Anomalous chromophore disruption enables an eight-step synthesis and stereochemical reassignment of (+)-marineosin A

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General Methods

Unless otherwise specified, reactions were performed in flame-dried glassware under an atmosphere of argon. Reagents were purchased from commercial vendors and used as received unless otherwise stated. Tetrahydrofuran (THF), diethyl ether (Et₂O), acetonitrile (CH₃CN) and toluene (PhMe) were passed through a Glass Contour solvent drying system. Methanol (MeOH) was distilled from Mg(OMe)₂, which was generated by refluxing methanol over magnesium turnings until all the turnings had converted into a white precipitate. The distilled MeOH was stored in a flame-dried flask over activated 3Å molecular sieves under argon. Magnesium turnings were polished by sequential rinsing with aqueous 1M HCl, absolute ethanol, and Et₂O. The washed turnings were placed under vacuum for several hours then stored under an atmosphere of argon.

Yields refer to chromatographically and spectroscopically (¹H NMR) homogeneous materials, unless otherwise stated. Thin-layer chromatography (TLC) was conducted on precoated plates (Sorbent Technologies, silica gel 60 PF254, 0.25 mm) visualized with UV 254 nm. For acid-sensitive compounds, TLC plates were neutralized with TEA/Hexane (1%) before use. Column chromatography was performed on silica gel 60 (SiliCycle, 240–400 mesh). For acid-sensitive compounds, silica gel was premixed with TEA/Hexane (1%) before being loaded into the column. Purification of 8 and 26 was performed using an Agilent 1200 HPLC system equipped with G1361A preparative pumps, a G1314A autosampler, a G1364B automated fraction collector, and a Waters Sunfire C18 column (5 μm, 19 mm × 250 mm), unless otherwise noted. Analytical HPLC was performed using the same system, but with a G1312A binary pump. Mass spectra were recorded using an Agilent 6130 LC/MS system equipped with an ESI source. High resolution mass spectra were recorded using Thermo Fisher Scientific Exactive Plus with IonSense ID-CUBE DART source and Orbitrap analyzer. NMR spectra were recorded on Bruker Avance spectrometers (400/100 MHz and 500/125 MHz).

Batch photoreactions were carried out in either a standard Ace Glass immersion well photoreactor or an Ace Glass low temperature immersion well photoreactor using a Hanovia 450W mercury arc lamp. Photoreactions were also examined in a Rayonet photoreactor with a 254 and 300 nm bulb set using quartz test tubes. For setup of photoreaction in flow format, 1/16" ID x 1/8" OD x 1/32" Wall Versilon™ FEP Tubing was coiled around an Ace Glass 7858 triple-walled quartz immersion well in either one or three layers. The reaction solution was propelled by a peristaltic pump (Binaca model 1001) through the FEP tubing under irradiation by a Hanovia 450W mercury arc lamp.
Experimental Procedures

![Chemical structure image]

Table S1. Optimization for the synthesis of pyridinophane 14.

| entry | Concentration (M) | Temperature (°C) | Grignard reagent addition time (h) | yields |
|-------|------------------|-----------------|-----------------------------------|--------|
| 1     | 0.4              | 30              | 2                                 | 27%    |
| 2     | 0.4              | 10              | 2                                 | 36%    |
| 3     | 0.4              | -10             | 2                                 | 5%     |
| 4     | 0.1              | 10              | 2                                 | 43%    |
| 5     | 0.1              | 10              | 6                                 | 50%    |

[8](2,6)pyridinophane (14)

To a flame-dried 500 mL 3-neck round bottom flask, equipped with an addition funnel, condenser, and stir bar, were added polished magnesium tunings (4.86 g, 0.2 mol, 2.0 eq.) and a single iodine crystal in anhydrous Et₂O (200 ml) under Ar. With vigorous stirring, from the addition funnel was added 1,8-dibromooctane (1 mL). The mixture was heated using a heat gun until the brown color dissipated. The remaining 1,8-dibromooctane (27.6 g in total, 0.1 mol, 1.0 eq.) was added dropwise into the flask at a rate such that the solution was maintained at a gentle reflux. After addition was complete, the addition funnel was rinsed with anhydrous diethyl ether (10 mL) into the reaction mixture. The resulting mixture was refluxed for another hour. (When stirring was stopped, the mixture separated into two layers; the top a translucent light gray and the bottom a viscous, opaque gray).

During the reflux, to a separate flame-dried 2 L 3-necked round bottom flask equipped with a thermometer was added 2,6-dichloropyridine 12 (14.8 g, 0.1 mol, 1.0 eq.) and NiCl₂(dppp) (0.43 g, 0.75 mmol, 0.8 mol %) in anhydrous Et₂O (1 L) under Ar. The mixture was cooled in an ice-water batch to 10 °C, followed by addition of the newly formed di-Grignard solution in Et₂O via syringe pump over 6 h. During the addition, the reaction solution was kept at 10 °C with vigorous stirring. When TLC monitoring (5% EtOAc/Hexane) confirmed that 12 was fully consumed, the reaction mixture was carefully poured into ice water then filtered through celite. The organic layer was separated and the aqueous layer was extracted with EtOAc (100 mL X 3). The organic layers were combined, washed with brine, dried over Na₂SO₄, filtered, and concentrated to an orange oil. The resulting 23 g of crude product was dry-loaded onto silica gel (30 g) and purified by flash column chromatography (EtOAc in Hexane: 3%) to yield compound 14 (9.48 g, 50 mmol, 50%) as a colorless oil. ¹H-NMR (400 MHz, CDCl₃) δ 7.46 (t, J = 7.6 Hz, 1H), 6.89 (d, J = 7.6 Hz, 2H), 2.84 (t, J = 6.38 Hz, 4H), 1.83 – 1.77 (m, 4H), 1.42 – 1.36 (m, 4H), 1.06 – 0.98 (m, 4H); ¹³C-NMR (100 MHz, CDCl₃) δ 160.6, 136.6, 120.0, 35.7, 26.3, 25.1, 23.2; HRMS (EI) calculated for C₁₃H₂₀N [M+H]⁺: 190.1590, found 190.1583.
[8](2,6)pyridinophane N-oxide (15)

To a stirred solution of 14 (34.4 g, 182 mmol, 1.0 eq.) in CHCl₃ (182 mL) in a 3 L flask submerged in a room temperature water bath was added mCPBA (62.8 g, 75% purity, 273 mmol, 1.5 eq.) in several portions. After 30 min, the reaction turned too thick to stir and another 100 mL of CHCl₃ was added. The resulting mixture was then stirred at r.t. for 16 h, and then diluted with CHCl₃ (2 L), followed by addition of K₂CO₃. The resulting white slurry was stirred at r.t. for 2 h then mixed with celite (200 g) and filtered through a layer of celite. The filter cake was rinsed with CHCl₃ until no product could be detected by TLC. The filtrate was then concentrated and purified by flash column chromatography (EtOAc in Hexane:10%-40%) to yield compound 15 (30.6 g, 149 mmol, 82%) as pale yellow crystalline solid, and recovered compound 14 (2.64 g, 14 mmol, 8%).

\[\text{1H-NMR (400 MHz, CDCl₃)} \delta 7.46 (t, J = 7.6 Hz, 1H), 6.89 (d, J = 7.6 Hz, 2H), 2.84 (t, J = 6.38 Hz, 4H), 1.82 – 1.76 (m, 4H), 1.42 – 1.36 (m, 4H), 1.04 – 0.98 (m, 4H); \text{13C-NMR (100 MHz, CDCl₃)} \delta 160.6, 136.6, 120.0, 35.7, 26.3, 25.1, 23.2; \text{HRMS (EI) calculated for C}_{13}H_{20}NO [M + H]^+ : 206.1539, found 206.1534.}

Table S2. Optimization of the photo-induced rearrangement.

| Entry | Solvent | Temp (°C) | % Yield | 14 | 16 | 17 | 18 |
|-------|---------|-----------|----------|----|----|----|----|
| 1     | c-hexane| r.t.      | 17       | 3  | 3  | 4  |
| 2     | DME     | r.t.      | 12       | 6  | 4  | 10 |
| 3     | EtOH    | r.t.      | 7        | 3  | 6  | 7  |
| 4     | MeCN    | r.t.      | 8        | 4  | 5  | 7  |
| 5     | THF     | r.t.      | 11       | 9  | 7  | 14 |
| 6     | THF     | -40       | 19       | 5  | 18 | 12 |
| 7     | THF     | -78       | 10       | 2  | 19 | 10 |
| 8     | DME     | -30       | 14       | 5  | 10 | 15 |
| 9a    | water   | r.t.      | nd       | nd | 4  | nd |
| 10b   | EtOH    | r.t.      | nd       | nd | 7  | nd |
| 11c   | THF     | r.t.      | nd       | nd | trace | nd |
| 12d   | THF     | -75       | 9        | 3  | 19 | 17 |
| 13e   | THF     | -75       | 15       | 5  | 25 | 18 |

*a 10 eq. CuSO₄ were added. *b The Cu(NO₃)₂ bis-adduct of 15 was used. *c Rh₂TFA₄ was added, complete decomposition of 15 was observed. *d Experiment performed in flow format (residence time = 2 min) with one layer of FEP tubing around the immersion well. *e Experiment performed in flow format with three layers of FEP tubing around the immersion well (residence time = 5 min). nd = not determined.
Batch Irradiation Conditions (Table S2, entry 6): A 1 L immersion well photoreactor was charged with a solution of 15 (3.9 g, 19.18 mmol) in THF (1 L, 0.02M). The solution was cooled to -40 °C and then irradiated with a 450 W Hanovia Mercury Arc lamp for 3h with stirring. The mixture was monitored by 1H-NMR spectrum analysis of aliquots. The lamp was removed and the mixture was warmed to room temperature and concentrated. The residue was then purified by flash column chromatography (EtOAc in Hexane: 10% - 20% - 22% - 30% - 40%).

Flow Irradiation Conditions (Table S2, entry 13): A quartz immersion well wrapped with 3 layers of FEP tubing was placed in a dewar and cooled to -75 °C with isopropanol and dry ice. The solution of 15 (6.32 g, 30.8 mmol) in anhydrous THF (0.01 M) was pumped through the FEP tubing with a residence time of 5 minutes. The resulting light yellow solution was concentrated, purified by flash column chromatography (EtOAc in Hexane: 10% - 20% - 22% - 30% - 40%). This resulted in 16 (292 mg, 1.42 mmol, 5%), 17 (1.56 g, 7.6 mmol, 25%), 18 (1.185 g, 5.3 mmol, 18%) and 14 (866 mg, 4.6 mmol, 15%).

5,6,7,8,9,10,11,12-octahydrocycloundeca[b]pyrrol-4(1H)-one (16)

White solid. M.P.: 154 °C. 1H-NMR (500 MHz, CDCl3) δ 8.14 (s, 1H), 6.63 (t, J = 2.7 Hz, 1H), 6.44 (t, J = 2.9 Hz, 1H), 3.09 (t, J = 6.35 Hz, 1H), 2.68 (t, J = 6.35 Hz, 1H), 1.75 (p, J = 6.2 Hz, 2H), 1.64 – 1.58 (m, 2H), 1.37 (p, J = 6.1 Hz, 2H), 1.23 (t, J = 8.9, 4.6 Hz, 2H), 1.12 (ddt, J = 10.3, 7.7, 4.6 Hz, 2H), 1.09 – 1.01 (m, 2H); 13C-NMR (126 MHz, CDCl3) δ 202.3, 136.9, 124.3, 116.6, 110.1, 41.7, 28.1, 27.8, 25.4, 25.1, 24.6, 24.5, 22.8; HRMS (EI) calculated for C13H20NO [M + H]+: 206.1545, found 206.1532.

1H-1(2,5)-pyrrolacyclodecaphan-2-one (17)

White solid. M.P.: 198 °C. 1H-NMR (500 MHz, CDCl3) δ 8.73 (s, 1H), 6.98 (t, J = 3.2 Hz, 1H), 6.09 (t, J = 3.2 Hz, 1H), 2.78 – 2.73 (m, 2H), 2.68 (t, J = 6.3 Hz, 2H), 1.79 (tq, J = 13.6, 6.8, 6.1 Hz, 4H), 1.60 – 1.49 (m, 2H), 1.37 (p, J = 6.0 Hz, 2H), 1.21 (p, J = 6.9 Hz, 2H), 1.08 (ddt, J = 12.3, 8.9, 5.4 Hz, 2H); 13C-NMR (125 MHz, CDCl3): 190.3, 137.9, 132.3, 115.9, 111.5, 36.1, 27.0, 26.7, 26.2, 23.5, 23.4, 23.3, 21.7; HRMS (EI) calculated for C13H21NO2 [M + H]+: 224.1651, found 224.1637.

(Z)-azacyclotetradec-13-ene-2,11-dione (18)

White solid. M.P.: 119 °C. 1H-NMR (500 MHz, CDCl3) δ 7.63 (d, J = 10.1 Hz, 1H), 6.90 (ddt, J = 10.4, 9.0, 1.3 Hz, 1H), 4.80 (dt, J = 9.1, 7.7 Hz, 1H), 3.15 (dd, J = 7.7, 1.2 Hz, 2H), 2.45 (t, J = 6.7 Hz, 2H), 2.36 – 2.33 (m, 2H), 1.69 – 1.61 (m, 4H), 1.35 (tt, J = 7.1, 3.0 Hz, 4H), 1.27 (q, J = 7.3 Hz, 2H), 1.17 (dq, J = 8.4, 6.5 Hz, 2H); 13C-NMR (126 MHz, CDCl3) δ 210.7, 170.9, 125.4, 101.0, 41.9, 40.7, 36.0, 26.8, 26.0, 25.3, 25.3, 24.3, 23.3; HRMS (EI) calculated for C13H21NO2 [M + H]+: 224.1651, found 224.1637.
Figure S1. Setup of flow chemistry for photolysis.
To a flame-dried 3-neck 100 mL round bottom flask, equipped with a low-temperature thermometer and a stir bar, was added anhydrous THF (10 mL) and iPr₂NH (0.9 mL, 6.2 mmol, 3.2 eq.) at r.t., and then cooled to -78 °C with an acetone-dry ice bath, followed by addition of n-BuLi (2.5 M in hexane, 2.5 mL, 6.2 mmol, 3.1 eq.). After addition, the resulting colorless solution was stirred for 10 min at -78 °C, then warmed up to 0 °C in ice-water bath. The solution of 17 (410 mg, 2 mmol, 1.0 eq.) in anhydrous THF (30 mL) was added into the formed LDA solution via syringe pump over 3 h while maintaining the LDA solution at 0 °C. The resulting light yellow solution was stirred for another 30 min at 0 °C, then cooled to -78 °C with an acetone-dry ice bath. (S)-Propylene oxide (0.7 mL, 10 mmol, 5.0 eq.) was added, followed by AlMe₃ solution (2.0 M in hexane, 1.1 mL, 2.2 mmol, 1.1 eq.). The reaction mixture was stirred at -78 °C for another 30 min, and then slowly warmed up to r.t. over 1 h, then allowed to stir at r.t. overnight. TLC monitoring showed products were the major spots. To quench the reaction, the mixture was carefully added into a stirred solution of potassium sodium tartrate and ice, then extracted with EtOAc (50 mL x 3). The organic layers were combined, washed with brine, dried over Na₂SO₄, filtered, concentrated, and purified by flash column chromatography using TEA neutralized silica gel (EtOAc in Hexane: 25% - 30% - 35% - 40%). The mixture of 6a and 6b (374 mg, 4.95 mmol, 71%, d.r. = 2:1) was obtained as a light yellow semisolid. 17 (60 mg, 15%) was also recovered. Two isomers 6a and 6b could be separated via flash column chromatography on TEA-neutralized silica gel (EtOAc in Hexane: 30% - 35\%)

(R)-3-((S)-2-hydroxypropyl)-11H-1(2,5)-pyrrolacyclodecaphan-2-one (6a)

\[ \text{1H-NMR} (500 MHz, C₆D₆) \delta 9.14 (s, 1H), 7.25 (t, J = 3.0 Hz, 1H), 5.94 (t, J = 3.0 Hz, 1H), 3.81 - 3.79 (m, 1H), 3.47 - 3.43 (m, 1H), 2.45 - 2.40 (m, 1H), 2.38 - 2.35 (m, 1H), 2.23 - 2.16 (m, 1H), 1.77 - 1.75 (m, 1H), 1.65 - 1.60 (m, 1H), 1.51 - 1.49 (m, 1H), 1.40-1.03 (m, 7H), 1.00 (d, J = 6.2 Hz, 3H), 0.98 – 0.75 (m, 4H); \text{13C-NMR} (125 MHz, C₆D₆) \delta 192.0, 137.9, 134.3, 115.9, 111.6, 66.4, 42.1, 41.1, 35.7, 27.2, 26.9, 24.9, 24.4, 24.1, 24.0, 22.3; \text{HRMS (EI) calculated for C}_{16}H_{25}NO_{2} [M]^+: 263.1885, found: 263.1844 \]

(S)-3-((S)-2-hydroxypropyl)-11H-1(2,5)-pyrrolacyclodecaphan-2-one (6b)

\[ \text{1H-NMR} (500 MHz, C₆D₆) \delta 9.23 (s, 1H), 7.22 (dd, J = 2.7, 3.7 Hz, 1H), 5.94 (t, J = 2.7 Hz, 1H), 3.70 – 3.80 (m, 1H), 3.25 – 3.32 (m, 1H), 2.49 (td, J = 3.9, 15.5 Hz, 1H), 2.15 – 2.32 (m, 3H), 1.63 – 1.72 (m, 1H), 1.50 – 1.61 (m, 2H), 1.40 – 1.11 (m, 5H), 1.09 (d, J = 6.2 Hz, 3H), 0.99 – 0.80 (m, 5H); \text{13C-NMR} (125 MHz, C₆D₆) \delta 193.0, 138.1, 133.8, 116.2, 111.6, 67.0, 41.52, 41.50, 35.2, 27.2, 27.0, 24.5, 24.3, 24.1, 24.0, 22.5; \text{HRMS (EI) calculated for C}_{16}H_{25}NO_{2} [M]^+: 263.1885, found: 263.1838 \]
**Figure S2.** Equilibrium of compound 6 isomers in wet CDCl₃.

To the mixture of 6a and 6b (683 mg, 2.6 mmol, 1.0 eq.) in toluene (26 mL, 0.1 M) and Na₂SO₄ (2.6 g) at 0 °C was added HCl (3.9 mL, 1M in MeOH, 1.5 eq), followed by addition of bipyrrrole 20 (0.82 g, 2.60 mmol, 1.0 eq) in toluene (20 mL) via syringe pump over 30 min. After addition, the resulting dark red solution was immediately quenched by dropwise addition into a solution of freshly prepared NaOMe (1M in MeOH, 10 mL, 3.85 eq) at 0 °C. The resulting orange solution was added dropwise into ice-water, then extracted with EtOAc (20 mL X 3). The organic layers were combined, washed with brine, dried over Na₂SO₄, filtered, and concentrated. The resulting crude product was immediately purified via flash column chromatography on TEA-neutralized silica gel (EtOAc in Hexane: 5%). Concentration resulted in compound 22 as a tan foam containing minor spectroscopic impurities due to oxygen contact. (1.27 g, 87% yield, 1:1 d.r.). These impurities do not affect subsequent reactions performed with this material, but an analytically pure, colorless sample may be isolated via subsequent chromatography, albeit with substantial
material loss. The mixture of compounds 22 (unstable when concentrated) was stored in toluene (0.1M) as a stock solution at -20 °C for later use. If the dark red solution of 21 was left at r.t. for 1h before quenching, it resulted in compound 22 (889 mg, 61% yield, 1:1 dr) as light yellow oil, and compound S27 (320 mg, 22% yield) as an orange oil.

(25S)-22-(4-methoxy-1'-tosyl-1'H,1'H-[2,2'-bipyrrrol]-5-yl)-25-methyl-22,23,24,25-tetrahydro-11H-1(2,5)-pyrrola-2(2,3)-furanacyclononaphane (22)

Spectra of this compound are of a colorless sample obtained via the aforementioned secondary purification. 

\[^{1}H\text{-NMR}\ (500 \text{MHz, CDCl}_3) \delta 8.96 \ (s, 1H), 8.84 \ (s, 1H), 8.76 \ (s, 1H), 8.69 \ (s, 1H), 7.39 – 7.36 \ (m, 2H), 7.26 \ (d, J = 3.0 Hz, 2H), 7.25 \ (d, J = 3.0 Hz, 2H), 6.92 \ (d, J = 8.0 Hz, 2H), 6.83 \ (d, J = 8.0 Hz, 2H), 6.23 \ (t, J = 3.3 Hz, 2H), 6.18 \ (ddd, J = 3.3, 1.8, 9.1Hz, 2H), 6.01 \ (dq, J = 3.1, 2.8Hz, 2H), 6.01 \ (dd, J = 3.2, 7.4 Hz, 2H), 5.82 \ (dt, J = 14.8, 2.8 Hz, 2H), 4.45 – 4.38 \ (m, 1H), 4.20 – 4.14 \ (m, 1H), 3.83 \ (s, 3H), 3.80 \ (s, 3H), 2.87 \ (q, J = 7.5 Hz, 1H), 2.76 \ (t, J = 6.1 Hz, 1H), 2.72-2.51 \ (m, 4H), 2.28 \ (s, 3H), 2.24 \ (s, 3H), 2.22 – 2.16 \ (m, 1H), 1.88 – 1.83 \ (m, 1H), 1.79 – 1.72 \ (m, 1H), 1.69 – 1.58 \ (m, 2H), 1.57 – 1.42 \ (m, 6H), 1.39 \ (d, J = 6.2 Hz, 3H), 1.35 \ (d, J = 6.2 Hz, 3H), 1.32 – 0.84 \ (m, 15H), 0.82 – 0.75 \ (m, 1H), 0.74 – 0.65 \ (m, 1H); \[^{13}C\text{-NMR}\ (125 \text{MHz, CDCl}_3) \delta 144.7, 144.6, 141.6, 139.7, 134.7, 130.9, 129.5, 129.4, 129.60, 127.56, 127.52, 127.4, 123.3, 123.11, 123.08, 121.6, 115.3, 114.9, 114.5, 114.1, 111.3, 111.1, 106.2, 105.3, 105.0, 104.9, 100.0, 99.9, 85.2, 84.5, 75.5, 73.7, 58.82, 58.80, 48.1, 48.0, 42.1, 41.0, 31.6, 31.5, 29.5, 28.2, 27.8, 27.3, 26.8, 26.7, 25.8, 25.5, 25.4, 23.8, 22.7, 21.6, 21.5, 21.3, 14.2, 14.1; \[^{HRMS}\ \text{(ESI) calculated for C}_{32}\text{H}_{40}\text{N}_{3}\text{O}_{4}\text{S \ [M + H]^+}: 562.2734, found: 562.2703.}

(S,E)-1-(2-(4-methoxy-1'-tosyl-1'H,1'H-[2,2'-bipyrrrol]-5-yl)-11H-1(2,5)-pyrrolacyclodecaphan-2-en-13-yl)propan-2-ol (S27)

\[^{1}H\text{-NMR}\ (500 \text{MHz, d}_6\text{-acetone}) \delta 9.30 \ (s, 1H), 9.11 \ (s, 1H), 7.38 \ (d, J = 8.4 Hz, 2H), 7.32 \ (dd, J = 3.2, 1.9 Hz, 1H), 7.30 \ (d, J = 8.4 Hz, 2H), 6.47 \ (t, J = 8.4 Hz, 1H), 6.26 \ (m, 2H), 6.08 \ (s, 1H), 5.79 \ (d, J = 2.8 Hz, 1H), 3.89 \ (q, J = 6.4 Hz, 1H), 3.75 \ (s, 3H), 2.64 \ (m, 2H), 2.44 \ (d, J = 7.3 Hz, 1H), 2.42 \ (d, J = 5.9 Hz, 1H), 2.36 \ (s, 3H), 1.92 \ (m, 2H), 1.60 \ (m, 2H), 1.53-1.13 \ (m, 7H), 1.11 \ (d, J = 6.2 Hz, 3H), 0.61 \ (m, 1H), 0.54 \ (m, 1H); \[^{13}C\text{-NMR}\ (125 \text{MHz, d}_6\text{-acetone}) \delta 146.1, 146.0, 136.2, 132.9, 130.7, 129.8, 129.2, 129.2, 127.9, 127.9, 127.4, 124.2, 123.9, 119.4, 118.5, 118.3, 117.3, 117.2, 115.2, 112.9, 106.3, 99.9, 99.8, 68.6, 58.1, 37.4, 30.1, 29.0, 28.5, 28.4, 27.7, 27.4, 26.3, 23.6, 21.5; \[^{HRMS}\ \text{(ESI) calculated for C}_{32}\text{H}_{40}\text{N}_{3}\text{O}_{4}\text{S \ [M + H]^+}: 562.2734, found: 562.2692.}
Procedure for ‘acidic’ MnO₂ preparation:

To a solution of MnSO₄•H₂O (8.45 g, 50 mmol, 5.0 eq.) in DI water (50 mL) cooled in an ice-water bath, a solution of KMnO₄ (1.58 g, 10 mmol, 1.0 eq) in DI water (50 mL) was added at a rate such that the reaction was maintained between 5-10 °C. After addition, the mixture was stirred for 1 h (pH ~ 2), then left standing for 12 h. The resulting mixture was filtered, and the filter cake was washed with DI water (100 mL x 3) and acetone (50 mL x 3). The resulting brown powder was stripped with benzene (50 mL x 3) on a rotavapor in a 25 °C water bath, then placed on a high-vac line for 3h, and stored under an atmosphere of Ar.

Table S3. Relative rates of benzylic oxidation mediated by MnO₂ forms.

| Eq. of MnO₂ | Yield of benzaldehyde | commercial MnO₂ | freshly prepared ‘acidic’ MnO₂ |
|------------|-----------------------|----------------|-------------------------------|
| 4          | 22                    | 22             | 0.8                           |
| 8          | 39                    | 39             | 2                             |
| 12         | 67                    | 67             | 2.7                           |
| 16         | 71                    | 71             | 4                             |
| 20         | 75                    | 75             | 5.6                           |

General procedure for oxidation of benzyl alcohol with MnO₂:

To a vial with MnO₂ solid and a stir bar, was added the solution of benzyl alcohol in CHCl₃ (0.1 M, 2 mL). The mixture was stirred at r.t. for 1 h, and then filtered through celite, concentrated on rotavapor (vacuum: 140 mbar) until dry. The yield was determined by ¹H-NMR using 3,5-dibromobenzadehyde (0.1 mmol) as internal standard.
Preparation of 24:

A dram vial was charged with a toluene stock solution of compound 22 (30 mg, 0.0535 mmol, 1.0 eq.), which was then concentrated and stripped with toluene (1 mL x 2). The resultant oil was then mixed with polished Mg (6.6 mg, 0.275 mmol, 5.0 eq.) under Ar and diluted with MeOH (0.6 mL). The resulting mixture was sonicated at r.t. for 20 min, at which point TLC showed complete conversion. The clear orange solution was transferred into a new vial under Ar and the reaction vial was rinsed with toluene (1 mL) while leaving the unreacted Mg behind. The orange solution was concentrated on a rotavapor to dryness and backfilled with Ar. This process was repeated twice with toluene (1 mL x 2) (after each addition of toluene, the heterogeneous mixture was sonicated to minimize bumping). The residue was taken up in toluene, mixed with celite and filtered through a celite plug into a flame-dried vial under Ar. The plug was rinsed with toluene until the filtrate turned colorless. This provided a solution of 23 in toluene in quantitative yield.

The solution of 23 was added dropwise over 15 min into a vigorously stirred slurry of commercial MnO2 (314 mg, 50 eq) in acetone (1 ml). After addition, the mixture was combined with celite and filtered through a celite plug. The resulting orange solution was concentrated and immediately purified by flash column chromatography (EtOAc/Hexane: 30-40%) to afford compound 24 (11.9 mg, 52% yield) as a mixture of four diastereomers.

4'-methoxy-5'-((25S)-25-methyl-22,23,24,25-tetrahydro-11H-1(2,5)-pyrrola-2(2,3)-furanacyclonaphane-22-yl)-[2,2'-bipyrrolylidene]-5(1H)-one (24)

1H-NMR (500 MHz, d6-acetone) δ 10.15 (s, 1H), 10.01 (s, 1H), 9.62 (s, 2H), 8.00 (t, J = 5.7 Hz, 2H), 7.81 (d, J = 5.6 Hz, 2H), 7.77 (d, J = 5.6 Hz, 2H), 7.24 – 7.10 (m, 6H), 6.69 (s, 1H), 6.63 (s,1H), 6.60 (s,1H), 6.57 (s,1H), 6.39 (dd, J = 5.7, 9.6 Hz, 2H), 6.36 (d, J = 5.7 Hz, 1H), 6.32 (d, J = 5.7 Hz, 1H), 5.91 (t, J = 2.6 Hz, 1H), 5.88 (t, J = 2.7 Hz, 1H), 5.74 – 5.72 (m, 2H), 5.68 – 5.66 (m, 2H), 5.61 (t, J = 2.6 Hz, 1H), 5.58 (t, J = 2.7 Hz, 1H), 4.42 – 4.38 (m, 2H), 4.27 – 4.25 (m, 1H), 4.20 – 4.16 (m, 1H), 3.81 (s, 3H), 3.80 (s, 3H), 3.74 (s, 3H), 3.72 (s, 3H), 3.28 – 3.24 (m, 2H), 3.05 – 2.95 (m, 2H), 2.70 – 2.57 (m, 8H), 2.55 (t, J = 2.2 Hz, 6H). The rest of peaks are not countable due to complexity. HRMS (EI) calculated for C25H31N3O3 [M + H]+: 422.2438, found: 422.2430.
Preparation of 8 and 26:

A solution of 23 was prepared following the procedure outlined in the preparation of 24. It was then concentrated to a volume of ~2 mL, then cooled in an ice-water bath for 5 min. Dry HCl solution (0.16 mL, 1M in MeOH, 3.0 eq.) was added and the yellow solution turned dark purple-red immediately. This solution was carefully concentrated without heating on a rotavapor until the pressure reached 20 mbar to remove any MeOH and excess HCl. The vial was placed back into an ice-water bath under Ar and the remaining toluene solution of 25 was diluted with dry acetone to a total volume of 4 mL.

Into each of a set of 4 flame dried dram vials was placed the ‘acidic’ MnO₂ reagent (68 mg, 0.784 mmol) and MgSO₄ (30 mg) under argon. To each vial was added dry acetone (0.5 mL). Under vigorous stirring, 1 mL of the dark red solution was added into each vial via syringe pump over 5 min. After addition, the mixture was filtered through a celite plug and rinsed with acetone until the filtrate turned colorless. The yellow filtrate was concentrated, diluted with CH₃CN, and purified by HPLC (CH₃CN/water, 0.1% formic acid, Sunfire C18 column, 40-47%, 2-8 min, 20 mL/min). 8 (1.2 mg, 6% yield) and 26 (1.2 mg, 6% yield) were collected.

(2R,3'S,4'S,6'S)-3-methoxy-6'-methyl-5-(1H-pyrrol-2-yl)spiro[pyrrole-2,2'-1(2,5)-pyrrola-2(3,4)-pyranacyclononaphan]-1-ium chloride (8)

1H-NMR (500 MHz, d₆-acetone) δ 13.78 (s, 1H), 12.63 (s, 1H), 10.56 (s, 1H), 7.69 (s, 1H), 7.40 (s, 1H), 6.48 (s, 1H), 6.21 (s, 1H), 5.66 (s, 1H), 4.46 – 4.42 (m, 1H), 4.11 (s, 3H), 2.93 (d, J = 12.6 Hz, 1H), 2.85 – 2.80 (m, 1H), 2.45 (d, J = 14.2 Hz, 1H), 2.25 (d, J = 13.1 Hz, 1H), 1.92 (d, J = 11.8 Hz, 1H), 1.73 – 1.61 (m, 4H), 1.47 – 1.25 (m, 12H), 1.08 – 0.73 (m, 7H), 0.60 – 0.50 (m, 1H); 13C-NMR (125 MHz, d₆-acetone) δ 181.5, 165.5, 134.4, 133.9, 126.7, 125.0, 121.8, 114.3, 110.4, 105.5, 97.0, 93.7, 77.2, 71.9, 60.9, 60.5, 47.2, 38.4, 28.9, 28.7, 26.1, 25.5, 25.4, 25.3, 21.5; HRMS (EI) calculated for C₂₅H₃₄N₃O₂ [M + H]⁺: 408.2646, found: 408.2632.

(2S,3'R,4'R,6'S)-3-methoxy-6'-methyl-5-(1H-pyrrol-2-yl)spiro[pyrrole-2,2'-1(2,5)-pyrrola-2(3,4)-pyranacyclononaphan]-1-ium chloride (26)
M.P.: 197-198 °C. $^1$H-NMR (500 MHz, CDCl$_3$) $\delta$ 13.35 (s, 1H), 12.92 (s, 1H), 9.82 (s, 1H), 7.50 – 7.45 (m, 1H), 7.08 – 7.03 (m, 1H), 6.41 (dq, $J = 2.1$, 2.1 Hz, 1H), 5.71 (t, $J = 2.8$ Hz, 1H), 5.57 – 5.54 (m, 2H), 4.26 – 4.18 (m, 1H), 4.05 (s, 3H), 2.93 (d, $J = 12.6$ Hz, 1H), 2.88 – 2.80 (m, 1H), 2.54 (td, $J = 4.2$, 14.6 Hz, 1H), 2.28 (d, $J = 5.0$, 15.0 Hz, 1H), 2.28 (dq, $J = 1.8$, 13.5 Hz, 1H), 2.09 – 1.98 (m, 2H), 1.92 – 1.82 (m, 1H), 1.54 – 1.48 (m, 1H), 1.47 – 1.39 (m, 1H), 1.26 (d, $J = 2.1$ Hz, 3H), 1.22 (d, $J = 13.3$ Hz, 1H), 1.17 – 1.11 (m, 1H), 1.04 – 0.98 (m, 2H), 0.89 – 0.83 (m, 2H), 0.82 – 0.73 (m, 1H), 0.48 – 0.38 (m, 1H); $^{13}$C-NMR (125 MHz, CDCl$_3$) $\delta$ 179.4, 164.2, 134.8, 133.4, 125.6, 124.2, 120.9, 113.7, 109.6, 104.4, 97.5, 92.7, 72.7, 60.1, 46.0, 40.5, 33.4, 28.2, 25.0, 24.8, 24.6, 24.5, 21.8; HRMS (EI) calculated for C$_{25}$H$_{34}$N$_3$O$_2$ [M + H$^+$]: 408.2646, found: 408.2618.

(2R,3S,3’S,4’S,6’S)-3-methoxy-6’-methyl-5-(1H-pyrrol-2-yl)-3,4-dihydrospiro[pyrrole-2,2’-1(2,5)-pyrrola-2(3,4)-pyranacyclonaphane], marineosin A (10)

Compound 8 (7.2 mg, 0.0177 mmol) and Pd/BaSO$_4$ (10.2 mg) in EtOAc (1 mL) was stirred vigorously (1500 rpm) under a hydrogen atmosphere (1 atm.) for 16 h. LCMS showed reaction was complete. The mixture was filtered through celite and rinsed with EtOAc. The filtrate was concentrated to afford 6.8 mg crude product, and then purified by PTLC (EtOAc in Hexane, 20%). Pure marineosin A (2.2 mg, 30% yield) was obtained as a colorless oil. [α]$_D$ = +138.7 (c = 0.02, MeOH), lit. $-101.7^\circ$ (c = 0.06, MeOH).$^{[1]}$ $^1$H-NMR (500 MHz, d$_6$-acetone) $\delta$ 10.96 (s, 1H), 8.23 (s, 1H), 6.98 (s, 1H), 6.38 (s, 1H), 6.12 (s, 1H), 5.69 (s, 1H), 5.45 (s, 1H), 4.28 – 4.20 (m, 1H), 3.90 – 3.82 (m, 1H), 3.42 (s, 3H), 2.95 – 2.92 (m, 1H), 2.90 – 2.86 (m, 1H), 2.40 – 2.29 (m, 1H), 2.27 – 2.20 (m, 2H), 1.94 – 1.84 (m, 1H), 1.79 (d, $J = 12.4$ Hz, 1H), 1.70 – 1.58 (m, 2H), 1.53 (d, $J = 6.6$ Hz, 3H), 1.41 – 1.25 (m, 6H), 1.24 – 1.14 (m, 1H), 1.08 – 0.99 (m, 1H), 0.93 – 0.83 (m, 2H), 0.76 – 0.65 (m, 1H), 0.57 – 0.47 (m, 1H); $^{13}$C-NMR (125 MHz, d$_6$-acetone) $\delta$ 164.4, 129.9, 129.2, 122.5, 113.5, 110.0, 106.1, 104.7, 90.0, 70.4, 58.5, 45.9, 39.6, 39.1, 32.0, 28.6, 28.1, 25.7, 25.6, 25.5, 22.8; HRMS (EI) calculated for C$_{25}$H$_{36}$N$_3$O$_2$ [M + H$^+$]: 410.2802, found: 410.2791.

The enantiomer of marineosin A was prepared using exactly the same procedures and reagents as marineosin A’s, except using (R)-propylene oxide for the alkylation.
Spectral data comparison between natural and synthetic material

Table S4. Comparison of Marineosin A NMR data in Acetone-d6.

|                  | ^1H-NMR (Natural) | ^1H-NMR (Synthetic) | ^13C-NMR (Natural) | ^13C-NMR (Synthetic) |
|------------------|-------------------|---------------------|-------------------|----------------------|
| 10.93 (br s, 1H) | 10.96 (br s, 1H)  | 164.4               | 164.4             |
| 8.23 (br s, 1H)  | 8.23 (br s, 1H)   | 129.9               | 129.9             |
| 6.97 (dd, J = 2.5, 1.5 Hz, 1H) | 6.98 (s, 1H) | 129.1               | 129.2             |
| 6.37 (dd, J = 2.5, 1.5 Hz, 1H) | 6.38 (s, 1H) | 122.5               | 122.5             |
| 6.11 (dd, J = 3.5, 2.5 Hz, 1H) | 6.12 (s, 1H) | 113.5               | 113.5             |
| 5.68 (d, J = 3.0 Hz, 1H) | 5.69 (s, 1H) | 110.1               | 110.0             |
| 5.44 (d, J = 3.0 Hz, 1H) | 5.45 (s, 1H) | 106.1               | 106.1             |
| 4.23 (m, 1H)     | 4.28 – 4.20 (m, 1H) | 104.7             | 104.7             |
| 3.85 (t, J = 8.5 Hz, 1H) | 3.90 – 3.82 (m, 1H) | 89.9               | 89.9               |
| 3.40 (s, 3H)     | 3.42 (s, 3H)      | 70.4                 | 70.4               |
| 2.91 (d, J = 12.0 Hz, 1H) | 2.95 – 2.92 (m, 1H) | 58.5               | 58.5               |
| 2.88 (dd, J = 16.0, 8.5 Hz, 1H) | 2.90 – 2.86 (m, 1H) | 45.9               | 45.9               |
| 2.32 (m, 1H)     | 2.40 – 2.29 (m, 1H) | 39.6               | 39.6               |
| 2.23 (m, 2H)     | 2.27 – 2.20 (m, 2H) | 39.0               | 39.1               |
| 1.88 (dd, J = 16.0, 8.5 Hz, 1H) | 1.94 – 1.84 (m, 1H) | 32.0               | 32.0               |
| 1.77 (m, 1H)     | 1.79 (d, J = 12.4 Hz, 1H) | 28.6               | 28.6               |
| 1.64 (m, 1H)     | 1.70-1.58 (m, 3H)  | 28.0               | 28.1               |
| 1.61 (td, J = 12.0, 6.5 Hz, 1H) | 25.7               | 25.7               |
| 1.52 (m, 1H)     | 25.5               | 25.6               |
| 1.51 (d, J = 6.5 Hz, 3H) | 1.53 (d, J = 6.6 Hz, 3H) | 25.4               | 25.5               |
| 1.37 (m, 1H)     | 1.41-1.25 (m, 4H)  | 22.8               | 22.8               |
| 1.35 (m, 1H)     | 1.24 – 1.14 (m, 1H) | 22.8               | 22.8               |
| 1.34 (m, 1H)     | 1.08 – 0.99 (m, 1H) | 22.8               | 22.8               |
| 1.28 (m, 1H)     | 0.93 – 0.83 (m, 2H) | 22.8               | 22.8               |
| 0.69 (m, 1H)     | 0.76 – 0.65 (m, 1H) | 22.8               | 22.8               |
| 0.52 (m, 1H)     | 0.57 – 0.47 (m, 1H) | 22.8               | 22.8               |
Crystal Structure Analysis

Crystals suitable for X-ray analysis were grown by slow diffusion of the samples in EtOAc into Hexane at room temperature. The diffraction data were measured 100K(2) on a Bruker Smart Apex2 CCD-based X-ray diffractometer system equipped with a Mo-Kα radiation ($\lambda = 0.71073$ Å). The frames were integrated with the Bruker Saint software package using a narrow-frame integration algorithm. The structure was solved and refined using the Bruker SHELXTL Software Package. All atoms were refined anisotropically, and hydrogen atoms were removed for clarity.

**ORTEP of 16 (50% probability ellipsoids)**
Table S5. Crystal data and structure refinement for Compound 16.

| Identification code       | cu_har1703s_a       |
|---------------------------|---------------------|
| Empirical formula         | C13 H19 N O         |
| Formula weight            | 205.29              |
| Temperature               | 100(2) K            |
| Wavelength                | 1.54178 Å           |
| Crystal system            | Monoclinic          |
| Space group               | P2₁/n               |
| Unit cell dimensions      |                     |
| a                         | 9.4220(3) Å         |
| b                         | 9.3471(3) Å         |
| c                         | 12.8767(5) Å        |
| a= 90°                    | b= 99.966(2)°       |
|                         | g = 90°             |
| Volume                    | 1116.92(7) Å³       |
| Z                         | 4                   |
| Density (calculated)      | 1.221 Mg/m³         |
| Absorption coefficient    | 0.594 mm⁻¹          |
| F(000)                    | 448                 |
| Crystal size              | .4 x .3 x .1 mm³    |
| Theta range for data collection | 5.397 to 69.880°   |
| Index ranges              | -11<=h<=11, -11<=k<=11, -15<=l<=12 |
| Reflections collected     | 8386                |
| Independent reflections   | 2062 [R(int) = 0.0213] |
| Completeness to theta = 67.679° | 99.2 %             |
| Absorption correction     | Semi-empirical from equivalents |
| Max. and min. transmission| 0.75 and 0.68       |
| Refinement method         | Full-matrix least-squares on F² |
| Data / restraints / parameters | 2062 / 0 / 145     |
| Goodness-of-fit on F²     | 1.098               |
| Final R indices [I>2sigma(I)] | R1 = 0.0389, wR2 = 0.0921 |
| R indices (all data)      | R1 = 0.0420, wR2 = 0.0934 |
| Extinction coefficient    | n/a                 |
| Largest diff. peak and hole | 0.330 and -0.198 e.Å⁻³ |
ORTEP of 17 (50% probability ellipsoids)
Table S6. Crystal data and structure refinement for Compound 17.

| Parameter                        | Value                        |
|----------------------------------|------------------------------|
| Identification code              | cu_har1702s_a                |
| Empirical formula                | C13 H19 N O                  |
| Formula weight                   | 205.29                       |
| Temperature                      | 0(2) K                       |
| Wavelength                       | 1.54178 Å                    |
| Crystal system                   | Monoclinic                   |
| Space group                      | P2\(/n\)                     |
| Unit cell dimensions             | a = 7.7866(3) Å, a= 90°      |
|                                 | b = 15.2172(7) Å, b= 112.279(3)° |
|                                 | c = 10.1883(5) Å, g = 90°    |
| Volume                           | 1117.09(9) Å³                |
| Z                                | 4                            |
| Density (calculated)             | 1.221 Mg/m³                  |
| Absorption coefficient           | 0.594 mm⁻¹                   |
| F(000)                           | 448                          |
| Crystal size                     | ? x ? x ? mm³                 |
| Theta range for data collection  | 5.520 to 69.358°              |
| Index ranges                     | -8<=h<=9, -18<=k<=15, -11<=l<=11 |
| Reflections collected            | 8118                         |
| Independent reflections          | 2005 [R(int) = 0.0742]       |
| Completeness to theta = 67.679°  | 98.0%                        |
| Refinement method                | Full-matrix least-squares on F² |
| Data / restraints / parameters   | 2005 / 0 / 145               |
| Goodness-of-fit on F²            | 0.958                        |
| Final R indices [I>2sigma(I)]    | R1 = 0.0400, wR2 = 0.0984    |
| R indices (all data)             | R1 = 0.0492, wR2 = 0.1006    |
| Extinction coefficient           | n/a                          |
| Largest diff. peak and hole      | 0.218 and -0.229 e.Å⁻³        |
ORTEP of 18 (50% probability ellipsoids)
Table S7. Crystal data and structure refinement for Compound 18.

Identification code: mo_har1704s_a
Empirical formula: C13 H21 N O2
Formula weight: 223.31
Temperature: 100(2) K
Wavelength: 0.71073 Å
Crystal system: Monoclinic
Space group: P2₁/n
Unit cell dimensions:
\[ a = 9.7653(9) \text{ Å, } \alpha = 90^\circ. \]
\[ b = 9.7181(9) \text{ Å, } \beta = 98.8330(10)^\circ. \]
\[ c = 13.3075(12) \text{ Å, } \gamma = 90^\circ. \]
Volume: 1247.9(2) Å³
Z: 4
Density (calculated): 1.189 Mg/m³
Absorption coefficient: 0.079 mm⁻¹
F(000): 488
Crystal size: 0.400 x 0.300 x 0.200 mm³
Theta range for data collection: 2.419 to 30.916°.
Index ranges: -13 ≤ h ≤ 13, -13 ≤ k ≤ 13, -18 ≤ l ≤ 19
Reflections collected: 18951
Independent reflections: 3718 [R(int) = 0.0224]
Completeness to theta = 25.242°: 100.0 %
Absorption correction: Semi-empirical from equivalents
Max. and min. transmission: 0.75 and 0.70
Refinement method: Full-matrix least-squares on F²
Data / restraints / parameters: 3718 / 0 / 145
Goodness-of-fit on F²: 1.072
Final R indices [I>2sigma(I)]: R1 = 0.0433, wR2 = 0.1111
R indices (all data): R1 = 0.0454, wR2 = 0.1133
Extinction coefficient: n/a
Largest diff. peak and hole: 0.360 and -0.341 e.Å⁻³
ORTEP of Cu(NO₃)₂•[15]₂ (50% probability ellipsoids)

Preparation: To a solution of Cu(NO₃)₂ (0.464g, 1.99 mmol) in EtOH (20 mL) at r.t., compound 15 was added. The reaction was then stirred for 40 min. The reaction was then diluted with EtOH and heated until all solids dissolved. The reaction was then allowed to cool to r.t. and then stored in -20 °C for 4-5 hours. The mother liquor was decanted and the green crystals were dried under vacuum.
| Identification code | Cu(NO$_3$)$_2$$[15]_2$ |
|---------------------|-------------------------|
| Empirical formula   | C$_{26}$ H$_{38}$ Cu N$_4$ O$_8$ |
| Formula weight      | 598.14                  |
| Temperature         | 298(2) K                |
| Wavelength          | 0.71073 Å               |
| Crystal system      | Monoclinic              |
| Space group         | P2$_1$/c                |
| Unit cell dimensions| a = 10.6090(9) Å, b = 7.8790(6) Å, c = 17.4437(14) Å |
|                     | a = 90°, b = 97.679(2)°, c = 90° |
| Volume              | 1445.0(2) Å$^3$        |
| Z                   | 2                       |
| Density (calculated)| 1.375 Mg/m$^3$          |
| Absorption coefficient | 0.808 mm$^{-1}$     |
| F(000)              | 630                     |
| Crystal size        | 0.1 x 0.1 x 0.04 mm$^3$|
| Theta range for data collection | 1.937 to 30.490° |
| Index ranges        | -14<=h<=14, -11<=k<=11, -24<=l<=24 |
| Reflections collected | 23281              |
| Independent reflections | 4275 [R(int) = 0.0311]     |
| Completeness to theta = 25.242° | 100.0 %               |
| Absorption correction | Semi-empirical from equivalents |
| Max. and min. transmission | 0.74 and 0.67         |
| Refinement method   | Full-matrix least-squares on F$^2$ |
| Data / restraints / parameters | 4275 / 0 / 178 |
| Goodness-of-fit on F$^2$ | 1.013                |
| Final R indices [I>2sigma(I)] | R1 = 0.0371, wR2 = 0.0994 |
| R indices (all data) | R1 = 0.0663, wR2 = 0.1119 |
| Extinction coefficient | n/a                  |
| Largest diff. peak and hole | 0.647 and -0.316 eÅ$^{-3}$ |
ORTEP of 26 (50% probability ellipsoids)
Table S9. Crystal data and structure refinement for 26.

| Identification code | compound 26 |
|---------------------|-------------|
| Empirical formula   | C25 H34 Cl N3 O2 |
| Formula weight      | 444.02 |
| Temperature         | 100(2) K |
| Wavelength          | 1.54178 Å |
| Crystal system      | Monoclinic |
| Space group         | C2 |
| Unit cell dimensions| a = 33.1593(15) Å, b = 8.7821(4) Å, c = 23.3882(10) Å |
|                     | a= 90°, b= 129.718(2)°, g = 90° |
| Volume              | 5238.9(4) Å³ |
| Z                   | 4 |
| Density (calculated)| 1.180 Mg/m³ |
| Absorption coefficient | 1.493 mm⁻¹ |
| F(000)              | 2004 |
| Crystal size        | 0.4 x 0.1 x 0.1 mm³ |
| Theta range for data collection | 2.456 to 69.424°. |
| Index ranges        | -37<=h<=39, -10<=k<=9, -28<=l<=28 |
| Reflections collected | 38002 |
| Independent reflections | 9489 [R(int) = 0.0573] |
| Completeness to theta = 67.679° | 98.6 % |
| Absorption correction | Semi-empirical from equivalents |
| Max. and min. transmission | 0.75 and 0.63 |
| Refinement method   | Full-matrix least-squares on F² |
| Data / restraints / parameters | 9489 / 55 / 609 |
| Goodness-of-fit on F² | 1.048 |
| Final R indices [I>2sigma(I)] | R1 = 0.0460, wR2 = 0.1163 |
| R indices (all data) | R1 = 0.0541, wR2 = 0.1198 |
| Absolute structure parameter | 0.015(8) |
| Extinction coefficient | n/a |
| Largest diff. peak and hole | 0.470 and -0.357 e.Å⁻³ |
Compounds 14 and 15 are known. Their spectra may be found in manuscript reference 10: Weber, H. et al. Chem. Ber. 1989, 122, 945-950.

$^1$H NMR of compound 16 (CDCl$_3$, 500 MHz)
$^{13}$C NMR of compound 16 (CDCl$_3$, 125 MHz)
$^1$H NMR of compound 18 (CDCl$_3$, 500 MHz)
$^{13}$C NMR of compound 18 (CDCl$_3$, 125 MHz)
$^{13}$C NMR of compound 17 (CDCl$_3$, 125 MHz)
$^1$H NMR of compound 6a ($C_{6}D_{6}$, 500 MHz)
$^{13}$C NMR of compound 6a (C$_6$D$_6$, 125 MHz)
$^1$H NMR of compound 6b (C$_6$D$_6$, 500 MHz)
$^{13}$C NMR of compound 6b (C$_6$D$_6$, 125 MHz)
$^1$H NMR of compound 22 (CDCl$_3$, 500 MHz)
$^1$H NMR of compound 22 (CDCl$_3$, 125 MHz)
HSQC of compound 22 (CDCl₃, 500 MHz)
HMBC of compound 22 (CDCl₃, 500 MHz)
COSY of compound 22 (CDCl₃, 500 MHz)
NOESY of compound 22 (CDCl₃, 500 MHz) (only isomer 22a has nOe between H24 and H29)
$^1$H NMR of compound 24 (d$_6$-acetone, 500 MHz)
COSY of compound 24 (d₆-acetone, 500 MHz)
$^{1}$H NMR of compound 27 (d$_6$-acetone, 500 MHz)
$^{13}$C NMR of compound 27 (d$_6$-acetone, 125 MHz)
HSQC of compound 27 (d$_6$-acetone, 500 MHz)
HMBC of compound 27 (d$_6$-acetone, 500 MHz)
COSY of compound 27 (d$_6$-acetone, 500 MHz)
NOESY of compound 27 (d₆-acetone, 500 MHz)
$^1$H NMR of compound 8 (d$_6$-acetone, 500 MHz)
$^{13}$C NMR of compound 8 (d$_6$-acetone, 125 MHz)
HSQC of compound 8 (d$_6$-acetone, 500 MHz)
HMBC of compound 8 (d$_6$-acetone, 500 MHz)
NOESY of compound 8 (d₆-acetone, 500 MHz)
NOESY of compound 8 (d$_6$-acetone, 500 MHz) (blowup, confirming the assignment of iminal spiral center)
$^1$H NMR of compound 26 (CDCl$_3$, 500 MHz)
$^{13}$C NMR of compound 26 (CDCl$_3$, 125 MHz)
HSQC of compound 26 (CDCl$_3$, 500 MHz)
HMBC of compound 26 (CDCl₃, 500 MHz)

gradient-selected HMBC
NOESY of compound 26 (CDCl₃, 500 MHz)
$^1$H NMR of compound 10 (d$_6$-acetone, 500 MHz)
$^1$H NMR of compound 10 (d$_6$-acetone, 125 MHz)
HSQC of compound 10 (d$_6$-acetone, 500 MHz)
HMBC of compound 10 (d₆-acetone, 500 MHz)
COSY of compound 10 (d$_6$-acetone, 500 MHz)
NOESY of compound 10 (d$_6$-acetone, 500 MHz)
Evidence for the reassignment of 10 from NOESY.
$^1$H NMR comparison of natural and synthetic marineosin A (10)

Natural Marineosin A

Synthetic Marineosin A
$^{13}$C NMR comparison of natural and synthetic marineosin A (10)