Studies Directed toward the Synthesis of the Unusual Antileukemic Diterpene Jatrophatrione. 1. A Solution to the Problem of Chirality Merger during Elaboration of the Entire Carbotricyclic Framework

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Received December 29, 1998

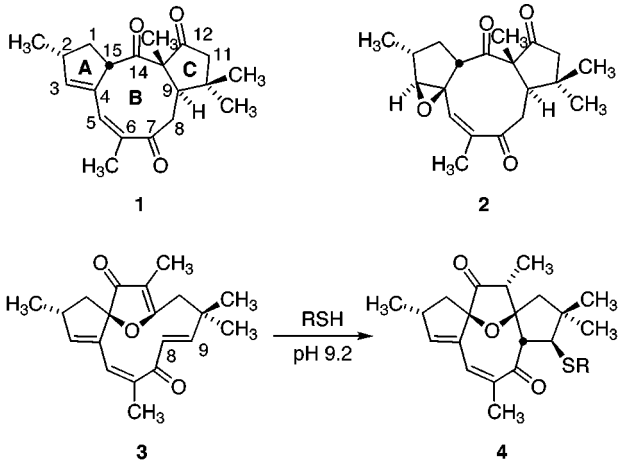
A practical route for elaboration of the [5.9.5] tricyclic nucleus of jatrophatrione (**1**) is reported. The two key steps involve an oxyanionic Cope rearrangement and a Grob fragmentation. The building blocks required to reach **44** are the bicyclo[3.3.0]octanone **29** and the cyclopentadienyl bromide **35**. The former was obtained in 12 steps from methylcyclopentadiene. The route to the latter began with 4,4-dimethylcyclopentenone. The charge-accelerated [3,3]-sigmatropic isomerization within **44** proceeds via a chairlike transition state to deliver, after enolate methylation, a highly strained product carrying a trans double bond in a medium-sized ring, one consequence of which is rapid transannular ring closure via an ene pathway. Acid hydrolysis of this enol ether and conversion to hydroxy mesylate **51** was followed by exposure to base. This sequence resulted in ring opening to provide the strategic advanced intermediate **52**. The synthetic pathway developed here is expected to open a route to 9-epijatrophatrione (**8**) for the ultimate purpose of examining its anticipated isomerization to **1** under mildly basic conditions.

Jatrophatrione (**1**) is an architecturally novel diterpene that has been isolated from the roots of *Jatropha macrorhiza* Benth and shown to possess very respectable inhibitory activity toward P-388 lymphocytic leukemia.[1] The detailed molecular structures of **1** and citlalitrione (**2**), a related epoxy trione obtained from *Jatropha dioica* var. *sessiliflora*,[2] have been independently secured by X-ray crystallographic analysis. Unfortunately, no chemistry surrounding these compounds has been reported. Their absolute configurations have instead been inferred on the basis of an obviously close structural relationship to jatrophone (**3**), previously isolated from *J. gossypiifolia*.[3] Early interest in **3** arose because of its strong inhibitory action against several carcinomas.[3,4]

Kupchan demonstrated that jatrophone (**3**) undergoes Michael addition to the C8−C9 enone double bond with concomitant transannular ring closure to give **4** when subjected to 1-propanethiol under basic conditions (pH 9.2).[5] This susceptibility to nucleophilic conjugate addition was proposed to be responsible for the pronounced anticancer activity of jatrophone (**3**).

To account for the fact that jatrophatrione (**1**) is biologically effective despite its lack of unsaturation at C8−C9, Torrance et al. proposed the interesting possibility that **1** is first subject to a retrograde Michael process to give **5**, which can be captured in a manner paralleling the **3** → **4** conversion (Scheme 1).[1] However, in a probe experiment, no reaction involving **1** and butanethiol occurred under conditions paralleling those described above. Note that competitive conjugate addition does not occur at C3 or C5 because of the lack of conjugation between the associated double bonds and neighboring carbonyl group. The crystallographically defined torsion angle for C5−C6−C7−O3, for example, is 61.0°.

In our view, the assignment of a negative connotation to this otherwise attractive concept is premature. It is plausible, for example, that the reverse Michael step would be facilitated (and therefore made more readily apparent) if one were to begin with the C9 epimer **8**. This single configurational change is estimated on the basis of MM2 calculations to cause **8** to be 6.5 kcal/mol *more strained* than **1**. As a consequence, the synthetic plan developed by us for ultimate arrival at jatrophatrione

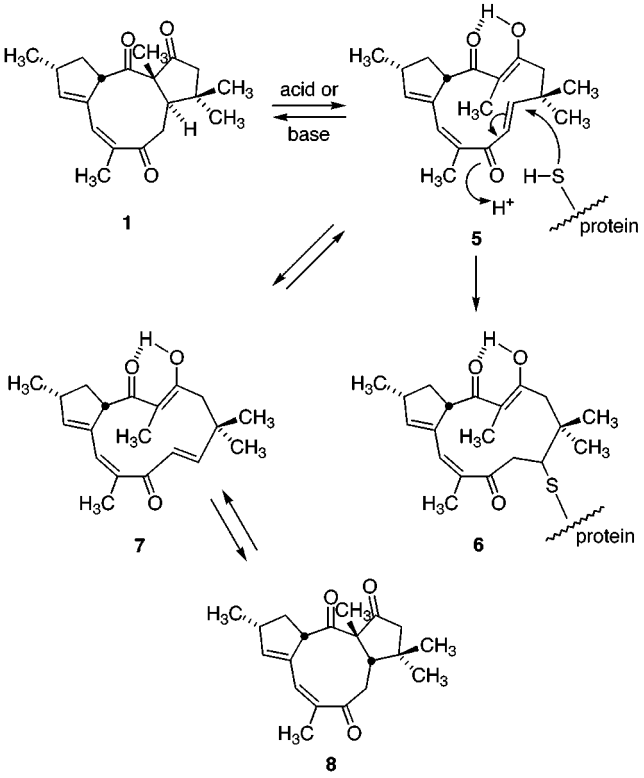


1 **2** **3** **4**

(1) Torrance, S. J.; Wiedhopf, R. M.; Cole, J. R.; Arora, S. K.; Bates, R. B.; Beavers, W. A.; Cutler, R. S. *J. Org. Chem.* **1976**, *41*, 1855.
(2) Villarreal, A. M.; Dominguez, X. A.; Williams, H. J.; Scott, A. I.; Reibenspies, J. *J. Nat. Prod.* **1988**, *51*, 749.
(3) (a) Kupchan, S. M.; Sigel, C. W.; Matz, M. J.; Saenz Renauld, J. A.; Haltiwanger, R. C.; Bryan, R. F. *J. Am. Chem. Soc.* **1970**, *92*, 4476. (b) Haltiwanger, R. C.; Bryan, R. F. *J. Chem. Soc., B* **1971**, 1598. (c) Kupchan, S. M.; Sigel, C. W.; Matz, M. J.; Gilmore, C. J.; Bryan, R. F. *J. Am. Chem. Soc.* **1976**, *98*, 2295.
(4) Taylor, M. D.; Smith, A. B., III.; Furst, G. T.; Gunasekara, S. P.; Bevelle, C. A.; Cordell, G. A.; Farnsworth, N. R.; Kupchan, S. M.; Uchida, H.; Branfman, A. R.; Dailey, R. G., Jr.; Sneden, A. T. *J. Am. Chem. Soc.* **1983**, *105*, 3177.
(5) Lillehaug, J. R.; Kleppe, K.; Sigel, C. W.; Kupchan, S. M. *Biochim. Biophys. Acta* **1973**, *327*, 92.

10.1021/jo9825254 CCC: $18.00
Published on Web 04/30/1999

Scheme 1



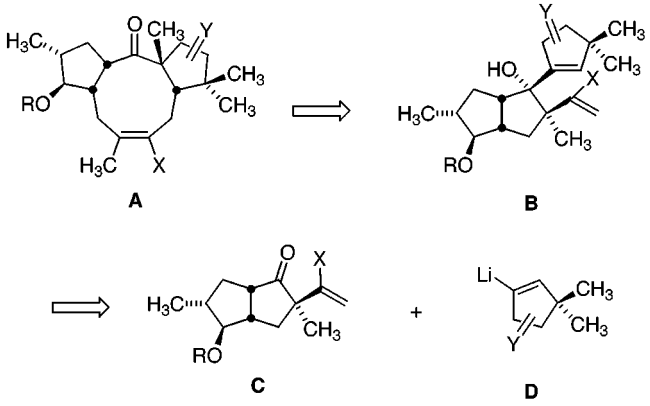
consists of a convergent approach to **8**, which we would hope to equilibrate to the more thermodynamically favored natural epimer by this mechanism. A perceived difficulty with this concept arises from the fact that the *E*-configured C8−C9 double bond in first-formed **7** must be subject to internal rotation about the adjacent single bonds prior to reclosure and delivery of **1**. Molecular mechanics calculations at the MACROMODEL version 5.0 level have provided indication that **5** is only 1.3 kcal/mol less stable than **7**.[6] The feasibility of attaining stereocontrol in tricyclic medium-ring *E*-olefinic precursors to taxusin has earlier been shown to be derivable from this very same theoretical principle.[7]

Herein, we report the details surrounding a projected racemic synthesis in which tactical advantage is taken of anionic sigmatropy in combination with Grob fragmentation technology to deliver the complete tricyclic framework of **8**. The following paper describes a variety of chemical reactions undertaken for the purpose of setting the requisite assortment of functional groups in their proper locale.[8]

Results and Discussion

Retrosynthetic Design. In its most concise form, the retrosynthetic analysis was envisioned to involve the formation of **A** from **B** via charge-accelerated oxy-Cope rearrangement with direct methylation of the enolate anion resulting from this [3,3]-sigmatropic shift (Scheme 2). The substituent X could, of course, be hydrogen. However, if it were an alkoxy group, its role in **A** would be that of an enol ether and a more immediate precursor

Scheme 2



to the carbonyl group in **8**. Several choices are also available for Y. Ideally, it can be envisioned to be part of a β-dicarbonyl subunit as required of the target. However, these circumstances could eventuate in undesirable O-methylation if steric crowding emerges as a serious consideration. Otherwise, a double bond within the five-membered ring could suffice.

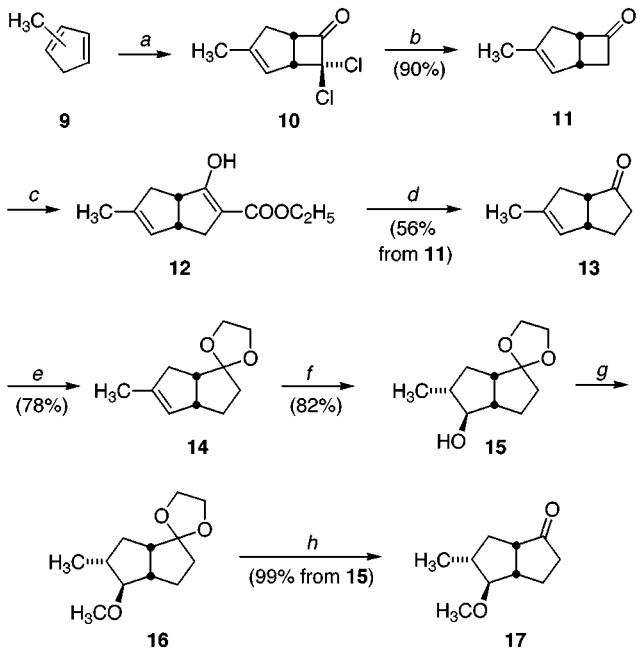
Two assumptions are intrinsic to the proposed **B** → **A** transformation. The first concerns the adoption of a chairlike transition-state arrangement during the electronic reorganization within **B** in accord with precedent derived from simpler structural analogues.[9,10] The second envisions that the entry of the angular methyl group will proceed from the more sterically accessible β face. Unbeknown to us at the outset was the ease and extent to which transannular ring closure can operate within the nine-membered ring of **A** under mild conditions.

Moving further along the retrosynthetic path, we contemplated that **B** could be obtained directly by the coupling of **C** with **D**. The 1,2-addition involved should occur from the less crowded β surface of the folded bicyclo[3.3.0]octanone. Beyond that, X and Y would need to be recalcitrant to attack by a vinyllithium species such as defined in **D**.

Construction of Building Blocks C and D. The strategy derived from the retrosynthetic analysis outlined in Scheme 2 prompted the construction of diquinanes **24** and **29**. Since our original plans called for ultimate base-promoted elimination of the OR substituent in **A**, the methoxy group was selected for the present purposes. Scheme 3 summarizes the synthesis of bicyclic ketone **17** from methylcyclopentadiene (**9**). The initial reaction of monomeric **9** with dichloroketene (generated in situ from dichloroacetyl chloride and triethylamine) gave predominantly the known [2 + 2] adduct **10**.[11] Subsequent dechlorination with zinc metal and ammonium chloride in a methanol−THF solvent system led to **11**[12] and set the stage for regioselective ring expansion of the cyclobutanone ring upon exposure to ethyl diazoacetate and antimony pentachloride.[13] Since the resulting product was a mixture of keto and enol tautomers, viz. **12**, hydrolytic decarboxylation was implemented prior to

(6) We thank John Hofferberth for performing these calculations.
(7) (a) Paquette, L. A.; Zhao, M. *J. Am. Chem. Soc.* **1993**, *115*, 354. (b) Paquette, L. A.; Zhao, M. *J. Am. Chem. Soc.* **1998**, *120*, 5203.
(8) Paquette, L. A.; Edmondson, S. C.; Monck, N.; Rogers. R. D. *J. Org. Chem.* **1999**, *64*, 3255.
(9) Kato, T.; Kondo, H.; Nishino, M.; Tanaka, M.; Hata, G.; Miyake, A. *Bull. Chem. Soc. Jpn.* **1980**, *53*, 2958.
(10) (a) Marvell, E. N.; Whalley, W. *Tetrahedron Lett.* **1970**, 509. (b) Fan, W.; White, J. B. *Tetrahedron Lett.* **1993**, *34*, 957.
(11) Brady, W. T.; Hieble, J. P. *J. Am. Chem. Soc.* **1972**, *94*, 4278.
(12) Grieco, P. A. *J. Org. Chem.* **1972**, *37*, 2363.
(13) For the use of boron trifluoride etherate as the promoter in this reaction, consult: Sugihara, Y.; Sugimura, T.; Murata, I. *J. Am. Chem. Soc.* **1981**, *103*, 6738.

Scheme 3[a]



[a] Key: (a) $Cl_2CHCOCl$, Et_3N, hexanes; (b) Zn, NH_4Cl, CH_3OH, THF, Δ, 48 h; (c) $SbCl_5$, $N_2CHCOOC_2H_5$, CH_2Cl_2, then $NaHCO_3$; (d) K_2CO_3, H_2O, dioxane, Δ, 24 h; (e) *p*-TsOH 2-ethyl-2-methyl 1,3-dioxolane; (f) BH_3·THF, THF, then H_2O_2, NaOH, H_2O; (g) CH_3I, NaH, THF; (h) *p*-TsOH, acetone, H_2O, Δ.

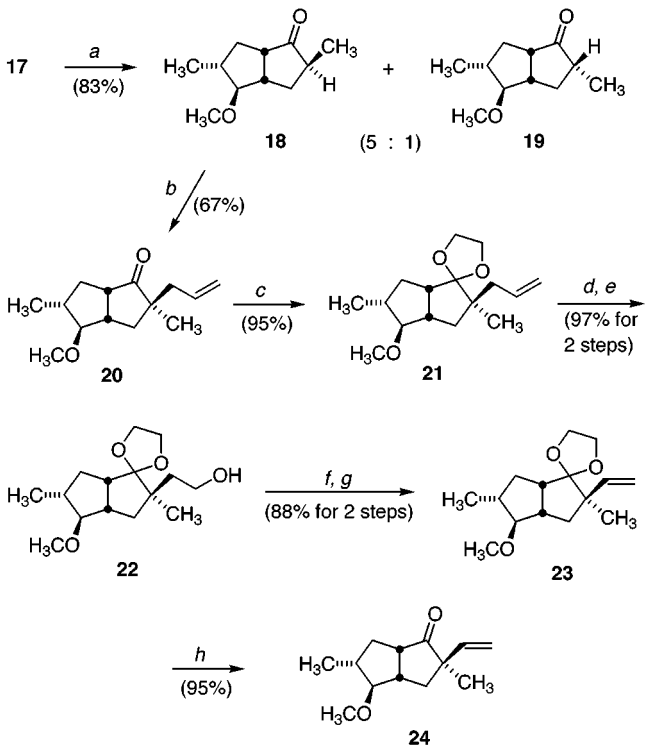
characterization. The small amount of regioisomer was removed during the chromatographic purification at this stage.

Protection of the carbonyl group in **13** was achieved efficiently by the method of Dauben.[14] The regio- and stereoselective transformation of **14** into **15** was readily accomplished with the borane·THF complex. Subsequent *O*-methylation and mild acid hydrolysis gave the desired ketone **17**.

With **17** available in this manner, the stage was set for introduction of the appropriate pair of α substituents. Generation of the less substituted enolate, undertaken with lithium diisopropylamide, made possible the regiocontrolled introduction of a methyl group by reaction with methyl iodide. The β isomer **18** was favored by a factor of 5:1 because of steric factors (Scheme 4). Of the conditions screened for arrival at the geminally allylated intermediate **20**, deprotonation of the **18/19** mixture with potassium hexamethyldisilazide in advance of the introduction of allyl bromide proved most suitable (67%).

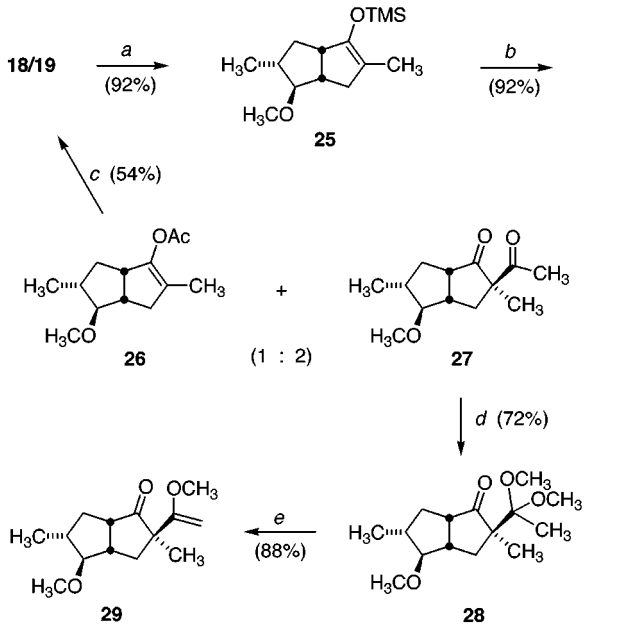
Following ketalization, a four-step procedure for degrading the allyl side chain to a vinyl substituent was undertaken. This operation began with oxidative cleavage to the acetaldehyde level by concomitant exposure of **21** to osmium tetraoxide and sodium periodate.[15] The carbonyl group was reduced with sodium borohydride in advance of 1,2-elimination via the primary *o*-nitrophenylselenide.[16] Hydrolysis of the resulting **23** afforded the targeted **24**.

Scheme 4[a]



[a] Key: (a) LDA, CH_3I, THF, HMPA; (b) KHMDS, allyl bromide, THF; (c) ethylene glycol, *p*-TsOH, C_6H_6; (d) OsO_4, $NaIO_4$, dioxane, H_2O; (e) $NaBH_4$, CH_3OH, CH_2Cl_2; (f) 2-nitrophenyl selenocyanate, $(n\text{-}Bu)_3P$, THF; (g) H_2O_2, H_2O, THF; (h) *p*-TsOH, acetone, H_2O.

Scheme 5[a]



[a] Key: (a) Me_3SiCl, Et_3N, THF; (b) CH_3Li, DME, HMPA, CH_3COCl; (c) KOH, CH_3OH, rt; (d) $HC(OCH_3)_3$, *p*-TsOH, CH_3OH (excess); (e) 450 °C, 0.4 Torr, quartz chips.

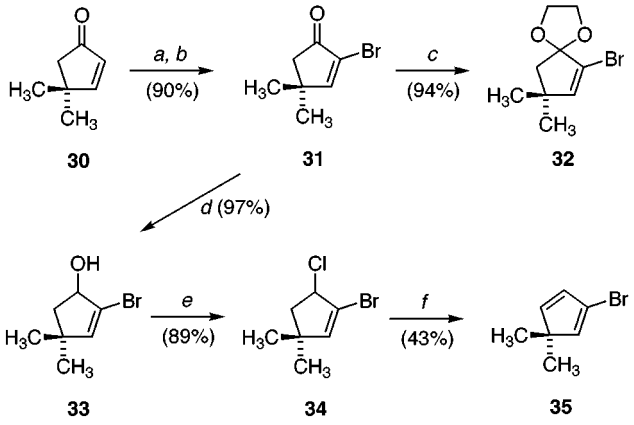
To reach the more highly oxygenated analogue **29**, the **18/19** mixture was first transformed into the corresponding silyl enol ether **25** under thermodynamic conditions (Scheme 5). Regeneration of the enolate anion by treatment with methyllithium followed by trapping with acetyl chloride in the presence of HMPA gave rise to the

(14) Dauben, H. J.; Löken, B.; Ringold, H. J. *J. Am. Chem. Soc.* **1954**, *76*, 1359.

(15) Wee, A. G.; Liu, B. In *Encyclopedia of Reagents for Organic Synthesis*; Paquette, L. A., Editor-in-Chief: John Wiley and Sons: Chichester, 1995; pp 4616−4620.

(16) Iwaoka, M.; Tomoda, S. In *Encyclopedia of Reagents for Organic Synthesis*; Paquette, L. A., Editor-in-Chief; John Wiley and Sons: Chichester, 1995; p 3752.

Scheme 6[a]



[a] Key: (a) Br_2, Et_3N, CCl_4; (b) Zn, CH_3OH, NH_4Cl, THF, Δ; (c) $HOCH_2CH_2OH$, *p*-TsOH, C_6H_6, Δ; (d) $NaBH_4$, CH_3OH, $CeCl_3 \cdot 7H_2O$; (e) CH_3SO_2Cl, Et_3N, CH_2Cl_2; (f) DBU, DMF, Δ.

easily separable isomers **26** and **27** in a ratio of 1:2. Conveniently, enol acetate **26** could be hydrolyzed in methanolic potassium hydroxide and reconverted to **18/19**, now with the α isomer predominating.

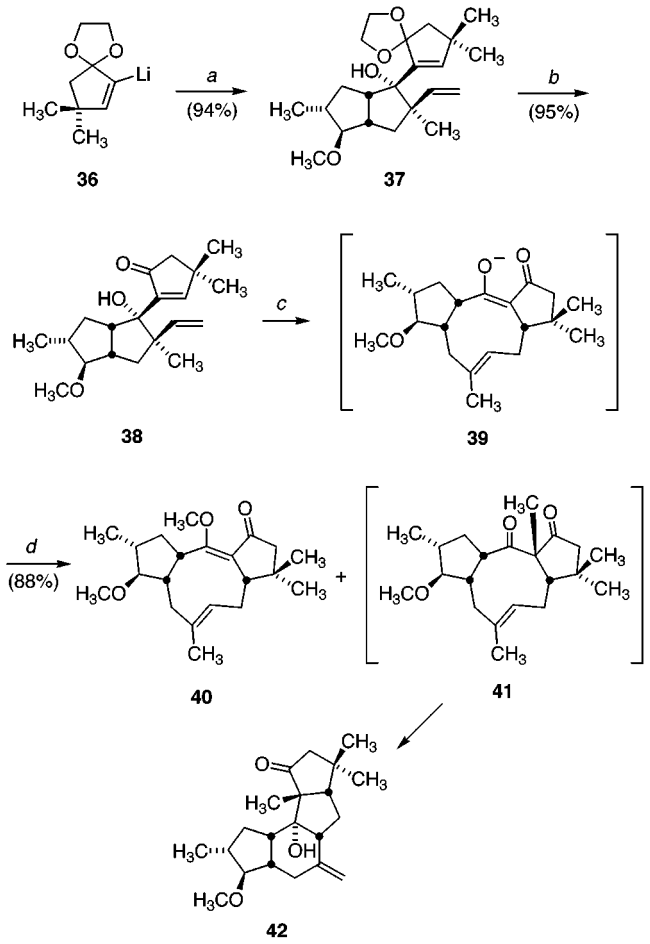
At this juncture, selective protection of the pendant methyl ketone was achieved by means of trimethyl orthoformate in excess methanol containing *p*-toluenesulfonic acid as catalyst. Exposure of the resulting ketal **28** to flash vacuum pyrolysis over quartz chips provided the desired **29** efficiently.

The starting material selected for preparation of the D subunit was the known 4,4-dimethylcyclopentenone (**30**).[17] Careful examination of the retrosynthetic options available to each of the diquinane ketones (see **C**, Scheme 2) suggested that the cyclopentenyl bromides **32** and **35** would best serve our needs (Scheme 6). Both involved initial generation of the bromo enone **31**.[18] Ketal **32** was formed readily without any indication of steric retardation.

Alternatively, Luche reduction[19] of **31** afforded the allyl alcohol **33**, reaction of which with methanesulfonyl chloride and triethylamine led directly to chloride **34**. The latter substance is particularly prone to elimination. Although this process operates on exposure of **34** to sodium iodide in acetone, greater reproducibility was noted with DBU in warm dimethylformamide. The resulting volatile bromocyclopentadiene **35** was routinely utilized as a solution in pentane for the critical coupling step.

Coupling of the C/D Fragments. The anhydrous cerium trichloride-promoted reaction[20] of cyclopentenyllithium **36** with ketone **24** gave **37** in 94% yield without any evidence for serious competing enolization (Scheme 7). The highly stereocontrolled course of this 1,2-addition was a most welcomed development that set the stage admirably for examination of the projected ring expansion. Prior to this event, the ketone carbonyl was unmasked by acidic hydrolysis to deliver **38**.

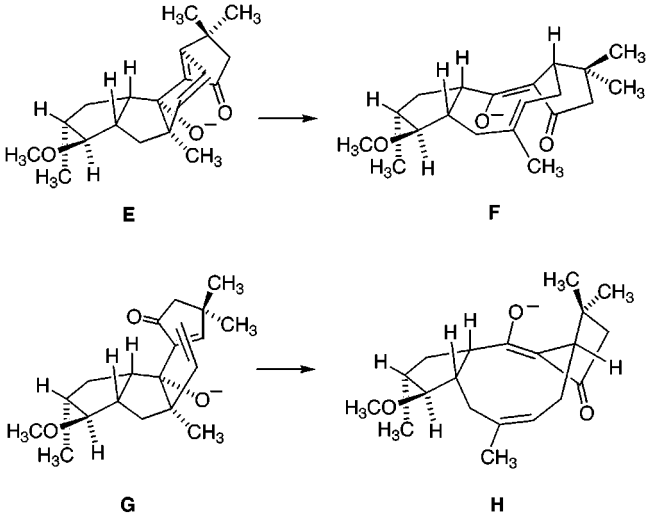
Scheme 7[a]



[a] Key: (a) $CeCl_3$, THF, −79 °C; **24**; (b) *p*-TsOH, acetone, H_2O; (c) KO*t*-Bu, 18-crown-6, THF, 0 °C; (d) CH_3I.

As alluded to earlier, the cisoid juxtapositioning of the two olefinic centers in **38**, while essential to the projected sigmatropic rearrangement, does not of itself guarantee the proper merger of chirality (i.e., matching of configuration at all stereogenic centers) so desirable to the direct acquisition of **8**. On the basis of analogy[9,10,21] and anticipated kinetic and thermodynamic control, the expectation was held by us that advancement to product would occur via chairlike transition state **E** rather than **G** or more congested boatlike alternatives with resultant introduction of two new double bonds as shown in **F** (= **39**). The alternative concerted trajectories such as **G** necessarily culminate in the formation of other double bond isomers typified by **H**. Indeed, when **38** was subjected to the action of potassium *tert*-butoxide and 18-crown-6 in THF at 0 °C for 1 h with subsequent introduction of excess methyl iodide, a 1:1.7 mixture of the anticipated **40** and the unexpected **42** was formed in 88% yield. Quite obviously, the enolate anion **39** had been generated efficiently and transformed via O- and C-alkylation into **40** and **41**, respectively. In our hands, the subsequent transannular ene reaction of **41** to deliver **42** could not be was arrested and must therefore occur quite

(17) Magnus, P. D.; Nobbs, M. S. *Synth. Commun.* **1980**, *10*, 273.
(18) This intermediate has previously been prepared by an alternative means: Wakui, T.; Otsuji, Y.; Imoto, E. *Bull. Chem. Soc. Jpn.* **1974**, *47*, 2267.
(19) (a) Luche, J.-L. *J. Am. Chem. Soc.* **1978**, *100*, 2226. (b) Luche, J.-L.; Rodriguez-Hahn, L.; Crabbe, P. *J. Chem. Soc., Chem. Commun.* **1978**, 601.
(20) Paquette, L. A. In *Encyclopedia of Reagents for Organic Synthesis*; Paquette, L. A., Editor-in-Chief: John Wiley and Sons: Chichester, 1995; p 1031.
(21) (a) Paquette, L. A. *Tetrahedron* **1997**, *53*, 13971. (b) Paquette, L. A. *Angew. Chem., Int. Ed. Engl.* **1990**, *29*, 609.



E **F** **G** **H**

rapidly.[22] The relative stereochemistry of **40** was assigned on the basis of the absence of NOE interaction between the methyl group at C6 and vinyl proton at C7 and by analogy to related products prepared in this and the related report.[8] The structural character of **42** was rigorously established by X-ray crystallographic analysis (Figure 1). The transoid B/C ring stereochemistry necessitates that the geometry of the double bond in **39**−**41** be *E* as shown.[23−27]

Although use of the anionic oxy-Cope rearrangement as a device for efficiently producing **40** and **42** from building blocks **24** and **36** had been demonstrated, the utility of tetracyclic product **42** was considered to be less than optimal. Although a variety of possibilities for central bond cleavage in this product can be identified, the steps needed to accomplish this chemistry would lengthen the synthesis appreciably. For these reasons, attention was focused instead in Scheme 8.

Adaptation of the cerium(III) chloride-mediated reaction conditions developed earlier to the coupling of **43** with **29** furnished **44** in 82% yield. The challenge of performing the oxy-Cope rearrangement/methylation step properly required only that molecular oxygen be stringently excluded in order to curtail adventitious oxygenation of enolate anion **45**.[28] In view of the excellent combined yield of **47** (64%) and **48** (34%) realized in this step, it follows that **45** experiences methylation exclusively at C_α and from the β direction to generate **46**. Once formed, **46** experiences transannular ene cyclization along a trajectory totally different from that followed by **41**. In the earlier example, proton loss was incurred from the extra-annular methyl substituent. In contrast, the kinetically favored ene reaction in **46** operates along that intra-annular pathway involving the allylic ring methylene adjacent to the methoxy group. In light of the ease with which **47** is transformed into **48** under conditions of acid hydrolysis, the real possibility exists that **48** is generated during neutralization of the strongly basic reaction medium.

Initially, **48** was difficult to characterize due to its fluxional behavior, with interconversion between two or

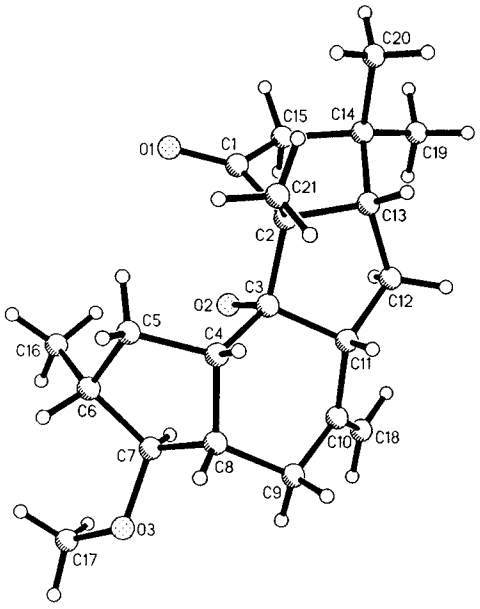
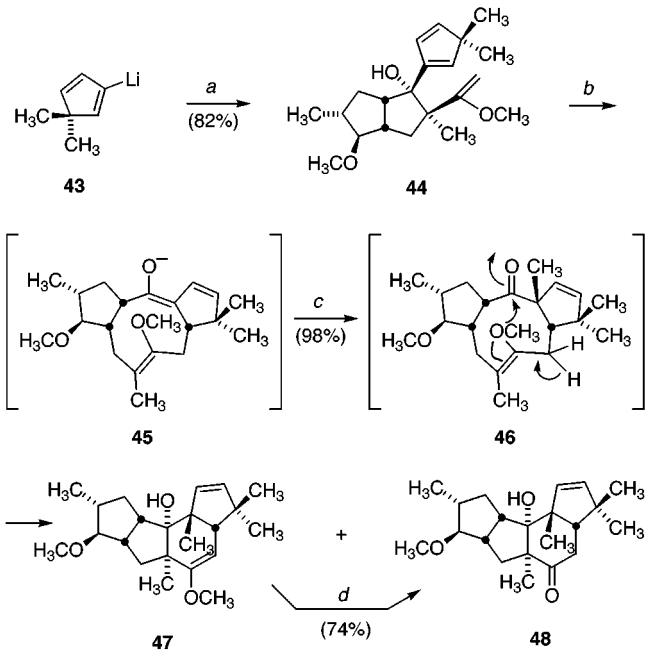


Figure 1. Computer-generated perspective drawing of **42** as determined by X-ray crystallography.

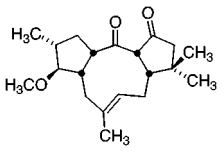
Scheme 8[a]



43 **44** **45** **46** **47** **48**

[a] Key: (a) $CeCl_3$, THF, −70 °C; **29**; (b) KO*t*-Bu, 18-crown-6, THF, 0 °C; (c) CH_3I; (d) *p*-TsOH, acetone, H_2O, Δ.

(22) The unwanted transannular ene reaction can be skirted if enolate anion **39** is quenched directly with saturated NH_4Cl solution at 0 °C. Under these circumstances, **i** was obtained in 92% yield. (Sun, L.-Q. Unpublished results).



i

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(24) Wender, P. A.; Hubbs, J. C. *J. Org. Chem.* **1980**, *45*, 365.
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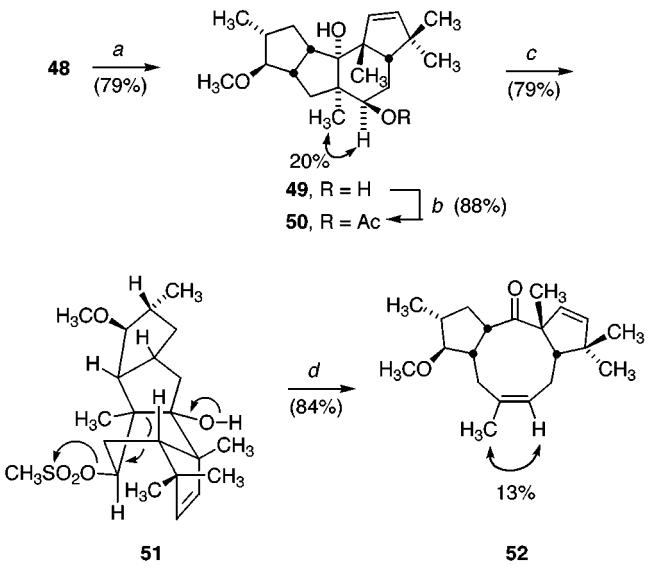
(26) (a) Srinivasan, R.; Rajagopalan, K. *Tetrahedron Lett.* **1998**, *39*, 4133. (b) Janardhanam, S.; Devan, B.; Rajagopalan, K. *Tetrahedron Lett.* **1993**, *34*, 6761. (c) Balakumar, A.; Janardhanam, S.; Rajagopalan, K. *J. Org. Chem.* **1993**, *58*, 5482.
(27) (a) Shanmugam, P. Rajagopalan, K. *Tetrahedron* **1996**, *52*, 7737. (b) Shanmugam, P.; Devan, B.; Srinivasan, R.; Rajagopalan, K. *Tetrahedron* **1997**, *53*, 12637.
(28) Paquette, L. A.; DeRussy, D. T.; Pegg, N. A.; Taylor, R. T.; Zydowsky, T. M. *J. Org. Chem.* **1989**, *54*, 4576.

Scheme 9[a]



[a] Key: (a) $LiAlH_4$, ether, 0 °C; (b) Ac_2O, Et_3N, DMAP, CH_2Cl_2; (c) CH_3SO_2Cl, Et_3N, CH_2Cl_2; (d) KO*t*-Bu, *t*-BuOH, 40 °C.

more conformations occurring slowly on the NMR time scale at room temperature. One consequence of this behavior is the appearance of the olefinic protons as a broad singlet instead of two sets of doublets. However, warming the sample to 77 °C was adequate to record a first-order spectrum.

Product **48** was recognized to be a β-hydroxy ketone and accordingly to be a substrate particularly well suited to a Grob fragmentation sequence.[29,30] To this end, **48** was reduced with lithium aluminum hydride in ether to generate a carbinol mixture with 10:1 selectivity (Scheme 9). Since olefin geometry in the impending Grob product is directly linked to the stereochemistry of the alcohol, it was important to rigorously establish that **49** was the major constituent. Although the ^{1}H NMR spectrum of **49** was too poorly resolved to permit unequivocal structural assignment, conversion to the corresponding acetate **50** solved this problem. The application of HETCOR and long-range C−H correlation techniques allowed each of the four methyl groups to be distinguished. Further, diagnostic NOE enhancements such as that shown on the structural formula revealed the hydroxyl to be oriented equatorially as a consequence of axial hydride delivery.

Following the conversion of **49** to its mesylate **51**under standard conditions, treatment with potassium *tert*-butoxide in *tert*-butyl alcohol gave rise to **52** in excellent yield. NOE enhancements confirmed the predicted *Z* configuration of the double bond resident in ring B. The stereoelectronic requirements for the Grob fragmentation dictate that the leaving group be antiplanar to the σ-bond experiencing scission. The requisite reactive conformation must adopt a boat geometry to satisfy this requirement as shown in **51**. As a consequence, the double bond newly introduced in **52** must have a *Z* configuration. The significant NOE interaction depicted in the structural formula corroborates this conclusion.

The chemistry detailed herein defines a concise convergent strategy for construction of the [5.9.5] tricyclic framework of jatrophatrione. More specifically, the route is very well tailored to cis alignment of the four ring juncture positions as required for the C9 epimer. At least two of the more advanced intermediates are expected to play a crucial role in making possible a de novo synthesis of **1**. Included in this group are the tetracyclic aldol **48** and the tricyclic enone **52**. The next step involved development of the chemistry of these compounds. This theme constitutes the substance of the accompanying report.[8]

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 mass 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.

***cis*-3-Methylbicyclo[3.2.0]hept-2-en-6-one (11).** To a mechanically stirred solution of **10**[11] (151 g, 0.79 mol) in 2400 mL of THF and 600 mL of methanol at 0 °C were added NH_4Cl (169 g, 3.16 mol) and activated zinc dust (207 g, 3.16 mol) in portions over 1 h. The suspension was warmed to room temperature and refluxed for 48 h. The solution was cooled to room temperature, diluted with CH_2Cl_2, filtered, and concentrated. Distillation (100 °C, 15 Torr) afforded 79.2 g (82%) of **11** as a pale yellow oil: IR (neat, cm^{-1}) 1750, 1680; ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.39 (m, 1 H), 3.81 (m, 1 H), 3.37 (m, 1 H), 3.21 (ddd, J = 17.2, 8.4, 2.9 Hz, 1 H), 2.62−2.37 (m, 3 H), 1.71 (s, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 213.3, 142.4, 126.6, 62.7, 54.0, 38.8, 37.0, 16.3; HRMS *m*/*z* ($M^+ - C_2H_2O$) calcd 80.0626, obsd 80.0623.

***cis*-3,3a,6,6a-Tetrahydro-5-methyl-1(2*H*)-pentalenone (13).** To a mechanically stirred solution of **11** (140 g, 1.14 mol) in 4000 mL of CH_2Cl_2 at −78 °C was added 1.0 M SbF_5 in CH_2Cl_2 (80 mL, 0.08 mol). The amber solution was stirred for 20 min before ethyl diazoacetate (202 g, 1.77 mol) was added dropwise over a period of 1.5 h. The mixture was stirred at −78 °C for 4 h, allowed to warm slowly to 0 °C, and poured into a vigorously stirred saturated solution of $NaHCO_3$ (2 L). The yellow suspension was stirred at room temperature for 14 h, separated, washed with water and brine, dried, and concentrated to afford an approximate 2:1 mixture of the β-keto ester and enol ester **12** as a cloudy orange oil. The crude mixture was dissolved in dioxane (2.4 L) and water (0.7 L), K_2CO_3 (400 g, 2.89 mol) was added, and the mixture was refluxed for 24 h. The red-black solution was cooled, diluted with ether, and washed with brine. The aqueous layer was extracted with ether, and the combined organic layers were dried, filtered, and concentrated. The residue was purified by flash chromatography on silica gel (elution with 39:1 petroleum ether/ethyl acetate) to give **13** (88.7 g, 56%) as a light yellow oil: IR (neat, cm^{-1}) 1730; ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.20 (s, 1 H), 3.49 (br s, 1 H), 2.67−1.89 (series of m, 7 H), 1.69 (s, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 224.2, 141.1, 127.5, 50.2, 47.7, 41.2, 36.3, 25.5, 16.2; HRMS *m*/*z* (M^+) calcd 136.0888, obsd 136.0884.

Anal. Calcd for $C_9H_{12}O$: C, 79.37; H, 8.88. Found: C, 79.05; H, 8.93.

***cis*-3′,3′a,6′,6′a-Tetrahydro-5′-methylspiro[1,3-dioxolane-2,1′(2′*H*)-pentalene] (14).** A solution of **13** (22.0 g, 0.161 mol) in 100 mL of 2-ethyl-2-methyl-1,3-dioxolane was treated with *p*-toluenesulfonic acid (5.0 g, 26 mmol), stirred for 1 h at room temperature, diluted with 2000 mL of ether, washed with saturated $NaHCO_3$ solution and brine, dried, filtered, and concentrated. The crude oil was purified by column chromatography (silica gel, elution with 2.5% ethyl acetate in petro-

(29) (a) Corey, E. J.; Mitra, R. B.; Uda, H. *J. Am. Chem. Soc.* **1963**, *85*, 362. (b) Corey, E. J.; Mitra, R. B.; Uda, H. *J. Am. Chem. Soc.* **1964**, *86*, 485.

(30) Tanabe, M.; Crowe, D. F. *Tetrahedron Lett.* **1964**, 2955.

leum ether) to give 19.5 g (67%) of **14** as a mobile oil: IR (neat, cm^{-1}) 1445, 1330, 1205; ^1H NMR (300 MHz, $CDCl_3$) δ 5.08 (t, J = 1.7 Hz, 1 H), 3.89 (series of m, 4 H), 3.21 (m, 1 H), 2.56 (m, 1 H), 2.34 (s, 2 H), 1.83−1.55 (m, 3 H), 1.67 (s, 3 H), 1.40 (m, 1 H); ^{13}C NMR (75 MHz, C_6D_6) δ 139.5, 127.8, 119.1, 64.8, 63.6, 49.2, 48.1, 39.6, 33.1, 28.9, 16.2; HRMS m/z (M^+) calcd 180.1550, obsd 180.1551.

(3′a*S,4′*S**,5′*R**,6′a*S**)-Hexahydro-4′-hydroxy-5′-methylspiro[1,3-dioxolane-2,1′(2′*H*)-pentalene] (15).** A solution of **14** (13.0 g, 72.2 mmol) in 300 mL of dry THF at 0 °C was treated with BH_3·THF (144 mL, 1.0 M in THF). The solution was stirred at 0 °C, treated sequentially with H_2O (30 mL), 6 N NaOH (150 mL), and 30% H_2O_2 solution (150 mL), warmed to room temperature, and stirred overnight prior to dilution with ether and washing with water and brine. The organic phase was dried, filtered, and concentrated. The crude oil was purified by flash chromatography on silica gel (elution with 1:1 petroleum ether in ethyl acetate) to afford 12.4 g (87%) of **15** as a colorless viscous oil; IR (neat, cm^{-1}) 3400, 1455, 1340; ^1H NMR (300 MHz, $CDCl_3$) δ 3.85 (m, 4 H), 3.18 (dd, J = 9.4, 7.3 Hz, 1 H), 2.40−2.15 (m, 2 H), 1.90−1.49 (m, 5 H), 1.46−1.34 (m, 2 H), 1.27−1.10 (m, 1 H), 1.01 (d, J = 6.3 Hz, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 118.1, 85.7, 64.5, 63.5, 49.3, 46.1, 42.7, 33.2, 33.0, 26.5, 16.4; HRMS m/z (M^+) calcd 198.1256, obsd 198.1269.

(3a*S,4*S**,5*R**,6a*S**)-Hexahydro-4-methoxy-5-methyl-1(2*H*)-pentalenone (17).** A slurry of NaH (7.82 g, 326 mmol) in 200 mL of dry THF at 0 °C was treated with **15** (29.37 g, 148 mmol) dissolved in 300 mL of dry THF, heated to reflux for 30 min, cooled to 0 °C, and treated with methyl iodide (16.8 mL, 0.266 mmol) over 30 min. The reaction mixture was allowed to warm to room temperature and stirred for 3 h, at which point TLC indicated the reaction to be complete. The reaction mixture was carefully quenched with water at 0 °C and concentrated. The resulting aqueous mixture was extracted with ether and the organic phases were combined and washed with brine, dried, filtered, and concentrated. The crude colorless oily **16** was used without further purification: IR (neat, cm^{-1}) 1748; ^1H NMR (300 MHz, $CDCl_3$) δ 3.84 (m, 4 H), 3.36 (s, 3 H), 2.88 (dd, J = 8.8, 5.9 Hz, 1 H), 2.38 (m, 2 H), 1.96−1.53 (series of m, 6 H), 1.19−0.95 (m, 1 H), 1.02 (d, J = 6.1 Hz, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 117.9, 95.4, 64.6, 63.7, 57.8, 47.1, 46.9, 41.3, 33.6, 33.5, 28.4, 17.2; HRMS m/z (M^+) calcd 212.1412, obsd 212.1410.

A solution of **16** dissolved in 500 mL of acetone and 50 mL of water was treated with *p*-toluenesulfonic acid (1.5 g), and the reaction mixture was heated to reflux for 16 h, cooled to room temperature, and concentrated. The residue was taken up in petroleum ether, washed with saturated $NaHCO_3$ solution and brine, dried, filtered, and concentrated. The crude oil was purified by flash chromatography on silica gel (10% ethyl acetate in petroleum ether) to give 24.58 g (99% over two steps) of **17** as a colorless oil: IR (neat, cm^{-1}) 1730, 1455, 1405, 1370; ^1H NMR (300 MHz, $CDCl_3$) δ 3.42 (s, 3 H), 3.05 (dd, J = 7.8, 5.1 Hz, 1 H), 2.65 (m, 2 H), 2.45−1.76 (series of m, 6 H), 1.23 (m, 1 H), 1.05 (d, J = 6.6 Hz, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 221.1, 94.2, 57.8, 49.1, 46.9, 41.9, 37.2, 33.9, 25.3, 18.0; HRMS m/z (M^+) calcd 168.1151, obsd 168.1151.

Anal. Calcd for $C_{10}H_{16}O_2$: C, 71.39; H, 9.59. Found: C, 71.27; H, 9.57.

(2*S,3a*S**,4*S**,5*R**,6a*S**)-Hexahydro-4-methoxy-2,5-dimethyl-1(2*H*)-pentalenone (18) and (2*R**,3a*S**,4*S**,5*R**,6a*S**)-Hexahydro-4-methoxy-2,5-dimethyl-1(2*H*)-pentalenone (19).** To a mechanically stirred solution of diisopropylamine (47.0 mL, 335 mmol) dissolved in 1000 mL of dry THF at −78 °C was added 1.4 M *n*-butyllithium in hexanes (225 mL, 315 mmol), and the resulting solution was warmed to 0 °C and stirred for 20 min. Ketone **17** (48.1 g, 286 mmol) dissolved in 100 mL of THF was added dropwise to this solution over 20 min at −78 °C, and the mixture was stirred for 1 h at this temperature. HMPA (100 mL, 574 mmol) followed by methyl iodide (54 mL, 856 mmol) was added to the solution, and the mixture was warmed to room temperature, stirred for 23 h, quenched with water, diluted with ether, washed with brine, dried, and concentrated. The residue was purified by flash chromatography on silica gel (elution with 19:1 petroleum ether in ethyl acetate) to give a light yellow oil (43.4 g, 83%) consisting of a 5:1 mixture of **18** and **19** (^1H NMR analysis). For the major isomer, which was obtained pure by rechromatography: IR (neat, cm^{-1}) 1725; ^1H NMR (300 MHz, $CDCl_3$) δ 3.46 (s, 3 H), 3.04 (dd, J = 8.7, 6.7 Hz, 1 H), 2.69−1.88 (series of m, 6 H), 1.73 (m, 2 H), 1.06 (d, J = 6.9 Hz, 3 H), 1.04 (d, J = 6.5 Hz, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 222.9, 93.7, 58.2, 48.1, 44.4, 41.7, 40.5, 34.8, 33.9, 17.6, 14.1; HRMS m/z (M^+) calcd 182.1307, obsd 182.1306.

(2*R,3a*R**,4*R**,5*S**,6a*R**)-2-Allylhexahydro-4-methoxy-2,5-dimethyl-1(2*H*)-pentalenone (20).** To a solution of **18** (11.7 g, 64.2 mmol) and HMPA (13.4 mL, 77.0 mmol) in THF (100 mL) at −78 °C was added potassium hexamethyldisilazide (134.8 mL of 0.5 M in toluene, 67.4 mmol). The reaction mixture was allowed to warm slowly to −10 °C during 1 h and recooled to −78 °C prior to the introduction of allyl bromide (10 mL, 128 mmol). After overnight stirring at room temperature, water was added, and the organic phase was washed with brine, dried, and concentrated. Flash chromatography of the residue on silica gel (elution with 5% ethyl acetate in hexanes) gave 9.5 g (67%) of **20**: IR (neat, cm^{-1}) 1732; ^1H NMR (300 MHz, $CDCl_3$) δ 5.71−5.61 (m, 1 H), 5.10−5.01 (m, 2 H), 3.36 (s, 3 H), 3.07 (dd, J = 6.8, 4.1 Hz, 1 H), 2.89 (ABq, J = 19.4, 9.5 Hz, 1 H), 2.59 (dq, J = 9.0, 4.1 Hz, 1 H), 2.30 (dd, J = 13.5, 8.1 Hz, 1 H), 2.26−1.98 (m, 4 H), 1.50 (dd, J = 13.6, 8.8 Hz, 1 H), 1.33−1.22 (m, 1 H), 1.05 (s, 3 H), 1.02 (d, J = 6.6 Hz, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 222.7, 133.1, 118.5, 96.2, 57.7, 51.5, 49.6, 43.0, 42.5, 42.2, 40.5, 34.0, 22.1, 18.1; HRMS m/z (M^+) calcd 222.1620, obsd 222.1626.

(2′*R,3′a*R**,4′*R**,5′*S**,6′a*R**)-2-Allylhexahydro-4′-methoxy-2′,5′-dimethylspiro[1,3-dioxolane-2,1′(2′*H*)-pentalene] (21).** A solution of **20** (2.42 g, 10.9 mmol), ethylene glycol (3.38 g, 54.5 mmol), and *p*-toluenesulfonic acid (121 mg) in benzene (100 mL) was refluxed under a Dean−Stark trap for 24 h, cooled to room temperature, quenched with saturated $NaHCO_3$ solution, washed with brine, dried, and freed of solvent. Purification of the residue by flash chromatography on silica gel (elution with 5% ethyl acetate in hexanes) afforded 2.75 g (95%) of **21**: IR (neat, cm^{-1}) 1732; ^1H NMR (300 MHz, $CDCl_3$) δ 5.85−5.72 (m, 1 H), 5.06−4.98 (m, 2 H), 3.93−3.77 (m, 4 H), 3.31 (s, 3 H), 2.91 (dd, J = 9.5, 7.2 Hz, 1 H), 2.74 (dt, J = 12.3, 9.0 Hz, 1 H), 2.33−2.04 (m, 3 H), 1.97−1.84 (m, 2 H), 1.69−1.60 (m, 1 H), 1.44−1.30 (m, 2 H), 1.01 (d, J = 6.4 Hz, 3 H), 0.87 (s, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 135.4, 117.9, 117.0, 95.2, 65.6, 65.3, 57.9, 51.2, 47.6, 44.8, 43.2, 40.9, 39.8, 30.4, 18.4, 17.4; HRMS m/z (M^+) calcd 266.1882, obsd 266.1884.

(2′*R,3′a*S**,4′*S**,5′*R**,6′a*R**)-Hexahydro-4′-methoxy-2′,5′-dimethylspiro[1,3-dioxolane-2,1′(2′*H*)-pentalene]-2′-ethanol (22).** A mixture of **21** (2.75 g, 10.3 mmol), osmium tetraoxide (1 mL of 0.5 M in pyridine, 0.5 mmol), and sodium metaperiodate (4.42 g, 20.7 mmol) in dioxane (25 mL) and water (25 mL) was stirred for 24 h, filtered, and concentrated. The residue was taken up in ethyl acetate, washed with brine, dried, and freed of solvent prior to chromatography on silica gel (elution with 10% ethyl acetate in hexanes). There was obtained 2.72 g (98%) of the aldehyde: IR (neat, cm^{-1}) 1717; ^1H NMR (300 MHz, $CDCl_3$) δ 9.80 (m, 1 H), 3.96−3.78 (m, 4 H), 3.32 (s, 3 H), 2.95 (dd, J = 9.3, 7.2 Hz, 1 H), 2.75 (dt, J = 12.2, 9.0 Hz, 1 H), 2.59 (dd, J = 15.1, 3.2 Hz, 1 H), 2.42−2.29 (m, 1 H), 2.23 (dd, J = 15.1, 2.7 Hz, 1 H), 2.01 (dd, J = 13.1, 8.6 Hz, 1 H), 1.95−1.85 (m, 1 H), 1.73−1.63 (m, 1 H), 1.58 (dd, J = 13.1, 8.6 Hz, 1 H), 1.38 (dt, J = 12.6, 9.0 Hz, 1 H), 1.13 (s, 3 H), 1.03 (d, J = 6.5 Hz, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 208, 117.3, 95.1, 65.9, 65.4, 58.0, 50.9, 50.1, 47.4, 44.8, 43.2, 43.0, 30.4, 19.5, 17.3; HRMS m/z (M^+) calcd 268.1675, obsd 268.1677.

The above aldehyde (1.07 g, 4.0 mmol) was dissolved in CH_2Cl_2 (5 mL) and methanol (5 mL), cooled to 0 °C, treated carefully with $NaBH_4$ (303 mg, 8.0 mmol), stirred for 1 h, quenched with saturated NH_4Cl solution, and concentrated in vacuo. The residue was taken up in ethyl acetate, washed with brine, dried, and freed of solvent. Chromatography of the residue on silica gel (elution with 50% ethyl acetate in hexanes)

afforded 1.07 g (98%) of **22**: IR (neat, cm^{-1}) 3415, 1455; ^1H NMR (300 MHz, $CDCl_3$) δ 3.98−3.58 (m, 6 H), 3.32 (s, 3 H), 2.93 (dd, J = 9.5, 7.4 Hz, 1 H), 2.82 (dt, J = 12.1, 9.0 Hz, 1 H), 2.41−2.29 (m, 1 H), 1.98−1.83 (m, 3 H), 1.71−1.62 (m, 1 H), 1.58−1.49 (m, 2 H), 1.38 (dd, J = 12.5, 8.9 Hz, 1 H), 1.02 (d, J = 6.4 Hz, 3 H), 0.96 (s, 3 H) (OH not observed); ^{13}C NMR (75 MHz, $CDCl_3$) δ 117.8, 95.1, 65.6, 59.4, 57.9, 50.4, 47.2, 44.7, 44.4, 43.1, 40.0, 30.2, 18.3, 17.3; HRMS m/z (M^+) calcd 270.1831, obsd 270.1831.

(2′*R,3′a*S**,4′*S**,5′*R**,6′a*S**)-Hexahydro-4′-methoxy-2′,5′-dimethyl-2′-vinylspiro[1,3-dioxolane-2,1′(2′*H*)-pentalene] (23).** To a solution of **22** (2.68 g, 10 mmol) and 2-nitrophenylselenocyanate (2.95 g, 13 mmol) in THF (100 mL) was added a solution of tri-*n*-butylphosphine (2.76 g, 13 mmol) in THF (20 mL). The mixture was stirred for 16 h, freed of THF, and passed through silica gel (5 → 20% ethyl acetate in hexanes) to give 4.5 g of crude selenide, which was dissolved in THF (50 mL), cooled to 0 °C, and treated with 30% hydrogen peroxide (10 mL). The reaction mixture was slowly warmed to room temperature, stirred overnight, and freed of THF below 25 °C. The residual aqueous phase was extracted with ethyl acetate, washed in sequence with 6 N sodium hydroxide solution, water, saturated $NaHSO_3$ solution, and brine, and then dried and concentrated. Purification of the residue by chromatography on silica gel (elution with 10% ethyl acetate in hexanes) furnished 2.20 g (88%) of **23**: IR (neat, cm^{-1}) 1456, 1122; ^1H NMR (300 MHz, $CDCl_3$) δ 6.05 (dd, J = 17.6, 10.8 Hz, 1 H), 5.12 (dd, J = 17.6, 1.3 Hz, 1 H), 5.04 (dd, J = 10.8, 1.3 Hz, 1 H), 3.99−3.79 (m, 4 H), 3.36 (s, 3 H), 2.95 (dd, J = 9.6, 7.8 Hz, 1 H), 2.68 (dt, J = 12.3, 8.8 Hz, 1 H), 2.37 (dt, J = 12.3, 8.5 Hz, 1 H), 2.11 (dd, J = 12.8, 8.6 Hz, 1 H), 1.96−1.84 (m, 1 H), 1.70−1.58 (m, 2 H), 1.30 (dt, J = 12.4, 8.4 Hz, 1 H), 1.03 (d, J = 6.5 Hz, 3 H), 1.00 (s, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 143.0, 117.5, 111.9, 95.1, 65.9, 65.6, 58.0, 54.5, 47.3, 44.8, 43.1, 41.0, 29.8, 19.5, 17.4; HRMS m/z (M^+) calcd 252.1725, obsd 252.1724.

(2*R,3a*S**,4*S**,5*R**,6a*S**)-2-Hexahydro-4-methoxy-2,5-dimethyl-2-vinyl-1(2*H*)-pentalenone (24).** A solution of **23** (2.20 g, 8.7 mmol) and *p*-toluenesulfonic acid (88 mg, 0.46 mmol) in acetone (50 mL) and water (5 mL) was refluxed for 24 h, cooled to room temperature, and worked up in the predescribed manner for **17** to provide 1.73 g (95%) of **24**: IR (neat, cm^{-1}) 1737; ^1H NMR (300 MHz, $CDCl_3$) δ 5.71 (dd, J = 17.2, 10.7 Hz, 1 H), 5.10 (d, J = 10.7 Hz, 1 H), 5.05 (d, J = 17.2 Hz, 1 H), 3.37 (s, 3 H), 3.10 (dd, J = 6.5, 3.7 Hz, 1 H), 2.95 (q, J = 9.6 Hz, 1 H), 2.64 (dq, J = 10.1, 3.7 Hz, 1 H), 2.44 (dd, J = 12.9, 8.7 Hz, 1 H), 2.15−2.00 (m, 2 H), 1.57 (dd, J = 13.3, 9.7 Hz, 1 H), 1.33−1.21 (m, 1 H), 1.15 (s, 3 H), 1.03 (d, J = 6.6 Hz, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 219.5, 140.5, 114.3, 96.1, 57.6, 55.7, 49.2, 43.0, 42.8, 41.3, 33.7, 22.4, 18.1; HRMS m/z (M^+) calcd 208.1663, obsd 208.1680.

Anal. Calcd for $C_{13}H_{20}O_2$: C, 74.96; H, 9.68. Found: C, 75.06; H, 9.71.

[[(3a*S,4*S**,5*R**,6a*S**)-3,3a,4,5,6,6a-Hexahydro-4-methoxy-2,5-dimethyl-1-pentalenyl]oxy]trimethylsilane (25).** Ketones **18** and **19** (7.2 g, 40 mmol) dissolved in 150 mL of dry DMF and 90 mL of triethylamine were treated with 90 mL of chlorotrimethylsilane, and the reaction mixture was heated to 85 °C for 23 h. The solution was cooled to room temperature, and excess silyl chloride was blown off in a stream of air. The reaction mixture was diluted with ether, washed with water, dried, filtered, and concentrated. The crude material was filtered through a pad of silica gel (elution with petroleum ether) to give 9.3 g (92%) of **25** as a colorless oil: ^1H NMR (300 MHz, $CDCl_3$) δ 3.39 (s, 3 H), 2.96 (m, 1 H), 2.58−1.83 (series of m, 5 H), 1.49 (d, J = 0.89 Hz, 3 H), 1.20−0.98 (m, 2 H), 1.02 (d, J = 6.4 Hz, 3 H), 0.17 (s, 9 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 149.0, 110.8, 96.3, 57.9, 47.3, 43.8, 40.9, 39.1, 36.1, 17.6, 12.0, 0.6 (3 C); HRMS m/z (M^+) calcd 254.1702, obsd 254.1692.

(2*S,3a*R**,4*R**,5*S**,6a*R**)-2-Acetylhexahydro-4-methoxy-2,5-dimethyl-1(2*H*)-pentalenone (27).** A solution of **25** (59.2 g, 223 mmol) dissolved in 350 mL of dry DME at 0 °C was treated with methyllithium (233 mL, 1.5 M in ether, 350 mmol), and the resulting solution was warmed to room temperature and stirred for 3 h. After the addition of HMPA (120 mL, 690 mmol), the mixture was cooled to −78 °C, and acetyl chloride (25.0 mL, 352 mmol) was introduced. The temperature was allowed to warm slowly to 20 °C, and the reaction mixture was stirred for 21 h, quenched with water, diluted with ether, washed with water and brine, dried, and concentrated. The crude oil was purified by flash chromatography on silica gel (elution with 10% ethyl acetate in petroleum ether) to give **26** (17.3 g, 33%) and **27** (34.6 g, 66%) as light yellow oils.

For **26**: IR ($CHCl_3$, cm^{-1}) 1727, 1703; ^1H NMR (300 MHz, $CDCl_3$) δ 3.40 (s, 3 H), 3.35−3.29 (m, 1 H), 3.03 (t, J = 6.9 Hz, 1 H), 2.70−2.60 (m, 1 H), 2.56−2.46 (m, 1 H), 2.20 (br d, J = 16.4 Hz, 1 H), 2.15 (s, 3 H), 1.98−1.83 (m, 2 H), 1.51 (t, J = 0.9 Hz, 3 H), 1.15−1.05 (m, 1 H), 1.02 (d, J = 6.1 Hz, 3 H); ^{13}C NMR (75 MHz,$CDCl_3$) δ 168.6, 146.4, 120.4, 96.1, 57.9, 45.3, 44.1, 40.8, 39.2, 35.6, 20.7, 17.5, 12.1; HRMS m/z (M^+) calcd 224.1413, obsd 224.1408.

For **27**: IR (neat, cm^{-1}) 1730, 1695; ^1H NMR (300 MHz, $CDCl_3$) δ 3.37 (s, 3 H), 3.06−3.00 (m, 1 H), 2.99−2.92 (m, 1 H), 2.88−2.80 (m, 1 H), 2.68−2.63 (m, 1 H), 2.12 (s, 3 H), 2.16−2.01 (m, 1 H), 1.43−1.35 (m, 1 H), 1.35 (s, 3 H), 1.31−1.27 (m, 1 H), 1.01 (d, J = 6.5 Hz, 3 H); ^{13}C NMR (75 MHz,$CDCl_3$) δ 216.1, 204.4, 95.8, 67.7, 57.5, 50.0, 43.1, 42.4, 38.3, 33.7, 25.1, 20.9, 17.9; HRMS m/z (M^+) calcd 224.1413, obsd 224.1403.

Anal. Calcd for $C_{13}H_{20}O_3$: C, 69.61; H, 8.99. Found: C, 69.35; H, 8.97.

(2*S,3a*S**,4*S**,5*R**,6a*S**)-2-(1,1-Dimethoxyethyl)hexahydro-4-methoxy-2,5-dimethyl-1(2*H*)-pentalenone (28).** A solution of **27** (16.4 g, 72.9 mmol) in 70 mL of dry methanol was treated with trimethyl orthoformate (50.0 mL, 457 mmol) and *p*-toluenesulfonic acid monohydrate (1.00 g, 5.26), and the resulting solution was stirred for 2 h at room temperature, treated with ether (100 mL) and K_2CO_3 (35 g, 0.25 mmol), filtered through a plug of Florisil, and concentrated. The crude oil was purified by flash chromatography on silica gel (elution with 1% triethylamine and 1% ethyl acetate in petroleum ether) to give **28** as a light yellow oil (14.3 g, 72%): IR (neat, cm^{-1}) 1740, 1465, 1385; ^1H NMR (300 MHz, C_6D_6) δ 3.19 (s, 3 H), 2.98 (s, 3 H), 2.97 (s, 3 H), 2.88−2.79 (m, 1 H), 2.50−2.22 (m, 1 H), 2.06−1.94 (m, 2 H), 1.46−1.33 (m, 2 H), 1.18 (s, 3 H), 1.16−1.04 (m, 2 H), 1.15 (s, 3 H), 0.89 (d, J = 6.4 Hz, 3 H); ^{13}C NMR (75 MHz, C_6D_6) δ 220.3, 104.0, 96.3, 59.5, 57.6, 51.6, 50.8, 50.1, 44.5, 42.3, 39.0, 33.6, 22.2, 18.2, 16.3; HRMS m/z (M^+) calcd 258.1831, obsd 258.1823.

(2*S,3a*R**,4*R**,5*S**,6a*R**)-Hexahydro-4-methoxy-2-(1-methoxyvinyl)-2,5-dimethyl-1(2*H*)-pentalenone (29).** A 16 in. × 0.75 in. quartz tube containing freshly broken quartz chips prewashed with dilute HCl solution was attached to a two-necked flask containing a neat sample of **28** (3.24 g, 12.0 mmol) and preequilibrated at 460 °C and 0.7 Torr for 3 h. The flask was heated with a heating mantle and later a naked flame while the product was collected in a receiving tube cooled with liquid N_2. After the transfer was complete, N_2 was purged through the flask and the apparatus was cooled to room temperature. The receiving tube was washed with ether and concentrated, and the dark yellow oil was purified by flash chromatography on SiO_2 (elution with 1% triethylamine in hexanes) to give **29** (2.20 g, 88%) as a light yellow oil: IR (neat, cm^{-1}) 1730, 1630, 1600; ^1H NMR (300 MHz, C_6D_6) δ 3.99 (d, J = 3 Hz, 1 H), 3.77 (d, J = 3 Hz, 1 H), 3.11 (s, 3 H), 3.05 (s, 3 H), 2.96−2.75 (series of m, 2 H), 2.68−2.56 (m, 2 H), 2.01−1.85 (m, 2 H), 1.34 (s, 3 H), 1.31−1.23 (m, 2 H), 0.92 (d, J = 6.3 Hz, 3 H); ^{13}C NMR (75 MHz, C_6D_6) δ 219.3, 164.4, 96.0, 80.6, 57.8, 57.0, 55.2, 49.9, 43.7, 42.7, 41.0, 33.7, 22.2, 18.1; HRMS m/z (M^+) calcd 238.1569, obsd 238.1569.

Anal. Calcd for $C_{14}H_{22}O_3$: C, 70.56; H, 9.30. Found: C, 70.29; H, 9.36.

6-Bromo-8,8-dimethyl-1,4-dioxaspiro[4.4]non-6-ene (32). A solution of **31** (9.45 g, 50 mmol), *p*-toluenesulfonic acid (380 mg, 2.0 mmol), and ethylene glycol (11.2 mL, 200 mmol) in benzene (100 mL) was refluxed under a Dean−Stark trap for 24 h, cooled to room temperature, and quenched with saturated $NaHCO_3$ solution. After solvent removal on a rotary evaporator, the residue was dissolved in ethyl acetate, washed

with brine, dried, and concentrated prior to chromatographic purification on silica gel (elution with 10% ethyl acetate in hexanes). There was obtained 10.95 g (94%) of **32** as a colorless oil: IR (neat, cm^{-1}) 1619, 1321, 1158; ^1H NMR (300 MHz, $CDCl_3$) δ 5.99 (s, 1 H), 4.21−4.15 (m, 2 H), 3.99−3.93 (m, 2 H), 1.99 (s, 2 H), 1.14 (s, 6 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 146.2, 121.9, 117.2, 65.7, 49.9. 42.0, 28.6; HRMS *m/z* (M^+) calcd 232.0099, obsd 232.0088.

2-Bromo-4,4-dimethyl-2-cyclopenten-1-ol (33). Ketone **31** (5.0 g, 26.5 mmol) dissolved in 100 mL of 0.4 M $CeCl_3 \cdot 7H_2O$ in methanol at 0 °C was carefully treated with sodium borohydride (1.2 g, 32 mmol). The resulting white slurry was stirred at 0 °C for 10 min, at which point the mixture was quenched with saturated NH_4Cl solution and diluted with ether. The separated organic layer was washed with saturated NH_4Cl solution, water, and brine, dried, and concentrated to afford 4.9 g (97%) of **33** as a white solid: mp 58 °C; IR (CH_2Cl_2, cm^{-1}) 3380, 1620; ^1H NMR (300 MHz, $CDCl_3$) δ 5.87 (d, *J* = 0.5 Hz, 1 H), 4.72 (dd, *J* = 7.5, 4.6 Hz, 1 H), 2.18 (dd, *J* = 13.4, 7.5 Hz, 1 H), 2.03 (br s, 1 H), 1.70 (dd, *J* = 13.4, 4.6 Hz, 1 H), 1.17 (s, 3 H), 1.09 (s, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 143.9, 123.1, 78.9, 47.6, 44.1, 29.5, 28.7; HRMS *m/z* (M^+) calcd 191.9929, obsd 199.9951.

Anal. Calcd for $C_7H_{11}BrO$: C, 44.00; H, 5.80. Found: C, 43.85; H, 5.70.

1-Bromo-5-chloro-3,3-dimethyl-1-cyclopentene (34). Alcohol **33** (14.7 g, 76.9 mmol) dissolved in 250 mL of dry CH_2Cl_2 at 0 °C was treated with triethylamine (16 mL, 115 mmol) and methanesulfonyl chloride (8.9 mL, 115 mmol). The resulting orange solution was stirred at 0 °C for 1 h, warmed to room temperature, stirred for 16 h, diluted with CH_2Cl_2, washed with water and brine, dried, and concentrated. The residue was purified by flash chromatography on silica gel (elution with petroleum ether) to afford 14.78 g (92%) of **34** as a colorless oil: IR (neat, cm^{-1}) 1615, 1330, 1225; ^1H NMR (300 MHz, $CDCl_3$) δ 5.95 (s, 1 H), 4.85 (dd, *J* = 7.7, 2.5 Hz, 1 H), 2.36 (dd, *J* = 14.3, 7.7 Hz, 1 H), 2.17 (dd, *J* = 14.3, 2.5 Hz, 1 H), 1.25 (s, 3 H), 1.12 (s, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 146.5, 120.2, 67.7, 48.5, 45.5, 28.6, 28.3; HRMS *m/z* (M^+) calcd 209.9625, obsd 209.9626.

Anal. Calcd for $C_7H_{10}BrCl$: C, 40.13; H, 4.81. Found: C, 40.00; H, 4.79.

1-Bromo-3,3-dimethylcyclopenta-1,4-diene (35). A solution of **34** (1.05 g, 5.0 mmol) in 2.5 mL of dry DMF at room temperature was treated with DBU (0.90 mL, 6.0 mmol), heated to 100 °C for 5 h, cooled to room temperature, and purified directly by flash chromatography on basic alumina (elution with pentane). The pentane eluant was distilled off at ambient pressure to give 0.37 g (43%) of **35**: IR (neat, cm^{-1}) 1578, 1523, 1346; ^1H NMR (300 MHz, C_6D_6) δ 6.03 (dd, *J* = 2.4, 1.5 Hz, 1 H), 5.99 (dd, *J* = 5.3, 1.4 Hz, 1 H), 5.83 (dd, *J* = 5.3, 2.5 Hz, 1 H), 0.87 (s, 6 H); ^{13}C NMR (75 MHz, C_6D_6) δ 148.0, 144.7, 131.2, 116.7, 53.9, 21.6; HRMS *m/z* (M^+) calcd 173.9867, obsd 173.9852.

(1*R,2*S**,3a*R**,4*R**,5*S**,6a*R**)-1-(8,8-Dimethyl-1,4-dioxaspiro[4.4]non-6-en-6-yl)octahydro-4-methoxy-2,5-dimethyl-2-vinyl-1-pentalenol (37).** A 5.33 g (14.3 mmol) sample of cerium trichloride heptahydrate was evacuated to 0.1 Torr and heated progressively at 50 °C (4 h), 60 °C (4 h), 70 °C (4 h), 80 °C (7 h), and 140 °C (14 h) while being stirred magnetically. After the mixture was returned to room temperature, dry THF (40 mL) was introduced under nitrogen, and the resulting milky mixture was stirred overnight prior to titration with *tert*-butyllithium (1 mL of 1 M in pentane) until a faint yellow-orange color persisted. Meanwhile, a solution of **32** (3.03 g, 13 mmol) in cold (−78 °C) THF (30 mL) was treated with *tert*-butyllithium (15.3 mL of 1.7 M in pentane, 26 mmol), stirred for 0.5 h, and transferred via cannula to the stirred cerium trichloride slurry. After an additional 2 h of stirring at −78 °C, ketone **24** (1.35 g, 6.5 mmol) was introduced, and the mixture was stirred for 2 h prior to warming to room temperature, quenching with water, and filtration. The filtrate was diluted with ethyl acetate, washed with brine, dried, and concentrated. Flash chromatography of the residue on silica gel (elution with 5% ethyl acetate in hexanes) furnished 2.21 g (94%) of **37** as a colorless oil: IR (neat, cm^{-1}) 3495, 1110; ^1H NMR (300 MHz, C_6D_6) δ 6.05 (dd, *J* = 17.6, 10.8 Hz, 1 H), 5.56 (s, 1 H), 5.19 (dd, *J* = 17.6, 1.5 Hz, 1 H), 5.06 (dd, *J* = 10.8, 1.5 Hz, 1 H), 4.41 (s, 1 H), 3.62−3.56 (m, 1 H), 3.47−3.25 (m, 4 H), 3.43 (s, 3 H), 2.93−2.87 (m, 1 H), 2.52 (dq, *J* = 11.7, 8.1 Hz, 1 H), 2.32−2.17 (m, 3 H), 1.83−1.66 (m, 4 H), 1.47 (s, 3 H), 1.33 (d, *J* = 6.5 Hz, 3 H), 1.08 (s, 3 H), 1.02 (s, 3 H); ^{13}C NMR (75 MHz, C_6D_6) δ 147.5, 145.1, 136.9, 120.7, 111.2, 95.5, 83.6, 63.4, 63.3, 57.6, 57.5, 51.3, 51.0, 46.6, 43.1, 42.4, 39.4, 28.9, 28.6, 28.5, 20.4, 17.8; HRMS *m/z* (M^+) calcd 362.2457, obsd 362.2458.

4,4-Dimethyl-2-[(1*R,2*S**,3a*R**,4*R**,5*S**,6a*R**)-octahydro-1-hydroxy-4-methoxy-2,5-dimethyl-2-vinyl-1-pentalenyl]-2-cyclopenten-1-one (38).** A solution of **37** (102 mg, 0.28 mmol) and *p*-toluenesulfonic acid (5 mg) in 10:1 acetone−water (2 mL) was stirred at room temperature for 10 h, quenched with saturated $NaHCO_3$ solution, and concentrated under reduced pressure. The product was extracted into ethyl acetate, dried, and freed of solvent prior to chromatography on silica gel (elution with 10% ethyl acetate in hexanes) to give 85 mg (95%) of **38** as a white solid: mp 86−87 °C; IR (neat, cm^{-1}) 3446, 1682; ^1H NMR (300 MHz, $CDCl_3$) δ 7.00 (s, 1 H), 5.66 (dd, *J* = 17.5, 10.8 Hz, 1 H), 5.28 (d, *J* = 2.0 Hz, 1 H), 4.98 (dd, *J* = 17.5, 1.4 Hz, 1 H), 4.96 (dd, *J* = 10.9, 1.4 Hz, 1 H), 3.39 (s, 3 H), 3.11−3.08 (m, 1 H), 2.95−2.85 (m, 1 H), 2.40−2.33 (m, 1 H), 2.31 (s, 2 H), 2.05−1.86 (m, 3 H), 1.63−1.53 (m, 2 H), 1.19 (s, 6 H), 1.04 (s, 3 H), 1.03 (d, *J* = 6.7 Hz, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 212.0, 169.9, 143.4, 139.6, 112.5, 95.0, 82.3, 58.2, 57.8, 50.7, 49.2, 46.7, 42.9, 41.9, 38.3, 28.6, 27.6, 27.5, 19.4, 17.3; HRMS *m/z* (M^+) calcd 318.2195, obsd 318.2187.

Anal. Calcd for $C_{20}H_{30}O_3$: C, 75.43; H, 9.50. Found: C, 75.32; H, 9.49.

(3a*R,7a*R**,8*R**,9*S**,10a*R**)-2,3,3a,4,7,7a,8,9,10,10a-Decahydro-8,11-dimethoxy-3,3,6,9-tetramethyl-1*H*-dicyclopenta[*a,d*]cyclononen-1-one (40) and (2*R**,3*S**,3a*S**,5a*R**,6a*S**,9a*R**,9b*S**,9c*S**)-Tetradecahydro-9b-hydroxy-3-methoxy-2,7,7,9a-tetramethyl-5-methylene-9*H*-cyclopent[*a*]-*as*-indacen-9-one (42).** To a solution of potassium *tert*-butoxide (168 mg, 1.5 mmol) and 18-crown-6 (420 mg, 1.59 mmol) in THF (12 mL) at 0 °C under N_2 was added 96 mg (0.30 mmol) of **38**. After 1 h of stirring at 0 °C, methyl iodide (2 mL) was introduced, and the reaction mixture was allowed to warm to room temperature and stirred for 2 h prior to quenching with saturated NH_4Cl solution. The solvents were removed in vacuo, and the product was extracted into ethyl acetate, washed with water and brine, dried, and concentrated. Chromatography of the residue on silica gel (gradient elution with 2.5 → 20% ethyl acetate in hexanes) afforded 55 mg (55%) of **40** and 33 mg (33%) of **42**.

For **40**: colorless oil; IR (neat, cm^{-1}) 1649, 1574; ^1H NMR (300 MHz, C_6D_6) δ 5.09 (m, 1 H), 3.28 (s, 3 H), 3.21 (s, 3 H), 3.17−3.03 (m, 2 H), 2.78−2.71 (m, 2 H), 2.33−2.29 (m, 1 H), 2.11 (dd, *J* = 16.5, 1.3 Hz, 1 H), 1.99−1.57 (m, 7 H), 1.55 (s, 3 H), 1.07 (d, *J* = 6.3 Hz, 3 H), 0.97 (s, 3 H), 0.82 (s, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 198.8, 166.1, 140.8, 129.2, 118.2, 94.0, 58.9, 57.4, 52.0, 46.6, 43.9, 40.5, 36.6, 35.7, 34.9, 31.8, 31.2, 24.0, 20.4, 17.2 (1 C not observed); HRMS *m/z* (M^+) calcd 332.2351, obsd 332.2349.

For **42**: colorless solid; IR (neat, cm^{-1}) 3528, 1735; ^1H NMR (300 MHz, C_6D_6) δ 4.96 (dd, *J* = 1.6, 0.8 Hz, 1 H), 4.73 (d, *J* = 1.6 Hz, 1 H), 3.33 (s, 3 H), 3.00 (dd, *J* = 9.7, 7.0 Hz, 1 H), 2.57 (m, 1 H), 2.53 (br s, 1 H), 2.23−2.14 (m, 2 H), 2.07−1.82 (m, 6 H), 1.74−1.52 (m, 3 H), 1.24 (d, *J* = 6.3 Hz, 3 H), 1.04 (s, 3 H), 0.99 (s, 1 H), 0.93 (s, 3 H), 0.87 (s, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 216.5, 145.8, 110.7, 91.5, 83.8, 62.3, 59.4, 58.4, 53.6, 52.5, 46.7, 41.3, 39.4, 34.7, 33.3, 31.4, 30.8, 28.9, 24.9, 23.5, 19.5; HRMS *m/z* (M^+) calcd 332.2351, obsd 332.2361.

(1*S,2*R**,3a*R**,4*R**,5*S**,6a*R**)-1-(3,3-Dimethyl-1,4-cyclopentadien-1-yl)octahydro-4-methoxy-2-(1-methoxyvinyl)-2,5-dimethyl-1-pentalenol (44).** A sample of cerium trichloride heptahydrate (4.9 g, 13.05 mmol) was evacuated to 0.1 Torr and stirred overnight at 110 °C (with slow elevation to this temperature). After additional heating to 130 °C for 60 min, the white solid was cooled slowly to room temperature

over 3 h, flushed with N_2, and added to THF (60 mL) via Schlenk glassware with vigorous stirring. The resulting white slurry was stirred for 4.5 h at room temperature and titrated with *tert*-butyllithium (1.8 mL) until a faint yellow-orange color persisted. Meanwhile, freshly prepared vinyl bromide **35** (1.5 g, 8.7 mmol) dissolved in 40 mL of dry THF was cooled to −78 °C and *tert*-butyllithium (10.7 mL, 18.3 mmol) was introduced via syringe. The resulting dark yellow solution was stirred for 30 min at −78 °C, transferred via cannula to the stirred $CeCl_3$ slurry, and stirred at −78 °C for 1.5 h. Ketone **29** (1.04 g, 4.35 mmol) dissolved in 30 mL of dry THF at −78 °C was added to this slurry via cannula. The reaction mixture was stirred at −78 °C for 90 min and at −30 °C for 3 h prior to quenching with saturated $NaHCO_3$ solution. This mixture was extracted with ether, and the combined organic layers were washed with saturated $NaHCO_3$ solution and brine, dried, and concentrated. The crude material was immediately purified by flash column on silica gel (elution with 1% triethylamine and 2% ethyl acetate in hexanes) to give 1.19 g (82%) of **44** as a colorless oil that forms transparent crystals upon standing at −20 °C: IR (neat, cm^{-1}) 3490, 1645, 1600; ^1H NMR (300 MHz, C_6D_6) δ 6.11 (dd, J = 5.3, 1.6 Hz, 1 H), 6.09 (dd, J = 5.3, 2.3 Hz, 1 H), 5.74−5.73 (m, 1 H), 4.04 (d, J = 2.6 Hz, 1 H), 3.76 (d, J = 2.6 Hz, 1 H), 3.30−3.06 (series of m, 3 H), 3.30 (s, 3 H), 3.02 (s, 3 H), 2.66−2.56 (m, 1 H), 2.37 (dd, J = 13.0, 8.9 Hz, 1 H), 2.18−2.08 (m, 1 H), 1.98 (dd, J = 13.0, 6.9 Hz, 1 H), 1.65−1.51 (m, 1 H), 1.43 (s, 3 H), 1.17 (d, J = 6.5 Hz, 3 H), 1.11 (s, 3 H), 1.09 (s, 3 H) (OH not observed); ^{13}C NMR (75 MHz, C_6D_6) δ168.2, 146.1, 145.8, 140.6, 129.2, 95.8, 82.5, 81.0, 60.1, 57.7, 54.0, 51.8, 49.2, 49.1, 43.8, 43.4, 29.6, 22.5, 22.4, 20.4, 18.1; HRMS m/z (M^+) calcd 318.2194, obsd 318.2188.

(3a*S,5a*S**,6a*S**,7*S**,8*R**,9a*S**,9b*R**,9c*R**)-3,3a,5a,6,-6a,7,8,9,9a,9c-Decahydro-5,7-dimethoxy-3,3,5a,8,9c-pentamethyl-9b*H*-cyclopent[*a*]-*as*-indacen-9b-ol (47) and (3a*S**,5a*R**,6a*S**,7*S**,8*R**,9a*S**,9b*R**,9c*R**)-3,3a,4,5,5a,6,-6a,7,8,9,9a,9c-Dodecahydro-9b-hydroxy-7-methoxy-3,3,-5a,8,9c-pentamethyl-9b*H*-cyclopent[*a*]-*as*-indacen-5-one (48).** A solution of potassium *tert*-butoxide (200 mg, 1.78 mmol) and 18-crown-6 (499 mg, 1.89 mmol) dissolved in 20 mL of dry THF at 0 °C was treated with a solution of **44** (120 mg, 0.36 mmol) in dry THF (5 mL), and the mixture was stirred at 0 °C for 1 h. Methyl iodide (10.0 mL, 159 mmol) was added to the yellow solution, and the resulting mixture was stirred at 0 °C for 1 h and at room temperature for 1 h prior to being quenched with water. The mixture was extracted with ether, and the combined organic phases were washed with brine, dried, and concentrated. The dark yellow oil was purified by flash chromatography on silica gel (elution with 1% triethylamine in petroleum ether) to give **47** (80 mg, 64%) and **48** (41 mg, 34%).

For **47**: white solid: mp 80−83 °C; IR (neat, cm^{-1}) 3640−3300 (br), 1670, 1460; ^1H NMR (300 MHz, C_6D_6) δ 5.69 (d, J = 5.7 Hz, 1 H), 5.15 (d, J = 5.7 Hz, 1 H), 4.26 (d, J = 4.4 Hz, 1 H), 3.27 (s, 3 H), 3.25 (s, 3 H), 2.88 (dd, J = 9.5, 7.1 Hz, 1 H), 2.73 (dd, J = 12.1, 9.3 Hz, 1 H), 2.68 (dd, J = 12.0, 7.9 Hz, 1 H), 2.33−2.19 (m, 1 H), 2.15 (d, J = 4.4 Hz, 1 H), 2.15−2.06 (m, 1 H), 1.54 (t, J = 9.6 Hz, 1 H), 1.51 (dd, J = 10.7, 10.7 Hz, 1 H), 1.25 (s, 3 H), 1.20 (s, 3 H), 1.18 (s, 3 H), 1.17 (d, J = 6.0 Hz, 3 H), 1.20−1.16 (s, 1 H), 0.98 (s, 3 H) (OH not observed); ^{13}C NMR (75 MHz, C_6D_6) δ 156.8, 137.2, 135.1, 95.7, 95.1, 82.8, 57.8, 55.1, 54.5, 54.2, 53.4, 50.1, 49.6, 46.5, 43.9, 42.1, 33.2, 31.3, 27.6, 26.1, 20.7, 17.8; HRMS m/z (M^+) calcd 346.2508, obsd 346.2515.

Anal. Calcd for $C_{22}H_{34}O_3$: C, 76.26; H, 9.89. Found: C, 76.03; H, 9.89.

For **48**: faint yellow solid: mp 115−116 °C; IR (neat, cm^{-1}) 3593−3417 (br), 1704, 1456; ^1H NMR (300 MHz, C_6D_6, 77 °C) δ 5.30 (d, J = 5.8 Hz, 1 H), 5.26 (d, J = 5.7 Hz, 1 H), 3.18 (s, 3 H), 2.92 (dd, J = 9.3, 6.3 Hz, 1 H), 2.67 (dd, J = 13.6, 7.1 Hz, 1 H), 2.57−2.45 (m, 1 H), 2.48 (dd, J = 13.7, 9.7 Hz, 1 H), 2.24−2.10 (m, 1 H), 2.17 (dd, J = 13.7, 8.6 Hz, 1 H), 2.02−1.88 (m, 1 H), 1.78 (dd, J = 8.6, 7.1 Hz, 1 H), 1.66 (dd, J = 13.7, 6.5 Hz, 1 H), 1.57 (ddd, J = 12.7, 12.4, 10.4 Hz, 1 H), 1.53−1.42 (m, 1 H), 1.30 (s, 1 H), 1.26 (s, 3 H), 1.11 (d, J = 6.3 Hz, 3 H), 0.98 (s, 3 H), 0.95 (s, 3 H), 0.89 (s, 3 H); ^{13}C NMR (75 MHz, C_6D_5Cl) δ 215.4, 142.1, 133.0, 97.7, 85.1, 57.9, 57.7, 54.7, 52.3, 49.4, 47.4, 44.7, 43.2, 38.2, 35.2, 32.6, 27.2, 24.8, 22.4, 17.8 (1 C not observed); HRMS m/z (M^+) calcd 332.2351, obsd 332.2360.

Anal. Calcd for $C_{21}H_{32}O_3$: C, 75.86; H, 9.70. Found: C, 75.56; H, 9.67.

Acid Hydrolysis of 47. A solution of **47** (247 mg, 0.713 mmol) in acetone (5.4 mL) and water (0.6 mL) was treated with *p*-toluenesulfonic acid (13.1 mg, 0.069 mmol), refluxed for 8 h, cooled, and partitioned between ether and water. The aqueous phase was extracted with ether, and the combined organic layers were dried, and concentrated. The residue was purified by flash chromatography (silica gel, elution with 19:1 → 9:1 petroleum ether in ethyl acetate) to give 175 mg (74%) of **48**.

(3a*S,5*R**,5a*R**,6a*S**,7*S**,8*R**,9a*S**,9b*R**,9c*R**)-3,3a,4,5,-5a,6,6a,7,8,9,9a,9c-Dodecahydro-7-methoxy-3,3,5a,8,9c-pentamethyl-9b*H*-cyclopent[*a*]-*as*-indacene-5,9b-diol (49).** A solution of **48** (163 mg, 0.489 mmol) in 2 mL of dry ether at 0 °C was treated with lithium aluminum hydride (40 mg, 1.05 mmol), and the resulting mixture was stirred at 0 °C for 15 min and at room temperature for 2 h prior to being quenched with methanol and water. The mixture was extracted with ether, and the combined organic layers were dried and concentrated. The residue was purified by MPLC (silica gel, elution with 2:1 petroleum ether in ethyl acetate) to give 130 mg (79%) of **49**: IR (neat, cm^{-1}) 3646−3131, 1461, 1375; ^1H NMR (300 MHz, C_6D_6) δ 5.49 (d, J = 5.6 Hz, 1 H), 5.25 (d, J = 5.6 Hz, 1 H), 3.48 (dd, J = 10.8, 3.5 Hz, 1 H), 3.29 (s, 3 H), 2.96 (dd, J = 9.3, 6.0 Hz, 1 H), 2.58−2.47 (m, 2 H), 2.42−2.30 (m, 1 H), 2.16−2.02 (m, 1 H), 1.70−1.57 (m, 3 H), 1.55−1.40 (m, 2 H), 1.28 (dd, J = 13.1, 8.2 Hz, 1 H), 1.20 (d, J = 6.4 Hz, 3 H), 1.17 (s, 3 H), 1.084 (s, 3 H), 1.075 (s, 3 H), 0.95 (s, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 140.5, 133.8, 96.7, 83.6, 72.7, 57.8, 57.0, 53.4, 52.0, 49.6, 48.1, 47.5, 42.8, 40.4, 34.3, 32.5, 30.1, 26.4, 25.1, 24.4, 17.4; HRMS m/z (M^+) calcd 334.2508, obsd 334.2530.

(3a*S,5*R**,5a*R**,6a*S**,7*S**,8*R**,9a*S**,9b*R**,9c*R**)-3,3a,4,5,-5a,6,6a,7,8,9,9a,9c-Dodecahydro-5-acetoxy-7-methoxy-3,3,5a,8,9c-pentamethyl-9b*H*-cyclopent[*a*]-*as*-indacen-9b-ol (50).** Diol **49** (37 mg, 0.12 mmol) was dissolved in 1.5 mL of CH_2Cl_2 and treated with 0.2 mL of triethylamine and 0.2 mL of acetic anhydride followed by 10 mg of DMAP. The reaction mixture was stirred for 5 min, diluted 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 purified by flash chromatography on silica gel (elution with 5% ethyl acetate in hexanes) to give 38 mg (88%) of **50** as a colorless oil: IR (neat, cm^{-1}) 3552, 3535, 1727, 1625; ^1H NMR (300 MHz, $CDCl_3$) δ 5.53 (d, J = 5.6 Hz, 1 H), 5.52 (d, J = 5.6 Hz, 1 H), 4.81 (dd, J = 7.9, 2.7 Hz, 1 H), 3.36 (s, 3 H), 3.03, (dd, J = 9.3, 5.9 Hz, 1 H), 2.67 (q, J = 10.0 Hz, 1 H), 2.31−2.18 (m, 2 H), 2.06 (s, 3 H), 1.92−1.31 (series of m, 8 H), 1.21 (s, 3 H), 1.13 (s, 3 H), 1.10 (s, 3 H), 1.06 (d, J = 6.4 Hz, 1 H), 1.04 (s, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 170.4, 142.1, 132.8, 96.7, 83.1, 75.7, 58.0, 57.3, 51.0, 50.8, 49.5, 48.3, 47.3, 42.4, 41.0, 34.9, 32.4, 26.2, 26.0, 25.3, 24.4, 21.3, 17.4; HRMS m/z (M^+) calcd 376.2614, obsd 376.2661.

(3a*S,5*R**,5a*R**,6a*S**,7*S**,8*R**,9a*S**,9b*R**,9c*R**)-3,3a,4,5,-5a,6,6a,7,8,9,9a,9c-Dodecahydro-7-methoxy-3,3,5a,8,9c-pentamethyl-9b*H*-cyclopent[*a*]-*as*-indacene-5,9b-diol 5-Methanesulfonate (51).** A solution of **49** (16.6 mg, 0.050 mmol) in dry CH_2Cl_2 (1 mL) at 0 °C was treated with triethylamine (0.14 mL, 1.00 mmol) and methanesulfonyl chloride (0.04 mL, 0.52 mmol), and the resulting mixture was stirred at 0 °C for 15 min and room temperature for 30 min, quenched with brine, and extracted with ether. The combined organic phases were dried and concentrated to leave an oil that was purified by flash chromatography on silica gel (elution with 4:1 petroleum ether−ethyl acetate) to give **51** (16 mg, 79%): IR (neat, cm^{-1}) 3446−3390, 1459, 1332; ^1H NMR (300 MHz, C_6D_6) δ 5.38 (d, J = 5.6 Hz, 1 H), 5.25 (d, J = 5.6 Hz, 1 H), 4.73 (dd, J = 10.2, 3.6 Hz, 1 H), 3.24 (s, 3 H), 2.94 (dd, J = 9.3, 5.7 Hz, 1 H), 2.47 (dd, J = 12.4, 8.9 Hz, 1 H), 2.43−2.33

(m, 2 H), 2.29 (s, 3 H), 2.12−2.00 (m, 1 H), 1.93 (ddd, J = 13.9, 5.4, 3.6 Hz, 1 H), 1.84−1.74 (m, 1 H), 1.69−1.64 (m, 1 H), 1.58 (dd, J = 12.7, 2.5 Hz, 1 H), 1.52−1.36 (m, 2 H), 1.27 (s, 1 H), 1.18 (s, 3 H), 1.16 (d, J = 6.4 Hz, 3 H), 1.09 (s, 3 H), 1.05 (s, 3 H), 1.01 (s, 3 H); ^{13}C NMR (75 MHz, C_6D_6) δ 140.9, 133.7, 96.8, 84.1, 83.7, 57.8, 57.1, 52.0, 49.8, 48.2, 47.8, 43.2, 41.8, 38.1, 34.6, 32.5, 30.8, 28.8, 26.2, 25.0, 24.6, 17.7; HRMS molecular ion too fleeting for accurate mass measurement.

(2*S,3*R**,3a*R**,5*Z*,7a*R**,10a*S**,11a*R**)-1,2,3,3a,4,7,7a,8,-10a,11a-Decahydro-3-methoxy-2,5,8,8,10a-pentamethyl-11*H*-dicyclopenta[*a*,*d*]cyclononen-11-one (52).** A solution of **51** (41.8 mg, 0.101 mmol) in 3 mL of dry *tert*-butyl alcohol at 40 °C was treated with potassium *tert*-butoxide (38.7 mg, 0.345 mmol) and the resulting solution was stirred at 40 °C for 20 min. The reaction mixture was partitioned between ether (100 mL) and brine (10 mL), and the organic layer was dried, filtered, and concentrated. The residue was purified by flash chromatography on silica gel (elution with 19:1 petroleum ether−ethyl acetate) to give 27.0 mg (84%) of **52** as a colorless oil: IR (neat, cm^{-1}) 1686, 1458, 1373; ^{1}H NMR (300 MHz, C_6D_6) δ 5.54 (d, J = 5.6 Hz, 1 H), 5.09 (d, J = 5.6 Hz, 1 H), 5.07 (dd, J = 12.4, 4.4 Hz, 1 H), 3.62 (dd, J = 9.4, 8.7 Hz, 1 H), 3.31 (s, 3 H), 3.18 (ddd, J = 9.1, 9.0, 4.7 Hz, 1 H), 2.68 (t, J = 12.4 Hz, 1 H), 2.53−2.28 (m, 2 H), 1.98 (dd, J = 12.9, 4.5 Hz, 1 H), 1.98−1.84 (m, 1 H), 1.79−1.74 (m, 2 H), 1.70 (dd, J = 8.9, 4.8 Hz, 1 H), 1.62 (s, 3 H), 1.28 (s, 3 H), 1.23 (s, 3 H), 1.15 (d, J = 6.6 Hz, 3 H), 1.12−1.06 (m, 1 H), 1.02 (s, 3 H); ^{13}C NMR (75 MHz, C_6D_6) δ 221.4, 142.3, 135.3, 133.9, 125.6, 92.6, 64.5, 62.9, 59.0, 50.6, 48.3, 43.0, 40.2, 35.2, 31.2, 30.4, 28.2, 26.2, 24.4, 23.4, 19.3; HRMS m/z (M^+) calcd 316.2402, obsd 316.2403.

Anal. Calcd for $C_{21}H_{32}O_2$: C, 79.70; H, 10.19. Found C, 79.56; H, 10.33.

Acknowledgment. This research was supported by the National Cancer Institute (Grant CA 12115). The authors thank Prof. Robin Rogers (The University of Alabama) for the crystallographic analysis of **42**, Dr. Kurt Loening for assistance with nomenclature, and Dr. Darryl Cleary for some preliminary studies.

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 **42**, together with high-field ^{1}H NMR spectra of those compounds lacking combustion analysis. This material is available free of charge via the Internet at http://pubs.acs.org.

JO9825254