# Studies Directed toward the Synthesis of the Unusual Antileukemic Diterpene Jatrophatrione. 2. Functionalization of Advanced Polycyclic Precursors to the 9-Epi and 8,9-Dehydro Congeners

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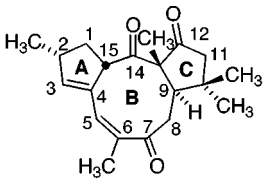
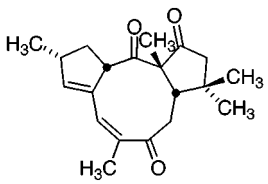
The synthesis of highly functionalized [5.9.5]tricyclic systems closely related to jatrophatrione (**1**) and 9-epijatrophatrione (**2**) is described. The first set of experiments provides a route to the conjugated 7-methylene ketones **8** and **9**, both of which resist migration of the exocyclic double bond to a position internal to the ring. Subsequent dihydroxylation studies define a convenient pathway from **3** to triketone **20**, which has yet to exhibit a tendency to undergo appropriate dehydration at the tertiary carbinol center. The presence of a carbonyl group in ring C was shown not to be contributory to this low reactivity. Finally, a protocol involving formation of a bromo oxetane with subsequent introduction of a C8−C9 double bond and Grob fragmentation has shown promise for arrival at **1** and/or **2** by making available the diene **36**.

In the preceding paper,[1] we outlined a retrosynthetic approach to jatrophatrione (**1**) that was founded on the possible isomerization of its C9 epimer **2** via a *β*-elimination-intramolecular Michael addition sequence. Also




**1**




**2**

described was a means for the stereocontrolled construction of advanced racemic intermediates that dealt quite satisfactorily with proper assembly of the remote stereocenters in these molecules. In this paper, we detail more advanced functionalization pathways for these compounds, define limitations associated with select types of transformations involving these complex tricyclic systems, and refine our focus as to suitable options potentially available for completing the total synthesis.

## Results and Discussion

**Is Exocyclic to Endocyclic Olefin Isomerization Feasible?** We chose preliminarily to examine initial reduction of the C14 carbonyl group in **3**[1] in order to explore regioselective functionalization tactics at the C7−C8 olefinic center. As expected on the basis of the notably concave nature of **3**, its exposure to lithium aluminum hydride in ether was met with nucleophilic attack from the convex surface to deliver **4** exclusively (Scheme 1). After protection of the alcohol functionality as a *p*-methoxybenzyl ether, **5** was treated with 1 equiv of *m*-chloroperbenzoic acid. As in the previous instance, epoxidation also proceeded stereospecifically. The stereochemical assignment to **6** parallels that made to a diol generated subsequently in which dihydroxylation from the α face was corroborated by crystallographic methods. When **6** was treated with diethylaluminum dicyclohexylamide at room temperature, isomerization to allylic alcohol **7** proceeded smoothly with proton abstraction occurring exclusively at the methyl substituent[2] to give **7**. Once oxidation of **7** with the Dess−Martin periodinane[3] had been completed, the option to remove the PMB protecting group from **8** was exercised to provide **9**.

With **8** and **9** in hand, the critical double bond isomerization to an endocyclic position as in **10** was attempted. Extensive experimentation with palladium on carbon[4] and with rhodium trichloride[5] showed these reagents to be totally ineffective in bringing about the desired positional shift of the unsaturated linkage. The application of forcing conditions to **8** resulted only in conversion to **9**. Heating either substrate for extended time periods eventuated in degradation.

To determine whether this potentially useful step might be implemented if the tricyclic substrate adopted a different conformation, the isomeric epoxide **11** was prepared (Scheme 2). The combination of iodine and silver(I) oxide in aqueous dioxane[6] proved well suited to this purpose. Not surprisingly, **11** proved recalcitrant to the action of diethylaluminum dicyclohexylamide, presumably because the methyl group is not now accessible

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(1) Paquette, L. A.; Nakatani, S.; Zydowsky, T. M.; Edmondson, S. D.; Sun, L.-Q.; Skerlj, R. *J. Org. Chem.* **1999**, *64*, 3244.

(2) Crandall, J. K.; Apparu, M. *Org. React.* **1983**, *29*, 345.

(3) (a) Dess, D. B.; Martin, J. C. *J. Org. Chem.* **1983**, *48*, 4155. (b) Dess, D. B.; Martin, J. C. *J. Am. Chem. Soc.* **1991**, *113*, 7277.

(4) Burn, D.; Kirk, D. N.; Petrow, V. *Tetrahedron* **1965**, *21*, 1619.

(5) (a) Andrieux, J.; Barton, D. H. R.; Patin, H. *J. Chem. Soc., Perkin Trans. 1* **1977**, 359. (b) Grieco, P. A.; Nishizawa, M.; Marinovic, N.; Ehmann, W. J. *J. Am. Chem. Soc.* **1976**, *98*, 7102. (c) Genet, J. P.; Ficini, J. *Tetrahedron Lett.* **1979**, 1499.

(6) (a) Parrilli, M.; Barone, G.; Adinolfi, M.; Mangoni, L. *Tetrahedron Lett.* **1976**, 207. (b) Polniaszek, R. P.; Stevens, R. V. *J. Org. Chem.* **1986**, *51*, 3023. (c) Paquette, L. A.; Wang, T.-Z.; Philippo, C. M. G.; Wang, S. *J. Am. Chem. Soc.* **1994**, *116*, 3367.

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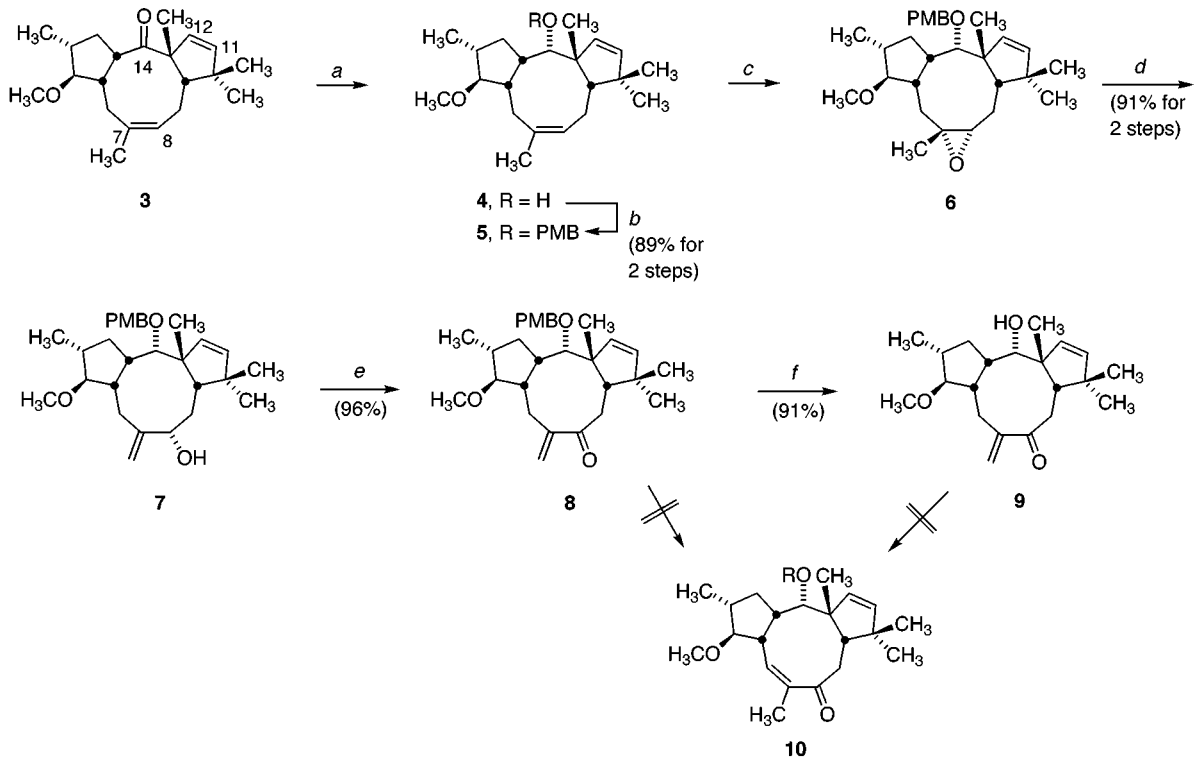
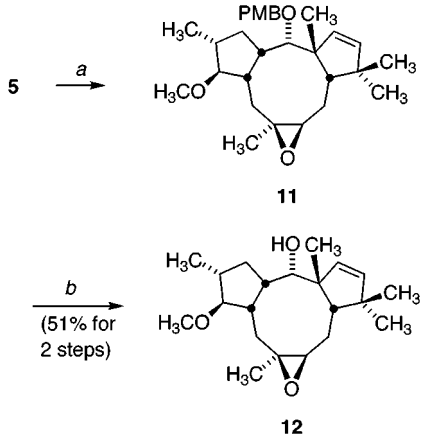
**Scheme 1**[a]



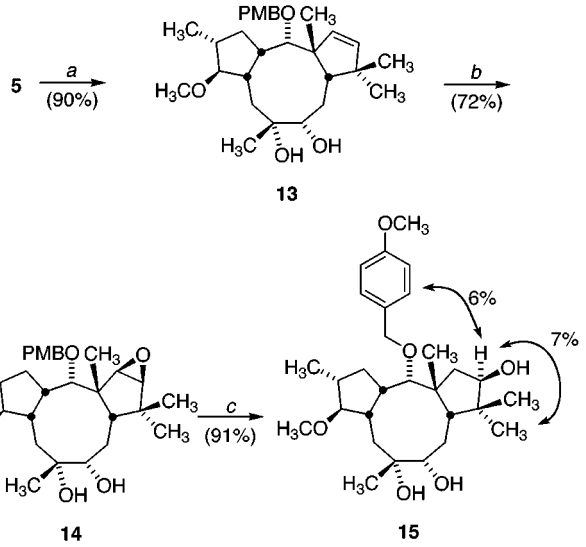

[a] Key: (a) $LiAlH_4$, ether, rt; (b) KH, PMBCl, $Bu_4Nl$, THF, rt; (c) MCPBA, $NaHCO_3$, $CH_2Cl_2$, rt; (d) $Et_2AlN(Cy)_2$ (4 equiv), $C_6H_6$, rt; (e) Dess−Martin periodinane, $CH_2Cl_2$; (f) $RhCl_3 \cdot 3H_2O$, $C_2H_5OH$, Δ, 7 h.

**Scheme 2**[a]




[a] Key: (a) $I_2$, $Ag_2O$, dioxane, $H_2O$; (b) $Et_2AlN(Cy)_2$, $C_6H_6$, Δ.

**Scheme 3**[a]




[a] Key: (a) $OsO_4$, py, −30 °C; $NaHSO_3$; (b) $CH_3CO_3H$, $Na_2HPO_4$, $NaH_2PO_4$, $CH_2Cl_2$, rt; (c) Dibal-H, toluene, −78 °C.

to attack by the base. Steric inhibition continued to be evident as the investigation was expanded to include less bulky amide ion reagents. When recourse was made to refluxing benzene as the reaction medium, removal of the PMB occurred with the formation of **12**.

As a consequence of these findings, it was quite apparent that an alternative approach had to be devised for installing the C7−C8 unsaturation.

**Addressing the Issue of Ring C Oxygenation.** In an effort to maximize efficiency, the decision was made to probe the preceding question concurrently with added functionalization within ring C. It was deemed unlikely from the outset that the appreciably hindered C11−C12 double bond located in the five-membered ring would prove more reactive than its counterpart in ring B. This kinetic bias, which has previously been exploited during the preparation of **6**, was likewise operative during the dihydroxylation of **5** with osmium tetraoxide. The single vicinal diol **13** was formed in 90% yield (Scheme 3). As a consequence of the crystallinity of **13**, its stereochemistry could be unequivocally ascertained by X-ray crystallographic analysis (Figure 1). The conformation adopted by the central ring of **13** in the solid state holds interest. Attention is called specifically to the exposed nature of the methyl group bonded to C6 (C10 in Figure 1), to the pseudoaxial projection of the *p*-methoxybenzyloxy substituent, and to the overall topology of the nine-membered core.

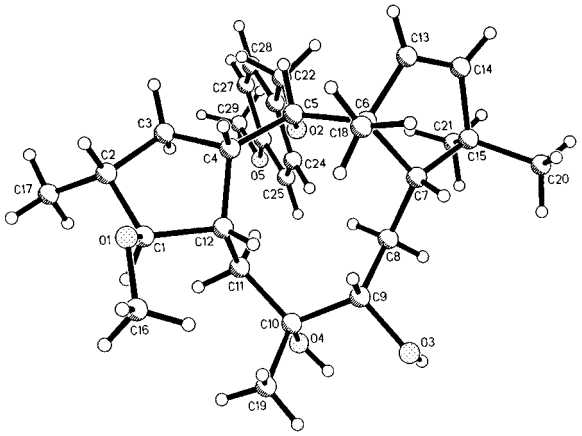



**Figure 1.** Computer-generated perspective drawing of **13** as determined by X-ray crystallography.

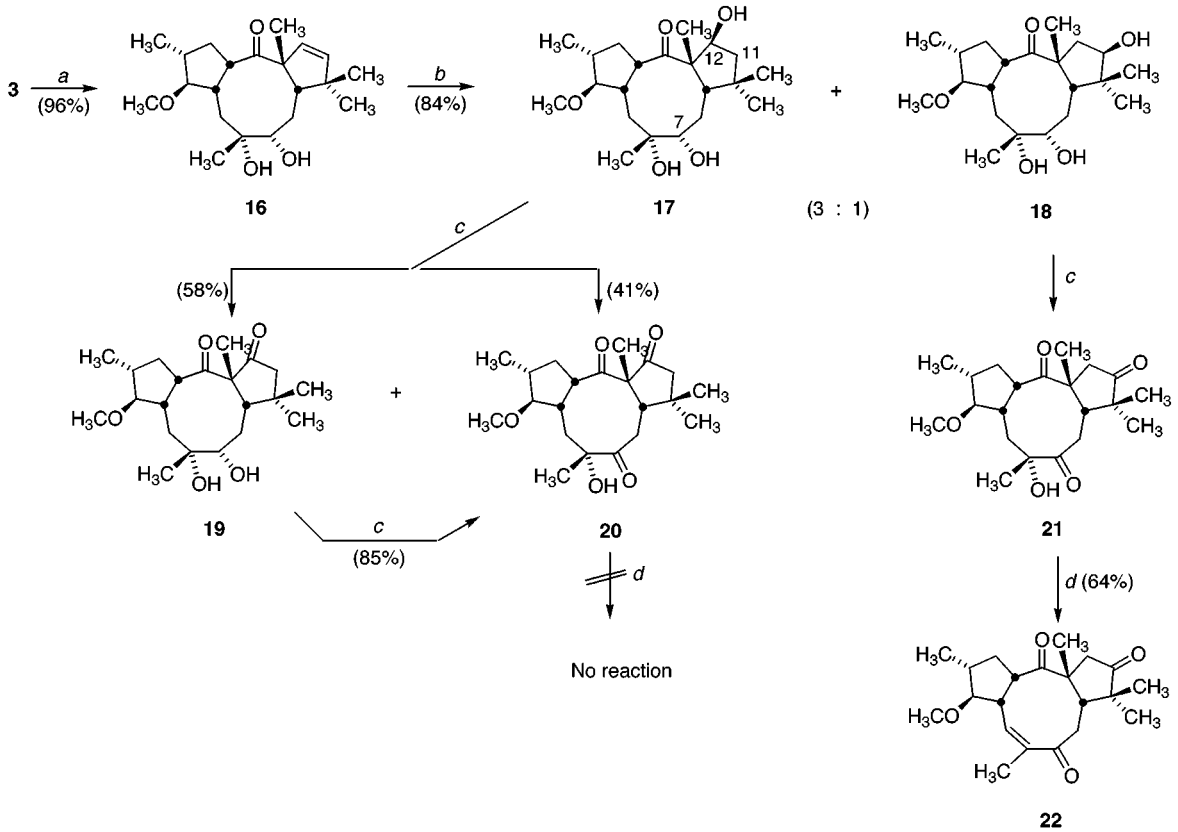
With a lone unsaturated center remaining in **13**, the next step was to examine its epoxidation and reductive cleavage of the resulting oxirane ring. Initial studies, conducted with *m*-chloroperbenzoic acid revealed the occurrence of a very slow reaction with concomitant removal of the PMB protecting group. Recourse to the less bulky peracetic acid reagent solved this problem, and epoxide **14** was now formed in good yield. While treatment of **14** with Dibal-H in THF for 12 h at the reflux temperature produced no chemical change, immediate ring opening occurred at −78 °C with Dibal-H in toluene. The process was entirely regioselective, giving rise to **15** in 91% isolated yield. The structure and stereochemistry of this carbinol was defined by means of C−H CORR and long-range H−C correlation experiments, coupled with relevant NOE enhancements (see Scheme 3).

Since this sequence resulted in the preferential oxygenation of C11 rather than C12, attempts were made to introduce an oxygen nucleophile properly on the α-face of **13** by means of oxymercuration or halohydrin protocols. However, these proved to be unsuccessful due either to steric inhibition or to the sensitivity of the PMB group. For these reasons, the decision was made to explore the osmylation step at an earlier stage of the synthesis.

In actuality, dienone **3** proved to be very reactive toward osmium tetraoxide at −78 °C and was transformed cleanly into diol **16** (96%) under these conditions (Scheme 4). Hydroboration−oxidation of **16** proceeded well to deliver a mixture of alcohols in a 3:1 ratio. Although these alcohols proved to be very difficult to separate completely, it was possible to enrich the major alcohol to greater than 90% purity by repeated chromatography. Through the application of 2D NMR methods, it proved possible to assign all of the carbon and proton signals. Ultimately, clear-cut evidence for structure **17** was provided by enhancement of the C11 methylene carbon peak upon irradiation of the *gem*-dimethyl protons. A particularly striking facet of the $^1$H NMR spectrum of **17** is the appreciable downfield shift of H-12 in **17** relative to that of H-11 in **18**. This is considered to be a reflection of the fact the carbinol proton in **17**, which is observed at 4.90 ppm, resides in the deshielding cone of the nearby carbonyl. This is not possible for the corresponding proton in **18**, which appears at 3.80 ppm.

With the proper oxygenation pattern realized as in **17**, conditions conducive to the oxidation of this intermediate

**Scheme 4**[a]




[a] Key: (a) $OsO_4$, py, THF, −78 °C; $NaHSO_3$; (b) $BH_3$·THF, THF, −70 °C; NaOH, $H_2O_2$, $H_2O$; (c) Dess−Martin periodinane, py, $CH_2Cl_2$; (d) AgOTf, $C_6H_6$, Δ.

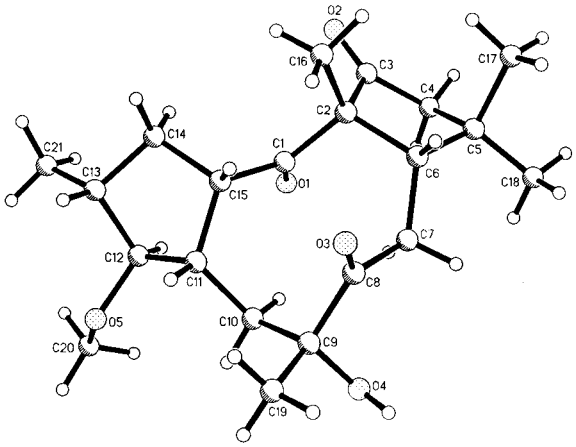


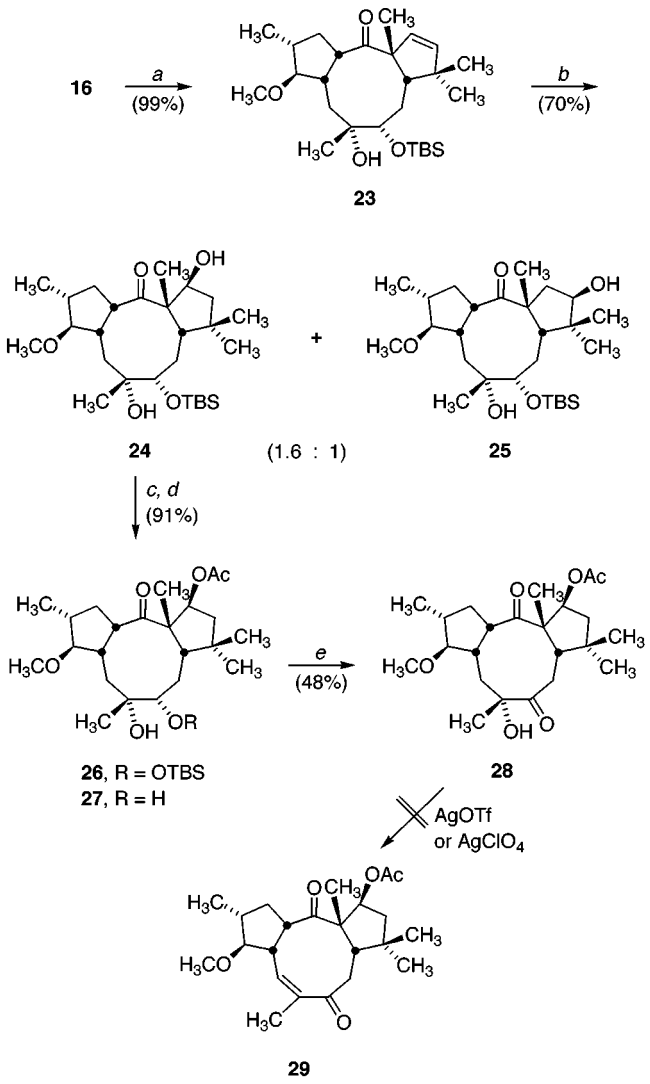

**Figure 2.** Computer-generated perspective drawing of **20** as determined by X-ray crystallography.

were sought. Protocols that rely on activated sulfur reagents such as Swern[7] and Corey−Kim methods[8] failed to accomplish reactions at C7 and led only to high yields of diketone **19** (and **21**). Chromium reagents were avoided because of anticipated cleavage of the glycol to the corresponding keto aldehyde. Indeed, utilization of the Dess−Martin periodinane[3,9] in dichloromethane solution triggered this undesirable transformation in moderate yield. However, the co-addition of pyridine to the latter reaction mixtures abated matters sufficiently[10] to permit isolation of dione **19** and trione **20**. Reexposure of **19** to the Dess−Martin reagent resulted in ready transformation into **20**. Single-crystal X-ray analysis of **20** confirmed the regioselectivity of the hydroboration step as well as the stereoselectivity of the osmylation of **3** (Figure 2).

The challenge remaining to arrive at 9-epijatrophatrione (**2**) resided in proper elimination of the elements of water from the tertiary alcohol and of methanol from the methyl ether.[11] While **20** was found to be remarkably recalcitrant to dehydration under a variety of conditions, its isomer **21** (admixed with **20**) was transformed readily under the influence of silver triflate or silver perchlorate[12] into enone **22**. In the final analysis, **20** came to be regarded as an intermediate unsuited to completion of the synthesis. For a variety of reasons, the wisdom of installing the $\beta$-dicarbonyl array was brought into question. Relegation of this step to the final stages of the synthesis would certainly skirt sensitivity arising from the potential for $\beta$-elimination. To explore this option, we have need to differentiate the two secondary hydroxyls in **17**.

**Alternative Elaboration of Highly Oxygenated Intermediates.** To determine if the above assumption

**Scheme 5**[a]



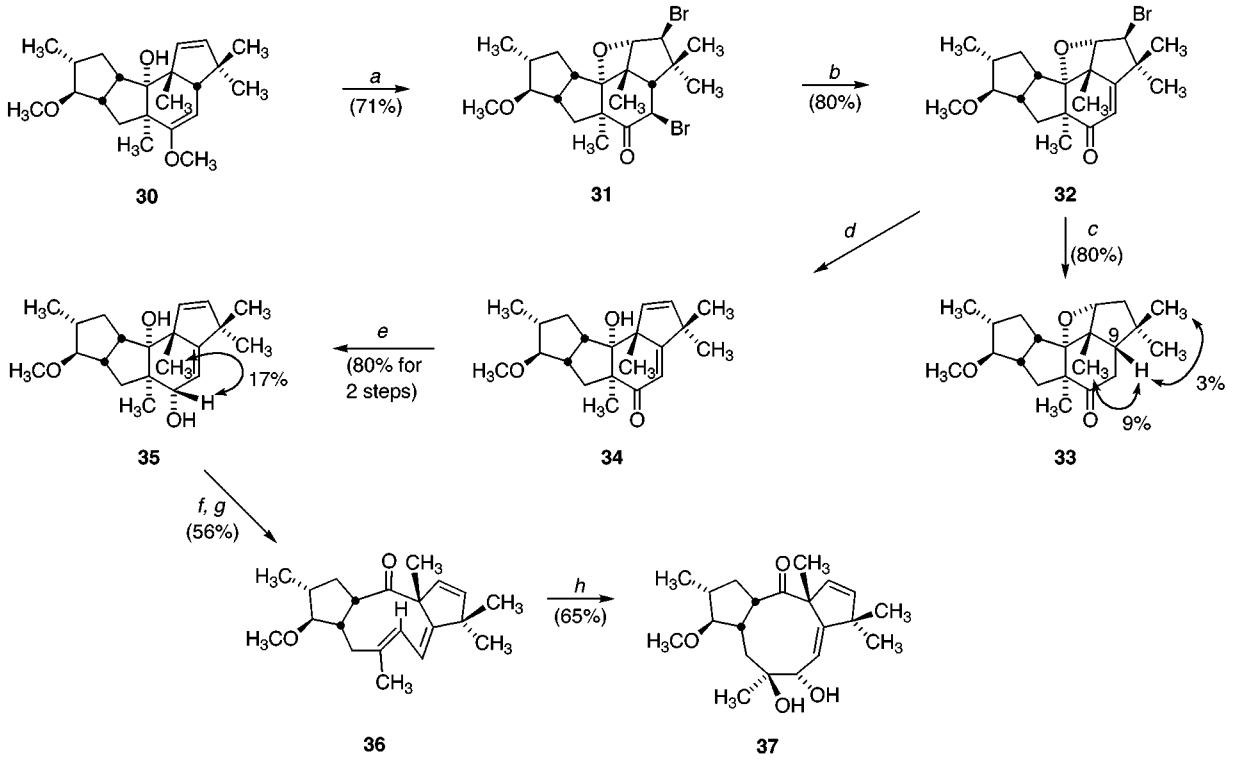

[a] Key: (a) TBSCl, imid, DMF; (b) $BH_3$·THF, THF, −70 °C; NaOH, $H_2O_2$, $H_2O$; (c) $Ac_2O$, $Et_3N$, DMAP, $CH_2Cl_2$; (d) TBAF, THF; (c) TPAP, NMO, 4 Å MS, $CH_2Cl_2$.

was correct, **16** was transformed into the *tert*-butyldimethylsilyl ether **23** in advance of hydroboration (Scheme 5). While the regioselectivity of this addition decreased from the 3:1 level observed for **17/18** to 1.6:1 in favor of the desired isomer, the two products were easily separated by flash chromatography. The structural assignments could be made with confidence by the comparative analysis of $^1$H NMR spectra. Once again, the striking downfield shift of H12 in **24** relative to H11 in **25** was considered to be particularly diagnostic.

The submission of **24** to sequential acetylation and desilylation gave rise efficiently to **27**, thereby setting the stage for oxidation to **28**. This process proved to be more troublesome than that involving **19**. The conditions developed earlier, which consisted of controlled application of the periodinane reagent, provided inappropriately small amounts of diketone **28**. Alternative recourse to Ley's perruthenate[13] led to useful improvements, although the isolation of **28** continued to prove troublesome and a maximum yield of 48% was realized. However,

(7) Review: Tidwell, T. T. *Org. React.* **1990**, *39*, 297.
(8) Corey, E. J.; Kim, C. U. *Tetrahedron Lett.* **1974**, 287.
(9) (a) Ireland, R. E.; Liu, L. *J. Org. Chem.* **1993**, *58*, 2899. (b) Meyer, S. D.; Schreiber, S. L. *J. Org. Chem.* **1994**, *59*, 7549.
(10) For previous examples of the use of pyridine as a moderator of the Dess−Martin oxidation, consult: (a) Chen, S.-H.; Horvath, R. F.; Joglar, J.; Fisher, M. J.; Danishefsky, S. J. *J. Org. Chem.* **1991**, *56*, 5834. (b) Vloon, W. J.; van den Bos, J. C.; Koomen, G.-J.; Pandit, U. K. *Tetrahedron* **1992**, *48*, 8317.
(11) For relevant examples of the $\beta$-elimination of alcohols to generate cyclic dienones, see: (a) Baettig, K.; Dallaire, C.; Pitteloud, R.; Deslongchamps, P. *Tetrahedron Lett.* **1987**, *28*, 5249. (b) Marinier, A.; Baettig, K.; Dallaire, C.; Pitteloud, R.; Deslongchamps, P. *Can. J. Chem.* **1989**, *67*, 1609. (c) Liu, H.-J.; Dieck-Abularach, T. *Heterocycles* **1987**, *25*, 245.
(12) For a lead reference, see: Mukaiyama, T.; Kuwahara, M.; Izawa, T.; Ueki, M. *Chem. Lett.* **1972**, 287.
(13) Ley, S. V.; Norman, J.; Griffith, W. P.; Marsden, S. P. *Synthesis* **1994**, 639.

**Scheme 6**[a]




[a] Key: (a) NBS, THF, $H_2O$; (b) LiBr, $Li_2CO_3$, DMF, Δ; (c) $H_2$, 10% Pd/C, $CH_3OH$, $Et_3N$; (d) Zn, $CH_3OH$, Δ; (c) Dibal-H, THF, −78 °C; (f) $CH_3SO_2Cl$, $Et_3N$, $CH_2Cl_2$; (g) KO*t*-Bu, *t*-BuOH, 40 °C; (h) $OsO_4$, py, THF, −78 °C.

since other methods failed to give this diketone, the use of TPAP was considered acceptable for its production.

Despite the availability of **28** via this route, we have again been unable to effect its dehydration to **29**. Seemingly, the functionality resident in **28** was dismantled upon heating with silver triflate or silver perchlorate. The degradation induced by thionyl chloride in pyridine was somewhat less, but $^1$H NMR analysis revealed only trace levels of exocyclic olefin to be formed. Thus, this approach likewise offered no obvious promise for ultimate introduction of the conjugated diene unit intrinsic to **1** and **2**.

**Construction of 8,9-Dehydro Precursors.** The demise of the intermediates described above prompted the consideration of unsaturated precursors to **1** and/or **2**, particularly across C8/C9, such that the stereochemistry at C9 could be controlled in the final step. To this end, **30**[1] was treated with *N*-bromosuccinimide in aqueous THF (Scheme 6). The expectation that bromo oxetane formation would take place concurrently with brominative substitution of the enol ether as in **31** was initially supported by NMR spectroscopy and ultimately corroborated by X-ray crystallographic methods (Figure 3). Exposure of **31** to lithium bromide and lithium carbonate in hot DMF[14] effected elimination of 1 equiv of HBr, affording conjugated ketone **32** in 80% yield. It will be recognized that one consequence of this step is the planarization of C9 without disruption of stereogenicity at the remaining nine chiral centers.

Catalytic hydrogenation of **32** resulted in saturation of the double bond and reductive debromination α to the carbonyl to furnish **33**. Unambiguous assignment to the $^1$H and $^{13}$C chemical shifts exhibited by **31** was made

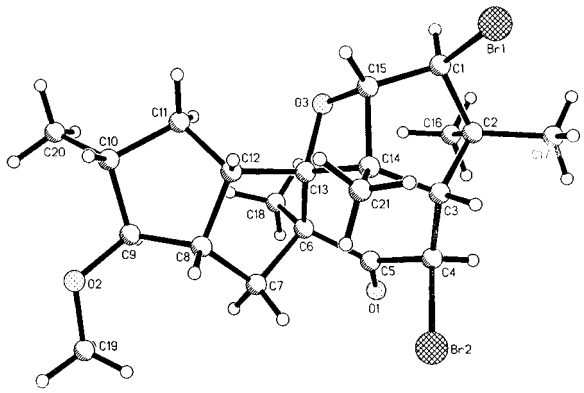



**Figure 3.** Computer-generated perspective drawing of **31** as determined by X-ray crystallography.

possible by $^1$H$^1$H COSY 90 and long-range H−C correlation experiments. The stereochemistry at C9 was subsequently deduced from the NOE enhancements shown. The installation of a β hydrogen by means of this chemistry likely stems from a combination of kinetic and thermodynamic factors. The C9 epimer represents a highly strained compound, due in large part to the presence of the oxetane ring. If this heterocyclic ring were opened, greater conformational flexibility would be gained and the chances of obtaining the α-C9 isomer improved.

The preceding analysis prompted the treatment of **32** with zinc in refluxing methanol, conditions that gave rise quantitatively to **34**. Disappointingly, this dienone proved resistant to the conjugate addition of hydride ion.[15] To side- step this lack of reactivity, we proceeded to generate

(14) For lead references, see: Wang, X.; Paquette, L. A. *Tetrahedron Lett.* **1993**, *34*, 4579.

(15) For example: Tsuda, T.; Hayashi, T.; Satomi, H.; Kawamoto, T.; Saegusa, T. *J. Org. Chem.* **1986**, *51*, 537.

the [5.9.5] tricyclic system in advance of further chemical change at this site.

Reduction of **34** with Dibal-H in THF at low temperature proceeded with 10:1 stereoselectivity for attack from the $\beta$-face to deliver predominantly **35** (note NOE). Regiocontrolled mesylation of this diol and ensuing Grob fragmentation proceeded without event to give trienone **36**. If the allylic mesylate is not subject to inversion of configuration, for example, by $S_N2$ displacement involving chloride ion, the newly formed double bond will possess *E* geometry as shown in **36**. Nucleophilic attack on allylic sulfonate esters by adventitious chloride ion is documented, and the present reaction did give varied results depending on reaction time and the proportion of methanesulfonyl chloride involved. In any case, the heavily predominating triene isomer underwent osmylation to give **37** in good yield. No effort was made to define in an unambiguous way the stereochemistry of this product.

## Overview

The tricyclic dienone **3** is shown to be amenable to stereocontrolled hydride reduction and subsequent regiospecific α-epoxidation in ring B. These conveniently executed transfomations allow for clean, positionally specific oxirane ring opening and ultimate arrival at **8** and **9**. Since it is crucial that the exocyclic double bond in these intermediates be internalized and it has not proven possible to implement this migration, the development of an alternative route was mandated. Some of the other key lessons learned include (i) a readiness on the part of **3** and **5** to undergo dihydroxylation from the identical $\pi$-surface approached during epoxidation; (ii) an ability to oxygenate the C-ring predominantly at C12 by hydroboration of an intermediate such as **16**; (iii) triketones typified by **20** exhibit a reactivity strikingly dissimilar from that of their isomers such as **21**; and (iv) application of a Grob fragmentation sequence after introduction of $\Delta^{8,9}$-unsaturation for the purpose of elaborating triene **36** and then the keto diol **37** proceeds advantageously without evidence of framework rearrangement.

The discovery that **36** can be chemoselectively dihydroxylated generates some degree of assurance that ongoing studies along these lines will ultimately culminate in the acquisition of jatrophatrione and bioactive analogues thereof. Clearly, however, other approaches are equally possible.

## Experimental Section

**General Methods.** Melting points are uncorrected. The column chromatographic separations were performed with Woelm silica gel (230−400 mesh). Solvents were reagent grade and in most cases dried prior to use. The purity of all compounds was shown to be >95% by TLC and high-field $^1$H and $^{13}$C NMR. The high-resolution and fast-atom-bombardment spectra were recorded at The Ohio State University Campus Chemical Instrumentation Center. Elemental analyses were performed at the Scandinavian Microanalytical Laboratory, Herlev, Denmark, or at Atlantic Microlab, Inc., Norcross, GA.

**(2*S**,3*R**,3a*R**,5*Z*,7a*R**,10a*S**,11*R**,11a*R**)-1,2,3,3a,4,7,-7a,8,10a,11a-Decahydro-11-hydroxy-3-methoxy-2,5,8,8,-10a-pentamethyl-11*H*-dicyclopenta[*a*,*d*]cyclononene (4).** A solution of **3**[1] (390 mg, 1.23 mmol) in 25 mL of ether at 0 °C was treated with lithium aluminum hydride (140 mg, 3.7 mmol) and the resulting slurry was stirred at room temperature for 20 min, quenched with 0.14 mL of $H_2O$, 0.14 mL of 15% NaOH solution, and 0.42 mL of $H_2O$, stirred with 500 mg of $Na_2SO_4$, and filtered through Celite. The filter cake was washed with ether, and the combined filtrates were concentrated. The residual white crystalline solid **4** (390 mg, 99%) was spectroscopically pure and used without further purification: mp 84−86 °C; IR (neat, cm$^{-1}$) 3443, 1461; $^1$H NMR (300 MHz, $C_6D_6$) $\delta$ 5.37 (d, $J$ = 5.6 Hz, 1 H), 5.28 (dd, $J$ = 11.0, 4.7 Hz, 1 H), 4.86 (d, $J$ = 5.6 Hz, 1 H), 3.46 (dd, $J$ = 9.6, 6.3 Hz, 1 H), 3.37 (s, 3 H), 3.37−3.30 (m, 1 H), 3.32 (d, $J$ = 11.1 Hz, 1 H), 3.14 (s, 1 H), 2.29−1.97 (series of m, 5 H), 1.84 (d, $J$ = 13.1 Hz, 1 H), 1.75 (s, 3 H), 1.70 (dd, $J$ = 13.7, 3.8 Hz, 1 H), 1.37−1.29 (m, 2 H), 1.23 (d, $J$ = 6.7 Hz, 3 H), 1.03 (s, 3 H), 0.95 (s, 3 H), 0.94 (s, 3 H); $^{13}$C NMR (75 MHz, $C_6D_6$) $\delta$ 140.2, 139.9, 136.3, 125.7, 93.5, 86.2, 58.7, 58.2, 57.0, 48.6, 48.3, 44.0, 38.7, 37.6, 31.2, 30.5, 29.1, 26.0, 24.6, 22.8, 21.0; HRMS *m*/*z* ($M^+$) calcd 318.2559, obsd 318.2576.

Anal. Calcd for $C_{21}H_{34}O_2$: C, 79.18; H, 10.76. Found: C, 79.30; H, 10.45.

**(2*R**,3*S**,3a*S**,5*Z**,7a*S**,10a*R**,11*S**11a*S**)-1,2,3,3a,4,7,-7a,8,10a,11a-Decahydro-11-[(*p*-methoxybenzyl)oxy]-3-methoxy-2,5,8,8,10a-pentamethyl-1*H*-dicyclopenta[*a*,*d*]-cyclononene (5).** To a dry 100 mL round-bottomed flask were added potassium hydride (120 mg, 2.99 mmol) and 10 mL of dry THF. Alcohol **4** (170 mg, 0.53 mmol) and *p*-methoxybenzyl chloride (0.9 mL, 6.6 mmol) dissolved in 20 mL of THF were introduced via cannula in advance of 10 mg of tetra-*n*-butylammonium iodide. The resulting mixture was stirred at room temperature for 8 h and quenched with 25 mL of water. The separated aqueous layer was extracted with ether, and the combined organic phases were washed with brine (2 × 30 mL), dried, filtered, and concentrated. The resulting oil was used without further purification.

For **5**: $^1$H NMR (300 MHz, $C_6D_6$) $\delta$ 7.31 (d, $J$ = 8.7 Hz, 2 H), 6.79 (dd, $J$ = 6.7, 2.0 Hz, 2 H), 5.39 (d, $J$ = 5.6 Hz, 1 H), 5.33 (ddd, $J$ = 11.1, 5.3, 0.9 Hz, 1 H), 5.20 (d, $J$ = 5.6 Hz, 1 H), 4.93 (d, $J$ = 11.5 Hz, 1 H), 4.41 (d, $J$ = 11.5 Hz, 1 H), 3.59−3.50 (m, 2 H), 3.40−3.28 (m, 1 H), 3.31 (s, 6 H), 3.22 (t, $J$ = 8.6 Hz, 1 H), 2.23−2.02 (m, 4 H), 1.92−1.72 (m, 3 H), 1.79 (br s, 3 H), 1.08 (d, $J$ = 6.7 Hz, 3 H), 1.06 (s, 3 H), 1.03 (s, 3 H), 0.97 (s, 3 H); $^{13}$C NMR (75 MHz, $C_6D_6$) $\delta$ 159.4, 141.4, 138.4, 135.8, 131.8, 128.2 (2 C), 126.2, 114.0 (2 C), 96.7, 93.0, 77.8, 59.5, 58.6, 56.8, 54.7, 48.7, 47.9, 42.8, 38.8, 38.1, 30.9, 30.8, 30.6, 26.1, 23.7, 22.9, 19.7; HRMS *m*/*z* ($M^+$) calcd 438.3134, obsd 438.3140.

**(2*R**,3*S**,3a*S**,5*R**,6*S**,7a*S**,10a*R**,11*S**,11a*S**)-5,6-Epoxy-2,3,3a,4,5,6,7,7a,8,10a,11,11a-dodecahydro-3-methoxy-11-[(*p*-methoxybenzyl)oxy]-2,5,8,8,10a-pentamethyl-1*H*-dicyclopenta[*a*,*d*]cyclononene (6).** A solution of **5** (26 mg, 0.059 mmol) in $CH_2Cl_2$ (4 mL) containing powdered sodium bicarbonate (150 mg) was treated at 1-h intervals with small portions of *m*-chloroperbenzoic acid until TLC analysis indicated that the consumption of starting material was complete. The reaction mixture was quenched with saturated $Na_2S_2O_3$ solution and extracted with ether (3×). The combined organic phases were washed with saturated $NaHCO_3$ solution, dried, and concentrated. The residue of **6** was used without further purification: IR (neat, cm$^{-1}$) 1511, 1458; $^1$H NMR (300 MHz, $C_6D_6$) $\delta$ 7.20 (d, $J$ = 8.6 Hz, 2 H), 6.72 (dd, $J$ = 6.8, 1.9 Hz, 2 H), 5.35 (d, $J$ = 5.6 Hz, 1 H), 5.15 (d, $J$ = 5.5 Hz, 1 H), 4.79 (d, $J$ = 11.5 Hz, 1 H), 4.34 (d, $J$ = 11.6 Hz, 1 H), 3.48 (d, $J$ = 1.6 Hz, 1 H), 3.28 (s, 3H), 3.22 (s, 3 H), 3.12 (t, $J$ = 7.5 Hz, 1 H), 2.70 (dd, $J$ = 10.7, 2.1 Hz, 1 H), 2.56−2.37 (m, 2 H), 2.37−2.23 (m, 1 H), 2.17−1.96 (m, 5 H), 1.80 (ddq, $J$ = 5.0, 2.0, 6.9 Hz, 1 H), 1.68 (dd, $J$ = 12.5, 2.1 Hz, 1 H), 1.38 (s, 3 H), 1.37−1.30 (m, 1 H), 1.21−1.08 (dq, $J$ = 12.7, 7.4 Hz, 1 H), 1.04 (d, $J$ = 6.8 Hz, 3 H), 1.03−0.95 (m, 1 H), 1.00 (s, 3 H), 0.88 (s, 3 H); $^{13}$C NMR (75 MHz, $C_6D_6$) $\delta$ 159.3, 140.9, 138.2, 131.2, 127.8 (2 C), 114.1 (2 C), 94.2, 93.9, 77.5, 65.3, 61.4, 58.4, 56.5, 56.2, 54.7, 49.4, 46.2, 41.9, 39.3, 38.5, 31.6, 30.5, 30.1, 26.7, 23.7, 22.5, 19.3; HRMS *m*/*z* ($M^+$) calcd 454.3083, obsd 454.3092.

Anal. Calcd for $C_{28}H_{42}O_4$: C, 76.63; H, 9.32. Found: C, 76.78; H, 9.53.

**(2*R**,3*S**,3a*S**,6*S**,7a*S**,10a*R**,11*S**,11a*S**)-2,3,3a,4,5,6,7,-7a,8,10a,11,11a-Dodecahydro-3-methoxy-11-[(*p*-methoxybenzyl)oxy]-2,8,8,10a-tetramethyl-5-methylene-1*H*-dicyclopenta[*a*,*d*]cyclononen-6-ol (7).** The unpurified epoxide

from above was dissolved in anhydrous benzene (2 mL) and treated with diethylaluminum dicyclohexylamide (1.8 mL of 0.17 M, 0.295 mmol). After 6 h at 20 °C, the reaction mixture was poured into 1 N HCl and extracted with ether (3×). The combined organic extracts were washed with saturated $NaHCO_3$ solution, dried, and concentrated. The residue was chromatographed on silica gel (elution with 35% ether in hexanes) to give **7** as a colorless oil (25 mg, 91% overall): IR (neat, $cm^{-1}$) 3425, 1613; $^1H$ NMR (300 MHz, $C_6D_6$) $\delta$ 7.23 (d, $J$ = 8.6 Hz, 2 H), 6.74 (dd, $J$ = 6.7, 2.0 Hz, 2 H), 5.39 (d, $J$ = 5.6 Hz, 1 H), 5.17 (s, 1 H), 5.11 (d, $J$ = 5.6 Hz, 1 H), 4.91 (d, $J$ = 1.5 Hz, 1 H), 4.68 (d, $J$ = 11.0 Hz, 1 H), 4.45 (d, $J$ = 4.5 Hz, 1 H), 4.27 (d, $J$ = 11.0 Hz, 1 H), 3.52 (q, $J$ = 7.5 Hz, 1 H), 3.47 (d, $J$ = 2.8 Hz, 1 H), 3.27 (s, 3 H), 3.21 (s, 3 H), 3.07 (t, $J$ = 5.0 Hz, 1 H), 3.00 (ddd, $J$ = 15.1, 13.3, 1.9 Hz, 1 H), 2.37−2.23 (m, 1 H), 2.25 (dd, $J$ = 14.2, 2.7 Hz, 1 H), 2.16−2.05 (m, 1 H), 2.07 (dd, $J$ = 13.0, 2.7 Hz, 1 H), 1.80−1.71 (m, 3 H), 1.42−1.35 (m, 2 H), 1.14 (s, 3 H), 1.10−1.07 (m, 3 H), 1.09 (d, $J$ = 6.4 Hz, 3 H), 0.89 (s, 3 H); $^{13}C$ NMR (75 MHz, $C_6D_6$) $\delta$ 159.6, 154.2, 140.3, 138.8, 131.4, 128.8 (2 C), 114.1 (2 C), 105.7, 97.7, 91.8, 77.5, 72.0, 57.6, 57.4, 57.0, 54.7, 49.5, 45.7, 43.2, 40.6, 38.1, 35.1, 34.8, 30.5, 30.4, 30.3, 24.3, 20.1; HRMS $m/z$ ($M^+$) calcd 454.3083, obsd 454.3088.

**(3a*R**,7a*R**,8*R**,9*S**,10a*R**,11*R**,11a*S**)-2,3,3a,4,5,6,7,-7a,8,10a,11,11a-Dodecahydro-3-methoxy-11-[(*p*-methoxybenzyl)oxy]-2,8,8,10a-tetramethyl-5-methylene-1*H*-dicyclopenta[*a*,*d*]cyclononen-6-one (8).** A solution of **7** (24 mg, 0.053 mmol) in $CH_2Cl_2$ (6 mL) was treated with the Dess−Martin periodinane (25 mg, 0.058 mmol) and stirred until TLC denoted the oxidation to be complete. Saturated $Na_2S_2O_3$ (2 mL) and $NaHCO_3$ solutions (2 mL) were added, and the mixture was stirred for 30 min, poured into saturated $NaHCO_3$ solution, and extracted with $CH_2Cl_2$ (3×). The combined organic phases were dried and concentrated to leave 23 mg (96%) of pure **8** as judged by TLC and $^1H$ NMR analysis: IR (neat, $cm^{-1}$) 1689; $^1H$ NMR (300 MHz, $C_6D_6$) $\delta$ 7.27 (d, $J$ = 8.6 Hz, 2 H), 6.79 (dd, $J$ = 6.8, 1.8 Hz, 2 H), 5.53 (d, $J$ = 2.0 Hz, 1 H), 5.31 (d, $J$ = 5.6 Hz, 1 H), 5.10 (d, $J$ = 5.6 Hz, 1 H), 4.83 (s, 1 H), 4.68 (d, $J$ = 10.6 Hz, 1 H), 4.25 (d, $J$ = 10.6 Hz, 1 H), 4.01 (dd, $J$ = 14.6, 12.6 Hz, 1 H), 3.72 (dd, $J$ = 13.6, 8.8 Hz, 1 H), 3.40 (d, $J$ = 3.9 Hz, 1 H), 3.31−3.25 (m, 1 H), 3.29 (s, 3 H), 3.18 (s, 3 H), 2.64 (dd, $J$ = 12.5, 3.0 Hz, 1 H), 2.29 (dd, $J$ = 13.8, 4.0 Hz, 1 H), 2.25−2.08 (m, 1 H), 1.97−1.75 (m, 3 H), 1.40−1.35 (m, 2 H), 1.36 (s, 3 H), 1.12 (d, $J$ = 7.0 Hz, 3 H), 1.09 (s, 3 H), 0.83 (s, 3 H); $^{13}C$ NMR (75 MHz, $C_6D_6$) $\delta$ 207.7, 159.6, 153.8, 139.3, 138.2, 131.1, 129.1 (2 C), 116.2, 114.0 (2 C), 94.6, 92.2, 76.9, 57.8, 57.4, 54.7, 53.8, 50.0, 49.6, 41.2, 40.9, 38.2, 36.2, 33.2, 30.4, 29.5, 25.0, 21.9; HRMS $m/z$ ($M^+$) calcd 452.2927, obsd 452.2903.

Anal. Calcd for $C_{29}H_{40}O_4$: C, 76.94; H, 8.91. Found: C, 77.22; H, 9.04.

**(2*R**,3*S**,3a*S**,5*S**,6*R**,7a*S**,10a*R**,11*S**,11a*S**)-5,6-Epoxy-2,3,3a,4,5,6,7,7a,8,10a,11,11a-dodecahydro-3-methoxy-11-[(*p*-methoxybenzyl)oxy]-2,5,8,8,10a-pentamethyl-1*H*-dicyclopenta[*a*,*d*]cyclononene (11).** Diene **5** (17 mg, 0.039 mmol) was dissolved in 1,4-dioxane (1.9 mL) and water (0.1 mL) and treated with iodine (11 mg, 0.043 mmol). Under a flow of nitrogen, silver(I) oxide (9.9 mg, 0.043 mmol) was added in one portion. The reaction mixture was stirred in the absence of light for 16 h, poured into water, and extracted with ether (3×). The combined organic layers were dried and concentrated. The residue was chromatographed on silica gel to give **11** as a colorless glass that was used directly: $^1H$ NMR (300 MHz, $CDCl_3$) $\delta$ 7.24−7.04 (m, 2 H), 6.76−6.71 (m, 2 H), 5.39 (d, $J$ = 5.5 Hz, 1 H), 5.30 (d, $J$ = 3.5 Hz, 1 H), 4.73 (c, $J$ = 11.6 Hz, 1 H), 4.34 (d, $J$ = 11.6 Hz, 1 H), 3.48 (d, $J$ = 1.6 Hz, 1 H), 3.33 (s, 3 H), 3.31 (s, 3 H), 3.17 (t, $J$ = 7.6 Hz, 1 H), 2.70 (dd, $J$ = 10.7, 2.2 Hz, 1 H), 2.56−2.34 (m, 2 H), 2.37−2.23 (m, 1 H), 2.15−1.92 (m, 6 H), 1.86−1.75 (m, 1 H), 1.67 (dd, $J$ = 2.1, 12.5 Hz, 1 H), 1.48−1.25 (m, 1 H), 1.38 (s, 3 H), 1.20−1.08 (m, 1 H), 1.04 (d, $J$ = 6.8 Hz, 3 H), 0.99 (s, 3 H), 0.88 (s, 3 H); HRMS $m/z$ ($M^+$) calcd 454.3083, obsd 454.3081.

**(2*R**,3*S**,3a*S**,5*S**,6*R**,7a*S**,10a*R**,11*S**,11a*S**)-5,6-Epoxy-2,3,3a,4,5,6,7,7a,8,10a,11,11a-dodecahydro-3-methoxy-2,5,8,8,10a-pentamethyl-1*H*-dicyclopenta[*a*,*d*]cyclononen-11-ol (12).** The preceding epoxide was dissolved in anhydrous benzene (1.6 mL), treated with diethylaluminum dicyclohexylamide (600 $\mu$L of 0.26 M, 0.16 mmol), refluxed for 48 h, cooled, and poured into 1 N HCl. The product was extracted into ether (3×), and the combined organic layers were washed with saturated $NaHCO_3$ solution, dried, and concentrated to leave a residue that was purified by chromatography on silica gel (elution with 50−60% ether in hexanes). There was obtained 6.6 mg (51% overall) of **12** as a colorless glass: IR (neat, $cm^{-1}$) 3430; $^1H$ NMR (300 MHz, $CDCl_3$) $\delta$ 5.39 (d, $J$ = 5.5 Hz, 1 H), 5.30 (d, $J$ = 5.6 Hz, 1 H), 3.72 (dd, $J$ = 11.2, 7.2 Hz, 1 H), 3.47 (d, $J$ = 5.9 Hz, 1 H), 3.34 (s, 3 H), 3.31 (t, $J$ = 3.1 Hz, 1 H), 3.18 (t, $J$ = 7.6 Hz, 1 H), 2.34 (qd, $J$ = 8.2, 3.8 Hz, 1 H), 2.25−2.15 (m, 2 H), 2.03 (m, 1 H), 1.93−1.72 (m, 4 H), 1.64 (dd, $J$ = 6.1, 2.7 Hz, 1 H), 1.58 (dd, $J$ = 14.0, 3.8 Hz, 1 H), 1.30 (s, 3 H), 1.12−1.09 (m, 9 H), 0.96 (s, 3 H); $^{13}C$ NMR (75 MHz, $CDCl_3$) $\delta$ 138.6, 138.0, 94.1, 82.7, 75.4, 75.3, 57.9, 53.0, 48.9, 47.7, 46.1, 42.2, 40.7, 39.1, 34.0, 31.3, 30.5, 26.0, 25.6, 22.6, 20.8; HRMS $m/z$ ($M^+$) calcd 334.2508, obsd 334.2532.

**(2*R**,3*S**,3a*S**,5*R**,6*S**,7a*S**,10a*R**,11*R**,11a*S**)-2,3,3a,-4,5,6,7,7a,8,10a,11,11a-Dodecahydro-3-methoxy-11-[(*p*-methoxybenzyl)oxy]-2,5,8,8,10a-pentamethyl-1*H*-dicyclopenta[*a*,*d*]cyclononene-5,6-diol (13).** Diene **5** (234 mg, 0.53 mmol) dissolved in 10 mL of dry pyridine was cooled to −30 °C, and osmium tetraoxide (134 mg, 0.53 mmol) in 8 mL of dry pyridine was introduced via pipet. The resulting yellow solution turned dark brown/black slowly while being stirred at −30 °C for 1 h and at room temperature for 2 h. The solution was quenched with 10 mL of saturated $NaHSO_3$ solution and stirred for 1 h at room temperature. The resulting mixture was diluted with 30 mL of water and extracted with ethyl acetate (4 × 50 mL). The combined organic layers were washed with 10% HCl (3×), $NaHCO_3$ solution (2×), and brine, dried, and concentrated. The crude material was purified by flash column on silica gel (elution with 60% ethyl acetate in hexanes) to give 240 mg of **13** (96% over 3 steps) as colorless crystals: IR ($CH_2Cl_2$, $cm^{-1}$) 3630, 3600, 1623; $^1H$ NMR (300 MHz, $CDCl_3$) $\delta$ 7.20 (d, $J$ = 8.6 Hz, 2 H), 6.83 (d, $J$ = 8.6 Hz, 2 H), 5.43 (d, $J$ = 5.5 Hz, 1 H), 5.23 (d, $J$ = 5.5 Hz, 1 H), 4.63 (d, $J$ = 10.9 Hz, 1 H), 4.33 (d, $J$ = 10.9 Hz, 1 H), 3.79 (s, 3 H), 3.63 (d, $J$ = 3.8 Hz, 1 H), 3.30 (s, 3 H), 3.06 (t, $J$ = 2.2 Hz, 1 H), 2.87 (dd, $J$ = 14.9, 14.9 Hz, 1 H), 2.59 (dd, $J$ = 13.9, 4.7 Hz, 1 H), 2.30 (m, 1 H), 1.92−1.78 (m, 6 H), 1.34 (s, 3 H), 1.31−1.24 (m, 2 H), 1.19 (s, 3 H), 1.11 (d, $J$ = 6.8 Hz, 3 H), 1.06 (s, 3 H), 1.02−0.83 (m, 2 H), 0.78 (s, 3 H); $^{13}C$ NMR (75 MHz, $CDCl_3$) $\delta$ 158.8, 139.8, 138.5, 131.0, 128.6, 113.6, 98.0, 89.3, 77.2, 76.8, 75.2, 57.4, 57.0, 56.9, 55.2, 49.7, 44.3, 41.3, 38.7, 38.5, 37.9, 31.4, 30.2, 29.5, 24.0, 23.9, 21.1; HRMS $m/z$ base peak ($C_8H_9O^+$) 121.0644.

**(1*S**,2*R**,3a*R**,5*R**,6*S**,7a*R**,8*R**,9*S**,10a*R**,11*R**11a*S**)-1,2-Epoxytetradecahydro-8-methoxy-11-[(*p*-methoxybenzyl)oxy]-3,3,6,9,11a-pentamethyl-1*H*-dicyclopenta[*a*,*d*]-cyclononene-5,6-diol (14).** A mixture of **13** (48 mg, 0.102 mmol), $Na_2HPO_4$ (280 mg, 2.03 mmol), and $NaH_2PO_4$ (288 mg, 203 mmol) was stirred in 5 mL of $CH_2Cl_2$. Peracetic acid (0.441 mL, 2.03 mmol, 35% solution) was added via syringe, and the solution was stirred for 17 h, quenched with 5 mL of saturated $NaHSO_3$ solution, diluted with 25 mL of water, and extracted with ethyl acetate (3×). The combined organic layers were washed with saturated $NaHSO_3$ and $NaHCO_3$ solutions, dried, and concentrated. The crude material was purified by flash chromatography on silica gel (elution with 50−80% ethyl acetate in hexanes) to give 36 mg (72%) of **14** as colorless crystals: mp 76−79 °C; IR ($CH_2Cl_2$, $cm^{-1}$) 3602, 3571, 1613; $^1H$ NMR (300 MHz, $CDCl_3$) $\delta$ 7.22 (d, $J$ = 8.5 Hz, 2 H), 6.85 (d, $J$ = 8.5 Hz, 2 H), 4.60 (d, $J$ = 11.1 Hz, 1 H), 4.45 (d, $J$ = 11.1 Hz, 1 H), 3.79 (brs, 4 H), 3.71 (d, $J$ = 3.7 Hz, 1 H), 3.29 (s, 3 H), 3.13 (d, $J$ = 2.0 Hz, 1 H), 3.07 (d, $J$ = 2.2 Hz, 1 H), 3.06 (s, 1 H), 2.66 (dd, $J$ = 14.5, 14.5 Hz, 1 H), 2.48 (dd, $J$ = 13.9, 3.5 Hz, 1 H), 2.42−2.31 (m, 1 H), 2.02−1.79 (m, 6 H), 1.52−1.42 (m, 2 H), 1.32 (s, 3 H), 1.22 (s, 3 H), 1.11 (d, $J$ = 6.8 Hz, 3 H), 1.05 (s, 3 H), 1.05−0.95 (m, 1 H), 0.78 (s, 3 H); $^{13}C$ NMR (75 MHz, $CDCl_3$) $\delta$ 159.2, 130.2, 128.7 (2 C), 113.7 (2 C), 98.2, 87.0, 76.4, 76.0, 73.8, 70.3, 67.0, 56.8, 55.2, 55.1, 51.0,

45.2, 43.3, 41.0, 38.2, 38.0, 37.8, 30.9, 25.0, 24.0, 23.2, 21.2, 17.9; HRMS *m/z* base peak ($C_8H_9O^+$) 121.0644.

**(2*S**,3a*R**,5*R**,6*S**,7a*R**,8*R**,9*S**,10a*R**,11*R**11a*S**)-2-Hydroxytetradecahydro-8-methoxy-11-[(*p*-methoxybenzyl)oxy]-3,3,6,9,11a-pentamethyl-1*H*-dicyclopenta[*a*,*d*]-cyclononene-5,6-diol (15).** Epoxide **14** (32 mg, 0.072 mmol) dissolved in 5 mL of dry toluene was cooled to −78 °C and treated with Dibal-H (1.4 mL, 1.0 M in toluene) via syringe. The resulting solution was stirred at −78 °C for 3 h, allowed to warm to room temperature, and stirred for an additional 2 h prior to being quenched with 3 mL of ethyl acetate and diluted with 35 mL of saturated $NH_4Cl$ solution and water. The mixture was extracted with ethyl acetate (4×), and the combined organic phases were washed with brine (3×), dried, and concentrated. The crude material was purified by flash chromatography on silica gel (elution with 60−90% ethyl acetate in hexanes) to give 29 mg (91%) of **15** as colorless crystals: mp 83−86 °C; IR ($CH_2Cl_2$, $cm^{-1}$) 3607, 3458, 1613; $^1H$ NMR (300 MHz, $CDCl_3$) $\delta$ 7.22 (d, $J$ = 8.6 Hz, 2 H), 6.84 (d, $J$ = 8.6 Hz, 2 H), 4.64 (d, $J$ = 10.9 Hz, 1 H), 4.53 (d, $J$ = 10.9 Hz, 1 H), 3.78 (s, 4 H), 3.70 (d, $J$ = 8.4 Hz, 1 H), 3.64 (d, $J$ = 4.2 Hz, 1 H), 3.59 (d, $J$ = 3.4 Hz, 1 H), 3.32 (dd, $J$ = 6.4, 6.4 Hz, 1 H), 3.30 (s, 3 H), 3.02 (dd, $J$ = 3.1, 3.1 Hz, 1 H), 2.88 (dd, $J$ = 14.3, 11.7 Hz, 1 H), 2.62 (dd, $J$ = 13.9, 4.7 Hz, 1 H), 2.44−2.35 (m, 1 H), 2.24 (dd, $J$ = 13.7, 4.4 Hz, 1 H), 2.08−1.92 (m, 1 H), 1.90−1.81 (m, 3 H), 1.51 (d, $J$ = 13.7 Hz, 1 H), 1.40 (m, 1 H), 1.31 (s, 3 H), 1.28 (s, 3 H), 1.31−1.23 (m, 2 H), 1.12 (d, $J$ = 7.1 Hz, 3 H), 1.00 (s, 3 H), 1.03−0.96 (m, 1 H), 0.69 (s, 3 H); $^{13}C$ NMR (75 MHz, $CDCl_3$) $\delta$ 158.9, 130.7, 128.5 (2 C), 113.7 (2 C), 97.1, 92.0, 80.9, 77.4, 76.8, 76.3, 57.0, 56.0, 55.2, 50.6, 49.9, 48.9, 42.6, 41.0, 39.6, 38.3, 38.0, 31.8, 30.6, 24.2, 22.4, 22.2, 20.9; HRMS *m/z* ($M^+$-$H_2O$) calcd 472.3188, obsd 472.3203.

**(3a*R**,5*R**,6*S**,7a*R**,8*R**,9*S**,10a*R**,11*R**,11a*S**)-1,2,3,-3a,4,5,6,7,7a,8,10a,11a-Dodecahydro-5,6-dihydroxy-8-methoxy-3,3,6,9,11a-pentamethyl-1*H*-dicyclopenta[*a*,*d*]cyclononen-11-one (16).** Diene **3** (82 mg, 0.26 mmol) dissolved in 1 mL of dry pyridine and 4 mL of THF was cooled to −70 °C, and osmium tetraoxide in dry pyridine (1.6 mL, 0.17 M) was added to the solution via syringe. The yellow solution turned dark brown/black slowly and was stirred at −70 °C for 2 h before being warmed to room temperature over 1 h, quenched with 10 mL of saturated $NaHSO_3$ solution, and stirred for 1 h at room temperature. The resulting mixture was diluted with 20 mL of water and extracted with ethyl acetate (4×). The organic phases were combined, washed with 10% HCl (2×), dried, and concentrated. The crude material was purified by flash chromatography on silica gel (elution with 70% ethyl acetate in hexanes) to give 87 mg (96%) of **16** as colorless crystals: mp 168−169 °C; IR ($CHCl_3$, $cm^{-1}$) 3576, 3458, 1683, 1633; $^1H$ NMR (300 MHz, $CDCl_3$) $\delta$ 5.58 (d, $J$ = 5.6 Hz, 1 H), 5.15 (d, 5.6 Hz, 1 H), 3.60−3.53 (m, 2 H), 3.45 (s, 3 H), 3.32 (t, $J$ = 8.1 Hz, 1 H), 2.17−2.00 (m, 2 H), 1.94−1.79 (series of m, 6 H), 1.66 (d, $J$ = 11.3 Hz, 1 H), 1.53 (s, 3 H), 1.30 (s, 3 H), 1.27−1.19 (m, 2 H), 1.10 (d, $J$ = 5.7 Hz, 3 H), 1.09 (s, 3 H), 0.95 (s, 3 H); $^{13}C$ NMR (75 MHz, $CDCl_3$) $\delta$ 220.7, 142.0, 132.5, 92.8, 75.8, 74.7, 65.5, 59.0, 58.4, 48.9, 46.1, 45.0, 38.4 (2 C), 35.9, 32.2, 30.2, 28.4, 24.8, 24.7, 19.0; HRMS *m/z* ($M^+$) calcd 350.2457, obsd 350.2457.

Anal. Calcd for $C_{21}H_{34}O_4$: C, 71.96; H, 9.78. Found: C, 71.44; H, 9.70.

**(1*S**,3a*S**,5*S**,6*R**,7a*S**,8*S**,9*R**,10a*S**,11a*S**)-Tetradecahydro-1,5,6-trihydroxy-8-methoxy-3,3,6,9,11a-pentamethyl-11*H*-dicyclopenta[*a*,*d*]cyclononen-11-one (17).** A solution of **16** (69 mg, 0.20 mmol) in 10 mL of THF was cooled to −30 °C and treated with borane·THF complex (6.0 mL of 1.0 M in THF). The reaction mixture was stirred for 3 h at −30 °C, allowed to warm to room temperature, and stirred for 2 h before being carefully quenched with 6 mL of 15% NaOH solution and 6 mL of 30% hydrogen peroxide. After 20 min of stirring, the mixture was diluted with $CH_2Cl_2$, washed with brine (2×), dried, filtered, and concentrated. The crude mixture was purified by flash chromatography on silica gel (elution with 70% ethyl acetate in hexanes) to give 61 mg (84%) of a 3:1 mixture of **17** and **18**.

For **17**: $^1H$ NMR (300 MHz, $CDCl_3$) $\delta$ 4.90 (dd, $J$ = 12.1, 6.1 Hz, 1 H), 3.57−3.53 (m, 1 H), 3.48 (s, 3 H), 3.44 (d, $J$ = 6.7 Hz, 1 H), 3.36 (t, $J$ = 9.0 Hz, 1 H), 2.08−2.01 (m, 1 H), 1.95−1.54 (series of m, 13 H), 1.37 (s, 3 H), 1.29 (s, 3 H), 1.10 (d, , $J$ = 6.5 Hz, 3 H), 0.98 (s, 3 H), 0.86 (s, 3 H); $^{13}C$ NMR (75 MHz, $CDCl_3$) $\delta$ 221.3, 92.1, 75.71, 75.66, 75.1, 60.8, 60.6, 59.3, 47.6, 46.2, 44.5, 38.5, 38.2, 37.5, 35.7, 31.7, 29.2, 24.8, 23.4, 22.2, 18.8; HRMS *m/z* ($M^+$) calcd 368.2563, obsd 368.2561.

**(3a*S**,6*R**,7a*S**,8*S**,9*R**,10a*S**,11a*S**)-Decahydro-6-hydroxy-8-methoxy-3,3,6,9,11a-pentamethyl-1*H*-dicyclopenta[*a*,*d*]cyclononene-1,5,11-trione (20).** Triol **17** (30 mg, 0.081 mmol) dissolved in 2 mL of $CH_2Cl_2$ and 2.4 mL of 0.2 M pyridine in $CH_2Cl_2$ was treated with Dess−Martin periodinane (103 mg, 0.244 mmol) and stirred for 20 h at room temperature. The reaction mixture was quenched with saturated $NaHCO_3$ (5 mL) and saturated $Na_2S_2O_5$ solutions (5 mL), and stirred until homogeneous. Following dilution with 10 mL of water and extraction with $CH_2Cl_2$ (4×), the combined organic phases were washed with 10% HCl (3×) and saturated $NaHCO_3$ solution (3×), dried, and concentrated. The crude material was purified by flash chromatography on silica gel (elution with 50−70% ethyl acetate in hexanes) to give 12.2 mg (41%) of **20** and 17.2 mg (58%) of **19**.

For **19**: IR ($CHCl_3$, $cm^{-1}$) 3606, 3574, 3479, 1741, 1683; $^1H$ NMR (300 MHz, $CDCl_3$) $\delta$ 3.47 (s, 3 H), 3.51−3.42 (m, 2 H), 3.28 (t, $J$ = 8.7 Hz, 1 H), 2.43 (d, $J$ = 16.5 Hz, 1 H), 2.33 (dd, $J$ = 13.5, 3.0 Hz, 1 H), 2.25 (d, $J$ = 16.5 Hz, 1 H), 2.10−2.01 (m, 1 H), 1.96−1.69 (series of m, 5 H), 1.59 (brs, 1 H), 1.55 (s, 3 H), 1.37−1.18 (m, 3 H), 1.31 (s, 3 H), 1.14 (s, 3 H), 1.11 (d, $J$ = 6.6 Hz, 3 H), 1.02 (s, 3 H); $^{13}C$ NMR (75 MHz, $CDCl_3$) $\delta$ 217.9, 216.4, 92.3, 75.8, 74.8, 65.8, 59.3, 58.1, 53.4, 46.3, 45.0, 38.6, 38.4, 37.4, 35.1, 31.7, 29.2, 26.2, 24.8, 23.2, 18.7; HRMS *m/z* ($M^+$) calcd 366.2406, obsd 366.2407.

Diol **19** (17.2 mg, 0.047 mmol) dissolved in 0.93 mL of 0.2 M pyridine in $CH_2Cl_2$ was treated with the Dess−Martin periodinane (39.6 mg, 0.093 mmol), and the white slurry was stirred for 12 h at room temperature, at which time an additional 30 mg (0.18 mmol) of the periodinane was introduced prior to an additional 40 h of stirring. The reaction slurry was quenched with saturated $NaHCO_3$ (5 mL) and saturated $Na_2S_2O_5$ solutions (5 mL), stirred until homogeneous, diluted with water, and extracted with $CH_2Cl_2$ (3×). The combined organic phases were washed with 10% HCl (3×) and saturated $NaHCO_3$ solutions (2×), dried, and concentrated. The crude material was purified by flash chromatography on silica gel (elution with 50−70% ethyl acetate in hexanes) to give 13.9 mg (81%) of **20** as colorless crystals: mp 129−132 °C; IR ($C_6H_6$, $cm^{-1}$) 3564, 1750, 1715, 1685; $^1H$ NMR (300 MHz, $C_6D_6$) $\delta$ 3.28−3.20 (m, 2 H), 3.21 (s, 3 H), 3.12 (dd, $J$ = 16.2, 4.3 Hz, 1 H), 3.12−3.04 (m, 1 H), 2.59 (dd, $J$ = 13.2, 3.8 Hz, 1 H), 2.34 (t, $J$ = 12.6 Hz, 1 H), 2.16 (d, $J$ = 16 Hz, 1 H), 2.14 (dd, $J$ = 17.5, 3.8 Hz, 1 H), 2.02 (d, $J$ = 16.0 Hz, 1 H), 1.89−1.74 (m, 2 H), 1.70−1.55 (m, 2 H), 1.46 (s, 3 H), 1.28 (s, 3 H), 1.16−1.07 (m, 1 H), 0.91 (d, $J$ = 6.2 Hz, 3 H), 0.82 (s, 3 H), 0.74 (s, 3 H); $^{13}C$ NMR (75 MHz, $C_6D_6$) $\delta$ 216.9, 214.6, 213.7, 92.5, 79.6, 65.6, 58.4, 53.3, 53.0, 45.4, 44.9, 40.3, 38.9, 36.2, 35.7, 35.4, 29.5, 24.2, 24.0, 22.8, 18.8; HRMS *m/z* ($M^+$) calcd 364.2250, obsd 368.2247.

Anal. Calcd for $C_{21}H_{32}O_5$: C, 69.20; H, 8.85. Found: C, 69.10; H, 8.66.

**(3a*S**,6*Z*,7a*S**,8*S**,9*R**,10a*S**,11a*R**)-1,3a,4,8,9,10,10a,-11a-Octahydro-8-methoxy-3,3,6,9,11a-pentamethyl-2*H*-dicyclopenta[*a*,*d*]cyclononene-2,5,11(3*H*,7a*H*)-trione (22).** A 2:1 mixture of triones **20** and **21** (39 mg, 0.11 mmol) and silver triflate (550 mg, 2.14 mmol) in 8.0 mL of benzene was heated to reflux (solution becomes homogeneous) for 18 h, cooled to room temperature, and diluted with 70 mL of ether and with 20 mL of 10% $NH_4OH$ solution. The aqueous layer was extracted once with ether, and the combined organic layers were washed with brine, dried, and concentrated. The residue was purified by flash chromatography on silica gel (elution with 20% ethyl acetate in hexanes) to give 11.3 mg of **22** and 20 mg of recovered **20**.

For **22**: colorless solid; mp 117−120 °C; IR ($C_6H_6$, $cm^{-1}$) 1731, 1684, 1637; $^1H$ NMR (300 MHz, $CDCl_3$) $\delta$ 5.89 (d, $J$ =

1.1 Hz, 1 H), 3.22 (s, 3 H), 2.84 (q, $J$ = 5.0 Hz, 1 H), 2.80 (d, $J$ = 14.2 Hz, 1 H), 2.30 (dd, $J$ = 12.7, 4.0 Hz, 1 H), 2.12 (dd, $J$ = 14.2, 4.0 Hz, 1 H), 2.12−2.08 (m, 1 H), 2.02 (d, $J$ = 1.1 Hz, 3 H), 1.90 (dd, $J$ = 13.4, 6.0 Hz, 1 H), 1.85−1.74 (m, 1 H), 1.72−1.44 (m, 3 H), 1.24 (s, 3 H), 1.18−1.08 (m, 1 H), 1.14 (d, $J$ = 6.4 Hz, 3 H), 1.13 (s, 3 H), 1.06 (s, 3 H); $^{13}$C NMR (75 MHz, $CDCl_3$) $\delta$ 217.9, 202.9, 159.3, 124.3, 93.9, 79.9, 74.5, 57.0, 52.5, 46.3, 44.1, 40.9, 38.7, 37.3, 34.0, 33.6, 25.6, 24.4, 23.5, 20.5, 20.0; HRMS $m/z$ ($M^+$) calcd 346.2144, obsd 346.2136.

**(3a*R**,5*R**,6*S**,7a*R**,8*R**,9*S**,10a*R**,11*R**11a*S**)-5-(*tert*-Butyldimethylsiloxy)-1,2,3,3a,4,5,6,7,7a,8,10a,11a-dodecahydro-5,6-dihydroxy-8-methoxy-3,3,6,9,11a-pentamethyl-1*H*-dicyclopenta[*a*,*d*]cyclononen-11-one (23).** To diol **16** (123 mg, 0.351 mmol) dissolved in 5 mL of dry DMF were added *tert*-butyldimethylsilyl chloride (264 mg, 1.75 mmol) and imidazole (119 mg, 1.75 mmol). The reaction mixture was stirred for 8 h at room temperature, quenched with 10 mL of water, and extracted with ether. The combined organic phases were washed with water (5×), dried, and concentrated. The residue was purified by flash chromatography on silica gel (elution with 7% ethyl acetate in hexanes) to give 162 mg (99%) of **23** as colorless crystals: mp 98−100 °C; IR ($CHCl_3$, $cm^{-1}$) 3565, 1688, 1652, 1636; $^1$H NMR (300 MHz, $CDCl_3$) $\delta$ 5.59 (d, $J$ = 5.6 Hz, 1 H), 5.15 (d, $J$ = 5.6 Hz, 1 H), 3.76 (d, $J$ = 4.0 Hz, 1 H), 3.51−3.44 (m, 1 H), 3.44 (s, 3 H), 3.37 (t, $J$ = 7.4 Hz, 1 H), 2.26 (br s, 1 H), 2.11−1.75 (series of m, 6 H), 1.62 (dd, $J$ = 14.1, 2.7 Hz, 1 H), 1.55 (s, 3 H), 1.36−1.29 (m, 1 H), 1.22 (s, 3 H), 1.20−1.13 (m, 1 H), 1.10 (d, $J$ = 6.7 Hz, 3 H), 1.06 (s, 3 H), 0.95 (s, 3 H), 0.92 (s, 9 H), 0.16 (s, 3 H), 0.13 (s, 3 H); $^{13}$C NMR (75 MHz, $CDCl_3$) $\delta$ 219.5, 142.0, 132.8, 93.6, 75.99, 75.97, 64.9, 59.0, 57.6, 49.6, 46.1, 45.6, 38.5, 36.8, 35.5, 32.0, 29.9, 28.2, 26.6, 26.1 (3 C), 24.6, 19.5, 18.2, −2.5, −4.2; HRMS $m/z$ ($M^+$) calcd 464.3322, obsd 464.3311.

**(1S*,3aS*,5S*,6R*,7aS*,8S*,9R*,10aS*,11aS*)-5-(*tert*-Butyldimethylsiloxy)tetradecahydro-1,6-dihydroxy-8-methoxy-3,3,6,9,11a-pentamethyl-11*H*-dicyclopenta[*a*,*d*]-cyclononen-11-one (24) and (2R*,3aS*,5S*,6R*,7aS*,8S*,-9R*,10aS*,11aS*)-5-(*tert*-Butyldimethylsiloxy)tetradecahydro-2,6-dihydroxy-8-methoxy-3,3,6,9,11a-pentamethyl-11*H*-dicyclopenta[*a*,*d*]cyclononen-11-one (25).** A solution of **23** (72 mg, 0.155 mmol) in 10 mL of THF was cooled to −70 °C and treated with borane−THF complex (2.0 mL of 1.0 M in THF), and the reaction mixture was stirred for 4 h at −70 °C, 2 h at 0 °C, and 1 h at room temperature prior to being quenched sequentially with 4 mL of water, 2 mL of 15% NaOH solution, and 2 mL of 30% hydrogen peroxide. After 45 min at room temperature, the mixture was diluted with water and extracted with ether. The combined organic layers were washed with brine, dried, and concentrated. The residue was purified by flash chromatography on silica gel (elution with 20% ethyl acetate in hexanes) to give 20.1 mg (27%) of **25** and 32.4 mg (43%) of **24**.

For **24**: white solid; mp 73−76 °C; IR ($CHCl_3$, $cm^{-1}$) 3686, 3614, 1684, 1602; $^1$H NMR (300 MHz, $CDCl_3$) $\delta$ 4.94 (dd, $J$ = 12.0, 6.1 Hz, 1 H), 3.60 (d, $J$ = 4.9 Hz, 1 H), 3.50 (s, 3 H), 3.50−3.40 (m, 2 H), 2.19−2.05 (m, 2 H), 1.93−1.47 (series of m, 9 H), 1.36 (s, 3 H), 1.25−1.18 (m, 1 H), 1.20 (s, 3 H), 1.11 (d, $J$ = 6.7 Hz, 3 H), 1.05−0.97 (m, 1 H), 0.95 (s, 3 H), 0.92 (s, 9 H), 0.85 (s, 3 H), 0.16 (s, 3 H), 0.13 (s, 3 H); $^{13}$C NMR (75 MHz, $CDCl_3$) $\delta$ 220.6, 92.3, 76.5, 75.9, 75.5, 60.0, 59.63, 59.56, 47.6, 46.1, 44.6, 38.7, 38.1, 36.6, 35.5, 31.7, 29.1, 26.9, 26.1 (3 C), 23.0, 22.2, 19.1, 18.2, −2.2, −4.1; HRMS $m/z$ ($M^+$) calcd 482.3428, obsd 482.3413.

For **25**: white solid; mp 70−73 °C; IR ($CHCl_3$, $cm^{-1}$) 3686, 3615, 3563, 1687, 1603; $^1$H NMR (300 MHz, $CDCl_3$) $\delta$ 3.82 (d, $J$ = 4.2 Hz, 1 H), 3.68 (d, $J$ = 4.8 Hz, 1 H), 3.61−3.54 (m, 1 H), 3.49 (s, 3 H), 3.49−3.43 (m, 1 H), 2.76 (dd, $J$ = 14.0, 4.4 Hz, 1 H), 2.26 (br s, 1 H), 2.20−2.05 (m, 2 H), 1.94−1.82 (m, 4 H), 1.73 (d, $J$ = 21.6 Hz, 1 H), 1.64 (s, 3 H), 1.60−1.46 (m, 2 H), 1.38−1.15 (m, 2 H), 1.21 (s, 3 H), 1.11 (d, $J$ = 6.7 Hz, 3 H), 0.99 (s, 3 H), 0.92 (s, 9 H), 0.84 (s, 3 H), 0.17 (s, 3 H), 0.13 (s, 3 H); $^{13}$C NMR (75 MHz, $CDCl_3$) $\delta$ 221.8, 92.4, 82.8, 76.3, 76.0, 59.5, 57.3, 56.3, 48.4, 46.2, 45.5, 43.8, 38.7, 36.6, 35.9, 31.4, 30.3, 26.8, 26.1 (3 C), 22.0, 21.3, 19.2, 18.2, −2.3, −4.2; HRMS $m/z$ ($M^+$) calcd 482.3428, obsd 482.3447.

**(1S*,3aS*,5S*,6R*,7aS*,8S*,9R*,10aS*,11aS*)-Tetradecahydro-1,5,6-trihydroxy-8-methoxy-3,3,6,9,11a-pentamethyl-11*H*-di-cyclopenta[*a*,*d*]cyclononen-11-one 1-Acetate (27).** To diol **24** (101 mg, 0.209 mmol) dissolved in 20 mL of $CH_2Cl_2$ was added pyridine (2.0 mL), acetic anhydride (1.0 mL), and DMAP (20 mg). The resulting solution was stirred for 60 min, quenched with water, and extracted with $CH_2Cl_2$. The combined organic phases were washed with 10% HCl and saturated $NaHCO_3$ solution, dried, and concentrated. The crude material was filtered through a column of silica gel and used without further purification.

For **26**: white solid; mp 94−97 °C; IR ($CHCl_3$, $cm^{-1}$) 3689, 3568, 1729, 1692, 1603; $^1$H NMR (300 MHz, $CDCl_3$) $\delta$ 5.45 (dd, $J$ = 11.9, 6.5 Hz, 1 H), 3.59 (d, $J$ = 5.2 Hz, 1 H), 3.48 (s, 3 H), 3.40−3.33 (m, 2 H), 1.99 (s, 3 H), 2.08−1.63 (series of m, 10 H), 1.28 (s, 3 H), 1.35−1.17 (m, 2 H), 1.20 (s, 3 H), 1.13 (d, $J$ = 6.7 Hz, 3 H), 0.97 (s, 3 H), 0.93 (s, 3 H), 0.92 (s, 9 H), 0.14 (s, 3 H), 0.12 (s, 3 H); $^{13}$C NMR (75 MHz, $CDCl_3$) $\delta$ 218.1, 170.3, 93.2, 79.6, 75.9, 75.8, 60.0, 59.2, 58.3, 45.8, 45.1, 44.8, 38.7, 38.4, 36.7, 36.0, 31.4, 28.8, 26.7, 26.1 (3 C), 22.8, 22.1, 19.1, 18.2, −2.3, −4.1; HRMS $m/z$ ($M^+$) calcd 524.3533, obsd 524.3526.

To a solution of **26** in 15 mL of dry THF was added 0.6 mL of TBAF (1.0 M in THF), and the resulting mixture was stirred for 45 min at room temperature and concentrated. The residue was purified by flash chromatography on silica gel (elution with 75% ethyl acetate in hexanes) to give 79 mg (91% from **24**) of crystalline diol **27**: white solid; mp 155−157 °C; IR ($CHCl_3$, $cm^{-1}$) 3575, 2994, 2965, 2936, 2879, 1729, 1686; $^1$H NMR (300 MHz, $CDCl_3$) $\delta$ 5.44 (dd, $J$ = 11.8, 6.4 Hz, 1 H), 3.46 (s, 3 H), 3.44 (dd, $J$ = 14.3, 7.1 Hz, 1 H), 3.28 (t, $J$ = 8.6 Hz, 1 H), 3.21−3.16 (m, 1 H), 1.98 (s, 3 H), 1.96−1.56 (series of m, 12 H), 1.47−1.39 (m, 1 H), 1.28 (s, 6 H), 1.11 (d, $J$ = 6.5 Hz, 3 H), 0.98 (s, 3 H), 0.92 (s, 3 H); $^{13}$C NMR (75 MHz, $CDCl_3$) $\delta$ 218.9, 170.3, 92.8, 79.7, 75.7, 74.2, 61.1, 59.0, 58.8, 46.0, 45.1, 44.3, 38.6, 38.3, 37.8, 36.4, 31.4, 28.7, 24.7, 22.9, 22.4, 20.7, 18.7; HRMS $m/z$ ($M^+$) calcd 410.2668, obsd 410.2669.

**(1S*,3aS*,5S*,6R*,7aS*,8S*,9R*,10aS*,11aS*)-Tetradecahydro-1,6-dihydroxy-8-methoxy-3,3,6,9,11a-pentamethyl-11*H*-di-cyclopenta[*a*,*d*]cyclononene-5,11-dione 1-Acetate (28).** A solution of **27** (23 mg, 0.056 mmol) in 4 mL of dry $CH_2Cl_2$ was treated with 50 mg of powdered 4 Å molecular sieves, *N*-methylmorpholine *N*-oxide (33 mg, 0.280 mmol), and finally tetrapropylammonium perruthenate (2.0 mg). The reaction mixure was stirred for 50 min and concentrated. The residue was taken up in ether and passed through a column of silica gel. Concentration of the appropriate fractions afforded 11 mg (48%) of **28** as a colorless oil: IR ($CHCl_3$, $cm^{-1}$) 3592, 1730, 1715, 1687, 1602; $^1$H NMR (300 MHz, $CDCl_3$) $\delta$ 5.38 (dd, $J$ = 11.8, 6.3 Hz, 1 H), 3.43 (s, 3 H), 3.29 (dd, $J$ = 13.6, 7.9 Hz, 1 H), 3.18 (dd, $J$ = 15.3, 8.5 Hz, 1 H), 2.92 (dd, $J$ = 17.3, 13.0 Hz, 1 H), 2.38−2.24 (m, 2 H), 2.10−1.68 (series of m, 7 H), 1.97 (s, 3 H), 1.32 (s, 3 H), 1.24 (s, 3 H), 1.22−1.12 (m, 1 H), 1.08 (d, $J$ = 6.6 Hz, 3 H), 1.01 (s, 3 H), 0.98 (s, 3 H), 0.95−0.84 (m, 1 H); $^{13}$C NMR (75 MHz, $CDCl_3$) $\delta$ 217.7, 213.8, 170.3, 93.3, 79.6, 79.0, 58.6, 58.5, 55.6, 44.70, 44.67, 44.6, 39.5, 38.6, 37.4, 36.0, 34.2, 28.9, 23.6, 22.5, 20.9, 20.7, 19.7; HRMS $m/z$ ($M^+$) calcd 408.2512, obsd 408.2527.

**(1S*,2aR*,3R*,4aS*,5aS*,6S*,7R*,8aS*,8bR*,9aS*,9bS*)-1,3-Dibromododecahydro-6-methoxy-2,2,4a,7,9b-pentamethylcyclopenta[7,8]-*as*-indaceno[1,8a-*bc*]oxet-4(4a*H*)-one (31).** A solution of **30**[1] (23 mg, 0.066 mmol) in 10 mL of 5:1 THF/water was treated with *N*-bromosuccinimide (90 mg, 0.50 mmol), stirred for 1 h, quenched with 4 mL of saturated $Na_2SO_3$ solution, diluted with water, and extracted with ether. The combined organic layers were washed with saturated $NaHCO_3$ solution (3×) and brine, dried, and concentrated. The residue was purified by flash chromatography on silica gel (elution with 5% ethyl acetate in hexanes) to give 24 mg (71%) of **31** as a yellow crystalline solid: mp 148−150 °C; IR ($CH_2Cl_2$, $cm^{-1}$) 1701; $^1$H NMR (300 MHz, $C_6D_6$) $\delta$ 4.57 (s, 1 H), 4.33 (d, $J$ = 1.7 Hz, 1 H), 3.64 (s, 1 H), 3.19−3.06 (m, 1 H), 3.06 (s, 3 H), 2.92 (dd, $J$ = 14.2, 10.7 Hz, 1 H), 2.68 (d, $J$ = 1.7 Hz, 1 H), 2.28−2.18 (m, 1 H), 2.00−1.88 (m, 1 H), 1.84 (dd, $J$ = 14.2, 1.7 Hz, 1 H), 1.72−1.50 (m, 2 H),1.48 (s, 3 H), 1.39 (s, 3 H),

1.37−1.16 (m, 1 H), 1.11 (d, $J$ = 6.5 Hz, 3 H), 0.91 (s, 3 H), 0.90 (s, 3 H); $^{13}$C NMR (75 MHz, $C_6D_6$) $\delta$ 206.8, 97.2, 95.0, 91.4, 65.3, 62.1, 57.6, 55.3, 49.9, 49.2, 47.6, 47.2, 46.4, 43.0, 41.8, 35.4, 31.2, 25.0, 23.7, 19.4, 17.7; HRMS $m/z$ ($M^+$ − Br) calcd 409.1468, obsd 409.1423.

Anal. Calcd for $C_{21}H_{30}Br_2O_3$: C, 51.45; H, 6.17. Found: C, 51.46; H, 6.20.

**(1*S**,4a*S**,5a*S**,6*S**,7*R**,8a*S**,8b*R**,9a*S**,9b*S**)-1-Bromo-1,2,5,5a,6,7,8,8a,9a,9b-decahydro-6-methoxy-2,2,4a,7,9b-pentamethylcyclopenta[7,8]-*as*-indaceno[1,8a-*bc*]oxet-4(4a*H*)-one (32).** Lithium bromide (180 mg, 2.1 mmol) was heated to 140 °C at 1.5 Torr for 16 h, allowed to cool to room temperature, and purged with nitrogen, at which time lithium carbonate (172 mg, 2.4 mmol) and **31** (230 mg, 0.45 mmol) were added followed by 10 mL of distilled DMF. The slurry was heated to reflux for 7 h, diluted with water, and extracted with ether. The organic layers were combined, washed with brine, dried, and concentrated. The crude material was purified by flash chromatography on silica gel (elution with 7% ethyl acetate in hexanes) to give 154 mg (80%) of **32** as colorless crystals: mp 117−119 °C; IR ($CCl_4$, cm$^{-1}$) 1685; $^1$H NMR (300 MHz, $C_6D_6$) $\delta$ 5.89 (s, 1 H), 4.64 (s, 1 H), 3.68 (s, 1 H), 3.08 (s, 3 H), 3.13−3.06 (m, 1 H), 2.95−2.86 (m, 2 H), 2.10−1.90 (m, 3 H), 1.37−1.18 (m, 2 H), 1.14 (s, 3 H), 1.11 (d, $J$ = 6.8 Hz, 3 H), 0.95 (s, 3 H), 0.87 (s, 3 H), 0.83 (s, 3 H); $^{13}$C NMR (75 MHz, $C_6D_6$) $\delta$ 201.2, 167.0, 120.7, 95.6, 93.5, 91.8, 63.4, 57.3, 57.0, 49.88, 49.14, 49.11, 45.8, 42.6, 37.4, 36.3, 26.9, 26.4, 24.3, 20.0, 17.8; HRMS $m/z$ ($M^+$) calcd 408.1300, obsd 408.1311.

Anal. Calcd for $C_{21}H_{29}BrO_3$: C, 61.42; H, 7.14. Found: C, 61.46; H, 7.12.

**(2a*R**,4a*S**,5a*S**,6*S**,7*R**,8a*S**,8b*R**,9a*S**,9b*S**)-Dodecahydro-6-methoxy-2,2,4a,7,9b-pentamethylcyclopenta[7,8]-*as*-indaceno[1,8a-*bc*]oxet-4(4a*H*)-one (33).** To **32** (38 mg, 0.093 mmol) was added 4 mL of methanol, 1.5 mL of triethylamine, and 10% Pd/C (25 mg). The resulting slurry was stirred under a hydrogen atmosphere for 18 h before being diluted with ether (30 mL) and filtered through a pad of Celite. The resulting soluton was concentrated, and the residue was purified by flash chromatography on silica gel (elution with 5% ethyl acetate in hexanes) to give 10 mg (32%) of **33** as a colorless crystalline solid: mp 151−152 °C; IR ($CHCl_3$, cm$^{-1}$) 1698; $^1$H NMR (300 MHz, $C_6D_6$) $\delta$ 4.62 (d, $J$ = 3.5 Hz, 1 H), 3.42−3.32 (m, 1 H), 3.34 (s, 3 H), 3.24 (dd, $J$ = 8.7, 6.3 Hz, 1 H), 2.59 (dd, $J$ = 15.7, 6.6 Hz, 1 H), 2.50 (dd, $J$ = 15.7, 4.1 Hz, 1 H), 2.26 (ddt, $J$ = 10.6, 6.3, 1.4 Hz, 1 H), 2.05−1.81 (m, 4 H), 1.65−1.56 (m, 3 H), 1.31 (s, 3 H), 1.29 (s, 3 H), 1.28−1.22 (m, 1 H), 1.10 (d, $J$ = 6.1 Hz, 3 H), 1.05 (s, 3 H), 1.04 (s, 3 H); $^{13}$C NMR (75 MHz, $C_6D_6$) $\delta$ 212.4, 97.4, 95.1, 87.2, 57.6 (2 C), 55.8, 50.5, 47.2 (2 C), 46.1, 44.3, 42.1, 41.9, 35.6, 33.4, 32.4, 26.9, 20.2, 17.8, 17.5; HRMS $m/z$ ($M^+$) calcd 332.2352, obsd 332.2350.

**(5*S**,5a*R**,6a*S**,7*S**,8*R**,9a*S**,9b*R**,9c*R**)-3,5,5a,6,6a,7,8,9,-9a,9c-Decahydro-7-methoxy-3,3,5a,8,9c-pentamethyl-9b*H*-cyclo-pent[*a*]-*as*-indacen-5,9b-diol (35).** To oxetane **32** (135 mg, 0.317 mmol) were added zinc metal (300 mg, 4.59 mmol) and dry methanol (10 mL). The mixture was heated to reflux for 6 h, cooled to room temperature, diluted with ether, filtered through a pad of Celite, and concentrated. The resulting pure **34** was used without further processing.

For **34**: white solid; mp 116−118 °C; IR ($CHCl_3$, cm$^{-1}$) 3590, 1668; $^1$H NMR (300 MHz, $CDCl_3$) $\delta$ 5.85 (s, 1 H), 5.81 (d, $J$ = 5.9 Hz, 1 H), 5.71 (d, $J$ = 5.9 Hz, 1 H), 3.36 (s, 3 H), 3.16 (dd, $J$ = 8.9, 5.8 Hz, 1 H), 2.82 (ddd, $J$ = 11.1, 11.1, 8.2 Hz, 1 H), 2.49 (dd, $J$ = 14.6, 11.3 Hz, 1 H), 2.36−2.26 (m, 1 H), 2.39 (dd, $J$ = 14.6, 3.2 Hz, 1 H), 1.89−1.73 (m, 2 H), 1.54 (ddd, $J$ = 12.3, 12.3, 12.3 Hz, 1 H), 1.33−1.22 (m, 1 H), 1.31 (s, 3 H), 1.27 (s, 3 H), 1.21 (s, 3 H), 1.19 (s, 3 H), 1.10 (d, $J$ = 6.2 Hz, 3 H); $^{13}$C NMR (75 MHz, $CDCl_3$) $\delta$ 205.7, 178.8, 141.8, 130.4, 117.0, 99.9, 98.2, 83.1, 58.7, 58.0, 57.4, 48.9, 48.6, 46.6, 43.3, 41.5, 36.0, 28.7, 27.2, 26.0, 17.5; HRMS $m/z$ ($M^+$) calcd 330.2195, obsd 330.2184.

Anal. Calcd for $C_{21}H_{30}O_3$: C, 76.33; H, 9.15. Found: C, 76.30; H, 9.10.

To ketone **34** (105 mg, 0.317 mmol) dissolved in 10 mL of dry THF at −78 °C was added Dibal-H (1.0 mL of 1.0 M in hexanes) via syringe. The resulting solution was stirred at −78 °C for 1 h, quenched with 1 mL of methanol and 1 mL of saturated $NH_4Cl$ solution, and stirred with $Na_2SO_4$ until a granular precipitate formed (60 min). The slurry was filtered through Celite and washed with ether. The ether layer in the filtrate was washed with brine, dried, and concentrated. The crude material was purified by flash chromatography on silica gel (elution with 20% ethyl acetate in hexanes) to give 84 mg (80% from **32**) of a 10:1 mixture of allylic alcohols.

For **35**: white solid; mp 117−119 °C; IR ($CHCl_3$, cm$^{-1}$) 3465, 3450; $^1$H NMR (300 MHz, $CDCl_3$) $\delta$ 5.70 (d, $J$ = 5.8 Hz, 1 H), 5.59 (d, $J$ = 5.8 Hz, 1 H), 5.50 (d, $J$ = 1.9 Hz, 1 H), 4.35 (d, $J$ = 2.2 Hz, 1 H), 3.33 (s, 3 H), 3.13 (dd, $J$ = 9.0, 5.5 Hz, 1 H), 2.75 (ddd, $J$ = 11.6, 8.4, 8.4 Hz, 1 H), 2.35−2.26 (m, 1 H), 2.17 (dd, $J$ = 13.7, 10.1 Hz, 1 H), 1.95−1.76 (m, 3 H), 1.63 (dd, $J$ = 13.8, 7.4 Hz, 1 H), 1.50 (ddd, $J$ = 12.1, 12.1, 12.1 Hz, 1 H), 1.42−1.03 (m, 1 H), 1.17 (s, 3 H), 1.13 (d, $J$ = 6.7 Hz, 3 H), 1.12 (s, 6 H), 0.99 (s, 3 H); $^{13}$C NMR (75 MHz, $CDCl_3$) $\delta$ 155.5, 141.5, 132.7, 121.5, 96.9, 84.8, 75.4, 59.1, 57.5, 53.7, 49.7, 47.5, 47.4, 46.1, 42.1, 36.5, 29.6, 28.0, 21.2, 20.0, 18.8; HRMS $m/z$ ($M^+$) calcd 332.2352, obsd 332.2322.

Anal. Calcd for $C_{21}H_{32}O_3$: C, 75.86; H, 9.70. Found: C, 75.95; H, 9.72.

**(2*S**,3*R**,3a*Z*,7a*R**,10a*S**,11a*R**)-1,2,3,7,7a,8,10a,11a-Octahydro-3-methoxy-2,5,8,8,10a-pentamethyl-11*H*-dicyclopenta[*a*,*d*]cyclononen-11-one (36).** Diol **35** (26 mg, 0.0782 mmol) dissolved in 5 mL of $CH_2Cl_2$ was treated with triethylamine (0.140 mL, 1.0 mmol) and methanesulfonyl chloride (0.080 mL, 1.0 mmol) at 0 °C. The solution was stirred at 0 °C for 15 min and at room temperature for 60 min before being quenched with 10 mL of water. The resulting mixture was extracted with $CH_2Cl_2$, and the organic layers were combined, washed with brine, dried, and concentrated. The crude residue was taken up in 8 mL of *tert*-butyl alcohol, and 200 mg of potassium *tert*-butoxide was added. The resulting mixture was stirred at 60 °C for 45 min, concentrated, taken up in water, and extracted with ether. The combined organic layers were washed with brine, dried, and concentrated. The residue was purified by flash chromatography on silica gel (elution with 5% ethyl acetate in hexanes) to give 13.5 mg (56%) of **36** as a single isomer: colorless oil; IR ($CHCl_3$, cm$^{-1}$) 1729, 1654; $^1$H NMR (300 MHz, $CDCl_3$) $\delta$ 6.26 (d, $J$ = 5.2 Hz, 1 H), 6.08 (d, $J$ = 5.2 Hz, 1 H), 5.80 (d, $J$ = 12.8 Hz, 1 H), 5.50 (d, 12.8 Hz, 1 H), 3.33 (s, 3 H), 3.02 (dd, $J$ = 7.1, 4.6 Hz, 1 H), 2.93 (t, $J$ = 9.4 Hz, 1 H), 2.71−2.52 (m, 2 H), 2.15−1.95 (m, 2 H), 1.83 (d, $J$ = 1.5 Hz, 3 H), 1.51 (dd, $J$ = 12.9, 7.8 Hz, 1 H), 1.33−1.23 (m, 1 H), 1.21 (s, 3 H), 1.08 (s, 3 H), 1.07 (s, 3 H), 1.01 (d, $J$ = 6.6 Hz, 3 H); $^{13}$C NMR (75 MHz, $CDCl_3$) $\delta$ 220.0, 146.2, 145.9, 134.2, 133.8, 131.5, 123.2, 96.0, 57.9, 55.5, 54.4, 48.8, 43.0, 42.6, 40.7, 33.8, 22.9, 22.8, 22.7, 18.0, 15.3; HRMS $m/z$ ($M^+$) calcd 314.2246, obsd 314.2254.

**(3a*Z*,7a*R**,8*R**,9*S**,10a*R**,11*R**11a*S**)-1,2,3,5,6,7,7a,8,-10a,11a-Decahydro-5,6-dihydroxy-8-methoxy-3,3,6,9,11a-pentamethyl-1*H*-dicyclopenta[*a*,*d*]cyclononen-11-one (37).** To an *E*/*Z* mixture of trienes **36** (40.2 mg, 0.128 mmol) dissolved in 3 mL of THF and cooled to −78 °C was added osmium tetraoxide (1.0 mL, 0.17 M in pyridine), and the resulting mixture was stirred at −78 °C for 30 min. Saturated $NaHSO_3$ solution (3 mL) was introduced, and the mixture was stirred for 1 h, diluted with water, and extracted with ethyl acetate. The combined organic layers were washed with $NaHSO_3$ solution, saturated $NaHCO_3$ solution, and brine prior to drying and solvent evaporation. The residue was purified by flash chromatography on silica gel (elution with 30−50% ethyl acetate in hexanes) to give 15 mg of a mixture of diol diastereomers and 14 mg of **37** (29 mg, 65%) as a single diastereomer.

For **37**: IR ($CHCl_3$, cm$^{-1}$) 3695−3554, 1684, 1602; $^1$H NMR (300 MHz, $CDCl_3$) $\delta$ 5.70 (d, $J$ = 5.8 Hz, 1 H), 5.32 (d, $J$ = 5.8 Hz, 1 H), 5.30 (d, $J$ = 8.4 Hz, 1 H), 4.60 (d, $J$ = 9.7 Hz, 1 H), 3.91 (m, 1 H), 3.46 (s, 3 H), 3.17 (t, $J$ = 9.4 Hz, 1 H), 2.29−1.79 (series of m, 7 H), 1.69−1.63 (m, 1 H), 1.58 (s, 3 H), 1.18 (s, 3 H), 1.17 (s, 3 H), 1.14 (d, $J$ = 6.4 Hz, 3 H), 1.11 (s, 3 H); $^{13}$C NMR (75 MHz, $CDCl_3$) $\delta$ 216.1, 155.8, 139.5, 132.1, 122.5, 91.4, 65.0, 58.8, 50.2, 43.9, 42.8, 42.5, 37.9, 35.8, 30.0, 29.8,

29.72, 29.67, 23.6, 23.3, 18.8; HRMS *m*/*z* ($M^+$) calcd 348.2301, obsd 348.2295.

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**Supporting Information Available:** Tables giving the crystal data and structure refinement information, bond lengths and bond angles, atomic and hydrogen coordinates, and isotropic and anisotropic displacement coordinates for **13**, **20**, and **31**, together with high-field $^1$H NMR spectra of those compounds lacking combustion analysis.

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