Synthesis and the absolute configuration of the sesquiterpene aldehyde tridensenal from the Taiwanese liverwort *Bazzania tridens*

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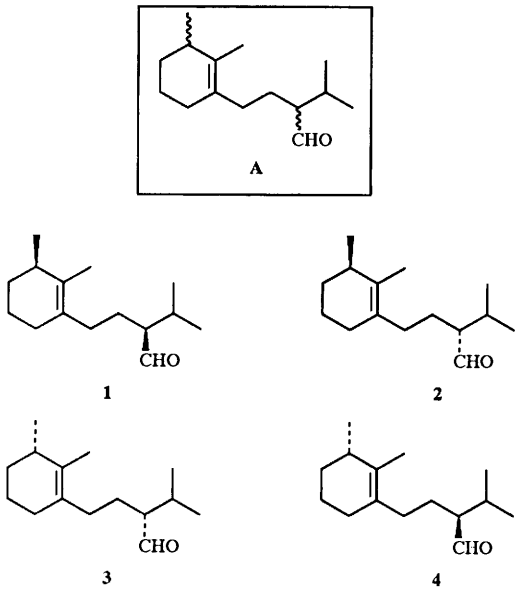
The absolute configuration of the sesquiterpene aldehyde tridensenal isolated from the Taiwanese liverwort *Bazzania tridens* has been determined by a total synthesis of the optically active compound as well as its diastereoisomer to have *S,R* configuration starting from (−)- and (+)-menth-1-ene and (+)-pulegone, respectively.

Liverworts still provide a variety of new terpenoids including those having novel skeletons.[1] Recently Wu *et al.*, isolated the sesquiterpene aldehyde tridensenal from the Taiwanese liverwort *Bazzania tridens*[2] and reported a planar structure for it as depicted in **A**.[3] Because this molecule has two, separate, chiral



centres, it is not possible to establish its relative configuration by use of spectroscopic techniques alone. Separation of a synthetic and diastereoisomeric mixture of tridensenal[3] proved impossible, the ^{1}H NMR spectrum of which was closely similar to that of natural tridensenal. The ^{13}C NMR spectrum of the diastereoisomeric mixture showed more than 15 peaks, few of which are congested in the highfield area. In view of these problems and in order to establish its absolute configuration we have synthesized optically active tridensenal and its diastereoisomer from (−)- and (+)-menth-1-ene and (+)-pulegone.

Results and discussion

It was recognized that natural tridensenal must be one of the four possible isomers, **1**–**4**, of which **1** and **3** and **2** and **4** are enantiomeric pairs. Compound **1** can be synthesized from (−)-menth-1-ene **5** and (+)-pulegone **7** (see Scheme 1). Since (+)-menth-1-ene is also available as a starting material compound **2** can be prepared in a similar manner. Therefore, the synthesis of compounds **1** and **2** and comparison of their spectral data and specific rotations with those of tridensenal enable the absolute configuration of the natural product to be determined.

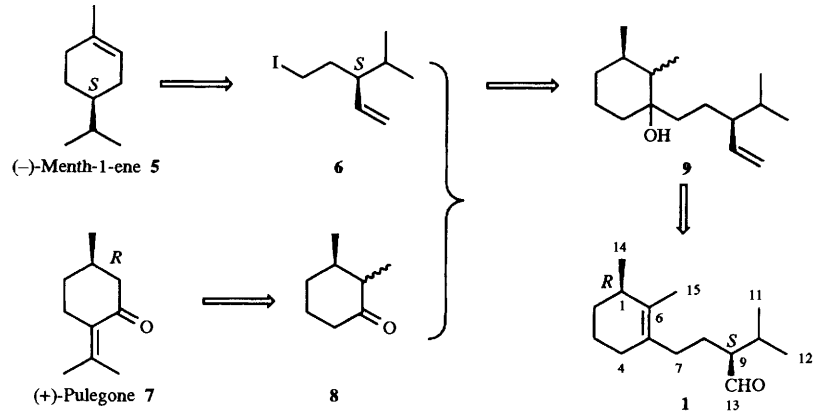
(−)-Menth-1-ene[4,5] was treated successively with ozone in MeOH–CH_2Cl_2 (1:1) and then with $NaBH_4$ at −78 °C. The diols were converted into a mono protected silyl alcohol followed by PDC† oxidation to afford the ketone **10**. The ketone **10** was treated with MCPBA to yield an acetate, which was hydrolysed to give an alcohol **11**. The alcohol **11** was converted into a vinyl alcohol **12** by Grieco and Nishizawa's method[6] followed by deprotection ($Bu_4N^+F^-$) of the silyl group. The alcohol **12** was converted into the iodide **6** in two steps (i, TsCl–Py; ii, NaI–acetone) (Scheme 2).

(+)-Pulegone **7** was methylated (LDA–MeI) and treated with KOH–MeOH to yield, by a retro aldol reaction, a diastereoisomeric mixture of 2,3-dimethylcyclohexanones **8**, the GC–MS analysis of which showed that they were present in a ratio of *ca.* 9:1. However, since the chiral centre at C-6 was to be lost at a later stage, we made no effort to purify compound **8**. A Grignard reagent was prepared from the aforementioned iodide **6** and the optically active ketone **8** was allowed to react with it to give a low yield of the adduct **9**, isolated as a single isomer as judged from its ^{13}C NMR spectrum. Thus, we assumed that the stereochemistry was that shown in the formula. Ozonolysis followed by $NaBH_4$ treatment afforded a diol, which was acetylated to give a mono acetate **13**, dehydration of which afforded a tetrasubstituted olefin along with a small amount of trisubstituted compound which was purified at the final stage. Deprotection of the acetyl group ($LiAlH_4$) and Swern oxidation afforded (+)-tridensenal **1** {$[\alpha]_D^{22}$ +55.0 (*c* 0.36)}‡ after purification by $AgNO_3$-impregnated silica gel PTLC (Scheme 3). Although both the ^{1}H and ^{13}C NMR spectra of the synthetic material were almost the same as those of the natural product, we felt that we needed to synthesize the other diastereoisomer in order to confirm the stereochemistry, particularly so since we knew that even the ^{13}C NMR spectra had closely similar signals.[3]

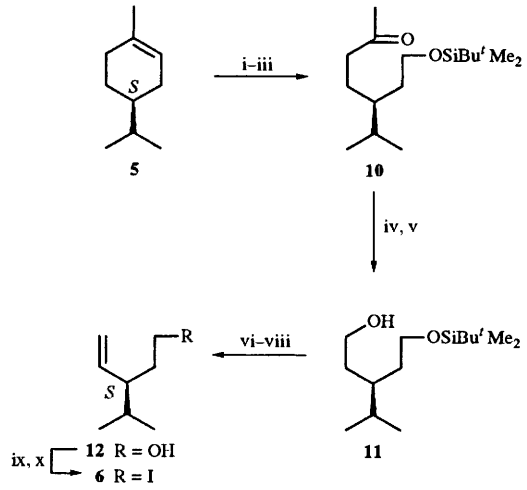
(+)-Menth-1-ene **14** was used as the starting material for the synthesis of the enantiomeric iodide **15**, which was prepared by the same route as shown in Scheme 2 (see Experimental section). The Grignard reaction of the iodide **15** with the ketone **8** derived from (+)-pulegone gave an adduct **16**. By similar reactions (Scheme 4), the diastereoisomer of tridensenal, **2**, was synthesized, whose spectral features were very similar to those

† Acronyms: PDC = pyridinium dichromate, TsCl = toluenesulfonyl chloride, Py = pyridine, LDA = lithium diisopropylamide, TBDMS = *tert*-butyldimethylsilyl, DMAP = 4-dimethylaminopyridine, MCPBA = *m*-chloroperbenzoic acid, THF = tetrahydrofuran and DMSO = dimethyl sulfoxide.

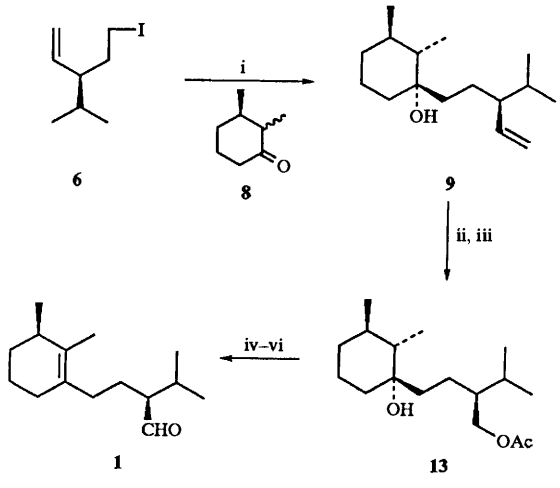
‡ Throughout, specific rotations $[\alpha]_D$ are given in units of 10^{-1} deg cm^2 g^{-1}.



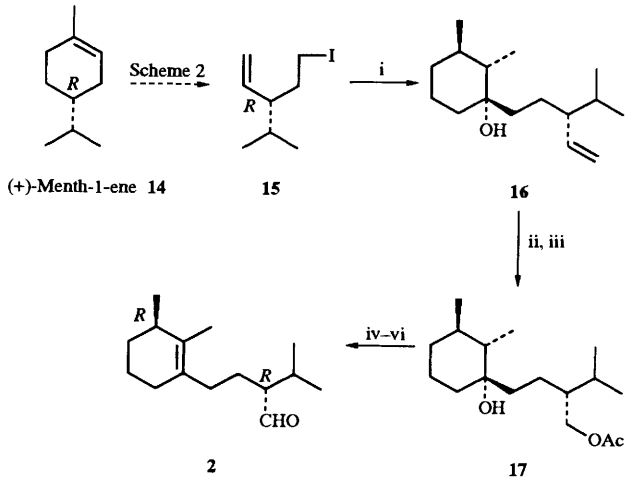
Scheme 1 Synthetic plan



Scheme 2 *Reagents:* i, O_3; then $NaBH_4$; ii, TBDMS–Cl, DMAP, Et_3N, CH_2Cl_2; iii, PDC, CH_2Cl_2; iv, MCPBA, CH_2Cl_2; v, KOH, MeOH; vi, *o*-nitrophenylseleno cyanate, Bu_3P; vii, H_2O_2, THF–H_2O; viii, Bu_4NF, THF; ix, TsCl, Py; x, NaI, acetone



Scheme 3 *Reagents:* i, Mg, THF; then **8**; ii, O_3; then $NaBH_4$; iii, Ac_2O, Py; iv, $SOCl_2$, Py; v, $LiAlH_4$; vi, $(COCl)_2$, DMSO, Et_3N



Scheme 4 *Reagents:* i, Mg, THF; then **8**; ii, O_3; then $NaBH_4$; iii, Ac_2O, Py; iv, $SOCl_2$, Py; v, $LiAlH_4$; vi, $(COCl)_2$, DMSO, Et_3N

Table 1 ^{13}C NMR data (in C_6D_6) for tridensenal and synthetic compounds

C	Natural[2]	**1** (*RS*)	**2** (*RR*)
15	17.27	17.27	17.30
11	19.53	19.50	19.49
14	20.08	20.06	19.97
12	20.18	20.17	20.18
7	20.41	20.40	20.27
3	24.40	24.37	24.30
10	28.36	28.33	28.30
4	30.21	30.20	30.20
8	31.80	31.78	31.72
2	32.07	32.05	32.04
1	35.07	35.04	35.03
9	57.98	57.98	57.93
6	129.88	129.88	129.85
5	131.28	131.28	131.22
13	203.75	203.71	203.74

of the natural compound. However, the signals for the two compounds around 2 ppm in their ^1H NMR spectra differed slightly as did the highfield area of the ^{13}C NMR spectra (see Table 1 and Fig. 1). Thus, these results clearly indicate that the synthetic product **1** is the real enantiomer of the natural tridensenal. (–)-Tridensenal should, therefore, be formulated as **3**.

Although biogenetic pathways to these compounds are not mentioned in the literature,[2] we believe that tridensenal **1** is produced from the eremophilane-type compound by C–C bond fission at C-5 and -6 (Fig. 2).

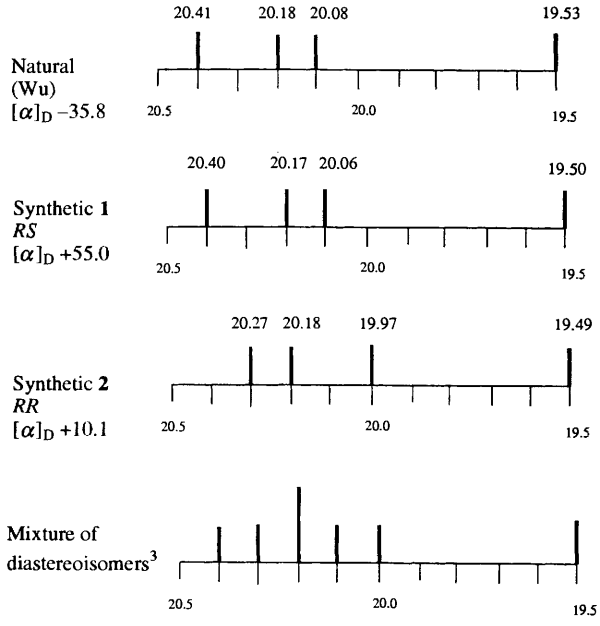


Fig. 1 Schematic comparison of the highfield area of the ^{13}C NMR signals for the three products

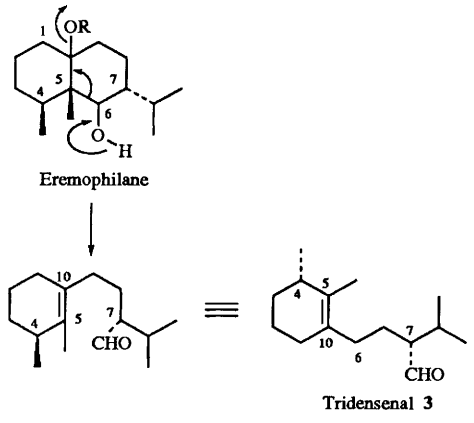


Fig. 2 Possible biogenetic route to tridensenal **3**

Experimental

General

IR spectra were measured on a JASCO FTIR 500 spectrophotometer. ^1H and ^{13}C NMR spectra were recorded on a JEOL JNM GX-400, a Varian Unity 200 or a Gemini 200 spectrometer. The solvent used for NMR spectra was $CDCl_3$ unless otherwise stated. Mass spectra were measured on a JEOL JMS HX-100 or a JEOL AX-500 spectrometer. The specific rotation and the CD spectra were taken on a JASCO DIP-140 polarimeter and a JASCO J-500 spectrometer, respectively. Chemcopak Nucleosil 50-5 (10 × 250 mm) and Develosil 60-10 (20 × 250 mm) columns were used for HPLC (JASCO pump system). Silica gel 60 for column chromatography was purchased from Merck. (−)-Menth-1-ene, $[\alpha]_D$ −109.4 (*c* 1.14, $CHCl_3$), (+)-menth-1-ene, $[\alpha]_D$ +112.5 (*c* 1.08, $CHCl_3$) and (+)-pulegone, $[\alpha]_D$ +17.9 (*c* 1.17, $CHCl_3$), were donated by the Nippon Terpene Company and were used as received.

Preparation of (*S*)-5-(*tert*-butyldimethylsiloxy)-3-isopropylpentyl methyl ketone 10

Ozone was bubbled through a solution of (−)-menth-1-ene **5** (21.6 g) in MeOH–CH_2Cl_2 (1:1; 200 cm^3) at −78 °C for 1 h, after which sodium boranuide ($NaBH_4$; 26.2 g) was added to it and the mixture was left overnight. Hydrochloric acid (1 mol dm^{-3}) was added to the mixture to bring it to pH 7.0, after which it was evaporated under reduced pressure to remove the MeOH. The residue was extracted with ether and the extract was washed with water and brine to give, upon work-up, a diol (27.7 g). A solution of the diol (27.7 g) in CH_2Cl_2 (350 cm^3) was treated with TBDMS–Cl (26 g), Et_3N (24 cm^3) and DMAP (2.8 g) at room temperature overnight. The mixture was washed with hydrochloric acid (1 mol dm^{-3}), 10% aq. $NaHCO_3$ and brine to afford, upon work-up, a residue (145.5 g), which was purified by silica gel column chromatography (hexane–EtOAc, gradient) to give a mono silyl ether (36 g; 80% from **5**). To a solution of the mono silyl ether (36 g) in dry CH_2Cl_2 (400 cm^3) was added PDC (240 g) and the mixture was stirred at room temperature overnight. It was then filtered first through Celite and then through silica gel. The filtrate was washed with hydrochloric acid (1 mol dm^{-3}), 10% aq. $NaHCO_3$ and brine to afford a residue (34 g), which was purified by silica gel column chromatography (hexane–EtOAc, gradient) to afford the ketone **10** (30.9 g, 85%) as an oil [Found: *m/z* (CI–CH_4) 287.2403 $(M + 1)^+$. $C_{16}H_{35}O_2Si$ requires *m/z* 287.2406]; $[\alpha]_D^{22}$ −4.1 (*c* 1.4, $CHCl_3$); ν_{max}(FT)/cm^{-1} 1715 (CO); δ_H(200 MHz) 0.04 (6 H, s, $SiMe_2$), 0.85 (6 H, d, *J* 6.9, $CHMe_2$), 0.89 (9 H, s, $SiBu^t$), 2.13 (3 H, s, COMe), 2.42 (2 H, t, *J* 8.0, $COCH_2$) and 3.61 (2 H, t, *J* 6.8, OCH_2); δ_C(50 MHz) −5.4 (Me × 2), 18.2 (C), 18.7 (Me), 19.0 (Me), 24.7 (CH_2), 25.9 (Me × 3), 29.3 (Me), 29.7 (CH), 33.4 (CH_2), 39.8 (CH), 42.0 (CH_2), 61.8 (CH_2) and 208.8 (CO); *m/z* (CI–CH_4) 287 $(M + 1)^+$, 271, 229, 155 (base) and 137.

Preparation of (*S*)-5-(*tert*-butyldimethylsiloxy)-3-isopropylpentan-1-ol 11

A solution of the ketone **10** (30.9 g) in chloroform (400 cm^3) was treated with MCPBA (53 g) at 40 °C overnight. The mixture was filtered and the filtrate was washed with 10% aq. $NaSO_3$, 10% aq. $NaHCO_3$ and brine to give, on work-up, an acetate (31 g). This was hydrolysed with 5% KOH in MeOH (400 cm^3) at room temperature overnight. After dilution with water and removal of MeOH under reduced pressure, the mixture was extracted with ether and the ethereal solution was washed with hydrochloric acid (1 mol dm^{-3}) and brine to afford, upon work-up, a residue. This was purified by silica gel column chromatography (hexane–EtOAc, gradient) to give the alcohol **11** (10 g, 35%) as an oil [Found: *m/z* (CI–CH_4) 261.2230 $(M + 1)^+$. $C_{14}H_{33}O_2Si$ requires *m/z* 261.2250]; $[\alpha]_D^{22}$ +0.28 (*c* 1.1, $CHCl_3$); ν_{max}(FT)/cm^{-1} 3340 (OH); δ_H(200 MHz) 0.06 (6 H, s, $SiMe_2$), 0.85 (6 H, d, *J* 6.8, $CHMe_2$), 0.90 (9 H, s, $SiBu^t$) and 3.61–3.70 (4 H, m, $HOCH_2$ and $SiOCH_2$); δ_C(50 MHz) −5.4 (Me × 2), 18.2 (C), 18.9 (Me × 2), 25.9 (Me × 3), 30.3 (CH), 33.6 (CH_2), 33.9 (CH_2), 36.9 (CH), 61.5 (CH_2) and 62.3 (CH_2); *m/z* (GC: CI–CH_4) 261 $(M + 1)^+$, 243, 203, 185, 173, 157, 145, 129, 111, 105, 89, 83, 75, 69 (base) and 55.

Preparation of (*S*)-3-isopropylpent-4-en-1-ol 12

A solution of the alcohol **11** (9.9 g) in THF (80 cm^3) was treated with *o*-nitrophenylseleno cyanate (17 g) and Bu_3P (19 cm^3) at room temperature for 5 h. After dilution with water and removal of THF, the mixture was extracted with ether. The extract was washed with brine and upon work-up gave a residue, which was purified by silica gel column chromatography (hexane–EtOAc, gradient) to afford a seleno compound (14.3 g, 84%). To a stirred solution of the seleno compound (14.3 g) in THF (300 cm^3) was added 30% H_2O_2 (160 cm^3) at 0 °C and the mixture was left overnight. It was then treated with 10% aq. $Na_2S_2O_3$ (160 cm^3) and after removal of THF was extracted with ether. The extract was washed with brine and, after work-up, afforded a residue. This was purified by silica gel column chromatography

(hexane–EtOAc, gradient) to give an olefin (1.9 g, 45%), a solution of which (1.9 g) in THF (10 cm^3) was treated with Bu_4NF (15 cm^3) at room temperature overnight. After dilution with water and removal of THF, the mixture was extracted with ether. The extract was washed with water and brine and, after work-up, gave a residue, which was purified by silica gel column chromatography (hexane–EtOAc, gradient) to afford the alcohol **12** (0.6 g, 64%) as an oil [Found: *m/z* (CI–CH_4) 129.1251 $(M + 1)^+$. $C_8H_{17}O$ requires *m/z* 129.1279]; $[\alpha]_D^{22}$ −12.5 (*c* 1.3, $CHCl_3$); ν_{max}(FT)/cm^{-1} 3400 (OH); δ_H(200 MHz) 0.82 (3 H, d, *J* 6.9, CH*Me*), 0.87 (3 H, d, *J* 6.9, CH*Me*), 3.54–3.67 (2 H, m, HOCH_2), 4.96 (1 H, dd, *J* 16.2 and 2.2, CH=CH_2), 5.01 (1 H, dd, *J* 10.2 and 2.2, CH=CH_2) and 5.58 (1 H, ddd, *J* 16.2, 10.2 and 9.5, C*H*=CH_2); δ_C(50 MHz) 18.7, 20.3, 31.6, 34.6, 47.1, 61.0, 115.6 and 140.2; *m/z* (GC: CI–CH_4) 129 $(M + 1)^+$, 111, 95, 83, 69 (base) and 55.

Preparation of (*S*)-3-isopropylpent-4-enyl iodide 6

A solution of the alcohol **12** (1.9 g) in dry pyridine (18 cm^3) was treated with TsCl (13.9 g) at room temperature for 5 h. After dilution with water the mixture was extracted with ether and the extract was washed with hydrochloric acid (1 mol dm^{-3}), 10% aq. $NaHCO_3$ and brine to give, upon work-up, a tosylate (1.1 g, 26%). A solution of the tosylate (1.1 g) in acetone (40 cm^3) was heated under reflux with NaI (2.9 g) overnight, after which the insoluble material was filtered off. After removal of acetone, the mixture was extracted with ether and the extract was washed with water and brine to give, upon work-up, a residue. This was purified by silica gel column chromatography (hexane–EtOAc, gradient) to afford the iodide **6** (483 mg, 52%) as an oil [Found: *m/z* (CI–CH_4) 239.0279 $(M + 1)^+$. $C_8H_{16}I$ requires *m/z* 239.0296]; $[\alpha]_D^{24}$ −50.2 (*c* 1.4, $CHCl_3$); ν_{max}(FT)/cm^{-1} 1650 (CH=CH_2); δ_H(200 MHz) 0.85 (3 H, d, *J* 6.8, CH*Me*), 0.889 (3 H, d, *J* 6.8, CH*Me*), 3.02 (1 H, dt, *J* 8.5 and 8.3), 3.25 (1 H, m), 5.05 (1 H, dd, *J* 16.5 and 2.2, CH=CH_2), 5.10 (1 H, dd, *J* 10.5 and 2.2, CH=CH_2) and 5.49 (1 H, ddd, *J* 16.5, 10.5 and 8.8, C*H*=CH_2); δ_C(50 MHz) 5.8 (CH_2), 19.1 (Me), 20.4 (Me), 31.4 (CH), 35.7 (CH_2), 51.3 (CH), 116.9 (CH_2=) and 138.7 (CH=); *m/z* (GC–EI) 238 $(M)^+$, 210, 196, 155, 141, 127, 83, 69 (base) and 55.

Preparation of 2,3-dimethylcyclohexanone 8

(+)-Pulegone **7** (5 g) was treated with LDA prepared from BuLi (1.6 mol dm^{-3}; 25 cm^3) and diisopropylamine (5 cm^3) in dry THF (40 cm^3) at −78 °C for 1 h. MeI (7.2 cm^3) was introduced to this mixture which was then stirred for 1 h at −78 °C and then at 0 °C for 1 h. Work-up afforded the methylated compound (4.5 g), which was treated with KOH (15 g) in water (80 cm^3) and MeOH (20 cm^3) under reflux overnight. The mixture was extracted with ether and the extract was washed with hydrochloric acid (1 mol dm^{-3}) and brine to afford, upon work-up, a residue. This was repeated 3 times after which the combined residues were distilled under reduced pressure to give the pure ketone **8** (2.8 g), bp 52–55 °C/9 Torr, $[\alpha]_D^{21}$ −12.2 (*c* 1.31, $CHCl_3$); ν_{max}(FT)/cm^{-1} 1710 (CO); GC–MS t_R 4.11: *m/z* 126 $(M)^+$, 111, 108, 98, 93, 83 (base), 70, 67, 55 and 41; t_R 4.41: *m/z* 126 $(M)^+$, 98, 83 (base), 70, 55 and 41.

Preparation of acetate 13

To a mixture of Mg (36 mg) and dry ether (5 cm^3) was added the iodide **6** (349 mg) and iodine (a small crystal). The mixture was stirred at room temperature for 1 h, after which a solution of 2,3-dimethylcyclohexanone **8** (184 mg) in dry ether (1 cm^3) was added to it at room temperature. After being stirred for 1 h, the mixture was treated with saturated aqueous NH_4Cl and then extracted with ether. The extract was washed with water and brine and, upon work-up, gave a residue, which was purified by silica gel column chromatography (hexane–EtOAc, gradient) to afford the adduct **9** (97 mg, 28%) [GC–MS: *m/z* 238 $(M)^+$ and 127 (base)]. Ozone was bubbled through a solution of the adduct **9** (97 mg) in CH_2Cl_2–MeOH (1:1, 20 cm^3) at −78 °C until a blue colour persisted. $NaBH_4$ (155 mg) was added at the same temperature to the mixture which was then left overnight. After removal of MeOH under reduced pressure the mixture was extracted with ether. The extract was washed with hydrochloric acid (1 mol dm^{-3}) and brine to give, upon work-up, an alcohol (96.7 mg). A solution of the alcohol (96.7 mg) in pyridine (0.5 cm^3) was treated with acetic anhydride (0.5 cm^3) for 2 h, after which it was diluted with MeOH and extracted with ether. The extract was washed with hydrochloric acid (1 mol dm^{-3}), 10% aq. $NaHCO_3$ and brine to give, upon work-up, a residue. This was purified by silica gel column chromatography (hexane–EtOAc, gradient) to afford the acetate **13** (40.7 mg, 35%) as an oil [Found: *m/z* (CI–CH_4) 267.2308 $(M - H_2O + 1)^+$. $C_{17}H_{31}O_2$ requires 267.2324]; $[\alpha]_D^{22}$ −12.1 (*c* 1.11, $CHCl_3$); ν_{max}($CHCl_3$)/cm^{-1} 3530 (OH), 1740 and 1240 (CO_2); δ_H(200 MHz; $CDCl_3$) 0.90 (12 H, m), 2.05 (3 H, s), 4.01 (1 H, dd, *J* 11.1 and 5.7) and 4.06 (1 H, dd, *J* 11.0 and 6.0); δ_C(50 MHz, $CDCl_3$) 12.5, 20.4, 20.8, 22.0, 22.2, 22.5, 23.6, 29.5, 34.8, 36.7, 37.7, 40.3, 44.9, 45.5, 66.7, 74.7 and 171.3; *m/z* (CI–CH_4) 267 $(M - H_2O + 1)^+$ (base), 223, 207, 181, 151, 137, 127, 123, 109, 97, 83, 69 and 55.

Preparation of tridensenal 1

A solution of the acetate **13** (40 mg) in dry pyridine (1 cm^3) was treated with thionyl chloride (6 drops) at 0 °C for 45 min, after which the mixture was diluted with water and extracted with ether. The extract was washed with hydrochloric acid (1 mol dm^{-3}) and brine to give, upon work-up, an olefin (41.4 mg) [GC–MS *m/z* 266 $(M)^+$ and 109 (base)]. $LiAlH_4$ (100 mg) was added to a solution of the olefin (41 mg) in dry ether (1 cm^3) and the mixture was stirred at room temperature for 2 h. After dilution with EtOAc, water (0.1 cm^3), 15% aq. NaOH (0.1 cm^3) and water (0.3 cm^3) were added to the mixture which was then filtered and worked-up to afford an alcohol (40.9 mg). Dimethyl sulfoxide (0.13 cm^3) in CH_2Cl_3 (3 cm^3) was added to a mixture of oxalyl chloride (0.16 cm^3) in CH_2Cl_2 (3 cm^3) at −78 °C and, after 3 min, a solution of the alcohol (41 mg) in dry CH_2Cl_2 (2 cm^3) was also added to it. After the mixture had been stirred for 15 min it was treated with Et_3N (1.25 cm^3) and stirred at 0 °C for 30 min. It was then diluted with water and extracted with CH_2Cl_2. The extract was washed with hydrochloric acid (1 mol dm^{-3}), saturated aq. $NaHCO_3$ and brine and, upon work-up, afforded a residue. This was purified by silver nitrate-impregnated PTLC to give tridensenal **1** (4 mg, 13%) as an oil; $[\alpha]_D^{23}$ +55.0 (*c* 0.36, $CHCl_3$); ν_{max}($CHCl_3$)/cm^{-1} 2680 and 1725; δ_H(400 MHz; C_6D_6) 0.72 (3 H, d, *J* 6.8, CHMe_2), 0.76 (3 H, d, *J* 6.8, CHMe_2), 0.99 (3 H, d, *J* 6.8, CHMe_2), 1.61 (3 H, s, C=C*Me*) and 9.44 (1 H, d, *J* 2.9, OCH); δ_C(50 MHz, C_6D_6) 17.27 (CH_3), 19.50 (CH_3), 20.06 (CH_3), 20.17 (CH_3), 20.40 (CH_2), 24.37 (CH_2), 28.33 (CH), 30.20 (CH_2), 31.78 (CH_2), 32.05 (CH_2), 35.04 (CH), 57.98 (CH), 129.88 (C), 131.28 (C) and 203.71 (CO); *m/z* (CI–CH_4) 222 $(M + 1)^+$, 204, 161, 136, 121, 109 (base), 81, 67 and 55; *ent*-**10** an oil; $[\alpha]_D^{21}$ +2.5 (*c* 1.01, $CHCl_3$); *ent*-**11** an oil; $[\alpha]_D^{18}$ −1.7 (*c* 1.7, $CHCl_3$); *ent*-**6** (≡**15**) an oil; $[\alpha]_D^{23}$ +50.7 (*c* 1.1, $CHCl_3$).

Preparation of acetate 17

A Grignard reagent was prepared from Mg (43 mg), the iodide **15** (418 mg) and iodine (small crystal) in dry ether (5 cm^3) and to it was added 2,3-dimethylcyclohexanone **8** (222 mg). The mixture was stirred for 1.5 h, after which it was treated with saturated aq. NH_4Cl and extracted with ether. The extract was washed with water and brine and then worked up to afford a residue. This was separated by silica gel column chromatography (hexane–EtOAc, gradient) to give the adduct **16** (124 mg, 30%). Ozone was bubbled through a solution of the alcohol

16 (103.5 mg) in MeOH–CH_2Cl_2 (1:1; 20 cm^3) at −78 °C until a blue colour persisted. Sodium boranuide (163 mg) was added to the mixture which was then left overnight before MeOH was removed from it under reduced pressure. The residue was extracted with CH_2Cl_2 and the extract was washed with hydrochloric acid (1 mol dm^{-3}) and brine to afford, upon work-up, a diol (117 mg). The diol (117 mg) was treated with acetic anhydride (0.5 cm^3) in Py (0.5 cm^3) for 1.5 h, after which work-up and silica gel column chromatography (hexane–EtOAc, gradient) afforded an acetate **17** (60 mg, 49%) as an oil [Found: *m/z* 267.2309 $(M - H_2O + 1)^+$ (CI–CH_4). $C_{17}H_{31}O_2$ requires 267.2324]; $[\alpha]_D^{24}$ −8.3 (*c* 1.1, $CHCl_3$); $\nu_{max}(CHCl_3)/cm^{-1}$ 3500, 1740, 1725 and 1240; δ_H(200 MHz; $CDCl_3$) 0.88 (12 H, br d, *J ca.* 7.0), 2.01 (3 H, s) and 4.01 (2 H, m); δ_C(50 MHz, $CDCl_3$) −11.2 (Me), 19.5 (Me × 2), 20.7 (Me), 21.0 (Me), 21.2 (CH_2), 22.3 (CH_2), 28.7 (CH), 33.5 (CH), 35.4 (CH_2), 36.4 (CH_2), 39.2 (CH_2), 43.7 (CH), 44.4 (CH), 65.3 (CH_2), 73.5 (C) and 171.3 (CO); *m/z* (CI–CH_4) 267 $(M - H_2O + 1)^+$, 223, 207 (base), 151, 137, 123, 109 and 97.

Preparation of 2

The acetate **17** (35 mg) was treated with thionyl chloride (6 drops) in Py (0.5 cm^3) at 0 °C for 1.5 h. Work-up afforded a residue (36.7 mg) which was deprotected with $LiAlH_4$ (100 mg) in dry ether (1 cm^3) to give, upon work-up, an alcohol (29 mg). This was subjected to Swern oxidation conditions to give a residue, which was purified by silver nitrate-impregnated silica gel PTLC to afford compound **2** (5.6 mg, 21%); $[\alpha]_D^{25}$ +10.1 (*c* 0.67, $CHCl_3$); ν_{max}(FT)/cm^{-1} 2700 and 1720; δ_H(400 MHz, C_6D_6) 0.72 (3 H, d, *J* 6.7), 0.76 (3 H, d, *J* 6.7), 1.00 (3 H, d, *J* 7.0), 1.61 (3 H, s) and 9.44 (1 H, d, *J* 3.1); δ_C(50 MHz, C_6D_6) 17.30 (Me), 19.49 (Me), 19.97 (Me), 20.18 (Me), 20.27 (CH_2), 24.30 (CH_2), 28.30 (CH), 30.20 (CH_2), 31.72 (CH_2), 32.04 (CH_2), 35.03 (CH), 57.93 (CH), 129.85 (C), 131.22 (C) and 203.74 (CO); *m/z* 222 (M^+), 204, 161, 136, 109, 81, 67 and 41.

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