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Synthesis of *E*-vinyl iodides via Pd-catalyzed hydrostannation of terminal alkynes

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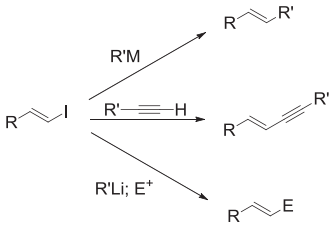
ABSTRACT

E-Vinyl iodides may be prepared via a one-pot reaction involving Pd-catalyzed hydrostannation of terminal alkynes followed by iodinolysis of the intermediate vinylstannane. The synthesis is tolerant of functional groups, such as alcohols and esters.

1. Introduction

Vinyl iodides are useful intermediates for organic synthesis. They have been used as coupling partners with various organometallic reagents,[1] most notably with tin (Stille),[2] boron (Suzuki),[3] zinc (Negishi),[4] and copper reagents[5] but also with antimony,[6] indium,[7] and zirconium[8] reagents. They have also been coupled with alkynes with Pd/Cu catalysis in Sonogashira-type couplings[9] or with Cu catalysis alone[10] as well as with TMS-alkynes.[11] Vinyl iodides can also serve as precursors to vinyllithium reagents (Scheme 1).[12] In all of these reactions, high degrees of retention of stereochemistry are typically observed.[13]



Scheme 1. Common applications of vinyl iodides.

A common approach to the synthesis of vinyl iodides is by addition to alkynes. Addition of HI, typically generated in situ, to terminal alkynes provides 2-iodo-1-alkenes.[14] Synthesis of (*E*)-1-iodo-1-alkenes may be achieved by hydrometalation (e.g., hydroalumination with DIBAL-H,[15] hydroboration with HBcat,[16] hydrozirconation with $HZrCp_2Cl$[17]) followed by electrophilic quench with an I^+ source, such as I_2. (*Z*)-1-Iodo-1-alkenes are typically prepared from 1-iodo-1-alkynes by hydroboration/protonolysis[18] or reduction with diimide.[19]

To make *E*-vinyl iodides, hydrometalation/iodination reactions proceed well with unfunctionalized alkynes but difficulties may be encountered when the alkyne possesses other functional groups. For example, hydroalumination of alkynols typically proceeds poorly or not at all unless the alcohol is protected as a *tert*-butyl ether.[20] In most cases, protection as a *tert*-butyl ether offers a satisfactory solution but in the case of 3-butyn-1-ol, this leads to the formation of the *Z*-iodide as the major product.[21] In cases where the desired product is an iodoalcohol, protection/deprotection adds two steps to the synthesis. Also hydroboration or hydrozirconation of alkynols requires the use of an extra equivalent of (expensive) reagent.

Hydrostannation/iodination could offer a solution to problems posed by the presence of other functional groups on an alkyne as hydrostannation should not be affected by alcohols or common protecting groups, such as TBS ethers (which are cleaved by DIBAL-H)[22] or acetates (which could be reduced). However, until recently, there has been a problem controlling the regiochemistry and stereochemistry in the hydrostannation of many 1-alkynes. The stereochemistry issue may be resolved by the use of Pd-catalysis developed in the 1980s, which proceeds with exclusive *syn*-selectivity but often gives regioisomeric stannanes with low (~2:1 to ~3:1) selectivities when $Pd(PPh_3)_4$ is used as the catalyst (except when R is a sterically large group).[23] The regiochemistry issue was

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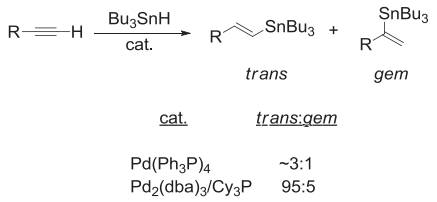
recently resolved when it was shown that the use of bulky electron-rich ligands, such as Cy_3P could routinely give regioselectivities of ~95:5 or better in favor of the 1-stannyl-1-alkene (Scheme 2).[24]



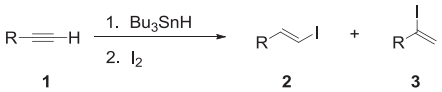
Scheme 2. Regioselective hydrostannation of alkynes.

We now report on our efforts to couple this chemistry with in situ iodination to develop a simple one-pot preparation of (*E*)-1-iodo-1-alkenes.

2. Results and discussion

Previous work had shown that vinyl stannanes react readily with I_2 in CH_2Cl_2 at 0 °C to provide the corresponding vinyl iodides.[25] Fortuitously, these conditions are compatible with the conditions developed for the Pd-catalyzed regioselective hydrostannation of alkynes. In particular, we had shown that the hydrostannation may be carried out in a variety of solvents including toluene and CH_2Cl_2.[24] Thus it was relatively straightforward to run the hydrostannation reaction in CH_2Cl_2 and subsequently add a solution of I_2 in CH_2Cl_2. After some experimentation, excellent results were obtained (Table 1).

Table 1
Synthesis of *E*-vinyl iodides from alkynes[a,b]



Entry	R	Ratio[c] **2**/**3** (iodides)	Isolated yield (%)
1	$(CH_2)_9OTBS$	95:5 (**2a**:**3a**)	88[d]
2		99:1 (**2a**:**3a**)	71[b,d]
3	$(CH_2)_8OH$	95:5 (**2b**:**3b**)	93[d]
4		99:1 (**2b**:**3b**)	75[b,d]
5	$(CH_2)_8OAc$	95:5 (**2c**:**3c**)	95[d]
6		99:1 (**2c**:**3c**)	76[b,d]
7	$(CH_2)_4OH$	95:5 (**2d**:**3d**)	94[d]
8		99:1 (**2d**:**3d**)	76[b,d]
9	CH_2OH	67:33 (**2e**:**3e**)	67[e]
10	$(CH_2)_2OH$	83:17 (**2f**:**3f**)	83[e]
11	$CH(OH)CH_3$	95:5 (**2g**:**3g**)	93[e]
12	$CH(OH)n\text{-}C_5H_{11}$	95:5 (**2h**:**3h**)	89[e]
13	CH(OH)Ph	82:18 (**2i**:**3i**)	80[e]

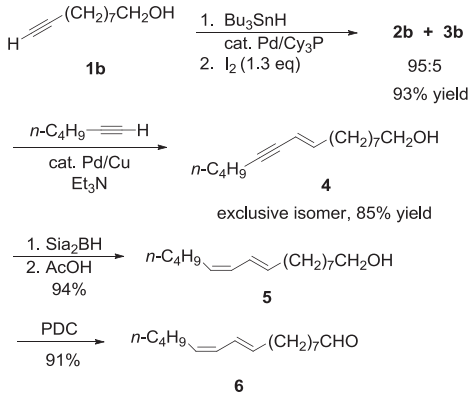
[a] Conditions: Bu_3SnH (1.2 equiv), cat. $Pd_2dba_3/Cy_3PHBF_4/i\text{-}Pr_2NEt$, CH_2Cl_2, 0 °C, 2 h, then I_2 (1.3 equiv), 0 °C, 10 min.
[b] I_2 (0.95 equiv) was used.
[c] Ratio was determined by ^1H NMR analysis of the crude mixture.
[d] Isolated yield of both inseparable isomers.
[e] Isolated yield of pure *trans* isomer **2**.

For alkynes with >3 methylene units separating the alkyne from another functional group, the regioselectivity of the hydrostannation was consistently *trans*/*gem*=95:5. Addition of excess iodine to the reaction mixture then provided **2** and **3** in a ratio of 95:5 in high yields (Table 1, entries 1, 3, 5, 7). However, these iodides proved to be inseparable by flash chromatography. In an attempt to selectively react the *trans* stannane,[26] the reaction mixture was treated with 0.95 equiv of I_2. It was pleasing to find that the *trans* stannane did react more quickly than the *gem* isomer resulting in an enhanced ratio of 99:1 for iodides **2** and **3** (entries 2, 4, 6, 8). Unfortunately, this higher purity came at a price as use of a limiting amount of I_2 gave lower yields. Attempts to further enhance the ratio of iodides by decreasing the reaction temperature to −15 °C or −78 °C were unsuccessful: ~1% of iodide **3** was still observed and yields were diminished.

With propargylic and homopropargylic alcohols, the isomeric iodides formed could be separated chromatographically; excess iodine could thus be used to obtain good yields of the desired *E*-vinyl iodide (Table 1, entries 9–12).

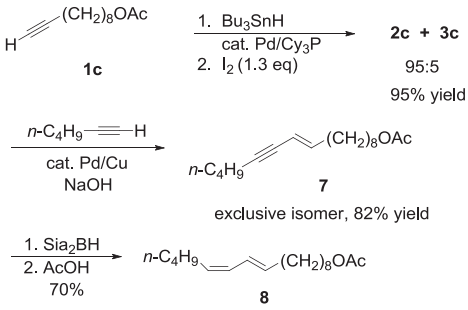
Although the purity of vinyl iodides **2** isolated was only 95% in some cases, this may not cause problems with subsequent reactions as the contaminating minor *gem* isomer **3** should be less reactive in coupling reactions. To test this hypothesis and to illustrate the synthetic utility of the one-pot hydrostannation/iodination sequence, we undertook the synthesis of two insect pheromones.

Dienal **6** is a sex pheromone of the sugar cane borer, *Diatraea saccharalis*[27] and the pecan nut casebearer, *Acrobasis nuxvorella*.[28] This pheromone was prepared from alkynyl alcohol **1b** in four steps (Scheme 3). Hydrostannation/iodination of **1b** provided *trans*-vinyl iodide **2b** in 93% isolated yield in a 95:5 ratio with the corresponding *gem*-vinyl iodide **3b**. The inseparable 95:5 mixture of vinyl iodides was subjected to Sonogashira coupling with excess 1-hexyne. To our delight, only the trans coupling product **4** was observed in 85% yield, and the *gem*-vinyl iodide **3b** was recovered. Reduction of the triple bond by hydroboration/protonolysis afforded diene **5** in 94% yield. Subsequent oxidation with PDC provided dienal **6** in 91% yield (overall 68% over four steps). It should be noted that this synthesis does not require the use of a protected alcohol as other similar approaches to dienals using other hydrometalation strategies do.[29]



Scheme 3. Synthesis of a sugar cane borer pheromone.

In a very similar manner, diene acetate **8**, another sex pheromone of the pecan nut casebearer *A. nuxvorella*, was prepared (Scheme 4).[30] In this case, treatment of the mixture of isomeric iodides **2c** and **3c** with 1-hexyne under Sonogashira conditions produced only the desired enyne **7** with germinal iodide **3c** remaining unreacted. Hydroboration/protonolysis of **7** furnished the desired pheromone in 70% yield (overall 55% over three steps). This synthesis allows for the presence of an acetate (which is part of **8** and many other insect pheromones) in the hydrometalation substrate, an approach that is not possible with hydroalumination or hydrozirconation strategies.



Scheme 4. Synthesis of a pecan nut casebearer sex pheromone.

3. Conclusion

In summary, we have shown that hydrostannation/iodination of terminal alkynes using Pd(0)/Cy_3P as the hydrostannation catalyst is a viable route to *E*-1-iodo-1-alkenes. Reactions are operationally simple (being carried out in one pot) and iodides are formed in high yields and with high regioselectivities. In cases where regioisomeric iodides are not separable, the 1-iodoalkene may be selectively reacted in the presence of the small amounts of contaminating 2-iodoalkene. Functional groups such as alcohols and acetates do not interfere with this hydrostannation/iodination process making it particularly attractive for alkynes bearing such groups.

4. Experimental section

4.1. General

All reactions were carried out under argon using flame-dried glassware. ^1H and ^{13}C NMR spectra were recorded in $CDCl_3$ at 300 MHz and 75 MHz, respectively. Dichloromethane and diisopropylethylamine were freshly distilled from calcium hydride. Tributyltin hydride was prepared by reduction of bis(tributyltin) oxide with $NaBH_4$ in ethanol[31] and was distilled (kugelrohr) before use. Samples were checked by ^{13}C NMR spectroscopy (in C_6D_6 since Bu_3SnH reacts with $CDCl_3$) for the presence of $Bu_3SnSnBu_3$ and were re-distilled if necessary.[32] Other reagents were purchased from Sigma–Aldrich and used without further purification. 10-Undecyn-1-ol **1b** was prepared by bromination/dehydrobromination of 10-undecen-1-ol,[33] commercially-unavailable propargylic alcohols were prepared by addition of lithium trimethylsilylacetylide to the appropriate aldehyde followed by treatment with K_2CO_3/MeOH.[34,35]

4.2. General procedure for the hydrostannation/iodination of alkynes

Pd_2dba_3 (65.0 mg, 0.147 mmol), tricyclohexylphosphonium tetrafluoroborate (99.0 mg, 0.294 mmol), and *i*-Pr_2NEt (76.0 mg, 0.588 mmol) were added successively to CH_2Cl_2 (300 mL) and the resulting mixture was stirred at rt for 15 min. Alkyne **1** was added (58.8 mmol) and the reaction was cooled to 0 °C Bu_3SnH (20.5 g, 70.5 mmol) diluted in CH_2Cl_2 (90 mL) was added dropwise via a dropping funnel over 1.5 h. The reaction was then allowed to stir at 0 °C for 2 h. Iodine (19.4 g, 76.4 mmol) dissolved in CH_2Cl_2 (300 mL) was added via a dropping funnel within 10 min at 0 °C and the mixture was stirred at 0 °C for a further 10 min. The reaction mixture was washed with saturated $Na_2S_2O_3$ solution (1×250 mL), and saturated KF solution (3×250 mL), passed through a silica plug and concentrated. The resulting oil was purified by silica gel chromatography (hexane/ether) to afford the corresponding *trans*-vinyl iodide **2** in a 95:5 ratio (with *gem* iodide 3, 1.3 equiv of I_2 was used) or 99:1 ratio (when 0.95 equiv of I_2 was used) for iodides **2a**–**d** or as a pure isomer (for iodides **2e**–**i**). The minor isomers **3a**–**d** were identified by the presence of broad singlets at ~δ 5.7 and 6.0 in ^1H NMR spectra.

*4.2.1. (E)-tert-Butyl(11-iodoundec-10-enyloxy)dimethylsilane (**2a**)*[36]. Vinyl iodide **2a** was isolated as a 95:5 (88% yield) or 99:1 (71% yield) mixture with **3a** from **1a** using the general procedure. ^1H NMR (300 MHz, $CDCl_3$) δ 6.49 (dt, 1H, *J*=14.3, 7.1 Hz), 5.94 (d, 1H, *J*=14.3 Hz), 3.57 (t, 2H, *J*=6.6 Hz), 2.08 (dt, 2H, *J*=7.2, 5.9 Hz), 1.56–1.25 (m, 14H), 0.87 (s, 9H), 0.03 (s, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 146.7, 74.1, 63.2, 35.9, 32.8, 29.4, 29.3, 29.2, 28.8, 28.3, 25.9, 25.7, 18.3, -5.4.

*4.2.2. (E)-10-Iododec-9-en-1-ol (**2b**)*[36]. Vinyl iodide **2b** was isolated as a 95:5 (93% yield) or 99:1 (75% yield) mixture with **3b** from **1b** using the general procedure. ^1H NMR (300 MHz, $CDCl_3$) δ 6.46 (dt, 1H, *J*=14.4, 7.1 Hz), 5.92 (d, 1H, *J*=14.4 Hz), 3.58 (t, 2H, *J*=6.6 Hz), 1.99 (app q, 2H, *J*=6.8 Hz), 1.82 (s, 1H), 1.53–1.14 (m, 12H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 146.8, 74.4, 63.0, 36.1, 32.8, 29.4 (2C), 28.9, 28.4, 25.8.

*4.2.3. (E)-10-Iododec-9-en-1-yl acetate (**2c**)*[20]. Vinyl iodide **2c** was isolated as a 95:5 (95% yield) or 99:1 (76% yield) mixture with **3c** from **1c** using the general procedure. ^1H NMR (300 MHz, $CDCl_3$) δ 6.44 (dt, 1H, *J*=14.3, 7.2 Hz), 5.91 (d, 1H, *J*=14.3 Hz), 3.98 (t, 2H, *J*=6.8 Hz), 1.99 (app q, 2H, *J*=7.0 Hz), 1.98 (s, 3H), 1.58–1.24 (m, 12H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 171.0, 146.6, 74.3, 64.5, 35.9, 29.1, 29.0, 28.7, 28.5, 28.2, 25.8, 20.9.

*4.2.4. (E)-6-Iodohex-5-en-1-ol (**2d**)*[37]. Vinyl iodide **2d** was isolated as a 95:5 (94% yield) or 99:1 (76% yield) mixture with **3d** from **1d** using the general procedure. ^1H NMR (300 MHz, $CDCl_3$) δ 6.47 (dt, 1H, *J*=14.3, 7.1 Hz), 5.97 (d, 1H, *J*=14.3 Hz), 3.59 (t, 2H, *J*=5.6 Hz), 2.05 (app q, 2H, *J*=6.9 Hz), 1.70 (s, 1H), 1.57–1.39 (m, 4H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 146.2, 74.8, 62.4, 35.7, 31.8, 24.8.

*4.2.5. (E)-3-Iodoprop-2-en-1-ol (**2e**)*[25]. Vinyl iodide **2e** was isolated in 67% yield from a 67:33 mixture of **2e** and **3e** formed from alkyne **1e** using the general procedure. ^1H NMR (300 MHz, $CDCl_3$) δ 6.67 (dt, 1H, *J*=14.6, 5.4 Hz), 6.37 (d, 1H, *J*=13.9 Hz), 4.07 (br s, 2H), 1.55 (s, 1H), 1.53–1.14 (m, 12H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 144.6, 77.8, 65.1.

*4.2.6. (E)-4-Iodobut-3-en-1-ol (**2f**)*[21]. Vinyl iodide **2f** was isolated in 83% yield from a 83:17 mixture of **2f** and **3f** formed from alkyne **1f** using the general procedure. ^1H NMR (300 MHz, $CDCl_3$) δ 6.51 (dt, 1H, *J*=14.4, 7.3 Hz), 6.13 (d, 1H, *J*=14.4 Hz), 3.65 (app q, 2H, *J*=6.0 Hz), 2.05 (app q, 2H, *J*=6.2 Hz), 1.62 (t, 1H, *J*=5.5 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 142.6, 77.2, 60.9, 39.1.

*4.2.7. (E)-4-Iodobut-3-en-2-ol (**2g**)*[38]. Vinyl iodide **2g** was isolated in 93% yield from a 95:5 mixture of **2g** and **3g** formed from alkyne **1g** using the general procedure. ^1H NMR (300 MHz, $CDCl_3$) δ 6.58 (dd, 1H, *J*=14.4, 6.0 Hz), 6.32 (dd, 1H, *J*=14.4, 1.1 Hz), 4.25 (m, 1H), 1.84 (d, 1H, *J*=4.2 Hz), 1.24 (d, 3H, *J*=6.5 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 149.5, 76.7, 70.6, 22.6.

*4.2.8. (E)-1-Iodooct-1-en-3-ol (**2h**)*[25]. Vinyl iodide **2h** was isolated in 89% yield from a 95:5 mixture of **2h** and **3h** formed from alkyne **1h** using the general procedure. ^1H NMR (300 MHz, CDCl3) δ 6.56 (dd, 1H, *J*=14.5, 6.3 Hz), 6.32 (d, 1H, *J*=14.5 Hz), 4.07 (m, 1H),

1.56–1.28 (m, 9H), 0.87 (t, 3H, J=6.2 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 148.6, 77.1, 74.7, 36.5, 31.6, 24.7, 22.5, 13.9.

*4.2.9. (E)-3-Iodo-1-phenylprop-2-en-1-ol (**2i**)*[39]. Vinyl iodide **2i** was isolated in 80% yield from a 82:18 mixture of **2i** and **3i** formed from alkyne **1i** using the general procedure. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.39–7.30 (m, 5H), 6.70 (dd, 1H, J=14.4, 5.9 Hz), 6.45 (dd, 1H, J=14.5, 1.1 Hz), 5.13 (m, 1H), 2.21 (d, 1H, J=3.4 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 147.1, 141.9, 128.7 (2C), 128.2, 126.3 (2C), 78.1, 76.6.

*4.2.10. (E)-Hexadec-9-en-11-yn-1-ol (**4**)*[40]. To a mixture of iodides **2b** and **3b** (95:5, 130 mg, 0.46 mmol), $Pd(PPh_3)_2Cl_2$ (32.0 mg, 0.046 mmol) and CuI (18.0 mg, 0.093 mmol) in Et_3N (10 mL) was added a dilute solution of hexyne (76.0 mg, 0.93 mmol) in Et_3N (2 mL) at rt. The reaction was allowed to stir at rt for 16 h. The reaction mixture was diluted with water (25 mL) and the aqueous layer was extracted with ether (2×25 mL). The organic layers were combined and washed with saturated NH_4Cl (2×30 mL) and brine (2×30 mL), then dried over Na_2SO_4 and concentrated. The resulting oil was purified by silica gel (7 g) chromatography (hexane/ether, 3:1) to afford enyne **4** in 85% (92 mg) yield as a colorless oil. ^{1}H NMR (300 MHz, $CDCl_3$) δ 6.02 (dt, 1H, J=15.8, 7.2 Hz), 5.42 (d, 1H, J=16.0 Hz), 3.61 (t, 2H, J=6.3 Hz), 2.27 (dt, 2H, J=7.2, 1.9 Hz), 2.03 (app q, 2H, J=7.3 Hz), 1.53–1.16 (m, 12H) (m, 4H), 0.89 (t, 3H, J=7.2 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 143.0, 109.7, 88.5, 79.0, 63.7 (CH_2OH), 32.8, 32.6, 30.8, 29.3, 29.2, 28.9, 28.7, 25.6, 21.8, 18.9, 13.5.

*4.2.11. (9E,11Z)-Hexadeca-9,11-dien-1-ol (**5**)*[27]. To a solution of 2-methyl-2-butene (0.15 mL, 1.44 mmol) in THF (5 mL) at 0 °C was added BH_3•SMe_2 (0.07 mL, 0.72 mmol). After 20 min, a solution of enyne **4** (85 mg, 0.36 mmol) in THF (1 mL) was added dropwise and the mixture was allowed to stir at 0 °C for 4 h. AcOH (0.16 mL, 2.9 mmol) was added slowly and the reaction was stirred at 55 °C for 6 h then allowed to cool to rt. This was followed by the addition of NaOH (0.29 mL, 50% w/v in H_2O) and H_2O_2 (0.16 mL, 30% in H_2O) and stirring for 30 min at 40 °C. The mixture was cooled, diluted with ether (30 mL), washed with brine (2×30 mL), dried over Na_2SO_4 and concentrated. The resulting oil was purified by silica gel (10 g) chromatography (hexane/ether, 3:1) to afford diene **5** (81 mg, 94% yield) as a colorless oil. ^{1}H NMR (300 MHz, $CDCl_3$) δ 6.27 (dd, 1H, J=14.6, 11.4 Hz), 5.90 (dd, 1H, J=10.8 Hz), 5.60 (dt, 1H, J=15.0, 6.9 Hz), 5.25 (dt, 1H, J=10.4, 7.7 Hz), 3.58 (t, 2H, J=6.6 Hz), 2.14–2.01 (m, 4H), 1.92 (s, 1H), 1.52–1.22 (m, 16H), 0.87 (t, 3H, J=6.7 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 134.5, 130.0, 128.5, 125.6, 62.8, 32.8, 32.7, 31.8, 29.4, 29.3 (2C), 29.1, 27.3, 25.7, 22.2, 13.7.

*4.2.12. (9E,11Z)-Hexadeca-9,11-dienal (**6**)*[27]. A solution of alcohol **5** (81 mg, 0.34 mmol) in CH_2Cl_2 (1 mL) was added dropwise to a mixture of PDC (192 mg, 0.51 mmol) and 3 Å sieves (100 mg) in CH_2Cl_2 (10 mL) and the mixture was stirred at rt for 18 h. The reaction mixture was diluted with ether, passed through a Celite plug and concentrated. The resulting oil was purified by silica gel chromatography (10 g, hexane/ether, 15:1) to afford aldehyde **6** (73 mg, 91% yield) as a colorless oil. ^{1}H NMR (300 MHz, $CDCl_3$) δ 9.74 (s, 1H), 6.28 (dd, 1H, J=14.3, 11.7 Hz), 5.91 (dd, 1H, J=10.8, 10.8 Hz), 5.62 (dt, 1H, J=15.0, 6.9 Hz), 5.27 (dt, 1H, J=10.2, 7.7 Hz), 2.39 (t, 2H, J=7.3 Hz), 2.14–2.09 (m, 2H), 1.62–1.16 (m, 18H), 0.88 (t, 3H, J=6.5 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 202.4, 134.2, 129.9, 128.5, 125.6, 43.0, 32.7, 31.7, 29.2 (2C), 32.7, 31.8, 29.2, 29.1, 29.0, 28.9, 27.3, 22.2, 21.9, 13.8.

*4.2.13. (E)-Hexadec-9-en-11-ynyl acetate (**7**)*[40]. To a degassed mixture of aqueous 10% NaOH (100 mL) and benzene (55 mL) was added successively iodides **2c** and **3c** (95:5 ratio, 16.54 g, 51.0 mmol), $BnNEt_3Cl$ (0.23 g, 1.0 mmol), $Pd(PPh_3)_4$ (1.1 g, 1.0 mmol), and CuI (0.38 g, 2.0 mmol). Hexyne (11.7 mL, 0.100 mol) was then added and the reaction mixture was stirred vigorously (to ensure the two phase system was emulsified) for 24 h. The reaction mixture was diluted with hexane. The layers were separated, and the aqueous layer was extracted with hexane (2×150 mL). The organic layers were combined and washed with saturated NH_4Cl (3×100 mL), brine (2×100 mL), dried over Na_2SO_4, and concentrated. The resulting oil was purified by silica gel (600 g) chromatography (hexane/ether, 25:1) to afford enyne **7** (11.7 g, 82% yield) as a colorless oil. ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.96 (dt, 1H, J=15.8, 7.0 Hz), 5.37 (d, 1H, J=15.0 Hz), 3.98 (t, 2H, J=6.7 Hz), 2.20 (dt, 2H, J=7.2, 1.9 Hz), 2.01 (s, 3H), 2.00 (app q, 2H, J=7.3 Hz), 1.55–1.23 (m, 12H), 1.15–1.06 (m, 4H), 0.85 (t, 3H, J=7.1 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 171.0, 143.0, 109.8, 88.5, 79.0, 64.5, 32.8, 30.8, 29.2, 29.1, 28.9, 28.7, 28.5, 25.8, 21.9, 20.9, 18.9, 13.5.

*4.2.14. (9E,11Z)-Hexadeca-9,11-dien-1-yl acetate (**8**)*[30b]. To a solution of 2-methyl-2-butene (20.8 mL, 195 mmol) in THF (65 mL) at 0 °C was added BH_3•SMe_2 (9.70 mL, 97.0 mmol). After 20 min, the disiamylborane was syringed, dropwise, into a solution of enyne **7** (17.5 g, 65.0 mmol) in THF (65 mL) at 0 °C over a period of 30 min. The mixture was allowed to stir at 0 °C for 4 h. AcOH (22 mL, 0.39 mol) was added slowly and the reaction was stirred at 55 °C for 6 h then allowed to cool to rt. This was followed by the addition of NaOH (82 mL, 25% w/v in H_2O) and H_2O_2 (22 mL, 30% in H_2O) and stirring for 30 min at 40 °C. The mixture was cooled, diluted with ether (200 mL), washed with brine (2×100 mL), dried over Na_2SO_4 and concentrated. The resulting oil was purified by silica gel (600 g) chromatography (hexane/ether, 30:1) to afford diene **8** (12.20 g, 70% yield) as a colorless oil. ^{1}H NMR (300 MHz, $CDCl_3$) δ 6.13 (dd, 1H, J=14.7, 11.3 Hz), 5.76 (dd, 1H, J=10.8 Hz), 5.46 (dt, 1H, J=15.0, 7.0 Hz), 5.11 (dt, 1H, J=10.5, 7.7 Hz), 3.88 (t, 2H, J=6.7 Hz), 2.01–1.90 (m, 4H), 1.84 (s, 3H), 1.62–1.16 (m, 16H), 0.75 (t, 3H, J=6.7 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 170.3, 133.9, 129.4, 128.6, 125.6, 64.1, 32.7, 31.7, 29.2 (2C), 29.0, 28.9, 28.5, 27.2, 25.7, 22.1, 20.5, 13.7.

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