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Total Synthesis of C_{31}-Methyl Ketone Apocarotenoids 3.† On the Structure of Hopkinsiaxanthin: First Total Synthesis of (all-*E*)-(3*S*)- and (9*Z*)-(3*S*)-7′-Apohopkinsiaxanthin

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Optically active (all-*E*)-(3*S*)-7′-apohopkinsiaxanthin, previously known as F1, and (9*Z*)-(3*S*)-7′-apohopkinsiaxanthin have been prepared by total synthesis for the first time in ca. 1% combined overall yield, including two unidentified geometrical isomers, in sixteen linear steps from (4*R*,6*R*)-actinol, (2*E*)-3-methyl-2-penten-4-yn-1-ol, (7-formyl-2-methyl-2,4,6-octatrienyl)triphenylphosphonium bromide, (3-formyl-2-butenyl)triphenylphosphonium bromide and methyllithium, by use of a $C_{15}+C_{10}+C_5+C_1$ approach.

By an alternative route from (2*Z*)-5-[(4*S*)-4-hydroxy-2,6,6-trimethyl-3-oxo-1-cyclohexenyl)-3-methyl-2-penten-4-ynyl]triphenylphosphonium bromide, (7-formyl-2-methyl-2,4,6-octatrienyl)triphenylphosphonium bromide and (2*E*)-3-methyl-4-oxo-2-pentenal, the same target compounds were obtained in a combined overall yield of >61%, including four unidentified geometrical isomers, over two steps, by use of a $C_{15}+C_{16}$ approach.

A hypothetical structure for hopkinsiaxanthin is discussed, based on present and previously reported spectroscopic and chemical data for (all-*E*)-(3*S*)- and (9*Z*)-(3*S*)-7′-apohopkinsiaxanthin and on data previously reported for hopkinsiaxanthin itself.

In 1949 Strain[1] reported the first isolation of hopkinsiaxanthin, assumed to be a keto carotenoid containing one or two hydroxy groups and eleven conjugated double bonds, from the nudibranch *Hopkinsia rosacea*. A re-examination of the carotenoids of *H. rosacea* was reported by McBeth[2] in 1972. Hopkinsiaxanthin, responsible for the pink colour of the animal, constituted 70% of total carotenoid. A less polar pigment referred to as F1 (fraction 1), constituting 8% of total carotenoid, and three other more polar minor pigments were also encountered. The three polar compounds were assumed to be isomers of hopkinsiaxanthin, in accordance with Strain's observation[1] that treatment of pure hopkinsiaxanthin with iodine in the presence of *N,N*-dimethylaniline resulted in the formation of small amounts of more polar compounds.

It is known that *H. rosacea* feeds exclusively on the pink bryozoan *Eurystomella bilabiata*.[3] The same pigment pattern was encountered in *E. bilabiata* and *H. rosacea*, indicating that the nudibranch deposits ingested carotenoids from the feed directly and unchanged.[2]

The structural elucidation of F1 (**1**), see Scheme 1, was based on functional group reactions,[4,5] chromatographic behaviour, partition between immiscible solvents and spectral data (UV–VIS, IR, MS).[2] F1 (**1**) is the second of only two known naturally occurring acetylenic C_{31}-methyl ketone apocarotenoids,[6] different from triophaxanthin (**2**)[7] only by the presence of a keto function at C-4 in **1**. The first total synthesis of (all-*E*)-(3*R*)-triophaxanthin (**2**) was recently reported.[8]

The structure of hopkinsiaxanthin remains unknown. McBeth[2] demonstrated that hopkinsiaxanthin was irreversibly converted into F1 (**1**) when treated with sodium hydroxide in the absence of oxygen, see Scheme 1. Hopkinsiaxanthin and F1 (**1**) had λ_{max}(hexane) 462 and 451 nm, respectively, with a somewhat higher spectral fine-structure[9] reported for **1**.[2] Hypsochromic shifts in the range 6–9 nm have been reported for the 9*Z* isomer, relative to the all-*E* isomer, of several different acetylenic

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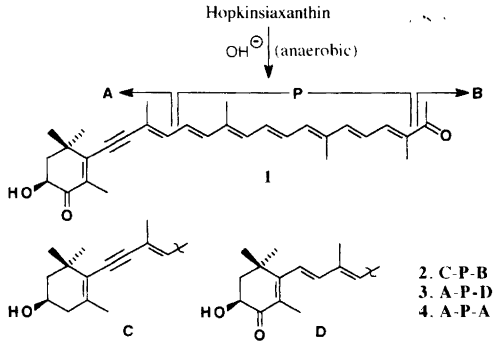


Scheme 1.

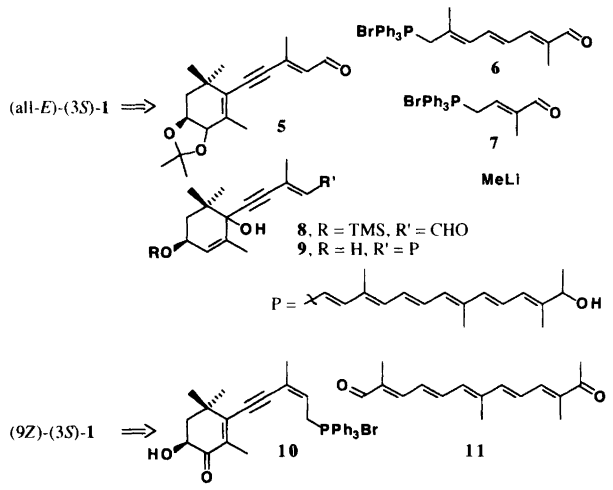
C_{40}-carotenoids.[10–12] It is well known that the all-*E* isomers of 7,8-didehydrocarotenoids readily undergo isomerisation, forming a mixture in which the 9*Z* isomer constitutes the major component.[10] However, the possibility that hopkinsiaxanthin and F1 (**1**) were *E*/*Z* isomers was disregarded by McBeth,[2] based on the observation that no F1 (**1**) was detected in the isomerisation mixture after iodine-catalysed, light-induced stereomutation of hopkinsiaxanthin.

The main objective of the present work was to carry out the first total synthesis of the naturally occurring F1 (**1**). No optical rotation data, or absolute configuration, has so far been published for **1**. Formally, F1 (**1**) may be considered as an apocarotenoid of asterinic acid,[13] representing a mixture of 7,8-didehydro- (**3**) and 7,8,7′,8′-tetradehydroastaxanthin (**4**), assigned the 3*S*,3′*S* configuration.[14] It appears likely that naturally occurring **1** may have the same absolute configuration as asterinic acid. Thus, the (all-*E*)-(3*S*) isomer of **1** was prepared in the present study. In order fully to rule out the possibility that F1 (**1**) is the 9*Z* isomer of hopkinsiaxanthin, i.e. that (all-*E*)-(3*S*)-**1** is identical with hopkinsiaxanthin, the (9*Z*)-(3*S*) isomer of **1** was synthesised for spectroscopic comparison with the (all-*E*)-(3*S*) isomer. We should point out straight away that the present results confirmed the previous conclusion,[2] that F1 (**1**) is not the 9*Z* isomer of hopkinsiaxanthin.

Surprisingly, naturally occurring **1** has been referred to as F1 since it was first described in 1972.[2,6] Since **1** is an apocarotenoid, also formed upon *in vitro* anaerobic alkali treatment of hopkinsiaxanthin via a plausible retroaldol cleavage, *vide infra*, we now suggest the name 7′-apohopkinsiaxanthin for this pigment (**1**). A hypothetical structure for hopkinsiaxanthin, based on the present data for F1 (**1**) and on data previously reported for hopkinsiaxanthin,[1,2] is discussed.

Results and discussion

Synthetic strategy. Five different building schemes were discussed for the preparation of acetylenic C_{31}-methyl ketone apocarotenoids in connection with the recently reported total synthesis of (3*R*)-triophaxanthin (**2**).[8] The $C_{15}+C_{10}+C_5+C_1$ approach elaborated for the synthesis of **2** was employed here for the total synthesis of (3*S*)-7′-apohopkinsiaxanthin (**1**). The acetylenic aldehyde **5**, see Scheme 2, was chosen as the key C_{15}-building block. The oxidation state at C-4 (carotenoid numbering) in **5** was kept at the alcohol level throughout the construction of the carbon backbone in order to avoid regio/chemoselectivity problems in the introduction of the terminal methyl group, see the discussion below. The syntheses of the C_{10}- and C_5-phosphonium salts **6**[15] and **7**[8,16] have previously been reported.



Scheme 2.

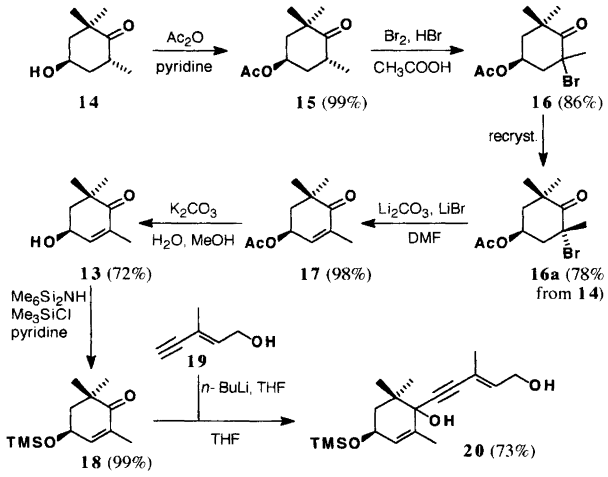
The aldehyde **8** represents an alternative C_{15}-building block for the synthesis of (3*S*)-7′-apohopkinsiaxanthin (**1**). Use of **8** in place of **5** may have reduced the number of steps in the synthesis of **1**. However, the allylic rearrangement of the 3,6-diol (carotenoid numbering) to form the 3,4-diol, which has been carried out effectively with a C_{15}-3,6,11-triol as discussed below, was unsuccessful when attempted with the corresponding C_{30}-3,6,8′-triol **9**.[17]

It is well known that acetylenic phosphonium salts such as **10**, regardless of the configuration of the exocyclic carbon–carbon double bond, predominantly form the thermodynamically favoured[10] 9*Z* isomeric Wittig condensation products.[18–20] Consequently, (9*Z*)-(3*S*)-7′-apohopkinsiaxanthin may be prepared according to a $C_{15}+C_{16}$ building scheme, by use of the previously described (2*Z*)-C_{15}-phosphonium salt **10**[18,19] and the C_{16}-keto aldehyde **11**.[15]

The preparation of the acetylenic C_{15}-aldehyde acetonide **5** and the synthesis of (all-*E*)-(3*S*)- (**1a**) and (9*Z*)-(3*S*)-7′-apohopkinsiaxanthin (**1b**) is discussed below. Preliminary results have been reported.[21]

Synthesis of the acetylenic C_{15}-aldehyde acetonide **5**. The synthesis of the key intermediate acetylenic C_{15}-aldehyde acetonide **5** is illustrated in Schemes 3 and 4. The C_{15}-triol **12**, see Scheme 4, was first prepared by Bernhard *et al.*[18] for the synthesis of asterinic acid (**3**,**4**). A key intermediate in their synthesis was the α,β-unsaturated

C_9-hydroxyketone **13**, see Scheme 3, originally prepared by Kienzle and Mayer[22] for the first total synthesis of (3*S*,3′*S*)-astaxanthin, **D-P-D** in Scheme 1. The present synthesis of **12** and **13** was carried out essentially according to previous methods.[18,22]



Scheme 3.

(4*R*,6*R*)-Actinol (**14**) was converted into the acetate **15** by standard acetylation. Treatment of **15** with bromine in acetic acid containing traces of hydrogen bromide afforded a 14:1 mixture of two epimeric α-bromo ketones **16**. Recrystallisation of the epimeric mixture afforded the pure 2*R*,4*S*-isomer **16a** as colourless needles. The relative configuration of **16a** was determined by X-ray crystallographic analysis.

A computer-generated perspective drawing of the α-bromo ketone **16a** is given in Fig. 1. There are two basically identical molecules in the asymmetric unit, the only distinction being the torsion angles C4–C5–O2–C10 which are 137.6° and 92.9°. Since the configuration at C-4 is known and no epimerisation of this centre occurs during the bromination,[22] the major product **16a** was assigned the 2*R*,4*S* absolute configuration. The overall yield of crystalline **16a** was 78% over two steps from (4*R*,6*R*-actinol) (**14**).

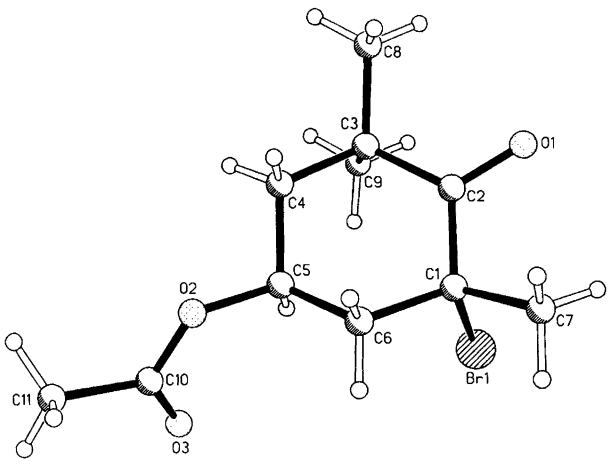
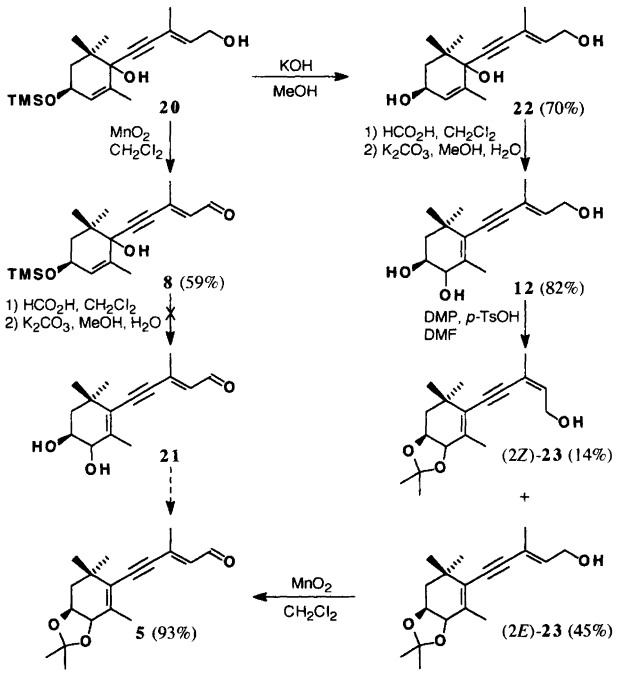


Fig. 1. A computer-generated perspective drawing of the α-bromo ketone **16a** according to the X-ray analysis.

Only the pure (2*R*,4*S*)-α-bromo ketone **16a** was employed in the subsequent steps of this synthesis. However, the epimeric mixture may be used since both diastereomers give rise to the same product. Treatment of **16a** with lithium carbonate in the presence of lithium bromide gave the α,β-unsaturated keto acetate **17** which upon hydrolysis afforded the α,β-unsaturated hydroxy ketone **13** in 55% overall yield from (4*R*,6*R*)-actinol (**14**). Treatment of **13** with a mixture of trimethylsilyl chloride and hexamethyldisilazane in pyridine afforded the TMS ether **18** in almost quantitative yield. Subsequent reaction of **18** with the dianion generated by treatment of the commercially available acetylenic (2*E*)-C_6-alcohol **19** with 2.1 equivalents of butyllithium, gave the C_{15}-diol **20**, in 73% yield, as a 3:1 mixture of two epimers. No attempt was made to separate the two epimers as they both provide the same final product after allylic rearrangement and oxidation, cf. the discussion below.

Allylic oxidation of **20** afforded the aldehyde **8** in 59% yield, see Scheme 4. However, allylic rearrangement of **8** with formic acid followed by basic hydrolysis, to yield the dihydroxy aldehyde **21**, was unsuccessful. A crude reaction mixture containing more than five different products was obtained. No attempt was made to isolate any of these products.

An alternative route to **5**, as already pointed out, was via the previously described[22] C_{15}-triol **12**. Treatment of the diol **20** with methanolic potassium hydroxide provided a 3:1 mixture of two C-1′ epimeric C_{15}-triols **22** in 70% yield. Allylic rearrangement of **22** effected with



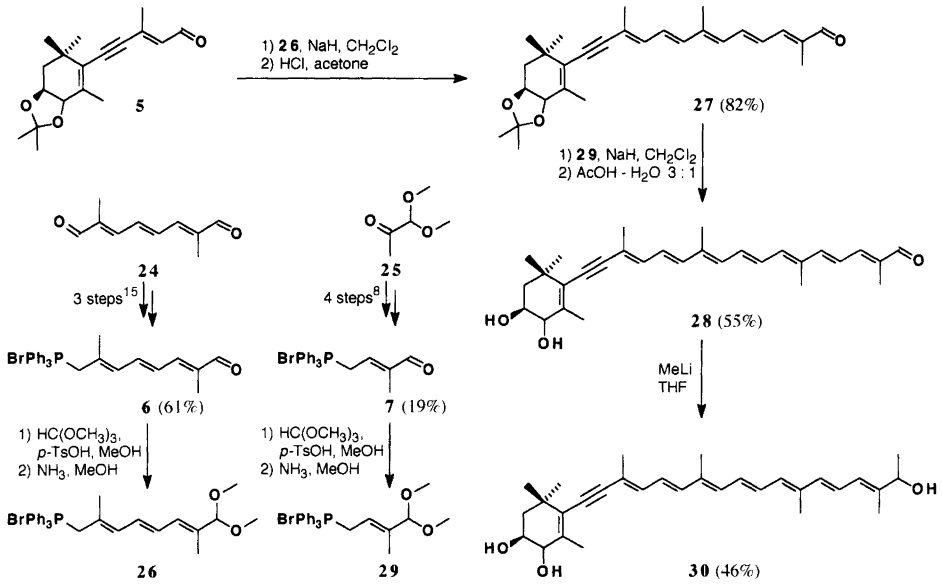
Scheme 4.

formic acid followed by basic hydrolysis of the intermediate formate ester, furnished the epimeric triols **12** in 82% yield. Protection of the 3,4-diol moiety as the acetonide was effected by treatment of **12** with 2,2-dimethoxypropane (DMP) in DMF containing catalytic amounts of *p*-toluenesulfonic acid. The reaction provided a mixture of geometrical isomers, which were separated by column chromatography to give (2*E*)-**23** and (2*Z*)-**23** in 45% and 14% yield respectively. Allylic oxidation of (2*E*)-**23** provided the epimeric C_{15}-aldehydes **5** in 93% yield. The overall yield of **5** was 10% over eleven steps from (4*R*,6*R*)-actinol (**14**).

*Synthesis of (all-*E*)-(3*S*)- (**1a**) and (9-Z)-(3*S*)-7′-apohopkinsiaxanthin (**1b**). Route 1.* The C_{10}- and C_5-phosphonium salts **6** and **7**, see Scheme 5, have previously been prepared, in 61% yield from the C_{10}-dial **24** and in 19% yield from the C_3-ketone **25** respectively.[8,15] The aldehyde moiety of the C_{10}-phosphonium salt **6** was protected, and the resulting dimethyl acetal phosphonium salt **26** underwent a Wittig reaction with the C_{15}-aldehyde **5** to give the C-4 epimeric C_{25}-aldehydes **27** in 82% yield after hydrolysis of the acetal. In a similar fashion, the C-4 epimeric C_{30}-dihydroxy aldehydes **28** were obtained in 55% yield after a Wittig reaction of the protected C_5-phosphonium salt **29** with the aldehydes **27** followed by hydrolysis of the acetal and acetonide moieties. The all-*E* isomers constituted 69% of total **28**, as determined by HPLC. Treatment of **28** with methyllithium furnished the C_{31}-triol **30** in 45% yield, as a complex mixture of stereoisomers which was used directly in the subsequent step.

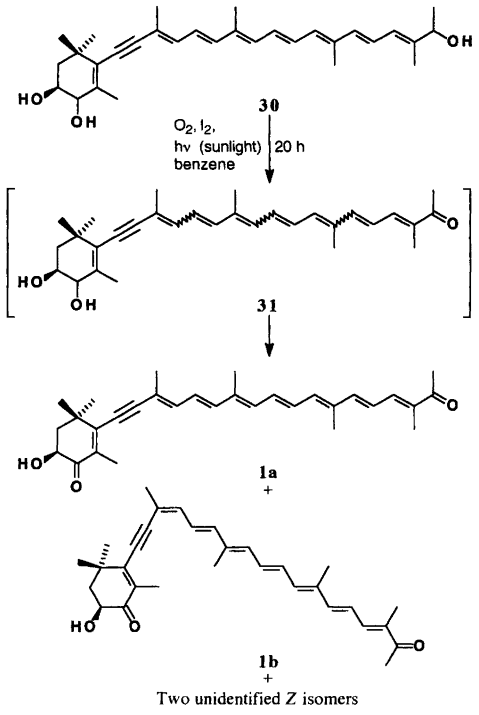
The main problem associated with the $C_{15}+C_{10}+C_5+C_1$ approach towards 7′-apohopkinsiaxanthin (**1**), not surprisingly, turned out to be the final oxidation step. Problems with the oxidation of the secondary allylic hydroxy group in the 3,4-dihydroxycyclohex-5-ene end group have previously been encountered in the partial synthesis of astaxanthin, **D-P-D** in Scheme 1.[23,24] Yields of astaxanthin in the range 2–20% have been obtained when DDQ, permanganate or air were used as oxidants in the final step.[24,25]

In the present work, oxidation of **30** with manganese dioxide in dichloromethane or acetone, or with DDQ in benzene, failed to give the desired (3*S*)-7′-apohopkinsiaxanthin (**1**). No oxidation product was observed when a sample of **30** was stirred under an atmosphere of air under irradiation (sunlight) for 13 h. Allylic oxidation of carotenols in air under the influence of iodine has been investigated and was found to be more effective than air oxidation in the absence of iodine.[25] Unfortunately, irradiation of carotenoids in the presence of iodine is a general method for effecting *cis/trans* isomerisation of polyenes.[26,27] Since the 9*Z* isomer is the thermodynamically favoured geometrical isomer in 7,8-didehydrocarotenoids,[10] iodine-induced air oxidation of **30** would be expected to give a mixture of isomers in which (9*Z*)-(3*S*)-7′-apohopkinsiaxanthin (**1b**) should be the major product. Only traces of **1**, as a mixture of isomers, in addition to a 3:2 mixture of the tentatively identified mono-oxidised product **31**, see Scheme 6, and the substrate **30** resulted from irradiation for 14 h of a sample of **30** with a 25 W sodium lamp in the presence of iodine. However, when **30** in the presence of 8 mol% iodine was stirred in direct sunlight for 20 h, (3*S*)-7′-apohopkinsiaxanthin (**1**) was obtained in 42% yield. The overall yield of **1** was 1% over 16 linear steps from (4*R*,6*R*)-actinol (**14**). The stereoisomeric mixture contained (all-*E*)-(3*S*)-(**1a**), (9*Z*)-(3*S*)-7′-apohopkinsiaxanthin (**1b**) and two unidentified geometrical isomers of **1** in a 1:5:4 ratio. Preparative HPLC provided pure **1a** and **1b** for spectroscopic characterisation.



Scheme 5.

In a separate experiment, the iodine-catalysed air oxidation of the triol **30** was interrupted after 6 h, when HPLC indicated complete conversion of the substrate. HPLC demonstrated the presence of the mono-oxidised **31** and 7′-apohopkinsiaxanthin (**1**) in a ca. 7:1 ratio. Preparative TLC provided the pure C_{31}-dihydroxy ketone **31** in 71% yield, as a mixture of five or more isomers with the tentatively identified (9*Z*)-(3*S*,4*RS*) isomers constituting 60% of total **31**.



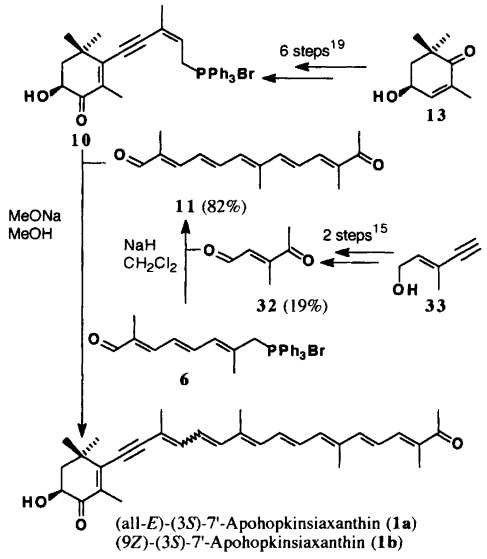
Yield **1a** + **1b** + two unidentified *Z* isomers: 42%
Isomeric ratio: **1a** - **1b** - unidentified isomers 1 : 5 : 4

Scheme 6.

*Synthesis of (all-*E*)-(3*S*)- (**1a**) and (9*Z*)-(3*S*)-7′-apohopkinsiaxanthin (**1b**). Route 2.* The synthesis of the C_{16}-keto aldehyde **11**, (see Scheme 7) by a Wittig reaction of the C_{10}-phosphonium salt **6** with the C_6-keto aldehyde **32**, prepared in 19% yield from the commercially available alcohol **33**, has been reported. The yield in the Wittig reaction was only 43%.[15] In the present work the yield was improved to 82% by employing freshly distilled **32** rather than a stored stock solution of **32** in dichloromethane. The all-*E* isomer constituted 64% of total **11**. Recrystallisation afforded the pure (all-*E*)-**11** which was employed in the subsequent step.

The acetylenic (2*Z*)-(4*S*)-phosphonium salt **10**, with the hydroxy function free or protected has, as already mentioned, been described by the Roche group.[18,19] The unprotected **10** may be prepared in six steps from the α,β-unsaturated hydroxy ketone **13**.[19] For use in the present work, **10** was obtained as a gift from Hoffmann–La Roche, Basel. The specific optical rotation $[\alpha]_D$ of the obtained sample of **10** was −55, as compared with the reported[19] −90. The discrepancy in the optical rotation data was ascribed to the presence of unidentified impurities in the present material rather than to the presence of substantial amounts of the (4*R*)-enantiomer of **10**. By ^{1}H NMR spectroscopy the purity of **10** was estimated to ca. 60%, corresponding to $[\alpha]_D \approx -92$ for pure material.

A Wittig reaction of the (2*Z*)-(4*S*)-phosphonium salt **10** with the C_{16}-keto aldehyde **11** provided (3*S*)-7′-apohopkinsiaxanthin (**1**) in >74% yield (74% based on 100% pure **10**). The overall yield of **1** was >61% over two steps from **32**. The stereoisomeric mixture contained (all-*E*)-(3*S*)-(**1a**), (9*Z*)-(3*S*)-7′-apohopkinsiaxanthin (**1b**) and four unidentified geometrical isomers in a 1:2:1 ratio. The fully characterised (9*Z*)-(3*S*) isomer **1b** crystallised from methanol as dark red–violet needles. Preparative HPLC provided pure (all-*E*)-(3*S*)-7′-apohopkinsiaxanthin (**1a**).



Yield **1a** + **1b** + Four unidentified *Z* isomers: > 74%
Isomeric ratio: **1a** - **1b** - unidentified isomers 1 : 2 : 1

Scheme 7.

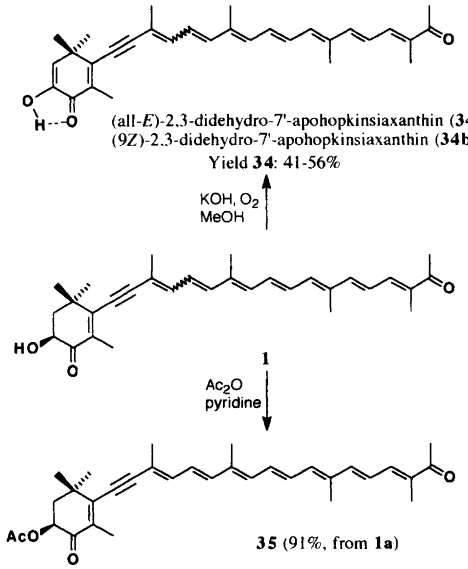
(all-*E*)-(3*S*)- (**1a**) and (9*Z*)-(3*S*)-7′-apohopkinsiaxanthin (**1b**) obtained by route 2 were identical with samples prepared by route 1. Furthermore, all spectral properties of synthetic (all-*E*)-(3*S*)-7′-apohopkinsiaxanthin (**1a**) were in good agreement with data reported[2] for the natural compound. A partial chemical characterisation of 7′-apohopkinsiaxanthin (**1**) is discussed below.

No obvious correlation was observed between the intermediate conservative[28,29] CD spectra of (all-*E*)-(3*S*)-(**1a**) and (9*Z*)-(3*S*)-7′-apohopkinsiaxanthin (**1b**). The isomerisation shifts $\Delta = \delta_{cis} - \delta_{trans}$ for **1b**, in both ^{1}H NMR and ^{13}C NMR spectra, were as expected for a 9*Z* isomer relative to the all-*E* isomer.[30]

Chemical characterisation of 7′-apohopkinsiaxanthin (**1**). The structural elucidation of F1 (**1** = 7′-apohopkinsiaxanthin) was, as already briefly mentioned, partly based on functional group reactions. As reported by McBeth,[2]

treatment of **1** with methanolic hydroxide in the presence of air provided the 2,3-didehydro oxidation product **34** named hopkinsianone, see Scheme 8. (all-*E*)-(3*S*)-7′-Apohopkinsiaxanthin (**1a**) provided **34** in 41% yield, as a 2:1 mixture of the all-*E* and 9*Z* isomers, while **1b** furnished **34** in 56% yield, as a 3:4 mixture of the all-*E* and 9*Z* isomers. The name hopkinsianone should be replaced by 7′-apohopkinsianone.

Treatment of (all-*E*)-(3*S*)-7′-apohopkinsiaxanthin (**1a**) with acetic anhydride in pyridine afforded the (all-*E*)-acetate **35** in 91% yield. The chemical properties demonstrated were as expected for 7′-apohopkinsiaxanthin (**1**).



Scheme 8.

A hypothetical structure of hopkinsiaxanthin. A comparison of the present spectroscopic data for (all-*E*)-(3*S*)-(**1a**) and (9*Z*)-(3*S*)-7′-apohopkinsiaxanthin (**1b**) confirmed the previous conclusion that F1 (**1**) is not a the 9*Z* isomer of hopkinsiaxanthin. The synthetic (all-*E*) isomer **1a** had a higher λ_{max}(hexane) than the natural compound, 453 vs. 451 nm, presumably due to the presence of contaminating *Z* isomers in the latter sample. The synthetic 9*Z* isomer **1b** displayed a UV–VIS spectrum with λ_{max}(hexane) 449 nm.

McBeth[2] reported the same molecular formula $C_{31}H_{38}O_3$, based on electron impact mass spectroscopy, for F1 (**1** = 7′-apohopkinsiaxanthin) and hopkinsiaxanthin. However, with the UV–VIS properties of the (all-*E*)-2,3-didehydro oxidation product **34** in mind, it is unlikely that any structural isomer of **1** will have λ_{max}(hexane) > 460 nm, as reported[1,2] for hopkinsiaxanthin. Thus, it appears that the molecular formula reported for hopkinsiaxanthin is incorrect.

It has been demonstrated that treatment of the allenic amarouciaxanthin A (**36**) or the acetylenic amarouciaxanthin B (**37**) with methanolic potassium hydroxide provides the C_{31}-methyl ketone apocarotenoids paracentrone **38** and triophaxanthin **2** respectively,[31] see Scheme 9, rationalised by a retroaldol cleavage. In a similar fashion McBeth[2] demonstrated that hopkinsiaxanthin was converted into F1 (**1**) when treated with sodium hydroxide with exclusion of oxygen. Strain[1] and McBeth[2] reported λ_{max}(petroleum ether) ≈467 nm and λ_{max}(hexane) 462 nm respectively for hopkinsiaxanthin. On the basis of the available data it appears likely that hopkinsiaxanthin may be a C_{40}-carotenoid in the amarouciaxanthin-series, more specifically the 4′-oxo derivative **39** of amarouciaxanthin B (**37**) or more likely the corresponding anhydro analogue **40**. This hypothetical structure is compatible with the VIS spectral properties reported[1,2] for hopkinsiaxanthin and also explains the base-promoted conversion of the pigment into 7′-apohopkinsiaxanthin, see Scheme 9.

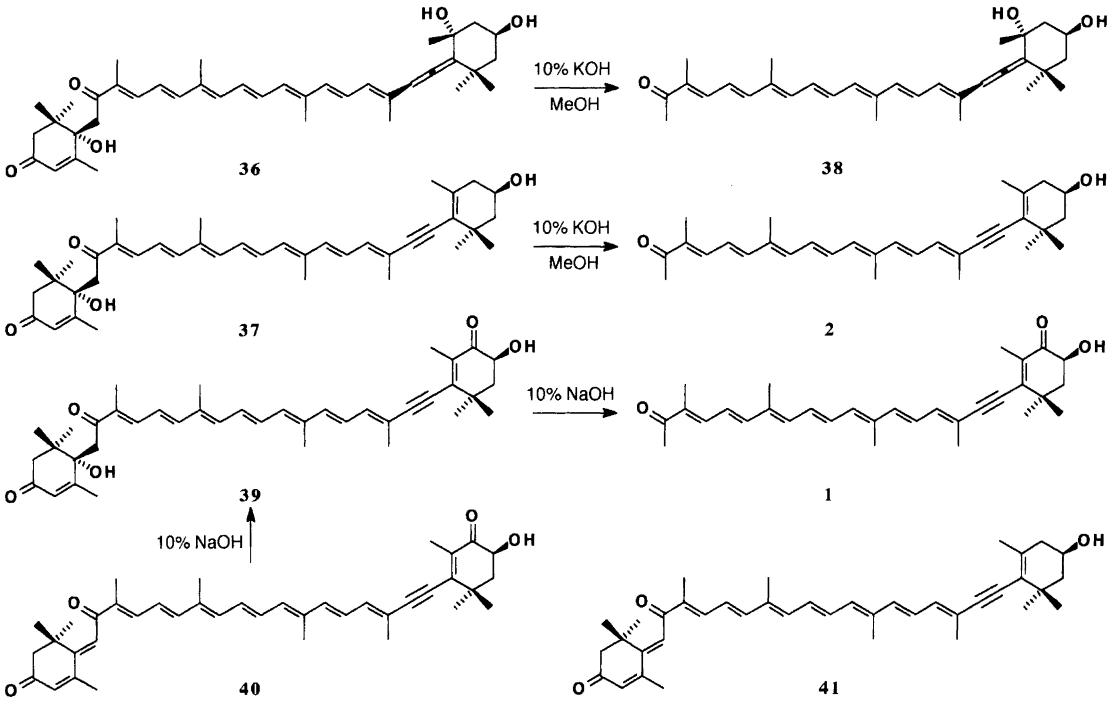
The chromophores of the apocarotenoids **38** and **2** correspond to those of the parent C_{40}-carotenoids **36** and **37**. Consequently, the λ_{max} values of the amarouciaxanthins[31] would be expected to be close to those of the C_{31}-compounds, and not at 16 nm longer wavelength as was indeed reported.[31] In fact, Hertzberg *et al.*[32] reported λ_{max}(hexane) 458 nm for anhydroamarouciaxanthin B (**41**), i.e. shorter than for amarouciaxanthin B (**37**) without cross-conjugation. Matsuno *et al.* [31] reported λ_{max}(diethyl ether) 463 nm for amarouciaxanthin B (**37**).

A reinvestigation of the carotenoids of *H. rosacea* and *E. bilabiata*, directed towards the structural elucidation of hopkinsiaxanthin, and determination of the absolute configuration of naturally occurring 7′-apohopkinsiaxanthin, is planned in the Trondheim laboratories.

Experimental

General methods. Solvents were of distilled or p.a. quality. Diethyl ether used for extraction was passed through alumina (neutral). Diethyl ether and THF used as solvents in reactions were distilled from sodium–benzophenone. Pyridine was distilled from solid potassium hydroxide. Dichloromethane, benzene, acetone, methanol and DMF were dried over freshly activated 3 Å molecular sieves before being employed as solvents in reactions. Sodium hydride was washed with hexane followed by dichloromethane before use. Solvents were evaporated from reaction mixtures at reduced pressure (ca. 20 mmHg) at temperatures not exceeding 35 °C. Melting points of polyenes were recorded in evacuated tubes, and are uncorrected.

Chromatography. Analytical thin layer chromatography (TLC) was performed on precoated 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. Preparative TLC was performed on silica gel 60 G (Merck Art. 7731) with ethyl acetate–heptane 2:3 (system 1) or 1:1 (system 2) as the eluent. Column chromatography (CC) was performed



Scheme 9.

on silica gel 60 (Merck Art. 7734) 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 Spherisorb S5W or Chromsphere 5 Si silica column, gradient elution with 100% hexane 0 min; 1% acetone min^{-1} to 30%; 15 min; flow = 1.25 ml min^{-1} (system 1), a Spherisorb S5W silica column, hexane–isopropyl acetate–*n*-propyl alcohol–*N*-ethyldiisopropylamine 83.9 : 14 : 2 : 0.1; flow = 1.00 ml min^{-1}, unless otherwise stated (system 2), or on a Brownlee Spheri-5 silica column modified with orthophosphoric acid, gradient elution with 100% hexane 0 min; 1% acetone min^{-1} to 30%; 15 min; flow = 1.25 ml min^{-1} (system 3). The orthophosphoric acid modified silica column was prepared as described by Vecchi *et al.*[33] by pumping a solution of 1% orthophosphoric acid in methanol (30 ml) through the column (1.0 ml min^{-1}). Subsequently, the column was equilibrated by pumping hexane (1.25 ml min^{-1}) through the column for 6 h. For analysis of coloured compounds, the diode array (DA) detector was set to detect at five different wavelengths simultaneously (330, 360, 390, 420, 445/450 nm). For analysis of colourless compounds, detection wavelengths relevant to the compounds in question were employed, as determined by UV spectroscopy. Gas liquid chromatography (GLC) was performed on a Varian 3700 instrument with a non-polar BP-1 capillary column (25 m × 0.25 mm) and a flame ionisation detector (FID), split ratio 1 : 9, temperature program: 40 °C 2 min; 10 °C min^{-1} to 280 °C; 10 min.

Spectroscopy. UV–VIS spectra were recorded on a Perkin Elmer 552 spectrophotometer. Spectral fine structure was measured as %III/II.[9] Solvents are specified in each case. IR spectra of solids were recorded for samples 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. Temperature and ionisation potential are specified in each case. 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 rotation was measured on a Jouan Dicrograph. ^1H NMR, ^{13}C NMR, ^1H–^1H COSY and ^1H–^{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 employed.

Primed numbers in the ^1H NMR assignments for compounds **5**, **8**, **10**, **12**, **20**, **22** and **23** refer to ring-protons.

(4R,6R)-4-Acetoxy-2,2,6-trimethylcyclohexanone (**15**). To a solution of (4*R*,6*R*)-4-hydroxy-2,2,6-trimethylcyclohexanone (actinol, **14**, $[\alpha]_D^{20} = -113.7$ ($c = 2.14$, methanol) consistent with reported data,[34] 20.00 g, 128.00 mmol) in dry pyridine (40 ml) was added acetic anhydride (26.10 g, 24.20 ml, 260.00 mol) dropwise over 15 min. The reaction mixture was stirred at 20 °C for 18 h and poured into ice–water and the product was extracted with dichloromethane. The extract was washed sequentially with 10% sulfuric acid (50 ml), half-saturated aqueous sodium hydrogen carbonate and brine and finally dried over anhydrous sodium sulfate. Evaporation of the solvent provided the acetate **15** as a colourless oil

in >99% yield (25.25 g, 127.53 mmol), >99% pure (GLC, ^{1}H NMR).

GLC t_R = 11.3 min. IR (liq.) cm^{-1}: 2987–2859s (CH), 1739s (C=O, acetate), 1708s (C=O), 1454m, 1377m, 1246s, 1222s, 1167m, 1132w, 1047w, 1024m, 994w, 942w. MS [IP 30 eV, 150 °C; *m/z* (% rel. int.)]: 198 (3, [*M*]), 156 (20, [*M*−42]), 138 (45, [*M*−60]), 110 (27, [*M*−88]), 105 (22), 95 (23), 83 (77), 43 (100). ^{1}H NMR ($CDCl_3$): δ 1.027 (d, 3 H, $J_{Me\text{-}6,H\text{-}6}$ 6.4 Hz, Me-6), 1.046 (s, 3 H, Me-2), 1.286 (s, 3 H, Me-2), 1.69 (dt, 1 H, *J* 3.4 Hz, *J* 13.8 Hz, H-5$_{ax}$), 1.80 (dd, 1 H, *J* 3.9 Hz, 14.7 Hz, H-3$_{ax}$), 2.09 (dt, 1 H, *J* 3.4 Hz, *J* 14.7 Hz, H-3$_{eq}$), 2.106 (s, 3 H, OAc), 2.19 (m, 1 H, H-5$_{eq}$), 3.03 (m, 1 H, H-6), 5.12 (m, 1 H, H-4). $[\alpha]_D^{25} = -84.9$ (*c* = 1.0, methanol).

(2R,4S)-4-Acetoxy-2-bromo-2,6,6-trimethylcyclohexanone (**16a**). A solution of bromine (23.40 g, 7.50 ml, 146.25 mmol) in conc. acetic acid (37 ml) was added dropwise to a solution of the acetate **15** (25.25 g, 127.53 mmol) in conc. acetic acid (45 ml), containing 1 drop of 48% hydrogen bromide in acetic acid, at 20 °C, at a rate which kept the reaction mixture colourless to light yellow (ca. 1 h). The reaction mixture was stirred at 20 °C for another 30 min and subsequently poured into ice–water. The product was extracted with dichloromethane. The extract was washed with saturated aqueous sodium hydrogen carbonate, water and brine, and dried over anhydrous sodium sulfate. Evaporation of the solvent afforded a 14:1 mixture (^{1}H NMR) of the diastereomeric bromides **16**, as a colourless oil in 86% yield (30.43 g, 109.90 mmol), >87% pure (GLC, ^{1}H NMR). Crystallisation from pentane at 20 °C yielded the major diastereomer (2*R*,4*S*)-**16** (**16a**) as colourless needles in 78% yield (27.41 g, 98.95 mmol) from **14**, 100% pure (GLC, ^{1}H NMR). Spectroscopic data are given for **16a** only.

An X-ray crystallographic analysis of **16a** was performed with the crystal mounted in a glass capillary. Intensity data were obtained using ω/2θ scans at room temperature on a Siemens R3m/V diffractometer using Cu Kα radiation (1.5418 Å). Three standard reflections were measured every 97 reflections. No crystal decay was detected. The data were reduced using the Siemens SHELXTL PLUS program package. The structure was solved by direct methods (SHELXS-86). Hydrogen atoms were introduced in calculated positions. In the subsequent full-matrix least-squares refinement (SHELXL-93) the $1/[s(F_o^2)^2 + (0.0958*P)^2 + 0.001*P]$ weighting scheme was used, where $P = (\max(F_o^2, 0) + 2*F_o^2)/3$. The final *R*1 was 5.27%.

GLC t_R = 15.1 min. IR (liq.) cm^{-1}: 2990–2862m (CH), 1719s (C=O), 1469w, 1445w, 1366m, 1249s, 1222w, 1135w, 1123w, 1062m, 1024m, 986w, 973w. MS [IP 30 eV, 160 °C; *m/z* (% rel. int.)]: 278 (3, [*M*, ^{81}Br]), 276 (3, [*M*, ^{79}Br]), 236 (19, [*M*−42, ^{81}Br]), 234 (27, [*M*−42, ^{79}Br]), 155 (8), 109 (13), 88 (100), 43 (36). ^{1}H NMR ($CDCl_3$): δ 1.137 (s, 3 H, Me-6), 1.538 (s, 3 H, Me-6), 1.69 (dd, 1 H, *J* 10.1 Hz, *J* 13.5 Hz, H-3$_{ax}$ or H-5$_{ax}$),1.836 (s, 3 H, Me-2), 2.042 (s, 3 H, OAc), 2.05 (dd, 1 H, *J* 10.4 Hz, *J* 14.8 Hz, H-3$_{ax}$ or H-5$_{ax}$), 2.24 (ddd, 1 H, *J* 3.0 Hz, *J* 4.6 Hz, *J* 13.5 Hz, H-3$_{eq}$ or H-5$_{eq}$), 2.76 (ddd, 1 H, *J* 3.0 Hz, 4.5 Hz, *J* 14.8 Hz, H-3$_{eq}$ or H-5$_{eq}$), 5.49 (m, 1 H, H-4). $[\alpha]_D^{26} = -111.7$ (*c* = 1.4, methanol).

(4S)-4-Acetoxy-2,6,6-trimethylcyclohex-2-enone (**17**). The preceding bromide **16a** (11.60 g, 41.88 mmol) was stirred with lithium bromide (6.20 g, 71.26 mmol) and lithium carbonate (8.50 g, 114.87 mmol) in dry DMF (170 ml) at 80 °C for 1.5 h. The reaction mixture was cooled to 20 °C, poured into water, and the resulting mixture was brought to pH ≈ 6 by addition of 1 M sulfuric acid. The product was extracted with dichloromethane. The extract was washed thoroughly with water and brine, and dried over anhydrous sodium sulfate. Evaporation of the solvent provided the acetate **17** as a colourless oil in 98% yield (8.08 g, 41.22 mmol), >99% pure (GLC, ^{1}H NMR).

GLC t_R = 13.2 min. UV–VIS λ_{max}(hexane): 224 nm. IR (liq.) cm^{-1}: 2965–2869s (CH), 1740s (C=O, acetate), 1679s (conj. C=O), 1454w, 1374m, 1356m, 1237s, 1184w, 1049m, 1024s, 980w, 959m. MS [IP 70 eV, 160 °C; *m/z* (% rel. int.)]: 196 (3, [*M*]), 154 (6, [*M*−42]), 136 (6, [*M*−60]), 98 (100, [*M*−98]), 93 (8), 49 (11). ^{1}H NMR ($CDCl_3$): δ 1.159 (s, 6 H, Me-6), 1.79 (m, 3 H, Me-2), 1.92 (dd, 1 H, *J* 9.8 Hz, *J* 12.7 Hz, H-5), 2.089 (s, 3 H, OAc), 2.13 (ddd, 1 H, *J* 2.0 Hz, *J* 5.4 Hz, *J* 12.7 Hz, H-5), 5.61 (m, 1 H, H-4), 6.50 (m, 1 H, H-3). $[\alpha]_D^{23} = -60.9$ (*c* = 1.5, methanol).

(4S)-4-Hydroxy-2,6,6-trimethylcyclohex-2-enone (**13**). The acetate **17** (8.08 g, 41.22 mmol) was stirred with potassium carbonate (4.50 g, 32.61 mmol) in a mixture of water (20 ml) and methanol (55 ml) at 20 °C for 1 h. The reaction mixture was subsequently poured into water and extracted with dichloromethane. The resulting extract was washed with water and brine, and dried over anhydrous sodium sulfate. Evaporation of the solvent afforded the alcohol **13** as a colourless oil in 72% yield (4.54 g, 29.48 mmol), >98% pure (GLC, ^{1}H NMR).

GLC t_R = 11.7 min. UV–VIS λ_{max}(methanol): 230 nm. IR (liq.) cm^{-1}: 3435s (OH), 3021–2871s (CH), 1668s (conj. C=O), 1453m, 1387m, 1354m, 1290w, 1258w, 1181w, 1149w, 1099m, 1046m, 1020m, 991w, 959w, 936m. MS [IP 70 eV, 150 °C; *m/z* (% rel. int.)]: 154 (19, [*M*]), 136 (2, [*M*−18]), 111 (10), 98 (100), 69 (14), 43 (6), 41 (13). ^{1}H NMR ($CDCl_3$): δ 1.117 (s, 3 H, Me-6), 1.152 (s, 3 H, Me-6), 1.77 (m, 3 H, Me-2), 1.81 (dd, 1 H, *J* 10.3 Hz, *J* 12.7 Hz, H-5), 2.13 (d, 1 H, *J* 6.4 Hz, OH), 2.14 (ddd, 1 H, *J* 2.0 Hz, *J* 5.3 Hz, *J* 12.8 Hz, H-5), 4.58 (m, 1 H, H-4), 6.61 (m, 1 H, H-3). $[\alpha]_D^{25} = -47.6$ (*c* = 1.3, methanol).

(4S)-2,6,6-Trimethyl-4-trimethylsiloxycyclohex-2-enone (**18**). A mixture of trimethylsilyl chloride (8.84 ml, 7.60 g, 69.84 mmol) and hexamethyldisilazane (17.87 ml, 13.76 g, 85.26 mmol) was added dropwise to a stirred

solution of the alcohol **13** (4.41 g, 28.64 mmol) in dry pyridine (50 ml) at 20 °C. The reaction mixture was stirred for 12 h and subsequently poured into ice-cold water. The product was extracted with diethyl ether. The extract was washed with water and brine and dried over anhydrous sodium sulfate. Evaporation of the solvent gave the silyl ether **18** as a colourless oil in 99% yield (6.43 g, 28.45 mmol), >99% pure (GLC, ^{1}H NMR).

GLC $t_R = 11.0$ min. UV–VIS λ_{max}(methanol): 231 nm. IR (liq.) cm^{-1}: 3021–2859s (CH), 1679s (conj. C=O), 1473w, 1452w, 1385w, 1352m, 1252s, 1154w, 1103m, 1078s, 1044w, 1026w, 995w, 964w, 942m, 884s, 843s, 755m. MS [IP 50 eV, 150 °C; *m/z* (% rel. int.)]: 226 (26, [*M*]), 211 (12), 198 (16), 183 (65), 170 (72), 127 (21), 91 (30), 75 (60), 73 (100), 45 (14). ^{1}H NMR ($CDCl_3$): δ 0.176 (s, 9 H, Me in TMSO–), 1.08 (s, 3 H, Me-6), 1.09 (s, 3 H, Me-6), 1.72 (m, 3 H, Me-2), 1.84 (dd, 1 H, *J* 9.9 Hz, *J* 12.9 Hz, H-5), 1.94 (ddd, 1 H, *J* 2.0 Hz, *J* 5.5 Hz, *J* 12.9 Hz, H-5), 4.50 (m, 1 H, H-4), 6.46 (m, 1 H, H-3). $[\alpha]_D^{20} = -59.7$ ($c = 1.7$, methanol).

(2E)-5-[(1RS,4S)-1-Hydroxy-2,6,6-trimethyl-4-trimethylsiloxycyclohex-2-enyl]-3-methyl-2-penten-4-ynol (**20**). *n*-Butyllithium in hexane (56.00 mmol, 35.00 ml of a 1.6 M solution) was added dropwise to a solution of (2*E*)-3-methyl-2-penten-4-ynol (**19**, 2.58 g, 26.88 mmol) in dry THF (150 ml) at 0 °C under N_2. The resulting suspension was stirred at 0 °C for 1 h, after which a solution of the C_9-ketone **18** (6.05 g, 26.77 mmol) in dry THF (50 ml) was added dropwise at 0 °C under N_2. The reaction mixture was allowed to warm to 20 °C and was stirred under N_2 in the dark for 15 h. Subsequently, the reaction mixture was cooled to 0 °C and cold saturated aqueous ammonium chloride was added. The resulting mixture was stirred at 0–20 °C for 1 h. The product was extracted with diethyl ether. The extract was washed with water and brine and dried over anhydrous sodium sulfate. Evaporation of the solvent gave an orange oil (8.14 g) which after CC afforded **20** as a 3:1 mixture (^{1}H NMR) of two epimers, as a light yellow oil in 73% yield (6.30 g, 19.57 mmol), >99% pure. No attempt was made to separate the two diastereomeric products.

UV–VIS λ_{max}(ethanol): 230 nm. IR (liq.) cm^{-1}: 3384s (OH), 3025–2867s (CH), 2213w (C≡C), 1450m, 1365m, 1252s, 1189w, 1065s, 1013m, 988m, 931w, 881m, 841s, 753w. MS [IP 70 eV, 170 °C; *m/z* (% rel. int.)]: 322 (1, [*M*]), 304 (5, [*M*−18]), 266 (11, [*M*−56]), 248 (4), 211 (19), 167 (19), 157 (16), 149 (16), 95 (10), 75 (38), 73 (100), 43 (15), 41 (16). ^{1}H NMR ($CDCl_3$) major epimer: δ 0.132 (s, 9 H, TMSO–), 1.005 (s, 3 H, Me-6′), 1.161 (s, 3 H, Me-6′), 1.57–1.75 (m, 2 H, H-5′), 1.81 (m, 3 H, Me-3), 1.85 (m, 3 H, Me-2′), 4.15–4.30 (m, 3 H, H-1 and H-4′), 5.38 (m, 1 H, H-3′), 5.96 (tq, 1 H, $J_{Me\text{-}3,H\text{-}2}$ 1.5 Hz, $J_{1,2}$ 6.8 Hz, H-2). ^{1}H NMR ($CDCl_3$) minor epimer: δ 0.132 (s, 9 H, TMSO–), 1.041 (s, 3 H, Me-6′), 1.118 (s, 3 H, Me-6′), 1.57–1.75 (m, 2 H, H-5′), 1.83 (m, 3 H, Me-3), 1.91 (m, 3 H, Me-2′), 4.15–4.30 (m, 3 H, H-1 and H-4′), 5.45 (m, 1 H, H-3′), 5.96 (tq, 1 H, $J_{Me\text{-}3,H\text{-}2}$ 1.5 Hz, $J_{1,2}$ 6.8 Hz, H-2).

(2E)-5-[(1RS,4S)-1-Hydroxy-2,6,6-trimethyl-4-trimethylsiloxycyclohex-2-enyl]-3-methyl-2-penten-4-ynal (**8**). The epimeric diols **20** (2.40 g, 7.45 mmol) were dissolved in dry THF (120 ml). Manganese dioxide (25.00 g) was added and the reaction mixture was stirred vigorously at 20 °C. The reaction was monitored by TLC (system 3). After 17 h, the reaction mixture was filtered through Celite and the solvent was evaporated off to afford a 4:1 mixture (^{1}H NMR) of two epimeric aldehydes **8** as a yellow oil in 59% yield (1.41 g, 4.41 mmol), >95% pure [TLC (system 3), ^{1}H NMR]. No attempt was made to separate the two epimers.

TLC (system 3) $R_f = 0.78$. UV–VIS λ_{max}(ethanol): 275 nm. IR (liq.) cm^{-1}: 3456m (OH), 2959–2753s (CH), 2205w (C≡C), 1672s (conj. C=O), 1603m, 1450w, 1408m, 1376m, 1313w, 1250s, 1218w, 1183w, 1134w, 1109w, 1067s, 1013w, 990m, 960w, 929w, 883s, 840s. MS [IP 50 eV, 170 °C; *m/z* (% rel. int.)]: 320 (2, [*M*]), 302 (1, [*M*−18]), 264 (7, [*M*−56]), 227 (10), 189 (32), 171 (10), 157 (13), 147 (31), 141 (16), 75 (42), 73 (100), 43 (11). ^{1}H NMR ($CDCl_3$) major epimer: δ 0.139 (s, 9 H, TMSO–), 1.024 (s, 3 H, Me-6′), 1.170 (s, 3 H, Me-6′), 1.55–1.80 (m, 2 H, H-5′), 1.85 (m, 3 H, Me-2′), 2.28 (d, 3 H, $J_{Me\text{-}3,H\text{-}2}$ 1.5 Hz, Me-3), 4.26 (m, 1 H, H-4′), 5.43 (m, 1 H, H-3′), 6.17 (dq, 1 H, $J_{Me\text{-}3,H\text{-}2}$ 1.5 Hz, $J_{1,2}$ 7.9 Hz, H-2), 10.01 (d, 1 H, $J_{1,2}$ 7.9 Hz, H-1). ^{1}H NMR ($CDCl_3$) minor epimer: δ 0.132 (s, 9 H, TMSO–), 1.052 (s, 3 H, Me-6′), 1.119 (s, 3 H, Me-6′), 1.55–1.80 (m, 2 H, H-5′), 1.92 (m, 3 H, Me-2′), 2.30 (d, 3 H, $J_{Me\text{-}3,H\text{-}2}$ 1.4 Hz, Me-3), 4.26 (m, 1 H, H-4′), 5.50 (m, 1 H, H-3′), 6.20 (dq, 1 H, $J_{Me\text{-}3,H\text{-}2}$ 1.5 Hz, $J_{1,2}$ 7.9 Hz, H-2), 10.02 (d, 1 H, $J_{1,2}$ 7.9 Hz, H-1).

Attempted synthesis of (2E)-5-[(3RS,4S)-3,4-dihydroxy-2,6,6-trimethylcyclohex-1-enyl]-3-methyl-2-penten-4-ynal (**21**). The diastereomeric aldehydes **8** (0.71 mg, 2.22 mmol) were stirred with formic acid (3 ml) in dichloromethane (10 ml) at 20 °C in the dark for 1 h. The reaction mixture was poured into ice–water and the product was extracted with dichloromethane. The extract was washed consecutively with water, saturated aqueous sodium hydrogen carbonate and water. The solvent was evaporated off and the resulting residue was dissolved in methanol (6 ml). A solution of potassium carbonate (1.50 g) in water (4 ml) was added and the reaction mixture was stirred at 20 °C in the dark for 15 min. The volume of the reaction mixture was reduced to ca. 5 ml. Water was added and the product was extracted with ethyl acetate. The extract was washed with water and brine and dried over anhydrous sodium sulfate. Evaporation of the solvent afforded a brown oily, viscous residue (0.38 g). TLC (system 3) indicated the presence of more than five different products. UV–VIS λ_{max}(dichloromethane): broad absorption 220–550 nm. ^{1}H NMR ($CDCl_3$) indicated a complex mixture of prod-

ucts: δ 1.0–2.05 (several singlets), 3.63 (m, 3 H), 3.77 (m, 3 H), 6.20 (m, 1 H), 9.97–10.97 [3 × d, *J* 9.7 Hz, 3 × CHO(?)]. No further work was carried out in order to purify or identify any of the products.

(2E)-5-[(1RS,4S)-1,4-Dihydroxy-2,6,6-trimethylcyclohex-2-enyl]-3-methyl-2-penten-4-ynol (**22**). The epimeric TMS ethers **20** (4.25 g,13.20 mmol) were stirred in 5% potassium hydroxide in methanol (100 ml) at 20 °C. The reaction was monitored by TLC (system 4). Complete conversion of the substrate was observed after 20 min. The volume of the reaction mixture was reduced to ca. 20 ml, water was added, and the product was extracted with ethyl acetate. The extract was washed with water and brine, and dried over anhydrous sodium sulfate. Evaporation of the solvent afforded a 3:1 mixture (^{1}H NMR) of the epimeric triols **22** as a light yellow oil in 70% yield (2.29 g, 9.16 mmol), >95% pure [TLC (system 4), ^{1}H NMR]. No attempt was made to separate the two epimers.

TLC (system 4) R_f=0.53 (diastereomers inseparable). UV–VIS λ_{max}(ethanol): 230 nm. IR (liq.) cm^{-1}: 3538s (OH), 3027–2732s (CH), 2213w (C≡C), 1723m, 1664w, 1634m, 1449m, 1378m, 1311w, 1256m, 1192w, 1141w, 1106w, 1061m, 1012s, 986s, 950m, 921w, 842w. MS [IP 70 eV, 150 °C; *m/z* (% rel. int.)]: 250 (3, [*M*]), 232 (5, [*M*−18]), 214 (1, [*M*−18−18]), 194 (66), 189 (13), 176 (96), 161 (100), 148 (35), 138 (63), 123 (32), 115 (22), 105 (54), 91 (56), 79 (43), 69 (36), 55 (25), 43 (48), 41 (75). ^{1}H NMR ($CDCl_3$) major epimer: δ 1.005 (s, 3 H, Me-6′), 1.177 (s, 3 H, Me-6′), 1.70 (dd, 1 H, *J* 9.0 Hz, *J* 13.0 Hz, H-5′), 1.82 (m, 3 H, Me-3), 1.88 (m, 1 H, H-5′), 1.89 (m, 3 H, Me-2′), 4.20 (m, 3 H, H-1 and H-4′), 5.49 (m, 1 H, H-3′), 5.97 (tq, 1 H, $J_{Me\text{-}3,H\text{-}2}$ 1.5 Hz, $J_{1,2}$ 6.8 Hz, H-2). ^{1}H NMR ($CDCl_3$) minor epimer: δ 1.040 (s, 3 H, Me-6′), 1.131 (s, 3 H, Me-6′), 1.84 (m, 3 H, Me-3), 1.94 (m, 3 H, Me-2′), 4.20 (m, 3 H, H-1 and H-4′), 5.58 (m, 1 H, H-3′), 5.99 (tq, 1 H, $J_{Me\text{-}3,H\text{-}2}$ 1.5 Hz, $J_{1,2}$ 7.0 Hz, H-2).

(2E)-5-[(3RS,4S)-3,4-Dihydroxy-2,6,6-trimethylcyclohex-1-enyl]-3-methyl-2-penten-4-ynol (**12**). The diastereomeric triols **22** (1.80 mg, 7.20 mmol) were stirred with formic acid (8 ml) in dichloromethane (28 ml) at 20 °C in the dark for 1 h. The reaction mixture was poured into ice–water and the product was extracted with dichloromethane. The extract was washed consecutively with water, saturated aqueous sodium hydrogen carbonate and water. The solvent was evaporated off and the resulting residue was dissolved in methanol (15 ml). A solution of potassium carbonate (3.70 g) in water (10 ml) was added and the reaction mixture was stirred at 20 °C in the dark for 15 min. The volume of the reaction mixture was reduced to ca. 10 ml. Water was added and the product was extracted with ethyl acetate. The extract was washed with water and brine, and dried over anhydrous sodium sulfate. Evaporation of the solvent afforded a brown oily residue (1.73 g) which, after CC, provided a ca. 3:1 mixture (^{1}H NMR) of the epimeric C_{15}-triols **12** as a yellow-brown oil in 82% yield (1.47 g, 5.88 mmol), >95% pure [TLC (system 4), ^{1}H NMR]. No attempt was made to separate the two epimers.

TLC (system 4) R_f=0.38 (diastereomers inseparable). UV–VIS λ_{max}(ethanol): 258, 269, 281 nm, %III/II=3. IR (liq.) cm^{-1}: 3360s (OH), 3033–2726s (CH), 2182w (C≡C), 1661m, 1629w, 1592m, 1409w, 1363m, 1330w, 1301w, 1250m, 1199m, 1177m, 1118m, 1062s, 1017m, 998m, 952m, 914w, 875w. MS [IP 70 eV, 150 °C; *m/z* (% rel. int.)]: 250 (100, [*M*]), 232 (14, [*M*−18]), 214 (3, [*M*−18−18]), 199 (18), 194 (32), 189 (24), 176 (39), 161 (34), 147 (34), 133 (34), 119 (30), 105 (44), 91 (50), 79 (25), 77 (35), 55 (25), 43 (49), 41 (47). ^{1}H NMR ($CDCl_3$) major epimer: δ 1.127 (s, 3 H, Me-6′), 1.177 (s, 3 H, Me-6′), 1.64 (m, 1 H, H-5′), 1.79 (m, 1 H, H-5′), 1.88 (d, 3 H, $J_{Me\text{-}3,H\text{-}2}$ 1.2 Hz, Me-3), 2.028 (m, 3 H, Me-2′), 3.82 (m, 1 H, H-3′ or H-4′), 3.98 (m, 1 H, H-3′ or H-4′), 4.25 (d, 2 H, $J_{1,2}$ 5.9 Hz, H-1), 6.00 (tq, 1 H, $J_{Me\text{-}3,H\text{-}2}$ 1.5 Hz, $J_{1,2}$ 6.9 Hz, H-2). The presence of the minor epimer was evident by a signal at 1.161 (s, Me-6′).

(2E)-5-[(3RS,4S)-3,4-Propane-2,2-diyldioxy-2,6,6-trimethylcyclohex-1-enyl]-3-methyl-2-penten-4-yn-1-ol and (2Z)-5-[(3RS,4S)-3,4-propane-2,2-diyldioxy-2,6,6-trimethylcyclohex-1-enyl]-3-methyl-2-penten-4-yn-1-ol (**23**). The epimeric C_{15}-triols **12** (0.49 g, 1.96 mmol) were stirred with 2,2-dimethoxypropane (1.02 g, 9.79 mmol) in dry DMF (50 ml) in the presence of *p*-toluenesulfonic acid (33.0 mg) at 30 °C for 20 h. Water was added and the product was extracted with dichloromethane. The extract was washed with water and brine and dried over anhydrous sodium sulfate. Evaporation of the solvent provided the C_{15}-acetonide **23** as a mixture of epimers and 2*E*/2*Z* geometrical isomers, forming a yellow–brown viscous oil in 83% yield (0.47 g, 1.62 mmol), >99% pure. CC provided (2*E*)-**23** as a yellow–brown oil in 45% yield, (0.26 g, 0.89 mmol), >99% pure [TLC (system 4), ^{1}H NMR]. No attempt was made to separate the two epimers. The corresponding (2*Z*)-**23** was obtained as a yellow–brown oil in 14% yield, (0.08 g, 0.28 mmol), >99% pure [TLC (system 4), ^{1}H NMR]. ^{1}H NMR assignments are given for the major epimer of each geometrical isomer only.

(2*E*)-**23**: TLC (system 3) R_f=0.48 (diastereomers inseparable). UV–VIS λ_{max} (methanol): 255, 267, 280 nm, %III/II=4. IR (liq.) cm^{-1}: 3376m (OH), 2989–2869s (CH), 2183w (C≡C), 1728w, 1675w, 1634w, 1613w, 1456m, 1377s, 1327w, 1214s, 1152m, 1057s, 1029s, 964w, 935w, 862m. MS [IP 70 eV, 180 °C; *m/z* (% rel. int.)]: 290 (65, [*M*]), 234 (11, [*M*−56]), 233 (13), 217 (45), 201 (28), 189 (46), 187 (21), 173 (29), 161 (26), 147 (26), 145 (26), 133 (25), 119 (27), 105 (34), 95 (21), 91 (38), 77 (23), 69 (19), 55 (27), 43 (100), 41 (49). ^{1}H NMR ($CDCl_3$): δ 1.073 (s, 3 H, Me-6′), 1.217 (s, 3 H, Me-6′), 1.377 (s, 3 H, Me in acetonide), 1.433 (s, 3 H, Me in acetonide), 1.67–1.72 (m, 2 H, H-5), 1.89 (m, 3 H, Me-3), 2.01 (d, 3 H, *J* 1.0 Hz, Me-2′), 4.26 (d, 2 H, $J_{1,2}$

6.2 Hz, H-1), 4.30–4.38 (m, 2 H, H-3′ and H-4′), 6.01 (tq, 1 H, $J_{Me\text{-}3,H\text{-}2}$ 1.4 Hz, $J_{1,2}$ 6.9 Hz, H-2).

(2*Z*)-**23**: TLC (system 3) R_f=0.78 (diastereomers inseparable). UV–VIS (methanol): 253, 267, 280 nm, %III/II=4. MS [IP 70 eV, 180 °C; *m/z* (% rel. int.)]: 290 (8, [*M*]), 273 (8), 231 (6), 215 (4), 201 (5), 187 (6), 173 (5), 159 (6), 145 (7), 131 (5), 119 (4), 115 (3), 105 (5), 91 (5), 77 (4), 73 (100), 55 (5), 43 (20), 41 (10). ^{1}H NMR ($CDCl_3$): δ 1.065 (s, 3 H, Me-6′), 1.210 (s, 3 H, Me-6′), 1.370 (s, 3 H, Me in acetonide), 1.431(s, 3 H, Me in acetonide), 1.67–1.72 (m, 2 H, H-5), 1.88 (m, 3 H, Me-3), 2.01 (d, 3 H, *J* 1.0 Hz, Me-2′), 4.05 (dq, 2 H, $J_{Me\text{-}3,H\text{-}1}$ 0.7 Hz, $J_{1,2}$ 6.7 Hz, H-1), 4.27–4.38 (m, 2 H, H-3′ and H-4′), 5.94 (tq, 1 H, $J_{Me\text{-}3,H\text{-}2}$ 1.5 Hz, $J_{1,2}$ 6.7 Hz, H-2).

(2E)-5-[(3RS,4S)-3,4-propane-2,2-diyldioxy-2,6,6-trimethylcyclohex-1-enyl]-3-methyl-2-penten-4-ynal (**5**). The epimeric acetonides (2*E*)-**23** (0.25 g, 0.86 mmol) were dissolved in dry dichloromethane (30 ml). Manganese dioxide (2.00 g) was added and the reaction mixture was stirred vigorously at 20 °C under N_2 in the dark. The reaction was monitored by TLC (system 3). After 1.5 h, the reaction mixture was filtered through Celite and the solvent was evaporated off to afford a mixture of two epimeric aldehydes **5** as a yellow oil in 93% yield (0.23 g, 0.80 mmol), >99% pure [TLC (system 3), ^{1}H NMR]. No attempt was made to separate the two epimers. ^{1}H NMR assignments are given for the major epimer only.

TLC (system 3) R_f=0.62. UV–VIS λ_{max}(methanol): 308, 321 nm, %III/II=30. IR (liq.) cm^{-1}: 3456m (OH), 2956–2725s (CH), 2183w (C≡C), 1675m (conj. C=O), 1595m, 1461s, 1377m, 1305w, 1216w, 1145w, 1113w, 1058w, 1029w, 862w. MS [IP 70 eV, 180 °C; *m/z* (% rel. int.)]: 288 (7, [*M*]), 230 (47, [*M*−58]), 215 (20), 187 (51), 175 (24), 173 (21), 159 (23), 147 (25), 131 (11), 121 (11), 115 (11), 105 (11), 91 (19), 77 (18), 69 (14), 58 (15), 55 (15), 43 (100). ^{1}H NMR ($CDCl_3$): δ 1.085 (s, 3 H, Me-6′), 1.229 (s, 3 H, Me-6′), 1.382 (s, 3 H, Me in acetonide), 1.430 (s, 3 H, Me in acetonide), 1.70–1.75 (m, 2 H, H-5′), 2.04 (m, 3 H, Me-2′), 2.35 (d, 3 H, $J_{Me\text{-}3,H\text{-}2}$ 1.4 Hz, Me-3), 4.33–4.40 (m, 2 H, H-3′ and H-4′), 6.20 (dq, 1 H, $J_{Me\text{-}3,H\text{-}2}$ 1.4 Hz, $J_{1,2}$ 8.0 Hz, H-2), 10.05 (d, 1 H, $J_{1,2}$ 9.8 Hz, H-1).

(all-E)-(3S,4RS)-3,4-propane-2,2-diyldioxy-7,8-didehydro-12′-apo-β-carotenal (**27**). A mixture of the protected C_{10}-phosphonium salt **26** [prepared from the available C_{10}-phosphonium salt **6** (0.72 g, 1.47 mmol) in methanol (10 ml) with *p*-toluenesulfonic acid (5 drops of a 1% solution in methanol) and trimethyl orthoformate (0.18 ml, 1.62 mmol) at 30–35 °C followed by treatment with ammonia (5 drops of a saturated solution in methanol) at 0 °C as previously reported[15]] and the epimeric C_{15}-aldehydes **5** (0.21 g, 0.73 mmol) in dry dichloromethane (20 ml), was added dropwise to a stirred suspension of sodium hydride (0.35 g, unwashed) in dry dichloromethane (30 ml) at 20 °C under N_2 in the dark. The reaction was monitored by TLC (system 3). Complete conversion of **5** was observed after 40 h. The reaction mixture was cooled to 0 °C and ice–water was added carefully to decompose excess sodium hydride. The product was extracted with dichloromethane. The extract was washed with water and brine and dried over anhydrous sodium sulfate. Evaporation of the solvent yielded a brown oily residue which was dissolved in acetone (20 ml). Hydrochloric acid (5 drops of a 1 M aqueous solution) was added and the reaction mixture was stirred at 20 °C under N_2 for 10 min. Solid potassium carbonate (0.20 g) was added to the resulting red solution. The precipitate formed was filtered off and the solvents were removed at reduced pressure to yield a deep red oily residue. CC provided a ca. 4:1 mixture (^{1}H NMR) of the C-4 epimeric C_{25}-aldehydes **27** as a red oil in 82% yield (0.25 g, 0.60 mmol), >99% pure [TLC (system 3), HPLC (system 1)]. HPLC (system 1) indicated a mixture of the all-*E* isomers (57%) and three *Z* isomers (4+24+15%). The C-4 epimers were not separated by HPLC (system 1). Spectroscopic data are given for the isomeric mixture. Complete ^{1}H NMR assignments are given for the major all-*E* isomer only.

TLC (system 3) R_f=0.74; HPLC (system 1) t_R= 8.6–9.6 min (isomeric mixture). UV–VIS λ_{max}(hexane) 408, 420 nm; λ_{max}(acetone) 408 nm. MS [IP 70 eV, 200 °C; *m/z* (% rel. int.)]: 420 (100, [*M*]), 405 (6, [*M*−15]), 362 (11, [*M*−58]), 319 (6), 305 (7), 277 (17), 263 (13), 223 (13), 209 (13), 195 (12), 183 (11), 165 (12), 157 (14), 145 (12), 143 (14), 129 (12), 119 (13), 105 (19), 95 (22), 91 (20), 77 (14), 43 (70). ^{1}H NMR ($CDCl_3$) major isomer: δ 1.094 (s, 3 H, Me-16 or Me-17), 1.240 (s, 3 H, Me-16 or Me-17), 1.382 (s, 3 H, Me in acetonide), 1.438 (s, 3 H, Me in acetonide), 1.65–1.78 (m, 2 H, H-2), 1.887 (s, 3 H, Me-18), 2.028 (s, 3 H, Me-19, Me-20 or Me-20′), 2.033 (s, 3 H, Me-19, Me-20 or Me-20′), 2.041 (s, 3 H, Me-19, Me-20 or Me-20′), 4.32–4.40 (m, 2 H, H-3 and H-4), 6.33 (d, 1 H, $J_{14,15}$ 12.0 Hz, H-14), 6.39 (d, 1 H, $J_{11,12}$ 15.0 Hz, H-12), 6.50 (d, 1 H, $J_{Me\text{-}19,H\text{-}10}$ 1.0 Hz, $J_{10,11}$ 11.1 Hz, H-10), 6.65 (dd, 1 H, $J_{10,11}$ 11.4 Hz, $J_{11,12}$ 14.9 Hz, H-11), 6.72 (dd, 1 H, $J_{14',15'}$ 11.7 Hz, $J_{15,15'}$ 14.5 Hz, H-15′), 6.97 (d, 1 H, $J_{14',15'}$ 11.4 Hz, H-14′), 7.03 (dd, 1 H, $J_{14,15}$ 11.9 Hz, $J_{15,15'}$ 14.5 Hz, H-15), 9.459 (s, 1 H, H-12′). The presence of the minor C-4 epimer was confirmed by resonances at δ 1.086 (s, Me-16 or Me-17), 1.231 (s, Me-16 or Me-17) and 1.878 (s, Me-18).

(all-E)-(3S,4RS)-3,4-Dihydroxy-7,8-didehydro-8′-apo-β-carotenal (**28**). A solution of the protected C_5-phosphonium salt **29** [prepared from the available C_5-phosphonium salt **7** (0.62 g, 1.45 mmol) in methanol (10 ml) with *p*-toluenesulfonic acid (5 drops of a 1% solution in methanol) and trimethyl orthoformate (0.18 ml, 1.62 mmol) at 30–35 °C followed by treatment with ammonia (5 drops of a saturated solution in methanol) at 0 °C as previously reported][8] and the C-4 epimeric C_{25}-aldehydes

27 (0.26 g, 0.62 mmol) in dry dichloromethane (20 ml), was added dropwise to a stirred suspension of sodium hydride (0.35 g, unwashed) in dry dichloromethane (30 ml) at 20 °C under N_2 in the dark. The reaction was monitored by TLC (system 3). Complete conversion of **27** was observed after 42 h. The reaction mixture was cooled to 0 °C and ice–water was added carefully to decompose excess sodium hydride. The product was extracted with dichloromethane. The solvent was evaporated off and the resulting residue was stirred in 75% aqueous acetic acid (50 ml) at 20 °C under N_2 in the dark for 3 h. The reaction mixture was cooled to 0 °C and neutralised with 15% aqueous potassium hydroxide. The product was extracted with diethyl ether. The extract was washed with water and brine, and dried over anhydrous sodium sulfate. Evaporation of the solvent provided a red oily residue which, after CC, afforded the C-4 epimeric C_{30}-dihydroxy aldehydes **28** as a red oil in 55% yield (152.8 mg, 0.34 mmol), >99% pure [HPLC (system 1), ^{1}H NMR]. HPLC indicated a mixture of one major all-*E* isomer (69%) and five minor isomers (1+7+16+6+1%). The spectroscopic analysis was performed on the isomeric mixture. ^{1}H NMR assignments are given for the all-*E* isomer only.

TLC (system 4) R_f=0.57; HPLC (system 1) t_R= 21.1–23.1 min (isomeric mixture). UV–VIS λ_{max}(acetone): 420, 446, 464 nm, %III/II=2. MS [IP 70 eV, 180 °C; *m/z* (% rel. int.)]: 446 (100, [*M*]), 444 (10, [*M*−2]), 428 (27, [*M*−18]), 412 (10, [*M*−18–16]), 221 (9), 209 (11), 197 (10), 183 (10), 171 (14), 169 (14), 157 (17), 145 (17), 131 (16), 128 (15), 119 (27), 109 (10), 107 (13), 105 (26), 95 (19), 93 (14), 91 (37), 83 (15), 81 (12), 79 (16), 77 (19), 69 (17), 55 (29), 43 (32), 41 (38). ^{1}H NMR ($CDCl_3$) major isomer: δ 1.153 (s, 3 H, Me-16 or Me-17), 1.207 (s, 3 H, Me-16 or Me-17), 1.64 (m, 1 H, H-2), 1.902 (s, 3 H, Me-19′), 1.985 (s, 3 H, Me-18), 2.012 (m, 6 H, Me-20 and Me-19 or Me-20′), 2.061 (s, 3 H, Me-19 or Me-20′), 2.11 (m, 1 H, H-2), 3.86 (m, 1 H, H-3), 4.00 (m, 1 H, H-4), 6.30 (d, 1 H, $J_{14,15}$ 10.9 Hz, H-14), 6.39 (d, 1 H, $J_{11,12}$ 14.4 Hz, H-12), 6.45 (d, 1 H, $J_{14',15'}$ 11.6 Hz, H-14′), 6.49 (dd, 1 H, $J_{Me\text{-}19,H\text{-}10}$ 1.2 Hz, $J_{10,11}$ 11.5 Hz, H-10), 6.58 (dd, 1 H, $J_{10,11}$ 10.1 Hz, $J_{11,12}$ 15.0 Hz, H-11), 6.63–6.73 (m, 3 H, H-11′, H-12′ and H-15′), 6.77 (dd, 1 H, $J_{14,15}$ 11.8 Hz, $J_{15,15'}$ 14.1 Hz, H-15), 6.94 (d, 1 H, $J_{Me\text{-}19',H\text{-}10'}$ 1.4 Hz, $J_{10',11'}$ 11.1 Hz, H-10′), 9.454 (s, 1 H, H-8′).

*(all-*E*)-(3*S*,4*RS*,8′*RS*)-3,4,8′-Trihydroxy-7,8-didehydro-7′,8′-dihydro-7′-apo-β-carotene* (**30**). Methyllithium (0.91 mmol, 0.65 ml of a 1.4 M solution in diethyl ether) was added dropwise to a stirred solution of the preceding C-4 epimeric C_{30}-dihydroxy aldehydes **28** (56.1 mg, 0.13 mmol) in dry diethyl THF (50 ml) at 20 °C under N_2 in the dark. The reaction mixture was stirred at 20 °C under N_2 in the dark for 1.5 h and subsequently cooled to 0 °C. Water was added carefully to decompose excess methyllithium and the product was extracted with diethyl ether. The organic phase was washed with water and brine, dried over anhydrous sodium sulfate and evaporated to dryness. CC of the resulting residue provided the C_{31}-diol **30** as a complex mixture of isomers (^{1}H NMR), isolated as a broad homogenous yellow zone, inseparable (broad zone) by TLC (system 3) and by HPLC (system 1), as an orange–red oil in 46% yield (29.3 mg, 0.06 mmol), >95% pure [TLC (system 3), HPLC (system 1), ^{1}H NMR]. The presence of *Z* isomers was demonstrated by HPLC (system 1). The spectroscopic characterisation was carried out on the diastereomeric mixture. Complete ^{1}H NMR assignments, exception for ring-methylene protons, are given for the major all-*E* isomer only.

TLC (system 3) R_f=0.52–0.29 (broad zone); HPLC (system 1) t_R=21–24 min (isomeric mixture). UV–VIS λ_{max}(acetone): 406, 427, 454 nm, %III/II=30. MS [IP 70 eV, 180 °C; *m/z* (% rel. int.)]: 463 (33, [*M*+1]), 462 (79, [*M*]), 445 (22, [*M*+1–18]), 444 (65, [*M*−18]), 426 (21, [*M*−18–18]), 308 (12), 211 (11), 195 (10), 183 (11), 171 (16), 169 (17), 157 (17), 149 (27), 145 (26), 143 (21), 133 (23), 119 (29), 105 (34), 91 (70), 69 (40), 55 (54), 43 (100), 41 (66). ^{1}H NMR ($CDCl_3$) major isomer: δ 1.151 (s, 3 H, Me-16 or Me-17), 1.203 (s, 3 H, Me-16 or Me-17), 1.30 (d, 3 H, $J_{Me\text{-}7',H\text{-}8'}$ 6.4 Hz, Me-7′), 1.826 (s, 3 H, Me-19′), 1.951 (m, 3 H, Me-19, Me-20 or Me-20′), 1.958 (s, 3 H, Me-18), 2.002 (s, 3 H, Me-19, Me-20 or Me-20′), 2.056 (s, 3 H, Me-19, Me-20 or Me.20′), 3.86 (m, 1 H, H-3), 3.99 (m, 1 H, H-4), 4.31 (*q*, 1 H, $J_{Me\text{-}7',H\text{-}8'}$ 6.7 Hz, H-8′), 6.17 (d, 1 H, $J_{10',11'}$ 11.3 Hz, H-10′), 6.23 (d, 1 H, *J* 11.0 Hz, H-14 or H-14′), 6.27 (d, 1 H, *J* 11.1 Hz, H-14 or H-14′), 6.33 (d, 2 H, *J* 15.0 Hz, H-12 and H-12′), 6.37 (d, 1 H, $J_{10,11}$ 11.0 Hz, H-10), 6.43 (m, 1 H, H-11), 6.51 (dd, 1 H, $J_{10',11'}$ 11.2 Hz, $J_{11',12'}$ 15.1 Hz, H-11′), 6.62 (m, 2 H, H-15 and H-15′).

*Synthesis of (all-*E*)- (**1a**) and (9*Z*)-(3*S*)-7′-apohopkinsiaxanthin (**1b**). Route 1.* (i) The triol **30** (11.3 mg, 24.46 μmol) was stirred with manganese dioxide (160.0 mg, 1.84 mmol) in acetone at 20 °C under N_2 in the dark. The reaction was monitored by TLC (system 3). Complete conversion of **30** was observed after 1.5 h. The reaction mixture was filtered through Celite, the solvent was evaporated off and CC of the resulting residue provided two unidentified products, fraction 1 (1.6 mg) and fraction 2 (0.9 mg), as red oils.

Fraction 1: TLC (system 3) R_f=0.64. UV–VIS λ_{max}(hexane): 450, 473, 506 nm, contaminated with a minor product absorbing in the region 400–480 nm.

Fraction 2: TLC (system 3) R_f=0.53. UV–VIS λ_{max}(hexane): 425, 452, 578 nm, contaminated with products absorbing in the regions 350–420 nm and >470 nm.

(ii) The triol **30** (4.6 mg, 9.97 μmol) was stirred with manganese dioxide (3.0 mg, 34.48 μmol) in acetone at 20 °C under N_2 in the dark. The reaction was monitored by TLC (system 3) and HPLC (system 1). No reaction was observed after 6 h. Additional manganese dioxide (6.0 mg, 68.97 μmol) was added and the reaction mixture was stirred at 20 °C under N_2 in the dark for an additional

1 h. Only traces of an oxidation product, tentatively identified as the mono-oxidised product by comparison with subsequent results, were observed by HPLC.

(iii) The triol **30** (3.2 mg, 6.93 μmol) in dry benzene (2 ml) was treated with DDQ (1.8 mg, 7.70 μmol) at 20 °C under N_2 in the dark. The reaction was monitored by TLC (system 3). Complete conversion of **30** was observed after 3 h. The main product had $R_f=0$. No coloured product less polar than the substrate was detected by TLC (system 3).

(iv) A solution of the triol **30** (1.0 mg, 2.16 μmol) and iodine (50 μg, 0.20 μmol) in dry benzene (5 ml) was stirred vigorously under an atmosphere of air while being irradiated with a 25 W sodium lamp. The reaction was monitored by HPLC (system 1). A ca. 3:2 mixture of the tentatively identified mono-oxidised product **31** and the substrate **30**, in addition to traces of the tentatively identified 7′-apohopkinsiaxanthin (**1**), were observed after 14 h.

(v) A solution of the triol **30** (0.5 mg, 1.08 μmol) in dry benzene (4 ml) was stirred under an atmosphere of air while being irradiated with dim sunlight. The reaction was monitored by HPLC (system 1). No reaction other than *cis–trans* isomerisation was observed during a 13 h period.

(vi) A solution of the triol **30** (12.7 mg, 27.49 μmol) and iodine (0.54 mg, 2.13 μmol) in dry benzene (50 ml) was stirred vigorously under an atmosphere of air while being irradiated with dim sunlight. The reaction was monitored by HPLC (system 1). Complete conversion of **30** was observed after 4 h. Complete oxidation to 7′-apohopkinsiaxanthin (**1**) was observed after 20 h. The reaction mixture turned from yellow to orange to dark orange–red during the course of the reaction. The solvent was evaporated off and CC of the resulting residue provided pure (3*S*)-7′-apohopkinsiaxanthin (**1**) in 42% yield (5.3 mg, 11.6 mmol), >99% pure [HPLC (system 1)]. HPLC (system 1) indicated a mixture of four geometrical isomers. The major isomer, constituting 51% of total **1**, and the isomer absorbing at the longest wavelength in the VIS region of the spectrum, constituting 10% of total **1**, recorded on-line [HPLC (system 1)], were isolated by preparative HPLC (system 2) and identified as (9*Z*)-(3*S*)-7′-apohopkinsiaxanthin (**1b**) and (all-*E*)-(3*S*)-7′-apohopkinsiaxanthin (**1a**) respectively. The two remaining isomers, constituting 9% and 30% of the total mixture, were not isolated or identified. All spectroscopic data for **1a** and **1b** were as given below (route 2).

(3S,4RS)-3,4-Dihydroxy-7,8-didehydro-7′,8′-dihydro-7′-apo-β-caroten-8′-one (**31**). A mixture of the diastereomeric C_{31}-triols **30** (3.0 mg, 6.49 μmol) and iodine (0.15 mg, 0.59 μmol) in benzene (10 ml) was stirred vigorously under an atmosphere of air while being irradiated with dim sunlight. The reaction was monitored by HPLC (system 1). Complete conversion of **30** was observed after 6 h. HPLC (system 1) indicated a mixture of the mono-oxidised product **31** (87%) and 7′-apohopkinsiaxanthin (**1**, 13%). The volume of the reaction mixture was concentrated to ca. 0.5 ml and preparative TLC (system 1) provided a mixture of geometrical isomers of the C-4 epimeric C_{31}-dihydroxy ketones **31** as an orange solid in 71% yield (2.1 mg, 4.57 μmol), >95% pure [HPLC (system 1)]. HPLC (system 1) indicated a mixture of five isomers (in order of elution: 3+6+12+19+60%). No attempt was made to isolate any pure isomer. The spectroscopic analysis was performed on the diastereomeric mixture. ^{1}H NMR assignments are given for the major (9*Z*)-diastereomer only.

HPLC (system 1) $t_R=20.5$–23.0 min (isomeric mixture). UV–VIS λ_{max}(acetone): 436, 461 nm. MS [IP 70 eV, 190 °C; *m/z* (% rel. int.)]: 461 (2, [*M*+1]), 460 (7, [*M*]), 442 (6, [*M*−18]), 426 (3, [*M*−18−16]), 209 (6), 197 (8), 183 (8), 173 (6), 161 (10), 145 (10), 119 (15), 109 (15), 107 (10), 105 (12), 95 (13), 91 (20), 85 (11), 83 (15), 81 (12), 77 (11), 69 (17), 67 (11), 57 (22), 43 (100), 41 (30). ^{1}H NMR ($CDCl_3$) major isomer: δ 1.150 (s, 3 H, Me-16 or Me-17), 1.200 (s, 3 H, Me-16 or Me-17), 1.94 (d, 3 H, $J_{Me\text{-}19',H\text{-}10'}\approx1.0$ Hz, Me-19′), 1.953 (m, 3 H, Me-18), 1.995 (s, 3 H, Me-20′), 2.100 (s, 3 H, Me-19 or Me-20), 2.110 (s, 3 H, Me-19 or Me-20), 2.366 (s, 3 H, Me-7′), 3.88 (m, 1 H, H-3), 4.03 (m, 1 H, H-4), 6.29 (d, 2 H, *J* 11.0 Hz, H-14 and H-14′), 6.38 (d, 1 H, $J_{11,12}\approx14$ Hz, H-12), 6.40 (d, 1 H, $J_{10,11}\approx11$ Hz, H-10), 6.55–6.67 (m, 2 H, H-11′ and/or H-15 and/or H-15′), 6.67 (d, 1 H, $J_{11',12'}\approx14$ Hz, H-12′), 6.72 (dd, 1 H, *J* 11.5 Hz, *J* 14.5 Hz, H-11′ or H-15 or H-15′), 6.84 (dd, 1 H, $J_{10,11}$ 11.2 Hz, $J_{11,12}$ 15.1 Hz, H-11), 7.14 (dq, 1 H, $J_{Me\text{-}19',H\text{-}10'}$ 1.3 Hz, $J_{10',11'}$ 10.0 Hz, H-10′).

(all-E)-2,7,11-Trimethyl-12-oxo-2,4,6,8,10-tridecapentaenal (**11**). The C_{16}-keto aldehyde **11** was prepared essentially according to a previously reported protocol,[15] but by using a sample of the isolated and purified C_6-keto aldehyde **32** rather than the usual stock solution of **32** in dichloromethane. The C_6-keto aldehyde **32** [1.50 g, 87% pure (GLC), corresponding to 1.30 g, 11.61 mmol] and the C_{10}-phosphonium salt **6** (5.65 g, 11.51 mmol) in dry dichloromethane (30 ml) were added dropwise to a stirred suspension of sodium hydride (0.90 g, unwashed) in dry dichloromethane at 20 °C under N_2 in the dark. The reaction mixture was stirred at 20 °C under N_2 in the dark for 22 h and cooled to 0 °C. Ice–water was added carefully to decompose excess sodium hydride. The product was extracted with dichloromethane. The organic phase was washed with water and brine, the solvent was evaporated off and the resulting red oily residue was subjected to CC. The C_{16}-keto aldehyde **11** was obtained as a brick-red solid in 82% yield (2.30 g, 9.43 mmol), 100% pure [TLC (system 1), HPLC (system 1)]. HPLC (system 1) indicated a mixture of the all-*E* isomer (64%) and two *Z* isomers (34+2%). Recrystallisation from acetone afforded the pure all-*E* isomer as a brick-red crystalline solid (753 mg).

All spectroscopic data for the C_{16}-keto aldehyde **11**

were as previously reported.[15] TLC (system 1) $R_f = 0.41$; HPLC (system 1) $t_R = 12.0$ min. UV–VIS λ_{max}(acetone): 366, 386 ($E^{1\%}_{1\,cm} = 3620$, $\varepsilon = 88350$), 390 nm. MS [IP 30 eV, 170 °C; *m/z* (% rel. int.)]: 244 ([$C_{16}H_{20}O_2$], measured: 244.147, calculated: 244.146).

*Synthesis of (all-*E*)- (**1a**) and (9*Z*)-(3*S*)-7′-apohopkinsiaxanthin (**1b**). Route 2.* Sodium methoxide (0.69 ml of a 1 M solution in methanol, 0.69 mmol) was added dropwise via a syringe to a solution of the available (2*Z*)-5-[((4*S*)-4-hydroxy-2,6,6-trimethyl-3-oxo-1-cyclohexenyl)-3-methyl-2-penten-4-ynyl]triphenylphosphonium bromide {**10**, 0.30 g, 0.52 mmol; $[\alpha]_D^{27} = -55$ (methanol, $c = 0.4$), reported[19] $[\alpha]_D^{20} = -90$, (ethanol, $c = 1.0$); tentative assignments ^{1}H NMR ($CDCl_3$): δ 1.14 (s, 3 H, Me-6′), 1.20 (s, 3 H, Me-6′), 1.70 (s, 6 H, Me-2′+contaminants), 1.93 (d, 3 H, $J_{P,H} \approx 3$ Hz, Me-3), 2.00–2.05 (m, 3 H, contaminants), 4.75 (m, 3 H, contaminants), 5.20 (m, 3 H, contaminants), 5.53 (dd, 1 H, $J_{1,2}$ 7.5 Hz, $J_{P,H}$ 12.5 Hz, H-1), 5.94 (m, 1 H, H-2), 7.00 (m, 5 H, contaminants), 7.30–7.65 (m, ≈10 H, contaminants), 7.65–8.00 (m, 15 H, aromatic protons); estimated purity from ^{1}H NMR spectrum ≈60%; optical rotation based on ≈60% purity $[\alpha]_D^{27} \approx -92$; 0.31 mmol employed in reaction based on ≈60% purity} and the C_{16}-keto aldehyde **11** (0.10 g, 0.41 mmol) in dry dichloromethane (50 ml) at 20 °C over 15 min with a continuous flow of N_2 being bubbled through the reaction mixture. The reaction mixture was stirred for another 2 h and subsequently poured into an ice-cold solution of a phosphate buffer (pH≈6). The product was extracted with dichloromethane. The extract was washed with water and brine and dried over anhydrous sodium sulfate. Evaporation of the solvent yielded a red oily residue. HPLC (system 2) demonstrated a mixture of six isomers (3+4+8+6+24+55%). The two major isomers were inseparable from (all-*E*)-(3*S*)-7′-apohopkinsiaxanthin (**1a**, 24% of total) and (9*Z*)-(3*S*)-7′-apohopkinsiaxanthin (**1b**, 55% of total) obtained by air-oxidation of the triol **30**, by HPLC (systems 2 and 3). Two fractions were isolated by CC of the crude product. Fraction 1 (70.5 mg, 0.15 mmol) consisted of the five less polar isomers, including the all-*E* isomer (33% of total). Fraction 2 (70.9 mg, 0.15 mmol) consisted of four isomers, including (all-*E*)-(3*S*)-7′-apohopkinsiaxanthin (**1a**, 10% of total) and (9*Z*)-(3*S*)-7′-apohopkinsiaxanthin (**1b**, 80% of total). Total yield of CC purified 7′-apohopkinsiaxanthin was 74% (141.4 mg, 0.30 mmol; based on 100% pure phosphonium salt **10**). (9*Z*)-(3*S*)-7′-Apohopkinsiaxanthin (**1b**) was obtained as dark red–violet needles upon crystallisation from methanol. HPLC purified (all-*E*)-(3*S*)-7′-apohopkinsiaxanthin {**1a**, >95% pure [HPLC (systems 2 and 3), ^{1}H NMR]} and crystalline (9*Z*)-(3*S*)-7′-apohopkinsiaxanthin {**1b**, >99% pure [HPLC (systems 2 and 3), ^{1}H NMR]} were employed for the spectroscopic analysis.

*(all-*E*)-(3*S*)-7′-Apohopkinsiaxanthin* (**1a**). TLC (system 3) $R_f = 0.48$; HPLC (system 1) $t_R = 15.1$ min; (system 3) $t_R = 8.5$ min. UV–VIS: λ_{max}(hexane) 430, 453, 482 nm, %III/II = 54; λ_{max}(acetone) 430, 457, 483 nm, %III/II = 8, λ_{max}(HPLC eluent) 430, 455, 485 nm, %III/II = 39. IR (KBr) cm^{-1}: 3434s (OH), 2959–2853m (CH), 2161m (C≡C), 1654s (conj. C=O). MS [IP 70 eV, 190 °C; *m/z* (% rel. int.)]: 459 (20, [*M*+1]), 458 (52, [$C_{31}H_{38}O_3$], measured: 458.283, calculated: 458.282), 442 (5, [*M*−16]), 295 (6), 223 (7), 173 (7), 161 (17), 157 (12), 149 (12), 143 (12), 119 (21), 109 (16), 105 (16), 91 (30), 83 (22), 77 (11), 69 (11), 55 (20), 43 (100), 41 (22). CD nm (Δε): 226 (+2.1), 242 (+1.6), 250 (0), 289 (−2.7), 322 (0), 359 (+0.9), 400 (0), 443 (−1.0), 449 (0). ^{1}H NMR ($CDCl_3$): δ 1.311 (s, 3 H, Me-17), 1.356 (s, 3 H, Me-16), 1.81 (dd, 1 H, $J_{2ax,3}$ 12.8 Hz, $J_{2ax,2eq}$ 13.2 Hz, H-2_{ax}), 1.944 (s, 3 H, Me-19′), 1.994 (m, 3 H, Me-20), 2.009 (s, 3 H, Me-20′), 2.027 (s, 3 H, Me-18), 2.051 (s, 3 H, Me-19), 2.22 (dd, 1 H, $J_{2eq,3}$ 6.8 Hz, $J_{2ax,2eq}$ 12.8 Hz, H-2eq), 2.369 (s, 3 H, Me-7′), 3.61 (d, 1 H, $J_{H\text{-}3,3\text{-}OH}$ 1.8 Hz, 3-OH), 3.34 (ddd, 1 H, $J_{H\text{-}3,3\text{-}OH}$ 1.8 Hz, $J_{2eq,3}$ 6.0 Hz, $J_{2ax,3}$ 13.8 Hz, H-3), 6.34 (d, 1 H, $J_{14,15}$ 10.3 Hz, H-14), 6.40 (d, 1 H, $J_{14',15'}$ 10.2 Hz, H-14′), 6.47 (d, 1 H, $J_{11,12}$ 14.1 Hz, H-12), 6.61 (m, 1 H, H-11), 6.64 (d, 1 H, $J_{10,11}$ 11.1 Hz, H-10), 6.65 (dd, 1 H, $J_{10,11}$ ≈11 Hz, $J_{11',12'}$ ≈14 Hz, H-11′), 6.67 (d, 1 H, $J_{11',12'}$ 14.4 Hz, H-12′), 6.69 (m, 1 H, H-15′), 6.71 (m, 1 H, H-15), 7.14 (d, 1 H, $J_{10',11'}$ 10.1 Hz, H-10′).

*(9*Z*)-(3*S*)-7′-Apohopkinsiaxanthin* (**1b**). M.p. 164 °C. TLC (system 3) $R_f = 0.44$; HPLC (system 1) $t_R = 15.6$ min, (system 3) $t_R = 10.1$ min. UV–VIS: λ_{max}(hexane) 427, 449, 479 nm, %III/II = 56; λ_{max}(acetone) 428, 452 ($E^{1\%}_{1\,cm}$ = 2160, $\varepsilon = 99\,000$), 477 nm, %III/II = 13. IR (KBr) cm^{-1}: 3465s (OH), 3031–2869m (CH), 2155m (C≡C), 1651s (conj. C=O), 1606w, 1575m, 1435w, 1363m, 1300w, 1274m, 1226s, 1178w, 1131w, 1075m, 1016w, 989m, 961s. MS [IP 70 eV, 190 °C; *m/z* (% rel. int.)]: 459 (33, [*M*+1]), 458 (100, [$C_{31}H_{38}O_3$], measured: 458.283, calculated: 458.282), 442 (6, [*M*−16]), 295 (9), 237 (6), 209 (10), 185 (11), 173 (8), 165 (11), 161 (32), 157 (15), 149 (17), 143 (14), 133 (11), 129 (11), 119 (27), 109 (22), 105 (23), 91 (35), 83 (31), 79 (11), 77 (13), 69 (9), 55 (20), 43 (96), 41 (24). CD nm (Δε): 228 (+3.0), 244 (0), 257 (−3.2), 272 (−2.1), 278 (−2.2), 318 (0), 334 (+0.3), 365 (0), 368 (−0.2), 375 (0), 386 (+0.1), 392 (0), 430 (−1.3), 438 (−0.7), 445 (−1.0), 450 (0). ^{1}H NMR ($CDCl_3$): δ 1.360 (s, 3 H, Me-17), 1.395 (s, 3 H, Me-16), 1.83 (t, 1 H, *J* 13.3 Hz, H-2_{ax}), 1.94 (d, 3 H, $J_{Me\text{-}19',H\text{-}10'}$ 1.0 Hz, Me-19′), 1.954 (m, 3 H, Me-20), 1.999 (s, 3 H, Me-20′), 2.051 (s, 3 H, Me-19), 2.080 (s, 3 H, Me-18), 2.24 (dd, 1 H, $J_{2eq,3}$ 5.7 Hz, $J_{2ax,2eq}$ 12.8 Hz, H-2eq), 2.365 (s, 3 H, Me-7′), 3.61 (d, 1 H, $J_{H\text{-}3,3\text{-}OH}$ 1.8 Hz, 3-OH; signal removed when 1 drop of D_2O was added to the sample), 3.35 (ddd, 1 H, $J_{H\text{-}3,3\text{-}OH}$ 1.8 Hz, $J_{2eq,3}$ 5.7 Hz, $J_{2ax,3}$ 13.8 Hz, H-3; signal changed to dd *J* 5.6 Hz, *J* 13.7 Hz, when 1 drop of D_2O was added to the sample), 6.32 (d, 1 H, $J_{14,15}$ 10.7 Hz, H-14), 6.40 (d,

1 H, $J_{14',15'}$ 11.1 Hz, H-14'), 6.45 (d, 1 H, $J_{11,12}$ 15.2 Hz, H-12), 6.48 (dq, 1 H, $J_{Me\text{-}19,H\text{-}10} \approx 1$ Hz, $J_{10,11}$ 11.2 Hz, H-10), 6.65 (m, 2 H, H-11' and H-15'), 6.67 (d, 1 H, $J_{11',12'}$ 15.4 Hz, H-12'), 6.68 (dd, 1 H, $J_{14,15}$ 11.1 Hz, $J_{15,15'}$ 15.3 Hz, H-15), 6.82 (dd, 1 H, $J_{10,11}$ 11.1 Hz, $J_{11,12}$ 15.1 Hz, H-11), 7.14 (dq, 1 H, $J_{Me\text{-}19',H\text{-}10'} \approx 1$ Hz, $J_{10',11'}$ 11.1 Hz, H-10'). ^{13}C NMR ($CDCl_3$): δ 11.7 (C-19'), 12.7 and 12.8 (C-20 and C-20'), 14.5 (C-18), 23.0 (C-19), 25.6 (C-7'), 26.2 (C-16), 31.1 (C-17), 36.6 (C-1), 44.1 (C-2), 69.3 (C-3), 93.4 (C-7), 106.0 (C-8), 118.6 (C-9), 124.2 (C-11'), 127.0 (C-11), 130.5 (C-15'), 131.8 (C-15), 133.9 (C-5), 134.1 (C-14), 135.8 (C-13'), 136.0 (C-13), 136.3 (C-14'), 137.2 (C-9'), 139.1 and 139.2 (C-10 and C-12), 139.8 (C-10'), 144.3 (C-12'), 147.5 (C-6), 199.3 and 199.4 (C-4 and C-8').

*(all-*E*)-2,3-Didehydro-7'-apohopkinsiaxanthin* (**34a**). (all-*E*)-(3*S*)-7'-Apohopkinsiaxanthin (**1a**, 0.1 mg, 0.22 μmol) was stirred in 5% methanolic potassium hydroxide (5 ml) under an atmosphere of air at 20 °C for 1 h. Water was added and the product was extracted with diethyl ether. The extract was washed with water until neutral followed by brine, and was subsequently dried over anhydrous sodium sulfate. The solvent was evaporated off and the resulting residue was subjected to preparative TLC (system 2). The product eluted as a broad zone with tailing on silica TLC-plates. The front of the broad zone was isolated by preparative TLC, affording 2,3-didehydro-7'-apohopkinsiaxanthin (**34**) as an oil in 41% yield (40.0 μg, 0.09 μmol, based on $E^{1\%}_{1\,cm}=2160$), >80% pure [TLC (system 3), HPLC (system 3), ^{1}H NMR]. HPLC (system 3) and ^{1}H NMR demonstrated a 2:1 mixture of the all-*E* and 9*Z* isomers. Synthetic 2,3-didehydro-7'-apohopkinsiaxanthin (**34**) was inseparable from a sample of **34** prepared from authentic (*ex. Hopkinsia rosacea*) (all-*E*)-7'-apohopkinsiaxanthin (**1a**), left over from an early collaboration with McBeth,[2] by TLC (system 3) and HPLC (system 2). No attempt was made to separate the two isomers on a preparative scale. The spectroscopic analysis was performed with the 2:1 mixture. Chromatographic properties and complete ^{1}H NMR assignments are given for the all-*E* isomer **34a** only.

TLC (system 3) $R_f=0.39$ (tailing); HPLC (system 3) $t_R=13.0$ min. UV–VIS: λ_{max}(hexane) 429, 453, 481 nm, %III/II = 38; λ_{max}(acetone) 423, 458, 481 nm; λ_{max} [HPLC-eluent, (all-*E*)-isomer] 436, 460, 487 nm, %III/II = 30. MS [IP 70 eV, 190 °C; *m/z* (% rel. int.)]: 457 (10, [*M*+1]), 456 (26, [*M*]), 236 (12), 228 (8, [*M*−228]), 161 (12), 125 (15), 119 (14), 109 (23), 107 (19), 105 (11), 97 (33), 91 (22), 85 (37), 83 (41), 71 (49), 57 (100), 63 (59), 41 (53). ^{1}H NMR ($CDCl_3$): δ 1.372 (s, 6 H, Me-16 and Me-17), 1.943 (s, 3 H, Me-19'), 2.000 (s, 3 H, Me-20 or Me-20'), 2.010 (s, 3 H, Me-20 or Me-20'), 2.076 (s, 3 H, Me-19), 2.161 (s, 3 H, Me-18), 2.368 (s, 3 H, Me-7'), 6.081 (s, 1 H, H-2), 6.34 (d, 1 H, $J_{14,15} \approx 11$ Hz, H-14), 6.40 (d, 1 H, $J_{14',15'}$ 11.1 Hz, H-14'), 6.50 (d, 1 H, $J_{11,12} \approx 15$ Hz, H-12), 6.60–6.65 (m, 3 H, H-10, H-11 and H-11'), 6.67 (d, 1 H, $J_{11',12'}$ 15.1 Hz, H-12'), 6.68–6.75 (m, 2 H, H-15 and H-15'), 7.14 (d, 1 H, $J_{10',11'} \approx 11$ Hz, H-10'). The presence of the (9*Z*) isomer **34b** was demonstrated by resonances at δ 1.419 (s, Me-16 and Me-17), 2.216 (s, Me-18), 6.111 (s, H-2).

(9Z)-2,3-Didehydro-7'-apohopkinsiaxanthin (**34b**). (9*Z*)-(3*S*)-7'-Apohopkinsiaxanthin (**1b**, 3.4 mg, 7.42 μmol) was stirred in 5% methanolic potassium hydroxide (50 ml) under an atmosphere of air at 20 °C for 1 h. Water was added and the product was extracted with diethyl ether. The extract was washed with water until neutral followed by brine, and was subsequently dried over anhydrous sodium sulfate. The solvent was evaporated off and the resulting residue was subjected to preparative TLC (system 2). The product eluted as a broad zone with tailing on silica TLC-plates. The front of the broad zone was isolated by preparative TLC, affording 2,3-didehydro-7'-apohopkinsiaxanthin (**34**) as a red solid in 56% yield (1.9 mg, 4.17 μmol, based on $E^{1\%}_{1\,cm}=2160$), >90% pure [TLC (system 3), HPLC (system 3), ^{1}H NMR]. HPLC (system 3) and ^{1}H NMR demonstrated a 4:3 mixture of the 9*Z* and all-*E* isomers. No attempt was made to separate the two isomers on a preparative scale. The spectroscopic analysis was performed on the 4:3 mixture. Chromatographic properties and complete ^{1}H NMR assignments are given for the 9*Z* isomer **34b** only.

TLC (system 3) $R_f=0.45$ (tailing); HPLC (system 3) $t_R=13.3$ min. UV–VIS: λ_{max}(hexane) 429, 451, 481 nm, %III/II = 33; λ_{max}(acetone) 423, 456, 480 nm; λ_{max} [HPLC-eluent, (9*Z*)-isomer] 432, 456, 483 nm, %III/II = 24. IR (KBr) cm^{-1}: 3430s (OH), 3033–2855s (CH), 2162m (C≡C), 1739s, 1654s (conj. C=O), 1401m, 1320w, 1253w, 1228w, 1176m, 1067w, 1033w, 992w, 966w. MS [IP 70 eV, 190 °C; *m/z* (% rel. int.)]: 457 (33, [*M*+1]), 456 (100, [*M*]), 279 (4), 261 (4), 228 (10, [*M*−228]), 215 (5), 197 (6), 189 (6), 161 (13), 145 (6), 119 (17), 109 (13), 105 (12), 91 (12), 83 (16), 55 (14), 43 (59), 41 (11). ^{1}H NMR ($CDCl_3$): δ 1.419 (s, 6 H, Me-16 and Me-17), 1.942 (s, 3 H, Me-19'), 2.000 (s, 6 H, Me-20 and Me-20'), 2.077 (s, 3 H, Me-19), 2.216 (s, 3 H, Me-18), 2.368 (s, 3 H, Me-7'), 6.110 (s, 1 H, H-2), 6.30–6.45 (m, 3 H, H-12, H-14 and H-14'), 6.50 (d, 1 H, $J_{10,11}$ 11.1 Hz, H-10), 6.55–6.75 (m, 4 H, H-11', H-12', H-15 and H-15'), 6.84 (dd, 1 H, $J_{10,11}$ 11.3 Hz, $J_{11,12}$ 15.1 Hz, H-11), 7.14 (d, 1 H, $J_{10',11'}$ 10.0 Hz, H-10'). The presence of the (all-*E*)-isomer **34a** was demonstrated by resonances at δ 1.372 (s, Me-16 and Me-17), 2.161 (s, Me-18), 6.081 (s, H-2).

*(all-*E*)-(3S)-7'-Apohopkinsiaxanthin 3-acetate* (**35**). (all-*E*)-(3*S*)-7'-Apohopkinsiaxanthin (**1a**, 0.1 mg, 0.22 μmol) was dissolved in dry pyridine (1 ml). Acetic anhydride (0.1 ml) was added and the reaction mixture was stirred at 20 °C under N_2 in the dark. The reaction was monitored by TLC (system 2). Complete conversion of **1a**

was observed after 3 h. Water was added and the product was extracted with diethyl ether. The extract was washed with water and brine and dried over anhydrous sodium sulfate. The solvent was evaporated off, and traces of pyridine were removed by azeotropic evaporation with toluene–acetone. Preparative TLC (system 1) provided (all-*E*)-(3*S*)-7′-apohopkinsiaxanthin 3-acetate (**35**) as a red oil in 91% yield (0.1 mg, 0.20 μmol), >85% pure [TLC (system 2), HPLC (system 2)], containing ca. 10% of the tentatively identified 9*Z* isomer [HPLC (system 2) t_R = 9.3 min. UV–VIS λ_{max}(HPLC-eluent): 446 nm, %III/II = 37].

TLC (system 2) R_f = 0.43; HPLC (system 3, flow = 0.75 min) t_R = 9.7 min. UV–VIS: λ_{max}(hexane) 426, 450, 478 nm, %III/II = 37; λ_{max}(HPLC-eluent) 428, 455, 484 nm, %III/II = 37. MS [IP 70 eV, 190 °C; *m/z* (% rel. int.)]: 500 (9, [*M*]), 458 (2, [*M* − 42]), 277 (19), 185 (5), 167 (5), 157 (5), 149 (18), 109 (7), 95 (8), 77 (11), 71 (11), 69 (13), 67 (13), 57 (28), 43 (100), 41 (33). ^{1}H NMR ($CDCl_3$): δ 1.323 (s, 3 H, Me-17), 1.378 (s, 3 H, Me-16), 1.941 (s, 3 H, Me-19′), 1.993 (m, 6 H, Me-18 and Me-20 or Me-20′), 2.005 (s, 3 H, Me-20 or Me-20′), 2.049 (s, 6 H, Me-19 and Me in OAc), 2.368 (s, 3 H, Me-7′), 5.53 (m, 1 H, H-3), 6.33 (d, 1 H, $J_{14,15} \approx 11$ Hz, H-14), 6.40 (d, 1 H, $J_{14',15'}$ 11.2 Hz, H-14′), 6.48 (d, 1 H, $J_{11,12} \approx 15$ Hz, H-12), 6.55–6.65 (m, 3 H, H-10, H-11 and H-11′), 6.68 (d, 1 H, $J_{11',12'}$ 14.8 Hz, H-12′), 6.67–6.73 (m, 2 H, H-15 and H-15′), 7.14 (d, 1 H, $J_{10',11'} \approx 11$ Hz, H-10′).

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