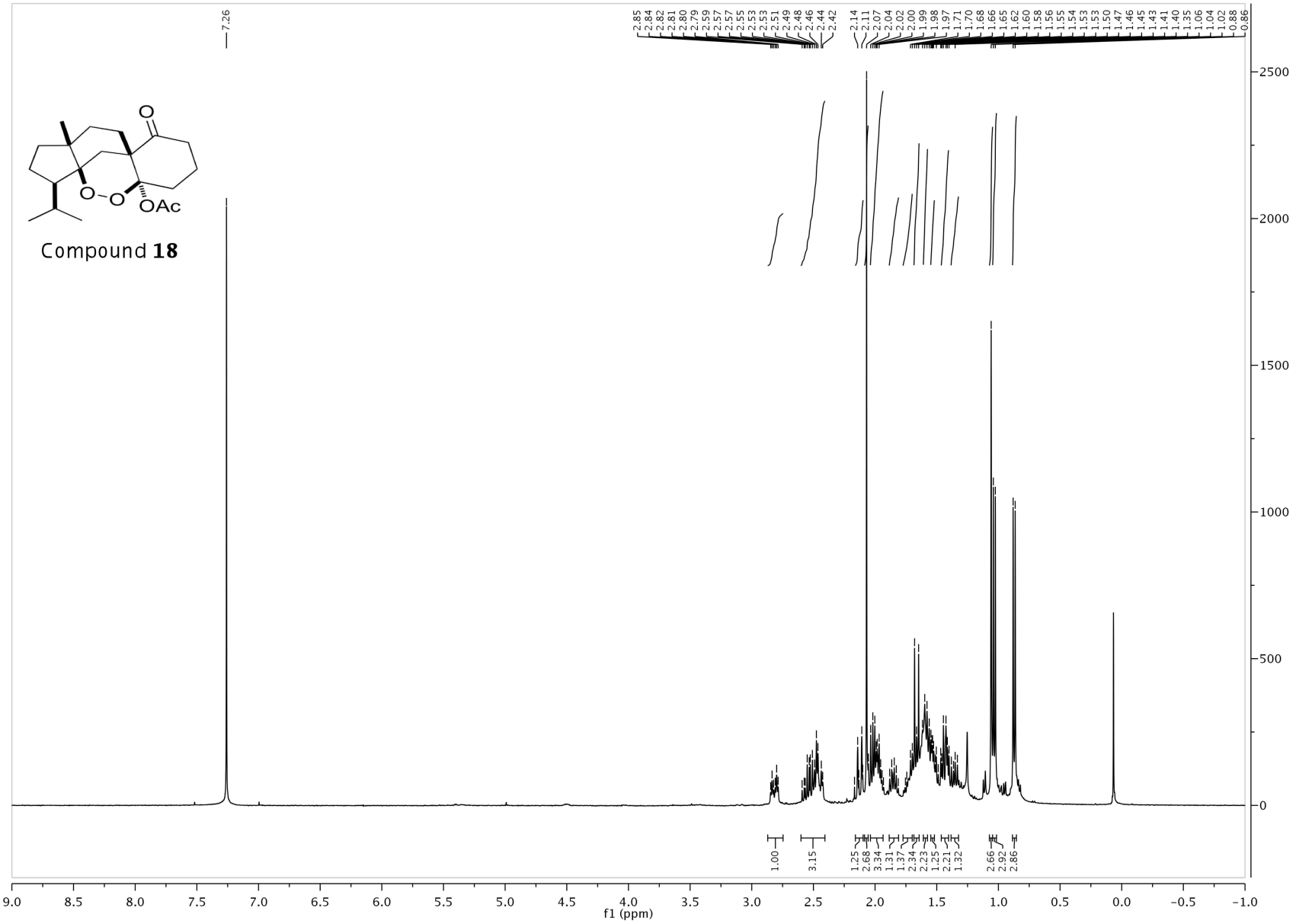

211.02
103.36
97.97
77.16
52.81
52.13
45.89
36.20
35.71
32.99
30.46
29.11
28.39
26.70
24.88
24.64
23.42
22.22
19.57
O
O
O
OH
Compound 12
f1 (ppm)

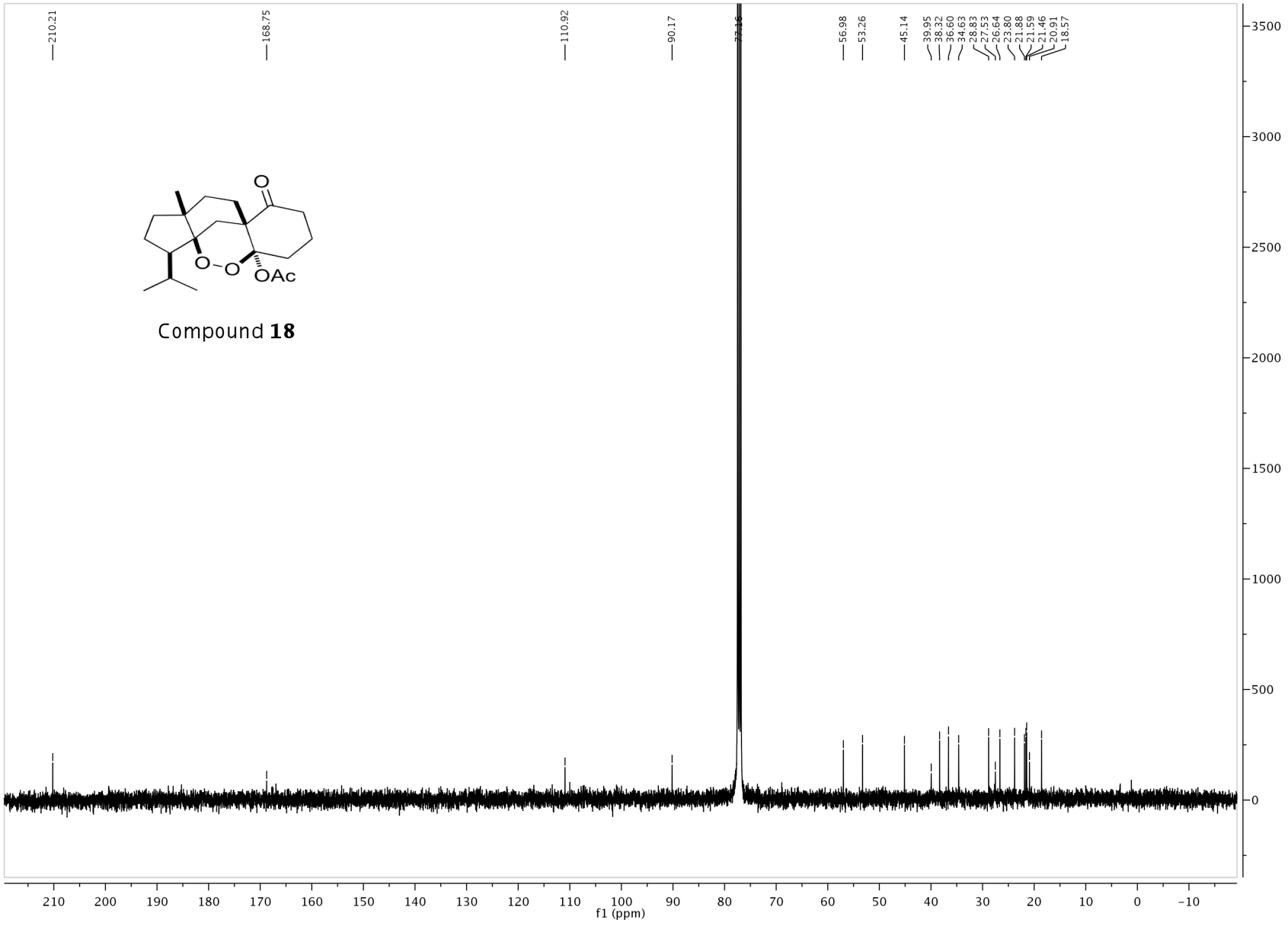

Compound 19
f1 (ppm)


211.74
106.71
89.14
77.16
57.40
53.80
49.76
45.39
42.44
37.66
36.79
34.23
29.34
27.17
24.13
24.03
22.53
21.81
21.50
18.50
O
O
O
OMe
Compound 19
f1 (ppm)


Compound 20
f1 (ppm)


211.07
105.30
97.51
77.16
52.87
51.92
47.73
45.85
36.10
35.80
32.89
30.35
29.09
26.66
24.57
23.92
23.31
22.32
22.21
19.28
O
O
O
OMe
Compound 20
f1 (ppm)


Compound 18
f1 (ppm)


210.21
168.75
110.92
90.17
77.16
56.98
53.26
45.14
39.95
38.32
36.60
34.63
28.83
27.53
26.64
23.80
21.88
21.59
21.46
20.91
18.57
O
O
O
OAc
Compound 18
3500
3000
2500
2000
1500
1000
500
0
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)