Supporting Information

Synthesis and Evaluation of a 2,11-Cembranoid-Inspired Library

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General experimental

All anhydrous solvents and reagents were obtained from commercial suppliers and used without further purification unless otherwise noted. Flash column chromatography was carried out on Merck silica gel 60 (0.040-0.063 mm).

All melting points were determined on a Stanford Research Systems MPA120 EZ-Melt melting point apparatus.

Analytical thin layer chromatography (TLC) was performed on pre-coated aluminium sheets of silica (60 F_{254}, Merck) and visualised by short-wave UV light, potassium permanganate vanillin or anisaldehyde dip. Infrared spectra were recorded on a Perkin Elmer Spectrum RX-1 or a Bruker Alpha-P FT-IR spectrometer. Optical rotations were recorded on a Bellingham and Stanley ADP440 Polarimeter.

$^1$H-nuclear magnetic resonance spectra were recorded at 500 MHz on Bruker Avance 500 spectrometers using an internal deuterium lock. Chemical shifts were measured in parts per million (ppm) relative to tetramethylsilane ($\delta = 0$) using the following internal references for residual protons in the solvent: CDCl$_3$ ($\delta$ 7.26), CD$_3$OD ($\delta$ 3.32), pyridine-d$_6$ ($\delta$ 8.74) and acetone-d$_6$ ($\delta$ 2.05).

$^{13}$C-nuclear magnetic resonance spectra were recorded at 126 MHz on Bruker Avance 500 spectrometers using an internal deuterium lock. All chemical shift values were reported in ppm relative to tetramethylsilane ($\delta = 0$). The following internal references were used: CDCl$_3$ ($\delta_C$ 77.0), CD$_3$OD ($\delta$ 49.0) and Pyridine-d$_5$ ($\delta$ 150.3).

LC-MS analyses were performed on a Micromass LCT / Water’s Alliance 2795 HPLC system using the column, flow rates and solvent gradient specified below at a temperature of 22 °C.

**UV Detector:** Waters 2487 Dual λ Absorbance Detector (detecting at 254nm)

**LCT Gradients:**

**Method A 6min Grad**

Flow rate 1 mL/min; Phenomenex Gemini 3u C18 column (3cm x 4.6mm i.d), solvent system-aqueous (0.1% Formic Acid) and methanol

| Time / min | % MeOH in MP |
|------------|--------------|
| 0          | 10           |
| 0.3        | 10           |
| 0.6        | 20           |
| 4.5        | 90           |
| 5.4        | 90           |
| 5.7        | 10           |
| 6.0        | 10           |
Method B 6min Non-Polar

Flow rate 1mL/min; Phenomenex Gemini 3u C18 column (3cm x 4.6mm i.d), solvent system aqueous (0.1% Formic Acid) & Methanol

| Time / min | % MeOH in MP |
|------------|--------------|
| 0          | 10           |
| 0.3        | 10           |
| 0.6        | 20           |
| 3          | 90           |
| 5.4        | 90           |
| 5.7        | 10           |
| 6.0        | 10           |

Method C Fast4min

Flow rate 2 mL/min; Merck Chromolith SpeedROD RP-18e 50x4.6mm column, solvents A = MeOH, B = Aqueous (0.1% Formic Acid)

| Time / min | A (%) | B (%) |
|------------|-------|-------|
| 0          | 10    | 90    |
| 2.25       | 90    | 10    |
| 3          | 90    | 10    |
| 3.3        | 10    | 90    |
| 3.5        | 10    | 90    |

Method D Fast4minLipophilic

Flow: 2 mL/min; Merck Chromolith SpeedROD RP-18e 50x4.6mm column, solvents A = MeOH, B = Aqueous (0.1% Formic Acid)

| Time/min | A (%) | B (%) |
|----------|-------|-------|
| 0        | 10    | 90    |
| 1.75     | 90    | 10    |
| 3        | 90    | 10    |
| 3.3      | 10    | 90    |
| 3.5      | 10    | 90    |

Method E Fast4minLipophilic II

Flow: 2 mL/min; Merck Chromolith SpeedROD RP-18e 50x4.6mm column, solvents A = MeOH, B = Aqueous (0.1% Formic Acid)

| Time/min | A (%) | B (%) |
|----------|-------|-------|
| 0        | 10    | 90    |
| 1        | 100   | 0     |
| 3        | 100   | 0     |
High resolution mass spectrometry data was collected using an Agilent 6210 Time Of Flight Mass Spectrometer with a Merck Chromolith SpeedROD RP-18e 50x4.6mm column and the solvent gradients as specified below:

**Flow:** 2 mL/min, Merck Chromolith SpeedROD RP-18e 50x4.6mm column, solvent A = MeOH, B = Aqueous (0.1% Formic Acid)

| Time / min | A (%) | B (%) |
|------------|-------|-------|
| 0          | 10    | 90    |
| 2.5        | 90    | 10    |
| 3.5        | 90    | 10    |
| 3.8        | 10    | 90    |
| 4          | 10    | 90    |

**Reference Masses:**

Caffeine [M+H]^+ = 195.087652; Reserpine [M+H]^+ = 609.280657; (1H,1H,3H-tetrafluoropentoxy)phosphazene [M+H]^+ = 922.009798.

UV detection was at 254 nm and ionisation was positive ion electrospray. Molecular weight scan range was 50-1000. Samples were prepared as 1 mg/mL in methanol or DMSO with 3 μL injected on a partial loop fill.

Microanalysis was carried out by Stephen Boyer, London Metropolitan Elemental Analysis Service. (Stephen Boyer, School of Human Sciences, Science Centre, London Metropolitan University, 29 Hornsey Road, London N7 7DD)
Experimental procedures

(S)-5-((tert-Butyldiphenylsilyloxy)methyl)furan-2-(5H)one 8

(S)-5-Hydroxymethylfuran-2-(5H)one 9 (1.00 g, 8.76 mmol) was added to a stirred solution of imidazole (660 mg, 9.76 mmol) in DMF (3 mL) and cooled to 0 °C. TBDPSCI (2.61 g, 2.47 mL, 9.76 mmol) was added dropwise and the reaction mixture was stirred for 30 min at 0 °C. The reaction was allowed to warm to RT and stirring continued for 2.5 h. The reaction mixture was quenched with sat. aq. NaHCO₃ (50 mL) and extracted with EtOAc (2 x 50 mL). The combined organic extracts were washed with water (50 mL) and brine (50 mL), then dried (MgSO₄) and concentrated to yield a clear oil which crystallised on standing. The product was recrystallised from hexane to yield 8 as white crystals (2.38 g, 87%). mp (79-81 °C) [lit.¹ 79-80 °C]; [α]²₃D -85 (c=1.50, CHCl₃) [lit.² -81.5]; IR (film) 2930, 2857, 1750 (CO), 1428, 1134 cm⁻¹; ¹H NMR (500 MHz, CDCl₃) δ 7.78-7.59 (4H, m, Ph), 7.53-7.34 (7H, m, Ph, H-4), 6.19 (1H, dd, J=2.0, 6.0, H-3), 5.09-5.07 (1H, m, H-5), 3.92 (1H, dd, J=5.0, 11.0, Ha-6), 3.88 (1H, dd, J=5.0, 11.0, Hb-6), 1.06 (9H, s, tBu); ¹³C NMR (125 MHz, CDCl₃) δ 172.8 (C2), 154.0 (C4), 135.6 (2 x Ph), 135.5 (2 x Ph), 132.8 (iPh), 132.5 (iPh), 130.0 (2 x Ph), 127.9 (4 x Ph), 122.7 (C3), 83.2 (C5), 63.4 (C6), 26.7 (tBu), 19.2 (Si-C); LC-MS (ESI⁺) m/z 375 [M+Na⁺], Rₜ 5.43 min [method B]; HRMS [M+Na⁺] calcd for C₂₁H₂₄O₃SiNa 375.1387; found 375.1390; Found: C, 71.33; H, 6.88%; C₂₁H₂₄O₃Si requires: C, 71.33; H, 6.86%.

(3S)-3-((tert-Butyldiphenylsilyloxy)methyl)-3a,4,7,7a-tetrahydroisobenzofuran-1-(3H)-one 10

Method A¹,³

(S)-5-((tert-Butyldiphenylsilyloxy)methyl)furan-2-(5H)one 8 (500 mg, 1.42 mmol) was added to a stirring solution of AlCl₃ (50 mg, 0.375 mmol) in CH₂Cl₂ (6 mL) in a pressure tube and cooled to 0 °C. A butadiene canister was cooled to 0 °C and butadiene (approx 3.0 mL, 25 equiv) poured into the pressure tube. The tube was sealed and heated to 55 °C for 6 d. The reaction was quenched in ice-cold sat. aq. NaHCO₃ (50 mL) and extracted with CH₂Cl₂ (25 mL x 2). The organic layers were separated, washed with brine (50 mL x 2) and dried over MgSO₄. The solvent was removed in vacuo. The crude mixture was purified by column chromatography on silica gel (15% EtOAc:hexane) to yield 10 as a clear oil (227 mg, 40%).

Method B
Carried out in triplicate- Trifluoromethanesulfonamide (465 mg, 3.125 mmol) was dissolved in 3.0 mL CH₂Cl₂ in a pressure tube. 1 M Dimethylaluminium chloride in hexane (6.25 mL, 6.250 mmol) was added slowly dropwise by syringe (ensuring no contact during addition with the vessel wall) under argon (gas evolution) and the solution stirred for 30 minutes. (S)-5-((tert-Butyldiphenylsilyloxy)methyl)furan-2-(5H)one 8 (1.00 g, 2.841 mmol) and butadiene (20% w/w in toluene, 9.5 mL, 28.4 mmol) were added, the tube sealed and heated to 60 °C for 2 d. The three reactions were combined for work-up; The vessels was cooled to 0 °C before opening and diluted with Et₂O (300 mL). The mixture was quenched cautiously by dropwise addition of 1M aqueous NaOH (200 mL). Gas was evolved. The aqueous layer was further extracted into Et₂O (60 mL x 2). The combined organics were washed with brine (100 mL) and dried over MgSO₄. The solvent was removed in vacuo. The crude mixture was purified by column chromatography on silica gel (10-20% EtOAc:hexane) to yield 10 as a clear oil (2.82 g, 82%). \([\alpha]^{20}_{D} +13.0 \; \text{(c=1.00, CHCl}_3) \; \text{[lit.} +19.8; \text{IR (film) 3070, 3046, 2930, 2856, 1778 (CO), 1589 cm}^{-1}; \text{\textsuperscript{1}H NMR (500 MHz, CDCl}_3) \; \delta \; 7.73-7.67 \; (4H, m, Ph), 7.50-7.39 \; (6H, m, Ph), 5.89-5.79 \; (2H, m, H-6, H-5), 4.17 \; (1H, dt, J=4.0, 4.0, H-3), 3.89 \; (1H, dd, J=4.0, 11.5, H-8), 3.79 \; (1H, dd, J=4.5, 11.5, H-8), 3.01 \; (1H, ddd, J=4.5, 8.5, 8.5, H-3a), 2.74-2.69 \; (1H, m, H-7a), 2.48-2.24 \; (3H, m, H-4, Ha-7), 1.97-1.90 \; (1H, m, Hb-7), 1.10 \; (9H, s, tBu); \text{\textsuperscript{13}C NMR (125 MHz, CDCl}_3) \; \delta \; 179.5 \; (C1), 135.6 \; (2 \; x \; Ph), 135.5 \; (2 \; x \; Ph), 132.9 \; (Ph), 132.6 \; (Ph), 129.9 \; (Ph), 127.9 \; (2x \; Ph), 126.4 \; (C5 or C6), 125.6 \; (C5 or C6), 84.8 \; (C3), 64.3 \; (C8), 37.4 \; (C7a), 34.1 \; (C3a), 26.8 \; (tBu), 25.5 \; (C7), 22.5 \; (C4), 19.1 \; (Si-C); \text{LC-MS (ESI')} \; m/z \; 429.18 \; [M+Na]\textsuperscript{+}, \; R_t \; 3.08 \; \text{[method A]; HRMS [M+Na\textsuperscript{+}]} \; \text{calcd for C}_{25}\text{H}_{30}\text{O}_{2} \; \text{Na} \; 429.1856; \; \text{found} \; 429.1866. \; \text{Found:} \; \text{C, } 73.97; \; \text{H, } 7.51\%, \; \text{C}_{25}\text{H}_{30}\text{O}_{2} \; \text{Na requires:} \; \text{C, } 73.85; \; \text{H, } 7.44\%.

\text{(3S,3aS,7aR)-3-((tert-Butyldiphenylsilyloxy)methyl)-1,3,3a,4,7,7a-hexahydroisobenzofuran-1-ol 11}

\begin{center}
\includegraphics[width=0.2\textwidth]{11.png}
\end{center}

(3S)-3-((tert-Butyldiphenylsilyloxy)methyl)-3a,4,7,7a-tetrahydroisobenzofuran-1-(3H)one 10 (150 mg, 0.37 mmol) was dissolved in anhydrous CH₂Cl₂ (1 mL) and cooled to -78 °C under N₂. DIBAL-H (1.0 M in toluene, 0.40 mL, 0.40 mmol) was added dropwise. The reaction was stirred at -78 °C for 80 min then quenched with EtOAc (4 mL). The solution was warmed to RT and a sat. aq. solution of Rochelles salt (6 mL) was added and the mixture was stirred for 3 h. The aqueous layer was separated and extracted with CH₂Cl₂ (3 x 5 mL). The organic layers were combined, dried over MgSO₄ and solvent removed in vacuo to yield 11 as a clear oil (145 mg, 97%). \([\alpha]^{23}_{D} -9.13 \; \text{(c=2.43 CH}_2\text{Cl}_2); \text{IR (film) 3409, 3024, 2929, 2856, 1427 \; cm}^{-1}; \text{\textsuperscript{1}H NMR (500 MHz, CDCl}_3) \; \delta \; 7.75-7.70 \; (4H, m, Ph), 7.51-7.39 \; (6H, m, Ph), 5.75-5.72 \; (1H, m, H-6), 5.64-5.58 \; (1H, m, H-5), 5.09 \; (1H, d, J=6.0, H-3), 3.87-3.82 \; (2H, m, H-1, Ha-8), 3.63 \; (1H, dd, J=3.0, 10.0, Hb-8), 2.90 \; (1H, d, J=6.0, OH), 2.74 \; (1H, dd, J=7.5, 15.0, H-7a),
2.31-2.16 (3H, m, H-3a, H-7, H-4), 1.88-1.79 (2H, m, H-7, H-4), 1.11 (9H, s, 'Bu); \(^{13}\)C NMR (125 MHz, CDCl\(_3\)) \(\delta\) 135.7 (2 x Ph), 135.6 (2 x Ph), 133.0 (Ph), 132.9 (Ph), 129.8 (Ph), 129.7 (Ph), 127.7 (2 x Ph), 127.6 (2 x Ph), 125.0 (C5 or C6), 124.4 (C5 or C6), 103.1 (C3), 83.5 (C1), 64.6 (C8), 41.7 (C3a), 32.2 (C7a), 26.9 ('Bu), 23.3 (C7 or C4), 19.2 (Si-C); LC-MS (ESI\(^+\)) m/z 431 [M+Na\(^+\)], Rt 3.19 min [method B], HRMS [M+Na\(^+\)] calcd for C\(_{25}\)H\(_{32}\)O\(_3\)SiNa 431.2013; found 431.2009.

\(((1S,3S,3aR,7aS)-3-Allyl-1,3,3a,4,7,7a-hexahydroisobenzofuran-1-yl)methoxy)(\textit{tert}-butyl)diphenylsilane 12

\(((1S,3S,3aR,7aS)-3-Allyl-1,3,3a,4,7,7a-hexahydroisobenzofuran-1-yl)methoxy)(\textit{tert}-butyl)diphenylsilane 12 (360 mg, 0.83 mmol) was dissolved in THF (4.2 mL). The solution was cooled to 0 °C under N\(_2\), then TBAF (2.49 mL, 1.0 Mol in THF, 1.49 mmol) was added by syringe. The reaction was stirred for 2 h at 0 °C before quenching with Et\(_2\)O (30 mL). The reaction mixture was washed with H\(_2\)O (30 mL) and extracted into Et\(_2\)O (2 x 30 mL). The combined organic layers were dried with MgSO\(_4\) and solvents were removed \textit{in vacuo} to yield the crude product as a clear oil. This was purified by column chromatography on silica gel (10% EtOAc:hexane) to yield 14 as a clear oil (132 mg, 82%).
[α]$_D^{22}$ +17.6 (c=2.60 CH$_2$Cl$_2$); IR (film) 3414, 3075, 3026, 2975, 2841, 1435 cm$^{-1}$; $^1$H NMR (500 MHz, CDCl$_3$) δ 5.79 (1H, tdd, $J$=7.0, 10.0, 17.5, H-10), 5.31 (1H, dd, $J$=6.5, 12.5, Hb-8), 2.39-2.28 (5H, m, Ha-9, H-7a, H-4a, Ha-7, Ha-4), 2.08 (1H, ddd, $J$=6.0, 6.5, 13.0, Hb-9), 1.97-1.93 (2H, Hb-7, Hb-4); $^{13}$C NMR (125 MHz, CDCl$_3$) δ 134.9 (C10), 125.8 (C5 or C6), 125.5 (C6 or C5), 117.1 (C11), 83.9 (C1 or C3), 83.7 (C1 or C3), 63.7 (C8), 39.7 (C4a or C7a), 39.5 (C9), 35.7 (C4a or C7a), 25.0 (C4 or C7), 24.4 (C4 or C7); LC-MS (ESI$^+$) m/z 217 [M+Na$^+$], R$_t$ 2.38 min [method D]; HRMS [M+Na$^+$] calcd for C$_{12}$H$_{18}$O$_3$Na 217.1192; found 217.1197.

But-2'-enoic acid (1S, 3S, 3aR, 7aS)-allyl-1, 3, 3a, 4, 7, 7a-hexahydro-isobenzofuran-8-ylmethyl ester 15

\[ \text{But-2'-enoic acid (1S, 3S, 3aR, 7aS)-allyl-1, 3, 3a, 4, 7, 7a-hexahydro-isobenzofuran-8-ylmethyl ester 15} \]

\[ \text{[((1S,3S,3aR,7aS)-3-Allyl-1,3,3a,4,7,7a-hexahydroisobenzofuran-1-yl)methanol 14 (40 mg, 0.21 mmol) was dissolved in CH$_2$Cl$_2$ (1.0 mL). Pyridine (0.05 mL, 0.63 mmol) and trans-crotonyl chloride (26 µL, 0.27 mmol) were added and the reaction stirred at RT for 16 h. The reaction mixture was then diluted with CH$_2$Cl$_2$ (10 mL), and washed with H$_2$O (2 x 10 mL) and brine (10 mL). The combined aqueous layers were extracted with CH$_2$Cl$_2$ (2 x 10 mL). The organic layer was dried with MgSO$_4$ and solvent was removed in vacuo. The resultant crude oil was purified by column chromatography on silica gel (15% EtOAc:hexane) to yield 15 as a clear oil (15 mg, 32%). [α]$^{19}$D -1.90 (c=0.8, CH$_2$Cl$_2$); IR (film) 3027, 2916, 2843, 1723 (CO), 1443 cm$^{-1}$; $^1$H NMR (500 MHz, CDCl$_3$) δ 7.01 (1H, qd, $J$=7.0, 14.0, H-3'), 5.98-5.80 (2H, m, H-2', H-10), 5.79-5.65 (2H, m, H-5, H-6), 5.15-5.04 (2H, m, H-11), 4.25 (1H, dd, $J$=4.0, 11.5, Ha-8), 4.11 (1H, dd, $J$=6.0, 11.5, Hb-8), 3.88 (1H, ddd, $J$=6.0, 6.0, 6.0 , H-1), 3.76 (1H, ddd, $J$=6.0, 6.0, 6.0, H-3'), 2.32-2.19 (5H, m, H-9, H-7a, H-7, H-4), 2.17-2.09 (1H, m, H-3a), 2.01-1.91 (2H, m, H-4, H-7), 1.89 (3H, dd, $J$=1.5, 7.0, H-4'); $^{13}$C NMR (125 MHz, CDCl$_3$) δ 199.4 (C1'), 145.0 (C3'), 134.9 (C2'), 125.7 (C5 or C6), 125.5 (C5 or C6), 122.5 (C10), 117.0 (C11), 83.9 (C3), 81.3 (C1), 65.8 (C8), 39.5 (C9), 39.1 (C3a), 37.0 (C7a), 24.8 (C4 or C7), 24.5 (C4 or C7), 17.9 (C4'); LC-MS (ESI$^+$) m/z 285 [M+Na$^+$], R$_t$ 2.83 min [method D]; HRMS [M+Na$^+$] calcd for C$_{16}$H$_{22}$O$_3$Na 285.1461; found 285.1465.} \]

((1S,3S,3aR,7aS)-3-Allyl-1,3,3a,4,7,7a-hexahydroisobenzofuran-1-yl)methyl but-3'-enoate 16

\[ \text{((1S,3S,3aR,7aS)-3-Allyl-1,3,3a,4,7,7a-hexahydroisobenzofuran-1-yl)methyl but-3'-enoate 16} \]

\[ \text{[((1S,3S,3aR,7aS)-3-Allyl-1,3,3a,4,7,7a-hexahydroisobenzofuran-1-yl)methanol 14 (40 mg, 0.213 mmol) was dissolved in CH$_2$Cl$_2$ (1.0 mL). Triethylamine (90 µL, 0.630 mmol) and trans-crotonyl chloride (26 µL,} \]
0.272 mmol) were added and the reaction left to stir at RT for 16 h. The reaction mixture was then diluted with CH₂Cl₂ (10 mL), and washed with H₂O (10 mL x 2) followed by brine (10 mL). The combined aqueous layers were extracted in to CH₂Cl₂ (10 mL x 2). The organic layer was dried with MgSO₄ and solvents were removed in vacuo. The resultant crude oil was purified by column chromatography on silica gel (15% EtOAc:hexane) to yield 16 as a clear oil (41 mg, 75%). [α]⁺²⁰ -6.06 (c=0.80 CH₂Cl₂); IR (film) 3353, 2906, 1752 (C=O), 1435, 1174 cm⁻¹; ¹H NMR (500 MHz, CDCl₃) δ 5.95 (1H, dddd, J=7.0, 7.0, 10.0, 17.0, H-3'), 5.85 (1H, dddd, J=7.0, 7.0, 10.0, 17.0, H-11), 5.73-5.69 (2H, m, H-5, H-6), 5.20-5.15 (2H, m H-12), 5.10-5.05 (2H, m, H-4'), 4.23 (1H, dd, J= 4.0, 11.5, Ha-8), 4.07 (1H, dd, J= 6.0, 11.5, Hb-8), 3.86 (1H, ddd, J=4.0, 6.0, 6.5, H-1), 3.76 (1H, ddd, J=6.0, 6.0, 6.0 H-3), 3.15 (2H, dd, J=1.5, 6.0, H-2'), 2.34-2.23 (5H, m, H-7a, H-10, H-4, H-7) 2.13-2.10 (1H, m, H-3a), 1.99-1.89 (2H, m, H-4, H-7); ¹³C NMR (125 MHz, CDCl₃) 171.5 (C1'), 134.8 (C3'), 130.2 (C11), 125.7 (C6 or C5), 125.3 (C6 or C5), 118.6 (C4'), 117 (C12), 83.9 (C3), 81.2 (C1), 66.3 (C8), 39.5 (C4a or C7a), 39.0 (C2'), 39.0 (C4a or C7a), 37.0 (C10), 24.8 (C4), 24.6 (C7); LC-MS (ESI⁺) m/z 285 [M+Na⁺], Rₜ 2.80 [method D]; HRMS [M+H⁺] calcd for C₁₆H₂₃O₃Si 263.1641; found 263.1645.

Pent-4’enoic acid (1S, 3S, 3aR, 7aS)-allyl-1, 3, 3a, 4, 7, 7a-hexahydro-isobenzofuran-8-ylmethyl ester 17

((1S,3S,3aR,7aS)-3-Allyl-1,3,3a,4,7,7a-hexahydroisobenzofuran-1-yl)methanol 14 (34 mg, 0.175 mmol) was dissolved in CH₂Cl₂ (0.6 mL). Triethylamine (73 μL, 0.525 mmol) and pentenonyl chloride (25 μL, 0.223 mmol) was added and the reaction was stirred at RT for 16 h. The reaction mixture was then diluted with CH₂Cl₂ (10 mL), washed with H₂O (10 mL x 2) and brine (10 mL). The combined aqueous layers were extracted into CH₂Cl₂ (10 mL x 2). The organic layer was dried with MgSO₄ and the solvent was removed in vacuo. The resultant crude oil was purified by column chromatography on silica gel (15% EtOAc:hexane) to yield 17 as a clear oil (45 mg, 95%). [α]⁺²⁰ -7.84 (c=0.30, CH₂Cl₂); IR (film) 2923, 2919, 2854, 1738, 1440 cm⁻¹; ¹H NMR (500 MHz, CDCl₃) δ 5.91-5.77 (2H, m, H-10, H-4''), 5.73-5.68 (2H, m, H-5, H-6), 5.14-4.98 (4H, m, H-5', H-11), 4.21 (1H, dd, J=4.0, 11.5, Ha-8), 4.03 (1H, dd, J=6.0, 6.0, Hb-8), 3.85 (1H, ddd, J=4.0, 6.5, 6.5, H-1), 3.76 (1H, ddd, J=6.0, 6.0, H-3), 2.52-2.35 (4H, m, H-2', H-3'); 2.35-2.16 (5H, m, H-9, H-7a, H-4, H-7), 2.12-2.16 (1H, m, H-3a), 2.01-1.88 (2H, m, H-4, H-7); ¹³C NMR (125 MHz, CDCl₃) δ 173.0 (C1'), 136.6 (C10 or C4'), 134.8 (C10 or C4'), 125.7 (C5 or C6), 125.3 (C5 or C6), 117.1 (C11), 115.5 (C5'), 83.8 (C3), 81.2 (C1), 66.1 (C8), 39.5 (C9), 38.9 (C7a or C3a) 36.9 (C3a or C7a), 33.5 (C3'), 28.1 (C2), 24.8 (C7 or C4), 24.5 (C4 or C7); LC-MS (ESI⁺) m/z 299 [M+Na⁺], Rₜ 2.97 min [method D]; HRMS [M+Na⁺] calcd for C₁₇H₂₆O₃Na 299.1618; found 299.1619.
((1S,3S,3aR,7aS)-3-Allyl-1,3,3a,4,7,7a-hexahydroisobenzofuran-1-yl)methyl hex-5-enoate 18

((1S,3S,3aR,7aS)-3-Allyl-1,3,3a,4,7,7a-hexahydroisobenzofuran-1-yl)methanol 14 (40 mg, 0.206 mmol) was dissolved in pyridine (1.0 mL). Hex-5-enoyl chloride (35 mg, 0.238 mmol) was added and the reaction stirred at RT for 16 h. The reaction mixture was then diluted with CH2Cl2 (10 mL) and solvent removed in vacuo to yield a brown residue. The residue was dissolved in CH2Cl2 (10 mL), then washed with H2O (10 mL) and brine (10 mL). The combined aqueous layers were extracted with CH2Cl2 (2 x 10 mL). The organic layer was dried with MgSO4 and solvent was removed in vacuo. The resultant crude oil was purified by column chromatography on silica gel (5% EtOAc:hexane) to yield 18 as a clear oil (20 mg, 32%). [α]D -1.9 (c=0.8 CH2Cl2); IR (film) 1731 (CO), 1459 cm⁻¹; ¹H NMR (500 MHz, CDCl3) δ 5.91-5.67 (4H, m, H-5, H-6, H-2'', H-7'), 5.15-4.96 (4H, m, H-3'', H-8'), 4.21 (1H, dd, J=4.0, 11.5, Hα-1'), 4.03 (1H, dd, J=6.0, 11.5, Hb-1'), 3.86 (1H, ddd, J=4.0, 6.0, 6.0, H-1), 3.76 (1H, ddd, J=6.0, 6.0, 6.0, H-3), 2.36 (2H, t, J=7.5, H-4'), 2.33-2.17 (5H, m, H-7, H-4, H-6', H-3a or H-7a), 2.15-2.07 (2H, m, H-1'', H-3a or H-7a), 2.02-1.87 (2H, m, H-7, H-4), 1.75 (2H, tt, J=7.5, 7.5, H-5'); ¹³C NMR (125 MHz, CDCl3) δ 173.6 (C3'), 137.7 (C2'' or C7'), 134.8 (C2'' or C7'), 125.7 (C5 or C6), 125.3 (C5 or C6), 117.5 (C8'), 115.4 (C3'), 83.9 (C1), 81.2 (C3), 66.0 (C1'), 39.5 (C6'), 39.0 (C3a or C7a), 36.9 (C3a or C7a), 33.5 (C4'), 33.1 (C1''), 24.8 (C4 or C7), 24.5 (C4 or C7), 24.0 (C5'); LC-MS (ESI⁺) m/z 313 [M+Na⁺], Rt 2.55 min [method D]; HRMS [M+Na⁺] calcd for C18H26O3Na 313.1774; found 313.1775.

(Z)-(1S,9S,10R,15S)-3,16-Dioxa-tricyclo[7.6.1.0¹⁰,¹⁵]hexadeca-6,12-diene-4-one 20

((1S,3S,3aR,7aS)-3-Allyl-1,3,3a,4,7,7a-hexahydroisobenzofuran-1-yl)methylbut-3’-enoate 16 (13 mg, 0.05 mmol) was dissolved in CH2Cl2 (100 mL, 0.0005 M). Argon was bubbled though the solution for 5 min. Grubbs II (4 mg, 0.005 mmol, 5 mol%) was added under argon and the reaction stirred for 16 h. DMSO (~10 µL) was added and the solution stirred overnight. The solvents were removed in vacuo and the resultant mixture purified by column chromatography on silica gel (15% EtOAc:hexane) to yield 20 as a white crystalline solid (2 mg, 10%). mp (79-81 °C); [α]D 132.0 (c=0.50 CH2Cl2); IR (film) 3020, 2952, 2889, 1731 cm⁻¹; ¹H NMR (500 MHz, CDCl3) δ 5.96-5.85 (1H, m, H-7), 5.76 (1H, ddd, J=2.5, 5.0, 10.0, H-12), 5.74-5.67 (1H, m, H-6), 5.67-5.62 (1H, m, H-13), 5.13 (1H, dd, J=3.5, 11.5, Hα-2), 3.89 (1H, dd, J=2.5, 11.5, H-9), 3.78 (1H, dd, J=3.5, 11.5, H-1), 3.59 (1H, dd, J=11.5, Hb-2), 3.23 (1H, ddd, J=2.0, 7.5, 11.5, H-5), 2.92 (1H, dd, J=12.0,
9.0, Hb-5), 2.82-2.68 (2H, m, H-15, Ha-8), 2.45-2.33 (1H, m, Ha-14), 2.33-2.20 (1H, m, Ha-11) 2.10-2.06 (1H, m, H-10), 2.05-1.88 (3H, m, Hb-8, Hb-11, Hb-14); 13C NMR (125 MHz, CDCl3) δ 172.4 (C4), 131.8 (C13), 125.6 (C6), 124.3 (C12), 123.4 (C7), 85.0 (C9), 80.7 (C1), 61.1 (C2), 39.4 (C10), 34.5 (C8), 34.4 (C15), 33.5 (C5), 26.1 (C11), 22.6 (C14); LC-MS (ESI+) m/z 257 [M+Na+], Rf 2.43 min [method D]; HRMS [M+H+] calcd for C14H18O3H 235.1329; found 235.1327.

(Z)-(1S,10S,11R,16S)-3,17-Dioxatricyclo[8.6.1.011,16]heptadeca-7,13-diene-4-one 21

Pent-4-enoic acid(1S,3S,3aR,7aS)-allyl-1,3,3a,4,7,7a-hexahydroisobenzofuran-8-ylmethyl ester 17 (23 mg, 0.083 mmol) was dissolved in CH2Cl2 (166 mL, 0.0005 M). Argon was bubbled though the solution for 5 min. Grubbs II (3.5 mg, 0.004 mmol, 5 mol%) was added under argon and the reaction mixture was stirred for 16 h. DMSO (~10 µL) was added and the solution was stirred overnight. The solvents were removed in vacuo and the resultant mixture purified by column chromatography on silica gel (15% EtOAc:hexane) to yield 21 as a white crystalline solid (10 mg, 49%). mp (81-86 °C); [α]22D -114.9 (c=0.10, CH2Cl2); IR (film) 3071, 2930, 2855, 1738, 1428 cm⁻¹; 1H NMR (500 MHz, CDCl3) δ 5.77-5.69 (1H, m, CH), 5.68-5.60 (1H, m, CH), 5.58-5.49 (2H, m, CH), 5.17 (1H, d, J=11.5, Ha-2), 3.97-3.88 (1H, dd, J=3.0, 11.5, H-10), 3.80 (1H, dd, J=3.0, 11.0, H-1), 3.60-3.47 (1H, d, J=12.0, Hb-2), 3.02-2.79 (1H, m, CH2), 2.78-2.53 (3H, m, H-11, CH2), 2.45-2.34 (2H, m, CH2), 2.33-2.22 (1H, m, CH2), 2.12-1.99 (3H, m, H-16, CH2), 1.98-1.81 (2H, m, CH2); 13C NMR (125 MHz, CDCl3) 172.1 (C4), 128.5 (CH), 128.0 (CH), 123.8 (CH), 123.7 (CH), 83.4 (C10), 79.4 (C1), 59.4 (C2), 39.7 (C16), 35.2 (CH2), 34.1 (CH2), 33.9 (C11), 26.1 (CH2), 23.0 (CH2), 22.6 (CH2); LC-MS (ESI+) m/z 271 [M+Na+], Rf 2.55 min [method D]; HRMS [M+Na+] calcd for C15H20O3Na 271.1310; found 271.1301.

(Z)-(1S,11S,12R,17S)-3,18-Dioxatricyclo[9.6.1.012,17]octadeca-8,14-dien-4-one 22

((1S,3S,3aR,7aS)-3-Allyl-1,3,3a,4,7,7a-hexahydroisobenzofuran-1-yl)methyl hex-5-enolate 18 (9 mg, 0.030 mmol) was dissolved in CH2Cl2 (63 mL, 0.0005 M). Argon was bubbled though the solution for 5 min. Grubbs II (3 mg, 0.003 mmol, 10 mol%) was added under argon and the reaction mixture was stirred for 16 h. DMSO (10 µL) was added and the solution was stirred overnight. The solvents were removed in vacuo and the resultant mixture purified by column chromatography on silica gel (10% EtOAc:hexane) to yield 22 as a white crystalline solid (4 mg, 51%). mp (122-126 °C); [α]19D -5.0 (c=1.0 CH2Cl2); IR (film) 3030, 2938, 2909, 1732 (CO), 1439 cm⁻¹; 1H NMR (500 MHz, CDCl3) δ 5.81-5.70 (2H, m, CH), 5.48-5.35 (2H, m, CH), 5.20 (1H, dd, J=3.0, 12.0, Ha-2), 3.02-2.79 (1H, m, CH2), 2.78-2.53 (3H, m, H-11, CH2), 2.45-2.34 (2H, m, CH2), 2.33-2.22 (1H, m, CH2), 2.12-1.99 (3H, m, H-16, CH2), 1.98-1.81 (2H, m, CH2); 13C NMR (125 MHz, CDCl3) 172.1 (C4), 128.5 (CH), 128.0 (CH), 125.8 (CH), 123.7 (CH), 83.4 (C10), 79.4 (C1), 59.4 (C2), 39.7 (C16), 35.2 (CH2), 34.1 (CH2), 33.9 (C11), 26.1 (CH2), 23.0 (CH2), 22.6 (CH2); LC-MS (ESI+) m/z 271 [M+Na+], Rf 2.55 min [method D]; HRMS [M+Na+] calcd for C15H20O3Na 271.1310; found 271.1301.
3.78 (1H, ddd, J=3.0, 3.0, 6.0, H-1), 3.75 (1H, ddd, J=1.5, 2.0, 5.0, H-11), 3.51 (1H, dd, J=3.0, 12.0, Hb-2), 2.48-2.22 (7H, m, CH₂), 2.18-2.01 (3H, m, CH₃), 1.97-1.84 (3H, m, CH₂), 1.73-1.65 (1H, m, CH₂); ¹³C NMR (125 MHz, CDCl₃) δ 173.8 (C4), 133.8 (CH), 126.7 (CH), 125.7 (CH), 125.5 (CH), 82.9 (C11 or C1), 82.8 (C11 or C1), 62.6 (C2), 37.4 (C12 or C17), 37.2 (C12 or C17), 34.4 (CH₂), 34.1 (CH₂), 33.6 (CH₂), 25.6 (CH₂), 24.4 (CH₂), 22.5 (CH₂); LC-MS (ESI⁺) m/z 285 [M+Na⁺], Rₜ 2.33 min [method D]; HRMS [M+Na⁺] calcd for C₁₆H₂₂O₃Na 285.1462; found 285.1465.

(3S,3aS,7aR)-3-((tert-Butyldiphenylsilyloxy)methyl)octahydroisobenzofuran-1-ol 23

(3S,3aS,7aR)-3-((tert-Butyldiphenylsilyloxy)methyl)-3a,4,7,7a-tetrahydroisobenzofuran n-1(3H)-one 10 (317 mg, 0.781 mmol) was dissolved in EtOAc (8 mL) and Pd/C (16 mg, 5% w/w Pd) was added. The solution was stirred overnight under H₂ (1 atm). The solution was filtered through silica eluted with EtOAc. The solvents were removed in vacuo to yield 23a as a white crystalline solid (318 mg, 100%), mp (95-98 °C); [α]⁺ 6.1 (c=1.00 CH₂Cl₂); IR (film) 3070, 2998, 2856, 1774 (CO) cm⁻¹; ¹H NMR (500 MHz, CDCl₃) δ 7.69 (4H, m, Ph), 7.43 (6H, m, Ph), 4.13 (1H, dd, J=7.0, 7.0, H-3), 3.83 (1H, dd, J=4.5, 11.5, Ha-8), 3.76 (1H, dd, J=4.5, 11.5, Hb-8), 2.84 (1H, dd, J=7.0, 11.5, H-7a), 2.41-2.50 (1H, m, H-3a), 2.05-1.94 (1H, m, Ha-7), 1.85-1.74 (1H, m, Ha-4), 1.71-1.48 (4H, m, H-5, H-6), 1.38-1.21 (2H, m, Hb-4, Hb-7), 1.06 (9H, s, tBu); ¹³C NMR (125 MHz, CDCl₃) δ 178.6 (C1), 135.6 (2 x Ph), 132.9 (2 x Ph), 132.7 (2 x Ph), 129.9 (2 x Ph), 127.8 (4 x Ph), 83.1 (C3), 64.1 (C8), 38.7 (C7a), 36.6 (C3a), 27.7 (C4), 26.8 (tBu), 23.2 (C5), 23.1 (C6), 22.8 (C7), 19.2 (Si-C); LC-MS (ESI⁺) m/z 431 [M+Na⁺], Rₜ 3.16 min [method D]; HRMS [M+Na⁺] calcd for C₂₅H₂₅O₃SiNa 431.2012; found 431.2020.

(3S,3aS,7aR)-3-((tert-Butyldiphenylsilyloxy)methyl)hexahydroisobenzofuran-1-(3H)one 23a (240 mg, 0.584 mmol) was dissolved in anhydrous CH₂Cl₂ (4.4 mL) and cooled to 78 °C under N₂. DIBAL-H (1.0 Mol in toluene, 0.97 mL, 0.97 mmol) was added dropwise. The reaction was stirred at 78 °C for 2 h then quenched with EtOAc (10 mL). The solution was warmed to RT and a sat. aq. solution of Rochelle’s salt (30 mL) was added and the mixture was stirred for 2 h. The organic layer was separated and washed with brine (30 mL). The aqueous layers were extracted with CH₂Cl₂ (3 x 30 mL). The combined organic layers were dried over MgSO₄ and solvent removed in vacuo to yield the product as a clear oil (241 mg, 100%). [α]⁺ 12.0 (c=0.15 Et₂O); IR (film) 3416, 3070, 2960, 2938, 2857, 1428 cm⁻¹; ¹H NMR (500 MHz, CDCl₃) δ 7.77-7.71 (4H, m, Ph), 7.52-5.43 (6H, m, Ph), 5.02 (1H, d, J=6.0, H-1), 4.02 (1H, dd, J=3.5, 6.0, H-3), 3.83 (1H, dd, J=3.0, 11.0, Ha-8), 3.60 (1H, dd, J=3.5, 11.0, Hb-8), 2.94 (1H, d, J=6.0, OH), S12
2.63-2.50 (1H, m, H-3a), 2.10 (1H, ddd, J= 6.0, 6.0, 6.0 H-7a), 1.74-1.46 (6H, m, CH₂), 1.29-1.16 (2H, m, CH₂), 1.05 (9H, s, tBu); ¹³C NMR (125 MHz, CDCl₃) δ 135.7 (2 x Ph), 135.7 (2 x Ph), 133.0 (Ph), 132.9 (Ph), 129.8 (Ph), 129.8 (Ph), 127.8 (2 x Ph), 127.8 (2 x Ph), 102.8 (C1), 81.2 (C3), 46.2 (C7a), 34.0 (3a), 26.9 (tBu), 25.2 (CH₂), 24.0 (CH₂), 23.7 (CH₂), 21.4 (CH₂), 19.2 (Si-C); LC-MS (ESI⁺) m/z 433 [M+Na⁺], Rₜ 3.27 min [method D], HRMS [M + Na⁺] calcd for C₂₅H₃₄O₃SiNa 433.2169; found 433.2166.

((1S,3S,3aR,7aS)-3-(Allyloctahydroisobenzofuran-1-ylmethoxy)tert-butyldiphenylsilane 24

((3S,3aS,7aR)-3-((tert-Butyldiphenylsilyloxy)methyl)octahydroisobenzofuran-1-ol 23 (120 mg, 0.618 mmol) was dissolved in CH₂Cl₂ (6 mL) and the solution was cooled to -78 °C. BF₃·OEt₂ (240 μL, 1.849 mmol) was added by syringe and the solution was stirred for 5 min. Allyltrimethylsilane (300 μL, 1.85 mmol) was added by syringe and the reaction then warmed to RT over 18 h. The reaction was diluted with 15 mL CH₂Cl₂ (15 mL) and washed with H₂O (7 mL). The aqueous layer was extracted with CH₂Cl₂ (2 x 20 mL). The combined organic layers were washed with brine (10 mL) and dried over MgSO₄. The solvents were removed in vacuo to yield 24 as a clear oil (268 mg, 100%). [α]²²D 2.11 (c=0.46 CH₂Cl₂); IR (film) 3072, 3050, 2929, 2858, 1472, 1428 cm⁻¹; ¹H NMR (500 MHz, CDCl₃) δ 7.80-7.65 (4H, m, Ph), 7.50-7.35 (6H, m, Ph), 5.86 (1H, tdd, J=7.0, 10.0, 17.0, H-2'), 5.10-5.02 (2H, m, H-3'), 3.91-3.83 (2H, m, H-1, H-3), 3.65 (2H, d, J=5.0, H-1''), 2.30-2.18 (3H, m, H-1', H-7a), 1.93 (1H, ddd, J=6.0, 6.0, 6.0, H-3a), 1.70-1.58 (2H, m, Ha-7, Ha-4), 1.57-1.45 (4H, m, Hb-4, Ha-5, Ha-6, Hb-7), 1.42-1.32 (2H, m, Hb-5, Hb-6), 1.08 (9H, s, tBu); ¹³C NMR (125 MHz, CDCl₃) 135.7 (2 x Ph), 135.6 (2 x Ph), 134.5 (Ph), 133.8 (Ph), 133.7 (Ph), 130.2 (C2'), 129.6 (Ph), 129.6 (Ph), 127.9 (Ph), 127.6 (Ph), 116.4 (C3'), 82.7 (C1), 81.7 (C3), 65.9 (C1''), 41.8 (C3a), 40.1 (C9), 38.9 (C7a), 26.9 (tBu), 26.0 (C7 or C4), 25.9 (C4 or C7), 23.4 (C5 or C6), 23.2 (C5 or C6), 19.2 (Si-C).

((1S,3S,3aR,7aS)-3-Allyloctahydro-isobenzofuran-1-yl)methanol 25

((1S,3S,3aR,7aS)-3-Allyloctahydroisobenzofuran-1-ylmethoxy)tert-butyldiphenylsilane 24 (410 mg, 0.945 mmol) was dissolved in THF (9.4 mL). The solution was cooled to 0 °C under N₂ and then TBAF (2.8 mL, 2.8 mmol, 1.0 M in THF) was added by syringe. The reaction was stirred for 2 h at 0 °C before quenching with Et₂O (30 mL). The reaction mixture was washed with H₂O (2 x 30 mL) and the aqueous layers extracted into Et₂O (2 x 30 mL). The combined organic layers were dried over MgSO₄ and the solvents were removed in vacuo. The crude residue was purified by column chromatography on silica gel (50% EtOAc:hexane) to yield 25 as a clear oil (131 mg, 74%). [α]²²D -9.0 (c=1.26

S13
CH₂Cl₂); IR (film) 3414, 2929, 2856, 1449 cm⁻¹; ¹H NMR (500 MHz, CDCl₃) δ 5.92-5.74 (1H, ddd, J=7.0, 7.0, 10.0, H-2’’), 5.19-5.03 (2H, m, H-3’’), 3.97-3.79 (2H, m, H-3, H-1), 3.67 (1H, dd, J=3.5, 11.5, H-1’’), 3.45 (1H, dd, J=5.5, 11.5, H-1’), 2.33-2.16 (3H, m, H-1’’), 2.11 (1H, ddd, J=6.5, 6.5, 12.5, H-7a), 1.70-1.69 (2H, m, CH₂), 1.59-1.28 (6H, m, 6 x CH₂); ¹³C NMR (125 MHz, CDCl₃) δ 135.1 (C2’’), 117.1 (C3’’), 82.2 (C3 or C1), 82.1 (C3 or C1), 64.3 (C1’’), 42.2 (C3a), 40.1 (C1’), 37.8 (C7a), 26.4 (CH₂), 25.6 (CH₂), 23.4 (CH₂), 22.8 (CH₂); LC-MS (ESI⁺) m/z 219 [M+Na⁺], Rₜ 2.47 min [method D]; HRMS [M+Na⁺] calcd for C₁₂H₂₀O₃Na 219.1362; found 219.1363.

(Z)-(1S,10S,11R,16S)-3,17-Dioxatricyclo[8.6.1.0₁₁,₁₆]heptadeca-7-en-4-one 26 and (E)-(1S,10S,11R,16S)-3,17-Dioxatricyclo[8.6.1.0₁₁,₁₆]heptadeca-7-en-4-one 27

((1S,3S,3aR,7aS)-3-Allyloctahydroisobenzofuran-1-yl)methyl pent-4-enoate 25 (40 mg, 0.203 mmol) was dissolved in CH₂Cl₂ (0.9 mL). Pent-4-enoyl chloride (29 µL, 0.275 mmol) and triethylamine (89 µL, 0.609 mmol) were added and the reaction mixture was stirred at RT for 18 h. The reaction mixture was diluted with CH₂Cl₂ (10 mL) and washed with H₂O (10 mL x 2) and brine (10 mL). The aqueous layers were combined and extracted with CH₂Cl₂ (10 mL x 2). The combined organic layers were dried with MgSO₄ and the solvents removed in vacuo. The crude reaction mixture was purified by column chromatography on silica gel (10% EtOAc:hexane) to yield 77 as a clear oil (39 mg, 69%)[α]₂₀⁺⁻¹.2 (c=1.0 CHCl₃); IR (CDCl₃ solution cell) 3081, 2932, 1732 (CO), 1641, 1451 cm⁻¹; ¹H NMR (500 MHz, CDCl₃) δ 5.93-5.73 (2H, m, H-6', H-2’’), 5.17-4.97 (4H, m, H-7’, H-3’’), 4.14 (1H, dd, J=6.5, 14.0, H-1’’), 4.03-3.93 (2H, m, Hb-1’, H-1), 3.86 (1H, dd, J=6.0, 11.5, H-3), 2.50-2.35 (4H, m, H-4’, H-5’), 2.29-2.17 (2H, m, H-1’’), 2.09-2.01 (1H, m, H-7a), 2.00-1.91 (1H, m, H-3a), 1.70-1.59 (2H, m, CH₂), 1.58-1.28 (6H, m, CH₂); ¹³C NMR (125 MHz, CDCl₃) δ 173.1 (C3’’), 136.7 (C6’ or C2’’), 135.0 (C6’ or C2’’), 116.9 (C7’ or C3’’), 115.5 (C7’ or C3’’), 82.4 (C3), 79.8 (C1), 66.6 (C1’’), 41.6 (C3a), 40.0 (C1’’), 39.1 (C7a), 33.5 (C4’’), 28.8 (C5’’), 26.2 (CH₂), 25.8 (CH₂), 23.2 (CH₂), 22.9 (CH₂); LC-MS (ESI⁺) m/z 301 [M+Na⁺], Rₜ 2.93 min [method D]; HRMS [M+Na⁺] calcd for C₁₇H₂₆O₃ Na 301.1774 found 301.1765.

((1S,3S,3aR,7aS)-3-Allyloctahydroisobenzofuran-1-yl)methyl pent-4-enoate 77 (23 mg, 0.083 mmol) was dissolved in CH₂Cl₂ (165 mL, 0.0005 M). Argon was bubbled though the solution for 5 min. Grubbs II (7 mg, 0.008 mmol, 10 mol%) was added under argon and the reaction...
mixture was stirred for 16 h. DMSO (10 µL) was added and the solution was stirred overnight. The solvents were removed in vacuo and the resultant mixture purified by column chromatography on silica gel (10% EtOAc:hexane) to yield 26 and 27 as a white crystalline solid (13 mg, 65%) and a clear oil (4 mg, 20%) respectively. 26: mp (141-143 °C); [α]19°D -1.9 (c=0.36 CH2Cl2); IR (film) 2980, 1732 (CO), 1551 cm⁻¹; ¹H NMR (500 MHz, Pyr-d5) δ 5.53-5.38 (2H, m, H-8, H-7), 5.25 (1H, d, J=11.5 Ha-2), 3.92 (1H, d, J=11.0, H-1), 3.71 (1H, d, J=11.5, H-10), 3.39 (1H, d, J=11.5, Hb-2), 2.85-2.81 (1H, m, Ha-6), 2.61-2.46 (2H, m, Ha-5, Ha-9), 2.43-2.27 (2H, m, H-16, Hb-5), 1.83-1.79 (1H, m, Hb-6), 1.75-1.61 (2H, m, Ha-9, H-11), 1.59-1.48 (4H, m, Ha-12, Ha-14, H-15), 1.38-1.36 (1H, m, Ha-13), 1.21-0.89 (3H, m, Hb-14, Hb-13, Hb-12)); ¹³C NMR (125 MHz, CDCl₃) δ 172.2 (C4), 129.7 (C8), 128.8 (C7), 83.5 (C10), 77.6 (C1), 60.3 (C2), 45.2 (C11), 36.7 (C16), 35.9 (C14), 35.0 (C9), 28.2 (C5), 25.6 (C12), 23.7 (C15), 23.5 (C13 or C14), 21.7 (C13 or C14); LC-MS (ESI⁺) m/z 273 [M+Na⁺], Rᵣ 2.30 min [method D]; HRMS [M+H⁺] calcd for C₁₅H₂₀O₃ 251.1642; found 251.1634. 27: [α]¹⁹°D -49.1 (c=0.24 CH2Cl2); IR (film) 2925, 1735 (CO) cm⁻¹; ¹H NMR (500 MHz, Pyr-d5) δ 5.57-5.50 (1H, m, H-8), 5.48-5.40 (1H, m, H-7), 4.92-4.68 (1H, m, Ha-2), 4.02-3.95 (1H, m, H-10), 3.77-3.74 (2H, m, Hb-2, H-1), 2.49-2.46 (1H, m, Ha-9), 2.39-2.30 (2H, m, Ha-5, Ha-6), 2.26-2.19 (3H, m Hb-5, Hb-6, H-11), 2.11-2.09 (1H, m, H-16), 1.95-1.91 (1H, m, Hb-9), 1.49-1.40 (2H, m, Hb-12, Ha-14, Ha-12), 1.39-1.35 (2H, m, Hb-12, Ha-15), 1.34-1.30 (3H, m, H-14, Hb-15), 1.22-1.17 (1H, m, Hb-13); ¹³C NMR (125 MHz, CDCl₃) δ 173.5 (C4), 131.2 (C7), 127.9 (C8), 82.2 (C1), 80.5 (C10), 64.9 (C2), 40.0 (C16), 38.8 (C11), 36.1 (C5), 34.2 (C9), 29.5 (C6), 27.3 (C15), 25.1 (C12), 23.9 (C13), 22.3 (C14); LC-MS (ESI⁺) m/z 273 [M+Na⁺], Rᵣ 2.27 min [method D]; HRMS [M+H⁺] calcd for C₁₅H₂₀O₃ 251.1642; found 251.1636.

(Z)-(15,11S,12R,17S)-3,18-Dioxatricyclo[9.6.1.012,17]octadec-8-en-4-one 28

((15,35,3aR,7aS)-3-Allyloctahydroisobenzofuran-1-yl)methanol 25 (35 mg, 0.178 mmol) was dissolved in CH₂Cl₂ (0.9 mL). Freshly prepared hex-5-enoyl chloride (30 mg, 0.267 mmol) and triethylamine (77 µL, 0.534 mmol) were added and the reaction mixture was stirred at RT for 18 h. The reaction mixture was diluted with CH₂Cl₂ (10 mL) and washed with H₂O (10 mL) and brine (10 mL). The aqueous layers were combined and extracted with CH₂Cl₂ (10 mL x 2). The combined organic layers were dried with MgSO₄ and the solvents removed in vacuo. The crude reaction mixture was purified by column chromatography on silica gel (5% EtOAc:hexane) to yield 78 as a clear oil (27 mg, 57%). [α]¹⁹°D -9.0 (c=1.0 CH₂Cl₂); IR (CDCl₃ solution cell) 3080, 2932, 1731 (CO), 1641, 1451 cm⁻¹; ¹H NMR (500 MHz, CDCl₃) δ 5.89-5.71 (2H, m, H-2”, H-7”), 5.13-4.95 (4H, m, H-3”, H-8”), 4.14 (1H, dd, J=6.5, 6.5, H-1”), 4.05-3.94
(2H, m, Hb-1', H-1), 3.87 (1H, dd, J=6.0, 11.5, H-3), 2.38 (2H, t, J=7.0, H-4'), 2.31-2.17 (2H, m, H-1"'), 2.14-2.00 (3H, m, H'-6', H-7a), 2.00-1.92 (1H, m, H-3a), 1.75 (2H, tt, J=7.5, 7.5, H-5"), 1.70-1.58 (2H, m, CH2), 1.57-1.23 (6H, m, CH2); 13C NMR (125 MHz, CDCl3) δ 173.7 (C3'), 137.7 (C7' or C2''), 135.1 (C7' or C8'), 115.4 (C3'' or C8'), 82.5 (C1), 79.4 (C3), 66.5 (C8), 41.6 (C3a), 40.0 (C1''), 39.2 (C7a), 33.5 (C6'), 33.1 (C6'), 26.2 (CH2), 25.7 (CH2), 24.0 (C5'), 23.3 (CH2), 22.9 (CH2); LC-MS (ESI+) m/z 315 [M+Na]+, R<sub>t</sub> 2.63 min [method D]; HRMS [M+Na]+ calcd for C<sub>18</sub>H<sub>28</sub>O<sub>3</sub>Na 315.1930; found 315.1935.

((1S,3S,3aR,7aS)-3-Allyloctahydroisobenzofuran-1-yl)methyl hex-5-enoate 78 (25 mg, 0.080 mmol) was dissolved in CH<sub>2</sub>Cl<sub>2</sub> (100 mL, 0.0008 M). Argon was bubbled though the solution for 5 min. Grubbs II (7 mg, 0.008 mmol, 10 mol%) was added under argon and the reaction mixture was stirred for 16 h. DMSO (10 µL) was added and the solution was stirred overnight.

The solvents were removed in vacuo and the resultant mixture purified by column chromatography on silica gel (10% EtOAc:hexane) to yield 28 as a white crystalline solid (10 mg, 51%). mp (141-143 °C); [α]<sub>25</sub>D -33.4 (c=1.0 CHCl3); IR (film) 3081, 2931, 2858, 1731, 1642, 1451 cm<sup>-1</sup>; 1H NMR (500 MHz, CDCl3) δ 5.39-5.35 (2H, m, H-8, H-9), 5.16 (1H, d, J=11.0, Ha-2), 3.95-3.91 (1H, m, H-11), 3.81-3.78 (1H, m, H-1), 3.47 (1H, d, J=11.0, Hb-2), 2.45-2.28 (3H, m, 3 x CH2), 2.26-2.18 (1H, m, H-17), 2.17-1.97 (4H, m, 4 x CH2), 1.95-1.85 (1H, m, CH2), 1.73-1.61 (4H, m, CH2), 1.57-1.29 (5H, m, CH2); 13C NMR (125 MHz, CDCl3) δ 173.8 (C4), 133.5 (C8 or C9), 125.8 (C8 or C9), 81.2 (C1), 80.3 (C11), 63.0 (C2), 39.8 (C17), 39.1 (C12), 34.7 (CH2), 34.0 (CH2), 33.7 (CH2), 27.1 (CH2), 25.5 (CH2), 23.9 (CH2), 22.9 (CH2), 22.5 (CH2); LC-MS (ESI+) m/z 287 [M+Na]+, R<sub>t</sub> 2.50 min [method D]; HRMS [M+H<sup>+</sup>] calcd for C<sub>18</sub>H<sub>26</sub>O<sub>3</sub> 265.1796 found 265.1796.

(1S,3S,3aS,7aR)-1-Allyl-3-(allyloxymethyl)-1,3,3a,4,7,7a-hexahydroisobenzofuran 29

((1S,3S,3aR,7aS)-3-Allyl-1,3,3a,4,7,7a-hexahydroisobenzofuran-1-yl)methanol 14 (48 mg, 0.247 mmol) was dissolved in DMF (1 mL). NaH (24 mg, 0.618 mmol, 60% dispersion in mineral oil) was then added to the solution followed by allyl bromide (25 µL, 0.296 mmol) by syringe. The reaction was stirred overnight at RT. The reaction was then quenched with H<sub>2</sub>O (2 mL) and extracted with Et<sub>2</sub>O (5 x 10 mL) and the organic layers subsequently washed with H<sub>2</sub>O (5 x 20 mL). The organic layer was dried with MgSO<sub>4</sub> and solvents removed in vacuo. The resultant crude oil was purified by column chromatography on silica gel (15% EtOAc:hexane) to yield 29 as a clear oil (28 mg, 49%). [α]<sup>19</sup>D -9.8 (c=2.20, CH2Cl2); IR (film) 3076, 3025, 2900, 2843, 1641, 1437 cm<sup>-1</sup>; 1H NMR (500 MHz, CDCl3) δ 6.01-5.76 (2H, m, H-2', H-10), 5.79-5.66 (2H, m, H-5, H-6), 5.33-5.32 (1H, m, Ha-3'), 5.23-5.13 (1H, m, Hb-3'), 5.13-5.02 (2H, m, H-11), 4.10-4.00 (2H, m, H-1''), 3.81 (1H, ddd, J=5.5, 5.5, 5.5, H-1), 3.73 (1H, dd, J=6.0, 6.0, 6.0, H-3), 3.52-3.44 (2H, m, H-8), 2.38-2.16 (5H, m, H-9, H-7a, Ha-4, Ha-7), 2.11 (1H, ddd, J=6.5, 6.5, 13.0, H-3a), 2.01-1.87 (2H, m, S16
Hb-7, Hb-4; $^{13}$C NMR (125 MHz, CDCl$_3$) δ 135.2 (C2'), 134.9 (C10), 125.8 (C5 or C6), 125.7 (C5 or C6), 116.7 (C3' or C11), 116.7 (C3' or C11), 83.6 (C3), 82.7 (C1), 72.5 (C8 or C1'), 72.4 (C8 or C1'), 39.5 (C9), 39.3 (C3a), 37.3 (C7a), 24.8 (C7), 24.8 (C4); LC-MS (ESI$^+$) m/z 257 [M+Na$^+$], R$_t$ 2.90 min [method D]; HRMS [M+Na$^+$] calcd for C$_{15}$H$_{22}$O$_2$Na 257.1512; found 257.1513.

(3aR,4aR,7S,7aS,8aS)-7-(tert-Butyldiphenylsilanyloxymethyl)-2,2-dimethyl-hexahydrofuro[3',4':4,5]benzo[1,2-d][1,3]dioxol-5-one 31

(3S)-3-((tert-Butyldiphenylsilyloxy)methyl)-3a,4,7,7a-tetrahydroisobenzofuran-1-(3H)-one 10 (1.30 g, 3.21 mmol) was dissolved in acetone:water (10:1, 32 mL). NMO (114 mg, 4.82 mmol) was added followed by Os EnCat (500 mg, 0.25 mmol/g, 0.125 mmol). The resulting solution was stirred at RT for 3 d. The Os Encat was removed by vacuum filtration, and washed with acetone (100 mL). Sat. aq Na$_2$S$_2$O$_5$ was added (100 mL) and stirred for 2 h. The acetone was removed in vacuo. The crude aqueous layer was extracted in the EtOAc (3 x 100 mL). The combined organic layers were dried over MgSO$_4$ and solvent removed in vacuo to yield a light brown oil. The oil was redissolved in CH$_2$Cl$_2$ (30 mL). 2,2-Dimethoxypropane (7.9 mL, 64.2 mmol) and pyridinium p-toluenesulfonate (241 mg, 1.08 mmol) were added and the reaction stirred at RT for 18 h. The reaction was then diluted in CH$_2$Cl$_2$ (100 mL) and washed with H$_2$O (50 mL) and sat aq NH$_4$Cl (50 mL). The aqueous layers were re-extracted into CH$_2$Cl$_2$ (100 mL) and the combined organic layers dried over MgSO$_4$. The solvent was removed in vacuo. The crude residue was recrystallised from Et$_2$O to yield 31 as a white crystalline solid (781 mg, 52%). mp (105-109 °C); [α]$^{22}_D$ -16.2 (c=1.0 CHCl$_3$); IR (film) 3071, 2931, 1770 cm$^{-1}$; $^1$H NMR (500 MHz, CDCl$_3$) δ 7.70-7.63 (4H, m, Ph), 7.49-7.39 (6H, m, Ph), 4.51 (1H, ddd, J=2.5, 2.5, 8.0, H-3a), 4.42 (1H, ddd, J=2.5, 2.5, 8.0, H-8a), 4.20-4.17 (1H, m, H-7), 3.88 (1H, dd, J=2.5, 11.0, Ha-9), 3.69 (1H, dd, J=2.5, 11.0, Hb-9), 3.13 (1H, ddd, J=7.5, 11.0, 11.0, H-4a), 2.94-2.87 (1H, m, H-7a), 2.43 (1H, ddd, J=3.0, 7.5, 15.0, Ha-4), 1.97 (1H, ddd, J=2.5, 4.5, 14.0, Ha-8), 1.59-1.44 (2H, m, Hb-4, Hb-8), 1.52 (3H, s, H-1'), 1.38 (3H, m, H-1'), 1.09 (9H, s, tBu); $^{13}$C NMR (125 MHz, CDCl$_3$) δ 180.2 (C5), 135.6 (2 x Ph), 135.5 (2 x Ph), 132.8 (iPh), 132.5 (iPh), 129.9 (2 x Ph), 127.9 (4 x Ph), 107.4 (C2), 82.8 (C7), 71.5 (C8a or C3a), 71.3 (C8a or C3a), 65.4 (C9), 34.4 (C4a), 30.2 (C7a), 29.6 (C8), 26.7 (tBu), 25.9 (C1'), 25.0 (C4), 23.8 (C1'), 19.2 (Si-C); LC-MS (ESI$^+$) m/z 503 [M+Na$^+$], R$_t$ 2.58 min [method D]; HRMS [M+Na$^+$] calcd for C$_{28}$H$_{36}$O$_5$SiNa 503.2224 found 503.2221.
(3aR,4aR,7S,7aS,8aS)-7-[(tert-Butyldiphenylsilanyloxymethyl)-2,2-dimethyloctahydrofuro[3',4':5,4,5]benzo[1,2-d][1,3]dioxol-5-ol 32

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\begin{align*}
\text{IR (film)} & : 3418, 2930, 1113, 1040 \text{ cm}^{-1}; \\
\text{Major Anomer} & : ^1H \text{ NMR (500 MHz, CDCl}_3 \delta 7.72-7.76 (4H, m, Ph), 7.49-7.36 (6H, m, Ph), 5.10 (1H, d, J= 9.0, H-5), 4.41-4.37 (2H, m, H-3a, H-8a), 4.15-4.10 (1H, m, OH), 3.92 (1H, dd, J=4.0, 4.0, H-7), 3.82 (1H, dd, J=3.0, 11.0, Hb-9), 3.60 (1H, dd, J=3.5, 11.0, Hb-9), 2.73-2.63 (1H, m, H-7a), 2.55-2.46 (1H, m, H-4a), 2.03 (1H, ddd, J=2.5, 5.0, 14.5, H-4a), 1.96 (1H, ddd, J=3.0, 6.0, 14.5, Ha-8), 1.50 (3H, s, H-1'), 1.36 (3H, s, H-1'), 1.37-1.28 (1H, m, Hb-8), 1.39-1.31 (1H, m, Hb-4), 1.09 (9H, s, tBu); \\
\text{13C NMR (125 MHz, CDCl}_3 \delta 135.8 (2 x Ph), 135.6 (2 x Ph), 132.4 (iPh), 132.3 (iPh), 130.1 (Ph), 129.7 (2 x Ph), 129.7 (2 x Ph), 127.9 (2 x Ph), 127.9 (2 x Ph), 107.1 (C2), 105.1 (C5), 87.6 (C7), 72.0 (C8a or C3a), 71.7 (C8a or C3a), 66.9 (C9), 41.5 (C4a), 32.0 (C7a), 29.0 (C8), 27.5 (C4), 26.8 (tBu), 26.0 (C1'), 23.8 (C1'), 19.2 (Si-C); \\
\text{Minor Anomer} & : ^1H \text{ NMR (500 MHz, CDCl}_3 \delta 7.72-7.67 (4H, m, Ph), 7.49-7.36 (6H, m, Ph), 5.53 (1H, dd, J= 2.0, 5.5, H-5), 4.52 (1H, dd, J= 3.0, 3.0, H-3a or H-8a), 4.51 (1H, dd, J= 3.0, 3.0, H-3a or H-8a), 4.15-4.10 (1H, m, OH), 3.96 (1H, ddd, J=4.5, 14.5, H-8a), 3.82 (1H, dd, J=2.0, 5.0, 14.5, H-4a), 2.73-2.63 (1H, m, H-7a), 2.55-2.46 (1H, m, H-4a), 1.96 (1H, ddd, J=3.0, 6.0, 14.5, Ha-8), 1.50 (3H, s, H-1'), 1.36 (3H, s, H-1'), 1.37-1.28 (1H, m, Hb-8), 1.39-1.31 (1H, m, Hb-4), 1.09 (9H, s, tBu); \\
\text{13C NMR (125 MHz, CDCl}_3 \delta 135.7 (2 x Ph), 135.2 (2 x Ph), 132.4 (iPh), 133.4 (iPh), 130.1 (Ph), 130.0 (Ph), 129.7 (2 x Ph), 129.7 (2 x Ph), 107.1 (C2), 105.1 (C5), 87.6 (C7), 72.0 (C8a or C3a), 71.7 (C8a or C3a), 66.9 (C9), 41.5 (C4a), 32.0 (C7a), 29.0 (C8), 27.5 (C4), 26.8 (tBu), 26.0 (C1'), 23.8 (C1'), 19.2 (Si-C); \\
\end{align*}
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(3aS,4aS,5S,7S,7aR,8aR)-7-allyl-2,2-dimethyloctahydroisobenzofuro[5,6-d][1,3]dioxol-5-yl)methanol 33

(3aR,4aR,7S,7aS,8aS)-7-(tert-Butyldiphenylsilanyloxymethyl)-2,2-dimethyloctahydrofuro[3’,4’:4,5]benzo[1,2-d][1,3]dioxol-5-ol 32 (95 mg, 0.197 mmol) was dissolved in CH₂Cl₂ (2.0 mL) and cooled to -78 °C. BF₃·OEt₂ (0.027 mL, 0.217 mmol) was added by syringe and the solution stirred for 5 min. Allyltrimethylsilane (0.096 mL, 0.519 mmol) was added by syringe and the reaction warmed to RT over 18 h. The reaction was quenched with H₂O (6 mL) and extracted into CH₂Cl₂ (6 mL x 3). The combined organic layers were dried over MgSO₄. The solvent was removed in vacuo to yield a clear oil. Partial acetal deprotection had occurred. The oil was dissolved in CH₂Cl₂ (2 mL). 2,2-Dimethoxypropane (0.5 mL, 3.94 mmol) and pyridinium p-toluene sulfonate (12 mg, 0.059 mmol) were added and the reaction stirred as RT overnight. The reaction was then diluted with CH₂Cl₂ (50 mL), washed with H₂O (50 mL) and sat. aqueous NH₄Cl (50 mL). The aqueous layers were extracted with CH₂Cl₂ (50 mL) and the combined organic layers were dried over MgSO₄. The solvent was removed in vacuo to yield 33a a clear oil (79 mg, 79%). [α]₂₀°+0.64 (c=2.0 CHCl₃); IR (film) 3049, 2931, 1472, 1428 cm⁻¹; ¹H NMR (500 MHz, CDCl₃) δ 7.75-7.69 (4H, m, Ph), 7.44-7.36 (6H, m, Ph), 5.89 (1H, dddd, J=7.5, 7.5, 10.0, 17.5, H-2”), 5.15-5.05 (2H, m, H-3”), 4.45-4.38 (2H, m, H-3a, H-8a), 3.79 (1H, dd, J=5.0, 10.5, Ha-9), 3.74 (1H, dd, J=5.0, 10.5, Hb-9), 3.57 (1H, ddd, J=4.5, 4.5, 7.5, H-7), 3.50 (1H, ddd, J=5.5, 5.5, 14.5, H-5), 2.32-2.22 (3H, m, H-7a, H-1”), 2.14-2.05 (1H, m, H-4a), 1.97 (1H, ddd, J=2.5, 6.0, 14.5, Ha-4 or Ha-8), 1.90 (1H, ddd, J=2.5, 5.5, 14.5, Ha-4 or Ha-8), 1.47 (3H, s, H-1’), 1.34 (3H, s, H-1’), 1.32-1.20 (2H, m, Hb-4, Hb-8), 1.07 (9H, s, tBu); ¹³C NMR (125 MHz, CDCl₃) δ 135.7 (2 x Ph), 135.7 (2 x Ph), 135.0 (C2”), 133.7 (2 x iPh), 129.5 (Ph), 129.5 (Ph), 127.6 (2 x Ph), 127.5 (2 x Ph), 116.8 (C3”), 107.1 (C2’), 85.5 (C5 or C7), 85.0 (C5 or C7), 72.6 (C3a or C8a), 72.4 (C3a or C8a), 65.8 (C9), 38.9 (C1”), 37.1 (C4a), 34.1 (C7a), 28.8 (C4 or C8), 27.7 (C4 or C8), 26.8 (tBu), 26.0 (C1’), 19.2 (Si-C); LC-MS (ESI⁺) m/z 529 [M+Na⁺], Rₜ 2.47 min [method E]; HRMS [M+Na⁺] calcd for C₃₁H₄₃O₄SiNa 529.2755 found 529.2744; Found: C, 73.58; H, 8.40%; C₃₁H₄₃O₄Si requires: C, 73.47; H, 8.35%.

(((3aS,4aS,5S,7S,7aR,8aR)-7-allyl-2,2-dimethyloctahydroisobenzofuro[5,6-d][1,3]dioxol-5-yl)methoxy)(tert-butyl)diphenylsilane 33a (506 mg, 1.09 mmol) was dissolved in THF (10
The solution was cooled to 0 °C under N₂ and TBAF (3.26 mL, 3.26 mmol, 1.0 M in THF) was added by syringe. The reaction was stirred for 3 h at 0 °C before diluted with Et₂O (50 mL). The reaction mixture was washed with H₂O (50 mL x 3) and extracted into Et₂O (50 mL x 2). The combined organic layers were washed with brine (50 mL) and dried over MgSO₄. The solvent was removed in vacuo to give the crude product. This was purified by column chromatography on silica gel (5% MeOH:CH₂Cl₂) to yield 33 as a clear oil (193 mg, 66%).

[α]²³D +6.9 (c=1.0, CHCl₃); IR (film) 3448, 2931, 1381, 1042 cm⁻¹; ¹H NMR (500 MHz, CDCl₃) δ 5.86 (1H, dddd, J=7.0, 7.0, 10.5, 17.0, H-2''), 5.16-5.06 (2H, m, H-3''), 4.45-4.40 (2H, m, H-3a, H-8a), 3.79 (1H, dd, J=2.5, 12.0, Ha-9), 3.63-3.51 (3H, m, Hb-9, H-7, H-5), 2.41-2.36 (2H, m, H-1''), 2.27-2.19 (1H, m, H-7a), 2.13-2.05 (1H, m, H-4a), 1.95-1.89 (2H, m, Ha-4, Ha-8), 1.46 (3H, s, H-1'), 1.33 (3H, s, H-1'), 1.32-1.21 (2H, m, Hb-4, Hb-8); ¹³C NMR (125 MHz, CDCl₃) δ 134.5 (C2''), 177.2 (C3''), 107.2 (C2), 85.7 (C5 or C7), 85.0 (C5 or C7), 72.3 (C8a or C3a), 64.0 (C9), 38.7 (C1''), 37.0 (C4a), 33.0 (C7a), 28.1 (C4 or C8), 26.0 (C1'), 23.7 (C1'); LC-MS (ESI⁺) m/z 291 [M+Na⁺], Rₜ 2.12 min [method D]; HRMS [M+Na⁺] calcd for C₁₅H₂₄O₄Na 291.1567 found 291.1575; Found: C, 67.21; H, 9.02%; C₁₅H₂₄O₄ requires: C, 67.14; H, 9.01%.

((3aS,4aS,5S,7S,7aR,8aR)-7-allyl-2,2-dimethyloctahydroisobenzofuro[5,6-d][1,3]dioxol-5-yl)methyl hex-5-enoate 34

((3aS,4aS,5S,7S,7aR,8aR)-7-allyl-2,2-dimethyloctahydroisobenzofuro[5,6-d][1,3]dioxol-5-yl)methanol 33 (92 mg, 0.343 mmol) was dissolved in CH₂Cl₂ (3.4 mL). Hex-5-enoyl chloride (136 mg, 1.029 mmol) and triethylamine (148 µL, 1.029 mmol) were added and the reaction mixture was stirred at RT for 18 h. The reaction mixture was diluted with CH₂Cl₂ (10 mL) and washed with sat. aqueous NaHCO₃ (15 mL) and H₂O (15 mL x 2). The combined organic layers were dried over MgSO₄ and the solvents removed in vacuo. The crude reaction mixture was purified by column chromatography on silica gel (10% EtOAc:hexane) to yield 34 as a clear oil (116 mg, 93%). The compound was observed to decomposed on RT storage over several weeks. [α]²³D +10.5 (c=1.0 CHCl₃); IR (film) 2937, 1732, 1381, 1163, 1040 cm⁻¹; ¹H NMR (500 MHz, CDCl₃) δ 5.90-5.74 (2H, m, H-2', H-5'''), 5.16-4.97 (4H, m, H-3''', H-6'''''), 4.45-4.40 (2H, m, H-3a, H-8a), 4.28 (1H, dd, J=3.5, 12.0, Ha-9), 4.09 (1H, dd, J=7.0, 12.0, Hb-9), 3.64 (1H, ddd, J=3.5, 7.0, 7.0, H-5), 3.52 (1H, ddd, J=6.0, 6.0, 7.5, H-7), 2.45-2.34 (4H, m, H-2'', H-1''), 2.20-2.07 (4H, m, H-4'', H-4a, H-7a), 1.94 (2H, m, Ha-4, Ha-8), 1.76 (1H, dddd, J=7.0, 7.0, 7.0, Ha-3'''), 1.75 (1H, dddd, J=7.0, 7.0, 7.0, Hb-3'''), 1.46 (3H, s, H-1'), 1.34 (3H, s, H-1'), 1.33-1.20 (2H, m, Hb-4, Hb-8); ¹³C NMR
(125 MHz, CDCl$_3$) δ 173.5 (C1''), 137.7 (C2' or C5''), 137.5 (C2' or C5''), 177.2 (C3' or C8'''), 115.3 (C3' or C8''), 107.2 (C2), 85.2 (C7), 82.7 (C5a or C8a), 72.3 (C3a or C8a), 65.7 (C9), 38.8 (C1''), 36.5 (C7a or C5a), 34.5 (C7a or C5a), 33.4 (C2''' or C4'''), 33.0 (C2''' or C4'''), 28.0 (C4 or C8), 28.0 (C4 or C8), 26.0 (C1'), 24.0 (C3'''), 23.7 (C1'); LC-MS (ESI$^+$) m/z 387 [M+Na$^+$], R$_t$ 2.78 min [method D]; Found: C, 69.17; H, 8.85%; C$_{21}$H$_{32}$O$_5$Na requires: C, 69.20; H, 8.85%.

(E)-[1S,11S,12R,14R,15S,17S]-14,15-Dihydroxy-3,18-dioxa-tricyclo[9.6.1.0$^{12,17}$]octadec-8-en-4-one 36

(1S,2R,4R,8S,10S,11S,18E)-6,6-dimethyl-5,7,13,21-tetraoxatetracyclo[9.9.1.0$^{2,10}$]henicos-18-en-14-one 35

(1S,2R,4R,8S,10S,11S,18E)-6,6-dimethyl-5,7,13,21-tetraoxatetracyclo[9.9.1.0$^{2,10}$]henicos-18-en-14-one 35 (17 mg, 0.051 mmol), was dissolved in THF (0.5 mL). HCl (0.100 mL, 1.00 mmol in H$_2$O) was added and the solution was stirred overnight at RT. The acid and ruthenium impurities from the previous step were removed by basic ion exchange chromatography to yield 36 as an
oil (13 mg, 88%). [α]24D -25.6 (c=1.0 CHCl3); IR (film) 3431, 2929, 1732, 1441 cm⁻¹; ¹H NMR (500 MHz, CDCl3) δ 5.42-5.34 (2H, m, H-8, H-9), 5.16 (2H, dd, J=2.0, 12.0, Ha-2), 3.91-3.79 (3H, m, H-11, H-14, H-15), 3.79-3.76 (1H, m, H-1), 3.49 (1H, dd, J=1.0, 12.5, Hb-2), 2.54-2.47 (1H, m, H-17), 2.49-2.31 (4H, m, Ha-5, Ha-6, Ha-10, H-12), 2.17-2.11 (2H, m, Hb-5, Hb-6), 2.12-1.88 (4H, m, Ha-7, Ha-13, Ha-16, Hb-10), 1.72-1.56 (3H, m, Hb-7, Hb-13, Hb-16); ¹³C NMR (125 MHz, CDCl3) δ 173.8 (C4), 133.9 (C8), 125.3 (C9), 80.8 (C14 or C15), 80.3 (C14 or C15), 68.9 (C1 or C11), 68.4 (C1 or C11), 62.8 (C2), 37.4 (C12), 36.2 (C17), 34.6 (C5 or C6 or C10), 33.9 (C5 or C6 or C10), 33.6 (C5 or C6 or C10), 30.6 (C7 or C13 or C16), 28.6 (C7 or C13 or C16), 22.5 (C7 or C13 or C16); LC-MS (ESI⁺) m/z 319 [M+Na⁺], R₁ 1.58 min [method D]; HRMS [M+Na⁺] calcd for C₁₆H₂₄O₅Na 319.1521 found 319.1518.

(3S,3aS,7aR)-3-(((tert-butyldiphenylsilyl)oxy)methyl)-5-methyl-3a,4,7,7a-tetrahydroisobenzofuran-1(3H)-one (37 major) and (3S,3aS,7aR)-3-(((tert-butyldiphenylsilyl)oxy)methyl)-6-methyl-3a,4,7,7a-tetrahydroisobenzofuran-1(3H)-one (37 minor)

Trifluoromethanesulfonamide (465 mg, 3.13 mmol) was dissolved in CH₂Cl₂ (3.0 mL) in a large pressure tube. Dimethylaluminium chloride (6.3 mL, 6.30 mmol) was added slowly under argon and the solution stirred for 30 min. (S)-5-(((tert-Butyldiphenylsilyloxy)methyl)furan-2-(5H)one 8 (1.00 g, 2.841 mmol) and isoprene (2.84 mL, 28.41 mmol) were added and the tube was sealed and heated to 60 °C for 2 d. The reaction was cooled and diluted with Et₂O (100 mL). The mixture was quenched with NaOH (70 mL, 1M aq soln) and gas was evolved. The aqueous layer was extracted into Et₂O (100 mL x 2) washed with brine (100 mL x 1) and dried over MgSO₄. The solvent was removed in vacuo. The crude mixture was purified by column chromatography on silica gel (10% EtOAc:hexane) to yield an inseparable mixture of products as a clear oil (1.190 g, 100%). [α]²⁴D +4.5 (c=1.0 CHCl₃); IR (CDCl₃ solution cell) 2929, 1769, 1427, 1113 cm⁻¹; ¹H NMR (500 MHz, CDCl₃) δ 7.66-7.64 (4H, m, Ph), 7.49-7.40 (6H, m, Ph), 5.56-5.51 (0.85H, m, H-6 major), 5.50-5.46 (0.15H, m, H-5 minor), 4.15-4.10 (1H, m, H-3), 3.89-3.84 (1H, m, Ha-8), 3.80-3.75 (1H, m, Hb-8), 3.03 (0.15H, ddd, J=4.0, 8.5, 8.5, H-7a minor), 2.93 (0.85H, m, ddd, J=4.0, 8.5, 8.5, H-7a major), 2.77-2.70 (0.85H, m, H-3a major), 2.68-2.63 (0.15H, m, H-3a minor), 2.44-2.37 (1H, m, Ha-7), 2.35-2.27 (1H, m, Hb-7), 2.21-2.17 (0.15H, m, H-4 minor), 2.16 (0.85H, dd, J=7.5, 16.0, Ha-4 major), 1.95-1.88 (0.15H, m, Hb-4 minor), 1.85 (0.85H, dd, J=6.5, 16.5, Hb-4 major), 1.74 (0.45H, br.s, H-9 minor), 1.71 (2.55H, br.s, H-9 major), 1.09 (1.5H, s, ³Bu), 1.07 (7.5H, s, ³Bu); ¹³C NMR (125 MHz, CDCl₃) δ 184.5 (C1), 135.6 (Ph), 135.5 (Ph), 134.7, 133.2, 132.9, 132.6, 129.9, 129.6, 127.8, 127.7, 119.8, 119.2, 110.7 (C6 major),...
110.2 (C5 minor), 84.7 (C3), 64.4 (C8), 37.2 (C7a), 34.8 (C3a), 30.7 (C4), 26.6 ('Bu major), 26.5 ('Bu minor), 23.7 (C9 major), 23.1 (C7), 22.6 (C9 minor), 14.0 (Si-C); LC-MS (ESI+) m/z 443 [M+Na+], R_t 2.70 min [method D].

(3S, 3aS, 5R, 6R, 7aR)-3-(tert-Butyldiphenylsilanyloxymethyl)-6-hydroxy-5-methylhexahydroisobenzofuran-1-one 38

(3S,3aS,7aR)-3-(((tert-Butyldiphenylsilyl)oxy)methyl)-5-methyl-3a,4,7,7a-tetrahydroisobenzofuran-1(3H)-one 37 (1.17 g, 2.66 mmol) was dissolved in THF (26 mL), and cooled to -78°C. BH_3.THF (5.3 mL, 5.3 mmol, 1.0 M solution in THF) was added dropwise and stirred at 0°C for 2 h. The reaction was quenched slowly with H_2O (6 mL). NaOH (6 mL, 20% aqueous solution) was then added dropwise, followed by H_2O_2 (6 mL, 30% aqueous solution). The mixture was left to stir for 30 min. Sat. sodium sulphite (40 mL) was then added, and the layers separated. The aqueous layer was extracted with Et_2O (100 mL x 3). The combined organic layers were dried over MgSO_4 and the solvent removed in vacuo to yield the crude product as a clear oil. The crude reaction mixture was purified by column chromatography on silica gel (33% EtOAc:hexane) to yield 38 as a white solid (612 mg, 55%). mp (117-120°C); [α]_D^24 +8.2 (c=1.0 CHCl_3); IR (film) 3421, 2932, 2859, 1772, 1428 cm^{-1}; ^1H NMR (500 MHz, CDCl_3) δ 7.66-7.63 (4H, m, Ph), 7.48-7.39 (6H, m, Ph), 4.05 (1H, dd, J=4.5, 4.5, H-3), 3.81 (1H, dd, J=4.5, 11.0, Ha-1'), 3.75 (1H, dd, J=4.0, 11.5, Hb-1'), 3.15 (1H, ddd, J=5.0, 10.5, 10.5, H-6), 3.09 (1H, dd, J=7.0, 7.0, H-7a), 2.49-2.40 (2H, m, Ha-4, Ha-7), 1.88-1.82 (1H, m, Hb-4), 1.54 (1H, ddd, J=7.0, 11.0, 14.0, Hb-7), 1.37 (1H, qddd, J=6.5, 3.0, 9.5, 12.5, H-5), 1.11-1.04 (1H, m, H-3a), 1.06 (9H, s, 'Bu), 1.01 (3H, d, J=6.5, H-8); ^13C NMR (125 MHz, CDCl_3) δ 177.9 (C1), 135.7 (2 x Ph), 135.6 (2 x Ph), 132.7 (iPh), 132.5 (iPh), 130.0 (2 x Ph), 127.9 (2 x Ph), 127.7 (2 x Ph), 83.3 (C3), 72.5 (C6), 64.4 (C8), 39.3 (C7a), 37.2 (C5), 36.5 (C4), 36.4 (C3a), 31.7 (C7), 26.8 (tBu), 19.1 (Si-C), 17.9 (C8); LC-MS (ESI+) m/z 461 [M+Na+]\], R_t 2.95 min [method D]; HRMS [M+Na+] calcd for C_{26}H_{34}O_4SiNa 461.2119 found 461.2116; Found: C,71.23; H, 7.75%; C_{26}H_{34}O_4Si requires: C, 71.19; H, 7.81%.

(1S,8E,11S,12R,14R,15R,17S)-14-hydroxy-15-methyl-3,18-dioxatricyclo[9.6.1.0^{12-17}]octadec-8-en-4-one 39
(3S, 3aS, 5R, 6R, 7aR)-3-(tert-Butyldiphenylsilyloxymethyl)-6-hydroxy-5-methylhexahydroisobenzofuran-1-one 38 (612 mg, 1.397 mmol) was dissolved in anhydrous CH₂Cl₂ (13 mL) and cooled to -78 °C under N₂. DIBAL-H (1.0 M in toluene, 1.53 mL, 1.53 mmol) was added dropwise. The reaction was stirred at -78 °C for 4 h then quenched with EtOAc (40 mL). The solution was warmed to RT and a sat. aq. solution of Rochelles salt (40 mL) was added and the mixture was stirred overnight. The aqueous layer was separated and extracted with CH₂Cl₂ (3 x 50 mL). The organic layers were combined, dried over MgSO₄ and the solvent was removed in vacuo NMR analysis showed only 50% conversion. Complete conversion was observed after a further 3 iterations of the above conditions. The final work up yielded a clear oil 39a (580 mg, 94%) as an inseparable mixture of anomers.

IR (film) 3312, 2930, 1428 cm⁻¹; MAJOR ¹H NMR (500 MHz, CDCl₃) δ 7.71-7.66 (4H, m, Ph), 7.47-7.37 (6H, m, Ph), 5.21 (1H, dd, J=6.0, 7.0, H-1), 3.81-3.78 (1H, m, H-3), 3.73-3.55 (2H, m, H-1'), 3.37-3.31 (1H, m, H-6), 2.83 (1H, d, J=7.5, OH), 2.34-2.28 (1H, m, H-7a), 2.15-2.09 (1H, m, H-3a), 1.75-1.66 (1H, m, HA-7), 1.57-1.44 (1H, m, HB-7), 1.44-1.35 (2H, m, H-5, H-3a), 1.11-1.05 (1H, m, HB-4), 1.09 (9H, s, tBu), 1.03 (3H, d, J=6.5, H-8); ¹³C NMR (125 MHz, CDCl₃) δ 135.6 (2 x Ph), 135.6 (2 x Ph), 133.2 (iPh), 133.1 (iPh), 129.9 (2 x Ph), 127.9 (2 x Ph), 127.7 (2 x Ph), 102.1 (C1), 85.2 (C3), 72.7 (C6), 66.0 (C1’'), 45.3 (C7a), 38.2 (C5), 37.8 (C3a), 35.3 (C4), 32.1 (C7), 26.8 (tBu), 19.2 (Si-C), 18.4 (C8); MINOR ¹H NMR (500 MHz, CDCl₃) δ 7.71-7.66 (4H, m, Ph), 7.47-7.37 (6H, m, Ph), 5.38 (1H, dd, J=3.0, 5.0, H-1), 4.00-3.97 (1H, m, H-3), 3.73-3.55 (3H, m, H-1’, H-6), 2.61-2.59 (1H, m, OH), 2.46-2.40 (1H, m, H-7a), 2.27-2.21 (1H, m, H-3a), 2.08-2.03 (1H, m, Ha-7), 1.75-1.66 (1H, m, HA-4), 1.57-1.44 (1H, m, Hb-7), 1.44-1.35 (1H, m, H-5), 1.11-1.05 (1H, m, Hb-4), 1.06 (9H, s, tBu), 1.04 (3H, d, J=6.5, H-8); ¹³C NMR (125 MHz, CDCl₃) δ 135.6 (2 x Ph), 135.6 (2 x Ph), 133.1 (iPh), 133.1 (iPh), 129.9 (2 x Ph), 127.9 (2 x Ph), 127.7 (2 x Ph), 101.1 (C1), 85.8 (C3), 73.5 (C6), 66.0 (C1’), 42.4 (C7a), 39.1 (C3a), 38.1 (C5), 35.3 (C4), 32.1 (C7), 26.8 (tBu), 19.2 (Si-C), 18.4 (C8); LC-MS (ESI⁺) m/z 463 [M+Na⁺], Rₜ 3.00 min [method D]; HRMS [M+Na⁺] calcd 463.2275 for C₂₆H₃₆O₄SiNa found 463.2279.
(3S,3aS,5R,6R,7aR)-3-((tert-Butyldiphenylsilyloxy)methyl)-5-methyloctahydroisobenzofuran-1,6-diol 39a (569 mg, 1.293 mmol) was dissolved in CH₂Cl₂ (13 mL) and cooled to -78 °C. BF₃·OEt₂ (0.50 mL, 3.880 mmol) was added and the solution stirred for 5 min. Allyltrimplsilyl silane (0.63 mL, 3.880 mmol) was then added and the reaction warmed to RT over 18 h. The reaction was quenched with H₂O (20 mL) and extracted into CH₂Cl₂ (30 mL x 3). The combined organic layers were dried over MgSO₄. The solvent was removed in vacuo to yield 39b as a clear oil (549 mg, 91%). [α]_D^20 -16.4 (c=1.0 CH₂Cl₂); IR (film) 3384, 2929, 2885, 1428 cm⁻¹; ^1H NMR (500 MHz, CDCl₃) δ 7.75-7.63 (4H, m, Ph), 7.48-7.37 (6H, m, Ph), 5.86 (1H, dddd, J=7.0, 7.0, 10.5, 17.5, H-2’’), 5.11-5.02 (2H, m, H-3’’), 3.85 (1H, ddd, J=4.0, 8.0, 10.5, H-1), 3.75 (1H, dd, J=4.0, 6.5, H-3), 3.60 (1H, dd, J=4.5, 10.5, H-1’’), 3.50 (1H, dd, J=6.5, 10.5, Hb-1’’), 3.02 (1H, dd, J=4.5, 10.5, 10.5, H-6), 2.89-2.32 (1H, m, Ha-1’’), 2.24 (1H, ddd, J=6.5, 6.5, 12.5, H-3a), 2.18 (1H, ddd, J=7.0, 7.5, 14.5, Hb-1’’), 2.10-2.04 (1H, m, H-7a), 1.93 (1H, ddd, J=2.0, 5.0, 14.0, Ha-7), 1.69 (1H, ddd, J=3.0, 5.5, 12.5, Ha-4), 1.55-1.49 (1H, m, Hb-7), 1.47-1.35 (1H, m, H-5), 1.29 (1H, ddd, J=12.5, 12.5, 12.5, Hb-4), 1.07 (9H, s, tBu), 1.05 (3H, d, J=6.5, H-8); ^13C NMR (125 MHz, CDCl₃) δ 135.6 (4 x Ph), 135.4 (C2’’), 133.7 (iPh), 133.6 (iPh), 129.7 (Ph), 129.6 (Ph), 127.9 (2 x Ph), 127.7 (2 x Ph), 116.8 (C3’’), 84.6 (C3), 79.6 (C1), 72.6 (C6), 66.1 (C1’), 42.6 (C7a), 40.6 (C3a), 39.2 (C1’’), 39.0 (C5), 36.3 (C4), 32.8 (C7), 26.8 (tBu), 19.2 (Si-C), 18.2 (C8); LC-MS (ESI⁺) m/z 487 [M+Na⁺], Rₜ 3.25 min [method D]; HRMS [M+Na⁺] calcd for C₂₉H₄₀O₃SiNa 487.2638 found 487.2647; Found: C, 74.87; H, 8.59%; C₂₉H₄₀O₃Si requires: C, 74.95; H, 8.68%.

(1S,3S,3aR,5R,6R,7aS)-3-Allyl-1-((tertbutyldiphenylsilyloxy)methyl)-6-methyloctahydroisobenzofuran-5-ol 39b (549 mg, 1.362 mmol) was dissolved in THF (13 mL). The solution was cooled to 0 °C under N₂ and TBAF (4.00 mL, 4.00 mmol, 1.0 M in THF) was added. The reaction was stirred for 4 h at 0 °C before diluting with Et₂O (50 mL). The reaction mixture was washed with H₂O (3 x 50 mL) and extracted into Et₂O (2 x 50 mL). The combined organic layers were washed with brine (50 mL) and dried over MgSO₄. The solvent was removed in vacuo to give the crude product. This was purified by column chromatography on silica gel (5% MeOH:CH₂Cl₂) to yield 86 as a clear oil (160 mg, 52%). [α]_D^20 –30.7 (c=1.0 CH₂Cl₂); IR (film) 3368, 2922, 1456, 1031 cm⁻¹; ^1H NMR (500 MHz, CDCl₃) δ 5.88 (1H, dddd, J=7.0, 7.0, 10.0, 17.0, H-2’’), 5.15-5.09 (2H, m, H-3’’), 3.92 (1H, ddd, J=4.0,
7.0, 10.5, H-1), 3.72-3.70 (1H, m, H-3), 3.53 (1H, dd, J=4.0, 11.0, Ha-1’), 3.43 (1H, dd, J=7.0, 11.5, Hb-1’), 3.31 (1H, ddd, J=4.5, 10.0, 10.0, H-6), 2.48-2.42 (1H, m, Ha-1’), 2.24-2.17 (1H, m, Hb-1’), 2.16-2.10 (1H, m, H-7a), 2.04 (1H, ddd, J=6.5, 6.5, 13.0, H-3a), 1.93 (1H, ddd, J=2.5, 4.5, 14.0, H-7), 1.72 (1H, ddd, J=3.0, 6.0, 14.0, Ha-4), 1.56 (1H, ddd, J=6.0, 11.0, 14.0, Hb-7), 1.38 (1H, dqqd, J=3.0, 6.5, 10.0, 13.0, H-5), 1.19 (1H, ddd, J=13.0, 13.0, 14.0, Hb-4), 1.04 (3H, d, J=6.5, H-8); 13C NMR (125 MHz, CDCl3) δ 134.5 (C2”), 117.5 (C3”), 84.5 (C3), 79.7 (C1), 72.4 (C6), 65.5 (C1’), 42.8 (C3a), 40.5 (C7a), 38.5 (C5), 38.7 (C1’), 36.0 (C4), 32.7 (C7), 18.2 (C8); LC-MS (ESI+) m/z 271 [M+Na+], Rf 2.55 min [method D].

(1S,3S,3aR,5R,6R,7aS)-3-Alllyl-1-(hydroxymethyl)-6-methyloctahydroisobenzofuran-5-ol 86 (50 mg, 0.221 mmol) was dissolved in CH2Cl2 (1.2 mL). Hex-5-enoyl chloride (32 mg, 0.243 mmol) and triethylamine (95 µL, 0.663 mmol) were added and the reaction mixture was stirred for 3 d. The solvents were removed in vacuo under argon and the reaction mixture was stirred for 3 d. DMSO (10 µL) was added and the solution was stirred overnight. The solvents were removed in vacuo and the resultant mixture purified by column chromatography on silica gel (15% EtOAc:hexane) to yield 39 as a clear oil (19 mg, 80%). [α]24D -20.8 (c=1.0 CHCl3); IR (film) 3432, 2919, 1738, 1446 cm⁻¹; 1H NMR (500 MHz, CDCl3) δ 5.42-5.35 (2H, m, H-8, H-9), 5.13 (1H, dd, J=3.0, 12.0, Ha-2), 3.94 (1H, ddd, J=3.0, 3.0, 11.0, H-11), 3.69 (1H, m, H-1), 3.42 (1H, d, J=12.0, Hb-2), 3.30 (1H, ddd,
J=5.0, 11.0, 11.0, H-14), 2.49-2.34 (4H, m, Ha-7, Ha-10, H-12, Ha-5 or Ha-6), 2.28-2.22 (1H, m, H-17), 2.17-2.03 (3H, m, Hb-7, Hb-10, Ha-5 or Ha-6), 1.95-1.87 (2H, m, Hb-13, Hb-5 or Hb-6), 1.74-1.70 (1H, m, Ha-16), 1.71-1.57 (2H, m, Hb-13, Hb-5 or Hb-6), 1.45-1.38 (1H, m, Ha-15), 1.18 (1H, ddd, J=13.0, 13.0, 13.0, Hb-16), 1.03 (3H, d, J=6.5, H-19); 13C NMR (125 MHz, CDCl3) δ 173.9 (C4), 133.1 (C8), 125.8 (C9), 81.9 (C1), 79.2 (C11), 72.5 (C14), 64.4 (C2), 41.5 (C17), 39.3 (C12), 38.9 (C15), 36.8 (C16), 33.8 (C5 or C6), 33.0 (C7), 32.3 (C10 or C13), 32.3 (C10 or C13), 21.8 (C5 or C6), 18.1 (C19); LC-MS (ESI+) m/z 317 [M+Na]+, R_t 1.90 min [method D]; HRMS [M+Na]+ calcd for C17H26O4Na 317.1723 found 317.1726.

(1R,2S,3S,10E,13S,14R,15S)-5,20-dioxatetracyclo[13.2.2.13,13.02,14]icosa-10,16-dien-6-one 40

Trifluoromethanesulfonamide (465 mg, 3.12 mmol) was dissolved in CH2Cl2 (3.0 mL) in a pressure tube. Dimethylaluminium chloride (6.2 mL, 6.2 mmol) was added slowly under argon and the solution stirred for 30 min. (S)-5-[(tert-Butyldiphenylsilyloxy)methyl]furan-2-(5H)one 8 (1.00 g, 2.841 mmol) and cyclohexadiene (2.7 mL, 28.4 mmol) were added and the tube was sealed and heated to 60 °C for 2 d. The reaction was cooled and diluted with EtO (100 mL), the mixture was quenched with NaOH (70 mL, 1M aq sol) and gas was evolved. The aqueous layer was extracted into Et2O (100 mL x 2) washed with brine (100 mL x 1) and dried over MgSO4. The solvent was removed in vacuo. The crude mixture was purified by column chromatography on silica gel (10% EtOAc:hexane) to yield 40a a clear oil (930 mg, 75%). [α]23° +10.0 (c=1.0 CHCl3); IR (film) 2934, 1767 (C=O) cm⁻¹; 1H NMR (500 MHz, CDCl3) δ 7.69-7.64 (4H, m, Ph), 7.48-7.39 (6H, m, Ph), 6.35-6.31 (1H, m, H-9), 6.27-6.23 (1H, m, H-8), 4.04 (1H, dd, J=3.5, 6.5, H-5), 3.80 (1H, dd, J=4.0, 11.0, Ha-1'), 3.67 (1H, dd, J=3.0, 11.0, Hb-1'), 3.10-3.06 (1H, m, H-1), 2.83 (1H, dd, J=3.5, 10.0, H-2), 2.67-2.63 (1H, m, H-7), 2.58 (1H, ddd, J=3.5, 3.5, 10.0, H-6), 1.62-1.56 (1H, m, Ha-10), 1.52-1.57 (1H, m, Ha-11), 1.35 (1H, dddd, J=3.0, 3.0, 12.0, 12.0, Hb-10), 1.30 (1H, dddd, J=3.0, 3.0, 12.0, 12.0, Hb-11).
\((1S,2R,5S,6S,7R)\)-5-\{\textit{tert}-Butyldiphenylsilylanyloxymethyl\}-4-oxatricyclo[5.2.2.0^{2,6}]\textit{undec}-8-en-3-one \textit{40a} (481 mg, 1.13 mmol) was dissolved in anhydrous \textit{CH}_{2}Cl_{2} (5.6 mL) and cooled to -78 °C under \textit{N}_{2}. \textit{DIBAL}-\textit{H} (1.0 M in toluene, 1.23 mL, 1.23 mmol) was added dropwise. The reaction was stirred at -78 °C for 3 h then quenched with \textit{EtOAc} (10 mL). The solution was warmed to RT and a sat. aq. solution of Rochelles salt (6 mM) was added and the mixture stirred overnight. The aqueous layer was separated and extracted with \textit{CH}_{2}Cl_{2} (20 mL x 3). The organic layers were combined, dried over \textit{MgSO}_{4} and the solvent was removed \textit{in vacuo}.

The crude mixture was purified by column chromatography on silica gel (15% \textit{EtOAc}:hexane) to yield a clear oil \textit{40b} (530 mg, 86%) as the kinetic anomer which converts to a mixture of anomers overnight in \textit{CDCl}_{3}. \([\alpha]^{23}_{D}=-15.6 \text{ (c=1.0 CHCl}_{3}\); IR (film) 3411, 2933, 1472, 1427 cm\(^{-1}\); \(^1\text{H NMR} (500 \text{MHz, CDCl}_{3}) \delta \text{ Anomer A} 7.74-7.66 (4H, m, Ph), 7.49-7.36 (6H, m, Ph), 6.28-6.20 (2H, m, H-9, H-8), 5.01 (1H, s, H-3), 3.82-3.76 (2H, m, H-5, Ha-1'), 3.58 (1H, dd, \textit{J}=2.0, 10.0, Hb-1'), 2.79-2.75 (1H, m, H-1), 2.53-2.48 (1H, m, H-7), 2.41-2.38 (2H, m, H-2, H-6), 1.56-1.14 (4H, m, H-10, H-11), 1.12 (9H, s, tBu); \text{ Anomer B} 7.74-7.66 (4H, m, Ph), 7.49-7.36 (6H, m, Ph), 6.25-6.18 (1H, m, H-9 or H-8), 6.11-6.08 (1H, m, H-9 or H-8), 4.80 (1H, d, J=2.0, H-3), 3.74-3.67 (2H, m, H-5, Ha-1'), 3.61-3.52 (1H, m, Hb-1'), 2.57-2.53 (1H, m, H-1 or H-7), 2.44-2.41 (1H, m, H-1 or H-7), 2.34 (1H, ddd, \textit{J}=3.5, 3.5, 10.0, H-6), 2.14 (1H, ddd, \textit{J}=2.0, 3.5, 10.0 H-2), 1.56-1.14 (4H, m, H-10, H-11), 1.09 (9H, s, tBu); \(^{13}\text{C NMR} (125 \text{MHz, CDCl}_{3}) \delta \text{ Anomer A} 135.8 (2 \text{ x Ph A or B}), 135.7 (2 \text{ x Ph A or B}), 135.6 (2 \text{ x Ph A or B}), 135.5 (2 \text{ x Ph A or B}), 133.8 (2 \text{ x Ph A or B}), 133.3 (2 \text{ x Ph A or B}), 133.3 (2 \text{ x Ph A or B}), 133.3 (2 \text{ x Ph A or B}), 133.2 (2 \text{ x Ph A or B}), 133.2 (2 \text{ x Ph A or B}), 133.2 (2 \text{ x Ph A or B}), 133.0 (2 \text{ x Ph A or B}), 129.9 (Ph A or B), 129.6 (Ph A or B), 127.8 (Ph A or B), 127.8 (Ph A or B), 127.6 (Ph A or B), 127.6 (Ph A or B), 105.7 (C3B), 104.6 (C3A), 86.5 (CA5), 85.6 (CA5), 67.3 (C1' A or B), 67.1 (C1' A or B), 55.5 (CA6 or CA2A), 52.2 (CA6 or CA2B), 47.3 (CA6 or CA2B), 46.1 (CA6 or CA2A), 34.9 (C1 or C7, A or B), 33.9 (C1 or C7, A or B), 33.9 (C1 or C7, A or B), 32.3 (C1A or C7A), 31.5 (C1A or C7A), 27.0 (tBu A or B), 26.9 (tBu A or B), 24.5 (C10 or C11, A or B), 24.5 (C10 or C11, A or B), 19.8 (Si-C, A or B), 19.8 (Si-C, A or B), 19.8 (Si-C, A or B), 19.8 (Si-C, A or B), 19.8 (Si-C, A or B), 19.8 (Si-C, A or B), 19.8 (Si-C, A or B), 19.8 (Si-C, A or B). LC-MS (ESI\(^{+}\)) \textit{m/z} 457 [M+Na\(^{+}\)], \textit{R}_{t} 2.78 min [method D]; HRMS [M+Na\(^{+}\)] calcd for \textit{C}_{27}\text{H}_{32}\text{O}_{3}\text{SiNa} 457.2169 found 457.2167; Found: C, 74.57; H, 7.92%; \textit{C}_{27}\text{H}_{32}\text{O}_{3}\text{Si} requires: C, 74.57; H, 7.92%.
into CH₂Cl₂ (6 mL x 3). The combined organic layers were dried over MgSO₄. The solvent was removed in vacuo to yield 40c as a clear oil (60 mg, 76%). [α]²³.⁷⁰ +5.5 (c=1.0 CH₂Cl₂); IR (film) 3046, 2932, 2860, 1472, 1428 cm⁻¹; ¹H NMR (500 MHz, CDCl₃) δ 7.76-7.71 (4H, m, Ph), 7.47-7.38 (6H, m, Ph), 6.22-6.19 (2H, m, H-8, H-9), 5.88 (1H, dddd, J=7.0, 7.0, 10.0, 17.0, H-2'), 5.15-5.05 (2H, m, H-3'), 3.80 (1H, dd, J=5.0, 10.5, Ha-1''), 3.70 (1H, dd, J=5.0, 10.5, Hb-1''), 3.60 (1H, ddd, J=5.0, 5.0, 8.0, H-3), 3.55 (1H, ddd, J=6.0, 6.0, 8.0, H-5), 2.55-2.49 (2H, m, H-1, H-7), 2.41-2.28 (2H, m, H-1''), 2.25 (1H, ddd, J=3.0, 8.0, 11.0, H-2), 2.05 (1H, ddd, J=3.0, 8.0, 11.0, H-6), 1.50-1.42 (2H, m, Ha-10, Ha-11), 1.34-1.26 (2H, m, Hb-10, Hb-11), 1.10 (9H, s, ³Bu); ¹³C NMR (125 MHz, CDCl₃) δ 135.7 (2 x Ph), 135.7 (2 x Ph), 135.3 (C₂'), 134.3 (C₈ or C₉), 134.1 (C₈ or C₉), 133.8 (iPh), 133.8 (iPh), 131.5 (C₁'), 131.5 (C₁'), 129.5 (2 x Ph), 127.6 (4 x Ph), 116.5 (C₃'), 83.6 (C₃), 82.9 (C₅), 66.3 (C₁''), 51.9 (C₆), 49.6 (C₂), 39.8 (C₁'), 32.1 (C₁ or C₇), 31.9 (C₁ or C₇), 26.9 (³Bu), 24.6 (C₁₀ or C₁₁), 24.6 (C₁₀ or C₁₁), 19.3 (Si-C); LC-MS (ESI⁺) m/z 481 [M+Na⁺], Rt 3.35 min [method E]; HRMS [M+Na⁺] calcd for C₃₀H₃₈O₂SiNa 481.2533 found 481.2547; Found: C, 78.56; H, 8.29%; C₃₀H₃₈O₂Si requires: C, 78.55; H, 8.35%.

((1R, 2S, 3S, 5S, 6R, 7S)-5-allyl-4-oxatricyclo[5.2.2.0²⁶]undec-8-en-3-ylmethoxy)tertbutyldiphenylsilane 40c (969 mg, 2.173 mmol) was dissolved in THF (22 mL). The solution was cooled to 0 °C under N₂ and TBAF (6.5 mL, 6.5 mmol, 1.0 M in THF) was added by syringe. The reaction was stirred for 3.5 h at 0 °C before diluting with Et₂O (50 mL). The reaction mixture was washed with H₂O (3 x 50 mL) and extracted into Et₂O (3 x 50 mL). The combined organic layers were dried over MgSO₄ and the solvent was removed in vacuo to give the crude product. This was purified by column chromatography on silica gel (50% EtOAc:hexane) to yield 41as as a clear oil (332 mg, 72%). [α]²³.⁷⁰ -23.5 (c=1.0 CHCl₃); IR (film) 3431, 2936 cm⁻¹; ¹H NMR (500 MHz, CDCl₃) δ 6.22-6.16 (2H, m, H-8, H-9), 5.84 (1H, dddd, J=7.0, 7.0, 10.0, 17.0, H-2'), 5.14-5.04 (2H, m, H-3'), 3.79-3.73 (1H, m, Ha-1''), 3.58-3.51 (3H, m, Hb-1''), 3.0, 8.0, 11.0, 17.0 (c=1.0 CHCl₃) and 1.58-1.51 (2H, m, Hb-1''), 2.62-2.45 (2H, m, H-1, H-7), 2.39-2.27 (3H, m, H-1'), OH), 1.25-1.19 (1H, m, H-2), 1.08-1.08 (1H, m, H-6), 1.21-1.18 (2H, m, Ha-10, Ha-11), 1.34-1.24 (2H, m, Hb-10, Hb-11); ¹³C NMR (125 MHz, CDCl₃) δ 134.8 (C₂'), 134.2 (C₈ or C₉), 134.1 (C₈ or C₉), 116.9 (C₃'), 83.9 (C₃ or C₅), 83.9 (2 x C₅), 66.2 (C₁''), 52.0 (C₆), 47.6 (C₂), 39.4 (C₁'), 31.8 (C₁ or C₇), 31.6 (C₁ or C₇), 24.5 (C₁₀ or C₁₁), 24.5 (C₁₀ or C₁₁); LC-MS (ESI⁺) m/z 243.24 [M+Na⁺], Rt 2.22 min [method D]; HRMS [M+H⁺] calcd for C₁₄H₂₁O₂ 221.1536 found 221.1538; Found: C, 76.21; H, 9.15%; C₁₄H₂₁O₂ requires: C, 76.33; H, 9.15%.

((1R, 2S, 3S, 5S, 6R, 7S)-5-Allyl-4-oxatricyclo[5.2.2.0²⁶]undec-8-en-3-yl)-methanol 84 (82 mg, 0.372 mmol) was dissolved in CH₂Cl₂ (3.0 mL). Hex-5-enoyl chloride (152 mg, 1.112 mmol) and triethylamine (160 µL, 1.112 mmol) were added and the reaction mixture was stirred at RT for 36 h. The reaction mixture was diluted with CH₂Cl₂ (10 mL) and washed with H₂O (10 mL x 2) and brine (10 mL). The aqueous layers were combined and extracted with CH₂Cl₂ (10 mL x 2). The combined organic layers were washed with brine (10 mL), dried with MgSO₄ and the solvents removed in vacuo. The crude reaction mixture was purified by column chromatography on silica gel (10% EtOAc:hexane) to yield 85 as a clear oil (81 mg, 70%).
[α]$^{23.7}_{D}$ +3.4 (c=1.0 CHCl$_3$); IR (film) 2938, 2868, 1737 cm$^{-1}$; $^1$H NMR (500 MHz, CDCl$_3$) δ 6.23-6.18 (2H, m, H-9, H-8), 5.89-5.75 (2H, m, H-2', H-7''), 5.14-4.94 (4H, m, H-3', H-8''), 4.25 (1H, dd, J=3.5, 11.5, Ha-1''), 4.03 (1H, dd, J=7.0, 11.5, Hb-1''), 3.66 (1H, ddd, J=3.5, 7.0, 7.0, H-3), 3.55 (1H, ddd, J=6.5, 6.5, 6.5, H-5), 2.55-2.49 (2H, m, H-1, H-7), 2.45-2.34 (2H, m, H-1, H-7), 2.34-2.27 (4H, m, H-1', H-4''), 2.14-2.04 (4H, m, H-2, H-6, H-6''), 1.78-1.73 (2H, m, H-5''), 1.48-1.43 (2H, m, Ha-10, Hb-11), 1.36-1.25 (2H, m, Hb-10, Hb-11). $^{13}$C NMR (125 MHz, CDCl$_3$) δ 173.6 (C2''), 137.2 (C2' or C7''), 134.7 (C2' or C7''), 134.5 (C8 or C9), 133.9 (C8 or C9), 116.9 (C8' or C3'), 115.3 (C8' or C3'), 83.2 (C5), 80.9 (C3), 66.1 (C1''), 51.4 (C2 or C6), 49.3 (C2 or C6), 39.4 (C1'), 33.5 (C4''), 33.0 (C6''), 31.8 (C1 or C6), 31.6 (C1 or C6), 24.5 (C10 or C11), 24.5 (C10 or C11), 24.0 (C5''); LC-MS (ESI$^+$) m/z 339 [M+Na$^+$], R$_t$ 3.05 min [method D]; HRMS [M+H$^+$] calcd for C$_{20}$H$_{29}$O$_3$ 317.2111 found 317.2107.

(1R,2S,3S,5S,6R,7S)-5-Allyl-4-oxatricyclo[5.2.2.0$^{2,6}$]undec-8-enylmethyl hex-5-enoate 85 (30 mg, 0.095 mmol) was dissolved in CH$_2$Cl$_2$ (94 mL, 0.001 M). Argon was bubbled though the solution for 5 min. Grubbs II (8 mg, 0.0095 mmol, 10 mol%) was added under argon and the reaction mixture was stirred for 5 d. DMSO (10 µL) was added and the solution was stirred overnight. The solvents were removed in vacuo and the resultant mixture purified by column chromatography on silica gel (15% EtOAc:hexane) to yield 40 as a crystalline solid (14 mg, 51%). mp (129-134 °C); [α]$^{24}_{D}$ -60.2 (c=1.0 CHCl$_3$); IR (film) 2930, 2865, 1738, 1433 cm$^{-1}$; $^1$H NMR (500 MHz, CDCl$_3$) δ 6.28-6.14 (2H, m, H-17, H-16), 5.46 (1H, dddd, J=1.5, 4.5, 10.0, 15.0, H-11), 5.37 (1H, dddd, J=1.0, 4.0, 11.0, 15.0, H-10), 5.18 (1H, dd, J=2.0, 11.5, H-4), 3.67-3.60 (2H, m, H-3, H-13), 3.44 (1H, d, J=11.5, Hb-4), 2.54-2.48 (3H, m, H-2, H-14, H-1 or H-15), 2.45-2.33 (3H, m, Ha-12, Ha-9, Ha-7), 2.29 (1H, ddd, J=3.0, 7.5, 10.5, H-1 or H-15), 2.12-2.01 (3H, m, Ha-8, Hb-7, Hb-12), 1.90-1.81 (1H, m, Hb-9), 1.67-1.60 (1H, m, Hb-8), 1.55-1.47 (2H, m, H-19 or H-18), 1.35-1.29 (2H, m, H-19 or H-18); $^{13}$C NMR (125 MHz, CDCl$_3$) δ 173.9 (C6), 134.7 (C16 or C17 or C10), 134.6 (C16 or C17 or C10), 134.1 (C16 or C17 or C10), 124.4 (C11), 82.7 (C3 or C13), 82.1 (C3 or C13), 61.3 (C4), 48.6 (C1 or C15), 47.8 (C1 or C15), 34.9 (C7 or C12 or C9), 34.7 (C7 or C12 or C9), 33.6 (C7 or C8 or C9), 32.1 (C2 or C14), 31.7 (C2 or C14), 24.6 (C18 or C19), 24.3 (C18 or C19), 22.4 (C8); LC-MS (ESI$^+$) m/z 311 [M+Na$^+$], R$_t$ 2.87 min [method D]; HRMS [M+H$^+$] calcd for C$_{17}$H$_{25}$O$_3$ 289.1804 found 289.1798; Found: C, 73.81; H, 8.63%; C$_{18}$H$_{24}$O$_3$ requires: C, 73.88; H, 8.75%.

(1R,7E/R,10S,11R,12R,15S,16S)-2,17-dioxatetracyclo[8.6.1.1$^{12,15}$,0$^{14,16}$]octadec-7-en-3-one 41
Dicyclopentadiene was cracked by heating to 170 °C and distillation of the monomer product. \((S)-5-(\text{tert-Butyldiphenylsilyloxy})\text{methyl}furan-2-(5H)\)-one 8 (500 mg, 1.433 mmol) was weighed into a pressure tube, and cyclopentadiene (4.6 mL, 56.0 mmol) was added. The tube was sealed and heated to 110 °C for 3 d. The pressure tube was then cooled to 0 °C to reduce excess pressure, and the reaction was diluted in CH$_2$Cl$_2$ (10 mL). Solvent and unreacted cyclopentadiene were removed in vacuo. Non-polar side-products were removed by loading the crude reaction mixture onto a plug of silica and washing with hexane. The products were then washed through the silica with EtOAc and concentrated in vacuo. The products were then separated by column chromatography (25% EtOAc:hexane) to give the endo product 41a as a white crystalline solid (305 mg, 69%) and the exo product as a clear oil (116 mg, 16%). Endo Product 41a [α]$^2$$^3$D -17.3 (c=2.78, CH$_2$Cl$_2$); IR (film) 3070, 2931, 2857, 1770 (CO), 1427 cm$^{-1}$; $^1$H NMR (500 MHz, CDCl$_3$) $\delta$ 7.70-7.65 (4H, m, Ph), 7.50-7.38 (6H, m, Ph), 6.32 (1H, dd, $J=3.0, 6.0, H-9$), 6.23 (1H, dd, $J=3.0, 6.5, H-8$), 3.97 (1H, dd, $J=3.0, 6.0, H-5$), 3.79 (1H, dd, $J=3.5, 11.0, Ha-1'$), 3.75 (1H, dd, 3.0, 11.0, Hb-1'), 3.50-3.35 (2H, m, H-7, H-2), 3.10-3.07 (1H, m, H-6), 3.05-3.01 (1H, m, H-1), 1.66 (1H, d, $J=8.5, Ha-10$), 1.46 (1H, d, $J=8.5, Hb-10$), 1.07 (9H, s, tBu); $^{13}$C NMR (125 MHz, CDCl$_3$) $\delta$ 177.8 (C3), 137.7 (C8), 137.3 (C9), 135.6 (Ph), 135.5 (Ph), 135.4 (Ph), 134.7 (Ph), 133.2 (iPh), 132.6 (iPh), 129.9 (Ph), 129.6 (Ph), 127.8 (2 x Ph), 127.8 (2 x Ph), 82.1 (C5), 65.7 (C1'), 51.7 (C10), 48.8 (C2), 45.9 (C1), 45.7 (C7), 43.1 (C6), 26.9 (tBu), 19.2 (Si-C); LC-MS (ESI$^+$) m/z 441 [M+Na$^+$], R$_t$ 5.80 min [method B]; HRMS [M+Na$^+$] calcld for C$_{26}$H$_{30}$O$_3$SiNa 441.1856; found 441.1857. Found: C, 74.58; H, 7.23%. Requires: C, 74.60; H, 7.22%. Exo Product [α]$^2$$^3$D -0.61 (c=2.14, CH$_2$Cl$_2$); IR (film) 3070, 3049, 2930, 2857, 1745 (CO), 1428 cm$^{-1}$; $^1$H NMR (500 MHz, CDCl$_3$) $\delta$ 7.70-7.65 (4H, m, Ph), 7.48-7.38 (6H, m, Ph), 6.26 (1H, dd, $J=3.0, 6.0, H-9$), 6.19 (1H, dd, $J=3.0, 6.0, H-8$), 4.20 (1H, dd, $J=3.0, 3.0, H-5$), 3.84 (1H, dd, $J=3.5, 11.0, Ha-1'$), 3.75 (1H, dd, 3.5, 11.0, Hb-1'), 3.29 (1H, m, H-1), 2.88 (1H, m, H-7), 2.72 (1H, d, $J=8.5, H-2$), 2.46 (1H, dd, $J=3, 8.5, H-6$) 1.53 (2H, m, H-10), 1.05 (9H, s, tBu); $^{13}$C NMR (125 MHz, CDCl$_3$) $\delta$ 177.4 (C8), 173.7 (C7), 137.8 (C8), 137.5 (C9), 135.7 (Ph), 135.6 (Ph), 135.2 (Ph), 134.8 (Ph), 133.1 (Ph), 129.5 (Ph), 129.9 (Ph), 127.8 (Ph), 137. (Ph), 135.6 (Ph), 135.2 (Ph), 134.8 (Ph), 133.1 (Ph), 132.5 (Ph), 129.9 (Ph), 129.9 (Ph), 127.8 (Ph)
(2 x Ph), 127.7 (2 x Ph), 83.3 (C5), 65.7 (C1’), 49.1 (C2), 47.6 (C7), 46.6 (C1), 44.8 (C6), 43.6 (C10), 26.7 (‘Bu), 19.1 (Si-C); LC-MS (ESI+) m/z 441 [M+Na+], Rf 5.80 min [method B]; HRMS [M+Na+] C26H30O3SiNa calcd for 441.1856; found 441.1857.

(15,2R,5S,6S,7R)-5-(tert-Butyldiphenylsilanoloxymethyl)-4-oxa-tricyclo[5.2.1.0.2,6]dec-8-en-3-one 41a (150 mg, 0.36 mmol) was dissolved in EtOAc (3.6 mL) and Pd/C (7.5 mg, 10% w/w Pd) was added. The solution was stirred under H2 (1 atm). The solution was stirred overnight at RT before being filtered through silica, washing with EtOAc. The solvent was removed in vacuo to yield 41b a white crystalline solid (149 mg, 100%). mp (78-81 °C) [α]22 D 36.9 (c=0.89 CH2Cl2); IR (film) 3076, 3026, 2910, 2841, 1740, 1641 cm⁻¹; 1H NMR (500 MHz, CDCl3) δ 7.73-7.60 (4H, m, Ph), 7.52-7.33 (6H, m, Ph), 4.39 (1H, dd, J=2.5, 5.0, H-5), 3.87 (1H, dd, J=3.0, 11.0, Ha-1’), 3.62 (1H, dd, J=3.0, 11.0, Hb-1’), 3.05 (1H, dd, J=5.5, 11.0, H-2), 2.76-2.74 (1H, m, H-6), 2.70-2.65 (1H, m, H-1), 2.42-2.30 (1H, m, H-7), 1.66-1.44 (6H, m, H-8, H-10, H-9), 1.06 (9H, s, 3‘Bu); 13C NMR (125 Hz, CDCl3) δ 178.4 (C3), 135.7 (2 x Ph), 135.6 (2 x Ph), 133.1 (Ph), 132.5 (Ph), 129.9 (2 x Ph), 127.8 (4 x Ph), 79.8 (C5), 66.2 (C1’), 48.2 (C2), 45.1 (C6), 41.6 (C10), 40.2 (C1), 39.7 (C7), 26.7 (‘Bu), 25.4 (C8 or C9), 19.1 (C8 or C9), 14.2 (Si-C); LC-MS (ESI+) m/z 443 [M+Na+], Rf 5.65 min [method B], HRMS [M+Na+] calcd for C26H32O3SiNa 443.2038; found 443.2037.

(15,2R,5S,6S,7R)-5-(tert-Butyldiphenylsilanoloxymethyl)-4-oxa-tricyclo[5.2.1.0.2,6]decan-3-one 41c (101 mg, 0.239 mmol) was dissolved in CH2Cl2 (1 mL) and cooled to -78 °C. BF3·OEt2 (90 µL, 0.718 mmol) was added and the solution stirred for 5 min. Allyltrimethylsilane (114 µL, 0.719 mmol) was added and the reaction then warmed to RT. The reaction was stirred for
18 h before quenching with H$_2$O (7 mL), and extracted with CH$_2$Cl$_2$ (3 x 7 mL). The combined organic layers were washed with brine (10 mL) and dried with MgSO$_4$. The solvent was removed in vacuo to yield **41d** a clear oil (97 mg, 92%). [α]$^{24.0}_{D}$ 4.1 (c=0.75, CH$_2$Cl$_2$); IR (film) 3071, 3048, 2956, 1427 cm$^{-1}$; $^1$H NMR (500 MHz, CDCl$_3$) δ 7.70-7.75 (4H, m, Ph), 7.41-7.48 (6H, m, Ph), 5.77-5.82 (1H, m, H-2”), 5.03-5.06 (2H, m, H-3”), 3.93 (1H, ddd, J=5.0, 6.0, 6.0, H-3), 3.85 (1H, ddd, J=5.0, 5.0, 7.0, H-5) 3.69 (1H, dd, J=5.5, 10.0, H-a’), 3.53 (1H, dd, J=6.5, 10.0, Hb’), 2.55-2.52 (1H, m, H-2), 2.35-2.29 (2H, m, H-6, Ha-1”) 2.20 (1H, br s, H-7), 2.15 (1H, br s, H-1), 2.17-2.11 (1H, m, Hb’), 1.68-1.60 (4H, m, H-8, H-9), 1.41 (2H, d, J=8.0, H-10), 1.05 (9H, s, tBu); $^{13}$C NMR (125 MHz, CDCl$_3$) δ 135.7 (2 x Ph), 135.7 (2 x Ph), 135.4 (C2”), 133.8 (Ph), 133.7 (Ph), 129.6 (Ph), 129.5 (Ph), 127.6 (4 x Ph), 116.5 (C3”), 79.7 (C3), 78.9 (C5), 67.4 (C1”), 52.6 (C6), 50.4 (C2), 44.0 (C8), 42.0 (C2”), 39.9 (C7), 39.9 (C1), 26.9 (tBu), 22.9 (C9), 19.2 (Si-C).

$\{(1R,25,35,55,6R,7S)-5$-Allyl-4-oxatricyclo$[5.2.1.0^{2,6}]$decane-3-ylmethoxy-tert-butyldiphenylsilane $\textbf{41d}$ (90 mg, 0.202 mmol) was dissolved in THF (1.1 mL). The solution was cooled to 0 °C under N$_2$ and TBAF (0.60 mL, 0.60 mmol, 1.0 M in THF) was added by syringe. The reaction was stirred for 2 h at 0 °C before diluting with Et$_2$O (10 mL). The reaction mixture was washed with H$_2$O (3 x 10 mL) and extracted into Et$_2$O (3 x 10 mL). The combined organic layers were dried over MgSO$_4$ and the solvent was removed in vacuo to give the crude product. This was purified by column chromatography on silica gel (15% EtOAc:hexane) to yield $\textbf{41e}$ as a clear oil (39 mg, 92%). [α]$^{22.0}_{D}$ 15.3 (c=0.53 CH$_2$Cl$_2$); IR (film) 3416, 2950, 2879, 1641, 1455, 1048 cm$^{-1}$; $^1$H NMR (500 MHz, CDCl$_3$) δ 5.76 (1H, tdd, J=7.0, 10.5, 17.0, Ha-3’), 5.11-5.06 (2H, m, H-3’), 4.04-3.99 (2H, m, H-3, H-5), 3.52 (1H, dd, J=4.0, 11.5, Ha-1”), 3.42 (1H, dd, J=8.0, 11.5, Hb’), 2.41-2.34 (3H, m, Ha-1”, H-7 or H-1, H-2 or H-6), 2.27-2.23 (3H, m, Hb’), H-1 or H-7, H-2 or H-6), 2.07 (1H, m, OH), 1.61-1.69 (4H, m, H-8, H-9), 1.46-1.49 (2H, m, H-10); $^{13}$C NMR (125 MHz, CDCl$_3$) δ 135.2 (C2’), 116.9 (C3’), 79.8 (C3), 78.8 (C5), 66.3 (C1”), 52.7 (C6 or C2), 49.0 (C6 or C2), 43.8 (C10), 42.4 (C1’), 39.9 (C1), 39.5 (C7), 22.9 (C8 or C9), 22.9 (C8 or C9); LC-MS (ESI$^+$) m/z 231 [M+Na$^+$], R$_t$ 2.20 min [method D]; HRMS [M+H$^+$] calcd for C$_{13}$H$_{21}$O$_{2}$ 209.1536; found 209.1539.

$\{(1R,25,35,55,6R,7S)-5$-Allyl-4-oxatricyclo$[5.2.1.0^{2,6}]$decane-3-yl)methanol $\textbf{41e}$ (50 mg, 0.243 mmol) was dissolved in pyridine (1.2 mL). Pent-4-enoyl chloride (83 µL, 0.762 mmol) was added and the reaction mixture was stirred at RT for 18 h. The solvents were removed in vacuo and the remaining residue was dissolved in CH$_2$Cl$_2$ (10 mL) and washed with H$_2$O (10 mL) and brine (10 mL). The aqueous layers were combined and extracted with CH$_2$Cl$_2$ (10 mL x 2). The combined organic layers were dried with MgSO$_4$ and the solvents removed in vacuo. The crude reaction mixture was purified by column chromatography on silica gel (25% EtOAc:hexane) to yield $\textbf{41f}$ as a clear oil (38 mg, 55%). [α]$^{25.0}_{D}$ +15.8 (c=1.0 CHCl$_3$); IR (film) 2952, 1737 cm$^{-1}$; $^1$H NMR (500 MHz, CDCl$_3$) δ 5.89-5.73 (2H, m, H-2”, H-6”), 5.11-4.94 (4H, m, H-3’, H-7”), 4.11-4.02 (3H, m, H-1”), 3.95 (1H, ddd, J=4.0, 7.0, 7.0, H-5), 2.49-2.32 (7H, m, H-5”, H-4”, H-6, H-2, HA-1”), 2.22-2.16 (3H, m, H-1, H-7, HB-1”), 1.65-1.56 (4H, S33
m, H-10, H-8 or H-9), 1.45-1.39 (2H, m, H-9 or H-8); $^{13}$C NMR (125 MHz, CDCl$_3$) δ 173.0 (C3’’), 136.7 (C2’ or C6’’), 134.9 (C2’ or C6’’), 116.8 (C3’ or C7’’), 115.5 (C3’ or C7’’), 79.2 (C5), 76.8 (C3), 67.6 (C1’’), 52.5 (C6 or C2), 50.0 (C6 or C2), 43.9 (C10), 41.9 (C1’), 39.8 (C1 or C7), 39.5 (C1 or C7), 33.5 (C5’’ or C4’’), 28.8 (C5’’ or C4’’); LC-MS (ESI$^+$) m/z 313 [M+Na$^+$], R$_t$ 2.50 min [method D]; HRMS [M+H$^+$] calcd for C$_{18}$H$_{27}$O$_3$ 291.1955 found 291.1955.

(1S,2S,3S,5S,6R,7R)-5-allyl-4-oxatricyclo[5.2.1.0$^2$6]dec-3-ylmethyl pent-5-enoate 41f (20 mg, 0.069 mmol) was dissolved in CH$_2$Cl$_2$ (137 mL, 0.0005 M). Argon was bubbled through the solution for 5 min. Grubbs II (6 mg, 0.008 mmol, 10 mol%) was added under argon and the reaction mixture was stirred for 16 h. DMSO (10 µL) was added and the solution was stirred overnight. The solvents were removed in vacuo and the resultant mixture purified by column chromatography on silica gel (15% EtOAc:hexane) to yield 41 as a mixture of E and Z (clear oil) (4 mg, 22%). [α]$^{20}$D -6.8 (c=0.5 CHCl$_3$); IR (film) 2951, 1737 (C=O), 1171, 1106 cm$^{-1}$; $^1$H NMR (500 MHz, CDCl$_3$) δ 5.59-5.42 (2H, m, H-7’, H-6’), 4.18-3.90 (4H, m, H-1’, H-3, H-5), 2.40-2.28 (6H, m, CH$_2$, CH), 2.26-2.14 (4H, m, CH, CH$_2$), 1.70-1.52 (4H, m, CH$_2$), 1.47-1.37 (2H, m, CH$_2$); $^{13}$C NMR (125 MHz, CDCl$_3$) δ 173.2, 173.0 (C3’), 130.2, 129.5, 129.0, 128.0 (2C, C7’, C6’), 79.8, 79.6, 77.6, 77.5 (2C, C3, C5), 67.4, 67.5 (C1’), 52.4, 52.4 (CH), 49.0, 49.0 (CH), 43.6, 43.5 (CH$_2$), 41.3 (CH$_2$), 40.6 (CH$_2$), 40.0, 39.8 (CH), 39.6 (CH), 34.4, 34.3 (CH$_2$), 28.0, 27.9 (CH$_2$), 22.9 (CH$_2$), 22.8 (CH$_2$); LC-MS (ESI$^+$) m/z 285 [M+Na$^+$], R$_t$ 2.32 min [method D]; HRMS [M+H$^+$] calcd for C$_{16}$H$_{23}$O$_3$ 263.1642 found 263.1643.

(E)-(1S,11S,12R,17S)-3,18-Dioxatetracyclo[9.6.1.1$^{13},16$.0$^{12},17$]nonadec-8-en-4-one 42

$((1R,2S,3S,5S,6R,7S)-5$-Allyl-4-oxatricyclo[5.2.1.0$^2$6]dec-3-yl)methanol 41e (50 mg, 0.243 mmol) was dissolved in pyridine 1.2 mL. Hex-5-enoyl chloride (100 mg, 0.762 mmol) was added and the reaction mixture was stirred at RT for 18 h. The solvents were removed in vacuo and the remaining residue was dissolved in CH$_2$Cl$_2$ (10 mL) and washed with H$_2$O (10 mL) and brine (10 mL). The aqueous layers were combined and extracted with CH$_2$Cl$_2$ (10 mL x 2). The combined organic layers were dried with MgSO$_4$ and the solvents removed in vacuo. The crude reaction mixture was purified by column chromatography on silica gel (15% EtOAc:hexane) to yield 83 as a clear oil (73 mg, 100%). [α]$^{25}$D -5.5 (c=1.0 CHCl$_3$); IR (film) 2952, 1737 cm$^{-1}$; $^1$H NMR (500 MHz, CDCl$_3$) δ 5.79 (1H, dddd, J=7.0, 7.0, 10.5, 17.0, H-2’
or H-7’”), 5.76 (1H, dddd, J=7.0, 7.0 10.0, 17.0, H-2’ or H-7’’), 5.09-4.97 (4H, m, H-3’, H-8’’), 4.09-4.00 (3H, m, H-1’’, H-3), 3.90 (1H, ddd, J=4.0, 7.0, 7.0, H-5), 2.45-2.32 (5H, m, HA-1’, H-4’’, H-2, H-6), 2.21-2.16 (3H, m, H-1, H-7, HB-1’), 2.16-2.08 (2H, m, H-6’’), 1.75 (2H, tt, J=7.5, 7.5, H-5’’), 1.63-1.56 (4H, m, HA-8, HA-9, H-10), 1.13-1.43 (2H, m, HB-9, HB-8); $^{13}$C NMR (125 MHz, CDCl$_3$) δ 173.5 (C3’’), 137.7 (C7’’), 134.9 (C2’’), 116.8 (C8’’ or C3’), 115.3 (C8’’ or C3’), 79.2 (C5), 76.7 (C3), 67.5 (C1’’), 52.5 (C6 or C2), 50.1 (C6 or C2), 43.9 (C10), 41.9 (C1’), 39.8 (C1 or C7), 39.5 (C1 or C7), 33.4 (C4’’), 33.0 (C6’’), 24.0 (C5’’), 22.8 (C9 or C8), 22.8 (C9 or C9); LC-MS (ESI+) m/z 327 [M+Na$^+$], Rf 2.55 min [method D]; HRMS [M+H$^+$] calcld for C$_{19}$H$_{30}$O$_3$ 305.2111 found 305.2115; Found: C, 74.91; H, 9.26%; C$_{17}$H$_{28}$O$_3$ requires: C, 74.96; H, 9.27%.

(1S,2S,3S,5S,6R,7R)-5- Allyl-4-oxatricyclo[5.2.1.0$^{2,6}$]dec-3-ylmethyl hex-5-enolate 83 (24 mg, 0.078 mmol) was dissolved in CH$_2$Cl$_2$ (156 mL, 0.0005 M). Argon was bubbled though the solution for 5 min. Grubbs II (7 mg, 0.008 mmol, 10 mol%) was added under argon and the reaction mixture was stirred for 5 d. DMSO (10 μL) was added and the solution was stirred overnight. The solvents were removed in vacuo and the resultant mixture purified by column chromatography on silica gel (15% EtOAc:hexane) to yield 42 as a white crystalline solid (11 mg, 51%). mp (94-96 °C); [α]$^{24}_D$ -10.4 (c=1.0 CHCl$_3$); IR (film) 2948, 1729, 1440 cm$^{-1}$; $^1$H NMR (500 MHz, CDCl$_3$) δ 5.54 (1H, ddd, J=7.0, 7.0, 14.0, H-9 or H-8), 5.28 (1H, ddd, J=7.0, 7.0, 14.0, H-9 or H-8), 4.33 (1H, dd, J=3.0, 12.0, Ha-2), 4.14-4.09 (2H, m, H-1, H-11), 3.69 (1H, dd, J=7.5, 12.0, Hb-2), 2.56-2.49 (1H, m, H-12 or H-17), 2.77-2.32 (3H, m, H-16 or H-17, CH$_2$, CH$_2$), 2.29-1.98 (7H, m, H-12 or H-17, H-16 or H-13, CH$_2$, CH$_2$, CH$_2$), 1.96-1.81 (2H, m, CH$_2$), 1.68-1.53 (4H, m, Ha-14, Ha-15, CH$_2$), 1.46-1.38 (2H, m, Hb-14, Hb-15); $^{13}$C NMR (125 MHz, CDCl$_3$) δ 175.3 (C4), 132.0 (C8 or C9), 127.4 (C8 or C9), 77.6 (C1 or C11), 76.1 (C1 or C11), 65.8 (C2), 51.5 (C12 or C17), 48.8 (C16 or C13), 43.7 (CH$_2$), 39.8 (CH), 39.5 (CH), 33.9 (CH$_2$), 33.8 (CH$_2$), 24.0 (CH$_2$), 22.9 (C14 or C15), 22.7 (C14 or C15); LC-MS (ESI+) m/z 299 [M+Na$^+$], Rf 2.43 min [method D]; HRMS [M+H$^+$] calcld for C$_{17}$H$_{26}$O$_3$ 277.1798 found 277.1799.

2-[[1R,3S,3aS,7aR]-3-[[ tert-butylidiphenylsilyloxy]methyl]-1,3,3a,4,7,7a-hexahydro-2-benzofuran-1-yl]-2-methylpropanal 44

2-[[1R,3S,3aS,7aR]-3-[[ tert-Butylidiphenylsilyloxy]methyl]-1,3,3a,4,7,7a-hexahydroisobenzofuran-1-ol 11 (100 mg, 0.245 mmol) was dissolved in CH$_2$Cl$_2$ (2.8 mL) and cooled to -78 °C. BF$_3$OEt$_2$ (94 μL, 0.735 mmol) was added and the solution was stirred for 5 min. Trimethyl(2-methylprop-1-enoxy)silane (49 μL, 0.269 mmol) was then added and the reaction was warmed to RT and stirred for 3 h. The reaction was diluted with CH$_2$Cl$_2$ (20 mL), and washed with H$_2$O (2 x 20 mL), followed by brine (20 mL). The organic layer was dried with MgSO$_4$. The solvents were removed in vacuo and the resultant crude residue was purified by column
chromatography on silica gel (15% EtOAc:hexane) to yield the product as a clear oil (110 mg, 97%). \([\alpha]_{D}^{21} +1.1\) (c=5.0 CHCl\(_3\)); IR (film) 3018, 1708, 1218 cm\(^{-1}\); \(^1\)H NMR (500 MHz, CDCl\(_3\)) \(\delta\) 9.66 (1H, s, H-3''), 7.73-7.68 (4H, m, Ph), 7.46-7.37 (6H, m, Ph), 5.81-5.78 (2H, m, H-5, H-6), 3.81-3.75 (2H, m, H-1', H-1 or H-3), 3.73-3.68 (2H, m, Hb-1', H-1 or H-3), 2.29-2.17 (4H, m, H-3a, H-7a, H-4, H-7), 1.97-1.86 (2H, Hb-4, Hb-7), 1.11 (3H, s, Me), 1.08 (3H, s, Me), 1.07 (9H, s, tBu); \(^{13}\)C NMR (125 MHz, CDCl\(_3\)) \(\delta\) 206.1 (C3''), 135.7 (2 x Ph), 135.6 (2 x Ph), 133.6 (iPh), 133.4 (iPh), 129.6 (Ph), 129.6 (Ph), 127.7 (4 x Ph), 127.0 (C5 or C6), 126.3 (C5 or C6), 89.1 (C1), 83.8 (C3), 64.7 (C1'), 49.6 (C2''), 37.8 (C3a or C7a), 37.2 (C3a or C7a), 27.4 (C7), 26.8 (tBu), 24.0 (C4), 19.2 (C-Si), 19.2 (Me), 17.6 (Me); LC-MS (ESI\(^+\)) m/z 485 [M+Na\(^+\)], R\(_t\) 2.60 min [method E]; Found: C, 75.35; H, 8.15%; C\(_{29}\)H\(_{38}\)O\(_3\)Si requires: C, 75.28; H, 8.28%.

2-((1S,3S,3aS,7aR)-3-((tert-butylidiphenylsilyloxy)methyl)-1,3,3a,4,7,7a-hexahydroisobenzofuran-1-yl)-1-phenylethanone 45

2-((1S,3S,3aS,7aR)-3-((tert-Butylidiphenylsilyloxy)methyl)-1,3,3a,4,7,7a-hexahydroisobenzofuran-1-ol 11 (100 mg, 0.245 mmol) was dissolved in CH\(_2\)Cl\(_2\) (2.8 mL) and cooled to -20 °C. BF\(_3\).OEt\(_2\) (63 µL, 0.490 mmol) was added and the solution was stirred for 5 min. Trimethyl(1-phenylvinylsilyloxy)silane (100 µL, 0.490 mmol) was then added and the reaction was warmed to RT and stirred for a further 16 h. The reaction was diluted with CH\(_2\)Cl\(_2\) (20 mL), and washed with H\(_2\)O (2 x 20 mL), followed by brine (20 mL). The organic layer was dried with MgSO\(_4\). The solvents were removed in vacuo and the resultant crude residue was a green oil. The product was isolated by column chromatography on silica gel (10% EtOAc:hexane) to yield 45 as a clear oil (95 mg, 78%). \([\alpha]_{D}^{21} = -1.66\) (c=1.0 CHCl\(_3\)); IR (film) 3070, 2930, 2857, 1684 (CO) cm\(^{-1}\); \(^1\)H NMR (500 MHz, CDCl\(_3\)) \(\delta\) 7.94-7.90 (2H, m, Ph), 7.75-7.67 (5H, m, Ph), 7.44-7.35 (8H, m, Ph), 5.77-5.68 (2H, m, H-5, H-6), 4.35 (1H, dd, J=6.0, 12.0, H-1), 3.82-3.77 (1H, m, H-3), 3.76 (1H, dd, J=4.5, 11.0, Ha-1''), 3.68 (1H, dd, J=4.0, 11.0, Hb-1''), 3.30 (1H, dd, J=6.5, 16.5, Ha-1'), 3.07 (1H, dd, J=6.0, 16.5, Hb-1'), 2.54-2.48 (1H, m, H-3a), 2.47-2.36 (2H, m, Ha-4, Hb-7), 2.26-2.18 (1H, m, H-7a), 2.03-1.93 (2H, m, Hb-4, Hb-7), 1.09 (9H, s, tBu); \(^{13}\)C NMR (125 MHz, CDCl\(_3\)) \(\delta\) 198.7 (C2''), 137.2 (iPh), 135.6 (2 x Ph), 135.6 (2 x Ph), 134.8 (Ph), 133.6 (Ph), 133.4 (iPh), 133.0 (iPh), 129.7 (Ph), 129.6 (Ph), 129.6 (Ph), 128.5 (Ph), 128.2 (Ph), 127.7 (Ph), 127.7 (2 x Ph), 127.7 (Ph), 125.4 (C5 or C6), 125.2 (C5 or C6), 84.1 (C3), 80.2 (C1), 64.9 (C1'), 44.4 (C1''), 40.1 (C7a), 35.5 (C3a), 26.9 (tBu), 24.8 (C4 or C7), 24.5 (C4 or C7), 19.3 (Si-C); LC-MS (ESI\(^+\)) m/z 533 [M+Na\(^+\)], R\(_t\) 2.52 min [method D]; HRMS [M+Na\(^+\)] calcd for C\(_{33}\)H\(_{38}\)O\(_3\)SiNa 533.2482 found 533.2492; Found: C, 77.51; H, 7.40%; C\(_{33}\)H\(_{38}\)O\(_3\)Si requires: C, 77.60; H, 7.50%.
3-[(1R,3S,3aS,7aR)-3-((Hydroxymethyl)-octahydro-2-benzofuran-1-yl]-3-methylbutan-2-one 46

trimethyl(3-methylbut-2-en-2-yl)oxy)silane (100 mg, 0.630 mmol) was added. The solution was cooled to -78 °C and TMSOTf (286 µL, 0.1 M in CH₂Cl₂, 0.029 mmol) was added and the reaction was warmed to -18 °C for 18 h. The reaction was quenched with sat. aqueous NaHCO₃ (20 mL) and extracted in CH₂Cl₂ (3 × 30 mL). The combined organic layers were dried over MgSO₄ and the solvent removed in vacuo. The crude residue was purified by column chromatography on silica gel (15% EtOAc:hexane) to yield 46a as a clear oil (101 mg, 36%). [α]₂⁴.₃D -22.7 (c=0.75 CHCl₃); IR (film) 2929, 2856, 1774 cm⁻¹; ¹H NMR (500 MHz, CDCl₃) δ 7.74-7.65 (4H, m, Ph), 7.46-7.35 (6H, m, Ph), 3.91 (1H, ddd, J=4.0, 4.0, 9.0, H-3'), 3.87 (1H, d, J=3.5, H-1'), 3.76 (1H, dd, J=4.0, 11.0, H-a-1'''), 3.67 (1H, dd, J=5.0, 11.0, H-b-1'') 2.17 (3H, s, H-1'''), 2.05-1.94 (2H, m, H-3a, H-7a), 1.73-1.54 (4H, m, CH₂), 1.49-1.23 (4H, m, CH₂), 1.14 (3H, s, Me), 1.09 (3H, s, Me), 1.08 (9H, s, tBu); ¹³C NMR (125 MHz, CDCl₃) δ 213.2 (C2''), 135.7 (2 x Ph), 135.6 (2 x Ph), 133.7 (iPh), 133.5 (iPh), 129.6 (Ph), 129.5 (Ph), 127.8 (2 x Ph), 127.6 (2 x Ph), 88.8 (C1), 80.7 (C3), 65.2 (C1'''), 51.5 (C3''), 39.3 (C7a or C3a), 38.8 (C7a or C3a), 29.6 (C1'), 26.7 (tBu), 26.7 (C1'), 24.3 (CH₂), 24.2 (CH₂), 22.2 (CH₂), 20.8 (C4A' or C4B'), 20.3 (C4A' or C4B''), 19.2 (C-Si); HRMS [M+Na⁺] calcd for C₃₀H₄₂O₃SiNa 501.2795 found 501.2799.

3-[(1R,3S,3aS,7aR)-3-[[tert-Butyldiphenylsilyl]oxy][methyl]-octahydro-2-benzofuran-1-yl]-3-methylbutan-2-one 46a (81 mg, 0.169 mmol), was dissolved in THF (2 mL). TBAF (1.0 M in THF, 0.51 mL, 0.51 mmol) and AcOH (0.31 mL, 0.508 mmol) were added and the reaction stirred at RT for 16 h. The solution was diluted with Et₂O (20 mL) and washed with H₂O (2 x 20 mL), brine (20 mL) and the organic layer was dried with MgSO₄. The crude residue was purified by column chromatography on silica gel to yield 46 as a clear oil (32 mg, 78%). [α]₂⁴.₆D +12.4 (c=1.0 CHCl₃); IR (film) 3428, 2926, 2857, 1698, 1450 cm⁻¹; ¹H NMR (500 MHz, CDCl₃) δ 3.89 (1H, ddd, J=3.0, 5.5, 13.0, H-3'), 3.87 (1H, d, J=3.5, H-1'), 3.74 (1H, d, J=3.0, 5.5, 13.0, H-3'), 3.65 (1H, dd, J=3.5, 3.5, 12.0, H-b-1'''), 2.18 (3H, s, H-1'''), 2.06-1.99 (2H, m, OH, H-7a), 1.96-1.90 (1H, m, H-3a), 1.74-1.52 (4H, m, CH₂), 1.43-1.21 (4H, m, CH₂), 1.11 (3H, s, Me), 1.09 (3H, s, Me); ¹³C NMR (125 MHz, CDCl₃) δ 212.8 (C2''), 89.3 (C1), 80.6 (C3), 63.8 (C1'), 51.5 (C3''), 39.6 (C7a), 38.0 (C3a), 29.8 (CH₂), 26.4 (C1'''), 24.2 (CH₂), 23.9 (CH₂), 21.9 (CH₂), 21.3 (Me), 19.8 (Me); LC-MS (ES⁺) m/z 263 [M+Na⁺], Rᵣ 1.42 min [method D]; HRMS [M+Na⁺] calcd for C₁₄H₂₄O₃SiNa 263.1797 found 263.1767.

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1-[(1S,3S,3aS,7aR)-3-(hydroxymethyl)-octahydro-2-benzofuran-1-yl]-3,3-dimethylbutan-2-one 47

(3S,3aS,7aR)-3-(((tert-Butyldiphenylsilyloxy)methyl)octahydroisobenzofuran-1-ol 23 (615 mg, 1.50 mmol) was dissolved in CH$_2$Cl$_2$ (15 mL) and cooled to -20 °C. BF$_3$.OEt$_2$ (578 µL, 4.50 mmol) was added and the solution was stirred for 5 min. (3,3-Dimethylbut-1-en-2-ol)trimethylsilane (797 µL, 4.50 mmol) was then added and the reaction was warmed to RT and stirred for 16 h. The reaction was diluted with CH$_2$Cl$_2$ (20 mL), and washed with H$_2$O (2 x 20 mL), followed by brine (20 mL). The organic layer was dried with MgSO$_4$. The product was isolated by column chromatography on silica gel (15% EtOAc:hexane) to yield 47a as a clear oil (483 mg, 65%).

$\alpha$$_{D}^{21}$ +9.0 (c=1.0 CHCl$_3$); IR (film) 2931, 2858, 1702, 1473 cm$^{-1}$; $^1$H NMR (500 MHz, CDCl$_3$) δ 7.71-7.66 (4H, m, Ph), 7.43-4.39 (6H, m, Ph), 4.30-4.25 (1H, m, H-1), 3.89-3.85 (1H, m, H-3), 3.68 (1H, dd, J=5.0, 11.0, Ha-1'), 3.61 (1H, dd, J=4.0, 11.0, Hb-1'), 2.78 (1H, dd, J=6.0, 17.0, Ha-1''), 2.53 (1H, dd, J=6.0, 17.0, Hb-1''), 2.27-2.22 (1H, m, H-7a), 1.93-1.87 (1H, m, 3a), 1.65-1.26 (8H, m, 4 x CH$_2$), 1.10 (9H, s, tBu), 1.08 (9H, s, tBu); $^{13}$C NMR (125 MHz, CDCl$_3$) δ 214.6 (C-3''), 135.6 (2 x Ph), 134.8 (2 x Ph), 133.7 (iPh), 133.5 (iPh), 129.6 (Ph), 129.6 (Ph), 127.7 (2 x Ph), 127.6 (2 x Ph), 82.3 (C3), 78.4 (C1), 65.0 (C1'), 44.1 (C3''), 43.1 (C3a), 42.7 (C1''), 38.3 (C7a), 26.1 (tBu), 25.9 (tBu), 25.9 (CH$_2$), 23.3 (CH$_2$), 23.1 (CH$_2$), 22.6 (CH$_2$), 19.3 (Si-C), HRMS [M+Na$^+$] calcd for C$_{31}$H$_{44}$O$_3$SiNa 515.2957 found 515.2938.

1-[(1S,3S)-3-(((tert-butylidiphenylsilyloxy)methyl)-octahydro-2-benzofuran-1-yl)-3,3-dimethylbutan-2-one 47a (467mg, 0.949 mmol) was dissolved in THF (10 mL). The solution was cooled to 0 °C under N$_2$, then TBAF (2.8 mL, 1.0 M in THF, 2.8 mmol) and AcOH (1.7 mL, 2.8 mmol) was added by syringe. The reaction was stirred for 16 h at RT before diluting with Et$_2$O (30 mL). The reaction mixture was washed with H$_2$O (30 mL) and extracted into Et$_2$O (2 x 30 mL). The combined organic layers were dried with MgSO$_4$ and solvents were removed in vacuo to yield the crude product as a clear oil. This was purified by column chromatography on silica gel (10% EtOAc:hexane) to yield 47 as a clear oil (161 mg, 67%).

$\alpha$$_{D}^{22}$ + 17.6 (c=2.60 CH$_2$Cl$_2$); IR (film) 3414, 3075, 3026, 2975, 2981, 1700, 1478 cm$^{-1}$; $^1$H NMR (500 MHz, CDCl$_3$) δ 4.26-4.21 (1H, m, H-1), 3.93-3.89 (1H, m, H-3), 3.76-3.71 (1H, m, Ha-1'), 3.49-3.44 (1H, m, Hb-1'), 2.71 (1H, dd, J=7.5, 15.5, Ha-1''), 2.63 (1H, dd, J=5.5, 15.5, Hb-1''), 2.24-2.18 (1H, m, H-3a), 1.95-1.89 (1H, m, H-7a), 1.79-1.71 (1H, m, CH$_2$), 1.68-1.51 (3H, m, 3 x CH$_2$), 1.38-1.35 (3H, m, 3 x CH$_2$) 1.35-1.26 (1H, m, CH$_2$), 1.16 (9H, s, tBu); $^{13}$C NMR
(125 MHz, CDCl$_3$) δ 82.0 (C3), 79.3 (C1), 63.8 (C1’), 44.3 (C3’), 43.7 (C1’’), 42.0 (C7a), 37.0 (C3a), 26.5, (CH$_2$), 26.4 (tBu), 25.1 (CH$_2$), 23.6 (CH$_2$), 22.5 (CH$_2$), missing quaternary C=O; LC-MS (ESI$^+$) m/z 255 [M+Na$^+$], R$_t$ 1.52 min [method E]; HRMS [M+Na$^+$] calcd for C$_{15}$H$_{26}$O$_3$Na 277.1779; found 217.1774.

1-[(1S,3S,3aS,7aR)-3-(hydroxymethyl)-1,3,3a,4,7,7a-hexahydro-2-benzofuran-1-yl]-3,3-imethylbutan-2-one 48

(3S,3aS,7aR)-3-((tert-Butyldiphenylsilyloxy)methyl)-1,3,3a,4,7,7a-hexahydroisobenzofuran-1-ol 11 (100 mg, 0.245 mmol) was dissolved in CH$_2$Cl$_2$ (2.8 ml) and cooled to -20 °C. BF$_3$.OEt$_2$ (94 µL, 0.735 mmol) was added and the solution was stirred for 5 min. (3,3-Dimethylbut-1-en-2-oxo)trimethylsilane (126 µL, 0.735 mmol) was then added and the reaction was warmed to RT and stirred for 16 h. The reaction was diluted with CH$_2$Cl$_2$ (20 ml), and washed with H$_2$O (2 x 20 ml), followed by brine (20 ml). The organic layer was dried with MgSO$_4$. The solvents were removed in vacuo and the resultant crude residue was analysed by $^1$H NMR and found to be a mixture of diastereoisomers (85:15). The major isomer was isolated by column chromatography on silica gel (10% EtOAc:hexane) to yield 48a as a clear oil (85 mg, 62%). [α]$^{21_D}$ +9.0 (c=1.0 CHCl$_3$); IR (film) 2931, 2858, 1702, 1473 cm$^{-1}$; $^1$H NMR (500 MHz, CDCl$_3$) δ 7.75–7.65 (4H, m, Ph), 7.47–4.36 (6H, m, Ph), 5.77–5.67 (2H, m, H-5, H-6), 4.21 (1H, dd, J=6.0, 12.0, H-1), 3.79 (2H, m, H-3, Ha-1’), 3.71–3.66 (1H, m, Hb-1’), 2.84 (1H, dd, J=6.0, 17.0, Ha-1’’), 2.59 (1H, dd, J=6.0, 17.0, Hb-1’’), 2.48–2.41 (1H, m, H-3a), 2.35–2.22 (2H, m, Ha-4, H-7), 2.18–2.15 (1H, m, H-7a), 2.12–2.06 (2H, m, Hb-4, Hb-7), 1.11 (9H, s, tBu), 1.08 (9H, s, tBu); $^{13}$C NMR (125 MHz, CDCl$_3$) δ 135.6 (2 x Ph), 134.8 (2 x Ph), 133.6 (iPh), 133.5 (iPh), 129.7 (Ph), 129.6 (Ph), 127.7 (2 x Ph), 127.7 (2 x Ph), 125.5 (C5 or C6), 125.2 (C5 or C6), 83.8 (C3), 80.0 (C1), 65.0 (C1’), 44.2 (C3’), 42.4 (C1’’), 40.1 (C7a), 35.7 (C3a), 26.9 (tBu), 26.1 (tBu), 24.9 (C4 or C5), 24.6 (C4 or C7), 19.3 (Si-C), missing quaternary C=O; LC-MS (ESI$^+$) m/z 513 [M+Na$^+$], R$_t$ 2.58 min [method E]; HRMS [M+Na$^+$] calcd for C$_{31}$H$_{42}$O$_3$SiNa 513.2795 found 513.2808; Found: C, 75.81; H, 8.73%; C$_{31}$H$_{42}$O$_3$Si requires: C, 75.87; H, 8.73%.

1-[(1S,3S,3aS,7aR)-3-((tert-Butyldiphenylsilyloxy)methyl)-1,3,3a,4,7,7a-hexahydroisobenzofuran-1-yl]-3,3-dimethylbutan-2-one 48a (216 mg, 0.485 mmol) was dissolved in THF (10.0 ml). The solution was cooled to 0 °C under N$_2$, then TBAF (1.45 ml, 1.0 M in THF, 1.45 mmol) was added by syringe. The reaction was stirred for 16 h at RT before quenching with

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Et<sub>2</sub>O (30 mL). The reaction mixture was washed with H<sub>2</sub>O (30 mL) and extracted into Et<sub>2</sub>O (2 x 30 mL). The combined organic layers were dried with MgSO<sub>4</sub> and solvents were removed in vacuo to yield the crude product as a clear oil. This was purified by column chromatography on silica gel (10% EtOAc:hexane) to yield 48 as a clear oil (84 mg, 67%).

$\alpha$<sup>22</sup>D +17.6 (c=2.60 CHCl<sub>3</sub>); IR (film) 3418, 3026, 2967, 2907, 1700, 1478 cm<sup>-1</sup>; <sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>) δ 5.77-5.67 (2H, m, H-5, H-6), 4.16 (1H, dd, J=6.0, 12.0, H-1), 2.59 (1H, dd, J=6.0, 17.0, Hb-1’’), 2.42-2.34 (2H, m, H-3a, OH), 2.31-2.27 (2H, m, Ha-4, Ha-7), 2.10-2.03 (1H, m, H-7a), 1.97-1.88 (2H, m, H-3a, OH); <sup>13</sup>C NMR (125 MHz, CDCl<sub>3</sub>) δ 125.5 (C5 or C6), 125.1 (C5 or C6), 83.8 (C3), 81.4 (C1), 63.2 (C1’), 44.4 (C3’), 42.2 (C1’’), 40.6 (C7a), 35.8 (C3a), 24.9 (C4 or C5), 23.6 (C4 or C7), missing quaternary C=O; LC-MS (ESI<sup>+</sup>) m/z 275 [M+Na<sup>+</sup>], R<sub>t</sub> 1.47 min [method E].

2-((1R,3S,3aS,7aR)-3-(hydroxymethyl)-1,3,3a,4,7,7a-hexahydroisobenzofuran-1-yl)-2-methylpropan-1-ol 49

2-((1R,3S,3aS,7aR)-3-{{(tert-Butyldiphenylsilyl)oxy}methyl}-1,3,3a,4,7,7a-hexahydro-2-benzofuran-1-yl)-2-methylpropanal 44 (110 mg, 0.239 mmol) was dissolved in THF:MeOH (4:1 ratio, 2.5 mL) and cooled to 0 °C. NaBH<sub>4</sub> (27 mg, 0.717 mmol) was added and the solution stirred for 1.5 h. The solution was diluted with Et<sub>2</sub>O (10 mL), then washed with H<sub>2</sub>O (10 mL) and brine (10 mL). The organic layer was then dried with MgSO<sub>4</sub>. The solvents were removed in vacuo to yield 49a as a clear oil (93 mg, 82%). $\alpha$<sup>22</sup>D -8.4 (c=1.0 CHCl<sub>3</sub>); IR (film) 3424, 1472 cm<sup>-1</sup>; <sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>) δ 7.76-7.67 (4H, m, Ph), 7.50-7.37 (6H, m, Ph), 5.88-5.74 (2H, m, H-5, H-6), 3.83 (1H, dd, J=5.0, 7.0, Ha-1’), 3.70-3.66 (2H, m, Hb-1’, H-3), 3.61 (1H, d, J=5.0, H-1), 3.51-3.47 (2H, m, H-3’’), 3.12 (1H, t, J=7.0, OH), 2.33-2.24 (2H, m, H-3a, H-7a), 2.24-2.14 (2H, m, Hb-4, Ha-7), 1.97-1.90 (1H, Ha-4, or Hb-7), 1.86-1.79 (1H, Hb-4, or Hb-7), 1.09 (9H, s, tBu), 1.01 (3H, s, Me), 0.90 (3H, s, Me); <sup>13</sup>C NMR (125 MHz, CDCl<sub>3</sub>) δ 135.7 (2 x Ph), 135.6 (2 x Ph), 133.4 (iPh), 133.4 (iPh), 129.7 (Ph), 129.6 (Ph), 127.7 (4 x Ph), 127.1 (C5 or C6), 126.7 (C5 or C6), 93.4 (C1), 83.7 (C3), 72.4 (C1’), 64.5 (C3’’), 37.9 (C2’’), 37.8 (C3a or C7a), 37.4 (C3a or C7a), 27.7 (C4 or C7), 26.8 (tBu), 23.9 (C4 or C7), 22.7 (Me), 19.2 (Si-C), 19.0 (Me); LC-MS (ESI<sup>+</sup>) m/z 487 [M+Na<sup>+</sup>], R<sub>t</sub> 3.12 min [method E]; HRMS [M+Na<sup>+</sup>] calcd for C<sub>29</sub>H<sub>40</sub>O<sub>3</sub>SiNa 487.2639 found 487.2637; Found: C, 75.07; H, 8.64%; C<sub>29</sub>H<sub>40</sub>O<sub>3</sub>SiNa requires: C, 74.95; H, 8.68%.
2-[(1R,3S,3aS,7aR)-3-{{[tert-butyldiphenylsilyl]oxy}methyl}-1,3,3a,4,7,7a-hexahydro-2-benzofuran-1-yl]-2-methylpropan-1-ol 49a (80 mg, 0.172 mmol) was dissolved in THF (0.5 mL) and TBAF (1.0 M in THF, 1.70 mL) was added. The reaction was stirred at RT for 16 h. The reaction mixture was then diluted with Et₂O (5 mL) and washed with H₂O (5 mL x 2). Solvents were removed in vacuo and the crude residue was purified by column chromatography on silica gel (15% EtOAc:hexane) to yield 49 as a clear oil (16 mg, 41%).

{2-[(1R,3S,3aS,7aR)-3-{{[tert-butyldiphenylsilyl]oxy}methyl}-1,3,3a,4,7,7a-hexahydro-2-benzofuran-1-yl]-2-methylpropyl}(benzyl)amine 50

2-[(1R,3S,3aS,7aR)-3-{{[tert-butyldiphenylsilyl]oxy}methyl}-1,3,3a,4,7,7a-hexahydro-2-benzofuran-1-yl]-2-methylpropanal 44 (107 mg, 0.232 mmol) and benzyl amine (25 µM, 0.232 mmol) was dissolved in 1,2-dichloroethane (3.0 mL). Sodium triacetoxyborohydride (68 mg, 0.324 mmol) was then added and the solution stirred at RT for 3 h. The reaction mixture was quenched by adding aqueous sat. NaHCO₃ (10 mL), and the solution was extracted with EtOAc. The organic extract was dried (MgSO₄), and the crude residue was purified by ionic exchange chromatography on acidic resin (5 g) to yield 50 as a clear oil (67 mg, 52%). [α]²⁰ -8.4 (c=1.0 CHCl₃); [H NMR (500 MHz, CDCl₃) 5.85-5.78 (2H, m, H-5, H-6), 3.84 (1H, dd, J=5.0, 7.0, Ha-1’), 3.71-3.68 (1H, m, H-1), 3.64-3.60 (2H, m, Hb-1’, H-3’), 3.50 (1H, d, J=11.0, Ha-3’’), 3.46 (1H, d, J=11.0, Hb-3’’), 2.31-2.17 (4H, m, H-3a, H-7a, Ha-4, Ha-7), 1.98-1.84 (2H, Hb-4, Hb-7), 0.94 (3H, s, Me), 0.91 (3H, s, Me); [¹³C NMR (125 MHz, CDCl₃) δ, 126.7 (C5 or C6), 126.6 (C5 or C6), 93.2 (C1), 83.6 (C3), 71.7 (C1’), 63.0 (C3’’), 38.1 (C2’’), 37.3 (C3a or C7a), 27.8 (C4 or C7), 19.3 (Me), LC-MS (ESI⁺) m/z 227 [M+Na⁺], Rₜ 1.38 min [method E]; HRMS [M+Na⁺] calcd for C₁₃H₂₂O₃ Na 249.1461 found 249.1463.

{2-[(1R,3S,3aS,7aR)-3-{{[tert-butyldiphenylsilyl]oxy}methyl}-1,3,3a,4,7,7a-hexahydro-2-benzofuran-1-yl]-2-methylpropyl}(benzyl)amine 50
{2-[(1R,3S,3aS,7aR)-3-[[[ tert-Butyldiphenylsilyl]oxy]methyl]-1,3,3a,4,7,7a-hexahydro-2-benzofuran-1-yl]-2-methylpropyl]}[[3-methoxyphenyl]methyl]amine 51

2-[(1R,3S,3aS,7aR)-3-[[[ tert-Butyldiphenylsilyl]oxy]methyl]-1,3,3a,4,7,7a-hexahydro-2-benzofuran-1-yl]-2-methylpropanal 44 (145 mg, 0.315 mmol) and (3-methoxyphenyl)methanamine (40 µM, 0.315 mmol) was dissolved in 1,2-dichloroethane (3.0 mL). Sodium triacetoxyborohydride (86 mg, 0.441 mmol) was then added and the solution stirred at RT for 3 h. The reaction mixture was quenched by adding aqueous sat. NaHCO₃ (10 mL), and the solution was extracted with EtOAc. The EtOAc extract was dried over MgSO₄, and the crude residue was purified by ionic exchange chromatography on acidic resin (2 g) to yield 51 as a clear oil (115 mg, 62%). [α]D -33.7 (c=1.0 CHCl₃); IR (film) 2931, 2857, 1600, 1586, 1488 cm⁻¹; ¹H NMR (500 MHz, CDCl₃) δ 7.74-7.70 (4H, m, Ph), 7.45-7.36 (6H, m, Ph), 7.21 (1H, dd, J=8.0, 8.0, H-8''), 6.96-6.89 (2H, m, H-9'', H-11''), 6.84-6.77 (1H, m, H-7''), 5.83-5.76 (2H, m, H-5, H-6), 3.85-3.68 (8H, m, H-1', H-5'', OMe, H-3), 3.58-3.55 (1H, d, J=4.0, H-1), 2.60 (1H, d, J=11.0, Ha-3''), 2.42 (1H, d, J=11.0, Hb-3''), 2.43-2.13 (4H, m, H-3a, H-7a, Ha-4, Hb-7), 1.97-1.86 (2H, Hb-4, Hb-7), 1.07 (9H, s, tBu), 0.93 (3H, s, Me), 0.93 (3H, s, Me); ¹³C NMR (125 MHz, CDCl₃) δ 159.7(C8''), 142.7(C6''), 135.7(2 x Ph), 135.6(2 x Ph), 133.7(iPh), 133.6(iPh), 129.5(Ph), 129.5(Ph), 129.1(C10''), 127.6(4 x Ph), 127.0(C5 or C6), 126.8(C5 or C6), 126.0(C11''), 113.3(C7'' or C9''), 112.4(C7'' or C9''), 91.3(C1), 83.3(C3), 65.4(C1'), 58.3(C3''), 55.2(C12''), 54.0(C5''), 38.2(C3a or C7a), 37.8(C2''), 36.9(C3a or C7a), 28.0(C4 or C7), 26.8(tBu), 24.1(C4 or C7), 22.9(Me), 21.9(Me), 19.2(Si-C); LC-MS (ESI⁺) m/z 584.37 [M+H⁺] calcd for C₃₇H₅₂O₅Si 584.3554 found 584.3568.

{2-[(1R,3S,3aS,7aR)-3-[[[ tert-Butyldiphenylsilyl]oxy]methyl]-1,3,3a,4,7,7a-hexahydro-2-benzofuran-1-yl]-2-methylpropyl} (methyl)amine 52

2-[(1R,3S,3aS,7aR)-3-[[[ tert-Butyldiphenylsilyl]oxy]methyl]-1,3,3a,4,7,7a-hexahydro-2-benzofuran-1-yl]-2-methylpropanal 44 (145 mg, 0.315 mmol) and methylamine (25 µM, 0.315 mmol) was dissolved in 1,2-dichloroethane (3.0 mL). Sodium triacetoxyborohydride (86 mg, 0.441 mmol) was then added and the solution stirred at RT for 3 h. The reaction mixture was quenched by adding aqueous sat. NaHCO₃ (10 mL), and the solution was extracted with EtOAc. The EtOAc extract was dried over MgSO₄, and the crude residue was purified by ionic exchange chromatography on acidic resin (2 g) to yield 52 as a clear oil (92 mg, 64%). [α]D -28.5 (c=0.41 CHCl₃); IR (film) 2931, 2857, 1472, 1428 cm⁻¹; ¹H NMR (500 MHz, CDCl₃) δ 7.75-7.68 (4H, m, Ph), 7.45-7.36 (6H, m, Ph), 5.83-5.76 (2H, m, H-5, H-6), 3.79
(1H, dd, J=4.0, 11.0, Ha-1’), 3.75-3.68 (2H, m, Hb-1’, H-3), 3.55-3.51 (1H, d, J=4.0, H-1), 2.59 (1H, d, J=11.5, Ha-3’’), 2.42 (3H, s, H-5’’), 2.37 (1H, d, J=11.5, Hb-3’’), 2.24-2.14 (4H, m, H-3a, H-7a, Ha-4, Ha-7), 1.99-1.85 (2H, m, Hb-4, Hb-7), 1.06 (9H, s, tBu), 0.93 (3H, s, Me), 0.91 (3H, s, Me); $^{13}$C NMR (125 MHz, CDCl$_3$) δ 135.7 (2 x Ph), 135.6 (2 x Ph), 133.8 (iPh), 133.6 (iPh), 129.6 (Ph), 129.5 (Ph), 127.6 (2 x Ph), 127.6 (2 x Ph), 127.0 (C5 or C6), 126.8 (C5 or C6), 91.4 (C1), 83.3 (C3), 65.2 (C1’), 61.9 (C3’’), 38.2 (C3a or C7a), 37.6 (C2’’), 37.6 (C5’’), 36.9 (C3a or C7a), 28.1 (C4 or C7), 26.8 (tBu), 24.0 (C4 or C7), 23.1 (Me), 21.1 (Me), 19.2 (Si-C); LC-MS (ESI$^+$) m/z 478 [M+H$^+$], R$_t$ 2.28 min [method D]; HRMS [M+H$^+$] calcd for C$_{30}$H$_{44}$NO$_2$ 478.3135 found 478.3114.

{2-[(1R,3S,3aS,7aR)-3-[[tert-Butyldiphenylsilyl]oxy]methyl]-1,3,3a,4,7,7a-hexahydro-2-benzofuran-1-yl]-2-methylpropyl}(propyl)amine 53

2-[(1R,3S,3aS,7aR)-3-[[tert-Butyldiphenylsilyl]oxy]methyl]-1,3,3a,4,7,7a-hexahydro-2-benzofuran-1-yl]-2-methylpropanal 44

(145 mg, 0.315 mmol) and n-propylamine (25 µM, 0.315 mmol) was dissolved in 1,2-dichloroethane (3.0 mL). Sodium triacetoxyborohydride (86 mg, 0.441 mmol) was added and the solution stirred at RT for 3 h. The reaction mixture was quenched by adding aqueous sat. NaHCO$_3$ (10 mL), and the solution was extracted with EtOAc. The EtOAc extract was dried (MgSO$_4$), and the crude residue was purified by ionic exchange chromatography on acidic resin (2 g) to yield 53 as a clear oil (92 mg, 62%). [α]$^{24}_{D}$ -21.3 (c=0.5 CHCl$_3$); IR (film) 2956, 2857, 1472 cm$^{-1}$; $^1$H NMR (500 MHz, CDCl$_3$) δ 7.75-7.68 (4H, m, Ph), 7.46-7.36 (6H, m, Ph), 5.82-5.74 (2H, m, H-5, H-6), 3.82-3.74 (3H, m, H-1’, H-3), 3.56 (1H, d, J=4.0, H-1), 2.63-2.50 (3H, m, H-5’’, Ha-3’’), 2.42 (1H, d, J=11.5, Hb-3’’), 2.25-2.13 (4H, m, H-3a, H-7a, Ha-4, Ha-7), 2.00-1.84 (2H, m, Hb-4, Hb-7), 1.50 (2H, ddddd, J=7.0, 7.0, 7.0, 7.0, 7.0, H-6’’), 1.07 (9H, s, tBu), 0.91-0.89 (9H, m, Me, Me, H-7’’); $^{13}$C NMR (125 MHz, CDCl$_3$) δ 135.6 (4 x Ph), 133.7 (iPh), 133.6 (iPh), 129.6 (Ph), 129.5 (Ph), 127.6 (4 x Ph), 127.0 (C5 or C6), 126.8 (C5 or C6), 91.5 (C1), 83.4 (C3), 65.2 (C1’), 59.0 (C3’’), 52.8 (C5’’), 38.3 (C3a or C4a), 37.6 (C2), 36.9 (C3a or C4a), 28.0 (C4 or C7), 26.0 (tBu), 24.0 (C4 or C7), 22.9 (C6’’), 22.9 (C1A’’ or C1B’’), 21.1 (C1A’’ or C1B’’), 19.2 (Si-C), 11.7 (C7’’); LC-MS (ESI$^+$) m/z 506 [M+H$^+$], R$_t$ 2.30 min [method D]; HRMS [M+H$^+$] calcd for C$_{32}$H$_{48}$NO$_2$SiNa 506.3449 found 506.3464.

{2-[(1R,3S,3aS,7aR)-3-[[tert-Butyldiphenylsilyl]oxy]methyl]-1,3,3a,4,7,7a-hexahydro-2-benzofuran-1-yl]-2-methylpropyl}(2-methoxyethyl)amine 54

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2-[(1R,3S,3aS,7aR)-3-[[[(tert-Butyldiphenylsilyl)oxy]methyl]-1,3,3a,4,7,7a-hexahydro-2-benzofuran-1-yl]-2-methylpropanal 44 (145 mg, 0.315 mmol) and methoxyethyl amine (27 µM, 0.315 mmol) was dissolved in 1,2-dichloroethane (3.0 mL). Sodium triacetoxyborohydride (86 mg, 0.441 mmol) was added and the solution stirred at RT for 3 h. The reaction mixture was quenched by adding aqueous sat. NaHCO₃ (10 mL), and the solution was extracted with EtOAc. The EtOAc extract was dried (MgSO₄), and the crude residue was purified by ionic exchange chromatography on acidic resin (2 g) to yield 54 as a clear oil (92 mg, 56%). 

\[\text{[α]}_{24.3}^{D} - 28.6 \text{ (c=1.0 CHCl₃)}; \text{IR (film)} 2930, 2857, 1472, 1428 \text{ cm}^{-1}; \text{¹H NMR (500 MHz, CDCl₃)} \delta 7.74-7.65 (4H, m, Ph), 7.44-7.36 (6H, m, Ph), 5.82-5.74 (2H, m, H-5, H-6), 3.80-3.66 (3H, m, H-1’, H-3’), 3.56 (1H, d, J=4.0, H-6’), 3.30 (3H, s, H-8’), 2.81-2.75 (2H, m, H-5’), 2.60 (1H, d J=11.5, Ha-3’), 2.42 (1H, d, J=11.5, Hb-3’), 2.25-2.09 (4H, m, H-3a, H-7a, Ha-4, Ha-7), 1.99-1.79 (2H, m, H-5, H-6), 1.05 (9H, s, tBu), 0.91 (3H, s, Me), 0.90 (3H, s, Me); \text{¹³C NMR (125 MHz, CDCl₃)} \delta 135.6 (4 x Ph), 133.7 (iPh), 133.6 (iPh), 129.6 (Ph), 129.5 (Ph), 127.6 (C5 or C6), 127.0 (C5 or C6), 126.8 (C5 or C6), 91.2 (C1), 83.2 (C3), 72.0 (C6’), 65.2 (C1’), 58.9 (C3’ or C8’), 58.7 (C3’ or C8’), 50.4 (C5’), 38.3 (C3a or C7a), 37.8 (C2’), 36.8 (C3a or C7a), 28.0 (C4 or C7), 24.3 (Me), 21.2 (Me), 19.2 (Si-C); \text{LC-MS (ESI⁺)} m/z 522 [M+H⁺], Rₜ 2.30 min [method D]; \text{HRMS [M+H⁺]} calcd for C₃₂H₄₈NO₃Si 522.3398 found 522.3409; Found: C, 73.75; H, 9.00%; C₃₂H₄₇NO₃Si requires: C, 73.66; H, 9.08%.

[(1S,3R,3aR,7aS)-3-[[1-(benzylamino)-2-methylpropan-2-yl]-1,3,3a,4,7,7a-hexahydro-2-benzofuran-1-yl]methanol 55

\[2-[(1R,3S,3aS,7aR)-3-[[[(tert-Butyldiphenylsilyl)oxy]methyl]-1,3,3a,4,7,7a-hexahydro-2-benzofuran-1-yl]-2-methylpropyl][benzyl]amine 50 (50 mg, 0.090 mmol) was dissolved in THF (1 mL). TBAF (1.0 M in THF, 0.27 mL, 0.27 mmol) was added and the reaction stirred at 0°C for 6 h. The solution was diluted with Et₂O (20 mL) and washed with H₂O (2 x 20 mL), brine (20 mL) and the organic layer was dried with MgSO₄. The crude residue was purified by ionic exchange chromatography on acidic resin (2 g) to yield 55 as a clear oil (18 mg, 63%). \[\text{[α]}_{21}^{D} - 10.5 \text{ (c=1.0 CHCl₃)}; \text{IR (film)} 3319, 2930, 2839, 1495, 1453 \text{ cm}^{-1}; \text{¹H NMR (500 MHz, CDCl₃)} \delta 7.35-7.34 (4H, m, Ph), 7.29-7.24 (1H, m, Ph), 5.81-5.74 (2H, m, H-5, H-6), 3.86-3.81 (2H, m, Ha-1’, Ha-5”), 3.73 (1H, d, J=13.0, Hb-5”), 3.68 (1H, ddd, J=3.0, 3.0, 8.5, H-3), 3.56-3.52 (2H, m, Hb-1’, H-1), 2.61 (1H, d, J=12.0, Hb-3”), 2.38 (1H, d, J=12.0, Hb-3”), 2.34-2.15 (4H, m, H-7a, H-3a, H-4, H-7), 1.97-1.83 (2H, m, Hb-4, Hb-7), 1.00 (3H, s, Me), 0.83 (3H, s, Me); \text{¹³C NMR...} \]
(125 MHz, CDCl$_3$) δ 128.4 (4x Ph), 128.3 (Ph), 127.2 (Ph), 126.5 (C5 or C6), 126.4 (C5 or C6), 92.7 (C1), 83.6 (C3), 62.5 (C1'), 57.3 (C3''), 24.5 (C5''), 37.5 (C2''), 37.0 (C3a or C7a), 36.2 (C3a or C7a), 27.9 (C4 or C7), 23.9 (C4 or C7), 23.8 (Me), 23.2 (Me); LC-MS (ESI$^+$) m/z 316 [M+H$^+$], R$_t$ 1.73 min [method D]; HRMS [M+H$^+$] calcd for C$_{20}$H$_{30}$NO$_3$ 316.2271 found 316.2278.

[(1S,3R,3aR,7aS)-3-{[(3-Methoxyphenyl)methyl]amino}-2-methylpropan-2-yl]-1,3,3a,4,7,7a-hexahydro-2-benzofuran-1-yl]methanol 56

![Diagram of 56](image)

{2-[[1R,3S,3aS,7aR]-3-{{(tert-Butyldiphenylsilyl)oxy}methyl}-1,3,3a,4,7,7a-hexahydro-2-benzofuran-1-yl]-2-methylpropyl}[(3-methoxyphenyl)methyl]amine 51 (69 mg, 0.118 mmol), was dissolved in THF (1.3 mL). TBAF (1.0 M in THF, 0.35 mL, 0.35 mmol) was added and the reaction stirred at 0 °C for 6 h. The solution was diluted with Et$_2$O (20 mL) and washed with H$_2$O (2 x 20 mL), brine (20 mL) and the organic layer was dried with MgSO$_4$. The crude residue was purified by ionic exchange chromatography on acidic resin (2 g) to yield 56 as a clear oil (26 mg, 63%). [α]$^{21}_D$ -6.7 (c=2.0 CHCl$_3$); IR (film) 2938, 1600, 1489, 1466, 1252 cm$^{-1}$; $^1$H NMR (500 MHz, CDCl$_3$) δ 7.29-7.24 (1H, m, Ph), 7.00-6.92 (2H, m, Ph), 6.85-6.80 (1H, m, Ph), 5.82-5.77 (2H, m, H-5, H-6), 3.89-3.79 (6H, m, Ha-1', H-3''), 3.76 (3H, s, H-13''), 3.70-3.65 (1H, m, H-3), 3.57-3.52 (2H, m, Hb-1', H-1), 2.66 (1H, d, j=12.0, Ha-5''), 2.42 (1H, d, j=12.0, Hb-5''), 2.32-2.14 (4H, m, H-3a, H-7a, Ha-4, Hb-7), 1.96-1.83 (2H, m, H-4, H-7), 1.01 (3H, s, Me), 0.92 (3H, s, Me); $^{13}$C NMR (125 MHz, CDCl$_3$) δ 159.3 (C8''), 128.9 (Ph), 126.1 (C5 or C6), 125.8 (C5 or C6), 120.8 (Ph), 119.9 (Ph), 113.5 (Ph), 113.1 (Ph), 92.3 (C1), 83.2 (C3), 61.9 (C1'), 56.5 (C5''), 54.7 (C13''), 53.6 (C3''), 36.9 (C2''), 36.5 (C3a or C7a), 35.8 (C3a or C7a), 27.4 (C4 or C7), 23.3 (C4 or C7), 23.0 (Me), 22.3 (Me); LC-MS (ESI$^+$) m/z 346 [M+H$^+$], R$_t$ 1.53 min [method D]; HRMS [M+H$^+$] calcd for C$_{21}$H$_{32}$NO$_3$ 346.2376 found 346.2386.

[(1S,3R,3aR,7aS)-3-{2-Methyl-1-(methylamino)propan-2-yl]-1,3,3a,4,7,7a-hexahydro-2-benzofuran-1-yl]methanol 57

![Diagram of 57](image)

{2-[[1R,3S,3aS,7aR]-3-{{(tert-Butyldiphenylsilyl)oxy}methyl}-1,3,3a,4,7,7a-hexahydro-2-benzofuran-1-yl]-2-methylpropyl}(methyl)amine 52 (84 mg, 0.176 mmol), was dissolved in THF (2 mL). TBAF (1.0 M in THF, 0.53 mL, 0.53 mmol) was added and the reaction stirred at 0 °C for 4 h. The solution was diluted with
Et₂O (20 mL) and washed with H₂O (2 x 20 mL), brine (20 mL) and the organic layer was dried with MgSO₄. The crude residue was purified by ionic exchange chromatography on acidic resin (2 g) to yield 57 as a clear oil (25 mg, 60%). [α]²⁰ -16.1 (c=1.0 CHCl₃; IR (film) 3327, 3027, 2932, 1472, 1443 cm⁻¹; ¹H NMR (500 MHz, CDCl₃) δ 5.83-5.72 (2H, m, H-5, H-6), 3.86 (1H, dd, J=2.5, 12.0, Ha-1'), 3.68 (1H, ddd, J=2.5, 9.0, H-3), 3.54-3.50 (2H, m, Hb-1', H-1), 2.58 (1H, d, J=12.0, Ha-3''), 2.36 (3H, s, H-5''), 2.35-2.16 (5H, m, Hb-3'', H-3a, H-7a, Ha-4, Ha-7), 1.98-1.82 (2H, m, Hb-4, Hb-7), 1.04 (3H, s, Me), 0.87 (3H, s, Me); ¹³C NMR (125 MHz, CDCl₃) δ 126.4 (C5 or C6), 126.1 (C5 or C6), 93.1 (C1), 83.7 (C3), 62.1 (C1'), 60.5 (C3''), 37.5 (C2''), 27.1 (C7a or C3a), 36.9 (C5''), 28.0 (C4 or C7), 23.8 (Me); LC-MS (ESI⁺) m/z 240 [M+H⁺], Rₜ 1.43 min [method D]; HRMS [M+H⁺] calcd for C₁₄H₂₆NO₂ 240.1958 found 240.1967.

[(1S,3R,3aR,7aS)-3-[2-methyl-1-(propylamino)propan-2-yl]-1,3,3a,4,7,7a-hexahydro-2-benzofuran-1-yl]methanol 58

[2-[(1R,3S,3aS,7aR)-3-[(tert-Butyldiphenylsilyl)oxy]methyl]-1,3,3a,4,7,7a-hexahydro-2-benzofuran-1-yl]-2-methylpropyl]propylamine 53 (84 mg, 0.144 mmol), was dissolved in THF (2 mL). TBAF (1.0 M in THF, 0.43 mL, 0.43 mmol) was added and the reaction stirred at 0 °C for 4 h. The solution was diluted with Et₂O (20 mL) and washed with H₂O (2 x 20 mL), brine (20 mL) and the organic layer was dried with MgSO₄. The crude residue was purified by ionic exchange chromatography on acidic resin (2 g) to yield 58 as a clear oil (36 mg, 93%). [α]²¹ -25.6 (c=1.0 CHCl₃; IR (film) 3313, 3027, 2932, 1467 cm⁻¹; ¹H NMR (500 MHz, CDCl₃) δ 5.83-5.72 (2H, m, H-5, H-6), 3.88 (1H, dd, J=2.0, 12.0, Ha-1'), 3.68 (1H, ddd, J=2.0, 9.0, H-3), 3.57-3.52 (2H, m, Hb-1', H-1), 2.69 (1H, d, J=12.0, Ha-3''), 2.66-2.59 (1H, m, Hb-5''), 2.55-2.49 (1H, m, Hb-5''), 2.40 (1H, d, J=12.0, Hb-3''), 2.32-2.17 (4H, m, Ha-4, Ha-7, H-3a, H-7a), 1.98-1.83 (2H, m, Hb-4, Hb-7), 1.67-1.50 (2H, m, H-6''), 1.06 (3H, s, Me), 0.94 (3H, s, Me), 0.92 (3H, t, J=7.0, J=7''); ¹³C NMR (125 MHz, CDCl₃) δ 126.7 (C5 or C6), 126.0 (C5 or C6), 93.7 (C1), 84.1 (C3), 61.2 (C1'), 60.5 (C3''), 37.5 (C2''), 27.1 (C7a or C3a), 36.9 (C5''), 35.0 (C3a or C7a), 28.0 (C4 or C7), 24.4 (Me), 23.9 (C4 or C7), 23.8 (Me); LC-MS (ESI⁺) m/z 268 [M+H⁺], Rₜ 1.43 min [method D]; HRMS [M+H⁺] calcd for C₁₆H₃₁NO₂ 268.2271 found 268.2273.

[(1S,3R,3aR,7aS)-3-1-[2-Methoxyethylamino]-2-methylpropan-2-yl]-1,3,3a,4,7,7a-hexahydro-2-benzofuran-1-yl]methanol 59

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[2-{(1R,3S,3aS,7aR)-3-{[(tert-Butyldiphenylsilyl)oxy]methyl}-1,3,3a,4,7,7a-hexahydro-2-benzofuran-1-yl}-2-methylpropyl][2-methoxyethyl]amine 54 (94 mg, 0.180 mmol), was dissolved in THF (2 mL). TBAF (1.0 M in THF, 0.54 mL, 0.54 mmol) was added and the reaction stirred at 0 °C for 6 h. The solution was diluted with Et<sub>2</sub>O (20 mL) and washed with H<sub>2</sub>O (2 x 20 mL), brine (20 mL) and the organic layer was dried with MgSO<sub>4</sub>. The crude residue was purified by ionic exchange chromatography on acidic resin (2 g) to yield 59 as a clear oil (25 mg, 49%). [α]<sup>21</sup>D -21.2 (c=1.0 CHCl<sub>3</sub>); IR (film) 3331, 2875, 2839, 1457, 1097 cm<sup>-1</sup>; <sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>) δ 5.81-5.76 (2H, m, H<sub>5</sub>, H<sub>6</sub>), 3.87 (1H, dd, J=2.0, 12.0, Ha<sub>1</sub>'), 3.69 (1H, ddd, J=3.0, 3.0, 9.0, H<sub>3</sub>), 3.57-3.51 (4H, Hb<sub>1</sub>'), H<sub>1</sub>, H<sub>6</sub>''), 3.38 (3H, s, H<sub>8</sub>''), 2.77-2.72 (2H, m, H<sub>5</sub>''), 2.66 (1H, d, J=12.0, Ha-3''), 2.43 (1H, d, J=12.0, Hb-3''), 2.35-2.31 (1H, m, H<sub>3a</sub>), 2.30-2.17 (3H, m, Ha-4, Ha-7, H<sub>7a</sub>), 1.98-1.84 (2H, m, Hb-4, Hb-7), 1.06 (3H, s, Me), 0.92 (3H, s, Me); LR-MS (ESI+)<em>m/z</em> 284 [M+H]+, R<sub>t</sub> 1.52 min [method D]; HRMS [M+H]+ calcd for C<sub>16</sub>H<sub>30</sub>N<sub>2</sub>O<sub>3</sub> 284.2220 found 284.2230; Found: C, 67.90; H, 10.36%; C<sub>16</sub>H<sub>29</sub>N<sub>2</sub>O<sub>3</sub> requires: C, 67.81; H, 10.31%.

[(1S,3S,3aR,7aS)-3-{(2-methoxy-3-phenylpropyl)-octahydro-2-benzofuran-1-yl}methanol 60

Trimethyl(phenyl)silane (0.155 mL, 0.903 mmol), Ph<sub>3</sub>PAuCl (11 mg, 0.023 mmol) and Selectfluor (346 mg, 0.903 mmol) was added to a solution of (1S,3S,3aR,7aS)-3-{allyl-octahydro-isobenzofuran-1-yl}methanol 25 (196 mg, 1.000 mmol) in MeOH:MeCN (1:5, 4.8 mL) and heated to 70 °C for 5 h. The reaction was cooled to RT and TBAF (1.0 M in THF, 1.35 mL, 1.35 mmol) was added. The resultant solution was stirred at RT for 16 h. The reaction mixture was then diluted with Et<sub>2</sub>O (10 mL) and washed with H<sub>2</sub>O (10 mL x 2). Solvents were removed in vacuo and the crude residue was purified by column chromatography on silica gel (15% EtOAc:hexane) to yield 60 as a mixture of diastereoisomers (39 mg, 29%). IR (film) 3406, 3028, 2926, 1451 cm<sup>-1</sup>; <sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>) δ 7.34-7.27 (2H, m, Ph), 7.25-7.20 (3H, m, Ph), 4.00 (0.8H, ddd, J=4.0, 4.0, 8.5, H-1), 3.93 (0.2H, ddd, J=3.5, 3.5, 8.5, H-3), 3.88-3.84 (0.8H, m, H-3), 3.80 (0.2H, ddd, J=4.0, 4.0, 10.0, H-1), 3.78 (0.2H, dd, J=3.0, 11.5, Ha-1'), 3.66-3.63 (0.8H, m, H-2''), 3.60-3.54 (1H, m, Ha-1', H-2''), 3.48-3.41 (0.2H, m, Hb-1'), 3.42 (2.4H, s, OMe), 3.36 (0.6H, s, OMe), 3.30-3.23 (0.8H, m, Hb-1'), 2.99 (0.8H, dd, J=5.5, 13.5, Ha-3''), 2.91 (0.2H, dd, J=5.5, 13.5, Ha-3''), 2.75 (0.2H, dd, J=7.0, 13.5, Hb-3''), 2.69 (0.8H, dd, J=7.5, 14.0, Hb-3''), 2.35-2.28 (0.2H, m, H-3a),
2.08-1.98 (0.8H, m, H-3a), 1.85-1.77 (1H m, H-7a), 1.68-1.24 (10H, m, H-4, H-5. H-6, H-7, H-1’’); 13C NMR (125 MHz, CDCl3) δ MAJOR: 139.3 (iPh), 130.3 (2 x Ph), 129.1 (2 x Ph), 127.0 (Ph), 82.7 (C3), 80.6 (C1), 80.5 (C2’’), 65.0 (C1’), 58.1 (OMe), 44.4 (C7a), 41.5 (C1’’), 40.8 (C3’’), 38.3 (C3a), 27.2 (CH2), 26.1 (CH2), 24.3 (CH2), 23.4 (CH2), MINOR: 139.0 (iPh), 130.1 (2 x Ph), 129.0 (2 x Ph), 126.9 (Ph), 83.1 (C3), 82.5 (C1), 63.6 (C1’), 57.5 (OMe), 44.6 (C7a), 41.1 (C3’’), 40.4 (C1’’), 36.8 (C3a), 27.7 (CH2), 25.5 (CH2), 24.8 (CH2), 22.6 (CH2); LC-MS (ESI+) m/z 327 [M+Na+], Rf 1.52 min [method E].

Ethyl (2E)-4-[[1R,3S,3aS,7aR]-3-[[[tert-Butyldiphenylsilyl]oxy]methyl]-1,3,3a,4,7,7a-hexahydro-2-benzofuran-1-yl]-4-methylpent-2-enoate 61

NaH (60 mg, 60% w/w mineral oil, 1.519 mmol) was added to THF (5 mL) to form a suspension. Triethylphosphonate (370 µL, 1.870 mmol) was added dropwise followed by a solution of 2-[[1R,3S,3aS,7aR]-3-[[[tert-Butyldiphenylsilyl]oxy]methyl]-1,3,3a,4,7,7a-hexahydro-2-benzofuran-1-yl]-2-methylpropanal 44 (469 mg, 1.167 mmol) in THF (7 mL). The reaction was stirred at RT for 16 h. The reaction was then diluted in Et2O (50 mL), washed with H2O (50 mL x 2) and brine (50 mL). The combined aqueous layers were extracted into CH2Cl2, and the organic layers dried over MgSO4. Solvents were removed in vacuo to yield the crude product as a clear oil (660 mg). The product was purified by column chromatography on silica gel (5% EtOAc:hexane) to yield 61 as a clear oil (361 mg, 58%). [α]24.7D -22.9 (c=1.0 CHCl3); IR (film) 2931, 2858, 1716 cm⁻¹; 1H NMR (500 MHz, CDCl3) δ 7.76-7.69 (4H, m, Ph), 7.47-7.37 (6H, m, Ph), 7.03 (1H, d, J=16.0, H-3’’), 5.81 (1H, d, J=16.0, H-4’’), 5.80-5.77 (2H, m, H-5, H-6), 4.19 (2H, dq, J= 1.5, 7.0, H-7’’), 3.80-3.72 (3H, m, H-1’, H-3), 3.51 (1H, J=5.0, H-1), 2.24-2.07 (4H, m, H-3a, H-7a, Ha-4, Hb-7), 1.95-1.88 (2H, m, Hb-4, Hb-7), 1.28 (3H, t, J=7.0, H-8’’), 1.11 (3H, s, H-1A’ or H-1B’), 1.10 (3H, s, H-1A’ or H-1B’’), 1.08 (9H, s, tBu); 13C NMR (125 MHz, CDCl3) δ 166.9 (C5’’), 155.4 (C3’’), 137.5 (2 x Ph), 135.6 (2 x Ph), 133.7 (ipPh), 133.6 (ipPh), 129.6 (Ph), 129.6 (Ph), 127.8 (2 x Ph), 127.7 (2 x Ph), 126.9 (C5 or C6), 126.4 (C5 or C6), 119.0 (C4’’), 91.6 (C1), 83.7 (C3), 65.3 (C1’), 60.2 (C7’’), 40.8 (C2’’), 38.1 (C3a or C7a), 37.2 (C3a or C7a), 27.6 (C4 or C7), 26.8 (tBu), 24.1 (C4 or C7), 23.4 (Me), 22.6 (Me), 19.2 (Si-C), 14.3 (C8’’); LC-MS (ESI+) m/z 555 [M+Na+], Rf 3.15 min [method E]; HRMS [M+H+] calcd for C33H44O4SiNa 555.2901 found 555.2917.

Ethyl 4-[[1R,3S,3aS,7aR]-3-[[[tert-Butyldiphenylsilyl]oxy]methyl} octahydro-2-benzofuran-1-yl]-4-methylpentanoate 62
Ethyl (2E)-4-[(1R,3S,3aS,7aR)-3-{{[(tert-butyldiphenylsilyl)oxy]methyl}-1,3,4,7,7a-hexahydro-2-benzofuran-1-yl]-4-methylpent-2-enoate 61 (587 mg, 1.105 mmol) was dissolved in EtOAc (11 mL). Palladium on activated carbon (30 mg, 10% w/w Pd) was added. The flask was evacuated and flushed with H₂, and left to stir under an atmosphere of H₂ for 5 d. The suspension was filtered through celite and the solvents removed in vacuo to yield 62 as a clear oil (592 mg, 97%). [α]²⁴.⁷ D -7.0 (c=1.0 CHCl₃); IR (film) 2930, 2858, 1733, 1472 cm⁻¹; ¹H NMR (500 MHz, CDCl₃) δ 7.66-7.60 (4H, m, Ph), 7.36-7.27 (6H, m, Ph), 4.03 (2H, q, J=7.5, H-7''), 3.84 (1H, ddd, J=4.5, 9.0, 9.0, H-3), 3.71 (1H, dd, J=4.0, 11.0, Ha-1'), 3.59 (1H, dd, J=4.5, 11.0, Hb-1'), 3.27 (1H, d, J=5.0, 10.5, Ha-4''), 2.29 (1H, dd, J=5.0, 10.5, Hb-4''), 1.99-1.91 (2H, m, H-3a, H-7a), 1.64-1.45 (8H, m, 8 x CH₂), 1.49-1.20 (2H, m, 2 x CH₂), 1.16 (3H, t, J=7.5, H-8''), 1.01 (9H, s, tBu), 0.77 (3H, s, Me), 0.75 (3H, s, Me); ¹³C NMR (125 MHz, CDCl₃) δ 174.5 (C5''), 135.7 (2 x Ph), 135.6 (2 x Ph), 133.8 (iPh), 133.6 (iPh), 129.5 (Ph), 129.5 (Ph), 127.6 (4 x Ph), 91.9 (C1), 80.1 (C3), 65.4 (C1'), 60.2 (C7''), 38.0 (C3a, C7a), 36.6 (C2''), 34.0 (CH₂), 30.3 (CH₂), 29.5 (CH₂), 26.8 (tBu), 24.6 (2 x CH₂), 24.0 (CH₂), 22.6 (Me), 22.4 (Me), 22.1 (CH₂), 19.21 (C-Si), 14.2 (C8''); LC-MS (ESI⁺) m/z 559 [M+Na⁺], Rₜ 3.50 min [method E]; HRMS [M+Na⁺] calcd for C₃₃H₄₈O₄SiNa 559.3214 found 559.3224; Found: C, 74.02; H, 8.91%; C₃₃H₄₈O₄Si requires: C, 73.83; H, 9.01%.

Ethyl 4-[(1R,3S)-3-(hydroxymethyl)octahydro-2-benzofuran-1-yl]-4-methylpentanoate 63

Ethyl 4-[(1R,3S,3aS,7aR)-3-{{[(tert-butyldiphenylsilyl)oxy]methyl}octahydro-2-benzofuran-1-yl]-4-methylpentanoate 62 (221 mg, 0.412 mmol) was dissolved in THF (4 mL). TBAF (1.0 Mol in THF, 1.23 mL, 1.23 mmol) was added and the reaction stirred at 0 °C for 4 h. The solution was diluted with Et₂O (20 mL) and washed with H₂O (2 x 20 mL), brine (20 mL) and the organic layer was dried with MgSO₄. The product was purified by column chromatography on silica gel (15% EtOAc:hexane) to yield 63 as a clear oil (89 mg, 72%). [α]²⁴.⁶ D +7.3 (c=3.0 CHCl₃); IR (film) 2931, 1723, 1450 cm⁻¹; ¹H NMR (500 MHz, CDCl₃) δ 4.11 (2H, dq, J= 1.5, 7.0, H-7''), 3.89 (1H, ddd, J=3.0, 6.0, 10.5, H-3), 3.76 (1H, br d, J=11.5, Ha-1'), 3.51 (1H, dd, J=6.0, 11.5, Hb-1'), 3.35 (1H, d, J=3.0, H-1), 2.32 (1H, ddd, J=6.5, 10.5, 15.5, Ha-4''), 2.27 (1H, ddd, J=6.5, 10.5, 15.5, Hb-4''), 2.07-1.99 (1H, m, H-7a), 1.92-1.86 (1H, m, H-3a), 1.67-1.52 (6H, m, CH₂), 1.50-1.44 (1H, m, CH₂), 1.41-1.20 (3H, m, CH₂), 1.24 (3H, t, J=7.0, H-8''), 0.83 (3H, s, Me), 0.81 (3H, s, Me); ¹³C NMR (125 MHz, CDCl₃) δ 174.4 (C5''), 92.3 (C1), 79.9 (C3), 64.2 (C1'), 60.3 (C4'), 39.1 (C7a), 38.1 (C3a), 36.5 (C2''), 34.0 (CH₂), 30.3 (CH₂), 29.5 (CH₂), 24.5 (CH₂), 23.8 (CH₂), 22.9 (Me), 22.3 (Me), 21.9.
(CH₂), 14.2 (C₈’’); LC-MS (ESI⁺) m/z 321.24 [M+Na⁺], Rₜ 1.72 min [method E]; HRMS [M+H⁺] calcd for C₁₇H₃₀O₄ 298.2144 found 298.2151;

4-[[1R,3S,3aS,7aR]-3-(hydroxymethyl)octahydro-2-benzofuran-1-yl]-4-methylpentanoic acid 64

Ethyl 4-[[1R,3S]-3-(hydroxymethyl)octahydro-2-benzofuran-1-yl]-4-methylpentanoate 63 (95 mg, 0.319 mmol) was dissolved in THF:H₂O (3.0 mL, 2:1 ratio) and LiOH.H₂O (23 mg, 0.79 mmol) was added. The solution was stirred at RT for 16 h. The reaction mixture was acidified to pH 4 with 1 M HCl. The solution was extracted with CH₂Cl₂ (4 x 5 mL). The combined organic layers were dried over MgSO₄ and the solvents removed in vacuo to yield 64 as a clear oil (81 mg, 99%). [α]₂₄.₂ D +17.8 (c=1.0 CHCl₃); IR (film) 2928, 2858, 1708, 1451 cm⁻¹; ¹H NMR (500 MHz, CDCl₃) δ 3.96 (1H, ddd, J=2.5, 6.0, 10.0, H-3), 3.77 (1H, dd, H=2.5, 12.0, Ha-1’), 3.55 (1H, dd, J=6.0, 12.0, Hb-1’), 3.40 (1H, d, J=3.0, H-1), 2.37 (1H, ddd, J=6.0, 12.0, 16.0, Ha-4’’), 2.30 (1H, ddd, J=6.0, 12.0, 16.0, Hb-4’’), 2.09-2.02 (1H, m, H-7a), 1.95-1.88 (1H, m, H-3a), 1.71-1.46 (7H, m, H-3’’, 3 x CH₂), 1.42-1.21 (3H, m, CH₂), 0.85 (3H, s, H-1A’’), 0.84 (3H, s, H-1B’’); ¹³C NMR (125 MHz, CDCl₃) δ 178.5 (C5’’), 92.3 (C1), 80.5 (C3), 64.2 (C1’), 39.1 (C7a), 38.0 (C3a), 36.4 (C2’’), 33.9 (C3’’), 30.3 (CH₂), 29.0 (C4’’), 24.5 (CH₂), 23.7 (CH₂), 23.1 (C1A’’), 22.1 (C1B’’), 21.8 (CH₂); LC-MS (ESI⁺) m/z 293 [M+Na⁺], Rₜ 1.58 min [method D lipol]; HRMS [M+Na⁺] calcd for C₁₅H₂₆O₄Na 293.1723 found 293.1726; Found: C, 66.59 H, 9.59%; C₁₅H₂₆O₄ requires: C, 66.64; H, 9.69%.

(1R,2R,7S,8S)-14,14-dimethyl-10,15-dioxatricyclo[6.6.1.0²,7]pentadecan-11-one 65

2-Methyl-6-nitrobenzoic anhydride (87 mg, 0.253 mmol) and DMAP (61 mg, 0.506 mmol) was dissolved in CH₂Cl₂ (90 mL). A solution of 4-[[1R,3S,3aS,7aR]-3-(hydroxymethyl)octahydro-2-benzofuran-1-yl]-4-methylpentanoic acid 64 (57 mg, 0.211 mmol) in CH₂Cl₂ (20 mL, 0.01 M) was added by syringe pump over 16 h at RT. Approximately 50% of the solvent was removed in vacuo and the remaining solution was washed with ice cold sat. aqueous NaHCO₃. The aqueous layer was extracted with CH₂Cl₂ (2 x 30 mL), and the combined organic layers were washed with brine (30 mL). The organic layer was dried with MgSO₄ and the solvents were removed in vacuo. The crude residue was purified by column chromatography on silica gel (5% MeOH:CH₂Cl₂) to yield the product as a white crystalline solid (18 mg, 30%), mp (56.6-57.1 °C); [α]₂²⁺ +14.0 (c=2.0 CHCl₃); IR (film) 2923, 2860, 1730, 1447 cm⁻¹; ¹H NMR (500 MHz, CDCl₃) δ 5.12 (1H, dd, J=4.0, 11.5, Ha-9), 3.90 (1H, dd, J=4.0, 8.0, H-8), 3.70 (1H, d, J=11.5, Hb-9), 3.50 (1H, d, J=3.0, H-1), 2.55-2.48 S50
(1H, m, H-7), 2.48-2.44 (2H, m, H-12), 2.27-2.20 (1H, m, H-2), 2.05 (1H, ddd, J=6.5, 10.5, 15.0, Ha-13), 1.69-1.60 (3H, m, CH3), 1.62-1.47 (2H, m, CH2), 1.40-1.09 (4H, m, CH2), 1.09 (3H, s, Me), 0.86 (3H, s, Me); 13C NMR (125 MHz, CDCl3) δ 175.7 (C11), 95.7 (C1), 79.5 (C8), 65.4 (C9), 39.0 (C2 or C7), 38.8 (C2 or C7), 37.3 (C14), 33.9 (C12), 32.5 (C13), 30.1 (CH2), 29.1 (Me), 25.4 (Me), 24.3 (CH2), 24.0 (CH2), 22.1 (CH2); LC-MS (ESI') m/z 253 [M+H'], Rt 1.63 min [method D]; HRMS [M+H]+ calcd for C15H25O3 253.1798 found 253.1799; Found: C, 71.45; H, 9.42%; C15H24O3 requires: C, 71.39; H, 9.59%.

2-[(1R,3S,3aS,7aR)-3-[[[tert-butyldiphenylsilyl]oxy]methyl]-octahydro-2-benzofuran-1-yl]-2-methylpropanal 66

(3S,3aS,7aR)-3-[[[Butyldiphenylsilyl]oxy]methyl]-octahydro-2-benzofuran-1-ol 23 (841 mg, 2.05 mmol) was dissolved in CH2Cl2 (20 mL) and cooled to -78 °C. BF3·OEt2 (0.78 mL, 6.15 mmol) was added and the solution was stirred for 5 min. Trimethyl(2-methylpropenyloxy)silane (0.41 mL, 2.25 mmol) was then added and the reaction was warmed to RT and stirred for 3 h. The reaction was diluted with CH2Cl2 (20 mL), and washed with H2O (2 x 50 mL), followed by brine (50 mL). The organic layer was dried with MgSO4. Solvent was removed in vacuo to yield 66 as a pale brown oil (950 mg, >98%). This compound was found to be unstable so was used immediately. 1H NMR (500 MHz, CDCl3) δ 9.63 (1H, s, H-3''), 7.75-7.64 (4H, m, Ph), 7.46-4.36 (6H, m, Ph), 3.96-3.89 (1H, m, H-3), 3.79-3.75 (2H, m, Ha-1', H-1), 3.65 (1H, ddd, J=5.0, 11.5, Hb-1''), 2.06-2.01 (2H, m, H-3a, H-7a), 1.70-1.56 (4H, 4 x CH2), 1.49-1.37 (2H, m, 2 x CH2), 1.37-1.21 (2H, m, 2 x CH2), 1.07 (3H, s, Me), 1.06 (9H, s, tBu), 1.06 (3H, s, Me); 13C NMR (125 MHz, CDCl3) δ 206.1 (C3'') 135.7 (2 x Ph), 135.6 (2 x Ph), 133.6 (iPh), 133.4 (iPh), 129.6 (Ph), 129.6 (Ph), 127.7 (4 x Ph), 88.3 (C1), 80.9 (C3), 64.9 (C1'), 49.9 (C2''), 39.0 (C3a or C7a), 38.6 (C3a or C7a), 29.4 (CH2), 26.8 (tBu), 24.2 (CH2), 24.0 (CH2), 22.2 (CH2), 19.2 (Me) 18.8 (C-Si), 17.6 (Me); LC-MS (ESI') m/z 487 [M+Na'], Rt 1.92 min [method E]; HRMS [M+Na]+ calcd for C29H40O3SiNa 487.2644 found 487.2639.

[(1S,3R,3aR,7aS)-3-(2-methyl-1-oxopropan-2-yl)octahydro-2-benzofuran-1-yl]methyl 2-bromoacacetate 68

2-[(1R,3S,3aS,7aR)-3-[[[tert-butyldiphenylsilyl]oxy]methyl]-octahydro-2-benzofuran-1-yl]-2-methylpropanal 66 (950 mg, 2.05 mmol) was dissolved in THF (20 mL). TBAF (1.0 M in THF, 6.2 mL, 6.2 mmol) was added and the reaction stirred at RT for 8 h. The solution was diluted with Et2O (30 mL) and washed with H2O (2 x 30 mL) and
the organic layer was dried with MgSO₄. The product was purified by column chromatography on silica gel (33% EtOAc:hexane) to yield the alcohol 67 as a clear oil (200 mg, 43%). This unstable product was taken immediately into the next step. The alcohol 67 (200 mg, 0.89 mmol) was dissolved in CH₂Cl₂ (9 mL) and Et₃N (257 µL, 1.78 mmol) was added. 2-Bromoacetyl bromide (154 µL, 1.78 mmol) was added and the solution was stirred at RT for 5 h. The solution was diluted with CH₂Cl₂ (20 mL), washed with H₂O (10 mL), brine (10 mL) and then the aqueous layers where extracted with CH₂Cl₂ (2 x10 mL). The organic layer was dried with MgSO₄. The solvents were removed in vacuo and the crude mixture was flushed through silica (4 cm x Ø 20 mm) with (33% EtOAc:hexane) to yield 68 as a pale brown oil (250 mg, 34% over 2 steps). This compound was unstable so limited characterisation was possible. ¹H NMR (500 MHz, CDCl₃) δ 9.61 (1H, s, H-3''), 4.31 (1H, dd, J=3.0, 11.5, Ha-1'), 4.17-4.10 (1H, m, Hb-1'), 4.04 (1H, ddd, J=3.0, 6.0, 9.0, H-3), 3.88 (2H, s, H-4'), 3.81 (1H, d, J=4.0, H-1), 2.14-2.08 (1H, m, H-7a), 1.96-1.89 (1H, m, H-3a), 1.75-1.58 (4H, m, 2 x CH₂), 1.46-1.25 (4H, m, 2x CH₂), 1.08 (3H, s, Me), 1.07 (3H, s, Me); ¹³C NMR (125 MHz, CDCl₃) δ 205.7 (C3''), 166.7 (C3'), 88.3 (C1), 77.4 (C3), 66.5 (C1'), 49.3 (C2''), 38.6 (C7a or C3a), 38.4 (C7a or C3a), 28.7 (CH₂), 25.1 (C4'), 23.5 (CH₂), 23.4 (CH₂), 21.3 (CH₂), 18.3 (C1A''), 17.3 (C1B''); LC-MS (ESI+) m/z 369 [M+Na]+, Rₜ 2.25 min [method D].

(1R,2R,7S,8S,13R)-13-hydroxy-14,14-dimethyl-10,15-dioxatricyclo[6.6.1.0²,7]pentadecan-11-one 69

[(1S,3R,3aR,7aS)-3-(2-Methyl-1-oxopropan-2-yl)octahydro-2-benzofuran-1-yl]methyl 2-bromoacetate 68 (240 mg, 0.581 mmol) was dissolved in THF (200 mL), and SmI₂ (0.1 M in THF) was added dropwise (~25 mL) until the colour change of the SmI₂ from blue to yellow on addition slowed and the reaction mixture remained green. The solution was then diluted with Et₂O (20 mL), and washed with H₂O (20 mL) and brine (20 mL). The organic layer was dried with MgSO₄. The crude yellow oil was purified by column chromatography on silica gel (5% MeOH:CH₂Cl₂) to yield 69 as a white crystalline solid (70 mg, 45%). mp (107.8-108.3 °C); [α]²¹D +14.3 (c=2.0 CHCl₃); IR (film) 3518, 1724, 1448 cm⁻¹; ¹H NMR (500 MHz, CDCl₃) δ 5.41 (1H, dd, J=4.0, 11.0, H-9A), 3.93 (1H, dd, J=4.0, 8.0, H-8), 3.82-3.78 (1H, m, H-13), 3.74 (1H, d, J=11.0, H-9B), 3.62 (1H, d, J=1.5, H-1), 2.86-2.77 (2H, m, H-12), 2.49-2.43 (3H, m, H-2, H-7, OH), 1.72-1.60 (3H, m, CH₂), 1.57-1.49 (2H, m, CH₂), 1.38-1.24 (3H, m, CH₂), 1.08 (3H, s, CH₃), 1.01 (3H, s, CH₃); ¹³C NMR (125 MHz, CDCl₃) δ 172.2 (C11), 94.7 (C1), 78.1 (C8), 75.4 (C13), 65.6 (C9), 41.9 (C14), 40.8 (C12), 38.8 (C2 or C7), 38.7 (C2 or C7), 30.1 (CH₂), 26.2 (Me), 23.6 (CH₂), 23.4 (CH₂), 23.1 (Me), 21.2 (CH₂); LC-MS (ESI+) m/z 269 [M+H]+, Rₜ 1.28 min [method E]; HRMS [M+Na⁺] calcd for C₁₅H₂₄O₄Na 291.1566 found 291.1572; Found: C, 67.26; H, 9.01%; C₁₅H₂₂O₄ requires: C, 67.14; H, 9.01%.
(1R,2R,7S,8S,13R)-14,14-dimethyl-11-oxo-10,15-dioxatricyclo[6.6.1.0²,⁷]pentadecan-13-yl acetate 70

(1R,2R,7S,8S,13R)-13-Hydroxy-14,14-dimethyl-10,15-dioxatricyclo[6.6.1.0²,⁷]pentadecan-11-one 69 (8 mg, 0.030 mmol) was dissolved in CH₂Cl₂ (1.0 mL) and Et₃N (8.3 µL, 0.060 mmol) was added. Acetic anhydride (6.6 µL, 0.070 mmol) was added and the reaction mixture was stirred for 18 h. The solution was diluted with CH₂Cl₂ (5 mL) and washed with H₂O (10 mL x 2). The combined aqueous layers were extracted in CH₂Cl₂ (10 mL) and the combined organic layers dried over MgSO₄. Solvent was removed in vacuo to yield 70 as a clear oil (9 mg, quant.). [α]²⁴ +42.3 (c=0.1 CHCl₃); IR (film) 2921, 2852, 1735, 1450 cm⁻¹; ¹H NMR (500 MHz, CDCl₃) δ 5.18 (1H, dd, J=4.0, 11.0, Ha-9), 4.95 (1H, dd, J=4.5, 4.5, H₁₃), 3.96 (1H, dd, J=4.0, 9.0, H₈), 3.74 (1H, d, J=11.5, Hb-9), 3.58 (1H, d, J=1.5, H₁), 2.83 (1H, obs dd, J=4.5, 15.0, Ha-12), 2.82-2.76 (1H, m, H₇), 2.68 (1H, dd, J=4.5, 15.0, Hb-12), 2.39-2.32 (1H, m, H₂), 2.11 (3H, s, H₃'), 1.72-1.50 (5H, m, CH₂), 1.37-1.21 (3H, m, CH₂), 1.07 (3H, s, Me), 0.98 (3H, s, Me); ¹³C NMR (125 MHz, CDCl₃) δ 172.4 (C₁₁), 169.9 (C₂'), 95.2 (C₁), 78.9 (C₈), 76.1 (C₁₃), 65.9 (C₉), 41.6 (C₁₄), 39.8 (C₂), 38.7 (C₁₂), 37.4 (C₇), 30.9 (CH₂), 25.9 (Me), 24.4 (CH₂), 24.4 (Me), 23.7 (CH₂), 21.7 (CH₂), 21.0 (C₃'); LC-MS (ESI⁺) m/z 311 [M+Na⁺], Rₜ 1.57 min [method D]; HRMS [M+Na⁺] calcd for C₁₇H₂₆O₅Na 333.1673 found 333.1691.

(1S,3S,3aR,7aS)-3-(Prop-2-en-1-yl)-octahydro-2-benzofuran-1-carbaldehyde 71

[(1S,3S,3aR,7aS)-3-(Prop-2-en-1-yl)-octahydro-2-benzofuran-1-yl]methanol 25 (146 mg, 0.753 mmol) was dissolved in CH₂Cl₂ (3 mL). Dess Martin reagent (3.0 mL, 0.3 M in CH₂Cl₂, 0.90 mmol) was added and the reaction was stirred at RT for 3 h. An aqueous quenching solution (10 mL, 1.0 g NaHCO₃ and 13 g Na₂S₂O₃ in 100 mL H₂O) was added and the mixture was stirred for 3 h. The organic layer was separated and washed with the quenching solution (5 mL), dried over MgSO₄ and flushed through silica gel (CH₂Cl₂). The solvent was removed in vacuo to yield 71 as a clear oil (146 mg, 100%). This compound was unstable so limited characterisation was possible and the compound was used immediately. ¹H NMR (500 MHz, CDCl₃) δ 9.69 (1H, d, J=2.0, H-1'), 5.90 (1H, dddd, J=7.0, 7.0, 17.0, H-2‘’), 5.20-5.06 (2H, m, H-3‘’), 4.09-3.99 (2H, m, H-1, H-3), 2.45-2.25 (3H, m, H-1‘’, H-7a or H-3a), 1.98-1.90 (1H, m, H-7a or H-3a), 1.81-1.32 (8H, m, CH₂); ¹³C NMR (125 MHz, CDCl₃) δ 203.2 (C₁'), 134.2 (C₂‘’), 116.8 (C₃‘’), 85.7 (C₁ or C₃), 82.8 (C₁ or C₃), 41.6 (C₃a or C₇a), 39.7 (C₃a or C₇a), 39.2 (C₁''), 25.2 (CH₂), 24.9 (CH₂), 22.5 (CH₂), 22.2 (CH₂).
(R)-1-((1S,3S,3aR,7aS)-3-allyl-1-methyloctahydroisobenzofuran-1-yl)pent-4-en-1-ol 72 and (S)-1-((1S,3S,3aR,7aS)-3-allyl-1-methyloctahydroisobenzofuran-1-yl)pent-4-en-1-ol 73

A solution of (1S,3S,3aR,7aS)-3-(Prop-2-en-1-yl)-octahydro-2-benzofuran-1-carbaldehyde 71 (160 mg, 0.824 mmol) in THF (8.2 mL) was added dropwise by syringe to a freshly prepared solution of but-3-enylmagnesium bromide (0.9 mL, 4.0 M in Et₂O) at 0 °C under nitrogen. The reaction was warmed to RT, quenched with sat. aqueous NH₄Cl (30 mL) and extracted with Et₂O (3 × 20 mL). The combined organic layers were dried over NaSO₄ and the solvents were removed in vacuo. The crude residue was purified by column chromatography (20% ethyl acetate in hexane) to give major isomer 72 (106 mg, 51%) and minor isomer 73 (59 mg, 29%) as clear oils. Major isomer [α]₂⁴D +35.1 (c=0.1 CHCl₃); IR (film) 3408, 2925, 2856, 1640 cm⁻¹; ¹H NMR (500 MHz, CDCl₃) δ 5.94-5.77 (2H, m, H-2”, H-4”), 5.22-4.96 (4H, m, H-3”, H-5”), 3.88 (1H, ddd, J=4.5, 7.0, 7.0, H-1), 3.70-3.62 (2H, m, H-1’, H-3), 2.40-2.10 (5H, m, H-3’, H-1”, H-3a), 2.00-1.88 (2H, m, H-7a, OH), 1.69-1.27 (10H, m, CH₂); ¹³C NMR (125 MHz, CDCl₃) δ 138.6 (C4’ or C2”), 135.2 (C4’ or C2’), 117.3 (C3” or C5’), 115.0 (C3’ or C5”), 86.3 (C3), 80.6 (C1), 72.6 (C1’), 42.5 (C7a), 39.1 (C1” or C3’), 37.7 (C3a), 31.9 (CH₂), 30.5 (C1” or C3’), 28.0 (CH₂), 25.3 (CH₂), 23.8 (CH₂), 22.8 (CH₂); LC-MS (ESI⁺) m/z 273 [M+Na⁺], Rₜ 1.45 min [method D]; HRMS [M+H⁺] calcd for C₁₅H₂₇O₂ 251.2006 found 251.2013. Minor Isomer- ¹H NMR (500 MHz, CDCl₃) δ 5.90-5.77 (2H, m, H-2”, H-4”), 5.14-4.93 (m, 4H, H-3”, H-5”), 3.89 (ddd, J = 7.0, 6.0, 5.2 Hz, 1H, H-1), 3.56 (t, J = 5.4 Hz, 1H, H-3), 3.35 (dq, J = 8.1, 5.2 Hz, 1H, H-1”), 2.38-2.05 (m, 6H, H-1”, H-3”, H-3a, OH), 1.98-1.89 (m, 1H, H-7a), 1.69-1.30 (m, 10H); ¹³C NMR (126 MHz, CDCl₃) δ 138.7 (C4’ or C2”), 135.2 (C4’ or C2”), 117.3 (C5” or C3”), 114.8 (C5’ or C3”), 85.4 (C3), 81.5 (C1), 71.8 (C1’), 42.2 (C7a), 40.0 (C1” or C3’), 39.0 (C3a), 34.0 (CH₂), 30.2 (C1” or C3’), 26.5 (CH₂), 25.9 (CH₂), 23.4 (CH₂), 23.2 (CH₂); LC-MS (ESI⁺) m/z 273 [M+Na⁺], Rₜ 1.53 min [method D]; HRMS [M+H⁺] calcd for C₁₆H₂₉O₂ 251.2006 found 251.2003.

((R)-1-((1S,3S,3aR,7aS)-3-allyl-1-methyloctahydroisobenzofuran-1-yl)oxy)(tert-butyl)dimethylsilane 74

1-((1S,3S,3aR,7aS)-3-{Prop-2-en-1-yl}-octahydro-2-benzofuran-1-yl)pent-4-en-1-ol 72 (70 mg, 0.283 mmol) was dissolved in CH₂Cl₂ (2.8 mL) and DIPEA (195 µL, 1.12 mmol) was added. TBSOTf (117 µL, 0.67 mmol) was added and the reaction was stirred at RT for 30 min. The reaction was quenched with sat. aqueous NH₄Cl (10 mL) and extracted in CH₂Cl₂ (3 × 10 mL). The combined organic layers were dried over
MgSO₄ and the solvent was removed in vacuo to yield 74 as a clear oil (102 mg, 100%). [α]²⁴⁺ₓ -33.5 (c=0.25 CHCl₃); IR (film) 3407, 2927, 2857, 1463 cm⁻¹; ¹H NMR (500 MHz, CDCl₃) δ 5.95-5.81 (2H, m, H-2'', H-4'), 5.14-4.92 (4H, m, H-5', H-3''), 3.87-3.85 (1H, m, H-1), 3.58-3.52 (2H, m, H-3, H-1'), 2.37-2.24 (1H, m, H-1''), 2.20-2.12 (2H, m, Hb-1'', H-3a or H-7a), 1.94-1.84 (1H, m, H-3a or H-7a), 1.74-1.26 (12H, m, CH₂), 0.91 (9H, s, 'Bu), 0.08 (6H, s, Si-CH₃); ¹³C NMR (125 MHz, CDCl₃) δ 139.2 (C2'' or C4'), 135.7 (C2'' or C4'), 116.5 (C3'' or C5'), 114.1 (C3'' or C5'), 85.8 (C3), 80.2 (C1), 73.6 (C1'), 41.6 (C3a or C7a), 39.7 (C3a or C7a), 39.6 (C1''), 33.4 (CH₂), 28.6 (CH₂), 28.2 (CH₂), 26.0 (tBu), 24.7 (CH₂), 24.3 (CH₂), 22.3 (CH₂), 18.1 (Si-C), -4.0 (Si-Me), -4.3 (Si-Me); HRMS [M+H⁺] calcd for C₂₂H₄₂O₂Si 365.2870 found 365.2875.

tert-butyl([4aS,5S,6R,12S,12aR,Z]-5,12-dimethyl-1,2,3,4,4a,5,6,7,8,11,12,12a-dodecahydro-5,12-epoxybenzo[10]annulen-6-yl)oxydimethylsilane 75

{(1-[{(5S,3aR,7aS)-(Prop-2-en-1-yl)-octahydro-2-benzofuran-1-yl]pent-4-en-1-yl)oxy}[(tert-butyldimethyl]silane 74 (42 mg, 0.115 mmol) was dissolved in CH₂Cl₂ (230 mL) and Grubbs II catalyst (9.7 mg, 0.01 mmol) was added. The solution was stirred at RT for 16 h. DMSO (10 µL) was added and the solution was stirred for 24 h, before pre-absorbing on to silica (~200 mg). The product was purified by column chromatography to yield 75 as a clear oil (36 mg, 97%). [α]²⁴⁺₀ -31.1 (c=0.75 CHCl₃); IR (film) 2930, 2857 cm⁻¹; ¹H NMR (Acetone-d₆, 500 MHz) δ 5.75 (1H, tdd, J=11.6, 5.6, 2.0 Hz, H-12), 5.62 (1H, ddd, J=11.0, 8.7, 6.3 Hz, H-13), 4.09 (1H, dt, J=9.9, 3.1 Hz, H-1), 3.45 (1H, ddd, J=9.6, 8.8, 4.9 Hz, H-9), 3.28 (1H, d, J=8.8 Hz, H-8), 3.01 (1H, qd, J=11.7, 8.7 Hz, H-11a), 2.56 (1H, dt, J=14.6, 6.3, 3.1, 2.0 Hz, H-14a), 2.18 (1H, dtd, J=10.3, 6.0, 4.8, 1.7 Hz, H-2), 2.07 (2H, ddd, J=14.8, 8.7, 2.7 Hz, H-14b), 1.96 (1H, dt, J=11.6, 5.9 Hz, H-7), 1.92 (1H, dtd, J=11.6, 4.8, 2.5, 1.2 Hz, H-11b), 1.73 – 1.66 (3H, m, H-5a, H-10), 1.66 – 1.54 (3H, m, H-6a, H-3), 1.54 – 1.48 (1H, m, H-4a), 1.40 – 1.29 (1H, m, H-4b), 1.29 – 1.14 (2H, m, H-5b, H-6b), 0.89 (9H, s, 'Bu), 0.08 (3H, s, Si-Me), 0.06 (3H, s, Si-Me); ¹³C NMR (126 MHz, Acetone) δ 133.2 (C12), 125.5 (C13), 89.9 (C9), 79.5 (C1), 72.1 (C8), 42.8 (C7), 36.4 (C2), 33.6 (C10), 28.5 (C14), 27.9 (C6), 25.5 (C11), 25.3 ('Bu), 24.9 (C5), 23.5 (C3), 21.1 (4), 17.6 ('Bu), -4.4 (Si-Me), -5.2 (Si-Me); LC-MS (ESI⁺) m/z 359 [M+Na⁺], Rᵣ 2.00 min [method E]; HRMS [M+H⁺] calcd for C₂₀H₃₇O₂Si 337.2557 found 337.2549.

(4aS,5S,6R,12S,12aR,Z)-5,12-dimethyl-1,2,3,4,4a,5,6,7,8,11,12,12a-dodecahydro-5,12-epoxybenzo[10]annulen-6-ol 76

tert-Butyldimethyl([15S,2R,7S,8S,12Z]-15-oxatricyclo[6.6.1.0²⁷]pentadec-12-en-9- yl)oxy]silane 75 (42 mg, 0.113 mmol), was dissolved in 1M HCl:EtOH:Et₂O (5 mL, 0.05:1:1) and stirred
at RT for 3 h. The solution was then basified with sat. aqueous NaHCO₃ (dropwise to neutral pH) and extracted into Et₂O (3 × 10 mL). The combined organic layers were washed in brine (10 mL) and dried over MgSO₄. The solvents were removed in vacuo to yield 76 as white crystals (14 mg, 55%). mp (102.3-103.2 °C); [α]D +23.0 (c=0.1 CHCl₃); IR (film) 3014, 2923, 2851, 1449 cm⁻¹; ¹H NMR (500 MHz, CDCl₃) δ 5.73 (1H, dddd, J=2.5, 5.5, 11.0, 12.0, H-12), 5.59 (1H, ddd, J=6.5, 8.5, 11.0, H-13), 4.12 (1H, ddd, J=2.5, 5.5, 11.0, H-12), 2.67-2.62 (1H, m, H-14), 2.20-2.16 (1H, m, H-2), 2.05-1.97 (3H, m, H-7, Hb-11), 1.82-1.75 (2H, m, H-10), 1.54-1.49 (3H, m, CH₂), 1.36-1.15 (3H, m, CH₂); ¹³C NMR (125 MHz, CDCl₃) δ 133.6 (C12), 125.5 (C13), 89.7 (C8), 80.0 (C1), 71.6 (C9), 42.9 (C7), 36.7 (C2), 33.9 (C10), 28.8 (C14), 27.8 (CH₂), 25.4 (C11), 24.9 (CH₂), 23.9 (C3), 21.4 (CH₂); LC-MS (ESI⁺) m/z 245 [M+Na⁺], Rₜ 1.47 min [method E]; HRMS [M+H⁺] calcd for C₁₄H₂₂O₂ 223.1693 found 223.1695.

(((1R,2S,3S,5S,6R,7S)-5-Allyl-4-oxatricyclo[5.2.1.0².₆]dec-8-en-3-yl)-methanol 79

(1S,2R,5S,6S,7R)-5-((tert-Butyldiphenylsilanoxymethyl)-4-oxatricyclo[5.2.1.0².₆]dec-8-en-3-one 41a (292 mg, 0.699 mmol) was dissolved in anhydrous CH₂Cl₂ (1.9 mL) and cooled to -78 °C under N₂. DIBAL-H (1.0 M in toluene, 0.77 mL, 0.77 mmol) was added dropwise. The reaction was stirred at 78 °C for 100 min then quenched with EtOAc (10 mL). The solution was warmed to RT and a sat. aq. solution of Rochelles salt (6 mL) was added and the mixture was stirred for 3 h. The aqueous layer was separated and extracted with CH₂Cl₂ (3 x 20 mL). The organic layers were combined, dried over MgSO₄ and the solvent was removed in vacuo to yield 79a as a clear oil (286 mg, 98%). [α]D +2.8 (c=0.34 CH₂Cl₂); IR (film) 3423, 2931, 2858, 1428 cm⁻¹; ¹H NMR (500 MHz, CDCl₃) δ 7.73-7.67 (4H, m, Ph), 7.49-7.41 (6H, m, Ph), 6.19-6.17 (2H, m, H-8, H-9), 4.87 (1H, d, J=9.5, H-3), 3.99 (1H, d, J=9.5, OH), 3.76 (1H, dd, J=3.0, 11.0, Ha-1'), 3.67-3.65 (1H, m, H-5), 3.55 (1H, dd, J=3.0, 11.0, Hb-1'), 3.08-3.05 (1H, m, H-7), 2.92-2.89 (1H, m, H-1), 2.88-2.84 (2H, m, H-2, 6), 1.48 (1H, d, J=8.0, Ha-10), 1.35 (1H, d, J=8.0, Hb-10), 1.09 (9H, s, tBu); ¹³C NMR (125 MHz, CDCl₃) δ 135.8 (2 x Ph), 135.7 (2 x Ph), 135.6 (Ph), 134.0 (C9), 134.0 (C8), 132.5 (Ph), 132.4 (Ph), 132.0 (Ph), 129.9 (Ph), 129.4 (Ph), 127.9 (Ph), 127.7 (Ph), 101.3 (C3), 83.6 (C5), 67.6 (C1'), 58.1 (C1), 51.6 (C10), 48.3 (C6), 46.0 (C2), 45.2 (C7), 27.0 (tBu), 19.2 (Si-C); LC-MS (ESI⁺) m/z 443 [M+Na⁺], Rₜ 3.22 min [method C]; HRMS [M+Na⁺] calcd for C₂₆H₃₂O₃SiNa 443.2013; found 443.2002.
(1S,2R,5S,6S,7R)-5-tert-Butyldiphenylsilanoxymethyl)-4-oxatricyclo[5.2.1.02,6]dec-8-en-3-ol 79a (286 mg, 0.90 mmol) was dissolved in CH2Cl2 (3 mL) and cooled to -78 °C. BF3·OEt2 (0.26 mL, 2.04 mmol) was added by syringe and the solution stirred for 5 min. Allyltrimethylsilane (0.32 mL, 2.04 mmol) was added by syringe and the reaction then warmed to RT over 18 h. The reaction was then quenched with H2O (6 mL) and extracted into CH2Cl2 (3 x 6 mL). The combined organic layers were dried over MgSO4. The solvent was removed in vacuo to yield 79b as a clear oil (289 mg, 96%). [α]25D 67.7 (c=0.10 CH2Cl2); IR (film) 2930, 2857, 1471, 1427 cm\(^{-1}\); H NMR (500 MHz, CDCl3) \(\delta\) 7.72-7.68 (4H, m, Ph), 7.45-7.39 (6H, m, Ph), 6.22-6.19 (2H, m, H-8, H-9), 5.85 (1H, ddd, \(J=7.0, 7.0, 10.0, 17.0, H-2'\)), 5.09-5.02 (2H, m, H-3'), 3.72 (1H, dd, \(J=5.0, 10.0, H-1''\)), 3.59 (1H, dd, \(J=6.0, 10.0, H-1''\)), 3.54 (1H, dd, \(J=6.0, 6.0, 6.0, H-3\)), 3.48 (1H, ddd, \(J=6.5, 6.0, 6.5, H-5\)), 2.89 (1H, ddd, \(J=4.0, 6.0, 10.0, H-2\)), 2.85-2.82 (1H, m, H-1), 2.80-2.78 (1H, m, H-7), 2.66 (1H, ddd, \(J=4.0, 6.0, 10.5, H-6\)), 2.38-2.32 (1H, m, H-1'), 2.20-2.15 (1H, m, H-1'), 1.71 (1H, dt, \(J=2.0, 8.0, H-10\)), 1.59-1.56 (1H, m, H-10), 1.09 (9H, s, \(^t\)Bu); 13C NMR (125 MHz, CDCl3) \(\delta\) 136.7 (C9), 136.6 (C8), 135.7 (4 x Ph), 135.1 (C1'), 133.8 (Ph), 133.7 (Ph), 129.6 (Ph), 129.6 (Ph), 127.6 (4 x Ph), 116.6 (C3'), 82.1 (C3), 81.5 (C5), 66.9 (C1''), 55.0 (C2), 53.8 (C10), 53.1 (C6), 45.0 (C1), 44.9 (C7), 41.0 (C1'), 26.9 (\(^t\)Bu), 19.3 (Si-C).

((1R,2S,3S,5S,6R,7S)-5-Allyl-4-oxatricyclo[5.2.1.02,6]dec-8-en-3-ylmethyl but-3-enoate 80

((1R,2S,3S,5S,6R,7S)-5-Allyl-4-oxatricyclo[5.2.1.02,6]dec-8-en-3-yl)methanol 79 (50 mg, 0.243 mmol) was dissolved in CH2Cl2 (0.5 mL, 2.04 mmol) and cooled to 0 °C under N2. Allyltrimethylsilane (178 mg, 0.403 mmol) was dissolved in CH2Cl2 (2.2 mL). The solution was cooled to 0 °C under N2 and TBAF (1.20 mL, 1.20 mmol, 1.0 M in THF) was added by syringe and the solution stirred for 5 min. Allyltrimethylsilane (0.32 mL, 2.04 mmol) was added by syringe and the reaction then warmed to RT over 18 h. The reaction was then quenched with H2O (6 mL) and extracted into CH2Cl2 (3 x 6 mL). The combined organic layers were dried over MgSO4. The solvent was removed in vacuo to give the crude product. This was purified by column chromatography on silica gel (15% EtOAc:hexane) to yield 79 as a clear oil (49 mg, 59%). [α]25D -5.7 (c=0.51 CH2Cl2); IR (film) 3420, 2965, 1653, 1558 cm\(^{-1}\); H NMR (500 MHz, d5-Pyr) \(\delta\) 6.23-6.11 (2H, m, H-8, H-9), 6.11-6.02 (1H, m, OH), 5.91 (1H, ddt, \(J=7.0, 10.5, 17.0, H-2'\)), 5.12 (1H, dd, \(J=1.5, 17.0, Ha-3'\)), 5.09-5.01 (1H, m, H-b3'), 3.90 (1H, dd, \(J=5.0, 11.0, Ha-1''\)), 3.84 (1H, dd, \(J=6.0, 11.0, Hb-1''\)), 3.75 (1H, ddd, \(J=5.5, 6.0, 6.0, H-3\)), 3.57 (1H, ddd, \(J=6.5, 6.5, 6.5, H-5\)), 2.93 (1H, ddd, \(J=4.0, 6.5, 10.5, H-2\)), 2.80-2.75 (1H, m, H-1) 2.70-2.64 (1H, m, H-7), 2.64 (1H, ddd, \(J=4.0, 6.5, 10.0, H-6\)), 2.43 (1H, m, H-1'), 2.29 (1H, ddd, \(J=7.0, 7.0, 13.5, H-1'\)), 1.63 (1H, d, \(J=8.0, H-10\)), 1.48 (1H, d, \(J=8.0, H-10\)); 13C NMR (125 MHz, CDCl3) \(\delta\) 137.6 (C8 or C9), 137.4 (C8 or C9), 136.4 (C2'), 117.1 (C3'), 83.9 (C3), 81.9 (C5), 66.1 (C1''), 56.0 (C2), 54.7 (C10), 53.5 (C6), 45.6 (C1 or C7), 45.5 (C1 or C7), 41.7 (C2'); LC-MS [ESI+] m/z 229 [M+Na]+, R\(t\) 2.12 min [method D]; HRMS [M+H]+ calcd for C13H19O2 207.1380; found 207.1377.
mL). Trans-crotonyl chloride (30 µL, 0.316 mmol) and triethylamine (105 µL, 0.725 mmol) were added and the reaction mixture was stirred at RT for 18 h. The reaction mixture was diluted with CH₂Cl₂ (10 mL) and washed with H₂O (10 mL) and brine (10 mL). The aqueous layers were combined and extracted with CH₂Cl₂ (10 mL x 2). The combined organic layers were dried with MgSO₄ and the solvents removed in vacuo. The crude reaction mixture was purified by column chromatography on silica gel (20% EtOAc:hexane) to yield 80 as a clear oil (44 mg, 66%). [α]²⁰° -19.0 (c=1.0 CHCl₃); IR (film) 3076, 2968, 1752 cm⁻¹; ¹H NMR (500 MHz, CDCl₃) δ 6.23-6.19 (2H, m, H-9, H-8), 5.93 (1H, tdd, J=6.5, 10.0, 17.0, H-5”), 5.78 (1H, tdd, J= 7.0, 10.0, 17.0, H-2’), 5.19-5.14 (2H, m, H-6”), 5.11-5.03 (2H, m, H-3’), 4.15 (1H, dd, J=4.0, 11.0, HA-1’”), 4.02 (1H, dd, J=7.0, 11.0, HB-1’”), 3.64 (1H, dd, J=6.0, 11.0, H-3), 3.51 (1H, dd, J=6.0, 12.5, H-5), 3.13 (2H, d, J=7.0, H-4”), 2.84-2.77 (2H, m, H-1, H-7), 2.76-2.67 (2H, m, H-2, H-6), 2.41-2.34 (1H, m, HA-1’), 2.24-2.18 (1H, m, HB-1’), 1.71 (1H, d, J=8.0, HA-10), 1.56 (1H, d, J=8.0, HB-10); ¹³C NMR (125 MHz, CDCl₃) δ 171.4 (C3”), 136.8 (C8 or C9), 136.3 (C8 or C9), 134.7 (C2”), 130.2 (C5”), 118.6 (C6”), 116.9 (C3”), 81.8 (C5), 79.2 (C3), 67.1 (C1’”), 54.9 (C2 or C6), 53.7 (C10), 52.9 (C2 or C6), 44.9 (C1 or C7), 44.5 (C1 or C7), 40.8 (C1’), 38.7 (C4’); LC-MS (ESI⁺) m/z 297 [M+Na⁺], Rᵣ 2.37 min [method D]; HRMS [M+Na⁺] calcd for C₁₂H₁₁O₃ H 275.1643, found 275.1642.

(1R,2S,3S,5S,6R,7S)-5-Allyl-4-oxatricyclo[5.2.1.0²,6]dec-8-en-3-ylmethyl pent-4-enoate 81

((1R,2S,3S,5S,6R,7S)-5-Allyl-4-oxatricyclo[5.2.1.0²,6]dec-8-en-3-yl)-methanol 79 (50 mg, 0.243 mmol) was dissolved in pyridine (1.2 mL). Pent-4-enoyl chloride (35 µL, 0.316 mmol) was added and the reaction mixture was stirred at RT for 18 h. The reaction mixture was diluted with CH₂Cl₂ (10 mL) and washed with H₂O (10 mL) and brine (10 mL). The aqueous layers were combined and extracted with CH₂Cl₂ (10 mL x 2). The combined organic layers were dried with MgSO₄ and the solvents removed in vacuo. The crude reaction mixture was purified by column chromatography on silica gel (20% EtOAc:hexane) to yield 81 as a clear oil (49 mg, 70%). [α]²⁰° +15.5 (c=2.0, CHCl₃); IR (film) 3075, 2965, 1741 cm⁻¹; ¹H NMR (500 MHz, CDCl₃) δ 6.22-6.21 (2H, m, H-9, H-8), 5.88-5.74 (2H, m, H-2’, H-6”), 5.12-4.99 (4H, m, H-3’, H-7”), 4.15 (1H, dd, J=4.5, 11.5, HA-1’”), 4.02 (1H, dd, J=6.5, 11.5, HB-1’”), 3.64 (1H, ddd, J=6.5, 6.5, 4.5, H-3), 3.15 (1H, ddd, J=5.5, 5.5, 7.5, H-5), 2.83-2.79 (2H, m, H-1, H-7), 2.76-2.69 (2H, m, H-2, H-6), 2.47-2.35 (5H, m, H-4’”, H-5’”, HA-1’), 2.20 (1H, ddd, J=7.5, 7.5, 7.5).
14.5, HB-1’), 1.71 (1H, ddd, J=1.5, 1.5, 8.5, HA-10), 1.57 (1H, br d, J=8.5, HB-10); $^{13}$C NMR (125 MHz, CDCl$_3$) δ 172.9 (C3’’), 136.9 (C8 or C9), 136.7 (C2’ or C6’’), 136.4 (C8 or C9), 134.6 (C2’ or C6’’), 117.0 (C3’ or C7’’), 115.5 (C3’ or C7’’), 81.8 (C5), 79.3 (C3), 66.9 (C1’’), 54.9 (C2 or C6), 53.9 (C10), 52.7 (C2 or C6), 44.9 (C1 or C7), 44.5 (C1 or C7), 40.8 (C1’), 33.5 (C4’’ or C5’’), 28.8 (C4’’ or C5’’); LC-MS (ESI+) m/z 311 [M+Na+] , Rt 2.43 min [method D]; HRMS [M+H$^+$] calcd for C$_{18}$H$_{24}$O$_3$ H 289.1798 found 289.1798.

((1R,2S,3S,5S,6R,7S)-5-Allyl-4-oxatricyclo[5.2.1.0$^{2,6}$]dec-8-en-3-yl)methanol 79 (50 mg, 0.243 mmol) was dissolved in pyridine (1.2 mL). Hex-5-enoyl chloride (42 mg, 0.317 mmol) was added and the reaction mixture was stirred at RT for 18 h. The reaction mixture was diluted with CH$_2$Cl$_2$ (10 mL) and washed with H$_2$O (10 mL) and brine (10 mL). The aqueous layers were combined and extracted with CH$_2$Cl$_2$ (10 mL x 2). The combined organic layers were dried over MgSO$_4$ and the solvents removed in vacuo. The crude reaction mixture was purified by column chromatography on silica gel (20% EtOAc:hexane) to yield 82 as a clear oil (33 mg, 46%). [α]$^{25}_D$ +19.6 (c=1.0 CHCl$_3$); IR (film) 3075, 2965, 1738 cm$^{-1}$; $^1$H NMR (500 MHz, CDCl$_3$) δ 6.25-6.22 (2H, m, H-9, H-8), 5.83-5.74 (2H, m, H-2’, H-7’’), 5.13-5.05 (2H, m, H-3’, 5.06-4.98 (2H, m, H-8’’), 4.18 (1H, dd, J=4.5, 11.0, Ha-1’’), 4.02 (1H, dd, J=7.0, 11.0, Hb-1’’), 3.63 (1H, ddd, J=4.5, 6.0, 6.5, H-3), 3.51 (1H, ddd, J=6.0, 7.0, 7.5, H-5), 2.84-2.79 (2H, m, H-1, H-7), 2.77-2.69 (2H, m, H-2, H-6), 2.42-2.35 (1H, m, H-1’), 2.38 (2H, t, J=7.5, H-4’’), 2.26-2.19 (2H, m, H-1’’), 2.14-2.08 (1H, m, H-5’’), 1.78-112 (3H, m, H-6’’, Ha-10), 1.61-1.56 (1H, m, Hb-10), $^{13}$C NMR (125 MHz, CDCl$_3$) δ 173.5 (C3’’), 137.6 (C7’’), 136.9 (C8 or C9), 136.3 (C8 or C9), 134.6 (C2’), 116.2 (C3’), 115.3 (C8’’), 81.7 (C5), 79.3 (C3), 66.8 (C1’’), 54.9 (C2 or C6), 53.8 (C10), 52.7 (C2 or C6), 44.9 (C1 or C7), 44.5 (C1 or C7), 40.8 (C1’), 33.7 (C4’’), 33.0 (C5’’), 24.0 (C6’’); LC-MS (ESI+) m/z 325 [M+Na$^+$], Rt 2.48 min [method D]; HRMS [M+H$^+$] calcd for C$_{19}$H$_{27}$O$_3$ 303.1955 found 303.1940.

[(1S,3R,3aR,7aS)-3-(2-methyl-3-oxobutan-2-yl)-octahydro-2-benzofuran-1-yl]methyl acetate 89
3-[(1R,3S,3aS,7aR)-3-(Hydroxymethyl)octahydro-2-benzofuran-1-yl]-3-methylbutan-2-one 46 (67 mg, 0.279) was dissolved in CH$_2$Cl$_2$ (3 mL) and Et$_3$N (80 µL, 0.558 mmol) was added. 2-Bromoaacetyl bromide (260 µL, 0.558 mmol) was added and the solution was stirred at RT for 5 h. The solution was diluted with CH$_2$Cl$_2$ (20 mL), washed with H$_2$O (10 mL), brine (10 mL), and then the aqueous layers where extracted with CH$_2$Cl$_2$ (2 x10 mL). The combined organic layers were dried with MgSO$_4$. The solvent was removed in vacuo and the crude residue purified by column chromatography on silica gel (33% EtOAc:hexane) to yield the product as a pale brown oil (67 mg, 67%). This compound was unstable so limited characterisation was possible. $^1$H NMR (500 MHz, CDCl$_3$) δ 4.29 (1H, dd, J=3.0, 12.0, Ha-1’), 4.16 (1H, dd, J=6.0, 12.0, Hb-1’), 4.03 (1H, ddd, J=3.0, 6.0, 9.0, H-3), 3.88 (2H, s, H-4’), 3.88-3.80 (1H, m, H-1), 2.18 (3H, s, H-1’’), 2.07-2.01 (1H, m, H-7a), 1.95-1.88 (1H, m, H-3a), 1.75-1.68 (1H, m, CH$_2$), 1.68-1.57 (3H, m, CH$_2$), 1.45-1.23 (4H, m, CH$_2$), 1.13 (3H, s, Me), 1.09 (3H, s, Me); LC-MS (ESI$^+$) m/z 361 [M+H$^+$], R$_t$ 1.50 min [method E]; HRMS [M+Na$^+$] calcd for C$_{16}$H$_{25}$BrO$_4$Na 361.1009 found 361.1013.

[(1S,3R,3aR,7aS)-3-(2-Methyl-3-oxobutan-2-yl)-octahydro-2-benzofuran-1-yl]methyl 2-bromoaacetate 89a (67 mg, 0.186 mmol) was dissolved in THF (37 mL) and SmI$_2$ (0.1 M in THF) was added dropwise (~9 mL) until the colour change of the SmI$_2$ from blue to yellow on addition slowed and the reaction mixture remained green for ~10 seconds before returning to a pale yellow. The solution was then diluted with Et$_2$O (20 mL) and washed with H$_2$O (20 mL) and brine (20 mL). The organic layer was dried with MgSO$_4$. The crude yellow oil was purified by column chromatography on silica gel (5% MeOH:CH$_2$Cl$_2$) to yield 89 as a clear oil (26 mg, 49%). [α]$^{24.3}_D$ +25.4 (c=1.0 CHCl$_3$); IR (film) 2929, 2858, 1739, 1701 cm$^{-1}$; $^1$H NMR (500 MHz, CDCl$_3$) δ 4.25-4.19 (1H, m, Ha-1’), 4.06-3.97 (2H, m, Hb-1’, H-3), 3.86 (1H, d, J=3.5, 1H-1), 2.17 (3H, s, H-4’’), 2.08 (3H, s, H-4’), 2.06-1.98 (1H, m, H-7a), 1.83-1.76 (1H, m, H-3a), 1.75-1.57 (4H, m, CH$_2$), 1.46-1.22 (4H, m, CH$_2$), 1.12 (3H, s, Me), 1.09 (3H, s, Me); $^{13}$C NMR (125 MHz, CDCl$_3$) δ 213.2 (C3”), 171.1 (C3’), 89.7 (C1), 78.0 (C3), 65.7 (C1’), 51.6 (C2”), 39.4 (C3a or C7a), 39.4 (C3a or C7a), 29.9 (CH$_2$), 27.0 (C4’’), 24.2 (CH$_2$), 24.1 (CH$_2$), 22.1 (CH$_2$), 21.0 (C4” or Me), 21.0 (C4” or Me), 20.6 (C4” or Me); LC-MS (ESI$^+$) m/z 305 [M+Na$^+$], R$_t$ 1.48 min [method E]; HRMS [M+H$^+$] calcd for C$_{16}$H$_{27}$O$_4$ 283.1904 found 283.1914; Found: C, 66.09; H, 8.81%; C$_{16}$H$_{26}$O$_4$ requires: C, 66.12; H, 8.72%.
Assay methods

SRB assay

Cells were seeded in 100μl medium into 96-well plates. After 36 hours, serial doubling dilutions of drug (or vehicle) were added to give the required dose range in sextuplicate across the plate. Cells were incubated for a further 96 hours. The medium was then removed and cells were fixed by adding 50μl of 10% (w/v) trichloroacetic acid (TCA) for one hour at room temperature. The plates were gently washed by immersion in tap water three times then air dried. 50μl of 0.4% (w/v) SRB in 1% (v/v) acetic acid was added to each well for one hour. Plates were then washed three times with 1% acetic acid and air dried. SRB was solubilised with 100ul/well 10mM Tris pH10.5. Absorbance at 570nm was measured using a SPECTRAmax 340PC plate reader.

Migration assay

Cells in standard tissue culture flasks were fluorescently labelled by incubation with 1umol/L CellTracker Green 5-chloromethylfluorescein diacetate (Invitrogen, Paisley) concomitant with serum starvation for two hours. Following trypsinisation cells were counted and added to the upper wells of 8um pore FluoroblokTM membrane inserts in 24-well companion plates (BD Biosciences, Franklin Lakes, NJ). The lower chambers were filled with 800μL medium containing 5% heat-inactivated FCS (to measure chemotaxis) or serum-free medium (to measure unstimulated random motility). The assay plates were incubated in a humidified atmosphere at 37°C in 5% CO2 in air for 16 hours. Cells which successfully migrated to the lower surface of the filter were visualised using an inverted fluorescence microscope.
PCA methodology

Principal Components Analysis (PCA) was conducted using SIMCA-P+\(^4\), and the scatter plot was created using Spotfire\(^5\). The descriptors used for the calculation of the PCA models are given in Table S1.

Table S1. Molecular descriptors calculated for the generation of the PCA model.

| Descriptor ID          | Descriptor Definition                                      |
|-----------------------|-----------------------------------------------------------|
| Molecular Weight      | Molecular weight                                          |
| No. Bonds             | Number of bonds                                           |
| No. Rings             | Number of rings                                           |
| AlogP                 | Calculated octanol/water partition coefficient             |
| No. Rotatable Bonds   | Number of rotatable bonds                                 |
| No. H acceptors       | Number of hydrogen-bond acceptors                          |
| No. H donors          | Number of hydrogen-bond donors                            |
| O count               | Number of oxygen atoms                                    |
| H count               | Number of hydrogen atoms                                  |
| No. Stereocentres     | Number of stereocentres                                   |
| N count               | Number of nitrogen atoms                                  |
| No. Aromatic Rings    | Number of aromatic rings                                  |
| No. Aromatic Bonds    | Number of aromatic bonds                                  |

The first two principal components of the PCA model explain 69% of the variance in the data which indicates that visualisation in a two-dimensional scatterplot is reasonable for interpretation of the chemistry spaces covered by the libraries.
Figure S1. The loading scores of the Principal Components Analysis.

The loadings plot is provided in Figure S1 and can assist in interpreting the PCA scores plot of Figure 5 in the main paper. The loadings plot illustrates those molecular descriptors that are most important for explaining the variance of the molecules in those regions of the scores plot when overlaid. Descriptors that lie proximate to each other on the loadings plot are correlated, such as aromatic rings and bonds in quadrant III. Furthermore, the magnitude of deviation from the origin indicates the importance of each descriptor in that region of the plot, as seen in those molecules in quadrant III being more nitrogen-rich in their composition. Therefore, it can be readily observed that the screening collection is enriched for nitrogen-containing compounds and aromaticity, as opposed to the cembranoid-like and cembranoid libraries.
Crystallography data for compound 26

Formula: C_{15}H_{22}O_{3}; M_r = 250.32; crystal dimensions: 0.62 x 0.22 x 0.06 mm; crystal system: orthorhombic; space group: P2_12_12_1; a = 5.25570(10) Å, b = 10.3241(4) Å, c = 24.6007(9) Å, α = 90°, β = 90°, γ = 90°; V = 1334.84(8) Å^3; Z = 4; ρ_{calcd} = 1.246 Mg/m^3; μ = 0.085 mm^{-1}; Mo Kα radiation, λ = 0.71073 Å; T = 120(2) K; 2Θ_{max} = 54.9°; 10722/3007 measured/independent reflections; R_{int}: 0.0442; R = 0.0418, wR = 0.0935; Δρ_{max} = 0.206 eÅ^{-3}, Δρ_{min} = −0.208 eÅ^{-3}. Colourless blade crystals gave good diffraction. The data were collected on a Nonius-Kappa CCD area detector mounted at the window of an FR591 rotating anode generator with a Mo anode and equipped with an Oxford Cryosystems cryostream device. Nonius COLLECT^6 was used to record images and HKL (Denzo and Scalepack)^7 was used for data integration. The structure was solved by direct methods using SHELXT^8 and refined on F_o^2 by full-matrix least squares refinement using SHELXL. All non-hydrogen atoms were refined with anisotropic displacement parameters. Hydrogen atoms were added at calculated positions and refined using a riding model with isotropic displacement parameters based on the equivalent isotropic displacement parameter (Ueq) of the parent atom. The structure was deposited on the Cambridge Structural Database with the deposition number CCDC 1010197.
Crystallography data for compound 40

Formula: C₁₈H₂₄O₃; Mr = 288.37; crystal dimensions: 0.3 x 0.2 x 0.19 mm; crystal system: monoclinic; space group: P2₁; a = 10.801(3) Å, b = 11.564(3) Å, c = 12.083(4) Å, α = 90°, β = 90.15(3)°, γ = 90°; V = 1509.2(8) Å³; Z = 4; ρcalcd = 1.269 Mg/m³; μ = 0.085 mm⁻¹; Mo Kα radiation, λ = 0.71073 Å; T = 120(2) K; 2θmax = 50.2°; 9752/9752 measured/independent reflections; Rint: N/A; R = 0.0899, wR = 0.2274; Δρmax = 0.348 eÅ⁻³, Δρmin = −0.308 eÅ⁻³.

Colourless block crystals were poorly diffracting with no significant data beyond 0.84Å resolution and also non-merohedrally twinned, with a twinning ratio of 0.537:0.463. The twinned components were related by 179.8° rotation about reciprocal lattice vector 001. The data were collected on a Nonius-Kappa CCD area detector mounted at the window of an FR591 rotating anode generator with a Mo anode and equipped with an Oxford Cryosystems cryostream device. Nonius COLLECT⁶ was used to record images and RigakuOD CrysAlisPro¹⁰ was used for data integration. The structure was solved by direct methods using SHELXT⁸ and refined on F² by full-matrix least squares refinement using SHELXL.⁹ All non-hydrogen atoms were refined with anisotropic displacement parameters. Hydrogen atoms were added at calculated positions and refined using a riding model with isotropic displacement parameters based on the equivalent isotropic displacement parameter (Ueq) of the parent atom. The structure was deposited on the Cambridge Structural Database with the deposition number CCDC 1011320.
Crystallography data for compound 42

Formula: C$_{17}$H$_{24}$O$_3$; $M_r$ = 276.36; crystal dimensions: 0.4 x 0.2 x 0.03 mm; crystal system: orthorhombic; space group: $P2_12_12_1$; $a = 5.7992(6)$ Å, $b = 12.0419(10)$ Å, $c = 20.795(2)$ Å, $\alpha = 90^{\circ}$, $\beta = 90^{\circ}$, $\gamma = 90^{\circ}$; $V = 1452.2(2)$ Å$^3$; $Z = 4$; $\rho_{calc} = 1.264$ Mg/m$^3$; $\mu = 0.085$ mm$^{-1}$; Mo K$\alpha$ radiation, $\lambda = 0.71073$ Å; $T = 120(2)$ K; $2\Theta_{max} = 54.9^{\circ}$; 17321/3252 measured/independent reflections; $R_{int}: 0.1130$; $R = 0.1002$, $wR = 0.2476$; $\Delta \rho_{max} = 0.534$ eÅ$^{-3}$, $\Delta \rho_{min} = -0.400$ eÅ$^{-3}$. Colourless plate crystals were poorly diffracting. The data were collected on a Nonius-Kappa CCD area detector mounted at the window of an FR591 rotating anode generator with a Mo anode and equipped with an Oxford Cryosystems cryostream device. Nonius COLLECT$^6$ was used to record images and RigakuOD CrysAlisPro$^10$ was used for data integration. The structure was solved by direct methods using SHELXT$^8$ and refined on $F_o^2$ by full-matrix least squares refinement using SHELXL.$^9$ All non-hydrogen atoms were refined with anisotropic displacement parameters. Hydrogen atoms were added at calculated positions and refined using a riding model with isotropic displacement parameters based on the equivalent isotropic displacement parameter (Ueq) of the parent atom. The structure was deposited on the Cambridge Structural Database with the deposition number CCDC 1435146.
Crystallography data for compound 69

Formula: C₁₅H₂₄O₄; Mr = 268.34; crystal dimensions: 0.45 x 0.4 x 0.38 mm; crystal system: orthorhombic; space group: P2₁2₁2₁; a = 9.16700(10) Å, b = 10.5275(2) Å, c = 14.3960(3) Å, α = 90°, β = 90°, γ = 90°; V = 1389.29(4) Å³; Z = 4; ρ_calc = 1.283 Mg/m³; μ = 0.091 mm⁻¹; Mo Kα radiation, λ = 0.71073 Å; T = 120(2) K; 2θ_max = 55.4°; 14418/3181 measured/independent reflections; R_int: 0.0361; R = 0.0324, wR = 0.0756; Δρ_max = 0.178 eÅ⁻³, Δρ_min = −0.174 eÅ⁻³.

Colourless block crystals diffracted well. The data were collected on a Nonius-Kappa CCD area detector mounted at the window of an FR591 rotating anode generator with a Mo anode and equipped with an Oxford Cryosystems cryostream device. Nonius COLLECT⁶ was used to record images and HKL (Denzo and Scalepack)⁷ was used for data integration. The structure was solved by direct methods using SHELXS¹¹ and refined on F₂ by full-matrix least squares refinement using SHELXL.⁹ All non-hydrogen atoms were refined with anisotropic displacement parameters. Hydrogen atoms were added at calculated positions and refined using a riding model with isotropic displacement parameters based on the equivalent isotropic displacement parameter (Ueq) of the parent atom. The structure was deposited on the Cambridge Structural Database with the deposition number CCDC 1435148.
Figure S2: Compounds screened at the NCI for cytotoxicity in a 60 cell line panel
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(S)-5-((tert-Butyldiphenylsilyloxy)methyl)furan-2-(5H)one 8
(S)-5-((tert-Butyldiphenylsilyloxy)methyl)furan-2-(5H)one 8
(3S)-3-((tert-Butyldiphenylsilyloxy)methyl)-3a,4,7,7a-tetrahydroisobenzofuran-1-(3H)-one 10
(3S)-3-((tert-Butyldiphenylsilyloxy)methyl)-3a,4,7,7a-tetrahydroisobenzofuran-1-(3H)-one 10
(3S,3aS,7aR)-3-((tert-Butyldiphenylsilyloxy)methyl)-1,3,3a,4,7,7a-hexahydroisobenzofuran-1-ol 11
(3S,3aS,7aR)-3-((tert-Butyldiphenylsilyloxy)methyl)-1,3,3a,4,7,7a-hexahydroisobenzofuran-1-ol 11
([(15,3S,3aR,7aS)-3-Allyl-1,3,3a,4,7,7a-hexahydroisobenzofuran-1-yl)methoxy](tert-butyl)diphenylsilane 12
(((1S,3S,3aR,7aS)-3- Allyl-1,3,3a,4,7,7a-hexahydroisobenzofuran-1-yl)methoxy)(tert-butyl)diphenylsilane 12
\([(1S,3S,3aR,7aS)-3\text{-}\text{Allyl}-1,3,3a,4,7,7a\text{-}\text{hexahydroisobenzofuran-1-yl})\text{methanol}\ 14\]
((1S,3S,3aR,7aS)-3-Allyl-1,3,3a,4,7,7a-hexahydroisobenzofuran-1-yl)methanol 14
But-2’-enoic acid (1S, 3S, 3aR, 7aS)-allyl-1, 3, 3a, 4, 7, 7a-hexahydro-isobenzofuran-8-ylmethyl ester 15
But-2′-enoic acid (1S, 3S, 3aR, 7aS)-allyl-1, 3, 3a, 4, 7, 7a-hexahydro-isobenzofuran-8-ylmethyl ester 15
((1S,3S,3aR,7aS)-3-Allyl-1,3,3a,4,7a-hexahydroisobenzofuran-1-yl)methyl but-3'-enoate 16
((1S,3S,3aR,7aS)-3-Allyl-1,3,3a,4,7,7a-hexahydroisobenzofuran-1-yl)methyl but-3'-enoate 16
Pent-4’enoic acid (1S, 3S, 3aR, 7aS)-allyl-1, 3, 3a, 4, 7, 7a-hexahydro-isobenzofuran-8-ylmethyl ester 17
Pent-4’enoic acid (1S, 3S, 3aR, 7aS)-allyl-1, 3, 3a, 4, 7, 7a-hexahydro-isobenzofuran-8-ylmethyl ester 17
((1S,3S,3aR,7aS)-3-Allyl-1,3,3a,4,7,7a-hexahydroisobenzofuran-1-yl)methyl hex-5-enoate 18
\( (1S,3S,3aR,7aS)-3\text{-Allyl}-1,3,3a,4,7,7a\text{-hexahydroisobenzofuran-1-yl})\text{methyl hex-5-enoate} \ 18 \)
(Z)-(15, 9S, 10R, 15S)-3, 16-Dioxa-tricyclo[7.6.1.0^{10,15}]hexadeca-6,12-diene-4-one 20
(Z)-(1S, 9S, 10R, 15S)-3, 16-Dioxa-tricyclo[7.6.1.0^{10,15}]hexadeca-6,12-diene-4-one 20
(Z)-(15,10S,11R,16S)-3,17-Dioxa-tricyclo[8.6.1.0\(^{11,16}\)]heptadeca-7,13-diene-4-one 21
(Z)-(15,10S,11R,16S)-3,17-Dioxa-tricyclo[8.6.1.0^{11,16}]heptadeca-7,13-diene-4-one 21 acetone contaminant
(Z)-(15,115,12R,17S)-3,18-Dioxatricyclo[9.6.1.0^{12,17}]octadeca-8,14-dien-4-one 22
(Z)-(15S,11S,12R,17S)-3,18-Dioxatricyclo[9.6.1.0^{12,17}]octadeca-8,14-dien-4-one 22
(3S,3aS,7aR)-3-((tert-Butyldiphenylsilyloxy)methyl)hexahydroisobenzofuran-1(3H)-one 23a
(3S,3aS,7aR)-3-((tert-Butyldiphenylsilyloxy)methyl)hexahydroisobenzofuran-1(3H)-one 23a
(3S,3aS,7aR)-3-((tert-Butyldiphenylsilyloxy)methyl)octahydroisobenzofuran-1-ol 23
(3S,3aS,7aR)-3-((tert-Butyldiphenylsilyloxy)methyl)octahydroisobenzofuran-1-ol 23
((1S,3S,3aR,7aS)-3-allyloctahydro-isobenzofuran-1-ylmethoxy)-tert-butyldiphenylsilane 24
((1S,3S,3aR,7aS)-3-Allyl-octahydro-isobenzofuran-1-ylmethoxy)-tert-butyldiphenylsilane 24
\((1S,3S,3aR,7aS)-3\text{-Allyl-octahydro-isobenzofuran-1-yl})\text{-methanol 25} \)
((1S,3S,3aR,7aS)-3-allyl-octahydro-isobenzofuran-1-yl)-methanol 25
\((1S,3S,3aR,7aS)-3\text{-allyloctahydroisobenzofuran-1-yl})\text{methyl pent-4-enoate 77}\)
((1S,3S,3aR,7aS)-3-allyloctahydroisobenzofuran-1-yl)methyl pent-4-enoate 77
(Z)-(1S,10S,11R,16S)-3,17-Dioxatricyclo[8.6.1.0^{11,16}]heptadeca-7-en-4-one 26
(Z)-(15,10S,11R,16S)-3,17-Dioxatricyclo[8.6.1.0^{11,16}]heptadeca-7-en-4-one 26
(E)-(1S,10S,11R,16S)-3,17-Dioxatricyclo[8.6.1.0^{11,16}]heptadeca-7-en-4-one 27
(E)-(15S,10S,11R,16S)-3,17-Dioxatricyclo[8.6.1.0^{11,16}]heptadeca-7-en-4-one 27
((1S,3S,3aR,7aS)-3-allyloctahydroisobenzofuran-1-yl)methyl hex-5-enoate 78
((1S,3S,3aR,7aS)-3-allyloctahydroisobenzofuran-1-yl)methyl hex-5-enoate 78
(Z)-{1S,11S,12R,17S}-3,18-Dioxatricyclo[9.6.1.0^{12,17}]octadec-8-en-4-one 28
(Z)-(15,15S,12R,17S)-3,18-Dioxatricyclo[9.6.1.0^{12,17}]octadec-8-en-4-one 28
(1S,3S,3aS,7aR)-1-allyl-3-(allyloxymethyl)-1,3,3a,4,7,7a-hexahydroisobenzofuran 29
(1S,3S,3aS,7aR)-1- Allyl 3- (allyloxymethyl) -1,3,3a,4,7,7a-hexahydroisobenzofuran \textbf{29}
(3aR,4aR,7S,7aS,8aS)-7-(tert-Butyldiphenylsilyloxy)methyl)-2,2-dimethyl-hexahydro-furo[3',4':4,5]benzo[1,2-d][1,3]dioxol-5-one 31

31

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(3aR,4aR,7S,7aS,8aS)-7-(tert-Butyldiphenylsilyloxymethyl)-2,2-dimethyl-hexahydro-furo[3′,4′:4,5]benzo[1,2-d][1,3]dioxol-5-one 31
(3aR,4aR,7S,7aS,8aS)-7-(tert-Butyldiphenylsilanyloxymethyl)-2,2-dimethyl-hexahydro-furo[3',4':4,5]benzo[1,2-d][1,3]dioxol-5-one 31
(3aR,4aR,7S,7aS,8aS)-7-(tert-Butyldiphenylsilanyloxymethyl)-2,2-dimethyl-hexahydro-furo[3',4':4,5]benzo[1,2-d][1,3]dioxol-5-one
(3aR,4aR,7S,7aS,8aS)-7-(tert-Butyldiphenylsilanyloxy)methyl)-2,2-dimethyloctahydrofuro [3',4':4,5]benzo[1,2-d][1,3]dioxol-5-ol 32
(3aR,4aR,7S,7aS,8aS)-7-\(\text{tert-Butyl diphenylsilyl oxymethyl}\)-2,2-dimethyloctahydrofuro [3′,4′:4,5]benzo[1,2-d][1,3]dioxol-5-ol 32
(((3aS,4aS,5S,7S,7aR,8aR)-7-allyl-2,2-dimethyloctahydroisobenzofuro[5,6-d][1,3]dioxol-5-yl)methoxy)(tert-butyl)diphenylsilane 33a
((3aS,4aS,5S,7S,7aR,8aR)-7-allyl-2,2-dimethyl-octahydroisobenzofuro[5,6-d][1,3]dioxol-5-yl) methoxy)(tert-butyl)diphenylsilane 33a
(3aS,4aS,5S,7S,7aR,8aR)-7-allyl-2,2-dimethyloctahydroisobenzofuro[5,6-d][1,3]dioxol-5-yl)methanol 33
((3aS,4aS,5S,7S,7aR,8aR)-7-allyl-2,2-dimethyloctahydroisobenzofuro[5,6-d][1,3]dioxol-5-yl)methanol 33
(3aS,4aS,5S,7S,7aR,8aR)-7-allyl-2,2-dimethyloctahydroisobenzofuro[5,6-d][1,3]dioxol-5-yl)methyl hex-5-enoate 34
((3aS,4aS,5S,7S,7aR,8aR)-7-allyl-2,2-dimethyl-1,3-dioxol[5,6-d][1,3]dioxol-5-yl)methyl hex-5-enoate 34
(1S,2R,4R,8S,10S,11S,18E)-6,6-dimethyl-5,7,13,21-tetraoxatetracyclo[9.9.1.0^{2,10}.0^{4,8}]henicos-18-en-14-one 35
(1S,2R,4R,8S,10S,11S,18E)-6,6-dimethyl-5,7,13,21-tetraoxatetracyclo[9.9.1.0².0⁴.⁸]henicos-18-en-14-one 35
(E)-(1S,11S,12R,14R,15S,17S)-14,15-Dihydroxy-3,18-dioxa-tricyclo[9.6.1.012,17]octadec-8-en-4-one 36
(E)-(1S,11S,12R,14R,15S,17S)-14,15-Dihydroxy-3,18-dioxa-tricyclo[9.6.1.012,17]octadec-8-en-4-one 36
(3S,3aS,7aR)-3-(((tert-butyldiphenylsilyl)oxy)methyl)-5-methyl-3a,4,7,7a-tetrahydroadenofuran-1(3H)-one 37
(3S,3aS,7aR)-3-(((tert-butyldiphenylsilyl)oxy)methyl)-5-methyl-3a,4,7,7a-tetrahydroisobenzofuran-1(3H)-one 37
(3S, 3aS, 5R, 6R, 7aR)-3-(tert-Butyldiphenylsilyloxy)methyl)-6-hydroxy-5-methylhexahydroisobenzofuran-1-one 38
(3S, 3aS, 5R, 6R, 7aR)-3-(tert-Butyldiphenylsilyloxymethyl)-6-hydroxy-5-methylhexahydroisobenzofuran-1-one \textbf{38}
(3S,3aS,5R,6R,7aR)-3-((tert-butyldiphenylsilyloxy)methyl)-5-methyloctahydroisobenzofuran-1,6-diol 39a
(3S,3aS,5R,6R,7aR)-3-((tert-butyldiphenylsilyloxy)methyl)-5-methyloctahydroisobenzofuran-1,6-diol 39a
(1S,3S,3aR,5R,6R,7aS)-3-allyl-1-((tert-butyldiphenylsilyloxy)methyl)-6-methyloctahydroisobenzofuran-5-ol 39b
(1S,3S,3aR,5R,6R,7aS)-3-allyl-1-((tert-butyldiphenylsilyloxy)methyl)-6-methyloctahydroisobenzofuran-5-ol 39b
(1S,3S,3aR,5R,6R,7aS)-3-allyl-1-((tert-butyldiphenylsilyloxy)methyl)-6-methyloctahydroisobenzofuran-5-ol 39b
(1S,3S,3aR,5R,6R,7aS)-3-allyl-1-((tert-butyldiphenylsilyloxy)methyl)-6-methyloctahydroisobenzofuran-5-ol 39b
(1S,3S,3aR,5R,6R,7aS)-3-allyl-1-(hydroxymethyl)-6-methyloctahydroisobenzofuran-5-ol 86
(1S,3S,3aR,5R,6R,7aS)-3-allyl-1-(hydroxymethyl)-6-methyloctahydroisobenzofuran-5-ol 86
((1S,3S,3aR,5R,6R,7aS)-3-Allyl-5-hydroxy-6-methyloctahydroisobenzofuran-1-yl)methyl hex-5-enoate 87
((1S,3S,3aR,5R,6R,7aS)-3-allyl-5-hydroxy-6-methyloctahydroisobenzofuran-1-yl)methyl hex-5-enoate 87
\((1S,8E,11S,12R,14R,15R,17S)\)-14-hydroxy-15-methyl-3,18-dioxatricyclo[9.6.1.0^{12,17}]octadec-8-en-4-one 39
(1S,8E,11S,12R,14R,15R,17S)-14-hydroxy-15-methyl-3,18-dioxatricyclo[9.6.1.0^{12,17}]octadec-8-en-4-one 39
(1S,2R,5S,6S,7R)-5-(tert-Butyldiphenylsilanyloxymethyl)-4-oxa-tricyclo[5.2.2.0^{2,6}]undec-8-en-3-one 40a
(1S,2R,5S,6S,7R)-5-(tert-Butyldiphenylsilanyloxymethyl)-4-oxa-tricyclo[5.2.2.0²6]undec-8-en-3-one 40a
(1S,2R,5S,6S,7R)-5-(tert-Butyldiphenylsilyloxy)methyl)-4-oxa-tricyclo[5.2.2.0^{2,6}]undec-8-en-3-ol 40b
(1S,2R,5S,6S,7R)-5-(tert-Butyldiphenylsilyloxymethyl)-4-oxa-tricyclo[5.2.2.02,6]undec-8-en-3-ol 40b
((1R, 2S, 3S, 5S, 6R, 7S)-5-allyl-4-oxatricyclo[5.2.2.0².⁶]undec-8-en-3-ylmethoxy)tertbutyl diphenylsilane 40c
((1R, 2S, 3S, 5S, 6R, 7S)-5-allyl-4-oxatricyclo[5.2.2.0^2.6]undec-8-en-3-ylmethoxy)tertbutyl diphenylsilane 40c

![Chemical Structure](image-url)
((1R, 2S, 3S, 5S, 6R, 7S)-5-allyl-4-oxatricyclo[5.2.2.02,6]undec-8-en-3-yl)-methanol 84
((1R, 2S, 3S, 5S, 6R, 7S)-5-allyl-4-oxatricyclo[5.2.2.0^{2.6}]undec-8-en-3-yl)-methanol 84
(1R,2S,3S,5S,6R,7S)-5-Allyl-4-oxatricyclo[5.2.2.0^2,6]undec-8-en-3-ylmethyl hex-5-enoate 85
(1R,2S,3S,5S,6R,7S)-5-Allyl-4-oxatricyclo[5.2.2.0^{2,6}]undec-8-en-3-ylmethyl hex-5-enoate 85

![ Molecular structure of compound 85 ]
(1R,2S,3S,10E,13S,14R,15S)-5,20- dioxatetracyclo[13.2.2.1^{3,13}.0^{2,14}]icos- 10,16-dien-6-one 40
(1R,2S,3S,10E,13S,14R,15S)-5,20-dioxatetracyclo[13.2.2.1^{3,13}.0^{2,14}]icosa-10,16-dien-6-one 40
(3S,3aS,4R,7S,7aR)-3-((tert-butyldiphenylsilyl)oxy)methyl)-3a,4,7,7a-tetrahydro-4,7-methanoisobenzofuran-1(3H)-one 41a
(3S,3aS,4R,7S,7aR)-3-((tert-butyldiphenylsilyl)oxy)methyl)-3a,4,7,7a-tetrahydro-4,7-methanoisobenzofuran-1(3H)-one 41a
(1S,2R,5S,6S,7R)-5-(tert-Butyldiphenylsilanoxymethyl)-4-oxa-tricyclo[5.2.1.0.2,6]decan-3-one 41b

\[ \text{OTBDPS} \]

\[ 41b \]
(1S,2R,5S,6S,7R)-5-(tert-Butyldiphenylsilanoxymethyl)-4-oxa-tricyclo[5.2.1.0².6]decan-3-one 41b
(1S,2R,5S,6S,7R)-5-(tert-Butyldiphenylsilanoxymethyl)-4-oxa-tricyclo[5.2.1.0.2,6]decan-3-ol 41c
(1S,2R,5S,6S,7R)-5-(tert-Butyldiphenylsilanoxymethyl)-4-oxa-tricyclo[5.2.1.0.2,6]decan-3-ol 41c
((1R,2S,3S,5S,6R,7S)-5-Allyl-4-oxa-tricyclo[5.2.1.0^{2,6}]decane-3-ylmethoxy-tert-butyldiphenylsilane 41d
\(((1R,2S,3S,5S,6R,7S)-5-\text{Allyl}-4-\text{oxa-tricyclo}[5.2.1.0^{2,6}]\text{decane}-3-\text{ylmethoxy-tert-butyldiphenylsilane} \ 41d\)
((1R,2S,3S,5S,6R,7S)-5-Allyl-4-oxa-tricyclo[5.2.1.0^2,6]decan-3-yl)-methanol 41e
((1R,2S,3S,5S,6R,7S)-5-Allyl-4-oxa-tricyclo[5.2.1.0^{2,6}]decan-3-yl)-methanol 41e
((1S,3S,3aR,4R,7S,7aS)-3-allyloctahydro-4,7-methanoisobenzofuran-1-yl)methyl pent-4-enoate 41f
\((1\text{S},3\text{S},3\text{aR},4\text{R},7\text{S},7\text{aS})-3\text{-allyloctahydro-4,7-methanosobenzofuran-1-yl)methyl pent-4-enoate}\) 41f
(1S,10S,10aR,11R,14S,14aS)-1,2,5,6,9,10,10a,11,12,13,14,14a-dodecahydro-4H-1,10-epoxy-11,14-methanobenzo[d][1]oxacyclododecin-4-one

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(1S,10S,10aR,11R,14S,14aS)-1,2,5,6,9,10,10a,11,12,13,14,14a-dodecahydro-4H-1,10-epoxy-11,14-methanobenzo[d][1]oxacyclododecin-4-one
(1S,2S,3S,5S,6R,7R)-5-Allyl-4-oxatricyclo[5.2.1.0^{2,6}]dec-3-ylmethyl hex-5-enoate 83
(1S,2S,3S,5S,6R,7R)-5-Allyl-4-oxatricyclo[5.2.1.0^{2,6}]dec-3-ylmethyl hex-5-enoate 83
(E)-(15S,11S,12R,17S)-3,18-Dioxatetracyclo[9.6.1.1\textsuperscript{13}16.0\textsuperscript{12}17]nonadec-8-en-4-one 42
(E)-(1S,11S,12R,17S)-3,18-Dioxatetracyclo[9.6.1.1^{13,16}.0^{12,17}]nonadec-8-en-4-one 42
2-[(1R,3S,3aS,7aR)-3-[(tert-butyldiphenylsilyl)oxy]methyl]-1,3,3a,4,7,7a-hexahydro-2-benzofuran-1-yl]-2-methylpropanal 44
2-[(1R,3S,3aS,7aR)-3-[(tert-butyldiphenylsilyl)oxy]methyl]-1,3,3a,4,7,7a-hexahydro-2-benzofuran-1-yl]-2-methylpropanal 44
2-((1S,3S,3aS,7aR)-3-(((tert-butyldiphenylsilyl)oxy)methyl)-1,3,3a,4,7,7a-hexahydroisobenzofuran-1-yl)-1-phenylethan-1-one 45
2-((1S,3S,3aS,7aR)-3-(((tert-butyldiphenylsilyl)oxy)methyl)-1,3,3a,4,7,7a-hexahydroisobenzofuran-1-yl)-1-phenylethano-1-one 45
3-[(1R,3S,3aS,7aR)-3-{[(tert-Butyldiphenylsilyl)oxy]methyl}-octahydro-2-benzofuran-1-yl]-3-methylbutan-2-one 46a
3-[(1R,3S,3aS,7aR)-3-[(tert-Butyldiphenylsilyl)oxy]methyl]-octahydro-2-benzofuran-1-yl]-3-methylbutan-2-one 46a
3-[(1R,3S,3aS,7aR)-3-(Hydroxymethyl)-octahydro-2-benzofuran-1-yl]-3-methylbutan-2-one 46
3-[[1R,3S,3aS,7aR]-3-{(Hydroxymethyl)}octahydro-2-benzofuran-1-yl]-3-methylbutan-2-one 46
1-((1S,3S,3aS,7aR)-3-((tert-butyldiphenylsilyloxy)methyl)octahydroisobenzofuran-1-yl)-3,3-dimethylbutan-2-one 47
1-((1S,3S,3aS,7aR)-3-(((tert-butyldiphenylsilyl)oxy)methyl)octahydroisobenzofuran-1-yl)-3,3-dimethylbutan-2-one 47
1-((1S,3S,3aS,7aR)-3-(hydroxymethyl)octahydroisobenzofuran-1-yl)-3,3-dimethylbutan-2-one 47
1-\{(1S,3S,3\text{a}S,7\text{a}R)-3\text{-}(hydroxymethyl)octahydroisobenzofuran-1-yl\}-3,3\text{-}dimethylbutan-2-one \textbf{47}
1-((1S,3S,3aS,7aR)-3-((tert-butyldiphenylsilyloxy)methyl)-1,3,3a,4,7,7a-hexahydroisobenzofuran-1-yl)-3,3-dimethylbutan-2-one 48a
1-((1S,3S,3aS,7aR)-3-((tert-butyldiphenylsilyloxy)methyl)-1,3,3a,4,7,7a-hexahydroisobenzofuran-1-yl)-3,3-dimethylbutan-2-one 48a
1-[[1S,3S,3aS,7aR]-3-(hydroxymethyl)-1,3,3a,4,7,7a-hexahydro-2-benzofuran-1-yl]-3,3-imethylbutan-2-one 48
1-[(1S,3S,3aS,7aR)-3-(hydroxymethyl)-1,3,3a,4,7,7a-hexahydro-2-benzofuran-1-yl]-3,3-imethylbutan-2-one 48

[Chemical Structure Image]

1H NMR (800 MHz, CDCl3) □

\[
\begin{array}{c}
\text{H} \\
8\text{H} \\
7\text{H} \\
6\text{H} \\
5\text{H} \\
4\text{H} \\
3\text{H} \\
2\text{H} \\
1\text{H} \\
\end{array}
\]

\[
\begin{array}{c}
\text{O} \\
\text{O} \\
\text{OH} \\
\end{array}
\]

[Chemical Structure Image]

1H NMR (800 MHz, CDCl3) □

\[
\begin{array}{c}
\text{H} \\
8\text{H} \\
7\text{H} \\
6\text{H} \\
5\text{H} \\
4\text{H} \\
3\text{H} \\
2\text{H} \\
1\text{H} \\
\end{array}
\]

\[
\begin{array}{c}
\text{O} \\
\text{O} \\
\text{OH} \\
\end{array}
\]
2-[(1R,3S,3aS,7aR)-3-(((tert-butyldiphenylsilyl)oxy)methyl)-1,3,3a,4,7a-hexahydro-2-benzofuran-1-yl]-2-methylpropan-1-ol 49a
2-[(1R,3S,3aS,7aR)-3-[(tert-butyldiphenylsilyl)oxy]methyl]-1,3,3a,4,7,7a-hexahydro-2-benzofuran-1-yl]-2-methylpropan-1-ol 49a
2-[(1R,3S,3aS,7aR)-3-(hydroxymethyl)-1,3,3a,4,7,7a-hexahydro-2-benzofuran-1-yl]-2-methylpropan-1-ol 49
2-[(1R,3S,3aS,7aR)-3-(hydroxymethyl)-1,3,3a,4,7,7a-hexahydro-2-benzofuran-1-yl]-2-methylpropan-1-ol **49**
{2-[[1R,3S,3a5,7aR]-3-[[tert-Butyldiphenylsilyl]oxy]methyl]-1,3,3a,4,7,7a-hexahydro-2-benzofuran-1-yl]-2-methylpropyl}(benzyl)amine 50
{2-[[1R,3S,3aS,7aR]-3-[[tert-Butyldiphenylsilyl]oxy]methyl]-1,3,3a,4,7,7a-hexahydro-2-benzofuran-1-yl]-2-methylpropyl}(benzyl)amine 50
{[1R,3S,3aS,7aR]-3-[[tert-Butyldiphenylsilyl]oxy]methyl]-1,3,3a,4,7a-hexahydro-2-benzofuran-1-yl}-2-methylpropyl][3-methoxyphenyl]methyl]amine 51
{2-[[1R,3S,3aS,7aR]-3-[[tert-Butyldiphenylsilyl]oxy]methyl]-1,3,3a,4,7,7a-hexahydro-2-benzofuran-1-yl-2-methylpropyl][3-methoxyphenyl]methyl]amine

51
{2-[(1R,3S,3aS,7aR)-3-[[tert-Butyldiphenylsilyl]oxy]methyl]-1,3a,4,7,7a-hexahydro-2-benzofuran-1-yl]-2-methylpropyl}(methyl)amine 52
(2-[(1R,3S,3aS,7aR)-3-[[tert-Butyldiphenylsilyl]oxy]methyl]-1,3a,4,7,7a-hexahydro-2-benzofuran-1-yl]-2-methylpropyl)(methyl)amine 52
(2-{[1R,3S,3aS,7aR]-3-{[(tert-Butyldiphenylsilyl)oxy]methyl}-1,3,3a,4,7,7a-hexahydro-2-benzofuran-1-yl]-2-methylpropyl}(propyl)amine 53
{(2-[(1R,3S,3aS,7aR)-3-[[tert-Butyldiphenylsilyl]oxy]methyl]-1,3,3a,4,7,7a-hexahydro-2-benzofuran-1-yl]-2-methylpropyl}(propyl)amine 53
(2-[(1R,3S,3aS,7aR)-3-[[tert-Butyldiphenylsilyl]oxy]methyl]-1,3,3a,4,7,7a-hexahydro-2-benzofuran-1-yl]-2-methylpropyl)(2-methoxyethyl)amine 54
(2-[[1R,3S,3aS,7aR]-3-[[tert-Butyldiphenylsilyl]oxy]methyl]-1,3,3a,4,7,7a-hexahydro-2-benzofuran-1-yl]-2-methylpropyl)(2-methoxyethyl)amine 54
[(1S,3R,3aR,7aS)-3-[1-(benzylamino)-2-methylpropan-2-yl]-1,3,3a,4,7,7a-hexahydro-2-benzofuran-1-yl]methanol 55
[(1S,3R,3aR,7aS)-3-[1-(benzylamino)-2-methylpropan-2-yl]-1,3,3a,4,7,7a-hexahydro-2-benzofuran-1-yl]methanol 55
[(1S,3R,3aR,7aS)-3-1-[(3-Methoxyphenyl)methyl]amino)-2-methylpropan-2-yl]-1,3,3a,4,7a-hexahydro-2-benzofuran-1-yl]methanol 56
[(1S,3R,3aR,7aS)-3-1-[[3-Methoxyphenyl)methyl]amino]-2-methylpropan-2-yl]-1,3,3a,4,7,7a-hexahydro-2-benzofuran-1-yl]methanol 56
[(1S,3R,3aR,7aS)-3-[2-Methyl-1-(methylamino)propan-2-yl]-1,3,3a,4,7,7a-hexahydro-2-benzofuran-1-yl]methanol 57
[(1S,3R,3aR,7aS)-3-[2-Methyl-1-(methylamino)propan-2-yl]-1,3,3a,4,7,7a-hexahydro-2-benzofuran-1-yl]methanol 57
[(1S,3R,3aR,7aS)-3-[2-methyl-1-(propylamino)propan-2-yl]-1,3,3a,4,7,7a-hexahydro-2-benzofuran-1-yl]methanol 58
[(1S,3R,3aR,7aS)-3-[2-methyl-1-(propylamino)propan-2-yl]-1,3,3a,4,7,7a-hexahydro-2-benzofuran-1-yl]methanol 58
[(1S,3R,3aR,7aS)-3-{1-[(2-Methoxyethyl)amino]-2-methylpropan-2-yl}-1,3,3a,4,7,7a-hexahydro-2-benzofuran-1-yl]methanol 59
[(1S,3R,3aR,7aS)-3-{1-[(2-Methoxyethyl)amino]-2-methylpropan-2-yl}-1,3,3a,4,7,7a-hexahydro-2-benzofuran-1-yl]methanol 59
[(1S,3S,3aR,7aS)-3-(2-methoxy-3-phenylpropyl)-octahydro-2-benzofuran-1-yl]methanol 60
[(1S,3S,3aR,7αS)-3-(2-methoxy-3-phenylpropyl)-octahydro-2-benzofuran-1-yl]methanol 60
Ethyl (2E)-4-[(1R,3S,3aS,7aR)-3-{{(tert-Butyldiphenylsilyl)oxy}methyl}-1,3,3a,4,7,7a-hexahydro-2-benzofuran-1-yl]-4-methylpent-2-enoate 61
Ethyl (2E)-4-[(1R,3S,3aS,7aR)-3-{{(tert-Butyldiphenylsilyl)oxy}methyl}-1,3,3a,4,7,7a-hexahydro-2-benzofuran-1-yl]-4-methylpent-2-enoate 61
Ethyl 4-[(1R,3S,3aS,7aR)-3-{{(tert-butyldiphenylsilyl)oxy}methyl} octahydro-2-benzofuran-1-yl]-4-methylpentanoate 62
Ethyl 4-[(1R,3S,3aS,7aR)-3-[[[tert-butyldiphenylsilyl]oxy]methyl] octahydro-2-benzofuran-1-yl]-4-methylpentanoate 62
Ethyl 4-[(1R,3S)-3-(hydroxymethyl)octahydro-2-benzofuran-1-yl]-4-methylpentanoate 63
Ethyl 4-[(1R,3S)-3-(hydroxymethyl)octahydro-2-benzofuran-1-yl]-4-methylpentanoate 63
4-[(1R,3S,3aS,7aR)-3-(hydroxymethyl)-octahydro-2-benzofuran-1-yl]-4-methylpentanoic acid 64
4-[(1R,3S,3aS,7aR)-3-(hydroxymethyl)-octahydro-2-benzofuran-1-yl]-4-methylpentanoic acid 64
(1R,2R,7S,8S)-14,14-dimethyl-10,15-dioxatricyclo[6.6.1.0^{2,7}]pentadecan-11-one 65
(1R,2R,7S,8S)-14,14-dimethyl-10,15-dioxatricyclo[6.6.1.0^2,7]pentadecan-11-one 65
2-[(1R,3S,3aS,7aR)-3-[[tert-butyldiphenylsilyl]oxy]methyl]-octahydro-2-benzofuran-1-yl]-2-methylpropanal 66
2-[(1R,3S,3aS,7aR)-3-[[tert-butyldiphenylsilyl]oxy]methyl]-octahydro-2-benzofuran-1-yl]-2-methylpropanal 66
[(1S,3R,3aR,7aS)-3-(2-methyl-1-oxopropan-2-yl)octahydro-2-benzofuran-1-yl]methyl 2-bromoacetate 68
(1R,2R,7S,8S,13R)-13-hydroxy-14,14-dimethyl-10,15-dioxatricyclo[6.6.1.0^{2,7}]pentadecan-11-one 69
(1R,2R,7S,8S,13R)-13-hydroxy-14,14-dimethyl-10,15-dioxatricyclo[6.6.1.0^{2,7}]pentadecan-11-one 69
(1R,2R,7S,8S,13R)-14,14-dimethyl-11-oxo-10,15-dioxatricyclo[6.6.1.0^{2,7}]pentadecan-13-yl acetate 70
(1R,2R,7S,8S,13R)-14,14-dimethyl-11-oxo-10,15-dioxatricyclo[6.6.1.0^{2,7}]pentadecan-13-yl acetate 70
(1S,3S,3aR,7aS)-3-(Prop-2-en-1-yl)-octahydro-2-benzofuran-1-carbaldehyde 71
(1S,3S,3aR,7aS)-3-(Prop-2-en-1-yl)-octahydro-2-benzofuran-1-carbaldehyde 71
(R)-1-((1S,3S,3aR,7aS)-3-allyl-1-methyloctahydroisobenzofuran-1-yl)pent-4-en-1-ol 72
(R)-1-(((1S,3S,3aR,7aS)-3-allyl-1-methyloctahydroisobenzofuran-1-yl)pent-4-en-1-ol 72
(S)-1-((1S,3S,3aR,7aS)-3-allyl-1-methyloctahydroisobenzofuran-1-yl)pent-4-en-1-ol 73
(S)-1-((1S,3S,3aR,7aS)-3-allyl-1-methyloctahydroisobenzofuran-1-yl)pent-4-en-1-ol 73
((R)-1-((1S,3S,3aR,7aS)-3-allyl-1-methyloctahydroisobenzofuran-1-yl)pent-4-en-1-yl)oxy)(tert-butyl)dimethylsilane 74
(((R)-1-((1S,3S,3aR,7aS)-3-allyl-1-methyloctahydroisobenzofuran-1-yl)pent-4-en-1-yl)oxy)(tert-butyl)dimethylsilane 74
tert-butyl(((4aS,5S,6R,12S,12aR,Z)-1,2,3,4,4a,5,6,7,8,11,12,12a-dodecahydro-5,12-epoxybenzo[10]annulen-6-yl)oxy)dimethylsilane 75
tert-butyl(((4aS,5S,6R,12S,12aR,Z)-1,2,3,4,4a,5,6,7,8,11,12,12a-dodecahydro-5,12-epoxybenzo[10]annulen-6-yl)oxy)dimethylsilane 75
The $^1$H-$^1$H NOESY spectrum for 75
(4aS,5S,6R,12S,12aR,Z)-5,12-dimethyl-1,2,3,4,4a,5,6,7,8,11,12,12a-dodecahydro-5,12-epoxybenzo[10]annulen-6-ol 76
(4aS,5S,6R,12S,12aR,Z)-5,12-dimethyl-1,2,3,4,4a,5,6,7,8,11,12,12a-dodecahydro-5,12-epoxybenzo[10]annulen-6-ol 76
(3S,3aS,4R,7S,7aR)-3-(((tert-butyldiphenylsilyl)oxy)methyl)-1,3,3a,4,7,7a-hexahydro-4,7-methanoisobenzofuran-1-ol 79a
(3S,3aS,4R,7S,7aR)-3-(((tert-butyldiphenylsilyl)oxy)methyl)-1,3,3a,4,7,7a-hexahydro-4,7-methanoisobenzofuran-1-ol 79a
(((1S,3S,3aR,4S,7R,7aS)-3-allyl-1,3,3a,4,7,7a-hexahydro-4,7-methanoisobenzofuran-1-yl)methoxy)(tert-butyl)diphenylsilane 79b
(((1S,3S,3aR,4S,7R,7aS)-3-allyl-1,3,3a,4,7,7a-hexahydro-4,7-methanoisobenzofuran-1-yl)methoxy)(tert-butyl)diphenylsilane 79b
((1S,3S,3aR,4S,7R,7aS)-3-allyl-1,3,3a,4,7,7a-hexahydro-4,7-methanoisobenzofuran-1-yl)methanol 79
((1S,3S,3aR,4S,7R,7aS)-3-allyl-1,3a,4,7,7a-hexahydro-4,7-methanoisobenzofuran-1-yl)methanol 79
((1S,3S,3aR,4S,7R,7aS)-3-allyl-1,3,3a,4,7,7a-hexahydro-4,7-methanoisobenzofuran-1-yl)methyl but-3-enoate 80
(1S,3S,3aR,4S,7R,7aS)-3-allyl-1,3,3a,4,7,7a-hexahydro-4,7-methanoisobenzofuran-1-yl)methyl but-3-enolate 80
((1S,3S,3aR,4S,7R,7aS)-3-allyl-1,3,3a,4,7,7a-hexahydro-4,7-methanoisobenzofuran-1-yl)methyl pent-4-enoate 81
((1S,3S,3aR,4S,7R,7aS)-3-allyl-1,3,3a,4,7,7a-hexahydro-4,7-methanoisobenzofuran-1-yl)methyl pent-4-enoate 81
\((1S,3S,3aR,4S,7R,7aS)\)-3-allyl-1,3,3a,4,7,7a-hexahydro-4,7-methanoisobenzofuran-1-yl)methyl hex-5-enoate 82
((1S,3S,3aR,4S,7R,7aS)-3-allyl-1,3,3a,4,7,7a-hexahydro-4,7-methanoisobenzofuran-1-yl)methyl hex-5-enoate 82
[(1S,3R,3aR,7aS)-3-(2-methyl-3-oxobutan-2-yl)-octahydro-2-benzofuran-1-yl]methyl 2-bromoacetate 89a
[(1S,3R,3aR,7aS)-3-(2-methyl-3-oxobutan-2-yl)-octahydro-2-benzofuran-1-yl]methyl acetate 89
[(1S,3R,3aR,7aS)-3-[(2-methyl-3-oxobutan-2-yl)-octahydro-2-benzofuran-1-yl]methyl acetate 89}