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Supporting Information

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Oxidative cyclizations of diols derived from 1,5-dienes: formation of enantiopure *cis*-tetrahydrofurans using catalytic osmium tetroxide and a formal synthesis of (+)-*cis*-solamin

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1) General procedures

Regioselective asymmetric dihydroxylation of dienes

A stirred solution of diene (1 mmol), ligand (0.02 mmol), potassium ferricyanide (2 mmol), potassium carbonate (2 mmol) and methane sulfonamide (1 mmol) in $^{t}BuOH/H_2O$ (1:1, 30 cm^3) at 0 ^0C was treated with potassium osmate (0.02 mmol) and stirred at 0 ^oC until the reaction was judged to have reached completion by TLC or no further oxidation was observed by TLC (c. a. 24 h), when the reaction was treated with sat. $Na_2SO_{3(aq)}$ and stirred for 30 min. The reaction mixture was extracted with EtOAc (3 x 30 cm^3), dried over Na_2SO_4 and concentrated. The compound was then purified as specified. The absolute stereochemistry of the products was assigned according to the Sharpless mnemonic.

10 **8**

Diol cyclization to give enantiopure THFs

A solution of the diol (1 mmol) in 9:1 acetone:water (20 cm^3) and trifluoroacetic acid (10 cm^3) was treated with trimethylamine N-oxide (5 mmol) and cyclohexene (5 mmol) [or isoprene (5 mmol) as specified] followed by osmium tetroxide (0.05 mmol) and stirred at RT until no diol was observed by TLC (typically 24 h). The reaction mixture was then basified with 40% NaOH solution saturated with NaCl, and queched with sodium sulfite (0.1 mmol). After stirring for 1 hour the resultant solution was poured onto H_20 (50 cm^3) and extracted into EtOAc (3 x 100 cm^3), dried over Na_2SO_4 and concentrated. The compound was then purified as specified.

HPLC analysis was carried out using a Water 600E system controller, a Waters Photodiode Array detector and a Daicel Chiralpak AD column using heptane – 30% ethanol-heptane as the mobile phase. Enantiomeric excesses of diols and/or THFs were measured against a racemic sample, prepared from the corresponding 1,5-diene.

2) Experimental details

(2*E*)-1-Benzyloxy-3,7-dimethyl-octa-2,6-diene 1[1]

A stirred solution of geraniol (2.2 cm^3, 13 mmol) in dry THF (50 cm^3) under argon at 0 ^{0}C was treated with sodium hydride (60% dispersion in mineral oil, 750 mg, 19 mmol) followed by benzyl bromide (2.3 cm^3, 19 mmol). After 20 hours the reaction mixture was quenched with sat. $NH_4Cl_{(aq)}$ (20 cm^3), extracted into Et_2O (2 x 30 cm^3), dried over $MgSO_4$, and concentrated to a yellow oil. Purification by column chromatography (petrol – 5% Et_2O/petrol) yielded the benzyl ether **1** (1.8 g, 56%) as an oil.

^{1}H NMR δ_H (400 MHz, $CDCl_3$) 7.37-7.27 (m, 5H, 5 x ArC*H*), 5.45-5.38 (m, 1H, C*H*CH_2OBn), 5.15-5.07 (m, 1H, $(CH_3)_2$C=C*H*), 4.51 (s, 2H, C*H*$_2$Ph), 4.06-4.02 (m, 2H, C*H*$_2$OBn), 2.17-2.00 (m, 4H, C*H*$_2$C*H*$_2$), 1.69 (s, 3H, C*H*$_3$), 1.65 (s, 3H, C*H*$_3$), 1.61 (s, 3H, C*H*$_3$); **^{13}C NMR** δ_C (100 MHz, $CDCl_3$) 140.4, 128.3, 127.8, 127.5, 124.0, 120.8, 71.9, 66.6, 39.6, 26.4, 25.7, 17.7, 16.4; **MS** *m/z* (CI+) 262 (81%, MNH_4^+), 154 (60%, MNH_4^+ - OBn), 137 (100%, M-OBn$^-$); **HRMS** $C_{17}H_{28}NO$ requires *M*, 262.2171. Found (MNH_4^+) 262.2182 (+4.2 ppm).

(*R,E*)-8-(Benzyloxy)-2,6-dimethyloct-6-ene-2,3-diol 3

Geraniol benzyl ether **1** (5.9 g, 24 mmol) was subjected to standard conditions for asymmetric dihydroxylation of dienes using $(DHQD)_2PHAL$ to give crude material Purification by column chromatography (20% acetone/petrol) yielded diol **3** (5.8 g, 87%) as an oil.

$[\alpha]_D^{20}$ 18 (c = 1, CH_2Cl_2); **^{1}H NMR** δ_H (400 MHz, $CDCl_3$) 7.36-7.27 (m, 5H, 5 x ArC*H*), 5.48-5.45 (m, 1H, C=C*H*), 4.53-4.51 (m, 2H, C*H*$_2$Ph), 4.04 (d, 2H, *J* 6.8, C*H*$_2$OBn), 3.35 (dd, 1H, *J* 10.4 and 2.0, C*H*OH), 2.32 (ddd, 1H, *J* 14.8, 9.6 and 5.2, C*H*$_2$C(CH_3)=CH), 2.20 (m, 2H, 2 x

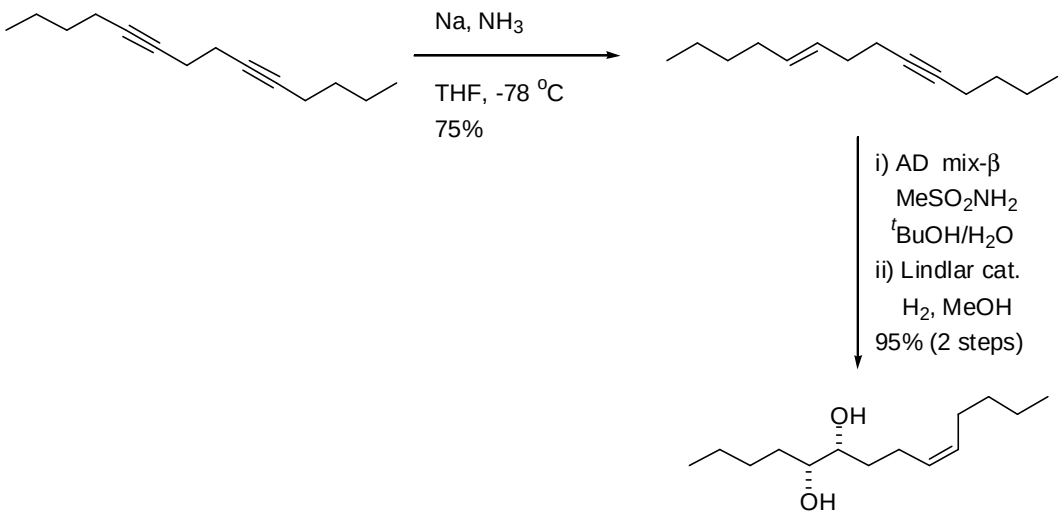
O*H*), 2.12 (ddd, 1H, *J* 14.8, 9.2 and 6.8, C*H*$_2$C(CH$_3$)=CH), 1.70-1.58 (m, 4H, C*H*$_3$C=CH and C*H*$_2$CHOH), 1.50-1.40 (m, 1H, C*H*$_2$CHOH), 1.20 (s, 3H, C*H*$_3$C(CH$_3$)OH), 1.16 (s, 3H, C*H*$_3$C(CH$_3$)OH); **^{13}C NMR** δ_C (100 MHz, CDCl$_3$) 140.2, 138.4, 128.3, 127.8, 127.6, 121.2, 78.1, 73.0, 72.2, 66.5, 36.6, 29.5, 26.5, 23.2, 16.5.

2-{(2*R*,5*S*)-5-[(*S*)-2-(Benzyloxy)-1-hydroxyethyl]-5-methyl-tetrahydrofuran-2-yl}propan-2-ol (-) 2

Geraniol benzyl ether diol **3** (200 mg, 0.72 mmol) was subjected to standard diol cyclization conditions to give the crude product as a brown oil. Purification by column chromatography (10% acetone/petrol) yielded *cis-THF* **2** (176 mg, 83%) as an off white solid.

m.p 94-95 ^{0}C; $[\alpha]_D^{20}$ -7.6 (c = 0.5, CH$_2$Cl$_2$); **^{1}H NMR** δ_H (400 MHz, CDCl$_3$) 7.39-7.29 (m, 5H, 5 x ArC*H*), 4.60 (d, 1H, *J* 12.0, C*H*$_2$Ph), 4.56 (d, 1H, *J* 12.0, C*H*$_2$Ph), 3.85 (t, 1H, *J* 7.2, THF C*H*), 3.75 (dd, 1H, *J* 8.4 and 3.2, C*H*OH), 3.67 (dd, 1H, *J* 9.2 and 3.2, CHOHC*H*$_2$), 3.58 (dd, 1H, *J* 9.2 and 8.4, CHOHC*H*$_2$), 2.63 (br s, 2H, 2 x O*H*), 2.24 (ddd, 1H, *J* 12.4, 8.8 and 6.4, C(3)*H*$_2$), 2.06-1.87 (m, 2H, C(4)*H*$_2$), 1.62 (ddd, 1H, *J* 12.4, 8.4 and 6.8), 1.23 (s, 3H, C*H*$_3$), 1.16 (s, 3H, C*H*$_3$), 1.10 (s, 3H, C*H*$_3$); **^{13}C NMR** δ_C (100 MHz, CDCl$_3$) 137.9, 128.5, 127.8, 85.8, 83.9, 75.4, 73.5, 71.8, 71.2, 35.1, 29.7, 27.8, 26.3, 25.0, 23.3; **MS** *m/z* (ES-) 292 (58%, M-H$^+$), 153 (100%); **HRMS** C$_{17}$H$_{26}$O$_4$^{23}Na requires *M*, 317.1729. Found (MNa$^+$) 317.1729 (-0.1 ppm); **IR** ν_{max} (film)/cm^{-1} 3400 (br), 1071.

Scheme for the synthesis of 4



(*E*)-Tetradec-5-en-9-yne

Freshly distilled ammonia (200 cm^3) was distilled onto sodium (2.0 g, 87 mmol) at - 78 ^{0}C. The dark blue solution was stirred for a further 30 minutes then treated with a solution of 5,9-tetradecadiyne (2.8 g, 15 mmol) in THF (10 cm^3). The resultant solution was stirred at - 78 ^{0}C for 1 hour before quenching with sat. $NH_4Cl_{(aq)}$ (10 cm^3). On warming to room temperature the biphasic mixture was extracted with petrol (3 x 15 cm^3) and the organics combined, dried over $MgSO_4$ and concentrated onto silica. Purification by column chromatography (petrol) yielded the *alkene* (2.1 g, 75%) as an oil.

^{1}H NMR δ_H (400 MHz, $CDCl_3$) 5.51-5.41 (m, 2H, C*H*=C*H*), 2.22-2.12 (m, 6H, CH_2-CC-CH_2CH_2), 2.03-1.97 (m, 2H, CH_2CH=CH), 1.50-1.27 (m, 8H, 2 x CH_2CH_2CH$_3$), 0.93-0.88 (m, 6H, 2 x CH_3); **^{13}C NMR** δ_C (100 MHz, $CDCl_3$) 131.6, 128.5, 80.5, 79.7, 32.3, 32.2, 31.7, 31.2, 22.1, 21.9, 19.3, 18.4, 13.9, 13.6; **MS** *m/z* (FI+) 192 (100%, M^+), 149 (98%, M^+-$CH_2CH_2CH_3$), 136 (65%); **HRMS** $C_{14}H_{24}$ requires M, 192.1878. Found (M^+) 192.1885 (+3.8 ppm); **IR** ν_{max} (film)/cm^{-1} 2958, 2929.

(5*R*,6*R*)-Tetradec-9-yne-5,6-diol 4

To a stirred solution of (*E*)-tetradec-5-en-9-yne (1.0 g, 5.2 mmol), potassium ferricyanide (5.75 g, 15 mmol), potassium carbonate (2.2 g, 15 mmol), $(DHQD)_2PHAL$ (81 mg, 0.10 mmol) and methane sulfonamide (0.50 g, 5.2 mmol) in 1:1 ^{t}BuOH:H_20 (80 cm^3) at 0 ^{0}C was added

potassium osmate (34 mg, 0.10 mmol). Stirring was continued until no starting alkene was observed by TLC (20 hr) and the reaction was quenched by addition of sat. $Na_2SO_{3(aq)}$, (50 cm^3) extracted into EtOAc (3 x 100 cm^3) and the organics combined, dried over Na_2SO_4 and concentrated. Purification by column chromatography (10% acetone/petrol) yielded the alkyne ***diol*** (1.1 g, 95%) as an oil.

A stirred solution of (5*R*,6*R*)-tetradec-9-yne-5,6-diol (250 mg, 1.1 mmol) in ethanol (15 cm^3) was treated with Lindlars catalyst (10 mg) and evacuated under high vacuum and filled with argon (x 5) followed by evacuation and filling with hydrogen (x 5). The suspension was vigorously stirred under hydrogen (1 atm) for 4 hours then carefully filtered through celite and the plug washed with methanol (3 x 20 cm^3). Concentration of the solution gave the cis-***alkene*** **4** (260 mg, quant.) as an oil.

$[\alpha]_D^{20}$ 18.4 (c = 1, CH_2Cl_2); **^{1}H NMR** δ_H (400 MHz, $CDCl_3$) 5.45-5.34 (m, 2H, C*H*=C*H*), 3.47-3.40 (m, 2H, C*H*(OH)C*H*OH), 2.28-1.19 (m, 6H, CH_2CH=CHCH_2 and 2 x O*H*), 1.59-1.30 (m, 12H, $CH_3CH_2CH_2CH_2$CHOH, CH(OH)CH_2 and $CH_2CH_2CH_3$), 0.95-0.89 (m, 6H, 2 x CH_3); **^{13}C NMR** δ_C (100 MHz, $CDCl_3$) 130.9, 128.9, 74.5, 74.2, 33.5, 33.3, 31.9, 27.8, 26.9, 23.4, 22.7, 22.3, 14.0, 14.0; **MS** *m/z* (CI+) 211 (100%, M-OH^-); **HRMS** $C_{14}H_{32}NO_2$ requires *M*, 246.2433. Found (MNH_4^+) 246.2422 (-4.6 ppm); **IR** ν_{max} (film)/cm^{-1} 3381 (br), 3006, 2957, 2931, 2860.

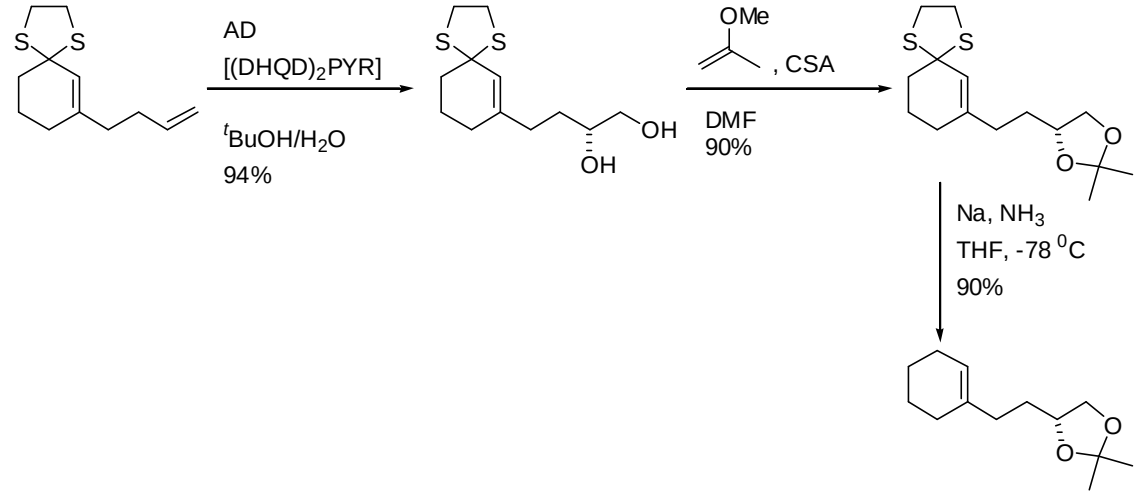
(1'*R*,1"*R*,2*S*,5*R*)-2-(1'-Hydroxypentyl)-5-(1"-hydroxypentyl)-terahydrofuran 5

Tetradecene diol **4** (200 mg, 0.88 mmol) was subjected to standard diol cyclization conditions using cyclohexene to give the crude product as a brown oil. Purification by column chromatography (10% acetone/petrol) yielded *cis-THF* **5** (152 mg, 71%) as a pale brown oil.

$[\alpha]_D^{20}$ 19.0 (c = 1, CH_2Cl_2); **^{1}H NMR** δ_H (400 MHz, $CDCl_3$) 3.29 (td, 1H, *J* 6.8 and 3.2, OC*H*CHOH), 3.86-3.80 (m, 2H, OC*H*C*H*OH), 3.48-3.41 (m, 1H, C*H*OH), 2.37 (br s, 2H, 2 x O*H*), 2.00-1.91 (m, 2H, THF CH_2CH_2), 1.84-1.71 (m, 2H, THF CH_2CH_2), 1.54-1.28 (m, 12H, 2 x $CH_2CH_2CH_2CH_3$), 0.92 (t, 6H, *J* 7.2, 2 x CH_3); **^{13}C NMR** δ_C (100 MHz, $CDCl_3$) 82.7, 82.2, 74.4, 72.3, 33.9, 32.8, 28.4, 28.1, 27.9, 24.3, 22.7, 22.7, 14.0, 14.0; **MS**

m/z (ES+) 267 (100%, MNa^+); **HRMS** $C_{14}H_{28}O_3Na$ requires *M*, 267.1936. Found (MNa^+) 267.1928 (-3.1 ppm); **IR** ν_{max} (film)/cm^{-1} 3387 (br), 2932.

Scheme for the synthesis of 6



(*R*)-7-(But-1′-an-3′,4′-diol)-1,4-dithia-spiro[4.5]dec-6-ene

7-(4′-But-1′-enyl)-1,4-dithia-spiro[4.5]dec-6-ene[5] (1.3 g, 5.8 mmol) was subjected to standard conditions for asymmetric dihydroxylation of dienes using $(DHQD)_2PYR$ to give crude material. Purification by column chromatography (20% acetone/petrol) yielded *diol* (1.4 g, 94%) as an oil.

$[\alpha]_D^{20}$ 3.7 (c = 1, CH_2Cl_2); **^{1}H NMR** δ_H (400 MHz, $CDCl_3$) 5.55 (s, 1H, C=C*H*), 3.84-3.76 (m, 2H, 2 x O*H*), 3.62-3.55 (m, 2H, C*H*(OH)CH_2OH), 3.39-3.23 (m, 5H, 1 x CH_2OH and SCH_2CH_2S), 2.10-1.87 (m, 6H, CH=CCH_2 and CH_2CH_2CH_2), 1.76-1.63 (m, 2H, CH_2CH_2CH_2), 1.48 (dd, 2H, *J* 14.4 and 7.6, CH_2CHOH); **^{13}C NMR** δ_C (100 MHz, $CDCl_3$) 139.3, 126.2, 71.8, 66.6, 65.7, 41.3, 39.9, 33.3, 30.7, 29.6, 27.6, 22.7; **MS** *m/z* (ES+) 319 (100%, M+MeCN+NH_4^+); **HRMS** $C_{12}H_{21}O_2S_2$ requires *M*, 261.0983. Found (MH^+) 261.0979 (-1.5 ppm); **IR** ν_{max} (film)/cm^{-1} 3375 (br), 2923.

(*R*)-4-[2′-(1″,4″-Dithia-spiro[4.5]oct-6-en-7-yl)ethyl]-2,2-dimethyl-1,3-dioxolane

To a stirred solution of (*R*)-7-(but-1′-an-3′,4′-diol)-1,4-dithia-spiro[4.5]dec-6-ene (500 mg, 1.9 mmol) and camphor sulfonic acid (44 mg, 0.19 mmol) in DMF (4 cm^3) at 20 ^{0}C was added 2-methoxypropene

(0.36 cm^3, 3.8 mmol). After stirring for 2 hours the reaction mixture was poured onto a mixture of Et_2O (40 cm^3) and sat. $NaHCO_{3(aq)}$ (20 cm^3), shaken and the organic phase washed with H_2O (4 x 40 cm^3), dried over $MgSO_4$ and concentrated , Purification by column chromatography (10% Et_2O/petrol) yielded the *acetonide* (520 mg, 90%) as an oil.

$[\alpha]_D^{20}$ 10.2 (c = 1, CH_2Cl_2); **^{1}H NMR** δ_H (400 MHz, $CDCl_3$) 5.60 (s, 1H, C=C*H*), 4.09-4.02 (m, 2H, C*H*(OR)C*H*$_2$OR), 3.50-3.49 (m, 1H, CH(OR)C*H*$_2$OR), 3.41-3.28 (m, 4H, SC*H*$_2$C*H*$_2$S), 2.18-1.93 (m, 6H, C*H*$_2$CH$_2$C*H*$_2$ and CH=CC*H*$_2$), 1.83-1.55 (m, 4H, CH$_2$C*H*$_2$CH$_2$ and C*H*$_2$CHOR), 1.41 (s, 3H, C*H*$_3$), 1.36 (s, 3H, C*H*$_3$); **^{13}C NMR** δ_C (100 MHz, $CDCl_3$) 138.9, 126.4, 108.7, 95.7, 75.7, 65.7, 41.4, 39.9, 33.4, 31.4, 27.7, 26.9, 25.7, 22.7; **MS** *m/z* (CI+) 301 (100%, MH^+); **HRMS** $C_{15}H_{25}O_2S_2$ requires *M*, 301.1296. Found (MH^+) 301.1301 (+1.8 ppm); **IR** ν_{max} (film)/cm^{-1} 2928.

(*R*)-4-(2-cyclohexenylethyl)-2,2-dimethyl-1,3-dioxolane 6

Freshly distilled ammonia (100 cm^3) was distilled onto sodium (150 mg, 6.5 mmol) at - 78 ^{0}C. The dark blue solution was stirred for a further 30 minutes then treated with a solution of (*R*)-4-[2′-(1″,4″-dithia-spiro[4.5]oct-6-en-7-yl)ethyl]-2,2-dimethyl-1,3-dioxolane (500 mg, 1.7 mmol) in THF (10 cm^3). The resultant solution was stirred at - 78 ^{0}C for 40 minutes before quenching with sat. $NH_4Cl_{(aq)}$ (20 cm^3). On warming to room temperature the biphasic mixture was extracted with Et_2O (3 x 15 cm^3) and the organics combined, washed with $NaOH_{(aq)}$,(1 M, 20 cm^3)dried over $MgSO_4$ and concentrated onto silica. Purification by column chromatography (5% Et_2O/petrol) yielded the *acetonide* **6** (315 mg, 90%) as an oil.

$[\alpha]_D^{20}$ 12.7 (c = 1, CH_2Cl_2); **^{1}H NMR** δ_H (400 MHz, $CDCl_3$) 5.43-5.41 (m, 1H, C=C*H*), 4.10-4.03 (m, 2H, C*H*(OR)C*H*$_2$OR), 3.55-3.49 (m, 1H, C*H*$_2$OR), 2.08-1.89 (m, 6H, C*H*$_2$CH$_2$CH$_2$C*H*$_2$ and CH=CC*H*$_2$), 1.82-1.73 (m, 1H, C*H*$_2$CHOR), 1.65-1.52 (m, 5H, CH$_2$C*H*$_2$C*H*$_2$CH$_2$ and 1 x C*H*$_2$CHOR), 1.42 (s, 3H, C*H*$_3$), 1.36 (s, 3H, C*H*$_3$); **^{13}C NMR** δ_C (100 MHz, $CDCl_3$) 136.9, 121.2, 108.5, 75.9, 69.4, 34.0, 31.7, 28.3, 26.9, 25.8, 25.2, 22.9, 22.5; **MS** *m/z* (CI+) 211 (100%, MH^+), 153 (98%, MH^+-acetone); **HRMS** $C_{13}H_{23}O_2$

requires *M*, 211.1698. Found (MH^+) 211.1695 (-1.7 ppm); **IR** ν_{max} (film)/cm^{-1} 2932.

(2*R*,5*S*,6*S*)-2-Hydroxymethyl-1-oxa-spiro[4.5]decan-6-ol 7

Acetonide **6** (100 mg, 0.48 mmol) was subjected to standard diol cyclization conditions using isoprene to give the crude product as a brown oil. Purification by column chromatography (10% acetone/petrol) yielded *cis-THF* **7** (72 mg, 67%) as a colourless oil. $[\alpha]_D^{20}$ 2.3 (c = 1, CH_2Cl_2) **^{1}H NMR** δ_H (400 MHz, $CDCl_3$) 4.13 (tdd, 1H, *J* 6.8, 4.4 and 2.8, C*H*CH_2OH), 3.79 (dd, 1H, *J* 11.6 and 2.8, C*H*$_2$OH), 3.51 (dd, 1H, *J* 11.6 and 4.4, C*H*$_2$OH), 3.42 (d, 1H, *J* 8.0 and 4.8, C*H*OH), 3.13 (br s, 2H, 2 x O*H*), 2.11 (ddd, 1H, *J* 12.4, 8.4 and 6.0, C(4)*H*$_2$), 1.95-1.86 (m, 2H, C(3)*H*$_2$), 1.84-1.78 (m, 1H, C(10)*H*$_2$), 1.69-1.59 (m, 4H, C(7)*H*$_2$, 1 x C(4)*H*$_2$ and 1 x C(9)*H*$_2$), 1.57-1.49 (m, 1H, C(9)*H*$_2$), 1.40-1.21 (m, 3H, 1 x C(10)*H*$_2$ and C(8)*H*$_2$); **^{13}C NMR** δ_C (100 MHz, $CDCl_3$) 85.2, 79.0, 74.1, 65.0, 35.4, 34.6, 31.6, 27.3, 22.8, 22.4; **MS** *m/z* (CI+) 204 (100%, MNH_4^+), 187 (40%, MH^+), 169 (59%, M-OH^-); **HRMS** $C_{10}H_{19}O_3$ requires *M*, 187.1334. Found (MH^+) 187.1338 (+2.2 ppm); **IR** ν_{max} (film)/cm^{-1} 3373 (br), 1078.

(3*S*)-3-(Benzyloxy)hexa-1,5-diene

To a stirred solution of (+)-*B*-allyldiisopinocampheylborane (assumed 25 mmol, prepared by the procedure of Brown *et al.*)[6] in Et_2O (10 cm^3) at -100 ^{0}C was slowly added a solution of acrolein (1.1 g, 20 mmol) in Et_2O (10 cm^3) pre-cooled to -78 ^{0}C. The resulting solution was stirred at -100 ^{0}C for 30 minutes before quenching with MeOH (1 cm^3) and warming to 20 ^{0}C, then treating with a mixture of $NaOH_{(aq)}$ (3 M, 10 cm^3) and 30% H_2O_2 (20 cm^3) (CARE – vigorous gas evolution causes reaction to foam on addition and during early stages of the subsequent reflux, necessitating the use of a column reservoir attached to the top of the reflux condenser to stop overflowing) and heating at reflux for 3 hours. On cooling the reaction was diluted with Et_2O (50 cm^3) and the organic layer separated, washed with H_2O (20 cm3), dried over $MgSO_4$ and concentrated to 20 cm^3 under a low

vacuum. With stirring, this solution was then treated with sodium hydride 60% dispersion in mineral oil, 2.0 g, 50 mmol) and tetrabutylammonium iodide (10 mg) followed by benzyl bromide (3.3 cm^3, 50 mmol). After 20 hours the reaction mixture was quenched with $NH_4Cl_{(aq)}$ (20 cm^3), extracted into Et_2O (2 x 30 cm^3), dried over $MgSO_4$ and concentrated to a yellow oil which was purified by column chromatography (petrol – 5% Et_2O/petrol) to yield the *benzyl ether* (1.1 g, 30%) as an oil.

^{1}H NMR δ_H (400 MHz, $CDCl_3$) 7.36-7.20 (m, 5H, 5 x ArC*H*), 5.94-5.67 (m, 2H, 2 x C*H*=CH_2), 5.28-5.04 (m, 4H, CH=C*H*$_2$), 4.63 (d, 1H, *J* 24.4, C*H*$_2$Ph), 4.39 (d, 1H, *J* 24.4, C*H*$_2$Ph), 3.87-3.77 (m, 1H, C*H*OBn), 2.52-2.45 (m, 2H, C*H*$_2$CHOBn); **^{13}C NMR** δ_C (100 MHz, $CDCl_3$) 138.6, 138.4, 134.6, 128.3, 127.7, 127.4, 117.4, 116.9, 80.0, 70.0, 40.0; **MS** *m/z* (CI+) 206 (87%, MNH_4^+), 108 (62%), 91 (100%, tol^+); **HRMS** $C_{13}H_{20}NO$ requires *M*, 206.1545. Found (MNH_4^+) 206.1551 (+2.8 ppm); **IR** ν_{max} (film)/cm^{-1} 3120, 1643, 1077.

(2*S*,4*S*)-4-(Benzyloxy)hex-5-ene-1,2-diol 8

(3*S*)-3-(Benzyloxy)hexa-1,5-diene (400 mg, 2.1 mmol) was subjected to standard conditions for asymmetric dihydroxylation of dienes using $(DHQ)_2PYR$ to give crude material. Purification by column chromatography (20% acetone/petrol) yielded *diol* **8** (2:1 mixture of inseparable diastereoisomers with **10**, 410 mg, 87%) as an oil.

^{1}H NMR δ_H (400 MHz, $CDCl_3$) 7.37-7.27 (m, 5H, 5 x ArC*H*), 5.82 (dddd, 1H, *J* 18.0, 10.4, 7.6 and 0.8, C*H*=CH_2), 5.32-5.27 (m, 2H, CH=C*H*$_2$), 4.62 (d, 1H, *J* 11.6, C*H*$_2$Ph), 4.33 (d, 1H, *J* 11.6, C*H*$_2$Ph), 4.12-4.03 (m, 1H, C*H*OBn), 3.99 (ddd, 1H, *J* 12.0, 7.2 and 3.6, C*H*OH), 3.59 (dd, 1H, *J* 11.2 and 3.2, C*H*$_2$OH), 3.44 (dd, 1H, *J* 11.2 and 7.2, C*H*$_2$OH), 2.97 (br s, 2H, 2 x O*H*), 1.77-1.66 (m, 2H, C*H*$_2$CH(OBn)); **^{13}C NMR** δ_C (100 MHz, $CDCl_3$) 138.1, 137.9, 128.5, 127.9, 127.8, 117.4, 77.7, 70.5, 69.0, 66.8, 38.4; **MS** *m/z* (ES+) 281 (91%, M+MeCN+NH_4^+), 245 (100%, MNa^+); **HRMS** $C_{13}H_{19}O_3$ requires *M*, 223.1334. Found (MH^+) 223.1340 (+2.7 ppm); **IR** ν_{max} (film)/cm^{-1} 3396 (br), 2922, 1069.

(2*S*,3*S*,5*S*)-3-(Benzyloxy)-2,5-*bis*-hydroxymethyl-tetrahydrofuran (+)-9

(*S*,*S*)-Benzyloxyhexene diol **8** (200 mg, 0.90 mmol- 2:1 mixture with **10**) was subjected to standard diol cyclization conditions using isoprene to give the crude product as a brown oil. Purification by column chromatography (20% acetone/petrol) yielded the undesired *cis/cis-THF* **10** (54 mg, 26%) as an oil followed by the-*THF* **11** (96 mg, 68% from the desired diastereoisomer) as an oil.

$[\alpha]_D^{20}$ +7.7 (c = 1, CH_2Cl_2); **^{1}H NMR** δ_H (400 MHz, $CDCl_3$) 7.36-7.27 (m, 5H, 5 x ArC*H*), 4.60 (d, 1H, *J* 12.0, C*H*$_2$Ph), 4.39 (d, 1H, *J* 12.0, C*H*$_2$Ph), 4.23 (ddd, 1H, *J* 7.6, 5.2 and 4.0, C*H*OBn), 4.10 (dddd, 1H, *J* 7.6, 7.6, 4.8 and 2.4, HOCH$_2$C*H*CH$_2$) 3.96 (td, 1H, *J* 5.2 and 3.6, CH(OBn)C*H*CH$_2$OH), 3.89 (dd, 1H, *J* 12.0 and 3.2, CH(OBn)CHC*H*$_2$OH)), 3.82 (dd, 1H, *J* 12.0 and 3.6, CH(OBn)CHC*H*$_2$OH)), 3.76 (dd, 1H, *J* 11.6 and 2.4, HOC*H*$_2$CHCH$_2$), 3.59 (dd, 1H, *J* 11.6 and 4.8, HOC*H*$_2$CHCH$_2$), 3.20 (br s, 2H, 2 x O*H*), 2.17 (ddd, 1H, *J* 13.2, 7.6 and 6.4, C*H*$_2$CH(OBn)), 1.99 (ddd, 1H, *J* 13.2, 7.6 and 4.0, C*H*$_2$CH(OBn)); **^{13}C NMR** δ_C (100 MHz, $CDCl_3$) 137.5, 128.5, 127.9, 127.6, 81.5, 79.8, 78.5, 71.5, 62.0, 33.2; **MS** *m/z* (ES+) 261 (100%, MNa^+); **HRMS** $C_{13}H_{19}O_4$ requires *M*, 239.1283. Found (MH^+) 239.1277 (-2.9 ppm); **IR** ν_{max} (film)/cm^{-1} 3387 (br), 2934 and 1054.

(2*R*,4*S*)-4-(Benzyloxy)hex-5-ene-1,2-diol 10

(3*S*)-3-(Benzyloxy)hexa-1,5-diene (400 mg, 2.1 mmol) was subjected to standard conditions for asymmetric dihydroxylation of dienes using $(DHQD)_2PYR$ to give crude material. Purification by column chromatography (20% acetone/petrol) yielded *diol* **10** (4:1 mixture of inseparable diastereomers with **8**, 430 mg, 92%) as an oil.

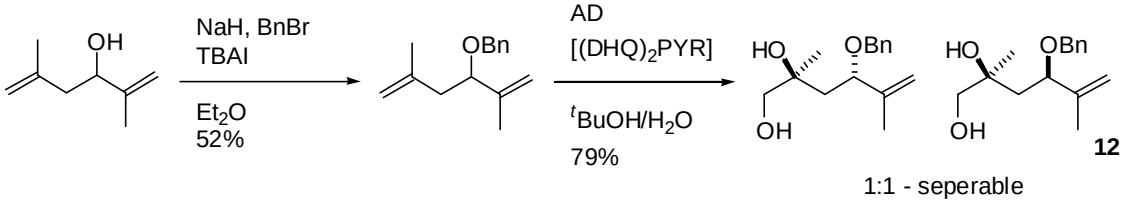
^{1}H NMR δ_H (400 MHz, $CDCl_3$) 7.37-7.27 (m, 5H, 5 x ArC*H*), 5.76 (ddd, 1H, *J* 18.0, 10.4 and 8.4, C*H*=CH$_2$), 5.30-5.26 (m, 2H, CH=C*H*$_2$), 4.63 (d, 1H, *J* 11.6, C*H*$_2$Ph), 4.37 (d, 1H, *J* 11.6, C*H*$_2$Ph), 4.10-4.03 (m, 1H, C*H*OBn), 3.89 (dddd, 1H, *J* 9.2, 6.0, 3.6 and 2.4, C*H*OH), 3.56 (dd, 1H, *J* 10.8 and 3.6, C*H*$_2$OH), 3.45 (dd, 1H, *J* 10.8 and 6.0, C*H*$_2$OH), 3.04 (br s, 2H, 2 x O*H*), 1.85 (dt, 1H, *J* 14.8 and 9.2, C*H*$_2$CH(OBn)), 1.62 (ddd, 1H, *J* 14.8, 4.0 and 2.4, C*H*$_2$CH(OBn)); **^{13}C NMR** δ_C (100 MHz, $CDCl_3$) 137.8, 137.7, 128.5, 128.0, 127.9, 118.1, 80.4, 71.2, 70.2, 66.6, 38.2; **MS** *m/z* (ES+) 281 (100%, M+MeCN+NH_4^+), 245

(98%, MNa^+); **HRMS** $C_{13}H_{19}O_3$ requires *M*, 223.1334. Found (MH^+) 223.1326 (-3.7 ppm); **IR** ν_{max} (film)/cm^{-1} 3406 (br), 2923, 1069.

(2*R*,3*S*,5*R*)-3-(Benzyloxy)-2,5-*bis*-hydroxymethyl-tetrahydrofuran 11

(*R*,*S*)-Benzyloxyhexene diol **10** (200 mg, 0.90 mmol) was subjected to standard diol cyclization conditions using isoprene to give the crude product as a brown oil. Purification by column chromatography (20% acetone/petrol) yielded THF **11** (130 mg, 76% from the desired diastereomer) as an oil followed by the undesired THF **9** (27 mg, 12%) as an oil.

$[\alpha]_D^{20}$ +21.8 (c = 1, CH_2Cl_2); **^{1}H NMR** δ_H (400 MHz, $CDCl_3$) 7.36-7.26 (m, 5H, 5 x ArC*H*), 4.55 (d, 1H, *J* 12.0, C*H*$_2$Ph), 4.49 (d, 1H, *J* 12.0, C*H*$_2$Ph), 4.32-4.26 (m, 1H, $HOCH_2CHCH_2$), 4.01-4.05 (m, 2H, C*H*(OBn)C*H*CH_2OH), 3.85 (dd, 1H, *J* 12.0 and 2.4, HOC*H*$_2$$CHCH_2$), 3.85 (dd, 1H, *J* 12.0 and 2.4, HOC*H*$_2$$CHCH_2$), 3.77 (dd, 1H, *J* 11.6 and 3.2, HOC*H*$_2$CHCH(OBn)), 3.70 (br s, 2H, 2 x O*H*), 3.56 (dd, 1H, *J* 12.0 and 4.0, HOC*H*$_2$$CHCH_2$), 3.51 (dd, 1H, *J* 11.6 and 4.0, HOC*H*$_2$CHCH(OBn)), 2.06-1.94 (m, 2H, CHC*H*$_2$CH(OBn)); **^{13}C NMR** δ_C (100 MHz, $CDCl_3$) 138.0, 128.5, 127.7, 127.6, 85.1, 80.6, 79.4, 71.3, 63.6, 63.3, 33.4; **MS** *m/z* (ES+) 261 (100%, MNa^+); **HRMS** $C_{13}H_{19}O_4$ requires *M*, 239.1283. Found (MH^+) 239.1280 (-1.4 ppm); **IR** ν_{max} (film)/cm^{-1} 3386 (br), 2928 and 1064.



(*RS*)-3-Benzyloxy-2,5-dimethylhexa-1,5-diene

A stirred solution of racemic 2,5-dimethylhexadiene-3-ol (5.0 g, 39 mmol) in Et_2O (50 cm^3) under argon at 0 ^{0}C was treated with sodium hydride (60% dispersion in mineral oil, 4.0 g, 100 mmol) and tetrabutylammonium iodide (5 mg) followed by benzyl bromide (2.3 cm^3, 78 mmol). After 20 hours the reaction mixture was quenched with sat. $NH_4Cl_{(aq)}$ (20 cm^3), extracted into Et_2O (2 x 30 cm^3), dried over

$MgSO_4$ and concentrated to a yellow oil which was purified by column chromatography (petrol – 5% Et_2O/petrol) to yield the *benzyl ether* (4.56 g, 52%) as an oil.

^{1}H NMR δ_H (400 MHz, $CDCl_3$) 7.36-7.27 (m, 5H, 5 x ArC*H*), 5.01-4.93 (m, 2H, CH(OBn)C(CH_3)=CH_2), 4.81-4.74 (m, 2H, CH_2C(CH_3)=CH_2), 4.52 (d, 1H, *J* 12.0, CH_2Ph), 4.28 (d, 1H, *J* 12.0, CH_2Ph), 3.94-3.91 (m, 1H, C*H*OBn), 2.43 (dd, 1H, *J* 14.0 and 8.0, CH_2CHOBn), 2.24 (dd, 1H, *J* 14.0 and 6.0, CH_2CHOBn), 1.74-1.72 (m, 6H, 2 x CH_3); **^{13}C NMR** δ_C (100 MHz, $CDCl_3$) 144.4, 142.6, 138.6, 128.3, 127.8, 127.4, 113.9, 112.4, 81.8, 69.9, 42.5, 22.6, 16.5; **MS** *m/z* (CI+) 161 (100%, M-CH_2=C(CH_3)CH_2^-); **HRMS** $C_{15}H_{24}NO$ requires *M*, 234.1858. Found (MNH_4^+) 234.1860 (+1.0 ppm); **IR** ν_{max} (film)/cm^{-1} 3072, 3031, 2971, 2943, 2863, 1454, 1070.

(2*S*,4*S*)-4-(Benzyloxy)-2,5-dimethylhex-5-ene-1,2-diol and **(2*S*,4*R*)-4-(benzyloxy)-2,5-dimethylhex-5-ene-1,2-diol 12**

3-Benzyloxy-2,5-dimethylhexa-1,5-diene (1 g, 4.6 mmol) was subjected to standard conditions for asymmetric dihydroxylation of dienes using $(DHQ)_2PYR$ to give crude material, as a 1:1 mixture of diastereomers. Purification by careful column chromatography (10% acetone/toluene) yielded first the *(S,S)-diol* (490 mg, 43%) followed by mixed fractions (240 mg, 21%) then the *(S,R)-diol* **12** (180 mg, 16%) as oils.

(*S*,*R*)-diol **12**

$[\alpha]_D^{20}$ -29.6 (c = 1, CH_2Cl_2); **^{1}H NMR** δ_H (400 MHz, $CDCl_3$) 7.39-7.29 (m, 5H, 5 x ArC*H*), 5.03-5.00 (m, 2H, C=CH_2), 4.51 (d, 1H, *J* 11.6, CH_2Ph), 4.24 (d, 1H, *J* 11.6, CH_2Ph), 4.07 (dd, 1H, *J* 10.8 and 2.0, C*H*OBn), 3.77 (br s, 1H, O*H*), 3.50 (d, 1H, *J* 11.6, CH_2OH), 3.36 (d, 1H, *J* 11.6, CH_2OH), 3.08 (br s, 1H, O*H*), 2.01 (dd, 1H, J 14.8 and 10.8, CH_2CHOBn), 1.76-1.74 (m, 3H, C(CH_3)=CH_2), 1.64 (dd, 1H, *J* 14.8 and 2.0, CH_2CHOBn), 1.16 (s, 3H, C(OH)CH_3); **^{13}C NMR** δ_C (100 MHz, $CDCl_3$) 144.3, 137.5, 128.5, 128.2, 127.9, 113.6, 80.7, 72.6, 70.2, 69.2, 42.8, 24.7, 16.8; **MS** *m/z* (ES+) 273 (100%, MNa^+); **HRMS** $C_{15}H_{22}O_3Na$ requires *M*, 273.1467. Found (MNa^+) 273.1464 (-1.1 ppm); **IR** ν_{max} (film)/cm^{-1} 3419 (br), 2922, 1050.

(2*S*,3*R*,5*S*)-2,5-*bis*(Hydroxymethyl)-2,5-dimethyl-3-benzyloxytetrahydrofuran 13

(2*S*,4*R*)-Benzyloxy diol **12** (100 mg, 0.40 mmol) was subjected to standard diol cyclization conditions using isoprene to give the crude product. Purification by column chromatography (20% acetone/petrol) yielded *cis-THF* **13** (78 mg, 74%) as prisms. The relative stereochemistry of **13** was proven by X-ray crystallography.

m.p 50-53 ^{0}C; $[\alpha]_D^{20}$ 20.5 (c = 1, CH_2Cl_2); **^{1}H NMR** δ_H (400 MHz, $CDCl_3$) 7.37-7.27 (m, 5H, 5 x ArC*H*), 4.59 (d, 1H, *J* 11.2, C*H*$_2$Ph), 4.50 (d, 1H, *J* 11.2, C*H*$_2$Ph), 4.33 (t, 1H, *J* 6.8, C*H*OBn), 3.59-3,47 (m, 5H, C*H*-$_2$OH, 1 x C*H*$_2$OH and 2 x O*H*), 3.35 (d, 1H, *J* 11.6, C*H*$_2$OH), 2.45 (dd, 1H, *J* 12.8 and 6.8, C*H*$_2$CHOBn), 1.92 (dd, 1H, *J* 12.8 and 6.8, C*H*$_2$CHOBn), 1.28 (s, 3H, C*H*$_3$), 1.20 (s, 3H, C*H*$_3$); **^{13}C NMR** δ_C (100 MHz, $CDCl_3$) 138.6, 128.3, 127.5, 127.2, 85.4, 82.1, 80.3, 72.1, 69.8, 67.6, 39.7, 25.9, 19.8; **MS** *m/z* (ES+) 289 (MNa^+); **HRMS** $C_{15}H_{23}O_4$ requires *M*, 267.1596. Found (MH^+) 267.1594 (-1.0 ppm); **IR** ν_{max} (film)/cm^{-1} 3375 (br), 2932, 1113, 1063.

(2*E*,6*E*)-Nonadeca-2,6-dien-1-ol 16

To a stirred solution of ethyl nonadecadienoate **15** (1.1 g, 3.4 mmol) in CH_2Cl_2 (50 cm^3) at -78 ^{0}C was added, dropwise, di-isobutylaluminiumhydride (1.5 M in toluene, 9.2 cm^3, 14 mmol) and the solution warmed to 20 ^{0}C. After quenching with $HCl_{(aq)}$ (3 M, 30 cm^3) the mixture was extracted into CH_2Cl_2 (3 x 100 cm^3), dried over $MgSO_4$ and concentrated. Purification by column chromatography (10% acetone/petrol) yielded **16** (870 mg, 91%) as a low melting solid.

m.p 35-38 ^{0}C; **^{1}H NMR** δ_H (400 MHz, $CDCl_3$) 5.72-5.60 (m, 2H, C*H*=C*H*CH$_2$OH), 5.46-5.34 (m, 2H, CH$_2$C*H*=C*H*CH$_2$), 4.07 (d, 2H, *J* 5.2, C*H*$_2$OH), 2.13-2.05 (m, 4H, CHC*H*$_2$C*H*$_2$CH), 1.96 (q, 2H, *J* 6.4, C*H*$_2$CH=CHCH$_2$), 1.36-1.20 (m, 20H, CH$_3$-(C*H*$_2$)$_{10}$-CH$_2$), 0.90-0.86 (m, 3H, C*H*$_3$); **^{13}C NMR** δ_C (100 MHz, $CDCl_3$) 132.7, 131.1, 129.2, 63.3, 32.5, 32.4, 32.3, 32.2, 31.9, 29.7, 29.6, 29.6, 29.5, 29.3, 29.2, 22.7, 14.1.

(6*S*,7*S*,*E*)-Nonadec-2-ene-1,6,7-triol 17

Nonadecadienol **16** (820 mg, 2.9 mmol) was subjected to standard conditions for asymmetric dihydroxylation of dienes using $(DHQ)_2PHAL$ to give crude material. Purification by column chromatography (30% acetone/petrol) yielded *diol* **17** (860 mg, 94%) as needles.

m.p 70-72 ^0C; $[\alpha]_D^{20}$ -17.7 (c = 1, MeOH); **^{1}H NMR** δ_H (400 MHz, $CDCl_3$) 5.76-5.66 (m, 2H, C*H*=C*H*), 4.13-4.10 (m, 2H, CH_2OH), 3.47-3.40 (m, 2H, C*H*(OH)C*H*(OH)), 2.32-2.13 (m, 2H, CH_2CH=CH), 1.82-1.22 (m, 27H, CH_2O*H* and CH_3-(CH_2)$_{11}$-CH(O*H*)CH(O*H*)CH_2), 0.89 (t, 3H, *J* 7.2, CH_3); **^{13}C NMR** δ_C (100 MHz, $CDCl_3$) 132.5, 129.5, 74.6, 73.9, 63.7, 33.6, 32.9, 31.9, 29.6, 29.6, 29.3, 28.4, 25.6, 22.7, 14.1; **MS** *m/z* (ES+) 337 (100%, MNa^+); **HRMS** $C_{19}H_{38}O_3Na$ requires *M*, 337.2719. Found (MNa^+) 337.2720 (+0.3 ppm); **IR** ν_{max} (film)/cm^{-1} 3257 (br), 2916, 2847.

(2*R*,5*S*,1'S,1"*R*)-1-(5-(-1'-Hydroxytridecyl)-tetrahydrofuran-2-yl)ethane-1",2"-diol 18[2]

Nonadecene triol **17** (150 mg, 0.48 mmol) was subjected to standard diol cyclization conditions using isoprene to give the crude product as a brown oil. Purification by column chromatography (30% acetone/petrol) yielded *cis*-THF **18** (128 mg, 81%) as a white solid.

$[\alpha]_D^{20}$ -4.5 (c = 1, MeOH); **^{1}H NMR** δ_H (400 MHz, $CDCl_3$) 3.98 (dd, 1H, *J* 6.4 and 4.4, C*H*CH(OH)CH_2OH), 3.82 (q, 1H, *J* 6.0, CH_2CH(OH)C*H*(OR)CH_2), 3.67-3.61 (m, 2H, CH_2OH), 3.56 (q, 1H, *J* 4.4, C*H*(OH)CH_2OH), 3.42-3.38 (m, 1H, CH_2C*H*(OH)CHO), 1.98-1.74 (m, 4H, THF CH_2CH_2), 1.47-1.21 (m, 22H, CH_3-(CH_2)$_{11}$-CH(OH)), 0.89 (t, 3H, *J* 6.8, CH_3); **^{13}C NMR** δ_C (100 MHz, $CDCl_3$) 82.8, 80.1, 74.1, 74.1, 64.8, 32.2, 31.9, 29.7, 29.7, 29.7, 29.6, 29.3, 28.0, 25.8, 22.7, 14.1.

(2*R*,5*S*,1'S,1"*R*)-1-(5-(-1'-Hydroxytridecyl)-tetrahydrofuran-2-yl)ethane-1"-ol-2"-(4"'-toluylsulphonate) 19[2]

A stirred solution of THF triol **18** (85 mg, 0.26 mmol) and dibutyltin oxide (77 mg, 0.31 mmol) in benzene (10 cm^3) were heated at reflux for 3 hours, then cooled to 20 ^0C and *para*-toluenesulphonyl chloride (54 mg, 0.29 mmol) and tetrabutylammonium bromide (42 mg, 0.13 mmol) added and stirring contined for 30 minutes. The reaction mixture was

concentrated onto silica and purified by column chromatography (10% acetone/petrol) to yield the tosyl diol **19** (121 mg, 97%) as needles. m.p 75-76 ^{0}C; $[\alpha]_D^{20}$ –11.4 (c = 1, CH_2Cl_2); **^{1}H NMR** δ_H (400 MHz, $CDCl_3$) 7.79 (d, 2H, *J* 8.4, ArC(2)*H*), 7.34 (d, 2H, *J* 8.4, ArC(3)*H*), 4.07 (d, 2H, *J* 6.0, C*H*$_2$OTs), 3.97 (td, 1H, *J* 6.4 and 2.4, C*H*CH(OH)CH$_2$OTs), 3.82 (td, 1H, *J* 6.4 and 4.0, CH$_2$CH(OH)C*H*O), 3.73 (td, 1H, *J* 6.0 and 2.4, C*H*(OH)CH$_2$OTs), 3.42-3.78 (m, 1H, CH*2*C*H*(OH)CHO), 2.44 (s, 3H, ARC*H*$_3$), 1.98-1.80 (m, 4H, THF C*H*$_2$C*H*$_2$), 1.48-1.20 (m, 22H, CH$_3$-(C*H*$_2$)$_{11}$-CH(OH)), 0.87 (t, 3H, *J* 6.8, CH$_2$C*H*$_3$); **^{13}C NMR** δ_C (100 MHz, $CDCl_3$) 144.9, 132.7, 129.9, 128.0, 82.5, 78.4, 74.0, 71.7, 71.2, 34.5, 31.9, 29.7, 29.6, 29.3, 28.1, 27.7, 25.8, 22.7, 21.6, 14.1.

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