Experimental

General

Chemicals were purchased from Sigma Aldrich and Acros organics. Haloethers 4 and 11a-e were prepared using literature procedures and used without purification. Where necessary, solvents were dried and stored for up to three weeks on molecular sieves. DCM and Et3N were dried over CaH2, THF and toluene over Na/benzophenone. AcCl was redistilled and used fresh. DMF was dried by storing a fresh bottle over activated molecular sieves under argon. All reactions were done under argon atmosphere and monitored on commercially available pre-coated TLC plates (layer thickness 0.25 mm) of Kieselgel 60 F254. Compounds were visualised by use of a UV lamp and/or a suitable dipping solution and heating. Column chromatography was performed manually when isocratic, or using an Argonaut Flashmaster where there was a gradient, using Merck 60 (40–60 mm) silica gel or aluminium oxide (activated, neutral, Bochmann grade I, ~150 mesh) as solid phase. Separation of enantiomers was done on a 25 cm Chiralcel OJ column. Mass spectrometric data (MS) were obtained by electrospray (ES) on a Waters LCT Premier Mass Spectrometer or electronic ionisation (EI) on a Waters GCT Premier Mass Spectrometer. NMR spectra were recorded on Bruker Avance DRX 500, 400 and 300 spectrometers operating at 500/125 MHz, 400/100 MHz or 300/75 MHz for 1H-NMR and 13C-NMR, respectively. Chemical shifts in NMR spectra are given in parts per million and J in Hertz using the deuterated solvent as an internal reference; CDCl3: δ 7.26/77.0, d4-MeOH: δ 3.31/49.1. Where chemical shifts overlap in 13C-NMR spectra, there can be a lower number of signals reported than actual carbon atoms in the compound.

Procedures

1-((ter-Butyldiphenylsilyloxy)-3-((trimethylsilyl)-methyl)but-3-en-2-ol (3)

3,4-Epoxytetrahydrofuran (14 g, 165 mmol, 1 eq) was dissolved in dry THF (400 mL) and cooled to -78 °C. [(trimethylsilyl)methyl]lithium (1.0 M in pentane, 440 mL, 440 mmol, 2.7 eq) was added drop wise. The solution was stirred at this temperature overnight, then allowed to warm to r.t. over 3 h. The reaction was then quenched with saturated aqueous NaHCO3 (500 mL) and the aqueous layer extracted with Et2O (2 x 500 mL). The combined organic layers were dried with MgSO4, filtered and concentrated in vacuo. The crude mixture was then dissolved in dry DCM (400 mL) at r.t. tert-Butyl(chloro)diphenylsilane (55 mL, 212 mmol, 1.3 eq), dry Et3N (29 mL, 208 mmol, 1.3 eq) and DMAP (0.78 g, 6.4 mmol, 0.04 eq) was added. The solution was stirred at this temperature overnight, then allowed to warm to r.t. over 3 h. The reaction was then quenched with saturated aqueous NaHCO3 (500 mL) and the aqueous layer extracted with Et2O (2 x 500 mL). The combined organic layers were dried with MgSO4, filtered and concentrated in vacuo. Column chromatography (5% EtOAc in pet.ether on aluminium oxide) yielded title compound 3 (60 g, 89%) as a colourless oil. νmax(KBr)/cm⁻¹: 3570 (m), 3072 (m), 2955 (s), 1638 (m), 1590 (w), 1473 (m), 1428 (s), 1249 (s), 1112 (s), 1033 (w), 770 (s). 1H(500 MHz; CDCl3): -0.02 (9H, s, Si-CH3), 1.07 (9H, s, Si-C=C), 1.16 (1H, d, J=13.8 Hz, TMS-CH2), 1.50 (1H, d, J=13.8 Hz, TMS-CH2), 2.71 (1H, d, J=3.1 Hz, OH), 3.51 (1H, dd, J=8.0, 10.3 Hz, TBDPSC-CH3), 3.74 (1H, dd, J=3.3, 10.3 Hz, TBDPSC-CH3), 3.99-4.04 (1H, m, CH2-CH3), 4.68 (1H, br m, C=C-CH3), 4.96 (1H, br m, C=C-CH3), 7.37-7.47 (6H, m, Ar-H), 7.65-7.69 (4H, m, Ar-H); δC(125 MHz; CDCl3): -1.4 (Si-CH3), 19.2 (Si-CH3), 23.3 (TMS-CH3), 26.9 (Si-C-CH3), 67.5 (TBDPS-CH3), 75.3 (CH2-CH3), 108.4 (C=C-CH3), 127.8 (Ar-CH), 127.8 (Ar-CH), 129.8 (Ar-CH), 133.1 (Ar=C), 133.2 (Ar=C), 135.6 (Ar-CH), 145.4 (C=C-CH3); m/z (ES): 435.2159 (M+Na+), calculated for C24H36O2Si2 + Na+: 435.2152 (1.6 ppm)

[Methoxy][1-[(ter-butyldiphenylsilyloxy)methyl-2-[(trimethylsilyl)methyl]prop-2-en-1-yloxymethyl]-benzene (5)

3 (0.2 g, 0.5 mmol, 1 eq) was dissolved in DCM (6 mL), added Et3N (0.3 mL, 2 mmol, 4 eq) and 4 (crude, approx 4 eq), and the reaction mixture stirred for 1h before it was warmed up to r.t and stirred over night. The solvent was then removed in vacuo. The residue was dissolved in EtOAc and filtered through a pad of aluminium oxide. The excess solvent was again removed in vacuo and purification was carried out by column chromatography (0-5% EtOAc in hexane gradient on aluminium oxide) to yield title compound 5 (0.2 g, 73%) as a colourless oil. Diastereomeric ratio of cis:trans was 1:1. These diastereomers separated partially during column chromatography, but was pooled together for the cyclisation step.

One diastereomer of 5: δH(500 MHz; CDCl3): 0.00 (9H, s, Si-CH3), 1.06 (9H, s, Si-C-CH3), 1.26 (1H, d, J=14.2 Hz, TMS-CH2), 1.46 (1H, d, J=14.2 Hz, TMS-CH2), 3.15 (3H, s, O-CH3), 3.69-3.80 (2H, m, TBDPSO-CH2), 4.33 (1H, dd, J=4.1, 6.6 Hz, CH2-CH3), 4.74 (1H, br s, C=C-CH3), 4.98 (1H, s, C=C-CH3), 5.62 (1H, s, O-CH-O), 7.30-7.45 (9H, m, Ar-H), 7.52-7.55 (2H, m, Ar-H), 7.73-7.78 (4H, m, Ar-H), δC(125 MHz; CDCl3): -1.2 (Si-CH3), 19.2 (Si-C-CH3), 22.8 (TMS-CH3), 26.8 (Si-C-CH3), 49.4 (O-CH3), 66.7 (TBDPSO-CH3), 80.1 (CH2-CH3), 98.0 (O-CH-O), 110.6 (C=C-CH3), 127.0 (Ar-CH), 127.5 (Ar-CH), 127.6 (Ar-CH), 128.1 (Ar-CH), 129.5 (Ar-CH), 129.6 (Ar-CH), 133.6 (Ar=C), 133.7 (Ar=C), 135.6 (Ar-CH), 135.7 (Ar-CH), 138.6 (Ar=C), 143.3 (C=C-CH3).
The other diastereomer of 5: $\delta_{1}$(500 MHz; CDC13): -0.01 (9H, s, Si-CH3), 1.00 (9H, s, Si-C-CH3), 1.26 (1H, d, $J=14.2$ Hz, TMS-CH3), 1.53 (1H, d, $J=14.2$ Hz, TMS-CH3), 3.20 (3H, s, O-CH3), 3.69-3.80 (2H, m, TBDPSO-CO), 4.09 (1H, dd, $J=3.5$, 7.0 Hz, CH2-C), 4.75 (1H, br s, C=CH2), 5.10 (1H, s, C=CH2), 5.77 (1H, s, O-CH=O), 7.30-7.45 (9H, m, Ar-H), 7.52-7.55 (2H, m, Ar-H), 7.61-7.64 (4H, m, Ar-H). $\delta_{i}$(125 MHz; CDC13): -1.2 (Si-CH3), 19.1 (Si-C-C), 23.1 (TMS-CH3), 26.8 (Si-C-CH3), 51.8 (O-CH3), 67.1 (TBDPSO-CH3), 81.1 (CH2-CH3), 102.3 (O-CH=O), 110.0 (C=CH2), 127.1 (Ar-CH), 127.6 (Ar-CH), 128.2 (Ar-CH), 129.5 (Ar-CH), 129.6 (Ar-CH), 133.4 (Ar-CH), 133.5 (Ar-C), 135.6 (Ar-CH), 135.7 (Ar-CH), 143.1 (C=CH2).

v$_{\text{max}}$(KBr)/cm$^{-1}$: 3071 (m), 1637 (m), 1478 (m), 1428 (m), 1258 (s), 1112 (s), 849 (s), 702 (s).

2-((Butyldiphenylsilyloxy)methyl)-3-methylene-5-phenyl-tetrahydrofuran (6)

5 (1.9 g, 3.5 mmol, 1 eq) was dissolved in dry DCM (50 mL) and the reaction mixture cooled to -78°C. Bis(trifluoromethane)sulfonimide (2.5 g, 6.9 mmol, 2 eq) was added and the reaction mixture stirred for 5 min. The solution was then filtered through a pad of silica gel using 25% EtOAc in Hexane as eluent. The filtrate was concentrated in vacuo until the colour changed to blue. Argon was then passed through for 30 min, the last 10 of which at r.t. The solution was then filtered through a pad of silica gel using 25% EtOAc in Hexane as eluent to yield title compound 7.

(9H, s, Si-C-CH3), 2.57-2.64 (1H, m, CH(Ar)-CH2), 2.89 (1H, dd, $J=5.5$, 15.1 Hz, CH(Ar)-CH3), 3.84 (1H, dd, $J=4.6$, 10.6 Hz, TBDPSO-CH3), 3.89 (1H, dd, $J=4.3$, 10.6 Hz, TBDPSO-CH3), 4.57-4.59 (1H, m, O-CH3), 4.93 (1H, dd, $J=5.5$, 10.7 Hz, O-CH-Ar), 5.01-5.02 (1H, m, C=C=O), 5.10-5.11 (1H, m, C=C=O), 7.27-7.46 (11H, m, Ar-H), 7.72-7.76 (4H, m, Ar-H). $\delta_{i}$(125 MHz; CDC13): 19.3 (Si-C-CH3), 26.8 (Si-C-CH3), 42.5 (CH(Ar)-CH3), 66.8 (TBDPSO-CH3), 80.5 (O-CH-Ar), 82.0 (O-CH=C=O), 105.7 (C=CH2), 126.2 (Ar-CH), 127.6 (Ar-CH), 128.3 (Ar-CH), 129.6 (Ar-CH), 133.4 (Ar-C), 133.6 (Ar-C), 135.7 (Ar-CH), 141.7 (Ar-C), 149.2 (C=CH2).

v$_{\text{max}}$(film)/cm$^{-1}$: 3070 (m), 1668 (m), 1428 (m), 1264 (m), 1112 (s), 892 (m), 700 (s).

2-((Butyldiphenylsilyloxy)methyl)-5-phenyl-tetrahydrofuran-3-one (7)

6a (0.28 g, 0.65 mmol, 1 eq) was dissolved in DCM (8 mL) and cooled to -78°C. O$_3$ was passed through the reaction mixture to yield 6a (0.73 g, 48%) as a colourless oil. Diastereomeric ratio of cis/trans was 2:1. The other diastereomers were separated with a second round of column chromatography (0-3% EtOAc in hexane) giving a 6a (0.37 g, 24%). It was later discovered that the diastereomers separate with only one round of chromatography after the oxidation step leading to compound 7.

(9H, s, Si-C-CH3), 2.57-2.67 (1H, m, CH(Ar)-CH2), 3.04 (1H, m, O-CH3), 3.20 (3H, s, O-CH3), 46.5 (CH(Ar)-C), 51.8 (O-C), 79.7 (O-C), 81.1 (O-C), 102.3 (O-C), 125.9 (Ar-C), 127.6 (Ar-CH), 128.3 (Ar-CH), 129.5 (Ar-CH), 133.4 (Ar-C), 133.6 (Ar-C), 135.6 (Ar-C), 135.7 (Ar-CH), 143.8 (C=CH2).

v$_{\text{max}}$(film)/cm$^{-1}$: 3070 (m), 2931 (s), 1668 (m), 1428 (m), 1264 (m), 1112 (s), 892 (m), 700 (s), 671 (s). m/z (ES): 451.2089 (M+Na$^+$), calculated for C$_{26}$H$_{36}$O$_2$Si$^{2+}$Na$^+$: 451.2069 (2.0 ppm).

2-(Hydroxymethyl)-5-phenyl-tetrahydrofuran-3-one (8)

5 (0.20 g, 0.46 mmol, 1 eq) was dissolved in DMF (5 mL) and the aqueous layer extracted with EtOAc (3 x 10mL). The combined organic layers were dried with MgSO$_4$, filtered and concentrated under reduced pressure. Purification by column chromatography (0-
50% EtOAc in hexane gradient on silica gel) yielded title compound 8 (50 mg, 56%) as a colourless oil. ν\textsubscript{max}(film)/cm\textsuperscript{-1}: 3452 (br, s), 2924 (s), 1759 (s), 1497 (w), 1457 (m), 1378 (m), 1106 (s), 752 (m), 700 (s). δ\textsubscript{H}(500 MHz; CDCl\textsubscript{3}): 2.04 (1H, t, J=6.4Hz, OH), 2.56 (1H, dd, J=11.0, 18.0 Hz, CH(=Ar)-CH\textsubscript{2}), 2.89 (1H, dd, J=5.8, 18.0 Hz, CH(=Ar)-CH\textsubscript{2}), 3.93-3.97 (2H, m, HO-CH\textsubscript{2}), 4.06 (1H, t, J=3.5 Hz, O-CH-CHO), 5.24 (1H, dd, J=5.8, 11.0 Hz, O-CH-CHO), 7.35-7.46 (5H, m, Ar-H). δ\textsubscript{C}(125 MHz; CDCl\textsubscript{3}): 45.3 (CH(=Ar)-CH\textsubscript{2}), 61.6 (HO-CH\textsubscript{2}), 77.7 (O-CH-Ar), 82.3 (O-C\textsubscript{Ar}), 126.2 (Ar-CH), 128.6 (Ar-CH), 128.8 (Ar-CH), 139.6 (Ar-C), 213.7 (CO). m/z (ES): 192.0790 (M+), calculated value for C\textsubscript{11}H\textsubscript{12}O\textsubscript{3}: 192.0786 (2.1 ppm).

Separation of enantiomers was done at GlaxoSmithKline with 15% EtOH in C\textsubscript{7} as eluent. Chiral trace is attached. NMR and high resolution mass of both fractions are identical to each other and the above reported data for the racemic mixture.


3 (3.5 g, 8.5 mmol, 1.0 eq) dissolved in DCM (35 mL) with Et\textsubscript{3}N (1.4 mL, 10 mmol, 1.2 eq) and purification was done by column chromatography (0-5% EtOAc in hexane gradient on aluminium oxide). The diastereomers were not separated, but where it was possible the signals in the NMR-spectrum are reported separately for the different diastereomers.
3-Bromo-[methoxy][1-[4-butyldiphenylsilyloxy]-methyl-2-[(trimethylsilylethyl]-prop-2-en-1-yl]oxy]-methyl[benzene (12b)

2 (3.5 g, 8.5 mmol, 1.0 eq) dissolved in DCM (50 mL) with Et3N (1.4 mL, 10 mmol, 1.2 eq) and 11b gave the title compound 12b (2.4 g, 47 %) as a colourless oil.

One diastereomer of 12b: $\delta_h$(500 MHz; CDCl3): -0.01 (9H, s, Si-CH$_3$), 1.06 (9H, s, Si-C-CH$_3$), 1.23 (1H, d, J=14.1 Hz, TMS-CH$_3$), 1.48 (1H, d, J=14.1 Hz, TMS-CH$_2$), 3.14 (3H, s, O-CH$_3$), 3.66-3.77 (2H, m, TBDPSO-CH$_2$), 4.30 (1H, dd, J=4.1, 6.1 Hz, CH$_2$-CH$_3$), 4.74 (1H, s, C=CH$_2$), 4.94 (1H, s, C=CH$_2$), 5.58 (1H, s, O-CH$_3$-O), 7.25 (1H, t, J=7.8 Hz, Ar-H), 7.37-7.47 (4H, m, Ar-H), 7.50 (1H, s, Ar-H), $\delta_c$(125 MHz; CDCl3): -1.2 (Si-CH$_3$), 19.2 (Si-C-CH$_3$), 22.8 (TMS-CH$_2$), 26.8 (Si-C-CH$_3$), 49.4 (O-CH$_3$), 80.3 (CH$_2$-CH$_3$), 81.6 (O-C=O), 110.6 (C=C-CH$_3$), 122.4 (Ar-C), 125.4 (Ar-CH), 127.6 (Ar-CH), 127.7 (Ar-CH), 129.6 (Ar-CH), 129.7 (Ar-CH), 130.1 (Ar-CH), 131.3 (Ar-CH), 133.2 (Ar-CH), 133.4 (Ar-C), 135.7 (Ar-CH), 135.8 (Ar-C), 140.4 (Ar-C), 143.0 (C=CH$_2$).

The other diastereomer of 12b: $\delta_h$(500 MHz; CDCl3): 0.00 (9H, s, Si-CH$_3$), 0.98 (9H, s, Si-C-CH$_3$), 1.23 (1H, d, J=14.1 Hz, TMS-CH$_3$), 1.51 (1H, d, J=14.1 Hz, TMS-CH$_2$), 3.17 (3H, s, O-CH$_3$), 3.66-3.77 (2H, m, TBDPSO-CH$_2$), 4.08 (1H, d, J=3.1, 7.5 Hz, CH$_2$-CH$_3$), 4.74 (1H, s, C=CH$_2$), 5.07 (1H, s, C=CH$_2$), 5.78 (1H, s, O-CH$_3$-O), 7.22 (1H, t, J=7.8 Hz, Ar-H), 7.34 (4H, t, J=7.3 Hz, Ar-H), 7.37-7.47 (4H, m, Ar-H), 7.40-7.43 (4H, m, Ar-H), 7.69 (1H, t, J=1.6 Hz).

The other diastereomer of 12b: $\delta_c$(125 MHz; CDCl3): -1.3 (Si-CH$_3$), 19.1 (Si-C-CH$_3$), 23.2 (TMS-CH$_2$), 26.8 (Si-C-CH$_3$), 51.5 (O-CH$_3$), 67.2 (TBDPSO-CH$_3$), 81.6 (CH$_2$-CH$_3$), 101.5 (O-C=O), 110.1 (C=CH$_2$), 122.3 (Ar-C), 125.8 (Ar-CH), 127.6 (Ar-CH), 127.7 (Ar-CH), 129.7 (Ar-CH), 129.8 (Ar-CH), 130.3 (Ar-C), 131.4 (Ar-C), 133.2 (Ar-C), 133.4 (Ar-C), 135.6 (Ar-CH), 135.6 (Ar-CH), 141.1 (Ar-C), 143.9 (C=CH$_2$).

$\nu_{\text{max}}$(film)/cm$^{-1}$: 3072 (m), 2932 (s), 1473 (m), 1428 (m), 1199 (m), 1112 (s), 850 (m), 702 (s). $m/z$ (ES): 564.2432 (M + H$^+$) Calculated value for C$_{31}$H$_{41}$NO$_3$Si$_2$+H$^+$: 564.2424 (1.4 ppm).

4-Bromo-2-[methoxy][1-[4-butyldiphenylsilyloxy]-methyl-2-[(trimethylsilylethyl]-prop-2-en-1-yl]-oxy]methyl[thiophene (12d)

2 (1.7 g, 4.1 mmol, 1.0 eq) dissolved in DCM (30 mL) with Et3N (0.7 mL, 4.8 mmol, 1.2 eq) and 11d gave the title compound 12d (0.75 g, 53 %) as an orange oil.

One diastereomer of 12d: $\delta_h$(500 MHz; CDCl3): 0.03 (9H, s, Si-CH$_3$), 1.09 (9H, s, Si-C-CH$_3$), 1.27 (1H, d, J=14.3 Hz, TMS-CH$_3$), 1.49 (1H, d, J=14.3 Hz, TMS-CH$_2$), 3.28 (3H, s, O-CH$_3$), 3.71-3.80 (2H, m, TBDPSO-CH$_2$), 4.29 (1H, dd, J=4.1, 6.0 Hz, CH$_2$-CH$_3$), 4.76 (1H, s, C=CH$_2$), 5.03 (1H, s, C=CH$_2$), 5.80 (1H, s, O-CH$_3$-O),
7.07 (1H, Ar-H), 7.23 (1H, Ar-H), 7.36-7.45 (6H, m, Ar-H), 7.74-7.79 (4H, m, Ar-H). δ (125 MHz; CDCl3): -1.3 (Si-CH3), 19.2 (Si-C(5)), 22.9 (TMS-CH3), 26.8 (Si-C(6)), 49.2 (OCH(OH)), 66.4 (TBDPSO-CH2), 80.4 (CH2-C(5)), 94.5 (O-CH(OH)), 109.2 (Ar, C(1)), 110.7 (C=C(5)), 123.1 (Ar, C(7)), 127.7 (Ar, C(5)), 127.7 (Ar, C(7)), 128.2 (Ar, C(5)), 129.7 (Ar, C(7)), 132.3 (Ar, C(3)), 133.4 (Ar, C), 135.6 (Ar, CH), 135.7 (Ar, CH), 142.7 (C=C(5)), 143.6 (Ar, C).

The other diastereomer of 12d: δ (500 MHz; CDCl3): 0.03 (9H, s, Si-CH3), 1.03 (9H, s, Si-C(5)), 1.27 (1H, d, J=14.2 Hz, TMS-CH3), 1.53 (1H, d, J=14.2 Hz, TMS-CH3), 3.25 (3H, s, O-CH(OH)), 3.71-3.80 (2H, m, TBDPSO-CH2), 4.15 (1H, dd, J=2.6, 7.1 Hz, CH2-CH2), 4.78 (1H, s, C=CH2), 5.09 (1H, s, C=CH2), 6.07 (1H, s, O-CH(OH)), 7.07 (1H, s, Ar-H), 7.23 (1H, s, Ar-H), 7.36-7.43 (6H, m, Ar-H), 7.66-7.67 (4H, m, Ar-H). δ (125 MHz; CDCl3): -1.2 (Si-CH3), 19.1 (Si-C(5)), 23.2 (TMS-CH2), 26.8 (Si-C(6)), 51.1 (O-CH(OH)), 67.3 (TBDPSO-CH2), 81.7 (CH2-C(5)), 98.6 (O-CH(OH)), 109.0 (Ar, C(11)), 123.1 (Ar, C(7)), 127.7 (Ar, C(5)), 128.2 (Ar, C(5)), 129.7 (Ar, C(7)), 133.3 (Ar, C), 133.5 (Ar, C(3)), 133.6 (Ar, CH), 136.7 (Ar, CH), 143.5 (C=C(5)), 143.8 (Ar, C).

νmax(film)/cm⁻¹: 3072 (s), 1638 (m), 1428 (m), 1249 (m), 1113 (s), 702 (s).

General procedure for the cyclisation reaction

The acetyls 12a-e were dissolved in dry DCM and the reaction mixture cooled to -78°C. The Lewis acid was added and the reaction mixture stirred for 1h. It was then filtered through a pod of silica gel using 25% EtOAc in Hexane or Pet. Ether as eluent. The filtrate was concentrated in vacuo.

Diastereomeric ratio is measured from the 1H-NMR spectrum of the mixture.

5-(4-Bromophenyl)-2-((t-butyldiphenyl-silyloxy)methyl)-3-methylene-tetrahydrofuran (13a)

δH(500 MHz; CDCl3): 0.03 (9H, s, Si-CH3), 1.03 (9H, s, Si-C(5)), 1.27 (1H, d, J=14.2 Hz, TMS-CH3), 1.53 (1H, d, J=14.2 Hz, TMS-CH3), 3.25 (3H, s, O-CH(OH)), 3.71-3.80 (2H, m, TBDPSO-CH2), 4.15 (1H, dd, J=2.6, 7.1 Hz, CH2-CH2), 4.78 (1H, s, C=CH2), 5.09 (1H, s, C=CH2), 6.07 (1H, s, O-CH(OH)), 7.07 (1H, s, Ar-H), 7.23 (1H, s, Ar-H), 7.36-7.43 (6H, m, Ar-H), 7.66-7.67 (4H, m, Ar-H). δ (125 MHz; CDCl3): -1.2 (Si-CH3), 19.1 (Si-C(5)), 23.2 (TMS-CH2), 26.8 (Si-C(6)), 51.1 (O-CH(OH)), 67.3 (TBDPSO-CH2), 81.7 (CH2-C(5)), 98.6 (O-CH(OH)), 109.0 (Ar, C(11)), 123.1 (Ar, C(7)), 127.7 (Ar, C(5)), 128.2 (Ar, C(5)), 129.7 (Ar, C(7)), 133.3 (Ar, C), 133.5 (Ar, C(3)), 133.6 (Ar, CH), 136.7 (Ar, CH), 143.5 (C=C(5)), 143.8 (Ar, C).

νmax(film)/cm⁻¹: 3072 (s), 1638 (m), 1428 (m), 1113 (s), 849 (m), 702 (s). m/z (ES): 639.1394 (M+Na) . Calculated value for C30H41BrO3SSi2+Na+: 639.1391 (0.5 ppm).

General procedure for the cyclisation reaction

The acetyl 12a-e were dissolved in dry DCM and the reaction mixture cooled to -78°C. The Lewis acid was added and the reaction mixture stirred for 1h. It was then filtered through a pod of silica gel using 25% EtOAc in Hexane or Pet. Ether as eluent. The filtrate was concentrated in vacuo and purification was done by column chromatography (0-5% EtOAc in hexane gradient on silica gel). The diastereomers were not separated, but where it was possible the signals in the NMR-spectrum are reported separately for the different diastereomers. Diastereomeric ratio is measured from the ¹H-NMR spectrum of the mixture.
H), δ(C125 MHz; CDCl3): 19.3 (Si-C-CH3), 26.8 (Si-C-CH3), 42.6 (CH(Ar)-CH2), 66.8 (TBDPSO-CH2), 79.8 (O-CH-Ar), 82.1 (O-C=C=), 106.0 (C=C=CH2), 121.3 (Ar-C), 127.6 (Ar-CH), 127.7 (Ar-CH), 127.8 (Ar-CH), 129.6 (Ar-CH), 131.3 (Ar-CH), 133.5 (Ar-CH2), 135.6 (Ar-CH2), 135.7 (Ar-CH1), 140.9 (Ar-C), 148.7 (C=C=CH2).

(R*, R*)-13a (trans): δ(C125 MHz; CDCl3): 1.07 (9H, s, Si-C-CH3), 2.50-2.56 (1H, m, CH(Ar)-CH2), 3.01 (1H, dddd, J=2.0, 2.0, 6.8, 15.6 Hz, CH(Ar)-CH3), 2.87 (1H, dd, J=5.0, 10.8 Hz, TBDPSO-CH2), 3.81 (1H, dd, J=5.0, 10.8 Hz, TBDPSO-CH2), 4.68-4.72 (1H, m, O-CH-CH2), 4.97 (1H, dd, J=2.1, 4.2 Hz, C=C=CH2), 5.06-5.09 (2H, m, O-CH-Ar + CH=CH2), 7.20-7.22 (2H, m, Ar-H), 7.34-7.44 (6H, m, Ar-H), 7.45-7.48 (2H, m, Ar-H), 7.70-7.73 (4H, m, Ar-H). δ(C75 MHz; CDCl3): 19.3 (Si-C-CH3), 26.8 (Si-C-CH3), 41.5 (CH(Ar)-CH2), 66.8 (TBDPSO-CH2), 79.0 (O-CH-Ar), 81.8 (O-C=C=CH2), 121.1 (Ar-CH2), 127.5 (Ar-CH), 127.6 (Ar-CH), 129.6 (Ar-CH), 131.4 (Ar-CH3), 133.4 (Ar-C), 133.5 (Ar-C), 135.6 (Ar-CH), 135.7 (Ar-CH), 141.8 (Ar-C), 148.1 (C=C=CH2).

vmax(film)/cm⁻¹: 3072 (m), 2927 (s), 1665 (w), 1470 (m), 1428 (m), 1113 (s), 892 (m), 702 (s).

5-(3-Bromophenyl)-2-((t-butyldiphenylsilyloxy)methyl)-3-methylene-tetrahydrofuran (13b)
12b (0.9 g, 1.5 mmol, 1.0 eq) with TMSNTf2 (1.0 g, 2.9 mmol, 2.0 eq) gave the title compound 13b (71 mg, 9 %) as a colourless oil. Diastereomeric ratio cis:trans was 1:7.1.

(R*, S*)-13b (cis): δ(C125 MHz; CDCl3): 1.08 (9H, s, Si-C-CH3), 2.51-2.60 (1H, m, CH(Ar)-CH2), 3.04 (1H, dddd, J=1.9, 3.7, 6.8, 15.5 Hz, CH(Ar)-CH3), 3.67-3.86 (2H, m, TBDPSO-CH2), 4.72 (1H, br s, O-CH=C=), 4.96-4.98 (1H, m, C=C=CH2), 5.06-5.12 (2H, m, O-CH-Ar + C=C=CH2), 7.29-7.43 (10H, m, Ar-H), 7.70-7.75 (14H, m, Ar-H), δ(C75 MHz; CDCl3): 19.2 (Si-C-CH3), 26.8 (Si-C-CH3), 42.5 (CH(Ar)-CH2), 66.8 (TBDPSO-CH2), 79.5 (O-CH-Ar), 81.9 (O-C=C=CH2), 106.0 (C=C=CH2), 121.4 (Ar-C), 125.4 (Ar-CH), 127.6 (Ar-CH), 127.7 (Ar-CH), 129.7 (Ar-CH), 129.8 (Ar-CH), 131.0 (Ar-CH), 131.3 (Ar-C), 133.2 (Ar-C), 133.3 (Ar-C), 135.5 (Ar-CH), 142.5 (Ar-C), 148.5 (C=C=CH2).

vmax(film)/cm⁻¹: 3072 (m), 2927 (s), 1665 (w), 1470 (m), 1428 (m), 1113 (s), 892 (m), 702 (s). m/z (ES): 529.1165 (M+Na`). Calculated value for C28H31BrO2SiNa+: 529.1169 (-0.7 ppm).

5-(5-((t-Butyldiphenylsilyloxy)methyl)-4-methylene-tetrahydrofuran-2-yl)thiophene-3-carbonitrile (13c)
12c (0.17 g, 0.3 mmol, 1.0 eq) with TMSNTf2 (0.2 g, 0.6 mmol, 2.0 eq) gave the title compound 13c (52 mg, 39 %) as a yellow oil. Diastereomeric ratio cis:trans was 2.3:1.

(R*, S*)-13d (cis): δ(C125 MHz; CDCl3): 1.07 (9H, s, Si-C-CH3), 2.64-2.71 (1H, m, CH(Ar)-CH2), 2.97 (1H, dd, J=5.6, 15.2 Hz, CH(Ar)-CH3), 3.77 (1H, dd, J=4.7, 10.8 Hz, TBDPSO-CH2), 3.84 (1H, dd, J=4.0, 10.8 Hz, TBDPSO-CH2), 4.54-4.58 (1H, m, O-CH=C=), 5.00-5.02 (1H, m, C=C=CH2), 5.12-5.15 (2H, m, O-CH-Ar + C=C=CH2), 7.14 (1H, dd, J=0.9, 1.3 Hz, Ar-H), 7.34-7.44 (6H, m, Ar-H), 7.67-7.73 (4H, m, Ar-H), 7.83 (1H, d, J=1.3 Hz, Ar-H), δ(C125 MHz; CDCl3): 19.3 (Si-C-CH3), 26.8 (Si-C-CH3), 42.5 (CH(Ar)-CH2), 66.5 (TBDPSO-CH2), 75.6 (O-CH-Ar), 82.4 (O-C=C=CH2), 106.8 (C=C=CH2), 115.2 (CN & Ar-C), 125.0 (Ar-CH), 127.6 (Ar-CH), 127.7 (Ar-CH), 129.6 (Ar-CH), 129.7 (Ar-CH), 133.2 (Ar-C), 133.4 (Ar-C), 134.8 (Ar-CH), 135.2 (Ar-C), 135.6 (Ar-CH), 135.7 (Ar-CH), 147.4 (C=C=CH2).

vmax(film)/cm⁻¹: 3072 (m), 2927 (s), 1665 (w), 1470 (m), 1428 (m), 1113 (s), 892 (m), 702 (s). m/z (ES): 529.1163 (M+Na`). Calculated value for C29H32BrO2SiNa+: 529.1169 (-1.1 ppm).
3-Bromo-5-(5-tert-butyldiphenylsilyloxy)methyl-4-methylene-tetrahydrofuran-2-ylthiophene (13d)

12d (0.20 g, 0.32 mmol, 1.0 eq) with TMSNTf₂ (0.23 g, 0.65 mmol, 2.0 eq) gave the title compound 13d (40 mg, 24 %) as a yellow oil. Diastereomeric ratio cis:trans was 1:1.1. Unfortunately this compound decomposed after recording of a 1H-NMR spectrum, so no other analysis were obtained.

\[ (R^* , S^*) ]-13c (cis): \delta_H(300 MHz; CDCl₃): 1.05 (9H, s, Si-C-CH₃), 2.65-2.71 (1H, m, Ar-H), 7.94 (1H, d, \( J=8.3 \) Hz, Ar-H), 8.01 (1H, dd, \( J=1.2, 7.0 \) Hz, Ar-H), 8.12 (1H, d, \( J=8.3 \) Hz, Ar-H). \delta_C(125 MHz; CDCl₃): 19.3 (Si-C-CH₃), 26.9 (Si-C-CH₃), 41.7 (Ar-CH₃), 66.7 (TBDPSO-CH₂), 77.4 (O-C=CH₂), 106.3 (O-CH=CH₂), 110.5 (C=CH₂), 122.5 (Ar-CH), 123.4 (Ar-CH), 125.4 (Ar-CH), 125.8 (Ar-CH), 126.9 (Ar-CH), 127.7 (Ar-CH), 128.4 (Ar-CH), 129.0 (Ar-CH), 129.5 (Ar-CH), 130.8 (Ar-C), 131.4 (Ar-C), 133.4 (Ar-C), 133.6 (Ar-C), 133.7 (Ar-C), 134.0 (Ar-C), 135.7 (Ar-CH), 135.8 (Ar-CH), 146.5 (C=CH₂).

\[ (R^* , R^*) ]-13c (trans): \delta_H(300 MHz; CDCl₃): 1.06 (9H, s, Si-C-CH₃), 2.65-2.71 (1H, m, CH-CH₃), 3.02-3.06 (2H, m, TBDPSO-CH₂), 3.16 (1H, dd, \( J=8.3 \) Hz, Ar-H), 7.94 (1H, d, \( J=8.3 \) Hz, Ar-H), 8.01 (1H, dd, \( J=1.2, 7.0 \) Hz, Ar-H), 8.12 (1H, d, \( J=8.3 \) Hz, Ar-H). \delta_C(125 MHz; CDCl₃): 19.3 (Si-C-CH₃), 26.9 (Si-C-CH₃), 41.7 (CH-CH₃), 66.7 (TBDPSO-CH₂), 77.4 (O-CH=CH₂), 81.6 (O-CH=CH₂), 105.9 (C=CH₂), 122.5 (Ar-CH), 123.4 (Ar-CH), 125.4 (Ar-CH), 125.8 (Ar-CH), 126.9 (Ar-CH), 127.7 (Ar-CH), 128.4 (Ar-CH), 129.0 (Ar-CH), 129.5 (Ar-CH), 130.8 (Ar-C), 131.4 (Ar-C), 133.4 (Ar-C), 133.6 (Ar-C), 133.7 (Ar-C), 134.0 (Ar-C), 135.7 (Ar-CH), 135.8 (Ar-CH), 146.5 (C=CH₂).

5-(1-Naphthyl)-2-(5-tert-butyldiphenylsilyloxy)methyl-3-methylene-tetrahydrofuran (13e)

12e (0.30 g, 0.5 mmol, 1.0 eq) with TMSNTf₂ (0.37 g, 1.0 mmol, 2.0 eq) gave the title compound 13e (45 mg, 18 %) as a colourless oil. Diastereomeric ratio cis:trans was 1:4:1.

\[ (R^* , S^*) ]-13e (cis): \delta_H(300 MHz; CDCl₃): 1.10 (9H, s, Si-C-CH₃), 2.61-2.74 (1H, m, CH-CH₃), 3.83-4.00 (2H, m, TBDPSO-CH₂), 4.68 (1H, br s, O-CH₂-C), 5.05 (1H, s, CH-CH₃), 5.13 (1H, s, C=CH₂), 5.89 (1H, dd, \( J=5.3 \) Hz, Ar-H), 7.72-7.79 (5H, m, Ar-H), 7.94 (1H, d, \( J=8.3 \) Hz, Ar-H), 8.10 (1H, dd, \( J=1.2, 7.0 \) Hz, Ar-H), 8.12 (1H, d, \( J=8.3 \) Hz, Ar-H). \delta_C(125 MHz; CDCl₃): 19.3 (Si-C-CH₃), 26.9 (Si-C-CH₃), 41.7 (Ar-CH₃), 66.7 (TBDPSO-CH₂), 77.4 (O-CH=CH₂), 81.6 (O-CH=CH₂), 105.9 (C=CH₂), 122.5 (Ar-CH), 123.4 (Ar-CH), 125.4 (Ar-CH), 125.8 (Ar-CH), 126.9 (Ar-CH), 127.7 (Ar-CH), 128.4 (Ar-CH), 129.0 (Ar-CH), 129.5 (Ar-CH), 130.8 (Ar-C), 131.4 (Ar-C), 133.4 (Ar-C), 133.6 (Ar-C), 133.7 (Ar-C), 134.0 (Ar-C), 135.7 (Ar-CH), 135.8 (Ar-CH), 146.5 (C=CH₂).

\[ (R^* , R^*) ]-13e (trans): \delta_H(500 MHz; CDCl₃): 1.16 (9H, s, Si-C-CH₃), 2.61-2.74 (1H, m, CH-CH₃), 3.83-4.00 (2H, m, TBDPSO-CH₂), 4.83 (1H, br s, O-CH₂-C), 5.01 (1H, s, C=CH₂), 5.08 (1H, s, C=CH₂), 5.08 (1H, s, C=CH₂), 5.89 (1H, t, \( J=7.0 \) Hz, O-CH₂-Ar), 7.32-7.49 (9H, m, Ar-H), 7.58-7.79 (5H, m, Ar-H), 7.72-7.79 (5H, m, Ar-H), 7.94 (1H, d, \( J=8.3 \) Hz, Ar-H), 8.01 (1H, dd, \( J=1.2, 7.0 \) Hz, Ar-H), 8.12 (1H, d, \( J=8.3 \) Hz, Ar-H). \delta_C(125 MHz; CDCl₃): 19.3 (Si-C-CH₃), 26.8 (Si-C-CH₃), 40.8 (CH₂-CH₂), 67.1 (TBDPSO-CH₂), 77.3 (O-CH-Ar), 81.7 (O-CH=CH₂), 106.3 (C=CH₂), 122.1 (Ar-CH), 123.2 (Ar-CH), 125.3 (Ar-CH), 125.5 (Ar-CH), 126.9 (Ar-CH), 127.7 (Ar-CH), 127.7 (Ar-CH), 128.4 (Ar-CH), 129.0 (Ar-CH), 129.5 (Ar-CH), 130.8 (Ar-C), 131.4 (Ar-C), 133.4 (Ar-C), 133.6 (Ar-C), 133.7 (Ar-C), 134.0 (Ar-C), 135.7 (Ar-CH), 135.8 (Ar-CH), 146.5 (C=CH₂).

5-(4-Bromophenyl)-2-((5-tert-butyldiphenylsilyloxy)methyl)-tetrahydrofuran-3-one (14)

13a (0.70 g, 1.4 mmol, 1 eq) was dissolved in DCM (15 mL) and cooled to -78°C. O₃ was passed through the solution until the colour changed to blue. Argon was then passed through for 30 min, the last 10 of which at r.t. PPh₃ (1.1 g, 4 mmol, 3 eq) was then added, and the reaction was stirred for 2 hours, before it was concentrated under reduced pressure. Purification by column chromatography (0-12% EtOAc in hexane gradient on silica gel) yielded title compound 14a (0.34 g, 48 %) and 14b (0.26 g, 37 %) as separated diastereomers (85 % total yield). 14a was a colourless oil, 14b a white solid. Mp 217-219°C (DCM).
(R<sup>+</sup>, S<sup>-</sup>)-14a (cis): J<sub>0</sub>(500 MHz; CDCl<sub>3</sub>): 1.02 (9H, s, Si-C-CH<sub>3</sub>), 2.51 (1H, dd, J<sup>z</sup>= 11.2, 17.5 Hz, CH(Ar)-CH<sub>2</sub>), 2.87 (1H, dd, J<sup>z</sup>=5.7, 17.5 Hz, CH(Ar)-CH<sub>2</sub>), 4.01 (2H, d, J<sup>z</sup>=2.3 Hz, TBDPSO-CH<sub>2</sub>), 4.06 (1H, t, J<sup>z</sup>=2.3 Hz, O-CH(CO)), 5.17 (1H, dd, J<sup>z</sup>=5.7, 11.2 Hz, O-CH(Ar)), 7.36-7.50 (10H, m, Ar-H), 7.66-7.72 (4H, m, Ar-H). δ<sub>0</sub>(100 MHz; CDCl<sub>3</sub>): 19.2 (Si-C-CH<sub>3</sub>), 26.7 (Si-C-CH<sub>3</sub>), 46.3 (CH(Ar)-CH<sub>2</sub>), 63.1 (TBDPSO-CH<sub>2</sub>), 76.9 (O-CH-Ar), 82.8 (O-CH-CO), 121.2 (Ar-C), 127.8 (Ar-CH), 131.7 (Ar-CH), 132.6 (Ar-C), 133.0 (Ar-C), 135.5 (Ar-CH), 135.6 (Ar-CH), 140.5 (Ar-C), 214.4 (CO). ν<sub>max</sub>(film)/cm<sup>-1</sup>: 3066 (m), 2931 (s), 1318 (Ar-CH), 132.4 (Ar-C), 132.8 (Ar-C), 135.5 (Ar-CH), 135.6 (Ar-CH), 140.5 (Ar-C), 214.4 (CO). δ<sub>max</sub>(film)/cm<sup>-1</sup>: 3068 (m).

(5-(4-Bromophenyl)-2-(hydroxymethyl)-tetrahydropyran-3-one (15)

NaBH(OAc)<sub>3</sub> (0.23 g, 1 mmol, 5 eq) was dissolved in MeCN (4 mL). After cooling the resulting solution to 0°C, AcOH (0.12 mL, 2 mmol, 10 eq ) was added. The ketone 15 (59 mg, 0.2 mmol, 1 eq) dissolved in MeCN (3 mL) was added to the cooled solution and stirred at 0°C for 1h. MeOH (3 x 8 mL) was subsequently added, with volatiles removed under reduced pressure between each portion added. Purification by column chromatography (0-50% EtOAc in hexane gradient on silica gel) yielded title compound 15 (70 mg, 33%) as a white solid. Mp 96-97°C (CDCl<sub>3</sub>). C<sub>23</sub>H<sub>20</sub>BrO<sub>3</sub>Si: 451.0365 (-0.4 ppm).

(R<sup>+</sup>, R<sup>-</sup>)-14b (trans): δ<sub>0</sub>(500 MHz; CDCl<sub>3</sub>): 1.05 (9H, s, Si-C-CH<sub>3</sub>), 2.55 (1H, dd, J<sup>z</sup>=1.0, 8.7, 18.0 Hz, CH(Ph)-CH<sub>2</sub>), 2.96 (1H, dd, J<sup>z</sup>=7.0, 18.0 Hz, CH(Ph)-CH<sub>2</sub>), 3.98 (2H, dd, J<sup>z</sup>=2.3, 11.1 Hz, TBDPSO-CH<sub>2</sub>), 4.07 (1H, dd, J<sup>z</sup>=2.3, 11.1 Hz, TBDPSO-CH<sub>2</sub>), 5.20 (1H, br t, J<sup>z</sup>=2.3 Hz, O-CH-CO), 5.69 (1H, dd, J<sup>z</sup>=7.0, 8.7 Hz, O-CH(Ar)), 7.27 (2H, d, J<sup>z</sup>=8.4 Hz, Ar-H), 7.38-7.46 (6H, m, Ar-H), 7.53 (2H, d, J<sup>z</sup>=8.4 Hz, Ar-H), 7.65-7.72 (4H, m, Ar-H). δ<sub>0</sub>(125 MHz; CDCl<sub>3</sub>): 19.2 (Si-C-CH<sub>3</sub>), 26.7 (Si-C-CH<sub>3</sub>), 45.1 (CH(Ar)-CH<sub>2</sub>), 65.4 (TBDPSO-CH<sub>2</sub>), 78.4 (O-CH-Ar), 81.5 (O-CH-CO), 125.9 (Ar-C) 127.5 (Ar-CH), 127.8 (Ar-CH), 129.9 (Ar-CH), 131.8 (Ar-CH), 132.4 (Ar-C), 132.8 (Ar-C), 135.5 (Ar-CH), 135.6 (Ar-CH), 140.5 (Ar-C), 214.4 (CO). δ<sub>max</sub>(film)/cm<sup>-1</sup>: 3068 (m), 2926 (s), 1764 (s), 1428 (m), 1399 (m), 1113 (s), 823 (m), 702 (s). m/z (EI): 451.0363 (M-tBu), calculated for C<sub>23</sub>H<sub>20</sub>BrO<sub>3</sub>Si: 451.0365 (-0.4 ppm).

5-(4-Bromophenyl)-2-(hydroxymethyl)-tetrahydropyran-3-one (16)

NaBH(OAc)<sub>3</sub> (0.23 g, 1 mmol, 5 eq) was dissolved in MeCN (4 mL). After cooling the resulting solution to 0°C, AcOH (0.12 mL, 2 mmol, 10 eq ) was added. The ketone 16 (55 mg, 93%) as a white solid. mp 105-106°C (CDCl<sub>3</sub>). C<sub>23</sub>H<sub>20</sub>BrO<sub>3</sub>Si: 451.0363 (M+), calculated value for C<sub>23</sub>H<sub>20</sub>BrO<sub>3</sub>Si: 451.0365 (-0.4 ppm).
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