Supporting Information
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Supplementary Information

A synthetic study towards the marmycins and analogues

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1. Chemistry
General experiments procedures

All starting materials were purchased from commercial sources and used without further purification, or purified according to Purification of Laboratory Chemicals (Armarego, W.L.F., Chai, C.L.L. 5th edition). Solvents were dried under standard conditions. Reactions were monitored by thin-layer chromatography (TLC) using TLC silica gel coated aluminum plates 60F-254 (Merck). Column chromatography was performed using Merck silica gel 60, 0.040-0.063 mm (230-400 mesh). Preparative TLC were carried out using 0.50 mm Merck silica gel plates (60F-254). NMR spectroscopy was performed on Bruker 300, and 500 MHz apparatus equipped with a cryoprobe. Spectra were run in CDCl₃ at 298 K unless otherwise stated. Molecular structures have been characterized using a comprehensive dataset including ¹H- and ¹³C-NMR spectra (1D and 2D experiments). ¹H chemical shifts are expressed in ppm using the residual non deuterated solvent as internal standard (CDCl₃ ¹H, 7.26 ppm). The following abbreviations are used: s, singlet; d, doublet; dd, double doublet; t, triplet; q, quartet; m, multiplet; bs, broad singlet. ¹³C chemical shifts are expressed in ppm using the residual non deuterated solvent as internal standard (CDCl₃ ¹³C, 77.16 ppm). Exact masses were recorded on a LCT Premier XE (Waters) equipped with an ESI ionization source and a TOF detector and on a Q-ToF 6540 (Agilent). Optical rotation measurements were performed on an Anton Paar Polarimeter MCP 300. The following parameters used were: temperature 20 °C, 100 mm path-length quartz cuvette, wavelength 589 nm. UV/vis absorption spectra were recorded on a Cary 5000 spectrophotometer from Agilent Technologies. Corrected emission spectra were obtained on a Fluorolog FL3-221 spectrofluorometer from Horiba Jobin-Yvon. Measurements were collected using a 1 cm path-length quartz cuvette. The following parameters used were: bandwidth 1 nm, response time 1 sec, wavelength scan range 200–800 nm.
2. Synthesis

9,10-dioxo-9,10-dihydroanthracen-1-yl trifluoromethanesulfonate (8).\(^1\)

A solution of 13 (1 g, 4.46 mmol) in dichloromethane (40 mL) was cooled to \(-78^\circ\) C prior the addition of triethylamine (2.5 mL, 17.9 mmol) and the reaction mixture was stirred for 30 min. Triflic anhydride (3.0 mL, 17.9 mmol) was then added dropwise and the reaction was allowed to warm to room temperature over 6 h. The mixture was diluted with dichloromethane and washed with sat. aq. NaHCO\(_3\). The combined organic layer was dried over MgSO\(_4\) and concentrated to dryness under reduced pressure. The crude residue was purified by flash chromatography (heptane/ethyl acetate, 8:2) to afford 8 (1.47 g, 93%) as a yellow solid. \(^1\)H NMR (300 MHz, CDCl\(_3\)) \(\delta\) 8.45 (dd, \(J = 7.8, 1.2\) Hz, 1H), 8.41−8.33 (m, 1H), 8.33−8.23 (m, 1H), 7.95−7.76 (m, 3H), 7.62 (d, \(J = 8.1\) Hz, 1H). \(^13\)C NMR (75 MHz, CDCl\(_3\)) \(\delta\) 181.6, 181.3, 147.9, 135.9, 135.3, 135.0, 134.7, 133.94, 132.5, 128.7, 128.2, 127.9, 127.3, 125.9. HRMS (APPI) calcd. for C\(_{15}\)H\(_8\)F\(_3\)O\(_5\)S\(^+\) [M+H]\(^+\), found: 357.0013.

Methyl 2,6-dideoxy-4-O-(methoxymethyl)-\(\alpha\)-L-erythrosepyranosid-3-dose (10). Compound 10 was prepared according to a modified procedure.\(^2\) A solution of Methyl 2,3-O-benzylidene-6-deoxy-4-O-(methoxymethyl)-\(\alpha\)-L-mannopyranoside (5 g, 16.1 mmol) in freshly distilled tetrahydrofuran (200 mL) was cooled to \(-40^\circ\) C under argon prior dropwise addition of sec-buthyllithium (1.6 M in hexane, 30 mL, 48.3 mmol). After 1.5 h, the mixture was poured into ice-water containing NH\(_4\)Cl and the organic material was extracted with
dichloromethane. The combined organic layer was dried over MgSO₄ and concentrated to dryness under reduced pressure. The crude product was purified by flash chromatography (heptane/ethyl acetate, 7:3) to afford **10** (2 g, 61%) as a white solid. ¹H NMR (300 MHz, CDCl₃) δ 5.05 (d, J = 4.5 Hz, 1H), 4.81 (d, J = 7.0 Hz, 1H), 4.67 (d, J = 7.0 Hz, 1H), 4.04–3.83 (m, 2H), 3.41 (s, 3H), 3.31 (s, 3H), 2.73 (ddd, J = 14.0, 4.5, 1.0 Hz, 1H), 2.56 (dd, J = 14.0, 1.0 Hz, 1H), 1.41 (d, J = 6.0 Hz, 3H). ¹³C NMR (75 MHz, CDCl₃) δ 203.0, 99.6, 96.5, 81.6, 69.2, 56.3, 54.9, 46.9, 18.9. HRMS (ESI-TOF) calcd. for C₉H₁₆O₅Na⁺ [M+Na]⁺ 227.0890, found: 227.0893.

**Methyl 4-O-methoxymethyl-2,6-dideoxy-α-L-threo-hexopyranosid-3-ulose O-benzylxime (11).**³ To a solution of **10** (0.30 g, 1.47 mmol) in ethanol (30 mL) was added O-benzylhydroxylamine hydrochloride (0.70 g, 4.41 mmol) and sodium acetate (0.80 g, 5.88 mmol). After stirring at room temperature for 2 h, the mixture was filtered, concentrated to dryness under reduced pressure and purified by flash chromatography (heptane/ethyl acetate, 7:3) to afford **11** (0.41 g, 90%) as a white solid. ¹H NMR (300 MHz, CDCl₃) δ 7.42–7.27 (m, 5H), 5.14 (s, 2H), 4.77–4.57 (m, 2H), 4.60 (d, J = 7.0 Hz, 1H), 4.04–3.91 (m, 1H), 3.85 (d, J = 8.5 Hz, 1H), 3.36 (s, 3H), 3.34 (s, 3H), 3.23 (dd, J = 14.5, 2.5 Hz, 1H), 2.38 (dd, J = 14.5, 4.5 Hz, 1H), 1.34 (d, J = 6.0 Hz, 3H). ¹³C NMR (75 MHz, CDCl₃) δ 152.7, 138.2, 128.4, 128.2, 127.8, 97.7, 95.7, 76.0, 75.9, 68.9, 56.2, 54.9, 30.6, 18.3. HRMS (ESI-TOF) calcd. for C₁₆H₂₄NO₅⁺ [M+H]⁺ 310.1649, found: 310.1653. [α]D²⁰ –239 (c 0.072, CHCl₃).

**O-benzyl-N-((2S,3R,4R,6R)-6-methoxy-3-(methoxymethoxy)-2,4-dimethyltetrahydro-2H-pyran-4-yl)hydroxylamine (12).**³ To a Schlenk tube containing dry CeCl₃ (3.98 g, 16.2 mmol) was added freshly distilled tetrahydofuran (50 mL) under argon and the solution was stirred at room temperature overnight. The reaction was cooled to –78 °C prior dropwise addition of
methyllithium (3 M in diethoxymethane, 4.32 mL, 13.0 mmol) and the reaction mixture was stirred for 1 h. After this time, a solution of 11 (1 g, 3.2 mmol) in freshly distilled tetrahydrofurane (10 mL) was added and the reaction was stirred at –78 ºC for another 2 h. The reaction mixture was allowed to warm to room temperature, quenched with sat. aq. NaHCO₃ and extracted with tert-butylmethyl ether. The combined organic layer was dried over MgSO₄, concentrated to dryness under reduced pressure and purified by flash chromatography (heptane/ethyl acetate, 8:2) to afford 12 (0.76 g, 72%) as a colorless oil. ¹H NMR (300 MHz, CDCl₃) δ 7.42–7.26 (m, 5H), 6.27 (bs, 1H), 4.87–4.86 (m, 5H), 3.97–3.90 (m, 1H), 3.39 (s, 3H), 3.35 (s, 3H), 3.15 (d, J = 9.0 Hz, 1H), 2.19 (dd, J = 14.5, 2.0 Hz, 1H), 1.56 (dd, J = 14.5, 5.0 Hz, 1H), 1.28 (s, 3H), 1.25 (d, J = 6.0 Hz, 3H). ¹³C NMR (75 MHz, CDCl₃) δ 138.4, 128.5, 128.3, 127.6, 98.9, 98.4, 85.6, 76.9, 64.5, 58.6, 56.5, 55.1, 36.5, 24.0, 18.7. HRMS (ESI-TOF) calcd. for C₁₇H₂₈NO₅⁺ [M+H]+ 326.1962, found: 326.1970. [α]D²⁰ –90 (c 0.123, CHCl₃).

(2S,3R,4R,6R)-6-methoxy-3-(methoxymethoxy)-2,4-dimethyltetrahydro-2H-pyran-4-amine (6).³ A solution of 12 (0.230 g, 0.71 mmol) and Pd/C 10% (0.034 g, 15% wt) in methanol (7 mL) was stirred at room temperature overnight under hydrogen atmosphere. The reaction mixture was filtered through celite and concentrated to dryness under reduced pressure. The crude residue was purified by flash chromatography (dichloromethane/methanol, 9:1) to afford 6 (0.136 g, 88%) as a colorless oil. CCDC 1484096. ¹H NMR (300 MHz, CDCl₃) δ 4.75 (d, J = 6.5 Hz, 1H), 4.68 (d, J = 6.5 Hz, 1H), 4.64 (d, J = 4.0 Hz, 1H), 3.93–3.66 (m, 3H), 3.42 (s, 3H), 3.31 (s, 3H), 3.02 (d, J = 9.5 Hz, 1H), 2.03 (d, J = 14.5 Hz, 1H), 1.68 (dd, J = 14.5, 4.0 Hz, 1H), 1.27 (d, J = 6.5 Hz, 3H), 1.20 (s, 3H). ¹³C NMR (75 MHz, CDCl₃) δ 98.9, 98.2, 85.0, 63.5, 56.7, 55.0, 52.2, 40.8, 28.3, 18.2. HRMS (ESI-TOF) calcd. for C₁₀H₂₂NO₄⁺ [M+H]+ 220.1543, found: 220.1542. [α]D²⁰ –130 (c 0.137, CHCl₃).
1-(((2S,3R,4R,6R)-6-methoxy-3-(methoxymethoxy)-2,4-
dimethyltetrahydro-2H-pyran-4-yl)amino)anthracene-9,10-
dione (5). A dry sealed tube was loaded with 8 (28.0 mg, 0.079
mmol), Cul (3.0 mg, 20 mol %), potassium carbonate (22.0 mg, 
0.157 mmol), amine 6 (68.0 mg, 0.314 mmol) and the mixture
was stirred in dry toluene (4 mL) at 160 °C for 8 days. The reaction was then cooled to room
temperature and washed with sat. aq. NaHCO₃. The combined organic layer was dried over
MgSO₄, concentrated to dryness under reduced pressure and purified by flash
cchromatography (heptane/ethyl acetate, 8:2) to afford 5 (19 mg, 57%) as a dark violet solid.

1H NMR (500 MHz, CDCl₃) δ 10.55 (s, 1H), 8.35 (dd, J = 7.5, 1.0 Hz, 1H), 8.22 (dd, J = 7.5,
1.0 Hz, 1H), 7.77–7.56 (m, 2H), 7.57 (dd, J = 7.5, 1.0 Hz, 1H), 7.49–7.42 (m, 1H), 7.38–7.32
(m, 1H), 4.88 (dd, J = 15.8, 6.8 Hz, 2H), 4.63 (d, J = 3.0 Hz, 1H), 4.30 (dq, J = 9.5, 6.5 Hz,
1H), 3.48 (s, 3H), 3.27 (d, J = 9.5 Hz, 1H), 3.14 (s, 3H), 2.77 (dd, J = 15.0, 1.5 Hz, 1H), 1.82
(dd, J = 15.0, 4.5 Hz, 1H), 1.65 (s, 3H), 1.39 (d, J = 6.5 Hz, 3H). 13C NMR (126 MHz,
CDCl₃) δ 184.8, 184.3, 151.7, 135.5, 135.3, 134.1, 133.9, 133.1, 132.8, 127.1, 126.6, 121.3,
115.5, 114.5, 99.1, 97.5, 87.5, 64.4, 56.8, 55.7, 54.9, 38.2, 26.4, 18.7. HRMS (ESI) calcd. for
C₂₄H₂₈NO₆ [M+H]+ 426.1911, found: 426.1904. [α]D²⁰ 500 (c 0.0002, CHCl₃).

1-(((2S,3R,4R,6R)-3-hydroxy-6-methoxy-2,4-
dimethyltetrahydro-2H-pyran-4-yl)amino)anthracene-9,10-
dione (14). To a solution of 5 (19 mg, 0.045 mmol) in dry
dichloromethane (3 mL) was added BF₃·OEt₂ (12 µL, 0.090
mmol) at −78 °C. The reaction mixture was allowed to warm to
room temperature and was stirred for 24 h. After this time, the reaction was washed with sat.
aq. NaHCO₃, dried over MgSO₄ and concentrated to dryness under reduced pressure. The
crude reaction product was purified by preparative TLC (petroleum ether/tert-butylmethylether, 1:1) to afford 14 (14 mg, 82%) as a dark violet solid. $^1$H NMR (300 MHz, CDCl$_3$) δ 10.48 (s, 1H), 8.34 (dd, $J = 7.5$, 1.5 Hz, 1H), 8.23 (dd, $J = 7.5$, 1.5 Hz, 1H), 7.81–7.56 (m, 2H), 7.54–7.42 (m, 1H), 7.34 (d, $J = 8.0$ Hz, 1H), 4.65 (d, $J = 2.8$ Hz, 1H), 4.21 (dq, $J = 9.5$, 6.5 Hz, 1H), 3.37 (dd, $J = 9.5$, 6.5 Hz, 1H), 3.18 (s, 3H), 2.72 (dd, $J = 14.5$, 1.5 Hz, 1H), 2.13 (d, $J = 6.5$ Hz, 1H), 2.04 (s, 1H), 1.83 (dd, $J = 14.5$, 4.0 Hz, 1H), 1.66 (s, 3H), 1.43 (d, $J = 6.5$ Hz, 3H). $^{13}$C NMR (126 MHz, CDCl$_3$) δ 185.2, 184.1, 148.1, 151.8, 135.3, 134.5, 134.0, 133.1, 133.0, 127.2, 126.7, 121.2, 116.1, 115.0, 97.7, 80.4, 64.8, 55.4, 55.0, 38.2, 25.9, 18.7. HRMS (ESI) calcd. for C$_{22}$H$_{25}$NO$_5$ $^+$ [M+H]$^+$ 382.1649, found [M+H-Me]$^+$: 368.4028. 

\[
\left[\alpha\right]_{D}^{20} = 237 (c 0.008, \text{CHCl}_3).
\]

(2R,3R,4S,6R)-3-hydroxy-2,4-dimethyl-3,4-dihydro-1H-2,6-methanoantra[2,1-c][1,5]oxazocine-9,14(2H,6H)-dione) (3). A solution of 5 (5.0 mg, 0.013 mmol) and 50% w/w aq. HBF$_4$ (1.5 μL, 0.013 mmol) in acetonitrile (2 mL) was refluxed for 7 h. The reaction was then cooled to room temperature, diluted with dichloromethane (5 mL) and washed with sat. aq. NaHCO$_3$. The organic layer was dried over MgSO$_4$ and concentrated to dryness under reduced pressure. The mixture was purified by preparative TLC (heptane/ethyl acetate, 1:1) to afford 3 (0.5 mg, 12%) as a red solid. $^1$H NMR (300 MHz, CDCl$_3$) δ 9.77 (s, 1H), 8.36–8.17 (m, $J = 7.5$ Hz, 2H), 7.85–7.67 (m, 2H), 7.63 (d, $J = 7.5$ Hz, 1H), 7.52 (d, $J = 7.5$ Hz, 1H), 4.81 (s, 1H), 3.24–3.06 (m, 2H), 2.18 (dd, $J = 13.0$, 3.5 Hz, 1H), 1.85 (dd, $J = 13.0$, 1.0 Hz, 1H), 1.54 (s, 3H), 1.24 (d, $J = 6.0$ Hz, 8H). $^{13}$C NMR (75 MHz, CDCl$_3$) δ 185.5, 183.5, 149.6, 136.2, 134.9, 134.2, 133.4, 133.1, 128.3, 127.0, 126.8, 116.1, 112.2, 79.2, 69.4, 51.8, 35.0, 25.1, 22.8, 18.5. HRMS (ESI-TOF) calcd. for C$_{21}$H$_{20}$NO$_4$ $^+$ [M+H]$^+$ 350.1387, found 350.1392.
(2S,4R,4aS,14aR)-2-methoxy-4,14a-dimethyl-1,2,4,4a,14,14a-hexahydroanthra[2,1-b]pyrano[4,3-e][1,4]oxazine-8,13-dione (15). To a solution of 14 (4.0 mg, 0.0102 mmol) in dry dimethylformamide (2 mL) was added NaH (60% in mineral oil, 4.1 mg, 0.1020 mmol) at 0 ºC. The reaction mixture was stirred at 0 ºC for 2 h prior addition of methanol. The mixture was concentrated to dryness under reduced pressure and the crude residue was purified by preparative TLC (petroleum ether/ethyl acetate, 8:2) to afford 15 (2.5 mg, 65%) as a violet solid. CCDC 1411860. \(^1\)H NMR (300 MHz, CDCl\(_3\)) \(\delta 9.57\) (s, 1H), 8.35–8.19 (m, 2H), 7.84–7.66 (m, 1H), 7.62 (d, \(J = 8.1\) Hz, 1H), 7.05 (d, \(J = 8.1\) Hz, 1H), 4.72 (d, \(J = 4.3\) Hz, 1H), 3.92 (dq, \(J = 12.4, 6.2\) Hz, 1H), 3.81 (d, \(J = 9.9\) Hz, 1H), 3.27 (s, 3H), 2.27 (d, \(J = 14.9\) Hz, 1H), 2.05 (dd, \(J = 14.9, 4.5\) Hz, 1H), 1.37 (s, \(J = 20.5, 14.4\) Hz, 1H), 1.30 (d, \(J = 6.1\) Hz, 1H). \(^{13}\)C NMR (126 MHz, CDCl\(_3\)) \(\delta 185.4, 182.8, 146.0, 137.4, 135.2, 133.7, 133.6, 133.2, 128.0, 126.9, 126.7, 119.6, 117.7, 113.6, 97.5, 79.5, 62.1, 55.6, 48.3, 41.9, 28.5, 17.4 HRMS (ESI-TOF) calcd. for C\(_{22}\)H\(_{22}\)NO\(_5^+\) [M+H]\(^+\) 380.1492, found 380.1516.
NMR spectra

$^1$H NMR spectrum of 11 in CDCl$_3$

$^{13}$C NMR spectrum of 11 in CDCl$_3$
$^1$H NMR spectrum of 12 in CDCl$_3$

$^{13}$C NMR spectrum of 12 in CDCl$_3$
$^1$H NMR spectrum of 6 in CDCl$_3$ 

$^{13}$C NMR spectrum of 6 in CDCl$_3$
$^1$H NMR spectrum of 8 in CDCl$_3$

$^{13}$C NMR spectrum of 8 in CDCl$_3$
$^1$H NMR spectrum of 14 in CDCl$_3$

$^{13}$C NMR spectrum of 14 in CDCl$_3$
$\text{H NMR spectrum of 15 in CDCl}_3$

$\text{C NMR spectrum of 15 in CDCl}_3$
$^1$H NMR spectrum of 3 in CDCl$_3$

$^{13}$C NMR spectrum of 3 in CDCl$_3$
### Crystallographic data

**Compound 6**

**Bond precision:**

\[ \text{C-C} = 0.0120 \text{ Å} \]

\[ \text{Wavelength} = 0.71073 \]

**Cell:**

\[ \begin{align*}
    a &= 14.199 (1) \\
    b &= 14.458 (1) \\
    c &= 28.391 (3) \\
    \alpha &= 90 \\
    \beta &= 90 \\
    \gamma &= 90
\end{align*} \]

**Temperature:** 293 K

**Calculated** | **Reported**
---|---
**Volume** | 5828.4(8) | 5828.4(8)
**Space group** | P 1 2 1 2 1 | P 1 2 1 2 1
**Hall group** | P 2ac 2ab | P 2ac 2ab
**Moiety formula** | C\(_{10}\) H\(_{22}\) N O\(_4\), C\(_1\) | C\(_{10}\) H\(_{22}\) N O\(_4\), C\(_1\)
**Sum formula** | C\(_{10}\) H\(_{22}\) Cl N O\(_4\) | C\(_{10}\) H\(_{22}\) Cl N O\(_4\)
**Mr** | 255.74 | 255.73
**Dx,g cm\(^{-3}\)** | 1.166 | 1.166
**Z** | 16 | 16
**\(\mu (\text{mm}^{-1})\)** | 0.263 | 0.263
**F000** | 2208.0 | 2208.0
**F000'** | 2211.42 |
**h,k,lmax** | 15,16,31 | 15,16,31
**Nref** | 8519[4742] | 8408
**Tmin, Tmax** | 0.919, 0.982 | 0.910, 0.980
**Tmin'** | 0.919 |

**Correction method:** # Reported T Limits: Tmin=0.910

**Data completeness:** 1.77/0.99  \(\text{Theta(max)} = 23.411\)

**R(reflections) = 0.0574( 5929)**  \(\text{wR2(reflections)} = 0.1730( 8390)\)

**S = 1.018**  \(\text{Npar} = 616\)
Compound 3

Bond precision: C-C = 0.0053 Å

Wavelength=1.54187

Cell: 

a=11.9155(3)  b=11.9155(3)  c=22.4912(15)
alpha=90  beta=90  gamma=120

Temperature: 193 K

Calculated  Reported
Volume  2765.5(3)  2765.5(2)
Space group  P 61  P 61
Hall group  P 61  P 61
Moiety formula  C22 H21 N O5  C22 H21 N O5
Sum formula  C22 H21 N O5  C22 H21 N O5
Mr  379.40  379.40
Dx,g cm-3  1.367  1.367
Z  6  6
Mu (mm-1)  0.799  0.799
F000  1200.0  1200.0
F000'  1203.89
h,k,lmax  14,14,27  14,14,27
Nref  3389[ 1741]  3276
Tmin,Tmax  0.800,0.894  0.770,0.890
Tmin'  0.800

Correction method= # Reported T Limits: Tmin=0.770
Tmax=0.890 AbsCorr = MULTI-SCAN
Data completeness= 1.88/0.97  Theta(max)= 68.208
R(reflections)= 0.0327( 2745)  wR2(reflections)= 0.0983( 3266)
S = 1.188  Npar= 260

Prob = 50
Temp = 193

NOMOVE FORCED
6. References

