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Total Synthesis of Acetylenic Carotenoids. 2. Synthesis of (all-*E*)-(3*R*,3′*R*)-Diatoxanthin and (all-*E*)-(3*R*)-7,8-Didehydrocryptoxanthin

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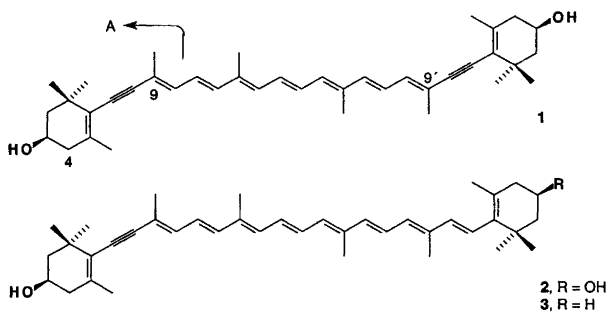
Optically active (all-*E*)-(3*R*,3′*R*)-diatoxanthin, indistinguishable from the natural carotenol, has been prepared by total synthesis for the first time with 34% overall yield in four steps from the available (2*E*)-5-[(4*R*)-4-hydroxy-2,6,6-trimethylcyclohex-1-enyl]-3-methylpent-2-en-4-ynal, 5-[(4*R*)-4-hydroxy-2,6,6-trimethylcyclohex-1-enyl]-3-methyl-2,4-pentadienyltriphenylphosphonium bromide and 2,7-dimethyl-2,4,6-octatrienedial by a $C_{15} + C_{10} + C_{15}$ approach.

By an alternative route from (2*E*)-5-[(4*R*)-4-hydroxy-2,6,6-trimethylcyclohex-1-enyl]-3-methylpent-2-en-4-ynal, 5-[(4*R*)-4-hydroxy-2,6,6-trimethylcyclohex-1-enyl]-3-methyl-2,4-pentadienyltriphenylphosphonium bromide and (7-formyl-2-methyl-2,4,6-octatrienyl)triphenylphosphonium bromide, the same target compound was obtained in 18% overall yield in two steps via (all-*E*)-(3*R*)-3-hydroxy-7,8-didehydro-12′-apo-β-caroten-12′-al.

The previously undescribed optically active (all-*E*)-(3*R*)-7,8-didehydrocryptoxanthin was synthesised with an overall yield of 34% in four steps from (2*E*)-5-3-methylpent-2-en-4-ynal, 5-[(4*R*)-4-hydroxy-2,6,6-trimethylcyclohex-1-enyl]-3-methyl-2,4-pentadienyltriphenylphosphonium bromide and 2,7-dimethyl-2,4,6-octatrienedial.

More than twenty different, naturally occurring acetylenic carotenoids are known.[1] Hitherto three monoacetylenic (crocoxanthin,[2] 7,8-didehydroastaxanthin[3] and pyrrhoxanthin[4]) and two diacetylenic [alloxanthin (**1**)[2,5] and 7,8,7′,8′-tetradehydroastaxanthin[3]] carotenoids have been prepared by total synthesis as optically neutral mixtures[2,4] or pure optical isomers.[3,5] In addition, partial syntheses of pyrrhoxanthin,[6,7] pectenol[8,9] and diatoxanthin (**2**)[10,11] have been reported. These acetylenic carotenoids all contain end groups A or the 4-keto analogue, Scheme 1.



Scheme 1.

Problems have been associated with construction of the 9*E* (9′*E*) double bonds.[2,3,5] Weedon and co-workers[2] synthesised alloxanthin (**1**) with the 9*Z*,9′*Z*-configuration, whereas the all-*E* isomer was obtained by Saucy *et al.*,[5] cf. also Bernhard *et al.*[3] An acetylenic C_{15} phosphonium salt/ylide intermediate results in the formation of the thermodynamically more stable 9*Z* (9′*Z*) isomer[12] in the subsequent Wittig reaction.[3]

It is surprising that no total synthesis of the monoacetylenic diatoxanthin (**2**) has been performed. (3*R*,3′*R*)-Diatoxanthin (**2**) is among the major carotenoids in several algal classes, including the Dinophyceae, Prymnesiophyceae, Bacillariophyceae, Xanthophyceae and Euglenophyceae.[13,14]

In this paper the first total synthesis of optically active (all-*E*)-(3*R*,3′*R*)-diatoxanthin (**2**) is reported. Also, the previously undescribed (all-*E*)-(3*R*)-7,8-didehydrocryptoxanthin (**3**) has been synthesised from available starting materials.

Results and discussion

*Synthesis of (all-*E*)-(3*R*,3′*R*)-diatoxanthin (**2**).* The strategy for the total synthesis of **2** was based on a $C_{15} + C_{10} + C_{15}$

approach with a final Wittig condensation (i) of a C_{25}-phosphonium salt with an acetylenic C_{15}-aldehyde or alternatively (ii) of a C_{15}-phosphonium salt with an acetylenic C_{25}-aldehyde.

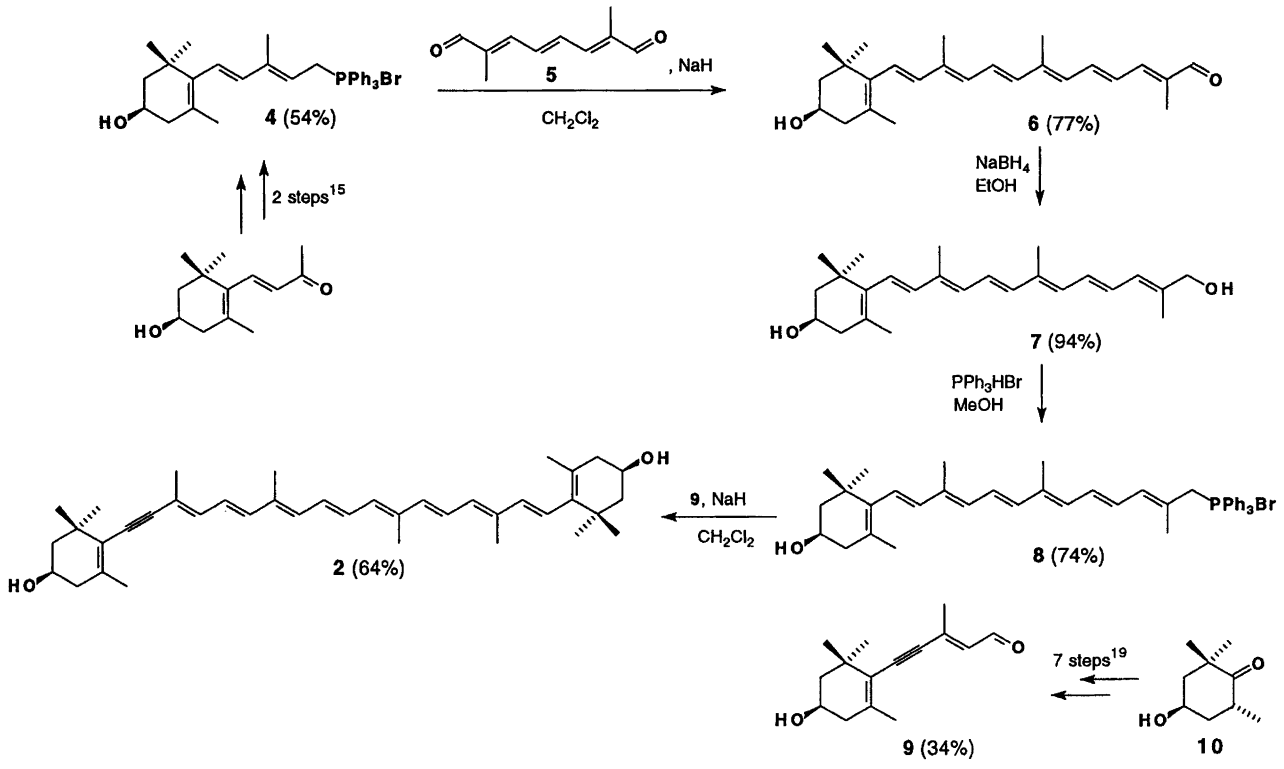
Route 1. The C_{15}-phosphonium salt **4**, Scheme 2, was available from a recent synthesis of (3*R*)-3-hydroxysintaxanthin.[15] A Wittig reaction between **4** and the available C_{10}-dial **5** provided the well known C_{25}-hydroxy aldehyde **6**.[16–18] Reduction of **6** with sodium borohydride gave the C_{25}-diol **7**, which was converted into the phosphonium salt **8** by treatment with triphenylphosphine hydrobromide. Finally the Wittig reaction between **8** and the acetylenic C_{15}-aldehyde **9** furnished diatoxanthin (**2**) in 64% yield. The synthesis of the optically active C_{15}-aldehyde **9** has recently been published separately.[19]

The overall yield of diatoxanthin (**2**) in this 13-step sequence from optically active actinol (**10**) was 22% based on actinol (**10**). The crude diatoxanthin (**2**) was shown by HPLC shown to be a mixture of the all-*E* isomer (63% of total) and three different *Z* isomers (13 + 13 + 11%). Pure (all-*E*)-diatoxanthin (**2**) crystallised from methanol–diethyl ether as a bright red crystalline powder. Its melting point, chromatographic behaviour and spectral data (UV–VIS, IR, MS, ^{1}H NMR and ^{13}C NMR) were as expected for structure **2**. The CD spectrum was consistent with that reported for natural diatoxanthin (**2**),[20,21] albeit with higher Δε values for the synthetic compound. No chromatographic separation could be achieved for synthetic **2** and a natural sample. This total synthesis represents a final proof for the structure, including the 3*R*,3′*R*-configuration of natural diatoxanthin (**2**).

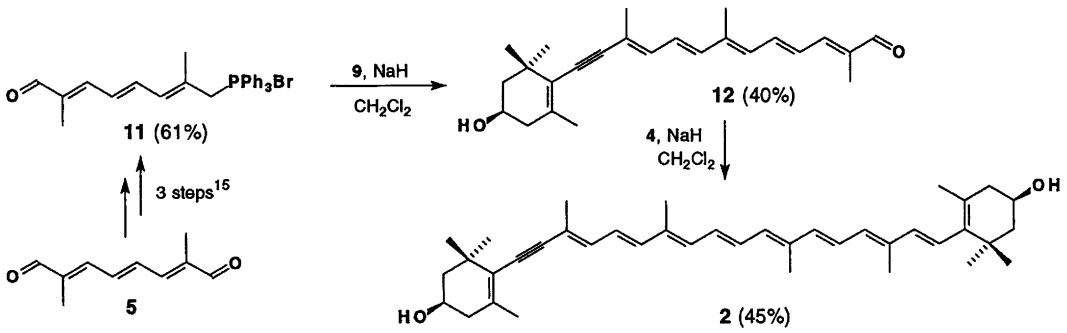
Route 2, Scheme 3. The C_{10}-phosphonium salt **11** was available from a recent synthesis of sintaxanthin and 3-hydroxysintaxanthin.[15] A Wittig reaction of **11** with the C_{15}-acetylenic aldehyde **9** afforded the C_{25} apocarotenal **12** in 40% yield, previously obtained by Weedon *et al.*[22] by a Wittig condensation between the C_{10}-dial **5** and the C_{15}-acetylenic hydroxy phosphonium salt. A Wittig reaction between the acetylenic C_{25}-carotenal **12** and the C_{15}-hydroxyphosphonium salt **4** furnished diatoxanthin (**2**).

The overall yield of diatoxanthin (**2**) by this 14-step sequence from actinol (**10**) was 6%, based on actinol. The crude diatoxanthin (**2**) was shown by HPLC to be a mixture of the all-*E* isomer (74% of the total) and three different *Z* isomers (7 + 3 + 16%). Judged by HPLC these *Z* isomers differed from those obtained in route 1 above. The (all-*E*)-(3*R*,3′*R*) isomer was crystallised from methanol–diethyl ether and had identical spectroscopic and chromatographic properties with diatoxanthin (**2**) obtained in route 1.

*Synthesis of (all-*E*)-(3*R*)-7,8-didehydrocryptoxanthin (**3**).* The C_{15}-phosphonium salt **13**, Scheme 4, was available from the synthesis of sintaxanthin.[15] A Wittig reaction between **13** and the C_{10}-dial **5** gave the well known C_{25}-



Scheme 2.



Scheme 3.

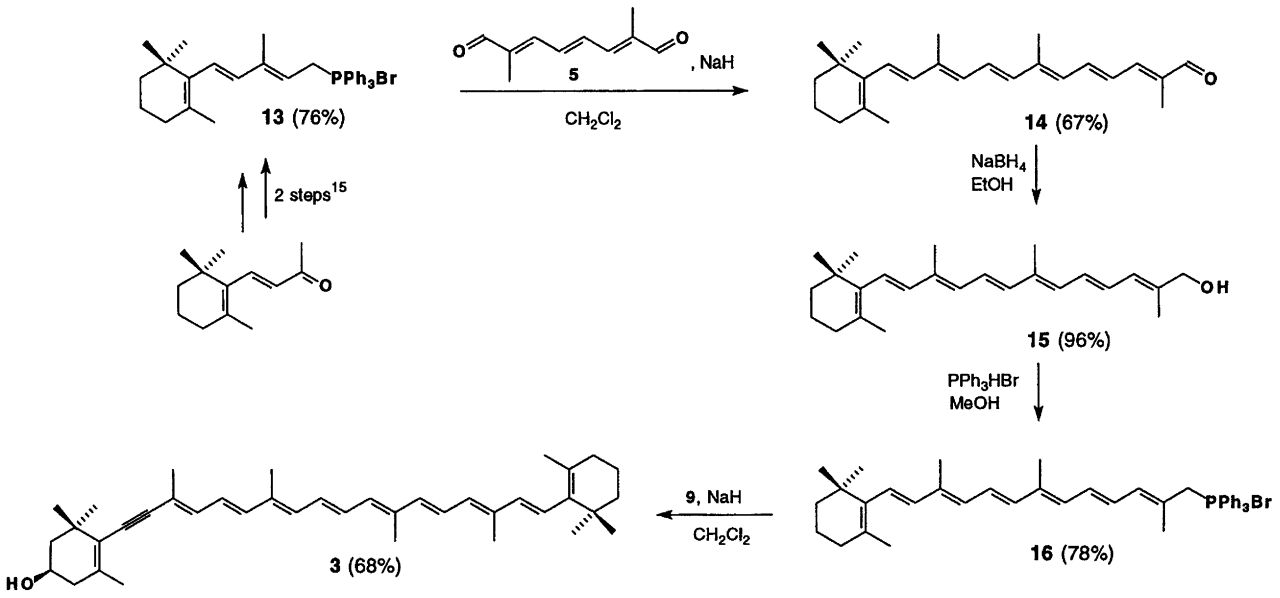
aldehyde **14**.[23] Reduction of the aldehyde moiety gave the C_{25}-allylic alcohol **15**, which upon treatment with triphenylphosphine hydrobromide furnished the corresponding phosphonium salt **16**. A final Wittig reaction between **16** and the C_{15}-acetylenic hydroxyaldehyde **9** afforded the acetylenic 7,8-didehydrocryptoxanthin (**3**).

The overall yield of 7,8-didehydrocryptoxanthin (**3**) by this 13-step $C_{15}+C_{10}+C_{15}$ sequence from actinol (**10**) was 23%, based on actinol. The crude carotenoid was a mixture of the all-*E* isomer (77% of total) and different *Z* isomers (10 + 7 + 6%), as indicated by HPLC. The pure all-*E* isomer was crystallised from methanol–diethyl ether. Spectroscopic data (UV–VIS, MS, IR, ^{1}H NMR and ^{13}C NMR) were as predicted for **3**. The CD spectrum exhibited a very weak negative Cotton effect, which in comparison with that of (all-*E*)-(3*R*,3′*R*)-alloxanthin (**1**)[5,21] was consistent with the 3*R*-configuration. The weak Cotton effect has been rationalised by the lack of an intrinsically chiral chromophore in chiral acetylenic carotenols such as **3**.[21]

Experimental

General methods. These were as recently given in detail.[15] Pyridine was distilled over solid potassium hydroxide. Assignments of NMR signals for each compound are based on ^{1}H–^{1}H COSY data, and on reported chemical shifts for protons and carbon atoms in carotenoids.[24] Carbon atoms and protons in side chains are given primed numbers.

General procedure for phosphonium salt formation. To the allylic alcohol dissolved in methanol was added triphenylphosphine hydrobromide and the mixture was kept in the dark, under a nitrogen atmosphere at 20 °C. The reaction was monitored by TLC. When TLC indicated 100% conversion of the alcohol, the reaction mixture was concentrated, water was added and the phosphonium salt extracted with dichloromethane. The organic phase was washed with water, dried over anhydrous sodium sulfate and the solvents evaporated off.



Scheme 4.

General procedure for Wittig condensations. This was adapted from Ref. 25. The phosphonium salt and the aldehyde in dry dichloromethane were added dropwise to a suspension of sodium hydride in dry dichloromethane at 20°C, under a nitrogen atmosphere in the dark. The reaction was monitored by TLC and cooled to 0°C when TLC indicated optimal conversion. Ice was added carefully to decompose the excess of sodium hydride, and the product was extracted with dichloromethane. The organic phase was washed several times with water, dried over anhydrous sodium sulfate and evaporated to dryness under reduced pressure. Chromatographic separation (TLC/CC) followed by crystallisation afforded the crystalline condensation product.

*Synthesis of (all-*E*)-(3*R*,3′*R*)-diatoxanthin (***2***). Route 1.*

*(all-*E*)-(3*R*)-3-Hydroxy-12′-apo-β-caroten-12′-al (***6***).* Compound **4** was available.[15] The C_{10}-dial **5** (0.49 g, 3.0 mmol) and **4** (0.54 g, 0.96 mol) in dry dichloromethane (30 ml) were added dropwise to a suspension of sodium hydride (0.46 g, unwashed) in dry dichloromethane (30 ml), 12 h reaction time, cf. the general procedure. Crystallisation from acetone–hexane furnished **6** as an orange-red solid in 77% yield (0.27 g, 0.77 mmol), 99% pure (HPLC).

M.p. 175–178°C; UV–VIS: λ_{max} (ethanol) 417 nm; MS [IP 50 eV; 180°C; *m/z* (% rel. int.)]: 366 (100, [*M*]), 348 (2, [*M* − 18]), 277 (3), 255 (3), 213 (6), 197 (6), 173 (12), 171 (10), 159 (13), 147 (17), 133 (14), 131 (13), 121 (11), 119 (25), 107 (14), 105 (22), 95 (19), 91 (19), 43 (18); ^{1}H NMR ($CDCl_3$): δ 1.076 (s, 3 H, Me-16 and Me-17), 1.48 (m, 1 H, H-2ax), 1.738 (s, 3 H, Me-18), 1.77 (m, 1 H, H-2ax), 1.884 (s, 3 H, Me-20′), 1.990 (s, 3 H, Me-19), 2.03 (m, 1 H, H-4ax), 2.045 (s, 3 H, Me-20), 2.39 (dd, 1 H, *J* 4.5 Hz, *J* 17.1 Hz, H-4eq), 4.00 (m, 1 H, H-3), 6.15–6.20 (m, 3 H, H-7, H-8 and H-10), 6.30 (d, 1 H, *J* 11.7 Hz, H-14), 6.38 (d, 1 H, *J* 14.7 Hz, H-12), 6.69 (dd, 1 H, *J* 11.7 Hz, *J* 14.2 Hz, H-15′), 6.79 (dd, 1 H, *J* 11.2 Hz, *J* 14.2 Hz, H-11), 6.96 (d, 1 H, *J* 11.7 Hz, H-14′), 7.03 (dd, 1 H, *J* 12.2 Hz, *J* 14.2 Hz, H-15), 9.45 (s, 1 H, H-12′).

*(all-*E*)-(3*R*)-3-Hydroxy-12′-apo-β-caroten-12′-ol (***7***).* To **6** (92 mg, 0.28 mmol) in ethanol (40 ml) was added sodium borohydride (10 mg, 0.26 mmol) in ethanol (15 ml) dropwise at 20°C. The reaction mixture was kept at 20°C for 2 h and then concentrated to ca. 5 ml. Water was added and the product was extracted with diethyl ether. The organic phase was washed with brine and water and dried over anhydrous sodium sulfate. Evaporation of the solvent and CC of the residue afforded **7** as a red oil in 94% yield (89 mg, 0.26 mmol) 96% pure [HPLC, 81% all-*E* and three *Z* isomers (4 + 3 + 8%)].

UV–VIS: λ_{max} (ethanol) 357, 373, 390 nm; MS [IP 70 eV, 180°C; *m/z* (% rel. int.)]: 368 (100, [*M*]), 350 (6, [*M* − 18]), 342 (4, [*M* − 26]), 332 (2, [*M* − 18 − 18]), 145 (10), 133 (10), 119 (15), 97 (16), 71 (18), 43 (46); ^{1}H NMR ($CDCl_3$): δ 1.069 (s, 6 H, Me-16 and Me-17), 1.47 (m, 1 H, H-2ax), 1.733 (s, 3 H, Me-18), 1.77 (m, 1 H, H-2eq), 1.831 (s, 3 H, Me-20′), 1.953 (s, 3 H, Me-19 or Me-20), 1.962 (s, 3 H, Me-19 or Me-20), 2.03 (m, 1 H, H-4ax), 2.35 (m, 1 H, H-4eq), 3.99 (m, 1 H, H-3), 4.10 (s, 2 H, H-12′), 6.09–6.15 (m, 3 H, H-7, H-8 and H-10), 6.19 (d, 1 H, *J* 11.2 Hz, H-14), 6.34 (d, 1 H, *J* 14.7 Hz, H-12), 6.49 (dd, 1 H, *J* 11.2 Hz, *J* 14.7 Hz, H-15′), 6.53 (d, 1 H, *J* 10.8 Hz, H-14′), 6.58 (dd, 1 H, *J* 11.2 Hz, *J* 15.1 Hz, H-11), 6.62 (dd, 1 H, *J* 11.2 Hz, *J* 14.7 Hz, H-15).

*[(3*R*)-3-Hydroxy-12′-apo-β-carotenyl]triphenylphosphonium bromide (***8***).* Compound **7** (0.34 g, 1.23 mmol) in methanol (130 ml) was treated with triphenylphosphine hydrobromide (0.63 g, 1.85 mmol), reaction time 48 h, cf. the general procedure. Crystallisation from methanol–ethyl acetate gave **8** as a yellow powder in 74% yield (0.63 mg, 0.91 mmol) > 95% pure (as indicated by ^{1}H NMR spectroscopy).

UV–VIS: λ_{max} 270, 360, 384, 403 nm; IR: (KBr) cm^{-1}, 3313s (OH), 3029–2853s (CH), 1436s, 1109s, 965m, 690s; ^{1}H NMR ($CDCl_3$): δ 1.057 (s, 3 H, Me-16 and Me-17), 1.47 (m, 1 H, H-2ax), 1.61 (d, *J* 4.4 Hz, Me-20′), 1.717 (s, 3 H, Me-18), 1.77 (m, 1 H, H-2eq), 1.887 (s, 3 H, Me-19 or Me-20), 1.950 (s, 6 H, Me-19 or Me-20), 2.04 (m, 1 H, H-4ax), 2.38 (dd, 1 H, *J* 5.4 Hz, *J* 16.6 Hz, H-4eq), 4.00 (m, 1 H, H-3), 4.88 (d, 2 H, *J* 15.6 Hz, H-12′), 6.08–6.40 (m, 9 H, olefinic protons), 6.63 (dd, 1 H, *J* 11.7 Hz, *J* 14.7 Hz, olefinic proton), 7.60–7.95 (m, 15 H, aromatic protons).

*(all-*E*)-(3*R*,3′*R*)-Diatoxanthin (***2***).* Compounds **8** (0.25 g, 0.38 mmol) and **9** (0.087 g, 0.38 mmol) in dry dichloromethane (40 ml) were added dropwise to a suspension of sodium hydride (0.15 g, unwashed) in dry dichloromethane (40 ml), reaction time 48 h, see the general procedure. CC of the residue afforded diatoxanthin (**2**) in 64% yield (138 mg, 0.244 mmol) 100% pure (HPLC) as a mixture of the all-*E* isomer (63%) and three *Z* isomers (13 + 13 + 11%). Repeated crystallisation from methanol–diethyl ether afforded (all-*E*)-diatoxanthin (**2**) as a bright red crystalline powder, 100% pure (HPLC).

M.p. 203°C; VIS: λ_{max} (acetone) 430, 453 ($E^{1\%}_{1cm}$ = 2720, ε = 154000), 480 nm, % III/II = 42; IR: (KBr) cm^{-1} 3376s (OH), 3027–2825s (CH), 2171w (C≡C), 1446m, 1360m, 1050s, 959s; MS [IP 70 eV, 200°C; *m/z* (% rel. int.)]: 566 (100, [*M*]), 548 (11, [*M* − 18]), 474 (6, [*M* − 92]), 408 (5, [*M* − 158]), 283 (15), 119 (31), 43 (34); CD nm (Δε): 216 (−6.5), 224 (−5.9), 239 (0), 252 (+4.5), 264 (0), 289 (−10.1), 319 (0), 347 (+2.8); ^{1}H NMR ($CDCl_3$): δ 1.073 (s, 6 H, Me-16′ and Me-17′), 1.147 (s, 3 H, Me-16), 1.200 (s, 3 H, Me-17), 1.45 (m, 1 H, H-2ax), 1.48 (m, 1 H, H-2′ax), 1.736 (s, 3 H, Me-18′), 1.77 (m, 1 H, H-2′eq), 1.84 (m, 1 H, H-2eq), 1.923 (s, 3 H, Me-18), 1.952 (s, 3 H, Me-20), 1.968 (s, 3 H, Me-20′), 1.975 (s, 3 H, Me-19′), 2.005 (s, 3 H, Me-20), 2.00–2.10 (m, 2 H, H-4ax and H-4′ax),

2.38 (dd, 1 H, *J* 5.4 Hz, *J* 15.6 Hz, H-4'eq), 2.43 (dd, 1 H, *J* 4.4 Hz, *J* 16.6 Hz, H-4eq), 4.00 (m, 2 H, H-3 and H-3'), 6.10–6.25 (m, 2 H, H-7' and H-8'), 6.16 (d, 1 H, *J* 11.2 Hz, H-10'), 6.25 (d, 1 H, *J* 10.3 Hz, H-14'), 6.27 (d, 1 H, *J* 10.8 Hz, H-14), 6.35 (d, 1 H, *J* 14.8 Hz, H-12), 6.36 (d, 1 H, *J* 15.1 Hz, H-12'), 6.46 (d, 1 H, *J* 11.3 Hz, H-10), 6.52 (dd, 1 H, *J* 11.3 Hz, *J* 14.2 Hz, H-11), 6.62–6.68 (m, 3 H, H-15, H-11' and H-15'); ^{13}C NMR ($CDCl_3$): δ 12.8 (C-20, C-19' and C-20'), 18.1 (C-19), 21.7 (C-18'), 22.5 (C-18), 28.7 (C-16 and C-16'), 30.3 (C-17 and C-17'), 36.6 (C-1), 37.1 (C-1'), 41.4 (C-4), 42.5 (C-4'), 46.7 (C-2), 48.4 (C-2'), 64.8 (C-3), 65.2 (C-3'), 89.0 (C-7), 98.6 (C-8), 118.9 (C-9), 124.1 (C-11), 124.2 (C-6), 125.1 (C-11'), 125.6 (C-7'), 126.2 (C-5'), 129.9 (C-15'), 130.5 (C-15), 131.3 (C-10'), 132.5 (C-14'), 133.5 (C-14), 135.2 (C-10), 135.8 (C-9'), 136.1 (C-13'), 136.8 (C-13), 137.3 (C-5), 137.5 (C-12'), 137.7 (C-6'), 138.1 (C-12), 138.5 (C-8').

*Synthesis of (all-*E*)-(3*R*,3'*R*)-diatoxanthin (***2***). Route 2.*

*(all-*E*)-(3*R*)-3-Hydroxy-7,8-didehydro-12'-apo-β-caroten-12'-al (***12***).* Compound **9** (0.087 g, 0.38 mmol) and the available **11** (0.18 g, 0.37 mmol) in dry dichloromethane (40 ml) were added dropwise to a suspension of sodium hydride (0.15 g, unwashed) in dry dichloromethane (40 ml), reaction time 40 h, see the general procedure. TLC (system 1) of the residue afforded **12** as a red oil in 40% yield (55.1 mg, 0.15 mmol) 100% pure (HPLC), as a mixture of the all-*E* (72%) and three *Z* isomers (15 + 10 + 3%).

UV–VIS: λ_{max} (acetone) 411 nm; MS [IP 70 eV, 180°C; *m/z* (% rel. int.)]: 364 (100, [*M*]), 346 (2, [*M* – 18]), 331 (4), 279 (6), 263 (5), 249 (10), 209 (11), 207 (10), 179 (12), 173 (15), 129 (20), 115 (16), 105 (28), 95 (30), 91 (34), 77 (29), 57 (40), 43 (65); ^{1}H NMR ($CDCl_3$): δ 1.118 (s, 3 H, Me-16), 1.170 (s, 3 H, Me-17), 1.45 (m, 1 H, H-2ax), 1.84 (m, 1 H, H-2eq), 1.874 (s, 3 H, Me-20'), 1.921 (s, 3 H, Me-18), 2.020 (s, 6 H, Me-19 and Me-20), 2.08 (m, 1 H, H-4ax), 2.45 (m, 1 H, H-4eq), 3.99 (m, 1 H, H-3), 6.31 (d, 1 H, *J* 12.2 Hz, H-14), 6.36 (d, 1 H, *J* 15.1 Hz, H-12), 6.45 (d, 1 H, *J* 12.2 Hz, H-10), 6.55–6.70 (m, 2 H, H-11 and H-15'), 6.95 (d, 1 H, *J* 11.7 Hz, H-14'), 7.11 (dd, 1 H, *J* 11.7 Hz, *J* 14.7 Hz, H-15), 9.44 (s, 1 H, H-12').

*(all-*E*)-(3*R*,3'*R*)-Diatoxanthin (***2***).* Compounds **4** (34 mg, 0.06 mmol) and **12** (21.2 mg, 0.06 mmol) in dry dichloromethane (30 ml) were added dropwise to a suspension of sodium hydride (86 mg, unwashed) in dichloromethane (30 ml), reaction time 48 h, cf. the general procedure. Work-up as described for diatoxanthin (**2**) above gave **2** in 45% yield (14.5 mg, 0.026 mmol) 100% pure (HPLC) as a mixture of the all-*E* (74%) and three *Z* isomers (7 + 3 + 16%). These *Z* isomers were not identical with the *Z* isomers obtained in the synthesis of diatoxanthin (**2**) in route 1.

Diatoxanthin (**2**) had identical chromatographic (HPLC, TLC) and spectroscopic (UV–VIS, MS) properties with **2** obtained by route 1.

*Synthesis of (all-*E*)-(3*R*)-7,8-didehydrocryptoxanthin (***3***).*

*(all-*E*)-12'-Apo-β-caroten-12'-al (***14***).* Compound **13** was available.[15] Compound **5** (0.70 g, 4.3 mmol) and **13** (0.77 g, 1.4 mmol) in dry dichloromethane (40 ml) were added dropwise to a suspension of sodium hydride (1.0 g, unwashed) in dry dichloromethane (40 ml), reaction time 64 h, cf. the general procedure. CC furnished **14** as a red oil in 67% yield (0.33 g, 0.94 mmol) 100% pure (HPLC) as a mixture of the all-*E* isomer (77%) and three *Z* isomers (10 + 11 + 2%).

UV–VIS: λ_{max} (acetone) 418 nm; MS [IP 70 eV, 180°C; *m/z* (% rel. int.)]: 350 (100, [*M*]), 324 (6, [*M* – 26]), 213 (7), 185 (11), 173 (21), 159 (21), 145 (25), 133 (24), 119 (40), 105 (44), 91 (45), 69 (50), 43 (44); ^{1}H NMR ($CDCl_3$): δ 1.040 (s, 3 H, Me-16 and Me-17), 1.47 (m, 2 H, H-2), 1.62 (m, 2 H, H-3), 1.727 (s, 3 H, Me-18), 1.884 (s, 3 H, Me-20'), 1.997 (s, 3 H, Me-19), 2.03 (m, 2 H, H-4), 2.045 (s, 3 H, Me-20), 6.15 (d, 1 H, *J* 16.1 Hz, H-8), 6.17 (d, 1 H, *J* 10.8 Hz, H-10), 6.25 (d, 1 H, *J* 16.1 Hz, H-7), 6.30 (d, 1 H, *J* 11.7 Hz, H-14), 6.37 (d, 1 H, *J* 15.1 Hz, H-12), 6.68 (dd, 1 H, *J* 11.7 Hz, *J* 14.2 Hz, H-15'), 6.81 (dd, 1 H, *J* 11.2 Hz, *J* 14.7 Hz, H-11), 6.96 (d, 1 H, *J* 11.3 Hz, H-14'), 7.03 (dd, 1 H, *J* 12.2 Hz, *J* 14.2 Hz, H-15), 9.45 (s, 1 H, H-12').

*(all-*E*)-12'-Apo-β-caroten-12'-ol (***15***).* To **14** (0.28 g, 0.80 mmol) in ethanol (100 ml) was added sodium borohydride (31 mg, 0.80 mmol) in ethanol (30 ml) dropwise at 20°C, under a nitrogen atmosphere in the dark. The reaction mixture was stirred for 3 h and concentrated to ca. 5 ml. Water was added and the product extracted with diethyl ether. The organic phase was washed with brine and water and dried over anhydrous sodium sulfate. TLC (system 1) indicated only one product, more polar than **14**. The solvents were evaporated off to give **15** as a red oil in 96% yield (0.27 g, 0.77 mmol) 97% pure (HPLC) as a mixture of the all-*E* isomer (73%) and *Z* isomers (27%).

UV–VIS: λ_{max} (ethanol) 351, 372, 389 nm, % III/II = 28; λ_{max} (acetone) 351, 376, 391 nm, % III/II = 30; MS [IP 70 eV, 180°C; *m/z* (% rel. int.)]: 352 (36, [*M*]), 334 (100, [*M* – 18]), 322 (11), 211 (13), 199 (11), 197 (18), 185 (18), 171 (21), 167 (17), 159 (39), 157 (38), 145 (48), 133 (39), 121 (46), 107 (40), 105 (72), 95 (50), 69 (73), 55 (75), 43 (52), 41 (91); ^{1}H NMR ($CDCl_3$): δ 1.029 (s, 6 H, Me-16 and Me-17), 1.47 (m, 2 H, H-2), 1.61 (m, 2 H, H-3), 1.716 (s, 3 H, Me-18), 1.819 (s, 3 H, Me-20'), 1.950 (s, 3 H, Me-19 or Me-20), 1.964 (s, 3 H, Me-19 or Me-20), 2.02 (m, 2 H, H-4), 4.09 (s, 2 H, H-2'), 6.10–6.15 (m, 3 H, H-7, H-8 and H-10), 6.20 (d, 1 H, *J* 12.2 Hz, H-14), 6.33 (d, 1 H, *J* 15.1 Hz, H-12), 6.49 (dd, 1 H, *J* 11.2 Hz, *J* 14.2 Hz, H-15'), 6.53 (d, 1 H, *J* 12.7 Hz, H-14'), 6.58 (dd, 1 H, *J* 11.2 Hz, *J* 14.7 Hz, H-11), 6.63 (dd, 1 H, *J* 11.7 Hz, *J* 15.1 Hz, H-15).

*(12′-Apo-β-carotenyl)triphenylphosphonium bromide (**16**).* Compound **15** (0.21 g, 0.60 mmol) was dissolved in methanol (60 ml) and triphenylphosphine hydrobromide (0.25 g, 0.73 mmol) was added, reaction time 48 h, cf. the general procedure. Crystallisation from methanol–ethyl acetate afforded **16** as a yellow crystalline powder in 78% yield (0.32 g, 0.47 mmol) > 90% pure (as indicated by ^{1}H NMR spectroscopy).

UV–VIS: λ_{max} (methanol) 270, 360, 385, 400 nm; ^{1}H NMR ($CDCl_3$): δ 1.020 (s, 3 H, Me-16 and Me-17), 1.47 (m, 2 H, H-2), 1.61 (m, 2 H, H-3), 1.61 (d, 3 H, *J* 4.4 Hz, Me-20′), 1.705 (s, 3 H, Me-18), 1.892 (s, 3 H, Me-19 or Me-20), 1.960 (s, 3 H, Me-19 or Me-20), 2.02 (m, 2 H, H-4), 4.91 (d, 2 H, *J* 16.1 Hz, H-12′), 6.03–6.40 (m, 8 H, olefinic protons), 6.64 (dd, 1 H, *J* 11.8 Hz, 14.5 Hz, olefinic proton), 7.62–7.95 (m, 15 H, aromatic protons).

*(all-E)-(3R)-7,8-Didehydrocryptoxanthin (**3**).* Compounds **16** (0.20 g, 0.30 mmol) and **9** (51 mg, 0.22 mmol) in dry dichloromethane (40 ml) were added dropwise to a suspension of sodium hydride (0.20 g, unwashed) in dry dichloromethane (40 ml); reaction time 44 h, cf. the general procedure. CC afforded **3** in 68% yield (82.3 mg, 0.15 mmol) 100% pure (HPLC) as a mixture of the all-*E* (77%) and *Z* isomers (23%). The pure all-*E* isomer crystallised from methanol–diethyl ether.

M.p. 173°C; UV–VIS: λ_{max} (acetone) 422, 452 ($E^{1\%}_{1cm}$ = 2808, ε = 155000), 480 nm, % III/II = 34; IR: (KBr) cm^{-1} 3414m (OH), 3025–2826s (CH), 2171w (C≡C), 1359w, 1175w, 1050w, 1027w, 962s (*trans* CH = CH); MS [IP 70 eV, 200°C; *m/z* (% rel. int.)]: 550 (100, [*M*]), 532 (5, [*M* − 18]), 524 (56, [*M* − 26]), 506 (3, [*M* − 18 − 26]), 275 (18), 221 (7), 183 (13), 157 (15), 43 (44); CD nm (Δε): 214 (−0.5), 226 (−2.0), 238 (−1.2), 268 (−0.4), 286 (−0.7), 337 (0), 352 (+0.6), 373 (0); ^{1}H NMR ($CDCl_3$): δ 1.026 (s, 6 H, Me-16′ and Me-17′), 1.146 (s, 3 H, Me-16), 1.200 (s, 3 H, Me-17), 1.46 (m, 2 H, H-2′), 1.48 (m, 1 H, H-2ax), 1.62 (m, 2 H, H-3′), 1.716 (s, 3 H, Me-18′), 1.83 (m, 1 H, H-2eq), 1.921 (s, 3 H, Me-18), 1.951 (s, 3 H, Me-20), 1.973 (s, 6 H, Me-19′ and Me-20′), 2.002 (s, 3 H, Me-19), 2.02 (m, 2 H, H-4′), 2.07 (m, 1 H, H-4ax), 2.43 (dd, 1 H, *J* 4.6 Hz, *J* 16.4 Hz, H-4eq), 3.99 (m, 1 H, H-3), 6.10–6.20 (m, 3 H, H-7′, H-8′ and H-10′), 6.25 (d, 1 H, *J* 11.2 Hz, H-14′), 6.27 (d, 1 H, *J* 10.3 Hz, H-14), 6.35 (d, 2 H, *J* 16.5 Hz, H-12 and H-12′), 6.64 (d, 1 H, *J* 11.3 Hz, H-10), 6.51 (dd, 1 H, *J* 11.3 Hz, *J* 14.7 Hz, H-11), 6.58–6.70 (m, 3 H, H-15, H-11′ and H-15′); ^{13}C NMR ($CDCl_3$): δ 12.8 (C-20, C-19′ and C-20′), 18.0 (C-19), 19.3 (C-3′), 21.8 (C-18′), 22.5 (C-18), 28.8 (C-16), 29.0 (C-16′ and C-17′), 30.5 (C-17), 33.1 (C-4′), 34.3 (C-1′), 36.6 (C-1), 39.7 (C-2′), 41.5 (C-4), 46.7 (C-2), 64.9 (C-3), 88.9 (C-7), 98.6 (C-8), 118.9 (C-9), 124.1 and 124.2 (C-6 and C-11), 125.1 (C-11′), 126.8 (C-7′), 129.4 (C-5′), 129.8 (C-15′), 130.6 (C-15), 130.8 (C-10′), 132.3 (C-14′), 133.6 (C-14), 135.2 (C-10), 136.0 (C-9′), 136.3 (C-13 and C-13′), 137.2 (C-12′), 137.3 (C-5), 137.7 (C-8′), 138.0 (C-6′), 138.1 (C-12).

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