

Supporting Information:

Total Synthesis of Sordaricin

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General methods: Most proton (^1H) and carbon (^{13}C) NMR spectra were recorded on a Varian Gemini 300, Varian Inova 300 and Varian Mercury 300 spectrometer operating at 300 MHz for proton and 75 MHz for carbon nuclei. Also used were a Varian Inova 500 and Varian Inova 600 spectrometer, operating at 500 and 600 MHz for proton, and 125 and 150 MHz for carbon spectra, respectively. Chemical shifts were recorded as δ values in parts per million (ppm). Spectra were acquired in deuteriochloroform (CDCl_3) at 20 $^\circ\text{C}$ unless otherwise stated. For ^1H NMR spectra recorded in CDCl_3 , the peak due to residual CHCl_3 (δ 7.26) was used as the internal reference. ^1H NMR spectra are reported as follows: chemical shift (δ) [multiplicity (where multiplicity is defined as: br = broad; s = singlet; d = doublet; t = triplet; q = quartet; m = multiplet, or combinations thereof), coupling constant(s) J (Hz), relative integral, and assignment (where possible)]. ^{13}C NMR spectra were conducted using the attached proton test (APT) and the central peak (δ 77.0) of the CDCl_3 triplet was used as the internal reference. For ^{13}C NMR spectra, the data are reported as: chemical shift (δ) [protonicity (where protonicity is defined as: C = quaternary; CH = methine; CH_2 = methylene; Me = methyl); assignment (where possible)]. The assignments of various NMR spectra were often assisted by homonuclear ($^1\text{H}/^1\text{H}$) correlation spectroscopy (COSY), nuclear Overhauser effect (nOe) and/or heteronuclear ($^1\text{H}/^{13}\text{C}$) correlation spectroscopy (HETCOR) experiments. For ^1H NMR spectra recorded in d_5 -pyridine the most downfield residual pyridine peak was used as a reference (8.60 ppm). For ^{13}C NMR spectra, the most downfield triplet was used as a reference (149.9 ppm).

Infrared spectra (ν_{max}) were recorded on a Perkin-Elmer Spectrum *One* instrument. Samples were analysed as thin films on NaCl discs.

Low and high resolution mass spectra were recorded on a VG Fisons AutoSpec three sector (E/B/E) double focussing mass spectrometer, using positive-ion electron impact techniques (unless otherwise stated). Mass spectra data are listed as follows:

mass-to-charge ratio (m/z) (assignment [where possible]; intensity as relative % of base peak).

Optical rotations were measured with a Perkin-Elmer 241 polarimeter at the sodium D-line (589 nm) using the spectroscopic grade solvents specified at 20 °C and at the concentrations (c) (g/100 mL) indicated. The measurements were carried out in a cell with a path length of 1 dm. Specific rotations ($[\alpha]_D^{20}$) were calculated using the equation $[\alpha]_D = (100 \cdot \alpha) / (c \cdot l)$ and are given in $10^{-1} \cdot \text{deg} \cdot \text{cm}^2 \cdot \text{g}^{-1}$.

Melting points were recorded on a Reichert hot-stage apparatus and are uncorrected.

Elemental analyses were performed by the Australian National University Microanalytical Services Unit based in the Research School of Chemistry, The Australian National University, Canberra, Australia.

Analytical thin layer chromatography (TLC) was conducted on aluminum backed 0.2 mm thick silica gel 60 F₂₅₄ plates (Merck) and the chromatographs visualised under a 254 nm UV lamp and/or by treatment with vanillin dip (1.7 g vanillin, 225 mL ethanol, 45 mL acetic acid and 15 mL conc. sulfuric acid), followed by heating. The retention factor (R_f) quoted is rounded to the nearest 0.1. Flash chromatography was conducted according to the method of Still and co-workers¹ using silica gel 60 (mesh size 0.040–0.063 mm) as the stationary phase and the analytical (AR) grade solvents indicated.

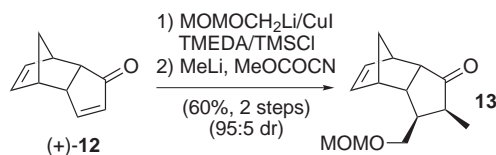
Many materials and reagents were available from the Aldrich Chemical Company and were used as supplied or simply dried and distilled. Magnesium sulfate for drying was purchased from the Aldrich Chemical Company, and other inorganic salts were purchased from BDH or Asia Pacific Specialty Chemicals. Reactions employing air and moisture sensitive reagents and intermediates were conducted under an atmosphere of dry, oxygen free nitrogen in flame dried apparatus.

Room temperature is assumed to be *ca.* 18 °C.

THF and diethyl ether were dried using sodium metal and then distilled, as required, from sodium benzophenone ketyl. DCM and benzene were distilled from calcium hydride.

Organic solutions obtained from workup of reaction mixtures were dried with magnesium sulfate (MgSO₄). Organic solutions were concentrated under reduced pressure on a Büchi rotary evaporator with the water bath generally not exceeding 40 °C. Samples were then subjected to high vacuum to remove any remaining solvent.

Compound 13



n-BuLi/hexanes (1.6 M, 5.5 mL, 13.7 mmol) was added dropwise to a stirred solution of *n*-Bu₃SnCH₂MOM (5.0 g, 13.7 mmol) in THF (30 mL) at -78°C under a nitrogen atmosphere. After 5 min the reaction mixture was transferred *via* cannula to a stirred solution of CuI (1.3 g, 6.84 mmol) and TMEDA (3.1 mL, 20.5 mmol) in THF (15 mL) at -78°C under a nitrogen atmosphere and the resulting mixture stirred for 30 min before TMSCl (2.6 mL, 20.5 mmol) and a solution of (+)-**12** (1.0 g, 6.84 mmol) in THF (20 mL) were added consecutively. After 45 min the reaction was quenched with saturated aqueous NH₄Cl solution (10 mL) and allowed to warm to room temperature. Following dilution with water (100 mL) and 10% aqueous ammonia solution (5 mL), the mixture was extracted twice with diethyl ether (150 mL) and the combined organic layers washed with brine (100 mL) and dried (MgSO₄). Concentration *in vacuo* followed by flash chromatography on a column of silica gel using petroleum spirits 60–80 $^{\circ}\text{C}$, then 5% ethyl acetate in petroleum spirits 60–80 $^{\circ}\text{C}$ as the eluant, afforded the unstable silyl enol ether (1.87g) which was used immediately in the next reaction.

MeLi/diethyl ether (1.0 M, 6.4 mL, 6.4 mmol) was added dropwise to a solution of the silyl enol ether (1.87 g, 6.4 mmol) in THF (50 mL) at -20°C under a nitrogen atmosphere, stirring was continued at -20°C for 30 min and then, after cooling to -78°C , HMPA (5.5 mL, 32 mmol) and MeI (1.98 mL, 32 mmol) were added. After 30 min the reaction mixture was allowed to gradually warm to -20°C and then stirred for a further 1 h before aqueous NH₄Cl solution (10 mL) was carefully added. The mixture was allowed to warm to room temperature then diluted with water (100 mL) and twice extracted with diethyl ether (100 mL). The combined organic layers were then washed with brine (75 mL) and dried (MgSO₄). Concentration *in vacuo* followed by flash chromatography on a column of silica gel using 10% ethyl acetate in petroleum spirits 60–80 $^{\circ}\text{C}$ as the eluant, gave the ketone **13** (95:5 diastereoselection, 881 mg, 60%) as a colourless oil.

Rf 0.50 (3:1, petroleum spirits 60–80 $^{\circ}\text{C}$:ethyl acetate)

[α]_D²⁰ +131.7 $^{\circ}$ (*c* 0.67 CHCl₃)

IR ν_{\max} 2933, 1730, 1455, 1182, 1149, 1108, 1052, 917 cm^{-1} .

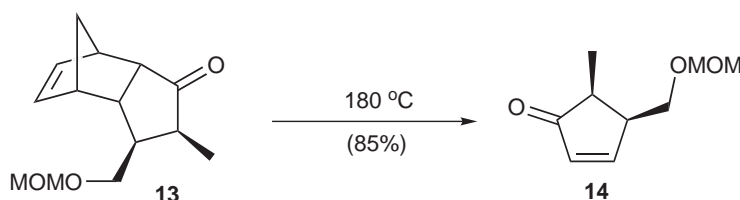
^1H NMR: 0.95 (d, 3 H, $J = 7.3$ Hz, CHMe), 1.41 (dt, 1 H, $J = 8.2, 1.4$ Hz, H8), 1.53 (dt, 1 H, $J = 8.2, 1.6$ Hz, H8'), 2.01 (m, 1 H, H3), 2.18 (m, 1 H, H2), 2.70 (ddd, 1 H, $J = 9.2, 4.1, 2.2$ Hz, H3a), 2.91 (dd, 1 H, $J = 9.2, 4.7$ Hz, H7a), 3.05 (m, 1 H, H4), 3.18 (m, 1 H, H7), 3.34 (s, 3 H, OMe), 3.45, 3.53 (AB d, 2 H, $J = 9.3$ Hz, CH_2OMOM), 4.55 (s, 2 H, OCH_2OMe), 6.07 (dd, 1 H, $J = 5.6, 2.9$ Hz, H6), 6.22 (dd, 1 H, $J = 5.6, 3.0$ Hz, H5).

^{13}C NMR: 9.5 (Me), 39.7 (CH), 44.1 (CH), 46.9 (CH), 47.1 (CH), 47.3 (CH), 52.4 (CH_2), 53.4 (CH), 55.3 (OMe), 69.3 (CH_2), 96.5 (CH_2), 134.6, 136.0 ($2 \times =\text{CH}$), 220.8 (C, CO).

MS: m/z 236 (M^+ , 5%), 191 (3), 171 (48), 139 (50), 109 (47), 91 (32), 81 (39), 66 (100).

HRMS: calcd for $\text{C}_{14}\text{H}_{20}\text{O}_3$ 236.1412, found 236.1415.

Compound 14



Nitrogen was bubbled through a stirred solution of ketone **13** (800 mg, 3.4 mmol) in 1,2-dichlorobenzene (6 mL) at reflux for 7 h. After cooling to room temperature the reaction mixture was subjected to immediate flash chromatography on a column of silica gel using petroleum spirits 60–80 °C, then 50% ethyl acetate in petroleum spirits 60–80 °C as the eluant, to give the enone **14** (507 mg, 85%) as a colourless oil.

Rf 0.27 (3:1, petroleum spirits 60–80 °C:ethyl acetate)

$[\alpha]_{\text{D}}^{20}$ +234.9° (c 0.48 CHCl_3)

IR ν_{\max} 2883, 1709, 1588, 1458, 1383, 1354, 1187, 1150, 1109, 1036 cm^{-1} .

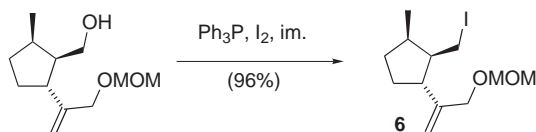
^1H NMR: 1.15 (d, 3 H, $J = 7.6$ Hz, CHMe), 2.52 (m, 1 H, H5), 3.52 (m, 1 H, H4), 3.35 (s, 3 H, OMe), 3.55 (dd, 1 H, $J = 10.5, 7.0$ Hz, CH_2OMOM), 3.70 (dd, 1 H, $J = 9.6, 6.9$ Hz, CH_2OMOM), 4.60 (s, 2 H, OCH_2OMe), 6.24 (dd, 1 H, $J = 5.9, 2.0$ Hz, H2), 7.67 (dd, 1 H, $J = 5.9, 2.6$ Hz, H3).

^{13}C NMR: 10.5 (Me), 42.1 (CH), 45.1 (CH), 55.4 (OMe), 67.0 (CH_2), 96.5 (CH_2), 133.5 (CH, C2), 164.2 (CH, C3), 211.8 (C, CO).

MS: m/z 170 (M^+ , 15%), 140 (100), 125 (5), 108 (34), 95 (21), 81 (51), 75 (39), 67 (29).

HRMS: calcd for $\text{C}_9\text{H}_{14}\text{O}_3$ 170.0943, found 170.0943

Compound 6



Iodine (3.6 g, 14.0 mmol) was added to a stirred solution of the alcohol (2.0 g, 9.3 mmol) and triphenylphosphine (3.7g, 14.0 mmol) in 3:1 diethyl ether:acetonitrile (80 mL) at room temperature under a nitrogen atmosphere. After 30 min the mixture was diluted with saturated aqueous sodium bicarbonate solution (100 mL) and twice extracted with diethyl ether (100mL). The combined organic layers washed with brine (100 mL), dried (MgSO_4) and the solvent removed *in vacuo*. The resulting residue was taken up in diethyl ether, and the insoluble triphenylphosphine oxide removed by filtration. The mother liquor was evaporated and the residue subjected to flash chromatography on a column of silica gel using 5% diethyl ether in hexanes as the eluant, to give **6** (2.9 g, 96%) as a pale oil.

Rf 0.92 (3:1, petroleum spirits 60–80 °C:ethyl acetate)

[α] $^{20}_{\text{D}}$ -64.7° (*c* 0.30 CHCl_3)

IR ν_{max} 2953, 1646, 1464, 1428, 1378, 1211, 1150, 1104, 1052 cm^{-1} .

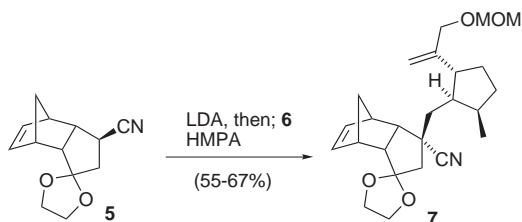
^1H NMR: 0.88 (d, 3 H, $J = 6.7$ Hz, CHMe), 1.37 (m, 1 H), 1.60 (m, 1 H), 1.86 (m, 1 H), 2.05 (m, 1 H), 2.31 (m, 3 H), 2.93 (apparent t, 1 H, $J = 9.8$ Hz, CH_2I), 3.28 (dd, 1 H, $J = 9.5, 3.5$ Hz, $\text{CH}_2\text{I}'$), 3.39 (s, 3 H, OMe), 4.01 (s, 2 H, CH_2OMOM), 4.64 (s, 2 H, OCH_2OMe), 4.97, 5.13 (br s, 2×1 H, $=\text{CH}_2$).

^{13}C NMR: 7.3 (CH_2I), 14.7 (Me), 31.5 (CH_2), 31.6 (CH_2), 36.0 (CH), 47.0 (CH), 50.2 (CH), 55.4 (OMe), 69.0 (CH_2), 95.6 (CH_2), 111.5 ($=\text{CH}_2$), 147.2 ($=\text{C}$).

MS: m/z 279 ($[\text{M}-45]^+$, 27%), 264 (6), 235 (36), 165 (18), 147 (42), 135 (64), 121 (32), 107 (64), 95 (90), 81 (100), 67 (59).

HRMS: calcd for $\text{C}_{12}\text{H}_{21}\text{O}_2\text{I}$ 324.0586, found 324.0590

Compound 7



A solution of LDA/THF (1.0 M, 23.1 mL, 23.1 mmol) was added dropwise to a stirred solution of nitrile **5** (2.0 g, 9.25 mmol) in THF (60 mL) at -78°C under a nitrogen atmosphere. After 30 min the reaction mixture was allowed to warm to room temperature and stir for 1h before being cooled to -78°C . HMPA (1.6 mL, 9.25 mmol) and a solution of iodide **6** (1.5 g, 4.63 mmol) in THF (40 mL) was added and the mixture stirred at -78°C for 2h. A saturated solution of aqueous ammonium chloride (10 mL) was added and the mixture warmed to room temperature, diluted with 1.0 M HCl (300 mL) and extracted three times with diethyl ether (150 mL). The combined organic layers were washed with brine (500 mL) and dried (MgSO_4). Concentration *in vacuo* followed by flash chromatography on a column of silica gel using 15% ethyl acetate in petroleum spirits $60\text{--}80^{\circ}\text{C}$ as the eluant, afforded the desired product **7** (1.1 g, 58% based on iodide) as a pale oil. Further elution afforded recovered nitrile **5** (1.2 g, 5.53 mmol). Product yield based on nitrile **5** was 73% (based on recovered **5**).

Rf 0.52 (3:1, petroleum spirits $60\text{--}80^{\circ}\text{C}$:ethyl acetate)

[α] $^{20}_{\text{D}}$ -19.9° (*c* 0.84 CHCl_3)

IR ν_{max} 2951, 2230, 1646, 1431, 1334, 1210, 1150, 1113, 1052 cm^{-1} .

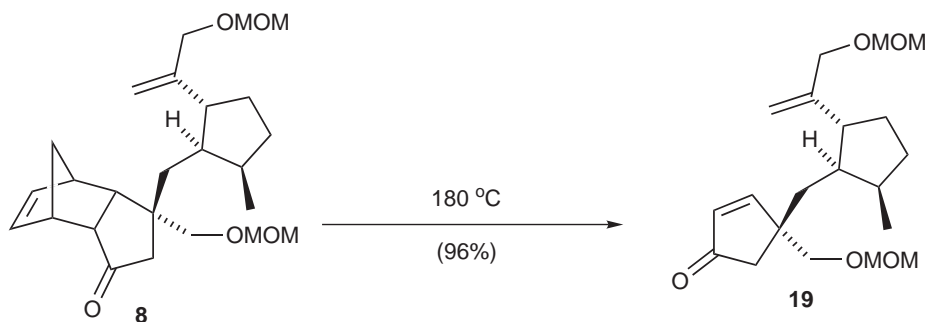
^1H NMR: 0.89 (d, 3 H, $J = 7.0$ Hz, CHMe), 1.27 (d, 1 H, $J = 8.2$ Hz, H'_8), 1.34–1.54 (m, 4 H), 1.68–2.08 (m, 4 H), 1.88 (d, 1 H, $J = 13.8$ Hz, H'_2), 2.14 (d, 1 H, $J = 13.9$ Hz, H'_2'), 2.28–2.46 (m, 2 H), 2.71 (m, 2 H), 2.93, 3.09 (s, 2×1 H, $\text{H}'_4 + \text{H}'_7$), 3.38 (s, 3 H, OMe), 3.78–3.94 (m, 4 H, $\text{H}_4, 4' + \text{H}_5, 5'$), 4.04 (s, 2 H, CH_2OMOM), 4.65 (s, 2 H, OCH_2OMe), 5.01, 5.15 (s, 2×1 H, $=\text{CH}_2$), 6.22 (dd, 1 H, $J = 5.7, 3.1$ Hz, H'_5 or H'_6), 6.41 (dd, 1 H, $J = 5.6, 2.9$ Hz, H'_6 or H'_5).

^{13}C NMR: 15.0 (Me), 28.2 (CH_2), 32.9 (CH_2), 35.0 (CH), 37.3 (C), 44.4 (CH), 46.0 (CH), 46.8 (CH), 47.5 (CH), 47.6 (CH_2), 51.0 (CH_2), 53.7 (CH), 54.3 (CH), 55.1 (OMe), 63.6 (CH_2), 64.2 (CH_2), 68.6 (CH_2), 95.4 (CH_2), 1115.5 ($=\text{CH}_2$), 115.8 (C, C2), 123.7 (CN), 133.4, 137.6 ($2 \times =\text{CH}$), 147.3 ($=\text{C}$).

MS: m/z 413 (M^+ , 3.2%), 284 (14), 268 (83), 352 (55), 316 (23), 286 (100), 261 (35), 229 (64), 216 (39), 164 (912), 89 (30), 66 (78).

HRMS: calcd for $\text{C}_{25}\text{H}_{36}\text{NO}_4$ 414.2622, found 414.2643.

Compound 19



A solution of ketone **8** (300 mg, 0.72 mmol) in 1,2-dichlorobenzene (3.0 mL) was heated at 180 °C under a stream of nitrogen gas from a cylinder for 24 h. After cooling to room temperature the mixture was subjected to flash chromatography on a column of silica gel using 40% ethyl acetate in hexanes, as the eluant, to afford enone **19** (243 mg, 96%) as a pale oil.

Rf 0.32 (3:1, petroleum spirits 60–80 °C:ethyl acetate)

[α]_D²⁰ –31.3° (*c* 0.75 CHCl₃)

IR ν_{max} 2949, 1715, 1675, 1587, 1465, 1442, 1379, 1213, 1150, 1109, 1044 cm^{–1}.

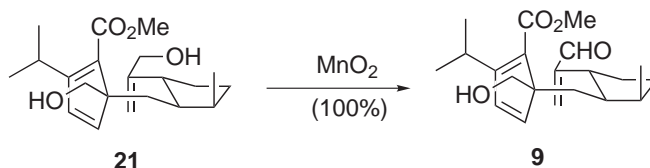
¹H NMR: 0.80 (d, 3 H, *J* = 7.0 Hz, CHMe), 1.25–2.10 (m, 8 H), 2.23 (m, 1 H), 2.24 (s, 2 H, H5), 3.30 (s, 3 H, OMe), 3.34 (s, 3 H, OMe), 3.45 (AB d, 2 H, *J* = 9.2 Hz, CH₂OMOM), 3.94 (s, 2 H, =CCH₂OMOM), 4.55, 4.60 (s, 2 × 2 H, 2 × OCH₂OMe), 4.89, 5.08 (s, 2 × 1 H, =CH₂), 6.11 (d, 1 H, *J* = 5.7 Hz, H2), 7.50 (d, 1 H, *J* = 5.7 Hz, H3).

¹³C NMR: 15.6 (Me), 28.8 (CH₂), 32.9 (CH₂), 33.0 (CH₂), 35.2 (CH), 42.9 (C), 43.3 (CH₂), 47.6 (CH), 49.7 (CH₂), 55.4 (2 × OMe), 68.9 (CH₂), 73.7 (CH₂), 95.7 (CH₂), 96.5 (CH₂), 112.1 (=CH₂), 134.0 (CH, C2), 147.5 (=C), 169.0 (CH, C3), 209.0 (CO).

MS: *m/z* 352 (M⁺, 1%), 291 (10), 277 (65), 217 (50), 159 (45), 122 (78), 107 (98), 95 (100), 67 (45).

HRMS: calcd for C₂₀H₃₂O₅ 352.2250, found 352.2247

Compound 9



Manganese dioxide (250 mg) was added to a solution of the diol **21** (50 mg, 0.15 mmol) in diethyl ether (2 mL) at room temperature. After 30 min the solution was filtered through a pad of celite and the solvent removed *in vacuo* to afford pure **9** (50 mg, 100%).

Rf 0.3 (3:1, petroleum spirits 60–80 °C:ethyl acetate)

[α]_D²⁰ −180.0° (*c* 0.38 CHCl₃)

IR ν_{max} 3435, 2954, 1639, 1527, 1464, 1435, 1377, 1324, 1241, 1191, 1096 cm^{−1}.

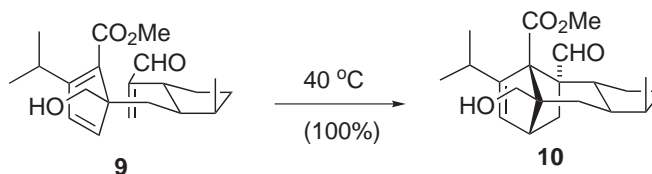
¹H NMR: 0.80 (d, 3 H, *J* = 6.9 Hz, CHMe), 1.11 (d, 3 H, *J* = 6.7 Hz, CHMe₂), 1.15 (d, 3 H, *J* = 6.7 Hz, CHMe₂'), 1.20–1.42 (m, 3 H), 1.64–2.00 (m, 5 H), 2.55 (m, 1 H), 3.54 (d, 1 H, *J* = 10.4 Hz, CH₂OH), 3.65 (obscured m, 1 H, CHMe₂), 3.74 (s, 3 H, OMe), 3.75 (obscured d, 1 H, CH₂OH'), 5.91 (s, 1 H, =CH₂), 6.09 (s, 1 H, =CH₂'), 6.49 (d, 1 H, *J* = 5.4 Hz, H3), 6.58 (d, 1 H, *J* = 5.4 Hz, H4), 9.48 (s, 1 H, CHO).

¹³C NMR: 14.7 (Me), 21.7 (Me), 21.9 (Me), 27.6 (CH), 28.7, 29.3, 32.9 (2 × CH₂ + C), 36.1 (CH), 41.9 (CH), 44.1 (CH), 51.1 (OMe), 62.5 (CH₂), 67.3 (CH₂), 130.3 (CH, C3), 131.1 (=CH₂), 133.4 (C, C1), 149.2 (CH, C4), 153.3 (=C), 166.0 (CO₂Me), 166.8 (C, C2), 194.4 (CHO).

MS: *m/z* 346 (M⁺, 13%), 328 (38), 316 (40), 284 (100), 269 (36), 256 (44), 241 (34), 180 (57), 147 (83), 133 (57), 119 (79), 105 (65), 91 (72).

HRMS: calcd for C₂₁H₃₀O₄ 346.2144 found 346.2147.

Methyl 19-Hydroxy-17-oxo-sordaric-1-en-18-oate (Compound 10)



A solution of aldehyde **9** (60 mg, 0.17 mmol) in d₈-toluene (1.5 mL) was heated at 40 °C for 3 days after which time the solvent was removed, *in vacuo*, to give pure ester **10** (60 mg, 100%).

Rf 0.3 (2:1, ethyl acetate:petroleum spirits 60–80 °C)

[α]²⁰_D synthetic: –65.1 ° (c 0.38 CHCl₃)

IR ν_{max} 3434, 2955, 2869, 1721, 1435, 1382, 1291, 1268, 1066 cm^{–1}.

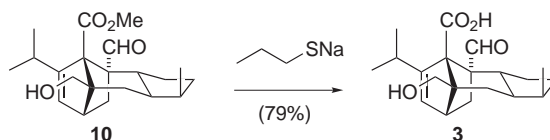
¹H NMR: 0.79 (d, 3 H, *J* = 7.2 Hz, H₂₀), 0.89, 1.05 (d, 2 × 3 H, *J* = 6.9 Hz, H₁₅ + H₁₆), 1.24 (m, 3H), 1.70–1.80 (m, 3 H), 1.90–2.12 (m, 5 H), 2.25 (heptet d, 1 H, *J* = 6.9, 1.0 Hz, H₁₄), 2.58 (t, 1 H, *J* = 4.1 Hz, H₃), 3.53, 3.90 (AB d, 2 × 1 H, *J* = 11.3 Hz, CH₂OH), 3.80 (s, 3 H, OMe), 6.08 (dd, 1 H, *J* = 3.5, 1.3 Hz, H₂), 9.64 (s, 1 H, CHO).

¹³C NMR: 17.4 (Me, C₂₀), 21.0, 22.1 (2 × Me, C₁₅ + C₁₆), 26.5 (CH₂, C₁₁), 27.8 (CH, C₁₄), 27.9, 30.0 (2 × CH₂, C₈ + C₁₂), 31.1 (CH, C₁₀), 32.0 (CH₂, C₄), 41.3, 41.4, 47.0 (3 × CH, C₃, C₉ + C₁₃), 52.3 (C, C₅), 66.8, 66.9 (2 × C, C₆ + C₇), 72.6 (CH₂, C₁₉), 130.5 (CH, C₂), 147.8 (C, C₁), 173.6 (C, C₁₈), 203.7 (CH, C₁₇).

MS: *m/z* 346 (M⁺, 34%), 328 (36), 315 (50), 284 (100), 269 (32), 255 (37), 239 (24), 180 (48), 147 (84), 133 (50), 119 (74), 105 (60), 91 (74).

HRMS: calcd for C₂₁H₃₀O₄ 346.2144, found 346.2144.

Sordaricin (Compound 3)



Freshly distilled propanethiol (700 μL , 7.72 mmol) was added to a stirred suspension of NaH (240 mg, 10 mmol) in HMPA (5.0 mL) at room temperature under a nitrogen atmosphere. The solution was stirred for 2 h, then allowed to stand for 1 h to give a 1.35 M solution of propanethiolate. To a dried flask containing the ester **10** (60 mg, 0.17 mmol) and a stirrer bar was added a solution propanethiolate/HMPA (1.35 M, 2.0 mL, 2.7 mmol) and the solution stirred under a nitrogen atmosphere for 48 h. The reaction mixture was diluted with ethyl acetate (20 mL) and washed twice with water (30 mL). The combined aqueous layers were extracted twice with ethyl acetate (20 mL), then the combined organic layers were washed with brine (25 mL) and dried (MgSO_4). Concentration *in vacuo* followed by flash chromatography on a column of silica gel using 20% ethyl acetate in hexanes, then 60% ethyl acetate in hexane as the eluent afforded sordaricin (**3**, 45 mg, 79%) as a white solid.

Rf 0.15 (1:1, petroleum spirits 60–80 $^\circ\text{C}$:ethyl acetate, 1 drop acetic acid)

mp 189–191 $^\circ\text{C}$, lit.² 190–191 $^\circ\text{C}$

$[\alpha]^{20}_{\text{D}}$ synthetic: -55.3° (*c* 0.19 MeOH), natural: -58.4° (*c* 0.19 MeOH), lit.² -64° (*c* 0.374 MeOH),

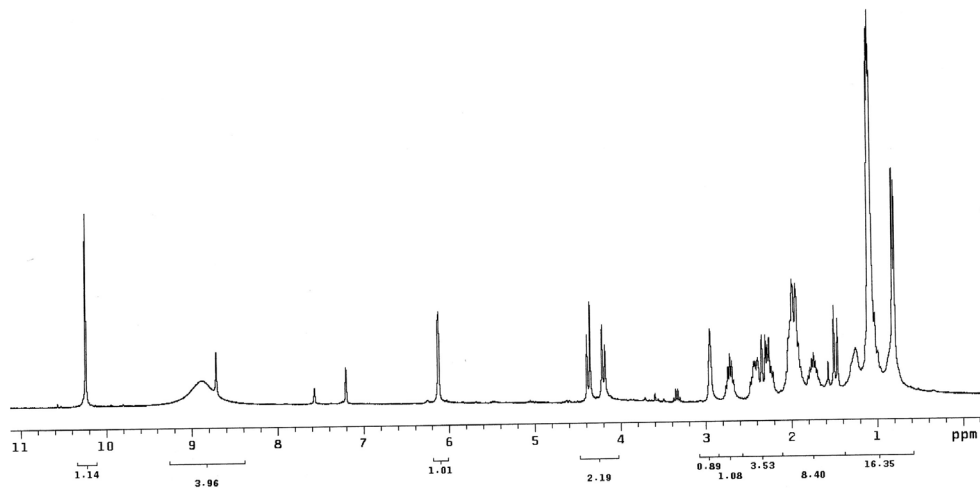
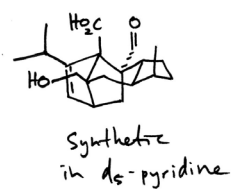
IR ν_{max} 3350, 2954, 2868, 1712, 1446, 1378, 1289, 1234, 1017 cm^{-1} .

^1H NMR: d_5 -pyridine: 0.80 (d, 3 H, $J = 6.6$ Hz, H20), 1.08 (m, 6 H, H15 + H16), 1.48 (d, 1 H, $J = 12.5$ Hz, H4 α), 1.74 (m, 1 H), 1.95 (m, 5 H), 2.20–2.50 (m, 3 H), 2.72 (heptet, 1 H, $J = 6.7$ Hz, H14), 2.97 (t, 1 H, $J = 3.8$ Hz, H3), 4.20, 4.37 (AB d, 2×1 H, $J = 10.5$ Hz, CH_2OH), 6.13 (d, 1 H, $J = 3.1$ Hz, H2), 8.85 (variable br s, 1 H, CO_2H), 10.24 (s, 1 H, CHO).

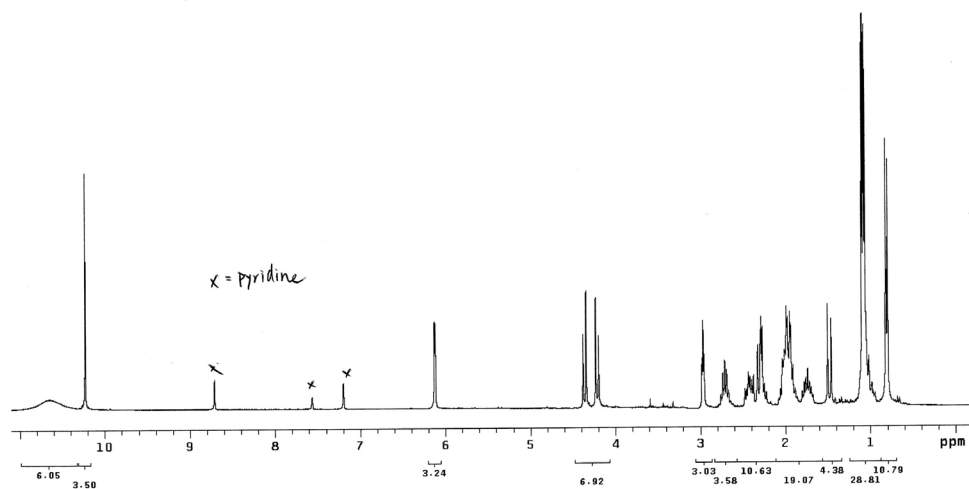
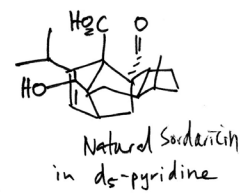
^{13}C NMR: d_5 -pyridine: 17.7 (Me, C20), 21.3, 22.7 ($2 \times$ Me, C15 + C16), 26.9 (CH_2 , C11), 28.2 (CH, C14), 29.1, 29.7 ($2 \times \text{CH}_2$, C8 + C12), 31.6 (CH, C10), 32.4 (CH_2 , C4), 41.9, 42.0, 47.1 ($3 \times \text{CH}$, C3, C9 + C13), 59.4 (C, C5), 66.9, 67.5 ($2 \times \text{C}$, C6 + C7), 73.8 (CH_2 , C19), 130.9 (CH, C2), 148.9 (C, C1), 176.0 (C, C18), 204.8 (CH, C17).

MS: m/z 332 (M^+ , 24%), 314 (33), 302 (40), 284 (90), 256 (37), 241 (40), 227 (35), 166 (64), 147 (67), 119 (64), 105 (72), 91 (100).

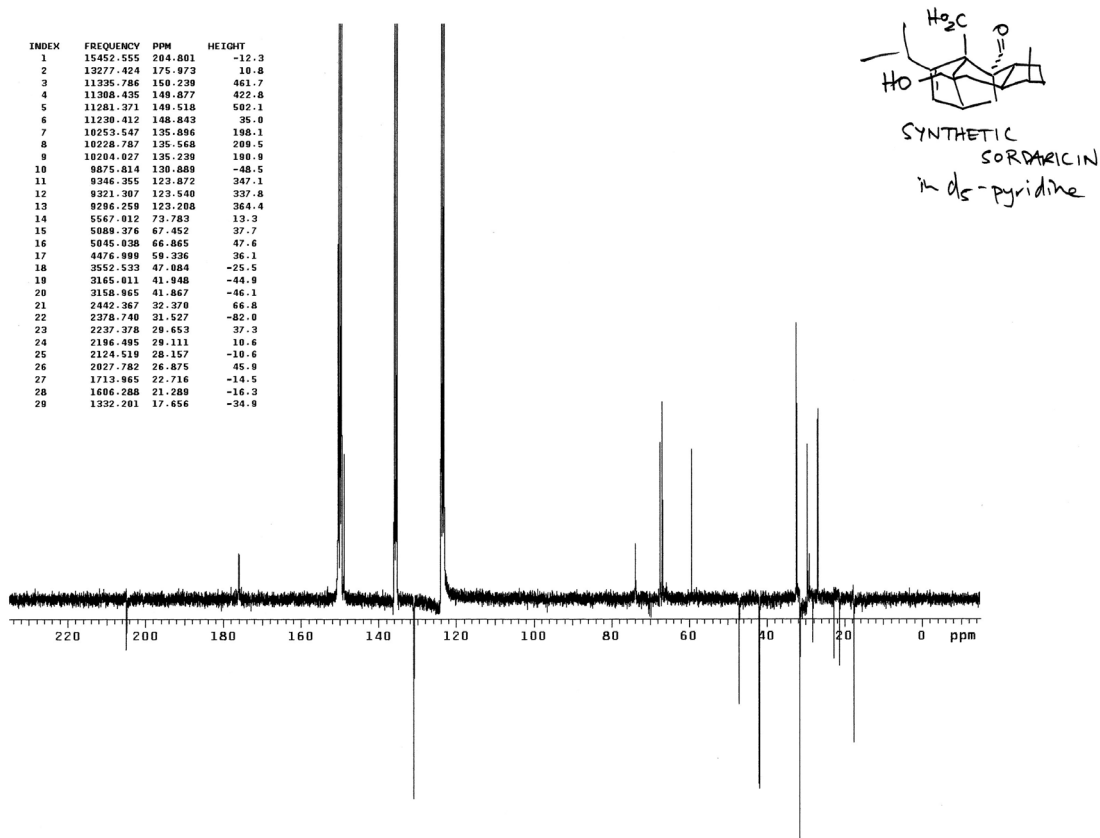
HRMS: calcd for $\text{C}_{21}\text{H}_{30}\text{O}_4$ 332.1988, found 332.1986.



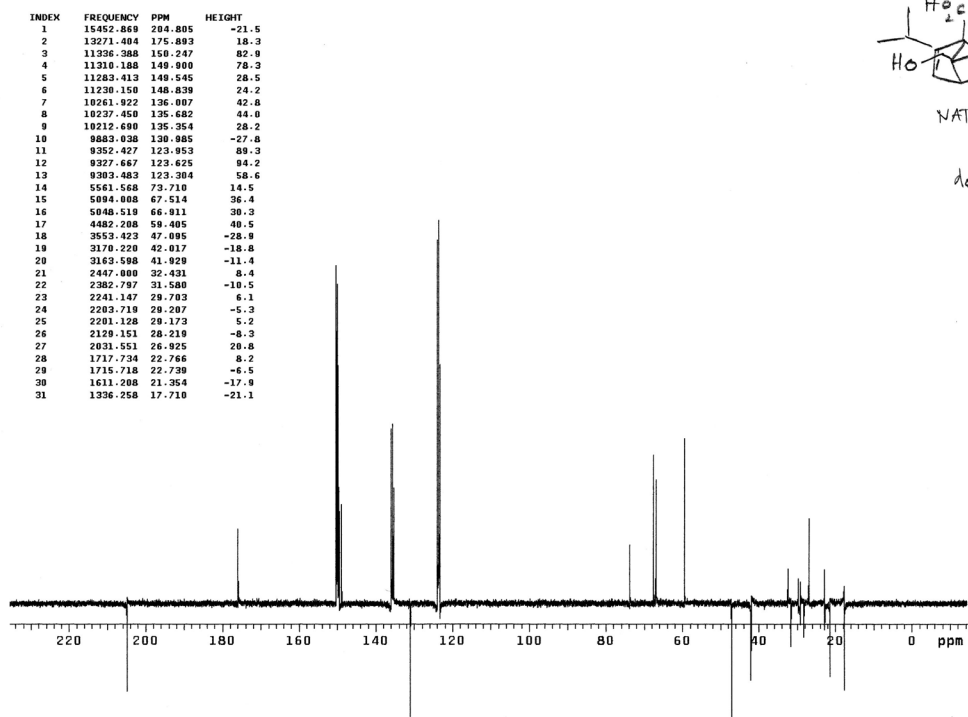
Proton spectra at 300 MHz of synthetic sordaricin in d_5 -pyridine



Proton spectra at 300 MHz of natural sordaricin in d_5 -pyridine



APT spectra at 75 MHz of synthetic sordaricin in d₅-pyridine



APT spectra at 75 MHz of natural sordaricin in d_5 -pyridine

1. Still, W.C.; Kahn, M.; Mitra, A. *J. Org. Chem.* **1978**, *43*, 2923.
2. Vasella, A. T. Ph.D. Dissertation. Eidgenossischen Technischen Hochschule, Zurich, 1972.