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# Stereoselective Synthesis Of Polyenic Alarm Pheromones Of Cephalaspidean Molluscs

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***Abstract***: The stereospecific thallium-accelerated palladium-catalyzed cross-coupling of 1-alkenyl boronic acids and 1-alkenyl iodides (the Suzuki reaction) is the key step in an efficient approach to several polyenic pheromones isolated from cephalaspidean opisthobranch molluscs.

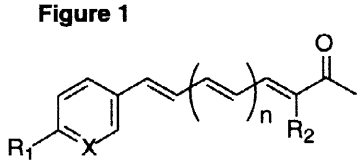


## Introduction

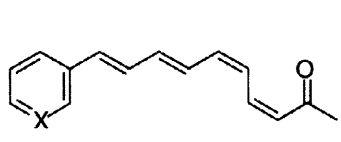
Opisthobranchs are marine molluscs wich, being scarcely protected by a shell, have been the subject of many chemical studies directed to investigate their defensive strategies.[1] Although most attention has been devoted to nudibranchs (which being completely devoid of a shell, are considered to be the most highly evolved opisthobranchs), in recent years there have also been several studies of cephalaspideans (characterized by a prominent head and a shell that is either small and fragile or internal), for some of which chemical communication seems to play an important role.[2]

The first chemical study of a cephalaspidean revealed the presence, in the Pacific aglajid *Navanax inermis*,[3] of a mixture of conjugated methyl ketones, navenones A, B and C (**1a**, **1b** and **1c**, respectively), together with the minor related compounds **1d-g** (Figure 1). When this mixture is secreted into the slime trail, acts as an alarm pheromone inducing an immediate escape reaction in following conspecifics. This study represented the first successful description of alarm pheromones in a marine mollusc.

**Figure 1**

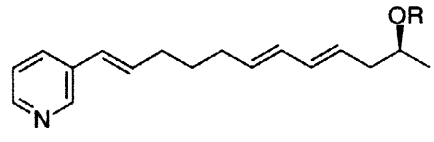



| | n | X | $R_1$ | $R_2$ |
|---|---|---|---|---|
| **1a** | 2 | N | H | H |
| **1b** | 2 | CH | H | H |
| **1c** | 2 | CH | OH | H |
| **1d** | 2 | N | H | $CH_3$ |
| **1e** | 2 | CH | H | $CH_3$ |
| **2b** | 1 | CH | H | $CH_3$ |



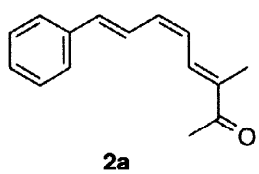

**1f** X= CH

**1g** X= N

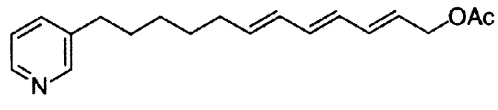



**3a** R= H

**3b** R= Ac




**2a**




**3c**

0040-4020/98/$19.00 
*PII:* S0040-4020(98)00363-9

More recently, metabolites with structures related to navenones have been found in Mediterranean cephalaspideans (Figure 1):[4-7] two new phenyl conjugated trienones, lignarenones A (**2a**) and B (**2b**), in the Cylichnidae *Scaphander lignarius*,[4] and nine polyenic pyridines, with alarm pheromone activity, in the Haminoeidae: haminols A (**3a**) and B (**3b**) in *Haminoea navicula*,[5] haminol C (**3c**) in *H. orteai*,[6] and haminols 1-2 and 3-6 in *H. orbignyana*, and *H. fusari*, respectively.[6]

The synthesis of natural products with highly unsaturated polyolefinic structures have represented a trial for a variety of olefin-formation reactions. These include, for the polyenic pheromones mentioned above, Wittig (or some of its variants) reaction,[8-13] the use of polyvinylogation reagents,[14] reductive elimination of 1,6-diol-2,4-diynes,[15] Sonogashira-type coupling of a halotriene to 1-butyn-3-ol followed by selective reduction of the propargylic alcohol function with Red-Al,[16] and the use of a "lipchin" stannylated dienyne suitable for bidirectional elaboration.[17] Most of these efforts have afforded unsubstituted conjugated polyenes with the extended all-(*E*) configuration.

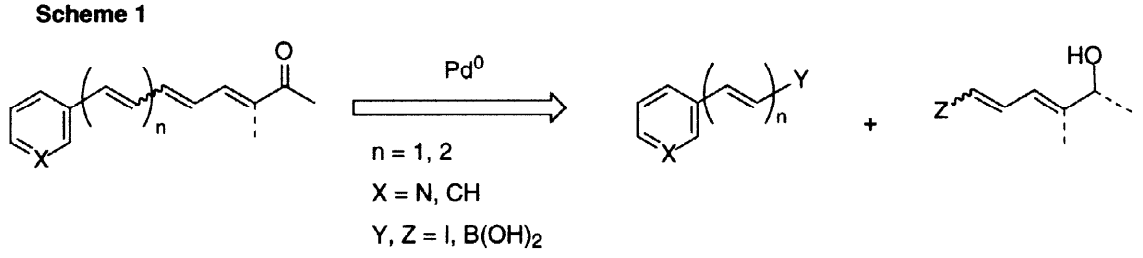
Our group has recently reported the application of the Suzuki[18] cross-coupling of boron derivatives with organic electrophiles to the preparation of retinoids and arotinoids.[19] By employing a variety of combinations of alkenyl- or arylboronic acids and electrophiles (alkenyl and aryl iodides, aryl bromides, aryl triflates), the procedure was shown to be of general application.

In a preliminary communication,[20] we have briefly described the application of this approach to the synthesis of 3-methylnavenone B (**1e**) and lignarenones A (**2a**) and B (**2b**); the thallium-accelerated, palladium-catalyzed cross-coupling of (*E*)-1-alkenylboronic acids and *E* or *Z* alkenyl iodides proved to be an efficient procedure for the preparation of alkyl-substituted polyenes with uniform configuration. We report here a full account of this work, including the stereoselective preparation of unsubstituted navenone B (**1b**) and the pyridine derivatives navenone A (**1a**) and haminol C (**3c**).

## Results and Discussion

The key step in our convergent approach is the construction of one of the single bonds of the pheromone side chain by cross-coupling of an alkenylboronic acid and an alkenyliodide (Scheme 1). Which moiety is the boronic acid and which the iodide depends upon the relative ease of preparation of the two possible combinations: **2a**, **2b**, **1e** and **1b** were obtained by coupling a phenylalkenylboronic acid (**4** or **5**[19a]) with an alkenyl iodide (**6**, **7** or **8**; Scheme 4); and **1a** and **3c** by coupling dienylboronic acid **9**[19b] with the pyridine derivatives **10** and **11**, respectively (Scheme 5).

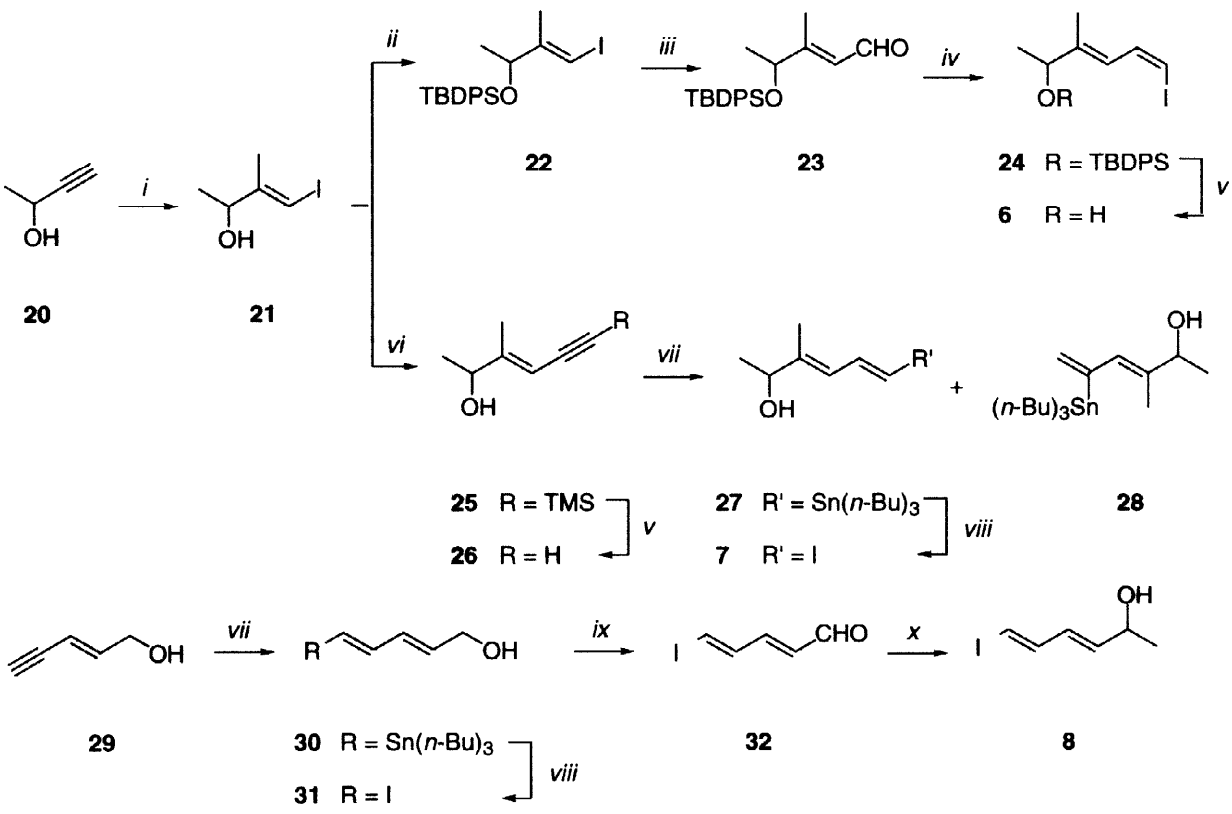
**Scheme 1**



All the boronic acids used in this work have been described elsewhere.[19a,b,21] Schemes 2 and 3 depict the preparation of the novel vinyl iodides **6-8**, **10** and **11**.

Compounds **6** and **7** were synthesized following standard sequences starting from the same precursor, the (*E*)-iodide **21**, which was itself obtained in 65% yield by zirconium-catalyzed methylalumination[22] of commercially available but-3-yn-2-ol (**20**) followed by Al-I exchange through slow addition of a solution of ICN in THF (Scheme 2). Protection of **21** with TBDPSCl gave the *tert*-butyldiphenylsilyl ether **22** (93%), which through *t*-BuLi treatment and organolithium trapping with DMF afforded enal **23** in 79% overall yield. (*Z*)-selective[23] Wittig reaction of **23** with iodomethylenetriphenylphosphorane afforded compound **24** in 92% yield stereoselectively (*5Z/5E* >20:1, as judged by $^1$H MNR). Deprotection of **24** with TBAF provided the (*Z*)-dienyl iodide **6** in 91% yield.

**Scheme 2**




Reagents and conditions. *i.* 1. $Me_3Al$, $Cl_2ZrCp_2$, $CH_2Cl_2$, 0 °C to 25 °C. 2. ICN, THF, 0 °C, 0.5 mL/h, 65%. *ii.* TBDPSCl, imidazole, DMF, 25 °C, 93%. *iii.* 1. *t*-BuLi, THF, -78 °C. 2. DMF, -78 °C, 79%. *iv.* $ICH_2PPh_3I$, $NaN(TMS)_2$, HMPA, THF, -78 °C to 25 °C, 92%. *v.* TBAF, THF, 25 °C, 91% for **6**, 65% for **26**. *vi.* $Pd(PPh_3)_4$, TMS-acetylene, CuI, pyrrolidine, 25 °C, 96%. *vii.* CuCN, *n*-BuLi, $(n\text{-}Bu)_3SnH$, THF, -30 ° C to 25 °C, 95% for **27** (**27/28** 15:1 ratio), 67% for **30**. *viii.* $I_2$, $CH_2Cl_2$, 25 °C, 93% for **7**, 95% for **31**. *ix.* $MnO_2$, $CH_2Cl_2$, 25 °C, 86%. *x.* MeLi, $Et_2O$, 0 °C, 53%.

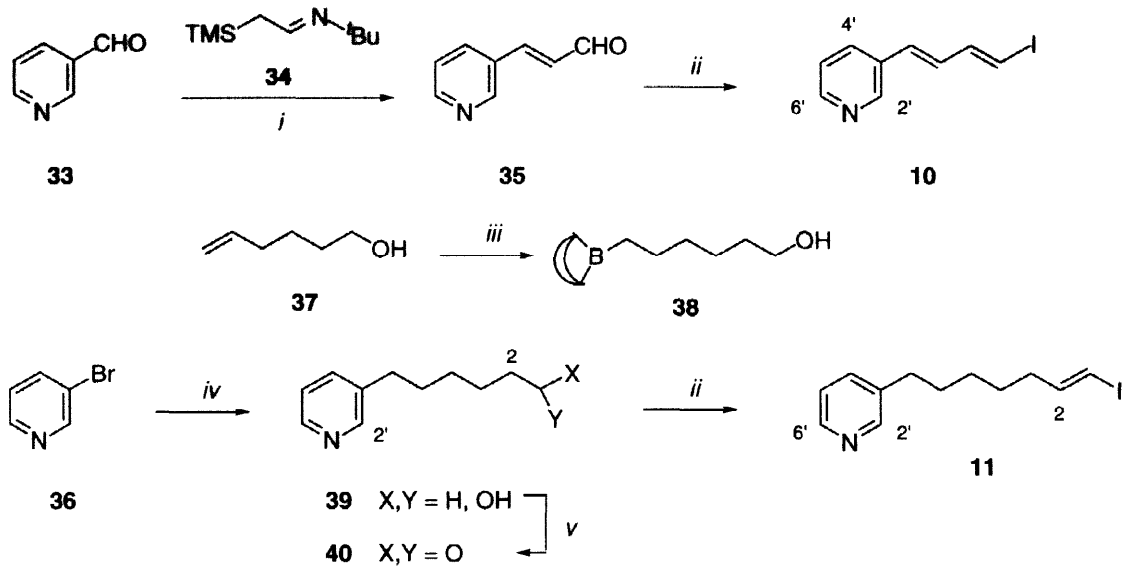
Sonogashira-type coupling of alkenyl iodide **21** with trimethylsilyl acetylene, under the modified conditions described by Linstrumelle (CuI, pyrrolidine)[24] (96%), followed by fluoride-induced deprotection of the product (**25**) provided the unstable enynol **26** (65%) which, by regioselective addition of a mixed

tributylstannylcuprate[25] at -30 °C, was converted in 95% yield into an easily separable 15:1 ratio mixture of the terminal dienyl stannane **27** and the corresponding internal stannane **28**. It is important to emphasize that the regioselectivity of this reaction depends heavily on the temperature at which the alkyne is added;[26] addition at -78 °C afforded a 2:1 mixture of **27** and **28** in 76% yield. Finally, metal-halogen exchange[27] provided the (*E*)-dienyliodide **7** in 93% yield.

Following a similar sequence (Scheme 2), the demethylated iodide **8** was prepared starting from commercially available pent-2-en-4-yn-1-ol (**29**). Treatment of **29** with $(Bu_3Sn)(Bu)Cu(CN)Li_2$ led to dienylstannane **30** (67%), which upon Sn/I conversion afforded the unstable vinyl iodide **31** (95%). $MnO_2$ oxidation to dienal **32** and treatment with MeLi provided the desired iodide **8** in 46% overall yield.

Scheme 3 depicts the preparation of alkenyl iodides **10** and **11**. Peterson olefination of 3-formylpyridine (**33**) with the anion derived from silylimine **34**[28] (*sec*-BuLi, -78 °C), followed by hydrolysis with trifluoroacetic acid and water, provided aldehyde **35** (77% yield), which was converted to a 4:1 mixture of *E/Z* alkenyl iodides **10** (72% yield) using Takai's procedure.[29] No attempts were made at separating both isomers at this stage, due to their instability. Iodide **11** was in turn synthesized by palladium-catalyzed cross-coupling of an alkylborane with an arylbromide using a modification of the method developed by Suzuki.[30] 3-Bromopyridine (**36**) and the 9-alkyl-9-BBN derivative **38**, generated by reaction of hex-5-en-1-ol **37** and 9-borabicyclo[3.3.1]nonane (9-BBN), were coupled ($K_2CO_3$, $Pd(PPh_3)_4$, $H_2O$, DMF, THF)[30] to afford alcohol **39** in 93% yield. Swern oxidation to aldehyde **40** (70%) and stereoselective iodoolefination as for compound **10** provided the desired (*E*)-iodide **11** stereochemically pure in 65% yield.[31]

**Scheme 3**

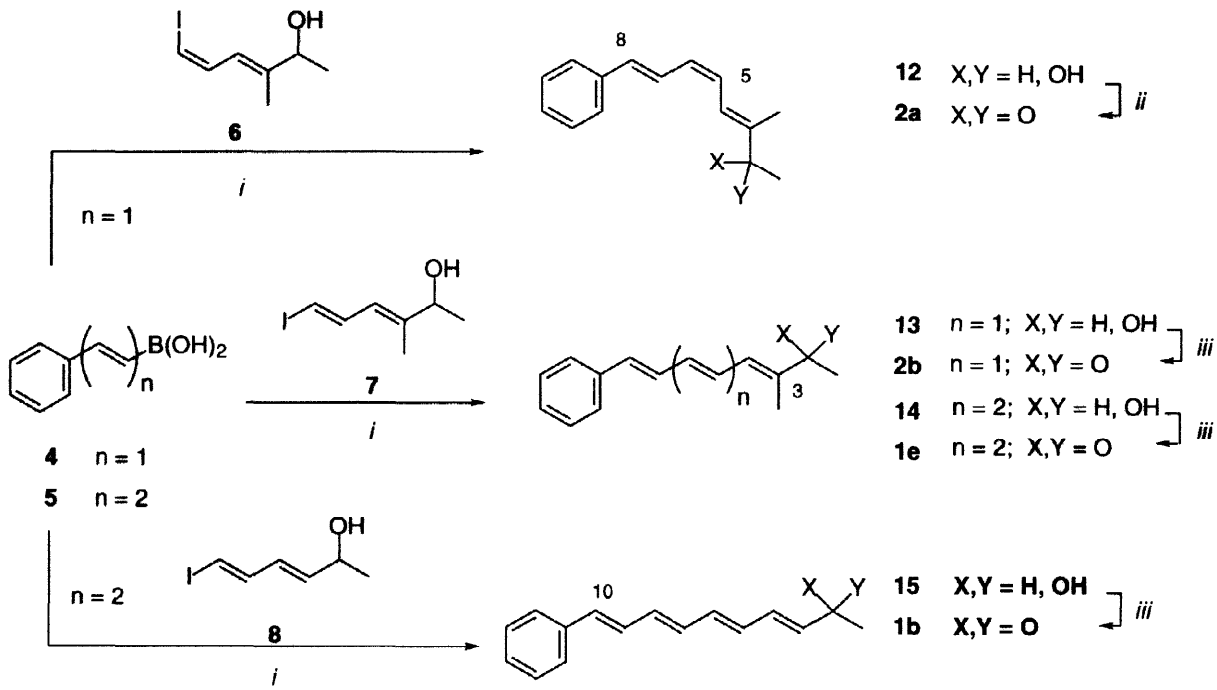



Reagents and conditions: *i.* 1. *sec*-BuLi, THF, -78 °C to -20 °C. 2. $CF_3COOH$, $H_2O$, -20 °C to 25 °C, 77%. *ii.* $CrCl_2$, $CHI_3$, THF, 0 °C to 25 °C, 72% for **10**, 65% for **11**. *iii.* 9-BBN, 25 °C. *iv.* **38**, $K_2CO_3$, $H_2O$, $Pd(PPh_3)_4$, DMF, THF, 25 °C, 93%. *v.* 1. $(COCl)_2$, DMSO, $CH_2Cl_2$, -60 °C. 2. $Et_3N$, 25 °C, 72 %.

The alkenyl iodides **6-8** were coupled with alkenylboronic acid **4** and/or **5** (Scheme 4) at room temperature using the modified Suzuki conditions due to Kishi (10% aqueous TlOH);[32] reactions completed in 1h

affording good yields of the conjugated polyenols **12**-**15** with excellent stereoselectivity. Transformation of **13**, **14** and **15** into the corresponding natural products lignarenone B (**2b**),[4] 3-methylnavenone B (**1e**)[3] and navenone B (**1b**)[3] was effected by allylic oxidation with $MnO_2$ in $CH_2Cl_2$. However, oxidation of **12** to lignarenone A (**2a**) proved troublesome because of its isomerization to lignarenone B (**2b**).[11a,12] Use of the Dess-Martin periodinane under basic conditions[33] afforded a 2:1 mixture of **2b** and **2a** in 57% yield. Compounds **2a** and **2b** were carefully separated by HPLC; their $^1H$ NMR spectra (500 MHz) matched both the published[4] spectral data for lignarenones A and B, respectively, and the actual spectra, copies of which were kindly provided by Prof. A. Spinella.

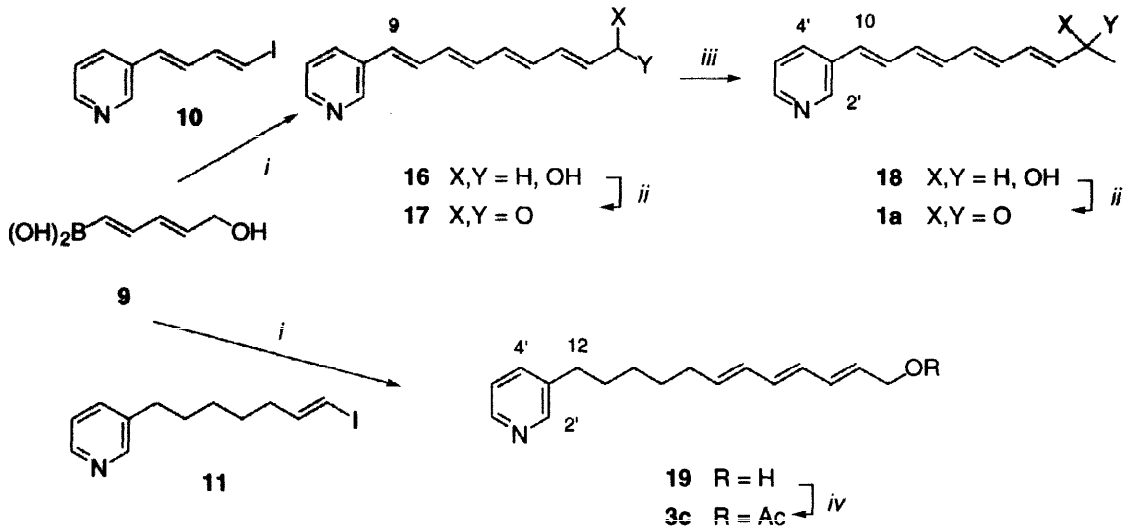
**Scheme 4**




Reagents and conditions: *i.* $Pd(PPh_3)_4$ (0.3 equiv), 10% aq TlOH (3.0 equiv), THF, 25 °C, 80% for **12**, 81% for **13**, 70% for **14**, and 81% for **15**. *ii.* Dess-Martin periodinane, 4 Å Sieves, $NaHCO_3$, $CH_2Cl_2$, 25 °C, 57%. *iii.* $MnO_2$, $CH_2Cl_2$, 25 °C, 65% for **2b**, 63% for **1e**, and 54% for **1b**.

Coupling of alkenyl iodides **10** (as a 4:1 *E/Z* mixture) and **11** with boronic acid **9** under the conditions specified above afforded the polyenols **16** (the pure *E* isomer was obtained by crystallization of the 4:1 mixture of *E/Z* isomeric coupled products) and **19**, respectively. Alcohol **19**, which was very unstable, was immediately acetylated by treatment with acetic anhydride in pyridine to produce haminol C (**3c**) (82%).[6] Navenone A (**1a**)[3] was obtained from **16** by allylic oxidation to aldehyde **17** (72%), reaction of **17** with MeLi to afford alcohol **18** (72%), and $MnO_2$ oxidation of **18** to give **1a** (92%). Spectral data of synthetic **1a**[3] and **3c**[6] also matched those reported for the natural products.

**Scheme 5**




Reagents and conditions: *i.* $Pd(PPh_3)_4$ (0.1 equiv), 10% aq TlOH (3.0 equiv), THF, 25 °C, 69 % for **16**, and 93 % for **19**. *ii.* $MnO_2$, $CH_2Cl_2$, 25 °C, 72 % for **17**, 92 % for **1a**. *iii.* MeLi, THF, 0 °C, 72 %. *iv.* $Ac_2O$, pyridine, 25 °C, 82%.

To summarize, we have found that the Suzuki reaction allows highly stereoselective synthesis of natural products with polyolefinic structures from readily accesible alkenyl fragments with the desired substitution patterns. Our previously reported syntheses of retinoids[19] and the syntheses of cephalaspidean polyenic pheromones described here confirm the potential of this stereoselective reaction for the preparation of unstable polyenes.

## Experimental Section[34]

**(*E*)-4-Iodo-3-methylbut-3-en-2-ol (21).** A suspension of $Cl_2ZrCp_2$ (4.18 g, 14.28 mmol) in $CH_2Cl_2$ (15 mL) was treated at 0 °C with trimethylaluminium (4.2 mL, 42.8 mmol) followed by addition of a solution of but-3-yn-2-ol (**20**; 1.0 g, 14.3 mmol) in $CH_2Cl_2$ (5 mL). The reaction mixture was stirred at room temperature for 12 h and then cooled down to 0 °C. A solution of ICN (6.6 g, 42.8 mmol) in THF (20 mL) was added dropwise through a mechanical syringe (0.5 mL/h). Addition of 100 mL of a 1:1 THF/$H_2O$ mixture was followed by extraction with $Et_2O$. The organic layer was washed with aqueous $Na_2S_2O_3$ and water, dried over $MgSO_4$ and concentrated. The residue was purified by chromatography on silica gel (80:20 hexane/ethyl acetate) to afford 1.97 g (65%) of compound **21** as a yellow oil. $^1H$ NMR (300.13 MHz, $CDCl_3$): δ 1.28 (3H, d, $J$ = 6.4 Hz, $3H_1$), 1.82 (3H, s, $C_3$-$CH_3$), 1.84 (1H, s, OH), 4.36 (1H, q, $J$ = 6.4 Hz, $H_2$), 6.29 (1H, s, $H_4$). $^{13}C$ NMR (62.89 MHz, $CDCl_3$): δ 19.8 (q, $C_3$-$CH_3$), 21.6 (q, $C_1$), 72.4 (d, $C_2$), 77.5 (d, $C_4$), 151.2 (s, $C_3$). IR (NaCl): ν 3600-3100 (br, O-H), 2982 (s, C-H), 2932 (s, C-H ) $cm^{-1}$. MS *m/z* (%): 212 ($M^+$, 14), 197 (16), 127 (12), 85 (66), 69 (10), 67 (21), 58 (base peak, 100), 55 (11).

***tert*-Butyldiphenylsilyl [(*E*)-4-Iodo-3-methylbut-3-en-2-yl] Ether (22).** To a cooled (0 °C) solution of alcohol **21** (0.7 g, 3.3 mmol) in DMF (5 mL) were added *tert*-butyldiphenylsilyl chloride (1.3 g, 4.73 mmol)

and imidazole (0.56 g, 8.3 mmol). The reaction mixture was stirred at room temperature for 5 h and then extracted with ether (3 x 50 mL). The combined organic extracts were washed with $H_2O$ (3 x 50 mL), dried over $MgSO_4$ and concentrated. Chromatographic purification ($SiO_2$, hexane) afforded 1.38 g (93%) of compound **22** as a brown oil. $^1H$ NMR (250.13 MHz, $CDCl_3$): δ 1.06 (9H, s, $C(CH_3)_3$), 1.16 (3H, d, $J$ = 6.3 Hz, $3H_1$), 1.77 (3H, s, $C_3$-$CH_3$), 4.30 (1H, q, $J$ = 6.3 Hz, $H_2$), 6.00 (1H, s, $H_4$), 7.3-7.7 (10H, m, ArH). $^{13}C$ NMR (62.89 MHz, $CDCl_3$): δ 19.2 (s, $C(CH_3)_3$), 19.6 (q), 22.9 (q), 26.9 (q, 3x, $C(CH_3)_3$), 73.9 (d, $C_2$), 77.8 (d, $C_4$), 127.6 (d, 4x), 129.7 (d, 2x), 133.6 (s, 2x), 134.1 (s, $C_3$), 135.9 (d, 4x). MS *m/z* (%): 393 ($M^+$ - *t*-Bu, base peak, 100), 315 (23), 309 (53), 223 (24), 200 (15), 199 (81), 197 (14), 181 (24), 135 (12), 105 (20), 77 (17), 57 (20).

**(*E*)-4-[(*tert*-Butyldiphenylsilyl)oxy]-3-methylpent-2-enal (23).** *t*-BuLi (3.96 mL, 1.48 M in pentane, 5.86 mmol) was slowly added to a cold (-78 °C) solution of iodide **22** (1.2 g, 2.67 mmol) in THF (24 mL). After the mixture had been stirred at -78 °C for 45 min, DMF (0.61 mL, 7.99 mmol) was added and the stirring was continued for 1h at the same temperature. Then saturated aqueous $NH_4Cl$ (20 mL) was added and the organic layer was extracted with $Et_2O$ (3 x 20 mL). The combined organic layers were washed with brine, dried over $Na_2SO_4$ and concentrated. Flash chromatography of the residue (80:20 hexane/ethyl acetate) gave 0.74 g (79%) of compound **23** as a yellow oil. $^1H$ NMR (250.13 MHz, $CDCl_3$): δ 1.07 (9H, s, $C(CH_3)_3$), 1.18 (3H, d, $J$ = 6.5 Hz, $3H_5$), 2.05 (3H, d, $J$ = 1.2 Hz, $C_3$-$CH_3$), 4.25 (1H, q, $J$ = 6.5 Hz, $H_4$), 6.02 (1H, dq, $J$ = 8.1, 1.2 Hz, $H_2$), 7.3-7.8 (10H, m, ArH), 9.97 (1H, d, $J$ = 8.1 Hz, $H_1$). $^{13}C$ NMR (62.89 MHz, $CDCl_3$): δ 13.8 (s, $C(CH_3)_3$), 19.7 (q), 23.1 (q), 27.3 (q, 3x, $C(CH_3)_3$), 73.8 (d, $C_2$), 125.3 (d), 128.2 (d, 4x), 130.2 (d, 2x), 134.4 (s, 2x), 136.2 (d, 4x), 149.1 (s), 192.1 (d, $C_1$). MS *m/z* (%): 295 ($M^+$-*t*-Bu, 53), 217 (34), 200 (19), 199 (base peak, 100), 181 (13), 139 (13), 77 (13). HRMS: calcd. for $C_{22}H_{28}O_2Si$ ($M^+$ - *t*-Bu), 295.1154; found, 295.1158.

***tert*-Butyldiphenylsilyl (3*E*,5*Z*)-6-Iodo-3-methylhexa-3,5-dien-2-yl Ether (24).** To a suspension of iodomethyltriphenylphosphonium iodide (1.13 g, 2.13 mmol) in THF (20 mL) was added sodium hexamethyldisilylazide (2.13 mL, 1 M in THF, 2.13 mmol) at room temperature. The resulting solution was stirred for 5 min and cooled down to -60 °C, and HMPA (0.5 mL, 2.55 mmol) was then added. After cooling to -78 °C, a solution of aldehyde **23** (0.6 g, 1.70 mmol) in THF (35 mL) was added through a cannula. The resulting mixture was stirred at room temperature for 3 h. Hexane was added (20 mL), and the mixture was washed with brine (2 x 20 mL) and water (2 x 20 mL). The combined organic extracts were dried over $MgSO_4$ and concentrated. The residue was purified by chromatography on silica gel (hexane) to afford 0.75 g (92%) of compound **24** as a brown oil which was used in the next step without further purification.

**(3*E*,5*Z*)-6-Iodo-3-methylhexa-3,5-dien-2-ol (6).** Tetrabutylammonium fluoride (2.3 mL, 1M in THF, 2.3 mmol) was added to a solution of silyl ether **24** (0.73 g, 1.53 mmol) in THF (10 mL), and the mixture was stirred at room temperature for 2 h, poured into $H_2O$ (30 mL) and extracted with $Et_2O$ (3 x 20 mL). The organic extracts were dried over $Na_2SO_4$ and concentrated. Chromatography of the residue ($SiO_2$, 80:20 hexane/ethyl acetate) afforded 0.33 g (91%) of compound **6** as a yellow oil. $^1H$ NMR (250.13 MHz, $CDCl_3$): δ 1.31 (3H, d, $J$ = 6.3 Hz, $3H_1$), 1.81 (3H, s, $C_3$-$CH_3$), 4.32 (1H, q, $J$ = 6.3 Hz, $H_2$), 6.20 (1H, d, $J$ = 10.1 Hz, $H_6$), 6.29 (1H, d, $J$ = 7.4 Hz, $H_4$), 6.92 (1H, dd, $J$ = 10.1, 7.4 Hz, $H_5$). $^{13}C$ NMR (75.89 MHz, $CDCl_3$): δ 13.5 (q, $C_3$-

$CH_3$), 21.4 (q, $C_1$), 72.6 (d, $C_2$), 83.3 (d, $C_6$), 124.1 (d, $C_4$), 134.1 (d, $C_5$), 146.8 (s, $C_3$). IR (NaCl): ν 3600-3000 (br, O-H), 2973 (s, C-H), 2927 (s, C-H) $cm^{-1}$. MS *m/z* (%): 238 ($M^+$, 23), 221 ($M^+$ - OH, 28), 199 (58), 163 (22), 127 ($I^+$, 23), 111 ($M^+$-I, base peak, 100), 109 (26), 107 (23), 105 (28), 97 (30), 96 (47), 95 (82), 93 (36), 91 (47), 86 (65), 84 (97), 81 (43).

**(*E*)-3-Methyl-6-(trimethylsilyl)hex-3-en-5-yn-2-ol (25).** Trimethylsilylacetylene (1.38 g, 14.15 mmol) was slowly added to a degassed solution of iodide **21** (1.50 g, 7.08 mmol), $Pd(PPh_3)_4$ (0.41 g, 0.345 mmol) and CuI (0.14 g, 0.71 mmol) in pyrrolidine (25 mL). After stirring at room temperature for 30 min, the reaction mixture was treated with a saturated aqueous $NH_4Cl$ solution (50 mL) and extracted with $Et_2O$ (4 x 20 mL). The combined organic layers were dried over $Na_2SO_4$ and concentrated. The residue was purified by chromatography ($SiO_2$, 80:20 hexane/ethyl acetate) to afford 1.24 g (96%) of compound **25** as a brown oil. $^1H$ NMR (300.13 MHz, $CDCl_3$): δ 0.20 (9H, s, $Si(CH_3)_3$), 1.28 (3H, d, $J$ = 6.5 Hz, $3H_1$), 1.57 (1H, br s, OH), 1.91 (3H, d, $J$ = 1.1 Hz, $C_3$-$CH_3$), 4.26 (1H, q, $J$ = 6.5 Hz, $H_2$), 5.60 (1H, q, $J$ = 1.1 Hz, $H_4$). $^{13}C$ NMR (75.89 MHz, $CDCl_3$): δ 0.4 (q, $Si(CH_3)_3$), 15.7 (q), 22.1 (q), 72.1 (d, $C_2$), 99.0 (s, $C_6$), 103.0 (s, $C_5$), 104.9 (d, $C_4$), 156.1 (s, $C_3$). IR (NaCl): ν 3600-3100 (br, O-H), 2957 (m, C-H), 2919 (m, C-H ), 2359 (s, C≡C ) $cm^{-1}$. MS *m/z* (%): 183 ($M^+$ +1, 21), 167 (23), 165 (80), 149 (22), 135 (24), 105 (45), 97 (44), 95 (53), 85 (46), 83 (64), 81 (53), 75 (base peak, 100). HRMS: calcd. for $C_{10}H_{18}OSi$, 182.1127; found, 182.1126.

**(*E*)-3-Methylhex-3-en-5-yn-2-ol (26).** Tetrabutylammonium fluoride (9.9 mL, 1M in THF, 9.9 mmol) was added to a solution of compound **25** (1.2 g, 6.59 mmol) in THF (15 mL), and the mixture was stirred at room temperature for 2 h, poured into $H_2O$ (20 mL) and extracted with $Et_2O$ (3 x 10 mL). The organic extracts were dried over $Na_2SO_4$ and concentrated. Chromatography of the residue ($SiO_2$, 80:20 hexane/ethyl acetate) yielded 0.47 g (65%) of the unstable enynol **26** as a colourless oil. $^1H$ NMR (250.13 MHz, $C_6D_6$): δ 0.96 (3H, d, $J$ = 6.2 Hz, $3H_1$), 1.80 (3H, s, $C_3$-$CH_3$), 2.87 (1H, s, $H_6$), 3.75 (1H, q, $J$ = 6.2 Hz, $H_2$), 5.55 (1H, s, $H_4$). $^{13}C$ NMR (62.89 MHz, $C_6D_6$): δ 15.1 (q, $C_3$-$CH_3$), 21.5 (q, $C_1$), 71.2 (d, 2x, $C_2$ + $C_6$), 81.5 (s, $C_5$), 103.6 (d, $C_4$), 156.3 (s, $C_3$). IR (NaCl): ν 3570-3000 (br, O-H), 2964 (s, C-H), 2356 (m, C≡C ) $cm^{-1}$. HRMS: calcd. for $C_7H_{10}O$, 110.0732; found, 110.0733.

**(3*E*,5*E*)-6-(tri-*n*-Butylstannyl)-3-methylhexa-3,5-dien-2-ol (27) and (*E*)-5-(tri-*n*-butylstannyl)-3-methylhexa-3,5-dien-2-ol (28).** *n*-BuLi (4.6 mL, 1.45 M in THF, 6.68 mmol) was slowly added to a cooled (-78 °C), stirred suspension of CuCN (0.313 g, 3.5 mmol) in 10 mL of THF and the mixture was stirred at room temperature until completely homogeneous. This solution was cooled down to -78 °C and then *n*-$Bu_3SnH$ (1.83 mL, 6.68 mmol) was added. The dark green mixture was stirred for 30 min under argon to allow slow release of hydrogen and then warmed to -30 °C. A solution of enynol **26** (0.35 g, 3.18 mmol) in THF (5 mL) was added and the reaction mixture was stirred for an additional 45 min. Then 30 mL of saturated aqueous $NH_4Cl/NH_4OH$ (90:10 v:v) was added and the mixture was stirred for 10 min and extracted with $Et_2O$ (4 x 20 mL). The combined organic layers were washed with saturated aqueous $NH_4Cl$ (3 x 20 mL), dried ($Na_2SO_4$) and concentrated. Chromatography of the residue (silica gel, 80:19:1 hexane/ethyl acetate/triethylamine) afforded 1.1 g (86%) of terminal vinyl stannane **27** and 0.11 g (9%) of internal stannane **28**.

Data for compound **27**. $^1$H NMR (250.13 MHz, $CDCl_3$): δ 0.8-1.0 (15H, m, Sn-*n*Bu), 1.2-1.4 (9H, m, Sn-*n*Bu + $3H_1$), 1.4-1.6 (6H, m, Sn-*n*Bu), 1.80 (3H, d, $J$ = 1.3 Hz, $C_3$-$CH_3$), 4.2-4.3 (1H, m, $H_2$), 6.03 (1H, d, $J$ = 10.3 Hz, $H_4$), 6.23 (1H, d, $J$ = 18.6 Hz, $H_6$), 6.76 (1H, dd, $J$ = 18.6, 10.3 Hz, $H_5$). $^{13}$C NMR (62.89 MHz, $C_6D_6$): δ 9.2 (q, 3x), 11.95 (t, 3x), 13.3 (t, 3x), 21.1 (t, 3x), 26.9 (q), 28.8 (q), 72.8 (d, $C_2$), 127.1 (d), 134.2 (d), 139.6 (s, $C_3$). IR (NaCl): ν 3600-3100 (br, O-H), 2921 (s, C-H) cm$^{-1}$. MS *m/z* (%): 291 ($M^+$-Bu, 65), 289 (61), 251 (88), 249 (66), 235 (51), 233 (50), 177 (base peak, 100), 175 (69), 137 (72), 135 (58), 121 (73), 119 (56), 57 (20). HRMS: calcd. for $C_{19}H_{38}O^{118}Sn$, 400.1938; found, 400.1946.

Data for compound **28**. $^1$H NMR (250.13 MHz, $CDCl_3$): δ 0.8-1.0 (15H, m, Sn-*n*Bu), 1.2-1.4 (9H, m, Sn-*n*Bu + $3H_1$), 1.4-1.6 (6H, m, Sn-*n*Bu), 1.69 (3H, d, $J$ = 1.3 Hz, $C_3$-$CH_3$), 4.2-4.3 (1H, m, $H_2$), 5.35 (1H, m, $H_6$), 5.67 (1H, m, $H_6$), 6.11 (1H, m, $H_4$). $^{13}$C NMR (62.89 MHz, $CDCl_3$): δ 9.9 (q, 3x), 12.4 (t, 3x), 13.6 (t, 3x), 21.6 (t, 3x), 27.3 (q), 29.0 (q), 73.4 (t, $C_6$), 127.3 (d, $C_4$), 130.1 (s), 151.3 (s). IR (NaCl): ν 3600-3100 (br, O-H), 2959 (s, C-H), 2926 (s, C-H) cm$^{-1}$. MS *m/z* (%): 291 ($M^+$ - Bu, 65), 289 (61), 235 (48), 233 (51), 179 (base peak, 100), 137 (79), 135 (65), 121 (82), 119 (63), 57 (27). HRMS: calcd. for $C_{19}H_{38}O^{120}Sn$, 402.1945; found, 402.1944.

**(3*E*,5*E*)-3-Methyl-6-iodohexa-3,5-dien-2-ol 7.** A solution of $I_2$ (0.8 g, 3.14 mmol) in $CH_2Cl_2$ (25 mL) was slowly added to a solution of compound **27** (1.15 g, 2.85 mmol) in 25 mL of $CH_2Cl_2$ and the mixture was stirred at room temperature for 30 min. After washing with saturated aqueous sodium thiosulfate solution, the organic layer was dried over $Na_2SO_4$ and evaporated *in vacuo*. The residue was purified by chromatography (silica gel, 80:20 hexane/ethyl acetate) to afford 0.63 g (93%) of compound **7**. $^1$H NMR (250.13 MHz, $CDCl_3$): δ 1.27 (3H, d, $J$ = 6.4 Hz, $3H_1$), 1.51 (1H, s, OH), 1.74 (3H, s, $C_3$-$CH_3$), 4.19 (1H, q, $J$ = 6.4 Hz, $H_2$), 6.02 (1H, d, $J$ = 11.5 Hz, $H_4$), 6.28 (1H, d, $J$ = 15.2 Hz, $H_6$), 7.25 (1H, dd, $J$ = 15.2, 11.5 Hz, $H_5$). $^{13}$C NMR (62.89 MHz, $CDCl_3$): δ 12.7 (q, $C_3$-$CH_3$), 21.5 (q, $C_1$), 72.3 (d, $C_2$), 79.0 (d, $C_6$), 123.7 (d, $C_4$), 141.5 (d, $C_5$), 142.4 (s, $C_3$). IR (NaCl): ν 3600-3100 (br, O-H), 2973 (s, C-H) cm$^{-1}$.

**(2*E*,4*E*)-5-(tri-*n*-Butylstannyl)penta-2,4-dien-1-ol (30).** Reaction of (*E*)-pent-2-en-4-yn-1-ol (**29**; 0.5 g, 6.09 mmol), CuCN (0.63 g, 7.06 mmol), *n*-BuLi (8.8 mL, 1.6 M in THF, 14.01 mmol) and *n*-$Bu_3SnH$ (3.8 mL, 14.01 mmol) in THF (25 mL) in accordance with the general procedure for addition of stannylcuprates to alkynes described for compound **27** afforded 1.52 g (67%) of compound **30**. $^1$H NMR (250.13 MHz, $CDCl_3$): δ 0.8-1.1 (15H, m, Sn-*n*Bu), 1.2-1.4 (6H, m, Sn-*n*Bu), 1.4-1.6 (6H, m, Sn-*n*Bu), 4.20 (2H, br s, $2H_1$), 5.79 (1H, dt, $J$ = 15.6, 5.8 Hz, $H_2$), 6.21 (1H, dd, $J$ = 15.6, 10.0 Hz, $H_3$), 6.26 (1H, dd, $^3J_{H\text{-}H}$= 18.5 Hz, $^2J_{Sn\text{-}H}$= 67.2 Hz, $H_5$), 6.54 (1H, ddd, $^3J_{H\text{-}H}$= 18.5, 10.0 Hz, $^3J_{Sn\text{-}H}$= 59.2 Hz, $H_4$). $^{13}$C NMR (62.89 MHz, $CDCl_3$): δ 9.6 (t, $^1J_{Sn\text{-}C}$= 344.2, 330.6 Hz, 3x), 13.8 (q, 3x), 27.4 (t, $^2J_{Sn\text{-}C}$= 53.7 Hz, 3x), 29.3 (t, $^3J_{Sn\text{-}C}$= 20.3 Hz, 3x), 65.3 (t, $C_1$), 131.0 (d), 134.9 (d, $^1J_{Sn\text{-}C}$= 315.4 Hz, $C_5$), 135.4 (d), 146.2 (d). IR (NaCl): ν 3600-3200 (br, O-H), 2960 (s, C-H), 2925 (s, C-H), 2864 (s, C-H), 1456 (C-O) cm$^{-1}$. MS *m/z* (%): 317 ($M^+$ - Bu, base peak, 100), 315 (75), 313 (42), 261 (48), 259 (37), 257 (21) 251 (31), 249 (23), 247 (16), 205 (56), 203 (47), 201 (29), 137 (64), 135 (49), 133 (29), 121 (36), 119 (28), 117 (16). HRMS: calcd. for $C_{17}H_{35}O^{118}Sn$, 373.1704; found, 373.1694.

**(2*E*,4*E*)-5-Iodo-penta-2,4-dien-1-ol (31).** Reaction of dienylstannane **30** (1.0 g, 2.68 mmol) with $I_2$ (0.75 g, 2.95 mmol) in $CH_2Cl_2$ (40 mL), in accordance with the procedure for metal-halogen exchange described

for compound **7**, afforded 0.54 g (95%) of iodide **31**. $^1$H NMR (250.13 MHz, $C_6D_6$): δ 3.66 (3H, m, $2H_1$ + OH), 5.33 (1H, dt, $J$ = 15.1, 5.1 Hz, $H_2$), 5.81 (1H, dd, $J$ = 15.1, 10.7 Hz, $H_3$), 5.93 (1H, d, $J$ = 14.4 Hz, $H_5$), 6.85 (1H, dd, $J$ = 14.4, 10.7 Hz, $H_4$). $^{13}$C NMR (62.89 MHz, $C_6D_6$): δ 62.2 (t, $C_1$), 78.9 (d, $C_5$), 129.8 (d), 134.0 (d), 144.9 (d). IR (NaCl): ν 3400-3200 (br, O-H), 2967 (s, C-H), 2925 (s, C-H) cm$^{-1}$.

**(2*E*,4*E*)-5-Iodo-penta-2,4-dienal (32).** $MnO_2$ (3.3 g, 38.4 mmol) was added at room temperature in one portion to a solution of alcohol **31** (0.45 g, 2.14 mmol) in $CH_2Cl_2$ (15 mL). The suspension was stirred at room temperature for 2 h, filtered through Celite and concentrated. The residue was purified by chromatography on silica gel (95:5:3 hexane/ethyl acetate/triethylamine) to afford 0.38 g (86%) of compound **32**. $^1$H NMR (250.13 MHz, $C_6D_6$) : δ 5.62 (1H, dd, $J$ = 15.3, 7.6 Hz, $H_2$), 5.88 (1H, dd, $J$ = 15.3, 10.8 Hz, $H_3$), 6.19 (1H, d, $J$ = 14.5 Hz, $H_5$), 6.53 (1H, dd, $J$ = 14.5, 10.8 Hz, $H_4$), 9.22 (1H, d, $J$ = 7.6 Hz, $H_1$). $^{13}$C NMR (62.89 MHz, $C_6D_6$): δ 90.7 (d, $C_5$), 131.3 (d), 143.2 (d), 148.2 (d), 191.9 (d). IR (NaCl): ν 2920 (s, C-H), 1666 (s, C=O) cm$^{-1}$. UV (MeOH): $\lambda_{max}$ 296 nm. MS *m/z* (%): 207 ($M^+$ - 1, 46), 175 (13), 149 (23), 127 (16), 97 (23), 95 (13), 86 (base peak, 100), 85 (22), 83 (27), 81 (41), 71 (25), 69 (22), 58 (99), 57 (40). HRMS: calcd. for $C_5H_5IO$, 207.9385; found, 207.9364.

**(3*E*,5*E*)-6-Iodo-hexa-3,5-dien-2-ol (8).** MeLi (1.24 mL, 1.6 M in $Et_2O$, 1.98 mmol) was added to a cold (0 °C) solution of dienal **32** (0.38 g, 1.80 mmol) in $Et_2O$ (36 mL), and the resulting solution was stirred at 0 °C for 2h. Then saturated aqueous $NH_4Cl$ (30 mL) and 0.1M aq HCl (50 mL) were sequentially added and the resulting mixture was vigorously stirred for 10 min at room temperature before extraction with $CH_2Cl_2$ (3 x 25 mL). The combined organic layers were washed with sat aq $NaHCO_3$ (3 x 25 mL) and brine (3 x 25 mL), dried ($Na_2SO_4$) and concentrated. Chromatography of the residue (silica gel, 80:20, hexane/ethyl acetate) afforded 0.21 g (53%) of compound **8** as a yellow oil. $^1$H NMR (250.13 MHz, $C_6D_6$): δ 1.00 (3H, d, $J$ = 6.4 Hz, $3H_1$), 3.85 (1H, m, $H_2$), 5.30 (1H, dd, $J$ = 15.4, 5.6 Hz, $H_3$), 5.73 (1H, dd, $J$ = 15.4, 10.7 Hz, $H_4$), 5.93 (1H, d, $J$ = 14.4 Hz, $H_6$), 6.83 (1H, dd, $J$ = 14.4, 10.7 Hz, $H_5$). $^{13}$C NMR (62.89 MHz, $C_6D_6$): δ 23.1 (q), 67.4 (d), 78.8 (d), 128.0 (d), 138.9 (d), 145.0 (d). IR (NaCl): ν 3500-3200 (br, O-H), 2960 (s, C-H), 2922 (s, C-H) cm$^{-1}$. MS *m/z* (%): 224 ($M^+$, 3), 207 (11), 167 (12), 132 (14), 117 (13), 97 (25), 85 (12), 83 (20), 82 (15), 81 (23), 80 (base peak, 100), 79 (36), 77 (14). HRMS: calcd. for $C_6H_9OI$, 223.9699; found, 223.9698.

**(*E*)-3-(3-Pyridyl)-prop-2-enal (35).** *sec*-BuLi (13.3 mL, 1.0 M in cyclohexane, 17.3 mmol) was added dropwise to a solution of silylimine **34**[28] (3.07 g, 18.08 mmol) in THF (30 mL) at -78 °C. The mixture was stirred at -78 °C for 30 min before addition of a solution of 3-pyridinecarboxaldehyde (**33**; 1.21 g, 13.29 mmol) in THF (30 mL). The resulting mixture was stirred at the same temperature for 1.5 h and then at -20 °C for 2h before addition of trifluoroacetic acid (3.2 mL, 40.36 mmol). After stirring at -20 °C for 1h, water (20 mL) was added and the mixture was stirred at 0 °C for 4h, poured into saturated aqueous $NaHCO_3$ solution (50 mL) and extracted with ethyl acetate (3 x 50 mL). The combined organic extracts were washed with brine (3 x 50 mL), dried over $MgSO_4$, and concentrated *in vacuo*. Chromatography of the residue (silica gel, 95:5 $CH_2Cl_2$/MeOH) afforded 1.15 g (77%) of compound **35** as a brown solid (m.p.: 54-56 °C, hexane/ethyl acetate). $^1$H NMR (250.13 MHz, $CDCl_3$): δ 6.76 (1H, dd, $J$ = 16.1, 7.6 Hz, $H_2$), 7.37 (1H, dd, $J$ = 8.0, 4.7 Hz, $H_5$'), 7.47 (1H, d, $J$ = 16.1 Hz, $H_3$), 7.88 (1H, dt, $J$ = 8.0, 2.1 Hz, $H_4$'), 8.64 (1H, dd, $J$ = 4.7, 1.6 Hz, $H_6$'), 8.77 (1H, d, $J$ = 2.1 Hz, $H_2$'), 9.72 (1H, d, $J$ = 7.5 Hz, $H_1$). $^{13}$C NMR (62.89 MHz, $CDCl_3$): δ 123.9 (d), 129.8 (s), 130.2

(d), 134.4 (d), 148.4 (d), 150.1 (d), 151.9 (d), 193.0 (d). IR (NaCl): ν 2968 (w, C-H), 1678 (s, C=O) $cm^{-1}$. MS *m/z* (%): 133 ($M^+$, 68), 132 (base peak, 100), 105 (42), 104 (69), 85 (11), 83 (14), 79 (43), 78 (35), 77 (29), 75 (12), 74 (8), 63 (7), 58 (86), 52 (19), 50 (45). HRMS: calcd. for $C_8H_7NO$, 133.0528; found, 133.0528.

**(1*E*,3*E*)-1-Iodo-4-(3-pyridyl)-buta-1,3-diene (10).** A solution of $CHI_3$ (1.78 g, 4.50 mmol) in THF (10 mL) was added to a cooled (0 °C) suspension of $CrCl_2$ (1.85 g, 15.03 mmol, previously flame-dried under argon) in THF (35 mL). A solution of aldehyde **35** (0.2 g, 1.50 mmol) in THF (10 mL) was then added, and the resulting mixture was stirred for 1h at 0 °C and 1.5 h at 25 °C. The reaction mixture was poured into a sat $NH_4Cl$ (30 mL)/2M NaOH (20 mL) mixture and extracted with ethyl acetate (3 x 50 mL). The combined organic extracts were washed with brine (3 x 50 mL), dried over $MgSO_4$, and concentrated *in vacuo*. Chromatography of the residue ($Al_2O_3$, ethyl acetate) afforded 0.28 g (72%) of compound **10** as a 4:1 *E/Z* isomer mixture, which was used in the next step without further purification.

**6-(3-Pyridyl)-hexan-1-ol (39).** A solution of hex-5-en-1-ol (0.3 g, 3.0 mmol) in THF (6 mL) was added to 9-BBN (18 mL, 0.5 M in THF, 8.99 mmol) and the mixture was stirred at room temperature for 2h. The 9-BBN derivative **38** thus generated was added, through a cannula, to a solution of $K_2CO_3$ (0.83 g, 6.0 mmol), $Pd(PPh_3)_4$ (0.35 g, 0.3 mmol), 3-bromopyridine (**37**; 0.52 g, 3.3 mmol) and $H_2O$ (2 mL) in DMF (15 mL), and the reaction mixture was stirred at room temperature for 1h and at 65 °C for 1h. Then $H_2O$ (20 mL) was added and the phases were separated. The aqueous layer was extracted with $Et_2O$ (3 x 25 mL) and the combined organic layers were washed with $H_2O$ (5 x 25 mL) and brine (3 x 25 mL), dried ($Na_2SO_4$) and concentrated. Purification of the residue by chromatography (silica gel, eluant gradient from hexane to ethyl acetate) afforded 0.5 g (93%) of compound **39** as an orange oil (b.p.: 175 °C, 0.05-0.1 mm Hg). $^1H$ NMR (400.13 MHz, $CDCl_3$): δ 1.3-1.4 (4H, m, $2H_4 + 2H_5$), 1.5-1.6 (4H, m, $2H_2 + 2H_3$), 2.32 (1H, s, OH), 2.59 (2H, t, $J$ = 7.7 Hz, $2H_6$), 3.62 (2H, t, $J$ = 6.5 Hz, $2H_1$), 7.20 (1H, dd, $J$ = 7.7 Hz, 4.8 Hz, $H_5$'), 7.48 (1H, d, $J$ = 7.7 Hz, $H_4$'), 8.41 (2H, br s, $H_2$' + $H_6$'). $^{13}C$ NMR (100.13 MHz, $CDCl_3$): δ 23.5 (t), 26.8 (t), 29.0 (t), 30.5 (t), 30.6 (t), 60.5 (t), 121.3 (d), 130.1 (s), 133.9 (d), 145.0 (d), 147.7 (d). MS *m/z* (%): 179 ($M^+$, 14), 178 ($M^+$ - 1, 11), 162 (15), 107 (14), 106 (base peak, 100), 105 (25), 93 (40), 92 (38), 65 (11). HRMS: calcd. for $C_{11}H_{17}NO$, 179.1310; found, 179.1304.

**6-(3-Pyridyl)-hexanal (40).** A solution of alcohol **39** (0.05 g, 0.31 mmol) in $CH_2Cl_2$ (1 mL) was added to a cold (-60 °C) solution of DMSO (58 mL, 0.76 mmol) and oxalyl chloride (31 mL, 0.36 mmol) in $CH_2Cl_2$ (1 mL). The reaction mixture was stirred for 15 min at -60 °C and, after addition of triethylamine (0.15 mL, 0.21 mmol), was warmed to room temperature, washed with $H_2O$ (3 x 5 mL) and brine (3 x 5 mL), dried over $Na_2SO_4$ and concentrated. Purification of the residue by chromatography (silica gel, eluant gradient from hexane to ethyl acetate) furnished aldehyde **40** in 70% yield. $^1H$ NMR (400.13 MHz, $CDCl_3$): δ 1.3-1.7 (6H, m), 2.45 (1H, dt, $J$ = 7.3, 1.6 Hz, $2H_2$), 2.62 (2H, m, $2H_6$), 7.20 (1H, m, $H_5$'), 7.49 (1H, d, $J$ = 7.8 Hz, $H_4$'), 8.43 (2H, s, $H_2$' + $H_6$'), 9.77 (1H, t, $J$ = 1.6 Hz, $H_1$). $^{13}C$ NMR (100.13 MHz, $CDCl_3$): δ 21.7 (t), 28.6 (t), 30.8 (t), 32.7 (t), 43.7 (t), 123.3 (d), 135.7 (d), 137.4 (s), 147.3 (d), 149.9 (d), 202.4 (d). IR (NaCl): ν 2931 (s, C-H), 1722 (m, C=O) $cm^{-1}$. MS *m/z* (%): 178 ($M^+$ + 1, 9), 162 (6), 149 (9), 148 (7), 120 (9), 118 (8), 107 (12),

106 (base peak, 100), 105 (18), 94 (44), 92 (46), 84 (7), 65 (14). HRMS: calcd. for $C_{11}H_{15}NO$, 177.1154; found, 177.1146.

**(*E*)-1-Iodo-7-(3-pyridyl)-hept-1-ene (11).** A solution of $CHI_3$ (1.13 g, 2.86 mmol) in THF (25 mL) was added to a cooled (0 °C) suspension of $CrCl_2$ (1.17 g, 9.54 mmol, previously flame-dried under argon) in THF (25 mL). A solution of aldehyde **40** (0.17 g, 0.95 mmol) in THF (10 mL) was then added, and the resulting mixture was stirred for 1h at 0 °C and 2 h at 25 °C. The reaction mixture was poured into a sat $NH_4Cl$ (30 mL)/2M NaOH (20 mL) mixture and extracted with ethyl acetate (3 x 50 mL). The combined organic extracts were washed with brine (3 x 50 mL), dried over $MgSO_4$, and concentrated *in vacuo*. Chromatography of the residue ($Al_2O_3$, ethyl acetate) afforded 0.18 g (65%) of compound **11** as an oil. $^1H$ NMR (400.13 MHz, $CDCl_3$): δ 1.2-1.5 (2H, m), 1.5-1.7 (4H, m), 2.0-2.1 (2H, m), 2.60 (2H, t, $J$ = 7.6 Hz, $2H_7$), 5.98 (1H, d, $J$ = 14.3 Hz, $H_1$), 6.50 (1H, dt, $J$ = 14.3, 7.2 Hz, $H_2$), 7.22 (1H, dd, $J$ = 7.5, 5.0 Hz, $H_5$'), 7.49 (1H, d, $J$ = 7.5 Hz, $H_4$'), 8.45 (2H, br s, $H_2$' + $H_6$'). $^{13}C$ NMR (100.13 MHz, $CDCl_3$): δ 28.3 (t), 28.5 (t), 30.8 (t), 32.9 (t), 35.9 (t), 82.5 (d), 123.3 (d), 135.8 (d), 141.1 (s), 146.4 (d), 147.2 (d), 149.9 (d). MS *m/z* (%): 174 ($M^+$ - I, base peak, 100), 167 (4), 134 (3), 118 (4), 106 (8), 105 (4), 93 (10), 92 (28), 65 (8).

**(3*E*,5*Z*,7*E*)-3-Methyl-8-phenylocta-3,5,7-trien-2-ol (12).** Iodide **6** (0.06 g, 0.25 mmol) in THF (10 mL) was added to a suspension of $Pd(PPh_3)_4$ (0.087 g, 0.08 mmol) in anhydrous THF (20 mL). After stirring for 30 min, a solution of (*E*)-β-phenylethenylboronic acid (**4**; 0.06 g, 0.38 mmol) in THF (5 mL) and 10% aqueous TlOH (1.64 mL, 0.78 mmol) were added sequentially. After stirring at room temperature for 2 h, the reaction mixture was diluted with $Et_2O$ (10 mL) and filtered through Celite. The filtrates were washed with saturated aqueous $NaHCO_3$ (3 x 10 mL) and the aqueous layer was extracted with ether (3 x 10 mL). The organic layers were dried over $MgSO_4$ and concentrated. Chromatography ($SiO_2$, 80:20:1 hexane/ethyl acetate/pyridine) afforded 0.043 g (79%) of compound **12** as a yellow oil. An analytical sample was obtained by HPLC (97:3 hexane/isopropanol, 2 mL/min; $t_R$ = 12.4 min). $^1H$ NMR (250.13 MHz, $CDCl_3$): δ 1.34 (3H, d, $J$ = 6.4 Hz, $3H_1$), 1.82 (3H, s, $C_3$-$CH_3$), 4.36 (1H, q, $J$ = 6.4 Hz, $H_2$), 6.19 (1H, t, $J$ = 10.8 Hz, $H_6$), 6.28 (1H, t, $J$ = 10.8 Hz, $H_5$), 6.58 (1H, d, $J$ = 15.4 Hz, $H_8$), 6.68 (1H, d, $J$ = 10.8 Hz, $H_4$), 7.2-7.4 (6H, m, ArH + $H_7$). $^{13}C$ NMR (62.89 MHz, $CDCl_3$): δ 12.3 (q), 21.7 (q), 73.2 (d), 119.2 (d), 124.2 (d), 125.4 (d), 126.6 (d, 2x), 127.7 (d), 128.7 (d, 2x), 129.4 (d), 133.4 (d), 137.5 (s), 142.9 (s). IR (NaCl): ν 3600-3100 (br, O-H), 2915 (s, C-H) $cm^{-1}$. UV (MeOH): $\lambda_{max}$ (ε) 240 (12 600), 246 (12 700), 260 (10 000), 310 (17 200), 322 (19 000) nm. MS *m/z* (%): 214 ($M^+$, 10), 213 (11), 199 (31), 178 (26), 155 (30), 149 (38), 143 (33), 131 (29), 129 (41), 128 (44), 127 (33), 115 (58), 105 (48), 97 (30), 95 (46), 91 (56), 86 (68), 84 (base peak, 100), 81 (63), 77 (48). HRMS: calcd. for $C_{15}H_{18}O$, 214.1358; found, 214.1362.

**(3*E*,5*Z*,7*E*)-3-Methyl-8-phenylocta-3,5,7-trien-2-one (2a).** A stirred solution of alcohol **12** (0.04 g, 0.19 mmol) in $CH_2Cl_2$ (4 mL) was treated with powdered 4Å molecular Sieves (0.073 g), $NaHCO_3$ (0.054 g) and Dess-Martin periodinane (0.12 g, 0.28 mmol). After stirring at room temperature for 20 min, the reaction mixture was diluted with ether (10 mL) and filtered through Celite. The solvents were removed under reduced pressure to afford 0.023 g (57%) of a 1:2 mixture of *Z* and *E* isomers (as shown by $^1H$ NMR), and **2a**[4,11a] was purified by HPLC in the dark [$t_R$(3*E*,5*Z*,7*E*) = 22.6 min, and $t_R$(3*E*,5*E*,7*E*) = 27.3 min].

**(3*E*,5*E*,7*E*)-3-Methyl-8-phenylocta-3,5,7-trien-2-ol (13).** Reaction of iodide **7** (0.075 g, 0.315 mmol), $Pd(PPh_3)_4$ (0.11 g, 0.095 mmol), boronic acid **4** (0.070 g, 0.473 mmol) and 10% aqueous TlOH (2.04 mL, 0.98 mmol) in THF, in accordance with the general coupling procedure described above, afforded compound **13** (0.054 g, 81%) as a yellow oil. An analytical sample was obtained by HPLC (97:3 hexane/isopropyl alcohol, 2 mL/min; $t_R$ = 13.8 min). $^1$H NMR (500.13 MHz, $CDCl_3$): δ 1.31 (3H, d, *J* = 6.4 Hz, $3H_1$), 1.82 (3H, d, *J* = 0.4 Hz, $C_3$-$CH_3$), 4.30 (1H, q, *J* = 6.4 Hz, $H_2$), 6.17 (1H, d, *J* = 11.1 Hz, $H_4$), 6.39 (1H, dd, *J* = 14.7, 10.8 Hz, $H_6$), 6.5-6.6 (2H, m, $H_5$ + $H_8$), 6.88 (1H, dd, *J* = 15.5, 10.8 Hz, $H_7$), 7.21 (1H, t, *J* = 7.4 Hz, $ArH_p$), 7.31 (2H, t, *J* = 7.4 Hz, $2ArH_m$), 7.40 (2H, d, *J* = 7.4 Hz, $2ArH_o$). $^{13}$C NMR (62.89 MHz, $CDCl_3$): δ 12.5 (q), 21.6 (q), 73.1 (d), 124.3 (d), 126.3 (d, 2x), 127.4 (d), 128.6 (d, 2x), 129.2 (d), 129.4 (d), 132.1 (d), 133.0 (d), 137.5 (s), 142.1 (s). IR (NaCl): ν 3600-3100 (br, O-H), 2915 (s, C-H) $cm^{-1}$. UV (MeOH): $\lambda_{max}$ (ε) 323 (14 200) nm. MS *m/z* (%): 214 ($M^+$, 50), 206 (16), 165 (17), 155 (15), 143 (base peak, 100), 142 (30), 141 (21), 129 (37), 128 (71), 127 (18), 117 (28), 115 (50), 91 (66), 84 (15), 77 (17). HRMS: calcd. for $C_{15}H_{18}O$, 214.1358; found, 214.1362.

**(3*E*,5*E*,7*E*)-3-Methyl-8-phenylocta-3,5,7-trien-2-one (2b).** $MnO_2$ (0.315 g, 3.62 mmol) was added to a solution of alcohol **13** (0.043 g, 0.2 mmol) in anhydrous $CH_2Cl_2$ (4 mL) and the mixture was stirred at room temperature for 9 h. The solid was removed by filtration through Celite and washed with $CH_2Cl_2$, and the filtrates were concentrated and purified ($SiO_2$, 90:10:1 hexane/ethyl acetate/pyridine) to afford 0.028 g (65%) of compound **2b** as yellow crystals (m.p. 62-64 °C (hexane/ethyl acetate); lit.:[11,12] 60-64 °C). An analytical sample was obtained by HPLC (93:7 hexane/ethyl acetate, 2 mL/min, $t_R$ = 27.4 min).[4,11a]

**(3*E*,5*E*,7*E*,9*E*)-3-Methyl-10-phenyldeca-3,5,7,9-tetraen-2-ol (14).** Reaction of iodide **7** (0.048 g, 0.20 mmol), $Pd(PPh_3)_4$ (0.071 g, 0.06 mmol), boronic acid **5** (0.053 g, 0.31 mmol) and 10% aq TlOH (1.33 mL, 0.63 mmol) in THF, in accordance with the coupling procedure described above, afforded compound **14** (0.034 g, 70%) as a yellow oil. $^1$H NMR (250.13 MHz, $CDCl_3$): δ 1.30 (3H, d, *J* = 6.4 Hz, $3H_1$), 1.56 (1H, br s, OH), 1.81 (3H, s, $C_3$-$CH_3$), 4.29 (1H, q, *J* = 6.4 Hz, $H_2$), 6.14 (1H, d, *J* = 10.9 Hz, $H_4$), 6.3-6.5 (4H, m, $H_5$ + $H_6$ + $H_7$ + $H_8$), 6.55 (1H, d, *J* = 15.5 Hz, $H_{10}$), 6.85 (1H, dd, *J* = 15.5, 9.6 Hz, $H_9$), 7.2-7-4 (5H, m, ArH). $^{13}$C NMR (62.89 MHz, $CDCl_3$): δ 12.5 (q), 21.6 (q), 73. 0 (d), 124.4 (d), 126.4 (d, 2x), 127.5 (d), 128.6 (d, 2x), 129.1 (d), 129.2 (d), 132.4 (d), 132.9 (d, 2x), 133.7 (d), 137.5 (s), 142.2 (s). UV (MeOH): $\lambda_{max}$ (ε) 258sh (6 500), 316sh (12 500), 328 (15 000), 346 (15 000), 364 (12 000) nm. MS *m/z* (%): 240 ($M^+$, 35), 199 (34), 178 (14), 169 (32), 168 (25), 167 (37), 149 (49), 141 (36), 129 (48), 128 (38), 117 (26), 115 (48), 105 (44), 91 (base peak, 100). HRMS: calcd. for $C_{17}H_{20}O$, 240.1514; found, 240.1513.

**(3*E*,5*E*,7*E*,9*E*)-3-Methyl-10-phenyldeca-3,5,7,9-tetraen-2-one (1e).** Reaction of alcohol **14** (20 mg, 0.08 mmol) and $MnO_2$ (132 mg, 1.52 mmol) in $CH_2Cl_2$, in accordance with the oxidation procedure described above, afforded ketone **1e** (12.5 mg, 63%) as a yellow solid (m.p. 113 °C, $CH_2Cl_2$/MeOH; lit.[3] 113-114 °C).[3a,c]

**(3*E*,5*E*,7*E*,9*E*)-10-phenyldeca-3,5,7,9-tetraen-2-ol (15).** Reaction of iodide **8** (0.2 g, 0.89 mmol), $Pd(PPh_3)_4$ (0.314 g, 0.265 mmol), boronic acid **5** (0.234 g, 1.35 mmol) and 10% aq TlOH (5.9 mL, 2.79 mmol) in THF, in accordance with the coupling procedure described above, gave compound **15** (0.163 g, 81%)

as a yellow oil. $^1$H NMR (500.13 MHz, $CDCl_3$): δ 1.30 (3H, d, $J$ = 6.4 Hz, $3H_1$), 4.0-4.3 (1H, m, $H_2$), 5.78 (1H, dd, $J$ = 14.2, 6.5 Hz, $H_3$), 6.2-6.4 (5H, m, $H_4 + H_5 + H_6 + H_7 + H_8$), 6.36 (1H, d, $J$ = 15.5 Hz, $H_{10}$), 6.84 (1H, dd, $J$ = 15.5, 9.7 Hz, $H_9$), 7.20 (2H, d, $J$ = 7.4 Hz, $2ArH_o$), 7.31 (2H, t, $J$ = 7.4 Hz, $2ArH_m$), 7.4 (1H, d, $J$ = 7.4 Hz, $ArH_p$). $^{13}$C NMR (62.89 MHz, $CDCl_3$): δ 23.4 (q), 68.6 (d), 126.4 (d, 2x), 127.6 (d), 128.7 (d, 2x), 129.0 (d), 129.9 (d), 132.4 (d), 132.8 (d), 133.2 (d), 133.3 (d), 133.6 (d), 137.5 (s), 137.6 (d). UV (MeOH): $\lambda_{max}$ (ε) 326sh, 340, 358 nm. MS *m/z* (%): 226 ($M^+$, base peak, 100), 208 (9), 193 (9), 180 (19), 179 (21), 168 (58), 167 (76), 165 (36), 153 (39), 149 (38), 141 (44), 128 (41), 115 (54), 91 (85). HRMS: calcd. for $C_{16}H_{18}O$, 226.1357; found, 226.1348.

**(3*E*,5*E*,7*E*,9*E*)-10-Phenyldeca-3,5,7,9-tetraen-2-one (1b).** Treatment of alcohol **15** (0.15 g, 0.66 mmol) with $MnO_2$ (1.04 g, 12.0 mmol) in $CH_2Cl_2$, in accordance with the oxidation procedure described above, afforded ketone **1b** (0.08 g, 54%) as a yellow oil.[3c]

**(2*E*,4*E*,6*E*,8*E*)-9-(3-Pyridyl)-nona-2,4,6,8-tetraen-1-ol (16).** Reaction of iodide **10** (4:1, *E/Z* mixture; 0.018 g, 0.848 mmol), $Pd(PPh_3)_4$ (0.098 g, 0.085 mmol), boronic acid **9** (0.141 g, 1.103 mmol) and 10% aqueous TlOH (2.63 mL, 5.3 mmol) in THF, in accordance with the coupling procedure described above and after purification ($SiO_2$, 50:50 hexane/ethyl acetate), afforded a 4:1 mixture of *E/Z* isomers in 74% yield. Stereochemically pure *E* alcohol **16** (0.133 g, 55%) crystallized as a yellow solid (m.p. 149-151 °C, hexane/ethyl acetate). $^1$H NMR (400.13 MHz, $CD_2Cl_2$): δ 4.21 (2H, m, $2H_1$), 5.92 (1H, dt, $J$ = 14.8, 5.8 Hz, $H_2$), 6.0-6.5 (5H, m), 6.56 (1H, d, $J$ = 15.7 Hz, $H_9$), 6.95 (1H, dd, $J$ = 15.7, 10.0 Hz, $H_8$), 7.26 (1H, dd, $J$ = 7.9, 4.7 Hz, $H_5$'), 7.75 (1H, dt, $J$ = 7.9, 1.9 Hz, $H_4$'), 8.41 (1H, dd, $J$ = 4.7, 1.5 Hz, $H_6$'), 8.60 (1H, d, $J$ = 2.1 Hz, $H_2$'). $^{13}$C NMR (100.13 MHz, $CDCl_3$): δ 63.6 (t), 123.5 (d), 128.4 (d), 130.9 (d), 131.2 (d), 131.9 (d), 132.0 (d), 132.1 (d), 132.4 (d), 132.7 (s), 132.8 (d), 133.2 (d), 134.4 (d), 148.2 (d). IR (NaCl): ν 3600-3100 (br, O-H), 2928 (s, C-H) $cm^{-1}$. UV (MeOH): $\lambda_{max}$ 266 nm. MS *m/z* (%): 213 ($M^+$, base peak, 100), 199 (11), 197 (13), 157 (17), 149 (16), 132 (10), 111 (59), 77 (11). HRMS: calcd. for $C_{14}H_{15}NO$, 213.1154; found, 213.1155.

**(2*E*,4*E*,6*E*,8*E*)-9-(3-Pyridyl)-nona-2,4,6,8-tetraenal (17).** Reaction of alcohol **16** (0.014 g, 0.067 mmol) with $MnO_2$ (1.13 g, 1.2 mmol) in $CH_2Cl_2$ (3 mL), in accordance with the oxidation procedure described above, afforded aldehyde **17** (10 mg, 72%) as a highly unstable orange oil, which was used in the next step without further purification. $^1$H NMR (400.13 MHz, $CD_2Cl_2$): δ 6.17 (1H, dd, $J$ = 15.2, 8.0 Hz, $H_2$), 6.5-6.6 (2H, m), 6.6-6.7 (2H, m), 6.83 (1H, dd, $J$ = 14.7, 11.1 Hz), 7.00 (1H, dd, $J$ = 15.7, 10.7 Hz), 7.20 (1H, dd, $J$ = 15.2, 11.3 Hz), 7.29 (1H, dd, $J$ = 7.9, 4.8 Hz, $H_5$'), 7.79 (1H, d, $J$ = 7.9 Hz, $H_4$'), 8.46 (1H, br s, $H_6$'), 8.65 (1H, br s, $H_2$'), 9.58 (1H, d, $J$ = 8.0 Hz, $H_1$). $^{13}$C NMR (100.13 MHz, $CD_3OD$): δ 123.9 (d), 130.6 (d), 131.1 (d), 131.8 (d), 131.9 (d), 132.8 (d), 132.9 (s), 133.4 (d), 138.3 (d), 142.4 (d), 148.9 (d), 149.3 (d), 151.7 (d), 193.6 (d).

**(3*E*,5*E*,7*E*,9*E*)-10-(3-Pyridyl)-deca-3,5,7,9-tetraen-2-ol (18).** Reaction of aldehyde **17** (10 mg, 0.047 mmol) and MeLi (0.1 mL, 1.6 M in hexane, 0.16 mmol) in THF (5 mL), in accordance with the same procedure as for compound **8** and after purification ($SiO_2$, AcOEt), gave alcohol **18** (0.024 g, 72%) as a yellow solid (m.p.: 149-151 °C; hexane/ethyl acetate). $^1$H NMR (400.13 MHz, $CDCl_3$): δ 1.32 (3H, d, $J$ = 6.5 Hz, $3H_1$), 1.62 (1H, br s, OH), 4.39 (1H, m, $H_2$), 5.8-5.9 (1H, m, $H_3$), 6.0-6.5 (5H, m, $H_4$-$H_8$), 6.52 (1H, d, $J$ =

15.7 Hz, $H_{10}$), 6.89 (1H, dd, $J$ = 15.7, 9.9 Hz, $H_9$), 7.24 (1H, m, $H_{5'}$), 7.72 (1H, d, $J$ = 8.0 Hz, $H_{4'}$), 8.43 (1H, d, $J$ = 4.3 Hz, $H_{6'}$), 8.60 (1H, br s, $H_{2'}$). $^{13}C$ NMR (100.13 MHz, $CDCl_3$): δ 23.5 (q), 68.6 (d), 123.8 (d), 128.7 (d), 129.5 (d), 131.3 (d), 132.6 (d), 132.9 (d, 2x), 133.8 (d), 134.8 (d), 139.0 (d), 145.0 (s), 148.5 (d), 148.6 (d). IR ($CHCl_3$): ν 3600-3100 (br, O-H), 2927 (s, C-H) $cm^{-1}$. UV (MeOH): $\lambda_{max}$ 254 (10 500), 274sh (10 800), 332 (35 600) nm. MS *m/z* (%): 227 ($M^+$, 55), 201 (13), 185 (14), 184 (base peak, 100), 182 (15), 170 (17), 168 (19), 156 (16), 144 (13), 130 (14), 117 (12), 106 (13), 93 (14), 92 (19), 91 (11). HRMS: calcd. for $C_{15}H_{17}NO$, 227.1310; found, 227.1301.

**(3*E*,5*E*,7*E*,9*E*)-10-(3-Pyridyl)-deca-3,5,7,9-tetraen-2-one (1a).** Treatment of alcohol **18** (0.006 g, 0.026 mmol) with $MnO_2$ (0.04 g, 0.475 mmol) in $CH_2Cl_2$ (2 mL), in accordance with the oxidation procedure described above, afforded ketone **1a** (0.005 g, 92%) as a yellow solid (m.p.: 142-144 °C; hexane/ethyl acetate).[3a,c]

**(2*E*,4*E*,6*E*)-12-(3-Pyridyl)-dodeca-2,4,6-trien-1-ol (19).** Reaction of iodide **11** (0.015 g, 0.05 mmol), $Pd(PPh_3)_4$ (0.006 g, 0.005 mmol), boronic acid **9** (0.009 g, 0.06 mmol) and 10% aqueous TlOH (0.34 mL, 0.155 mmol) in THF in accordance with the coupling procedure described above and after purification ($SiO_2$, eluant gradient from hexane to ethyl acetate), afforded compound **19** (0.012 g, 93%) as a yellow oil which was used immediately in the next step due to its high instability.

**(2*E*,4*E*,6*E*)-1-Acetoxy-12-(3-pyridyl)-dodeca-2,4,6-triene (3c).** $Ac_2O$ (0.03 mL, 0.56 mmol) was added to a solution of alcohol **19** (0.01 g, 0.04 mmol) in pyridine (0.035 mL) and the mixture was reacted at room temperature for 4h. After the solvents were evaporated, the residue was dissolved in $CHCl_3$ (5 mL), washed with $H_2O$ (3 x 2 mL), aq sat $NaHCO_3$ (2 mL) and brine (2 mL), and concentrated. Chromatography (silica gel, ethyl acetate) afforded acetate **3c** in 82% yield as a yellow oil.[6]

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32. Compared to saturated analogs, iodoolefination of unsaturated aldehydes is not highly stereoselective.[29]

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35. For General Procedures, see ref. 19b. Multiplicities in $^{13}C$ NMR, determined by the DEPT pulse sequence, refer only to H-C splitting, and do not take into account the presence of Sn. For stannanes, large Sn-$^{1}H$ or Sn-$^{13}C$ coupling constants (250-300 Hz) are frequently observed as two close pairs of satellites corresponding to both $^{117}Sn$ and $^{119}Sn$ isotopes. For small coupling constants (<100 Hz), the two pairs of satellites are not discernible, and only one value is reported.