Total synthesis of C_{31}-methyl ketone apocarotenoids. Part 4.† First total synthesis of (3*S*,5*R*,6*R*)-paracentrone

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Optically active (all-*E*)-(3*S*,5*R*,6*R*)-paracentrone has been prepared by total synthesis for the first time, in 3% overall yield over 13 linear steps from the readily available (4*R*,6*R*)-actinol, (2*E*)-3-methylpent-2-en-4-yn-1-ol, (all-*E*)-2,7-dimethylocta-2,4,6-triene-1,8-dial and 1,1-dimethoxypropan-2-one. All spectral data for synthetic (all-*E*)-(3*S*,5*R*,6*R*)-paracentrone are in accordance with data reported for the natural compound.

Introduction

The structural elucidation of paracentrone **1** (see Scheme 1), first isolated from the sea urchin *Paracentrotus lividus*, was reported by Weedon and co-workers in 1969.[1] Paracentrone **1** was the second naturally occurring C_{31}-methyl ketone apocarotenoid to be reported and is one of two known naturally occurring allenic C_{31}-apocarotenoids.[2] Optical rotatory dispersion (ORD) studies demonstrated that paracentrone **1** has the same (3*S*,5*R*,6*R*)-configuration as reported for the allenic end group of fucoxanthin **2**.[3–5]

Direct *in vitro* conversion, upon Oppenauer oxidation, of the allenic C_{40}-carotenoid fucoxanthin **2** into paracentrone 3-acetate **3** has been reported. Hydrolysis of **3** afforded paracentrone **1** in 6% overall yield.[6] It was inferred that natural paracentrone **1** probably results from *in vivo* degradation of dietary fucoxanthin **2** in the animal.[6] More recently, the formation of paracentrone **1** upon base-induced retro aldol cleavage of the marine C_{40}-carotenoid amarouciaxanthin A **4**, isolated from the tunicate *Amaroucium pliciferum*, has been reported.[7]

A communication describing the first total synthesis of optically active (3*S*,5*R*,6*R*)-paracentrone **1** was recently published.[8] A full account of these results are presented here.

† For Part 3, see *Acta Chem. Scand.*, in the press.

Results and discussion

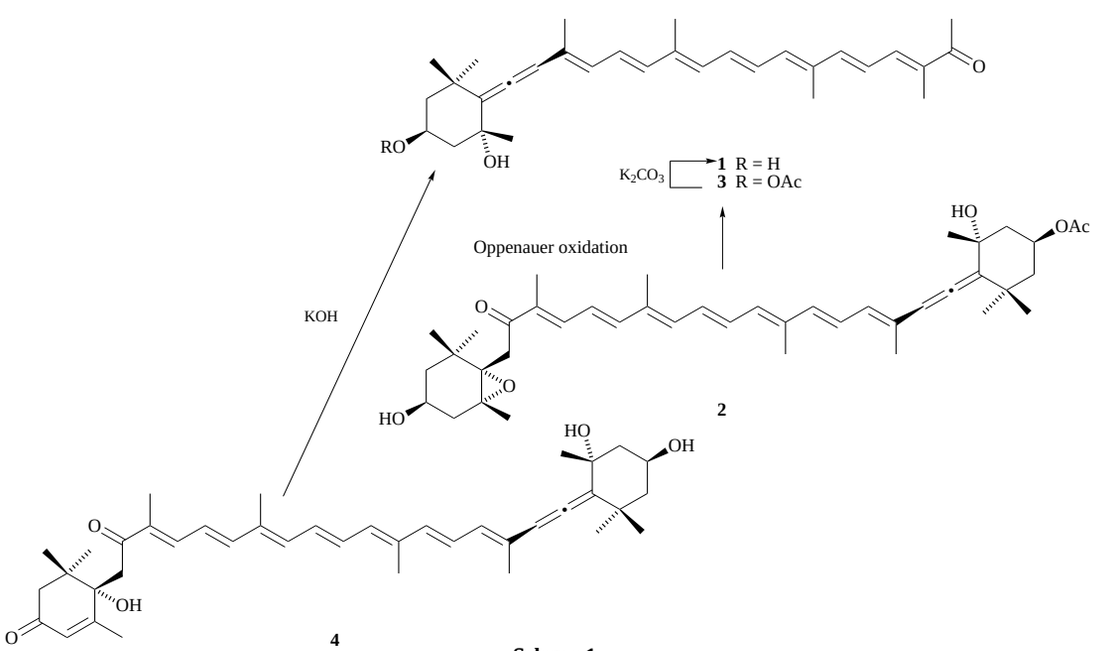
The synthetic strategy

The $C_{15} + C_{10} + C_5 + C_1$ building scheme first elaborated for the total synthesis of (all-*E*)-(3*R*)-triophaxanthin,[9] and subsequently employed as one of two successful strategies in the total synthesis of (9*Z*)- and (all-*E*)-(3*S*)-7′-apohopkinsiaxanthin,[10] was here adopted for the synthesis of (3*S*,5*R*,6*R*)-paracentrone **1**. A key intermediate in the synthesis of **1** was the allenic C_{15}-aldehyde **5a** (see Scheme 2) previously described as an intermediate in the synthesis of allenic carotenoids including mimulaxanthin,[11] neoxanthin,[12] peridinin[13] and fucoxanthin.[14] The syntheses of the C_{10}- and C_5-phosphonium salts **6**[15] and **7**[9,16] have previously been reported.

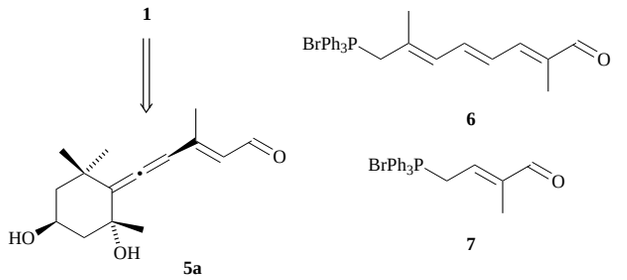
The preparation of the allenic C_{15}-aldehyde **5a** and the synthesis of (3*S*,5*R*,6*R*)-paracentrone **1** is discussed below.

Synthesis of the allenic C_{15}-aldehyde 5a

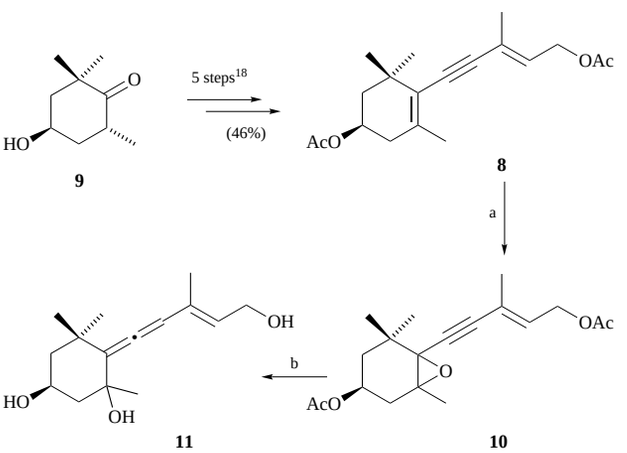
The allenic C_{15}-aldehyde **5a** was prepared essentially according to previous methods,[13,17] starting from the acetylenic C_{15}-diacetate **8** (see Scheme 3) which was prepared in 5 steps from (4*R*,6*R*)-actinol **9** for a recent synthesis of diatoxanthin.[18,19] Epoxidation of **8** with MCPBA in chloroform provided the epoxide **10**, as a *ca.* 3:2 mixture of the *syn* and *anti* epoxides in 40% combined yield. Ito and co-workers separated the two pure



Scheme 1



Scheme 2



Scheme 3 *Reagents and conditions:* a, MCPBA, $CHCl_3$, 4 °C, 8 h (40%); b, DIBAH, DCM, 0 °C, <2 h (73%)

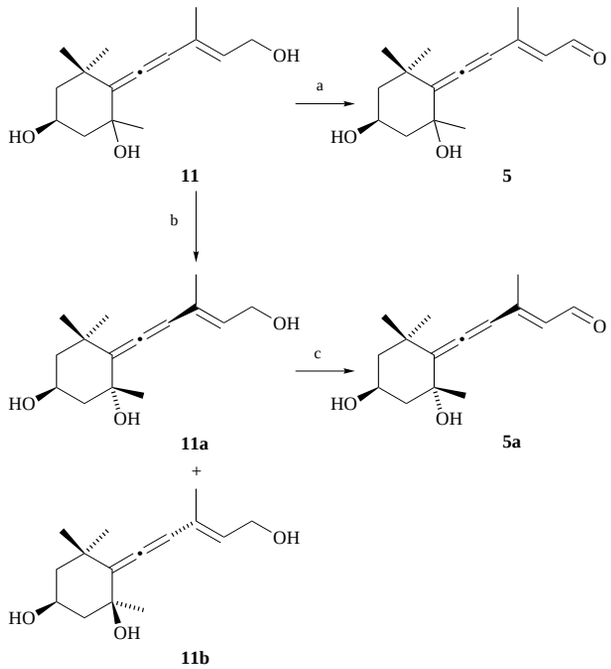
diastereoisomeric epoxides **10** by low-pressure column chromatography for their synthesis of peridinin.[13,20] In the present work, treatment of a mixture of the two diastereoisomeric epoxides **10** with DIBAH provided the two diastereoisomeric allenic C_{15}-triols (4*R*,2′*R*,4′*S*)-**11** and (4*S*,2′*S*,4′*S*)-**11**, as a *ca.* 5:4 mixture, in 73% combined yield.

Allylic oxidation of the diastereoisomeric triols **11** with manganese dioxide afforded the C_{15}-dihydroxy aldehyde **5**, as a *ca.* 5:4 mixture of the (4*R*,2′*R*,4′*S*) and (4*S*,2′*S*,4′*S*) diastereoisomers in 66% combined yield (see Scheme 4). Attempted chromatographic separation of the two diastereoisomeric aldehydes **5** was unsuccessful. The separation of the diastereoisomeric allenic triols **11** by column chromatography has been reported, albeit with no experimental details.[21] In the present work, flash chromatography of crude **11** provided the optically pure (4*R*,2′*R*,4′*S*)-triol **11a** and (4*S*,2′*S*,4′*S*)-triol **11b**, in 19 and 5% yield, respectively, from the epoxide **10**. The (4*R*,2′*R*,4′*S*)-triol **11a** provided the optically active (4*R*,2′*R*,4′*S*)-dihydroxy aldehyde **5a** in 92% yield upon allylic oxidation with manganese dioxide.

Synthesis of (3*S*,5*R*,6*R*)-paracentrone 1

The C_{10}- and C_5-phosphonium salts **6** and **7** were available from the symmetrical C_{10}-dial **12** in 61% yield over 3 steps[15] and from the C_3-ketone **13** in 19% yield over 4 steps[9] respectively (see Scheme 5). As previously discussed,[9] the aldehyde moieties of **6** and **7** were protected as the dimethyl acetals **14** and **15**, respectively, eliminating potential problems caused by use of excess of phosphonium salt in subsequent Wittig reactions.

A Wittig reaction between the optically active (4*R*,2′*R*,4′*S*)-dihydroxy aldehyde **5a** and the C_{10}-phosphonium salt **14**, followed by hydrolysis of the acetal moiety, provided the optically active C_{25}-dihydroxy aldehyde **16** in 94% yield. HPLC indicated a mixture of geometrical isomers, the all-*E* isomer constituting 75% of total **16**. A subsequent Wittig reaction of **16** with the C_5-phosphonium salt **15**, followed by hydrolysis of the dimethyl acetal, afforded the optically active C_{30}-dihydroxy aldehyde **17**



Scheme 4 *Reagents and conditions:* a, MnO_2, THF, 20 °C, 2 h (66%); b, flash chromatography, silica gel, ethyl acetate–hexane, **11a** (19% from **10**), **11b** (5% from **10**); c, MnO_2, THF, 20 °C, 1 h (92%)

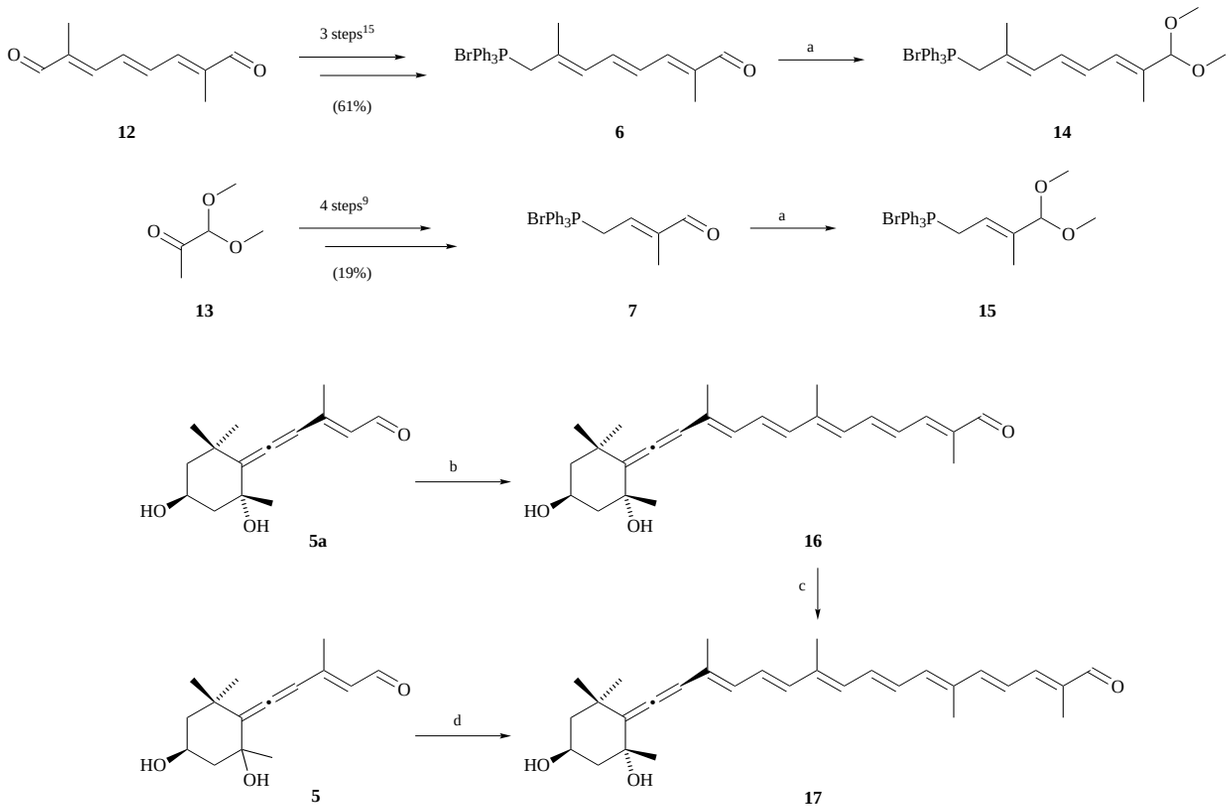
in 84% yield. The all-*E* isomer constituted 79% of total **17**. The overall yield of **17** by this route was 3% from (4*R*,6*R*)-actinol **9**.

In an alternative approach, a 5:4 mixture of the two diastereoisomeric aldehydes **5** was treated with the C_{10}-phosphonium salt **14**, followed by hydrolysis, to yield the diastereoisomeric aldehydes (3*S*,5*RS*,6*RS*)-**16** in 52% yield. HPLC and ^{1}H NMR spectroscopy demonstrated that the chromatographically purified product was enriched in the desired (3*S*,5*R*,6*R*) isomer, (all-*E*)-(3*S*,5*R*,6*R*) and (all-*E*)-(3*S*,5*S*,6*S*) constituting 50 and 25% of total **16**, respectively. However, no further purification was carried out at this stage. A Wittig reaction of (3*S*,5*RS*,6*RS*)-**16** with the C_5-phosphonium salt **15**, again followed by hydrolysis of the acetal moiety, furnished (3*S*,5*RS*,6*RS*)-**17**. In contrast to the case of the C_{15}-aldehydes, the corresponding diastereoisomeric C_{30}-compounds were readily separated by chromatography. Thus, column chromatography of crude (3*S*, 5*RS*,6*RS*)-**17** gave the pure C_{30}-(3*S*,5*R*,6*R*)-dihydroxy aldehyde **17** in 60% yield, or 32% overall yield from **5**. The all-*E* isomer constituted 78% of total **17**. The overall yield of **17** by this approach was 4% from (4*R*,6*R*)-actinol **9**.

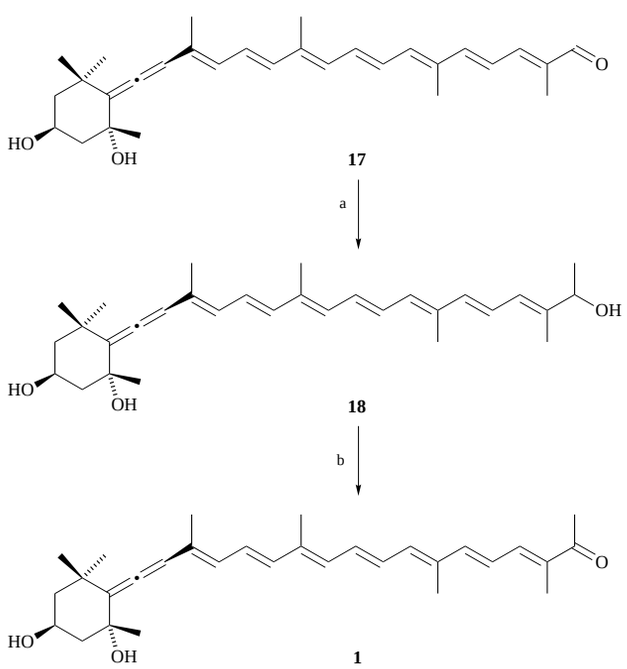
Treatment of the C_{30}-dihydroxy aldehyde **17** with methyllithium provided the C-8′ epimeric C_{31}-triols **18** in 96% yield (see Scheme 6). HPLC indicated a mixture of isomers in which the two all-*E* isomers constituted 84% of total **18**. Finally, allylic oxidation of **18** with manganese dioxide in acetone furnished (3*S*,5*R*,6*R*)-paracentrone **1** in 75% yield, as a mixture of geometrical isomers. The all-*E* isomer constituted 85% of total **1**. The total overall yield of **1** was 3% over 13 linear steps from (4*R*,6*R*)-actinol **9**.

Pure (all-*E*)-(3*S*,5*R*,6*R*)-paracentrone **1** was obtained by crystallisation from benzene. All spectral data for synthetic (all-*E*)-(3*S*,5*R*,6*R*)-paracentrone **1** were in accordance with data reported for the natural compound[1] and for two semisynthetic samples.[6,7] The melting point for synthetic **1** was considerably higher than what was reported for the natural or semisynthetic compound, 184–185 °C *vs.* 147–149 and 148–150 °C respectively, presumably due to contaminants in the two last samples.

The CD spectrum of (all-*E*)-(3*S*,5*R*,6*R*)-paracentrone **1** was intermediate conservative[22,23] with relatively weak Cotton effects and two sign shifts. It was *a priori* expected that the CD



Scheme 5 *Reagents and conditions:* a, (i) $HC(OMe)_3$, *p*-TsOH, MeOH, 30–35 °C, 16–20 h; (ii) NH_3, MeOH, 0 °C, 30 min (quantitative); b, (i) **14**, NaH, DCM, 20 °C, 40 h; (ii) AcOH–H_2O–DCM (1:1:5), 0 °C, 30 min (94%); c, (i) **15**, NaH, DCM, 20 °C, 40 h; (ii) AcOH–H_2O–DCM (1:1:5), 0 °C, 30 min (84%); d, (i) **14**, NaH, DCM, 20 °C, 22 h; (ii) AcOH–H_2O–DCM (1:1:5), 0 °C, 30 min; (iii) **15**, NaH, DCM, 20 °C, 40 h; (iv) AcOH–H_2O–DCM (1:1:4), 0 °C, 30 min; (v) column chromatography, silica gel, ethyl acetate–hexane (31%)



Scheme 6 *Reagents and conditions:* a, MeLi, THF, Et_2O, 20 °C, 1.5 h (96%); b, MnO_2, acetone, 20 °C, 75 min (75%)

spectrum of **1** would be similar to that of (all-*E*)-(3*S*,5*R*,6*S*,3′*S*,5′*R*,6′*R*)-fucoxanthin **2**.[24] This was not the case, indicating that the 5,6-epoxy-8-keto terminal group contributes more to the CD properties of fucoxanthin **2** than had been assumed.[25]

Experimental

General methods

Solvents were of distilled or p.a. quality. Diethyl ether used for extraction was passed through alumina (neutral). THF was distilled from sodium–benzophenone. Acetone, chloroform, dichloromethane (DCM), hexane and methanol were dried over freshly activated 3 Å molecular sieves. Sodium hydride was washed with hexane followed by DCM before use. Solvents were evaporated at reduced pressure (~20 mmHg) at temperatures not exceeding 35 °C. Melting points of polyenes were recorded in evacuated tubes. All melting points are uncorrected.

Chromatography

Analytical thin layer chromatography (TLC) was performed on pre-coated silica gel 60 F_{254} (Merck Art. 5554) plates with ethyl acetate–heptane 3:7 (system 1), 2:3 (system 2), 1:1 (system 3) or 4:1 (system 4) as the eluent. Methanolic sulfuric acid (30%) was used to develop TLC plates in order to detect the presence of non-UV active compounds. Column chromatography (CC) and flash chromatography were performed on silica gel 60 (Merck Art. 7734 or Merck Art. 9385, respectively) with mixtures of ethyl acetate in hexane as the eluent. High performance liquid chromatography (HPLC) was carried out on a Hewlett Packard series 1050 instrument on a Techsphere 5 CN nitrile column with gradient elution starting at 100% hexane 0 min; 1% acetone min^{-1} to 30%; 15 min, flow = 1.25 ml min^{-1} (system 1), or on a Spherisorb S5W silica column with hexane–isopropyl acetate–isopropyl alcohol–*N*-ethyldiisopropylamine 83.9:14:2:0.1 as the mobile phase, flow = 1.5 ml min^{-1} (system 2). The diode array (DA) detector was set to detect at five different wavelengths simultaneously (330, 360, 390, 420, 450 nm). The presence of *Z* isomers in synthetic samples was determined by inspection of on-line recorded UV–VIS spectra (λ_{max} and spectral fine structure). Relative amounts of geometrical isomers were determined by HPLC, assuming identical extinction coefficients for *E* and *Z* isomers.

Spectroscopy

UV–VIS spectra were recorded on a Perkin-Elmer 552 spec-

trophotometer. Spectral fine structure was measured as %III/II.[26] Solvents are specified in each case. IR spectra of solids were recorded in KBr discs and of liquids as a film between NaCl discs, on a Nicolet 20 SXC FT-IR spectrophotometer. Mass spectra were recorded on an AEI 902 spectrometer with a direct inlet to the ion source. CD spectra were recorded on a Jobin Yvon Auto Dicrograph Mark IV in EPA (diethyl ether–isopentane–ethanol, 5:5:2) solution at room temperature. Optical rotations were measured on a Jouan Dicrograph with methanol as the solvent and are recorded in units of 10^{-1} deg cm^2 g^{-1}. ^{1}H NMR, ^{13}C NMR, ^{1}H-^{1}H COSY and ^{1}H-^{13}C COSY spectra were recorded on a 300 MHz (75 MHz for ^{13}C) Bruker Avance DPX300, a 400 MHz (100 MHz for ^{13}C) Bruker Avance DPX400 or on a 400 MHz JEOL EX400 instrument with $CDCl_3$ as the solvent. Standard Bruker or JEOL software was used.

(2*E*)-[(1′*RS*,2′*RS*,4′*S*)-4′-Acetoxy-1′,2′-epoxy-2′,6′,6′-trimethylcyclohexyl]-3-methylpent-2-en-4-yn-1-yl acetate 10

MCPBA (1.76 g, 7.16 mmol) in chloroform (20 ml) was added dropwise to a stirred solution of the available[18] acetylenic diacetate **8** (1.80 g, 5.66 mmol) in chloroform (18 ml) at 4 °C. The reaction mixture was stirred at 4 °C in the dark for 8 h, when TLC (system 1) indicated complete conversion of **8**. The reaction mixture was poured into saturated aqueous sodium hydrogen carbonate and the product was extracted with chloroform. The organic phase was washed with water and brine, dried (Na_2SO_4) and evaporated to yield a yellow oily residue which was subjected to CC. The two diastereoisomeric epoxides **10**, inseparable by TLC (systems 1, 2 and 3), were obtained as a light yellow oil (40%, 0.76 g, 2.28 mmol), >99% pure (^{1}H NMR). No further attempt was made to separate the two diastereoisomeric epoxides. ^{1}H NMR indicated a *ca.* 3:2 mixture of the *syn* and *anti* epoxides. ^{1}H NMR assignments were based on data previously reported for the pure compounds;[20] TLC (system 1) R_f 0.40 (Found: $M^+ - C_2H_4O_2$, 274.157. $C_{17}H_{22}O_3$ requires *M*, 274.157); *m/z* (EI) 334 (1%) and 274 (4); compound **10**-*anti*: δ_H 1.14 (3 H, s, Me at 6′-C), 1.25 (3 H, s, Me at 6′-C), 1.38 (1 H, m, 5′-H^{ax}), 1.49 (3 H, s, Me at 2′-C), 1.63 (1 H, m, 5′-H^{eq}), 1.81 (1 H, m, 3′-H^{ax}), 1.86 (3 H, d, $J_{Me\ at\ 3\text{-}C,2\text{-}H}$ 1, Me at 3-C), 2.00 (3 H, s, AcO), 2.06 (3 H, s, AcO), 2.38 (1 H, m, 3′-H^{eq}), 4.63 (1 H, d, $J_{1\text{-}H,2\text{-}H}$ 7, 1-H), 4.86 (1 H, m, 4′-H) and 5.91 (1 H, tq, $J_{Me\ at\ 3\text{-}C,2\text{-}H}$ 1, $J_{1\text{-}H,2\text{-}H}$ 7, 2-H); compound **10**-*syn*: δ_H 1.17 (3 H, s, Me at 6′-C), 1.22 (3 H, s, Me at 6′-C), 1.41 (1 H, m, 5′-H^{ax}), 1.46 (3 H, s, Me at 2′-C), 1.58 (1 H, m, 5′-H^{eq}), 1.84 (1 H, m, 3′-H^{ax}), 1.86 (3 H, d, $J_{Me\ at\ 3\text{-}C,2\text{-}H}$ 1, Me at 3-C), 2.00 (3 H, s, AcO), 2.07 (3 H, s, AcO), 2.33 (1 H, m, 3′-H^{eq}), 4.63 (1 H, d, $J_{1\text{-}H.2\text{-}H}$ 7, 1-H), 4.86 (1 H, m, 4′-H) and 5.93 (1 H, tq, $J_{Me\ at\ 3\text{-}C,2\text{-}H}$ 1, $J_{1\text{-}H,2\text{-}H}$ 7, 2-H).

(2*E*)-(4*R*)-[(2′*R*,4′*S*)-2′,4′-Dihydroxy-2′,6′,6′-trimethylcyclohexylidene]-3-methylpenta-2,4-dien-1-ol 11a and (2*E*)-(4*S*)-[(2′*S*,4′*S*)-2′,4′-dihydroxy-2′,6′,6′-trimethylcyclohexylidene]-3-methylpenta-2,4-dien-1-ol 11b

DIBAH (1 M solution in DCM; 19.00 mmol, 19.0 ml) was added dropwise over 15 min to a solution of a mixture of the two (2*E*)-(1′*RS*,2′*RS*,4′*S*) diastereoisomeric C_{15}-epoxides **10** (0.78 g, 2.34 mmol) in dry DCM (40 ml) at 0 °C under an N_2 atm. in the dark. The reaction mixture was stirred at 0 °C for a further 1.5 h after which it was treated dropwise with water at 0 °C to decompose the excess of DIBAH. The mixture was then saturated with sodium chloride and extracted thoroughly with DCM. The combined extracts were washed with water and brine, dried (Na_2SO_4) and evaporated to yield the two diastereoisomeric C_{15}-triols **11a** and **11b**, *ca.* 5:4 mixture (^{1}H NMR), as a yellow–orange oil (73%, 0.43 g, 1.71 mmol), >90% pure [TLC (system 4), ^{1}H NMR]. Flash chromatography provided the (2*E*)-(4*R*,2′*R*,4′*S*) isomer **11a** as a white solid (19% from **10**, 0.11 g, 0.44 mmol), >95% pure [TLC (system 4), ^{1}H NMR] and the (2*E*)-(4*S*,2′*S*,4′*S*) isomer **11b** as a light yellow oil (5% from **10**, 30.0 mg, 0.12 mmol), >80% pure [TLC (system 4), ^{1}H NMR]; compound **11a**: TLC (system 4) R_f 0.29; λ_{max}(ethanol)/nm 224 (Found: $M^+ - H_2O$, 234.162. $C_{15}H_{22}O_2$ requires *M*, 234.162); *m/z* (EI) 252 (1%), 234 (27), 219 (7), 161 (23), 135 (27), 109 (59), 105 (18), 95 (23), 91 (27), 77 (15) and 43 (100); δ_H 1.06 (3 H, s, Me at 6′-C), 1.24–1.42 (5 H, m, 3′-H^{ax}, 5′-H^{ax} and 3 × OH), 1.33 (3 H, s, Me at 6′-C), 1.35 (3 H, s, Me at 2′-C), 1.68 (3 H, d, $J_{Me\ at\ 3\text{-}C,2\text{-}H}$ 1, Me at 3-C), 1.94 (1 H, ddd, *J* 2, *J* 4, $J_{5'\text{-}H,5'\text{-}H}$ 12, 5′-H^{eq}), 2.25 (1 H, ddd, *J* 2, *J* 4, $J_{3'\text{-}H,3'\text{-}H}$ 13, 3′-H^{eq}), 4.26 (2 H, dd, $J_{1\text{-}H,OH\ at\ 1\text{-}C}$ 6, $J_{1\text{-}H,2\text{-}H}$ 7, 1-H), 4.31 (1 H, m, 4′-H), 5.60 (1 H, tq, $J_{Me\ at\ 3\text{-}C,2\text{-}H}$ 1, $J_{1\text{-}H,2\text{-}H}$ 7, 2-H) and 5.95 (1 H, s, 4-H); $[\alpha]_D^{21}$ −60.0 (*c* 0.8, methanol); compound **11b**: TLC (system 4) R_f 0.23; λ_{max}(ethanol)/nm 225 (Found: $M^+ - H_2O$, 234.162. $C_{15}H_{22}O_2$ requires *M*, 234.162); *m/z* (EI) 252 (1%), 234 (22), 219 (6), 179 (8), 161 (20), 155 (22), 135 (26), 109 (53), 105 (18), 95 (20), 91 (29) and 43 (100); δ_H 1.12 (3 H, s, Me at 6′-C), 1.17–1.40 (5 H, m, 3′-H^{ax}, 5′-H^{ax} and 3 × OH), 1.32 (3 H, s, Me at 6′-C), 1.40 (3 H, s, Me at 2′-C), 1.69 (3 H, s, Me at 3-C), 1.94 (1 H, m, 5′-H^{eq}), 2.24 (1 H, m, 3′-H^{eq}), 4.15 (1 H, m, 4′-H), 4.26 (2 H, dd, $J_{1\text{-}H,OH\ at\ 1\text{-}C}$ 6, $J_{1\text{-}H,2\text{-}H}$ 7, 1-H), 5.63 (1 H, t, $J_{1\text{-}H,2\text{-}H}$ 7, 2-H) and 6.10 (1 H, s, 4-H); $[\alpha]_D^{27}$ + 20.4 (*c* 1.0, MeOH).

(2*E*)-(4*RS*)-[(2′*RS*,4′*S*)-2′,4′-Dihydroxy-2′,6′,6′-trimethylcyclohexylidene]-3-methylpenta-2,4-dien-1-al 5

A 5:4 mixture of the preceding diastereoisomeric triols **11** (88.0 mg, 0.35 mmol) was dissolved in dry THF (10 ml) and manganese dioxide (0.90 g) was added to the solution. The reaction mixture was stirred vigorously at 20 °C under an N_2-atm. in the dark for 2 h and subsequently filtered through Celite. The filtrate was evaporated and CC of the resulting residue provided a 5:4 mixture (^{1}H NMR) of the two diastereoisomeric C_{15}-dihydroxy aldehydes **5**, as an orange oil (66%, 58.0 mg, 0.23 mmol), >90% pure [TLC (system 4), ^{1}H NMR]. The two diastereoisomers were inseparable by TLC (systems 3 and 4); TLC (system 4) R_f 0.77; λ_{max}(EtOH)/nm 286; ^{1}H NMR data for the (2*E*)-(4*R*)-(2′*R*,4′*S*) diastereoisomer **5a** were the same as those given for the pure isomer below. Compound (2*E*)-(4*S*,2′*S*,4′*S*)-**5**: δ_H 1.11 (3 H, s, Me at 6′-C), 1.39 (3 H, s, Me at 2′-C), 1.41 (3 H, s, Me at 6′-C), 2.16 (3 H, d, $J_{Me\ at\ 3\text{-}C,2\text{-}H}$ 1, Me at 3-C), 4.21 (1 H, m, 4′-H), 5.96 (1 H, d, $J_{1\text{-}H,2\text{-}H}$ 7, 2-H), 6.17 (1 H, s, 4-H) and 10.03 (1 H, d, $J_{1\text{-}H,2\text{-}H}$ 8, 1-H).

(2*E*)-(4*R*)-[(2′*R*,4′*S*)-2′,4′-Dihydroxy-2′,6′,6′-trimethylcyclohexylidene]-3-methylpenta-2,4-dien-1-al 5a

The preceding (2*E*)-(4*R*,2′*R*,4′*S*)-triol **11a** (0.16 g, 0.63 mmol) was dissolved in dry THF (20 ml) and manganese dioxide (1.50 g) was added to the solution. The reaction mixture was stirred vigorously at 20 °C under an N_2-atm. in the dark. UV–VIS spectroscopy and TLC (system 4) indicated complete conversion of the substrate after 1 h. The reaction mixture was filtered through Celite and the filtrate was evaporated. CC of the resulting residue provided the dihydroxy aldehyde **5a** as a white solid (92%, 0.15 g, 0.60 mmol), >98% pure, containing less than 2% of the (2*E*)-(4*S*,2′*S*,4′*S*)-isomer [TLC (system 4), ^{1}H NMR]; mp 178–179 °C; TLC (system 3) R_f 0.26; λ_{max}(EtOH)/nm 287; ν_{max}(KBr)/cm^{-1} 3353 (OH), 2995–2851 (CH), 1933 (C=C=C), 1662 (conj. C=O), 1601, 1456, 1373, 1194, 1161, 1139, 1102, 1041 and 874 (Found: M^+, 250.157. $C_{15}H_{22}O_3$ requires *M*, 250.157); *m/z* (EI) 250 (9%), 235 (8), 232 (24), 217 (11), 214 (1), 199 (7), 189 (13), 175 (19), 161 (14), 149 (60), 133 (69), 105 (31), 95 (19), 91 (26), 77 (25) and 43 (100); δ_H 1.10 (3 H, s, Me at 6′-C), 1.25–1.45 (2 H, m, 3′-H^{ax} and 5′-H^{ax}), 1.36 (3 H, s, Me at 2′-C), 1.38 (3 H, s, Me at 6′-C), 1.98 (1 H, ddd, *J* 2, *J* 4, $J_{5'\text{-}H,5'\text{-}H}$ 13, 5′-H^{eq}), 2.15 (3 H, d, $J_{Me\ at\ 3\text{-}C,2\text{-}H}$ 1, Me at 3-C), 2.28 (1 H, ddd, *J* 2, *J* 4, $J_{3'\text{-}H,3'\text{-}H}$ 13, 3′-H^{eq}), 4.33 (1 H, m, 4′-H), 5.94 (1 H, dq, $J_{Me\ at\ 3\text{-}C,2\text{-}H}$ 1, $J_{1\text{-}H,2\text{-}H}$ 8, 2-H), 6.07 (1 H, s, 4-H) and 10.03 (1 H, d, $J_{1\text{-}H,2\text{-}H}$ 8, 1-H); $[\alpha]_D^{22}$ −63.0 (*c* 0.5, MeOH).

(all-*E*)-(3*S*,5*R*,6*R*)-3,5-Dihydroxy-6,7-didehydro-5,6-dihydro-12′-apo-β-caroten-12′-al 16

The available[15] C_{10}-phosphonium salt **6** (0.46 g, 0.94 mmol) in dry methanol (10 ml) was warmed to 30–35 °C and toluene-*p*-sulfonic acid (1% solution in methanol; 3 drops) and trimethyl orthoformate (0.11 ml, 1.03 mmol) were added to the solution. The reaction mixture was stirred at 30–35 °C in the dark for 16 h and subsequently cooled to 0 °C. Ammonia (saturated solution in methanol; 3 drops) was added to the mixture which was then stirred at 0 °C for 30 min. Evaporation of the solvent and removal of the excess of formate, ammonia and methanol at 30 °C under reduced pressure (0.01 mmHg) yielded the protected C_{10}-phosphonium salt **14** as a yellow solid. The ^{1}H NMR data for **14** were as previously reported.[9] The (2*E*)-(4*R*,2′*R*,4′*S*)-dihydroxy aldehyde **5a** (0.12 mg, 0.48 mmol) and **14** in dry DCM (20 ml) were added dropwise to a stirred suspension of sodium hydride (0.23 g, unwashed) in dry DCM (30 ml) at 20 °C under an N_2-atm. in the dark. The reaction was monitored by TLC (system 3) and UV–VIS spectroscopy. Complete conversion of **5a** was observed after 40 h. The reaction mixture was cooled to 0 °C and an ice-cold mixture of acetic acid–water (1:1; 20 ml) was added dropwise to it with vigorous stirring. After 30 min at 0 °C, the mixture was diluted with water and extracted with DCM. The extract was washed with water and brine, dried (Na_2SO_4) and evaporated to yield a red oily residue. CC provided the (3*S*,5*R*,6*R*)-dihydroxy aldehyde **16** as a red oil (94%, 0.17 mg, 0.45 mmol), >95% pure [TLC (system 3), HPLC (system 1), ^{1}H NMR]. HPLC (system 1) indicated a mixture of the all-*E* isomer (75%) and three *Z* isomers (4 + 2 + 19%). The all-*E* isomer crystallised from an aliquot in benzene as an orange crystalline powder, >80% pure (^{1}H NMR), containing ~2% benzene after 8 h at 20 °C under reduced pressure (0.01 mmHg). ^{1}H NMR demonstrated the presence of two unidentified *Z* isomers in the crystalline sample. Complete ^{1}H NMR assignments are given for the all-*E* isomer only; mp 193–195 °C; TLC (system 3) R_f 0.13; HPLC (system 1) R_T 23.4 min; λ_{max}(hexane)/nm 386, 403 and 427, %III/II 18; λ_{max}(acetone)/nm 409 ($E^{1\%}_{1\,cm}$ 1570, ε 60 000, corrected for 2% benzene in the crystalline sample: $E^{1\%}_{1\,cm}$ 1600, ε 61 100); ν_{max}(KBr)/cm^{-1} 3395 (OH), 3032–2864 (CH), 1927 (C=C=C), 1668 (conj. C=O), 1609, 1553, 1454, 1384, 1286, 1265, 1186, 1157, 1044 and 956 (Found: M^+, 382.251. $C_{25}H_{34}O_3$ requires *M*, 382.251); *m/z* (EI) 382 (72%), 364 (42), 346 (26), 277 (14), 233 (22), 195 (23), 183 (23), 171 (24), 165 (25), 157 (35), 145 (26), 119 (33), 105 (40), 95 (49), 91 (46) and 43 (100); CD nm ($\Delta\varepsilon$) 220 (0), 233 (−2.0), 248 (−0.8), 272 (−0.2), 298 (−2.0), 343 (−0.1), 348 (0), 359 (+0.2) and 368 (0); δ_H 1.08 (3 H, s, 17-Me), 1.34 (1 H, m, 2-H^{ax}), 1.34 (3 H, s, 16-Me), 1.36 (3 H, s, 18-Me), 1.41 (1 H, m, 4-H^{ax}), 1.80 (3 H, s, 19-Me), 1.89 (3 H, s, 20′-Me), 1.95 (1 H, ddd, *J* 1, *J* 4, $J_{2\text{-}H,2\text{-}H}$ 13, 2-H^{eq}), 2.03 (3 H, s, 20-Me), 2.27 (1 H, ddd, *J* 2, *J* 4, $J_{4\text{-}H,4\text{-}H}$ 13, 4-H^{eq}), 4.32 (1 H, m, 3-H), 6.05 (1 H, s, 8-H), 6.13 (1 H, d, $J_{10\text{-}H,11\text{-}H}$ 12, H-10), 6.30 (1 H, d, $J_{14\text{-}H,15\text{-}H}$ 12, 14-H), 6.34 (1 H, d, $J_{11\text{-}H,12\text{-}H}$ 14, 12-H), 6.69 (1 H, dd, $J_{10\text{-}H,11\text{-}H}$ 12, $J_{11\text{-}H,12\text{-}H}$ 15, 11-H), 6.70 (1 H, dd, $J_{14'\text{-}H,15'\text{-}H}$ 11, $J_{15\text{-}H,15'\text{-}H}$ 15, 15′-H), 6.98 (1 H, d, $J_{14'\text{-}H,15'\text{-}H}$ 12, 14′-H), 7.03 (1 H, dd, $J_{14\text{-}H,15\text{-}H}$ 11, $J_{15\text{-}H,15'\text{-}H}$ 14, 15-H) and 9.46 (1 H, s, 12′-H).

(all-*E*)-(3*S*,5*R*,6*R*)-3,5-Dihydroxy-6,7-didehydro-5,6-dihydro-8′-apo-β-caroten-8′-al 17

(i) The available[9] C_5-phosphonium salt **7** (0.45 g, 1.06 mmol) was dissolved in dry methanol (10 ml) and the solution was heated to 30–35 °C. Toluene-*p*-sulfonic acid (1% solution in methanol; 5 drops) and trimethyl orthoformate (0.11 g, 0.11 ml, 1.00 mmol) were added to the solution and the reaction mixture was stirred at 30–35 °C for 16 h and subsequently cooled to 0 °C and treated with ammonia (saturated solution in methanol; 5 drops). The reaction mixture was stirred at 0 °C for 30 min after which evaporation of the solvent and removal of the excess of ammonia and methanol at 30 °C under reduced pressure (0.01 mmHg) yielded the protected phosphonium salt **15** as a white solid, >90% pure (^{1}H NMR), which was employed in the subsequent Wittig reaction without further purification; ν_{max}(KBr)/cm^{-1} 3057–2827 (CH), 1626, 1586, 1485, 1439, 1397, 1345, 1191, 1145, 1111, 1032 and 996; δ_H 1.31 (3 H, d, $J_{Me\ at\ 3\text{-}C,P}$ 4, Me at 3-C), 3.11 (6 H, s, MeO), 4.35 (1 H, d, $J_{4\text{-}H,P}$ 2, 4-H), 4.61 (2 H, dd, $J_{1\text{-}H,P}$ 15, $J_{1\text{-}H,2\text{-}H}$ 8, 1-H), 5.55 (1 H, dt, $J_{2\text{-}H,P}$ 6, $J_{1\text{-}H,2\text{-}H}$ 7, 2-H) and 7.60–7.90 (15 H, m, ArH). The protected C_5-phosphonium salt **15** and the (3*S*,5*R*,6*R*)-dihydroxy aldehyde **16** (0.14 mg, 0.37 mmol) in dry DCM (20 ml) were added dropwise to a stirred suspension of sodium hydride (0.22 g, unwashed) in dry DCM (30 ml) at 20 °C under an N_2-atm. in the dark. The reaction was monitored by TLC (system 3) and UV–VIS spectroscopy. Complete conversion of **16** was observed after 40 h. The reaction mixture was cooled to 0 °C and ice-cold acetic acid–water (1:1; 20 ml) was added dropwise to it with vigorous stirring. After 30 min at 0 °C, the mixture was diluted with water and extracted with DCM. The organic phase was washed with water and brine, dried (Na_2SO_4) and evaporated. CC of the resulting red residue provided the C_{30}-dihydroxy aldehyde **17** as a red solid (84%, 0.14 mg, 0.31 mmol), >99% pure [TLC (system 3), HPLC (system 1), ^{1}H NMR]. HPLC (system 1) indicated a mixture of the all-*E* isomer (79%) and two *Z* isomers (6 + 15%). Recrystallisation of an aliquot from diethyl ether provided the (all-*E*)-(3*S*,5*R*,6*R*) isomer as a red crystal powder, >95% pure (^{1}H NMR).

(ii) The aldehyde moiety of the available[15] C_{10}-phosphonium salt **6** (0.33 g, 0.67 mmol) was protected as the dimethyl acetal by treatment with toluene-*p*-sulfonic acid (1% solution in methanol; 3 drops) and trimethyl orthoformate (0.09 ml, 0.80 mmol) in dry methanol (10 ml) at 30–35 °C for 20 h, followed by treatment of the reaction mixture with ammonia (saturated solution in methanol; 5 drops) at 0 °C for 30 min. After solvent evaporation from the mixture, the resulting residue was warmed at 30 °C under reduced pressure (0.01 mmHg) to remove the excess of formate, ammonia and methanol and yield the C_{10}-dimethyl acetal phosphonium salt **14** as a light yellow solid. A 5:4 mixture of the two diastereoisomeric C_{15}-dihydroxy aldehydes **5** (56.0 mg, 0.25 mmol) and **14** in dry DCM (20 ml) were added dropwise to a stirred suspension of sodium hydride (0.16 g, unwashed) in dry DCM (30 ml) at 20 °C under an N_2-atm. in the dark. The reaction was monitored by TLC (system 3) and UV–VIS spectroscopy. Complete conversion of **5** was observed after 22 h. The reaction mixture was cooled to 0 °C and an ice-cold mixture of acetic acid–water (1:1; 20 ml) was added dropwise to it with vigorous stirring. The resulting mixture was stirred at 0 °C for 30 min, and then diluted with water and extracted with DCM. The organic phase was washed with water and brine, dried (Na_2SO_4) and evaporated. CC of the resulting red oily residue afforded a mixture of the two diastereoisomeric (3*S*,5*RS*,6*RS*)-dihydroxy aldehydes **16** as a red oil (52%, 48.0 mg, 0.13 mmol), >80% pure [TLC (system 3), HPLC (system 1), ^{1}H NMR]. HPLC (system 1) indicated a mixture of >5 isomers. The (all-*E*)-(3*S*,5*R*,6*R*) and (all-*E*)-(3*S*,5*S*,6*S*) isomers constituted 50 and 25% of total **16**, respectively. The isomeric mixture obtained in the reaction formed a broad zone on TLC plates (systems 3 and 4). No further attempt was made to isolate the pure allenic isomers. UV–VIS and mass spectra were as reported for the pure (all-*E*)-(3*S*,5*R*,6*R*) isomer **16** above. ^{1}H NMR data for (all-*E*)-(3*S*,5*R*,6*R*)-**16** were as reported for the pure compound above. The presence of (all-*E*)-(3*S*,5*S*,6*S*)-**16** was demonstrated by a singlet at 1.12 ppm for Me-17, a multiplet at 4.15 ppm for H-3, and a singlet at 6.17 ppm for the allenic proton (H-8). The isomeric mixture was used directly in the subsequent Wittig reaction. The available[9] C_5-phosphonium salt **7** (0.14 g, 0.33 mmol) was treated with toluene-*p*-sulfonic acid (1% solution in methanol; 3 drops) and trimethyl orthoformate (0.04 ml, 0.36 mmol) in dry methanol (10 ml) at 30–35 °C for 20 h, followed by treatment of the reaction mixture with ammonia (saturated solution in methanol; 5

drops) at 0 °C for 30 min. Evaporation of the solvent and removal of the excess of formate, ammonia and methanol at 30 °C under reduced pressure (0.01 mmHg) yielded the protected C_5-phosphonium salt **15** as a light yellow solid. The protected C_5-phosphonium salt **15** and the above described diastereoisomeric C_{25}-dihydroxy aldehydes **16** (48.0 mg, 0.13 mmol) in dry DCM (20 ml) were added dropwise to a stirred suspension of sodium hydride (0.10 g, unwashed) in dry DCM (20 ml) at 20 °C under an N_2-atm. in the dark. The reaction was monitored by TLC (system 3) and UV–VIS spectroscopy. Complete conversion of **16** was observed after 40 h. The reaction mixture was cooled to 0 °C and ice-cold acetic acid–water (1:1; 20 ml) was added dropwise to it with vigorous stirring. After 30 min at 0 °C, the mixture was diluted with water and extracted with DCM. The extract was washed with water and brine, dried (Na_2SO_4) and evaporated. CC of the resulting residue provided the (3*S*,5*R*,6*R*)-C_{30}-dihydroxy aldehyde **17** as a red solid (60%, 34.0 mg, 0.08 mmol), >95% pure [TLC (system 3), HPLC (system 1), ^{1}H NMR]. HPLC (system 1) indicated a mixture of the all-*E* isomer (78%) and two *Z* isomers (9 + 13%). The (3*S*,5*S*,6*S*) isomer was not obtained in the pure form. Crystallisation of (3*S*,5*R*,6*R*)-**17** from diethyl ether provided (all-*E*)-(3*S*,5*R*,6*R*)-**17** as a red crystal powder, >98% pure [HPLC (system 1), ^{1}H NMR]; mp 209–210 °C; TLC (system 3) R_f 0.18; HPLC (system 1) R_T 23.7 min; λ_{max}(hexane)/nm 423, 445 and 474, %III/II 42; λ_{max}(acetone)/nm 420, 446 ($E^{1\%}_{1\,cm}$ 2020, ε 90 500) and 464; ν_{max}(KBr)/cm^{-1} 3392 (OH), 3031–2707 (CH), 1924 (C=C=C), 1668 (conj. C=O), 1609, 1572, 1527, 1453, 1376, 1273, 1170, 1153, 1069, 1042, 1004 and 960 (Found: M$^+$, 448.298. $C_{30}H_{40}O_3$ requires *M*, 448.298); *m/z* (EI) 448 (51%), 430 (34), 412 (21), 247 (10), 233 (16), 215 (15), 207 (20), 197 (25), 195 (20), 171 (22), 157 (29), 145 (29), 119 (46), 105 (46), 91 (57), 55 (55) and 43 (100); CD nm ($\Delta\varepsilon$) 223 (−0.2), 230 (−0.8), 236 (−0.5), 260 (−1.4), 280 (−0.9), 306 (−0.4), 318 (−0.6), 324 (−0.5), 332 (−0.6), 353 (0), 364 (+0.1) and 377 (0); δ_H 1.07 (3 H, s, 17-Me), 1.32 (1 H, m, 2-H^{ax}), 1.34 (3 H, s, 16-Me), 1.35 (3 H, s, 18-Me), 1.41 (1 H, m, 4-H^{ax}), 1.81 (3 H, s, 19-Me), 1.90 (3 H, d, $J_{19'\text{-Me},10'\text{-H}}$ 1, 19′-Me), 1.95 (1 H, ddd, *J* 2, *J* 4, $J_{2\text{-H},2\text{-H}}$ 13, 2-H^{eq}), 1.99 (3 H, s, 20-Me), 2.00 (3 H, s, 20′-Me), 2.27 (1 H, ddd, *J* 2, *J* 4, $J_{4\text{-H},4\text{-H}}$ 13, 4-H^{eq}), 4.32 (1 H, m, H-3), 6.04 (1 H, s, 8-H), 6.12 (1 H, d, $J_{10\text{-H},11\text{-H}}$ 11, 10-H), 6.27 (1 H, d, $J_{14\text{-H},15\text{-H}}$ 11, 14-H), 6.34 (1 H, d, $J_{11\text{-H},12\text{-H}}$ 15, 12-H), 6.45 (1 H, d, $J_{14'\text{-H},15'\text{-H}}$ 11, 14′-H), 6.61 (1 H, dd, $J_{10\text{-H},11\text{-H}}$ 11, $J_{11\text{-H},12\text{-H}}$ 15, 11-H), 6.67 (1 H, dd, $J_{14'\text{-H},15'\text{-H}}$ 11, $J_{15\text{-H},15'\text{-H}}$ 15, 15′-H), 6.72 (1 H, dd, $J_{10'\text{-H},11'\text{-H}}$ 12, $J_{11'\text{-H},12'\text{-H}}$ 14, 11′-H), 6.74 (1 H, d, $J_{11'\text{-H},12'\text{-H}}$ 14, 12′-H), 6.77 (1 H, $J_{14\text{-H},15\text{-H}}$ 11, $J_{15\text{-H},15'\text{-H}}$ 15, 15-H), 6.94 (1 H, d, $J_{10'\text{-H},11'\text{-H}}$ 11, 10′-H) and 9.45 (1 H, s, 8′-H).

(all-*E*)-(3*S*,5*R*,6*R*,8′*RS*)-3,5,8′-Trihydroxy-6,7-didehydro-5,6,7′,8′-tetrahydro-7′-apo-β-carotene 18

Methyllithium (1.4 M solution in diethyl ether; 1.54 mmol, 1.10 ml) was added dropwise to a stirred solution of the preceding C_{30}-dihydroxy aldehyde **17** (98.1 mg, 0.22 mmol) in dry THF (50 ml) at 20 °C under an N_2-atm. in the dark. The reaction mixture was stirred at 20 °C under an N_2-atm. in the dark for 1.5 h and subsequently cooled to 0 °C. It was then treated with water, added carefully to decompose the excess of methyllithium, and extracted with diethyl ether. The extract was washed with water and brine, dried (Na_2SO_4) and evaporated to dryness. CC of the resulting residue provided the two C-8′epimeric C_{31}-triols **18**, inseparable by TLC (systems 3 and 4) as a *ca.* 1:1 mixture [HPLC (system 1)], as a red solid in 96% combined yield (97.7 mg, 0.21 mmol), >95% pure [TLC (system 4), HPLC (system 1), ^{1}H NMR]. HPLC (system 1) indicated a mixture of the all-*E* isomers (84%) and four *Z* isomers (1 + 2 + 3 + 10%). The pure all-*E* C-8′ epimeric triols **18** were obtained as a 1:1 mixture by crystallisation of an aliquot from diethyl ether; mp 131–138 °C; TLC (system 4) R_f 0.43–0.31 (broad zone); HPLC (system 3) R_T 25.6 and 25.8 min; λ_{max}(acetone)/nm 395, 418 and 446, %III/II 74 (Found: M$^+$, 464.329. $C_{31}H_{44}O_3$ requires *M*, 464.329); *m/z* (EI) 464 (26%), 446 (60), 428 (23), 410 (10), 233 (19), 221 (10), 197 (24), 195 (15), 171 (27), 157 (37), 133 (37), 119 (53), 105 (52), 91 (67), 55 (50) and 43 (100); δ_H 1.06 (3 H, s, 17-Me), 1.30 (3 H, d, $J_{7'\text{-Me},8'\text{-H}}$ 6, 7′-Me), 1.33 (3 H, s, 16-Me), 1.33 (1 H, m, 2-H^{ax}), 1.35 (3 H, s, 18-Me), 1.42 (1 H, m, 4-H^{ax}), 1.80 (3 H, s, 19-Me), 1.83 (3 H, s, 19′-Me), 1.95 (1 H, m, 2-H^{eq}), 1.95 (6 H, s, 20-Me and 20′-Me), 2.26 (1 H, s, 4-H^{eq}), 4.30 (2 H, m, 3-H and 8′-H), 6.03 (1 H, s, 8-H), 6.11 (1 H, d, $J_{10\text{-H},11\text{-H}}$ 11, 10-H), 6.17 (1 H, d, $J_{10'\text{-H},11'\text{-H}}$ 11, 10′-H), 6.24 (2 H, m, 14-H and 14′-H), 6.31 and 6.32 (2 H, 2 × d, $J_{11\text{-H},12\text{-H}}$ and $J_{11'\text{-H},12'\text{-H}}$ 15, 12-H and 12′-H), 6.48 (1 H, m, 11′-H), 6.55 (1 H, m, 11-H) and 6.62 (2 H, m, 15-H and 15′-H).

(all-*E*)-(3*S*,5*R*,6*R*)-paracentrone 1

The C-8′ epimeric C_{31}-triols **18** (56.8 mg, 0.12 mmol) in acetone (50 ml) were stirred with manganese dioxide (0.85 g) at 20 °C under an N_2-atm. in the dark. The reaction was monitored by TLC (system 4) and HPLC (system 1). Complete conversion of **18** was observed after 75 min. The reaction mixture was filtered and evaporated. CC of the resulting residue afforded **1** as a red solid (75%, 43.1 mg, 0.09 mmol), >99% pure [TLC (system 4), HPLC (systems 1 and 2)]. HPLC (system 2) indicated a mixture of the all-*E* isomer (85%) and four *Z* isomers (7 + 2 + 4 + 2%). The all-*E* isomer crystallised from benzene, >95% pure [HPLC (system 2), ^{1}H NMR], containing ~4% benzene after 8 h at 20 °C under reduced pressure (0.01 mmHg); mp 184–185 °C; TLC (system 4) R_f 0.50; HPLC (system 1) R_T 23.7 min, (system 2) R_T 50.1 min; λ_{max}(hexane)/nm 417, 439 and 467, %III/II 54; λ_{max}(acetone)/nm 416, 442 ($E^{1\%}_{1\,cm}$ 1960, ε 90 600, corrected for 4% benzene in the crystalline sample: $E^{1\%}_{1\,cm}$ 2050, ε 95 000) and 464, %III/II 8; λ_{max}(diethyl ether)/nm 417, 440 and 464, %III/II 10; ν_{max}(KBr)/cm^{-1} 3406 (OH), 3020–2863 (CH), 1926 (C=C=C), 1652 (conj. C=O), 1606, 1576, 1528, 1452, 1365, 1318, 1278, 1227, 1155, 1069, 1040 and 958 (Found: M$^+$, 462.314. $C_{31}H_{42}O_3$ requires *M*, 462.313); *m/z* (EI) 462 (34%), 444 (28), 426 (24), 261 (7), 233 (11), 221 (10), 209 (13), 197 (20), 195 (12), 183 (13), 167 (29), 157 (34), 149 (27), 119 (32), 109 (29), 105 (32), 95 (15), 91 (32) and 43 (100); CD nm ($\Delta\varepsilon$) 222 (−0.9), 228 (−1.1), 240 (−0.8), 250 (−1.0), 261 (−0.8), 267 (−0.9), 350 (0), 366 (+0.3) and 386 (0); δ_H 1.07 (3 H, s, 17-Me), 1.35 (1 H, m, 2-H^{ax}), 1.33 (3 H, s, 16-Me), 1.35 (3 H, s, 18-Me), 1.41 (1 H, m, 4-H^{ax}), 1.81 (3 H, s, 19-Me), 1.94 (3 H, d, $J_{19'\text{-Me},10'\text{-H}}$ 1, 19′-Me), 1.96 (1 H, m, 2-H^{eq}), 1.98 (3 H, s, 20-Me), 1.99 (3 H, s, 20′-Me), 2.27 (1 H, ddd, *J* 2, *J* 4, $J_{4\text{-H},4\text{-H}}$ 13, 4-H^{eq}), 2.36 (3 H, s, 7′-Me), 4.32 (1 H, m, 3-H), 6.03 (1 H, s, 8-H), 6.12 (1 H, d, $J_{10\text{-H},11\text{-H}}$ 11, 10-H), 6.26 (1 H, d, $J_{14\text{-H},15\text{-H}}$ 11, 14-H), 6.34 (1 H, d, $J_{11\text{-H},12\text{-H}}$ 15, 12-H), 6.39 (1 H, d, $J_{14'\text{-H},15'\text{-H}}$ 12, 14′-H), 6.58 (1 H, dd, $J_{10\text{-H},11\text{-H}}$ 11, $J_{11\text{-H},12\text{-H}}$ 15, 11-H), 6.60 (1 H, dd, $J_{10'\text{-H},11'\text{-H}}$ 12, $J_{11'\text{-H},12'\text{-H}}$ 16, 11′-H), 6.62 (1 H, dd, $J_{14'\text{-H},15'\text{-H}}$ 11, $J_{15\text{-H},15'\text{-H}}$ 15, 15′-H), 6.67 (1 H, d, $J_{11'\text{-H},12'\text{-H}}$ 16, 12′-H), 6.74 (1 H, dd, $J_{14\text{-H},15\text{-H}}$ 11, $J_{15\text{-H},15'\text{-H}}$ 14, 15-H) and 7.14 (1 H, dq, $J_{19'\text{-Me},10'\text{-H}}$ 1, $J_{10'\text{-H},11'\text{-H}}$ 10, 10′-H); δ_C 11.6 (C-19′), 12.8 and 12.9 (C-20 and C-20′), 14.0 (C-19), 25.6 (C-7′), 29.3 (C-16), 31.4 (C-18), 32.2 (C-17), 35.8 (C-1), 48.9 (C-4), 49.4 (C-2), 64.2 (C-3), 73.0 (C-5), 103.2 (C-8), 117.7 (C-6), 123.8 (C-11′), 125.6 (C-11), 128.3 (C-10), 129.4 (C-15′), 132.1 (C-14), 132.2 (C-15), 132.6 (C-9), 135.5 (C-14′), 136.2 (C-12), 137.1 (C-9′) 137.9 (C-13 and C-13′), 140.0 (C-10′), 144.5 (C-12′), 199.4 (C-8′) and 202.4 (C-7).

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