Synthetic Study on 1,3-Polyols. An Efficient Enantioselective Synthesis of Tarchonanthuslactone

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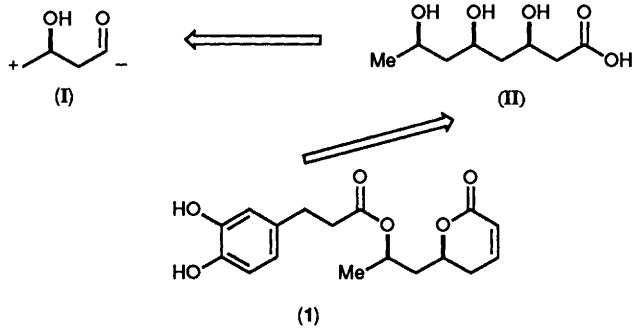
Tarchonanthuslactone, a *syn*-1,3-polyol-derived α,β-unsaturated δ-lactone, has been synthesized. The coupling reaction of a chiral dithiane with a chiral epoxide and highly *syn*-stereoselective 1,3-asymmetric reduction of the derived hydroxy ketone led to the synthesis of tarchonanthuslactone in a stereocontrolled manner.

A 1,3-polyhydroxylated chain is often found as the backbone of biologically important polyene macrolide antibiotics.[1] The acyclic nature of a 1,3-polyol chain and a regular array of many hydroxy groups are the main obstacles to synthetic studies of 1,3-polyols. Therefore the stereoselective synthesis of continuous 1,3-diol units is of importance and many synthetic efforts have been made to this end.[2] We recently developed a method for the preparation of *syn*-1,3-polyols using 1,3-asymmetric reduction.[3] The method was stereoselective and iterative and led to the synthesis of an all-*syn*-1,2,4,6,8,10,12-heptol derivative.[3b] We report here an efficient stereoselective synthesis of tarchonanthuslactone (**1**), an α,β-unsaturated δ-lactone derived from a 1,3-polyol compound.

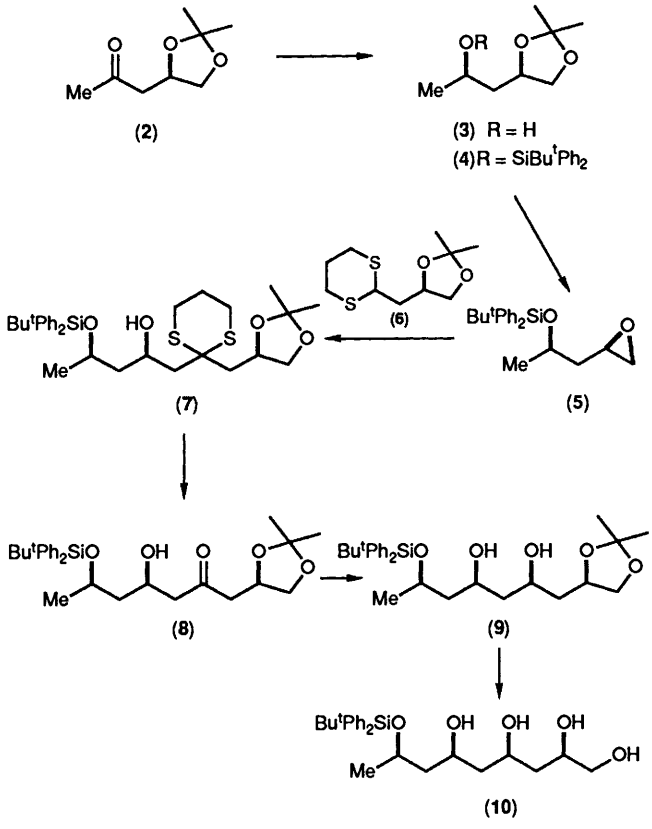
Higher plants produce several α,β-unsaturated δ-lactones,[4] which seem to originate biogenetically from the corresponding 1,3-polyhydroxylated acid. One member of this group is tarchonanthuslactone (**1**), which was isolated from *Tarchonanthus trilobus* (Compositae)[5] and whose absolute configuration was established by synthesis.[6] A key feature of our synthesis lies in the stereocontrolled formation of a *syn*-1,3-triol acid (**II**) or its equivalent that could be prepared from a C_4 chiral unit (**I**) (Scheme 1).



Scheme 1.

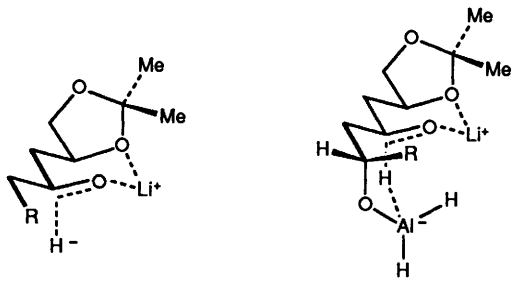
Results and Discussion

The starting ketone (**2**) was prepared from (3*S*)-3,4-isopropylidenedioxybutanal[7] by addition of methyl-lithium followed by oxidation with pyridinium chlorochromate in good yield. Reduction of the ketone (**2**) with lithium aluminium hydride in the presence of lithium iodide in diethyl ether at −78 °C provided the *syn*-triol derivative (**3**) in 84% yield. The *syn*:*anti* ratio was 94:6. The hydroxy group was protected with t-butylchlorodiphenylsilane and then the acetonide group was transformed into an oxirane ring in three steps [i, pyridinium toluene-*p*-sulphonate, methanol; ii, toluene-*p*-sulphonyl chloride, pyridine; iii, KH, diethyl ether–methanol], giving the epoxide (**5**) in 67% overall yield (Scheme 2).



Scheme 2.

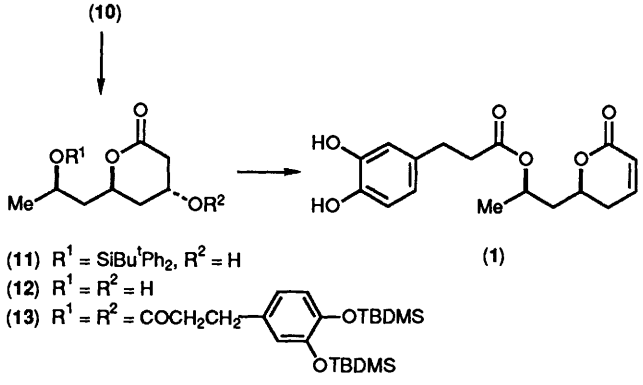
The coupling reaction of the anion generated from the chiral dithiane (**6**), an equivalent to the C_4 unit (**I**), with the chiral epoxide (**5**) yielded the dithiane (**7**) in 87% yield. Deprotection of the dithioacetal group with *N*-bromosuccinimide (NBS)–$AgNO_3$[8] gave the β-hydroxy ketone (**8**) in 87% yield. The ketone (**8**) was reduced to the *syn*-diol derivative (**9**) (88%) with excellent *syn*-selectivity (*syn*:*anti* 96:4) by reaction with lithium aluminium hydride–lithium iodide in diethyl ether at −100 °C. (Reduction at −78 °C decreased the *syn*:*anti* ratio to 89:11.) The high *syn*-selectivity of lithium aluminium hydride–lithium iodide reduction of compounds (**2**) and (**8**) arises from β-chelation of lithium cation with the ketone and an ether oxygen of the 1,3-dioxolane ring to form intermediate complexes (**III**) and (**IV**) (Figure), and hydride then attacks from the less hindered α-side, resulting in the formation of the *syn*-products.



(III) (IV)

Figure.

The correct array of hydroxy groups on the chain having been established (*vide infra*), it remained to remove one carbon unit and to form a lactone ring to achieve the synthesis of the target lactone (**1**). Removal of the acetonide group of compound (**9**) afforded the all-*syn*-1,2,4,6,8-pentol compound (**10**) in 91% yield, which is a synthetic equivalent to the triol acid (**II**). Oxidative cleavage of the 1,2-diol moiety of compound (**10**) with sodium metaperiodate followed by oxidation of the resulting lactol with manganese dioxide afforded the lactone (**11**). Desilylation of lactone (**11**) gave the hydroxy lactone (**12**) in 68% overall yield from the tetraol (**10**). The stereochemical assignment of the reduction product (**9**) was established unequivocally by ^{1}H NMR analysis of the lactone (**11**). The signal assigned to 3-H appeared at δ 4.39 as a quintet with a coupling constant of 3.4 Hz, indicating that 3-H was β equatorial and that the C-3 hydroxy group was thus α axial. Therefore, the configuration of the C-4 hydroxy group of compound (**9**) was determined to be β.



(**11**) R^1 = $SiBu^tPh_2$, R^2 = H
(**12**) R^1 = R^2 = H
(**13**) R^1 = R^2 = $COCH_2CH_2$–(OTBDMS, OTBDMS)

Scheme 3. 7 BDMS = $SiMe_2Bu^t$.

Completion of the synthesis required three more steps; (i) diesterification of diol lactone (**12**) to (**13**) with 3,4-dihydroxyhydrocinnamic acid, protected with t-butyldimethylsilyl groups, by using dicyclohexylcarbodi-imide (DCC); (ii) formation of an α,β-unsaturated δ-lactone by treatment with 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU) in benzene; and (iii) deprotection of the silyl groups by tetrabutylammonium fluoride in the presence of benzoic acid in tetrahydrofuran (THF), yielding tarchonanthuslactone (**1**), $[\alpha]_D^{25}$ −76.5° (*c* 0.4 in $CHCl_3$) {lit.,[5] $[\alpha]_D$ −67.2° (*c* 2.3 in $CHCl_3$)}, in 72% overall yield from lactone (**12**) (Scheme 3). The spectroscopic data (NMR, IR, and MS) were identical with the reported values.[5]

In conclusion the stereoselective synthesis of tarchonanthuslactone has been accomplished, where a new methodology for *syn*-1,3-polyol synthesis originally developed by us was successfully applied.

Experimental

Optical rotations were determined on a JASCO DIP-181 digital polarimeter, and IR spectra were recorded on a Hitachi 251 infrared spectrometer. ^{1}H NMR spectra were recorded on a JEOL JNM GX-400 spectrometer with tetramethylsilane as internal standard. Chemical ionization mass spectra (CIMS) were taken on a Shimadzu GCMS QP-1000 spectrometer, and secondary ionization mass spectra (SIMS) and high-resolution mass spectra were recorded on a Hitachi M-80 mass spectrometer. Flash chromatography was performed on silica gel 60 (230–400 mesh). Organic solutions were dried over $MgSO_4$, and, after filtration, were concentrated under reduced pressure on a rotary evaporator.

(2R,4R)-4,5-(*Isopropylidenedioxy*)*pentan*-2-*ol* (**3**).—A stirred solution of the ketone (**2**) (750 mg) and LiI (1.9 g) in dry diethyl ether (50 ml) was cooled to −78 °C under nitrogen and $LiAlH_4$ (540 mg) was added. The mixture was stirred for 30 min and was then quenched with MeOH (2 ml) and 2M-KOH (1.5 ml), and stirred at room temperature until precipitates formed. The mixture was filtered through a short column of Celite and the filtrate was evaporated. The residue was purified by flash chromatography with acetone–$CHCl_3$ (6:94) to give *compound* (**3**) (630 mg, 84%) as an oil, b.p. (Kugelrohr distillation) 80 °C at 15 mmHg (Found: C, 59.8; H, 10.2. $C_8H_{16}O_3$ requires C, 59.98; H, 10.07%); $[\alpha]_D^{23}$ −14.7° (*c* 1.0 in $CHCl_3$); ν_{max} 3 450 cm^{-1}; $\delta_H(C_6D_6)$ 1.09 (3 H, d, *J* 6.4 Hz, 1-H_3), 1.24 (3 H, s, Me), 1.31 (3 H, s, Me), 2.64 (1 H, s, OH), 3.23 (1 H, t, *J* 7.6 Hz, 5-H), 3.70 (1 H, dd, *J* 5.8 and 7.8 Hz, 5-H), 3.80 (1 H, m, 2-H), and 3.89 (1 H, m, 4-H).

(2R,4R)-4-(*t-Butyldiphenylsiloxy*)-1,2-(*isopropylidenedioxy*)-*pentane* (**4**).—A mixture of compound (**3**) (700 mg), imidazole (1.19 g), and t-butylchlorodiphenylsilane (2.4 g) in *N*,*N*-dimethylformamide (2 ml) was stirred for 13 h at room temperature and extracted with diethyl ether. The extract was washed successively with water and brine, dried, and evaporated to dryness. Flash chromatography with EtOAc–hexane (5:95) gave the *title compound* (**4**) (1.6 g, 92%) as an oil (Found: M^+, 398.2143. $C_{24}H_{34}O_3Si$ requires *M*, 398.2118); $[\alpha]_D^{24}$ −1.88° (*c* 1.0 in $CHCl_3$); $\nu_{max}(CHCl_3)$ 1 422, 1 380, 1 108, 1 040, 815, and 695 cm^{-1}; $\delta_H(CDCl_3)$ 1.06 (9 H, s, Bu^t), 1.12 (3 H, d, *J* 6.1 Hz, 5-H_3), 1.30 (3 H, s, Me), 1.32 (3 H, s, Me), 1.61 (1 H, dt, *J* 13. 5 and 6.4 Hz, 3-H), 1.91 (1 H, dt, *J* 13.5 and 5.9 Hz, 3-H), 3.40 (1 H, t, *J* 7.6 Hz, 1-H), 3.90 (1 H, dd, *J* 8.1 and 5.9 Hz, 1-H), 3.99 (1 H, sextet, *J* 5.9 Hz, 4-H), 4.20 (1 H, quint, *J* 6.5 Hz, 2-H), 7.35–7.44 (6 H, ArH), and 7.66–7.68 (4 H, ArH); CIMS, *m*/*z* 399 (MH^+).

(2R,4R)-4-(*t-Butyldiphenylsiloxy*)-1,2-*epoxypentane* (**5**).—A solution of compound (**4**) (1.6 g) and pyridinium toluene-*p*-sulphonate (40 mg) in MeOH (30 ml) was heated at 50 °C for 4 h and then Et_3N (0.1 ml) was added to the solution. After evaporation of the solvent the oily residue was purified by flash chromatography with EtOAc–hexane (1:1) to give the 1,2-diol product (1.1 g, 77%); $[\alpha]_D^{23}$ −15.56° (*c* 0.25 in $CHCl_3$); $\nu_{max}(CHCl_3)$ 3 450 cm^{-1}; $\delta_H(CDCl_3)$ 1.03 (3 H, d, *J* 6.4 Hz, 5-H_3), 1.04 (9 H, s, Bu^t), 1.50–1.79 (2 H, m, 3-H), 1.97 (1 H, t, *J* 6.1 Hz, OH), 3.11 (1 H, d, *J* 2.7 Hz, OH), 3.43 (1 H, dt, *J* 11.1 and 6.1 Hz, 1-H), 3.58 (1 H, ddd, *J* 10.1, 6.7, and 3.7 Hz, 1-H), 3.94 (1 H, m, 4-H), and 4.14 (1 H, m, 2-H); CIMS, *m*/*z* 359 (MH^+).

The product (1.1 g) obtained above was dissolved in pyridine (10 ml) at 0 °C and toluene-*p*-sulphonyl chloride (1.5 g) was added. The mixture was stirred at 0 °C for 4.5 h and extracted with diethyl ether. The extract was washed successively with 1% HCl and brine, dried, and concentrated. Flash chromatography with EtOAc–hexane (15:85) gave the monotosyl ester (1.4 g, 89%).

The monotosyl ester (1.4 g) was dissolved in diethyl ether–methanol (5:1) (40 ml) and excess of KH (suspension in mineral oil) was added to the stirred solution at 0 °C. The mixture was stirred for 1 h and extracted with diethyl ether. The extract was washed successively with water and brine, dried, and concentrated. Flash chromatography of the residue with EtOAc–hexane (6:94) gave the *epoxide* (**5**) (0.9 g, 97%) as an oil (Found: M^+, 340.2157. $C_{21}H_{28}O_2Si$ requires M, 340.2184); $[\alpha]_D^{24}$ +11.37° (*c* 0.67 in $CHCl_3$); $\nu_{max}(CHCl_3)$ 1 422, 1 105, 820, and 695 cm^{-1}; $\delta_H(CDCl_3)$ 1.07 (9 H, s, Bu^t), 1.17 (3 H, d, *J* 6.1 Hz, 5-H_3), 1.61 (1 H, dt, *J* 13.9 and 5.6 Hz, 3-H), 1.73 (1 H, dt, *J* 13.9 and 5.7 Hz, 3-H), 2.37 (1 H, dd, *J* 5.1 and 2.7 Hz, 1-H), 2.68 (1 H dd, *J* 5.1 and 4.2 Hz, 1-H), 3.04 (1 H, m, 2-H), 4.08 (1 H, sextet, *J* 5.4 Hz, 4-H), 7.36–7.45 (6 H, ArH), and 7.67–7.69 (4 H, ArH).

(2R,4R,8R)-2-(*t-Butyldiphenylsiloxy*)-8,9-(*isopropylidenedioxy*)-6,6-(*trimethylenedithio*)*nonan-4-ol* (**7**).—A solution of compound (**6**) (260 mg, 1.1 mmol) in dry THF (3 ml) was treated with 1.6M-BuLi in hexane (1 ml, 1.6 mmol) at −40 °C under nitrogen. After the mixture had been stirred at −30 °C for 2 h a solution of the epoxide (**5**) (350 mg, 0.94 mmol) in dry THF (3 ml) was added. The reaction vessel was closed under positive pressure of nitrogen and stored at −20 °C for 40 h. The reaction mixture was extracted with diethyl ether, and the extract was washed successively with water and brine, dried, and concentrated. The residue was purified by flash chromatography with EtOAc–hexane (1:9) to give the *title compound* (**7**) (514 mg, 87%) as an oil (Found: M^+, 574.2461. $C_{31}H_{46}O_4S_2Si$ (requires M, 574.2419); $[\alpha]_D^{24}$ −1.4° (*c* 0.85 in $CHCl_3$); $\nu_{max}(CHCl_3)$ 3 480, 1 425, 1 380, 1 115, 820, and 700 cm^{-1}; $\delta_H(CDCl_3)$ 1.06 (9 H, s, Bu^t), 1.08 (3 H, d, *J* 6.1 Hz, 1-H_3), 1.31 (3 H, s, Me), 1.39 (3 H, s, Me), 1.80–2.06 (4 H), 2.20–2.31 (3 H), 2.73–3.05 (4 H), 3.36 (1 H, d, *J* 1.7 Hz, OH), 3.52 (1 H, t, *J* 8.1 Hz, 9-H), 4.11 (1 H, m, 4-H), 4.13 (1 H, dd, *J* 8.1 and 6.1 Hz, 9-H), 4.17 (1, H, m, 2-H), 4.41 (1 H, m, 8-H), 7.35–7.44 (6 H, ArH), and 7.69–7.72 (4 H, ArH); CIMS, *m/z* 575 (MH^+).

(2R,6R,8R)-8-(*t-Butyldiphenylsiloxy*)-6-*hydroxy*-1,2-(*isopropylidenedioxy*)*nonan-4-one* (**8**).—A solution of compound (**7**) (122 mg) in 85% aq. MeCN (4 ml) was added to a stirred suspension of NBS (227 mg), $AgNO_3$ (228 mg), and 2,6-lutidine (0.3 ml) in 85% aq. MeCN (6 ml) and the mixture was stirred for 7 min. After successive additions of saturated aq. Na_2SO_3 (1 ml), aq. $NaHCO_3$ (0.5 ml), and brine (0.5 ml) at one minute intervals, the mixture was diluted with CH_2Cl_2–hexane (1:1) and filtered through a short column of Celite. The filtrate was concentrated and the residue was purified by flash chromatography with EtOAc–hexane (2:8) to give the *hydroxy ketone* (**8**) (69 mg, 68%) as an oil (Found: M^+, 484.2261. $C_{28}H_{40}O_5Si$ requires M, 484.2237); $[\alpha]_D^{24}$ −13.48° (*c* 2.13 in $CHCl_3$); $\nu_{max}(CHCl_3)$ 3 480, 1 705, 820, and 700 cm^{-1}; $\delta_H(CDCl_3)$ 1.04 (9 H, s, Bu^t), 1.05 (3 H, d, *J* 6.1 Hz, 9-H_3), 1.35 (3 H, s, Me), 1.41 (3 H, s, Me), 1.52 (1 H, dt, *J* 13.7 and 4.9 Hz, 7-H), 1.76 (1 H, dt, *J* 13.7 and 8.1 Hz, 7-H), 2.48 (1 H, dd, *J* 17.1 and 4.4 Hz, 5-H), 2.54 (1 H, dd, *J* 17.1 and 7.6 Hz, 5-H), 2.55 (1 H, dd, *J* 16.9 and 6.8 Hz, 3-H), 2.85 (1 H, dd, *J* 16.9 and 6.4 Hz, 3-H), 3.28 (1 H, d, *J* 2.7 Hz, OH), 3.54 (1 H, dd, *J* 8.3 and 5.8 Hz, 1-H), 4.10 (1 H, m, 6-H), 4.17 (1 H, dd, *J* 8.3 and 6.1 Hz, 1-H), 4.25 (1 H, m, 8-H), 4.45 (1 H, quintet, *J* 6.4 Hz, 2-H), 7.36–7.45 (6 H, ArH), and 7.68–7.71 (4 H, ArH).

(2R,4R,6S,8R)-8-(*t-Butyldiphenylsiloxy*)-1,2-(*isopropylidenedioxy*)*nonane-4,6-diol* (**9**).—A stirred solution of the hydroxy ketone (**8**) (64 mg) and LiI (30 mg) in dry diethyl ether (6 ml) under nitrogen was cooled to −100 °C and $LiAlH_4$ (20 mg) was added. The reaction mixture was stirred at −100 °C for 30 min and then quenched with MeOH (0.5 ml) and 2M-KOH (0.5 ml). After being stirred for 30 min at room temperature the organic layer was separated, dried, and concentrated. Flash chromatography of the residue with EtOAc–hexane (3:7) gave the *syn*-diol (**9**) (58 mg, 91%) as an oil; $[\alpha]_D^{24}$ −6.52° (*c* 1.0 in $CHCl_3$); $\nu_{max}(CHCl_3)$ 3 480, 1 425, 1 380, 1 110, 818, and 700 cm^{-1}; $\delta_H(CDCl_3)$ 1.04 (3 H, d, *J*, 6.1 Hz, 9-H_3), 1.05 (9 H, s, Bu^t), 1.37 (3 H, s, Me), 1.42 (3 H, s, Me), 1.40-1.82 (6 H, 3-, 5-, and 7-H_2), 3.57 (1 H, t, *J* 7.6 Hz, 1-H), 3.79 (1 H, s, OH), 3.87 (1 H, s, OH), 3.98–4.16 (3 H, 4-, 6-, and 8-H), 4.11 (1 H, dd, *J* 8.1 and 5.9 Hz, 1-H), 4.28 (1 H, m, 2-H), 7.36–7.45 (6 H, ArH), and 7.69–7.73 (4 H, ArH); SIMS, *m/z* 487 (MH^+) and 199 (base peak).

(2R,4R,6R,8R)-8-(*t-Butyldiphenylsiloxy*)*nonane*-1,2,4,6-*tetraol* (**10**).—A solution of compound (**9**) (62 mg) and pyridinium toluene-*p*-sulphonate (3 mg) in MeOH (6 ml) was heated at 50 °C for 4 h. After addition of Et_3N (0.1 ml) the solvent was evaporated off. The residue was purified by flash chromatography with EtOAc to give the title tetraol (**10**) (52 mg, 91%) as an oil; $[\alpha]_D^{24}$ −13.88° (*c* 1.0 in $CHCl_3$); $\nu_{max}(CHCl_3)$ 3 450, 1 425, 1 110, and 700 cm^{-1}; $\delta_H(CDCl_3)$ 1.00 (3 H, d, *J* 6.1 Hz, 9-H_3), 1.05 (9 H, s, Bu^t), 1.40–1.79 (6 H, 3-, 5-, and 7-H_2), 2.64 (1 H, br, OH), 3.51 (1 H, dd, *J* 11.0 and 5.6 Hz, 1-H), 3.63 (1 H, dd, *J* 11.0 and 4.0 Hz, 1-H), 3.89 (1 H, br, OH), 3.96 (1 H, br, OH), 3.98 (1 H, m, 2-H), 4.08–4.18 (3 H, 4-, 6-, and 8-H), 4.59 (1 H, br, OH), 7.38–7.48 (6 H, ArH), and 7.70–7.74 (4 H, ArH); SIMS, *m/z* 447 (MH^+) and 199 (base peak).

(3R,5R,7R)-7-(*t-Butyldiphenylsiloxy*)-3,5-*dihydroxyoctanoic Acid* δ-*Lactone* (**11**).—The pentaol derivative (**10**) (45 mg) was dissolved in MeOH (2 ml)–water (2 ml) and $NaIO_4$ (43 mg) was added. After being stirred for 20 min at room temperature the mixture was extracted with EtOAc. The extract was washed with brine, dried, and concentrated to give a lactol (42 mg, 99%).

The lactol (42 mg) was dissolved in EtOAc (5 ml) and freshly prepared MnO_2 (300 mg) was added. After being stirred for 38 h at room temperature the mixture was passed through a short column of silica gel with EtOAc. The eluate was concentrated and the residue was purified by flash chromatography with EtOAc–hexane (4:6) to give the silyl lactone (**11**) (36 mg, 87%) as an oil; $[\alpha]_D^{24}$ +26.2° (*c* 0.7 in $CHCl_3$); $\nu_{max}(CHCl_3)$ 3 600, 3 430, 1 720, 1 310, 818, and 700 cm^{-1}; $\delta_H(CDCl_3)$ 1.06 (9 H, s, Bu^t), 1.17 (3 H, d, *J* 6.1 Hz, 8-H_3), 1.55–2.06 (4 H, 4- and 6-H_2), 2.54 (1 H, ddd, *J* 17.6, 4.2, and 1.7 Hz, 2-H), 2.65 (1 H, dd, *J* 17.6 and 5.1 Hz, 2-H), 4.10 (1 H, sextet, *J* 6.1 Hz, 7-H), 4.26 (1 H, quintet, *J* 4.4 Hz, 3-H), 4.84 (1 H, m, 5-H), 7.36–7.45 (6 H, ArH), and 7.65–7.71 (4 H, ArH); CIMS, *m/z* 413 (MH^+) and 317 (base peak).

(3R,5R,7R)-3,5,7-*Trihydroxyoctanoic Acid* δ-*Lactone* (**12**).—A solution of 1M-Bu_4NF in THF (0.12 ml) was added to a stirred solution of compound (**11**) (17.8 mg) and benzoic acid (15 mg) in dry THF (1 ml), and the mixture was stirred for 12 h at room temperature. After evaporation of the solvent, the residue was purified by flash chromatography with MeOH–EtOAc (4:96) to give the lactone (**12**) (5.8 mg, 78%) as an oil; $[\alpha]_D^{24}$ +18.9° (*c* 0.6 in $CHCl_3$); $\nu_{max}(CHCl_3)$ 3 400, 1 725, 1 268, and 1 078 cm^{-1}; $\delta_H(CDCl_3)$ 1.26 (3 H, d, *J* 6.4 Hz, 8-H_3), 1.70 (1 H, ddd, *J* 14.2, 5.1, and 3.9 Hz, 6-H), 1.79 (1 H, ddd, *J* 14.6, 11.5, and 2.9 Hz, 4-H), 1.94 (1 H, dt, *J* 14.2 and 8.1 Hz, 6-H), 2.03 (1 H, br d, *J* 14.6 Hz, 4-H), 2.65 (1 H, ddd, *J* 17.9, 3.4, and 1.7 Hz, 2-H), 2.73 (1 H, dd, *J* 17.9 and 4.9 Hz, 2-H), 4.08 (1 H, m, 7-H), 4.39 (1 H, quintet, *J* 3.4 Hz, 3-H), and 4.92 (1 H, m, 5-H); CIMS, *m/z* 175 (MH^+).

Tarchonanthuslactone (**1**).—(i) *Diesterification of compound* (**12**). The lactone (**12**) (4.7 mg) was dissolved in CH_2Cl_2 (2 ml) and to this solution were added successively 3,4-bis-(t-butyldimethylsiloxy)hydrocinnamic acid (33 mg), DCC (28 mg), and

4-(dimethylamino)pyridine (3 mg). The reaction mixture was stirred for 13 h at room temperature. After dilution with CH_2Cl_2 (5 ml) the mixture was filtered to remove precipitates and the filtrate was concentrated. Flash chromatography with EtOAc–hexane (15:85) gave a diester (**13**) (20 mg, 77%) as an oil; $[\alpha]_D^{24}$ −0.96° (*c* 1.0 in $CHCl_3$); $\nu_{max}(CHCl_3)$ 1 725, 1 305, 1 250, 900, and 835 cm^{-1}; $\delta_H(CDCl_3)$ 0.18 (24 H, s, SiMe), 0.97 (18 H, s, Bu^t), 1.24 (3 H, d, *J* 6.4, 8-H_3), 1.73 (2 H, m, 4-H_2), 2.06 (2 H, m, 6-H_2), 2.50–2.84 (10 H, 2-H_2 and ArCH_2CH_2CO), 4.56 (1 H, m, 5-H), 5.13 (1 H, m, 7-H), 5.22 (1 H, m, 3-H), and 6.58–6.75 (6 H, ArH); SIMS, *m/z* 959 (MH^+).

(ii) *DBU treatment of the diester* (**13**). The diester (**13**) (15 mg) obtained above was dissolved in benzene (1 ml) and DBU (5 μl) was added. After being stirred for 10 min at room temperature the mixture was extracted with EtOAc, and the extract was washed successively with 1% HCl and brine, dried, and concentrated. Flash chromatography of the residue with EtOAc–hexane (1:3) gave an α,β-unsaturated δ-lactone (8.4 mg, 98%) as an oil; $[\alpha]_D^{24}$ −44.74° (*c* 0.7 in $CHCl_3$); $\nu_{max}(CHCl_3)$ 1 723, 1 505, 1 255, 900, and 840 cm^{-1}; $\delta_H(CDCl_3)$ 0.18 (6 H, s, SiMe), 0.19 (6 H, s, SiMe), 0.98 (9 H, s, Bu^t), 0.99 (9 H, s, Bu^t), 1.26 (3 H, d, *J* 6.4 Hz, 8-H_3), 1.81 (1 H, ddd, *J* 14.4, 6.8, and 4.4 Hz, 6-H), 2.21–2.41 (2 H, m, 4-H), 2.56 (2 H, t, *J* 7.5 Hz), 2.81 (2 H, t, *J* 7.5 Hz), 4.43 (1 H, m, 5-H), 5.10 (1 H, m, 7-H), 6.00 (1 H, dd, *J* 9.7 and 2.4 Hz, 2-H), 6.62 (1 H, dd, *J* 8.1 and 2.0 Hz, ArH), 6.65 (1 H, d, *J* 2.0 Hz, ArH), 6.70 (1 H, d, *J* 8.1 Hz, ArH), and 6.84 (1 H, ddd, *J* 9.0, 5.9, and 2.2 Hz, 3-H); CIMS, *m/z* 566 ($M + NH_4^+$).

(iii) *Tarchonanthuslactone* (**1**). The unsaturated lactone (8.2 mg) obtained above was dissolved in dry THF (0.5 ml) and benzoic acid (5.6 mg) and 1M-Bu_4NF in THF (38 μl) were added to the solution. The reaction mixture was stirred for 30 min at room temperature and then extracted with EtOAc. The extract was washed with brine, dried, and concentrated. Flash chromatography with MeOH–EtOAc (1.5:98.5) gave *tarchonanthuslactone* (**1**) (4.6 mg, 96%) as an oil (Found: M^+, 320.1251. $C_{17}H_{20}O_6$ requires *M*, 320.1234); $[\alpha]_D^{25}$ −76.5° (*c* 0.4 in $CHCl_3$); $\nu_{max}(CHCl_3)$ 3 600–3 200, 1 720, 1 600, 1 520, 1 445, 1 380, 1 260, and 1 040 cm^{-1}; $\delta_H(CDCl_3)$ 1.25 (3 H, d, *J* 6.4 Hz, 8-H_3), 1.76 (1 H, ddd, *J* 14.7, 7.1, and 3.9 Hz, 6-H), 2.07 (1 H, ddd, *J* 14.7, 8.6, and 6.1 Hz, 6-H), 2.19 (1 H, ddt, *J* 18.3, 11.7, and 2.6 Hz, 4-H), 2.35 (1 H, dddd, *J* 18.3, 5.9, 3.9, and 1.0 Hz, 4-H), 2.61 (2 H, t, *J* 7.1 Hz), 2.84 (2 H, t, *J* 7.1 Hz), 4.16 (1 H, dddd, *J* 13.2, 11.2, 6.1, and 3.9 Hz, 5-H), 5.06 (1 H, ddq, *J* 8.6, 3.9, and 6.4 Hz, 7-H), 6.00 (1 H, ddd, *J* 9.8, 2.7, and 1.0 Hz, 2-H), 6.60 (1 H, dd, *J* 8.1 and 2.2 Hz, ArH), 6.73 (1 H, d, *J* 2.2 Hz, ArH), 6.75 (1 H, d, *J* 8.1 Hz, ArH), and 6.84 (1 H, ddd, *J* 9.8, 6.1, 2.4 Hz, 3-H).

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