Part 2: Efficient strategies for the construction of variably substituted bicyclo[5.3.1]undecenones (AB-taxane ring systems) and their conversion to tricyclo[9.3.1.0^{3,8}]pentadecenones (ABC taxane ring systems) and bicyclo[2.2.2]octanones[1]

Nidia P. Villalva-Servín, Alain Laurent, and Alex G. Fallis

Abstract: The extension of our strategies for the construction of cyclic molecules containing variably substituted bicyclo[5.3.1]undecenones (AB taxane ring systems) for the synthesis of the tricyclo[9.3.1.0^{3,8}]pentadecenone (ABC taxane ring system) and bicyclo[2.2.2]octanones are described. These routes employ a multi-component coupling protocol that employs sequential magnesium-mediated carbometallation of allyl-substituted propargyl alcohols followed by diastereoselective Lewis acid catalyzed intramolecular Diels–Alder reactions (IMDA). Subsequent ring-closing metathesis (RCM) afforded the ABC taxane core structure. Enone accelerated [3,3] sigmatropic rearrangements (Cope rearrangements) generated the bicyclo[2.2.2]octanone nucleus. In the presence of a Lewis acid, the dienophile precursor underwent a tandem reaction via the adduct directly to the bicyclo[2.2.2]octanones. This is the first example of a novel enone accelerated carbocycle Cope rearrangement and provides direct access to bicyclo[2.2.2]octanones by a new route that compliments the traditional cyclohexadiene cycloaddition approach.

Key words: magnesium chelate, Lewis acid, taxanes, Diels–Alder, sigmatropic rearrangement, oxy-Cope, ring-closing metathesis, bicyclo[2.2.2]octanone.

Résumé : On décrit une extension de nos stratégies développées pour la construction de molécules cycliques contenant des bicyclo[5.3.1]undécénones (noyaux AB du taxane) portant divers substituants à la synthèse d'un tricyclo[9.3.1.0^{3,8}]pentadécénone (noyaux ABC du taxane) et de bicyclo[2.2.2]octanones. Ces voies impliquent un protocole de couplage à plusieurs composants qui fait appel à des réactions séquentielles de carbométallation catalysée par le magnésium d'alcools propargyliques portant un substituant allyle et de réactions diastéréosélectives de Diels–Alder intramoléculaires catalysées par un acide de Lewis. La réaction subséquente de métathèse de fermeture de cycle conduit au noyau fondamental ABC du taxane. Des réarrangements sigmatropiques [3,3] accélérés de l'énone (réarrangements de Cope) génèrent le noyau bicyclo[2.2.2]octanone. En présence d'un acide de Lewis, le précurseur diénophile donne lieu à une réaction en tandem, par le biais de l'adduit, qui conduit directement à la bicyclo[2.2.2]octanone. Cette réaction correspond au premier exemple d'un nouveau réarrangement de carbocycle de Cope accéléré par une énone et elle permet d'accéder directement aux bicyclo[2.2.2]octanones par une nouvelle voie qui est un complément à l'approche traditionnelle des cycloadditions au cyclohexadiène.

Mots clés : chélate magnésien, acide de Lewis, taxanes, Diels–Alder, réarrangement sigmatropique, oxy-Cope, métathèse avec cyclisation, bicyclo[2.2.2]octanone.

[Traduit par la Rédaction]

Introduction

The preceding paper provides a brief introduction to the importance of Taxol® (**1**, paclitaxel) and Taxotere® (**2**, docetaxel). It outlines briefly their utility as cancer chemotherapeutic agents and the synthetic challenge they present to organic chemists. We also described our approach to the synthesis of key AB taxane building blocks possessing the

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This paper is dedicated to Professor Edward Piers on the occasion of his 65th birthday. Presented with respect and gratitude for his contributions to organic chemistry and to our friendship.

N.P. Villalva-Servin, A. Laurent,[2] and A.G. Fallis.[3] Centre for Research in Biopharmaceuticals, Department of Chemistry, University of Ottawa, 10 Marie Curie, Ottawa, ON K1N 6N5, Canada.

[1]This article is part of a Special Issue dedicated to Professor Ed Piers.
[2]Present address: Aegera Therapeutics, Inc., 810, chemin du Golf, Nun's Island, QC H3E 1A8, Canada.
[3]Corresponding author (e-mail: afallis@science.uottawa.ca).

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bicyclo[5.3.1]undecenone skeleton. These investigations have been expanded to a synthesis of the carbocyclic ABC taxane core via a carbometallation–cycloaddition-ring-closing metathesis strategy. In addition, the Diels–Alder dienophile precursors may be converted in a tandem reaction to bicyclo[2.2.2]octanones (Fig. 1).

Carbometallation – intramolecular cycloaddition strategy

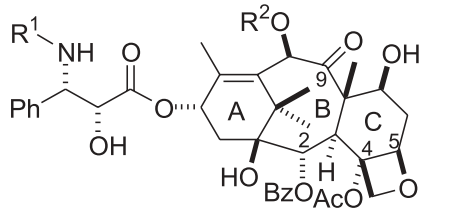
We have described our magnesium-mediated carbometallation of propargyl alcohols followed by diastereoselective Lewis acid catalyzed intramolecular Diels–Alder reactions for the preparation of bicyclo[5.3.1]undecenones (AB-taxane ring systems), as illustrated in Scheme 1. Unfortunately, as discussed in the preceding paper, the proposed [4 + 2] combinations with the family represented by **9** or **11** failed to give the desired adduct(s) **10**.

Cope rearrangements towards ring C taxanes and bicyclo[2.2.2]octanones

Clearly, a new approach was required to extend and build on this knowledge and capitalize on our ring assembly protocol. An efficient method was required to attach the C ring and assemble the complete ABC taxane nucleus. Two additional options appeared attractive, but both required repeating the synthesis from the beginning. Our initial plan was to prepare **14** from **9d**, as illustrated in Scheme 2. Based on previous studies, we have established that nucleophilic attack at the C2 carbonyl occurred from the underside of **9a**. Thus, it was anticipated that an anion-based [3,3] sigmatropic rearrangement would deliver the allyl group from the concave side of the molecule and thus establish, after protonation, the correct *trans* ring stereochemistry of the taxane natural products. Addition of allyl Grignard to **9d** should generate the bis-allyl secondary alcohol **12**. A subsequent oxy-Cope rearrangement could then be employed to install the allyl functionality in **13** for ring-closing metathesis to the tricyclic skeleton **14** (Scheme 2). However, this sequence had an inherent risk, owing to the very reactive nature of the ring A and ring B olefins. This complication affected our plans but also provided an unexpected, synthetically useful transformation, discovered earlier (1) and summarized below.

The existence of atropisomerism in taxane ring systems is well established (2, 3). Variable temperature ^{1}H NMR was investigated to determine the conformational bias in the bicyclo[5.3.1]undecene type synthon **9a**. It was anticipated that the details of the carbonyl-*exo* and carbonyl-*endo* conformers could be examined for their synthetic potential and stereochemical bias. However, rather than the conformational isomerization expected, the enone **9a** underwent a facile Cope rearrangement (commencing at ~60 °C), to give the bicyclo[2.2.2]octanone product **15a** (Scheme 3). Experimentally, this [3,3]-sigmatropic rearrangement afforded the same bicyclic ketone **15a** directly in 71% yield after 3 h in refluxing toluene (Scheme 3). The temperature required (110 °C) to effect this transformation is significantly lower than most carbocyclic rearrangements of this type (4). Consequently, this rearrangement provides an attractive method

Fig. 1. Current taxoid drugs.



Paclitaxel **1** (Taxol®) R^1 = Bz, R^2 = Ac

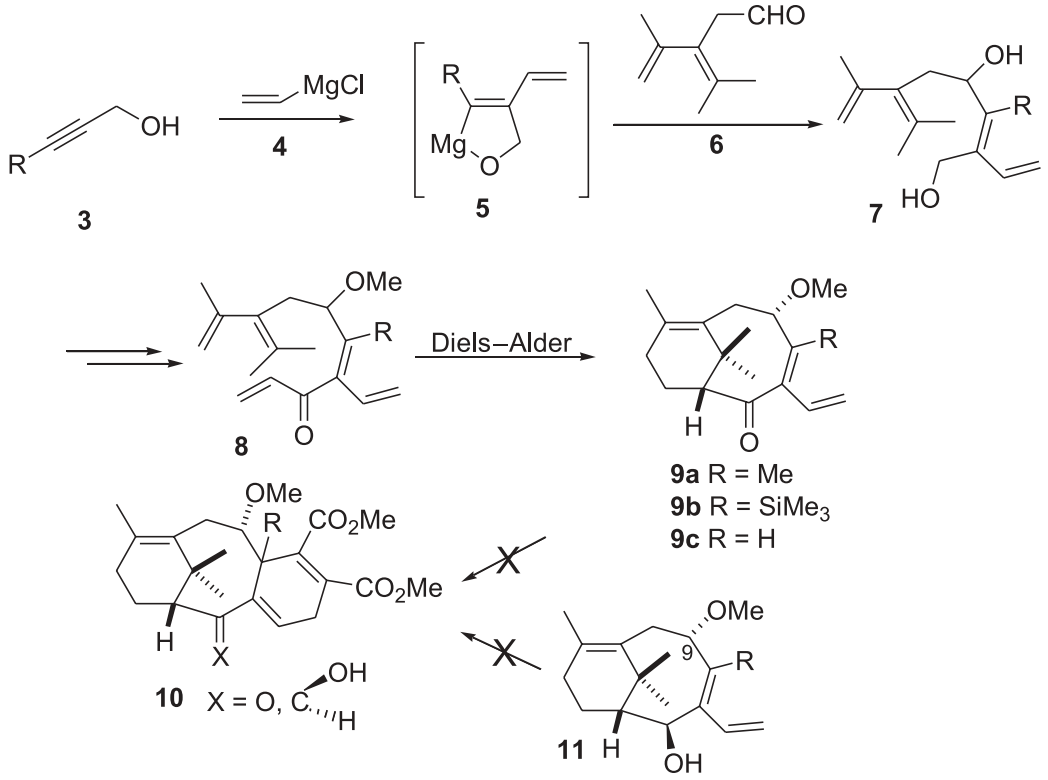
Docetaxel **2** (Taxotere®) R^1 = Boc, R^2 = H

for the preparation of densely substituted bicyclooctenones **15**. The reverse transformation from an oxy-Cope bicyclo[2.2.2]octene precursor was employed in previous approaches to the taxane AB ring system (5). The ease of the rearrangement in **9a** is a consequence of the excellent alignment of the reactive diene units in a pre-organized chair-like conformation that mimics the required transition state. Our published X-ray analysis of **9a** (1) revealed that the C3—C8 separation is 3.13 Å, a separation less than the 3.2–3.3 Å c-d separation required for enediynes to undergo spontaneous cycloaromatization at room temperature (6, 7). However, an additional, beneficial influence from the carbonyl group is also implicated. Reduction of the carbonyl in **9a** to provide alcohol **11** (Scheme 1) and subsequent protection as the *p*-methoxybenzyl ether produced compound **16**, which was stable to prolonged reflux (20 h) in toluene, and none of **17** was observed (Scheme 3). Additional evidence for the importance of the conjugated carbonyl and its electronic influence was illustrated by the ease with which the tandem rearrangement **8** to **9** to **15** occurred at 0–22 °C in the presence of a catalytic amount of Lewis acid (Et_2AlCl, 70%–92%).

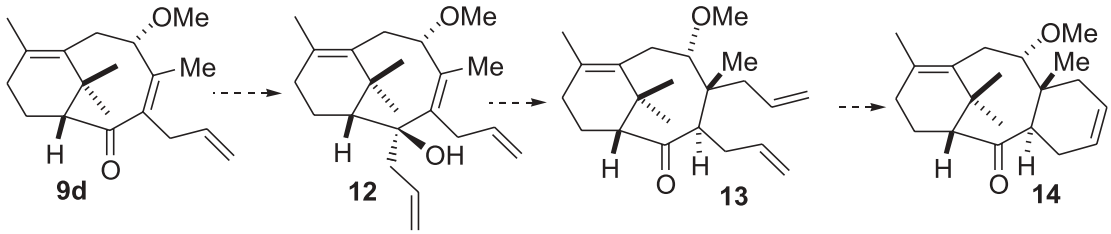
For subsequent synthetic applications this tandem conversion provides an attractive entry to highly functionalized bicyclo[2.2.2]octanones, which will complement the traditional route from cycloaddition of cyclohexadienes. These substitution patterns are difficult to achieve by traditional routes (for example, sorbiquinol, Fig. 2, (8)). This accelerating influence exerted by a conjugated carbonyl group in a carbocyclic [3,3] sigmatropic rearrangement does not appear to have been observed prior to our discovery. We are currently investigating the potential and generality of this interesting transformation.

Based on the data above, it seemed reasonable to conclude that the anionic oxy-Cope rearrangement of a potassium salt should proceed at approximately 40–50 °C (9), and thus, the carbocyclic [3,3] rearrangement would not be competitive, as a consequence of the higher energy required. The adduct **9d** was synthesized in a parallel fashion to examine the validity of this assumption, as outlined in Scheme 4. Allylation of the ketone **9d** provided the allyl alcohol **13**. However, at room temperature the potassium salt derived from treatment with potassium *tert*-butoxide did not rearrange to the desired bis-allyl ketone **18** (Scheme 5) but followed a different pathway. Instead, the loss of the allyl substituent followed by double bond migration to **19** was observed. The use of potassium hydride provided no improvement and generated the isomeric ketone **20**. The failure of these mild conditions prompted a single experiment under more forcing conditions

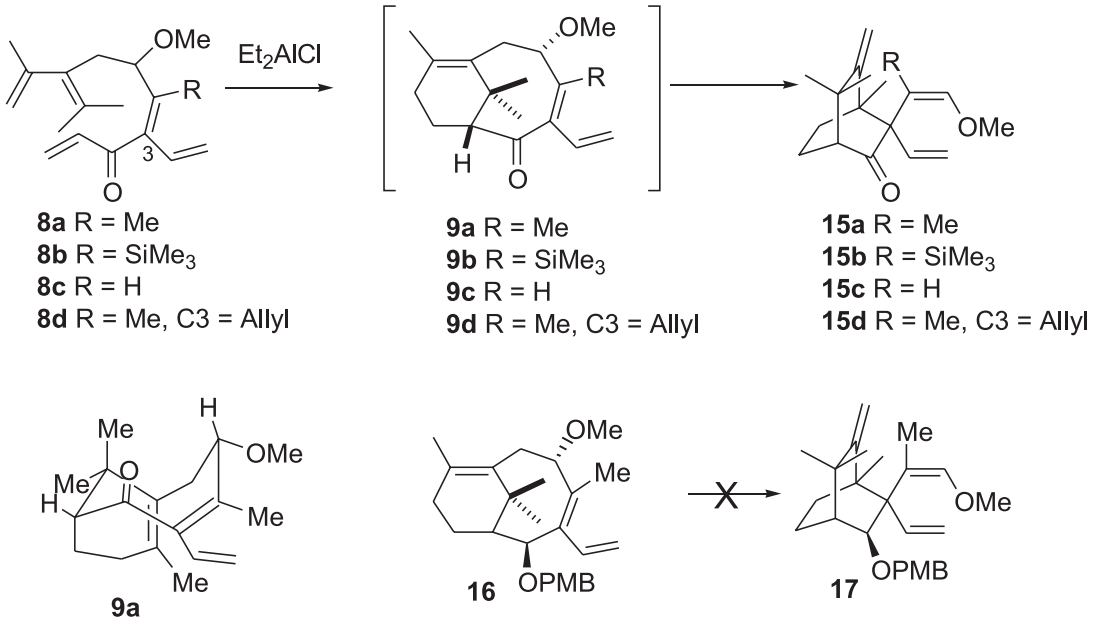
Scheme 1.



Scheme 2.



Scheme 3.



Scheme 4. Reagents and conditions: (*a*) (*i*) CH_2=$CHCH_2MgCl$, cyclohexane–THF, room temperature (rt) to 70 °C, 18 h; (*ii*) **6**, –78 °C to rt, 3 h, 40%; (*b*) TBDMSCl, DMAP, CH_2Cl_2, rt, 18 h, 81%; (*c*) NaH, MeI, THF, rt, 18 h, 89%; (*d*) TBAF, THF, rt, 2 h, 93%; (*e*) IBX, DMSO–THF, 0 °C to rt, 3 h, 86%; (*f*) CH_2=$CHMgCl$, Et_2O, –78 to 0 °C, 2 h, 50%; (*g*) IBX, DMSO–THF, 0 °C to rt, 3 h, 86%; (*h*) Et_2AlCl, CH_2Cl_2, –78 to 0 °C, 2 h, 70% or $BF_3{\cdot}(OEt)_2$, CH_2Cl_2, –78 to 10 °C, 2 h, 68%.

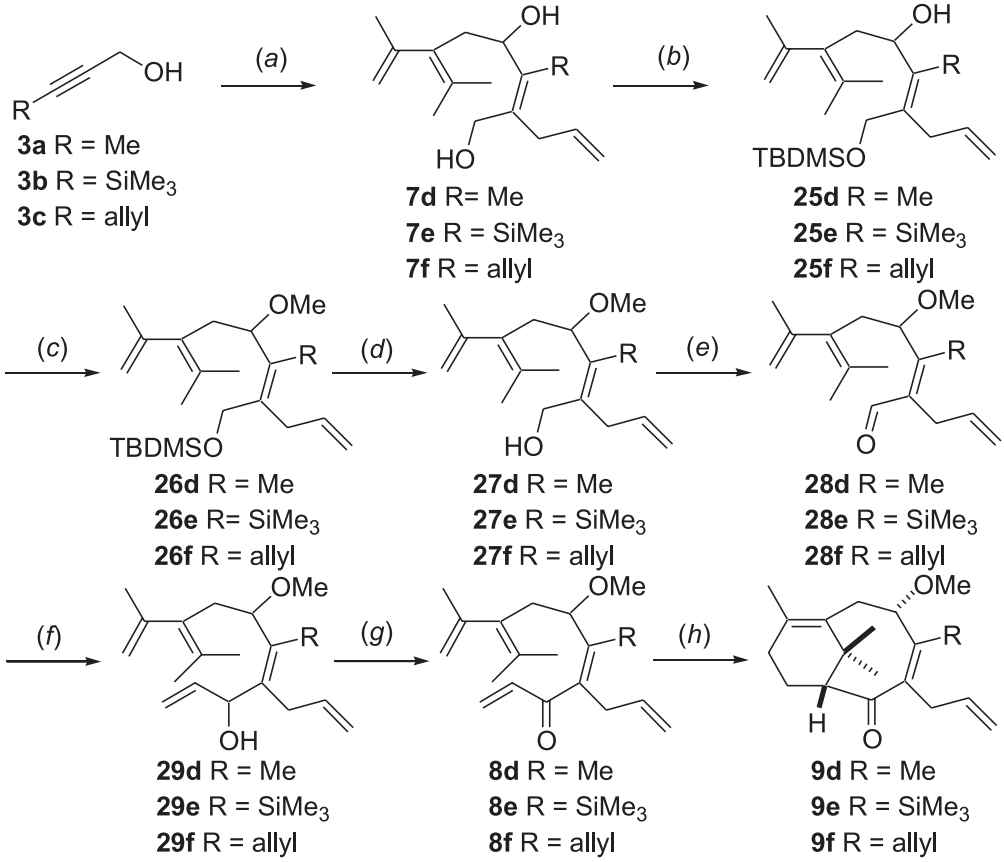
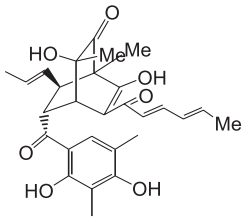


Fig. 2. Sorbiquinol.



in which treatment of **13** with 1,8-diazobiocyclo[5.4.0]undec-7-ene (DBU) under microwave irradiation also failed to produce the desired ring C precursor but gave instead the mixture of bicyclo[2.2.2]octenes **21** (7%), **22** (16%), and **23** (19%).

Ring-closing metathesis (RCM) for ring C

Despite the failure of the previous approach, the idea of installing the C ring by ring-closing metathesis was attractive. This variation for ring C is represented by the transformation **9f** to **24** in Scheme 6. One option was the introduction of a C3 allyl group by modification of the vinyl silyl group present in **9e** (Scheme 4). However, bromodesilylation failed and thus eliminated the possibility of direct palladium coupling from an advanced intermediate.

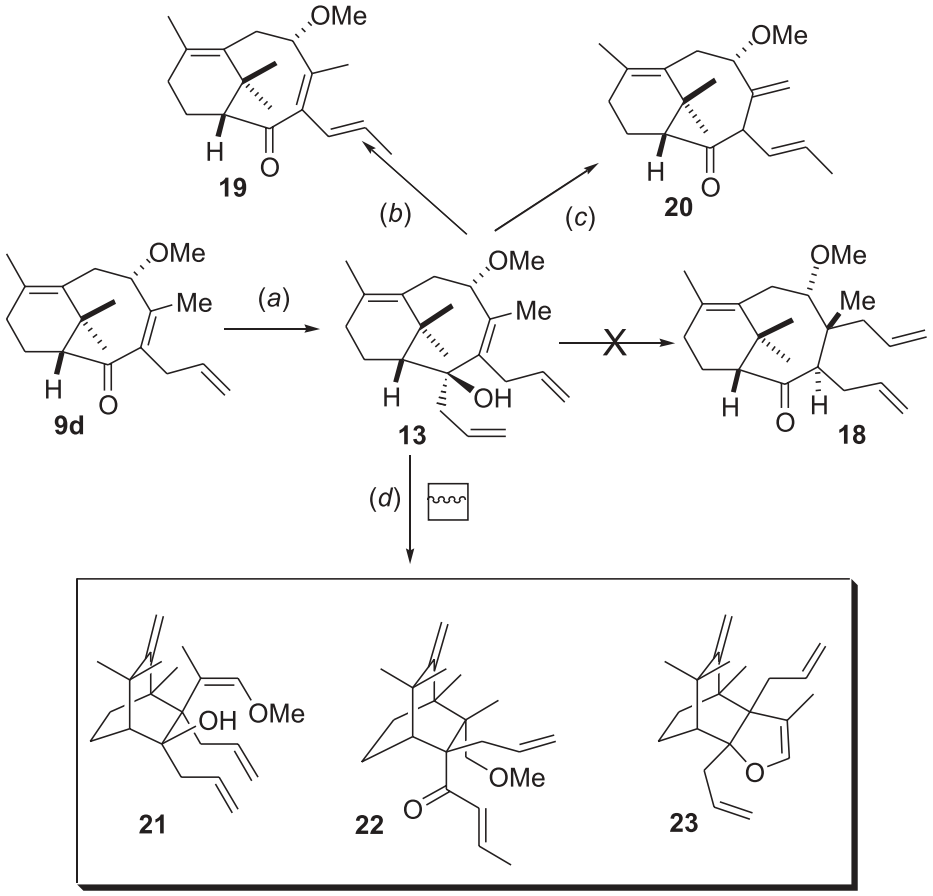
Consequently the strategy was modified (Scheme 6) to commence with an allyl-substituted propargyl alcohol **3c** followed by exposure to an allyl Grignard reagent for conversion to **8f**. Cycloaddition would generate the bicyclic ketone **9f** for conversion to the tricyclic compound **24**. The preparation of the desired Diels–Alder adduct **9f** and the precursor compounds is outlined in Scheme 4.

There appear to be two reports in which RCM approaches have been employed for the assembly of taxane AB (10) and BC (11) ring systems. However, the route in Scheme 6 for the construction of taxane ABC ring systems has not been explored. With the synthesis of the bicyclo[5.3.1]undecene **9f** completed it was anticipated that generation of the requisite cyclohexadiene **24** could be easily achieved. Indeed, treatment of **9f** with the second generation Grubbs' catalyst **30** ((4,5-dihydroIMES)(PCy_3)Cl_2Ru=CHPh) (12) gave rise to the desired tricyclo[$9.3.1.0^{3,8}$]pentadecane nucleus **24** in high yield (93%) (Scheme 7).

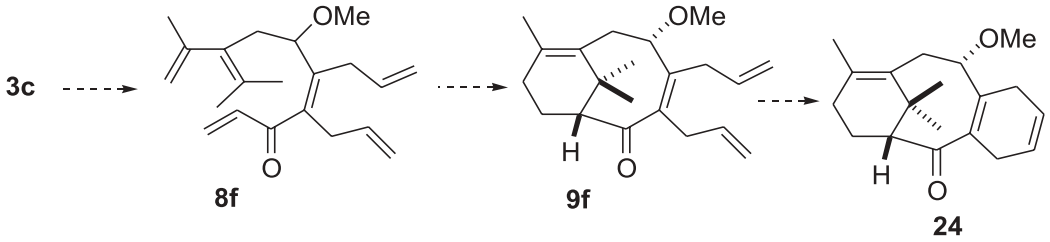
Experimental section

See preceding paper for general experimental details (13).

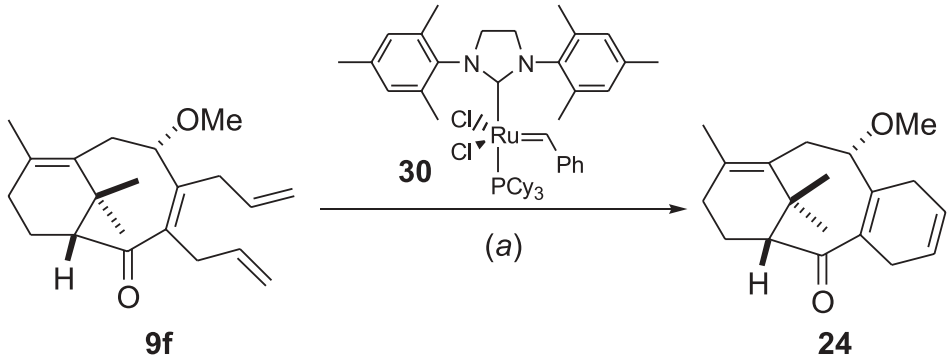
Scheme 5. Reagents and conditions: (*a*) CH_2=$CHCH_2MgCl$, Et_2O, –78 to 0 °C, 1 h, 59%; (*b*) . KO*t*Bu, DMF, 40 °C, 3 h, 51%; (*c*) KH, 18-crown-6, THF, rt, 1 h, 69%; (*d*) DBU, toluene, microwave, 220 °C, 1 h, **2**1 6%, **2**2 9%, **2**3 19%.



Scheme 6.



Scheme 7. Reagents and conditions: (*a*) **30**, CH_2Cl_2, 21 °C, 2 h, 93%.



3-Trimethylsilanyl-prop-2-yn-1-ol (3b)

Butyl lithium (189 mL, 434 mmol, 2.3 mol L^{-1} in hexane) was added to a solution of propargyl alcohol (11.0 mL, 189 mmol) in THF (300 mL) cooled to –78 °C. After 45 min, chlorotrimethylsilane (57.6 mL, 453 mmol) was added, and the solution was warmed to 21 °C for 3 h. After cooling to 0 °C, 10% aqueous sulfuric acid (250 mL) was added, and the layers were separated after 15 min, and the aqueous layer was extracted with ether (2 × 150 mL). The combined organic extracts were washed with brine (2 × 100 mL), dried ($MgSO_4$), filtered, and concentrated under reduced pressure. Purification by flash chromatography (silica gel, ether – petroleum ether) provided the title compound as a colorless oil (15.1 g, 62%). IR (neat) (cm^{-1}) ν: 3324, 2961, 2901, 2177. ^1H NMR ($CDCl_3$, 300 MHz) δ: 0.15 (s, 9H), 1.8 (s, 1H), 4.24 (s, 2H). ^{13}C NMR ($CDCl_3$, 75 MHz) δ: 0.13, 51.9, 91.0, 104.2. HR-MS (EI) *m/z* calcd. for $C_6H_{12}OSi$ ($[M]^+$): 128.0657; found: 128.0686.

3-Allyl-prop-2-yn-1-ol (3c) (14)

Propargyl alcohol (5.8 mL, 0.10 mol) was added to a stirred solution of acetone (400 mL), followed by allyl bromide (10.4 mL, 0.120 mol), potassium carbonate (27.6 g, 0.200 mol), sodium iodide (30 g, 0.20 mol), and copper iodide (19.0 g, 0.100 mol). The reaction was stirred under nitrogen at 21 °C for 5 h, quenched with 1 N HCl (120 mL), diluted with water (500 mL), and stirred for 10 min. The reaction mixture was subsequently filtered and extracted with diethyl ether (5 × 100 mL). The combined organic extracts were dried ($MgSO_4$), filtered, and concentrated under reduced pressure. The title compound was isolated as a colourless oil and purified by distillation (80–82 °C at 3 mmHg (1 mmHg = 133.322 Pa), 92%). IR (neat) (cm^{-1}) ν: 3351, 3086–2983, 2918–2872, 1420, 918, 780. ^1H NMR (C_6D_6, 300 MHz) δ: 2.33 (s, 1H), 2.94–2.98 (m, 2H), 4.24 (t, *J* = 2.2 Hz, 2H), 5.07 (ddd, *J* = 10.0, 3.3, 1.6 Hz, 1H), 5.27 (ddd, *J* = 17.0, 3.5, 1.7 Hz, 1H), 5.80 (dddd, *J* = 16.6, 10.6, 6.0, 5.6 Hz, 1H). ^{13}C NMR (C_6D_6, 75 MHz) δ: 23.2, 51.1, 81.9, 82.3, 116.1, 132.8. HR-MS (EI) *m/z* calcd. for C_6H_8O ($[M]^+$): 96.05752; found: 96.05597.

General procedure for the carbometallation of the propargylic alcohols

Vinyl- or allylmagnesium chloride (2.5 equiv.) was added to a solution of the propargylic alcohol (1.0 equiv.) in cyclohexane ([alcohol] = 1.0 mol L^{-1}) at 21 °C. The solution was heated at reflux for 20 h and cooled to –78 °C, and 4-methyl-3-vinyl-pent-3-enal **6** (0.5 equiv.) in ether ([aldehyde] = 0.3 mol L^{-1}) was added. The solution was stirred for 30 min at –78 °C, for 1 h at 0 °C, and for 1 h at 21 °C. The reaction was subsequently cooled to 0 °C, and a saturated aqueous solution of NH_4Cl added. The layers were separated, and the aqueous layer was extracted with dichloromethane. The combined organic extracts were washed with brine, dried ($MgSO_4$), filtered, and concentrated under reduced pressure. The crude material was purified by flash chromatography (silica gel, ether – petroleum ether).

2-Allyl-6-isopropenyl-3,7-dimethyl-octa-2,6-diene-1,4-diol (7d)

79% from **3a**. IR (neat) (cm^{-1}) ν: 3361, 3076, 2976, 2915, 1635, 1010, 996, 902. ^1H NMR (C_6D_6, 300 MHz) δ: 1.67 (s, 3H), 1.74 (s, 3H), 1.75 (s, 3H), 1.77 (s, 3H), 2.25 (dd, *J* = 13.9, 5.6 Hz, 1H), 2.6 (dd, *J* = 13.9, 8.1 Hz, 1H), 2.95 (d, *J* = 6.2 Hz, 2H), 3.00 (s, br, 2H), 3.93 (d, *J* = 11.6 Hz, 1H), 4.31 (d, *J* = 11.6 Hz, 1H), 4.69 (dd, *J* = 2.6, 0.8 Hz, 1H), 4.83 (dd, *J* = 8.1, 5.7 Hz, 1H), 4.99 (dd, *J* = 10.0, 2.0 Hz, 1H), 5.00 (d, 1H), 5.05 (dd, *J* = 17.1, 2.0 Hz, 1H), 5.78 (dddd, *J* = 16.9, 10.2, 6.4, 6.4 Hz, 1H). ^{13}C NMR (C_6D_6, 75 MHz) δ: 13.0, 20.3, 22.1, 22.6, 36.3, 37.2, 60.8, 69.6, 114.3, 115.2, 128.9, 132.5, 133.6, 136.1, 137.3, 146.7. HR-MS (EI) *m/z* calcd. for $C_{16}H_{24}O$ ($[M^+ – H_2O]$): 232.1827; found: 232.1829.

2-Allyl-6-isopropenyl-7-methyl-3-trimethylsilanyl-octa-2,6-diene-1,4-diol (7e)

43% from **3b**. IR (neat) (cm^{-1}) ν: 3386, 3077, 2962–2852, 1442, 1250, 1088–996, 838. ^1H NMR (C_6D_6, 500 MHz) δ: 0.31 (s, 9H), 1.66 (s, 3H), 1.69 (s, 3H), 1.73 (s, 3H), 2.10 (d, *J* = 14.2 Hz, 1H), 2.31 (s, br, 1H), 2.76 (dd, *J* = 14.2, 10.4 Hz, 2H), 3.04–3.14 (m, 2H), 4.14 (d, *J* = 11.8 Hz, 1H), 4.30 (d, *J* = 11.8 Hz, 1H), 4.65 (dd, *J* = 1.8, 0.7 Hz, 1H), 4.74 (dd, *J* = 10.4, 3.1 Hz, 1H), 4.98 (dd, *J* = 2.4, 1.4 Hz, 1H), 5.03 (ddd, *J* = 10.1, 3.0, 1.5 Hz, 1H), 5.08 (ddd, *J* = 17.1, 3.5, 1.7 Hz, 1H), 5.80 (dddd, *J* = 16.9, 10.4, 6.3, 6.3 Hz, 1H). ^{13}C NMR (C_6D_6, 125 MHz) δ: 2.2, 20.3, 22.0, 22.6, 39.0, 40.1, 61.7, 72.1, 114.2, 116.6, 129.2, 133.9, 137.1, 142.3, 146.7, 149.0. HR-MS (EI) *m/z* calcd. for $C_{18}H_{30}OSi$ ($[M^+ – H_2O]$): 290.2066; found: 290.2012.

2,3-Diallyl-6-isopropenyl-7-methyl-octa-2,6-diene-1,4-diol (7f)

64% from **3c**. IR (neat) (cm^{-1}) ν: 3303, 2955–2872, 1637, 1448, 1060, 993, 890. ^1H NMR (C_6D_6, 300 MHz) δ: 1.70 (s, 3H), 1.71 (s, 3H), 1.77 (d, 3H), 2.13 (d, br, *J* = 14.2 Hz, 2H), 2.18 (s, br, 1H), 2.62 (dd, *J* = 14.1, 10.2 Hz, 1H), 2.81 (dd, *J* = 15.6, 6.5 Hz, 1H), 2.88–2.96 (m, 3H), 4.03 (d, *J* = 11.8 Hz, 1H), 4.16 (d, *J* = 11.8 Hz, 1H), 4.54 (dd, *J* = 10.1, 3.5 Hz, 1H), 4.61 (t, br, 1H), 4.98–5.02 (m, 4H), 5.06 (dd, *J* = 5.1, 1.7 Hz, 1H), 5.70–5.87 (m, 2H). ^{13}C NMR (C_6D_6, 75 MHz) δ: 20.6, 22.4, 22.9, 33.5, 36.4, 37.7, 61.4, 71.1, 114.7, 115.7, 116.1, 130.3, 133.3, 135.4, 136.3, 137.3, 138.2, 146.4. HR-MS (EI) *m/z* calcd. for $C_{16}H_{26}O$ ($[M^+ – H_2O]$): 258.1984; found: 258.1978.

General procedure for silylation of the primary alcohols

tert-Butyldimethylsilyl chloride (1.1 equiv.) and DMAP (1.1 equiv.) were sequentially added to a solution of the diol (1.0 equiv.) in dichloromethane ([diol] = 1.0 mol L^{-1}) at 0 °C, and the solution was stirred for 18 h at 21 °C. A saturated aqueous solution of $NaHCO_3$ was then added; the layers were separated, and the aqueous layer was extracted with ether. The combined organic extracts were washed with brine, dried ($MgSO_4$), filtered, and concentrated under reduced pressure. The crude material was purified by flash chromatography (silica gel, ether – petroleum ether).

7-(*tert*-Butyl-dimethyl-silanyloxymethyl)-3-isopropylidene-2,6-dimethyl-deca-1,6,9-trien-5-ol (25d)

94% from **7d**. IR (neat) (cm^{-1}) ν: 3370, 3076, 2857, 1636, 1255, 1070, 837, 776. ^1H NMR ($CDCl_3$, 500 MHz) δ: 0.03

(s, 6H), 0.87 (s, 9H), 1.70 (s, 3H), 1.71 (s, 3H), 1.73 (s, br, 1H), 1.73 (s, 3H), 1.78 (s, 3H), 2.04 (dd, *J* = 14.0, 4.0 Hz, 1H), 2.59 (dd, *J* = 14.0, 9.6 Hz, 1H), 2.87 (dd, *J* = 14.4, 6.4 Hz, 2H), 4.02 (d, *J* = 11.4 Hz, 1H), 4.17 (d, *J* = 11.5 Hz, 1H), 4.61 (dd, *J* = 2.0, 0.8 Hz, 1H), 4.70 (dd, *J* = 9.6, 4.1 Hz, 1H), 4.95 (dd, *J* = 10.2, 1.6 Hz, 1H), 4.97 (dd, *J* = 17.4, 1.9 Hz, 1H), 4.96–4.99 (m, 1H), 5.73 (dddd, *J* = 17.2, 10.0, 6.5, 6.4 Hz, 1H). ^{13}C NMR ($CDCl_3$, 125 MHz) δ: –5.4, 12.4, 18.4, 20.1, 21.9, 22.6, 26.0, 34.8, 36.8, 60.7, 69.0, 114.0, 114.8, 129.2, 132.0, 133.0, 135.4, 135.8, 146.2. HR-MS (EI) *m/z* calcd. for $C_{22}H_{38}OSi$ ([$M^+ - H_2O$]): 346.2692; found: 346.2688.

7-(*tert*-Butyl-dimethyl-silanyloxymethyl)-3-isopropylidene-2-methyl-6-trimethylsilanyl-deca-1,6,9-trien-5-ol (25e)

71% from **7e**. IR (neat) (cm^{-1}) ν: 3371, 3043, 2956, 1433, 1259, 1084–990, 841. ^{1}H NMR ($CDCl_3$, 300 MHz) δ: 0.02 (s, 6H), 0.23 (s, 9H), 0.88 (s, 9H), 1.70 (s, 3H), 1.74 (s, 3H), 1.78 (s, 4H), 1.97 (d, *J* = 12.8 Hz, 1H), 2.65 (dd, *J* = 14.3, 10.7 Hz, 1H), 3.00 (dd, *J* = 14.1, 6.3 Hz, 1H), 3.12 (dd, *J* = 14.2, 6.5 Hz, 1H), 4.10 (d, *J* = 12.2 Hz, 1H), 4.32 (d, *J* = 12.2 Hz, 1H), 4.63 (dd, *J* = 2.4, 0.9 Hz, 1H), 4.69 (dd, *J* = 10.7, 2.9 Hz, 1H), 4.99–5.03 (m, 3H), 5.75 (dddd, *J* = 17.0, 10.1, 6.6, 6.6 Hz, 1H). ^{13}C NMR ($CDCl_3$, 75 MHz) δ: –5.4, 2.6, 18.3, 20.3, 21.9, 22.7, 25.9, 37.2, 38.6, 60.8, 71.6, 114.0, 115.8, 129.0, 133.5, 137.1, 140.3, 146.2, 148.1. Anal calcd. for $C_{24}H_{46}O_2Si_2$ (%): C 73.78, H 10.84; found: C 73.67, H 10.64.

6-Allyl-7-(*tert*-butyl-dimethyl-silanyloxymethyl)-3-isopropylidene-2-methyl-deca-1,6,9-trien-5-ol (25f)

81% from **7f**. IR (neat) (cm^{-1}) ν: 3298, 1643, 1412, 1095, 982, 885. ^{1}H NMR ($CDCl_3$, 300 MHz) δ: 0.02 (s, 6H), 0.86 (s, 9H), 1.70 (s, 3H), 1.71 (s, 3H), 1.78 (d, 3H), 1.81 (s, 1H), 1.98 (d, 1H), 2.60 (dd, *J* = 14.1, 10.3 Hz, 1H), 2.81–2.96 (m, 4H), 4.06 (d, *J* = 11.6 Hz, 1H), 4.19 (d, *J* = 11.6 Hz, 1H), 4.62 (d, 1H), 4.68 (dd, *J* = 10.3, 3.5 Hz, 1H), 4.94–5.09 (m, 5H), 5.74 (dddd, *J* = 16.9, 10.3, 6.4, 6.4 Hz, 1H), 5.86 (dddd, *J* = 16.9, 10.4, 6.2, 6.2 Hz, 1H). ^{13}C NMR ($CDCl_3$, 75 MHz) δ: –5.0, 18.7, 20.6, 22.3, 23.0, 26.3, 32.2, 34.8, 37.9, 60.7, 69.8, 114.4, 115.2, 115.6, 129.8, 133.3, 134.7, 136.6, 136.8, 138.1, 146.4. Anal calcd. for $C_{24}H_{42}O_2Si$ (%): C 73.78, H 10.84; found: C 73.67, H 10.64.

General procedure for methylation of the secondary alcohols

Sodium hydride (3.0 equiv., 60% dispersion in mineral oil) was added to a solution of the alcohol (1.0 equiv.) in THF ([alcohol] = 1.0 mol L^{-1}) at 0 °C. After 30 min, iodomethane (20.0 equiv.) was added, and the solution was stirred for 18 h at 21 °C. A saturated aqueous solution of NH_4Cl was subsequently added; the layers were separated, and the aqueous layer was extracted with dichloromethane. The combined organic extracts were washed with brine, dried ($MgSO_4$), filtered, and concentrated under reduced pressure. The crude material was purified by flash chromatography (silica gel, ether – petroleum ether).

(2-Allyl-6-isopropenyl-4-methoxy-3,7-dimethyl-octa-2,6-dienyloxy)-*tert*-butyl-dimethyl-silane (26d)

92% from **25d**. IR (neat) (cm^{-1}) ν: 3077, 2956–2820, 1255, 1100–1051, 837, 775. ^{1}H NMR ($CDCl_3$, 500 MHz) δ: 0.02 (s, 6H), 0.87 (s, 9H), 1.61 (s, 3H), 1.65 (s, 3H), 1.66 (s, 3H), 1.7 (s, 3H), 2.08 (dd, *J* = 14.3, 5.6 Hz, 1H), 2.52 (dd, *J* = 14.2, 7.8 Hz, 1H), 2.90 (d, br, 2H), 2.97 (s, 3H), 3.91 (d, *J* = 11.4 Hz, 1H), 4.17 (dd, *J* = 7.8, 5.7 Hz, 1H), 4.23 (d, *J* = 11.4 Hz, 1H), 4.56 (d, *J* = 2.7 Hz, 1H), 4.94 (dd, *J* = 16.9, 1.5 Hz, 1H), 4.95–4.96 (m, 1H), 4.97 (dd, *J* = 10.1, 1.7 Hz, 1H), 5.74 (dddd, *J* = 16.9, 10.4, 6.3, 6.3 Hz, 1H). ^{13}C NMR ($CDCl_3$, 125 MHz) δ: –5.3, –5.4, 11.9, 20.2, 21.9, 22.7, 25.9, 34.7, 35.7, 56.0, 60.3, 78.2, 113.7, 114.6, 127.3, 133.1, 133.2, 134.1, 135.9, 146.3. Anal calcd. for $C_{23}H_{42}O_2Si$ (%): C 72.95, H 11.18; found: C 73.16, H 11.12.

4-(*tert*-Butyl-dimethyl-silanyloxymethyl)-8-isopropenyl-6-methoxy-9-methyl-5-trimethylsilanyl-deca-1,4,8-triene (26e)

90% from **25e**. IR (neat) (cm^{-1}) ν: 3077–2814, 1255, 1102, 839, 775. ^{1}H NMR ($CDCl_3$, 300 MHz) δ: 0.02 (s, 6H), 0.21 (s, 9H), 0.88 (s, 9H), 1.66 (s, 3H), 1.69 (s, 3H), 1.76 (s, 3H), 1.95 (dd, *J* = 14.4, 3.2 Hz, 1H), 2.65 (dd, *J* = 14.5, 9.3 Hz, 1H), 3.04 (dd, br, 1H), 3.10 (dd, br, 1H), 3.12 (s, 3H), 3.99 (s, broad, 1H), 4.14 (d, *J* = 5.3 Hz, 1H), 4.35 (d, *J* = 11.8 Hz, 1H), 4.59 (q, 1H), 4.98 (q, 1H), 5.01 (d, *J* = 9.1 Hz, 1H), 5.02 (d, *J* = 17.9 Hz, 1H), 5.77 (dddd, *J* = 16.8, 10.5, 6.4, 6.4 Hz, 1H). ^{13}C NMR ($CDCl_3$, 75 MHz) δ: –5.5, 2.3, 18.2, 20.2, 21.9, 22.7, 25.9, 37.6, 37.7, 56.5, 60.3, 80.7, 113.6, 115.8, 126.8, 133.7, 136.9, 140.9, 146.3, 149.5.

4-(*tert*-Butyl-dimethyl-silanyloxymethyl)-8-isopropenyl-6-methoxy-9-methyl-5-allyl-deca-1,4,8-triene (26f)

89% from **25f**. IR (neat) (cm^{-1}) ν: 3077–2814, 1636, 1463, 1255, 1102–1069, 837, 775. ^{1}H NMR ($CDCl_3$, 300 MHz) δ: 0.03 (s, 6H), 0.87 (s, 9H), 1.66 (s, 6H), 1.75 (d, 3H), 1.99 (d, br, 1H), 2.60 (dd, *J* = 14.5, 9.3 Hz, 1H), 2.82–2.86 (m, br, 2H), 2.91 (dd, *J* = 6.2, 4.8 Hz, 2H), 3.09 (s, 3H), 4.02 (d, *J* = 11.4 Hz, 1H), 4.10 (dd, *J* = 9.3, 4.1 Hz, 1H), 4.25 (d, *J* = 11.4 Hz, 1H), 4.59 (d, br, 1H), 4.95–5.07 (m, 5H), 5.71–5.83 (m, 2H). ^{13}C NMR ($CDCl_3$, 75 MHz) δ: –5.0 (2), 18.7, 20.5, 22.3, 23.1, 26.3, 32.5, 34.7, 36.8, 57.0, 60.3, 79.3, 114.1, 115.4, 115.6, 127.5, 133.7, 135.2, 136.2, 136.8, 137.8, 146.6.

General procedure for deprotection of the primary alcohols

Tetrabutylammonium fluoride (1.5 equiv., 1.0 mol L^{-1} in THF) was added to a solution of silane (1.0 equiv.) in THF ([silane] = 1.0 mol L^{-1}) at 0 °C, and the resulting solution was stirred for 18 h at 21 °C. A saturated aqueous solution of NH_4Cl was then added; the layers were separated, and the aqueous layer was extracted with ether. The combined organic extracts were washed with brine, dried ($MgSO_4$), filtered, and concentrated under reduced pressure. The crude material was purified by flash chromatography (silica gel, ether – petroleum ether).

2-Allyl-6-isopropenyl-4-methoxy-3,7-dimethyl-octa-2,6-dien-1-ol (27d)

96% from **26d**. IR (neat) (cm^{-1}) ν: 3442, 3077, 2976, 2919, 2818, 1636, 1445, 1098, 996, 898. ^{1}H NMR ($CDCl_3$, 300 MHz) δ: 1.39 (s, br, 1H), 1.61 (s, 3H), 1.65 (s, 6H), 1.74 (s, 3H), 2.19 (dd, *J* = 14.0, 7.3 Hz, 1H), 2.50 (dd, *J* = 14.0,

6.4 Hz, 1H), 2.90 (t, 2H), 3.03 (s, 3H), 4.00 (d, *J* = 11.9 Hz, 1H), 4.09 (d, *J* = 11.9 Hz, 1H), 4.17 (d, *J* = 6.8 Hz, 1H), 4.56 (d, *J* = 2.0 Hz, 1H), 4.94–4.98 (m, 2H), 5.00 (ddd, *J* = 11.8, 3.3, 1.6 Hz, 1H), 5.77 (dddd, *J* = 16.7, 10.0, 6.6, 6.4 Hz, 1H). ^{13}C NMR ($CDCl_3$, 75 MHz) δ: 12.4, 20.5, 22.2, 23.0, 35.6, 36.3, 56.2, 61.2, 78.7, 114.2, 115.6, 128.6, 133.7, 134.9, 135.3, 135.9, 146.5. Anal calcd. for $C_{17}H_{28}O_2$ (%): C 77.22, H 10.67; found: C 77.36, H 10.51.

2-Allyl-6-isopropenyl-4-methoxy-7-methyl-3-trimethylsilanyl-octa-2,6-dien-1-ol (27e)

90% from **26e**. IR (neat) (cm^{-1}) ν: 3433, 3076, 2963–2814, 1636, 1443, 1250, 1100, 996, 838. ^{1}H NMR ($CDCl_3$, 300 MHz) δ: 0.19 (s, 9H), 1.65 (s, 3H), 1.68 (s, 3H), 1.75 (s, 3H), 2.04 (dd, *J* = 14.5, 3.8 Hz, 1H), 2.18 (s, br, 1H), 2.71 (dd, *J* = 14.5, 8.9 Hz, 1H), 3.04 (dd, *J* = 6.1, 1.1 Hz, 2H), 3.16 (s, 3H), 4.08 (d, *J* = 12.7 Hz, 1H), 4.11 (dd, *J* = 8.7, 4.4 Hz, 1H), 4.18 (d, *J* = 12.7 Hz, 1H), 4.60 (d, *J* = 1.9 Hz, 1H), 5.02 (d, br, *J* = 18.0 Hz, 1H), 5.05 (s, br, 1H), 5.08 (ddd, *J* = 11.0, 3.6, 1.6 Hz, 1H), 5.78 (dddd, *J* = 17.6, 9.6, 6.1, 6.1 Hz, 1H). ^{13}C NMR ($CDCl_3$, 75 MHz) δ: 2.2, 20.6, 22.3, 23.1, 37.9, 40.2, 57.2, 62.2, 81.6, 114.3, 117.1, 127.9, 134.0, 137.0, 141.2, 146.6, 149.7. Anal calcd. for $C_{19}H_{34}O_2Si$ (%): C 73.78, H 10.84; found: C 73.67, H 10.64.

2,3-Diallyl-6-isopropenyl-4-methoxy-7-methyl-octa-2,6-dien-1-ol (27f)

93% from **26f**. IR (neat) (cm^{-1}) ν: 3423, 3077, 2977–2814, 1635, 1446, 1100, 992, 909. ^{1}H NMR ($CDCl_3$, 300 MHz) δ: 1.63 (s, 6H), 1.79 (s, 3H), 1.88 (s, 1H), 2.12 (dd, *J* = 14.4, 4.6 Hz, 1H), 2.62 (dd, *J* = 14.3, 8.3 Hz, 1H), 2.74 (dd, *J* = 15.2, 7.1 Hz, 1H), 2.85 (d, *J* = 5.9 Hz, 1H), 2.90 (d, *J* = 6.0 Hz, 1H), 2.94 (d, *J* = 6.1 Hz, 1H), 3.17 (s, 3H), 4.03 (dd, *J* = 8.2, 5.0 Hz, 1H), 4.07 (d, *J* = 12.2 Hz, 1H), 4.16 (d, *J* = 12.2 Hz, 1H), 4.58 (s, 1H), 4.96–5.07 (m, 5H), 5.68–5.85 (m, 2H). ^{13}C NMR ($CDCl_3$, 75 MHz) δ: 20.5, 22.3, 23.0, 33.5, 36.1, 36.6, 57.2, 61.4, 80.2, 114.3, 115.8, 116.2, 128.2, 133.7, 136.1, 136.4, 136.9, 137.1, 146.6. Anal calcd. for $C_{19}H_{30}O_2$ (%): C 78.57, H 10.41; found: C 77.09, H 9.97.

General procedures for oxidation of the primary alcohols

Oxalyl chloride (1.5 equiv.) was added to a solution of DMSO (3.0 equiv.) in dichloromethane ([oxalyl chloride] = 1.0 mol L^{-1}) at –78 °C. After 5 min, the alcohol (1.0 equiv.) was added, and the solution was stirred for 1 h at –78 °C. Triethylamine (7.0 equiv.) was added, and the solution was warmed to 0 °C for 1 h. A saturated aqueous solution of NH_4Cl was added; the layers were separated, and the aqueous layer was extracted with ether. The combined organic extracts were washed with brine, dried ($MgSO_4$), filtered, and concentrated under reduced pressure. The crude material was purified by flash chromatography (silica gel, ether – petroleum ether).

The alcohol (1.0 equiv.) in THF was added to a solution of *o*-iodoxybenzoic acid (IBX) (1.5 equiv.) in DMSO (such that [alcohol] = 1.0 mol L^{-1}) at 0 °C. The resulting solution was stirred for 3 h at 21 °C prior to the addition of water. Following filtration, the solution was extracted with ether. The combined organic extracts were washed with brine, dried ($MgSO_4$), filtered, and concentrated. The crude material was purified by flash chromatography (silica gel, ether – petroleum ether).

2-Allyl-6-isopropenyl-4-methoxy-3,7-dimethyl-octa-2,6-dienal (28d)

90% from **27d**. IR (neat) (cm^{-1}) ν: 2924, 1671, 1443, 1100, 906. ^{1}H NMR ($CDCl_3$, 300 MHz) δ: 1.62 (s, 6H), 1.73 (s, 3H), 1.88 (s, 3H), 2.27 (dd, *J* = 14.2, 6.8 Hz, 1H), 2.60 (dd, *J* = 14.1, 7.8 Hz, 1H), 2.95 (dd, *J* = 15.1, 5.8 Hz, 1H), 3.08 (dd, *J* = 15.1, 5.8 Hz, 1H), 3.16 (s, 3H), 4.78 (t, *J* = 6.8 Hz, 1H), 4.89 (d, *J* = 17.8 Hz, 1H), 4.92 (d, *J* = 10.6 Hz, 1H), 4.97 (s, 1H), 5.67 (ddd, *J* = 16.6, 11.0, 6.0 Hz, 1H), 10.07 (s, 1H). ^{13}C NMR ($CDCl_3$, 75 MHz) δ: 14.7, 20.4, 22.3, 22.8, 30.4, 35.8, 56.9, 76.8, 115.3 (2), 129.5, 132.0, 134.8, 138.3, 145.7, 158.9, 189.4. HR-MS (EI) *m*/*z* calcd. for $C_{16}H_{23}O_2$ ($[M^+ - CH_3]$): 247.1698; found: 247.1721 or calcd. for $C_{16}H_{22}O$ ($[M^+ - CH_3OH]$): 230.1671; found: 230.1643.

2-Allyl-6-isopropenyl-4-methoxy-7-methyl-3-trimethylsilanyl-octa-2,6-dienal (28e)

73% from **27e**. IR (neat) (cm^{-1}) ν: 3077–2817, 1673, 1252, 1100, 905. ^{1}H NMR ($CDCl_3$, 300 MHz) δ: 0.24 (s, 9H), 1.65 (s, 3H), 1.66 (s, 3H), 1.74 (s, 3H), 2.14 (dd, *J* = 14.7, 3.2 Hz, 1H), 2.71 (dd, *J* = 14.7, 9.2 Hz, 1H), 3.15 (s, 3H), 3.11–3.17 (m, 2H), 4.48 (dd, *J* = 8.8, 3.2 Hz, 1H), 4.58 (d, *J* = 2.0 Hz, 1H), 4.92 (dd, *J* = 17.8, 1.6 Hz, 1H), 4.96 (s, 1H), 4.97 (dd, *J* = 10.8, 1.3 Hz, 1H), 5.77 (dddd, *J* = 16.9, 10.9, 5.6, 5.6 Hz, 1H), 10.19 (s, 1H). ^{13}C NMR ($CDCl_3$, 75 MHz) δ: 1.5, 20.6, 22.3, 23.0, 34.4, 38.7, 57.3, 80.4, 114.8, 116.2, 128.7, 132.9, 136.3, 146.1, 147.8, 193.5.

2,3-Diallyl-6-isopropenyl-4-methoxy-7-methyl-octa-2,6-dienal (28f)

93% from **27f**. .IR (neat) (cm^{-1}) ν: 3079–2821, 1671, 1446, 1101, 911. ^{1}H NMR (C_6D_6, 300 MHz) δ: 1.59 (s, 3H), 1.66 (s, 3H), 1.68 (s, 3H), 2.16 (dd, *J* = 14.4, 4.5 Hz, 1H), 2.73 (dd, *J* = 14.4, 8.6 Hz, 1H), 2.84 (dd, *J* = 14.3, 7.3 Hz, 1H), 2.91 (s, 3H), 2.99 (dd, *J* = 13.7, 5.1 Hz, 1H), 3.06 (dd, *J* = 14.3, 5.3 Hz, 1H), 3.24 (dd, *J* = 15.0, 6.2 Hz, 1H), 4.51 (dd, *J* = 8.5, 4.6 Hz, 1H), 4.66 (d, 1H), 4.95 (dd, br, 3H), 5.01 (dd, *J* = 16.7, 1.6 Hz, 2H), 5.66 (dddd, *J* = 16.8, 10.2, 6.5, 6.5 Hz, 1H), 5.82 (dddd, *J* = 16.9, 10.4, 6.3, 6.3 Hz, 1H), 10.49 (s, 1H). ^{13}C NMR (C_6D_6, 75 MHz) δ: 20.4, 22.2, 22.6, 30.6, 34.8, 37.5, 57.0, 79.0, 114.9, 115.4, 117.2, 128.8, 132.9, 134.9, 135.9, 138.3, 146.1, 157.1, 189.9. HR-MS (EI) *m*/*z* calcd. for $C_{18}H_{24}O$ ($[M^+ - CH_3OH]$): 256.1827; found: 256.1808.

General procedure for vinyl Grignard addition to the aldehydes

Vinylmagnesium chloride (2.0 equiv., 1.60 mol L^{-1} in THF) was added to a solution of the aldehyde (1.0 equiv.) in ether ([aldehyde] = 1.0 mol L^{-1}) at –78 °C. The solution was stirred for 1 h at –78 °C and for 30 min at 0 °C. A saturated aqueous solution of NH_4Cl was then added; the layers were separated, and the aqueous layer was extracted with ether. The combined organic extracts were washed with brine, dried ($MgSO_4$), filtered, and concentrated under reduced

pressure. The crude material was purified by flash chromatography (silica gel, ether – petroleum ether).

4-Allyl-8-isopropenyl-6-methoxy-5,9-dimethyl-deca-1,4,8-trien-3-ol (29d)

75% from **28d**. IR (neat) (cm^{-1}) ν: 3456, 3076, 2976, 2910, 2815, 1634, 1445, 1100, 992, 919.

Isomer A

65%. ^{1}H NMR (C_6D_6, 300 MHz) δ: 1.61 (s, br, 1H), 1.67 (s, 6H), 1.70 (s, 3H), 1.76 (s, 3H), 2.28 (dd, *J* = 14.1, 5.9 Hz, 1H), 2.71 (dd, *J* = 14.1, 7.4 Hz, 1H), 2.81 (dd, *J* = 15.7, 5.8 Hz, 1H), 2.92 (dd, *J* = 15.7, 6.0 Hz, 1H), 3.01 (s, 3H), 4.35 (t, *J* = 6.7 Hz, 1H), 4.78 (s, 1H), 4.97 (d, *J* = 10.2 Hz, 2H), 5.04 (d, *J* = 17.3 Hz, 2H), 5.26 (s, broad, 1H), 5.35 (d, *J* = 17.1 Hz, 1H), 5.82 (m, 2H). ^{13}C NMR (C_6D_6, 75 MHz) δ: 12.8, 20.4, 22.2, 22.8, 32.8, 36.2, 56.1, 71.1, 78.6, 114.2, 114.3, 114.9, 127.6, 133.9, 135.3, 135.4, 137.3, 139.5, 146.8.

Isomer B

10%. ^{1}H NMR (C_6D_6, 300 MHz) δ: 1.60 (d, br, 1H), 1.69 (s, 6H), 1.71 (s, 3H), 1.76 (s, 3H), 2.06 (dd, *J* = 14.1, 4.4 Hz, 1H), 2.76 (dd, *J* = 14.2, 8.6 Hz, 1H), 2.86 (d, *J* = 6.0 Hz, 2H), 3.06 (s, 3H), 4.38 (dd, *J* = 8.6, 4.6 Hz, 1H), 4.76 (d, *J* = 2.1 Hz, 1H), 4.96–5.03 (m, 3H), 5.07 (d, 1H), 5.29 (s, br, 1H), 5.36 (ddd, *J* = 17.1, 1.7, 1.7 Hz, 1H), 5.77 (ddd, *J* = 17.1, 10.5, 4.5 Hz, 1H), 5.84 (dddd, *J* = 16.9, 10.4, 6.3, 6.2 Hz, 1H). ^{13}C NMR (C_6D_6, 75 MHz) δ: 12.8, 20.3, 22.2, 22.9, 32.6, 36.0, 56.0, 70.8, 78.0, 114.0, 114.1, 114.9, 127.8, 133.6, 135.0, 135.5, 137.7, 139.8, 147.0. HR-MS (EI) *m/z* calcd. for $C_{19}H_{28}O$ ([M^+ – H_2O]): 272.2140; found: 272.2112.

4-Allyl-6-methoxy-9-methyl-5-trimethylsilanyl-8-vinyl-deca-1,4,8-trien-3-ol (29e)

57% from **28e**. IR (neat) (cm^{-1}) ν: 3445, 3076–2814, 1443, 1250, 1100, 851–839. ^{1}H NMR (C_6D_6, 300 MHz) δ: 0.31 (s, 9H), 1.73 (s, 3H), 1.80 (s, 6H), 2.17 (d, *J* = 14.0 Hz, 1H), 3.07 (s, 3H), 2.96–3.11 (m, 3H), 4.36 (s, br, 1H), 4.81 (d, *J* = 2.0 Hz, 1H), 4.98 (ddd, *J* = 10.2, 1.7 Hz, 1H), 5.04–5.12 (m, 3H), 5.37 (d, *J* = 17.1 Hz, 2H), 5.88 (dddd, *J* = 17.0, 10.5, 6.1, 6.1 Hz, 1H), 5.98 (ddd, *J* = 17.2, 10.4, 5.4 Hz, 1H). ^{13}C NMR (C_6D_6, 75 MHz) δ: 2.6, 20.5, 22.2, 23.0, 37.2, 38.3, 57.3, 73.6, 81.2, 114.3, 114.7, 116.2, 127.8, 128.1, 128.4, 134.2, 139.2, 140.1, 146.9.

4,5-Diallyl-8-isopropenyl-6-methoxy-9-methyl-deca-1,4,8-trien-3-ol (29f)

60% from **28f**. IR (neat) (cm^{-1}) ν: 3421, 3077–2819, 1636, 1444, 1100, 992, 909.

Isomer A

42%. ^{1}H NMR (C_6D_6, 300 MHz) δ: 1.73 (s, 3H), 1.74 (s, 3H), 1.79 (s, 3H), 1.93 (d, br, 1H), 2.22 (dd, *J* = 14.3, 3.1 Hz, 1H), 2.85 (s, 1H), 2.78–2.90 (m, 1H), 2.93–3.01 (m, 3H), 3.06 (s, 3H), 4.18 (dd, *J* = 9.3, 3.8 Hz, 1H), 4.78 (d, br, 1H), 4.99 (dd, *J* = 9.2, 1.8 Hz, 2H), 5.02–5.08 (m, 3H), 5.11 (dd, *J* = 11.9, 1.8 Hz, 1H), 5.32–5.39 (m, 2H), 5.74–5.84 (m, 2H), 5.90 (ddd, *J* = 17.2, 10.3, 4.7 Hz, 1H). ^{13}C NMR (C_6D_6, 75 MHz) δ: 20.4, 22.2, 22.9, 33.0, 34.1, 37.3, 57.1, 72.0, 80.3, 114.2, 114.4, 115.2, 115.8, 128.0, 134.0, 136.6, 136.8, 137.1, 137.9, 139.9, 146.9.

Isomer B

18%. ^{1}H NMR (C_6D_6, 300 MHz) δ: 1.38 (d, *J* = 3.6 Hz, 1H), 1.74 (s, 3H), 1.75 (s, 3H), 1.79 (s, 3H), 2.06 (d, *J* = 14.4 Hz, 1H), 2.92 (dd, *J* = 14.4, 10.0 Hz, 1H), 2.94–3.05 (m, 4H), 3.06 (s, 3H), 4.28 (dd, *J* = 10.0, 3.3 Hz, 1H), 4.79 (d, br, 1H), 4.95–5.06 (m, 5H), 5.35 (ddd, *J* = 18.0, 1.7, 1.7 Hz, 1H), 5.42 (s, br, 1H), 5.81 (ddd, *J* = 16.0, 10.3, 7.3 Hz, 2H), 5.90 (ddd, *J* = 16.7, 10.4, 6.1 Hz, 1H). ^{13}C NMR (C_6D_6, 75 MHz) δ: 20.3, 22.4, 22.9, 33.0, 34.1, 37.3, 57.1, 72.0, 80.3, 114.2, 114.4, 115.2, 115.8, 128.0, 134.0, 136.6, 136.8, 137.2, 137.9, 139.9, 146.9.

General procedures for oxidation of the secondary alcohols

Oxalyl chloride (1.5 equiv.) was added to a solution of DMSO (3.0 equiv.) in dichloromethane ([oxalyl chloride] = 1.0 mol L^{-1}) at –78 °C. After 5 min, the alcohol (1.0 equiv.) was added, and the solution was stirred for 1 h at –78 °C. Triethylamine (7.0 equiv.) was added, and the solution was warmed to 0 °C for 1 h. A saturated aqueous solution of NH_4Cl was added; the layers were separated, and the aqueous layer was extracted with ether. The combined organic extracts were washed with brine, dried ($MgSO_4$), filtered, and concentrated under reduced pressure. The crude material was purified by flash chromatography (silica gel, ether – petroleum ether).

The alcohol (1.0 equiv.) in THF was added to a solution of IBX (1.5 equiv.) in DMSO ([alcohol] = 1.0 mol L^{-1}) at 0 °C. The resulting solution was stirred for 3 h at 21 °C prior to the addition of water. Following filtration, the solution was extracted with ether. The combined organic extracts were washed with brine, dried ($MgSO_4$), filtered, and concentrated. The crude material was purified by flash chromatography (silica gel, ether – petroleum ether).

4-Allyl-8-isopropenyl-6-methoxy-5,9-dimethyl-deca-1,4,8-trien-3-one (8d)

97% from **29d**. IR (neat) (cm^{-1}) ν: 2978, 2923, 1660, 1638, 1443, 1399, 1099, 992. ^{1}H NMR (C_6D_6, 300 MHz) δ: 1.63 (s, 3H), 1.72 (s, 3H), 1.73 (s, 3H), 1.83 (s, 3H), 2.18 (dd, *J* = 14.1, 2.6 Hz, 1H), 2.72 (dd, *J* = 14.1, 9.3 Hz, 1H), 2.82 (d, *J* = 6.5 Hz, 2H), 3.05 (s, 3H), 4.10 (ddd, *J* = 9.2, 4.0, 1.6 Hz, 1H), 4.76 (d, 1H), 4.94 (dd, *J* = 10.1, 1.5 Hz, 1H), 5.01 (t, 1H), 5.03 (dd, *J* = 16.5, 1.0 Hz, 1H), 5.33 (dd, *J* = 10.4, 1.5 Hz, 1H), 5.66 (dddd, *J* = 16.8, 10.3, 6.4, 6.4 Hz, 1H), 5.95 (dd, *J* = 17.5, 1.5 Hz, 1H), 6.30 (dd, *J* = 17.5, 10.4 Hz, 1H). ^{13}C NMR (C_6D_6, 75 MHz) δ: 11.9, 20.3, 22.2, 22.8, 34.9, 35.8, 56.4, 80.3, 114.2, 116.2, 127.7, 129.0, 133.6, 134.5, 136.1, 137.3, 139.9, 146.7, 197.6. HR-MS (EI) *m/z* calcd. for $C_{19}H_{28}O_2$ ([$M]^+$): 288.2089; found: 288.2056 or calcd. for $C_{18}H_{24}O$ ([M^+ – CH_3OH]): 256.1827; found: 256.1837.

4-Allyl-8-isopropenyl-6-methoxy-9-methyl-5-trimethysilanyl-deca-1,4,8-trien-3-one (8e)

83% from **29e**. IR (neat) (cm^{-1}) ν: 3075–2821, 1664, 1251, 1102, 852–840. ^{1}H NMR (C_6D_6, 300 MHz) δ: 0.31 (s, 9H), 1.74 (s, 3H), 1.78 (s, 3H), 1.82 (s, 3H), 2.13 (d, *J* =

14.0 Hz, 1H), 2.88 (dd, *J* = 14.3, 10.5 Hz, 1H), 3.04 (s, 3H), 3.11 (d, br, 2H), 4.01 (dd, *J* = 10.4, 2.9 Hz, 1H), 4.75 (d, *J* = 2.3 Hz, 1H), 4.94–5.05 (m, 3H), 5.34 (dd, *J* = 10.4, 1.1 Hz, 1H), 5.69 (dddd, *J* = 16.9, 10.2, 6.7, 6.7 Hz, 1H), 5.91 (dd, *J* = 17.0, 1.1 Hz, 1H), 6.23 (dd, *J* = 17.6, 10.4 Hz, 1H). ^{13}C NMR (C_6D_6, 75 MHz) δ: 2.0, 20.5, 22.2, 22.9, 37.6, 38.7, 57.0, 83.0, 114.2, 117.5, 127.4, 128.9, 134.0, 134.7, 137.5, 142.5, 146.7, 150.3, 199.5.

4,5-Diallyl-8-isopropenyl-6-methoxy-9-methyl-deca-1,4,8-trien-3-one (8f)

72% from **29f**. IR (neat) (cm^{-1}) ν: 3077–2823, 1662, 1637, 1102, 991, 897. ^{1}H NMR (C_6D_6, 300 MHz) δ: 1.62 (s, 6H), 1.69 (s, 3H), 1.98 (d, *J* = 14.5 Hz, 1H), 2.59 (dd, *J* = 14.5, 10.0 Hz, 1H), 2.89 (d, *J* = 6.6 Hz, 2H), 3.03 (s, 3H), 2.90–3.10 (m, 2H), 3.73 (dd, *J* = 10.0, 3.1 Hz, 1H), 4.51 (d, *J* = 2.4 Hz, 1H), 4.91 (s, 1H), 4.99 (d, *J* = 9.6 Hz, 1H), 5.04 (d, *J* = 16.9 Hz, 1H), 5.05 (d, *J* = 9.8 Hz, 1H), 5.11 (d, *J* = 17.2 Hz, 1H), 5.69 (dddd, *J* = 17.1, 10.5, 6.9, 6.9 Hz, 1H), 5.93 (dddd, *J* = 17.1, 10.5, 6.7, 6.7 Hz, 1H), 5.89 (d, *J* = 10.4 Hz, 1H), 6.10 (d, *J* = 17.5 Hz, 1H), 6.38 (dd, *J* = 17.6, 10.4 Hz, 1H). ^{13}C NMR (C_6D_6, 75 MHz) δ: 20.4, 22.3, 22.9, 31.9, 35.3, 36.1, 57.3, 81.0, 114.2, 116.4, 117.2, 127.8, 130.2, 133.4, 134.5, 136.3, 137.3, 138.0, 139.5, 146.3, 199.9. HR-MS (EI) *m*/*z* calcd. for $C_{21}H_{30}O_2$ ($[M]^+$): 314.2246; found: 314.2261.

General procedures for Diels–Alder cyclizations

Diethylaluminum chloride (1.1 equiv., 1.0 mol L^{-1} in hexane) was added to a solution of ketone (1.0 equiv.) in dichloromethane ([ketone] = 1.0 mol L^{-1}) at –78 °C. The solution was slowly warmed to 0 °C and, after 5 min, cooled to –78 °C. A saturated aqueous solution of $NaHCO_3$ was added; the layers were separated, and the aqueous layer was extracted with ether. The combined organic extracts were washed with brine, dried ($MgSO_4$), filtered, and concentrated under reduced pressure. The crude material was purified by flash chromatography (silica gel, ether – petroleum ether).

Borontrifluoride etherate (1.0 equiv.) was added to a solution of ketone (1.0 equiv.) in dichloromethane (such that [ketone] = 1.0 mol L^{-1}) at –78 °C, and the solution was stirred for 2 h. A saturated aqueous solution of $NaHCO_3$ was then added; the layers were separated, and the aqueous layer was extracted with ether. The combined organic extracts were washed with brine, dried ($MgSO_4$), filtered, and concentrated under reduced pressure. The crude material was purified by flash chromatography (silica gel, ether – petroleum ether).

3-Allyl-5-methoxy-4,8,11,11-tetramethyl-bicyclo[5.3.1]-undeca-3,7-dien-2-one (9d)

72% from **8d**. IR (neat) (cm^{-1}) ν: 3077–2824, 1669, 1464, 1103. ^{1}H NMR (C_6D_6, 300 MHz) δ: 0.89 (s, 3H), 1.22 (s, 3H), 1.35 (s, 3H), 1.58 (s, 3H), 1.61–1.69 (m, 2H), 1.74–1.82 (m, 1H), 2.12–2.23 (m, 1H), 2.43–2.51 (m, 2H), 2.52–2.64 (m, 2H), 2.87 (dd, *J* = 15.8, 6.6 Hz, 1H), 3.06 (s, 3H), 4.05 (dd, *J* = 11.1, 6.3 Hz, 1H), 4.98 (ddd, *J* = 10.0, 3.3, 1.6 Hz, 1H), 5.06 (ddd, *J* = 17.0, 3.5, 1.7 Hz, 1H), 5.83 (dddd, *J* = 16.8, 10.2, 6.5, 6.5 Hz, 1H). ^{13}C NMR (C_6D_6, 75 MHz) δ: 12.1, 19.2, 21.6, 25.1, 28.5, 28.8, 35.6, 36.4, 37.9, 57.6, 63.0, 82.3, 115.8, 131.5, 132.2, 134.0, 135.2, 138.8, 213.4. HR-MS (EI) *m*/*z* calcd. for $C_{19}H_{28}O_2$ ($[M]^+$): 288.2089; found: 288.2078.

3-Allyl-5-methoxy-4,8,11,11-trimethyl-4-trimethylsilanyl-bicyclo[5.3.1]undeca-3,7-dien-2-one (9e)

65% from **8e**. IR (neat) (cm^{-1}) ν: 3074–2819, 1667, 1464, 1245, 1128–1095, 841. ^{1}H NMR (C_6D_6, 300 MHz) δ: 0.36 (s, 9H), 0.92 (s, 3H), 1.22 (s, 3H), 1.34 (s, br, 1H), 1.47 (s, 3H), 1.63–1.76 (m, 2H), 2.16–2.22 (m, 1H), 2.32 (t, *J* = 11.8 Hz, 1H), 2.43 (d, *J* = 5.9 Hz, 1H), 2.56–2.65 (m, 2H), 3.06 (s, 3H), 3.25 (dd, *J* = 16.1, 6.0 Hz, 1H), 4.15 (dd, *J* = 11.4, 5.7 Hz, 1H), 5.00 (ddd, *J* = 10.1, 3.2, 1.6 Hz, 1H), 5.09 (ddd, *J* = 17.1, 3.4, 1.7 Hz, 1H), 5.89 (dddd, *J* = 17.0, 10.1, 6.9, 6.9 Hz, 1H). ^{13}C NMR (C_6D_6, 75 MHz) δ: 3.4, 19.1, 22.4, 24.9, 28.7, 28.9, 35.8, 37.6, 38.4, 57.5, 63.0, 86.1, 116.4, 133.2, 133.4, 135.5, 136.2, 152.7, 213.8. HR-MS (EI) *m*/*z* calcd. for $C_{21}H_{34}O_2Si$ ($[M]^+$): 346.2328; found: 346.2339.

3,4-Diallyl-5-methoxy-8,11,11-trimethyl-bicyclo[5.3.1]-undeca-3,7-dien-2-one (9f)

68% from **8f**. IR (neat) (cm^{-1}) ν: 3076, 2934–2827, 1672, 1637, 1448, 1098, 911. ^{1}H NMR (C_6D_6, 300 MHz) δ: 0.89 (s, 3H), 1.21 (s, 3H), 1.34 (s, 3H), 1.67–1.75 (m, 2H), 1.80 (s, br, 1H), 2.13–2.20 (m, 1H), 2.35 (t, *J* = 11.8 Hz, 1H), 2.44 (d, *J* = 6.4 Hz, 1H), 2.59 (d, *J* = 6.8 Hz, 1H), 2.63 (d, *J* = 6.7 Hz, 1H), 2.70 (d, *J* = 6.0 Hz, 1H), 3.05–3.07 (m, 2H), 3.11 (s, 3H), 4.08 (dd, *J* = 11.0, 6.1 Hz, 1H), 4.97 (d, *J* = 10.5 Hz, 1H), 4.99–5.03 (d, br, 2H), 5.14 (d, *J* = 17.3 Hz, 1H), 5.81–5.98 (m, 2H). ^{13}C NMR (C_6D_6, 75 MHz) δ: 18.8, 21.6, 25.0, 28.6, 28.6, 31.7, 35.9, 36.3, 37.9, 58.6, 63.0, 82.2, 115.1, 116.4, 131.8, 132.4, 134.0, 135.7, 137.1, 141.0, 214.5. HR-MS (EI) *m*/z calcd. for $C_{21}H_{30}O_2$ ($[M]^+$): 314.2246; found: 314.2255.

5-Methoxy-4,8,11,11-tetramethyl-3-propenyl-bicyclo[5.3.1]undeca-3,7-dien-2-one (19)

Potassium *tert*-butoxide (0.042 g, 0.37 mmol) was added to a solution of **13** (0.081 g, 0.24 mmol) in DMF (10 mL) at 21 °C, and the solution was subsequently warmed to 40 °C. After stirring for 3 h, the suspension was filtered, neutralized, and extracted with ether (2 × 30 mL). The combined organic extracts were washed with brine (2 × 30 mL), dried ($MgSO_4$), filtered, and concentrated under reduced pressure. Purification by flash chromatography (silica gel, ether – petroleum) provided the title compound as a white solid (0.041 g, 51%). IR (neat) (cm^{-1}) ν: 3025–2819, 1663, 1456–1438, 1101, 961. ^{1}H NMR (C_6D_6, 300 MHz) δ: 0.94 (s, 3H), 1.29 (s, 3H), 1.40 (s, 3H), 1.51 (d, *J* = 6.5 Hz, 3H), 1.52 (s, 3H), 1.70 (s, 3H), 1.66–1.80 (m, 1H), 1.81–1.97 (m, 2H), 2.17 (t, br, 1H), 2.53–2.57 (m, 2H), 2.62 (dd, br, 1H), 3.04 (s, 3H), 4.15 (dd, *J* = 10.9, 6.6 Hz, 1H), 5.51 (dd, *J* = 15.8, 6.7 Hz, 1H), 6.24 (dd, *J* = 15.8, 1.7 Hz, 1H). ^{13}C NMR (C_6D_6, 75 MHz) δ: 12.2, 18.7, 19.9, 21.7, 25.2, 28.2, 29.2, 35.6, 38.0, 57.7, 63.3, 82.4, 126.7, 128.4, 131.8, 132.0, 134.5, 141.2, 212.8. HR-MS (EI) *m*/*z* calcd. for $C_{19}H_{28}O_2$ ($[M]^+$): 288.2089; found: 288.2076.

5-Methoxy-8,11,11-trimethyl-4-methylene-3-propenyl-bicyclo[5.3.1]undec-7-en-2-one (20)

Potassium hydride (0.240 g, 2.10 mmol, 35% in mineral

oil) was washed with pentane (3 × 1 mL) and suspended in THF (2 mL). The resultant mixture was treated with iodine (0.053 g, 0.21 mmol) in THF (0.5 mL). After 15 min, 18-crown-6 (0.554 g, 2.10 mmol) and alcohol **13** (0.120 g, 0.420 mmol) in THF (1 mL) were sequentially added, and the resultant mixture was stirred for 1 h at 21 °C. The reaction was then cooled to –78 °C and quenched with ethanol (2 mL). A saturated aqueous solution of NH_4Cl (10 mL) and ether (10 mL) were added; the layers were separated, and the aqueous layer was extracted with ether (2 × 30 mL). The combined organic extracts were washed with brine (2 × 30 mL), dried ($MgSO_4$), filtered, and concentrated under reduced pressure. Purification by flash chromatography (silica gel, petroleum ether – ether) provided the title compound as a colorless oil (0.083 g, 69%). IR (neat) (cm^{-1}) ν: 2950, 1705, 1640. ^1H NMR (C_6D_6, 300 MHz) δ: 0.95 (s, 3H), 1.11 (s, 3H), 1.52 (dd, *J* = 6.5, 1.6 Hz, 3H), 1.54–1.68 (m, 1H), 1.70–1.82 (m, 1H), 1.91 (dd, *J* = 9.3, 1.6 Hz, 1H), 1.97 (s, 3H), 2.35 (dd, *J* = 14.5, 5.2 Hz, 2H), 2.66 (dd, *J* = 9.8, 1.7 Hz, 1H), 2.91 (s, br, 1H), 2.95 (s, 3H), 3.50 (dd, *J* = 4.9, 1.6 Hz, 1H), 4.37 (d, *J* = 9.8 Hz, 1H), 4.88 (s, 1H), 5.27 (dddd, *J* = 14.5, 7.0, 7.0, 7.0 Hz, 1H), 5.47 (s 1H), 6.17 (ddd, *J* = 15.1, 9.9, 1.7 Hz, 1H). ^{13}C NMR (C_6D_6, 75 MHz) δ: 17.7, 19.2, 23.4, 28.9, 29.1, 29.3, 33.9, 37.2, 50.5, 56.0, 63.1, 87.3, 118.6, 124.2, 131.7, 133.6, 134.3, 148.9, 210.4. HR-MS (EI) *m/z* calcd. for $C_{19}H_{28}O_2$ ($[M]^+$): 288.2089; found: 288.2090.

Carbocyclic Cope rearrangements

A solution of trienone **9** in toluene ([trieneone] = 0.05 mol L^{-1}) was heated in a sealed tube at an external temperature of 110 °C for 3 h. Following removal of the solvent under reduced pressure, the residue was purified by flash chromatography (silica gel, ether – petroleum ether).

3-(2-Methoxy-1-methyl-vinyl)-4,6,6-trimethyl-5-methylene-3-vinyl-bicyclo[2.2.2]octan-2-one (15a)

71% from **9a**. IR (neat) (cm^{-1}) ν: 2959, 2930, 17016, 1660, 1461, 1382, 1229, 1131, 764, 750, 621. ^1H NMR (C_6D_6, 500 MHz) δ: 0.99 (s, 3H), 1.00 (s, 3H), 1.15 (s, 3H), 1.55–1.71 (m, 4H), 1.84 (d, *J* = 1.3 Hz, 3H), 2.03 (d, *J* = 2.2 Hz, 1H), 3.17 (s, 3H), 4.80 (s, 1H), 4.85 (s, 1H), 5.05 (dd, *J* = 10.8, 1.3 Hz, 1H), 5.35 (dd, *J* = 17.5, 1.3 Hz, 1H), 5.87 (dd, *J* = 17.5, 10.8 Hz, 1H), 5.94 (m, 1H). ^{13}C NMR (C_6D_6, 125 MHz) δ: 13.9, 18.2, 19.1, 29.8, 30.6, 31.0, 38.3, 45.4, 56.3, 58.9, 62.4, 106.9, 114.2, 116.7, 137.0, 148.9, 161.6, 212.1. HR-MS (EI) *m/z* calcd. for $C_{18}H_{26}O_2$ ($[M]^+$): 274.1934; found: 274.1945. Anal calcd. for $C_{18}H_{26}O_2$ (%): C 78.79, H 9.55; found: C 78.75, H 9.47.

3-(2-Methoxy-1-trimethylsilanyl-vinyl)-4,6,6-trimethyl-5-methylene-3-vinyl-bicyclo[2.2.2]octan-2-one (15b)

78% from **9b**. IR (neat) (cm^{-1}) ν: 2955, 2891, 1725. ^1H NMR (C_6D_6, 500 MHz) δ: 0.43 (s, 9H), 0.99 (s, 3H), 1.03 (s, 3H), 1.10 (s, 3H), 1.16–1.22 (m, 1H), 1.53–1.60 (m, 3H), 1.98 (s, 1H), 3.07 (s, 3H), 4.79 (s, 1H), 4.83 (s, 1H), 5.09 (d, *J* = 10.7 Hz, 1H), 5.39 (d, *J* = 17.3 Hz, 1H), 5.95 (dd, *J* = 17.3, 10.7 Hz, 1H), 6.45 (s, 1H). ^{13}C NMR (C_6D_6, 125 MHz) δ: 2.9, 18.2, 19.6, 29.8, 30.3, 30.4, 37.8, 46.5, 56.4, 58.8, 61.8, 106.6, 115.8, 118.2, 139.2, 159.4, 161.0, 213.8. HR-MS (EI) *m/z* calcd. for $C_{20}H_{32}O_2Si$ ($[M]^+$): 332.2172; found: 332.2179.

3-(2-Methoxy-vinyl)-4,6,6-trimethyl-5-methylene-3-vinyl-bicyclo[2.2.2]octan-2-one (15c)

92% from **9c**. IR (neat) (cm^{-1}) ν: 2966, 2830, 1722, 1642. ^1H NMR (C_6D_6, 500 MHz) δ: 0.89 (s, 3H), 0.96 (s, 3H), 1.03 (s, 3H), 1.17–1.22 (m, 1H), 1.51–1.70 (m, 3H), 2.00 (m, 1H), 3.11 (s, 3H), 4.68 (d, *J* = 12.7 Hz, 1H), 4.85 (s, 1H), 4.87 (s, 1H), 5.09 (dd, *J* = 10.7, 1.3 Hz, 1H), 5.32 (dd, *J* = 17.3, 1.3 Hz, 1H), 5.64 (dd, *J* = 17.5, 10.7 Hz, 1H), 6.62 (d, *J* = 12.7 Hz, 1H). ^{13}C NMR (C_6D_6, 125 MHz) δ: 17.7, 18.5, 28.3, 29.4, 30.6, 37.3, 45.2, 55.8, 55.9, 58.2, 102.5, 107.3, 117.1, 136.8, 153.1, 160.4, 212.3. HR-MS (EI) *m/z* calcd. for $C_{17}H_{24}O_2$ ($[M]^+$): 260.1776; found: 260.1771.

3-Allyl-3-(2-methoxy-1-methyl-vinyl)-4,6,6-trimethyl-5-methylene-bicyclo[2.2.2]octan-2one (15d)

79% from **9d**. IR (neat) (cm^{-1}) ν: 2923, 1718, 1637. ^1H NMR ($CDCl_3$, 500 MHz) δ: 0.93 (s, 3H), 0.96 (s, 3H), 1.12 (s, 3H), 1.17–1.23 (m, 1H), 1.48 (d, *J* = 9.3 Hz, 2H), 1.64 (dd, *J* = 12.2, 3.3 Hz, 1H), 1.78 (s, 3H), 1.99 (s, 1H), 2.35 (dd, *J* = 15.5, 5.4 Hz, 1H), 2.51 (dd, *J* = 15.6, 7.3 Hz, 1H), 3.16 (s, 3H), 4.79 (d, *J* = 6.5 Hz, 2H), 4.97 (d, *J* = 17.3 Hz, 1H), 5.04 (d, *J* = 10.1 Hz, 1H), 5.79 (s, 1H), 6.25–6.38 (m, 1H). ^{13}C NMR ($CDCl_3$, 125 MHz) δ: 13.7, 19.8, 20.3, 29.5, 29.7, 30.9, 36.6, 37.3, 46.6, 56.6, 58.7, 59.0, 106.8, 110.7, 115.8, 136.7, 149.9, 160.3, 214.5. HR-MS (EI) *m/z* calcd. for $C_{19}H_{28}O_2$ ($[M]^+$): 288.2089; found: 288.2089.

2,3-Diallyl-5-methoxy-4,8,11,11-tetramethyl-bicyclo[5.3.1]undeca-3,7-dien-2-ol (13)

Allylmagnesium chloride (1.3 mL, 2.6 mmol, 1.6 mol L^{-1} in THF) was added to a solution of ketone **9d** (0.376 g, 1.3 mmol) in ether (20 mL) at –78 °C. The solution was stirred for 1 h at –78 °C and for 30 min at 0 °C. A saturated aqueous solution of NH_4Cl (30 mL) was then added; the layers were separated, and the aqueous layer was extracted with ether (2 × 30 mL). The combined organic extracts were washed with brine (2 × 30 mL), dried ($MgSO_4$), filtered, and concentrated under reduced pressure. Purification by flash chromatography (silica gel, ether – petroleum ether) provided the title compound as a viscous oil (0.253 g, 59%). IR (neat) (cm^{-1}) ν: 3458, 3052–2814, 1640, 1463, 1093, 911. ^1H NMR (C_6D_6, 300 MHz) δ: 0.99 (s, 1H), 1.04 (s, 3H), 1.27–1.35 (m, 1H), 1.43 (s, 3H), 1.64 (s, 3H), 1.67–1.69 (m, 2H), 1.76 (s, 3H), 1.79–1.84 (m, 1H), 2.18 (dd, br, 1H), 2.33 (dd, *J* = 14.0, 6.2 Hz, 1H), 2.51 (dd, *J* = 17.3, 5.7 Hz, 1H), 2.58–2.70 (m, 2H), 2.74–2.90 (m, 2H), 3.30 (s, 3H), 4.99 (dd, *J* = 17.3 Hz, 2H), 5.05 (dd, *J* = 9.6 Hz, 2H), 5.73 (dddd, *J* = 16.7, 10.4, 6.1, 4.8 Hz, 1H), 5.87 (dddd, *J* = 17.2, 10.2, 7.6, 5.8 Hz, 1H), 5.93 (dd, *J* = 11.0, 6.3 Hz, 1H). ^{13}C NMR (C_6D_6, 75 MHz) δ: 15.0, 20.8, 21.3, 28.3, 29.3, 32.8, 36.5, 38.0, 39.9, 45.8, 52.3, 57.3, 81.1, 82.4, 115.1, 119.1, 131.2, 133.2, 135.6, 135.8, 137.7, 138.5. HR-MS (EI) *m/z* calcd. for $C_{22}H_{34}O_2$ ($[M]^+$): 330.2559; found: 330.2559.

Attempted oxy-Cope rearrangement

A solution of alcohol **13** (0.119 g, 0.360 mmol) and DBU (0.110 g, 0.720 mmol) in dry, deoxygenated toluene (10 mL) was heated in a quartz tube for 1 h at 220 °C. The solution

was then cooled to 21 °C, transferred to a round-bottom flask, and concentrated under reduced pressure. The residue was purified by flash chromatography (silica gel, ether – petroleum ether) to afford the compounds **21** (7%), **22** (16%), and **23** (19%) as a mixture of white solids.

2,3-Diallyl-3-(2-methoxy-1-methyl-vinyl)-4,6,6-trimethyl-5-methylene-bicyclo[2.2.2]octan-2-ol (21)

7% from **13**. IR (neat) (cm^{-1}) ν: 3559, 3076–2827, 1637, 1467, 1098, 998, 883. ^{1}H NMR ($CDCl_3$, 500 MHz) δ: 1.18 (s, 3H), 1.26 (s, br, 2H), 1.27 (s, 3H), 1.37 (s, 3H), 1.68 (s, 3H), 1.69–1.72 (m, 2H), 1.78–1.83 (m, 1H), 2.02 (s, 1H), 2.06–2.12 (m, 1H), 2.38 (ddd, *J* = 14.5, 7.4, 7.4 Hz, 1H), 2.41 (dd, *J* = 14.5, 8.1 Hz, 1H), 2.66 (dd, *J* = 14.6, 6.5 Hz, 1H), 3.19 (s, 3H), 4.70 (s, 1H), 4.80 (s, 1H), 5.01 (dd, *J* = 10.2, 1.1 Hz, 1H), 5.08 (dd, *J* = 17.1, 1.5 Hz, 1H), 5.17 (dd, *J* = 15.7, 5.6 Hz, 1H), 5.20 (d, *J* = 9.6 Hz, 1H), 5.22 (dd, *J* = 8.4, 5.5 Hz, 1H), 5.81 (dddd, *J* = 18.0, 10.3, 7.0, 7.0 Hz, 1H), 5.96 (dddd, *J* = 18.4, 8.8, 8.8, 6.5 Hz, 1H). ^{13}C NMR ($CDCl_3$, 125 MHz) δ: 13.7, 19.5, 25.6, 30.4, 33.6, 36.6, 38.6, 38.6, 44.1, 47.7, 49.5, 55.7, 78.1, 78.8, 101.5, 116.0, 119.4, 133.6, 134.5, 136.0, 144.6, 163.3. Anal calcd. for $C_{22}H_{34}O_2$ (%): C 79.95, H 10.37; found: C 76.62, H 9.57.

1-(2-Allyl-3-methoxymethyl-3,4,6,6-tetramethyl-5-methylene-bicyclo[2.2.2]oct-2-yl)-but-2-en-1-one (22)

16% from **13**. IR (neat) (cm^{-1}) ν: 3072–2813, 1690, 1660.7, 1625, 1442, 1095, 906. ^{1}H NMR ($CDCl_3$, 500 MHz) δ: 0.93 (s, 3H), 1.04 (dd, *J* = 13.9, 4.2 Hz, 1H), 1.14 (s, 3H), 1.29 (s, 3H), 1.48 (dd, *J* = 13.9, 3.6 Hz, 1H), 1.69 (s, 3H), 1.86 (dd, *J* = 6.9, 1.6 Hz, 3H), 2.07 (dd, *J* = 12.4, 3.4 Hz, 1H), 2.27 (dd, *J* = 14.5, 3.4 Hz, 1H), 2.57 (dd, *J* = 12.3, 3.7 Hz, 1H), 3.03 (dd, *J* = 15.9, 7.2 Hz, 1H), 3.12–3.16 (m, 1H), 3.24 (s, 3H), 3.90 (d, *J* = 10.7 Hz, 1H), 4.16 (d, *J* = 10.7 Hz, 1H), 4.99 (dd, *J* = 10.1, 1.3 Hz, 1H), 5.03 (dd, *J* = 17.2, 1.6 Hz, 1H), 5.09 (d, *J* = 6.5 Hz, 2H), 5.76 (dddd, *J* = 17.2, 10.1, 7.1, 5.4 Hz, 1H), 6.14 (dd, *J* = 15.6, 3.4, 1.6 Hz, 1H), 6.80 (ddd, *J* = 15.5, 13.8, 6.8 Hz, 1H). ^{13}C NMR ($CDCl_3$, 125 MHz) δ: 18.2, 18.8, 23.1, 23.9, 30.1, 32.0, 35.1, 40.3, 41.1, 46.2, 58.1, 58.9, 72.7, 108.4, 115.1, 130.9, 133.3, 137.9, 139.1, 141.9, 162.7, 202.3. HR-MS (EI) *m*/*z* calcd. for $C_{22}H_{34}O_2$ ($[M]^+$): 330.2559; found: 330.2555.

2,6-Diallyl-5,7,9,9-tetramethyl-8-methylene-3-oxa-tricyclo[5.2.2.0^{2,6}]undec-4-ene (23)

19% from **13**. IR (neat) (cm^{-1}) ν: 3068, 3032–2867, 1671, 1631, 1154, 1120, 1002, 921, 888, 859. ^{1}H NMR ($CDCl_3$, 500 MHz) δ: 1.07 (s, 3H), 1.10 (s, 3H), 1.28 (s, 3H), 1.21–1.32 (m, 1H), 1.42–1.47 (m, 1H), 1.50 (d, *J* = 1.5 Hz, 3H), 1.56–1.65 (m, 2H), 1.70–1.81 (m, 1H), 2.44 (dd, *J* = 16.3, 8.1 Hz, 2H), 2.55–2.60 (m, 1H), 2.62–2.64 (m, 1H), 4.78 (d, *J* = 8.3 Hz, 2H), 4.98 (d, *J* = 9.8 Hz, 1H), 5.00 (d, *J* = 15.9 Hz, 1H), 5.02 (d, *J* = 17.9 Hz, 1H), 5.08 (d, *J* = 8.8 Hz, 1H), 5.90 (d, *J* = 1.3 Hz, 1H), 5.80–5.94 (m, 2H). ^{13}C NMR ($CDCl_3$, 125 MHz) δ: 11.2, 19.1, 21.6, 28.8, 31.7, 32.7, 35.2, 37.4, 42.5, 43.7, 44.3, 57.6, 94.2, 103.8, 114.1, 115.3, 117.1, 135.9, 138.6, 140.3, 163.6. HR-MS (EI) *m*/*z* calcd. for $C_{21}H_{30}O$ ($[M]^+$): 298.2297; found: 298.2305.

9-Methoxy-12,15,15-trimethyl-tricyclo[9.3.1.0^{3,8}]pentadeca-3(8),5,11-trien-2-one (24)

Grubbs' catalyst **30** ((4,5-dihydroIMES)(PCy_3)Cl_2Ru=CHPh, 5 mol%) dissolved in dichloromethane (3 mL) was added to a solution of **9f** in dichloromethane ([**30**] = 0.02 mol L^{-1}). The solution was subsequently stirred at 21 °C for 2 h, at which point the solvent was removed under reduced pressure. The residue was purified by flash chromatography to afford the title compound as a white solid (93%), mp 90 to 91 °C. IR (neat) (cm^{-1}) ν: 3031–2822, 1665, 1465, 1103, 1072, 949. ^{1}H NMR (C_6D_6, 300 MHz) δ: 0.89 (s, 3H), 1.21(s, 3H), 1.42 (s, 3H), 1.54 (dd, *J* = 10.4, 3.2 Hz, 1H), 1.63–1.78 (m, 1H), 1.82 (dd, *J* = 10.3, 3.8 Hz, 1H), 2.14 (t, br, 1H), 2.42–2.50 (m, 3H), 2.63 (ddd, *J* = 12.4, 6.3, 2.1 Hz, 1H), 2.71–2.85 (m, 2H), 2.90 (dd, br, 1H), 3.03 (s, 3H), 4.07 (dd, *J* = 10.9, 6.4 Hz, 1H), 5.47 (dd, *J* = 9.8, 2.2 Hz, 1H), 5.58 (dd, *J* = 10.1, 2.9 Hz, 1H). ^{13}C NMR (C_6D_6, 75 MHz) δ: 20.3, 21.3, 24.9, 25.3, 28.1, 28.8, 30.6, 35.5, 37.6, 57.9, 63.3, 82.4, 123.4, 124.4, 127.5, 131.9, 134.6, 136.5, 214.5. HR-MS (EI) *m*/*z* calcd. for $C_{19}H_{26}O_2$ ($[M]^+$): 286.1933; found: 286.1906.

Conclusion

We have demonstrated the utility of bis-allylpropargyl alcohol in our magnesium-mediated carbometallation protocol for the synthesis of the AB taxane ring by a *cis*-alkene tether controlled intramolecular Diels–Alder reaction, followed by closing metathesis (RCM), to generate a substituted tricyclo[9.3.1.0^{3,8}]pentadecenone (ABC taxane) ring system. We have discovered the first example of an enone accelerated Cope rearrangement. This isomerization of conjugated bicyclo[5.3.1]undecadienes provides a rapid entry into bicyclo[2.2.2]octanone skeletons that complements the more traditional [4 + 2] cyclizations from cyclohexadienes. We are examining the generality of this conjugative effect. In total, the procedures described above provide direct access to a number of useful unsaturated compounds and bicyclic ring systems, which may be employed for a variety of synthetic objectives.

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