Carotenoids and related polyenes. Part 8.[1] Total synthesis of optically active mytiloxanthin applying the stereoselective rearrangement of tetrasubstituted epoxide †

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Received (in Cambridge, UK) 1st February 2002, Accepted 14th May 2002
First published as an Advance Article on the web 7th June 2002

Biomimetic synthesis of mytiloxanthin **1** was accomplished with stereoselective rearrangement of the tetrasubstituted epoxide **5** as a key reaction. This is the first total synthesis of optically active all-*E* mytiloxanthin **1**.

Introduction

Mytiloxanthin **1**, with a unique cyclopentyl enolic β-diketone group conjugated to a polyene chain, was first isolated from *Mytilus californianus* by Scheer in 1940.[2] Its structure and synthesis of the 9*Z*-isomer were reported by Weedon's group,[3] they developed the new synthetic route to polyene β-diketones using Claisen type condensation between polyene esters and methyl ketones. The absolute configuration was determined by Maoka and Fujiwara in 1996.[4] The cyclopentyl end group of mytiloxanthin **1** is believed[3] to be formed in Nature from the epoxide end group of 5,6-epoxy carotenoids such as halocynthiaxanthin **2** by cleavage of the oxirane ring at the C-5 position and successive ring contraction (a pinacolic rearrangement) (Scheme 1, route *a*).

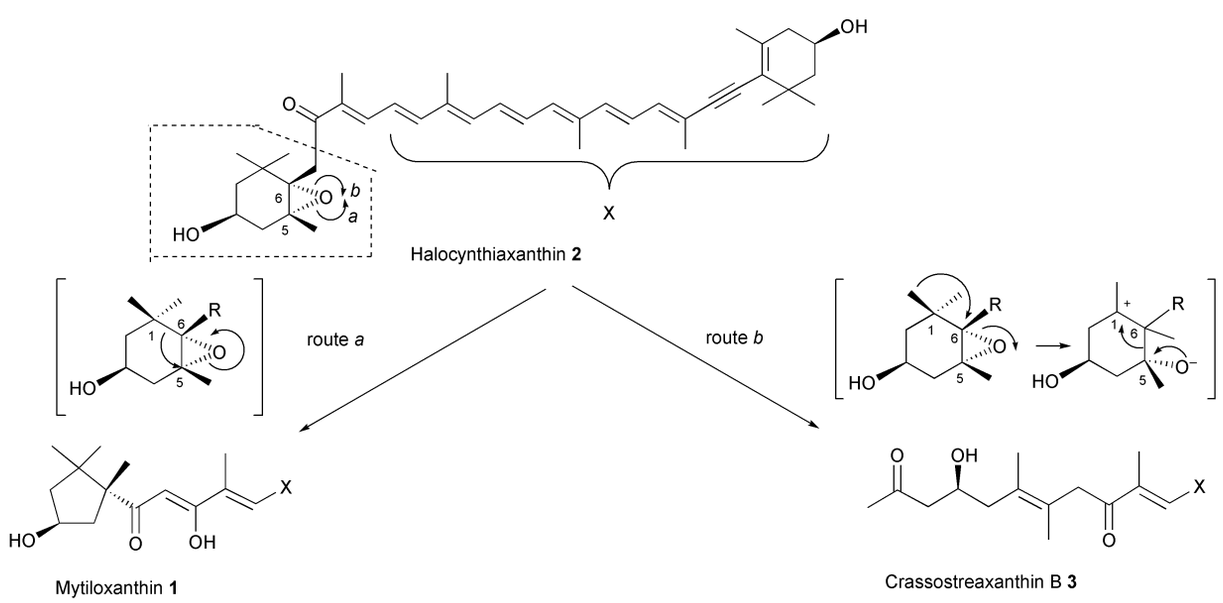
We found[5] that the acyclic-tetrasubstituted olefinic compounds and the cyclopentyl ketone were derived by Lewis acid-promoted stereoselective rearrangement of epoxy compounds. Then, the biomimetic total synthesis[1,6] of crassostreaxanthin B **3** possessing the acyclic-tetrasubstituted olefinic end group was achieved using this rearrangement reaction.

† We have employed the numbering system used in carotenoids.

In a previous communication,[7] we reported the first total synthesis of mytiloxanthin **1** which includes the new construction of conjugated β-diketones **10a**,**b** through the cyclopentyl compound **8** (Scheme 2), prepared by application of the stereoselective rearrangement of epoxide **5**. The present paper is concerned with a full account of the experiments.

Results and discussion

It has been previously reported[5b] that $BF_3{\cdot}OEt_2$-treatment of the epoxide **4** (Scheme 2) with the acetoxy ethyl group at the C-6 position resulted in a very slow reaction and in a low-yield formation of the C-5 diastereomer **6** instead of the desired compound **7**. Efficient preparation of **7** was obtained from the investigation of other Lewis acids with an aminium salt. Thus, treatment of the epoxide **4** with tris(4-bromophenyl)aminium hexachloroantimonate **9**[8] in CH_2Cl_2 was found to afford **7** in reasonable yield (69%) (Scheme 2). In order to accomplish the biomimetic synthesis of **1** in an analogous manner to the successful synthesis of **3**, the acetoxy group at the C-3 position in **4** was replaced by the *tert*-butyldimethylsilyl (TBS) ether leading to epoxide **5**. The synthetic route of mytiloxanthin **1** was therefore planned through conversion of **5** to the cyclopentyl ketone



Scheme 1

DOI: 10.1039/b201228f

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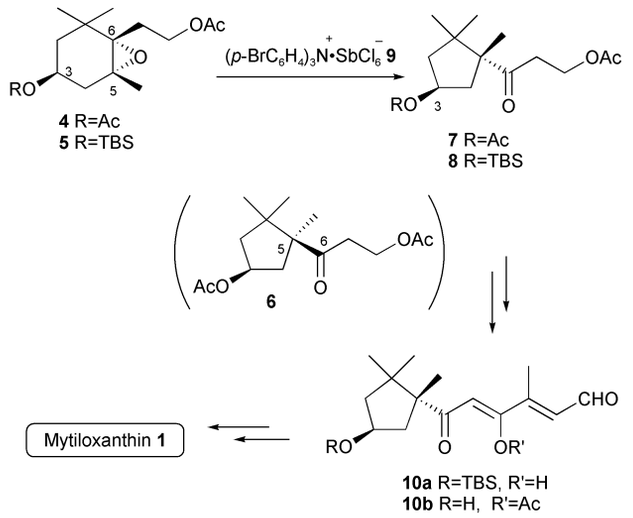


Scheme 2

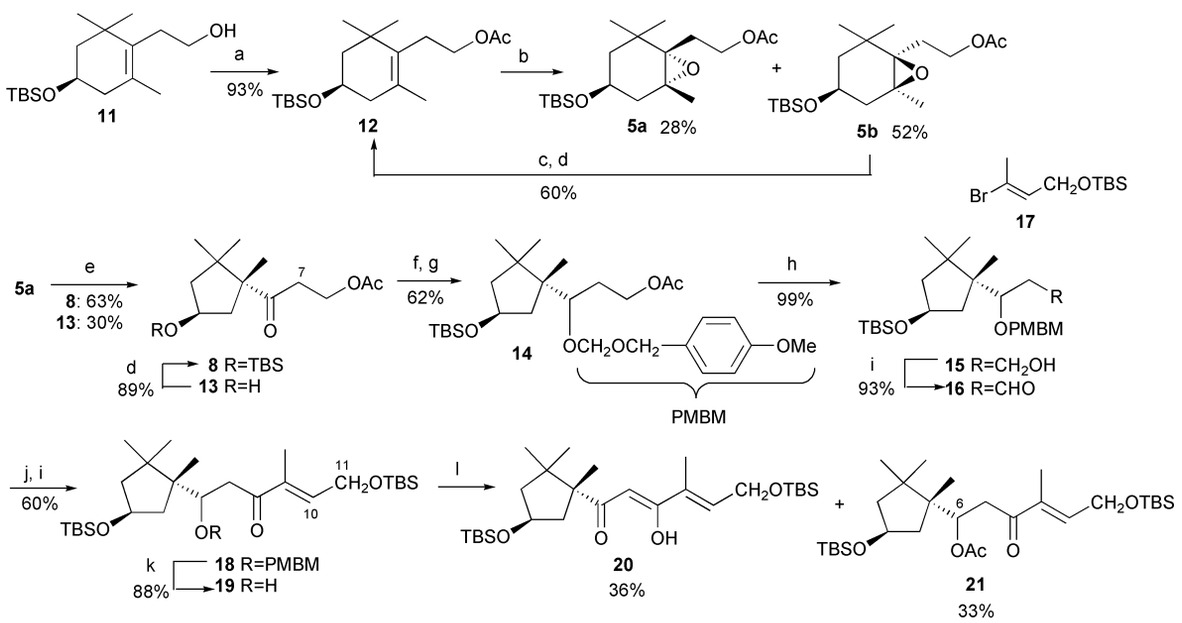
8 and subsequent construction of enolic β-diketone as shown in Scheme 2.

Starting from the previously prepared optically active alcohol[1] **11** (Scheme 3), acetylation followed by epoxidation with MCPBA gave epoxides **5a**,**b** (**5a**: 26% from **11**; **5b**: 48% from **11**), in which the relative configurations between the silyloxy and epoxy groups were confirmed by ^{1}H NMR.[9] The undesired isomer **5b** was returned to the tetrasubstituted olefin **12** by the following deepoxidation procedure. Treatment of **5b** with TMSCl and NaI in dry acetonitrile[10] followed by silylation gave **12** in 60% yield. Reaction of *anti*-epoxide **5a** with aminium salt **9** provided the desired cyclopentyl compound **8** (63%) and its deprotected alcohol **13** (30%) which was easily resilylated to give **8** (89%). Consequently, the cyclopentyl ketone **8** was synthesized by the stereoselective rearrangement of **5a** in high yield. The structure of **8** was determined from the following spectral data. Its IR absorption showed a new carbonyl frequency at 1699 cm^{-1}. In its ^{1}H NMR spectrum, the methylene signal of the C-7 position appeared at δ 2.75 (t), further downfield than the corresponding signal [δ 2.01 (2H, m)] of **5a**, in addition, proton signals on the cyclopentane ring were observed analogous to results reported previously.[5b]

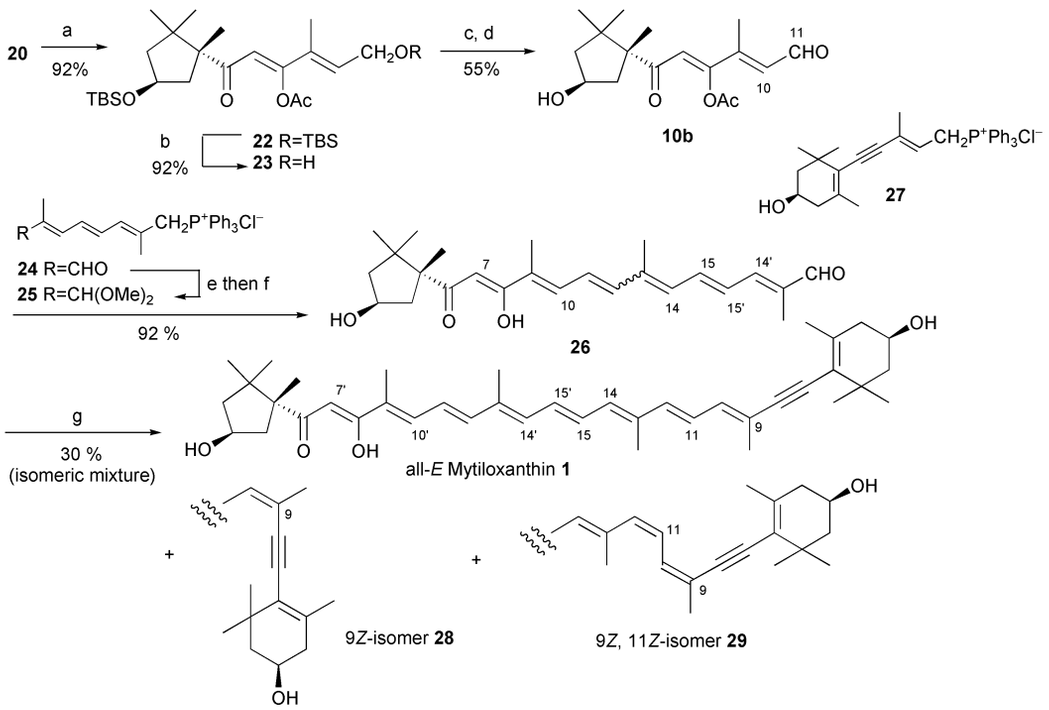
Reduction of **8** with $NaBH_4$ followed by protection of the resulting hydroxy group with *p*-methoxybenzyloxymethyl (PMBM) chloride[11] gave compound **14** (62% from **8**), which was reduced with LAH to provide the alcohol **15** (99%). This was subjected to oxidation with *o*-iodoxybenzoic acid[12] (IBX) to yield the aldehyde **16** (93%), which was reacted with vinyllithium prepared from the vinyl bromide **17**[13] and Bu^{t}Li followed by oxidation with IBX to provide the ketone **18** (60% from **16**). Its structure was confirmed by IR (ν 1669 cm^{-1}) and ^{1}H NMR data [δ 6.53 (1H, tq-like, *J* 5, 1, 10-H), 4.26 (2H, m, 11-H$_2$)]. Deprotection of the PMBM group in **18** with DDQ[11b] gave the alcohol **19** (88%), which was treated with DMSO and Ac_2O to afford the enolic β-diketone **20** (36%) and the acetate **21** (33%). Attempts to prepare **20** from **19** under other oxidation conditions (*e.g.*, DMSO–oxalyl chloride, DMSO–TFAA, DMSO–SO_3·Py, NMO–TPAP and IBX) were unsuccessful. The ^{1}H NMR spectrum of **20** had a broad one-proton signal at δ 16.15 and a sharp one-proton resonance at δ 5.81. In addition, its IR spectrum showed an absorption at 1583 cm^{-1} exhibiting the presence of a strongly hydrogen-bonded carbonyl group. These spectral data confirmed the presence of a completely enolic β-diketone structure. The structure of **21** was revealed by the following ^{1}H NMR data [an acetoxy methyl signal appeared at δ 2.14 (3H, s) and a proton signal (δ 4.23) due to C-6 shifted downfield compared to the corresponding signal (δ 4.04) of **19**].

Unfortunately, direct conversion of **20** into the C_{15}-β-diketone aldehyde **10a** (Scheme 2) by deprotection of the allylic TBS group and subsequent oxidation of the resulting alcohol using several reagents (IBX, MnO_2, *etc.*) was unsuccessful, probably due to the instability of the β-diketone part. Thus, after protection of the β-diketone moiety in **20** by acetylation, the resulting acetate **22** was partly deprotected with TBAF to give the allylic alcohol **23** (92%) which was oxidized with IBX followed by removal of another TBS group with HF to afford the C_{15}-aldehyde **10b** (55% from **23**) as shown in Scheme 4. Its ^{1}H NMR spectrum showed no signal from the TBS group but it did display a pair of doublets attributable to the 11-H (δ 10.17, d, *J* 7.5) and 10-H (δ 6.37, d, *J* 7.5).

The Wittig reaction of **10b** with the C_{10}-phosphonium salt **25**[14] in the presence of KOH as a base in a mixture of water and propan-2-ol gave condensed products which, after acid hydrolysis, provided an isomeric mixture of C_{25}-apocarotenals **26** (92% from **10b**). Investigations of alternative conditions (*e.g.*, NaOMe–MeOH, Bu^{n}Li–CH_2Cl_2–THF) for optimization



Scheme 3 *Reagents and conditions*: a, Ac_2O, Py; b, MCPBA; c, TMSCl, NaI; d, TBSCl, Et_3N, DMAP; e, **9**; f, $NaBH_4$; g, PMBMCl, Pr^i_2NEt; h, LAH; i, IBX; j; **17**, Bu^{t}Li; k, DDQ; l, DMSO, Ac_2O.



Scheme 4 *Reagents and conditions*: a, Ac_2O, Et_3N, DMAP; b, TBAF; c, IBX; d, HF; e; $HC(OMe)_3$, cat. H^+ then 1 M NaOMe; f, KOH then H^+; g, **27**, KOH.

of this condition resulted in the formation of an unexpected complex mixture. This is presumably owing to the presence of the conjugated β-diketone moiety in the molecule. It was notable that KOH was the best base in the condensation of the conjugated polyenes including the β-diketone part. Finally, the isomeric mixture **26** was condensed with the acetylenic C_{15}-Wittig salt **27**[15] in the presence of KOH in propan-2-ol at 0 °C to yield the products (30%), a part of which was separated by repeated preparative HPLC (PHPLC) in the dark to afford all-*E* mytiloxanthin **1**, 9*Z*-isomer **28**, 9*Z*,11*Z*-one **29** and unidentified isomers. Three isomers (**1**, **28** and **29**) were respectively obtained in pure form (all-*E* **1**–9*Z* **28**–9*Z*,11*Z* **29** = *ca.* 1 : 1 : 1). Spectral data (UV–VIS, ^{1}H NMR and CD) of synthetic mytiloxanthins (all-*E* and 9*Z*-isomers) were in good agreement with those of natural specimens, respectively.[4] Their configurations were confirmed from 2D-nuclear Overhauser enhancement spectroscopy (NOESY) experiments in ^{1}H NMR spectra (see Experimental section). 9*Z*,11*Z*-Stereochemistry in **29** was determined by ^{1}H NMR data in comparison with those[16] of 9′*Z*,11′*Z*-isomer of halocynthiaxanthin **2** skeletal compound. This is the first biomimetic total synthesis of optically active all-*E* mytiloxanthin **1** by application of the stereoselective rearrangement of the epoxide **5a** with aminium salt **9**.

Experimental

UV–VIS spectra were recorded on a JASCO Ubest-55 instrument for ethanol solutions unless otherwise stated. IR spectra were measured on a Perkin Elmer FT-IR spectrometer, model Paragon 1000, for chloroform solutions. ^{1}H NMR spectra at 300 or 500 MHz were determined on a Varian Gemini-300 or a Varian VXR-500 superconducting FT-NMR spectrometer, respectively, for deuteriochloroform solutions (tetramethylsilane as internal reference). *J*-Values are given in Hz. NMR assignments are given using the carotenoid numbering system. Mass spectra were taken on a Hitachi M-4100 spectrometer. Optical rotations were measured on a JASCO DIP-181 polarimeter ($[\alpha]_D$-values are in units of 10^{-1} deg cm^2 g^{-1}). CD spectra were measured on a Shimadzu-AVIV 62A DS circular dichroism spectrometer.

Column chromatography (CC) was performed on silica gel (Merck Art. 7734). Short-column chromatography (SCC) was carried out on silica gel (Merck Art. 7739) under reduced pressure. Preparative TLC (PTLC) was conducted on silica gel plates (Merck silica gel $60F_{254}$ precoated plates, 0.5 mm thickness). Low-pressure CC was performed on a Yamazen Low Pressure Liquid Chromatography System using a Lobar column (Merck LiChroprep Si 60). Analytical and PHPLC were carried out on Shimadzu LC-6A, or Waters 510 instruments with UV–VIS detectors.

Standard work-up means that the organic layers or extracts 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. Hexane refers to *n*-hexane.

Rearrangement of the epoxide 4 with aminium salt 9

To a solution of **4** (142 mg, 0.5 mmol) in CH_2Cl_2 (1.5 ml) was added aminium salt **9**[8] (8.17 mg, 0.01 mmol) at rt and the mixture was stirred at rt for 2 h. Evaporation of the reaction mixture gave a residue, which was purified by SCC (Et_2O–hexane, 2 : 3) to afford the cyclopentyl compound **7** (98 mg, 69%) as a colorless oil. Spectral data (IR and ^{1}H NMR) of this compound were in agreement with those of our previous report.[5b]

2-[(4*R*)-4-*tert*-Butyldimethylsilyloxy-2,6,6-trimethylcyclohex-1-enyl]ethyl acetate 12

To a solution of the alcohol **11**[1] (11.9 g, 0.04 mol) in dry Py (20 ml) was added Ac_2O (15 ml) at rt and the mixture was stirred at rt for 16 h. The mixture was poured into ice–water and extracted with Et_2O. The extracts were washed successively with aq. 5% HCl, saturated aq. $NaHCO_3$ and brine. Evaporation of the dried extracts gave a residue, which was purified by SCC (Et_2O–hexane, 1 : 9) to afford the acetate **12** (12.6 g, 93%) as a colorless oil; $[\alpha]_D^{26}$ −42.6 (*c* 1.22, MeOH); ν_{max}/cm^{-1} 1732 (OAc); δ_H (300 MHz) 0.06 (6H, s, $SiMe_2$), 0.89 (9H, s, $SiBu^t$), 1.02 and 1.04 (each 3H, s, *gem*-Me), 1.44 (1H, t, *J* 12, 2-H_{ax}), 1.61 (1H, m, 2-H_{eq}), 1.65 (3H, s, 5-Me), 1.99 (1H, dd, *J* 17 and 9, 4-H_{ax}), 2.05 (3H, s, OAc), 2.11 (1H, dd, *J* 17 and 7, 4-H_{eq}), 2.34 (2H, dt,

J 13 and 8.5, 7-H_2), 3.88 (1H, m, 3-H), 3.99 (2H, t, *J* 8.5, 8-H_2) (Found: M^+, 340.2416. $C_{19}H_{36}O_3Si$ requires *M*, 340.2435).

2-[(1*S*,4*S*,6*R*)- and (1*R*,4*S*,6*S*)-4-*tert*-Butyldimethylsilyloxy-2,2,6-trimethyl-7-oxabicyclo[4.1.0]heptan-1-yl]ethyl acetate 5a and 5b

A solution of MCPBA (72%, 552 mg, 2.29 mmol) in dry CH_2Cl_2 (5 ml) was added to an ice-cooled solution of the acetate **12** (600 mg, 1.76 mmol) in dry CH_2Cl_2 (5 ml). After being stirred at 0 °C for 1 h, the reaction mixture was diluted with Et_2O and washed successively with aq. 1% $Na_2S_2O_3$, saturated aq. $NaHCO_3$ and brine. Evaporation of the dried solvent gave a residue, which was purified by SCC (Et_2O–hexane, 1 : 5) followed by low-pressure CC (Et_2O–benzene, 1 : 19) to afford the *anti*-epoxide **5a** (174 mg, 28%) and the *syn*- epoxide **5b** (328 mg, 52%) as colorless oils, respectively.

***anti*-Epoxide 5a.** $[\alpha]_D^{22}$ −10.0 (*c* 1.00, MeOH); ν_{max}/cm^{-1} 1733 (OAc); δ_H (300 MHz) 0.03 (6H, s, $SiMe_2$), 0.86 (9H, s, $SiBu^t$), 1.03 and 1.15 (each 3H, s, *gem*-Me), 1.18 (1H, dd, *J* 13 and 9.5, 2-H_{ax}), 1.33 (3H, s, 5-Me), 1.44 (1H, ddd, *J* 13, 3.5 and 1.5, 2-H_{eq}), 1.64 (1H, dd, *J* 14.5 and 7.5, 4-H_{ax}), 2.01 (2H, m, 7-H_2), 2.04 (3H, s, OAc), 2.19 (1H, ddd, *J* 14.5, 5 and 1.5, 4-H_{eq}), 3.77 (1H, m, 3-H), 4.15 (2H, m, 8-H_2) (Found: M^+, 356.2352. $C_{19}H_{38}O_4Si$ requires *M*, 356.2380).

***syn*-Epoxide 5b.** $[\alpha]_D^{22}$ −30.0 (*c* 1.00, MeOH); ν_{max}/cm^{-1} 1733 (OAc); δ_H (300 MHz) 0.03 (6H, s, $SiMe_2$), 0.86 (9H, s, $SiBu^t$), 1.06 (6H, s, *gem*-Me), 1.12 (1H, ddd, *J* 13, 4 and 2, 2-H_{eq}), 1.28 (3H, s, 5-Me), 1.51 (1H, t, *J* 12.5, 2-H_{ax}), 1.81 (1H, dd, *J* 15 and 9.5, 4-H_{ax}), 1.96 (2H, m, 7-H_2), 2.00 (1H, ddd, *J* 14.5, 7 and 1.5, 4-H_{eq}), 2.03 (3H, s, OAc), 3.75 (1H, m, 3-H), 4.07 (2H, m, 8-H_2) (Found: M^+, 356.2360. $C_{19}H_{36}O_4Si$ requires *M*, 356.2380).

Conversion of epoxide 5b to alkene 12

To a solution of NaI (1.35 g, 9 mmol) in dry acetonitrile (10 ml) was added TMSCl (0.56 ml, 4.5 mmol) at rt and the mixture was stirred at rt for a few minutes. To this mixture was added a solution of the epoxide **5b** (1.07 g, 3 mmol) in dry CH_2Cl_2 (5 ml) at rt. After being stirred at rt for 30 min, the reaction mixture was diluted with Et_2O and washed successively with aq. 1% $Na_2S_2O_3$ and brine. Evaporation of the dried solvent gave a residue, which was purified by SCC (acetone–hexane, 1 : 4) to afford the alcohol (542 mg, 80%) as a colorless oil. To a solution of the alcohol (542 mg, 2.4 mmol) in dry CH_2Cl_2 (5 ml) was added Et_3N (0.64 ml, 4.8 mmol), DMAP (586 mg, 4.8 mmol) and a solution of TBSCl (433 mg, 2.9 mmol) in dry CH_2Cl_2 (3 ml) at rt and the mixture was stirred at rt for 15 h. The reaction mixture was poured into ice–water and extracted with Et_2O. The extracts were washed successively with aq. 5% HCl, saturated aq. $NaHCO_3$ and brine. Evaporation of the dried extracts gave a residue, which was purified by SCC (Et_2O–hexane, 1 : 9) to yield **12** (611 mg, 75%; 60% from **5b**) as a colorless oil. Spectral data of this compound were identical with those of **12** derived from **11** in this paper.

Rearrangement of epoxide 5a by aminium salt 9

To a solution of the epoxide **5a** (178 mg, 0.5 mmol) in CH_2Cl_2 (4 ml) was added aminium salt **9**[8] (42 mg, 0.05 mmol) at rt and the mixture was stirred at rt for 30 min. Evaporation of the reaction mixture gave a residue, which was purified by SCC (Et_2O–hexane, 3 : 17 ⟶ acetone–hexane, 1 : 5) to afford the cyclopentyl compound **8** (112 mg, 63%) and the deprotected compound **13** (36 mg, 30%) as colorless oils, respectively.

Cyclopentyl compound 8. $[\alpha]_D^{22}$ +10.0 (*c* 1.00, MeOH); ν_{max}/cm^{-1} 1736 (OAc), 1699 (C=O); δ_H (300 MHz) 0.01 (6H, s, $SiMe_2$), 0.82 (3H, s, 1-Me_α), 0.86 (9H, s, $SiBu^t$), 1.14 (3H, s, 1-Me_β), 1.29 (3H, s, 5-Me), 1.44 (1H, dd, *J* 14 and 3, 4-H_β), 1.66 (1H, dd, *J* 13.5 and 4.5, 2-H_β), 1.90 (1H, dd, *J* 13.5 and 7.5, 2-H_α), 2.01 (3H, s, OAc), 2.71 (1H, dd, *J* 14 and 8, 4-H_α), 2.75 (2H, t, *J* 6.5, 7-H_2), 4.32 (2H, td, *J* 6.5 and 2, 8-H_2), 4.35 (1H, m, 3-H) (Found: M^+, 356.2356. $C_{19}H_{36}O_4Si$ requires *M*, 356.2380).

Deprotected compound 13. $[\alpha]_D^{23}$ +5.00 (*c* 1.00, MeOH); ν_{max}/cm^{-1} 3612 and 3468 (OH), 1736 (OAc), 1701 (C=O); δ_H (300 MHz) 0.81 (3H, s, 1-Me_α), 1.14 (3H, s, 1-Me_β), 1.28 (3H, s, 5-Me), 1.43 (1H, dd, *J* 14.5 and 3.5, 4-H_β), 1.66 (1H, dd, *J* 13.5 and 4.5, 2-H_β), 1.95 (1H, dd, *J* 13.5 and 8, 2-H_α), 1.98 (3H, s, OAc), 2.74 (2H, t, *J* 6, 7-H_2), 2.78 (1H, dd, *J* 14.5 and 8.5, 4-H_α), 4.27 and 4.31 (each 1H, dt, *J* 11 and 6.5, 8-H_2), 4.44 (1H, m, 3-H) (Found: M^+, 242.1535. $C_{13}H_{22}O_4$ requires *M*, 242.1519).

Reprotection of the alcohol 13

To a solution of the alcohol **13** (145 mg, 0.60 mmol) in dry CH_2Cl_2 (3 ml) was added Et_3N (0.5 ml, 3.6 mmol), DMAP (110 mg, 0.90 mmol) and a solution of TBSCl (106 mg, 0.70 mmol) in dry CH_2Cl_2 (3 ml) at rt and the mixture was stirred at rt for 15 h. The reaction mixture was poured into ice–water, and extracted with Et_2O. The extracts were washed successively with aq. 5% HCl, saturated aq. $NaHCO_3$ and brine. Evaporation of the dried extracts gave a residue, which was purified by SCC (Et_2O–hexane, 1 : 4) to afford **8** (191 mg, 89%) as a colorless oil. Spectral properties of this compound were in agreement with those of the cyclopentyl compound **8** in the above rearrangement.

3-[(1*R*,4*S*)-4-*tert*-Butyldimethylsilyloxy-1,2,2-trimethylcyclopentyl]-3-{[(4-methoxyphenyl)methoxy]methoxy}propyl acetate 14

To a solution of the cyclopentyl compound **8** (255 mg, 0.72 mmol) in MeOH (5 ml) was added $NaBH_4$ (27.2 mg, 0.72 mmol) at 0 °C and the mixture was stirred at 0 °C for 30 min. The reaction mixture was poured into ice–water, and extracted with Et_2O. Standard work-up afforded a residue, which was purified by SCC (Et_2O–hexane, 1 : 5) to yield the alcohol (200 mg, 78%) as a colorless oil. Pr^i_2NEt (0.98 ml, 5.60 mmol) and PMBMCl[11] (626 mg, 3.36 mmol) were added to a solution of the above alcohol (200 mg, 0.56 mmol) in dry CH_2Cl_2 (2 ml) at rt. After being stirred at rt for 16 h, the reaction mixture was diluted with Et_2O and the organic layer was washed successively with aq. 5% HCl, saturated aq. $NaHCO_3$ and brine. Evaporation of the dried solution gave a residue, which was purified by SCC (acetone–hexane, 1 : 19) to afford the PMBM ether **14** (229 mg, 80%; 62% from **8**) as a colorless oil; ν_{max}/cm^{-1} 1732 (OAc), 1612 and 1514 (Ph); δ_H (300 MHz) 0.00 (6H, s, $SiMe_2$), 0.86 (9H, s, $SiBu^t$), 0.90, 1.06 and 1.12 (each 3H, s, *gem*-Me and 5-Me), 1.30 (1H, dd, *J* 14 and 2, 2-H_β), 1.80 (4H, m, 4-H_2 and 7-H_2), 1.94 (1H, dd, *J* 14 and 9, 2-H_α), 2.03 (3H, s, OAc), 3.50 (1H, t-like, *J* 4, 6-H), 3.80 (3H, s, OMe), 4.22 (1H, m, 3-H), 4.24 (2H, m, 8-H_2), 4.52 and 4.60 (each 1H, d, *J* 11.5, CH_2Ph), 4.71 and 4.82 (each 1H, d, *J* 7, –OCH_2O–), 6.87 and 7.25 (each 2H, d, *J* 8.5, Ar-H_4) (Found: M^+, 508.3236. $C_{28}H_{48}O_6Si$ requires *M*, 508.3232).

3-[(1*R*,4*S*)-4-*tert*-Butyldimethylsilyloxy-1,2,2-trimethylcyclopentyl]-3-{[(4-methoxyphenyl)methoxy]methoxy}propan-1-ol 15

To a suspension of LAH (24 mg, 0.64 mmol) in dry Et_2O (5 ml) was added dropwise a solution of **14** (323 mg, 0.64 mmol) in dry Et_2O (15 ml) at 0 °C. After being stirred at 0 °C for 30 min, the excess of LAH was decomposed by dropwise addition of water. The mixture was extracted with Et_2O and the extracts were washed successively with aq. 5% HCl, saturated aq. $NaHCO_3$ and brine. Evaporation of the dried solvent gave a residue, which was purified by SCC (acetone–hexane, 1 : 9) to

afford the alcohol **15** (292 mg, 99%) as a colorless oil; ν_{max}/cm^{-1} 3465 (OH), 1613 and 1514 (Ph); δ_H (300 MHz) 0.01 (6H, s, $SiMe_2$), 0.86 (9H, s, SiBu^t), 0.92, 1.05 and 1.13 (each 3H, s, *gem*-Me and 5-Me), 1.30 (1H, dd, *J* 14 and 2, 2-H$_\beta$), 1.78 (4H, m, 4-H_2 and 7-H_2), 1.98 (1H, dd, *J* 14 and 9, 2-H$_\alpha$), 3.66 (1H, t, *J* 5.5, 6-H), 3.77 (2H, m, 8-H_2), 3.81 (3H, s, OMe), 4.23 (1H, m, 3-H), 4.52 and 4.68 (each 1H, d, *J* 11.5, CH_2Ph), 4.81 and 4.87 (each 1H, d, *J* 6.5, –OCH_2O–), 6.89 and 7.27 (each 2H, d, *J* 8.5, Ar-H_4) (Found: M$^+$, 466.3105. $C_{26}H_{46}O_5Si$ requires *M*, 466.3112).

3-[(1*R*,4*S*)-4-*tert*-Butyldimethylsilyloxy-1,2,2-trimethylcyclopentyl]-3-{[(4-methoxyphenyl)methoxy]methoxy}propanal 16

To a solution of the alcohol **15** (125 mg, 0.27 mmol) in DMSO (1 ml) was added a solution of IBX[12] (188 mg, 0.67 mmol) in DMSO (0.67 ml) at rt and the mixture was stirred at rt for 1 h. The reaction mixture was diluted with water (5 ml) and the white precipitate was filtered. The filtrate was extracted with Et_2O. Standard work-up gave a residue, which was purified by SCC (acetone–hexane, 1 : 9) to provide the aldehyde **16** (116 mg, 93%) as a colorless oil; ν_{max}/cm^{-1} 1721 (CHO), 1613 and 1514 (Ph); δ_H (300 MHz) 0.01 (6H, s, $SiMe_2$), 0.86 (9H, s, SiBu^t), 0.93, 1.06 and 1.12 (each 3H, s, *gem*-Me and 5-Me), 1.23 (1H, dd, *J* 13.5 and 2.5, 2-H$_\beta$), 1.80 (2H, d, *J* 7.5, 4-H_2), 1.92 (1H, dd, *J* 13.5 and 8.5, 2-H$_\alpha$), 2.37 (1H, dd, *J* 17 and 2.5, 7-H), 2.78 (1H, ddd, *J* 17, 7 and 2, 7-H), 3.80 (3H, s, OMe), 4.13 (1H, dd, *J* 7 and 2.5, 6-H), 4.24 (1H, m, 3-H), 4.42 and 4.54 (each 1H, d, *J* 11.5, CH_2Ph), 4.70 and 4.76 (each 1H, d, *J* 7, –OCH_2O–), 6.87 and 7.23 (each 2H, d, *J* 8.5, Ar-H_4), 9.76 (1H, d, *J* 2, CHO) (Found: M$^+$, 464.2967. $C_{26}H_{44}O_5Si$ requires *M*, 464.2960).

(4*E*)-6-*tert*-Butyldimethylsilyloxy-1-[(1*R*,4*S*)-4-*tert*-butyldimethylsilyloxy-1,2,2-trimethylcyclopentyl]-1-{[(4-methoxyphenyl)methoxy]methoxy}-4-methylhex-4-en-3-one 18

To a solution of the vinyl bromide **17**[13] (403 mg, 1.52 mmol) in dry Et_2O (4 ml) was added Bu^{t}Li (1.64 M in pentane; 0.93 ml, 1.52 mmol) at −78 °C and the mixture was stirred at −78 °C for 10 min. A solution of the aldehyde **16** (235 mg, 0.51 mmol) in dry Et_2O (6 ml) was added to this mixture at −78 °C for 1 h. After being quenched with saturated aq. NH_4Cl, the mixture was extracted with Et_2O. Standard work-up gave a residue, which was purified by SCC (Et_2O–hexane, 1 : 4) to afford the adduct (313 mg, 95%) as a colorless oil. Then, to a solution of the adduct (313 mg, 0.48 mmol) in DMSO (1.5 ml) was added a solution of IBX[12] (337 mg, 1.20 mmol) in DMSO (1.2 ml) at rt and the mixture was stirred at rt for 16 h. The reaction mixture was diluted with water (5 ml) and the white precipitate was filtered. The filtrate was extracted with Et_2O. Standard work-up gave a residue, which was purified by SCC (Et_2O–hexane, 3 : 17) to provide the conjugated ketone **18** (197 mg, 63%; 60% from **16**) as a colorless oil; ν_{max}/cm^{-1} 1669 (conj. C=O), 1613 and 1514 (Ph); δ_H (300 MHz) −0.02 and 0.09 (each 6H, s, $SiMe_2$ × 2), 0.86 and 0.92 (each 9H, s, SiBu^t × 2), 0.96, 1.06 and 1.16 (each 3H, s, *gem*-Me and 5-Me), 1.18 (1H, m, 2-H$_\beta$), 1.63 (3H, d, *J* 1, 9-Me), 1.79 (2H, d, *J* 7, 4-H_2), 1.92 (1H, dd, *J* 14 and 9, 2-H$_\alpha$), 2.45 (1H, dd, *J* 17 and 2, 7-H), 3.16 (1H, dd, *J* 17 and 7, 7-H), 3.79 (3H, s, OMe), 4.26 (4H, m, 3-H, 6-H and 11-H_2), 4.38 and 4.65 (each 1H, d, *J* 12, CH_2Ph), 4.62 and 4.65 (each 1H, d, *J* 6.5, –OCH_2O–), 6.53 (1H, tq-like, *J* 5 and 1, 10-H), 6.83 and 7.17 (each 2H, d, *J* 9, Ar-H_4) (Found: M$^+$, 648.4236. $C_{36}H_{64}O_6Si_2$ requires *M*, 648.4244).

(4*E*)-6-*tert*-Butyldimethylsilyloxy-1-[(1*R*,4*S*)-4-*tert*-butyldimethylsilyloxy-1,2,2-trimethylcyclopentyl]-1-hydroxy-4-methylhex-4-en-3-one 19

To a solution of the ketone **18** (197 mg, 0.30 mmol) dissolved in a mixture of CH_2Cl_2–H_2O (18 : 1, 6.54 ml) was added DDQ[11b] (86 mg, 0.36 mmol). After being stirred at rt for 2 h, the reaction mixture was filtered through Celite. Evaporation of the filtrate gave a residue, which was purified by SCC (Et_2O–hexane, 1 : 9) to afford the alcohol **19** (133 mg, 88%) as a colorless oil; λ_{max}/nm 228; ν_{max}/cm^{-1} 3558 (OH), 1659 (conj. C=O); δ_H (300 MHz) 0.01 and 0.11 (each 6H, s, $SiMe_2$ × 2), 0.87 and 0.93 (each 9H, s, SiBu^t × 2), 0.98, 1.10 and 1.11 (each 3H, s, *gem*-Me and 5-Me), 1.29 (1H, dd, *J* 14 and 2.5, 2-H$_\beta$), 1.74 (3H, d, *J* 1, 9-Me), 1.78 (2H, d, *J* 7, 4-H_2), 1.88 (1H, dd, *J* 13.5 and 9, 2-H$_\alpha$), 2.73 (1H, s, OH), 2.71 and 2.90 (each 1H, d-like, *J* 3, 7-H_2), 4.04 (1H, m, 6-H), 4.25 (1H, m, 3-H), 4.42 (2H, br d, *J* 5, 11-H_2), 6.64 (1H, td-like, *J* 5 and 1, 10-H) (Found: M$^+$, 498.3531. $C_{27}H_{54}O_4Si_2$ requires *M*, 498.3557).

Oxidation of the β-hydroxy ketone 19

To a solution of the alcohol **19** (200 mg, 0.40 mmol) in dry DMSO (14 ml) was added Ac_2O (7 ml) at rt and the mixture was stirred at rt for 16 h. The reaction mixture was poured into ice-water and extracted with Et_2O. The extracts were washed with water and saturated aq. $NaHCO_3$ and brine. Evaporation of the dried solvent gave a residue, which was purified by SCC (Et_2O–hexane, 1 : 19) to afford the conjugated β-diketone **20** (71 mg, 36%) and the acetate **21** (72 mg, 33%) as colorless oils, respectively.

(2*E*,4*E*)-6-*tert*-Butyldimethylsilyloxy-1-[(1*R*,4*S*)-4-*tert*-butyldimethylsilyloxy-1,2,2-trimethylcyclopentyl]-3-hydroxy-4-methylhexa-2,4-dienone 20. $[\alpha]_D^{23}$ −23.4 (*c* 0.47, $CHCl_3$); λ_{max}/nm 305; ν_{max}/cm^{-1} 1583 (hydrogen-bonded conj. C=O); δ_H (300 MHz) 0.03 and 0.09 (each 6H, s, $SiMe_2$ × 2), 0.81 (3H, s, 1-Me$_\alpha$), 0.88 and 0.92 (each 9H, s, SiBu^t × 2), 1.15 (3H, s, 1-Me$_\beta$), 1.30 (3H, s, 5-Me), 1.51 (1H, dd, *J* 14 and 2.5, 4-H$_\beta$), 1.69 (1H, dd, *J* 13.5 and 4.5, 2-H$_\beta$), 1.80 (3H, d, *J* 1, 9-Me), 1.98 (1H, dd, *J* 13.5 and 7.5, 2-H$_\alpha$), 2.73 (1H, dd, *J* 14 and 8, 4-H$_\alpha$), 4.38 (1H, m, 3-H), 4.39 (2H, d, *J* 6, 11-H_2), 5.81 (1H, s, 7-H), 6.59 (1H, t, *J* 6, 10-H), 16.15 (1H, s, enolic OH) (Found: M$^+$, 496.3412. $C_{27}H_{52}O_4Si_2$ requires *M*, 496.3407).

(4*E*)-1-Acetyloxy-6-*tert*-butyldimethylsilyloxy-1-[(1*R*,4*S*)-4-*tert*-butyldimethylsilyloxy-1,2,2-trimethylcyclopentyl]-4-methylhex-4-en-3-one 21. $[\alpha]_D^{27}$ +10.0 (*c* 0.40, MeOH); λ_{max}/nm 231; ν_{max}/cm^{-1} 1668 (conj. C=O); δ_H (300 MHz) 0.02 and 0.11 (each 6H, s, $SiMe_2$ × 2), 0.85 and 0.93 (each 9H, s, SiBu^t × 2), 0.99, 1.07 and 1.13 (each 3H, s, *gem*-Me and 5-Me), 1.16 (1H, m, 2-H$_\beta$), 1.76 (3H, d, *J* 1, 9-Me), 1.78 (2H, d, *J* 8, 4-H_2), 1.93 (1H, dd, *J* 14 and 9, 2-H$_\alpha$), 2.14 (3H, s, OAc), 2.59 (1H, dd, *J* 17.5 and 2.5, 7-H), 3.07 (1H, dd, *J* 17.5 and 6.5, 7-H), 4.23 (2H, m, 3-H and 6-H), 4.42 (2H, d, *J* 5, 11-H_2), 6.66 (1H, td-like, *J* 5 and 1, 10-H) [Found: (M − Ac)$^+$, 497.3463. $C_{27}H_{53}O_4Si_2$ requires *M* − Ac, 497.3485].

(2*E*,4*E*)-3-Acetyloxy-6-*tert*-butyldimethylsilyloxy-1-[(1*R*,4*S*)-4-*tert*-butyldimethylsilyloxy-1,2,2-trimethylcyclopentyl]-4-methylhexa-2,4-dienone 22

Ac_2O (0.5 ml) was added to a solution of the β-diketone **20** (104 mg, 0.21 mmol), Et_3N (0.04 ml, 0.29 mmol) and DMAP (28 mg, 0.23 mmol) in dry CH_2Cl_2 (1 ml) at rt. After being stirred at rt for 30 min, the mixture was poured into ice–water and extracted with Et_2O. The extracts were washed successively with aq. 5% HCl, saturated aq. $NaHCO_3$ and brine. Evaporation of the dried extracts gave a residue, which was purified by SCC (Et_2O–hexane, 1 : 4) to afford the enol acetate **22** (104 mg, 92%) as a colorless oil; $[\alpha]_D^{20}$ −10.3 (*c* 0.98, $CHCl_3$); λ_{max}/nm 277; ν_{max}/cm^{-1} 1766 (OAc), 1673 (conj. C=O), 1586 (conj. C=C); δ_H (300 MHz) 0.01 and 0.07 (each 6H, s, $SiMe_2$ × 2), 0.86 and 0.90 (each 9H, s, SiBu^t × 2), 0.82, 1.16 and 1.31 (each 3H, s, *gem*-Me and 5-Me), 1.42 (1H, m, 4-H$_\beta$), 1.68 (1H, dd, *J* 13 and 5, 2-H$_\beta$), 1.80 (3H, d, *J* 1, 9-Me), 1.88 (1H, dd, *J* 13 and 7.5, 2-H), 2.31 (3H, s, OAc), 2.78 (1H, m, 4-H$_\alpha$), 4.33 (1H, m, 3-H),

4.38 (2H, d, *J* 5.5, 11-H_2), 6.20 (1H, m, 10-H), 6.25 (1H, s, 7-H) (Found: M^+, 538.3509. $C_{29}H_{54}O_5Si_2$ requires *M*, 538.3512).

(2*E*,4*E*)-3-Acetyloxy-1-[(1*R*,4*S*)-4-*tert*-butyldimethylsilyloxy-1,2,2-trimethylcyclopentyl]-6-hydroxy-4-methylhexa-2,4-dienone 23

A solution of TBAF (1 M in THF; 0.19 ml, 0.19 mmol) was added to a solution of the acetate **22** (104 mg, 0.19 mmol) in dry THF (4 ml) at 0 °C and the mixture was stirred at 0 °C for 1 h. The reaction mixture was diluted with Et_2O. Standard work-up gave a residue, which was purified by SCC (Et_2O–hexane, 1 : 4 ⟶ acetone–hexane, 1 : 4) to afford the alcohol **23** (75 mg, 92%) as a colorless oil; $[\alpha]_D^{24}$ +0.98 (*c* 1.02, $CHCl_3$); λ_{max}/nm 277; ν_{max}/cm^{-1} 3604 and 3508 (OH), 1767 (OAc), 1674 (conj. C=O), 1587 (conj. C=C); δ_H (300 MHz) 0.01 (6H, s, $SiMe_2$), 0.86 (9H, s, $SiBu^t$), 0.82 and 1.16 (each 3H, s, *gem*-Me), 1.31 (3H, s, 5-Me), 1.42 (1H, m, 4-H_β), 1.68 (1H, dd, *J* 14 and 5, 2-H_β), 1.85 (3H, s, 9-Me), 1.87 (1H, m, 2-H_α), 2.31 (3H, s, OAc), 2.78 (1H, m, 4-H_α), 4.33 (1H, m, 3-H), 4.38 (2H, d, *J* 6, 11-H_2), 6.25 (1H, m, 10-H), 6.28 (1H, s, 7-H) (Found: M^+, 424.2632. $C_{23}H_{40}O_5Si$ requires *M*, 424.2647).

(2*E*,4*E*)-4-Acetyloxy-6-[(1*R*,4*S*)-4-hydroxy-1,2,2-trimethylcyclopentyl]-3-methyl-6-oxohexa-2,4-dienal 10b

To a solution of the alcohol **23** (54 mg, 0.13 mmol) in DMSO (0.25 ml) was added a solution of IBX[12] (72 mg, 0.26 mmol) in DMSO (0.26 ml) at rt and the mixture was stirred at rt for 1 h. The reaction mixture was diluted with water (3 ml) and the white precipitate was filtered. The filtrate was extracted with Et_2O. Standard work-up gave a residue, which was purified by SCC (acetone–hexane, 3 : 17) to afford the aldehyde (33 mg, 60%) as a pale yellow oil. A mixture of 47% aq HF–CH_3CN (1 : 19; 0.4 ml) was added to a solution of this aldehyde (33 mg, 0.08 mmol) in a mixture of CH_3CN–THF (9 : 1; 4 ml) at rt. After being stirred at rt for 1.5 h, the reaction mixture was quenched with saturated aq. $NaHCO_3$ and extracted with Et_2O. Standard work-up gave a residue, which was purified by SCC (acetone–hexane, 3 : 7) to provide the desilylated aldehyde **10b** (22 mg, 92%; 55% from **23**) as a pale yellow oil; $[\alpha]_D^{26}$ −10.0 (*c* 0.40, $CHCl_3$); λ_{max}/nm 283; ν_{max}/cm^{-1} 3611 and 3476 (OH), 1773 (OAc), 1674 (conj. C=O and conj. CHO), 1588 (conj. C=C); δ_H (300 MHz) 0.84 (3H, s, 1-Me_α), 1.19 (3H, s, 1-Me_β), 1.35 (3H, s, 5-Me), 1.46 (1H, dd, *J* 14.5 and 3, 4-H_β), 1.70 (1H, dd, *J* 14 and 5, 2-H_β), 1.96 (1H, dd, *J* 14 and 8, 2-H_α), 2.31 and 2.33 (each 3H, s, 9-Me and OAc), 2.85 (1H, dd, *J* 14.5 and 8.5, 4-H_α), 4.47 (1H, m, 3-H), 6.37 (1H, d, *J* 7.5, 10-H), 6.60 (1H, s, 7-H), 10.17 (1H, d, *J* 7.5, 11-H) (Found: M^+, 308.1648. $C_{17}H_{24}O_5$ requires *M*, 308.1625).

(2*E*,4*E*,6*E*,8*E*,10*E*,12*E*)-12-Hydroxy-14-[(1*R*,4*S*)-4-hydroxy-1,2,2-trimethylcyclopentyl]-2,7,11-trimethyl-14-oxotetradeca-2,4,6,8,10,12-hexaenal 26

An acidic solution (0.1 ml) prepared from PTSA (500 mg) and H_3PO_4 (725 mg) in MeOH (37.5 ml) and trimethyl orthoformate (0.1 ml, 0.91 mmol) were added to a solution of the Wittig salt **24**[14] (35.6 mg, 0.08 mmol) in MeOH (1 ml). The mixture was stirred at rt for 1 h and neutralized with NaOMe (1 M in MeOH) until just before the red color of an ylide appeared. Evaporation of the solvent provided the Wittig salt **25**, to which a solution of the aldehyde **10b** (9.8 mg, 0.03 mmol) in propan-2-ol (1.5 ml) was added. To the mixture, a basic solution (1 ml) of KOH (500 mg) dissolved in water (1 ml) and propan-2-ol (10 ml) was added dropwise at 0 °C. After being stirred at 0 °C for 1 h, the mixture was poured into ice–water, and extracted with Et_2O. The extracts were shaken with aq. 5% HCl until the fine structure disappeared on UV–VIS, washed successively with saturated aq. $NaHCO_3$ and brine. Evaporation of the dried extracts provided a residue, which was purified by SCC (acetone–hexane, 1 : 4) to afford an isomeric mixture of apocarotenal **26** (12 mg, 92%) in which the main product was all-*E* isomer. Purification of a part of the isomeric mixture by PTLC (acetone–hexane, 3 : 7) provided the all-*E* isomer as an orange solid; λ_{max}/nm 419 and 440(sh); ν_{max}/cm^{-1} 3610 and 3476 (OH), 1665 (conj. CHO), 1605 and 1568 (conj. C=C or hydrogen-bonded conj. C=O); δ_H (300 MHz) 0.85 (3H, s, 1-Me_α), 1.19 (3H, s, 1-Me_β), 1.35 (3H, s, 5-Me), 1.55 (1H, dd, *J* 14.5 and 3, 4-H_β), 1.72 (1H, dd, *J* 13.5 and 4, 2-H_β), 1.90 (3H, s, 13′-Me), 2.00 (3H, s, 9-Me), 2.06 (3H, s, 13-Me), 2.09 (1H, dd, *J* 13.5 and 8, 2-H_α), 2.88 (1H, dd, *J* 14.5 and 8.5, 4-H_α), 4.53 (1H, m, 3-H), 5.87 (1H, s, 7-H), 6.41 (1H, d, *J* 11.5, 14-H), 6.65 (1H, d, *J* 15, 12-H), 6.74 (1H, dd, *J* 15 and 10.5, 11-H), 6.77 (1H, dd, *J* 14.5 and 11.5, 15′-H), 6.97 (1H, d, *J* 11.5, 14′-H), 7.03 (1H, dd, *J* 14.5 and 11.5, 15-H), 7.23 (1H, d, *J* 10.5, 10-H), 9.48 (1H, s, 12′-H) (Found: M^+, 398.2439. $C_{25}H_{34}O_4$ requires *M*, 398.2458).

Synthesis of mytiloxanthin

A basic solution (3 ml) of KOH (500 mg) dissolved in water (1 ml) and propan-2-ol (10 ml) was added dropwise to a solution of the apocarotenal **26** (11.7 mg, 0.03 mmol) and the Wittig salt **27**[15] (61 mg, 0.12 mmol) in propan-2-ol (6 ml) at 0 °C. After being stirred at 0 °C for 30 min, the reaction mixture was extracted with Et_2O and washed with saturated aq. NH_4Cl and brine. Evaporation of the dried extracts gave a residue, which was purified by SCC (acetone–hexane, 3 : 7) to afford an isomeric mixture of mytiloxanthin (5.2 mg, 30%). Purification of a part of the isomeric mixture by PHPLC [CHEMCOSORB 7ODS-H 1.0 × 30 cm; H_2O–MeOH, 4 : 96; 460 nm detect.] provided the all-*E* isomer **1**, 9*Z* one **28** and 9*Z*,11*Z* one **29** as red solids respectively, in a pure state. Spectral properties of the synthetic all-*E* isomer **1** and 9*Z* one **28** were in agreement with those of a natural specimen.[4]

all-*E* Isomer 1. CD (Et_2O)/nm ($\Delta\varepsilon$) 230 (−0.5), 275 (0), 294 (+0.7), 310 (0), 360 (−0.3); λ_{max}/nm 470, λ_{max}(Et_2O)/nm 467; ν_{max}/cm^{-1} 3530 and 3321 (OH), 1602 (hydrogen-bonded conj. C=O); δ_H (500 MHz) 0.85 (3H, s, 1′-Me_α), 1.14 (3H, s, 1-Me_{ax}), 1.19 (3H, s, 1′-Me_β), 1.20 (3H, s, 1-Me_{eq}), 1.35 (3H, s, 5′-Me), 1.45 (1H, t, *J* 11.5, 2-H_{ax}), 1.55 (1H, m, 4′-H_β), 1.71 (1H, dd, *J* 13.5 and 4, 2′-H_β), 1.83 (1H, m, 2-H_{eq}), 1.92 (3H, s, 5-Me), 1.98 (6H, s, 13-Me and 13′-Me), 1.99 (3H, s, 9′-Me), 2.01 (3H, s, 9-Me), 2.07 (1H, m, 4-H_{ax}), 2.09 (1H, dd, *J* 13.5 and 8, 2′-H_α), 2.43 (1H, br dd, *J* 18 and 5.5, 4-H_{eq}), 2.88 (1H, dd, *J* 14.5 and 9, 4′-H_α), 4.00 (1H, m, 3-H), 4.52 (1H, m, 3′-H), 5.86 (1H, s, 7′-H), 6.28 (1H, d, *J* 11.5, 14-H), 6.36 (1H, d, *J* 15, 12-H), 6.38 (1H, d, *J* 10.5, 14′-H), 6.46 (1H, d, *J* 11.5, 10-H), 6.55 (1H, dd, *J* 15 and 11.5, 11-H), 6.60 (1H, dd, *J* 15 and 10.5, 11′-H), 6.64 (1H, dd, *J* 14 and 11, 15′-H), 6.65 (1H, d, *J* 15.5, 12′-H), 6.71 (1H, dd, *J* 14 and 11.5, 15-H), 7.23 (1H, d, *J* 10.5, 10′-H) (Found: M^+, 598.4016. $C_{40}H_{54}O_4$ requires *M*, 598.4025).

9*Z*-Isomer 28. CD (Et_2O)/nm ($\Delta\varepsilon$) 230 (−0.8), 247 (0), 258 (+1.0), 280 (0), 300 (−0.3), 310 (0), 350 (+1.0), 370 (0); λ_{max}/nm 467, 358 λ_{max}(Et_2O)/nm 465, 358; ν_{max}/cm^{-1} 3530 and 3321 (OH), 1602 (hydrogen-bonded conj. C=O); δ_H (500 MHz) 0.85 (3H, s, 1′-Me_α), 1.19 (6H, s, 1-Me_{ax} and 1′-Me_β), 1.26 (3H, s, 1-Me_{eq}), 1.35 (3H, s, 5′-Me), 1.48 (1H, t, *J* 12, 2-H_{ax}), 1.56 (1H, m, 4′-H_β), 1.72 (1H, dd, *J* 13.5 and 4.5, 2′-H_β), 1.93 (1H, ddd, *J* 11.5, 3 and 2, 2-H_{eq}), 1.95 (3H, s, 13-Me), 1.97 (6H, s, 5-Me and 9′-Me), 1.99 (3H, s, 13′-Me), 2.01 (3H, s, 9-Me), 2.09 (1H, dd, *J* 14 and 8, 2′-H_α), 2.10 (1H, m, 4-H_{ax}), 2.46 (1H, br dd, *J* 17.5 and 4.5, 4-H_{eq}), 2.88 (1H, dd, *J* 14.5 and 9, 4′-H_α), 4.01 (1H, m, 3-H), 4.53 (1H, m, 3′-H), 5.86 (1H, s, 7′-H), 6.27 (1H, d, *J* 11, 14-H), 6.30 (1H, d, *J* 11.5, 10-H), 6.35 (1H, d, *J* 15.5, 12-H), 6.37 (1H, d, *J* 10.5, 14′-H), 6.63 (1H, dd, *J* 15.5 and 12, 15′-H), 6.64 (1H, dd, *J* 15 and 10.5, 11′-H), 6.65 (1H, d, *J* 15, 12′-H), 6.71 (1H, dd, *J* 14 and 11, 15-H), 6.87 (1H, dd, *J* 15 and 11, 11-H), 7.23 (1H, d, *J* 10.5, 10′-H) (the cross peak was

observed between 11-H and 5-Me in the NOESY spectrum) (Found: M^+, 598.4001. $C_{40}H_{34}O_4$ requires *M*, 598.4025).

9*Z*,11*Z*-Isomer 29. λ_{max}/nm 463 and 296, $\lambda_{max}(Et_2O)$/nm 460, 447, 294; ν_{max}/cm^{-1} 3530 and 3321 (OH), 1602 (hydrogen-bonded conj. C=O); δ_H (500 MHz) 0.83 (3H, s, 1′-Me_α), 1.15 (3H, s, 1-Me_{ax}), 1.17 (3H, s, 1′-Me_β), 1.21 (3H, s, 1-Me_{eq}), 1.33 (3H, s, 5′-Me), 1.45 (1H, t, *J* 12, 2-H_{ax}), 1.56 (1H, m, 4′-H_β), 1.70 (1H, dd, *J* 14 and 5, 2′-H_β), 1.83 (1H, m, 2-H_{eq}), 1.93 (3H, s, 5-Me), 1.96 (3H, s, 9′-Me), 1.97 (3H, s, 13′-Me), 2.01 (3H, s, 9-Me), 2.05 (1H, m, 4-H_{ax}), 2.07 (1H, dd, *J* 13.5 and 8, 2′-H_α), 2.08 (3H, s, 13-Me), 2.43 (1H, br dd, *J* 17 and 5.5, 4-H_{eq}), 2.86 (1H, dd, *J* 14.5 and 8.5, 4′-H_α), 3.99 (1H, m, 3-H), 4.51 (1H, m, 3′-H), 5.84 (1H, s, 7′-H), 5.95 (1H, d, *J* 12.5, 12-H), 6.27 (1H, d, *J* 10, 14-H), 6.36 (1H, d, *J* 10.5, 14′-H), 6.50 (1H, t, *J* 12.5, 11-H), 6.58 (1H, dd, *J* 15 and 10.5, 11′-H), 6.61 (1H, dd, *J* 15 and 10.5, 15′-H), 6.63 (1H, d, *J* 15, 12′-H), 6.66 (1H, dd, *J* 15 and 10.5, 15-H), 6.78 (1H, d, *J* 12.5, 10-H), 7.21 (1H, d, *J* 10.5, 10′-H) (the cross peak was observed between 11-H and 12-H in the NOESY spectrum) (Found: M^+, 598.4018. $C_{40}H_{54}O_4$ requires *M*, 598.4025).

Acknowledgements

We thank Dr T. Maoka, Kyoto Pharmaceutical University for his kind gift of spectral data on natural mytiloxanthins. We are also grateful for the chemical support from Drs U. Hengartner and K. Bernherd, Hoffmann-La Roche Ltd., Basel, Switzerland.

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