Stereoselective Synthesis of Exocyclic Alkenes by Cu-Catalyzed Allylmagnesiation, Pd-Catalyzed Alkylation, and Ru-Catalyzed Ring-Closing Metathesis: Highly Stereoselective Synthesis of (*Z*)- and (*E*)-γ-Bisabolenes

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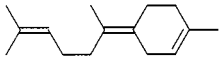
Dedicated to Professor Jean François Normant on the occasion of his 65th birthday

Keywords: Asymmetric synthesis / Natural products / Alkylation / Catalysis / Cyclization / Bisabolenes

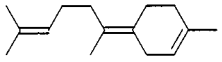
Highly efficient stereoselective syntheses of both (*Z*)- and (*E*)-γ-bisabolenes (**1**) were achieved by ring closing metathesis of stereodefined tetrasubstituted alkenes. Both (*Z*)- and (*E*)-tetrasubstituted alkene precursors were obtained by Cu-catalyzed stereoselective addition of allylmagnesium bromide to propargyl alcohols, followed by Pd-catalyzed cross coupling of alkylzinc derivatives. This represents the first application of ring-closing metathesis to the stereoselective synthesis of exocyclic alkenes.

Introduction

Various types of natural and non-natural products containing stereodefined exocyclic alkenes have been shown to possess significant biological and medicinal activities. They include prostacyclin,[1] carbacyclin,[2] punaglandins and chlorovulones,[3] pumiliotoxins,[4] freelingyne,[5] senkynnolides,[6] and γ-bisabolene[7] (**1**). Collectively, these stereodefined exocyclic alkenes have provided a major synthetic challenge for the organic chemist. Such alkenes can also serve as convenient intermediates for the synthesis of compounds of defined stereochemistry. Although various stereoselective methods for the synthesis of these exocyclic alkenes have been developed,[8] the extent of the stereoselectivity has often been marginal.



(*Z*)-γ-bisabolene (**1a**)



(*E*)-γ-bisabolene (**1b**)

Based on an organometallic strategy for the synthesis of exocyclic alkenes we introduced in 1986,[9] we envisioned a ring-closing metathesis (RCM) route to stereodefined exocyclic alkenes, as depicted in Scheme 1. Addition of allylmagnesium bromide to propargylic alcohols (**2**) in the presence of a catalytic quantity of CuI, followed by iodinolysis, is known to produce **3** in a completely stereo- and regioselective manner. After converting **3** into **4** and then into **5** through a series of C−C bond formations, **5** may be subjected to ring closing metathesis[10] to produce the exocyclic alkenes **6**.

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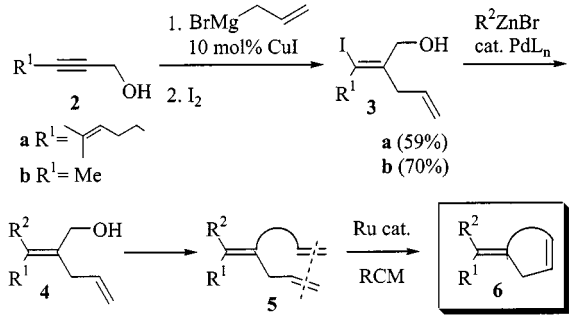

Scheme 1

Since the recent development of a few very efficient Ru[11] and Mo[12] complexes for RCM,[10] a wide variety of cyclic compounds have been synthesized using this methodology.[13] To the best of our knowledge, however, the use of RCM for the synthesis of exocyclic alkenes such as those shown in Scheme 1 does not appear to have been reported previously. We therefore chose (*E*)- and (*Z*)-γ-bisabolene (**1**)[7] as targets for testing and demonstrating the potential synthetic value of this protocol.

Results and Discussion

With the above mentioned goal in mind, the propargylic alcohols **2a** and **2b**[14] were converted into **3a** and **3b** in 59 and 70% yields, respectively, by Cu-catalyzed allylmagnesiation[15] followed by iodinolysis. As is well known, the Cu-catalyzed carbomagnesiation of propargyl alcohols gives tetrasubstituted alkenes with four different groups in a completely regio- and stereoselective manner. Indeed, both **3a** and **3b** were found to be ≥99% isomerically pure.[16] (*Z*)-γ-Bisabolene (**1a**) was then synthesized as a ≥98% isomerically pure compound[16] from **3a**, as summarized in

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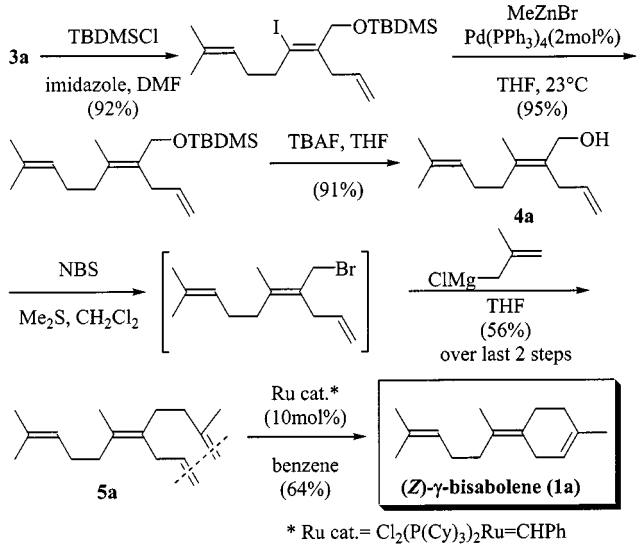
Scheme 2, in five isolation steps and 29% overall yield. Throughout the synthesis, there was no sign of stereoisomerization. After protection of **3a** with TBDMSCl, the Pd-catalyzed alkylation[17] with MeZnBr in the presence of 2 mol % of $Pd(PPh_3)_4$ in THF followed by deprotection with TBAF cleanly produced **4a** of ≥98% isomeric purity[16] in 80% overall yield. It was then converted into the bromide with NBS and Me_2S in CH_2Cl_2.[18] After workup without isolation, the bromide was subjected to a coupling reaction with methallylmagnesium chloride in THF to provide the tetraenic precursor **5a** in 56% yield as a ≥98% isomerically pure substance.[16]

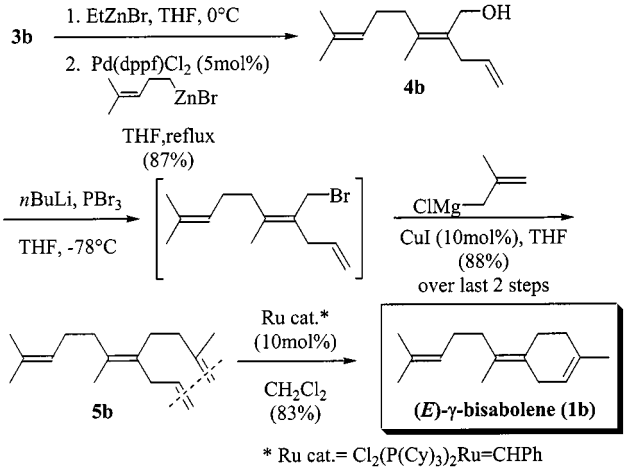


Scheme 2

The RCM reaction of **5a** with 10 mol % of $[Cl_2(PCy_3)_2Ru{=}CHPh]$[19] in benzene at 23 °C proceeded smoothly to produce the desired (*Z*)-γ-bisabolene (**1a**) in 64% yield as a ≥98% pure compound. The overall yield over six steps starting from **2a** was 17%. As satisfactory as the synthesis of **1a** shown in Scheme 2 was, it was desirable to avoid the protection-deprotection of the allylic alcohol **2a** before and after methylation. Indeed, we earlier demonstrated the feasibility of using EtZnBr as a sacrificial alkylzinc reagent.[20] Rather than improve the synthesis of (*Z*)-γ-bisabolene shown in Scheme 2, we chose to synthesize the *E* isomer **1b** to demonstrate the practical applicability of the above-mentioned strategy for providing an ultimately satisfactory and selective route to γ-bisabolenes and other related exocyclic alkenes in general.

As summarized in Scheme 3, **3b** was converted into **4b** in 87% yield. For the Pd-catalyzed alkylation with alkylzinc reagents containing β-hydrogens, certain palladium catalysts with bidentate phosphanes (dppf and dppp in particular) have been shown to be superior to $[Pd(PPh_3)_4]$ and other Pd complexes.[21]

Conversion of **4b** to the corresponding bromide proved to be much more difficult than that of **4a**, presumably due to the *syn* relationship of the 4-methyl-3-pentenyl and hydroxy- or bromomethyl groups. After some unsatisfactory



Scheme 3

attempts, including the use of NBS-Me_2S, which led to the formation of unwanted by-products including the stereoisomer, it was judged to be essential to avoid the presence of an acid during the reaction. Indeed, pretreatment of **4b** with 1 equiv. of *n*BuLi before the addition of PBr_3 (1 equiv.) led to the clean formation of the desired bromide, as judged by NMR spectroscopy of the reaction mixture.[22] After workup without purification, this bromide was subjected to the Cu-catalyzed reaction with methallylmagnesium bromide to provide **5b**, in a highly selective manner, in 88% yield based on **4b**. The final RCM reaction with 10 mol % of $[Cl_2(PCy_3)_2Ru{=}CHPh]$[19] was similarly satisfactory in providing (*E*)-γ-bisabolene (**1b**) as a ≥98% isomerically pure substance in 83% yield (44% overall yield in four steps from **2b**). The *E* geometry of **1b** was unequivocally established by NOE measurements, which revealed a significant NOE between the CH_2 (δ = 2.72) flanked by two C=C bonds, the adjacent olefinic proton (δ = 5.40), and the CH_3 (δ = 1.66) on the tetrasubstituted C=C bond.[23]

Conclusion

In summary, a combination of Cu-catalyzed allylation of propargylic alcohols, Pd-catalyzed cross coupling, and ring-closing metathesis provides a new protocol for the synthesis of stereodefined tetrasubstituted exocyclic alkenes, which further expands the scope of the carbometallation-based efficient and stereoselective methodology for the exocyclic alkene synthesis we have been developing during the past 15 years.[8,9,24]

Experimental Section

General Remarks: All manipulations involving organometallic reagents were carried out under an atmosphere of Ar using standard techniques. Organolithium and organomagnesium halides were titrated with 2-butanol/1,10-phenanthroline. THF was distilled from sodium benzophenone ketyl, and benzene was distilled from $LiAlH_4$. All other commercial solvents were dried over 4 Å molecular

sieves. The other commercial reagents were used as received. ^1H and ^{13}C NMR spectra were recorded in $CDCl_3$ on Varian Gemini-200 (200 MHz) and Innova-300 NMR (300 MHz) spectrometers using $CDCl_3$ as an internal standard, unless otherwise noted.

Synthesis of (*Z*)-γ-Bisabolene

7-Methyl-6-octen-2-yn-1-ol (2a):[14] To a mixture of Mg turnings (8.7 g, 360 mmol), I_2 (one crystal) and $HgCl_2$ (50 mg, 0.1 mmol) in THF (20 mL) was added a solution of propargyl bromide (9 mL, 120 mmol) dissolved in THF (100 mL). After the addition of the first 10 mL, the reaction mixture was heated to reflux to initiate the reaction, and the remaining part of the solution of propargyl bromide in THF was added at such a rate as to maintain a slight reflux. After the addition was complete, the reaction mixture was refluxed for 30 min., and then added to a solution of 1-bromo-3-methyl-2-butene (6.67 g, 5.2 mL, 44 mmol) in THF (40 mL) at 23 °C. The resulting reaction mixture was refluxed for 2 h, quenched with aqueous NH_4Cl, extracted with pentane, washed with aqueous $NaHCO_3$, dried over $MgSO_4$, and filtered. Evaporation of the solvent followed by distillation afforded 3.5 g (74%) of 6-methyl-5-hepten-1-yne. To a solution of this enyne (2.80 g, 25.9 mmol) in THF (65 mL) at −78 °C were added successively a solution of *n*BuLi (2.5 M in hexanes, 11.4 mL, 28.5 mmol) and, after 1 h, paraformaldehyde (1.17 g, 38.8 mmol). The reaction mixture was then warmed to 23 °C, quenched with aqueous NH_4Cl, extracted with Et_2O, washed with aqueous $NaHCO_3$, dried over $MgSO_4$, filtered, and concentrated. Chromatography on silica gel (pentane/Et_2O, 70:30 v/v) afforded 4.1 g (68%) of 7-methyl-6-octen-2-yn-1-ol: ^1H NMR ($CDCl_3$) δ = 1.62 (s, 3 H), 1.70 (s, 3 H), 1.72 (s, 1 H), 2.15−2.25 (m, 4 H), 4.25 (s, 2 H), 5.15−5.2 (m, 1 H).

(2*Z*)-2-Allyl-3-iodo-7-methyl-2,6-octadien-1-ol (3a):[15] To a solution of 7-methyl-6-octen-2-yn-1-ol (3.45 g, 25 mmol) and copper(I) iodide (0.475 g, 2.5 mmol) in dry Et_2O (25 mL) was added allylmagnesium bromide (1 M in Et_2O, 75 mL, 75 mmol) dropwise at 0 °C. After the addition was complete, the reaction mixture was stirred at 23 °C for 20 h, and then cooled to −78 °C. A solution of I_2 (19 g, 75 mmol) in THF (50 mL) was added by cannula, and the reaction mixture was slowly warmed to 23 °C, stirred for 1 h, and washed successively with aqueous NH_4Cl, aqueous $NaHCO_3$, and aqueous $Na_2S_2O_3$. Drying over $MgSO_4$, filtration, concentration, and purification by chromatography (pentane/Et_2O, 90:10 v/v) provided (2*Z*)-2-allyl-3-iodo-7-methyl-2,6-octadien-1-ol (4.5 g, 59%, with a stereoselectivity >98%[16]): ^1H NMR ($CDCl_3$) δ = 1.54 (s, 3 H), 1.60 (s, 3 H), 2.17 (apparent q, *J* = 7.0 Hz, 2 H), 2.53 (t, *J* = 7.0 Hz, 2 H), 3.02 (d, *J* = 6.0 Hz, 2 H), 4.19 (s, 2 H), 5.0−5.1 (m, 3 H), 5.65−5.8 (m, 1 H). − ^{13}C NMR ($CDCl_3$) δ = 17.79, 25.60, 27.82, 34.29, 41.57, 71.42, 107.13, 116.16, 122.07, 132.93, 134.84, 140.06.

(2*Z*)-2-Allyl-1-(*tert*-butyldimethylsiloxy)-3-iodo-7-methyl-2,6-octadiene: To a solution of (2*Z*)-2-allyl-3-iodo-2-methyl-2,6-octadien-1-ol (3.43 g, 11.2 mmol) in DMF (15 mL) were added imidazole (1.53 g, 22.4 mmol) and *tert*-butyldimethylsilyl chloride (2.04 g, 13.5 mmol) at 23 °C. The reaction mixture was stirred overnight, poured into pentane, washed with aqueous NH_4Cl and then with aqueous $NaHCO_3$, dried over $MgSO_4$, filtered, and concentrated. Chromatography (pentane/Et_2O, 90:10 v/v) provided (2*Z*)-2-allyl-1-(*tert*-butyldimethylsiloxy)-3-iodo-7-methyl-2,6-octadiene (4.3 g, 92%): ^1H NMR ($CDCl_3$) δ = 0.08 (s, 6 H), 0.88 (s, 9 H), 1.63 (s, 3 H), 1.67 (s, 3H), 2.23 (q, *J* = 7.0 Hz, 2 H), 2.57 (t, *J* = 7.0 Hz, 2 H), 3.05 (d, *J* = 6.0 Hz, 2 H), 4.25 (s, 2 H), 5.0−5.1 (m, 3 H), 5.6−5.8 (m, 1 H). − ^{13}C NMR ($CDCl_3$): δ = −5.19, 17.86, 18.25, 25.70, 25.93, 27.87, 33.36, 41.54, 71.95, 104.32, 115.52, 122.39, 132.78, 135.23, 140.32.

(2*E*)-2-Allyl-1-(*tert*-butyldimethylsiloxy)-3,7-dimethyl-2,6-octadiene: To a solution of dry $ZnBr_2$ (4.49 g, 19.9 mmol) in THF (25 mL) at 0 °C was added a solution of methylmagnesium bromide (3 M in Et_2O, 5.3 mL, 16 mmol). The reaction mixture was stirred at 23 °C for 30 min., and then a mixture of [$Pd(PPh_3)_4$] (277 mg, 0.24 mmol) and (2*Z*)-2-allyl-1-(*tert*-butyldimethylsiloxy)-3-iodo-2-methyl-2,6-octadiene (5.04 g, 12 mmol) in THF (12 mL) was added by cannula at 0 °C. The reaction mixture was stirred for 18 h, diluted with Et_2O, washed with aqueous NH_4Cl and then with aqueous $NaHCO_3$, dried over $MgSO_4$, filtered, and concentrated. Filtration on a pad of silica (pentane) gave (2*E*)-2-allyl-1-(*tert*-butyldimethylsiloxy)-3,7-dimethyl-2,6-octadiene (3.51 g, 95%): ^1H NMR ($CDCl_3$) δ = 0.16 (s, 6 H), 0.90 (s, 9 H), 1.70 (s, 3 H), 1.77 (s, 3 H), 2.15−2.25 (m, 2 H), 2.45−2.5 (m, 2H) 3.01 (d, *J* = 6.0 Hz, 2 H), 4.23 (s, 2 H), 5.0−5.2 (m, 3 H), 5.85−5.9 (m, 1 H). − ^{13}C NMR ($CDCl_3$): δ = −5.28 (2 C), 17.55, 17.82, 18.36, 25.66, 25.96 (3 C), 26.71, 33.68, 34.71, 61.69, 114.42, 124.28, 130.19, 131.40, 132.54, 137.13.

(2*E*)-2-Allyl-3,7-dimethyl-2,6-octadien-1-ol (4a): To a solution of (2*Z*)-2-allyl-1-(*tert*-butyldimethylsiloxy)-2,3-dimethyl-2,6-octadiene (3.51 g, 11.38 mmol) in THF (8 mL) was added tetrabutylammonium fluoride (1 M in THF, 14 mL, 14 mmol) at 23 °C. After 5 h, the reaction mixture was diluted with Et_2O, washed with aqueous NH_4Cl and then with aqueous $NaHCO_3$, dried over $MgSO_4$, filtered, and concentrated to afford (2*E*)-2-allyl-3,7-dimethyl-2,6-octadien-1-ol (2.0 g, 92%): ^1H NMR ($CDCl_3$) δ = 1.57 (s, 3 H), 1.65 (s, 3 H), 1.74 (s, 3 H), 2.03 (br. s, 4 H), 2.89 (d, *J* = 6.0 Hz, 2 H), 4.07 (s, 2 H), 4.95−5.1 (m, 3 H), 5.7−5.8 (m, 1 H). − ^{13}C NMR ($CDCl_3$) δ = 17.46, 17.78, 25.54, 26.66, 34.55, 34.61, 61.75, 114.90, 123.95, 129.82, 131.57, 134.86, 136.93.

(5*Z*)-5-Allyl-2,6,10-trimethyl-1,5,9-undecatriene (5a): To a solution of *n*-bromosuccinimide (804 mg, 4.5 mmol) in CH_2Cl_2 (15 mL) was added dimethyl sulfide (5.4 mmol, 0.40 mL) dropwise at 0 °C.[18] To this reaction mixture was added (2*E*)-2-allyl-3,7-dimethyl-2,6-octadien-1-ol (582 mg, 3 mmol) in CH_2Cl_2 (6 mL) dropwise at −78 °C. After stirring at 0 °C for 5 h and then at 23 °C for 18 h, the reaction mixture was diluted with pentane, and poured into cold water (4 mL). The organic layer was separated, washed with cold brine, filtered quickly on a pad of silica, and concentrated to give (2*E*)-2-allyl-3,7-dimethyl-2,6-octadienyl bromide, which was used immediately without purification, as described below. To a solution of (2*E*)-2-allyl-3,7-dimethyl-2,6-octadienyl bromide in THF (8 mL) was added methallylmagnesium chloride (0.5 M in THF, 12 mL, 6 mmol) at 0 °C, and the resultant mixture was stirred overnight at 23 °C. It was then diluted with pentane, poured onto ice, washed with aqueous NH_4Cl and then with aqueous $NaHCO_3$, dried over $MgSO_4$, filtered, and concentrated. Chromatography on silica gel (pentane) gave (5*Z*)-5-allyl-2,6,10-dimethyl-1,5,9-undecatriene (**4a**) (390 mg, 56%): ^1H NMR ($CDCl_3$) δ = 1.62 (s, 3 H), 1.70 (s, 6 H), 1.76 (s, 3 H), 2.05−2.15 (m, 8 H), 2.80 (d, *J* = 6.0 Hz, 2 H), 4.71 (s, 2H), 4.95−5.15 (m, 3 H), 5.7−5.8 (m, 1 H). − ^{13}C NMR ($CDCl_3$) δ = 17.60, 17.99, 22.54, 25.69, 27.08, 30.84, 34.47, 36.52, 36.55, 109.48, 114.66, 124.43, 130.18, 130.27, 131.35, 137.23, 146.30. − HRMS calcd. for $C_{17}H_{28}$ [M + 1]: 233.2269; found 233.2270.

(*Z*)-γ-Bisabolene (1a): To a solution of (5*Z*)-5-allyl-2,6,10-dimethyl-1,5,9-undecatriene (116 mg, 0.5 mmol) in benzene (30 mL) was added [$Cl_2(PCy_3)_2Ru{=}CHPh$] (44 mg, 0.05 mmol, 10% mmol).[19] The reaction mixture turned dark purple, and an evolution of gas, presumably ethylene, was observed. After 1 day, the reaction mixture was exposed to air for 5 h to destroy the catalyst. The reaction mixture was then concentrated. No aqueous workup was necessary,

and the residue was purified by chromatography on silica gel (pentane) to provide (*Z*)-γ-bisabolene[7] (65.4 mg, 64%): ^{1}H NMR ($CDCl_3$) δ = 1.60 (s, 3 H), 1.67 (s, 6 H), 1.70 (s, 3 H), 1.95−2.1 (m, 6 H), 2.31 (t, *J* = 6.0 Hz, 2 H), 2.75 (br. s, 2 H) 5.12 (br. s, 1 H), 5.36 (br. s, 1 H). − ^{13}C NMR ($CDCl_3$) δ = 17.60, 17.82, 23.39, 25.70, 26.78, 26.83, 29.31, 31.56, 34.45, 120.85, 124.48, 125.65, 128.39, 131.39, 134.13. − IR (neat): ν̃ = 2965, 2910, 2853, 1670, 1440, 1373, 1108, 830, 795 cm^{-1}.

Synthesis of (*E*)-γ-Bisabolene

(Z)-2-Allyl-3-iodo-2-buten-1-ol (3b):[15] The title compound was prepared according to the literature procedure: ^{1}H NMR ($CDCl_3$, Me_4Si) δ = 2.31 (br. s, 1 H), 2.55 (s, 3 H), 3.08 (d, *J* = 6.1 Hz, 2 H), 4.23 (br. s, 2 H), 5.0−5.1 (m, 2 H), 5.7−5.8 (m, 1 H). − ^{13}C NMR ($CDCl_3$) δ = 30.34, 33.71, 71.37, 97.94, 115.95, 134.32, 140.02.

(2*Z*)-2-Allyl-3,7-dimethyl-2,6-octadien-1-ol (4b): To a mixture of Mg turnings (0.9 g, 36.8 mmol), I_2 (one crystal), and CH_2Br_2 (20 μL) in THF (2 mL) was added a solution of commercially available 5-bromo-2-methyl-2-pentene (3 g, 18.4 mmol) and dry $ZnBr_2$ (4.4 g, 19.6 mmol) dissolved in THF (20 mL). The reaction mixture was heated to gentle reflux for 7 h. In another flask a solution of **3b** (2.9 g, 12.3 mmol) in THF (30 mL) was added dropwise to a solution of EtMgBr (1 M in THF, 12.28 mL) and $ZnBr_2$ (2.76 g, 12.28 mmol) in THF (10 mL) at 0 °C. The first reaction mixture was then transferred by cannula to the second flask, and then [$PdCl_2$(dppf)] (317 mg, 0.37 mmol) was added. The reaction mixture was then heated to reflux for 10 h, diluted with Et_2O, washed with aqueous NH_4Cl and then with aqueous $NaHCO_3$, dried over $MgSO_4$, filtered, and concentrated. Chromatography on silica gel (hexane/EtOAc, 90:10 v/v) gave (2*Z*)-2-allyl-3,7-dimethyl-2,6-octadien-1-ol (**4b**) (2.08 g, 87%): ^{1}H NMR ($CDCl_3$, Me_4Si) δ = 1.59 (s, 3 H), 1.68 (s, 3 H), 1.70 (s, 3 H), 2.1−2.9 (m, 4 H), 2.91 (d, *J* = 6.0 Hz, 2 H), 4.07 (s, 2 H), 4.95−5.1 (m, 3 H), 5.75−5.8 (m, 1 H). − ^{13}C NMR ($CDCl_3$) δ = 17.45, 18.22, 25.50, 26.49, 34.08, 34.97, 61.48, 114.56, 123.92, 130.33, 132.22, 134.84, 136.22.

(5*Z*)-5-Allyl-2,6,10-trimethyl-1,5,9-undecatriene (5b): To a solution of **4b** (500 mg, 2.57 mmol) in THF (10 mL) was added *n*BuLi (2.5 M in hexanes, 1.03 mL) at −78 °C. After the addition was complete, phosphorus tribromide (0.70 g, 0.24 mL, 2.57 mmol) was added dropwise, and the reaction mixture was stirred at −78 °C for 3 h, diluted with pentane, and poured into cold water (10 mL).[22] The organic layer was separated, washed with cold brine, filtered quickly on a pad of celite, and concentrated to give (2*Z*)-2-allyl-3,7-dimethyl-2,6-octadienyl bromide, which was used immediately without purification, as described below. To a solution of (2*Z*)-2-allyl-3,7-dimethyl-2,6-octadienyl bromide and CuI (49 mg, 0.26 mmol) in THF (8 mL) was added methallylmagnesium chloride (0.5 M in THF, 7.7 mL, 3.8 mmol) at −78 °C. The reaction mixture was stirred for 1 h at −78 °C, diluted with pentane, poured onto ice, washed with aqueous NH_4Cl and then with aqueous $NaHCO_3$, dried over $MgSO_4$, filtered, and concentrated. Chromatography on silica gel (pentane) gave (5*E*)-5-allyl-2,6,10-dimethyl-1,5,9-undecatriene (**5b**) (525 mg, 88%): ^{1}H NMR ($CDCl_3$, Me_4Si) δ = 1.61 (s, 3 H), 1.65 (s, 3 H), 1.68 (s, 3 H), 1.68 (s, 3 H), 1.95−2.2 (m, 8 H), 2.77 (d, *J* = 6.0 Hz, 2 H), 4.68 (s, 2 H), 4.95−5.15 (m, 3 H), 5.7−5.75 (m, 1 H). − ^{13}C NMR ($CDCl_3$) δ = 17.54, 17.96, 22.52, 25.67, 27.20, 30.82, 34.41, 36.78, 37.18, 109.46, 114.35, 124.47, 130.10, 130.42, 131.32, 136.45, 146.21. − HRMS calcd. for $C_{17}H_{28}$ [M + 1]: 233.2269; found 233.2271.

(*E*)-γ-Bisabolene (1b): To a solution of (5*E*)-5-allyl-2,6,10-dimethyl-1,5,9-undecatriene (125 mg, 0.54 mmol) in CH_2Cl_2 (30 mL) was added [$Cl_2(PCy_3)_2Ru$=CHPh] (44 mg, 0.054 mmol, 10% mmol).[19] The reaction mixture turned dark purple, and an evolution of gas, presumably ethylene, was observed. After 2 h, the reaction mixture was exposed to air for 3 h to destroy the catalyst. The reaction mixture was then concentrated. No aqueous workup was necessary, and the residue was purified by chromatography on silica gel (pentane) to provide (*E*)-γ-bisabolene[7] (91 mg, 83%): ^{1}H NMR ($CDCl_3$, Me_4Si) δ = 1.60 (s, 3 H), 1.66 (s, 6 H), 1.68 (s, 3 H), 1.95−2.15 (m, 6 H), 2.32 (t, *J* = 6.4 Hz, 2 H), 2.72 (br. s, 2H), 5.1−5.2 (m, 1 H), 5.37 (br. s, 1 H). − ^{13}C NMR ($CDCl_3$) δ = 17.59, 18.37, 23.41, 25.72, 26.51, 27.31, 29.71, 31.80, 34.18, 120.74, 124.52, 125.87, 128.35, 131.37, 134.19.

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