Carotenoids and related polyenes. Part 7.[1] Total synthesis of crassostreaxanthin B applying the stereoselective rearrangement of tetrasubstituted epoxides †

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(3*R*,3′*S*)- and (3*R*,3′*R*)-Crassostreaxanthin B isomers are synthesized by application of the stereoselective rearrangement of tetrasubstituted epoxides **5a**,**b**. As a result, the absolute configuration at C-3′ of **1** is determined to be *S*.

Introduction

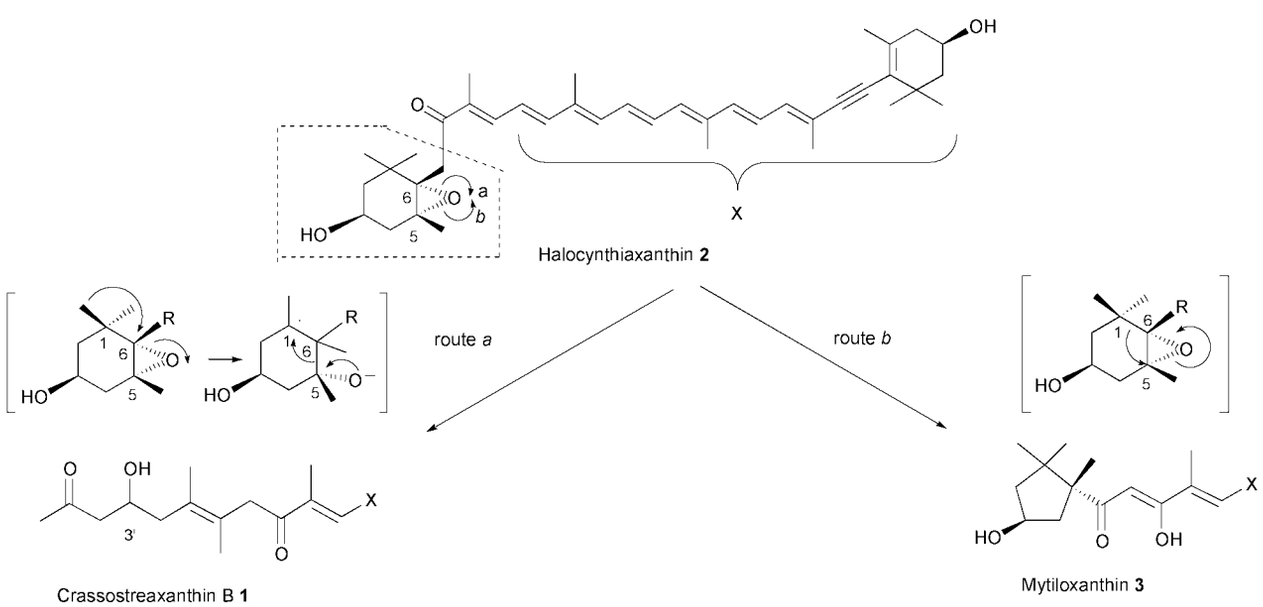
In 1992, crassostreaxanthin B **1** (Scheme 1) was isolated by Fujiwara *et al.*[2] from the viscera of the edible oyster *Crassostrea gigas*. The structure of **1** including the novel acyclic tetrasubstituted olefinic end group and β-end group with 3*R* chirality was determined by extensive modern NMR techniques and CD data. However, its absolute configuration at C-3′ has remained undetermined. We assumed that the tetrasubstituted olefinic end group was formed in Nature from the epoxide end group of 5,6-epoxy carotenoids such as halocynthiaxanthin[3] **2** by opening of the C-6–oxygen bond of the oxirane ring and subsequent rearrangement of the methyl group at C-1 (Scheme 1, route *a*). Thus, the absolute configuration at C-3′ in **1** is considered to be *S*, since chiralities at C-3 in most of the known natural epoxy carotenoids are *R*. On the other hand, mytiloxanthin[3b,4] **3** is also believed[5] to arise from 5,6-epoxy carotenoids by cleavage of the oxirane ring at C-5 and successive ring contraction (a pinacolic rearrangement) (Scheme 1, route *b*). In the previous communication,[6] we reported the first total synthesis of crassostreaxanthin B **1** *via* the tetrasubstituted olefinic compound **7** (Scheme 2), prepared by Lewis acid-promoted stereoselective rearrangement of epoxides **5a**,**b**, and the determination of the absolute configuration at C-3′ in **1**. Here, we give a full account of the experimental details.

† We have employed the numbering system used in carotenoids.

Results and discussion

Synthesis of the tetrasubstituted olefinic compound 7

Among several epoxides previously investigated,[7] epoxides **4a**,**b** (Scheme 2) with the acetoxypropyl group at the C-6 position provided, by treatment with $BF_3{\cdot}OEt_2$, the tetrasubstituted olefinic compound **6** in reasonable yield. It is significant that **6** was stereoselectively produced from both isomers **4a**,**b**. However, this reaction was accompanied by the elimination by-product **8** (Scheme 2). Thus, in order to accomplish the biomimetic synthesis of **1**, the acetoxy group at the C-3 position in **4a**,**b** was replaced by the *tert*-butyldimethylsilyl (TBS) ether leading to epoxides **5a**,**b**.



Scheme 1

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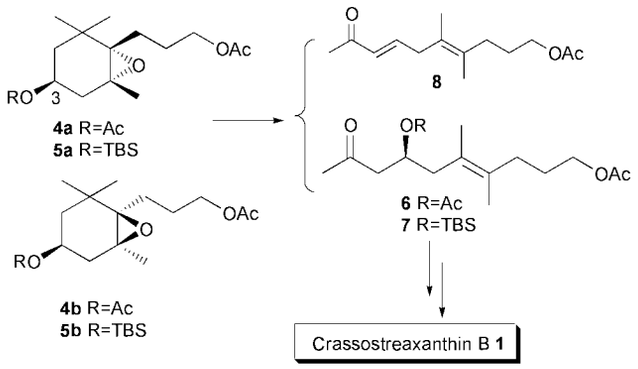


Scheme 2

As shown in Scheme 3, epoxides **5a**,**b** were synthesized starting from the known optically active ketone **9**,[8] which was treated with lithium trimethylsilylacetylide followed by basic hydrolysis to give the α-acetylenic alcohol **10** as a single product (98% from **9**). By rearrangement using tris(triphenylsilyl)vanadate (TPSV) catalyst,[9,10] this was converted to the β,γ-unsaturated aldehyde **11** quantitatively. Reduction of the formyl group in **11** with $NaBH_4$ gave the alcohol **12**, which was mesylated with MsCl in pyridine (Py) followed by treatment with KCN in the presence of 18-crown-6 to provide the nitrile **13** (89% from **12**). The nitrile **13** was transformed by DIBAL-H and successive $NaBH_4$ reduction into the alcohol **14** (73%), which was acetylated to provide compound **15** (94%). Epoxidation of **15** with MCPBA led to a mixture of the *anti*-epoxide **5a** and the *syn*-epoxide **5b** (98%; **5a** : **5b** = *ca.* 2 : 3), which were separated by column chromatography (CC) to yield the respective isomers in pure state. The relative configurations between the silyloxy and epoxy groups in the two isomers were confirmed by their ^1H NMR data.[8] Thus, epoxides **5a**,**b** were prepared in 10 steps from the ketone **9** in excellent overall yield (58%).

Reaction of *syn*-epoxide **5b** with $BF_3{\cdot}OEt_2$ as a Lewis acid provided the desired olefinic compound **7** (66%) and its deprotected alcohol **16** (19%). Resilylation of **16** resulted in the easy formation of **7**. On the other hand, the same treatment of *anti*-epoxide **5a** gave **16** (29%) and the cyclopentyl compound **17a** (32%), both of which were deprotected products. This is presumably due to the longer reaction time of **5a** than that of **5b**. Consequently, the change (Ac to TBS) of protecting group at the C-3 position was found to block the production of the elimination product **8** (Scheme 2). Structures of the products **7**, **16** and **17a** were deduced on the basis of their spectral data in comparison with previous results.[7] As the result of optimization of this rearrangement, it was found that treatment of a mixture of **5a**,**b** using $SnCl_4$ as a Lewis acid at low temperature provided the tetrasubstituted olefinic compounds **7** and **16** in high yield.

Synthesis of (3*R*,3′*S*)-crassostreaxanthin B 1a

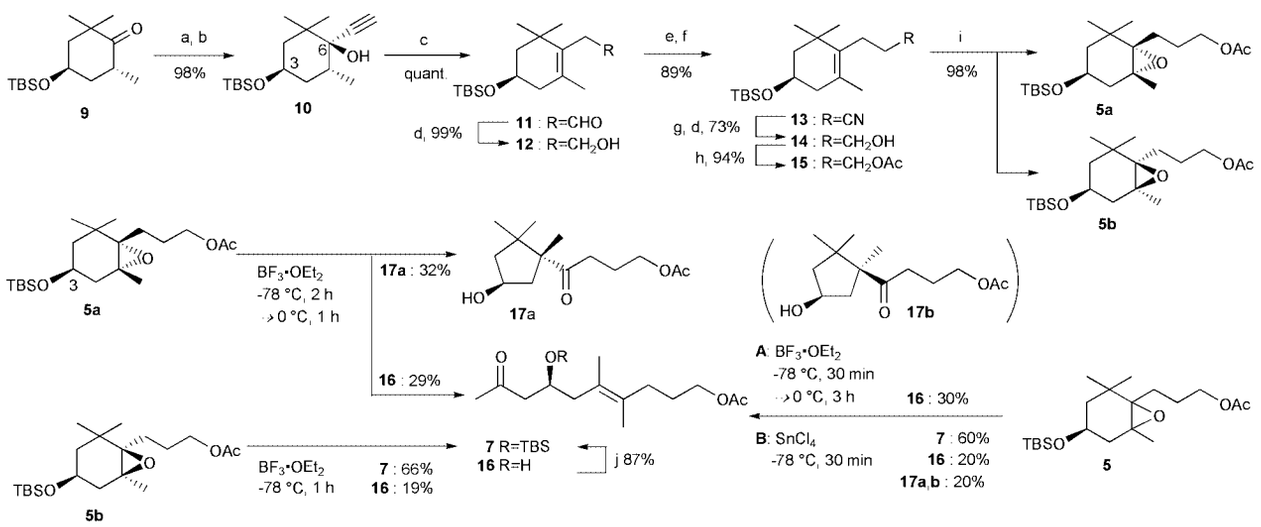
Synthesis of (3*R*,3′*S*)-crassostreaxanthin B **1a** was accomplished in 15 steps from the tetrasubstituted olefin **7** (Scheme 4). Ketalization[11] of **7** with ethylene glycol TMS ether (78%) followed by resilylation (92%) of the alcohol **18** gave **19** whose acetate moiety was reduced with LAH followed by PDC oxidation[12] to afford the carboxylic acid **20**. Treatment of **20** with $TMSCHN_2$[13] yielded the methyl ester **21** (64% from **19**). According to the developed method by Davis *et al.*,[14] the hydroxy group was introduced into the ester **21** by use of (+)-camphorylsulfonyloxaziridine **22** in the presence of LDA to give the α-hydroxy ester **23** (52%) as a diastereomeric mixture which, without separation, was reduced with LAH and the resulting glycol **24** was cleaved with $NaIO_4$ to afford the aldehyde **25** (92% from **23**). Reaction of this aldehyde **25** with vinyllithium prepared from the vinyl bromide **26**[15] and ^{t}BuLi gave the allyllic alcohol **27**, which was subjected to oxidation with MnO_2 and partial deprotection with TBAF followed by MnO_2 oxidation to yield the C_{15}-aldehyde **28** (53% from **25**).

The Wittig condensation of **28** with the C_{10}-phosphonium salt **30**[16] in the presence of NaOMe as a base followed by acid hydrolysis provided an isomeric mixture of C_{25}-apocarotenal **31** whose main isomer was shown to be all-*E* one by HPLC and ^1H NMR analysis.

Finally, the Wittig condensation between C_{25}-apocarotenal **31** and C_{15}-phosphonium salt **32**[17] using NaOMe as a base followed by deprotection of all protecting groups with PTSA gave an isomeric mixture of target compound, which was purified by repeated preparative HPLC (PHPLC) in the dark to afford (3*R*,3′*S*-all-*E*)-crassostreaxanthin B **1a** (6% from **28**) and a small amount of other isomers. Spectral data (IR, UV-VIS, ^1H NMR and MS) of synthetic **1a** were in good agreement with those of a natural specimen.[2] However, the absolute configuration at C-3′ in the native sample[18] could not be confirmed by comparison of CD data of synthetic and natural samples because these did not exhibit a clear Cotton effect.

Synthesis of (3*R*,3′*R*)-crassostreaxanthin B 1b and determination of the absolute configuration of natural crassostreaxanthin B

In order to confirm the absolute configuration at C-3′ in the native sample, (3*R*,3′*R*)-crassostreaxanthin B **1b** was independ-



Scheme 3 *Reagents and conditions*: a, LiC≡CTMS; b, 10% aq. KOH; c, TPSV (0.02 eq.), $PhCO_2H$ (0.02 eq.), commercial xylenes, reflux; d, $NaBH_4$; e, MsCl, Py; f, KCN, 18-crown-6; g, DIBAL-H; h, Ac_2O, Py; i, MCPBA: j, TBDMSCl, Et_3N, DMAP.

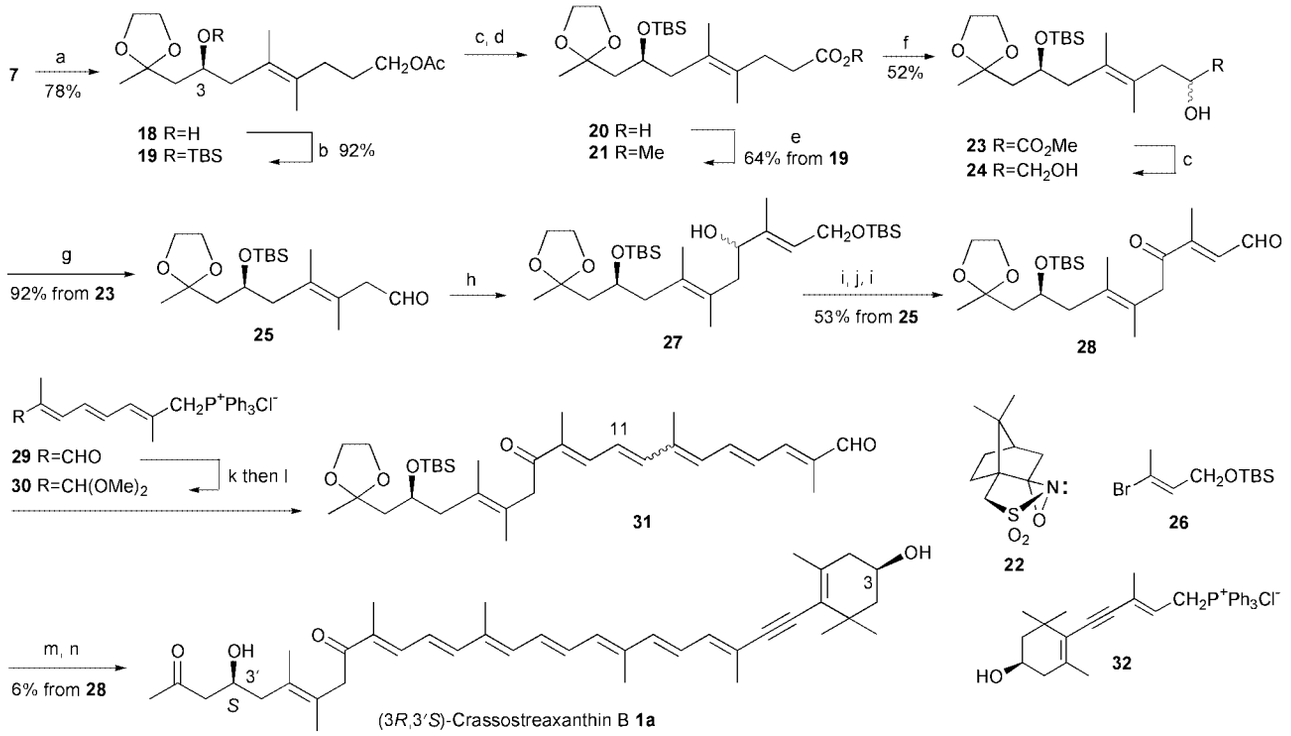
ently synthesized *via* (3*S*)-aldehyde **11** from the (4*S*,6*R*)-hydroxy ketone **33**[19] (Scheme 5) in the same manner as that described in the synthesis of (3*R*,3′*S*)-isomer **1a**. High optical purity of the (3*S*)-aldehyde **11** was confirmed from the result that the absolute value of specific rotation $\{[\alpha]_D^{26} +17 \times 10^{-1}$ deg cm^2 g^{-1} (*c* 1.00 MeOH)$\}$ of (3*S*)-**11** was the same as that of (3*R*)-aldehyde **11** $\{[\alpha]_D^{26} -18$ (*c* 1.00 MeOH)$\}$.

Separation of (3*R*,3′*S*)-**1a** and (3*R*,3′*R*)-**1b** on HPLC using a chiral column (CHIRALCEL OD; DAICEL) was achieved. By co-chromatography with the synthetic samples **1a** and **1b**, the native specimen[18] was shown to be identical with **1b**. Accordingly, the absolute configuration at the C-3′ position of natural crassostreaxanthin B was confirmed to be *S*.

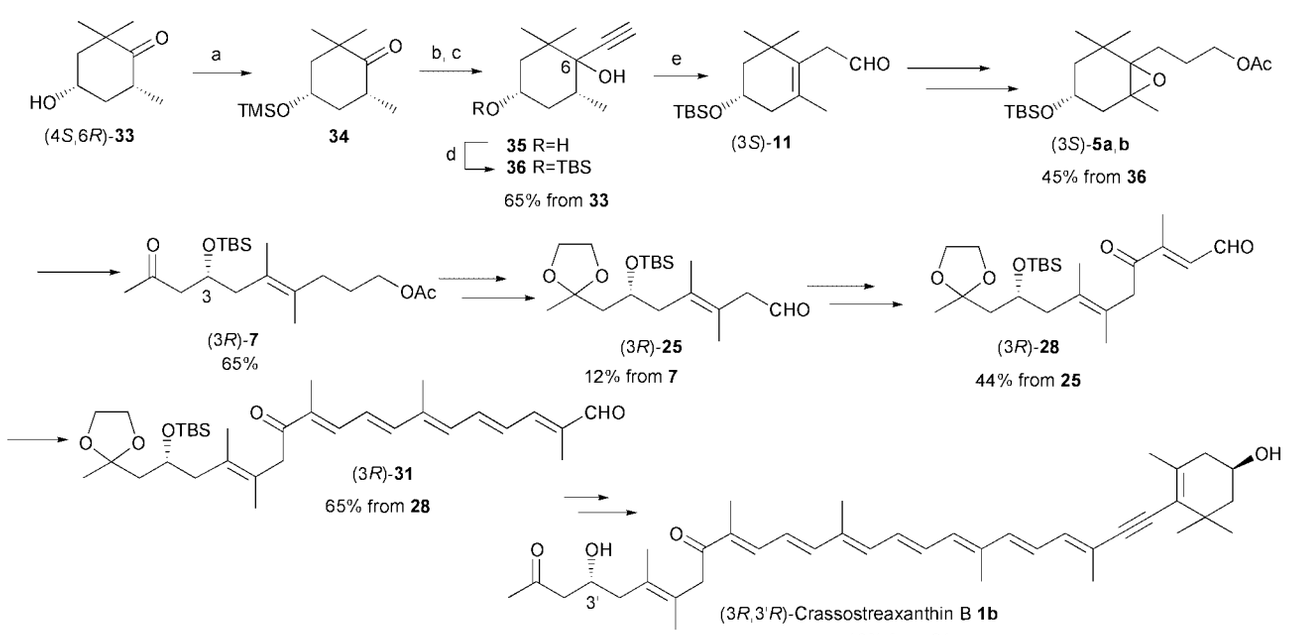
This is the first biomimetic total synthesis of optically active crassostreaxanthin B **1** by application of the stereoselective rearrangement of epoxides **5a**,**b** with $SnCl_4$.

Experimental

UV-VIS spectra were recorded on a JASCO Ubest-55 instrument. IR spectra were measured on a Shimadzu IR-27G 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 Gemini-200, a Varian Gemini-300, or a Varian VXR-500 superconducting FT-NMR spectrometer, respectively, for



Scheme 4 *Reagents and conditions*: a, $(CH_2OTMS)_2$, cat. TMSOTf; b, TBSOTf, 2,6-lutidine; c, LAH; d, PDC, DMF; e, $TMSCHN_2$; f, LDA, **22**; g, $NaIO_4$; h, **26**, ^{t}BuLi; i, MnO_2; j, TBAF; k, $HC(OMe)_3$, cat. H^+; l, 1 M NaOMe, then H^+; m, **32**, 1 M NaOMe; n, PTSA.



Scheme 5 *Reagents and conditions*: a, TMSCl, Et_3N; b, LiC≡CTMS; c, 10% aq. KOH; d, TBSCl, Et_3N, DMAP; e, TPSV (0.02 eq.), $PhCO_2H$ (0.02 eq.), commercial xylenes, reflux.

deuteriochloroform solutions (tetramethylsilane as internal reference). *J*-Values are given in Hz. Locants reported in the NMR spectra follow the carotenoid numbering displayed in the Schemes, and do not necessarily follow the systematic nomenclature used to name each individual compound. 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}).

Column chromatography (CC) was performed on silica gel (Merck Art. 7734). Short-column chromatography (SCC) was performed on silica gel (Merck Art. 7739) under reduced pressure. Analytical and PHPLC was carried out on Shimadzu LC-5A and 6A, or Waters 510 and 515 instruments with a UV-VIS detector.

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.

(1*S*,4*R*,6*R*)-4-*tert*-Butyldimethylsilyloxy-1-ethynyl-2,2,6-trimethylcyclohexanol 10

BuLi (1.53 M in hexane; 49 ml, 75 mmol) was added to a solution of TMSacetylene (10.6 ml, 75 mmol) in dry THF (25 ml) at 0 °C and the mixture was stirred for a further 30 min. To this mixture was added dropwise a solution of the ketone **9**[8] (13.5 g, 50 mmol) in dry THF (25 ml) at 0 °C and the reaction mixture was stirred for 30 min. The reaction was quenched with saturated aq. NH_4Cl. After evaporation off of the THF, the residue was extracted with Et_2O. Standard work-up gave the crude compound which, without purification, was dissolved in MeOH (50 ml), and 10% aq. KOH (20 ml) was added to it. After being stirred at rt for 1 h, the reaction mixture was evaporated to remove the MeOH, and the residue was extracted with Et_2O. Standard work-up afforded a residue, which was purified by CC (Et_2O–hexane, 1 : 9) to give the acetylenic alcohol **10** (14.56 g, 98%) as a colorless oil; ν_{max}/cm^{-1} 3608 (OH), 3305 (≡CH), 2107 (C≡C); δ_H (300 MHz) 0.02 (6H, s, SiMe × 2), 0.89 (9H, s, Si^{t}Bu), 1.06 (3H, d, *J* 6.5, 5-Me), 1.08 and 1.20 (each 3H, s, *gem*-Me), 1.46–1.71 (4H, m, 2-H_2 and 4-H_2), 1.86 (1H, s, OH), 2.31 (1H, m, 5-H), 2.45 (1H, s, 8-H), 3.94 (1H, quint, *J* 3, 3-H) [Found: (M − CH_3)$^+$, 281.1928. $C_{16}H_{29}O_2Si$ requires *M* − CH_3, 281.1938].

[(4*R*)-4-*tert*-Butyldimethylsilyloxy-2,6,6-trimethylcyclohex-1-enyl]acetaldehyde 11

To a solution of the acetylenic alcohol **10** (14.42 g, 49 mmol) in xylenes (100 ml) were added $(Ph_3SiO)_3VO$ (869 mg, 0.97 mmol) and $PhCO_2H$ (119 mg, 0.97 mmol), then the reaction mixture was refluxed for 3.5 h. After evaporation off of the solvent, the residue was purified by SCC (acetone–hexane, 1 : 9) to give the β,γ-unsaturated aldehyde **11** (14.42 g, quant.) as a colorless oil; $[\alpha]_D^{26}$ −18.0 (*c* 1.00, MeOH); ν_{max}/cm^{-1} 1718 (CHO); δ_H (300 MHz) 0.08 (6H, s, SiMe × 2), 0.90 (9H, s, Si^{t}Bu), 0.99 and 1.00 (each 3H, s, *gem*-Me), 1.52 (1H, t, *J* 12, 2-H_{ax}), 1.58 (3H, s, 5-Me), 1.67 (1H, ddd, *J* 12, 3.5 and 2.5, 2-H_{eq}), 2.09 (1H, dd, *J* 16.5 and 9, 4-H_{ax}), 2.21 (1H, dd, *J* 16.5 and 5.5, 4-H_{eq}), 3.08 (2H, br s, 7-H_2), 3.94 (1H, m, 3-H), 9.50 (1H, t, *J* 2.5, CHO) [Found: (M − CH_3)$^+$, 281.1916. $C_{16}H_{29}O_2Si$ requires *M* − CH_3, 281.1938].

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

$NaBH_4$ (1.85 g, 49 mmol) was added to an ice-cooled solution of the aldehyde **11** (14.42 g, 49 mmol) in MeOH (80 ml). The mixture was stirred at 0 °C for 10 min and then poured into ice–water, and extracted with Et_2O. Standard work-up afforded a residue, which was purified by SCC (acetone–hexane, 1 : 4) to yield the alcohol **12** (14.44 g, 99%) as a colorless oil; $[\alpha]_D^{27}$ −48.0 (*c* 1.00, MeOH); ν_{max}/cm^{-1} 3621 and 3453 (OH); δ_H (300 MHz) 0.07 (6H, s, SiMe × 2), 0.89 (9H, s, Si^{t}Bu), 1.02 and 1.03 (each 3H, s, *gem*-Me), 1.44 (1H, t, *J* 12, 2-H_{ax}), 1.61 (1H, m, 2-H_{eq}), 1.64 (3H, s, 5-Me), 1.99 (1H, ddd, *J* 16.5, 9.5 and 1, 4-H_{ax}), 2.11 (1H, br dd, *J* 16.5 and 6, 4-H_{eq}), 2.33 (2H, m, 7-H_2), 3.59 (2H, m, 8-H_2), 3.89 (1H, m, 3-H) [Found: (M − CH_3)$^+$, 283.2084. $C_{16}H_{31}O_2Si$ requires *M* − CH_3, 283.2094].

3-[(4*R*)-4-*tert*-Butyldimethylsilyloxy-2,6,6-trimethylcyclohex-1-enyl]propanenitrile 13

MsCl (4.64 ml, 60 mmol) was added to a solution of the alcohol **12** (9.18 g, 31 mmol) in dry Py (20 ml) at 0 °C and the mixture was stirred at rt for 1 h. The reaction mixture was poured into ice–water, and extracted with Et_2O. The extracts were washed successively with 5% aq. HCl, saturated aq. $NaHCO_3$ and brine. Evaporation of the dried extracts gave a residue, which was purified by SCC (Et_2O–hexane, 3 : 17) to afford the mesylester (10.55 g, 91%) as a colorless oil. KCN (3.65 g, 56 mmol) was added to a solution of the mesylester (10.55 g, 28 mmol) and 18-crown-6 (740 mg, 2.8 mmol) in dry DMSO (60 ml) at rt and the mixture was stirred vigorously and warmed at 120 °C for 16 h. After cooling, the mixture was poured into ice–water carefully and extracted with Et_2O. Standard work-up gave a residue, which was purified by SCC (Et_2O–hexane, 1 : 9) to afford the nitrile **13** (7.64 g, 89%) as a colorless oil; $[\alpha]_D^{25}$ −41.0 (*c* 1.00, MeOH); ν_{max}/cm^{-1} 2247 (CN); δ_H (300 MHz) 0.06 (6H, s, SiMe × 2), 0.88 (9H, s, Si^{t}Bu), 1.02 and 1.03 (each 3H, s, *gem*-Me), 1.44 (1H, t, *J* 12, 2-H_{ax}), 1.62 (1H, m, 2-H_{eq}), 1.63 (3H, s, 5-Me), 1.99 (1H, br dd, *J* 17 and 9, 4-H_{ax}), 2.13 (1H, ddd, *J* 17, 5.5 and 1, 4-H_{eq}), 2.38 (4H, m, 7-H_2 and 8-H_2), 3.88 (1H, m, 3-H) [Found: (M − CH_3)$^+$, 292.2122. $C_{17}H_{30}NOSi$ requires *M* − CH_3, 292.2096].

3-[(4*R*)-4-*tert*-Butyldimethylsilyloxy-2,6,6-trimethylcyclohex-1-enyl]propan-l-ol 14

A solution of DIBAL-H (1.0 M in hexane; 43 ml, 43 mmol) was added to a solution of the nitrile **13** (6.28 g, 20.5 mmol) in dry Et_2O (70 ml) at 0 °C and the mixture was stirred at 0 °C for 1 h. The excess of DIBAL-H was destroyed by addition of water and the mixture was extracted with Et_2O. Standard work-up gave the aldehyde which, without purification, was dissolved in MeOH (35 ml). $NaBH_4$ (780 mg, 20.5 mmol) was added to the solution at 0 °C and this was stirred at 0 °C for 20 min. After evaporation of MeOH, the residue was extracted with Et_2O. Standard work-up gave a residue, which was purified by SCC (acetone–hexane, 1 : 4) to afford the alcohol **14** (4.66 g, 73%) as a colorless oil; $[\alpha]_D^{25}$ −44.0 (*c* 1.00, MeOH); ν_{max}/cm^{-1} 3624 and 3453 (OH); δ_H (300 MHz) 0.07 (6H, s, SiMe × 2), 0.89 (9H, s, Si^{t}Bu), 1.01 and 1.03 (each 3H, s, *gem*-Me), 1.45 (1H, t, *J* 12, 2-H_{ax}), 1.62 (3H, m, 2-H_{eq} and 7-H_2), 1.60 (3H, s, 5-Me), 2.02 (4H, m, 4-H_2 and 8-H_2), 3.64 (2H, t, *J* 6.5, 9-H_2), 3.90 (1H, m, 3-H) [Found: (M − CH_3)$^+$, 297.2263. $C_{17}H_{33}O_2Si$ requires *M* − CH_3, 297.2254].

3-[(4*R*)-4-*tert*-Butyldimethylsilyloxy-2,6,6-trimethylcyclohex-1-enyl]propyl acetate 15

Ac_2O (6 ml) was added to a solution of the alcohol **14** (3.04 g, 9.74 mmol) in dry Py (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 successively with 5% aq. 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 **15** (3.24 g, 94%) as a colorless oil; $[\alpha]_D^{26}$ −42.0 (*c* 1.00, MeOH); ν_{max}/cm^{-1} 1731 (C=O); δ_H (300 MHz) 0.06 (6H, s, SiMe × 2), 0.89 (9H, s, Si^{t}Bu), 1.00 and 1.01 (each 3H, s, *gem*-Me), 1.44 (1H, t, *J* 12, 2-H_{ax}), 1.59 (3H, s, 5-Me), 1.59 (1H, m, 2-H_{eq}), 1.68 (2H, m, 7-H_2), 1.91 (2H, m, 8-H_2), 1.99 (1H, dd, *J* 16.5 and 9, 4-H_{ax}), 2.05 (3H, s, OAc),

2.09 (1H, br dd, *J* 16.5 and 6, 4-H_{eq}), 3.89 (1H, m, 3-H), 4.05 (2H, t, *J* 6.5, 9-H_2) [Found: $(M - CH_3)^+$, 339.2367. $C_{19}H_{35}O_3Si$ requires $M - CH_3$, 339.2357].

3-[(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]propyl acetate 5a and 5b

A solution of MCPBA (70%, 1.88 g, 7.62 mmol) in dry CH_2Cl_2 (30 ml) was added to an ice-cooled solution of the acetate **15** (2.08 g, 5.88 mmol) in dry CH_2Cl_2 (20 ml). After being stirred at 0 °C for 2 h, the reaction mixture was diluted with Et_2O and washed successively with 1% aq. $Na_2S_2O_3$, 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 a diastereomeric mixture of epoxides **5a** and **5b** (*ca.* 2 : 3) (2.13 g, 98%) as a colorless oil. Purification of a part of this mixture by CC (benzene–hexane, 2 : 98) gave each isomer, the *anti*-epoxide **5a** and *syn*-epoxide **5b**, in a pure form.

***anti*-Epoxide 5a.** $[\alpha]_D^{26}$ −16.0 (*c* 1.00, MeOH); ν_{max}/cm^{-1} 1732 (C=O); δ_H (300 MHz) 0.03 (6H, s, SiMe × 2), 0.87 (9H, s, Si^{t}Bu), 1.03 and 1.15 (each 3H, s, *gem*-Me), 1.19 (1H, dd, *J* 13 and 10, 2-H_{ax}), 1.31 (3H, s, 5-Me), 1.43 (1H, ddd, *J* 13, 3.5 and 2, 2-H_{eq}), 1.62 (1H, dd, *J* 14.5 and 8, 4-H_{ax}), 1.79 (4H, m, 7-H_2 and 8-H_2), 2.04 (3H, s, OAc), 2.18 (1H, ddd, *J* 14.5, 5 and 2, 4-H_{eq}), 3.77 (1H, m, 3-H), 4.03 (2H, m, 9-H_2) [Found: $(M - CH_3)^+$, 355.2289. $C_{19}H_{35}O_4Si$ requires $M - CH_3$, 355.2306].

***syn*-Epoxide 5b.** $[\alpha]_D^{25}$ −27.0 (*c* 1.00, MeOH); ν_{max}/cm^{-1} 1732 (C=O); δ_H (300 MHz) 0.03 (6H, s, SiMe × 2), 0.86 (9H, s, Si^{t}Bu), 1.03 and 1.07 (each 3H, s, *gem*-Me), 1.10 (1H, ddd, *J* 12.5, 4 and 2, 2-H_{eq}), 1.25 (3H, s, 5-Me), 1.52 (1H, t, *J* 12, 2-H_{ax}), 1.68 (4H, m, 7-H_2 and 8-H_2), 1.80 (1H, dd, *J* 15 and 9.5, 4-H_{ax}), 1.99 (1H, ddd, *J* 15, 7.5 and 2, 4-H_{eq}), 2.04 (3H, s, OAc), 3.76 (1H, m, 3-H), 4.03 (2H, m, 9-H_2) [Found: $(M - CH_3)^+$, 355.2303. $C_{19}H_{35}O_4Si$ requires $M - CH_3$, 355.2306].

Rearrangement of *syn*-epoxide 5b using $BF_3{\cdot}OEt_2$

To a solution of **5b** (200 mg, 0.54 mmol) in dry CH_2Cl_2 (10 ml) was added dropwise 47% $BF_3{\cdot}OEt_2$ (0.49 g, 1.62 mmol) at −78 °C and the mixture was stirred at −78 °C for 1 h. The reaction mixture was diluted with Et_2O and 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 (Et_2O–hexane, 3 : 7) to afford the tetrasubstituted olefinic compound **7** (131 mg, 66%) and the deprotected compound **16** (27 mg, 19%) as colorless oils, respectively.

Tetrasubstituted olefin 7. $[\alpha]_D^{26}$ +8.12 (*c* 1.11, MeOH); ν_{max}/cm^{-1} 1724 (C=O); δ_H (500 MHz) 0.02 and 0.05 (each 3H, s, SiMe × 2), 0.85 (9H, s, Si^{t}Bu), 1.65 and 1.66 (each 3H, s, 5-Me and 6-Me), 1.67 (2H, quint-like, *J* 8, 8-H_2), 2.04 (3H, s, OAc), 2.06 (2H, m, 7-H_2), 2.14 (3H, s, 1-Me), 2.22 (2H, d, *J* 6.5, 4-H_2), 2.41 (1H, dd, *J* 15.5 and 4.5, 2-H), 2.55 (1H, dd, *J* 15 and 7.5, 2-H), 4.02 (2H, t, *J* 7, 9-H_2), 4.28 (1H, m, 3-H) [Found: $(M - CH_3)^+$, 355.2282. $C_{19}H_{35}O_4Si$ requires $M - CH_3$, 355.2306].

Deprotected compound 16. $[\alpha]_D^{27}$ +3.64 (*c* 1.10, MeOH); ν_{max}/cm^{-1} 3673 and 3468 (OH), 1728 (C=O); δ_H (300 MHz) 1.67 (6H, s, 5-Me and 6-Me), 1.70 (2H, tt, *J* 8 and 6.5, 8-H_2), 2.04 (3H, s, OAc), 2.12 (2H, t, *J* 8, 7-H_2), 2.13 (1H, dd, *J* 13.5 and 4,2-H), 2.18 (3H, s,1-Me), 2.33 (1H, dd, *J* 13.5 and 7.5, 2-H), 2.56 (1H, d, *J* 7.5, 4-H), 2.56 (1H, d, *J* 4.5, 4-H), 4.02 (2H, br t, *J* 6.5, 9-H_2), 4.17 (1H, m, 3-H) (Found: M^+, 256.1687. $C_{14}H_{24}O_4$ requires *M*, 256.1676).

Treatment of the *anti*-epoxide 5a with $BF_3{\cdot}OEt_2$

In the same manner as described above, *anti*-epoxide **5a** 200 mg (0.54 mmol) was treated with 47% $BF_3{\cdot}OEt_2$ (0.49 g, 1.62 mmol) at −78 °C for 2 h and at 0 °C for 1 h to provide the cyclopentyl compound **17a** (87 mg, 32%) and the tetrasubstituted olefinic compound **16** (81 mg, 29%) as colorless oils, respectively.

Cyclopentyl compound 17a. $[\alpha]_D^{28}$ +10.1 (*c* 0.89, MeOH); ν_{max}/cm^{-1} 3611 and 3504 (OH), 1725 (OAc); δ_H (300 MHz) 0.81, 1.16 and 1.31 (each 3H, s, Me × 3), 1.47 (1H, dd *J* 14.5 and 3, 4-H_β), 1.67 (1H, dd, *J* 13.5 and 4.5, 2-H_β), 1.86 (2H, m, 8-H_2), 1.98 (1H, dd, *J* 13.5 and 7.5, 2-H_α), 2.03 (3H, s, OAc), 2.47, 2.56 (each, 1H, dt, *J* 18 and 6.5, 7-H_2), 2.81 (1H, dd, *J* 14.5 and 8.5, 4-H_α), 4.06 (2H, t, *J* 6.5, 9-H_2), 4.48 (1H, m, 3-H) [Found: $(M + H)^+$, 226.1751. $C_{14}H_{25}O_4$ requires M + H, 226.1574].

Treatment of the mixture of epoxides 5a,b with $SnCl_4$

To a solution of the above mixture of epoxides **5a** and **5b** (*ca.* 2 : 3) (4.43 g, 12 mmol) in dry CH_2Cl_2 (40 ml) was added dropwise $SnCl_4$ (1 M in CH_2Cl_2; 36 ml, 36 mmol) at −78 °C and the mixture was stirred at −78 °C for 30 min. The reaction mixture was diluted with Et_2O and 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 (Et_2O–hexane, 3 : 17) to afford the cyclopentyl compounds **17a**,**b** (0.60 g, 20%), the tetrasubstituted olefinic compound **7** (2.82 g, 60%) and the deprotected olefinic compound **16** (0.62 g, 20%) as colorless oils, respectively. Spectral data (IR, ^{1}H NMR and MS) of **7** and **16** were in agreement with data already shown.

Reprotection of the alcohol 16

TBSCl (0.82 g, 5.5 mmol) was added to a stirred solution of the alcohol **16** (1.08 g, 4.2 mmol), Et_3N (1.76 ml, 12.6 mmol) and DMAP (1.03 g, 8.4 mmol) in dry CH_2Cl_2 (10 ml) at rt. After being stirred at rt for 15 h, the mixture was poured into ice–water and extracted with Et_2O. The extracts were washed successively with 5% aq. HCl, saturated aq. $NaHCO_3$ and brine. Evaporation of the dried extracts gave a residue, which was purified by SCC (Et_2O–hexane, 3 : 17) to afford compound **7** (1.35 g, 87%) as a colorless oil. Spectral data (IR, ^{1}H NMR and MS) of **7** was in agreement with the rearranged compound of **5b** by $BF_3{\cdot}OEt_2$.

(4*E*,7*S*)-7-*tert*-Butyldimethylsilyloxy-4,5-dimethyl-8-(2-methyl-1,3-dioxolan-2-yl)oct-4-enyl acetate 19

A solution of TMSOTf (0.6 ml, 2.9 mmol) in dry CH_2Cl_2 (6 ml) was added dropwise to a stirred solution of the tetrasubstituted olefinic compound **7** (1.68 g, 4.5 mmol) and ethylenedioxydi-(trimethylsilane) (1.87 g, 9.1 mmol) in dry CH_2Cl_2 (15 ml) at −78 °C and the mixture was stirred at −78 °C for 1 h. Then, Py (0.2 ml) was added to the reaction mixture at −78 °C and the mixture was stirred for 10 min and was poured into saturated aq. $NaHCO_3$ and extracted with Et_2O. The organic layer was dried over a mixture of anhydrous Na_2SO_4 and anhydrous Na_2CO_3 (1 : 1) and evaporated to afford a residue, which was purified by SCC (Et_2O–hexane, 1 : 9 ⟶ acetone–hexane, 1 : 3) to give the ethylenedioxy alcohol **18** (1.06 g, 78%) as a colorless oil. Then, to a stirred solution of the alcohol **18** (1.06 g, 3.53 mmol) and 2,6-dimethylpyridine(2,6-lutidine) (1.67 ml, 10 mmol) in dry THF (20 ml) was added TBSOTf (1.54 ml, 6.7 mmol) at 0 °C and the mixture was stirred at 0 °C for 3 h. The reaction mixture was diluted with Et_2O and the organic layer was washed successively with saturated aq. oxalic acid, saturated aq. $NaHCO_3$ and brine. Evaporation of the dried solution gave a residue, which was purified by SCC (Et_2O–hexane, 2 : 8) to afford compound **19** (1.27 g, 92%) as a colorless oil; $[\alpha]_D^{26}$ +11.1 (*c* 0.90, MeOH); ν_{max}/cm^{-1} 1731 (OAc); δ_H (500 MHz) 0.01 and 0.06 (each 3H, s, SiMe × 2), 0.87 (9H, s, Si^{t}Bu), 1.35 (3H, s, 1-Me), 1.65 and 1.66 (each 3H, br s, 5-Me and 6-Me), 1.68 (2H, m, 8-H_2), 1.80 (2H, br d, *J* 5, 2-H_2), 2.05

(3H, s, OAc), 2.09 (2H, m, 7-H_2), 2.18 (1H, dd, *J* 14 and 7.5, 4-H), 2.34 (1H, dd, *J* 14 and 5.5, 4-H), 3.90 (4H, m, OCH_2-CH_2O), 3.97 (1H, m, 3-H), 4.03 (2H, t, *J* 6.5, 9-H_2) (Found: M^+, 414.2815. $C_{22}H_{42}O_3Si$ requires *M*, 414.2803).

Methyl (4*E*,7*S*)-7-*tert*-butyldimethylsilyloxy-4,5-dimethyl-8-(2-methyl-1,3-dioxolan-2-yl)oct-4-enoate 21

A solution of the acetate **19** (614 mg, 1.48 mmol) in dry Et_2O (13 ml) was added dropwise to a stirred suspension of LAH (56.2 mg, 1.48 mmol) in dry Et_2O (13 ml) at 0 °C and the mixture was stirred at 0 °C for 20 min. The excess of LAH was decomposed by dropwise addition of water and the mixture was extracted with Et_2O. Standard work-up gave the hydroxy compound which, without purification, was dissolved in dry DMF (4 ml). To this solution was added PDC (2.05 g, 5.34 mmol) and the mixture was stirred at rt for 15 h. The reaction mixture was filtered through Celite and the filtrate was diluted with AcOEt and washed with brine. Evaporation of the dried solution gave a residue, which was purified by SCC (acetone–hexane, 3 : 7) to afford the carboxylic acid **20** (428 mg, 75%) as a colorless oil; ν_{max}/cm^{-1} 3000 and 1709 (COOH). This carboxylic acid **20** was dissolved in a mixture of MeOH–benzene (2 : 7), and $TMSCHN_2$ (2 M in hexane; 0.83 ml, 1.66 mmol) was added dropwise to the solution. After being stirred at rt for 30 min, the reaction mixture was concentrated to give a residue, which was purified by SCC (Et_2O–hexane, 3 : 17) to afford the ester **21** (377 mg, 85%) as a colorless oil; $[\alpha]_D^{26}$ −2.00 (*c* 1.00, MeOH); ν_{max}/cm^{-1} 1731 (C=O); δ_H (300 MHz) 0.02 and 0.05 (each 3H, s, SiMe × 2), 0.87 (9H, s, Si^{t}Bu), 1.35 (3H, s, 1-Me), 1.67 (6H, s, 5-Me and 6-Me), 1.81 (2H, d, *J* 5.5, 2-H_2), 2.19 (1H, dd, *J* 13.5 and 7.5, 4-H), 2.34 (1H, dd, *J* 13.5 and 5.5, 4-H), 2.34 (4H, m, 7-H_2 and 8-H_2), 3.67 (3H, s, CO_2Me), 3.93 (5H, m, 3-H and OCH_2CH_2O) (Found: M^+, 400.2636. $C_{21}H_{40}O_5Si$ requires *M*, 400.2647).

(3*E*,6*S*)-6-*tert*-Butyldimethylsilyloxy-3,4-dimethyl-7-(2-methyl-1,3-dioxolan-2-yl)hept-3-enal 25

A solution of the ester **21** (400 mg, 1 mmol) in dry THF (5 ml) was added to a stirred solution of LDA, prepared from BuLi (1.59 M in hexane; 1.26 ml, 2 mmol) and diisopropylamine (0.28 ml, 2 mmol) in THF (2 ml), at −78 °C and the mixture was stirred at −78 °C for 10 min and at 0 °C for 1 h. Then to the reaction mixture was added a solution of Davis reagent **22** [(+)-camphorylsulfonyloxaziridine] (344 mg, 1.5 mmol) in dry THF (4 ml) at 0 °C and the mixture was stirred at 0 °C for 1.5 h. The reaction mixture was quenched with saturated aq. NH_4Cl and then extracted with AcOEt. The extracts were washed with saturated aq. $Na_2S_2O_3$, dried and evaporated to give a residue, which was purified by SCC (acetone–hexane, 1 : 9) to afford the hydroxy ester **23** (217 mg, 52%) as a colorless oil. Next, a solution of **23** (210 mg, 0.5 mmol) in dry Et_2O (8 ml) was added dropwise to a suspension of LAH (20.1 mg, 0.53 mmol) at 0 °C and the mixture was stirred at 0 °C for 30 min. The excess of LAH was decomposed by dropwise addition of water and the mixture was extracted with AcOEt. Standard work-up gave the 1,2-diol **24** which, without purification, was dissolved in a mixture of 1,4-dioxane–water (3 : 1; 12 ml). To this solution was added $NaIO_4$ (208 mg, 0.97 mmol) and the mixture was stirred at rt for 1 h. The reaction mixture was extracted with Et_2O. Standard work-up afforded a residue, which was purified by SCC (acetone–hexane, 1 : 9) to yield the aldehyde **25** (166 mg, 92% from **23**) as a colorless oil; $[\alpha]_D^{27}$ −4.69 (*c* 0.64, MeOH); ν_{max}/cm^{-1} 1719 (CHO); δ_H (300 MHz) 0.01 and 0.06 (each 3H, s, SiMe × 2), 0.87 (9H, s, Si^{t}Bu), 1.36 (3H, s, 1-Me), 1.71 and 1.76 (each 3H, s, 5-Me and 6-Me), 1.85 (2H, m, 2-H), 2.28 (1H, dd, *J* 13.5 and 8, 4-H), 2.46 (1H, dd, *J* 13.5 and 5, 4-H), 3.08 and 3.16 (each 1H, dd, *J* 15.5 and 2.5, 7-H_2), 3.91 (4H, m, OCH_2-CH_2O), 3.97 (1H, m, 3-H), 9.57 (1H, t, *J* 2.5, CHO) (Found: M^+, 356.2356. $C_{19}H_{36}O_4Si$ requires *M*, 356.2385).

(2*E*,6*E*,9*S*)-9-*tert*-Butyldimethylsilyloxy-3,6,7-trimethyl-10-(2-methyl-1,3-dioxolan-2-yl)-4-oxodeca-2,6-dienal 28

To a stirred solution of the vinyl bromide **26** (199 mg, 0.75 mmol) in dry Et_2O (2 ml) was added ^{t}BuLi (1.64 M in pentane; 0.46 ml, 0.75 mmol) at −78 °C and the mixture was stirred at −78 °C for 10 min. Then the aldehyde **25** (107 mg, 0.3 mmol) was added to this mixture at −78 °C and the reaction mixture was stirred 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 alcohol **27** (133 mg, 81%) as a colorless oil. Then, a solution of the alcohol **27** (133 mg, 0.25 mmol) in Et_2O–hexane (1 : 2; 6 ml) was shaken with active MnO_2 (1.33 g) at rt for 8 h. The mixture was filtered through Celite. Evaporation of the filtrate gave crude products which, without purification, were dissolved in THF (3.5 ml). A solution of TBAF (1 M in THF; 0.24 ml, 0.24 mmol) was added to the above solution and the mixture was stirred at rt for 30 min. This was diluted with AcOEt and the organic layer was washed with brine. Evaporation of the dried solution gave a residue, which was purified by SCC (acetone–hexane, 1 : 4) to provide the allyl alcohol (103 mg, 98%, from **27**) as a colorless oil. Again, a solution of the alcohol (103 mg, 0.24 mmol) in a mixture of Et_2O–hexane (1 : 2; 6 ml) was shaken with active MnO_2 (513 mg) at rt for 3 h. The mixture was filtered through Celite. Evaporation of the filtrate gave a residue, which was purified by SCC (acetone–hexane, 3 : 17) to give the aldehyde **28** (69 mg, 67%; 53% from **25**) as a colorless oil; $[\alpha]_D^{22}$ −3.00 (*c* 1.00, MeOH); λ_{max}(EtOH)/nm 242; ν_{max}/cm^{-1} 1681 (conj. C=O and conj. CHO); δ_H (300 MHz) 0.01 and 0.07 (each 3H, s, SiMe × 2), 0.87 (9H, s, Si^{t}Bu), 1.36 (3H, s, 1-Me), 1.65 and 1.67 (each 3H, s, 5-Me and 6-Me), 1.80 (1H, dd, *J* 14.5 and 5, 2-H), 1.88 (1H, dd, *J* 14.5 and 6, 2-H), 2.25 (1H, dd, *J* 14 and 7.5,4-H), 2.26 (3H, d, *J* 1.5, 9-Me), 2.44 (1H, dd, *J* 13.5 and 6, 4-H), 3.41 and 3.54 (each 1H, d, *J* 16.5, 7-H_2), 3.93 (4H, m, OCH_2CH_2O), 3.97 (1H, m, 3 H), 6.58 (1H, dq, *J* 7.5 and 1.5, 10-H), 10.26 (1H, d, *J* 7.5, CHO) (Found: M^+, 424.2645. $C_{23}H_{40}O_5Si$ requires *M*, 424.2643).

(2*E*,4*E*,6*E*,8*E*,10*E*,14*E*, 17*S*)- and (2*E*,4*E*,6*E*,8*Z*,10*E*,14*E*,17*S*)-17-*tert*-Butyldimethylsilyloxy-2,7,11,14,15-pentamethyl-18-(2-methyl-1,3-dioxolan-2-yl)-12-oxooctadeca-2,4,6,8,10,14-hexaenal 31a and 31b

An acidic solution (0.29 ml) prepared from PTSA (500 mg) and H_3PO_4 (725 mg) in MeOH (37.5 ml) and trimethyl orthoformate (0.29 ml, 2.65 mmol) was added to a solution of the Wittig salt **29**[16] (316.3 mg, 0.71 mmol) in MeOH (4 ml). The mixture was stirred at rt for 1 h and neutralized with NaOMe until just before the red color of an ylide appeared, to give a solution of the Wittig salt **30**. To this solution were added a solution of the aldehyde **28** (60 mg, 0.14 mmol) in CH_2Cl_2 (2 ml) and a solution of NaOMe (1 M in MeOH; 0.64 ml, 0.64 mmol), successively. After being stirred at rt for 30 min, the mixture was poured into ice–water and extracted with Et_2O. The extracts were shaken with 5% aq. HCl until the fine structure disappeared on UV, and then washed successively with saturated aq. $NaHCO_3$ and brine. Evaporation of the dried extracts provided a residue, which was purified by SCC (Et_2O–hexane, 3 : 7) to give an isomeric mixture of apocarotenal **31** (50 mg, 64%) in which the main product was all-*E* isomer **31a**. Purification of a part of the isomeric mixture by PHPLC [LiChrosorb Si 60 (7 μm) 1.0 × 30 cm; acetone–hexane, 1 : 9; 400 nm detect.] followed by PHPLC [LiChrosorb Si 60 (7 μm) 1.0 × 30 cm; Et_2O–hexane, 3 : 7; 345 nm detect.] provided the all-*E* isomer **31a** and the 11*Z* one **31b** as orange solids.

All-*E* isomer 31a. λ_{max}(EtOH)/nm 392 and 412sh; ν_{max}/cm^{-1} 1673 (conj. C=O and conj. CHO), 1605 (C=C); δ_H (300 MHz) 0.02 and 0.06 (each 3H, s, SiMe × 2), 0.87 (9H, s, Si^{t}Bu), 1.36

(3H, s, 1-Me), 1.67 (6H, br s, 5-Me and 6-Me), 1.78 (1H, dd, *J* 14.5 and 5, 2-H), 1.89 (1H, dd, *J* 13.5 and 6.5, 2-H), 1.90 (3H, s, 13′-Me), 1.95 (3H, s, 9-Me), 2.06 (3H, s, 13-Me), 2.25 (1H, dd, *J* 13.5 and 7.5, 4-H), 2.44 (1H, dd, *J* 13.5 and 6, 4-H), 3.42 and 3.51 (each 1H, d, *J* 16, 7-H_2), 3.92 (4H, m, OCH_2CH_2O), 3.99 (1H, m, 3-H), 6.43 (1H, d, *J* 11.5, 14-H), 6.64 (1H, d, *J* 15, 12-H), 6.73 (1H, dd, *J* 15 and 10.5, 11-H), 6.77 (1H, dd, *J* 14.5 and 12, 15′-H), 6.97 (1H, d, *J* 11, 14′-H), 7.03 (1H, dd, *J* 14.5 and 11, 15-H), 7.15 (1H, d, *J* 10, 10-H), 9.54 (1H, s, CHO) (Found: M^+, 556.3586. $C_{33}H_{52}O_5Si$ requires *M*, 556.3586).

11*Z* Isomer 31b. λ_{max}/nm 290, 372, 387 and 409sh; ν_{max}/cm^{-1} 1660 (conj. C=O and conj. CHO), 1606 (C=C); δ_H (300 MHz) 0.05 (6H, s, SiMe × 2), 0.86 (9H, s, Si′Bu), 1.35 (3H, s, 1-Me), 1.64 and 1.67 (each 3H, s, 5-Me and 6-Me), 1.88 (3H, s, 13′-Me), 1.93 (3H, s, 9-Me), 2.15 (3H, s, 13-Me), 1.58 (1H, m, 2-H), 1.76 (1H, m, 2-H), 2.25 (1H, m, 4-H), 2.43 (1H, m, 4-H), 3.39 and 3.48 (each 1H, d, *J* 16.5, 7-H_2), 3.92 (4H, m, OCH_2-CH_2O), 3.98 (1H, m, 3-H), 6.31 (1H, d, *J* 11.5, 12-H), 6.39 (1H, d, *J* 11.5, 14-H), 6.43 (1H, t, *J* 11.5, 11-H), 6.75 (1H, dd, *J* 15 and 12, 15′-H), 6.97 (1H, d, *J* 12, 14′-H), 6.99 (1H, dd, *J* 15 and 12, 15-H), 7.61 (1H, d, *J* 11.5, 10-H), 9.48 (1H, s, CHO) (Found: M^+, 556.3602. $C_{33}H_{52}O_5Si$ requires *M*, 556.3586).

Synthesis of (3*R*,3′*S*)-crassostreaxanthin B 1a

A solution of NaOMe (1 M in MeOH; 0.36 ml, 0.36 mmol) was added to an ice-cooled solution of the isomeric mixture of apocarotenal **31** (50.4 mg, 0.09 mmol) and the Wittig salt **32**[17] (186.7 mg, 0.36 mmol) in CH_2Cl_2 (5 ml). After being stirred at 0 °C for 5 min, the reaction mixture was diluted with Et_2O followed by standard work-up to give a residue, which was purified by SCC (acetone–hexane, 1 : 9) to afford an isomeric mixture of condensed products (73 mg). Then, PTSA (10 mg) was added to an ice-cooled solution of this isomeric mixture in acetone (9 ml) and the reaction mixture was stirred at 0 °C for 3 h. The mixture was diluted with Et_2O and washed successively with 5% aq. HCl, saturated aq. $NaHCO_3$ and brine. Evaporation of the dried solution gave a residue, which was purified by SCC (acetone–hexane, 3 : 7) followed by PHPLC [LiChrosorb Si 60 (7 μm) 1.0 × 30 cm; acetone–hexane, 3 : 7] to provide the all-*E* isomer **1a** (5.2 mg, 6% from **28**). Spectral properties of the synthetic crassostreaxanthin B were in agreement with those of a natural specimen;[2] λ_{max}/nm 450 and 475sh; ν_{max}/cm^{-1} 3601 and 3448 (OH), 1706 (conj. C=O and C=O); δ_H (300 MHz) 1.15 and 1.20 (each 3H, s, *gem*-Me), 1.46 (1H, t, *J* 12, 2-H_{ax}), 1.64 (3H, s, 6′-Me), 1.68 (3H, s, 5′-Me), 1.84 (1H, ddd, *J* 12.5, 3.5 and 2, 2-H_{eq}), 1.93 (3H, s, 5-Me), 1.95 (3H, s, 9′-Me), 1.98 (3H, s, 13-Me), 2.00 (3H, s, 13′-Me), 2.02 (3H, s, 9-Me), 2.07 (1H, dd, *J* 18.5 and 9.5, 4-H_{ax}), 2.21 (3H, s, 1′-Me), 2.22 (1H, dd, *J* 13.5 and 5.5, 4′-H), 2.42 (1H, m, 4-H_{eq}), 2.44 (1H, dd, *J* 13.5 and 8, 4′-H), 2.65 (2H, d, *J* 7.5, 2′-H_2), 3.49 and 3.58 (each 1H, d, *J* 16.5, 7′-H_2), 3.99 (1H, m, 3-H), 4.20 (1H, m, 3′-H), 6.29 (1H, d, *J* 11, 14-H), 6.36 (1H, d, *J* 14.5, 12-H), 6.40 (1H, d, *J* 10.5, 14′-H), 6.46 (1H, d, *J* 11, 10-H), 6.56 (1H, dd, *J* 14.5 and 11, 11-H), 6.64 (1H, dd, *J* 15.5 and 9.5, 11′-H), 6.66 (1H, d, *J* 15.5, 12′-H), 6.69 (1H, dd, *J* 16 and 10.5, 15′-H), 6.74 (1H, dd, *J* 16 and 11, 15-H), 7.19 (1H, d, *J* 9.5, 10′-H) (Found: M^+, 598.4037. $C_{40}H_{54}O_4$ requires *M*, 598.4025).

(4*S*,6*R*)-4-*tert*-Butyldimethylsilyloxy-1-ethynyl-2,2,6-trimethylcyclohexanol 36

TMSCl (75 ml, 0.60 mol) was added to a stirred solution of the (4*S*,6*R*)-hydroxy ketone **33**[19] (85 g, 0.54 mol), Et_3N (90 ml, 0.65 mol) in dry Et_2O (750 ml) at 0 °C. The mixture was stirred at rt for 4 h, poured into ice–water and extracted with Et_2O. The extracts were washed successively with 5% aq. HCl, saturated aq. $NaHCO_3$ and brine. Evaporation of the dried solution followed by distillation (68–71 °C/0.62 mmHg) gave the (4*S*)-siloxy ketone **34** (118 g, 95%) as a colorless oil. Then, in the same manner as described for the preparation of α-acetylenic alcohol **10**, the (4*S*)-siloxy ketone **34** (10.7 g, 47 mmol) was treated with lithium trimethylsilylacetylide to give a crude product, which was purified by recrystallization (from AcOEt–hexane) to provide the (4*S*)-diol **35** (diastereomeric mixture) (7.81 g, 91%). TBSCl (4.78 g, 0.03 mol) was added to a stirred solution of the diol **35** (5.5 g, 0.03 mol), Et_3N (5 ml, 0.04 ml) and DMAP (4.42 g, 0.04 mol) in dry CH_2Cl_2 (20 ml) at rt. The mixture was stirred at rt for 1.5 h, poured into ice–water and extracted with Et_2O. The extracts were washed successively with 5% aq. HCl, saturated aq. $NaHCO_3$ and brine. Evaporation of the dried solution followed by CC (Et_2O–hexane, 1 : 9) afforded the TBS ether **36** (8.4 g, 94%; 65% from **33**) as a colorless oil; ν_{max}/cm^{-1} 3609, 3477 (OH), 3306 (≡CH), 2107 (C≡C); δ_H (300 MHz) 0.05 (6H, s, SiMe × 2), 0.876 (9H, s, Si′Bu), 1.00 and 1.12 (each 3H, s, *gem*-Me), 1.06 (3H, d, *J* 6.5, 5-Me), 1.44 (1H, td-like, *J* 13 and 11, 4-H_{ax}), 1.52 (1H, ddd, *J* 13, 5 and 2.5, 2-H_{eq}), 1.64 (1H, dd, *J* 13 and 11, 2-H_{ax}), 1.72 (1H, m, 4-H_{eq}), 1.94 (1H, m, 5-H), 2.50 (1H, br s, 8-H), 3.83 (1H, tt, *J* 11 and 5, 3-H) (Found: M^+, 296.2161. $C_{17}H_{32}O_2Si$ requires *M*, 296.2173).

[(4*S*)-4-*tert*-Butyldimethylsilyloxy-2,6,6-trimethylcyclohex-1-enyl]acetaldehyde 11

In the same manner as described for the preparation of (3*R*)-aldehyde **11**, (3*S*)-aldehyde **11** (8.2 g, quant.) was obtained as a colorless oil from (3*S*)-α-acetylenic alcohol **36** (8.2 g, 28 mmol); $[a]_D^{26}$ +17.0 (*c* 1.00, MeOH).

2-[(4*S*)-4-*tert*-Butyldimethylsilyloxy-2,6,6-trimethylcyclohex-1-enyl]ethanol 12

In the same manner as described for the preparation of (3*R*)-alcohol **12**, (3*S*)-alcohol **12** (7.8 g, 96%) was obtained as a colorless oil from (3*S*)-aldehyde **11** (8.1 g, 27 mmol); $[a]_D^{27}$ +48.0 (*c* 1.00, MeOH).

3-[(4*S*)-4-*tert*-Butyldimethylsilyloxy-2,6,6-trimethylcyclohex-1-enyl]propanenitrile 13

In the same manner as described for the preparation of (3*R*)-nitrile **13**, (3*S*)-nitrile **13** (4.5 g, 57%) was obtained as a colorless oil from (3*S*)-alcohol **12** (7.7 g, 26 mmol); $[a]_D^{27}$ +48.0 (*c* 1.00, MeOH).

3-[(4*S*)-4-*tert*-Butyldimethylsilyloxy-2,6,6-trimethylcyclohex-1-enyl]propan-1-ol 14

In the same manner as described for the preparation of (3*R*)-alcohol **14**, (3*S*)-alcohol **14** (4.0 g, 91%) was obtained as a colorless oil from (3*S*)-nitrile **13** (4.3 g, 14 mmol); $[a]_D^{25}$ +50.0 (*c* 1.00, MeOH).

3-[(4*S*)-4-*tert*-Butyldimethylsilyloxy-2,6,6-trimethylcyclohex-1-enyl]propyl acetate 15

In the same manner as described for the preparation of (3*R*)-acetate **15**, (3*S*)-acetate **15** (4.0 g, 91%) was obtained as a colorless oil from (3*S*)-alcohol **14** (3.8 g, 12 mmol); $[a]_D^{25}$ +39.0 (*c* 1.00, MeOH).

3-[(1*R*,4*R*,6*S*)- and (1*S*,4*R*,6*R*)-4-*tert*-Butyldimethylsilyloxy-2,2,6-trimethyl-7-oxabicyclo[4.1.0]heptan-1-yl]propyl acetate 5a and 5b

In the same manner as described for the preparation of (3*R*)-epoxide **5**, a mixture of (3*S*)-epoxides **5a**,**b** (3.98 g, 99%) was obtained as a colorless oil from (3*S*)-acetate **15** (3.84 g, 11 mmol). A part of the epoxides was purified by SCC (Et_2O–hexane, 4 : 96) to provide the *anti*-epoxide **5a** and *syn*-epoxide **5b**, each as a colorless oil.

***anti*-Epoxide 5a.** $[\alpha]_D^{27}$ +21.7 (*c* 0.46, MeOH).

***syn*-Epoxide 5b.** $[\alpha]_D^{27}$ +34.0 (*c* 0.50, MeOH).

(6*E*,4*R*)-10-Acetoxy-4-*tert*-butyldimethylsilyloxy-6,7-dimethyldec-6-en-2-one 7

In the same manner as described for the rearrangement of (3*R*)-epoxides **5a**,**b** with $SnCl_4$, (3*R*)-tetrasubstituted olefinic compound **7** (2.50 g, 65%) was obtained as a colorless oil from (3*S*)-epoxides **5a**,**b** (3.86 g, 10 mmol); $[\alpha]_D^{27}$ −8.40 (*c* 1.31, MeOH).

(4*E*,7*R*)-7-*tert*-Butyldimethylsilyloxy-4,5-dimethyl-8-(2-methyl-1,3-dioxolan-2-yl)oct-4-enyl acetate 19

In the same manner as described for the preparation of (3*S*)-ketal **19**, (3*R*)-ketal **19** (2.26 g, 81%) was obtained as a colorless oil from (3*R*)-tetrasubstituted olefinic compound **7** (2.50 g, 6.76 mmol); $[\alpha]_D^{27}$ −10.4 (*c* 1.06, MeOH).

Methyl (4*E*,7*R*)-7-*tert*-butyldimethylsilyloxy-4,5-dimethyl-8-(2-methyl-1,3-dioxolan-2-yl)oct-4-enoate 21

In the same manner as described for the preparation of (3*S*)-methyl ester **21**, (3*R*)-methyl ester **21** (0.83 g, 45%) was obtained as a colorless oil from (3*R*)-ketal **19** (1.93 g, 4.66 mmol); $[\alpha]_D^{26}$ +11.7 (*c* 0.94, MeOH).

(3*E*,6*R*)-6-*tert*-Butyldimethylsilyloxy-3,4-dimethyl-7-(2-methyl-1,3-dioxolan-2-yl)hept-3-enal 25

In the same manner as described for the preparation of (3*S*)-aldehyde **25**, (3*R*)-aldehyde **25** (236 mg, 32%) was obtained as a colorless oil from (3*R*)-methyl ester **21** (820 mg, 2.05 mmol); $[\alpha]_D^{27}$ +3.33 (*c* 0.3, MeOH).

(2*E*,6*E*,9*R*)-9-*tert*-Butyldimethylsilyloxy-3,6,7-trimethyl-10-(2-methyl-1,3-dioxolan-2-yl)-4-oxodeca-2,6-dienal 28

In the same manner as described for the preparation of (3*S*)-aldehyde **28**, (3*R*)-aldehyde **28** (113 mg, 44%) was obtained as a colorless oil from (3*R*)-aldehyde **25** (214 mg, 0.60 mmol); $[\alpha]_D^{23}$ +8.00 (*c* 1.0, MeOH).

(2*E*,4*E*,6*E*,8*E*,10*E*,14*E*,17*R*)-17-*tert*-Butyldimethylsilyoxy-2,7,11,14,15-pentamethyl-18-(2-methyl-1,3-dioxolan-2-yl)-12-oxooctadeca-2,4,6,8,10,14-hexaenal 31

In the same manner as described for the preparation of (3*S*)-apocarotenal **31**, (3*R*)-apocarotenal **31** (94 mg, 65%) was obtained as an orange solid from (3*R*)-aldehyde **28** (110 mg, 0.26 mmol).

Synthesis of (3*R*,3′*R*)-crassostreaxanthin B 1b

In the same manner as described for the preparation of (3*R*,3′*S*)-crassostreaxanthin B **1a**, (3*R*,3′*R*)-crassostreaxanthin B **1b** (10 mg, 10%) was obtained as a red solid from (3*R*)-apocarotenal **31** (94 mg, 0.17 mmol).

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