Total synthesis of capsanthin and capsorubin using Lewis acid-promoted regio- and stereoselective rearrangement of tetrasubsutituted epoxides†‡

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The synthesis of capsanthin **1** and capsorubin **2** was accomplished *via* the C_{15}-cyclopentyl ketone **6** prepared by Lewis acid-promoted regio- and stereoselective rearrangement of the epoxy dienal **5**.

Introduction

There are many xanthophylls that are hypothetically assumed to be derived from 5,6-epoxycarotenoids through ring opening of the epoxy moiety. Capsanthin **1** and capsorubin **2**, having a κ-end group, are major pigments of red paprika *Capsicum annuum*[2,3] and attract interest due to their strong antioxidant activity.[4] Both carotenoids are also considered[3] to be formed in nature from 5,6-epoxycarotenoids *via* a pinacolic type rearrangement. Previously, we reported the first biomimetic type total synthesis of both crassostreaxanthin B **3**,[5] possessing a novel acyclic tetrasubstituted olefinic end group, and mytiloxanthin **4**,[6] containing a cyclopentyl enolic β-diketone group, applying stereoselective rearrangement of tetrasubstituted epoxides. In these syntheses, we employed epoxides in which substituents at the C-6[7] position were alkyl groups having an oxygen functional group as shown in Scheme 1.

In a previous communication,[8] we disclosed the reaction of various 5,6-epoxides having an olefinic group at C-6 with Lewis acids and the total synthesis of capsanthin **1** through the C_{15}-cyclopentyl ketone **6** (Scheme 1), efficiently prepared by regio- and stereoselective rearrangement of the C_{15}-epoxy dienal **5**. Recently we have also synthesized capsorubin **2** using the common intermediate **6**. Here, we describe a full account of these experiments.

Results and discussion

It has been reported that the treatment of epoxide **7a**[9] (Scheme 2) with hydrochloric acid and that of **7b**[10] with $BF_3{\cdot}OEt_2$ only provided the 5,8-epoxides **8a** and **8b**, respectively, by opening of the C-6–oxygen bond of the oxirane ring (route *a*) and subsequent migration of the 7,8-double bond. On the other hand, the treatment of epoxide **7c** with $ZnBr_2$ or tris(4-bromophenyl)aminium hexachloroantimonate has been known[11] to predominantly give the cyclopentyl ketone **9c**, by cleavage of the oxirane ring at the C-5 position (route *b*) and subsequent ring contraction. It is considered that the selective cleavage of epoxide **7c** at C-5 was promoted by destabilization of the cation at C-6 due to the electron deficiency of the 7(β)-carbon of the α,β-unsaturated carbonyl group, whereas the π-orbital of the 7,8-double bond in epoxides **7a** and **7b** acted as an activator for C-6–oxygen bond cleavage.

Thus, the reaction of epoxides **7d–f**, having olefinic groups conjugated to carbonyl groups at C-6, was investigated toward the synthesis of **1** and **2**. The epoxides **7d–f** were prepared starting from β-ionone **10** as shown in Scheme 3. Emmons–Horner reaction of the ketone **10** with triethyl phosphonoacetate in the presence of sodium hydride and subsequent epoxidation with *m*-chloroperbenzoic acid (MCPBA) gave an isomeric mixture of the epoxy dienoates **7d**, which was cleanly separated by column chromatography (CC) to afford each pure isomer (all-*E*-isomer, 48%; 9*Z*-isomer, 6%). Reduction of the all-*E*-epoxy dienoate **7d** with $LiAlH_4$ followed by oxidation with MnO_2 yielded the epoxy dienal **7e** (96%). This dienal **7e** was condensed with triethyl phosphonoacetate using *n*-BuLi as a base to give the epoxy trienoate **11** (83%), which was transformed into the epoxy trienal **7f** in good yield.

Treatment of the epoxy dienoate **7d** with $SnCl_4$ (2.2 equiv.) or tris(4-bromophenyl)aminium hexachloroantimonate[11] (0.1 equiv.) gave the 5,8-epoxide **8d** (75% for the former, 86% for the latter; 5,8-*trans* : 5,8-*cis*,[12] ~8 : 1) accompanied by a trace of the cyclopentyl ketone **9d**. On the other hand, the epoxy dienal **7e** predominantly provided the cyclopentyl ketone **9e** (91%) after treatment of $SnCl_4$. Treatment of **7e** with tris(4-bromophenyl)aminium hexachloroantimonate afforded a complex mixture, probably due to oxidative effect of the aminium salt. The epoxy trienal **7f** was treated with $SnCl_4$ to preferentially give the 5,8-epoxide **8f** (53%; 5,8-*trans* : 5,8-*cis*, 5 : 1). These results show that the direction of C–O bond cleavage in the oxirane ring depends upon both the length of the conjugated double bond system and the electron-withdrawing ability of the substituent adjacent to the double bond.

In order to synthesize capsanthin **1** and capsorubin **2**, the C_{15}-epoxy dienal **5** with an oxygen function at C-3 was prepared by two methods as shown in Scheme 4. The known[13] terminal alkyne **13**, prepared from the optically active hydroxyketone **12**,[14] was heated at 130 °C for 20 min with an excess amount (4 equiv.) of azobisisobutyronitrile (AIBN)[15] to give stereoselectively the *E*-vinylstannane **14** in 88% yield. The regio- and stereochemical structure of the stananne **14** was deduced from ^{1}H NMR data (see ESI‡), especially from the coupling patterns J_{HH}, $J_{^{117}SnH}$, $J_{^{119}SnH}$ of vinylic protons.[15,16] Cross-coupling reaction of the stannane **14** with the vinyl triflate **23**[17] by the combined use of tris(dibenzylideneacetone)dipalladium (Pd_2dba_2) and $AsPh_3$ (ligand)[18] in *N*,*N*-dimethylformamide (DMF) at 50 °C gave the all-*E*-trienoate **15** (92%), whose hydroxy group at C-3 was

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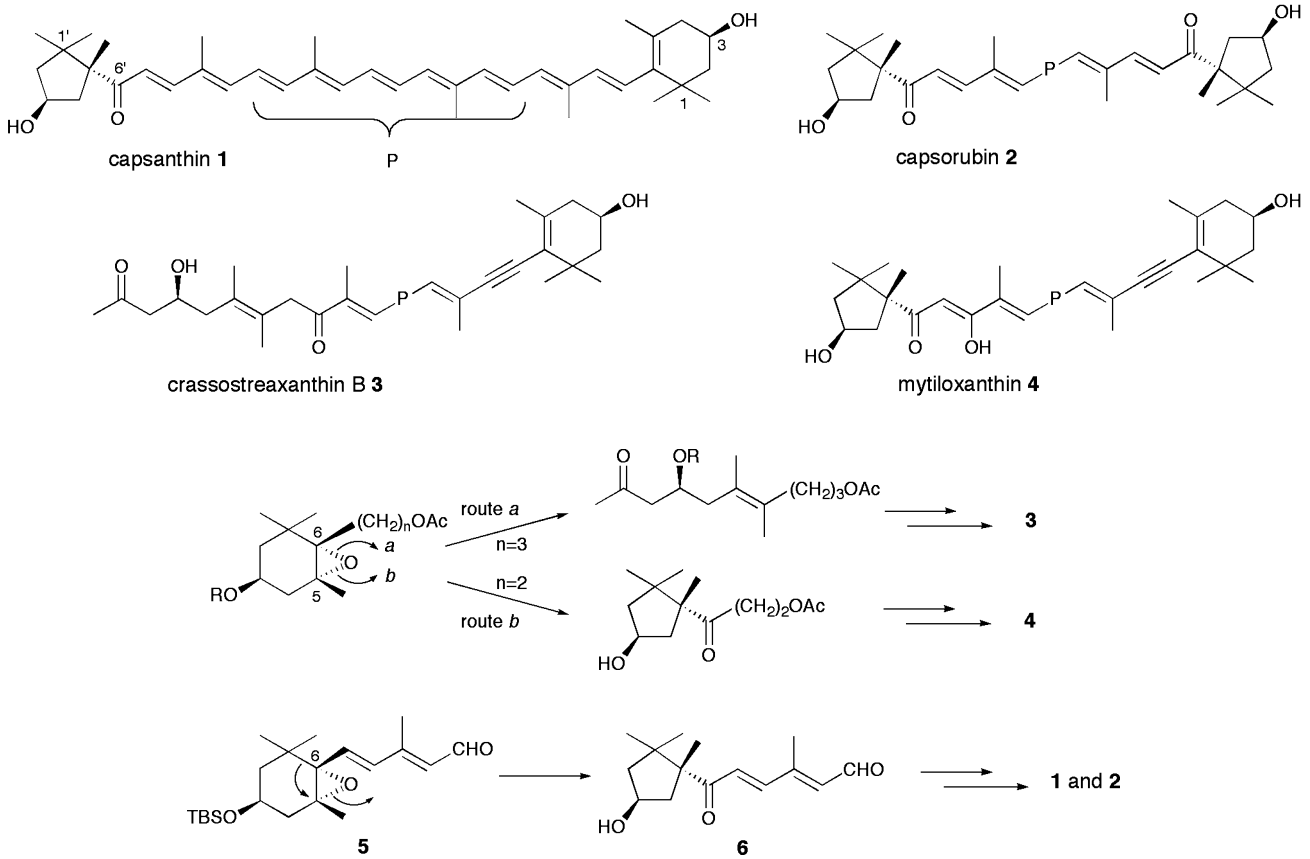
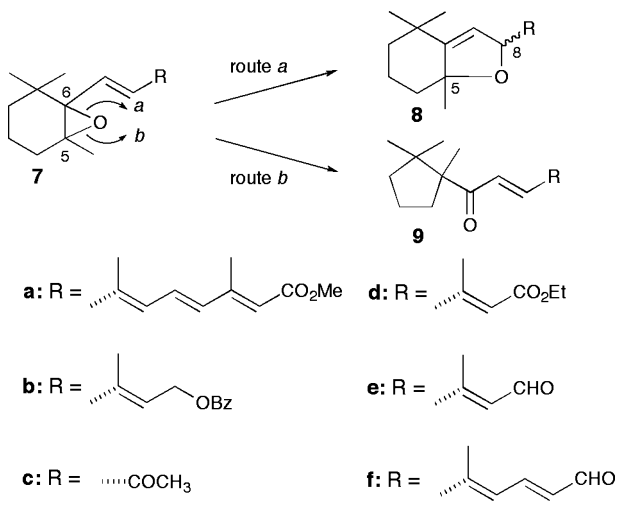
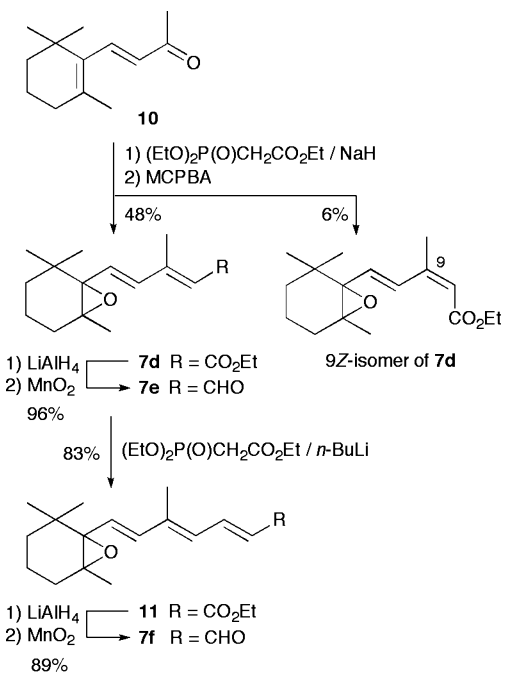
‡ Electronic supplementary information (ESI) available: Synthesis and characterization data of compounds **7d–f**, **8d**, **8f**, **9d**, **9e**, **11**, **14–17** and **5**. Spectral data of compounds **1** and **2**.



Scheme 1

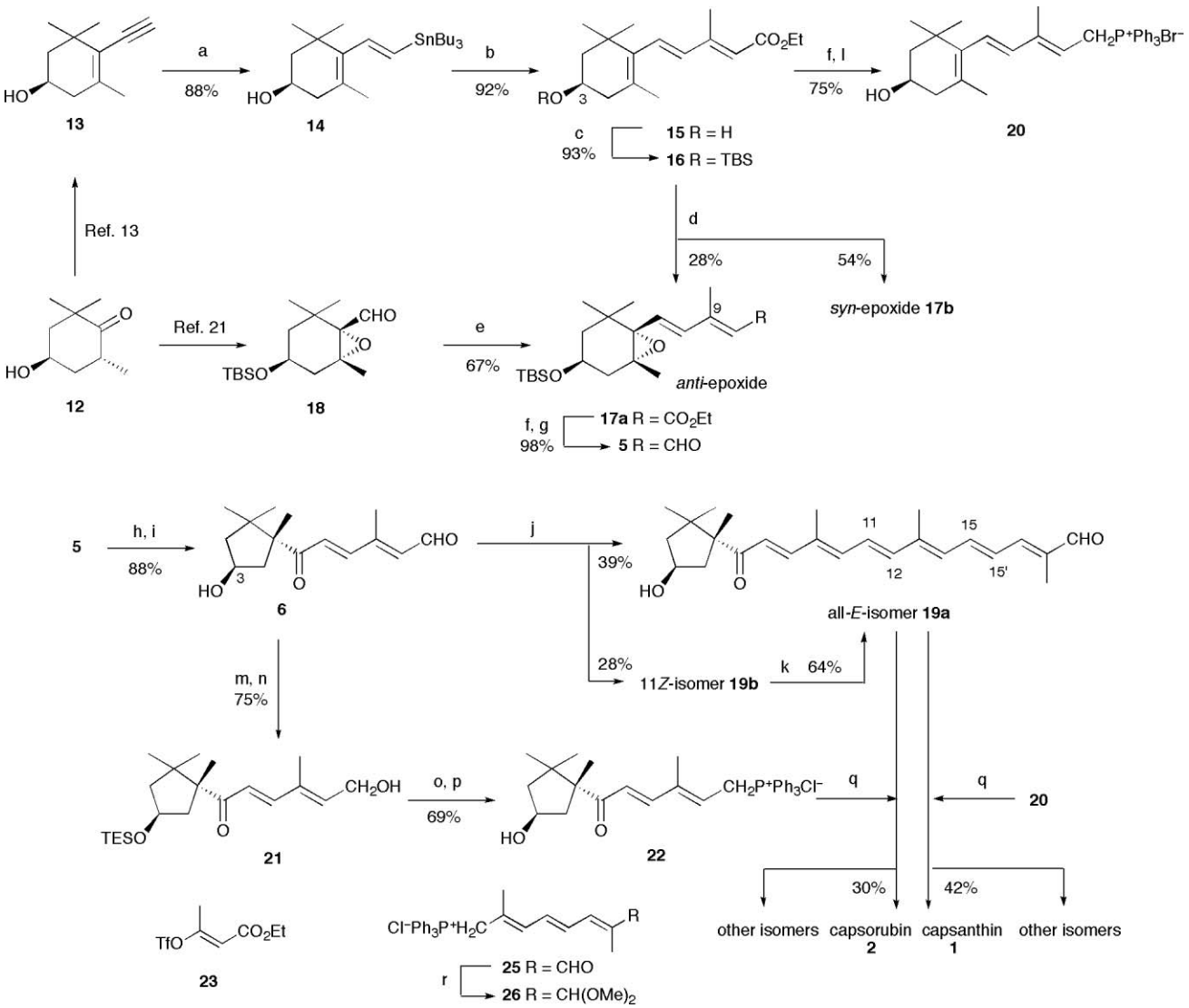


Scheme 2



Scheme 3

protected (93%) with a *tert*-butyldimethylsilyl (TBS) group. The resulting TBS ether **16** was then treated with MCPBA to give a mixture of the *anti* (α)-epoxide **17a** (28%) and *syn* (β)-epoxide **17b** (54%). The relative configurations between the silyloxy and epoxy groups in the two isomers were confirmed by their ^{1}H NMR data.[19] The *anti* (α)-epoxide **17a** could be effectively prepared[20] from the known C_{10}-epoxy aldehyde **18**, which was recently synthesized by Katsumura's group[21] *via* a Sharpless asymmetric epoxidation of the corresponding allylic alcohol derived from the hydroxyketone **12**. Emmons–Horner reaction of the aldehyde **18** with the phosphonate **24** in the presence of *n*-BuLi gave the all-*E*-dienoate **17a** (67%) and its 9*Z*-isomer (26%). Reduction of



Scheme 4 *Reagents and conditions*: a, Bu_3SnH, cat. AIBN, 130 °C; b, **23**, cat. $AsPh_3$, cat. $Pd_2dba_2{\cdot}CHCl_3$, 50 °C; c, TBSCl, cat. DMAP, Et_3N; d, MCPBA; e, $(EtO)_2P(O)CH_2C(Me)=CHCO_2Et$ **24**, *n*-BuLi; f, $LiAlH_4$; g, MnO_2; h, $SnCl_4$; i, aq. HF; j, **26**, NaOMe then Dowex (H^+); k, cat. $PdCl_2(MeCN)_2$, Et_3N; l, $PPh_3{\cdot}HBr$; m, TESCl, cat. DMAP, Et_3N; n, $NaBH_4$; o, LiCl, γ-collidine, MsCl; p, PPh_3, CH_2Cl_2, reflux; q, NaOMe; r, $CH(OMe)_2$, H^+, MeOH.

17a with $LiAlH_4$ followed by MnO_2 oxidation gave the C_{15}-epoxy dienal **5** in 98% yield.

Treatment of the epoxide **5** with $SnCl_4$ followed by desilylation yielded the regio- and stereoselectively rearranged cyclopentyl ketoaldehyde **6** in good yield. The stereostructure of **6** was determined by the comparison of its ^1H NMR data with those of known[22] cyclopentyl ketones. This C_{15}-compound **6** was then condensed with the C_{10}-Wittig salt **26**[23] in the presence of NaOMe as a base, followed by one-pot treatment with ion exchange resin, Dowex 50W-X8 (H^+), to give an isomeric mixture of C_{25}-apocarotenals. Separation by preparative HPLC (PHPLC) provided the all-*E*-isomer **19a** (39%) and the 11*Z*-isomer **19b** (28%), each in pure form. The latter was isomerized to the desired all-*E*-isomer in 65% yield by treatment[24] with a palladium catalyst. Stereochemistries of the newly formed 11,12-double bonds of these isomers were determined from the coupling constants (**19a**: 15 Hz; **19b**: 12 Hz) between 11- and 12-Hs in the ^1H NMR spectra.

Wittig reaction of the C_{25}-apocarotenal **19a** with the C_{15}-Wittig salt **20**,[25] which was prepared from the trienoate **15** by $LiAlH_4$ reduction and subsequent treatment with $PPh_3{\cdot}HBr$, gave the condensed products. PHPLC purification afforded all-*E*-capsanthin **1** (42%) accompanied by some isomers. Spectral data of purified capsanthin **1** were in good agreement with those reported.[22a]

Next, the cyclopentyl ketoaldehyde **6** was transformed into the C_{15}-phosphonium salt **22** toward the synthesis of capsorubin **2**. Protection of the hydroxy group of compound **6** at C-3 with a triethylsilyl (TES) group and subsequent partial reduction of the formyl group of the resulting TES ether with $NaBH_4$ provided the alcohol **21** in 75% yield. This was then allowed to react with LiCl and methanesulfonyl chloride (MsCl) followed by treatment of the resulting chloride with PPh_3 under reflux in CH_2Cl_2 to provide the deprotected Wittig salt **22** in 69% yield from the alcohol **21**. Finally, the C_{25}-apocarotenal **19a** was condensed with the

C_{15}-phosphonium salt **22** to give the condensed products, which were separated by PHPLC to provide all-*E*-capsorubin **2** (30%) along with some isomers. Spectral data of purified capsorubin **2** were in good accordance with those reported.[22a]

In summary, consideration of the ring formation in biosynthesis has led us to apply the regio- and stereoselective rearrangement of epoxy dienal **5** with $SnCl_4$ to accomplish the total synthesis of optically active capsanthin **1** and capsorubin **2**.

Experimental

UV spectra were recorded on a JASCO Ubest-55 instrument. IR spectra were measured on a Perkin Elmer FT-IR spectrometer, model Paragon 1000, using chloroform solutions. ^{1}H NMR and ^{13}C NMR spectra were determined on a Varian Gemini-300 or a Varian VXR-500 superconducting FT-NMR spectrometer, using deuteriochloroform solutions unless otherwise stated (tetramethylsilane as internal reference). *J*-Values are given in Hz. 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}) and CD spectra on a Shimadzu-AVIN 62A DS circular dichroism spectrometer.

CC was performed on silica gel (Merck Art. 7734). Short-column chromatography (SCC) was conducted on silica gel (Merck Art. 7739) under reduced pressure. Low-pressure CC was conducted on a Yamazen low pressure liquid chromatography system using a Lobar column (Merck LiChroprep Si 60). PHPLC was carried out on a Shimadzu LC-6A with a UV–vis detector.

All operations were carried out under nitrogen or argon. Evaporation of the extract or the filtrate was carried out under reduced pressure. Ether refers to diethyl ether, and hexane to *n*-hexane. NMR assignments are given using the carotenoid numbering system.

(2*E*,4*E*)-6-[(1*R*,4*S*)-4-Hydroxy-1,2,2-trimethylcyclopentyl]-3-methyl-6-oxohexa-2,4-dienal 6

To a solution of the epoxy dienoate **5** (1.24 g, 3.40 mmol) in dry CH_2Cl_2 (20 ml) was added $SnCl_4$ (1 M in CH_2Cl_2; 7.5 ml, 7.5 mmol) at 0 °C. The mixture was stirred at 0 °C for 45 min and then poured into saturated aq. $NaHCO_3$ and extracted with ether. The extracts were washed with brine and dried. Evaporation of the solvent gave a residue which, without purification, was dissolved in CH_3CN (10 ml) and aq. 48% HF (0.5 ml) was added to it at 0 °C. After being stirred at rt for 15 min, the mixture was poured into saturated aq. $NaHCO_3$ and extracted with ether. The extracts were washed with brine, dried and evaporated to give a residue, which was purified by SCC (acetone–hexane, 3 : 7) to afford the cyclopentyl ketone **6** (697 mg, 82%) as a pale yellow oil; $[\alpha]_D^{21}$ −15.2 (*c* 1.12, MeOH); λ_{max} (EtOH)/nm 287; ν_{max}/cm^{-1} 3605 and 3466 (OH), 1667 (conj. CHO + conj. CO), 1589 (C=C); δ_H (300 MHz) 0.85 and 1.22 (each 3H, s, *gem*-Me), 1.39 (3H, s, 5-Me), 1.52 (1H, dd, *J* 14.5 and 3.5, 4-H$_\beta$), 1.74 (1H, dd, *J* 13.5 and 4.5, 2-H$_\beta$), 1.99 (1H, dd, *J* 13.5 and 8, 2-H$_\alpha$), 2.32 (3H, d, *J* 1.5, 9-Me), 2.91 (1H, dd, *J* 14.5 and 8.5, 4-H$_\alpha$), 4.51 (1H, m, 3-H), 6.21 (1H, br d, *J* 8, 10-H), 6.88 (1H, d, *J* 15.5, 7-H), 7.26 (1H, d, *J* 15.5, 8-H), 10.18 (1H, d, *J* 8, CHO) ppm; δ_C (75 MHz) 13.28 (9-Me), 20.89, 25.08 and 25.83 (*gem*-Me and 5-Me), 44.09 (C1), 45.02 (C4), 50.70 (C2), 59.24 (C5), 69.91 (C3), 128.29 (C7), 134.33 (C10), 143.89 (C8), 151.36 (C9), 191.19 (C11), 202.64 (C6) ppm; *m*/*z* (EI) 250.1560 (M$^+$, $C_{15}H_{22}O_3$ requires 250.1568).

(2*E*,4*E*,6*E*,8*E*,10*E*,12*E*)-, (2*E*,4*E*,6*E*,8*Z*,10*E*,12*E*)-14-[(1*R*,4*S*)-4-Hydroxy-1,2,2-trimethylcyclopentyl]-2,7,11-trimethyl-14-oxotetradeca-2,4,6,8,10,12-hexaenal 19a,b

An acidic solution (3.0 ml) prepared from toluene-*p*-sulfonic acid (*p*-TsOH) (500 mg) and H_3PO_4 (725 mg) in MeOH (38 ml) and methyl orthoformate (3.0 ml) was added to a solution of the C_{10}-phosphonium chloride **25**[23] (2.40 g, 5.37 mmol) in MeOH (30 ml). The reaction mixture was stirred at rt for 2 h and neutralized with NaOMe (1 M in MeOH) until just before the red colour of an ylide appeared to give a solution of the Wittig salt **26**. To this solution was added a solution of the aldehyde **6** (350 mg, 1.4 mmol) in MeOH (4 ml) and NaOMe (1 M in MeOH; 6 ml, 6 mmol) at rt. After stirring at rt for 30 min, Dowex 50W-X8 (H$^+$) (12 g) was added to the reaction mixture and this was stirred at rt for 20 min. After Dowex was filtered off, the filtrate was evaporated. The resulting residue was purified by CC (acetone–hexane, 1 : 2) and then PHPLC [LiChrosorb Si 60 (7 μm) 2 × 25 cm; acetone–hexane, 22 : 78] to provide all-*E*-apocarotenal **19a** (208 mg, 39%) and the 11*Z*-isomer **19b** (159 mg, 28%) as orange foams.

Compound 19a

λ_{max} (EtOH)/nm 399 sh, 423 and 442; ν_{max}/cm^{-1} 3612 and 3487 (OH), 1662 (conj. CHO + conj. CO), 1611, 1573 and 1542 (C=C); δ_H (500 MHz) 0.84, 1.21 (each 3H, s, *gem*-Me), 1.37 (3H, s, 5-Me), 1.50 (1H, dd, *J* 14.5 and 3, 4-H$_\beta$), 1.72 (1H, dd, *J* 13.5 and 4.5, 2-H$_\beta$), 1.90 (3H, s, 13′-Me), 1.98 (3H, s, 9-Me), 2.00 (1H, dd, *J* 13.5 and 7.5, 2-H$_\alpha$), 2.05 (3H, s, 13-Me), 2.95 (1H, dd, *J* 14.5 and 8, 4-H$_\alpha$), 4.51 (1H, m, 3-H), 6.39 (1H, br d, *J* 11.5, 14-H), 6.49 (1H, d, *J* 15, 7-H), 6.53 (1H, d, *J* 15, 12-H), 6.56 (1H, br d, *J* 11.5, 10-H), 6.75 (1H, dd, *J* 14 and 11.5, 15′-H), 6.76 (1H, dd, *J* 15 and 11.5, 11-H), 6.96 (1H, br d, *J* 11.5, 14′-H), 7.02 (1H, dd, *J* 14 and 11.5, 15-H), 7.32 (1H, d, *J* 15, 8-H), 9.47 (1H, s, CHO) ppm; *m*/*z* (EI) 382.2506 (M$^+$, $C_{25}H_{34}O_3$ requires 382.2506).

Compound 19b

λ_{max} (EtOH)/nm 313, 399 sh, 421 and 439 sh; ν_{max}/cm^{-1} 3611 and 3492 (OH), 1663 (conj. CHO + conj. CO), 1609 and 1573 (C=C); δ_H (500 MHz) 0.84, 1.21 (each 3H, s, *gem*-Me), 1.37 (3H, s, 5-Me), 1.50 (1H, dd, *J* 14.5 and 3, 4-H$_\beta$), 1.72 (1H, dd, *J* 13.5 and 4.5, 2-H$_\beta$), 1.90 (3H, s, 13′-Me), 1.96 (3H, s, 9-Me), 2.00 (1H, dd, *J* 13.5 and 8, 2-H$_\alpha$), 2.13 (3H, s, 13-Me), 2.95 (1H, dd, *J* 14.5 and 8.5, 4-H$_\alpha$), 4.51 (1H, m, 3-H), 6.18 (1H, d, *J* 12, 12-H), 6.38 (1H, br d, *J* 12, 14-H), 6.44 (1H, t, *J* 12, 11-H), 6.52 (1H, d, *J* 15, 7-H), 6.74 (1H, dd, *J* 15 and 12, 15′-H), 6.97 (1H, br d, *J* 12, 14′-H), 6.99 (1H, dd, *J* 15 and 12, 15-H), 7.03 (1H, br d, *J* 12, 10-H), 7.34 (1H, d, *J* 15, 8-H), 9.48 (1H, s, CHO) ppm; *m*/*z* (EI) 382.2510 (M$^+$, $C_{25}H_{34}O_3$ requires 382.2506).

Isomerization of 11*Z*-isomer 19b

A solution (1 ml) prepared from $PdCl_2(MeCN)_2$ (13 mg), Et_3N (7 μl) and water (1.2 ml) in MeCN (10 ml) was added to a solution of compound **19b** (150 mg, 0.39 mmol) in MeCN (30 ml) and the mixture was stirred at rt for 40 min. The solvent was evaporated off

to give a residue, which was purified by SCC (acetone–hexane, 3 : 7) and then PHPLC [LiChrosorb Si 60 (7 μm) 2 × 25 cm; acetone–hexane, 22 : 78] to provide all-*E*-apocarotenal **19a** (96 mg, 64%).

Preparation of the Wittig salt 20

A solution of the ester **15** (1.00 g, 3.6 mmol) in dry ether (40 ml) was added dropwise to a stirred suspension of $LiAlH_4$ (165 mg, 4.3 mmol) in dry ether at 0 °C. After being stirred at 0 °C for 15 min, the excess of $LiAlH_4$ was decomposed by dropwise addition of water and the mixture was extracted with ether. The extracts were dried and evaporated to give a residue, which was purified by SCC (acetone–hexane, 3 : 7) to afford the corresponding alcohol (723 mg, 85%). A solution of this alcohol (3.1 mmol) and triphenylphosphine hydrobromide (1.05 g, 3.1 mmol) in MeOH (20 ml) was stirred at rt for 48 h. Evaporation of the methanol gave a residue, which was washed with ether to provide crude phosphonium salt **20**[25]; δ_H (300 MHz) 0.97 and 0.99 (each 3H, s, *gem*-Me), 1.39 (3H, d, *J* 4, 9-Me), 1.45 (1H, t, *J* 12, 2-H_{ax}), 1.62 (3H, s, 5-Me), 1.78 (1H, br d, *J* 12, 2-H_{eq}), 2.03 (1H, br dd, *J* 16.5 and 9.5, 4-H_{ax}), 2.35 (1H, br dd, *J* 16.5 and 5.5, 4-H_{eq}), 3.99 (1H, m, 3-H), 4.77 (2H, br dd, *J* 15.5 and 7.5, 11-H_2), 5.33 (1H, br q-like, *J* 7, 10-H), 5.93 (2H, s, 7-H and 8-H), 7.5–7.9 (15H, m, ArH) ppm.

Preparation of capsanthin 1

To a solution of the phosphonium salt **20** (400 mg, 0.71 mmol) and the all-*E*-apocarotenal **19a** (75 mg, 0.20 mmol) in MeOH (15 ml) was added NaOMe (1 M in MeOH; 1.0 ml, 1.0 mmol) at rt. After stirring at rt for 1.5 h, Dowex 50 W-X8 (H^+) (2 g) was added to the reaction mixture and this was stirred at rt for 20 min. After Dowex was filtered off, the filtrate was evaporated. The resulting residue was purified by CC (acetone–CH_2Cl_2, 15 : 85) and then PHPLC (CHEMCOSORB 7-ODS-H 1 × 30 cm; MeOH–H_2O, 96 : 4) to provide all-*E*-capsanthin **1** (48 mg, 42%) as a red solid. Its spectral data were in agreement with those reported.[22a]

(2*E*,4*E*)-1-[(1*R*,4*S*)-4-Triethylsilyloxy-1,2,2-trimethylcyclopentyl]-6-hydroxy-4-methylhexa-2,4-dienone 21

A solution of TESCl (307 mg, 2.04 mmol) in dry CH_2Cl_2 (2 ml) was added to a stirred solution of the hydroxy compound **6** (340 mg, 1.36 mmol), DMAP (17 mg, 0.14 mmol) and Et_3N (0.38 ml, 2.72 mmol) in dry CH_2Cl_2 (2 ml) at 0 °C. The mixture was stirred at rt for 20 min, poured into chilled water and extracted with ether. The extracts were washed successively with aq. 3% HCl, saturated aq. $NaHCO_3$ and brine. Evaporation of the dried solution gave a residue, which was purified by CC (ether–hexane, 5 : 95) to afford the TES ether of **6** (456 mg, 92%) as a pale yellow oil. To a stirred solution of this TES ether in MeOH (10 ml) was added slowly a solution of $NaBH_4$ (48 mg) in MeOH (4 ml) at −20 °C. The reaction was monitored by TLC. After being quenched with saturated aq. NH_4Cl, the mixture was extracted with ether. The extracts were washed with brine, dried and evaporated to give a residue, which was purified by SCC (acetone–hexane, 1 : 4) to provide the alcohol **21** (377 mg, 82%; 75% from **6**) as a pale yellow oil; $[\alpha]_D^{26}$ +8.2 (*c* 1.10, MeOH); λ_{max} (EtOH)/nm 280; ν_{max}/cm^{-1} 3610 and 3449 (OH), 1671 (conj. CO), 1625 and 1598 (C=C); δ_H (300 MHz) 0.57 (6H, q, *J* 7.5, $SiCH_2CH_3$ × 3), 0.81 and 1.17 (each 3H, s, *gem*-Me), 0.95 (9H, t, *J* 7.5, CH_2CH_3 × 3), 1.33 (3H, s, 5-Me), 1.47 (1H, dd, *J* 14.5 and 3.5, 4-H_β), 1.71 (1H, dd, *J* 13.5 and 5, 2-H_β), 1.83 (3H, d, *J* 1, 9-Me), 1.89 (1H, dd, *J* 13.5 and 8, 2-H_α), 2.85 (1H, dd, *J* 14.5 and 8.5, 4-H_α), 4.36 (2H, d, *J* 6.5, 11-H_2), 4.38 (1H, m, 3-H), 6.06 (1H, br t, *J* 6.5, 10-H), 6.46 (1H, d, *J* 16, 7-H), 7.23 (1H, d, *J* 16, 8-H) ppm; *m*/*z* (EI) 366.2597 (M^+, $C_{21}H_{38}O_3Si$ requires 366.2588).

Preparation of the Wittig salt 22

A solution of LiCl (162 mg, 3.82 mmol) in dry DMF (5 ml) was added to a stirred mixture of the alcohol **21** (830 mg, 2.27 mmol) in γ-collidine (0.60 ml, 4.5 mmol) at 0 °C and the mixture was stirred at 0 °C for 10 min. To this mixture was added MsCl (0.26 ml, 3.4 mmol) and the mixture was stirred at 0 °C for a further 30 min. The mixture was poured into ice-water and extracted with ether. The extracts were washed successively with 3% aq. HCl, saturated aq. $NaHCO_3$ and brine. Evaporation of the dried solution provided a residue, which was purified by SCC (ether–hexane, 1 : 4) to afford the corresponding chloride (818 mg, 94%). Subsequently, triphenylphosphine (615 mg, 2.34 mmol) was added to a solution of this chloride in CH_2Cl_2 (20 ml) and the mixture was refluxed for 17 h. Evaporation of the solvent gave a residue, which was washed with ether to provide the phosphonium chloride **22** (835 mg, 69%) as a pale yellow solid; δ_H (300 MHz) 0.76, 1.13 and 1.28 (each 3H, s, *gem*-Me and 5-Me), 1.50 (1H, dd, *J* 14.5 and 3.5, 4-H_β), 1.55 (3H, d, *J* 3, 9-Me), 1.70 (1H, dd, *J* 14 and 5, 2-H_β), 1.92 (1H, dd, *J* 14 and 7.5, 2-H_α), 2.83 (1H, dd, *J* 14.5 and 8.5, 4-H_α), 4.45 (1H, m, 3-H), 5.00 (2H, dd, *J* 16 and 8, 11-H_2), 5.79 (1H, q-like, *J* 6.5, 10-H), 6.35 (1H, dd, *J* 15.5 and 2, 7-H), 7.03 (1H, d, *J* 15.5, 8-H), 7.6–7.9 (15H, m, ArH) ppm.

Preparation of capsorubin 2

To a solution of the phosphonium salt **22** (835 mg, 1.57 mmol) and the all-*E*-apocarotenal **19a** (210 mg, 0.55 mmol) in MeOH (15 ml) was added NaOMe (1 M in MeOH; 2.0 ml, 2.0 mmol) at rt. After stirring at rt for 2 h, Dowex 50 W-X8 (H^+) (2 g) was added to the reaction mixture and this was stirred at rt for 20 min. After Dowex was filtered off, the filtrate was evaporated. The resulting residue was purified by SCC (acetone–hexane, 1 : 3) and then PHPLC (CHEMCOSORB 7-ODS-H 1 × 30 cm; MeOH–H_2O, 95 : 5) to provide all-*E*-capsorubin **2** (99 mg, 30%) as a red solid. Its spectral data were in agreement with those reported.[22a,26,27]

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