SUPPORTING INFORMATION

Synthetic procedures

All solvents were of analytical grade and used as supplied. Solketal (2,3-isopropylidene glycerol), oxalyl chloride, oleyl alcohol (99%), phytol (3,7,11,15-tetramethyl-hexadec-2-en-1-ol), 97% mixture of isomers, and farnesol (3,7,11-trimethyl-dodecan-1-ol), 95% mixture of isomers, were used as obtained from Aldrich.

Analytical HPLC was performed on a Phenomenex Luna C18 column (150 x 4.6 mm), using MeOH/water, pumped at 1.1 ml/minute. The results were monitored by a UV detector at 205 nm.

Preparative HPLC separation was carried out using a Waters Deltapak C18 column (300 x 40 mm) with methanol/water mixtures. The progress was monitored by a UV detector at 205 nm, the output of which was recorded on a chart recorder. 1 g of the material was used for each injection and the solvent was pumped at 80 ml/minute. Fractions were cut over the main product bands, and only those analysing > 95% were combined as product.

Column chromatography was performed on Merck silica gel 60 (0.040–0.063 mm).

NMR spectra were recorded on a Bruker AC-200 or Av400 spectrometer and analysed using SwaN-MR (written by Guiseppi Belacco). Where coupling constants (J) are stated, they are the result of spectral simulation using SwaN-MR, otherwise they are given merely as a "splitting".

3,7,11,15-Tetramethyl-hexadecan-1-ol (phytanol)

A solution of phytol (17.8 g, 58.6 mmol) in ethanol (100 ml) was stirred under hydrogen atmosphere over Raney nickel (Aldrich) (1.78 g, 50% slurry in water) for 50 hours. The catalyst was removed by filtration through a short layer of silica gel and the filtrate concentrated under reduced pressure (~ 50 mm Hg; water bath 70°C) to give 17 g of phytanol as a colourless oil. Yield 97%.

^{1}H NMR ($CDCl_3$): sl br d, δ0.84, 6H, splitting 6.3 Hz, CH_3; d, δ0.86, 6H, splitting 6.5 Hz, CH_3; d, δ0.89, 3H, splitting 6.5 Hz, CH_3; m, δ0.95–1.72, 24H, CH + CH_2; m δ3.57–3.77, 2H, **CH_2**OH; sl br s, δ4.80, OH.

GC: r_t 17.3 min (25 m BPX5 column, SGE); initial temp. 100°C; initial time 2 min, rate 10 deg./min)

3,7,11-Trimethyl-dodecan-1-ol (hexahydrofarnesol)

A solution of farnesol (11.12 g, 50 mmol) in ethanol (100 ml) was stirred under hydrogen atmosphere over Raney nickel (3.3 g, 50% slurry in water, Aldrich) for 3 days. While the allylic double bond was fully reduced, the other unsaturation partially remained. Very little progress in reduction was detected over additional two days. The nickel catalyst was removed and 5% w/w of Pd/C (5% palladium, LR, BDH) was added. Stirring in hydrogen atmosphere overnight resulted in a 4:1 mixture of hexahydrofarnesol and 3,7,11- trimehyldodecane, which were subsequently separated by distillation (80°C at 0.2-0.3 mm Hg). 7.34 g of hexahydrofarnesol as a colourless oil was obtained. Yield 64.2%.

GC: 25 m BPX5 column, SGE; initial temp. 70°C; initial time 2 min, rate 10°C/min)

hexahydrofarnesol: r_t 15.5 min

trimehyldodecane : r_t 11.8min

^{1}H NMR ($CDCl_3$): sl br d, δ0.84, 3H, splitting 6.3 Hz, CH_3; d, δ0.86, 6H, splitting 6.5 Hz, CH_3; sl br d, δ0.90, 3H, splitting 6.3 Hz, CH_3; m, δ0.95–1.43, 14H, CH_2 + CH; m, δ1.43–1.71, 3H CH_2 + CH; m, δ3.58–3.78, 2H **CH_2**OH.

2,2-Dimethyl-[1,3]dioxolane-4-carbonyl chloride (2,3-isopropylidene glyceroyl chloride)

(a) ***Potassium 2,2-Dimethyl-[1,3]dioxolane-4-carboxylate.***

Solketal (2,3-isopropylidene-glycerol) (67.3g) and potassium hydroxide (45g) were dissolved in water (400 ml). It was cooled to about 5°C and a solution of potassium permanganate (118g) in water (2000 ml) was added in aliquots, with stirring below 5°C. After the addition, the mixture was allowed to warm to room temperature and stirred until all the residual permanganate had changed to manganese dioxide, as indicated by the decolourisation of the supernatant liquid. 50% Sulphuric acid was added until the pH was 7.5 (as read by a pH meter). The mixture was vacuum filtered and the dark brown solid washed twice with water (about 100 ml). The combined filtrates were evaporated to give an off white solid (70°C/1 mm Hg). This was treated with hot ethanol (150 ml), cooled to 4°C, filtered and the filtered solid potassium sulphate solid washed twice with ethanol (50 ml). The ethanol was evaporated to

give potassium 2,3-isopropylidene-glycerate as an off white solid. (79.3 g; 84% theoretical yield). It was dried at room temperature/0.02 mm for 4–5 hours.

^{1}H NMR (D_2O) s δ1.42, 3H, isopropylidene CH_3; s, δ1.47, 3H, isopropylidene CH_3; dd, δ3.94, 1H, J -8.4 Hz 6.8 Hz, C3-H_2; dd, δ4.31, 1H, J -8.4 Hz 7.7 Hz, C3-H_2; dd, δ4.53, 1H, J 6.8 Hz 7.7 Hz, C2-H.

(b) ***2,3-isopropylidene glyceroyl chloride.*** Potassium 2,3-isopropylidene glycerate (76.9 g) was suspended in sodium dried ether (500 ml, 99.6%) and the mixture was chilled to <5°C in an ice bath. Oxalyl chloride (59.3 g, 1.2 mole equivalent) was slowly added with stirring so that the temperature stayed below 8°C. After the addition, the mixture was stirred overnight at room temperature. The precipitated KCl was filtered, resuspended in dry ether (100 ml), refiltered, and then washed twice with more dry ether (50 ml). The ether and excess oxalyl chloride were removed from the combined filtrates (35°C/500 mm Hg). It was then pumped at 35°C/1 mm Hg for 5 minutes. The golden yellow oil was dissolved in pentane (400 ml) and allowed to stand at -12°C for 3 hours so that the undissolved oily material settled. The pentane solution was separated from the oil and passed through a 5 mm bed of celite to remove the last of the undissolved oil. The solution was evaporated (25–30°C/400–500 mm Hg, then 25–30°C/10 mm) to give a light golden oil (54.3 g, 79% yield).

^{1}H NMR ($CDCl_3$) s, δ1.41, 3H, isopropylidene CH_3; s, δ1.52, 3H, isopropylidene CH_3; d, δ4.33, 2H, J 5.75 Hz, C3-H_2; t, δ4.82, 1H, J 5.75 Hz, C2-H.

2,3-dihydroxy-propionic acid cis-Octadec-9-enyl ester (Oleyl glycerate)

(a) 2,2-Dimethyl-[1,3]dioxolane-4-carboxylic acid cis-Octadec-9-enyl ester (Oleyl 2,3-isopropylidene-glycerate). Oleyl alcohol (50.5g, 188 mmole, 99%) was dissolved in dry dichloromethane (200 ml) and dry pyridine (35 ml). This was chilled in an ice bath, vigorously stirred and 2,3-isopropylidene-glyceroyl chloride (35 g) dripped in over 10 minutes. It was stirred for a further 20 minutes and then allowed to warm to room temperature for 2 hours. An NMR spectrum of an aliquot showed the presence of only a trace amount of oleyl alcohol. The mixture was extracted three times with water and the solvent removed (45°C/1 mm Hg). The product (76.8 g) was dissolved in 1 litre of cyclohexane and passed through a short silica gel column (76 g, 55 mm diameter). All cyclohexane solutions were evaporated at 45°C/50 mm Hg. The product (68.9 g) was a golden yellow oil. An NMR spectrum showed a trace of oleyl alcohol present in the ester. Yield 92%.

NMR (CDCl3) sl br t, δ0.88, splitting 6.3 Hz, 3H oleyl CH_3; m, δ1.10–1.45, 22H oleyl CH_2; s, δ1.41, 3H, isopropylidene CH_3; s, δ1.50, 3H, isopropylidene CH_3; m, δ1.54–1.75, 2H, **CH_2**CH_2CO_2; m, δ1.9–2.1, 4H, **CH_2**CH=CH**CH_2**; dd, δ4.10, 1H, J -8.6 Hz 5.3 Hz, glyceryl C3-H_2; m, δ4.15, 1H, J -11.7 Hz 6.7 Hz, oleyl CH_2O; m, δ4.18, 1H, J -11.7 Hz 6.7 Hz, oleyl CH_2O; dd, δ4.24, 1H, J -8.6 Hz 7.3 Hz, glyceryl C3-H_2; dd, δ4.58, 1H, J 5.3 Hz 7.3 Hz, glyceryl C2-H; m, δ5.3–5.4, 2H, CH=CH.

(b) ***Oleyl Glycerate.*** The oleyl 2,3-isopropylidene-glycerate (64.5 g) was dissolved in a mixture of acetic acid (440 ml) and water (110 ml) and heated with rapid stirring in an oil bath preheated to 132°C. After about 16 minutes the mixture became homogenous. It was refluxed for 15 minutes, then cooled rapidly and the solvent removed (45°C/9 mm Hg) to give 62.0 g golden yellow product. The crude product was dissolved in methanol (60 ml) and allowed to crystallise, first at 4°C and then at -12°C. The crystals were filtered at -10°C, redissolved in methanol (55 ml) and allowed to crystallise again as before. A third crystallisation was performed as before using 100 ml methanol. The mother liquors from the crystallisations (about 12 g) were purified using preparative HPLC, using 82.5% methanol/water as a mobile phase. 4 g of the material was injected each time. Fractions were cut so as to exclude impurities that overlapped the first and the last of the product. Fractions containing < 95% of the glycerate were recycled. The pure material was recrystallised three times from methanol (55 ml) and dried at 0.02 mm Hg at room temperature for 18 hours. A total of 48.5 g was recovered. Yield 84%. Melting point 33.2- 34.2^{o}C.

δ($CDCl_3$) sl br t, δ0.88, 3H, splitting 6.3 Hz, oleyl CH_3; m, δ1.2–1.45, 22H oleyl CH_2; m, δ1.55–1.75, 2H, **CH_2**CH_2CO_2; m, δ1.9–2.1, 4H, **CH_2**CH=CH**CH_2**; v br s*, δ2.05–2.45, 1H, OH; v br s*, δ3.05–3.40, 1H, OH; dd, δ3.83, 1H, J –11.7 Hz 3.7 Hz, glyceryl C3-H; dd, δ3.90, 1H, J –11.7 Hz 3.3 Hz, glyceryl C3-H; t, δ4.22, 2H, J 6.7 Hz, oleyl **CH_2**O; dd, δ4.26, 1H, J 3.7 Hz 3.3 Hz, glyceryl C2-H; m, 2H, δ5.3–5.4, CH=CH.

* The resonances at 2.2 and 3.2 disappear on D_2O treatment.

Elemental analysis for $C_{21}H_{40}O_4$ (356.29) Calcd: C, 70.74; H, 11.31; O, 17.95. Found: C, 70.39; H, 10.92; O, 18.69.\

2,3-dihydroxy-propionic acid 3,7,11,15-tetramethyl-hexadecyl ester

(Phytanyl glycerate)

(a) ***2,2-Dimethyl-[1,3]dioxolane-4-carboxylic acid 3,7,11,15-tetramethyl-hexadecyl ester (Phytanyl 2,3-isopropylidene-glycerate).*** Phytanol (55g, 184 mmole) was dissolved in dried dichloromethane (200 ml) and dry pyridine (35ml). This was chilled in an ice bath, vigorously stirred and 2,3-isopropylidene-glyceroyl chloride (35.7 g) dripped in over 20 minutes. It was then allowed to warm to room temperature for 1 hour, after which phytanol presence was still detectable by NMR. More 2,3-isopropylidene-glyceroyl chloride (3.6 g) was added, and after a further hour stirring, the mixture was extracted 3 times with water and the solvent removed (45°C/1 mm Hg). The product (85.4 g) was dissolved in 1 litre of cyclohexane and passed through a short silica gel column (75 g, 55 mm diameter). All cyclohexane solutions were evaporated at 45°C/50 mm Hg. A NMR spectrum of the product, a golden yellow oil (72.5 g), showed a trace amount of phytanyl alcohol present in the ester. Yield 92%.

NMR (CDCl3) sl br d, δ0.84, 6H, splitting 6.3 Hz, CH_3; d, δ0.86, 6H, splitting 6.6 Hz, CH_3; d, δ0.90, 3H, splitting 6.3 Hz, CH_3; m, δ0.94–1.80, 24H, phytanyl CH_2 + phytanyl CH; s, δ1.40, 3H, isopropylidene CH3; s, δ1.50, 3H, isopropylidene CH3; dd, δ4.09, 1H, J -8.7 Hz 5.1 Hz, glyceryl C3-H; m, δ4.15–4.32, 2H, Phytanyl CH_2O; dd,δ4.23, 1H, J -8.7 Hz 7.4 Hz, glyceryl C3-H; dd, δ4.57, 1H, J 5.1 Hz 7.4 Hz, glyceryl C2-H.

(b) (Phytanyl glycerate) The phytanyl 2,3-isopropylidene-glycerate (83.5 g) was added to acetic acid (480 ml, 99.8%) and water (120 ml). It was heated in an oil bath at 132°C with rapid stirring. The mixture was two phase initially but became clear in about 19 minutes. After 15 minutes reflux the mixture was rapidly cooled. NMR analysis of a sample showed that the acetonide had been completely cleaved. The acetic acid / water was evaporated using a rotary evaporator (45°C/ 9 mm Hg), and the product was dissolved in an equal volume of ether, extracted twice with 50 ml of saturated $NaHCO_3$ solution to remove residual acetic acid, and then washed two times with water (50 ml). Evaporation of the ether gave a deep golden oil (76.7 g. It was purified by preparative HPLC, using 82.5% MeOH/water as a mobile phase. 4.5 g was separated each time on the column. A total of 55.3 g was recovered. To remove the last trace of solvent, the sample was pumped on a rotary evaporator at room temperature/0.03 mm Hg for 20 hours. Yield 73%.

^{1}H NMR ($CDCl_3$): sl br d, δ0.84, 6H, splitting 6.3 Hz, CH_3; d, δ0.86, 6H, splitting 6.6 Hz, CH_3; sl br d, δ0.90, 3H, splitting 6.3 Hz, CH_3; m, δ0.95–1.80, 24H, phytanyl CH_2 + phytanyl CH; dd, δ2.13, 1H, J 8.5 Hz 4.6 Hz, glyceryl C3-OH; d, δ3.16, 1H, J 4.6 Hz, glyceryl C2-OH; ddd, δ3.83, 1H, J -11.4 Hz 4.1 Hz 8.5Hz, glyceryl C3-H; ddd, 1H, δ3.90, J -11.4 Hz 3.4 Hz 4.6 Hz,

glyceryl C3-H; t, δ4.22, 2H, J 6.7 Hz, CH_2CO_2; ddd, δ4.27, 1H, J 4.6 Hz 4.1 Hz 3.4 Hz, glyceryl C2-H.

NMR after treatment with D2O sl br d, δ0.84, 6H, splitting 6.3 Hz, CH_3; d, δ0.86, 6H, splitting 6.6 Hz, CH_3; sl br d, δ0.90, 3H, splitting 6.3 Hz, CH_3; m, δ0.95–1.80, 24H, phytanyl CH_2 + phytanyl CH; dd, δ3.83, 1H, J -11.7 Hz 3.8 Hz, glyceryl C3-H2; dd, δ3.89, 1H, J -11.7 Hz 3.3 Hz, glyceryl C3-H2; t, δ4.22, 2H, J 6.7 Hz, phytanyl CH_2O; dd, v4.25, 1H, J 3.8 Hz 3.3 Hz, glyceryl C2-H. The resonances previously at 2.13 and 3.16 have disappeared.

Elemental analysis for $C_{21}H_{40}O_4$ (356.29) Calcd: C, 71.45; H, 11.99; O, 16.55. Found: C, 70.78; H, 12.24; O, 16.98.

2,3-dihydroxy-propionic acid octadecyl ester

(Octadecyl glycerate)

(a) ***2,2-Dimethyl-[1,3]dioxolane-4-carboxylic acid octadecyl ester (Octadecyl 2,3-isopropylidene-glycerate)***. This was prepared by the same procedure as oleyl isopropylidene glycerate. Octadecanol (1 g) was reacted with 2,3-isopropylidene-glyceroyl chloride (0.91 g) in dry dichloromethane (4 ml) and dry pyridine (1 ml). Work up, extraction and filtration through silica gel (1.4 g) gave a product (1.38 g), which crystallised on the evaporation of the solvent. M.p. 34.5–40.0°C.

NMR ($CDCl_3$) sl br t, δ0.87, splitting 6.4 Hz, 3H octadecyl CH_3; m, δ1.15–1.43, 30H octadecyl CH_2; s, δ1.41, 3H, isopropylidene CH_3; s, δ1.50, 3H, isopropylidene CH_3; tt, δ1.65, 2H, J 7.1Hz 6.6 Hz, $\mathbf{CH_2}CH_2CO_2$; dd, δ4.10, 1H, J -8.6 Hz 5.1 Hz, glyceryl C3-H_2; m, δ4.14, 1H, J -10.6 Hz 6.6 Hz, octadecyl CH_2O; t, δ4.17, 1H, J -10.6 Hz 6.6 Hz, octadecyl CH_2O; dd, δ4.24, 1H, J -8.6 Hz 7.2 Hz, glyceryl C3-H_2; dd, δ 4.58, 1H, J 5.1 Hz 7.2 Hz, glyceryl C2-H.

(b) ***Octadecyl glycerate.*** This followed the procedure of oleyl glycerate. Octadecyl isopropylidene glycerate (1.38 g) was treated with 80% acetic acid (10 ml). After removal of the solvent, the product was crystallised from methanol (10 ml), and then petroleum spirit (10 ml; b.p. 60–80°). The product (1.11 g) was dried at room temperature at 0.06 mm for 45 minutes. M.p. 73.0–74.2°C.

δ($CDCl_3$) sl br t, δ0.88, 3H, splitting 6.4 Hz, octadecyl CH_3; m, δ1.15–1.42, 30H octadecyl CH_2; tt, δ1.66, 2H, J 7.1Hz 6.7 Hz, $\mathbf{CH_2}CH_2CO_2$; dd, δ2.04, 1H, J 8.1Hz 5.2 Hz, glyceryl C(3)-OH; d, δ3.09, 1H, J 4.6 Hz, C(2)-OH; ddd, δ3.83, 1H, J 8.1 Hz -11.7 Hz 3.9 Hz, glyceryl C(3)-

H_2; ddd, δ3.89, 1H, J 5.2 Hz -11.7 Hz 3.3 Hz, glyceryl C(3)-H_2; t, δ4.22, 2H, J 6.7 Hz, octadecyl **CH_2**O; dd, δ4.22–4.30, 1H, glyceryl C(2)-H.

On treatment with D_2O the protons at δ2.14 and δ3.16 are removed and the spectrum resolves to:- sl br t, δ0.88, 3H, splitting 6.4 Hz, oleyl CH_3; m, δ1.15–1.42, 30H octadecyl CH_2; tt, δ1.66, 2H, J 7.1Hz 6.7 Hz, **CH_2**CH_2CO_2; dd, δ3.83, 1H, J –11.6 Hz 3.9 Hz, glyceryl C(3)-H; dd, δ3.89, 1H, J –11.6 Hz 3.3 Hz, glyceryl C(3)-H; t, δ4.22, 2H, J 6.7 Hz, octadecyl **CH_2**O; dd, δ4.25, 1H, J 3.9 Hz 3.3 Hz, glyceryl C(2)-H.

2,3-Dihydroxy-propionic acid 3,7,11-trimethyl-dodecyl ester (hexahydrofarnesyl glycerate)

(a) ***2,2-Dimethyl-[1,3]dioxolane-4-carboxylic acid 3,7,11-trimethyl-dodecyl ester (Hexahydrofarnesyl 2,3isopropylidene-glycerate).*** Hexahydrofarnesol (3.52 g, 15.4 mmol) in dry dichloromethane (30 ml) and dry pyridine (1.2 ml, 15.4 mmol) was reacted with 2,3-isopropylidene glyceroyl chloride (2.37 g, 14.38 mmol) following the same procedure as for oleyl isopropylidene-glycerate. The crude product, 5.7g was dissolved in of 40/60 petroleum spirit (100 ml) and filtered through 6 g layer of silica gel, to remove traces of pyridine.

^{1}H NMR ($CDCl_3$): sl br d, δ0.84, 3H, splitting 6.3 Hz, CH_3; d, δ0.86, 6H, splitting 6.6 Hz, CH_3; sl br d, δ0.90, 3H, splitting 6.3 Hz, CH_3; m, δ0.97–1.75, 17H, CH_2 + CH; s, δ1.41, 3H, isopropylidene CH_3; s, δ1.50, 3H, isopropylidene CH_3; dd, δ4.08, 1H, J -8.6 Hz 5.1 Hz, glyceryl C(3)H; m, δ4.10–4.35, 2H, CO_2-**CH_2**; dd, δ4.22, 1H, J -8.6 Hz 7.3 Hz, glyceryl C(3)H; dd, δ 4.57, 1H, J 5.1 Hz 7.3 Hz, glyceryl C(2)H

(b) ***Hexahydrofarnesyl glycerate***. 1-Hexahydrofarnesyl-2,3-isopropylidene glycerate (2.34 g) was treated with 80% acetic acid (23.4 g) in the same manner as oleyl glycerate. The crude product (96% yield) was purified by preparative HPLC using 75% methanol/water. Fractions were cut over the main product band, and only those analysing > 95% were combined as product. 1.2 g of product was recovered from HPLC, giving 40% yield, as calculated for the pure product (fractions less pure were kept apart for further processing).

^{1}H NMR ($CDCl_3$): sl br d, δ0.84, 3H, splitting 6.3 Hz, CH_3; d, δ0.86, 6H, splitting 6.6 Hz, CH_3; sl br d, δ0.91, 3H, splitting 6.3 Hz, CH_3; m, δ0.97–1.75, 17H, CH_2 + CH; m, δ1.37–1.60, 3H, CH_2 + CH; m, δ1.60–1.78, 1H, CH_2; v br s, δ1.75–2.55, 2H, OH; dd, δ3.83, 1H, J –

11.5 Hz 4.0 Hz, glyceryl-C(3)H_2; dd, δ3.90, 1H, J –11.5 Hz 3.2 Hz, glyceryl-C(3)H_2; dd, δ4.25, 1H, J 4.0 Hz 3.2 Hz, glyceryl C(2)H; t, δ4.27, 2H, J 6.6 Hz, $CO_2\mathbf{CH_2}$.

3-(*cis*-Octadec-9-enyloxy)-propane-1,2-diol (1-glyceryl oleyl ether)

(a) cis-*Octadec-9-enyl bromide (oleyl bromide)*

Oleyl alcohol (4.03 g, 15 mmole, technical) and 1.5 eq. of carbon tetrabromide (7.46 g, 22.5 mmole) was dissolved in dichloromethane (50 ml, dried over 3A molecular sieve) and cooled to ~ 3°C. A solution of triphenylphosphine (5.90 g, 22.5 mmole) in 50 ml dichloromethane was added to it dropwise, maintaining the temperature 3°C. The mixture was stirred for a further hour at 0-5°C. NMR spectrum of an aliquot showed complete conversion from the alcohol to the bromide. Pentane (400 ml) and diethyl ether (200 ml) was added to the reaction mixture (that gives 4:2:1 pentane/Et_2O/DCM ratio). A white precipitate came out immediately. The mixture was left at –12°C overnight for a better separation. The white precipitate was cold filtered and the solvent evaporated. As the product still contained some triphenylphosphine oxide, it was taken up in pentane (100 ml). The white precipitate that formed was filtered, and the solvent evaporated to give a dark yellow oil. The crude product was redissolved in pentane (25 ml) and filtered through a pad of silica gel (2 g). The solvent was evaporated, and the product was further pumped on the rotary evaporator (70°C/1mm) to give a clear colourless oil (4.5 g). Yield 90.5%.

NMR ($CDCl_3$) sl br t, δ0.88, splitting 6.4 Hz, 3H oleyl CH_3; m, δ1.15–1.53, 22H oleyl CH_2 tt, δ1.86, 1H, J 6.8 Hz 7.3 Hz, $\mathbf{CH_2}CH_2Br$; m, δ1.93–2.11, 3.5H, $\mathbf{CH_2}CH{=}CH\mathbf{CH_2}$; t, δ3.41, 1H, J 6.8 Hz , CH_2Br; m, δ 5.25–5.45, 1.75H, CH=CH.

(b) *2,2-Dimethyl-4-(*cis*-octadec-9-enyloxymethyl)-[1,3]dioxolane (Oleyl 2,3-isopropylidene-glyceryl ether).* This procedure followed that of P.Sahai and R.A. Vishwakarma[1]. Solketol (900 mg) and oleyl bromide (2.71 g, 1.2 equiv) were dissolved in dry DMF (10 ml), maintaining an argon atmosphere. Sodium hydride (408 mg, 60% dispersion in oil, 1.5 equiv.) was added in four portions; the reaction mixture became dark brown. It was stirred at room temperature for about 30 hours and poured into an ice/water slurry (50 ml). After a few minutes stirring, this was extracted with petroleum spirit (bp 60–80°C). The petroleum spirit phase was separated, washed with water followed by brine, and then dried over Na_2SO_4. Evaporation of the solvent gave 2.42 g of a crude product, still containing some oleyl bromide. This material was submitted for deprotection, without further purification.

NMR ($CDCl_3$) sl br t, δ0.88, splitting 6.3 Hz, 3H oleyl CH_3; m, δ1.15–1.47, 22H oleyl CH_2; s, δ1.36, 3H, isopropylidene CH_3; s, δ1.42, 3H, isopropylidene CH_3; m, δ1.47–1.66, 2H, **CH_2**CH_2O; m, δ1.92–2.12, 3.5H, **CH_2**$CH=CH$**CH_2**; dd, δ3.42, 1H, J –9.9 Hz 5.7 Hz, glyceryl C(1)-H_2; dd, δ3.44, 1H, J –9.4 Hz 6.6 Hz, oleyl CH_2O; dd, δ3.48, 1H, J –9.4 Hz 6.6 Hz, oleyl CH_2O; dd, δ3.51, 1H, J –9.9 Hz 5.7 Hz, glyceryl C(1)-H_2; dd, δ3.73, 1H, J –8.3 Hz 6.4 Hz, glyceryl C(3)-H_2; dd, δ3.99, 1H, J –8.3 Hz 6.4 Hz, glyceryl C(3)-H_2; dddd, δ4.19, 1H, J 5.7 Hz 5.7 Hz 6.4 Hz 6.4 Hz, glyceryl C(2)-H; m, δ5.28–5.43, 1.75H, CH=CH.

(c) **1-*Glyceryl oleyl ether.*** The oleyl 2,3-isopropylidene-glyceryl ether (2.42 g) mixed with 10% HCl (10 ml) was immersed in 120°C oil bath and stirred for 30 minutes . Petroleum spirit (60 ml; bp 60–80°C) was added to dissolve the beige sludge and the phases separated. The petroleum phase was washed twice with water (30 ml) and dried over Na_2SO_4, The solvent was evaporated to give 1.68 g of a mobile brown oil. Column chromatography (50% $CHCl_3$/ petroleum spirit, then 100% $CHCl_3$, and finally 5% MeOH/$CHCl_3$) resulted in 500 mg of pure product and 450 mg of a material still showing some impurities. The pure product was slightly yellowish, so it was dissolved in EtOH/water and treated with activated carbon. Filtration and evaporation of the solvent gave a colourless waxy material.

Recrystallisation of this from EtOH/water was unsuccessful, so it was used with no further treatment.

NMR ($CDCl_3$) sl br t, δ0.86, splitting 6.4 Hz, 3H oleyl CH_3; m, δ1.15–1.43, 22H oleyl CH_2; m, δ1.47–1.64, 2H, **CH_2**CH_2O; m, δ1.88–2.10, 3.4H, **CH_2**$CH=CH$**CH_2**; sl br s, δ2.79, 2H, OH; t, δ3.38, 2H, J 6.7 Hz, oleyl CH_2O; dd, δ3.41, 1H, J –9.9 Hz 6.3 Hz, glyceryl C(1)-H_2; dd, δ3.43, 1H, J –9.9 Hz 4.1 Hz, glyceryl C(1)-H_2; dd, δ3.55, 1H, J –11.4 Hz 5.7 Hz, glyceryl C(3)-H_2; dd, δ3.62, 1H, J –11.4 Hz 3.6 Hz, glyceryl C(3)-H_2; dddd, δ3.78, 1H, J 6.3 Hz 4.1 Hz 5.7 Hz 3.6 Hz, glyceryl C(2)-H; m, δ5.26–5.43, 1.7H, CH=CH.

3,7,11-Trimethyl-dodecanoic acid 2-hydroxy-1-hydroxymethyl-ethyl ester

(2-Glyceryl-hexahydrofarnesoate)

(a) ***3,7,11-trimethyl-dodecanoic acid (Hexahydrofarnesoic acid.)*** 4.56g (20 mmol) of 3,7,11-trimethyl-dodecan-1-ol was dissolved in a mixture of acetic acid (121 ml) and acetone (242 ml) and cooled in an ice bath to about 5°C. A solution of chromic oxide CrO_3, 4.84 g (48.4 mmol) in water (6 ml) was added over 25 min, maintaining the temperature not higher than 5°C. After a further 5 min the ice bath was removed and the mixture was stirred at room

temperature for 2 hours. Water (100 ml) was added, followed by finely powdered potassium metabisulphite until the mixture turned purplish green. The solvent was removed under vacuum, the residue taken up in water (100 ml) and extracted twice with 50 ml portions of diethyl ether. The combined organic extracts were washed with brine, water and brine again then dried over Na_2SO_4 and the solvent was removed under reduced pressure. 3.87 g of a greenish oil was obtained. The crude product was distilled at 110-115°/0.025 mm Hg, using a Buchi Kugelrohr to give a colourless oil (2.85 g). Yield 58.5%.

^{1}H NMR ($CDCl_3$): sl br d, δ0.84, 3H, splitting 6.2 Hz, CH_3; d, δ0.86, 6H, splitting 6.6 Hz, CH_3; sl br d, δ0.96, 3H, splitting 6.5 Hz, CH_3; m, δ0.97–1.40, 13H, CH_2 + CH; m, δ1.40–1.62, 1H, CH; m, δ1.85–2.05, 1H, CH; ddd, δ2.14, 1H, J –15.0 Hz 8.2 Hz 1.2 Hz, **CH_2**CO_2; sl br dd, δ2.35, 1H, J –15.0 Hz 5.9 Hz, **CH_2**CO_2.

(b) ***3,7,11-Trimethyl-dodecanoic acid 2-benzyloxy-1-benzyloxymethyl-ethyl ester***

(1.3-dibenzyloxy-2-glyceryl hexahydrofarnesoate). The process was conducted in Ar atmosphere. Hexahydrofarnesoic acid (2.76 g, 11.37 mmol), 1,3-benzyloxy-2-propanol (3.10 g, 11.37 mmol; 97% purity, Aldrich) and 4-dimethylaminopyridine (0.15 g, 1.205 mmol) were dissolved in dry DCM (50ml). N,N' dicyclohexylcarbodiimide (99% purity, Aldrich; 3.03g, 1.3 eq., 14.78 mmol) dissolved in 20 ml of dry DCM was added dropwise at RT over 40 min. Before the end of addition some white particles started precipitating. After 20 h at RT, stirring was turned off and the precipitate was allowed to sediment. NMR analysis of an aliquot showed that reaction was not completed. An additional 100 mg of DMAP was added and stirring was continued overnight. No progress could be observed. A fresh dose of DCC (2 g) was added and reaction mixture was stirred again overnight. Since no further reaction took place, as judged by NMR, the whole reaction mixture was worked up. It was filtered through a thin layer of celite, the DCM phase was washed with 5% $NaHCO_3$ (25 ml), brine (30 ml) and evaporated at RT. The residual material (8 g) contained the desired product plus DCC and DHU. None of the contaminants could be crystallized out; hence the whole material was diluted with petroleum spirit (bp 40/60; 150ml) and filtered through a 3 cm layer of silica gel. DHU was removed but DCC was still present in the crude product. The mixture was taken up in 90 ml of ethanol and 2g of acetic acid and stirred at RT for 2 h, to hydrolyse DCC to DHU. The DHU was removed by re-filtering through the same silica gel (as above) and washed with 5% sodium bicarbonate. The organic phase was filtered through a 1 cm layer of fresh silica gel and evaporated to give 4.32g of 1.3-dibenzyloxy-glyceryl 2-hexahydrofarnesoate as a colourless oil.

^{1}H NMR ($CDCl_3$): sl br d, δ0.83, 3H, splitting 6.3 Hz, CH_3; d, δ0.86, 6H, splitting 6.6 Hz, CH_3; sl br d, δ0.93, 3H, splitting 6.5 Hz, CH_3; m, δ0.97–1.40, 13H CH_2 + CH; m, δ1.40–1.62, 1H, CH; m̩δ1.85–2.05, 1H, CH; dd, δ2.14, 1H, J –14.7 Hz 8.6 Hz, **CH_2**CO_2; dd, δ2.35, 1H, J –14.7 Hz 5.9 Hz, **CH_2**CO_2; d, δ3.64, 4H, J 5.1 Hz, glyceryl C(1 + 3)H_2; d, δ4.52, 2H, J –12.0 Hz, OC**H_2**Bz; d, δ4.55, 2H, J –12.0 Hz, OC**H_2**Bz; pentet, δ5.24, 1H, J 5.1 Hz, glyceryl C(2)H; m, δ7.20–7.40, 10H, phenyl.

(c) ***2-Glyceryl hexahydrofarnesoate.*** 1.3-dibenzyloxy-glyceryl 2-hexahydrofarnesoate (4.22g) dissolved in 50ml of ethanol mixed with 10 drops of 1N hydrochloric acid, was hydrogenated over 0.4 g 10% Pd/carbon, at RT. As a result of overnight hydrogenation, a mixture of glyceryl-2-hexahydrofarnesoate (target compound) and glyceryl-1-hexahydrofarnesoate (product of acyl migration) in 1:0.4 ratio was obtained. The reaction time required to complete the deprotection was probably shorter, and monitoring of the progress could help to minimise acyl migration. The catalyst was removed by filtration and ethanol was evaporated at 25°C. The residue was treated with water and 5% sodium bicarbonate solution (to adjust pH to 7) and extracted with DCM. Evaporation at 25°C resulted in 2.68g of a colourless oil (quantitative recovery). It was estimated that there was ~30% of isomer **1** and ~70% of isomer **2** of glyceryl hexahydrofarnesoate. Those were separated by means of preparative HPLC, using 75% methanol/water for elution. Fractions were cut over the main product bands, and only those analysing > 95% were combined as product. The 2-glyceryl ester eluted first and partially overlapped the 1-glyceryl ester, which followed. 1.3 g of a pure isomer **2** and 500 mg of the isomer 1 was collected.

^{1}H NMR ($CDCl_3$): sl br d, δ0.83, 3H, splitting 6.2 Hz, CH_3; d, δ0.86, 6H, splitting 6.6 Hz, CH_3; sl br d, δ0.94, 3H, splitting 6.6 Hz, CH_3; m, δ0.97–1.40, 13H CH_2 + CH; m, δ1.40–1.62, 1H, CH; m̩δ1.85–2.05, 1H, CH; dd, δ2.17, 1H, J –14.7 Hz 8.3 Hz, **CH_2**CO_2; v br s, δ2.1–2.4, 2H, OH; dd, δ2.38, 1H, J –14.7 Hz 5.9 Hz, **CH_2**CO_2; d, δ3.83, 4H, J 4.7 Hz, glyceryl C(1,3)H_2; pentet, δ4.93, 1H, J 4.7 Hz, glyceryl C(2)H.

1-Glyceryl hexahydrofarnesoate (Glyceryl mono-hexahydrofarnesoate)

^{1}H NMR ($CDCl_3$): sl br d, ™0.83, 3H, splitting 6.2 Hz, CH_3; d, ™0.86, 6H, splitting 6.6 Hz, CH_3; sl br d, ™0.94, 3H, splitting 6.6 Hz, CH_3; m, ™0.97–1.40, 13H CH_2 + CH; m, ™1.40–1.62, 1H, CH; m™1.85–2.05, 1H, CH; dd, ™2.17, 1H, J –14.7 Hz 8.3 Hz, **CH_2**CO_2; v br s, ™2.1–2.4, 2H, OH; dd, ™2.38, 1H, J –14.7 Hz 5.9 Hz, **CH_2**CO_2; dd, ™3.60, 1H, J –11.5 Hz 5.9 Hz, glyceryl C(3)H_2; dd, ™3.70, 1H, J –11.5 Hz 3.6 Hz, glyceryl C(3)H_2; dddd, ™3.93, 1H, J

5.9 Hz 3.6 Hz 6.1 Hz 4.6 Hz, glyceryl C(2)H; dd, ™4.15, 1H, J –11.7 Hz 6.1 Hz, glyceryl C(1)H_2; dd, ™4.20, 1H, J –11.7 Hz 4.6 Hz, glyceryl C(1)H_2

3,7,11,15-Tetramethyl-hexadecanoic acid 2,3-dihydroxy-propyl ester

(Glyceryl monophytanoate)

(a) ***3,7,11,15-tetramethyl-hexadecanoic acid (Phytanoic acid).*** Phytanol (30 g) was dissolved in a mixture of acetic acid (600 ml) and acetone (1200 ml). This was chilled in an ice bath to about 5°C, and a solution of chromic oxide (Aldrich 99.9% CrO_3, 24 g) in water (30 ml) was added slowly so that the temperature of the reaction mixture did not rise above 5°C. At the end of the CrO_3 addition, the temperature was allowed to rise, and the mixture stirred at room temperature for 1.5 hours. Water (500 ml) was added, and then powdered potassium metabisulphite was added until the mixture turned purplish green. The solvent was removed and the sticky material obtained was dissolved in water (400 ml), and extracted three times with diethyl ether (50 ml). The combined ether extracts were washed once with water, once with pH 2 aqueous HCl, and a second time with water. A little NaCl was added to each extraction to assist in phase separation. After evaporation of the ether, a dark green oil (28.6 g) was obtained. This was distilled at 143–145°C at 0.025 mm Hg to give a colourless oil (20.88 g). The foreruns, residues and washings from the distillation were redistilled using a Buchi Kugelrohr at 0.04 mm Hg at 170°C. A further 2.24 g of product was obtained.

^{1}H NMR ($CDCl_3$) sl br d, δ0.84, 6H, splitting 6.3 Hz, CH_3; d, δ0.87, 6H, splitting 6.6 Hz, CH_3; d, δ0.97, 3H, splitting 6.5Hz, CH_3; m, δ0.95–1.45, 20H, CH_2 + CH; m, δ1.42–1.63, 1H CH; m δ1.85-2.05, 1H, C(3)H; ddd δ2.14, 1H, J -14.7 Hz, 8.5 Hz, 1.0 Hz, **CH_2**CO_2; sl br dd, δ2.35, 1H, J -14.7 Hz, 6.0 Hz, **CH_2**CO_2.

(b) ***3,7,11,15-tetramethyl-hexadecanoyl chloride (Phytanoyl chloride).***

Phytanoic acid (20.34 g) was dissolved in dried benzene (25 ml). The solution was rapidly stirred while oxalyl chloride (12.4 g, 1.2 mole equivalent) was added dropwise. The mixture was allowed to stir at room temperature overnight, and then the excess oxalyl chloride and benzene was evaporated at 50°/50 mm. The product was distilled in a Buchi Kugelrohr at 135°C oven temperature and 0.22 mm Hg to give a colourless oil (18.2 g).

^{1}H NMR ($CDCl_3$) sl br d, δ0.85, 6H, splitting 6.2 Hz, CH_3; d, δ0.87, 6H, splitting 6.5 Hz, CH_3; d, δ0.99, 3H, splitting 6.7 Hz, CH_3; m, δ0.95–1.45, 20H, CH_2 + CH; m, δ1.42–1.63, 1H CH; m

δ1.95-2.17, 1H, C(3)H; sl br dd δ2.68, 1H, J -16.1 Hz, 7.9 Hz, **CH_2**COCl; sl br dd, δ2.88, 1H, J -16.1 Hz, 5.6 Hz, **CH_2**COCl.

(c) ***3,7,11,15-tetramethyl-hexadecanoic acid 2,2-dimethyl-[1,3]dioxolan-4-ylmethyl ester (2,3-isopropylidene-glyceryl 1-phytanoate).*** 3.64 g (11 mmol) of phytanoyl chloride in 10 ml of dry DCM was added dropwise to a cold solution of solketal (1.815g, 13.75 mmol; 25% excess) and 0.87 g (11 mmol) of dry pyridine in 25 ml DCM at ~0°C. The syringe was rinsed with additional 8 ml of DCM. The reaction vessel was protected against moisture by maintaining Ar atmosphere. Addition took 0.5 h. The reaction mixture was left in the ice bath, allowing it to slowly come to RT. It was left with stirring overnight to give a clear yellow solution (pyridine chloride did not precipitate). An aliquot was withdrawn for NMR analysis, quenched with water, extracted with chloroform and evaporated. The NMR spectrum showed completion of the acylation process. 50 ml of brine was added to the reaction flask, stirred well and the reaction mixture was transferred to a separation funnel. The aqueous phase was extracted second time with chloroform and the combined organic extract was back-washed with 40 ml of brine. It was filtered through a phase separating paper filter, evaporated and dried under vacuum. 4.7 g of 3,7,11,15-tetramethyl-hexadecanoic acid 2,2-dimethyl-[1,3]dioxalan-4-ylmethyl ester as an yellow oil was obtained (quantitative yield).

^{1}H NMR ($CDCl_3$): sl br d, δ0.83, 6H, splitting 6.3 Hz, CH_3; d, δ0.85, 6H, splitting 6.4 Hz, CH_3; sl br d, δ0.92, 3H, splitting 6.5 Hz, CH_3; m, δ0.97–1.61, 21H, CH_2 + CH; s, δ1.36, 3H, isopropylidene CH_3; s, δ1.42, 3H, isopropylidene CH_3; m, 1.83–2.05, 1H, CH; dd, δ2.14, 1H, J –14.9 Hz 8.0 Hz, **CH_2**CO_2; dd, δ2.34, 1H, J –14.9 Hz 5.8 Hz, **CH_2**CO_2; dd, δ3.73, 1H, J –8.4 Hz 6.2 Hz, glyceryl C(3)H_2; dd, δ4.07, 1H, J –8.4 Hz 6.7 Hz, glyceryl C(3)H_2; dd, δ4.09, 1H, J –11.7 Hz 5.6 Hz, glyceryl C(1)H_2; dd, δ4.15, 1H, J –11.7 Hz 4.9 Hz, glyceryl C(1)H_2; dddd, δ4.15, 1H, J 6.2 Hz 5.6 Hz 6.6 Hz 4.9 Hz, glyceryl C(2)H.

(d) ***Glyceryl monophytanoate.*** 4.7 g of 3,7,11,15-tetramethyl-hexadecanoic acid 2,2-dimethyl-[1,3]dioxalan-4-ylmethyl ester was diluted with methanol (70 ml) and brought to reflux. 5.5 ml of 1M HCl was added by means of a pipette and reflux continued for 10 min. During HCl addition the reaction mixture became turbid but cleared up immediately. It was cooled down and poured into diethyl ether (250 ml). That resulted in the formation of two layers. The etheral layer was washed with brine (75ml) and the aqueous phase back-washed with ether. The combined etheral phase was washed with $NaHCO_3$ saturated solution, brine (100 ml) and after overnight separation, dried with Na_2SO_4. Evaporation and drying (1

mm/RT) gave 3.77 g of a yellow clear oil. Yield calculated for the crude material: 88.7%. It was purified by preparative HPLC, using 85% methanol/water as a mobile phase.

2.428 g of a pure product was obtained. Overall yield 57.1%.

^{1}H NMR ($CDCl_3$): sl br d, δ0.84, 6H, splitting 6.3 Hz, CH_3; d, δ0.86, 6H, splitting 6.5 Hz, CH_3; sl br d, δ0.94, 3H, splitting 6.6 Hz, CH_3; m, δ0.97–1.42, 20H, CH_2 + CH; m, δ1.42–1.63, 1H, CH; m, 1.83–2.05, 1H, CH; m, 1.83–2.05, 1H, CH; dd, δ2.15, 1H, J –14.9 Hz 8.0 Hz, CH_2CO_2; dd, δ2.36, 1H, J –14.9 Hz 5.8 Hz, CH_2CO_2; dd, δ3.60, 1H, J –11.5 Hz 5.9 Hz, glyceryl C(3)H_2; dd, δ3.70, 1H, J –11.5 Hz 3.9 Hz, glyceryl C(3)H_2; dddd, δ3.93, 1H, J 5.9 Hz 3.9 Hz 6.0 Hz 4.6 Hz, glyceryl C(2)H; dd, δ4.15, 1H, J –11.7 Hz 6.0 Hz, glyceryl C(1)H_2; dd, δ4.20, 1H, J –11.7 Hz 4.6 Hz, glyceryl C(1)H_2.

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