Construction of the Tricyclic Core of Steenkrotin-Type Diterpenoids via Intramolecular [3+2] Cycloaddition

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Supporting Information Available

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I) Experimental Section

Experimental Data for Compounds

General Procedures. All reactions were carried out under a nitrogen or argon atmosphere with dry solvents under anhydrous conditions, unless otherwise noted. Dry acetonitrile (MeCN), 1,4-dioxane, tetrahydrofuran (THF), methylene chloride (CH$_2$Cl$_2$), toluene and triethylamine (Et$_3$N) were obtained by passing commercially available pre-dried, oxygen-free formulations through activated alumina columns. Methanol (MeOH), benzene, $N$,$N$-dimethylformamide (DMF) and dimethyl sulfoxide (DMSO) were purchased in anhydrous form and used without further purification. Water, ethyl acetate (EtOAc), diethyl ether (Et$_2$O), methylene chloride (CH$_2$Cl$_2$),
acetone and hexanes were purchased at the highest commercial quality and used without further purification, unless otherwise stated. Reagents were purchased at the highest commercial quality and used without further purification, unless otherwise stated. Yields refer to chromatographically and spectroscopically (¹H NMR) homogeneous materials, unless otherwise stated. Reactions were monitored by thin-layer chromatography (TLC) carried out on 0.25 mm E. Merck silica gel plates (60F-254) using UV light as visualizing agent and an ethanolic solution of ammonium molybdate, anisaldehyde, and heat as developing agents. E. Merck silica gel (60, particle size 0.040–0.063 mm) was used for flash column chromatography. NMR spectra were recorded on a Bruker AV-400 instrument and calibrated using residual undeuterated solvent as an internal reference. The following abbreviations were used to explain the multiplicities: s = singlet, d = doublet, t = triplet, q = quartet, quint = quintet, m = multiplet, pent = pentet, hex = hexet, br = broad. IR spectra were recorded on a Perkin-Elmer Spectrum One FTIR spectrometer with diamond ATR accessory. High-resolution mass spectra (HRMS) were recorded on an Agilent ESI TOF (time of flight) mass spectrometer at 3500 V emitter voltage.

**Alcohol 12**: To a stirred solution of i-Pr₂NH (15.25 g, 0.15 mol) in THF (150 mL) at –78°C was added n-BuLi (2.5 M in hexane, 55 mL, 0.14 mol). The resulting mixture was stirred at –78 °C for 0.5 h before it was added a solution of 3-ethoxy-2-cyclohexenone 10¹ (14.8 g, 0.11 mol) in THF (20 mL). After stirring at –78 °C for further 0.5 h, the resulting
mixture was added a solution of aldehyde 11\(^2\) (27 g, 0.13 mol) in THF (30 mL) at –78 °C. The resulting mixture was stirred at –78 °C for 15 min before it was diluted with EtOAc (50 mL) and quenched with NH\(_4\)Cl (50 mL, sat. aq.). The layers were separated, and the aqueous layer was extracted with EtOAc (3 × 50 mL). The combined organic layers were dried (Na\(_2\)SO\(_4\)) and concentrated \textit{in vacuo}. Flash column chromatography (silica gel, hexanes:EtOAc 6:1) afforded alcohol 12 (34.8 g, 90\%, \textit{dr} = 1.5:1) as a light yellow oil. 12: \(R_f = 0.25\) (hexanes:EtOAc 5:1); IR (film) \(\nu_{\text{max}}\) 3437, 2933, 2859, 1644, 1603, 1468, 1382, 1359, 1250, 1193, 1104, 916, 837, 770, 740, 664 cm\(^{-1}\); \(^1\)H NMR (400 MHz, CDCl\(_3\)): \(\delta = 5.35\) (d, \(J = 11.7\) Hz, 1 H), 4.71–4.57 (m, 1 H), 3.98–3.86 (m, 2 H), 3.70 (dt, \(J = 10.9, 7.1\) Hz, 2 H), 2.61–2.23 (m, 6 H), 2.11–1.96 (m, 1 H), 1.77–1.60 (m, 1 H), 1.36 (t, \(J = 7.0\) Hz, 3 H), 0.87 (d, \(J = 2.8\) Hz, 9 H), 0.05 ppm (d, \(J = 2.7\) Hz, 6 H); \(^{13}\)C NMR (100 MHz, CDCl\(_3\)): \(\delta = 202.0, 200.7, 179.0, 178.6, 103.2, 102.5, 83.7, 83.5, 80.1, 79.8, 64.9, 64.7, 64.4, 63.6, 62.0, 61.9, 50.3, 49.9, 29.0, 28.9, 26.0 (6C), 24.3, 23.3 (2C), 23.0, 18.4 (2C), 14.2 (2C), -5.2 ppm (4C); HRMS(ESI): calcd for C\(_{19}\)H\(_{33}\)O\(_4\)Si\(^+\)[M+H\(^+\)] 353.2143, found 353.2146.

**MOM ether 13**: To a stirred solution of alcohol 12 (22.0 g, 0.063 mol) in CH\(_2\)Cl\(_2\) (100 mL) at 0 °C was added \(i\)-Pr\(_2\)NEt (44.0 mL, 0.25 mol) and MOMCl (14.4 mL, 0.19 mol). The resulting mixture was warmed to room temperature and stirred for 12 h before it was quenched with NaHCO\(_3\) (30 mL, sat. aq.). The layers were separated, and the aqueous layer was extracted with CH\(_2\)Cl\(_2\) (3 × 30 mL). The combined organic layers were dried

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(Na$_2$SO$_4$) and concentrated $\textit{in vacuo}$. Flash column chromatography (silica gel, hexanes:EtOAc 12:1) afforded MOM ether 13 (22.8 g, 92%) as a colorless oil. 13: $R_f$ =0.25 (hexanes:EtOAc 8:1); IR (film) $\nu_{\text{max}}$ 2933, 2887, 1655, 1606, 1467, 1380, 1360, 1250, 1189, 1099, 1034, 915, 836, 777, 734, 664 cm$^{-1}$; $^1$H NMR (400 MHz, CDCl$_3$): $\delta$ = 5.34 (s, 1 H), 5.11–5.04 (m, 1 H), 4.93 (d, $J$ = 6.6 Hz, 1 H), 4.58 (d, $J$ = 6.6 Hz, 1 H), 3.89 (dd, $J$ = 6.9, 4.6 Hz, 2 H), 3.66 (t, $J$ = 7.2 Hz, 2 H), 3.35 (s, 3 H), 2.64–2.54 (m, 1 H), 2.46 (d, $J$ = 4.5 Hz, 2 H), 2.38 (t, $J$ = 6.5 Hz, 2 H), 2.24–2.08 (m, 2 H), 1.35 (t, $J$ = 7.0 Hz, 3 H), 0.86 (s, 9 H), 0.03 ppm (s, 6 H); $^{13}$C NMR (100 MHz, CDCl$_3$): $\delta$ = 197.3, 177.4, 102.7, 94.2, 84.7, 65.6, 64.3, 61.8, 55.7, 49.9, 28.4, 25.8 (4C), 23.2, 22.1, 18.2, 14.1, -5.2 ppm (2C); HRMS(ESI): calcd for C$_{21}$H$_{37}$O$_5$Si$^+\text{[M+H$^+$]}$ 397.2405, found 397.2408.

Enone 9: To a stirred solution of MOM ether 13 (8.1 g, 20.5 mmol) in THF (50 mL) at $-78^\circ$C was added Dibal-H (1.5 M in toluene, 20.5 mL, 30.8 mmol). The resulting mixture was warmed to $-20^\circ$C and stirred for 0.5 h before it was acidified (HCl, 2.0 M aq.) to pH 1. The layers were separated, and the aqueous layer was extracted with EtOAc (3 $\times$ 20 mL). The combined organic layers were washed with NaHCO$_3$ (20 mL, sat. aq.) and brine (20 mL), dried (Na$_2$SO$_4$), and concentrated $\textit{in vacuo}$. Flash column chromatography (silica gel, hexanes:EtOAc 4:1) afforded the crude alcohol as a colorless oil.

To a stirred solution of the alcohol (crude, obtained above) in THF/H$_2$O (20:1, v/v, 30 mL) at room temperature was added $n$-Bu$_4$NF·3H$_2$O (5.38 g, 17.0 mmol). The
resulting mixture was stirred for 2 h before it was quenched with NH₄Cl (20 mL, sat. aq.). The layers were separated, and the aqueous layer was extracted with EtOAc (3 × 20 mL). The combined organic layers were dried (Na₂SO₄) and concentrated in vacuo.

Flash column chromatography (silica gel, hexanes:EtOAc 1:1) afforded enone 9 (3.2 g, 65% over the two steps) as a colorless oil. **9:** \( R_f = 0.25 \) (hexanes:EtOAc 1:1); IR (film) \( \nu \text{max} 3409, 2959, 2886, 2235, 1673, 1390, 1332, 1213, 1147, 1097, 1024, 921, 844, 780 \text{ cm}^{-1}; \) \(^1\text{H} \text{NMR (400 MHz, CDCl}_3\): \( \delta = 7.03 \) (d, \( J = 10.2 \text{ Hz, 1 H} \)), 6.05 (dd, \( J = 10.2, 2.0 \text{ Hz, 1 H} \)), 4.95 (d, \( J = 6.9 \text{ Hz, 1 H} \)), 4.59 (d, \( J = 6.8 \text{ Hz, 1 H} \)), 4.35 (dd, \( J = 4.0, 1.8 \text{ Hz, 1 H} \)), 3.69 (dd, \( J = 8.4, 4.2 \text{ Hz, 2 H} \)), 3.36 (s, 3 H), 2.73 (dd, \( J = 4.7, 2.3 \text{ Hz, 1 H} \)), 2.63–2.27 (m, 5 H), 2.20–2.12 (m, 1 H), 1.99 ppm (ddd, \( J = 13.4, 10.6, 4.4 \text{ Hz, 1 H} \)); \(^{13}\text{C} \text{NMR (100 MHz, CDCl}_3\): \( \delta = 199.6, 150.3, 130.4, 94.2, 85.2, 78.1, 68.2, 60.9, 55.9, 41.6, 36.8, 25.2, 23.0 \text{ ppm; HRMS(ESI): calcd for C}_{13}\text{H}_{19}\text{O}_4\right)^+ [\text{M+H}^+] \) 239.1278, found 239.1280.

Alkene 14: To a stirred solution of alkyne 9 (2.6 g, 10.9 mmol) in toluene (20 mL) at room temperature was added Pd/CaCO₃ (260 mg). The resulting mixture was stirred under hydrogen atmosphere (1 atm) for 0.5 h before it was filtered through a short pad of celite. The filtrate was concentrated in vacuo. Flash column chromatography (silica gel, hexanes:EtOAc 1:1) afforded alkene 14 (2.5 g, 95%) as a colorless oil. **14:** \( R_f = 0.25 \) (hexanes:EtOAc 1:1); IR (film) \( \nu \text{max} 3436, 2947, 2887, 1673, 1390, 1349, 1216, 1147, 1094, 1030, 923, 878, 845, 749 \text{ cm}^{-1}; \) \(^1\text{H} \text{NMR (400 MHz, CDCl}_3\): \( \delta = 7.15 \) (d, \( J = 10.2 \text{ Hz, 1 H} \)), 6.07 (dd, \( J = 10.2, 2.1 \text{ Hz, 1 H} \)), 5.86–5.76 (m, 1 H), 5.44 (t, \( J = 10.4 \text{ Hz, 1 H} \)), 4.79 (d, \( J = 6.8 \text{ Hz, 1 H} \)), 4.75 (m, 1 H), 4.35 (d, \( J = 7.4 \text{ Hz, 1 H} \)), 4.06 (d, \( J = 7.2 \text{ Hz, 1 H} \)), 3.69 (ddd, \( J = 13.2, 10.6, 4.4 \text{ Hz, 1 H} \)); \(^{13}\text{C} \text{NMR (100 MHz, CDCl}_3\): \( \delta = 199.6, 150.3, 130.4, 94.2, 85.2, 78.1, 68.2, 60.9, 55.9, 41.6, 36.8, 25.2, 23.0 \text{ ppm; HRMS(ESI): calcd for C}_{13}\text{H}_{19}\text{O}_4\right)^+ [\text{M+H}^+] \) 239.1278, found 239.1280.
Hz, 1 H), 4.54 (d, J = 6.8 Hz, 1 H), 4.3–4.23 (m, 1 H), 3.69 (ddt, J = 13.3, 10.4, 5.3 Hz, 2 H), 3.38 (s, 3 H), 2.59–2.43 (m, 3 H), 2.41–2.34 (m, 1 H), 2.34–2.25 (m, 1 H), 2.04 (ddd, J = 22.2, 9.8, 5.1 Hz, 2 H), 1.80–1.68 ppm (m, 1 H); ¹³C NMR (100 MHz, CDCl₃): δ = 199.5, 151.0, 132.9, 130.0, 129.6, 93.5, 72.9, 61.8, 55.7, 41.1, 37.0, 31.4, 25.4 ppm; HRMS(ESI): calcd for C₁₃H₂₁O₄⁺ [M+H⁺] 241.1434, found 241.1436.

**Nitro compound 8:** To a stirred solution of alcohol 14 (1.23 g, 5.13 mmol) in CH₂Cl₂ (15 mL) at 0 °C were added PPh₃ (2.01 g, 7.69 mmol), imidazole (5.23 g, 7.69 mmol) and iodine (1.95 g, 7.69 mmol). The resulting mixture was warmed to room temperature and stirred for 4 h before it was filtered through a short pad of celite. The filtrate was concentrated in vacuo.

Flash column chromatography (silica gel, hexanes:EtOAc 2:1) afforded the crude iodide as a colorless oil, which was used directly without further purification.

To a stirred solution of iodide (crude, obtained above) in Et₂O/H₂O (1:3, v/v, 15 mL) at room temperature was added AgNO₂ (3.2 g, 20.6 mmol). The resulting mixture was stirred for 12 h before it was filtered through a short pad of celite. The layers were separated, and the aqueous layer was extracted with Et₂O (3 × 15 mL). The combined organic layers were dried (Na₂SO₄) and concentrated in vacuo. Flash column chromatography (silica gel, hexanes:EtOAc 4:1) afforded nitro compound 8 (677 mg, 55% over the two steps) as a colorless oil. 8: Rₚ = 0.45 (hexanes:EtOAc 2:1); IR (film) νₘₐₓ 3491, 2949, 2892, 2362, 1678, 1553, 1382, 1215, 1147, 1095, 1030, 921, 791, 754 cm⁻¹; ¹H NMR (400 MHz, CDCl₃): δ = 7.12 (d, J = 10.3 Hz, 1 H), 6.08 (dd, J = 10.3, 2.2 Hz, 1 H), 5.73 (dt, J = 11.0, 7.4 Hz, 1 H), 5.49 (dd, J = 10.9,
9.9 Hz, 1 H), 4.67 (d, J = 6.8 Hz, 1 H), 4.51 (d, J = 6.8 Hz, 1 H), 4.44 (dd, J = 13.1, 6.5 Hz, 2 H), 4.32–4.23 (m, 1 H), 3.38 (s, 3 H), 2.83 (d, J = 7.1 Hz, 2 H), 2.53 (ddd, J = 12.7, 9.3, 4.8 Hz, 2 H), 2.44–2.27 (m, 1 H), 2.09–1.98 (m, 1 H), 1.82–1.66 ppm (m, 1 H); \(^{13}\)C NMR (100 MHz, CDCl\(_3\)): \(\delta = 199.2, 150.4, 131.4, 130.2, 129.2, 93.4, 74.5, 72.1, 55.8, 41.0, 37.0, 25.7, 25.4 \) ppm; HRMS(ESI): calcd for C\(_{13}\)H\(_{20}\)NO\(_5\)\([\text{M+H}^+]\) 270.1336, found 270.1334.

**Tricyclic isoxazoline 15:** To a stirred solution of nitro compound 8 (600 mg, 2.23 mmol) in toluene (20 mL) at room temperature was added Boc\(_2\)O (2.43 g, 11.1 mmol) and 4-DMAP (134 mg, 1.1 mmol). The resulting mixture was stirred at 90 °C for 5 h before it was concentrated in vacuo. Flash column chromatography (silica gel, hexanes:EtOAc 2:1) afforded tricyclic isoxazoline 15 (420 mg, 75%) as a white solid. 15: \(R_f = 0.48\) (hexanes:EtOAc 1:1); m.p. = 131–133 °C; IR (film) \(\nu_{\text{max}} = 3437, 2947, 2892, 2360, 1724, 1604, 1280, 1220, 1148, 1101, 1037, 917, 840, 744, 667 \) cm\(^{-1}\); \(^1\)H NMR (400 MHz, CDCl\(_3\)): \(\delta = 5.85–5.75 \) (m, 1 H), 5.69 (d, \(J = 10.9 \) Hz, 1 H), 4.76–4.65 (m, 3 H), 4.59 (s, 1 H), 3.90 (dd, \(J = 10.9, 5.8 \) Hz, 1 H), 3.43–3.32 (m, 4 H), 2.94 (d, \(J = 15.8 \) Hz, 1 H), 2.74–2.63 (m, 1 H), 2.44–2.28 (m, 2 H), 2.03 (d, \(J = 8.0 \) Hz, 1 H), 1.77–1.67 ppm (m, 1 H); \(^{13}\)C NMR (100 MHz, CDCl\(_3\)): \(\delta = 205.8, 152.6, 134.9, 123.2, 95.0, 83.1, 74.9, 55.8, 55.6, 39.0, 36.8, 25.7, 20.1 \) ppm; HRMS(ESI): calcd for C\(_{13}\)H\(_{18}\)NO\(_4\)\([\text{M+H}^+]\) 252.1230, found 252.1234.

**Isoxazoline 7:** To a stirred solution of tricyclic isoxazoline 15 (246 mg, 0.98 mmol) in EtOAc (10 mL) at room temperature was added Pd/C (10% wt/wt, 26.5 mg). The
resulting mixture was stirred under hydrogen atmosphere (1 atm) for 0.5 h before it was filtered through a short pad of celite. The filtrate was concentrated in vacuo. Flash column chromatography (silica gel, hexanes:EtOAc 1:1) afforded isoxazoline 7 (238 mg, 96%) as a colorless oil. 7: \( R_f = 0.25 \) (hexanes:EtOAc 1:1); IR (film) \( \nu_{\text{max}} \) 3851, 3634, 2942, 2886, 2360, 1725, 1452, 1279, 1223, 1148, 1099, 1035, 918, 840, 746 cm\(^{-1}\); \(^1\)H NMR (400 MHz, CDCl\(_3\)):
\[
\begin{align*}
\delta & = 4.68 (d, J = 7.4 \text{ Hz}, 2 \text{ H}), 4.64 (d, J = 7.0 \text{ Hz}, 1 \text{ H}), 3.82 (d, J = 6.5 \text{ Hz}, 1 \text{ H}), 3.73 (dd, J = 7.6, 3.2 \text{ Hz}, 1 \text{ H}), 3.38 (s, 3 \text{ H}), 2.81–2.68 (m, 2 \text{ H}), 2.53 (dd, J = 12.4, 3.1 \text{ Hz}, 1 \text{ H}), 2.44 (dd, J = 10.2, 6.0 \text{ Hz}, 2 \text{ H}), 2.35–2.26 (m, 1 \text{ H}), 2.25–2.17 (m, 1 \text{ H}), 2.06–1.83 (m, 3 \text{ H}), 1.50 ppm (d, J = 5.6 \text{ Hz}, 1 \text{ H}); \quad ^{13}\text{C NMR (100 MHz, CDCl}_3\text{):} \\
\delta & = 206.7, 160.1, 95.4, 83.2, 79.7, 55.8, 53.6, 39.5, 38.1, 31.2, 26.7, 21.4, 20.7 \text{ ppm;} \\
\text{HRMS(ESI): calcd for C}_{13}\text{H}_{20}\text{NO}_4^{+} [M+H]^+ & 254.1387, \text{ found 254.1386.}
\end{align*}
\]

**Alcohol 16:** To a stirred solution of isoxazoline 7 (556 mg, 2.20 mmol) in THF (50 mL) at –78 °C was added allylmagnesium bromide (0.35 M in THF, 6.8 mL, 2.40 mmol). The resulting mixture was stirred for 20 min before it was quenched with NH\(_4\)Cl (20 mL, sat. aq.). The layers were separated, and the aqueous layer was extracted with Et\(_2\)O (3 × 20 mL). The combined organic layers were dried (Na\(_2\)SO\(_4\)) and concentrated in vacuo. Flash column chromatography (silica gel, hexanes:EtOAc 5:1) afforded alcohol 16 (591 mg, 91%) as a colorless oil. 16: \( R_f = 0.50 \) (hexanes:EtOAc 1:1); \(^1\)H NMR (400 MHz, CDCl\(_3\)):
\[
\begin{align*}
\delta & = 5.85 (td, J = 16.7, 8.5 \text{ Hz}, 1 \text{ H}), 5.12 (t, J = 13.4 \text{ Hz}, 2 \text{ H}), 4.66 (s, 2 \text{ H}), 4.46 (d, J = 9.5 \text{ Hz}, 1 \text{ H}), 3.79–3.67 (m, 1 \text{ H}), 3.47–3.40 (m, 1 \text{ H}), 3.38 (s, 3 \text{ H}),
\end{align*}
\]
2.61 (dd, $J = 16.1, 8.5$ Hz, 1 H), 2.55–2.41 (m, 1 H), 2.31 (dd, $J = 13.6, 6.4$ Hz, 1 H), 2.25–2.13 (m, 2 H), 2.07 (d, $J = 9.6$ Hz, 2 H), 1.92 (d, $J = 14.0$ Hz, 1 H), 1.85–1.66 (m, 3 H), 1.54 (dd, $J = 12.5, 9.9$ Hz, 2 H), 1.23 ppm (d, $J = 16.0$ Hz, 1 H); $^{13}$C NMR (100 MHz, CDCl$_3$): $\delta = 161.0, 133.0, 120.6, 94.9, 83.8, 79.8, 72.0, 55.4, 50.1, 43.9, 33.3, 30.8, 29.2, 26.8, 21.3, 16.5$ ppm; HRMS(ESI): calcd for C$_{16}$H$_{26}$NO$_4$$^[M+H^+]$ 296.1856, found 296.1854.

**TMS ether 17**: To a stirred solution of alcohol 16 (591 mg, 2.0 mmol) in CH$_2$Cl$_2$ (50 mL) at −78 °C was added 2,6-lutidine (2.3 mL, 20 mmol) and TMSOTf (1.8 mL, 10 mmol). The resulting mixture was stirred for 0.5 h before it was quenched with NH$_4$Cl (30 mL, sat. aq.). The layers were separated, and the aqueous layer was extracted with CH$_2$Cl$_2$ (3 × 20 mL). The combined organic layers were dried (Na$_2$SO$_4$) and concentrated in vacuo.

Flash column chromatography (silica gel, hexanes:EtOAc 10:1) afforded TMS ether 17 (631 mg, 86%) as a colorless oil. 17: $R_f = 0.50$ (hexanes:EtOAc 5:1); IR (film) $\nu_{max}$ 3783, 2947, 2884, 2361, 1725, 1640, 1445, 1251, 1147, 1100, 1037, 918, 842, 756, 686 cm$^{-1}$; $^1$H NMR (400 MHz, CDCl$_3$): $\delta = 5.91$ (ddt, $J = 17.2, 10.3, 7.0$ Hz, 1 H), 5.21–5.05 (m, 2 H), 4.64 (q, $J = 6.9$ Hz, 2 H), 4.51 (d, $J = 11.0$ Hz, 1 H), 3.70 (dt, $J = 11.2, 3.8$ Hz, 1 H), 3.45 (d, $J = 11.0$ Hz, 1 H), 3.37 (s, 3 H), 2.99–2.88 (m, 1 H), 2.71 (d, $J = 17.6$ Hz, 1 H), 2.56–2.34 (m, 2 H), 2.27 (dd, $J = 14.7, 6.7$ Hz, 1 H), 1.97 (d, $J = 7.3$ Hz, 1 H), 1.86–1.73 (m, 2 H), 1.69–1.63 (m, 3 H), 1.51 (dd, $J = 18.6, 7.0$ Hz, 1 H), 1.40 (td, $J = 13.1, 6.6$ Hz, 1 H), 0.16 ppm (s, 9 H); $^{13}$C NMR (100 MHz, CDCl$_3$): $\delta = 158.4, 131.3, 115.6, 92.1, 81.2, 76.9, 74.0, 53.0, 47.6, 40.7, 30.4, 28.1, 26.9, 24.4,
Enone 18: To a stirred solution of TMS ether 17 (587 mg, 1.6 mmol) in MeCN (30 mL) at room temperature was added Mo(CO)₆ (522 mg, 2.0 mmol). The resulting mixture was stirred at 90 °C for 1.5 h before it was added H₂O (3 mL). The resulting mixture was stirred at 90 °C for further 5 h before it was filtered through a short pad of celite. The filtrate was extracted with Et₂O (3 × 30 mL). The combined organic layers were dried (Na₂SO₄) and concentrated in vacuo. Flash column chromatography (silica gel, hexanes:EtOAc 1:1) afforded enone 18 (237 mg, 42%) as a colorless oil. 18: Rᶠ = 0.25 (hexanes:EtOAc 1:1); IR (film) νmax 3880, 3696, 3637, 3430, 2926, 2858, 2362, 1735, 1689, 1629, 1461, 1377, 1152, 1073, 1042, 917, 845, 751 cm⁻¹; ¹H NMR (400 MHz, CDCl₃): δ = 6.52 (s, 1 H), 5.76 (ddt, J = 17.4, 10.4, 7.2 Hz, 1 H), 5.04 (dd, J = 9.8, 8.9 Hz, 2 H), 4.63 (d, J = 6.9 Hz, 1 H), 4.51 (d, J = 6.9 Hz, 1 H), 3.88 (d, J = 4.9 Hz, 1 H), 3.33 (s, 3 H), 2.59–2.43 (m, 3 H), 2.38 (dd, J = 13.7, 7.2 Hz, 1 H), 2.32–2.22 (m, 2 H), 1.97 (ddd, J = 24.3, 13.2, 2.5 Hz, 1 H), 1.88–1.66 (m, 4 H), 1.60 (d, J = 5.6 Hz, 1 H), 1.42 (td, J = 13.3, 2.7 Hz, 1 H), 0.13 ppm (s, 9 H); ¹³C NMR (100 MHz, CDCl₃): δ = 203.5, 140.2, 139.2, 133.8, 117.8, 95.3, 79.0, 71.5, 55.9, 47.7, 43.8, 41.3, 34.7, 33.8, 25.7, 20.1, 2.6 ppm (3C); HRMS(ESI): calcd for C₁₉H₃₄NO₄Si⁺[M+H⁺] 353.2143, found 353.2146.

Alcohol 6: To a stirred solution of enone 18 (106 mg, 0.30 mmol) in THF (20 mL) at room temperature was added n-Bu₄NF (1.0 M in toluene, 0.43 mL, 0.43 mmol). The
resulting mixture was stirred at room temperature for 0.5 h before it was quenched with NH₄Cl (20 mL, sat. aq.). The layers were separated, and the aqueous layer was extracted with Et₂O (3 × 10 mL). The combined organic layers were dried (Na₂SO₄) and concentrated in vacuo. Flash column chromatography (silica gel, hexanes:EtOAc 1:1) afforded alcohol 6 (72 mg, 90%) as a colorless oil. 6: Rᵣ = 0.25 (hexanes:EtOAc 1:1); IR (film) νₘₐₓ 3786, 3697, 3636, 3440, 2926, 2858, 2362, 1729, 1687, 1627, 1460, 1152, 1040, 991, 916, 752, 674 cm⁻¹; ¹H NMR (400 MHz, CDCl₃): δ = 6.56 (s, 1 H), 5.85 (ddt, J = 17.6, 10.5, 7.3 Hz, 1 H), 5.19–5.02 (m, 2 H), 4.66 (d, J = 7.1 Hz, 1 H), 4.54 (d, J = 7.1 Hz, 1 H), 3.87 (d, J = 4.9 Hz, 1 H), 3.33 (s, 3 H), 2.62–2.51 (m, 3 H), 2.34 (d, J = 7.3 Hz, 2 H), 2.31–2.23 (m, 1 H), 2.19 (s, 1 H), 2.00–1.88 (m, 1 H), 1.88–1.68 (m, 4 H), 1.57–1.53 (m, 1 H), 1.49 ppm (dd, J = 13.2, 3.3 Hz, 1 H); ¹³C NMR (100 MHz, CDCl₃): δ = 203.7, 140.7, 137.9, 133.0, 119.0, 95.9, 79.8, 68.2, 56.1, 46.4, 43.6, 40.8, 34.2, 33.9, 25.2, 20.2 ppm; HRMS(ESI): calcd for C₁₆H₂₅O₄[M+H⁺] 281.1747, found 281.1746.

**MOM ether 19:** To a stirred solution of alcohol 6 (78 mg, 0.28 mmol) in THF (20 mL) at 0 °C was added NaBH₄ (11 mg, 0.28 mmol) and CeCl₃·7H₂O (104 mg, 0.28 mmol). The resulting mixture was stirred at 0 °C for 0.5 h before it was quenched with NH₄Cl (10 mL, sat. aq.). The layers were separated, and the aqueous layer was extracted with Et₂O (3 × 10 mL). The combined organic layers were dried (Na₂SO₄) and concentrated in vacuo. Flash column chromatography (silica gel, hexanes:EtOAc 1:2)
afforded crude diol as a colorless oil, which was used directly without further purification.

To a stirred solution of the diol (crude, obtained above) in CH$_2$Cl$_2$ (20 mL) at 0 °C was added $i$-Pr$_2$NEt (0.24 mL, 1.40 mmol) and MOMCl (64 μL, 0.84 mmol). The resulting mixture was warmed to room temperature and stirred for 12 h before it was quenched with NaHCO$_3$ (10 mL, sat. aq.). The layers were separated, and the aqueous layer was extracted with CH$_2$Cl$_2$ (3 × 10 mL). The combined organic layers were dried (Na$_2$SO$_4$) and concentrated in vacuo. Flash column chromatography (silica gel, hexanes:EtOAc 1:1) afforded MOM ether 19 (74 mg, 81% over the two steps) as a colorless oil. 19: $R_f$ = 0.25 (hexanes:EtOAc 1:1); IR (film) $\nu_{\text{max}}$ 3876, 3790, 3638, 3467, 2929, 2361, 1725, 1639, 1445, 1278, 1149, 1100, 1037, 995, 946, 915, 748, 646 cm$^{-1}$; $^1$H NMR (400 MHz, CDCl$_3$): $\delta$ = 5.91 (s, 1 H), 5.88–5.74 (m, 1 H), 5.16–5.01 (m, 2 H), 4.63 (dd, $J$ = 15.1, 6.8 Hz, 2 H), 4.56 (d, $J$ = 6.7 Hz, 1 H), 4.47 (d, $J$ = 6.7 Hz, 1 H), 4.15–4.02 (m, 1 H), 3.92–3.82 (m, 1 H), 3.36 (d, $J$ = 5.2 Hz, 6 H), 2.54–2.47 (m, 1 H), 2.36–2.28 (m, 2 H), 2.10–2.01 (m, 2 H), 1.93–1.77 (m, 3 H), 1.72 (s, 1 H), 1.63 (ddd, $J$ = 14.0, 8.7, 2.6 Hz, 2 H), 1.48 (dd, $J$ = 15.7, 6.9 Hz, 2 H), 1.43 ppm (d, $J$ = 4.7 Hz, 1 H); $^{13}$C NMR (100 MHz, CDCl$_3$): $\delta$ = 143.9, 133.9, 128.0, 118.7, 95.0, 93.9, 74.4, 69.2, 55.7, 55.6, 47.7, 41.7, 37.8, 34.8, 29.9 (2C), 23.8, 19.7 ppm; HRMS(ESI): calcd for C$_{18}$H$_{31}$O$_5$$^+[\text{M}+\text{H}]^+$ 327.2166, found 327.2165.

Alcohol 21: To a stirred solution of $i$-Pr$_2$NH (28.9 mL, 0.21 mol) in THF (150 mL) at −78 °C was added $n$-BuLi (2.5 M in hexane, 75 mL, 0.19 mol). The resulting mixture was stirred at −78 °C for 0.5 h before it was
added a solution of cyclohexenone 20 (13.9 g, 0.14 mol) in THF (20 mL). After stirring at –78 °C for further 0.5 h, the resulting mixture was added a solution of aldehyde 11 (35 g, 0.17 mol) in THF (30 mL). The resulting mixture was stirred at –78 °C for 15 min before it was diluted with EtOAc (50 mL) and quenched with NH₄Cl (50 mL, sat. aq.). The layers were separated, and the aqueous layer was extracted with EtOAc (3 × 50 mL). The combined organic layers were dried (Na₂SO₄) and concentrated in vacuo. Flash column chromatography (silica gel, hexanes:EtOAc 5:1) afforded alcohol 21 (32.3 g, 75%, dr = 3:1) as a yellow oil. 21: R₇ = 0.25 (hexanes:EtOAc 4:1); IR (film) \( \nu \) max 3461, 2932, 2859, 1674, 1467, 1390, 1333, 1252, 1223, 1105, 1053, 991, 915, 839, 778, 666 cm⁻¹; \(^1\)H NMR (400 MHz, CDCl₃): \( \delta \) = 7.03 (dt, \( J = 4.5, 4.0 \) Hz, 1 H), 6.02 (dd, \( J = 9.2, 7.8 \) Hz, 1 H), 4.80–4.55 (m, 1 H), 3.98 (d, \( J = 2.6 \) Hz, 1 H), 3.70 (dd, \( J = 11.4, 4.3 \) Hz, 2 H), 2.63–2.27 (m, 6 H), 1.85–1.67 (m, 1 H), 0.88 (s, 9 H), 0.05 ppm (s, 6 H); \(^1^3\)C NMR (100 MHz, CDCl₃): \( \delta \) = 202.0, 200.8, 151.7, 151.4, 130.0, 129.5, 83.8, 83.4, 79.8, 79.3, 63.7, 62.9, 61.8, 61.7, 51.9, 51.4, 25.9 (6C), 25.8, 25.3 (2C), 24.0, 23.2 (2C), 18.3 (2C), -5.3 ppm (4C); HRMS(ESI): calcd for C₁₇H₂₉O₃Si+[M+H+] 309.1880, found 309.1883.

MOM ether 22: To a stirred solution of alcohol 21 (30 g, 0.097 mmol) in CH₂Cl₂ (100 mL) at 0 °C was added \( \mathit{i} \)-Pr₂NEt (85.3 mL, 0.49 mol) and MOMCl (22.6 mL, 0.29 mol). The resulting mixture was warmed to room temperature and stirred for 12 h before it was quenched with NaHCO₃ (50 mL, sat. aq.). The layers were separated, and the aqueous layer was extracted with CH₂Cl₂ (3 × 50 mL). The combined organic layers were dried (Na₂SO₄)
and concentrated \textit{in vacuo}. Flash column chromatography (silica gel, hexanes:EtOAc 12:1) afforded MOM ether \textit{22} (32.4 g, 95\%) as a light yellow oil. \textit{22}: $R_f = 0.50$
(hexanes:EtOAc 4:1); $^1$H NMR (400 MHz, CDCl$_3$): $\delta$ = 7.03–6.88 (m, 1 H), 6.00 (d, $J = 10.1$ Hz, 1 H), 5.05–5.00 (m, 1 H), 4.94 (d, $J = 6.7$ Hz, 1 H), 4.58 (d, $J = 6.7$ Hz, 1 H), 3.66 (t, $J = 7.1$ Hz, 2 H), 3.35 (s, 3 H), 2.68 (dt, $J = 12.1$, 4.7 Hz, 1 H), 2.47–2.33 (m, 4 H), 2.26 (ddd, $J = 12.9$, 8.4, 4.2 Hz, 1 H), 2.20–2.05 (m, 1 H), 0.86 (s, 9 H), 0.03 ppm (s, 6 H); $^{13}$C NMR (100 MHz, CDCl$_3$): $\delta$ = 197.7, 150.2, 129.7, 94.1, 84.7, 76.9, 64.9, 61.8, 55.7, 51.3, 25.8 (3C), 25.2, 23.7, 23.1, 18.2, -5.3 ppm (2C); HRMS(ESI): calcd for C$_{19}$H$_{33}$O$_4$Si$^+$$[M+H]^+$ 353.2143, found 353.2146.

\textbf{Enone 24}: To a stirred solution of MOM ether \textit{22} (6.0 g, 0.017 mol) in THF (20 mL) at \textit{-20 °C} was added \textit{23} (0.65M in THF, 41.3 mL, 0.026 mol). The resulting mixture was stirred for 0.5 h before it was quenched with NH$_4$Cl (30 mL, sat. aq.). The layers were separated, and the aqueous layer was extracted with EtOAc (3 × 30 mL). The combined organic layers were dried (Na$_2$SO$_4$) and concentrated \textit{in vacuo}. Flash column chromatography (silica gel, hexanes:EtOAc 5:1) afforded the crude alcohol as a colorless oil, which was used directly without further purification.

To a stirred solution of the alcohol (crude, obtained above) in CH$_2$Cl$_2$ (20 mL) at room temperature was added silica gel (7.25 g) and pyridinium chloroformate (7.25 g, 0.034 mol). After stirring for 12 h, the resulting mixture was quenched with Et$_2$O (100 mL). The resulting mixture was stirred for further 0.5 h before it was filtered through
a short pad of celite. The filtrate was concentrated in vacuo. Flash column chromatography (silica gel, hexanes:EtOAc 5:1) afforded the crude enone as a yellow oil, which was used directly without further purification.

To a stirred solution of the enone (crude, obtained above) in THF/H2O (20:1, v/v, 20 mL) at room temperature was added n-Bu4NF·3H2O (4.1 g, 13.0 mmol). The resulting mixture was stirred for 2 h before it was quenched with NH4Cl (20 mL, sat. aq.). The layers were separated, and the aqueous layer was extracted with EtOAc (3 × 20 mL). The combined organic layers were dried (Na2SO4) and concentrated in vacuo. Flash column chromatography (silica gel, hexanes:EtOAc 1:1) afforded enone 24 (3.0 g, 50% over the three steps) as a colorless oil. 24: Rf = 0.25 (hexanes:EtOAc 1:1); IR (film) vmax 3785, 3461, 2950, 2854, 2361, 2232, 1663, 1379, 1335, 1246, 1145, 1032, 900, 853, 749 cm⁻¹; ¹H NMR (400 MHz, CDCl₃): δ = 5.94 (s, 1 H), 4.95 (d, J = 6.8 Hz, 1 H), 4.64 (dd, J = 16.4, 6.2 Hz, 2 H), 4.55 (t, J = 4.6 Hz, 1 H), 4.09 (d, J = 7.8 Hz, 2 H), 3.74 (t, J = 11.1 Hz, 2 H), 3.67 (dd, J = 11.6, 5.7 Hz, 2 H), 3.36 (s, 3 H), 2.77–2.58 (m, 2 H), 2.47 (dd, J = 15.3, 8.0 Hz, 4 H), 2.36–2.23 (m, 2 H), 2.21–1.99 (m, 4 H), 1.87–1.75 (m, 1 H), 1.34 ppm (d, J = 13.4 Hz, 1 H); ¹³C NMR (100 MHz, CDCl₃): δ = 199.6, 164.3, 127.4, 101.1, 94.3, 85.7, 78.2, 67.4, 66.9 (2C), 60.9, 55.9, 43.0, 34.6, 32.6, 30.4, 25.7, 24.4, 23.2 ppm; HRMS(ESI): calcd for C₁₉H₂₉O₆⁺[M+H⁺] 353.1959, found 353.1963.

Alkene 25: To a stirred solution of alkyne 24 (1.2 g, 3.4 mmol) in toluene (20 mL) at room temperature was added Pd/CaCO₃ (300 mg). The resulting mixture was stirred under the hydrogen atmosphere for 0.5 h
before it was filtered through a short pad of celite. The filtrate was concentrated in vacuo. Flash column chromatography (silica gel, hexanes:EtOAc 1:1) afforded alkene 25 (1.2 g, 100%) as a colorless oil. 25: Rf = 0.25 (hexanes:EtOAc 1:1); IR (film) νmax 3459, 2950, 2861, 2732, 2361, 1662, 1347, 1283, 1211, 1143, 1080, 1027, 971, 898, 752, 641 cm⁻¹; ¹H NMR (400 MHz, CDCl₃): δ = 5.89 (s, 1 H), 5.79 (td, J = 9.9, 6.3 Hz, 1 H), 5.36 (t, J = 10.5 Hz, 1 H), 4.72 (d, J = 6.8 Hz, 1 H), 4.61–4.51 (m, 2 H), 4.45 (d, J = 6.8 Hz, 1 H), 4.08 (dd, J = 11.0, 3.9 Hz, 2 H), 3.71 (dd, J = 31.1, 19.3 Hz, 4 H), 3.26 (s, 3 H), 2.60–2.34 (m, 5 H), 2.32–2.18 (m, 2 H), 2.09–1.96 (m, 3 H), 1.83 (dd, J = 13.6, 9.5 Hz, 2 H), 1.74 (dd, J = 9.0, 5.4 Hz, 1 H), 1.33 ppm (d, J = 13.3 Hz, 1 H); ¹³C NMR (100 MHz, CDCl₃): δ = 199.2, 168.5, 133.3, 129.7, 126.0, 101.3, 93.0, 73.0, 66.9 (2C), 61.8, 55.4, 42.3, 33.8, 32.7, 32.4, 31.4, 25.7, 25.0 ppm; HRMS(ESI): calcd for C₁₉H₂₃O₆ [M+H⁺] 355.2115, found 355.2116.

Nitro compound 26: To a stirred solution of alcohol 25 (0.99 g, 2.8 mmol) in CH₂Cl₂ (10 mL) at 0 °C were added PPh₃ (1.1 g, 4.2 mmol), imidazole (0.29 g, 4.2 mmol) and iodine (1.1 g, 4.2 mmol). The resulting mixture was warmed to room temperature and stirred for 4 h before it was filtered through a short pad of celite. The filtrate was concentrated in vacuo. Flash column chromatography (silica gel, hexanes:EtOAc 4:1) afforded the crude iodide as a colorless oil, which was used directly without further purification.

To a stirred solution of iodide (crude, obtained above) in Et₂O/H₂O (1:3, v/v, 10 mL) at room temperature was added AgNO₂ (1.73 g, 11.2 mmol). The resulting
mixture was stirred for 12 h before it was filtered through a short pad of celite. The filtrate was extracted with Et₂O (3 × 15 mL). The combined organic layers were dried (Na₂SO₄) and concentrated in vacuo. Flash column chromatography (silica gel, hexanes:EtOAc 3:1) afforded 26 (676 mg, 63% over the two steps) as a colorless oil. 

26: Rᵣ = 0.50 (hexanes:EtOAc 2:1); IR (film) νₛmax 3778, 3492, 2951, 2857, 2733, 2361, 1665, 1622, 1551, 1431, 1378, 1283, 1247, 1210, 1143, 1082, 1027, 898, 745, 642 cm⁻¹; ¹H NMR (400 MHz, CDCl₃): δ = 5.92 (s, 1 H), 5.74–5.62 (m, 1 H), 5.44 (t, J = 10.4 Hz, 1 H), 4.64–4.51 (m, 3 H), 4.49–4.37 (m, 3 H), 4.09 (dd, J = 11.4, 4.2 Hz, 2 H), 3.74 (td, J = 12.1, 2.0 Hz, 2 H), 3.26 (s, 3 H), 2.82 (qd, J = 15.2, 7.8 Hz, 2 H), 2.59–2.45 (m, 3 H), 2.36 (dd, J = 11.0, 6.1 Hz, 2 H), 2.02 (dt, J = 12.6, 9.5, 4.5 Hz, 3 H), 1.84 (ddd, J = 15.0, 10.3, 5.3 Hz, 1 H), 1.79–1.69 (m, 1 H), 1.34 ppm (d, J = 12.7 Hz, 1 H); ¹³C NMR (100 MHz, CDCl₃): δ = 198.8, 167.6, 131.6, 129.2, 126.4, 101.2, 93.1, 74.5, 72.2, 66.9 (2C), 55.5, 42.3, 33.8, 32.7, 32.3, 25.7, 25.7, 24.8 ppm; HRMS(ESI): calcd for C₁₉H₃₀NO₇ [M+H⁺] 384.2017, found 384.2021.

Tricyclic isoxazoline 28: To a stirred solution of nitro compound 26 (532 mg, 1.39 mmol) in toluene (20 mL) at room temperature was added PhNCO (1.5 mL, 13.9 mmol) and Et₃N (0.19 mL, 1.39 mmol). The resulting mixture was stirred at 90 °C for 5 h before it was concentrated in vacuo. Flash column chromatography (silica gel, hexanes:EtOAc 2:1) afforded tricyclic isoxazoline 27 (315 mg, 65%) as a white solid, which was used immediately in the next step due to its instability.
To a stirred solution of tricyclic isoxazoline 27 (315 mg, 0.90 mmol) in EtOAc (10 mL) at room temperature was added Pd/C (10% wt/wt, 20 mg). The resulting mixture was stirred under hydrogen atmosphere (1 atm) for 1 h before it was filtered through a short pad of celite. The filtrate was concentrated in vacuo. Flash column chromatography (silica gel, hexanes:EtOAc 1:1) afforded tricyclic isoxazoline 28 (284 mg, 90%) as a colorless oil. 28: \( R_f = 0.25 \) (hexanes:EtOAc 1:1); IR (film) \( \nu_{\text{max}} \) 3877, 3660, 2930, 2857, 2361, 2248, 1726, 1670, 1446, 1407, 1379, 1326, 1239, 1216, 1143, 1081, 1022, 919, 899, 735, 697, 646 cm\(^{-1}\); \( ^1\)H NMR (400 MHz, CDCl\(_3\)) \( \delta = 4.61 \) (d, \( J = 7.0 \) Hz, 1 H), 4.55 (dd, \( J = 7.7, 3.9 \) Hz, 2 H), 4.30 (s, 1 H), 4.08 (dd, \( J = 11.2, 4.5 \) Hz, 2 H), 3.85 (d, \( J = 8.5 \) Hz, 1 H), 3.74 (t, \( J = 11.5 \) Hz, 2 H), 3.35 (s, 3 H), 2.74 (ddd, \( J = 15.2, 11.1, 5.2 \) Hz, 2 H), 2.42–2.28 (m, 2 H), 2.24 (d, \( J = 9.5 \) Hz, 1 H), 2.05 (ddd, \( J = 20.3, 12.6, 7.7 \) Hz, 1 H), 1.97–1.88 (m, 2 H), 1.88–1.78 (m, 3 H), 1.78–1.66 (m, 4 H), 1.53–1.41 (m, 1 H), 1.33 ppm (d, \( J = 13.2 \) Hz, 1 H); \( ^{13}\)C NMR (100 MHz, CDCl\(_3\)): \( \delta = 206.7, 161.0, 101.0, 95.5, 88.0, 77.9, 66.9 \) (2C), 63.1, 56.0, 43.3, 36.2, 30.3, 29.5, 29.0, 25.7, 24.2, 21.1, 20.4 ppm; HRMS(ESI): calcd for C\(_{19}\)H\(_{30}\)NO\(_6\)\([\text{M+H}^+]\) 368.2068, found 368.2069.

Hydroxyl ketone 29: To a stirred solution of isoxazoline 28 (570 mg, 1.63 mmol) in MeCN/H\(_2\)O (10:1, v/v, 50 mL) at room temperature was added Mo(CO)\(_6\) (517 mg, 1.94 mmol). The resulting mixture was heated to 90 °C and stirred for 1.5 h before it was filtered through a short pad of celite. The filtrate was extracted with Et\(_2\)O (3 × 50 mL). The combined organic layers were dried (Na\(_2\)SO\(_4\)) and concentrated in vacuo. Flash
column chromatography (silica gel, hexanes:EtOAc 2:1) afforded hydroxyl ketone 29 (413 mg, 72%) as a colorless oil. 29: Rf = 0.50 (CH2Cl2:Et2O 1:1); IR (film) νmax 3914, 3490, 2951, 2857, 2361, 2248, 1719, 1689, 1547, 1405, 1380, 1279, 1243, 1141, 1093, 1033, 912, 863, 843, 731, 696, 647 cm⁻¹; ¹H NMR (400 MHz, CDCl3): δ = 4.73 (d, J = 6.9 Hz, 1 H), 4.68 (d, J = 6.9 Hz, 1 H), 4.65–4.59 (m, 1 H), 4.19–4.00 (m, 4 H), 3.84–3.72 (m, 3 H), 3.67 (d, J = 4.9 Hz, 1 H), 3.40 (s, 3 H), 2.68 (dd, J = 16.2, 7.0 Hz, 1 H), 2.60 (dd, J = 15.5, 4.0 Hz, 1 H), 2.50–2.37 (m, 2 H), 2.31 (d, J = 12.9 Hz, 1 H), 2.26–2.10 (m, 4 H), 2.07 (dd, J = 11.1, 6.2 Hz, 1 H), 1.97–1.82 (m, 3 H), 1.56–1.42 (m, 2 H), 1.35 ppm (d, J = 13.4 Hz, 1 H); ¹³C NMR (100 MHz, CDCl3): δ = 212.8, 208.2, 101.9, 96.0, 77.4, 76.9, 67.1 (2C), 62.7, 55.7, 41.8, 41.1, 36.9, 29.0, 28.9, 25.9, 22.7, 20.7, 20.6 ppm ; HRMS(ESI): calcd for C₁₉H₃₁O₇ [M+H⁺] 371.2064, found 371.2063.

Ketone 30: To a stirred solution of hydroxyl ketone 29 (336 mg, 0.95 mmol) in CH₂Cl₂ (30 mL) at 0 °C were added Et₃N (0.65 mL, 4.68 mmol), Ac₂O (0.45 mL, 4.71 mmol) and DMAP (23 mg, 0.19 mmol). The resulting mixture was allowed to warmed to room temperature and stirred for 1 h before it was quenched with NaHCO₃ (30 mL, sat. aq.). The layers were separated, and the aqueous layer was extracted with CH₂Cl₂ (3 × 30 mL). The combined organic layers were dried (Na₂SO₄) and concentrated in vacuo. Flash column chromatography (silica gel, hexanes:EtOAc 3:1) afforded the crude acetate as a colorless oil, which was used directly without further purification.
To a stirred solution of acetate (crude, obtained above) in THF/MeOH (2:1, v/v, 15 mL) at \(-78\, ^\circ\text{C}\) was added \(\text{SmI}_2\) (0.1M in THF, 24 mL, 2.40 mmol). The resulting mixture was stirred for 15 min before it was quenched with \(\text{NH}_4\text{Cl}\) (50 mL, sat. aq.). The layers were separated, and the aqueous layer was extracted with \(\text{Et}_2\text{O}\) (3 × 50 mL). The combined organic layers were dried (\(\text{Na}_2\text{SO}_4\)) and concentrated in vacuo.

Flash column chromatography (silica gel, hexanes:EtOAc 2:1) afforded ketone 30 (253 mg, 79%) as a colorless oil. 30: \(R_f = 0.50\) (hexanes:EtOAc 1:1); IR (film) \(\nu_{\text{max}}\) 3912, 3789, 3637, 2945, 2885, 2361, 1708, 1463, 1407, 1379, 1239, 1215, 1144, 1097, 1077, 1036, 919, 884, 854, 744, 699, 644 cm\(^{-1}\); \(^1\)H NMR (400 MHz, CDCl\(_3\)): \(\delta = 4.69\) (d, \(J = 6.9\) Hz, 1 H), 4.64 (d, \(J = 6.9\) Hz, 1 H), 4.47 (t, \(J = 4.4\) Hz, 1 H), 4.17–3.99 (m, 3 H), 3.72 (t, \(J = 11.6\) Hz, 2 H), 3.38 (s, 3 H), 2.84 (d, \(J = 15.2\) Hz, 1 H), 2.71 (d, \(J = 14.8\) Hz, 1 H), 2.59–2.36 (m, 2 H), 2.24–2.13 (m, 3 H), 2.11–1.94 (m, 3 H), 1.91–1.63 (m, 7 H), 1.37–1.27 ppm (m, 2 H); \(^{13}\)C NMR (100 MHz, CDCl\(_3\)): \(\delta = 213.0, 209.8, 101.3, 95.5, 79.1, 66.8\) (2C), 56.0, 55.9, 47.0, 44.9, 41.1, 38.8, 31.1, 30.2, 29.5, 25.7, 24.2, 20.9 ppm; HRMS(ESI): calcd for \(\text{C}_{19}\text{H}_{31}\text{O}_6\)\([\text{M+H}^+]\) 355.2115, found 355.2117.

**Core structure 4**: To a stirred solution of ketone 30 (206 mg, 0.61 mmol) in THF (15 mL) at room temperature was added HCl (10% wt/wt, aq., 15 mL). The resulting mixture was heated to reflux and stirred for 0.5 h before it was quenched with \(\text{NaHCO}_3\) (100 mL, sat. aq.) The layers were separated, and the aqueous layer was extracted with \(\text{Et}_2\text{O}\) (3 × 50 mL). The combined organic layers were dried (\(\text{Na}_2\text{SO}_4\)) and concentrated in vacuo. Flash
column chromatography (silica gel, hexanes:EtOAc 1:1) afforded core structure 4 (114 mg, 80%) as a colorless oil. 4: $R_t = 0.25$ (hexanes:EtOAc 1:1); IR (film)$\nu_{\text{max}}$ 3912, 3853, 3660, 3410, 2938, 2862, 2361, 2247, 1682, 1612, 1334, 1284, 1254, 1217, 1081, 1027, 1002, 967, 938, 911, 881, 856, 824, 767, 740, 642 cm$^{-1}$; $^1$H NMR (400 MHz, CDCl$_3$): $\delta = 6.97$ (s, 1 H), 4.09 (s, 1 H), 2.80 (s, 1 H), 2.61–2.50 (m, 1 H), 2.39 (tdd, $J = 11.4$, 8.1, 4.6 Hz, 3 H), 2.26 (d, $J = 18.8$ Hz, 1 H), 2.22–2.12 (m, 2 H), 2.06–1.93 (m, 1 H), 1.91–1.74 (m, 6 H), 1.48 ppm (d, $J = 10.0$ Hz, 1 H); $^{13}$C NMR (100MHz, CDCl$_3$): $\delta = 200.1$, 145.6, 143.6, 105.1, 78.3, 61.3, 45.8, 34.6 (2C), 33.4, 30.6, 29.2, 24.9, 17.7 ppm; HRMS(ESI): calcd for C$_{14}$H$_{19}$O$_3$ [M+H$^+$] 235.1329, found 235.1330.
II) Abbreviations

MOMCl  chloromethylmethyl ether
PCC  pyridinium chlorochromate
DMAP  4-dimethylaminopyridine
Dibal-H  diisobutylaluminium hydride
THF  tetrahydrofuran
Tf  trifluoromethanesulfonyl
DIPEA  \(N,N\)-Diisopropylethylamine

III) References


IV) $^1$H and $^{13}$C NMR Spectra of Compounds

$^1$H NMR spectrum (400 MHz, CDCl$_3$) (ca. 1.5:1 mixture of diastereomers)

$^{13}$C NMR spectrum (100 MHz, CDCl$_3$)
$^{13}$C NMR spectrum (100 MHz, CDCl$_3$)

$^1$H NMR spectrum (400 MHz, CDCl$_3$)
$^1$H NMR spectrum (400 MHz, CDCl$_3$)

$^{13}$C NMR spectrum (100 MHz, CDCl$_3$)

S25
\[1\text{H NMR spectrum (400 MHz, CDCl}_3\text{)}\]

\[13\text{C NMR spectrum (100 MHz, CDCl}_3\text{)}\]
$^1$H NMR spectrum (400 MHz, CDCl$_3$)

$^{13}$C NMR spectrum (100 MHz, CDCl$_3$)
$^{1}$H NMR spectrum (400 MHz, CDCl$_3$)

$^{13}$C NMR spectrum (100 MHz, CDCl$_3$)

15

OMOM

OMOM

H

H

H

H
$^1$H NMR spectrum (400 MHz, CDCl$_3$)

$^{13}$C NMR spectrum (100 MHz, CDCl$_3$)
$^1$H NMR spectrum (400 MHz, CDCl$_3$)

$^{13}$C NMR spectrum (100 MHz, CDCl$_3$)
$\text{^1H NMR spectrum (400 MHz, CDCl}_{3}\text{)}$

$\text{^13C NMR spectrum (100 MHz, CDCl}_{3}\text{)}$
$^1$H NMR spectrum (400 MHz, CDCl$_3$)

$^{13}$C NMR spectrum (100 MHz, CDCl$_3$)
$^{1}H$ NMR spectrum (400 MHz, CDCl$_3$)

$^{13}C$ NMR spectrum (100 MHz, CDCl$_3$)
$^1$H NMR spectrum (400 MHz, CDCl$_3$)  
(ca. 3:1 mixture of diastereomers)
\[ ^1H \text{ NMR spectrum (400 MHz, CDCl}_3 \] \]

\[ ^{13}C \text{ NMR spectrum (100 MHz, CDCl}_3 \] \]
$^1$H NMR spectrum (400 MHz, CDCl$_3$)

$^{13}$C NMR spectrum (100 MHz, CDCl$_3$)
$^{1}\text{H NMR spectrum (400 MHz, CDCl}_3\text{)}$

$^{13}\text{C NMR spectrum (100 MHz, CDCl}_3\text{)}$
$^1$H NMR spectrum (400 MHz, CDCl$_3$)

$^{13}$C NMR spectrum (100 MHz, CDCl$_3$)
$^1$H NMR spectrum (400 MHz, CDCl$_3$)

$^{13}$C NMR spectrum (100 MHz, CDCl$_3$)
\(^1\)H NMR spectrum (400 MHz, CDCl\(_3\))

\(^{13}\)C NMR spectrum (100 MHz, CDCl\(_3\))
$^1$H NMR spectrum (400 MHz, CDCl$_3$)

$^{13}$C NMR spectrum (100 MHz, CDCl$_3$)
$^1$H NMR spectrum (400 MHz, CDCl$_3$)

$^{13}$C NMR spectrum (100 MHz, CDCl$_3$)