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Total Syntheses of (±)-Omphadiol and (±)-Pyxidatol C through a *Cis*-Fused 5,7-Carbocyclic Common Intermediate

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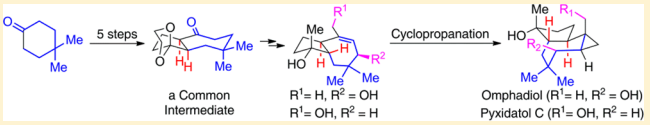
Supporting Information

ABSTRACT: Total syntheses of omphadiol and pyxidatol C, two isomeric africanane sesquiterpenes sharing identical 5-7-3 tricyclic carbon skeletons yet containing distinct oxidation patterns, are reported. The *trans*-fused 5,7-carbocycles in the terpenoids characterized by specific oxidation patterns were derived from a readily available *cis*-fused 5,7-carbocyclic common intermediate.



Omphadiol (**1**) and pyxidatol C (**2**) (Figure 1) are two isomeric natural products belonging to the africanane

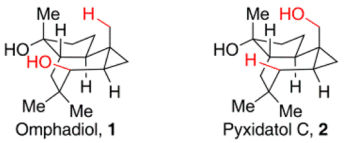


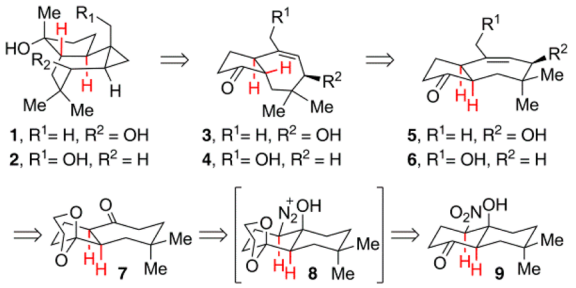
Figure 1. Molecular structures of omphadiol and pyxidatol C.

family of sesquiterpenes. Omphadiol was first isolated from the basidiomycete *Omphalotus illudens* by McMorris and co-workers in 2000.[1] Later, in 2008, omphadiol and its analogue pyxidatol C were also found to be produced by a different genus of fungi named *Clavicorona pyxidata*.[2] Although the wild mushroom *C. pyxidata* has been widely used in traditional Chinese medicine to cure gastric pain, dyspepsia, gout, and heat toxicity,[2] the limited quantity of isolated materials have prevented a full evaluation of the bioactivities of both omphadiol and pyxidatol C. Structurally, these two analogous terpenoids contain the same 5-7-3 tricyclic carbon skeleton elaborated with two hydroxyl groups. While one hydroxyl group is identically located in the two molecules, the position of the other one is different (highlighted in red in Figure 1), resulting in distinct stereochemistry. Further structural complexities of the two terpenoids involve a panel of contiguous stereogenic centers within the *trans*-fused 5,7-carbocycle. Dense stereochemical complexity on a relatively flexible skeleton and difficult levels of oxidation have rendered africananes containing such structural motifs to be appealing synthetic targets and have inspired elegant synthetic solutions to this family of terpenoids.[3−7]

To date, the only documented total synthesis of omphadiol was achieved in an asymmetric fashion by Romo and co-workers.[8] In 2011, they reported a concise synthesis of (+)-omphadiol featuring highly stereocontrolled introduction of the six contiguous stereogenic centers and olefin metathesis for efficient construction of the seven-membered ring in the molecule. Unlike omphadiol, the total synthesis of its analogue pyxidatol C has not been disclosed in the literature. Herein we report our divergent syntheses of these two structurally intriguing isomeric sesquiterpenes from a readily available *cis*-fused 5,7-carbocyclic common intermediate.

Our synthetic strategy toward omphadiol and pyxidatol C is depicted in Scheme 1. We envisioned that two *trans*-fused 5,7-

Scheme 1. Synthetic Design of Omphadiol and Pyxidatol C



carbocycles **3** and **4** could be elaborated to produce omphadiol **1** and pyxidatol C **2**, respectively, after addition of a methyl group to the ketone functionality and cyclopropanation on the double bond. Considering that a *trans*-fused 5,7-carbocycle is thermodynamically more stable than a *cis*-fused one,[9] we anticipated that *trans*-fused **3** and **4** could be derived from their *cis*-fused counterparts **5** and **6** through epimerization of the bridging carbon adjacent to the carbonyl group.[10] To obtain **5** and **6** possessing different oxidation patterns, we selected the *cis*-fused 5,7-carbocyclic common intermediate **7** as a suitable precusor. Then we assumed that compound **7** could be readily prepared from *trans*-decalin **9** through a reactive intermediate **8** using a Tiffeneau−Demjanov rearrangement.[11] We assumed that an aldol−Henry reaction cascade, which was previously

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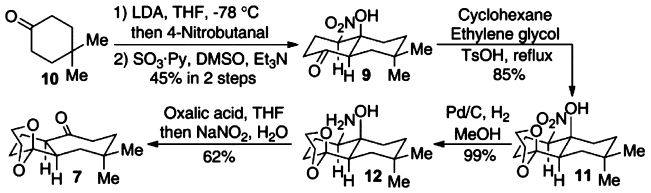
developed in our group in the total synthesis of echinopines,[12] would be well-suited for construction of *trans*-decalin **9**.

Our synthetic practice commenced from commercially available ketone **10** (Scheme 2). Gratifyingly, by applying the

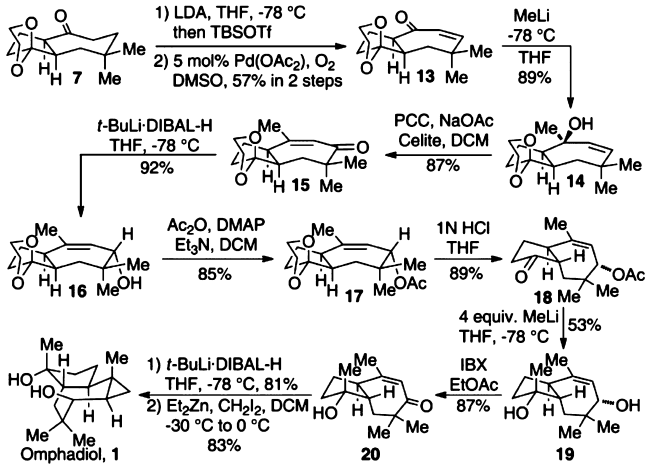
Scheme 2. Synthesis of the Key *Cis*-Fused 5,7-Carbocylic Intermediate 7



aldol−Henry reaction cascade and subsequent Parikh−Doering oxidation,[13] we readily obtained *trans*-decalin **9** in 45% yield. The stereochemistry of **9** was unambiguously confirmed by single-crystal X-ray crystallographic analysis.[14] Protection of the carbonyl group in **9** provided **11**, which underwent facile palladium-catalyzed hydrogenation of the nitro group to afford the corresponding amine **12** in nearly quantitative yield.[15] The desired Tiffeneau−Demjanov rearrangement went smoothly to generate the desired *cis*-fused 5,7-carbocycle **7** in 62% yield with complete diastereocontrol. This short synthetic sequence allowed us to conveniently synthesize **7** from the inexpensive ketone **10** in an overall yield of 23% through straightforward chemical transformations.

With a sufficient supply of the key intermediate **7**, we proceeded to complete the total synthesis of omphadiol (Scheme 3). Adjustment of the oxidation state in **7** to that in

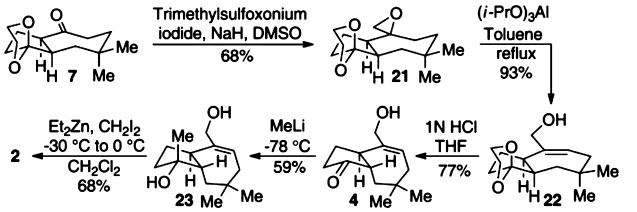
Scheme 3. Total Synthesis of Omphadiol



intermediate **15** was accomplished through a combination of Saegusa oxidation,[16] methyllithium addition, and Dauben oxidation.[17] More specifically, we obtained the desired unsaturated ketone **13** in a reasonable yield by applying Larock's protocol for Saegusa oxidation.[18] Subsequent Dauben oxidation of **14** following 1,2-addition of methyllithium to **13** delivered **15**. When unsaturated ketone **15** was treated with a DIBAL-H/*t*-BuLi complex,[8,19] allylic alcohol **16** was produced smoothly in 92% yield with high selectivity (d.r. > 19:1). Notably, the stereochemistry of the newly formed hydroxyl group in **16** is opposite to what is present in the natural product. At this point, direct exposure of compound **16** to acidic conditions for removal of the acetal protecting group led to a complex mixture of products. Assuming that the free hydroxyl group in the allylic alcohol became vulnerable under the acidic conditions, we converted it to an acetyl ester for protection and delivered **17**, which was then treated with 1 N HCl in THF. Remarkably, by using this new substrate **17**, we were able to remove the acetal protecting group and simultaneously accomplish complete epimerization to generate the desired *trans*-fused product **18** in 89% yield! Subsequent treatment of **18** with 4 equiv of methyllithium produced the desired diol **19** as the major diastereomer in 53% yield.[20] To convert **19** to omphadiol, we oxidized the allylic hydroxyl group using 2-iodoxybenzoic acid in ethyl acetate to yield **20**,[21] an advanced intermediate reported in Romo's synthesis.[8] Following their procedure of reduction and Simmons−Smith cyclopropanation,[22] we achieved a total synthesis of omphadiol starting from the common intermediate **7**.

The synthesis of pyxidatol C starting from **7** was fulfilled in a more straightforward manner than that of omphadiol (Scheme 4). First, the external hydroxyl group in the terpenoid was

Scheme 4. Total Synthesis of Pyxidatol C



introduced through a Corey−Chaykovsky epoxidation[23] and epoxide isomerization sequence. The epoxidation of **7** went smoothly upon treatment with trimethylsulfoxonium iodide in the presence of NaH in DMSO to afford **21** in 68% yield. To our delight, upon treatment with $(i\text{-PrO})_3$Al in refluxing toluene, epoxide **21** was isomerized to the allylic alcohol **22** in excellent yield with exclusive regioselectivity.[24] With no need to protect the allylic alcohol in this case, the *cis*-fused compound **22** was directly converted to *trans*-fused 5,7-carbocyle **4** in good yield upon treatment with 1 N HCl in THF. Addition of methyllithium to **4** then yielded the desired diol **23** in 59% yield.[25] Again, a Simmons−Smith cyclopropanation of **23** generated pyxidatol C in 68% yield with excellent stereochemical control (d.r. > 19:1).

In summary, we have achieved the divergent total syntheses of two isomeric sesquiterpenes, omphadiol and pyxidatol C, through a readily available *cis*-fused 5,7-carbocyclic common intermediate. The analytical data for our synthetic samples completely matched those previously reported.[26] A key strategy of our total syntheses was to convert *cis*-fused 5,7-carbocycles to their thermodynamically more stable *trans*-fused counterparts through equilibration. The synthesis of the common intermediate **7** was achieved through a concise sequence of stereospecific Tiffeneau−Demjanov rearrangement and a two-step preparation of *trans*-decalin **9** involving an aldol−Henry cascade. Furthermore, our strategy of combining Saegusa oxidation and Dauben oxidation fulfilled the introduction of the specific oxidation pattern in omphadiol, whereas in pyxidatol C a different oxidation pattern was established through Corey−Chaykovsky epoxidation and a highly regioselective epoxide isomerization to an allylic alcohol. Considering that the 5,7-carbocycle is a common motif in

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terpenoids, we envision that the chemistry demonstrated in this work will have potential for the total syntheses of other structurally challenging terpenes containing similar motifs.

EXPERIMENTAL SECTION

(4*S*,4a*S*,8a*R*)-4a-Hydroxy-7,7-dimethyl-4-nitrooctahydronaphthalen-1(2*H*)-one (9). To a solution of **10** (6.31 g, 50.0 mmol) in THF (90.0 mL) was added newly prepared LDA (65.0 mmol) at −78 °C dropwise.[27] The mixture was stirred at −78 °C for 30 min before a solution of 4-nitrobutanal in THF (8.78 g, 75.0 mmol) was added. The reaction mixture was stirred for 1 h and allowed to warm to room temperature. The reaction was quenched with a saturated aqueous solution of NH_4Cl (50.0 mL) upon completion, and the mixture was extracted with ethyl acetate (3 × 100 mL). The combined organic layers were washed with brine, dried over anhydrous $MgSO_4$, and filtered. The solvent was removed under reduced pressure to give a yellow oil that was used in next step without further purification.

To a solution of the above yellow oil in CH_2Cl_2 (250 mL) were added DMSO (27.3 g, 350 mmol) and Et_3N (25.3 g, 250 mmol) before SO_3·pyridine (23.9 g, 150 mmol) was added in two portions at 0 °C. The reaction mixture was allowed to warm to room temperature and stirred overnight before it was diluted with water (100 mL) and extracted with CH_2Cl_2 (3 × 100 mL). The combined organic layers were washed with brine, dried over anhydrous $MgSO_4$, and filtered. The solvent was removed under reduced pressure to give a brown oil. The crude product was purified by column chromatography (4:1 petroleum ether/ethyl acetate) to give **9** (5.40 g, 45%) as a white solid. R_f 0.28 (4:1 petroleum ether/ethyl acetate); ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.91 (dd, J = 12.6, 3.8 Hz, 1H), 2.86−2.75 (m, 1H), 2.65−2.54 (m, 2H), 2.50−2.31 (m, 3H), 1.78 (td, J = 13.5, 4.1 Hz, 1H), 1.68−1.55 (m, 2H), 1.54−1.39 (m, 2H), 1.24 (dd, J = 13.5, 1.9 Hz, 1H), 0.99 (s, 3H), 0.86 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 206.0, 91.2, 74.1, 50.5, 37.9, 32.7, 32.4, 32.4, 31.5, 29.5, 26.2, 23.6; IR (thin film) ν_{max} 3474, 2969, 2949, 2929, 2863, 1721, 1550, 1458, 1371, 1221, 1152, 1115, 1022, 982, 889, 847 cm^{-1}; HRMS (ESI) calcd for $C_{12}H_{18}NO_4$ $[M - H]^-$ 240.1241, found 240.1245; mp 117−119 °C.

(4′*R*,4a′*S*,8a′*R*)-7′,7′-Dimethyl-4′-nitrooctahydro-2′*H*-spiro[[1,3]dioxolane-2,1′-naphthalen]-4a′-ol (11). To a solution of **9** (2.00 g, 8.30 mmol) in cyclohexane (80.0 mL) were added ethylene glycol (2.30 mL, 41.5 mmol) and *p*-TsOH (143 mg, 0.830 mmol). The mixture was heated to reflux and stirred for 10 h before it was allowed to cool to room temperature. The reaction was quenched with a saturated aqueous solution of $NaHCO_3$ (30.0 mL), and the mixture was extracted with ethyl acetate (3 × 50.0 mL). The combined organic layers were washed with brine, dried over anhydrous $MgSO_4$, and filtered. The solvent was removed under reduced pressure to give a yellow solid. The crude product was purified by column chromatography (4:1 petroleum ether/ethyl acetate) to give **11** (2.00 g, 85%) as a white solid. R_f 0.26 (4:1 petroleum ether/ethyl acetate); ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.38 (dd, J = 12.9, 3.8 Hz, 1H), 4.02−3.89 (m, 4H), 3.78 (s, 1H), 2.55 (ddd, J = 27.4, 13.6, 3.9 Hz, 1H), 2.03−1.98 (m, 1H), 1.92 (dt, J = 13.7, 3.3 Hz, 1H), 1.85 (dd, J = 11.5, 4.8 Hz, 1H), 1.65−1.54 (m, 4H), 1.41−1.29 (m, 2H), 1.19 (d, J = 8.3 Hz, 1H), 0.95 (s, 3H), 0.90 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 108.6, 91.4, 72.3, 65.7, 64.7, 44.9, 33.4, 33.0, 32.8, 31.8, 31.3, 29.7, 24.0, 23.1; IR (thin film) ν_{max} 3495, 2997, 2951, 2936, 2901, 2868, 1541, 1459, 1443, 1354, 1261, 1160, 1103, 1077, 1030, 994, 952, 923, 870 cm^{-1}; HRMS (ESI) calcd for $C_{14}H_{23}NO_5Na$ $[M + Na]^+$ 308.1468, found 308.1475; mp 128−130 °C.

(4′*R*,4a′*S*,8a′*R*)-4′-Amino-7′,7′-dimethyloctahydro-2′*H*-spiro[[1,3]dioxolane-2,1′-naphthalen]-4a′-ol (12). To a solution of **11** (2.00 g, 7.00 mmol) in MeOH (70.0 mL) was added 10% Pd/C (100 mg) at room temperature. The mixture was purged with nitrogen three times and then connected to a balloon filled with hydrogen. After the reaction mixture was stirred at room temperature for 10 h, Pd/C was removed by filtration, and the filtrate was concentrated under reduced pressure to give **12** (1.77 g, 99%) as a colorless oil, which was used in next step without further purification. ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.9−3.80 (m, 4H), 3.39 (s, 1H), 2.41−2.33 (m, 1H), 1.82−1.71 (m, 3H), 1.67 (d, J = 12.5 Hz, 1H), 1.59−1.45 (m, 3H), 1.35−1.22 (m, 2H), 1.22−1.10 (m, 2H), 0.92 (s, 3H), 0.85 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 109.9, 72.6, 65.4, 64.4, 57.0, 44.5, 34.3, 33.6, 33.0, 32.0, 30.9, 29.8, 28.5, 24.1.

(8a*R*)-7,7-Dimethylhexahydro-2*H*-spiro[azulene-1,2′-[1,3]-dioxolan]-4(5*H*)-one (7). To a solution of **12** (1.77 g, 6.90 mmol) in THF (70 mL) was added a solution of oxalic acid (495 mg, 5.50 mmol) in THF (14.0 mL) dropwise. The mixture was stirred for 30 min to afford a slurry. The slurry was concentrated under reduced pressure to give a sticky solid. The solid was dissolved in H_2O (125 mL) before sodium nitrite (1.43 g, 20.7 mmol) was added in one portion. The reaction mixture was stirred for 12 h before it was extracted with ethyl acetate (3 × 50.0 mL). The combined organic layers were washed with brine, dried over anhydrous $MgSO_4$, and filtered. The solvent was removed under reduced pressure to give a yellow oil. The crude product was purified by column chromatography (4:1 petroleum ether/ethyl acetate) to give **7** (1.02 g, 62%) as a white solid. R_f 0.34 (4:1 petroleum ether/ethyl acetate); ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.88−3.80 (m, 4H), 3.20 (dt, J = 11.2, 7.9 Hz, 1H), 2.42 (t, J = 11.5 Hz, 1H), 2.33 (dd, J = 10.0, 4.1 Hz, 2H), 2.23−2.15 (m, 1H), 1.81−1.69 (m, 2H), 1.60−1.51 (m, 2H), 1.40−1.33 (m, 1H), 1.29 (d, J = 13.5 Hz, 1H), 1.09 (d, J = 13.5 Hz, 1H), 0.97 (s, 3H), 0.88 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 212.3, 117.4, 64.9, 64.6, 49.7, 41.9, 398.0, 37.4, 36.0, 33.8, 32.0, 30.1, 28.0, 20.9; IR (thin film) ν_{max} 2955, 2866, 1699, 1473, 1408, 1386, 1321, 1299, 1281, 1254, 1110, 1094, 1025, 970, 922, 894, 846 cm^{-1}; HRMS (ESI) calcd for $C_{14}H_{22}O_3Na$ $[M + Na]^+$ 261.1461, found 261.1465; mp 70−72 °C.

(8a*R*)-7,7-Dimethyl-3,3a,8,8a-tetrahydro-2*H*-spiro[azulene-1,2′-[1,3]dioxolan]-4(7*H*)-one (13). To a newly prepared LDA solution was added a solution of **7** (834 mg, 3.50 mmol) in THF (30.0 mL) at −78 °C dropwise. The reaction mixture was stirred for 30 min before TBSOTf (0.200 mL, 0.400 mmol) was added. The reaction was quenched with a saturated aqueous solution of $NaHCO_3$ (10.0 mL) upon completion, and the mixture was extracted with ethyl acetate (3 × 50.0 mL). The combined organic layers were washed with brine, dried over anhydrous $MgSO_4$, and filtered. The solvent was removed under reduced pressure to give a yellow oil that was used in next step without purification.

To a solution of the yellow oil (1.11 g, 3.15 mmol) in DMSO (40.0 mL) was added $Pd(OAc)_2$ (35.4 mg, 0.160 mmol). The reaction mixture was allowed to warm to 40 °C and stirred under an atmosphere of O_2 until the starting material was completely consumed. The reaction mixture was diluted water (100 mL) and extracted with ethyl acetate (3 × 80.0 mL). The combined organic layers were washed with brine, dried over anhydrous $MgSO_4$, and filtered. The solvent was removed under reduced pressure to give **13** (471 mg, 57%) as a brown oil, which was used without further purification. R_f 0.36 (4:1 petroleum ether/ethyl acetate); ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.00 (d, J = 12.3 Hz, 1H), 5.74 (d, J = 12.3 Hz, 1H), 3.84 (dd, J = 9.0, 3.2 Hz, 4H), 3.13 (t, J = 8.8 Hz, 1H), 2.49 (dd, J = 18.0, 8.3 Hz, 1H), 2.25 (dd, J = 12.6, 5.6 Hz, 1H), 1.77 (dd, J = 14.4, 6.1 Hz, 1H), 1.67 (dd, J = 10.3, 6.7 Hz, 2H), 1.57 (t, J = 7.8 Hz, 2H), 1.11 (s, 3H), 1.04 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 203.5, 152.3, 127.9, 117.4, 65.0, 64.7, 53.1, 43.4, 37.7, 37.6, 33.7, 32.6, 24.9, 21.1; IR (thin film) ν_{max} 2958, 2883, 1674, 1471, 1362, 1308, 1254, 1104, 1044, 949, 893, 837 cm^{-1}; HRMS (ESI) calcd for $C_{14}H_{20}O_3Na$ $[M + Na]^+$ 259.1310, found 259.1327.

(4*S*,8a*R*)-4,7,7-Trimethyl-3,3a,4,7,8,8a-hexahydro-2*H*-spiro-[azulene-1,2′-[1,3]dioxolan]-4-ol (14). To a solution of **13** (236 mg, 1.00 mmol) in THF (10 mL) was added MeLi (1.00 M in diethyl ether, 1.50 mL, 1.50 mmol) dropwise at −78 °C. The mixture was stirred at −78 °C until completion of the reaction. The reaction was quenched with a saturated aqueous solution of NH_4Cl (10.0 mL), and the mixture was extracted with ethyl acetate (3 × 20.0 mL). The combined organic layers were washed with brine, dried over anhydrous $MgSO_4$, and filtered. The solvent was removed under reduced pressure to give a yellow oil. The crude product was purified by column chromatography (4:1 petroleum ether/ethyl acetate) to give **14** (225 mg, 89%) as a white solid. R_f 0.33 (4:1 petroleum ether/ethyl acetate); ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.34 (d, J = 12.1 Hz, 1H), 5.26 (d, J =

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12.2 Hz, 1H), 3.96−3.80 (m, 4H), 3.11 (s, 1H), 2.43−2.28 (m, 2H), 1.98 (dd, J = 16.8, 9.2 Hz, 1H), 1.85−1.70 (m, 3H), 1.54 (q, J = 11.2 Hz, 1H), 1.35 (d, J = 13.6 Hz, 1H), 1.12 (s, 3H), 0.98 (s, 3H), 0.96 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 141.7, 134.0, 117.1, 71.3, 65.5, 64.8, 45.7, 43.9, 35.2, 35.0, 34.2, 33.2, 30.3, 26.1, 23.0; IR (thin film) ν_{max} 3504, 2975, 2952, 2880, 2865, 1733, 1653, 1455, 1374, 1325, 1284, 1246, 1147, 1041, 946, 864, 806 cm^{-1}; HRMS (ESI) calcd for $C_{15}H_{24}O_3Na$ $[M + Na]^+$ 275.1618, found 275.1621; mp 70−72 °C.

(8a*R*)-4,7,7-Trimethyl-3,3a,8,8a-tetrahydro-2*H*-spiro-[azulene-1,2′-[1,3]dioxolan]-6(7*H*)-one (15). To a stirred suspension of PCC (203 mg, 0.940 mmol), AcONa (38.7 mg, 0.470 mmol), and Celite (75.5 mg) in CH_2Cl_2 (4.00 mL) was added a solution of **14** (106 mg, 0.470 mmol) in CH_2Cl_2 (2.00 mL). The reaction mixture was stirred at room temperature for 4 h until the starting material was completely consumed. Et_2O was added, and the suspension was filtered. The filtrate was concentrated under reduced pressure. The crude product was purified by column chromatography (8:1 petroleum ether/ethyl acetate) to give **15** (102 mg, 87%) as a white solid. R_f 0.20 (8:1 petroleum ether/ethyl acetate); ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.75 (s, 1H), 4.03−3.86 (m, 4H), 2.88 (d, J = 4.2 Hz, 1H), 2.10 (ddd, J = 13.1, 8.7, 4.0 Hz, 1H), 2.07−1.91 (m, 2H), 1.85 (s, 4H), 1.65 (d, J = 3.2 Hz, 3H), 1.18 (s, 3H), 1.09 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 208.8, 152.5, 125.9, 117.8, 64.6, 63.7, 47.3, 46.7, 44.0, 34.3, 32.0, 29.2, 25.1, 24.5, 23.9; IR (thin film) ν_{max} 2959, 2879, 1703, 1659, 1472, 1440, 1381, 1320, 1182, 1055, 1018, 947, 907, 851 cm^{-1}; HRMS (ESI) calcd for $C_{15}H_{22}O_3Na$ $[M + Na]^+$ 273.1461, found 273.1460; mp 46−48 °C.

(6*S*,8a*R*)-4,7,7-Trimethyl-3,3a,6,7,8,8a-hexahydro-2*H*-spiro-[azulene-1,2′-[1,3]dioxolan]-6-ol (16). To a solution of DIBAL-H (1.20 M in hexane, 0.330 mL) was added *t*-BuLi (1.60 M in toluene, 0.250 mL) slowly at 0 °C. The clear solution was stirred at 0 °C for 10 min before it was added to a solution of **15** (25.0 mg, 0.10 mmol) in THF (1.00 mL) at −78 °C dropwise. The reaction mixture was stirred until the starting material was completely consumed. The reaction was quenched with MeOH (1.00 mL) carefully, and the mixture was diluted with CH_2Cl_2 and 20% aqueous NaOH, allowed to warm to room temperature, and stirred for 30 min. The resulting white precipitate was removed by filtration through a pad of silica gel, and the filtrate was concentrated under reduced pressure to give a colorless oil. The crude product was purified by column chromatography (4:1 petroleum ether/ethyl acetate) to give **16** (23.2 mg, 92%) as a white solid. R_f 0.36 (4:1 petroleum ether/ethyl acetate); ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.27 (s, 1H), 3.90−3.78 (m, 4H), 2.67−2.50 (m, 1H), 2.09 (dd, J = 9.1, 4.2 Hz, 1H), 1.89 (dd, J = 17.2, 7.9 Hz, 3H), 1.70 (s, 3H), 1.51−1.40 (m, 2H), 1.29−1.13 (m, 2H), 0.93 (s, 3H), 0.84 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 137.4, 127.9, 118.8, 77.5, 64.5, 63.5, 45.1, 42.2, 36.8, 35.9, 32.5, 30.0, 26.4, 25.1, 19.1; IR (thin film) ν_{max} 3363, 3296, 2978, 2947, 2881, 1718, 1671, 1474, 1359, 1203, 1103, 1056, 988, 950, 898, 838 cm^{-1}; HRMS (ESI) calcd for $C_{15}H_{25}O_3$ $[M + H]^+$ 253.1798, found 253.1800; mp 89−91 °C.

(6*S*,8a*R*)-4,7,7-Trimethyl-3,3a,6,7,8,8a-hexahydro-2*H*-spiro-[azulene-1,2′-[1,3]dioxolan]-6-yl acetate (17). To a solution of **16** (134 mg, 0.530 mmol) in CH_2Cl_2 (3.00 mL) were added Et_3N (536 mg, 5.30 mmol), Ac_2O (433 mg, 4.24 mmol), and DMAP (6.50 mg, 0.0530 mmol) at room temperature. The mixture was stirred until the starting material was completely consumed. The reaction was quenched with a saturated aqueous solution of $NaHCO_3$ (8.00 mL), and the mixture was extracted with CH_2Cl_2 (3 × 20.0 mL). The combined organic layers were washed with brine, dried over anhydrous $MgSO_4$, and filtered. The solvent was removed under reduced pressure to give a brown oil. The crude product was purified by column chromatography (8:1 petroleum ether/ethyl acetate) to give **17** (133 mg, 85%) as a white solid. R_f 0.32 (8:1 petroleum ether/ethyl acetate); ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.13 (s, 1H), 5.00 (s, 1H), 3.92−3.74 (m, 4H), 2.69−2.59 (m, 1H), 2.18−2.10 (m, 1H), 1.99 (d, J = 7.9 Hz, 3H), 1.89 (t, J = 10.9 Hz, 2H), 1.71 (d, J = 12.6 Hz, 4H), 1.61−1.41 (m, 2H), 1.34 (t, J = 13.7 Hz, 1H), 0.87 (d, J = 9.4 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.2, 139.1, 123.5, 118.6, 78.9, 64.5, 63.5, 45.0, 42.1, 36.6, 35.1, 32.6, 29.6, 25.9, 25.3, 21.0, 20.5; IR (thin film) ν_{max} 2974, 2954, 2893, 1722, 1470, 1387, 1301, 1249, 1161, 1130, 1020, 979, 945, 935 cm^{-1}; HRMS (ESI) calcd for $C_{17}H_{26}O_4Na$ $[M + Na]^+$ 317.1729, found 317.1715; mp 73−75 °C.

(3a*S*,6*S*)-5,5,8-Trimethyl-3-oxo-1,2,3,3a,4,5,6,8a-octahydroazulen-6-yl acetate (18). To a solution of **17** (133 mg, 0.450 mmol) in THF (2.50 mL) was added 1.0 M aqueous HCl (0.20 mL) dropwise. The reaction mixture was stirred until the starting material was completely consumed. The reaction mixture was treated with water (2.00 mL) and extracted with ethyl acetate (3 × 10.0 mL). The combined organic layers were washed with water and brine, dried over anhydrous $MgSO_4$, and filtered. The solvent was removed under reduced pressure to give a pale-yellow oil. The crude product was purified by column chromatography (8:1 petroleum ether/ethyl acetate) to give **18** (100 mg, 89%) as a colorless oil. R_f 0.28 (8:1 petroleum ether/ethyl acetate); ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.57 (d, J = 7.2 Hz, 1H), 4.72 (d, J = 7.4 Hz, 1H), 2.91−2.78 (m, 1H), 2.39−2.26 (m, 1H), 2.13−2.06 (m, 2H), 1.98 (d, J = 4.2 Hz, 4H), 1.84 (dd, J = 14.1, 2.3 Hz, 1H), 1.76 (d, J = 5.6 Hz, 3H), 1.73−1.64 (m, 2H), 0.89 (d, J = 7.0 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 219.6, 170.3, 142.8, 123.9, 77.6, 49.0, 44.4, 38.0, 37.6, 33.8, 29.2, 24.5, 24.1, 21.9, 20.8; IR (thin film) ν_{max} 2966, 2871, 1738, 1674, 1473, 1444, 1371, 1244, 1141, 1019, 975, 894, 882 cm^{-1}; HRMS (ESI) calcd for $C_{15}H_{22}O_3NH_4$ $[M + NH_4]^+$ 268.1907, found 268.1908.

(1*R*,6*S*,8a*S*)-1,4,7,7-Tetramethyl-1,2,3,3a,6,7,8,8a-octahydroazulene-1,6-diol (19). To a solution of **18** (47.5 mg, 0.190 mmol) in THF (2.00 mL) was added MeLi (1.00 M in diethyl ether, 0.760 mL, 0.760 mmol) dropwise at −78 °C. The mixture was stirred until the reaction was complete. The reaction was quenched with a saturated aqueous solution of NH_4Cl (5.00 mL) carefully, and the mixture was extracted with ethyl acetate (3 × 10.0 mL). The combined organic layers were washed with water and brine, dried over anhydrous $MgSO_4$, and filtered. The solvent was removed under reduced pressure to give a yellow oil. The crude product was purified by column chromatography (2:1 petroleum ether/ethyl acetate) to give the major diastereomer **19** (22.6 mg, 53%) as a white solid and a minor diastereomer (10.2 mg, 24%) as a colorless oil.

Data for the major diastereomer **19**: R_f 0.16 (2:1 petroleum ether/ethyl acetate); ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.48 (d, J = 6.1 Hz, 1H), 3.84 (d, J = 6.3 Hz, 1H), 2.90 (dd, J = 19.9, 9.9 Hz, 1H), 1.96−1.85 (m, 1H), 1.81 (d, J = 12.7 Hz, 1H), 1.74 (s, 3H), 1.69 (dd, J = 6.6, 4.5 Hz, 1H), 1.58−1.44 (m, 3H), 1.39−1.31 (m, 1H), 1.22 (s, 3H), 1.00 (s, 3H), 0.92 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 142.5, 126.3, 80.4, 76.2, 48.9, 46.0, 40.0, 36.6, 35.7, 28.7, 26.8, 26.1, 23.6; IR (thin film) ν_{max} 3384, 3292, 2957, 2890, 1720, 1648, 1473, 1384, 1211, 1165, 1147, 1077, 1020, 998, 943, 827 cm^{-1}; HRMS (ESI) calcd for $C_{14}H_{24}O_2Na$ $[M + Na]^+$ 247.1669, found 247.1669; mp 78−80 °C.

Data for the minor diastereomer: R_f 0.13 (2:1 petroleum ether/ethyl acetate); ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.53 (d, J = 6.6 Hz, 1H), 3.80 (d, J = 6.7 Hz, 1H), 2.80−2.63 (m, 1H), 1.85−1.81 (m, 1H), 1.76 (s, 3H), 1.73−1.68 (m, 3H), 1.49−1.45 (m, 1H), 1.24 (d, J = 9.0 Hz, 2H), 1.17 (s, 3H), 1.02 (s, 3H), 0.93 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 143.4, 126.1, 80.2, 76.6, 50.0, 46.0, 41.0, 38.2, 35.7, 29.5, 25.5, 25.3, 24.0, 23.0; IR (thin film) ν_{max} 3387, 2964, 2929, 2867, 1730, 1657, 1548, 1464, 1447, 1378, 1302, 1284, 1261, 1200, 1150, 1110.

(3*R*,3a*S*)-3-Hydroxy-3,5,5,8-tetramethyl-1,3,3a,4,5,8a-hexahydroazulen-6(2*H*)-one (20). To a solution of **19** (58.3 mg, 0.260 mmol) in ethyl acetate (3.00 mL) was added 2-iodoxybenzoic acid (218 mg, 0.780 mmol) in one portion. The mixture was allowed to warm to 75 °C and stirred until the starting material was completely consumed. The reaction mixture was diluted with petroleum ether, filtered, and concentrated under reduced pressure. The crude product was purified by column chromatography (4:1 petroleum ether/ethyl acetate) to give **20** (50.3 mg, 87%) as a white solid. R_f 0.19 (4:1 petroleum ether/ethyl acetate); ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.79 (d, J = 1.2 Hz, 1H), 2.70 (q, J = 9.1 Hz, 1H), 2.12−2.04 (m, 1H), 1.88 (s, 3H), 1.85−1.78 (m, 3H), 1.65−1.59 (m, 2H), 1.34−1.30 (m, 2H), 1.29 (s, 3H), 1.17 (s, 3H), 1.13 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 209.0, 154.1, 126.6, 80.1, 52.2, 51.4, 47.3, 38.9, 36.8, 29.3, 27.4, 26.8, 25.8, 24.4; IR (thin film) ν_{max} 3426, 2979, 2959, 2917, 2867, 1619,

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1454, 1371, 1243, 1198, 1152, 1074, 1020, 977, 947, 880 cm^{-1}; HRMS (ESI) calcd for $C_{14}H_{23}O_2$ $[M + H]^+$ 223.1693, found 223.1693; mp 79−81 °C.

Omphadiol (1). To a solution of DIBAL-H (1.20 M in hexane, 1.67 mL) was added *t*-BuLi (1.60 M in toluene, 1.25 mL) slowly at 0 °C. The clear solution was stirred at 0 °C before it was added to a solution of **20** (111 mg, 0.50 mmol) in THF (5.0 mL) at −78 °C dropwise. The mixture was stirred until the starting material was completely consumed. The reaction was quenched with MeOH (3.00 mL) carefully, and the mixture was diluted with CH_2Cl_2 and a 20% aqueous solution of NaOH. The mixture was stirred at ambient temperature for 30 min. The resulting white precipitate was removed by filtration through a pad of silica gel, and the filtrate was concentrated under reduced pressure to give a colorless oil. The crude product was purified by column chromatography (2:1 petroleum ether/ethyl acetate) to give an intermediate (90.8 mg, 81%) as a white solid. R_f 0.30 (2:1 petroleum ether/ethyl acetate); ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.23 (s, 1H), 4.14 (s, 1H), 2.70−2.60 (m, 1H), 1.93−1.82 (m, 1H), 1.76 (s, 3H), 1.74−1.64 (m, 3H), 1.60−1.44 (m, 3H), 1.33−1.24 (m, 2H), 1.22 (s, 3H), 1.04 (s, 3H), 0.84 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 138.6, 130.2, 80.5, 77.3, 48.5, 45.5, 42.3, 40.8, 35.5, 29.1, 26.2, 24.4, 21.8, 19.2; IR (thin film) ν_{max} 3427, 2958, 2921, 2866, 1732, 1658, 1456, 1302, 1258, 1186, 1132, 1098, 969, 934, 867, 831 cm^{-1}; HRMS (ESI) calcd for $C_{14}H_{24}O_2$ $[M + Na]^+$ 247.1669, found 247.1674; mp 127−129 °C.

To a solution of the above intermediate (49.4 mg, 0.220 mmol) in CH_2Cl_2 (5.5 mL) cooled to −30 °C was added diethylzinc (1.00 M in toluene, 2.00 mL, 2.00 mmol) dropwise. The mixture was stirred for 10 min before CH_2I_2 was added dropwise. The mixture was allowed to warm to 0 °C slowly and stirred at this temperature until the starting material was completely consumed. The reaction was quenched with H_2O (2.00 mL), and the mixture was extracted with ethyl acetate (3 × 10.0 mL). The combined organic layers were washed with 1.00 M aqueous NaOH and brine, dried over anhydrous $MgSO_4$, and filtered. The solvent was removed under reduced pressure. The crude product was purified by column chromatography (2:1 petroleum ether/ethyl acetate) to give omphadiol (**1**) (43.5 mg, 83%) as an amorphous solid. R_f 0.23 (2:1 petroleum ether/ethyl acetate); ^{1}H NMR (400 MHz, $(CD_3)_2CO$) δ 3.40 (d, J = 4.5 Hz, 1H), 3.03 (dd, J = 8.5, 4.4 Hz, 1H), 2.89 (s, 1H), 1.79 (ddd, J = 18.1, 10.5, 5.0 Hz, 1H), 1.66−1.60 (m, 2H), 1.60−1.51 (m, 2H), 1.46 (dd, J = 10.5, 3.6 Hz, 1H), 1.42 (t, J = 3.5 Hz, 1H), 1.30−1.22 (m, 1H), 1.21 (s, 3H), 0.98 (s, 3H), 0.97 (s, 3H), 0.94 (s, 3H), 0.61 (dd, J = 8.1, 3.9 Hz, 1H), 0.56−0.51 (m, 1H), 0.34 (t, J = 4.3 Hz, 1H); ^{13}C NMR (100 MHz, $(CD_3)_2CO$) δ 80.8, 80.4, 50.2, 49.3, 43.4, 42.4, 38.8, 31.3, 29.8, 26.0, 23.9, 23.4, 20.1, 19.9, 19.8; IR (thin film) ν_{max} 3398, 3069, 2958, 2931, 1457, 1381, 1229, 1211, 1188, 1152, 1124, 1078, 1017, 966, 875, 842 cm^{-1}; HRMS (ESI) calcd for $C_{15}H_{26}O_2Na$ $[M + Na]^+$ 261.1830, found 261.1817; mp 125−127 °C.

Epoxide 21. To NaH (360 mg of 60% oil dispersion) that had been washed with hexane to remove the oil was added DMSO (1.5 mL) at 0 °C. The mixture was stirred for 15 min before trimethyloxosulfonium iodide (343 mg, 1.56 mmol) was added. The mixture was stirred for 30 min at room temperature, and then a solution of **7** (71.5 mg, 0.300 mmol) in DMSO (4.50 mL) was added dropwise. The mixture was stirred until the starting material was completely consumed. The reaction was quenched with pH 7 phosphate buffers, and the mixture was extracted with ethyl acetate (3 × 10.0 mL). The combined organic layers were washed with brine, dried over anhydrous $MgSO_4$, and filtered. The solvent was removed under reduced pressure. The crude product was purified by chromatography (8:1 petroleum ether/ethyl acetate) to give **21** (51.3 mg, 68%) as a white solid. R_f 0.33 (8:1 petroleum ether/ethyl acetate); ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.97−3.77 (m, 4H), 2.63 (d, J = 4.8 Hz, 1H), 2.49 (d, J = 4.8 Hz, 1H), 2.16 (dt, J = 11.9, 9.1 Hz, 1H), 1.96 (t, J = 11.1 Hz, 1H), 1.87−1.77 (m, 1H), 1.68 (t, J = 8.1 Hz, 2H), 1.57 (t, J = 10.8 Hz, 1H), 1.33 (dddd, J = 19.4, 17.8, 16.9, 12.4 Hz, 6H), 0.92 (d, J = 3.0 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 118.0, 64.9, 64.2, 59.8, 53.3, 46.9, 44.4, 40.1, 36.4, 34.2, 31.9, 31.5, 31.1, 28.5, 19.9; IR (thin film) ν_{max} 3048, 2952, 2892, 2864, 1728, 1468, 1324, 1285, 1247, 1154, 1114, 1058, 957, 879, 827 cm^{-1}; HRMS (ESI) calcd for $C_{15}H_{24}O_3Na$ $[M + Na]^+$ 275.1623, found 275.1615; mp 66−68 °C.

((8a*R*)-7,7-Dimethyl-3,3a,6,7,8,8a-hexahydro-2*H*-spiro-[azulene-1,2′-[1,3]dioxolan]-4-yl)methanol (22). To a solution of **21** (90.7 mg, 0.360 mmol) in toluene (4.0 mL) was added $(i\text{-PrO})_3Al$ (221 mg, 1.08 mmol) in one portion. The mixture was allowed to warm to reflux and stirred until the starting material was completely consumed. The reaction mixture was cooled to room temperature, and the reaction was quenched with a saturated aqueous solution of potassium sodium tartrate (4.00 mL). The resulting mixture was extracted with ether (3 × 10.0 mL), and the combined organic layers were washed with 1 M aqueous NaOH (3.00 mL) and brine, dried over anhydrous $MgSO_4$, and filtered. The solvent was removed under reduced pressure to give a colorless oil. The crude product was purified by chromatography (2:1 petroleum ether/ethyl acetate) to give **22** (84.5 mg, 93%) as a colorless oil. R_f 0.33 (2:1 petroleum ether/ethyl acetate); ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.60 (t, J = 6.4 Hz, 1H), 4.04 (d, J = 6.0 Hz, 2H), 3.90−3.83 (m, 2H), 3.76 (ddd, J = 14.3, 6.2, 2.8 Hz, 2H), 2.55 (dd, J = 18.5, 9.4 Hz, 1H), 2.08 (dd, J = 14.3, 5.1 Hz, 1H), 1.87−1.69 (m, 5H), 1.66−1.59 (m, 1H), 1.54−1.36 (m, 2H), 1.21 (ddd, J = 20.2, 15.2, 11.3 Hz, 1H), 0.91 (s, 3H), 0.80 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 143.4, 126.3, 117.6, 65.7, 64.6, 64.0, 46.5, 44.5, 43.8, 40.3, 36.2, 33.9, 30.6, 24.8, 24.2; IR (thin film) ν_{max} 3427, 2950, 2922, 2869, 1731, 1659, 1469, 1363, 1306, 1265, 1149, 1093, 948, 895 cm^{-1}; HRMS (ESI) calcd for $C_{15}H_{24}O_3Na$ $[M + Na]^+$ 275.1623, found 275.1620.

(8a*S*)-4-(Hydroxymethyl)-7,7-dimethyl-3,3a,6,7,8,8a-hexahydroazulen-1(2*H*)-one (4). To a solution of **22** (101 mg, 0.400 mmol) in THF (4.00 mL) was added 1.00 M aqueous HCl (0.20 mL) dropwise. The mixture was stirred until the starting material was completely consumed. The mixture was treated with water (4.00 mL) and extracted with ethyl acetate (3 × 10.0 mL). The combined organic layers were washed with water and brine, dried over anhydrous $MgSO_4$, and filtered. The solvent was removed under reduced pressure to give a yellow oil. The crude product was purified by column chromatography (2:1 petroleum ether/ethyl acetate) to give **4** (63.8 mg, 77%) as a colorless oil. R_f 0.24 (2:1 petroleum ether/ethyl acetate); ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.74 (dd, J = 6.3, 5.6 Hz, 1H), 4.16 (q, J = 12.4 Hz, 2H), 2.74 (td, J = 11.8, 6.3 Hz, 1H), 2.46−2.33 (m, 1H), 2.33−2.21 (m, 1H), 2.16−2.11 (m, 1H), 2.11−2.07 (m, 4H), 2.06−2.03 (m, 1H), 2.02−1.98 (m, 1H), 1.98−1.89 (m, 2H), 1.86 (dd, J = 12.0, 1.7 Hz, 1H), 1.22 (t, J = 13.0 Hz, 1H), 0.96 (s, 3H), 0.84 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 220.8, 142.3, 128.3, 65.8, 49.3, 45.0, 44.4, 40.5, 38.0, 33.4, 30.5, 24.2, 23.2; IR (thin film) ν_{max} 3434, 2952, 2922, 2869, 1735, 1633, 1456, 1385, 1326, 1245, 1209, 1056, 998, 898, 851, 827 cm^{-1}; HRMS (ESI) calcd for $C_{13}H_{20}O_2NH_4$ $[M + NH_4]^+$ 226.1802, found 226.1802.

(1*R*,8a*S*)-4-(Hydroxymethyl)-1,7,7-trimethyl-1,2,3,3a,6,7,8,8a-octahydroazulen-1-ol (23). To a solution of **4** (33.3 mg, 0.160 mmol) in THF (1.00 mL) was added MeLi (1.00 M in diethyl ether, 0.640 mL, 0.640 mmol) dropwise at −78 °C. The mixture was stirred at −78 °C until the starting material was completely consumed. The reaction was quenched a saturated aqueous solution of NH_4Cl (2.00 mL) carefully, and the mixture was extracted with ethyl acetate (3 × 10.0 mL). The combined organic layers were washed with water and brine, dried over anhydrous $MgSO_4$, and filtered. The solvent was removed under reduced pressure to give a yellow oil. The crude product was purified by column chromatography (2:1 petroleum ether/ethyl acetate) to give the major diastereomer **23** (21.1 mg, 59%) as a white solid and a minor diastereomer (5.40 mg, 15%) as a colorless oil.

Data for the major diastereomer **23**: R_f 0.20 (2:1 petroleum ether/ethyl acetate); ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.64 (t, J = 6.5 Hz, 1H), 4.12 (s, 2H), 2.87 (q, J = 8.7 Hz, 1H), 2.16 (dd, J = 14.3, 5.3 Hz, 1H), 1.96−1.86 (m, 3H), 1.79−1.72 (m, 2H), 1.58 (dd, J = 10.5, 1.9 Hz, 1H), 1.49−1.35 (m, 2H), 1.23 (s, 3H), 0.99 (s, 3H), 0.87 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 144.7, 126.3, 80.6, 66.8, 49.5, 44.4, 43.7, 40.9, 40.3, 34.0, 30.9, 26.4, 25.2, 24.0; IR (thin film) ν_{max} 3304, 2952, 2923, 2869, 1730, 1652, 1461, 1366, 1210, 1139, 1074, 1006, 918, 887,

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860, 804 cm^{-1}; HRMS (ESI) calcd for $C_{14}H_{24}O_2Na$ $[M + Na]^+$ 247.1669, found 247.1671; mp 116−118 °C.

Data for the minor diastereomer: R_f 0.16 (2:1 petroleum ether/ethyl acetate); ^1H NMR (400 MHz, $CDCl_3$) δ 5.64 (t, J = 5.4 Hz, 1H), 4.15 (s, 2H), 2.55 (q, J = 8.5 Hz, 1H), 2.13 (dd, J = 14.3, 5.3 Hz, 1H), 2.01−1.86 (m, 2H), 1.81−1.70 (m, 3H), 1.69−1.61 (m, 2H), 1.23 (t, J = 2.3 Hz, 1H), 1.15 (s, 3H), 0.98 (s, 3H), 0.88 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 144.6, 126.4, 80.2, 66.4, 50.4, 45.7, 45.0, 41.7, 40.4, 34.1, 31.1, 24.9, 23.7, 23.3; IR (thin film) ν_{max} 3370, 2949, 2924, 2866, 1720, 1630, 1460, 1363, 1262, 1114, 1090, 1057, 1001, 952, 863, 825, 800.

Pyxidatol C (2). To a solution of **23** (20.2 mg, 0.090 mmol) in CH_2Cl_2 (2.00 mL) cooled to −30 °C was added diethylzinc (1.00 M in toluene, 0.800 mL, 0.800 mmol) dropwise. The mixture was stirred for 10 min before CH_2I_2 was added dropwise. The reaction mixture was allowed to warm to 0 °C slowly and stirred at this temperature until the starting material was completely consumed. The reaction was quenched with H_2O (2.00 mL), and the mixture was extracted with ethyl acetate (3 × 10.0 mL). The combined organic layers were washed with a 1.00 M aqueous solution of NaOH and brine, dried over anhydrous $MgSO_4$, and filtered. The solvent was removed under reduced pressure. The crude product was purified by column chromatography (2:1 petroleum ether/ethyl acetate) to give pyxidatol C (**2**) (14.6 mg, 68%) as a colorless oil. R_f 0.27 (2:1 petroleum ether/ethyl acetate); ^1H NMR (400 MHz, $(CD_3)_2CO$) δ 3.59 (dd, J = 11.1, 4.6 Hz, 1H), 3.48 (dd, J = 11.1, 5.6 Hz, 1H), 3.42 (t, J = 5.0 Hz, 1H), 2.79 (s, 1H), 2.00−1.92 (m, 2H), 1.85−1.81 (m, 1H), 1.81−1.78 (m, 1H), 1.73−1.69 (m, 1H), 1.69−1.64 (m, 1H), 1.63−1.61 (m, 1H) 1.45−1.41 (m, 1H), 1.19 (s, 3H), 1.22−1.15 (m, 1H), 1.10 (dd, J = 10.1, 4.3 Hz, 1H), 1.04 (s, 3H), 0.89 (s, 3H), 0.79−0.72 (m, 1H), 0.69 (dd, J = 8.5, 3.7 Hz, 1H), 0.14 (t, J = 4.1 Hz, 1H); ^{13}C NMR (100 MHz, $(CD_3)_2CO$) δ 80.3, 66.9, 50.0, 49.2, 44.7, 44.1, 42.5, 34.8, 33.7, 27.7, 26.4, 24.6, 24.0, 20.7, 19.8; IR (thin film) ν_{max} 3339, 3055, 2951, 2925, 2869, 1727, 1676, 1457, 1363, 1271, 1176, 1075, 925, 876, 824, 803; HRMS (ESI) calcd for $C_{15}H_{26}O_2Na$ $[M + Na]^+$ 261.1830, found 261.1824.

■ ASSOCIATED CONTENT

Supporting Information

Tables comparing the NMR spectroscopic data for our synthetic samples with the previously reported data, copies of ^1H and ^{13}C NMR spectra for new compounds, and crystallographic data (CIF) for compound **9**. This material is available free of charge via the Internet at http://pubs.acs.org.

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Notes

The authors declare no competing financial interest.

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