Supporting Information

Total Synthesis, and structural revision of chaetoviridins A

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I. Materials and Methods

General Information

All solvents were dried following standard procedures: toluene, methylene chloride (DCM) was obtained from MB SPS-800 apparatus from MBRAUN. THF: distillation over Na°/benzophenone. Cyclohexane and ethyl acetate (EtOAc) were purchased at ACS grade quality and used without further purification, unless otherwise stated. Commercially available reagents were used without further purification, unless otherwise stated. All reactions involving air- and moisture sensitive reagents were performed under Argon using syringe-septum cap technique. Column chromatography purifications were performed on silica gel (40-63 μm). Thin-layer chromatography (TLC) analyses were carried out on Merck DC Kieselgel 60 F-254 aluminum sheets. The spots were visualized through illumination with UV lamp (λ = 254 nm) and/or staining with $KMnO_4$. Phosphate buffer PB (0.1 M, pH 7.4) was prepared using water purified with a Milli-Q system (purified to 18.2 MΩ.cm).

Instruments and methods

Circular dichroism (CD) spectra were acquired on a MOS 500 dichrograph (Bio-Logic, Claix, France). Each chaetoviridin was dissolved in MeOH at a final concentration of 0.2 mg/mL. Data points were collected from 200 to 500 nm at a scan rate of 1nm/s with a 1 mm optical path length quartz cell, and were measured at room temperature (20 °C). IR spectra were recorded with a universal ATR sampling accessory. ^{1}H and ^{13}C NMR spectra (C13APT or C13CPD experiments) were recorded on a 300 MHz spectrometer. Chemical shifts are expressed in parts per million (ppm) from the residual non-deuterated solvent signal contained in $CDCl_3$ (δH = 7.26, δC = 77.16). Multiplicities are described as s (singlet), d (doublet), t (triplet), q (quartet), qn (quintet), st (sextet), sp (septet), m (multiplet), bs (broad singlet), dm (doublet of multiplets) and associated combinations dd, ddd, etc. (doublet of doublets, doublet of doublets of doublets, etc.). Coupling constants, J values, are reported in Hz. High-resolution mass spectra (HRMS) were obtained using an orthogonal acceleration time-of-flight (oa-TOF) mass spectrometer equipped with an electrospray source and in the positive and negative modes (ESI+/-). Optical rotations were determined on a Perkin Elmer 341 digital polarimeter at λ = 589 nm (*i.e.*, sodium D line), using a 1.0 mL cell (l = 1 dm), and are given as $[\alpha]^{T}_{D}$, which were calculated as following: $[\alpha]^{T}_{D} = 100 \times (\alpha / l \times c)$ where *c*: concentration in g/100 mL solvent.

II. Chiral HPLC traces for compound 12 and its racemic mixture

Column: Chiralpak IC (5 µm, 4.6 × 250 mm);

Eluent system: Heptane/isopropanol A (95:5);

Flow rate: 1 mL/min;

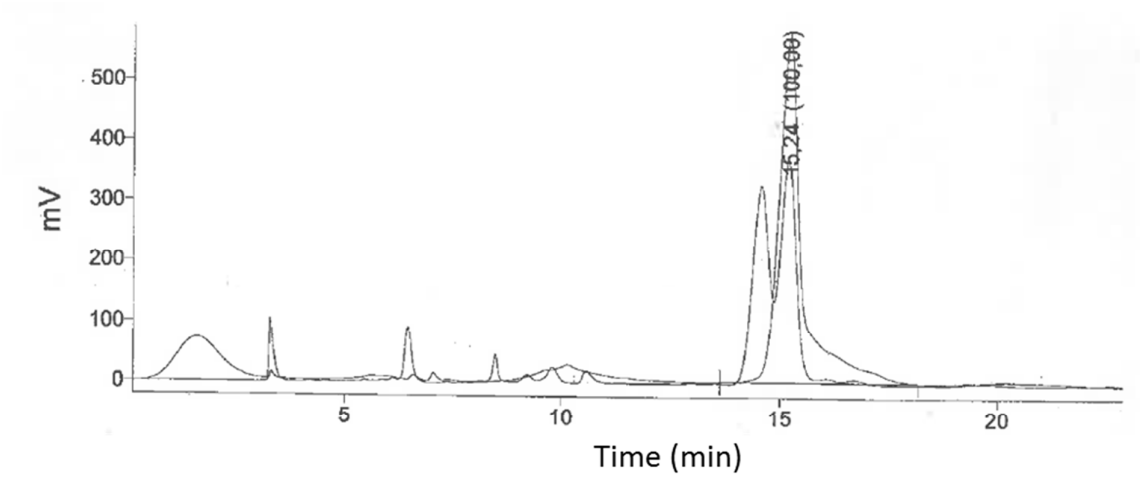


Figure S1. Chiral HPLC trace overlay of the enantiopure lactone **12** and its racemic mixture.

III. Circular dichroism spectroscopy of chaetoviridins 24, 25, 29-32

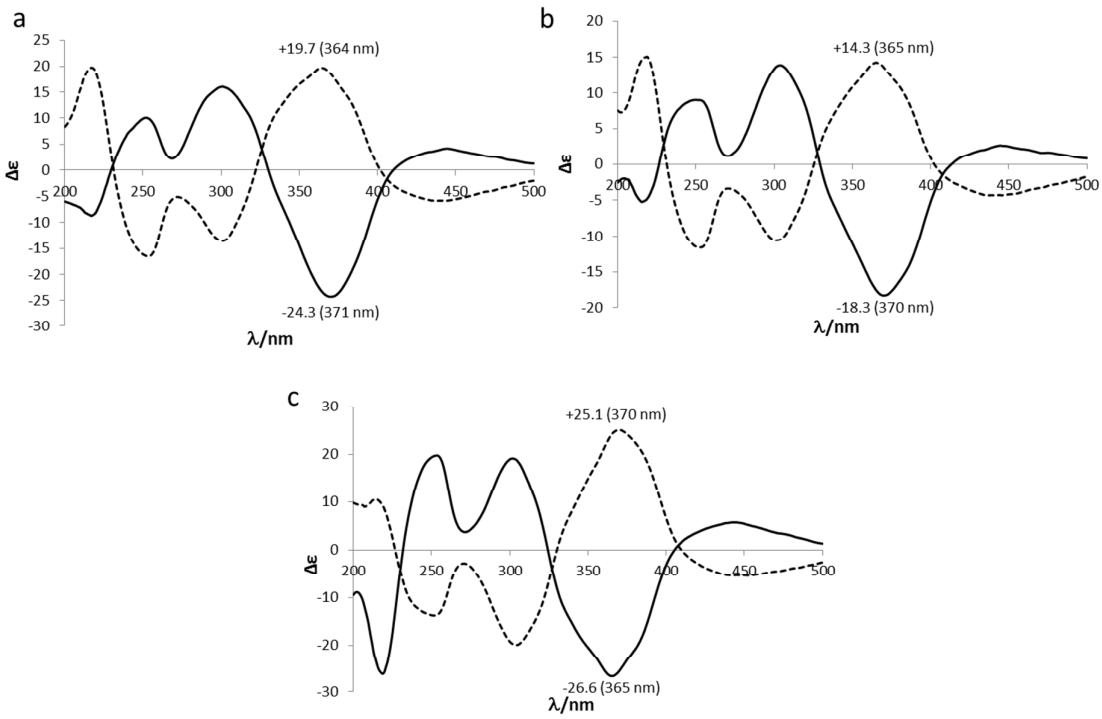
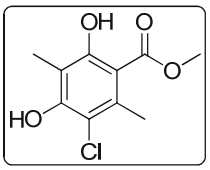


Figure S2. Circular dichroism spectra of chaetoviridins: (**a**) **24** (black line), **25** (dotted line); (**b**) **29** (black line), **30** (dotted line); (**c**) **31** (black line), **32** (dotted line), recorded in MeOH at 20 °C.

IV. Experimental procedures

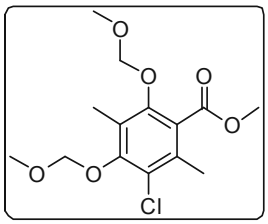
IV.1. Synthesis of the (7*S*, 4'*S*, 5'*R*, 11*S*)-chaetoviridin-A 24 and its epimer (7*R*, 4'*S*, 5'*R*, 11*S*)-chaetoviridin-A 25

Methyl 3-chloro-4,6-dihydroxy-2,5-dimethylbenzoate:



To a solution of methyl atratate **7** (20 g, 101.9 mmol, 1 eq.) in MeCN (150 mL) was added N-chlorosuccinimide (16.3 g, 122 mmol, 1.2 eq.) at room temperature. The mixture was then heated at 50 °C for 5 h. The reaction mixture was concentrated under reduced pressure. The crude product was then purified by flash chromatography (silica gel, cyclohexane/EtOAc 95:5) to give the title compound (23 g, 100 mmol, 98%) as a white solid. R_f = 0.5 (Cyclohexane/EtOAc 95:5); m.p.: 94-96 °C; ^{1}H NMR (300MHz, $CDCl_3$) δ (ppm): 11.70 (s, 1H), 6.16 (brs, 1H), 3.94 (s, 3H), 2.59 (s, 3H), 2.16 (s, 3H); ^{13}C NMR (300MHz, $CDCl_3$) δ (ppm): 172.0, 160.9 153.9, 135.7, 113.7, 110.5, 106.4, 52.3, 19.8, 8.8; IR (Neat) ν (cm^{-1}): 3465, 2783, 1725, 1653, 1581, 1433, 1409, 1381, 1300, 1269, 1193, 1163, 1098; HRMS (ESITOF): calculated for $C_10H_{10}O_4Cl$ ([M^{35}Cl+H]$^+$) ([M^{35}Cl-H]$^-$): 229.0268, found 229.0258.

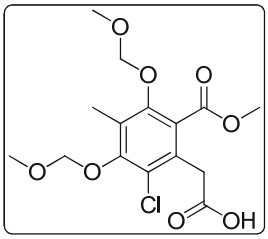
Methyl 3-chloro-4,6-bis(methoxymethoxy)-2,5-dimethylbenzoate 8:



To a solution of methyl 3-chloro-4,6-dihydroxy-2,5-dimethylbenzoate (13.2 g, 57.2 mmol, 1 eq.) in DMF (250 mL) at 0 °C was added NaH (60% in mineral oil, 6.86 g, 171.6 mmol, 3 eq.). The resulting mixture was stirred at 0 °C for 20 min, then a solution of chloromethyl methyl ether (2.1 M in toluene, 83.6 mL, 171.6 mmol, 3 eq.) was slowly added. The resulting mixture was warmed to room temperature and stirred for 3 h before it was quenched with a solution of saturated aq NH_4Cl. The layers were separated and the aqueous layer was extracted with cyclohexane (4 $\times$ 200 mL). The combined organic layers were washed with a solution of saturated aq $NaHCO_3$, dried over anhydrous $MgSO_4$ and concentrated under reduced pressure. Finally, the crude product was purified by chromatography (silica gel, cyclohexane/EtOAc 90:10) to afford the corresponding ester **8** (13.6 g, 43, 75 %) as pale yellow oil. R_f = 0.5 (cyclohexane/EtOAc 80:20); ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm): 5.06 (s, 2H), 4.96 (s, 2H), 3.91 (s, 3H), 3.63 (s, 3H), 3.53 (s, 3H), 2.29 (s, 3H), 2.27 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm): 168.0, 153.9, 151.9, 132.4, 126.8, 125.4, 124.9, 100.5, 99.6, 57.9, 57.6, 52.5, 17.7, 11.2; IR (Neat) *v* (cm^{-1}): 2952, 2830, 1730, 1590, 1561, 1433,

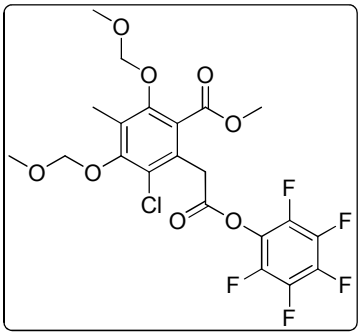
1384, 1322, 1302, 1270, 1210, 1193, 1154, 1111, 1086, 1041, 994. HRMS (ESITOF): calculated for $C_{14}H_{20}O_6Cl$ ($[M^{35}Cl+H]^+$): 319.0948, found 319.0936.

2-(2-chloro-6-(methoxycarbonyl)-3,5-bis(methoxymethoxy)-4-methylphenyl)acetic acid 9:



To a stirred solution of DIPA (5.74 mL, 41.7 mmol, 1.3 eq.) in THF (200 mL) at -78 °C was slowly added 15.5 mL of *n*-BuLi solution (2.5 M in hexane, 11.2 mmol, 1.2 eq.). The resulting mixture was warmed to 0 °C and stirred for 20 min before re-cooling to -78 °C. Then a solution of ester **8** (10 g, 31.3 mmol, 1 eq.) in THF (10 mL) was added. The resulting reddish mixture was stirred at -78 °C for 20 min before adding dry ice. Then, the reaction mixture was stirred for 10 min at -78 °C before warming up to room temperature. Aqueous 1M HCl was carefully added until pH = 1. The layers were separated and the aqueous layer was extracted with EtOAc (5 × 60 mL), washed with brine (100 mL), dried over anhydrous $MgSO_4$ and concentrated under reduced pressure to furnish the crude product **9** as pale yellowish solid (10.9 g, 30.1 mmol, 95%). R_f = 0.4 (cyclohexane/EtOAc 50:50); m.p.: 80-82 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm): 5.08 (s, 2H), 4.96 (s, 2H), 3.90 (s, 3H), 3.85 (s, 2H), 3.63 (s, 3H), 3.53 (s, 3H), 2.30 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm): 175.4, 167.3, 154.5, 152.9, 128.8, 127.9, 126.6, 125.9, 100.6, 99.7, 58.0, 57.7, 52.7, 36.7, 11.4; IR (Neat), ν (cm^{-1}): 2953, 2831, 1728, 1561, 1423, 1384, 1299, 1276, 1210, 1195, 1154, 1046, 974; HRMS (ESITOF): calculated for $C_{14}H_{18}O_6Cl$ $[M^{35}Cl\text{-}CO_2]^-$ 317.0792, found 317.0797.

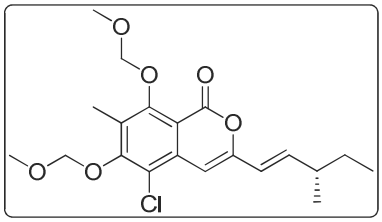
Methyl 3-chloro-4,6-bis(methoxymethoxy)-5-methyl-2-(2-oxo-2-(perfluorophenoxy)ethyl)benzoate 10:



To a stirred solution of acid **9** (5 g, 13.8 mmol, 1 eq.) and pentafluorophenol (3.1 g, 16.5 mmol, 1.2 eq.) in CH_2Cl_2 (30 mL) at 0 °C were added EDCI (3.2 g, 16.5 mmol, 1.2 eq.) and DMAP (337 mg, 2.76 mmol, 0.2 eq.). The mixture was stirred at rt for 1h before it was quenched with a solution of saturated aq NH_4Cl. The layers were separated and the aqueous layer was extracted with CH_2Cl_2 (3 × 40 mL), and the organic layers were combined and dried over anhydrous $MgSO_4$, filtered, and concentrated under reduced pressure. Finally, the crude product was purified by chromatography (silica gel, cyclohexane/EtOAc 93:7) to afforded ester **10** (4.7 g, 1.7 mmol, 65 %) as a white solid: R_f = 0.4 (cyclohexane/EtOAc 85:15); mp: 74-76 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm) : 5.10 (s, 2H), 4.99 (s, 2H), 4.15 (s, 2H), 3.92 (s, 3H), 3.64 (s, 3H), 3.54 (s, 3H), 2.32 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm) : 166.9, 165.7, 154.7, 153.3, 141.2 (dm, J = 247.5 Hz, 2C), 139.6

(dm, J = 255 Hz), 137.9 (dm, J = 255 Hz, 2C), 128.6, 127.6, 126.7, 125.8, 125.1, 100.7, 99.8, 58.0, 57.7, 52.6, 36.0, 11.5; ^{19}F NMR (282 MHz, $CDCl_3$) δ (ppm) : 152.5 (d, *J* = 16.9 Hz, 2F), 157.8 (t, *J* = 21.4 Hz, 1F), 162.4 (t, *J* = 19.7 Hz, 2F); IR (Neat), ν (cm-1) : 2961, 1783, 1745, 1516, 1434, 1416, 1327, 1302, 1251, 1155, 1102, 1085, 992 ; HRMS (ESITOF): calculated for $C_{21}H_{18}ClF_5KO_8$ $[M^{35}Cl+K]^+$ 567.0247, found 567.0248.

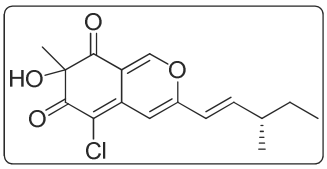
(*S*,E)-5-chloro-6,8-bis(methoxymethoxy)-7-methyl-3-(3-methylpent-1-en-1-yl)-1*H*-isochromen-1-one 12:



To a stirred solution of dimethyl (trimethylsilyl)methylphosphonate[1] (5.09 g, 26.0 mmol, 2.2 eq.) in THF (30 mL) at −78 °C was added *n*-BuLi (10 mL, 2.5 M in hexane, 24.8 mmol, 2.1 eq.). The mixture was stirred for 30 min at −78 °C before adding a solution of ester **10** (6.24 g, 11.8 mmol, 1 eq.) in THF (20 mL). After stirring for 1h at -78 °C, the orange reaction medium was hydrolyzed by addition of saturated aqueous NH_4Cl was added and allowed to reach room temperature. The mixture was extracted with EtOAc (4 × 100 mL). The combined organic layers were dried over anhydrous $MgSO_4$, filtered and concentrated under reduced pressure. The crude product was filtered through a thick pad of silica gel, eluting with CH_2Cl_2/MeOH 99:1 to give a yellow oil containing a 65:35 (^{1}H NMR estimation) mixture of ketophosphonate **11** and dimethylphosphonate which was used in the next step without further purification. 1.6 g of this crude mixture dissolved in anhydrous EtOH (25 mL) and anhydrous K_2CO_3 (920 mg, 6.63 mmol, 3 eq.) at room temperature. The reaction mixture was stirred 20 min and the freshly prepared aldehyde (*S*)-**13**[2] (571 mg, 6.63 mmol, 3 eq.) was added. The resulting mixture was stirred at room temperature overnight before it was quenched with a solution of saturated aq NH_4Cl (15 mL). The aqueous layer was extracted with EtOAc (3 × 40 mL), then combined organic layers were washed with brine (50 mL), dried over anhydrous $MgSO_4$, filtered and concentrated under reduced pressure. The crude product was purified by chromatography on silica gel, eluting with cyclohexane/EtOAc 95:5 to afford the lactone **12** (660 mg, 1.78 mmol), as a white solid in 37% yield on the three steps (phosphonatation, wittig and lactonization). R_f = 0.4 (cyclohexane/EtOAc : 80/20); m.p.: 53-55 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm) : 6.61 (s, 1H), 6.52 (dd, *J* = 15, 9 Hz, 1H), 6.00 (d, *J* = 15.6 Hz, 1H), 5.15 (s, 2H), 5.13 (s, 2H), 3.63 (s, 3H), 3.61 (s, 3H), 2.36 (s, 3H), 2.21 (sp, *J* = 9 Hz, 1H), 1.40 (q, *J* = 7.2 Hz, 2H), 1.05 (d, *J* = 6 Hz, 3H), 0.87 (t, J = 7.2 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm) : 158.7, 158.4, 158.3, 153.1, 143.4, 136.3, 128.0, 120.2, 118.8, 110.6, 101.9, 100.2, 99.8, 58.1, 57.8, 38.8, 29.4, 19.6, 11.8, 11.5; IR (Neat), *v* (cm^{-1}): 2961, 2918,1737, 1651, 1617, 1571, 1537, 1438, 1383, 1360, 1301, 1277, 1236, 1161, 1111, 1083,

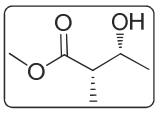
1054, 979. HRMS (ESITOF): calculated for $C_{20}H_{25}O_6{}^{35}ClNa$ $[M^{35}Cl+Na]^+$ 419.1237, found 419.1232; $[\alpha]_D{}^{25.0}$ = +22 (*c* = 1.0, $CHCl_3$).

7*RS*,11*S* cazisochromene 14:



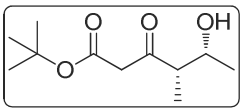
To a stirred solution of lactone **12** (530 mg, 1.33 mmol, 1 eq.) in toluene (20 mL) at -78 °C was added DiBAl-H (1.2 M in toluene, 1.44 mL, 1.72 mmol, 1.3 eq.). The resulting mixture was stirred at -78 °C for 20 min before it was quenched with an aqueous solution of 1 M HCl. The reaction medium was diluted with EtOAc and the two layers were separated. The combined organic layers were washed with an aqueous solution of 1 M HCl (4 × 10 mL), brine, dried over anhydrous $MgSO_4$, filtered and concentrated under reduced pressure to afford the lactol as a yellow oil containing a mixture of diastereomers, which was immediately used without further purification. The crude product was dissolved in CH_2Cl_2 (15 mL) at room temperature, and TFA (717 μL, 9.31 mmol, 7 eq.) was added, followed by water (480 μL, 26.6 mmol, 20 eq.) and IBX (1.12, 4 mmol, 3 eq.). The resulting mixture was stirred for 3 h before it was filtered to remove the insoluble IBX residue and the filtrate was dried over anhydrous $MgSO_4$, then concentrated under reduced pressure. The crude product was purified by chromatography (silica gel, cyclohexane/EtOAc from 80:20 to 60:40) afforded alcohol **14** as an inseparable mixture of C-7 epimers (138 mg, 0.45 mmol, 34 %) and as an orange/brown oil. R_f = 0.2 (cyclohexane/EtOAc 60:40); ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm): 7.92 (s, 1H), 6.58 (s, 1H), 6.57 (dd, *J* = 9.0; 15.0 Hz, 1H), 6.07 (d, *J* = 15.0 Hz, 1H), 2.29 (qn, *J* = 6.0 Hz, 1H), 1.58 (s, 3H), 1.45 (qn, *J* = 6.0 Hz, 2H), 1.09 (d, *J* = 9.0 Hz, 3H), 0.91 (t, *J* = 6.0 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm): 194.0, 189.9, 157.7, 151.7, 148.0, 140.0, 119.8, 115.3, 109.5, 105.7, 84.1, 39.1 and 39.0 (2 dias), 29.2, 28.7, 19.3 and 19.3 (2 dias), 11.8; IR (Neat), *v* (cm^{-1}): 3361, 2970, 1719, 1615, 1518, 1420, 1241, 1215, 1173, 1139, 1100, 1016, 977; HRMS (ESITOF): calculated for $C_{16}H_{18}O_4{}^{35}Cl$ $[M^{35}Cl+H]^+$ 309.0894, found 309.0896.

(2S,3R)-methyl 3-hydroxy-2-methylbutanoate 17: [3]



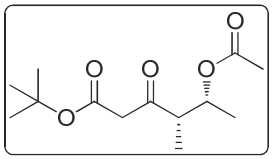
To a stirred solution of aldol **16**[4] (1,00 g, 3.2 mmol, 1 eq.) in MeOH (50 mL) was added DMAP (100 mg, 0.8 mmol, 0.25 eq.) at room temperature. The mixture was stirred for 16 h and the solvent was removed under reduced pressure. The crude product was purified by chromatography (silica gel, cyclohexane/EtOAc 85:15) to afford ester **17** (230 mg, 55 %) as a colorless oil. R_f = 0.2 (cyclohexane/EtOAc 70:30); ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm): 4.07 (m, 1H), 3.71 (s, 3H), 2.56 (bs, 1H), 2.52 (qd, *J* = 7.2, 3.9 Hz, 1H), 1.19 (d, *J* = 7.2 Hz, 3H), 1.17 (d, *J* = 6.4 Hz, 3H). This ^{1}H NMR analysis was consistent with reported data.[3]

(4S,5R)-tert-butyl 5-hydroxy-4-methyl-3-oxohexanoate 18:[3]



To a stirred solution of DIPA (1.4 mL, 9.9 mmol, 3.3 eq.) in THF (20 mL) at -78 °C was slowly added *n*-BuLi (2.5 M in hexane, 3.7 mL, 9.3 mmol, 3.2 eq.). The resulting mixture was warmed to 0 °C and stirred for 20 min before re-cooling to -78 °C. Then, a solution of ester **17** (400 mg, 3.03 mmol, 1 eq.) in THF (5 mL) was added, and the resulting mixture was stirred at -78 °C for 1.5 h before it was warmed to room temperature. The reaction was quenched by addition of 15 mL of a solution of saturated aqueous NH_4Cl and the two layers were separated. The aqueous layer was extracted with EtOAc (3 × 10 mL), then combined organic layers were washed with brine (20 mL) dried over anhydrous $MgSO_4$, filtered and concentrated under reduced pressure. The crude was purified by column chromatography on silica gel, eluting with cyclohexane/AcOEt 70:30 to afford the β-ketoester **18** in equilibrium with minor amounts of its enol form (600 mg, 2.77 mmol, 91 %) as a colorless oil. R_f = 0.3 (cyclohexane/EtOAc 80:20); ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm): 4.17 (dq, *J* = 6.6, 3.6 Hz, 1H), 3.48 (d, *J* = 15.3 Hz, 1H), 3.41 (d, *J* = 15.3 Hz, 1H), 2.71 (dq, *J* = 7.2, 3.3 Hz, 1H), 1.46 (s, 9H), 1.17 (d, *J* = 6.6 Hz, 3H), 1.16 (d, J = 7.2 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm): 208.0, 166.6, 82.3, 67.3, 51.9, 49.9, 28.1, 20.0, 9.9; IR (Neat), *v* (cm^{-1}): 3432, 2976, 2930, 1729, 1704, 1456, 1368, 1317, 1250, 1145, 1073, 951; HRMS (ESITOF): calculated for $C_{11}H_{20}O_4Na$ ($[M+Na]^+$) 239.1259, found 239.1261; The ^{1}H NMR analysis was consistent with reported data.[3]

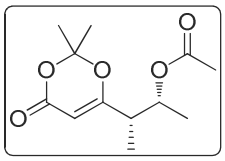
(4*S*,5*R*)-tert-butyl 5-acetoxy-4-methyl-3-oxohexanoate 19a:



To a stirred solution of β-ketoester **18** (550 mg, 2.54 mmol, 1 eq.) in dry CH_2Cl_2 (33 mL) at room temperature were successively added Et_3N (696 μL, 5.09 mmol, 2 eq.), 4-DMAP (62 mg, 0.51 mmol, 0.2 eq.) and acetic anhydride (264 μL, 2.81 mmol, 1.1 eq.). The resulting mixture was stirred for 2h before it was quenched by 15 mL a solution of saturated aqueous NH_4Cl and the two layers were separated. The aqueous layer was extracted with CH_2Cl_2 (3 × 20), then organic layers were dried over anhydrous $MgSO_4$, filtered and concentrated under reduced pressure. The crude product was purified by chromatography (silica gel, cyclohexane/EtOAc 80:20) to afford the corresponding acetylated product **19a** in equilibrium with minor amounts of its enol form (577 mg, 2.23 mol, 88 %) as a pale orange oil. R_f = 0.4 (cyclohexane/EtOAc 80:20); ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm): 5.17 (qn, *J* = 6.3 Hz, 1H), 3.46 (d, *J* = 15.6 Hz, 1H), 3.39 (d, J = 15.6 Hz, 1H), 2.91 (qn, *J* = 6.9 Hz, 1H), 2.04 (s, 3H), 1.46 (s, 9H), 1.21 (d, *J* = 6.3 Hz, 3H), 1.12 (d, *J* = 6.3 Hz, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm) : 204.2, 170.3, 166.4, 82.1, 70.8, 50.5, 50.3, 28.1, 21.2, 17.5, 11.8 ; IR, *v* (cm^{-1}) : 2984, 1734, 1712, 1644, 1456,

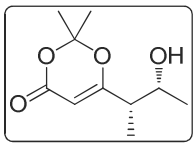
1368, 1320, 1236, 1145, 1075, 1021, 946 ; HRMS (ESITOF): calculated for $C_{13}H_{22}O_5Na$ ($[M+Na]^+$) 281.1365, found 281.1359.

(2R,3S)-3-(2,2-dimethyl-4-oxo-4H-1,3-dioxin-6-yl)butan-2-yl acetate 20:



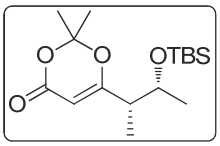
To a stirred solution of acetylated β-ketoester **19a** (400 mg, 1.54 mmol, 1 eq.) in acetone (1.13 mL, 15.4 mmol, 10 eq.) at 0 °C were successively added acetic anhydride (2.2 mL, 23.1 mmol, 15 eq.) and sulfuric acid (83 µL, 1.54 mmol, 1 eq.). The resulting mixture was stirred for 1 h before it was quenched with a solution of saturated aq $NaHCO_3$ and the two layers were separated. The aqueous layer was extracted with EtOAc (3 ×), then organic layers were dried over $MgSO_4$, filtered and concentrated under reduced pressure. The crude product was purified by chromatography (silica gel, cyclohexane/EtOAc 90:10) afforded the dioxinone **20** (277 mg, 75 %) as a white solid: R_f = 0.5 (cyclohexane/EtOAc 80:20); mp: 48-50°C; ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm) : 5.24 (s, 1H), 5.02 (qn, *J* = 6.3 Hz, 1H), 2.46 (qn, *J* = 6.9 Hz, 1H), 2.00 (s, 3H), 1.65 (s, 3H), 1.62 (s, 3H), 1.21 (d, *J* = 6.3 Hz, 3H), 1.13 (d, *J* = 6.9 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm): 171.9, 170.3, 161.1, 106.5, 94.1, 70.5, 43.0, 25.6, 24.3, 21.1, 17.9, 12.5; IR (Neat), ν (cm^{-1}): 2929, 1721, 1634, 1457, 1365, 1314, 1271, 1238, 1203, 1079, 1054, 1024, 998 ; HRMS (ESITOF): calculated for $C_{12}H_{18}O_5Na$ ($[M+Na]^+$) 265.1052, found 265.1060; $[a]_D^{22} =$ +25 (c = 1.0, $CHCl_3$).

6-((2*S*,3*R*)-3-hydroxybutan-2-yl)-2,2-dimethyl-4H-1,3-dioxin-4-one:



To a suspension of lipase *Candida cylindracea* in 0.1 M phosphate buffer (pH = 7.4, 12 mL) was added dioxinone **20** (256 mg, 1.05 mmol, 1 eq.) in THF (3.5 mL) at room temperature. The resulting mixture was stirred for 6 days at 30 °C before it was quenched by a mixture of water/EtOAc (1:1) and the two layers were separated. The aqueous layer was extracted with EtOAc (5 × 10 mL), then organic layers were dried over anhydrous $MgSO_4$, filtered and concentrated under reduced pressure to afford the deprotected dioxinone (186 mg, 0.93 mmol, 88 %) as a pale yellow residue which was used without further purification ; R_f = 0.2 (cyclohexane/EtOAc 50:50); ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm) : 5.28 (s, 1H), 3.93 (qn, *J* = 6.3 Hz, 1H), 2.2 (qn, *J* = 6.9 Hz, 1H), 1.90 (bs, 1H), 1.67 (s, 6H), 1.21 (d, *J* = 6.3 Hz, 1H), 1.16 (d, *J* = 7.2 Hz, 1H); ^{13}C NMR (75 MHz, CDCl3) δ (ppm) : 172.4, 160.3, 105.4, 92.6, 67.8, 44.2, 24.3, 23.6, 20.2, 10.9; IR (neat), ν (cm-1) : 3437, 2974, 2928, 1708, 1626, 1456, 1391, 1377, 1274, 1253, 1203, 1145, 1096, 1014, 996; HRMS (ESITOF): calculated for $C_{10}H_{17}O_4$ ($[M+H]^+$) 201.1127, found 201.1115; $[a]_D^{22} =$ +10 (*c* = 1.0, $CHCl_3$).

6-((2*S*,3*R*)-3-((tert-butyldimethylsilyl)oxy)butan-2-yl)-2,2-dimethyl-4*H*-1,3-dioxin-4-one 21:

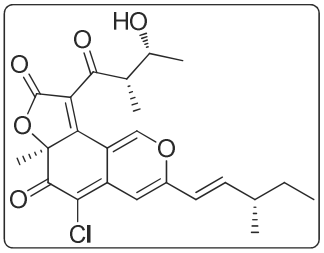


To a stirred solution of dioxinone **33** (96 mg, 0.48 mmol, 1 eq.) in CH_2Cl_2 (4 mL) were successively added imidazole (95 mg, 0.72 mmol, 1.5 eq.) and TBDMSCl (95 mg, 0.62 mmol, 1.3 eq.). The resulting mixture was stirred for 48 h at room temperature before addition of supplementary imidazole (95 mg, 0.72 mmol, 1.5 eq.) and TBDMSCl (95 mg, 0.62 mmol, 1.3 eq). The reaction was concentrated under reduced pressure. The crude product was purified by column chromatography on silica gel, eluting with cyclohexane/EtOAc (95:5) to afford the dioxinone **21** (119 mg, 0.38 mmol, 79 %) as a yellow oil: R_f = 0.5 (cyclohexane/EtOAc : 80/20); ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm): 5.24 (s, 1H), 3.89 (qn, *J* = 6 Hz, 1H), 2.25 (qn, *J* = 7.2 Hz, 1H), 1.68 (s, 6H), 1.15 (d, *J* = 6.3 Hz, 3H), 1.12 (d, J = 7.2 Hz, 3H), 0.87 (s, 9H), 0.05 (s, 3H), 0.04 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm): 173.8, 161.5, 106.3, 93.8, 69.3, 46.5, 25.8, 25.2, 25.1, 21.9, 18.1, 12.9, -4.0, -4.7; IR (Neat), *v* (cm-1): 2929, 2863, 1732, 1628, 1464, 1389, 1376, 1271, 1250, 1203, 1100, 1030, 995; HRMS (ESITOF): calculated for $C_{16}H_{31}O_2Si$ ($[M+H]^+$) 315.1992, found 315.1996; $[a]_D^{22} =$ -5 (*c* = 1.0, $CHCl_3$).

Procedure for the condensation of dioxinone 21 on dearomatized alcohol 14.

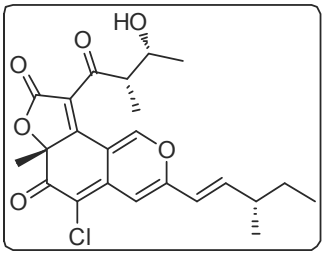
To a stirred solution of dearomatized alcohol **14** (109 mg, 0.35 mmol, 1.0 equiv.) in dry toluene (4 mL) under were added 4Å molecular sieves (50 mg) and the dioxinone **21** (133 mg, 0.42 mmol, 1.2 equiv.). The resulting mixture was stirred for 10 min at room temperature then 1h under toluene reflux. Triethylamine (91 µL, 0.706 mmol, 2.0 equiv.) was added and the reaction was stirred for 1h under reflux. The reaction was then cooled down to room temperature, hydrolyzed with 10 mL 1M aqueous HCl, extracted with EtOAc (4 × 10 mL), washed with brine (15 mL), dried over $MgSO_4$, filtered and concentrated under reduced pressure. ^{1}H NMR analysis of the crude indicated the formation of two products. The crude mixture was dissolved in dry THF (5 mL), and HF·pyridine complex was added was added portionwise every 6 h (*i.e.* 70% HF basis, 1.1 mL, 105 mmol, 300 equiv.) until complete reaction. Reaction was quenched by slow addition of saturated aqueous sodium bicarbonate (30 mL). The layers were separated and the aqueous layer was extracted with EtOAc (3 × 20 mL), washed with brine (50 mL), dried over $MgSO_4$, filtered and concentrated under reduced pressure. Diastereiosomers **24** and **25** were separated by column chromatography on silica gel, eluting with cyclohexane/EtOAc 85:15 to furnish (7*R*,4'*S*,5'*R*,11*S*)-chaetoviridine A **25** as a yellow oil (30 mg, 0.07 mmol, 20%) and with cyclohexane/EtOAc 60:40 to furnish (7S,4'S,5'R,11S)-chaetoviridine A **24** as an orange oil (25 mg, 0.06 mmol, 17%). Overall yield 37%.

(7*S*,4'*S*,5'*R*,11*S*)-chaetoviridine-A 24



R_f= 0.23 (cyclohexane/EtOAc : 70/30); ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm) : 8.77 (s, 1H), 6.63 (dd, *J* = 15.7, 8.1 Hz, 1H), 6.58 (s, 1H), 6.09 (d, *J* = 15.9 Hz, 1H), 4.31 (dq, *J* = 6.4, 3.1 Hz, 1H), 3.70 (dq, *J* = 7.2, 3.0 Hz, 1H), 2.39-2.23 (m, 1H), 1.72 (s, 3H), 1.45 (qn, *J* = 7.5 Hz, 2H), 1.24 (d, *J* = 6.5 Hz, 3H), 1.11.10 (d, *J* = 6.7 Hz, 3H), 1.06 (d, *J* = 7.2 Hz, 3H), 0.91 (t, *J* = 7.4 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm): 201.2, 183.2, 168.0, 165.3, 157.2, 152.1, 148.5, 139.8, 123.2, 119.8, 110.4, 109.2, 105.5, 88.0, 67.4, 48.8, 39.2, 30.5, 29.3, 26.4, 19.7, 19.5, 11.95, 9.9; IR, v (cm$^-$1): 3441, 2964, 2928, 1764, 1684, 1643, 1620, 1513; HRMS (ESITOF): calculated for $C_{23}H_{26}O_6{}^{37}Cl$ ([$M^{35}Cl$+H]$^+$): 433.1418, found 433.1434. calculated for $C_{32}H_{26}O_6{}^{37}Cl$ ([$M^{37}Cl$+H]$^+$): 435.1388, found 435.1422. $[\alpha]_D^{26} =$ +139 (*c* = 0.7, $CHCl_3$) (lit.: $[\alpha]_D^{30}$ = -44 (*c* = 0.03, $CHCl_3$), [5] and $[\alpha]_D^{20}$ + 16 (*c* = 0.002, $CHCl_3$)[6]); CD (*c* = 4.6 × 10^{-4} M, MeOH) λ_{max} (Δε) = 371 (-24.3).

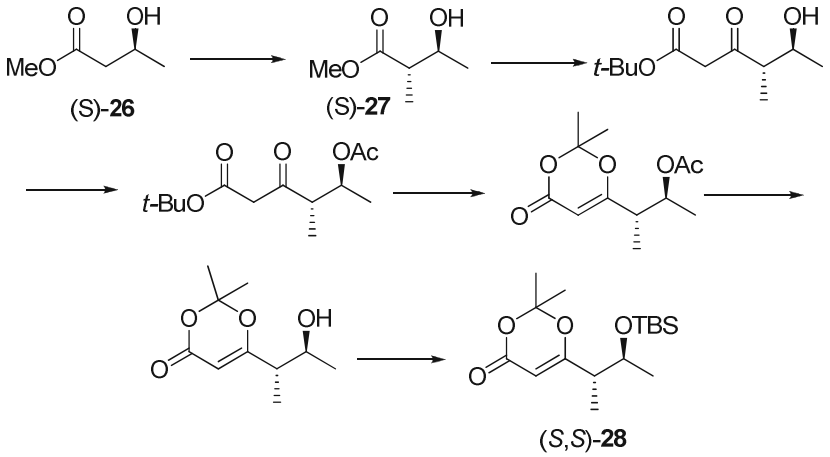
(7*R*,4'*S*,5'*R*,11*S*)-chaetoviridine-A 25



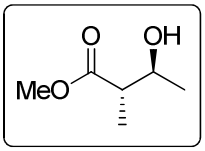
R_f= 0.34 (cyclohexane/EtOAc : 70/30); ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm) : 8.77 (s, 1H), 6.61 (dd, *J* = 15.7, 8.0 Hz, 1H), 6.56 (s, 1H), 6.08 (d, *J* = 15.6 Hz, 1H), 4.15-4.03 (m, 1H), 3.72 (dq, *J* = 6.8, 3.2 Hz, 1H), 2.39-2.21 (m, 1H), 1.72 (s, 3H), 1.45 (qn, *J* = 7.2 Hz, 2H), 1.17 (d, *J* = 6.8 Hz, 3H), 1.14 (d, *J* = 6.8 Hz, 3H), 1.10 (d, *J* = 6.7 Hz, 3H), 0.92 (t, *J* = 7.4 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm): 200.1, 183.3, 168.0, 163.8, 157.1, 151.6, 148.2, 139.7, 124.2, 119.7, 110.4, 109.1, 105.4, 87.7, 68.3, 49. 7, 39.0, 29.2, 26.3, 20.5, 19.3, 11.7, 8.8; IR, *v* (cm^{-1}): 3476, 2966, 2927, 2874, 1762, 1683, 1644, 1616, 1511, 1167, 895, 851, 734, 692; HRMS (ESITOF): calculated for $C_{23}H_{26}O_6{}^{37}Cl$ ([$M^{35}Cl$+H]$^+$): 433.1418, found 433.1438. calculated for $C_{32}H_{26}O_6{}^{37}Cl$ ([$M^{37}Cl$+H]$^+$): 435.1388, found 435.1423. $[\alpha]_D^{25} =$ -36 (*c* = 0.2, $CHCl_3$); CD (*c* = 4.6 × 10^{-4} M, MeOH) λ_{max} (Δε) = 364 (+19.7).

IV.2. Synthesis of the (7*S*,4'*S*,5'*S*,11*S*)-chaetoviridin-A 29 and its epimer (7*R*,4'S,5'*S*,11*S*)-chaetoviridin-A 30

Synthesis of the dioxinone (*S*,*S*)-28:

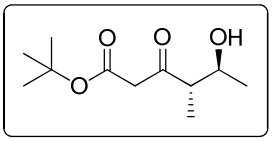


(2*S*, 3*S*)-methyl 3-hydroxy-2-methylbutanoate (*S,S*)-27



To a stirred solution of *N,N*-di*iso*propylamine (3.57 mL, 25.4 mmol, 3.0 equiv.) in dry THF (10 mL) was added *n*-BuLi (2.5 M in hexanes, 9.8 mL, 24.5 mmol, 2.9 equiv.) at -78 °C. After 30 min at -78 °C, (S)-methyl-3-hydroxybutyrate (*S*)-**26** (950 µL, 8.47 mmol, 1.0 equiv.). The resulting mixture was stirred for 30 min at -78 °C, after which time methyl iodide (3.13 mL, 50.82 mmol, 6.0 equiv.) was added. The reaction was stirred at -78 °C for further 1.5 h after which time it was allowed to reach room temperature and aqueous 1M HCl (10 mL) was added. The product was extracted with CH_2Cl_2 (3 × 10 mL) and the organic layer was washed with brine (15 mL), dried over $MgSO_4$, filtered and concentrated under reduced pressure. The oily crude was purified by column chromatography on silica gel, eluting with cyclohexane/EtOAc 4:1 to 1:1 to furnish the desired compound as a pale yellow oil (884 mg, 79%). IR (neat): ν_{max} 3435, 2978, 1717, 1457, 1437 cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$): δ 3.86 (bq, *J* = 6.3 Hz, 1H), 3.70 (s, 3H), 2.74 (bd, *J* = 5.7 Hz, 1H), 2.45 (p, *J* = 7.2, 1H), 1.20 (d, *J* = 6.3 Hz, 3H), 1.16 (d, *J* = 7.2 Hz, 3H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 176.5, 69.5, 51.9, 47.0, 20.8, 14.2. $[\alpha]_D^{20}$ = +27 (c = 1.1, $CHCl_3$). ^{1}H and ^{13}C NMR spectra were consistent with reported data.[9]

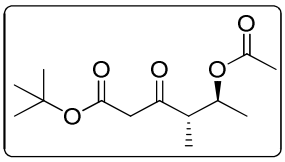
(4*S*,5*S*)-*tert*butyl 5-hydroxy-4-methyl-3-oxohexanoate



To a stirred solution of *N,N*-di*iso*propylamine (4.73 mL, 33.68 mmol, 3.2 equiv.) in dry THF (35 mL) at -78 °C was added *n*-BuLi (2.5 M in hexane, 13.05 mL, 32.60 mmol, 3.1 equiv.). The resulting mixture was stirred at -78 °C for 30 min after which time *tert*butylacetate (4.31 mL, 31.57 mmol, 3.0 equiv.). Then, a solution of ester (*S,S*)-**27** (1.39 g, 10.52 mmol, 1 equiv.) in THF (9 mL) was added, and

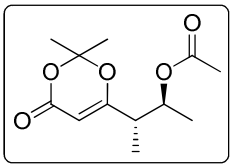
the resulting mixture was stirred at -78 °C for 1.5 h and allowed to warm up to room temperature overnight. The reaction was quenched by addition of a solution of saturated aqueous NH_4Cl (15 mL) and the two layers were separated. The aqueous layer was extracted with EtOAc (4 × 20 mL), then combined organic layers were washed with brine (20 mL), dried over anhydrous $MgSO_4$, filtered and concentrated under reduced pressure to afford the crude β-ketoester which was purified by column chromatography on silica gel, eluting with cyclohexane/EtOAc 80:20 to furnish the titled compound in equilibrium with minor amounts of its enol form (1.179 mg, 52%)as a pale yellow oil. R_f: 0.37 (Cyclohexane/EtOAc 70:30); IR (neat): ν_{max} 3430, 2979, 2935, 2881, 1730, 1705,1644, 1369, 1262 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$): δ 3.87 (m, 1H), 3.45 (d, *J* = 15.4 Hz, 1H), 3.39 (d, *J* = 15.4 Hz, 1H), 2,69 (m, 2H), 1.43 (s, 9H), 1.18 (d, *J* = 6.3 Hz, 3H), 1.07 (d, *J* = 7.2 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 208.1, 166.6, 82.2, 69.8, 53.7, 50.6, 28.1 (3C), 21.1, 13.6; HRMS (ESITOF): calculated for $C_{11}H_{24}NO_4$ $[M+NH_4]^+$: 234.1705, found 234.1709; $[\alpha]_D^{20}$ = +27 (*c* = 0.4, $CHCl_3$). ^{1}H and ^{13} C NMR spectra were consistent with reported data.[7]

(4*S*,5*S*)-tert-butyl 5-acetoxy-4-methyl-3-oxohexanoate



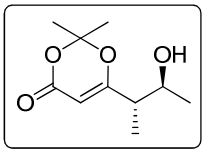
To a stirred solution of β-ketoester (257 mg, 11.86 mmol, 1.0 equiv.) in dry CH_2Cl_2 (13 mL) were successively added 4-*N,N*-dimethyl-4-aminopyridine (29 mg, 0.23 mmol, 0.2 equiv.), triethylamine (177 µL, 2.38 mmol, 2.0 equiv.) and acetic anhydride (124 µL, 1.30 mmol, 1.1 equiv). The resulting solution was stirred at room temperature for 2h after which time a solution of saturated aqueous NH_4Cl (10 mL) was added and the two layers were separated. The aqueous layer was extracted with CH_2Cl_2 (3 × 10 mL), then combined organic layers were washed with brine (20 mL), dried over anhydrous $MgSO_4$, filtered and concentrated under reduced pressure. The crude acetylated β-ketoester was purified by column chromatography on silica gel, eluting with cyclohexane/EtOAc 90:10 to furnish the compound in a 50:50 mixture with corresponding enol form, as a colorless oil (234 mg, 76 %). R_f: 0.61 (Cyclohexane/EtOAc 80:20); IR (neat): ν_{max} 2982, 2933, 1775, 1733, 1715, 1659, 1457, 1369, 1238 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$): 5.55 (s, 1H), 5.13 – 4.91 (m, 3H), 3.42 (s, 2H), 2.92 (p, J = 7.1 Hz, 1H), 2.59 – 2.53 (m, 1H), 2.23 (d, J = 1.4 Hz, 2H), 2.02 (d, J = 3.5 Hz, 6H), 1.46 (d, J = 7.3 Hz, 18H), 1.22 (dd, J = 6.3, 4.5 Hz, 6H), 1.11 (dd, J = 7.0, 2.0 Hz, 6H). 13C NMR (76 MHz, CDCl3) : ^{13}C NMR (75 MHz, $CDCl_3$) δ 204.6, 170.5, 170.2, 167.7, 166.3, 163.4, 161.2, 110.3, 82.1, 80.7, 71.7, 71.0, 51.0, 50.3, 44.5, 28.5, 28.3, 28.1, 21.4, 21.3, 21.2, 17.2, 16.7, 13.0, 12.1; HRMS (ESITOF): calculated for $C_{13}H_{26}NO_5$ $[M+NH_4]^+$: 276.1811, found 276.1812; $[\alpha]_D^{23}$ = +20 (*c* = 0.4, $CHCl_3$).

(2*S*,3*S*)-3-(2,2-dimethyl-4-oxo-4*H*-1,3-dioxin-6-yl)-butan-2-yl acetate (*S,S*)



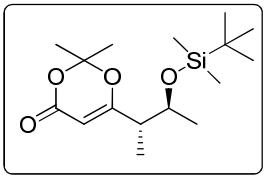
To a stirred solution of acetylated β-ketoester (200 mg, 0.77 mmol, 1.0 equiv.) in acetone (1.0 mL) at 0°C were successively added acetic anhydride (1.0 mL, 11.6 mmol, 15.0 equiv) and sulfuric acid (41 µL, 0.77 mmol, 1.0 equiv). The reaction solution was stirred at 0 °C for 2 hours and at room temperature for 2h. The reaction mixture was diluted in EtOAc (10 mL) and cooled down to 0 °C. A satured aqueous sodium bicarbonate solution was added dropwise until no bubbling appeared. aqueous layer was extracted with EtOAc (3 × 10 mL), then the combined organic layers were washed with brine (20 mL), dried over anhydrous $MgSO_4$, filtered and concentrated under reduced pressure. The crude was purified by column chromatography on silica gel, eluting with cyclohexane/EtOAc 90:10 to furnish the desired compound as a pale yellow oil (126 mg, 68 %). R_f: 0.28 (Cyclohexane/EtOAc 80:20); IR (neat): ν_{max} 2988, 2921, 2852, 1725, 1632, 1391, 1370 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ 5.29 (s, 1H), 5.01 (m, 1H), 2.54 (dq, *J* = 14.6 and 7.2 Hz, 1H), 2.01 (s, 3H), 1.68 (s, 3H), 1.64 (s, 3H), 1.23 (d, *J* = 6.3 Hz, 3H), 1.15 (d, *J* = 7.1 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 172.1, 170.3, 161.3, 106.6, 94.1, 71.0, 43.4, 25.4, 24.7, 21.3, 17.4, 13.3; LRMS (ESITOF): 243 (35, $[M+H]^+$), 260 (100, $[M+NH_4]^+$), 284 (26, $[M+ACN+H]^+$); HRMS (ESITOF): calculated for $C_{12}H_{22}NO_5$ ($[M+NH_4]^+$): 260.1498, found 260.1507; $[\alpha]_D^{20}$ = +11 (c = 0.4, $CHCl_3$).

6-[(2*S*,3*S*)-3-hydroxybutan-2-yl]-2,2-dimethyl-4*H*-1,3-dioxin-4-one:



To a stirred solution of acetylated dioxinone (106 mg, 0.77 mmol, 1.0 equiv.) in THF (1.6 mL) at room temperature were successively added 0.1 M aqueous phosphate buffer at pH = 7.41 (6 mL) and the Lipase from *Candida Cylindracea* (424 mg, 0.007 mmol, 0.01 equiv). The resulting mixture was gently stirred at 35°C for 6 days (0.01 equiv. of enzyme were added each 48 h). Reaction was then diluted in EtOAC (10 mL), extracted with EtOAc (4 × 10 mL), then the combined organic layers were washed with brine (30 mL), dried over anhydrous $MgSO_4$, filtered and concentrated under reduced pressure to furnish the pure dioxinone as a yellow oil without further purification (79 mg, 90 %). R_f: 0.4 (Cyclohexane/EtOAc 50:50); IR (neat): ν_{max} 3440, 2977, 2883, 1705, 1625, 1391, 1377 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ 5.29 (s, 1H), 3.87 (dq, *J* = 12.7 and 6.3 Hz, 1H), 2.32 (dq, *J* = 12.7 and 7.1 Hz, 1H), 1.69 (s, 3H), 1.68 (s, 3H), 1.22 (d, *J* = 6.3 Hz, 1H), 1.11 (d, *J* = 7.1 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 173.3, 161.4, 106.7, 94.2, 69.3, 46.3, 25.19 and 25.16, 21.0, 13.8; HRMS (ESITOF): calculated for $C_{10}H_{17}O_4$ ($[M+H]^+$): 201.1127, found 201.1125; $[\alpha]_D^{20}$ = +17 (c = 0.6, $CHCl_3$).

6-[(2*S*,3*S*)-3-*tert*butyldimetylsilyloxybutan-2-yl]-2,2-dimethyl-4*H*-1,3-dioxin-4-one (*S,S*)-28:



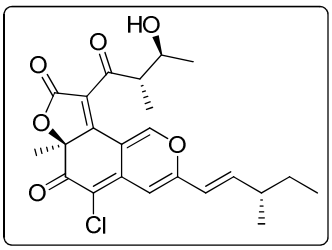
To a stirred solution of crude dioxinone (74 mg, 0.37 mmol, 1.0 equiv.) in dry CH_2Cl_2 (2.0 mL) at room temperature were successively added 1*H*-imidazole (38 mg, 0.48 mmol, 1.5 equiv) and *tert*butyl(chloro)dimethylsilane (72 mg, 0.56 mmol, 1.3 equiv). The reaction solution was stirred at room temperature for 24 hours after which time additional 1*H*-imidazole (38 mg, 0.48 mmol, 1.5 equiv) and *tert*butyl(chloro)dimethylsilane (72 mg, 0.56 mmol, 1.3 equiv) were added and reaction was stirred for 24 h at room temperature. The reaction mixture was concentrated under reduced pressure and purified by column chromatography on silica gel, eluting with cyclohexane/EtOAc 95:5 to furnish the silylated dioxinone compound (*S,S*)-**28** as a pale yellow oil (126 mg, 68 %).; R_f: 0.17 (Cyclohexane/EtOAc 95:5); IR (neat): ν_{max} 2959,2933, 2855, 1732, 1631 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$): δ 5.28 (s, 1H), 3.92 (p, *J* = 6.2 Hz, 1Hz), 2.33 (m, 1H), 1.69 (s, 3H), 1.66 (s, 3H), 1.13 (d, *J* = 6.2 Hz, 3H), 1.07 (d, *J* = 7.1 Hz, 3H), 0.87 (s, 9H), 0.05 (s, 3H), 0.03 (s, 3H); 13C NMR (75 MHz, $CDCl_3$): δ 173.6, 161.6, 106.3, 94.2, 69.6, 46.4, 26.1, 25.9 (3C), 24.3, 21.0, 18.1, 13.2, -4.2, -4.9.; LRMS (ESITOF): 315 (36, $[M+H]^+$), 332 (95, $[M+NH_4]^+$), 356 (100, $[M+ACN+H]^+$); HRMS (ESITOF): calculated for $C_{16}H_{31}O_4Si$ ($[M+H]^+$): 315.1992, found 315.1986.; $[\alpha]_D^{20}$ = + 30 (*c* = 1.0, $CHCl_3$).

Reaction condensation starting from (*S,S*)-dioxinone enantiomer :

To a stirred solution of dearomatized alcohol **14** (74 mg, 0.24 mmol, 1.0 equiv.) in dry toluene (4 mL) under were added 4Å molecular sieves (50 mg) and the dioxinone (*S,S*)-**28** (90 mg, 0.29 mmol, 1.2 equiv.). The resulting mixture was stirred for 10 min at room temperature then 1h under toluene reflux. Triethylamine (61 µL, 0.706 mmol, 2.0 equiv.) was added and the reaction was stirred for 1h under reflux. The reaction was then cooled down to room temperature, hydrolyzed with 10 mL 1M aqueous HCl, extracted with EtOAc (4 × 10 mL), washed with brine (15 mL), dried over $MgSO_4$, filtered and concentrated under reduced pressure. ^{1}H NMR analysis of the crude indicated the formation of two products. The crude mixture was dissolved in dry THF (5 mL), and HF·pyridine complex was added was added portionwise every 6 h (*i.e.* 70% HF basis, 1.1 mL, 105 mmol, 300 equiv.) until complete reaction. Reaction was quenched by slow addition of saturated aqueous sodium bicarbonate (30 mL). The layers were separated and the aqueous layer was extracted with EtOAc (3 × 20 mL), washed with brine (50 mL), dried over $MgSO_4$, filtered and concentrated under reduced pressure. Diastereiosomers were separated by column chromatography on silica gel, eluting with cyclohexane/EtOAc 85:15 to furnish (7*R*,4'*S*,5'*S*,11*S*)-chaetoviridin A **30** as an orange oil (15 mg,

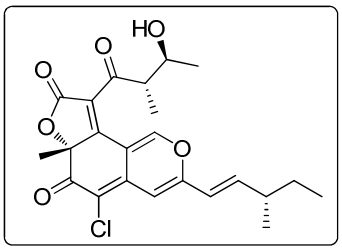
0.03 mmol, 15%) and with cyclohexane/EtOAc 60:40 to furnish (7*S*,4'*S*,5'*S*,11*S*)-chaetoviridin A **29** as an orange oil (14 mg, 0.04 mmol, 14%). Overall yield 29%.

(7*S*,4'*S*,5'*S*,11*S*)-chaetoviridin-A 29:



R_f: 0.29 (Cyclohexane/ EtOAc 70:30); IR (neat): ν_{max} 3385, 2969, 2924, 1768, 1685, 1645, 1621, 1510 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ 8.88 (s, 1H), 6.63 (dd, *J* = 15.7 and 8.0 Hz, 1H), 6.57 (s, 1H), 6.09 (d, *J* = 15.7 Hz, 1H), 3.90 (m, 1H), 3.64 (m, 1H), 2.30 (m, 1H), 1.73 (s, 3H), 1.45 (m, 2H), 1.33 (d, *J* = 6.3 Hz, 3H), 1.10 (d, *J* = 6.7 Hz, 3H), 1.02 (d, *J* = 7.0 Hz, 3H), 0.91 (t, *J* = 7.4 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 201.0, 183.3, 168.8, 165.0, 157.2, 152.4, 148.5, 139.9, 123.8, 119.8, 110.4, 109.1, 105.5, 88.1, 71.9, 50.6, 39.2, 29.3, 26.3, 21.8, 19.5, 14.4, 11.9; LRMS (ESITOF): 433 (100, $[M+H]^+$); HRMS (ESITOF): calculated for $C_{23}H_{26}O_6{}^{35}Cl$ ($[M+H]^+$): 433.1418, found 433.142; $[a]_D^{25}$ = + 69 (*c* = 0.5, $CHCl_3$) (lit.: $[a]_D^{20}$ = + 40 (*c* = 0.002, $CHCl_3$)[6]); CD (*c* = 4.6 × 10^{-4} M, MeOH) λ_{max} ($\Delta\varepsilon$) = 370 (-18.3).

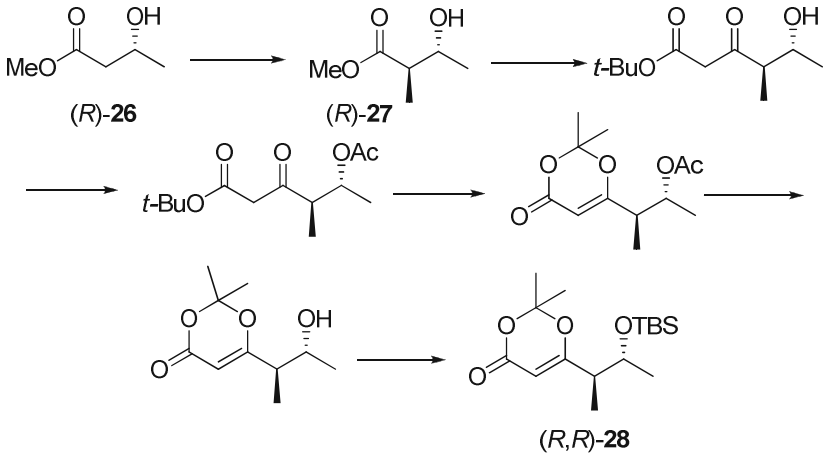
(7*R*,4'*S*,5'*S*,11*S*)-chaetoviridin-A 30:



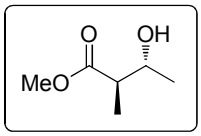
R_f: 0.51 (Cyclohexane/ EtOAc 70:30); IR (neat): ν_{max} 2962, 1768, 1683, 1617, 1512, 1414 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ 8.78 (s, 1H), 6.61 (dd, *J* = 15.7 and 8.0 Hz, 1H), 6.55 (s, 1H), 6.08 (d, *J* = 15.7 Hz, 1H), 3.86(p, *J* = 6.3 Hz, 1H), 3.63 (m, 1H), 2.29 (m, 1H), 1.71 (s, 3H), 1.44 (m, 2H), 1.17 (d, *J* = 6.9 Hz, 3H), 1.17 (d, *J* = 6.0 Hz, 3H), 1.09 (d, *J* = 6.7 Hz, 3H), 0.91 (t, *J* = 7.4 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 201.3, 183.5, 168.1, 163.1, 157.2, 151.7, 148.2, 139.8, 125.1, 119.9, 110.6, 109.1, 105.6, 87.8, 71.1, 51.1, 39.1, 29.3, 26.5, 21.7, 19.4, 13.8, 11.9; LRMS (ESITOF): 433 (100, $[M+H]^+$); HRMS (ESITOF): calculated for $C_{23}H_{26}O_6{}^{35}Cl$ ($[M+H]^+$): 433.1418, found 433.141; $[a]_D^{20}$ = +34 (*c* = 0.6, MeOH) (lit.: $[a]_D^{27}$ = + 39 (*c* = 0.4, $CHCl_3$)[8]); CD (*c* = 4.6 × 10^{-4} M, MeOH) λ_{max} ($\Delta\varepsilon$) = 365 (+14.3).

IV.3. Synthesis of the revised structure of chaetoviridin-A, (7*S*,4'*R*,5'*R*,11*S*)-chaetoviridin-A 31 and its (7*R*)-epimer (7*R*,4'*R*,5'*R*,11*S*)-chaetoviridin-A 32

Synthesis of the dioxinone (*R*,*R*)-28:

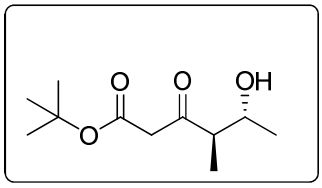


(2*R*,3*R*)-methyl 3-hydroxy-2-methylbutanoate (*R,R*)-27



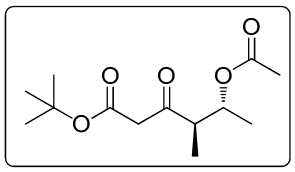
The same procedure as for the preparation of the (*R,R*) enantiomer was used starting from (*S*)-methyl-3-hydroxybutyrate (*R*)-**26** (950 µL, 8.47 mmol, 1.0 equiv.). The oily crude was purified by column chromatography on silica gel, eluting with cyclohexane/EtOAc 4:1 to 1:1 to furnish the desired compound as a pale yellow oil as (839 mg, 75%). IR (neat): ν_{max} 3423, 2977, 1717, 1457, 1436 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ 3.87 (m, 1H), 3.69 (s, 3H), 2.76 (bd, *J* = 4.3 Hz, 1H), 2.44 (p, *J* = 7.2 Hz, 1H), 1.19 (d, *J* = 6.3Hz, 3H), 1.16 (d, *J* = 7.2 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 176.5, 69.5, 51.9, 47.0, 20.8, 14.1. $[\alpha]_D^{20}$= - 30 (*c* = 1.0, $CHCl_3$). ^1H and ^{13} C NMR spectra were consistent with reported data.[9]

(4*R*,5*R*)-tert-butyl 5-hydroxy-4-methyl-3-oxohexanoate



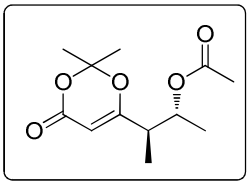
The same procedure as for the preparation of the (*S,S*) enantiomer was used starting from (*R,R*)-**27** (789 g, 5.97 mmol, 1.0 equiv.). The oily crude was purified by column chromatography on silica gel, eluting with cyclohexane/EtOAc 80:20. It was obtained in equilibrium with minor amounts of its enol form (579 mg, 45 %), as colorless oil. R_f: 0.37 (Cyclohexane/EtOAc 70:30); IR (neat): ν_{max} 3430, 2978, 2937, 2885, 1730, 1704, 1645, 1368, 1262 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ 3.87 (m, 1H), 3.45 (d, *J* = 15.4 Hz, 1H), 3.39 (d, *J* = 15.4 Hz, 1H), 1.43 (s, 9H), 1.18 (d, *J* = 6.3 Hz, 3H), 1.07 (d, *J* = 7.2 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 208.1, 166.7, 82.2, 69.7, 53.7, 50.6, 28.0 (3C), 21.0, 13.5; HRMS (ESITOF): calculated for $C_{11}H_{24}NO_4$ $[M+NH_4]^+$: 234.1705, found 234.1699; $[\alpha]_D^{20}$ = -36 (*c* = 0.8, $CHCl_3$).

(4*R*,5*R*)-*tert*butyl 5-acetoxy-4-methyl-3-oxohexanoate



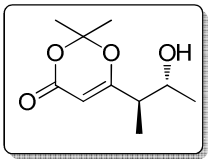
The same procedure as for the preparation of the (*R,R*) enantiomer was used starting from (4*S*,5*S*)-*tert*butyl 5-hydroxy-4-methyl-3-oxohexanoate (492 mg, 2.27 mmol, 1.0 equiv.). The oily crude was purified by column chromatography on silica gel, eluting with cyclohexane/EtOAc 90:10 to furnish the compound in equilibrium with minor amounts of its enol form (354 mg, 60 %)as a pale yellow oil. R_f: 0.61 (Cyclohexane/EtOAc 80:20); IR (neat): ν_{max} 2981, 2937, 2886, 1733, 1713, 1646, 1456, 1369, 1235 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): 5.04 (m, 1H), 3.40 (s, 2H), 2.92 (p, J = 6.1 Hz, 1H), 1.99 (s, 3H), 1.44 (m, 9H), 1.20 (d, J = 6.0 Hz, 3H), 1.09 (d, J = 6.0 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 204.5, 170.1, 166.2, 82.1, 71.7, 50.9, 50.3, 29.1 (3C), 21.2, 17.1, 12.1; HRMS (ESITOF): calculated for $C_{13}H_{26}NO_5$ $[M+NH_4]^+$: 276.1811, found 276.1822; $[a]_D^{20}$ = -19 (c = 2.5, $CHCl_3$)

(2*R*,3*R*)-3-(2,2-dimethyl-4-oxo-4*H*-1,3-dioxin-6-yl)-butan-2-yl acetate



The same procedure as for the preparation of the (*S,S*) enantiomer was used starting from (4*R*,5*R*)-tert-butyl 5-acetoxy-4-methyl-3-oxohexanoate (310 mg, 1.20 mmol, 1.0 equiv.). The oily crude was purified by column chromatography on silica gel, eluting with cyclohexane/EtOAc 80:20 to furnish the pure dioxinone compound as a yellow oil (204 mg, 70 %); R_f**:** 0.28 (Cyclohexane/EtOAc 80:20); IR (neat): ν_{max} 2991, 2923, 2852, 1725, 1633, 1392, 1370 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ 5.29 (s, 1H), 5.01 (dq, J = 12.7 and 6.3 Hz, 1H), 2.54 (dq, *J* = 12.7 and 7.2 Hz, 1H), 2.01 (s, 3H), 1.68 (s, 3H), 1.64 (s, 3H), 1.23 (d, *J* = 6.3 Hz, 3H), 1.15 (d, *J* = 7.1 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 172.1, 170.2, 161.3, 106.6, 93.9, 70.9, 43.3, 25.3, 24.6, 21.2, 17.4, 13.4.; HRMS (ESITOF): calculated for $C_{12}H_{22}NO_5$ ($[M+NH_4]^+$): 260.1498, found 260.1501; $[a]_D^{20}$ = -7 (*c* = 0.7, $CHCl_3$).

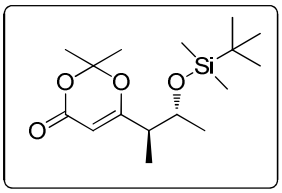
6-[(2*R*,3*R*)-3-hydroxybutan-2-yl]-2,2-dimethyl-4*H*-1,3-dioxin-4-one:



The same procedure as for the preparation of the (S,*S*) enantiomer was used starting from (2*R*,3*R*)-3-(2,2-dimethyl-4-oxo-4*H*-1,3-dioxin-6-yl)-butan-2-yl acetate (160 mg, 1.20 mmol, 1.0 equiv.). Pure dioxinone was obtained as a yellow oil without further purification (127 mg, 96 %). R_f: 0.4 (Cyclohexane/EtOAc 50:50); IR (neat): ν_{max} 3420, 2977, 2887, 1705, 1625, 1391, 1377 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ 5.29 (s, 1H), 3.87 (dq, *J* = 12.7 and 6.3 Hz, 1H), 2.32 (dq, *J* = 12.7 and 7.1 Hz, 1H), 1.69 (s, 3H), 1.68 (s, 3H), 1.22 (d, *J* = 6.3 Hz, 1H), 1.11 (d, *J* = 7.1 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 173.5, 161.5, 106.6, 94.1, 69.2, 46.2, 25.13 and 25.11, 21.0, 13.8; LRMS (ESITOF): 201 (100, $[M+H]^+$),

218 (40, $[M+NH_4]^+$), 242 (40, $[M+ACN+H]^+$); HRMS (ESITOF): calculated for $C_{10}H_{17}O_4$ ($[M+H]^+$): 201.1127, found 201.1129; $[\alpha]_D^{20}$ = -25 (*c* = 1.2, $CHCl_3$).

6-[(2*R*,3*R*)-3-*tert*butyldimetylsilyloxybutan-2-yl]-2,2-dimethyl-4*H*-1,3-dioxin-4-one (*R,R*)-28:

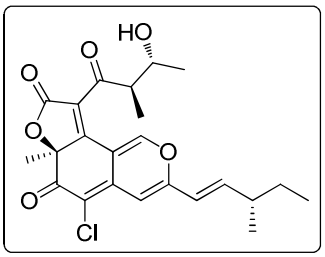


The same procedure as for the preparation of the (*R,R*) enantiomer was used starting from 6-[(2*S*,3*S*)-3-hydroxybutan-2-yl]-2,2-dimethyl-4*H*-1,3-dioxin-4-one (112 mg, 0.56 mmol, 1.0 equiv.). The oily crude was purified by column chromatography on silica gel, eluting with cyclohexane/EtOAc 95:5 to furnish the desired compound (*R,R*)-**28** as a pale yellow oil (137 mg, 78 %). R_f: 0.17 (Cyclohexane/EtOAc 95:5); IR (neat): ν_{max} 2961,2926, 2851, 1732, 1637 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ 5.28 (s, 1H), 3.92 (p, *J* = 6.2 Hz, 1Hz), 2.33 (m, 1H), 1.69 (s, 3H), 1.66 (s, 3H), 1.13 (d, *J* = 6.2 Hz, 3H), 1.07 (d, *J* = 7.1 Hz, 3H), 0.87 (s, 9H), 0.05 (s, 3H), 0.03 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 173.6, 161.6, 106.3, 94.2, 69.6, 46.4, 26.1, 25.9 (3C), 24.3, 21.0, 18.1, 13.2, -4.2, -4.9; LRMS (ESITOF): 315 (34, $[M+H]^+$), 332 (78, $[M+NH_4]^+$), 356 (100, $[M+ACN+H]^+$); HRMS (ESITOF): calculated for $C_{16}H_{31}O_4Si$ ($[M+H]^+$): 315.1992, found 315.1989; $[\alpha]_D^{20}$ = -30 (*c* = 1.0, $CHCl_3$).

Reaction condensation starting from (*R,R*)-dioxinone enantiomer

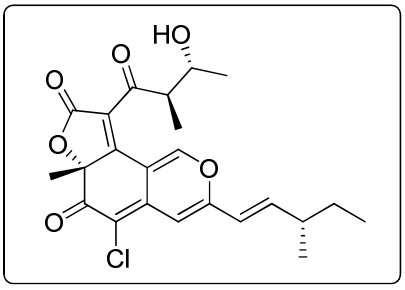
To a stirred solution of dearomatized alcohol **14** (48 mg, 0.16 mmol, 1.0 equiv.) in dry toluene (2 mL) under argon were added 4Å molecular sieves (20 mg) and the dioxinone (*R,R*)-**28** (60 mg, 0.19 mmol, 1.2 equiv.). The resulting mixture was stirred for 5 min at room temperature then 1.5 h under toluene reflux. Triethylamine (45 µL, 0.32 mmol, 2.0 equiv.) was added and the reaction was stirred for 1.5 h under reflux. The reaction was then cooled down to room temperature, hydrolyzed with 10 mL 1M aqueous HCl, extracted with EtOAc (4 × 15 mL), washed with brine (20 mL), dried over $MgSO_4$, filtered and concentrated under reduced pressure. ^1H NMR analysis of the crude indicated the formation of two products. The crude mixture was dissolved in dry THF (2 mL), and HF·pyridine complex was added was added portionwise every 2 h (*i.e.* 70% HF basis, 290 µL, 16 mmol, 100 equiv.) until complete reaction. Reaction was slowly poured into saturated aqueous sodium bicarbonate (10 mL). The layers were separated and the aqueous layer was extracted with EtOAc (3 × 10 mL), washed with brine (50 mL), dried over MgSO4, filtered and concentrated under reduced pressure. Diastereiosomers were separated by preparative TLC on silica gel, eluting with cyclohexane/EtOAc 55:45 to furnish (7*S*,4'*R*,5'*R*,11*S*)-chaetroviridin-A **31** as a yellow oil (8 mg, 0.018 mmol, 11%) and (7*R*,4'*R*,5'*R*,11*S*)-chaetroviridin-A **32** as an orange oil (10 mg, 0.023 mmol, 14%). Overall yield 25%.

(7*S*,4'*R*,5'*R*,11*S*)-chaetroviridin-A 31 :



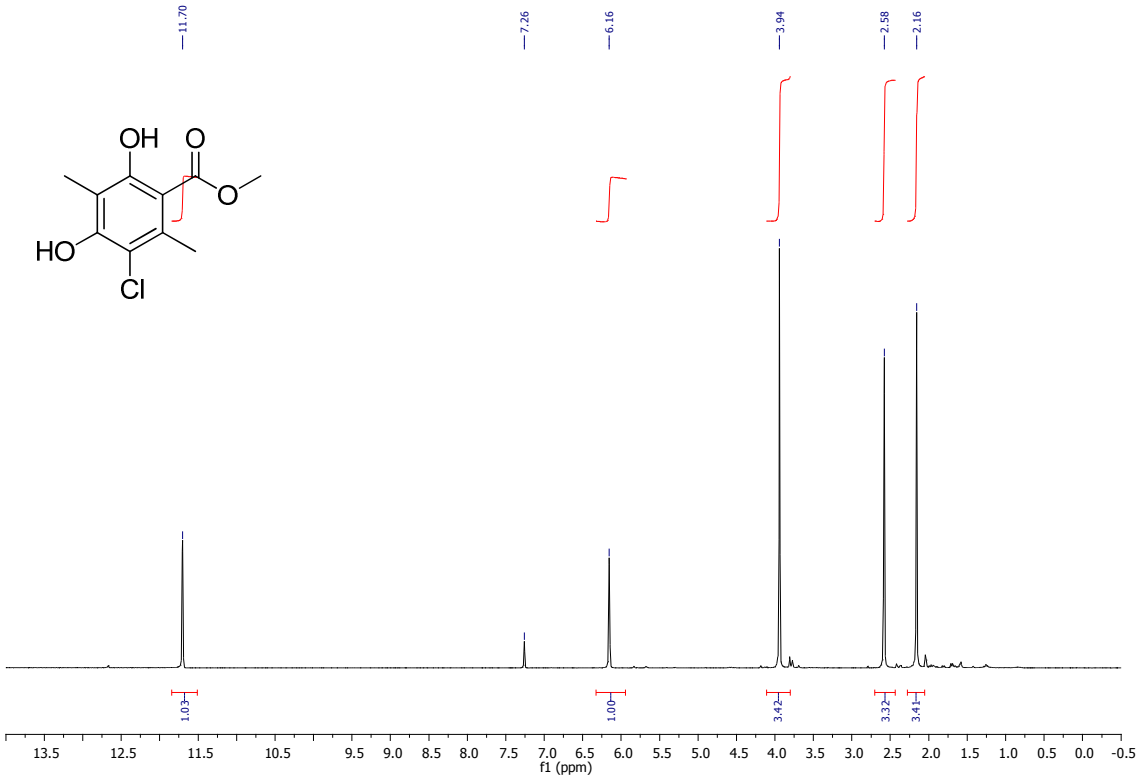
R_f: 0.53 (Cyclohexane/EtOAc 70:30); IR (neat): ν_{max} 3363, 2974, 2928, 1766, 1683, 1645, 1620, 1512 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ 8.79 (s, 1H), 6.61 (dd, *J* = 15.7 and 8.1 Hz, 1H), 6.55 (s, 1H), 6.08 (d, *J* = 15.9 Hz, 1H), 3.87 (p, *J* = 6.6 Hz, 1H), 3.64 (m, 1H), 2.28 (m, 1H), 1.71 (s, 3H), 1.45 (m, 2H), 1.18 (d, *J* = 6.2 Hz, 3H), 1.17 (d, *J* = 6.8 Hz, 3H), 1.10 (d, *J* = 6.7 Hz, 3H), 0.91 (t, *J* = 7.4 Hz, 3H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 201.2, 183.5, 168.1, 163.2, 157.1, 151.8, 148.2, 139.7, 125.0, 119.9, 110.6, 109.2, 105.5, 87.8, 71.1, 51.1, 39.2, 29.3, 26.5, 21.7, 19.5, 13.8, 11.9. LRMS (ESITOF): 433 (100, $[M+H]^+$). HRMS (ESITOF): calculated for $C_{23}H_{26}O_6{}^{35}Cl$ ($[M+H]^+$): 433.1418, found 433.1410. $[a]_D^{20}$ = +96 (*c* = 1.0, $CHCl_3$); (lit.: $[a]_D^{30}$ = + 98 (*c* = 0.05, $CHCl_3$),[10] and $[a]_D^{27}$ + 97 (*c* = 1.0, $CHCl_3$)[11]) CD (*c* = 4.6 × 10^{-4} M, MeOH) λ_{max} (Δε) = 365 (-26.6).

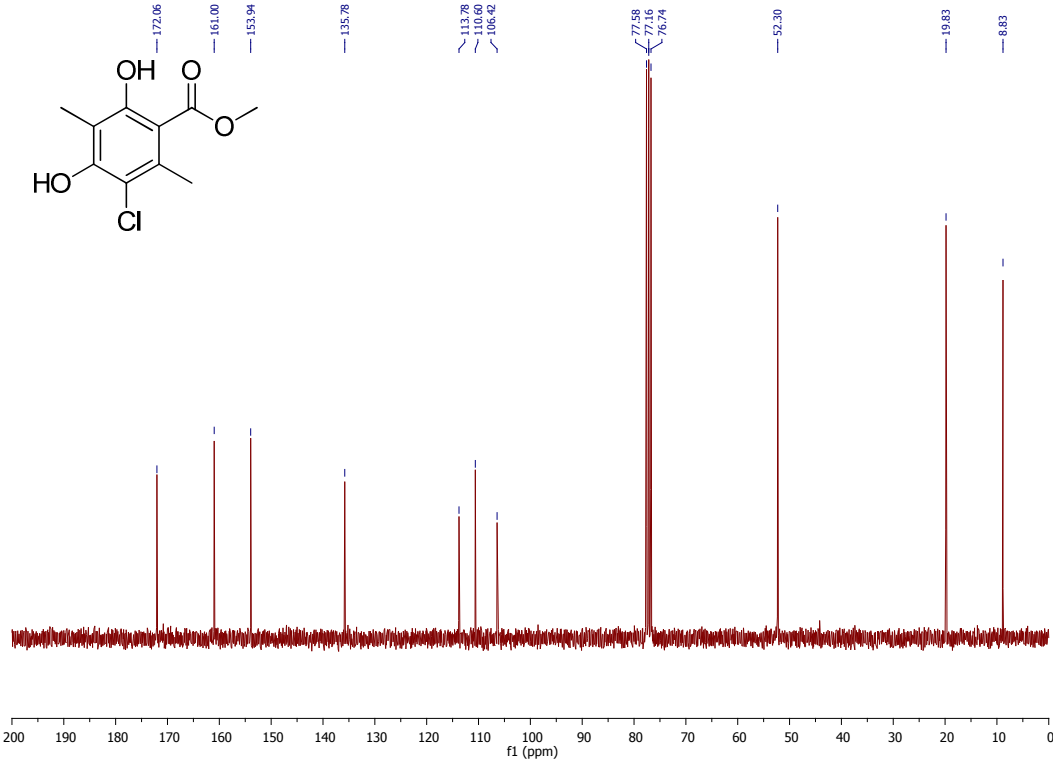
(7*R*,4'*R*,5'*R*,11*S*)-chaetroviridin-A 32

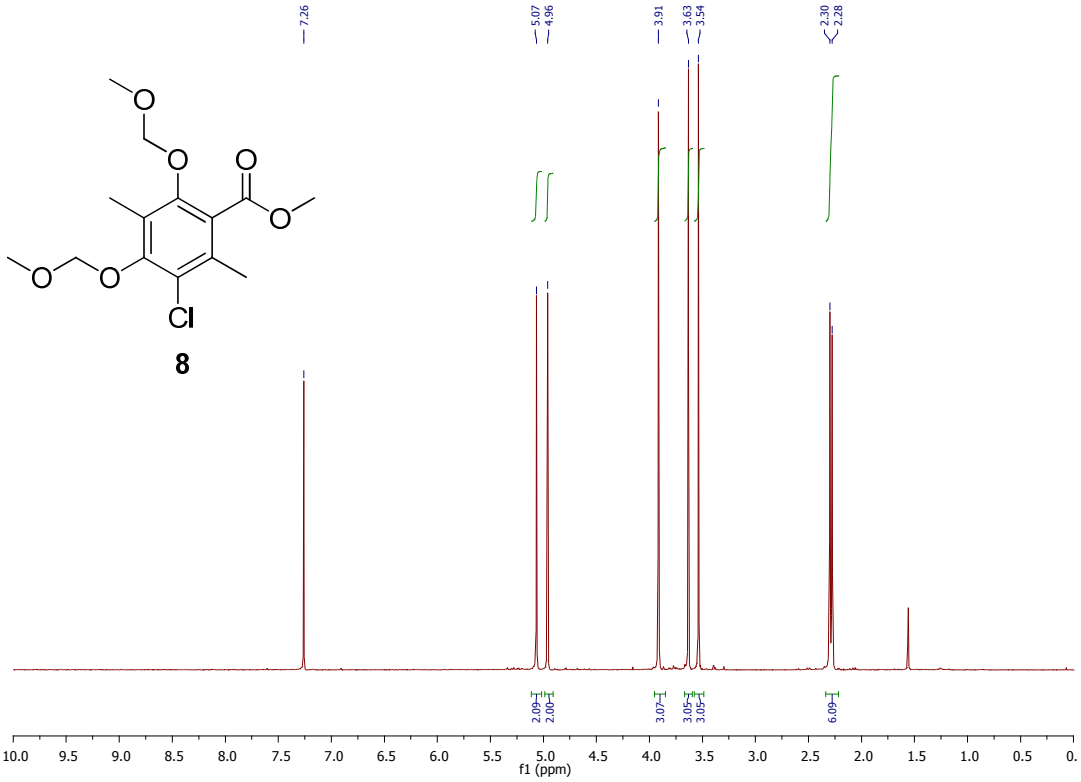


R_f: 0.28 (Cyclohexane/ EtOAc 70:30); IR (neat): ν_{max} 3471, 2962, 2926, 2855, 1765, 1685, 1645, 1621, 1513 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ 8.87 (s, 1H), 6.64 (dd, J = 15.7, 8.0 Hz, 1H), 6.57 (s, 1H), 6.09 (d, J = 15.7 Hz, 1H), 3.96 – 3.81 (m, 1H), 3.68 – 3.56 (m, 1H), 2.38 – 2.23 (m, 2H), 1.73 (s, 3H), 1.52 – 1.39 (m, 3H), 1.33 (d, *J* = 6.3 Hz, 3H), 1.29 – 1.20 (m, 3H), 1.10 (d, *J* = 6.7 Hz, 3H), 1.02 (d, *J* = 7.0 Hz, 3H), 0.92 (t, *J* = 7.4 Hz, 3H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 201.0, 183.3, 168.8, 165.0, 157.2, 152.3, 148.5, 139.9, 123.8, 119.9, 110.5, 109.2, 105.5, 88.1, 71.9, 50.6, 39.2, 29.9, 29.3, 26.3, 21.8, 19.4, 14.4, 11.9. HRMS (ESITOF) : calculated for $C_{23}H_{24}O_6{}^{35}Cl$ ($[M-H]^-$): 431.1295, found 431.1273. $[a]_D^{23}$ = -9.4 (*c* = 0.2, $CHCl_3$); CD (*c* = 4.6 × 10^{-4} M, MeOH) λ_{max} (Δε) = 370 (+25.1).

V. Copies of ^{1}H and ^{13}C NMR



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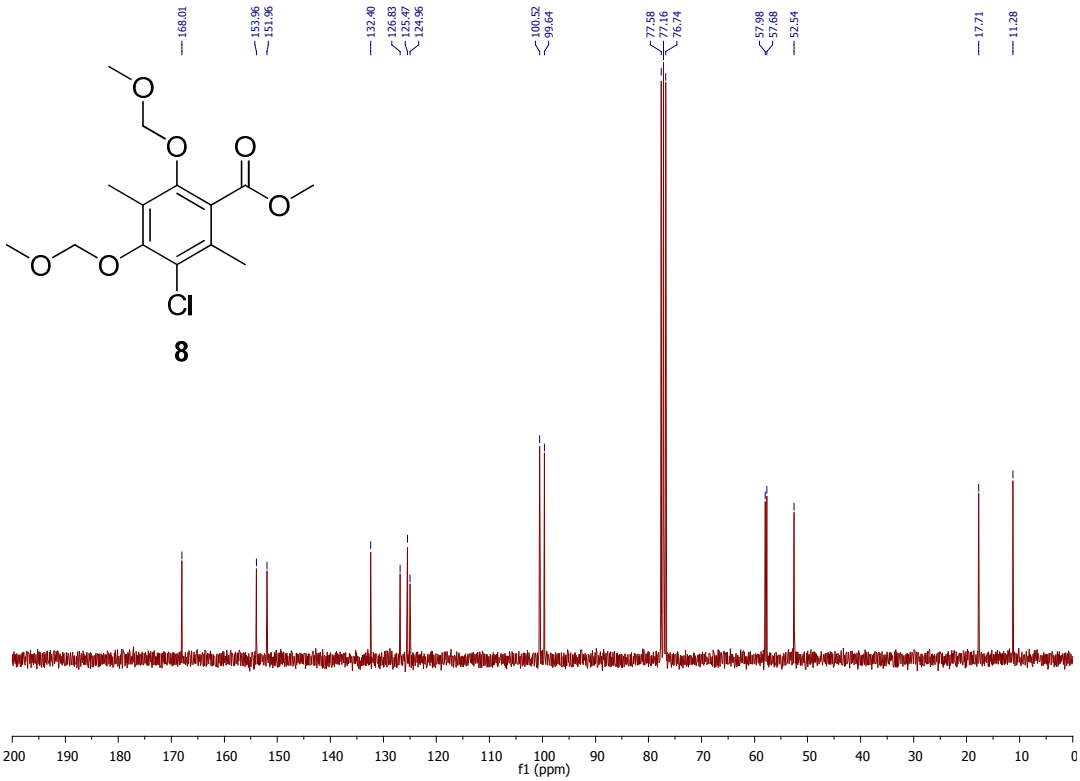
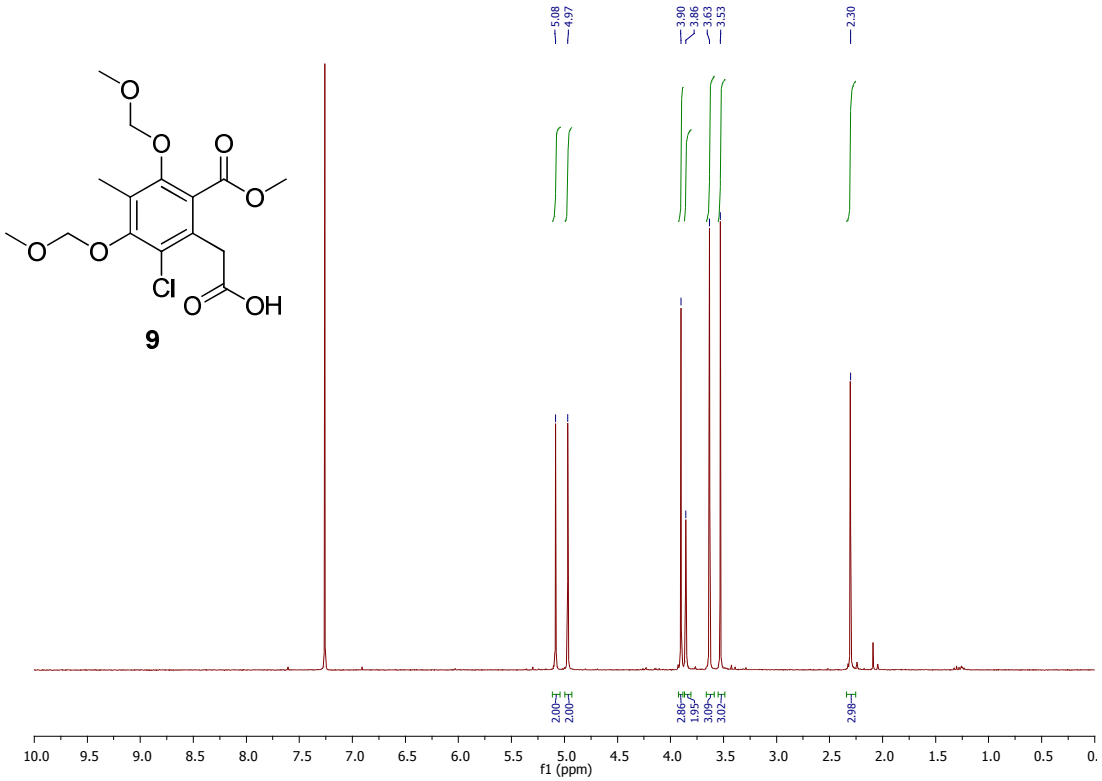
5.07
4.96
3.91
3.63
3.54
2.30
2.28
2.09
2.00
3.07
3.05
3.05
6.09
f1 (ppm)

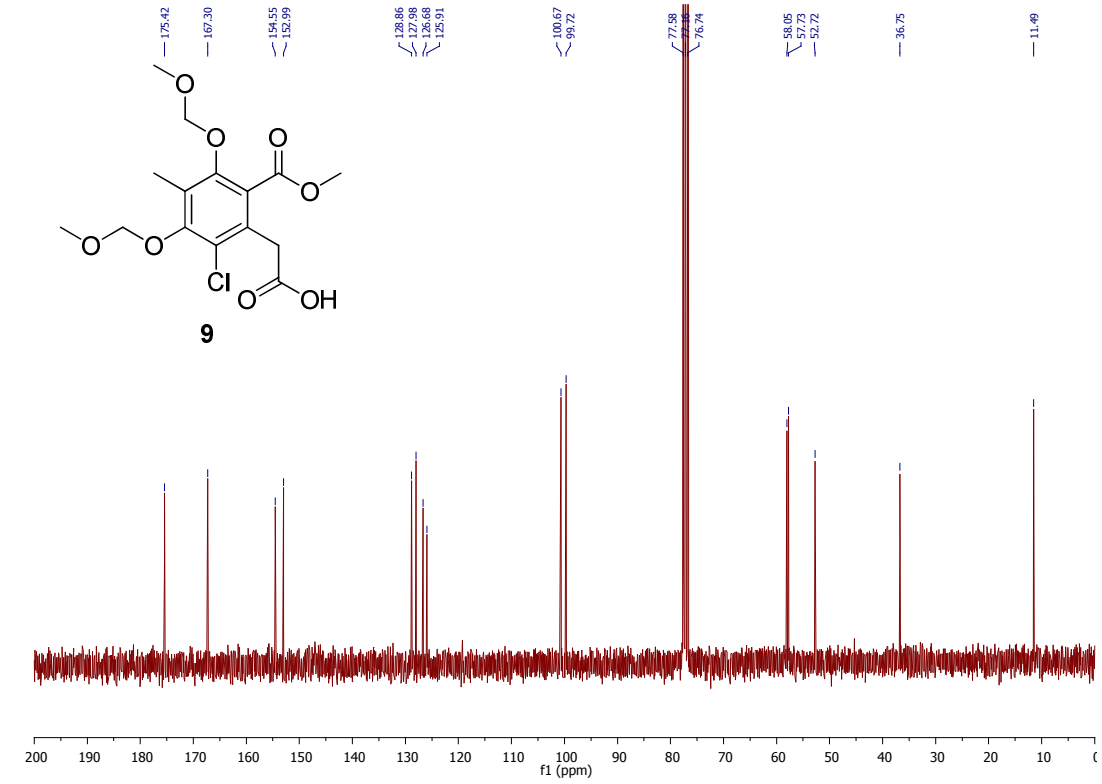
8


168.01
153.96
151.96
132.40
126.83
125.47
124.96
100.52
99.64
77.58
77.16
76.74
57.98
57.68
52.54
17.71
11.28
f1 (ppm)

8


5.08
4.97
3.90
3.86
3.63
3.53
2.30
2.00
2.00
2.86
1.95
3.09
3.02
2.98
f1 (ppm)

9


175.42
167.30
154.55
152.99
128.86
127.98
126.68
125.91
100.67
99.72
77.58
77.16
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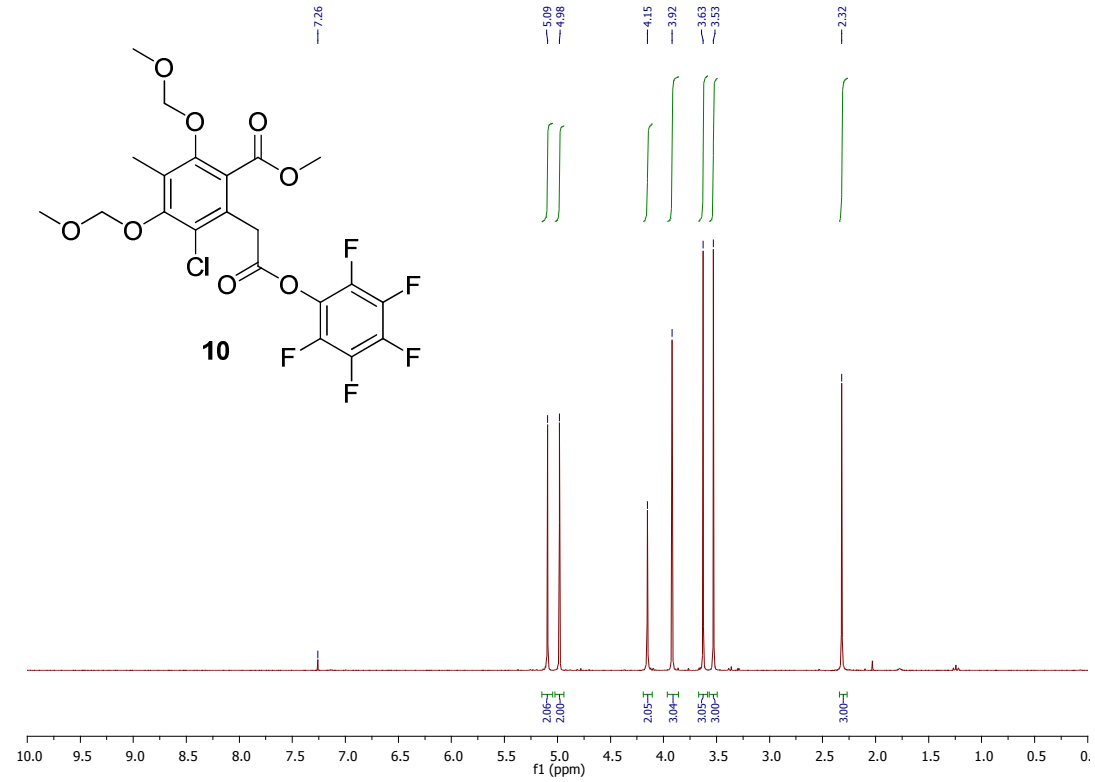
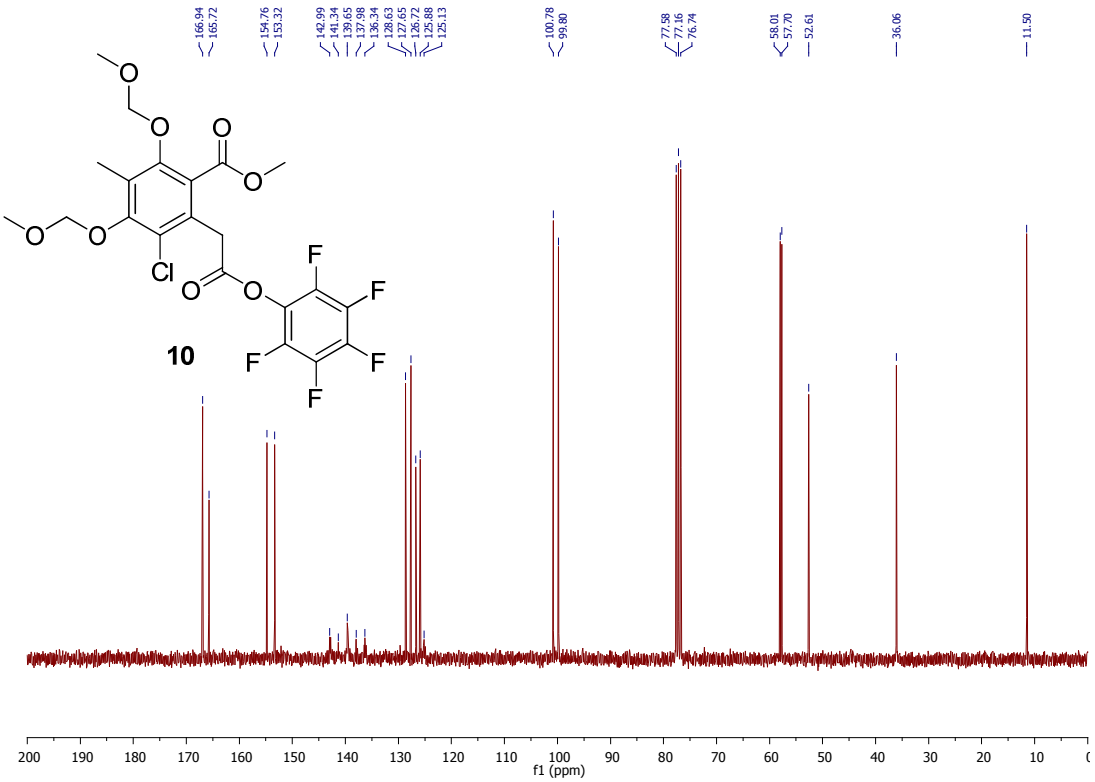
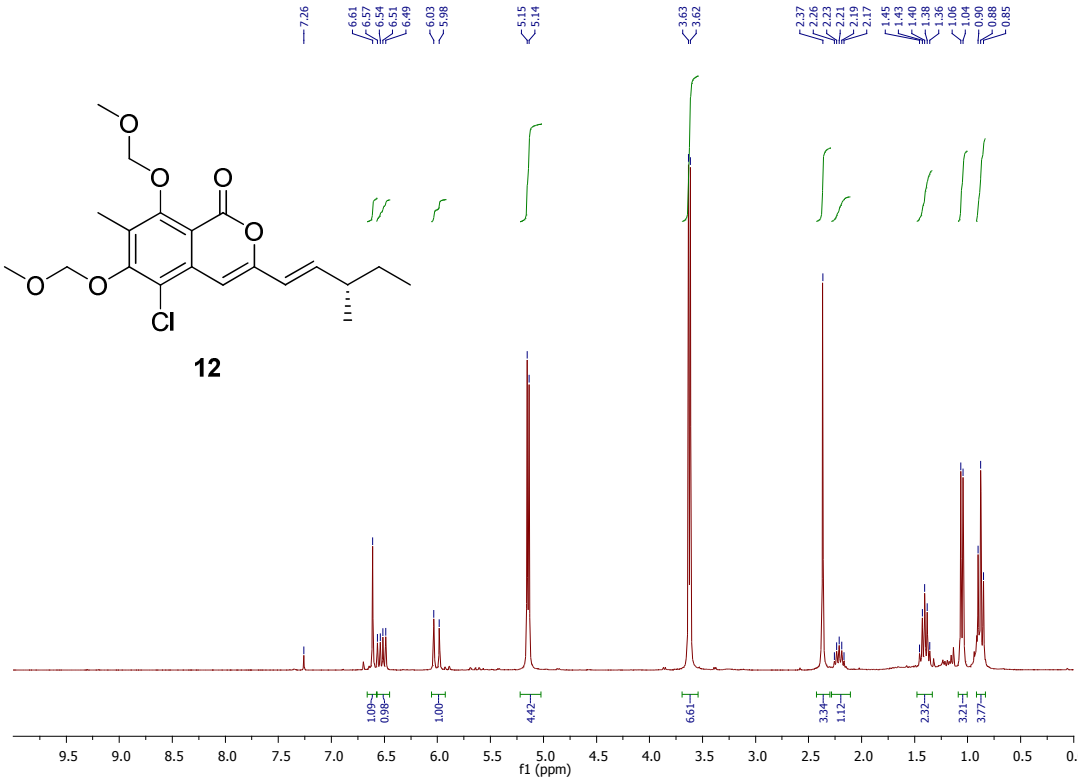
57.73
52.72
36.75
11.49
f1 (ppm)

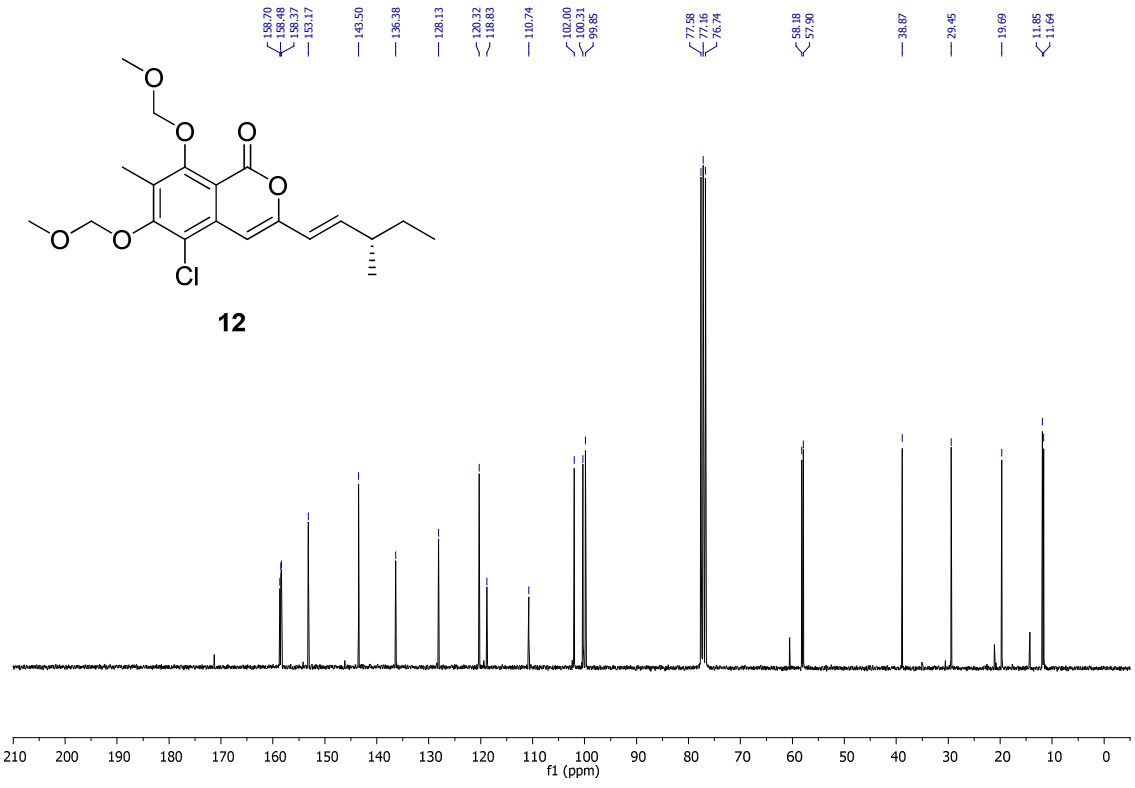
9


7.26
5.09
4.98
4.15
3.92
3.63
3.53
2.32
10
2.06
2.00
2.05
3.04
3.05
3.00
3.00
f1 (ppm)

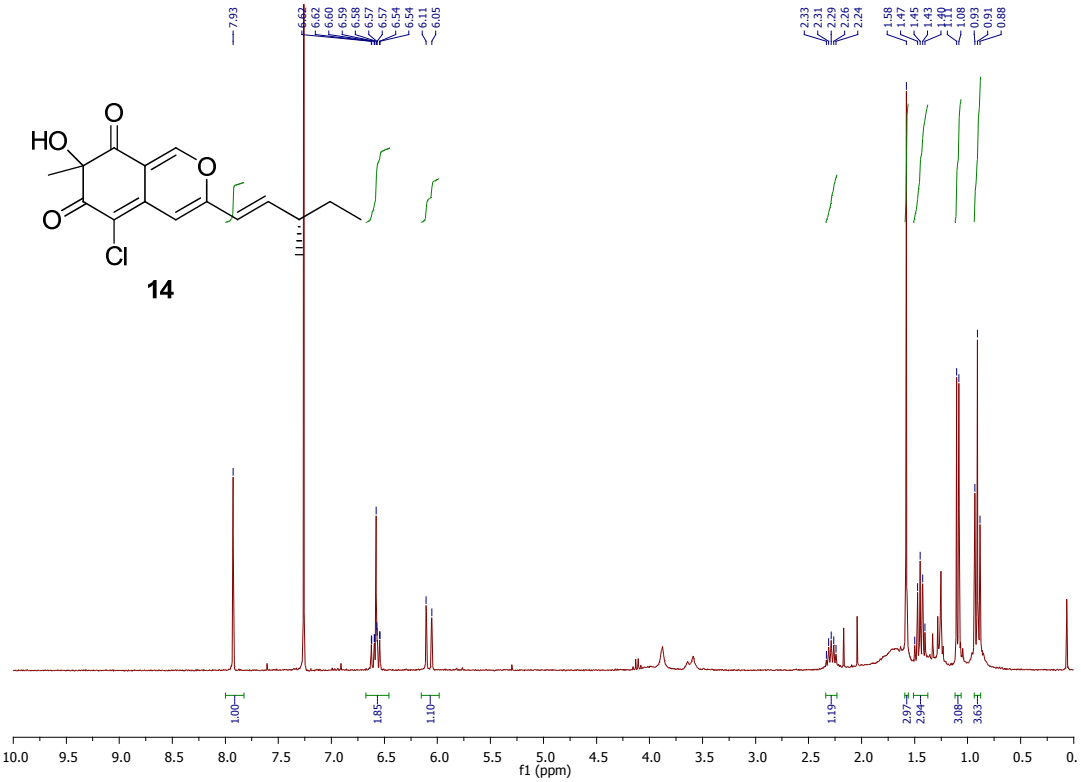

166.94
165.72
154.76
153.32
142.99
141.34
139.65
137.98
136.34
128.63
127.65
126.72
125.68
125.13
100.78
99.80
77.58
77.16
76.74
58.01
57.70
52.61
36.06
11.50
10
f1 (ppm)

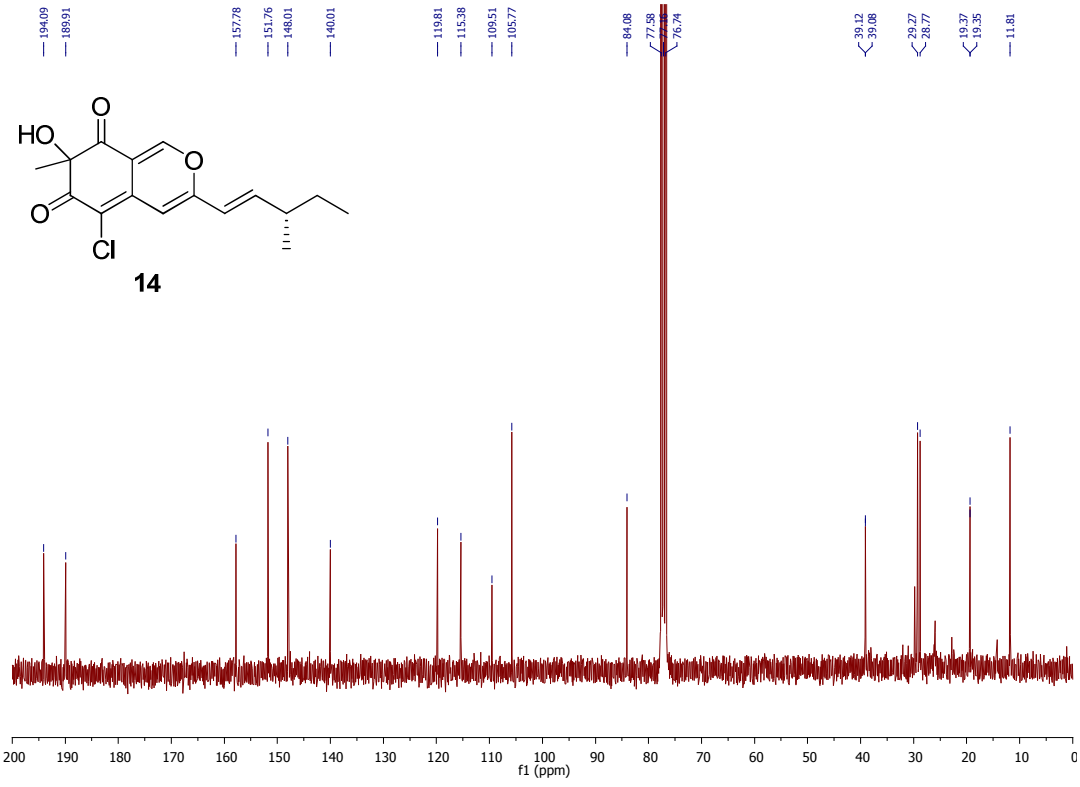

7.26
6.61
6.57
6.54
6.51
6.49
6.03
5.98
5.15
5.14
3.63
3.62
2.37
2.26
2.23
2.21
2.19
2.17
1.45
1.43
1.40
1.38
1.36
1.06
1.04
0.90
0.88
0.85
1.09
0.98
1.00
4.42
6.61
3.34
1.12
2.32
3.21
3.77
f1 (ppm)

12


158.70
158.48
158.37
153.17
143.50
136.38
128.13
120.32
118.83
110.74
102.00
100.31
99.85
77.58
77.16
76.74
58.18
57.90
38.87
29.45
19.69
11.85
11.64
f1 (ppm)

12


HO
O
O
O
Cl
14
7.93
6.62
6.62
6.60
6.59
6.58
6.57
6.57
6.54
6.54
6.11
6.05
2.33
2.31
2.29
2.26
2.24
1.58
1.47
1.45
1.43
1.40
1.11
1.08
0.93
0.91
0.88
1.00
1.85
1.10
1.19
2.97
2.94
3.08
3.63
f1 (ppm)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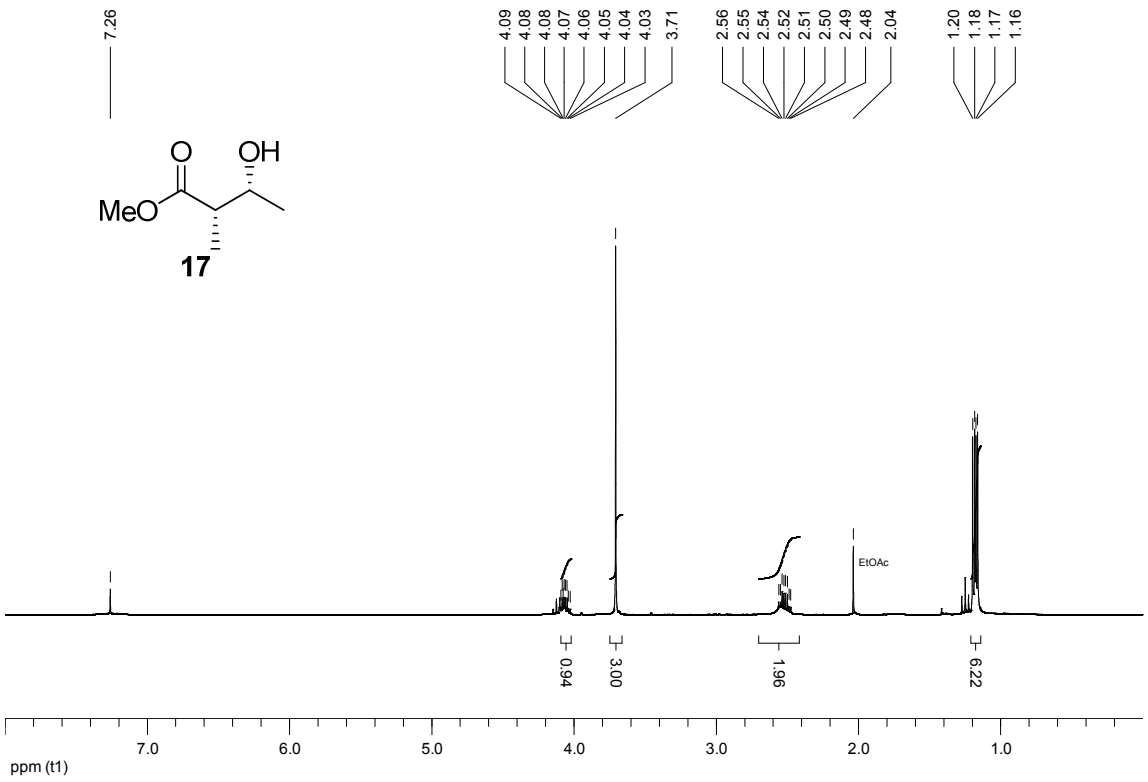
O
O
O
Cl
14
194.09
189.91
157.78
151.76
148.01
140.01
119.81
115.38
109.51
105.77
84.08
77.58
77.32
76.74
39.12
39.08
29.27
28.77
19.37
19.35
11.81
f1 (ppm)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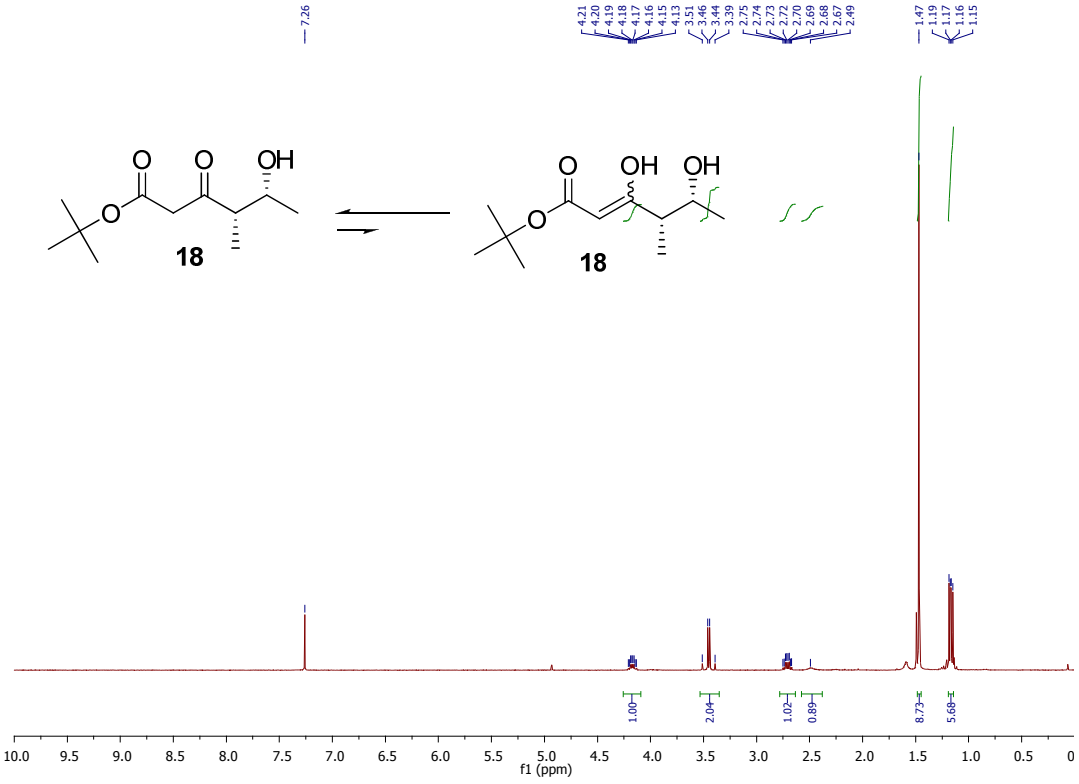
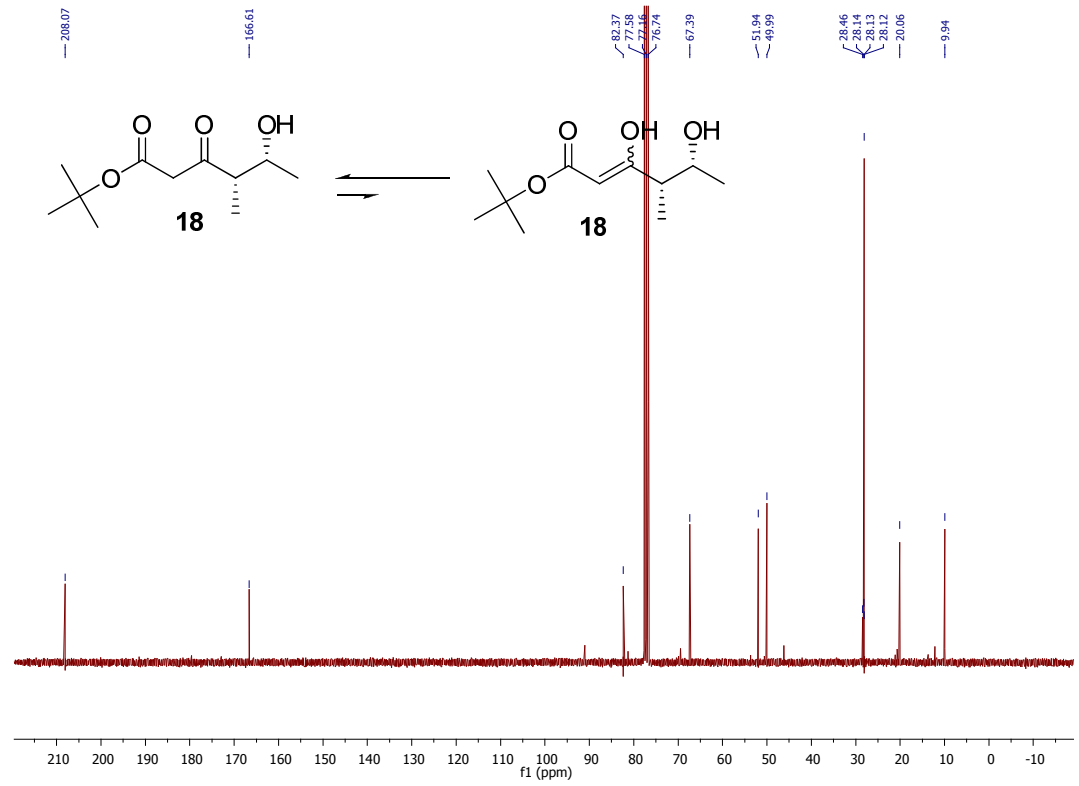
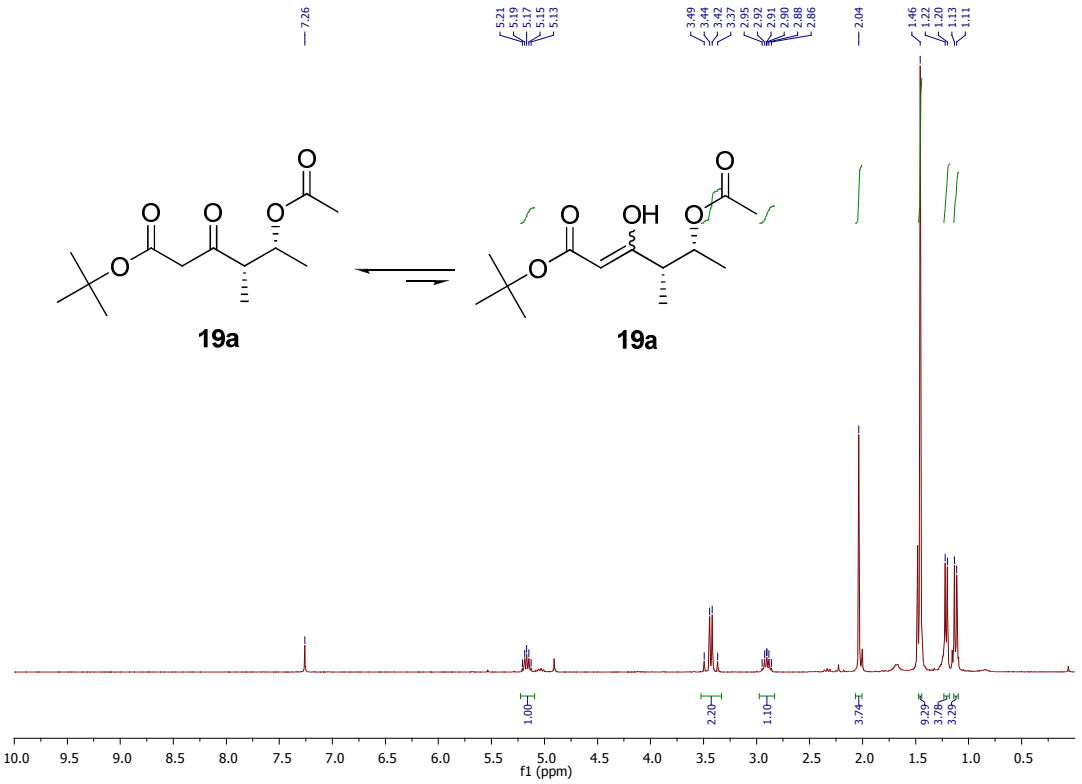
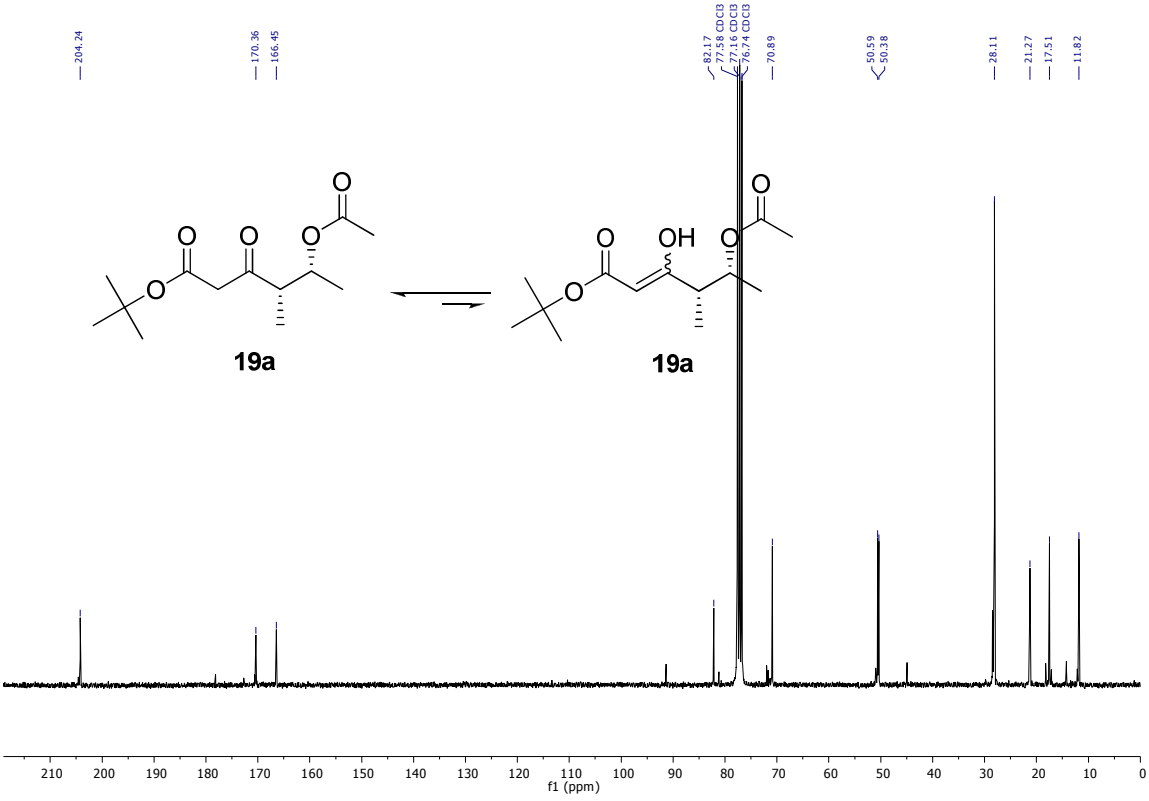
4.09
4.08
4.08
4.07
4.06
4.05
4.04
4.03
3.71
2.56
2.55
2.54
2.52
2.51
2.50
2.49
2.48
2.04
1.20
1.18
1.17
1.16
O
OH
MeO
17
EtOAc
0.94
3.00
1.96
6.22
7.0
6.0
5.0
4.0
3.0
2.0
1.0
ppm (t1)


7.26
4.21
4.20
4.19
4.18
4.17
4.16
4.15
4.13
3.51
3.46
3.44
3.39
2.75
2.74
2.73
2.72
2.70
2.69
2.68
2.67
2.49
1.47
1.19
1.17
1.16
1.15
O
O
OH
O
18
OH
OH
O
18
1.00
2.04
1.02
0.89
8.73
5.68
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0
f1 (ppm)


208.07
166.61
82.37
77.58
77.16
76.74
67.39
51.94
49.99
28.46
28.14
28.13
28.12
20.06
9.94
O
O
OH
O
18
OH
OH
O
18
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)


7.26
5.21
5.19
5.17
5.15
5.13
3.49
3.44
3.42
3.37
2.95
2.92
2.91
2.90
2.88
2.86
2.04
1.46
1.22
1.20
1.13
1.11
19a
19a
1.00
2.20
1.10
3.74
9.29
3.78
3.29
f1 (ppm)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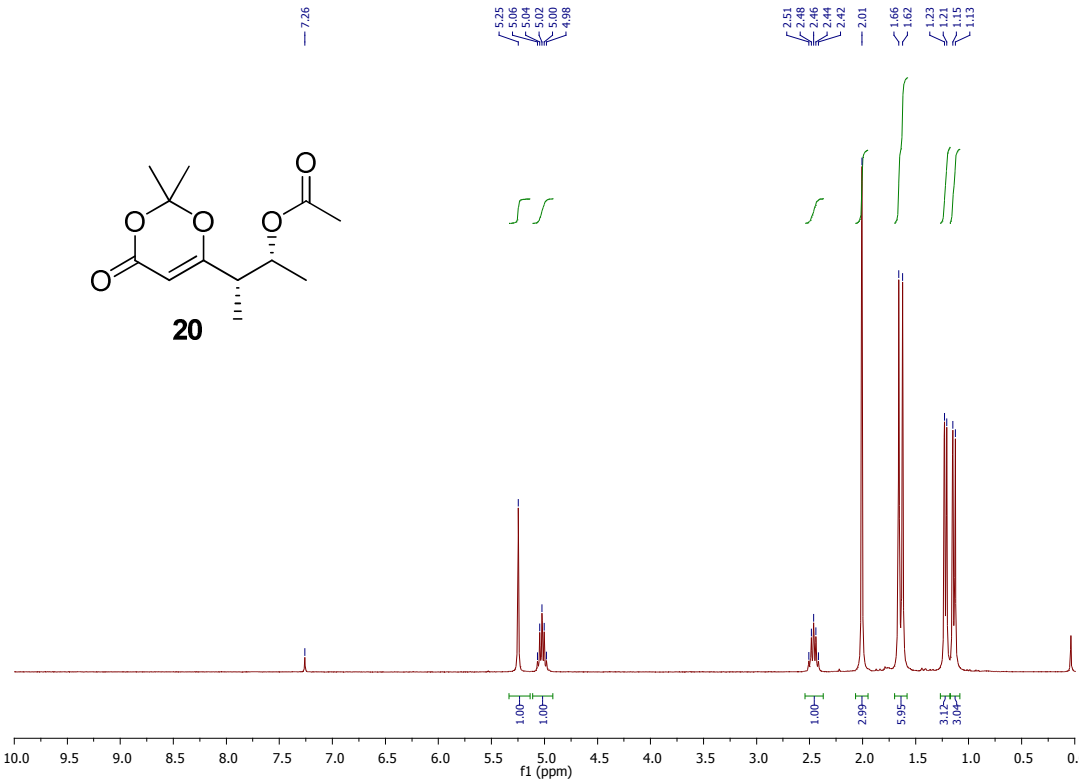
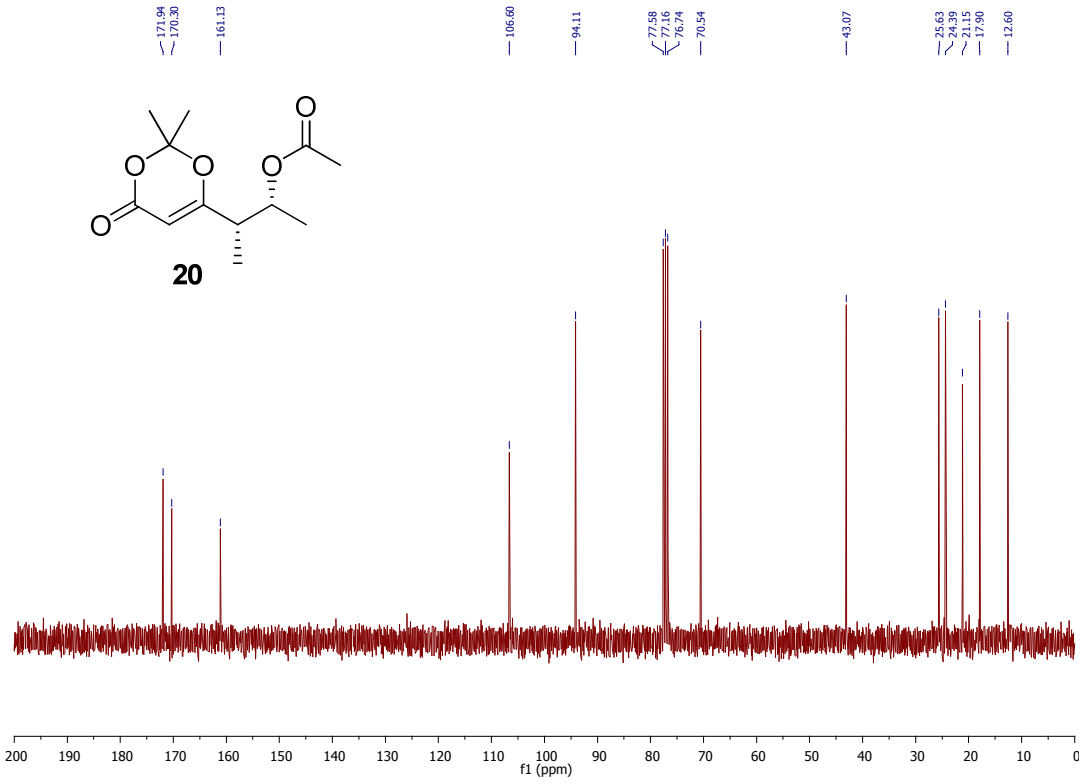
170.36
166.45
82.17
77.58 CDCl3
77.16 CDCl3
76.74 CDCl3
70.89
50.59
50.38
28.11
21.27
17.51
11.82
19a
19a
f1 (ppm)


7.26
5.25
5.06
5.04
5.02
5.00
4.98
2.51
2.48
2.46
2.44
2.42
2.01
1.66
1.62
1.23
1.21
1.15
1.13
1.00
1.00
1.00
2.99
5.95
3.12
3.04
f1 (ppm)

20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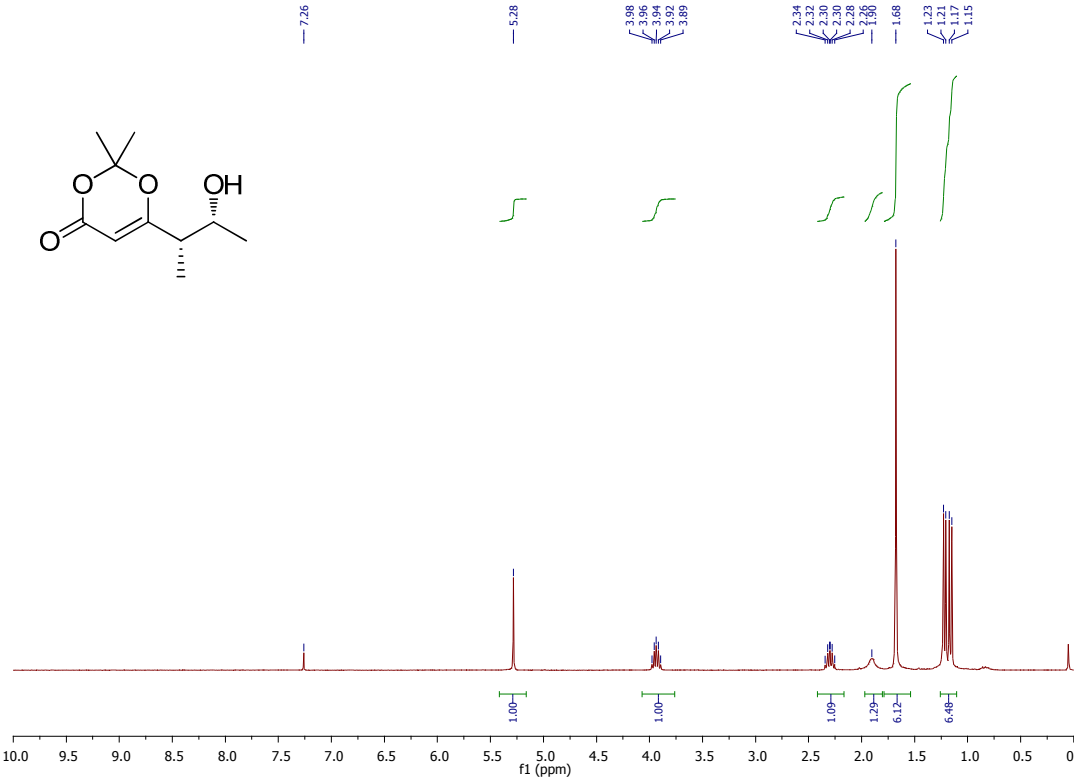
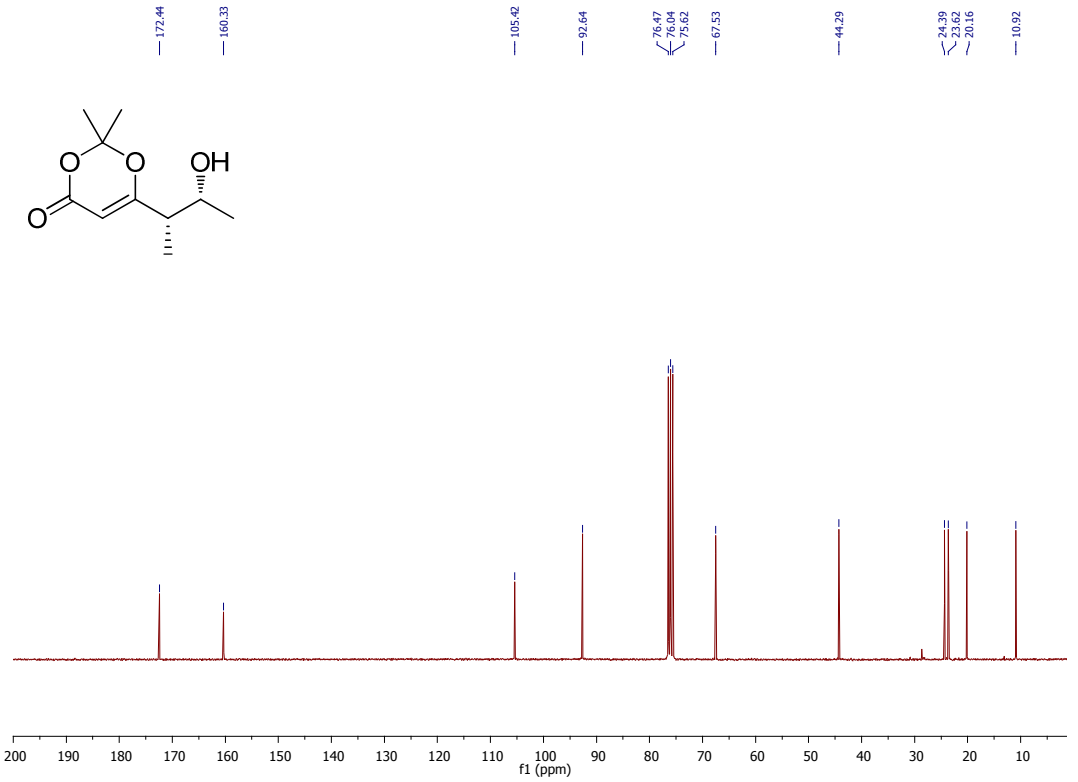
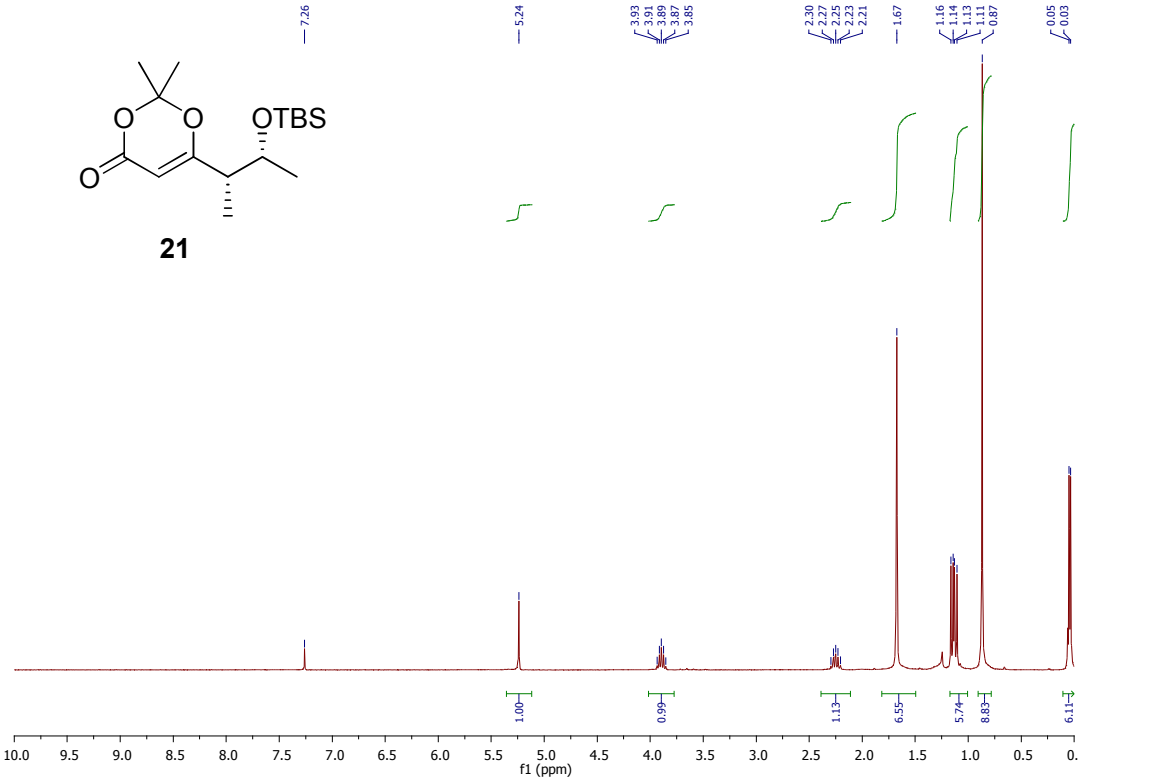
170.30
161.13
106.60
94.11
77.58
77.16
76.74
70.54
43.07
25.63
24.39
21.15
17.90
12.60
f1 (ppm)

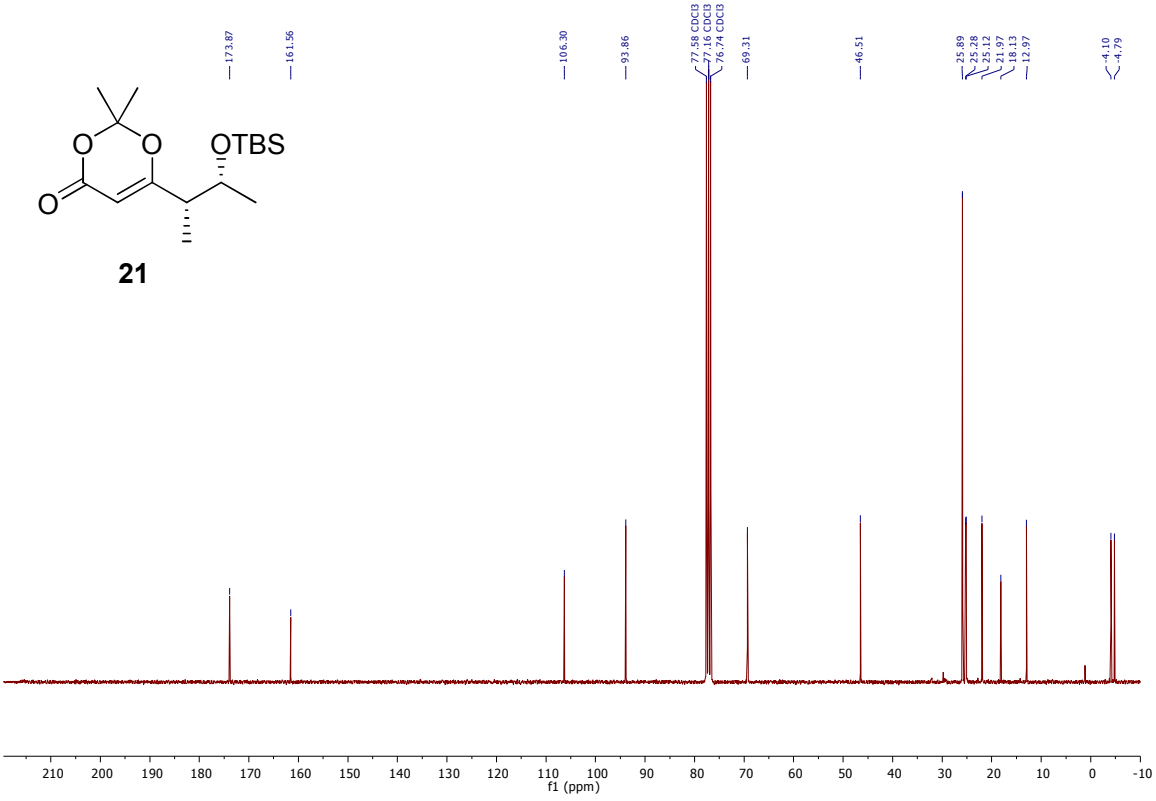
20


7.26
5.28
3.98
3.96
3.94
3.92
3.89
2.34
2.32
2.30
2.30
2.28
1.68
1.23
1.21
1.17
1.15
O
O
OH
O
1.00
1.00
1.09
1.29
6.12
6.48
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0
f1 (ppm)

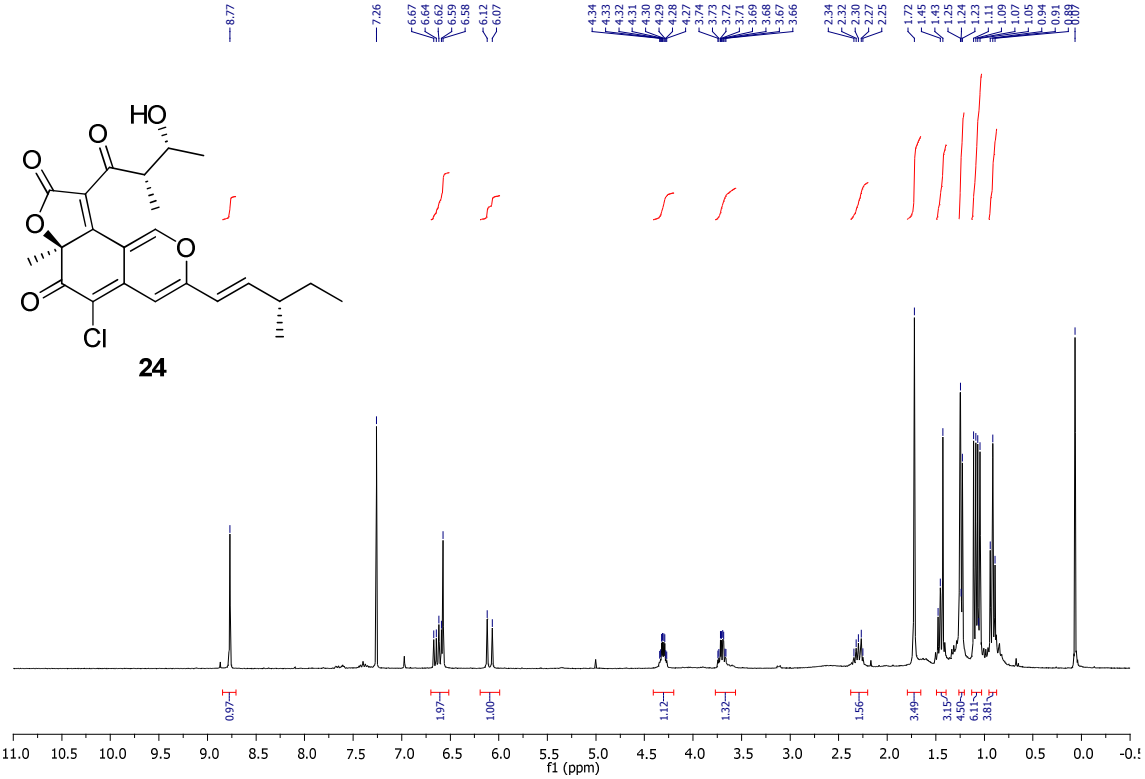

172.44
160.33
105.42
92.64
76.47
76.04
75.62
67.53
44.29
24.39
23.62
20.16
10.92
O
O
OH
O
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10
f1 (ppm)

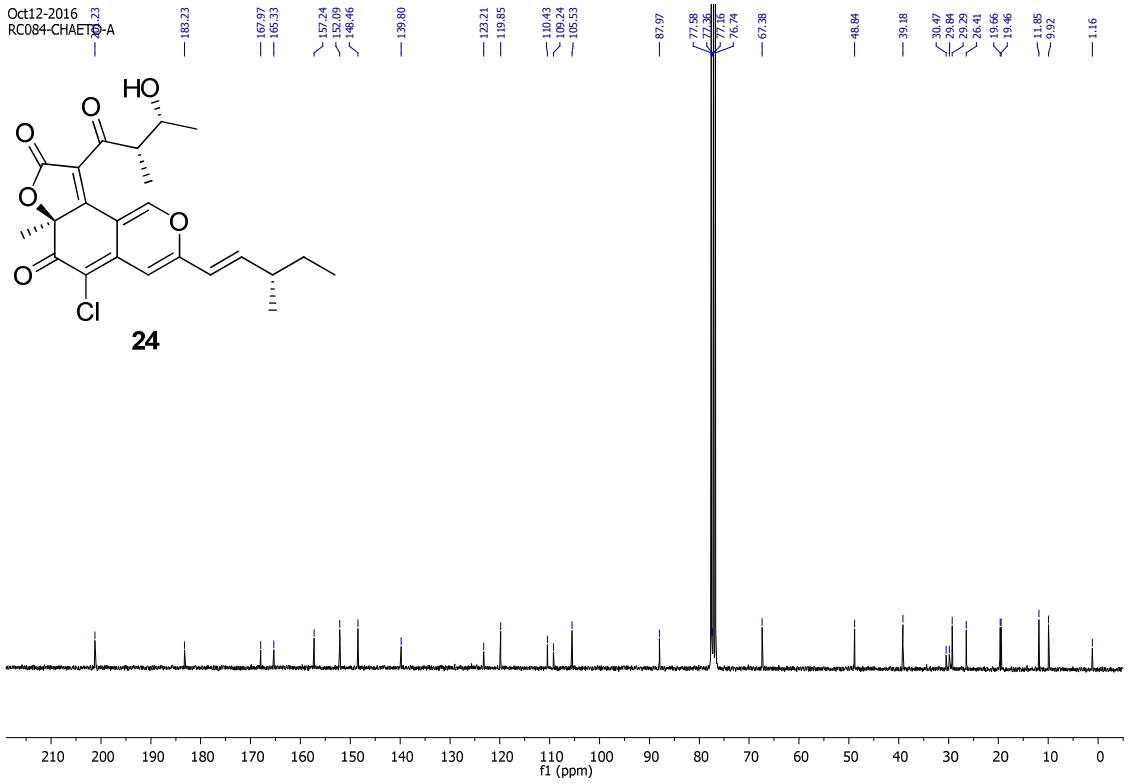

7.26
5.24
3.93
3.91
3.89
3.87
3.85
2.30
2.27
2.25
2.23
2.21
1.67
1.16
1.14
1.13
1.11
0.87
0.05
0.03
O
O
OTBS
O
1.00
0.99
1.13
6.55
5.74
8.83
6.11
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.
f1 (ppm)

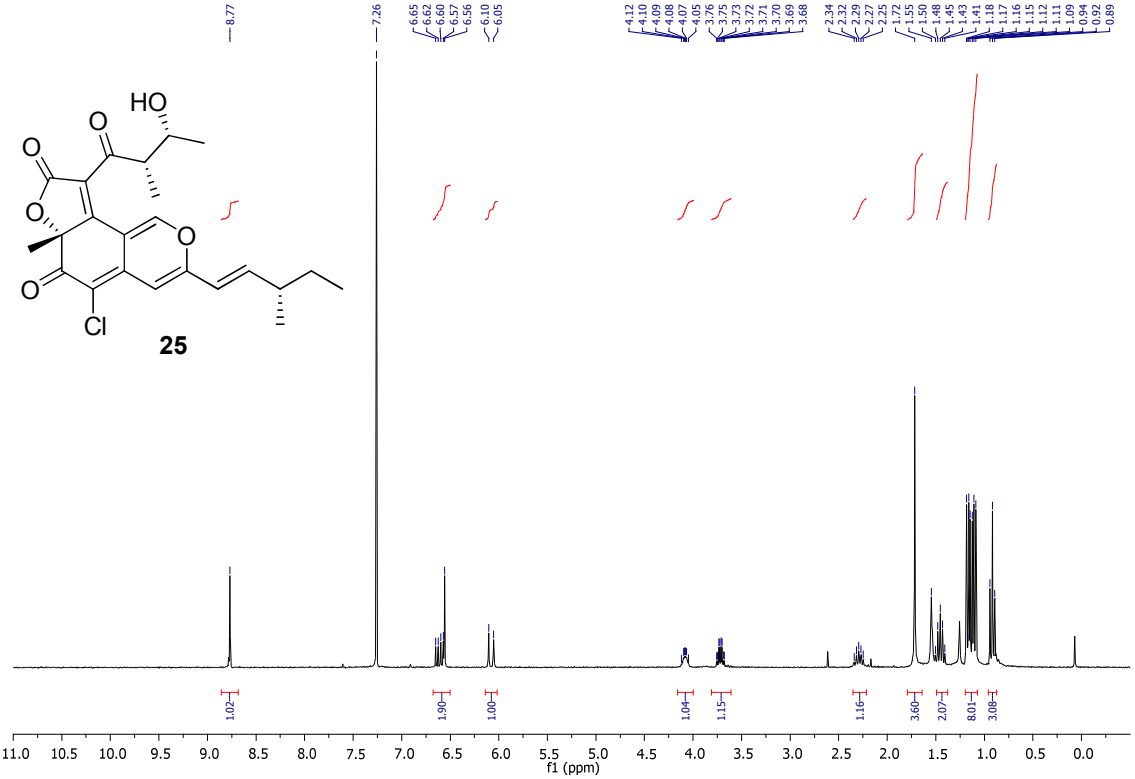
21


173.87
161.56
106.30
93.86
77.58 CDCl3
77.16 CDCl3
76.74 CDCl3
69.31
46.51
25.89
25.38
25.12
21.97
18.13
12.97
-4.10
-4.79
O
O
OTBS
O
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)

21


HO
O
O
O
O
O
Cl
24
f1 (ppm)


Oct12-2016
RC084-CHAETO-A
HO
O
O
O
O
O
Cl
24
f1 (ppm)


HO
O
O
O
O
O
Cl
25
8.77
7.26
6.65
6.62
6.60
6.57
6.56
6.10
6.05
4.12
4.10
4.09
4.08
4.07
4.05
3.76
3.75
3.73
3.72
3.71
3.70
3.69
3.68
2.34
2.32
2.29
2.27
2.25
1.72
1.55
1.50
1.48
1.45
1.43
1.41
1.18
1.17
1.16
1.15
1.12
1.11
1.09
0.94
0.92
0.89
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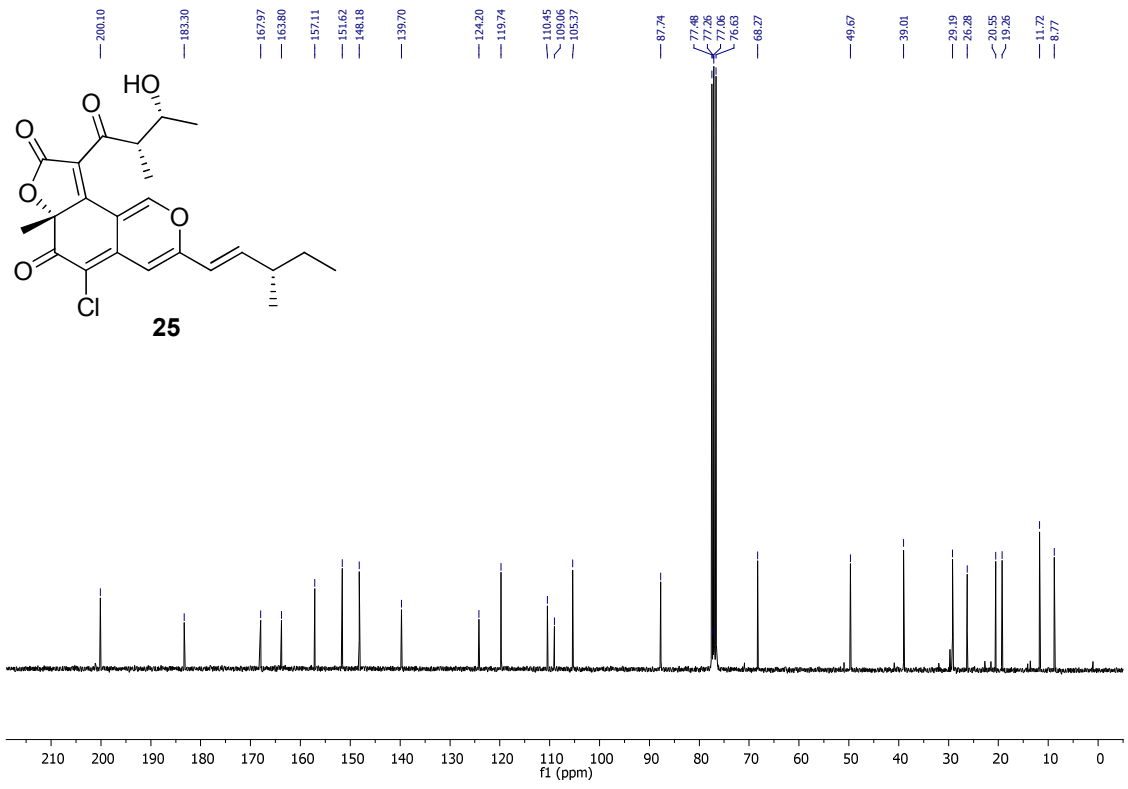
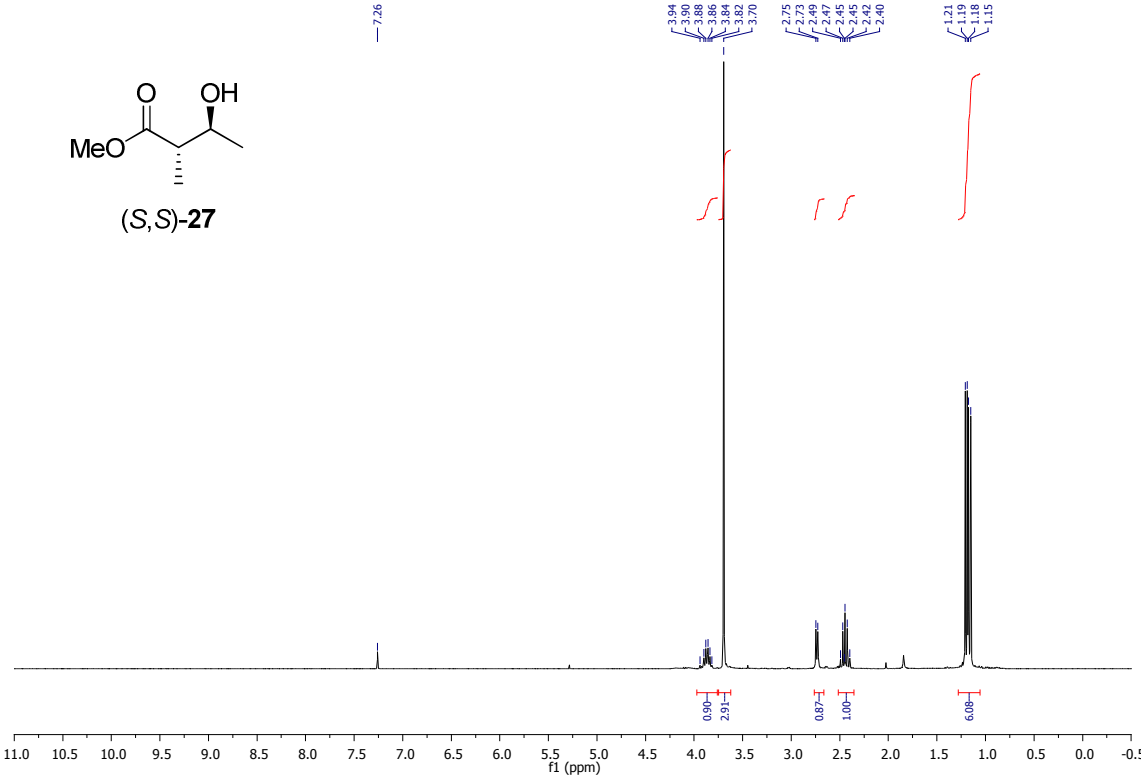
1.00
1.04
1.15
1.16
3.60
2.07
8.01
3.08
f1 (ppm)


HO
O
O
O
O
O
Cl
25
200.10
183.30
167.97
163.80
157.11
151.62
148.18
139.70
124.20
119.74
110.45
109.06
105.37
87.74
77.48
77.26
77.06
76.63
68.27
49.67
39.01
29.19
26.28
20.55
19.26
11.72
8.77
f1 (ppm)


O
OH
MeO
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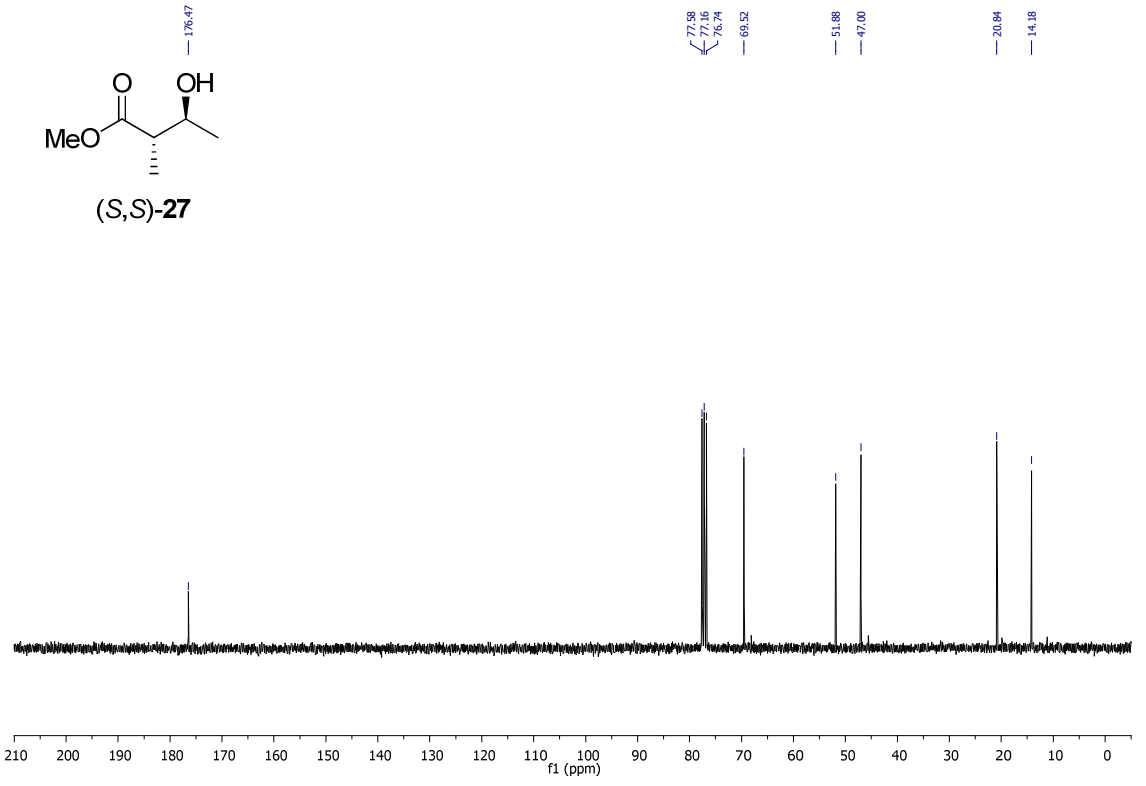
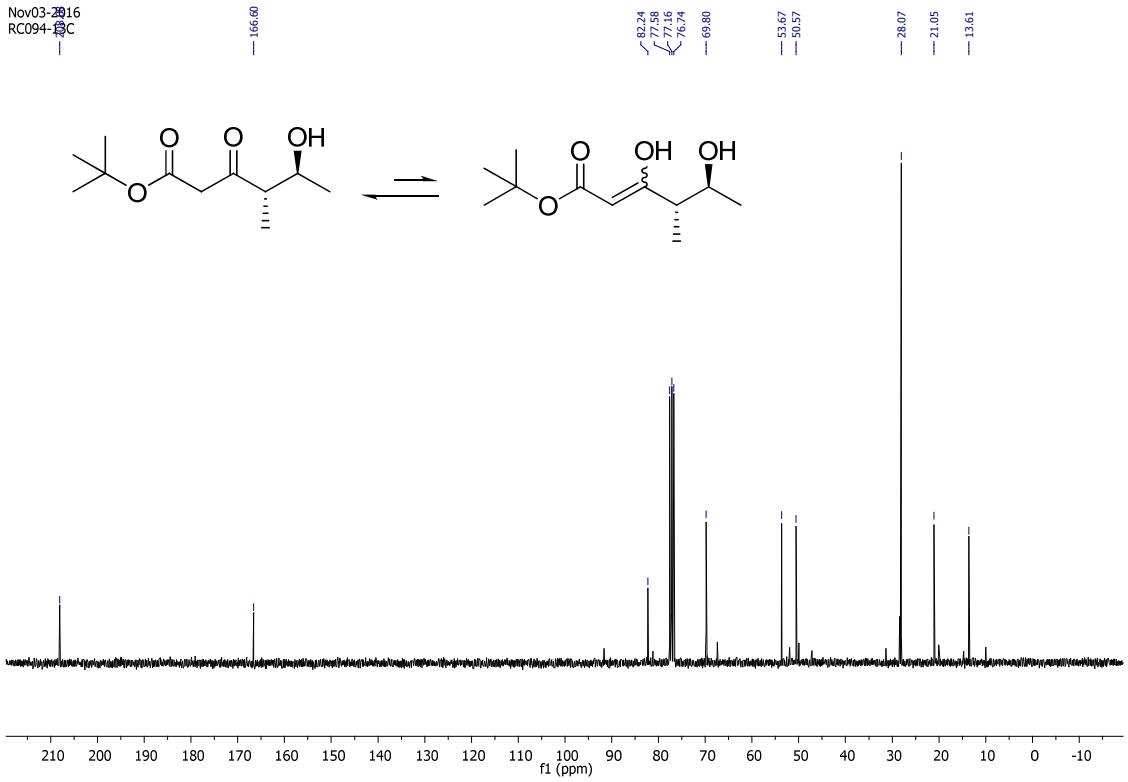
3.94
3.90
3.88
3.86
3.84
3.82
3.70
2.75
2.73
2.49
2.47
2.45
2.45
2.42
2.40
1.21
1.19
1.18
1.15
0.90
2.91
0.87
1.00
6.08
f1 (ppm)

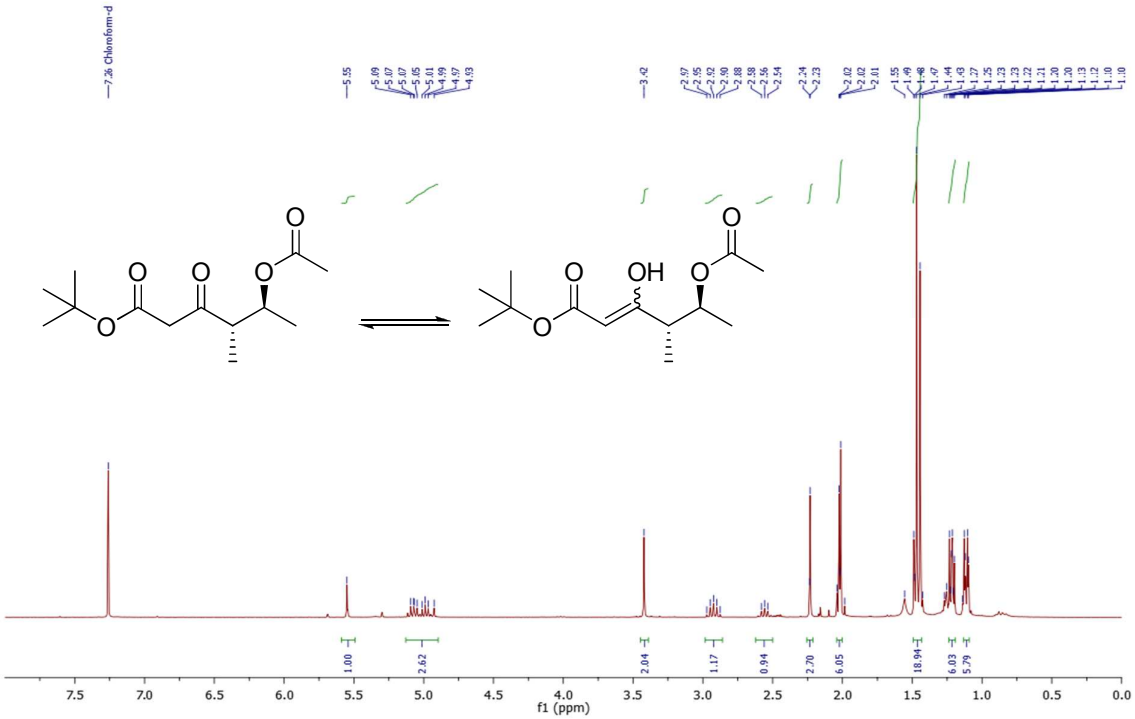
(*S*,*S*)-**27**

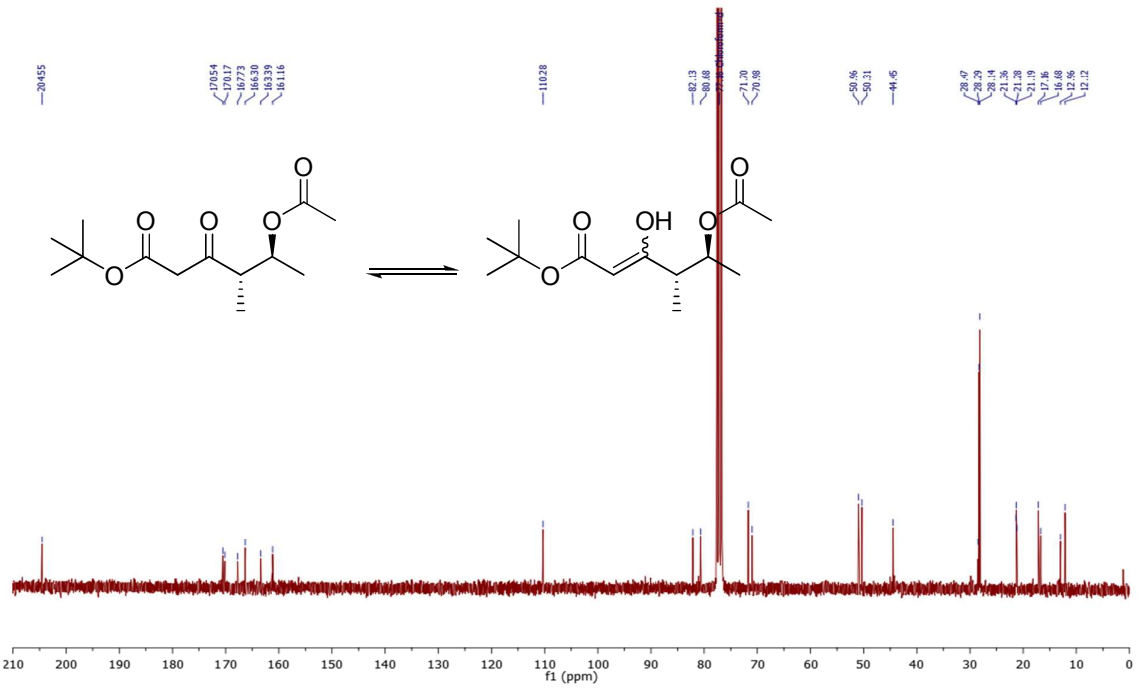

O
OH
MeO
176.47
77.58
77.16
76.74
69.52
51.88
47.00
20.84
14.18
f1 (ppm)

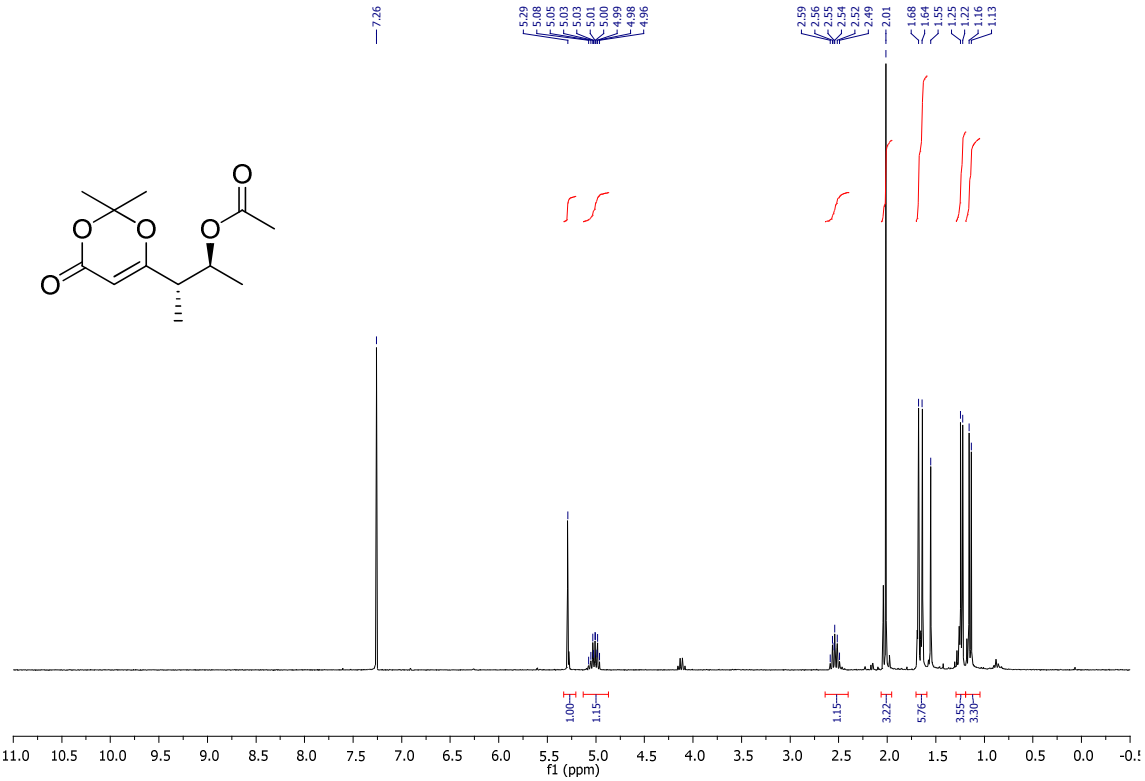
(*S*,*S*)-**27**

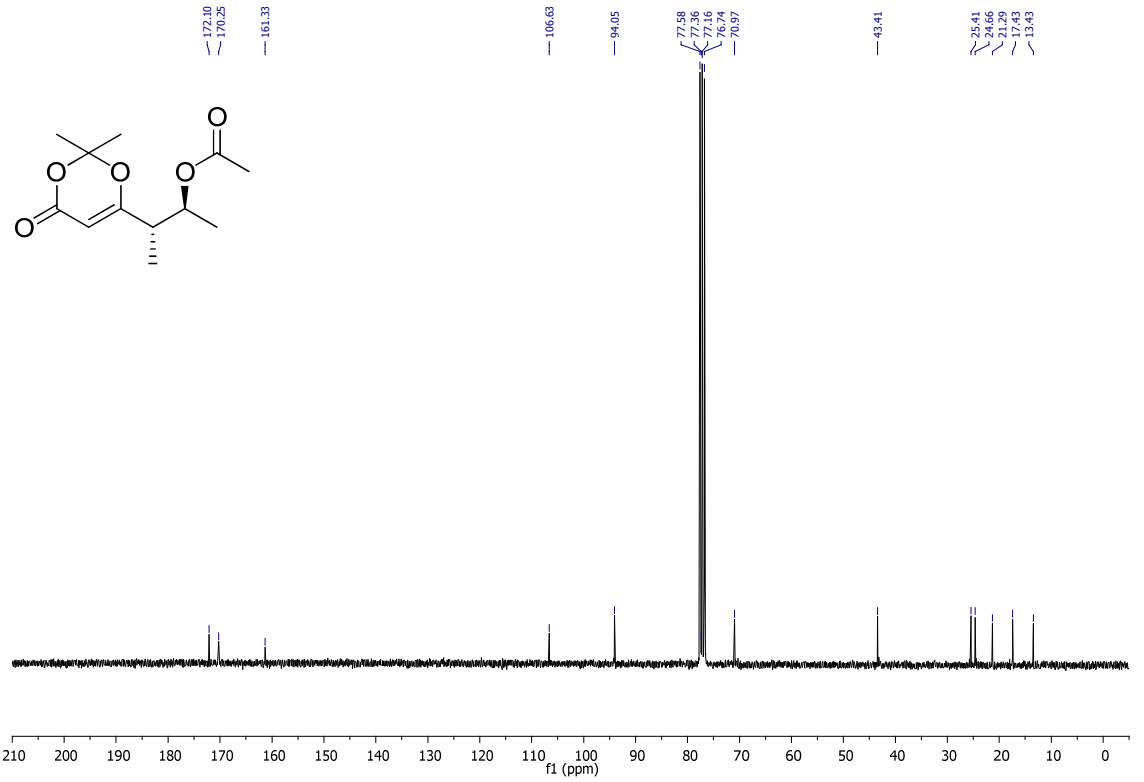

7.26
4.94
3.94
3.92
3.90
3.87
3.85
3.45
3.44
3.43
3.38
2.72
2.70
2.69
2.67
2.65
2.63
2.59
1.47
1.45
1.22
1.19
1.11
1.09
O
O
OH
O
OH
OH
1.00
2.01
1.91
9.74
6.85
11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

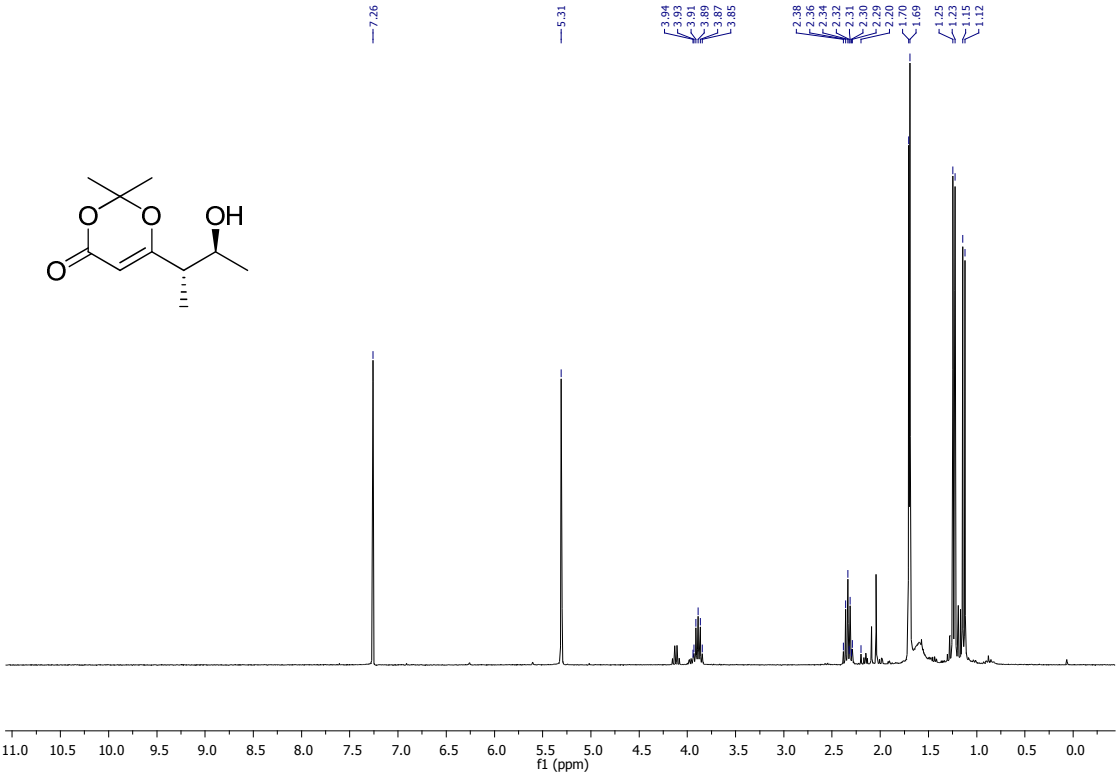

Nov03-2016
RC094-13C
166.60
82.24
77.58
77.16
76.74
69.80
53.67
50.57
28.07
21.05
13.61
O
O
OH
O
OH
OH
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

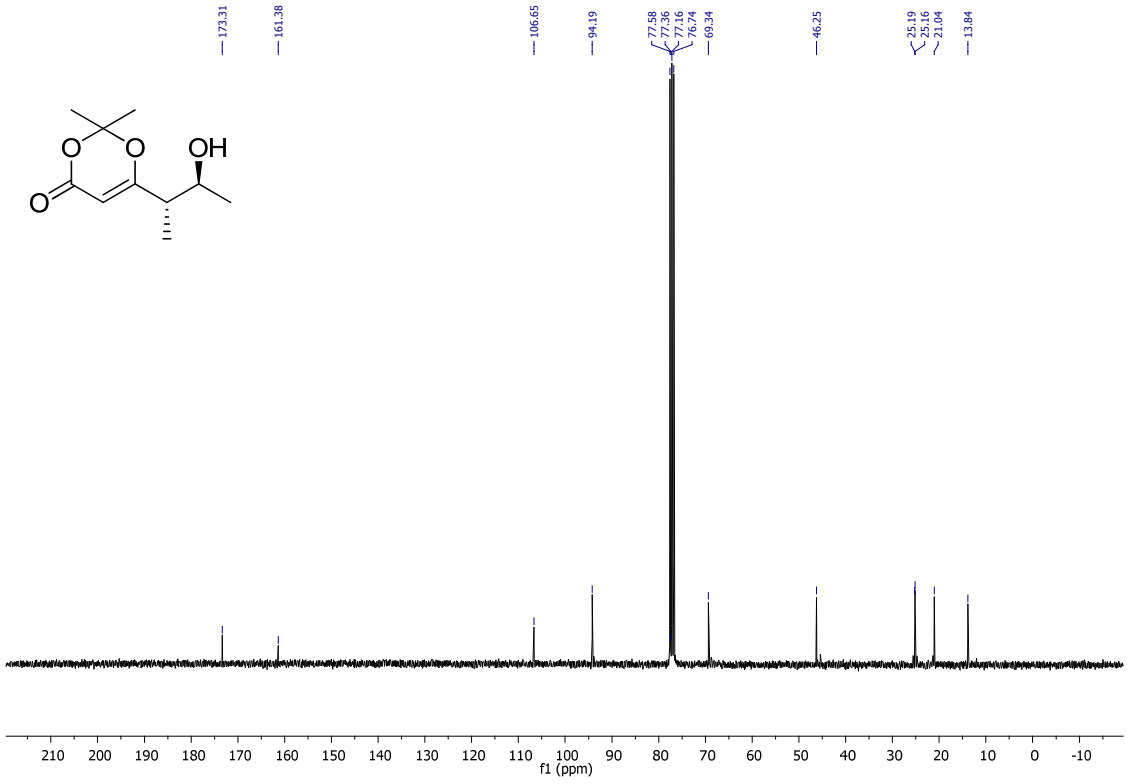

7.26 Chloroform-d
5.55
5.09
5.07
5.07
5.05
5.01
4.99
4.97
4.93
3.42
2.97
2.95
2.92
2.90
2.88
2.58
2.56
2.54
2.24
2.23
2.02
2.02
2.01
1.55
1.49
1.48
1.47
1.44
1.43
1.27
1.25
1.23
1.23
1.22
1.21
1.20
1.20
1.13
1.12
1.10
1.10
O
O
O
O
O
O
OH
O
1.00
2.62
2.04
1.17
0.94
2.70
6.05
18.94
6.03
5.79
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

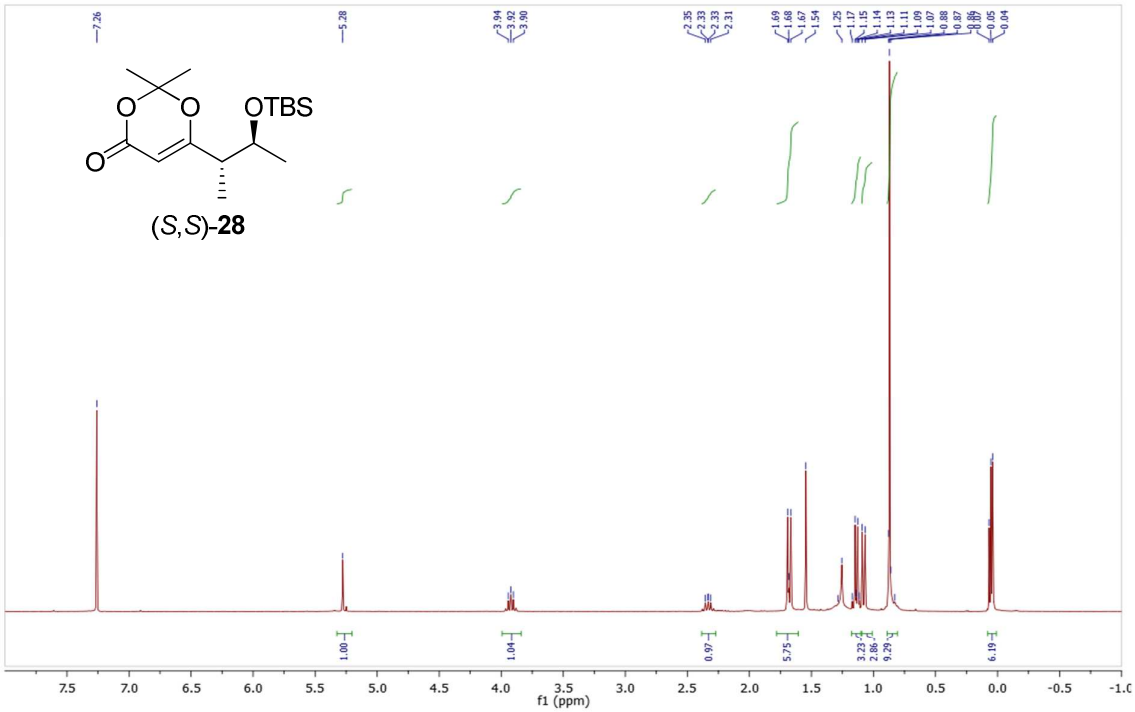

20.455
170.54
170.17
167.73
166.30
163.39
161.16
110.28
82.13
80.68
77.48 Chloroform-d
71.20
70.98
50.56
50.31
44.45
28.47
28.29
28.14
21.36
21.28
21.19
17.36
16.68
12.56
12.12
O
O
O
O
O
O
OH
O
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

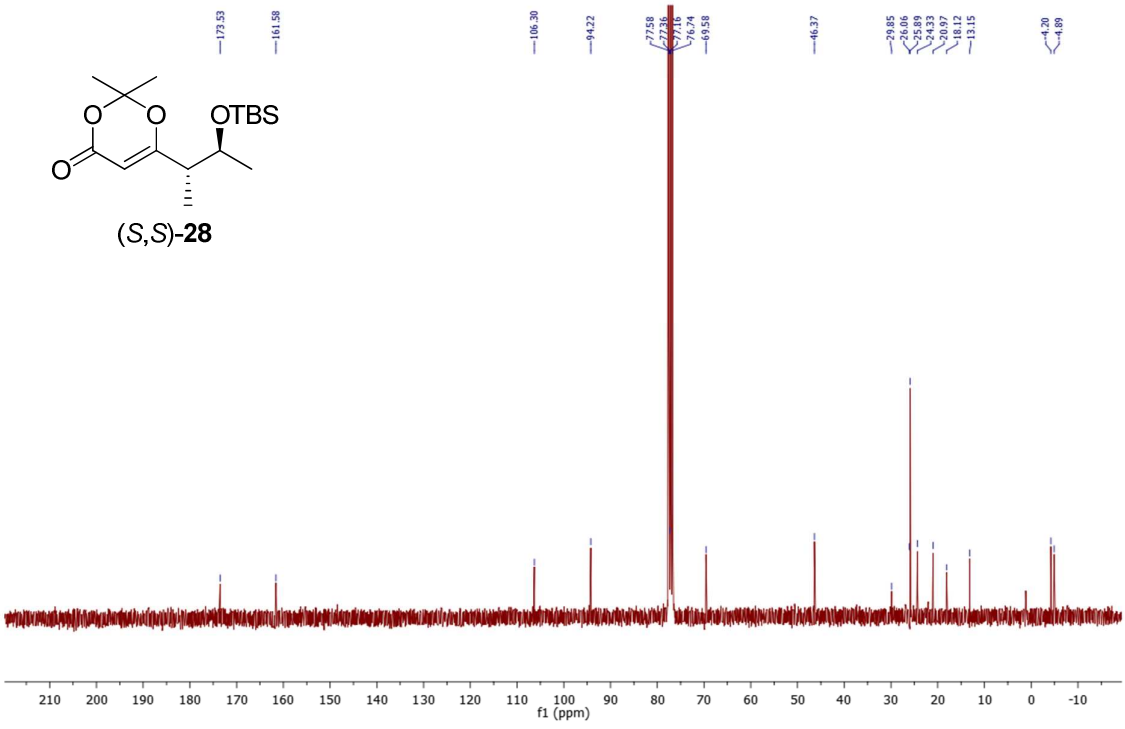

7.26
5.29
5.08
5.05
5.03
5.03
5.01
5.00
4.99
4.98
4.96
2.59
2.56
2.55
2.54
2.52
2.49
2.01
1.68
1.64
1.55
1.25
1.22
1.16
1.13
1.00
1.15
1.15
3.22
5.76
3.55
3.30
f1 (ppm)

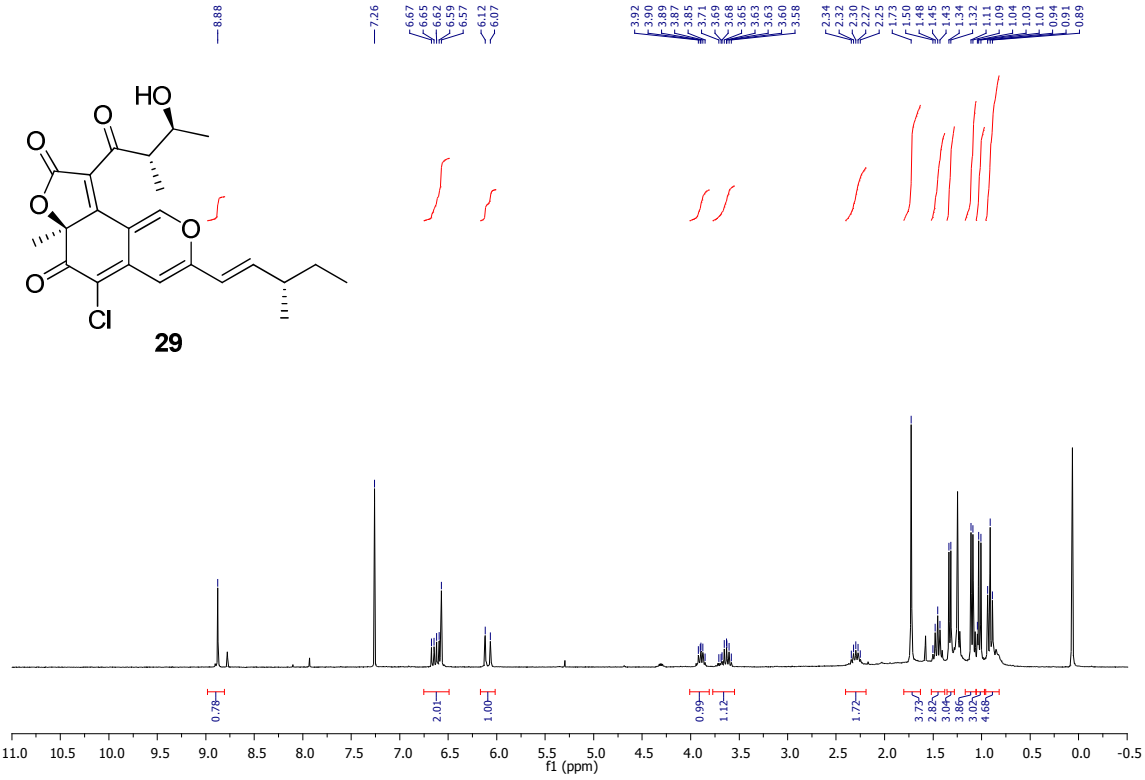

172.10
170.25
161.33
106.63
94.05
77.58
77.36
77.16
76.74
70.97
43.41
25.41
24.66
21.29
17.43
13.43
f1 (ppm)

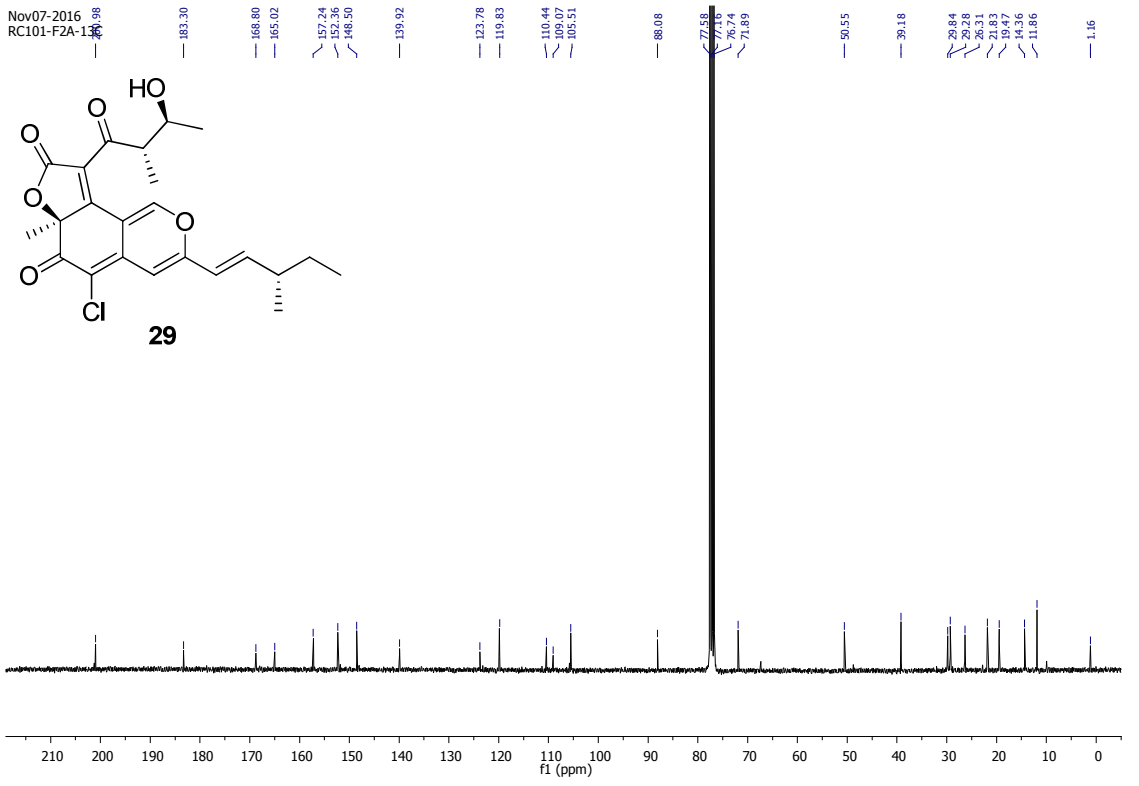

7.26
5.31
3.94
3.93
3.91
3.89
3.87
3.85
2.38
2.36
2.34
2.32
2.31
2.30
2.29
2.20
1.70
1.69
1.25
1.23
1.15
1.12
O
O
OH
O
11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

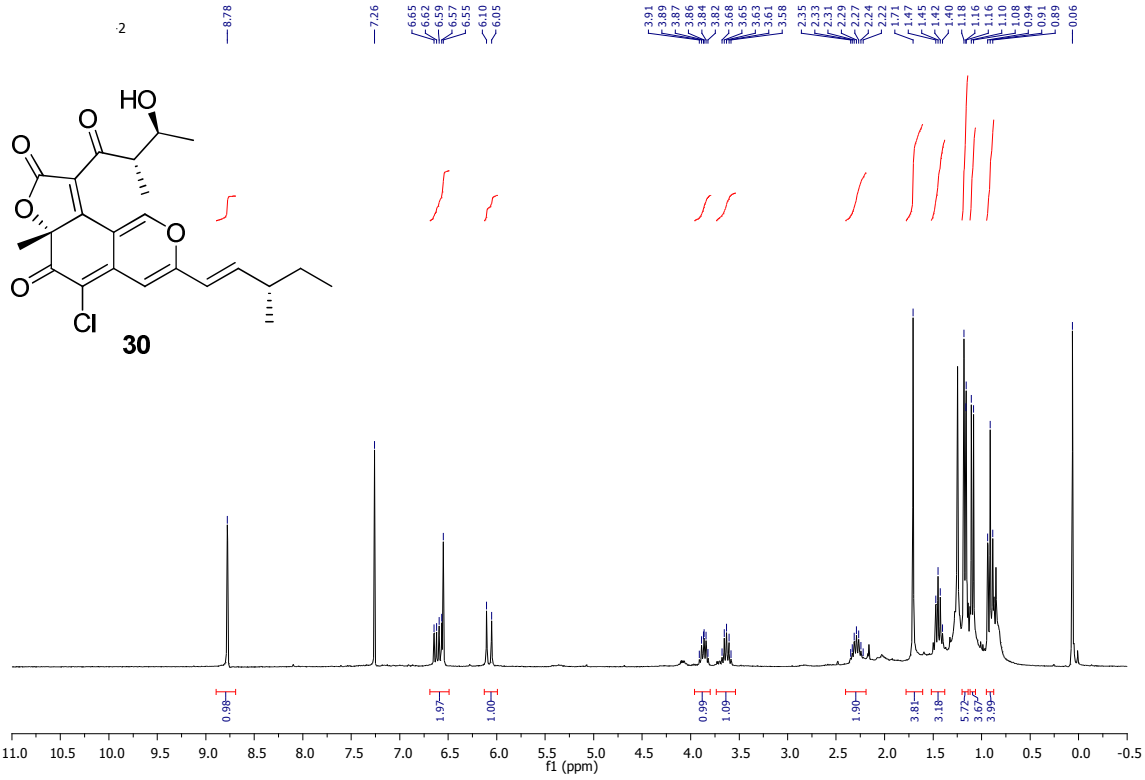

173.31
161.38
106.65
94.19
77.58
77.36
77.16
76.74
69.34
46.25
25.19
21.16
21.04
13.84
O
O
OH
O
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

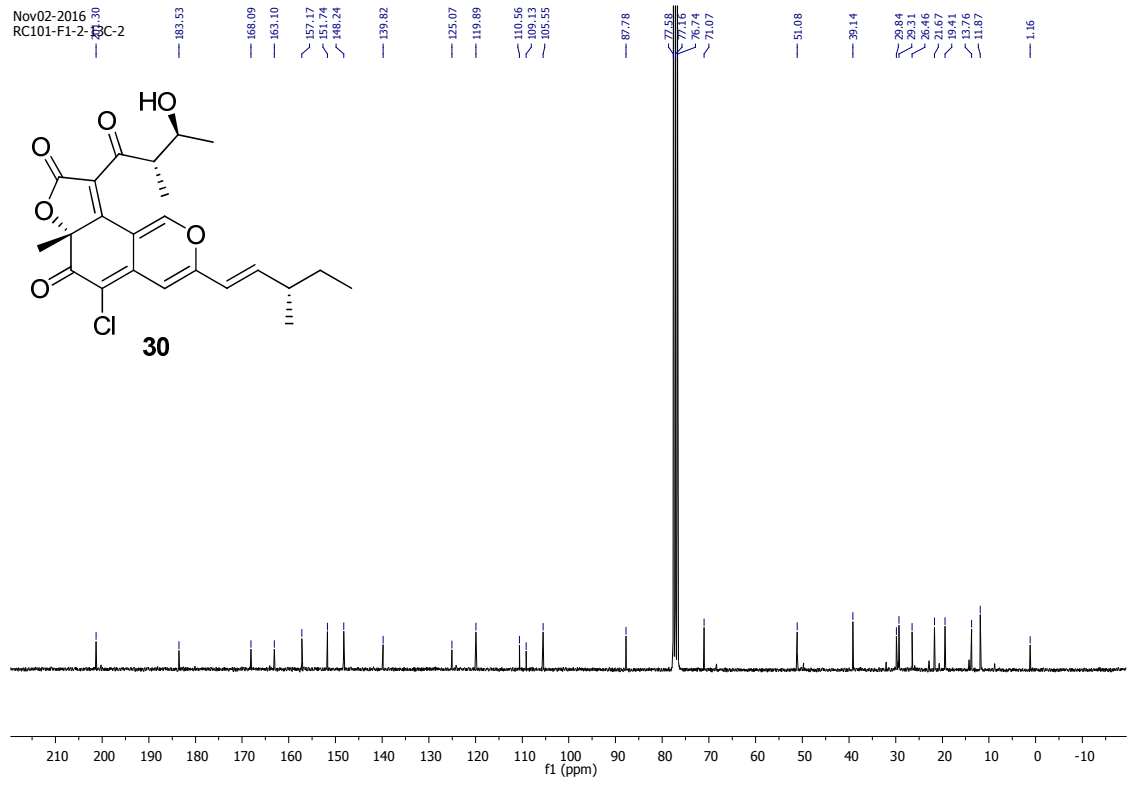

OTBS
O
O
O
(S,S)-28
f1 (ppm)

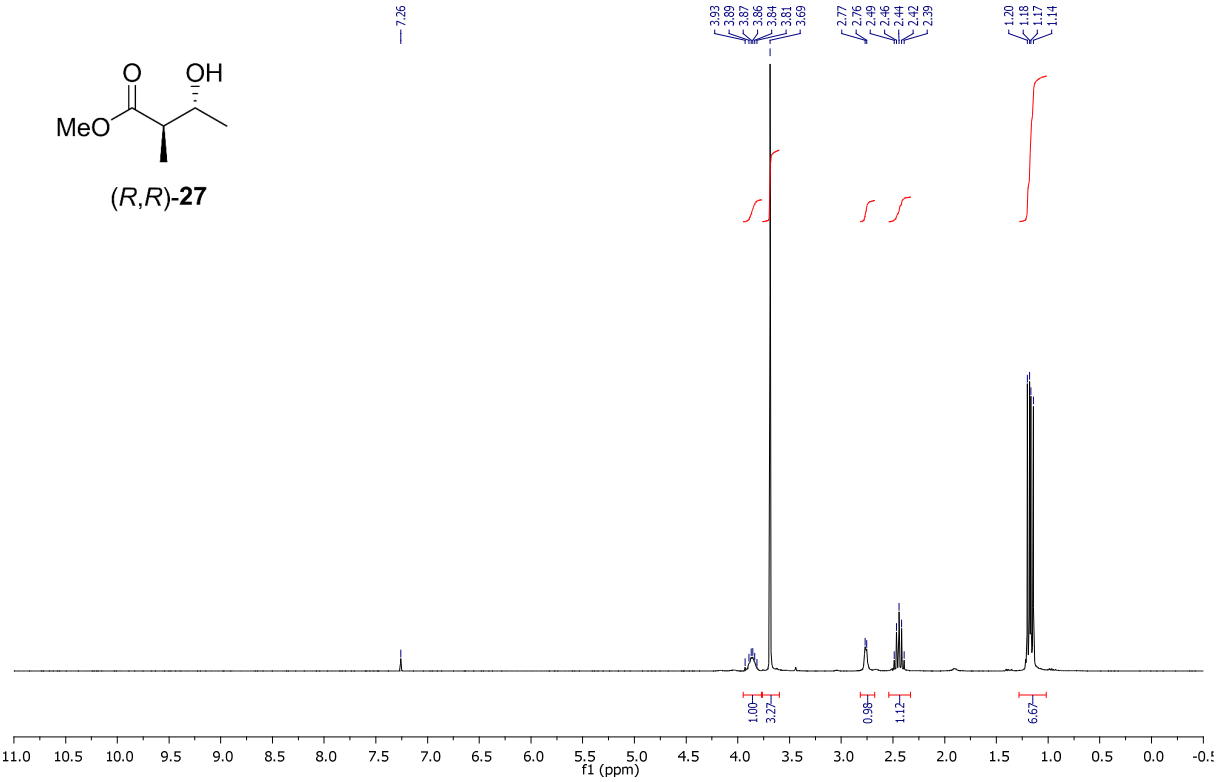

OTBS
O
O
O
(S,S)-28
f1 (ppm)

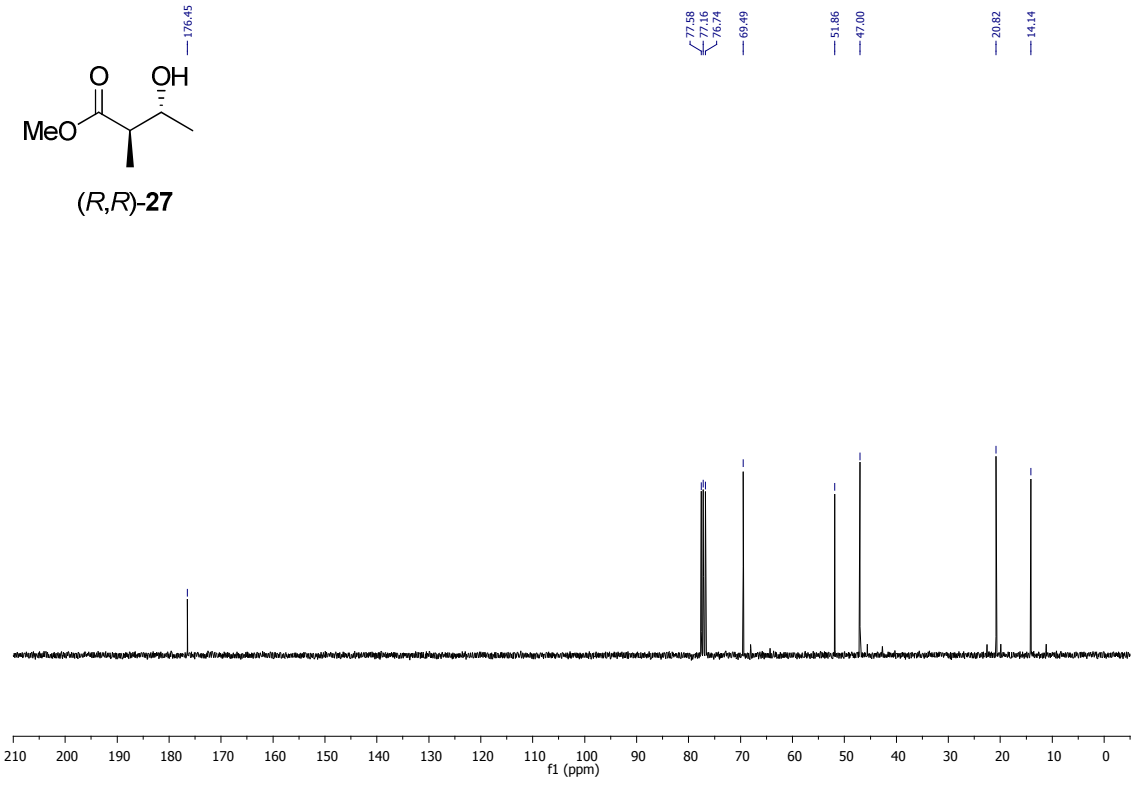

HO
O
O
O
O
O
Cl
29
f1 (ppm)

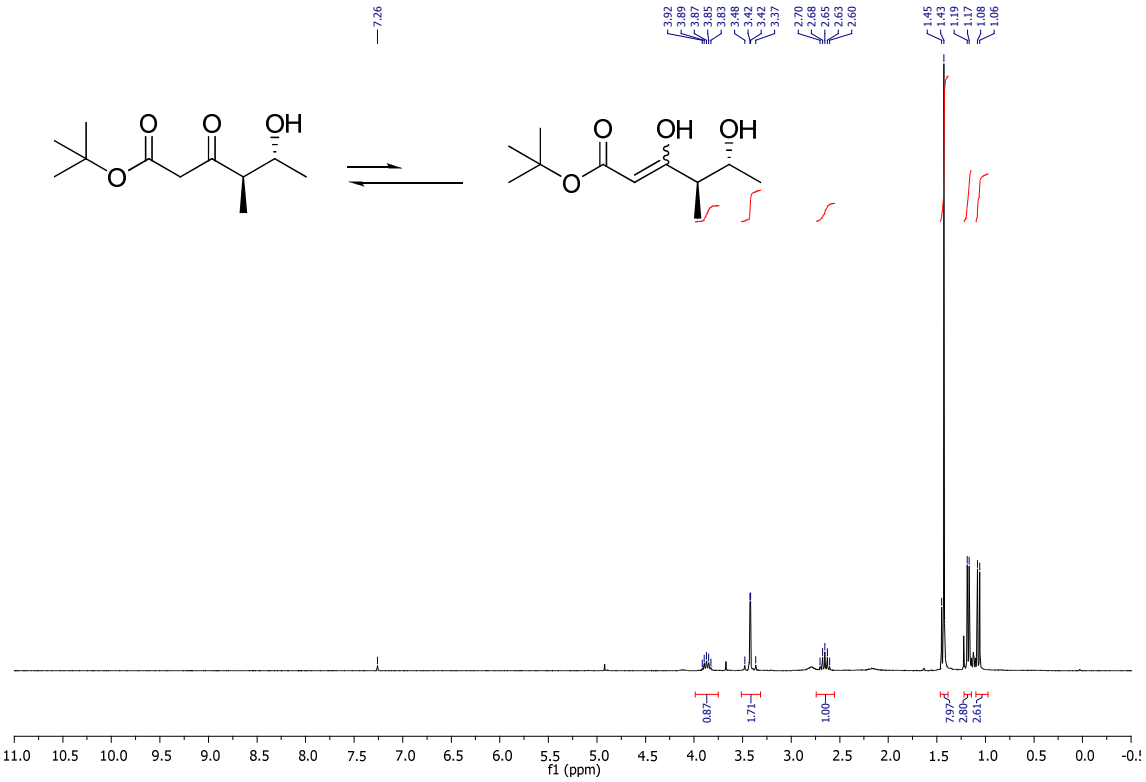

Nov07-2016
RC101-F2A-13C
HO
O
O
O
O
O
Cl
29
f1 (ppm)

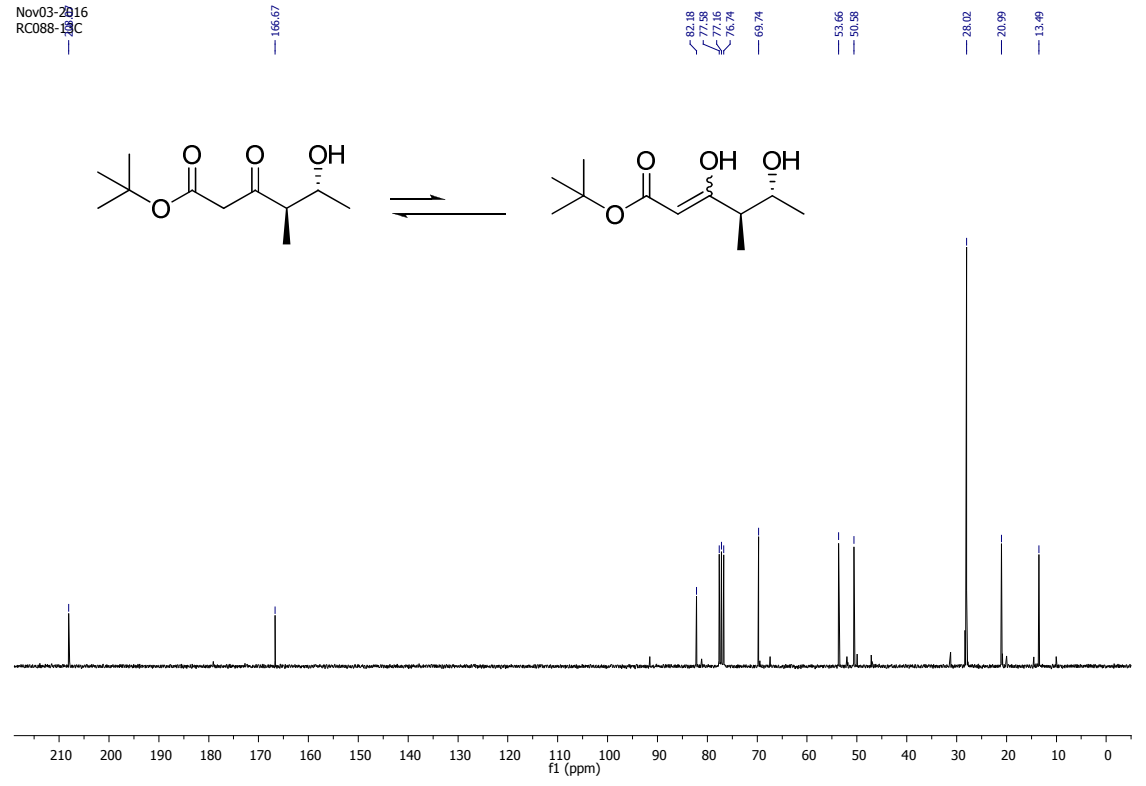

HO
O
O
O
O
O
Cl
30
8.78
7.26
6.65
6.62
6.59
6.57
6.55
6.10
6.05
3.91
3.89
3.87
3.86
3.84
3.82
3.68
3.65
3.63
3.61
3.58
2.35
2.33
2.31
2.29
2.27
2.24
2.22
1.71
1.47
1.45
1.42
1.40
1.18
1.16
1.16
1.10
1.08
1.04
0.91
0.89
0.06
0.98
1.97
1.00
0.99
1.09
1.90
3.81
3.18
5.72
3.67
3.99
f1 (ppm)

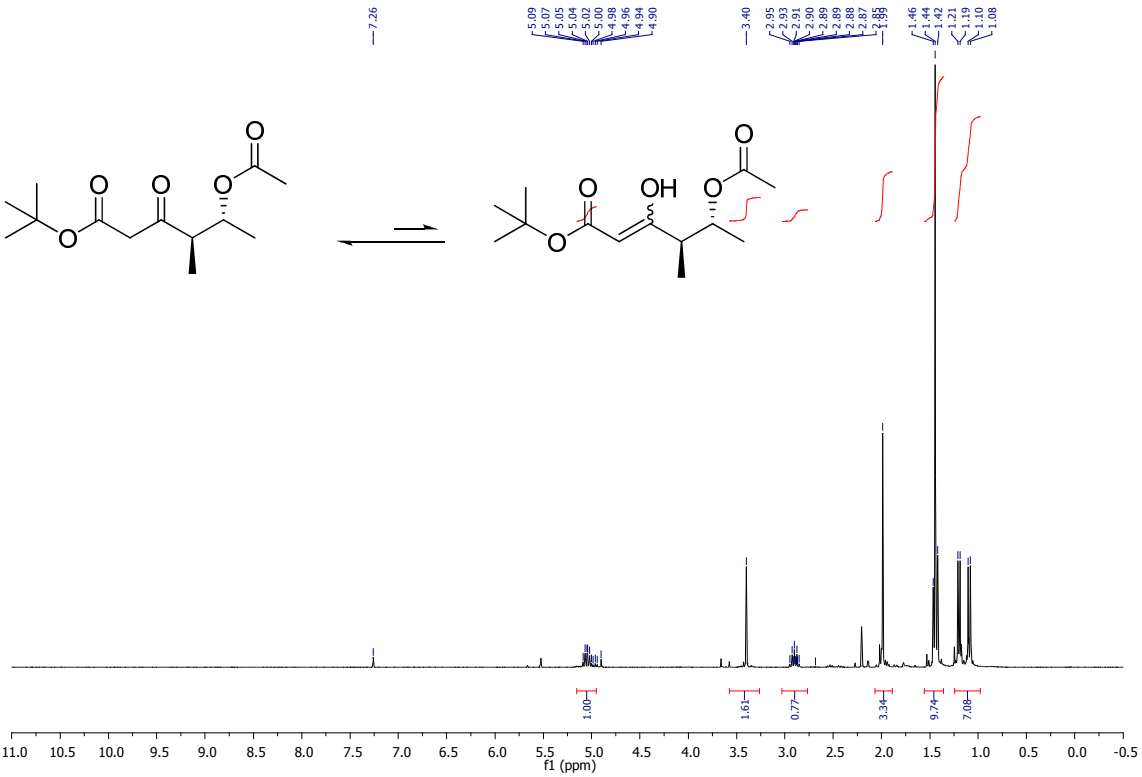

Nov02-2016
RC101-F1-2-13C-2
183.53
168.09
163.10
157.17
151.74
148.24
139.82
125.07
119.89
110.56
109.13
105.55
87.78
77.58
77.16
76.74
71.07
51.08
39.14
29.84
29.31
26.46
21.67
19.41
13.76
11.87
1.16
HO
O
O
O
O
O
Cl
30
f1 (ppm)

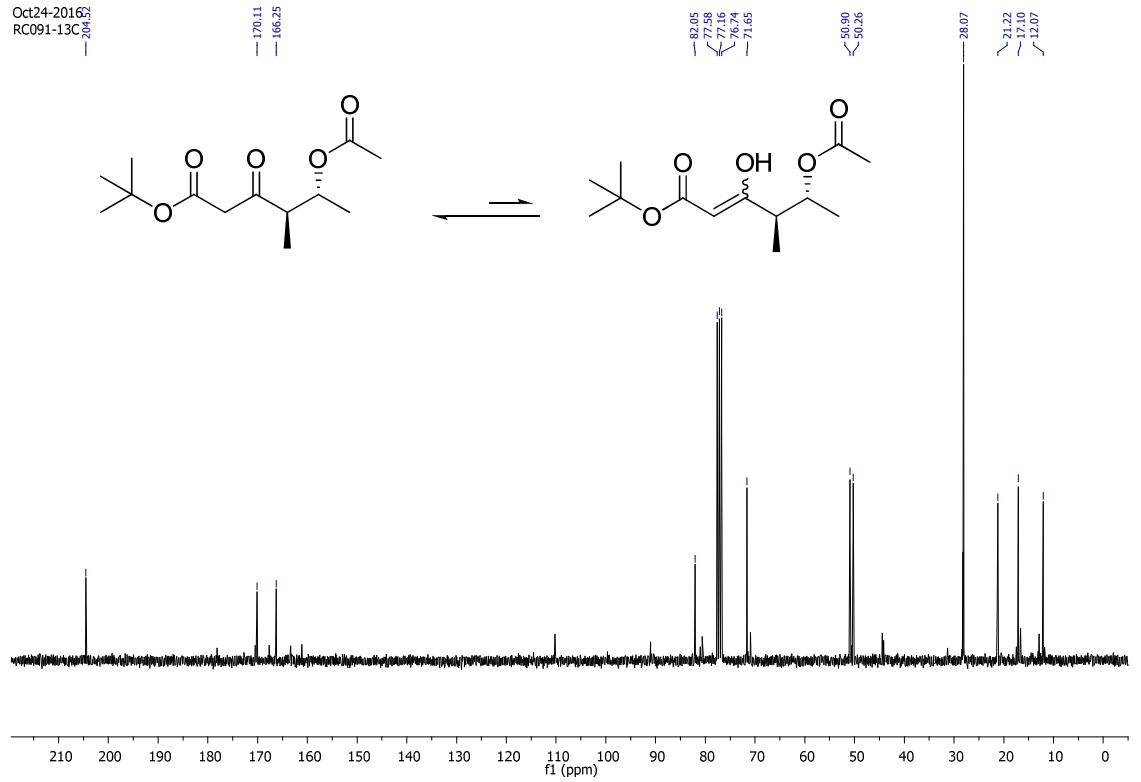

O
OH
MeO
(R,R)-27
7.26
3.93
3.89
3.87
3.86
3.84
3.81
3.69
2.77
2.76
2.49
2.46
2.44
2.42
2.39
1.20
1.18
1.17
1.14
1.00
3.27
0.98
1.12
6.67
f1 (ppm)

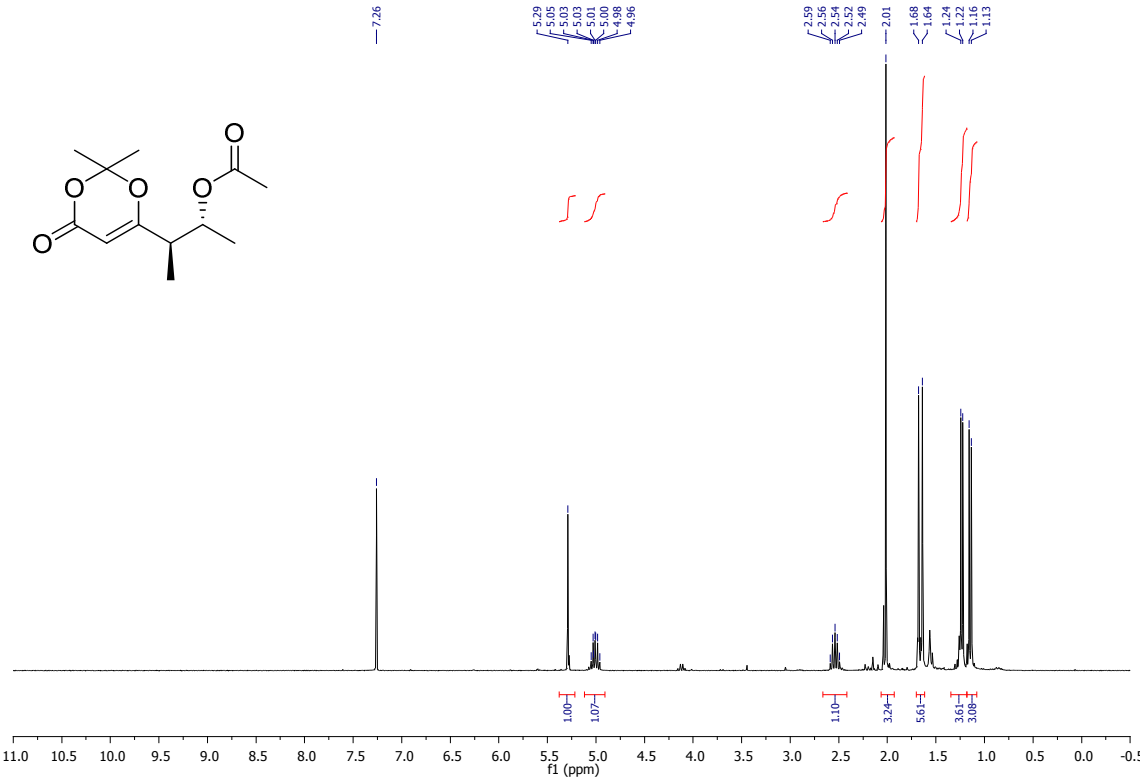

O
OH
MeO
(R,R)-27
176.45
77.58
77.16
76.74
69.49
51.86
47.00
20.82
14.14
f1 (ppm)

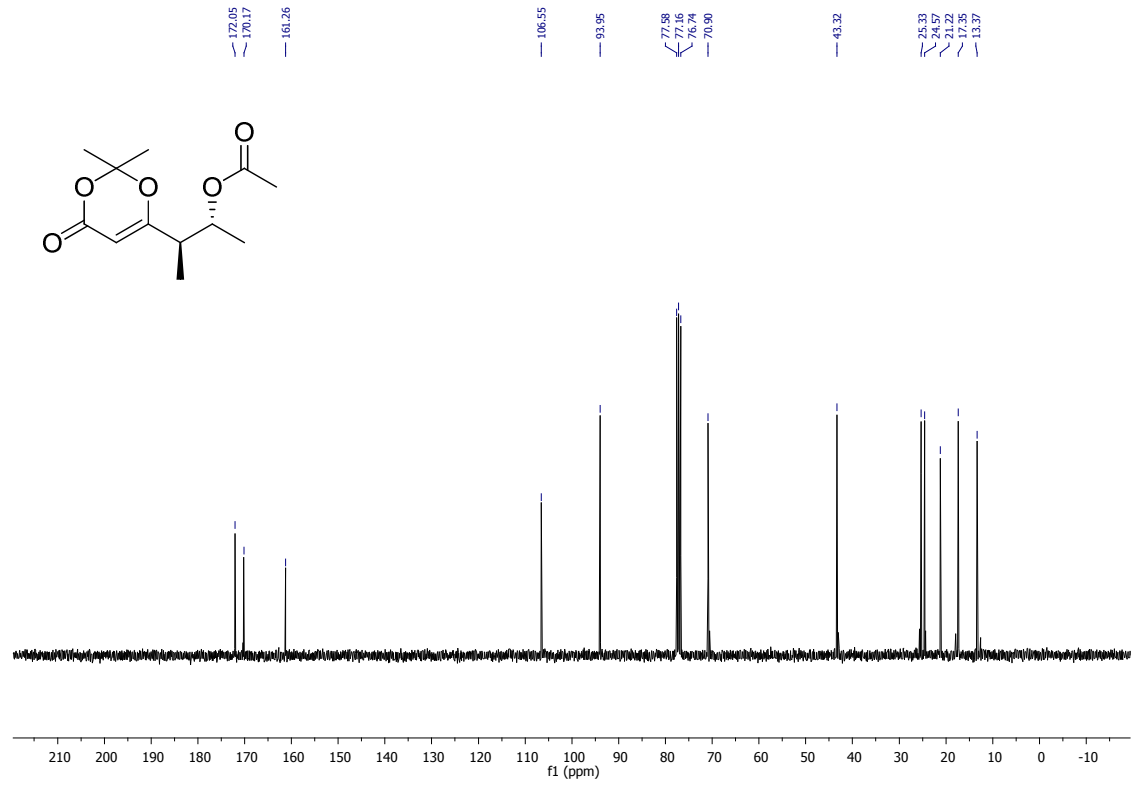

7.26
3.92
3.89
3.87
3.85
3.83
3.48
3.42
3.42
3.37
2.70
2.68
2.65
2.63
2.60
1.45
1.43
1.19
1.17
1.08
1.06
0.87
1.71
1.00
7.97
2.80
2.61
f1 (ppm)

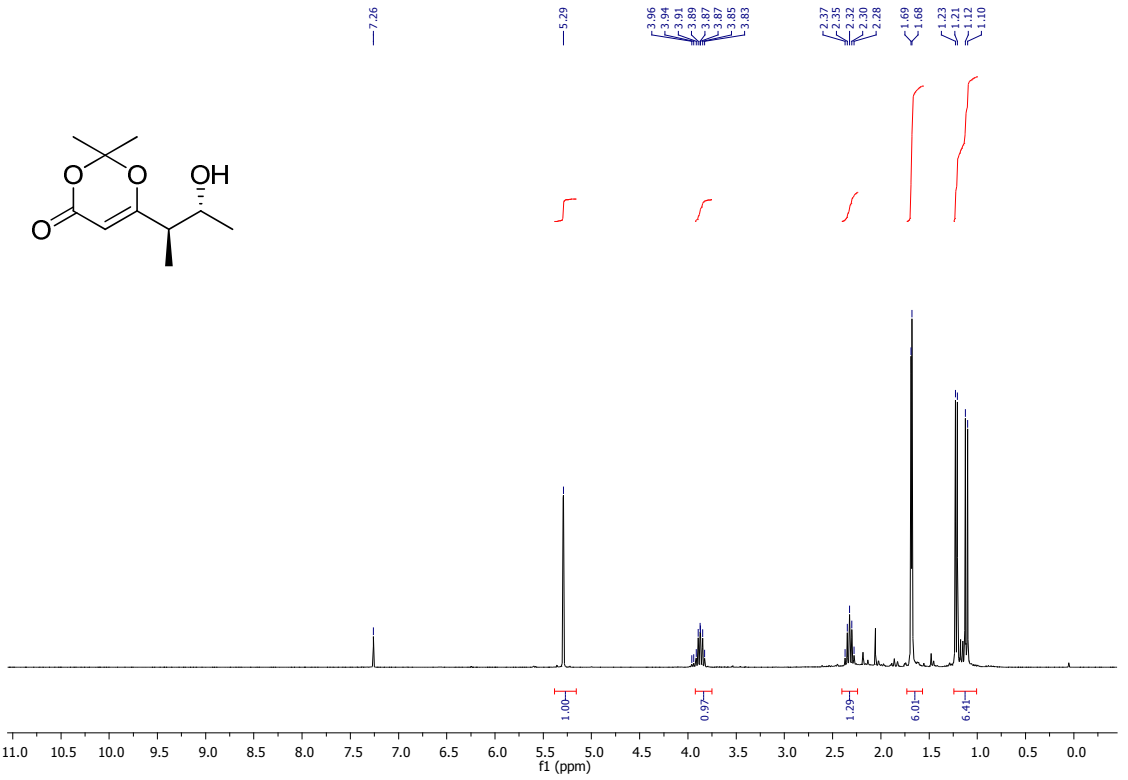

Nov03-2016
RC088-13C
166.67
82.18
77.58
77.16
76.74
69.74
53.66
50.58
28.02
20.99
13.49
f1 (ppm)

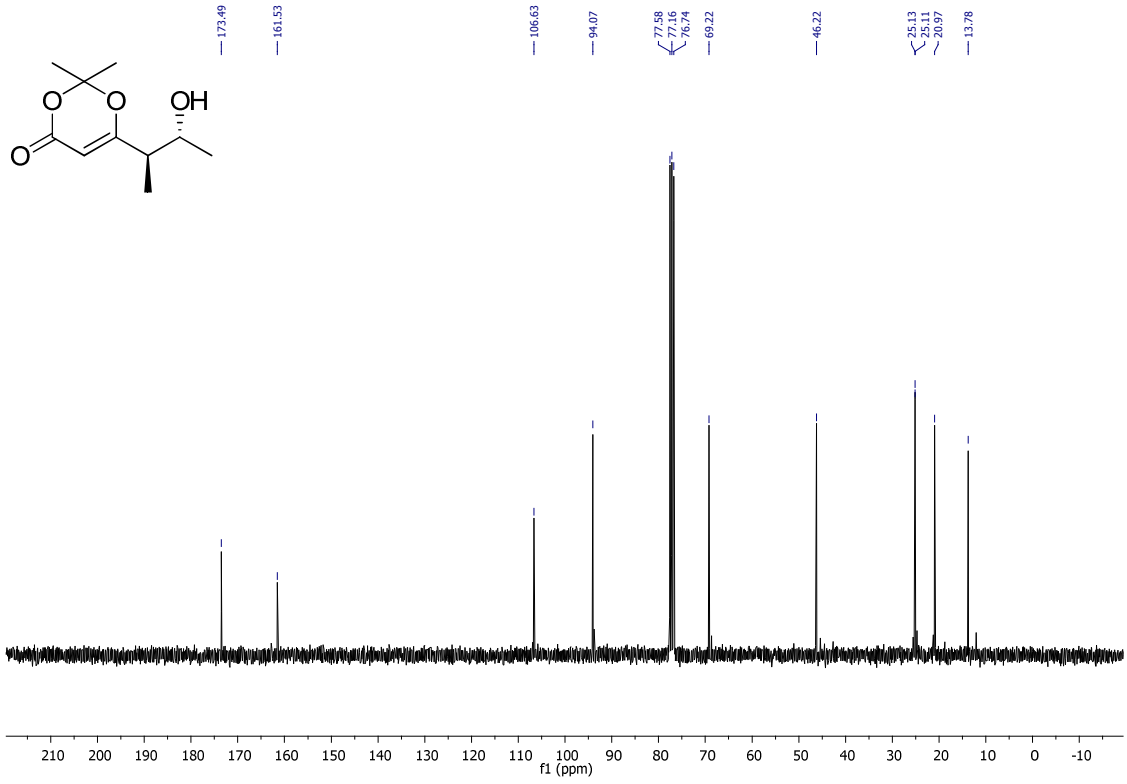

7.26
5.09
5.07
5.05
5.04
5.02
5.00
4.98
4.96
4.94
4.90
3.40
2.95
2.93
2.91
2.90
2.89
2.89
2.88
2.87
1.46
1.44
1.42
1.21
1.19
1.10
1.08
O
O
O
O
O
O
OH
1.00
1.61
0.77
3.34
9.74
7.08
f1 (ppm)

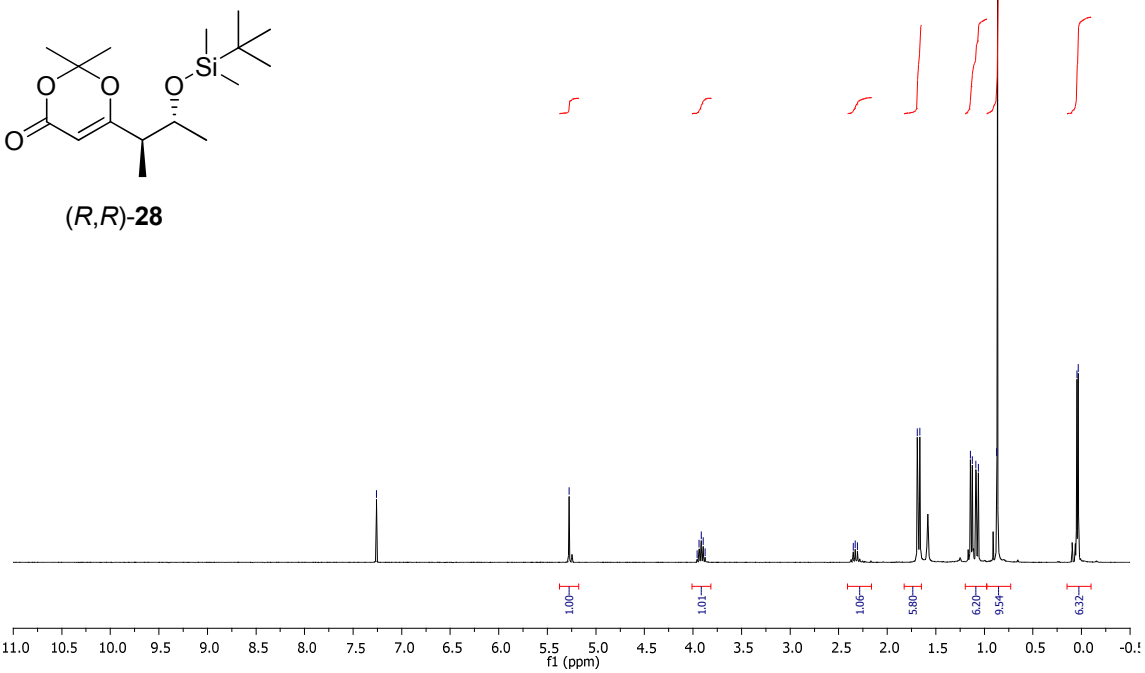

Oct24-2016
RC091-13C
204.52
170.11
166.25
82.05
77.58
77.16
76.74
71.65
50.90
50.26
28.07
21.22
17.10
12.07
O
O
O
O
O
O
OH
f1 (ppm)


7.26
5.29
5.05
5.03
5.03
5.01
5.00
4.98
4.96
2.59
2.56
2.54
2.52
2.49
2.01
1.68
1.64
1.24
1.22
1.16
1.13
1.00
1.07
1.10
3.24
5.61
3.61
3.08
f1 (ppm)

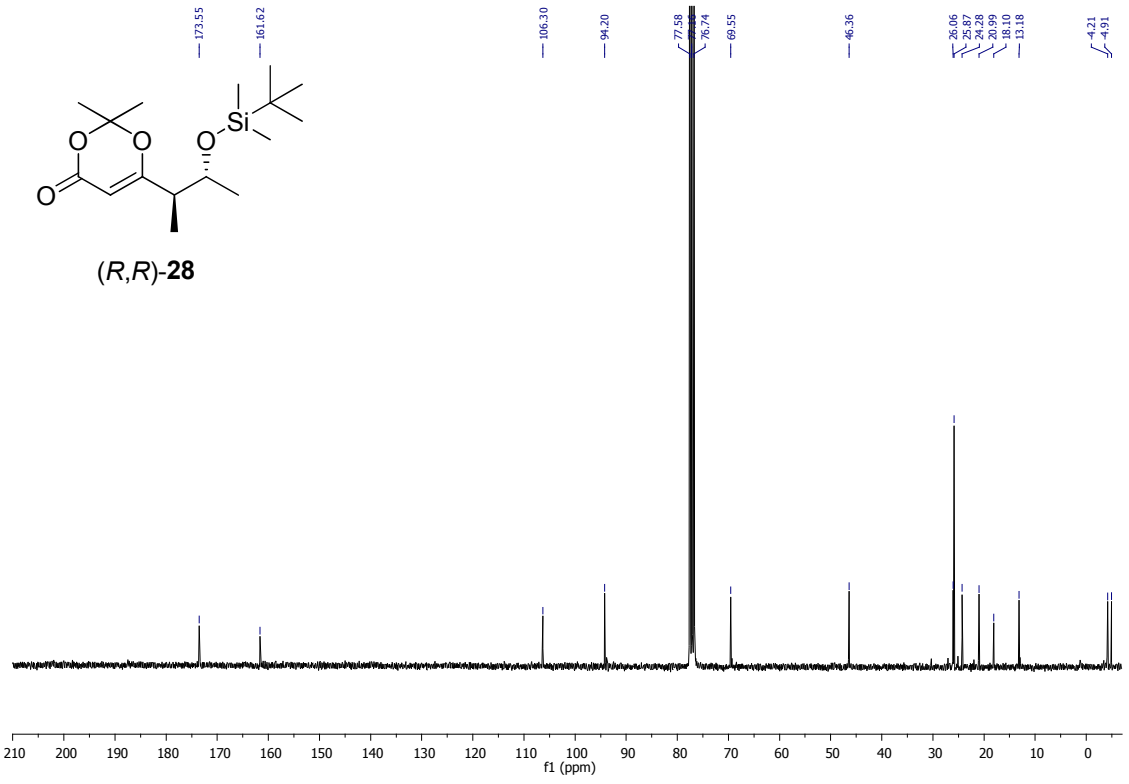

172.05
170.17
161.26
106.55
93.95
77.58
77.16
76.74
70.90
43.32
25.33
24.57
21.22
17.35
13.37
f1 (ppm)


7.26
5.29
3.96
3.94
3.91
3.89
3.87
3.87
3.85
3.83
2.37
2.35
2.32
2.30
2.28
1.69
1.68
1.23
1.21
1.12
1.10
O
O
OH
O
1.00
0.97
1.29
6.01
6.41
11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

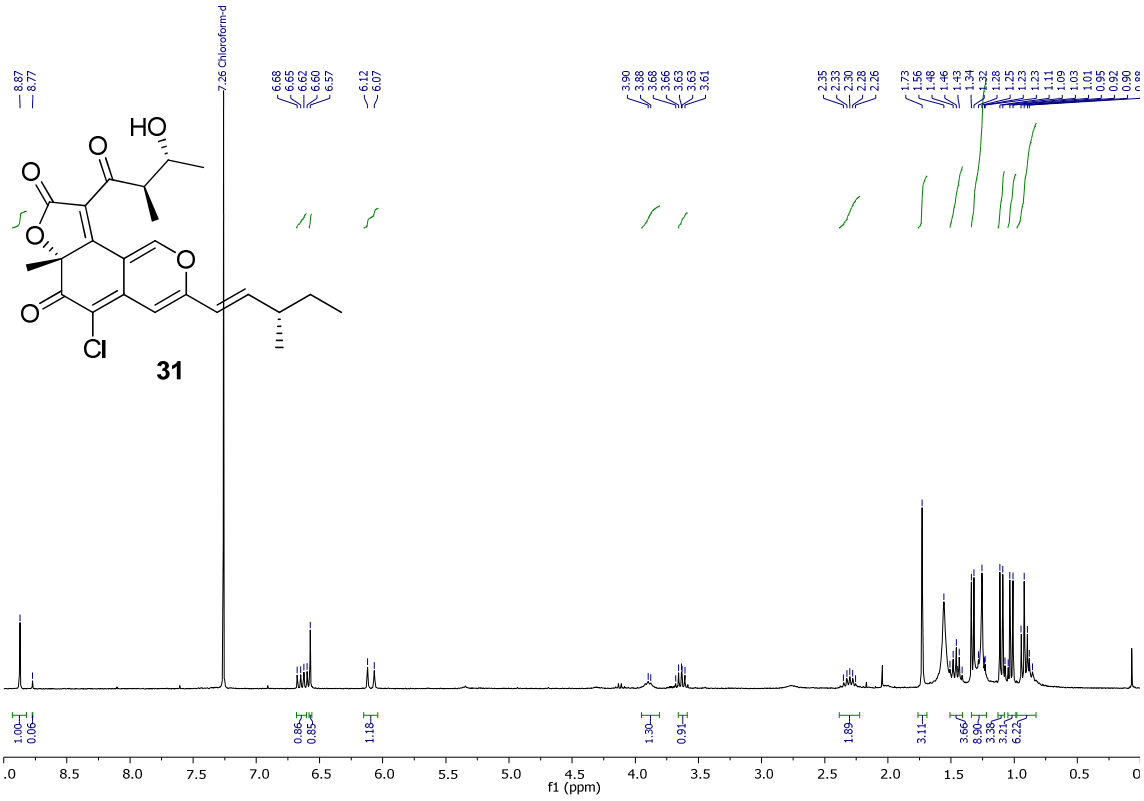

173.49
161.53
106.63
94.07
77.58
77.16
76.74
69.22
46.22
25.13
25.11
20.97
13.78
O
O
OH
O
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

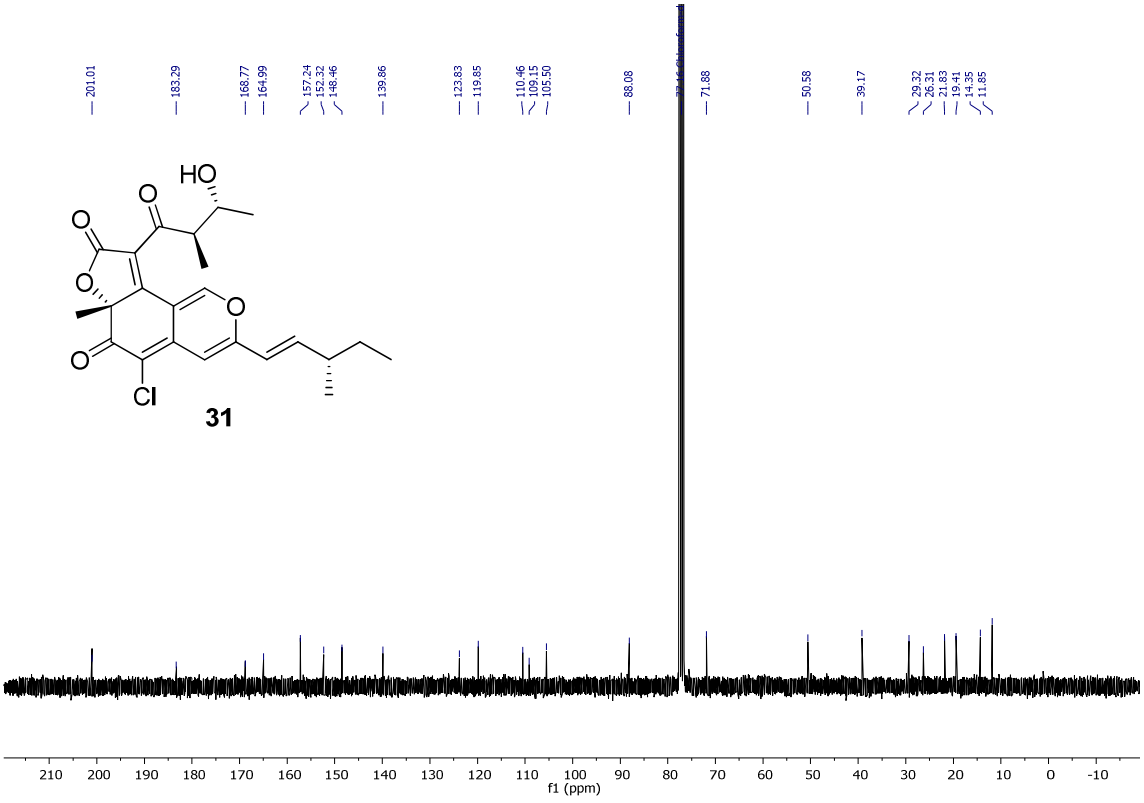

7.26
5.28
3.96
3.94
3.92
3.90
3.88
2.35
2.33
2.31
1.69
1.66
1.14
1.12
1.09
1.06
0.87
0.86
0.05
0.03
1.00
1.01
1.06
5.80
6.20
9.54
6.32
f1 (ppm)

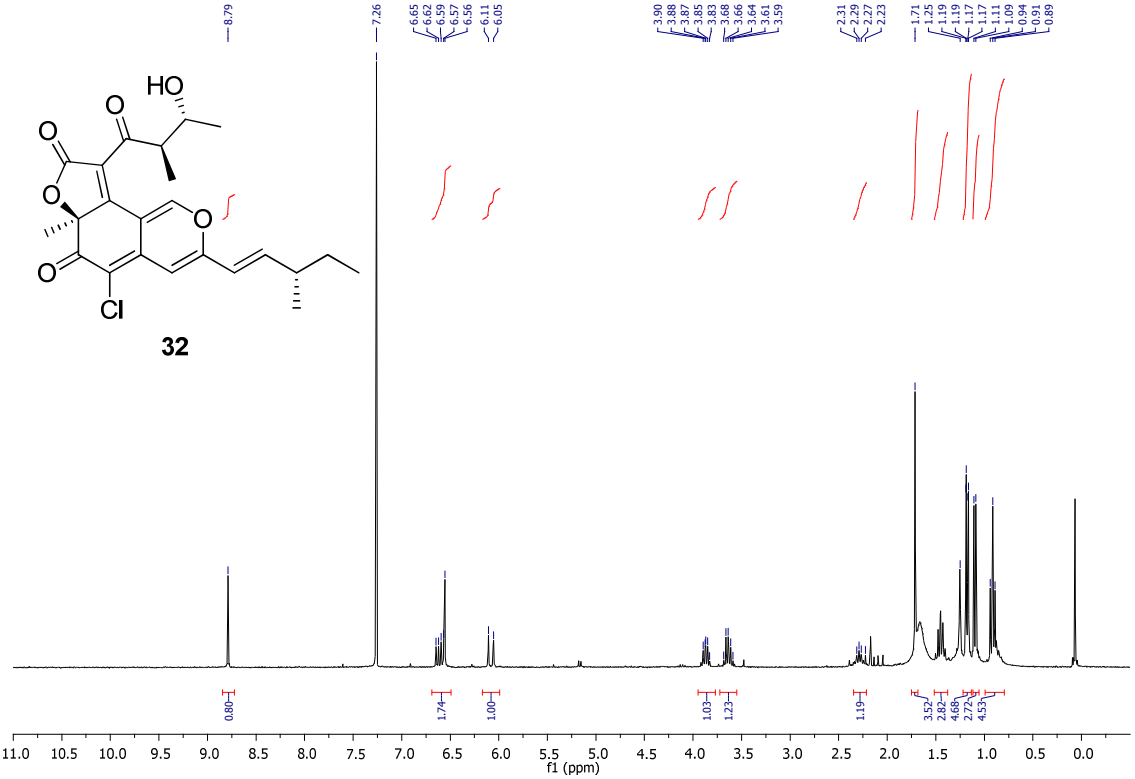
(*R*,*R*)-**28**

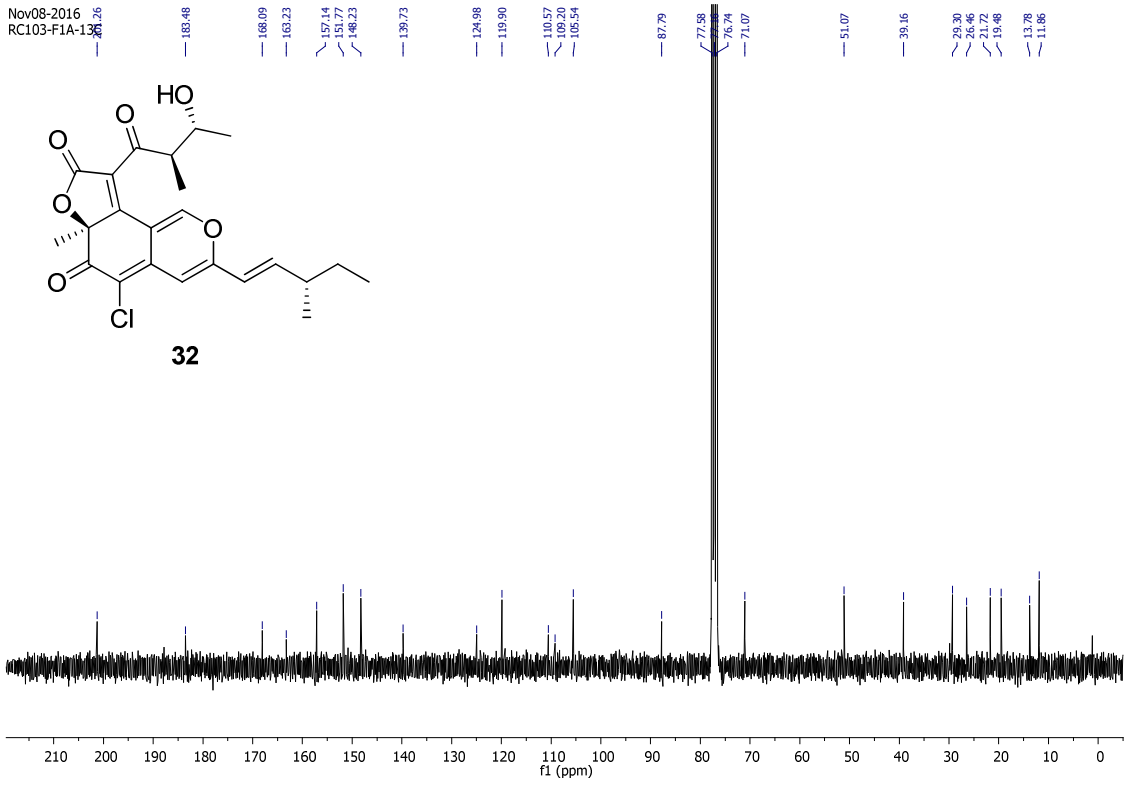

173.55
161.62
106.30
94.20
77.58
77.16
76.74
69.55
46.36
26.06
25.87
24.28
20.99
18.10
13.18
-4.21
-4.91
f1 (ppm)

(*R*,*R*)-**28**


HO
O
O
O
O
O
Cl
31
8.87
8.77
7.26 Chloroform-d
6.68
6.65
6.62
6.60
6.57
6.12
6.07
3.90
3.88
3.66
3.63
3.61
2.35
2.33
2.30
2.28
2.26
1.73
1.56
1.48
1.46
1.43
1.34
1.32
1.28
1.25
1.23
1.23
1.11
1.09
1.03
1.01
0.95
0.92
0.90
1.00
0.06
0.86
0.85
1.18
1.30
0.91
1.89
3.11
3.66
8.90
3.36
2.21
6.24
f1 (ppm)


HO
O
O
O
O
O
Cl
31
201.01
183.29
168.77
164.99
157.24
152.32
148.46
139.86
123.83
119.85
110.46
109.15
105.50
88.08
71.88
50.58
39.17
29.32
26.31
21.83
19.41
14.35
11.85
f1 (ppm)


HO
O
O
O
O
O
Cl
32
8.79
7.26
6.65
6.62
6.59
6.57
6.56
6.11
6.05
3.90
3.88
3.87
3.85
3.83
3.68
3.66
3.64
3.61
3.59
2.31
2.29
2.27
2.23
1.71
1.25
1.19
1.19
1.17
1.17
1.11
1.09
0.94
0.91
0.89
0.80
1.74
1.00
1.03
1.23
1.19
3.52
2.82
4.68
2.72
4.53
f1 (ppm)


Nov08-2016
RC103-F1A-13C
183.48
168.09
163.23
157.14
151.77
148.23
139.73
124.98
119.90
110.57
109.20
105.54
87.79
77.58
76.74
71.07
51.07
39.16
29.30
26.46
21.72
19.48
13.78
11.86
HO
O
O
O
O
O
Cl
32
f1 (ppm)

VI. References

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