Notes

Radical Cyclization of Polyenes Initiated by Attack of Trialkyltin or Germanium Radical on an Ynone

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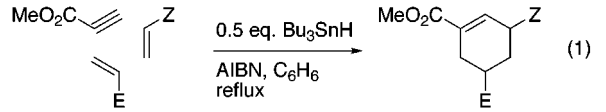
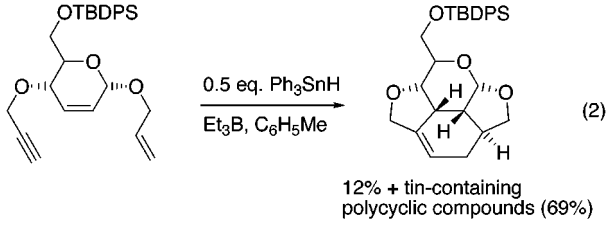
Radical multicyclizations on polyunsaturated chains have been distinctively useful for the construction of polycyclic molecules.[1−3] Several elaborate polycyclizations to triquinane and triterpene skeletons[1] and the attempt by Curran and co-workers to build the steroid framework via a formidable tandem radical macrocyclization/cascade radical cyclizations strategy[4] underscore the advances made in this field in recent years. In most examples of radical reactions though, a metal hydride is used in a stoichiometric amount. Radical cyclizations in which the metal radical source is used in a catalytic amount are rare despite the few available methods.[5] Lee and co-workers described the cyclization of functionally complementary alkenes and alkynes into six-membered rings in modest yields (eq 1) using 0.5 equiv of tin hydride.[6] Marco-Contelles reported intramolecular cyclizations of polyenes in 12−14% yield as byproducts in a strategy for the formation of polycyclic molecules (eq 2).[7] Catalytic versions of metal hydride mediated radical cyclizations are desirable in view of the cost and/or toxicity of stannyl, germyl, or silyl hydrides.



E = electron-withdrawing, Z = electron-donating



12% + tin-containing polycyclic compounds (69%)

Scheme 1

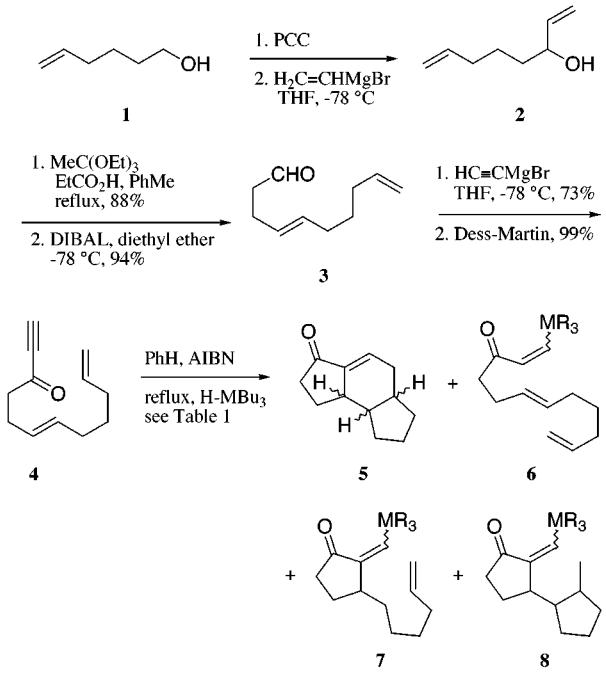


Table 1. Results of the Radical Polycyclization of 4 with Various Metal Hydrides

entry	M-H (equiv)	initiation condition	solvent (conc, mM)	time (h)	**5**	**6**
1	*n*-Bu_3SnH (0.5)	AIBN, Δ	PhH (30)	4	22	23
2	*n*-Bu_3SnH (0.1)	AIBN, Δ	PhH (30)	23	15	0
3	*n*-Bu_3GeH (0.3)	AIBN, Δ	PhH (30)	24	11	0
4	*n*-Bu_3GeH (1.0)	AIBN, Δ	PhH (30)	4	29	13
5	*n*-Bu_3GeH (1.0)	AIBN, Δ	PhH (h.d.)[a]	16	25	10
6	*n*-Bu_3GeH (1.0)	AIBN, Δ	PhH (4.5)	9	28	9
7	*n*-Bu_3GeH (1.0)	ACCN, Δ	PhH (h.d.)[a]	23	38	10
8	*n*-Bu_3GeH (0.3)	ACCN, Δ	PhMe	4	40	0
9	(*n*-$Bu_3Sn)_2$ (0.2)	AIBN, *hν*, Δ	PhH (30)	72	12	0
10	$(PhS)_2$ (0.1)	AIBN, *hν*	PhH (30)	48	15	0
11	$(PhS)_2$ (0.2)	AIBN, *hν*	PhH (4.5)	96	5	0
12	(*n*-$BuS)_2$ (0.25)	*hν*	PhH (30)	4	0	0

[a] h.d. = high dilution from slow addition over 7 h.

We wish to report our initial attempt at developing a polyenyne cyclization method using a catalytic amount of metal hydride. In our strategy, an ynone moiety serves as the pivotal functionality to allow the initial attack by the metal radical. The requisite precursor **4** was synthesized in a straightforward manner from 5-hexen-1-ol as described in Scheme 1. Swern oxidation followed by addition of vinylmagnesium bromide furnished alcohol **2**, which underwent a Claisen rearrangement and further reduction to give aldehyde **3**. This aldehyde was reacted with ethynylmagnesium bromide, and the resulting alcohol was oxidized to yield **4**. The latter suffered a radical polycyclization to give tricyclic enone **5** in modest yields under various conditions (Table 1). Proton and carbon NMR and GCMS analysis confirmed the presence of four diastereomers of **5** in an approximately 2:2:1:1 ratio. Of course, in such a simple model, we did not expect

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(1) For a review see: Malacria, M. *Chem. Rev.* **1996**, *96*, 289.
(2) Curran, D. P. *Synthesis* **1988**, 417 and 489.
(3) Giese, B. *Radicals in Organic Synthesis: Formation of C−C bonds*; Pergamon Press: New York, 1986.
(4) Jahn, U.; Curran, D. P. *Tetrahedron Lett.* **1995**, *36*, 8921.
(5) For versions of classical radical reactions using catalytic tin hydride see: Terstiege, I.; Maleczka, R. E., Jr. *J. Org. Chem.* **1999**, *64*, 342 and references therein.
(6) Lee, E.; Hur, C. U.; Rhee, Y. H.; Park, Y. C.; Kim, S. Y. *J. Chem. Soc., Chem. Commun.* **1993**, 1466.
(7) Marco-Contelles, J. *J. Chem. Soc., Chem. Commun.* **1996**, 2629.

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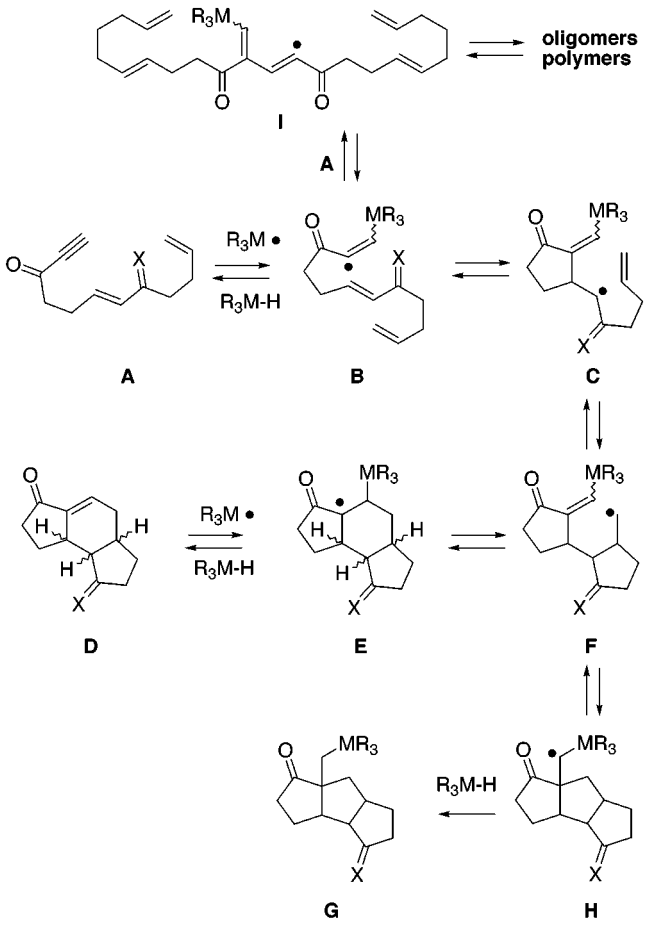
Scheme 2

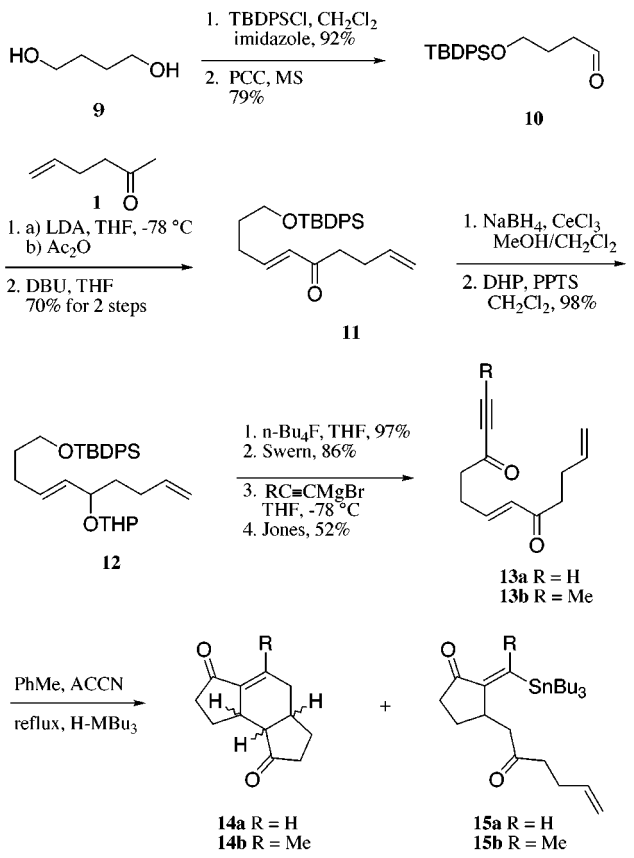


any control over the stereochemistry.[8] This model was chosen because the first two cyclizations are 5-exo-trig cyclizations and thought to be favorable ones.[2] However, the all-syn isomer of **5** seems fairly strained, and its formation is surprising. We could not assign the stereochemistry of the major isomers or any particular isomer mostly because of signal overlap in the NMR spectra.

Scheme 2 depicts the steps necessary for the formation of **5** and possible byproducts (X = H_2). Table 1 lists the various conditions that were tried on this system. Unfortunately, in all entries that produced **5**, the desired product was accompanied by many byproducts (possibly oligomers or polymers), which made purification difficult. We believe the actual yields of **5** were higher (ca. 50% range). Although modest, these yields are promising considering a conversion in which three new bonds and three rings were formed. We often had to add more metal hydride to consume more of the starting material (entries 4−7). The process to form **5** was nevertheless catalytic in metal radical, but the latter was consumed in the process of oligomerization which does not regenerate it. This caused the metal radical source to slowly vanish during the reaction and accounts for the incomplete conversions. Indeed, the desired tricyclic compound **5** started to appear at the beginning of each reaction at the same time as byproducts. After a while, the reaction stopped, and more hydride and initiator had to be added.

Germanium seems to be more efficient than tin and gave better conversions with smaller amounts of mono-

Scheme 3



addition product **6**. Germanium is a poorer hydride donor than tin, and that may be responsible for a cleaner reaction. Decreasing the hydride concentration, though, changed little of the outcome (entries 5 and 6). Silanes were not used in the polycyclization. They are known to efficiently add to many alkenes under radical reaction conditions, and it is unlikely that the silyl radical would be ejected in the last step (**E** → **D** in Scheme 2).[9]

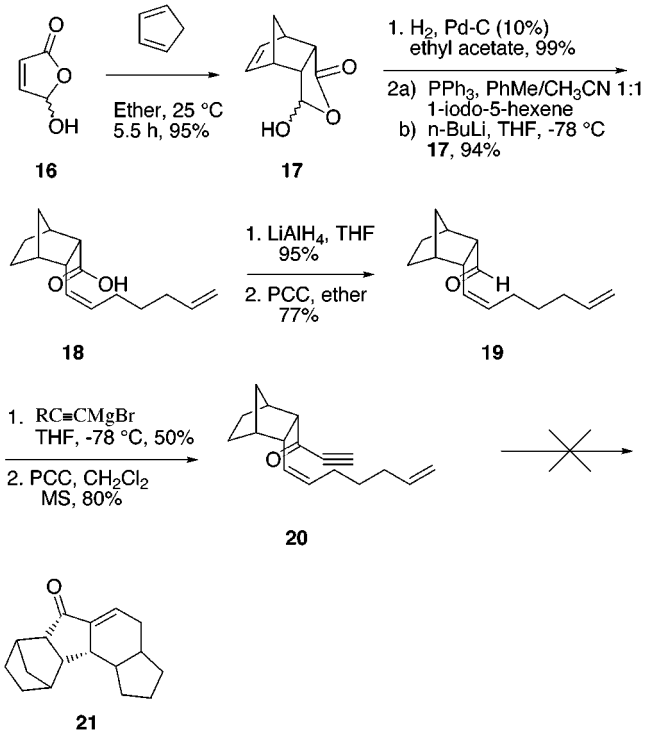
Surprisingly, little or no monocyclization or bicyclization product **7** or **8** was detected in any of the experiments tried. The strong signals for both remaining double bonds in the proton NMR spectra of the byproducts were evidence of this. The absence of mono- and bicyclization products seemed to indicate that the first cyclization was slower than intermolecular attack or hydride abstraction by the vinyl radical. This problem should have been solved by using hydride-free conditions (entries 9−12). Unfortunately, the starting ynone and/or the product enone were decomposed by light sources necessary in some of these hydride-free conditions. Others gave no product or only byproducts. The ynone functionality is not only necessary to accelerate the initial addition of metal radical but also to ensure formation of the six-membered final ring. The competing final 5-exo-trig cyclization would give a metal-containing tricyclic adduct (cf. **G** Scheme 2). Triethyl borane as an initiator (not listed) led to no reaction at all.

We reasoned that conjugating an electron-withdrawing group to the internal alkene could enhance the rate of the first cyclization and probably the yield of the final product (cf. Scheme 2, X = O). Although α to a carbonyl,

(8) For a review of stereochemical control in radical reactions see: Curran, D. P.; Porter, N. A.; Giese, B. *Stereochemistry of radical reactions*; VCH: Weinheim, 1996.

(9) See, for example: Kopping, B.; Chatgilialoglu, C.; Zehnder, M.; Giese, B. *J. Org. Chem.* **1992**, *57*, 3994.

Scheme 4



radical **B** (Scheme 2) is moderately nucleophilic because it is not conjugated to the carbonyl and the polarity of the C−M bond imparts a higher electron density.[6] Lee pointed out that such radicals only add to electron-deficient alkenes when the reaction is intermolecular.[6] Moreover, the resulting radical **C** (X = O) would become electrophilic and should react well with an electron-rich double bond. To that effect, we built compound **13a** as shown in Scheme 3 and submitted it to the usual conditions. Disappointingly, the yield of tricycle **14a** was no higher, and side products still formed. Installing a methyl group on the alkyne led to a very clean reaction but gave monocyclization product **15b** only. A trace of tricyclic product **14b** was detected, but none of the mono-addition or biscyclization products were found. This result indicates that the unsubstituted ynones in **4** and **13a** are probably responsible for the high amount of byproducts that was found. A substituted ynone, however, is slower to react intermolecularly because of the added bulk, but it may understandably slow the second and perhaps third cyclizations as well.

Restricting the freedom of rotation of the chain to increase the rate of the first cyclization proved futile as **20**, prepared as per Scheme 4, gave no discernible tricyclic product and only a collection of byproducts. Although these initial results are modest, they do supply important clues to making the method successful. It seems terminal ynones will lead to unclean reactions, whereas internal ones should provide clean adducts. However, presumably because of steric congestion around the olefin, so far only monocyclization adducts have been obtained. Other R groups on model **13**, including ones that could be removed after the cyclization, should be screened so as to maximize the cyclization rate while minimizing byproduct formation. Other sources of metal radical or reaction conditions for hydride-free metal radicals should also be designed and prepared. Although hydride-free conditions will not solve the oligomerization or polymerization problem on terminal ynones, it could allow substituted ones to cyclize cleanly without interruption. We are presently developing and optimizing the method further.

Experimental Section

All reactions were performed under nitrogen, otherwise noted. Solvents such as diethyl ether, THF, benzene, toluene, and *tert*-butylbenzene were distilled over sodium−benzophenone. Dichloromethane, triethylamine, diisopropylamine, and acetonitrile were distilled over calcium hydride, and methanol was distilled over magnesium and iodine. Flash column chromatography was performed on silica gel, 230−400 mesh.

1,7-Octadien-3-ol (2). Molecular sieves (4 Å) (2.5 g) were added to a 0 °C solution of 5-hexen-1-ol (1.2 mL, 1.0 g, 10.0 mmol) in dichloromethane (100 mL). The reaction mixture was stirred for 5 min. Pyridinium chlorochromate (3.23 g, 15.0 mmol) was added by portions over a 5 min period, and the mixture was stirred at room temperature for 4 h. The reaction was diluted with diethyl ether (100 mL) and filtered on a fritted glass funnel containing silica gel, activated charcoal, and Celite. The residue was washed with diethyl ether (200 mL). The greenish solution was concentrated by distillation under normal pressure. The greenish oil was used without further purification. ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm): 9.77 (t, 1H, J = 1.5 Hz), 5.39 (ddt, 1H, J = 17.0, 10.5 and 6.5 Hz), 5.06−4.98 (m, 2H), 2.45 (td, 2H, J = 7.3, 1.5 Hz), 2.10 (m, 2H), 1.74 (quintet, 2H, J = 7.3 Hz).

Vinylmagnesium bromide (1.0 M) (12 mL, 12.0 mmol) was added dropwise to a −78 °C solution of 5-hexenal (979 mg, 10.0 mmol) in THF (100 mL), and the solution was stirred for 45 min. The reaction was quenched with 50 mL of a saturated solution of NH_4Cl and allowed to warm to room temperature. The layers were separated, and the aqueous phase was extracted with diethyl ether (3 × 30 mL). The organic portions were combined, washed with brine (30 mL), dried over magnesium sulfate, filtered, and concentrated by rotary evaporation to give 1.07 g of 1,7-octadien-3-ol (**2**), which was used without further purification. ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm): 5.92−5.73 (m, 2H), 5.25−4.94 (m, 4H), 4.14−4.08 (m, 1H), 2.11−2.04 (m, 2H), 1.59−1.41 (m, 4H). GCMS (*m*/*z*, relative intensity): 125 ($M^+ - 1$, 0.2).

(*E*)-4,9-Decadienal (3). Propionic acid (164 μL, 163 mg, 2.2 mmol), triethyl orthoacetate (14 mL, 12.5 g, 77 mmol), and 1,7-octadien-3-ol (**2**) (1.4 g, 11.1 mmol) were heated to reflux in toluene (20 mL) for 15 h. Then, the toluene was removed by rotary evaporation, leaving an oil that was vacuum distilled to yield ethyl (*E*)-4,9-decadienoate (1.91 g, 88%) as a clear oil. Bp: 78−82 °C (0.1−0.5 mmHg). ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm): 5.79 (ddt, 1H, J = 17.0, 10.5, and 6.5 Hz), 5.51−5.37 (m, 2H), 5.02−4.92 (m, 2H), 4.14 (q, 2H, J = 7.0 Hz), 2.39−2.26 (m, 4H), 2.07−1.96 (m, 4H), 1.43 (quintet, 2H, J = 7.5 Hz), 1.25 (t, 3H, J = 7 Hz). IR ($CHCl_3$, cm^{-1}): 1727. LRMS (*m*/*z*, relative intensity): 196 (M^+, 0.8). HRMS calculated for $C_{12}H_{20}O_2$: 196.1463, observed 196.1469. Anal. Calcd for $C_{12}H_{20}O_2$: H 10.28, C 73.41, O 16.31. Found: H 10.12 C 73.44.

Diisobutylaluminum hydride (1.0 M) (19.6 mL, 19.6 mmol) was added dropwise to a −78 °C solution of ethyl (*E*)-4,9-decadienoate (3.5 g, 17.8 mmol) in diethyl ether (220 mL), and the solution was stirred for 15 min. The reaction mixture was quenched with a 1 N HCl solution (30 mL). The separated aqueous layer was extracted with diethyl ether (3 × 50 mL). The organic phases were combined, washed with brine (50 mL), dried over magnesium sulfate, filtered, and concentrated by rotary evaporation. The crude oil was purified by flash chromatography on silica gel using a 1:9 solution of ethyl acetate and hexanes to yield (*E*)-4,9-decadienal (**3**) (2.56 g, 94%) as an oil. ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm): 9.76 (t, 1H, J = 1.5 Hz), 5.79 (ddt, 1H, J = 17.0, 10.2, and 6.8 Hz), 5.51−5.35 (m, 2H), 5.03−4.92 (m, 2H), 2.49 (td, 2H, J = 7.0, 1.5 Hz), 2.36−2.30 (m, 2H), 2.07−1.96 (m, 4H), 1.43 (quintet, 2H, J = 7.0 Hz). IR ($CHCl_3$, cm^{-1}): 1723. LRMS (*m*/*z*, relative intensity): 151 ($M^+ - 1$, 1.0), 134 ($M^+ - H_2O$, 3). HRMS calculated for $C_{10}H_{15}O$ ($M^+ - 1$): 151.1123, observed 151.1131.

(*E*)-6,11-Dodecadien-1-yn-3-one (4). Ethynylmagnesium bromide (0.5 M) (90 mL, 45.0 mmol) was added over a 10 min period to a −78 °C solution of (*E*)-4,9-decadienal (**3**) (2.27 g, 14.9

mmol) in THF (150 mL), and the solution was stirred for 5 h, allowing the temperature to reach 0 °C slowly. The reaction was quenched with a saturated ammonium chloride solution (80 mL) and warmed to room temperature. The separated aqueous layer was extracted with diethyl ether (3 × 50 mL), and the organic portions were combined, washed with brine (80 mL), dried over magnesium sulfate, filtered, and concentrated by rotary evaporation. The crude oil was purified by flash chromatography on silica gel using a 1:9 solution of ethyl acetate and hexanes to yield (*E*)-6,11-dodecadien-1-yn-3-ol (1.93 g, 73%) as a colorless oil. ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm): 5.80 (ddt, 1H, J = 17.0, 10.0, and 7.0 Hz), 5.53−5.36 (m, 2H), 5.03−4.93 (m, 2H), 4.38 (td, 1H, J = 7.0, 2.0 Hz), 2.47 (d, 1H, J = 2.0 Hz), 2.18 (q, 2H, J = 7.0 Hz), 2.08−1.97 (m, 4H), 1.82−1.74 (m, 2H), 1.44 (quintet, 2H, J = 7.0 Hz). IR (neat, cm^{-1}): 3550−3200 (br). LRMS (*m*/*z*, relative intensity): 196 (MNH_4^+, 0.8), 177 ($M^+ - 1$, 6), 160 ($M^+ - H_2O$, 8). HRMS calculated for $C_{12}H_{22}NO$ (MNH_4^+): 196.1701, observed 196.1704. Anal. Calcd for $C_{12}H_{18}O$: H 10.18, C 80.84, O 8.98. Found: H 10.09, C 80.81.

A solution of (*E*)-6,11-dodecadien-1-yn-3-ol (180 mg, 1.01 mmol) in dichloromethane (5 mL) was added to a solution of Dess-Martin's periodinane (471 mg, 1.11 mmol) in dichloromethane (10 mL). The resulting mixture was stirred at room temperature for 15 min. Then, the mixture was diluted with diethyl ether (15 mL) and a saturated aqueous bicarbonate solution (15 mL) containing sodium thiosulfate (3 g), which had been previously stirred for 5 min. A second portion of diethyl ether was added (15 mL), and the layers were separated. The organic layer was washed with a saturated aqueous bicarbonate solution (30 mL), water (30 mL) and brine (30 mL), dried over magnesium sulfate, filtered, and concentrated by rotary evaporation. The crude oil was purified by flash chromatography on silica gel using a 4:96 solution of ethyl acetate and hexanes to yield (*E*)-6,11-dodecadien-1-yn-3-one (**4**) (176 mg, 99%) as a colorless oil. ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm): 5.79 (ddt, 1H, J = 17.0, 10.2, and 6.8 Hz), 5.50−5.35 (m, 2H), 5.03−4.93 (m, 2H), 3.21 (s, 1H), 2.65 (t, 2H, J = 7.0 Hz), 2.37 (q, 2H, J = 7.0 Hz), 2.07−1.95 (m, 4H), 1.43 (quintet, 2H, J = 7.5 Hz).^{13}C NMR (75.5 MHz, $CDCl_3$) δ (ppm): 186.8 (s), 138.7 (d), 131.8 (d), 127.6 (d), 114.5 (t), 81.4 (d), 78.6 (s), 45.2 (t), 33.1 (t), 31.8 (t), 28.5 (t), 26.7 (t). IR (neat, cm^{-1}): 2093, 1683. LRMS (*m*/*z*, relative intensity): 194 (MNH_4^+, 2), 161 ($M^+ - CH_3$, 3). HRMS calculated for $C_{12}H_{20}NO$ (MNH_4^+): 194.1545, observed 194.1550. Anal. Calcd for $C_{12}H_{16}O$: H 9.16, C 81.76, O 9.08. Found: H 9.18, C 81.69.

Tricyclo[7.3.0.0^{2,6}]dodec-8-en-10-one (5). See Table 1 for the different conditions. A typical procedure (entry 8) is as follows: AIBN (28 mg, 0.17 mmol) and tributylgermanium hydride (193 mg, 146 μL, 0.57 mmol) were added to a solution of **4** (100 mg, 0.57 mmol) in benzene (20 mL), and the solution was stirred under reflux for 4 h. The solution was concentrated under reduced pressure without complete drying. The crude product was purified by flash chromatography on silica gel using a (0:100 to 20:80) solution of ethyl acetate and hexanes to yield two mixtures of two products. The two compounds in the first mixture could not be separated, but the other two were isolated by preparative chromatography on a plate of silica gel, eluting with a solution of ethyl acetate and hexanes to yield **5** as four isomers (A + B, 11.3 mg, 11%), (C, 7.6 mg, 8%), and (D, 9.5 mg, 10%). Isomers A + B: ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm): 6.77−6.65 (m, 1HA + 1HB), 2.58−1.04 (m, 15H). Isomer C: ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm): 5.81 (s, 1H), 2.89−1.14 (m, 15H). Isomer D: ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm): 5.89 (s, 1H), 2.89−2.80 (m, 2H), 2.67−2.60 (m, 1H), 2.57 (dd, 1H, J = 16.2, 8.1 Hz), 2.46 (ddd, 1H, J = 16.5, 4.3, and 2.6 Hz), 2.30 (ddd, 1H, J = 16.5, 14.4 and 4.9 Hz), 2.18−1.92 (m, 3H), 1.81−1.12 (m, 6H). ^{13}C NMR (75.5 MHz, $CDCl_3$) δ (ppm): 200.1 (s), 175.3 (s), 122.9 (d), 47.8 (d0, 44.7 (d), 41.2 (d), 39.8 (t), 37.4 (t), 33.5 (t), 27.5 (t), 26.0 (t), 25.7 (t). IR (neat, cm^{-1}): 1670. LRMS (*m*/*z*, relative intensity): 176 (M^+, 42). HRMS calculated for $C_{12}H_{16}O$: 176.1201, observed 176.1198.

(6*E*)-1-Tributylstannyl-1,6,11-dodecatrien-3-one (6). Isomer A: ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm): 7.17 (d, 1H, J = 12.4 Hz), 7.10 (d, 1H, J = 12.4 Hz), 5.80 (ddt, 1H, J = 17.0, 10.0, and 7.0 Hz), 5.44−5.40 (m, 2H), 5.03−4.91 (m, 2H), 2.58 (t, 2H, J = 7.2 Hz), 2.33−2.28 (m, 2H), 2.04−1.96 (m, 4H), 1.52−1.40 (m, 6H), 1.36−1.22 (m, 8H), 0.98−0.83 (m, 15H). GCMS (*m*/*z*, relative intensity): 411 (M^+ − Bu, 70). Isomer B: ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm): 7.57 (d, 1H, J = 19.7 Hz), 6.54 (d, 1H, J = 19.7 Hz), 5.79 (ddt, 1H, J = 17.0, 10.4, and 6.6 Hz), 5.45−5.42 (m, 2H), 5.02−4.92 (m, 2H), 2.66 (t, 2H, J = 7.4 Hz), 2.38−2.29 (m, 2H), 2.07−1.95 (m, 4H), 1.56−1.41 (m, 8H), 1.31 (sextet, 6H, J = 7.3 Hz), 1.00−0.87 (m, 15H). GCMS (*m*/*z*, relative intensity): 411 (M^+ − Bu, 41).

(*E*)-10-*tert*-Butyldiphenylsilyloxy)deca-1,6-dien-5-one (11). At −78 °C, *n*-butyllithium (2.00 M) (2.5 mL, 5.05 mmol) was added dropwise to a solution of diisopropylamine (710 μL, 510 mg, 5.05 mmol) in THF (40 mL), and the solution was stirred at 0 °C during 10 min. At −78 °C, 5-hexen-2-one (590 μL, 496 mg, 5.05 mmol) was added slowly, and the solution was stirred for 1 h. Then, **10** (1.5 g, 4.59 mmol) in THF (10 mL) was added slowly to the reaction mixture, which was stirred at −78 °C for 2 h. Acetic anhydride (around 5 mL) was added, and the reaction was allowed to warm to room temperature and stirred for 20 min. Water (10 mL) and a 1 N HCl solution (5 mL) were poured over the mixture, and the layers were separated. The aqueous phase was extracted with diethyl ether (3 × 50 mL), and the combined organic portions were stirred with a saturated aqueous sodium bicarbonate solution (50 mL) for 1 h. The layers were separated, and the organic phase was dried over magnesium sulfate, filtered, and concentrated by rotary evaporation to yield (*E*)-10-(*tert*-butyldiphenylsilyloxy)-5-acetoxy-1,6-decadiene as a colorless oil, which was used without further purification. ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm): 7.65 (dd, 4H, J = 7.6, 1.7 Hz), 7.45−7.35 (m, 6H), 5.79 (ddt, 1H, J = 17.0, 10.5, and 6.5 Hz), 5.29−5.20 (m, 1H), 5.06−4.96 (m, 2H), 3.65 (t, 2H, J = 6.0 Hz), 2.72 (dd, 1H, J = 16.1, 7.4 Hz), 2.58−2.48 (m, 3H), 2.31 (q, 2H, J = 6.9 Hz), 1.99 (s, 3H), 1.69−1.52 (m, 4H), 1.04 (s, 9H). IR (neat, cm^{-1}): 1739, 1717. LRMS (*m*/*z*, relative intensity): 467 (MH^+, 0.6). HRMS calculated for $C_{28}H_{39}O_4Si$ (MH^+): 467.2617, observed 467.2610.

1,8-Diazabicyclo[5.4.0]undec-7-ene (DBU) (690 μL, 699 mg, 4.59 mmol) was added dropwise to a 0 °C solution of (*E*)-10-(*tert*-butyldiphenylsilyloxy)-5-acetoxy-1,6-decadiene (2.14 g, 4.59 mmol) in THF (50 mL), and the solution was stirred at room temperature for 2.5 h. The reaction mixture was diluted with water (20 mL) and a 1 N HCl solution (1.0 M) (10 mL). The layers were separated, and the aqueous phase was extracted with ethyl acetate (3 × 50 mL). The combined organic portions were washed with a saturated aqueous sodium bicarbonate solution (50 mL), water (50 mL), and brine (50 mL), dried over magnesium sulfate, filtered, and concentrated by rotary evaporation. The crude oil was purified by flash chromatography on silica gel using a 3:97 solution of ethyl acetate and hexanes to yield **11** (1.32 g, 70%, 2 steps) as a colorless oil. ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm): 7.65 (dd, 4H, J = 7.6, 1.7 Hz), 7.46−7.35 (m, 6H), 6.82 (dt, 1H, J = 15.9, 6.9 Hz), 6.09 (d, 1H, J = 15.9 Hz), 5.83 (ddt, 1H, J = 17.0, 10.5 and 6.5 Hz), 5.08−4.96 (m, 2H), 3.68 (t, 2H, J = 6.1 Hz), 2.61 (t, 2H, J = 7.1 Hz), 2.39−2.27 (m, 4H), 1.71 (quintuplet, 2H, J = 6.1 Hz), 1.05 (s, 9H). IR (neat, cm^{-1}): 1697. LRMS (*m*/*z*, relative intensity): 349 (M^+ − *t*-Bu, 92). HRMS calculated for $C_{22}H_{25}O_2Si$ (M^+ − *t*-Bu): 349.1624, observed 349.1618.

(*E*)-1-(*tert*-Butyldiphenylsilyloxy)-6-(tetrahydropyran-2-yloxy)deca-4,9-diene (12). Sodium borohydride (54 mg, 1.43 mmol) was added to a solution of **11** (580 mg, 1.43 mmol) and cerium(III) chloride heptahydrate (531 mg, 1.43 mmol) in a mixture of methanol/dichloromethane (10 mL/10 mL). The resulting suspension was stirred for 15 min. The reaction was concentrated by rotary evaporation and diluted with water (20 mL) and a 1 N HCl solution (10 mL). The layers were separated, and the aqueous phase was extracted with diethyl ether (3 × 20 mL). The combined organic portions were washed with brine (20 mL), dried over magnesium sulfate, filtered, and concentrated by rotary evaporation to yield (*E*)-10-(*tert*-butyldiphenylsilyloxy)deca-1,6-dien-5-ol (583 mg, 100%) as a clear oil, which was used without further purification. ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm): 7.66 (dd, 4H, J = 7.5, 1.6 Hz), 7.43−7.35 (m, 6H), 5.82 (ddt, 1H, J = 17.0, 10.5, and 6.5 Hz), 5.60 (dt, 1H, J = 15.4, 6.6 Hz), 5.44 (dd, 1H, J = 15.4, 7.0 Hz), 5.06−4.95 (m, 2H), 4.04 (q, 1H, J = 7.0 Hz), 3.66 (t, 2H, J = 6.3 Hz), 2.17−2.06 (m, 4H), 1.69−1.58 (m, 4H), 1.05 (s, 9H). IR (neat, cm^{-1}): 3500−3200 (br). LRMS (*m*/*z*, relative intensity): 351 (M^+ − *t*-Bu,

3). HRMS calculated for $C_{22}H_{25}O_2Si$ ($M^+ - t$-Bu): 351.1780, observed 351.1775.

3,4-Dihydro-2*H*-pyran (400 μL, 371 mg, 4.40 mmol) was added to a solution of (*E*)-10-(*tert*-butyldiphenylsilyloxy)deca-1,6-dien-5-ol (900 mg, 2.20 mmol) and pyridinium *p*-toluenesulfonate (221 mg, 0.88 mmol) in dichloromethane (30 mL), and the solution was stirred overnight. The reaction mixture was concentrated under rotary evaporation and diluted with diethyl ether (20 mL) and a saturated aqueous sodium bicarbonate solution (20 mL). The layers were separated, and the aqueous phase was extracted with diethyl ether (2 × 20 mL). The combined organic portions were washed with brine (20 mL), dried over magnesium sulfate, filtered, and concentrated by rotary evaporation. The crude product was purified by flash chromatography on silica gel using a 3:97 solution of ethyl acetate and hexanes to yield a mixture of inseparable diastereomers of **12** (1.06 g, 98%) as a colorless oil. ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm): 7.66 (dd, 4H, J = 7.5, 1.4 Hz), 7.42−7.34 (m, 6H), 5.85−5.79 (m, 1H), 5.64−5.54 (m, 1H), 5.47 (dd, 1HA, J = 15.5, 7.1 Hz), 5.21 (dd, 1HB, J = 15.4, 8.4 Hz), 5.04−4.93 (m, 2H), 4.67−4.63 (m, 1H), 4.04−3.97 (m, 1H), 3.89−3.82 (m, 1H), 3.66 (t, 2H, J = 6.3 Hz), 3.49−3.42 (m, 1H), 2.17−2.01 (m, 4H), 1.84−1.48 (m, 10H), 1.05 (s, 9H). IR (neat, cm^{-1}): 1471. LRMS (*m*/*z*, relative intensity): 435 ($M^+ - t$-Bu, 3). HRMS calculated for $C_{27}H_{35}O_3Si$ ($M^+ - t$-Bu): 435.2355, observed 435.2361. Anal. Calcd for $C_{31}H_{44}O_3Si$: H 9.00, C 75.56, O 9.74, Si 5.70. Found: H 8.87, C 75.62.

(*E*)-Dodeca-6,11-dien-1-yn-3,8-dione (13a). Tetrabutylammonium fluoride (1.0 M) (11 mL, 11 mmol) was added dropwise to a 0 °C solution of **12** (4.81 g, 9.77 mmol) in THF (100 mL), and the solution was stirred at room temperature for 1.5 h. The reaction mixture was diluted with water (60 mL). The layers were separated, and the aqueous phase was extracted with diethyl ether (2 × 60 mL). The combined organic portions were washed with brine (100 mL), dried over magnesium sulfate, filtered, and concentrated by rotary evaporation. The crude oil was purified by flash chromatography on silica gel using a (2:98 to 30:70) solution of ethyl acetate and hexanes to yield a 1:1 mixture of inseparable diastereomers A and B of (*E*)-6-(tetrahydropyran-2-yloxy)deca-4,9-dien-1-ol (2.40 g, 97%) as a colorless oil. ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm): 5.91−5.74 (m, 1H), 5.69−5.58 (m, 1H), 5.52 (dd, 1HA, J = 15.5, 7.1 Hz), 5.26 (dd, 1HB, J = 15.3, 8.3 Hz), 5.05−4.94 (m, 2H), 4.66 (t, 1H, J = 3.3 Hz), 4.05 (q, 1HB, J = 7.0 Hz), 3.98 (q, 1HA, J = 6.6 Hz), 3.93−3.83 (m, 1H), 3.69−3.63 (m, 2H), 3.52−3.41 (m, 1H), 2.18−2.04 (m, 4H), 1.86−1.50 (m, 10H). IR (neat, cm^{-1}): 3550−3150 (br). LRMS (*m*/*z*, relative intensity): 254 (M^+, 0.01), 237 ($M^+ - OH$, 1). HRMS calculated for $C_{15}H_{25}O_2$ ($M^+ - OH$): 237.1854, observed 237.1857. Anal. Calcd for $C_{15}H_{26}O_3$: H 10.31, C 70.81, O 18.88. Found: H 10.37, C 70.73.

Oxalyl chloride (420 μL, 614 mg, 4.84 mmol) was dissolved in dichloromethane (20 mL) and cooled to −78 °C. Dimethyl sulfoxide (660 μL, 727 mg, 9.30 mmol) was added, and the solution was stirred at −78 °C for 15 min. The alcohol from **12** (947 mg, 3.72 mmol) in dichloromethane (20 mL) was added via cannula, and the solution was stirred at −78 °C during 45 min. At −78 °C, triethylamine (2.9 mL, 2.1 g, 20.8 mmol) was added in one portion to the reaction, which was stirred for another 45 min, diluted with water (20 mL), and allowed to warm to room temperature. The layers were separated, and the aqueous phase was extracted with dichloromethane (2 × 30 mL). The combined organic portions were washed with water (2 × 20 mL) and brine (30 mL), dried over magnesium sulfate, filtered, and concentrated by rotary evaporation. The crude product was purified by flash chromatography on silica gel using a (5:95 to 15:85) solution of ethyl acetate and hexanes to yield a 1:1 mixture of inseparable diastereomers A and B of (*E*)-6-(tetrahydropyran-2-yloxy)deca-4,9-dienal (811 mg, 86%) as a colorless oil. ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm): 9.77 (t, 1H, J = 1.4 Hz), 5.90−5.73 (m, 1H), 5.69−5.49 (m, 1H + 1HA), 5.28 (dd, 1HB, J = 15.5, 8.2 Hz), 5.04−4.93 (m, 2H), 4.65−4.60 (m, 1H), 4.13−3.97 (m, 1H), 3.89−3.82 (m, 1H), 3.51−3.40 (m, 1H), 2.53 (td, 2H, J = 7.3, 1.4 Hz), 2.38 (q, 2H, J = 6.8 Hz), 2.20−2.02 (m, 2H), 1.88−1.49 (m, 8H). IR (neat, cm^{-1}): 1726. LRMS (*m*/*z*, relative intensity): 252 (M^+, 0.01), 197 ($M^+ - C_4H_7$, 56). HRMS calculated for $C_{11}H_{17}O_3$ ($M^+ - C_4H_7$): 197.1178, observed 197.1174.

Ethynylmagnesium bromide (0.5 M) (19.0 mL, 9.57 mmol) was added to a −60 °C solution of the previous aldehyde (804 mg, 3.19 mmol) in THF (30 mL), and the solution was stirred for 3 h, allowing the temperature to reach 0 °C. The reaction mixture was quenched at −60 °C with a saturated aqueous ammonium chloride solution (20 mL) and warmed to room temperature. The layers were separated, and the aqueous phase was extracted with ethyl acetate (3 × 20 mL). The combined organic portions were washed with brine (20 mL), dried over magnesium sulfate, filtered, and concentrated by rotary evaporation to yield a 1:1 mixture of two diastereomers of (*E*)-8-(tetrahydropyran-2-yloxy)-dodeca-6,11-dien-1-yn-3-ol, which was used without further purification. ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm): 5.88−5.76 (m, 1H), 5.68−5.50 (m, 1H + 1HA), 5.30 (dd, 1HB, J = 15.4, 8.3 Hz), 5.04−4.93 (m, 2H), 4.66 (t, 1H, J = 3.3 Hz), 4.42−4.35 (m, 1H), 4.09−3.82 (m, 2H), 3.52−3.43 (m, 1H), 2.48 (d, 1HB, J = 2.1 Hz), 2.46 (d, 1HA, J = 2.1 Hz), 2.31−2.03 (m, 4H), 1.89−1.49 (m, 10H). IR (neat, cm^{-1}): 3550−3100 (br). LRMS (*m*/*z*, relative intensity): 223 ($M^+ - C_4H_7$, 6). HRMS calculated for $C_{13}H_{19}O_3$ ($M^+ - C_4H_7$): 223.1334, observed 223.1332.

Jones reagent (5 mL) was added to a 0 °C solution of the previous alcohol (880 mg, 3.16 mmol) in acetone (20 mL). An excess of Jones reagent (10 mL) was added by portions over a period of 5 h. The reaction was followed by TLC. Chromium excesses were reduced with propan-2-ol (10 mL) until a green color persisted. Water (15 mL) was added, and the acetone was removed by rotary evaporation. The aqueous mixture was extracted with diethyl ether (3 × 30 mL). The combined organic portions were washed with brine (40 mL), dried over magnesium sulfate, filtered, and concentrated by rotary evaporation. The crude product was purified by flash chromatography on silica gel using a (5:95 to 10:90) solution of ethyl acetate and hexanes to yield **13** (311 mg, 52%, 2 steps) as a colorless oil. ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm): 6.79 (dt, 1H, J = 15.9, 6.6 Hz), 6.13 (dt, 1H, J = 15.9, 1.5 Hz), 5.82 (ddt, 1H, J = 17.0, 10.5, and 6.5 Hz), 5.07−4.96 (m, 2H), 3.27 (s, 1H), 2.79 (t, 2H, J = 7.2 Hz), 2.65−2.54 (m, 4H), 2.35 (q, 2H, J = 7.0 Hz). ^{13}C NMR (75.5 MHz, $CDCl_3$) δ (ppm): 199.2 (s), 185.2 (s), 143.8 (d), 137.0 (d), 130.9 (d), 115.1 (t), 80.9 (d), 79.3 (s), 43.3 (t), 39.2 (t), 27.8 (t), 25.8 (t). IR (neat, cm^{-1}): 3242, 1679. GCMS (*m*/*z*, relative intensity): 190 (M^+, 2). HRMS calculated for $C_{12}H_{14}O_2$: 190.0994, observed 190.0987. Anal. Calcd for $C_{12}H_{14}O_2$: H 7.42, C 75.75, O 16.83. Found: H 7.47, C 75.77.

Tricyclo[7.3.0.0^{2,6}]dodeca-6-en-5,12-dione (14a). Typical Procedure. 1,1′-Azobis(cyclohexanecarbonitrile) (ACCN, 11 mg, 0.04 mmol) and tributylgermanium hydride (22 μL, 21 mg, 0.09 mmol) were added to a solution of (*E*)-dodeca-6,11-dien-1-yn-3,8-dione (**13**) (54.9 mg, 0.29 mmol) in toluene (25 mL), and the solution was stirred at reflux temperature for 3 h. Three portions of tributylgermanium hydride (10 μL, 9 mg, 0.04 mmol) and ACCN (5 mg, 0.02 mmol) were added every 2 h for a total of 7 h. The reaction mixture was stirred for another 30 min and then cooled to room temperature. The solution was concentrated by rotary evaporation until 5 mL of toluene remained. The crude product was purified by flash chromatography on silica gel using a (0:100 to 20:80) solution of ethyl acetate and hexanes to yield a mixture of four inseparable compounds, which was further purified by preparative plate of silica gel with a solution of 20:80 ethyl acetate and hexanes as eluent to yield tricyclo[7.3.0.0^{2,6}]-dodeca-6-en-5,12-dione **14** as four isomers A, B, C, and D (11 mg, 20%). ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm): 6.91 (dd, 1HA, J = 7.7 et 3.0 Hz), 6.75−6.71 (m, 1HB), 6.65−6.62 (m, 1HC + 1HD), 2.98−1.07 (m, 13H). ^{13}C NMR (75.5 MHz, $CDCl_3$) δ (ppm): 218.6 (s), 216.9 (s), 212.1 (s), 211.3 (s), 205.4 (s), 204.8 (s), 204.7 (s), 204.3 (s), 142.8 (s), 141.0 (s), 140.3 (s), 138.5 (s), 134.2 (d), 132.6 (d), 131.7 (d), 131.0 (d), 56.7 (d), 52.4 (d), 48.2 (d), 47.4 (d), 41.5 (d), 41.1 (d), 39.3 (d), 38.5 (d), 37.9 (t), 37.6 (t), 37.0 (t), 36.6 (t), 36.0 (t), 35.7 (t), 35.0 (t), 34.4 (d), 34.1 (t), 33.8 (d), 32.2 (t), 31.3 (t), 31.0 (t), 29.0 (d), 28.8 (d), 28.0 (t), 27.6 (t), 27.3 (t), 27.0 (t), 26.9 (t), 26.6 (t), 25.5 (t), 25.0 (t), 24.1 (t). IR (neat, cm^{-1}): 1737, 1718. GCMS (*m*/*z*, relative intensity): 190 (M^+, 100). HRMS calculated for $C_{12}H_{14}O_2$: 190.0994, observed 190.0991.

(*E*)-Trideca-7,12-dien-2-yn-4,9-dione (13b). Propyne (1 mL, 706 mg, 17.6 mmol) was condensed in THF (30 mL) at −78 °C. *n*-Butyllithium (1.21 M) (7.8 mL, 9.3 mmol) was added dropwise, and the solution was stirred for 15 min. A solution of (*E*)-6-(tetrahydropyran-2-yloxy)deca-4,9-dienal (940 mg, 3.72 mmol) in THF (10 mL) was added via cannula, and the solution was

stirred for 1.5 h at −78 °C. The reaction mixture was quenched with a saturated solution of NH_4Cl (20 mL) and warmed to room temperature. The layers were separated, and the aqueous phase was extracted with ethyl acetate (3 × 20 mL). The combined organic portions were washed with brine (20 mL), dried over magnesium sulfate, filtered, and concentrated by rotary evaporation. The crude product was purified by flash chromatography on silica gel using a (5:95 to 20:80) solution of ethyl acetate and hexanes to yield a 1:1 mixture of inseparable diastereomers A and B of (*E*)-9-(tetrahydropyran-2-yloxy)trideca-7,12-dien-2-yn-4-ol (821 mg, 75%) as a colorless oil. ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm): 5.91−5.74 (m, 1H), 5.68−5.49 (m, 1H+1HA), 5.28 (dd, 1HB, J = 15.4, 8.3 Hz), 5.05−4.93 (m, 2H), 4.66−4.64 (m, 1H), 4.38−4.30 (m, 1H), 4.08−3.96 (m, 1H), 3.93−3.82 (m, 1H), 3.52−3.41 (m, 1H), 2.30−2.03 (m, 4H), 1.85 (d, 3H, J = 1.8 Hz), 1.83−1.49 (m, 10H). IR (neat, cm^{-1}): 3700−3150 (br). LRMS (*m*/*z*, relative intensity): 310 (MNH_4^+, 7), 292 (M^+, 1). HRMS calculated for $C_{18}H_{32}NO_3$ (MNH_4^+): 310.2382, observed 310.2388.

Jones reagent (5 mL) was added to a 0 °C solution of (*E*)-9-(tetrahydropyran-2-yloxy)trideca-7,12-dien-2-yn-4-ol (807 mg, 2.76 mmol) in acetone (30 mL). An excess of Jones reagent (10 mL) was added by portions over a period of 5 h. The reaction mixture was monitored by thin-layer chromatography. The excess chromium was reduced with propan-2-ol (10 mL) until a green color persisted. Water (20 mL) was then added, and the acetone was removed by rotary evaporation. The aqueous mixture was extracted with diethyl ether (3 × 30 mL). The combined organic portions were washed with brine (40 mL), dried over magnesium sulfate, filtered, and concentrated by rotary evaporation. The crude product was purified by flash chromatography on silica gel using a (5:95 to 12:88) solution of ethyl acetate and hexanes to yield **13b** (318 mg, 56%). ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm): 6.80 (dt, 1H, J = 15.9, 6.6 Hz), 6.11 (dt, 1H, J = 15.9, 1.3 Hz), 5.82 (ddt, 1H, J = 17.0, 10.4, and 6.5 Hz), 5.05−4.96 (m, 2H), 2.72 (t, 2H, J = 7.2 Hz), 2.63 (t, 2H, J = 7.2 Hz), 2.59−2.52 (m, 2H), 2.38−2.29 (m, 2H), 2.03 (s, 3H). ^{13}C NMR (75.5 MHz, $CDCl_3$) δ (ppm): 199.0 (s), 185.6 (s), 144.2 (d), 136.9 (d), 130.6 (d), 114.8 (t), 90.7 (s), 79.6 (s), 43.0 (t), 38.9 (t), 27.6 (t), 26.1 (t), 3.8 (q). IR (neat, cm^{-1}): 3325. GCMS (*m*/*z*, relative intensity): 204 (M^+, 6). HRMS calculated for $C_{13}H_{16}O_2$: 204.1150, observed 204.1146. Anal. Calcd for $C_{13}H_{16}O_2$: H 7.90, C 76.43, O 15.67. Found: H 7.92, C 76.49.

2-(1-Tributylstannyl-1-ethylidene)-3-(2-oxohex-5-enyl)-cyclopentanone (15b). Typical Procedure. α,α′-Azobis-(isobutyronitrile) (AIBN, 2 mg, 0.01 mmol) and tributyltin hydride (20 μL, 21 mg, 0.07 mmol) were added to a solution of **13b** (50 mg, 0.24 mmol) in benzene (8 mL), and the solution was stirred at reflux temperature during a total of 10 h. Two other portions of tributyltin hydride and AIBN were added after 2 and 6 h (20 μL and 34 μL, respectively, for Bu_3SnH and 5 mg each time for AIBN). The reaction was cooled to room temperature. The solution was concentrated by rotary evaporation until 2 mL of benzene remained. The crude product was purified by flash chromatography on silica gel using a (0:100 to 20:80) solution of ethyl acetate and hexanes to yield two separable isomers of 2-(1-tributylstannyl-1-ethylidene)-3-(2-oxohex-5-enyl)cyclopentanone (**15b**) (A: 19 mg, 15% and B: 25 mg, 21%). Isomer A: ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm): 5.80 (ddt, 1H, J = 17.0, 10.5, and 6.5 Hz), 5.07−4.96 (m, 2H), 3.62 (q, 1H, J = 7.1 Hz), 2.55−2.48 (m, 4H), 2.41−2.31 (m, 4H), 2.09 (s, 3H), 1.99−1.92 (m, 1H), 1.79−1.71 (m, 1H), 1.49−1.39 (m, 6H), 1.27 (sextet, 6H, J = 7.1 Hz), 1.00−0.80 (m, 15H). Isomer B: ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm): 5.81 (ddt, 1H, J = 17.0, 10.6 and 6.4 Hz), 5.08−4.98 (m, 2H), 2.89 (sextet, 1H, J = 4.3 Hz), 2.68−2.52 (m, 4H), 2.39−2.32 (m, 4H), 2.09−2.00 (m, 1H), 1.96 (s, 3H), 1.76 (dq, 1H, J = 13.5, 4.5 Hz), 1.51−1.40 (m, 6H), 1.30 (sextet, 6H, J = 7.2 Hz), 1.07−0.86 (m, 6H), 0.87 (t, 9H, J = 7.2 Hz). ^{13}C NMR (75.5 MHz, $CDCl_3$) δ (ppm): 208.3 (s), 202.3 (s), 171.6 (s), 142.2 (s), 136.7 (d), 115.6 (t), 43.9 (t), 42.4 (t), 37.0 (t), 33.0 (t), 29.2 (t), 29.1 (t), 27.3 (t), 26.7 (t), 24.9 (q), 13.7 (q), 11.8 (t). IR (neat, cm^{-1}): 1718. GCMS (*m*/*z*, relative intensity): 439 (M^+ − Bu, 100). HRMS calculated for $C_{21}H_{35}O_2Sn$ (M^+ − Bu): 439.1659, observed 439.1665.

***rac*-(1*R*,2*S*,6*R*,7*S*)-4-Oxa-3-oxotricyclo[5.2.1.0^{2,6}]dec-8-en-5-ol (17).** A 50 mL three-neck round-bottom flask, equipped with a 20 cm Vigreux column and a distillation system, was charged with paraffin oil (20 mL) and heated to 240 °C. Dicyclopentadiene (50 mL) was added dropwise to the hot oil while the rate of addition was regulated so that the temperature stayed over 210 °C and the top of the column was below 42 °C. Cyclopentadiene was recovered in an ice-cold flask and added (40 mL, 26.4 g, 400 mmol) to a solution of 5-hydroxy-2(5*H*)-furanone (2.0 g, 20.0 mmol) in diethyl ether (10 mL). The reaction mixture was stirred for 5.5 h at room temperature. The solvent was removed by rotary evaporation to give a white solid. The crude product was purified by flash chromatography on silica gel using a (30:70 to 80:20) solution of ethyl acetate and hexanes to yield **17** (3.14 g, 95%) as a white solid. Mp: 101−4 °C. ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm): 6.25−6.18 (m, 2H), 5.23 (s, 1H), 4.3−3.7 (bs, 1H), 3.39 (dd, 1H, J = 8.7, 4.7 Hz), 3.32 (m, 1H), 3.21 (bs, 1H), 2.95 (ddd, 1H, J = 8.7, 4.3 and 1.3 Hz), 1.63 (dt, 1H, J = 8.6, 1.5 Hz), 1.45 (d, 1H, 8.7 Hz). IR (neat, cm^{-1}): 3700−3200 (br), 1766, 1738. LRMS (*m*/*z*, relative intensity): 166 (M^+, 1.5). HRMS calculated for $C_9H_{10}O_3$: 166.0630, observed 166.0633. Anal. Calcd for $C_9H_{10}O_3$: H 6.07, C 65.04, O 28.9. Found: H 6.02, C 64.96.

1-Iodohex-5-ene. Triphenylphosphine (8.7 g, 33.2 mmol), imidazole (2.26 g, 33.2 mmol), and iodine (8.4 g, 33.2 mmol) were successively added to 5-hexen-1-ol (2.0 mL, 1.67 g, 16.6 mmol) in a mixture of diethyl ether/acetonitrile (80 mL/20 mL). The reaction mixture was stirred for 20 min. Diethyl ether (50 mL) was added, and the mixture was filtered on Celite and washed with diethyl ether (20 mL). The yellow solution recovered was washed with a saturated sodium bicarbonate solution (2 × 50 mL) and brine (50 mL), dried over magnesium sulfate, filtered, and concentrated by rotary evaporation. The crude oil was purified by flash chromatography on silica gel using hexanes to yield 1-iodohex-5-ene (3.40 g, 98%) as an oil. ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm): 5.79 (ddt, 1H, J = 17.0, 10.3, and 6.6 Hz), 5.06−4.96 (m, 2H), 3.19 (t, 2H, J = 7.0 Hz), 2.07 (q, 2H, J = 7.1 Hz), 1.84 (quintet, 2H, J = 7.1 Hz), 1.50 (quintet, 2H, J = 7.2 Hz). IR (neat, cm^{-1}): 1640. GCMS (*m*/*z*, relative intensity): 210 (M^+, 3). HRMS calculated for $C_6H_{11}I$: 209.9905, observed 209.9911.

***rac*-(*Z*)-(1*R*,2*S*,3*R*,4*S*)-2-Carboxy-3-(1,6-heptadienyl)bicyclo[2.2.1]heptane (18).** Palladium on charcoal (10%) (1.5 g) was mixed with ethyl acetate (80 mL), and the solution was stirred under hydrogen (1 atm) during 20 min. A solution of **17** (3.14 g, 18.9 mmol) in ethyl acetate (20 mL) was added, and the mixture was stirred for 3 h under a hydrogen atmosphere. The mixture was filtered on Celite and washed with ethyl acetate (50 mL). The solution was concentrated by rotary evaporation to give a white solid, which was recrystallized with hot ethyl acetate and pentane to yield *rac*-(1*R*,2*S*,6*R*,7*S*)-4-oxa-3-oxotricyclo-[5.2.1.0^{2,6}]decan-5-ol (3.15 g, 99%) as colorless crystals. Mp: 115−116 °C. ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm): 5.69 (s, 1H), 3.75−3.60 (bs, 1H), 3.11 (dd, 1H, J = 10.6, 5.6 Hz), 2.68−2.61 (m, 1H), 2.54 (m, 1H), 1.75−1.40 (m, 5H), 1.42 (dd, 1H, J = 9.6, 4.7 Hz). IR (neat, cm^{-1}): 3600−3100 (br), 1770, 1746. LRMS (*m*/*z*, relative intensity): 168 (M^+, 0.4). HRMS calculated for $C_9H_{12}O_3$: 168.0786, observed 168.0782. Anal. Calcd for $C_9H_{12}O_3$: H 7.2, C 64.26, O 28.55. Found: H 7.23, C 64.28.

Triphenylphosphine (7.5 g, 28.6 mmol) was added to 1-iodohex-5-ene (3.0 g, 14.3 mmol) in a mixture of toluene/acetonitrile (60 mL/60 mL). The reaction mixture was heated at 75 °C for 72 h, after which time it was cooled to 0 °C and solvent was removed under vacuum to give a white solid (the flask was flushed with dry nitrogen after solvent removal). A suspension of the phosphonium salt (6.7 g, 14.3 mmol) in THF (70 mL) was cooled to −78 °C. *n*-Butyllithium (1.87 M) (7.7 mL, 14.3 mmol) was added dropwise, and the solution was stirred for 1 h at −78 °C. Then a solution of *rac*-(1*R*,2*S*,6*R*,7*S*)-4-oxa-3-oxotricyclo[5.2.1.0^{2,6}]decan-5-ol (1.2 g, 7.15 mmol) in THF (10 mL) was added to the reaction mixture, and the resulting solution was stirred during 16 h at room temperature. Distilled water (20 mL) and a 1 N HCl solution (10 mL) were added, and the layers were separated. The aqueous layer was extracted with ethyl acetate (3 × 50 mL). The organic phases were combined, washed with brine (50 mL), dried over magnesium sulfate, filtered and concentrated by rotary evaporation. The crude product was purified by flash chromatography on silica gel using a (10:90 to 80:20) solution of ethyl acetate and hexanes to yield **18** (1.57 g, 94%). ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm): 5.81 (ddt, 1H, J = 17.0, 10.3, and 6.6 Hz), 5.60 (dd, 1H, J = 10.9, 9.7 Hz), 5.45 (dt, 1H, J = 10.9, 7.2 Hz), 5.04−4.93 (m, 2H), 3.06 (td,

1H, J = 10.7, 4.2 Hz), 2.90 (ddd, 1H, J = 11.8, 3.9 and 1.7 Hz), 2.52 (s, 1H), 2.20 (s, 1H), 2.09−1.94 (m, 5H), 1.73−1.65 (m, 1H), 1.51−1.32 (m, 6H). IR (neat, cm^{-1}): 3450−2450 (br), 1770, 1704. LRMS (*m*/*z*, relative intensity): 234 (M^+, 2). HRMS calculated for $C_{15}H_{22}O_2$: 234.1620, observed 234.1624. Anal. Calcd for $C_{15}H_{22}O_2$: H 9.47, C 76.87, O 13.66. Found: H 9.41, C 76.79.

***rac*-(*Z*)-(1*R*,2*S*,3*R*,4*S*)-2-Hydroxymethyl-3-(1,6-heptadienyl)bicyclo[2.2.1]heptane (19).** Lithium aluminum hydride (1.0 M) (1.7 mL, 1.66 mmol) was added dropwise to a 0 °C solution of **18** (379 mg, 1.62 mmol) in THF (15 mL). When the bubbling stopped, the mixture was allowed to warm to room temperature and stirred for 24 h. Water (10 mL) was slowly added, then a 1 N HCl solution (5 mL) was added, and the layers were separated. The aqueous layer was extracted with ethyl acetate (3 × 20 mL). The combined organic portions were washed with brine (20 mL), dried over magnesium sulfate, filtered, and concentrated by rotary evaporation to yield *rac*-(*Z*)-(1*R*,2*S*,3*R*,4*S*)-2-hydroxymethyl-3-(1,6-heptadienyl)bicyclo[2.2.1]heptane (349.4 mg, 95%) as a colorless oil, which was used without further purification. ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm): 5.80 (ddt, 1H, J = 17.0, 10.3, and 6.7 Hz), 5.60−5.47 (m, 2H), 5.04−4.94 (m, 2H), 3.66 (dd, 1H, J = 11.1, 8.1 Hz), 3.52 (dd, 1H, J = 11.2, 7.9 Hz), 2.87 (ddd, 1H, J = 12.3, 8.1 and 3.3 Hz), 2.29 (s, 1H), 2.19−2.02 (m, 5H), 1.60 (td, 1H, J = 7.3, 2.3 Hz), 1.52−1.32 (m, 8H). IR (neat, cm^{-1}): 3600−3050 (br), 1707. LRMS (*m*/*z*, relative intensity): 220 (M^+, 0.01), 202 ($M^+ - H_2O$, 1). HRMS calculated for $C_{15}H_{22}$ ($M^+ - H_2O$): 202.1721, observed 202.1720.

Molecular sieves (4 Å) (125 mg) were added to a 0 °C solution of *rac*-(*Z*)-(1*R*,2*S*,3*R*,4*S*)-2-hydroxymethyl-3-(1,6-heptadienyl)-bicyclo[2.2.1]heptane (50 mg, 0.23 mmol) in dichloromethane (3 mL), and the solution was stirred for 5 min. Pyridinium chlorochromate (54 mg, 0.25 mmol) was added to the reaction mixture, and the solution was stirred at room temperature during 1 h. Diethyl ether (5 mL) was added, and the solution was filtered on a fritted glass containing silica gel, activated charcoal, and Celite and washed with diethyl ether (15 mL). The solution was concentrated by rotary evaporation, and the crude product was purified by flash chromatography on silica gel using a (0:100 to 10:90) solution of ethyl acetate and hexanes to yield **19** (38.3 mg, 77%) as a colorless oil. ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm): 9.73 (t, 1H, J = 2.2 Hz), 5.80 (ddt, 1H, J = 17.0, 10.3, and 6.7 Hz), 5.55−5.52 (m, 2H), 5.03−4.94 (m, 2H), 3.22−3.13 (m, 1H), 2.63−2.58 (m, 2H), 2.26−2.25 (m, 1H), 2.09−2.01 (m, 4H), 1.74−1.64 (m, 2H), 1.51−1.40 (m, 6H). IR (neat, cm^{-1}): 1716. LRMS (*m*/*z*, relative intensity): 218 (M^+, 2). HRMS calculated for $C_{15}H_{22}O$: 218.1671, observed 218.1667.

***rac*-(*Z*)-(1*R*,2*S*,3*R*,4*S*)-2-(1-Oxopropynyl)-3-(1,6-heptadienyl)bicyclo[2.2.1]heptane (20).** Ethynylmagnesium bromide (0.5 M) (4.6 mL, 2.29 mmol) was added to a −78 °C solution of **19** (200 mg, 0.92 mmol) in THF (10 mL), and the solution was stirred for 4 h, during which time the temperature was allowed to reach 0 °C. The reaction mixture was quenched with a 1 N HCl solution (10 mL) and allowed to warm to room temperature. The layers were separated, and the aqueous phase was extracted with ethyl acetate (3 × 20 mL). The combine organic portions were washed with brine (20 mL), dried over magnesium sulfate, filtered, and concentrated by rotary evaporation. The crude product was purified by flash chromatography on silica gel using a (5:95 to 10:90) solution of ethyl acetate and hexanes to yield two separable diastereomers A and B of *rac*-(*Z*)-(1*R*,2*S*,3*R*,4*S*)-2-(1-hydroxy-2-propynyl)-3-(1,6-heptadienyl)-bicyclo[2.2.1]-heptane (A: 112.5 mg, 50% and B: 83.5 mg, 37%) as colorless oils. Isomer A: ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm): 5.86−5.60 (m, 3H), 5.04−4.94 (m, 2H), 4.46 (dd, 1H, J = 10.8, 2.1 Hz), 2.91 (td, 1H, J = 10.9, 4.1 Hz), 2.46−2.44 (m, 1H), 2.45 (d, 1H, J = 2.1 Hz), 2.22−2.02 (m, 6H), 1.72−1.41 (m, 8H). IR (neat, cm^{-1}): 3550−3150 (br). LRMS (*m*/*z*, relative intensity): 243 ($M^+ - 1$, 2). HRMS calculated for $C_{17}H_{23}O$: 243.1749, observed 243.1754. Anal. Calcd for $C_{17}H_{23}O$: H 9.53, C 83.89, O 6.58. Found: H 9.53, C 83.89. Isomer B: ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm): 5.81 (ddt, 1H, J = 17.0, 10.3, and 6.7 Hz), 5.47−5.44 (m, 2H), 5.03−4.93 (m, 2H), 4.29 (dd, 1H, J = 11.3, 2.0 Hz), 2.97−2.91 (m, 1H), 2.43 (s, 1H), 2.38 (d, 1H, J = 2.0 Hz), 2.23 (dd, 1H, J = 11.4, 3.4 Hz), 2.19−2.00 (m, 5H), 1.67−1.32 (m, 8H).

Molecular sieves (4 Å) (400 mg) were added to a 0 °C solution of a mixture of the isomers of the previous alcohols (167 mg, 0.68 mmol) in dichloromethane (10 mL), and the solution was stirred for 5 min. Pyridinium chlorochromate (220 mg, 1.02 mmol) was added to the reaction, and the solution was stirred at room temperature during 1 h. Diethyl ether (10 mL) was added, and the mixture was filtered on a fritted glass containing silica gel, activated charcoal, and Celite. The residue was washed with diethyl ether (20 mL). The solution was concentrated by rotary evaporation. The crude product was purified by flash chromatography on silica gel using a (0:100 to 2:98) solution of ethyl acetate and hexanes to yield a mixture of inseparable isomers of **20** (132.1 mg, 80%) as an oil (unstable). ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm): 5.85−5.74 (m, 1H), 5.55−5.32 (m, 2H), 5.04−4.93 (m, 2H), 3.19 (s, 1HB), 3.17−3.12 (m, 1H), 3.08 (s, 1HA), 2.64 (s, 1H), 2.22 (s, 1H), 2.19−2.01 (m, 4H), 1.77−1.23 (m, 9H). GCMS (*m*/*z*, relative intensity): 241 ($M^+ - 1$, 0.5).

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Supporting Information Available: ^{1}H NMR spectra of compounds **14a** (mixture of all isomers), **15** (mixture of two isomers **A** and **B**), **15** (mixture of two isomers **C** and **D**), **15** (one isomer **C**). ^{13}C NMR spectra as well as the DEPT 90 and DEPT 135 of compounds **14a** (mixture of all isomers), **15** (one isomer **C**). This material is available free of charge via the Internet at http://pubs.acs.org.

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