

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.¹ 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 was 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-(*t*-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 r.t. for 48 h. It was then washed with brine (400 mL) and the aqueous layer extracted with DCM (2 x 400 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. ν_{\max} (KBr)/cm⁻¹: 3570 (m), 3072 (m), 2955 (s), 1638 (m), 1590 (w), 1473 (m), 1428 (s), 1249 (s), 1112 (s), 850 (s), 702 (s). δ_{H} (500 MHz; CDCl₃): -0.02 (9H, s, Si-CH₃), 1.07 (9H, s, Si-C-CH₃), 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, TBDPSO-CH₂), 3.74 (1H, dd, *J*=3.3, 10.3 Hz, TBDPSO-CH₂), 3.99-4.04 (1H, m, CH₂-CH), 4.68 (1H, br m, C=CH₂), 4.96 (1H, br m, C=CH₂), 7.37-7.47 (6H, m, Ar-H), 7.65-7.69 (4H, m, Ar-H); δ_{C} (125 MHz; CDCl₃): -1.4 (Si-CH₃), 19.2 (Si-C-CH₃), 23.3 (TMS-CH₂), 26.9 (Si-C-CH₃), 67.5 (TBDPSO-CH₂), 75.3 (CH₂-CH), 108.4 (C=CH₂), 127.8 (Ar-CH), 127.8 (Ar-CH), 129.8 (Ar-CH), 129.8 (Ar-CH), 133.1 (Ar-C), 133.2 (Ar-C), 135.6 (Ar-CH), 135.6 (Ar-CH), 145.4 (C=CH₂); *m/z* (ES): 435.2159 (M+Na⁺), calculated for C₂₄H₃₆O₂Si₂ + Na⁺: 435.2152 (1.6 ppm)

[Methoxy]([1-(*t*-butyldiphenylsilyloxy)methyl-2-[(trimethylsilyl)methyl]prop-2-en-1-yl)oxy)methyl]-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**: δ_{H} (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-CH), 4.74 (1H, br s, C=CH₂), 4.98 (1H, s, C=CH₂), 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). δ_{C} (125 MHz; CDCl₃): -1.2 (Si-CH₃), 19.2 (Si-C-CH₃), 22.8 (TMS-CH₂), 26.8 (Si-C-CH₃), 49.4 (O-CH₃), 66.7 (TBDPSO-CH₂), 80.1 (CH₂-CH), 98.0 (O-CH-O), 110.6 (C=CH₂), 127.0 (Ar-CH), 127.6 (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=CH₂).

The other diastereomer of **5**: δ_{H} (500 MHz; CDCl_3): -0.01 (9H, s, Si- CH_3), 1.00 (9H, s, Si-C- CH_3), 1.26 (1H, d, $J=14.2$ Hz, TMS- CH_2), 1.53 (1H, d, $J=14.2$ Hz, TMS- CH_2), 3.20 (3H, s, O- CH_3), 3.69-3.80 (2H, m, TBDPSO- CH_2), 4.09 (1H, dd, $J=3.5, 7.0$ Hz, CH_2 - CH), 4.75 (1H, br s, C= CH_2), 5.10 (1H, s, C= CH_2), 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). δ_{C} (125 MHz; CDCl_3): -1.2 (Si- CH_3), 19.1 (Si-C- CH_3), 23.1 (TMS- CH_2), 26.8 (Si-C- CH_3), 51.8 (O- CH_3), 67.1 (TBDPSO- CH_2), 81.1 (CH_2 - CH), 102.3 (O- CH -O), 110.0 (C= CH_2), 127.1 (Ar-CH), 127.6 (Ar-CH), 127.6 (Ar-CH), 128.2 (Ar-CH), 129.5 (Ar-CH), 129.6 (Ar-CH), 133.4 (Ar-C), 133.5 (Ar-C), 135.6 (Ar-CH), 135.7 (Ar-CH), 138.7 (Ar-C), 144.1 (C= CH_2).

ν_{max} (KBr)/ cm^{-1} : 3071 (m), 1637 (m), 1473 (m), 1428 (m), 1250 (s), 1112 (s), 849 (s), 702 (s). m/z (ES): 555.2725 (M+Na⁺), calculated for $\text{C}_{32}\text{H}_{44}\text{O}_3\text{Si}_2+\text{Na}^+$: 555.2727 (-0.4 ppm).

2-((*t*-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* and purification was performed by column chromatography (0-5% EtOAc in hexane gradient on silica gel) to yield title compound **6** (1.1 g, 72%) as a colourless oil. Diastereomeric ratio of *cis:trans* was 2:1. These diastereomers were separated with a second round of column chromatography (0-3% EtOAc in hexane gradient on silica gel) giving a **6a** (0.73 g, 48%) and **6b** (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**.

(**R***, **S***)-**6a** (*cis*): δ_{H} (500 MHz; CDCl_3): 1.07 (9H, s, Si-C- CH_3), 2.57-2.64 (1H, m, CH(Ar)- CH_2), 2.89 (1H, dd, $J=5.5, 15.1$ Hz, CH(Ar)- CH_2), 3.84 (1H, dd, $J=4.6, 10.6$ Hz, TBDPSO- CH_2), 3.89 (1H, dd, $J=4.3, 10.6$ Hz, TBDPSO- CH_2), 4.57-4.59 (1H, m, O- CH -C=), 4.93 (1H, dd, $J=5.5, 10.7$ Hz, O- CH -Ar), 5.01-5.02 (1H, m, C= CH_2), 5.10-5.11 (1H, m, C= CH_2), 7.27-7.46 (11H, m, Ar-H), 7.72-7.76 (4H, m, Ar-H). δ_{C} (125 MHz; CDCl_3): 19.3 (Si-C- CH_3), 26.8 (Si-C- CH_3), 42.5 (CH(Ar)- CH_2), 66.8 (TBDPSO- CH_2), 80.5 (O- CH -Ar), 82.0 (O- CH -C=), 105.7 (C= CH_2), 126.2 (Ar-CH), 127.6 (Ar-CH), 127.6 (Ar-CH), 128.3 (Ar-CH), 129.6 (Ar-CH), 129.6 (Ar-CH), 133.4 (Ar-C), 133.6 (Ar-C), 135.7 (Ar-CH), 135.8 (Ar-CH), 141.7 (Ar-C), 149.2 (C= CH_2).

(**R***, **R***)-**6b** (*trans*): δ_{H} (500 MHz; CDCl_3): 1.09 (9H, s, Si-C- CH_3), 2.57-2.67 (1H, m, CH(Ar)- CH_2), 3.04 (1H, dddd, $J=1.9, 3.7, 6.7, 15.6$ Hz, CH(Ar)- CH_2), 3.78-3.85 (2H, m, TBDPSO- CH_2), 4.74 (1H, br s, O- CH -C=), 4.99 (1H, dd, $J=2.1, 4.2$ Hz, C= CH_2), 5.10 (1H, dd, $J=2.1, 4.2$ Hz, C= CH_2), 5.15 (1H, t, $J=7.2$ Hz, O- CH -Ar), 7.28-7.45 (11H, m, Ar-H), 7.72-7.76 (4H, m, Ar-H). δ_{C} (125 MHz; CDCl_3): 19.3 (Si-C- CH_3), 26.8 (Si-C- CH_3), 41.6 (CH(Ar)- CH_2), 66.9 (TBDPSO- CH_2), 79.7 (O- CH -Ar), 81.7 (O- CH -C=), 106.0 (C= CH_2), 125.9 (Ar-CH), 127.6 (Ar-CH), 127.7 (Ar-CH), 128.3 (Ar-CH), 129.5 (Ar-CH), 129.6 (Ar-CH), 133.4 (Ar-C), 133.6 (Ar-C), 135.6 (Ar-C), 135.7 (Ar-CH), 135.8 (Ar-CH), 148.6 (C= CH_2).

ν_{max} (film)/ cm^{-1} : 3071 (m), 2931 (s), 1668 (m), 1428 (m), 1264 (m), 1112 (s), 892 (m), 700 (s). m/z (ES): 451.2089 (M+Na⁺), calculated for $\text{C}_{28}\text{H}_{32}\text{O}_2\text{Si}+\text{Na}^+$: 451.2069 (2.0 ppm).

2-((*t*-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 solution until the colour changed to blue. Argon was then passed through for 30 min, the last 10 of which at r.t. PPh_3 (0.5 g, 2.0 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 **7** (0.22 g, 78%) as a colourless oil. ν_{max} (film)/ cm^{-1} : 3070 (m), 2928 (s), 1763 (s), 1472 (w), 1428 (m), 1376(m), 1113 (s), 742 (m), 700(s). δ_{H} (500 MHz; CDCl_3): 1.03 (9H, s, Si-C- CH_3), 2.59 (1H, dd, $J=11.3, 17.5$ Hz, CH(Ar)- CH_2), 2.88 (1H, dd, $J=5.6, 17.5$ Hz, CH(Ar)- CH_2), 4.01 (2H, d, $J=2.4$ Hz, TBDPSO- CH_2), 4.07 (1H, t, $J=2.4$ Hz, O- CH -CO), 5.21 (1H, dd, $J=5.6, 11.3$ Hz, O- CH -Ar), 7.34-7.43 (9H, m, Ar-H), 7.53 (2H, dd, $J=1.9, 7.6$ Hz, Ar-H), 7.67-7.76 (4H, m, Ar-H). δ_{C} (125 MHz; CDCl_3): 19.2 (Si-C- CH_3), 26.7 (Si-C- CH_3), 46.5 (CH(Ar)- CH_2), 63.2 (TBDPSO- CH_2), 77.6 (O- CH -Ar), 82.9 (O- CH -CO), 126.3 (Ar-CH), 127.7 (Ar-CH), 127.6 (Ar-CH), 128.3 (Ar-CH), 129.6 (Ar-CH), 129.7 (Ar-CH), 129.8 (Ar-CH), 132.7 (Ar-C), 133.1 (Ar-C), 135.6 (Ar-CH), 135.7 (Ar-CH), 140.5 (Ar-C), 213.9 (CO). m/z (EI): 373.1247 (M-tBu), calculated for $\text{C}_{23}\text{H}_{21}\text{O}_3\text{Si}$: 373.1260 (-3.5 ppm).

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

7 (0.20 g, 0.46 mmol, 1 eq) was dissolved in DMF (5 mL) and added *p*-toluenesulfonic acid (0.1 g, 0.5 mmol, 1.1 eq). This mixture was stirred at 60°C for 4 days. The reaction was then quenched with saturated aqueous NaHCO_3 (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_{\max} (film)/ cm^{-1} : 3452 (br, s), 2924 (s), 1759 (s), 1497 (w), 1457 (m), 1378 (m), 1106 (s), 752 (m), 700(s). δ_{H} (500 MHz; CDCl_3): 2.04 (1H, t, $J=6.4$ Hz, OH), 2.56 (1H, dd, $J=11.0, 18.0$ Hz, CH(Ar)-CH₂), 2.89 (1H, dd, $J=5.8, 18.0$ Hz, CH(Ar)-CH₂), 3.93-3.97 (2H, m, HO-CH₂), 4.06 (1H, t, $J=3.5$ Hz, O-CH-CO), 5.24 (1H, dd, $J=5.8, 11.0$ Hz, O-CH-Ar), 7.35-7.46 (5H, m, Ar-H). δ_{C} (125 MHz; CDCl_3): 45.3 (CH(Ar)-CH₂), 61.6 (HO-CH₂), 77.7 (O-CH-Ar), 82.3 (O-CH-CO), 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 $\text{C}_{11}\text{H}_{12}\text{O}_3$: 192.0786 (2.1 ppm).

2-(Hydroxymethyl)-5-phenyl-tetrahydrofuran-3-ol (**9**)

$\text{NaBH}(\text{OAc})_3$ (0.22 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 **8** (40 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 (0-5% MeOH in DCM gradient on silica gel) yielded title compound **9** (38 mg, 94%) as a white solid. mp 81-83°C (MeOH). ν_{\max} (film)/ cm^{-1} : 3369 (br, s), 2923 (s), 1494 (w), 1455 (m), 1216 (w), 1048 (s), 756 (m), 699(s). δ_{H} (500 MHz; d_4 -MeOH): 1.94 (1H, ddd, $J=5.9, 10.6, 13.2$ Hz, CH(Ph)-CH₂), 2.19 (1H, ddd, $J=1.6, 5.4, 13.2$ Hz, CH(Ph)-CH₂), 3.65 (1H, dd, $J=5.3, 11.8$ Hz, HO-CH₂), 3.69 (1H, dd, $J=5.3, 11.8$ Hz, HO-CH₂), 3.94 (1H, dt, $J=2.4, 5.4$ Hz, O-CH-CHOH), 4.31-4.33 (1H, m, HO-CH), 5.12 (1H, dd, $J=5.4, 10.6$ Hz, O-CH-Ph), 7.23-7.27 (1H, m, Ar-H), 7.30-7.33 (2H, m, Ar-H), 7.38-7.40 (2H, m, Ar-H). δ_{C} (125 MHz; CDCl_3): 45.0 (CH(Ph)-CH₂), 64.1 (HO-CH₂), 74.5 (HO-CH), 81.7 (O-CH-CHOH), 89.2 (O-CH-Ph), 127.2 (Ar-CH), 128.6 (Ar-CH), 129.4 (Ar-CH), 143.2 (Ar-C). m/z (EI): 194.0938 (M^+), calculated for $\text{C}_{11}\text{H}_{14}\text{O}_3$: 194.0943 (-2.6 ppm).

Separation of enantiomers was done at GlaxoSmithKline with 15% EtOH in C7 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.

General procedure for the synthesis of [methoxy-[(1-[*t*-butyldiphenylsilyloxy]methyl-2-[(trimethylsilyl)methyl]prop-2-en-1-yl)oxy]methyl]aromatics

3 was dissolved in dry DCM, added Et_3N and cooled to 0°C. The 2-(chloro-(methoxy)methyl)aromatic (1.2 eq) was added and the reaction mixture stirred for 1h before it was allowed to go to r.t. and stir over night. The solvent was then removed *in vacuo*, the residue dissolved in EtOAc and filtered through a plug of aluminium oxide. Solvent was again removed *in vacuo* 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.

4-Bromo-[methoxy[(1-[*t*-butyldiphenylsilyloxy]-methyl-2-[(trimethylsilyl)methyl]prop-2-en-1-yl)oxy]-methyl]-benzene (**12a**)

3 (3.5 g, 8.5 mmol, 1.0 eq) dissolved in DCM (35 mL) with Et_3N (1.4 mL, 10 mmol, 1.2 eq) and **11a** gave the title compound **12a** (2.6 g, 50 %) as a colourless oil.

One diastereomer of **12a**: δ_{H} (500 MHz; CDCl_3): 0.02 (9H, s, Si-CH₃), 1.08 (9H, s, Si-C-CH₃), 1.26 (1H, d, $J=14.3$ Hz, TMS-CH₂), 1.48 (1H, d, $J=14.3$ Hz, TMS-CH₂), 3.16 (3H, s, O-CH₃), 3.67-3.82 (2H, m, TBDPSO-CH₂), 4.33 (1H, dd, $J=5.1, 5.2$ Hz, CH₂-CH), 4.76 (1H, br s, C=CH₂), 4.96 (1H, s, C=CH₂), 5.60 (1H, s, O-CH-O), 7.32-7.46 (8H, m, Ar-H), 7.48-7.55 (2H, m, Ar-H), 7.74-7.80 (4H, m, Ar-H). δ_{C} (125 MHz; CDCl_3): -1.2 (Si-CH₃), 19.2 (Si-C-CH₃), 22.8 (TMS-CH₂), 26.8 (Si-C-CH₃), 49.3 (O-CH₃), 66.6 (TBDPSO-CH₂), 80.2 (CH₂-CH), 97.3 (O-CH-O), 110.6 (C=CH₂), 122.2 (Ar-C), 127.6 (Ar-CH), 127.7 (Ar-CH), 128.8 (Ar-CH), 129.6 (Ar-CH), 129.7 (Ar-CH), 131.2 (Ar-CH), 133.5 (Ar-C), 133.6 (Ar-C), 135.7 (Ar-CH), 135.7 (Ar-CH), 137.6 (Ar-C), 143.1 (C=CH₂).

The other diastereomer of **12a**: δ_{H} (500 MHz; CDCl_3): 0.03 (9H, s, Si-CH₃), 1.02 (9H, s, Si-C-CH₃), 1.26 (1H, d, $J=14.3$ Hz, TMS-CH₂), 1.54 (1H, d, $J=14.3$ Hz, TMS-CH₂), 3.20 (3H, s, O-CH₃), 3.67-3.82 (2H, m, TBDPSO-CH₂), 4.08 (1H, dd, $J=3.3, 7.2$ Hz, CH₂-CH), 4.76 (1H, br s, C=CH₂), 5.10 (1H, s, C=CH₂), 5.77 (1H, s, O-CH-O), 7.32-7.46 (8H, m, Ar-H), 7.48-7.55 (2H, m, Ar-H), 7.62-7.67 (4H, m, Ar-H). δ_{C} (125 MHz; CDCl_3): -1.3 (Si-CH₃), 19.1 (Si-C-CH₃), 23.2 (TMS-CH₂), 26.8 (Si-C-CH₃), 51.6 (O-CH₃), 67.2 (TBDPSO-CH₂), 81.4 (CH₂-CH), 101.6 (O-CH-O), 110.1 (C=CH₂), 122.3 (Ar-C), 127.7 (Ar-CH), 127.8 (Ar-CH), 128.9 (Ar-CH), 129.7 (Ar-CH), 129.8 (Ar-CH), 131.3 (Ar-CH), 133.3 (Ar-C), 133.4 (Ar-C), 135.6 (Ar-CH), 135.6 (Ar-CH), 137.8 (Ar-C), 143.9 (C=CH₂).

ν_{\max} (film)/ cm^{-1} : 3072 (m), 2956 (s), 1592 (m), 1428 (m), 1250 (m), 1113 (s), 850 (m), 702 (s), m/z (ES): 633.1840 ($\text{M}+\text{Na}^+$), calculated value for $\text{C}_{32}\text{H}_{43}\text{BrO}_3\text{Si}_2+\text{Na}$: 633.1832 (1.3 ppm).

3-Bromo-[methoxy[(1-[*t*-butyldiphenylsilyloxy]-methyl-2-[(trimethylsilyl)methyl]-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**: δ_{H} (500 MHz; CDCl₃): -0.01 (9H, s, Si-CH₃), 1.06 (9H, s, Si-C-CH₃), 1.23 (1H, d, $J=14.1$ Hz, TMS-CH₂), 1.48 (1H, d, $J=14.1$ Hz, TMS-CH₂), 3.14 (3H, s, O-CH₃), 3.66-3.77 (2H, m, TBDPSO-CH₂), 4.30 (1H, dd, $J=4.1, 6.1$ Hz, CH₂-CH), 4.74 (1H, s, C=CH₂), 4.94 (1H, s, C=CH₂), 5.58 (1H, s, O-CH-O), 7.25 (1H, t, $J=7.8$ Hz, Ar-H), 7.37-7.47 (8H, m, Ar-H), 7.72-7.77 (5H, m, Ar-H). δ_{C} (125 MHz; CDCl₃): -1.2 (Si-CH₃), 19.2 (Si-C-CH₃), 22.8 (TMS-CH₂), 26.8 (Si-C-CH₃), 49.4 (O-CH₃), 66.7 (TBDPSO-CH₂), 80.3 (CH₂-CH), 97.0 (O-CH-O), 110.6 (C=CH₂), 122.4 (Ar-C), 125.4 (Ar-CH), 127.6 (Ar-CH), 127.7 (Ar-CH), 129.6 (Ar-CH), 129.7 (Ar-CH), 129.9 (Ar-CH), 130.1 (Ar-CH), 131.3 (Ar-CH), 133.2 (Ar-C), 133.4 (Ar-C), 135.7 (Ar-CH), 135.7 (Ar-CH), 140.4(Ar-C), 143.0 (C=CH₂).

The other diastereomer of **12b**: δ_{H} (500 MHz; CDCl₃): 0.00 (9H, s, Si-CH₃), 0.98 (9H, s, Si-C-CH₃), 1.23 (1H, d, $J=14.1$ Hz, TMS-CH₂), 1.51 (1H, d, $J=14.1$ Hz, TMS-CH₂), 3.17 (3H, s, O-CH₃), 3.66-3.77 (2H, m, TBDPSO-CH₂), 4.08 (1H, dd, $J=3.1, 7.5$ Hz, CH₂-CH), 4.74 (1H, s, C=CH₂), 5.07 (1H, s, C=CH₂), 5.78 (1H, s, O-CH-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), 7.60-7.63 (4H, m, Ar-H), 7.69 (1H, t, $J=1.6$ Hz). δ_{C} (125 MHz; CDCl₃): -1.3 (Si-CH₃), 19.1 (Si-C-CH₃), 23.2 (TMS-CH₂), 26.8 (Si-C-CH₃), 51.5 (O-CH₃), 67.2 (TBDPSO-CH₂), 81.6 (CH₂-CH), 101.5 (O-CH-O), 110.1 (C=CH₂), 122.3 (Ar-C), 125.8 (Ar-CH), 127.6 (Ar-CH), 127.7 (Ar-CH), 129.7 (Ar-CH), 129.8 (Ar-CH), 129.9 (Ar-CH), 130.3 (Ar-CH), 131.4 (Ar-CH), 133.2 (Ar-C), 133.4 (Ar-C), 135.6 (Ar-CH), 135.6 (Ar-CH), 141.1 (Ar-C), 143.9 (C=CH₂).

ν_{max} (film)/cm⁻¹: 3072 (m), 2932 (s), 1473 (m), 1428 (m), 1199 (m), 1112 (s), 850 (m), 702 (s). m/z (ES): 633.1833 (M+Na⁺), calculated value for C₃₂H₄BrO₃Si₂ + Na⁺: 633.1832 (0.2 ppm).

5-[Methoxy[(1-[*t*-butyldiphenylsilyloxy]methyl-2-[(trimethylsilyl)methyl]prop-2-en-1-yl)oxy]methyl]-thiophene-3-carbonitrile (12c)

2 (0.9 g, 2.2 mmol, 1.0 eq) dissolved in DCM (40 mL) with Et₃N (0.4 mL, 2.7 mmol, 1.2 eq) and **11c** gave the title compound **12c** (0.22 g, 18%) as an orange oil.

One diastereomer of **12c**: δ_{H} (500 MHz; CDCl₃): -0.01 (9H, s, Si-CH₃), 0.98 (9H, s, Si-C-CH₃), 1.19 (1H, d, $J=14.1$ Hz, TMS-CH₂), 1.49 (1H, d, $J=14.1$ Hz, TMS-CH₂), 3.22 (3H, s, O-CH₃), 3.66-3.71 (1H, m, TBDPSO-CH₂), 3.76 (1H, dd, $J=3.0, 11.2$ Hz, TBDPSO-CH₂), 4.10 (1H, dd, $J=2.9, 8.1$ Hz, CH₂-CH), 4.73 (1H, s, C=CH₂), 5.04 (1H, s, C=CH₂), 6.07 (1H, d, $J=0.8$ Hz, O-CH-O), 7.25-7.26 (1H, m, Ar-H), 7.34-7.46 (6H, m, Ar-H), 7.70-7.74 (4H, m, Ar-H), 7.92 (1H, d, $J=1.4$ Hz, Ar-H). δ_{C} (125 MHz; CDCl₃): -1.3 (Si-CH₃), 19.1 (Si-C-CH₃), 23.2 (TMS-CH₂), 26.7 (Si-C-CH₃), 51.3 (O-CH₃), 67.4 (TBDPSO-CH₂), 82.1 (CH₂-CH), 98.4 (O-CH-O), 110.3 (Ar-C), 110.6 (C=CH₂), 115.2 (CN), 126.6 (Ar-CH), 127.7 (Ar-CH), 127.7 (Ar-CH), 129.7 (Ar-CH), 129.8 (Ar-CH), 133.1 (Ar-C), 133.4 (Ar-C), 135.5 (Ar-CH), 135.6 (Ar-CH), 135.7 (Ar-CH), 143.2(C=CH₂), 145.2 (Ar-C).

The other diastereomer of **12c**: δ_{H} (500 MHz; CDCl₃): -0.01 (9H, s, Si-CH₃), 1.05 (9H, s, Si-C-CH₃), 1.20 (1H, d, $J=14.0$ Hz, TMS-CH₂), 1.45 (1H, d, $J=14.0$ Hz, TMS-CH₂), 3.24 (3H, s, O-CH₃), 3.66-3.71 (2H, m, TBDPSO-CH₂), 4.24-4.26 (1H, m, CH₂-CH), 4.76 (1H, s, C=CH₂), 4.96 (1H, s, C=CH₂), 5.78 (1H, d, $J=0.8$ Hz, O-CH-O), 7.25-7.26 (1H, m, Ar-H), 7.34-7.46 (6H, m, Ar-H), 7.61-7.62 (4H, m, Ar-H), 7.89 (1H, d, $J=1.4$ Hz, Ar-H). δ_{C} (125 MHz; CDCl₃): -1.3 (Si-CH₃), 19.2 (Si-C-CH₃), 22.9 (TMS-CH₂), 26.8 (Si-C-CH₃), 49.3 (O-CH₃), 66.3 (TBDPSO-CH₂), 80.6 (CH₂-CH), 94.2 (O-CH-O), 110.1 (Ar-C), 110.2 (C=CH₂), 115.2 (CN), 126.5 (Ar-CH), 127.7 (Ar-CH), 127.7 (Ar-CH), 129.8 (Ar-CH), 129.8 (Ar-CH), 133.0 (Ar-C), 133.3 (Ar-C), 135.5 (Ar-CH), 135.6 (Ar-CH), 135.7 (Ar-CH), 142.5 (C=CH₂), 144.9 (Ar-C).

ν_{max} (film)/cm⁻¹: 3072 (m), 2931 (s), 2231 (m), 1686 (m), 1428 (m), 1250 (s), 1113 (s), 851 (m), 702 (s). m/z (ES): 564.2432 (M + H⁺) Calculated value for C₃₁H₄₁NO₃SSi₂+H⁺: 564.2424 (1.4 ppm).

4-Bromo-2-[methoxy[(1-[*t*-butyldiphenylsilyloxy]methyl-2-[(trimethylsilyl)methyl]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, 30%) as an orange oil.

One diastereomer of **12d**: δ_{H} (500 MHz; CDCl₃): 0.03 (9H, s, Si-CH₃), 1.09 (9H, s, Si-C-CH₃), 1.27 (1H, d, $J=14.3$ Hz, TMS-CH₂), 1.49 (1H, d, $J=14.3$ Hz, TMS-CH₂), 3.28 (3H, s, O-CH₃), 3.71-3.80 (2H, m, TBDPSO-CH₂), 4.29 (1H, dd, $J=4.1, 6.0$ Hz, CH₂-CH), 4.76 (1H, s, C=CH₂), 5.03 (1H, s, C=CH₂), 5.80 (1H, s, O-CH-O),

7.07 (1H, s, Ar-H), 7.23 (1H, s, Ar-H), 7.36-7.45 (6H, m, Ar-H), 7.74-7.79 (4H, m, Ar-H). δ_c (125 MHz; CDCl₃): -1.3 (Si-CH₃), 19.2 (Si-C-CH₃), 22.9 (TMS-CH₂), 26.8 (Si-C-CH₃), 49.2 (O-CH₃), 66.4 (TBDPSO-CH₂), 80.4 (CH₂-CH), 94.5 (O-CH-O), 109.2 (Ar-C), 110.7 (C=CH₂), 123.1 (Ar-CH), 127.7 (Ar-CH), 127.7 (Ar-CH), 128.2 (Ar-CH), 129.7 (Ar-CH), 129.7 (Ar-CH), 133.2 (Ar-C), 133.4 (Ar-C), 135.6 (Ar-CH), 135.7 (Ar-CH), 142.7 (C=CH₂), 143.6 (Ar-C).

The other diastereomer of **12d**: δ_H (500 MHz; CDCl₃): 0.03 (9H, s, Si-CH₃), 1.03 (9H, s, Si-C-CH₃), 1.27 (1H, d, J =14.2 Hz, TMS-CH₂), 1.53 (1H, d, J =14.2 Hz, TMS-CH₂), 3.25 (3H, s, O-CH₃), 3.71-3.80 (2H, m, TBDPSO-CH₂), 4.15 (1H, dd, J =2.6, 7.1 Hz, CH₂-CH), 4.78 (1H, s, C=CH₂), 5.09 (1H, s, C=CH₂), 6.07 (1H, s, O-CH-O), 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_c (125 MHz; CDCl₃): -1.2 (Si-CH₃), 19.1 (Si-C-CH₃), 23.2 (TMS-CH₂), 26.8 (Si-C-CH₃), 51.1 (O-CH₃), 67.3 (TBDPSO-CH₂), 81.7 (CH₂-CH), 98.6 (O-CH-O), 109.0 (Ar-C), 110.2 (C=CH₂), 123.1 (Ar-CH), 127.7 (Ar-CH), 127.7 (Ar-CH), 128.2 (Ar-CH), 129.7 (Ar-CH), 129.7 (Ar-CH), 133.3 (Ar-C), 133.5 (Ar-C), 135.6 (Ar-CH), 137.6 (Ar-CH), 143.5 (C=CH₂), 143.8 (Ar-C).

ν_{\max} (film)/cm⁻¹: 3072 (m), 2956 (s), 1638 (m), 1428 (m), 1249 (m), 1113 (s), 849 (m), 702 (s). m/z (ES): 639.1394 (M+Na⁺). Calculated value for C₃₀H₄₁BrO₃SSi₂+Na⁺: 639.1391 (0.5 ppm).

1-[Methoxy[(1-*t*-butyldiphenylsilyloxy)-methyl-2-[(trimethylsilyl)methyl]prop-2-en-1-yl)oxy]-methyl]-naphthalene (**12e**)

3 (3.0 g, 7.3 mmol, 1.0 eq) dissolved in DCM (35 mL) with Et₃N (1.2 mL, 10 mmol, 1.2 eq) and **11e** gave the title compound **12e** (1.6 g, 38 %) as a colourless oil.

One diastereomer of **12e**: δ_H (500 MHz; CDCl₃): 0.00 (9H, s, Si-CH₃), 1.12 (9H, s, Si-C-CH₃), 1.32 (1H, d, J =14.3 Hz, TMS-CH₂), 1.47 (1H, d, J =14.3 Hz, TMS-CH₂), 3.13 (3H, s, O-CH₃), 3.81 (1H, dd, J = 3.9, 10.9 Hz, TBDPSO-CH₂), 3.86 (1H, dd, J =6.7, 10.9 Hz, TBDPSO-CH₂), 4.46 (1H, dd, J =3.9, 6.7 Hz, CH₂-CH), 4.75 (1H, s, C=CH₂), 4.99 (1H, s, C=CH₂), 6.12 (1H, s, O-CH-O), 7.34-7.50 (9H, m, Ar-H), 7.75-7.79 (4H, m, Ar-H), 7.82-7.86 (4H, m, Ar-H). δ_c (125 MHz; CDCl₃): -1.2 (Si-CH₃), 19.2 (Si-C-CH₃), 22.8 (TMS-CH₂), 26.8 (Si-C-CH₃), 50.0 (O-CH₃), 66.7 (TBDPSO-CH₂), 80.5 (CH₂-CH), 97.2 (O-CH-O), 110.6 (C=CH₂), 124.5 (Ar-CH), 124.8 (Ar-CH), 125.4 (Ar-CH), 125.5 (Ar-CH), 126.0 (Ar-CH), 127.6 (Ar-CH), 127.6 (Ar-CH), 128.4 (Ar-CH), 129.0 (Ar-CH), 129.6 (Ar-CH), 129.6 (Ar-C), 131.0 (Ar-C), 133.4 (Ar-C), 133.6 (Ar-C), 133.7 (Ar-C), 133.8 (Ar-C), 135.7 (Ar-CH), 135.7 (Ar-CH), 143.3 (C=CH₂).

The other diastereomer of **12e**: δ_H (500 MHz; CDCl₃): 0.02 (9H, s, Si-CH₃), 1.06 (9H, s, Si-C-CH₃), 1.37 (1H, d, J =14.3 Hz, TMS-CH₂), 1.58 (1H, d, J =14.3 Hz, TMS-CH₂), 3.21 (3H, s, O-CH₃), 3.75-3.80 (2H, m, TBDPSO-CH₂), 4.24 (1H, dd, J =4.0, 6.3 Hz, CH₂-CH), 4.80 (1H, d, C=CH₂), 5.16 (1H, s, C=CH₂), 6.32 (1H, s, O-CH-O), 7.34-7.50 (9H, m, Ar-H), 7.59-7.62 (4H, m, Ar-H), 7.66-7.68 (4H, m, Ar-H). δ_c (125 MHz; CDCl₃): -1.3 (Si-CH₃), 19.1 (Si-C-CH₃), 23.2 (TMS-CH₂), 26.7 (Si-C-CH₃), 52.0 (O-CH₃), 67.3 (TBDPSO-CH₂), 81.1 (CH₂-CH), 100.9 (O-CH-O), 110.1 (C=CH₂), 124.5 (Ar-CH), 124.8 (Ar-CH), 125.3 (Ar-CH), 125.5 (Ar-CH), 125.9 (Ar-CH), 127.5 (Ar-CH), 127.6 (Ar-CH), 128.3 (Ar-CH), 129.0 (Ar-CH), 129.5 (Ar-CH), 129.6 (Ar-C), 131.0 (Ar-C), 133.4 (Ar-C), 133.6 (Ar-C), 133.7 (Ar-C), 133.8 (Ar-C), 135.6 (Ar-CH), 135.6 (Ar-CH), 144.2 (C=CH₂).

ν_{\max} (film)/cm⁻¹: 3049 (m), 2955(s), 1468 (w), 1428 (m), 1248 (m), 1113 (s), 850 (m), 702 (s), m/z (ES): 605.2890 (M+Na⁺), calculated value for C₃₆H₄₆O₃Si₂+Na: 605.2883 (1.2 ppm).

General procedure for the cyclisation reaction

The acetals **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 pad 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.

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

12a (0.16 g, 0.26 mmol, 1.0 eq) with TMSNTf₂ (0.18 g, 0.52 mmol, 2.0 eq) gave the title compound **13a** (85 mg, 65 %) as a colourless oil. Diastereomeric ratio *cis:trans* was 1.3:1

(**R***, **S***)-**13a** (*cis*): δ_H (500 MHz; CDCl₃): 1.06 (9H, s, Si-C-CH₃), 2.51-2.57 (1H, m, CH(Ar)-CH₂), 2.88 (1H, dd, J =5.6, 15.1 Hz, CH(Ar)-CH₂), 3.82 (1H, dd, J =4.6, 10.7 Hz, TBDPSO-CH₂), 3.89 (1H, dd, J =4.0, 10.7 Hz, TBDPSO-CH₂), 4.55-4.58 (1H, m, O-CH-C=), 4.89 (1H, dd, J =5.5, 10.6 Hz, O-CH-Ar), 4.99-5.00 (1H, m, C=CH₂), 5.10-5.11 (1H, m, C=CH₂), 7.29-7.32 (2H, m, Ar-H), 7.35-7.45 (8H, m, Ar-H), 7.70-7.74 (4H, m, Ar-

H). δ_{C} (125 MHz; CDCl_3): 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-CH-C=), 106.0 (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), 133.3 (Ar-C), 133.5 (Ar-C), 135.6 (Ar-CH), 135.7 (Ar-CH), 140.9 (Ar-C), 148.7 (C=CH₂).

(R*, R*)-13a (trans): δ_{H} (500 MHz; CDCl_3): 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)-CH₂), 3.77 (1H, dd, $J=5.0, 10.8$ Hz, TBDPSO-CH₂), 3.81 (1H, dd, $J=4.0, 10.8$ Hz, TBDPSO-CH₂), 4.68-4.72 (1H, m, O-CH-C=), 4.97 (1H, dd, $J=2.1, 4.2$ Hz, C=CH₂), 5.06-5.09 (2H, m, O-CH-Ar + C=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_{C} (125 MHz; CDCl_3): 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-CH-C=), 106.3 (C=CH₂), 121.1 (Ar-CH), 127.5 (Ar-CH), 127.6 (Ar-CH), 127.6 (Ar-CH), 129.6 (Ar-CH), 131.4 (Ar-CH), 133.4 (Ar-C), 133.5 (Ar-C), 135.6 (Ar-CH), 135.7 (Ar-CH), 141.8 (Ar-C), 148.1 (C=CH₂).

ν_{max} (film)/ cm^{-1} : 3072 (m), 2930 (s), 1668 (w), 1590 (m), 1428 (m), 1113 (s), 892 (m), 702 (s). m/z (ES): 529.1165 (M+Na⁺). Calculated value for C₂₈H₃₁BrO₂Si+Na⁺: 529.1169 (-0.7 ppm).

5-(3-Bromophenyl)-2-((*t*-butyldiphenylsilyloxy)-methyl)-3-methylene-tetrahydrofuran (13b)

12b (0.90 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_{H} (300 MHz; CDCl_3): 1.06 (9H, s, Si-C-CH₃), 2.51-2.62 (1H, m, CH(Ar)-CH₂), 2.89 (1H, dd, $J=5.6, 15.1$ Hz, CH(Ar)-CH₂), 3.81 (1H, dd, $J=4.5, 10.7$ Hz, TBDPSO-CH₂), 3.89 (1H, dd, $J=4.0, 10.7$ Hz, TBDPSO-CH₂), 4.55-4.58 (1H, m, O-CH-C=), 4.89 (1H, dd, $J=5.6, 10.6$ Hz, O-CH-Ar), 4.98-5.00 (1H, m, C=CH₂), 5.09-5.11 (1H, m, C=CH₂), 7.28-7.45 (10H, m, Ar-H), 7.70-7.76 (4H, m, Ar-H). δ_{C} (75 MHz; CDCl_3): 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-CH-C=), 106.0 (C=CH₂), 121.4 (Ar-C), 125.4 (Ar-CH), 127.6 (Ar-CH), 127.7 (Ar-CH), 129.6 (Ar-CH), 129.7 (Ar-CH), 129.8 (Ar-CH), 130.0 (Ar-CH), 131.3 (Ar-CH), 133.2 (Ar-C), 133.3 (Ar-C), 135.6 (Ar-CH), 135.7 (Ar-CH), 142.5(Ar-C), 148.6 (C=CH₂).

(R*, R*)-13b (trans): δ_{H} (300 MHz; CDCl_3): 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)-CH₂), 3.67-3.86 (2H, m, TBDPSO-CH₂), 4.72 (1H, br s, O-CH-C=), 4.96-4.98 (1H, m, C=CH₂), 5.06-5.12 (2H, m, O-CH-Ar + C=CH₂), 7.29-7.43 (10H, m, Ar-H), 7.70-7.75 (14H, m, Ar-H). δ_{C} (75 MHz; CDCl_3): 19.2 (Si-C-CH₃), 26.8 (Si-C-CH₃), 41.6 (CH(Ar)-CH₂), 66.8 (TBDPSO-CH₂), 78.9 (O-CH-Ar), 81.6 (O-CH-C=), 106.2 (C=CH₂), 121.4 (Ar-C), 125.4 (Ar-CH), 127.6 (Ar-CH), 127.7 (Ar-CH), 129.6 (Ar-CH), 129.7 (Ar-CH), 129.8 (Ar-CH), 130.0 (Ar-CH), 131.3 (Ar-CH), 133.2 (Ar-C), 133.3 (Ar-C), 135.6 (Ar-CH), 135.7 (Ar-CH), 142.5(Ar-C), 148.2 (C=CH₂).

ν_{max} (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 C₂₈H₃₁BrO₂Si+Na⁺: 529.1169 (-1.1 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_{H} (500 MHz; CDCl_3): 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)-CH₂), 3.77 (1H, dd, $J=4.7, 10.8$ Hz, TBDPSO-CH₂), 3.84 (1H, dd, $J=4.0, 10.8$ Hz, TBDPSO-CH₂), 4.54-4.56 (1H, m, O-CH-C=), 5.00-5.02 (1H, m, C=CH₂), 5.12-5.15 (2H, m, O-CH-Ar & 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_{C} (125 MHz; CDCl_3): 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-CH-C=), 106.8 (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=CH₂).

(R*, R*)-13d (trans): δ_{H} (500 MHz; CDCl_3): 1.05 (9H, s, Si-C-CH₃), 2.64-2.71 (1H, m, CH(Ar)-CH₂), 3.07-3.13 (1H, m, CH(Ar)-CH₂), 3.73-3.85 (2H, m, TBDPSO-CH₂), 4.64 (1H, br s, O-CH-C=), 5.00-5.02 (1H, m, C=CH₂), 5.12-5.15 (1H, m, C=CH₂), 5.33 (1H, t, $J=6.6$ Hz, O-CH-Ar), 7.08 (1H, dd, $J=1.0, 1.3$ 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_{C} (125 MHz; CDCl_3): 19.3 (Si-C-CH₃), 26.6 (Si-C-CH₃), 41.6 (CH(Ar)-CH₂), 66.7 (TBDPSO-CH₂), 75.3 (O-CH-Ar), 81.7 (O-CH-C=), 107.3 (C=CH₂), 115.2 (CN & Ar-C), 124.6 (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=CH₂).

$\nu_{\max}(\text{film})/\text{cm}^{-1}$: 3071 (m), 2930 (s), 2229 (m), 1667 (w), 1472 (m), 1428 (s), 1113 (s), 823 (m), 703 (s). m/z (EI): 396.1409 (M-C(CH₃)₃) Calculated value for C₂₅H₂₂NO₂Si: 396.1420 (-1.1 ppm).

3-Bromo-5-(5-((*t*-butyldiphenylsilyloxy)methyl)-4-methylene-tetrahydrofuran-2-yl)thiophene (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*): δ_{H} (300 MHz; CDCl₃): 1.05 (9H, s, Si-C-CH₃), 2.65-2.71 (1H, m, CH(Ar)-CH₂), 2.92 (1H, dd, $J=5.3, 15.0$ Hz, CH(Ar)-CH₂), 3.71-3.83 (2H, m, TBDPSO-CH₂), 4.54 (1H, br s, O-CH-C=), 4.98-5.01 (1H, m, C=CH₂), 5.10-5.14 (2H, m, O-CH-Ar & C=CH₂), 6.86 (1H, dd, $J=0.8, 1.2$ Hz, Ar-H), 7.14 (1H, d, $J=1.2$ Hz, Ar-H), 7.37-7.42 (6H, m, Ar-H), 7.65-7.72 (4H, m, Ar-H).

(**R***, **R***)-**13c** (*trans*): δ_{H} (300 MHz; CDCl₃): 1.06 (9H, s, Si-C-CH₃), 2.65-2.71 (1H, m, CH(Ar)-CH₂), 3.02-3.10 (1H, m, CH(Ar)-CH₂), 3.71-3.83 (2H, m, TBDPSO-CH₂), 4.63 (1H, br s, O-CH-C=), 4.98-5.01 (1H, m, C=CH₂), 5.10-5.14 (1H, m, C=CH₂), 5.33 (1H, t, $J=6.7$ Hz, O-CH-Ar), 6.93 (1H, dd, $J=0.9, 1.2$ Hz, Ar-H), 7.14 (1H, d, $J=1.2$ Hz, Ar-H), 7.37-7.42 (6H, m, Ar-H), 7.65-7.72 (4H, m, Ar-H).

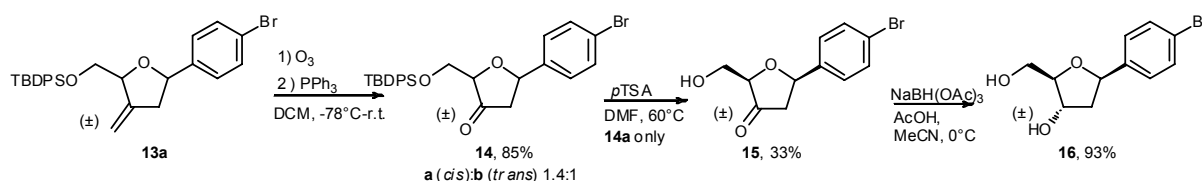
5-(1-Naphthyl)-2-((*t*-butyldiphenylsilyloxy)-methyl)-3-methylene-tetrahydrofuran (13e)

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*): δ_{H} (500 MHz; CDCl₃): 1.10 (9H, s, Si-C-CH₃), 2.61-2.74 (1H, m, CH(Ar)-CH₂), 3.16 (1H, dd, $J=5.6, 15.5$ Hz, CH(Ar)-CH₂), 3.83-4.00 (2H, m, TBDPSO-CH₂), 4.68 (1H, br s, O-CH-C=), 5.05 (1H, s, C=CH₂), 5.13 (1H, s, C=CH₂), 5.89 (1H, dd, $J=5.3, 10.4$ Hz, O-CH-Ar), 7.32-7.49 (9H, m, Ar-H), 7.58-7.79 (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). δ_{C} (125 MHz; CDCl₃): 19.3 (Si-C-CH₃), 26.9 (Si-C-CH₃), 41.7 (CH(Ar)-CH₂), 66.7 (TBDPSO-CH₂), 77.4 (O-CH-Ar), 81.6 (O-CH-C=), 105.9 (C=CH₂), 122.5 (Ar-CH), 123.4 (Ar-CH), 125.4 (Ar-CH), 125.8 (Ar-CH), 126.9 (Ar-CH), 127.6 (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*): δ_{H} (500 MHz; CDCl₃): 1.06 (9H, s, Si-C-CH₃), 2.61-2.74 (1H, m, CH(Ar)-CH₂), 3.29 (1H, dd, $J=7.3, 15.3$ Hz, CH(Ar)-CH₂), 3.83-4.00 (2H, m, TBDPSO-CH₂), 4.83 (1H, br s, O-CH-C=), 5.01 (1H, s, C=CH₂), 5.08 (1H, s, C=CH₂), 5.89 (1H, t, $J=7.0$ Hz, O-CH-Ar), 7.32-7.49 (9H, m, Ar-H), 7.58-7.79 (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). δ_{C} (125 MHz; CDCl₃): 19.3 (Si-C-CH₃), 26.8 (Si-C-CH₃), 40.8 (CH(Ar)-CH₂), 67.1 (TBDPSO-CH₂), 77.3 (O-CH-Ar), 81.7 (O-CH-C=), 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).

$\nu_{\max}(\text{film})/\text{cm}^{-1}$: 3055 (m), 2857 (s), 1510 (m), 1428 (s), 1113 (s), 801 (s), 703 (s). m/z (EI): 501.2220 (M+Na⁺) Calculated value for C₃₂H₃₄O₂Si + Na⁺: 501.2226 (-1.2 ppm).



5-(4-Bromophenyl)-2-((*t*-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*, S*)-14a (*cis*): δ_{H} (500 MHz; CDCl₃): 1.02 (9H, s, Si-C-CH₃), 2.51 (1H, dd, J = 11.2, 17.5 Hz, CH(Ar)-CH₂), 2.87 (1H, dd, J =5.7, 17.5 Hz, CH(Ar)-CH₂), 4.01 (2H, d, J =2.3 Hz, TBDPSO-CH₂), 4.06 (1H, t, J =2.3 Hz, O-CH-CO), 5.17 (1H, dd, J =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_{C} (100 MHz; CDCl₃): 19.2 (Si-C-CH₃), 26.7 (Si-C-CH₃), 46.3 (CH(Ar)-CH₂), 63.1 (TBDPSO-CH₂), 76.9 (O-CH-Ar), 82.8 (O-CH-CO), 122.1 (Ar-C), 127.8 (Ar-CH), 127.9 (Ar-CH), 129.8 (Ar-CH), 129.8 (Ar-CH), 131.7 (Ar-CH), 132.6 (Ar-C), 133.0 (Ar-C), 135.6 (Ar-CH), 135.5 (Ar-CH), 139.7 (Ar-C), 213.4 (CO). ν_{max} (film)/cm⁻¹: 3066 (m), 2931 (s), 1764 (s), 1428 (m), 1113 (s), 823 (m), 702 (s). m/z (EI): 451.0363 (M-*t*Bu), calculated for C₂₃H₂₀BrO₃Si: 451.0365 (-0.4 ppm).

(R*, R*)-14b (*trans*): δ_{H} (500 MHz; CDCl₃): 1.05 (9H, s, Si-C-CH₃), 2.55 (1H, ddd, J =1.0, 8.7, 18.0 Hz, CH(Ar)-CH₂), 2.96 (1H, dd, J =7.0, 18.0 Hz, CH(Ar)-CH₂), 3.98 (2H, dd, J =2.3, 11.1 Hz, TBDPSO-CH₂), 4.07 (1H, dd, J =2.3, 11.1 Hz, TBDPSO-CH₂), 5.20 (1H, br t, J =2.3 Hz, O-CH-CO), 5.69 (1H, dd, J =7.0, 8.7 Hz, O-CH-Ar), 7.27 (2H, d, J =8.4 Hz, Ar-H), 7.38-7.46 (6H, m, Ar-H), 7.53 (2H, d, J =8.4 Hz, Ar-H), 7.65-7.72 (4H, m, Ar-H). δ_{C} (125 MHz; CDCl₃): 19.2 (Si-C-CH₃), 26.7 (Si-C-CH₃), 45.1 (CH(Ar)-CH₂), 65.4 (TBDPSO-CH₂), 78.4 (O-CH-Ar), 81.5 (O-CH-CO), 125.9 (Ar-C), 127.5 (Ar-CH), 127.8 (Ar-CH), 129.8 (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). ν_{max} (film)/cm⁻¹: 3068 (m), 2926 (s), 1753 (s), 1428 (m), 1399 (m), 1122 (s), 990 (s), 823 (s), 702 (s). m/z (EI): 451.0359 (M-*t*Bu), calculated for C₂₃H₂₀BrO₃Si: 451.0365 (-1.3 ppm)

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

14a (0.40 g, 0.46 mmol, 1 eq) was dissolved in DMF (10 mL) and added *p*-toluenesulfonic acid (0.16 g, 0.9 mmol, 1.1eq). This mixture was stirred at 60 °C for 4 days. The reaction was then quenched with saturated aqueous NaHCO₃ (10 mL) and the aqueous layer extracted with EtOAc (3 x 20mL). The combined organic layers were dried with MgSO₄, filtered and concentrated under reduced pressure. 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 (CDCl₃). ν_{max} (film)/cm⁻¹: 3367 (br, s), 2926 (s), 1765 (s), 1491 (m), 1377 (m), 1099 (s), 818 (m). δ_{H} (500 MHz; CDCl₃): 1.97 (1H, t, J =6.4 Hz, OH), 2.49 (1H, dd, J =11.0, 18.0 Hz, CH(Ar)-CH₂), 2.89 (1H, dd, J =5.9, 18.0 Hz, CH(Ar)-CH₂), 3.96 (2H, dd, J =3.4, 6.4 Hz, HO-CH₂), 4.05 (1H, t, J =3.4 Hz, O-CH-CO), 5.19 (1H, dd, J =5.9, 11.0 Hz, O-CH-Ar), 7.31-7.35 (2H, m, Ar-H), 7.52-7.56 (2H, m, Ar-H). δ_{C} (125 MHz; CDCl₃): 45.3 (CH(Ar)-CH₂), 61.5 (HO-CH₂), 77.0 (O-CH-Ph), 82.3 (O-CH-CO), 122.4 (Ar-CH), 127.8 (Ar-CH), 131.9 (Ar-CH), 138.8 (Ar-C), 213.2 (CO). m/z (EI): 269.9881 (M⁺), calculated value for C₁₁H₁₁BrO₃: 269.9892 (-4.1 ppm).

5-(4-Bromophenyl)-2-(hydroxymethyl)-tetrahydrofuran-3-ol (16)

NaBH(OAc)₃ (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 (0-5% MeOH in DCM gradient on silica gel) yielded title compound **16** (55 mg, 93%) as a white solid. mp 105-106°C (CDCl₃). ν_{max} (film)/cm⁻¹: 3335 (br, s), 2919 (s), 1490 (s), 1456 (m), 1069 (s), 999 (s), 820 (s). δ_{H} (300 MHz; CDCl₃): 1.81 (2H, br s, OH), 1.99 (1H, ddd, J =6.3, 10.3, 13.3 Hz, CH(Ph)-CH₂), 2.27 (1H, ddd, J =1.9, 5.6, 13.3 Hz, CH(Ph)-CH₂), 3.76 (1H, dd, J =4.6, 11.7 Hz, HO-CH₂), 3.85 (1H, dd, J =4.3, 11.7 Hz, HO-CH₂), 4.03 (1H, dt, J =3.1, 4.3, 4.6 Hz, O-CH-CHOH), 4.44-4.47 (1H, m, HO-CH), 5.14 (1H, dd, J =5.6, 10.3 Hz, O-CH-Ph), 7.22-7.24 (m, 2H, Ar-H), 7.46-7.49 (m, 2H, Ar-H). δ_{C} (125 MHz; CDCl₃): 44.1 (CH(Ph)-CH₂), 63.4 (HO-CH₂), 73.8 (HO-CH), 79.4 (O-CH-CHOH), 87.3 (O-CH-Ph), 121.5 (Ar-C), 127.6 (Ar-CH), 131.6 (Ar-CH), 140.3 (Ar-C). m/z (EI): 272.0046 (M⁺), calculated for C₁₁H₁₃BrO₃: 272.0048 (-0.7 ppm).

