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Bidirectional Hiyama-Denmark Cross-Coupling Reactions of Bissilyldeca-1,3,5,7,9-pentaenes for the Synthesis of Symmetrical and Non-symmetrical Carotenoids

Aurea Rivas, Víctor Pérez-Revenga, Rosana Alvarez,* and Angel R. de Lera* [a]

Abstract: The construction of the carotenoid skeleton by Pd-catalyzed Csp^2-Csp^2 cross-coupling reactions of symmetrical and non-symmetrical 1,10-bissilyldeca-1,3,5,7,9-pentaenes and the corresponding complementary alkenyl iodides has been developed. Reaction conditions for these bidirectional and orthogonal Hiyama-Denmark cross-coupling reactions of bis-functionalized pentaenes are mild and the carotenoid products preserve the stereochemical information of the corresponding oligoene partners. The carotenoids synthesized in this manner include β,β-carotene and (3*R*,3´*R*)-zeaxanthin (symmetrical) as well as 9-*cis*-β,β-carotene, 7,8-dihydro-β,β-carotene and β-cryptoxanthin (non-symmetrical).

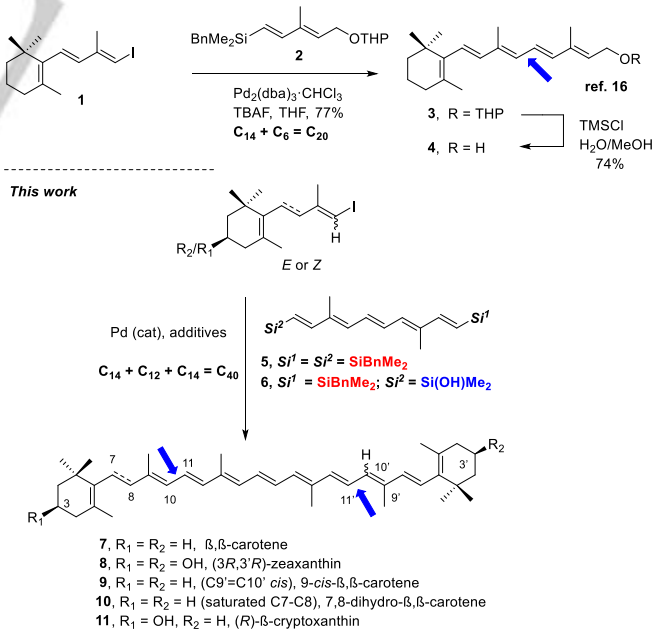
Introduction

Polyene substructures are present in a large number of molecular skeletons of natural products that display diverse biological activities.[1] Notably, the polyene fragments of retinoids and carotenoids are considered to be responsible for some fundamental biological functions, including animal vision (11-*cis*-retinal), bacterial proton- and ion-pumping activities (all-*trans*-retinal)[2] and plant photosynthesis (selected carotenoids)[3] among others.[4] More than 800 natural carotenoids have been isolated from biological materials,[3a, 5] with a large number of them still remaining incompletely characterized due to their instability or to the scarcity of material isolated from the natural sources.

Csp^2=Csp^2 condensation reactions (Wittig, Horner-Wadsworth-Emmons or HWE, Julia-Kocienski...) are considered as classical methods[6] for the synthesis of the polyene substructures of retinoids and carotenoids.[7] Despite their efficiency, these procedures have some drawbacks, notably the lack of stereocontrol leading to mixtures of isomers, and a laborious purification requiring also the separation of by-products.[7] Alternatively these polyenes are constructed using palladium-catalyzed Csp^2-Csp^2 cross-coupling reactions. These processes are more functional group-tolerant and require in general milder reaction conditions, thus leading to the preservation of the stereochemical information of the reacting oligoenes.[6b, 7]

Both the Stille[8] and the Suzuki-Miyaura cross-coupling reactions[9] have been thoroughly explored for the synthesis of apocarotenoids (including the retinoids or vitamin A analogues) and carotenoids[10] using mono- and bis-functionalized alkenyl linchpins.[11] In fact, these synthetic challenges have contributed to illustrate the scope and limitations[6b, 12, 13] of the Pd-catalyzed Csp^2-Csp^2 cross-coupling reactions for the preparation of highly unstable polyenes.[7]

Similarly, the Hiyama-Denmark cross-coupling reaction,[14] which utilizes organosilicon reagents,[15] has also been applied to the stereocontrolled synthesis of the all-*trans*- and 11-*cis*-isomers of vitamin A by the highly convergent C_{14} + C_6 strategy.[7] For example, dienylsilane **2** was found to couple to trienyl iodide **1** under mild reaction conditions to afford the retinoid pentaene structure **3** in high yield (Scheme 1).[16] Organosilicon reagents are in general easier to prepare and handle than structurally related organometallic compounds. In addition, they are also more stable due to the low polarizability of the C-Si bond, and show lower toxicity than stannanes. Moreover, mechanistic studies have provided an in-depth understanding of the cross-coupling reaction,[17] including the effect of silicon substituents on their reactivity[18] and the electronic demands for efficient transmetalation.[19] All of these features have contributed to the current status of organosilanes as powerful synthetic tools for the preparation of unsaturated fragments of natural polyenes.[14c, 17a, e, 20]



Scheme 1. Reported synthetic approach to vitamin A (**4**)[16a] and extension to β,β-carotene (**7**), (3*R*,3´*R*)-zeaxanthin (**8**), 9-*cis*-β-carotene (**9**), 7,8-dihydro-β-carotene (**10**) and (*R*)-β-cryptoxanthin (**11**) using a bidirectional Hiyama-Denmark cross-coupling reactions of alkenyl iodides with symmetrical (**5**) and non-symmetrical (**6**) 1,10-bissilyldeca-1,3,5,7,9-pentaenes.

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A popular strategy in the construction of the polyene skeleton of carotenoids involves connecting a central C_{12}-pentaenyl fragment to two C_{14} end groups, the so-called C_{14} + C_{12} + C_{14} strategy (Scheme 1).[7] The application of the Hiyama-Denmark transformation in this strategy would imply the generation of both the C_{10}-C_{11} and the $C_{10'}$-$C_{11'}$ bonds of carotenoids by using bis-metallated organosilanes **5/6** and alkenyl iodides (such as **1**, for example).

In order for this bidirectional strategy using bismetallated organometallic reagents to be of general applicability, it would have to be able to provide access to both symmetrical (**7,8**) and non-symmetrical (**9-11**) polyene structures (Scheme 1), implying that selective activation of each of the metallic fragments associated to the central pentaene core (as in **5/6**) is needed.

Denmark has already demonstrated that, while both types of silyl groups are activated using fluoride anion sources through the formation of pentavalent Si species,[17b, c, 21] the treatment of silanols under basic conditions provides a second alternative pathway for activation via generation of active silanolate species.[22] He has also taken advantage of this dual behavior in the bidirectional preparation of simple non-symmetrical bisarylbutadienes, hexatrienes and octatetraenes, devoid of substitution at the diene or tetraene moieties, using mixed silanol-silane 1,4-bissilylbutadienes.[23] However, the preparation/use of higher analogues of these bissilyl reagents has not been reported, while literature reports on other alkenyl bissilanes appear to be restricted to the synthesis of symmetrical unsubstituted butadienyl-, hexatrienyl-,[24] and octatetraenyl-bissilanes,[25] and their related use in mono- and bis-acylation reaction with aroyl chlorides.

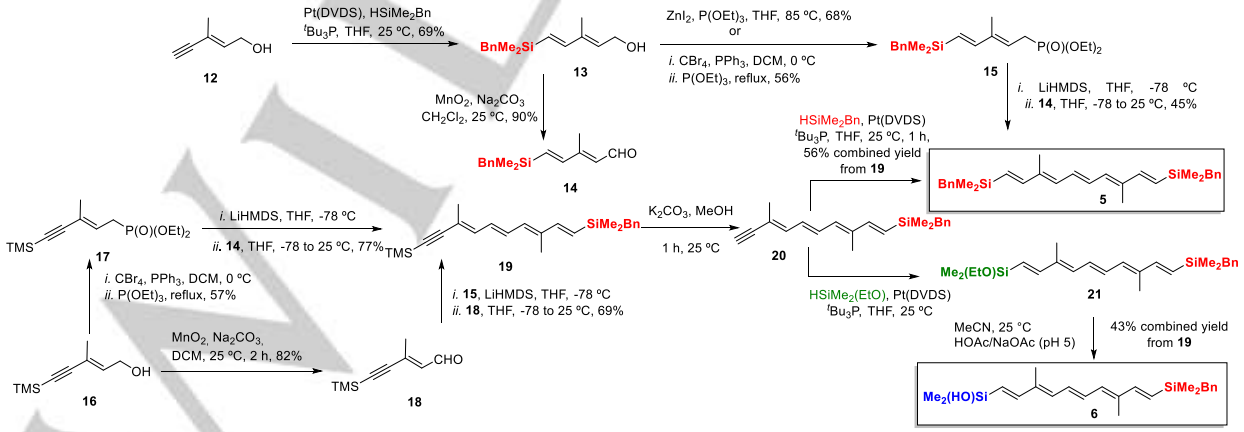
With these precedents, in this paper we describe the preparation of pentaenyl-bissilane reagents **5** and **6**, and their application to the synthesis of both symmetrical (β,β-carotene **7**, (3*R*,3´*R*)-zeaxanthin **8**) and non-symmetrical (9-*cis*-β-carotene **9**, 7,8-dihydro-β-carotene **10** and (*R*)-β-cryptoxanthin **11**) carotenoids (Scheme 1). To further add to the attractiveness of this strategy, it is noted that the oligoene skeleton that comprises the central region of carotenoids (integrated in structures **7-11**) is biosynthetically preserved in most of these natural products, while structural modifications (in the form of changes in oxidation state, ring contractions, etc...) are found at the ring carbons and/or at their more proximal double bonds.[3a, 5] This makes reagents **5** and **6** potentially useful for the synthesis of a wide variety of carotenoid structures.

Results and Discussion

Synthesis of 1,10-bissilyldeca-1,3,5,7,9-pentaenes 5 and 6

Starting from either enynol **12** or TMS-substituted derivative **16** (Scheme 2), two routes were employed that differed in the order of hydrosilylation[26] relative to oxidation[27] and HWE[28] steps. The first route started with a regioselective Pt-catalyzed *syn*-hydrosilylation[26] of enynol **12** with $HSiMe_2Bn$ and Karstedt's catalyst [(*t*Bu_3P)Pt(DVDS), (DVDS = 1,3-divinyl-1,1,3,3-tetramethyldisiloxane, generated from Pt(DVDS) and *t*Bu_3P], which stereoselectively provided the corresponding silyldienol **13** in 69% yield.[16b] Oxidation of silyldienol **13** with MnO_2 afforded silyldienal **14** in 90% yield.[27] Allylic phosphonate **15** was prepared from **13** by reaction with triethylphosphite[29] of the corresponding iodide[30] or bromide[31] intermediates in 68 and 56% overall yields, respectively. Finally, unsaturated chain extension of silyldienal **14** by HWE reaction with phosphonate **15** under Barbier conditions provided the symmetrical 3,8-dimethyl-1,10-bissilyl-1,3,5,7,9-decapentaene **5** in 45% yield.

A more efficient approach (Scheme 2) to both **5** and the non-symmetrical 1,10-bissilyl-1,3,5,7,9-decapentaene **6** was devised involving silyltetraenyne **20** as intermediate. Thus, TMS-enynol **16**, itself obtained by reduction of the corresponding enynoate precursor,[32] was transformed into allylic phosphonate **17** along the same lines indicated for **15**,[31] and the subsequent HWE reaction with silyldienal **14** gave rise to tetraenynyl derivative **19** in 69% yield. A better yield (77%) resulted from the exchange of the functionalities between the reaction partners, thus performing the HWE process between enynal **18** and phosphonate **15**.[27]

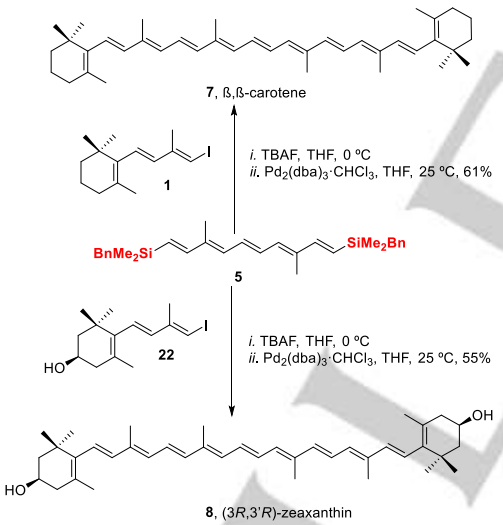


Scheme 2. Synthesis of symmetrical (**5**) and non-symmetrical (**6**) pentaenylbissilanes from enynols **12** and **16**.

Then, regio- and stereoselective Pt-catalyzed hydrosilylation[26a, b, d] of deprotected alkyne **20** with $HSiBnMe_2$ or $HSi(OEt)Me_2$ and Karstedt's catalyst afforded 1,10-bissilyldeca-1,3,5,7,9-pentaenes **5** and **21** in 56 and 88% overall yields (from **19**), respectively. Alternatively, upon stirring crude **21** in aqueous buffer (1M HOAc/NaOAc, pH 5),[23a] the corresponding silanol **6** was obtained in an overall 43% yield from **19** (Scheme 2).[23a] The all-*E* geometry of pentaenes **5** and **6** was assigned based on the magnitude of the C_{sp2}-H-C_{sp2}-H vicinal coupling constants (J = 18 – 20 Hz) on their ^{1}H NMR spectra[33] and the observed nuclear Overhauser effects (nOe).

Bidirectional Hiyama-Denmark cross-coupling of 1,10-bissilyldeca-1,3,5,7,9-pentaenes 5 and 6

The two-fold bidirectional Hiyama-Denmark cross-coupling reaction[20h, 34] using the homodimeric 1,10-bissilyldeca-1,3,5,7,9-pentaene **5** was performed following the protocol previously described for the synthesis of retinoids.[16b] Upon treatment with TBAF [35] in the presence of $Pd_2(dba)_3{\cdot}CHCl_3$ as catalyst, the coupling of **5** with trienyl iodide **1**[36] took place at ambient temperature and afforded β,β-carotene **7** in 61% yield (Scheme 3). Similarly, (3*R*,3´*R*)-zeaxanthin **8** was also synthesized, in 55% yield, upon two-fold Hiyama-Denmark cross-coupling of **5** and trienyl iodide **22**,[36] thus showing the compatibility of the unprotected hydroxyl group with the reaction conditions.[37]



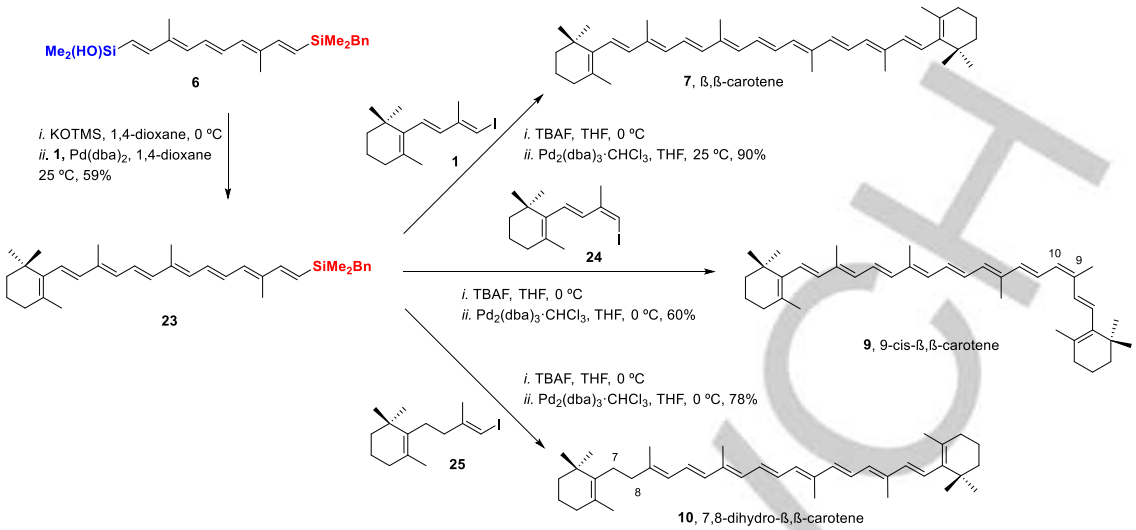
Scheme 3. Total synthesis of symmetrical carotenoids (**7**, **8**) by Hiyama-Denmark cross-coupling of symmetrical pentaenylbissilane (**5**) and trienyl iodides (**1** and **22**).

In order to explore the sequential Hiyama-Denmark cross-coupling[26d] of a non-symmetrical 1,10-bissilyldeca-1,3,5,7,9-pentaene with modulated reactivity,[23a] the silanol group of pentaenylbissilane **6** was selectively activated by treatment with KOTMS. Then, addition of $Pd(dba)_2$ and trienyl iodide **1** afforded, at ambient temperature, octaenylsilane **23** with good efficiency (59% yield; Scheme 4).[38] Thus, the reactivity of the non-symmetrical 1,10-bissilyldeca-1,3,5,7,9-pentaene follows the same trends described for the shorter unsubstituted 1,4-bissilylbutadienes,[23a] and the observed selectivity can be diverted to the preparation of non-symmetrical carotenoids. This is clearly another advantage of the Hiyama-Denmark coupling for stepwise polyene construction.

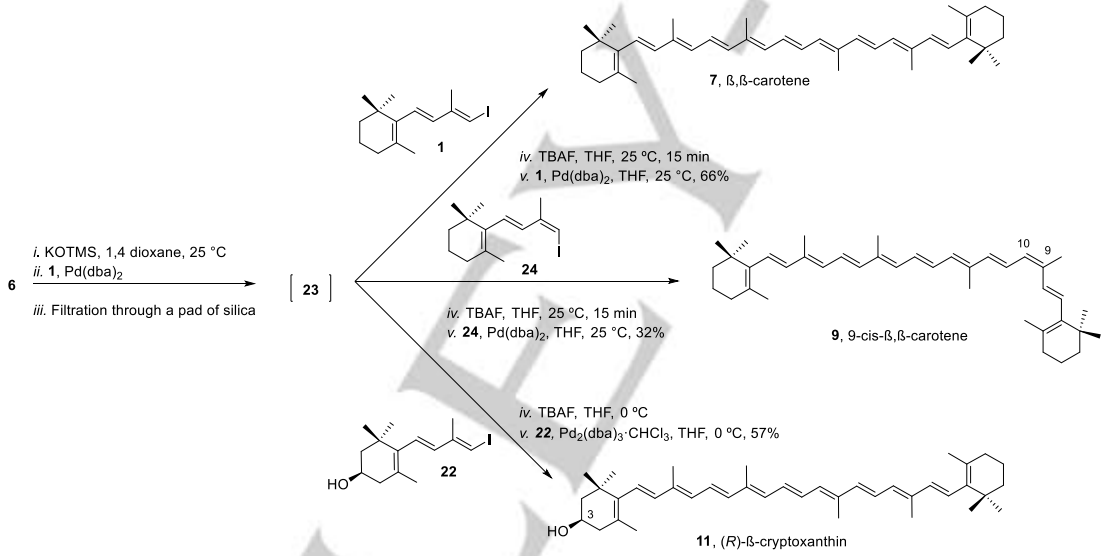
Further coupling of octaenylsilane **23** with trienyl iodide **1** or its *Z*-isomer **24** (Scheme 4) took place following activation with TBAF and using $Pd_2(dba)_3{\cdot}CHCl_3$ as catalyst. This afforded, in 90 and 60% yields, respectively, β,β-carotene **7** and the highly unstable 9-*cis* isomer **9**.[39] Thus, the geometry of the starting trienyl iodides appears to be preserved in the Hiyama-Denmark cross-coupling reaction. Similarly, 7,8-dihydro-β,β-carotene **10**, which has been isolated from the extracts of genetically modified *E. coli*,[40] could be obtained in 78% yield when the isolated octaenylsilane intermediate **23** was subjected to a second Hiyama-Denmark cross-coupling with the non-conjugated dienyl iodide **25**, upon activation with TBAF using $Pd_2(dba)_3{\cdot}CHCl_3$ as catalyst.

Additionally, the bis-coupling process could be carried out without isolation of the octaenylsilane intermediate **23**. Thus, heterodimeric 1,10-bissilyldecapentaene **6** was also converted into β,β-carotene **7**, 9-*cis*-β,β-carotene **9**,[39] and (*R*)-β-cryptoxanthin **11**[37, 41]) in 66, 30 and 57% yield, respectively, in a sequential double Hiyama-Denmark cross-coupling reaction of **6** with trienyl iodides **1**, **24** and **22** (Scheme 5).

This protocol involved first a Hiyama-Denmark cross-coupling with *E*-trienyl iodide **1** at the silanol terminus of **6**[22-23, 42] followed, after filtration of the crude mixture through a silica gel plug in order to remove Pd black, by a second coupling[35] between the putative octaenylsilane intermediate **23** and trienyl iodides **1**, **24** or **22**, respectively.



Scheme 4. Synthesis of silylated octaenylapocarotenoid **23** by position-selective mono-Hiyama-Denmark cross-coupling of non-symmetrical 1,10-bissilyldecapentaene **6** and trienyl iodide **1**, and synthesis of symmetrical (β,β-carotene **7**) and non-symmetrical (9-*cis*-β,β-carotene **9** and 7,8-dihydro-β,β-carotene **10**) by Hiyama-Denmark cross-coupling reaction of octaenylsilane **23**.



Scheme 5. Synthesis of symmetrical (β,β-carotene **7**) and non-symmetrical (9-*cis*-β,β-carotene **9**; (*R*)-β-cryptoxanthin **11**) by sequential selective mono-Hiyama-Denmark cross-coupling reaction of non-symmetrical 1,10-bissilyldecapentaene **6**.

Conclusions

To summarize, as an extension of the Hiyama-Denmark cross-coupling approach[17a, 20g, h] to polyenes, we have developed a new synthesis of symmetrical and non-symmetrical carotenoids by bidirectional Pd-catalyzed Csp^2-Csp^2 bond formation using conjunctive pentaenyl-1,□□-bissilanes and the apropriately matched (tri)enyl iodide building blocks. Conceptually, the application of transition metal catalyzed processes[43][12b] to carotenoids complements the general condensation approaches based on olefination, with the construction of polyenes by single-bond formation between unsaturated carbons.[7] These procedures are mild (ambient temperature) and functional group (OH) tolerant and the synthesis of the desired isomer can be achieved by choosing the geometries of the conjunctive reagents, since the oligoene products preserve the stereochemical information of the cross-coupling partners.[1a] The stability of the cross-coupling organosilane reagents, the cost-effectiveness and low environmental impact of their preparation are additional advantages of these protocols, particularly when used as tandem processes to more efficiently generate molecular complexity. In the case at hand, it is expected that using these procedures the synthesis of unstable (as exemplified by **9**) natural carotenoids will allow their full characterization and provide samples for comprehensive biological studies.

Experimental Section

General Procedures (see S. I.)

Diethyl (2*E*-4*E*)-5-(Benzyldimethylsilyl)-3-methylpenta-2,4-dienylphosphonate (15).

Method A: A solution of **13**[16] (0.40 g, 1.62 mmol) in THF (6.5 mL) was added to a mixture of ZnI_2 (0.78 g, 2.44 mmol) and $P(OEt)_3$ (0.84 mL, 4.87 mmol). The reaction mixture was stirred for 4 h at 85 °C. After cooling down to 25 °C, the solvent was removed, the residue was diluted with EtOAc and washed with a 2 M aqueous solution of NaOH and the aqueous layer was extracted with EtOAc (3x). The combined organic layers were dried (Na_2SO_4) and the solvent was evaporated. The residue was purified by column chromatography (C18 - silica gel, 55:45 v/v CH_3CN/H_2O) to afford 0.42 g (68%) of **15** as a yellow oil.

Method B: To a cooled (0 °C) stirred solution of **13**[16] (0.30 g, 1.22 mmol) in CH_2Cl_2 (4 mL) were added CBr_4 (0.53 g, 1.58 mmol) and PPh_3 (0.48 g, 1.83 mmol). The reaction mixture was stirred for 15 min at 0 °C and the solvent was evaporated in *vacuo*. The residue was dissolved in $P(OEt)_3$ (0.29 mL, 1.79 mmol) and the mixture was refluxed for 30 min. After being cooled down to ambient temperature, toluene (1 mL) was added and the mixture was concentrated. The residue was purified by column chromatography (C18 - silica gel, 55:45 v/v CH_3CN/H_2O) to afford 0.25 g (56%) of **15** as a yellow oil. **^{1}H-NMR** (400.13 MHz, C_6D_6): δ 7.44 -7.20 (m, 2H, ArH), 7.01 (t, *J* = 6.9 Hz, 1H, ArH), 6.97 (d, *J* = 8.0 Hz, 2H, ArH), 6.64 (d, *J* = 19.0 Hz, 1H, H_4 or H_5), 5.80 (d, *J* = 19.0 Hz, 1H, H_5 or H_4), 5.73 – 5.63 (m, 1H, H_2), 3.98 – 3.82 (m, 4H, 2xO$\underline{CH_2}CH_3$), 2.57 (dd, *J* = 8.0 Hz, J_{HP} = 23.0 Hz, 2H, $2H_1$), 2.06 (s, 2H, $SiMe_2\underline{CH_2}Ph$), 1.68 (d, *J* = 3.9 Hz, 3H, C_3-CH_3), 1.02 (t, *J* = 7.1 Hz, 6H, 2xO$CH_2\underline{CH_3}$), 0.05 (s, 6H, $Si\underline{Me_2}Bn$) ppm. **^{13}C-NMR** (100.61 MHz, C_6D_6): δ 149.3 (d, $^4J_{C\text{-}P}$ = 5.0 Hz), 140.2 (s), 139.1 (s, $^3J_{C\text{-}P}$ = 14.5 Hz), 128.6 (d, 2x), 128.5 (d, 2x), 125.2 (d), 124.5 (d), 122.9 (d, $^2J_{C\text{-}P}$ = 12.2 Hz), 61.7 (t, 2x), 27.7 (t, $^1J_{C\text{-}P}$ = 139.6 Hz), 26.3 (t), 16.5 (q, 2x), 12.1 (q), -3.2 (q, 2x) ppm. **IR** (NaCl): υ 2982 (s, C-H), 2957 (m, C-H), 1492 (w), 1250 (s), 1027 (s) cm^{-1}. **HRMS** (ESI^+): Cald. for $C_{19}H_{32}O_3PSi$ ($[M+H]^+$), 367.1853; found, 367.1856.

(2*E*,4*E*)-5-(Benzyldimethylsilyl)-3-methylpenta-2,4-dienal (14). To a cooled (0 °C) solution of **13**[16] (2.3 g, 9.33 mmol) in Et_2O (373 mL), MnO_2 (8.11 g, 93.34 mmol) and Na_2CO_3 (9.89 g, 93.34 mmol) were added and the reaction was stirred at 25 °C for 1.5 h. The mixture was filtered through Celite®, the solids were washed with CH_2Cl_2, and the solvent was evaporated to afford 2.05 g (89%) of **14** as a yellow oil. **^{1}H-NMR** (400.13 MHz, C_6D_6): δ 9.96 (d, *J* = 7.8 Hz, 1H, H_1), 7.19 – 7.13 (m, 2H, ArH), 7.03 (t, *J* = 7.4 Hz, 1H, ArH), 6.92 (d, *J* = 8.2 Hz, 2H, ArH), 6.39 (d, *J* = 19.0 Hz, 1H, H_5), 6.15 (d, *J* = 19.0 Hz, 1H, H_4), 5.85 (d, *J* = 8.3 Hz, 1H, H_2), 2.00 (s, 2H, $SiMe_2\underline{CH_2}Ph$), 1.65 (s, 3H, C_3-CH_3), -0.01 (s, 6H, $Si\underline{Me_2}Bn$) ppm**.** **^{13}C-NMR** (100.63 MHz, C_6D_6): δ 190.7 (d), 152.9 (s), 147.8 (d), 139.5 (s), 135.9 (d), 130.8 (d), 128.6 (d, 2x), 128.5 (d, 2x), 124.8 (d), 25.8 (t), 12.0 (q), -3.6 (q, 2x) ppm. **UV** (MeOH): λ_{max} 274 nm. **IR** (NaCl): 2956 (w, C-H), 1663 (s, C=O), 1204 (m), 839 (s) cm^{-1}. **HRMS** (ESI^+): Calcd. for $C_{15}H_{21}OSi$ ($[M+H]^+$), 245.1356; found, 245.1355.

Diethyl (*E*)-(3-Methyl-5-(trimethylsilyl)pent-2-en-4-yn-1-yl)phosphonate (17). To a cooled (0 °C) stirred solution of **16**[16] (0.398 g, 2.365 mmol) in CH_2Cl_2 were added CBr_4 (1.02 g, 3.075 mmol) and PPh_3 (0.931 g, 3.548 mmol). The reaction mixture was stirred for 15 min at 0 °C and the solvent was evaporated. The residue was dissolved in triethylphosphite (0.56 mL, 3.005 mmol) and the resulting mixture was refluxed at 130 °C for 30 min. After being cooled down to room temperature, toluene (1 mL) was added and the mixture was concentrated. The residue was purified by column chromatography (C18 - silica gel, 55:45 v/v CH_3CN/H_2O) to afford 0.29 g (57%) of **17** as a yellow oil. **^{1}H-NMR** (400.13 MHz, C_6D_6): δ 6.17 – 6.09 (m, 1H, H_2), 3.91 – 3.78 (m, 4H, $PO(O\underline{CH_2}CH_3)_2$), 2.38 (dd, $J_{H\text{-}H}$ = 8.6 Hz, $^1J_{P\text{-}H}$ = 23.5 Hz, 2H, $2H_1$), 1.73 (d, $^5J_{H\text{-}P}$ = 5.1 Hz, 3H, C_3-CH_3), 0.97 (t, *J* = 7.1 Hz, 6H, $PO(OCH_2\underline{CH_3})_2$), 0.18 (s, 9H, $Si\underline{Me_3}$) ppm. **^{13}C-NMR** (100.63 MHz, C_6D_6): δ 128.1 (d, $^2J_{C\text{-}P}$ = 12.1 Hz), 122.3 (s, $^3J_{C\text{-}P}$ = 15.2 Hz), 108.4 (s, $^4J_{C\text{-}P}$ = 5.9 Hz), 91.9 (s, $^5J_{C\text{-}P}$ = 2.9 Hz), 61.7 (t), 61.6 (t), 27.8 (t, $^1J_{C\text{-}P}$ = 139.7 Hz), 17.5 (q $^4J_{C\text{-}P}$ = 5.6 Hz), 16.5 (q), 16.4 (q), 0.1 (q, 3x) ppm. **IR** (NaCl): ν 2966 (m, C-H), 2145 (m, C≡C), 1254 (s), 1029 (s), 848 (s) cm^{-1}. **MS** (ESI^+-TOF): *m/z* 311 ($[M+Na]^+$, 28), 289 ($[M+H]^+$, 100). **HRMS** (ESI^+): Cald. for $C_{13}H_{26}O_3PSi$ ($[M+H]^+$), 289.1386; found, 289.1383.

(1*E*,3*E*,5*E*,7*E*,9*E*)-1,10-Di(benzyldimethylsilyl)-3,8-dimethyldeca-1,3,5,7,9-pentaene (5).

Procedure A (Barbier conditions): n-BuLi (0.075 mL, 2.45 M in hexanes, 0.184 mmol) was added to a solution of HMDS (0.039 mL, 0.184 mmol) in THF (0.2 mL). After stirring at -78 °C for 30 min, this solution was added dropwise to a mixture of **15** (0.067 g, 0.184 mmol) and **14** (0.03 g, 0.123 mmol) in THF (0.25 mL) and the temperature was allowed to reach 25 °C over 21 h. Water was added and the resulting mixture was extracted with Et_2O (3x). The combined organic layers were washed with H_2O (3x) and brine (3x), and dried (Na_2SO_4). The solvent was evaporated and the residue was purified by column chromatography (silica gel, 98:2 hexane/EtOAc) to afford 0.032 g (45%) of **5** as a colourless oil.

Procedure B: n-BuLi (0.12 mL, 2.45 M in hexanes, 0.027 mmol) was added to a solution of HMDS (0.06 mL, 0.285 mmol) in THF (0.2 mL). After stirring at -78 °C for 30 min, this solution was added dropwise to a solution of **15** (0.112 g, 0.305 mmol) in THF (0.25 mL) and the resulting solution was stirred at this temperature for 30 min. A solution of **14** (0.05 g, 0.205) in THF (0.25 mL) was then added. The reaction mixture was allowed to stir at 25 °C for a total of 5 h. Water was added and the resulting mixture was extracted with Et_2O (3x). The combined organic layers were washed with H_2O (3x) and brine (3x), and dried (Na_2SO_4). The solvent was evaporated and the residue was purified by column chromatography (silica gel, 98:2 hexane/EtOAc) to afford 0.023 g (25%) of **5** as a colourless oil.

Procedure C: To a cooled (0 °C) solution of **19** (0.39 g, 1.03 mmol) in MeOH (4.7 mL), K_2CO_3 (1.71 g, 12.36 mmol) was added. The mixture was stirred at 25 °C for 1 h and water was added. The resulting mixture was extracted with Et_2O (4x), the combined organic layers were dried (Na_2SO_4) and the solvent was evaporated. To a degassed solution of Pt(DVDS) (0.11 mL, 2% in xylene, 0.005 mmol) and ^{t}Bu$_3$P (0.005 mL, 1M in toluene, 0.005 mmol) in THF (2.7 mL), $BnMe_2SiH$ (0.95 mL, 1.47 mmol) was added. After stirring for 30 min at 25 °C, a solution of the residue obtained above (expected to be **20**) in THF (2.7 mL) was added and the reaction mixture was stirred at 25 °C for 2.5 h. The solvent was evaporated and the residue was purified by column chromatography (silica gel, 98-2 hexane/EtOAc) to afford 0.25 g (56%) of **5** as a yellow oil. **^{1}H-NMR** (400.16 MHz, C_6D_6): δ 7.33 – 7.22 (m, 4H, ArH), 7.17 – 7.07 (m, 6H, ArH), 6.86 (d, *J* = 19.4 Hz, 2H, $2H_1$ or $2H_2$), 6.75 (d, *J* = 10.1 Hz, 2H, $2H_4$ or $2H_5$), 6.32 (d, *J* = 10.1 Hz, 2H, $2H_5$ or $2H_4$), 6.07 (d, *J* = 19.4 Hz, 2H, $2H_2$ or $2H_1$), 2.26 (s, 4H, 2x$SiMe_2\underline{CH_2}Ph$), 1.95 (s, 6H, 2xC_3-CH_3), 0.27 (s, 12H, 2x$Si\underline{Me_2}Bn$) pm. **^{13}C-NMR** (100.62 MHz, C_6D_6): δ 149.8 (d, 2x), 140.2 (s, 2x), 137.2 (s, 2x), 133.8 (d, 2x), 131.2 (d, 2x), 128.7 (d, 2x), 128.6 (d, 4x), 126.6 (d, 4x), 124.6 (d, 2x), 26.5 (t, 2x), 12.4 (q, 2x), -3.1 (q, 4x) ppm. **IR** (NaCl): υ 2954 (m, C-H), 2854 (m, C-H), 1568 (m), 1249 (m), 1151 (m), 772 (s) cm^{-1}. **MS** (ESI^+-TOF): *m/z* 458 (30), 457 ($[M+H]^+$, 100), 419 (72). **HRMS** (ESI^+): Calcd. for $C_{30}H_{41}Si_2$ ($[M+H]^+$), 457.2741; found, 457.2742.

(3*E*,5*E*,7*E*,9*E*)-10-(benzyldimethylsilyl)-3,8-dimethyl-1-trimethylsilyl-deca-3,5,7,9-tetraen-1-yne (19).

Procedure A: n-BuLi (4.7 mL, 2.3 M in hexanes, 10.93 mmol) was added to a solution of HMDS (2.3 mL, 10.93 mmol) in THF (20 mL). After stirring at -78 °C for 30 min, this solution was added dropwise to a solution of **17** (3.151 g, 10.93 mmol) in THF (70 mL) and the resulting solution was stirred at this temperature for 30 min. After stirring at -78 °C for 0.5 h, a solution of **14** (1.78 g, 7.28 mmol) in THF (70 mL) was added and the reaction mixture was allowed to warm slowly from -78 °C to 25 °C over 2 h. Water was added and the resulting mixture was extracted with Et_2O (3x). The combined organic layers were washed with H_2O (3x) and a saturated aqueous solution of NaCl (3x), and dried (Na_2SO_4). The solvent

was evaporated and the residue was purified by column chromatography (silica gel, 98:2 hexane/EtOAc) to afford 1.3 g (77% yield) of **19** as a red oil.

Procedure B: *n*-BuLi (0.68 mL, 2.45 M in hexanes, 1.66 mmol) was added to a solution of HMDS (0.42 mL, 1.99 mmol) in THF (3 mL). After stirring at -78 °C for 30 min, this solution was added dropwise to a solution of **15** (0.61 g, 1.66 mmol) in THF (5 mL) and the resulting solution was stirred at this temperature for 30 min. After stirring at -78 °C for 0.5 h, a solution of **18** (0.18 g, 1.1 mmol) in THF (5 mL) was added and the reaction mixture was allowed to warm slowly from -78 °C to 25 °C over 2 h. Water was added and the resulting mixture was extracted with Et_2O (3x). The combined organic layers were washed with H_2O (3x) and a saturated aqueous solution of NaCl (3x), and dried (Na_2SO_4). The solvent was evaporated and the residue was purified by column chromatography (silica gel, 98:2 hexane/EtOAc) to afford 0.25 g (60% yield) of **19** as a red oil. **^{1}H-NMR** (400.13 MHz, C_6D_6): δ 7.20 – 7.10 (m, 5H, $SiMe_2CH_2\underline{Ph}$), 7.09 – 6.96 (m, 2H), 6.51 – 6.32 (m, 2H), 6.04 (d, *J* = 11.0 Hz, 1H), 5.92 (d, *J* = 18.8 Hz, 1H), 2.11 (s, 2H, $SiMe_2\underline{CH_2}Ph$), 1.84 (s, 3H, C-CH_3), 1.70 (s, 3H, C-CH_3), 0.26 (s, 6H, $Si(\underline{CH_3})_3$), 0.11 (s, 6H, $Si\underline{Me_2}Bn$) ppm. **^{13}C-NMR** (100.16 MHz, C_6D_6): δ 149.6 (d), 140.1 (s), 138.2 (s), 137.8 (d), 133.3 (d), 131.4 (d), 129.9 (d), 128.6 (d, 2x), 128.5 (d, 2x), 127.1 (d), 124.6 (d), 119.3 (s), 110.2 (s), 95.4 (s), 30.4 (d), 26.4 (t), 17.6 (q), 12.4 (q), 0.2 (q, 2x), -3.1 (q, 3x) ppm. **IR** (NaCl): v 2961 (m, C-H), 2847 (w, C-H), 2143 (w, C-C≡H), 1668 (s), 1250 (m), 844 (s) cm^{-1}. **UV** (MeOH): λ_{max} 239 nm. **MS** (ESI$^+$-TOF): *m/z* 379 ([M+H]$^+$, 100), 149 (23). **HRMS** (ESI$^+$): Calcd. for $C_{24}H_{35}Si_2$ ([M+H]$^+$), 379.2276; found, 379.2272.

(1*E*,3*E*,5*E*,7*E*,9*E*)-10-[9-(Benzyldimethylsilyl)-3,8-dimethyl-1,3,5,7,9-pentaen-1-yl]-dimethylsilanol (6). To a cooled (0 °C) solution of **19** (0.614 g, 1.621 mmol) in MeOH (7.4 mL), K_2CO_3 (2.688 g, 19.452 mmol) was added. The reaction mixture was stirred at 25 °C for 1 h and water was added. The mixture was extracted with Et_2O (4x), 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 Pt(DVDS) (0.157 mL, 2% in xylene, 0.007 mmol) and ^{t}Bu$_3$P (7 µL, 1 M in toluene, 0.007 mmol) in THF (5 mL), ethoxydimethylsilane (0.224 g, 2.153 mmol) was added. After stirring for 30 min at 25 °C a solution of **20** (0.406 g, 1.435 mmol) in THF (1 mL) was added and the reaction mixture was stirred at 25 °C for 1 h. Then the solvent was evaporated. To a solution of the residue obtained above in CH_3CN (15 mL) an aqueous buffer solution of HOAc/NaOAc (1.0 M, 5 mL, pH 5.0) was added and the resulting mixture was stirred at 25 °C for 15 h. Water was added and the aqueous layers were extracted with Et_2O (3x). The combined organic layers were washed with water (2x) and a saturated aqueous solution of NaCl (2x) and dried and the solvent was evaporated. The residue was purified by column chromatography (silica gel, 85:15 hexane/EtOAc) to afford 0.237 g (43%) of **6** as a yellow oil. **^{1}H-NMR** (400.13 MHz, C_6D_6): δ 7.21 – 7.17 (m, 2H, ArH), 7.07 – 6.95 (m, 3H, ArH), 6.86 (d, *J* = 18.8 Hz, 1H), 6.73 (d, *J* = 18.8 Hz, 1H), 6.69-6.60 (m, 2H), 6.30-6.20 (m, 2H), 5.93 (d, *J* = 18.8 Hz, 1H), 5.92 (d, *J* = 18.8 Hz, 1H), 2.13 (s, 2H, $SiMe_2\underline{CH_2}Ph$), 1.82 (s, 6H, 2xC-CH_3), 0.23 (s, 6H, Si(OH)$\underline{Me_2}$ or $Si\underline{Me_2}Bn$), 0.13 (s, 6H, Si(OH)$\underline{Me_2}$ or $Si\underline{Me_2}Bn$) ppm. **^{13}C-NMR** (100.16 MHz, C_6D_6): δ 149.7 (d, 2x), 140.2 (s), 137.3 (s), 137.2 (s), 134.2 (d), 133.7 (d), 131.3 (d), 131.2 (d), 128.7 (d, 2x), 128.6 (d, 2x), 127.5 (d), 126.6 (d), 124.6 (d), 26.5 (t), 12.4 (q, 2x), 0.6 (q, 2x), -3.1 (q, 2x) ppm. **IR** (NaCl): v 2956 (m, C-H), 1568 (w), 1214 (w), 843 (m), 771 (s) cm^{-1}. **UV** (MeOH): λ_{max} 372, 353 nm. **MS** (ESI$^+$-TOF): *m/z* 383 ([M+H]$^+$, 100), 362 (18), 341 (13), 301 (15), 270 (19), 242 (18). **HRMS** (EI$^+$): Calcd. for $C_{23}H_{35}OSi_2$ ([M+H]$^+$), 383.2218; found, 383.2210.

(1*E*,3*E*,5*E*,7*E*,9*E*)-10-Benzyldimehtylsilyl-benzyl-10-(ethoxydimethylsilyl)-3,8-dimethyldeca-1,3,5,7,9-pentaene) (21). To a cooled (0 °C) solution of **19** (0.65 g, 1.72 mmol) in MeOH (7.8 mL), K_2CO_3 (2.85 g, 20.60 mmol) was added. The mixture was stirred at 25 °C for 1 h and water was added. The resulting mixture was extracted with Et_2O (4x), the combined organic layers were dried (Na_2SO_4) and the solvent was evaporated.

To a solution of Pt(DVDS) (0.18 mL, 2% in xylene, 0.008 mmol) and ^{t}Bu$_3$P (8 µL, 1 M in toluene, 0.008 mmol) in THF (5 mL), ethoxydimethylsilane (0.25 g, 2.45 mmol) was added and the mixture was stirred for 30 min at 25 °C. A solution of the residue obtained above (0.5 g, 1.63 mmol) in THF (5 mL) was added and the reaction mixture was stirred for 1 h. The solvent was evaporated and the residue was purified by column chromatography (C18 - silica gel, MeCN) to afford 0.45 g (68% yield) of a yellow oil identified as (1*E*,3*E*,5*E*,7*E*,9*E*)-benzyl-10-(ethoxydimethylsilyl)-3,8-dimethyldeca-1,3,5,7,9-tetraen-1-yl)dimethylsilane **21**. **^{1}H-NMR** (400.16 MHz, C_6D_6): δ 7.20 – 7.15 (m, 2H, ArH), 7.07 – 7.00 (m, 3H, ArH), 6.93 (d, *J* = 18.9 Hz, 1H), 6.73 (d, *J* = 18.8 Hz, 1H), 6.62 (m, 2H), 6.21 (m, 2H), 6.01 (d, *J* = 18.9 Hz, 1H), 5.95 (d, *J* = 18.8 Hz, 1H), 3.66 (q, *J* = 7.0 Hz, 2H, $SiMe_2O\underline{CH_2}CH_3$), 2.13 (s, 2H, $SiMe_2\underline{CH_2}Ph$), 1.81 (s, 6H, 2xCH_3), 1.19 (t, *J* = 7.0 Hz, 3H, $SiMe_2OCH_2\underline{CH_3}$), 0.31 (s, 6H, $Si\underline{Me_2}OEt$), 0.12 (s, 6H, $Si\underline{Me_2}Bn$) ppm. **^{13}C-NMR** (100.62 MHz, C_6D_6): δ 150.3 (d), 149.5 (d), 140.2 (d), 137.3 (s), 137.2 (s), 134.3 (s), 133.7 (d), 131.4 (d), 131.1 (d), 128.7 (d, 2x), 128.5 (d, 2x), 126.7 (d), 126.2 (d), 124.6 (d), 58.5 (t), 26.5 (t), 19.0 (q), 12.4 (q, 2x), -1.2 (q, 2x), -3.1 (q, 2x) ppm. **IR** (NaCl): υ 1644 (m), 1219 (m), 834 (s), 679 (s) cm^{-1}. **HRMS** (EI$^+$): Calcd. for $C_{25}H_{39}OSi_2$ ([M+H]$^+$), 411.2538; found, 411.2534.

(1*E*,3*E*,5*E*,7*E*,9*E*,11*E*,13*E*)-Benzyldimethyl-[3,8,12-trimethyl-14-(2,6,6-trimethylcyclohex-1-en-1-yl)-tetradeca-1,3,5,7,9,11,13-heptaen-1-yl)-silane (23). To a solution of **6** (24.1 mg, 0.063 mmol) in dioxane (0.126 mL) was added TMSOK (0.063 mL, 2M in THF, 0.126 mmol). After stirring for 15 min at 25 °C, a solution of **1** (20 mg, 0.063 mmol) in dioxane (0.126 mL) and $Pd(dba)_2$ (1.2 mg, 0.002 mmol) were added and the reaction mixture was stirred at 25 °C for 1.5 h. Then, the reaction mixture was filtered through a silica gel plug, the solids were washed with EtOAc (3x) and the solvent was evaporated. The residue was purified by column chromatography (silica gel, 98:2 hexane/EtOAc) to afford 18.4 mg (59%) of **24** as an orange oil. **^{1}H-NMR** (400.13 MHz, $(CD_3)_2CO$): δ 7.27 – 7.16 (m, 2H, ArH), 7.14 – 6.99 (m, 3H, ArH), 6.84 – 6.70 (m, 3H), 6.66 (d, *J* = 18.8 Hz, 1H), 6.41 (d, *J* = 15.0 Hz, 1H), 6.4 – 6.32 (d, *J* = 10.5 Hz, 2H), 6.26 – 6.17 (m, 3H), 5.91 (d, *J* = 18.8 Hz, 1H), 2.20 (s, 2H, $SiMe_2\underline{CH_2}Ph$), 2.04 (m, 2H), 1.99 (s, 6H, 2xC-CH_3), 1.89 (s, 3H, C-CH_3), 1.71 (s, 3H, C-CH_3), 1.66 – 1.58 (m, 2H), 1.52 – 1.46 (m, 2H), 1.04 (s, 6H, C_1-$(CH_3)_2$), 0.08 (s, 6H, $Si\underline{Me_2}Bn$) ppm. **^{13}C-NMR** (100.16 MHz, $(CD_3)_2CO$): δ 150.3 (d), 141.1 (s), 139.0 (d), 138.9 (s), 138.4 (d), 137.9 (s), 137.5 (s), 136.9 (s), 134.6 (d), 133.4 (d, 2x), 132.2 (d), 131.0 (s), 129.9 (d, 2x), 129.3 (d, 2x), 129.1 (d), 127.5 (d), 127.0 (d), 126.5 (d), 125.0 (d), 40.6 (t), 35.1 (s), 33.8 (t), 29.5 (q, 2x), 26.7 (q), 22.1 (t), 20.1 (q), 13.0 (t), 12.5 (q), 12.5 (q), -2.9 (q, 2x) ppm. **IR** (NaCl): v 2921 (s, C-H), 1566 (w), 960 (s), 847 (s) cm^{-1}. **UV** (MeOH): λ_{max} 403, 373, 352 nm. **MS** (ESI$^+$-TOF): *m/z* 497 ([M+H]$^+$, 2), 413 (8), 285 (18), 356 (13), 255 (100). **HRMS** (ESI$^+$): Calcd. for $C_{35}H_{49}Si$ ([M+H]$^+$), 497.3595; found, 497.3598.

β,β-Carotene (7).

Procedure A: (Preparation of **7** from symmetrical bissilylpentaene reagent **5**) To a cooled (0 °C) solution of **5** (12.2 mg, 0.027 mmol) in THF (0.76 mL) was added TBAF (0.061 mL, 1M in THF, 0.061 mmol). After stirring for 40 min at 0 °C, a solution of **1** (12.0 mg, 0.038 mmol) in THF (0.76 mL) and $Pd_2dba_3{\cdot}CHCl_3$ (5.9 mg, 0.006 mmol) were added and the reaction mixture was stirred at 0 °C for 1 h and at 25 °C for 15 min. After reaction completion (as indicated by tlc), a saturated aqueous solution of NH_4Cl was added and the mixture was extracted with Et_2O (3x). The combined organic layers were washed with brine (1x), dried (Na_2SO_4) and concentrated. After purification by column chromatography (CN-silica gel, 98:2 hexane/EtOAc), 20.4 mg (61%) of an orange oil identified as β,β-carotene **7** were isolated.[36]

Procedure B: (One-pot sequential preparation of **7** from bissilylpentaene reagent **6** without isolation of octaenylsilane **23**) To a solution of **6** (36.4 mg, 0.095 mmol) in dioxane (0.45 mL) was added KOTMS (0.095 mL,

2M in THF, 0.190 mmol). After stirring for 15 min at 25 °C, a solution of **1** (30 mg, 0.095 mmol) in dioxane (0.5 mL) and $Pd(dba)_2$ (1.2 mg, 0.002 mmol) were added and the reaction mixture was stirred at 25 °C for 1.5 h. Then, the reaction mixture was filtered through a silica gel plug, the solids were washed with EtOAc (3x), and the solvent was evaporated. The residue was dissolved in THF (0.5 mL) and TBAF (0.190 mL, 1M in THF, 0.190 mmol) was then added. After stirring for 15 min at 25 °C, a solution of **6** (30 mg, 0.095 mmol) in THF (0.5 mL) and $Pd(dba)_2$ (1.2 mg, 0.002 mmol) were added and the reaction mixture was stirred at 25 °C for 1.5 h. Then, the reaction mixture was filtered through a silica gel plug, the solids were washed with EtOAc (3x) and the solvent was evaporated. After purification by column chromatography (CN-silica gel, 98:2 hexane/EtOAc), 33.8 mg (66%) of an orange oil identified as β,β-carotene **7** were isolated.[36]

*Procedure C: (Preparation of **7** from octaenylsilane **23**)* TBAF (0.066 mL, 0.066 mmol, 1M in THF) was added to a cooled (0 °C) solution of **23** (33 mg, 0.066 mmol) in THF (0.6 mL). After stirring for 30 min at 0 °C, a solution of **1** (20 mg, 0.063 mmol) in THF (0.766 mL) and $Pd_2dba_3{\cdot}CHCl_3$ (3.3 mg, 0.003 mmol) were added and the reaction mixture was stirred at 0 °C for 1 h and at 25 °C for 15 min. After completion, a saturated aqueous solution of NH_4Cl was added and the reaction mixture was extracted with Et_2O (3x). The combined organic layers were washed with a saturated aqueous solution of NaCl (1x), dried and concentrated. After purification by column chromatography (CN-silica gel, 98:2 hexane/EtOAc), 30.5 mg (90%) of an orange oil identified as β,β-carotene **7** were isolated.[36]

(3*R*,3'*R*)-Zeaxanthin (8). TBAF (0.072 mL, 1M in THF, 0.072 mmol) was added to a cooled (0 °C) solution of **5** (14.4 mg, 0.032 mmol) in THF (0.9 mL). After stirring for 40 min at 0 °C, a solution of **22**[36] (15.0 mg, 0.045 mmol) in THF (0.9 mL) and $Pd_2dba_3{\cdot}CHCl_3$ (7.1 mg, 0.007 mmol) were added and the reaction mixture was stirred at 0 °C for 1h and at 25 °C for 15 min. After completion, a saturated aqueous solution of NH_4Cl was added and the resulting mixture was extracted with EtOAc (3x). The combined organic layers were washed with brine (1x), dried and concentrated. After purification by column chromatography (CN-silica gel, 90:10 hexane/EtOAc), 14 mg (55%) of an orange oil identified as (3*R*,3'*R*)-zeazanthin **8** were isolated.[36]

9-*cis*-β,β-Carotene (9).

Procedure A: TBAF (0.205 mL, 1 M in THF, 0.205 mmol) was added to a cooled (0 °C) solution of **23** (45.2 mg, 0.091 mmol) in THF (1.6 mL). After stirring for 30 min, a solution of **24** (25 mg, 0.079 mmol) in THF (1.6 mL) and $Pd_2dba_3{\cdot}CHCl_3$ (8.3 mg, 0.008 mmol) were added. After stirring at 25 °C for 2.5 h, a saturated aqueous solution of NH_4Cl was added. The mixture was extracted with EtOAc (3x) and the combined organic layers were washed with a saturated aqueous solution of NaCl (3x) and dried (Na_2SO_4) and the solvent was evaporated. The residue was purified by column chromatography (silica gel, 90:7:3 hexane/EtOAc/Et_3N) to afford 25.4 mg (60%) of a red oil identified as 9-*cis*-β,β-carotene **9**.

Procedure B: (one pot) KOTMS (0.026 mL, 2M in THF, 0.052 mmol) was added to a solution of **6** (9.9 mg, 0.026 mmol) in dioxane (0.3 mL). After stirring for 15 min at 25 °C, (1*E*,3*E*)-4-iodo-3-methylbuta-1,3,3-trimethylcyclohex-1-ene **1** (8.3 mg, 0.026 mmol) in dioxane (0.3 mL) and $Pd(dba)_2$ (0.6 mg, 0.001 mmol) were added and the reaction mixture was stirred at 25°C for 1.5 h. Then, the reaction mixture was filtered through a silica gel plug, washing with EtOAc (3x) and the solvent was evaporated. TBAF (0.052 mL, 1M in THF, 0.052 mmol) was then added to the solution of the residue in THF (0.5 mL). After stirring for 15 min at 25 °C, a solution of **24** (8.2 mg, 0.026 mmol) in THF (0.5 mL) and $Pd(dba)_2$ (0.6 mg, 0.001 mmol) were added and the reaction mixture was stirred at 25 °C for 1.5 h. Then, the reaction mixture was filtered through a silica gel plug, washing with EtOAc (3x) and the solvent was evaporated. After purification by column chromatography (CN-silica gel, 98:2 hexane/EtOAc), 4.5 mg (32%) of an orange oil identified as 9-*cis*-β,β-carotene **9** were isolated. **^{1}H-NMR** (400.13 MHz, $CDCl_3$): δ 6.74 (dd, *J* = 14.8, 11.6 Hz, 2H), 6.68 (d, *J* = 7.9 Hz, 1H), 6.66 – 6.54 (m, 3H), 6.28 (d, *J* = 14.9 Hz, 1H), 6.26 – 6.19 (m, 2H), 6.19 – 6.08 (m, 4H), 6.05 (d, *J* = 11.5 Hz, 1H), 2.08 – 1.99 (m, 4H), 1.97 (s, 6H), 1.95 (s, 6H), 1.76 (s, 3H), 1.71 (s, 3H), 1.66 – 1.59 (m, 4H), 1.51 – 1.39 (m, 4H), 1.04 (s, 6H), 1.03 (s, 6H) ppm. **^{13}C-NMR** (100.16 MHz, $CDCl_3$): δ 138.4 (s), 138.1 (s), 137.8 (d), 136.7 (d), 136.4 (s, 2x), 136.1 (s), 134.6 (d), 130.9 (d), 132.4 (d), 130.2 (d, 3x), 130.0 (d), 129.6 (s, 2x), 129.5 (d, 2x), 128.5 (d), 127.1 (s), 127.0 (d), 123.8 (d), 39.7 (t, 2x), 34.4 (s, 2x), 33.3 (t, 2x), 29.1 (q), 28.6 (q, 2x), 22.0 (q), 21.9 (q), 20.9 (q), 19.4 (t, 2x), 13.0 (q), 12.9 (q) ppm. **UV** (MeOH): λ_{max} 426 nm. **HRMS** (ESI^+): Calcd. for $C_{40}H_{56}$ ($[M+H]^+$), 536.4375; found, 536.4376.

7,8-Dihydro-β,β-carotene (10).[40] TBAF (0.33 mL, 0.33 mmol, 1M in THF) was added to a cooled (0 °C) solution of **23** (72 mg, 0.145 mmol) in THF (1.3 mL). After stirring for 30 min at 0 °C, a solution of **25** (40 mg, 0.126 mmol) in THF (1.3 mL) and $Pd_2dba_3{\cdot}CHCl_3$ (13 mg, 0.013 mmol) were added, and the reaction mixture was stirred at 0 °C for 1h and at 25 °C for 15 min. After completion, a saturated aqueous solution of NH_4Cl was added and the resulting mixture was extracted with Et_2O (3x). The combined organic layers were washed with a saturated aqueous solution of NaCl (1x), dried and concentrated under *vacuum*. After purification by column chromatography (CN-silica gel, 98:2 hexane/EtOAc), 53 mg (78%) of an orange solid identified as 7,8-dihydro-β,β-carotene **10** were isolated. **^{1}H-NMR** (400.13 MHz, $CDCl_3$): δ 6.50 – 6.09 (m, 11H), 5.98 (d, *J* = 11.1 Hz, 1H), 2.02 (t, *J* = 6.0 Hz, 4H, $2xCH_2$), 1.97 (s, 6H, $C\text{-}CH_3$ + $C\text{-}CH_3$), 1.95 (s, 3H, $C\text{-}CH_3$), 1.94 – 1.89 (m, 4H, $2xCH_2$), 1.87 (s, 3H, $C\text{-}CH_3$), 1.72 (s, 3H, $C\text{-}CH_3$), 1.63 (s, 3H, $C\text{-}CH_3$), 1.62 – 1.54 (m, 4H, $2xCH_2$), 1.49 – 1.45 (m, 4H, $2xCH_2$), 1.45 – 1.41 (m, 4H, $2xCH_2$), 1.03 (s, 6H, $C\text{-}(CH_3)_2$), 1.01 (s, 6H, $C\text{-}(CH_3)_2$) ppm.[40] **^{13}C-NMR** (100.16 MHz, $CDCl_3$): δ 140.8 (s), 138.1 (s), 138.0 (d), 137.4 (d), 136.6 (d), 136.3 (s), 136.0 (d), 135.5 (s), 135.4 (d), 132.6 (d), 131.6 (d), 131.0 (d), 130.2 (d), 129.6 (d), 129.5 (s), 127.4 (s), 126.7 (s), 125.3 (d), 125.2 (s), 125.0 (d), 41.0 (t), 40.0 (t), 39.8 (t), 35.2 (s), 34.4 (s), 33.3 (t), 32.9 (t), 29.1 (q, 2x), 28.8 (q, 3x), 27.9 (t), 21.9 (q), 20.0 (q), 19.7 (t), 19.4 (t), 17.2 (q), 13.0 (q, 2x) ppm. **IR** (NaCl): v 2927 (s, C-H), 2364 (w, C-H), 1447 (w), 965 (s) cm^{-1}. **HRMS** (ESI^+): Calcd. for $C_{40}H_{58}$ ($[M+H]^+$), 538.4525; found, 538.4533.

(3*R*)-β-Cryptoxanthin (11). KOTMS (0.057 mL, 2M in THF, 0.114 mmol) was added to a solution of **6** (22 mg, 0.057 mmol) in dioxane (0.5 mL). After stirring for 15 min at 25 °C, a solution of **1** (18 mg, 0.057 mmol) in dioxane (0.5 mL) and $Pd(dba)_2$ (1 mg, 0.001 mmol) were added and the reaction mixture was stirred at 25°C for 1.5 h. Then, the reaction mixture was filtered through a silica gel plug, washing with EtOAc (3x) and the solvent was evaporated. TBAF (0.114 mL, 1M in THF, 0.114 mmol) was added to the solution of the residue in THF (0.5 mL). After stirring for 15 min at 25 °C a solution of **22**[36] (22 mg, 0.057 mmol) in THF (0.5 mL) and $Pd(dba)_2$ (1 mg, 0.001 mmol) were added and the reaction mixture was stirred at 25 °C for 1.5 h. Then, the reaction mixture was filtered through a silica gel plug, washing with EtOAc (3x) and the solvent was evaporated. After purification by column chromatography (CN-silica gel, 90:10 hexane/EtOAc), 18 mg (57%) of an orange oil identified as (3*R*)-β-cryptoxanthin **11** were isolated. ^{1}H-NMR data matched those previously reported.[41] **^{1}H-NMR** (400.13 MHz, $CDCl_3$): δ 6.70 – 6.58 (m, 4H), 6.36 (dd, *J* = 14.9, 3.8 Hz, 4H), 6.24 (m, 2H), 6.19 – 6.09 (m, 4H), 4.05 – 3.95 (m, 1H), 2.44 – 2.34 (m, 1H), 2.06 – 1.99 (m, 1H), 1.99 – 1.94 (m, 10H), 1.79 – 1.76 (m, 1H), 1.74 (s, 3H), 1.72 (s, 3H), 1.65 – 1.59 (m, 1H), 1.51 – 1.44 (m, 2H), 1.25 (s, 6H), 1.07 (s, 6H), 1.03 (s, 6H) ppm. **HRMS** (ESI^+): Calcd. for $C_{40}H_{56}O$($[M+H]^+$), 553.4385 found, 553.4404**.**

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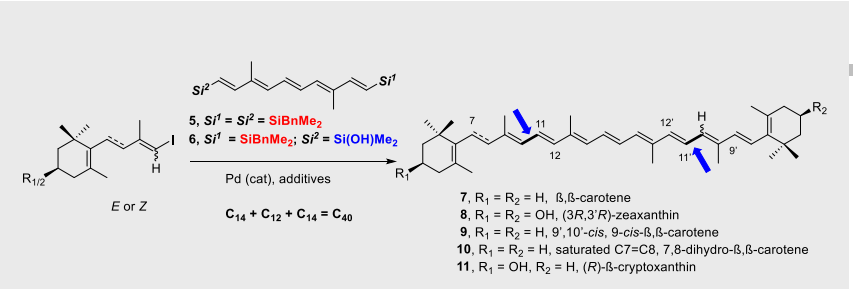

The Hiyama-Denmark cross-coupling reaction has been extended to the preparation of symmetrical and nonsymmetrical carotenoids using bissilyldeca-1,3,5,7,9-pentaenes.

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Bidirectional Hiyama-Denmark Cross-Coupling Reactions of Bissilyldeca-1,3,5,7,9-pentaenes for the Synthesis of Symmetrical and Non-Symmetrical Carotenoids