Supplementary Material (ESI) for Organic and Biomolecular Chemistry

Electronic Supplementary Material

Synthesis and assignment of the absolute configuration of the anti-*Helicobacter pylori* agents CJ-12,954 and CJ-13,014

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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 F_{254} 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}deg cm^2 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}). ^{1}H 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 $CDCl_3$. All *J* values are given in Hz. Assignments are made with the aid of DEPT 135, COSY and HSQC experiments. ^{19}F 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 $CFCl_3$. 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.

1-(3',5'-Dimethoxyphenyl)-but-3-en-1-one (8)

To a stirred suspension of magnesium (0.95 g, 39.50 mmol) in diethyl ether (30 mL) under nitrogen at room temperature was added an iodine crystal and the mixture stirred until the solution decolourised. Allyl bromide (1.46 mL, 15.8 mmol) was added to the mixture over 15 min to initiate the reaction. The reaction mixture was heated under reflux for 1 h then added over 30 min to a solution of 3,5-dimethoxybenzaldehyde (0.75 g, 4.52 mmol) in tetrahydrofuran at –10 °C. The resultant mixture was warmed to room temperature and stirred for 12 h. The reaction was quenched by the addition of saturated aqueous ammonium chloride (20 mL) followed by water (10 mL). The layers were separated and the aqueous layer

extracted with ethyl acetate (3 x 50 mL). The combined organic extracts were washed with brine (20 mL), dried over magnesium sulfate and the solvent removed under reduced pressure. The resultant oil was purified by flash column chromatography using hexane-ethyl acetate (4:1-1:1) as eluent to afford racemic alcohol **9** (0.93 g, 98%) as a colourless oil for which the NMR and mass spectrometry data was in agreement with that reported for the (1*S*) enantiomer **9** reported below. To a solution of this alcohol (0.50 g, 2.40 mmol) in dichloromethane (30 mL) under nitrogen at room temperature was added pyridinium chlorochromate (0.67 g, 3.13 mmol) and the mixture stirred for 4 h. The reaction mixture was diluted with dry diethyl ether (50 mL) and filtered through Florisil®. The solvent was removed under reduced pressure and quickly purified by flash column chromatography using hexane-ethyl acetate (9:1) as eluent to afford the *title compound* **8** (0.41 g, 83%) as a colourless oil; ν_{max}(film)/cm^{-1} 3080, 2839, 1685s (CO), 1594, 1457, 1353, 1206, 1156, 1067, 1028, 924, 843, 749, 680; δ_H (300 MHz, $CDCl_3$) 3.70 (2H, d, *J* 6.7 Hz, H2), 3.81 (3H, s, OMe), 3.81 (3H, s, OMe), 5.17-5.23 (2H, m, H4), 6.07 (1H, dddd, *J* 17.3, 10.6, 6.7, 6.7 Hz, H3), 6.63 (1H, dd, *J* 2.3, 2.3 Hz, H4'), 7.07 (2H, d, *J* 2.4 Hz, H2', H6'); δ_C (75.5 MHz, $CDCl_3$) 43.3 (CH_2, C2), 55.3 (CH_3, OMe), 105.0 (CH, C4'), 105.8 (CH, C2', C6'), 118.4 (CH_2, C4), 130.9 (CH, C3), 138.2 (quat., C1'), 160.6 (quat., C3', C5'), 197.3 (quat., C1); *m/z* (EI+) 206 (M^+, 14%), 165 (100), 137 (34), 122 (23), 107 (11), 77 (11); HRMS (EI+): Found M^+, 206.0941; $C_{14}H_{14}O_3$ requires 206.0943.

(1*S*)-(3',5'-Dimethoxyphenyl)but-3-en-1-ol (9)

(*R*)-2-Methyl-CBS-oxazaborolidine reagent (3.64 mL, 1 M in toluene, 3.64 mmol) was added to a solution of borane-dimethyl sulfide (1.82 mL, 2 M in THF, 3.64 mmol) and stirred for 15 min under an atmosphere of nitrogen at room temperature.

The mixture was then cooled to -20 °C and a solution of ketone **8** (0.75 g, 3.64 mmol) in tetrahydrofuran (10 mL) added dropwise. The solution was stirred at -20 °C for 2 h then quenched by the slow addition of methanol (10 mL) and warmed to rt over 1 h. The solvent was removed under reduced pressure and the crude oil purified by flash column chromatography using hexane-ethyl acetate (9:1) as eluent to yield the *title compound* **9** (0.69 g, 92%) as a clear colourless oil; $[\alpha]_D$ –42.3 (*c* 1.02 in $CHCl_3$); ν_{max} (film)/cm^{-1} 3432s (OH), 2933, 2833, 1598, 1429, 1204, 1155, 1060, 920, 837; δ_H (300 MHz, $CDCl_3$) 2.29 (1H, s, OH), 2.46-2.51 (2H, m, H2), 3.78 (3H, s, OMe), 3.80 (3H, s, OMe), 4.64 (1H, dd, *J* 7.1, 5.8 Hz, H1), 5.13 (1H, d, *J* 10.1 Hz, H4A), 5.16 (1H, dd, *J* 17.2, 1.5 Hz, H4B), 5.80 (1H, dddd, *J* 17.2, 10.1, 7.1, 7.1 Hz, H3), 6.37 (1H, t, *J* 2.3 Hz, H4'), 6.51 (2H, d, *J* 2.3 Hz, H2', H6'); δ_C (75.5 MHz, $CDCl_3$) 43.61 (CH_2, C2), 55.1 (CH_3, OMe), 55.2 (CH_3. OMe), 73.3 (CH, C1), 99.3 (CH, C4'), 103.5 (CH, C2'), 103.6 (CH, C6'), 118.2 (CH_2, C4), 134.4 (CH, C3), 146.5 (quat.., C1'), 160.7 (quat.., C3', C5'); HRMS (EI+): Found M^+, 208.1098; $C_{12}H_{16}O_3$ requires 208.1099.

Conversion to Mosher ester

Alcohol **9** (16 mg, 0.08 mmol) was added to a suspension of (*S*)-2-methoxy-2-trifluoromethyl-2-phenylacetic acid (27 mg, 0.12 mmol), dicyclohexylcarbodiimide (40 mg, 0.19 mmol) and *N*,*N*-4-dimethylaminopyridine (2 mg, 0.02 mmol) in dichloromethane (1 mL) at 0 °C. The mixture was warmed to room temperature and stirred for 48 h then the solvent removed under reduced pressure. The crude oil was purified by flash column chromatography using hexane-ethyl acetate (95:5) as eluent to afford the *Mosher ester* (32 mg, 97%) as a clear colourless oil; ν_{max} (film)/cm^{-1} 2939, 2846, 1747, 1599, 1461, 1361, 1254, 1157, 1121, 1066, 1018, 923, 837, 765, 720, 697; δ_H (300 MHz, $CDCl_3$) 2.51-2.61 (1H, m, H2'A), 2.67 (1H, ddd, *J* 1.0, 5.5,

16.3 Hz, H2'B), 3.48 (3H, s, OMe), 3.77 (6H, s, OMe), 5.00-5.07 (2H, m, H4'), 5.63 (1H, dddd, *J* 7.0, 7.0, 10.2, 17.1 Hz, H3'), 5.95 (1H, dd, *J* 5.5, 8.0 Hz, H1'), 6.42 (1H, dd, *J* 2.3, 2.3 Hz, H4''), 6.50 (2H, d, *J* 2.3 Hz, H2'', H6''), 7.31-7.39 (3H, m, Ph, *m* and *p*), 7.40-7.47 (2H, m, Ph, *o*); δ_C (75.5 MHz, $CDCl_3$) 40.4 (CH_2, C2'), 50.1 (CH_3, OMe), 55.3 (CH_3, OMe), 55.4 (CH_3, OMe), 77.8 (CH, C1'), 100.4 (CH, C4''), 104.7 (quat, C2), 106.1 (CH, C2'', C6''), 118.6 (CH_2, C4'), 121.5 (quat, C3), 127.5 (CH, Ph, *p*), 128.3 (CH, Ph, *m*), 129.5 (CH, Ph, *o*), 132.4 (quat, Ph), 134.4 (CH, C3'), 141.0 (quat, C1''), 160.9 (quat, C3'', C5''), 165.8 (quat, C1); *m/z* (EI+) 424 (M^+, 4%), 359 (2), 251 (5), 191 (63), 189 (100), 126 (42), 105 (16), 83 (80), 55 (28); δ_F (282 MHz, $CDCl_3$) -72.42 (79.31F, CF_3), -72.48 (2.45F, CF_3); HRMS (EI+): Found M^+, 424.1494, $C_{22}H_{23}F_3O_5$ requires 424.1498.

(1*S*)-1-(2'-bromo-3',5'-dimethoxyphenyl)-but-3-en-1-ol (10)

To a stirred solution of (*S*)-alcohol **9** (0.69 g, 3.33 mmol) in diethyl ether (20 mL) was added *N*-bromosuccinimide (0.62 g, 3.50 mmol) and ammonium acetate (0.03 g, 0.33 mmol) and the mixture stirred at room temperature for 24 h. The solution was filtered and the solvent removed under reduced pressure. The crude oil was purified by flash column chromatography using hexane-ethyl acetate (9:1) as eluent to afford the *title compound* **10** (0.86 g, 90%) as a bright yellow oil; $[\alpha]_D$ -49.5 (*c* 1.11 in $CHCl_3$); ν_{max} (film)/cm^{-1} 3435s (OH), 3003, 2840, 1590, 1454, 1429, 1323, 1202, 1160, 1022, 921, 839, 701; δ_H (300 MHz, $CDCl_3$) 1.69 (1H, s, OH), 2.29-2.31 (1H, m, H2A), 2.58-2.67 (1H, m, H2B), 3.81 (3H, s, OMe), 3.86 (3H, s, OMe), 5.11-5.12 (1H, m, H1), 5.14-5.23 (2H, m, H4), 5.89 (1H, dddd, *J* 17.1, 10.1, 7.1, 7.1 Hz, H3), 6.40 (1H, d, *J* 2.8 Hz, H4'), 6.76 (1H, d, *J* 2.8 Hz, H6'); δ_C (75.5 MHz, $CDCl_3$) 41.9 (CH_2, C2), 55.5 (CH_3, OMe), 56.3 (CH_3, OMe), 72.0 (CH, C1), 98.8 (CH, C4'), 102.1 (quat., C2'),

103.1 (CH, C6'), 118.4 (CH_2, C4), 134.4 (CH, C3), 144.9 (quat., C1'), 156.3 (quat., C3'), 159.9 (quat., C5'); *m/z* (EI+) 288 ($M[^{81}Br]^+$, 7%), 286 ($M[^{79}Br]^+$, 7%), 247 (62), 245 (65), 207 (32), 189 (16), 166 (56), 138 (100), 77 (8); HRMS (EI+): Found M^+, 286.0204; $C_{12}H_{15}{}^{79}BrO_3$ requires 286.0205. Found M^+, 288.0188; $C_{12}H_{15}{}^{81}BrO_3$ requires 288.0184.

(1*S*)-1-(2-Bromo-3',5'-dimethoxyphenyl)but-3-en-1-yl *N*,*N*-diethyl carbamate (11)

To a solution of sodium hydride (0.62 g, 25.66 mmol) in tetrahydrofuran (20.0 mL) was added (*S*)-alcohol **10** (2.95 g, 10.26 mmol) in tetrahydrofuran (20.0 mmol) at 0 °C under an atmosphere of nitrogen and the mixture stirred for 90 min. To the mixture was added *N*,*N* diethylcarbamyl chloride (1.43 mL, 1.29 mmol) and the solution warmed to room temperature overnight. The reaction was quenched with water (25 mL) and the tetrahydrofuran removed under reduced pressure. Ethyl acetate (150 mL) was added and the two layers separated. The organic layer was washed with saturated aqueous sodium bicarbonate (2 x 100 mL) and water (1 x 100 mL) then dried over magnesium sulfate and the solvent removed under reduced pressure. The crude oil was purified by flash column chromatography using hexane-ethyl acetate (9:1) as eluent to give the *title compound* **11** (3.56 g, 90%) as a clear yellow oil; $[\alpha]_D$ -11.5 (*c* 1.01 in $CHCl_3$); ν_{max} (film)/cm^{-1} 3076, 2973, 2935, 2839, 1702, 1641, 1595, 1456, 1427, 1355, 1277, 1202, 1161, 1066, 1024, 921, 836, 703; δ_H (300 MHz, $CDCl_3$) 1.11-1.21 (6H, m, NCH_2CH_3), 2.48-2.62 (2H, m, H2), 3.31 (4H, s br, NCH_2CH_3), 3.77 (3H, s, OMe), 3.84 (3H, s, OMe), 5.06 (1H, d, *J* 10.2 Hz, H4A), 5.09 (1H, dd, *J* 17.1, 1.6 Hz, H4B), 5.80 (1H, dddd, *J* 17.1, 10.2, 7.0, 7.0 Hz, H3), 6.10 (1H, dd, *J* 7.9, 4.4 Hz, H1), 6.38 (1H, d, *J* 2.8 Hz, H4'), 6.51 (1H, d, *J* 2.8 Hz, H6'); δ_C (75.5

MHz, $CDCl_3$) 13.4 (CH_3, NCH_2CH_3), 14.2 (CH_3, CH_2CH_3), 39.6 (CH_2, C2), 41.3 (CH_2, CH_2CH_3), 41.9 (CH_2, CH_2CH_3), 55.3 (CH_3, OMe), 56.2 (CH_3, OMe), 74.8 (CH, C1), 98.4 (CH, C4'), 102.2 (quat., C2'), 103.5 (quat., C6'), 117.6 (CH_2, C4), 133.6 (CH, C3), 142.6 (quat., C1'), 154.7 (quat., $CONEt_2$), 156.5 (quat., C5'), 159.7 (quat., C3'); *m/z* (CI+, NH_3) 388 ($M[^{81}Br]^+$, 5%), 386 ($M[^{79}Br]^+$, 5%), 306 (32), 271 (100), 269 (90), 218 (21), 209 (38), 193 (23), 191 (31), 100 (37), 72 (59); HRMS (CI+, NH_3): Found MH^+, 386.0955; $C_{17}H_{25}{}^{79}BrNO_4$ requires 386.0967. Found MH^+, 388.0950; $C_{17}H_{25}{}^{81}BrNO_4$ requires 388.0947.

(3*S*)-3-Allyl-5,7-dimethoxy-3*H*-isobenzofuran-1-one (12)

To a stirred solution of (*S*)-carbamate **11** (0.50 g, 1.30 mmol) in tetrahydrofuran (10.0 mL) under an atmosphere of nitrogen at -78 °C was added *t*-BuLi (1.68 mL, 1.7 M in pentane, 2.86 mmol) and the mixture stirred for 2 h at -78 °C. Methanol (2 mL) was slowly added and the mixture warmed to room temperature. (1*S*)-(+)-Camphorsulfonic acid (20 mg) was added to the solution and the mixture stirred overnight. The mixture was diluted with dichloromethane (30 mL), washed with water (1 x 10 mL) and brine (1 x 10 mL). The organic layer was dried over magnesium sulfate and the solvent removed under reduced pressure. The crude oil was purified by flash column chromatography using hexane-ethyl acetate (1:1) as eluent to afford the *title compound* **12** (0.21 g, 70%) as a colourless solid; m.p. 93-94 °C; $[\alpha]_D$ -28.1 (*c* 0.99 in $CHCl_3$); ν_{max} (film)/cm^{-1} 2975, 1943, 1751, 1613, 1495, 1431, 1333, 1218, 1159, 1037, 925, 839, 754; δ_H (300 MHz, $CDCl_3$) 2.48-2.55 (1H, m, H1A'), 2.61-2.68 (1H, m, H1B'), 3.83 (3H, s, OMe), 3.88 (3H, s, OMe), 5.05-5.15 (2H, m, H3'), 5.26-5.30 (1H, m, H3), 5.69 (1H, dddd, *J* 16.8, 10.1, 7.2, 7.2 Hz, H2'), 6.37 (1H, d, *J* 1.7 Hz, H4), 6.40 (1H, d, *J* 1.7 Hz, H6); δ_C (75.5 MHz, $CDCl_3$) 38.5

(CH_2, C1'), 55.8 (CH_3, OMe), 55.9 (CH_3, OMe), 78.7 (CH, C3), 97.7 (CH, C6), 98.6 (CH, C4), 106.7 (quat., C7a), 119.2 (CH_2, C3'), 131.2 (CH, C2'), 154.2 (quat., C3a), 159.4 (quat., C7), 166.5 (quat., C5), 168.1 (quat., C1); *m/z* (EI+) 234 (M^+, 8%), 193 (100), 165 (3), 150 (3), 135 (3), 121 (6), 106 (3), 91 (3), 77(4); HRMS (EI+): Found M^+, 234.0891; $C_{13}H_{14}O_4$ requires 234.0892.

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

Disiamylborane was prepared as according to the method of Brown and Zweifel.[i] To a solution of borane-dimethyl sulfide (3.0 mL, 10 M in tetrahydrofuran, 30.0 mmol) in tetrahydrofuran (12.0 mL) under a nitrogen atmosphere was added a solution of 2-methyl-2-butene (6.45 mL, 92.0 mmol) in tetrahydrofuran (18.6 mL) over 1 h at 0 °C. This was stirred for 6 h at 0 °C to prepare the disiamylborane. To a solution of alkene **12** (0.42 g, 1.79 mmol) in tetrahydrofuran (10 mL) was added disiamylborane (2.0 mL, 2.0 mmol) and the mixture stirred for 3 h at 0 °C. Methanol (1.0 mL) was added to quench the excess disiamylborane then sodium hydroxide (0.3 mL, 2.5 M) and 30% w/w hydrogen peroxide (0.4 mL, 8 M) added slowly. The solution was warmed to room temperature overnight, then concentrated to a third of the original volume before the layers were separated. The aqueous layer was extracted with ethyl acetate (3 x 10 mL). The combined organic extracts were washed with water (1 x 10 mL), dried over magnesium sulfate and the solvent removed under reduced pressure. The crude oil was purified by flash column chromatography using dichloromethane-acetone (9:1-1:1) as eluent to afford (3*S*)-3-(3'-Hydroxyprop-1'-yl)-5,7-dimethoxy-3*H*-isobenzofuran-1-one (0.32 g, 71%) as a colourless solid; m.p. 117-118 °C; $[\alpha]_D$ -40.6 (*c* 7.8 in $CHCl_3$); ν_{max} (film)/cm^{-1} 3208 (OH), 2971, 1744, 1605, 1466, 1431, 1340, 1215, 1159, 1055, 1007, 980, 932, 840, 755, 668; δ_H (400 MHz, $CDCl_3$) 1.68-

1.80 (3H, m, H1A', H2'), 2.13-2.19 (1H, m, H1B'), 3.66-3.72 (2H, m, H3'), 3.87 (3H, s, OMe), 3.93 (3H, s, OMe), 5.34 (1H, dd, *J* 7.2, 3.7 Hz, H3), 6.40 (1H, d, *J* 1.5 Hz, H4), 6.40 (1H, s, H6); δ_C (100 MHz, $CDCl_3$) 27.8 (CH_2, C2'), 31.2 (CH_2, C1'), 55.9 (CH_3, OMe), 55.9 (CH_3. OMe), 62.0 (CH_2. C3'), 79.7 (CH, C3), 97.4 (CH, C6), 98.7 (CH, C4), 106.7 (quat., C7a), 154.9 (quat., C3a), 159.5 (quat., C7), 166.8 (quat., C5), 168.4 (quat., C1); *m/z* (EI+) 252 (M^+, 35%), 207 (25), 193 (100), 165 (7), 135 (7), 122 (5), 105 (3), 77 (6); HRMS (EI+): Found M^+, 252.0994; $C_{13}H_{16}O_5$ requires 252.0998.

To a stirred solution of the above alcohol (70 mg, 0.28 mmol) in dichloromethane (0.6 mL) was added powdered 4Å molecular sieves (140 mg), tetrapropylammonium perruthenate (5 mg, 0.01 mmol) and 4-methylmorpholine *N*-oxide (49 mg, 0.42 mmol). The mixture was stirred for 6 h then filtered through Celite® and the solvent removed under reduced pressure. The crude oil was purified using flash column chromatography using dichloromethane-acetone (9:1) as eluent to give the *title compound* **5a** (50 mg, 72%) as a colourless solid; m.p. 95-96 °C; $[\alpha]_D$ -46.2 (*c* 1.07 in $CHCl_3$); ν_{max} (film)/cm^{-1} 2945, 2845, 1755, 1614, 1464, 1338, 1220, 1159, 1119, 1030, 984, 840, 752, 690; δ_H (300 MHz, $CDCl_3$) 1.97 (1H, dddd, *J* 13.5, 8.3, 8.3, 5.0 Hz, H1A'), 2.44 (1H, dddd, *J* 13.5, 7.5, 7.5, 3.3 Hz, H1B'), 2.60 (1H, ddd, *J* 18.4, 8.3, 5.1 Hz, H2A'), 2.72 (1H, ddd, *J* 18.4, 7.5, 7.5 Hz, H2B'), 3.88 (3H, s, OMe), 3.93 (3H, s, OMe), 5.33 (1H, dd, *J* 8.4, 3.3 Hz, H3), 6.41 (1H, dd, *J* 1.8 Hz, H4), 6.43 (1H, d, *J* 1.8 Hz, H6), 9.79 (1H, s, H3'); δ_C (75.5 MHz, $CDCl_3$) 26.9 (CH_2, C1'), 38.8 (CH_2, C2'), 55.9 (CH_3, OMe), 56.0 (CH_3, OMe), 78.4 (CH, C3), 97.4 (CH, C6), 99.0 (CH, C4), 106.6 (quat., C7a), 154.2 (quat., C3a), 159.6 (quat., C7), 166.9 (quat., C5), 168.0 (quat., C1), 200.7 (CH, C3'); *m/z* (FAB+) 251 (MH+, 100%), 233 (12), 205 (9), 193

(14), 165 (9), 115 (7), 89 (24); HRMS (FAB+): Found MH^+, 251.0913; $C_{13}H_{15}O_5$ requires 251.0920.

4-(*tert*-Butyldiphenylsilyloxy)butanal (13)

To a solution of 4-(*tert*-butyldiphenylsilyloxy)butan-1-ol[ii] (9.6 g, 29.3 mmol) in dichloromethane (50 mL) under an atmosphere of nitrogen was added pyridinium chlorochromate (8.2 g, 38.1 mmol) and the reaction mixture stirred at room temperature for 2.5 h. The reaction mixture was poured into diethyl ether (100 mL) and filtered through a pad of Celite® and silica gel. Removal of the solvent at reduced pressure afforded a brown oil that was purified by flash chromatography using hexane-diethyl ether (1:1) as eluent to give the *title compound* **13** (8.4 g, 88%) as a colourless oil that solidified upon storage in the freezer; ν_{max} (film)/cm^{-1} 2931, 2857, 1655 (C=0), 1589, 1111, 822, 701; δ_H (300 MHz, $CDCl_3$) 1.04 (9H, s, Si^t*Bu*Ph_2), 1.84-1.91 (2H, m, H3), 2.54 (2H, td, *J* = 7.2, 1.6 Hz, H2), 3.69 (1H, t, *J* = 6.0 Hz, H4), 7.35-7.45 (6H, m, Si^{t}Bu*Ph*$_2$, *m* and *p*), 7.63-7.70 (4H, m, Si^{t}Bu*Ph*$_2$, *o*), 9.77 (1H, t, *J* = 1.6 Hz, H1); δ_C (75.5 MHz, $CDCl_3$) 19.2 (quat., Si^t*Bu*Ph_2), 25.2 (CH_2, C3), 26.8 (CH_3, Si^t*Bu*Ph_2), 40.7 (CH_2, C2), 62.9 (CH_2, C4), 127.7 (CH, Si^{t}Bu*Ph*$_2$, *m*), 129.7 (CH, Si^{t}Bu*Ph*$_2$, *p*), 133.6 (quat., Si^{t}Bu*Ph*$_2$), 135.5 (CH, Si^{t}Bu*Ph*$_2$, *o*), 202.5 (CHO, C1). This data was in agreement with that reported in literature.[ii,iii]

(4*S*)-7-(*tert*-Butyldiphenylsilyloxy)hept-1-en-4-ol‡ (14)

To a stirred suspension of magnesium powder (1.10 g, 46.01 mmol) and an iodine crystal in diethyl ether (20 mL) was added allyl bromide (2.02 mL, 22.09 mmol) very

‡ (4*S*)-1-*tert*-butyldiphenylsilyloxy)hept-6-en-4-ol

slowly. The mixture was heated for 1 h then transferred *via* cannula into a solution of (+)-β-diisopinocampheylmethoxyborane (6.99 g, 22.09 mmol) in diethyl ether (30 mL) that had been cooled to -78 °C. The mixture was stirred for 2 h at -78 °C then warmed to room temperature for 1 h. The solution was transferred *via* cannula into a solution of aldehyde **13** (6.00 g, 18.40 mmol) in diethyl ether (70 mL) which had been cooled to -78 °C. The resultant mixture was stirred at -78 °C for 5 h then warmed to room temperature overnight. The reaction was quenched by the slow addition of sodium hydroxide (2 M, 24 mL) and hydrogen peroxide (27% w/w, 8 M, 12 mL). The mixture was heated under reflux for 3 h, then cooled to room temperature and the two layers separated. The aqueous layer was extracted with ethyl acetate (2 x 100 mL) and the combined organic layers were dried over magnesium sulfate and the solvent removed under reduced pressure. The crude oil was repeatedly purified by flash column chromatography using hexane-diethyl ether (100:0-9:1) as eluent to afford the title compound **14** (5.55 g, 82%) as a clear pale yellow oil; $[\alpha]_D$ = -2.81 (*c* 1.1, $CHCl_3$) (lit.[iv] $[\alpha]_D$ = -2.68 (*c* 1.2, $CHCl_3$)); ν_{max} (film)/cm^{-1} 3390s (O-H), 2930, 2857, 1641, 1427, 1111s (C-OSi), 998, 914, 822, 701; δ_H (300 MHz, $CDCl_3$) 1.05 (9H, s, Si*t*-*Bu*Ph_2), 1.50-1.53 (2H, m, H5), 1.61-1.71 (2H, m, H6), 2.00 (1H, s, OH), 2.16-2.31 (2H, m, H3), 3.64-3.71 (3H, m, H4, H7), 5.10-5.14 (2H, m, H1), 5.83 (1H, dddd, *J* = 17.1, 10.0, 7.4, 7.4 Hz, H2), 7.36-7.44 (6H, m, Si^{t}Bu*Ph*$_2$, *m* and *p*), 7.66-7.71 (4H, m, Si^{t}Bu*Ph*$_2$, *o*); *m/z* (EI) 369 (MH^+, 100%), 327 (12), 216 (16), 196 (18), 95 (36); HRMS (EI): Found MH^+, 369.2258; $C_{23}H_{33}O_2Si$ requires 369.2250. The ^{1}H NMR data was in agreement with that reported in literature.[iv]

Conversion to Mosher ester

Alcohol **14** (20 mg, 0.05 mmol) was added to a solution of (*S*)-2-methoxy-2-trifluoromethyl-2-phenylacetic acid (26 mg, 0.11 mmol), dicyclohexylcarbodiimide

(22 mg, 0.11 mmol) and *N*,*N*-4-dimethylaminopyridine (2 mg, 0.02 mmol) in dichloromethane (1 mL) at 0 °C under an atmosphere of nitrogen. The mixture was stirred for 72 h then the solvent removed under reduced pressure. The crude oil was purified by flash column chromatography using hexane-ethyl acetate (99:1-9:1) as eluent to afford the *Mosher ester* (26 mg, 83%) as a pale yellow oil; ν_{max} (film)/cm^{-1} 2930, 2855, 2119, 1745, 1643, 1450, 1360, 1259, 1169, 1111, 1021, 891, 823, 702; δ_H (300 MHz, $CDCl_3$) 1.03 (9H, s, Si^t*Bu*Ph$_2$), 1.38-1.54 (2H, m, H2'), 1.61-1.75 (2H, m, H3'), 2.41 (2H, t, *J* 6.5 Hz, H5'), 3.54 (3H, s, OMe), 3.57 (2H, t, *J* 6.2 Hz, H1'), 5.08-5.14 (2H, m, H7'), 5.18 (1H, pentet, *J* 6.1 Hz, H4'), 5.75 (1H, dddd, *J* 7.0, 7.0, 9.5, 16.7 Hz, H6'), 7.33-7.45 (9H, m, Si^{t}Bu*Ph$_2$*, *p* and *m*, ArH, *p* and *m*), 7.52-7.54 (2H, m, ArH, *o*), 7.61-7.65 (4H, m, Si^{t}Bu*Ph$_2$*, *o*); δ_C (75.5 MHz, $CDCl_3$) 19.2 (quat, Si^t*Bu*Ph$_2$), 26.5 (CH_3, Si^t*Bu*Ph$_2$), 29.7 (CH_2, C2'), 34.9 (CH_2, C3'), 38.3 (CH_2, C5'), 55.5 (CH_3, OMe), 63.2 (CH_2, C1'), 76.4 (CH, C4'), 110.9 (quat, C2), 118.5 (CH_2, C7'), 121.6 (quat, C3), 127.3 (CH, Ph, *p*), 127.6 (CH, Si^{t}Bu*Ph$_2$*, *m*), 128.3 (CH, Ph, *m*), 129.5 (CH, Si^{t}Bu*Ph$_2$*, *p*), 129.6 (CH, Ph, *o*), 132.7 (CH, C6'), 133.1 (quat, Ph), 135.5 (CH, Si^{t}Bu*Ph$_2$*, *o*), 166.2 (quat, C1); δ_F (282 MHz, $CDCl_3$) -72.43 (15.60F, CF_3), -72.48 (1.00F, CF_3); *m/z* (FAB+) 585 (MH^+, 2%), 415 (9), 351 (18), 239 (8), 197 (28), 189 (34), 165 (13), 105 (24), 105 (24), 95 (100); HRMS (FAB+): Found MH^+, 585.2646, $C_{33}H_{40}F_3O_4Si$ requires 585.2648.

(4*S*)-4-(*tert*-Butyldimethylsilyloxy)-7-(*tert*-butyldiphenylsilyloxy)hept-1-ene‡ (15)

tert-Butyldimethylsilyl chloride (0.24 g, 1.59 mmol) was added portionwise to a solution of alcohol **14** (0.45 g, 1.22 mmol), imidazole (0.10 g, 1.41 mmol) and *N*,*N*-4-

‡ (4*S*)-1-(*tert*-butyldiphenylsilyloxy)-4-(*tert*-butyldimethylsilyloxy)-hept-6-ene

dimethylaminopyridine (0.01 g, 0.06 mmol) in dichloromethane (10 mL) and the mixture stirred for 12 h at room temperature. The solution was diluted with dichloromethane (20 mL), washed with saturated aqueous sodium chloride (10 mL), then the aqueous layer was extracted with dichloromethane (2 x 10 mL) and the combined organic layers were dried over magnesium sulfate. Removal of the solvent under reduced pressure followed by flash column chromatography using hexane-diethyl ether (99:1) as eluent gave the *title compound* **15** (0.53 g, 90%) as a colourless oil; $[\alpha]_D$ = -2.83 (*c* 1.00, $CHCl_3$); ν_{max} (film)/cm^{-1} 2955, 2857, 1701, 1641, 1472, 1254, 1111, 836, 701; δ_H (400 MHz, $CDCl_3$) 0.04 (6H, s, Si^{t}Bu*Me*$_2$), 0.88 (9H, s, Si^t*Bu*Me$_2$), 1.04 (9H, s, Si^t*Bu*Ph$_2$), 1.46-1.63 (4H, m, H5, H6), 2.20 (2H, dd, *J* = 6.8, 5.8 Hz, H3), 3.65 (2H, t, *J* = 6.1 Hz, H7), 3.70 (1H, pentet, *J* = 5.8 Hz, H4), 5.00-5.04 (2H, m, H1), 5.79 (1H, dddd, *J* = 16.6, 10.7, 7.2, 7.2 Hz, H2), 7.24-7.43 (4H, m, Si^{t}Bu*Ph*$_2$, *m* and *p*), 7.65-7.67 (6H, m, Si^{t}Bu*Ph*$_2$, *o*); δ_C (75 MHz, $CDCl_3$) -4.5 (CH_3, Si^{t}Bu*Me*$_2$), 18.1 (quat., Si^t*Bu*Me$_2$), 19.2 (quat., Si^t*Bu*Ph$_2$), 25.9 (CH_3, Si^t*Bu*Me$_2$), 26.9 (CH_3, Si^t*Bu*Ph$_2$), 28.4 (CH_2, C6), 33.0 (CH_2, C5), 41.9 (CH_2, C3), 64.1 (CH_2, C7), 71.8 (CH, C4), 116.6 (CH_2, C1), 127.6 (CH, Si^{t}Bu*Ph*$_2$, *m*), 129.5 (CH, Si^{t}Bu*Ph*$_2$, *p*), 134.1 (quat., Si^{t}Bu*Ph*$_2$), 135.6 (CH, Si^{t}Bu*Ph*$_2$, *o*), 135.4 (CH, C2); *m/z* (CI, NH_3) 483 (MH^+, 13%), 369 (100), 216 (17), 199 (21), 95 (61).HRMS (CI): Found MH^+, 483.2916; $C_{29}H_{47}O_2Si$ requires 483.2907.

(4*S*)-4-(*tert*-Butyldimethylsilyloxy)-7-(*tert*-butyldiphenylsilyloxy)heptan-1-ol (16)

Disiamylborane was prepared by an adaptation of the method of Brown and Zweifel.[i] To a solution of borane-dimethyl sulfide (3.0 mL, 10 M in THF, 30.0 mmol) in tetrahydrofuran (12.0 mL) under a nitrogen atmosphere was added a solution of 2-methyl-2-butene (6.45 mL, 9.2 mmol) in tetrahydrofuran (8.6 mL) over 1 h at 0 °C.

The reaction mixture was stirred at 0 °C for 6 h to form the disiamylborane. Disiamylborane (5 mL) was added dropwise to a solution of (4*S*)-alkene **15** (0.47 g, 0.96 mmol) in tetrahydrofuran (5 mL) at 0 °C. After stirring for 20 h, methanol (*ca*. 0.5 mL) was added until gas evolution ceased. Aqueous sodium hydroxide (1.5 mL of 2.5M, 3.6 mmol) and 30% w/w hydrogen peroxide (0.4 mL, 3.6 mmol) were added dropwise causing the mixture to warm. The mixture was stirred for 30 min then extracted with ethyl acetate (3 x 15 mL) and the organic layers washed with water (5 mL) and dried over magnesium sulfate. Removal of the solvent under reduced pressure followed by flash column chromatography using hexane-diethyl ether (19:1) afforded the *title compound* **16** (0.36 g, 76%) as a pale yellow oil; $[\alpha]_D$ = +3.02 (*c* 0.98, $CHCl_3$); ν_{max} (film)/cm^{-1} 3433s (O-H), 2956, 2856, 1472, 1254, 1111, 836, 775, 701; δ_H (300 MHz, $CDCl_3$) 0.04 (6H, s, Si^{t}Bu*Me*$_2$), 0.91 (9H, s, Si*^{t}Bu*Me$_2$), 1.05 (9H, s, Si*^{t}Bu*Ph$_2$), 1.55-1.63 (6H, m, H2, H5, H6), 1.81 (1H, s, OH), 3.55 (1H, t, *J* = 6.1 Hz, H1), 3.62 (2H, td, *J* = 6.2, 1.1 Hz, H7), 3.72 (1H, pentet, *J* = 5.1 Hz, H4), 7.26-7.44 (6H, m, Si^{t}Bu*Ph*$_2$, *m* and *p*), 7.66 (4H, m, 1.8 Hz, Si^{t}Bu*Ph*$_2$, *o*); δ_C (75 MHz, $CDCl_3$) -4.4 (CH_3, Si^{t}Bu*Me*$_2$), 18.2, 19.2 (quat., Si*^{t}Bu*Me$_2$), 25.9 (CH_3, Si*^{t}BuMe*$_2$), 26.9 (CH_3, Si*^{t}Bu*Ph$_2$), 28.2 (CH_2, C2), 28.5 (CH_2, C6), 32.9 (CH_2, C3), 33.3 (CH_2, C5), 63.2 (CH_2, C1), 64.0 (CH_2, C7), 71.9 (CH, C4), 127.6 (CH, Si^{t}Bu*Ph*$_2$, *m*), 129.5 (CH, Si^{t}Bu*Ph*$_2$, *p*), 134.1 (quat., Si^{t}Bu*Ph*$_2$), 135.6 (CH, Si^{t}Bu*Ph*$_2$, *o*).

(4*S*)-4-(*tert*-Butyldimethylsilyloxy)-7-(*tert*-butyldiphenylsilyloxy)heptanal (17)

Dess-Martin periodinane (2.97 g, 7.01 mmol) was added to a solution of (4*S*)-alcohol **16** (1.40 g, 2.81 mmol) and pyridine (0.93 mL, 11.22 mmol) in dichloromethane (25 mL). After stirring at room temperature for 3 h the reaction mixture was filtered through Celite® and washed with dichloromethane (100 mL). Removal of solvent

under reduced pressure afforded a semi-solid which was purified by flash column chromatography using hexane-diethyl ether (4:1) as eluent to give the *title compound* **17** (1.08 g, 77%) as a colourless clear oil; $\alpha]^{20}_{D}$ = +3.24 (*c* 1.03, $CHCl_3$); ν_{max} (film)/cm^{-1}2930, 2857, 1727s (C=O), 1472, 1428, 1255, 1111s (C-OSi); δ_H (300 MHz, $CDCl_3$) 0.04 (6H, s, Si^{t}Bu*Me*$_2$), 0.88 (9H, s, Si*^{t}Bu*Me$_2$), 1.06 (9H,s, Si*^{t}Bu*Ph$_2$), 1.54-1.61 (4H, m, H5, H6), 1.67-1.87 (2H, m, H3), 2.47 (2H, td, *J* 7.5, 1.6 Hz, H2), 3.67 (2H, t, *J* 5.3 Hz, H7), 3.73 (1H, pentet, *J* 5.4 Hz, H4), 7.35-7.46 (6H, m, Si^{t}Bu*Ph*$_2$, *m* and *p*), 7.66-7.69 (4H, m, Si^{t}Bu*Ph*$_2$, *o*), 9.78 (1H, t, *J* 1.6 Hz, H1); δ_C (75.5 MHz, $CDCl_3$) –4.6 (CH_3, Si^{t}Bu*Me*$_2$), 18.0 (quat., Si*^{t}Bu*Me$_2$), 19.2 (quat., Si*^{t}Bu*Ph$_2$), 25.8 (quat., Si*^{t}Bu*Me$_2$), 26.9 (CH_3, (quat., Si*^{t}Bu*Ph$_2$), 28.3 (CH_2, C6), 28.8 (CH_2, C3), 33.3 (CH_2, C5), 39.7 (CH_2, C2), 63.9 (CH_2, C7), 71.0 (CH, C4), 127.6 (CH, Si^{t}Bu*Ph*$_2$, *m*), 129.5 (CH, Si^{t}Bu*Ph*$_2$, *p*), 134.0 (quat., Si^{t}Bu*Ph*$_2$), 135.6 (CH, Si^{t}Bu*Ph*$_2$, *o*), 202.6 (CH, CHO); *m/z* (CI, NH_3) 499 (MH^+, 19%), 419 (6), 367 (100), 309 (18), 185 (10), 111 (20); HRMS (CI): Found MH^+, 499.3061; $C_{29}H_{47}O_3Si_2$ requires 499.3064.

(2*S*)-2-(*tert*-Butyldimethylsilyloxy)but-3-yne (18)

(*S*)-3-Butyn-2-ol (0.11 mL, 1.43 mmol) was added dropwise to a stirred solution of *tert*-butyldimethylsilyl chloride (0.32 g, 2.14 mmol) and imidazole (0.29 g, 4.28 mmol) in dry diethyl ether (2.0 mL) under an atmosphere of nitrogen at room temperature. After stirring for 3 h, ethyl acetate (3mL) was added, then the solution quenched by the addition of saturated aqueous ammonium chloride (3 mL). The layers were separated and the aqueous layer extracted with ethyl acetate (3 x 10 mL). The organic layer was dried over magnesium sulfate followed by removal of the solvent under reduced pressure. The crude oil was purified by flash column

chromatography using hexane-diethyl ether (33:1) as eluent to give the title compound **18** (0.24 g, 92%) as a clear colourless oil; $[\alpha]_D$ = -44.9 (*c* 1.17, $CHCl_3$) (lit.[v] $[\alpha]_D$ = -46.0 (*c* 1.0, $CHCl_3$)); ν_{max} (film)/cm^{-1}) 3312 s (≡C-H), 2956, 2858, 2115m (C≡C), 1742, 1472, 1253, 1122, 836; δ_H (300 MHz, $CDCl_3$) 0.13 (6H, d, *J* 2.8 Hz, Si^{t}Bu*Me*$_2$), 0.90 (9H, s, Si^t*Bu*Me$_2$), 1.41 (3H, d, *J* 6.5 Hz, H1), 2.36 (1H, d, *J* 2.1 Hz, H4), 4.50 (1H, qd, *J* 6.5, 2.1 Hz, H2). This data was in agreement with that reported in the literature.[v]

(2*S*,8*S*)-*2*,8-bis(*tert*-Butyldimethylsilyloxy)-11-(*tert*-butyldiphenylsilyloxy)undec-3-yn-5-ol (19)

To a stirred solution of 2-(*tert*-butyldimethylsilyloxy)but-3-yne **18** (0.81 g, 4.42 mmol) in tetrahydrofuran (15 mL) at -78 °C under an atmosphere of nitrogen was added *n*-butyllithium (2.89 mL, 1.6 M in hexanes, 4.62 mmol) dropwise and stirred for 15 min. A suspension of lithium bromide (0.17 g, 2.01 mmol) in tetrahydrofuran (4 mL) was added and the mixture stirred at -78 °C for 30 min. A solution of aldehyde **17** (2.00 g, 4.02 mmol) in tetrahydrofuran (10 mL) was added dropwise and the mixture stirred at -78 °C for 4 h before being quenched with water (10 mL). The solution was warmed to room temperature and the layers separated. The aqueous layer was washed with ethyl acetate (2 x 20 mL) and the combined organic layers dried over magnesium sulfate and the solvent removed under reduced pressure. The crude oil was purified by flash column chromatography using hexane-ethyl acetate (99:1-95:5) as eluent to give the *title compound* **19** (2.31 g, 84%) as a clear colourless oil; $[\alpha]_D$ = -11.2 (*c* 1.1, $CHCl_3$); ν_{max} (film)/cm^{-1}) 3428s (O-H), 2955, 2857, 2115, 1642, 1471, 1254, 1104, 883, 774; δ_H (300 MHz, $CDCl_3$) 0.04 (3H, s, Si^{t}Bu*Me*$_2$), 0.05 (3H, s, Si^{t}Bu*Me*$_2$), 0.11 (3H, s, Si^{t}Bu*Me*$_2$), 0.12 (3H, s, Si^{t}Bu*Me*$_2$), 0.89 (9H, s, Si^t*Bu*Me$_2$),

0.90 (9H, s, Si*t*-*Bu*Me$_2$), 1.05 (9H, s, Si*t*-*Bu*Ph$_2$), 1.40 (3H, d, *J* 6.5 Hz, H1), 1.55-1.61 (6H, m, H7, H9, H10), 1.73-1.75 (2H, m, H6), 2.22 (1H, s, OH), 3.64-3.76 (3H, m, H8, H11), 4.39 (1H, t, *J* 5.5 Hz, H5), 4.54 (1H, q, *J* 6.5 Hz, H2), 7.34-7.45 (6H, m, Si^{t}Bu*Ph$_2$*, *m* and *p*), 7.65-7.68 (4H, dd, *J* 7.6, 1.7 Hz, Si^{t}Bu*Ph$_2$*, *o*); δ_C (75.5 MHz, $CDCl_3$) –4.9 (CH_3, Si^{t}Bu*Me$_2$*), –4.9 (CH_3, Si^{t}Bu*Me$_2$*), 18.1 (quat., Si*t*-*Bu*Me$_2$), 18.2 (quat., Si*t*-*Bu*Me$_2$), 19.2 (quat., Si*t*-*Bu*Ph$_2$), 25.4 (CH_3, C1), 25.8 (CH_3, Si*t*-*Bu*Me$_2$), 25.9 (CH_3, Si*t*-*Bu*Me$_2$), 26.9 (CH_3, Si*t*-*Bu*Ph$_2$), 28.4 (CH_2, C10), 32.4 (CH_2, C7), 32.9 (CH_2, C6), 33.5 (CH_2, C9), 59.0 (CH, C2), 62.7 (CH, C5), 64.0 (CH_2, C11), 71.7 (CH, C8), 84.1 (quat., C4), 87.3 (quat., C3), 127.6 (CH, Si^{t}Bu*Ph$_2$*, *m*), 129.5 (CH, Si^{t}Bu*Ph$_2$*, *p*), 134.0 (quat., Si^{t}Bu*Ph$_2$*), 135.6 (CH, Si^{t}Bu*Ph$_2$*, *o*); *m/z* (FAB+) 683 (MH^+, 1%), 620 (1), 551 (1), 493 (1), 211 (7), 197 (13), 115 (10), 91 (18), 73 (100); HRMS (FAB+): Found MH^+, 683.4348; $C_{39}H_{67}O_4Si_3$ requires 683.4347.

(2*S*,8*S*)-2,8-bis(*tert*-Butyldimethylsilyloxy)-11-(*tert*-butyldiphenylsilyloxy)undec-3-yn-5-one (20)

To a solution of alkyne **19** (0.58 g, 0.85 mmol) in dichloromethane (1.7 mL) was added 4Å molecular sieves (0.43 g), tetrapropylammonium perruthenate (0.02 g, 0.04 mmol) and 4-methylmorpholine *N*-oxide (0.15 g, 1.28 mmol). The mixture was stirred for 30 min then filtered through a pad of silica and washed with dichloromethane (25 mL). The solvent was removed under reduced pressure to yield the *title compound* **20** (0.54 g, 94%) as a clear colourless oil; $[\alpha]_D$ = -16.03 (*c* 0.89, $CHCl_3$); ν_{max} (film)/cm^{-1}) 2954, 2857, 2213, 1681 (C=O), 1472, 1255, 1110, 835, 701; δ_H (300 MHz, $CDCl_3$) 0.03 (3H, s, Si^{t}Bu*Me$_2$*), 0.04 (3H, s, Si^{t}Bu*Me$_2$*), 0.12 (3H, s, Si^{t}Bu*Me$_2$*), 0.14 (3H, s, Si^{t}Bu*Me$_2$*), 0.91 (9H, s, Si*t*-*Bu*Me$_2$), 0.93 (9H, s, Si*t*-*Bu*Me$_2$), 1.08 (9H, s, Si*t*-*Bu*Ph$_2$), 1.48 (3H, d, *J* 6.6 Hz, H1), 1.55-1.63 (4H, m, H9, H10), 1.70-1.91 (2H, m, H7), 2.63

(2H, t, *J* 7.6 Hz, H6), 3.69 (2H, t, *J* 5.4 Hz, H11), 3.73 (1H, pentet, *J* 5.5 Hz, H8), 4.68 (1H, q, *J* 6.6 Hz, H2), 7.36-7.46 (6H, m, Si^{t}Bu*Ph$_2$*, *m* and *p*), 7.67-7.70 (4H, m, Si^{t}Bu*Ph$_2$*, *o*); δ_C (100 MHz, $CDCl_3$) –5.0 (CH_3, Si^{t}Bu*Me$_2$*), –4.6 (CH_3, Si^{t}Bu*Me$_2$*), 18.1 (quat., Si^t*Bu*Me$_2$), 19.2 (quat., Si^t*Bu*Ph$_2$), 24.5 (CH_3, C1), 25.7 (CH_3, Si^t*Bu*Me$_2$), 26.9 (CH_3, Si^t*Bu*Ph$_2$), 28.2 (CH_2, C10), 30.4 (CH_2, C7), 33.4 (CH_2, C9), 41.3 (CH_2, C6), 58.8 (CH, C2), 64.0 (CH_2, C11), 70.8 (CH, C8), 82.3 (quat., C4), 93.6 (quat., C3), 127.6 (CH, Si^{t}Bu*Ph$_2$*, *m*), 129.5 (CH, Si^{t}Bu*Ph$_2$*, *p*), 134.0 (quat., Si^{t}Bu*Ph$_2$*), 135.6 (CH, Si^{t}Bu*Ph$_2$*, *o*), 187.7 (quat., C5); *m/z* (EI+) 680 (M^+, 1%), 623 (18), 491 (80), 367 (20), 199 (23), 135 (39), 73 (100); HRMS (EI+): Found M^+, 680.4119; $C_{39}H_{64}O_4Si_3$ requires 680.4113.

(2*S*,8*S*)-2,8-bis(*tert*-Butyldimethylsilyloxy)-11-(*tert*-butyldiphenylsilyloxy)undecan-5-one (21)

To a stirred solution of alkyne **20** (1.73 g, 2.55 mmol) in tetrahydrofuran:methanol (1:1, 15 mL) was added potassium carbonate (1.06 g, 7.64 mmol) and Adams'catalyst (PtO_2) (10 mg, catalytic). The mixture was stirred for 6 h under hydrogen then filtered through a pad of silica and Celite® and the solvent removed under reduced pressure. The crude oil was purified by flash column chromatography using hexane-ethyl acetate (95:5) as eluent to give the *title compound* **21** (1.64 g, 94%) as a clear colourless oil; $[\alpha]_D$ = +3.05 (*c* 0.89, $CHCl_3$); ν_{max} (film)/cm^{-1}) 2955, 2857, 1694, 1472, 1255, 1112, 836, 775, 701; δ_H (300 MHz, $CDCl_3$) 0.04 (6H, s, Si^{t}Bu*Me$_2$*), 0.05 (6H, s, Si^{t}Bu*Me$_2$*), 0.89 (18H, s, Si^t*Bu*Me$_2$), 1.05 (9H, s, Si^t*Bu*Ph$_2$), 1.12 (3H, d, *J* 6.1 Hz, H1), 1.47-1.79 (8H, m, H3, H7, H9, H10), 2.43-2.51 (4H, m, H4, H6), 3.65 (2H, t, *J* 5.8 Hz, H11), 3.69 (1H, pentet, *J* 5.7 Hz, H8), 3.84 (1H, sextet, *J* 6.1 Hz, H2), 7.34-7.45 (6H, m, Si^{t}Bu*Ph$_2$*, *m* and *p*), 7.67 (4H, dd, *J* 7.6 Hz, 1.7 Hz, Si^{t}Bu*Ph$_2$*, *o*); δ_C

(75.5 MHz, $CDCl_3$) –4.9 (CH_3, Si^{t}Bu*Me*$_2$), –4.5 (CH_3, Si^{t}Bu*Me*$_2$), 18.1 (quat., Si^t*Bu*Me$_2$), 19.2 (quat., Si^t*Bu*Ph$_2$), 24.5 (CH_3, C1), 25.7 (CH_3, Si^t*Bu*Me$_2$), 25.9 (CH_3, Si^t*Bu*Me$_2$), 26.9 (CH_3, Si^t*Bu*Ph$_2$), 28.2 (CH_2, C10), 30.4 (CH_2, C7), 33.3 (CH_2, C9), 33.4 (CH_2, C3), 38.3 (CH_2, C4), 38.8 (CH_2, C6), 64.0 (CH_2, C11), 67.6 (CH, C2), 70.8 (CH, C8), 127.6 (CH, Si^{t}Bu*Ph$_2$*, *m*), 129.5 (CH, Si^{t}Bu*Ph$_2$*, *p*), 134.0 (quat., Si^{t}Bu*Ph$_2$*), 135.5 (CH, Si^{t}Bu*Ph$_2$*, *o*), 211.1 (quat., C5); *m/z* (CI, NH_3) 686 (MH^+, 2%), 625 (2), 553 (2), 495 (6), 421 (8), 363 (5), 154 (82), 73 (100); HRMS (CI): Found MH^+, 685.4478; $C_{39}H_{69}O_4Si_2$ requires 685.4503.

(2''*S*, 5''*R*, 7''*S*)- and (2''*S*, 5''*S*, 7''*S*)-2-(3'-(2''-Methyl-1'',6''-dioxaspiro[4.4]non-7''-yl)propylsulfonyl)benzothiazole (30) and (31)

To a solution of (2*S*, 5*R*, 7*S*)-7-(3'-hydroxypropyl)-2-methyl-1,6-dioxaspiro[4.4]nonane **25** and (2*S*, 5*S*, 7*S*)-7-(3'-hydroxypropyl)-2-methyl-1,6-dioxaspiro[4.4]nonane **24** (0.104 g, 0.52 mmol) in tetrahydrofuran (10 mL) under an atmosphere of nitrogen at room temperature was added triphenylphosphine (0.15 g, 0.57 mmol) and 2-mercaptobenzothiazole (0.10 g, 0.57 mmol) and the mixture then cooled to 0 °C. A solution of diethyl azodicarboxylate (0.10 mL, 0.57 mmol) in tetrahydrofuran (1 mL) was added dropwise to the mixture *via* syringe. The bright yellow solution was warmed to room temperature over 12 h then the solvent removed under reduced pressure. The residue was treated with a solution of hexane-ethyl acetate (5:1, v/v, 10 mL) causing a precipitate to form which was removed by filtration. The precipitate was washed twice with hexane-ethyl acetate (5:1, v/v, 10 mL) then the solvent removed from the filtrate at reduced pressure. The crude residue was purified by flash column chromatography using hexane-diethyl ether (9:1) as eluent to afford (2"*S*, 5"*R*, 7"*S*)- and (2"*S*, 5"*S*, 7"*S*)-2-(3'-(2"-methyl-1",6"-

dioxaspiro[4.4]non-7''-yl)propylsulfanyl)benzothiazole (0.15 g, 83%) as a clear yellow oil and as a 1:1 mixture of diastereomers; ν_{max} (film)/cm^{-1}) 2940, 2869, 1643, 1560, 1456, 1427, 1380, 1340, 1309, 1274, 1238, 1155, 1074, 995, 892, 869, 756, 726; δ_H (300 MHz, $CDCl_3$)[#] 1.20 (2H, d, *J* 6.2 Hz, Me[‡]), 1.27 (1H, d, *J* 6.2 Hz, Me [ø]), 1.38-1.52 (2H, m, H3''A, H8''A), 1.63-1.73 (2H, m, H3'), 1.81-1.93 (2H, m, H2'), 1.95-2.15 (6H, m, H3''B, H4'', H8''B, H9''), 3.36 (2H, t, *J* 7.3 Hz, H1'), 3.93-3.99 (0.33H, m, H7'' [ø]), 4.05-4.09 (0.67H, m, H7''[‡]), 4.11-4.21 (1H, m, H2''), 7.25 (1H, td, *J* 7.7, 1.1 Hz, H6), 7.38 (1H, td, *J* 7.7, 1.1 Hz, H5), 7.72 (1H, d, *J* 8.1 Hz, H7), 7.84 (1H, d, *J* 8.1 Hz, H4); δ_C (75.5 MHz, $CDCl_3$)[#] 21.0 (CH_3, Me[‡]), 22.9 (CH_3, Me [ø]), 25.8 (CH_2, C2'), 26.0 (CH_2, C2'*), 30.2 (CH_2, C8''), 30.6 (CH_2, C8''*), 32.1 (CH_2, C3''), 32.5 (CH_2, C3''*), 33.5 (CH_2, C1'), 33.5 (CH_2, C1'*), 34.5 (CH_2, C3'), 35.3 (CH_2, C4''), 35.5 (CH_2, C4''*), 35.9 (CH_2, C9''), 36.4 (CH_2, C9''*), 74.0 (CH, C2''[‡]), 75.8 (CH, C2'' [ø]), 77.3 (CH, C7''[‡]), 79.0 (CH, C7''[ø]), 114.3 (quat., C5''[ø]), 114.7 (quat., C5''[‡]), 120.8 (CH, C7), 121.3 (CH, C4), 123.9 (CH, C5), 124.0 (CH, C5*), 125.8 (CH, C6), 125.9 (CH, C6*), 135.1 (quat., C7a), 153.2 (quat., C3a), 167.0 (quat., C2), 167.1 (quat., C2*); *m/z* (CI, NH_3) 350 (MH^+, 100%), 332 (15), 251 (17), 183 (17), 168 (17), 141 (9), 111 (11), 85 (12); HRMS (CI): Found MH^+, 350.1253; $C_{18}H_{24}NO_2S_2$ requires 350.1249. Found M^+, 349.1174; $C_{18}H_{23}NO_2S_2$ requires 349.1170.

To a solution of the above sulfides (1:1 mixture) (0.10 g, 0.29 mmol) in dichloromethane (4 mL) under an atmosphere of nitrogen at rt was added sodium bicarbonate (0.12 g, 1.43 mmol) and a solution of *m*-chloroperoxybenzoic acid (0.12 g, 0.72 mmol) in dichloromethane (2 mL). The mixture was stirred for 15 h then a solution of saturated aqueous sodium bicarbonate (2.5 mL) and sodium thiosulfate

[#] The symbol * is used to denote either the (2*S*, 5*R*, 7*S*) or the (2*S*, 5*S*, 7*S*) isomer.
The symbol [‡] is used to denote the (2*S*, 5*R*, 7*S*) isomer.
The symbol [ø] is used to denote the (2*S*, 5*S*, 7*S*) isomer.

(2.5 mL) added dropwise to the mixture. The layers were separated and the aqueous layer extracted with dichloromethane (2 x 20 mL). The combined organic extracts were dried over potassium carbonate and the solvent removed under reduced pressure. The crude oil was purified by flash column chromatography using hexane-diethyl ether (9:1-1:1) as eluent to give the *title compounds* **30** and **31** (0.08 g, 67%) as a clear yellow oil and as a 1:1 mixture of diastereomers; ν_{max} (film)/cm^{-1}) 2970, 2873, 2241, 1634, 1472, 1329, 1236, 1147, 911, 854, 762, 731, 647; δ_H (300 MHz, $CDCl_3$)[#] 1.16 (2H, d, *J* 6.2 Hz, Me[‡]), 1.20 (1H, d, *J* 6.2 Hz, Me [ø]), 1.35-1.47 (2H, m, H3"A, H8"A), 1.58-1.72 (3H, m, H3', H4"A), 1.79-1.87 (1H, m, H9"A), 1.88-2.00 (5H, m, H2', H3"B, H4"B, H9"B), 2.00-2.10 (1H, m, H8"B), 3.50-3.61 (2H, m, H1'), 3.89-3.93 (0.33H, m, H7"[ø]), 3.96-4.03 (0.67H, m, H7"[‡]), 4.04-4.12 (1H, m, H2"), 7.56 (1H, td, *J* 7.6, 1.5 Hz, H6), 7.61 (1H, td, *J* 7.6, 1.5 Hz, H5), 7.99 (1H, dd, *J* 7.2, 1.4 Hz, H7), 8.18 (1H, dd, *J* 7.2, 1.4 Hz, H4); δ_C (75.5 MHz, $CDCl_3$)[#] 19.2 (CH_2, C2'), 19.4 (CH_2, C2'*), 21.0 (CH_3, Me[‡]), 22.7 (CH_3, Me [ø]), 30.1 (CH_2, C8"), 30.5 (CH_2, C8"*), 32.0 (CH_2, C3"), 32.5 (CH_2, C3"*), 33.7 (CH_2, C3'), 35.1 (CH_2, C4"), 35.4 (CH_2, C4"*), 35.8 (CH_2, C9"), 36.3 (CH_2, C9"*), 54.6 (CH_2, C1'), 54.6 (CH_2, C1'*), 74.0 (CH, C2"[‡]), 75.9 (CH, C2"[ø]), 76.9 (CH, C7"[‡]), 78.6 (CH, C7"[ø]), 114.4 (quat., C5"[ø]), 114.8 (quat., C5"[‡]), 122.2 (CH, C7), 125.3 (CH, C4), 127.5 (CH, C5), 127.5 (CH, C5*), 127.8 (CH, C6), 127.9 (CH, C6*), 136.6 (quat., C7a), 152.6 (quat., C3a), 165.7 (quat., C2); *m/z* (CI, NH_3) 382 (MH^+, 27%), 364 (16), 166 (5), 154 (100), 120 (12), 89 (21); HRMS (CI): Found MH^+, 382.1140; $C_{18}H_{24}NO_4S_2$ requires 382.1113.

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The symbol [‡] is used to denote the (2*S*, 5*R*, 7*S*) isomer.
The symbol [ø] is used to denote the (2*S*, 5*S*, 7*S*) isomer.

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