Supporting Information for

Reengineering an Azaphilone Biosynthesis Pathway in *Aspergillus nidulans* to create Lipoxygenase Inhibitors

Amber D. Somoza, Kuan-Han Lee, Yi-Ming Chiang, Berl R. Oakley, and Clay C.C. Wang

Table of Contents

General Information

^{1}H and ^{13}C NMR spectra were recorded on a Varian Mercury Plus 400 spectrometer. Chemical shifts are reported in ppm relative to $CDCl_3$ (^{1}H, δ 7.26; ^{13}C, δ 77.0) or acetone-d_6 (^{1}H, δ 2.05; ^{13}C, δ 30.0, 206.0). ^{1}H NMR data is reported as: chemical shift, multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet), coupling constant, and integration. Infrared spectra were recorded on a JASCO FTIR-4100. Infrared frequencies are reported in reciprocal centimeters. High resolution electrospray ionization mass was obtained on an Agilent 6210 time of flight LC-MS. Reactions were monitored by analytical thin-layer chromatography on EMD silica gel-60^{F254} plates. Flash chromatography was performed on EMD silica gel 60, 70-230 mesh. All reagents were used without further purification unless otherwise noted. Reagents were purchased from Sigma-Aldrich, and Alfa Aesar. Diethyl ether (anhydrous) and 1,2-dichloroethane (anhydrous) were used directly from the bottle. Water sensitive reactions were performed

under a nitrogen atmosphere with oven-dried glassware. Kinetic experiments for lipoxygenase inhibition were recorded on a Shimadzu UV-2401PC at 26˚C. Materials for the lipoxygenase assay such as linoleic acid, 15-Lipoxygenase (soybean P_1), and (+)-sclerotiorin were purchased from Cayman Chemicals.

Supplemental Methods

Optimization of Cyclopentanone Inducing Time. Five flasks inoculated with *alcA*(p)-*afoA, afoD*Δ *A. nidulans* containing 1 x 10^6 spores per mL in a liquid lactose minimal medium (lactose 15g, $NaNO_3$ 6g, KCl 0.52g, $MgSO_4 \bullet 7H_2O$ 0.52g, KH_2PO_4 1.52g, H_2O 1 L supplemented with 1 mL of trace elements and adjusted to a pH of 6.5) were incubated at 37°C in a Barnstead/Lab-Line MaxQ 4000 rotary shaker at a speed of 180 rpm. After incubation for the times shown, the chemical inducer, cyclopentanone was added in a single dose to a final concentration of 30 mM. After induction, the strain was cultured for three days under the same conditions.

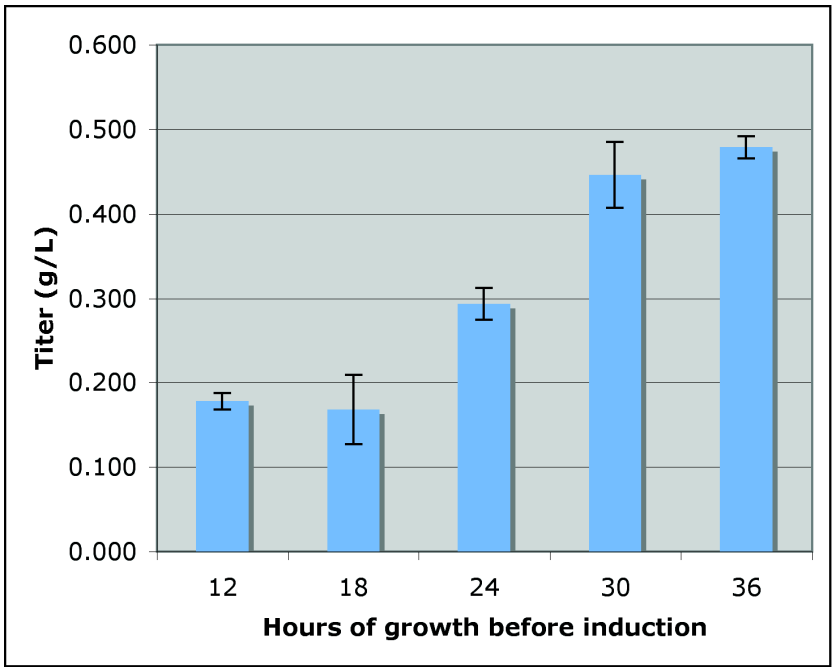
Extraction and isolation. The mycelium was collected by filtration and then immersed in 50 mL of acetone The mycelium-acetone mixture was subjected to stirring for 0.5 h and filtered to isolated the organic solution. The solvent was removed in vacuo to leave a light yellow solid residue analyzed by LC-MS and ^{1}H NMR to be compound **5**.

Optimization of Culture Time. The *A. nidulans* strain, *alcA*(p)-*afoA, afoD*Δ , at a concentration of 1 x 10^6 spores per mL was incubated 37°C in 25 mL of liquid lactose minimal medium (lactose 15g, $NaNO_3$ 6g, KCl 0.52g, $MgSO_4 \bullet 7H_2O$ 0.52g, KH_2PO_4 1.52g, H_2O 1 L supplemented with 1 mL of trace elements and adjusted to a pH of 6.5) at a speed of 180 rpm. For induction, cyclopentanone at a final concentration of 30 mM was introduced to the medium at 30 h of incubation. The strain was cultured for several days, and the mycelia were collected from day 3 to day 7 and analyzed for production of **5**.

Table S1. *A. nidulans* strain used in this study[S1,S2]

strain	genotype
LO2955	*pyrG89; pyroA4, nkuA::argB; riboB2, stcJ::riboB; afoA::AfpyrG-alcA*(p)-*afoA*; *afoD::AfpyroA*

afoA::AfpyrG-alcA(p)-*afoA* is a replacement of the endogenous promoter of *afoA* with the *alcA* promoter and the *a. fumigatus pyrG* gene (*AfpyrG*). *AfpyroA* is the *A. fumigatus pyroA* gene.



Figures S1. Optimization of Induction Time

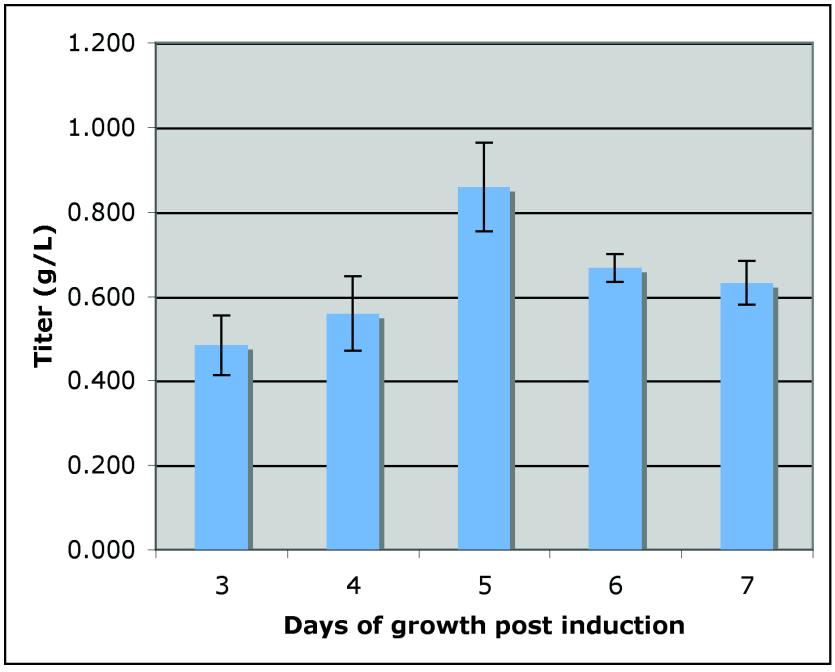
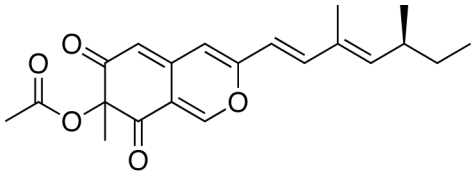


Figure S2. Optimization of Culture Time (post-induction)

Experimental Procedures

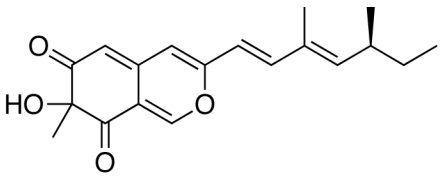
Compound 7



To 2,4-dihydroxy-6-(5,7dimethyl-2-oxo-*trans*-3-*trans*-5-nonadienyl)-3-methylbenzaldehyde **5** (151 mg, 0.48 mmol) in 60 mL of acetic acid at room temperature was added in one portion p-TsOH·H_2O (940 mg, 4.94 mmol). The reaction was warmed in an oil bath to 100˚C and stirred for 2 hours. Then the reaction was cooled to room temperature and purged with nitrogen for 1.5 hours. It was further cooled to 18˚C and then treated with lead tetraacetate (276 mg, 0.621 mmol) in three portions over a 15-minute period. The solution stirred for 1 hour, and was quenched with 200 mL of ice water. The reaction mixture was extracted with dichloromethane 3x, and the combined organic layers were dried over magnesium sulfate, filtered and concentrated under reduced pressure. The crude product was purified by flash chromatography on silica gel (15% EtOAc/DCM) to afford 50.3 mg of compound 4. Isolated yield: 30%

^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.91 (s, 1H), 6.98 (d, J = 16 Hz, 1H), 6.17 (s, 1H), 5.96 (d, J = 15.6 Hz, 1H), 5.65 (d, J = 9.6 Hz, 1H), 5.57 (d, J = 1.2 Hz, 1H), 2.47 (m, 1H), 2.18 (s, 3H), 1.82 (d, J = 1.2 Hz, 3H), 1.55 (s, 3H), 1.43 (m, 1H), 1.30 (m, 1H), 1.01 (d, J = 5.6 Hz, 3H), 0.86 (t, J = 7.2 Hz, 3H); ^{13}C NMR ($CDCl_3$, 400 MHz) δ 193.3, 192.5, 170.1, 156.5, 153.5, 147.9, 142.8, 141.6, 131.8, 115.6, 114.8, 109.2, 107.3, 84.3, 35.0, 30.1, 22.4, 20.25 20.18, 12.3, 11.9; IR [acetone solution, ν_{max} cm^{-1}] 3079, 2965, 2933, 2877, 1746, 1717, 1639, 1247; HRMS (EIS) *m/z* calculated for $C_{21}H_{25}O_5$ 357.1697, experimental 357.1696 $[M+H]^+$

Compound 11

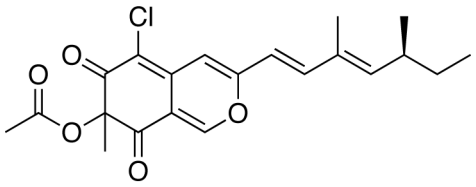


To 2,4-dihydroxy-6-(5,7-dimethyl-2-oxo-*trans*-3-*trans*-5-nonadienyl)-3-methylbenzaldehyde **5** (200 mg, 0.635 mmol) in 2.5 mL of acetic acid at room temperature was added p-TsOH (425 mg, 2.47 mmol). The suspension stirred for 1.5 hours under nitrogen leaving an orange precipitate, 2-benzopyrilium salt (**6**). The acetic acid was removed and the precipitate redissolved in 1,2-dichloroethane (5mL) and then treated with freshly prepared 2-iodoxybenzoic acid (IBX)[S3] (182 mg, 0.65 mmol), which was followed by the addition of tert-n-butyl ammonium iodide (23 mg, 0.062 mmol). The solution stirred for six hour and quenched with saturated NaS_2O_3 and ethyl acetate. The mixture was extracted with ethyl acetate 4x, and the combined organic layers were washed with saturated $NaHCO_3$, water and brine. It was subsequently dried with anhydrous sodium sulfate, filtered and concentrated under reduced pressure. The crude product was purified by flash chromatography on silica gel (60% EtOAc/n-hexanes) to afford 79.4 mg of compound **11**. Isolated yield: 40%

^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.91 (s, 1H), 7.01 (d, J = 15.6 Hz, 1H), 6.19 (s, 1H), 5.97 (d, J = 16 Hz, 1H), 5.67 (d, J = 10 Hz, 1H), 5.57 (d, J = 0.8 Hz, 1H), 3.94 (br 1, 1H), 2.46 (m, 1H), 1.82 (d, J = 1.2 Hz, 3H), 1.56 (s, 3H), 1.43 (m, 1H), 1.30 (m, 1H), 1.01 (d, J = 6.8 Hz, 3H), 0.85 (t, J = 7.6 Hz, 3H); ^{13}C NMR ($CDCl_3$, 400 MHz) δ 196.0, 195.7, 156.9,

152.5, 148.3, 144.2, 142.1, 131.8, 117.9, 115.5, 108.8, 105.5, 83.3, 35.1, 30.1, 28.7, 20.2, 12.3, 11.9; IR [acetone solution, ν_{max} cm^{-1}] 3431, 2965, 2930, 2874, 1715, 1624, 1236; HRMS (ESI) *m/z* calculated for $C_{19}H_{23}O_4$ 315.1591, experimental 315.1595 $[M+H]^+$

Compound 8

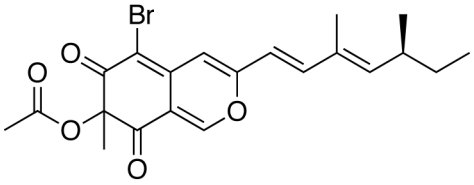


To a stirring solution of compound 7 (28.4 mg, 0.078 mmol) in acetic acid (0.93 mL) was added N-chlorosuccinimide (14 mg, 0.105 mmol) at room temperature. The solution stirred for 3 hours and then quenched with saturated $Na_2S_2O_3$ aqueous solution and diluted with ethyl acetate. The resulting mixture was extracted with ethyl acetate and the combined organic layers washed with $NaHCO_3$, water, and brine. It was dried over anhydrous sodium sulfate, filtered and concentrated under reduced pressure. The crude product was purified by flash chromatography on silica gel (25 % EtOAc/n-hexanes) to afford 16 mg of compound 8. Isolated yield: 52%

The diastereomers of **8** were separated by analytical chiral HPLC (Diacel CHIRALCEL ® OD column 0.46 x 25 cm, 10% EtOH-hexanes, 1.0 mL/min, 360 nm, t_R = 7.5 min 7-*epi*-sclerotiorin, 9.5 min (+)-sclerotiorin compared with commercial available (+)-sclerotiorin.

Compound 8 (diastereomeric mixture): ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.93 (s, 1H), 7.06 (d, J = 15.6 Hz, 1H), 6.64 (s, 1H), 6.08 (d, J = 15.6 Hz, 1H), 5.70 (d, J = 9.6 Hz, 1H), 2.47 (m, 1H), 2.17 (s, 3H), 1.85 (d, J = 0.8 Hz, 3H), 1.57 (s, 3H), 1.42 (m, 1H), 1.32 (m, 1H), 1.01 (d, J = 6.8 Hz, 3H), 0.86 (t, J = 0.8 Hz, 3H); ^{13}C NMR ($CDCl_3$, 400 MHz) δ 191.8 185.9, 170.1, 158.1, 152.6, 148.8, 142.8, 138.6, 131.9, 115.6, 114.5, 110.8, 106.4, 84.5, 35.1, 30.0, 22.5, 20.2, 20.1, 12.3, 11.9; IR [acetone solution, ν_{max} cm^{-1}] 2961, 2927, 2872, 1740, 1719, 1634, 1527, 1246, 1131, 1089; HRMS (ESI) *m/z* calculated for $C_{21}H_{24}ClO_5$ 391.1307, experimental 391.131 $[M+H]^+$

Compound 9

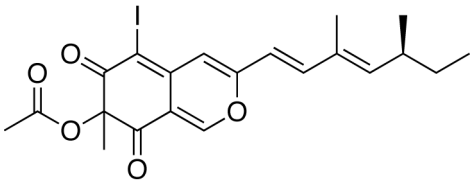


To a stirring solution of compound 7 (13.9 mg, 0.39 mmol) in acetonitrile (0.650 mL) was added N-bromosuccinimide (10 mg, 0.056 mmol) at room temperature. The solution stirred for 4 hours after which it was quenched with water and extracted with ethyl acetate. The organic layers were combined, washed with brine, dried over anhydrous sodium sulfate, filtered and concentrated under reduced pressure. The crude product was purified by flash chromatography on silica gel (20% EtOAc/n-hexanes) to afford 68.9 mg of compound 9. Isolated yield: 41%

^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.91 (s, 1H), 7.07 (d, J = 15.6 Hz, 1H), 6.68 (s, 1H), 6.08 (d, J = 15.6 Hz), 5.71 (d, J = 10 Hz, 1H), 2.48 (m, 1H), 2.17 (s, 3H), 1.85 (d, J = 0.8 Hz, 3H), 1.57 (s, 3H), 1.42 (m, 1H), 1.32 (m, 1H), 1.03 (d, J = 6.8 Hz, 3H), 0.86 (t, J = 7.6 Hz, 3H); ^{13}C NMR ($CDCl_3$, 400 MHz) δ 191.9, 186.0 170.0, 158.4, 152.7, 148.9, 142.9, 140.9, 132.0, 115.6, 115.2, 109.1, 103.1, 84.4, 35.1, 30.0, 22.6, 20.2, 20.1, 12.3, 11.9; IR

[acetone solution, ν_{max} cm^{-1}] 2962, 2928, 1735, 1718, 1633, 1520, 1245, 1126; HRMS (ESI) *m/z* calculated for $C_{21}H_{24}BrO_5$ 435.0802, experimental 435.0807 $[M+H]^+$

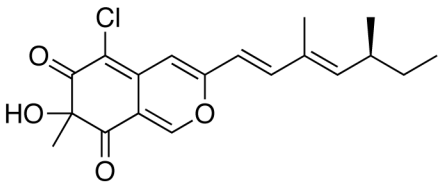
Compound 10



To a stirring solution of compound 7 (19.1 mg, 0.054 mmol) in acetonitrile (1.3 mL) was added N- iodosuccinimide (14 mg, 0.059 mmol) at room temperature. The solution stirred for 30 minutes and quenched with water. The mixture was extracted with ethyl acetate; combined organic layers were washed with brine, dried over anhydrous sodium sulfate, and concentrated under reduced pressure. Crude extract was purified by flash chromatography on silica gel (20% EtOAc/n-hexanes) to afford 7.2 mg of compound 10. Isolated yield: 28%

^1H NMR ($CDCl_3$, 400 MHz) δ 7.81 (s, 1H), 7.07 (d, J = 15.6 Hz, 1H), 6.67 (s, 1H), 6.10 (d, J = 15.6 Hz, 1H), 5.71 (d, J = 10 Hz, 1H), 2.49 (m, 1H), 2.17 (s, 3H), 1.86 (d, J = 1.2 Hz, 3H), 1.56 (s, 3H), 1.42 (m, 1H), 1.31 (m, 1H), 1.01 (d, J = 6.8 Hz, 3H), 0.86 (t, J = 7.6 Hz, 3H); ^{13}C NMR ($CDCl_3$, 400 MHz) δ 192.4, 187.5, 170.0, 158.8, 152.7, 149.9, 144.9, 142.9, 132.0, 115.9, 115.6, 114.2, 83.5, 83.4, 35.1, 30.0, 22.7, 20.2, 20.1, 12.4, 11.9; IR [acetone solution, ν_{max} cm^{-1}] 2961, 2927, 2872, 1739, 1718, 1630, 1509, 1245; HRMS (ESI) *m/z* calculated for $C_{21}H_{24}IO_5$ 483.0663, experimental 483.0667 $[M+H]^+$

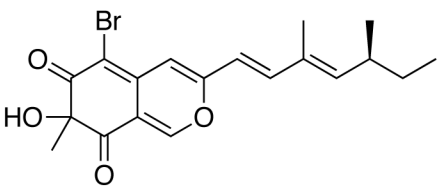
Compound 12



To a stirring solution of compound 11 (59.3 mg, 0.188 mmol) in 3.0 mL of acetonitrile at room temperature was added N-chlorosuccinimide (27 mg, 0.202 mmol). The solution stirred for 48 hours and quenched with water then extracted with ethyl acetate. The combined organic layers were washed with brine, dried over anhydrous sodium sulfate, filtered and concentrated under reduced pressure. Crude extract was purified by flash chromatography on silica gel (45% EtOAc/n-hexanes) to afford 29.3 mg of compound 12. Isolated yield: 45%

^1H NMR ($CDCl_3$, 400 MHz) δ 7.94 (s, 1H), 7.09 (d, J = 15.6 Hz, 1H), 6.62 (s, 1H), 6.08 (d, J = 15.6 Hz, 1H), 5.72 (d, J = 9.6 Hz, 1H), 3.90 (br s, 1H), 2.48 (m, 1H), 1.85 (d, J = 1.2 Hz, 3H), 1.59 (s, 3H), 1.42 (m, 1H), 1.32 (m, 1H), 1.01 (d, J = 6.4 Hz, 3H), 0.86 (t, J = 7.6 Hz, 3H); ^{13}C NMR ($CDCl_3$, 400 MHz) δ 194.0, 189.6, 158.6, 151.7, 149.4, 143.4, 140.0, 132.0, 115.6, 115.1, 108.9, 105.9, 83.9, 35.2, 30.1, 28.8, 20.2, 12.4, 12.0; IR [acetone solution, ν_{max} cm^{-1}] 3444, 3085, 3065, 3039, 2871, 1724, 1635, 1527, 1178, 670; HRMS (ESI) *m/z* calculated for $C_{19}H_{22}ClO_4$ 349.1201, experimental 349.1205 $[M+H]^+$

Compound 13

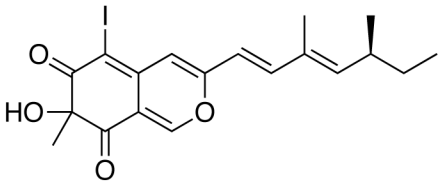


To a stirring solution of compound 11 (122.09 mg, 0.39 mmol) in acetonitrile (6.5 mL) was added N-bromosuccinimide (77.0 mg, 0.43 mmol) at room temperature. The solution stirred for 45 minutes and was then quenched with water. The mixture was extracted with ethyl acetate and the combined organic layers were dried over anhydrous sodium sulfate, filtered and concentrated under

reduced pressure. The crude product was purified by flash chromatography on silica gel (20% EtOAc/n-hexanes) to afford 71 mg of compound 13. Isolated yield: 46%

^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.92 (s, 1H), 7.11 (d, J = 15.6 Hz, 1H), 6.66 (s, 1H), 6.10 (d, J = 15.6 Hz, 1H), 5.74 (d, J = 9.6 Hz, 1H), 3.92 (s, 1H), 2.49 (m, 1H), 1.86 (d, J = 1.2 Hz, 3H), 1.56 (s, 3H), 1.43 (m, 1H), 1.32 (m, 1H), 1.02 (d, J = 6.8 Hz, 3H), 0.87 (t, J = 7.6 Hz, 3H); ^{13}C NMR ($CDCl_3$, 400 MHz) δ 194.1, 190.0, 158.9, 151.7, 149.4, 143.5, 142.2, 132.0, 115.9, 115.6, 108.6, 100.5, 83.9, 35.2, 30.0, 28.8, 20.2, 12.4, 12.0; IR [acetone solution, ν_{max} cm^{-1}] 3451, 3081, 2964, 2931, 2875, 1719, 1633, 1518, 1172, 1144; HRMS (ESI) *m/z* calculated for $C_{19}H_{22}BrO_4$ 393.0696, experimental 393.0700 $[M+H]^+$

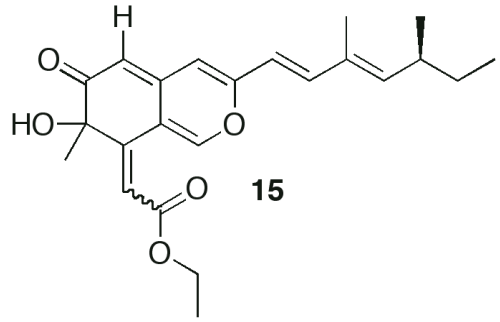
Compound 14



To a stirring solution of compound 11 (33.2 mg, 0.106 mmol) in acetonitrile (2.1 mL) was added N-iodosuccinimide (28 mg, 0.124 mmol) at room temperature. The solution stirred for 1 hour and quenched with water. The mixture was extracted with ethyl acetate; organic layers were combined and washed with brine, dried over anhydrous sodium sulfate and concentrated under reduced pressure. The crude product was purified by flash chromatography on silica gel (35% EtOAc/n-hexanes) to afford 23.7 mg of compound 14. Isolated yield: 51%

^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.81 (s, 1H), 7.10 (d, J = 16 Hz, 1H), 6.64 (s, 1H), 6.10 (d, J = 15.6 Hz, 1H), 5.74 (d, J = 9.6 Hz, 1H), 3.94 (s, 1H), 2.49 (m, 1H), 1.86 (d, J = 1.2 Hz, 3H), 1.57 (s, 3H), 1.42 (m, 1H), 1.32 (m, 1H), 1.02 (d, J = 6.8 Hz, 3H), 0.86 (t, J = 7.6 Hz, 3H); ^{13}C NMR ($CDCl_3$, 400 MHz) δ 194.4, 191.6, 159.3, 151. 6, 149.4, 146.2, 143.5, 132.0, 116.7, 115.4, 113.5, 83.2, 79.3, 35.2, 30.0, 28.9, 20.2, 12.4, 11.9; IR [acetone solution, ν_{max} cm^{-1}] 3458, 3070, 2963, 2928, 2873, 1721, 1633, 1504, 1166; HRMS (ESI) *m/z* calculated for $C_{19}H_{22}IO_4$ 441.0557, experimental 441.056 $[M+H]^+$

Compound 15

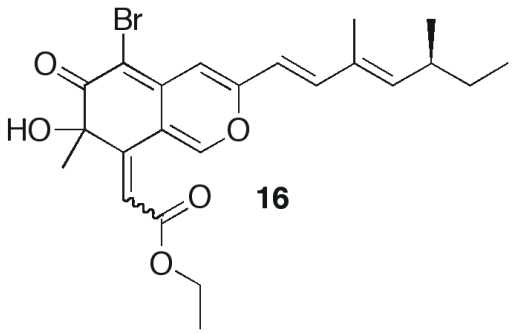


To a stirring solution of compound 11 (55 mg, 0.175 mmol) in anhydrous diethyl ether (6 mL) was added Wittig reagent, Ph_3=$CHCO_2Et$, (68 mg, 0.193 mmol). The solution stirred for 7 hours at room temperature. The solvent was removed under reduced pressure and crude extract purified by flash chromatography on silica gel (15% acetone/n-hexanes) to afford 11 mg of compound 15. Isolated yield: 17%

^{1}H NMR (acetone-d_6, 400 MHz) δ 8.13 (s, 1H), 7.07 (d, J = 16 Hz, 1H), 6.47 (s, 1H), 6.27 (d, J = 15.6 Hz, 1H), 5.71 (d, J = 9.6 Hz, 1H), 5.38 (s, 1H), 4.6 (s, 1H), 4.18 (q, J = 7.2 Hz, 2H), 2.53 (m, 1H), 1.87 (d, J = 1.2 Hz, 3H), 1.49 (m, 1H), 1.37 (s, 3H), 1.33 (m, 1H), 1.25 (t, J = 7.2 Hz, 3H), 1.01 (d, J = 6.4 Hz, 3H), 0.86 (t, J = 7.6 Hz, 3H); ^{13}C NMR (acetone-d_6, 400 MHz) δ 197.1, 166.5, 157.0, 150.8, 147.2, 147.1, 141.4, 133.4, 117.9, 115.1, 110.0, 109.3, 104.6, 77.7, 61.0, 35.7, 31.0, 29.2, 20.8, 14.6, 12.7, 12.4; IR [acetone

solution, ν_{max} cm^{-1}] 3441, 2967, 2955, 2877, 1716, 1623, 1543, 1179; HRMS (ESI) *m/z* calculated for $C_{23}H_{29}O_5$ 385.201, experimental 385.2014 $[M+H]^+$

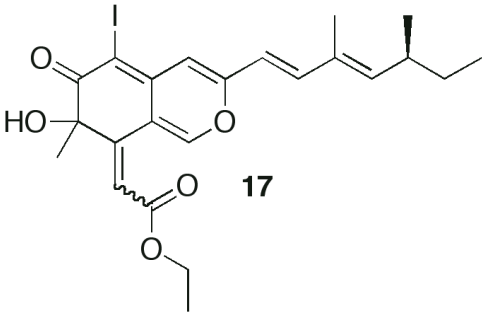
Compound 16



To a stirring solution of compound 13 (20.5 mg, 0.052 mmol) in anhydrous diethyl ether (2.6 mL) was added Ph_3=$CHCO_2Et$, (23 mg, 0.066 mmol). The solution stirred for 6 hours at room temperature. The solvent was removed under reduced pressure and crude extract purified by flash chromatography on silica gel (15% acetone/n-hexanes) to afford 16.3 mg of compound 16. Isolated yield: 68%

^{1}H NMR (acetone-d_6, 400 MHz) δ 8.12 (s, 1H), 7.18 (d, J = 16 Hz, 1H), 6.78 (s, 1H), 6.51 (d, J = 16 Hz, 1H), 6.50 (s, 1H), 5.78 (d, J = 9.2 Hz, 1H), 4.86 (s, 1H), 4.18 (q, J = 7.2 Hz, 2H), 2.55 (m, 1H), 1.91 (d, J = 1.2 Hz, 3H), 1.45 (m, 1H), 1.40 (s, 3H), 1.33 (m, 1H), 1.24 (t, J = 7.2 Hz, 3H), 1.02 (d, J = 6.8 Hz, 3H), 0.86 (t, J = 7.2 Hz, 3H); ^{13}C NMR (acetone-d_6, 400 MHz) δ 190.9, 166.3, 159.4, 150.0, 148.3, 145.7, 144.9, 142.9, 133.6, 118.0, 116.1, 109.4, 108.6, 99.2, 78.6, 61.2, 35.9, 30.9, 28.8, 20.7, 14.6, 12.7, 12.4; IR [acetone solution, ν_{max} cm^{-1}] 3464, 2961, 2933, 2874, 1717, 1627, 1554, 1515, 1174, 669; HRMS (ESI) *m/z* calculated for $C_{23}H_{28}BrO_5$ 463.1115, experimental 463.1118 $[M+H]^+$

Compound 17

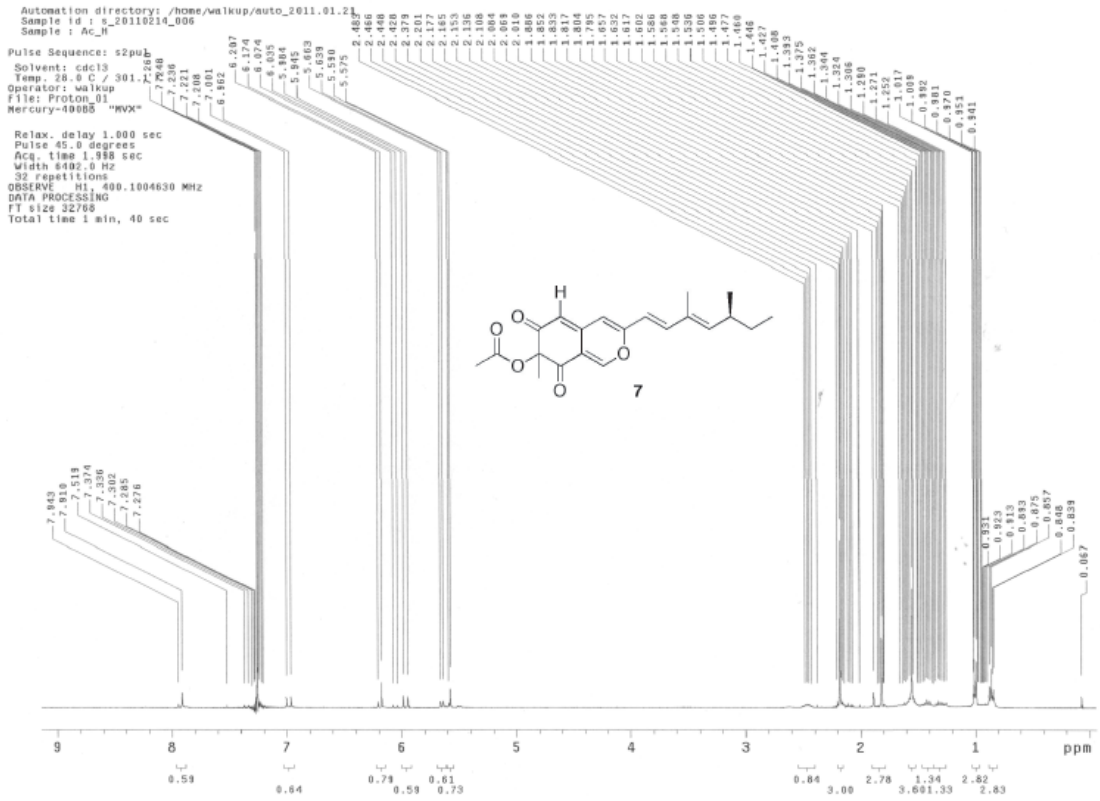


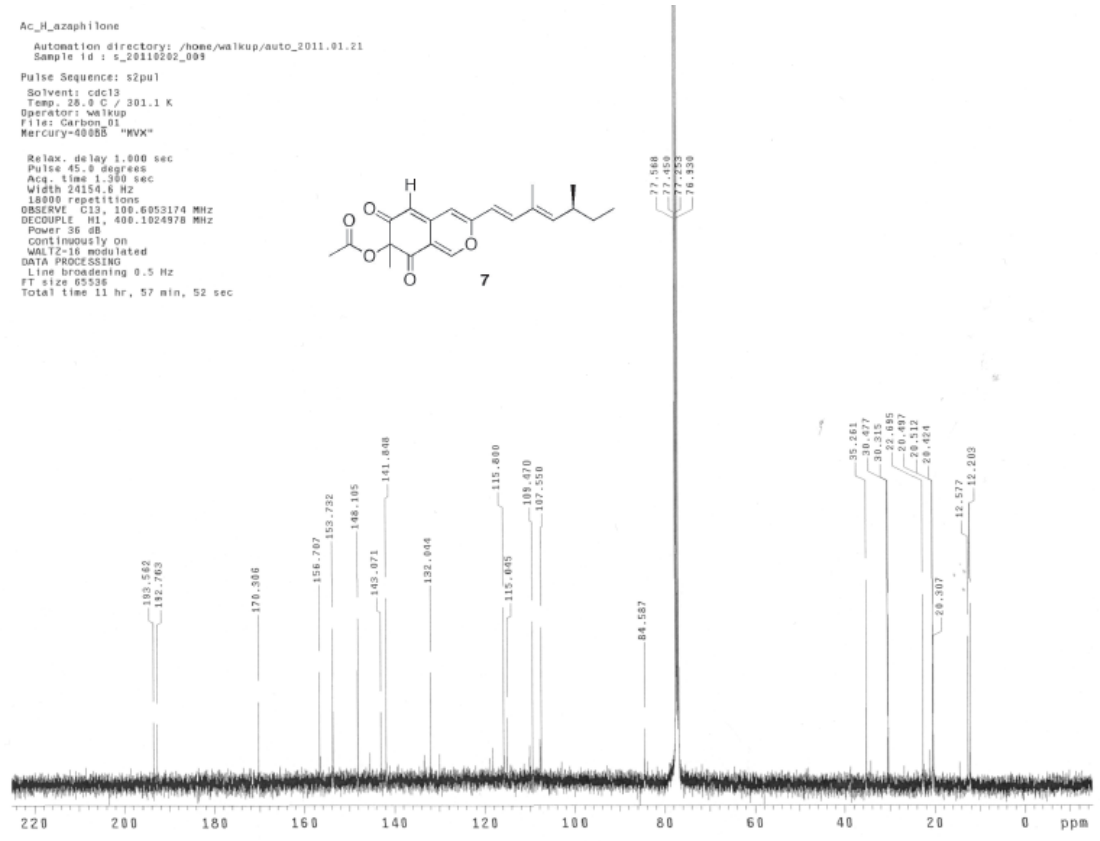
To a stirring solution of compound 14 (48 mg, 0.109 mmol) in diethyl ether (5.0 mL) was added Ph_3=$CHCO_2Et$, (46 mg, 0.132 mmol). The solution stirred for 6 hours at room temperature. The solvent was removed under reduced pressure and crude extract purified by flash chromatography on silica gel (15% acetone/n-hexanes) to afford 31.8 mg of compound 17. Isolated yield: 57%

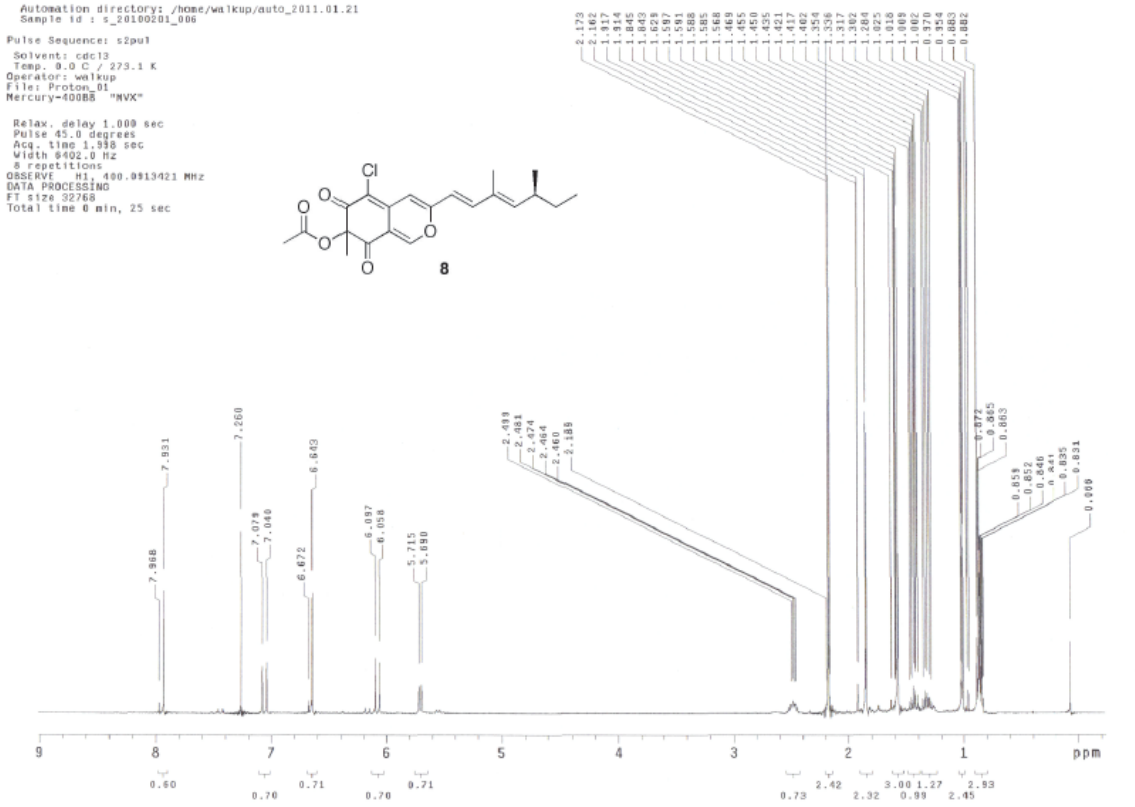
^{1}H NMR (acetone-d_6, 400 MHz) δ 8.01 (s, 1H), 7.18 (d, J = 16 HZ, 1H), 6.76 (s, 1H), 6.53 (d, J = 16 Hz, 1H), 6.50 (s, 1H), 5.78 (d, J = 9.6 Hz, 1H), 4.82 (s, 1H), 4.18 (q, J = 7.2 Hz, 2H), 2.55 (m, 1H), 1.97 (d, J = 1.2 Hz, 3H), 1.44 (m, 1H), 1.40 (s, 3H), 1.32 (m, 1H), 1.24 (t, J = 7.2 Hz, 3H), 1.02 (d, J = 4.8 Hz, 3H), 0.87 (t, J = 7.6 Hz, 3H); ^{13}C NMR (acetone-d_6, 400 MHz) δ 192.8, 166.3, 159.7, 149.9, 149.0, 148.3, 142.9, 133.6, 118.0, 115.9, 114.3, 113.6, 105.8, 78.0, 61.2, 35.9, 30.9, 28.9, 20.7, 14.6, 12.7, 12.4; IR [acetone solution, ν_{max} cm^{-1}] 3456, 2965, 2930, 2873, 1717, 1624, 1555, 1502, 1176, 530; HRMS (ESI) *m/z* calculated for $C_{23}H_{28}IO_5$ 511.0976, experimental 511.0977 $[M+H]^+$

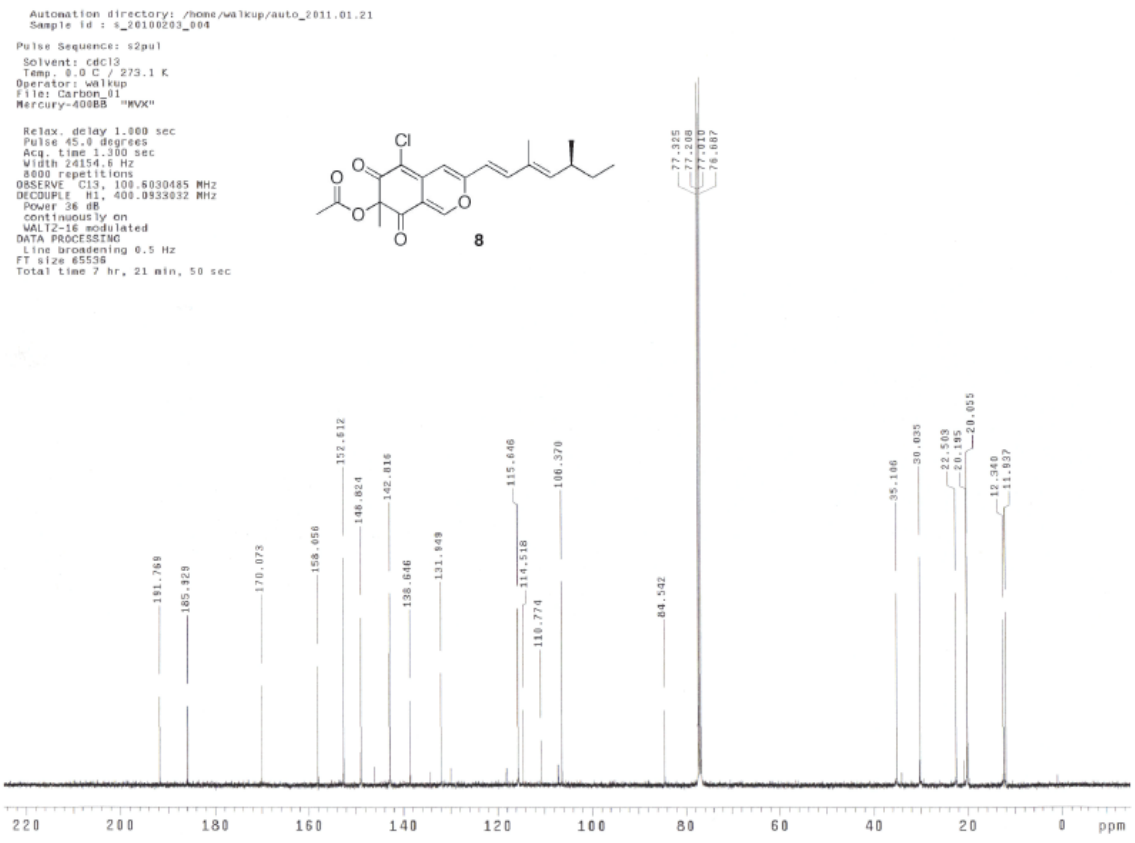
Supplemental References

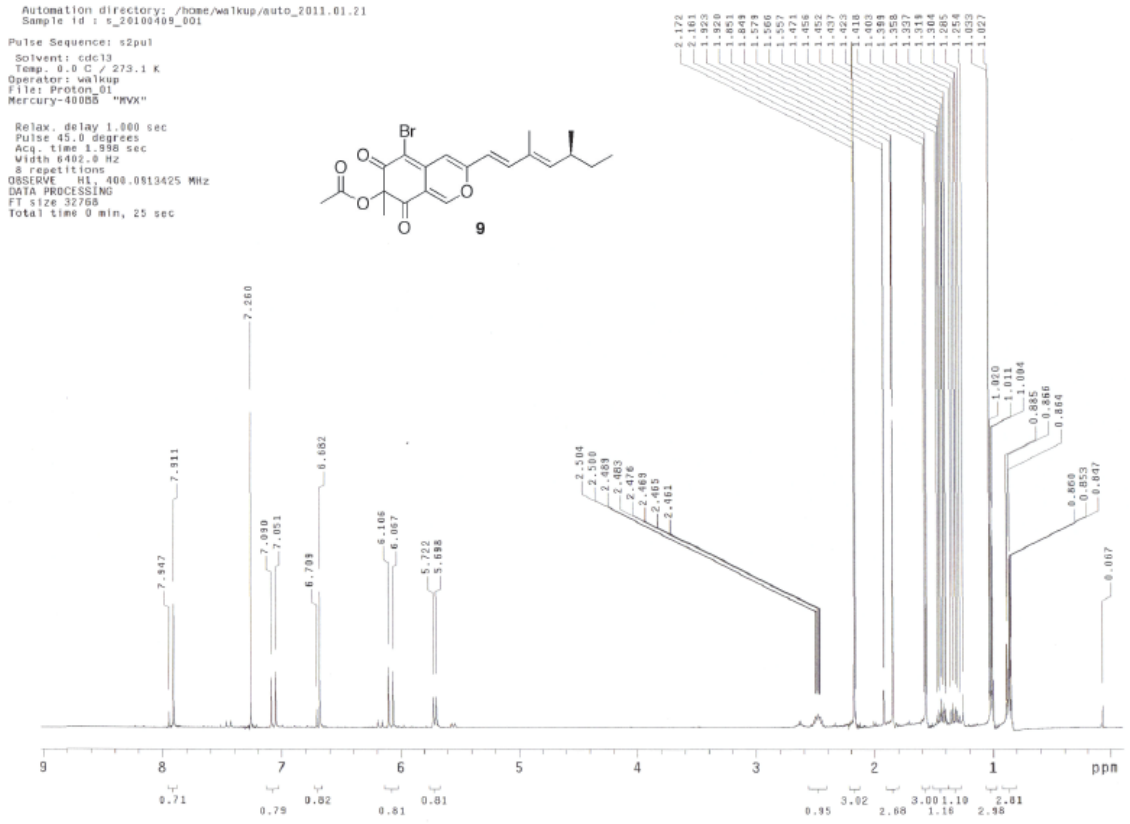
(1) Chiang, Y.-M.; Szewczyk, E.; Oakley, B. R.; Wang, C. C. C. *J. Am. Chem. Soc.* **2009**, *131,* 2965.
(2) Szewczyk, E.; Nayak, T.; Oakley, C. E.; Edgerton, H.; Xiong, Y.; Taheri-Talesh, N.; Osmani, S. A.; Oakley, B. R. Nat. Protoc. 2006, 1, 3111–3120.
(3) Frigerio, M.; Santagostino, M.; Sputore, S. *J. Org. Chem.* **1999**, *64*, 4537.
(4) Axelrod, B.; Cheesbrough, T.M.; Laakso, S. *Meth. Enzymol.* **1981**, *71*, 441.

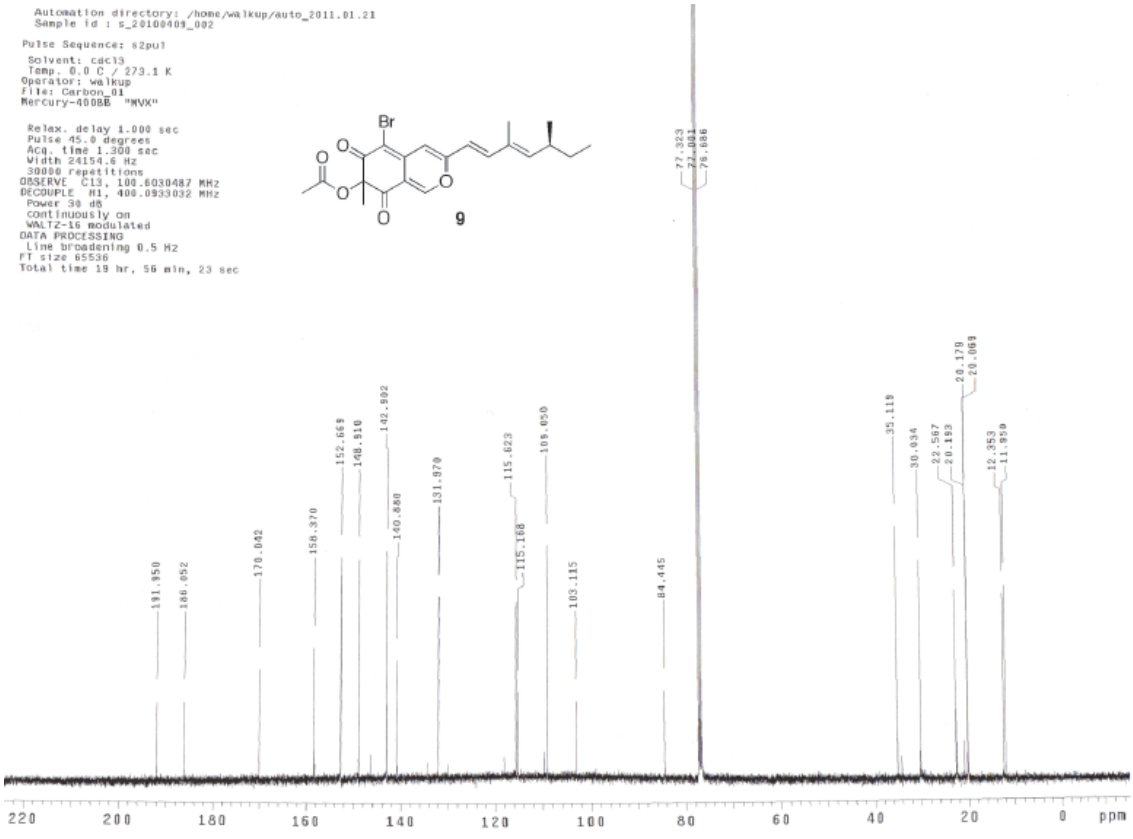

Automation directory: /home/walkup/auto_2011.01.21
Sample id : s_20110214_006
Sample : Ac_H
Pulse Sequence: s2pul
Solvent: cdcl3
Temp. 28.0 C / 301.1 K
Operator: walkup
File: Proton_01
Mercury-400BB "MVX"
Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 1.988 sec
Width 6402.0 Hz
32 repetitions
OBSERVE H1, 400.1004630 MHz
DATA PROCESSING
FT size 32768
Total time 1 min, 40 sec
7
ppm

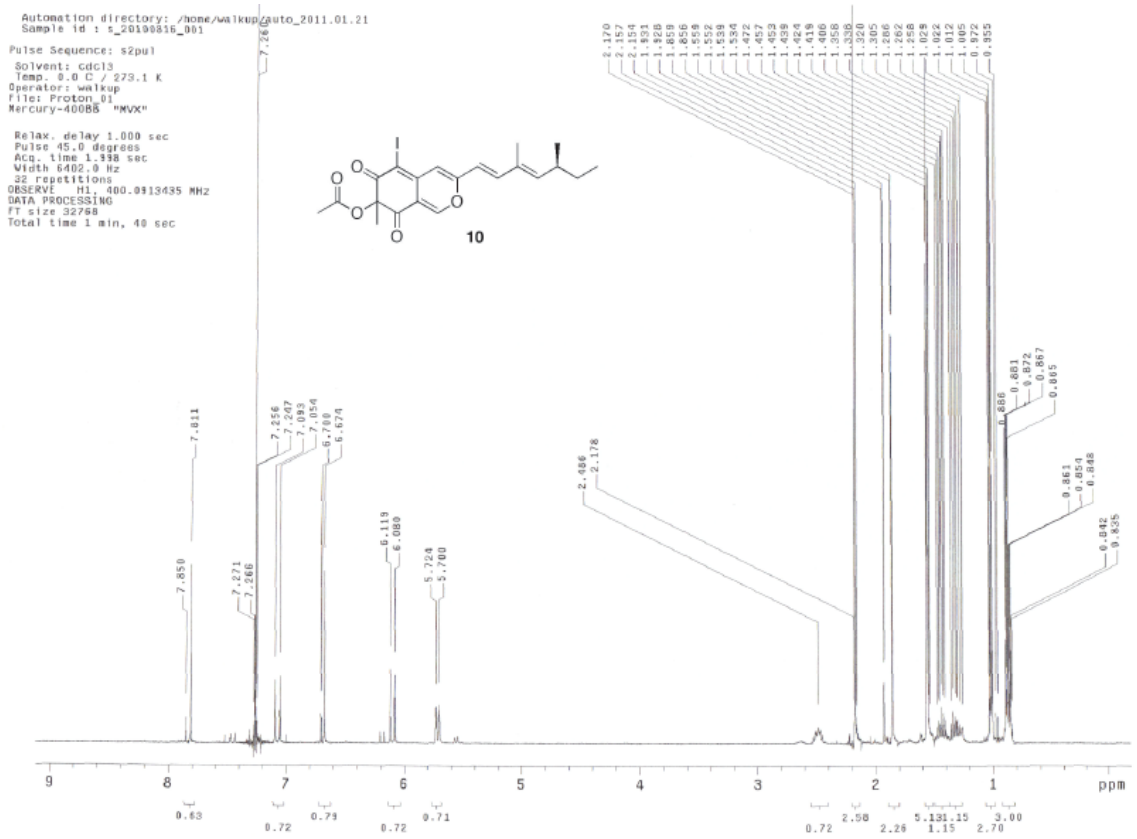

Ac_H_azaphilone
Automation directory: /home/walkup/auto_2011.01.21
Sample id : s_20110202_009
Pulse Sequence: s2pul
Solvent: cdcl3
Temp. 28.0 C / 301.1 K
Operator: walkup
File: Carbon_01
Mercury-400BB "MVX"
Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 1.300 sec
Width 24154.6 Hz
18000 repetitions
OBSERVE C13, 100.6053174 MHz
DECOUPLE H1, 400.1024978 MHz
Power 36 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 0.5 Hz
FT size 65536
Total time 11 hr, 57 min, 52 sec
7
ppm

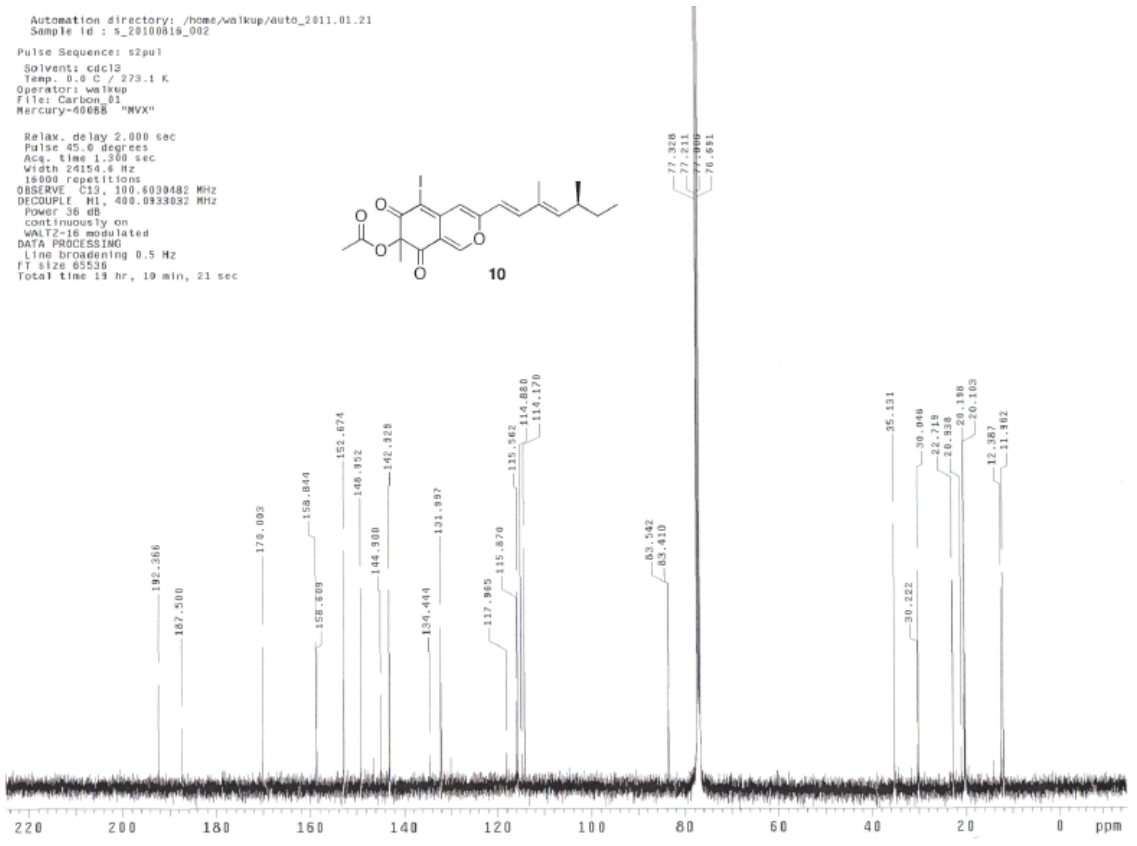

Automation directory: /home/walkup/auto_2011.01.21
Sample id : s_20100201_006
Pulse Sequence: s2pul
Solvent: cdcl3
Temp. 0.0 C / 273.1 K
Operator: walkup
File: Proton_01
Mercury-400BB "MVX"
Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 1.936 sec
Width 8402.0 Hz
8 repetitions
OBSERVE H1, 400.0813421 MHz
DATA PROCESSING
FT size 32768
Total time 0 min, 25 sec
Cl
O
O
O
O
O
8
7.968
7.931
7.260
7.079
7.040
6.672
6.643
6.097
6.058
5.715
5.690
2.499
2.481
2.474
2.464
2.460
2.189
2.173
2.162
2.152
1.917
1.914
1.845
1.843
1.628
1.597
1.581
1.568
1.585
1.568
1.469
1.455
1.450
1.435
1.421
1.417
1.402
1.354
1.336
1.317
1.302
1.284
1.025
1.016
1.008
1.002
0.970
0.954
0.883
0.882
0.872
0.865
0.863
0.859
0.852
0.846
0.841
0.835
0.831
0.809
9
8
7
6
5
4
3
2
1
ppm
0.60
0.70
0.71
0.70
0.71
0.73
2.42
2.32
3.00
0.99
1.27
2.45
2.93

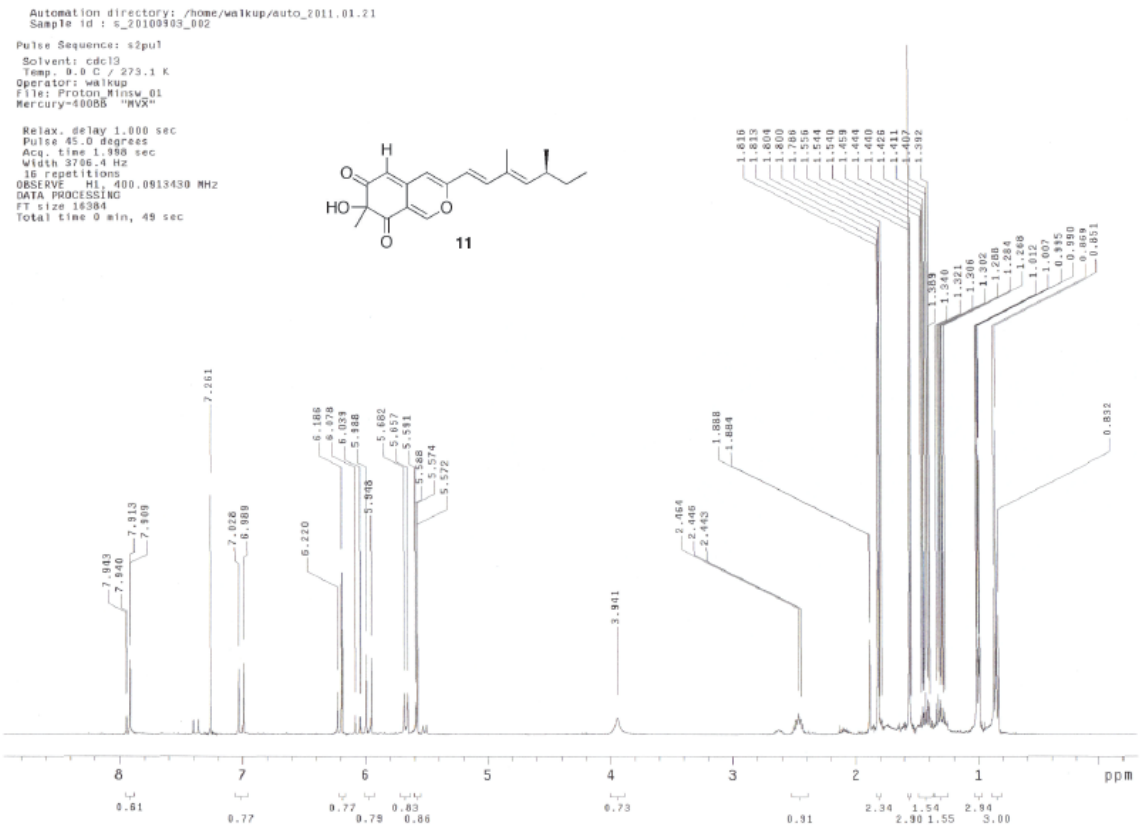

Automation directory: /home/walkup/auto_2011.01.21
Sample id : s_20100203_004
Pulse Sequence: s2pul
Solvent: cdcl3
Temp. 0.0 C / 273.1 K
Operator: walkup
File: Carbon_01
Mercury-400BB "MVX"
Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 1.300 sec
Width 24154.6 Hz
8000 repetitions
OBSERVE C13, 100.6030485 MHz
DECOUPLE H1, 400.0933032 MHz
Power 36 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 0.5 Hz
FT size 65536
Total time 7 hr, 21 min, 50 sec
Cl
O
O
O
O
O
8
191.769
165.328
170.073
158.656
152.612
140.824
142.816
138.646
131.949
115.646
114.518
110.774
106.370
84.542
77.325
77.208
77.010
76.687
35.106
30.035
28.568
28.195
20.055
12.340
11.937
220
200
180
160
140
120
100
80
60
40
20
0
ppm

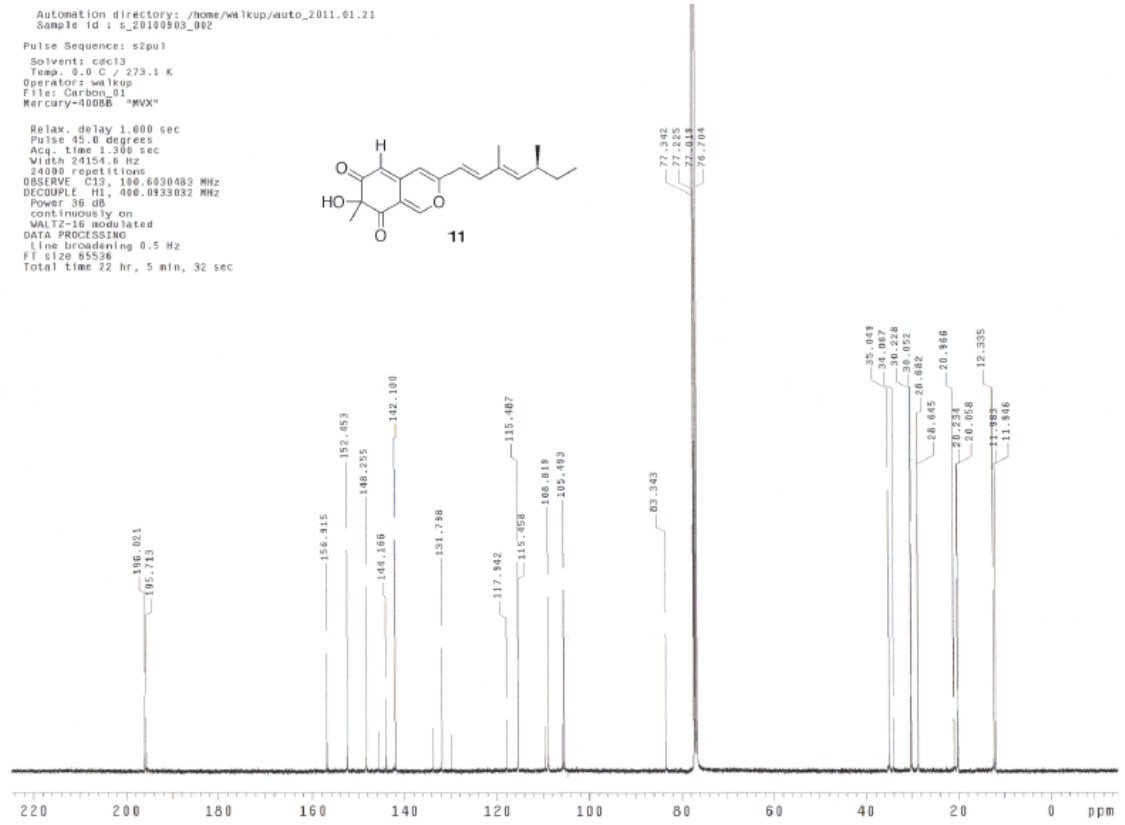

Automation directory: /home/walkup/auto_2011.01.21
Sample id : s_20100409_001
Pulse Sequence: s2pul
Solvent: cdcl3
Temp. 0.0 C / 273.1 K
Operator: walkup
File: Proton_01
Mercury-400BB "MVX"
Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 1.998 sec
Width 6402.0 Hz
8 repetitions
OBSERVE H1, 400.0513425 MHz
DATA PROCESSING
FT size 32768
Total time 0 min, 25 sec
Br
O
O
O
O
O
9
7.947
7.911
7.260
7.050
7.051
6.709
6.682
6.106
6.087
5.722
5.688
2.504
2.500
2.489
2.483
2.476
2.469
2.465
2.461
1.920
1.011
1.004
0.885
0.866
0.864
0.860
0.853
0.847
0.067
9
8
7
6
5
4
3
2
1
ppm
0.71
0.79
0.82
0.81
0.81
0.95
3.02
2.68
3.00
1.10
1.16
2.98
2.01

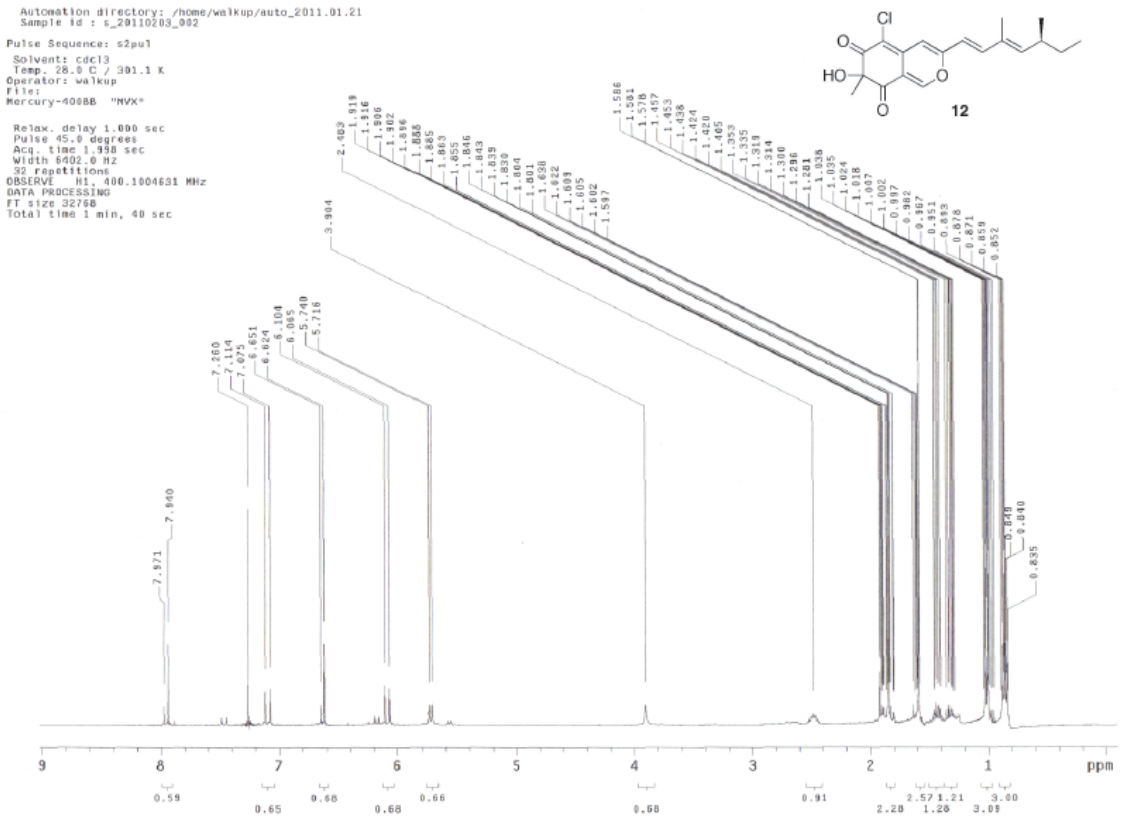

Automation directory: /home/walkup/auto_2011.01.21
Sample id : s_20100409_002
Pulse Sequence: s2pul
Solvent: cdcl3
Temp. 0.0 C / 273.1 K
Operator: walkup
File: Carbon_01
Mercury-400BB "MVX"
Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 1.300 sec
Width 24154.6 Hz
30000 repetitions
OBSERVE C13, 100.6030487 MHz
DECOUPLE H1, 400.0933032 MHz
Power 38 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
line broadening 0.5 Hz
FT size 65536
Total time 19 hr, 56 min, 23 sec
Br
O
O
O
O
O
9
191.950
166.052
170.042
158.370
152.669
148.510
142.902
140.880
131.970
115.623
115.168
109.050
103.115
84.445
77.323
77.001
76.686
35.119
30.034
22.567
20.193
20.179
20.069
12.353
11.950
220
200
180
160
140
120
100
80
60
40
20
0
ppm

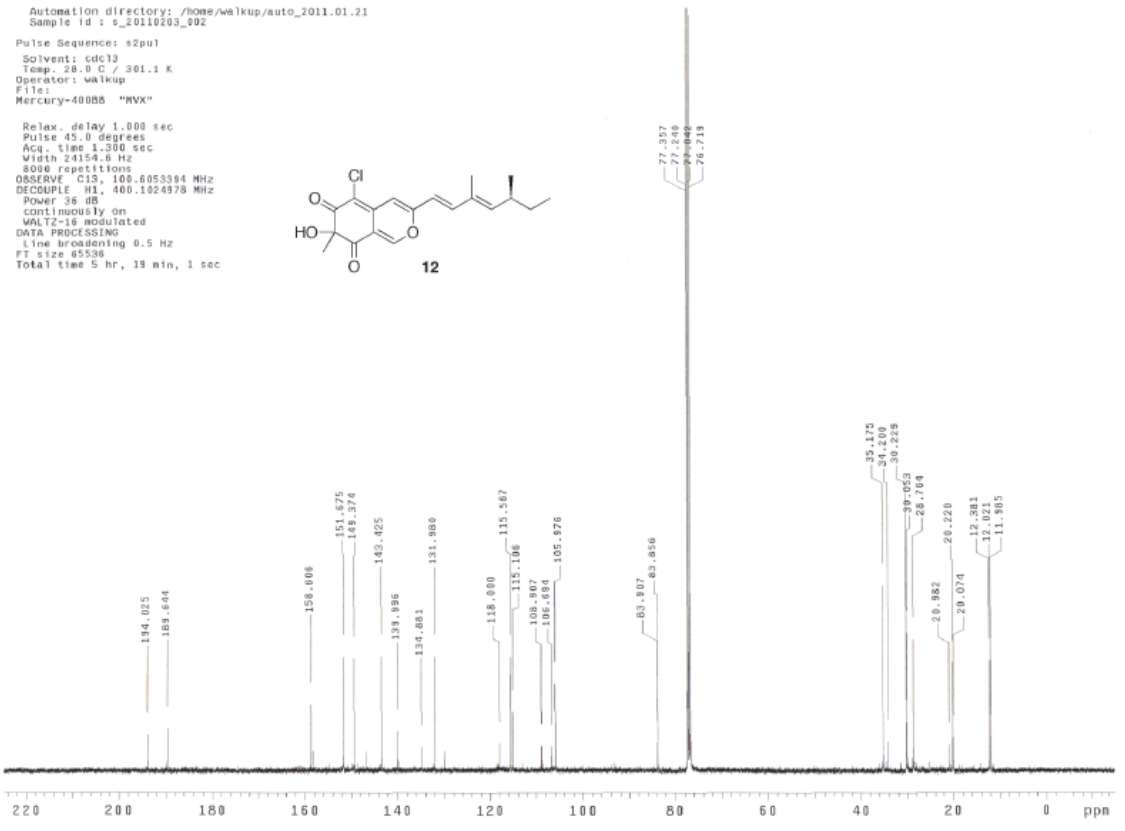

Automation directory: /home/walkup/auto_2011.01.21
Sample id : s_20190816_001
Pulse Sequence: s2pul
Solvent: cdcl3
Temp. 0.0 C / 273.1 K
Operator: walkup
File: Proton_01
Mercury-400BB "MVX"
Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 1.998 sec
Width 6402.0 Hz
32 repetitions
OBSERVE H1, 400.0813435 MHz
DATA PROCESSING
FT size 32768
Total time 1 min, 40 sec
10
ppm

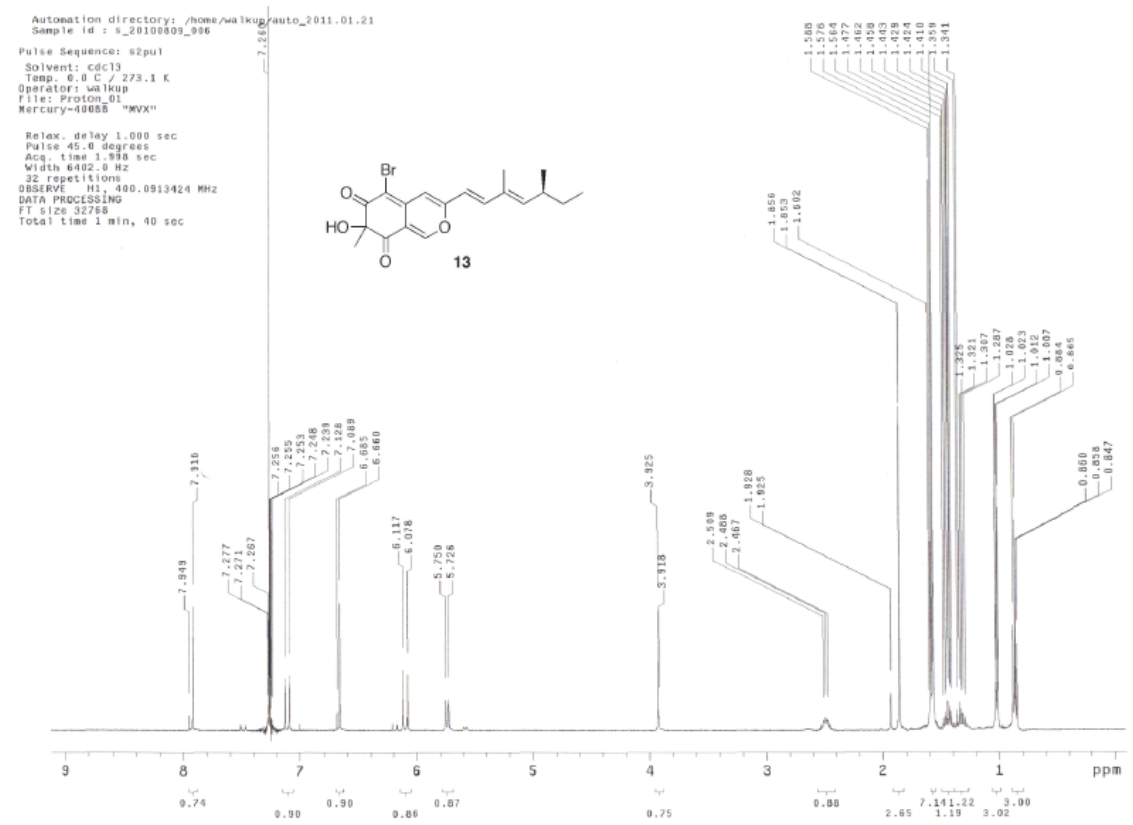

Automation directory: /home/walkup/auto_2011.01.21
Sample id : s_20100816_002
Pulse Sequence: s2pul
Solvent: cdcl3
Temp. 0.0 C / 273.1 K
Operator: walkup
File: Carbon_01
Mercury-400BB "MVX"
Relax. delay 2.000 sec
Pulse 45.0 degrees
Acq. time 1.300 sec
Width 24154.6 Hz
16000 repetitions
OBSERVE C13, 100.6030482 MHz
DECOUPLE H1, 400.0933032 MHz
Power 36 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 0.5 Hz
FT size 65536
Total time 19 hr, 10 min, 21 sec
10
ppm

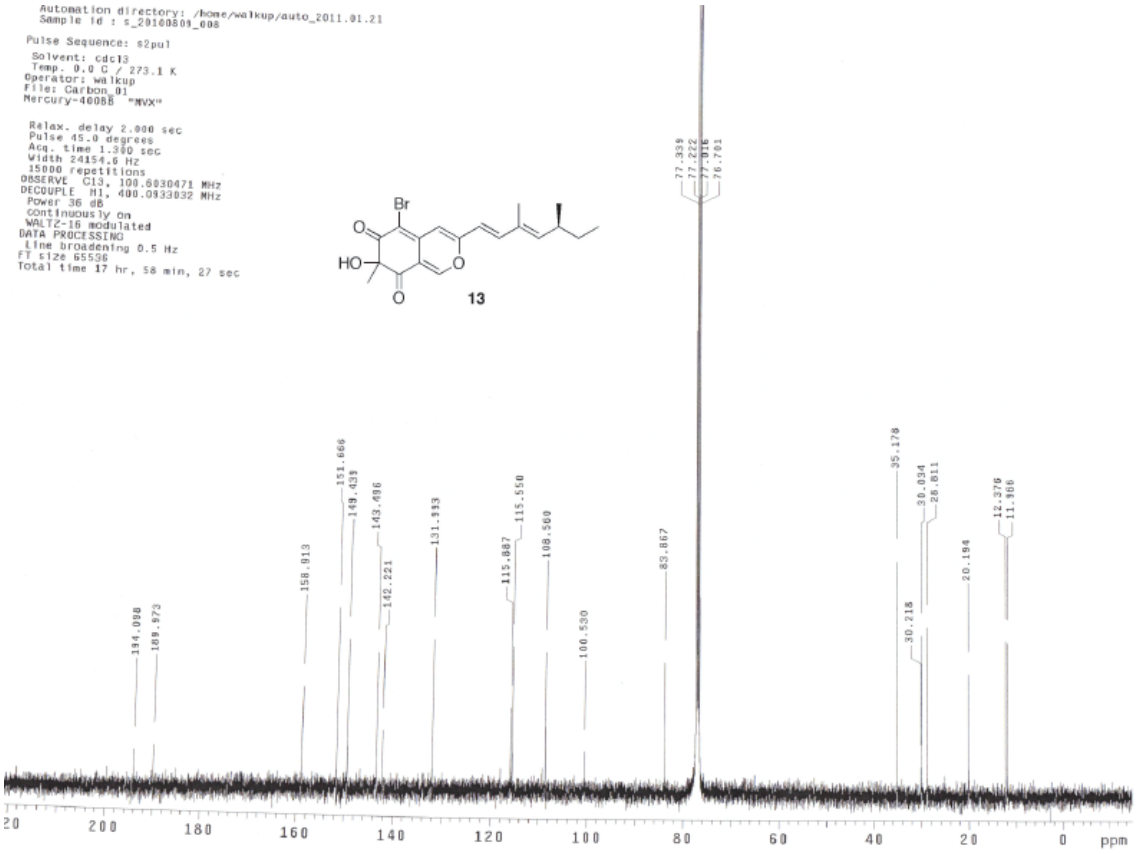

Automation directory: /home/walkup/auto_2011.01.21
Sample id : s_20100903_002
Pulse Sequence: s2pul
Solvent: cdcl3
Temp. 0.0 C / 273.1 K
Operator: walkup
File: Proton_Minsw_01
Mercury-400BB "MVX"
Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 1.998 sec
Width 3786.4 Hz
16 repetitions
OBSERVE H1, 400.0813430 MHz
DATA PROCESSING
FT size 16384
Total time 0 min, 49 sec
11
ppm

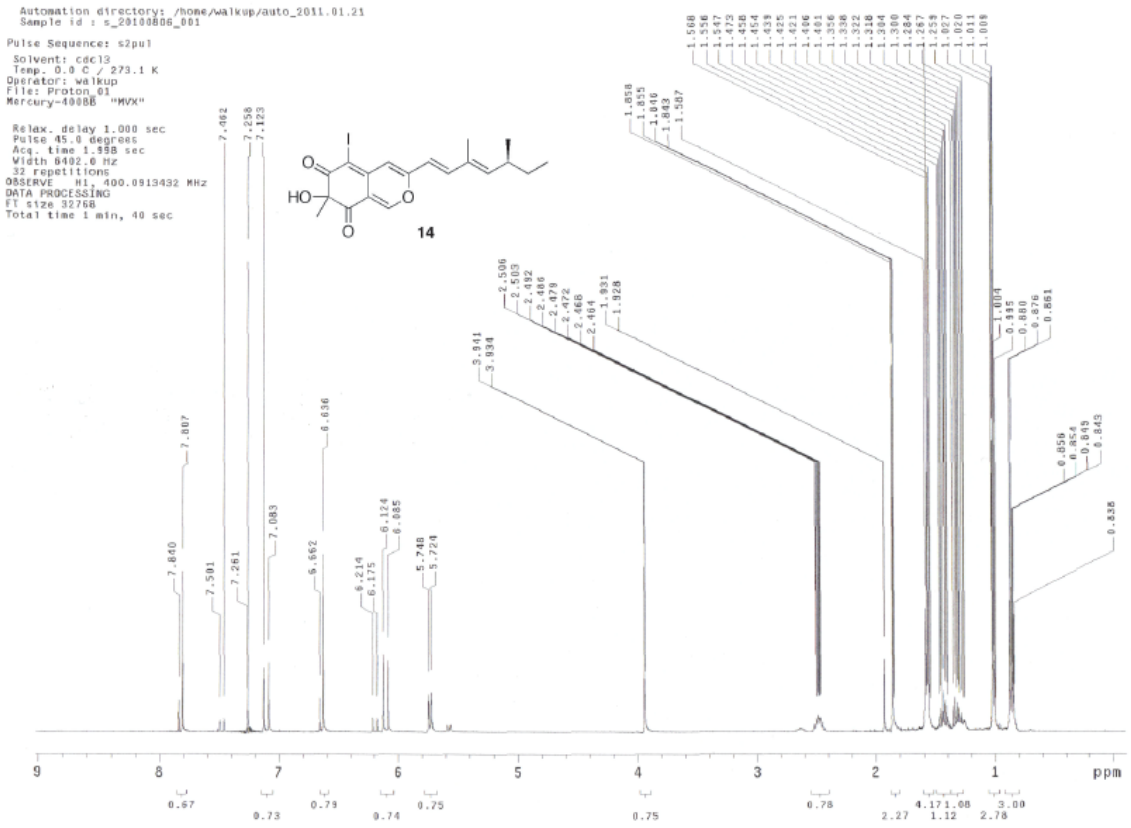

Automation directory: /home/walkup/auto_2011.01.21
Sample id : s_20100903_002
Pulse Sequence: s2pul
Solvent: cdcl3
Temp. 0.0 C / 273.1 K
Operator: walkup
File: Carbon_01
Mercury-400BB "MVX"
Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 1.300 sec
Width 24154.6 Hz
24000 repetitions
OBSERVE C13, 100.6030483 MHz
DECOUPLE H1, 400.0933032 MHz
Power 36 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 0.5 Hz
FT size 65536
Total time 22 hr, 5 min, 32 sec
11
ppm

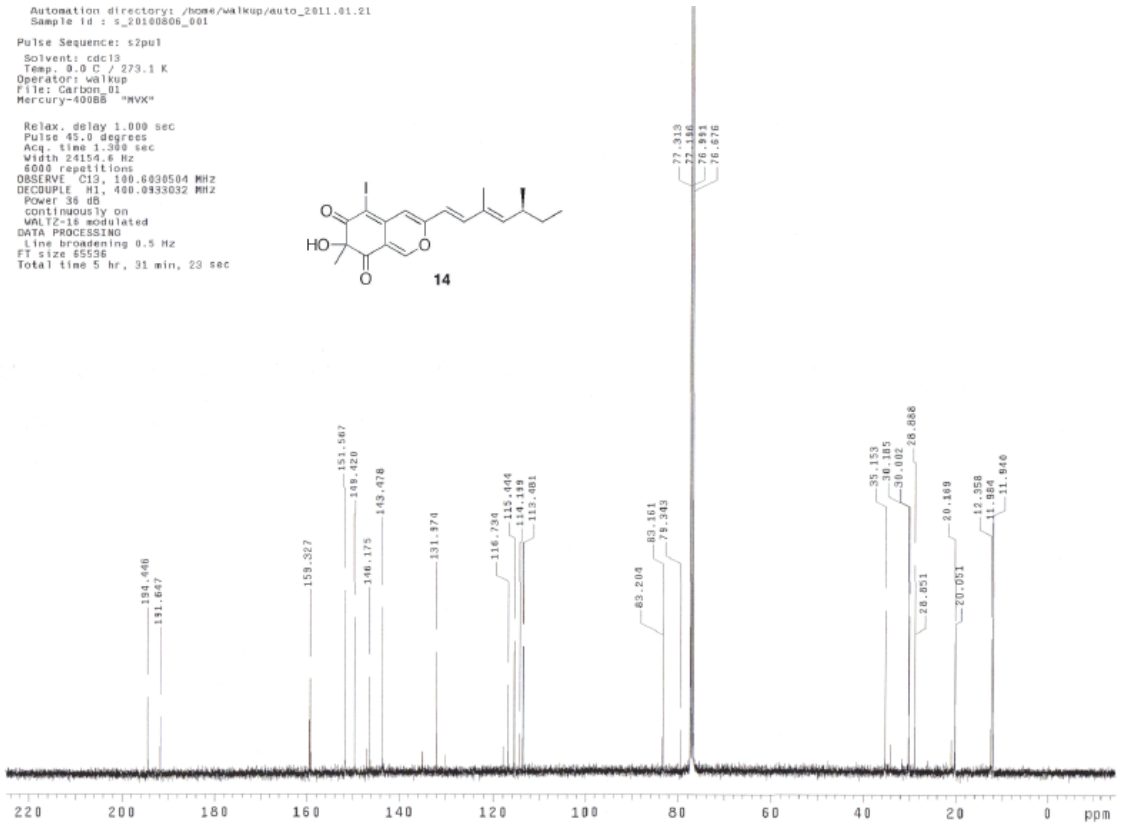

Automation directory: /home/walkup/auto_2011.01.21
Sample id : s_20110203_002
Pulse Sequence: s2pul
Solvent: cdcl3
Temp. 28.0 C / 301.1 K
Operator: walkup
File:
Mercury-400BB "MVX"
Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 1.998 sec
Width 6402.0 Hz
32 repetitions
OBSERVE H1, 400.1804631 MHz
DATA PROCESSING
FT size 32768
Total time 1 min, 40 sec
12
ppm

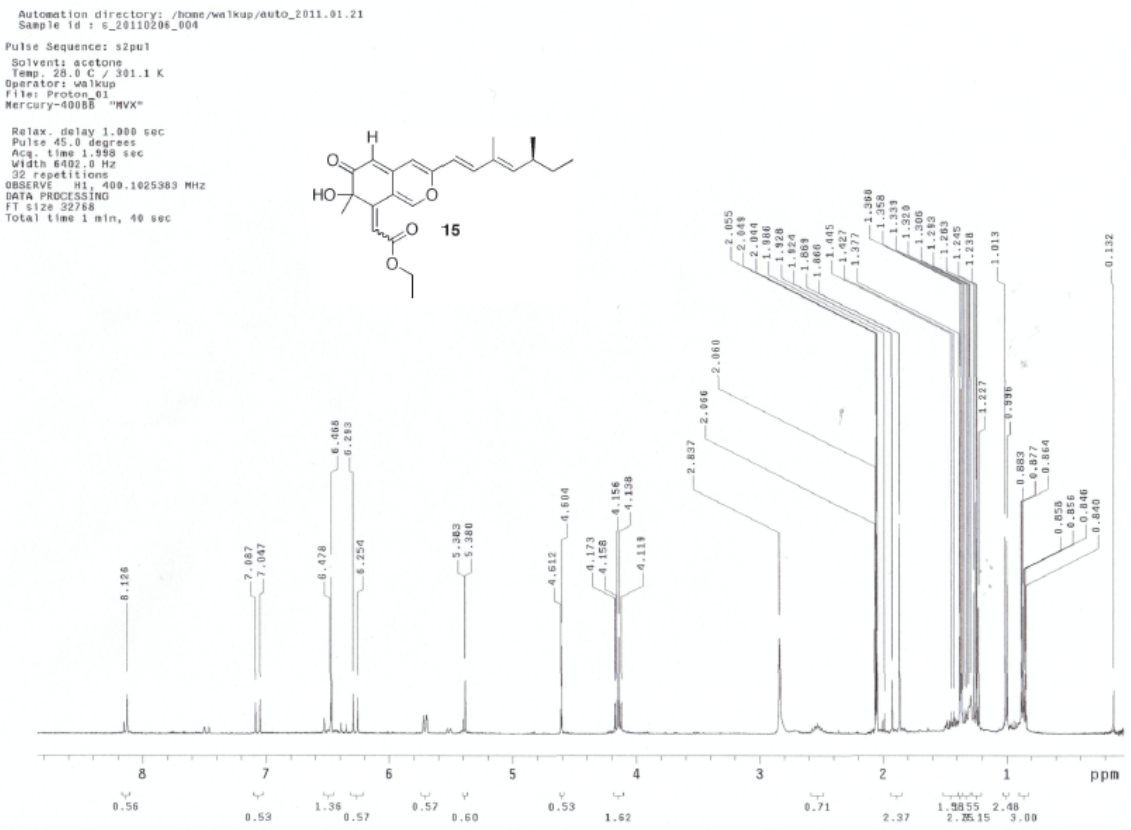

Automation directory: /home/walkup/auto_2011.01.21
Sample id : s_20110203_002
Pulse Sequence: s2pul
Solvent: cdcl3
Temp. 28.0 C / 301.1 K
Operator: walkup
File:
Mercury-400BB "MVX"
Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 1.300 sec
Width 24154.6 Hz
8000 repetitions
OBSERVE C13, 100.6053394 MHz
DECOUPLE H1, 400.1324378 MHz
Power 36 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
line broadening 0.5 Hz
FT size 65536
Total time 5 hr, 19 min, 1 sec
12
ppm

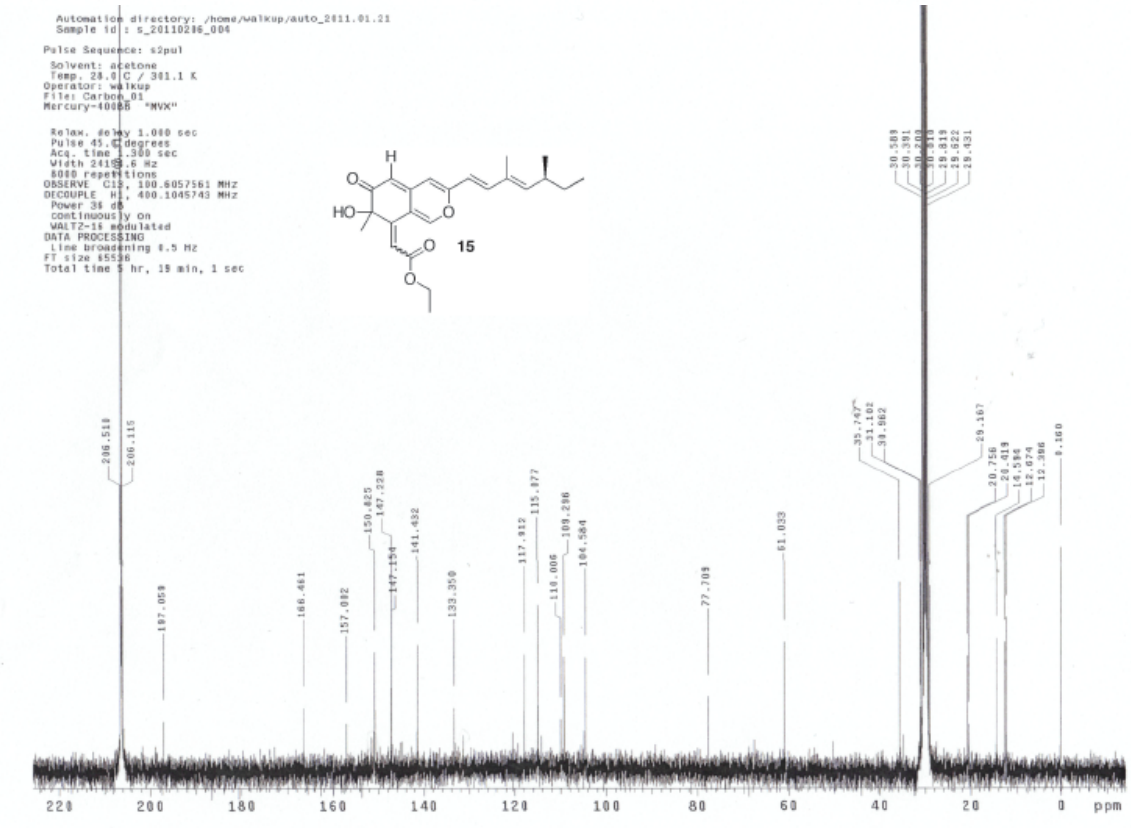

Automation directory: /home/walkup/auto_2011.01.21
Sample id : s_20100809_006
Pulse Sequence: s2pul
Solvent: cdcl3
Temp. 0.0 C / 273.1 K
Operator: walkup
File: Proton_01
Mercury-400BB "MVX"
Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 1.998 sec
Width 6402.0 Hz
32 repetitions
OBSERVE H1, 400.0913424 MHz
DATA PROCESSING
FT size 32768
Total time 1 min, 40 sec
Br
O
HO
O
O
13
ppm

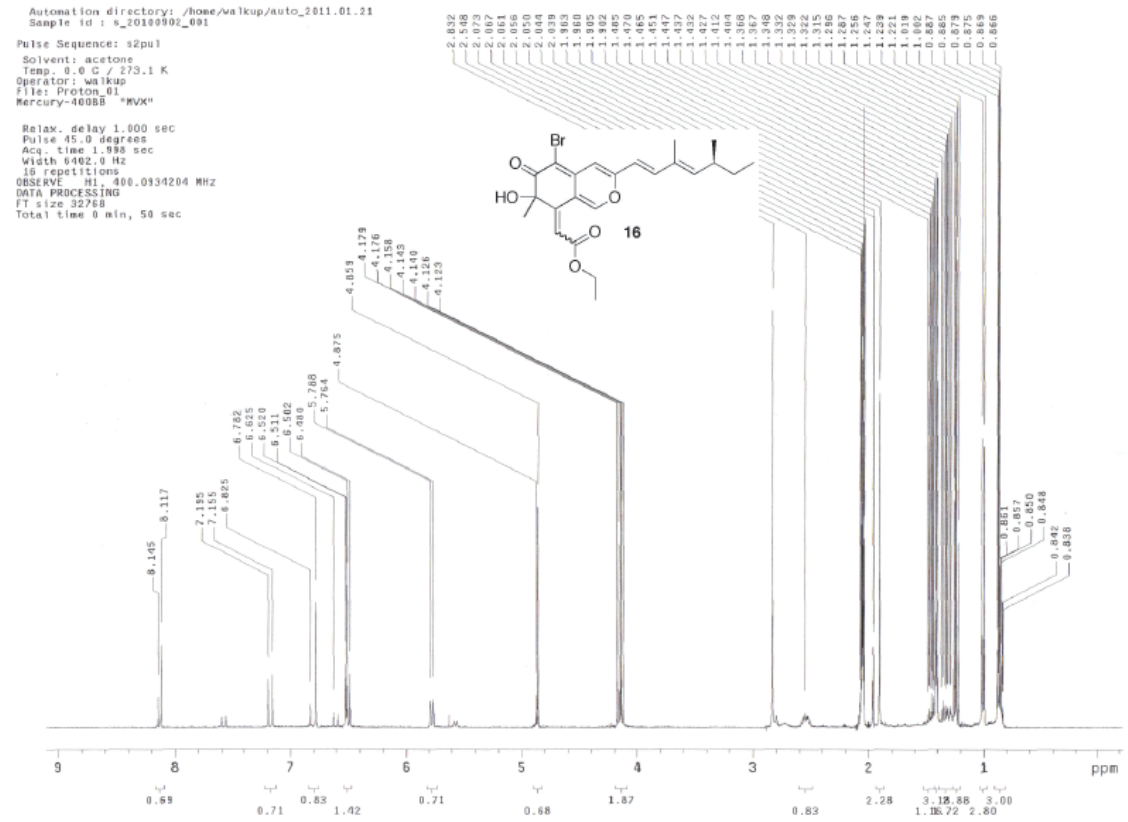

Automation directory: /home/walkup/auto_2011.01.21
Sample id : s_20100809_008
Pulse Sequence: s2pul
Solvent: cdcl3
Temp. 0.0 C / 273.1 K
Operator: walkup
File: Carbon_01
Mercury-400BB "MVX"
Relax. delay 2.000 sec
Pulse 45.0 degrees
Acq. time 1.300 sec
Width 24154.6 Hz
15000 repetitions
OBSERVE C13, 100.6030471 MHz
DECOUPLE H1, 400.0933032 MHz
Power 36 dB
continuously On
WALTZ-16 modulated
DATA PROCESSING
line broadening 0.5 Hz
FT size 65536
Total time 17 hr, 58 min, 27 sec
Br
O
HO
O
O
13
ppm

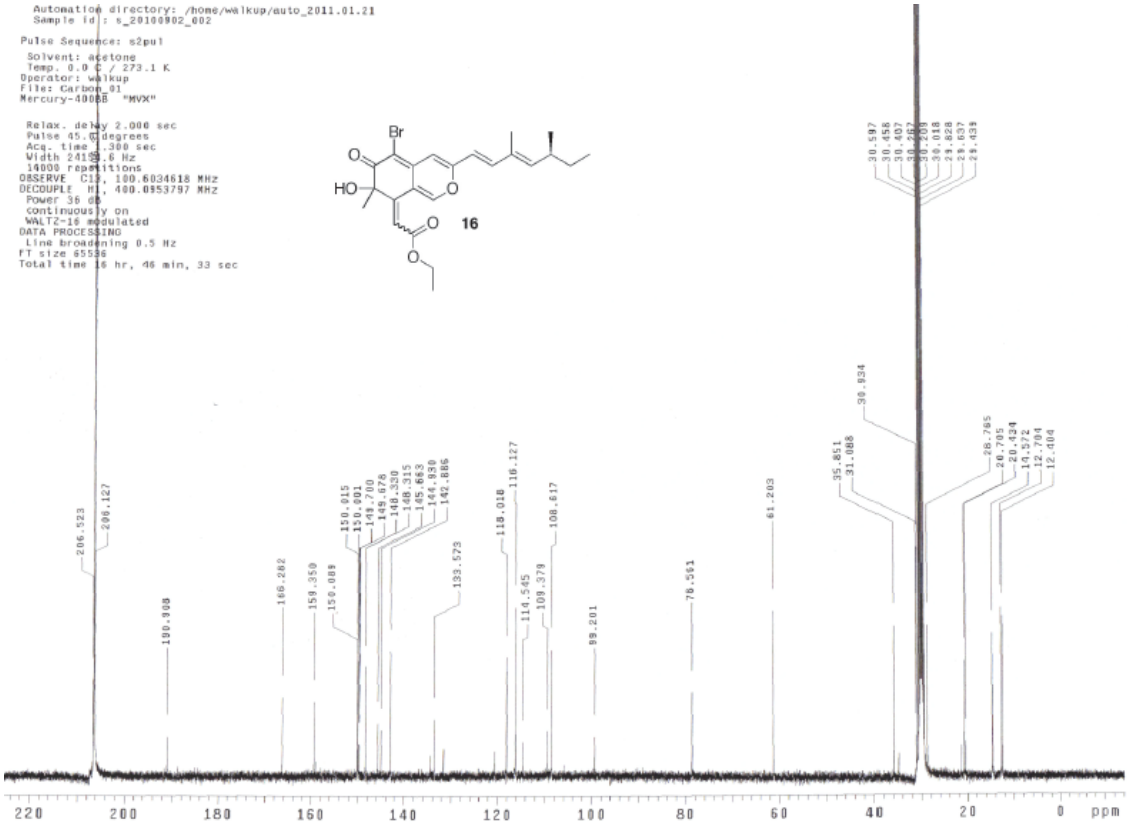

Automation directory: /home/walkup/auto_2011.01.21
Sample id : s_20100806_001
Pulse Sequence: s2pul
Solvent: cdcl3
Temp. 0.0 C / 273.1 K
Operator: walkup
File: Proton_01
Mercury-400BB "MVX"
Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 1.998 sec
Width 8402.6 Hz
32 repetitions
OBSERVE H1, 400.0913432 MHz
DATA PROCESSING
FT size 32768
Total time 1 min, 40 sec
14
ppm

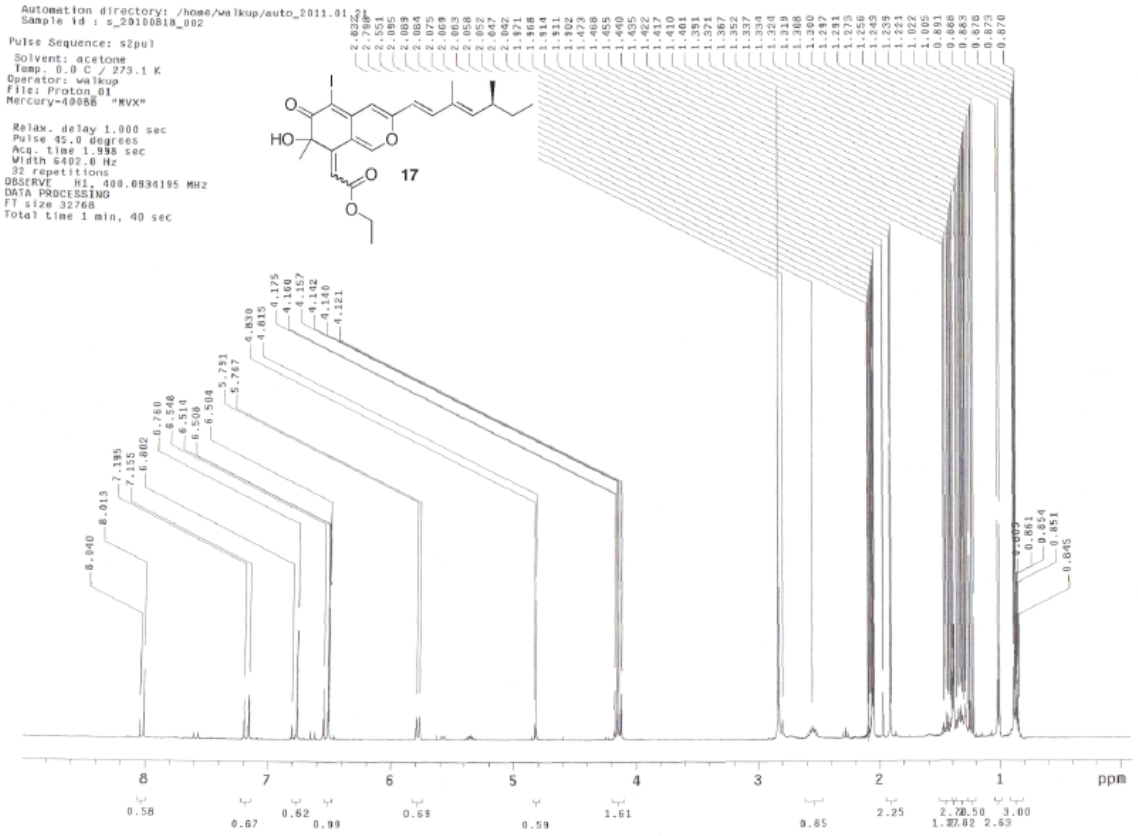

Automation directory: /home/walkup/auto_2011.01.21
Sample id : s_20100806_001
Pulse Sequence: s2pul
Solvent: cdcl3
Temp. 0.0 C / 273.1 K
Operator: walkup
File: Carbon_01
Mercury-400BB "MVX"
Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 1.300 sec
Width 24154.6 Hz
6000 repetitions
OBSERVE C13, 100.6030504 MHz
DECOUPLE H1, 400.0933032 MHz
Power 36 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
line broadening 0.5 Hz
FT size 65536
Total time 5 hr, 31 min, 23 sec
14
ppm

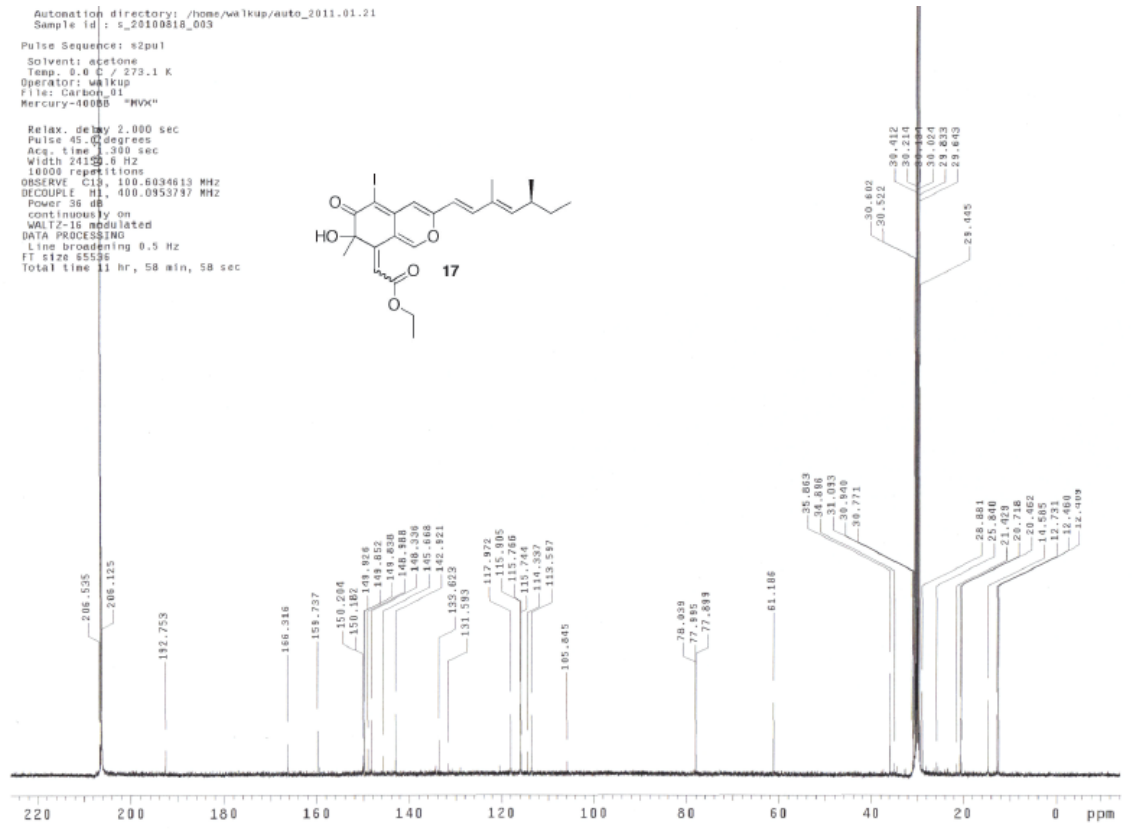

Automation directory: /home/walkup/auto_2011.01.21
Sample id : s_20110206_004
Pulse Sequence: s2pul
Solvent: acetone
Temp. 28.0 C / 301.1 K
Operator: walkup
File: Proton_01
Mercury-400BB "MVX"
Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 1.998 sec
Width 6402.0 Hz
32 repetitions
OBSERVE H1, 400.1025383 MHz
DATA PROCESSING
FT size 32768
Total time 1 min, 40 sec
15
ppm

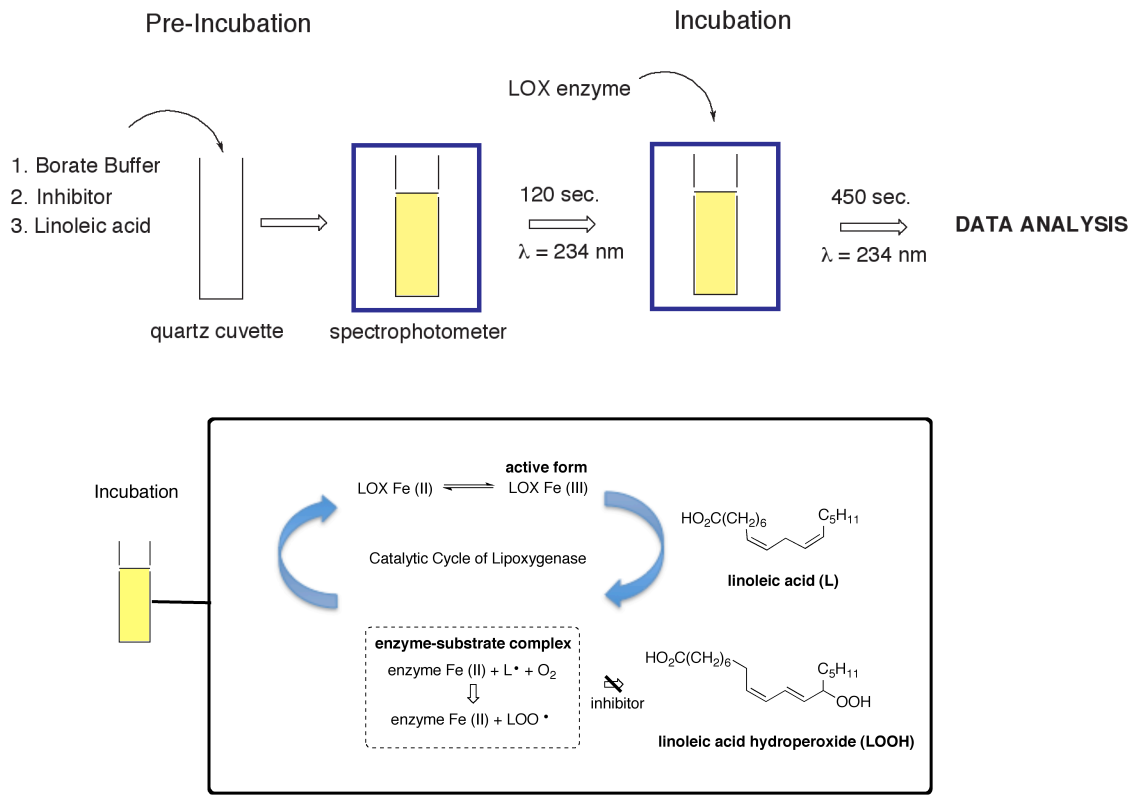

Automation directory: /home/walkup/auto_2011.01.21
Sample id : s_20110206_004
Pulse Sequence: s2pul
Solvent: acetone
Temp. 28.0 C / 301.1 K
Operator: walkup
File: Carbon_01
Mercury-400BB "MVX"
Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 1.300 sec
Width 24155.6 Hz
8000 repetitions
OBSERVE C13, 100.6057561 MHz
DECOUPLE H1, 400.1045743 MHz
Power 36 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 0.5 Hz
FT size 65536
Total time 5 hr, 19 min, 1 sec
15
ppm


Automation directory: /home/walkup/auto_2011.01.21
Sample id : s_20100902_001
Pulse Sequence: s2pul
Solvent: acetone
Temp. 0.0 C / 273.1 K
Operator: walkup
File: Proton_01
Mercury-400BB "MVX"
Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 1.998 sec
Width 6402.0 Hz
16 repetitions
OBSERVE H1, 400.0934204 MHz
DATA PROCESSING
FT size 32768
Total time 0 min, 50 sec
Br
HO
O
16
ppm


Automation directory: /home/walkup/auto_2011.01.21
Sample id : s_20100902_002
Pulse Sequence: s2pul
Solvent: acetone
Temp. 0.0 C / 273.1 K
Operator: walkup
File: Carbon_01
Mercury-400BB "MVX"
Relax. delay 2.000 sec
Pulse 45.0 degrees
Acq. time 1.300 sec
Width 24154.6 Hz
14000 repetitions
OBSERVE C13, 100.6034618 MHz
DECOUPLE H1, 400.0353797 MHz
Power 36 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 0.5 Hz
FT size 65536
Total time 16 hr, 46 min, 33 sec
Br
HO
O
16
ppm


Automation directory: /home/walkup/auto_2011.01.21
Sample id : s_20100818_002
Pulse Sequence: s2pul
Solvent: acetone
Temp. 0.0 C / 273.1 K
Operator: walkup
File: Proton_01
Mercury-400BB "MVX"
Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 1.998 sec
Width 6402.8 Hz
32 repetitions
OBSERVE H1, 400.6934195 MHz
DATA PROCESSING
FT size 32768
Total time 1 min, 40 sec
17
ppm


Automation directory: /home/walkup/auto_2011.01.21
Sample id : s_20100818_003
Pulse Sequence: s2pul
Solvent: acetone
Temp. 0.0 C / 273.1 K
Operator: walkup
File: Carbon_01
Mercury-400BB "MVX"
Relax. delay 2.000 sec
Pulse 45.0 degrees
Acq. time 1.300 sec
Width 24154.6 Hz
16000 repetitions
OBSERVE C13, 100.6034613 MHz
DECOUPLE H1, 400.0953797 MHz
Power 36 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 0.5 Hz
FT size 65536
Total time 11 hr, 58 min, 58 sec
17
ppm



Scheme 1. Soybean Lipoxgyenase-1 Assay

Soybean Lipoxygenase-1 Assay. The enzyme assay was performed according to Axelrod *et. al*. [S4] Each solution was prepared and measured at room temperature. Enzyme kinetics was measured on a Shimadzu UV-2401PC at a wavelength of 234 nm in a quartz cuvette. For the assay, the linoleic acid substrate was prepared by mixing 20 µL linoleic acid (Cayman Chemical #760716) with 20 µL KOH (Cayman Chemical #760713) and 40 µL double distilled water. Lipoxygenase-1 (Cayman Chemical #60712) was diluted from original stock concentration to a concentration of 100 U/mL in the cuvette. The semisynthetic azaphilones were prepared as stock concentrations in dimethylsulfoxide (DMSO) from 20 µM to 10 mM; 5 µL was added to the assay mixture to give the desired final concentration of the inhibitor with 1% of DMSO in the assay.

Lipoxygenase-1 Inhibition Assay: The spectrophotometric assay is based on monitoring the reaction, catalyzed by LOX-1 to convert linoleic acid (L) to the hydroperoxide (LOOH), at 234 nm. The substrate L does not absorb at the indicated wavelength, so that any absorption is due to the generation of LOOH. The reaction is initiated when the non-

heme iron of LOX-1 in the ferric state is reduced by the substrate L. While in the enzyme-substrate complex, L is oxidized and converted to the peroxide free radical (LOO•), and subsequently released from the enzyme as LOOH. Inhibitors can interfere in the process in several different ways to prevent the generation of LOOH by the chelation of iron, removal of oxygen or prevention of free radical formation.

Procedure: Prior to measurements, a sample with buffer was used as a blank. In a quartz cuvette, each sample was prepared with 482.5 µL 0.2 M borate buffer (at a pH of 9.0) mixed with 5 µL inhibitor and 5 µL substrate by pipetting the solution. The cuvette was placed in the spectrophotometer and measured for 120 seconds and then rapidly 7.5 µL lipoxygenase-1 was added and mixed to initiate the reaction. Measurements were recorded every 30 seconds for 7.5 minutes. All measurements were carried out in triplicate.

IC_{50} calculation: Inhibition of an enzyme at 50 % can be experimentally measured by monitoring enzyme kinetics. A kinetic study generates a curve where the slope provides the initial velocity (V_o) of the enzyme. For each sample with different inhibitor concentrations the initial velocity was derived from a linear segment between 210-300 nm. The absorbance was used directly and not converted into concentration units. These data points (V_o, [Inhibitor]) were fitted to a curve using the software Curve Expert Professional 1.5.0 to provide an equation for the curve; the best mathematical model for the data was the MMF model. The concentration of inhibitor at which 50% inhibition occurred (as measured by change in V_o) was reported as the IC_{50}.

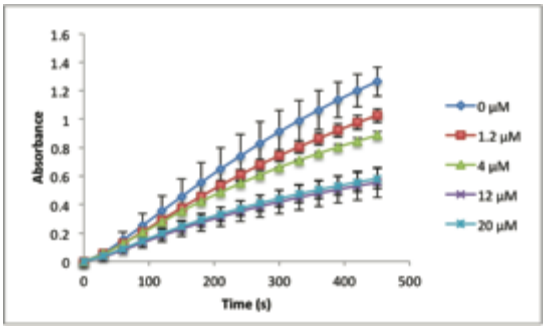


Figure S3a. LOX-1 enzyme kinetics with varying concentrations of (+)-sclerotiorin measured at λ = 234 nm.

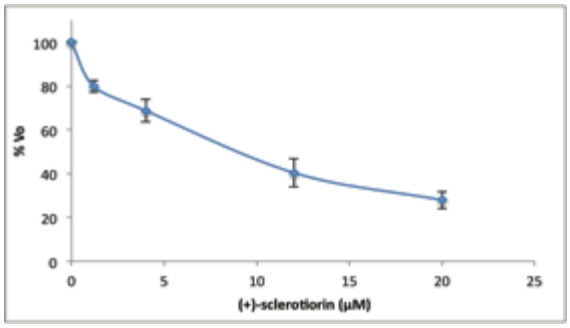


Figure S3b. Initial Velocity (V_o) of LOX-1 vs. concentration of inhibitor, where V_o of enzyme incubated in the absence of inhibitor designated a value of 1.

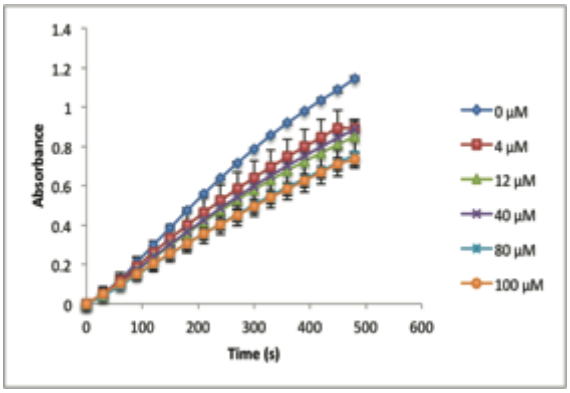


Figure S4a. LOX-1 enzyme kinetics with varying concentrations of compound 4 measured at λ = 234 nm.

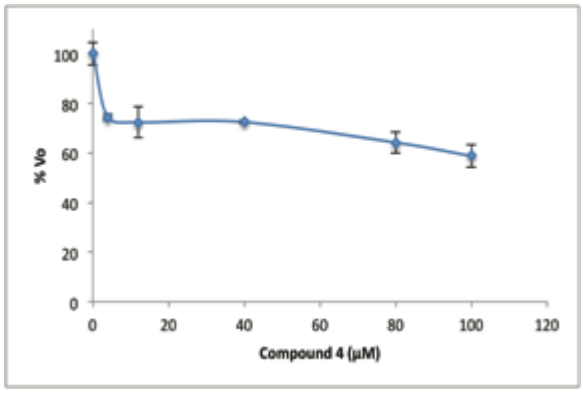


Figure S4b. Initial Velocity (V_o) of LOX-1 vs. concentration of inhibitor, where V_o of enzyme incubated in the absence of inhibitor designated a value of 1.

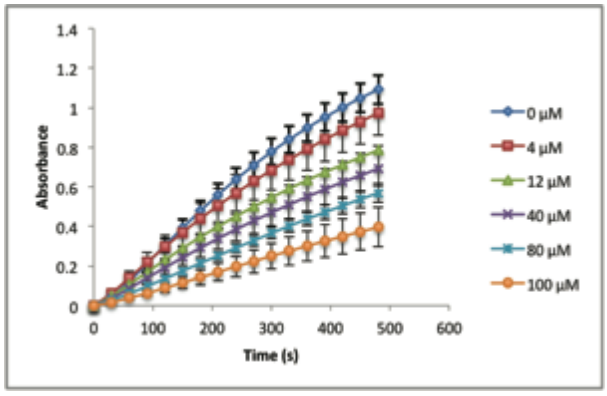


Figure S5a. LOX-1 enzyme kinetics with varying concentrations of compound 5 measured at λ = 234 nm.

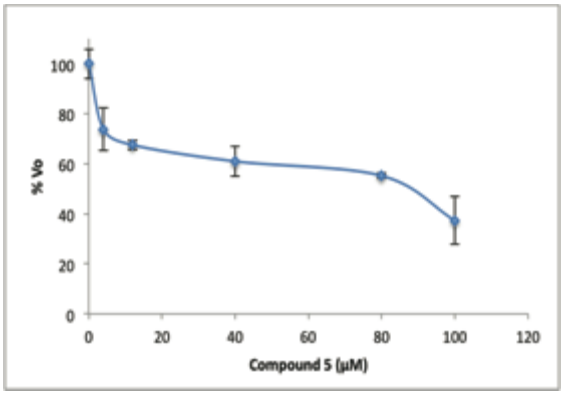


Figure S5b. Initial Velocity (V_o) of LOX-1 vs. concentration of inhibitor, where V_o of enzyme incubated in the absence of inhibitor designated a value of 1.

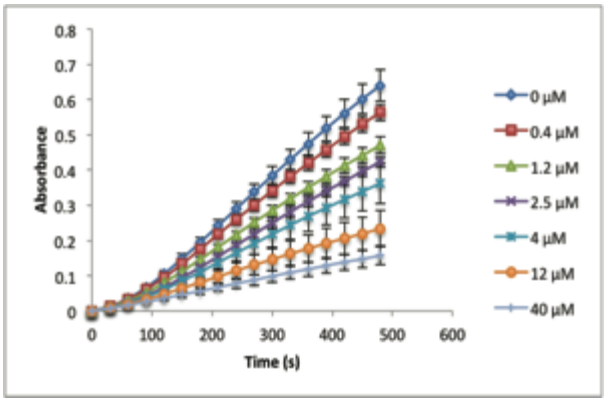


Figure S6a. LOX-1 enzyme kinetics with varying concentrations of compound 7 measured at λ = 234 nm.

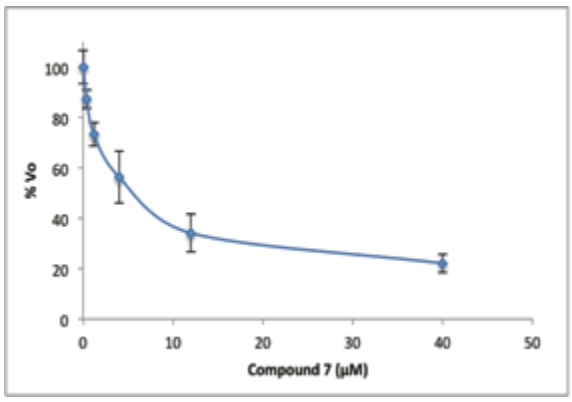


Figure S6b. Initial Velocity (V_o) of LOX-1 vs. concentration of inhibitor, where V_o of enzyme incubated in the absence of inhibitor designated a value of 1.

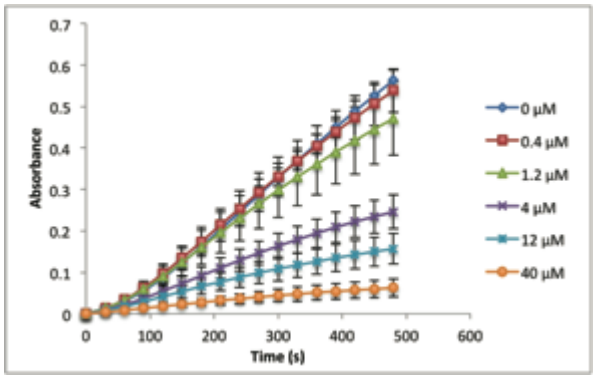


Figure S7a. LOX-1 enzyme kinetics with varying concentrations of compound 8 measured at λ = 234 nm.

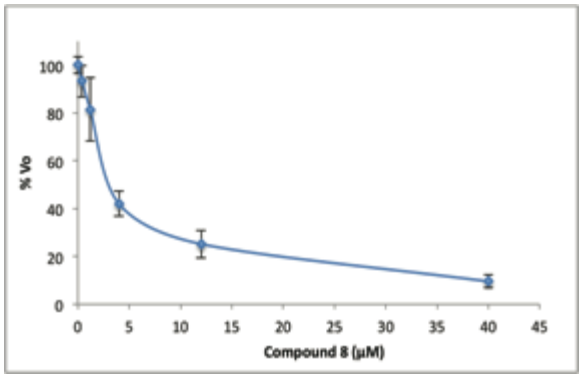


Figure S7b. Initial Velocity (V_o) of LOX-1 vs. concentration of inhibitor, where V_o of enzyme incubated in the absence of inhibitor designated a value of 1.

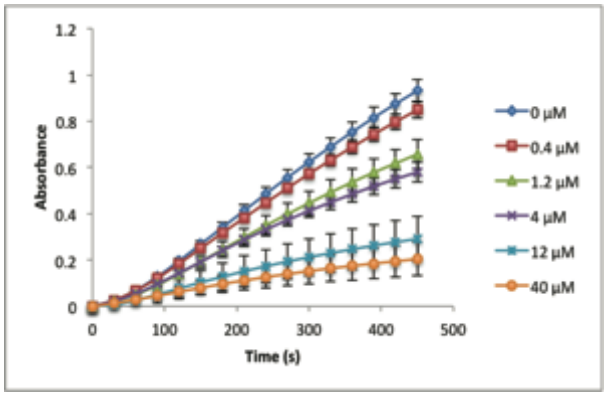


Figure S8a. LOX-1 enzyme kinetics with varying concentrations of compound 9 measured at λ = 234 nm.

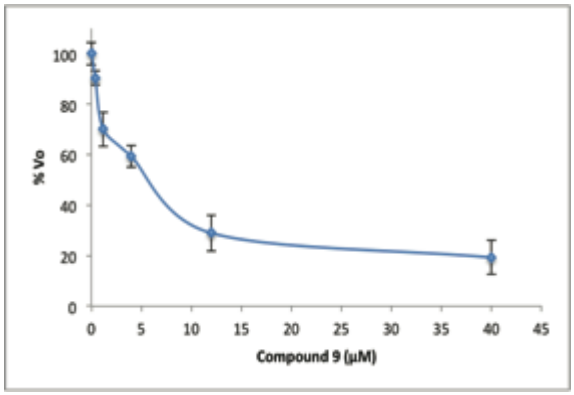


Figure S8b. Initial Velocity (V_o) of LOX-1 vs. concentration of inhibitor, where V_o of enzyme incubated in the absence of inhibitor designated a value of 1.

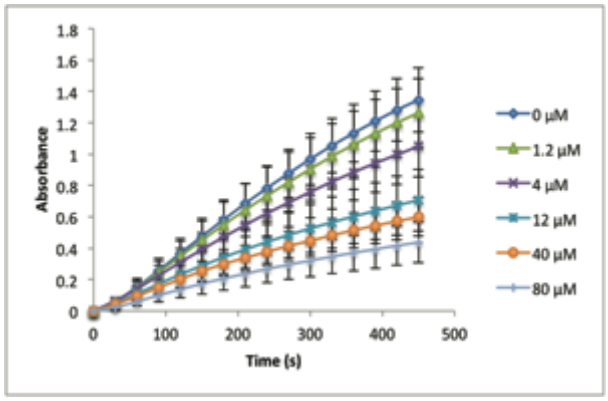


Figure S9a. LOX-1 enzyme kinetics with varying concentrations of compound 10 measured at λ = 234 nm.

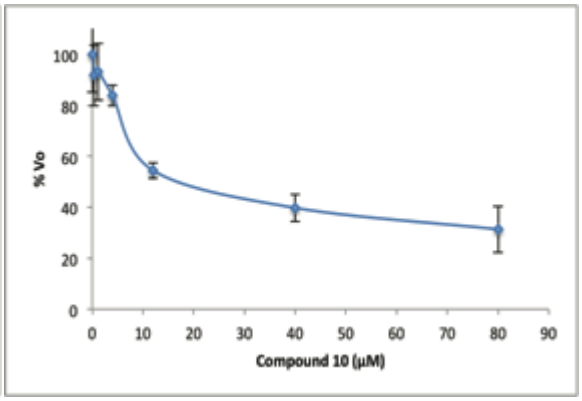


Figure S9b. Initial Velocity (V_o) of LOX-1 vs. concentration of inhibitor, where V_o of enzyme incubated in the absence of inhibitor designated a value of 1.

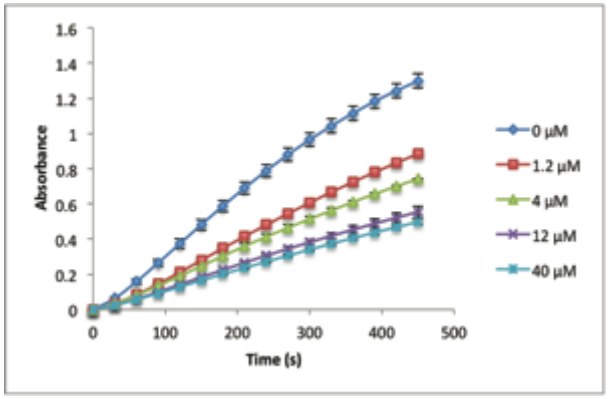


Figure S10a. LOX-1 enzyme kinetics with varying concentrations of compound 11 measured at λ = 234 nm.

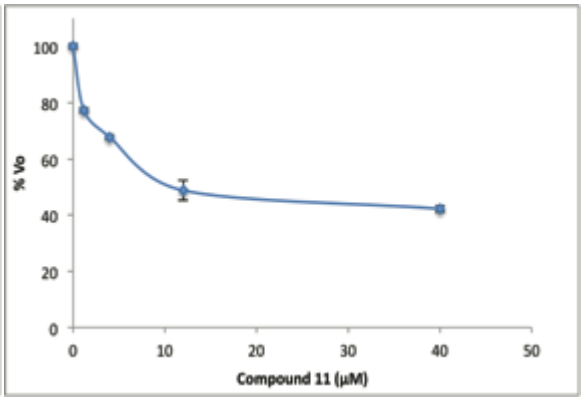


Figure S10b. Initial Velocity (V_o) of LOX-1 vs. concentration of inhibitor, where V_o of enzyme incubated in the absence of inhibitor designated a value of 1.

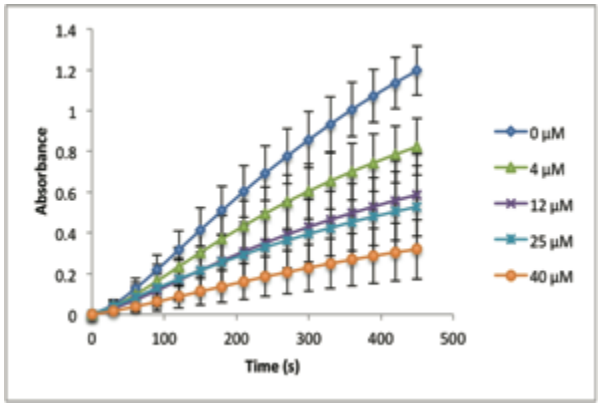


Figure S11a. LOX-1 enzyme kinetics with varying concentrations of compound 12 measured at λ = 234 nm

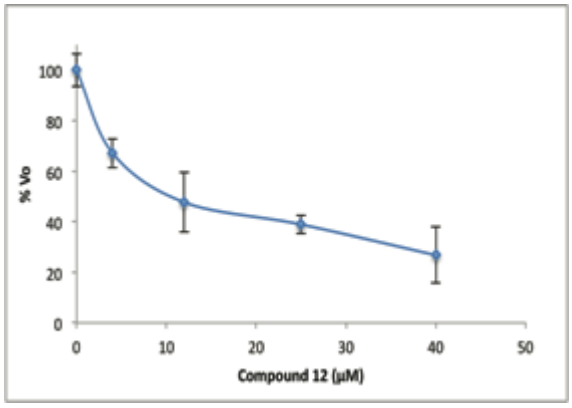


Figure S11b. Initial Velocity (V_o) of LOX-1 vs. concentration of inhibitor, where V_o of enzyme incubated in the absence of inhibitor designated a value of 1.

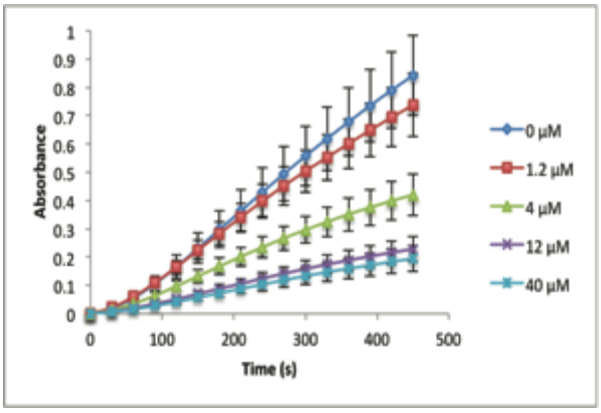


Figure S12a. LOX-1 enzyme kinetics with varying concentrations of compound 13 measured at λ = 234 nm.

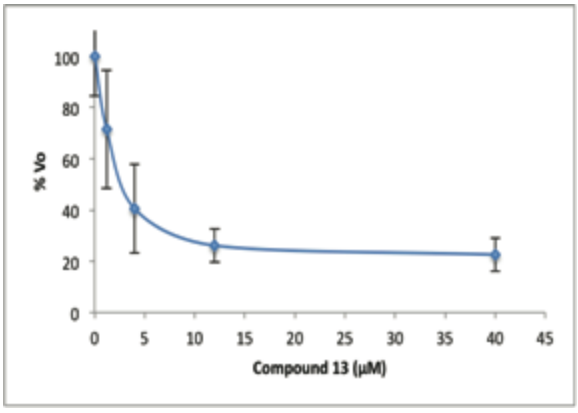


Figure S12b. Initial Velocity (V_o) of LOX-1 vs. concentration of inhibitor, where V_o of enzyme incubated in the absence of inhibitor designated a value of 1.

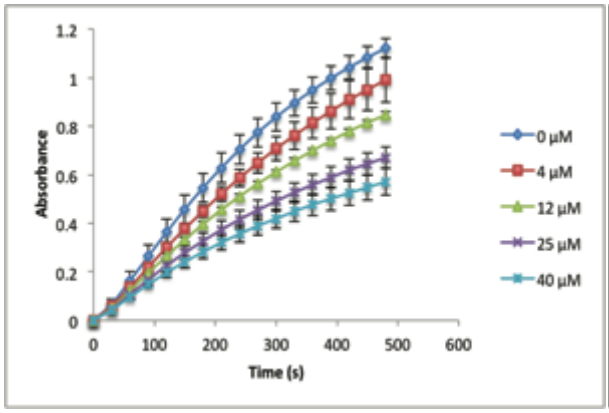


Figure S13a. LOX-1 enzyme kinetics with varying concentrations of compound 14 measured at λ = 234 nm.

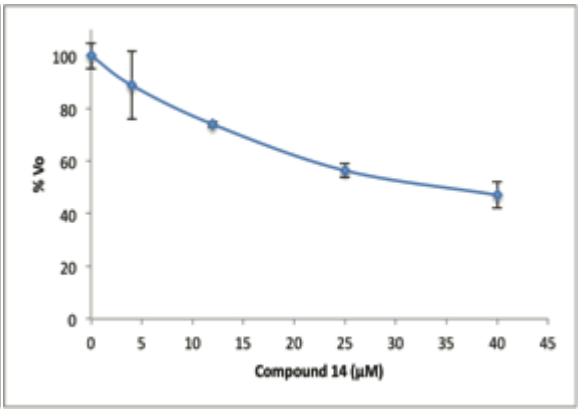


Figure S13b. Initial Velocity (V_o) of LOX-1 vs. concentration of inhibitor, where V_o of enzyme incubated in the absence of inhibitor designated a value of 1.

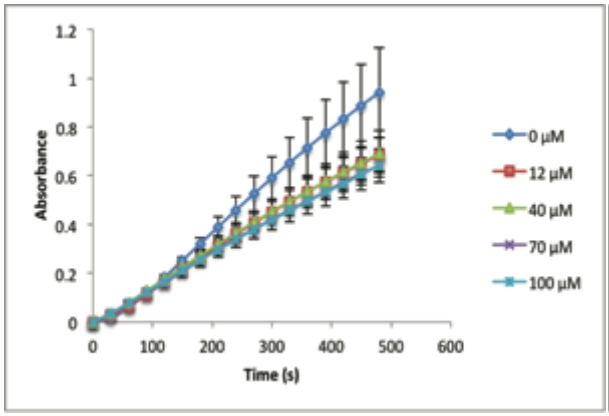


Figure S14a. LOX-1 enzyme kinetics with varying concentrations of compound 15 measured at λ = 234 nm

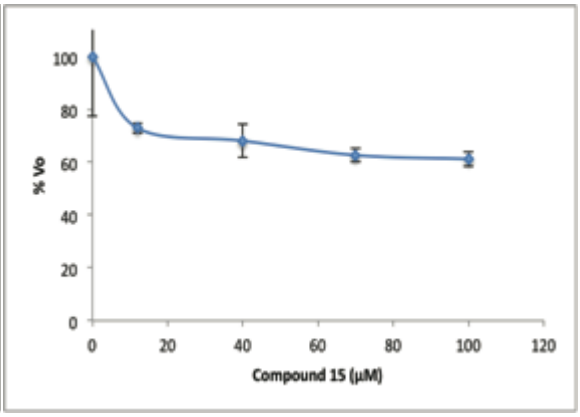


Figure S14b. Initial Velocity (V_o) of LOX-1 vs. concentration of inhibitor, where V_o of enzyme incubated in the absence of inhibitor designated a value of 1.

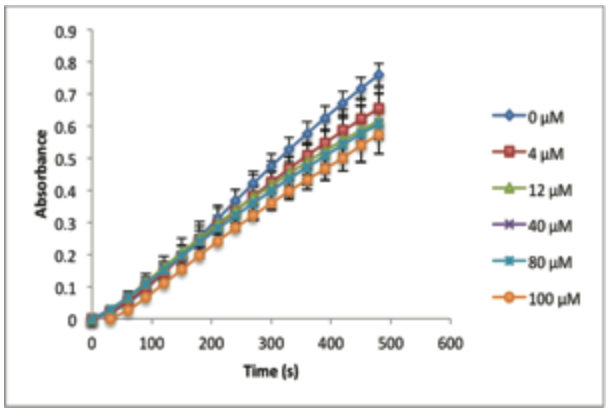


Figure S15a. LOX-1 enzyme kinetics with varying concentrations of compound 16 measured at λ = 234 nm.

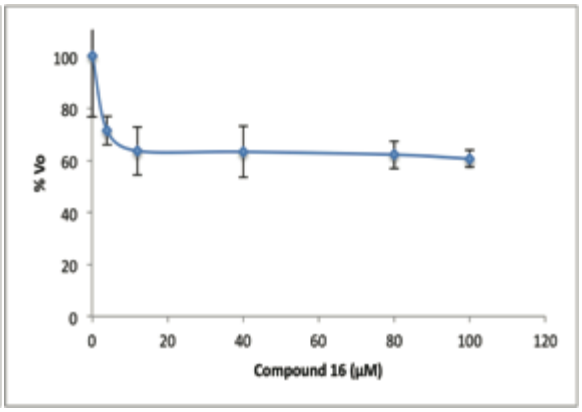


Figure S15b. Initial Velocity (V_o) of LOX-1 vs. concentration of inhibitor, where V_o of enzyme incubated in the absence of inhibitor designated a value of 1.

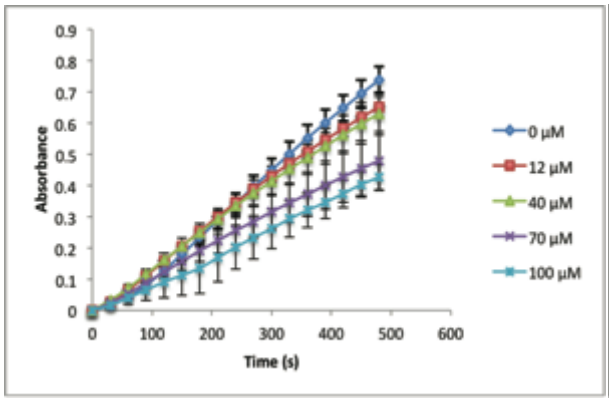


Figure S16a. LOX-1 enzyme kinetics with varying concentrations of compound 17 measured at λ = 234 nm.

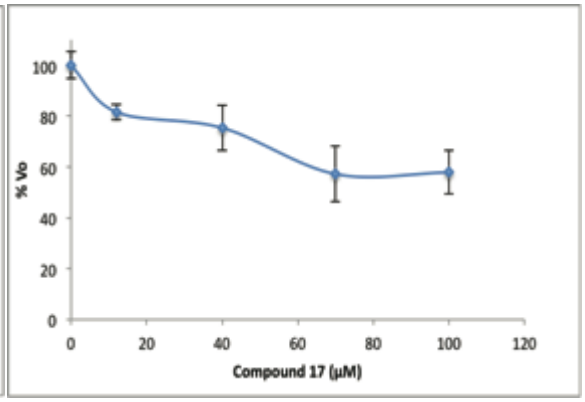


Figure S16b. Initial Velocity (V_o) of LOX-1 vs. concentration of inhibitor, where V_o of enzyme incubated in the absence of inhibitor designated a value of 1.