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CONVENIENT SYNTHETIC ROUTE TO (+)-FARANAL AND (+)-13-NORFARANAL; THE TRAIL PHEROMONE OF PHARAOH'S ANT AND ITS CONGENER [1]

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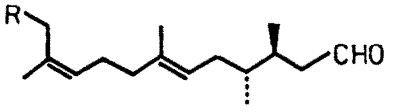
Abstract: (+)-Faranal 1a, the trail pheromone of Pharaoh's ant, and its congener, (+)-13-norfaranal 1b were synthetized from chiral building block 4 employing diastereoselective carbon-carbon bond formation. The application of crude pig liver esterase enzyme for the preparation of 4 is also discussed.

(+)-Faranal is the most attractive component of the trail pheromone produced by Pharaoh's ant (Monomorium pharaonis, L.), which is a serious houshold pest in most of the world. This compound has a very high behavioural efficiency and the detection threshold is about 1 pg cm^{-1} of a trail. The structure of (+)-faranal was assigned to be (3S,4R,6E,10Z)-3,4,7,11-tetramethyl-6,10-tridecadienal 1a [2-4]



1a: R= Me
1b: R= H

All four optical isomers of faranal have some biological activity. However, racemic faranal has only one tenth of the trail pheromone activity of the natural product. Surprisingly, the 3-epimer (3R,4R-faranal) was also weakly active and does not interfere with the activity of natural product, since ants follow a trail made of a 1:1 mixture of stereoisomeric compounds. Furthermore, structure modification study showed that among structurally related compounds a 40 : 60 mixture of (3S,4R)- and (3R,4R)-13-norfaranal (1b and its 3-epimer) had also the ability to release trail-following activity [4,5].

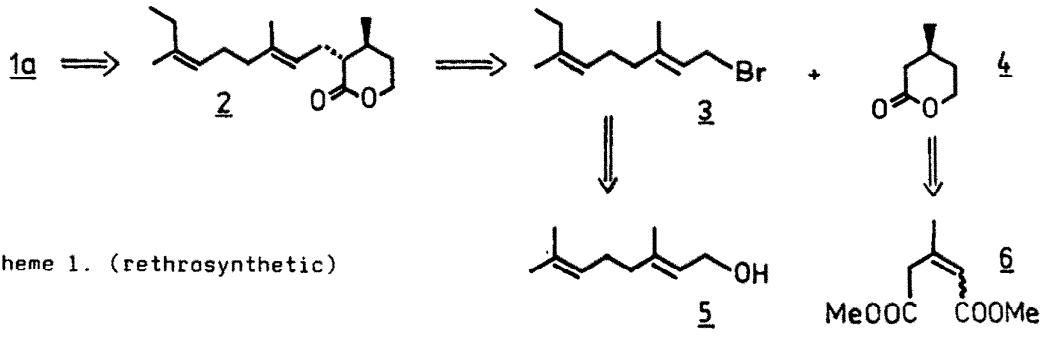
(+)-Faranal has been an attractive synthetic target of considerable current interest because of its challenging structural features and extremely high level of biological activity. Four different synthetic approaches to faranal have been reported. In cooperation with Japanese group, Ritter et al. elaborated the first synthesis of faranal [4]. Actually, this small scale bioorganic synthesis leading to a 40 : 60 mixture of (+)-faranal and its (3R)-epimer, established its absolute stereochemistry.

Mori and Ueda have confirmed the structural assignments of (+)-faranal by synthetising both enantiomers. Their attractive linear approach is rather lenghty and required the chemical resolution of an intermediate [6,7].

Recently, two convergent approaches for the synthesis of racemic faranal

were reported. Knight and Ojhara assembled the sesquiterpenoid skeleton of faranal by Wittig condensation, which yielded an approximately 1 : 1 mixture of (E)- and (Z)-isomers. Racemic faranal and its (6Z)-isomer were then separated by preparative scale g.l.c. [8,9]. In an alternative synthesis of racemic faranal, Baker's group employed the addition of an alkylcopper complex to terminal acetylene for the stereoselective construction of the 6E double bond [10,11].

Recent interest in the use of trail pheromone to increase the rate of toxic bait pick-up has led us to develop new synthetic method for the preparation of enantiomerically pure (+)-faranal and (+)-13-norfaranal (1a and 1b, respectively). Our approach is strategically quite different from the existing ones in the construction of the skeleton of faranal (Scheme 1.). Namely, we formed the

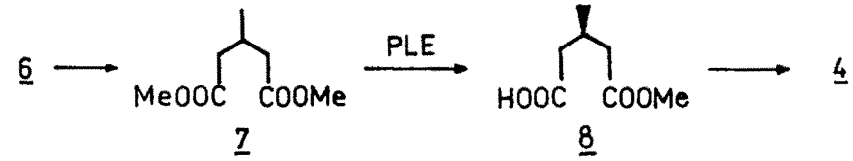


Scheme 1. (rethrosynthetic)

4,5-bond of the molecule stereoselectively by electrophilic enolate alkylation of an appropriately functionalized chiral building block (4) with (Z)-homogeranyl bromide (3).These key intermediates can be easily prepared from geraniol (5) and glutaconic ester (6), respectively.

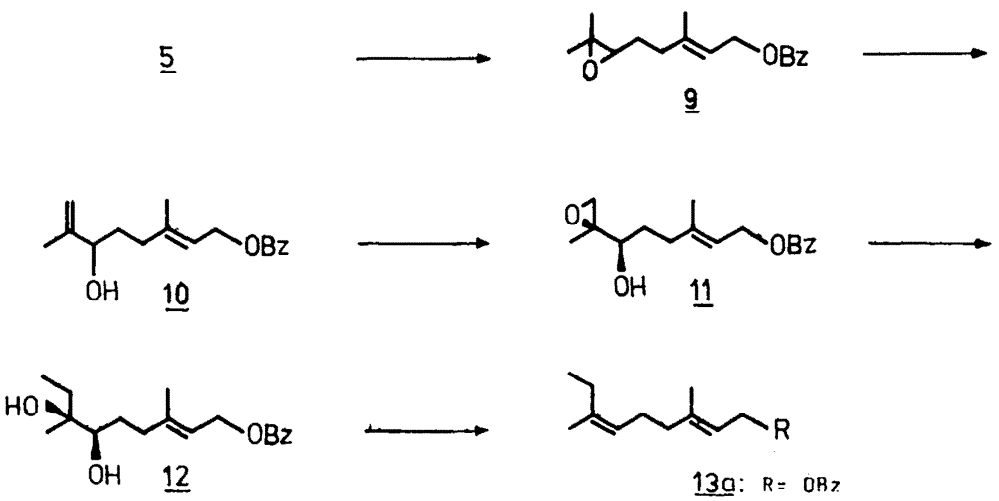
(3S)-Methyl valerolactone (4), our chiral key intermediate, was prepared from dimethyl 3-methylglutarate (7) obtained by catalytic hydrogenation of glutaconic ester (6) [12] (Scheme 2.).

Scheme 2:



Recently, this compound was enantiotopically-selectively hydrolysed with pig liver esterase (PLE) enzyme system [13-16]. The enzyme attacked preferentially at the pro-(S)-methoxycarbonyl group and (R)-monoester (8) was isolated in above 80 % yield and in 80 - 90 % optical purity. However, the commercially available pure pig liver esterase is rather expensive. Therefore, we tried to perform the selective hydrolysis of diester (7) with crude enzyme. Thus, molar amount of diester (7) was suspended in 0.1 M phosphate buffer (pH 7) extract of pig liver acetone powder [17]. The pH value of the resulting mixture was kept within 6.9 - 7.1 range by continuous addition of 10 % sodium hyroxide solution. After consumption of one equivalent of base (approximately 5 h), the mixture was worked up to yield the (R)-enantiomer of monoester (7) in 72 % yield and in 85 % optical purity. Since the optical purity was not satisfactory, the crystalline l-cinchonidine salt of monoester (8) was formed and recrystallized from water-acetone. Acidification of this salt yielded optically pure (R)-monoester (8, e.e.>96 %), which was selectively reduced with sodium in NH_3-EtOH [18] or $LiBH_4$ in THF [13] to give (3S)-methyl valerolactone (4).

(Z)-Homogeranyl bromide (3), another key intermediate, was prepared from the readily available geraniol (5) by the combination of known methods with some modification (Scheme 3.).

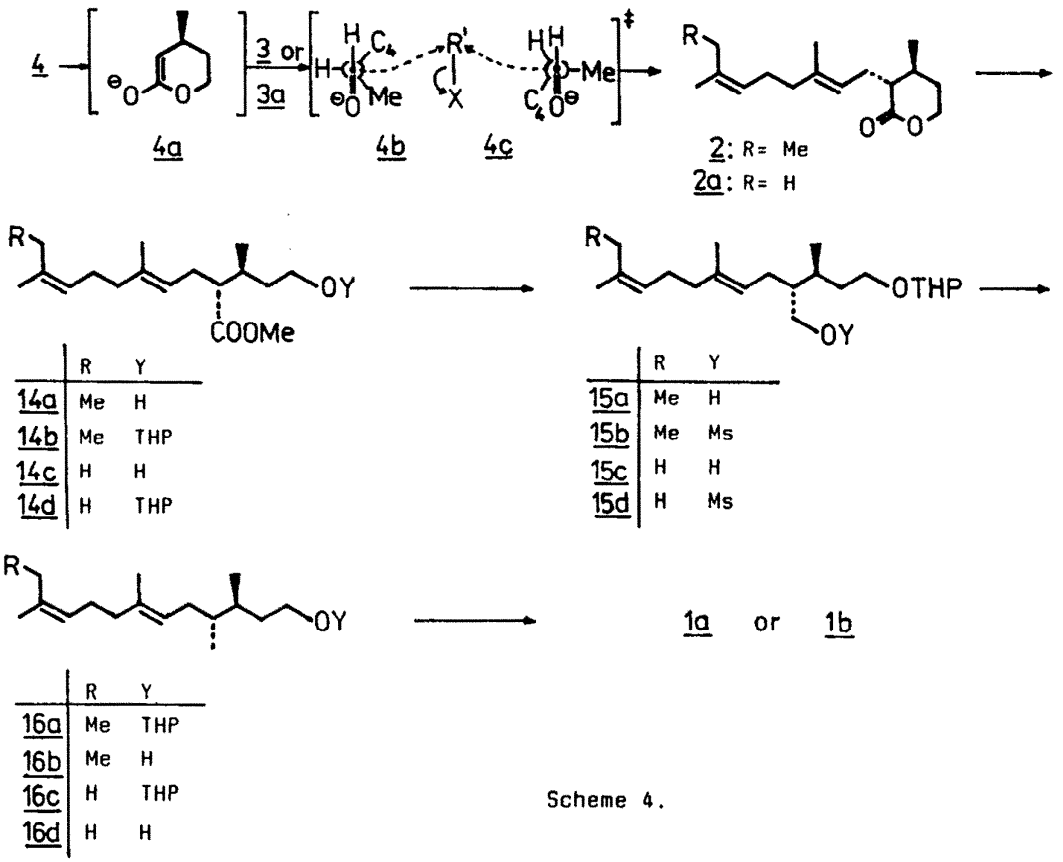


Scheme 3.

Thus, reaction of geraniol with sodium hydride and benzyl bromide gave geranyl benzyl ether [19], which was generally not purified, but directly treated with 3-chloroperoxybenzoic acid to produce epoxy compound (9). A number of reagents (e.g. sodium glass [20], lithium perchlorate [21], lithium diethylamide [22], aluminium isopropoxide [23]) were then examined for the conversion of epoxide (9) to allylic alcohol (10). In our hands, aluminium isopropoxide proved to be superior to the other reagents. The reaction was performed in refluxing toluene and afforded the desired product (10) in good yield. Catalytic epoxidation of alcohol (10) with t-butyl hydroperoxide in the presence of catalytic amount of $VO(acac)_2$ in benzene afforded epoxy alcohol (11), which was then converted into (Z)-homogeranyl benzyl ether (13a) by the sequence involving oxirane reaction with lithium dimethyl cuprate and elimination of the hydroxy groups of the resulting diol (12) by treatment with dimethylformamide dimethyl acetale and acetic anhydride [24]. HPLC analysis showed that the product (13a) was contaminated by less than 8 % of (E)-isomer , which was removed after deprotection by treatment with lithium in liquid ammonia by column chromatography. The resultant (Z)-homogeraniol (13b) was then converted to diastereomerically pure (Z)-homogeranyl bromide (3) by treatment with phosphorous tribromide, in 24 % overall yield (based on geraniol).

Next task was to connect the two building blocks (3 and 4). For this, we plan a diastereoselective carbon-carbon bond formation by an electrophilic enolate alkylation (Scheme 4.).

Enolate (4a) generated from the lactone (4) seemed particularly attractive for this purpose by virtue of its rigidity and conformationally enforced proximity of its reacting center (C_2). Furthermore, in the transition state of alkylation only one of the possible conformers (4c, methyl group in perpendicular position) is stabilized by hyperconjugative interaction. Here, the incoming electrophile preferentially attacks on the opposite side of the plan and renders the (R)-configuration at the newly created chiral center (Scheme 4.).



	R	Y
14a	Me	H
14b	Me	THP
14c	H	H
14d	H	THP

	R	Y
15a	Me	H
15b	Me	Ms
15c	H	H
15d	H	Ms

	R	Y
16a	Me	THP
16b	Me	H
16c	H	THP
16d	H	H

Scheme 4.

Coupling reaction between enolate (4a) generated from the lactone (4) with lithium diethylamide, and (Z)-homogeranyl bromide (3) proceeded as expected to give predominantly the desired anti-isomer (2R,3S)-2, together with a small amount (less than 6 %) of syn-isomer (2S,3S). This high anti stereofacial selectivity was evidenced by the trans relationship found between the substituents of lactone moiety in the product (2), as deduced from the coupling constant value $J_{2,3}$ in NMR spectra, that requires trans-arrangement for this substituent.

Trivial reactions were then used to convert lactone (2) into (+)-faranal (1a). Thus, transesterification of 2 with MeOH and Et_3N led to a hydroxy ester (14a) which was converted to protected ester (14b) by treatment with dihydropyran in the presence of pyridinium p-toluenesulfonate. Reduction of 14b with excess lithium aluminium hidride gave the alcohol (15a) which was converted to the corresponding mesylate (15b) by mesyl chloride in the presence of triethylamine. The mesylate (15b) was reduced with lithium aluminium hidride in refluxing THF and then the protecting group of the resulting ether (16a) was removed by acid catalyzed hydrolysis. Finally, oxidation of the resulting alcohol (16b) with pyridinium dichromate afforded (+)-faranal (1a) in 1.9 % and 3.5 % overall yield (based on 5 and 6, respectively).

Chiral lactone (4) also served as the key intermediate in the first stereocontrolled synthesis of (+)-13-norfaranal (1b)(Scheme 4.). Here, in the electrophilic ester enolate alkylation we used geranyl bromide (3a) and isolated the desired anti-isomer 2b, together with a small amount of syn-isomer (6 %). This was converted to stereoisomerically 94 % pure (+)-13-norfaranal (1b) by the method described above for (+)-faranal, via intermediates 14c, 14d, 15c, 15d, 16c an 16d in 19.4 % overall yield from lactone 4.

EXPERIMENTAL

IR spectra were obtained with a Specord IR-75 (Carl Zeiss, Jena) spectrophotometer. ^{1}H- and ^{13}C-NMR spectra were recorded on a JEOL FX-100 FT-NMR instrument at 100 and 25 MHz, respectively, and are reported in ppm downfield from internal TMS. Mass spectra were taken on a JEOL-20K and a JMS-01SG-2 combined GC-MS system at 75 eV ionizing energy. HPLC measurements were carried out on a Du Pont 830 instrument. For the capillary GLC analyses a Packard 428 instrument equipped with FID was used. Thin layer chromatography was carried out using Kieselgel 60 F_{254} on alumina plates (E. Merck Co,FRG) and hexane-acetone=5:0.2(A), hexane-acetone=10:1(B), hexane-acetone=5:2(C) or hexane-ethyl acetate=2:1(D) eluant systems. Spots were visualised by immersing the plates into 5 % ethanolic solution of phosphomolibdenic acid and then heating. All solvents used were freshly distilled and anhydrous, and operations with alkyl lithiums, cuprates, $LiBH_4$ and $LiAlH_4$ were carried out under dry argon atmosphere.

Dimethyl 3-methylglutarate (7)

Dimethyl glutaconate (6, 435 g, 2.5 moles) was catalytically hydrogenated by 10 % palladium on active carbon under 4 atm hydrogene pressure at 65°C. After consumption of the calculated 61 l (2.5 moles) hydrogene the catalyst was filtered off and the product was distilled in vacuo to yield 7 (349 g, 91 %) as a colorless oil Bp.: 115°C(0.5 torr); TLC(B):Rf=0.29; IR(film), ν_{max}: 2900, 1725, 1440, 1370, 1260, 1190, 1150, 1080, 1010 cm^{-1}; ^{1}H-NMR(CCl_4, δ): 1.01 (d,J=5Hz, 3H,-CH_3), 2.26 (m,5H, 2-CH_2- and 1-CH=), 3.55 (s,6H, 2 $COOCH_3$); MS m/e: 174(2)[M^+], 143(100), 142(51), 115(51), 114(92), 101(94), 83(20), 82(28), 73(60), 69(91), 59(75), 55(60), 43(61), 42(38), 41(65), 39(40).

(3R)-Hydrogen-methyl 3-methylglutarate (8)

Pig liver acetone powder[17] (100 g) was homogenized with 0.1 M phosphate buffer (pH=8, 1200 mL) and then centrifuged at 3000 g at room temperature for five minutes. To this obtained supernatant (pH value changed to about 7.0 during the extraction process) having 31 U/mL enzyme activity (measured on ethyl butyrate as a substrate at 25°C, pH=8) compound 7 (314 g, 1.8 moles) was added and the pH value of the resulted well stirred emulsion was kept within 6.9-7.1 range by continous addition of 10 % (2.78 M) sodium hydroxide solution. After consumption of 1 equivalent of base (645 mL) the mixture was acidified to pH=2 by the addition of concentrated hydrochloric acid. To the emulsion sodium chloride (150 g) was added and the resulting mixture was centrifuged at 3000 g for five minutes. The precipitated part was washed with ethyl acetate (400 mL) and the supernatant was extracted three times with ethyl acetate (800 mL, each). The combined ethyl acetate solutions were washed with brine (200 mL) and dried over $MgSO_4$. Evaporation of the solvent in vacuo gave crude 8, which was further purified by vacuum-distillation to yield pure 8 (213 g, 74 %) as a colorless oil. Bp.: 106-107°C (0.05 torr); $[\alpha]_D^{22}$=0.49°(neat). Lit.[28]: $[\alpha]_D^{22}$=0.58°(neat, 100 % ee).
Recrystallzation of this product (8, 12 g, 75 mmol) with l-cinchonidine (22.2 g, 75 mmol) from water (210 mL) containing acetone (60 mL) resulted chrystalline salt of 8 as white needles. Chrystals were then solved in 1M hydrochloric acid (60 mL) and extracted three times with ether (30 mL, each). The combined ethereal solutions were then washed with brine (15 mL) and dried over $MgSO_4$. After evaporation of the solvent in vacuo optically pure 8 (7.7 g, 64 %) was obtained as a pale yellow oil. $[\alpha]_D^{22}$= 0.57°(neat); TLC (C): Rf= 0.35; IR(film), ν_{max}: 3200, 2900, 1725, 1700, 1440, 1380, 1290, 1200, 1160, 1080, 1010 cm^{-1}; ^{1}H-NMR (CCl_4,δ): 1.08 (d,J=5,5Hz, 3H,-CH_3), 2.31 (m, 5H,2-CH_2- and 1-CH=), 3.62 (s,3H,$COOCH_3$), 11.3 (br s, 1H,COOH); MS m/e: 160(1)[M^+], 143(11), 142(25), 129(65), 128(27), 114(66), 101(66), 100(50), 87(18), 83(16), 82(21), 74(67), 72(21), 69(78), 60(13), 59(100), 56(12), 55(42), 45(13), 44(77), 43(33), 42(46), 39(27).

(-)-(3S)-Methylvalerolactone (4)

a) To a stirred and boiling solution of distilled ammonia (700 mL) containing dry ethanol (60 mL) and 8 (32 g, 700 mmol) sodium pieces were added portionwise. After complete sodium addition the mixture was boiled and stirred for 1 h and then solid ammonium chloride was added until the disappearance of the deep blue color of the mixture. Ammonia was evaporated and the residue was dissolved in water (400 mL). The aqueous solution was acidified to pH 2 at 0°C with 50 % H_2SO_4 and then extracted three times with ethyl acetate (400 mL, each). Ethyl acetate solutions were combined and washed with brine (80 mL), dried over $MgSO_4$. After evaporation of the solvent in vacuo the residue was vacuum-chromatographed (VLC)[27] (on 200 g of 63-100 μm Kieselgel 60 with hexane-acetone= 10:1 eluant) to yield 4 (12.8 g, 56 %).
Product can only be stored without decomposition at 4°C in diluted aprotic (e.g.ethereal) solution for a longer period.
b) To an ice cooled and stirred solution of 8 (101 g, 0.63 mol) in methanol (500 mL) LiOH H_2O

(26.3 g, 0.63 mol) was added portionwise maintaining the inner temperature under 15°C. After complete dissolution of the LiOH H_2O methanol and water was evaporated from the resulted salty product in vacuo to yield dry lithium salt of 8 (100.4 g, 95 %). 80 g (0.48 mol) of this salt was suspended in dry THF (800 mL) under dry argon atmosphere and then $LiBH_4$(16.5 g, 0.76 mol) was added to the vigorously stirred suspension. The resulted mixture was refluxed for 1 h and after cooling to room temperature poured into ice-water (500 mL), which was then acidified to pH=2 by dropwise addition of concentrated hydrochloric acid. The acidified aqueous mixture was extracted four times with ethyl acetate (400 mL, each) and then the combined organic layers were washed with brine (150 mL) and dried over $MgSO_4$. After evaporation of the solvent in vacuo and VLC purification (as above) pure 4 (29.9 g, 55 %) was obtained.
$[\alpha]_D^{23}$=-23.5° (c=5.21, $CHCl_3$, from unrecrystallized 8) and $[\alpha]_D^{23}$=-26.9°(c=4.98, $CHCl_3$, from recrytallized 8), Lit.[28]: $[\alpha]_D^{22}$=+27.6° (c=5.72, $CHCl_3$, 3R-enantiomer, 100 % ee); TLC(C):Rf=0.39; IR (film), ν_{max}: 2900, 1720, 1460, 1440, 1400, 1370, 1310, 1280, 1240, 1220, 1160, 1080, 1060, 1000, 920 cm^{-1}; ^{1}H-NMR ($CDCl_3$, δ): 1.09 (d, J=6.5Hz,-CH_3), 1.4-2.3 (br m, 5H, 2-CH_2- and 1-CH=), 4.0-4.5 (m,2H,-CH_2-O); MS m/e: 115(4)[M+1]$^+$, 114(21)[M$^+$],85(1),84(2),71(3),70(23), 55(100),42(83),41(54),39(40).

(2E)-1- Benzyloxy-6,7-epoxy-3,7-dimethyl-2-octene (9)

To an ice-cooled and stirred solution of geranyl benzyl ether[23] (30 g, 0.122 mol) in dry dichloromethane (300 mL) 3-chloro-peroxybenzoic acid (31.5 g, 0.128 mmol, 75 % content) was added portionwise maintaining the inner temperature under 5°C. After complete addition the resulted mixture was stirred at 0°C for 1 h and then the precipitated white solid was filtered off. Filtrate was washed two times with 10 % sodium hydroxide solution (80 mL, each) and then brine (50 mL). After evaporation of the solvent VLC of the residue (on 300 g of silica gel with hexane-acetone=5:0.1 eluant) resulted 9 (21.9, 69 %) as an oil. TLC (B):Rf=0.36; IR(film), ν_{max}: 2900, 2840, 1660, 1445, 1370, 1240, 1190, 1100, 1080, 1060, 1020, 725, 690 cm^{-1}; ^{1}H-NMR (CCl_4, δ): 1.18 (m, 6H, 2-CH_3), 1.4-1.8 (m, 5H,-CH_2- and -CH_3), 2.12 (mc, 2H,-CH_2-), 2.49 (t, J=6Hz, 1H,C_6 -CH=), 3.90 (d, J=7Hz, 2H, -CH_2-OBz), 4.38 (s, 2H, O-CH_2-Ph), 5.33 (t, J=7Hz, 1H,-CH=C), 7.19 (m,5H,Ar-H);MS m/e: 210(1)[M$^+$], 174(6), 154(4), 123(7),107(7), 91(100), 85(13), 71(19), 59(20), 43(7).

(2E)-1-Benzyloxy-6-hydroxy-3,7-dimethyl-2,7-octadiene (10)

A solution of 9 (15.6 g, 60 mmol) and aluminium isopropoxide (12.3 g, 60 mmol) in dry toluene (100 mL) was refluxed and stirred for 8 h. After cooling to room temperature hexane (100 mL) was added to the resulting mixture and then the organic solution was washed with 2M hydrochloric acid (100 mL), saturated $NaHCO_3$ solution (40 mL) and brine (40 mL). The organic layer was then dried over $MgSO_4$ and the solvent was removed in vacuo to give 10 (14.6 g, 93 %) as a pale yellow oil. TLC(C): Rf=0.47; IR (film) ν_{max}: 3400, 2900, 2850, 1670, 1500, 1460, 1380, 1075, 1040, 900, 740, 700 cm^{-1}; ^{1}H-NMR ($CDCl_3$,δ): 1.66 (s, 3H,-CH_3), 1.71 (s, 3H,-CH_3), 1.95 (mc, 4H, 2-CH_2-), 3.57 (m, 1H,=CH-O), 3.99 (d, J=6.5 Hz, 2H,-CH_2-OBz), 4.47 (s, 2H, O-CH_2-Ph), 4.80 and 4.92 (m,m,2H, C=CH_2), 5.38 (t, J=6,5Hz,1H,-CH=C), 7.27 (br s, 5H, Ar-H); MS m/e: 260(1)[M$^+$], 242(1), 174(3), 169(4), 151(13),125(7), 123(10), 109(8), 107(18), 97(6), 95(8), 93(10), 92(17), 91(100), 82(12), 81(19), 71(16), 69(15), 68(11), 67(15), 55(12), 44(22), 42(19).

(2E)-1-Benzyloxy-7,8-epoxy-6-hydroxy-3,7-dimethyl-2-octene (11)

To a solution of 10 (10.4 g, 40 mmol) in dry benzene (100 mL) 20 mg of $VO(acac)_2$ catalyst was added and then t-BuOOH (8.0 g, 90 % content, 80 mmol) was dropped to the resulting mixture over a period of 15 min. After stirring at room temperature for 2 h, additional $VO(acac)_2$ catalyst (20 mg) was added to the reaction mixture and stirring was continued for another 2h. The obtained mixture was then diluted with hexane (100 mL) and washed with 10 % Na_2CO_3 solution (30 mL) and brine(30 mL). After drying ($MgSO_4$) and evaporation in vacuo the resulting residue was purified by VLC(on 200 g of 63-200 μm silica gel with hexane-acetone=10:1 eluant) to yield pure 11 (8.6 g, 78 %) as an oil. TLC(C):Rf=0.38; IR (film), ν_{max}: 3350, 2900, 2830, 1660, 1500, 1450, 1380, 1360, 1190, 1060, 1020, 940, 900, 740, 700 cm^{-1}; ^{1}H-NMR (CCl_4, δ): 1.30 (s,3H,-CH_3), 1.50 (m,2H,-CH_2-), 1.66(s,3H,-CH_3), 2.22 (m,2H,-CH_2-), 2.61 (mc,2H, C_8-CH_2-), 3.48 (m,1H,OH), 3.96 (d,J=6.5Hz,2H,-CH_2-OBz), 4.36(s,2H,O-CH_2-Ph), 5.39 (t,J=6.5Hz, 1H,-CH=C), 7.29 (br s,5H,Ar-H); MS m/e: 276(< 1)[M$^+$], 174(2), 170(2), 169(3), 167(3), 153(3), 141(3), 123(4), 121(4), 111(9), 97(9), 91(100), 87(10), 81(26), 43(31), 41(25).

(2E,6,7-anti)-1-Benzyloxy-6,7-dihydroxy-3,7-dimethyl-2-octene (12)

To a suspension of copper(I) iodide (9.4 g, 48.4 mmol) in dry ether (100 mL) 1.38 M ethereal methyl lithium solution (70 mL, 97 mmol) was added below -20°C under dry argon atmosphere. After stirring at -20°C for 10 minutes the mixture became homogenous and then 11 (6.67 g, 24.2 mmol) in dry ether (30 mL) was added to this solution at -20°C. The resulting mixture was stirred at 0°C for 4 h and then was quenched by addition of 10 % NH_4Cl solution (30 mL). The ethereal layer was washed with two additional portion of 10 % NH_4Cl solution (30 mL,each) and brine (30 mL) and dried over $MgSO_4$. The VLC (100 g of 63-200 μm silica gel , hexane-acetone=10:1 eluant) of the residue of the evaporation in vacuo gave 12 (4.45 g, 63 %). TLC(C):Rf=0.34; IR (film), ν_{max}: 3350, 2900, 2840, 1660, 1450, 1380,

1060, 1000, 730, 695 cm^{-1}; ^{1}H-NMR ($CDCl_3$, δ): 0.91 (t, J=6,5Hz, 3H,-CH_3), 1.12 (s, 3H,-CH_3), 1.45 (mc, 4H,2-CH_2-), 1.65 (s, 3H,-CH_3), 2.12 (t, J=6Hz, 2H,-CH_2-), 2.36 (br s, 2H,2 OH), 3.35 (m, 1H,=CH -O), 4.01 (d, J=7Hz, 2H,-CH_2-OBz), 4.47 (s, 2H, O-CH_2-Ph), 5.42 (t, J=7Hz, 1H,-CH=C), 7.28 (br s, 5H, Ar-H); MS m/e: 292(< 1)[M^+], 274(3), 219(5), 183(4), 166(3), 163(3), 155(5), 137(5), 112(8), 111(14), 91(100), 81(20), 73(58), 68(30), 57(22), 43(22), 41(15).

(2E,6Z)-1-Benzyloxy-3,7-dimethyl-2,6-nonadiene (13a; Z-homogeranyl benzyl ether)

A solution of 12 (9.8 g, 29.8 mmol) in N,N-dimethylformamide dimethyl acetale (30 mL) was stirred overnight at room temperature and then evaporated in vacuo. To the residue acetic anhydride (30 mL) was added and the solution was boiled and stirred for 8 h. After cooling to room temperature the mixture was diluted with hexane (250 mL) and washed with water (50 mL), two times with 10 % sodium hydroxide solution and brine (50 mL). After drying over $MgSO_4$ the solvent was removed in vacuo and the residue was purified by VLC (100 g silica gel, hexane-acetone=5:0.1 eluant) to yield 13a (5.05 g, 65 %) as an oil. TLC (A):Rf=0.62; IR (film), ν_{max}: 2970, 2930, 2850, 1660, 1450, 1370, 1230, 1100, 1060, 1020, 725, 690 cm^{-1}; ^{1}H-NMR (CCl_4,δ): 0.95 (t, J=6.5Hz, 3H,-CH_3), 1.65 (s, 3H,-CH_3), 1.72 (s, 3H,-CH_3), 2.10 (m, 4H, 2-CH_2-), 3.94 (d, J=6.5Hz, 2H,-CH_2OBz), 4.46 (s, 2H, O-CH_2-Ph),5.05 (m, 1H,-CH=C), 5.33 (t, J=6.5Hz, 1H,-CH=C), 7.29 (br s,5H,Ar-H); MS m/e: 258(11)[M^+], 229(2),176(6), 167(7), 150(25), 137(26), 121(17), 91(100), 83(66), 55(66), 41(29); HPLC: t_R= 147 s (main component, 95 %, (2E,6E)-isomer:t_R= 138 s, 5 %; 250x4.5 mm LiChrosorb RP-8 10 μm,1 ml/min acetonitrile eluant, λ = 254 nm).

(2E,6Z)-3,7-Dimethyl-2,6-nonadien-1-ol (13b; Z-homogeraniol)

To a stirred boiling solution of $LiNH_2$[prepared from lithium (1.4 g, 167 mmol)] in dry ammonia (300 mL) was added a solution of 13a (4.3 g, 16.7 mmol) in dry n-hexane (30 mL). After stirring for 30 min, an excess of ammonium chloride was added, and the mixture was diluted with n-hexane (800 mL). The ammonia was evaporated, and water (150 mL) was added. The separated aqueous layer was extracted with hexane (200 mL) and the hexane layer was washed with saturated NH_4Cl solution (100 mL), and dried over $MgSO_4$. After removing the solvent the residue was purified by low presure liquid chromatography (LPLC) (on 10-40 μm Kieselgel HR using hexane-acetone=10:1 as eluant) to afford 13b (2.37 g, 84 %). TLC(C):Rf=0.50; IR (film), ν_{max}: 3350, 2980, 2940, 2880, 1660, 1450, 1380, 1000 cm^{-1}; ^{1}H-NMR (CCl_4,δ): 0.96 (t, J=6.5Hz, 3H,-CH_3), 1.64 (br s, 6H,2-CH_3), 2.01 (m, 4H,2-CH_2-), 2.03 (q, J=6.5Hz, 2H,-CH_2-), 3.76 (m,1H,OH), 4.03 (d, J=6.5Hz,2H,-CH_2-O), 5.07 (m, 1H,-CH=C), 5.37 (t,J=6.5Hz, 1H,-CH=C); MS m/e: 168(1)[M^+], 151(1), 150 (1), 137(3), 121(3), 111(2), 107(2), 93(7), 83(32), 67(17), 55(100), 53(18), 43(12), 41(81), 39(38).

(2E,6Z)-1-Bromo-3,7-dimethyl-2,6-nonadiene (3; Z-homogeranyl bromide)

To a stirred solution of 13b (1.68 g, 10 mmol) in dry ether (50 mL) there was added a solution of phosphorous tribromide (1.25 g, 4.5 mmol) in dry ether (5 mL) under dry argon atmosphere at -5°C in darkness. The resulting mixture was stirred at 0°C for 45 min, and then brine (20 mL) was added. After extraction of the aqueous layer with ether (20 mL), the combined ethereal solutions were washed with ice-cooled and saturated $NaHCO_3$ solution (10 mL) and brine (10 mL) and dried over $MgSO_4$. Evaporation of the solvent in vacuo at 0-5°C gave 3 (2.19 g, 95 %)as a pale yellow oil. The product is sensitive for light, heat, wet and was used up immediately for the next step. TLC(hexane): Rf=0.80; IR (CCl_4), ν_{max}: 3030, 2980, 2945, 2880, 2870, 1650, 1450, 1380, 1200, 1105, 1060 cm^{-1}; ^{1}H-NMR (CCl_4,δ): 0.90 (t, J=6.5Hz, 3H,-CH_3), 1.60 (s, 3H,-CH_3), 1.66 (s,3H,-CH_3), 1.93 (q, J=6.5Hz, 2H,-CH_2-), 2.0 (m, 4H, 2-CH_2-), 3.86 (d, J=8.5Hz, 2H,-CH_2Br), 4.96 (m, 1H,-CH=C), 5.44 (t, J=8.5Hz, 1H,-CH=C); MS m/e: 232(3), 230(2),[M^+], 175(2), 171(2), 151(18), 123(2), 109(2), 95(11), 83(100), 81(17), 68(12), 67(11), 55(72), 41(23).

(2R,3S,2'E,6'Z)-2-(3,7-Dimethyl-2,6-nonadienyl)-3-methyl-5-pentanolide (2)

To a solution of lithium diethyl amide [prepared from diethyl amine (0.60 g, 8.2 mmol) and n-buthyl lithium (8.2 mmol, 1.1 M hexane solution)] in dry THF (20 mL) there was added a solution of 4 (0.94 g, 8.2 mmol, >95 % ee) in dry THF (5 mL) below -70°C, and the resulting mixture was stirred at -78°C for 1 h. Then 3 (1.89 g, 8.2 mmol) dissolved in dry THF (5 mL) and dry HMPA (0.8 mL) was added below -70°C. The resulting mixture was stirred at -78°C for 1 h and then stayed at -30°C overnight. The reaction was diluted with ether (50 mL) and quenched by 10 % hydrochloric acid (20 mL) and the acidic layer was extracted two times with ether (20 mL; each). The combined organic solutions were washed with saturated $NaHCO_3$ solution (10 mL) and brine (20 mL) and dried over $MgSO_4$. After evaporation of the solvent in vacuo, the residual oil was chromatographed at low pressure (on 40-60 μm LiChroprep Si 60 with hexane-acetone=10:0.5 as eluant) to afford 2 (1.07 g, 48 %) as an oil. $[\alpha]^{25}_{546}$= -8.8°, $[\alpha]^{25}_{D}$= -6.8° (c=2.89, $CHCl_3$); TLC(C):Rf=0.58; IR (film), ν_{max}: 2970, 2940, 2890, 1730, 1660, 1450, 1380, 1270, 1200, 1145, 1100, 1060 cm^{-1}; ^{1}H-NMR ($CDCl_3$, δ): 0.95 (t, J=7.5Hz, 3H,-CH_3), 1.08 (d, J=6Hz, 3H,-CH_3), 1.65 (br s, 6H,2-CH_3), 1.7-2.8 (br m, 10H,4-CH_2- and 2-CH=), 4.0-4.5 (m, 2H,-CH_2-O), 5.09 (m, 2H,2-CH=C); ^{13}C-NMR ($CDCl_3$): 12.81(-CH_3), 16.26(-CH_3),20.68(-CH_3), 22.85(-CH_3), 24.81(-CH_2-), 26.15(-CH_2-), 27.79(-CH_2-), 29.89(-CH<) 30.98(-CH_2-), 40.16(-CH_2-), 48.32(-CH<), 67.48(O-CH_2-), 120.69(-CH=), 123.79(-CH=), 137.16(=C=), 137.72(=C=), 173.69(C=O);

MS m/e: 265(7)[M+1]$^+$, 264(27)[M$^+$], 207(15), 194(7), 183(27), 181(23), 150(18), 127(17), 123(17), 115(16), 114(100), 99(34), 95(21), 93(16), 83(26), 82(19), 81(23), 69(16), 55(75), 43(17), 41(62); GLC: t_R= 13,84 min (94 %, (2R,3S)-isomer; t_R= 13.67 min, 6 %, (2S, 3S)-isomer; 30 m x 0,25 mm SP-2100 glass capillary column, t_k= 160-260°C, 3°C/min, N_2).

(2R,3S,2'E)-2-(3,7-Dimethyl-2,6-octadienyl)-3-methyl-5-pentanolide (2a)

Enolate generated from 4(31 g, 0.272 mol, 95 % ee) by LiNEt$_2$ (0.272 mol) and geranyl bromide[25] (59.1 g, 0.272 mol) was coupled as describe for the preparation of 2 to give 2a (34.6 g, 51 %) as a pale yellow oil TLC (C):Rf = 0.57 ; $[\alpha]_{546}^{23}$= -8.6°, $[\alpha]_D^{23}$= -6.8° (c=3.35, $CHCl_3$); IR(film), ν_{max}: 2970, 2930, 2880, 1730, 1660, 1450, 1380, 1265, 1140, 1100, 1070 cm^{-1}; ^{1}H-NMR($CDCl_3$, δ): 1.09 (d, J=6Hz, 3H,-CH_3), 1.4-1.9 (br m,3H,-CH_2- and -CH=), 1.60 (s, 3H,-CH_3), 1.65 (s, 3H,-CH_3), 2.03 (mc, 6H, 3-CH_2-), 2.4 (m, 1H, CH-COO), 4.25 (mc, 2H,-CH_2-O), 5.09 (m, 2H,2-CH=C); ^{13}C-NMR($CDCl_3$): 16.23 (C_3,-CH_3), 17.67 (C_7,-CH_3), 20.65 (C_4-CH_3), 25.71 (C_8,), 26.50 (C_5,), 27.67 (C_5), 29.84 (C_4), 30.95 (C_1,), 39.89 (C_4,), 48.26 (C_3), 67.54 (C_6), 120.63 (C_2,), 124.17 (C_6,), 131.31 (C_7,), 137.66 (C_3,), 173.75 (C_2), (main component, ~ 94 %); MS m/e: 250(37) [M$^+$], 207(18), 194(3), 181(30),137(23), 136(23), 127(19), 114(100), 109(26), 99(39), 69(74), 55(25), 41(84); GC: t_R= 11.83 min,(2R,3S)-isomer, 94 % (t_R= 11,64 min,(2S,3S)-isomer, 6 %, 30 m x 0.25 mm SP-2100 column, t_k= 160-260°C, 3°C/min,N_2).

Methyl(2R,1'S,4E,8Z)-5,9-dimethyl-2-(1-methyl-3-hydroxy-propyl)-4,8-undecadienoate (14a)

A solution of 2 (1.05 g, 3.98 mmol) in dry methanol (6 mL) and triethylamine (3 mL) was stirred at room temperature overnight, and then methanol and triethylamine was removed by vacuum evaporation. LPLC of the residue on 40-60 μm LiChroprep Si 60 using hexane-acetone=10:1 as eluant gave 14a(0.88 g, 75 %) as an oil. TLC(C):Rf=0.44; IR (film), ν_{max}: 3350, 2950, 2900, 1730, 1660, 1450, 1380, 1185, 1150, 1100, 1050 cm^{-1}; ^{1}H-NMR ($CDCl_3$, δ): 0.95 (m, (d and t), 6H, 2-CH_3), 1.4-1.9 (br m, 3H,-CH_2- and -CH=), 1.61 (s, 3H,-CH_3), 1.66 (s, 3H,-CH_3), 1.9-2.4 (br m, 9H,4-CH_2- and CH-COO), 3.63 (s, 3H, COO-CH_3), 3.75 (t, J=6.5Hz, 2H,-CH_2-O), 5.07 (m, 2H,2-CH=C); MS m/e: 296(10)[M$^+$], 239(7), 207(10), 195(9), 181(16), 153(8), 135(16), 123(14), 107(14), 97(14), 93(16), 83(44), 82(21), 81(23), 79(16), 69(13), 68(10), 67(22), 55(100), 43(19), 41(65).

Methyl(2R,1'S,4E,8Z)-5,9-dimethyl-2-(1-methyl-3-tetrahydropyranyloxy-propyl)-4,8-undecadienoate (14b)

To a solution of 14a (830 mg, 2.8 mmol) and 2H-dihydropyran (300 mg, 3.6 mmol) in dry dichloromethane (15 mL) was added piridinium tosylate catalyst (30 mg) and the mixture was stirred at room temperature for 6 h. The resulted solution was washed with water (3 mL) and brine (3 mL) and dried over $MgSO_4$. Evaporation of the solvent in vacuo and LPLC of the residue (on LiChroprep Si 60 by hexane-acetone=5:0.1 as eluant) gave 14b (1020 mg, 95 %) as an oil TLC(B):Rf=0.52; IR (film), ν_{max}: 2940, 2880, 1735, 1450, 1440, 1390, 1360, 1330, 1260, 1200, 1170, 1150, 1125, 1080, 1030, 990, 980, 905, 870, 810 cm^{-1}; ^{1}H-NMR ($CDCl_3$,δ): 0.93 (d, J=6Hz, 3H,-CH_3), 0.96 (t, J=7Hz, 3H,-CH_3), 1.4-1.8 (m, 15H, 2-CH_3 and 4-CH_2- and -CH=), 1.8-2.4 (m, 9H, 4-CH_2- and =CH-COO), 3.1-4.0 (m, 4H, 2-CH_2O), 3.64 (s, 3H,COO-CH_3), 4.57 (m, 1H, O-CH-O), 5.05 (m, 2H, 2-CH=C).

Methyl(2R,1'S,4E)-5,9-dimethyl-2-(1-methyl-3-hyroxy-propyl)-4,8-decadienoate (14c)

2a (32.5 g, 0.13 mol) was converted to 14c (29.2 g, 80 %) as described for the preparation of 14a. TLC(C):Rf=0.46; IR (film), ν_{max}: 3400, 2940, 2900, 1730, 1660, 1440, 1380, 1185, 1150, 1100, 1050 cm^{-1}; ^{1}H-NMR($CDCl_3$,δ): 0.95 (d, J=6Hz, 3H,-CH_3), 1.4-1.95 (br m, 3H,-CH_2- and -CH=), 1.60 (br s, 6H, 2-CH_3), 1.66 (s, 3H,-CH_3), 1.9-2.4 (br m, 7H,3-CH_2- and -CH-COO), 3.64 (s, 3H, O-CH_3), 3.65 (t, J=6Hz, 2H, O-CH_2-), 5.06 (m, 2H, 2-CH=C); MS m/e: 282(10)[M$^+$], 250(6), 239(10), 207(16), 195(11), 181(24), 145(13), 134(20), 113(22), 108(31), 96(19), 93(20), 81(29), 79(16), 69(100), 55(22), 43(12), 41(63), 39(8).

Methyl(2R,1'S,4E)-5,9-dimethyl-2-(1-methyl-3-tetrahydropyranyloxy-propyl) -4,8-decadienoate (14d)

14c (26.0 g, 92 mmol) was converted to 14d (32.8 g,97 %) as described for the preparation of 14b. TLC(B):Rf=0.51; IR(film), ν_{max}: 2940, 2875, 1730, 1665, 1450, 1440, 1385, 1360, 1320, 1260, 1200, 1160, 1140, 1120, 1075, 1030, 995, 980, 905, 875, 810 cm^{-1}; ^{1}H-NMR ($CDCl_3$,δ): 0.93 (d,J=6Hz, 3H,-CH_3), 1.4-1.8 (br m, 18H, 3-CH_3 and 4-CH_2- and -CH=), 1.8-2.4 (br m, 7H,3-CH_2- and CH-COO), 3.1-4.0 (m, 4H, 2-CH_2-O), 3.63 (s, 3H,COO-CH_3), 4.55 (m,1H, O-CH-O), 5.05 (m, 2H, 2-CH=C);

(3S,4R,6E,10Z)-4-Hydroxymethyl-1 - tetrahydropyranyloxy-3,7,11-trimethyl-6,10-tridecadiene (15a)

To a stirred suspension of lithium aluminium hydride (0.21 g, 5.4 mmol) in dry ether (8 mL) was added a solution of 14b (1000 mg, 2.7 mmol) in dry ether (3 mL) and the resulting mixture was stirred at room temperature for 1 h. The reaction was quenched by careful dropwise addition of water (3 mL) and then 15 % hydrochloric acid (5 mL) was added to the mixture to dissolve the precipitates. After fast separation the acidic layer was extracted with ether (10 mL) and the combined ethereal solutions were washed with saturated $NaHCO_3$ solution (5 mL) and brine (5 mL). After drying over $MgSO_4$ the solvent was evaporated in vacuo to afford 15a (803 mg, 87 %) as an oil. TLC(C):Rf=0.64; IR (film), ν_{max}: 3370, 2940, 2910, 2860, 1655, 1440, 1425, 1370, 1340, 1250, 1190, 1170, 1120, 1060, 1020, 970, 895, 860, 800 cm^{-1}; ^{1}H-NMR($CDCl_3$,δ): 0.89 (d,J=6Hz, 3H,-CH_3), 0.95 (t, J=7Hz, 3H,-CH_3), 1.3-1.9 (br m, 16H,2-CH_3 and 4-CH_2- and 2-CH=), 1.9-2.4 (m, 8H, 4-CH_2-), 3.1-4.1 (br m, 6H, 3-CH_2-O), 4.54 (m, 1H, O-CH-O), 5.07 (m, 2H, 2-CH=C).

(3S,4R,6E,10Z)-4-Mesyloxymethyl-1-tetrahydropyranyloxy-3,7,11-trimethyl-6,10-tridecadiene (15b)

To a stirred solution of 15a (780 mg, 2.21 mmol) and triethylamine (310 mg, 3.09 mmol) in dry ether (6 mL) was added a solution of mesyl chloride (290 mg, 2.54 mmol) in dry ether (3 mL) at 0°C, and the resulting mixture was stirred at room temperature for 1 h. The mixture was then diluted with ether (6 mL) and 10 % hydrochloric acid (6 mL) was added. After separation and extraction of the acidic layer with ether (6 mL) the combined ethereal solutions were washed with saturated $NaHCO_3$ solution (3 mL) and brine (3 mL) and were dried over $MgSO_4$. Evaporation of the solvent in vacuo yielded 15b (836 mg, 88 %). TLC (D):Rf=0.61; IR (film), ν_{max}: 2960, 2940, 2870, 2860, 1670, 1440, 1430, 1350, 1250, 1200, 1180, 1130, 1110, 1070, 1030, 970, 950, 860, 830, 810 cm^{-1}; ^{1}H-NMR ($CDCl_3$,δ): 0.93 (mc(d and t), 6H, 2-CH_3), 1.4-1.9 (br m, 16H, 2-CH_3 and 4-CH_2 and 2-CH=), 2.0 (mc, 8H, 4-CH_2), 2.88 (s, 3H, SO_2-CH_3), 3.1.-4.0 (br m, 4H, 2-CH_2O), 4.06 (d, J=6Hz, 2H,-CH_2-OMs), 4.55 (m, 1H, O-CH-O), 5.05 (m, 2H, 2-CH=C).

(3S,4R,6E)-4-Hydroxymethyl-1-tetrahydropyranyloxy-3,7,11-trimethyl-6,10-dodecadiene (15c)

Lithium aluminium hydride reduction of 14d (32.8 g, 89 mmol) according to the method desribed at 15a afforded 15 (27.3 g, 90 %) as an oil. TLC (C):Rf=0.63; IR (film), ν_{max}: 3400, 2940, 2920, 2865, 1645, 1440, 1430, 1370, 1340, 1310, 1250, 1190, 1170, 1150, 1120, 1105, 1060, 1015, 970, 895, 860, 800 cm^{-1}; ^{1}H-NMR ($CDCl_3$,δ): 0.92 (d, J=6Hz, 3H,-CH_3), 1.3-1.95 (br m, 19H, 3-CH_3 and 4-CH_2- and 2-CH=), 2.03 (mc, 6H, 3-CH_2-), 3.2-4.2 (br m, 4H, 2-CH_2-O), 3.58 (d, J=6Hz, 2H, O-CH_2-), 4.56 (m, 1H, O-CH-O), 5.11 (m, 2H, 2-CH=C).

(3S,4R,6E)-4-Mesyloxymethyl-1-tetrahydropyranyloxy-3,7,11-trimethyl-6,10-dodecadiene (15d)

Mesylation of 15c (26.3 g, 78 mmol) by the process desribed at 15b gave 15d (29.0 g, 89 % as an oil. TLC (D):Rf=0.61; IR (film), ν_{max}: 2960, 2930, 2870, 1670, 1445, 1350, 1250, 1200, 1180, 1130, 1115, 1070, 1060, 1025, 970, 950, 910, 860, 840, 810 cm^{-1}; ^{1}H-NMR ($CDCl_3$,δ): 0.93 (d, J=6.5Hz, 3H, -CH_3), 1.4-1.9 (br m, 19H, 3-CH_3 and 4-CH_2- and 2-CH=), 2.01 (mc, 6H, 3-CH_2-), 2.94 (s, 3H, SO_2CH_3), 3.2-4.1 (br m, 4H, 2-CH_2-O), 4.11 (d, J=6Hz, 2H, -CH_2-OMs), 4.56 (M, 1H, O-CH-O), 5.08 (m,2H,2-CH=C).

(3S,4R,6E,10Z)-1-Tetrahydropyranyloxy-3,4,7,11-tetramethyl-6,10-tridecadiene (16a)

To a stirred suspension of lithium aluminium hydryde (0.30 g, 7.9 mmol) in dry THF (8 mL) was added a solution of 15b (805 mg, 1.98 mmol) in dry THF (8 mL) and the resulting mixture was refluxed for 1h. After cooling the reaction was quenched by careful dropwise addition of water (4 mL). Then 15 % hydrochloric acid (5 mL) was added to solubilize the precipitate and the mixture was extracted three times with ether (12 mL, each). The combined organic solutions were washed with saturated $NaHCO_3$ solutions (4 mL) and brine (4 mL) and dried over $MgSO_4$. After removal of the solvent in vacuo 16a (586 mg, 90 %) was yielded as an oil. TLC (A):Rf=0.61; IR(film), ν_{max}: 2950, 2930, 2870, 1665, 1445, 1430, 1375, 1350, 1315, 1260, 1200, 1160, 1120, 1110, 1080, 1070, 1030, 990, 980, 900, 870, 810 cm^{-1}; ^{1}H-NMR ($CDCl_3$, δ): 0.83, 0.89, 0.95 (d, d, t, 9H, 3-CH_3), 1.4-1.9 (br m, 16H, 2-CH_3 and 4-CH_2- and 2-CH=), 2.0 (mc, 8H, 4-CH_2-), 3.2-4.1 (br m, 4H, 2-CH_2-O), 4.55 (m, 1H, O-CH-O), 5.10 (m, 2H, 2-CH=C).

(3S,4R,6E,10Z)-3,4,7,11-Tetramethyl-6,10-tridecadien-1-ol (16b)

A solution of 16a (531 mg, 1.58 mmol) and p-toluene sulfonic acid (5 mg) in methanol (10 mL) was stirred at room temperatura overnight. After addition of 10 µL of triethylamine the solution was concentrated in vacuo and the residue was purified by LPLC (on LiChroprep Si 60 with hexane--acetone=10:1 as eluant) to give 16b (373 mg, 94 %) as an oil. TLC (C):Rf=0.48; $[\alpha]_{546}^{22}$=-5.7°, $[\alpha]_{D}^{22}$=-4.5° (c=4,87, $CHCl_3$); IR (film), ν_{max}: 3350, 2970, 2930, 2880, 1660, 1450, 1380, 1110, 1055, 1015, 1000 cm^{-1}; ^{1}H-NMR (CCl_4,δ): 0.83, 0.88, 0.97 (d, d, t, 9H, 3-CH_3), 1.4-1.9 (m, 4H,-CH_2- and 2-CH=), 1.59 (s, 3H,-CH_3), 1.66 (s, 3H,-CH_3) 2.0 (m, 8H, 4-CH_2-), 3.46 (s, 1H, OH), 3.55 (t, J=6Hz, 2H,-CH_2-O), 5.06 (m, 2H, 2-CH=C); MS m/e: 252(13)[M^+], 223(3), 195(12), 179(5), 177(5), 151(7), 137(35), 123(17), 113(13), 109(19), 99(29), 95(49), 83(100), 69(37), 55(79), 41(32).

(3S,4R,6E)-1-Tetrahydropyranyloxy-3,4,7,11-tetramethyl-6,10-dodecadiene (16c)

Lithium aluminium hydride reduction of the mesylate 15d (29.6 g, 72 mmol) according to the method described at 16a yielded 16c (22.0 g,95 %) as an oil. TLC (A):Rf=0.62; IR (film), ν_{max}:2960, 2940, 2870, 1665, 1450, 1440, 1380, 1350, 1320, 1260, 1200, 1160, 1130, 1110, 1070, 1060, 1030, 990, 900, 870, 810 cm^{-1}; ^{1}H-NMR ($CDCl_3$,δ): 0.83 (d, J=6Hz, 3H,-CH_3), 0.88 (d, J=6Hz, 3H,-CH_3), 1.4-1.9 (br m, 19H,3-CH_3 and 4-CH_2- and 2-CH=), 2.02 (m, 6H, 3-CH_2-), 3.2-4.1 (br m, 4H, 2-CH_2-O), 4.57 (m, 1H, O-CH-O), 5.12 (m, 2H, 2-CH=C).

(3S,4R,6E)-3,4,7,11-Tetramethyl-6-10-dodecadien-1-ol (16d)

Deprotection of 16c (21.7 g, 67 mmol) by the process described at 16b but purified by VLC the crude product (on 200 g of 63-200 µm silica gel with hexane-acetone=10:1 as eluant) gave 16d(15.2 g, 96 %) as an oil. TLC (C):Rf=0.49;$[\alpha]_{546}^{23}$=-5.9°,$[\alpha]_{D}^{23}$=-4.6° (c=4.21, $CHCl_3$); IR (film), ν_{max}: 3350, 2980, 2945, 2890, 1660, 1455, 1380, 1205, 1105, 1055, 1010 cm^{-1}; ^{1}H-NMR ($CDCl_3$, δ): 0.82 (d,J=6.5Hz, 3H,-CH_3), 0.87 (d, J=6.5Hz, 3H,-CH_3), 1.4-1.9 (br m, 4H,-CH_2- and 2-CH=), 1.60 (br s, 6H, 2-CH_3), 1.68 (s, 3H,-CH_3), 2.03 (mc, 6H, 3-CH_2-), 3.62 (t, J=6Hz, 2H,-CH_2-O), 5.10 (m, 2H,-CH=C); ^{13}C-NMR ($CDCl_3$): 16.09 (C_4-$\underline{C}H_3$ and C_7-$\underline{C}H_3$), 16.76 (C_3-$\underline{C}H_3$), 17.67 (C_{11}-$\underline{C}H_3$), 25.71 (C_{12}), 26.71 (C_9),

31.53 (C_5), 33.73 (C_3) 35.95 (C_2) 38.78 (C_4), 39.90 (C_8), 61.63 (C_1), 123.91 (C_6), 124.44 (C_{10}), 131.22 (C_{11}), 135.32 (C_7), (main component, ~ 94 %); MS m/e: 238(11)[M^+], 195(12), 177(4), 165(4), 137(7), 123(39), 109(25), 99(24), 95(49), 83(42), 81(37), 69(100), 55(41), 41(48).

(+)-(3S,4R,6E,10Z)-3,4,7,11-Tetramethyl-6,10-tridecadienal (1a; (+)-Faranal)

To a solution of 16b (332 mg, 1.32 mmol) in dry dichloromethane (15 mL) was added piridinium dichromate (505 mg, 1.35 mmol) portionwise at room temperature. After stirring for 3 h the resulting mixture was filtered through a small column containing 15 g of Kieselgel 60 and the column was eluted with ether (50 mL). The resulted solution was then evaporated in vacuo and purified by LPLC (on LiChroprep Si 60 with hexane-acetone=5:0.1 as eluant) to yield 1a (214 mg, 65 %) as an oil that froze keeping at -30°C. Mp.:-25°C, TLC (A):Rf=0.51; $[\alpha]_{546}^{24}$= +19.4°,$[\alpha]_D^{24}$= +17.4° (c= 4.12, $CHCl_3$, > 95 % ee), Lit.[7]:$[\alpha]_D^{23}$= +16.2° (c= 0,5, hexane, 90 % ee); IR (film), ν_{max}: 2970, 2940, 2880, 2720, 1730, 1655, 1450, 1380, 1120, 1080, 1020 cm^{-1}; ^{1}H-NMR ($CDCl_3$,δ): 0.84 (d, J=6.5Hz, 3H,-CH_3), 0.93 (d, J=6.5Hz, 3H,-CH_3), 0.97 (t, J=7Hz, 3H,-CH_3), 1.60 (s, 3H,-CH_3), 1.67 (s, 3H,-CH_3), 1.8-2.6 (br m, 12H,-5-CH_2- and 2-CH=), 5.09 (m, 2H, 2-CH=C), 9.74 (t, J=2Hz,-CHO); ^{13}C-NMR ($CDCl_3$,δ): 12.81 (C_{13}), 16.00 (C_4-$\underline{C}H_3$), 16.12 (C_7-CH_3), 17.55 (C_3-$\underline{C}H_3$),22.87(C_{11}-$\underline{C}H_3$), 24.81 (C_{12}), 26.27 (C_9), 30.97 (C_5), 32.02 (C_3), 38.49 (C_4), 40.11 (C_8), 47.43 (C_2), 123.12 (C_6), 123.91 (C_{10}), 135.96 C_7), 137.18 (C_{11}), 203.21 (C_1), (main component, ~ 94 %); MS m/e: 250(6)[M^+], 232(2), 221(2), 206(2), 203(3), 193(26), 177(3), 175(8), 137(21), 123(20), 107(11), 95(18), 83(100), 69(22), 55(78),43(17), 41(33); HPLC: t_R= 4.12 min (250 x 4.6 mm column,10 µm LiChrosorb RP-18,2.0 ml/min MeOH-water=9:1 eluant, λ=215 mm/; GLC: t_R= 21.11 min, (3S,4R)-isomer, 94 % (t_R=20.87 min, (3S,4S)-isomer, 6 %; 40 m x 0.128 mm OV-1 capillary column, t_k= 180°C, N_2).

(+)-(3S,4R,6E)-3,4,7,11-Tetramethyl-6,10-dodecadienal (1b; (+)-13-Norfaranal)

Oxidation of 16d (10.0 g, 42 mmol) by the method described above afforded 1b (6.63 g 67 %) as an oil. TLC (A):Rf=0.52;$[\alpha]_{546}^{22}$= +19.6°,$[\alpha]_D^{22}$= +17.5° (c=4.46, $CHCl_3$); IR (film), ν_{max}: 2980, 2945, 2880, 2720, 1730, 1660, 1450, 1380, 1115, 1080, 1020 cm^{-1}; ^{1}H-NMR ($CDCl_3$, δ): 0.84 (d, J=6.5Hz, 3H,-CH_3), 0.94 (d, J=6.5Hz, 3H,-CH_3), 1.59 (s, 6H, 2-CH_3), 1.68 (s, 3H, -CH_3), 1.8-2.6 (m, 10H, 4-CH_2- and 2-CH=), 5.10 (m,2H,2-CH=C), 9.75 (t, J=2Hz, 1H,CHO); ^{13}C-NMR ($CDCl_3$): 15.97 (C_4-$\underline{C}H_3$), 16.09 (C_7-$\underline{C}H_3$), 17.55 (c_3-$\underline{C}H_3$), 17.67 (C_{11}-CH_3), 25.71 (C_{12}), 26.62 (C_9), 31.91 (C_5), 32.00 (C_3), 38.49 (C_4), 39.84 (C_8), 47.42 (C_2), 123.09 (C_6), 124.29 (C_{10}), 131.31 (C_{11}), 135.90 (C_7), 203.21 (C_1); (main component, 94 %); MS m/e: 236(4)[M^+], 193(22), 175(5), 149(5), 137(5), 123(33), 109(17), 81(23), 69(100), 41(40), GLC: t_R= 17.46 min, (3S,4R)-isomer, 94 % (t_R= 17.22 min, (3S,4S)-isomer, 6 %; 40 m x 0.128 mm OV-1 capillary column, t_k= 180°C, N_2).

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