Supplementary data

Experimental

General procedure

Unless otherwise stated, commercially available reagents were used without purification and solvents were dried according to standard procedures. Product purification was carried out using flash chromatography on silica gel (Merck silica gel 60 (230-400mesh). ^{1}H and ^{13}C NMR spectra were recorded on a Bruker DPX-300 spectrometer (300 MHz for ^{1}H and 75MHz for ^{13}C) using $CDCl_3$ as the solvent and TMS as internal reference. Spectra were recorded in ppm downfield from TMS (δ=0) for ^{1}H NMR and relative to the $CDCl_3$ resonance (δ=77.0) for ^{13}C spectra. Mass spectra were recorded on a Fisons VG Autospec Mass Spectrometer. Optical rotations were measured on a Perkin Elmer 241 polarimeter.

1. (*E*)-2-Methyl-2-pentene-1-o1 (11)^{13}: Sodium borohydride (60.6 g, 1.56 mol) was added with vigorous stirring over 2 hours to 2-methyl-2-pentenal (153.3 g, 1.56 mol, Aldrich) in methanol (1 dm^3) keeping the temperature below 30^{o}C (vigorous gas evolution occurred). The reaction mixture was stirred for 15 minutes at room temperature and quenched by the careful addition of aqueous ammonium chloride (1 dm^3). The mixture was extracted with dcm (3 x 300 cm^3) and the combined organic layers were dried over $MgSO_4$, filtered and concentrated under reduced pressure. Distillation (94.5^{o}C, 77 mmHg) yielded the title compound (**11**) as a clear colourless liquid (139.72 g, 90%), (R_f = 0.20 in 20% diethyl ether / pentane). ν_{max} (thin film) / cm^{-1} 3427 (b, OH), 2965 (s, CH), 2933 (s, CH), 2874 (s, CH), 1671 (w), 1461 (s), 905 (s); δ_H 5.41 (1H, bt, *J* 7.5, 3-H), 3.99 (2H, s, 1-H), 2.05 (2H, p, *J* 7.5, 4-H), 1.66 (3H, s, 6-H), 1.50 (1H, bs, OH), 0.97 (3H, t, *J* 7.5, 5-H); δ_C 133.95 (C-2), 127.91 (CH-3), 68.64 (CH_2-1), 20.76 (CH_2-4), 13.89 (CH_3-5), 13.33 (CH_3-6); $^m/_z$ EI 82 (M^+-H_2O, 23%), 67 (M^+-H_2O-Me, 88), 39 (100); CI 100 (M+NH_4^+-H_2O, 51%), 83 (MH^+-H_2O, 100).

2. (2*R*,3*R)*-2,3-Epoxy-2-methylpentan-1-ol (+) (11a)^{14}: A solution of *tert*-butylhydroperoxide (5.0 M in dichloromethane, 264 cm^3, 1.32 mol) was added over 15 minutes at –25^{o}C to a mixture of titanium tetraisopropoxide (9.9 cm^3, 33 mmol), (-)-diethyl tartrate (8.3 g, 14 mmol) and powdered 4Å molecular sieves (ca. 20 g) in dichloromethane (1.3 dm^3) and the reaction mixture stirred for 30 minutes. A solution of allylic alcohol (**11**) (66.0 g, 0.66 mol, pre-dried with 4Å molecular sieves) in dichloromethane (160 cm^3) was added dropwise over 1 hour to the reaction mixture and the temperature was maintained at -20^o to -25^{o}C. The reaction mixture was stirred at this temperature for an additional 1 hour and tlc analysis indicated that the reaction was complete. A freshly prepared solution of citric acid monohydrate (6.9 g, 33 mmol) in 500 cm^3 of a 10% acetone / diethyl ether mixture was added, with stirring, to the reaction mixture over 2 minutes. The cooling bath was removed and the mixture allowed to warm to room temperature for over 1 hour. The mixture was filtered through a pad of silica gel and concentrated under reduced pressure. Distillation (82 – 84°C, 12 mmHg) yielded the title compound (+)-(**11a**) as a clear colourless liquid (56.1 g, 85%). (R_f = 0.28 in 70% ether / petrol); $[\alpha]^{24}_D$ +16.5 (*c* 3.00, $CHCl_3$) [lit.[14] enantiomer $[\alpha]^{24.4}_D$ -21.3 (*c* 1.78, $CHCl_3$)]; ν_{max} (thin film) / cm^{-1} 3327 (b, OH), 2971 (s, C-H), 2937 (s, C-H), 2877 (s), 1460 (s), 1384 (s), 1035 (s), 875 (s); δ_H 3.69 (1H, dd, *J* 12.0 and 4.0, 1-H), 3.56 (1H, dd, *J* 12.0 and 8, 1-H), 3.01 (1H, t, *J* 7, 3-H), 2.18 (1H, dd, *J* 8 and 4, OH), 1.62 (1H, dp, *J* 14 and 7, 4-H), 1.55 (1H, dp, *J* 14 and 7, 4-H), 1.27 (3H, s, 6-H), 1.03 (3H, t, *J* 7, 5-H); δ_C 65.51 (CH_2-1), 61.38 (CH-3), 61.15 (C-2), 21.37 (CH_2-4), 13.87 (CH_3-6), 10.35 (CH_3-5); $^m/_z$ EI 98 (M^+-H_2O, 3%), 82 (2), 58 (66), 29 (100); CI 134 (M+NH_4^+, 52%), 116 (M+NH_4^+-H_2O, 90), 100 (M+NH_4^+-H_2O-O, 73), 58 (100).

3. (2*S*,3*R*)-2,3-Epoxy-2-methylpentanal (-)-(12): Collins reagent[15] (186 g, 0.72 mol) was added portionwise to the epoxyalcohol (+)-(**11a**) (13.9 g, 0.12 mol) and powdered 4Å molecular sieves (10 g) in dichloromethane (2.0 dm^3) at room temperature over 5 minutes and stirred for 30 minutes. The reaction mixture was filtered through a silica gel plug and washed with diethyl ether (400 cm^3). The solvent was carefully removed under reduced pressure to leave approximately 50 cm^3 of solvent. This was absorbed onto silica gel and purified by chromatography using 20% diethyl ether / pentane (R_f = 0.20 as eluant to obtain the desired product (-)-(**12**) as a pale yellow oil (8.70 g, 64%). (R_f = 0.50 in 30% ether/petrol); $[\alpha]^{24}_D$ -86 (*c* 2.48, $CHCl_3$) [lit.[16] enantiomer $[\alpha]^{23}_D$ +93 (*c* 2.3, $CHCl_3$)]; ν_{max} (thin film) / cm^{-1} 2975 (m), 1725 (s, C=C), 870 (m); δ_H 8.88 (1H, s, 1-H), 3.12 (1H, t, *J* 7, 3-H), 1.74 (1H, dp, *J* 14 and 7, 4-H), 1.62 (1H, dp, *J* 14 and 7, 4-H), 1.40 (3H, s, 6-H), 1.10 (3H, t, *J* 7, 5-H); δ_C 200.20 (CH-1), 62.36 (C-2), 61.03 (CH-3), 21.42 (CH_2-4), 10.36 (CH_3-5), 9.82 (CH_3-6); $^m/_z$ EI 98 (M^+-O, 44%), 69 (60), 41 (100); CI 132 (M+NH_4^+, 4%), 116 (M+NH_4^+-O, 100).

4. (3*S*,4*S*,5*R*)-4,5-Epoxy-4-methyl-2-trimethylsilylmethylhept-1-en-3-ol (13a):
(3*R*,4*S*,5*R*)-4,5-Epoxy-4-methyl-2-trimethylsilylmethylhept-1-en-3-ol (13b):
2-Bromo-3-(trimethylsilyl)propene (10.6 cm^3, 0.06 mol) was added dropwise over 15 minutes to a suspension of magnesium (1.45 g, 0.06 mol) and 1,2-dibromethane (0.52 cm^3, 6 mmol) in THF (100 cm^3) at such a rate as to maintain a gentle reflux. Upon cooling to 0°C an opaque olive mixture containing a gelatinous precipitate was obtained. The aldehyde (-)-(**12**) (4.56 g, 0.04 mol) in THF (10 cm^3) was added dropwise to the Grigard reagent over 20 minutes and the reaction mixture then warmed to room temperature over 30 minutes. Aqueous ammonium chloride (500 cm^3) was added carefully to the reaction mixture with stirring. The mixture was filtered, the layers separated and the aqueous layer extracted with diethyl ether (3 x 100 cm^3). The combined organic layers were dried over $MgSO_4$, filtered through a silica plug and concentrated under reduced pressure. The residue was purified by chromatography on silica gel using 20% diethyl ether / hexane as eluant to yield the diastereomeric products as clear colourless oils:

(**13a**) (3.10 g, 34%), (R_f = 0.27) in 20% diethyl ether / hexane); $[\alpha]^{24}_D$ –22 (*c* 1.00, $CHCl_3$). Anal. (Found: C, 62.77; H, 10.59. $C_{12}H_{24}O_2Si$ requires C, 63.10; H, 10.6%);

ν_{max} (thin film) / cm^{-1} 3470 (b, OH), 2975 (s, CH), 1640 (w), 1250 (s), 850 (s); δ_H 5.08 (1H, s, 1-H), 4.78 (1H, s, 1-H), 3.63 (1H, d, *J* 4, 3-H), 2.94 (1H, t, *J* 7, 5-H), 2.25 (1H, d, *J* 4, OH), 1.69 (1H, dp, *J* 14 and 7, 6-H), 1.65 (1H, d, *J* 14, 9-H), 1.54 (1H, dp, *J* 14 and 7, 6-H), 1.34 (1H, d, *J* 14, 9-H), 1.20 (3H, s, 8-H), 1.05 (3H, t, *J* 7, 7-H), 0.04 (9H, s, TMS); δ_C 144.85 (C-2), 109.03 (CH_2-1), 79.19 (CH-3), 63.86 (CH-5), 63.19 (C-4), 23.03 (CH_2-6), 21.47 (CH_2-9), 11.31 (CH_3-8), 10.42 (CH_3-7), -1.25 (CH_3-TMS); $^{m}/_{z}$ EI 210 (M^+-H_2O, 1%), 195 (M^+-H_2O-Me, 2), 170 (8), 155 (33), 73 (TMS^+, 100); HRMS calc. 228.1546, found 228.1546.

(**13b**) (2.82 g, 31%), (R_f = 0.33 (v) in 20% diethyl ether / hexane); $[\alpha]^{24}_{D}$ –51 (*c* 1.01, $CHCl_3$). Anal. (Found: C, 62.61; H, 10.56. $C_{12}H_{24}O_2Si$ requires C, 63.10; H, 10.6%); ν_{max} (thin film) / cm^{-1} 3480 (b, OH), 2970 (s, CH), 1640 (w, C=C), 1250 (s), 850 (s); δ_H 4.95 (1H, s, 1-H), 4.80 (1H, s, 1-H), 3.93 (1H, s, 3-H), 3.09 (1H, t, *J* 6.5, 5-H), 2.14 (1H, bs, OH), 1.75-1.48 (4H, m, 6 and 9-H), 1.25 (3H, s, 8-H), 1.05 (3H, t, *J* 7.5, 7-H), 0.06 (9H, s, TMS); δ_C 145.77 (C-2), 110.56 (CH_2-1), 77.22 (CH-3), 62.24 (CH-4), 61.03 (CH-5), 23.12 (CH_2-9), 21.59 (CH_2-6), 14.25 (CH_3-8), 10.53 (CH_3-7), -1.16 (CH_3-TMS); $^{m}/_{z}$ EI 210 (M^+-H_2O, 1%), 195 (M^+-H_2O-Me, 1), 170 (18), 155 (22), 73 (TMS^+, 100); HRMS calc. 228.1546, found 228.1546.

5. (3*S*,4*S*,5*R*)-4,5-Epoxy-4-methyl-2-trimethylsilylmethylhept-1-en-3-yl propanoate (14a): Propionyl chloride (0.45 cm^3, 5.30 mmol) was added dropwise over 1 minute to a solution of the alcohol (**13a**) (600 mg, 2.60 mmol) and pyridine (0.43 cm^3, 5.30 mmol) in dichloromethane (10 cm^3) at room temperature. The reaction mixture was stirred for 2 hours at room temperature, then poured onto a silica gel column and eluted with 10% diethyl ether / hexane (R_f = 0.24) to yield the title compound (**14a**) as a colourless oil (709 mg, 96%). Anal. (Found: C, 63.35; H, 10.01. $C_{15}H_{28}O_3Si$ requires C, 63.33; H, 9.9%); $[\alpha]^{23}_{D}$ –91 (*c* 0.86, $CHCl_3$); ν_{max} (thin film) / cm^{-1} 2970 (s, CH), 1746 (s, C=O), 638 (m, C=C), 1248 (s), 1180 (s), 850 (s); δ_H 4.88 (1H, s, 1-H), 4.78 (1H, s, 3-H), 4.73 (1H, s, 1-H), 2.89 (1H, t, *J* 6.5, 5-H), 2.44 (1H, dq, *J* 14 and 7.5, 11-H), 2.42 (1H, dq, *J* 14 and 7.5, 11-H), 1.76-1.46 (2H, m, 6-H), 1.64 (1H, d, *J* 14, 9-H), 1.38 (1H, d, *J* 14, 9-H), 1.25 (3H, s, 8-H), 1.18 (3H, t, *J* 7.5, 12-H), 1.04 (3H, t, *J* 7.5, 7-H), 0.06 (9H, s, TMS); δ_C 173.06 (C-10), 142.39 (C-2), 108.92 (CH_2-1), 80.49 (CH-3), 63.64 (CH-5), 60.71 (C-4), 27.69 (CH_2-11), 25.38 (CH_2-9), 21.35 (CH_2-6), 12.22 (CH_3-8), 10.44 (CH_3-7), 9.15 (CH_3-12), -1.28 (CH_3-TMS); $^{m}/_{z}$ EI 73 (TMS^+, 100%); CI 285 (MH^+, 12%), 211 (12), 197 (41), 123 (100). HRMS calc. 285.1886, found 285.1884.

6. (3*R*,4*S*,5*R*)-4,5-Epoxy-4-methyl-2-trimethylsilylmethylhept-1-en-3-yl propanoate (14b): Propionyl chloride (0.30 cm^3, 3.50 mmol) was added dropwise over 1 minute to a solution of the alcohol (**13b**) (400 mg, 1.75 mmol) and pyridine (0.28 cm^3, 3.50 mmol) in dichloromethane (10 cm^3) at room temperature. The reaction mixture was stirred for 2 hours at room temperature, then poured onto a silica gel column and eluted with 10% diethyl ether / hexane (R_f = 0.27) to yield the title compound (**14b**) as a colourless oil (477 mg, 96%). $[\alpha]^{23}_{D}$ +74 (*c* 0.80, $CHCl_3$); ν_{max} (thin film) / cm^{-1} 2971 (s, CH), 1746 (s, C=O), 1639 (m, C=C), 1249 (s), 1180 (s), 853 (s); δ_H 4.89 (1H, s, 1-H), 4.86 (1H, s, 3-H), 4.77 (1H, s, 1-H), 2.84 (1H, t, *J* 6.5, 5-H), 2.38 (2H, q, *J* 7.5, 11-H), 1.72-1.37 (4H, m, 6 and 9-H), 1.22 (3H, s, 8-H), 1.17 (3H, t, *J* 7.5, 12-H), 1.01 (3H, t, *J* 7.5, 7-H), 0.04 (9H, s, TMS); δ_C 175.60 (C-10), 145.49 (C-2), 112.29 (CH_2-1), 81.86 (CH-3), 65.07 (CH-5), 62.93 (C-4), 30.52 (CH_2-11), 26.08

(CH_2-9), 24.46 (CH_2-6), 15.45 (CH_3-8), 13.16 (CH_3-7), 11.99 (CH_3-12), -1.46 (CH_3-TMS); $^{m}/_{z}$ EI 227 (M^+-C(O)Et, 1%), 181 (13), 73 (TMS^+, 77), 57 ($C(O)Et^+$, 100); HRMS calc. 284.1807, found 284.1800.

7. (5*E*)-(2S,7R)-2,6-Dimethyl-7-hydroxy-4-methylene-non-5-enoic acid (10): *tert*-Butyldimethylsilyl chloride (301 mg, 2.0 mmol) in THF (1 cm^3) was added over 5 minutes to hydrocarbon free LDA (2.0 mmol) in THF (8 cm^3) at –78°C. A solution of the ester (**14a**) (284 mg, 1.0 mmol), in THF (1 cm^3) was added to the reaction mixture over 10 minutes at –78°C followed by the addition of dimethyltetrahydropyrimidinone (1 cm^3). After stirring at –78°C for 20 minutes the reaction mixture was warmed to room temperature giving a pale yellow solution. The reaction mixture was heated at reflux for 2 hours, cooled to room temperature, quenched by the addition of aqueous ammonium chloride (20 cm^3). The solution was vigorously stirred at room temperature for 30 minutes and then extracted with diethyl ether (3 x 10 cm^3). The combined organic layers were washed with brine (2 x 10 cm^3), dried over $MgSO_4$, filtered and concentrated under reduced pressure. The residue was dissolved in THF (10 cm^3) and 2 M aqueous HCl (10 cm^3), vigorously stirred for 30 minutes and then H_2O (20 cm^3) added. The solution was extracted with diethyl ether (3 x 10 cm^3) and the combined organic layers washed with 1 M aqueous sodium hydroxide (3 x 10 cm^3). The basic extracts were washed with diethyl ether (10 cm^3), acidified with conc. HCl (≈ pH 3) to give a cloudy solution which was extracted with diethyl ether (3 x 10 cm^3). The combined organic layers from the final extraction were washed with brine (2 x 10 cm^3), dried over $MgSO_4$, filtered and concentrated under reduced pressure to yield the title compound (**10**), as a clear colourless oil (190 mg, 90%). Ratio of *E*- to *Z*-isomers > 20:1. ν_{max} (thin film) / cm^{-1} 3700-2400 (b, OH), 2980 (m, CH), 2965 (m, CH), 1717 (s, C=O), 1415 (m), 1295 (m), 907 (m); δ_H 5.78 (1H, s, 5-H), 5.10 (1H, s, 11-H), 4.91 (1H, s, 11-H), 3.97 (1H, t, *J* 6.5, 7-H), 2.65-2.38 (2H, m, 3-H), 2.30-2.12 (1H, m, 2-H), 1.75 (3H, s, 10-H), 1.61 (2H, p, *J* 7, 8-H), 1.14 (3H, d, *J* 7, 12-H), 0.87 (3H, t, *J* 7, 9-H); δ_C 181.99 / 181.91* (C-1), 142.36 / 142.18* (C-4 or 6), 140.50 (C-4 or 6), 126.19 / 126.08* (CH-5), 116.05* / 115.99 (CH_2-11), 79.33 (CH-7), 41.51 / 41.42* (CH_2-3), 38.47 /38.26* (CH-2), 27.66 / 27.60* (CH_2-8), 16.54 / 16.34* (CH_3-12), 13.08* / 13.01 (CH_3-10), 9.95 (CH_3-9); $^{m}/_{z}$ EI 212 (M^+, 8%), 194 (M^+-H_2O, 30), 183 (M^+-Et, 9), 165 (25), 155 (35), 138 (57), 136 (56), 121 (69), 109 (100), 57 (100); CI 442 ($2M+NH_4^+$, 6%), 424 ($2M+NH_4^+$-H_2O, 13), 230 ($M+NH_4^+$, 100), 212 ($M+NH_4^+$-H_2O, 72), 195 ($(M-H_2O)H^+$, 50); HRMS calc. 212.1412, found 212.1409

8. (5*E*)-(2S,7R)-2,6-Dimethyl-7-hydroxy-4-methylene-non-5-enoic acid (10): Dimethyltetrahydropyrimidinone (4.5 cm^3) was added over 10 minutes with vigorous stirring to hydrocarbon free LDA (2.0 mmol) in THF (4 cm^3) at –78°C. The reaction mixture was stirred for 10 minutes at –78°C and the *tert*-butyldimethylsilyl chloride (301 mg, 2.0 mmol) in THF (0.5 cm^3) was added over 5 minutes with vigorous stirring. A solution of the ester (**14b**) (284 mg, 1.0 mmol), in THF (1 cm^3) was added at –78°C to the LDA solution. After stirring at –78°C for 10 minutes the reaction mixture was warmed to room temperature giving a clear brown solution. The reaction mixture was heated at reflux for 2 hours, cooled to room temperature, quenched by the addition of aqueous ammonium chloride (20 cm^3). The solution was vigorously stirred at room temperature for 30 minutes and then extracted with diethyl ether (3 x 10 cm^3). The combined organic layers were washed with brine (2 x 10 cm^3), dried over $MgSO_4$, filtered and concentrated under reduced pressure. The residue was dissolved in THF (10 cm^3) and 2 M aqueous HCl (10 cm^3), vigorously stirred for 30 minutes and then H_2O (20 cm^3) added. The solution was extracted with diethyl ether (3 x 10 cm^3) and the combined organic layers washed with 1 M aqueous sodium hydroxide (3 x 10 cm^3). The basic extracts were washed with diethyl ether (10 cm^3), acidified with conc. HCl (≈ pH 3) to give a cloudy solution which was extracted with diethyl ether (3 x 10 cm^3). The combined organic layers from the final extraction were washed with brine (2 x 10 cm^3), dried over $MgSO_4$, filtered and concentrated under reduced pressure to yield the title compound (**10**), as a clear colourless oil (187 mg, 88%). Ratio of *E*- to *Z*-isomers > 20:1. Spectrascopic data as above.

9. Methyl (5*E*)-(2*S*,7*R*)-2,6-dimethyl-7-hydroxy-4-methylenenon-5-enoate (19): To the acid (**10**) (10.18 g, 0.048 mol) and 1,8-diazabicyclo[5.4.0]-undeca-7-ene (14.31 cm^3, 0.096 mol) in dichloromethane (100 cm^3) was added methyl iodide (5.98 cm^3, 0.96 mol) at 0^{o}C over 5 minutes. The reaction mixture was stirred for 30 minutes at 0^{o}C and a further 18 hours at room temperature then quenched with dil. aqueous HCl (100 cm^3) and extracted with dichloromethane (3 x 25 cm^3). The combined organic layers were washed with 1M aqueous sodium hydroxide (25 cm^3), brine (25 cm^3), dried over $MgSO_4$, filtered and concentrated under reduced pressure. The residue was purified by chromatography on silica gel using a gradient elution of 10, 20, 30, 40% diethyl ether / hexane to yield the title compound (**19**) (8.11 g, 75%). $[\alpha]^{24}_{D}$ +21 (*c* 0.94, $CHCl_3$); ν_{max} (thin film) / cm^{-1} 3450 (b, OH), 2954 (s, CH), 1738 (s, C=O), 1630 (w, C=C), 1460 (m), 1437 (m), 1168 (m), 905 (m); δ_H 5.77 (1H, s, 5-H), 5.06 (1H, s, 11-H), 4.89 (1H, s, 11-H), 3.97 (1H, t, *J* 7, 7-H), 3.67 (3H, s, 13-H), 2.63-2.46 (2H, m, 2 or 3-H), 2.22-2.09 (1H, m, 2 or 3-H), 1.75 (3H, s, 10-H), 1.70 (1H, bs, OH), 1.61 (2H, p, *J* 7, 8-H), 1.11 (3H, d, *J* 6.5, 12-H), 0.91 (3H, t, *J* 7, 9-H); δ_C 176.82 (C-1), 142.42 / 140.61 (C-4 and 6), 125.92 (CH-5), 115.77 (CH_2-11), 79.23 (CH-7), 51.54 (CH_3-13), 41.65 (CH_2-3), 38.33 (CH-2), 27.68 (CH_2-8), 16.58 (CH_3-12), 13.06 (CH_3-10), 9.96 (CH_3-9); ${}^{m}/_{z}$ EI 226 (M^+, 1%), 208 (M^+-H_2O, 11), 149 (M^+-H_2O-CO_2Me, 12), 121 (100), 105 (49); HRMS calc. 226.1569, found 226.1574.

10. (5*E*)-(2*S*,7*R*)-Methyl-2,6-dimethyl-4-methylene-7-triethylsilyl-oxynon-5-enoate (20): Triethylsilyl chloride (2.50 cm^3, 0.015 mol) was added to a solution of alcohol (**19**) (300 g, 0.013 mol), triethylamine (3.50 cm^3, 0.025 mmol) and *N,N*-dimethylaminopyridine (100 mg) in dichloromethane (30 cm^3) at room temperature and stirred for 40 minutes. The reaction mixture was quenched by the addition of aqueous ammonium chloride (200 cm^3), the layers separated and the aqueous layer extracted with diethyl ether (3 x 50 cm^3). The combined organic layers were washed with brine (100 cm^3), dried over $MgSO_4$, filtered and concentrated under reduced pressure. The residue was purified by chromatography on silica gel using 10% diethyl ether / hexane. (R_f = 0.46) as eluant to yield the title compound (**20**) as a clear colourless oil (4.44 g, 99%). $[\alpha]^{22}_{D}$ +46 (*c* 1.00, $CHCl_3$); ν_{max} (thin film) / cm^{-1} 2957 (s, C-H), 2914 (s, C-H), 2878 (s, C-H), 1742 (s, C=O), 1629 (w), 1459 (m); δ_H 5.71 (1H, bs, 5-H), 5.03 (1H, bs, 11-H), 4.87 (1H, bs, 11-H), 4.02 (1H, t, *J* 6.5, 7-H), 3.67 (3H, s, 13-H), 2.62-2.47 (2H, m, 2 and 3-H), 2.19-2.05 (1H, m, 3-H), 1.72 (3H, bs, 10-H), 1.54 (2H, qd, *J* 7.5 and 6.5, 8-H), 1.12 (3H, d, *J* 7, 12-H), 0.96 (9H, t, *J* 7.5, TES), 0.83 (3H, t, *J* 7.5, 9-H), 0.59 (6H, q, *J* 7.5, TES); δ_C 176.81 (C-1), 142.70 (C-4), 141.17 (C-6), 125.12 (CH-5), 115.30 (CH_2-11), 79.68 (CH-7), 51.45 (CH_3-13), 41.73 (CH_2-3), 38.22 (CH-2), 29.05 (CH_2-8), 16.53 (CH_3-12), 13.04 (CH_3-10), 10.04 (CH_3-9), 6.83 (CH_3-TES), 4.78 (CH_2-TES); ${}^{m}/_{z}$ EI 340 (M^+, 20%), 311 (M^+-Et, 97), 279 (23), 253 (12), 239 (30), 115 (57), 87 (100); CI 358 (M+NH_4^+, 12%), 341 (MH^+, 2); HRMS calc. 340.2434, found 340.2436.

11. (5*E*)-(2*S*,7*R*)-2,6-Dimethyl-4-methylene-7-triethylsiloxynon-5-en-1-ol (21): Diisobutylaluminium hydride solution (28.5 cm^3, 1.0 M in dichloromethane, 0.0285 mol) was added dropwise to (5*E*)-(2*S*,7*R*)-methyl- 2,6-dimethyl-4-methylene-7-triethylsilyloxynon-5-enoate **(20)** (4.30 g, 0.0126 mol) in dichloromethane (70 cm^3) at 0^{o}C over 15 minutes with stirring. The reaction mixture was stirred 0^{o}C for 20 minutes and quenched by the careful addition of aqueous potassium sodium tartrate (100 g/ 1 dm^3). The reaction mixture was stirred for 10 minutes and the layers separated. The aqueous layer was extracted with diethyl ether (3 x 200 cm^3) and the combined organic layers washed with brine (400 cm^3), dried over $MgSO_4$, filtered and concentrated under reduced pressure. This yielded the title compound as a pale yellow oil (3.96 g, 100%). This sample was used without further purification; ν_{max} (thin film) / cm^{-1} 3342 (b, OH), 2959 (s, C-H), 2916 (s, C-H), 2878 (s, C-H), 1628 (w), 1459 (m), 1095 (m), 1064 (s), 1037 (s), 1005 (s), 743 (s); δ_H 5.72 (1H, bs, 5-H), 5.02 (1H, bs, 11-H), 4.87 (1H, bs, 11-H), 3.91 (1H, t, *J* 6.5, 11-H), 3.55-3.39 (2H, m, 1-H), 2.23 (1H, dd, *J* 14 and 7, 3-H), 1.90 (1H, dd, *J* 14 and 7.5, 3-H), 1.83-1.68 (1H, m, 2-H), 1.73 (3H, d, *J* 1.5, 10-H), 1.53 (2H, qd, *J* 7.5 and 6.5, 8-H), 1.30 (1H, bs, OH), 0.94 (9H, t, *J* 7.5, TES), 0.89 (3H, d, *J* 6.5, 12-H), 0.82 (3H, t, *J* 7, 9-H), 0.58 (6H, q, *J* 7.5, TES); δ_C 144.01 (C-4), 140.66 (C-6), 125.75 (CH-5), 114.80 (CH_2-11), 79.83 (CH-7), 68.09 (CH_2-1), 42.00 (CH_2-3), 34.46 (CH-2), 29.17 (CH_2-8), 16.45 (CH_3-12), 13.06 (CH_3-10), 10.14 (CH_3-9), 6.85 (CH_3-TES), 4.80 (CH_2-TES); $^{m}/_{z}$ EI 312 (M^+, 2%), 297 (M^+-Me, 1), 283 (M^+-Et, 18), 151 (100); CI 330 (M+NH_4^+, 3%), 313 (MH^+, 2); HRMS calc. 312.2485, found 312.2486.

12. (5*E*)-(2*S*,7*R*)-2,6-Dimethyl-4-methylene-7-triethylsiloxynon-5-en-l-al (22): *N*-methylmorpholine-*N*-oxide (2.0g, 0.0189 mol), 4Å molecular sieves (30g) and (5*E*)-(2*S*,7*R*)-2,6-dimethyl-4-methylene-7-triethyl siloxynon-5-en-1-o1 (**21**) (3.96 g, 0.0126 mol) were vigorously stirred in dichloromethane (70 cm^3) for 10 minutes at room temperature. Tetrapropylammonium perruthenate (221 mg, 0.63 mmol) was then added in one portion. The reaction mixture was stirred for 30 minutes at room temperature and then poured onto a silica gel column and eluted with 20% diethyl ether / hexane ($R_f = 0.59$) to yield the title compound which was used crude: ν_{max} (thin film) / cm^{-1} 2960 (s, CH), 2938 (s, CH), 2878 (s, C-H), 1729 (s, C=O), 1629 (w), 1457 (m), 1064 (s), 1006 (s), 901 (m), 839 (w), 743 (s); δ_H 9.64 (1H, d, *J* 1.5, 1-H), 5.71 (1H, bs, 5-H), 5.06 (1H, bs, 11-H), 4.91 (1H, bs, 11-H), 4.01 (1H, t, *J* 7, 7-H), 2.57 (1H, dd, *J* 14 and 7, 3-H), 2.52-2.38 (1H, m, 2-H), 2.07 (1H, dd, *J* 14 and 8.5, 3-H), 1.73 (3H, d, *J* 1.5, 10-H), 1.62-1.45 (2H, m, 8-H), 1.07 (3H, d, *J* 7, 12-H), 0.94 (9H, t, *J* 7.5, TES), 0.83 (3H, t, *J* 7, 9-H), 0.58 (6H, q, *J* 7.5, TES); δ_C 204.63 (CH-1), 142.17 (C-4), 141.86 (C-6), 124.82 (CH-5), 115.78 (CH_2-11), 79.53 (CH-7), 44.97 (CH-2), 38.85 (CH_2-3), 29.16 (CH_2-8), 13.16 / 13.01 (CH_3-10 and 12), 10.01 (CH_3-9), 6.85 (CH_3-TES), 4.83 (CH_2-TES); $^{m}/_{z}$ EI 310 (M^+, 9%), 281 (M^+-Et, 100); CI 328 (M+-NH_4^+, 10%), 311 (MH^+, 1); HRMS calc. for (M^+-Et) 281.1937, found 281.1928.

13. (7*E*)-(4*S*,9*R*)-6-Methylene-9-triethylsiloxy-2,4,8-trimethyl-undeca-1,7-dien-3-ol (9): 2-Bromopropene (2.22 cm^3, 0.025 mmol) was added dropwise over 30 minutes to a suspension (600 mg, 0.025 mol) and 1,2-dibromoethane (1 drop) in THF (60 cm^3) so as to maintain a gentle reflux and then heated at reflux for a further 1.5 hours. The reaction mixture was cooled to -10^{o}C and

(5*E*)-(2*S*,7*R*)-2,6-dimethyl-4-methylene-7-triethylsiloxynon-5-en-l-al (**22**) (0.0126 mol) in THF (10 cm^3) was added dropwise over 10 minutes. The reaction mixture was allowed to warm to room temperature over 2 hours and quenched by the slow addition of aqueous ammonium chloride (200 cm^3). The layers were separated and the aqueous layer extracted with diethyl ether (3 x 50 cm^3). The combined organic layers were washed with brine (100 cm^3), dried over $MgSO_4$, filtered and concentrated under reduced pressure. The residue was purified by chromatography on silica gel using 20% diethyl ether / hexane (R_f = 0.32 / 0.28) as eluant to yield the title compound (**9**) as a beige clear oil in a 1 : 1 ratio of diastereomers (3.35 g, 76% for reduction, oxidation and Grignard); ν_{max} (thin film) / cm^{-1} 3449 (b, OH), 2960 (s, C-H), 2936 (s, C-H), 2877 (s, C-H), 1648 (w), 1627 (w), 1455 (m), 1064 (m), 1012 (s), 897 (s), 743 (s); δ_H (1 : 1 ratio of diastereomers) 5.71 (1H, bs, 7-H), 5.05 (1H, bs, 13-H), 4.96 / 4.92 (1H, bs, 1-H), 4.91-4.83 (2H, m, 1 and 13-H), 3.95-3.85 (1.5H, m, 9 and 3-H), 3.82-3.76 (0.5H, m, 3-H), 2.53 (0.5H, bd, *J* 10, 5-H), 2.23 (0.5H, dd, *J* 13 and 5.5, 5-H), 1.92 (0.5H, dd, *J* 13 and 8.5, 5-H), 1.85-1.40 (3.5H, m, 4 and 5 and 10-H), 1.76 / 1.74 (3H, d, *J* 1.5, 12-H), 1.70 / 1.67 (3H, bs, 15-H), 0.95 (9H, t, *J* 7.5, TES), 0.86-0.74 (6H, m, 11 and 14-H), 0.58 (6H, q, *J* 7.5, TES); δ_C 146.67 / 146.40 / 144.42 / 143.98 / 140.51 / 140.28 (C-2 and 6 and 8), 126.08 / 125.76 (CH-7), 115.00 / 114.79 (CH_2-13), 112.36 / 111.08 (CH_2-1), 80.88 / 80.00 / 79.80 / 78.25 (CH-3 and 9), 42.23 / 40.26 (CH_2-5), 34.56 / 33.98 (CH-4), 29.02 / 28.90 (CH_2-10), 18.54 / 17.42 (CH_3-15), 15.93 / 12.97 (CH_3-14), 13.11 (CH_3-12), 10.06 / 10.02 (CH_3-11), 6.85 (CH_3-TES), 4.81 / 4.79 (CH_2-TES); $^m/_z$ EI 352 (M$^+$, 1%), 323 (M$^+$-Et, 29), 225 (38), 191 (40), 115 (63), 103 (71), 87 (100); CI 370 (M+-NH_4^+, 12%), 353 (MH$^+$, 10); HRMS calc. for (M$^+$-Et) 323.2506, found 323.2420.

14. Ethyl (4*E*,9*E*)-(6*S*,11*R*)-8-Methylene-11-triethylsiloxy-4,6,10-trimethytrideca-4,9-dienoate (23a): The alcohol (**9**) (2.20 g, 6.25 mmol) and hexanoic acid (0.04 cm^3, 0.3 mmol) in triethyl orthoacetate (11.5 cm^3, 62.5 mmol) were heated at reflux (approx. 140°C) for 5.5 hours and then cooled to room temperature. The reaction mixture was poured directly onto a silica gel column and eluted with 20% diethyl ether / hexane (R_f = 0.58) to yield the title compound (**23a**) as a clear colourless oil (2.42 g, 92%); $[\alpha]^{23}_D$ +36 (*c* 1.48, $CHCl_3$); ν_{max} (thin film) / cm^{-1} 2959 (s, C-H), 2877 (s, C-H), 1738 (s, C=O), 1627 (w), 1453 (m), 1371 (m), 1238 (m), 1156 (m), 1064 (m), 1005 (m), 896 (w), 840 (w), 743 (m); δ_H 5.70 (1H, bs, 9-H), 4.98-4.88 (2H, m, 5 and 15-H), 4.80 (1H, bs, 15-H), 4.12 (2H, q, *J* 7, 18-H), 4.00 (1H, t, *J* 7, 11-H), 2.51-2.33 (3H, m, 6 and 2 or 3-H), 2.32-2.21 (2H, m, 2 or 3-H), 2.12-1.89 (2H, m, 7-H), 1.69 (3H, d, *J* 1.5, 14-H), 1.64-1.47 (2H, m, 12-H), 1.57 (3H, bs, 17-H), 1.25 (3H, t, *J* 7, 19-H), 0.92 (9H, t, *J* 7.5, TES), 0.87 (3H, d, *J* 7, 16-H), 0.82 (3H, t, *J* 7, 13-H), 0.58 (6H, q, *J* 7.5, TES); δ_C 173.51 (C-1), 144.13 (C-8), 140.05 (C-10), 131.80 (CH-5), 131.76 (C-4), 126.23 (CH-9), 114.60 (CH_2-15), 79.94 (CH-11), 60.23 (CH_2-18), 45.77 (CH_2-7), 34.68 (CH_2-2), 33.37 (CH_2-3), 31.06 (CH-6), 29.08 (CH_2-12), 20.43 (CH_3-16), 16.02 (CH_3-17), 14.28 (CH_3-19), 13.03 (CH_3-14), 10.16 (CH_3-13), 6.90 (CH_3-TES), 4.86 (CH_2-TES); $^m/_z$ EI 422 (M$^+$, 18%), 393 (M$^+$-Et, 49), 290 (33), 169 (88), 123 (74), 95 (100); CI 440 (M+-NH_4^+, 24%), 423 (MH$^+$, 8); HRMS calc. 422.3216, found 422.3213.

15. (4*E*,9*E*)-(6*S*,11*R*)-8-Methylene-11-triethylsiloxy-4,6,10-trimethytrideca-4,9-dienoic acid (23b): Potassium hydroxide (1.20 g, 21.0 mmol) in water (10 cm^3) was added to ester (**23a**) (2.20 g, 5.20 mmol) in ethanol (100 cm^3) at room temperature and the reaction was stirred vigorously for 4 hours. The reaction was quenched with dilute HCl (50 cm^3) and extracted with diethyl ether (3 x 10 cm^3). The combined organic layers were washed with brine (20 cm^3), dried over MgSO$_4$, filtered and concentrated under reduced pressure to yield the title compound (**23b**) as a clear colourless oil (1.96 g, 92%). The material was used as obtained; $[\alpha]^{24}_D$ +38 (*c* 0.70, CHCl$_3$); ν_{max} (thin film) / cm^{-1} 3600-2200 (b, CO$_2$H), 2959 (s, C-H), 2877 (s, C-H), 1710 (s, C=O), 1627 (w), 1451 (m), 1065 (m), 1005 (s), 743 (s); δ_H 5.71 (1H, bs, 9-H), 5.00-4.88 (2H, m, 5 and 15-H), 4.80 (1H, bs, 15-H), 4.01 (1H, t, *J* 7, 11-H), 2.52-2.37 (3H, m, 6 and 2 or 3-H), 2.34-2.22 (2H, m, 2 or 3-H), 2.11-1.91 (2H, m, 7-H), 1.82-1.46 (2H, m, 12-H), 1.70 (3H, d, *J* 1.5, 14-H), 1.59 (3H, bs, 17-H), 0.97 (9H, t, *J* 7.5, TES), 0.87 (3H, d, *J* 6.5, 16-H), 0.83 (3H, t, *J* 7, 13-H), 0.59 (6H, q, *J* 7.5, TES); δ_C 179.70 (C-1), 144.08 (C-8), 140.02 (C-10), 132.04 (CH-5), 131.36 (C-4), 126.20 (CH-9), 114.59 (CH$_2$-15), 79.93 (CH-11), 45.73 (CH$_2$-7), 34.31 (CH$_2$-3), 33.06 (CH$_2$-2), 31.08 (CH-6), 29.05 (CH$_2$-12), 20.41 (CH$_3$-16), 15.97 (CH$_3$-17), 13.02 (CH$_3$-14), 10.13 (CH$_3$-13), 6.86 (CH$_3$-TES), 4.83 (CH$_2$-TES); $^m/_z$ EI 394 (M$^+$, 3%), 365 (M$^+$-Et, 39), 262 (54), 161 (79), 141 (90), 87 (100); CI 412 (M+NH$_4^+$, 4%), 395 (MH$^+$, 2); HRMS calc. 394.2903, found 394.2909.

16. *S-tert*-Butyl (6*E*,11*E*)-(8*S*,13*R*)-10-methylene-3-oxo-13-triethylsiloxy-2,6,8,12-tetramethylpentadeca-6,11-dienethioate (7): 1,1′- Carbonyldiimidazole (0.50 g, 3.10 mmol) was added to the acid (**23b**) (990 mg, 2.50 mmol) in THF (10 cm^3) at room temperature and stirred for 4 hours. Then magnesium di[(*S-tert*-butylthio)carbonyl propinate] (5 mmol) in THF (20 cm^3) was added and the reaction mixture stirred at room temperature for 18 hours. The reaction was quenched with aqueous ammonium chloride (100 cm^3) and extracted with diethyl ether (3 x 30 cm^3). The combined organic layers were dried over MgSO$_4$, filtered and concentrated under reduced pressure. The residue was purified by chromatography on silica gel using 5% diethyl ether / hexane (R$_f$ = 0.52) as eluant to yield the title compound (**7**) as a pale yellow gum (1.26 g, 97%); $[\alpha]^{25}_D$ +32 (*c* 0.60, CHCl$_3$); ν_{max} (thin film) / cm^{-1} 2960 (s, C-H), 2876 (s, C-H), 1726 (s, C=O), 1675 (s, C=O), 1604 (w), 1452 (m), 1365 (m), 1064 (m), 1004 (m); δ_H 5.70 (1H, bs, 11-H), 4.98-4.85 (2H, m, 7 and 17-H), 4.80 (1H, bs, 17-H), 3.90 (1H, t, *J* 6.5, 13-H), 3.65 (1H, q, *J* 7, 2-H), 2.67-2.55 (2H, m, 4-H), 2.52-2.35 (1H, m, 8-H), 2.22 (2H, bt, *J* 7, 5-H), 2.11-1.88 (2H, m, 9-H), 1.71 (3H, d, *J* 1.5, 16-H), 1.65-1.38 (2H, m, 14-H), 1.55 (3H, bs, 19-H), 1.48 (9H, s, *S-t*-Bu), 1.32 (3H, d, *J* 7, 20-H), 0.95 (9H, t, *J* 7.5, TES), 0.87 (3H, d, *J* 7, 18-H), 0.82 (3H, t, *J* 7, 15-H), 0.58 (6H, q, *J* 7.5, TES); δ_C 204.65 / 204.62 (C-3), 197.19 (C-1), 144.05 (C-10), 140.41 (C-12), 131.78 (C-6), 131.76 (CH-7), 126.01 (CH-11), 114.64 (CH$_2$-17), 79.90 (CH-13), 62.10 / 62.06 (CH-2), 48.77 (C, S-*t*-Bu), 45.96 (CH$_2$-9), 40.13 (CH$_2$-4), 33.34 / 33.32 (CH$_2$-5), 31.00 (CH-8), 29.63 (CH$_3$-S-*t*-Bu), 29.21 (CH$_2$-14), 20.34 (CH$_3$-18), 16.07 (CH$_3$-19), 13.44 (CH$_3$-20), 13.02 (CH$_3$-16), 10.14 (CH$_3$-15), 6.88 (CH$_3$-TES), 4.84 (CH$_2$-TES); $^m/_z$ EI 522 (M$^+$, 1%), 493 (M$^+$-Et, 3), 229 (43), 57 (100); CI 540 (M+-NH$_4^+$, 1%); HRMS calc. for (M$^+$-Et) 493.3172, found 493.3157.

17. *S-tert*-Butyl (6*E*,11*E*)-(8*S*,13*R*)-13-hydroxy-10-methylene-3-oxo-2,6,8,12-tetramethylpentadeca-6,11-dienethioate (24): The silyl ether (**7**) (1.10 g, 2.11 mmol) was vigorously stirred at room temperature in a mixture of acetic acid (20 cm^3), water (20 cm^3) and THF (10 cm^3) for 5 hours. The reaction mixture was carefully quenched by slow addition to aqueous potassium carbonate (500 cm^3). The solution was extracted with diethyl ether (3 x 100 cm^3) and the combined organic layers were dried over MgSO$_4$, filtered and concentrated under reduced pressure. The residue was purified by chromatography on silica gel using 20% EtOAc / hexane as eluant ($R_f = 0.26$). This was further purified by HPLC (Sorbsil 30Å 5 μm) using 15% EtOAc / hexane as eluant yielding the title compound (**24**) as a clear colourless oil (565 mg, 66%): $[\alpha]^{22}_{D}$ +15 (*c* 0.60, $CHCl_3$); ν_{max} (thin film) / cm^{-1} 3393 (b, OH), 2961 (s, C-H), 2876 (s, C-H), 1723 (s, C=O), 1673 (s, C=O), 1605 (w), 1453 (m), 1365 (m), 940 (m), 734 (m); δ_H 5.77 (1H, bs, 11-H), 4.97 (1H, bs, 17-H), 4.89 (1H, bd, *J* 9, 7-H), 4.82 (1H, bs, 17-H), 3.97 (1H, t, *J* 7, 13-H), 3.65 (1H, q, *J* 7, 2-H), 2.72-2.51 (2H, m, 4-H), 2.52–2.34 (1H, m, 8-H), 2.22 (2H, bt, *J* 7, 5-H), 2.02 (2H, d, *J* 7.5, 19-H), 1.74 (3H, d, *J* 1.5, 16-H), 1.68-1.40 (2H, m, 14-H), 1.56 (3H, bs, 19-H), 1.47 (9H, s, S-*t*-Bu), 1.31 (3H, d, *J* 7, 20-H), 0.89 (3H, t, *J* 7.5, 15-H), 0.87 (3H, d, *J* 7, 18-H); δ_C 204.69 / 204.65 (C-3), 197.22 (C-1), 143.92 (C-10), 139.48 (C-12), 131.79 (C-6), 131.53 (CH-7), 127.08 (CH-11), 114.95 (CH_2-17), 79.43 (CH-13), 62.07 / 62.04 (CH-2), 48.78 (C, S-*t*-Bu), 45.70 (CH_2-9), 40.03 (CH_2-4), 33.29 / 33.32 (CH_2-5), 31.18 (CH-8), 29.61 (CH_3-S-*t*-Bu), 27.75 (CH_2-14), 20.58 (CH_3-18), 16.13 (CH_3-19), 13.43 (CH_3-20), 13.03 (CH_3-16), 10.07 (CH_3-15); $^{m}/_{z}$ EI 390 (M^+-H_2O, 1%), 229 (M^+-Et, 48), 173 (49), 57 (100); CI 426 ($M+NH_4^+$, 27%); HRMS calc. for (M^+-H_2O) 390.2593, found 390.2597.

18. (6*E*,11*E*)-(2*R*,8*S*,13*R*)-10-Methylene-3-oxo-2,6,8,12-tetramethylpentadeca-6,11-dien-13-olide (26):

(6*E*,11*E*)-(2S,8*S*,13*R*)-10-Methylene-3-oxo-2,6,8,12-tetramethylpentadeca-6,11-dien-13-olide (27):

Mercuric acetate (489 mg, 1.53 mmol) was added to a solution of the thioester (**24**) (125 mg, 0.303 mmol) and *N,N*-diisopropylethylamine (267 mm^3, 1.53 mmol) in THF (150 cm^3) at room temperture and stirred for 48 hours. The reaction was filtered through a pad of celite and the filtrate quenched with aqueous ammonium chloride (300 cm^3) and extracted with diethyl ether (3 x 100 cm^3). The combined organic layers were washed with brine (100 cm^3), dried over $MgSO_4$, filtered and concentrated under reduced pressure. The residue was chromatographed on silica gel using 10% EtOAc / hexane as eluant (R_f = 0.22 / 0.20) . The diastereomers were separated by HPLC (Sorbsil 30Å 5 μm) using 7% EtOAc / hexane as eluant to yield the diastereomeric macrocycles (**25**) as clear colourless oils.

(**26**) (48.2 mg, 50%): Sample crystallised after trituration in diethyl ether / pentane and cooling at –18°C. Recrystallation from acetone / water yielded a beige waxy solid; m.p. 37-38°C. $[\alpha]^{24}_{D}$ -104 (*c* 0.128, $CHCl_3$); ν_{max} (thin film) / cm^{-1} 2968 (s, CH), 2926 (s, C-H), 1739 (s, C=O), 1715 (s, C=O), 1619 (w), 1451 (m), 1378 (m), 1322 (m), 1187 (s), 1119 (m), 1085 (m), 898 (m); δ_H (400 MHz; $CDCl_3$; Me_4Si) 5.78 (1H, bs, 11-H), 5.17 (1H, t, *J* 7, 13-H), 5.07 (1H, bs, 17-H), 4.97-4.89 (2H, m, 7 and 17-H), 3.49 (1H, q, *J* 7.5, 2-H), 2.72 (1H, ddd, *J* 18, 8.5 and 8, 4-H), 2.62-2.50 (1H, m, 8-H), 2.51 (1H, ddd, *J* 18, 8.5 and 6.5, 4-H), 2.33-2.21 (1H, m, 5-H), 2.21 (1H, dd, *J* 14 and 4.5, 9-H), 2.13-2.02 (1H, m, 5-H), 2.02 (1H, dd, *J* 14 and 7, 9-H), 1.84 (3H, d, *J* 2, 16-H), 1.73 (2H, p, *J* 7, 14-H), 1.54 (3H, bs, 19-H), 1.32 (3H, d, *J* 7.5, 20-H), 0.97 (3H, d, *J* 7, 18-H), 0.87 (3H, t, *J* 7.5, 15-H); δ_C 204.99 (C-3), 170.56 (C-1), 143.48 (C-10), 133.22 (C-12), 132.46 (C-6), 131.99 (CH-11), 130.25 (CH-7), 117.39 (CH_2-17), 81.43 (CH-13), 53.63 (CH-2), 44.49 (CH_2-9), 39.22 (CH_2-4), 33.42 (CH-8), 32.20 (CH_2-5), 25.99 (CH_2-14), 21.20 (CH_3-18), 17.07 (CH_3-19), 14.85 (CH_3-16), 12.41 (CH_3-20), 9.76 (CH_3-15); $^{m}/_{z}$ EI 318 (M^+, 1%), 274 (M^+-CO_2, 3), 161 (21), 113 (52), 107 (42), 93 (100); CI 336 ($M+NH_4^+$, 50%), 319 (MH^+, 100); HRMS (CI) calc. for (MH^+) 319.2273, found 319.2282.

(**27**) (47.9 mg, 49%): $[\alpha]^{24}_{D}$ -120 (*c* 0.196, $CHCl_3$); ν_{max} (thin film) / cm^{-1} 2968 (s, C-H), 2927 (s, C-H), 1717 (bs, C=O), 1648 (w), 1620 (w), 1451 (m), 1383 (m), 1239 (m), 1127 (w), 1068 (m), 1026 (m), 896 (m); δ_H (400 MHz; $CDCl_3$; Me_4Si) 5.63 (1H, bs, 11-H), 5.09 (1H, bt, *J* 7, 13-H), 5.06 (1H, bs, 17-H), 4.98 (1H, bd, *J* 10.5, 7-H), 4.87 (1H, bs, 17-H), 3.48 (1H, q, *J* 7, 2-H), 2.78-2.67 (1H, m, 4-H), 2.62-2.38 (2H, m, 5 and 8H), 2.18 (1H, dd, *J* 13.5 and 3, 9-H), 2.01-1.87 (1H, m, 5-H), 1.92 (1H, dd, *J* 13.5 and 9.5, 9-H), 1.78 (3H, d, *J* 1.5, 16-H), 1.78-1.68 (1H, m, 4-H), 1.64 (2H, p, *J* 7, 14-H), 1.58 (3H, d, *J* 1.5, 19-H), 1.36 (3H, d, *J* 7, 20-H), 0.95 (3H, d, *J* 7, 18-H), 0.85 (3H, t, *J* 7, 15-H); δ_C 203.67 (C-3), 169.61 (C-1), 144.38 (C-10), 133.45 (C-12), 131.98 (C-6), 131.79 (CH-7), 128.66 (CH-11), 115.95 (CH_2-17), 79.54 (CH-13), 54.39 (CH-2), 44.71 (CH_2-9), 39.95 (CH_2-4), 34.45 (CH-8), 31.76 (CH_2-5), 25.86 (CH_2-14), 21.96 (CH_3-18), 16.22 (CH_3-19), 15.69 (CH_3-16), 12.49 (CH_3-20), 9.24 (CH_3-15); $^{m}/_{z}$ EI 318 (M^+, 1%), 274 (M^+-CO_2, 3), 161 (20), 113 (53), 107 (48), 93 (100); CI 336 ($M+NH_4^+$, 8%), 319 (MH^+, 9); HRMS (CI) calc. for (MH^+) 319.2273, found 319.2290.

19. (4*E*,9*E*)-(6*S*,11*R*)-2-(2-Methylacryloyl)-8-methylene-4,6,10-trimethyltrideca-6,11-dien-11-olide (28): The macrocycles (**25**) (8 mg, 0.025 mmol) in THF (0.5 cm^3) were added to LDA (0.025 mmol) in THF (0.5 cm^3) and DMPU (0.1 cm^3) at -15°C and the reaction mixture stirred for 20 minutes. A stream of depolymerised (160°C) paraformaldehyde was bubbled through the reaction mixture for 10 minutes with the aid of a stream of nitrogen and the reaction was stirred for 30 minutes at room temperature. The reaction was quenched with aqueous ammonium chloride (10 cm^3) and extracted with diethyl ether (3 x 5 cm^3). The combined organic layers were washed with brine (10 cm^3), dried over $MgSO_4$, filtered and concentrated under reduced pressure. The residue was purified by chromatography on silica gel using 20% EtOAc / hexane ($R_f = 0.14$) as eluant to yield the title compound (**28**) as a thin film (3.1 mg, 39%); $[\alpha]^{24}_{D}$ -15 (*c* 0.075, $CHCl_3$); ν_{max} (thin film) / cm^{-1} 2958 (s, C-H), 2937 (s, C-H), 1716 (s, C=O), 1637 (w), 1451 (m), 1289 (m), 1162 (s); δ_H (400 MHz; $CDCl_3$; Me_4Si) 6.11 (1H, dq, *J* 2 and 1, 20-H), 5.81 (1H, bs, 9-H), 5.55 (1H, p, *J* 2, 20-H), 5.15 (1H, t, *J* 7, 11-H), 4.97 (1H, bs, 15-H), 4.92 (1H, dq, *J* 9 and 1.5, 5-H), 4.80 (1H, bs, 15-H), 2.47-2.38 (2H, m, 6 and 2-H), 2.30-2.23 (2H, m, 3-H), 2.05 (1H, dd, *J* 12.5 and 6.5, 7-H), 1.98 (1H, dd, *J* 12.5 and 6.5, 7-H), 1.95 (3H, dd, *J* 2 and 1, 21-H), 1.85-1.61 (2H, m, 12-H), 1.74 (3H, d, *J* 1.5, 14-H), 1.52 (3H, d, *J* 1.5, 17-H), 0.89 (3H, t, *J* 7.5, 13-H), 0.87 (3H, d, *J* 7.5, 16-H); irradiation of 2.47-2.38 (2H, m, 6 and 2-H), collapses 2.05 (1H, dd, *J* 12.5, 7-H), 1.98 (1H, d, *J* 12.5, 7-H), 4.92 (1H, bs, 5-H); irradiation 2.05 (1H, dd, *J* 12.5 and 6.5, 7-H), 1.98 (1H, dd, *J* 12.5 and 6.5, 7-H) collapses 4.97 (1H, d, *J* 2.5, 15-H), and simplifies 5.81 (1H, bs, 9-H), 4.80 (1H, bs, 15-H); $^{m}/_{z}$ EI 262 (M^+-C_4H_4O, 23%), 189 (20), 161 (82), 41 (100); CI 280 ($M+NH_4^+$-C_4H_4O, 28), 263 (MH^+-C_4H_4O, 28); HRMS calc. for (M^+-C_4H_4O) 262.1933, found 262.1930.