Enantioselective Synthesis of the ent-Lomaiviticin A Bicyclic Core

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General Experimental

Moisture- and oxygen-sensitive reactions were carried out in flame-dried glassware under an inert nitrogen atmosphere. Dry ether (Et₂O), toluene, dichloromethane (CH₂Cl₂), and tetrahydrofuran (THF) were purified by passing these solvents through activated alumina columns. Reagents were purchased at the highest commercial quality and used without further purification unless otherwise stated. Reactions were monitored by thin layer chromatography carried out on 0.25 mm E. Merck silica gel plates (60F-254) with UV visualization and KMnO₄ staining. Purification of products via flash chromatography was performed with 40-63 μ m silica gel and the solvent system indicated.



8

(*R*,*R*)-1,6-Diphenyl-hexa-2,4-diyne-1,6-diol (8). To a stirring solution of CuCl (0.98 g, 9.3 mmol) in 450 mL of acetone was added TMEDA (1.50 mL, 10.0 mmol) dropwise followed by bubbling O₂ through the solution. A solution of propargyl alcohol $7^{1,2}$ (12.3 g, 92.7 mmol) in 50 mL of acetone was added and the solution was heated to 40 °C. After stirring for 14 h at this temperature while bubbling O₂ through the solution, the mixture was concentrated in vacuo. To the crude mixture was added 250 mL of 1M HCl. The resulting solution was partitioned between EtOAc and H₂O and the aqueous layer was extracted with EtOAc (3 x 50 mL). The combined organic fractions were dried over Na₂SO₄, filtered, and concentrated in vacuo to give an orange solid. Purification of this solid by SiO₂ flash column chromatography (gradient, 3 → 30% EtOAc/hexanes as

eluent) gave (*R*,*R*)-diyne diol **8** (8.54 g, 70%) as an orange solid. mp 82-84 °C; $[\alpha]^{20}_{D} =$ -34 (*c* 10.0, MeOH); IR (thin film) 3272, 2355 cm⁻¹; ¹H NMR (360 MHz, MeOD) δ 7.39 (d, *J* = 3.6 Hz, 4H), 7.26-7.18 (m, 6H), 5.40 (s, 2H); ¹³C NMR (90 MHz, MeOD) δ 141.4, 129.4, 129.2, 127.5, 81.1, 70.4, 65.0; LRMS (ESI) *m/z* (relative intensity) 371.2 (5%, M + Na⁺). HRMS (ESI) *m/z* calcd for [C₁₈H₁₃O]⁺, 245.0966, found 245.0972.





(*S*,*S*)-1,6-Diphenyl-hexa-2,4(*Z*,*Z*)-diene-1,6-diol (9). Argon was bubbled through a stirring suspension of Zn dust (70 g, 1.1 mol) in 420 mL of H₂O. After 15 min, Cu(OAc)₂·H₂O (7.0 g, 35 mmol) was added. After an additional 15 min, AgNO₃ (7.0 g, 41 mmol) was added. After stirring for 30 min, the mixture was filtered and the solid was washed successively with H₂O, MeOH, acetone, and Et₂O. The solid was added to 250 mL of a 1:1 mixture of MeOH/H₂O followed by a solution of (*R*,*R*)-diyne diol **8** (3.50 g, 13.3 mmol) in 30 mL of MeOH. The reaction mixture was heated at 40 °C for 36 h, filtered through Celite with MeOH, and concentrated in vacuo. The remaining aqueous layer was extracted with EtOAc (3 x 400 mL). The combined organic fractions were dried over Na₂SO₄, filtered, and concentrated in vacuo to give a crude orange solid. Purification of this solid by SiO₂ flash column chromatography (gradient, 15 \rightarrow 60 % EtOAc/hexanes as eluent) gave (*S*,*S*)-diene diol **9** (2.71 g, 76%) as an orange solid. mp 107-110 °C; $[\alpha]^{20}_{D} = +69$ (*c* 6.20, MeOH); IR (thin film) 3284 cm⁻¹; ¹H NMR (400 MHz, THF-d₈) δ 7.35 (d, *J* = 7.3 Hz, 4H), 7.24 (t, *J* = 7.5 Hz, 4H), 7.14 (t, *J* = 7.3 Hz, 2H), 6.60-6.58 (m, 2H), 5.63 (s, 4H), 4.53 (m, 2H); ¹³C NMR (75 MHz, THF-d₈) δ 145.8, 137.4, 128.8, 127.4, 126.6, 123.7, 69.4; LRMS (ESI) *m*/*z* (relative intensity) 249.1 (100%, M – OH⁻); HRMS (ESI) *m*/*z* calcd for [C₁₈H₁₇O], 249.1279, found 249.1261.



(S,S)-2-(4-(Methoxy)benzyloxy)butyric Acid 6-[2-(4-(Methoxy)benzyloxy)butyryloxy]-1,6-diphenylhexa-(Z,Z)-2,4-dienyl Ester (10). To a stirring solution of 2-(4-(methoxy)benzyloxy)butyric acid³ (5.90 g, 26.3 mmol) and (S,S)-diene diol**9**(3.19 g,12.0 mmol) in 120 mL of CH₂Cl₂ was added DMAP (365 mg, 4.00 mmol) and DCC (5.92 g, 28.7 mmol). After 16 h at room temperature, the solution was concentrated in vacuo to give a crude yellow oil. Purification of this oil by deactivated silica (2% Et₃N in hex) flash column chromatography (gradient, $5 \rightarrow 15$ % EtOAc/hexanes as eluent) gave bis PBM glycolate 10 (5.41 g, 67%) as a colorless oil (1:1 mixture of diastereomers). An 84% yield was obtained on a 94 mg scale. IR (thin film) 1737 cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ 7.43-7.33 (m, 10H), 7.29 (d, J = 8.1 Hz, 4H), 6.90 (d, J = 9.3 Hz, 4H), 6.86 (d, J = 4.2 Hz, 2H), 6.82-6.79 (m, 2H), 5.93-5.85 (m, 2H), 4.68 (d, J = 9.5 Hz, 1H), 4.65 (d, J = 9.5 Hz, 1H), 4.37 (d, J = 12.5 Hz, 2H), 3.95 (t, J = 7.0 Hz, 2H), 3.84 (s, 6H), 1.87-1.80 (m, 4H), 1.00 (t, J = 7.7 Hz, 3H), 0.96 (t, J = 7.6 Hz, 3H); ¹³C NMR (75 MHz, CDCl₃) δ 171.84, 171.78, 159.3 (x2), 139.0, 138.9, 131.3, 131.2 (2 carbons), 131.1, 129.6 (2 carbons), 128.6 (2 carbons), 128.2, 128.1, 126.6, 126.5, 125.7, 125.5, 113.7 (2 carbons), 78.9, 78.8, 71.7 (2 carbons), 71.4, 71.2, 55.2 (2 carbons), 26.2, 26.1; LRMS (ESI) m/z (relative intensity) 696.4 (20%, M + NH₄⁺). HRMS (ESI) m/z calcd for $[C_{42}H_{50}NO_8]^+$, 696.3536, found 696.3520.



13

(2R,3S,4S,5R)-2,5-Diethyl-2,5-bis-(4-(methoxy)benzyloxy)-3,4-

(distyryl)hexanedioic Acid (13). To a stirring solution of KHMDS (0.50 M in toluene, 31.6 mL, 15.8 mmol) in 20 mL of Et₂O at -100 °C was added a solution of bis PMB glycolate 10 (1.58 g, 2.32 mmol) in 10 mL of Et₂O. After stirring for 40 min at that temperature, TIPSOTf (2.49 mL, 9.28 mmol) was added dropwise. After stirring for an additional 30 min at -100 °C, the solution was warmed to -60 °C. After stirring for 2 h at -60 °C, the solution was warmed to -20 °C. After stirring for 2 h at -20 °C, the solution was warmed to room temperature. After stirring for 2.5 h at room temperature, saturated NaHCO₃ (40 mL) was added. The resulting solution was partitioned between Et₂O and H_2O and the aqueous layer was extracted with Et_2O (3 x 40 mL). The combined organic fractions were dried over Na₂SO₄, filtered, and concentrated in vacuo to give bis TIPS ester 12 (1.81 g, 79%) as a yellow oil that was used without further purification. IR (thin film) 1713 cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ 7.37-7.20 (m, 14H), 6.79 (d, J = 8.5 Hz, 4H), 6.51 (d, J = 15.8 Hz, 2H), 6.23 (dd, J = 15.8, 10.9 Hz, 2H), 4.56 (d, J = 10.0 Hz, 2H), 4.41 (d, J = 10.1 Hz, 2H), 3.84-3.81 (m, 2H), 3.81 (s, 6H), 2.07-1.89 (m, 4H), 1.22-1.14 (m, 6H), 1.00-0.91 (m, 42H); ¹³C NMR (90 MHz, CDCl₃) δ 171.8, 158.6, 137.5, 134.3, 131.4, 129.0, 128.1, 127.4, 126.9, 126.4, 113.2, 84.8, 65.5, 55.2, 45.7, 25.7, 17.8, 17.71, 17.67, 12.3, 11.9, 7.4; LRMS (ESI) m/z (relative intensity) 948.8 (100%, M + NH_4^+).

To a stirring solution of crude bis TIPS ester 12 (1.28 g, 1.29 mmol) in 15 mL of THF at 0 °C was added Bu₄NF (1.0 M in hexanes, 3.89 mL, 3.9 mmol) dropwise. After stirring for 30 min, H₂O (20 mL) was added. The resulting solution was partitioned between EtOAc and H_2O and the aqueous layer was extracted with EtOAc (3 x 20 mL). The combined organic fractions were dried over Na₂SO₄, filtered, and concentrated in vacuo to give a crude yellow solid. CH₃CN (20 mL) was added and this solution was washed with hexanes (5 x 20 mL) and the CH₃CN phase was separated and concentrated in vacuo to give diacid 13 (0.876 g, 100%) as a white solid which was used without further purification. mp 116-118 °C; $[\alpha]_{D}^{20} = -42$ (*c* 5.00, MeOH); IR (thin film) 3354, 1702 cm⁻¹; ¹H NMR (360 MHz, CDCl₃) δ 7.37 (d, J = 7.3 Hz, 4H), 7.28 (t, J = 7.2 Hz, 4H), 7.22 (d, J = 7.2 Hz, 2H), 7.17 (d, J = 8.2 Hz, 4H), 6.81 (d, J = 8.5 Hz, 4H), 6.50 (d, J = 15.8 Hz, 2H), 6.37 (dd, J = 15.6, 10.6 Hz, 2H), 4.29 (d, J = 9.2 Hz, 2H), 4.20 (d, J = 15.6 H 9.4 Hz, 2H), 3.80 (s, 6H), 3.32 (d, J = 10.4 Hz, 2H), 1.73-1.58 (m, 4H), 0.82 (t, J = 7.1Hz, 6H); ¹³C NMR (75 MHz, CDCl₃) δ 175.2, 159.9, 137.6, 135.4, 130.2, 128.9, 127.3, 127.1, 125.8, 114.1, 83.8, 65.0, 55.7, 45.4, 26.5, 7.1; LRMS (ESI) *m/z* (relative intensity) 696.3 (100%, M + NH₄⁺). HRMS (ESI) m/z calcd for $[C_{42}H_{50}NO_8]^+$, 696.3536, found 696.3550.



14

(2R,3S,4S,5R)-2,5-Diethyl-2,5-bis-(4-(methoxy)benzyloxy)-3,4-

(distyryl)hexanedioic Acid Bis-(methoxymethylamide) (14). To a stirring solution of diacid 13 (0.045 g, 0.066 mmol) in 1 mL of benzene was added pyridine (32 μ L, 0.40 mmol). After stirring for 15 min, oxalyl chloride (23 μ L, 0.26 mmol) was added dropwise. After stirring for an additional 30 min, the reaction mixture was concentrated in vacuo, Et₂O (10 mL) was added, and the suspension was filtered through a thin pad of Celite with Et₂O rinsing (10 mL). The combined organics were concentrated in vacuo to afford the bis acid chloride, which was used without further purification. IR (thin film) 1778 cm⁻¹; ¹H NMR (300 MHz, CDCl₃) δ 7.43-7.25 (m, 14H), 6.84 (d, *J* = 10.0 Hz, 4H), 6.66 (d, *J* = 15.5 Hz, 2H), 6.34 (dd, *J* = 15.8, 10.7 Hz, 2H), 4.53 (d, *J* = 10.1 Hz, 2H), 4.47 (d, *J* = 10.2 Hz, 2H), 3.85 (s, 6H), 3.65 (d, *J* = 10.6 Hz, 2H), 2.14-2.00 (m, 4H), 0.98 (t, *J* = 7.3 Hz, 6H); ¹³C NMR (75 MHz, CDCl₃) δ 177.2, 159.0, 136.9, 136.7, 129.7, 128.9, 128.5, 127.7, 126.6, 124.2, 113.5, 90.3, 65.5, 55.2, 47.3, 27.0, 7.2; LRMS (ESI) *m/z* (relative intensity) 677.5 (100%, M - H – CI⁻).

To a stirring solution of this crude bis acid chloride in 45 mL of benzene was added pyridine (32 μ L, 0.40 mmol) dropwise followed by *N*,*O*-dimethylhydroxylamine⁴ (23 μ L, 0.26 mmol). After stirring for 15 h, the reaction mixture was concentrated in vacuo to afford a crude pale yellow oil. Purification of this oil by SiO₂ flash column chromatography (gradient, 20 \rightarrow 50 % EtOAc/hexanes as eluent) gave bis Weinreb amide **14** (0.037 g, 73% from **13**) as a yellow solid. A 42% yield was obtained from **10** on a 2.69 g scale. mp. 51-54 °C; $[\alpha]^{20}_{D}$ = +13 (*c* 2.67, MeOH); IR (thin film) 1637 cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ 7.39 (d, *J* = 7.5 Hz, 4H), 7.32-7.19 (m, 10H), 6.74 (d, *J* = 8.2 Hz, 4H), 6.55-6.50 (m, 4H), 4.50 (d, *J* = 9.5 Hz, 2H), 4.42-4.37 (m, 2H), 3.79 (s, 6H), 3.63-3.57 (m, 2H), 3.46 (s, 6H), 3.08 (br s, 6H), 2.13-2.07 (m, 4H), 0.99 (t, *J* = 6.7 Hz, 6H); ¹³C NMR (90 MHz, CDCl₃) δ 172.5, 158.7, 138.0, 132.5, 130.9, 129.5, 128.8, 128.4, 126.8, 126.4, 113.2, 87.3, 64.9, 60.7, 55.2, 47.8, 35.5, 26.4, 8.5; LRMS (ESI) *m/z* (relative intensity) 765.4 (100%, M + H⁺). HRMS (ESI) *m/z* calcd for [C₄₆H₅₆N₂O₈]⁺, 765.4115, found 765.4119.



15

(2R,3S,4S,5R)-5,8-Diethyl-5,8-bis-(4-(methoxy)benzyloxy)-6,7-

(distyryl)dodeca-1,11-diene-4,9-dione (15). To a stirring solution of freshly prepared allyllithium⁵ (0.48 M in 2:1 THF/Et₂O, 14.5 ml, 6.7 mmol) at -78 °C was added dropwise a solution of bis Weinreb amide 14 (1.28 g, 1.67 mmol) in 4 mL of THF. After stirring for 1 h at -78 °C, saturated NH₄Cl (25 mL) was added. The resulting solution was partitioned between Et₂O and H₂O and the aqueous layer was extracted with Et₂O (3 x 25 mL). The combined organic fractions were dried over Na₂SO₄, filtered, and concentrated in vacuo to give a yellow oil. Purification of this oil by SiO₂ flash column chromatography (2 \rightarrow 8% Et₂O/hexanes then 15% EtOAc/hexanes as eluent) gave tetraene 15 (0.83 g, 72%) as a yellow solid. A 77% yield was obtained on a 109 mg scale. A sample of this solid was crystallized from EtOH to give an X-ray quality crystal. mp 116-118°C; $[\alpha]^{20}_{D} = -58$ (*c* 2.10, MeCN); IR (thin film) 1713 cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ 7.43 (d, *J* = 7.4 Hz, 4H), 7.34 (t, *J* = 7.5 Hz, 4H), 7.28-7.25 (m, 6H), 6.95 (d, *J* = 8.5 Hz, 4H), 6.52 (dd, *J* = 15.8, 9.4 Hz, 2H), 6.43 (d, *J* = 15.8 Hz, 2H), 5.51-5.37 (m, 2H), 4.86 (d, *J* = 10.3 Hz, 2H), 4.67 (d, *J* = 17.2 Hz, 2H), 4.45 (d, *J* = 11.2 Hz, 2H), 4.41 (d, *J* = 11.2 Hz, 2H), 3.88 (s, 6H), 3.47 (dd, *J* = 19.0, 6.0 Hz, 2H), 3.39 (d, *J* = 9.3 Hz, 2H), 3.32 (dd, *J* = 19.0, 7.6 Hz, 2H), 2.00-1.91 (m, 2H), 1.80-1.71 (m, 2H), 0.76 (t, *J* = 7.3 Hz, 6H); ¹³C NMR (75 MHz, CDCl₃) δ 212.9, 158.8, 136.9, 133.4, 130.9, 130.2, 128.4, 127.6, 127.4, 127.3, 126.5, 117.8, 113.7, 88.5, 62.5, 55.2, 48.6, 47.1, 28.4, 7.6; LRMS (ESI) *m/z* (relative intensity) 744.5 (100%, M + NH₄⁺). HRMS (ESI) *m/z* calcd for [C₄₈H₅₈NO₆]⁺, 744.4264, found 744.4262.

X-ray Data for 15



A colorless pyramid shaped crystal of **15** (C46 H54 O6) with approximate dimensions 0.11 x 0.16 x 0.17 mm, was used for the X-ray crystallographic analysis. The X-ray intensity data were measured at 298(2) K, on a Bruker SMART APEX CCD area detector system equipped with a graphite monochromator and a MoK α fine-focus sealed

tube ($\lambda = 0.71073$ Å) operated at 1600 watts power (50 kV, 32 mA). The detector was placed at a distance of 5.8 cm from the crystal.

A total of 1850 frames were collected with a scan width of 0.3° in ω and an exposure time of 10 seconds/frame. The total data collection time was about 8 hours. The frames were integrated with the Bruker SAINT software package using a narrow-frame integration algorithm. The integration of the data using a Tetragonal unit cell yielded a total of 21947 reflections to a maximum θ angle of 28.42° (0.90 Å resolution), of which 5331 were independent, completeness = 99.5 %, R_{int} = 0.0795, R_{sig} = 0.1063 and 1917 were greater than $2\sigma(I)$. The final cell constants: a = 8.966(2)Å, b = 8.966(2)Å, c = 53.26(2)Å, $\alpha = 90^{\circ}$, $\gamma = 90^{\circ}$, volume = 4282(2)Å³, are based upon the refinement of the XYZ-centroids of 1195 reflections above $20\sigma(I)$ with 1.886° < θ <15.811°. Analysis of the data showed negligible decay during data collection. Data were corrected for absorption effects using the multiscan technique (SADABS). The ratio of minimum to maximum apparent transmission was 0.0506.

The structure was solved and refined using the Bruker SHELXTL (Version 6.1) Software Package, using the space group P4(3)2(1)2, with Z = 4 for the formula unit, C48 H54 O6. The final anisotropic full-matrix least-squares refinement on F² with 247 variables converged at R1 = 14.00 %, for the observed data and wR2 = 42.75 % for all data. The goodness-of-fit was 1.136. The largest peak on the final difference map was 0.512 e⁷/Å³ and the largest hole was -0.268 e⁷/Å³. Based on the final model, the calculated density of the crystal is 1.128 g/cm³ and F(000) amounts to 1560 electrons.

Note that this structure determination has an A-level error: PLAT241_alert_2_A for high Ueq for O2. This structure has a unit cell with a long axis of 53.264 angstroms.

The asymmetric unit is 1/8th of the unit cell contents and the disorder in this part of the molecule is causing this error. We tried SIMU and DELU to dampen the atomic displacement parameters.



16

(1S,1'S,2R,2'R)-2,2'-Diethyl-2,2'-bis-(4-(methoxy)benzyloxy)-bicyclohexyl-

5,5'-diene-3,3'-dione (16). To a freeze-pump-thawed solution of tetraene **15** (0.147 g, 0.202 mmol) in 10 mL of toluene in a sealable tube was added Grubbs II catalyst (0.069 g, 0.081 mmol) and the tube was sealed. After freeze-pump-thawing the solution again, the reaction mixture was heated at 100 °C. After heating at this temperature for 4 h, the crude solution was cooled to room temperature and concentrated in vacuo to give a green oil. Purification of this oil by SiO₂ flash column chromatography (10 \rightarrow 30% EtOAc/hexanes as eluent) gave bis cyclohexenone **16** (0.067 g, 64%) as a green solid. mp 135-137 °C; [α]²⁰_D = -100 (*c* 1.00, MeCN); IR (thin film) 1719 cm⁻¹; ¹H NMR (360 MHz, CDCl₃) δ 7.39 (d, *J* = 8.6 Hz, 4H), 6.93 (d, *J* = 8.6 Hz, 4H), 5.76-5.70 (m, 4H), 4.81 (d, *J* = 10.8 Hz, 2H), 4.41 (d, *J* = 10.9 Hz, 2H), 3.85 (s, 6H), 3.41 (d, *J* = 3.6 Hz, 2H), 2.87 (s, 4H), 1.99-1.85 (m, 4H), 0.82 (t, *J* = 7.3 Hz, 6H); ¹³C NMR (90 MHz, CDCl₃) δ 209.8, 158.9,130.9, 128.3, 126.8, 126.3, 113.7, 83.7, 64.3, 55.2, 45.3, 40.7, 24.8, 7.1; (ESI) *m/z* (relative intensity) 536.4 (100%, M + NH₄⁺); HRMS (ESI) *m/z* calcd for [C₃₂H₄₂NO₆]⁺, 536.3012, found 536.3008.



18

Pentacyclic Bis Hemiacetal Diene (18). To a solution of bis cyclohexenone 16 (0.022 g, 0.042 mmol) in 1 mL of CH₂Cl₂ at 0 °C was added TFA (32 µL, 0.42 mmol). After stirring for 15 min at 0 °C, the reaction mixture was concentrated in vacuo to give a crude yellow oil. Purification of this oil by SiO₂ flash column chromatography (10 \rightarrow 15 % EtOAc/hexanes as eluent) gave pentacyclic bis hemiketal diene 18 (8 mg, 70%) as a yellow solid. mp. 167-170 °C; $[\alpha]^{20}_{D} = -64$ (*c* 0.44, MeCN);IR (thin film) 3413 cm⁻¹; ¹H NMR (300 MHz, CDCl₃) δ 5.77 (m, 2H), 5.47 (m, 2H), 3.84 (s, 2H), 2.48-2.31 (m, 6H), 1.83 (m, 2H), 1.46 (m, 2H), 0.91 (t, *J* = 7.2 Hz, 6H); ¹³C NMR (75 MHz, CDCl₃) δ 130.5, 123.0, 97.9, 73.4, 41.2, 38.2, 23.8, 6.9; LRMS (ESI) *m/z* (relative intensity) 261.1 (100%, M – OH⁻); HRMS (ESI) *m/z* calcd for [C₁₆H₂₁O₃]⁻, 261.1491, found 261.1474.



20

1,1'-Bis-(tert-butyl(dimethyl)silanyloxy)-6,6'-diethyl-6,6'-bis-(4-

(methoxy)benzyloxy)-[5,5']bi[2,3-dioxabicyclo[2.2.2]octyl]-7,7'-diene (20). To a stirring solution of KHMDS (0.50 M in toluene, 848 μ L, 0.42 mmol) in 800 μ L of THF at -78 °C was added dropwise a solution of bis cyclohexenone 16 (0.055 g, 0.11 mmol) in 400 μ L of THF. After stirring for 40 min at -78 °C, TBSOTf (98 μ L, 0.42 mmol) was added. After stirring for 2 h at -78 °C, saturated NaHCO₃ solution (10 mL) was added.

The resulting solution was partitioned between EtOAc and H_2O and the aqueous layer was extracted with EtOAc (3 x 15 mL). The combined organic fractions were dried over Na_2SO_4 , filtered, and concentrated in vacuo to give bis TBS dienol ether **19** as a crude yellow oil that was used without further purification.

To a solution of this crude bis OTBS dienyl ether 19 in 10 mL of CH₂Cl₂ at -78 °C was added tetraphenylporphine (2 mg, 0.003 mmol). The sample was irradiated with a 275W sun lamp while bubbling O_2 through the solution. After irradiation for 45 min at -78 °C, the reaction mixture was concentrated in vacuo to give a pink oil. Purification of this oil by SiO₂ flash column chromatography (gradient, $2 \rightarrow 20\%$ Et₂O/hexanes as eluent) gave bis endoperoxide **20** (0.057 g, 67% over 2 steps) as a pink solid. A sample of this solid was crystallized from 1:1 hexanes/THF to obtain colorless X-ray quality crystals. mp 120-122 °C; $[\alpha]^{20}_{D} = +94$ (c 1.80, MeCN); IR (thin film) 1243 cm⁻¹; ¹H NMR (300 MHz, CDCl₃) δ 7.18 (d, J = 8.4 Hz, 4H), 6.88 (d, J = 8.5 Hz, 4H), 6.58 (dd, J= 8.6, 5.6 Hz, 2H), 6.38 (d, J = 8.3 Hz, 2H), 4.81 (d, J = 6.1 Hz, 2H), 4.64 (d, J = 11.2Hz, 2H), 4.53 (d, J = 11.3 Hz, 2H), 3.81 (s, 6H), 3.04 (br s, 2H), 2.19-2.16 (m, 4H), 1.18 (t, J = 7.3 Hz, 6H), 1.01 (s, 18H), 0.24 (s, 12H); ¹³C NMR (90 MHz, CDCl₃) δ 158.6, 135.1, 131.8, 131.2, 127.8, 113.8, 103.5, 82.4, 74.2, 65.8, 55.2, 43.3, 25.7, 21.7, 18.0, 8.5, -2.4, -3.3; LRMS (ESI) *m/z* (relative intensity) 811.6 (100%, M + H⁺). HRMS (ESI) *m/z* calcd for $[C_{44}H_{67}O_{10}Si_2]^+$, 811.4273, found 811.4238.

X-ray Data for 20



A colorless block shaped crystal of **20** (C44 H66 O10 Si2) with approximate dimensions 0.15 x 0.18 x 0.23 mm, was used for the X-ray crystallographic analysis. The X-ray intensity data were measured at 298(2) K, on a Bruker SMART APEX CCD area detector system equipped with a graphite monochromator and a MoK α fine-focus sealed tube ($\lambda = 0.71073$ Å) operated at 1600 watts power (50 kV, 32 mA). The detector was placed at a distance of 5.8 cm from the crystal.

A total of 1850 frames were collected with a scan width of 0.3° in ω and an exposure time of 30 seconds/frame. The total data collection time was about 17 hours. The frames were integrated with the Bruker SAINT software package using a narrow-frame integration algorithm. The integration of the data using a Monoclinic unit cell yielded a total of 22112 reflections to a maximum θ angle of 28.35° (0.90 Å resolution), of which 10354 were independent, completeness = 99.2%, R_{int} = 0.0361, R_{sig} = 0.0596 and 7105 were greater than $2\sigma(I)$. The final cell constants: a = 7.2313(12)Å, b = 21.911(4)Å, c = 14.668(2)Å, $\alpha = 90^{\circ}$, $\beta = 94.760(3)^{\circ}$, $\gamma = 90^{\circ}$, volume = 2316.0(7)Å³, are based upon the refinement of the XYZ-centroids of 4621 reflections above $20\sigma(I)$ with 2.323° < θ <21.984°. Analysis of the data showed negligible decay during data collection. Data were corrected for absorption effects using the multiscan technique (SADABS). The ratio of minimum to maximum apparent transmission was 0.6951.

The structure was solved and refined using the Bruker SHELXTL (Version 6.1) Software Package, using the space group P2(1), with Z = 2 for the formula unit, C44 H66 O10 Si2. The final anisotropic full-matrix least-squares refinement on F^2 with 519 variables converged at R1 = 7.39%, for the observed data and wR2 = 20.81% for all data. The goodness-of-fit was 1.013. The largest peak on the final difference map was 1.346 e⁻ $/\text{Å}^3$ and the largest hole was -0.534 e⁻/Å³. Based on the final model, the calculated density of the crystal is 1.163 g/cm³ and F(000) amounts to 876 electrons.



2,2'-Diethyl-6,6'-dihydroxy-2,2'-bis-(4-(methoxy)benzyloxy)-bicyclohexyl-

4,4'-diene-3,3'-dione (2). To a stirring solution of bis endoperoxide **20** (0.036 g, 0.045 mmol) in 1 mL of MeCN at 0 °C was added dropwise fluorosilicic acid (117 μ L, 20-25 wt% in H₂O, ~ 0.2 mmol). After stirring for 40 min at 0 °C, H₂O (1 mL) was added. The resulting solution was partitioned between EtOAc (10 mL) and H₂O (10 mL) and the aqueous layer was extracted with EtOAc (3 x 10 mL). The combined organic fractions were dried over Na₂SO₄, filtered, and concentrated in vacuo to give crude bis peroxide **21** as a yellow oil that was used without further purification.

To a stirring solution of the crude bis peroxide **21** in 1 mL of CH₂Cl₂ at 0 °C was added PPh₃ (0.035 g, 0.13 mmol). After stirring for 30 min at 0 °C, the crude mixture was concentrated in vacuo to give a crude yellow oil. Purification of this oil by SiO₂ flash column chromatography (gradient, $15 \rightarrow 30\%$ EtOAc/hexanes as eluent) gave lomaiviticinone core **2** (0.014 g, 57% over 2 steps) as a yellow oil contaminated by a small amount of an inseparable unidentified compound. $[\alpha]^{20}_{D} = +131$ (MeCN); IR (thin film) 3425, 1672 cm⁻¹; ¹H NMR (360 MHz, CDCl₃, major isomer) δ 7.08 (d, J = 8.5 Hz, 4H), 6.97 (d, J = 10.3 Hz, 2H), 6.82 (d, J = 8.4 Hz, 4H), 6.01 (d, J = 10.2 Hz, 2H), 5.53 (s, 2H), 4.76 (d, J = 8.0 Hz, 2H), 4.41 (d, J = 10.3 Hz, 2H), 4.12 (d, J = 10.2 Hz, 2H), 3.77 (s, 6H), 2.71 (d, J = 8.4 Hz, 2H), 2.31 (m, 2H), 1.89 (m, 2H), 1.63 (m, 2H), 0.96 (t, J = 7.3 Hz, 6H); ¹³C NMR (90 MHz, CDCl₃, major isomer) δ 195.3, 159.6, 153.9, 129.8, 127.7, 124.6, 114.0, 83.8, 66.7, 64.8, 55.2, 49.6, 21.4, 8.7; LRMS (ESI) *m/z* (relative intensity) 573.2 (80%, M + Na⁺). HRMS (ESI) *m/z* calcd for [C₃₂H₃₈O₈Na]⁺, 573.2464, found 573.2449.



22

6,6'-Diethyl-6,6'-bis-(4-(methoxy)benzyloxy)-bicyclohexyl-3,3'-diene-2,5,2',5'tetraone (22). To a solution of crude bis peroxide 21 (0.0050 g, 0.0085 mmol) in 500 µL of acetic anhydride was added pyridine (2 µL, 0.03 mmol). After 14 h of stirring at room temperature, the reaction mixture was concentrated in vacuo to give a crude yellow oil. Purification of this oil by SiO₂ flash column chromatography (gradient, $10 \rightarrow 30\%$ EtOAc/hexanes as eluent) gave bis enedione 22 (0.014 g, 49% from 20) as a light yellow oil. IR (thin film) 1691cm⁻¹; ¹H NMR (360 MHz, CDCl₃) δ 7.19 (d, J = 8.6 Hz, 4H), 6.87 (d, J = 8.5 Hz, 4H), 6.27 (br s, 4H), 4.88 (m, 2H), 4.43 (d, J = 10.5 Hz, 2H), 3.84 (s, 6H), 3.79 (s, 2H), 2.08 (m, 2H), 1.94 (m, 2H), 0.95 (t, J = 7.2 Hz, 6H); ¹³C NMR (150 MHz, CDCl₃) δ 197.5(2 carbons), 159.1, 139.2 (2 carbons), 129.9, 129.6, 113.5, 93.8, 82.2, 68.0, , 55.2, , 25.6, 7.7; LRMS (ESI) m/z (relative intensity) 564.2 (100%, M + NH₄⁺). HRMS (ESI) m/z calcd for [C₃₂H₃₈NO₈]⁺, 564.2597, found 564.2595.







¹H NMR of **9**



¥

¹³C NMR of **9**





¹³C NMR of **10**









¹H NMR of **14**



÷.







¹H NMR of **16**







4



¹H NMR of **20**



6



¹H NMR of **2**



¹³C NMR of **2**



 1 H NMR of **22**



¹³C NMR of **22**

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