Part 1: Efficient strategies for the construction of variably substituted bicyclo[5.3.1]undecenones (AB taxane ring systems)[1]

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Abstract: Strategies for the construction of cyclic molecules containing variably substituted bicyclo[5.3.1]undecenones (AB taxane ring systems) are described. These routes employ a multi-component coupling protocol that utilizes sequential magnesium-mediated carbometallation of propargyl alcohols and intramolecular Diels–Alder reactions (IMDA). The cycloaddition generates the key eight-membered taxane ring as a single diastereomer, induced by preferential Lewis acid (diethylaluminum chloride or boron trifluoride etherate) complexation with the cross-ring oxygens. Both the electronic nature of the dienophile and the neighbouring group non-bonded interactions contribute to the success of these cycloadditions.

Key words: magnesium chelate, Lewis acid, intramolecular Diels–Alder, cycloaddition.

Résumé : On décrit des stratégies permettant de construire des molécules cycliques contenant des bicyclo[5.3.1]undécénones (cycles AB du taxane). Ces routes font appel à un protocole de couplage à plusieurs composants qui utilise en séquence des réactions de carbométallation d'alcools propargyliques catalysées par le magnésium et des réactions de Diels–Alder intramoléculaires. La cycloaddition génère le cycle à huit chaînons du taxane sous la forme d'une seul diastéréomère en raison de la complexation préférentielle de l'acide de Lewis (chlorure de diéthylaluminium ou éthérate du trifluorure de bore) avec les atomes d'oxygène dans la partie opposée du cycle. La nature électronique du diénophile ainsi que les interactions non liées du groupe voisin jouent toutes les deux en faveur du succès de ces cycloadditions.

Mots clés : chélate magnésien, acide de Lewis, Diels–Alder intramoléculaire, cycloaddition.

[Traduit par la Rédaction]

Introduction

Taxol® (paclitaxel) and Taxotere® (docetaxel) are now established chemotherapeutic agents (selling more than $1 billion US each annually) for the treatment of ovarian and breast cancer. These drugs operate by a novel mechanism of action that differs from other spindle poisons such as vincristine. Based on a long tradition of natural products isolation and discovery, nature has provided a novel structure that represents a new chemotherapeutic lead. Thus, as previously demonstrated for penicillins and tetracyclines, modified taxoid structures have provided new understanding of the mode of action. Eventually novel compounds with improved water solubility and better therapeutic properties will be developed. We hope that eventually our own research will be able to contribute to this area with new, improved drugs. Paclitaxel **1** (Taxol®) and docetaxel **2** (Taxotere®) (Fig. 1) continue to receive increased medicinal attention because of their increased utility, particularly for mixed chemotherapy. These diterpenoids, classified as alkaloids (!), have elicited considerable interest over the last two decades, principally as a result of their proven chemotherapeutic utility and their attraction as highly challenging synthetic targets (1). The total synthesis of Taxol® has been surmounted by six different groups (2). However, new, efficient strategies for construction of the unique taxane tricyclo[9.3.1.$0^{3,8}$]pentadecane nu-

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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.

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Scheme 1.

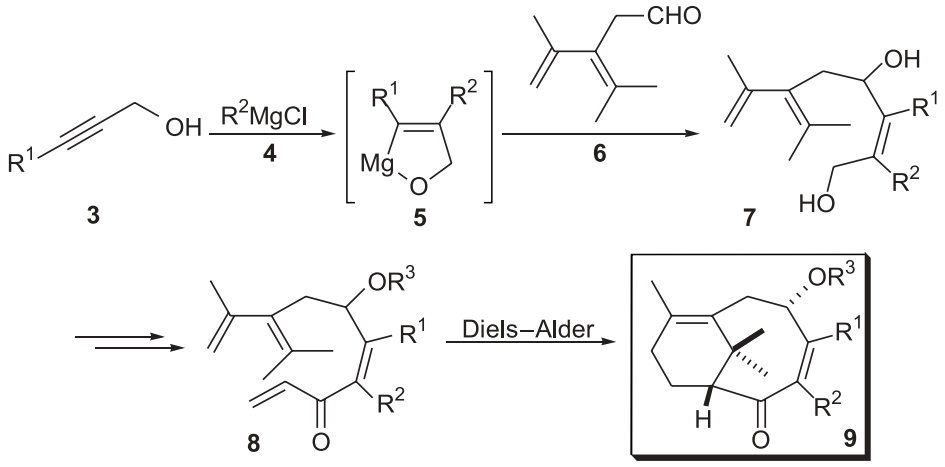
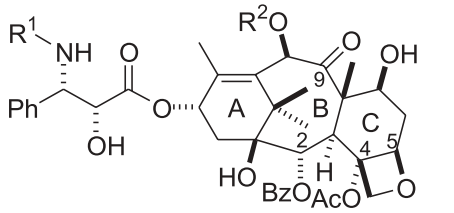


Fig. 1. Current taxoid drugs.



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

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

cleus are still required if we are to make new, improved analogues.

Carbometallation – intramolecular cycloaddition strategy

We have a long-standing interest in the area of taxane synthesis. We have examined different protocols, but particularly those that involve diverse strategies and that encompass intramolecular Diels–Alder sequences (3). We continue to develop more efficient and convergent routes for the preparation of the carbocyclic taxane skeleton via versatile approaches to the AB ring system. We wish to report the details of our recent progress, involving combinations of carbometallation reactions of propargyl alcohols and type II intramolecular Diels–Alder (IMDA) reactions (4) to generate eight-membered rings, induced by the presence of an endocyclic *cis*-akene (5). The following paper (6) describes further studies with related building blocks and their conversion to the tricyclic ABC taxane nucleus.

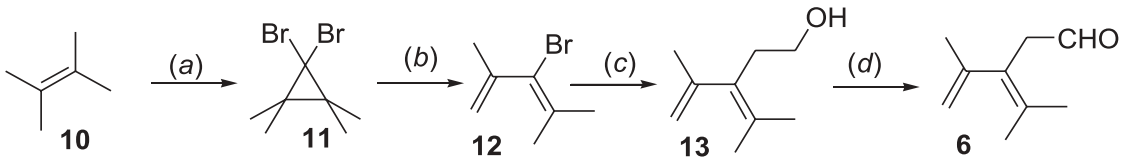
We have previously described the versatility of the magnesium-mediated carbometallation of propargyl alcohols for the assembly of several diverse structures generated in a single reaction. This three-component coupling strategy allows the direct regio- and stereocontrolled synthesis of halodienes, diene-diols, enediynes, tetraenes, tetrasubstituted alkenes, substituted furans, and 2(5*H*)-furanones (butenolides) with vinyl and related Grignard reagents (7).

We have also established the beneficial influence of "planar" double bonds and aromatic rings in the side chain, to control the stereochemistry of IMDA reactions (8). For oxygenated targets, isopropylidene acetal tether control groups direct the enantioselectivity of the adducts, especially for *cis*-decalins (9). A related concept, namely the possibility of controlling the geometry of the side chain with a *cis* double bond, appeared attractive for the construction of the eight-membered ring embedded in the bicyclo[5.3.1]undecene AB skeleton of taxoids. We envisaged that a carbometallation strategy would allow efficient access to suitable cycloaddition precursors, which in turn would lead to the rapid assembly of variably functionalized taxane AB-ring systems.

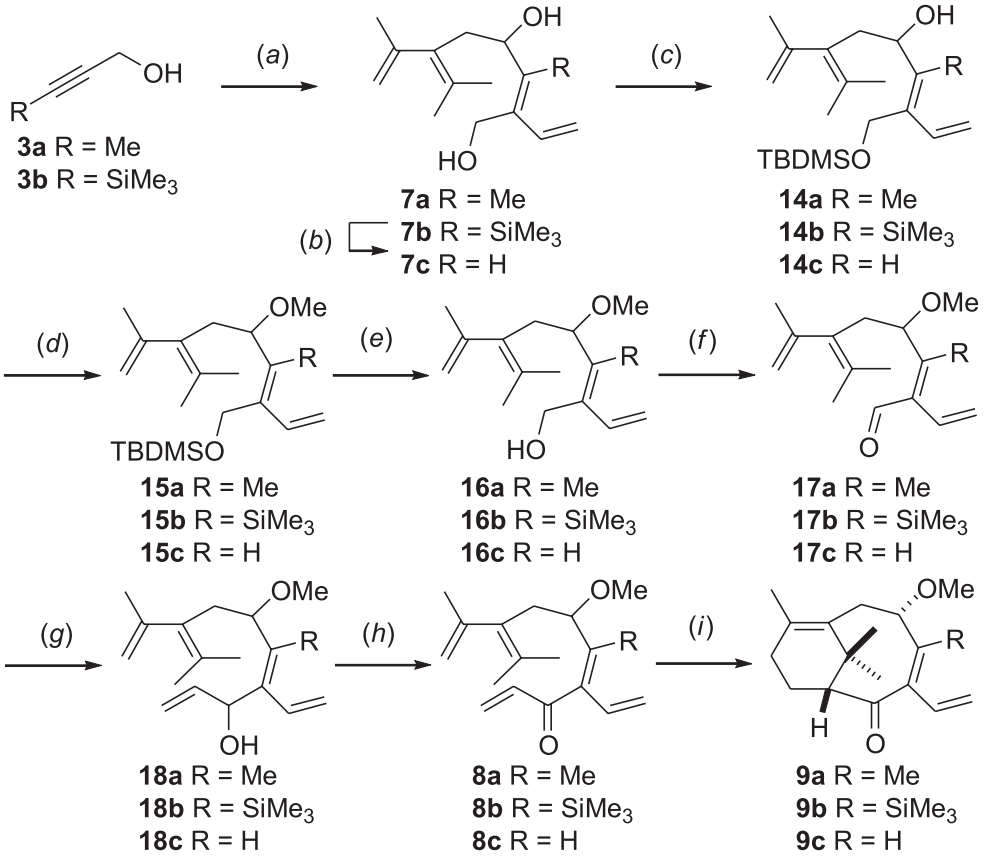
This general strategy, via the magnesium chelate **5** and the cycloaddition precursor **8**, is outlined in Scheme 1 (5). We anticipated that the synthesis of key intermediate diols of type **7** could be conducted in one pot via the addition of Grignard reagents **4** to terminally substituted propargylic alcohols **3** and subsequent trapping of the putative magnesium chelate **5** with diene aldehyde **6**. Further elaboration would allow access to Diels–Alder precursors such as **8**. These cross-conjugated dienones were expected to readily undergo intramolecular cyclization to afford the desired bicyclo[5.3.1]undecenone skeletons **9** in the presence of a Lewis acid. Molecular modeling suggested that modest stereoselection might be achieved during the cycloaddition created by the preferential complexation between the cross-ring oxygens. In view of the flexibility available for the carbometallation partners, these cores could be constructed with sufficient functionality for the eventual attachment of the C-ring by annulation, cycloaddition, or ring-closing metathesis procedures.

Current structure activity relationships (SAR) data for Taxol® have established that the C2 benzoate, the C4 acetate, and the oxetane or hydrogen bond acceptor on the "southern" perimeter of the molecule are crucial for activity. In contrast, the "northern" perimeter C7 hydroxyl and C10 acetate substituents can be omitted without compromising efficacy (1). Although not essential, the C9 hydroxyl increases activity slightly and acts as a useful handle for the formation of resolvable derivatives (10) or the introduction of solubilizing groups (11). We elected to employ diene aldehyde **6** as a source of the future C9 oxygen to take advantage of the rapid AB-ring assembly afforded by an IMDA

Scheme 2. Reagents and conditions: (*a*) *t*-BuOK, $HCBr_3$, pentane, 0 °C, 3 h, 71%; (*b*) 120–140 °C, 80%; (*c*) (*i*) *t*-BuLi, THF, –78 °C, 30 min; (*ii*) ethylene oxide, –78 °C to room temperature (rt) (22 °C), 2 h, 83%; (*d*) Dess–Martin periodinane, CH_2Cl_2, rt, 30 min, 95%.



Scheme 3. Reagents and conditions: (*a*) (*i*) CH_2=CHMgCl, cyclohexane–THF, rt (22 °C) to 70 °C, 20 h; (*ii*) **6**, –78 °C to rt, 3 h, 71%; (*b*) NaOMe, MeOH, rt to 80 °C, 2 h, 87%; (*c*) TBDMSCl, DMAP, CH_2Cl_2, rt, 18 h, 92%; (*f*) Dess–Martin periodinane, CH_2Cl_2, rt, 1 h, 89%; (*g*) CH_2=CHMgCl, Et_2O, –78 °C to 0 °C, 2 h, 97%; (*h*) Dess–Martin periodinane, CH_2Cl_2, rt, 1 h, 80%; (*i*) Et_2AlCl, CH_2Cl_2, –78 °C to 0 °C, 5 min, 72%.



strategy for **9**, while the propargylic alcohol **3** would contribute the requisite C2 oxygen.

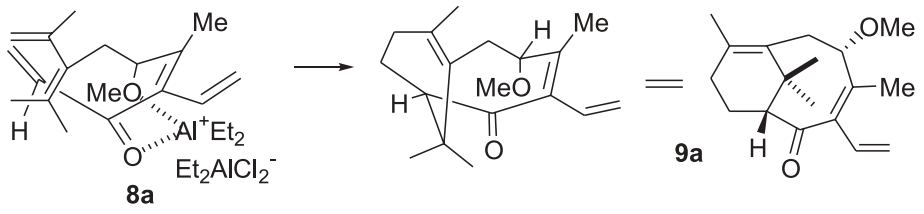
Magnesium-mediated carbometallation – intramolecular Diels–Alder studies

Diene aldehyde **6** was readily prepared in multigram quantities and 45% overall yield via our reported four-step sequence from 2,3-dimethyl-2-butene **10** (Scheme 2) (3*d*). Subsequent thermal rearrangement of the initially formed 1,1-dibromo-2,2,3,3-tetramethylcyclopropane **11** gave bromodiene **12**, and lithium–halogen exchange followed by alkylation with ethylene oxide afforded diene alcohol **13**. Diene aldehyde **6** was somewhat sensitive to prolonged storage, so it was prepared immediately prior to use by oxidation of diene alcohol **13** with Dess–Martin periodinane (12).

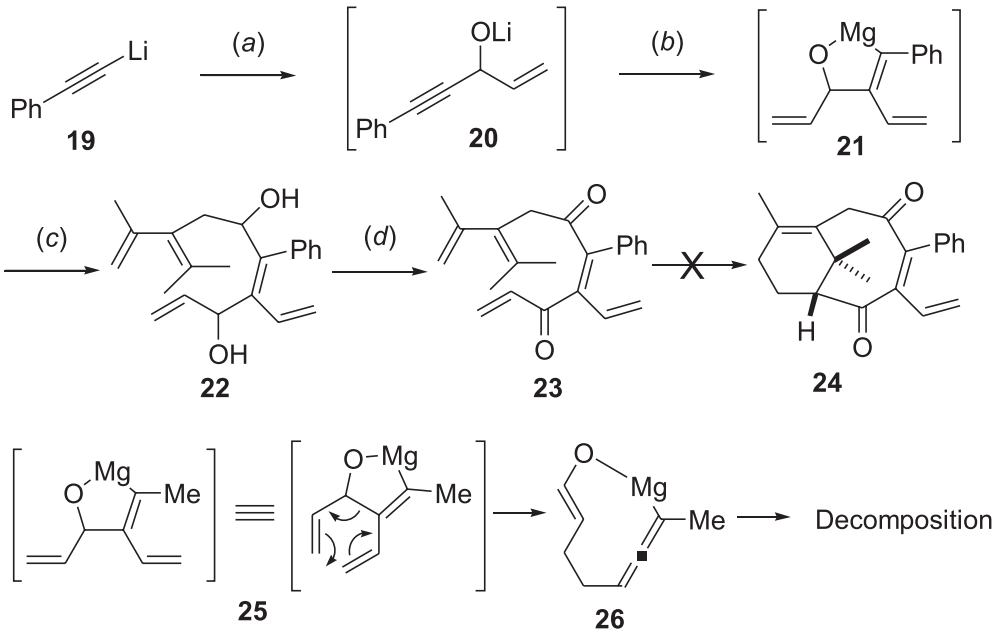
Our route for the preparation of the keto-pentaene **8a** began with the addition of vinylmagnesium chloride to 2-butynol (**3a**) and followed by quenching of the intermediate magnesium anion with diene aldehyde **6** (Scheme 3). Selective protection of the primary allylic alcohol, as silyl ether **14a**, permitted methylation of the secondary allylic alcohol in diol **7a** and subsequent fluoride-mediated desilylation of the methylated intermediate **15a** to afford alcohol **16a**. Swern, *o*-iodoxybenzoic acid (IBX), or Dess–Martin oxidation to aldehyde **17a** was followed by the addition of vinylmagnesium chloride and a second IBX or Dess–Martin oxidation of alcohol **18a** to give the Diels–Alder precursor **8a**.

The Diels–Alder cycloaddition of substrate **8a** proceeded smoothly in the presence of Et_2AlCl to afford the taxane AB-ring building block **9a** as a single diastereomer (Scheme 3). The observed stereoselectivity, confirmed by X-

Fig. 2. Diastereoselective Lewis-acid complexation of **8a**.



Scheme 4. Reagents and conditions: (*a*) CH_2=CHCHO; (*b*) CH_2=CHMgCl; (*c*) **6**; (*d*) Dess–Martin periodinane, CH_2Cl_2, rt, 1 h, 80%.



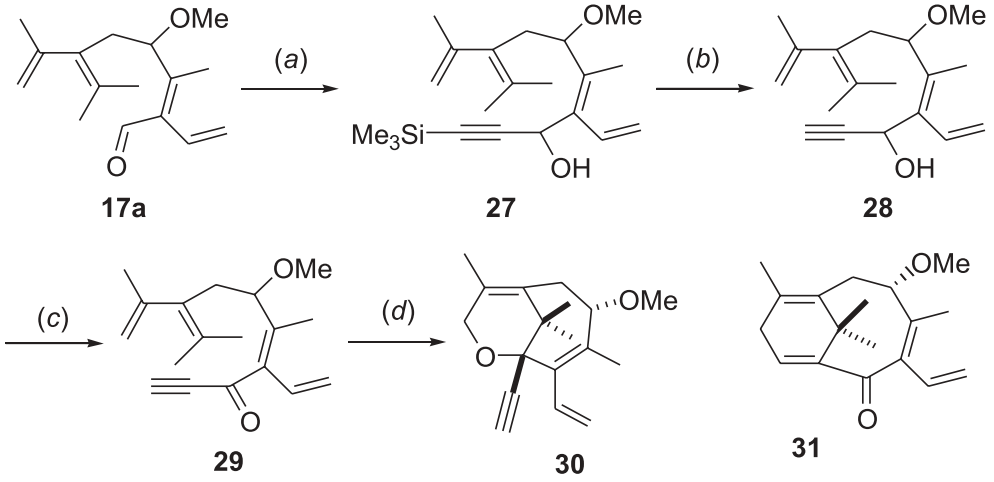
ray crystallographic analysis (5), arose from chelation control provided by complexation of the Lewis acid between the C2 carbonyl and C9 methoxy substituents (Fig. 2). The geometry appears particularly favourable, created by the chair-like arrangement of the atoms involved. Related chelation effects have been shown to control the selectivity of both intermolecular (13) and intramolecular cycloadditions (14) mediated by Lewis acids.

This direct route to the bicyclo[5.3.1]undecenone **9a** was also utilized to construct compounds **9b** and **9c** in a parallel fashion. Trimethylsilyl acetylene propargyl alcohol provided access to intermediate **7b**, from which the silyl group could be readily removed to afford the corresponding carbometallation product **7c**. This ultimately provided access to the bicyclo[5.3.1]undecenone **9c**, or alternatively, the silyl group could be retained until the adduct **9b**, to afford a second source of **9c**, as illustrated in Scheme 3.

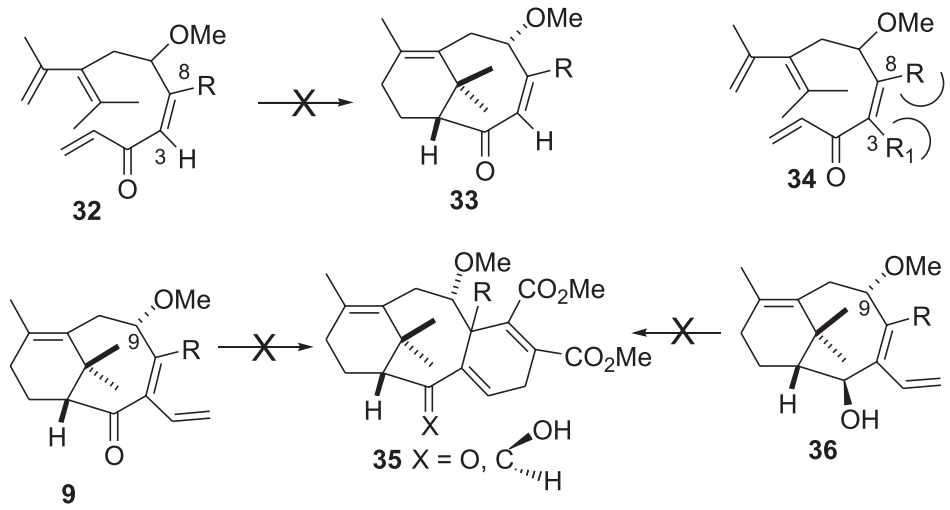
An attempt to shorten this sequence, as we had done for our furan syntheses (7) with an acetylenic anion, gave variable results. The in situ generation of a secondary alkoxide by carbometallation to install the dienophilic olefin worked well with a phenyl substituent (Scheme 4). Thus the lithium salt of phenyl acetylene **19** was condensed with acrolein, treated with excess vinylmagnesium chloride, and quenched with diene aldehyde **6** to afford the phenyl pentadiene diol **22** directly. Subsequent oxidation of the allylic alcohols provided the diketone **23**. Unfortunately, this cross-conjugated diketone readily decomposed in the presence of Lewis acids. In addition, attempted thermal cycloadditions of **23** failed to give **24**. This appears to be a consequence of the reduced dienophilic character of **23** due to its extended conjugation, combined with the bulky phenyl group and the presence of a single methylene unit in the tether. This excessive planarity precluded the formation of the required Diels–Alder transition-state conformation. The phenyl acetylide was replaced with propynyllithium, and the sequence was repeated; however, a second complication was discovered. The modified electronic environment and reduced size of the methyl substituent in the chelate resulted in a rapid oxy-Cope rearrangement of the intermediate magnesium alkoxide **25**. The resulting allene aldehyde enolate **26** decomposed under the reaction conditions and necessitated the abandonment of this procedure.

Another variation was investigated, based on related studies by Shea and co-workers (4) who incorporated an oxygen in the tether, to prepare an A-ring cycloheaxadiene. Ring systems of type **31** are desirable because of the increased potency of C14-substituted taxoids (1). The addition of trimethylsilylethynyl lithium to the unsaturated aldehyde **17a** was converted to the alternative Diels–Alder precursor **29**

Scheme 5. Reagents and conditions: (*a*) (*i*) TMS–acetylene, BuLi, THF, –78 °C, 30 min; (*ii*) **17a**, –78 °C, 1 h, 89%; (*b*) TBAF, THF, rt, 1 h, 85%; (*c*) Dess–Martin periodinane, CH_2Cl_2, rt, 1 h, 86%; (*d*) Et_2AlCl, CH_2Cl_2, –78 °C to 0 °C, 5 min, 62%.



Scheme 6.



with the intention of preparing **31**. Experimentally, the heterocyclic cycloaddition adduct **30**, containing a seven-membered ring, was formed exclusively (Scheme 5).

In the course of these investigations, several additional subtleties of these Diels–Alder precursors were uncovered. It was anticipated, in view of the success of the cyclization of **8** to **9**, that the cyclization of **32** under Lewis-acid conditions should also be straightforward. This would permit a "Robinson annulation"-type approach for the attachment of the C ring (Scheme 6). However, when members of the family represented by **32** in which the C3 substituent is hydrogen were investigated, they were completely inert under the cycloaddition reaction conditions above. These experiments revealed that an important nonbonded interaction played a key role in the success of these cycloadditions. A substituent at the C3 position (taxane numbering, **34**) is required to ensure the dienophile attains the required conformation. This interaction causes the enone to fold under the diene, to ensure the requisite transition state for the cycloaddition. The examples in Scheme 3 confirm this effect.

Additional examples with C3 allyl substituents are discussed in the following paper. Thus the vinyl methyl at C8 may be replaced by hydrogen (**8c**), but the group at C3 is more important than the substituent at C8.

It will be obvious that we intended to attach the C ring to the diene adducts **9** by a second Diels–Alder reaction of either an intermolecular or intramolecular variety, the latter via attachment of an ester dienophile to the C9 centre. However, a number of attempts to elaborate the ABC-ring core from **9** with a suitable C-ring dienophile via Diels–Alder protocols were unsuccessful (Scheme 6). Several activated dienophiles (maleic anhydride, *N*-phenylmaleimide) and even "relatively flat" diethyl acetylenedicarboxylate were investigated, but these reactions failed to yield significant amounts of the desired adducts. The stereochemical control available from an allylic hydroxyl or ether group in cycloadditions is well established (15). Reduction of the carbonyl in **9a** gave **36**, and protection afforded the *p*-methoxybenzyl ether (not illustrated). These compounds also failed to react with the same three dienophiles, although in these cases,

only the starting materials were recovered. Consequently, other variations were examined. These alternative protocols initially included modification of the vinyl silyl group present in **8b** (Scheme 3). Halodesilylation to afford the vinyl bromide in place of the C8 methyl substituent would have permitted subsequent palladium couplings for ring C appendages. Unfortunately, the desired transformation failed. However, an efficient method for attaching the C ring is described in the following paper.

Experimental section

Reagents, unless otherwise noted, were purchased from the Aldrich Chemical Company and used as received. Reaction solvents were distilled under a nitrogen atmosphere prior to use unless otherwise stated. Diethyl ether (Et_2O) and tetrahydrofuran (THF) were distilled from Na metal and benzophenone ketyl, while dichloromethane (CH_2Cl_2) was distilled from calcium hydride (CaH_2). All other solvents used were reagent grade.

All manipulations were carried out under a nitrogen atmosphere in flame-dried glassware. Analytical thin-layer chromatography (TLC) was performed on commercial aluminum sheets precoated (0.2 mm layer thickness) with silica gel 60 F_{254} (E. Merck), visualized with a UV_{254} lamp (Spectroline Longlife filter), and stained with 20% phosphomolybdic acid in ethanol (Aldrich Chemical Company). Column chromatography on silica gel (60 Å, 230–400 mesh, E. Merck) was performed with hexanes and ethyl acetate (EtOAc).

Melting points were determined in capillary tubes with a Thomas-Hoover unit-melt apparatus and are uncorrected. FT-IR spectra were recorded on a Bomem Michelson 100 FT-IR spectrometer, with samples loaded as neat films on NaCl plates. All ^{1}H and ^{13}C NMR spectra were obtained on a 500 MHz Brüker AMX500 or a 300 MHz Brüker AMX300 in $CDCl_3$ (referenced to the residual solvent signals at δ 7.24 and 77.00 ppm for ^{1}H and ^{13}C, respectively) or C_6D_6 (referenced to the residual solvent signals at δ 7.15 and 127.00 ppm for ^{1}H and ^{13}C, respectively). Features of peaks in the ^{1}H NMR spectra are labeled in brackets after each chemical shift in the following order: multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet), coupling constant, and integration. Mass spectra (MS) were determined on a V.G. micromass 7070 HS instrument, using an ionization energy of 70 eV. Elemental analyses were conducted by M-H-W Laboratories (Phoenix, Arizona, U.S.A.). The purity of the title compounds were judged to be >95% pure, as determined by a combination of GC–MS, ^{1}H NMR, and ^{13}C NMR analysis.

1,1-Dibromo-2,2,3,3-tetramethyl-cyclopropane (11)

Bromoform (80.0 mL, 916 mmol) was added dropwise by means of an addition funnel to a stirred suspension of 2,3-dimethyl-2-butene **10** (50.0 mL, 421 mmol) and potassium *tert*-butoxide (86.4 g, 770 mmol) in pentane (150 mL) at 0 °C over a period of 1 h. After warming to 21 °C, stirring was continued for another 2 h prior to the addition of water (200 mL). The layers were separated, and the aqueous layer was extracted with hexanes (2 × 150 mL). The combined organic extracts were washed with brine (4 × 80 mL), dried ($MgSO_4$), filtered, and concentrated under reduced pressure. Cold methanol (100 mL) was added to the residue, and the solution was cooled to 0 °C. The resulting precipitate was then collected by filtration, washed with cold methanol (20 mL), and allowed to dry in air. The mother liquor was concentrated under reduced pressure, and the precipitation cycle was repeated to yield more of the white crystalline solid (75 g, 71%). mp = 77 to 78 °C. ^{1}H NMR ($CDCl_3$, 300 MHz) δ: 1.25 (s, 12H). ^{13}C NMR ($CDCl_3$, 75 MHz) δ: 18.4, 35.5, 58.7.

3-Bromo-2,4-dimethyl-penta-1,3-diene (12)

1,1-Dibromo-2,2,3,3-tetramethyl-cyclopropane **11** (28.7 g, 118 mmol) was slowly heated with a propane torch, and the resulting liquid was collected by distillation between 120–140 °C. The distillate was further purified by two additional distillations. The product was treated with NaOH pellets for 0.5 h and then filtered through glass wool to afford a colorless liquid (15.7 g, 80%). The product was stored at –20 °C over grains of NaOH. ^{1}H NMR ($CDCl_3$, 300 MHz) δ: 1.73 (s, 3H), 1.75 (s, 3H), 1.82 (s, 3H), 4.73–4.75 (m, 1H), 4.89–4.91 (m, 1H). ^{13}C NMR ($CDCl_3$, 75 MHz) δ: 17.0, 17.2, 19.8, 107.8, 111.9, 133.4, 145.7.

3-Isopropenyl-4-methyl-pent-3-en-1-ol (13)

A solution of 3-bromo-2,4-dimethylpenta-1,3-diene **12** (13.5 g, 77.0 mmol) in THF (235 mL) at –78 °C was added to a stirred solution of *tert*-butyllithium (100.0 mL, 170.0 mmol, 1.7 mol L^{-1} in pentane) cooled to –78 °C. After 0.5 h, ethylene oxide (39 mL) was added via a cannula. The resulting solution was subsequently stirred for 1 h at –78 °C and then for 1 h at 21 °C. Water (200 mL) was then added; the layers were separated, and the aqueous layer was extracted with ether (4 × 100 mL). The combined organic extracts were dried ($MgSO_4$), filtered, and concentrated under reduced pressure. Purification by flash chromatography (silica gel, ethyl acetate – hexanes) provided the title compound as a colorless liquid (9.0 g, 83%). IR (neat) (cm^{-1}) ν: 3357, 2923, 1623. ^{1}H NMR ($CDCl_3$, 300 MHz) δ: 0.90 (s, 1H), 1.67 (s, 3H), 1.69 (s, 3H), 1.75 (s, 3H), 2.37 (t, J = 6.7 Hz, 2H), 3.60 (t, J = 6.7 Hz, 2H), 4.54–4.56 (m, 1H), 4.93–4.95 (m, 1H). ^{13}C NMR ($CDCl_3$, 75 MHz) δ: 20.3, 22.2, 22.9, 34.2, 61.6, 113.9, 128.9, 132.9, 146.7. HR-MS (EI) *m*/*z* calcd. for $C_9H_{16}O$: 140.1201; found: 140.1213.

4-Methyl-3-vinyl-pent-3-enal (6)

Dess–Martin periodinane (8.30 g, 19.6 mmol) was added to a solution of 3-isopropenyl-4-methyl-pent-3-en-1-ol **13** (2.50 g, 17.8 mmol) in dichloromethane (30 mL) at 21 °C. The resulting solution was stirred for 0.5 h prior to dilution with a 10% aq. solution of NaOH (30 mL). The layers were separated, and the organic layer was extracted with dichloromethane (3 × 30 mL). The combined organic extracts were dried ($MgSO_4$), filtered, and concentrated under reduced pressure to afford the title compound as a colorless liquid (2.34 g, 95%). IR (neat) (cm^{-1}) ν: 2923, 1706, 1630. ^{1}H NMR ($CDCl_3$, 300 MHz) δ: 1.66 (s, 3H), 1.73 (s, 6H), 3.12 (d, J = 2.6 Hz, 2H), 4.62–4.64 (m, 1H), 4.93–4.96 (m, 1H), 9.52 (t, J = 2.6 Hz, 1H). ^{13}C NMR ($CDCl_3$, 75 MHz) δ: 20.5, 22.2, 22.5, 47.1, 114.6, 127.4, 131.9, 146.3, 200.3. HR-MS (EI) *m*/*z* calcd. for $C_9H_{14}O$: 138.1045; found: 138.1049.

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% aq. sulfuric acid (250 mL) was added; 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.

General procedure for the carbometallation of the propargylic alcohols

Vinylmagnesium 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).

6-Isopropenyl-3,7-dimethyl-2-vinyl-octa-2,6-diene-1,4-diol (7a)

71% from **3a**. IR (neat) (cm^{-1}) ν: 3355, 2964, 2917, 1630, 1442, 1374, 998, 900. ^1H NMR ($CDCl_3$, 500 MHz) δ: 1.65 (s, 3H), 1.66 (s, 3H), 1.73 (s, 3H), 1.82 (s, 3H), 2.19 (dd, *J* = 14.0, 5.2 Hz, 1H), 2.54 (s, 1H), 2.63 (dd, *J* = 14.0, 8.5 Hz, 1H), 4.24 (d, *J* = 11.9 Hz, 1H), 4.36 (d, *J* = 11.9 Hz, 1H), 4.67 (s, 1H), 4.85 (dd, *J* = 8.5, 5.2 Hz, 1H), 4.98 (s, 1H), 5.09 (dd, *J* = 11.1, 1.2 Hz, 1H), 5.42 (dd, *J* = 17.5, 1.2 Hz, 1H), 6.62 (dd, *J* = 17.5, 11.1 Hz, 1H). ^{13}C NMR ($CDCl_3$, 125 MHz) δ: 13.0, 20.2, 22.0, 22.6, 36.9, 57.5, 70.1, 114.1, 114.2, 129.0, 132.5, 133.4, 134.8, 141.0, 146.7. HR-MS (EI) *m/z* calcd. for $C_{15}H_{24}O_2$ ($[M]^+$): 236.1777; found: 236.1791.

6-Isopropenyl-7-methyl-3-trimethylsilanyl-2-vinyl-octa-2,6-diene-1,4-diol (7b)

56% from **3b**. IR (neat) (cm^{-1}) ν: 3408, 3075, 2958, 2913, 1631. ^1H NMR ($CDCl_3$, 500 MHz) δ: 0.21 (s, 9H), 1.72 (s, 3H), 1.76 (s, 3H), 1.79 (s, 3H), 2.06 (dd, *J* = 14.4, 2.8 Hz, 1H), 2.69 (dd, *J* = 14.4, 10.8 Hz, 1H), 4.25 (d, *J* = 11.7 Hz, 1H), 4.54 (d, *J* = 11.7 Hz, 1H), 4.62 (s, 1H), 4.67 (dd, *J* = 10.8, 2.8 Hz, 1H), 5.03 (s, 1H), 5.17 (dd, *J* = 11.0, 0.9 Hz, 1H), 5.47 (dd, *J* = 17.3, 0.9 Hz, 1H), 6.69 (dd, *J* = 17.3, 11.0 Hz, 1H). ^{13}C NMR ($CDCl_3$, 125 MHz) δ: 1.3, 20.2, 21.9, 23.3, 38.1, 58.6, 72.1, 114.3, 114.6, 130.2, 133.1, 138.0, 146.0, 146.6, 147.5. HR-MS (EI) *m/z* calcd. for $C_{17}H_{28}OSi$ ($[M^+ – H_2O]$): 276.1909; found: 276.1932.

6-Isopropenyl-7-methyl-2-vinyl-octa-2,6-diene-1,4-diol (7c)

Sodium methoxide (1.93 g, 34.0 mmol) was added to a solution of diol **7b** (2.50 g, 8.50 mmol) in methanol (40 mL) at 21 °C. The solution was heated at reflux for 2 h and then concentrated. A saturated aqueous solution of NH_4Cl (50 mL) was added; the layers were separated, and the aqueous layer was extracted with ether (2 × 40 mL). The combined organic extracts were washed with brine (2 × 50 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 (1.64 g, 87%). IR (neat) (cm^{-1}) ν: 3308, 2908, 2859, 1630, 1606. ^1H NMR ($CDCl_3$, 500 MHz) δ: 1.69 (s, 3H), 1.70 (s, 3H), 1.76 (s, 3H), 2.27 (dd, *J* = 13.9, 5.1 Hz, 1H), 2.50 (dd, *J* = 13.9, 8.5 Hz, 1H), 4.27 (d, *J* = 12.1 Hz, 1H), 4.32 (d, *J* = 12.1 Hz, 1H), 4.35 (ddd, *J* = 8.5, 7.8, 5.1 Hz, 1H), 4.58 (s, 1H), 4.98 (s, 1H), 5.10 (d, *J* = 10.9 Hz, 1H), 5.38 (d, *J* = 17.6 Hz, 1H), 5.61 (d, *J* = 7.8 Hz, 1H), 6.25 (dd, *J* = 17.6, 10.9 Hz, 1H). ^{13}C NMR ($CDCl_3$, 125 MHz) δ: 20.2, 21.9, 22.4, 38.6, 57.2, 66.9, 114.0, 114.2, 129.8, 132.2, 136.3, 138.1, 139.5, 146.2. HR-MS (EI) *m/z* calcd. for $C_{14}H_{20}O$ ($[M^+ – H_2O]$): 204.1514; found: 204.1503.

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).

3-(*tert*-Butyl-dimethyl-silanyloxymethyl)-7-isopropenyl-4,8-dimethyl-nona-1,3,7-trien-5-ol (14a)

92% from **7a**. IR (neat) (cm^{-1}) ν: 3469, 2941, 2858, 1631, 1472, 1377, 1254, 1053, 898, 776. ^1H NMR ($CDCl_3$, 500 MHz) δ: 0.10 (s, 6H), 0.96 (s, 9H), 1.66 (s, 6H), 1.77 (s, 3H), 1.86 (s, 3H), 2.12 (dd, *J* = 14.0, 3.1 Hz, 1H), 2.68 (dd, *J* = 14.0, 9.7 Hz, 1H), 4.35 (d, *J* = 11.4 Hz, 1H), 4.43 (d, *J* = 11.4 Hz, 1H), 4.71 (m, 1H), 4.95 (s, 1H), 5.03 (s, 1H), 5.16 (dd, *J* = 11.2, 1.4 Hz, 1H), 5.49 (dd, *J* = 17.5, 1.4 Hz, 1H), 6.69 (dd, *J* = 17.5, 11.2 Hz, 1H). ^{13}C NMR ($CDCl_3$, 125 MHz) δ: –5.1, 12.8, 18.4, 20.1, 22.0, 22.8, 26.1, 37.1, 58.4, 69.6, 114.0, 114.1, 129.3, 132.1, 133.3, 135.2, 140.8, 146.7. HR-MS (EI) *m/z* calcd. for $C_{21}H_{36}OSi$ ($[M^+ – H_2O]$): 332.2537; found: 332.2552. Anal calcd. for $C_{21}H_{38}O_2Si$ (%): C 71.95, H 10.65; found: C 71.86, H 10.65.

3-(*tert*-Butyl-dimethyl-silanyloxymethyl)-7-isopropenyl-8-methyl-4-trimethylsilanyl-nona-1,3,7-trien-5-ol (14b)

74% from **7b**. IR (neat) (cm^{-1}) ν: 3462, 2955, 2930, 2857. ^1H NMR ($CDCl_3$, 500 MHz) δ: 0.04 (s, 6H), 0.25 (s, 9H), 0.86 (s, 9H), 1.70 (s, 3H), 1.75 (s, 3H), 1.79 (s, 3H), 1.89 (s, 1H), 2.01 (dd, *J* = 14.2, 2.5 Hz, 1H), 2.66 (dd, *J* = 14.2,

10.7 Hz, 1H), 4.35 (d, *J* = 11.5 Hz, 1H), 4.39 (d, *J* = 11.5 Hz, 1H), 4.64 (s, 1H), 4.81 (dd, *J* = 10.7, 2.5 Hz, 1H), 5.01 (s, 1H), 5.13 (dd, *J* = 11.1, 1.1 Hz, 1H), 5.34 (dd, *J* = 17.3, 1.1 Hz, 1H), 6.62 (dd, *J* = 17.3, 11.1 Hz, 1H). ^{13}C NMR ($CDCl_3$, 125 MHz) δ: –5.2, 2.5, 18.2, 20.3, 21.9, 22.7, 25.9, 38.4, 58.8, 72.0, 114.1, 115.0, 128.9, 133.2, 137.9, 146.1, 146.2, 146.8. HR-MS (EI) *m/z* calcd. for $C_{23}H_{42}OSi$ ([$M^+ - H_2O$]): 390.2274; found: 390.2770.

3-(*tert*-Butyl-dimethyl-silanyloxymethyl)-7-isopropenyl-8-methyl-nona-1,3,7-trien-5-ol (14c)

78% from **7c**. IR (neat) (cm^{-1}) ν: 3432, 3075, 2954, 2929, 2857, 1631, 1607. ^{1}H NMR ($CDCl_3$, 500 MHz) δ: 0.06 (s, 3H), 0.07 (s, 3H), 0.87 (s, 9H), 1.69 (s, 3H), 1.72 (s, 3H), 1.77 (s, 3H), 2.24 (dd, *J* = 13.9, 5.3 Hz, 1H), 2.28 (s, 1H), 2.50 (dd, *J* = 13.9, 8.3 Hz, 1H), 4.25 (s, 2H), 4.57 (ddd, *J* = 8.3, 8.1, 5.3 Hz, 1H), 4.58 (s, 1H), 4.97 (s, 1H), 5.05 (d, *J* = 11.0 Hz, 1H), 5.31 (d, *J* = 17.6 Hz, 1H), 5.62 (d, *J* = 8.1 Hz, 1H), 6.24 (dd, *J* = 17.6, 11.0 Hz, 1H). ^{13}C NMR ($CDCl_3$, 125 MHz) δ: –5.4 (2), 18.2, 20.1, 21.8, 22.5, 25.8, 38.4, 58.1, 66.6, 113.6, 113.9, 129.2, 132.4, 136.4, 138.4, 146.2. HR-MS (EI) *m/z* calcd. for $C_{20}H_{34}OSi$ ([$M^+ - H_2O$]): 318.2379; found: 318.2383.

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).

3-(*tert*-Butyl-dimethyl-silanyloxymethyl)-7-isopropenyl-5-hydroxy-8-methyl-4-methyl-nona-1,3,7-triene (15a)

91% from **14a**. IR (neat) (cm^{-1}) ν: 2929, 2858, 1633, 1463, 1383, 1255, 1100, 1068, 898, 851, 837, 774. ^{1}H NMR ($CDCl_3$, 500 MHz) δ: 0.11 (s, 6H), 0.96 (s, 9H), 1.73 (s, 3H), 1.74 (s, 3H), 1.79 (s, 3H), 1.82 (s, 3H), 2.11 (dd, *J* = 14.2, 4.3 Hz, 1H), 2.79 (dd, *J* = 14.2, 8.9 Hz, 1H), 3.13 (s, 3H), 4.30 (d, *J* = 11.2 Hz, 1H), 4.48 (dd, *J* = 8.9, 4.3 Hz, 1H), 4.74 (d, *J* = 11.2 Hz, 1H), 4.81 (s, 1H), 5.09 (s, 1H), 5.16 (dd, *J* = 11.2, 1.1 Hz, 1H), 5.50 (dd, *J* = 17.5, 1.1 Hz, 1H), 6.69 (dd, *J* = 17.5, 11.2 Hz, 1H). ^{13}C NMR ($CDCl_3$, 125 MHz) δ: –5.2, 12.2, 18.5, 20.2, 22.1, 22.9, 26.1, 36.2, 56.3, 57.9, 79.1, 114.0, 127.6, 128.3, 133.5, 133.9, 135.0, 139.1, 147.0. HR-MS (EI) *m/z* calcd. for $C_{22}H_{40}O_2Si$ ([M]$^+$): 364.2799; found: 364.2801. Anal calcd. for $C_{22}H_{40}O_2Si$ (%): C 72.97, H 11.06; found: C 73.13, H 11.06.

3-(*tert*-Butyl-dimethyl-silanyloxymethyl)-7-isopropenyl-5-methoxy-8-methyl-4-trimethylsilanyl-nona-1,3,7-triene (15b)

95% from **14b**. IR (neat) (cm^{-1}) ν: 2956, 2858, 1630. ^{1}H NMR ($CDCl_3$, 500 MHz) δ: 0.10 (s, 3H), 0.11 (s, 3H), 0.38 (s, 9H), 0.95 (s, 9H), 1.74 (s, 3H), 1.79 (s, 3H), 1.83 (s, 3H), 2.09 (d, *J* = 14.4 Hz, 1H), 2.91 (dd, *J* = 14.4, 9.8 Hz, 1H), 3.20 (s, 3H), 4.35 (m, 1H), 4.49 (s, 2H), 4.83 (s, 1H), 5.12 (s, 1H), 5.13 (d, *J* = 11.1 Hz, 1H), 5.48 (d, *J* = 17.3 Hz, 1H), 6.83 (dd, *J* = 17.3, 11.1 Hz, 1H). ^{13}C NMR ($CDCl_3$, 125 MHz) δ: –5.1, 2.6, 18.4, 20.5, 22.1, 22.9, 26.1, 38.3, 57.1, 58.4, 81.9, 114.2, 114.9, 127.4, 127.9, 128.3, 134.0, 138.1, 146.9.

3-(*tert*-Butyl-dimethyl-silanyloxymethyl)-7-isopropenyl-5-methoxy-8-methylnona-1,3,7-triene (15c)

89% from **14c**. IR (neat) (cm^{-1}) ν: 2956, 2929, 2858, 1615. ^{1}H NMR ($CDCl_3$, 500 MHz) δ: 0.06 (s, 6H), 0.87 (s, 9H), 1.65 (s, 3H), 1.66 (s, 3H), 1.75 (s, 3H), 2.17 (dd, *J* = 14.1, 5.9 Hz, 1H), 2.51 (dd, *J* = 14.1, 7.4 Hz, 1H), 3.19 (s, 3H), 4.08 (ddd, *J* = 9.2, 7.4, 5.9 Hz, 1H), 4.22 (d, *J* = 11.3 Hz, 1H), 4.31 (d, *J* = 11.3 Hz, 1H), 4.56 (s, 1H), 4.95 (s, 1H), 5.06 (d, *J* = 11.0 Hz, 1H), 5.37 (d, *J* = 17.6 Hz, 1H), 5.41 (d, *J* = 9.2 Hz, 1H), 6.26 (dd, *J* = 17.6, 11.0 Hz, 1H). ^{13}C NMR ($CDCl_3$, 125 MHz) δ: –5.4, 18.3, 20.2, 21.9, 22.6, 25.9, 37.3, 56.3, 57.9, 75.8, 113.7, 113.9, 127.7, 132.5, 134.7, 138.3, 139.5, 146.4. HR-MS (EI) *m/z* calcd. for $C_{21}H_{38}O_2Si$ ([M]$^+$): 350.2641; found: 350.2642.

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).

6-Isopropenyl-4-methoxy-3,7-dimethyl-2-vinyl-octa-2,6-dien-1-ol (16a)

99% from **15a**. IR (neat) (cm^{-1}) ν: 3445, 2922, 1629, 1444, 1364, 1099, 996, 898, 691, 630. ^{1}H NMR ($CDCl_3$, 500 MHz) δ: 1.65 (s, 6H), 1.66 (s, 3H), 1.72 (s, 3H), 2.18 (dd. *J* = 14.1, 5.9 Hz, 1H), 2.67 (dd, *J* = 14.1, 7.6 Hz, 1H), 3.00 (s, 3H), 4.29–4.40 (m, 3H), 4.72 (s, 1H), 4.99 (s, 1H), 5.10 (d, *J* = 11.1 Hz, 1H), 5.44 (d, *J* = 17.7 Hz, 1H), 6.59 (dd, *J* = 17.7, 11.1 Hz, 1H). ^{13}C NMR ($CDCl_3$, 125 MHz) δ: 12.2, 20.1, 22.0, 22.7, 36.0, 56.0, 57.4, 79.1, 114.1, 114.2, 128.5, 133.8, 134.5, 134.9, 139.3, 146.8. HR-MS (EI) *m/z* calcd. for $C_{16}H_{26}O_2$ ([M]$^+$): 250.1934; found: 250.1938.

6-Isopropenyl-4-methoxy-7-methyl-3-trimethylsilanyl-2-vinyl-octa-2,6-dien-1-ol (16b)

83% from **15b**. IR (neat) (cm^{-1}) ν: 3415, 2910, 2858, 2816, 1631. ^{1}H NMR ($CDCl_3$, 300 MHz) δ: 0.23 (s, 9H), 1.66 (s, 3H), 1.69 (s, 3H), 1.76 (s, 3H), 1.93 (dd, *J* = 7.6, 4.5 Hz, 1H), 2.07 (dd, *J* = 14.5, 4.5 Hz, 1H), 2.71 (dd, *J* = 14.5, 8.6 Hz, 1H), 3.17 (s, 3H), 4.22 (dd, *J* = 8.6, 4.5 Hz, 1H), 4.32 (dd, *J* = 12.1, 7.6 Hz, 1H), 4.45 (dd, *J* = 12.1, 4.5 Hz, 1H), 4.61–4.63 (m, 1H), 4.99–5.02 (m, 1H), 5.20 (dd, *J* = 11.1, 0.8 Hz, 1H), 5.43 (dd, *J* = 17.3, 0.8 Hz, 1H),

6.70 (dd, *J* = 17.3, 11.1 Hz, 1H). ^{13}C NMR ($CDCl_3$, 75 MHz) δ: 2.2, 20.6, 22.3, 23.1, 37.8, 57.5, 58.6, 82.0, 114.5, 115.1, 128.2, 133.8, 137.9, 146.6, 147.6, 147.8.

6-Isopropenyl-4-methoxy-7-methyl-2-vinyl-octa-2,6-dien-1-ol (16c)

90% from **15c**. IR (neat) (cm^{-1}) ν: 3438, 3076, 2925, 2820, 1630, 1606. ^{1}H NMR ($CDCl_3$, 500 MHz) δ: 1.65 (s, 3H), 1.66 (s, 3H), 1.76 (s, 3H), 2.29 (dd, *J* = 13.9, 7.6 Hz, 1H), 2.52 (dd, *J* = 13.9, 6.1 Hz, 1H), 3.23 (s, 3H), 4.07 (ddd, *J* = 8.9, 7.6, 6.1 Hz, 1H), 4.27 (s, 2H), 4.55 (s, 1H), 4.97 (s, 1H), 5.12 (d, *J* = 10.9 Hz, 1H), 5.39 (d, *J* = 17.6 Hz, 1H), 5.46 (d, *J* = 8.9 Hz, 1H), 6.27 (dd, *J* = 17.6, 10.9 Hz, 1H). ^{13}C NMR ($CDCl_3$, 125 MHz) δ: 20.2, 21.9, 22.6, 36.7, 56.2, 57.3, 76.1, 113.9, 114.0, 128.4, 132.4, 135.7, 138.1, 139.9, 146.2. HR-MS (EI) *m/z* calcd. for $C_{15}H_{24}O_2$ ($[M]^+$): 236.1776; found: 236.1786.

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 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).

6-Isopropenyl-4-methoxy-3,7-dimethyl-2-vinyl-octa-2,6-dienal (17a)

80% from **16a**. IR (neat) (cm^{-1}) ν: 3076, 2981, 2925, 2821, 1683, 1629. ^{1}H NMR ($CDCl_3$, 500 MHz) δ: 1.58 (s, 3H), 1.65 (s, 3H), 1.71 (s, 3H), 1.73 (s, 3H), 2.19 (dd, *J* = 14.1, 6.0 Hz, 1H), 2.63 (dd, *J* = 14.1, 7.5 Hz, 1H), 2.88 (s, 3H), 4.69 (dd, *J* = 7.5, 6.0 Hz, 1H), 4.68 (s, 1H), 4.98 (s, 1H), 5.26 (dd, *J* = 11.6, 1.7 Hz, 1H), 5.67 (dd, *J* = 17.8, 1.7 Hz, 1H), 6.34 (dd, *J* = 17.8, 11.6 Hz, 1H), 10.19 (s, 1H). ^{13}C NMR ($CDCl_3$, 125 MHz) δ: 14.3, 20.2, 22.0, 22.5, 35.9, 56.3, 77.6, 114.7, 119.8, 128.9, 130.4, 132.5, 136.5, 146.1, 154.8, 189.6. HR-MS (EI) *m/z* calcd. for $C_{16}H_{24}O_2$ ($[M]^+$): 248.1776; found: 248.1795.

6-Isopropenyl-4-methoxy-7-methyl-3-trimethylsilanyl-2-vinyl-octa-2,6-dienal (17b)

91% from **16b**. IR (neat) (cm^{-1}) ν: 3074, 2914, 2820, 2718, 1699, 1630. ^{1}H NMR ($CDCl_3$, 500 MHz) δ: 0.22 (s, 9H), 1.65 (s, 3H), 1.66 (s, 3H), 1.75 (s, 3H), 2.05 (dd, *J* = 14.8, 3.1 Hz, 1H), 2.64 (dd, *J* = 14.8, 9.9 Hz, 1H), 3.08 (s, 3H), 4.13 (dd, *J* = 9.9, 3.1 Hz, 1H), 4.57 (s, 1H), 4.98 (s, 1H), 5.27 (d, *J* = 11.2 Hz, 1H), 5.29 (d, *J* = 17.6 Hz, 1H), 6.52 (dd, *J* = 17.6, 11.2 Hz, 1H), 10.16 (s, 1H). ^{13}C NMR ($CDCl_3$, 125 MHz) δ: 0.6, 19.9, 21.8, 22.6, 37.4, 56.6, 81.4, 114.0, 118.7, 128.0, 132.3, 132.6, 145.8, 146.5, 195.5. HR-MS (EI) *m/z* calcd. for $C_{17}H_{27}O_2Si$ ($[M^+ – CH_3]$): 291.1780; found: 291.1732.

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).

8-Isopropenyl-6-methoxy-5,9-dimethyl-4-vinyl-deca-1,4,8-trien-3-ol (18a)

72% from **17a**. IR (neat) (cm^{-1}) ν: 3458, 2923, 1629, 1445, 1100, 991, 919, 896, 638. ^{1}H NMR ($CDCl_3$, 500 MHz) δ: 1.60 (d, *J* = 5.1 Hz, 1H), 1.69 (s, 3H), 1.72 (s, 3H), 1.77 (s, 3H), 1.78 (s, 3H), 2.26 (dd, *J* = 14.1, 5.7 Hz, 1H), 2.67 (dd, *J* = 14.1, 7.7 Hz, 1H), 3.01 (s, 3H), 4.41 (dd, *J* = 7.7, 5.7 Hz, 1H), 4.83 (s, 1H), 5.02–5.06 (m, 2H), 5.17 (dd, *J* = 11.6, 1.9 Hz, 1H), 5.32–5.36 (m, 2H), 5.43 (dd, *J* = 17.9, 1.9 Hz, 1H), 6.04 (m, 1H), 6.36 (dd, *J* = 17.9, 11.6 Hz, 1H). ^{13}C NMR ($CDCl_3$, 125 MHz) δ: 13.7, 20.2, 22.1, 22.7, 36.0, 56.2, 70.4, 79.0, 114.1, 114.2, 117.9, 128.3, 133.4, 133.6, 136.5, 137.2, 140.4, 146.7. HR-MS (EI) *m/z* calcd. for $C_{18}H_{28}O_2$ ($[M]^+$): 276.2089; found: 276.2090.

8-Isopropenyl-6-methoxy-9-methyl-5-trimethylsilanyl-4-vinyl-deca-1,4,8-triene-3-ol (18b)

83% from **17b**. IR (neat) (cm^{-1}) ν: 3450, 3076, 2979, 1631. ^{1}H NMR ($CDCl_3$, 500 MHz) δ: 0.18 (s, 9H), 1.67 (s, 3H), 1.69 (s, 3H), 1.76 (s, 3H), 2.05 (dd, *J* = 14.7, 3.5 Hz, 1H), 2.77 (dd, *J* = 14.7, 9.7 Hz, 1H), 3.14 (s, 3H), 4.12 (dd, *J* = 9.7, 3.5 Hz, 1H), 4.61 (s, 1H), 5.00 (s, 1H), 5.11 (d, *J* = 10.5 Hz, 1H), 5.21 (dd, *J* = 11.5, 1.6 Hz, 1H), 5.25 (d, *J* = 17.3 Hz, 1H), 5.26 (d, *J* = 11.2 Hz, 1H), 5.32 (dd, *J* = 17.7, 1.6 Hz, 1H), 5.34 (s, 1H), 5.99 (ddd, *J* = 17.3, 11.2, 10.5 Hz, 1H), 6.47 (dd, *J* = 17.7, 11.5 Hz, 1H). ^{13}C NMR ($CDCl_3$, 125 MHz) δ: 2.3, 20.1, 21.8, 22.7, 37.3, 57.4, 71.6, 81.9, 113.7, 114.8, 118.2, 127.3, 133.3, 136.4, 139.6, 146.1, 146.2, 149.6.

8-Isopropenyl-6-methoxy-9-methyl-4-vinyl-deca-1,4,8-triene-3-ol (18c)

88% from **17c**. IR (neat) (cm^{-1}) ν: 3434, 3079, 2977, 2920, 1632. ^{1}H NMR ($CDCl_3$, 500 MHz) δ: 1.67 (s, 3H), 1.68 (s, 3H), 1.76 (s, 3H), 2.30 (dd, *J* = 13.9, 7.3 Hz, 1H), 2.40 (s, 1H), 2.53 (dd, *J* = 13.9, 6.3 Hz, 1H), 3.21 (s, 3H), 4.10 (ddd, *J* = 8.6, 7.3, 6.3 Hz, 1H), 4.59 (s, 1H), 4.98 (s, 1H), 5.02 (d, *J* = 4.8 Hz, 1H), 5.07 (d, *J* = 11.1 Hz, 1H),

5.14 (d, J = 10.5 Hz, 1H), 5.31 (d, J = 17.2 Hz, 1H), 5.40 (d, J = 17.6 Hz, 1H), 5.51 (d, J = 8.6 Hz, 1H), 5.95 (ddd, J = 17.2, 10.5, 4.8 Hz, 1H), 6.21 (dd, J = 17.6, 11.1 Hz, 1H). ^{13}C NMR ($CDCl_3$, 125 MHz) δ: 20.2, 21.9, 22.6, 36.6, 56.3, 69.9, 75.9, 113.9, 114.8, 115.2, 128.3, 132.3, 132.5, 136.2, 138.6, 141.5, 146.2. HR-MS (EI) m/z calcd. for $C_{17}H_{24}O$ ($[M^+ - H_2O]$): 244.1827; found: 244.1879.

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).

8-Isopropenyl-6-methoxy-5,9-dimethyl-4-vinyl-deca-1,4,8-trien-3-one (8a)

82% from **18a**. IR (neat) (cm^{-1}) ν: 2970, 2925, 1738, 1444, 1366, 1228, 1217, 772, 686. ^{1}H NMR (C_6D_6, 500 MHz) δ: 1.67 (s, 3H), 1.70 (s, 3H), 1.71 (s, 3H), 1.79 (s, 3H), 2.09 (dd, J = 14.2, 3.7 Hz, 1H), 2.69 (dd, J = 14.2, 9.6 Hz, 1H), 3.01 (s, 3H), 3.91 (dd, J = 9.6, 3.7 Hz, 1H), 4.73 (s, 1H), 4.98–5.03 (m, 3H), 5.39 (dd, J = 10.4, 1.4 Hz, 1H), 5.95 (dd, J = 17.6, 1.4 Hz, 1H), 6.28 (dd, J = 17.6, 10.4 Hz, 1H), 6.47 (dd, J = 17.7, 11.0 Hz, 1H). ^{13}C NMR (C_6D_6, 125 MHz) δ: 20.2, 22.1, 22.7, 30.4, 35.5, 56.5, 80.6, 114.0, 117.2, 128.3, 129.7, 130.1, 131.6, 133.3, 137.8, 138.0, 139.1, 197.9. HR-MS (EI) m/z calcd. for $C_{18}H_{26}O_2$ ($[M]^+$): 274.1934; found: 274.1935. Anal calcd. for $C_{18}H_{26}O_2$ (%): C 78.79, H 9.55; found: C 78.88, H 9.41.

8-Isopropenyl-6-methoxy-9-methyl-5-trimethylsilanyl-4-vinyl-deca-1,4,8-trien-3-one (8b)

90% from **18b**. IR (neat) (cm^{-1}) ν: 2977, 2921, 2819, 1660, 1622, 1604. ^{1}H NMR (C_6D_6, 500 MHz) δ: 0.33 (s, 9H), 1.72 (s, 3H), 1.77 (s, 3H), 1.82 (s, 3H), 1.98 (dd, J = 14.5, 2.8 Hz, 1H), 2.89 (dd, J = 14.5, 10.6 Hz, 1H), 3.03 (s, 3H), 4.02 (dd, J = 10.6, 2.8 Hz, 1H), 4.74 (s, 1H), 5.01 (d, J = 10.9 Hz, 1H), 5.02 (s, 1H), 5.07 (d, J = 17.5 Hz, 1H), 5.38 (dd, J = 10.5, 1.2 Hz, 1H), 5.95 (dd, J = 17.6, 1.2 Hz, 1H), 6.27 (dd, J = 17.6, 10.5 Hz, 1H), 6.73 (dd, J = 17.5, 10.9 Hz, 1H). ^{13}C NMR (C_6D_6, 125 MHz) δ: 1.8, 20.4, 22.1, 22.7, 37.3, 57.2, 82.9, 114.1, 118.4, 127.5, 129.3, 133.8, 134.2, 137.8, 146.4, 146.6, 150.0, 198.8. Anal calcd. for $C_{20}H_{32}O_2Si_2$ (%): C 72.23, H 9.69; found: C 72.09, H 9.76.

8-Isopropenyl-6-methoxy-9-methyl-4-vinyl-deca-1,4,8-trien-3-one (8c)

84% from **18c**. IR (neat) (cm^{-1}) ν: 2978, 2925, 2822, 1670, 1631, 1606. ^{1}H NMR (C_6D_6, 500 MHz) δ: 1.68 (s, 3H), 1.70 (s, 3H), 1.77 (s, 3H), 2.23 (dd, J = 14.1, 5.6 Hz, 1H), 2.61 (dd, J = 14.1, 8.1 Hz, 1H), 3.11 (s, 3H), 3.89 (ddd, J = 8.8, 8.1, 5.6 Hz, 1H), 4.74 (s, 1H), 4.90 (d, J = 10.8 Hz, 1H), 5.05 (s, 1H), 5.01 (d, J = 17.6 Hz, 1H), 5.37 (d, J = 10.6 Hz, 1H), 5.51 (d, J = 8.8 Hz, 1H), 5.97 (d, J = 17.6 Hz, 1H), 6.12 (dd, J = 17.6, 10.8 Hz, 1H), 6.27 (dd, J = 17.6, 10.6 Hz, 1H). ^{13}C NMR (C_6D_6, 125 MHz) δ: 20.3, 22.1, 22.7, 37.3, 56.8, 77.4, 114.2, 116.8, 128.3, 130.3, 132.9, 135.8, 136.1, 137.5, 142.4, 146.7, 196.7. HR-MS (EI) m/z calcd. for $C_{17}H_{24}O_2$ ($[M]^+$): 260.1776; found: 260.1778.

8-Isopropenyl-6-methoxy-5,9-dimethyl-4-vinyl-deca-4,8-diene-1-yn-3-one (29)

86% from **28**. IR (neat) (cm^{-1}) ν: 3253, 3076, 2979, 2926, 2824, 2089, 1662, 1629. ^{1}H NMR (C_6D_6, 500 MHz) δ: 1.60 (s, 3H), 1.71 (s, 3H), 1.72 (s, 3H), 1.80 (s, 3H), 2.20 (dd, J = 14.2, 4.5 Hz, 1H), 2.47 (s, 1H), 2.72 (dd, J = 14.2, 8.9 Hz, 1H), 3.08 (s, 3H), 4.18 (dd, J = 8.9, 4.5 Hz, 1H), 4.79 (s, 1H), 5.04 (s, 1H), 5.07 (d, J = 11.1 Hz, 1H), 5.23 (d, J = 17.8 Hz, 1H), 6.34 (dd, J = 17.8, 11.1 Hz, 1H). ^{13}C NMR (C_6D_6, 75 MHz) δ: 12.7, 20.2, 22.2, 22.6, 35.7, 56.6, 78.9, 80.6, 83.5, 114.3, 118.0, 128.3, 130.4, 133.1, 138.1, 142.5, 146.4, 181.5. HR-MS (EI) calcd. for $C_{18}H_{24}O_2$ ($[M]^+$): 272.1776; found: 272.1768.

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).

5-Methoxy-4,8,11,11-tetramethyl-3-vinyl-bicyclo[5.3.1]undeca-3,7-dien-2-one (9a)

76% from **8a**. mp = 76–81 °C. IR (neat) (cm^{-1}) ν: 2927, 1673, 1378, 1463, 911, 750. ^{1}H NMR (C_6D_6, 500 MHz) 0.92 (s, 3H), 1.26 (s, 3H), 1.36 (s, 3H), 1.64–1.66 (m, 1H), 1.66 (s, 3H), 1.79 (ddd, J = 18.3, 10.2, 3.6 Hz, 1H), 1.90–1.96 (m, 1H), 2.10–2.16 (m, 1H), 2.51–2.56 (m, 2H), 2.62 (dd, J = 12.5, 6.4, 2.5 Hz, 1H), 3.00 (s, 3H), 4.12 (dd, J = 11.1, 6.4 Hz, 1H), 4.92 (dd, J = 11.0, 0.5 Hz, 1H), 5.65 (dd, J =

17.5, 0.5 Hz, 1H), 6.42 (dd, *J* = 17.5, 11.0 Hz, 1H). ^{13}C NMR (C_6D_6, 125 MHz) δ: 12.1, 19.8, 21.6, 25.1, 28.1, 29.0, 35.4, 37.8, 57.6, 63.4, 82.3, 115.5, 131.6, 131.8, 134.5, 135.1, 141.3, 212.3. HR-MS (EI) *m/z* calcd. for $C_{18}H_{26}O_2$ ([M]$^+$): 274.1934; found: 274.1951. Anal calcd. for $C_{18}H_{26}O_2$ (%): C 78.79, H 9.55; found: C 78.65, H 9.50.

5-Methoxy-8,11,11-trimethyl-4-trimethylsilanyl-3-vinyl-bicyclo[5.3.1]undeca-3,7-dien-2-one (9b)

62% from **8b**. mp = 81 to 82 °C. IR (neat) (cm^{-1}) ν: 2898, 1672. ^{1}H NMR (C_6D_6, 500 MHz) δ: 0.35 (s, 9H), 0.95 (s, 3H), 1.26 (s, 3H), 1.49 (s, 3H), 1.60–1.69 (m, 1H), 1.74–1.82 (m, 1H), 1.88–1.93 (m, 1H), 2.14–2.20 (m, 1H), 2.40 (dd, *J* = 12.2, 11.4 Hz, 1H), 2.50 (d, *J* = 7.6 Hz, 1H), 2.64 (dd, *J* = 12.2, 5.8 Hz, 1H), 3.05 (s, 3H), 4.26 (dd, *J* = 11.4, 5.8 Hz, 1H), 4.96 (d, *J* = 11.0 Hz, 1H), 5.07 (d, *J* = 17.5 Hz, 1H), 6.73 (dd, *J* = 17.5, 11.0 Hz, 1H). ^{13}C NMR (C_6D_6, 125 MHz) δ: 3.4, 19.7, 22.4, 24.9, 28.5, 28.9, 35.8, 37.6, 57.5, 63.2, 86.0, 117.4, 132.6, 133.9, 134.3, 141.2, 153.4, 213.2. HR-MS (EI) *m/z* calcd. for $C_{20}H_{32}O_2Si$ ([M]$^+$): 332.2172; found: 332.2163. Anal calcd. for $C_{20}H_{32}O_2Si$ (%): C 72.23, H 9.69; found: C 71.37, H 9.51.

5-Methoxy-8,11,11-trimethyl-3-vinyl-bicyclo[5.3.1]undeca-3,7-dien-2one (9c)

53% from **8c**. mp = 62 to 63 °C. IR (neat) (cm^{-1}) ν: 2947, 2828, 1679. ^{1}H NMR (500 MHz) δ: 0.90 (s, 3H), 1.15 (s, 3H), 1.38 (s, 3H), 1.63–1.68 (m, 1H), 1.73–1.81 (m, 2H), 2.11–2.14 (m, 1H), 2.45 (dd, *J* = 12.6, 9.7 Hz, 1H), 2.51 (m, 1H), 2.69 (dd, *J* = 12.6, 7.6 Hz, 1H), 3.06 (s, 3H), 4.11 (ddd, *J* = 9.7, 7.6, 6.5 Hz, 1H), 4.78 (d, *J* = 10.7 Hz, 1H), 4.96 (d, *J* = 17.6 Hz, 1H), 5.36 (d, *J* = 6.5 Hz, 1H), 5.98 (dd, *J* = 17.6, 10.7 Hz, 1H). ^{13}C NMR (125 MHz) δ: 19.2, 21.6, 25.8, 27.9, 28.3, 36.4, 37.3, 57.1, 63.6, 80.5, 114.7, 131.7, 132.9, 134.0, 136.9, 145.4, 210.9. HR-MS (EI) *m/z* calcd. for $C_{17}H_{24}O_2$ ([M]$^+$): 260.1776; found: 260.1773.

8-Isopropenyl-6-methoxy-5,9-dimethyl-1-trimethylsilyl-4-vinyl-deca-4,8-dien-1-yn-3-ol (27)

Butyl lithium (7.93 mL, 19.1 mmol, 2.4 mol L^{-1} in hexane) was added to a solution of trimethylsilylacetylene (2.44 mL, 17.3 mmol) in THF (50 mL) cooled to –78 °C. After 30 min, aldehyde **17a** (2.15 g, 8.66 mmol) in THF (20 mL) was added, and the solution was then stirred for 1 h at –78 °C. A saturated aqueous solution of N_4Cl (100 mL) was then added; the layers were separated, and the aqueous layer was extracted with ether (2 × 100 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 (2.66 g, 89%). IR (neat) (cm^{-1}) ν: 3334, 3075, 2930, 2165, 1625. ^{1}H NMR (C_6D_6, 300 MHz) δ: 0.12 (s, 9H), 1.73 (s, 3H), 1.74 (s, 3H), 1.77 (s, 3H), 1.86 (s, 3H), 2.29 (dd, *J* = 14.2, 4.8 Hz, 1H), 2.75 (dd, *J* = 14.2, 8.3 Hz, 1H), 3.11 (s, 3H), 4.57 (dd, *J* = 8.3, 4.8 Hz, 1H), 4.90 (s, 1H), 5.09 (s, 1H), 5.19 (dd, *J* = 11.6, 1.4 Hz, 1H), 5.63 (s, 1H), 5.66 (dd, *J* = 17.8, 1.4 Hz, 1H), 6.48 (dd, *J* = 17.8, 11.6 Hz, 1H). ^{13}C NMR (C_6D_6, 75 MHz) δ: –0.2, 13.6, 20.2, 22.2, 22.8, 35.8, 56.3, 59.8, 79.0, 89.4, 107.4, 114.2, 117.0, 128.3, 132.9, 133.5, 134.5, 139.0, 146.8. HR-MS (EI) *m/z* calcd. for $C_{21}H_{32}OSi$ ([M$^+$ – H_2O]): 328.2222; found: 328.2182.

8-Isopropenyl-6-methoxy-5,9-dimethyl-4-vinyl-deca-4,8-dien-1-yn-3-ol (28)

Tetrabutylammonium fluoride (6.35 mL, 6.35 mmol, 1.0 mol L^{-1} in THF) was added to a solution of silane **27** (1.10 g, 3.17 mmol) in THF (10 mL) at 0 °C, and the solution was stirred for 1 h at 21 °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 × 40 mL). The combined organic extracts were washed with brine (2 × 40 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 (0.738 g, 85%). IR (neat) (cm^{-1}) ν: 3421, 3307, 3076, 2929, 2821, 1630. ^{1}H NMR ($CDCl_3$, 300 MHz) δ: 1.66 (s, 6H), 1.74 (s, 3H), 1.76 (s, 3H), 2.22 (dd, *J* = 14.2, 6.2 Hz, 1H), 2.48 (d, *J* = 2.4 Hz, 1H), 2.51 (d, *J* = 6.4 Hz, 1H), 2.57 (dd, *J* = 14.2, 7.3 Hz, 1H), 3.15 (s, 3H), 4.09 (dd, *J* = 7.3, 6.2 Hz, 1H), 4.60 (s, 1H), 4.98 (s, 1H), 5.35 (dd, *J* = 11.7, 1.4 Hz, 1H), 5.52 (dd, *J* = 6.4, 2.4 Hz, 1H), 5.64 (dd, *J* = 17.9, 1.4 Hz, 1H), 6.47 (dd, *J* = 17.9, 11.6 Hz, 1H). ^{13}C NMR ($CDCl_3$, 75 MHz) δ: 14.9, 20.5, 22.3, 22.9, 35.6, 57.0, 59.6, 73.9, 79.9, 84.2, 114.5, 118.6, 128.8, 132.2, 133.0, 134.3, 137.9, 146.4. HR-MS (EI) *m/z* calcd. for $C_{18}H_{24}O$ ([M$^+$ – H_2O]): 256.1827; found: 256.1840.

6-Ethynyl-3-methoxy-4,9,10,10-tetramethyl-5-vinyl-7-oxa-bicyclo[4.3.1]deca-1(9),4-diene (30)

Diethylaluminium chloride (1.10 mL, 1.10 mmol, 1.0 mol L^{-1} in hexane) was added to a solution of ketone **29** (0.272 g, 1.00 mmol) in dichloromethane (20 mL) at –78 °C. The solution was slowly warmed to 0 °C and, after 5 min, cooled to –78 °C. A saturated aqueous solution of $NaHCO_3$ (20 mL) was 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 colorless oil (0.167 g, 62%). IR (neat) (cm^{-1}) ν: 3285, 2974, 2931, 2821, 1608, 1561. ^{1}H NMR (C_6D_6, 500 MHz) δ: 1.18 (d, *J* = 13.5 Hz, 1H), 1.36 (s, 3H), 1.37 (s, 3H), 1.44 (s, 3H), 1.51 (dd, *J* = 13.8, 10.2 Hz, 1H), 1.92 (d, *J* = 13.5 Hz, 1H), 2.01 (s, 3H), 2.72 (s, 1H), 2.85 (dd, *J* = 13.8, 7.0 Hz, 1H), 3.14 (s, 3H), 3.53 (dd, *J* = 10.2, 7.0 Hz, 1H), 5.10 (dd, *J* = 11.9, 1.5 Hz, 1H), 5.38 (dd, *J* = 18.0, 1.5 Hz, 1H), 6.89 (dd, *J* = 18.0, 11.9 Hz, 1H). ^{13}C NMR (C_6D_6, 75 MHz) δ: 21.5, 22.0, 22.2, 24.8, 30.7, 37.6, 44.2, 57.0, 77.6, 78.9, 79.7, 81.3, 113.9, 127.3, 129.2, 131.3, 133.0, 136.3. HR-MS (EI) *m/z* calcd. for $C_{18}H_{24}O_2$ ([M]$^+$): 272.1776; found: 272.1743.

Conclusion

We have successfully extended the magnesium-mediated carbometallation protocol developed in our laboratories to more complex systems and studied various aspects in more depth. In addition, the nuances of the *cis*-alkene tether controlled intramolecular Diels–Alder reactions to bicyclo-

[5.3.1]undecenones have been delineated. A key feature is the diastereoselectivity derived from Lewis acid complexation, which implies that enantioselective cycloaddition may eventually be feasible. A direct route to these taxane AB-ring building blocks has been established for future elaboration into the complete nucleus by different procedures. In total, these procedures provide direct access to functionalized molecules that may be employed for a variety of synthetic objectives.

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