A Total Synthesis of (±)-Faranal, the True Trail Pheromone of Pharaoh's Ant, *Monomorium pharaonis*

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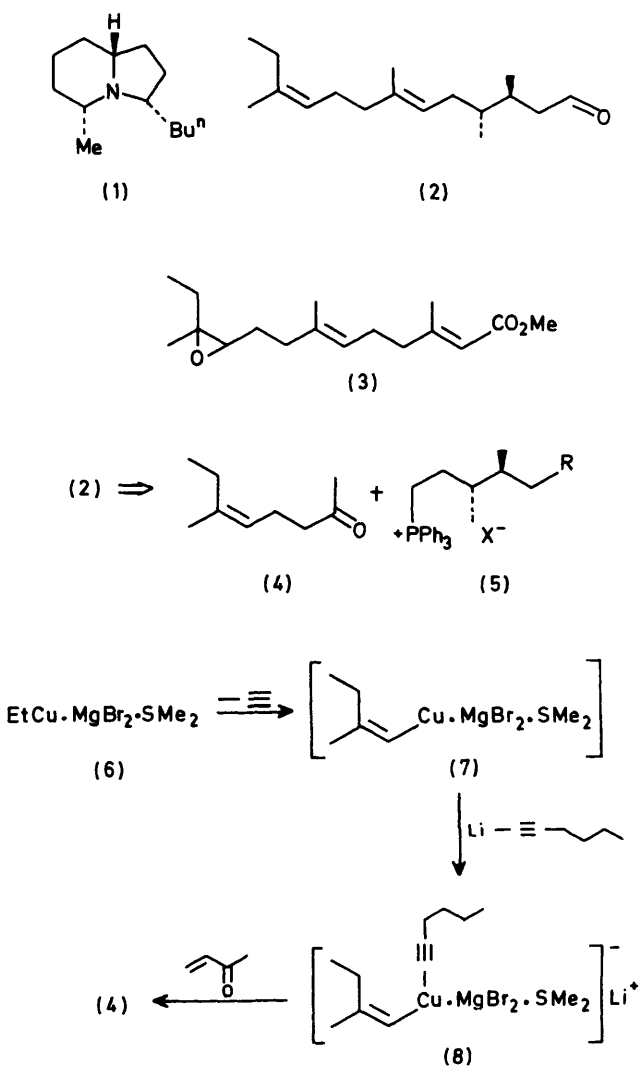
A relatively short total synthesis of the true trail pheromone of Pharaoh's ant, (±)-faranal [(3*SR*,4*RS*)-(6*E*,10*Z*)-3,4,7,11-tetramethyltrideca-6,10-dienal (2)] is reported. The carbon skeleton was assembled by a Wittig condensation between (*Z*)-6-methyloct-5-en-2-one (4) and the 5-carboxypentylphosphonium salt (15). The ketone (4) was prepared in 'one-pot' and in a stereoselective manner using vinyl cuprate chemistry, while the relative stereochemistry of the two methyl substituents in the phosphonium salt (15) was established by using the Diels–Alder adduct (16) of buta-1,3-diene and maleic anhydride, which, after reduction and oxidative cleavage of the resulting *cis*-1,2-dimethylcyclohex-4-ene (18), gave only *meso*-3,4-dimethyladipic acid (19); this in turn was converted into the salt (15) in six straightforward steps.

Pharaoh's ant, *Monomorium pharaonis* L, is a small, brown ant which, although a native of the tropics, occurs in the U.K., generally in buildings, where it depends on artificial heating for survival. Such infestations are particularly dangerous in hospitals, as the animal has been shown to carry a number of pathogenic bacteria, and to be responsible for the contamination of such items as food, laundry, and sterile dressings and even for the infection of wounds of post-operative patients.[1] Its occurrence in environments such as artificial heating units tends to preclude its control by many conventional insecticides,[2] although some success has been achieved using juvenile hormone analogues.[3]

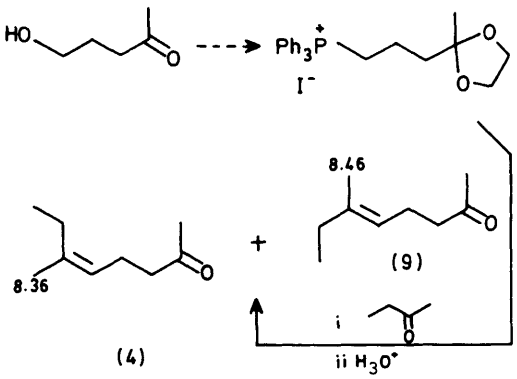
The ants are known to follow lengthy trails (at least 72 ft [1]), presumably marked by a pheromone; clearly such a compound, if non-toxic, could be of use in their control. In the early 1970's Ritter *et al.*[4] isolated an alkaloidal fraction (the monomorines), having trail pheromone activity, from the poison gland of the ant. Their work, together with the synthetic studies of Sonnet *et al.*[5] and some trail-following tests carried out by Edwards and Pinniger,[6] led to the conclusion that the major active pheromone was the (3*S*,5*R*,9*R*)-octahydroindolizine (1). However, later work by the Dutch group led to the isolation of a much more active trail pheromone from the Dufour's gland of pharaoh's ant.[7] This compound, given the trivial name of faranal, and now regarded as the true trail pheromone of the ant (trails followed at concentrations of <1 pg cm^{-1}) was shown to be a (6*E*,10*Z*)-3,4,7,11-tetramethyltrideca-6,10-dienal. The two chiral centres in the molecule were originally thought [7] to have the (3*S*,4*S*) or (3*R*,4*R*) geometry, but further examination of the ozonolysis products of faranal [8,9] established them as (3*S*,4*R*) or (3*R*,4*S*). Subsequently, a rather unusual, small-scale, bio-organic synthesis showed conclusively that natural (+)-faranal is the (3*S*,4*R*)-isomer (2).[9] This was further confirmed by a more conventional if somewhat lengthy total synthesis, involving a classical resolution step.[10] The structure of faranal is very reminiscent of Juvenile Hormone II (3),[11] and herein, we report a relatively brief total synthesis of racemic faranal, (3*SR*,-4*RS*)-(2), which could be of use in the preparation of reasonable quantities of the compound.[12] A similar racemic mixture has been reported to possess good trail-following activity [13] and hence could be useful in various methods for controlling the ant.

Our strategy was to construct the central double bond of (2) using a Wittig condensation. Therefore we required the (*Z*)-ketone (4) and a suitable phosphonium salt (5) in which the distal substituent, R, could be readily converted into the aldehyde function of (2). [In formula (5) and in all subsequent diagrams, where applicable, the structures are racemates.]

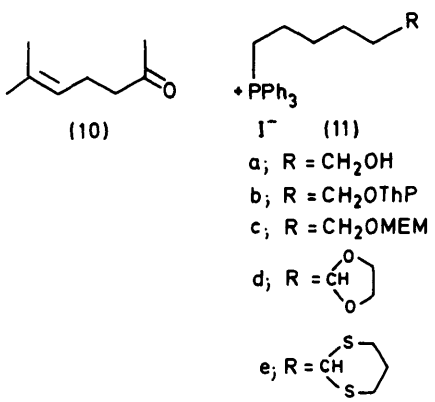


Scheme 1.

The ketone (4) was prepared by the method of Helquist *et al.*,[14] by a selective *syn*-addition of complex (6), formed from ethyl magnesium bromide and cuprous bromide–dimethyl sulphide, to propyne followed by conversion of the resulting vinyl



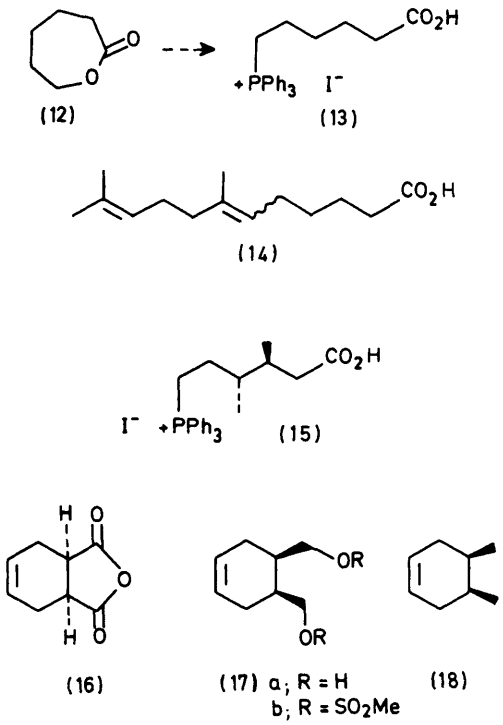
Scheme 2.



Thp — tetrahydropyranyl, MEM — methoxyethoxymethyl

cuprate (7) into the ' ate ' complex (8), using hex-1-ynyl-lithium, and finally condensation with methyl vinyl ketone (Scheme 1).* The overall yield of the ketone (4) was only 29% but this was compensated for by the fact that the compound was assembled in ' one-pot ' from simple materials and, crucially, that it was >98% stereochemically pure, according to g.l.c. and ^{1}H n.m.r. data. For comparison, we prepared a mixture of (4) and the (*E*)-isomer (9) by a previously described Wittig condensation (Scheme 2).[15] The two isomers could be cleanly resolved by g.l.c. and in the ^{1}H n.m.r. spectrum of the mixture, the vinyl methyl resonances of (4) and (9) appeared at τ 8.36 and 8.46 respectively. Using these methods of analysis, we did not detect any of the (*E*)-isomer (9) in the sample of (4), prepared as shown in Scheme 1.

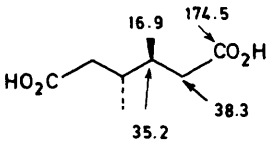
We next examined the key Wittig condensation which we planned to use for the construction of the central double bond of faranal. For this, we used the commercially available ketone (10) and the phosphonium salts (11a—e), which were all prepared from 1-chloro-6-hydroxyhexane using standard methodology. Under a variety of conditions, the ylides derived from (11a—e) gave only low yields (0—20%) of the desired olefins when treated with (10). However, condensation of compound (10) with the 5-carboxypentylphosphonium salt (13) [16] [derived from commercial ε-caprolactone (12) by sequential reactions with hydrogen bromide–sulphuric acid,[17] sodium iodide and triphenylphosphine] using two equivalents of sodium hydride in dimethyl sulphoxide did produce the desired product (14) in *ca.* 70% yield. Therefore, for a synthesis of (±)-faranal (2), we required the phosphonium salt (15). As (15) can be regarded as a 1,6-disubstituted hexane, an obvious precursor was an appropriately substituted cyclohexene; such a precursor also offered the possibility of controlling the final, relative stereochemistries of the two methyl substituents in (15).



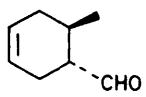
The Diels–Alder adduct (16) of buta-1,3-diene and maleic anhydride, a cheap, commercially available compound, was chosen as the starting material. The anhydride (16) was reduced to the corresponding diol (17a) using lithium aluminium hydride and thence converted into the bis-mesylate (-methanesulphonate) (17b) according to the procedures described in detail by Photis and Paquette [18] for the corresponding cyclohexane derivatives. Further reduction of (17b), again using lithium aluminium hydride, then gave the *cis*-dimethylcyclohexene (18). A number of reagents (*e.g.* ozone, osmium tetraoxide, potassium permanganate in acetone) were then examined for the oxidative cleavage of (18) to the *meso*-diacid (19). In our hands, the best procedure was found to be oxidation by potassium permanganate under phase-transfer conditions.[19] An additional advantage of this method is that the by-product, manganese dioxide, is reduced to more easily handled manganous salts, using sodium sulphite, before isolation of the diacid. The *meso*-diacid (19) was >99% pure according to ^{13}C n.m.r. spectroscopy. A sample of the corresponding ±-diacid (22) was prepared from the commercially available aldehyde (20; *ca.* 70% *trans*-isomer) by sequential reduction of the aldehyde group, tosylation of the resulting alcohol, and further reduction to the cyclohexene (21) followed by oxidative cleavage, as for (18), and finally fractional crystallisation from water. The two isomers were clearly distinguished by ^{13}C n.m.r. spectroscopy [see data associated with formulae (19) and (22)].

The *meso*-diacid (19) was then converted into the half-ester (23) in excellent yield by continuous extraction of a mixture of (19) and aqueous ethanol containing sulphuric acid.[20] This method was superior to other partial esterification procedures and to various partial saponifications of diesters derived from (19). Reduction of the half-ester (23) with borane–tetrahydrofuran [21] then provided the hydroxy-ester (24a) which

* The formulae (6)—(8) only represent the stoicheiometry of the reaction scheme and do not necessarily represent the actual structures of these intermediates.



(19)



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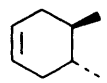

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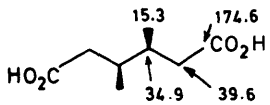

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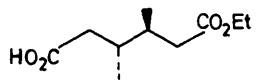

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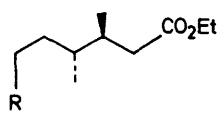
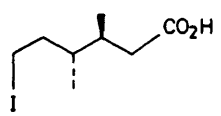
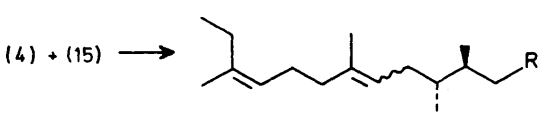


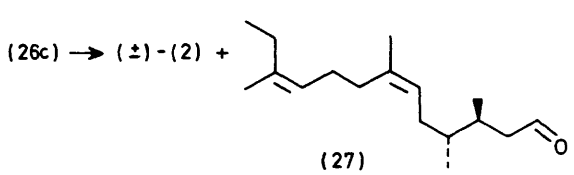


(24) a; R = OH
b; R = $OSO_2C_6H_4Me$-*p*
c; R = I

(25)



(26) a; R = CO_2H
b; R = CO_2Me
c; R = CH_2OH



(27)

was converted into the iodo-ester (24c), *via* the tosylate (toluene-*p*-sulphonate) (24b), using established methodology. Saponification of the iodo-ester (24c) then gave the iodo-acid (25) which was quaternized with triphenylphosphine to give the required phosphonium salt (15).

The Wittig condensation between the salt (15) and the (*Z*)-ketone (4) proceeded as expected to give the desired acids (26a) which were esterified with ethereal diazomethane and filtered through silica gel to remove some residual phosphorus-containing impurities. In this way, the esters (26b), pure by ^{1}H n.m.r. spectroscopy and g.l.c., were obtained in 64% yield from the ketone (4). The isomer ratio of the esters was found to be (6*E*) : (6*Z*) = 46 : 54 by g.l.c. analysis, assuming that the order of elution was the same as for faranal (2) and its (6*Z*)-isomer (27). The esters (26b) were then reduced to the corresponding alcohols (26c) using lithium aluminium hydride and finally oxidised to the aldehydes (2) and (27) using pyridinium chlorochromate.[22] The aldehydes were then separated by preparative scale g.l.c. to give (±)-faranal (2), which exhibited identical spectral data with those reported for the natural material,[7,10] and the (6*Z*)-isomer (27). This isomer was readily distinguished from (2) by ^{1}H n.m.r. spectroscopy, both in the overall appearance of the spectra, and particularly by the occurrence of two, separate broadened triplets at τ 4.80 and 4.88 for the two olefinic protons [in faranal (2), these occur as overlapping triplets at τ 4.82 and 4.85] and of the 7-methyl resonance at τ 8.32 (τ 8.45 in faranal).

An alternative synthesis of (±)-faranal has been achieved by Baker, Billington, and Ekanayake.[23] They used similar strategies to ours for the stereoselective construction of the (10*Z*) double bond and to establish the relative stereochemistries of the 3- and 4-methyl groups, but made further use of vinyl cuprate chemistry in a stereoselective synthesis of the (6*E*) double bond.

Experimental

M.p.s were determined on a Kofler hot-stage apparatus, and are corrected. I.r. spectra were obtained using a Perkin-Elmer 710B spectrometer. ^{1}H N.m.r. spectra were obtained at 90 MHz using a Perkin-Elmer R32 spectrometer or a Bruker WM-250 operating at 250 MHz; the latter instrument was also used for the ^{13}C n.m.r. spectra. Tetramethylsilane was used as the internal standard throughout. Mass spectra and molecular weights were determined using an A.E.I. MS 902 spectrometer.

All organic solutions were dried over anhydrous magnesium sulphate. Ether refers to diethyl ether throughout.

(*Z*)-6-*Methyloct-5-en-2-one* (4).—A solution of cuprous bromide–dimethyl sulphide complex [24] (6.16 g, 30 mmol) in dimethyl sulphide (50 ml) and ether (20 ml) was added dropwise to a stirred solution of ethylmagnesium bromide [from magnesium (0.69 g, 30 mmol) and ethyl bromide (2.25 ml, 30 mmol)] in ether (25 ml), maintained at −50 °C under nitrogen. The resulting yellow-brown suspension was stirred at −45 °C for 1.5 h, then cooled to −65 °C while gaseous propyne (670 ml, *ca.* 30 mmol) was condensed into the solution at a flow rate of 75 ml min^{-1}. The mixture was warmed to −30 °C and stirred at this temperature for 1.75 h. The resulting dark green solution was cooled to −78 °C and treated with a freshly prepared suspension of hex-1-ynyl-lithium in ether–hexane [prepared by adding Bu^{n}Li (18 ml of a 1.66M-solution in hexane, 30 mmol) to an ice-cold solution of hex-1-yne (3.44 ml, 30 mmol) in ether (50 ml)]. The mixture was stirred at −78 °C for 0.5 h, then freshly distilled methyl vinyl ketone (2.43 ml, 30 mmol) was added; after 1 h at −78 °C, the mixture was warmed to room temperature and treated with ether (50 ml) and water (5 ml), then washed with water (2 × 70 ml), dried, filtered and evaporated under reduced pressure (T < 30 °C). The semi-solid residue was stirred with n-pentane, then filtered and evaporated. Distillation of the residue then gave the *ketone* (4) as a colourless oil (1.2 g, 29%), b.p. 88—90 °C at 17 mmHg, $\nu_{max.}$ (film) 1 716 cm^{-1}, τ($CDCl_3$) 4.96 (bt, *J ca.* 7 Hz, =C*H*CH_2), 7.56—7.77 (m, 2 × CH_2), 7.91 (CH_3-CO), 7.98 (q, *J* 7 Hz, CH_2CH_3), 8.36 (bs, CH_3C=), and 9.05 (t, *J* 7 Hz, CH_2CH_3); *m/e* 140(1%), 82(23), 67(27), 55(51), and 43(100) (Found: C, 77.5; H, 11.7. $C_9H_{16}O$ requires C, 77.1; H, 11.4%) (Found: M^+, 140.1209. $C_9H_{16}O$ requires M, 140.1201).

The ketone was stereochemically pure according to ^{1}H n.m.r. and g.l.c. A mixture of (4) and its (6*E*)-isomer (9), prepared by a Wittig procedure,[15] could be clearly separated by g.l.c. (5% OV17, 80 °C) and the (6*E*)-isomer (9) displayed a vinyl methyl resonance at τ($CDCl_3$) 8.46.

cis-1,2-*Dimethylcyclohex-4-ene* (18).—Commercial *cis*-cyclohex-4-ene-1,2-dicarboxylic anhydride (16) was reduced to 1,2-bis(hydroxymethyl)cyclohex-4-ene (17a) and thence converted into the bis-mesylate (17b) using the procedures described by Photis and Paquette for the corresponding cyclohexane derivatives.[18] Similar yields were obtained. The bis-

mesylate (17b) had m.p. 86—87 °C (MeOH) (lit.,[25] m.p. 82.5—83 °C), τ($CDCl_3$) 4.32 (bs, 2 × =CH), 5.76 (m, 2 × OCH_2), 6.94 (2 × $MeSO_2$), and 7.44—8.20 (m, 6 H).

The bis-mesylate (59.6 g, 0.2 mol) was added to a stirred suspension of lithium aluminium hydride (23 g, 0.6 mol) in ether (800 ml). The mixture was refluxed for 48 h, then cooled and treated with methanol (5 ml), water (100 ml), and 2M-hydrochloric acid (200 ml). The ether layer was separated and the aqueous layer extracted with ether (2 × 50 ml). The combined ether solutions were washed with water (1 × 100 ml), 2M-aqueous potassium hydroxide (2 × 100 ml), and saturated brine (1 × 100 ml), then dried and fractionally distilled, collecting the cyclohexene (18) as a colourless oil (15 g, 68%), b.p. 121—124 °C (lit.,[25,26] b.p. 123—124.2 °C); τ(CCl_4) 4.63 (bs, 2 × =CH), 7.80—8.47 (m, 6 H), and 9.15 (d, *J* 7 Hz, 2 × $CHCH_3$).

meso-3,4-*Dimethylhexane*-1,6-*dioic Acid* (19).—A mixture of potassium permanganate (56.9 g, 0.35 mol), water (350 ml), benzene (120 ml), and tetra-n-butylammonium hydrogen sulphate (1 g) was vigorously stirred and to it was added a solution of *cis*-1,2-dimethylcyclohex-4-ene (18) (13.0 g, 0.118 mol) in benzene (70 ml) at such a rate that the temperature remained just below 40 °C.[19] After the addition, the mixture was stirred until it cooled to room temperature, then further cooled in an ice-bath and treated with sodium sulphite (70.4 g) followed by sufficient concentrated hydrochloric acid to completely reduce the precipitated manganese dioxide. The mixture was filtered and the solid thoroughly washed with ether. The combined filtrate was separated and the aqueous layer extracted with ether (4 × 100 ml). The combined organic solutions were dried and evaporated. Crystallisation of the residue from water gave the diacid (19) as colourless prisms (12.7 g, 62%), m.p. 134.5—135.5 °C (lit.,[27] m.p. 133—134 °C), τ[$(CD_3)_2CO$] 7.56—8.22 (m, 6 H), and 9.06 (d, *J* 7 Hz, 2 × $CHCH_3$); δ(^{13}C) [$(CD_3)_2CO$] 16.9, 35.2, 38.3, and 174.5 p.p.m.

(±)-3,4-*Dimethylhexane*-1,6-*dioic Acid* (22).—Commercial 1-formyl-2-methylcyclohex-4-ene (20) (*ca.* 70% *trans*) (49.6 g, 0.4 mol) in ether (100 ml) was added dropwise to a vigorously stirred suspension of lithium aluminium hydride (5 g) in ether (500 ml) at such a rate that the ether gently refluxed. After a further 0.5 h, the mixture was worked up in the usual way to give a *cis–trans* mixture of 1-hydroxymethyl-2-methylcyclohex-4-ene (46 g), b.p. 86—90 °C at 16 mmHg. The foregoing alcohol (46 g, 0.365 mol) was added dropwise to an ice-cold solution of toluene-*p*-sulphonyl chloride (73 g) in dry pyridine (400 ml) and the resulting solution left at 0 °C for 16 h, then poured into water (2 l) and ether extracted (3 × 200 ml). The combined ether solutions were washed with water (1 × 300 ml), 2M-hydrochloric acid (2 × 200 ml), and saturated brine (1 × 200 ml), then dried and evaporated to leave the crude tosylate (97 g) which was thoroughly dried azeotropically using benzene. A solution of the tosylate (70 g) in tetrahydrofuran (100 ml) was added to a vigorously stirred ice-cold suspension of lithium aluminium hydride (10.3 g) in tetrahydrofuran (THF) (250 ml). The mixture was stirred for 48 h, then refluxed for 1 h, cooled and diluted with methanol (5 ml), water (1 l) and 2M-hydrochloric acid (500 ml), and extracted with n-pentane (3 × 100 ml). The combined extracts were washed with water (3 × 100 ml) and saturated brine, then dried and fractionally distilled to give a *cis–trans* mixture of 1,2-dimethylcyclohex-4-ene (21) (13 g), b.p. 119—126 °C.

The cyclohexene was oxidatively cleaved using potassium permanganate under phase-transfer conditions, as described above, to give 3,4-dimethylhexane-1,6-dioic acid (m.p. 109—111 °C) containing *ca.* 70% of the (±)-isomer. Crystallisation (5×) from water then provided a pure sample of the ±-isomer (22), m.p. 115—116 °C (lit.,[27] m.p. 115—116.5 °C), δ(^{13}C) [$(CD_3)_2CO$] 15.3, 34.9, 39.6, and 174.6 p.p.m.

Ethyl (3SR,4RS)-5-*Carboxy*-3,4-*dimethylpentanoate* (23).—A mixture of *meso*-3,4-dimethylhexane-1,6-dioic acid (19) (9.5 g, 55 mmol), water (360 ml), ethanol (64 ml), and concentrated sulphuric acid (8 ml) was continuously extracted with cyclohexane for 10 days.[20] The cooled cyclohexane solution was extracted with 7% aqueous potassium hydroxide (4 × 25 ml) and water (1 × 25 ml), then dried and evaporated to leave *meso*-diethyl 3,4-dimethylhexane-1,6-dioate (0.6 g, crude). The combined aqueous extracts were washed once with ether then acidified with solid citric acid. (Acidification with dilute hydrochloric acid tended to cause rapid hydrolysis of the half-ester.) The mixture was then ether extracted (3 × 100 ml) and the combined extracts were dried and evaporated, and the residue extracted with light petroleum (b.p. 40—60 °C) (4 × 50 ml). A small amount (0.4 g) of the starting diacid (19) remained undissolved. The light petroleum extracts were evaporated and the residue distilled to give the *half-ester* (23) (9.1 g, 90%) as a colourless oil, b.p. 119—120 °C at 0.02 mmHg, $\nu_{max.}$ (film) 1 740 and 1 708 cm^{-1}; τ($CDCl_3$) 5.85 (q, *J* 7 Hz, OCH_2CH_3), 7.40—8.05 (m, 6 H), 8.72 (t, *J* 7 Hz, OCH_2CH_3), 9.01 (d, *J* 7 Hz, $CHCH_3$), and 9.05 (d, *J* 7 Hz, $CHCH_3$), *m/e* 157(10%), 143(13), 115(9), 97(8), 89(26), 73(19), and 69(100) (Found: C, 59.2; H, 9.0. $C_{10}H_{18}O_4$ requires C, 59.4; H, 8.9%).

Ethyl (3SR,4RS)-6-*Hydroxy*-3,4-*dimethylhexanoate* (24a).—Borane–THF (33.2 ml of 1M-solution) was added dropwise to a stirred solution of ethyl (3*SR*,4*RS*)-5-carboxy-3,4-dimethylpentanoate (23) (6.6 g, 33 mmol) in THF (30 ml), maintained at −20 °C under nitrogen.[21] The resulting solution was allowed to warm slowly to room temperature and stirred overnight, then cooled in ice and treated with water (30 ml) and anhydrous potassium carbonate (14 g). The mixture was stirred for 5 min, then the organic layer was separated and the aqueous layer extracted with ether (2 × 30 ml). The combined organic solutions were washed with saturated brine (1 × 20 ml), dried, evaporated, and distilled to give the *hydroxy-ester* (24a) as a colourless oil (5.7 g, 92%), b.p. 108—110 °C at 0.2 mmHg, $\nu_{max.}$(film) 3 400 and 1 740 cm^{-1}; τ($CDCl_3$) 5.85 (q, *J* 7 Hz, OCH_2CH_3), 6.32 (bt, *J ca.* 7 Hz, CH_2OH), 7.58—8.08 (m, 2 × CH_2), 8.27—8.57 (m, 2 × $CHCH_3$), 8.72 (t, *J* 7 Hz, $O{\cdot}CH_2CH_3$), 9.05 (d, *J* 7 Hz, $CHCH_3$), and 9.09 (d, *J* 7 Hz, $CH{\cdot}CH_3$); *m/e* 188 (<1%), 143(15), 115(31), 88(54), 83(51), and 69(100) (Found: C, 63.4; H, 10.6. $C_{10}H_{20}O_3$ requires C, 63.8; H, 10.6%).

Ethyl (3SR,4RS)-6-*Iodo*-3,4-*dimethylhexanoate* (24c).—Ethyl (3*SR*,4*RS*)-6-hydroxy-3,4-dimethylhexanoate (24a) (5.7 g, 30.3 mmol) was added dropwise to an ice-cold solution of toluene-*p*-sulphonyl chloride (5.82 g, 30.5 mmol) in dry pyridine (50 ml). The resulting solution was stored at 0 °C overnight, then diluted with water (300 ml) and extracted with ether (3 × 70 ml). The combined extracts were washed with water (1 × 100 ml), 2M-hydrochloric acid (2 × 50 ml), saturated brine (1 × 50 ml), and finally dried and evaporated to leave the crude *tosylate* (24b) (9.5 g, 91%) as a colourless oil, $\nu_{max.}$ (film) 1 732 cm^{-1}, τ($CDCl_3$) 2.03 (d, *J* 8 Hz, 2 H), 2.46 (d, *J* 8 Hz, 2 H), 5.82 (q, *J* 7 Hz, OCH_2CH_3), 5.84 (t, *J* 7 Hz, CH_2OTs), 7.49 (CH_3Ar), 7.66—8.20 (m, 2 × CH_2), 8.26—8.60 (m, 2 × $CHCH_3$), 8.74 (t, *J* 7 Hz, OCH_2CH_3), 9.13 (d, *J* 7 Hz, $CHCH_3$), and 9.20 (d, *J* 7 Hz, $CHCH_3$).

The tosylate (9.5 g) was dried azeotropically using benzene, then added to a solution of sodium iodide (16.8 g) in dry acetone (95 ml). The mixture was stirred at room temperature

for 1.5 h, then refluxed for 0.5 h. The cooled solution was filtered and the residue thoroughly washed with ether. The combined filtrate and washings were evaporated and the residue partitioned between ether (70 ml) and water (70 ml). The ether layer was separated and the aqueous layer extracted with fresh ether (2 × 30 ml). The combined ether solutions were washed with 1% aqueous sodium thiosulphate (1 × 30 ml) and saturated brine (1 × 30 ml), then dried, evaporated, and the residue distilled to give the *iodo-ester* (24c) as a colourless oil (7.8 g, 94%), b.p. 96—98 °C at 0.5 mmHg, $\nu_{max.}$(film) 1 740 cm^{-1}, τ($CDCl_3$) 5.85 (q, *J* 7, Hz OCH_2CH_3), 6.83 (m, CH_2I), 7.61—8.14 (m, 2 × CH_2), 8.29—8.50 (m, 2 × $CHCH_3$), 8.75 (t, *J* 7 Hz, OCH_2CH_3), 9.09 (d, *J* 7 Hz, $CH{\cdot}CH_3$), and 9.15 (d, *J* 7 Hz, $CHCH_3$); *m/e* 298 (<1%), 253 (24), 171 (94), 125 (28), 115 (29), 97 (60), 88 (82), 83 (100), and 69 (59) (Found: C, 40.3 H, 6.2. $C_{10}H_{19}IO_2$ requires C, 40.3; H, 6.4%).

[(3SR,4RS)-5-*Carboxy*-3,4-*dimethylpentyl*]*triphenylphosphonium Iodide* (15).—Ethyl (3*SR*,4*RS*)-6-iodo-3,4-dimethylhexanoate (24c) (3.0 g) was added to an ice-cold solution of potassium hydroxide (1.2 g) in ethanol (50 ml) and water (8 ml), and the mixture stirred until t.l.c. indicated that saponification was complete (*ca.* 1.5 h). The solution was concentrated under reduced pressure, then diluted with water (30 ml) and washed with ether (2 × 10 ml). The aqueous solution was cooled and acidified with concentrated hydrochloric acid, then extracted with ether (4 × 15 ml). The combined extracts were dried and evaporated to leave the crude acid (25) (2.3 g), τ($CDCl_3$) 6.83 (m, CH_2I), 7.57—8.50 (m, 6 H), 9.05 (d, *J* 7 Hz, $CHCH_3$), and 9.14 (d, *J* 7 Hz, $CHCH_3$), which was refluxed with triphenylphosphine (2.3 g) in benzene for three days. The cooled mixture was evaporated to dryness and the residue crystallised from acetone–light petroleum (b.p. 60—80 °C) containing a few drops of methanol to give the *salt* (15) as colourless prisms (3.2 g, 70%), m.p. 218—219 °C (Found: C, 58.8; H, 6.0. $C_{26}H_{30}IO_2P$ requires C, 58.7; H, 5.6%).

(6E)- *and* (6Z)-*Isomers of* (3SR,4RS)-(10Z)-3,4,7,11-*Tetramethyltrideca*-6,10-*dienal* [(±)-*Faranal* (2) *and the* (6Z)-*Isomer* (27)].—Sodium hydride (0.2 g of a 50% dispersion, 4 mmol) was added to dry dimethyl sulphoxide (20 ml) and the mixture stirred at 70 °C under nitrogen for 0.75 h, by which time a clear solution was obtained. The solution was cooled to room temperature and to it was added the phosphonium salt (15) (1.1 g, 2.06 mmol). The resulting bright red solution was stirred for 5 min, then treated with (*Z*)-6-methyloct-5-en-2-one (4) (0.28 g, 2 mmol) after which the mixture was heated to 50 °C and maintained at this temperature for 1 h. The cooled mixture was diluted with water (50 ml), washed with chloroform (3 × 30 ml), acidified with concentrated hydrochloric acid and ether extracted (3 × 20 ml). The combined extracts were washed with water (2 × 20 ml), and saturated brine (1 × 20 ml), then dried and evaporated to leave a crude mixture of the (6*E*)- and (6*Z*)-acids (26a) which was treated with ethereal diazomethane. After 1 h, the excess of diazomethane was destroyed by adding acetic acid and the resulting solution was filtered through silica gel. Evaporation of the filtrate left a mixture of the (6*E*)- and (6*Z*)-esters (26b) (0.36 g) as a colourless oil, τ($CDCl_3$) 6.30 and 6.33 (CO_2Me). Analytical g.l.c. of this mixture using a 5 ft × ¼ in 10% OV 17 column at 170 °C showed the ratio of (6*E*) : (6*Z*) to be 46 : 54 assuming that the order of elution was the same as for faranal (2) and the (6*Z*)-isomer (27).

A solution of the mixed esters (0.34 g) in dry ether (2 ml) was added dropwise to a vigorously stirred suspension of lithium aluminium hydride (0.07 g) in ether (5 ml). After 0.5 h, saturated aqueous ammonium chloride (5 ml) was added and the ether layer separated. The aqueous layer was extracted with ether (2 × 5 ml) and the combined ether solutions washed once with saturated brine (5 ml) then dried and evaporated to leave a mixture of the (6*E*)- and (6*Z*)-alcohols (26c) (0.25 g) as a colourless oil, τ($CDCl_3$) 6.17—6.42 (m, CH_2OH).

A solution of the foregoing alcohols (0.09 g) in dry dichloromethane (1 ml) was added dropwise to a vigorously stirred, ice-cold suspension of pyridinium chlorochromate [22] (0.155 g) in dichloromethane (5 ml). The cooling bath was removed and, after 1 h, dry ether (40 ml) was added and the mixture filtered through Florisil. The filtrate was evaporated and the residue (0.063 g; virtually pure by ^1H n.m.r.) separated by preparative g.l.c., using a 10 ft × ¼ in 20% carbowax-20M on chromosorb W column at 200 °C, to give (±)-*faranal* (2) (eluted second) as a colourless oil, $\nu_{max.}$ (film) 2 850, 2 700, and 1 729 cm^{-1}; τ(250 MHz; C_6D_6) 0.62 (dd, *J* 2.75 and 1.75 Hz, CH_2CHO), 4.82 (bt, *J ca.* 7 Hz, $=CHCH_2$), 4.85 (bt, *J ca.* 7 Hz, $=CHCH_2$), 7.8—8.3 (m, 8 H), 7.98 (q, *J* 7.5 Hz, 12-CH_2), 8.31 (d, *J* 1 Hz, 11-CH_3), 8.45 (bs, 7-CH_3), 8.63—8.78 (m, 2 × $CHCH_3$), 9.05 (t, *J* 7.5 Hz, 13-CH_3), 9.27 (d, *J* 7 Hz, $CHCH_3$), and 9.31 (d, *J* 7 Hz, $CHCH_3$) (Found: M^+, 250.2307. $C_{17}H_{30}O$ requires *M*, 250.2296), and the (6*Z*)-isomer (27) (eluted first), as a colourless oil, $\nu_{max.}$ (film) 2 850, 2 705, and 1 730 cm^{-1}; τ(250 MHz; C_6D_6) 0.63 (dd, *J* 2.75 and 1.5 Hz, CH_2CHO), 4.80 (bt, *J ca.* 7 Hz, $=CHCH_2$), 4.88 (bt, *J ca.* 7 Hz, $=CHCH_2$), 7.8—8.25 (m, 8 H), 7.97 (q, *J* 7.5 Hz, 12-CH_2), 8.29 (d, *J* 1.25 Hz, 11-CH_3), 8.32 (d, *J* 1.25 Hz, 7-CH_3), 8.61—8.79 (m, 2 × $CHCH_3$), 9.04 (t, *J* 7.5 Hz, 13-CH_3), 9.27 (d, *J* 7 Hz, $CHCH_3$), and 9.29 (d, *J* 7 Hz, $CHCH_3$) (Found: M^+, 250.2276).

The data reported for compound (2) are indistinguishable from those reported [7,10] for natural (+)-faranal.

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