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The Stille Reaction in the Synthesis of the C_{37}-Norcarotenoid Butenolide Pyrrhoxanthin. Scope and Limitations

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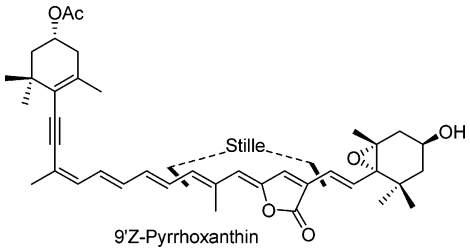

The sequential Stille cross-coupling reactions of the dihalogenated γ-alkylidenebutenolide **7** with stannanes **9** and **6** afforded the carbon skeleton of pyrrhoxanthin, a highly functionalized C7′−C8′ acetylenic C_{37}-norcarotenoid butenolide. Although the first halogen-selective Stille coupling takes place in 90% yield at ambient temperature, double isomerization of the *Z,E*- to the *E,Z*-C7′−C10′ enyne, likely induced by the catalyst, accompanyied the bond formation, leading to 9′*Z*-**20** and, ultimately, to 9′*Z*-pyrrhoxanthin 9′*Z*-**1**.

Introduction

Pyrrhoxanthin **1**[1] is a naturally occurring C_{37}-norcarotenoid characterized by having a structural truncation on the polyene chain and an abnormal arrangement of methyl groups relative to parent C_{40}-carotenoids.[2] Isolated from microalgae and planktonic dinoflagellates responsible for "red tide" episodes, its structure was elucidated by Liaaen-Jensen and co-workers.[3] With a similar skeleton up to C8′ (Figure 1), pyrrhoxanthin **1** contains an enyne in place of the allenol moiety of congener peridinin **2** and is therefore included in the C7′−C8′ acetylenic carotenoid group. As in peridinin **2**, a polyene chain of all-trans geometry comprising a γ-alkylidenebutenolide ring connects two highly oxygenated cyclohexenyl end groups decorated with 4 stereocenters.

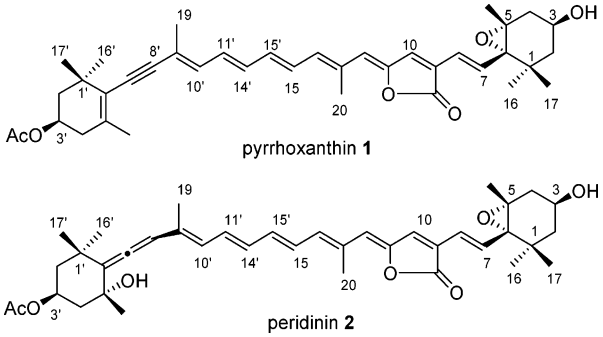

FIGURE 1. Representative C_{37}-norcarotenoid butenolides isolated from planktonic dinoflagellates with the IUPAC carotenoid-specific numbering.

Particularly challenging to synthetic chemists is the control of the relative and absolute configurations of the stereogenic elements of these C_{37}-norcarotenoids not only during the preparation of all required fragments but also in the assembly of the entire carotenoid structure. Not surprisingly, only one synthesis of *racemic* pyrrhoxanthin **1** has been reported to date.[4]

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(1) Johansen, J. E.; Svec, W. A.; Liaaen-Jensen, S.; Haxo, F. T. *Phytochemistry* **1974**, *13*, 2261.

(2) For recent monographs, see the following: (a) Britton, G., Liaaen-Jensen, S., Pfander, H., Eds.; *Carotenoids. Part 1A. Isolation and Analysis*; Birkhäuser: Basel, Germany, 1995. (b) Britton, G., Liaaen-Jensen, S., Pfander, H., Eds.; *Carotenoids. Part 1B. Spectroscopy*; Birkhäuser: Basel, Germany, 1995. (c) Britton, G., Liaaen-Jensen, S., Pfander, H., Eds.; *Carotenoids. Part 2. Synthesis*; Birkhäuser: Basel, Germany, 1996.

(3) (a) Johansen, J. E.; Borch, G.; Liaaen-Jensen, S. *Phytochemistry* **1980**, *19*, 441. (b) Aakermann, T.; Liaaen-Jensen, S. *Phytochemistry* **1992**, *31*, 1779.

(4) a) Yamano, Y.; Ito, M. *J. Chem. Soc., Perkin Trans 1* **1993**, 1599. (b) Ito, M.; Hirata, Y.; Tsukida, K.; Tanaka, N.; Hamada, K.; Hino, R.; Fujiwara, T. *Chem. Pharm. Bull.* **1988**, *36*, 3328.

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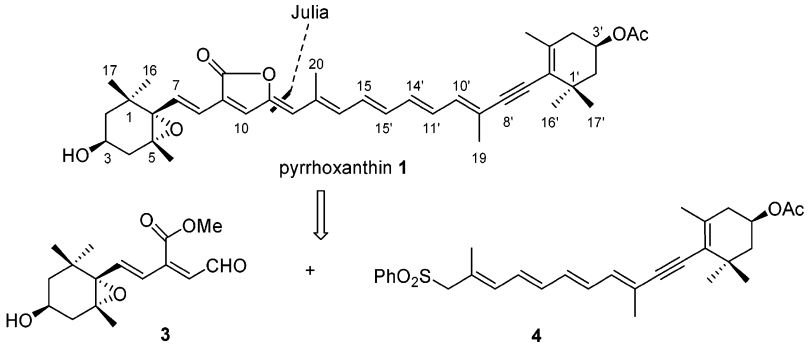


FIGURE 2. Key condensation step of the synthesis of *rac*-pyrrhoxanthin **1** reported by Ito et al.

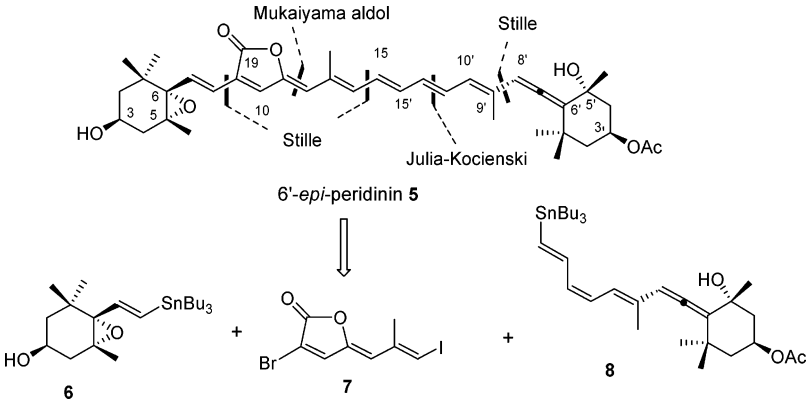


FIGURE 3. Approach to 6′-*epi*-peridinin **5** using the Julia−Stille−Stille sequence.

In his approach to highly functionalized C_{37}-norcarotenoid butenolides, Ito assembled the entire skeleton of pyrrhoxanthin **1** using a classical Julia reaction between aldehyde **3** and allyl phenyl sulfone **4**. This critical step (Figure 2), which also constructed the butenolide ring of *rac*-**1**, proved inefficient (13% yield of a 50:50 mixture of the 11*E*/11*Z* γ-alkylidenebutenolide isomers). This limitation and additional drawbacks found along the synthetic sequence call for novel, more efficient routes to these complex natural products.

Metal-catalyzed cross-coupling reactions are undoubtedly a method of choice for C−C bond formation, particularly for the connection of unsaturated fragments. In the carotenoid field, novel approaches to symmetrical C_{40} compounds using organozinc (Negishi coupling)[5] or organotin (Stille coupling)[6] derivatives and their halogenated polyenyl counterparts assisted by palladium have been disclosed. In addition, we recently reported the application of the Stille coupling to the construction of three key bonds of allenic C_{37}-norcarotenoids, including the last two connective steps that assembled the skeleton of 6′-*epi*-peridinin **5** (Figure 3).[7] We noticed, gratifyingly, a selective and efficient *Z* to *E* isomerization of the C11′−C12′ olefin (itself obtained stereoselectively by a Julia-Kocienski reaction) under the quite drastic coupling conditions required for the last Stille coupling (the C8−C9 bond formation), which set the correct geometry of the final C_{37}-norcarotenoid.[8] This was in retrospect a fortunate outcome since *Z* isomers of the C11′−C12′ double bond proved to be more stable than the corresponding *E* counterparts, and polyene degradation was minimized along the sequence.

Given the fact that enantiopure pyrrhoxanthin **1** has not yielded to synthesis, and that the Julia−Stille−Stille approach to 6′-*epi*-peridinin **5** depicted in Figure 3 appears versatile and therefore suitable for this endeavor, we decided to include this C7′−C8′ acetylenic carotenoid in our synthetic program. We hereby validate the above approach as a highly efficient route to the C_{37}-norcarotenoid butenolides. However, we also show an additional limitation of palladium-catalyzed cross-coupling processes applied to the synthesis of highly functionalized carotenoids, namely, the thus far unavoidable double isomerization of the C7′−C10′ enyne fragment which occurred at the stage of the advanced intermediate **20**.

Results and Discussion

The presence of a common γ-alkylidenebutenolide system with additional conjugation through the Cα-position in these natural C_{37}-norcarotenoids called for the use of a common central dihalogenated C_8-butenolide unit **7** as a linchpin.[9] We anticipated a regio(halogen)selective Stille coupling with the polyenylstannane **9** occurring at the alkenyl iodide end, which would then be followed by the final Stille reaction at the butenolide bromide position using alkenylstannane **6** (Figure

(5) Zeng, F.; Negishi, E. *Org. Lett.* **2001**, *3*, 719.
(6) Vaz, B.; Alvarez, R.; de Lera, A. R. *J. Org. Chem.* **2002**, *67*, 5040. See the stereochemical correction in ref 24.
(7) Vaz, B.; Alvarez, R.; Brückner, R.; de Lera, A. R. *Org. Lett.* **2005**, *7*, 545.
(8) For other approaches to enantiopure peridinin **2**, see the following: (a) Furuichi, N.; Hara, H.; Osaki, T.; Mori, H.; Katsumura, S. *Angew. Chem. 114*, 1065; *Angew. Chem., Int. Ed.* **2002**, *41*, 1023. (b) Furuichi, N.; Hara, H.; Osaki, T.; Takano, M.; Mori, H.; Katsumura, S. *J. Org. Chem.* **2004**, *69*, 7949−7959.
(9) This halogen-differentiated γ-alkylidenebutenolide was constructed using a Mukaiyama aldol reaction followed by dehydration as described in ref 7.

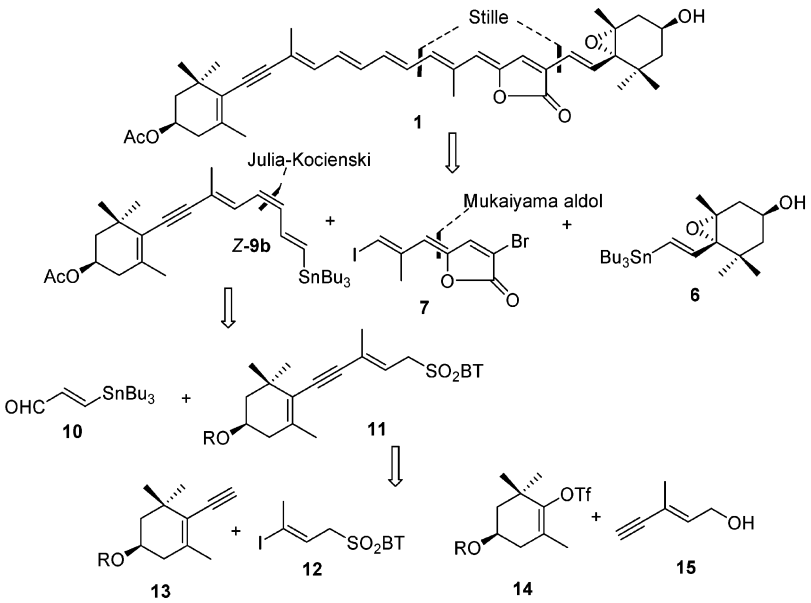
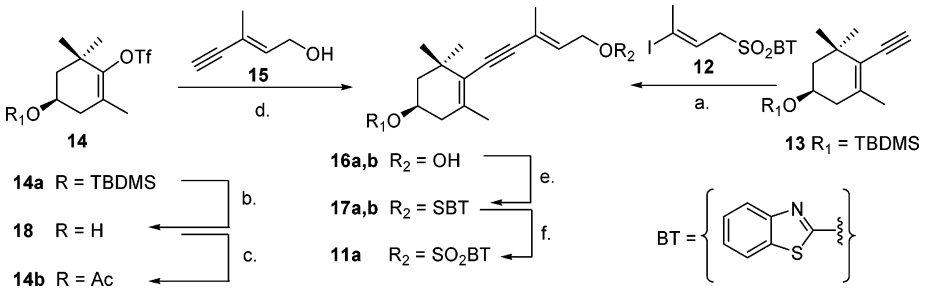


FIGURE 4. Retrosynthetic analysis of pyrrhoxanthin **1** using the dihalogenated C_8-butenolide **7** as a linchpin.

SCHEME 1[a]



[a](a) $Pd(PPh_3)_4$, K_2CO_3, DMF, 60 °C; (b) $(n\text{-Bu})_4NF$, THF, 25 °C, 4 h; (c) Ac_2O, Py, 25 °C, 13 h, (89%, b−c); (d) $Pd(PPh_3)_4$, K_2CO_3, DMF, 60 °C (90% for **16a**, 76% for **16b**); (e) BTSH, DIAD, PPh_3, THF, −10 °C for **17a** (98%; 10:1 *E*/*Z*); BTSH, DIAD, PPh_3, THF, 25 °C for **17b** (88%; 1.4:1 *E*/*Z*); (f) 35% H_2O_2, $(NH_4)_6Mo_7O_{24}\cdot 4H_2O$, EtOH, 0 °C for **11a** (65%).

4).[10] Polyenylstannane **9** stood out as the only remaining fragment for attempting the convergent sequential halogen-selective Stille cross-coupling approach[11] to pyrrhoxanthin **1**. In exploiting the greater stability of the *Z* isomers in this series, we conceived that **9** could be obtained by a *Z*-selective Julia-Kocienski olefination of β-stannylacrolein **10** and allyl benzothiazolyl-(BT)-sulfone **11**.[7] This sulfone could in turn be acquired through a cross-coupling reaction[12] that combines either alkenyliodide **12** and enyne **13**[13] or cycloalkenyl triflate **14**[14] and enynol **15**, followed by the appropriate functional group transformations. The former option was discarded following the observation that coupling between **12** and **13** under Heck conditions [$Pd(PPh_3)_4$, K_2CO_3, DMF] furnished only a mixture of isomers of the starting allyl BT-sulfone **12** at ambient temperature and degradation of the starting materials upon heating (up to 60 °C).

Enol triflate **14a**[15] derived from enantiopure actinol[16] was treated with enynol **15** under the reaction conditions indicated above [$Pd(PPh_3)_4$, K_2CO_3, DMF, 60 °C] to afford the expected alcohol **16a** in good yield (90%). Mitsunobu-like BT-sulfide formation (**17a**) and subsequent oxidation following the Kocienski method[17] transformed this alcohol into the corresponding allyl BT-sulfone **11a** (Scheme 1). Both processes required a rigorous control of the temperature, which should not exceed 0 °C, to minimize the isomerization of the C9′−C10′ double bond (carotenoid numbering).

(10) Fragment **6** has already been described in enantiopure form starting from actinol through a sequence involving the preparation of an epoxycyclohexanol through a Sharpless asymmetric epoxidation, followed by Swern oxidation, alkyne formation using Shioiri's lithium diazomethane, and palladium-assisted hydrostannation. See ref 7 for details.

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(13) Enyne **13** was synthesized by coupling triflate **14a** with TMS-acetylene [$Pd(PPh_3)_4$, K_2CO_3, DMF, 60 °C, 93%) and alkyne desilylation (K_2CO_3, MeOH, 25 °C, 2 h, 98%).

(14) (a) Ito, M.; Hirata, Y.; Shibata, Y.; Tsukida, K. *J. Chem. Soc., Perkin Trans. 1* **1990**, 197. (b) Ito, M.; Yamano, Y.; Sumiya, S.; Wada, A. *Pure Appl. Chem.* **1994**, *66*, 939. (c) Yamano, Y.; Tode, C.; Ito, M. *J. Chem. Soc., Perkin Trans. 1* **1995**, 1895.

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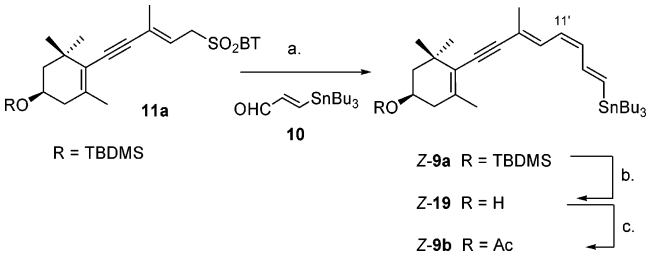
SCHEME 2[a]



[a] (a) NaHMDS, THF, −78 °C → 25 °C (78%); (b) (n-Bu)$_4$NF, THF, 25 °C, 3 h; (c) Ac_2O, Py, 25 °C, 4 h (50%, b−c).

Deprotection of allyl BT-sulphone **11a** faced unanticipated problems. Treatment with (n-Bu)$_4$NF (THF, 25 °C, 1.5 h) led to degradation, probably due to the basicity of the fluoride ion, especially under anhydrous conditions,[18] which appears to be incompatible with the sensitive sulphone. The use of HF (48% HF, pyridine, THF, 25 °C, 3.5 h) furnished the deprotected allyl BT-sulfone, but with the undesired C9′−C10′ *Z* geometry.[19] Alternative conditions were explored, but unfortunately either complete or partial isomerization of the double bond of the starting sulfone **11a** resulted: PPTS/MeOH at 50 °C (only *Z*),[20] CAN/MeOH at 0 °C (1:3 *E/Z*) or $LiBF_4/CH_3CN$ (CH_2Cl_2, H_2O, 25 °C, 40 h, only *Z*).[21,22]

Because of incompatibility of the various silyl ether deprotection conditions with the allyl BT-sulfone group or with its geometrical integrity, the incorporation of the required acetate was attempted earlier in the synthesis, thus avoiding manipulation of unstable intermediates. Triflate **14a** was desilylated (TBAF, THF, 25 °C) and acetylated (Ac_2O, Py, 25 °C, 89% combined yield) to provide the substrate for the subsequent cross coupling reaction with enynol **15** (Scheme 1). Despite the success of this Pd catalyzed process (76% yield), the coupled product **16b** showed high geometrical instability, and isomerization of the double bond under the Mitsunobu-type S-alkylation conditions was observed (a 1.4:1 *E*/*Z* mixture of **17b** was obtained). The deprotection-acetylation of the secondary alcohol was therefore postponed until a later stage in the sequence.

The synthesis of the enantiopure polyenylstannane **9** relied on the precedented cis-selective (Sylvestre) Julia olefination between allyl BT-sulfone **11a** and β-stannylacrolein **10** which uneventfully provided *Z*-**9a**.[23] The $Z > E$ stereoselectivity resulting from the condensation of this (formally) allyl 2,6-dien-4-yn-1-yl BT-sulfone (Scheme 2) confirms the general trend exhibited by other allyl BT-sulfones in their condensation with unsaturated aldehydes.[24] Although the stereochemical outcome is opposite to that required for natural pyrrhoxanthin **1**, we considered this to be inconsequential, since several methods that induce the isomerization of a cis-polyene to the all-trans geometry are known, including our observation that Stille reaction conditions are efficient in this setting. At this stage the hydroxyl group at C3′ of *Z*-**9a** was deprotected to *Z*-**19** and acetylated, affording the corresponding C_{18} polyenyl stannane *Z*-**9b** (50% combined yield) required for the construction of the C_{37} skeleton of pyrrhoxanthin **1**.

The stage was now set for the connective Stille cross-coupling reactions, under the optimized conditions developed in our laboratory for carotenoid synthesis. Using $Pd_2(dba)_3$·$CHCl_3$ and $AsPh_3$ as catalyst in a thoroughly deoxygenated BHT-added THF in the presence of tetrabutylammonium phosphinate[25] $Bu_4NPh_2PO_2$ as Bu_3SnX scavenger, stannane *Z*-**9b** was coupled to γ-alkylidenebutenolide **7** in an excellent yield (90%, Scheme 3). The geometry of the sole reaction product was determined as corresponding to 9′*Z*-**20** after careful analysis and interpretation of the NMR spectra (^{1}H, COSY, HSQC) and nuclear Overhauser effect (NOE) interactions (the most significant of which are depicted in Figure 5). Additionally, the value of the vicinal coupling constants for the vinyl protons across the double bonds (between 14 and 14.5 Hz) confirmed the trans geometry at the C11′−C14′ and C15′−C15 diene fragments. Given the short reaction times and the mild temperatures used, the occurrence of this highly selective double isomerization process during a Stille coupling is quite remarkable. We surmise that the isomerization could be due to ligand exchange processes at palladium, involving the alkyne and neighboring olefins.

For the completion of the C_{37}-norcarotenoid skeleton, coupling of 9′*Z*-**20** and alkenylstannane **6** provided 9′*Z*-**1** as a single isolable product in moderate yield (37%, Scheme 3). As in the case of peridinin **2**, the final step of the synthesis required heating to 55 °C for extended periods (43 h) under the same conditions indicated above, owing to the poor reactivity of **6**.

The structure of the final carotenoid was established through rigorous data analysis from ROESY experiments (Figure 5), which confirmed in particular the 9′*Z* geometry as well as the trans geometry of the remaining polyene bonds of the synthetic 9′*Z*-pyrrhoxanthin 9′*Z*-**1**.

In summary, the Julia−Stille−Stille sequence is a valuable convergent approach to construct the complete skeleton of highly functionalized acetylenic C_{37}-norcarotenoid butenolides. The palladium-induced isomerization, which proved beneficial during the second Stille coupling in the case of peridinin **2**, can be a limitation, as shown in the present approach to pyrrhoxanthin **1**. A double isomerization of a *Z*,*E*- to the *E*,*Z*-enyne occurs during the first Stille coupling, despite the moderate temperatures and relatively short reaction times employed, affording the thermodynamically more stable C9′-*Z*-pyrrhoxanthin.[26] This feature represents an important drawback in the preparation of unstable naturally occurring acetylenic carotenoids such as pyrrhoxanthin **1** using Pd-catalyzed cross-coupling reactions. Notwithstanding this limitation, our experience with polyenes indicates that Pd-catalyzed processes represent a valuable synthetic tool for the preparation of the adequate fragments for carotenoid synthesis in an exquisite stereoselective manner. Our efforts are now directed toward the stereoselective synthesis of

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(17) Blakemore, P. R.; Cole, W. J.; Kocienski, P.; Morley, A. *Synlett* **1998**, 26.
(18) (a) Corey, E. J.; Venkateswarlu, A. *J. Am. Chem. Soc.* **1972**, *94*, 6190. (b) Clark, J. H. *Chem. Rev.* **1980**, *80*, 429.
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(22) Metcalf, B. W.; Burkhart, K. P.; Jund, K. *Tetrahedron Lett.* **1980**, *21*, 35.
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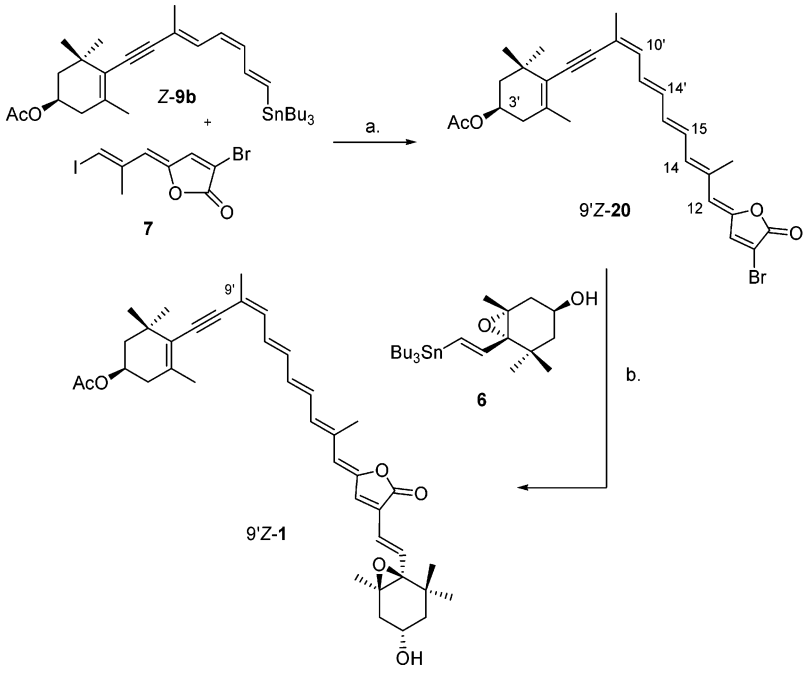
(26) Bernhard, K.; Kienzle, F.; Mayer, H.; Müller, R: K. *Helv. Chim. Acta* **1980**, *63*, 1473.

SCHEME 3[a]



[a] (a) $Pd_2(dba)_3$·$CHCl_3$, $AsPh_3$, $Bu_4NPh_2PO_2$, BHT, THF, 25 °C, 6.5 h (90%); (b) $Pd_2(dba)_3$·$CHCl_3$, $AsPh_3$, $Bu_4NPh_2PO_2$, BHT, THF, 55 °C, 43 h (37%).

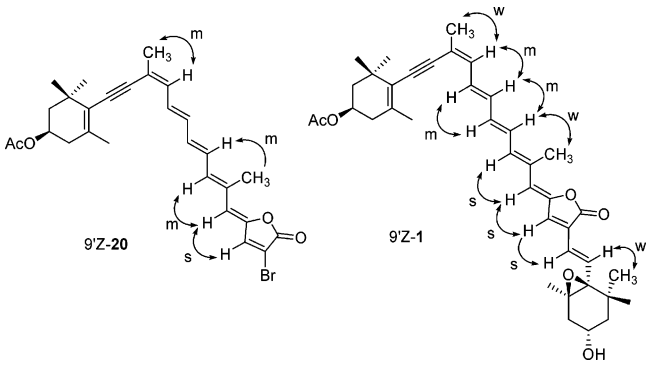


FIGURE 5. NOEs for 9′*Z*-**20** and 9′*Z*-pyrrhoxanthin 9′*Z*-**1** extracted from the NOESY spectra. The intensities are indicated as s (strong > 7%), m (medium, 3−7%), and w (weak, < 3%).

all-trans pyrrhoxanthin **1,** avoiding the use of palladium catalysts during the late stages of the sequence and ensuring the stereocontrolled preparation of these very unstable and highly functionalized carotenoids.

Experimental Section.

(*R*)-4-Acetoxy-2,6,6-trimethylcyclohex-1-en-1-yl Trifluoromethanesulfonate 14b. To a solution of (*R*)-4-(*tert*-butyldimethylsilyloxy)-2,6,6-trimethylcyclohex-1-en-1-yl trifluoromethanesulfonate **14a** (1.30 g, 3.23 mmol) in THF (30 mL) was added (*n*-Bu)$_4$NF (4.85 mL, 4.85 mmol), and the mixture was stirred at 25 °C for 4 h. The reaction mixture was poured into a saturated $NaHCO_3$ solution and extracted with Et_2O (3x). The combined organic layers were dried (Na_2SO_4), and the solvent was evaporated. The residue was used in the next step without further purification. To a solution of this residue in pyridine (10 mL) was added Ac_2O (1.51 mL, 16.17 mmol). After stirring at 25 °C for 13 h, the mixture was diluted with *t*-BuOMe (3x) and washed with a saturated $CuSO_4$ solution (2x). The organic layer was dried (Na_2SO_4), and the solvent was evaporated. The residue was purified by column chromatography (90:10 hexane/ethyl acetate) to afford 0.949 g (89%) of a colorless oil identified as (*R*)-4-acetoxy-2,6,6-trimethylcyclohex-1-en-1-yl trifluoromethanesulfonate **14b**. $[\alpha]^{26}_D$ −8.79 (*c* 0.264, MeOH). ^{1}H NMR (400 MHz, $CDCl_3$): δ 5.1−4.9 (m, 1H), 2.53 (dd, J = 17.0, 5.7 Hz, 1H), 2.19 (dd, J = 17.0, 8.6 Hz, 1H), 2.00 (s, 3H), 1.9−1.8 (m, 1H), 1.8−1.7 (m, 1H), 1.72 (s, 3H), 1.20 (s, 3H), 1.14 (s, 3H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ 170.4 (s), 148.8 (s), 123.2 (s), 118.7 (q, $^1J_{C-F}$ = 319.7 Hz), 66.4 (d), 44.4 (t), 37.2 (t), 36.4 (s), 27.0 (q), 26.5 (q), 21.1 (q), 17.4 (q) ppm. MS (EI$^+$) *m*/*z* (%): 353 (M^+ + 23, 78), 348 (12), 332 (M^+ + 2, 12), 331 (M^+ + 1, 100), 271 (13). HRMS (EI$^+$): Calcd for $C_{12}H_{18}F_3O_5S$, 331.0821; found, 331.0822.

(1*R*,3′*E*)-4-(5-Hydroxy-3-methylpent-3-en-1-yn-1-yl)-3,5,5-trimethylcyclohex-3-en-1-yl Acetate 16b. To a solution of (*R*)-4-acetoxy-2,6,6-trimethylcyclohex-1-en-1-yl trifluoromethanesulfonate **14b** (0.804 g, 2.43 mmol) in DMF (29 mL) was added $Pd(PPh_3)_4$ (0.18 g, 0.24 mmol) and K_2CO_3 (1.01 g, 7.30 mmol). After addition of 3-methylpent-2-en-4-yn-1-ol **15** (0.444 g, 4.62 mmol), the reaction mixture was stirred at 60 °C for 6 h. The mixture was diluted with Et_2O, and the layers were separated. The aqueous layer was washed with H_2O (3x), the combined organic layers were dried (Na_2SO_4), and the solvent was evaporated. The residue was purified by column chromatography (80:20 hexane/ethyl acetate) to afford 0.514 g (76%) of a colorless oil identified as (1*R*,3′*E*)-4-(5-hydroxy-3-methylpent-3-en-1-yn-1-yl)-3,5,5-trimethylcyclohex-3-en-1-yl acetate **16b**. $[\alpha]^{26}_D$ −47.39 (*c* 0.34, MeOH). ^{1}H NMR (400 MHz, $(CD_3)_2CO$): δ 5.94 (t, J = 6.5 Hz, 1H), 5.1−4.9 (m, 1H), 4.19 (t, J = 5.9 Hz, 2H), 3.73 (t, J = 5.5 Hz, 1H), 2.47 (dd, J = 17.7, 5.5 Hz, 1H), 2.14 (dd, J = 17.8, 9.1 Hz, 1H), 2.00 (s, 3H), 1.89 (s, 3H), 1.85 (s, 3H), 1.9−1.8 (m, 1H), 1.55 (t, J = 11.8 Hz, 1H), 1.19 (s, 3H), 1.16 (s, 3H) ppm. ^{13}C NMR (100 MHz, $(CD_3)_2CO$): δ 169.5 (s), 136.2 (s), 136.1 (d), 123.7 (s), 119.0 (s), 96.3 (s), 84.6 (s), 67.1 (d), 58.0 (t), 42.0 (t), 36.9 (t), 35.6 (s), 29.5 (q), 27.9 (q), 21.4 (q), 20.1 (q), 16.8 (q) ppm. MS (EI$^+$) *m*/*z* (%): 299 (M^+ + 23, 100), 199 (51). HRMS (EI$^+$): Calcd for $C_{17}H_{24}NaO_3$, 299.1618; found, 299.1619.

(−)-(2*E*,4′*R*)-5-(4-*tert*-Butyldimethylsilyloxy-2,6,6-trimethylcyclohex-1-en-1-yl)-3-methylpent-2-en-4-yn-1-ol 16a. To a solution of (*R*)-4-(*tert*-butyldimethylsilyloxy)-2,6,6-trimethylcyclohex-1-en-1-yl trifluoromethanesulfonate **14a** (0.50 g, 1.25 mmol) in

DMF (15 mL) was added $Pd(PPh_3)_4$ (0.14 g, 0.12 mmol) and K_2CO_3 (0.52 g, 3.73 mmol). After the addition of 3-methylpent-2-en-4-yn-1-ol **15** (0.36 mL, 3.73 mmol), the reaction mixture was stirred at 60 °C for 6 h. The mixture was diluted with Et_2O, and the layers were separated. The aqueous layer was washed with H_2O (3x), the combined organic layers were dried (Na_2SO_4), and the solvent was evaporated. The residue was purified by column chromatography (80:20 hexane/ethyl acetate) to afford 0.073 g (98%) of a colorless oil identified as (−)-(2*E*,4′*R*)-5-(4-*tert*-butyldimethylsilyloxy-2,6,6-trimethylcyclohex-1-en-1-yl)-3-methylpent-2-en-4-yn-1-ol **16a**. $[\alpha]^{26}_D$ −78.36 (*c* 0.16, $CHCl_3$). ^{1}H NMR (400 MHz, $(CD_3)_2CO$): δ 5.82 (tq, J = 6.5 and 1.3 Hz, 1H), 4.08 (t, J = 6.5 Hz, 2H), 3.9−3.8 (m, 1H), 2.23 (ddd, J = 17.7, 5.4, 1.4 Hz, 1H), 1.95 (ddd, J = 17.7 Hz, 9.3, 1.4 Hz, 1H), 1.77 (s, 3H), 1.74 (d, J = 1.3 Hz, 3H), 1.64 (ddd, J = 12.0, 3.5, 1.9 Hz, 1H), 1.33 (t, J = 12.0 Hz, 1H), 1.06 (s, 3H), 1.03 (s, 3H), 0.81 (s, 9H), 0.00 (s, 6H) ppm. ^{13}C NMR (100 MHz, $(CD_3)_2CO$): δ 138.6 (s), 137.3 (d), 124.9 (s), 120.5 (s), 97.5 (s), 86.4 (s), 66.5 (d), 59.4 (t), 48.2 (t), 42.9 (t), 37.4 (s), 31.2 (q), 29.4 (q), 26.6 (q, 3x), 22.9 (q), 19.0 (s), 18.2 (q), −4.1 (q, 2x) ppm. MS (EI$^+$) *m*/*z* (%): 348 (M^+, 4), 291 (17), 273 (38), 235 (65), 218 (19), 217 (100), 157 (15), 143 (18), 75 (23). HRMS (EI$^+$): Calcd for $C_{21}H_{36}O_2Si$, 348.2485; found, 348.2473. FT-IR (NaCl): ν 3600−3100 (br, OH), 2950 (s, C−H), 2928 (s, C−H), 2857 (s, C−H), 1469 (m), 1377 (m), 1253 (m), 1086 (s, Si−O), 836 (m) cm^{-1}

(−)-(2*E*,4′*R*)-1-(Benzothiazol-2-yl)sulfanyl-5-(4-*tert*-butyldimethylsilyloxy-2,6,6-trimethylcyclohex-1-en-1-yl)-3-methylpent-2-en-4-yne 17a. A solution of diisopropyl azodicarboxylate (DIAD, 0.083 mL, 0.43 mmol) and PPh_3 (0.123 g, 0.47 mmol), in THF (1 mL) was stirred at −10 °C for 5 min. A solution of (2*E*,4′*R*)-5-(4-*terc*-butyldimethylsilyloxy-2,6,6-trimethylcyclohex-1-en-1-yl)-3-methylpent-2-en-4-yn-1-ol **16a** (0.10 g, 0.29 mmol) in THF (1 mL) and 2-mercaptobenzothiazole (0.07 g, 0.43 mmol) were added, and the resulting mixture was stirred at −10 °C for 2 h. The solvent was evaporated, and the residue was purified by chromatography (96:2:2 hexane/ethyl acetate/Et_3N) to afford 0.14 g (98%) of a colorless oil identified as (−)-(2*E*,4′*R*)-1-(benzothiazol-2-yl)sulfanyl-5-(4-*tert*-butyldimethylsilyloxy-2,6,6-trimethylcyclohex-1-en-1-yl)-3-methylpent-2-en-4-yne **17a**. $[\alpha]^{25}_D$ −85.58 (*c* 0.03, $CHCl_3$). ^{1}H NMR (400 MHz, $(CD_3)_2CO$): δ 7.95 (dd, J = 8.0, 0.5 Hz, 1H), 7.86 (dd, J = 8.1, 0.5 Hz, 1H), 7.48 (ddd, J = 8.1, 7.3, 1.2 Hz, 1H), 7.37 (ddd, J = 8.0, 7.3, 1.2 Hz, 1H), 6.04 (td, J = 8.0, 1.5 Hz, 1H), 4.21 (d, J = 8.0 Hz, 2H), 4.0−3.9 (m, 1H), 2.31 (ddd, J = 17.7, 5.6, 1.3 Hz, 1H), 2.04 (s, 3H), 2.00 (m, 1H), 1.85 (s, 3H), 1.73 (ddd, J = 12.6, 3.5, 2.0 Hz, 1H), 1.41 (t, J = 12.0 Hz, 1H), 1.14 (s, 3H), 1.10 (s, 3H), 0.90 (s, 9H), 0.09 (s, 6H) ppm. ^{13}C NMR (100 MHz, $(CD_3)_2CO$): δ 166.8 (s), 154.3 (s), 139.1 (s), 136.3 (s), 130.1 (d), 127.2 (d), 125.5 (d), 124.4 (s), 124.3 (s), 122.4 (d), 122.3 (d), 96.8 (s), 87.9 (s), 66.1 (d), 47.9 (t), 42.6 (t), 37.1 (s), 31.9 (t), 30.9 (q), 29.0 (q), 26.3 (q, 3x), 22.7 (q), 18.7 (s), 18.2 (q), −4.4 (q, 2x) ppm. MS (EI$^+$) *m*/*z* (%): 499 ($M^+ + 2$, 8), 498 ($M^+ + 1$, 16), 497 (M^+, 42), 332 (14), 331 (48), 330 (13), 199 (36), 174 (14), 173 (100), 157 (15), 143 (21), 129 (11), 75 (27), 73 (43). HRMS (EI$^+$): Calcd for $C_{28}H_{39}OS_2Si$, 497.2242; found, 497.2238. FT-IR (NaCl): ν 2956 (s, C−H), 2921 (s, C−H), 2856 (s, C−H), 2186 (w, C═C), 1460 (s), 1427 (s), 1083 (s, Si−O), 996 (m) cm^{-1}.

(2*E*,4′*R*)-1-(Benzothiazol-2-yl)sulfanyl-5-(4-*tert*-butyldimethylsilyloxy-2,6,6-trimethylcyclohex-1-en-1-yl)-3-methylpent-2-en-4-yne 11a. To a solution of (2*E*,4′*R*)-1-(benzothiazol-2-yl)sulfanyl-5-(4-*tert*-butyldimethylsilyloxy-2,6,6-trimethylcyclohex-1-en-1-yl)-3-methylpent-2-en-4-yne **17a** (0.20 g, 0.40 mmol) in EtOH (5 mL), at 0 °C, was added a solution of $(NH_4)_6Mo_7O_{24}\cdot 4H_2O$, (0.05 g, 0.04 mmol) in aqueous hydrogen peroxide (35%, 0.60 mL, 2.0 mmol). After stirring for 48 h, the mixture was quenched with brine and extracted with Et_2O (3x). The combined organic layers were washed with brine (2x) and dried (Na_2SO_4), and the solvent was removed. The residue was purified by chromatography (silicagel, 85:12:3 hexane/EtOAc/Et_3N) to afford 0.14 g (65%) of a white solid identified as (2*E*,4′*R*)-1-(benzothiazol-2-yl)sulfonyl-5-(4-*tert*-butyldimethylsilyloxy-2,6,6-trimethylcyclohex-1-en-1-yl)-3-methylpent-2-en-4-yne **11a. *E*-11a**: $[\alpha]^{26}_D$ −25.12 (*c* 0.23, MeOH). ^{1}H NMR (600 MHz, $CDCl_3$): δ 8.19 (d, J = 8.1 Hz, 1H), 7.98 (d, J = 8.1 Hz, 1H), 7.58 (m, 2H), 5.74 (t, J = 8.1 Hz, 1H), 4.31 (d, J = 8.2 Hz, 2H), 3.9−3.8 (m, 1H), 2.21 (dd, J = 17.7, 5.3 Hz, 1H′), 2.02 (dd, J = 17.8, 9.3 Hz, 1H), 1.79 (s, 3H), 1.78 (s, 3H), 1.65 (d, J = 12.6 Hz, 1H), 1.39 (t, J = 12.1 Hz, 1H), 1.06 (s, 3H), 1.03 (s, 3H), 0.85 (s, 9H), 0.03 (s, 6H) ppm. ^{13}C NMR (150 MHz, $CDCl_3$): δ 165.7 (s), 152.6 (s), 139.7 (s′), 137.1 (s), 129.4 (s), 128.0 (d), 127.6 (d), 125.4 (d), 123.3 (s), 122.3 (d), 117.7 (d), 94.9 (s), 89.1 (s), 65.3 (d), 54.9 (t), 46.9 (t′), 42.0 (t), 36.4 (s), 30.3 (q), 28.6 (q), 25.9 (q, 3x), 22.4 (q), 18.3 (q), 18.2 (s), −4.7 (q), −4.6 (q) ppm. MS (EI$^+$) *m*/*z* (%): 529 (M^+, 1), 332 (28), 331 (100), 200 (16), 199 (90), 174 (10), 173 (68), 157 (12), 143 (16), 75 (18), 73 (28). HRMS (EI$^+$): Calcd for $C_{24}H_{30}NO_3S_2Si$, 472.1436; found, 472.1424. FT-IR (NaCl): ν 2956 (s, C−H), 2928 (s, C−H), 2856 (s, C−H), 2186 (m, C≡C), 1612 (w), 1473 (s), 1334 (s), 1146 (s), 1085 (s) cm^{-1}. Anal. Calcd for $C_{28}H_{39}NO_3S_2Si$: C, 63.47; H, 7.42; N, 2.64; S, 12.10. Found: C, 63.20; H, 7.39; N, 2.69; S, 12.05.

***Z*-11a:** ^{1}H NMR (600 MHz, $CDCl_3$): δ 8.18 (d, J = 8.0 Hz, 1H), 8.00 (d, J = 8.1 Hz, 1H), 7.60 (m, 2H), 5.70 (t, J = 7.6 Hz, 1H), 4.47 (d, J = 7.6 Hz, 2H), 3.9−3.8 (m, 1H), 2.25 (dd, J = 17.7, 5.2 Hz, 1H), 2.05 (dd, J = 17.7, 9.3 Hz, 1H), 1.94 (s, 3H), 1.79 (s, 3H), 1.67 (d, J = 12.4 Hz, 1H), 1.40 (t, J = 12.1 Hz, 1H), 1.02 (s, 3H), 1.00 (s, 3H), 0.91 (s, 9H), 0.08 (s, 6H) ppm. ^{13}C NMR (150 MHz, $CDCl_3$): δ 165.3 (s), 152.7 (s), 140.1 (s′), 137.3 (s), 129.9 (s), 127.9 (d), 127.4 (d), 125.6 (d), 123.2 (s), 122.2 (d), 117.8 (d), 94.9 (s), 90.7 (s), 65.2 (d), 57.4 (t), 46.9 (t), 42.1 (t), 36.3 (s), 30.4 (q), 28.6 (q), 25.9 (q, 3x), 23.8 (q), 22.6 (q), 18.2 (s), −4.6 (q, 2x) ppm. MS (FAB$^+$) *m*/*z* (%): 529 (M^++1, 11), 332 (32), 331 (100), 286 (16), 215 (16), 200 (20), 199 (70), 189 (17), 180 (16), 178 (17), 173 (46), 169 (16), 167 (20), 166 (17), 165 (29), 157 (18), 155 (24), 154 (65). HRMS (FAB$^+$): Calcd for $C_{28}H_{40}NO_3SiS_2$, 530.2219; found, 530.2209. FT-IR (NaCl): ν 2956 (s, C−H), 2928 (s, C−H), 2856 (s, C−H), 2184 (m, C≡C), 1612 (w), 1471 (s), 1335 (s), 1146 (s), 1085 (s) cm^{-1}. Anal. Calcd for $C_{28}H_{39}NO_3SiS_2$: C, 63.47; H, 7.42; N, 2.64; S, 12.10. Found: C, 63.21; H, 7.39; N, 2.60; S, 11.94.

(*R*)-*tert*-Butyldimethylsilyl 4-[(3′*E*,5′*Z*,7′*E*)-3-Methyl-8-(tributylstannyl)octa-3,5,7-trien-1-yn-1-yl]-3,5,5-trimethylcyclohex-3-en-1-yl Ether 11′*Z*-9a. To a solution of (2*E*,4′*R*)-1-(benzothiazol-2-yl)sulfanyl-5-[4-*tert*-butyldimethylsilyloxy-2,6,6-trimethylcyclohex-1-en-1-yl]-3-methylpent-2-en-4-yne **11a** (0.045 g, 0.085 mmol) in THF (4 mL), was added NaHMDS (0.25 mL, 1 M in THF, 0.25 mmol), and the reaction mixture was stirred for 30 min. A solution of 3-tri-*n*-butylstannylpropen-1-al **10** (0.044 g, 0.13 mmol) in THF (2 mL) was added, and the reaction mixture was stirred for 2 h. H_2O was slowly added, and the reaction mixture was allowed to reach ambient temperature. It was then diluted with Et_2O, and the separated aqueous layer was further extracted with Et_2O (3x). The combined organic layers were dried (Na_2SO_4), and the solvent was removed. The residue was purified by chromatography (C-18 silicagel, 80:20 CH_3CN/CH_2Cl_2), to afford 53.2 mg (78%) of a yellow oil identified as (*R*)-*tert*-butyldimethylsilyl 4-[(3′*E*,5′*Z*,7′*E*)-3-methyl-8-(tributystannyl)octa-3,5,7-trien-1-yn-1-yl]-3,5,5-trimethylcyclohex-3-en-1-yl ether 11′*Z*-**9a**. ^{1}H NMR (400 MHz, C_6D_6): δ 7.36 (dd, J = 18.5, 10.8 Hz, 1H), 7.0−6.9 (m, 2H), 6.47 (d, J = 18.5 Hz, 1H), 6.19 (t, J = 9.5 Hz, 1H), 4.0−3.8 (m, 1H), 2.24 (dd, J = 17.8, 5.3 Hz, 1H), 2.12 (dd, J = 17.8, 9.2 Hz, 1H), 1.90 (s, 3H), 1.88 (s, 3H), 1.78 (ddd, J = 12.6, 3.3, 1.7 Hz, 1H), 1.7−1.5 (m, 7H), 1.4−1.3 (m, 6H), 1.31 (s, 3H), 1.23 (s, 3H), 1.1−1.0 (m, 15H), 1.0−0.9 (m, 9H), 0.09 (s, 3H), 0.08 (s, 3H) ppm. ^{13}C NMR (100 MHz, C_6D_6): δ 142.3 (d), 138.2 (s), 136.3 (d), 132.3 (d), 129.8 (d), 126.5 (d), 124.2 (s), 121.5 (s), 95.4 (s), 93.6 (s), 65.4 (d), 47.2 (t), 42.1 (t), 36.4 (s), 30.5 (q, 3x), 29.2 (t, 3x $^3J_{Sn}$ = 10.4 Hz), 28.6 (q), 27.3 (t, 3x), 25.7 (q, 3x), 23.6 (q), 22.4 (q), 18.0 (s), 13.5 (q, 3x), 9.5 (t, 3x), −4.8 (q, 2x) ppm. MS (FAB$^+$) *m*/*z* (%): 660 ($M^+ + 2$, 13), 659 ($M^+ + 1$, 13), 658 ($M^+ + 1$, 12), 604 (27),

603 (67), 602 (34), 601 (51), 600 (25), 599 (27), 547 (28), 545 (39), 543 (26), 369 (22), 291 (69), 290 (26), 289 (56), 288 (22), 287 (34), 237 (34), 235 (63), 234 (23), 233 (48), 231 (30), 195 (24), 193 (22), 183 (22), 181 (28), 179 (100), 178 (32), 177 (93), 176 (31), 175 (62). HRMS (EI^+): calcd for $C_{36}H_{65}OSi^{116}Sn$, 657.3821; found, 659.3851; calcd for $C_{36}H_{65}OSi^{118}Sn$, 659.3827; found, 661.3817; calcd for $C_{36}H_{65}OSi^{120}Sn$, 661.3827; found, 661.3817.

(1*R*,3′*E*,5′*Z*,7′*E*)-4-[3-Methylocta-8-(tributylstannyl)-3,5,7-trien-1-yn-1-yl]-3,5,5-trimethylcyclohex-3-enyl Acetate *Z*-19. A solution of (*R*)-*tert*-butyldimethylsilyl 4-[(3*E*,5*Z*,7*E*)-3-methyl-8-(tributylstannyl)octa-3,5,7-trien-1-yn-1-yl]-3,5,5-trimethylcyclohex-3-en-1-yl ether ***Z*-9a** (0.51 g, 0.078 mmol) in THF (1 mL) was treated with *n*Bu_4NF (0.12 mL, 0.12 mmol), and the mixture was stirred at 25 °C for 2 h. It was then poured over an aqueous saturated $NaHCO_3$ solution and extracted with AcOEt (3x). The residue was used in the next step without purification. Acetic anhydride (0.036 mL, 0.39 mmol) was added to a solution of the residue above in pyridine (1 mL). After being stirred for 16 h at ambient temperature, EtOAc was added and the mixture was washed with a saturated $CuSO_4$ solution (2x), dried (Na_2SO_4), and the solvent was removed. The residue was purified by chromatography (silicagel, hexane/EtOAc/Et_3N 90:10:0 → 77:20:3 gradient), to afford 0.016 g (50%) of a yellow oil identified as (1*R*,3′*E*,5′*Z*,7′*E*)-4-[3-methylocta-8-(tributylstannyl)-3,5,7-trien-1-yn-1-yl]-3,5,5-trimethylcyclohex-3-en-1-yl acetate ***Z*-9b** and 0.011 g (0.017 mmol) of starting material ***Z*-9a**. ^1H NMR (400 MHz, C_6D_6): δ 7.36 (dd, J = 18.5, 10.8 Hz, 1H), 6.9−6.8 (m, 2H), 6.48 (d, J = 18.5 Hz, 1H), 6.2−6.1 (m, 1H), 5.4−5.2 (m, 1H), 2.31 (dd, J = 17.7, 5.4 Hz, 1H), 1.97 (dd, J = 17.8, 9.1 Hz, 1H), 1.87 (s, 3H), 1.80 (s, 3H), 1.8−1.7 (m, 1H), 1.71 (s, 3H), 1.7−1.6 (m, 6H), 1.6−1.5 (m, 1H), 1.4−1.3 (m, 6H), 1.26 (s, $3H_3$), 1.22 (s, 3H), 1.1−1.0 (m, 6H), 1.0−0.9 (m, 9H) ppm. ^{13}C NMR (100 MHz, C_6D_6): δ 169.3 (s), 142.3 (d), 137.0 (s), 136.5 (d), 132.4 (d), 130.0 (d), 126.4 (d), 124.4 (s), 121.4 (s), 95.0 (s), 93.7 (s), 67.4 (d), 42.3 (t), 37.3 (t), 35.9 (s), 30.1 (q), 29.2 (t, 3x, $^3J_{Sn-C}$ = 10.4 Hz), 28.5 (q), 27.3 (t, 3x, $^2J_{Sn-C}$ = 27.4 Hz), 23.5 (q), 22.1 (q), 20.5 (q), 13.5 (q, 3x), 9.5 (t, 3x) ppm. MS (FAB^+) *m*/*z* (%): 535 (M^+ -Bu, 6), 533 (M^+ -Bu, 7), 532 (M^+ -Bu, 11), 531 (M^+ -Bu, 35), 530 (M^+ -Bu, 17), 529 (M^+ -Bu, 28), 528 (M^+ -Bu, 14), 527 (M^+ -Bu, 17), 471 (26), 357 (24), 355 (24), 297 (20), 295 (36), 293 (79), 292 (30), 291 (100), 290 (38), 289 (72), 287 (29), 239 (41), 238 (39), 237 (79), 235 (85), 234 (30), 233 (62), 232 (24), 231 (37), 223 (27), 222 (30), 221 (99), 207 (49), 205 (22), 193 (25), 191 (25), 179 (62), 177 (61), 175 (40). HRMS (EI^+): Calcd for $C_{28}H_{43}O_2{}^{116}Sn$, 527.2280; found, 527.2297; calcd for $C_{28}H_{43}O_2{}^{118}Sn$, 529.2279; found, 529.2255; calcd for $C_{28}H_{43}O_2{}^{120}Sn$, 531.2285; found, 531.2289.

***9′Z*-20.** To a solution of $Pd_2(dba)_3{\cdot}CHCl_3$ (5×10^{-4} g, 0.005 mmol) in THF (0.3 mL) was added $AsPh_3$ (0.001 g, 0.004 mmol). After stirring for 5 min at 25 °C, (5*Z*,1′*E*)-3-bromo-5-(3-iodo-2-methyl-propenyliden)-5*H*-furan-2-one **7** (0.008 g, 0.023 mmol) was added, and the mixture was stirred for 10 min at 25 °C. A solution of (1*R*,3′*E*,5′*Z*,7′*E*)-4-[3-methylocta-8-(tributylstannyl)-3,5,7-trien-1-yn-1-yl]-3,5,5-trimethylcyclohex-3-en-1-yl acetate ***Z*-9b** (0.016 g, 0.028 mmol) in THF (0.3 mL) and $Bu_4NPh_2PO_2$ (0.011 g, 0.023 mmol) were added, and the reaction mixture was stirred for at 25 °C for 6.5 h. Brine was added, and the mixture was extracted with EtOAc/CH_2Cl_2 (90:10) (3x). The combined organic layers were dried (Na_2SO_4), and the solvent was removed. The residue was purified by chromatography (silicagel, hexane/EtOAc 60:40 → 50:50 gradient), to afford 10.5 mg (90%) of a red solid identified as ***9′Z*-20**. ^1H NMR (600 MHz, $(CD_3)_2CO$): δ 7.93 (s, 1H), 6.87 (dd, J = 14.5, 11.4 Hz, 1H), 6.79 (dd, J = 14.0, 11.9 Hz, 1H), 6.66 (d, J = 11.9 Hz, 1H), 6.62 (dd, J = 14.0, 11.5 Hz, 1H), 6.55 (dd, J = 14.4, 10.9 Hz, 1H), 6.41 (d, J = 10.8 Hz, 1H), 6.10 (s, 1H), 5.2−5.0 (m, 1H), 2.52 (dd, J = 17.9, 5.5 Hz, 1H), 2.21 (s, 3H), 2.2−2.1 (m, 1H), 2.00 (s, 6H, C_9'-CH_3), 1.96 (s, 3H), 1.87 (ddd, J = 12.4, 3.5, 1.8 Hz, 1H), 1.58 (t, J = 11.8 Hz, 1H), 1.24 (s, 3H), 1.21 (s, 3H) ppm. ^{13}C NMR (100 MHz, $(CD_3)_2CO$): δ 171.6 (s), 167.0 (s), 148.4 (s), 145.3 (d), 141.2 (d), 139.7 (d), 136.7 (d), 135.3 (d, 2x), 134.6 (s), 132.2 (s), 131.6 (d), 125.9 (s), 123.6 (s), 121.7 (d), 110.4 (s), 110.2 (s), 97.3 (s), 69.1 (d), 44.0 (t), 39.1 (t), 37.7 (s), 31.7 (q), 30.1 (q), 24.8 (q), 23.7 (q), 22.2 (q), 16.3 (q) ppm. MS (FAB^+) *m*/*z* (%): 513 (M^+ -Ac + 1, 57), 512 (M^+ -Ac, 100), 511 (M^+ -Ac − 1, 58), 510 (M^+ -Ac, 90), 461 (34), 460 (63), 453 (37), 451 (40), 327 (55), 325 (34), 309 (38). HRMS (IE^+): Calcd for $C_{28}H_{31}{}^{79}BrO_4$, 510.1406; found, 510.1394; calcd for $C_{28}H_{31}{}^{81}BrO_4$, 512.1385; found, 512.1379.

***9′Z*-Pyrrhoxanthin 9′*Z*-1.** To a solution of $Pd_2(dba)_3{\cdot}CHCl_3$ (0.001 g, 0.001 mmol) in THF (0.5 mL) was added $AsPh_3$ (0.002 g, 0.008 mmol). After stirring at 25 °C for 5 min, a solution of ***9′Z*-20** (0.010 g, 0.020 mmol) was added, and the mixture was stirred for at 25 °C for 10 min. A solution of tributyl{(1*E*,1′*S*,6′*R*)-2-(2,2,6-trimethyl-7-oxa-bicyclo[4.1.0]heptan-1-yl)vinyl}stannane **6** (0.011 g, 0.020 mmol) in THF (1.0 mL) and $Bu_4NPh_2PO_2$ (0.009 g, 0.020 mmol) were added, and the reaction was thoroughly degassed using freeze−thaw cycles (3x). After being stirred at 55 °C for 43 h, brine was added and the mixture was extracted with EtOAc/CH_2Cl_2 (90:10) (3x). The combined organic layers were dried (Na_2SO_4), and the solvent was removed. The residue was purified by chromatography (silicagel, 67:20:3 hexane/acetone/Et_3N), to afford 4.5 mg (37%) of a red solid identified as 9′*Z*-pyrroxanthin ***9′Z*-1**. ^1H NMR (600 MHz, $CDCl_3$): δ 7.16 (d, J = 15.6 Hz, 1H), 7.01 (s, 1H), 6.79 (dd, J = 14.4, 11.3 Hz, 1H), 6.61 (dd, J = 13.8, 11.6 Hz, 1H), 6.46 (d, J = 11.1 Hz, 1H), 6.45 (dd, J = 14.3, 12.1 Hz, 1H), 6.4−6.3 (m, 1H), 6.36 (d, J = 15.5 Hz, 1H), 6.28 (d, J = 11.1 Hz, 1H), 5.71 (s, 1H), 5.2−5.0 (m, 1H), 4.0−3.8 (m, 1H), 2.52 (dd, J = 17.5, 5.5 Hz, 1H), 2.39 (ddd, J = 14.3, 5.0, 1.6 Hz, 1H), 2.21 (s, 3H), 2.15 (dd, J = 17.3, 9.4 Hz, 1H), 2.04 (s, 3H), 2.00 (s, 3H), 1.94 (s, 3H), 1.85 (ddd, J = 12.5, 3.4, 1.6 Hz, 1H′), 1.7−1.6 (m, 3H), 1.3−1.2 (m, 1H), 1.21 (s, 3H), 1.20 (s, 3H), 1.19 (s, 6H), 0.96 (s, 3H) ppm. ^{13}C NMR (100 MHz, C_6D_6): δ 170.7 (s), 168.7 (s), 146.8 (s), 137.9 (d), 137.5 (s), 137.1 (d), 136.3 (d), 134.8 (d), 134.1 (s), 133.7 (d), 133.4 (d), 132.9 (d), 129.4 (d_5), 124.9 (s), 124.3 (s), 121.9 (s), 121.8 (d), 119.1 (d), 95.4 (s), 94.0 (s), 70.4 (s), 67.9 (d), 67.5 (s), 64.2 (d), 47.1 (t), 42.3 (t′), 40.9 (t), 37.6 (t), 36.1 (s), 35.3 (s), 30.3 (q), 29.5 (q), 28.8 (q), 24.9 (q), 23.8 (q), 22.5 (q), 21.4 (q), 19.9 (q), 15.4 (q) ppm. MS (EI^+) *m*/*z* (%): 636 (M^+ + 24, 37), 635 (M^+ + 23, 89), 614 (M^+ + 2, 44), 613 (M^+ + 1, 100), 539 (20), 451 (24), 391 (29), 315 (48), 279 (45). HRMS (EI^+): Calcd for $C_{39}H_{49}O_6$, 613.3524; found, 613.3511; calcd for $C_{39}H_{48}NaO_6$, 635.3343; found, 635.3327.

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Supporting Information Available: Physical and spectroscopic data of all compounds. This material is available free of charge via the Internet at http://pubs.acs.org.

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