**SUPPORTING INFORMATION**

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**General.** Otherwise noted, all reactions were carried out in flame-dried glassware under dry nitrogen atmosphere. The solvents were purified with the solvent purification system Pure Solv MD-6 (THF, Et₂O, CH₂Cl₂, benzene, toluene, hexane). Dry acetone was purchased from VWR. Flash chromatography: Merck silica gel 60 (230-400 mesh). NMR: Spectra were recorded on a Bruker DRX 500 and a Bruker DPX 400 spectrometers in CDCl₃; chemical shifts (δ) are given in ppm. The solvent signals were used as references and the chemical shifts converted to the TMS scale (CDCl₃: δC = 77.0 ppm; residual CHCl₃ in CDCl₃: δH = 7.26 ppm); apparent splitting patterns are designated using the following abbreviations: s (singlet), d (doublet), t (triplet), q (quartet), quint. (quintuplet), m (multiplet), br (broad), and the appropriate combinations. IR: PerkinElmer Spectrum 100 FT-IR spectrometer, wavenumbers (ν) in cm⁻¹. HRMS determined at the University of Liverpool on micromass LCT mass spectrometer (ES+) and Trio-1000 or Agilent QTOF 7200 mass spectrometers (Cl). Melting points: Griffin melting point apparatus (not corrected). Elemental analyses: University of Liverpool. Optical rotations were measured on a PerkinElmer Model 343 plus polarimeter with a sodium lamp (D line, 589 nm) at ambient temperature (indicated in °C as superscript) using a 1 mL quartz cell of 100 mm length; solution concentration (c) are given in g/100 mL. All commercially available compounds were used as received.

Preparation of compound 3a–3c  
Preparation of common intermediate 4  
Preparation of compounds 5a–5c, 6a–6c and 7a–7c  
Preparation of compounds 8 and 9  
Preparation of compounds 10 and 11  
Bioassays conducted on 7a–7c, 10 and 11  
NMR spectra of compounds 3a–c, SI-19–21, 4, 5a–c, 6a–c, 7a–c, 8–11
Preparation of compounds 3a–3c

\[ \text{Me}_3\text{Si} \equiv \text{OH} \xrightarrow{\text{a,b}} \text{Me}_3\text{Si} \equiv \text{OH} \xrightarrow{\text{c}} \text{Me}_3\text{Si} \equiv \text{OMe} \equiv \text{N} \xrightarrow{\text{d}} \text{Me}_3\text{Si} \equiv \text{OMe} \equiv \text{OH} \]

\( \textbf{SI-1}, n = 7 \)
\( \textbf{SI-2}, n = 6 \)
\( \textbf{SI-3}, n = 5 \)
\( \textbf{SI-4} \)
\( \textbf{SI-5}, n = 7 \)
\( \textbf{SI-6}, n = 6 \)
\( \textbf{SI-7}, n = 5 \)
\( \textbf{SI-8}, n = 7 \)
\( \textbf{SI-9}, n = 6 \)
\( \textbf{SI-10}, n = 5 \)
\( \textbf{3a}, n = 7 \)
\( \textbf{3b}, n = 6 \)
\( \textbf{3c}, n = 5 \)

\((a) (\text{COCl})_2, \text{DMSO, Et}_3\text{N, CH}_2\text{Cl}_2. \) (b) i) SI-4, Et3N, Bu2BOTf, CH2Cl2; ii) SI-1–SI-3; iii) pH 7-buffer, H2O2, MeOH. (c) Me3O•BF4, proton sponge, CH2Cl2. (d) LiAlH4, Et2O.

**Compound SI-1.** This compound was prepared according to a literature procedure.\(^1\) To ethylenediamine (50 mL) at 0 °C under N2 was added NaH (2.07 g, 51.9 mmol, 60% in oil) portionwise. The reaction mixture was stirred at 0 °C for 15 minutes then at room temperature for 1 hour. The purple/brown reaction mixture was heated at 60 °C for 1 hour, cooled to 40 °C and 3-decyn-1-ol (2 g, 13.0 mmol) was added. The reaction was stirred at 40 °C for 1.5 hours then at 65 °C for 2 hours. The reaction mixture was cooled to 0 °C and quenched by addition of H2O (50 mL) and 1M HCl (50 mL). The reaction was extracted with Et2O (50 mL) and EtOAc (50 mL), the combined organics were washed with brine, dried (Na2SO4) and the solvent removed under reduced pressure. Purification by flash chromatography (SiO2, petroleum ether/Et2O, 4:1 to 2:1) afforded 9-decyn-1-ol as a pale yellow oil (1.42 g, 71%). Some of this material (1.3 g, 8.44 mmol) was diluted in THF (42 mL) under N2 at 0 °C and MeMgBr (7.8 mL, 23.6 mmol, 3M in Et2O) was added dropwise. The reaction was warmed to ambient temperature and stirred for 16 hours. TMSCl (3.0 mL, 23.6 mmol) was added and the reaction stirred for 8 hours. 1M HCl (50 mL) was added carefully and the reaction stirred for 15 minutes. The mixture was extracted with Et2O (2 x 100 mL), the combined organics dried (Na2SO4) and the solvent removed under reduced pressure. Purification by flash column chromatography (SiO2, petroleum ether/Et2O, 4:1) yielded **SI-1** as a pale yellow oil (960 mg, 50%). \(^1\)H-NMR (CDCl3, 500 MHz) δ 3.63 (t, J = 6.6 Hz, 2H), 2.18 (td, J = 7.2 and 2.7 Hz, 2H), 1.94 (t, J = 2.7 Hz, 1H), 1.59-1.49 (m, 4H) and 1.43-1.29 (m, 8H), 0.17 (s, 9H), in agreement with previously published data.\(^2\)

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Compound SI-2. 8-nonyl-1-ol was prepared analogously from 3-nonyl-1-ol and SI-2 (pale yellow oil, 55% over 2 steps) was then obtained following the same procedure as the one used for the preparation of SI-1. $^1$H-NMR (CDCl$_3$, 500 MHz) $\delta$ 3.66-3.60 (m, 2H), 2.21 (t, $J = 7.1$ Hz, 2H), 1.59-1.48 (m, 4H), 1.42-1.30 (m, 6H) and 0.13 (s, 9H), in agreement with previously published data.$^3$

Compound SI-3. 7-octyn-1-ol (964 mg, 71%) was prepared analogously from 3-octyn-1-ol and SI-3 (pale yellow oil, 85%) was then obtained following the same procedure as the one used for the preparation of SI-1.$^1$H-NMR (CDCl$_3$, 500 MHz) $\delta$ 3.67 (q, $J = 6.8$ Hz, 2H), 2.25 (t, $J = 7.1$ Hz, 2H), 1.63-1.52 (m, 4H), 1.47-1.37 (m, 4H), 1.27-1.23 (m, 1H), 0.17 (s, 9H) in agreement with previously published data.$^4$

Compound SI-5. This compound was prepared from SI-1 (344 mg, 1.29 mmol) using the same procedure as described for the preparation of SI-7. Colourless oil (442 mg, 75% over 2 steps). $^1$H-NMR (500 MHz, CDCl$_3$) $\delta$ = 7.38-7.34 (m, 2H), 7.33-7.30 (m, 1H), 7.24-7.21 (m, 2H), 4.73 (ddt, $J = 9.4$, 7.8 and 2.9 Hz, 1H), 4.25 (dd, $J = 9.1$ and 7.7 Hz, 1H), 4.21 (dd, $J = 9.1$ and 2.9 Hz, 1H), 3.99-3.95 (m, 1H), 3.77 (dq, $J = 7.1$ and 2.5 Hz, 1H), 3.27 (dd, $J = 13.4$ and 3.1 Hz, 1H), 2.89 (d, $J = 2.3$ Hz, 1H(OH)), 2.81 (dd, $J = 13.3$ and 9.5 Hz, 1H), 2.23 (t, $J = 2.3$ Hz, 2H), 1.60-1.47 (m, 4H), 1.46-1.30 (m, 8H), 1.28 (d, $J = 7.3$ Hz, 3H), 0.17 (s, 9H); $^{13}$C-NMR (125 MHz, CDCl$_3$) $\delta$ = 177.6, 153.0, 134.9, 129.4 (2C), 129.0 (2C), 127.4, 107.7, 84.2, 71.4, 66.2, 55.1, 42.1, 37.8, 33.8, 29.4, 29.0, 28.7, 28.6, 25.9, 19.8, 10.3, 0.2 (3C); IR (neat): $\tilde{\nu}$ = 3517 (br), 3029, 2931, 2856, 2172, 1778, 1696, 1604, 1497, 1481, 1415, 1383, 1350, 1289, 1247, 1208, 1109, 1075, 1048, 1014, 970, 920, 760, 701 cm$^{-1}$; HRMS (ES$^+$) calcd for C$_{29}$H$_{39}$NO$_4$SiNa 480.2546, found 480.2545; [$\alpha$]$^\circ_{D} = -27.1$ (c = 0.9, CHCl$_3$).  

Compound SI-6. This compound was prepared from SI-2 (495 mg, 2.33 mmol) using the same procedure as described for the preparation of SI-7. Colourless oil (438 mg, 49% over two steps). $^1$H-NMR (500 MHz, CDCl$_3$) $\delta$ = 7.36-7.32 (m, 2H), 7.30-7.27 (m, 1H), 7.22-7.19 (m, 2H), 4.74-4.68 (m, 1H), 4.23 (dd, $J = 9.0$ and 7.7 Hz, 1H), 4.19 (dd, $J = 9.0$ and 2.9 Hz, 1H), 3.97-3.92 (m, 1H), 3.76 (qd, $J = 7.0$ and 2.5 Hz, 1H), 3.25 (dd, $J = 13.4$ and 3.2 Hz, 1H), 2.88 (br s, 1H(OH)), 2.79 (dd, $J = 13.4$ and 9.4 Hz, 1H), 2.21 (t, $J = 7.0$ Hz, 2H), 1.59-1.47 (m, 4H), 1.44-1.29 (m, 6H), 1.25 (d, $J = 7.0$ Hz, 3H), 0.15 (s, 9H); $^{13}$C-NMR (125 MHz, CDCl$_3$) $\delta$ = 177.5, 153.0, 135.0, 129.4 (2C), 128.9 (2C), 127.4, 107.6, 84.2, 71.4, 66.1, 55.0, 42.1, 37.8, 33.7, 29.0, 28.7, 28.5, 25.8, 19.8, 10.3, 0.1 (3C); IR (neat): $\tilde{\nu}$ = 3528 (br), 2932, 2857, 2172, 1779, 1695, 1497, 1455, 1384, 1350, 1289, 1247, 1209, 1107, 1048, 1013, 970, 842, 760, 701 cm$^{-1}$; HRMS (ES$^+$) calcd for C$_{25}$H$_{37}$NO$_4$SiNa 466.2390, found 466.2387; [$\alpha$]$^\circ_{D} = -25.9$ (c = 1.25, CHCl$_3$).  

Compound SI-7. Under N$_2$ atmosphere, DMSO (0.96 mL, 13.47 mmol) was added via syringe to oxalychloride (0.700 mL, 8.09 mmol) in CH$_2$Cl$_2$ (50 mL) at -78 $^\circ$C. The reaction was stirred for 10 minutes and SI-3 (1.06 g, 5.39 mmol) in CH$_2$Cl$_2$ (3 mL) was added dropwise. The reaction was stirred for 1 hour, Et$_3$N (3.74 mL, 26.9 mmol) was added and the reaction warmed to room temperature. Saturated aqueous NH$_4$Cl (30 mL) was added and the reaction mixture was extracted with CH$_2$Cl$_2$ (3 × 50 mL). The combined organic layers were dried (Na$_2$SO$_4$) and the solvent removed under reduced pressure. The crude aldehyde was used without further purification in the next step. Under N$_2$ atmosphere, Bu$_2$OTf (4.35 mL, 4.35

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mmol, 1M in CH₂Cl₂) was added dropwise to SI-4 (930 mg, 3.99 mmol) in CH₂Cl₂ (36 mL) at 0 °C. The reaction was stirred for 10 minutes and Et₃N (0.655 mL, 4.71 mmol) was added. The mixture was cooled to -78 °C and a solution of the aldehyde previously obtained (0.711, 3.63 mmol) in CH₂Cl₂ (2 mL) was added and the mixture was then stirred at -78 °C for 90 minutes. The reaction mixture was warmed to 0 °C and stirred for 90 minutes. A pH7 buffer (10 mL) in MeOH (30 mL) and H₂O₂ (2 mL) in MeOH (10 mL) were added and the reaction mixture stirred at 0 °C for 1 hour. The volatiles were removed under reduced pressure and the reaction extracted with Et₂O (3 × 50 mL). The combined organics were washed with saturated aqueous NaHCO₃ (50 mL) and brine (50 mL), dried (Na₂SO₄) and the solvent removed under reduced pressure. Purification by flash column chromatography on silica gel (petroleum ether/Et₂O, 9:1 to 4:1 to 1:1) gave SI-7 as a colourless oil (790 mg, 51%). ¹H-NMR (CDCl₃, 500 MHz) δ 7.36-7.31 (m, 2H), 7.30-7.26 (m, 1H), 7.22-7.18 (m, 2H), 4.72-4.68 (m, 1H), 4.22 (dd, J = 9.1 and 7.7 Hz, 1H), 4.19 (dd, J = 9.1 and 3.0 Hz, 1H), 3.97-3.92 (m, 1H), 3.75 (qd, J = 7.1 and 2.6 Hz, 1H), 3.24 (dd, J = 13.4 and 3.3 Hz, 1H), 2.86 (br s, 1H(OH)), 2.79 (dd, J = 13.4 and 9.5 Hz, 1H), 2.21 (t, J = 7.1 Hz, 2H), 1.59-1.30 (m, 8H), 1.25 (d, J = 7.1 Hz, 3H) and 0.14 (s, 9H); ¹³C-NMR (CDCl₃, 125 MHz) δ 177.6, 153.0, 135.0, 129.4 (2C), 129.0 (2C), 127.4, 107.5, 84.0, 71.4, 66.2, 55.1, 42.1, 37.8, 33.7, 28.7, 28.5, 25.6, 19.8, 10.4, 0.2 (3C); IR (neat): ν = 3517 (br), 3029, 2937, 2860, 2172, 1777, 1697, 1604, 1497, 1481, 1455, 1383, 1350, 1289, 1247, 1209, 1109, 1075, 1049, 1011, 977, 921, 840, 760, 700 cm⁻¹; MS (ES⁺) m/z (rel. intensity) 452 (100 %, [M+Na]⁺); HRMS calcd for C₂₉H₃₅O₄NSiNa, 452.2233, found 452.2249; [α]D²⁰ = -36.4 (c = 1, CHCl₃).

**Compound SI-8.** This compound was prepared from SI-5 (442 mg, 0.97 mmol) using the same procedure as described for the preparation of SI-10. Colourless oil (295 mg, 65%). ¹H-NMR (CDCl₃, 500 MHz) δ = 7.37-7.33 (m, 2H), 7.31-7.28 (m, 1H), 7.25-7.22 (m, 2H), 4.67 (ddt, J = 9.9, 6.9 and 2.8 Hz, 1H), 4.21 (dd, J = 9.2 and 7.5 Hz, 1H), 4.18 (dd, J = 9.2 and 2.9 Hz, 1H), 4.10-4.02 (m, 1H), 3.43-3.39 (m, 1H), 3.38 (s, 3H), 3.32 (dd, J = 13.4 and 3.0 Hz, 1H), 2.78 (dd, J = 13.4 and 10.1 Hz, 1H), 2.22 (t, J = 7.2 Hz, 2H), 1.55-1.35 (m, 5H), 1.35-1.28 (m, 7H), 1.25 (d, J = 6.7 Hz, 3H), 0.16 (s, 9H); ¹³C-NMR (CDCl₃, 125 MHz) δ = 175.4, 153.1, 135.3, 129.4 (2C), 128.9 (2C), 127.3, 107.7, 84.2, 82.7, 66.0, 58.4, 55.8, 41.0, 37.8, 31.9, 29.6, 29.0, 28.7, 28.6, 25.8, 19.8, 12.6, 0.2 (3C); IR (neat): ν = 2931, 2856, 2817, 1772, 1699, 1497, 1481, 1379, 1349, 1289, 1247, 1208, 1194, 1107, 1050, 1013, 966, 921, 839, 759, 700 cm⁻¹; MS (ES⁺) m/z (rel. intensity) 494 (100 %, [M+Na]⁺); HRMS calcd for C₂₉H₃₅O₄NSiNa, 494.2702, found 494.2702; [α]D²⁰ = -55.6 (c = 1.3, CHCl₃).

**Compound SI-9.** This compound was prepared from SI-6 (295 mg, 0.66 mmol) using the same procedure as described for the preparation of SI-10. Colourless oil (195 mg, 65%). ¹H-NMR (CDCl₃, 500 MHz) δ = 7.35-7.31 (m, 2H), 7.30-7.27 (m, 1H.), 7.23-7.21 (m, 2H), 4.65 (ddt, J = 9.9, 7.0 and 2.9 Hz, 1H), 4.21-4.15 (m, 2H), 4.10-4.02 (m, 1H), 3.42-3.38 (m, 1H), 3.37 (s, 3H), 3.31 (dd, J = 13.0 and 3.1 Hz, 1H), 2.77 (dd, J = 13.0 and 9.8 Hz, 1H), 2.21 (t, J = 7.0 Hz, 2H), 1.55-1.28 (m, 10H), 1.24 (d, J = 7.0 Hz, 3H), 0.14 (s, 9H); ¹³C-NMR (CDCl₃, 125 MHz) δ = 175.4, 153.1, 135.3, 129.4 (2C), 128.9 (2C), 127.3, 107.6, 84.3, 82.6, 65.9, 58.4, 55.7, 41.0, 37.8, 31.9, 29.2, 28.7, 28.5, 25.7, 19.8, 12.6, 0.1 (3C); IR (neat): ν = 2933, 2858, 2172, 1779, 1696, 1604, 1497, 1481, 1455, 1379, 1349, 1288, 1247, 1208, 1194, 1106, 1050, 1014, 966, 924, 841, 760, 701 cm⁻¹; MS (ES⁺) m/z (rel. intensity) 480 (100 %, [M+Na]⁺); HRMS calcd for C₂₆H₃₉NO₄SiNa, 480.2546, found 480.2557; [α]D²⁰ = -49.5 (c = 0.85, CHCl₃).
**Compound SI-10.** Under N₂ atmosphere, proton sponge (850 mg, 6.96 mmol) and Me₃SiBF₄ (1.02 g, 6.96 mmol) were added to SI-7 (750 mg, 1.74 mmol) in CH₂Cl₂ (17.4 mL, 0.1M) in a flask covered with aluminum foil. The reaction was stirred in the dark at room temperature for 40 hours. The reaction mixture was diluted with CH₂Cl₂ (30 mL), washed with saturated aqueous NH₄Cl (20 mL) and brine (20 mL), dried (Na₂SO₄) and the solvent removed under reduced pressure. Purification by flash column chromatography on silica gel (petroleum ether/Et₂O, 20:1) afforded SI-10 as a pale yellow oil (632 mg, 82%). ¹H-NMR (500 MHz, CDCl₃) δ = 7.35-7.30 (m, 2H), 7.28-7.25 (m, 1H), 7.22-7.19 (m, 2H), 4.65 (dt, J = 9.9, 7.1 and 2.9 Hz, 1H), 4.21-4.15 (m, 2H), 4.10-4.02 (m, 1H), 3.41 (q, J = 5.9 Hz, 1H), 3.39 (s, 3H), 3.30 (dd, J = 13.4 and 3.2 Hz, 1H), 2.76 (dd, J = 13.4 and 9.8 Hz, 1H), 2.21 (t, J = 7.2 Hz, 2H), 1.55-1.28 (m, 8H), 1.24 (d, J = 7.0 Hz, 3H), 0.13 (s, 9H); ¹³C-NMR (125 MHz, CDCl₃) δ = 175.4, 153.1, 135.3, 129.4 (2C), 128.9 (2C), 127.3, 107.5, 84.3, 82.7, 66.0, 58.4, 55.7, 41.0, 37.8, 31.8, 28.8, 28.6, 25.3, 19.8, 12.7, 0.2 (3C); IR (neat): ν = 3029, 2936, 2860, 2172, 1778, 1696, 1604, 1497, 1454, 1378, 1349, 1289, 1247, 1209, 1194, 1106, 1049, 1012, 967, 920, 840, 760, 701 cm⁻¹; MS (ES⁺) m/z (rel. intensity) 444 (100 %, [M+H⁺]); HRMS calcd for C₂₅H₃₇O₄NSi 444.2565, found 444.2583.

**Compound 3a.** This compound was prepared from SI-8 (215 mg, 0.456 mmol) using the same procedure as described for the preparation of 3c. Colourless oil (109 mg, 80%). ¹H-NMR (500 MHz, CDCl₃) δ = 3.69 (ddd, J = 10.6, 7.5 and 3.4 Hz, 1H), 3.58 (dt, J = 10.6 and 4.8 Hz, 1H), 3.40 (s, 3H), 3.27-3.24 (m, 1H), 3.27-3.23 (m, 1H), 2.76-2.72 (m, 1H(OH)), 2.22 (t, J = 7.2 Hz, 2H), 2.10-2.00 (m, 1H), 1.60-1.49 (m, 3H), 1.46-1.24 (m, 9H), 0.87 (d, J = 7.3 Hz, 3H), 0.16 (s, 9H); ¹³C-NMR (125 MHz, CDCl₃) δ = 107.6, 85.0, 84.2, 66.4, 57.6, 39.6, 29.6 (2C), 29.0, 28.7, 28.6, 26.2, 19.8, 11.6, 0.1 (3C); IR (neat): ν = 3407 (br), 2930, 2856, 2173, 1460, 1378, 1248, 1091, 1028, 841, 759, 698 cm⁻¹; MS (ES⁺) m/z (rel. intensity) 321 (100 %, [M+N⁺⁺]); HRMS (ES⁺) calcd for C₁₀H₁₄O₂SiNa 321.2226, found 321.2226; [α]D²⁰ = +10.2 (c = 0.85, CHCl₃).

**Compound 3b.** This compound was prepared from SI-9 (150 mg, 0.33 mmol) using the same procedure as described for the preparation of 3c. Colourless oil (65 mg, 69%). ¹H-NMR (500 MHz, CDCl₃) δ = 3.69 (ddd, J = 10.5 and 7.6 Hz, 1H), 3.58 (dd, J = 10.8 and 4.7 Hz, 1H), 3.39 (s, 3H), 3.27-3.23 (m, 1H), 2.64 (brs, 1H (OH)), 2.22 (t, J = 7.2 Hz, 2H), 2.07-2.00 (m, 1H), 1.59-1.48 (m, 3H), 1.46-1.36 (m, 4H), 1.36-1.24 (m, 3H), 0.86 (d, J = 7.0 Hz, 3H), 0.15 (s, 9H); ¹³C-NMR (125 MHz, CDCl₃) δ = 107.4, 84.9, 84.4, 66.3, 57.7, 36.4, 29.5, 28.9, 28.5, 28.3, 25.7, 19.8, 11.6, 0.1 (3C); IR (neat): ν = 3400 (br), 2933, 2858, 2174, 1461, 1379, 1248, 1194, 1157, 1091, 1029, 924, 839, 758, 694 cm⁻¹; MS (ES⁺) m/z (rel. intensity) 307 (100 %, [M+N⁺⁺]); HRMS calcd for C₁₀H₂₃O₂SiNaN 307.2069, found 307.2076; [α]D²⁰ = +8.0 (c = 0.15, CHCl₃).

**Compound 3c.** Under N₂ atmosphere, SI-10 (602 mg, 1.35 mmol) in Et₂O (1 mL) was added dropwise via cannula to a suspension of LiAlH₄ (26 mg, 0.68 mmol) in Et₂O (14 mL) at 0 °C. The reaction was stirred for 30 minutes at 0 °C and a second portion of LiAlH₄ (26 mg, 0.68 mmol) was added. The reaction was warmed slowly to room temperature and stirred for 2 hours. The reaction was diluted with Et₂O (10 mL) and saturated aqueous Na₂SO₄ was added dropwise (slowly) until a white precipitate had formed. The reaction mixture was filtered through Celite and the solvent removed under reduced pressure. Purification by flash column chromatography on silica gel (petroleum ether/Et₂O, 10:1 to 2:1) afforded 3c as a pale yellow oil (235 mg, 64%). ¹H-NMR (500 MHz, CDCl₃) δ = 3.69 (ddd, J = 10.8, 7.6 and 4.7 Hz, 1H), 3.58 (ddd, J = 10.7, 5.7 and 4.7 Hz, 1H), 3.40 (s, 3H), 3.28-3.23 (m, 1H), 2.65-2.61 (m, 1H(OH)), 2.23 (t, J = 7.1 Hz, 2H), 2.09-2.01 (m, 1H), 1.60-1.50 (m, 3H), 1.47-1.37 (m, 4H), 1.35-1.27 (m, 1H), 0.86 (d, J = 7.2 Hz, 3H), 0.15 (s, 9H); ¹³C-NMR (125 MHz, CDCl₃) δ = 107.4, 84.9,
84.4, 66.3, 57.7, 36.4, 28.9, 25.7, 19.8, 11.6, 0.1 (3C); IR (neat): $\tilde{\nu} = 3391$ (br), 2934, 2173, 1459, 1379, 1248, 1193, 1161, 1091, 1032, 841, 759, 697 cm$^{-1}$; MS (ES$^+$) $m/z$ (rel. intensity) 293 (100 %, [M+Na]$^+$); HRMS calcd for C$_{15}$H$_{30}$O$_2$SiNa 293.1913, found 293.1913; $[\alpha]_D^{20} = +8.2$ (c = 1.1, CHCl$_3$).

A Mosher ester analysis was performed with one derivative to ascertain the stereochemistry of the products.

(a) SI-13, pyridine, CH$_2$Cl$_2$. (b) SI-14, pyridine, CH$_2$Cl$_2$.

**Compound SI-11.** A solution of SI-6 (35 mg, 0.072 mmol), SI-13 (24 µL, 0.13 mmol) and pyridine (17 µL, 0.22 mmol) in CH$_2$Cl$_2$ (0.35 mL) was stirred for 12h at room temperature under N$_2$. The mixture was quenched with water and extracted with Et$_2$O (3 × 5 mL). The combined organic layers were dried (Na$_2$SO$_4$) and the solvent removed under reduced pressure. Purification by flash column chromatography on silica gel (petroleum ether/Et$_2$O, 20:1 to 10:1) afforded SI-11 as a colourless oil (21 mg, 44%).

$^1$H-NMR (500 MHz, CDCl$_3$) $\delta$ 7.59-7.54 (m, 2H, ArH), 7.42-7.39 (m, 3H, ArH), 7.36-7.32 (m, 2H, ArH), 7.30-7.27 (m, 1H, ArH), 7.21-7.19 (m, 2H, ArH), 5.43 (ddd, $J = 9.0, 4.0$ and 2.9 Hz, 1H, H-2), 4.57-4.52 (m, 1H, H-13), 4.33 (t, $J = 8.2$ Hz, 1H, H-14$^B$), 4.17 (dd, $J = 8.9$ and 2.2 Hz, 1H, H-14$^B$), 4.02 (qd, $J = 7.0$ and 3.4 Hz, 1H, H-1), 3.64 (s, 3H, OMe), 3.29 (dd, $J = 13.3$ and 3.4 Hz, 1H, H-12$^B$), 2.79 (dd, $J = 13.4$ and 9.6 Hz, 1H, H-12$^B$), 2.17 (t, $J = 7.1$ Hz, 2H, H-8), 1.73-1.64 (m, 1H, H-3$^A$), 1.59-1.50 (m, 1H, H-3$^B$), 1.45-1.38 (m, 2H, H-7), 1.35-1.20 (m, 5H), 1.24 (d, $J = 7.0$ Hz, 3H, H-11), 1.20-1.04 (m, 1H), 0.15 (s, 9H, SiMe$_3$).

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Compound SI-12. This compound was prepared from SI-6 (25 mg, 0.050 mmol) and SI-14 (17 µL, 0.095 mmol) using the same procedure as described for the preparation of SI-11. Colourless oil (16 mg, 48%). \(^1\)H-NMR (500 MHz, CDCl\(_3\)) \(\delta\) 7.58-7.54 (m, 2H, ArH), 7.43-7.39 (m, 3H, ArH), 7.36-7.31 (m, 2H, ArH), 7.30-7.27 (m, 1H, ArH), 7.20-7.17 (m, 2H, ArH), 5.45-5.40 (m, 1H, H-2), 4.60-4.54 (m, 1H, H-13), 4.00 (qd, \(J = 7.0\) and 3.4 Hz, 1H, H-1), 3.55 (s, 3H, OMe), 3.28 (dd, \(J = 13.4\) and 3.4 Hz, 1H, H-12A), 2.76 (dd, \(J = 13.4\) and 9.8 Hz, 1H, H-12B), 2.21 (t, \(J = 7.2\) Hz, 2H, H-8), 1.84-1.75 (m, 1H, H-3A), 1.70-1.62 (m, 1H, H-3B), 1.52-1.45 (m, 2H, H-7), 1.40-1.26 (m, 6H), 1.17 (d, \(J = 7.0\) Hz, 3H, H-11), 0.15 (s, 9H, SiMe\(_3\)).

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<th>SI-11 δ (ppm)</th>
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<th>Hz</th>
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</table>
Preparation of intermediate 4

(a) Pd(OAc)$_2$, PPh$_3$, (S)-but-3-yn-2-yl methanesulfonate, Et$_2$Zn, THF. (b) NaH, MeI, THF. (c) i) Cp$_2$ZrHCl, THF; ii) N-iodosuccinimide. (d) Tetrbutylammonium fluoride, THF. (e) Dess-Martin periodinane, NaHCO$_3$, CH$_2$Cl$_2$. (f) dimethyl methylphosphonate, nBuLi, THF. (g) Dess-Martin periodinane, NaHCO$_3$, CH$_2$Cl$_2$.

**Compound SI-16.** Under N$_2$, Pd(OAc)$_2$ (97 mg, 0.435 mmol, 5 mol%) was dissolved in degassed THF (90 mL). The reaction was cooled to -78 °C, then PPh$_3$ (113 mg, 0.435 mmol, 5 mol%), SI-21 (2.84 g, 8.7 mmol) in THF (5 mL) and (S)-but-3-yn-2-yl methanesulfonate (1.54 g, 10.4 mmol) were added. Et$_2$Zn (26.1 mL, 26.1 mmol, 1M in hexane) was then added dropwise to the reaction mixture which was stirred for ten minutes at -78 °C before warming to -20 °C. The reaction was stirred at this temperature for 16 hours. The reaction mixture was poured into a stirred mixture of NH$_4$Cl (100 mL) and Et$_2$O (100 mL) and stirred for 30 minutes. The layers were separated and the aqueous phase washed with Et$_2$O (100 mL). The combined organics were washed with brine (100 mL), dried (Na$_2$SO$_4$), stirred with charcoal, and filtered through silica on a Celite plug. The solvent was removed under reduced pressure. Purification by flash column chromatography on silica gel (petroleum ether/Et$_2$O, 20:1 to 10:1) afforded SI-16 as a colourless oil (2.74 g, 7.23 mmol, 83%).

1H-NMR (500 MHz, CDCl$_3$) δ 7.73-7.70 (m, 4H), 7.49-7.40 (m, 6H), 3.80 (dd, $J$ = 10.2 and 4.6 Hz, 1H), 3.72 (dd, $J$ = 10.2 and 7.4 Hz, 1H), 3.53 (d, $J$ = 4.6 Hz, 1H), 3.46-3.42 (m, 1H), 2.75-2.70 (m, 1H), 2.12 (d, $J$ = 2.3 Hz, 1H), 2.11-2.04 (m, 2H), 1.34 (d, $J$ = 7.3 Hz, 3H), 1.08 (s, 9H), 0.87 (d, $J$ = 6.9 Hz, 3H), in agreement with literature data.

Mosher esters SI-17 and SI-18 of SI-16 were prepared for confirmation of its stereochemistry.

**Compound SI-17.** This compound was prepared from SI-16 (21 mg, 0.056 mmol) and SI-13 (20 µL, 0.107 mmol) using the same procedure as described for the preparation of SI-11. Purification by flash column chromatography on silica gel (petroleum ether/Et$_2$O, 50:1 to 20:1) afforded SI-17 as a colourless oil (2.74 g, 7.23 mmol, 83%). 1H-NMR (500 MHz, CDCl$_3$) δ 7.73-7.70 (m, 4H), 7.49-7.40 (m, 6H), 3.80 (dd, $J$ = 10.2 and 4.6 Hz, 1H), 3.72 (dd, $J$ = 10.2 and 7.4 Hz, 1H), 3.53 (d, $J$ = 4.6 Hz, 1H), 3.46-3.42 (m, 1H), 2.75-2.70 (m, 1H), 2.12 (d, $J$ = 2.3 Hz, 1H), 2.11-2.04 (m, 2H), 1.34 (d, $J$ = 7.3 Hz, 3H), 1.08 (s, 9H), 0.87 (d, $J$ = 6.9 Hz, 3H), in agreement with literature data. [α]$_D^{20}$ = +20.1 (c = 1.0, CHCl$_3$).

Compound SI-18. This compound was prepared from SI-16 (17 mg, 0.045 mmol) and SI-14 (16 μL, 0.085 mmol) using the same procedure as described for the preparation of SI-11. Purification by flash column chromatography on silica gel (petroleum ether/Et₂O, 50:1 to 20:1) afforded SI-18 as a colourless oil (10 mg, 37%). ¹H-NMR (500 MHz, CDCl₃) δ 7.66-7.63 (m, 4H, ArH), 7.57 (d, J = 7.4 Hz, 2H, ArH), 7.46-7.31 (m, 9H, ArH), 5.18 (dd, J = 6.9 and 4.7 Hz, 1H, H₃), 3.67 (dd, J = 10.4 and 5.0 Hz, 1H, H¹⁴), 3.50 (dd, J = 10.4 and 6.4 Hz, 1H, H¹⁸), 3.43 (s, 3H, OMe), 2.94 (qdd, J = 7.2, 4.7 and 2.4 Hz, 1H, H¹⁸), 2.28-2.20 (m, 1H, H¹⁷), 1.97 (d, J = 2.4 Hz, 1H, H⁸), 1.14 (d, J = 7.2 Hz, 3H, H⁸), 1.07 (s, 9H, sBu), 1.04 (d, J = 7.0 Hz, 3H, H¹³).

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<td>H¹³</td>
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Compound SI-19. Sodium hydride (560 mg, 14.0 mmol, 60% dispersion in mineral oil) was added to a solution of SI-16 (2.65 g, 7.0 mmol) and iodomethane (5.9 mL, 42.0 mmol) in THF (70 mL) at 0 °C under N₂. The reaction was slowly warmed to room temperature and stirred for 4 hours. The reaction was carefully quenched with saturated aqueous NH₄Cl (50 mL) and extracted with EtOAc (3 × 100 mL). The combined organic layers were dried (Na₂SO₄) and stirred over charcoal before filtration and removal of the solvent under reduced pressure. Purification by flash column chromatography on silica gel (petroleum ether/Et₂O, 20:1) afforded SI-19 as a pale yellow oil (2.40 g, 87%). ¹H-NMR (500 MHz, CDCl₃) δ 7.72-7.67 (m, 4H, 7.47-7.43 (m, 2H), 7.42-7.38 (m, 4H), 3.86 (dd, J = 9.9 and 4.8 Hz, 1H), 3.70 (dd, J = 9.9 and 3.6 Hz, 1H), 3.47 (s, 3H), 3.10 (dd, J = 8.5 and 3.6 Hz, 1H), 2.80-2.75 (m, 1H), 2.08 (d, J = 2.4 Hz, 1H), 2.07-1.99 (m, 2H), 1.31 (d, J = 7.0 Hz, 3H), 1.10 (m, 9H), 1.03 (d, J = 7.0 Hz, 3H); ¹³C-NMR (125 MHz, CDCl₃) δ = 135.7 (2C), 135.6 (2C), 133.8, 133.7, 129.6 (2C), 127.56 (2C), 127.55 (2C), 85.7, 85.0, 69.7, 65.3, 61.0, 39.1, 29.0, 26.9 (3C), 19.3, 18.2, 14.4; IR (neat): ν = 3309, 3071, 2960, 2931, 2857, 1589, 1472, 1427, 1389, 1391, 1191, 1111, 1089, 1007, 936, 823, 739, 702 cm⁻¹; MS (ES⁺) m/z (rel. intensity) 417 (100 %, [M+Na⁺]; HRMS calcd for C₁₉H₁₄O₂SiNa 417.2226, found 417.2242; [α]₂⁰° = -11.3 (c = 1.1, CHCl₃).

Compound SI-20. A solution of SI-19 (2.40 g, 6.10 mmol) in THF (5 mL) was added dropwise to a stirred suspension of Cp₂ZrHCl (2.04 g, 7.94 mmol) in THF (60 mL) at 0 °C in the dark and under N₂. The reaction was stirred for 90 minutes at 0 °C. N-iodosuccinimide (2.73 g, 12.2 mmol) was then added in one portion and the mixture was stirred for 30 minutes. Saturated aqueous Na₂S₂O₃ solution (50 mL) was added and after 15 minutes stirring at room temperature, the reaction mixture was extracted with EtOAc (3 × 70 mL). The combined organic layers were washed with brine (50 mL), dried (Na₂SO₄) and the solvent removed under reduced pressure. Purification by flash column chromatography on silica gel (petroleum ether/Et₂O, 100:0 to 30:1) afforded SI-20 as a pale yellow gum (2.29 g, 75%). ¹H-NMR (500 MHz, CDCl₃) δ 7.66-7.62 (m, 4H), 7.42-7.34 (m, 6H), 6.50 (dd, J = 14.4
and 8.6 Hz, 1H), 5.94 (d, J = 14.4 Hz, 1H), 3.71 (dd, J = 9.9 and 5.3 Hz, 1H), 3.63 (dd, J = 9.9 and 4.0 Hz, 1H), 3.35 (s, 3H), 2.97 (dd, J = 7.8 and 3.5 Hz, 1H), 2.47-2.39 (m, 1H), 1.77-1.68 (m, 1H), 1.05-1.04 (m, 12H), 0.89 (d, J = 6.9 Hz, 3H); 13C-NMR (125 MHz, CDCl3) δ = 148.2, 135.70 (2C), 135.65 (2C), 133.8, 133.7, 129.6, 129.5, 127.6 (4C), 86.1, 74.7, 65.3, 61.1, 43.1, 38.7, 26.9 (3C), 19.3, 17.7, 14.2; IR (neat): ʋ = 3070, 3048, 2960, 2929, 2894, 2857, 1600, 1589, 1471, 1460, 1427, 1389, 1361, 1268, 1240, 1180, 1138, 1103, 1092, 1066, 1008, 971, 952, 907, 863, 822, 791, 738, 698 cm⁻¹; MS (ES⁺) m/z (rel. intensity) 545 (100 %, [M+Na]⁺); HRMS calcld for C25H35IO5SiNa 545.1349, found 545.1364; [α]D⁰ = −1.9 (c = 0.65, CHCl₃).

**Compound SI-21.** TBAF (2.0 mL, 2.04 mmol, 1M in THF) was added to SI-20 (510 mg, 1.02 mmol) in THF (5 mL) at 0 °C under N₂. The reaction was stirred at room temperature for 16 hours. The volatiles were removed under reduced pressure and the crude residue was purified by flash column chromatography on silica gel (petroleum ether/Et₂O, 10:1 to 4:1 to 1:1) to yield SI-21 as a colourless oil (223 mg, 77%). 1H-NMR (500 MHz, CDCl₃) δ 6.56 (dd, J = 14.5 and 8.4 Hz, 1H), 6.07 (d, J = 14.5 Hz, 1H), 3.70-3.59 (m, 2H), 3.48 (s, 3H), 2.95 (dd, J = 7.5 and 4.4 Hz, 1H), 2.57 (dd, J = 6.5 and 4.7 Hz, 1H(OH)), 2.54-2.47 (m, 1H), 1.85-1.76 (m, 1H), 1.10 (d, J = 7.1 Hz, 3H), 0.93 (d, J = 7.0 Hz, 3H); 13C-NMR (125 MHz, CDCl₃) δ = 147.9, 89.9, 75.3, 66.1, 61.4, 43.6, 37.7, 16.9, 14.8; IR (neat): ʋ = 3397 (br), 3047, 2963, 2929, 2828, 1600, 1455, 1427, 1372, 1268, 1178, 1149, 1060, 1031, 969, 952, 905, 859, 820, 741, 702 cm⁻¹; MS (Cl(NH₃)) m/z (rel. intensity) 285 (100 %, [M+H]⁺); HRMS calcld for C₉H₁₇IO₂ 285.0346, found 285.0349; [α]D⁰ = −11.2 (c = 0.9, CHCl₃).

**Compound 4.** Dess-Martin periodinane (958 mg, 2.94 mmol) was added in one portion to SI-21 (642 mg, 2.26 mmol) and NaHCO₃ (379 mg, 4.52 mmol) in CH₂Cl₂ (23 mL, 0.1M) at 0 °C. The reaction was stirred at room temperature for 2 hours. Saturated aqueous NaHCO₃ (10 mL) and saturated aqueous Na₂S₂O₃ (10 mL) were added. After stirring for 15 minutes, the mixture was diluted with CH₂Cl₂ (30 mL), and the aqueous layer washed with CH₂Cl₂ (2 × 50 mL). The combined organic phases were dried (Na₂SO₄) and concentrated under reduced pressure. The crude aldehyde was used without further purification in the next step. A solution of nBuLi (2.4 mL, 6.10 mmol, 2.5M in hexanes) was added dropwise to freshly distilled dimethyl methylphosphonate (0.60 mL, 5.65 mmol) in THF (22 mL) at -78 °C under N₂. The cloudy solution was stirred at this temperature for 30 minutes and a solution of the aldehyde obtained previously in THF (2 mL) was added dropwise to give a yellow solution. The reaction was stirred at -78 °C for 1 hour and quenched by addition of saturated aqueous NH₄Cl (50 mL). The reaction was warmed to room temperature and extracted with EtOAc (3 × 70 mL). The combined organic layers were dried (Na₂SO₄) and the solvent removed under reduced pressure. Purification by flash column chromatography on silica gel (petroleum ether/Et₂O, 2:1 to 0:1) afforded a secondary alcohol (0.832 g, 73 % over two steps, pale yellow oil, 1:1 mixture of diastereoisomers). Dess-Martin periodinane (869 mg, 2.05 mmol) was added in one portion to a fraction of this material (800 mg, 1.58 mmol) and NaHCO₃ (265 mg, 3.16 mmol) in CH₂Cl₂ (16 mL) at 0 °C, as described above. After the same aqueous work-up as described above, purification by flash chromatography on silica gel (petroleum ether/EtOAc, 4:1 to EtOAc only) afforded 4 as a colourless oil (701 mg, 87%). 1H-NMR (500 MHz, CDCl₃) δ 6.53 (dd, J = 14.5 and 9.0 Hz, 1H), 6.03 (d, J = 14.5 Hz, 1H), 3.80 (d, Jp = 9.0 Hz, 3H), 3.78 (d, Jp = 9.0 Hz, 3H), 3.28 (s, 3H), 3.27 (dd, J = 22.0 and 14.5 Hz, 1H), 3.13 (dd, J = 9.5 and 9.0 Hz, 1H), 3.07 (dd, J = 22.0 and 14.5 Hz, 1H), 2.88 (dq, J = 9.0 and 7.0 Hz, 1H), 2.39 (ddq, J = 14.3, 7.0 and 2.9 Hz, 1H), 1.08 (d, J = 7.0 Hz, 3H), 0.94 (d, J = 7.0 Hz, 3H); 13C-NMR (125 MHz, CDCl₃) δ = 205.7 (d, Jp = 7.5 Hz), 146.8, 87.5, 75.8, 61.2, 53.0 (d, Jp = 23.8 Hz), 52.9 (d, Jp = 23.1 Hz), 49.5, 43.1, 42.8 (d, Jp = 128.5 Hz), 17.2, 13.3; IR (neat): ʋ = 2929, 2850, 1712, 1601, 1456, 1374, 1351, 1255, 1179, 1088, 971, 954, 925, 880, 808, 738, 705 cm⁻¹; MS (ES⁺) m/z (rel. intensity) 427 (100 %, [M+Na]⁺); HRMS calcld for C₁₂H₂₂O₃IPNa 427.0147, found 427.0161; [α]D⁰ = −99.1 (c = 1.14, CHCl₃).

S10
Preparation of compounds 5a–5c, 6a–6c and 7a–7c

(a) Dess–Martin periodinane, NaHCO₃, CH₂Cl₂. (b) i) 4, Ba(OH)₂, THF; ii) aldehydes, THF/water (40:1), rt. (c) [CuH₃PPh₃]Br, toluene, water. (d) Cul (0.2 equiv), 1,2-trans-cyclohexyldiamine (0.4 equiv), K₂PO₃ (2 equiv), MeNCHO (10 equiv), 1,4-dioxane, 80 °C. (e) AgNO₃ (4 equiv), THF/EtOH/water/2,6-lutidine (1:1:1:0.1), rt, 48h.

**Compound 5a.** This compound was prepared from 3a (108 mg, 0.36 mmol) using the same procedure as described for the preparation of 5c. Colourless oil (121 mg, 59% over two steps). ¹H-NMR (500 MHz, CDCl₃) δ 6.88 (dd, J = 16.0 and 7.5 Hz, 1H), 6.60 (dd, J = 14.6 and 9.2 Hz, 1H), 6.16 (dd, J = 16.0 and 0.9 Hz, 1H), 6.07 (d, J = 14.6 Hz, 1H), 3.37 (s, 3H), 3.31-3.27 (m, 4H (MeO + 1H)), 3.11-3.07 (m, 1H), 2.96 (dq, J = 9.5 and 7.0 Hz, 1H), 2.63-2.55 (m, 1H), 2.48-2.40 (m, 1H), 2.20 (t, J = 7.2 Hz, 2H), 1.53-1.46 (m, 2H), 1.45-1.21 (m, 10H), 1.12 (d, J = 7.6 Hz, 3H), 1.07 (d, J = 7.1 Hz, 3H), 0.94 (d, J = 7.1 Hz, 3H), 0.14 (s, 9H); ¹³C-NMR (125 MHz, CDCl₃) δ = 203.2, 149.9, 147.1, 129.8, 107.6, 86.6, 84.4, 84.2, 75.4, 61.1, 57.8, 46.4, 43.1, 39.6, 31.3, 29.6, 29.0, 28.7, 28.6, 25.6, 19.8, 17.6, 14.7, 13.8, 0.1 (3C); IR (neat): ν = 2931, 2856, 2173, 1693, 1668, 1624, 1456, 1373, 1248, 1179, 1093, 971, 953, 841, 759, 698 cm⁻¹; MS (ES⁺) m/z (rel. intensity) 597 (100 %, [M+Na]+); HRMS (ES⁺) calcd for C₂₇H₄₇IO₃SiNa 597.2237, found 597.2235; [α]D³₀ = −92.3 (c = 1.02, CHCl₃).

**Compound 5b.** This compound was prepared from 3b (65 mg, 0.23 mmol) using the same procedure as described for the preparation of 5c. Colourless oil (79 mg, 46% over two steps). ¹H-NMR (500 MHz, CDCl₃) δ 6.86 (dd, J = 15.9 and 7.8 Hz, 1H), 6.60 (dd, J = 14.7 and 9.5 Hz, 1H), 6.17 (dd, J = 15.9 and 1.2 Hz, 1H), 6.07 (d, J = 14.7 Hz, 1H), 3.37 (s, 3H), 3.30 (s, 3H), 3.30-3.27 (m, 1H), 3.12-3.07 (m, 1H), 2.96 (dq, J = 9.9 and 6.8 Hz, 1H), 2.63-2.56 (m, 1H), 2.45 (dq, J = 9.0, 7.0 and 2.6 Hz, 1H), 2.20 (t, J = 7.0 Hz, 2H), 1.58-1.47 (m, 2H), 1.45-1.34 (m, 6H), 1.33-1.26 (m, 2H), 1.12 (d, J = 6.7 Hz, 3H), 0.95 (d, J = 7.0 Hz, 3H), 0.14 (s, 9H); ¹³C-NMR (125 MHz, CDCl₃) δ = 203.1, 149.8, 147.2, 129.8, 107.6, 86.7, 84.4, 84.3, 75.4, 61.2, 57.9, 46.4, 43.2, 39.6, 31.3, 29.2, 28.7, 28.6, 25.6, 19.8, 17.6, 14.7, 13.8, 0.2 (3C); IR (neat): ν = 2932, 2857, 2172, 1692, 1667, 1623, 1456, 1373, 1354, 1248, 1179, 1093, 971, 953, 842, 760, 733, 697 cm⁻¹; MS (ES⁺) m/z (rel. intensity) 583 (100 %, [M+Na]+); HRMS calcd for C₂₅H₄₅O₃SiNa 583.2080, found 583.2079; [α]D³₀ = −76.6 (c = 1.33, CHCl₃).
Compound 5c. Dess-Martin periodinane (369 mg, 0.87 mmol) was added in one portion to 3c (127 mg, 0.47 mmol) and NaHCO₃ (79 mg, 0.94 mmol) in CH₂Cl₂ (5 mL) at 0 °C. The reaction was stirred at room temperature for 2 hours. Saturated aqueous NaHCO₃ (10 mL) and saturated aqueous Na₂S₂O₅ (10 mL) were added. After stirring for 15 minutes, the mixture was diluted with CH₂Cl₂ (30 mL), and the aqueous layer washed with CH₂Cl₂ (2 × 30 mL). The combined organic phases were dried (Na₂SO₄) and concentrated under reduced pressure. The crude aldehyde thus obtained was passed through a short silica plug (eluting with 10:1 petroleum ether/Et₂O) to remove residual impurities and was used without further purification (100 mg, 0.37 mmol) in the next step. Under N₂, Ba(OH)₂ (70 mg, 0.41 mmol)⁹ was added to 4 (150 mg, 0.37 mmol) in THF (3 mL). The mixture was stirred for 30 minutes at room temperature, before adding the aldehyde prepared above (100 mg, 0.37 mmol) as a THF/H₂O (40:1, 1 mL) solution. After stirring for 1 hour, the reaction was diluted with CH₂Cl₂ (10 mL) and saturated aqueous NaHCO₃ (10 mL) was added and the mixture was stirred for 15 minutes. The mixture was separated and the aqueous layer washed with CH₂Cl₂ (2 × 20 mL). The combined organic layers were dried (Na₂SO₄) and the solvent removed under reduced pressure. Purification by flash column chromatography (SiO₂, petroleum ether/Et₂O, 4:1) yielded 5c as a colourless oil (142 mg, 55% over two steps). ¹H-NMR (500 MHz, CDCl₃) δ 6.85 (dd, J = 15.9 and 7.6 Hz, 1H), 6.59 (dd, J = 14.6 and 9.3 Hz, 1H), 6.16 (dd, J = 15.9 and 1.0 Hz, 1H), 6.06 (d, J = 14.6 Hz, 1H), 3.37 (s, 3H). 3.30 (s, 3H), 3.30-3.26 (m, 1H), 3.12-3.07 (m, 1H), 2.95 (dq, J = 9.5 and 7.0 Hz, 1H), 2.64-2.56 (m, 1H), 2.44 (ddq, J = 9.3, 6.8 and 2.0 Hz, 1H), 2.20 (t, J = 7.2 Hz, 2H), 1.51 (quint, J = 7.2 Hz, 2H), 1.46-1.26 (m, 6H), 1.12 (d, J = 7.0 Hz, 3H). ¹³C-NMR (125 MHz, CDCl₃) δ = 203.1, 149.7, 147.2, 129.9, 107.5, 86.6, 84.4, 84.3, 75.4, 61.2, 57.9, 46.4, 43.2, 39.6, 31.3, 28.9, 28.5, 25.2, 19.8, 17.6, 14.7, 13.8, 0.2 (3C); IR (neat): ν = 2031, 1497, 1472, 1299, 1075, 8330, 2855, 2173, 1713, 1601, 1457, 1373, 1248, 1179, 1093, 971, 908, 842, 759, 733, 698 cm⁻¹; MS (ES⁺) m/z (rel. intensity) 569 (100 %, [M+Na⁺]); HRMS calcd for C₂₅H₃₃O₃SiNa 569.1924, found 569.1938; [α]D²⁰ = -83.3 (c = 1.0, CHCl₃).

Compound 6a. This compound was prepared from 5a (97 mg, 0.17 mmol) using the same procedure as described for the preparation of 6c. Colourless oil (68 mg, 70 %). ¹H-NMR (500 MHz, CDCl₃) δ 6.57 (dd, J = 14.6 and 9.1 Hz, 1H), 6.04 (d, J = 14.6 Hz, 1H), 3.34 (s, 3H), 3.30 (s, 3H), 3.25 (dd, J = 9.6 and 2.4 Hz, 1H), 2.99-2.94 (m, 1H), 2.68 (dq, J = 9.6 and 7.0 Hz, 1H), 2.54-2.48 (m, 1H), 2.45-2.37 (m, 1H), 2.20 (t, J = 7.2 Hz, 2H), 1.78-1.68 (m, 1H), 1.68-1.60 (m, 1H), 1.55-1.46 (m, 2H), 1.46-1.33 (m, 6H), 1.32-1.23 (m, 6H). 1.11 (d, J = 6.9 Hz 3H), 0.90 (d, J = 7.0 Hz, 3H), 0.85 (d, J = 6.8 Hz, 3H), 0.14 (s, 9H); ¹³C-NMR (125 MHz, CDCl₃) δ = 214.2, 247.1, 107.8, 86.6, 85.3, 84.3, 75.4, 61.3, 57.9, 48.9, 43.1, 42.3, 34.8, 30.4, 29.8, 29.1, 28.8, 28.7, 26.1, 26.0, 19.9, 17.5, 14.7, 13.5, 0.2 (3C); IR (neat): ν = 3071, 2985, 2917, 1713, 1601, 1457, 1407, 1373, 1248, 1179, 1153, 1091, 969, 954, 922, 841, 759, 698 cm⁻¹; MS (ES⁺) m/z (rel. intensity) 599 (100 %, [M+Na⁺]); HRMS calcd for C₂₇H₄₀O₃SiNa 599.2393, found 599.2384; [α]D²⁰ = -53.1 (c = 1.0, CHCl₃).

Compound 6b. This compound was prepared from 5b (55 mg, 0.098 mmol) using the same procedure as described for the preparation of 6c. The material thus obtained contained approximately 12% of desilylated analogue and 10% of PPh₃ and was not fully characterised before being used in the following step (colourless oil, 47 mg, yield = 71% after correction). ¹H-NMR (500 MHz, CDCl₃) δ 6.57 (dd, J = 14.6 and 9.1 Hz, 1H), 6.05 (d, J = 14.6 Hz, 1H), 3.35 (s, 3H), 3.31 (s, 3H), 3.25 (dd, J = 9.6

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⁹ Ba(OH)₂·8H₂O was dried at 120 °C under vacuum for 2h prior to use, see I. Paterson, K.-S. Yeung and J. B. Smaill, Synlett, 1993, 774
and 2.4 Hz, 1H), 3.01-2.96 (m, 1H), 2.69 (dq, J = 9.6 and 7.0 Hz, 1H), 2.55-2.49 (m, 1H), 2.47-2.38 (m, 1H), 2.21 (t, J = 7.2 Hz, 2H), 1.79-1.70 (m, 1H), 1.69-1.61 (m, 1H), 1.56-1.49 (m, 2H), 1.48 (m, 9H), 1.33-1.23 (m, 2H), 1.12 (d, J = 7.0 Hz, 3H), 0.91 (d, J = 7.2 H, 3H), 0.86 (d, J = 6.8 Hz, 3H), 0.14 (s, 9H); HRMS (ESI) caleed for C_{26}H_{27}O_{3}SiNa 585.2237, found 585.2236.

**Compound 6c.** [Cu(HPPh)_3]_6 (123 mg, 0.063 mmol) was added to a solution of 5c (117 mg, 0.21 mmol) in toluene (4.3 mL, 0.055M) followed by deionised H_2O (35 μL, 2.10 mmol) was added. After stirring at room temperature for 2 hours, the reaction was filtered through deactivated neutral alumina and the solvent removed under reduced pressure. Purification by flash column chromatography on silica gel (petroleum ether/Et_2O, 100:1 to 50:1 to 40:1) afforded 6 as a colourless oil (83 mg, contains 12% of desilylated analogue; yield = 64% after correction). ^1H-NMR (500 MHz, CDCl_3) δ 6.57 (dd, J = 14.6 and 9.1 Hz, 1H), 5.05 (d, J = 14.6 Hz, 1H), 3.36 (s, 3H), 3.31 (s, 3H), 3.25 (dd, J = 9.8 and 2.5 Hz, 1H), 3.00-2.96 (m, 1H), 2.69 (dq, J = 9.6 and 7.0 Hz, 1H), 2.55-2.50 (m, 1H), 2.46-2.39 (m, 1H), 2.22 (t, J = 6.7 Hz, 2H), 1.78-1.70 (m, 1H), 1.69-1.62 (m, 1H), 1.56-1.49 (m, 2H), 1.48 (m, 7H), 1.33-1.23 (m, 2H), 1.12 (d, J = 7.0 Hz, 3H), 0.91 (d, J = 7.2 H, 3H), 0.86 (d, J = 7.0 Hz, 3H). 0.15 (s, 9H); ^13C-NMR (125 MHz, CDCl_3) δ = 214.1, 147.1, 107.6, 86.6, 85.2, 84.3, 75.4, 61.2, 57.8, 48.8, 43.0, 42.3, 34.8, 30.3, 29.0, 28.6, 25.9, 25.6, 19.8, 17.4, 14.7, 13.5, 0.2 (3C); IR (neat): v = 2933, 2173, 1713, 1601, 1457, 1407, 1373, 1248, 1180, 1155, 1090, 970, 954, 922, 840, 759, 697 cm⁻¹; MS (ESI) m/z (rel. intensity) 571 (100 %, [M+Na]^+); HRMS caleed for C_{25}H_{33}O_{3}SiNa 571.2080, found 571.2065; [α]_D^25 = -63.9 (c = 0.9, CHCl_3).

**Compound 7a.** This compound was prepared from 6a (65 mg, 0.11 mmol) using the same procedure as described for the preparation of 7c. Colourless oil (29 mg, 60% over 2 steps, d.r. = 90:10). ^1H-NMR (500 MHz, CDCl_3) δ 8.27 (s, 0.65H, H^1), 8.06 (s, 0.35H, H^1), 7.12 (d, J = 14.7 Hz, 0.35H, H^2), 6.44 (d, J = 14.4 Hz, 0.65H, H^3), 5.14-5.06 (m, 1H, H^5), 3.34 (s, 6H, H^6 + H^5), 3.30-3.29 (m, 1H, H^5), 3.06 (s, 1.05H, H^5), 3.03 (s, 1.95H, H^A), 2.99-2.94 (m, 1H, H^11), 2.68 (dq, J = 9.7 and 7.1 Hz, 0.65H^6), 2.65 (dq, J = 9.8 and 7.0 Hz, 0.35H^5), 2.56-2.46 (m, 2H, H^8), 2.45-2.34 (m, 1H, H^8), 2.16 (td, J = 7.0 and 2.6 Hz, 2H, H^18), 1.92 (t, J = 2.6 Hz, 1H, H^20), 1.79-1.70 (m, 1H, H^9q), 1.69-1.61 (m, 1H, H^10), 1.57-1.50 (m, 2H, H^17), 1.47-1.25 (m, 11H, H^9p + H^11 + H^13 + H^14 + H^15 + H^16), 1.15 (d, J = 6.9 Hz, 3H, H^9o), 0.91 (d, J = 7.0 Hz, 1.8H, H^D), 0.90 (d, J = 7.0 Hz, 1.2H, H^D), 0.85 (d, J = 7.0 Hz, 1.8H, H^D), 0.84 (d, J = 7.0 Hz, 1.2H, H^D); ^13C-NMR (125 MHz, CDCl_3) δ = 214.3 (C^7min), 214.2 (C^7maj), 162.1 (C^1maj), 160.8 (C^1min), 128.7 (C^2maj), 124.7 (C^2min), 113.1 (C^5min), 111.3 (C^3maj), 87.4 (C^5maj), 87.3 (C^5maj), 85.3 (C^11), 84.7 (C^19), 68.0 (C^20), 61.4 (C^Cmin), 61.3 (C^Cmaj), 57.7 (C^F), 49.1 (C^6min), 49.0 (C^6maj), 42.3 (C^8maj), 42.2 (C^8min), 37.6 (C^4min), 37.4 (C^4maj), 35.0 (C^10min), 34.77 (C^10maj), 33.1 (C^Amin), 30.4 (C^12min), 30.3 (C^12maj), 29.7 (C^14), 29.0 (C^15), 28.7 (C^16), 28.4 (C^17), 27.6 (C^Amax), 26.06 (C^13), 26.03 (C^9min), 26.00 (C^9maj), 19.4 (C^Bmaj), 19.3 (C^Bmin), 18.2 (C^18), 14.7 (C^Emin), 14.6 (C^Emaj), 13.6 (C^Dmaj), 13.5 (C^Dmin), IR (neat): v = 3265, 2930, 2856, 1692, 1653, 1457, 1371, 1318, 1274, 1194, 1155, 1090, 1069, 939, 877, 725, 686 cm⁻¹; MS (ESI) m/z (rel. intensity) 458 (100 %, [M+Na]^+); HRMS caleed for C_{26}H_{34}N_{3}O_{3}Na 458.3246, found 458.3239; [α]_D^25 = -63.3 (c = 1.35, CHCl_3).

**Compound 7b.** This compound was prepared from 6b (46 mg, 0.082 mmol) using the same procedure as described for the preparation of 7a. Colourless oil (19 mg, 55% over 2 steps, d.r. = 92:8). ^1H-NMR (500 MHz, CDCl_3) δ 8.21 (s, 0.65H, H^1), 8.06 (s, 0.35H, H^1), 7.12 (d, J = 14.6 Hz, 0.35H, H^3), 6.44 (d, J = 14.3 Hz,
0.65H, H²), 5.15-5.06 (m, 1H, H¹), 3.33 (s, 6H, H⁴ + H⁵), 3.33-3.29 (m, 1H, H⁶), 3.06 (s, 1.05H, H⁴), 3.03 (s, 1.95H, H³), 3.00-2.93 (m, 1H, H¹¹), 2.68 (dq, J = 9.6 and 7.0 Hz, 0.65H⁶), 2.65 (dq, J = 9.7 and 7.0 Hz, 0.35H⁵), 2.56-2.47 (m, 2H, H²), 2.47-2.34 (m, 1H, H⁵), 2.18 (td, J = 7.0 and 2.6 Hz, 2H, H¹⁴), 1.94 (t, J = 2.6 Hz, 1H, H¹⁹), 1.80-1.70 (m, 1H, H⁷), 1.69-1.61 (m, 1H, H¹⁰), 1.58-1.50 (m, 2H, H¹⁶), 1.47-1.25 (m, 9H, H⁹ + H¹² + H¹³ + H¹⁴ + H¹⁵), 1.15 (d, J = 7.0 Hz, 3H, H³), 0.92 (d, J = 7.0 Hz, 1.8H, H²), 0.91 (d, J = 7.0 Hz, 1.2H, H⁴), 0.85 (d, J = 7.0 Hz, 1.8H, H⁷), 0.84 (d, J = 7.0 Hz, 1.2H, H²); ¹³C-NMR (125 MHz, CDCl₃) δ = 141.3 (C⁷min), 214.25 (Cºmaj), 162.1 (C¹maj), 160.8 (C¹min), 128.7 (C³maj), 124.7 (Cºmin), 113.1 (C³min), 111.3 (Cºmaj), 87.4 (C⁵min), 87.3 (C³maj), 85.3 (C¹¹), 84.7 (C¹⁸), 68.1 (C⁶⁵), 61.41 (C⁵maj), 61.38 (C³maj), 57.8 (C⁶), 49.1 (C⁸ºmin), 49.0 (C⁵maj), 42.3 (C⁸maj), 42.2 (C⁸min), 37.6 (C⁴maj), 37.4 (C⁴maj), 34.77 (C¹⁰maj), 34.74 (C³maj), 33.1 (C⁸min), 30.33 (C¹²maj), 30.29 (C¹²min), 29.3 (C¹⁴), 28.7 (C¹⁶), 27.4 (C³maj), 26.0 (Cºmin + C¹³), 25.97 (C³maj), 19.40 (Cºmaj), 19.37 (C³min), 18.4 (C¹⁷), 17.43 (C³maj), 14.67 (Cºmin), 13.6 (C³min), 13.5 (C³maj); IR (neat): ν = 3262, 2931, 2858, 1693, 1655, 1457, 1371, 1319, 1274, 1194, 1156, 1092, 1070, 938, 726, 686 cm⁻¹; MS (ES⁺) m/z (rel. intensity) 444 (100 %, [M+Na]⁺); HRMS calcd for C₂₅H₄₉O₃Na 444.3090, found 444.3082; [α] D = −102 (c = 0.43, CHCl₃).

**Compound 7c.**¹⁰ Cu(II) (2.5 mg, 0.013 mmol), K₃PO₄ (28 mg, 0.13 mmol), 1,2-trans-cyclohexyldiamine (2.9 mg, 0.025 mmol) and MeNCHO (38 mg, 0.65 mmol) were added to a dried resealable J-Young Schlenk tube in a glovebox. The tube was removed from the glovebox and 6c (36 mg, 0.065 mmol) in dioxane (2 mL) was added. The tube was then sealed and heated at 80 °C for 16 hours. The reaction was cooled to room temperature, diluted with EtOAc and filtered through a short pad of Celite. The solvent was removed under reduced pressure and the crude residue was diluted in THF:EtOH:H₂O:2:6-lutidine (2 mL, 1:1:1:0.1) before adding added AgNO₃ (44 mg, 0.26 mmol). The reaction mixture was then diluted and filtered through a pad of Celite. The solvent was removed under reduced pressure. Purification by flash column chromatography on silica gel (petroleum ether/EtO₂O, 2:1 to 1:2) gave 7c as a colourless oil (11.3 mg, 43% over 2 steps, d.r. = 88:12). ¹H-NMR (500 MHz, CDCl₃) δ 8.29 (s, 0.6H, H¹), 8.08 (s, 0.4H, H¹), 7.13 (d, J = 14.9 Hz, 0.4H, H²), 6.64 (d, J = 14.3 Hz, 0.6H, H³), 5.17-5.07 (m, 1H, H⁴), 3.35 (s, 6H, H⁴ + H⁵), 3.33-3.29 (m, 1H, H⁵), 3.08 (s, 1.2H, H⁶), 3.04 (s, 1.8H, H¹⁶), 3.00-2.95 (m, 1H, H¹¹), 2.68 (dq, J = 9.5 and 7.0 Hz, 0.6H⁶), 2.65 (dq, J = 9.8 and 7.1 Hz, 0.4H¹⁴), 2.56-2.47 (m, 2H, H²), 2.47-2.34 (m, 1H, H⁵), 2.19 (td, J = 7.1 and 2.7 Hz, 2H, H¹⁶), 1.94 (t, J = 2.7 Hz, 1H, H¹⁵), 1.80-1.70 (m, 1H, H¹¹), 1.69-1.61 (m, 1H, H¹⁰), 1.58-1.50 (m, 2H, H¹⁵), 1.48-1.30 (m, 7H, Hº⁹ + H¹² + H¹³ + H¹⁴), 1.16 (d, J = 7.0 Hz, 3H, H³), 0.93 (d, J = 7.0 Hz, 1.8H, H²), 0.92 (d, J = 7.0 Hz, 1.2H, H⁴), 0.86 (d, J = 7.0 Hz, 1.8H, H²), 0.85 (d, J = 7.0 Hz, 1.2H, H²); ¹³C-NMR (125 MHz, CDCl₃) δ = 214.3 (Cºmin), 214.2 (Cºmaj), 162.1 (Cºmaj), 160.8 (Cºmin), 128.7 (Cºmaj), 124.7 (Cºmin), 113.1 (Cºmin), 111.3 (Cºmaj), 87.4 (Cºmin), 87.3 (Cºmaj), 85.3 (C¹¹), 84.7 (C¹⁸), 68.1 (Cºmin), 61.41 (Cºmaj), 61.38 (Cºmaj), 57.8 (Cº), 49.1 (Cººmin), 49.0 (Cºmaj), 42.3 (Cºmaj), 42.2 (Cºmin), 37.6 (Cºmaj), 37.4 (Cºmaj), 34.77 (C¹⁰maj), 34.74 (Cºmaj), 33.1 (Cºmin), 30.33 (C¹²maj), 30.29 (C¹²min), 29.3 (C¹⁴), 28.7 (C¹⁶), 27.4 (Cºmaj), 26.0 (Cºmin + C¹³), 25.97 (Cºmaj), 19.40 (Cºmaj), 19.37 (Cºmin), 18.4 (C¹⁷), 17.43 (Cºmaj), 14.67 (Cºmin), 13.6 (Cºmin), 13.5 (Cºmaj); IR (neat): ν = 3262, 2931, 2858, 1693, 1655, 1457, 1371, 1319, 1274, 1194, 1156, 1092, 1070, 938, 726, 686 cm⁻¹; MS (ES⁺) m/z (rel. intensity) 444 (100 %, [M+Na]⁺); HRMS calcd for C₂₅H₄₉O₃Na 444.3090, found 443.3092; [α] D = −66.2 (c = 1.1, CHCl₃).

¹⁰ Two rotamers were observed at room temperature. In the description of the ¹³C NMR spectrum, the signals specific to each rotamer are indicated with the terms maj and min for the major and minor rotomer, respectively.
Preparation of compounds 8 and 9

(a) HCl•H₂NValOMe, hydroxybenzotriazole, 1-ethyl-3-(3-dimethylaminopropyl)carbodiimide hydrochloride, Et₃N, CH₂Cl₂.  
(b) i) pTsOH, Et₂O; ii) SI-22, hydroxybenzotriazole, 1-ethyl-3-(3-dimethylaminopropyl)carbodiimide hydrochloride, Et₃N, CH₂Cl₂.  
(c) i) pTsOH, Et₂O; ii) SI-26, hydroxybenzotriazole, 1-ethyl-3-(3-dimethylaminopropyl)carbodiimide hydrochloride, Et₃N, CH₂Cl₂.  
(d) CH₂Cl₂, trifluoroacetic acid.

Compound SI-23. Compound SI-22 was suspended in CH₂Cl₂ (15 mL) with the hydrochloride salt of H₂NValOMe (227 mg, 1.66 mmol), hydroxybenzotriazole (224 mg, 1.66 mmol) and 1-ethyl-3-(3-dimethylaminopropyl)carbodiimide hydrochloride (317 mg, 1.66 mmol), before adding Et₃N (0.42 mL, 3.02 mmol). The reaction mixture was stirred at room temperature for 16 hours. The reaction was diluted with EtOAc (50 mL), washed sequentially with citric acid (0.5M, 50 mL) and saturated aqueous NaHCO₃ (50 mL). The organic phase was dried (Na₂SO₄) and the solvent removed under reduced pressure to give the title compound as a colourless oil (737 mg, 1.47 mmol, 97%), which was used without further purification in the following step. ¹H-NMR (500 MHz, CDCl₃) δ 6.67-6.49 (m, 1H(NH)), 5.17-4.94 (m, 1H(NH)), 4.82-4.66 (m, 1H(NH)), 4.52 (dd, J = 8.8 and 4.9 Hz, 1H), 4.19-4.03 (m, 3H), 3.73 (s, 3H), 3.21-3.07 (m, 2H), 2.22-2.12 (m, 1H), 1.88-1.71 (m, 1H), 1.67-1.57 (m, 1H), 1.56-1.47 (m, 2H), 1.44 (s, 9H), 1.43-1.33 (m, 2H), 1.01-0.91 (m, 2H), 0.92 (d, J = 6.7 Hz, 3H), 0.89 (d, J = 6.9 Hz, 3H), 0.02 (s, 9H); IR (neat): ν ~ 3320 (br), 2954, 1742, 1691, 1662, 1521, 1456, 1438, 1392, 1366, 1337, 1248, 1212, 1171, 1045, 1022, 937, 859, 837, 778, 733, 694 cm⁻¹; MS (ES⁺) m/z (rel. intensity) 526 (100 %, [M+Na]⁺); HRMS calcd for C₂₃H₄₅N₃O₇SiNa 526.2924, found 526.2924.
Compound SI-24. *p*-toluenesulfonic acid (293 g, 1.54 mmol) was added to a solution of SI-23 (706 mg, 1.40 mmol) in EtO (50 mL). The reaction was held at 30 °C for 30 minutes. The solvent was removed under reduced pressure at 30 °C and held at this temperature under vacuum for 1 hour. The crude product was kept under high vacuum for 16 hours to give a glass residue (MS (ES\(^+\)) m/z (rel. intensity) 404 (100 %, [M+H]+), 426 (50 %, [M+Na]+); HRMS calcd for C\(_{35}\)H\(_{38}\)N\(_3\)O\(_7\)Si\(_4\) 404.2581, found 404.2578) which was suspended in CH\(_2\)Cl\(_2\) (14 mL) with SI-22 (491 mg, 1.26 mmol), hydroxybenzotriazole (207 mg, 1.54 mmol) and 1-ethyl-3-(3-dimethylaminopropyl)carbodiimide hydrochloride (294 mg, 1.54 mmol) before adding Et\(_3\)N (0.39 mL, 2.8 mmol). The same procedure as described for the preparation of SI-23 was then applied to give crude SI-24 as a colourless oil (926 mg, 85%), which was used without further purification in the following step. \(^1\)H-NMR (500 MHz, CDCl\(_3\)) \(\delta\) 4.52 (dd, \(J = 8.8\) and 4.9 Hz, 1H), 4.46-4.38 (m, 1H), 4.22-4.03 (m, 5H), 3.73 (s, 3H), 3.2-3.03 (m, 4H), 2.22-2.12 (m, 1H), 1.92-1.73 (m, 2H), 1.73-1.58 (m, 2H), 1.58-1.46 (m, 4H), 1.43 (s, 9H), 1.42-1.31 (m, 4H), 1.05-0.90 (m, 4H), 0.91 (d, \(J = 6.7\) Hz, 3H), 0.89 (d, \(J = 6.9\) Hz, 3H), 0.03 (s, 18H)\(^1\) IR (neat): \(\tilde{\nu}\) = 3311 (br), 2953, 1693, 1648, 1524, 1457, 1438, 1392, 1366, 1337, 1249, 1172, 1059, 912, 859, 836, 778, 731, 694 cm\(^{-1}\); MS (ES\(^+\)) m/z (rel. intensity) 798 (100 %, [M+Na]\(^+\)); HRMS calcd for C\(_{35}\)H\(_{39}\)N\(_3\)O\(_{10}\)Si\(_4\)Na 798.4481, found 798.4501.

Compound 8. *p*-toluenesulfonic acid (224 mg, 1.28 mmol) was added to a solution of SI-24 (914 mg, 1.17 mmol) in EtO (40 mL). The reaction was held at 30 °C for 30 minutes. The solvent was removed under reduced pressure at 30 °C and held at this temperature under vacuum for 1 hour. The crude product was kept under high vacuum for 16 hours to give a glass residue (MS (ES\(^+\)) m/z (rel. intensity) 698 (100 %, [M+Na]+); HRMS calcd for C\(_{30}\)H\(_{51}\)N\(_3\)O\(_8\)Si\(_2\)Na 698.3964, found 698.3956) which was suspended in CH\(_2\)Cl\(_2\) (12 mL) with SI-26\(^2\) (239 mg, 1.52 mmol), hydroxybenzotriazole (197 mg, 1.29 mmol) and 1-ethyl-3-(3-dimethylaminopropyl)carbodiimide hydrochloride (244 mg, 1.29 mmol), before adding Et\(_3\)N (0.30 mL, 2.34 mmol). The reaction mixture was stirred at room temperature for 16 hours. The reaction was diluted with EtOAc (40 mL), washed sequentially with citric acid (0.5M, 40 mL) and saturated aqueous NaHCO\(_3\) (40 mL). The organic phase was dried (Na\(_2\)SO\(_4\)) and the solvent removed under reduced pressure to give SI-25 as a colourless oil (MS (ES\(^+\)) m/z (rel. intensity) 837 (100 %, [M+Na]+); HRMS calcd for C\(_{36}\)H\(_{70}\)N\(_8\)O\(_{32}\)Si\(_2\)Na 837.4702, found 837.4711). This crude material was then diluted in CH\(_2\)Cl\(_2\)/TFA (18 mL, 4:1, 0.1M) at 0 °C. After stirring at room temperature for 2 hours, the solvent was removed under reduced pressure. Purification by flash chromatography on deactivated silica gel\(^3\) (CH\(_2\)Cl\(_2\) then CH\(_3\)Cl/MeOH, 9:1) afforded 8 as a pale orange glass residue (441 mg, 50%). \(^1\)H-NMR (500 MHz, CD\(_3\)OD) \(\delta\) 4.45-3.49 (m, 1H), 4.35-4.27 (m, 2H), 3.85 (dd, \(J = 8.5\) and 6.0 Hz, 1H), 3.71 (s, 3H), 3.01-2.90 (m, 4H), 2.18-2.11 (m,

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\(^1\) Not all the rapidly exchangeable protons are visible in CDCl\(_3\). However, several poorly resolved signals were visible between 6.89 and 4.83 ppm: 6.89-4.83 (m, 0.7H), 6.73-6.60 (m, 0.7H), 5.30-5.18 (m, 0.8H), 5.08-4.85 (m, 1.7H).


\(^3\) The silica was treated with EtSiCl\(_3\) prior to the chromatography. See: P. Panne and M. J. Fox, J. Am. Chem. Soc., 2007, 129, 22.
1H), 1.89-1.78 (m, 2H), 1.76-1.61 (m, 8H), 1.57-1.39 (m, 5H), 0.98-0.92 (m, 12H);\textsuperscript{14} \textsuperscript{13}C-NMR (125 MHz, CD\textsubscript{3}OD) \(\delta = 175.0, 174.9, 174.4, 173.3, 63.2, 60.1, 55.4, 55.2, 53.3, 42.1, 41.4, 41.3, 33.2, 33.1, 32.6, 28.8 (2C), 27.0, 24.5 (2C), 24.1, 22.9, 20.2, 19.4; IR (neat): \(\tilde{v} = 3288 \text{ (br)}, 2961, 2873, 2407, 2111, 1735, 1640, 1541, 1436, 1390, 1372, 1314, 1267, 1200, 1179, 1132, 1011, 977, 836, 799, 721 \text{ cm}^{-1}; MS (ES\textsuperscript{+}) \text{m/z} \text{ (rel. intensity) 599 (100 \%, [M+Na]\textsuperscript{+}); MS (ES\textsuperscript{+}) \text{m/z} \text{ (rel. intensity) 527 (100 \%, [M+H]\textsuperscript{+}); HRMS calcd for C\textsubscript{24}H\textsubscript{47}N\textsubscript{8}O\textsubscript{5} 527.3669, found 527.3672.}

\begin{itemize}
\item \textsuperscript{(a)} i) pTsOH, Et\textsubscript{2}O; ii) BocAlaOH, hydroxybenzotriazole, 1-ethyl-3-(3-dimethylaminopropyl)carbodiimide hydrochloride, Et\textsubscript{3}N, CH\textsubscript{2}Cl\textsubscript{2}. \textsuperscript{(b)} i) pTsOH, Et\textsubscript{2}O; ii) SI-26, hydroxybenzotriazole, 1-ethyl-3-(3-dimethylaminopropyl)carbodiimide hydrochloride, Et\textsubscript{3}N, CH\textsubscript{2}Cl\textsubscript{2}. \textsuperscript{(c)} CH\textsubscript{2}Cl\textsubscript{2}, trifluoroacetic acid.
\end{itemize}

**Compound SI-27.** This compound was prepared from SI-23 (116 mg, 0.23 mmol) and BocAlaOH (34 mg, 0.21 mmol) using the same procedure as described for the preparation of SI-24. The crude material thus obtained was a colourless oil (92 mg, 76\%) and it was used without further purification in the following step. \(^1\)H-NMR (500 MHz, CDCl\textsubscript{3}) \(\delta = 6.83-6.69 \text{ (m, 1H(NH))}, 6.67-6.50 \text{ (m, 1H(NH))}, 5.22-4.99 \text{ (m, 1H(NH))}, 4.92-4.75 \text{ (m, 1H(NH))}, 4.52 \text{ (dd, } J = 8.8 \text{ and } 4.9 \text{ Hz, 1H}), 4.46-4.37 \text{ (m, 1H), 4.22-4.03 \text{ (m, 3H), 3.74 \text{ (s, 3H)}, 3.23-3.07 \text{ (m, 2H), 2.22-2.12 \text{ (m, 1H), 1.94-1.81 \text{ (m, 1H), 1.75-1.63 \text{ (m, 1H), 1.58-1.45 \text{ (m, 2H), 1.43 \text{ (s, 9H)}, 1.42-1.31 \text{ (m, 2H), 1.36 \text{ (d, } J = 7.2 \text{ Hz, 3H), 1.01-0.91 \text{ (m, 2H), 0.92 \text{ (d, } J = 6.9 \text{ Hz, 3H), 0.89 \text{ (d, } J = 7.4 \text{ Hz, 3H), 0.03 \text{ (s, 9H).}}}

\textsuperscript{14} Not all the rapidly exchangeable protons are visible in CD\textsubscript{3}OD: 8.38 \text{ (d, } J = 7.5 \text{ Hz, 0.2H), 8.30 \text{ (d, } J = 7.5 \text{ Hz, 0.2H), 8.28 \text{ (d, } J = 7.5 \text{ Hz, 0.4H).}

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Compound 9. This compound was prepared from SI-27 (92 mg, 0.016 mmol) following the same sequence of steps as described for the preparation of 8. Pale orange glass (40 mg, 53%) \( ^1 \)H-NMR (400 MHz, CD\(_3\)OD, 313 K) \( \delta \) 4.50-4.42 (m, 1H), 4.40-4.31 (m, 2H), 3.91-3.85 (m, 1H), 3.74 (s, 3H), 3.00-2.93 (m, 2H), 2.17 (sextet, \( J = 6.0 \) Hz, 1H), 1.93-1.83 (m, 1H), 1.82-1.63 (m, 6H), 1.59-1.45 (m, 2H), 1.40 (d, \( J = 6.7 \) Hz, 3H), 1.02-0.94 (m, 12H); \( ^{13} \)C-NMR (100 MHz, CD\(_3\)OD, 313 K) \( \delta \) = 174.8, 174.2, 173.7, 172.9, 62.4, 59.4, 54.2, 52.6, 50.8, 41.5, 40.8, 32.5, 31.9, 28.1, 26.3, 23.7, 23.4, 22.3, 19.5, 18.6, 18.0; IR (neat): \( \tilde{\nu} \) = 3288 (br), 2961, 2419, 2112, 1743, 1644, 1543, 1460, 1371, 1204, 1019, 722 cm\(^{-1}\); MS (ES\(^+\)) \( m/z \) (rel. intensity) 470 (100 %, [M+H]\(^+\)); HRMS calcd for C\(_{21}\)H\(_{40}\)N\(_7\)O\(_5\) 470.3078, found 470.3078.

\(^{15}\) Not all the rapidly exchangeable protons are visible in CD\(_3\)OD: 8.31 (d, \( J = 6.0 \) Hz, 0.3H), 8.15-8.11 (m, 0.4H), 8.03 (d, \( J = 8.1 \) Hz, 0.7H).
Preparation of compounds 10 and 11

**Compound 10**\(^{16}\) Compound 7c (7.4 mg, 0.017 mmol), 8 (12.8 mg, 0.017 mmol), CuSO\(_4\) (0.017 mL, 0.1 M in water, 10 mol%) and sodium-L-ascorbate (0.6 mg, 0.0034 mmol, 40 mol%) were stirred in \(\text{tBuOH}\) (0.17 mL, 0.1 M) for 48 hours at 35 °C. The reaction mixture was diluted with ethanol and filtered through a short pad of celite. The solvent was removed under reduced pressure and the crude residue purified by flash column chromatography on silylated silica gel\(^{12}\) (EtOAc/EtOH, 20:1 to 1:1) to give 10 as a gum (8.0 mg, 39%, d.r. = 87:13). \(^1\)H-NMR (500 MHz, CD\(_3\)OD) δ 8.32 (s, 0.55H, H\(_1\)), 8.06 (s, 0.35H, H\(^3\)), 7.93-7.85 (m, 1H, H\(^{20}\)), 7.10 (d, J = 14.8 Hz, 0.35H, H\(^2\)), 6.71 (d, J = 14.2 Hz, 0.65H, H\(^5\)), 5.50-5.40 (m, 1H, H\(_G\)), 5.26 (dd, J = 14.7 and 9.4 Hz, 0.35H, H\(^3\)), 5.19 (dd, J = 14.1 and 9.2 Hz, 0.65H, H\(^3\)), 4.43 (dd, J = 8.8 and 5.6 Hz, 1H, H\(^K\)\(^{1}\)/H\(^K\)\(^{10}\)), 4.36-4.27 (m, 2H, H\(^M\) + H\(^I\)\(^{1}\)/H\(^I\)\(^{10}\)), 3.72 (s, 3H, H\(^O\)), 3.36 (s, 6H, H\(^C\) + H\(^F\)), 3.11 (s, 1.05H, H\(^A\)), 3.06-2.99 (m, 1H, H\(^5\)), 3.03 (s, 1.95H\(^A\)), 2.98-2.93 (m, 2H, H\(^W\)/H\(^W'\)), 2.92-2.87 (m, 2H, H\(^W\)/H\(^W'\)), 2.80-2.74 (m, 1H, H\(^6\)), 2.74-2.66 (m, 2H, H\(^{18}\)), 2.59-2.53 (m, 2H, H\(^8\)), 2.51-2.43 (m, 1H, H\(^{10}\)), 2.42-2.34 (m, 1H, H\(^7\)), 2.02-2.00 (m, 1H, H\(^5\)), 2.00-0.88 (m, 15H, H\(^D\) + H\(^F\) + H\(^S\) + H\(^Y\) + H\(^Z\)), 0.85 (d, J = 6.8 Hz, 3H, H\(^5\)); MS (ES\(^+\)) m/z (rel. intensity) 962 (100 %, [M+H]\(^+\)); IR (neat): \(\tilde{\nu}\) = 3306 (br), 3068, 2934, 2870, 1740, 1652, 1547, 1459, 1438, 1373, 1275, 1202, 1180, 1136, 1094, 972, 835, 799, 722 cm\(^{-1}\); HRMS calcd for C\(_{50}\)H\(_{92}\)N\(_9\)O\(_9\) 962.7018, found 962.7047.

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\(^{16}\)Two rotamers were visible in the \(^1\)H NMR spectrum. The signal for H\(^{11}\) is masked by CD\(_3\)OD. The rapidly exchangeable protons were mostly invisible in CD\(_3\)OD and are therefore not listed in the description.
Compound 11. This compound was obtained from 7c (5.0 mg, 0.011 mmol) and 9 (6.7 mg, 0.011 mmol) using the same procedure as described for the preparation of 10. Gum (7.1 mg, 63%, d.r. = 87:13).

\[ \text{H-NMR (500 MHz, CD}_3\text{OD) } \delta 8.32 (s, 0.65H, H^1), 8.09 (s, 0.35H, H^1), 7.90-7.82 (m, 1H, H^20), 7.10 (d, J = 14.6 Hz, 0.35H, H^2), 6.70 (d, J = 14.2 Hz, 0.65H, H^3), 5.45-5.38 (m, 1H, H^G)), 5.26 (dd, J = 14.6 and 9.0 Hz, 0.35H, H^3), 5.19 (dd, J = 14.2 and 9.3 Hz, 0.65H, H^3), 4.44 (dd, J = 8.4 and 5.4 Hz, 1H, H^K), 4.32 (d, J = 7.0 Hz, 1H, H^M), 4.26 (q, J = 6.9 Hz, H^1), 3.72 (s, 3H, H^O), 3.36 (s, 6H, H^C + H^F), 3.11 (s, 1.05H, H^A), 3.06-2.99 (m, 1H, H^5), 3.03 (s, 1.95H^A), 2.98-2.93 (m, 2H, H^W), 2.80-2.74 (m, 1H, H^6), 2.74-2.66 (m, 2H, H^18), 2.58-2.52 (m, 2H, H^8), 2.51-2.42 (m, 1H, H^9), 2.20-2.12 (m, 1H, H^X), 2.12-2.02 (m, 1H, H^P), 2.02-1.94 (m, 1H, H^P), 1.89-1.78 (m, 1H, H^15w), 1.76-1.62 (m, 7H, H^9u + H^10 + H^11 + H^V + H^10p), 1.55-1.25 (m, 18H, H^10b + H^12 + H^13 + H^14 + H^15 + H^16 + H^9 + H^12 + H^2), 1.17 (d, J = 7.0 Hz, 3H, H^B), 1.01-0.88 (m, 15H, H^D + H^R + H^S + H^V + H^2), 0.85 (d, J = 6.8 Hz, 3H, H^E); IR (neat): v ~ 3306 (br), 3302 (br), 2930, 2414, 1793, 1740, 1651, 1547, 1457, 1371, 1272, 1202, 1148, 1092, 723 cm\(^{-1}\); MS (ES\(^+\)) m/z (rel. intensity) 905 (100 %, [M+H]\(^+\)); HRMS calcd for C\(_{47}\)H\(_{83}\)N\(_{8}\)O\(_9\) 905.6440, found 905.6470.
Bioassays conducted on 7a–7c, 10 and 11

Rabbit muscle actin was prepared as described in Winder and Walsh 1990. For G-actin interaction assays, actin was labelled with acrylodan according to a previously published method. Compounds were incubated with 2µM prodan-actin and following excitation at 380nm any interaction was monitored by scanning the emission between 400 and 650nm using a Varian Cary Eclipse fluorescence spectrophotometer.

The effect of compounds on 6µM F-actin in vitro was determined following a high speed centrifugation pelleting assay and SDS-PAGE analysis of resultant supernatant (G-actin) and pellet (F-actin) fractions as described previously. SDS-gels were scanned with a Biorad ChemiDoc XRS+ and quantified with Image Lab software using volume integration and local background subtraction. Representative results are depicted in Figure S1.

Actin polymerisation assays were conducted with varying concentrations of compounds using 5µM pyrenyl G-actin in a Varian fluorescence spectrophotometer according to previously described procedures. Representative results are depicted in Figure S2.

REF52 rat embryo fibroblasts were grown in DMEM with 10% FCS as described previously. Cells were seeded in flat bottomed 96 well tissue culture plates and incubated with various concentrations of the compounds for either 2 or 24 hours. Following incubation, cells were fixed with 3.7% formaldehyde in PBS (10 min) permeabilised in 0.1% Triton X-100 in PBS (1 min) and incubated with 1µg/ml rhodamine phalloidin for one hour. Following 3 washes in PBS cells were mounted directly in the 96 well plate by addition of 20µl of Hydromount containing DAPI. Cells were visualised on a Leica DMIRE2 microscope and images captured using Leica Q-fluoro software.

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**Figure S1.** Coomassie blue stained SDS gel of equivalent volumes of supernatant (S) and pellet (P) fractions following incubation of 6μM F-actin with the indicated concentrations of compounds and separation by high speed centrifugation {7a (A), 7b (C), 7c (E), 10 (G) and 11 (I)}. At higher concentrations of 10, there is a clear shift of actin from pellet to supernatant fraction indicative of depolymerisation of F-actin. Quantification of the amount of actin in the supernatant was performed for 7a-c, 10, 11 and DMSO control. In the presence of DMSO only, between 1 and 2% of actin is in the supernatant fraction. A compound was deemed to have a significant effect at a concentration that resulted in 5% of actin in the supernatant fraction. Quantification of the gels in A, C, E, G and I is shown in B, D, F, H and J, respectively.
Figure S2. Effect of compounds 7a-c, 10 and 11 on the polymerisation rate of 2µM pyrenyl actin as monitored by the increase in pyrenyl fluorescence at 384nm on polymerisation. Reactions were monitored for 120 minutes and recorded as arbitrary fluorescence units. The initial rate of polymerisation is the most reliable parameter to determine an effect of a compound on simple actin polymerisation. Rates were calculated for compounds in the initial linear phase of polymerisation up to 20 minutes. The minimum concentration that reduced the polymerisation rate by 10% compared to DMSO control was deemed significant and is indicated in Table 1 of the manuscript.