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Structure and Synthesis of Anhydrobisfarnesol from *Euphorbia lateriflora* and Asymmetric Synthesis of (*R*)-Sesquilavandulol

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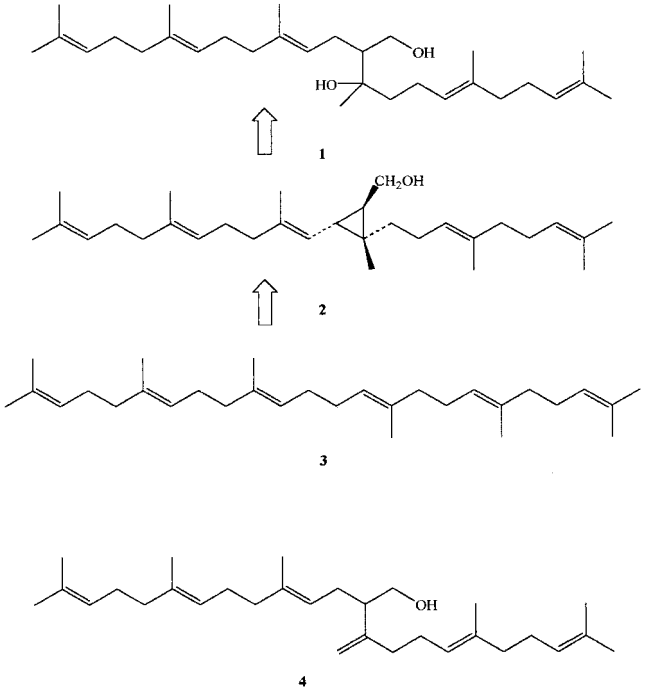
Abstract—Anhydrobisfarnesol has been isolated from the latex of *Euphorbia lateriflora* and assigned structure **4** on the basis of its spectroscopic properties. Its structure has been confirmed by synthesis using a photochemical isomerisation procedure. A similar approach has been used for the total synthesis of (*R*)-sesquilavandulol.

Introduction

The formation of bisfarnesol **1** seems the obvious first step in the conversion of farnesol into presqualene alcohol **2** on the biosynthetic route[1] to squalene **3** (Scheme 1). To date neither bisfarnesol nor any of its derivatives has been found in Nature. We now report the isolation of an anhydro-derivative of bisfarnesol from the latex of *Euphorbia lateriflora*. Structure **4**, assigned to this compound on the basis of its spectroscopic properties, has been confirmed by synthesis.

Anhydrobisfarnesol shows a small parent ion in the mass spectrum at *m/z* 426, corresponding to $C_{30}H_{50}O$. The ^1H and ^{13}C data (vide infra) indicated the presence of six double bonds and hence the molecule is acyclic. The ^1H NMR spectrum shows resonances for five vinyl protons [δ_H 5.09 (m, 5H)], an exomethylene group [δ_H 4.94 and 4.85 (each bs)], a two proton doublet [δ_H 3.53 (2H, d, J=5.8 Hz, CH_2OH)] and seven vinyl methyl groups [δ_H 1.66 (6H) and 1.59 (15H)]. Also present is a large methylene envelope at approximately 2.10 ppm. The ^{13}C NMR spectrum confirmed the presence of the above functional groups. Thus, there are resonances for five trisubstituted double bonds [δ_C 136.3, 135.4, 135.0, 131.2, 131.1 (all C), 124.3, 124.2, 124.0, 123.8, 122.1 (all CH)], an exomethylene [δ_C 149.5 (C) and 110.9 (CH_2)], a primary alcohol [δ_C 63.9 (CH_2)] and seven methyl groups [δ_C 15.9, 16.0, 16.1, 17.6 (2), 25.6 (2)]. The remaining resonances include nine methylenes [δ_C 26.2, 26.5, 26.6, 26.7, 29.0, 34.3, 39.62, 39.66, 39.7] and one methine [δ_C 48.7].

The above data suggest that the unknown compound is a triterpenoid related to squalene but lacking the regular



Scheme 1.

Keywords: terpenes; anhydrobisfarnesol; sesquilavandulol; photoisomerisation.

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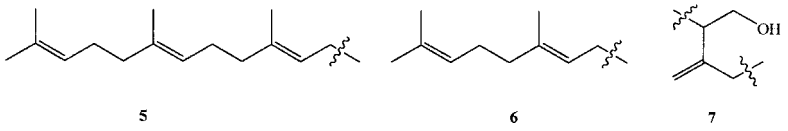


5 6 7

Figure 1.

arrangement of the isoprenoid groups. A careful examination of the ^{13}C chemical shifts and comparison with model systems enabled us to identify a farnesyl moiety **5** and a geranyl moiety **6**. The chemical shifts are in good agreement with literature values.[2] The remaining unit **7** consists of a methylene, an exomethylene, a methine and a primary alcohol (Fig. 1).

The three part structures **5**–**7** can be assembled to give two structures: **4**, which may be formally derived from coupling of two farnesol units, and **8**, which can arise from coupling of geraniol and geranylgeraniol (Fig. 2). In view of the accepted biosynthetic pathway to squalene, structure **4** seems more attractive.[3] Since the sample of natural product decomposed before definitive spectroscopic experiments were carried out a synthesis was undertaken in order to confirm the structure.

Some years ago, in connection with our work on the asymmetric photochemical isomerisations of α,β-unsaturated esters into their β,γ-unsaturated isomers,[4] we reported a total synthesis of lavandulol **9** in good yield and with high enantiomeric excess.[4b] We have now applied our methodology to the synthesis of related systems, the proposed structure of the *E. lateriflora* compound **4** (Scheme 2) and sesquilavandulol **10**.

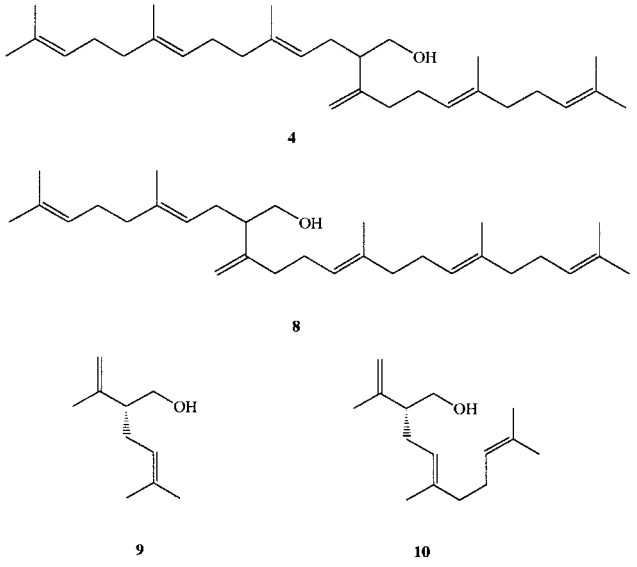
Methyl acetoacetate **11** was conveniently γ-alkylated with geranyl bromide after double deprotonation using standard conditions (NaH, then *n*-BuLi) to give **12** in good yield.[5] α-Alkylation of **12** to give **13** was achieved using DBU as base and farnesyl bromide as the electrophile.[6] The preparation of the α,β-unsaturated ester **15** was carried out via a 1,4-addition/elimination process of methyl cuprate on the enol phosphate **14** according to a procedure already described by Wolf and Pfander.[7] Photochemical isomerisation of the unsaturated ester **15** afforded an inseparable mixture of three β,γ-unsaturated isomers **16**, **(*E*)-17** and **(*Z*)-17** in excellent yield with the ratio 53/28/19. Reduction of the mixture of the deconjugated esters with $LiAlH_4$ gave the corresponding alcohols in quantitative yield. By preparative thin-layer chromatography, compound **4** was partially isolated in pure form from the other isomers **18** and **18′**. Its spectroscopic data were identical to those of the isolated compound from *E. lateriflora*.

The poor regioselectivity of the hydrogen abstraction results probably from *E*/*Z* isomerisation of the starting material during the irradiation. This lack of regiocontrol has been already observed for a similar process during the synthesis of the San Jose scale pheromone by Lombardo et Weedon.[8] Moreover, these authors pointed out the role of the added base on the ratio of the different isomers: amines such as 1,2-dimethylimidazole (or dimethylaminoethanol, this work) allow a rapid equilibration between the dienols and the dienolates which are kinetically reprotonated to afford the deconjugated compounds (Scheme 3). Therefore, addition of bases prevents the reverse thermal 1,5-sigmatropic hydrogen shift of the dienol to the starting material.

Another strategy for the preparation of ester **16** in pure form could involve the direct methylenation of the keto-ester **13**.[9] However, while a such methylenation has been already reported on a β-keto-acid anion with moderate selectivity,[10] a β-ketoester like **13** bearing on the α-position a highly acidic proton (p*K*a<12) would probably not undergo such a transformation.[11]

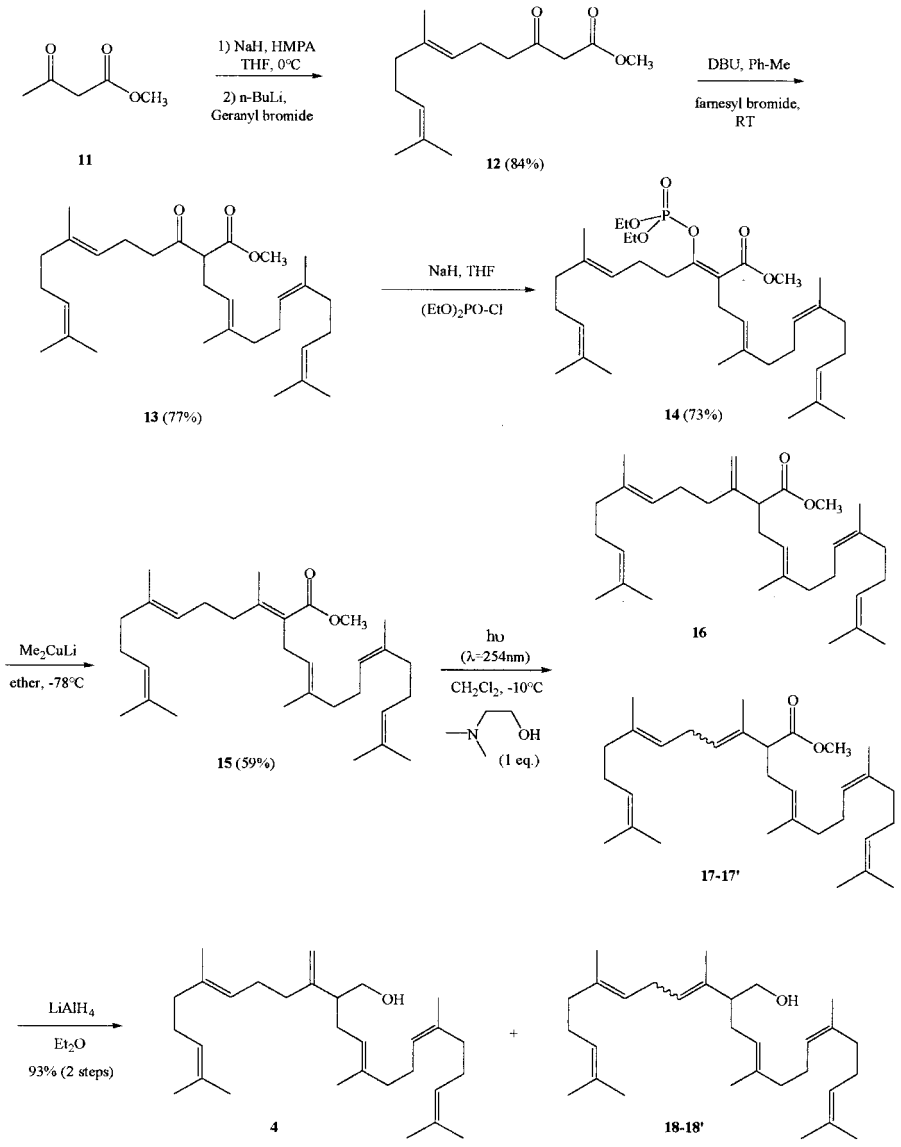
The synthetic route to sesquilavandulol **10** is shown in Scheme 4. β-Ketoester **19**,[4b] bearing the diacetone D-glucose (DAG) moiety as chiral auxiliary, was selectively mono-alkylated with geranyl bromide following a literature method.[6,12] The geranyl derivative **20** was converted into the corresponding enol phosphate ester **22** which was smoothly transformed into **23** on treatment with dimethylcuprate in ether.[7] Irradiation of **23** in dichloromethane and in the presence of *N*,*N*-dimethylaminoethanol afforded the expected βγ-unsaturated ester **24** as the sole product. The ^1H NMR spectrum of the crude product indicated a diastereoselectivity of greater than 94%. The absolute configuration of the new chiral centre was established according to previous results[4a–d] obtained in lavandulol series. Finally, ester **24** was reduced with $LiAlH_4$ to give sesquilavandulol **10** in good yield.

It should be noted that direct α-alkylation/isomerisation of DAG ester **25** under basic conditions also afforded **24** but with a much lower diastereoisomeric excess (74%) (Scheme 5). The sense of induction remained the same.[13]

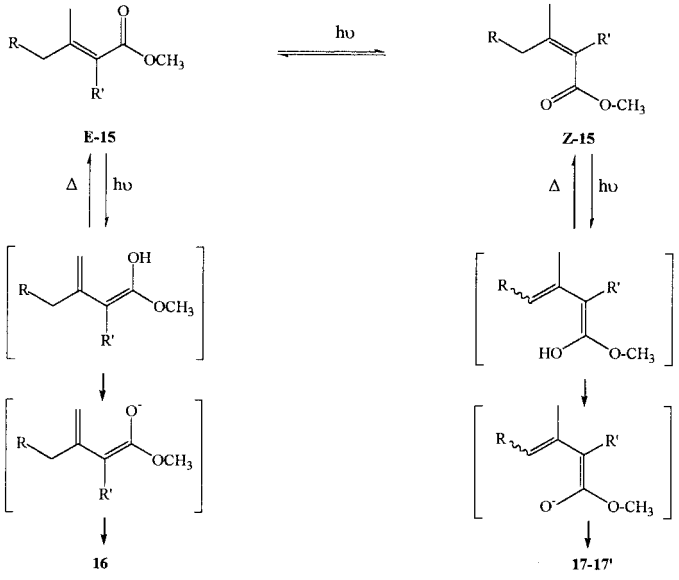


4 8 9 10

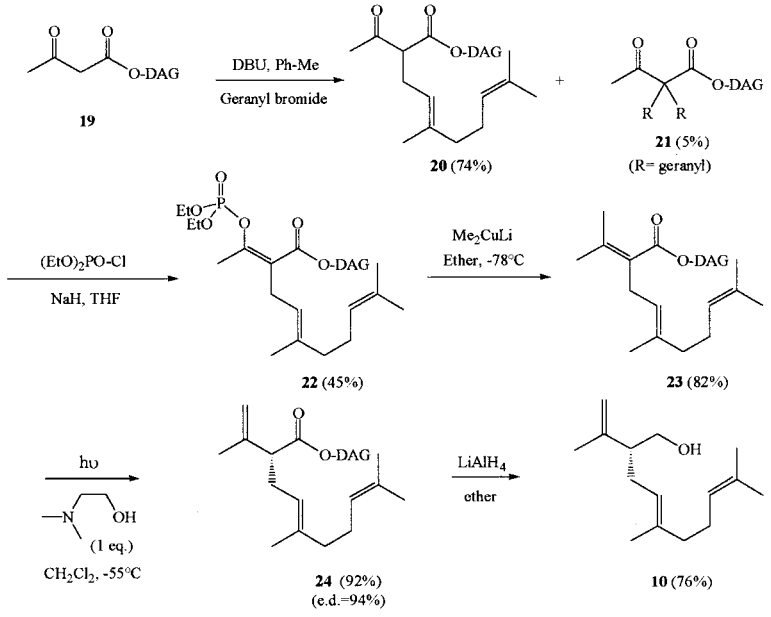
Figure 2.



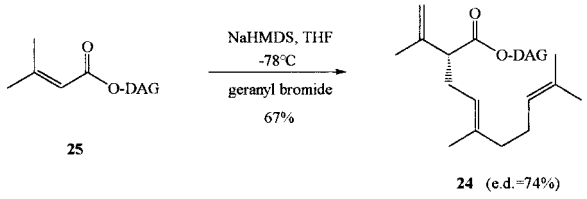
Scheme 2.



Scheme 3.



Scheme 4.



Scheme 5.

In conclusion, we have reported here the structure of anhydrobisfarnesol, first isolated in nature from the latex of *E. lateriflora*. The structure assigned was confirmed by a total synthesis using a photochemical isomerisation as the key-step. A structurally related alcohol, (*R*)-sesquilavandulol, was prepared in optically active form using an asymmetrical version of the photochemical process.

Experimental

General

Solvents were distilled before use under an argon atmosphere: THF, toluene and diethyl ether over sodium/benzophenone; methylene chloride, pentane over calcium hydride. ^{1}H and ^{13}C NMR spectra were recorded on Bruker AC 250 MHz or DRX 500 MHz spectrometers in deuteriochloroform, using tetramethylsilane as internal standard, chemical shifts are expressed in ppm. IR spectra were recorded on a IR Mirdac spectrometer. Elemental analyses were performed on a CHN 2400 Perkin–Elmer apparatus. Mass spectra were recorded at the Faculty of Pharmacy, University of Reims, on a JEOL D300 spectrometer.

Plant material. The latex of *E. lateriflora* was collected, over a period of four months, from plants growing on the campus of Obafemi Awolowo University, Nigeria. The plant material was authenticated by Mr Jaiyeola of the Department of Botany, O.A.U., Ife-Ife, where a voucher specimen has been deposited.

Isolation of anhydrobisfarnesol 4

Extraction of the latex of *E. lateriflora*.[14] Latex (250 ml) was dissolved in EtOH and kept frozen. Subsequent extraction with cold EtOH (2.5 l) afforded a solution which was concentrated under vacuum and extracted with Et_2O. The ethereal extract was washed with H_2O, dried over $MgSO_4$, and finally evaporated to a gum (28 g) which contained the irritant components of the latex. Flash chromatography of a portion of the crude petroleum extract followed by preparative thin layer chromatography afforded compound **4** as an oil. ^{1}H NMR: 1.61 (12H, s), 1.69 (6H, s), 1.90–2.30 (21H, m), 3.56 (2H, d, J=6.5 Hz), 4.88 (1H, brs), 4.96 (1H, brs), 5.00–5.20 (5H, m). ^{13}C NMR: 15.9 ($2CH_3$), 16.0 (CH_3), 16.1 (CH_3), 17.6 (CH_3), 25.6 (CH_3), 26.2 (CH_2), 26.6 (CH_2), 26.7 (CH_2), 26.75 (CH_2), 29.1 (CH_2), 29.7 (CH_2), 34.4 (CH_2), 39.7 (CH_2), 48.8, 64.0 (CH_2), 110.9 (CH_2), 122.2 (CH), 123.8 (CH), 124.1 (CH), 124.3 (CH), 124.4 (CH), 131.2 (C), 131.3 (C), 135.0 (C), 135.5 (C), 136.5 (C), 149.6 (C). IR: 3340, 2922, 1717, 1454 cm^{-1}. MS (70 eV), *m/z*: 426 ($M^{+\cdot}$, $C_{30}H_{50}O$, 8), 357 (5), 289 (4), 121 (12), 109 (13), 107 (12), 93 (12), 81 (23), 69 (100). No rotation was measured.

Methyl 7,11-dimethyl-3-oxo-dodeca-6,10-dienoate: 12. To a suspension of sodium hydride (1.22 g, 50.9 mmol) in THF (100 ml) placed under argon, methyl acetoacetate **11** (5.0 ml, 46.3 mmol) was added dropwise at 0°C. After 15 min, HMPA (16.1 ml, 92 mmol) was added to give a colourless solution. A 1.6 M solution in hexanes of *n*-butyl lithium (28.9 ml, 46.3 mmol) was added carefully and the orange coloured mixture was stirred at the same temperature for 0.5 h. Geranyl bromide (9.3 ml, 46.3 mmol) diluted in THF (10 ml) was then added and the resulting mixture was stirred 4 h at rt. After hydrolysis

with a 2N HCl solution (30 ml), the aqueous layers were extracted with ether (3×10 ml). The organic layer was washed with water, dried over $MgSO_4$ and concentrated under vacuum. Purification by flash-chromatography (AcOEt/hexanes: 12/88) afforded **12** (9.81 g, 38.9 mmol) as a pale yellow oil. Yield: 84%. ^{1}H NMR: 1.60 (3H, s), 1.61 (3H, s), 1.68 (3H, s), 1.90–2.15 (4H, m), 2.29 (2H, dt, J=7.25, 6.5 Hz), 2.57 (2H, t, J=7.25 Hz), 3.54 (2H, s), 3.74 (3H, s), 5.07 (2H, t, J=6.5 Hz). ^{13}C NMR: 15.9 (CH_3), 17.5 (CH_3), 22.1 (CH_2), 25.5 (CH_3), 26.5 (CH_2), 39.5 (CH_2), 42.9 (CH_2), 48.9 (CH_2), 52.2 (CH_3), 121.9 (CH), 124.0 (CH), 131.3 (C), 136.7 (C), 167.5 (CO_2R), 202.3 (C═O). IR: 2922, 2860, 1743, 1718, 1630, 1441, 1315, 1228, 1153 cm^{-1}. MS (70 eV), m/z: 252 ($M^{+\cdot}$, 38), 234 (31), 209 (52), 191 (46), 183 (43), 151 (43), 136 (67), 129 (48), 123 (65), 116 (49), 109 (100), 105 (67). Elemental analysis: Calcd for $C_{15}H_{24}O_3$: C 71.39, H 9.58. Found: C 71.66, H 9.68.

Methyl 2-(5,9-dimethyldeca-4,8-dienoyl)-5,9,13-trimethyltetradeca-4,8,12-trienoate: 13. A solution of farnesyl bromide (10.04 g, 35.2 mmol) in toluene (5 ml) was added to a solution of methyl ester **12** (8.06 g, 32 mmol) and DBU (5.35 g, 35.2 mmol) in the same solvent (25 ml). The mixture was stirred overnight at rt, then washed with water. The organic layer was dried over $MgSO_4$ and concentrated. The crude mixture was filtered over a small silica pad, then purified by flash-chromatography (eluent: hexanes/AcOEt: 90/10) and afforded **13** (11.30 g, 24.7 mmol). Yield: 77%. ^{1}H NMR: 1.59 (6H, s), 1.60 (6H, s), 1.62 (3H, s), 1.68 (6H, s), 1.90–2.11 (12H, m), 2.26 (2H, dt, J=7.6, 7.2 Hz), 2.49–2.58 (4H, m), 3.47 (1H, t, J=7.4 Hz), 3.71 (3H, s), 5.04 (5H, m). ^{13}C NMR: 15.9 ($2CH_3$), 16.1 (CH_3), 17.6 ($2CH_3$), 22.1 ($2CH_2$), 25.7 ($2CH_3$), 26.5 (CH_2), 26.6 (CH_2), 26.7 (CH_2), 26.9 (CH_2), 39.7 ($2CH_2$), 42.3 (CH_2), 52.2 (CH_3), 58.9 (CH), 119.7 (CH), 122.3 (CH), 123.9 (CH), 124.2 (CH), 124.3 (CH), 131.3 (C), 131.4 (C), 135.2 (C), 136.5 (C), 138.5 (C), 170.0 (CO_2R), 204.8 (C═O). IR: 2922, 2847, 1730, 1466, 1379, 1278, 1128, 1064 cm^{-1}. MS (70 eV), m/z: 456 (M^+, 100), 245 (30), 233 (48), 121 (47). Elemental analysis: Calcd for $C_{30}H_{48}O_3$: C 78.89, H 10.59. Found: C 78.28, H 10.31.

Methyl 2-(1′-diethoxyphosphoryloxy-5,9-dimethyldeca-4,8-dienylidene)-5,9,13-trimethyltetradeca-4,8,12-trienoate: 14. To a suspension of sodium hydride (55 mg, 2.3 mmol) in ether (3 ml) under argon was added dropwise at 0°C a solution of ketoester **13** (0.490 g, 1.07 mmol) in the same solvent (10 ml). After 2 h at this temperature, diethylchlorophosphate (0.18 ml, 1.25 mmol) was added and the mixture stirred overnight (12 h) and heated for one additional hour at 40°C. After cooling, brine was added and the aqueous solution twice extracted with ether. After drying, the organic layer was concentrated to give **14** (0.465 g, 0.79 mmol) which was used without further purification. Yield: 73%. ^{1}H NMR: 1.33 (3H, t, J=6.9 Hz), 1.34 (3H, t, J=6.9 Hz), 1.58 (3H, s), 1.59 (6H, s), 1.62 (3H, s), 1.63 (3H, s), 1.67 (6H, s), 1.90–2.10 (12H, m), 2.31 (2H, m), 2.45 (2H, m), 2.98 (2H, d, J=6.5 Hz), 3.71 (3H, s), 4.16 (2H, q, J=7.25 Hz), 4.19 (2H, q, J=7.25 Hz), 5,00–5,16 (5H, m). ^{13}C NMR: 15.9 ($3CH_3$), 16.1 ($2CH_3$), 17.6 ($2CH_3$), 25.5 (CH_2), 25.6 ($2CH_3$), 26.6 ($2CH_2$), 26.7 (CH_2), 27.7 (CH_2), 31.7 ($2CH_2$), 39.7 ($2CH_2$), 51.5 (CH_3), 64.3 (CH_2), 64.4 (CH_2), 120.5 (CH), 122.3 (CH), 123.9 (CH), 124.2 (CH), 124.3 (CH), 131.2 (C), 131.4 (C), 135.1 (C), 136.7 (C), 137.0 (C), 152.2 (2C), 167.3 (CO_2R). IR: 2972, 2922, 1847, 1730, 1441, 1379, 1278, 1203, 1128, 1028 cm^{-1}. MS (70 eV), m/z: 594 (M^++1, 6), 558 (78), 524 (31), 317 (37), 263 (32), 239 (100), 227 (37).

Methyl 2-(1,5,9-dimethyldeca-4,8-dienylidene)-5,9,13-trimethyltetradeca-4,8,12-trienoate: 15. To a suspension of copper iodide (74 mg, 0.39 mmol) in ether (5 ml) and under argon was added dropwise at 0°C a 1.6 M ether solution of methyl lithium (1.0 ml, 1.6 mmol). After 30 min stirring, enol phosphate **14** (0.219 g, 0.37 mmol), diluted in ether (2 ml), was introduced at −78°C. The resulting mixture was stirred overnight at rt, then hydrolysed with an aqueous saturated solution of ammonium chloride. After extraction with dichloromethane, the organic layers were dried over $MgSO_4$, filtered and concentrated under vacuum. The unsaturated ester **15** (0.102 g, 0.22 mmol) was purified by preparative thin-layer chromatography (eluent: hexanes/AcOEt: 85/15). Yield: 59%. ^{1}H NMR: 1.58 (3H, s), 1.60 (9H, s), 1.64 (3H, s), 1.68 (6H, s), 1.96 (3H, s), 1.90–2.20 (16H, m), 3.01 (2H, d, J=6.8 Hz), 3.70 (3H, s), 5.03 (1H, t, J=6.7 Hz), 5.09 (3H, brt, J=6.5 Hz), 5.13 (1H, t, J= 6.5 Hz). ^{13}C NMR: 15.9 ($2CH_3$), 16.1 (CH_3), 17.7 ($2CH_3$), 20.9 (CH_3), 25.7 ($2CH_3$), 26.4 (CH_2), 26.7 ($2CH_2$), 26.8 (CH_2), 28.5 (CH_2), 29.7 (CH_2), 35.7 (CH_2), 39.7 ($2CH_2$), 51.1 (CH_3), 121.9 (CH), 123.4 (CH), 124.1 (CH), 124.3 (CH), 124.4 (CH), 127.2 (C), 131.3 (C), 131.4 (C), 135.0 (C), 135.8 (C), 135.9 (C), 145.4 (C), 170.2 (CO_2R). IR: 2922, 2847, 1718, 1215, 1064 cm^{-1}. UV (CH_2Cl_2): ϵ_{231}=7140. MS (70 eV), m/z: 454 (M^+, 18), 191 (39), 147 (30), 137 (65), 121 (100), 109 (97).

Irradiation of ester 15. Argon was bubbled through a solution of ester **15** (0.100 g, 0.2 mmol) and *N*,*N*-dimethylaminoethanol (0.18 g, 0.2 mmol) in dichloromethane (20 ml) and the solution was then poured into quartz tubes. The tubes were placed around a quartz Dewar containing a short wave length OSRAM lamp. The irradiation was carried out at 10°C. After disappearance of the starting material (TLC control), the solvent was removed. The crude mixture dissolved in diethyl ether (5 ml) was added dropwise to a suspension of $LiAlH_4$ in the same solvent (30 ml) at 0°C. The resulting mixture was stirred overnight at rt, then hydrolysed with wet ether. After extraction with ether, the organic layer was dried over $MgSO_4$, concentrated and purified by preparative thin-layer chromatography.

2-[5,9-Dimethyl-1-methylenedeca-4,8-dienyl]-5,9,13-trimethyltetradeca-4,8,12-trien-1-ol: 4. Yield: 21%. (data identical with above).

2-[1,5,9-Trimethyldeca-1,4,8-trienyl]-5,9,13-trimethyltetradeca-4,8,12-trien-1-ols: 18 and 18′. Characteristic signals detected in the spectrum of the crude mixture: ^{1}H NMR: 5.27 (t, 1H, J=6.5 Hz) and 5.39 ppm (t, 1H, J= 6.5 Hz).

Alkylation of (1,2:5,6-di-*O*-isopropylidene-α-D-glucofuranos-3-*O*-yl) 3-oxobutanoate 19. DBU (1.55 ml, 10.17 mmol) and geranylbromide (2.35 ml, 10.17 mmol) were successively added to a solution of **19** (3.17 g,

9.23 mmol) in toluene. The mixture was stirred for 72 h at rt. After concentration, the crude product was purified by flash-chromatography (AcOEt/hexanes: 20/80) giving the monoalkylated compound **20** (3.61 g, 7.52 mmol) and the dialkylated product **21** (0.32 g, 0.51 mmol).

(1,2:5,6-Di-*O*-isopropylidene-α-D-glucofuranos-3-*O*-yl) 2-acetyl-5,9-dimethyldeca-4,8-dienoate: 20. Yield: 74% (2 diastereoisomers 50/50). ^{1}H NMR: 1.30 (6H, s), 1.39 (3H, s), 1.59 (3H, s), 1.63 (3H, s), 1.67 (3H, s), 1.90–2.10 (4H, m), 2.23 (1.5H, s), 2.24 (1.5H, s), 2.55 (1H, dd, *J*=7.6, 3.05 Hz), 2.58 (1H, dd, *J*=7.2, 3.05 Hz), 3.45 (0.5H, t, *J*=7.6 Hz), 3.51 (0.5H, t, *J*=7.2 Hz), 3.90–4.20 (4H, m), 4.45 (1H, d, *J*=3.4 Hz), 5.04 (2H, m), 5.28 (0.5H, d, *J*= 2.6 Hz), 5.31 (0.5H, d, *J*=2.6 Hz), 5.82 (0.5H, d, *J*=3.8 Hz), 5.87 (0.5H, d, *J*=3.8 Hz). ^{13}C NMR: 16.0 ($4CH_3$), 17.6 ($2CH_3$), 25.0 (CH_3), 25.1 (CH_3), 25.6 (CH_3), 26.1 (CH_3), 26.3 (CH_2), 26.4 (CH_2), 26.6 ($2CH_3$), 26.7 ($2CH_3$), 28.6 (CH_3), 29.2 (CH_3), 39.6 ($2CH_2$), 59.4 (CH), 59.7 (CH), 67.3 (CH_2), 67.5 (CH_2), 72.1 (CH), 72.2 (CH), 76.7 (CH), 76.7 (CH), 79.7 (CH), 79.9 (CH), 83.0 (CH), 83.2 (CH), 105.0 (2CH), 109.4 (2 C), 112.3 (2 C), 119.2 (CH), 119.3 (CH), 123.7 (2CH), 131.6 (2C), 138.6 (2 C), 168.1 (CO_2R), 168.3 (CO_2R), 202.0 (2C=O). IR: 2986, 2936, 1743, 1718, 1454, 1379, 1228, 1153, 1078, 1028, 852 cm^{-1}. MS (70 eV), *m/z*: 481 (M^++1, 5), 465 (75), 422 (27), 379 (62), 321 (25), 185 (61), 177 (41), 151 (38), 136 (91), 127 (94), 109 (100). Elemental analysis calcd for $C_{26}H_{40}O_8$: C 64.59, H 8.34. Found: C 64.71, H 8.54.

(1,2:5,6-Di-*O*-isopropylidene-α-D-glucofuranos-3-*O*-yl) 2-acetyl-2-(3′,7′-dimethylocta-2′,6′-dienyl)-5,9-dimethyldeca-4,8-dienoate: 21. Yield: 5%. ^{1}H NMR: 1.28 (3H, s), 1.29 (3H, s), 1.39 (3H, s), 1.52 (3H, s), 1.59 (6H, s), 1.60 (6H, s), 1.68 (6H, s), 1.90–2.10 (8H, m), 2.14 (3H, s), 2.55 (2H, dl, *J*=3.81 Hz), 2.63 (2H, d, *J*=5.7 Hz), 3.95–4.20 (4H, m), 4.39 (1H, d, *J*=3.81 Hz), 4.88 (1H, t, *J*=7.25 H), 4.92 (1H, *J*=6.87 Hz), 4.90–5.10 (2H, m), 5.25 (1H, d, *J*= 2.6 Hz), 5.78 (1H, d, *J*=3.81 Hz). ^{13}C NMR: 16.2 ($2CH_3$), 16.3 ($2CH_3$), 17.6 ($2CH_3$), 25.0 (CH_3), 25.6 (CH_3), 26.1 (CH_3), 26.4 ($2CH_2$), 26.7 (CH_3), 26.8 (CH_3), 29.7 (CH_2), 30.1 (CH_2), 39.9 ($2CH_2$), 63.4 (C), 67.4 (CH_2), 72.1 (CH), 76.9 (CH), 80.0 (CH), 83.0 (CH), 105.1 (CH), 109.4 (C), 112.3 (C), 117.4 (CH=), 117.7 (CH=), 123.8 (CH=), 123.9 (CH=), 131.5 (C), 131.6 (C), 138.9 (C), 139.2 (C), 171.0 (CO_2R), 204.2 (C=O). IR: 2986, 2910, 2860, 1718, 1441, 1365, 1228, 1153, 1078, 1028, 852 cm^{-1}. $[\alpha]_D^{24}$= −51.5 (0.8, $CHCl_3$). MS (70 eV), *m/z*: 616 (M^+, 5), 601 (42), 515 (41), 353 (40), 245 (37), 219 (100), 151 (65), 127 (62).

(1,2:5,6-Di-*O*-isopropylidene-α-D-glucofuranos-3-*O*-yl) 2-[1′-(diethoxyphosphoryloxy)ethylidene]-5,9-dimethyldeca-4,8-dienoate: 22. Compound **20** (3.45 g, 7.2 mmol) in ether 25 ml was added at 0°C to a suspension of NaH (0.21 g, 9 mmol) in the same solvent (75 ml). After 1 h, diethylphosphorochloridate (1.30 ml, 9 mmol) was added. The reaction was stirred at rt overnight. After hydrolysis with brine, the aqueous layer was extracted three times with ether. The organic layers were combined, dried over $MgSO_4$ and concentrated. The crude product was purified by flash-chromatography (AcOEt/hexanes 30/70) giving **22** as an oil (2.00 g, 3.25 mmol). Yield: 45%. ^{1}H NMR: 1.30 (6H, s), 1.35 (3H, t, *J*=6.9 Hz), 1.36 (3H, t, *J*=6.7 Hz), 1.40 (3H, s), 1.52 (3H, s), 1.59 (3H, s), 1.63 (3H, s), 1.67 (3H, s), 1.97 (2H, m), 2.04 (2H, m), 2.13 (3H, d, *J*=1.6 Hz), 2.92 (1H, dd, J_{AB}=16.6 Hz, *J*=6.3 Hz), 2.99 (1H, J_{AB}=16.6 Hz, *J*=6.7 Hz), 4.05 (2H, m), 4.16–4.25 (6H, m), 4.61 (1H, d, *J*=3.7 Hz), 5.05 (2H, t, *J*=6.1 Hz), 5.28 (1H, d, *J*=2.1 Hz), 5.88 (1H, d, *J*=3.7 Hz). ^{13}C NMR: 16.0 (CH_3), 16.1 ($2CH_3$), 17.6 (CH_3), 17.9 (CH_3), 25.2 (CH_3), 25.6 (CH_3), 26.2 (CH_3), 26.6 (CH_2), 26.7 (CH_3), 26.8 (CH_3), 27.6 (CH_2), 39.6 (CH_2), 64.5 (CH_2), 64.6 (CH_2), 67.1 (CH_2), 72.5 (CH), 76.2 (CH), 79.8 (CH), 83.1 (CH), 105.1 (CH), 109.2 (C), 112.1 (C), 117.9 (C), 120.2 (CH), 123.9 (CH), 131.9 (C), 137.1 (2 C), 165.1 (CO_2R). IR: 2986, 2936, 1730, 1454, 1379, 1278, 1165, 1028, 852 cm^{-1}. MS (70 eV), *m/z*: 617 (M^++1, 5), 601 (60), 507 (19), 465 (29), 379 (24), 245 (21), 185 (29), 155 (94), 143 (28), 127 (100).

(1,2:5,6-Di-*O*-isopropylidene-α-D-glucofuranos-3-*O*-yl) 2-(1′-methylethylidene)-5,9-dimethyldeca-4,8-dienoate: 23. Methyllithium (4.4 ml, 6.7 mmol) in ether was added dropwise at 0°C to a suspension of CuI (0.638 g, 3.35 mmol) in dried ether (40 ml). The solution was cooled to −65°C and compound **22** (1.84 g, 3.0 mmol) was slowly added. The solution was stirred for 2 h at this temperature and subsequently quenched with an aqueous saturated solution of ammonium chloride. After extraction three times with ether, the combined organic layers were dried over $MgSO_4$ and concentrated under vacuum. **23** (1.184 g, 2.48 mmol) was obtained pure after flash-chromatography (AcOEt/hexanes 10/90). Yield: 82%. ^{1}H NMR: 1.29 (3H, s), 1.30 (3H, s), 1.41 (3H, s), 1.53 (3H, s), 1.59 (3H, s), 1.64 (3H, s), 1.67 (3H, s), 1.83 (3H, s), 1.90–2.10 (4H, m), 2.02 (3H, s), 2.99 (2H, d, *J*=6.87 Hz), 3.95–4.10 (2H, m), 4.23 (2H, m), 4.49 (1H, d, *J*=3.81 Hz), 4.90–5.10 (2H, m), 5.29 (1H, d, *J*=1.9 Hz), 5.84 (1H, d, *J*=3.81 Hz). ^{13}C NMR: 16.0 ($2CH_3$), 17.6 (CH_3), 22.1 (CH_3), 23.1 (CH_3), 25.1 (CH_3), 25.6 (CH_3), 26.1 (CH_3), 26.6 (CH_2), 26.7 (CH_3), 28.6 (CH_2), 39.6 (CH_2), 67.3 (CH_2), 72.4 (CH), 75.8 (CH), 80.0 (CH), 83.4 (CH), 105.0 (CH), 109.2 (C), 112.1 (C), 121.6 (CH=), 123.9 (CH=), 125.8 (C), 132.1 (C), 135.7 (C), 144.8 (C), 167.8 (CO_2R). IR: 2986, 2910, 2847, 1718, 1630, 1441, 1379, 1253, 1203, 1153, 1078, 1028, 852 cm^{-1}. UV (CH_2Cl_2): ϵ_{231}=5600. MS (70 eV), *m/z*: 478 (M^+, 5), 463 (92), 420 (7), 218 (16), 149 (28), 136 (100), 121 (21). $[\alpha]_D^{24}$=−27 (0.5, $CHCl_3$). Elemental analysis calcd for $C_{27}H_{42}O_7$: C 67.75, H 8.84. Found: C 67.74, H 9.09.

(2*R*)-(1,2:5,6-Di-*O*-isopropylidene-α-D-glucofuranos-3-*O*-yl) 2-isoproprenyl-5,9-dimethyldeca-4,8-dienoate: 24. Argon was bubbled through a solution of ester **23** (1.195 g, 2.5 mmol) and *N*,*N*-dimethylaminoethanol (0.223 g, 2.5 mmol) in dichloromethane (250 ml) and the solution was poured into quartz tubes. The tubes were placed around a quartz Dewar containing a short wave length OSRAM lamp. The irradiation was carried out at −55°C. After disappearance of the starting material (TLC control), the solvent was removed and ester **24** (1.100 g, 2.30 mmol) purified by preparative thin-layer chromatography. Yield: 92%. ^{1}H NMR: 1.28 (3H, s), 1.29 (3H, s), 1.39 (3H, s), 1.54 (3H, s), 1.58 (3H, s), 1.62 (3H, s), 1.67 (3H, s), 1.74 (3H, s), 1.92–2.10 (4H, m), 2.30 (1H, m), 2.52 (1H, m), 3.05 (1H, t, *J*=7.7 Hz), 3.92–4.00 (1H, m), 4.05–4.20 (3H, m), 4.41 (1H, d, *J*=3.7 Hz), 4.90 (2H, sl), 5.00–5.10 (2H, m),

5.28 (1H, d, J=1.65 Hz), 5.86 (1H, d, J=3.7 Hz). ^{13}C NMR: 14.1 (CH_3),16.0 (CH_3), 17.6 (CH_3), 20.1 (CH_3), 25.0 (CH_3), 25.6 (CH_3), 26.1 (CH_3), 26.5 (CH_2), 26.6 (CH_3), 28.5 (CH_2), 39.6 (CH_2), 53.2 (CH), 67.4 (CH_2), 72.1 (CH), 75.8 (CH), 80.2 (CH), 83.3 (CH), 105.0 (CH), 109.2 (C), 112.2 (C), 114.1 (CH_2=), 120.7 (CH=), 123.9 (CH=), 137.3 (C), 141.7 (2 C), 171.9 (CO_2R). IR: 1745, 1454, 1153, 1143 cm^{-1}. MS (70 eV), *m/z*: 478 ($M^{+\cdot}$, 8), 463 (100), 420 (80), 351 (35), 284 (55), 218 (31), 190 (26), 136 (24), 121 (48). $[\alpha]_D^{24}=-44.5$ (0.9, $CHCl_3$). Elemental analysis calcd for $C_{27}H_{42}O_7$: C 67.75, H 8.84. Found: C 67.52, H 9.15.

Sesquilavandulol: 10. A solution of ester **24** (0.650 g, 1.35 mmol) in ether (5 ml) was added to a suspension of $LiAlH_4$ (0.064 g, 1.69 mmol) in the same solvent (25 ml) at 0°C. The mixture was stirred for 4 h. After complete disappearance of the starting material, the mixture was hydrolysed with wet ether. The aqueous layer was extracted with ether, the organic phases combined, dried over $MgSO_4$ and concentrated. After flash-chromatography, **10** (0.227 g, 1.02 mmol) was obtained pure as an oil. Yield: 76%. ^{1}H NMR: 1.59 (6H, s), 1.67 (3H, s), 1.69 (3H, s), 1.90–2.15 (6H, m), 2.24–2.35 (1H, m), 3.48 (1H, dd, J_{AB}=10.7 Hz, J= 8 Hz), 3.58 (1H, dd, J_{AB}=10.7 Hz, J=5.3 Hz), 4.81 (1H, sl), 4.93 (1H, sl), 5.09 (2H, m). ^{13}C NMR: 16.0 (CH_3), 17.6 (CH_3), 19.4 (CH_3), 25.6 (CH_3), 26.5 (CH_2), 28.2 (CH_2), 39.6 (CH_2), 49.9 (CH), 63.5 (CH_2), 113.0 (CH_2=), 121.9 (CH=), 124.1 (CH=), 131.3 (C), 136.2 (C), 145.3 (C).

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