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Supporting Information

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General

Unless stated otherwise, all reactions were performed in flame-dried glassware using anhydrous solvents under Argon. Organic solvents were dried using a Pure Solv solvent purification system. Liquid reagents (i-Pr₂NEt, Et₃N, TiCl₄, Me₃SiCl) were distilled prior to use if needed. All reagents were purchased from commercial suppliers and used without further purification except where it is stated.

Column chromatography was performed under pressure using silica gel (Fluorochem LC60A, 35-70 micron or Merck Geduran Si60, 40-63 micron) as solid support and reagent-graded solvents as eluent. Petroleum ether used for column chromatography was the 40•60 °C fraction.

Reactions were monitored by thin-layer chromatography (TLC) on Fisher and Merck silica gel 60 covered alumina plates. TLC plates were developed under UV light and/or with a KMnO₄ solution (3 g KMnO₄, 20 g K₂CO₃, 5 mL 5% NaOH aq. and 300 mL H₂O) or in an anisaldehyde solution (15 g anisaldehyde, 250 mL EtOH, 2.5 mL concentrated H₂SO₄).

Specific rotations of the chiral non-racemic compounds were recorded with an error d±0.1 using an automatic polarimeter Autopol V. The wavelength of the light was 589 nm.

IR spectra were recorded using a type IIa diamond single reflection element on a Shimadzu FTIR-8400S instrument. The IR spectrum of the compound was recorded directly on a thin film (liquid) or powder (solid) at ambient temperature.

¹H NMR spectra were recorded on a Bruker Avance iii 400 MHz or Bruker Avance iii UltraShield 500 MHz spectrometer at ambient temperature. Data are reported as follows: chemical shift in ppm relative to CDCl₃ (7.26) on the ‘ scale, integration, multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, br = broad, or a combination of these), coupling constant(s) J (Hz) and assignment. ¹³C NMR spectra were recorded at 101 MHz or 126 MHz at ambient temperature. Data are reported as follows: chemical shift in ppm, relative to CHCl₃ (77.16) on the ‘ scale, and assignment.

High resolution mass spectra (HRMS) were obtained by the analytical services of the University of Glasgow on a J eol MSstation J MS-700 High Resolution Mass Spectrometer (EI or CI using isobutane) or a Bruker micro TOFq High Resolution Mass Spectrometer (ESI).

Melting points were recorded with an Electrothermal IA 9100 apparatus.
**Experimental Procedures**

**Enone 5.**

To a stirred solution of Co$_2$(CO)$_8$ (2.3 g, 6.9 mmol) in toluene (100 mL) was added (R)-BINAP (4.3 g, 6.9 mmol) in one portion. The mixture was sparged with carbon monoxide for 15 min and stirred under an atmosphere of carbon monoxide for 1 h at 65 °C. A solution of the alkene 4 (6.0 g, 23 mmol) in toluene (20 mL) was added dropwise to the reaction. The mixture was stirred at 65 °C for 6 h and then concentrated in vacuo. Purification of the residue by flash column chromatography on silica gel (petroleum ether: EtOAc, 6:4) provided the enone 5 (4.8 g, 72%, 97% ee) as a pale yellow solid. Enantiomeric excess was determined by HPLC analysis: column Chiralpak OD-H, temperature 25 °C, hexane:propan-2-ol 67:33, flow rate 0.5 mL.min$^{-1}$, retention time 17.2 min. R$_f$ = 0.18 (petroleum ether:EtOAc, 5:5); [±]$^{[a]}$ = 97.3 (c = 5.00, CHCl$_3$); m.p. 124-126 °C; $\nu_{max}$ (film) 2980, 2870, 1708, 1342, 1155, 788 cm$^{-1}$; $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 7.65 (2H, d, J = 8.0 Hz), 7.34 (2H, d, J = 8.0 Hz), 6.00 (1H, t, J = 1.7 Hz), 4.72 (1H, dd, J = 13.3, 1.4 Hz), 3.95 (1H, ddq, J = 12.4, 2.6, 1.9 Hz), 3.20 (1H, d, J = 13.3 Hz), 2.61–2.46 (3H, m), 2.44 (3H, s), 2.13–2.05 (1H, m), 2.05–1.97 (1H, m), 1.46 (1H, qd, J = 12.4, 4.0 Hz); $^{13}$C NMR (101 MHz, CDCl$_3$) $\delta$ 207.3, 172.4, 144.2, 132.9, 129.9, 129.0, 127.8, 47.5, 45.7, 41.3, 39.2, 32.0, 21.5; HRMS (EI) for C$_{15}$H$_{17}$NO$_3$S [M]$^+$ calcd. 291.0929, found 291.0932.

**Ketone 6.**

Allylmagnesium chloride (1.7 mL of a 1.6 M solution in THF, 2.7 mmol) was added dropwise to a solution of copper(I) iodide (0.50 g, 2.7 mmol) and lithium chloride (0.11 g, 2.7 mmol) in THF (30 mL) at −10 °C. This was followed by the rapid addition of a mixture of the ketone 5 (0.26 g, 0.89 mmol) and chlorotrimethylsilane (0.12 mL, 1.0 mmol) as a solution in THF (10 mL). The mixture was stirred at −10 °C for 1 h and then allowed to reach rt. The reaction was quenched by addition of saturated
aqueous NH₄Cl solution (30 mL), saturated aqueous Na₂CO₃ solution (30 mL) and EtOAc (50 mL). The phases were separated and the aqueous phase was extracted with EtOAc (3 × 50 mL). The combined organic phases were washed with water (150 mL) and brine (150 mL), dried over Na₂SO₄, filtered and concentrated in vacuo. Purification of the residue by flash column chromatography on silica gel (petroleum ether:EtOAc, 8:1 to 4:1) provided the ketone 6 (0.27 g, 91%) as a colourless solid. Rₛ = 0.29 (petroleum ether: EtOAc, 4:1); [±]D²₂ +32.3 (c = 1.80, CHCl₃); m.p. 134–137 °C; νₘₐₓ (film) 2901, 2856, 1728, 1597, 1334, 1157 cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ 7.61 (2H, d, J = 7.8 Hz), 7.32 (2H, d, J = 7.8 Hz), 5.73 (1H, ddt, J₁ = 16.7, 10.3, 7.5 Hz), 5.17–5.10 (2H, m), 3.13–3.06 (1H, m), 3.00 (1H, d, J₁ = 12.1 Hz), 2.90–2.82 (1H, m), 2.58 (1H, d, J = 12.1 Hz), 2.48–2.38 (1H, m), 2.43 (3H, s), 2.31 (1H, dd, J₂ = 18.5, 7.9 Hz), 2.23 (1H, dd, J₂ = 14.0, 7.4 Hz), 2.22–2.18 (2H, m), 2.12 (1H, ddd, J₂ = 13.5, 7.6, 6.0 Hz), 2.05–1.95 (2H, m), 1.55 (1H, dtd, J₂ = 14.2, 6.2, 3.6 Hz); ¹³C NMR (101 MHz, CDCl₃) δ 216.7, 143.9, 133.0, 132.6, 129.9, 127.7, 119.8, 49.6, 46.5, 42.7, 41.6, 41.2, 40.5, 37.0, 25.4, 21.6; HRMS (El) for C₁₈H₂₃NO₃S [M+Na]+ calcd. 333.1399, found 333.1401.

**Allylic alcohol 8.**

The TBS ether 7[1] (1.4 g, 7.5 mmol) was added to a solution of the alkene 6 (0.50 g, 1.5 mmol) and the Hoveyda-Grubbs second-generation catalyst (47 mg, 5 mol %) in dichloromethane (50 mL). The mixture was then heated at 50 °C for 12 h and then a 1 M aqueous solution of HCl (20 mL) was added. The biphasic mixture was stirred for 2 h and then neutralised by addition of saturated aqueous NaHCO₃ solution (40 mL). The phases were separated and the aqueous phase was extracted with EtOAc (3 × 50 mL). The organic phases were combined and washed with brine (100 mL), dried over MgSO₄, filtered and concentrated in vacuo. Purification of the residue by flash column chromatography on silica gel (petroleum ether:EtOAc, 3:1 to 1:1) afforded the allylic alcohol 8 (481 mg, 85%) as a colourless foam. Rₛ = 0.26 (petroleum ether: EtOAc, 1:2); [±]D²₂ +40 (c = 0.50, CHCl₃); νₘₐₓ (film) 3492 (br), 2969, 2926, 2851, 1738, 977, 934, 816, 754, 661 cm⁻¹; ¹H NMR (500 MHz,
CDCl₃) 7.60 (2H, d, J = 8.0 Hz), 7.33 (2H, d, J = 8.0 Hz), 5.68 (1H, dd, J = 15.2, 6.5 Hz), 5.58–5.50 (1H, m), 4.29 (1H, dq, J = 6.5, 6.5 Hz), 3.25–3.18 (1H, m), 3.09 (1H, d, J = 12.1 Hz), 2.76–2.72 (1H, m), 2.50 (1H, dd, J = 13.8, 8.2 Hz), 2.44 (3H, s), 2.39 (1H, d, J = 12.1 Hz), 2.30 (1H, dd, J = 18.7, 8.1 Hz), 2.20–2.00 (3H, m), 2.16 (2H, s), 2.02 (1H, dd, J = 18.6, 8.5 Hz), 1.58 (1H, dt, J = 14.1, 5.3, 3.5 Hz), 1.27 (3H, d, J = 6.5 Hz); ¹³C NMR (126 MHz, CDCl₃) 216.3, 144.0, 139.8, 133.0, 130.0, 127.7, 124.1, 68.7, 49.5, 47.3, 42.5, 41.8, 40.9, 39.1, 37.3, 25.1, 23.7, 21.7; HRMS (ESI) for C₂₀H₂₇NNaO₄S [M+Na]⁺ calcd. 400.1553, found 400.1535.

Trifluoroacetamide 11.

To a solution of the allylic alcohol 8 (4.0 mg, 10.5 mmol) in THF (40 mL) at −30 °C was added NaHMDS (11.5 mL of 1 m solution in THF, 11.5 mmol). The bromide 9 (6.3 g of a 47% w/w solution in pentane, 11.5 mmol) was added over 5 min and the mixture was stirred at −30 °C for 1 h. Anhydrous K₂CO₃ (1.6 g, 11.5 mmol) and toluene (80 mL) were then added and the resulting mixture was heated at 115 °C for 2 d with vigorous stirring. After cooling to rt, the mixture was filtered through a short pad of Celite and the filter cake was washed with EtOAc (100 mL). The combined filtrate was concentrated in vacuo and the residue was purified by flash column chromatography on silica gel (petroleum ether:EtOAc, 4:1 to 2:1) to afford the trifluoroacetamide 11 (4.3 g, 73% yield over two steps) as a colourless gum. R₆ = 0.66 (petroleum ether: EtOAc, 1:1); [α]D²³ +32.5 (c = 2.15, CHCl₃); ¾max (film) 2951, 2924, 2855, 1744, 1686, 980, 930, 816, 756 cm⁻¹; ¹H NMR (500 MHz, CDCl₃) 7.56 (2H, d, J = 8.0 Hz), 7.29 (2H, d, J = 8.0 Hz), 5.96 (1H, dd, d, J = 15.4, 9.3, 1.5 Hz), 5.85–5.70 (2H, m), 5.03–4.91 (2H, m), 4.10–4.00 (1H, m), 3.51 (1H, d, J = 10.8 Hz), 3.42–3.22 (3H, m), 2.43–2.27 (2H, m), 2.40 (3H, s), 2.23–2.02 (8H, m), 1.97–1.85 (2H, m), 1.78–1.69 (2H, m), 1.67 (3H, dd, d, J = 6.4, 1.5 Hz), 1.62–1.52 (1H, m), 1.41–1.33 (2H, m); ¹³C NMR (101 MHz, CDCl₃) 216.2, 156.2 (q, JCF = 35.0), 144.1, 138.4, 132.5, 131.2, 130.0, 129.9, 129.0, 116.5 (q, JCF = 288.6), 114.8, 61.4, 50.1, 49.3, 47.7, 41.8, 40.5, 38.7, 38.3, 36.9, 33.2, 28.7, 26.0, 23.4, 21.6, 17.9; HRMS (ESI) for C₂₈H₃₇F₃N₂NaO₄S [M+Na]⁺ calcd. 601.1935, found 601.1929.
Azocine S1.

A solution of the diene 11 (1.3 g, 2.3 mmol) in dichloromethane (20 mL) was added to a solution of the Grubbs second-generation catalyst (0.20 g, 0.23 mmol) in dichloromethane (1 L). The resulting solution was heated at reflux for 4 h. The solution was cooled to rt, MeOH (10 mL) was added and the mixture was concentrated in vacuo. Purification of the residue by flash column chromatography on silica gel (petroleum ether: EtOAc, 2:1) afforded the azocine S1 (0.97 g, 81%) as a colourless foam. \( R_f \) = 0.52 (petroleum ether:EtOAc, 1:1); \( \lambda_{\text{max}} \) (film) 2926, 2859, 1744, 1684, 978, 936, 816, 756 cm\(^{-1}\); \( ^1\)H NMR (400 MHz, CDCl\(_3\)) \( \delta \) 7.51 (2H, d, \( J = 8.3 \) Hz), 7.25 (2H, d, \( J = 8.3 \) Hz), 5.83−5.65 (2H, m), 4.87−4.61 (1H, m), 3.80−3.92 (1H, m), 3.62−3.38 (2H, m), 3.22 (1H, d, \( J = 12.5 \) Hz), 2.55−2.45 (2H, m), 2.45 (3H, s) 2.41−2.05 (9H, m), 2.02−1.90 (3H, m), 1.85−1.60 (3H, m); \( ^{13}\)C NMR (101 MHz, CDCl\(_3\)) \( \delta \) 215.6, 156.6 (q, \( J_{\text{CF}} = 35.3 \)), 144.0, 132.5, 131.1, 130.2, 129.9, 127.4, 116.5 (q, \( J_{\text{CF}} = 288.6 \)), 54.6, 48.7, 48.4, 47.9, 41.8, 41.0, 39.0, 37.9, 37.5, 28.2, 26.4, 24.8, 23.8, 21.5; HRMS (ESI) for C\(_{25}\)H\(_{31}\)F\(_3\)N\(_2\)NaO\(_4\)S [M+Na]\(^+\) calcd 535.1849, found 535.1838.

Amino ketone 12.

To a stirred solution of the amide S1 (475 mg, 1.14 mmol) in methanol (40 mL) at rt was added 2 M aqueous K\(_2\)CO\(_3\) solution (20 mL) and the mixture was then stirred at rt for 2 d. The reaction mixture was diluted with EtOAc (80 mL) and then 1 M aqueous HCl solution (40 mL) was added. The phases were separated and the aqueous phase was extracted with EtOAc (3 × 60 mL). The combined
organic extracts were washed with brine (200 mL), dried over anhydrous Na$_2$SO$_4$, filtered and concentrated in vacuo. Purification of the residue by flash column chromatography on silica gel (petroleum ether: EtOAc, 2:1) gave the amino ketone 12 (341 mg, 88%) as a pale yellow oil. R$_f$ = 0.28 (EtOAc:MeOH:Et$_3$N, 87:10:3); [±]$^2$ +83 (c = 0.47, CHCl$_3$); $\nu_{max}$ (film) 3464 (br), 2924, 2853, 1740, 754 cm$^{-1}$; $^1$H NMR (500 MHz, CDCl$_3$) ` 7.57 (2H, d, $J$ = 8.3 Hz), 7.29 (2H, d, $J$ = 8.3 Hz), 5.82 (1H, td, $J$ = 9.1, 8.2 Hz), 5.07 (1H, td, $J$ = 9.8, 1.1 Hz), 3.77–3.68 (2H, m), 3.46–3.38 (1H, m), 3.37 (1H, d, $J$ = 12.0 Hz), 2.95 (1H, dd, $J$ = 13.5, 9.3 Hz), 2.70 (1H, dd, $J$ = 13.5, 7.9 Hz), 2.53–2.45 (1H, m), 2.35–2.25 (1H, m), 2.23–2.05 (9H, m), 1.95 (1H, dd, $J$ = 16.7, 8.1 Hz), 1.85–1.70 (3H, m), 1.59–1.45 (3H, m), 1.26–1.19 (1H, m); $^{13}$C NMR (126 MHz, CDCl$_3$) ` 216.7, 143.7, 132.8, 132.0, 131.3, 129.8, 127.5, 67.9, 49.5, 49.1, 48.0, 45.6, 42.3, 41.7, 41.0, 39.3, 38.2, 28.6, 28.2, 26.4, 25.6, 23.9, 21.5; HRMS (ESI) for C$_{23}$H$_{33}$N$_2$O$_3$S [M+H]$^+$ calcd. 417.2182, found 417.2175.

**Ketone 13.**

To a stirred solution of the amine 12 (106 mg, 0.206 mmol) in THF (10 mL) at 0 °C was added pyrrolidone hydrotribromide (113 mg, 0.227 mmol) in one portion. The mixture was stirred overnight before addition of DMAP (50.5 mg, 0.413 mmol). The reaction mixture was stirred at rt for 12 h and then washed with saturated aqueous Na$_2$S$_2$O$_3$ solution (20 mL), saturated aqueous Na$_2$CO$_3$ solution (20 mL) and brine (20 mL). The phases were separated and the organic phase was dried over anhydrous Na$_2$SO$_4$, filtered and concentrated in vacuo. Purification of the residue by flash column chromatography on silica gel (petroleum ether:EtOAc, 2:1) afforded the ketone 13 (95 mg, 90%) as a pale yellow solid. R$_f$ = 0.42 (petroleum ether:EtOAc, 1:1); [±]$^4$ -47 (c = 0.48, CHCl$_3$); m.p. 128–132 °C; $\nu_{max}$ (powder) 2953, 2926, 2855, 1732, 1467, 1160, 966, 901, 837, 815, 777, 746 cm$^{-1}$; $^1$H NMR (500 MHz, C$_6$D$_6$) ` 7.63 (2H, d, $J$ = 8.2 Hz), 6.80 (2H, d, $J$ = 8.2 Hz), 5.59–5.51 (1H, m), 5.27 (1H, dd, $J$ = 10.9, 6.5 Hz), 3.48 (1H, td, $J$ = 6.9, 6.6 Hz), 3.42 (1H, d, $J$ = 11.7 Hz), 3.24 (1H, dt, $J$ = 13.2, 4.6 Hz), 3.17–3.06 (1H, m), 2.97 (1H, s), 2.95–2.87 (1H, m), 2.49–2.35 (2H, m), 2.30 (1H, dd, $J$
= 10.6, 9.8 Hz), 2.04 (1H, dtd, J = 13.1, 8.9, 4.3 Hz), 1.92 (3H, s), 1.88 (1H, dd, J = 17.7, 7.4 Hz), 1.67
(1H, dd, J = 13.6, 8.4 Hz), 1.62−1.55 (3H, m), 1.45−1.24 (4H, m), 1.24−1.17 (1H, m), 0.81 (1H, dtd, J = 13.8, 9.7, 4.0 Hz); 13C NMR (126 MHz, C6D6) ’ 215.0, 143.1, 134.9, 132.5, 130.5, 129.7, 128.6, 72.3, 59.7, 52.3, 49.3, 48.8, 44.8, 44.7, 44.2, 36.9, 28.3, 27.4, 26.5, 26.0, 21.2; HRMS (ESI) for C23H31N2O3S [M+H]+ calcd. 415.2050, found 415.2037.

(R)-5,6-di(tert-butyldimethylsilyloxy)-1-hexyne (S2).[3]

To a stirred solution of the alcohol (R)-1-(tert-butyldimethylsilyloxy)hex-5-yn-2-ol (3.42 g, 15.0 mmol) and imidazole (2.10 g, 30.0 mmol) in dichloromethane (40 mL) at 0 °C was added t-BuMe2SiCl (3.40 g, 22.5 mmol). The mixture was stirred at 0 °C for 1.5 h and then allowed to reach rt over 30 min. The reaction was quenched by addition of saturated aqueous NH4Cl solution (50 mL) and the resulting mixture was extracted with Et2O (3 × 100 mL). The organic extracts were washed with brine (80 mL), dried over anhydrous MgSO4, filtered and concentrated in vacuo. Purification of the residue by flash column chromatography on silica gel (100% petroleum ether to 50:1 petroleum ether: Et2O) afforded the title compound S2 (4.80 g, 94%) as a colourless oil. Rf = 0.91 (petroleum ether: Et2O, 10:1); [±]D27 +21.2 (c = 1.44, CHCl3); γmax (film) 3316, 2955, 2930, 2859, 1472, 1005, 993, 939, 836, 812, 775 cm–1; 1H NMR (400 MHz, CDCl3) ’ 3.77 (1H, dddd, J = 7.7, 6.7, 5.1, 3.9 Hz), 3.55 (1H, dd, J = 10.0, 5.2 Hz), 3.39 (1H, dd, J = 10.0, 6.7 Hz), 2.34–2.19 (2H, m), 1.93 (1H, t, J = 2.6 Hz), 1.82 (1H, dddd, J = 13.6, 8.0, 6.8, 3.9 Hz), 1.59 (1H, dd, J = 13.6, 7.7, 6.0 Hz), 0.89 (9H, s), 0.88 (9H, s), 0.08 (3H, s), 0.07 (3H, s), 0.05 (3H, s), 0.04 (3H, s); 13C NMR (101 MHz, CDCl3) ’ 84.6, 71.6, 68.2, 67.1, 33.2, 26.0, 25.9, 18.4, 18.1, 14.4, −4.3, −4.8, −5.3, −5.4; HRMS (ESI) for C18H38NaO2Si2 [M+Na]+ calcd. 365.2303, found 365.2290.

Methyl (R)-9,10-bis(tert-butyldimethylsilyloxy)dec-5-ynoate (S3).

To a stirred solution of the alkyne S2 (2.5 g, 7.3 mmol) in THF (60 mL) at −78 °C was added n-BuLi (3.8 mL of a 2.32 m solution in THF, 8.8 mmol). The mixture was stirred at −78 °C for 30 min before
addition of HMPA (5.0 mL, 29 mmol) and the trimethyl ortho-4-bromobutanoate[4] (1.5 mL, 8.8 mmol). The reaction mixture was then stirred at −78 °C for 1 h and allowed to reach rt overnight. The reaction was quenched by addition of saturated aqueous NH₄Cl solution (50 mL) and the resulting mixture was extracted with Et₂O (3 × 100 mL). The combined organic extracts were washed with brine (50 mL), dried over anhydrous MgSO₄, filtered and concentrated in vacuo. Purification of the residue by flash column chromatography on silica gel (petroleum ether: Et₂O, 100:1 to 50:1) afforded the title compound S₃ (2.6 g, 80%) as a colourless oil. Rf = 0.45 (petroleum ether:Et₂O, 10:1); [±]D²⁷ +25.3 (c = 1.70, CHCl₃); ½max (film) 2953, 2928, 2857, 1742, 1472, 1005, 986, 835, 814, 775 cm⁻¹; ¹H NMR (500 MHz, CDCl₃) ´ 3.74 (1H, dddd, J = 7.8, 6.4, 5.2, 4.1 Hz), 3.64 (3H, s), 3.52 (1H, dd, J = 10.0, 5.3 Hz), 3.39 (1H, dd, J = 10.0, 6.5 Hz), 2.41 (2H, t, J = 7.5), 2.23−2.16 (4H, m), 1.81−1.70 (3H, m), 1.55−1.48 (1H, m), 0.87 (9H, s), 0.86 (9H, s), 0.86 (9H, s), 0.04 (3H, s), 0.03 (3H, s), 0.02 (3H, s); ¹³C NMR (126 MHz, CDCl₃) ´ 173.6, 81.0, 78.9, 71.8, 67.3, 51.4, 33.7, 32.8, 25.9, 25.9, 24.2, 18.3, 18.2, 18.1, 14.7, −4.3, −4.8, −5.3, −5.4; HRMS (ESI) for C₂₃H₄₆NaO₄Si₂ [M+Na]⁺ calcd. 465.2827, found 465.2805.

**Methyl (9R,5Z)-9,10-bis(tert-butyldimethylsilyloxy)dec-5-enoate (S₄).**

To a stirred solution of the alkyne S₃ (1.5 g, 3.4 mmol) in EtOAc (20 mL) at rt was added Lindlar catalyst (722 mg, 0.34 mmol) and quinoline (44 mg, 0.34 mmol). The mixture was sparged with hydrogen for 10 min, and then stirred under a static hydrogen atmosphere at rt for 1h. The reaction was then filtered through a short pad of Celite and the filter cake was washed with EtOAc (100 mL). The filtrate was concentrated in vacuo. Purification of the residue by flash column chromatography on silica gel (petroleum ether:Et₂O, 50:1) afforded the title compound S₄ (1.5 g, 99%) as a colourless oil. Rf = 0.51 (petroleum ether:Et₂O, 10:1); [±]D²¹ +14 (c = 0.63, CHCl₃); ½max (film) 2953, 2928, 2907, 2857, 1742, 939, 831, 814, 773 cm⁻¹; ¹H NMR (500 MHz, CDCl₃) ´ 5.45•5.36 (1H, m), 5.35−5.27 (1H, m), 3.68−3.62 (1H, m), 3.65 (3H, s), 3.51 (1H, dd, J = 10.0, 5.4 Hz), 3.39 (1H, dd, J = 10.0, 6.4 Hz), 2.28 (2H, t, J = 7.6), 2.17−2.10(1H, m), 2.09−2.03 (2H, m), 2.02−1.96 (1H, m), 1.61 (2H, tt, J = 7.6,
7.4 Hz), 1.62–1.54 (1H, m), 1.41 (1H, dddd, J = 13.6, 10.5, 6.8, 5.6 Hz), 0.83 (18H, s), 0.05 (6H, s), 0.04 (3H, s), 0.03 (3H, s); $^{13}$C NMR (126 MHz, CDCl$_3$) ´ 174.0, 130.9, 128.5, 72.8, 67.2, 51.4, 34.4, 33.5, 26.6, 25.9, 25.9, 24.9, 23.0, 18.4, 18.1, −4.3, −4.8, −5.3, −5.4; HRMS (ESI) for C$_{23}$H$_{48}$NaO$_4$Si$_2$ [M+Na]$^+$ calcd. 467.2983, found 467.2967.

**Methyl (9R,5Z)-9-(tert-butyldimethylsilyloxy)-10-hydroxydec-5-enoate (S5).**

![Methyl (9R,5Z)-9-(tert-butyldimethylsilyloxy)-10-hydroxydec-5-enoate (S5).](image)

To a stirred solution of the bis-TBS ether S4 (2.5 g, 5.6 mmol) in THF (60 mL) at −10 °C was added HF·pyridine (23 mL of a 4.81 M solution in THF, 110 mmol). The mixture was stirred at −10 °C for 2 d. The reaction was quenched by addition of saturated aqueous NaHCO$_3$ solution (100 mL) and the resulting mixture was extracted with Et$_2$O (3 × 100 mL). The combined organic phases were washed with brine (100 mL), dried over anhydrous MgSO$_4$, filtered and concentrated in vacuo. Purification of the residue by flash column chromatography on silica gel (petroleum ether:Et$_2$O, 10:1 to 5:1) afforded the title compound S5 (1.5 g, 81%) as a colourless oil. R$_f$ = 0.31 (petroleum ether: Et$_2$O, 4:1); [α]$_{D}^{23}$ = −1.8 (c = 0.73, CHCl$_3$); ½max (film) 3499 (br), 2951, 2930, 2857, 1740, 995, 835, 775 cm$^{-1}$; $^1$H NMR (500 MHz, CDCl$_3$) ´ 5.35–5.21 (2H, m), 3.68–3.63 (1H, m), 3.57 (3H, s), 3.49–3.43 (1H, m), 3.42–3.45 (1H, m), 2.22 (2H, t, J = 7.6), 2.05–1.85 (4H, m), 1.60 (2H, tt, J = 7.5, 7.4 Hz), 1.53–1.39 (2H, m), 0.82 (9H, s), 0.00 (6H, s); $^{13}$C NMR (126 MHz, CDCl$_3$) ´ 174.0, 130.3, 128.8, 72.5, 66.0, 51.4, 33.9, 33.4, 26.5, 25.8, 24.8, 23.1, 18.0, −4.5, −4.6; HRMS (ESI) for C$_{17}$H$_{34}$NaO$_4$Si [M+Na]$^+$ calcd. 353.2119, found 353.2108.
Methyl (9R,5Z)-9-(tert-butyldimethylsilyloxy)-10-oxodec-5-enoate (14).

To a stirred solution of the alcohol S5 (500 mg, 1.51 mmol) in dichloromethane (30 mL) at 0 °C was added NaHCO₃ (378 mg, 4.52 mmol) and Dess-Martin periodinane (1.27 g, 3.02 mmol) in one portion. The mixture was stirred overnight before addition of saturated aqueous Na₂S₂O₃ solution (30 mL). The reaction was then stirred for 10 min and the phases were separated. The organic phase was washed with saturated aqueous Na₂CO₃ solution (30 mL), brine (30 mL), dried over anhydrous MgSO₄, filtered and concentrated in vacuo. Purification of the residue by flash column chromatography on silica gel (petroleum ether: ether, 4:1) afforded the title compound 14 (488 mg, 98%) as a colourless oil. Rᵡ = 0.42 (petroleum ether:Et₂O, 4:1); [±]D²³ +28 (c = 0.89, CHCl₃); ½max (film) 2953, 2930, 2857, 1736, 837, 777, 727, 702 cm⁻¹; ¹H NMR (500 MHz, CDCl₃) ´  9.60 (1H, d, J = 1.5 Hz), 5.40−5.31 (2H, m), 3.99 (1H, ddd, J = 6.6, 5.6, 1.5 Hz), 3.64 (3H, s), 2.35 (2H, t, J = 7.5), 2.20−1.98 (4H, m), 1.71−1.62 (4H, m), 0.87 (9H, s), 0.05 (3H, s), 0.04 (3H, s); ¹³C NMR (126 MHz, CDCl₃) ´ 204.1, 174.0, 129.8, 129.5, 77.4, 51.5, 33.5, 32.8, 26.6, 25.8, 24.8, 22.3, 18.2, −4.6, −4.9; HRMS (ESI) for C₁₇H₃₂NaO₄Si [M+Na]⁺ calcd. 351.1962, found 351.1969.

Enone 15.

To a stirred solution of diisopropylamine (26 µL, 0.19 mmol) in THF (2 mL) at −78 °C was added n-BuLi (88 µL of a 2.16 M solution in THF, 0.19 mmol). The mixture was stirred at −78 °C for 10 min and a solution of the ketone 13 (70 mg, 0.17 mmol) in THF (1 mL) was added. The mixture was then stirred at −78 °C for 30 min and then a solution of the aldehyde 14 (61 mg, 0.19 mmol) in THF (1 mL)
was added. The mixture was stirred at −78 °C for 2 h and allowed to reach rt over 12 h. The reaction was quenched by addition of saturated aqueous NH₄Cl solution (5 mL) and the resulting mixture was extracted with EtOAc (3 × 10 mL). The combined organic extracts were washed with brine (30 mL), dried over anhydrous Na₂SO₄, filtered and concentrated in vacuo. Purification of the residue by flash column chromatography on silica gel (gradient, petroleum ether:EtOAc, 10:1 to 2:1) afforded the enone 15 (56 mg, 46%) as a yellow gum along with the alcohol (38 mg, 30%) arising from the aldol reaction without dehydration. Rᵣ = 0.78 (petroleum ether:EtOAc, 2:1); [±]D₂¹ −23.7 (c = 1.06, CHCl₃); ¾max (film) 3005, 2951, 2928, 2855, 1738, 982, 835, 775, 758 cm⁻¹; ¹H NMR (400 MHz, C₆D₆) δ 7.71 (2H, d, J = 8.2 Hz), 6.83 (2H, d, J = 8.2 Hz), 6.67 (1H, dd, J = 8.9, 1.5 Hz), 5.53−5.25 (4H, m), 4.21 (1H, ddd, J = 8.6, 8.4, 4.0), 4.19−4.13 (1H, m), 3.77−3.64 (2H, m), 3.54 (1H, s), 3.50−3.42 (1H, m), 3.39 (3H, s), 3.26−3.16 (1H, m), 3.14−3.03 (1H, m), 2.26−1.87 (11H, m), 1.92 (3H, s), 1.66−1.20 (10H, m), 1.09−1.03 (1H, m), 0.93 (9H, s), 0.05 (3H, s), 0.00 (3H, s); ¹³C NMR (101 MHz, C₆D₆) δ 206.8, 172.8, 142.7, 139.8, 137.3, 134.7, 134.6, 129.7, 129.6, 129.3, 127.8, 127.6, 71.4, 69.4, 59.5, 51.5, 50.8, 50.6, 49.9, 46.0, 44.2, 39.7, 37.0, 32.9, 30.1, 26.8, 25.8, 25.6, 25.0, 24.8, 24.8, 23.0, 20.8, 17.9, −4.1, −4.9; HRMS (ESI) for C₄₀H₆₁N₂O₆SSi [M+H]+ calcd. 725.4014, found 725.3961.

**Ester 16.**

To a stirred solution of the TBS ether 15 (10 mg, 16 µmol) in toluene (3 mL) at rt was added p-toluenesulfonic acid monohydrate (3.8 mg, 20 µmol). The mixture was stirred vigorously at rt for 12 h. The reaction was quenched by addition of saturated aqueous Na₂CO₃ solution (10 mL) and the resulting mixture was extracted with EtOAc (3 × 10 mL). The combined organic extracts were washed with brine (20 mL), dried over anhydrous Na₂SO₄, filtered and concentrated in vacuo. Purification of the residue by flash column chromatography on silica gel (petroleum ether:EtOAc, 4:1 to 2:1) afforded the ester 16 compound (7.8 mg, 95%) as a pale yellow oil. Rᵣ = 0.21 (petroleum ether:EtOAc, 4:1 to 2:1).
EtOAc, 3:2); [±]D<sup>27</sup> = −7.3 (c = 0.70, CHCl<sub>3</sub>); ½max (film) 3007, 2924, 2855, 1736, 988, 964, 937, 812, 802, 756, 733 cm<sup>−1</sup>; ¹H NMR (400 MHz, MeOD) ´ 7.66 (2H, d, J = 8.3 Hz), 7.40 (2H, d, J = 8.3 Hz), 5.93 (1H, s), 5.83–5.75 (1H, m), 5.48–5.31 (3H, m), 4.11 (1H, s), 3.65 (3H, s), 3.61–3.53 (1H, m), 3.51 (1H, d, J = 12.5 Hz), 2.95 (1H, dd, J = 13.9, 6.9 Hz), 2.84 (1H, td, J = 5.4, 1.5 Hz), 2.66 (2H, t, J = 7.3 Hz), 2.44 (3H, s), 2.41–2.28 (3H, m), 2.31 (1H, t, J = 7.4), 2.23–2.16 (2H, m), 2.10–1.96 (3H, m), 1.72–1.50 (9H, m); ¹³C NMR (101 MHz, MeOD) ´ 174.3, 162.0, 153.0, 143.6, 134.8, 133.0, 131.8, 130.0, 129.5, 129.3, 129.0, 126.9, 102.4, 70.3, 58.0, 56.6, 50.6, 49.5, 49.3, 45.6, 41.5, 40.8, 32.7, 28.4, 27.8, 27.6, 26.1, 25.7, 24.7, 24.5, 24.4, 20.1; HRMS (ESI) for C<sub>34</sub>H<sub>45</sub>N<sub>2</sub>O<sub>5</sub>S [M+H]<sup>+</sup> calcd. 593.3044, found 593.3022.

(R)-1-(tert-Butyldimethylsilyloxy)hex-5-en-2-ol (S6).<sup>[5]</sup>

To a stirred solution of the tert-butyldimethylsilyl (R)-glycidyl ether (7.09 g, 37.6 mmol) in Et<sub>2</sub>O (150 mL) at −30 °C was added allyl magnesium chloride (54 mL of a 1.40 M solution in THF, 75 mmol). The mixture was stirred at −30 °C for 1 h and allowed to reach rt over 2 h. The reaction was quenched by addition of saturated aqueous NH₄Cl solution (150 mL) and the resulting mixture was extracted with Et<sub>2</sub>O (3 × 300 mL). The combined organic phases were washed with brine (150 mL), dried over anhydrous MgSO₄, filtered and concentrated in vacuo. Purification of the residue by flash column chromatography on silica gel (petroleum ether:Et<sub>2</sub>O, 100:1 to 50:1) gave the title compound S6 (8.50 g, 98%) as a colourless oil. R<sub>r</sub> = 0.52 (petroleum ether:EtOAc, 10:1); ½max (film) 3520 (br), 3314, 2956, 2928, 2852, 836, 776 cm<sup>−1</sup>; ¹H NMR (500 MHz, CDCl<sub>3</sub>) ´ 5.76 (1H, ddt, J = 16.9, 10.2, 6.6 Hz), 5.03–4.85 (2H, m), 3.64–3.51 (2H, m), 3.34 (1H, dd, J = 9.7, 7.2 Hz), 2.37 (1H, d, J = 3.5 Hz), 2.21–1.97 (2H, m), 1.51–1.37 (2H, m), 0.83 (9H, s), 0.00 (6H, s); ¹³C NMR (126 MHz, CDCl<sub>3</sub>) ´ 138.5, 114.7, 71.4, 67.3, 32.1, 30.0, 26.0, 18.4, −5.2, −5.3.
(R)-5,6-Di(tert-butyldimethylsilyloxy)hex-1-ene (S7). \[6\]

To a stirred solution of the alcohol S6 (7.20 g, 31.2 mmol) in dichloromethane (300 mL) was added imidazole (3.13 g, 46.0 mmol), DMAP (719 mg, 5.89 mmol) and t-BuMe2SiCl (5.70 g, 37.8 mmol). The mixture was stirred at rt for 16 h. The reaction was quenched with saturated aqueous NH₄Cl solution (100 mL) and phases were separated. The aqueous phase was extracted with dichloromethane (3 × 100 mL) and the combined organic extracts were washed with brine (100 mL), dried over anhydrous Na₂SO₄ and concentrated in vacuo. Purification of the residue by flash column chromatography on silica gel (petroleum ether:EtOAc, 97.5:2.5) provided bis-TBS ether S7 (10.6 g, 98%) as a colourless oil. Rᵣ = 0.91 (petroleum ether:Et₂O, 10:1); [±]D²⁷ +21 (c = 1.44, CHCl₃); ½max (film) 3316, 2957, 2930, 2859, 835, 776 cm⁻¹; ¹H NMR (500 MHz, CDCl₃) ' 5.83 (1H, ddt, J = 16.8, 10.2, 6.5 Hz), 5.03–4.98 (1H, m), 4.96–4.93 (1H, m), 3.70–3.65 (1H, m), 3.53 (1H, dd, J = 9.9, 5.4 Hz), 3.41 (1H, dd, J = 9.9, 6.5 Hz), 2.21–2.02 (2H, m), 1.66 (1H, dddd, J = 13.6, 10.3, 5.9, 4.3 Hz), 1.47 (1H, dddd, J = 13.6, 10.2, 7.1, 5.6 Hz), 0.90 (9H, s), 0.89 (9H, s), 0.07–0.04 (12H, m); ¹³C NMR (126 MHz, CDCl₃) ' 139.0, 114.2, 72.6, 67.3, 33.6, 29.4, 26.0, 25.9, 18.4, 18.2, –4.2, –4.7, –5.3, –5.4.

(R)-2-(tert-Butyldimethylsilyloxy)hex-5-en-1-ol (S8).

To a stirred solution of the bis-TBS ether S7 (2.5 g, 7.3 mmol) in THF (60 mL) at −10 °C was added HF-pyridine (23 mL of a 4.81 M solution in THF, 110 mmol). The mixture was stirred at −10 °C for 2 d. The reaction was quenched by addition of saturated aqueous NaHCO₃ solution (100 mL) and the resulting mixture was extracted with Et₂O (3 × 100 mL). The combined organic phases were washed with brine (100 mL), dried over anhydrous MgSO₄, filtered and concentrated in vacuo. Purification of the residue by flash column chromatography on silica gel (petroleum ether:Et₂O, 100:1 to 50:1) gave the alcohol S8 (1.5 g, 90%) as a colourless oil. Rᵣ = 0.48 (petroleum ether: EtOAc, 10:1); [±]D²¹ –8.2 (c = 0.85, CHCl₃); ½max (film) 3395 (br), 2953, 2930, 2886, 2859, 984, 939, 910, 833, 773 cm⁻¹; ¹H NMR (500 MHz, CDCl₃) ' 5.81 (1H, ddt, J = 16.9, 10.2, 6.5 Hz), 5.05–4.99 (1H, m), 4.98–4.94 (1H, m), 3.76 (1H, dtd, J = 6.3, 5.2, 3.7 Hz), 3.58 (1H, ddd, J = 11.0, 5.8, 3.7 Hz), 3.47 (1H, ddd, J = 11.0, 6.3,
5.4 Hz), 2.11–2.04 (2H, m), 1.86 (1H, t, J = 6.2 Hz), 1.63–1.57 (2H, m), 0.91 (9H, s), 0.09 (3H, s), 0.08 (3H, s); 13C NMR (126 MHz, CDCl3) 138.3, 114.7, 72.3, 66.1, 33.1, 29.5, 25.9, 18.1, • 4.4, • 4.5; HRMS (ESI) for C12H26NaO2Si [M+Na]+ calcd. 253.1594, found 253.1587.

(R)-2-(tert-Butyldimethylsilyloxy)hex-5-enal (18).

To a stirred solution of the alcohol S8 (1.4 g, 6.1 mmol) in dichloromethane (50 mL) at 0 °C was added NaHCO3 (1.5 g, 18 mmol) and Dess-Martin periodinane (6.1 g, 12 mmol) in one portion. The mixture was stirred at 0 °C for 2 h, then allowed to warm to rt over 1 h and saturated aqueous Na2S2O3 solution (60 mL) was added. The mixture was then stirred for 30 min and the phases were separated. The organic phase was washed with saturated aqueous Na2CO3 (60 mL), brine (60 mL), dried over anhydrous MgSO4, filtered and concentrated in vacuo. Purification of the residue by flash column chromatography on silica gel (petroleum ether:Et2O, 4:1) gave the title compound 18 (1.3 g, 94%) as a colourless oil. Rf = 0.88 (petroleum ether:EtOAc, 4:1); [±]D21 +34 (c = 0.99, CHCl3); νmax (film) 2955, 2930, 2897, 2859, 1736, 1642, 912, 881, 837, 814, 777 cm−1; 1H NMR (500 MHz, CDCl3) 9.58 (1H, d, J = 1.6 Hz), 5.75 (1H, ddt, J = 16.9, 10.2, 6.6 Hz), 5.04–4.99 (1H, m), 4.98–4.95 (1H, m), 3.97 (1H, ddd, J = 7.2, 5.2, 1.6 Hz), 2.20–2.06 (2H, m), 1.77–1.64 (2H, m), 0.90 (9H, s), 0.06 (3H, s), 0.05 (3H, s); 13C NMR (126 MHz, CDCl3) 204.0, 137.5, 115.4, 77.0, 32.0, 28.7, 25.7, 18.1, • 4.6, −5.0; HRMS (ESI) for C12H24NaO2Si [M+Na]+ calcd. 251.1438, found 251.1426.

Enone 19.

To a stirred solution of i-Pr2NEt (81 µL, 0.58 mmol) in THF (5 mL) at −78 °C was added n-BuLi (247 µL of a 2.27 M solution in THF, 0.56 mmol). The mixture was stirred at −78 °C for 10 min before
addition of the ketone 13 (192 mg, 0.464 mmol) in THF (3 mL). The mixture was then stirred at 
−78 °C for 30 min before addition of the aldehyde 18 (212 mg, 0.928 mmol) in THF (3 mL). The
mixture was stirred at −78 °C for 2 h and allowed to warm to rt overnight. The reaction was quenched
by addition of saturated aqueous NH₄Cl (10 mL) and the resulting mixture extracted with EtOAc (3 × 20 mL). The combined organic extracts were washed with brine (50 mL), dried over anhydrous
Na₂SO₄, filtered and concentrated in vacuo. Purification of the residue by flash column
chromatography on silica gel (petroleum ether:EtOAc, 10:1 to 2:1) gave the enone 19 (145 mg, 50%)
as a yellow gum. Rᵣ = 0.31 (petroleum ether:EtOAc, 2:1); [±]D²⁷ −40 (c = 1.78, CHCl₃); ½max (film) 2953,
2926, 2855, 1721, 1651, 978, 912, 835, 814, 802, 775, 758 cm⁻¹; ¹H NMR (500 MHz, CD₂Cl₂)  δ 7.65
(2H, d, J = 8.2 Hz), 7.37 (2H, d, J = 8.2 Hz), 6.37 (1H, dd, J = 8.9, 1.5 Hz), 5.79 (1H, ddt, J = 17.0,
10.2, 6.7 Hz), 5.57–5.46 (1H, m), 5.41 (1H, dd, j = 11.2, 4.6 Hz), 5.04–4.98 (1H, m), 4.98–4.93 (1H,
m), 4.23 (1H, td, J = 8.5, 4.0 Hz), 3.85 (1H, dd, J = 12.0, 1.7 Hz), 3.77–3.70 (1H, m), 3.47–3.33 (2H,
m), 3.40 (1H, s), 3.10 (1H, td, J = 12.2, 1.5 Hz), 2.83–2.72 (1H, m), 2.53 (1H, ddt, J = 11.9, 6.0, 1.5
Hz), 2.44 (3H, s), 2.33 (1H, td, J = 12.1, 2.4 Hz), 2.21 (1H, d, J = 12.1 Hz), 2.19–2.04 (3H, m), 1.94
(1H, dd, J = 13.8, 9.8 Hz), 1.85–1.47 (6H, m), 1.45–1.33 (3H, m), 0.85 (9H, s), 0.01 (3H, s), −0.05
(3H, s); ¹³C NMR (126 MHz, CD₂Cl₂)  δ 208.1, 143.8, 139.4, 138.1, 138.0, 134.4, 133.5, 129.7, 127.9,
127.6, 114.7, 71.5, 69.1, 59.0, 51.6, 49.8, 46.1, 45.0, 44.2, 39.9, 37.4, 30.7, 29.3, 27.0, 25.5, 25.2,
24.6, 21.3, 17.9, −4.4, −5.0; HRMS (ESI) for C₃₅H₅₃N₂O₄SSi [M+H]⁺ calcd. 625.3490, found
625.3460.

**Furan 20.**

![Furan 20](image)

To a stirred solution of TBS ether 19 (60 mg, 98 µmol) in dichloromethane (10 mL) at rt was added
p-toluenesulfonic acid monohydrate (39 mg, 0.21 mmol). The mixture was stirred vigorously
overnight at rt. The reaction was quenched by addition of saturated aqueous Na₂CO₃ (20 mL) and
the resulting mixture was extracted with EtOAc (3 × 20 mL). The combined organic extracts were
washed with brine (50 mL), dried over anhydrous Na₂SO₄, filtered and concentrated in vacuo. Purification of the residue by flash column chromatography on silica gel (petroleum ether:EtOAc, 4:1 to 2:1) gave the furan 20 (44.2 mg, 93%) as a pale yellow oil. R₂ = 0.45 (petroleum ether: Et₂O, 10:1); [±]D²⁶ + 36 (c = 0.23, CHCl₃); ½max (film) 2924, 2855, 1764, 987, 964, 935, 912, 814, 801, 731 cm⁻¹; ¹H NMR (500 MHz, MeOD) ´ 7.55 (2H, d, J = 8.1 Hz), 7.30 (2H, d, J = 8.1 Hz), 5.84 (1H, ddt, J = 17.0, 10.2, 6.7 Hz), 5.83–5.76 (1H, m), 5.45 (1H, dd, J = 10.2, 7.6 Hz) 5.07–5.01 (1H, m), 4.99–4.95 (1H, m), 4.10 (1H, s), 3.59–3.53 (1H, m), 3.52 (1H, d, J = 12.6 Hz), 3.08–3.03 (4H, m), 2.95 (1H, dd, J = 13.6, 7.1 Hz), 2.85 (1H, dd, J = 5.3, 1.4 Hz), 2.71 (2H, t, J = 7.4 Hz), 2.33 (3H, s), 2.41–2.35 (2H, m), 2.24–2.14 (2H, m), 2.05–1.98 (2H, m), 1.70–1.00 (8H, m); ¹³C NMR (126 MHz, MeOD) ´ 161.9, 143.6, 137.2, 134.8, 133.2, 129.8, 129.5, 127.8, 126.9, 121.0, 114.4, 102.3, 70.3, 58.0, 56.5, 49.4, 49.2, 45.5, 41.5, 40.7, 32.1, 29.4, 28.0, 25.1, 24.7, 24.3, 20.1; HRMS (ESI) for C₉H₇N₂O₃S [M+H]+ calcd. 493.2519, found 493.2507.

Amide 21.

![Amide 21](image)

To a stirred solution of furan 20 (24 mg, 49 µmol) in DME (5 mL) at −78 °C was added sodium naphthalenide (1.0 mL, 0.1 M solution in DME, 0.10 mmol). The mixture was stirred at −78 °C for 10 min before the addition of triethylamine (20 µL, 0.15 mmol) and hex-5-enoyl chloride (9.7 mg, 74 µmol). The mixture was then allowed to reach rt in 2 h. The reaction was quenched by addition of saturated aqueous NH₄Cl (5 mL) and the resulting mixture extracted with EtOAc (3 × 10 mL). The combined organic extracts were washed with brine (30 mL), dried over anhydrous Na₂SO₄, filtered and concentrated in vacuo. Purification of the residue by flash column chromatography on silica gel (petroleum ether:EtOAc, 2:1 to 1:2) gave the amide 20 (19 mg, 90%, 5:4 ratio of rotamers) as a colourless oil. R₁ = 0.09 (petroleum ether:EtOAc, 1:1); [±]D²¹ −13 (c = 1.40, MeOH); ½max (film) 3005, 2924, 2857, 933, 910, 800, 758 cm⁻¹; ¹H NMR (500 MHz, MeOD) ´ 5.99 (0.55H, s), 5.97 (0.44H, s), 5.89–5.72 (3H, m), 5.50–5.44 (1H, m), 5.06–4.93 (4H, m), 4.18 (0.55H, d, J = 13.5 Hz), 4.04 (0.44H, S17
s), 4.02 (0.55H, s), 3.70–3.52 (2H, m), 3.48–3.39 (0.55H, m), 3.37 (0.55H, d, J = 13.5 Hz), 3.33–3.27 (0.55H, m), 3.19 (0.55H, dd, J = 14.4, 7.9 Hz), 3.13–2.90 (3.51H, m), 2.72 (2H, t, J = 7.4 Hz), 2.46–2.36 (3H, m), 2.28–1.99 (7.59H, m), 1.87–1.32 (8H, m); \(^\text{13C}\) NMR (126 MHz, MeOD) \(\delta\) 174.2, 173.6, 162.0, 161.8, 153.0, 137.9, 137.8, 137.3, 137.2, 133.3, 133.1, 131.5, 131.0, 130.2, 129.5, 114.4, 114.3, 114.2, 102.4, 102.3, 69.9, 69.8, 58.7, 58.1, 56.0, 55.9, 55.8, 55.8, 49.2, 49.1, 48.7, 46.0, 45.0, 44.6, 42.3, 42.2, 40.9, 39.1, 33.0, 32.9, 32.3, 32.1, 31.9, 28.0, 27.8, 25.0, 24.8, 24.7, 24.6, 24.2, 24.2, 24.1, 24.1, 24.0; HRMS (ESI) for \(\text{C}_{28}\text{H}_{39}\text{N}_{2}\text{O}_{2}\) [M+H]\(^+\) calcd. 435.3006, found 435.2895.

**Triene 22.**\(^7\)

To a stirred solution of amide 21 (14 mg, 32 µmol) in toluene (10 mL) at 0 °C was added Red-Al (14 µL, 65% w/w solution in toluene, 48 µmol). The mixture was stirred at 0 °C for 30 min and then heated at reflux for 3 h. The mixture was then cooled to 0 °C and the reaction was quenched by the addition of saturated aqueous solution of Rochelle’s salt (5 mL). The resulting mixture was extracted with EtOAc (3 × 15 mL) and the combined organic extracts were then washed with brine (30 mL), dried over anhydrous Na\(_2\)SO\(_4\), filtered and concentrated in vacuo. Purification of the residue by flash column chromatography on silica gel (petroleum ether:EtOAc, 2:1 to 1:1) gave the triene 22 (11 mg, 81%) as a colourless oil. \(R_f = 0.23\) (petroleum ether:EtOAc, 1:1); \([\pm]\)D\(_{23}\) +17.1 (c = 1.05, CHCl\(_3\)); \(\lambda_{\text{max}}\) (film) 3077, 3007, 2922, 2855, 2799, 2760, 1641, 966, 937, 910, 800, 733 cm\(^{-1}\); \(^1\)H NMR (600 MHz, CDCl\(_3\)) \(\delta\) 5.84 (1H, ddt, J = 16.9, 10.2, 6.6 Hz), 5.80 (1H, ddt, J = 16.7, 10.2, 6.7 Hz), 5.83 (1H, m), 5.58–5.52 (1H, m), 5.48 (1H, dd, J = 10.6, 6.0 Hz), 5.09–5.03 (1H, m), 5.02–4.97 (2H, m), 4.95–4.91 (1H, m), 4.15 (1H, s), 3.33–3.25 (1H, m), 3.12–3.04 (1H, m), 3.00 (1H, ddd, J = 12.8, 5.9, 2.0 Hz), 2.92 (1H, d, J = 11.9 Hz), 2.68 (2H, t, J = 7.6 Hz), 2.59–2.50 (3H, m), 2.41–2.26 (4H, m), 2.21–2.13 (1H, m), 2.10 (1H, dd, J = 13.0, 8.0 Hz), 2.07–2.01 (4H, m), 2.00–1.94 (1H, m), 1.83–1.72 (1H, m), 1.69–1.55 (2H, m), 1.55–1.46 (3H, m), 1.42–1.27 (4H, m); \(^{13}\)C NMR (151
MHz, CDCl₃) 160.1, 155.7, 139.1, 137.8, 134.0, 133.1, 129.1, 115.3, 114.5, 102.7, 70.9, 62.6, 58.8, 58.8, 56.7, 51.8, 51.3, 48.3, 41.0, 33.8, 32.4, 31.7, 28.6, 27.7, 27.0, 26.6, 25.3, 25.0; HRMS (ESI) for C₂₈H₄₁N₂O [M+H]+ calcd. 421.3213, found 421.3199.


The diene 22 (10 mg, 23 µmol) in dichloromethane (10 mL) was added to a solution of the Grubbs second-generation catalyst (3.9 mg, 4.6 µmol) in dichloromethane (100 mL) and the resulting solution was heated at reflux for 2 h. The solution was cooled to rt, MeOH (10 mL) was added and the mixture was concentrated in vacuo. Purification of the residue by flash column chromatography on silica gel (petroleum ether:EtOAc, 4:1 to pure EtOAc) afforded a mixture of the lactams Z-24 and E-24 (7.7 mg, 80%, Z/E 1.45:1) as a colourless oil. The mixture of geometrical isomers was separated by chromatography on basic alumina (petroleum ether:EtOAc, 8:1 to 2:1).

Z-24. Rf = 0.15 (petroleum ether: EtOAc, 2:1); [±]D²⁴ −36.8 (c = 1.00, CHCl₃); ½max (film) 3005, 2926, 2854, 1642 cm⁻¹; ¹H NMR (400 MHz, MeOD) 5.93 (1H, s), 5.87–5.79 (1H, m), 5.52–5.46 (1H, m), 5.36–5.30 (2H, m), 4.54 (1H, d, J = 13.5 Hz), 4.06 (1H, s), 3.78–3.70 (1H, m), 3.41 (1H, dd, J = 11.2, 6.2 Hz), 3.21–3.12 (1H, m), 3.06–3.03 (1H, m), 3.05 (1H, d, J = 13.5 Hz), 2.95 (1H, dd, J = 13.5, 9.7 Hz), 2.78–2.71 (2H, m), 2.64–2.55 (1H, m), 2.54–2.42 (3H, m), 2.31–2.20 (2H, m), 2.18–2.10 (2H, m), 2.05 (1H, dd, J = 12.5, 4.8 Hz), 1.98–1.86 (3H, m), 1.72–1.62 (7H, m) ¹³C NMR (101 MHz, MeOD) 174.6, 161.9, 154.6, 133.4, 131.5, 130.8, 129.3, 128.8, 104.0, 70.2, 60.1, 56.5, 49.3, 44.5, 42.8, 41.8, 41.2, 29.8, 29.4, 27.7, 27.6, 27.5, 25.7, 24.9, 23.5, 22.0; HRMS (ESI) for C₂₆H₃₅N₂O₂ [M+H]+ calcd. 407.2693, found 407.2677.

E-24. Rf = 0.26 (petroleum ether:EtOAc, 2:1); [±]D²⁴ −87 (c = 0.50, CHCl₃); ½max (film) 3003, 2922, 2853, 950, 849, 802, 799 cm⁻¹; ¹H NMR (400 MHz, MeOD) 6.01 (1H, s), 5.91–5.83 (1H, m), 5.50 (1H, dd, J = 10.4, 8.0, 1.1 Hz), 5.33–5.24 (1H, m), 5.13 (1H, dd, J = 15.1, 8.5, 5.0 Hz), 4.51 (1H, d, J = 13.3 Hz), 4.12 (1H, brs), 3.84–3.76 (1H, m), 3.33–3.29 (2H, m), 3.07–3.04 (1H, m), 3.05 (1H, d, J = 13.3 Hz), 2.95–2.88 (2H, m), 2.83–2.75 (2H, m), 2.72–2.67 (1H, m), 2.18–2.10 (2H, m), 2.05 (1H, dd, J = 12.5, 4.8 Hz), 1.98–1.86 (3H, m), 1.72–1.62 (7H, m) ¹³C NMR (101 MHz, MeOD) 174.6, 161.9, 154.6, 133.4, 131.5, 130.8, 129.3, 128.8, 104.0, 70.2, 60.1, 56.5, 49.3, 44.5, 42.8, 41.8, 41.2, 29.8, 29.4, 27.7, 27.6, 27.5, 25.7, 24.9, 23.5, 22.0; HRMS (ESI) for C₂₆H₃₅N₂O₂ [M+H]+ calcd. 407.2693, found 407.2677.
Hz), 2.97 (1H, dd, J = 13.5, 9.3), 2.82–2.77 (1H, m), 2.76 (2H, dd, J = 6.8, 6.0 Hz), 2.55–2.45 (1H, m), 2.34–1.95 (8H, m), 1.86 (1H, ddd, J = 17.0, 7.8, 4.3 Hz), 1.80–1.33 (8H, m); ¹³C NMR (101 MHz, MeOD) \( \delta \) 175.3, 163.3, 155.9, 135.2, 132.9, 132.3, 131.6, 130.3, 104.7, 71.6, 62.6, 58.4, 50.8, 46.3, 43.4, 43.2, 42.1, 32.9, 31.8, 30.6, 29.1, 29.0, 26.2, 25.9, 23.2, 22.6; HRMS (ESI) for C₂₆H₃₅N₂O₂ [M+H]⁺ calcd. 407.2693, found 407.2676.

24E-Nakadomarin A (23).

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To a stirred solution of amide E-24 (8.3 mg, 20 µmol) in toluene (10 mL) at 0 °C was added Red-Al (14 µL, 65% w/w solution in toluene, 48 µmol). The mixture was stirred at 0 °C for 30 min and then heated at reflux for 3 h. The mixture was then cooled to 0 °C and the reaction was quenched by the addition of saturated aqueous solution of Rochelle’s salt (10 mL). The resulting mixture was extracted with EtOAc (3 × 15 mL). The combined organic extracts were washed with brine (30 mL), dried over anhydrous Na₂SO₄, filtered and concentrated in vacuo. Purification of the residue by flash column chromatography on silica gel (EtOAc) gave the title compound 23 (6.7 mg, 84%) as a colourless oil. R\(_f\) = 0.31 (EtOAc:MeOH, 3:1); \([±]D^{23}\) 73 (c = 1.66, MeOH); \(\lambda_{max}\) (film) 2922, 2876, 2855, 958, 937, 800, 736 cm⁻¹; \(¹\)H NMR (400 MHz, MeOD) \( \delta \) 5.92 (1H, s), 5.88–5.79 (1H, m), 5.53–5.46 (1H), 5.27–5.22 (2H, m), 4.07 (1H, s), 3.77–3.69 (1H, m), 3.08 (1H, d, J = 12.0 Hz), 3.10–3.03 (1H, m), 2.86–2.74 (3H, m), 2.73–2.60 (2H, m), 2.44–2.37 (2H, m), 2.32 (1H, d, J = 12.3 Hz), 2.33–2.15 (3H, m), 2.12–1.96 (4H, m), 1.92 (1H, dd, J = 12.4, 4.9 Hz), 1.83 (1H, ddd, J = 14.0, 6.6, 2.3 Hz), 1.74–1.55 (4H, m), 1.52 (1H, dd, J = 12.4, 10.3 Hz), 1.46–1.02 (5H, m); \(¹³\)C NMR (101 MHz, MeOD) \( \delta \) 163.0, 155.0, 135.2, 135.0, 133.7, 131.1, 129.2, 104.1, 74.6, 63.1, 60.2, 59.4, 58.1, 50.9, 46.4, 43.9, 34.6, 33.3, 29.3, 29.1, 28.9, 27.7, 26.0, 25.7, 23.1; HRMS (ESI) for C₂₆H₃₃N₂O [M+H]⁺ calcd. 393.2900, found 393.2887.
To a stirred solution of amide **Z-24** (11 mg, 27 µmol) in toluene (10 mL) at 0 °C was added Red-Al (18 µL, 65% w/w solution in toluene, 62 µmol). The mixture was stirred at 0 °C for 30 min and then heated reflux for 3 h. The mixture was then cooled to 0 °C and the reaction was quenched by the addition of saturated aqueous solution of Rochelle’s salt (10 mL). The resulting mixture was extracted with EtOAc (3 × 20 mL) and the combined organic extracts were washed with brine (30 mL), dried over anhydrous Na₂SO₄, filtered and concentrated *in vacuo*. Purification of the residue by flash column chromatography on silica gel (EtOAc) gave (−)-nakadomarin A (1) (9.5 mg, 89%) as a colourless oil. \( R_f = 0.31 \) (EtOAc:MeOH, 3:1); \( [\pm]_{D}^{23} = -69 \) (c = 1.06, MeOH); \( \lambda_{\text{max}} \) (film) 3077, 3003, 2928, 2855, 2801, 2758, 966, 937, 910, 799, 758 cm⁻¹; \( ^1\text{H NMR} \) (400 MHz, MeOD) \( \delta \) 5.88 (1H, s), 5.86–5.78 (1H, m), 5.54–5.41 (2H, m), 5.31–5.22 (1H, m), 3.94 (1H, s), 3.79–3.72 (1H, m), 3.05 (1H, d, \( J = 12.1 \) Hz), 3.06–3.00 (1H, m), 2.84 (1H, brs), 2.81–2.69 (2H, m), 2.64–2.58 (2H, m), 2.53–2.28 (4H, m), 2.32 (1H, d, \( J = 12.0 \) Hz), 2.21–1.96 (4H, m), 1.92 (1H, dd, \( J = 12.4, \) 4.8 Hz), 1.95–1.89 (1H, m), 1.83 (1H, ddd, \( J = 14.0, \) 7.1 Hz, 2.6 Hz), 1.76–1.58 (4H, m), 1.51 (1H, dd, \( J = 12.4, \) 10.1 Hz), 1.43–1.23 (2H, m), 1.11–1.02 (2H, m), 0.94–0.82 (1H, m); \( ^{13}\text{C NMR} \) (101 MHz, MeOD) \( \delta \) 162.5, 156.2, 135.4, 134.7, 132.2, 131.3, 129.3, 104.8, 74.8, 63.6, 60.6, 59.3, 58.4, 50.9, 46.1, 43.4, 43.1, 29.5, 29.2, 29.1, 28.8, 27.2, 27.1, 26.0, 25.8, 23.0; HRMS (ESI) for C₂₆H₃₇N₂O [M+H]^+ calcd. 393.2900, found 393.2887.
References


S1
X-Ray Data for Ketone 13

Empirical formula: $\text{C}_{23}\text{H}_{30}\text{N}_{2}\text{O}_{3}\text{S}$

Formula weight: 414.55

Temperature: 150(2) K

Wavelength: 0.71073

Crystal system: orthorhombic

Space group: $P \bar{2}1 \bar{2}1 \bar{2}1$

Unit cell dimension:
- $a = 12.6438(12)$ Å, $\pm = 90^\circ$
- $b = 17.2238(18)$ Å, $\pm = 90^\circ$
- $c = 29.188(3)$ Å, $\pm = 90^\circ$

Volume: $6356.4(11)$ Å$^3$

Z: 12

Density (calculated): 1.300 mg/m$^3$

Radiation type: MoK$\alpha$

Absorption coefficient: 0.180 μ/mm

$F(000)$: 2664

Crystal size: $0.512 \times 0.120 \times 0.048$

Index ranges: $-15 \leq h \leq 15$, $-20 \leq k \leq 20$, $-34 \leq l \leq 34$

Number of reflections measured: 74994

Number of independent reflections: 11253

$R_{int}$: 0.093

Completeness to $\theta = 25.242^\circ$: 0.981

Absorption correction type: Multi-scan

Max. and min. transmission: 0.862 and 0.698

Refinement method: Full-matrix least-squares on $F^2$

Data / restraints / parameters: 11253 / 0 / 788

Goodness-of-fit on $F^2$: 1.018

Final $R$ indices [$I > 2\sigma(I)$]: $R_1 = 0.0608$, $wR_2 = 0.1060$

$R$ indices (all data): $R_1 = 0.0399$, $wR_2 = 0.0938$

Largest diff. peak and hole: 0.219 and $-0.253$ e.Å$^{-3}$

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