

Supplementary Material (ESI) for Chemical Communications
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SUPPLEMENTARY MATERIALS

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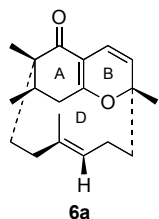
Unique Structural Topology and Reactivities of the ABD Tricycle in Phomactin A.

authored by

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(±)-2β,6β,7β-Trimethyl-2α,6α-(3'-methyl-3'E-hexeno)-2,6,7,8-tetrahydro-5-chromenone (6a).



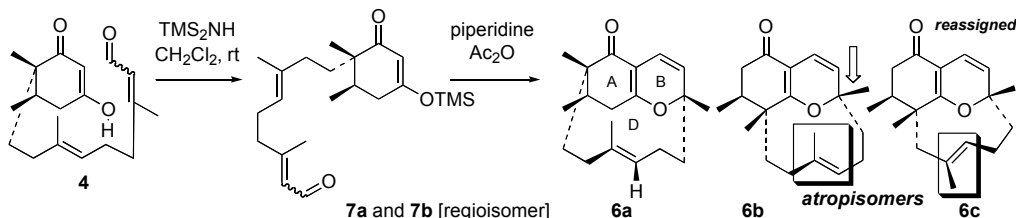
Original procedure:

Enal **4** (39.1 mg, 0.128 mmol) was taken up in THF (200 mL) and piperidinium acetate (37.2 mg, 0.256 mmol) was added. The solution was stirred overnight at rt. The following morning the THF was removed *in vacuo* and the residue subjected to silica gel flash column chromatography (5-15% EtOAc/hexanes) to afford the desired isomer **6a** (8.4 mg, 23%) and a 4:1 unassignable mixture of **6b** and **6c** (19.4 mg, 53%) as colorless oils.

6a: R_f = 0.41 (10% EtOAc/hexanes);

^1H NMR (500 MHz, CDCl_3) δ (ppm) 6.45 (d, 1 H, J = 10.5 Hz), 5.15 (brd, 1 H, J = 10.5 Hz), 4.99 (d, 1 H, J = 10.5 Hz), 2.87 (dd, 1 H, J = 6.5, 20.0 Hz), 2.40-2.29 (m, 2 H), 2.12(m, 1 H), 2.10 (d, 1 H, J = 19.5 Hz), 2.06 (ddd, 1 H, J = 1.5, 7.5, 14.5 Hz), 1.94 (dt, 1 H, J = 3.5, 14.0 Hz), 1.94 (ddd, 1 H, J = 2.0, 4.0, 14.5 Hz), 1.89 (ddd, 1 H, J = 3.5, 12.5, 15.0 Hz), 1.80 (td, 1 H, J = 3.5, 14.5 Hz), 1.70 (ddd, 1 H, J = 3.0, 6.0, 15.0 Hz), 1.47 (s, 3 H), 1.38 (brm, 3 H), 1.07 (s, 3 H), 1.02 (d, 3 H, J = 7.0 Hz); ^{13}C NMR (75 MHz, CDCl_3) δ (ppm) 198.6, 169.1, 134.6, 125.3, 119.8, 118.0, 116.0, 82.9, 47.1, 46.1, 39.5, 37.0, 35.7, 34.5, 31.3, 25.2, 24.6, 20.0, 16.1; IR (neat) cm^{-1} 2976 (m), 2929 (m), 2901 (m), 2835 (w), 1640 (vs), 1607 (s), 1449 1449 (m), 1416 (s); mass spectrum (ESI) m/e (% relative intensity) 309.2 ($\text{M}+\text{Na}^+$) (100), 197.0 (13); m/e calcd for $\text{C}_{19}\text{H}_{26}\text{O}_2\text{Na}$ ($\text{M}+\text{Na}^+$) 309.1830, found 309.1818 [δ = 3.89 ppm].

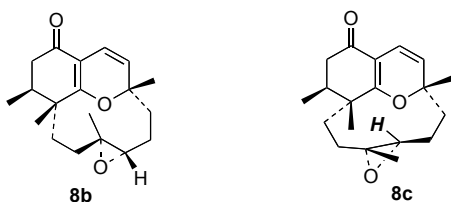
Modified [3 + 3] Procedure:



Enal **4** (1 equiv.) was taken up in CH_2Cl_2 (50 mL/mmol) and TMS_2NH (1.5 equiv.) was added. The solution was stirred for 2 h at rt. Piperidine (1.2 equiv.) was then added, and after

stirring for 10 min, acetic anhydride (6 equiv.) was added. The solution was then stirred at ambient temperature overnight. The following morning, the solution was washed with 1 *M* NaOH until the washings remained basic. The solution was dried and concentrated *in vacuo*. Silica gel flash column chromatography (10-30% EtOAc in hexanes, gradient elution) afforded the desired tricycle **6a** (19%) and a mixture of undesired isomers **6b** and **6c** (19%), which could only be unambiguously characterized through epoxides **8b** and **8c**.

Epoxides 8b and 8c and Characterizations of 6b and 6c:



The mixture of cycloadducts **6b** and **6c** (133.1 mg, 0.465 mmol) was taken up in CH₂Cl₂ (2.0 mL) and cooled to 0 °C with an ice bath. To this solution was added solid *m*-CPBA (77%, 112.1 mg, 0.50 mmol) in a single portion. TLC indicated consumption of starting material within 5 min, at which time dimethyl sulfide (100 μL) was added. It was noted that the product mixture seemed to form two separate spots in the TLC; the upper spot was observed to be highly fluorescent under the short wave UV lamp used for UV indication; the lower spot did not exhibit fluorescence. The solution was diluted with CH₂Cl₂ (15 mL) and washed successively with 1 *M* NaOH (2 mL), water (5 mL), and sat aq. NaCl (5 mL). The organic phase was dried with Na₂SO₄ and the crude ¹H NMR indicated clean and quantitative conversion of both isomers to the corresponding epoxides. The mixture of isomers was partially separated using silica gel flash column chromatography to afford analytical samples of **8b** and **8c**.

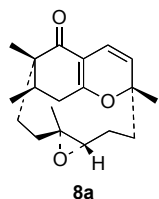
8b: *R_f* = 0.39 (60% EtOAc in hexanes); white solid, mp = 110-114 °C;

¹H NMR (300 MHz, toluene *d*₈, 80 °C: significant line broadening at rt) δ 0.66 (d, 3H, *J* = 6.9 Hz), 0.81 (s, 3H), 1.06 (s, 3H), 1.10 (s, 3H), 1.20-1.41 (m, 5H), 1.50-1.60 (m, 3H), 1.61-1.72 (m, 2H), 1.76-1.86 (m, 2H), 2.04 (d, 1H, *J* = 17.1 Hz), 2.37 (dd, 1H, *J* = 4.8, 17.1 Hz), 2.71 (d, 1H, *J* = 9.9 Hz), 4.61 (d, 1H, *J* = 10.2 Hz), 6.64 (d, 1H, *J* = 10.2 Hz); ¹³C NMR: **Not possible given the line broadening even at 80 °C in toluene *d*₈**; mass spectrum (ESI) *m/e* (% relative intensity) 627.3 (2M + Na)⁺ (35), 325.2 (M + Na)⁺ (100), 303.2 (M + H)⁺ (93); *m/e* calcd for C₁₉H₂₆NaO₃⁺ 325.1774, found 325.1781 [δ = 2.15 ppm].

8c: R_f = 0.41 (60% EtOAc in hexanes); white solid; mp = 85-88 °C;

^1H NMR (500 MHz, CDCl_3) δ 0.91 (d, 3H, J = 6.5 Hz), 1.07 (dd, 1H, J = 10.5, 14.5 Hz), 1.08 (s, 3H), 1.36 (s, 3H), 1.39 (m, 1H), 1.39 (s, 3H), 1.70 (m, 2H), 1.93 (m, 3H), 2.20 (m, 2H), 2.28 (s, 1H), 2.29 (d, 1H, J = 2.0 Hz), 2.73 (dd, 1H, J = 6.0, 9.0 Hz), 5.18 (d, 1H, J = 10.0 Hz), 6.51 (d, 1H, J = 11.0 Hz); ^{13}C NMR (75 MHz, CDCl_3) δ 15.1, 17.3, 19.6, 26.1, 29.9, 30.5, 31.7, 33.2, 37.7, 41.4, 42.3, 60.3, 62.7, 84.1, 108.7, 117.3, 120.0, 175.1, 193.8; IR (film, cm^{-1}) 2967 (m), 1653 (vs), 1584 (s), 1454 (m), 1413 (m); mass spectrum (ESI) m/e (% relative intensity) 929.5 $(3\text{M} + \text{Na})^+$ (30), 627.3 $(2\text{M} + \text{Na})^+$ (100), 325.2 $(\text{M} + \text{Na})^+$ (22), 303.2 $(\text{M} + \text{H})^+$ (82); m/e calcd for $\text{C}_{19}\text{H}_{26}\text{NaO}_3^+$ 325.1774, found 325.1780 [δ = 1.85 ppm].

(±)-2 β ,6 β ,7 β -trimethyl-2 α ,6 α -(3'-methyl-3',4'-epoxy-hexano)-2,6,7,8-tetrahydro-5-chromenone (8a).

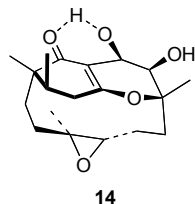


The tricycle **6a** (17.6 mg, 6.14 μmol) was taken up in CH_2Cl_2 (1 mL) and cooled to 0 °C., and after which, solid *m*-CPBA (75%, 20.6 mg, 9.21 μmol) was added in one portion. TLC indicated consumption of the starting material within 2 min. The solution was transferred to a separatory funnel, diluted with CH_2Cl_2 (10 mL), washed with 1 *M* NaOH (1 mL) and sat aq. NaCl (1 mL), and dried with Na_2SO_4 . Silica gel flash column chromatography (20% EtOAc in hexanes) afforded epoxide **8a** (17.8 mg, 96%) as colorless oil.

R_f = 0.34 (30% EtOAc in hexanes);

^1H NMR 1.00 (s, 3H), 1.02 (d, 3H, J = 7.5 Hz), 1.07 (s, 3H), 1.50 (s, 3H), 1.59-1.74 (m, 5H), 1.83-1.97 (m, 3H), 2.09 (quintet, 1H, J = 6.5 Hz), 2.18 (d, 1H, J = 20.0 Hz), 2.88 (d, 1H, J = 6.5 Hz), 3.01 (dd, 1H, J = 6.5, 20.0 Hz), 5.04 (d, 1H, J = 10.5 Hz), 6.62 (d, 1H, J = 10.0 Hz); ^{13}C NMR (75 MHz, toluene d_8 , 80 °C) δ 19.2, 19.3, 24.8, 24.9, 30.8, 35.1, 35.3, 35.6, 38.5, 40.5, 47.5, 61.8, 65.2, 82.5, 111.7, 119.5, 119.6, 167.8, 196.7; IR (neat, cm^{-1}) 2978 (s), 2932 (s), 1641 (vs), 1605 (vs), 1461 (m), 1420 (vs), 1360 (m), mass spectrum (ESI) m/e (% relative intensity) 627.4 $(2\text{M} + \text{Na})^+$ (63), 558.3 (26), 325.2 $(\text{M} + \text{Na})^+$ (45), 307.1 (12), 303.2 $(\text{M} + \text{H})^+$ (100), 277.2 (28), 256.1 (41); m/e calcd for $\text{C}_{19}\text{H}_{26}\text{NaO}_3^+$ 325.1774, found 325.1769 [δ = 1.54 ppm].

(±)-2β,6β,7β-trimethyl-2α,6α-(3'-methyl-3',4'-epoxy-hexano)-5(6*H*)-oxo-7,8-dihydro-chroman-3β,4β-diol (14**).**

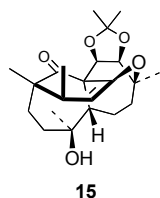


Epoxide **8a** (17.8 mg, 58.9 μmol) was taken up in acetone (1 mL) and water (100 μL). NMO (20.0 mg 170.7 μmol) was added and the solution was cooled to 0 °C. To this acetone solution, 1 drop of a 4% (w/v) solution of OsO₄ was added. The solution was stirred for 4 h, at which time TLC indicated complete conversion. The mixture was transferred to a separatory funnel and 1 mL of a 10% aq. Na₂S₂O₃ (w/v) was added along with EtOAc (10 mL). The mixture was shaken, while the aqueous portion turned dark. The organic layer was washed with sat aq. NaCl (2 mL) and dried with Na₂SO₄. Concentration *in vacuo* and silica gel flash column chromatography (50% EtOAc in hexanes) afforded diol **14** (10.3 mg, 52%) as colorless oil.

R_f = 0.16 (40% EtOAc in hexanes);

¹H NMR (500 MHz, CDCl₃) δ 1.06 (d, 3H, *J* = 7.5 Hz), 1.07 (s, 3H), 1.12 (s, 3H), 1.54 (s, 3H), 1.58-1.73 (m, 4H), 1.80-2.00 (m, 4H), 2.10 (quintet, 1H, *J* = 7.5 Hz), 2.32 (d, 1H, *J* = 20.0 Hz), 2.96 (ddd, 1H, *J* = 2.0, 6.5, 20.0 Hz), 2.98 (d, 1H, *J* = 2.0 Hz), 3.38 (br, 1H), 3.83 (d, 1H, *J* = 5.5 Hz), 4.79 (d, 1H, *J* = 4.0 Hz), 4.91 (s, 1H); ¹³C NMR (75 MHz, toluene *d*₈, 80 °C) δ 19.1, 19.2, 24.6, 25.7, 25.8, 34.4, 35.0 (2C), 35.6, 47.6, 60.9, 63.2, 63.7, 66.4, 69.6, 83.6, 110.2, 169.1, 204.9; IR (neat, cm⁻¹) 3471 (br), 2928 (m), 2882 (m), 1613 (vs), 1461 (m), 1422 (m), 1386 (m), 1364 (m), 1239 (s); mass spectrum (ESI) *m/e* (% relative intensity) 847.6 (21), 435.3 (100), 413.3 (25), 359.2 (M + Na)⁺ (72), 307.1 (19), 277.2 (44), 256.1 (57), 213.1 (35), 191.1 (50); *m/e* calcd for C₁₉H₂₈NaO₅⁺ 359.1829. found 359.1841 [δ = 3.34 ppm].

Acetonide **15.**

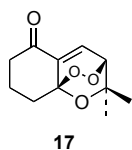


Acetonide **15** was obtained using standard conditions for acetonide formation using PPTS and 2,2-dimethoxypropane.

R_f = 0.30 (50% EtOAc in hexanes);

^1H NMR (500 MHz, CDCl_3) δ 0.87 (d, 3H, J = 7.0 Hz), 1.00 (s, 3H), 1.18 (s, 3H), 1.25-1.30 (m, 2H), 1.34 (s, 3H), 1.35 (s, 3H), 1.38 (s, 3H), 1.75 (dt, 1H, J = 5.0, 15.0 Hz), 1.79 (m, 2H), 1.90 (ddd, 1H, J = 2.5, 4.5, 15.0 Hz), 1.97 (tdd, 1H, J = 2.5, 4.5, 14.0 Hz), 2.30 (td, 1H, J = 7.0, 12.5 Hz), 2.44 (dd, 1H, J = 2.0, 13.0 Hz), 2.51 (td, 1H, J = 7.5, 14.0 Hz), 4.16 (d, 1H, J = 8.0 Hz), 4.86 (d, 1H, J = 8.0 Hz), 4.99 (d, 1H, J = 5.5 Hz); ^{13}C NMR (125 MHz, CDCl_3) δ 19.9, 20.3, 20.8, 24.2, 26.0, 26.1 (2C), 32.8, 38.4, 39.5, 40.1, 51.8, 53.6, 54.5, 73.6, 76.4, 76.6, 76.9, 101.4, 107.6, 151.2, 210.7; IR (neat, cm^{-1}) 3505 (br), 2972 (m), 2934 (m), 1712 (s), 1683 (m), 1377 (s); mass spectrum (ESI) m/e (% relative intensity) 791.7 ($2\text{M} + \text{K}$) $^+$ (15), 775.7 ($2\text{M} + \text{Na}$) $^+$ (30), 415.3 ($\text{M} + \text{K}$) $^+$ (26), 399.3 ($\text{M} + \text{Na}$) $^+$ (52), 377.4 ($\text{M} + \text{H}$) $^+$ (100); m/e calcd for $\text{C}_{22}\text{H}_{32}\text{NaO}_5$ $^+$ 399.2142, found 399.2145 [δ = 0.80 ppm].

(±)-2,2-Dimethyl-3 β ,8 $\alpha\beta$ -peroxy-2,3,6,7,8,8a-hexahydro-5-chromenone (17).

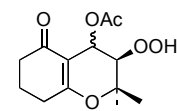


Chromene **16** (121.1 mg, 0.68 mmol) was taken up in THF (10 mL) and a few crystals of Rose Bengal were added. The solution was swirled to ensure complete dissolution of the sensitizer before it was cooled to $-78\text{ }^\circ\text{C}$. A fritted gas filter was connected to an air supply and lowered into the flask with a low rate of bubbling. A 300-W tungsten lamp was placed approximately 0.3 m away from the flask and plugged in. The solution was maintained at $-78\text{ }^\circ\text{C}$, and after 15 min, TLC indicated complete consumption of the starting material. The lamp was turned off, and the flask warmed to rt. Concentration *in vacuo* afforded a pink solid. Filtration through silica (30% EtOAc in hexanes) afforded peroxide **17** (134.3 mg, 94%) as a white solid.

R_f = 0.30 (30% EtOAc in hexanes);

^1H NMR (500 MHz, CDCl_3) δ 1.03 (s, 3H), 1.59 (s, 3H), 1.84-2.80 (m, 4H), 2.42 (ddd, 1H, J = 4.5, 9.5, 18.0 Hz), 2.51 (dddd, 1H, J = 1.0, 4.5, 5.0, 18.5 Hz), 4.53 (d, 1H, J = 6.0 Hz), 7.49 (d, 1H, J = 6.5 Hz); ^{13}C NMR (125 MHz, CDCl_3) δ 18.2, 25.3, 26.3, 30.8, 38.6, 74.9, 98.7, 134.0, 138.4, 194.4; IR (film, cm^{-1}) 2977 (m), 2938 (m), 1694 (vs), 1624 (s), 1265 (s), 1017 (s); mass spectrum (ESI) m/e (% relative intensity) 265.2 ($\text{M} + \text{Na} + \text{MeOH}$) $^+$ (100), 249.2 ($\text{M} + \text{K}$) $^+$ (5).

(±)-4 α -Acetoxy-2,2-dimethyl-3 β -hydroperoxy-5-oxo-3,4,5,6,7,8-hexahydro-2H-chromene **350a** and (±)-4 β -Acetoxy-2,2-dimethyl-3 β -hydroperoxy-5-oxo-3,4,5,6,7,8-hexahydro-2H-chromene **18a** and **18b**.



18: *cis:trans* = 2.5:1

Endoperoxide **17** (37.1 mg, 176.4 μ mol) was dissolved in glacial HOAc and stirred at rt overnight. In the following morning, TLC indicated complete consumption of the starting material. The acid was removed under high vacuum (*ca.* 0.15 mmHg) and a tan solid was obtained. The crude ^1H NMR indicated a diastereomeric ratio of 7 : 3. The isomers were separated by silica gel flash column chromatography (40% EtOAc in hexanes) to afford **18a** (29.1 mg, 61%) as a white solid and **18b** (11.9 mg, 25%) as a white solid.

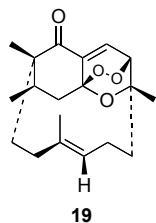
18a: R_f = 0.31 (60% EtOAc in hexanes);

^1H NMR (500 MHz, CDCl_3) δ 1.27 (s, 3H), 1.55 (s, 3H), 1.91-2.09 (m, 2H), 2.12 (s, 3H), 2.40-2.46 (m, 4H), 4.12 (d, 1H, J = 3.5 Hz), 6.01 (d, 1H, J = 4.0 Hz), 11.01 (s, 1H); ^{13}C NMR (125 MHz, CDCl_3) δ 20.6, 21.0, 21.2, 27.9, 29.1, 36.5, 61.1, 78.3, 84.8, 107.5, 172.9, 174.3, 196.3; IR (film, cm^{-1}) 3302 (br), 2984 (w), 2948 (w), 2898 (w), 1748 (m), 1708 (s), 1661 (s), 1621 (vs), 1398 (vs), 1376 (s), 1256 (vs), 1135 (s); mass spectrum (ESI) m/e (% relative intensity) 309.1 ($\text{M} + \text{K}$) $^+$ (21), 293.1 ($\text{M} + \text{Na}$) $^+$ (100), 277.2 ($\text{M} + \text{H}$) $^+$ (17), 256.1 256.1 (16), 211.1 ($\text{M} + \text{H} - \text{AcOH}$) $^+$ (13), 194.1 (26); m/e calcd for $\text{C}_{13}\text{H}_{18}\text{NaO}_6^+$ 293.0996, found 293.1001 [δ = 1.71 ppm].

18b: R_f = 0.45 (60% EtOAc in hexanes);

^1H NMR (500 MHz, CDCl_3) δ 1.46 (s, 3H), 1.47 (s, 3H), 1.96-2.08 (m, 2H), 2.06 (s, 3H), 2.40-2.43 (m, 4H), 3.96 (d, 1H, J = 4.5 Hz), 6.02 (d, 1H, J = 4.0 Hz), 10.75 (brm, 1H); ^{13}C NMR (125 MHz, CDCl_3) δ 20.4, 21.2, 23.3, 25.2, 29.2, 36.7, 62.4, 80.1, 84.6, 108.3, 171.7, 173.3, 197.6; IR (film, cm^{-1}) 3185 (br), 2955 (w), 2838 (w), 1739 (s), 1628 (m), 1606 (vs), 1414 (vs), 1407 (vs), 1233 (vs), 1138 (vs); mass spectrum (ESI) m/e (% relative intensity) 649.3 (32), 563.2 ($2\text{M} + \text{Na}$) $^+$ (75), 379.2 (29), 309.1 ($\text{M} + \text{K}$) $^+$ (12), 293.1 ($\text{M} + \text{Na}$) $^+$ (100), 271.1 ($\text{M} + \text{H}$) $^+$ (10), 256.1 (12), 211.1 ($\text{M} + \text{H} - \text{AcOH}$) $^+$ (19), 194.1 (20); m/e calcd for $\text{C}_{13}\text{H}_{18}\text{NaO}_6^+$ 293.0996, found 293.0982 [δ = 4.78 ppm].

Peroxide 19.



Using a 50 mL round bottom flask, chromenone **6a** (215.4 mg, 0.752 mmol) was taken up in CH₂Cl₂ (15.0 mL) and Rose Bengal (10.0 mg) was added. The solution was swirled to ensure that the sensitizer completely dissolved to give a bright pink solution. A dry ice/acetone bath was made in a clear Pyrex crystallizing dish and placed on a lab-jack, which was covered with white paper. The flask was lowered into the ice bath and cooled to -78 °C. The airflow from a tygon tube connected to a pressurized air source was adjusted such that a small, barely noticeable stream of air was flowing through the tubing, and a fritted gas bubbling tube was connected. The gas bubbler was cautiously lowered into the solution and secured with a clamp. The bubbling in the solution should be somewhat vigorous, but not so violent that droplets are observed splattering against the ground glass joint of the flask.

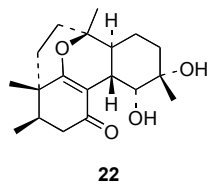
At this point, a 300-W tungsten lamp was positioned no more than 0.3 m away from the flask surface and aimed directly at the flask. The lamp was then turned on. The cooling bath was carefully maintained during the reaction, as the lamp generated copious amounts of heat. During larger runs, which required additional time, additional CH₂Cl₂ was used to rinse the sides of the flask, which had small spatters of reaction mixture of it, this also served to replace the small amount of DCM lost to evaporation.

When TLC indicated consumption of starting material (generally 70-90 min for the reaction duration), the light was unplugged with the air source removed from the flask. The solution was taken out of the cooling bath and allowed to warm to rt at which time the solvent was removed *in vacuo* to afford a pink solid. The solid was taken up in a minimal amount of CH₂Cl₂ and loaded onto a column packed with silica gel, and was flash chromatographed with 15% EtOAc in hexanes. When the peroxide had eluted, small crystals that rapidly grew into larger crystals were noted in some of the more concentrated fractions. The crystals were sparingly soluble in acetone, so CHCl₃ was used to rinse the test tubes. Concentration afforded the peroxide **19** (146.1 mg, 61%) as clear prisms.

R_f = 0.34 (20% EtOAc in hexanes); mp = 154-159 °C;

^1H NMR (500 MHz, C_6D_6) δ 0.56 (d, 3H, J = 7.0 Hz), 0.76 (s, 3H), 0.88 (ddd, 1H, J = 3.0, 5.0, 15.5 Hz), 1.19 (m, 1H), 1.26 (ddd, 1H, J = 3.0, 4.5, 14.0 Hz), 1.26 (s, 3H), 1.41 (ddd, 1H, J = 4.0, 13.5, 17.5 Hz), 1.53 (s, 3H), 1.62 (md, 1H, J = 18.0 Hz), 1.66 (t, 1H, J = 13.5 Hz), 1.71 (m, 1H), 2.04 (dt, 1H, J = 4.5, 13.5 Hz), 2.36 (dt, 1H, J = 5.0, 14.5 Hz), 2.72 (dq, 1H, J = 3.5, 6.5, 13.5 Hz), 3.67 (d, 1H, J = 5.5 Hz), 5.30 (d, 1H, J = 9.0 Hz), 6.82 (d, 1H, J = 6.0 Hz); ^{13}C NMR (75 MHz, CDCl_3) δ 15.3, 16.2, 20.0, 26.1 (2C), 27.9, 32.8, 35.2, 35.3, 37.1, 48.7, 76.3, 80.5, 97.0, 127.7, 129.2, 133.0, 139.7, 198.1; IR (film, cm^{-1}) 3074 (m), 3046 (m), 2996 (s), 2969 (vs), 2930 (vs), 2878 (s), 2854 (s), 2824 (m), 1681 (m), 1632 (s), 1447 (s), 1426 (s), 1381 (s), 1366 (s); mass spectrum (ESI) m/e (% relative intensity) 707.6 (11), 691.1 (23), 675.6 ($2\text{M} + \text{K}$) $^+$ (19), 659.6 ($2\text{M} + \text{Na}$) $^+$ (40), 643.6 ($2\text{M} + \text{K} - \text{O}_2$) $^+$ (50), 627.6 ($2\text{M} + \text{Na} - \text{O}_2$) $^+$ (23), 611.6 (24), 595.6 (58), 373.3 (17), 357.3 ($\text{M} + \text{K}$) $^+$ (36), 341.3 ($\text{M} + \text{Na}$) $^+$ (54), 325.3, 319.3 ($\text{M} + \text{H}$) $^+$ (33), 309.3 ($\text{M} + \text{Na} - \text{O}_2$) $^+$ (26), 303.3 (25), 287.3 ($\text{M} + \text{H} - \text{O}_2$) $^+$ (100); m/e calcd for $\text{C}_{19}\text{H}_{26}\text{NaO}_4^+$ 341.1723, found 341.1722 [δ = 0.29 ppm].

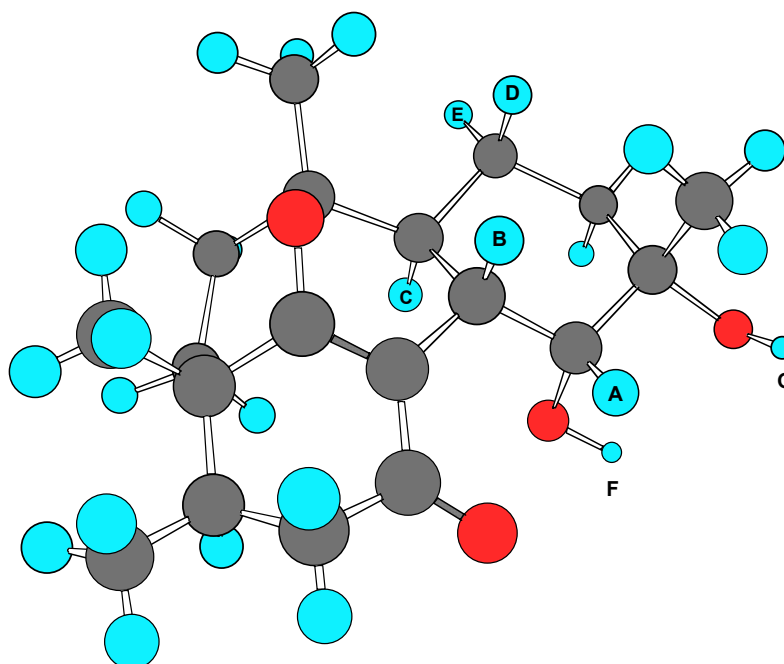
Tetracycle 22.



R_f = 0.37 (50% EtOAc in hexanes);

^1H NMR (500 MHz, CDCl_3) δ 0.97 (d, 3H, J = 7.0 Hz), 1.17 (s, 3H), 1.25 (s, 3H), 1.35 (dt, 1H, J = 3.0, 13.5 Hz), 1.41-1.49 (m, 4H), 1.43 (s, 3H), 1.61-1.65 (m, 2H), 1.66-1.78 (m, 2H), 1.95 (ddd, 1H, J = 3.5, 9.5, 12.5 Hz), 2.05 (m, 1H), 2.10 (dd, 1H, J = 17.5, 20.5 Hz), 2.52 (d, 1H, J = 14.5 Hz), 2.57 (dd, 1H, J = 1.5, 12.5 Hz), 3.35 (s, 1H -OH), 4.16 (d, 1H, J = 3.8 Hz), 4.40 (d, 1H, J = 3.8 Hz, -OH); ^{13}C NMR (125 MHz, CDCl_3) δ 15.4, 15.5, 23.1, 24.0, 26.0, 35.8, 36.1, 36.3, 37.3, 42.6, 45.2, 45.4, 50.0, 71.0, 73.5, 92.3, 131.5, 186.1, 200.9; IR (neat, cm^{-1}) 3445 (br), 2966 (s), 2936 (s), 2873 (s), 1652 (vs), 1607 (s), 1357 (s); mass spectrum (ESI) m/e (% relative intensity) 321 ($\text{M} + 2\text{H}$) $^+$ (20), 321 ($\text{M} + \text{H}$) $^+$ (100), 303 ($\text{M} - \text{H}_2\text{O}$) $^+$ (55), 285 (5), 138 (10); m/e calcd for $\text{C}_{19}\text{H}_{28}\text{O}_4$ 320.1988, found 320.1987 [δ = 8.06 ppm].

Key Coupling Constants for the Stereochemical Assignment of Tetracycle 22.



proton B: δ 2.57 (dd, 1H): J_{BA} = 1.5 Hz; J_{BC} = 12.5 Hz.

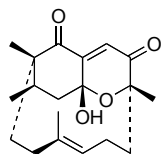
proton C: δ 1.95 (ddd, 1H): J_{CE} = 3.5 Hz; J_{CD} = 9.5 Hz; J_{CB} = 12.5 Hz

proton A: δ 4.16 (brd, 1H): J_{AF} = 3.8 Hz; J_{BA} = small but seen in COSY.

proton F: δ 4.40 (d, 1H): J_{FA} = 3.8 Hz.

proton G: δ 3.35 (brs, 1H).

(\pm)-2 β ,6 β ,7 β -trimethyl-2 α ,6 α -(3'-methyl-3'*E*-hexeno)-3,5(6*H*)-dioxo-2,7,8,8a-tetrahydro-chromen-8a β -ol (23).



23

Peroxide **19** (146.1 mg, 0.459 mmol) was taken up in THF (4.0 mL). To this solution were added 18-Crown-6 (12.1 mg, 45.9 μ mol) and KOAc (4.5 mg, 45.9 μ mol), and the resulting solution (KOAc was often slow to dissolve) was stirred at rt. During the reaction, a bright yellow color developed. After about 45 min, TLC indicated complete consumption of the

starting material. Most of the THF was blown off using a stream of nitrogen, and the residue was loaded directly onto a short silica gel column, and was flash chromatographed (30% EtOAc in hexanes) to afford **23** (137.3 mg, 94%) as a yellow solid. The yellow color is believed to be an impurity as the color persists in the next step, but is then separated by chromatography.

R_f = 0.20 (20% EtOAc in hexanes); mp = 97-99 °C;

^1H NMR (500 MHz, CDCl_3) δ 0.97 (d, 3H, J = 7.0 Hz), 1.03 (s, 3H), 1.18 (s, 3H), 1.54 (td, 1H, J = 3.0, 14.0 Hz), 1.56 (s, 3H), 1.66-1.74 (m, 2H), 1.82-1.97 (m, 3H), 2.06 (dd, 1H, J = 2.0, 13.0 Hz), 2.16 (dt, 1H, J = 4.0 13.5 Hz), 2.24 (dt, 1H, J = 4.5, 13.5 Hz), 2.84 (dq, 1H, J = 2.0, 7.0, 13.5 Hz), 3.21 (br, 1H), 5.39 (d, 1H, J = 10.0 Hz), 6.38 (s, 1H); ^{13}C NMR (125 MHz, CDCl_3) δ 15.0, 15.4, 20.4, 25.2, 25.8, 28.8, 34.7, 36.0, 40.4, 40.5, 49.7, 85.2, 93.3, 124.3, 130.9, 131.3, 152.8, 202.6, 204.8; IR (film, cm^{-1}) 3417 (br), 2975 (m), 2938 (s), 2878 (w), 2857 (w), 1683 (vs), 1617 (m), 1455 (m), 1368 (m); mass spectrum (ESI) m/e (% relative intensity) 675.6 ($2\text{M} + \text{K}$) $^+$ (14), 659.6 ($2\text{M} + \text{Na}$) $^+$ (38), 357.3 ($\text{M} + \text{K}$) $^+$ (25), 341.3 ($\text{M} + \text{Na}$) $^+$ (40), 319.3 ($\text{M} + \text{H}$) $^+$ (8), 301.3 ($\text{M} + \text{H} - \text{H}_2\text{O}$) $^+$ (100), 287.3 (11); m/e calcd for $\text{C}_{19}\text{H}_{26}\text{NaO}_4$ $^+$ 341.1723, found 341.1707 [δ = 4.69 ppm].