

ELECTRONIC SUPPLEMENTARY MATERIAL

Synthesis of the anti-*Helicobacter pylori* agent (+)-spiroloxine methyl ether and the unnatural (2''S)-diastereomer

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Experimental

General

All reactions were carried out in oven-dried or flame-dried glassware under a nitrogen atmosphere using standard syringe and septum techniques unless otherwise stated. Diethyl ether and tetrahydrofuran were freshly distilled from sodium/benzophenone. Hexane, pentane, dichloromethane, triethylamine and diethylamine were distilled from calcium hydride. Thin layer chromatography was performed on pre-coated 0.2 mm Merck Kieselgel 60 F₂₅₄ silica plates and compounds were visualized under 365 nm ultraviolet irradiation followed by staining either alkaline permanganate or ethanolic vanillin solution. Flash column chromatography was performed using Reidel-de Häen Kieselgel or Merck Kieselgel 60 F (both 230-400 mesh) with the indicated solvent. Melting points were determined on an Electrothermal melting point apparatus and are uncorrected. Optical rotations were measured using a Perkin-Elmer 341 polarimeter at $\lambda = 598$ nm and are given in $10^{-1} \text{deg cm}^2 \text{g}^{-1}$. Infrared spectra were recorded with a Perkin-Elmer Spectrum One Fourier Transform IR spectrophotometer as thin films between sodium chloride plates. Absorption maxima are expressed in wavenumbers (cm^{-1}). ^1H and ^{13}C

NMR spectra were obtained using either a Bruker DRX-400 spectrophotometer operating at either 400 MHz or 100 MHz or a Bruker Avance 300 spectrometer operating at 300 MHz or 75 MHz, respectively. Data are expressed in parts per million downfield shift from tetramethylsilane as an internal standard or relative to CDCl₃. All *J* values are given in Hz. Assignments are made with the aid of DEPT 135, COSY and HSQC experiments. ¹⁹F NMR spectra were obtained using a Bruker Avance 300 spectrometer operating at 282 MHz and data are expressed in parts per million downfield shift from CFC1₃. High resolution mass spectra were recorded using a VG70-SE spectrometer operating at a nominal accelerating voltage of 70 eV. Chemical ionization (CI) mass spectra were obtained with the indicated reagent gas and fast atom bombardment (FAB) mass spectra were obtained using 3-nitrobenzyl alcohol as the matrix.

Nomenclature

All compounds are systematically named according to IUPAC conventions, but in some cases strict adherence to the priority order of substituents has been neglected in order to permit comparison of spectroscopic data among related compounds. The relevant compounds are indicated by the symbol phi (ϕ) and the correct IUPAC name is included as a footnote.

(3R)-3-(3'-Oxopropyl)-5,7-dimethoxy-3H-isobenzofuran-1-one (3a)

To a stirred mixture of (*R*)-alcohol **17** (150 mg, 0.59 mmol) and Celite[®] (200 mg) in dichloromethane (10 cm³) at 0 °C was added pyridinium chlorochromate (192 mg, 0.89 mmol). After stirring for 12 h., the mixture was filtered through a pad of Celite[®] and the solid washed with dichloromethane (3 x 15 cm³). Removal of the solvent under reduced pressure and purification of the resultant oil by flash column chromatography using hexane-ethyl acetate (2:8) as eluent gave the *title compound* **3a** (107 mg, 72%) as a white solid; m.p. 99-102 °C,

$[\alpha]_D^{25} +51.1$ (c 0.74 in CHCl_3); $\nu_{\text{max}}(\text{film})/\text{cm}^{-1}$ 2928, 2951, 1755s (CO), 1602s (CO), 1463, 1338, 1218, 1158, 1028, 837 and 734; δ_{H} (300 MHz, CDCl_3): 1.88 (1 H, dddd, J 14.4, 8.3, 8.3 and 5.1, H1'_a), 2.44 (1 H, dddd, J 14.4, 7.4, 7.4 and 3.2, H1'_b), 2.54 (1 H, ddd, J 18.7, 8.3 and 5.1, H2'_a), 2.75 (1 H, dd, J 18.7, 7.4 and 7.4, H2'_b), 3.88 (3 H, s, OMe), 3.94 (3 H, s, OMe), 5.34 (1 H, dd, J 8.3 and 3.2, H3), 6.42 (1 H, s, H4) and 6.43 (1 H, s, H6), 9.80 (1 H, apparent s, H3'); δ_{C} (75 MHz, CDCl_3): 26.9 (CH_2 , C1'), 38.9 (CH_2 , C2'), 56.0 (CH_3 , OMe), 56.0 (CH_3 , OMe), 78.4 (CH, C3), 97.4 (CH, C6), 99.1 (CH, C4), 106.7 (quat., C7a), 154.3 (quat., C3a), 159.7 (quat., C7), 167.0 (quat., C5), 168.0 (quat., C1) and 200.7 (CH, C3'); m/z (EI): 250 (M^+ , 30%), 206 (61), 193 ($M-\text{C}_3\text{H}_5\text{O}$, 100), 165 (21), 135 (20) and 77 (10); HRMS (EI): Found M^+ , 250.08333. $\text{C}_{13}\text{H}_{14}\text{O}_5$ requires M , 250.08412.

(1'*R*)-1-(3,5-Dimethoxyphenyl)but-3'-en-1'-ol (14)

Following an adaptation of the procedure used by Gauthier and Carreira¹ (*R*)-(+)-BINOL (1.04 g, 3.64 mmol) was dissolved in acetonitrile (50 cm³) and cooled to 0 °C under an atmosphere of argon. To this stirred solution was added a solution of titanium tetrafluoride in acetonitrile (3.64 cm³, 1.82 mmol, 0.5 mol dm⁻³) dropwise *via* syringe. After stirring the resultant deep orange solution at room temperature for 0.25 h. the solvent was removed *in vacuo* and the residue taken up in a solution of dichloromethane and acetonitrile (75 cm³, 97:3). The solution was cooled to 0 °C and allyltrimethylsilane (7.53 cm³, 47.37 mmol) added dropwise. After stirring for 1.5 h., the solution was cooled to -20 °C and a solution of 3,5-dimethoxybenzaldehyde (6.06 g, 36.44 mmol) in dichloromethane and acetonitrile (75 cm³, 97:3) was added dropwise *via* cannula. The solution was stirred at -20 °C for 72 h. before quenching the reaction with aqueous ammonium fluoride (50 cm³, 1 mol dm⁻³). The mixture was poured into brine (50 cm³) and extracted with dichloromethane (3 x 200 cm³). The combined extracts were washed with aqueous sodium hydroxide³³⁶ (2 x 100 cm³, 1 mol dm⁻³) and saturated aqueous sodium

bicarbonate ($1 \times 200 \text{ cm}^3$) before drying over magnesium sulfate. Filtration and removal of the solvent under reduced pressure gave an oil that was purified by flash column chromatography using hexane-diethyl ether (7:3-1:1) as eluent to afford the *title compound* **14** (5.32 g, 70%) as a yellow oil in 86%# enantiomeric excess; $[\alpha]_{\text{D}} +39.6$ (c 1.57 in CHCl_3); $\nu_{\text{max}}(\text{film})/\text{cm}^{-1}$ 3434br (OH), 2937, 2938, 1598, 1463, 1429, 1204, 1154, 1059, 920, 838 and 696; δ_{H} (400 MHz, CDCl_3): 2.10 (1 H, br s, OH), 2.43-2.55 (2 H, m, H2'), 3.79 (6 H, s, OMe), 4.66 (1 H, dd, J 7.5 and 5.3, H1'), 5.13-5.18 (2 H, m, H4'), 5.81 (1 H, dddd, J 17.2, 10.2, 7.1 and 7.1, H3'), 6.37 (1 H, t, J 2.2, H4), and 6.52 (2 H, d, J 2.2, H2); δ_{C} (100 MHz, CDCl_3): 43.7 (CH_2 , C2'), 55.3 (CH_3 , OMe), 73.3 (CH, C1'), 99.4 (CH, C4), 103.7 (CH, C2), 118.3 (CH_2 , C4'), 134.4 (CH, C3'), 146.5 (quat., C1) and 160.8 (quat., C3); m/z (EI): 208 (M^+ , 23%), 167 ($\text{M}-\text{C}_3\text{H}_5$, 92), 139 ($\text{M}-\text{C}_3\text{H}_5$, $-\text{CH}_3\text{O}$, 100), 124 (24), 77 (11) and 41 (7); HRMS (EI): Found M^+ , 208.10973. $\text{C}_{12}\text{H}_{16}\text{O}_3$ requires M , 208.10994.

(1'R)-1-(2-Bromo-3,5-dimethoxyphenyl)but-3'-en-1'-ol (12)

(*R*)-Alcohol **14** (5.10 g, 24.49 mmol) and *N*-bromosuccinimide (4.36 g, 24.49 mmol) were dissolved in chloroform (150 cm^3) and the mixture heated at reflux for 12 h. under an atmosphere of nitrogen. The solution was filtered through a pad of Celite[®] and the solvent removed under reduced pressure. Purification by flash column chromatography using hexane-diethyl ether (6:4) as eluent gave the *title compound* **12** (6.19 g, 88%) as an orange oil; $[\alpha]_{\text{D}} +57.5$ (c 3.40 in CHCl_3); $\nu_{\text{max}}(\text{film})/\text{cm}^{-1}$ 3435br (OH), 2939, 2839, 1589, 1454, 1431, 1323, 1200, 1160, 1071, 1052, 1022, 919 and 838; δ_{H} (300 MHz, CDCl_3): 2.26-2.36 (1 H, m, H2'a), 2.40 (1 H, br s, OH), 2.57-2.65 (1 H, m, H2'b), 3.80 (3 H, s, OMe), 3.85 (3 H, s, OMe), 5.10-5.21 (3 H, m, H4' and H1'), 5.88 (1 H, dddd, J 17.1, 10.1, 7.1 and 7.1, H3'), 6.39 (1 H, d, J 2.8,

HPLC Conditions: Chiracel[®] OD-H column, *i*-propanol:hexane 1:9, flow rate $0.5 \text{ cm}^3 \text{ min}^{-1}$, retention times: 17.8 min (major, *R*-isomer) and 22.4 min (minor, *S*-isomer).

H4) and 6.75 (1 H, d, J 2.8, H6); δ_{C} (75 MHz, CDCl_3): 41.8 (CH_2 , C2'), 55.5 (CH_3 , OMe), 56.2 (CH_3 , OMe), 71.9 (CH , C1'), 98.8 (CH , C4), 101.9 (quat., C2), 103.0 (CH , C6), 118.3 (CH_2 , C4'), 134.4 (CH , C3'), 144.9 (quat., C1), 156.2 (quat., C5) and 159.9 (quat., C3); m/z (EI): 288 ($\text{M}^{+}[\text{Br}^{81}]$, 6%), 286 ($\text{M}^{+}[\text{Br}^{79}]$, 6), 247 ($\text{M}^{+}[\text{Br}^{81}]-\text{C}_3\text{H}_5$, 58), 245 ($\text{M}^{+}[\text{Br}^{79}]-\text{C}_3\text{H}_5$, 62), 207 ($\text{M}-\text{Br}$, 31), 166 (55) and 138 (100); HRMS (EI): Found M^{+} , 286.01990. $\text{C}_{12}\text{H}_{15}^{79}\text{BrO}_3$ requires M , 286.02046. Found M^{+} , 288.01915. $\text{C}_{12}\text{H}_{15}^{81}\text{BrO}_3$ requires M , 288.01841.

(1'R)-1-(2-Bromo-3,5-dimethoxyphenyl)but-3'-en-1'-yl *N,N*-diethyl carbamate (15)

To a suspension of sodium hydride (0.40 g, 15.81 mmol, 95%) in tetrahydrofuran (25 cm^3) at 0°C under an atmosphere of nitrogen was added a solution of (*R*)-bromoalcohol **12** (4.13 g, 14.37 mmol) in tetrahydrofuran (15 cm^3) dropwise. After stirring for 0.5 h., *N,N*-diethylcarbamoyl chloride (2.74 cm^3 , 21.56 mmol) was added dropwise. The mixture was stirred for 12 h. before the addition of saturated ammonium chloride (20 cm^3). The aqueous layer extracted with diethyl ether (3 x 40 cm^3) and the combined organic extracts were dried over magnesium sulfate. Filtration and removal of the solvent under reduced pressure provided an oil that was purified by flash column chromatography using hexane-diethyl ether (8:2) as eluent to give the *title compound* **15** (4.60 g, 82%) as a yellow oil. $[\alpha]_{\text{D}} -9.1$ (c 1.60 in CHCl_3); ν_{max} (film)/ cm^{-1} 2974, 2836, 1703s (CO), 1589, 1455, 1422, 1325, 1276, 1163, 1067, 1024, 920, 835, 767 and 734; δ_{H} (300 MHz, CDCl_3): 1.11-1.26 (6 H, m, NCH_2CH_3), 2.47-2.68 (2 H, m, H2'), 3.33 (4 H, br s, NCH_2CH_3), 3.79 (3 H, s, OMe), 3.85 (3 H, s, OMe), 5.04-5.12 (2 H, m, H4'), 5.82 (1 H, m, H3'), 6.10 (1 H, dd, J 8.0 and 4.3, H1'), 6.42 (1 H, d, J 2.8, H4) and 6.52 (1 H, d, J 2.8, H6); δ_{C} (75 MHz, CDCl_3): 13.4 (CH_3 , NCH_2CH_3), 14.3 (CH_3 , NCH_2CH_3), 39.6 (CH_2 , C2'), 41.3 (CH_2 , NCH_2CH_3), 41.9 (CH_2 , NCH_2CH_3), 55.3 (CH_3 , OMe), 56.3 (CH_3 , OMe), 74.8 (CH , C1'), 98.4 (CH , C4), 102.2 (quat., C2), 103.4 (CH , C6), 117.7 (CH_2 , C4'), 133.6 (CH , C3'), 142.7 (quat., C1), 154.7 (quat., CO), 156.5 (quat., C5) and 159.7 (quat., C3); m/z (CI): 388

(M[⁸¹Br]H⁺, 6%), 386 (M[⁷⁹Br]H⁺, 6), 344 (2), 342 (2), 306 (M-Br, 31), 288 (M[⁸¹Br]H-C₅H₁₀NO, 4), 286 (M[⁷⁹Br]H-C₅H₁₀NO, 4), 271 (M[⁸¹Br]-C₅H₁₀NO₂, 100), 269 (M[⁷⁹Br]-C₅H₁₀NO₂, 97), 190 (13), 100 (C₅H₁₀NO, 22) and 72 (24); HRMS (CI, NH₃): Found MH⁺, 386.09538. C₁₇H₂₅⁷⁹BrNO₄ requires *M*, 386.09669. Found MH⁺, 388.09559. C₁₇H₂₅⁸¹BrNO₄ requires *M*, 388.09465.

(3R)-3-Allyl-5,7-dimethoxy-3H-isobenzofuran-1-one (16)

To a stirred solution of (*R*)-carbamate **15** (4.48 g, 11.60 mmol) in tetrahydrofuran (60 cm³) at -78 °C under an atmosphere of nitrogen was added *tert*-butyllithium (18.62 cm³, 25.52 mmol, 1.37 mol dm⁻³) dropwise. After stirring for 0.75 h. the reaction was quenched by the addition of methanol (10 cm³) and the solution allowed to warm to room temperature. A catalytic amount of *p*-toluenesulfonic acid (0.05 g) was added and the solution stirred for 12 h. The solvent was removed under reduced pressure and the resultant oil purified by flash column chromatography using hexane-ethyl acetate (1:1-1:9) as eluent to give the *title compound* **16** (2.06 g, 76%) as a white solid; m.p. 95-98 °C; [α]_D +31.5 (*c* 1.37 in CHCl₃); ν_{max}(film)/cm⁻¹ 2948, 1750, 1615, 1460, 1332, 1221, 1159, 1030 and 839; δ_H (300 MHz, CDCl₃): 2.50-2.56 (1 H, m, H1'_a), 2.63-2.70 (1 H, m H1'_b), 3.85 (3 H, s, OMe), 3.91 (3 H, s, OMe), 5.07-5.17 (2 H, m, H3'), 5.30 (1 H, dd, *J* 10.6 and 5.5, H3), 5.64-5.80 (1 H, m, H2'), 6.38-6.39 (1 H, m, H4) and 6.41 (1 H, s, H6); δ_C (75 MHz, CDCl₃): 38.4 (CH₂, C1'), 55.7 (CH₃, OMe), 55.7 (CH₃, OMe), 78.6 (CH, C3), 97.6 (CH, C6), 98.4 (CH, C4), 106.5 (quat., C7a), 119.0 (CH₂, C3') 131.1 (CH, C2'), 154.0 (quat., C3a), 159.2 (quat., C7), 166.5 (quat., C5) and 167.9 (quat., C1); *m/z* (FAB): 235 (MH⁺, 100), 203 (M-OMe, 11) and 193 (M-C₃H₇O, 26); HRMS (FAB): Found MH⁺, 235.09691. C₁₃H₁₅O₄ requires *M*, 235.09703.

(3R)-3-(3'-Hydroxyprop-1'-yl)-5,7-dimethoxy-3H-isobenzofuran-1-one (17)

Alkene **16** (1.21 g, 5.17 mmol) was dissolved in dry tetrahydrofuran (30 cm³) and cooled to 0 °C under an atmosphere of nitrogen. Borane dimethylsulfide complex (0.62 cm³, 6.20 mmol, 10 mol dm⁻³) was added and the solution allowed to warm to room temperature over 12 h. Oxidative workup with aqueous sodium hydroxide (12.91 cm³, 25.83 mmol, 2 mol dm⁻³) and hydrogen peroxide (2.93 cm³, 25.83 mmol, 8.8 mol dm⁻³) gave a biphasic mixture that was extracted with diethyl ether (3 x 50 cm³). The combined organic extracts were dried over magnesium sulfate, filtered and the solvent removed under reduced pressure. The resultant residue was purified by flash chromatography using dichloromethane-acetone (1:1) as eluent to give the *title compound* **17** (0.73 g, 56%) as a white solid; m.p. 118-120 °C; [α]_D +67.5 (*c* 0.88 in CHCl₃); ν_{\max} (film)/cm⁻¹ 3305br (OH), 2951, 2958, 1738s (CO), 1603, 1430, 1340, 1204, 1160, 1053, 980, 840 and 737; δ_{H} (300 MHz, CDCl₃): 1.63-1.82 (4 H, m, H1'_a, H2' and OH), 2.08-2.21 (1 H, m, H1'_b), 3.62-3.75 (2 H, m, H3'), 3.87 (3 H, s, OMe), 3.92 (3 H, s, OMe), 5.33 (1 H, dd, *J* 7.2 and 3.7, H3), 6.40 (1 H, d, *J* 1.7, H4) and 6.41 (1 H, apparent s, H6); δ_{C} (75 MHz, CDCl₃): 27.8 (CH₂, C2'), 31.3 (CH₂, C1'), 55.9 (CH₃, OMe), 56.0 (CH₃, OMe), 62.1 (CH₂, C3'), 79.7 (CH, C3), 97.5 (CH, C6), 98.8 (CH, C4), 106.8 (quat., C7a), 155.0 (quat., C3a), 159.6 (quat., C7), 166.8 (quat., C5) and 168.4 (quat., C1); *m/z* (EI): 252 (M⁺, 34%), 207 (30), 193 (M-C₃H₇O, 100), 165 (21), 135 (9) and 77 (8); HRMS (EI): Found M⁺, 252.09955. C₁₃H₁₆O₅ requires *M*, 252.09977.

(3R)-3-(3'-Oxopropyl)-5,7-dimethoxy-3H-isobenzofuran-1-one (3a)

To a stirred mixture of (*R*)-alcohol **17** (150 mg, 0.59 mmol) and Celite[®] (200 mg) in dichloromethane (10 cm³) at 0 °C was added pyridinium chlorochromate (192 mg, 0.89 mmol). After stirring for 12 h., the mixture was filtered through a pad of Celite[®] and the solid washed with dichloromethane (3 x 15 cm³). Removal of the solvent under reduced pressure and purification of the resultant oil by flash column chromatography using hexane-ethyl acetate

(2:8) as eluent gave the *title compound* **3a** (107 mg, 72%) as a white solid; m.p. 99-102 °C, $[\alpha]_D^{25} +51.1$ (*c* 0.74 in CHCl₃); $\nu_{\max}(\text{film})/\text{cm}^{-1}$ 2928, 2951, 1755s (CO), 1602s (CO), 1463, 1338, 1218, 1158, 1028, 837 and 734; δ_{H} (300 MHz, CDCl₃): 1.88 (1 H, dddd, *J* 14.4, 8.3, 8.3 and 5.1, H1'_a), 2.44 (1 H, dddd, *J* 14.4, 7.4, 7.4 and 3.2, H1'_b), 2.54 (1 H, ddd, *J* 18.7, 8.3 and 5.1, H2'_a), 2.75 (1 H, dd, *J* 18.7, 7.4 and 7.4, H2'_b), 3.88 (3 H, s, OMe), 3.94 (3 H, s, OMe), 5.34 (1 H, dd, *J* 8.3 and 3.2, H3), 6.42 (1 H, s, H4) and 6.43 (1 H, s, H6), 9.80 (1 H, apparent s, H3'); δ_{C} (75 MHz, CDCl₃): 26.9 (CH₂, C1'), 38.9 (CH₂, C2'), 56.0 (CH₃, OMe), 56.0 (CH₃, OMe), 78.4 (CH, C3), 97.4 (CH, C6), 99.1 (CH, C4), 106.7 (quat., C7a), 154.3 (quat., C3a), 159.7 (quat., C7), 167.0 (quat., C5), 168.0 (quat., C1) and 200.7 (CH, C3'); *m/z* (EI): 250 (M⁺, 30%), 206 (61), 193 (M-C₃H₅O, 100), 165 (21), 135 (20) and 77 (10); HRMS (EI): Found M⁺, 250.08333. C₁₃H₁₄O₅ requires *M*, 250.08412.

(2S)-2-Bromobutanedioic acid (18)

(S)-Aspartic acid **9** (20.0 g, 15.0 mmol) was dissolved in aqueous sulfuric acid (390.9 cm³, 97.7 mmol, 2.5 mol dm⁻³) with potassium bromide (82.3 g, 69.2 mmol) and the mixture cooled to -10 °C. To this vigorously stirred mixture was added a solution of sodium nitrite (18.7 g, 27.1 mmol) in water (39 cm³) *via* an addition funnel. The resultant dark brown suspension was allowed to warm to room temperature over 5 h. then extracted with ethyl acetate (4 x 600 cm³). The combined organic extracts were dried over magnesium sulfate, filtered, and the solvent removed *in vacuo* to give the title compound **18** (27.2 g, 92%) as a white solid; m.p. 176-179 °C (lit.,ⁱⁱ 178-180 °C); $[\alpha]_D^{25} -38.1$ (*c* 1.00 in H₂O) (lit.,ⁱⁱ $[\alpha]_D^{25} -38.1$ (*c* 1.00 in H₂O)); δ_{H} (300 MHz, CD₃OD): 2.95 (1 H, dd, *J* 17.2 and 6.3, H3b), 3.20 (1 H, dd, *J* 17.2 and 8.6, H3a) and 4.56 (1 H, dd, *J* 8.6 and 6.3, H2); δ_{C} (75 MHz, CD₃OD): 40.1 (CH₂, C3), 40.8 (CH, C2), 172.3 (quat., C4) and 173.1 (quat., C1). This data was in agreement with that reported in the literature.ⁱⁱ

(2S)-2-Bromobutane-1,4-diol (19)

(S)-Bromosuccinic acid **18** (6.31 g, 32.05 mmol) was dissolved in dry tetrahydrofuran (100 cm³) under nitrogen and cooled to -10 °C. Borane dimethylsulfide complex (9.62 cm³, 96.15 mmol, 10 mol dm⁻³) was added dropwise and the solution allowed to warm to room temperature over 12 h. The reaction was quenched by the addition of methanol (50 cm³) and the trimethylborate azeotropically removed *in-vacuo*. The resultant residue was taken up in methanol (50 cm³) and the solvent removed under reduced pressure. This process was repeated three times. Flash column chromatography using acetone-dichloromethane (1:1) as eluent gave the title compound **19** (5.25 g, 97%) as a yellow oil; [α]_D -31.2 (*c* 1.02 in CHCl₃) (lit.,ⁱⁱⁱ [α]_D -31.9 (*c* 15.2 in CHCl₃)); δ _H (300 MHz, CD₃OD): 1.86-1.94 (1 H, m, H3b), 2.11-2.18 (1 H, m, H3a), 3.68-3.79 (4 H, m, H1 and H4), 4.17-4.22 (1 H, m, H2) and 4.81 (2 H, br s, OH); δ _C (75 MHz, CD₃OD): 39.0 (CH₂, C3), 54.7 (CH, C2), 60.5 (CH₂, C4) and 67.9 (CH₂, C1). This data was in agreement with that reported in the literature.^{ii,iii}

(3R)-1-(tert-Butyldiphenylsilyloxy)-3,4-epoxybutane (20)

Sodium hydride (2.35 g, 92.97 mmol, 95%) was suspended in dry tetrahydrofuran (150 cm³) under an atmosphere of nitrogen and cooled to 0 °C. A solution of (S)-bromodiol **19** (5.24 g, 30.10 mmol) in tetrahydrofuran (50 cm³) was then added dropwise. After 1 h. *tert*-butyldiphenylsilylchloride (8.86 cm³, 34.08 mmol) in tetrahydrofuran (30 cm³) was added and the mixture allowed to warm to room temperature. After stirring for 5 h. saturated aqueous sodium bicarbonate (50 cm³) was added. The aqueous layer was extracted with diethyl ether (3 x 100 cm³). The combined organic extracts were dried over magnesium sulfate, filtered and the solvent removed *in vacuo*. Flash column chromatography using hexane-diethyl ether (9:1) as

eluent gave the title compound **20** (8.29 g, 82%) as a white solid; m.p. 38-40 °C (lit^{iv} 38-40 °C); $[\alpha]_D +5.9$ (c 1.00 in CHCl₃) (lit.,^v $[\alpha]_D +6.3$ (c 1.00 in CHCl₃)); δ_H (300 MHz, CDCl₃): 1.07 (9 H, s, Si^tBuPh₂), 1.74-1.79 (2 H, m, H₂), 2.52 (1 H, m, H_{4a}), 2.76-2.78 (1 H, m, H_{4b}), 3.10 (1 H, m, H₃), 3.83-3.84 (2 H, m, H₂), 7.38-7.40 (6 H, m, Si^tBuPh₂, *m* and *p*) and 7.68 (4 H, m, Si^tBuPh₂, *o*); δ_C (75 MHz, CDCl₃): 19.2 (quat., Si^tBuPh₂), 26.8 (CH₃, Si^tBuPh₂), 35.7 (CH₂, C₂), 47.2 (CH, C₄), 50.1 (CH₂, C₃), 60.9 (CH₂, C₁), 127.7 (CH, Si^tBuPh₂, *m*), 129.7 (CH, Si^tBuPh₂, *p*), 133.6 (quat., Si^tBuPh₂*), 133.7 (quat., Si^tBuPh₂) and 135.5 (CH, Si^tBuPh₂, *o*). This data was in agreement with that reported in the literature.^{iv,v}

(5S)-7-(tert-Butyldiphenylsilyloxy)hept-1-en-5-ol^φ (21)

Allyltributyltin (22.81 cm³, 73.58 mmol) was dissolved in tetrahydrofuran (80 cm³) and cooled to -78 °C under an atmosphere of nitrogen. To this stirred solution was added methyllithium (45.99 cm³, 73.58 mmol, 1.6 mol dm⁻³). The solution was stirred for 2 h. and then added *via* cannula to a mixture of anhydrous lithium chloride (1.56 g, 36.79 mmol) and copper (I) cyanide (3.29 g, 36.79 mmol) in tetrahydrofuran (60 cm³) at -78 °C. The resultant deep golden-yellow solution was stirred for 3 h., then a solution of (*R*)-epoxide **20** (8.00 g, 24.53 mmol) in tetrahydrofuran (20 cm³) was added dropwise. After stirring at -78 °C for 2 h., the solution was allowed to warm to -40 °C and quenched by the addition 10% ammonia in saturated aqueous ammonium chloride (60 cm³). The aqueous layer was extracted with diethyl ether (3 x 200 cm³) and the combined organic extracts dried over magnesium sulfate. Filtration and removal of the solvent *in vacuo* gave a crude oil that was purified by flash chromatography using hexane-diethyl ether (9:1-7:3) as eluent to afford the *title compound* **21** (20 g, 90%) as a yellow oil; $[\alpha]_D -4.3$ (c 1.05 in CHCl₃); ν_{\max} (film)/cm⁻¹ 3442br (OH), 3071, 2930, 2857, 1472, 1428, 1112, 997, 910, 822, 736 and 701; δ_H (300 MHz, CDCl₃): 1.05 (9 H, s, Si^tBuPh₂), 1.53-1.70 (4 H, m,

^φ (3S)-1-(tert-butyldiphenylsilyloxy)hept-6-en-3-ol

H6 and H4), 2.17-2.27 (2 H, m, H3), 3.85-3.92 (3 H, m, H5 and H7), 3.28 (1 H, br s, OH), 4.95-5.07 (2 H, m, H1), 5.77-5.89 (1 H, m, H2), 7.39-7.46 (6 H, m, Si^tBuPh₂, *m* and *p*) and 7.68-7.69 (4 H, m, Si^tBuPh₂, *o*); δ_C (75 MHz, CDCl₃): 19.2 (quat., Si^tBuPh₂), 26.8 (CH₃, Si^tBuPh₂), 29.8 (CH₂, C3), 36.6 (CH₂, C4), 38.3 (CH₂, C6), 63.4 (CH₂, C7), 71.1 (CH, C5), 114.6 (CH₂, C1), 127.8 (CH, Si^tBuPh₂, *m*), 129.8 (CH, Si^tBuPh₂, *p*), 132.9 (quat., Si^tBuPh₂), 133.0 (quat., Si^tBuPh₂*), 135.5 (CH, Si^t-BuPh₂, *o*) and 138.6 (CH, C2); *m/z* (EI): 311 (M-^tBu⁺, 6%), 229 (17), 199 (100), 139 (9), 95 (37) and 77 (8); HRMS (CI, NH₃): Found MH⁺, 369.2253. C₂₃H₃₃O₂Si requires *M*, 369.2250.

Conversion to Mosher ester

A solution of alcohol **21** (50 mg, 0.14 mmol) in dichloromethane (1 cm³) was added to a suspension of (*S*)-2-methoxy-2-trifluoromethyl-2-phenylacetic acid (48 mg, 0.20 mmol), *N,N*-4-dimethylaminopyridine (3 mg, 0.03 mmol) and dicyclohexylcarbodiimide (70 mg, 0.34 mmol) in dichloromethane (1 cm³). After stirring the mixture at room temperature for 72 h., the reaction was quenched by the addition of brine (2 cm³) and the mixture diluted with diethyl ether (5 cm³). The aqueous layer was extracted with diethyl ether (3 x 5 cm³) and the combined extracts dried over magnesium sulfate. Filtration and removal of the solvent under reduced pressure gave an oil that was purified by flash column chromatography using hexane-diethyl ether (9:1) as the eluent to afford the *Mosher ester* (65 mg, 82%) as a colourless oil; δ_H (300 MHz, CDCl₃): 1.05 (9 H, s, Si^tBuPh₂), 1.67-1.74 (2 H, m, H4), 1.82-1.89 (2 H, m, H2), 1.90-2.02 (2 H, m, H5), 3.45 (3 H, s, OMe), 3.70 (2 H, t, *J* 6.3, H1), 4.92-4.98 (2 H, m, H7), 5.36 (1 H, quintet, *J* 6.3, H3), 5.71 (1 H, dddd, *J* 17.6, 9.7, 6.5 and 6.5, H6), 7.38-7.42 (9 H, m, Si^tBuPh₂, *p* and *m* and ArH, *p* and *o* or *m*), 7.50-7.52 (2 H, m, ArH, *o* or *m*), 7.62-7.66 (4 H, m, Si^tBuPh₂, *o*); The ¹⁹F NMR spectrum of the *Mosher ester* exhibited two resonances for the trifluoromethyl group at δ -72.47 and δ -72.29, in the ratio 32.3:1, corresponding to an enantiomeric excess of 94%.

(5S)-7-(*tert*-Butyldiphenylsilyloxy)-5-(*tert*-butyldimethylsilyloxy)hept-1-ene^φ 22

tert-Butyldimethylsilylchloride (2.53 g, 16.76 mmol), imidazole (1.14 g, 16.76 mmol) and 4-(*N,N*-dimethylamino)pyridine (0.08 g, 0.64 mmol) were dissolved in dichloromethane (90 cm³) under an atmosphere of nitrogen and cooled to 0 °C. To this stirred solution was added (*S*)-alcohol **21** (4.75 g, 12.90 mmol) in dichloromethane (10 cm³). After stirring for 12 h. brine (30 cm³) was added and the mixture extracted with dichloromethane (3 x 100 cm³). The combined extracts were dried over magnesium sulfate, filtered and the solvent removed under reduced pressure. Flash column chromatography using hexane-diethyl ether (9:1) as eluent gave the *title compound 22* (6.10 g, 98%) as a yellow oil; $[\alpha]_D +3.7$ (*c* 0.98 in CHCl₃); $\nu_{\max}(\text{film})/\text{cm}^{-1}$ 2928, 1471, 1427, 1255, 1111, 909, 835, 774, 736 and 701; δ_{H} (300 MHz, CDCl₃): 0.01 (3 H, s, Si^tBuMe₂), 0.04 (3 H, s, Si^tBuMe₂), 0.85 (9 H, s, Si^tBuMe₂), 1.05 (9 H, s, Si^tBuPh₂), 1.43-1.59 (2 H, m, H4), 1.70 (2 H, m, H6), 2.03-2.11 (2 H, m, H3), 3.72 (2 H, td, *J* 6.3, *J*_w 2.4, H7), 3.91 (1 H, quintet, *J* 6.3, H5), 4.91-5.03 (2 H, m, H1), 5.80 (1 H, dddd, *J* 17.1, 10.3, 6.6 and 6.6, H2), 7.34-7.45 (6 H, m, Si^tBuPh₂, *m* and *p*) and 7.64-7.68 (4 H, m, Si^tBuPh₂, *o*); δ_{C} (75 MHz, CDCl₃): -4.5 (CH₃, Si^tBuMe₂), -4.4 (CH₃, Si^tBuMe₂), 18.1 (quat., Si^tBuMe₂), 19.2 (quat., Si^tBuPh₂), 25.9 (CH₃, Si^tBuMe₂), 26.9 (CH₃, Si^tBuPh₂), 29.5 (CH₂, C3), 36.5 (CH₂, C4), 39.8 (CH₂, C6), 60.8 (CH₂, C7), 68.8 (CH, C5), 114.2 (CH₂, C1), 127.6 (CH, Si^tBuPh₂, *m*), 129.5 (CH, Si^tBuPh₂, *p*), 133.9 (quat., Si^tBuPh₂), 135.6 (CH, Si^tBuPh₂, *o*) and 138.9 (CH, C2); *m/z* (EI): 425 (M-^tBu⁺, 24%), 313 (57), 271 (52), 209 (70), 197 (50), 175 (39), 135 (86), 95 (100), 91 (65) and 73 (44); HRMS (FAB): Found MH⁺, 483.31171. C₂₉H₄₇O₂Si₂ requires *M*, 483.31146.

(5S)- 7-(*tert*-Butyldiphenylsilyloxy)-5-(*tert*-butyldimethylsilyloxy)heptan-1-ol (23)

^φ (3S)-1-(*tert*-butyldiphenylsilyloxy)-3-(*tert*-butyldimethylsilyloxy)-hept-6-ene

Alkene **22** (5.75 g, 11.91 mmol) was dissolved in dry tetrahydrofuran (30 cm³) and the solution cooled to 0 °C under an atmosphere of nitrogen. Borane dimethylsulfide complex (11.91 cm³, 23.83 mmol, 2 mol dm⁻³) was added and the solution allowed to warm to room temperature over 12 h. Oxidative workup with aqueous sodium hydroxide (29.78 cm³, 59.57 mmol, 2 mol dm⁻³) and hydrogen peroxide (6.77 cm³, 59.57 mmol, 8.8 mol dm⁻³) gave a biphasic mixture that was extracted with diethyl ether (3 x 100 cm³). The combined organic extracts were dried over magnesium sulfate, filtered and the solvent removed under reduced pressure. The resultant residue was purified by flash chromatography using hexane-diethyl ether (9:1) as eluent to give the *title compound* **23** (4.95 g, 83%) as a yellow oil; $[\alpha]_D +3.9$ (*c* 1.17 in CHCl₃); $\nu_{\max}(\text{film})/\text{cm}^{-1}$ 3346br (OH), 2930, 2858, 1471, 1427, 1256, 1112, 835, 774, 738 and 701; δ_{H} (300 MHz, CDCl₃): 0.00 (3 H, s, Si^tBuMe₂), 0.02 (3 H, s, Si^tBuMe₂), 0.84 (9 H, s, Si^tBuMe₂), 1.04 (9 H, s, Si^tBuPh₂), 1.31-1.46 (4 H, m, H3 and H4), 1.53 (2 H, quintet, *J* 6.6, H2), 1.68 (2 H, m, H6), 3.62 (2 H, t, *J* 6.6, H1), 3.71 (2 H, td, *J* 6.2, *J*_w 1.7, H7), 3.86 (1 H, quintet, *J* 6.2, H5), 7.33-7.44 (6 H, m, Si^tBuPh₂, *m* and *p*) and 7.63-7.68 (4 H, m, Si^tBuPh₂, *o*); δ_{C} (75 MHz, CDCl₃): -4.6 (CH₃, Si^tBuMe₂), -4.4 (CH₃, Si^tBuMe₂), 18.1 (quat., Si^tBuMe₂), 19.2 (quat., Si^tBuPh₂), 21.3 (CH₂, C3), 25.9 (CH₃, Si^tBuMe₂), 26.9 (CH₃, Si^tBuPh₂), 33.0 (CH₂, C2), 37.1 (CH₂, C4), 39.8 (CH₂, C6), 61.0 (CH₂, C7), 63.0 (CH₂, C1), 69.2 (CH, C5), 127.6 (CH, Si^tBuPh₂, *m*), 129.6 (CH, Si^tBuPh₂, *p*), 134.0 (quat., Si^tBuPh₂) and 135.6 (CH, Si^tBuPh₂, *o*); *m/z* (EI): 443 (M-^tBu⁺, 1%), 311 (67), 199 (31), 135 (37), 95 (100) and 73 (25); HRMS (FAB): Found MH⁺, 501.32137. C₂₉H₄₉O₃Si₂ requires *M*, 501.32203.

(5S)-7-(tert-Butyldiphenylsilyloxy)-5-(tert-butyltrimethylsilyloxy)heptanal (7)

A solution of alcohol **23** (3.85 g, 7.69 mmol) in dichloromethane (40 cm³) was added dropwise to a suspension of Dess-Martin periodinane (6.52 g, 15.38 mmol) and pyridine (1.86 cm³, 23.07 mmol) in dichloromethane (40 cm³) at 0 °C under an atmosphere of nitrogen. After stirring at

room temperature for 2 h. the solution was filtered through a pad of Celite[®] and the solid washed with dichloromethane (3 x 10 cm³). Removal of the solvent *in vacuo* and purification of the resultant residue by flash column chromatography using hexane-diethyl ether (8:2) as eluent afforded the *title compound 7* (3.30 g, 86%) as a yellow oil; $[\alpha]_D +1.5$ (*c* 1.05 in CHCl₃); $\nu_{\max}(\text{film})/\text{cm}^{-1}$ 2954, 2930, 2857, 1728s (CO), 1472, 1428, 1255, 1111, 835, 774, 738 and 701; δ_{H} (300 MHz, CDCl₃): 0.00 (3 H, s, Si^tBuMe₂), 0.03 (3 H, s, Si^tBuMe₂), 0.85 (9 H, s, Si^tBuMe₂), 1.04 (9 H, s, Si^tBuPh₂), 1.41-1.54 (2 H, m, H4), 1.61-1.74 (4 H, m, H6 and H3), 2.37 (2 H, td, *J* 7.3 and 1.8, H2), 3.71 (2 H, t, *J* 6.1, H7), 3.88 (1 H, quintet, *J* 5.6, H5), 7.34-7.44 (6 H, m, Si^tBuPh₂, *m* and *p*), 7.63-7.67 (4 H, m, Si^tBuPh₂, *o*) and 9.73 (1 H, t, *J* 1.8, H1); δ_{C} (75 MHz, CDCl₃): -4.6 (CH₃, Si^tBuMe₂), -4.5 (CH₃, Si^tBuMe₂), 17.8 (CH₂, C3), 18.0 (quat., Si^tBuMe₂), 19.1 (quat., Si^tBuPh₂), 25.8 (CH₃, Si^tBuMe₂), 26.9 (CH₃, Si^tBuPh₂), 36.5 (CH₂, C4), 39.7 (CH₂, C6), 43.9 (CH₂, C2), 60.7 (CH₂, C7), 68.9 (CH, C5), 127.6 (CH, Si^tBuPh₂, *m*), 129.6 (CH, Si^tBuPh₂, *p*), 133.9 (quat., Si^tBuPh₂), 135.5 (CH, Si^tBuPh₂, *o*) and 202.5 (CH, C1); *m/z* (EI): 441 (M^tBu⁺, 74%), 271 (29), 255 (65), 241 (38), 209 (38) 199 (73), 135 (100), 111 (27) and 91 (37); HRMS (CI, NH₃): Found MH⁺, 499.30572. C₂₉H₄₇O₃Si₂ requires *M*, 499.30638.

(2S)-2-(tert-Butyldimethylsilyloxy)but-3-yne (24a)

tert-Butyldimethylsilylchloride (2.97 g, 19.71 mmol) and imidazole (2.68 g, 39.41 mmol) were dissolved in diethyl ether (15 cm³) under an atmosphere of nitrogen and cooled to 0 °C. To this stirred solution was added (*S*)-but-3-yn-2-ol (1.03 cm³, 13.14 mmol) in diethyl ether (10 cm³). After stirring for 12 h. saturated aqueous ammonium chloride (20 cm³) was added and the mixture extracted with diethyl ether (3 x 40 cm³). The combined extracts were dried over magnesium sulfate, filtered and the solvent removed under reduced pressure. Flash column chromatography using hexane-diethyl ether (97:3) as eluent gave the title compound **24a** (1.70

g, 70%) as a yellow oil; $[\alpha]_D -43.8$ (c 1.29 in CHCl_3) (lit.,^{vi} -46.0 (c 0.09 in CHCl_3)); δ_H (300 MHz, CDCl_3): 0.10 (3 H, s, Si^tBuMe_2), 0.12 (3 H, s, Si^tBuMe_2), 0.89 (9 H, s, Si^tBuMe_2), 1.40 (3 H, d, J 6.6, H1), 2.34 (1 H, s, H4) and 4.49 (1 H, q, J 6.6, H2); δ_C (75 MHz, CDCl_3): -5.0 (CH_3 , Si^tBuMe_2), -4.7 (CH_3 , Si^tBuMe_2), 18.2 (quat., Si^tBuMe_2), 25.3 (CH_3 , C1), 25.7 (CH_3 , Si^tBuMe_2), 58.8 (CH, C2), 71.1 (CH, C4) and 86.4 (quat., C3). This data was in agreement with that reported in the literature.^{vi}

(2R)-2-(tert-Butyldimethylsilyloxy)but-3-yne (24b)

tert-Butyldimethylsilylchloride (2.97 g, 19.71 mmol) and imidazole (2.68 g, 39.41 mmol) were dissolved in diethyl ether (15 cm^3) under an atmosphere of nitrogen and cooled to 0 °C. To this stirred solution was added (*R*)-but-3-yn-2-ol (1.03 cm^3 , 13.14 mmol) in diethyl ether (10 cm^3). After stirring for 12 h. saturated aqueous ammonium chloride (30 cm^3) was added and the mixture extracted with diethyl ether (3 x 20 cm^3). The combined extracts were dried over magnesium sulfate, filtered and the solvent removed under reduced pressure. Flash column chromatography using pentane-diethyl ether (97:3) as eluent gave the title compound **24b** (2.28 g, 94%) as a yellow oil; $[\alpha]_D +44.3$ (c 1.29 in CHCl_3). The spectroscopic data was identical to that reported above for (*S*)-**24a** and was in agreement with that reported in the literature.^{vi}

(2S, 5R, 9S)- and (2S, 5S, 9S)-2,9-Bis-(tert-butyldimethylsilyloxy)-11-(tert-butyldiphenylsilyloxy)undec-3-yn-5-ol (25a)

n-Butyllithium (6.19 cm^3 , 9.90 mmol, 1.6 mol dm^{-3}) was added to a stirred solution of (*S*)-silyl ether **24a** (1.67 g, 9.07 mmol) in tetrahydrofuran (30 cm^3) at -78 °C under an atmosphere of nitrogen and the resultant pale yellow solution stirred for 0.5 h. before the addition of anhydrous lithium bromide (0.36 g, 4.12 mmol) in tetrahydrofuran (5 cm^3). After 0.25 h a

solution of aldehyde **7** (4.11 g, 8.25 mmol) in tetrahydrofuran (40 cm³) was added dropwise and the solution stirred for 6 h. Saturated aqueous ammonium chloride (30 cm³) was added and the mixture extracted with diethyl ether (3 x 100 cm³). The combined extracts were dried over magnesium sulfate, filtered and the solvent removed under reduced pressure. Flash column chromatography using hexane-diethyl ether (9:1-7:3) as eluent afforded the *title compound 25a* (4.85 g, 86%) as a yellow oil; $[\alpha]_D -12.6$ (*c* 1.00 in CHCl₃); $\nu_{\max}(\text{film})/\text{cm}^{-1}$ 3400br (OH), 2954, 2930, 2857, 1472, 1462, 1428, 1254, 1104, 835, 775, 738 and 701; δ_{H} (300 MHz, CDCl₃): 0.00 (3 H, s, Si^tBuMe₂), 0.03 (3 H, s, Si^tBuMe₂), 0.11 (3 H, s, Si^tBuMe₂), 0.12 (3 H, s, Si^tBuMe₂), 0.85 (9 H, s, Si^tBuMe₂), 0.90 (9 H, s, Si^tBuMe₂), 1.05 (9 H, s, Si^tBuPh₂), 1.40 (3 H, d, *J* 6.5, H1), 1.41-1.47 (4 H, m, H7 and H8), 1.63-1.75 (4 H, m, H6 and H10), 3.71 (2 H, t, *J* 6.1, H11), 3.87 (1 H, m, H9), 4.36 (1 H, m, H5), 4.54 (1 H, qd, *J* 6.5, *J*_w 1.4, H2), 7.35-7.44 (6 H, m, Si^tBuPh₂, *m* and *p*) and 7.64-7.68 (4 H, m, Si^tBuPh₂, *o*); δ_{C} (75 MHz, CDCl₃): -4.9 (CH₃, Si^tBuMe₂), -4.6 (CH₃, Si^tBuMe₂), -4.5 (CH₃, Si^tBuMe₂), -4.4 (CH₃, Si^tBuMe₂), 18.1 (quat., Si^tBuMe₂), 18.2 (quat., Si^tBuMe₂), 19.2 (quat., Si^tBuPh₂), 20.8 (CH₂, C7), 20.8 (CH₂, C7*), 25.4 (CH₃, C1), 25.8 (CH₃, Si^tBuMe₂), 25.9 (CH₃, Si^tBuMe₂), 26.9 (CH₃, Si^tBuPh₂), 36.5 (CH₂, C8), 37.9 (CH₂, C6), 38.0 (CH₂, C6*), 39.8 (CH₂, C10), 59.0 (CH, C2), 60.9 (CH₂, C11), 62.4 (CH, C5), 69.2 (CH, C9), 84.1 (quat., C4), 87.4 (quat., C3), 127.6 (CH, Si^tBuPh₂, *m*), 129.5 (CH, Si^tBuPh₂, *p*), 134.0 (quat., Si^tBuPh₂) and 135.6 (CH, Si^tBuPh₂, *o*); *m/z* (EI): 625 (M-^tBu⁺, 1%), 493 (6), 441 (8), 361 (8), 313 (10), 271 (16), 255 (18), 209 (26), 199 (34), 159 (21), 145 (35), 135 (70), 91 (46) and 73 (100); HRMS (FAB): Found MH⁺, 683.43080. C₃₉H₆₇O₄Si₃ requires *M*, 683.43472.

(2*S*, 9*S*)-2,9-Bis-(*tert*-butyldimethylsilyloxy)-11-(*tert*-butyldiphenylsilyloxy)undec-3-yn-5-one (26a)

Alcohol **25a** (5.65 g, 8.27 mmol) was dissolved in dichloromethane (20 cm³) containing 4 Å molecular sieves and the mixture cooled to 0 °C under an atmosphere of nitrogen. To the stirred mixture was added *N*-methylmorpholine *N*-oxide (1.45 g, 12.41 mmol) and tetrapropylammonium perruthenate (0.15 g, 0.41 mmol). After stirring at room temperature for 2 h. the solvent was removed under reduced pressure. Purification of the resultant residue by flash column chromatography using hexane-diethyl ether (9:1-7:3) as eluent gave the *title compound 26a* (5.47 g, 97%) as a yellow oil; $[\alpha]_D -15.7$ (*c* 0.498 in CHCl₃); $\nu_{\max}(\text{film})/\text{cm}^{-1}$ 2955, 2930, 2857, 2213 (C=C), 1680s (CO), 1472, 1462, 1428, 1255, 1155, 1111, 836, 776, 738 and 701; δ_{H} (300 MHz, CDCl₃): 0.01 (3 H, s, Si^tBuMe₂), 0.04 (3 H, s, Si^tBuMe₂), 0.12 (3 H, s, Si^tBuMe₂), 0.14 (3 H, s, Si^tBuMe₂), 0.85 (9 H, s, Si^tBuMe₂), 0.91 (9 H, s, Si^tBuMe₂), 1.05 (9 H, s, Si^tBuPh₂), 1.41-1.46 (2 H, m, H8), 1.45 (3 H, d, *J* 6.6, H1), 1.61-1.75 (4 H, m, H7 and H10), 2.52 (2 H, t, *J* 7.6, H6), 3.71 (2 H, td, *J* 6.5, *J*_w 1.8, H11), 3.88 (1 H, quintet, *J* 5.8, H9), 4.65 (1 H, q, *J* 6.6, H2), 7.35-7.42 (6 H, m, Si^tBuPh₂, *m* and *p*) and 7.64-7.68 (4 H, m, Si^tBuPh₂, *o*); δ_{C} (75 MHz, CDCl₃): -5.0 (CH₃, Si^tBuMe₂), -4.6 (CH₃, Si^tBuMe₂), -4.6 (CH₃, Si^tBuMe₂), -4.5 (CH₃, Si^tBuMe₂), 18.0 (quat., Si^tBuMe₂), 18.1 (quat., Si^tBuMe₂), 19.1 (quat., Si^tBuPh₂), 19.6 (CH₂, C7), 24.5 (CH₃, C1), 25.7 (CH₃, Si^tBuMe₂), 25.9 (CH₃, Si^tBuMe₂), 26.9 (CH₃, Si^tBuPh₂), 36.4 (CH₂, C8), 39.7 (CH₂, C10), 45.5 (CH₂, C6), 58.8 (CH, C2), 60.8 (CH₂, C11), 68.9 (CH, C9), 82.3 (quat., C4), 93.6 (quat., C3), 127.6 (CH, Si^tBuPh₂, *m*), 127.6 (CH, Si^tBuPh₂, *m**), 129.5 (CH, Si^tBuPh₂, *p*), 129.6 (CH, Si^tBuPh₂, *p**), 133.9 (quat., Si^tBuPh₂), 135.5 (CH, Si^tBuPh₂, *o*) and 187.5 (quat., C5); *m/z* (FAB): 623 (M^tBu⁺, 1%), 549 (1), 491 (1), 413 (2), 271 (3), 209 (7), 197 (18), 135 (32) and 73 (100); HRMS (FAB): Found MH⁺, 681.42118. C₃₉H₆₅O₄Si₃ requires *M*, 681.41907.

(2*S*, 9*S*)-2,9-Bis-(*tert*-butyldimethylsilyloxy)-11-(*tert*-butyldiphenylsilyloxy)undecan-5-one (6a)

Ynone **26a** (5.47 g, 8.03 mmol) was dissolved in a solution of methanol (40 cm³) and dilute sulfuric acid (0.02 cm³, 0.05 mmol, 2.5 mol dm⁻³) added. After hydrogenation of the solution using a hydrogen filled double balloon in the presence of 10% Pd/C (0.27 g) for 48 h. the catalyst was removed by filtration through a pad of silica gel. The solvent was removed under reduced pressure and the resultant oil purified by flash column chromatography using hexane-diethyl ether (9:1) as eluent to give the *title compound* **6a** (4.73 g, 86%) as a yellow oil; $[\alpha]_D^{25} +8.2$ (*c* 1.30 in CHCl₃); $\nu_{\max}(\text{film})/\text{cm}^{-1}$ 2955, 2929, 2857, 1716s (CO), 1472, 1428, 1255, 1111, 1005, 836, 774, 738 and 701; δ_{H} (300 MHz, CDCl₃): 0.00 (3 H, s, Si^tBuMe₂), 0.02 (3 H, s, Si^tBuMe₂), 0.03 (3 H, s, Si^tBuMe₂), 0.04 (3 H, s, Si^tBuMe₂), 0.84 (9 H, s, Si^tBuMe₂), 0.88 (9 H, s, Si^tBuMe₂), 1.04 (9 H, s, Si^tBuPh₂), 1.11 (3 H, d, *J* 6.1, H1), 1.36-1.44 (2 H, m, H8), 1.51-1.62 (2 H, m, H7), 1.64-1.72 (4 H, m, H3 and H10), 2.17-2.51 (4 H, m, H4 and H6), 3.70 (2 H, td, *J* 6.5, *J*_w 1.7, H11), 3.79-3.90 (2 H, m, H2 and H9), 7.33-7.44 (6 H, m, Si^tBuPh₂, *m* and *p*) and 7.63-7.67 (4 H, m, Si^tBuPh₂, *o*); δ_{C} (75 MHz, CDCl₃): -4.8 (CH₃, Si^tBuMe₂), -4.6 (CH₃, Si^tBuMe₂), -4.4 (CH₃, Si^tBuMe₂), -4.4 (CH₃, Si^tBuMe₂), 18.0 (quat., Si^tBuMe₂), 18.1 (quat., Si^tBuMe₂), 19.2 (quat., Si^tBuPh₂), 19.6 (CH₂, C7), 23.7 (CH₃, C1), 25.9 (CH₃, Si^tBuMe₂), 26.0 (CH₃, Si^tBuMe₂), 26.9 (CH₃, Si^tBuPh₂), 33.2 (CH₂, C3), 36.8 (CH₂, C8), 38.6 (CH₂, C4), 39.7 (CH₂, C10), 42.9 (CH₂, C6), 43.0 (CH₂, C6*), 60.8 (CH₂, C11), 67.6 (CH, C9), 69.1 (CH, C2), 127.6 (CH, Si^tBuPh₂, *m*), 129.5 (CH, Si^tBuPh₂, *p*), 129.5 (CH, Si^tBuPh₂, *p**), 134.0 (quat., Si^tBuPh₂), 135.6 (CH, Si^tBuPh₂, *o*) and 211.0 (quat., C5); *m/z* (FAB): 685 (MH⁺, 2%), 627 (M^tBu, 2), 553 (3), 495 (2), 421 (6), 343 (2), 297 (3), 269 (4), 239 (8), 197 (18), 135 (43) and 73 (100); HRMS (FAB): Found MH⁺, 685.45024. C₃₉H₆₉O₄Si₃ requires *M*, 685.45037.

References

i D. R. Gauthier and E. M. Carreira, *Angew. Chem. Int. Ed. Engl.*, 1996, **35**, 2363.

- ii T. Shibata, K. Iiono and Y. Sugimura, *Heterocycles*, 1986, **24**, 1331.
- iii J. A. Frick, J. B. Klassen, A. Bathe, J. M. Abramson and H. Rapoport, *Synthesis*, 1992, 621.
- iv B. Achmatowicz, M. M. Kabat and J. Krajewski, *Tetrahedron*, 1992, **48**, 10201.
- v Y. Mori and M. Suzuki, *Tetrahedron Lett.*, 1989, **38**, 4383.
- vi A. S. Cotterill, M. Gill, A. Gimenez and N. M. Milanovic, *J. Chem. Soc. Perkin Trans. 1*, 1994, 3269.