Carotenoids and related polyenes. Part 4.[1] Synthesis of carotenoid analogues containing a conjugated carbonyl group and their fluorescence properties

Yumiko Yamano,[a] Mamoru Mimuro[b] and Masayoshi Ito*,[a]

[a] *Kobe Pharmaceutical University, Motoyamakita-machi, Higashinada-ku, Kobe 658, Japan*
[b] *Department of Information Science, Faculty of Science, Yamaguchi University, Yamaguchi 753, Japan*

Fluorescence properties of several synthetic carotenoid analogues have been investigated in order to assess the relationship between molecular structures and function as a photosynthetic antenna. The origin of fluorescence is determined by two factors; the length of the conjugated double bond system and the presence of a carbonyl group. For efficient energy transfer to chlorophyll *a*, eight conjugated double bonds and an associated carbonyl group are required, which ensures that fluorescence occurs from the S_1 state.

Introduction

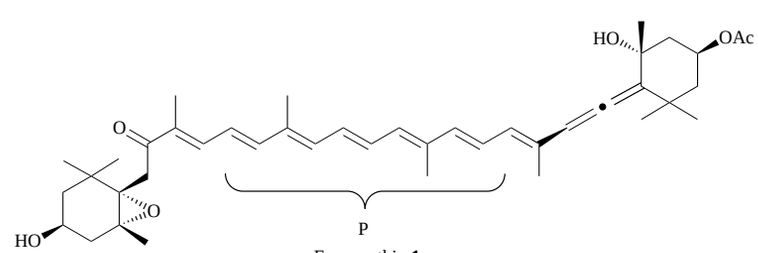
In photosynthesis of algae, three carotenoids, fucoxanthin **1**, peridinin **2** and siphonaxanthin **3**, function as efficient light-harvesting antennas in pigment systems;[2,3] their energy-transfer efficiency to an acceptor molecule, chlorophyll (Chl) *a*, was estimated to be very high. These carotenoids show a stronger emission from the forbidden S_1 state than that from the allowed S_2 state and their S_1 lifetimes were longer than those of the unsubstituted carotenoids.[4,5] Their S_1 fluorescence spectra exhibit a greater overlap with the absorption spectrum of Chl *a* and thus a higher transition probability from the S_1 state takes place in the energy-transfer sequence. These are of the utmost importance for the antenna function in algal photosynthetic pigment systems.[3]

Previously, our group reported that the fluorescence spectra of carbonyl-containing carotenoids were characterized by dual emissive properties.[4–7] The origin of fluorescence is determined by the presence of a carbonyl group; for example, neoxanthin **4**, in which a carbonyl group of fucoxanthin **1** was replaced with a normal double bond, showed its origin from the S_2 state. However, in the case of spheroidenone **5**, even though the carbonyl group was contained in the conjugated system, its main emission originated from the S_2 state (Fig. 1). This suggests that the origin of fluorescence is determined not only by the presence of a carbonyl group but also by the molecular structure of the carotenoids. Thus we investigated this point by using several synthetic carotenoid analogues.

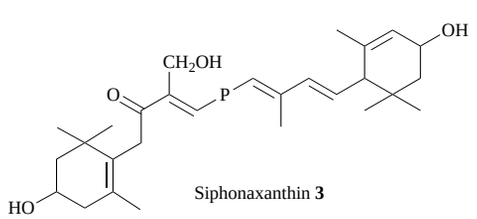
Results and discussion

Effect of β-ionone rings on the fluorescence properties

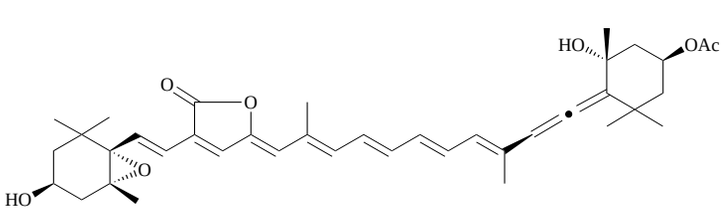
A characteristic molecular structure of antenna carotenoids is the presence of β-ionone rings and a carbonyl group in a chain of eight conjugated C=C double bonds. First, in order to study the effect of β-ionone rings on the fluorescence properties, we synthesized four analogues **6**,[7] **7**, **8** and **9**[7] of fucoxanthin **1**.



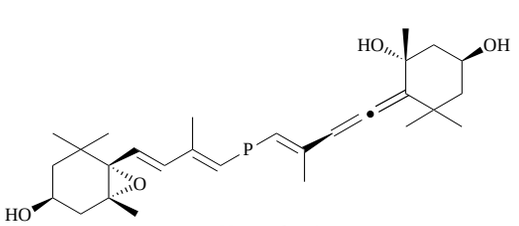
Fucoxanthin **1**



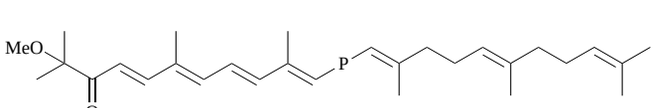
Siphonaxanthin **3**



Peridinin **2**



Neoxanthin **4**



Spheroidenone **5**

Structure of carotenoids of interest

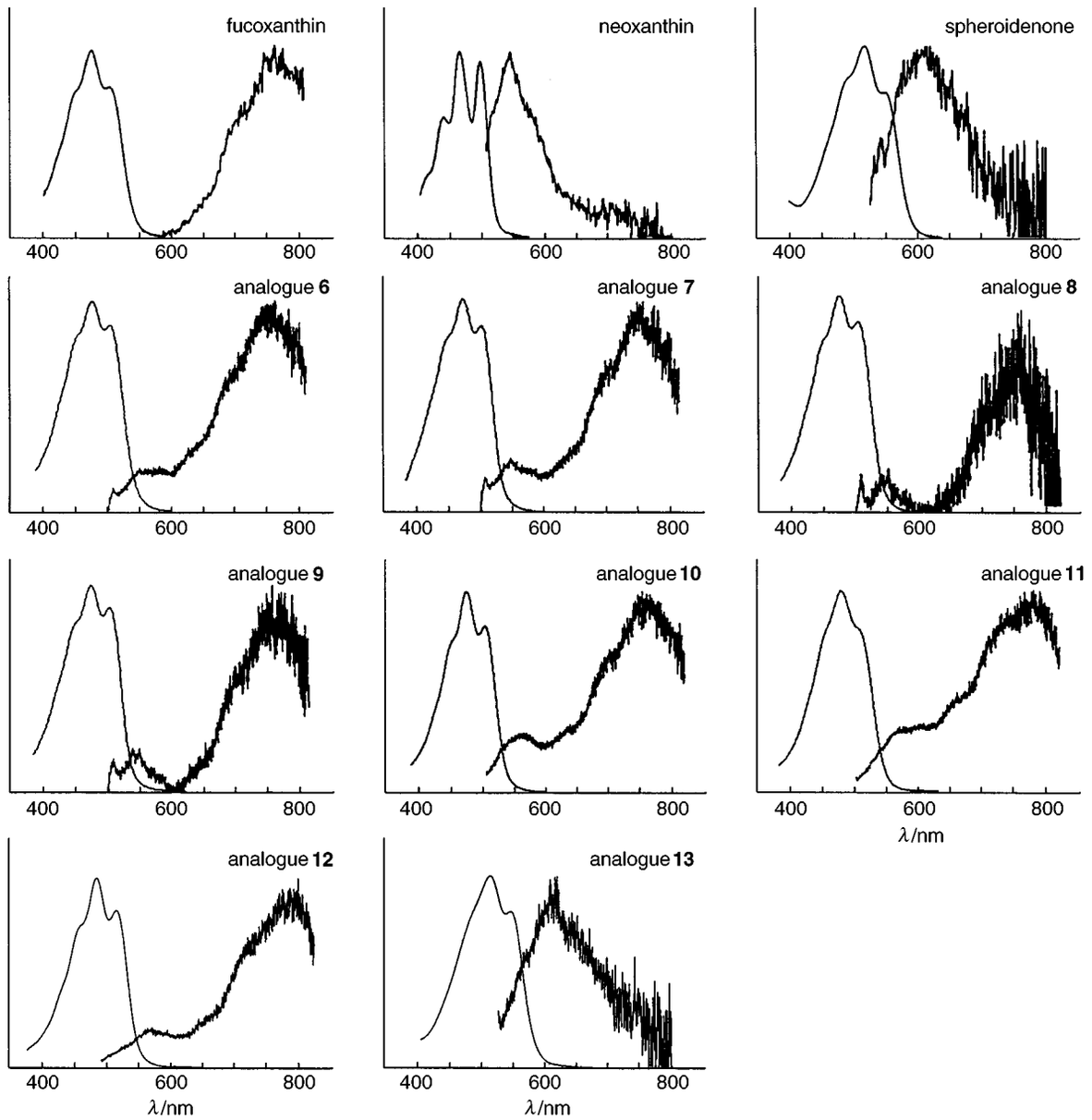


Fig. 1 Absorption spectra (smooth curves; left side) and fluorescence spectra (noisy curves; right side) of fucoxanthin **1**, neoxanthin **4**, spheroidenone **5** and analogues **6**–**13**, for solutions in CS_2

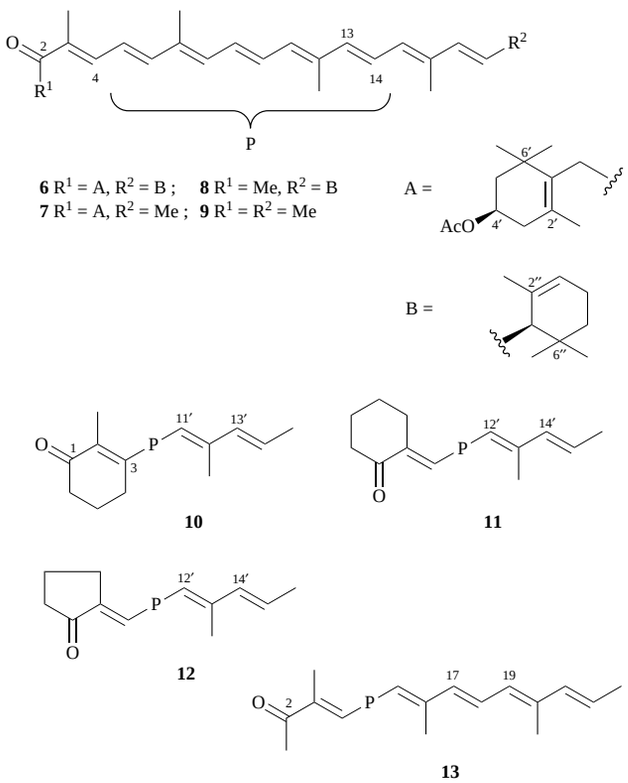
Analogues **6** and **7** were derived from the oxo pentaenal **14**, which was previously prepared[1] for the first total synthesis of fucoxanthin **1** (Scheme 1). Wittig condensation of the phosphonium salt **15**[8] with the aldehyde **14** in the presence of sodium methoxide as base, followed by acetylation, afforded an isomeric mixture [50% from **14**; all-*E* (analogue **6**):13*Z* ~1:1] of the condensed products, which was cleanly separated by preparative HPLC (PHPLC) in the dark. The stereochemistry of the newly formed 13,14-double bonds of these isomers was determined from the coupling constants (*E*: 15 Hz; *Z*: 12 Hz) between 13- and 14-H in the ^{1}H NMR spectra. The analogue **7** was also synthesized [64% from **15**; all-*E*:11*Z* ~1:1] using the Wittig salt **16**, which was derived from the formyl ester **17**[9] in 3 steps (64%) as shown in Scheme 1.

Analogues **8** and **9**, not possessing a β-ionone ring on the left side of the polyene chain, were prepared by reaction of the Wittig salt **15** or **16** with the oxo pentaenal **24a**. Condensed products (**8**: 74%; **9**: 87%; as isomeric mixtures) were purified by PHPLC to give each pure analogue. The aldehyde **24a** was derived from the formyl ester **17**. Introduction of a methyl group into aldehyde **17** and subsequent protection of the resulting hydroxy group gave the *tert*-butyldimethylsilyl (TBS) ether **20** (80%). Reduction of the ester group in compound **20** with lithium aluminium hydride (LAH) provided the alcohol **21** (83%), which was treated with lithium chloride and methanesulfonyl chloride (MsCl) followed by treatment with triphenylphosphine in chloroform under reflux to afford the Wittig salt **22** (73% from **21**). Wittig condensation of the phosphonium salt **22** with the C_{10}-dialdehyde **23** gave a mixture of the condensed products, which was desilylated using tetrabutylammonium fluoride (TBAF), oxidized with MnO_2, and subsequently separated by PHPLC to provide the all-*E*-oxo pentaenal **24a** (42% from **23**) and its 8*Z*-isomer **24b** (8% from **23**). The steady-state fluorescence spectra of these analogues **6**–**9** in CS_2 are shown in Fig. 1. The main emissions from these analogues were all observed at around 750 nm, indicating their origin from the S_1 state as in the case of antenna carotenoids **1**–**3**. These results show that β-ionone rings on both sides of a polyene chain do not affect its fluorescence properties.

Effect of the direction of a carbonyl group with respect to a polyene chain on the fluorescence properties

The carbonyl group in antenna carotenoids **1**,[10] **2** and **3**[11] is arranged in s-*trans* form. The s-*trans* configuration of fucoxanthin **1** was confirmed[10] by ^{1}H NMR spectroscopy, including nuclear Overhauser enhancement (NOE) experiments. In

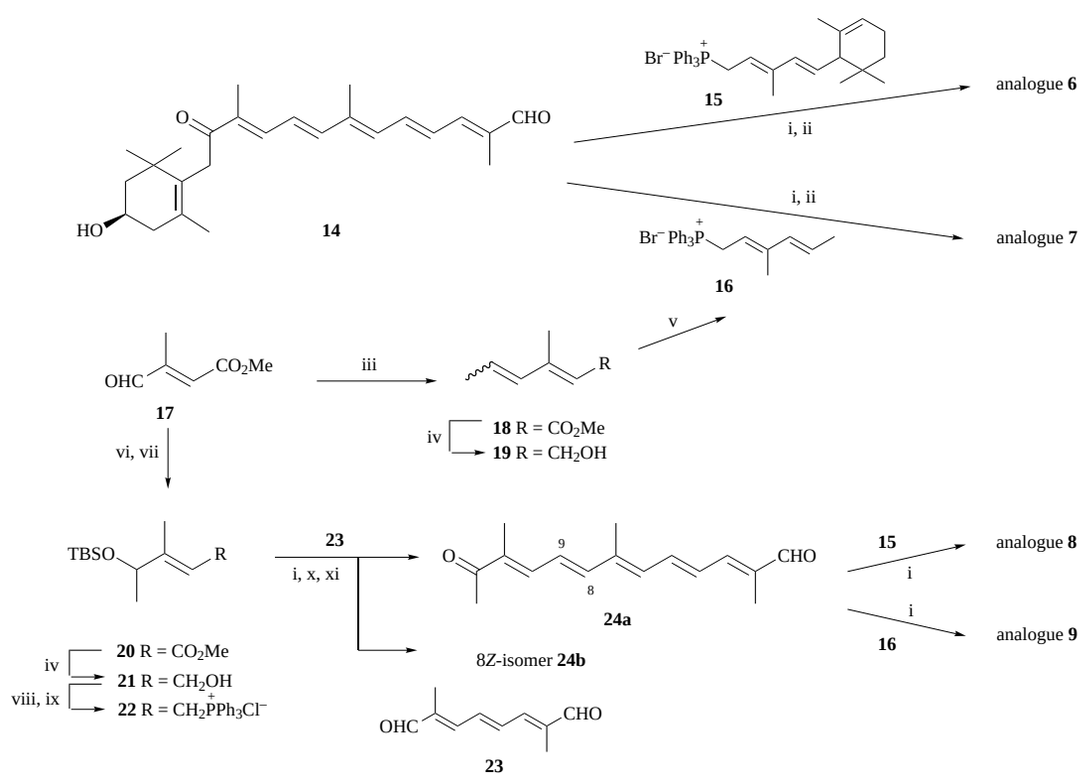
siphonaxanthin **3**, the oxygen atom of the carbonyl group is fixed in the same plane as that of conjugated double bonds by intramolecular hydrogen bonding with the alcohol.[11] This is also the case in peridinin **2**, which has an ylidene butenolide ring structure. The carbonyl group in analogues **6**–**9** was also confirmed to be s-*trans* from ^{1}H NMR spectroscopy including NOE experiments (cross-peaks between 1-H_2 or 1-H_3 and 4-H). On the other hand, the carbonyl group in spheroidenone **5** (emission from S_2 state is dominant) is known[12] to be in the s-*cis* form. Therefore, it is expected[7] that coplanarity of a carbonyl group with a polyene chain in the ground state is correlated with the origin of fluorescence. Thus, in order to study the effect of a carbonyl group on the fluorescence properties, we synthesized analogues **10**–**12**, whose configuration of the carbonyl group with respect to the eight conjugated double bonds is fixed in s-*cis* or s-*trans* form by the terminal ring structure.



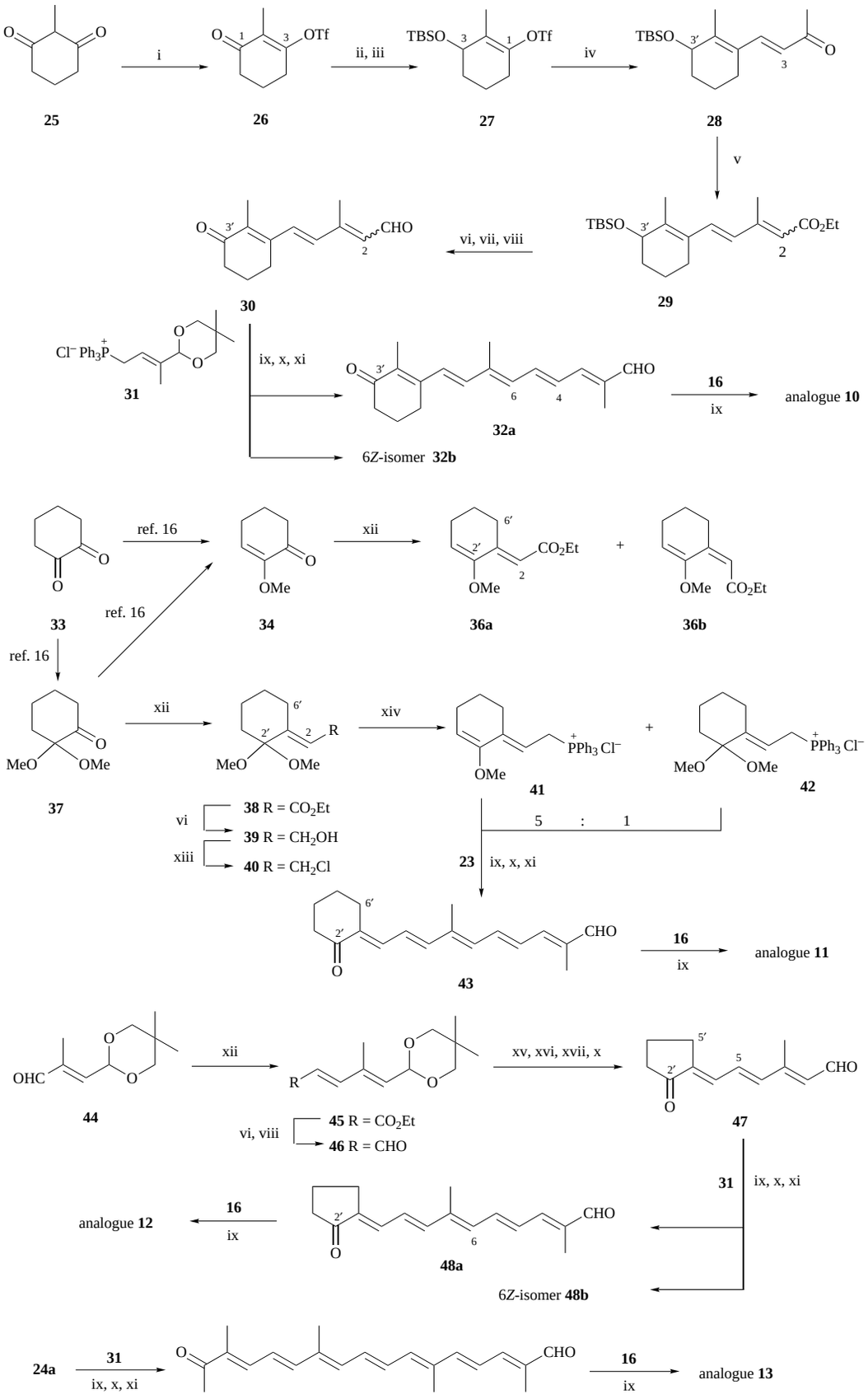
Structure of synthetic carotenoid analogues

The analogue **10**, possessing an s-*trans* carbonyl group, was synthesized starting from 2-methylcyclohexane-1,3-dione **25** (Scheme 2). Treatment of dione **25** with 1 mol equiv. of *N*-phenyltrifluoromethanesulfonimide (Tf_2NPh) in the presence of sodium hydride as a base gave the oxo enol triflate **26** (98%). Reduction of the carbonyl group of compound **26** with sodium borohydride followed by protection of the resulting hydroxy group gave the TBS ether **27** (68%), which underwent a coupling reaction[13] with methyl vinyl ketone in the presence of palladium catalyst to afford the dienone **28** (91%). Peterson olefination of compound **28** with ethyl (trimethylsilyl)(TMS)-acetate and lithium diisopropylamide (LDA) at −78 °C afforded the trienoate **29** (2*E*:2*Z* = 4:3) (95%), which without separation was transformed into the trienal **30** (2*E*:2*Z* = 3:2) in 3 steps (63%) as shown in Scheme 2. Wittig condensation of the phosphonium salt **31**[14] with aldehyde **30** and subsequent acid hydrolysis gave a crude isomeric mixture of the oxo pentaenal **32**, which without separation was treated with a palladium catalyst[1,15] and then purified by PHPLC to give the all-*E*-oxo pentaenal **32a** (76% from **30**) and its 6*Z*-isomer **32b** (13% from **30**). Finally, compound **32a** was condensed with the phosphonium salt **16** (Scheme 1) to give the analogue **10** (62%; all-*E*:9′*Z* ~1:1).

The analogue **11** was derived from cyclohexane-1,2-dione **33** as shown in Scheme 2. Treatment of the dione **33** with methoxytrimethylsilane at 0 °C in the presence of a catalytic amount of trifluoromethanesulfonic acid (TfOH) gave the dione monoketal **37** as the major initial product, which was converted into the diosphenol methyl ether **34** by keeping the reaction mixture at room temperature for several hours.[16] Emmons–Horner reaction of enone **34** with the phosphonate **35** provided an isomeric



Scheme 1 *Reagents*: i, **15**, **16** or **23**, NaOMe; ii, Ac_2O, Py; iii, $EtPPh_3Br$, ^{n}BuLi; iv, LAH; v, PPh_3·HBr; vi, MeMgBr; vii, TBSOTf, γ-collidine; viii, LiCl, MsCl, γ-collidine; ix, PPh_3; x, TBAF; xi, MnO_2



Scheme 2 *Reagents*: i, NaH, Tf_2NPh; ii, $NaBH_4$; iii, TBSCl, Et_3N, DMAP; iv, methyl vinyl ketone, cat. $PdCl_2(PPh_3)_2$, Et_3N; v, $TMSCH_2CO_2Et$, LDA; vi, LAH; vii, TBAF; viii, MnO_2; ix, **31**, **16** or **23**, NaOMe; x, *p*-TsOH; xi, cat. $PdCl_2(MeCN)_2$, Et_3N; xii, $(EtO)_2P(O)CH_2CO_2Et$ **35**, ^{n}BuLi; xiii, LiCl, MsCl, γ-collidine; xiv, PPh_3; xv, cyclopentanone, LDA; xvi, Ac_2O, DMAP; xvii, DBU

mixture of ylidene-esters **36a** (31%) and **36b** (36%), while the same reaction of ketal **37** afforded the *E*-ylidene-ester **38** (95%) as a single isomer. Therefore, the ester **38** was used for further reaction. Stereochemistry of those isomers was confirmed by ^{1}H NMR spectroscopy including 2D NOE and exchange spectroscopy (NOESY) experiments: in *E*-isomers **36a** and **38**, cross-peaks between 2-H and 2′-OMe were observed, whereas cross-peaks between 2-H and 6′-H_2 appeared in the *Z*-isomer

36b. Similar treatment of the ester **38** as in the case of the preparation of the Wittig salt **22** from **20** (Scheme 1) gave a mixture of Wittig salts **41** and **42**, which without purification was allowed to react with the C_{10}-dialdehyde **23**. The resulting condensed products were deprotected by acid hydrolysis and subsequently treated with palladium catalyst and then purified by PHPLC to give the all-*E*-oxo pentaenal **43** (81% from **23**). Finally, aldehyde **43** was condensed with the phosphonium salt **16** to furnish the analogue **11** (79%; all-*E*:10′*Z* ~1:1).

The analogue **12** was synthesized through reaction of cyclopentanone with the dienal **46**, which was prepared from the enal **44**[14] by Emmons–Horner reaction with the phosphonate **35** (98%) and subsequent reduction with LAH and oxidation with MnO_2 (50% from **45**). Treatment of the dienal **46** with the lithium enolate of cyclopentanone gave the aldol, which was acetylated, treated with 1,8-diazabicyclo[5.4.0]-undec-7-ene (DBU), and then hydrolysed to provide the all-*E*-oxo trienal **47** (64% from **46**). The newly formed ylidene double bond in compound **47** was determined to be *E* from ^{1}H NMR spectroscopy including NOE experiments (cross-peaks between 5′-H_2 and 5-H). The oxo trienal **47** was transformed into the analogue **12** in the same manner as in the case of synthesis of the analogue **10**, as shown in Scheme 2.

The steady-state fluorescence spectra of analogues **10**–**12** (Fig. 1) were similar to those of antenna carotenoids **1**–**3** and analogues **6**–**9**; the main emission originated from the S_1 state (~750 nm). This shows that coplanarity of a carbonyl group with a polyene chain is not significant for the S_1 emission.

Effect of length of conjugated double-bond system on the fluorescence properties

The number of conjugated double bonds (*n*) in antenna carotenoids **1**–**3** and synthetic analogues **6**–**12** is nine [C=C (or C=C=C) × 8 + C=O × 1]† and show, preferentially, S_1 emission, whereas the emission from the S_2 state is dominant in spheroidenone **5** (*n* = 11; C=C × 10 + C=O × 1). Therefore, in order to study the effect of the length of the conjugated double-bond system on the fluorescence properties, we synthesized the analogue **13** as shown in Scheme 2 and measured its fluorescence spectrum (Fig. 1). The main emission from analogue **13** was observed at ~600 nm, indicating S_2 emission. This clearly shows that the origin of fluorescence is affected by the length of the conjugated double-bond system.

Previously, our group reported that the presence of a carbonyl group had a large effect on the origin of fluorescence of polyenes.[4–7] For example, in the case of fucoxanthin **1**, replacement of a carbonyl group with a normal double bond (neoxanthin **4**) changed the origin of fluorescence from the S_1 state to the S_2 state (Fig. 1), even though the number *n* was the same in the two carotenoids.[5] From the above results, it appears that the origin of fluorescence is determined not only by the presence of a carbonyl group but also by the length of the conjugated double-bond system. However, neither the substituent group (for example, β-ionone ring) nor the direction of a carbonyl group with respect to a polyene chain is so significant for the S_1 emission.

As pointed out by one of us,[17] a main determinant for the origin of fluorescence is assigned to the energy gap between the S_2 and S_1 states (ΔE_{21}). On the other hand, the direction of a carbonyl group with respect to a polyene chain is known to be a major determinant in some aspects in the excited S_2 state;[18] this might be additional to the relaxation processes from the S_2 state.

In summary, it is expected that a common molecular structure, *viz*. eight conjugated double bonds, with one carbonyl group associated with the conjugated double-bond system, might be necessary for these carotenoids to function as efficient light-harvesting antennas in pigment systems.

† One of the eight double bonds in peridinin is cross-conjugated with the carbonyl group.

Experimental

UV–VIS spectra were recorded on a JASCO Ubest-55 instrument. IR spectra were measured on a Shimadzu IR-27G spectrometer, a Shimadzu FT-IR 4000 spectrometer or a Perkin-Elmer FT-IR spectrometer, model Paragon 1000, for chloroform solutions unless otherwise stated. ^{1}H NMR spectra at 200, 300 or 500 MHz were determined on a Varian XL-200, a Varian Gemini-200, a Varian Gemini-300 or a Varian VXR-500 superconducting Fourier-transform (FT)-NMR spectrometer, respectively, for deuteriochloroform solutions (tetramethylsilane as internal reference). ^{13}C NMR spectrum at 75 MHz was measured on a Varian Gemini-300 superconducting FT-NMR spectrometer for samples in deuteriochloroform solution with tetramethylsilane as internal standard. *J*-Values are given in Hz. Mass spectra were taken on a Hitachi M-80 or a Hitachi M-4100 spectrometer.

Absorption and fluorescence spectra shown in Fig. 1 were measured with a Hitachi 330 spectrophotometer and a Hitachi 850 spectrofluorometer, respectively, at 20 °C for solutions in carbon disulfide. For the fluorescence spectra, the maximum absorbance of sample solutions was kept <0.3. Measurements were repeated several times to increase the signal-to-noise ratio. The excitation wavelength was between 410 and 460 nm depending on the sample. The bandwidths for fluorescence analysis were 5 nm for excitation and 3 nm for emission. Data were transferred to a microcomputer for processing and to correct the spectral sensitivity of the fluorometer numerically.

Short-column chromatography (SCC) was performed on silica gel (Merck Art. 7739) under reduced pressure, and open column chromatography (CC) on silica gel (Merck Art. 7734). Preparative TLC (PLC) was performed on silica gel plates (Merck silica gel 60F_{254} precoated plates, 0.5 mm thickness). Analytical and preparative HPLC was carried out on Shimadzu LC-3A, 5A, 6A and Waters Model 510 instruments with a UV–VIS detector.

Standard work-up means that the organic layers were finally washed with brine, dried over anhydrous sodium sulfate (Na_2SO_4), filtered and concentrated *in vacuo* below 30 °C, using a rotary evaporator. All operations were carried out under nitrogen or argon. Ether refers to diethyl ether and hexane to *n*-hexane.

Preparation of the analogue 6

A solution of NaOMe (1.0 mol dm^{-3} in MeOH; 1.54 cm^3, 1.54 mmol) was added to an ice-cooled solution of the Wittig salt **15**[8] (690 mg, 1.28 mmol) and the aldehyde **14**[1] (98 mg, 0.26 mmol) in CH_2Cl_2 (10 cm^3). After being stirred at 0 °C for 1.5 h, the reaction mixture was diluted with ether. The organic layer was followed by standard work-up to give a residue, which was purified by SCC (acetone–hexane, 2:8) to afford an isomeric mixture of condensed products. Without separation, this was dissolved in a mixture of pyridine (Py) (6 cm^3) and acetic anhydride (2 cm^3). The mixture was stirred at room temp. for 16 h, poured into ice–water and extracted with ether. The extracts were washed successively with aq. 3% HCl, saturated aq. $NaHCO_3$ and brine. Evaporation of the dried extracts gave a residue, which was purified by SCC (ether–hexane, 1:3) to provide an isomeric mixture [78 mg, 50% from **14**; all-*E* (analogue **6**):13*Z* ~1:1]. PHPLC separation [LiChrosorb Si 60 (5 μm) 1.0 × 30 cm; tetrahydrofuran (THF)–hexane, 5:95] of the mixture in the dark gave the analogue **6** and its 13*Z*-isomer as red solids. *Analogue* **6**: λ_{max}(EtOH)/nm 267, 449 and 464sh; λ_{max}(hexane)/nm 264, 424, 446 and 474; ν_{max}(KBr)/cm^{-1} 1730 (OAc), 1659 (conj. CO) and 1607 (C=C); δ_H(500 MHz) 0.82 and 0.91 (each 3 H, s, 6″-*gem*-Me), 0.93 (3 H, s, 6′-Me^{eq}), 1.03 (3 H,

s, 6′-Me^{ax}), 1.48 (3 H, s , 2′-Me), 1.59 (3 H, d, *J* 1.5, 2″-Me), 1.65 (1 H, t, *J* 12, 5′-H^{ax}), 1.74 (1 H, ddd, *J* 12, 3.5 and 2, 5′-H^{eq}), 1.92 (3 H, s, 16-Me), 1.97 (3 H, s, 3-Me), 1.99 (3 H, s, 12-Me), 2.00 (3 H, s, 7-Me), 2.05 (3 H, s, OAc), 2.19 (1 H, d, *J* 10, 1″-H), 2.19 (1 H, br dd, *J* 16 and 10, 3′-H^{ax}), 2.39 (1 H, br dd, *J* 16 and 6, 3′-H^{eq}), 3.44 and 3.48 (each 1 H, d, *J* 18, 1-H$_2$), 5.07 (1 H, m, 4′-H), 5.42 (1 H, br s, 3″-H), 5.55 (1 H, dd, *J* 15 and 10, 18-H), 6.12 (1 H, d, *J* 15, 17-H), 6.13 (1 H, br d, *J* 11, 15-H), 6.26 (1 H, br d, *J* 11.5, 11-H), 6.35 (1 H, d, *J* 15, 13-H), 6.40 (1 H, br d, *J* 12, 8-H), 6.60 (1 H, dd, *J* 15 and 11, 5-H), 6.64 (1 H, dd, *J* 15 and 12, 9-H), 6.67 (1 H, dd, *J* 15 and 11, 14-H), 6.68 (1 H, d, *J* 15, 6-H), 6.74 (1 H, dd, *J* 15 and 11.5, 10-H) and 7.24 (1 H, br d, *J* 11, 4-H) (Found: M$^+$, 610.440. Calc. for $C_{42}H_{58}O_3$: M, 610.438).

13Z-*Isomer*: λ_{max}(EtOH)/nm 269, 333 and 446; λ_{max}(hexane)/nm 266, 316, 425, 444 and 472; ν_{max}(KBr)/cm^{-1} 1730 (OAc), 1665 and 1659 (split) (conj. CO) and 1609 (C=C); δ_H(500 MHz) 0.83 and 0.91 (each 3 H, s, 6″-*gem*-Me), 0.93 (3 H, s, 6′-Me^{eq}), 1.03 (3 H, s, 6′-Me^{ax}), 1.48 (3 H, s , 2′-Me), 1.59 (3 H, d, *J* 1.5, 2″-Me), 1.65 (1 H, t, *J* 12, 5′-H^{ax}), 1.74 (1 H, ddd, *J* 12, 3.5 and 2, 5′-H^{eq}), 1.89 (3 H, s, 16-Me), 1.97 (3 H, s, 3-Me), 2.00 (3 H, s, 7-Me), 2.05 (3 H, s, OAc), 2.13 (3 H, s, 12-Me), 2.19 (1 H, br dd, *J* 16 and 10, 3′-H^{ax}), 2.19 (1 H, d, *J* 10, 1″-H), 2.39 (1 H, br dd, *J* 16 and 6, 3′-H^{eq}), 3.44 and 3.48 (each 1 H, d, *J* 18, 1-H$_2$), 5.07 (1 H, m, 4′-H), 5.42 (1 H, br s, 3″-H), 5.58 (1 H, dd, *J* 15 and 10, 18-H), 5.97 (1 H, d, *J* 12, 13-H), 6.14 (1 H, d, *J* 15, 17-H), 6.32 (1 H, br d, *J* 11, 11-H), 6.34 (1 H, t, *J* 12, 14-H), 6.41 (1 H, br d, *J* 11, 8-H), 6.60 (1 H, dd, *J* 15 and 11, 5-H), 6.63 (1 H, br d, *J* 12, 15-H), 6.64 (1 H, dd, *J* 14.5 and 11, 9-H), 6.68 (1 H, d, *J* 15, 6-H), 6.72 (1 H, dd, *J* 14.5 and 11, 10-H) and 7.24 (1 H, br d, *J* 11, 4-H) (Found: M$^+$, 610.439).

Methyl (2*E*,4*E*/*Z*)-3-methylhexa-2,4-dienoate 18

A solution of butyllithium (1.68 mol dm^{-3} in hexane; 18.5 cm^3, 31 mmol) was added to a stirred suspension of ethyltriphenylphosphonium bromide (11.50 g, 31 mmol) in dry THF (50 cm^3) at 0 °C. The mixture was stirred for a further 40 min, after which a solution of the aldehyde **17**[9] (3.84 g, 30 mmol) in dry THF (20 cm^3) was added, and stirring was continued at room temp. for 15 min. After being quenched with saturated aq. NH_4Cl, the mixture was extracted with ether followed by standard work-up to give a residue, which was purified by CC (ether–hexane, 2:8) to afford an isomeric mixture of the *ester* **18** (3.16 g, 75%; 4*E*:4*Z* = 2:3) as an oil, λ_{max}(EtOH)/nm 260; ν_{max}/cm^{-1} 1712 (conj. CO_2Me) and 1640 and 1612 (C=C); δ_H(300 MHz) 1.83 (3 H, d-like, *J* 7, 5-Me), 2.27 (3 H, s-like, 3-Me), 3.70 (6/5 H) and 3.71 (9/5 H) (each s, CO_2Me), 5.69 (2/5 H) and 5.73 (3/5 H) (each br s, 2-H), 5.72 (3/5 H, dq, *J* 12 and 7) and 6.12–6.23 (2/5 H, m) (together 5-H) and 5.91 (3/5 H, br d, *J* 12) and 6.11 (2/5 H, d, *J* 15) (together 4-H) (Found: M$^+$, 140.085. $C_8H_{12}O_2$ requires M, 140.084).

(2*E*,4*E*/*Z*)-3-Methylhexa-2,4-dien-1-ol 19

A solution of the ester **18** (4.00 g, 28.6 mmol) in dry ether (30 cm^3) was added dropwise to a stirred suspension of LAH (0.81 g, 21.3 mmol) in dry ether (100 cm^3) at 0 °C and the mixture was stirred for a further 15 min. The excess of LAH was decomposed by dropwise addition of water. The mixture was extracted with ether followed by standard work-up to provide a residue, which was purified by SCC (ether–hexane, 2:8) to afford an isomeric mixture of the *alcohol* **19** (2.94 g, 92%; 4*E*:4*Z* = 2:3) as an oil, ν_{max}/cm^{-1} 3630 and 3460 (OH); δ_H(300 MHz) 1.68 (1 H, br s, OH), 1.77 (9/5 H) and 1.82 (6/5 H) (each s, 3-Me), 1.81 (9/5 H, d, *J* 7.2) and 1.81 (6/5 H, d, *J* 6.7) (together 5-Me), 4.25 (2 H, d, *J* 6.5, 1-H$_2$), 5.51 (3/5 H, dq, *J* 12 and 7.2) and 5.72 (2/5 H, dq, *J* 15.5 and 6.7) (together 5-H), 5.52–5.58 (1 H, m, 2-H), 5.83 (3/5 H, br d, *J* 12) and 6.09 (2/5 H, dd-like, *J* 15.5 and 1) (together 4-H) (Found: M$^+$, 112.090. $C_7H_{12}O$ requires M, 112.089).

Preparation of the phosphonium salt 16

A solution of the alcohol **19** (2.94 g, 26.3 mmol) and triphenylphosphine hydrobromide (9.01 g, 26.3 mmol) in methanol (100 cm^3) was stirred at room temp. for 48 h. Evaporation of the methanol gave a residue, which was washed with ether to provide crude *phosphonium salt* **16** (10.69 g, 93%) as a foam, δ_H(200 MHz) 1.35 (3 H, d, *J* 4, 3-Me), 1.71 (3 H, m, 5-Me), 4.71 (2 H, dd, *J* 15.5 and 8, 1-H$_2$), 5.21 (1 H, m, 2-H), 5.75 (1 H, m, 5-H), 5.94 (1 H, br d, *J* 15, 4-H) and 7.60–7.90 (15 H, m, ArH).

Preparation of the analogue 7

In the same manner as described for the preparation of the analogue **6**, the Wittig reaction between the phosphonium salt **16** (192 mg, 0.44 mmol) and the aldehyde **14** (56 mg, 0.15 mmol) followed by acetylation gave a residue, which was purified by SCC (ether–hexane, 1:3) to afford an isomeric mixture [47 mg, 64% from **14**; all-*E* (analogue **7**):13*Z* ~1:1]. PHPLC separation [LiChrosorb Si 60 (5 μm) 1.0 × 30 cm; THF–hexane, 4:96] of the mixture in the dark provided the analogue **7** and its 13*Z*-isomer as red solids.

Analogue **7**: λ_{max}(EtOH)/nm 265, 447 and 462sh; λ_{max}(hexane)/nm 262, 420, 443 and 471; ν_{max}(KBr)/cm^{-1} 1730 (OAc), 1659 (conj. CO) and 1607 (C=C); δ_H(500 MHz) 0.93 (3 H, s, 6′-Me^{eq}), 1.03 (3 H, s, 6′-Me^{ax}), 1.48 (3 H, s, 2′-Me), 1.65 (1 H, t, *J* 12, 5′-H^{ax}), 1.74 (1 H, ddd, *J* 12, 3.5 and 2, 5′-H^{eq}), 1.83 (3 H, br d, *J* 7, 18-Me), 1.91 (3 H, s, 16-Me), 1.97 (3 H, s, 3-Me), 1.99 (3 H, s, 12-Me), 2.00 (3 H, s, 7-Me), 2.05 (3 H, s, OAc), 2.18 (1 H, br dd, *J* 16 and 10, 3′-H^{ax}), 2.39 (1 H, br dd, *J* 16 and 6, 3′-H^{eq}), 3.44 and 3.48 (each 1 H, d, *J* 18, 1-H$_2$), 5.07 (1 H, m, 4′-H), 5.77 (1 H, dq, *J* 15.5 and 7, 18-H), 6.09 (1 H, br d, *J* 11, 15-H), 6.16 (1 H, dd-like, *J* 15.5 and 1, 17-H), 6.26 (1 H, br d, *J* 12, 11-H), 6.34 (1 H, d, *J* 15, 13-H), 6.40 (1 H, br d, *J* 11, 8-H), 6.60 (1 H, dd, *J* 15 and 11, 5-H), 6.63 (1 H, dd, *J* 14 and 11, 9-H), 6.66 (1 H, dd, *J* 15 and 11, 14-H), 6.68 (1 H, d, *J* 15, 6-H), 6.74 (1 H, dd, *J* 14 and 12, 10-H) and 7.24 (1 H, dd-like, *J* 11 and 1, 4-H) (Found: M$^+$, 502.343. $C_{34}H_{46}O_3$ requires M, 502.344).

13Z-*Isomer*: λ_{max}(EtOH)/nm 267, 330 and 443; λ_{max}(hexane)/nm 264, 314, 327, 423, 441 and 469; ν_{max}(KBr)/cm^{-1} 1730 (OAc), 1659 (conj. CO) and 1607 (C=C); δ_H(500 MHz) 0.93 (3 H, s, 6′-Me^{eq}), 1.03 (3 H, s, 6′-Me^{ax}), 1.48 (3 H, s, 2′-Me), 1.65 (1 H, t, *J* 12, 5′-H^{ax}), 1.74 (1 H, ddd, *J* 12, 3.5 and 2, 5′-H^{eq}), 1.83 (3 H, br d, *J* 7, 18-Me), 1.89 (3 H, s, 16-Me), 1.97 (3 H, s, 3-Me), 2.00 (3 H, s, 7-Me), 2.05 (3 H, s, OAc), 2.11 (3 H, s, 12-Me), 2.19 (1 H, br dd, *J* 16 and 9.5, 3′-H^{ax}), 2.39 (1 H, br dd, *J* 16 and 6, 3′-H^{eq}), 3.44 and 3.48 (each 1 H, d, *J* 18, 1-H$_2$), 5.07 (1 H, m, 4′-H), 5.80 (1 H, dq, *J* 15.5 and 7, 18-H), 5.96 (1 H, d, *J* 11.5, 13-H), 6.19 (1 H, dd-like, *J* 15.5 and 1.5, 17-H), 6.31 (1 H, br d, *J* 11.5, 11-H), 6.33 (1 H, t, *J* 11.5, 14-H), 6.40 (1 H, br d, *J* 11, 8-H), 6.58 (1 H, br d, *J* 11.5, 15-H), 6.60 (1 H, dd, *J* 15 and 11, 5-H), 6.64 (1 H, dd, *J* 14.5 and 11, 9-H), 6.68 (1 H, d, *J* 15, 6-H), 6.71 (1 H, dd, *J* 14.5 and 11.5, 10-H) and 7.24 (1 H, br d, *J* 11, 4-H) (Found: M$^+$, 502.343).

Methyl (*E*)-4-(*tert*-butyldimethylsiloxy)-3-methylpent-2-enoate 20

A solution of methylmagnesium bromide (0.92 mol dm^{-3} in THF; 94.5 cm^3, 86.9 mmol) was added dropwise to a stirred solution of the formyl ester **17**[9] (10.60 g, 82.8 mmol) in dry THF (50 cm^3) at 0 °C and the mixture was stirred for a further 30 min. After the reaction had been quenched with saturated aq. NH_4Cl, the organics were extracted with ether followed by standard work-up to give a residue, which was purified by SCC (ether–hexane, 2:8) to afford the corresponding alcohol (11.63 g, 98% from **17**) as an oil, ν_{max}/cm^{-1} 3608 and 3482 (OH), 1715 (conj. CO_2Me) and 1655 (C=C); δ_H(300 MHz) 1.32 (3 H, d, *J* 6.5, 5-H$_3$), 2.12 (3 H, d, *J* 1, 3-Me), 3.70 (3 H, s, CO_2Me), 4.27 (1 H, qd, *J* 6.5 and 1, 4-H) and 5.98 (1 H, quint, *J* 1, 2-H).

Subsequently, *tert*-butyldimethylsilyl trifluoromethanesulfonate (TBSOTf) (20.4 cm^3, 88.8 mmol) was added to a stirred solution of this alcohol (11.63 g, 80.8 mmol) and 2,4,6-

trimethylpyridine (γ-collidine) (16.0 cm^3, 121 mmol) in dry ether (50 cm^3) at 0 °C. After being stirred at 0 °C for 1.5 h, the reaction mixture was poured into ice–water and extracted with ether. The organic layer was washed successively with aq. 3% HCl, saturated aq. $NaHCO_3$ and brine. Evaporation of the dried extracts provided a residue, which was purified by CC (ether–hexane, 2:8) to yield the *TBS ether* **20** (17.08 g, 80% from **17**) as an oil, ν_{max}/cm^{-1} 1712 (conj. CO_2Me) and 1657 (C=C); δ_H(300 MHz) 0.03 and 0.05 (each 3 H, s, SiMe × 2), 0.90 (9 H, s, Bu^t), 1.24 (3 H, d, *J* 6.5, 5-H_3), 2.10 (3 H, s, 3-Me), 3.70 (3 H, s, CO_2Me), 4.19 (1 H, qd, *J* 6.5 and 1, 4-H) and 5.94 (1 H, *J* 1, 2-H) (Found: M^+, 258.163. $C_{13}H_{26}O_3Si$ requires M, 258.165).

(*E*)-4-(*tert*-Butyldimethylsiloxy)-3-methylpent-2-en-1-ol 21

According to the procedure described for the preparation of the alcohol **19** from the ester **18**, reduction of the ester **20** (4.91 g) with LAH followed by purification by SCC (ether–hexane, 3:7) afforded the *alcohol* **21** (3.63 g, 83%) as an oil, ν_{max}/cm^{-1} 3613 and 3460 (OH); δ_H(300 MHz) 0.02 and 0.05 (each 3 H, s, SiMe × 2), 0.89 (9 H, s, Bu^t), 1.20 (3 H, d, *J* 6.5, 5-H_3), 1.47 (1 H, br s, OH), 1.64 (3 H, br s, 3-Me), 4.18 (2 H, d, *J* 6.5, 1-H_2), 4.18 (1 H, br q, *J* 6.5, 4-H) and 5.60 (1 H, tquint, *J* 6.5 and 1.5, 2-H) [Found: $(M - Me)^+$, 215.146. $C_{11}H_{23}O_2Si$ requires *m*/*z*, 215.147].

Preparation of the phosphonium salt 22

A solution of LiCl (738 mg, 17.4 mmol) in dry dimethylformamide (DMF) (15 cm^3) was added to a stirred mixture of the alcohol **21** (3.63 g, 15.8 mmol) in γ-collidine (2.55 cm^3, 19.0 mmol) at 0 °C and the mixture was stirred at 0 °C for 15 min. To this reaction mixture was added MsCl (1.34 cm^3, 17.3 mmol) and stirring of the mixture was continued at 0 °C for 1 h and at room temp. for 3 h. The mixture was poured into ice–water and extracted with ether. The organic layer was washed successively with aq. 3% HCl, saturated aq. $NaHCO_3$ and brine. Evaporation of the dried extracts provided a residue, which was purified by SCC (ether–hexane, 5:95) to afford the corresponding chloride (3.38 g, 86% from **21**) as an oil, δ_H(300 MHz) 0.02 and 0.05 (each 3 H, s, SiMe × 2), 0.89 (9 H, s, Bu^t), 1.20 (3 H, d, *J* 6.5, CH*Me*), 1.68 (3 H, d, *J* 1.5, =CMe), 4.10 (2 H, d, *J* 8, CH_2Cl), 4.17 (1 H, br q, *J* 6.5, C*H*OTBS) and 5.64 (1 H, tquint, *J* 8 and 1.5, =CH).

Subsequently, triphenylphosphine (4.28 g, 16.3 mmol) and triethylamine (0.1 cm^3) were added to a solution of the above chloride (3.38 g, 13.6 mmol) in $CHCl_3$ (15 cm^3) and the mixture was refluxed for 20 h. Evaporation off of the solvent gave a residue, which was washed with ether to provide the *phosphonium salt* **22** (5.88 g, 73% from **21**) as a solid, δ_H(300 MHz) −0.14 and −0.04 (each 3 H, s, SiMe × 2), 0.74 (9 H, s, Bu^t), 1.08 (3 H, d, *J* 6, CH*Me*), 1.42 (3 H, br d, *J* 3, =CMe), 4.04 (1 H, br quint, *J* 6, C*H*OTBS), 4.53 and 4.71 (each 1 H, td, *J* 15.5 and 7.5, CH_2P), 5.47 (1 H, br q, *J* 7.5, =CH) and 7.65–7.89 (15 H, m, ArH).

(2*E*,4*E*,6*E*,8*E*/*Z*,10*E*)-2,7,11-Trimethyl-12-oxotrideca-2,4,6,8,10-pentaenal 24a and 24b

A solution of NaOMe (1.0 mol dm^{-3} in MeOH; 3.10 cm^3, 3.10 mmol) was added to an ice-cooled solution of the phosphonium salt **22** (1.06 g, 2.08 mmol) and the C_{10}-dialdehyde **23** (200 mg, 1.22 mmol) in CH_2Cl_2 (20 cm^3). After being stirred at room temp. for 30 min, the reaction mixture was diluted with ether. The organic layer was treated by standard work-up to give a residue, which was purified by SCC (acetone–hexane, 15:85) to afford an isomeric mixture of condensed products. This was dissolved in THF (20 cm^3) and a solution of TBAF (1.0 mol dm^{-3} in THF; 2.5 cm^3, 2.5 mmol) was added. After being stirred at room temp. for 3 h, the reaction mixture was diluted with ether. The organic layer was followed by standard work-up to provide a residue, which was purified by SCC (acetone–hexane, 2:8). The resulting hydroxy compound was dissolved in a mixture of ether–hexane (1:1) and shaken with active MnO_2 (4.0 g) at room temp. for 5 h. The mixture was filtered through Celite. Evaporation of the filtrate gave a residue, which was purified by SCC (acetone–hexane, 2:8) and then PHPLC [LiChrosorb CN 60 (7 μm) 1.0 × 25 cm; THF–hexane, 15:85] to afford the all-*E*-oxo pentaenal **24a** (125 mg, 42% from **23**) and the 8*Z*-isomer **24b** (23 mg, 8% from **23**) as yellow solids.

Compound **24a**: λ_{max}(EtOH)/nm 393 and 413; ν_{max}/cm^{-1} 1660 (conj. CO and conj. CHO) and 1606 (C=C); δ_H(500 MHz) 1.91 (3 H, d, *J* 0.5, 2-Me), 1.96 (3 H, d, *J* 1.5, 11-Me), 2.07 (3 H, br s, 7-Me), 2.38 (3 H, s, MeCO), 6.43 (1 H, br d, *J* 11.5, 6-H), 6.67 (1 H, d, *J* 14.5, 8-H), 6.74 (1 H, dd, *J* 14.5 and 10.5, 9-H), 6.79 (1 H, dd, *J* 14.5 and 11.5, 4-H), 6.97 (1 H, br d, *J* 11.5, 3-H), 7.03 (1 H, dd, *J* 14.5 and 11.5, 5-H), 7.14 (1 H, dd-like, *J* 10.5 and 1.5, 10-H) and 9.49 (1 H, s, CHO) (Found: M^+, 244.147. $C_{16}H_{20}O_2$ requires M, 244.146).

Compound **24b**: λ_{max}(EtOH)/nm 231, 288, 389 and 409; ν_{max}/cm^{-1} 1655 (conj. CO and conj. CHO) and 1605 (C=C); δ_H(500 MHz) 1.90 (3 H, br s, 2-Me), 1.93 (3 H, d, *J* 1, 11-Me), 2.18 (3 H, br s, 7-Me), 2.36 (3 H, s, MeCO), 6.34 (1 H, d, *J* 12, 8-H), 6.40 (1 H, br d, *J* 12, 6-H), 6.44 (1 H, t, *J* 12, 9-H), 6.77 (1 H, dd, *J* 14.5 and 11.5, 4-H), 6.98 (1 H, br d, *J* 11.5, 3-H), 7.00 (1 H, dd, *J* 14.5 and 11.5, 5-H), 7.62 (1 H, br d, *J* 12, 10-H) and 9.49 (1 H, s, CHO) (Found: M^+, 244.147).

Preparation of the analogue 8

A solution of NaOMe (1.0 mol dm^{-3} in MeOH; 1.3 cm^3, 1.3 mmol) was added to an ice-cooled solution of the Wittig salt **15**[8] (560 mg, 1.04 mmol) and the aldehyde **24a** (63 mg, 0.26 mmol) in CH_2Cl_2 (10 cm^3). After being stirred at 0 °C for 1.5 h, the reaction mixture was diluted with ether. The organic layer was followed by standard work-up to provide a residue, which was purified by SCC (ether–hexane, 1:3) followed by PLC (ether–hexane, 1:3) to afford an isomeric mixture [82 mg, 74% from **24a**; all-*E* (analogue **8**):13*Z* ~1:1]. PHPLC separation [LiChrosorb Si 60 (5 μm) 1.0 × 25 cm; THF–hexane, 4:96] of the mixture provided the analogue **8** and its 13*Z*-isomer as red solids. *Analogue* **8**: λ_{max}(EtOH)/nm 267, 447 and 460sh; λ_{max}(hexane)/nm 263, 421, 444 and 472; ν_{max}(KBr)/cm^{-1} 1649 (conj. CO) and 1613 (C=C); δ_H(500 MHz) 0.82 and 0.91 (each 3 H, s, 6′-*gem*-Me), 1.59 (3 H, d, *J* 1.5, 2′-Me), 1.92 (3 H, s, 16-Me), 1.94 (3 H, s, 3-Me), 1.99 (6 H, s, 7- and 12-Me), 2.19 (1 H, d, *J* 9.5, 1′-H), 2.37 (3 H, s, MeCO), 5.42 (1 H, br s, 3′-H), 5.56 (1 H, dd, *J* 15.5 and 9.5, 18-H), 6.11 (1 H, d, *J* 15.5, 17-H), 6.13 (1 H, br d, *J* 11.5, 15-H), 6.26 (1 H, br d, *J* 11.5, 11-H), 6.35 (1 H, d, *J* 15, 13-H), 6.40 (1 H, br d, *J* 11.5, 8-H), 6.58 (1 H, dd, *J* 15 and 10.5, 5-H), 6.63 (1 H, dd, *J* 14 and 11.5, 9-H), 6.67 (1 H, dd, *J* 15 and 11.5, 14-H), 6.67 (1 H, d, *J* 15, 6-H), 6.74 (1 H, dd, *J* 14 and 11.5, 10-H) and 7.14 (1 H, dd-like, *J* 10.5 and 1.5, 4-H) (Found: M^+, 430.323. $C_{31}H_{42}O$ requires M, 430.323).

13Z-*Isomer*: λ_{max}(EtOH)/nm 268, 332 and 445; λ_{max}(hexane)/nm 265, 319, 328, 421, 442 and 470; ν_{max}(KBr)/cm^{-1} 1659 and 1649 (split) (conj. CO) and 1609 (C=C); δ_H(500 MHz) 0.83 and 0.91 (each 3 H, s, 6′-*gem*-Me), 1.59 (3 H, d, *J* 1.5, 2′-Me), 1.89 (3 H, d, *J* 1, 16-Me), 1.94 (3 H, s, 3-Me), 1.99 (3 H, s, 7-Me), 2.13 (3 H, s, 12-Me), 2.19 (1 H, br d, *J* 9.5, 1′-H), 2.37 (3 H, s, MeCO), 5.42 (1 H, br s, 3′-H), 5.58 (1 H, dd, *J* 15.5 and 9.5, 18-H), 5.97 (1 H, d, *J* 12, 13-H), 6.14 (1 H, d, *J* 15.5, 17-H), 6.32 (1 H, br d, *J* 11.5, 11-H), 6.34 (1 H, t, *J* 12, 14-H), 6.41 (1 H, br d, *J* 11.5, 8-H), 6.58 (1 H, dd, *J* 15 and 10.5, 5-H), 6.63 (1 H, br d, *J* 12, 15-H), 6.64 (1 H, dd, *J* 14 and 11.5, 9-H), 6.67 (1 H, d, *J* 15, 6-H), 6.72 (1 H, dd, *J* 14 and 11.5, 10-H) and 7.14 (1 H, dd-like, *J* 10.5 and 1, 4-H) (Found: M^+, 430.323).

Preparation of the analogue 9

Following the procedure described for the preparation of the analogue **8**, Wittig reaction between the phosphonium salt **16** (242 mg, 0.55 mmol) and the aldehyde **24a** (54 mg, 0.22 mmol) followed by purification by SCC (ether–hexane, 2:3)

gave an isomeric mixture [62 mg, 87% from **24a**; all-*E* (analogue **9**):13*Z* ~1:1]. PHPLC separation [LiChrosorb Si 60 (5 μm) 1.0 × 30 cm; THF–hexane, 4:96] of the mixture in the dark provided the analogue **9** and its 13*Z*-isomer as red solids. *Analogue* **9**: λ_{max}(EtOH)/nm 265, 447 and 460sh; λ_{max}(hexane)/nm 261, 418, 441 and 469; ν_{max}(KBr)/cm^{-1} 1655 and 1645 (split) (conj. CO) and 1611 (C=C); ν_{max}/cm^{-1} 1647, 1607, 1574 and 1530 (conj. CO and C=C); δ_H(500 MHz) 1.83 (3 H, dd, *J* 7 and 1, 18-Me), 1.91 (3 H, s, 16-Me), 1.94 (3 H, d, *J* 1, 3-Me), 1.99 (6 H, s, 7-Me and 12-Me), 2.37 (3 H, s, MeCO), 5.77 (1 H, dq, *J* 15.5 and 7, 18-H), 6.09 (1 H, br d, *J* 11, 15-H), 6.16 (1 H, dd-like, *J* 15.5 and 1, 17-H), 6.26 (1 H, br d, *J* 12, 11-H), 6.34 (1 H, d, *J* 15, 13-H), 6.39 (1 H, br d, *J* 11.5, 8-H), 6.58 (1 H, dd, *J* 15 and 10.5, 5-H), 6.62 (1 H, dd, *J* 14 and 11.5, 9-H), 6.65 (1 H, dd, *J* 15 and 11, 14-H), 6.66 (1 H, d, *J* 15, 6-H), 6.73 (1 H, dd, *J* 14 and 12, 10-H) and 7.14 (1 H, dd-like, *J* 10.5 and 1, 4-H) (Found: M$^+$, 322.230. Calc. for $C_{23}H_{30}O$: M, 322.230).

13*Z*-*Isomer*: λ_{max}(EtOH)/nm 266, 329 and 442; λ_{max}(hexane)/nm 262, 312, 325, 418, 439 and 468; ν_{max}(KBr)/cm^{-1} 1644 (conj. CO) and 1611 (C=C); δ_H(500 MHz) 1.83 (3 H, dd, *J* 7 and 1, 18-Me), 1.88 (3 H, s, 16-Me), 1.94 (3 H, d, *J* 1, 3-Me), 1.99 (3 H, s, 7-Me), 2.10 (3 H, s, 12-Me), 2.37 (3 H, s, MeCO), 5.80 (1 H, dq, *J* 16 and 7, 18-H), 5.96 (1 H, d, *J* 12, 13-H), 6.19 (1 H, dd-like, *J* 16 and 1, 17-H), 6.30 (1 H, br d, *J* 11, 11-H), 6.33 (1 H, t, *J* 12, 14-H), 6.40 (1 H, br d, *J* 11.5, 8-H), 6.58 (1 H, br d, *J* 12, 15-H), 6.59 (1 H, dd, *J* 15 and 11, 5-H), 6.63 (1 H, dd, *J* 14.5 and 11.5, 9-H), 6.66 (1 H, d, *J* 15, 6-H), 6.71 (1 H, dd, *J* 14.5 and 11, 10-H) and 7.15 (1 H, dd-like, *J* 11 and 1, 4-H) (Found: M$^+$, 322.230).

2-Methyl-3-(trifluoromethylsulfonyloxy)cyclohex-2-enone 26

A suspension of sodium hydride (60% oil dispersion; 1.80 g, 45 mmol) was added to a stirred, dry solution of 2-methylcyclohexane-1,3-dione **25** (3.78 g, 30 mmol) in THF (20 cm^3)–DMF (20 cm^3) at 0 °C. The mixture was stirred at 0 °C for 30 min, after which a solution of Tf_2NPh (11.25 g, 31.5 mmol) in dry THF (50 cm^3) was added dropwise at the same temperature. The mixture was stirred at room temp. for 30 min. After the reaction had been quenched with saturated aq. NH_4Cl, the mixture was extracted with ether. The extracts were followed by standard work-up to give a residue, which was purified by CC (acetone–hexane, 1:3) to provide the *oxo enol triflate* **26** (7.58 g, 98%) as an oil, ν_{max}/cm^{-1} 1680 (conj. CO) and 1414 and 1132 (OSO_2); δ_H(300 MHz) 1.86 (3 H, s, 2-Me), 2.09 (2 H, quint-like, *J* 6.5, 5-H_2), 2.49 (2 H, dd, *J* 6.5 and 7.5, 4-H_2) and 2.75 (2 H, m, 6-H_2); δ_C(75 MHz) 9.19 (CH_3), 20.71, 28.83 and 36.66 (CH_2 × 3), 118.36 (q, *J* 318, CF_3), 128.14 (2-C), 162.11 (3-C) and 197.66 (CO) (Found: M$^+$, 258.016. $C_8H_9F_3O_4S$ requires M, 258.017).

3-(*tert*-Butyldimethylsiloxy)-2-methylcyclohex-1-enyl trifluoromethanesulfonate 27

$NaBH_4$ (380 mg, 10.0 mmol) was added to a stirred solution of the oxo enol triflate **26** (2.58 g, 10.0 mmol) in MeOH (20 cm^3) 0 °C. After being stirred for a further 15 min, the reaction mixture was poured into ice–water. The organics were extracted with ether followed by standard work-up to give the crude alcohol, which was dissolved in CH_2Cl_2 (20 cm^3). To this solution was added triethylamine (1.54 cm^3, 11.0 mmol), 4-(dimethylamino)pyridine (DMAP) (1.34 g, 11.0 mmol) followed by TBSCl (1.58 g, 10.5 mmol). The mixture was stirred at room temp. for 5 h, poured into chilled water and extracted with ether. The extracts were washed successively with aq. 3% HCl, saturated aq. $NaHCO_3$ and brine. Evaporation of the dried extracts gave a residue, which was purified by SCC (ether–hexane, 5:95) to afford the *TBS ether* **27** (2.54 g, 68% from **26**) as an oil, ν_{max}/cm^{-1} 1402 and 1133 (OSO_2); δ_H(200 MHz) 0.09 and 0.10 (each 3 H, s, SiMe × 2), 0.90 (9 H, s, Si^{t}Bu), 1.6–2.0 (6 H, m, 4-, 5- and 6-H_2), 1.79 (3 H, t, *J* 2, 2-Me) and 4.21 (1 H, br t-like, *J* 5, 3-H) (Found: M$^+$, 374.119. $C_{14}H_{25}F_3O_4SSi$ requires M, 374.120).

(*E*)-4-[3′-(*tert*-Butyldimethylsiloxy)-2′-methylcyclohex-1′-enyl]-but-3-en-2-one 28

$PdCl_2(PPh_3)_2$ (273 mg, 0.39 mmol) was added to a solution of the vinyl triflate **27** (4.84 g, 12.9 mmol), methyl vinyl ketone (5.24 cm^3, 64.7 mmol) and triethylamine (6.32 cm^3, 45.2 mmol) in dry DMF (50 cm^3). The mixture was heated and stirred at 75 °C for 7 h. After cooling, the reaction mixture was diluted with ether and washed successively with aq. 3% HCl, saturated aq. $NaHCO_3$ and brine. Evaporation of the dried solution provided a residue, which was purified by SCC (ether–hexane, 1:9) to furnish the *dienone* **28** (3.47 g, 91%) as an oil, λ_{max}(EtOH)/nm 291; ν_{max}/cm^{-1} 1660 (conj. CO) and 1613 and 1585 (C=C); δ_H(200 MHz) 0.11 and 0.13 (each 3 H, s, SiMe × 2), 0.91 (9 H, s, Si^{t}Bu), 1.5–1.9 (4 H, m, 4′- and 5′-H_2), 1.96 (3 H, br s, 2′-Me), 2.1–2.4 (2 H, m, 6′-H_2), 2.30 (3 H, s, MeCO), 4.13 (1 H, br t, *J* 5, 3′-H), 6.15 (1 H, d, *J* 16, 3-H) and 7.66 (1 H, d, *J* 16, 4-H) (Found: M$^+$, 294.202. $C_{17}H_{30}O_2Si$ requires M, 294.202).

Ethyl (2*E*/*Z*,4*E*)-5-[3′-(*tert*-butyldimethylsiloxy)-2′-methylcyclohex-1′-enyl]-3-methylpenta-2,4-dienoate 29

A solution of BuLi (1.71 mol dm^{-3} in hexane; 7.02 cm^3, 12 mmol) was added to a stirred solution of diisopropylamine (1.68 cm^3, 12 mmol) in dry THF (10 cm^3) at −78 °C and the mixture was stirred for a further 30 min. To this LDA solution was added dropwise a solution of ethyl TMSacetate (1.92 g, 12 mmol) in dry THF (15 cm^3). The mixture was stirred for 30 min at −78 °C, after which a solution of the ketone **28** (2.94 g, 10 mmol) in dry THF (15 cm^3) was added dropwise at the same temp. and stirring was continued for a further 15 min. After being quenched with saturated aq. NH_4Cl, the mixture was extracted with ether followed by standard work-up to give a residue, which was purified by SCC (ether–hexane, 5:95) to afford an isomeric mixture of the *trienoate* **29** (3.44 g, 95%; 2*E*:2*Z* = 4:3) as a solid, λ_{max}(EtOH)/nm 310; ν_{max}/cm^{-1} 1700 (conj. CO_2Et) and 1607 (C=C); δ_H(200 MHz) 0.10 and 0.12 (each 3 H, s, SiMe × 2), 0.91 (9 H, s, Si^{t}Bu), 1.28 (3 H, t, *J* 7, OCH_2CH_3), 1.45–1.90 (4 H, m, 4′- and 5′-H_2), 1.90 (3 H, br s, 2′-Me), 2.05–2.38 (2 H, m, 6′-H_2), 2.06 (9/7 H) and 2.35 (12/7 H) (each d, *J* 1, 3-Me), 4.12 (1 H, m, 3′-H), 4.17 (2 H, q, *J* 7, OCH_2CH_3), 5.66 (3/7 H) and 5.80 (4/7 H) (each s, 2-H), 6.26 (4/7 H) and 7.84 (3/7 H) (each d, *J* 16, 4-H) and 7.06 (1 H, d, *J* 16, 5-H) (Found: M$^+$, 364.242. $C_{21}H_{36}O_3Si$ requires M, 364.244).

(2*E*/*Z*,4*E*)-3-Methyl-5-(2′-methyl-3′-oxocyclohex-1′-enyl)penta-2,4-dienal 30

According to the procedure for the preparation of the alcohol **19** from the ester **18**, reduction of the trienoate **29** (750 mg, 2.06 mmol) with LAH produced a crude alcohol, which without purification was dissolved in THF (20 cm^3) and a solution of TBAF (1.0 mol dm^{-3} in THF; 4.3 cm^3, 4.3 mmol) was added. After being stirred at room temp. for 24 h, the reaction mixture was diluted with ether followed by standard work-up to give an oil, which was purified by SCC (acetone–hexane, 2:3) to afford an isomeric mixture of the corresponding diol (375 mg, 87% from **29**; 2*E*:2*Z* = 3:2) as an oil, ν_{max}/cm^{-1} 3606 and 3444 (OH) and 1624 (C=C); δ_H(300 MHz) 1.85 (9/5 H, s) and 1.94 (21/5 H, br s) (2′- and 3-Me), 4.07 (1 H, br s, 3′-H), 4.30 (6/5 H) and 4.32 (4/5 H) (each d, *J* 7, 1-H_2), 5.58 (2/5 H) and 5.70 (3/5 H) (each br t, *J* 7, 2-H) and 6.30 (3/5 H), 6.62 (2/5 H), 6.71 (2/5 H) and 6.64 (3/5 H) (each d, *J* 16, 4- and 5-H).

Subsequently, a solution of the diol (375 mg, 1.80 mmol) in CH_2Cl_2 was shaken with active MnO_2 (7.5 g) at room temp. for 4 h. The mixture was filtered through Celite. Evaporation of the filtrate followed by purification by SCC (MeOH–CH_2Cl_2, 2:98) provided the *oxo trienal* **30** (265 mg, 63% from **29**) as an orange solid, λ_{max}(EtOH)/nm 329; ν_{max}/cm^{-1} 1656 (conj. CO and conj. CHO) and 1599 (C=C); δ_H(300 MHz) 1.98 (3 H, s, 2′-Me), 2.05 (2 H, m, 5′-H_2), 2.19 (6/5 H) and 2.37 (9/5 H) (each s, 3-Me), 2.49 (2 H, m, 4′-H_2), 2.58 (2 H, m, 6′-H_2), 6.03 (2/5 H, d, *J* 7.5)

and 6.09 (3/5 H, d, *J* 8) (together 2-H), 6.71 (3/5 H) and 7.66 (2/5 H) (each d, *J* 16, 4-H), 7.17 (2/5 H) and 7.26 (3/5 H) (each d, *J* 16, 5-H) and 10.18 (3/5 H, d, *J* 8) and 10.22 (2/5 H, d, *J* 7.5) (CHO) (Found: M^+, 204.115. $C_{13}H_{16}O_2$ requires M, 204.115).

(2*E*,4*E*,6*E*/*Z*,8*E*)-2,7-Dimethyl-9-(2′-methyl-3′-oxocyclohex-1′-enyl)nona-2,4,6,8-tetraenal 32a and 32b

In the same manner as described for the preparation of the analogue **8**, Wittig reaction between the phosphonium salt **31**[14] (1.21 g, 2.59 mmol) and the aldehyde **30** (265 mg, 1.30 mmol) followed by purification by SCC (acetone–hexane, 1:4) provided condensed products, which were dissolved in THF (30 cm^3). To this solution were added water (1.5 cm^3) and a solution of toluene-*p*-sulfonic acid (*p*-TsOH) (0.1 mol dm^{-3} in THF; 10 cm^3, 1.0 mmol) and the mixture was stirred at room temp. for 30 min, before being diluted with ether. The organic layer was washed successively with saturated aq. $NaHCO_3$ and brine. Evaporation of the dried solution gave crude products, which without purification were dissolved in CH_3CN (40 cm^3). To this solution was added a solution (10 cm^3) prepared from $PdCl_2(CH_3CN)_2$ (65 mg), triethylamine (0.035 cm^3) and water (6 cm^3) in CH_3CN (50 cm^3) and the mixture was stirred at room temp. for 3 h. The solvent was evaporated off to give a residue, which was purified by SCC (acetone–hexane, 1:3) and then PHPLC [LiChrosorb Si 60 (5 μm) 1.0 × 30 cm; THF–hexane, 13:87] to afford the all-*E*-oxo pentaenal **32a** (265 mg, 76% from **30**) and the 6*Z*-isomer **32b** (47 mg, 13% from **30**) as orange solids. *Compound* **32a**: λ_{max}(EtOH)/nm 395 and 413; ν_{max}/cm^{-1} 1655 (conj. CO and conj. CHO) and 1600 (C=C); δ_H(500 MHz) 1.91 (3 H, d, *J* 1, 2-Me), 1.97 (3 H, t, *J* 1.5, 2′-Me), 2.02 (2 H, quint-like, *J* 6.5, 5′-H_2), 2.08 (3 H, d, *J* 0.5, 7-Me), 2.47 (2 H, dd, *J* 7.5 and 6, 4′-H_2), 2.56 (2 H, br t, *J* 6, 6′-H_2), 6.46 (1 H, br d, *J* 12, 6-H), 6.73 (1 H, d, *J* 16, 8-H), 6.78 (1 H, dd, *J* 14.5 and 11.5, 4-H), 6.91 (1 H, d, *J* 16, 9-H), 6.98 (1 H, br d, *J* 11.5, 3-H), 7.05 (1 H, dd, *J* 14.5 and 12, 5-H) and 9.49 (1 H, s, CHO) (Found: M^+, 270.161. $C_{18}H_{22}O_2$ requires M, 270.162).

Compound **32b**: λ_{max}(EtOH)/nm 238, 295, 389 and 407sh; ν_{max}/cm^{-1} 1655 (conj. CO and conj. CHO) and 1600 (C=C); δ_H(500 MHz) 1.90 (3 H, d, *J* 1, 2-Me), 1.97 (3 H, t, *J* 1.5, 2′-Me), 2.04 (2 H, quint-like, *J* 6.5, 5′-H_2), 2.09 (3 H, s, 7-Me), 2.49 (2 H, dd, *J* 7.5 and 6, 4′-H_2), 2.63 (2 H, br t, *J* 6, 6′-H_2), 6.35 (1 H, br d, *J* 11.5, 6-H), 6.71 (1 H, dd, *J* 14.5 and 11.5, 4-H), 6.92 (1 H, d, *J* 16, 9-H), 6.98 (1 H, br d, *J* 11.5, 3-H), 7.19 (1 H, dd, *J* 14.5 and 11.5, 5-H), 7.26 (1 H, d, *J* 16, 8-H) and 9.48 (1 H, s, CHO) (Found: M^+, 270.162).

Preparation of the analogue 10

In the same manner as described for the preparation of the analogue **8**, Wittig reaction between the phosphonium salt **16** (675 mg, 1.54 mmol) and the aldehyde **32a** (104 mg, 0.39 mmol) followed by purification by SCC (MeOH–CH_2Cl_2, 3:97) furnished an isomeric mixture [83 mg, 62% from **32a**; all-*E* (analogue **10**):9′*Z* ~1:1]. PHPLC separation [LiChrosorb Si 60 (5 μm) 1.0 × 30 cm; THF–hexane, 4:96] of the mixture in the dark provided the analogue **10** and its 9′*Z*-isomer as red solids. *Analogue* **10**: λ_{max}(EtOH)/nm 268, 445 and 460sh; λ_{max}(hexane)/nm 264, 416, 439 and 467; ν_{max}/cm^{-1} 1643, 1600, 1574 and 1532 (conj. CO and C=C); δ_H(500 MHz) 1.82 (3 H, dd, *J* 7 and 1, 14′-Me), 1.91 (3 H, s, 12′-Me), 1.95 (3 H, t, *J* 1, 2-Me), 1.97–2.02 (2 H, m, 5-H_2), 1.98 (3 H, s, 8′-Me), 2.00 (3 H, s, 3′-Me), 2.45 (2 H, dd, *J* 7.5 and 6, 6-H_2), 2.56 (2 H, br t, *J* 6, 4-H_2), 5.76 (1 H, dq, *J* 15.5 and 7, 14′-H), 6.08 (1 H, br d, *J* 11.5, 11′-H), 6.16 (1 H, dd-like, *J* 15.5 and 1, 13′-H), 6.26 (1 H, br d, *J* 11.5, 7′-H), 6.34 (1 H, d, *J* 15, 9′-H), 6.42 (1 H, br d, *J* 11.5, 4′-H), 6.64 (1 H, dd, *J* 14 and 11.5, 5′-H), 6.65 (1 H, dd, *J* 15 and 11.5, 10′-H), 6.72 (1 H, d, *J* 16, 2′-H), 6.73 (1 H, dd, *J* 14 and 11.5, 6′-H) and 6.76 (1 H, d, *J* 16, 1′-H) (Found: M^+, 348.246. $C_{25}H_{32}O$ requires M, 348.245).

9′*Z*-*Isomer*: λ_{max}(EtOH)/nm 269, 332 and 442; λ_{max}(hexane)/nm 265, 314sh, 327, 417sh, 437 and 465; ν_{max}/cm^{-1} 1642, 1600, 1566 and 1532 (conj. CO and C=C); δ_H(500 MHz) 1.83 (3 H, dd, *J* 7 and 1, 14′-Me), 1.88 (3 H, s, 12′-Me), 1.96 (3 H, t, *J* 1.5, 2-Me), 1.97–2.02 (2 H, m, 5-H_2), 2.00 (3 H, s, 3′-Me), 2.10 (3 H, s, 8′-Me), 2.45 (2 H, dd, *J* 7.5 and 6, 6-H_2), 2.56 (2 H, br t, *J* 6, 4-H_2), 5.80 (1 H, dq, *J* 15.5 and 7, 14′-H), 5.96 (1 H, d, *J* 12, 9′-H), 6.19 (1 H, dd-like, *J* 15.5 and 1, 13′-H), 6.30 (1 H, br d, *J* 10.5, 7′-H), 6.33 (1 H, t, *J* 12, 10′-H), 6.43 (1 H, br d, *J* 10.5, 4′-H), 6.57 (1 H, br d, *J* 12, 11′-H), 6.64 (1 H, dd, *J* 14 and 10.5, 5′-H), 6.70 (1 H, dd, *J* 14 and 10.5, 6′-H), 6.73 (1 H, d, *J* 16, 2′-H) and 6.77 (1 H, d, *J* 16, 1′-H) (Found: M^+, 348.246).

Ethyl 2-[2-methoxycyclohex-2-en-(*E*/*Z*)-ylidene]acetate 36a and 36b

A solution of BuLi (1.62 mol dm^{-3} in hexane; 1.62 cm^3, 2.62 mmol) was added to a stirred solution of ethyl (diethoxyphosphoryl)acetate **35** (587 mg, 2.62 mmol) in dry THF (3 cm^3) at 0 °C and the mixture was stirred for a further 30 min. To this mixture was added dropwise a solution of the ketone **34**[16] (110 mg, 0.87 mmol) in dry THF (3 cm^3) at 0 °C, and the mixture was refluxed for 1 h. After cooling, the reaction was quenched with saturated aq. NH_4Cl. The mixture was extracted with ether followed by standard work-up to give an oil, which was purified by SCC (ether–hexane, 1:4) to furnish the *E*-isomer **36a** (53 mg, 31%) and the *Z*-isomer **36b** (61 mg, 36%) as pale yellow oils. *Compound* **36a**: λ_{max}(EtOH)/nm 221 and 285; ν_{max}/cm^{-1} 1700 (conj. CO_2Et) and 1625 and 1610 (C=C); δ_H(200 MHz) 1.28 (3 H, t, *J* 7, OCH_2CH_3), 1.67 (2 H, quint-like, *J* 6.5, 5′-H_2), 2.25 (2 H, q-like, *J* 5, 4′-H_2), 3.01 (2 H, ddd, *J* 6.5, 5 and 1.5, 6′-H_2), 3.58 (3 H, s, OMe), 4.16 (2 H, q, *J* 7, OCH_2CH_3), 5.26 (1 H, t, *J* 5, 3′-H) and 6.19 (1 H, br s, 2-H) (Found: M^+, 196.110. $C_{11}H_{16}O_3$ requires M, 196.110).

Compound **36b**: λ_{max}(EtOH)/nm 210 and 256; ν_{max}/cm^{-1} 1708 (conj. CO_2Et) and 1610 (C=C); δ_H(200 MHz) 1.31 (3 H, t, *J* 7, OCH_2CH_3), 1.73 (2 H, quint, *J* 6, 5′-H_2), 2.24 (2 H, td, *J* 6 and 4, 4′-H_2), 2.37 (2 H, ddd, *J* 6, 4 and 1.5, 6′-H_2), 3.52 (3 H, s, OMe), 4.20 (2 H, q, *J* 7, OCH_2CH_3), 5.02 (1 H, td, *J* 4 and 1.5, 3′-H) and 5.54 (1 H, br s, 2-H) (Found: M^+, 196.110).

Ethyl (*E*)-2-[2,2-dimethoxycyclohexylidene]acetate 38

Following the procedure described for the preparation of the ylidene esters **36ab**, Emmons–Horner reaction between the phosphonate **35** (9.82 g, 43.8 mmol) and the ketone **37**[16] (2.31 g, 14.6 mmol) followed by purification by CC (ether–hexane, 1:4) provided the *E*-ylidene ester **38** (3.16 g, 95%) as an oil, ν_{max}/cm^{-1} 1704 (conj. CO_2Et) and 1652 (C=C); δ_H(200 MHz) 1.29 (3 H, t, *J* 7.5, OCH_2CH_3), 1.53–1.86 (6 H, m, CH_2 × 3), 2.82 (2 H, t-like, *J* 6, CH_2), 3.14 (6 H, s, OMe × 2), 4.17 (2 H, q, *J* 7.5, OCH_2CH_3) and 6.18 (1 H, s, =CH) (Found: M^+, 228.134. $C_{12}H_{20}O_4$ requires M, 228.136).

(*E*)-2-[2,2-Dimethoxycyclohexylidene]ethanol 39

According to the procedure for the preparation of the alcohol **19** from the ester **18**, reduction of the ester **38** (3.00 g, 13.2 mmol) with LAH produced a crude product, which was purified by SCC (acetone–hexane, 35:65) to yield the *alcohol* **39** (2.36 g, 96%) as an oil, ν_{max}/cm^{-1} 3600 and 3400 (OH); δ_H(200 MHz) 1.42–1.80 (6 H, m, CH_2 × 3), 2.16 (3 H, t-like, *J* 6, CH_2 and OH), 3.13 (6 H, s, OMe × 2), 4.24 (2 H, dd, *J* 6.5 and 5, CH_2OH) and 5.94 (1 H, t, *J* 6.5, =CH) (Found: M^+, 186.124. $C_{10}H_{18}O_3$ requires M, 186.126).

Preparation of the phosphonium salts 41 and 42

A solution of LiCl (180 mg, 4.24 mmol) in dry DMF (4 cm^3) was added to a stirred mixture of the alcohol **39** (750 mg, 4.03 mmol) in γ-collidine (0.60 cm^3, 4.46 mmol) at 0 °C and the mixture was stirred at 0 °C for 15 min. To this reaction mixture was added MsCl (0.33 cm^3, 4.26 mmol) and stirring of the mixture was continued for a further 1.5 h. The mixture was poured into ice–water and extracted with ether. The organic layer was washed successively with aq. 3% HCl, saturated aq. $NaHCO_3$

and brine. Evaporation of the dried extracts provided a residue, which was purified by SCC (ether–hexane, 3:97) to afford the chloride **40** (810 mg, 98%) as an oil, δ_H(300 MHz) 1.48–1.80 (6 H, m, CH_2 × 3), 2.22 (2 H, t, *J* 6, CH_2), 3.12 (6 H, s, OMe × 2), 4.13 (2 H, d, *J* 8, CH_2Cl) and 6.03 (1 H, t, *J* 8, =CH).

Subsequently, triphenylphosphine (1.13 g, 5.12 mmol) and triethylamine (0.05 cm^3) were added to a solution of the chloride **40** (810 mg, 3.95 mmol) in $CHCl_3$ (30 cm^3) and the mixture was refluxed for 15 h. Evaporation of the solvent gave a residue, which was washed with ether to give a mixture of the phosphonium salts **41** and **42** (1.77 g; **41**:**42** ~5:1) as a foam, δ_H(200 MHz) (*inter alia*) 3.42 (s, *gem*-OMe) and 3.63 (s, =COMe).

(2*E*,4*E*,6*E*,8*E*)-2,7-Dimethyl-10-[2′-oxocyclohex-(*E*)-ylidene]-deca-2,4,6,8-tetraenal 43

In the same manner as described for the preparation of the oxo pentaenals **32ab**, Wittig reaction between a mixture of the phosphonium salts **41** and **42** (880 mg, ~2 mmol) and the C_{10}-dialdehyde **23** (164 mg, 1.0 mmol) and successive hydrolysis with *p*-TsOH followed by treatment with the palladium complex catalyst gave a crude product. This was purified by SCC (THF–CH_2Cl_2, 5:95) and then PHPLC [LiChrosorb Si 60 (5 μm) 1.0 × 30 cm; THF–hexane, 13:87] to afford the *all*-E-*oxo pentaenal* **43** (220 mg, 81% from **23**) as an orange solid, λ_{max}(EtOH)/nm 403 and 420; ν_{max}/cm^{-1} 1668 (conj. CO and conj. CHO) and 1596 and 1573 (C=C); δ_H(300 MHz) 1.76–1.93 (4 H, m, 4′- and 5′-H_2), 1.90 (3 H, s, 2-Me), 2.04 (3 H, s, 7-Me), 2.48 (2 H, t, *J* 7, 3′-H_2), 2.70 (2 H, br t, *J* 6.5, 6′-H_2), 6.42 (1 H, br d, *J* 11.5, 6-H), 6.59 (1 H, dd, *J* 15 and 11, 9-H), 6.71 (1 H, d, *J* 15, 8-H), 6.78 (1 H, dd, *J* 14.5 and 11.5, 4-H), 6.96 (1 H, br d, *J* 11.5, 3-H), 7.02 (1 H, dd, *J* 14.5 and 11.5, 5-H), 7.20 (1 H, dt, *J* 11 and 2, 10-H) and 9.48 (1 H, s, CHO) (Found: M^+, 270.163. $C_{18}H_{22}O_2$ requires M, 270.162).

Preparation of the analogue 11

In the same manner as described for the preparation of the analogue **8**, Wittig reaction between the phosphonium salt **16** (300 mg, 0.69 mmol) and the aldehyde **43** (54 mg, 0.20 mmol) followed by purification by SCC (ether–hexane, 2:3) gave an isomeric mixture [55 mg, 79% from **43**; all-*E* (analogue **11**):10′*Z* ~1:1]. PHPLC separation [LiChrosorb Si 60 (5 μm) 1.0 × 30 cm; THF–hexane, 4:96] of the mixture in the dark provided the analogue **11** and its 10′*Z*-isomer as red solids. *Analogue* **11**: λ_{max}(EtOH)/nm 270 and 459; λ_{max}(hexane)/nm 267, 425sh, 447 and 475; ν_{max}/cm^{-1} 1661, 1597, 1558 and 1520 (conj. CO and C=C); δ_H(500 MHz) 1.76–1.89 (4 H, m, 4- and 5-H_2), 1.82 (3 H, dd, *J* 7 and 1, 15′-Me), 1.91 (3 H, s, 13′-Me), 1.96 (3 H, s, 4′-Me), 1.98 (3 H, s, 9′-Me), 2.46 (2 H, t, *J* 6.5, 6-H_2), 2.67 (2 H, td, *J* 7 and 2, 3-H_2), 5.76 (1 H, dq, *J* 15.5 and 7, 15′-H), 6.08 (1 H, br d, *J* 11.5, 12′-H), 6.16 (1 H, dd-like, *J* 15.5 and 1, 14′-H), 6.25 (1 H, br d, *J* 11.5, 8′-H), 6.33 (1 H, d, *J* 14.5, 10′-H), 6.39 (1 H, br d, *J* 12, 5′-H), 6.50 (1 H, dd, *J* 15 and 12, 2′-H), 6.61 (1 H, dd, *J* 14.5 and 12, 6′-H), 6.65 (1 H, dd, *J* 14.5 and 11.5, 11′-H), 6.70 (1 H, d, *J* 15, 3′-H), 6.73 (1 H, dd, *J* 14.5 and 11.5, 7′-H) and 7.23 (1 H, dt, *J* 12 and 2, 1′-H) (Found: M^+, 348.244. $C_{25}H_{32}O$ requires M, 348.245).

10′Z-*Isomer*: λ_{max}(EtOH)/nm 272, 336, 447 and 455sh; λ_{max}(hexane)/nm 260sh, 268, 320sh, 333, 425sh, 445 and 475; ν_{max}/cm^{-1} 1660, 1597, 1558 and 1523 (conj. CO and C=C); δ_H(500 MHz) 1.76–1.90 (4 H, m, 4- and 5-H_2), 1.83 (3 H, dd, *J* 7 and 1.5, 15′-Me), 1.88 (3 H, s, 13′-Me), 1.97 (3 H, s, 4′-Me), 2.10 (3 H, s, 9′-Me), 2.46 (2 H, t, *J* 6.5, 6-H_2), 2.67 (2 H, td, *J* 7 and 2, 3-H_2), 5.80 (1 H, dq, *J* 15.5 and 7, 15′-H), 5.95 (1 H, d, *J* 12, 10′-H), 6.19 (1 H, dd-like, *J* 15.5 and 1.5, 14′-H), 6.29 (1 H, br d, *J* 11.5, 8′-H), 6.32 (1 H, t, *J* 12, 11′-H), 6.39 (1 H, br d, *J* 11.5, 5′-H), 6.45 (1 H, dd, *J* 15 and 12, 2′-H), 6.57 (1 H, br d, *J* 12, 12′-H), 6.61 (1 H, dd, *J* 14.5 and 11.5, 6′-H), 6.70 (1 H, d, *J* 15, 3′-H), 6.71 (1 H, dd, *J* 14.5 and 11.5, 7′-H) and 7.23 (1 H, dt, *J* 12 and 2, 1′-H) (Found: M^+, 348.245).

Ethyl (2*E*,4*E*)-5-(5,5-dimethyl-1,3-dioxolan-2-yl)-4-methyl-penta-2,4-dienoate 45

A solution of BuLi (1.63 mol dm^{-3} in hexane; 13.0 cm^3, 21.2 mmol) was added to a stirred solution of the phosphonate **35** (4.65 g, 20.8 mmol) in dry THF (35 cm^3) at 0 °C and the mixture was stirred for a further 30 min. To this mixture was added dropwise a solution of the aldehyde **44**[14] (3.00 g, 16.3 mmol) in dry THF (50 cm^3) at 0 °C and stirring was continued at room temp. for 1 h. After being quenched with saturated aq. NH_4Cl, the mixture was extracted with ether followed by standard work-up to give an oil, which was purified by CC (ether–hexane, 1:3) to furnish the *dienoate* **45** (4.06 g, 98%) as an oil, ν_{max}/cm^{-1} 1707 (conj. CO_2Et) and 1626 (C=C); δ_H(300 MHz) 0.76 and 1.23 (each 3 H, s, *gem*-Me), 1.30 (3 H, t, *J* 7, OCH_2CH_3), 1.88 (3 H, s, 4-Me), 3.53 and 3.67 (each 2 H, d, *J* 11, OCH_2 × 2), 4.21 (2 H, q, *J* 7, OCH_2CH_3), 5.20 (1 H, d, *J* 6, OCHO), 5.86 (1 H, br d, *J* 6, 5-H), 5.95 (1 H, d, *J* 16, 2-H) and 7.30 (1 H, d, *J* 16, 3-H) (Found: M^+, 254.151. $C_{14}H_{22}O_4$ requires M, 254.152).

(2*E*,4*E*)-5-(5,5-Dimethyl-1,3-dioxolan-2-yl)-4-methylpenta-2,4-dienal 46

According to the procedure for the preparation of the alcohol **19** from the ester **18**, reduction of the dienoate **45** (6.71 g, 26.4 mmol) with LAH produced a crude alcohol, which without purification was dissolved in ether–hexane (1:3) and shaken with active MnO_2 (48 g) at room temp. for 6 h. The mixture was filtered through Celite. Evaporation of the filtrate gave a residue, which was purified by SCC (ether–hexane, 1:4) to provide the *dienal* **46** (2.79 g, 50%) as a solid, ν_{max}/cm^{-1} 1681 (conj. CHO) and 1643 and 1608 (C=C); δ_H(300 MHz) 0.77 and 1.24 (each 3 H, s, *gem*-Me), 1.92 (3 H, s, 4-Me), 3.55 and 3.68 (each 2 H, d, *J* 11, OCH_2 × 2), 5.22 (1 H, d, *J* 6, OCHO), 5.97 (1 H, br d, *J* 6, 5-H), 6.23 (1 H, dd, *J* 16 and 7.5, 2-H), 7.11 (1 H, d, *J* 16, 3-H) and 9.60 (1 H, d, *J* 7.5, CHO) (Found: M^+, 210.127. $C_{12}H_{18}O_3$ requires M, 210.125).

(2*E*,4*E*)-3-Methyl-6-[2′-oxocyclopent-(*E*)-ylidene]hexa-2,4-dienal 47

A solution of BuLi (1.63 mol dm^{-3} in hexane; 3.86 cm^3, 6.29 mmol) was added to a stirred solution of diisopropylamine (0.88 cm^3, 6.29 mmol) in dry THF (20 cm^3) at −78 °C and the mixture was stirred for a further 30 min. To this LDA solution was added dropwise a solution of cyclopentanone (480 mg, 5.71 mmol) in dry THF (10 cm^3). The mixture was stirred for 30 min at −78 °C, after which a solution of the aldehyde **46** (1.00 g, 47.6 mmol) in dry THF (20 cm^3) was added dropwise at the same temperature and stirring was continued for a further 45 min. After being quenched with saturated aq. NH_4Cl, the mixture was extracted with ether followed by standard work-up to give a residue, which was purified by SCC (acetone–hexane, 1:4) to afford the adduct (1.24 g, 89%) as an oil, ν_{max}/cm^{-1} 3493 (OH), 1722 (CO) and 1635 (C=C).

Subsequently, acetic anhydride (0.68 cm^3, 7.2 mmol) was added to a stirred solution of this adduct (1.24 g, 4.2 mmol) and DMAP (930 mg, 7.62 mmol) in dry benzene (30 cm^3). The mixture was stirred at room temp. for 1.5 h, after which DBU (0.63 cm^3, 4.2 mmol) was added. After being stirred at room temp. for 2 h, the mixture was diluted with ether and washed successively with aq. 3% HCl, saturated aq. $NaHCO_3$ and brine. Evaporation of the dried solution provided the crude product, which without purification was dissolved in a mixture of acetone (15 cm^3) and THF (40 cm^3). To this solution were added water (5 cm^3) and a solution of *p*-TsOH (0.1 mol dm^{-3} in THF; 10 cm^3, 1.0 mmol) and the mixture was stirred at room temp. for 2.5 h, before being diluted with ether. The organic layer was washed successively with saturated aq. $NaHCO_3$ and brine. Evaporation of the dried solution gave a residue, which was purified by SCC (acetone–hexane, 1:3) to provide the *oxo trienal* **47** (578 mg, 64% from **46**) as a yellow solid, ν_{max}/cm^{-1}

1707 (conj. CO and conj. CHO) and 1634 and 1618 (split) (C=C); δ_H(300 MHz) 2.03 (2 H, quint, *J* 7.5, 4′-H_2), 2.34 (3 H, s, 3-Me), 2.41 (2 H, t, *J* 7.5, 3′-H_2), 2.81 (2 H, td, *J* 7.5 and 2.5, 5′-H_2), 6.06 (1 H, d, *J* 7.5, 2-H), 6.70 (1 H, d, *J* 15, 4-H), 6.82 (1 H, dd, *J* 15 and 11, 5-H), 7.00 (1 H, dt, *J* 11 and 2.5, 6-H) and 10.16 (1 H, d, *J* 7.5, CHO) (Found: M^+, 190.099. $C_{12}H_{14}O_2$ requires M, 190.099).

(2*E*,4*E*,6*E*/*Z*,8*E*)-2,7-Dimethyl-10-[2′-oxocyclopent-(*E*)-ylidene]deca-2,4,6,8-tetraenal 48a and 48b

In the same manner as described for the preparation of the oxo pentaenals **32ab**, Wittig reaction between the phosphonium salt **31**[14] (1.10 g, 2.35 mmol) and the aldehyde **47** (224 mg, 1.78 mmol) followed by acid hydrolysis and then treatment with the palladium complex catalyst gave a crude product, which was purified by SCC (acetone–hexane, 3:7) and then PHPLC [LiChrosorb Si 60 (5 μm) 1.0 × 30 cm; THF–hexane, 13:87] to provide the all-*E*-oxo pentaenal **48a** (130 mg, 43% from **47**) and the 6*Z*-isomer **48b** (26 mg, 9% from **47**) as orange solids. *Compound* **48a**: λ_{max}(EtOH)/nm 296, 401 and 421; ν_{max}/cm^{-1} 1698 (conj. CO), 1665 (conj. CHO) and 1601 and 1557 (C=C); δ_H(300 MHz) 1.90 (3 H, s, 2-Me), 2.00 (2 H, quint, *J* 7.5, 4′-H_2), 2.04 (3 H, s, 7-Me), 2.38 (2 H, t, *J* 7.5, 3′-H_2), 2.78 (2 H, td, *J* 7.5 and 2, 5′-H_2), 6.44 (1 H, br d, *J* 11.5, 6-H), 6.48 (1 H, dd, *J* 15 and 11.5, 9-H), 6.71 (1 H, d, *J* 15, 8-H), 6.79 (1 H, dd, *J* 14.5 and 11.5, 4-H), 6.97 (1 H, dd-like, *J* 11.5 and 1, 3-H), 7.01 (1 H, dt, *J* 11.5 and 2, 10-H), 7.02 (1 H, dd, *J* 14.5 and 11.5, 5-H) and 9.48 (1 H, s, CHO) (Found: M^+, 256.146. $C_{17}H_{20}O_2$ requires M, 256.146).

Compound **48b**: λ_{max}(EtOH)/nm 297, 397 and 416; ν_{max}/cm^{-1} 1699 (conj. CO), 1663 (conj. CHO) and 1603 and 1571 (C=C); δ_H(300 MHz) 1.89 (3 H, s, 2-Me), 2.01 (2 H, quint, *J* 7.5, 4′-H_2), 2.06 (3 H, s, 7-Me), 2.40 (2 H, t, *J* 7.5, 3′-H_2), 2.78 (2 H, td, *J* 7.5 and 2, 5′-H_2), 6.31 (1 H, br d, *J* 12, 6-H), 6.48 (1 H, dd, *J* 15 and 12, 9-H), 6.70 (1 H, dd, *J* 14 and 11.5, 4-H), 6.97 (1 H, br d, *J* 11.5, 3-H), 7.06 (1 H, dt, *J* 12 and 2, 10-H), 7.16 (1 H, dd, *J* 14 and 12, 5-H), 7.25 (1 H, d, *J* 15, 8-H) and 9.49 (1 H, s, CHO) (Found: M^+, 256.147).

Preparation of the analogue 12

Following the procedure described for the preparation of the analogue **8**, Wittig reaction between the phosphonium salt **16** (850 mg, 1.95 mmol) and the aldehyde **48a** (200 mg, 0.78 mmol) followed by purification by SCC (ether–hexane, 2:3) afforded an isomeric mixture [130 mg, 50% from **48a**; all-*E* (analogue **12**):10′*Z* ~1:1]. PHPLC separation [LiChrosorb Si 60 (5 μm) 1.0 × 30 cm; THF–hexane, 5:95] of the mixture in the dark provided the analogue **12** and its 10′*Z*-isomer as red solids.

Analogue **12**: λ_{max}(EtOH)/nm 260sh, 269 and 462; λ_{max}(hexane)/nm 257sh, 266, 425, 449 and 447; ν_{max}/cm^{-1} 1694, 1604, 1571 and 1523 (conj. CO and C=C); δ_H(500 MHz) 1.82 (3 H, br d, *J* 6, 15′-Me), 1.91 (3 H, s, 13′-Me), 1.97 (3 H, s, 4′-Me), 1.98 (3 H, s, 9′-Me), 1.98 (2 H, quint, *J* 7.5, 4-H_2), 2.37 (2 H, t, *J* 7.5, 5-H_2), 2.75 (2 H, td, *J* 7.5 and 2, 3-H_2), 5.76 (1 H, dq, *J* 15.5 and 6, 15′-H), 6.08 (1 H, br d, *J* 11.5, 12′-H), 6.16 (1 H, dd-like, *J* 15.5 and 1.5, 14′-H), 6.25 (1 H, br d, *J* 11.5, 8′-H), 6.33 (1 H, d, *J* 15, 10′-H), 6.34 (1 H, dd, *J* 15 and 12, 2′-H), 6.40 (1 H, br d, *J* 11.5, 5′-H), 6.61 (1 H, dd, *J* 14.5 and 11.5, 6′-H), 6.65 (1 H, dd, *J* 15 and 11.5, 11′-H), 6.70 (1 H, d, *J* 15, 3′-H), 6.73 (1 H, dd, *J* 14.5 and 11.5, 7′-H) and 7.04 (1 H, dt, *J* 12 and 2, 1′-H) (Found: M^+, 334.231. $C_{24}H_{30}O$ requires M, 334.230).

10′*Z*-*Isomer*: λ_{max}(EtOH)/nm 262sh, 271, 337 and 457; λ_{max}(hexane)/nm 257sh, 267, 318, 332, 426, 448 and 477; ν_{max}/cm^{-1} 1695, 1604, 1560 and 1523 (conj. CO and C=C); δ_H(500 MHz) 1.83 (3 H, br d, *J* 6.5, 15′-Me), 1.88 (3 H, s, 13′-Me), 1.97 (3 H, s, 4′-Me), 1.99 (2 H, quint, *J* 7.5, 4-H_2), 2.10 (3 H, s, 9′-Me), 2.38 (2 H, t, *J* 7.5, 5-H_2), 2.76 (2 H, td, *J* 7.5 and 2, 3-H_2), 5.80 (1 H, dq, *J* 15 and 6.5, 15′-H), 5.95 (1 H, br d, *J* 11.5, 10′-H), 6.19 (1 H, dd-like, *J* 15 and 1, 14′-H), 6.30 (1 H, br d, *J* 11.5, 8′-H), 6.33 (1 H, t, *J* 11.5, 11′-H), 6.34 (1 H, dd, *J* 14.5 and 12, 2′-H), 6.41 (1 H, br d, *J* 11.5, 5′-H), 6.58 (1 H, br d, *J* 11.5, 12′-H), 6.61 (1 H, dd, *J* 14.5 and 11.5, 6′-H), 6.71 (1 H, d, *J* 14.5, 3′-H), 6.72 (1 H, dd, *J* 14.5 and 11.5, 7′-H) and 7.04 (1 H, dt, *J* 12 and 2, 1′-H) (Found: M^+, 334.230).

(2*E*,4*E*,6*E*,8*E*,10*E*,12*E*,14*E*)-2,6,11,15-Tetramethyl-16-oxo-heptadeca-2,4,6,8,10,12,14-heptaenal 49

In the same manner as described for the preparation of the oxo pentaenals **32ab**, Wittig reaction between the phosphonium salt **31**[14] (1.03 g, 2.21 mmol) and the aldehyde **24a** (216 mg, 0.89 mmol) followed by acid hydrolysis and successive treatment with the palladium complex catalyst gave a crude product, which was purified by SCC (acetone–hexane, 2:8) and then PHPLC [LiChrosorb CN 60 (7 μm) 2.5 × 30 cm; THF–hexane, 13:87] to provide the *all*-E-*oxo heptaenal* **49** (159 mg, 58% from **24a**) as an orange solid, λ_{max}(EtOH)/nm 264, 420sh, 442 and 467; ν_{max}/cm^{-1} 1721, 1662, 1611 and 1576 (conj. CO, conj. CHO and C=C); δ_H(500 MHz) 1.91 (3 H, s, 2-Me), 1.95 (3 H, d, *J* 1, 15-Me), 2.02 and 2.03 (each 3 H, s, 6- and 11-Me), 2.37 (3 H, s, MeCO), 6.40 (1 H, br d, *J* 10.5, 10-H), 6.46 (1 H, br d, *J* 10, 7-H), 6.64 (1 H, dd, *J* 15 and 8.5, 13-H), 6.68 (1 H, d, *J* 15, 12-H), 6.73 (1 H, dd, *J* 14.5 and 9, 4-H), 6.72–6.80 (3 H, m, 5-, 8- and 9-H), 6.95 (1 H, br d, *J* 9, 3-H), 7.14 (1 H, br d, *J* 8.5, 14-H) and 9.47 (1 H, s, CHO) (Found: M^+, 310.195. $C_{21}H_{26}O_2$ requires M, 310.193).

Preparation of the analogue 13

According to the procedure described for the preparation of the analogue **8**, Wittig reaction between the phosphonium salt **16** (350 mg, 0.80 mmol) and the aldehyde **49** (82 mg, 0.26 mmol) gave a residue, which was purified by SCC (acetone–hexane, 1:3) and then PLC (acetone–hexane, 1:3) to afford an isomeric mixture (92 mg, 90%). PHPLC separation [LiChrosorb Si 60 (5 μm) 1.0 × 30 cm; THF–hexane, 7:93] of the mixture in the dark provided the analogue **10** as a red solid, λ_{max}(EtOH)/nm 292, 446sh, 471 and 494sh; λ_{max}(hexane)/nm 277sh, 289, 340, 357, 443, 470 and 502; ν_{max}/cm^{-1} 1647, 1607, 1584, 1558 and 1515 (conj. CO and C=C); δ_H(500 MHz) 1.83 (3 H, br d, *J* 5.5, 22-Me), 1.91 (3 H, s, 20-Me), 1.94 (3 H, d, *J* 1, 3-Me), 1.99 (3 H) and 2.00 (6 H) (each s, 7-, 12- and 16-Me), 2.37 (3 H, s, MeCO), 5.75 (1 H, dq, *J* 15.5 and 7, 22-H), 6.08 (1 H, br d, *J* 11, 19-H), 6.16 (1 H, dd-like, *J* 15.5 and 1.5, 21-H), 6.23 (1 H, br d, *J* 11.5, 15-H), 6.28 (1 H, br d, *J* 11.5, 11-H), 6.34 (1 H, d, *J* 15, 17-H), 6.38 (1 H, d, *J* 15, 13-H), 6.40 (1 H, br d, *J* 11.5, 8-H), 6.59 (1 H, dd, *J* 15 and 11, 5-H), 6.62 (1 H, dd, *J* 15 and 11, 18-H), 6.64 (1 H, dd, *J* 14 and 11.5, 9-H), 6.66 (1 H, d, *J* 15, 6-H), 6.69 (1 H, dd, *J* 15 and 11.5, 14-H), 6.74 (1 H, dd, *J* 14 and 11.5, 10-H) and 7.14 (1 H, dd-like, *J* 11 and 1, 4-H) (Found: M^+, 388.278. $C_{28}H_{36}O$ requires M, 388.276).

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