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Total Syntheses and Absolute Configuration Assignment of (+)-Sootepdienone, (−)-Jambolanin C, (−)-Jambolanin I, and (−)-Gibberodione

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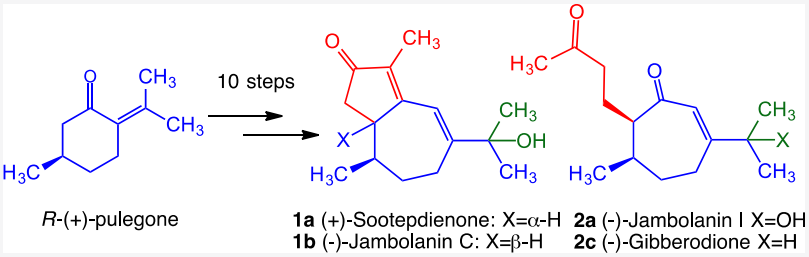

ABSTRACT: Total syntheses of the sesquiterpenes (+)-sootepdienone, (−)-jambolanin C, (−)-jambolanin I, and (−)-gibberodione have been accomplished in 10 steps each from *R*-(+)-pulegone, allowing assignment of the absolute configuration of the natural products. A key step in the synthetic pathways involves the one-carbon ring expansion of a cyclic allylic phosphonate to a substituted cycloheptenone by a tandem oxidative cleavage/intramolecular Horner−Wadsworth−Emmons reaction.

In 1998, Rukachaisirikul, Taylor, and Bubb detailed the isolation of the sesquiterpene sootepdienone from the twigs of the shrub *Gardenia sootepensis* in Thailand (Figure 1).[1] Subsequently, Huang and Li, who reported the isolation of 11 similar sesquiterpenoids (Jambolanins A−K) from the seeds of *Eugenia jambolana* fruit, revealed that sootepdienone inhibits the growth of the Gram-positive bacterium *Staphylococcus aureus*.[2] Jambolanin C was discovered to be the C-1 diastereomer of sootepdienone, and jambolanins I, J, and gibberodione (previously isolated by Sheu et al.)[3] lack the cyclopentenone moiety of sootepdienone and jambolanins A−C. Given the interesting biological profile of sootepdienone, we decided to undertake synthetic studies directed toward this family of sesquiterpenes,[4] in the hope that a short and flexible pathway would allow the preparation of derivatives with heightened antibacterial activities.[5]

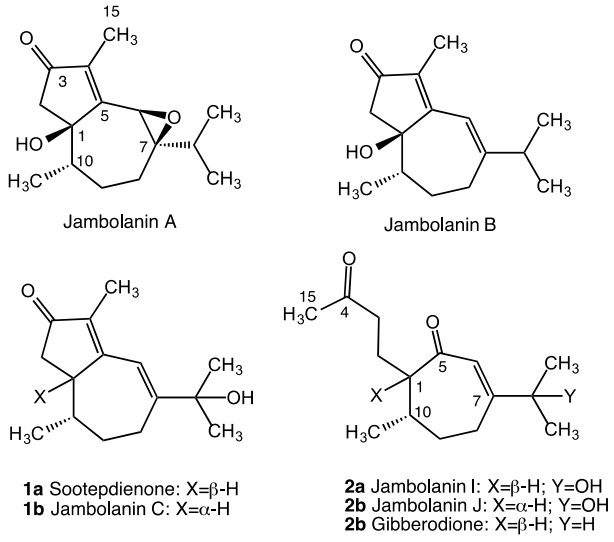

Figure 1. Proposed chemical structures of jambolanins A−C, I, J, sootepdienone, and gibberodione.

We envisioned that sootepdienone and jambolanins C, I, and gibberodione could be accessed from a common cycloheptenone core; furthermore, we viewed the readily available monoterpene pulegone as a starting material for the syntheses. Key to the success of this strategy would be a one-carbon ring expansion of a cyclohexenone to a cycloheptenone, and we anticipated that our recently developed homologation process involving oxidative cleavage of cyclic allylic phosphonates and base-mediated intramolecular Horner−Wadsworth−Emmons reaction[6] would allow us to achieve this desired transformation.[7] In addition, we expected that construction of the cyclopentenone ring of jambolanin C and sootepdienone

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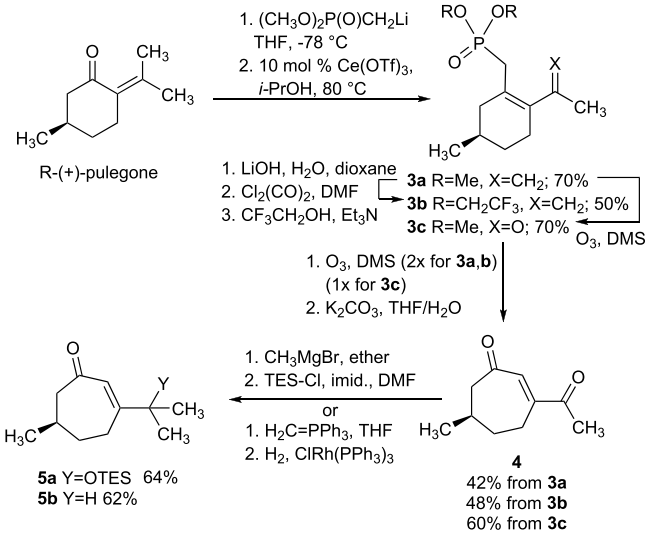
could be achieved by installation of a 2-butanone side chain (or equivalent) by ketone α-alkylation, followed by intramolecular aldol condensation. The realization of this plan is detailed in the present *Note*.

Addition of 2 equiv of (1-lithiomethyl)dimethylphosphonate to *R*-(+)-pulegone in THF at −78 °C,[8] followed by reaction quench and aqueous workup gave the expected tertiary hydroxyphosphonate, which was immediately dehydrated by treatment with substoichiometric amounts of cerium triflate (2 mol %) in isopropanol at 80 °C for 2 h[9] to provide diene **3a** in 70% overall yield (Scheme 1). Ozonolyses of **3a** in methanol at

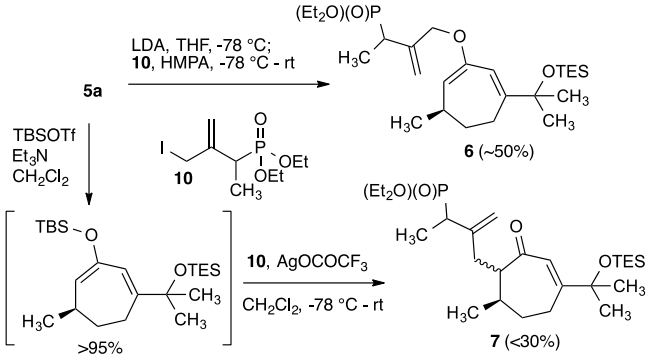
Scheme 1. Preparation of Cycloheptenones 5a and 5b



−78 °C resulted in selective cleavage of the isopropenyl double bond to provide intermediate enone **3c** (70%), which was directly subjected to ozonolysis again at −78 °C for 2 h. After workup with dimethylsulfide, dissolution of the resulting crude α-diketone in 1:1 THF/H_2O (0.05 M) and treatment with 4.5 equiv of K_2CO_3 at room temperature for 1 h then gave cycloheptenone **4** in 60% yield from **3c** (42% overall from **3a**). Use of other base/solvent systems for the intramolecular HWE reaction (DBU, CH_2Cl_2; NaH, THF; Cs_2CO_3, THF, H_2O) gave lower overall yields. Conversion of **3a** into the bis(trifluoroethyl)phosphonate **3b**,[10a] followed by exhaustive ozonolysis and intramolecular HWE reaction, gave **4** in 48% overall yield from **3b**.[10b] Introduction of the tertiary alcohol was then accomplished by treatment of an ethereal solution of **4** at −78 °C with 1.1 equiv of CH_3MgBr and warming to room temperature. Direct silylation of the tertiary alcohol then gave rise to cycloheptenone **5a** in 64% overall yield from **4**. Alternatively, Wittig reaction of **4** with methylene triphenylphosphorane, followed by selective hydrogenation of the isopropenyl group with Wilkinson's catalyst,[11] gave rise to **5b** in 62% overall yield.

Next, we desired to introduce an allylic phosphonate side chain at the ketone α-carbon atom of enone **5a**, in the hopes that a similar oxidative cleavage/intramolecular HWE reaction sequence would give rise to the cyclopentannulated product (Scheme 2). However, treatment of **5a** with LDA in THF at −78 °C, followed by reaction of the lithium enolate with allyl iodide **10**[7] in the presence or absence of HMPA, provided primarily the *O*-alkylation product **6**[21] in ∼50% yield. In light of this result, formation of the *tert*-butyldimethyl-silyl enol

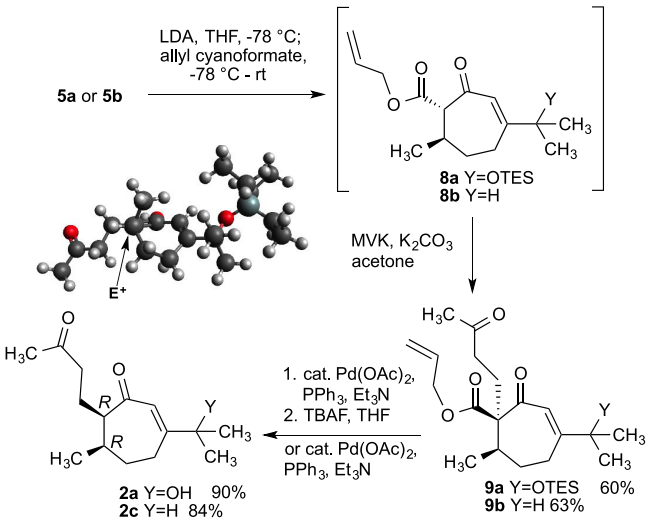
Scheme 2. Attempted Side Chain Introduction onto 5a



ether of **5a** proceeded uneventfully (TBSOTf, Et_3N, CH_2Cl_2, −78 °C) to provide the corresponding siloxy diene in >95% yield (by NMR). Combination of the siloxy diene with 2 equiv **10** in the presence of 2 equiv of silver trifluoracetate in dichloromethane (−78 °C−rt)[12] led primarily to the *C*-alkylated product **7**, albeit in low (<30%) yields. All attempts to improve the yields of **7** by varying the reaction solvent and by decreasing the amounts of **10** or silver trifluoroacetate employed proved fruitless. Thus, alternative strategies were required for α-alkylation of cycloheptenone **5a**.

Shifting our focus to the preparation of jambalonin I, we attempted direct conjugate addition of the lithium enolate of **5a** to MVK (−78 °C−rt) either in the presence or absence of diisopropylamine; however no discernible 1,4-addition product could be isolated from the reaction mixture.[13] Following the precedent of Stoltz,[14] deprotonation of **5a** with LDA (1.1 equiv, THF, −78 °C) followed by addition of allyl cyanoformate[20] gave rise to allyl-β-keto ester **8a**, which upon exposure to MVK in the presence of excess K_2CO_3 in acetone at 40 °C produced the 1,4-adduct **9a** in 60% overall yield with >10:1 diastereomeric excess (Scheme 3).[15] Finally, treatment of **9a** with 10 mol % palladium acetate in the presence of Et_3N (1.1 equiv) and PPh_3 (2 mol %) in 9:1 CH_3CN/H_2O[16] resulted in smooth deallyloxycarbonylation to provide the intermediate 1,5-diketone, which was subsequently exposed to

Scheme 3. Syntheses of Jambolanin I and Gibberodione; Model for Electrophilic Addition to the Enol of 2a (Y = $OSiEt_3$) *anti* to the C-10 Methyl Group



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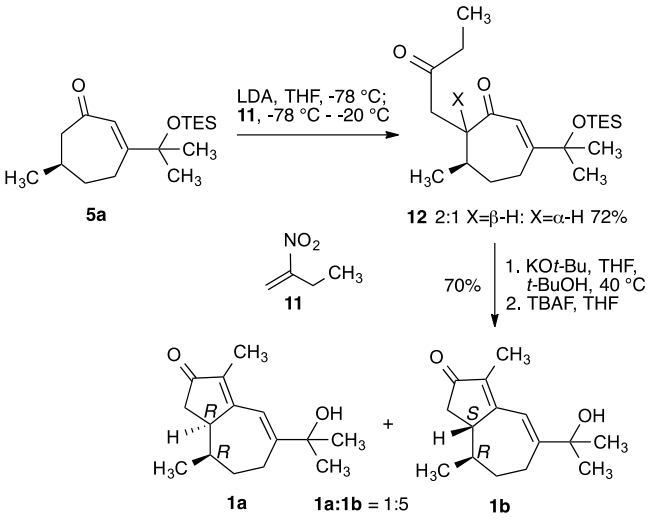
TBAF (2 equiv) in THF at room temperature for 1 h to provide Jambolanin I (**2a**) in 90% overall yield (from **9a**) and with >10:1 diastereoselectivity. The spectroscopic data obtained for synthetic **2a** (^{1}H NMR,^{13}C NMR, IR, MS, α_D^{25}) were in accord with those reported for natural jambolanin I (see Experimental Section); however, the proposed structure reported for jambolanin I is the enantiomer of our synthetic material, derived from *R*-(+)-pulegone. The absolute configuration of Jambolanin I may therefore be assigned as (1*R*, 10*R*). All attempts to isomerize **2a** to jambolanin J (**2b**) under acidic or basic conditions[17a] were unsuccessful; ab initio calculations[17b] on the enol form of **2a** (Y = $OSiEt_3$) indicate that the C-10 methyl group adopts a pseudoxial orientation in the lowest energy conformer, which shields the top face of C-1 from electrophilic attack (Scheme 3). Subjection of enone **5b** to an analogous sequence as **5a** provided intermediate dione **9b** in 63% yield; palladium-catalyzed deallyloxycarbonylation then gave rise to **2c** in 84% yield with >10:1 diasteroselectivity. The ^{1}H NMR,^{13}C NMR, IR, and MS data for **2c** were in accord with those reported for natural gibberodione (see Experimental Section); however, the optical rotation of synthetic **2c** (α_D^{25} = −21.8) was of opposite sign as that reported for gibberodione (α_D^{25} = +20.8),[3] confirming that the absolute configuration of gibberodione is (1*S*, 10*S*), as in the proposed chemical structure.

Despite the reluctance of the lithium enolate of **5a** to undergo 1,4-addition with MVK, we anticipated that conjugate addition to a suitable nitroalkene instead might be possible given the precedent of Alexakis.[18] Thus, deprotonation of enone **5a** with 1.1 equiv of LDA, followed by addition of 2-methylenenitropropane and reaction quench at −20 °C with 2 M aqueous HCl, gave rise to a 72% yield of dione **12** as an inseparable 2:1 mixture of diastereomers (Scheme 4, 2:1 X = *β*-H:X = *α*-H). Exposure of the diastereomeric mixture to 1.5 equiv KO*t*Bu in 1:1 THF/*t*-BuOH at 40 °C for 1 h[19] provided the expected TES-protected cyclopentenone, which upon treatment with TBAF (1.5 equiv) in THF at room temperature for 1 h gave a 1:5 mixture of **1a** and **1b** in 70% overall yield; the diastereomers were readily separated by column chromatography. All attempts to alter the diastereomer ratio to favor **1a** by employing different cyclization reaction conditions (0 °C or room temperature, 20 h) or bases (NaOMe in MeOH, rt −40 °C, NaHMDS/THF, −78 °C − rt) were unsuccessful. The spectroscopic data obtained for synthetic **1b** (^{1}H NMR,^{13}C NMR, IR, MS, and α_D) were in accord with those reported for natural jambolanin C (see Experimental Section); however, the proposed structure reported for jambolanin C is the enantiomer of our synthetic material, derived from *R*-(+)-pulegone. Thus, we assign the absolute configuration of jambolanin C as (1*S*, 10*R*). Similarly, the spectroscopic data obtained for synthetic **1a** (^{1}H NMR,^{13}C NMR, IR, MS, and α_D) were in accord with those reported for natural sootepdienone (see Experimental Section); once again, the proposed structure reported for sootepdienone is the enantiomer of our synthetic material, and we assign the absolute configuration of sootepdienone as (1*R*, 10*R*).

Scheme 4. Syntheses of Jambolanin C and Sootepdienone



In summary, we have developed a concise route to four sesquiterpenes of the sootepdienone/jambolanin/gibberodione family, which has led to a revision of the absolute configuration of three of the natural products. A one-carbon ring expansion of an *R*-(+)-pulegone-derived allylic phosphonate was achieved by tandem oxidative cleavage and intramolecular Horner−Wadsworth−Emmons reactions to provide the substituted cycloheptenone precursor to the four natural products.

EXPERIMENTAL SECTION

General Experimental Procedures. All reagents and solvents were purchased and used without further purification. Distilled water was used in all of the experiments. Organic extracts were dried over Na_2SO_4, filtered, and concentrated using a rotary evaporator at aspirator pressure (20−30 mm Hg). Chromatography refers to flash chromatography and was carried out on SiO_2 (silica gel 60, 230−400 mesh). All glassware used in the reactions described below were flame-dried under vacuum and then flushed with argon gas at room temperature prior to the addition of reagents and solvents. Heating of reactions was performed in an oil bath equipped with a thermostat. ^{1}H and ^{13}C{^{1}H} NMR spectra were measured in $CDCl_3$ at 400 and 100 MHz, respectively, using Me_4Si as internal standard. Chemical shifts are reported in ppm downfield (δ) from Me_4Si.

Dimethyl ((*R*)-5-Methyl-2-(prop-1-en-2-yl)cyclohex-1-enyl)-methylphosphonate (3a). *n*-BuLi (3.16 mL, 7.3 mmol, 2.3 M in hexanes 1.1 equiv) was added dropwise to a solution of dimethylmethyl phosphonate (0.93 mL, 8.6 mmol 1.3 equiv) in THF (17 mL) at −78 °C. The solution was stirred for 20 min at −78 °C, and *R*-(+)-pulegone (1 g, 6.6 mmol) was added. The mixture was allowed to stir for 1 h at −78 °C and was then quenched by the addition of saturated $NaHCO_3$ solution (20 mL) and allowed to warm to room temperature. The reaction mixture was diluted with ethyl acetate (30 mL), and the phases were separated. The aqueous layer was extracted with ethyl acetate (2 × 20 mL). The combined organic extracts were washed once with saturated aqueous NaCl (30 mL), dried over anhydrous Na_2SO_4, and concentrated under reduced pressure to give a crude oil. Rapid filtration of the residue through silica gel (90:10 → 70:30 hexanes/EtOAc) afforded an intermediate hydroxyphosphonate that was used immediately in the next step. The hydroxyphosphonate (1.57 g, 5.7 mmol) was dissolved in isopropanol (20 mL, 0.25 M), and cerium triflate (84 mg, 0.114 mmol, 2 mol %) was added. The mixture was then heated to 80 °C in an oil bath for 14 h. Upon cooling to room temperature the mixture was diluted with saturated $NaHCO_3$ solution (20 mL) and concentrated *in vacuo*. Ethyl acetate (20 mL) was added, and the phases were separated. The aqueous layer was then extracted with ethyl acetate (2 × 20 mL). The combined organic extracts were washed once with saturated aqueous NaCl (20 mL), dried over anhydrous Na_2SO_4, and concentrated under reduced pressure to give a crude oil. Purification of the residue by flash chromatography (4:1 → 1.5:1 hexanes/EtOAc) afforded diene **3a** as a pale yellow oil (1.18 g, 4.6 mmol, 70% from *R*-(+)-pulegone). ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.91 (s, 1H); 4.70 (s,

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1H); 3.72 (s, 3H); 3.69 (s, 3H); 2.82−2.61 (m, 2H); 2.24−2.19 (d, J = 17.3 Hz, 1H); 2.10 (m, 2H); 1.81 (m, 1H); 1.78 (s, 3H); 1.71−1.67 (m, 2H); 1.25−1.18 (m, 1H); 0.96−0.95 (d, J = 6.4 Hz, 3H). $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 146.6, 138.9, 120.1, 112.8, 52.4, 38.2, 31.6, 30.9, 29.6, 28.8, 22.0, 21.9. HRMS (ESI-TOF) m/z: $[M + Na]^+$ calcd for $C_{13}H_{23}NaO_3P$ 281.1283; found 281.1276. $[\alpha]_D^{25}$ = −24.8 (c = 0.08, $CHCl_3$). IR (film): 2951, 2914, 2850, 1631 cm^{-1}.

Bis(2,2,2-trifluoroethyl) ((*R*)-5-Methyl-2-(prop-1-en-2-yl)-cyclohex-1-enyl)methylphos-phonate (3b). Diene **3a** (258 mg, 1 mmol) was dissolved in a 1:1 mixture of H_2O and Dioxane (0.5 M), and LiOH (144 mg, 6 mmol) was added; the mixture was then stirred overnight at 120 °C on an oil bath. The mixture was cooled to room temperature and concentrated *in vacuo* to remove dioxane. The residue was diluted with 1 M NaOH (20 mL) and ether (20 mL), and the layers were separated. The aqueous layer was then acidified to pH 2 with 1 M HCl and extracted with EtOAc (3 × 20 mL). The combined organic extracts were washed once with saturated aqueous NaCl (20 mL), dried over anhydrous Na_2SO_4, and concentrated under reduced pressure to give a crude oil. To a solution of the crude product in DCM (2.5 mL) was added DMF (1 drop) and oxalyl chloride (236 μL, 3.0 mmol, 3.0 equiv). The mixture was stirred for 3 h at 50 °C on an oil bath, diluted with toluene (10 mL), and then concentrated *in vacuo*. The crude product was immediately taken up in THF (5 mL) and added to a stirring solution of triethylamine (0.83 mL, 6 mmol, 6 equiv), trifluoroethanol (0.18 mL, 2.5 mmol, 2.5 equiv), and THF (2 mL) at 0 °C. The mixture was allowed to stir overnight and was quenched with saturated aqueous NH_4Cl (10 mL). The phases were separated, and the aqueous layer was extracted with EtOAc (2 × 20 mL). The combined organic extracts were washed once with saturated aqueous NaCl (20 mL), dried over anhydrous Na_2SO_4, and concentrated under reduced pressure to give a crude oil. Purification by flash chromatography (4:1 → 1:1 hexanes/EtOAc) afforded **3b** as a clear oil (191 mg, 0.5 mmol, 50% from **3a**). ^1H NMR (400 MHz, $CDCl_3$) δ 4.93 (s, 1H); 4.70 (s, 1H); 4.42−4.26 (m, 2H); 3.75−3.72 (dd, J = 11.1, 1.4 Hz, 3H); 2.89−2.71 (m, 2H); 2.24−2.11 (m, 3H); 1.78 (s, 3H); 1.73−1.69 (m, 2H); 1.25−1.18 (m, 1H); 0.97 (d, J = 6.5 Hz, 3H). $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 146.4, 139.8, 229.2, 119.1, 112.9, 62.1, 61.7, 52.3, 38.2, 32.1, 30.8, 29.6, 28.8, 21.9, 21.5. HRMS (ESI-TOF) m/z: $[M + Na]^+$ calcd for $C_{15}H_{21}F_6NaO_3P$ 417.1030; found 417.1066. α_D^{25} = +31.2 (c = 0.01, $CHCl_3$). IR (film): 2955, 2919, 2874, 2848, 1632 cm^{-1}.

Dimethyl ((*R*)-2-Acetyl-5-methylcyclohex-1-enyl)-methylphosphonate (3c). Diene **3a** (260 mg, 1 mmol) was dissolved in 20 mL of methanol and cooled to −78 °C. Ozone was bubbled through the reaction mixture for 1 h at −78 °C, at which time TLC indicated complete consumption of the starting material. Air was bubbled through the reaction mixture for 5 min, and then DMS (4 mL) was added; the reaction mixture was then allowed to warm to room temperature. The solution was concentrated *in vacuo*, and water (20 mL) and ethyl acetate (20 mL) were added. The phases were separated, and the aqueous layer was then extracted with ethyl acetate (2 × 20 mL). The combined organic extracts were washed once with saturated aqueous NaCl (20 mL), dried over anhydrous Na_2SO_4, and concentrated under reduced pressure to give a crude oil. Purification of the residue by flash chromatography (4:1 → 1:1 hexanes/EtOAc) afforded enone **3c** as a pale yellow oil (182 mg, 0.7 mmol, 70% from **3a**). ^1H NMR (400 MHz, $CDCl_3$) δ 3.69 (s, 3H); 3.67 (s, 3H); 3.23−3.13 (dd, J = 23.6, 14.0 Hz, 1H), 2.92−2.82 (dd, J = 23.6, 14.0 Hz, 1H), 2.32−2.30 (m, 3H), 2.20 (s, 3H), 1.90−1.83 (m, 1H), 1.77−1.66 (m, 2H), 1.22 (m, 1H), 0.95 (d, J = 6.4 Hz, 3H). $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 203.7, 203.6, 135.6, 135.5, 133.7, 133.5, 52.5, 52.4, 52.4, 52.3, 40.5, 40.4, 31.1, 30.1, 29.7, 27.9, 27.5, 27.4, 21.2. HRMS (ESI-TOF) m/z: $[M + Na]^+$ calcd for $C_{12}H_{21}NaO_4P$ 283.1075; found 283.1100. α_D^{25} = +22.2 (c = 0.03, $CHCl_3$). IR (film): 2952, 2927, 2854, 1684 cm^{-1}.

***E*-3-Acetyl-6*R*-methylcyclohept-2-enone (4).** Diene **3a** (260 mg, 1 mmol) or **3b** (394 mg, 1.0 mmol) was dissolved in 20 mL of methanol and cooled to −78 °C. Ozone was bubbled through the reaction mixture for 1 h at −78 °C, at which time TLC indicated complete consumption of the starting material. Air was bubbled through the reaction mixture for 5 min, and then DMS (4 mL) was added; the reaction mixture was then allowed to warm to room temperature. The solution was concentrated *in vacuo*, and water (20 mL) and ethyl acetate (20 mL) were added. The phases were separated, and the aqueous layer was then extracted with ethyl acetate (2 × 20 mL). The combined organic extracts were washed once with saturated aqueous NaCl (20 mL), dried over anhydrous Na_2SO_4, and concentrated under reduced pressure to give a crude oil, which was used directly in the next step. The crude product or **3c** (260 mg, 1 mmol) was dissolved in methanol (20 mL) and cooled to −78 °C. Ozone was bubbled through the reaction mixture for 2.5 h at −78 °C, at which time complete disappearance of the starting material was observed by TLC. Air was bubbled through the reaction mixture for 5 min, and then DMS (4 mL) was added. The mixture was allowed to warm to room temperature and was then concentrated *in vacuo*. Water (20 mL) and ethyl acetate (20 mL) were added. The phases were separated, and the aqueous layer was then extracted with ethyl acetate (2 × 20 mL). The combined organic extracts were washed once with saturated aqueous NaCl (30 mL), dried over anhydrous Na_2SO_4, and concentrated under reduced pressure to give a crude oil. The crude oil was dissolved in 1:1 THF/H_2O (20 mL, 0.05 M), and potassium carbonate (624 mg, 4.5 mmol) was added. The mixture was stirred at room temperature for 2 h and was then diluted with saturated NH_4Cl solution (10 mL) and ethyl acetate (10 mL). The phases were separated, and the aqueous layer was extracted with EtOAc (2 × 20 mL). The combined organic extracts were washed once with saturated aqueous NaCl (20 mL), dried over anhydrous Na_2SO_4, and concentrated under reduced pressure to give a crude oil. Purification of the residue by flash chromatography (80:20 hexanes/EtOAc) afforded **4** as a colorless oil (70 mg, 0.42 mmol, 42% from **3a**; 80 mg, 0.48 mmol, 48% from **3b**; 100 mg, 0.6 mmol, 60% from **3c**). ^1H NMR (400 MHz, $CDCl_3$) δ 6.61 (s, 1H); 2.71−2.66 (dd, J = 13.6, 5.3 Hz, 1H); 2.59−2.56 (m, 2H); 2.42−2.37 (dd, J = 13.5, 8.0 Hz, 1H); 2.33 (s, 3H); 2.10−2.05 (m, 1H); 1.88−1.83 (m, 1H); 1.41−1.33 (m, 1H); 0.97−0.96 (d, J = 6.8 Hz, 3H). $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 203.6, 199.9, 152.6, 136.7, 50.3, 33.9, 28.9, 25.9, 24.0, 21.6. HRMS (ESI-TOF) m/z: $[M + Na]^+$ calcd for $C_{10}H_{14}NaO_2$ 189.0891; found 189.0902. $[\alpha]_D^{25}$ = +16.4 (c = 0.01, $CHCl_3$). IR (film): 2957, 2973, 2872, 1670 cm^{-1}.

***E*-6*R*-Methyl-3-(1-methyl-1-triethylsilanoxyethyl)cyclohept-2-enone (5a).** Compound **4** (200 mg, 1.2 mmol) was dissolved in Et_2O (0.5 M) and cooled to −40 °C. Then CH_3MgBr (0.44 mL, 1.32 mmol, 3 M in ether) was added, and the mixture was stirred for 10 min. The solution was warmed to room temperature and stirred for 15 min, and then was diluted with saturated NH_4Cl solution (10 mL) and ethyl acetate (10 mL). The phases were separated, and the aqueous layer was extracted with EtOAc (2 × 20 mL). The combined organic extracts were washed once with saturated aqueous NaCl (20 mL), dried over anhydrous Na_2SO_4, and concentrated under reduced pressure to give a crude oil. The crude oil was dissolved in DMF (1 M), and imidazole (179.5 mg, 2.64 mmol 2.2 equiv) and TESCl (272 mg, 1.8 mmol, 1.5 equiv) were added. The reaction mixture was stirred for 16 h at room temperature and was quenched with saturated NH_4Cl. The phases were separated, and the aqueous layer was extracted with EtOAc (2 × 20 mL). The combined organic extracts were washed once with saturated aqueous NaCl (20 mL), dried over anhydrous Na_2SO_4, and concentrated under reduced pressure to give a crude oil. Purification by flash chromatography (15:1 hexanes/EtOAc) afforded compound **5a** as a light yellow oil (229 mg, 0.77 mmol, 64% from **4**). ^1H NMR (400 MHz, $CDCl_3$) δ 6.08 (s, 1H); 2.61−2.58 (dd, J = 13.8, 4.7 Hz, 1H); 2.45−2.32 (m, 3H); 2.05−2.00 (m, 1H); 1.89−1.85 (m, 1H); 1.38 (m, 1H); 1.33 (s, 6H); 0.98−0.96 (d, J = 6.8 Hz, 3H); 0.92−0.88 (t, J = 8.0 Hz, 9H); 0.59−0.53 (q, J = 8.0 Hz, 6H). $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 240.1, 167.6, 125.7, 75.8, 49.6, 34.7, 28.9, 28.6, 28.0, 26.2, 21.8, 6.9, 6.5. HRMS (ESI-TOF) m/z: $[M + Na]^+$ calcd for $C_{17}H_{32}NaO_2Si$ 319.2069; found 319.2070. $[\alpha]_D^{25}$ = +16.1 (c = 0.007, $CHCl_3$). IR (film): 2955, 2876, 1662, 1627 cm^{-1}.

***E*-3-Isopropyl-6*R*-methylcyclohept-2-enone (5b).** To a solution of *t*-BuOK (134 mg, 1.2 mmol) and CH_3PPh_3Br (427 mg, 1.2

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mmol) in THF (3 mL) at room temperature was added compound **4** (166 mg, 1 mmol) in THF (1 mL) dropwise, and the mixture was stirred for 1 h. The reaction was quenched by the addition of saturated NH_4Cl solution (10 mL) and ethyl acetate (10 mL). The phases were separated, and the aqueous layer was extracted with EtOAc (2 × 20 mL). The combined organic extracts were washed once with saturated aqueous NaCl (20 mL), dried over anhydrous Na_2SO_4, and concentrated under reduced pressure to give a crude oil. Purification by flash chromatography (10:1 hexanes/EtOAc) afforded a yellow oil. The diene (∼121 mg, 0.74 mmol) was dissolved in THF and tBuOH (1:1, 5.3 mL, 0.14 M), and Wilkinson's catalyst (68 mg, 0.1 mmol, 10 mol %) was added. The reaction was then stirred under a H_2 atmosphere for 3.5 h. The mixture was concentrated under vacuum to give a crude oil. Purification by flash chromatography (10:1 hexanes/EtOAc) afforded **5b** (103 mg, 0.62 mmol, 62%) as a colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ 5.87 (s, 1H); 2.65−2.60 (dd, J = 4.8, 0.9 Hz, 1H); 2.47−2.28 (m, 4H); 2.10−2.02 (m, 1H); 1.95−1.87 (m, 1H); 1.46−1.38 (m, 1H); 1.07 (d, J = 8.0 Hz, 6H); 1.05−0.99 (d, J = 6.8 Hz, 3H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 203.5, 168.7, 126.9, 50.0, 38.1, 34.7, 29.1, 28.2, 22.0, 20.8, 20.7. HRMS (ESI-TOF) m/z: [M + H]$^+$ calcd for $C_{11}H_{19}O$ 167.1436; found 167.1447. α_D^{25} = +38.1 (c = 0.003, $CHCl_3$). IR (film): 2958, 2927, 2872, 1656, 1626 cm^{-1}.

(*E*)-Allyl-4-(1-methyl-1-triethylsilanoxyethyl)-7*R*-methyl-2-oxo-1*R*-(3-oxobutyl)cyclohept-3-ene carboxylate (9a). *n*-BuLi (0.56 mL, 1.3 mmol, 2.3 M in hexanes) was added dropwise to a solution of diisopropylamine (0.2 mL, 1.4 mmol) in THF (3 mL) at 0 °C. The solution was stirred for 10 min and then cooled to −78 °C. Compound **5a** (296 mg, 1 mmol) in THF (1 mL) was then added dropwise, and the reaction mixture was stirred for 1 h at −78 °C. Then allyl cyanoformate (166 mg, 1.5 mmol) was added dropwise, and the mixture was stirred for 15 min. The solution was warmed to room temperature and was allowed to stir for 15 min, at which point it turned dark red. The reaction was quenched with saturated NH_4Cl solution (10 mL). The phases were separated, and the aqueous layer was extracted with EtOAc (2 × 20 mL). The combined organic extracts were washed once with saturated aqueous NaCl (20 mL), dried over anhydrous Na_2SO_4, and concentrated *in vacuo* to give a crude oil, which was purified by flash chromatography (10:1 hexanes/EtOAc). The resulting colorless oil (289 mg, 0.74 mmol) was dissolved in acetone (1.5 mL, 0.5 M). MVK (0.1 mL, 1.1 mmol, 1.5 equiv) and K_2CO_3 (253 mg, 1.1 mmol, 1.5 equiv) were added, and the reaction mixture was allowed to stir overnight at 40 °C in an oil bath. The reaction was diluted with saturated NH_4Cl solution (10 mL) and ethyl acetate (10 mL). The phases were separated, and the aqueous layer was extracted with EtOAc (2 × 20 mL). The combined organic extracts were washed once with saturated aqueous NaCl (20 mL), dried over anhydrous Na_2SO_4, and concentrated under reduced pressure to give a crude oil. Purification of the residue by flash chromatography (4:1 hexanes/EtOAc) afforded **9a** (266 mg, 0.60 mmol, 60%) as a pale yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ 6.04 (s, 1H); 5.92−5.84 (m, 1H); 5.34−5.30 (m, 1H); 5.22−5.19 (m, 1H); 4.61 (m, 2H); 2.65−2.59 (m, 1H); 2.51−2.44 (m, 1H); 2.42−2.38 (m, 1H); 2.30−2.27 (d, J = 11.3 Hz, 2H); 2.24−2.16 (m, 1H); 2.06 (s, 3H); 1.87−1.77 (m, 2H); 1.63−1.58 (m, 1H); 1.36 (d, J = 4.6 Hz, 6H); 0.98 (d, J = 7.1 Hz, 3H); 0.94 (t, J = 8.0 Hz, 9H); 0.61−0.55 (q, J = 7.8 Hz, 6H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 207.9, 203.8, 170.9, 162.1, 131.8, 123.2, 118.5, 75.7, 68.6, 65.3, 39.0, 37.9, 31.5, 31.2, 30.1, 29.9, 29.6, 29.5, 17.8, 7.0, 6.6. HRMS (ESI-TOF) m/z: [M + Na]$^+$ calcd for $C_{25}H_{42}NaO_5Si$ 473.2699; found 473.2719. α_D^{25} = +98.3 (c = 0.004, $CHCl_3$). IR (film): 2955, 2934, 2913, 2876, 1733, 1718, 1650 cm^{-1}.

(*E*)-Allyl-4-isopropyl-7*R*-methyl-2-oxo-1*R*-(3-oxobutyl)-cyclohept-3-ene Carboxylate (9b). *n*-BuLi (0.34 mL, 0.78 mmol, 1.3 equiv, 2.3 M in hexanes) was added dropwise to a solution of diisopropylamine (0.12 mL, 0.84 mmol 1.4 equiv) in THF (2 mL) at 0 °C. The solution was stirred for 10 min and then cooled to −78 °C. Compound **5b** (100 mg, 0.6 mmol) in THF (1 mL) was then added dropwise, and the reaction mixture was stirred for 1 h at −78 °C. Then allyl cyanoformate (100 mg, 0.9 mmol) was added dropwise, and the mixture was stirred for 15 min. The solution was warmed to room temperature and was allowed to stir for 15 min. The reaction was quenched with saturated NH_4Cl solution (10 mL). The phases were separated, and the aqueous layer was extracted with EtOAc (2 × 20 mL). The combined organic extracts were washed once with saturated aqueous NaCl (20 mL), dried over anhydrous Na_2SO_4, and concentrated *ion vacuo* to give a crude oil, which was purified by flash chromatography (10:1 hexanes/EtOAc). The resulting colorless oil (114 mg, 0.45 mmol) was dissolved in acetone (0.9 mL, 0.5 M). MVK (0.06 mL, 0.7 mmol, 1.5 equiv) and K_2CO_3 (95 mg, 0.68 mmol, 1.5 equiv) were added, and the reaction mixture was allowed to stir overnight at 40 °C on an oil bath. The reaction was diluted with saturated NH_4Cl solution (10 mL) and ethyl acetate (10 mL). The phases were separated, and the aqueous layer was extracted with EtOAc (2 × 20 mL). The combined organic extracts were washed once with saturated aqueous NaCl (20 mL), dried over anhydrous Na_2SO_4, and concentrated under reduced pressure to give a crude oil. Purification of the residue by flash chromatography (4:1 hexanes/EtOAc) afforded **9b** (122 mg, 0.38 mmol, 63%) as a yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ 5.92 (m, 1H); 5.73 (s, 1H); 5.33−5.28 (m, 1H); 5.20−5.17 (m, 1H); 4.60 (d, J = 5.8 Hz, 2H); 2.67−2.58 (m, 1H); 2.45−2.40 (m, 1H); 2.33−2.23 (m, 5H); 2.06 (s, 3H); 1.83−1.75 (m, 2H); 1.58 (m, 1H); 1.05 (m, 6H); 0.95 (d, J = 7.2 Hz, 3H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 208.0, 203.1, 170.9, 163.1, 131.8, 123.9, 118.4, 69.1, 65.3, 39.0, 38.3, 36.8, 34.2, 30.9, 29.9, 29.6, 21.7, 21.6, 17.9. HRMS (ESI-TOF) m/z: [M + Na]$^+$ calcd for $C_{19}H_{28}NaO_4$ 343.1885; found 343.1865. α_D^{25} = +91.4 (c = 0.008, $CHCl_3$). IR (film): 2963, 2932, 2878, 1732, 1716 cm^{-1}.

Jambolanin I (2a). Compound **9a** (450 mg, 1.0 mmol) was dissolved in 9:1 MeCN/H_2O (2.5 mL, 0.4 M). Et_3N (0.15 mL, 1.10 mmol), PPh_3 (5.3 mg, 0.02 mmol), and $Pd(OAc)_2$ (22.0 mg, 0.10 mmol) were added, and the reaction mixture was allowed to stir for 2 h at rt. The mixture was quenched with saturated NH_4Cl solution (10 mL) and ethyl acetate (10 mL). The phases were separated, and the aqueous layer was extracted with EtOAc (2 × 20 mL). The combined organic extracts were washed once with saturated aqueous NaCl (20 mL), dried over anhydrous Na_2SO_4, and concentrated under reduced pressure to give a crude oil. Purification of the residue by flash chromatography (10:1 hexanes/EtOAc) afforded a pale yellow oil. This oil (∼367 mg, 1 mmol) was dissolved in THF (1 mL, 1 M), and TBAF (1.5 mL, 1.5 mmol, 1 M solution in THF) was added. The reaction mixture was then stirred for 1 h at room temperature. The reaction mixture was diluted with saturated aqueous $NaHCO_3$ solution (20 mL). The phases were separated, and the aqueous layer was extracted with EtOAc (2 × 20 mL). The combined organic extracts were washed once with saturated aqueous NaCl (20 mL), dried over anhydrous Na_2SO_4, and concentrated *in vacuo* to give a crude oil. Purification of the residue by flash chromatography (1:1 hexanes/EtOAc) gave **2a** (226 mg, 0.9 mmol, 90%) as a colorless oil. **2a**: ^{1}H NMR (400 MHz, DMSO-d_6): δ 6.09 (s, 1H); 4.86 (s, 1H); 2.85−2.80 (m, 1H); 2.56 (m, 1H); 2.39−2.30 (m, 3H); 2.19−2.16 (m, 1H); 2.06 (s, 3H); 2.04 (m, 1H); 1.92−1.85 (m, 1H); 1.47−1.40 (m, 1H); 1.24 (s, 6H); 0.93−0.84 (m, 1H); 0.68 (d, J = 6.6 Hz, 3H). ^{13}C{^{1}H} NMR (100 MHz, DMSO-d_6): δ 208.8, 203.3, 170.9, 126.4, 72.6, 52.2, 41.5, 36.8, 32.8, 30.1, 28.8, 28.4, 27.4, 22.1, 16.4. HRMS (ESI-TOF) m/z: [M + Na]$^+$ calcd for $C_{15}H_{24}NaO_3$ 275.1623; found 275.1622. α_D^{25} = −28.2 (c = 0.006, MeOH). IR (film): 3423, 2968, 2925, 2003, 1719, 1654 cm^{-1}. Jambolanin I[2]: ^{1}H NMR (400 MHz, DMSO-d_6) δ 6.08 (s, 1H); 4.86 (s, 1H); 2.82 (dt, J = 8.9, 5.6 Hz, 1H); 2.53 (m, 1H); 2.34 (m, 1H); 2.32 (m, 2H); 2.17 (m, 1H); 2.06 (s, 3H); 2.04 (m, 1H); 1.87 (m, 1H); 1.43 (m, 1H); 1.24 (s, 3H); 1.24 (s, 3H); 0.86 (m, 1H); 0.67 (d, J = 6.7 Hz, 3H). ^{13}C{^{1}H} NMR (150 MHz, DMSO-d_6) δ 208.8, 203.3, 170.9, 126.4, 72.6, 52.3, 41.5, 36.8, 32.9, 30.1, 28.8, 28.4, 27.5, 22.2, 16.5. HRMS (ESI-TOF) m/z: [M + Na]$^+$ calcd for $C_{15}H_{24}O_3Na$ 275.1623; found 275.1624. α_D^{20} = −28 (c = 1.0, MeOH). IR (film) 3451, 2969, 2921, 2875, 1711, 1654 cm^{-1}.

***ent*-Gibberodione (2c).** Compound **9b** (32 mg, 0.1 mmol) was dissolved in 9:1 MeCN/H_2O (2.5 mL, 0.04 M). Et_3N (0.02 mL, 0.13 mmol), PPh_3 (5.6 mg, 0.02 mmol), and $Pd(OAc)_2$ (2.4 mg, 0.01

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mmol) were added, and the reaction mixture was allowed to stir for 2 h at rt. The reaction was quenched with saturated NH_4Cl solution (10 mL) and ethyl acetate (10 mL). The phases were separated, and the aqueous layer was extracted with EtOAc (2 × 20 mL). The combined organic extracts were washed once with saturated aqueous NaCl (20 mL), dried over anhydrous Na_2SO_4, and concentrated *in vacuo* to give a crude oil. Purification of the residue by flash chromatography (4:1 hexanes/EtOAc) gave **2c** (20 mg, 0.084 mmol, 84%) as a yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ 5.89 (s, 1H); 2.83 (m, 1H); 2.54−2.46 (m, 1H); 2.43 (m, 1H); 2.38 (m, 2H); 2.31 (m, 1H); 2.20−2.12 (m, 2H); 2.11 (s, 3H); 2.10−2.03 (m, 1H); 1.62−1.54 (m, 1H); 1.09 (m, 1H); 1.06 (d, J = 6.8 Hz, 6H); 0.79 (d, J = 6.6 Hz, 3H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 208.9, 203.4, 170.2, 127.9, 52.8, 41.9, 37.9, 36.3, 33.6, 29.9, 29.8, 22.3, 20.9, 20.6, 16.2. HRMS (ESI-TOF) m/z: [M + Na]$^+$ calcd for $C_{15}H_{24}NaO_2$ 259.1674; found 259.1670. α_D^{25} = −21.8 (c = 0.003, $CHCl_3$). IR (film): 2964, 2929, 2874, 1716, 1661 cm^{-1}. Gibberodione:[3] ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.89 (br s, 1H); 2.83 (dd, J = 10.6, 5.2, 5.2 Hz, 1H); 2.54 (dd, J = 10.8, 9.9 Hz, 1H); 2.46 (m, 1H); 2.33−2.41 (m, 2H); 2.31 (m, 1H); 2.15 (m, 1H); 2.11 (s, 3H); 2.10 (m, 2H); 1.61 (m, 1H); 1.08 (m, 1H); 1.06 (d, J = 6.9 Hz, 6H); 0.79 (d, J = 6.9 Hz, 3H). ^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$) δ 206.0, 203.4, 170.2, 128.0, 52.8, 42.0, 38.0, 36.3, 33.6, 29.9, 29.9, 22.3, 20.9, 20.6, 16.2. HRMS (ESI-TOF) m/z: [M]$^+$ calcd for $C_{15}H_{24}O_2$ 236.1777; found 236.1781. α_D^{25} = +20.8 (c = 0.72, $CHCl_3$). IR (neat) 3020, 2975, 2932, 2872, 1715, 1603 cm^{-1}.

***E*-6*R*-Methyl-3-(1-methyl-1-triethylsilanoxyethyl)-7*S*-(2-oxobutyl)cyclohept-2-enone and *E*-6*R*-Methyl-3-(1-methyl-1-triethylsilanoxyethyl)-7*R*-(2-oxobutyl)cyclohept-2-enone (12).** *n*-BuLi (0.5 mL, 1.1 mmol, 2.3 M in hexanes) was added dropwise to a solution of diisopropylamine (0.2 mL, 1.2 mmol) in THF (40 mL) at 0 °C. The solution was stirred for 10 min and then cooled to −78 °C. Compound **5a** (296 mg, 1 mmol) in THF (2 mL) was then added, and the reaction mixture was stirred for 1 h at −78 °C. A solution of 2-methylenenitropropane (121 mg, 1.2 mmol) in THF (1 mL) was added dropwise, and the mixture was stirred for 1 h at −78 °C and warmed to −20 °C. A 2 M aqueous HCl solution (10 mL) was added, and the reaction mixture was warmed to 0 °C and stirred for 30 min. The phases were separated, and the aqueous layer was extracted with EtOAc (2 × 20 mL). The combined organic extracts were washed once with saturated aqueous NaCl (20 mL), dried over anhydrous Na_2SO_4, and concentrated under reduced pressure to give a crude oil. Purification by flash chromatography (10:1 hexanes/ethyl acetate) afforded compound **12** as an inseparable 2:1 mixture of diastereomers (263 mg, 0.72 mmol, 72%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.14, 6.11 (2s, 1H); 3.49, 2.94 (m, t, J = 8.0 Hz, 1 H); 3.19−3.06 (m, 1H); 2.70−2.19 (m, 6H); 1.69−1.63 (m, 2H); 1.35 (s, 6H); 1.04−1.00 (q, J = 7.3 Hz, 5H); 0.94−0.90 (t, J = 7.9 Hz, 9H); 0.77−0.75 (d, J = 6.7 Hz, 1H); 0.60−0.54 (q, J = 8.1 Hz, 6H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$; peaks for both diastereomers listed) δ 210.6, 210.2, 204.6, 203.0, 169.4, 167.4, 126.5, 125.8, 75.9, 75.6, 51.9, 48.3, 42.1, 41.1, 36.5, 36.2, 36.1, 35.2, 32.8, 32.7, 29.4, 29.2, 28.8, 28.7, 26.9, 24.1, 19.6, 16.7, 7.6, 7.0, 6.5. HRMS (ESI-TOF) m/z: [M + Na]$^+$ calcd for $C_{21}H_{38}NaO_3Si$ 389.2488; found 389.2500. IR (film): 2956, 2876, 1716, 1666, 1627 cm^{-1}.

Sootepdienone (1a) and Jambolanin C (1b). Compound **12** (366 mg, 1 mmol, as a 2:1 mixture of diastereomers) was dissolved in THF (10 mL) and *t*-BuOH (0.5 m). A 1 M solution of *t*-BuOK (1.1 mL, 1.1 mmol) in THF was added, and the reaction mixture was stirred for 1 h at 40 °C on an oil bath. The mixture was diluted with a saturated solution of ammonium chloride (10 mL). The phases were separated, and the aqueous layer was extracted with EtOAc (2 × 20 mL). The combined organic extracts were washed once with saturated aqueous NaCl (20 mL), dried over anhydrous Na_2SO_4, and concentrated under reduced pressure to give a crude oil. Rapid filtration through a plug of silica gel (10:1 hexanes/EtOAc) gave a pale yellow oil. The product was dissolved in THF (1 mL, 1 M), and TBAF (1.5 mL, 1.5 mmol, 1 M solution in THF) was added. The reaction mixture was then stirred for 1 h at room temperature. The reaction mixture was diluted with saturated aqueous $NaHCO_3$ solution (20 mL). The phases were separated, and the aqueous layer was extracted with EtOAc (2 × 20 mL). The combined organic extracts were washed once with saturated aqueous NaCl (20 mL), dried over anhydrous Na_2SO_4, and concentrated under reduced pressure to give a crude oil. Purification of the residue by flash chromatography (5:1 hexanes/EtOAc) gave **1a** (27 mg, 0.12 mmol, 12%) as an off-white solid and **1b** (135 mg, 0.58 mmol, 58%) as a white solid. **1a**: ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.74 (s, 1H); 3.32 (m, 1H); 2.60−2.56 (m, 1H); 2.51−2.45 (dd, J = 18.7, 8.8 Hz, 1H); 2.37−2.30 (ddd, J = 16.1, 8.0, 3.5 Hz, 1H); 2.24−2.19 (m, 2H); 2.15−2.09 (m, 1H); 1.76 (d, J = 3.5 Hz, 3H); 1.50−1.44 (m, 1H); 1.41 (s, 6H); 0.70−0.68 (d, J = 6.8 Hz, 3H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 209.2, 167.1, 160.5, 137.2, 118.0, 74.5, 43.4, 39.6, 34.9, 32.7, 28.7, 28.5, 26.4, 14.4, 8.2. HRMS (ESI-TOF) m/z: [M + Na]$^+$ calcd for $C_{15}H_{22}NaO_2$ 257.1517; found 257.1530. α_D^{25} = +73.1 (c = 0.004, $CHCl_3$). IR (film): 3349, 2970, 2922, 2877, 1665, 1618, 1585 cm^{-1}. Mp = 108−111 °C. Sootepdienone:[1] ^{1}H NMR (400 MHz) δ 6.75 (d, J = 1.75 Hz, 1H); 3.33 (m, 1H); 2.58 (m, 1H); 2.50 (dd, J = 18.6, 6.6 Hz, 1H); 2.35 (ddd, J = 16.5, 7.8, 2.7 Hz, 1H); 2.24 (dd, J = 18.6, 2.1 Hz, 1H); 2.23 (m, 1H); 2.15 (m, 1H); 1.70 (d, J = 1.8 Hz, 3H); 1.48 (m, 1H); 1.41 (s, 6H); 0.71 (d, J = 6.6 Hz, 3H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) 209.3, 167.1, 160.4, 137.4, 118.2, 74.4, 43.6, 39.7, 35.1, 32.9, 28.8, 28.6, 26.5, 14.5, 8.3. HRMS (ESI-TOF) m/z: [M]$^+$ calcd $\varphi o \rho$ $C_{15}H_{22}O_2$ 234.1620; found 234.1612. α_D^{20} = +12 (c = 0.1, $CHCl_3$). IR ($CHCl_3$): 3240, 1680 cm^{-1}. Mp = 47−50°. **1b**: ^{1}H NMR (400 MHz, DMSO-d_6) δ 6.67 (s, 1H); 4.83 (s, 1H); 2.64 (m, 1H); 2.51(m, 1H) 2.44 (m, 1H); 2.29−2.22 (dd, J = 19.5, 8.4 Hz, 1H); 2.01 (d, J = 16.4 Hz, 1H); 1.68 (m, 1H); 1.64 (s, 3H); 1.57−1.49 (m, 2H); 1.26 (s, 6H); 1.02−1.00 (d, J = 6.4 Hz, 3H). ^{13}C{^{1}H} NMR (100 MHz, DMSO-d_6) δ 207.5, 168.6, 163.7, 134.8, 117.4, 73.1, 46.0, 41.9, 38.7, 35.5, 28.9, 28.8, 22.2, 8.4. HRMS (ESI-TOF) m/z: [M + Na]$^+$ calcd for $C_{15}H_{22}NaO_2$ 257.1517; found 257.1520. α_D^{25} = −168.6 (c = 0.005, MeOH). IR (film): 3366, 2971, 2924, 2875, 1666, 1619, 1585 cm^{-1}. Mp = 95−99 °C. Jambolanin C:[2] ^{1}H NMR (600 MHz, DMSO-d_6) δ 6.67 (s, 1H); 4.84 (s, 1H); 2.64 (m, 1H); 2.44 (dd, J = 17.0, 7.8 Hz, 1H); 2.26 (dd, J = 17.0, 10.8 Hz, 1H); 2.50 (dd, J = 18.4, 2.0 Hz, 1H); 2.02 (dd, J = 18.4, 2.0 Hz, 1H); 1.69 (m, 1H); 1.64 (s, 3H); 1.56 (m, 1H); 1.27 (s, 3H); 1.27 (s, 3H); 1.02 (d, J = 6.6 Hz, 3H). ^{13}C{^{1}H} NMR (150 MHz, DMSO-d_6) 207.6, 168.6, 163.8, 134.8, 117.4, 71.3, 46.1, 42.0, 38.7, 35.5, 29.0, 28.8, 22.2, 8.5. HRMS (ESI-TOF) m/z: [M + H]$^+$ calcd for $C_{15}H_{23}O_2$ 235.1698; found 235.1725. α_D^{20} = −70 (c = 0.4, MeOH). IR (film) 3408, 2958, 2924, 2860, 1723, 1676, 1625, 1586.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge at https://pubs.acs.org/doi/10.1021/acs.joc.0c02747.

^{1}H and ^{13}C NMR spectra for all compounds in Schemes 1, 3, and 4 (PDF)

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Notes

The authors declare no competing financial interest.

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(17) (a) Attempted C.1 epimerization of Jambolanin I to Jambolanin H under a variety of acidic ($Ce(OTf)_3$, *i*-PrOH, 80 °C, 5 h; HCl, MeOH) or basic (KO*t*-Bu, THF, *t*BuOH, rt; $NaOCH_3$, CH_3OH, rt−40 °C) conditions was unsuccessful. Furthermore, attempted palladium-catalyzed deallyloxycarbonylation of **9a** at elevated temperatures (80 °C) and high concentrations (>1 M) did not alter the **2a**:**2b** diastereomer ratio obtained. (b) Ab initio Hartree−Fock calculations of the equilibrium geometry of the enol of **2a** (Y = $OSiEt_3$) using the 3-21G basis set reveal that the lowest energy conformer possesses a pseudoaxial C-10 methyl group at approximately 90° to the plane of enolate C═C bond. This geometry appears to be favored due to an avoidance of steric interaction between the C-10 methyl group and the C-1 substituent. Furthermore, the presence of the bulky quaternary substituent at C-7 contorts the seven-membered ring in such a way that there are no other (pseudo)axial hydrogen atoms on the ring to interact with the C-10 methyl group (see Scheme 3). The positioning of this methyl group effectively shields the top face of the enol/enolate from attack by electrophiles. This observation may explain the diastereoselectivity obtained in the formation of **9a** and **9b** from **8a** and **8b**, respectively, and in the conversion of **9a** and **9b** into **2a** and **2c**, respectively. In addition, the stereochemistry proposed for the C-1 quaternary center of **9a** and **9b** is based on the assumption of the MVK approach to the enolate derived from **8a** and **8b** *anti* to the C-10 methyl group.

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(21) No evidence of Claisen rearrangement product **7** was observed when compound **6** was heated in toluene at 110 °C for 12 h. (b) Previous reports on the reaction of allyl halides with 2-cyclohepten-1-one enolates indicate that the *C*-allylated product is formed in low to moderate yields, and it is likely that the allyl enol ether is a prominant side product: see: (a) Weinmann, H.; Winterfeldt, E. A Predictable Enantioselective Total Synthesis of (+)-Clavularin. *Synthesis* **1995**, *1995*, 1097−1101. (b) Litman, Z. C.; Sharma, A.; Hartwig, J. F. Oxidation of Hindered Allylic C-H Bonds with Applications to the Functionalization of Complex Molecules. *ACS Catal.* **2017**, *7*, 1998−2001.

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