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Retinoids and Related Compounds. XI.[1] Synthesis and Stereochemistry of (±)-C_{22}-Acetylenic and Allenic Apocarotenals

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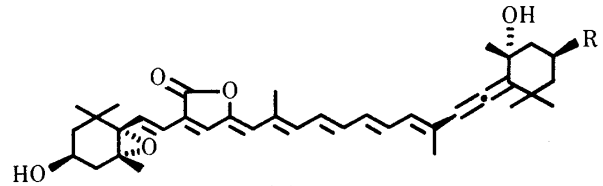
C_{22}-Acetylenic and allenic apocarotenals (**9**, **17**, **31**—**34**) were synthesized by the $C_{15}+C_7 \rightarrow C_{22}$ route. Their stereostructures are discussed.

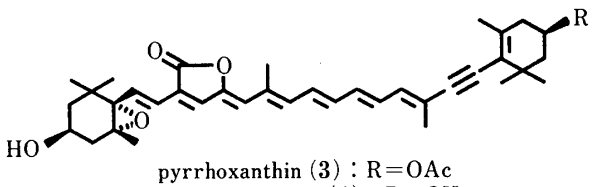
Keywords——C_{37}-norcarotenoid; C_{22}-acetylenic apocarotenal; C_{22}-allenic apocarotenal; Wittig condensation; X-ray crystallographic analysis; Fourier-transform infrared spectrum

The unique C_{37}-tricyclic carotenoid peridinin (**1**)[2] occurs together with carotenoids possessing the ordinary isoprenoid C_{40}-carbon skeleton in dinoflagellates causing "red tide," and functions as an auxiliary light-harvesting pigment for photosynthesis.[3] Other structural variations of **1**, peridininol (**2**), pyrrhoxanthin (**3**), and pyrroxanthinol (**4**) were also isolated in an investigation of the photosynthetic dinoflagellates.[4] These unusual C_{37}-skeletal norcarotenoids contain the ylidenebutenolide structure carrying an allene or an acetylene function.

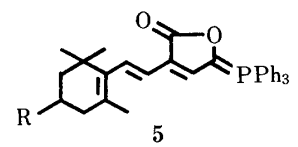
In our previous communication,[5] we reported the first syntheses of carotenoidal ylidenebutenolides *via* a Wittig reaction of the conjugated phosphanylidenebutenolides [a C_{15}-component, (**5**)] with conjugated aldehydes (**6**). Therefore, for the total synthesis of C_{37}-skeletal norcarotenoids, C_{22}-acetylenic and allenic conjugated aldehydes (**7**, **8**) possessing the



peridinin (1) : R=OAc
peridininol (2) : R=OH



pyrrhoxanthin (3) : R=OAc
pyrrhoxanthinol (4) : R=OH



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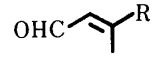
R=H or OH



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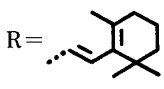
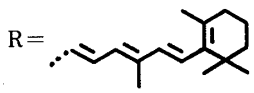
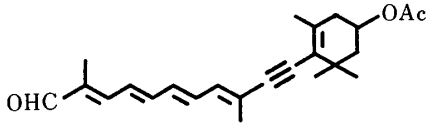


or





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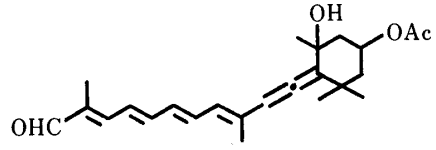

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Chart 1

abnormal arrangement of the in-chain methyl group are required (Chart 1). On the other hand, in order to understand the biological function of prosthetic groups in a variety of light-sensitive retinoidal proteins, geometrical isomers of retinal homologues as well as retinal analogs (C_{20}) are currently required.[6] In this paper, we wish to describe the synthesis and stereochemistry of C_{22}-acetylenic and allenic apocarotenals containing the unusual polyene system.

Synthesis of C_{22}-Acetylenic Apocarotenals

The exceptional stability of (9*Z*)-isomers in the case of carotenoids with a 7,8-triple bond has been noted in the synthesis of alloxanthin and other acetylenes through a Wittig reaction.[7] Previous synthetic studies[8] on the acetylenic carotenoids and related compounds showed that the condensation between the C_{15}-acetylenic phosphonium salt and the conjugated aldehydes was accompanied with stereomutation to give a product with a (9*Z*)-configuration. To avoid isomerization at position 9, the reverse Wittig reaction was successfully conducted.[8] Thus, in our case the C_{22}-acetylenic apocarotenal (**9**) was synthesized *via* a Wittig condensation of the C_{15}-acetylenic aldehyde (**10**) with the C_7-phosphonium salt (**11**) which was derived from methyl (*E*)-β-formylcrotonate (**12**)[9] as follows (Chart 2). After acetalization ($HC(OMe)_3/H^+$) of **12**, the ester group of the resulting acetal was converted to the aldehyde group (**13**) by lithium aluminum hydride (LAH) reduction and subsequent MnO_2 oxidation in 57% yield from **12**. An Emmons–Horner reaction of **13** with diethyl ethoxycarbonylmethylphosphonate in the presence of *n*-butyllithium (*n*-BuLi) gave the

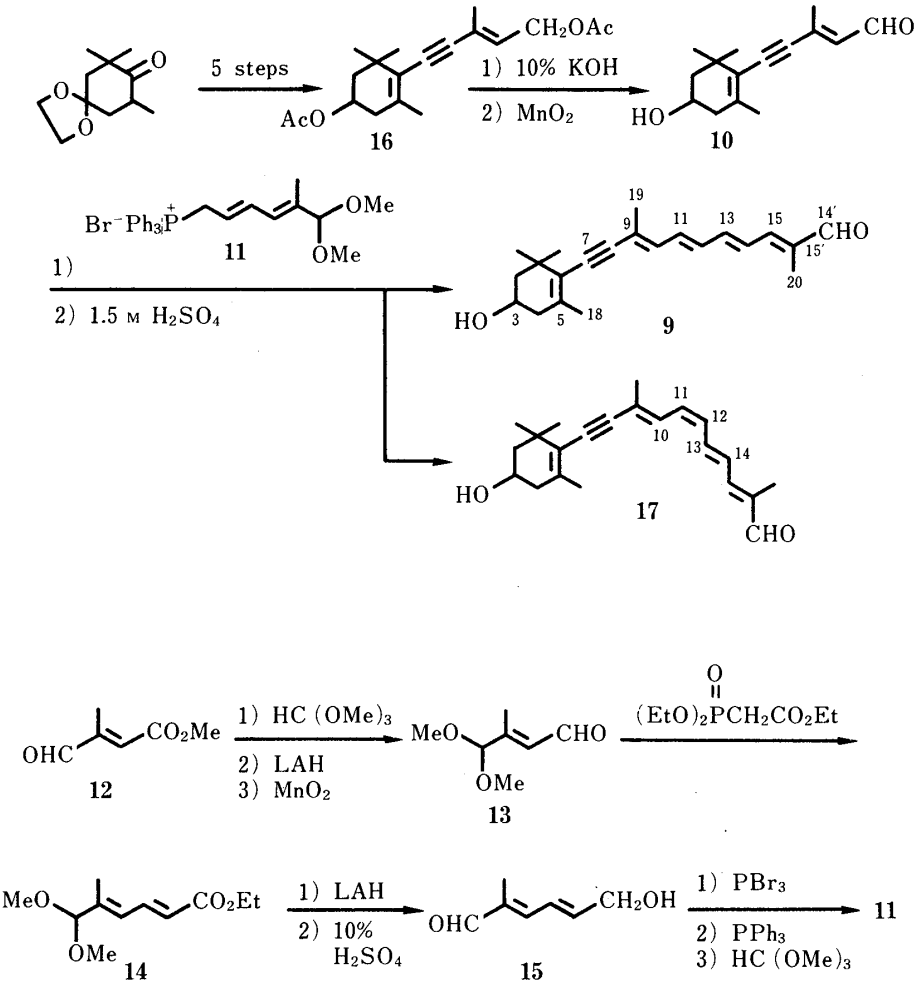


Chart 2

(*E,E*)-acetal ester (**14**), which was reduced with LAH followed by deprotection (10% H_2SO_4) to afford the formyl alcohol (**15**) in 69% yield from **13**. Bromination of **15** with PBr_3 and subsequent treatment of the resulting bromide with PPh_3 gave the phosphonium salt in which the aldehyde group was protected with orthoformate in the presence of an acid catalyst to provide the acetal phosphonium salt (**11**). The aldehyde **10** was derived from the diacetate (**16**)[7] by alkaline hydrolysis and MnO_2 oxidation in 71% yield. Reaction of **10** with the phosphorane (a C_7-component) prepared by treating the Wittig salt (**11**) with sodium methoxide (NaOMe) in methanol gave the condensation products which, after deprotection (1.5 M H_2SO_4) followed by short column chromatography (CC) under reduced pressure, produced a mixture of C_{22}-acetylenic apocarotenals. Separation by preparative high-performance liquid chromatography (pHPLC) in the dark provided the all-(*E*)-isomer (**9**, 39%) and the (11*Z*)-one (**17**, 23%) in a pure form. The stereostructures of two isomers were determined on the basis of the proton and the carbon-13 nuclear magnetic resonance (^{1}H- and ^{13}C-NMR) spectral data. A 200 MHz ^{1}H-NMR spectrum of the faster eluted isomer (**9**) showed no clear separation of the olefinic protons in both $CDCl_3$ and C_6D_6 solutions, whereas that of the other isomer (**17**) exhibited clear resolution in a $CDCl_3$ solution. All olefinic protons of the former (**9**) were clearly assigned as shown in Table I by homonuclear chemical shift correlated 2D spectroscopy at 500 MHz ^{1}H-NMR in a C_6D_6 solution, and an all-(*E*)-configuration was deduced for **9**. Confirmation of a (9*E*)-geometry in **9** was obtained from the chemical shift[10] of 19-C (18.22 ppm) in its ^{13}C-NMR spectrum. Decoupling experiments (200 MHz ^{1}H-NMR) on the latter (**17**) gave an unambiguous assignment of the olefinic protons (Table I), from which a (*Z*)-configuration was assigned to the newly formed 11,12-double bond in **17**. Both 9,10- and 15,15′-double bonds in **17** were determined to be *E* from the respective chemical shifts[10,11] of 19-C (18.03 ppm) in ^{13}C-NMR and 14-H (6.71 ppm) in ^{1}H-NMR. The 13-H signal appears downfield due to the anisotropic effect of the 9,10-double bond and 10-H also resonates at lower field owing to the effect of the 13,14-double bond. The coupling constants (*ca.* 12 Hz) for 2-H_{ax}s in the ^{1}H-NMR spectra of **9** and **17** showed the presence of an equatorial hydroxyl group at C-3.

Synthesis of C_{22}-Allenic Apocarotenals

Chiral allenic synthons (**24′** and **28**) [a C_{15}-component] (Chart 4) were synthesized by Bernhard *et al.*,[12] starting from the optically active acetylenic diacetate (**16**). Compound **24′** is the product of the *cis* addition of diisobutyl aluminum hydride (DIBAL) to the triple bond in the epoxide (**18**), whereas **28** is the compound arising from the *trans* addition of DIBAL to the triple bond in the epoxide (**19**). Thus, the structure of either **24′** or **28** should be reexamined. Therefore, we followed the reaction and determined the stereostructures of the products independently (Charts 3 and 4).

TABLE I. Characteristic Spectral Data for C_{22}-Acetylenic Apocarotenals (**9** and **17**)

		All-(*E*)-isomer (**9**)	(11*Z*)-isomer (**17**)
UV λ_{max}^{EtOH} nm (ε)		398 (55000)	391 (43000), 285 (18000)
^{1}H-NMR δ [a)]	10-H	6.43 (d, J=11.0)	6.87 (d, J=11.5)
(J in Hz)	11-H	6.33 (dd, J=14.0, 11.0)	6.49 (t, J=11.5)
	12-H	6.25 (dd, J=14.0, 11.0)	6.19 (t, J=11.5)
	13-H	6.05 (dd, J=14.7, 11.0)	7.16 (dd, J=14.5, 11.5)
	14-H	6.51 (dd, J=14.7, 11.6)	6.71 (dd, J=14.5, 11.5)
	15-H	6.65 (d, J=11.6)	6.98 (d, J=11.5)
	CHO	9.43 (s)	9.48 (s)
	3-H	3.77 (m)	4.00 (m)

a) 500 MHz, C_6D_6 for **9**; 200 MHz, $CDCl_3$ for **17**.

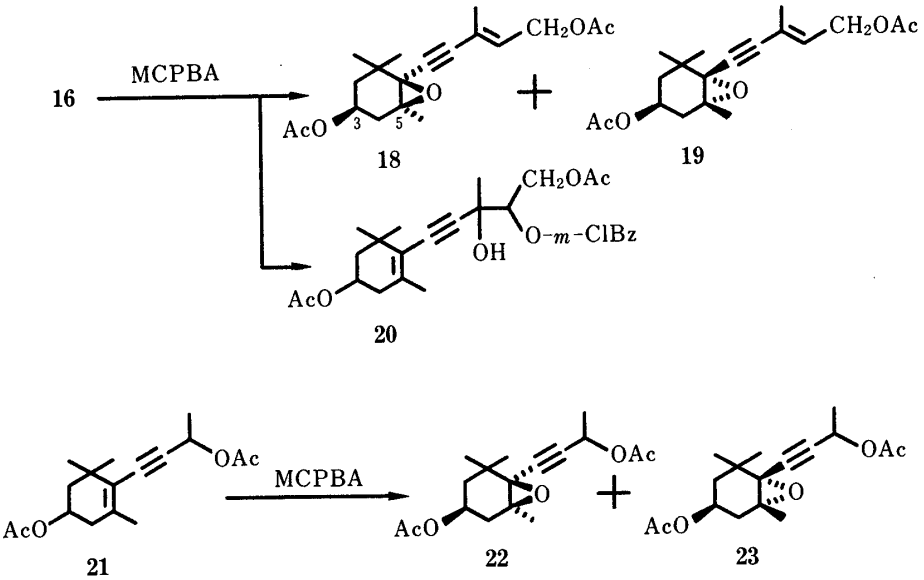


Chart 3

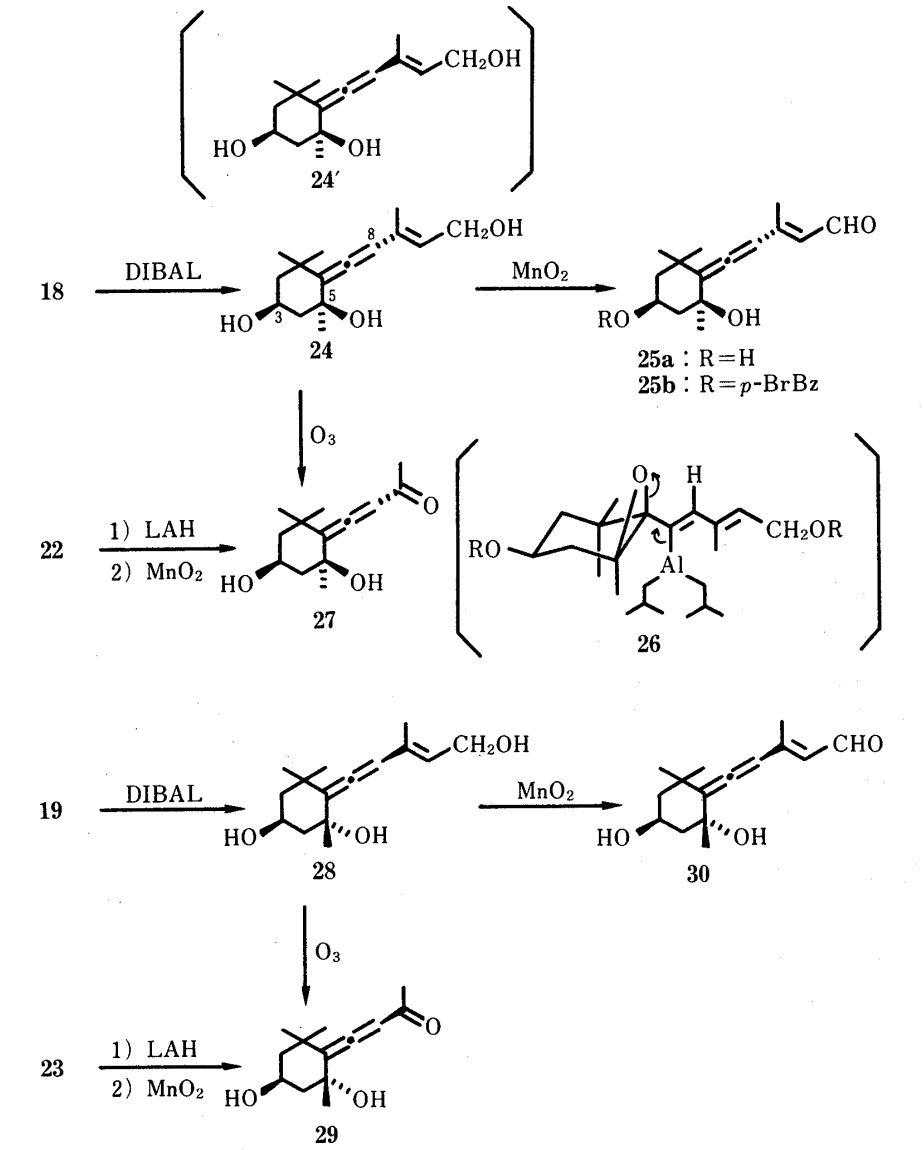
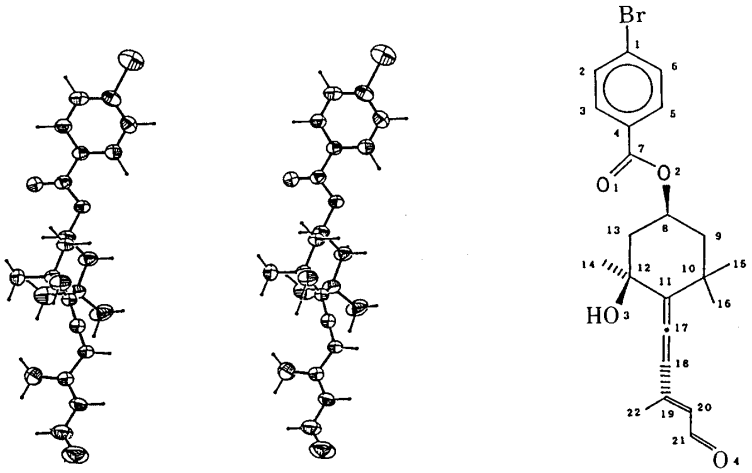


Chart 4

Treatment of **16** with *m*-chloroperbenzoic acid (MCPBA) in dry CH_2Cl_2 led to a mixture of two diastereomeric epoxides [(**18**, 28%) and (**19**, 20%)] and the more polar compound (**20**, 11%), which were separated by means of short CC followed by low-pressure CC. The more strongly adsorbed isomer (**19**) of the two epoxides was assigned as *trans* and the other one (**18**) was decided to be *cis* concerning the relative configuration between acetoxy and epoxy groups, based on a comparison of their ^{1}H-NMR data with those[13] of the epoxidation products (**22** and **23**) of the compound (**21**). The structure of the most polar compound (**20**) was assumed from the spectral data (see Experimental). DIBAL reduction of the *cis* epoxide (**18**) in CH_2Cl_2 gave the allenic triol (**24**) in 77% yield. The structure of **24** was chemically proved by ozonolysis to the dihydroxyallenic ketone (**27**), whose spectral data and chromatographic behavior were identical with those of an authentic specimen (**27**)[13] derived from the epoxide (**22**). Therefore, it was determined that the tertiary hydroxy-group at C-5 of **24** was *cis* to both the hydroxy group at C-3 and the allenic hydrogen at C-8. Thus, in the transformation of **18** to **24**, an organoaluminum intermediate of the type (**26**) is probably involved in the *trans* addition of DIBAL to the triple bond in **18**. Compound **24** was converted by MnO_2 oxidation to the dihydroxyallenic aldehyde (**25a**) in 71% yield. Its stereostructure was established unambiguously by X-ray crystallographic analysis of its *p*-bromobenzoate (**25b**) (see Experimental). The crystal contains two indepedent molecules in an asymmetric unit, and they are very similar to each other in dimensions and conformations. One of the molecular structures of **25b** is depicted in Fig. 1. Decoupling experiments (200 MHz ^{1}H-NMR) on **25a** showed that 3-H was equatorial, based on the coupling constants, $J_{2ax,3}=J_{4ax,3}=4$ Hz. The Fourier-transform infrared (FT-IR) spectrum of **25a** in a diluted solution (4.8×10^{-3} mol in CCl_4) exhibited absorptions due to both free OH at 3623 and 3608 cm^{-1} and intramolecularly hydrogen-bonded OH at 3537 cm^{-1}. Therefore, the hydroxyl groups at the C-3 and C-5 positions in **25a** are in a diaxial orientation. However, it was found from the ^{1}H-NMR analysis and X-ray data that the benzoyloxy group at C-3 in **25b** was equatorial both in $CDCl_3$ solution and in the crystal structure. Treatment of the *trans* epoxide (**19**) with DIBAL under the same conditions as in the case of **18** gave the allenic triol (**28**) in 76% yield; its structure was also chemically confirmed by ozonolysis to the grasshopper ketone (**29**)[13] which was derived from **23**. Thus, the reduction process from **19** to **28** also involves the *trans* addition of DIBAL to the triple bond. Treatment of **28** with MnO_2 afforded the dihydroxyal-



25b

Fig. 1. An ORTEP Stereodrawing of the Molecule of **25b**

The thermal ellipsoid was drawn at the 50% probability level.

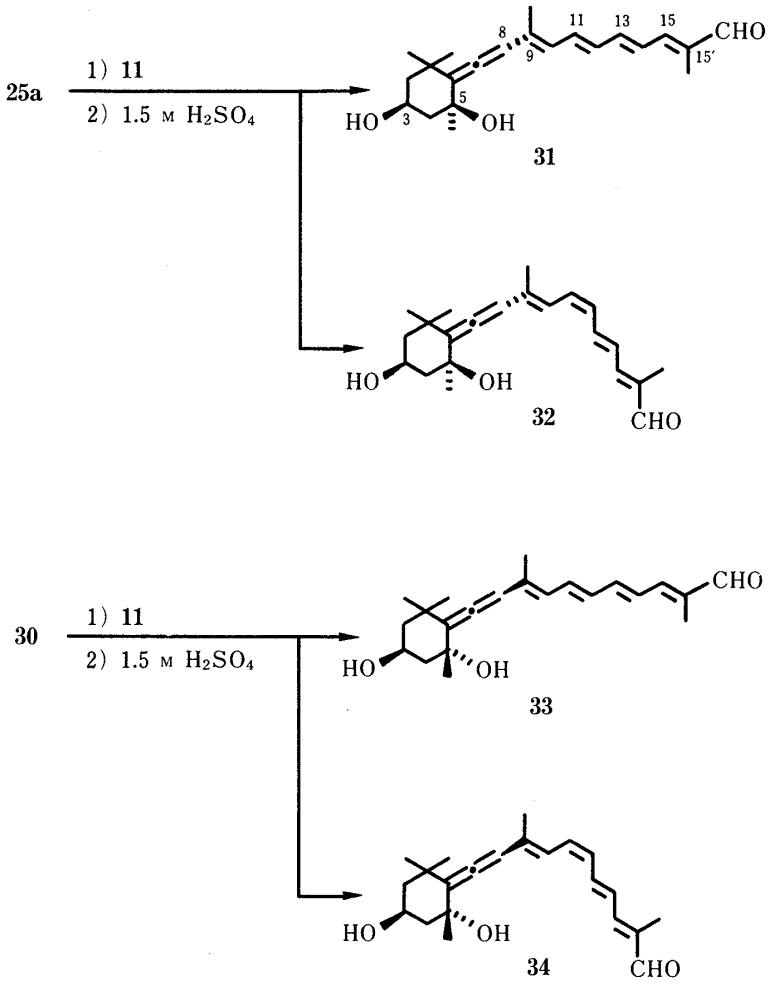


Chart 5

TABLE II. Characteristic Spectral Data for C_{22}-Allenic Apocarotenals (**31** and **32**)

		All-(*E*)-isomer (**31**)	(11*Z*)-isomer (**32**)
UV (nm) (ε)[a]		398 (57000)	394 (49000), 270 (16500), 243 (11000)
IR (cm^{-1})[b]		3600, 3470, 1928, 1659, 1612, 1569	3600, 3460, 1925, 1675, 1660, 1612, 1572
FT-IR (cm^{-1})[c]		3623, 3607, 3543	3623, 3607, 3544
^{1}H-NMR δ[d]	8-H	6.20 (s)	6.24 (s)
	10-H	6.16 (d, J=11.6)	6.59 (d, J=12.2)
	11-H	6.77 (dd, J=14.7, 11.6)	6.54 (dd, J=12.2, 9.8)
	12-H	6.41 (dd, J=14.7, 11.0)	6.21 (dd, J=12.2, 9.8)
	13-H	6.76 (dd, J=14.7, 11.0)	7.20 (dd, J=14.7, 12.2)
	14-H	6.67 (dd, J=14.7, 11.0)	6.71 (dd, J=14.7, 11.6)
	15-H	6.91 (dd-like, J=11.0, 1.2)	6.98 (d, J=11.6)
	CHO	9.47 (s)	9.48 (s)
	3-H	4.19 (br s)	4.20 (br s)

a) In EtOH. *b*) In $CHCl_3$. *c*) In CCl_4 (0.0037 M solution in all cases). *d*) 500 MHz, in $CDCl_3$, J in Hz.

lenic aldehyde (**30**) in 87% yield. The hydroxyl group at C-3 was definitely assigned as equatorial from the coupling constant ($J_{4ax,3}$=11.5 Hz) in the ^{1}H-NMR, and the FT-IR spectrum showed no absorption due to intramolecularly hydrogen-bonded OH.

TABLE III. Characteristic Spectral Data for C_{22}-Allenic Apocarotenals (**33** and **34**)

		All-(*E*)-isomer (**33**)	(11*Z*)-isomer (**34**)
UV (nm) (ε)[a]		398 (52000)	394 (44000), 271 (13000), 245 (9000)
IR (cm^{-1})[b]		3600, 3315, 1927, 1660, 1615, 1570	3600, 3430, 1927, 1676 (sh), 1660, 1612, 1572
^{1}H-NMR δ[c]	8-H	6.03 (s)	6.09 (s)
	10-H	6.11 (d, J=11.5)	6.56 (m)
	11-H	6.77 (dd, J=15, 11.5)	
	12-H	6.39 (dd, J=15, 10.5)	6.22 (dd, J=12, 10)
	13-H	6.77 (dd, J=15, 10.5)	7.19 (dd, J=15, 12)
	14-H	6.64 (dd, J=15, 10.5)	6.69 (dd, J=15, 11)
	15-H	6.91 (d, J=10.5)	6.97 (dd-like, J=11, 1)
	CHO	9.45 (s)	9.48 (s)
	3-H	4.32 (tt, J=11.5, 4)	4.34 (tt, J=11.5, 4)

a) In EtOH. *b*) In $CHCl_3$. *c*) 200 MHz, in $CDCl_3$, J in Hz.

The Wittig condensation of the C_{15}-allenic aldehyde (**25a**) with the C_7-phosphonium salt (**11**) in the presence of NaOMe and subsequent deprotection (1.5 M H_2SO_4) of the products gave a mixture of the all-(*E*)-C_{22}-allenic aldehyde (**31**, 26%) and the (11*Z*)-isomer (**32**, 32%) which was separated by short CC followed by pHPLC in the dark (Chart 5). The structures of both isomers were determined by spectral (ultraviolet (UV), IR, and ^{1}H-NMR) analyses (Table II). Assignments of all olefinic protons of **31** and **32** in the ^{1}H-NMR were accomplished by comparison of their chemical shifts and coupling constants with those[14] of retinal analogs and by means of decoupling experiments (500 MHz ^{1}H-NMR). The underlined values in Table II indicate anomalous chemical shifts. These can be rationalized in terms of the anisotropy of double bonds—10-H due to the 13,14-double bond and 13-H owing to the 9,10-double bond. In addition, it was found from decoupling experiments on **31** and **32** that 3-H was equatorial ($J_{2ax,3}$ = *ca.* 4 Hz and $J_{4ax,3}$ = 3.7 Hz). The FT-IR spectra of both **31** and **32** in a diluted solution exhibited absorptions due to intramolecularly hydrogen-bonded OH at 3543 and 3544 cm^{-1}. Therefore, the hydroxyl groups at the C-3 and C-5 positions are in a diaxial conformation. Reaction of **30** with **11** using NaOMe as a base followed by deprotection (1.5 M H_2SO_4) gave a mixture of all-(*E*)-allenic apocarotenal (**33**, 37%) and the (11*Z*)-isomer (**34**, 39%), which were clearly separated by a combination of short CC and pHPLC in the dark. Spectral data for both isomers are summarized in Table III. Their ^{1}H-NMR data were assigned by analogy with **31** and **32**. The conformation of the hydroxyl group at C-3 in **33** and **34** was determined to be equatorial from the same considerations as in the cases of **30**—**32**. Comparison of chemical shifts of allenic hydrogens of **31**—**34** indicates that β-8-H signals are observed further downfield than the corresponding α-H signals. Using the C_{22}-apocarotenals obtained here, work is in progress on the synthesis of the C_{37}-skeletal norcarotenoids, **1** and **3**.

Experimental

UV spectra were recorded on Shimadzu UV 200S and UV-160 instruments and IR spectra on a Shimadzu IR-27G spectrometer. FT-IR spectra were measured on a Shimadzu FT-IR 4000 spectrometer. ^{1}H-NMR spectra at 60, 200, and 500 MHz were determined on JEOL JNM-PMX 60, Varian XL-200, and JEOL JNM-GX 500 superconducting FT-NMR spectrometers using tetramethylsilane (TMS) as an internal reference. ^{13}C-NMR spectra at 50 MHz were determined on a Varian XL-200 superconducting FT-NMR spectrometer using TMS as an internal standard. Assignments of spectral lines were conducted by use of a DEPT technique. Mass spectra (MS) were

determined on a Hitachi M-80 double-focusing GC mass spectrometer. Short CC was performed on silica gel (Merck Art. 7739) using a short column under reduced pressure and CC was carried out on a silica gel (Merck Art. 7734) under atmospheric pressure. Low-pressure CC was conducted using a Lobar column (LiChroprep Si 60 (Merck)). Preparative thin layer chromatography (TLC) was carried out on silica gel plates (Merck Silica gel $60F_{254}$ precoated plates, 0.25 or 0.5 mm thickness). pHPLC was carried out in the dark on Shimadzu LC-3A, 5A, and 6A instruments with a UV-VIS detector using a column of LiChrosorb Si-60-5 (30 × 1 cm i.d.). Unless otherwise stated, solvent extracts were dried over anhydrous Na_2SO_4 and all operations were carried out under nitrogen or argon. Evaporation of the extract or the filtrate was carried out *in vacuo*. Ether refers to dietyl ether and hexane to *n*-hexane. The acetylenic diacetate (**16**) was prepared in an improved yield by a modification of Weedon's procedure.[7] Methyl (*E*)-*β*-formylcrotonate (**12**) was supplied by Kuraray Co., Ltd.

(2*E*)-4,4-Dimethoxy-3-methylbut-2-enal (13)——A solution of **12** (10.2 g), trimethyl orthoformate (9.9 g), and *p*-toluenesulfonic acid (*p*-TsOH) (250 mg) in methanol (50 ml) was stirred at room temperature for 2 h. The mixture was poured into water and extracted with ether. The extract was washed with saturated aqueous $NaHCO_3$ solution and brine. Evaporation of the dried extract gave the acetal ester (12.3 g, 89%). A solution of this acetal ester (12.3 g) in dry ether (150 ml) was added slowly to a stirred suspension of LAH (2.5 g) in dry ether (150 ml) at 0 °C and stirring was continued for a further 30 min. The excess reagent was decomposed by dropwise addition of water. The mixture was saturated with NaCl and then thoroughly extracted with ether. The extract was dried and evaporated to give the corresponding alcohol (9 g), which was shaken with active MnO_2 (140 g) in CH_2Cl_2 at room temperature for 20 h. The mixture was filtered through Celite. Evaporation of the dried solvent gave an oil which was submitted to CC (ether : hexane = 2 : 1) to afford the acetal aldehyde (**13**, 6.49 g (64% from the acetal ester)) as a colorless oil. bp 74 °C/1 mmHg. UV λ_{max}^{EtOH} nm: 231. IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1675 (conj. CHO), 1625 (C=C). ^{1}H-NMR (60 MHz, $CDCl_3$) δ: 2.13 (3H, s-like, 3-Me), 3.33 (6H, s, 2 × OMe), 4.66 (1H, s, 4-H), 6.11 (1H, br d, J = 8 Hz, 2-H), 10.03 (1H, d, J = 8 Hz, CHO). MS *m/z*: 145.086 ($M^+ + 1$, $C_7H_{12}O_3 + 1$ requires 145.086).

(2*E*,4*E*)-Ethyl 6,6-Dimethoxy-5-methylhexa-2,4-dienoate (14)——A solution (31.7 ml) of *n*-BuLi (10% (w/v) in hexane) was added to a stirred solution of diethyl ethoxycarbonylmethylphosphonate (11.1 g) in dry ether (10 ml) at 0 °C and the mixture was stirred for a further 30 min. A solution of the acetal aldehyde (**13**, 6.49 g) in dry ether (10 ml) was added to the above cooled mixture and stirring was continued at room temperature for 1.5 h. The reaction mixture was poured into water and extracted with ether. The ethereal extracts were washed with brine, dried, and evaporated to give an oil which was purified by CC (ether : hexane = 2 : 3) to afford the acetal diene-ester (**14**, 9.14 g (95%)) as a pale yellow oil. UV λ_{max}^{EtOH} nm: 267. IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1700 (conj. CO_2Et), 1643 and 1615 (C=C). ^{1}H-NMR (60 MHz, $CDCl_3$) δ: 1.30 (3H, t, J = 7 Hz, OCH_2CH_3), 1.87 (3H, br s, 5-Me), 3.28 (6H, s, 2 × OMe), 4.19 (2H, q, J = 7 Hz, OCH_2), 4.60 (1H, s, 6-H), 5.89 (1H, d, J = 15 Hz, 2-H), 6.17 (1H, br d, J = 12 Hz, 4-H), 7.53 (1H, dd, J = 15, 12 Hz, 3-H). MS *m/z*: 214.119 (M^+, $C_{11}H_{18}O_4$ requires 214.120).

(2*E*,4*E*)-6-Hydroxy-2-methylhexa-2,4-dienal (15)——A solution of the preceding acetal diene-ester (**14**, 9.14 g) in dry ether (80 ml) was added slowly to a stirred suspension of LAH (1.62 g) in dry ether (80 ml) at 0 °C and stirring was continued for a further 30 min. The excess reagent was decomposed by dropwise addition of water. The mixture was saturated with NaCl and then thoroughly extracted with ether. The extracts were dried and evaporated to give the corresponding alcohol (7.15 g), which was dissolved in tetrahydrofuran (THF) (150 ml). To this solution was added 10% H_2SO_4 (30 ml). The mixture was stirred at room temperature for 30 min, then a slight excess of saturated aqueous $NaHCO_3$ solution was added. THF was evaporated under reduced pressure. The aqueous phase was saturated with NaCl and then extracted with ether. The extracts were washed with brine, dried, and evaporated to give a residue which was purified by CC (ether : hexane = 3 : 1) to provide the formyl dienol (**15**, 3.93 g (73%)). UV λ_{max}^{EtOH} nm: 275. IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3600 and 3340 (OH), 1672 (conj. CHO), 1635 and 1633 (C=C). ^{1}H-NMR (200 MHz, $CDCl_3$) δ: 1.87 (3H, s, 2-Me), 2.13 (1H, br s, OH), 4.38 (2H, br s, 6-H_2), 6.35 (1H, dt, J = 13, 5 Hz, 5-H), 6.80 (1H, tt-like, J = 13, 1.5 Hz, 4-H), 6.91 (1H, br d, J = 13 Hz, 3-H), 9.46 (1H, s, CHO). MS *m/z*: 126.068 (M^+, $C_7H_{10}O_2$ requires 126.068).

(2*E*)-5-(4-Hydroxy-2,6,6-trimethylcyclohex-1-enyl)-3-methylpent-2-en-4-yn-1-al (10)——The acetylenic diacetate (**16**,[7] 1.33 g) was hydrolyzed according to the literature[7] to give the crude alcohol, which was dissolved in a mixture of ether and hexane. The solution was shaken with active MnO_2 (20 g) at room temperature for 17 h. The mixture was filtered through Celite. Evaporation of the dried filtrate gave a yellow oil which was purified by short CC (ether : hexane = 3 : 1) to afford the C_{15}-acetylenic aldehyde (**10**, 688 mg (71%)). UV λ_{max}^{EtOH} nm: 337, 286. IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3600 and 3350 (OH), 2170 (C≡C), 1660 (conj. CHO), 1588 (C=C). ^{1}H-NMR (60 MHz, $CDCl_3$) δ: 1.13, 1.19 (each 3H, s, gem-Me), 1.92 (3H, s, 5-Me[15]), 2.31 (3H, d, J = 1.5 Hz, 9-Me), 3.97 (1H, m, 3-H), 6.13 (1H, br d, J = 8 Hz, 10-H), 9.92 (1H, d, J = 8 Hz, CHO). MS *m/z*: 232.144 (M^+, $C_{15}H_{20}O_2$ requires 232.146).

C_{22}-Acetylenic Apocarotenals (9 and 17)——PBr_3 (0.6 ml) was added to a stirred solution of the formyl alcohol (**15**, 1.1 g) in dry ether (50 ml) and pyridine (0.7 ml) at −20 °C and stirring was continued for a further 20 min. The mixture was poured into water and extracted with ether. Ethereal extracts were washed with 3% HCl, saturated aqueous $NaHCO_3$ solution, and brine. Evaporation of the dried extracts gave a residue which was purified by short CC (ether : hexane = 1 : 1) to afford the bromide (310 mg). Subsequently, PPh_3 (470 mg) was added to a solution of the above bromide (310 mg) in CH_2Cl_2 (20 ml) and the mixture was refluxed for 2 h. Evaporation of the solvent gave a

crude phosphonium salt which was washed with ether and dissolved in MeOH (5 ml). To this solution were added an acidic solution (0.5 ml) prepared from *p*-TsOH (150 mg) and H_3PO_4 (0.2 ml) in MeOH (50 ml), and methyl orthoformate (0.4 ml). The reaction mixture was stirred at room temperature for 18 h and neutralized with NaOMe until just before the red color of a ylide appeared to give a Wittig salt (**11**) solution, to which a solution of the C_{15}-acetylenic aldehyde (**10**, 280 mg) in CH_2Cl_2 (15 ml) and an NaOMe solution prepared from Na (90 mg) and MeOH (2 ml) were added. The reaction mixture was stirred at room temperature for 20 min, then poured into water and extracted with CH_2Cl_2. Extracts were washed with water and dried. Evaporation of the solvent gave a residue, which was dissolved in acetone (5 ml) and the solution was stirred with 1.5 M H_2SO_4 (0.2 ml) at room temperature for 20 min. The reaction mixture was poured into water and extracted with ether. The ethereal extracts were washed with brine, dried, and evaporated to give a residue which was purified by short CC (acetone : hexane = 1 : 3) to afford an isomeric mixture (319 mg) of acetylenic apocarotenals. pHPLC (isopropanol : ether : hexane = 1 : 35 : 64) separation provided the all-(*E*)-isomer (**9**, 152 mg (39%)) and the (11*Z*)-isomer (**17**, 88 mg (23%)), as orange solids, respectively. The all-(*E*)-C_{22}-acetylenic apocarotenal (**9**). UV: see Table I. IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3610 and 3450 (OH), 2170 (C≡C), 1660 (conj. CHO), 1613 and 1565 (C=C). ^{1}H-NMR (500 MHz, C_6D_6) δ: see Table I, 1.25, 1.36 (each 3H, s, *gem*-Me), 1.41 (1H, t, J = 12.2 Hz, 2_{ax}-H), 1.70 (1H, br d, J = 12.2 Hz, 2_{eq}-H), 1.80 (3H, s, 5-Me), 1.94 (6H, s, 9-Me and 15′-Me), 2.20 (1H, dd, J = 18.0, 5.2 Hz, 4_{eq}-H). ^{13}C-NMR ($CDCl_3$) δ: 9.61 (20-C), 18.22 (19-C), 22.52 (18-C), 28.77, 30.47 (16-C, 17-C), 36.56 (1-C), 41.49 (4-C), 46.59 (2-C), 64.70 (3-C), 91.04 (7-C), 98.08 (8-C), 123.18 (9-C or 6-C), 124.09 (6-C or 9-C), 137.41 (5-C or 15′-C), 138.52 (15′-C or 5-C), 148.34 (15-C), 194.50 (14′-C), 127.78, 132.38, 133.37, 133.91, 141.43 (10-C or 11-C or 12-C or 13-C or 14-C). MS *m/z*: 324.209 (M^+, $C_{22}H_{28}O_2$ requires 324.209). The (11*Z*)-isomer (**17**). UV: see Table I. IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3610 and 3460 (OH), 2160 (C≡C), 1675 and 1660 (split) (conj. CHO), 1610 and 1565 (C=C). ^{1}H-NMR (200 MHz, $CDCl_3$) δ: see Table I; 1.16, 1.22 (each 3H, s, *gem*-Me), 1.46 (1H, t, J = 12 Hz, 2_{ax}-H), 1.85 (1H, ddd, J = 12, 3.5, 2 Hz, 2_{eq}-H), 1.89, 1.95, 2.03 (each 3H, s, 5-Me, 9-Me, 15′-Me), 2.08 (1H, dd, J = 18, 9 Hz, 4_{ax}-H), 2.46 (1H, br dd, J = 18, 5.5 Hz, 4_{eq}-H). ^{13}C-NMR ($CDCl_3$) δ: 9.61 (20-C), 18.03 (19-C), 22.58 (18-C), 28.79, 30.51 (16-C, 17-C), 36.59 (1-C), 41.49 (4-C), 46.61 (2-C), 64.71 (3-C), 90.87 (7-C), 98.02 (8-C), 123.39 (6-C or 9-C), 137.88 (5-C or 15′-C), 138.57 (15′-C or 5-C), 147.84 (9-C or 6-C), 148.24 (15-C), 194.52 (14′-C), 128.54 (2 × C), 128.65, 129.29, 135.95 (10-C or 11-C or 12-C or 13-C or 14-C). MS *m/z*: 324.209 (M^+, $C_{22}H_{28}O_2$ requires 324.209).

Epoxidation of the C_{15}-Acetylenic Diacetate (16)——A solution of MCPBA (1.23 g) in CH_2Cl_2 (10 ml) was added to a cooled solution of the acetylenic diacetate (**16**, 1.25 g) in CH_2Cl_2 (13 ml). The mixture was stirred at 5 °C for 20 h, then poured into an excess of aqueous $NaHCO_3$ solution and extracted with CH_2Cl_2. The extracts were washed with brine, dried, and evaporated to give a light yellow oil which was purified by low-pressure CC (ether : benzene = 1 : 9) to yield the *cis*-epoxide (**18**, 365 mg (28%)), the *trans*-epoxide (**19**, 266 mg (20%)), and the acetylenic *m*-Cl-benzoate (**20**, 260 mg (11%)), each as a colorless oil. Then, the starting material (160 mg (13%)) was recovered. The *cis*-epoxide (**18**). UV λ_{max}^{EtOH} nm: 234. IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1735 (sh) and 1730 (OAc). ^{1}H-NMR (200 MHz, $CDCl_3$) δ: 1.18, 1.23 (each 3H, s, *gem*-Me), 1.41 (1H, ddd, J = 12.5, 4.5, 1.5 Hz, 2_{eq}-H), 1.47 (3H, s, 5-Me), 1.58 (1H, t, J = 12.5 Hz, 2_{ax}-H), 1.84 (1H, dd, J = 15, 9.5 Hz, 4_{ax}-H), 1.87 (3H, s-like, 9-Me), 2.01, 2.07 (each 3H, s, 2 × OAc), 2.35 (1H, ddd, J = 15, 8.5, 1.5 Hz, 4_{eq}-H), 4.68 (2H, dd, J = 7, 0.5 Hz, 11-H_2), 4.91 (1H, m, 3-H), 5.98 (1H, tq, J = 7, 1.5 Hz, 10-H). MS *m/z*: 291.158 (($M^+ - CH_3CO$), $C_{17}H_{23}O_4$ requires 291.160). The *trans*-epoxide (**19**). UV λ_{max}^{EtOH} nm: 234. IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1735 (sh) and 1730 (OAc). ^{1}H-NMR (200 MHz, $CDCl_3$) δ: 1.15, 1.26 (each 3H, s, *gem*-Me), 1.39 (1H, dd, J = 13.5, 8Hz, 2_{ax}-H), 1.50 (3H, s, 5-Me), 1.63 (1H, ddd, J = 13.5, 3.5, 1 Hz, 2_{eq}-H), 1.81 (1H, dd, J = 15, 7 Hz, 4_{ax}-H), 1.88 (3H, s-like, 9-Me), 2.01, 2.07 (each 3H, s, 2 × OAc), 2.40 (1H, ddd, J = 15, 6, 1 Hz, 4_{eq}-H), 4.68 (1H, br d, J = 7 Hz, 11-H_2), 4.91 (1H, m, 3-H), 5.98 (1H, tq, J = 7, 1.5 Hz, 10-H). MS *m/z*: 291.158 (($M^+ - CH_3CO$), $C_{17}H_{23}O_4$ requires 291.160). The acetylenic *m*-Cl-benzoate (**20**). UV λ_{max}^{EtOH} nm: 232. IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3600 and 3440 (OH), 2200 (C≡C), 1724 (OAc). ^{1}H-NMR (200 MHz, $CDCl_3$) δ: 1.13, 1.16 (each 3H, s, *gem*-Me), 1.52 (1H, t, J = 11 Hz, 2_{ax}-H), 1.62 (3H, s, 9-Me), 1.82 (1H, ddd, J = 11, 3.5, 1.5 Hz, 2_{eq}-H), 1.86 (3H, s, 5-Me), 2.01, 2.04 (each 3H, s, 2 × OAc), 2.09 (1H, dd, J = 18, 9 Hz, 4_{ax}-H), 2.47 (1H, br dd, J = 18, 6 Hz, 4_{eq}-H), 4.45 (1H, dd, J = 12, 8.5 Hz, 11-H), 4.74 (1H, dd, J = 12, 3 Hz, 11-H), 5.02 (1H, m, 3-H), 5.47 (1H, dd, J = 8.5, 3 Hz, 10-H), 7.44 (1H, t, J = 7.5 Hz, Ar-H), 7.60 (1H, ddd, J = 7.5, 2, 1 Hz, Ar-H), 8.01 (1H, ddd, J = 7.5, 2, 1 Hz, Ar-H), 8.09 (1H, t, J = 2 Hz, Ar-H). MS *m/z*: 370.137 (($M^+ - 2 \times AcOH$), $C_{22}H_{23}ClO_3$ requires 370.133).

Epoxidation of the C_{13}-Acetylenic Diacetate (21)——In the same manner as described for MCPBA-oxidation of **16**, the acetylenic diacetate (**21**, 250 mg) was treated with MCPBA to give oxidation products, which were purified by preparative TLC (ether : benzene = 3 : 17) to afford the *cis*-epoxide (**22**, 98 mg (37%)) and the *trans*-epoxide (**23**, 39 mg (15%)), respectively. The *cis*-epoxide (**22**). IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1730 (OAc). ^{1}H-NMR (200 MHz, $CDCl_3$) δ: 1.16 (3H, d, J = 2 Hz, *gem*-Me), 1.21 (3H, d, J = 1.5 Hz, *gem*-Me), 1.38 (1H, ddd, J = 12.5, 4.5, 1.5 Hz, 2_{eq}-H), 1.45 (3H, s, 5-Me), 1.49 (3H, d, J = 6.5 Hz, 9-Me), 1.54 (1H, t, J = 12.5 Hz, 2_{ax}-H), 1.81 (1H, dd, J = 15, 10 Hz, 4_{ax}-H), 2.00, 2.06 (each 3H, s, 2 × OAc), 2.32 (1H, ddd, J = 15, 8, 1.5 Hz, 4_{eq}-H), 4.88 (1H, m, 3-H), 5.49 (1H, qd, J = 6.5, 2 Hz, 9-H). The *trans*-epoxide (**23**). IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1730 (OAc). ^{1}H-NMR (200 MHz, $CDCl_3$) δ: 1.13 (3H, d, J = 2 Hz, *gem*-Me), 1.24 (3H, br s, *gem*-Me), 1.40 (1H, dd, J = 13.5, 8 Hz, 2_{ax}-H), 1.48 (3H, s, 5-Me), 1.50 (3H, d, J = 7 Hz, 9-Me), 1.63 (1H, ddd, J = 13.5, 3.5, 1 Hz, 2_{eq}-H), 1.81 (1H, dd, J = 15, 7 Hz, 4_{ax}-H), 2.01, 2.07 (each 3H, s, 2 × OAc), 2.40 (1H, ddd, J = 15, 6, 1 Hz, 4_{eq}-H), 4.89 (1H, m, 3-H), 5.51 (1H, qd, J = 7, 2 Hz, 9-H).

Dihydroxyallenic Ketones (27 and 29)——**22** and **23** were respectively converted to the dihydroxyallenic ketones

(**27** and **29**) according to the literature.[13] The dihydroxyallenic ketone (**27**). UV λ_{max}^{EtOH} nm: 231. IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3600 and 3425 (OH), 1935 (C=C=C), 1670 (conj. C=O). ^{1}H-NMR (200 MHz, $CDCl_3$) δ: 1.19 (3H, s, 1-Me),1.43, 1.44 (each 3H, s, 1-Me and 5-Me), 1.73 (1H, dd, J=14, 4 Hz, 2_{ax}-H), 1.88 (1H, dd, J=14, 4 Hz, 4_{ax}-H), 1.90 (1H, ddd, J=14, 5, 1 Hz, 2_{eq}-H), 2.11 (1H, ddd, J=14, 5, 1 Hz, 4_{eq}-H), 2.19 (3H, s, 9-Me), 3.28 (1H, br d, J=5 Hz, 3-OH), 3.79 (1H, s, 5-OH), 4.27 (1H, m, 3-H), 5.92 (1H, s, 8-H). MS *m/z*: 224.141 (M^+, $C_{13}H_{20}O_3$ requires 224.141). The dihydroxyallenic ketone (**29**). UV λ_{max}^{EtOH} nm: 233. IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3600 and 3325 (OH), 1937 (C=C=C), 1670 (conj. C=O). ^{1}H-NMR (200 MHz, $CDCl_3$) δ: 1.16 (3H, s, 1-Me), 1.37 (1H, dd, J=13, 11.5 Hz, 2_{ax}-H), 1.43 (1H, dd, J=13, 11.5 Hz, 4_{ax}-H), 1.39, 1.43 (each 3H, s, 1-Me and 5-Me), 2.03 (1H, ddd, J=13, 4, 2 Hz, 2_{eq}-H), 2.19 (3H, s, 9-Me), 2.31 (1H, ddd, J=13, 4, 2 Hz, 4_{eq}-H), 4.34 (1H, tt, J=11.5, 4 Hz, 3-H), 5.86 (1H, s, 8-H). MS *m/z*: 224.141 (M^+, $C_{13}H_{20}O_3$ requires 224.141).

(±)-(2*E*,4*S*)-5-((2*S*,4*S*)-2,4-Dihydroxy-2,6,6-trimethylcyclohexylidene)-3-methylpenta-2,4-dien-1-ol (24)——A solution of DIBAL (1.98 g) in dry CH_2Cl_2 (40 ml) was added to a stirred solution of the *cis*-epoxide (**18**, 600 mg) in dry CH_2Cl_2 (40 ml) at 0 °C. The mixture was stirred for a further 1 h. The excess reagent was decomposed by dropwise addition of water. The mixture was saturated with NaCl and then thoroughly extracted with CH_2Cl_2. The extracts were washed with brine, dried, and evaporated to give a residue which was submitted to CC (acetone : hexane = 2 : 3) to provide the allenic triol (**24**, 350 mg (77%)) as a colorless solid. IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3610 and 3450 (OH), 1938 (C=C=C). ^{1}H-NMR (200 MHz, $CDCl_3$) δ: 1.12, 1.29 (each 3H, s, *gem*-Me), 1.38 (3H, s, 5-Me), 1.69 (3H, s, 9-Me), 1.90 (2H, m, 4-H_2), 4.10 (1H, m, 3-H), 4.22 (2H, d, J=7 Hz, 11-H_2), 5.60 (1H, br t, J=7 Hz, 10-H), 6.09 (1H, s, 8-H). MS *m/z*: 234.162 (($M^+ - H_2O$), $C_{15}H_{22}O_2$ requires 234.163).

Ozonolysis of 24——Ozone gas was introduced into a stirred solution of the allenic triol (**24**, 85 mg) in AcOEt (15 ml) at −78 °C until the spot of **24** disappeared on TLC. Nitrogen gas was introduced into the reaction solution for 20 min, and dimethylsulfide (0.05 ml) was added at −78 °C. The mixture was stirred for 30 min at −78 °C and for 1 h at room temperature. Evaporation of the solvent under reduced pressure gave a residue which was purified by preparative TLC (acetone : hexane = 1 : 1) to afford the allenic ketone (**27**, 15 mg (20%)) as a colorless solid. Spectral properties and chromatographic behavior of the product was identical with those of an authentic specimen (**27**) derived from **22**.

(±)-(2*E*,4*S*)-5-((2*S*,4*S*)-2,4-Dihydroxy-2,6,6-trimethylcyclohexylidene)-3-methylpenta-2,4-dien-1-al (25a)——A solution of the allenic triol (**24**, 720 mg) in THF was shaken with active MnO_2 (12 g) at room temperature for 20 h. The mixture was worked up by the same method as described for the preparation of the C_{15}-acetylenic aldehyde (**10**). Evaporation of the solvent gave a residue which was purified by CC (acetone : hexane = 1 : 2) to give the allenic aldehyde (**25a**, 510 mg (71%)). UV λ_{max}^{EtOH} nm: 287. IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3600 and 3410 (OH), 1933 (C=C=C), 1655 (conj. CHO), 1602 (C=C). FT-IR $\nu_{max}^{CCl_4(0.0048M)}$ cm^{-1}: 3623 (*sec*-OH), 3608 (*tert*-OH), 3537 (hydrogen-bonded OH). ^{1}H-NMR (200 MHz, $CDCl_3$) δ: 1.15 (3H, s, 1-Me), 1.40, 1.41 (each 3H, s, 1-Me and 5-Me), 1.72 (1H, dd, J=14, 4 Hz, 2_{ax}-H), 1.87 (1H, dd, J=14, 5 Hz, 2_{eq}-H), 1.89 (1H, dd, J=14, 4 Hz, 4_{ax}-H), 2.07 (1H, dd, J=14, 5 Hz, 4_{eq}-H), 2.16 (3H, d, J=1 Hz, 9-Me), 4.23 (1H, tt, J=5, 4 Hz, 3-H), 5.97 (1H, d, J=8 Hz, 10-H), 6.17 (1H, s, 8-H), 10.03 (1H, d, J=8 Hz, CHO). MS *m/z*: 250.168 (M^+, $C_{15}H_{22}O_3$ requires 250.167).

Preparation of the *p*-Bromobenzoate (25b)——*p*-Bromobenzoyl chloride (165 mg) was added to a stirred solution of the allenic aldehyde (**25a**, 125 mg) and pyridine (0.5 ml) in CH_2Cl_2 (10 ml) at room temperature. The mixture was stirred for 4 h, poured into water, and extracted with ether. The ethereal extract was washed with 3% HCl, saturated aqueous $NaHCO_3$ solution, and brine. Evaporation of the dried extract gave a residue, which was purified by short CC (acetone : hexane = 3 : 7) to afford the *p*-bromobenzoate (**25b**, 202 mg (96%)). Recrystallization (EtOH) of the crude solid yielded light yellow crystals, mp 195—197 °C, this product was used for X-ray analysis. IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3600 (OH), 1934 (C=C=C), 1713 (OCO-*p*-Br-Ph), 1658 (conj. CHO), 1602 and 1593 (C=C). ^{1}H-NMR (200 MHz, $CDCl_3 + CD_3OD$) δ: 1.29 (6H, s, *gem*-Me), 1.56 (3H, s, 5-Me), 1.85 (1H, dd, J=13, 9 Hz, 2_{ax}-H), 1.96 (1H, dd, J=13, 9 Hz, 4_{ax}-H), 2.00 (1H, ddd, J=13, 4.5, 1 Hz, 2_{eq}-H), 2.10 (3H, d, J=1 Hz, 9-Me), 2.26 (1H, ddd, J=13, 4.5, 1 Hz, 4_{eq}-H), 5.33 (1H, tt, J=9, 4.5 Hz, 3-H), 5.97 (1H, d, J=8 Hz, 10-H), 6.29 (1H, s, 8-H), 7.60, 7.61 (each 1H, dd, J=9, 2 Hz, 2 × Ar-H), 7.91, 7.92 (each 1H, dd, J=9, 2 Hz, 2 × Ar-H). *Anal.* Calcd for $C_{22}H_{25}BrO_4$: C, 60.97; H, 5.82. Found: C, 60.69; H, 5.71.

Structural Determination of 25b——(i) Crystal Data: $BrC_{22}H_{25}O_4$ (M_r = 433.3); triclinic, space group, $P\bar{1}$, Z=4, unit cell dimensions; a = 17.627(6) Å, b = 17.458(7) Å, c = 7.600(3) Å, α = 102.60(3)°, β = 77.68(3)°, γ = 107.78(3)°, U = 2146(1) Å^{-3}, D_m = 1.339(5) Mgm^{-3} by flotation with citric acid aqueous solution, D_x = 1.341 Mgm^{-3}, μ = 30.87 cm^{-1} for Cu-K_α radiation.

(ii) X-Ray Crystallgraphic Analysis: A large crystal was cut to the size of 0.30 × 0.30 × 0.41 mm and then used for the collection of X-ray diffraction data. The precise cell parameters were determined by least-squares fit with 25 reflections in the range of 21° < 2θ < 44°, using Cu-K_α radiation monochromated by the use of a graphite plate. The intensities of 7156 reflections were obtained within the maximum 2θ value of 125°, and 5869 reflections gave $F_O > 3\sigma(F_O)$. The structure was solved by the heavy atom method, and refined by the block-diagonal least-squares procedure. All the hydrogen atoms were found on the difference Fourier map. The final R value was 0.054 for 5869 reflections. Atomic coordinates and equivalent isotropic temperature factors are given in Table IV, in which the apostrophe is used to distinguish one of the two molecules in an asymmetric unit.

TABLE IV. Final Atomic Coordinates and Isotropic Temperature Factors with e.s.d.'s in Parentheses of **25b**

Atom	x	y	z	B_{eq}
Br	0.33938 (3)	1.07796 (5)	0.22026 (9)	7.13 (1)
Br′	1.16007 (3)	1.41898 (4)	−0.01919 (8)	7.01 (1)
O1	0.6717 (2)	0.9725 (2)	0.3018 (5)	5.29 (4)
O2	0.7016 (1)	1.1033 (2)	0.4338 (4)	4.01 (3)
O3	0.9758 (2)	1.1602 (2)	0.1574 (4)	4.75 (4)
O4	1.3688 (2)	1.3593 (2)	0.5495 (6)	8.01 (6)
C1	0.4367 (2)	1.0675 (3)	0.2660 (6)	4.36 (5)
C2	0.4505 (2)	0.9916 (3)	0.2156 (6)	4.56 (5)
C3	0.5225 (2)	0.9827 (3)	0.2432 (6)	4.08 (4)
C4	0.5786 (2)	1.0488 (2)	0.3210 (5)	3.41 (4)
C5	0.5622 (2)	1.1247 (3)	0.3723 (6)	4.29 (4)
C6	0.4908 (3)	1.1340 (3)	0.3438 (6)	4.65 (5)
C7	0.6537 (2)	1.0367 (2)	0.3494 (5)	3.66 (4)
C8	0.7797 (2)	1.0980 (2)	0.4588 (5)	3.52 (4)
C9	0.8028 (2)	1.1600 (3)	0.6231 (6)	4.33 (5)
C10	0.8856 (2)	1.1638 (3)	0.6652 (5)	4.15 (5)
C11	0.9476 (2)	1.1717 (2)	0.4891 (5)	3.30 (4)
C12	0.9258 (2)	1.1210 (2)	0.3055 (5)	3.46 (4)
C13	0.8399 (2)	1.1183 (3)	0.2883 (5)	3.69 (4)
C14	0.9361 (3)	1.0354 (3)	0.2802 (7)	4.85 (5)
C15	0.9095 (3)	1.2373 (4)	0.8121 (7)	6.52 (7)
C16	0.8812 (3)	1.0863 (3)	0.7404 (7)	5.92 (7)
C17	1.0196 (2)	1.2214 (2)	0.4923 (5)	3.74 (4)
C18	1.0915 (2)	1.2726 (2)	0.4936 (6)	3.85 (4)
C19	1.1623 (2)	1.2515 (2)	0.5205 (6)	3.88 (4)
C20	1.2326 (2)	1.3114 (3)	0.5213 (6)	4.29 (5)
C21	1.3084 (3)	1.3016 (3)	0.5407 (7)	5.47 (6)
C22	1.1515 (3)	1.1659 (3)	0.5439 (8)	5.74 (7)
O1′	0.8284 (2)	1.5262 (2)	0.4996 (4)	5.05 (4)
O2′	0.7984 (1)	1.3959 (2)	0.5318 (4)	4.08 (3)
O3′	0.5239 (2)	1.3391 (2)	0.4738 (4)	4.57 (3)
O4′	0.1313 (2)	1.1411 (2)	1.0561 (6)	8.12 (5)
C1′	1.0631 (2)	1.4326 (3)	0.1354 (6)	4.32 (5)
C2′	1.0492 (2)	1.5086 (3)	0.1747 (6)	4.55 (5)
C3′	0.9770 (2)	1.5171 (3)	0.2834 (6)	3.99 (4)
C4′	0.9213 (2)	1.4505 (2)	0.3504 (5)	3.29 (4)
C5′	0.9376 (2)	1.3752 (3)	0.3102 (6)	4.24 (4)
C6′	1.0091 (3)	1.3653 (3)	0.2007 (6)	4.57 (5)
C7′	0.8453 (2)	1.4632 (2)	0.4671 (5)	3.57 (4)
C8′	0.7201 (2)	1.4016 (2)	0.6402 (5)	3.53 (4)
C9′	0.6977 (2)	1.3395 (3)	0.7654 (6)	4.25 (5)
C10′	0.6146 (2)	1.3367 (3)	0.8879 (6)	4.23 (5)
C11′	0.5526 (2)	1.3277 (2)	0.7653 (5)	3.35 (4)
C12′	0.5741 (2)	1.3786 (2)	0.6108 (5)	3.44 (4)
C13′	0.6598 (2)	1.3809 (3)	0.5102 (5)	3.73 (4)
C14′	0.5635 (3)	1.4643 (3)	0.6818 (7)	4.80 (5)
C15′	0.6192 (3)	1.4129 (3)	1.0349 (6)	5.96 (7)
C16′	0.5911 (3)	1.2610 (4)	0.9826 (8)	6.57 (7)
C17′	0.4803 (2)	1.2782 (2)	0.7909 (5)	3.77 (4)
C18′	0.4082 (2)	1.2270 (2)	0.8119 (6)	3.83 (4)
C19′	0.3377 (2)	1.2480 (3)	0.9305 (6)	3.97 (4)
C20′	0.2675 (2)	1.1884 (3)	0.9413 (6)	4.40 (5)
C21′	0.1915 (3)	1.1982 (3)	1.0477 (7)	5.51 (6)
C22′	0.3491 (3)	1.3341 (3)	1.0302 (7)	5.96 (6)

$B_{eq} = (4/3) \sum_i \sum_j B_{ij} \boldsymbol{a}_i \cdot \boldsymbol{a}_j$.

(±)-(2*E*,4*R*)-5-((2*R*,4*S*)-2,4-Dihydroxy-2,6,6-trimethylcyclohexylidene)-3-methylpenta-2,4-dien-1-ol (28)——The *trans*-epoxide (**19**, 228 mg) was treated with DIBAL by the same method as described for the preparation of **24** to give the allenic triol (**28**, 131 mg (76%)) as a white solid. UV λ_{max}^{EtOH} nm: 227, 238 (sh). IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3600 and 3430 (OH), 1935 (C=C=C). ^{1}H-NMR (200 MHz, $CDCl_3+CD_3OD$) δ: 1.05 (3H, s, 1-Me), 1.36 (6H, s, 1-Me+5-Me), 1.23—1.41 (2H, m, 2_{ax}-H+4_{ax}-H), 1.67 (3H, s, 9-Me), 1.91 (1H, br d, J=13.5 Hz, 2_{eq}-H), 2.20 (1H, br d, J=13.5 Hz, 4_{eq}-H), 4.22 (2H, d, J=7 Hz, 11-H_2), 4.17—4.32 (1H, m, 3-H), 5.56 (1H, t, J=7 Hz, 10-H), 5.94 (1H, s, 8-H). MS *m/z*: 234.163 ((M^+-H_2O), $C_{15}H_{22}O_2$ requires 234.162).

Ozonolysis of 28——The allenic triol (**28**, 50 mg) was oxidized with ozone gas by the same method as used for the ozonolysis of **24** to give the allenic ketone (**29**, 9 mg (20%)) as a colorless solid. Spectral properties and chromatographic behavior of the product were identical with those of an authentic specimen (**29**) derived from **23**.

(±)-(2*E*,4*R*)-5-((2*R*,4*S*)-2,4-Dihydroxy-2,6,6-trimethylcyclohexylidene)-3-methylpenta-2,4-dien-1-al (30)——MnO_2 oxidation of **28** (150 mg) was carried out by the same method as described for the preparation of **25** to give the allenic aldehyde (**30**, 130 mg (87%)) as a yellow oil. UV λ_{max}^{EtOH} nm: 289. IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3605 and 3410 (OH), 1933 (C=C=C), 1658 (conj. CHO), 1602 (C=C). FT-IR $\nu_{max}^{CCl_4(0.003\,M)}$ cm^{-1}: 3621 (*sec*-OH), 3609 (*tert*-OH). ^{1}H-NMR (200 MHz, $CDCl_3$) δ: 1.10 (3H, s, 1-Me), 1.37, 1.38 (each 3H, s, 1-Me and 5-Me), 1.42 (1H, dd, J=13, 11.5 Hz, 4_{ax}-H), 1.98 (1H, ddd, J=13, 4, 2 Hz, 2_{eq}-H), 2.16 (3H, d, J=1 Hz, 9-Me), 2.29 (1H, ddd, J=13, 4, 2 Hz, 4_{eq}-H), 4.33 (1H, tt, J=11.5, 4 Hz, 3-H), 5.95 (1H, d, J=8 Hz, 10-H), 6.08 (1H, s, 8-H), 10.08 (1H, d, J=8 Hz, CHO). MS *m/z*: 250.156 (M^+, $C_{15}H_{22}O_3$ requires 250.157).

C_{22}-Allenic Apocarotenals (31 and 32)——In a manner similar to that used for the preparation of **9** and **17** from **10**, the allenic aldehyde (**25a**, 380 mg) produced an isomeric mixture of apocarotenals which was purified by pHPLC (isopropanol : *tert*-butyl methyl ether : hexane = 3 : 40 : 57) to give the all-(*E*)-isomer (**31**, 137 mg (26%)) and the (11*Z*)-isomer (**32**, 166 mg (32%)), as orange solids, respectively. The all-(*E*)-isomer (**31**). UV: see Table II. IR: see Table II. FT-IR: see Table II. ^{1}H-NMR (500 MHz, $CDCl_3$) δ: see Table II, 1.15 (3H, s, 1-Me), 1.36, 1.42 (each 3H, s, 1-Me and 5-Me), 1.75 (1H, dd, J=14.0, 4.0 Hz, 2_{ax}-H), 1.81 (1H, dd, J=14.0, 5.8 Hz, 2_{eq}-H), 1.85 (3H, s, 9-Me), 1.89 (3H, d, J=1.2 Hz, 15′-Me), 1.94 (1H, dd, J=13.6, 3.7 Hz, 4_{ax}-H), 2.00 (1H, dd, J=13.6, 5.2 Hz, 4_{eq}-H). MS *m/z*: 342.219 (M^+, $C_{22}H_{30}O_3$ requires 342.219). The (11*Z*)-isomer (**32**). UV: see Table II. IR: see Table II. FT-IR: see Table II. ^{1}H-NMR (500 MHz, $CDCl_3$) δ: see Table II, 1.15 (3H, s, 1-Me), 1.38, 1.43 (each 3H, s, 1-Me and 5-Me), 1.76 (1H, dd, J=13.7, 3.7 Hz, 2_{ax}-H), 1.82 (1H, dd, J=13.7, 6.1 Hz, 2_{eq}-H), 1.85 (3H, s, 9-Me), 1.91 (3H, d, J=1.2 Hz, 15′-Me), 1.95 (1H, dd, J=13.1, 3.7 Hz, 4_{ax}-H), 2.02 (1H, dd, J=13.1, 6.1 Hz, 4_{eq}-H). MS *m/z*: 342.221 (M^+, $C_{22}H_{30}O_3$ requires 342.219).

C_{22}-Allenic Apocarotenals (33 and 34)——In the same manner as described for the preparation of **31** and **32** from **25a**, the allenic aldehyde (**30**, 260 mg) provided an isomeric mixture of the allenic apocarotenals which was purified by pHPLC (isopropanol : THF : hexane = 1 : 35 : 64) to yield the all-(*E*)-isomer (**33**, 130 mg (37%)) and the (11*Z*)-isomer (**34**, 138 mg (39%)), as orange solids, respectively. The all-(*E*)-isomer (**33**). UV: see Table III. IR: see Table III. ^{1}H-NMR (200 MHz, $CDCl_3$) δ: see Table III, 1.06 (3H, s, 1-Me), 1.33, 1.34 (each 3H, s, 1-Me and 5-Me), 1.40 (1H, dd, J=13, 11.5 Hz, 4_{ax}-H), 1.82 (3H, s, 9-Me), 1.87 (3H, d, J=1 Hz, 15′-Me), 1.95 (1H, ddd, J=13, 4, 2 Hz, 2_{eq}-H), 2.29 (1H, ddd, J=13, 4, 2 Hz, 4_{eq}-H). MS *m/z*: 342.217 (M^+, $C_{22}H_{30}O_3$ requires 342.219). The (11*Z*)-isomer (**34**). UV: see Table III. IR: see Table III. ^{1}H-NMR (200 MHz, $CDCl_3$) δ: see Table III, 1.08 (3H, s, 1-Me), 1.34 (1H, dd, J=13, 11.5 Hz, 2_{ax}-H), 1.35, 1.36 (each 3H, s, 1-Me and 5-Me), 1.41 (1H, dd, J=13, 11.5 Hz, 4_{ax}-H), 1.83 (3H, s, 9-Me), 1.89 (3H, d, J=1 Hz, 15′-Me), 1.96 (1H, ddd, J=13, 4, 2 Hz, 2_{eq}-H), 2.28 (1H, ddd, J=13, 4, 2 Hz, 4_{eq}-H). MS *m/z*: 342.219 (M^+, $C_{22}H_{30}O_3$ requires 342.219).

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References and Notes

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