Total Synthesis of (+)-Epoxydictymene. Application of Alkoxy-Directed Cyclization to Diterpenoid Construction

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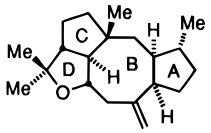
Abstract: An enantioselective synthesis of (+)-epoxydictymene (**1**) is reported. Condensation of the enantiopure aldehydo ester **5** with (*S*)-3-isopropylcyclopentenyllithium proceeds selectively to afford **13**. Once this lactone was methylenated with the Tebbe reagent, the newly formed allyl vinyl ether was induced into Claisen rearrangement under catalysis with triisobutylaluminum. Sequential hydroboration−oxidation of the resulting dicyclopentacyclooctenone derivative was followed by angular methylation and deoxygenation of the carbonyl functionality. Following epimerization at C-11, an α-hydroxyl was introduced regio- and stereoselectively. Some functional group manipulation led to **57** and **58**, both of which underwent efficient cyclization to deliver the complete framework of the target molecule when irradiated with visible light in cyclohexane solution containing iodosobenzene diacetate and iodine. The generality of this key reaction, which efficiently constructs the strained oxabicyclo[3.3.0]octane subunit of **1**, is demonstrated. This significant development permitted the conversion of **57** to **1** in two additional steps.

In the early 1980s, Matsumoto and co-workers at Hokkaido University were actively investigating the nature of the constituents produced by brown algae of the *Dictyotaceae* family. Their focus on *Dictyota dichotoma* was initially rewarded with the isolation of cyclononane and hydroazulene diterpenoids of novel structure.[2]

Subsequently, they identified epoxydictymene (**1**) to be present as well.[3] The fusicoccin-like tricyclic framework of **1**, established by X-ray crystal structure analysis of a derivative, was recognized to feature a strained trans-fused 3-oxabicyclo-[3.3.0]octane subunit. This unusual constitutional characteristic arguably defines **1** as the most complex of the fusicoccanes. The absolute configuration of epoxydictymene is as depicted.[3]



1

Schreiber *et al.* succeeded in 1994 to access natural (+)-**1** by deployment of a Pauson−Khand reaction in a key step.[4] This ring-building protocol delivered a dehydro derivative of epoxydictymene, from which the target molecule was produced only after cleavage and reconstruction of the C ring.

We have successfully exploited an alkoxy-directed cyclization route to **1** which highlights the facility and efficiency with which the strained tetrahydrofuran sector (ring D) can be assembled late in the synthesis.[5] Herein are described the full experimental details of this route, along with details of other exploratory thrusts carried out in support of this venture. These latter studies feature some unique aspects of the chemistry of cyclooctane rings.[6]

Results and Discussion

Synthetic Planning. In line with the general guidelines set above, we considered **2** (X being a substituent capable of E_2 elimination) to be a reasonable penultimate precursor to the target molecule. Elaboration of its entire tricyclic framework was expected to best be realized by subjecting **4** to Claisen rearrangement (Scheme 1).[7−11] The chairlike characteristics of the transition state expected to be adopted during this interconversion[12−17] would serve to interrelate properly the rather distal stereogenic centers in rings A and C. Left unspecified for the moment was the manner in which the oxygen-substituted center in **3** would be transposed, the angular methyl group introduced, and one ring-juncture hydrogen atom epimerized. Although one can imagine a variety of ways to achieve the orderly functionalization of **3** in mandated fashion, particular

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(2) (a) Enoki, N.; Ishida, R.; Matsumoto, T. *Chem. Lett.* **1982**, 1749. (b) Enoki, N.; Ishida, R.; Urano, S.; Ochi, M.; Tokoroyama, T.; Matsumoto, T. *Chem. Lett.* **1982**, 1837.

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(14) (a) Kang, H.-J.; Paquette, L. A. *J. Am. Chem. Soc.* **1990**, *112*, 3252. (b) Paquette, L. A.; Kang, H.-J. *J. Am. Chem. Soc.* **1991**, *113*, 2610.

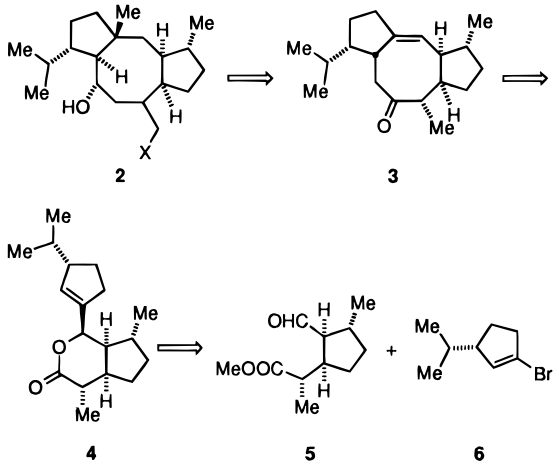
(15) (a) Philippo, C. M. G.; Vo, N. H.; Paquette, L. A. *J. Am. Chem. Soc.* **1991**, *113*, 2762. (b) Paquette, L. A.; Philippo, C. M. G.; Vo, N. H. *Can. J. Chem.* **1992**, *70*, 1356.

(16) Paquette, L. A.; Wang, T.-Z.; Vo, N. H. *J. Am. Chem. Soc.* **1993**, *115*, 1676.

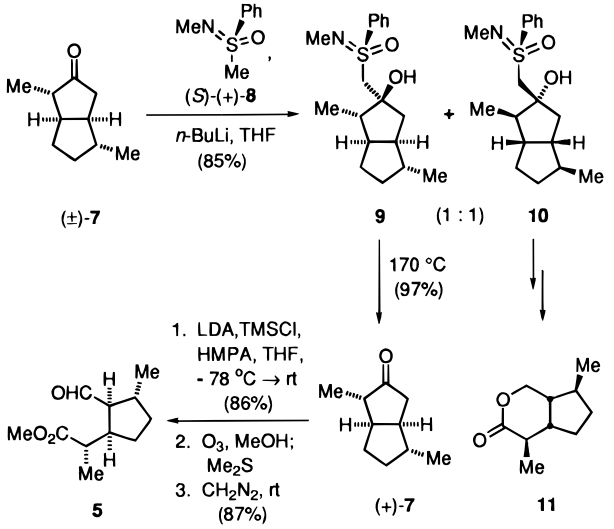
(17) Paquette, L. A.; Friedrich, D.; Rogers, R. D. *Q. Rev., Chem. Soc.* **1991**, *56*, 3841.

S0002-7863(97)01526-6 CCC: $14.00

Scheme 1

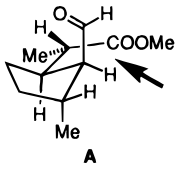


Scheme 2



attention had to be accorded to those hazards inherent in the chemistry of medium-sized rings.[6,18]

The stereocontrol projected for the condensation of **5** with **6** was founded on the results of model studies involving closely related systems.[19] A key consideration in this scenario was the anticipation that nucleophilic attack at the aldehyde carbonyl would occur most readily on the conformer depicted in **A** from the front right quadrant. This trajectory has previously been considered to involve the minimum level of nonbonded steric interactions.[19]



A

The Sigmatropic Event and First Attempt at Functionalization of the Cyclooctane Core. Whereas **6** was generated from (*R*)-carvone and was therefore of high enantiomeric purity,[20] it was necessary to resolve racemic **7**[19] prior to arrival at **5**. This task was easily accomplished by means of Johnson's sulfoximine technology.[21] The adducts **9** and **10** produced upon coupling of (*S*)-(+)-**8** to **7** were readily amenable to chromatographic separation. Elucidation of absolute stereochemistry was accomplished by the conversion of **10** into (−)-isoiridomyrmecin (**11**) of well established configuration[22] (Scheme 2). Following the thermal cracking of **9** to return (+)-**7**, sequential formation of the silyl enol ether, ozonolysis, and esterification with diazomethane delivered enantiopure **5**.

Addition of the cycloalkenyllithium reagent derived from (*S*)-**6** to **5** in THF at −78 °C did indeed prove to be usefully diastereoselective, providing a mixture of **12** and **13** rich in the latter (71%). Treatment of the chromatographically purified **13** with carefully generated Tebbe reagent[23] provided vinyl ether **14** in high yield. Without delay, this sensitive compound was immediately exposed to triisobutylaluminum (Tribal) in CH_2Cl_2 at −78 °C. Following warming to room temperature, the resulting mixture of cyclooctenols was directly oxidized with PCC to the homogeneous ketone **15**. Oshima and co-workers had earlier recognized the appreciable capability of Tribal for accelerating the Claisen rearrangement.[24] Concomitant reduction of the carbonyl products under the mild reaction conditions was also noted. The stereocontrolled conversion to **15** provides clear indication that **14** makes exclusive use of the chairlike arrangement depicted in **B**.[25,26] Although nonbonded steric interactions involving the isopropyl substitutent are notably apparent in **B**, the major driving force behind adoption of this geometry is the *Z* selectivity with which the newly developing double bond is being generated within the eight-membered ring.[7,17] The stereochemical assignment to **15** was initially derived from decoupling, NOED, and H,H-COSY/C,H-COSY experiments and was later corroborated by X-ray crystallographic analysis of a more advanced intermediate (see Scheme 4).

With **15** in hand, we initially chose to examine the option of its possible conversion into the carbonyl-transposed conjugated ketone **26**. This prospect was alluring in that suitable deployment of existing functionalities within this enone could plausibly be exploited for arrival at **1**. With **26** as the interim goal, the kinetic enolate of **15** was generated and allowed to be captured by diphenyl disulfide.[27] These sulfenylating conditions gave rise exclusively to **16** (94%), which underwent Dibal-H reduction smoothly again from the β face to produce **17** quantitatively (Scheme 4). Two methods for oxidizing **17** to the sulfoxide stage were screened. In the first approach, the two-phase H_2O_2/$PhSeO_2H$ combination devised by Reich[28] served as the reagent

(18) Cope, A. C.; Martin, M. M.; McKervey, M. A. *Q. Rev., Chem. Soc.* **1966**, *20*, 119.

(19) Friedrich, D.; Paquette, L. A. *J. Org. Chem.* **1991**, *56*, 3831.

(20) Paquette, L. A.; Dahnke, K.; Doyon, J.; He, W.; Wyant, K.; Friedrich, D. *J. Org. Chem.* **1991**, *56*, 6199.

(21) Johnson, C. R.; Zeller, J. R. *J. Am. Chem. Soc.* **1982**, *104*, 4021.

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(23) (a) Tebbe, F. N.; Parshall, G. W.; Reddy, G. S. *J. Am. Chem. Soc.* **1978**, *100*, 3611. (b) Pine, S. H.; Zahler, R.; Evans, D. A.; Grubbs, R. H. *J. Am. Chem. Soc.* **1980**, *102*, 3270. (c) Brown-Wensley, K. A.; Buchwald, S. L.; Cannizzo, L.; Clawson, L.; Ho, S.; Meinhardt, D.; Stille, J. R.; Straus, D.; Grubbs, R. H. *Pure Appl. Chem.* **1983**, *55*, 1733. (d) Pine, S. H.; Pettit, R. J.; Geib, G. D.; Cruz, S. G.; Gallego, C. H.; Tijerina, T.; Pine, R. D. *J. Org. Chem.* **1985**, *50*, 1212.

(24) (a) Takai, K.; Mori, I.; Oshima, K.; Nozaki, H. *Tetrahedron Lett.* **1981**, *22*, 3985. (b) Takai, K.; Mori, I.; Oshima, K.; Nozaki, H. *Bull. Chem. Soc. Jpn.* **1984**, *57*, 446. (c) Mori, I.; Takai, K.; Oshima, K.; Nozaki, H. *Tetrahedron* **1984**, *40*, 4013. See, also: Lutz, R. P. *Chem. Rev.* **1984**, *84*, 205.

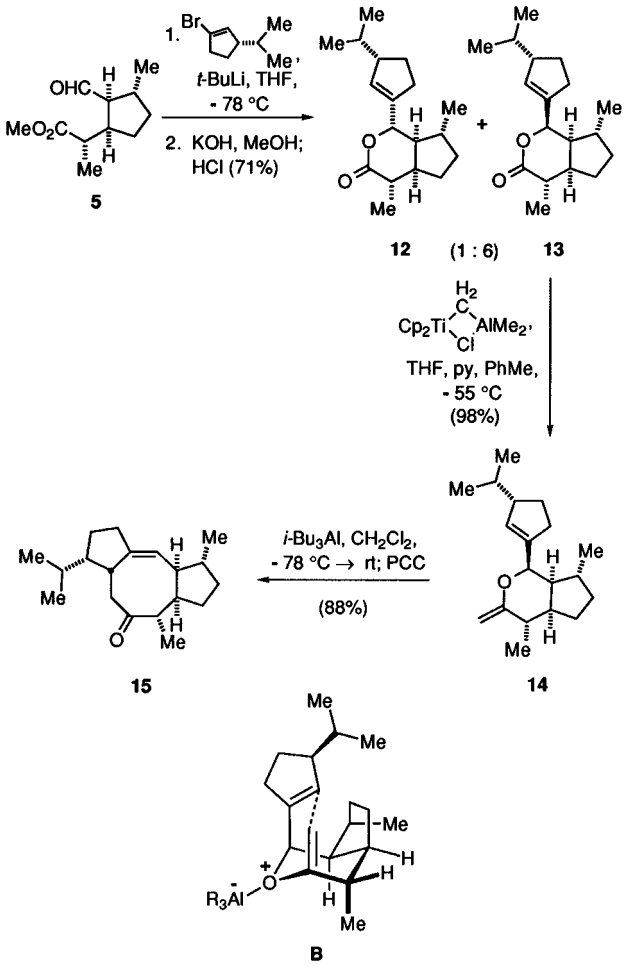
(25) Although Yamamoto has proposed an axial orientation for the complexation of bulky aluminum reagents to ether oxygen,[26] recent crystallographic and spectroscopic evidence suggests that the geometries of these complexes may be rather planar, and we have therefore adopted this formulation in **B**.

(26) (a) Maruoka, K.; Nonoshita, K.; Banno, H.; Yamamoto, H. *J. Am. Chem. Soc.* **1988**, *110*, 7922. (b) Nonoshita, K.; Banno, H.; Maruoka, K.; Yamamoto, H. *J. Am. Chem. Soc.* **1990**, *112*, 316.

(27) Trost, B. M.; Salzmann, T. N.; Hiroi, K. *J. Am. Chem. Soc.* **1976**, *98*, 4887.

(28) Reich, H. J.; Chow, F.; Peake, S. L. *Synthesis* **1978**, 299.

Scheme 3



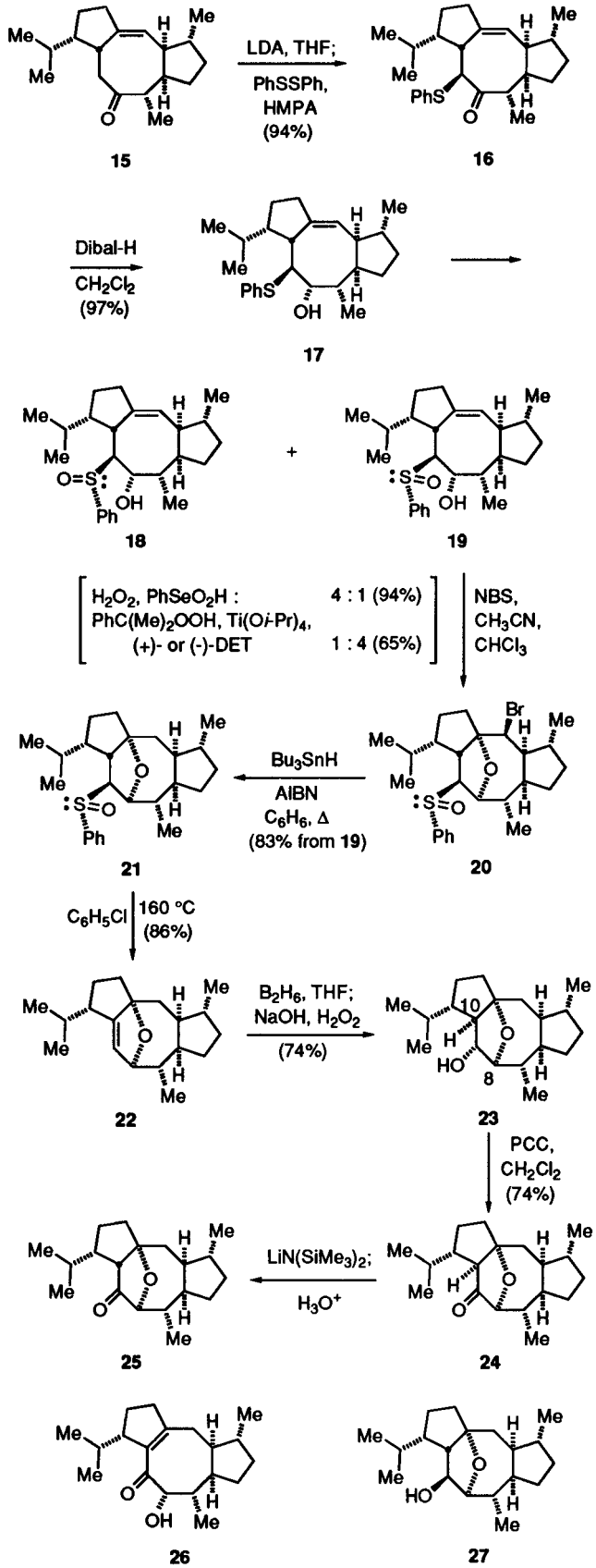
system. Reaction was complete in less than 5 min at 20 °C. The major product was the less polar isomer **18** (74%), which was accompanied by the highly polar diastereomer **19** (20%) along with 2% of the sulfone. The infrared and ^{1}H NMR spectra of **18** and the sulfone are convincingly diagnostic of the existence of intramolecular hydrogen bonding. Inspection of molecular models showed that only that sulfoxide with the *R* configuration on sulfur (**18**) is able to engage in this type of interaction without experiencing strong repulsion between the phenyl and isopropyl substituents. As will be seen, these considerations carry over as well into the thermal extrusion processes described below.

Our attempt to alter the **18**/**19** ratio through use of Kagan's chiral reagent system[29] gave an unexpected result. Use of either (+)- or (−)-diethyl tartrate afforded the identical inverse composition of these sulfoxides (now 1:4). Reagent control was obviously ineffective here.

Sequential brominative cyclization and reduction of **19** proceeded smoothly via **20** to **21**. Elimination on a preparative scale was performed in chlorobenzene at 160 °C (sealed tube) and afforded **22** in good yield. The same sequence of steps involving **18** was found to occur with diminished efficiency such that the amount of **22** obtained by this route was lower. In agreement with the stereochemical formulations, however, the rate at which **22** is generated in the elimination step differs significantly, with **21** ($t_{1/2} \approx 10$ h, reaction still incomplete after 24 h) being appreciably less reactive than the *R*-sulfoxide ($t_{1/2} < 60$ min; complete reaction after 7 h). The hydroboration of **22** required several hours at 20 °C for completion and afforded

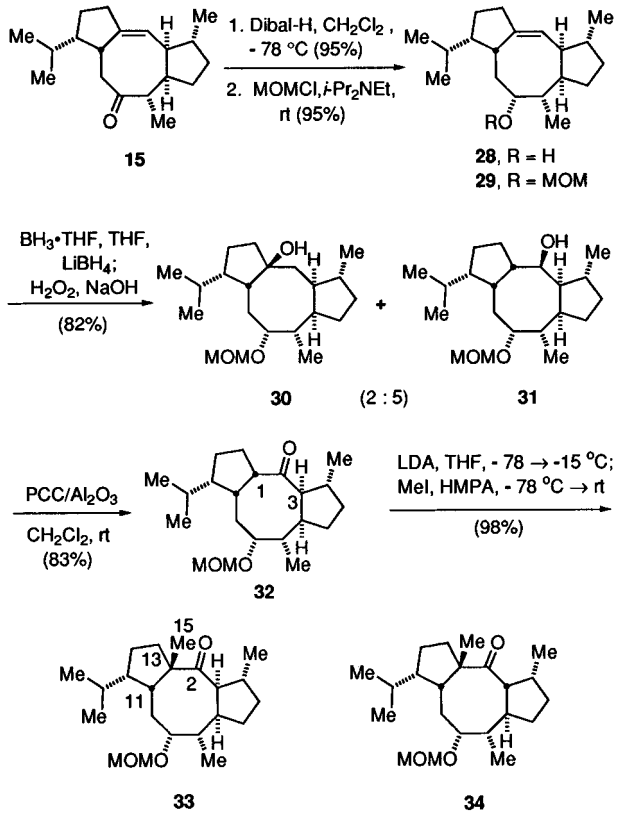
(29) Kagan, H. B.; Rebiere, F. *Synlett* **1990**, 643.

Scheme 4

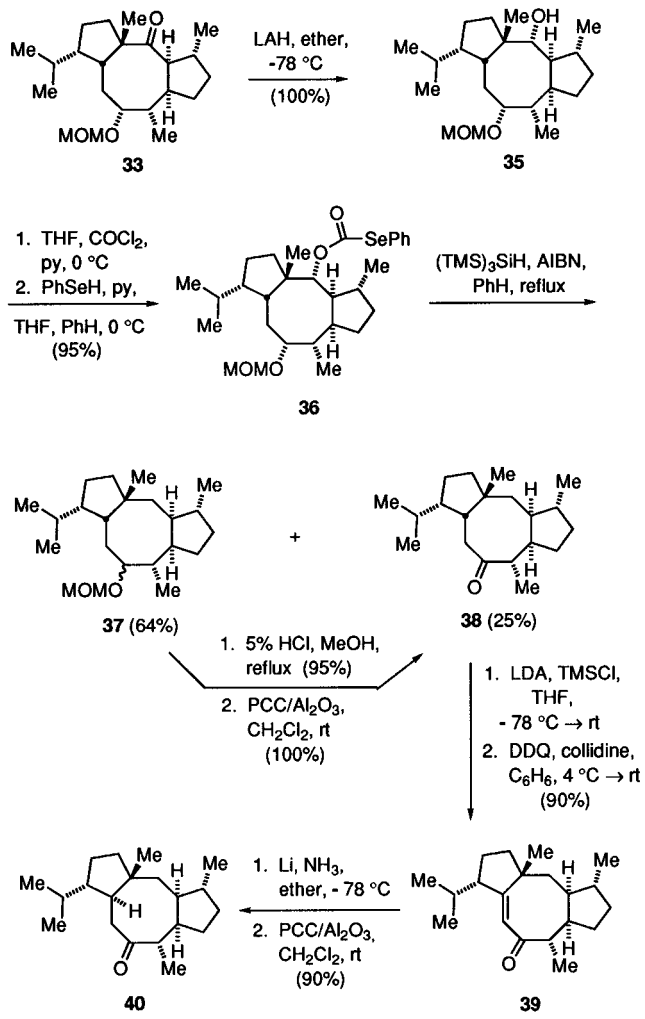


the lone alcohol **23** formed by attack on the α surface, as verified at the stage of ketone **24** obtained by PCC oxidation. In this advanced intermediate, the observed bidirectional NOEs between H-8 and H-10 (2%) can only be accommodated by the relative configuration shown. The desired β-alkoxide elimination to form enone **26** was next attempted by means of LiN(SiMe$_3$)$_2$

Scheme 5



Scheme 6



in toluene, benzene, or THF. However, even after prolonged exposure the only observed product was **25**. Molecular models show the β epimer to be considerably less strained than **24**, supporting the NMR-derived stereochemical assignment. Attempts to cleave the furanone ring in the opposite direction by reductive cleavage of the α-alkoxy functionality in **25** with samarium iodide in anhydrous THF[30] was also to no avail. Prolonged standing at room temperature left **25** unchanged, while further addition of water led simply to ketone reduction and formation of **27**.

Ultimately, it proved more expedient to prepare ketone **32** and to take advantage of its expected tendency to undergo regioselective deprotonation (Scheme 5). The conformation adopted by **15**, previously recognized to be conducive to kinetically controlled β-attack by electrophiles in the southern sector of the central ring, also enabled stereospecific reduction with Dibal-H to provide **28**. In this instance, the assignment of relative stereochemistry was founded on direct comparison of diagnostic ^{1}H NMR features with those earlier observed in model series, where extensive stereochemical studies had been undertaken.[17]

An abbreviated protocol for the conversion of lactone **13** to alcohol **28** was subsequently developed, which takes advantage of the significantly greater rate at which ketone **15** is reduced by Dibal-H compared to Tribal. Sequential addition to vinyl ether **14** of Tribal and Dibal-H at −78 °C effected Claisen rearrangement followed by stereospecific reduction to produce solely **28** of sufficient purity for direct conversion to MOM ether **29**. This modification raised the overall efficiency of the **13** to **29** conversion to 88% (see Experimental Section).

As a consequence of the very sluggish rate of hydroboration of **29** and the associated erratic efficiencies, our attention was drawn to a report describing the strong acceleration of catecholborane additions by lithium borohydride.[31] Gratifyingly, the presence of $LiBH_4$ in reactions involving **29** gave rise to much improved reproducibility and dramatically increased efficiency. The distribution of **30**:**31** was consistently 2:5, a ratio which could not be manipulated by making recourse to more bulky boranes since the latter failed to react at all.

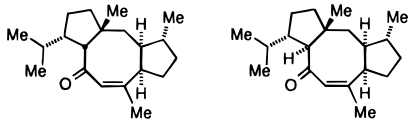
The oxidation of **31** to **32** was followed by monomethylation under conventional conditions. The misalignment of H-3 in **32** with the carbonyl π bond was recognized early in the tactical design stages. In contrast, the stereodisposition of C(1)−H is ideally suited to conjugative overlap, although abstraction of H-1 is confronted with significant steric hindrance. Accordingly, while LDA did not effect deprotonation of **32** at −78 °C, warmup to −15 °C for 1 h followed by introduction of methyl iodide at −78 °C succeeded in producing **33** exclusively. That the methyl group in **33** was β-oriented as required was clearly apparent from a strong NOE between H-15 and H-11 and a diagnostic W-coupling between H-15 and H-13α.

Now that the angular methylation was complete, the time had arrived to remove the C-2 oxygen that had served us so well. The steric crowding at this position came to the fore when an attempt at Wolff−Kishner reduction under quite forcing conditions returned only a mixture of **33** and its epimer **34**. Ketone **33** was therefore reduced with $LiAlH_4$ to pursue radical deoxygenation of an alcohol derivative (Scheme 6). While the resulting diastereomerically pure alcohol **35** proved unreactive

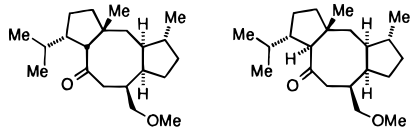
(30) (a) Molander, G. A.; Hahn, G. *J. Org. Chem.* **1986**, *51*, 1135. (b) Pratt, D. W.; Hopkins, P. B. *Tetrahedron Lett.* **1987**, *28*, 3065. (c) Hamelin, O.; Deprés, J.-P.; Greene, A. E. *J. Am. Chem. Soc.* **1996**, *118*, 9992.

(31) Arase, A.; Nunokawa, Y.; Masuda, Y.; Hoshi, M. *J. Chem. Soc., Chem. Commun.* **1991**, 205.

Table 1. Comparison of Two Sets of Energy Minimized Diastereomers[a]



ΔH_f	-67.0	-73.2 [a]
Strain energy	40.5	33.9
Total energy	51.5	44.9



ΔH_f	-127.9	-129.6 [b]
Strain energy	38.0	36.2
Total energy	55.4	53.6

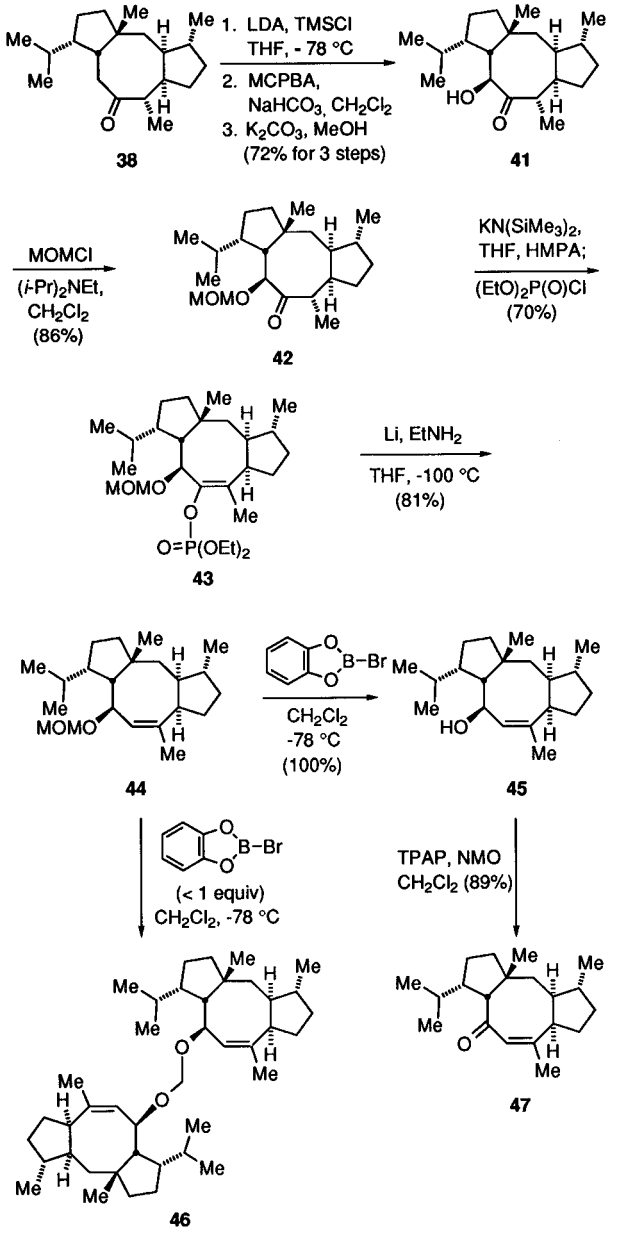
[a] MODEL version 2.99 was employed. [b] MODEL version 2.96 was utilized. [c] All values in kcal/mol.

to xanthate formation under a variety of conditions, conversion to the selenocarbonate[32a] proceeded smoothly to produce **36**. Exposure to tris(trimethylsilyl)silane[32b] and AIBN in refluxing benzene led to formation of **37** (*ca.* 1:1 mixture of epimers) as well as **38**, which is taken as evidence that transannular hydrogen abstraction by the initially formed secondary radical had occurred. Conversion to **38** was completed by sequential hydrolysis and oxidation of **37**.

The overall strategy next called for the specific epimerization of C-11. To this end, **38** was deprotonated under kinetically controlled conditions[33] in advance of conversion to the less substituted silyl enol ether. Oxidation of this reactive intermediate with DDQ[34] gave rise to **39** in acceptably high yield. This cyclooctenone underwent dissolving metal reduction to provide uniquely the trans-fused isomer **40** in 90% yield. The thermodynamic bias made evident in this experiment was in direct agreement with MM2 calculations[35] performed on model ketones which unmistakingly reveal the trans isomers to be more stable (Table 1).

The critical introduction of the ethereal oxygen projected to reside in ring D, with proper regard for the preservation of unsaturation in ring B, was first attempted from the cis-fused tricyclic ketone **38** (Scheme 7). Under kinetically-controlled deprotonation conditions, formation of the less substituted silyl enol ether was heavily favored. When this intermediate was oxidized with *m*-chloroperbenzoic acid, the α-ketol **41** was formed as the major product. When initial experiments designed to transform **41** into cyclooctene **44** proved unrewarding, recourse was made to formation of the enol phosphate **43** in preparation for dissolving metal reduction.[36] By proper optimization of concentration, reaction temperature, and the relative amount of lithium metal, the yield of **44** was maximized (81%) at the expense of competing overreduction. Careful monitoring of the subsequent deprotection of the MOM ether under a variety of conditions revealed **44** to be prone to acid-promoted elimination. In order to skirt this unwanted reaction pathway, use was made of bromocatecholborane.[37] When

Scheme 7



somewhat more than 1 equiv of this reagent was employed, the conversion to **45** proceeded quantitatively, allowing for subsequent perruthenate oxidation[38] to enone **47**. On one occasion, an insufficient amount of bromocatecholborane was mistakingly introduced, an event which led to isolation of the highly crystalline methylene acetal **46**. The opportunity to confirm the stereochemical assignments made to this advanced stage of the synthesis was seized in the form of an X-ray analysis. As shown in Figure 1, all seven stereogenic centers in each half of this symmetric structure possess the absolute configuration assigned to them. Beyond that, the cyclooctene rings adopt as much of a tub formation as the cyclopentanes cis-annealed along the periphery allow.

Despite these successes, ketone **47** proved not to be a notably useful precursor to epoxydictymene. Although MM2 calculations suggested that the trans isomer of **47** is about 6.7 kcal/mol more stable (Table 1), means were not found to effect

(32) (a) Pfenninger, J.; Heuberger, C.; Graf, W. *Helv. Chim. Acta* **1980**, *63*, 2328. (b) Chatgilialoglu, C.; Griller, D.; Lesage, M. *J. Org. Chem.* **1988**, *53*, 3641.

(33) Corey, E. J.; Gross, A. W. *Tetrahedron Lett.* **1984**, *25*, 495.

(34) Fleming, I.; Paterson, I. *Synthesis* **1979**, 736.

(35) MODEL version 2.96 and 2.99 obtained from Prof. K. Steliou was utilized.

(36) Ireland, R. E.; Pfister, G. *Tetrahedron Lett.* **1969**, 2145.

(37) Boeckman, R. K., Jr.; Potenza, J. C. *Tetrahedron Lett.* **1985**, *26*, 1411.

(38) (a) Griffith, W. P.; Ley, S. V. *Aldrichim. Acta* **1990**, *23*, 13. (b) Ley, S. V.; Norman, J.; Griffith, W. P.; Marsden, S. P. *Synthesis* **1994**, 639.

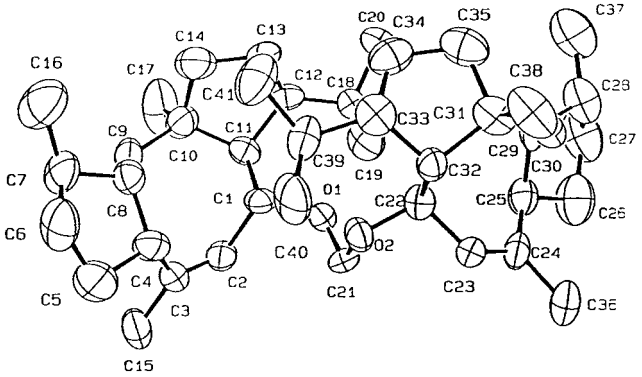
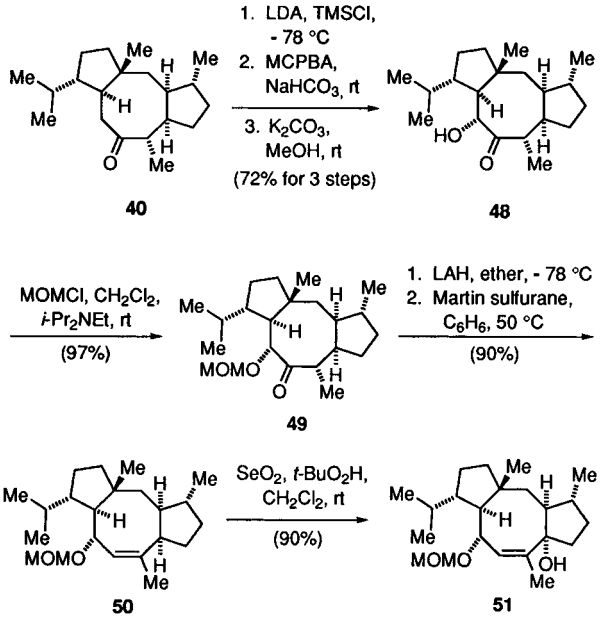
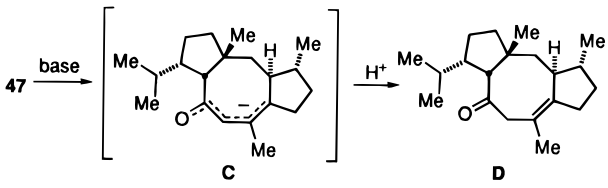


Figure 1. ORTEP drawing of **46**. The non-hydrogen atoms are represented by 50% probability thermal ellipsoids.

Scheme 8



epimerization at this position. In every instance, deprotonation occurred to generate the extended enolate **C**, protonation of



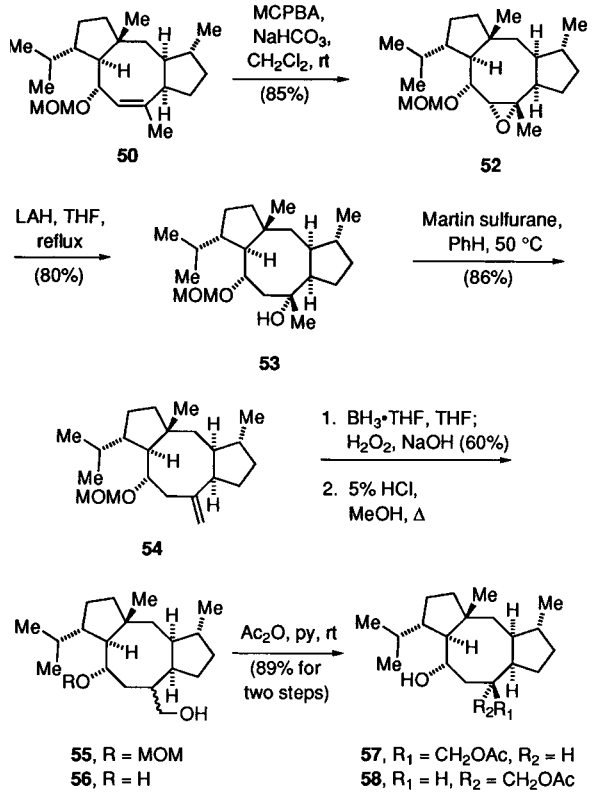
which gave rise to **D** with obliteration of a key stereogenic center. Under no circumstances did the double bond provide indication that it could be migrated to the exocyclic site. Consequently, attention was directed alternatively to the trans-fused ketone **40**.

Once the α-MOM substituent had been introduced as before (Scheme 8), a critical improvement in the introduction of the cyclooctene double bond was realized.

Through sequential hydride reduction and alcohol dehydration with the Martin sulfurane reagent,[39] the conversion to **50** could be accomplished conveniently without painstaking provisions to monitor and control reaction parameters closely. Note, however, that all attempts to functionalize **50** at its allylic methyl group proved unsuccessful. The conversion to **51** under the influence of selenium dioxide is illustrative of the greater

(39) Martin, J. C.; Arhart, R. J. *J. Am. Chem. Soc.* **1971**, *93*, 4327.

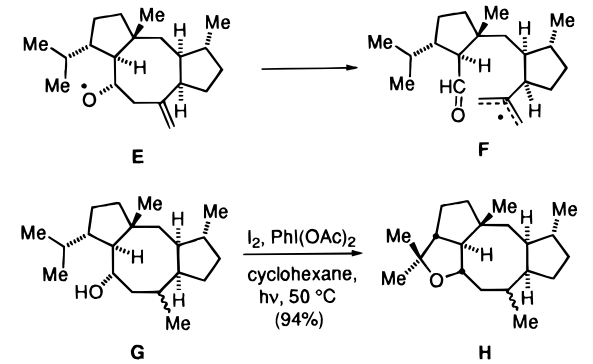
Scheme 9



reactivity of the tertiary allylic center as seen earlier in a different context.

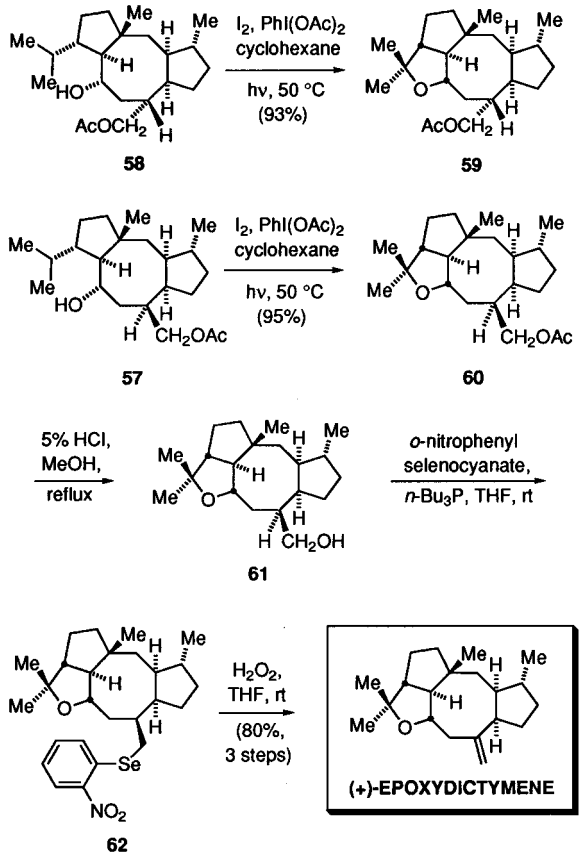
In order to override the regioselectivity of those processes characterized by the production of **D** and **51**, we chose to epoxidize **50** and to reduce the oxirane **52** with lithium aluminum hydride (Scheme 9). Although steric factors contributed in an important way to kinetic retardation of the C−O bond cleavage, formation of tertiary carbinol **53** was not adversely affected. The latter could be unidirectionally dehydrated to the exomethylene derivative **54** in the presence of Martin's sulfurane.

With this protected alcohol in hand, we recognized that little chance existed for its direct conversion to **1** via alkoxy-directed cyclization. The disadvantage materializes because of the fact that oxygen-centered radical **E** has open to it a facile ring-cleavage fragmentation that would generate the delocalized allylic radical **F**. Indeed, when this reaction was attempted, only ill-defined products resulted. Since it was our intention to exploit formation of the tetrahydrofuran ring in this manner, the dihydro derivatives **G** available from the catalytic hydro-



genation of **54** were subjected to irradiation in cyclohexane solution containing iodobenzene diacetate and iodine.[40] Both

Scheme 10



isomers underwent intramolecular abstraction of the tertiary isopropyl hydrogen and subsequent cyclization to generate the strained *trans*-oxabicyclo[3.3.5]octanes **H**.

With this precedent established, **54** was sequentially hydroborated, deprotected to the diols **56**, and monoacetylated. Ideally, the primary acetates **57** and **58** proved to be chromatographically separable. When each isomer was independently subjected to irradiation in the predescribed manner, cyclization to **59** and **60**, respectively, proceeded once again with exceptional efficiency (Scheme 10).

Following acetate hydrolysis, the more reactive exo alcohol **61** was dehydrated via the Scheme 10 *o*-nitrophenylselenide **62**[41] to deliver (+)-epoxydictymene (**1**), spectroscopically identical to the natural material.[3]

Conclusion

A total synthesis of (+)-epoxydictymene has been successfully realized. The most rewarding aspects of the synthesis were the ability to carry out effective closure of the oxabicyclooctane ring in a complex structural setting and to fix the majority of the relevant stereogenic centers in a catalyzed Claisen rearrangement. The introduction of an angular methyl group and other approaches to regio- and stereocontrol provide additional information of tactical value. The least satisfying stage in the synthetic route revolves about our inability to expedite the conversion of **50** to the target molecule. Notwithstanding, the study defines useful limits within which a significantly strained C−O bond can be formed strategically as part of the "end game" of a complex synthesis. Further exploitation of this tactic appears to be warranted.

(40) Concepción, J. I.; Francisco, C. G.; Hernández, R.; Salazar, J. A.; Suárez, E. *Tetrahedron Lett.* **1984**, *25*, 1953.

(41) Grieco, P. A.; Gilman, S.; Nishizawa, M. *J. Org. Chem.* **1976**, *41*, 1485.

Experimental Section

Melting points are uncorrected. ^{1}H NMR spectra were recorded at 300 MHz and ^{13}C NMR spectra at 75 MHz unless otherwise noted. Elemental analyses were performed at the Scandinavian Microanalytical Laboratory, Herlev, Denmark. All MPLC separations were conducted with Merck Lobar columns (Lichroprep Si-60) with a Fluid Metering INC pump and a Waters Associates Model R403 differential refractometer detector. The organic extracts were dried over anhydrous $MgSO_4$. Solvents were reagent grade and in most cases dried prior to use. All other commercially available reagents were used as received.

(*S*)-*N*-Methyl-*S*-[[(1*S*,2*S*,3a*S*,4*R*,6a*R*)-octahydro-2-hydroxy-1,4-dimethyl-2-pentalenyl]methyl]-*S*-phenylsulfoximine (9) and (*S*)-*N*-Methyl-*S*-[[(1*R*,2*R*,3a*R*,4*S*,6a*S*)-octahydro-2-hydroxy-1,4-dimethyl-2-pentalenyl]-methyl]-*S*-phenylsulfoximine (10). A solution of (*S*)-(+)-**8**[21] (9.86 g, 58.3 mmol), $[\alpha]^{19}_D$ +178.4° (*c* 1.60, acetone) (≥ 97% ee) in dry THF (100 mL) was treated at −10 °C with *n*-butyllithium (33.8 mL of 1.6 M in hexanes, 54.1 mmol). After 10 min, racemic **7** (6.34 g, 41.6 mmol) in dry THF (20 mL) was added during 10 min at −78 °C. Two hours later, saturated NH_4Cl solution was introduced at −78 °C, and the product was extracted into ether. The combined organic phases were washed with 5% HCl and brine, dried, and evaporated to provide a brown residue. Flash chromatrography on silica gel (elution with 10:1 hexanes−ethyl acetate) gave 6.0 g (45%) of **9**, mp 124−125 °C (from ether), as the more polar diastereomer and 5.35 g (40%) of **10**, mp 137−138 °C.

For **9**: IR ($CHCl_3$, cm^{-1}) 3480, 1240, 1210, 1145; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.89−7.83 (m, 2 H), 7.64−7.51 (m, 3 H), 5.98 (br s, 1 H), 3.26 (d, J = 14 Hz, 1 H), 3.20 (dd, J = 14, 1 Hz, 1 H), 2.70 (s, 3 H), 2.23 (dd, J = 12.5, 8 Hz, 1 H), 1.92−1.63 (m, 5 H), 1.52 (dddd, J = 9, 8, 8, 5 Hz, 1 H), 1.43−1.32 (m, 1 H), 1.33 (br dd, J = 12.5, 8 Hz, 1 H), 1.20−1.06 (m, 1 H), 0.89 (d, J = 7 Hz, 3 H), 0.78 (d, J = 6.5 Hz, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) ppm 139.9, 133.0, 129.4, 128.8, 82.0, 60.4, 51.4, 48.8, 47.3, 43.6, 41.6, 34.5, 31.0, 29.2, 19.8, 14.2; MS *m*/*z* (M^+) calcd 321.1763, obsd 321.1753; $[\alpha]^{20}_D$ +74.4 (*c* 1.22, $CHCl_3$).

Anal. Calcd for $C_{18}H_{27}NO_2S$: C, 67.25; H, 8.47. Found: C, 67.17; H, 8.54.

For **10**: IR ($CHCl_3$, cm^{-1}) 3350, 1245, 1215, 1155; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.90−7.84 (m, 2 H), 7.66−7.53 (m, 3 H), 6.72 (s, 1 H), 3.20 (dd, J = 13.5, 2 Hz, 1 H), 3.10 (dd, J = 13, 8 Hz, 1 H), 2.98 (d, J = 13.5 Hz, 1 H), 2.59 (s, 3 H), 1.94 (br dddd, J = 9.5, 9, 8.5, 3.5 Hz, 1 H), 1.88−1.72 (m, 4 H), 1.61 (dq, J = 9, 7 Hz, 1 H), 1.45 (ddd, J = 13, 9.5, 2 Hz, 1 H), 1.26−1.19 (m, 2 H), 0.89 (d, J = 6.5 Hz, 1 H), 0.79 (d, J = 7 Hz, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) ppm 139.1, 133.1, 129.6, 128.9, 82.2, 58.9, 51.9, 47.4, 47.1, 43.5, 41.4, 33.7, 30.3, 28.9, 19.9, 12.6; MS *m*/*z* (M^+) calcd 321.1763, obsd 321.1771; $[\alpha]^{20}_D$ +15.3 (*c* 0.95, $CHCl_3$).

Anal. Calcd for $C_{18}H_{27}NO_2S$: C, 67.25; H, 8.47. Found: C, 67.06; H, 8.48.

Conversion of 10 to (−)-Isoiridomyrmecin (11). A 218 mg (0.68 mmol) sample of **10** was placed in a flask and heated at 170 °C under 1 mm in a Kugelrohr apparatus until the ketone was completely liberated. Filtration of the crude product through TLC grade silica gel afforded 86 mg (83%) of (−)-**7**, $[\alpha]^{20}_D$ −34.9° (*c* 1.0, $CHCl_3$). This material was converted in turn into its kinetic silyl enol ether, subjected to ozonolytic cleavage, and reduced with sodium borohydride in a manner paralleling that detailed previously.[19] There was isolated 36 mg (65%) of **11**, $[\alpha]^{20}_D$ −58.0 (*c* 1.01, CCl_4).

Conversion of 9 to (1*S*,3a*S*,4*R*,6a*R*)-Hexahydro-1,4-dimethyl-2(1*H*)-pentalenone (7). A 2.32 g (7.22 mmol) sample of **9** was heated from 60 °C to 170 °C during 10 min in a Kugelrohr apparatus evacuated to 1 mm. The distillate was chromatographed on silica gel (elution with 4:1 petroleum ether−ether) to give 1.07 g (97%) of pure **7** as a colorless oil, $[\alpha]^{20}_D$ +40.1° (*c* 2.23, $CHCl_3$). This ketone was transformed into **5** via the silyl enol ether with 86% overall efficiency, as described previously for the racemic compound.[19]

(1*S*,4*S*,4a*R*,7*R*,7a*S*)-Hexahydro-1-[(3*S*)-3-isopropyl-1-cyclopenten-1-yl]-4,7-dimethylcyclopenta[*c*]pyran-3(1*H*)-one (12) and (1*R*,4*S*,-4a*R*,7*R*, 7a*S*)-Hexahydro-1-[(3*S*)-3-isopropyl-1-cyclopenten-1-yl]-4,7-dimethylcyclopenta[*c*]pyran-3(1*H*)-one (13). *tert*-Butyllithium in pentane (42 mL of 1.7 M, 71.4 mmol) was added dropwise during 15

min at −78 °C to a solution of (*S*)-**6** (8.10 g, 42.8 mmol) in dry THF (300 mL). After 2.5 h of further stirring at −78 °C, the resulting alkenyllithium was slowly (*ca.* 30 min) transferred via a cooled cannula into a cold (−78 °C) stirred solution of **15** (6.14 g, 31.0 mmol) in dry THF (500 mL). After 3 h, the reaction mixture was quenched with saturated NH_4Cl solution and partitioned between ether and water. The organic phase was washed with 5% HCl (2×) and brine, dried, and evaporated. The partially lactonized product (10.66 g) was stirred overnight at 20 °C with 10 equiv of aqueous potassium hydroxide in sufficient methanol to produce a homogeneous solution. After evaporative removal of the methanol, the neutrals were removed by extraction with CH_2Cl_2. Acidification with dilute HCl and exhaustive $CHCl_3$ extraction was followed by washing of the combined $CHCl_3$ extracts with brine, drying, and solvent evaporation. ^{1}H NMR analysis showed the **12**/**13** ratio to be 14:86. Flash chromatography of the mixture on silica gel (elution with 2:1 petroleum ether−ether) afforded pure **12** (850 mg, 10%) and pure **13** (5.22 g, 61%).

For **12**: colorless crystals, mp 85−86 °C (from pentane); IR (CCl_4, cm^{-1}) 1750; ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.73 (ddd, J = 2, 2, 1.5 Hz, 1 H), 4.66 (br d, J = 11 Hz, 1 H), 2.56−2.38 (m, 2 H), 2.37−1.94 (m, 5 H), 1.94−1.80 (m, 2 H), 1.70-1.48 (m, 3 H), 1.36−1.17 (m, 2 H), 1.20 (d, J = 6.5 Hz, 3 H), 0.91 (d, J = 6.5 Hz, 3 H), 0.90 (d, J = 6.5 Hz, 3 H), 0.86 (d, J = 6.5 Hz, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) ppm 176.2, 140.6, 133.6, 80.3, 52.6, 48.0, 43.8, 39.2, 38.6, 35.8, 33.1, 32.4, 30.1, 27.5, 20.6, 20.4, 19.5, 14.0; MS *m*/*z* (M^+) calcd 276.2089, obsd 276.2091.

Anal. Calcd for $C_{18}H_{28}O_2$: C, 78.21; H, 10.21. Found: C, 78.13; H, 10.30.

For **13**: colorless crystals, mp 90−91 °C (from pentane); IR (CCl_4, cm^{-1}) 1745; ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.82 (dddd, J = 2, 2, 2, 2 Hz, 1 H), 5.10 (br s, 1 H), 2.53−2.41 (m, 1 H), 2.51 (dq, J = 1.5, 7.5 Hz, 1 H), 2.35 (dddd, J = 9, 7, 7, 2.5 Hz, 1 H), 2.32−2.22 (m, 2 H), 2.07−1.85 (m, 4 H), 1.73 (dddd, J = 12, 6.5, 6, 4.5 Hz, 1 H), 1.58 (dddd, J = 13, 8, 8, 6 Hz, 1 H), 1.52 (dqq, J = 7, 7, 7 Hz, 1 H), 1.34 (d, J = 7.5 Hz, 3 H), 1.31−1.07 (m, 2 H), 0.90 (d, J = 6.5 Hz, 3 H), 0.89 (d, J = 7 Hz, 3 H), 0.85 (d, J = 7 Hz, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) ppm 175.8, 139.8, 129.3, 76.9, 52.8, 46.5, 43.7, 41.3, 34.3, 34.1, 33.8, 33.0, 32.7, 27.4, 20.8, 20.5, 20.3, 18.2; MS *m*/*z* (M^+) calcd 276.2089, obsd 276.2059; $[\alpha]^{20}_D$ +2.1 (*c* 0.86, $CHCl_3$).

Anal. Calcd for $C_{18}H_{28}O_2$: C, 78.21; H, 10.21. Found: C, 78.27; H, 10.31.

(1*R*,4*S*,4a*R*,7*R*,7a*S*)-Octahydro-1-[(3*S*)-3-isopropyl-1-cyclopenten-1-yl]-4,7-dimethyl-3-methylenecyclopenta[*c*]pyran (14). To a solution of **13** (2.00 g, 7.25 mmol) in a cold (−55 °C) mixture of THF (29 mL), toluene (58 mL), and pyridine (0.6 mL) was added the Tebbe reagent (29 mL of 0.44 M in toluene, 12.8 mmol), and stirring was maintained under N_2 for 1 h. The reaction mixture was diluted with petroleum ether, quenched with 20% NaOH solution (7.25 mL) at −55 °C, allowed to warm to room temperature, washed with 20% NaOH and with brine, quickly dried, and evaporated. Flash chromatography of the residue on grade III basic alumina (elution with petroleum ether) afforded 1.94 g (98%) of **14** as a colorless oil: IR (CCl_4, cm^{-1}) 1645, 1465, 1215, 1100, 1085, 1010; ^{1}H NMR (300 MHz, C_6D_6) δ 6.03 (dddd, J = 2, 2, 2, 2 Hz, 1 H), 4.75 (d, J = 0.5 Hz, 1 H), 4.58 (br s, 1 H), 4.22 (d, J = 1 Hz, 1 H), 2.56−2.45 (m, 1 H), 2.38−2.15 (m, 3 H), 2.06 (dddq, J = 7, 7, 1, 0.5 Hz, 1 H), 1.99 (dddd, J = 12.5, 8.5, 8.5, 4.5 Hz, 1 H), 1.87 (dddd, J = 12.5, 8, 7.5, Hz, 1 H), 1.80 (dddd, J = 7.5, 7, 7, 4.5 Hz, 1 H), 1.67−1.37 (m, 4 H), 1.54 (ddd, J = 9.5, 8, 3 Hz, 1 H), 1.09 (dddd, J = 12.5, 9, 8, 6 Hz, 1 H), 1.07 (d, J = 7 Hz, 3 H), 0.97 (d, J = 6.5 Hz, 3 H), 0.95 (d, J = 6.5 Hz, 3 H), 0.92 (d, J = 6.5 Hz, 3 H); ^{13}C NMR (75 MHz, C_6D_6) ppm 165.1, 143.6, 127.3, 90.1, 77.0, 53.3, 48.7, 46.2, 35.8, 33.9, 33.4, 33.3, 32.4, 30.8, 27.9, 21.6, 20.8, 20.6, 19.2; MS *m*/*z* (M^+) calcd 274.2297, obsd 274.2273.

This material was utilized without delay.

(1*R*,3a*R*,5*S*.6a*R*.7*S*,10*S*)-2,3,3a,4,6,6a,7,8,9,10a-Decahydro-7-isopropyl-1,4-dimethyldicyclopenta[*a,d*]cycloocten-5(1*H*)-one (15). A solution of **14** (52.4 mg, 0.19 mmol) in dry CH_2Cl_2 (10 mL) was treated at −78 °C with triisobutylaluminum (0.70 mL of 1.0 M in toluene, 0.70 mmol) during 2 min, allowed to warm slowly to 20 °C, and stirred overnight prior to quench with saturated NH_4Cl solution. The product was extracted into ether, and the combined organic phases were washed with 5% HCl, water, and brine prior to drying and concentration. ^{1}H NMR analysis of this material showed it to be a 4:1 mixture of the α- and *β*-alcohols, which was directly oxidized with pyridinium chlorochromate (150 mg, 696 mmol) and pyridine (0.1 mL) in dry CH_2Cl_2 (5 mL) during 3 h at room temperature to give 46 mg (88%) of **15** as a colorless oil: IR (CCl_4, cm^{-1}) 1710; ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.43 (dddd, J =9, 2.5, 2.5, 1 Hz, 1 H), 3.20 (br ddd J = 13, 6, 5 Hz, 1 H), 2.78 (br dq, J = 11, 6.5 Hz, 1 H), 2.54 (dd, J = 13, 5 Hz, 1 H), 2.45 (ddddd, J = 17, 10, 2.5, 2, 1.5 Hz, 1 H), 2.30 (br dddd, J = 17, 10, 9, 2.5 Hz, 1 H), 2.23−2.10 (br m, 1 H), 2.09−1.92 (m, 2 H), 2.02 (br dd, J = 13, 12.5 Hz, 1 H), 1.92−1.62 (m, 4 H), 1.55 (dddd, J = 13.5, 9, 5, 2.5 Hz, 1 H), 1.50−1.29 (m, 2 H), 1.11 (dddd, J = 12.5, 10, 7.5, 5 Hz, 1 H), 1.00 (pair of unresolved d, J = 6.5 Hz, 2 × 3 H), 0.94 (d, J = 6.5 Hz, 3 H), 0.90 (d, J = 6.5 Hz, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) ppm 216.4, 148.0, 120.8, 52.0, 51.6, 46.9, 45.5, 43.5, 40.1, 36.5, 32.0, 31.0, 28.8, 27.8, 26.3, 22.1, 21.4, 20.4, 17.1; MS *m*/*z* (M^+) calcd 274.2297, obsd 274.2299; $[\alpha]^{20}_D$ +18.5 (*c* 1.9, $CHCl_3$).

Anal. Calcd for $C_{19}H_{30}O$: C, 83.15; H, 11.02. Found: C, 83.10; H, 10.99.

(1*R*,3a*R*,4*S*,5*R*,6a*R*,7*S*,10a*S*)-1,2,3,3a,4,5,6,6a,7,8,9,10a-Dodecahydro-7-isopropyl-1,4-dimethyldicyclopenta[*a,d*]cycloocten-5-ol (28). A solution of **15** (52 mg, 0.19 mmol) in CH_2Cl_2 (5 mL) at −78 °C was treated with Dibal-H (0.6 mL of 1 M in toluene, 0.60 mmol), allowed to warm to 20 °C during 4 h, and quenched at −20 °C with saturated NH_4Cl solution. After dilution with ether, the separated organic phase was washed with 5% HCl, water, and brine, dried, and concentrated. Purification of the residue on silica gel (elution with 3:1 petroleum ether−ether) gave 50 mg (95%) of **28** as a colorless crystalline solid, mp 114−116 °C (from pentane): IR (CCl_4, cm^{-1}) 3620; ^{1}H NMR (300 MHz, $CDCl_3$) (most signals are very broad at 25 °C) δ 4.87 (m, 1 H), 3.69 (br ddd, J = 9.5, 7.5, 1.5 Hz, 1 H), 2.75 (m, 1 H), 2.45−0.75 (series of m, 16 H), 1.03 (d, J = 7 Hz, 3 H), 0.96 (d, J = 7 Hz, 3 H), 0.83 (d, J = 7 Hz, 3 H), 0.73 (d, J = 6.5 Hz, 3 H) (OH not observed); ^{13}C NMR (75 MHz, $CDCl_3$) ppm 146.2, 124.0, 78.1, 48.3, 46.2, 44.7, 43.7, 41.9, 37.0, 33.3, 32.7, 30.9, 30.7, 27.8, 22.7, 22.3, 22.2, 18.9, 17.6; MS *m*/*z* (M^+) calcd 276.2453, obsd 26.2446.

Anal. Calcd for $C_{19}H_{32}O$: C, 82.55; H, 11.67. Found: C, 82.65; H, 12.09.

(1*R*,3a*R*,4*S*,5*R*,6a*R*,7*S*,10a*S*)-1,2,3,3a,4,5,6,6a,7,8,9,10a-Dodecahydro-7-isopropyl-5-(methoxymethoxy)-1,4-dimethyldicyclopenta[*a,d*]-cyclooctene (29). A solution of **28** (600 mg, 2.17 mmol) and diisopropylethylamine (3.02 mL, 17.4 mmol) in CH_2Cl_2 (30 mL) was treated with methoxymethyl chloride (0.66 mL, 8.68 mmol) at −10 °C. The reaction mixture was allowed to warm slowly to 20 °C, stirred for 8 h, and quenched with 5% HCl. The organic phase was washed with brine, dried, and concentrated to leave a residue that was chromatographed on silica gel (elution with 20:1 hexanes−ether) to give 660 mg (95%) of **29** as a colorless oil: IR (CCl_4, cm^{-1}) 1465, 1445, 1365, 1145, 1095, 1085; ^{1}H NMR (300 MHz, C_6D_6) (all signals except the upfield doublets are broad at 25 °C) δ 4.98 (br s, 1 H), 4.27 (d, J = 7 Hz, 1 H), 4.56 (d, J = 7 Hz, 1 H), 3.53 (br dd, J = 9.5, 7.5 Hz, 1 H), 3.25 (s, 3 H), 2.92 (m, 1 H), 2.44−2.25 (m, 2 H), 2.25−1.96 (m, 4 H), 1.96−1.65 (m, 6 H), 1.58−1.46 (m, 2 H), 1.24−0.98 (m, 2 H), 1.11 (d, J = 7 Hz, 3 H), 0.95 (d, J = 7 Hz, 3 H), 0.81 (d, J = 7 Hz, 3 H), 0.79 (d, J = 7 Hz, 3 H); ^{13}C NMR (75 MHz, C_6D_6) ppm 146.5, 124.9, 96.1, 83.3, 55.3, 48.8, 46.7, 45.1, 44.0, 43.5, 37.1, 33.7, 31.2, 31.0, 30.2, 28.2, 23.0, 22.7, 22.5, 19.6, 17.9, 17.9; MS *m*/*z* (M^+) calcd 320.2715, obsd 320.2726.

Abbreviated Procedure for Preparation of 29 from Lactone 13. Lactone **13** (5.22 g, 18.9 mmol) was reacted with Tebbe reagent (40 mL of 0.88 M in toluene, 35 mmol) as described earlier. The resulting vinyl ether **14** was immediately dissolved in dry CH_2Cl_2 (400 mL) and treated with triisobutylaluminum (50 mL of 1.0 M in toluene, 50 mmol) at −78 °C. After 1 h of stirring, Dibal-H (50 mL of 1.0 M in hexanes, 50 mmol) was introduced at −78 °C followed by slow warmup to 20 °C during 4 h. Customary workup afforded alcohol **28** (5.00 g) of sufficient purity to be carried forward without purification. This material and diisopropylethylamine (25 mL, 144 mmol) were dissolved in CH_2Cl_2 (200 mL) and treated with methoxymethyl chloride (5.6 mL, 74 mmol) at −10 °C followed by slow warmup to 20 °C and overnight stirring. Excess reagent was then destroyed by addition of methanol, and workup and purification as above provided pure **29** (5.30 g, 88% overall from **13**) as a colorless oil.

(1*R*,3a*R*,4*S*,5*R*,6a*R*,7*S*,9a*S*,10a*S*)-Dodecahydro-7-isopropyl-5-(methoxymethoxy)-1,4-dimethyldicyclopenta[*a*,*d*]cyclooctene-9a(1*H*)-ol (30) and (1*R*,3a*S*,4*S*,5*R*,6a*R*,7*S*,9a*S*,10*R*,10a*S*)-Tetradecahydro-7-isopropyl-5-(methoxymethoxy)-1,4-dimethyldicyclopenta[*a*,*d*]-cyclooctene-10-ol (31). The protected cyclooctenol **29** (4.13 g, 12.9 mmol) and lithium borohydride (350 mg, 16.1 mmol) were dissolved in dry THF (250 mL), cooled to −15 °C, and treated with the borane−THF complex (50 mL of 1 M in THF, 50 mmol) during 5 min. The reaction mixture was stirred overnight at 20 °C, carefully quenched with water (15 mL) followed by 20% NaOH (15 mL) and 30% hydrogen peroxide solutions (15 mL), stirred for an additional 3 h, and diluted with ether (250 mL). The combined organic layers were washed with 5% HCl (200 mL), water (200 mL), and brine (200 mL), then dried, and concentrated. Flash chromatography of the residue on silica gel (elution with 4:1 petroleum ether−ether) afforded 1.02 g (23%) of **30** and 2.56 g (59%) of **31**.

For **30**: colorless gum; IR (film, cm^{-1}) 3529, 1466, 1150, 1028; ^1H NMR (300 MHz, C_6D_6) δ 4.44 (d, J = 7.0 Hz, 1 H), 4.26 (d, J = 7.0 Hz, 1 H), 4.17 (br s, 1 H), 3.37 (ddd, J = 11.8, 6.3, 2.9 Hz, 1 H), 3.07 (s, 3 H), 2.28−2.24 (m, 1 H), 1.95−0.90 (series of m, 18 H), 1.34 (d, J = 6.7 Hz, 3 H), 1.17 (d, J = 7.1 Hz, 3 H), 0.81 (d, J = 6.6 Hz, 3 H), 0.69 (d, J = 6.6 Hz, 3 H); ^{13}C NMR (75 MHz, C_6D_6) ppm 96.1, 85.8 (2 C), 59.9, 55.4, 50.5, 47.6, 47.3, 43.7, 41.1, 40.9, 37.0, 33.9, 31.5, 30.4, 28.5, 23.7, 22.7, 22.5, 18.3, 16.5; MS *m*/*z* (M^+) calcd 338.2821, obsd 338.2819.

For **31**: colorless gum; IR (CCl_4, cm^{-1}) 3620; ^1H NMR (300 MHz, C_6D_6) δ 4.74 (d, J = 6.5 Hz, 1 H), 4.60 (d, J = 6.5 Hz, 1 H), 3.52 (ddd, J = 11.5, 5.5, 2.5 Hz, 1 H), 3.45 (br d, J = 2 Hz, 1 H), 3.26 (s, 3 H), 3.00 (ddq, J = 10.5, 2.5, 7 Hz, 1 H), 1.88−0.95 (series of m, 17 H), 1.16 (d, J = 7 Hz, 3 H), 0.95 (d, J = 6 Hz, 3 H), 0.91 (d, J = 6.5 Hz, 3 H), 0.89 (d, J = 6.5 Hz, 3 H) (OH not observed); ^{13}C NMR (75 MHz, C_6D_6) ppm 96.5, 84.4, 77.6, 55.3, 55.1, 52.4, 46.9, 43.4, 41.2, 36.3, 34.6, 34.4, 34.3, 30.3, 26.6, 26.4, 25.3, 22.2, 21.9, 20.6, 18.6; MS *m*/*z* (M^+) calcd 338.2821, obsd 338.2839.

(1*R*,3a*S*,4*S*,5*R*,6a*R*,7*S*,9a*S*,10a*S*)-Dodecahydro-7-isopropyl-5-(methoxymethoxy)-1,4-dimethyldicyclopenta[*a*,*d*]cyclooctene-10(1*H*)-one (32). To a solution of **31** (2.56 g, 7.55 mmol) in CH_2Cl_2 (250 mL) and ether (150 mL) was added pyridinium chlorochromate on alumina (60 g, 54 mmol). After 3 h, the reaction mixture was filtered through Celite and concentrated. The concentrate was chromatographed on silica gel (elution with 9:1 petroleum ether−ether) to provide 2.11 g (83%) of **32** as colorless crystals, mp 109.5−110 °C (from petroleum ether): IR (CCl_4, cm^{-1}) 1680; ^1H NMR (300 MHz, C_6D_6) δ 4.63 (d, J = 7 Hz, 1 H), 4.49 (d, J = 7 Hz, 1 H), 3.30 (ddd, J = 10.5, 6, 2.5 Hz, 1 H), 3.20 (s, 3 H), 3.11 (dd, J = 9.5, 4.5 Hz, 1 H), 2.80−2.62 (m, 2 H), 2.39 (dddd, J = 11.5, 11.5, 9.5, 6.5 Hz, 1 H), 2.04−1.93 (m, 1 H), 1.88−1.50 (m, 9 H), 1.44 (dqq, J = 9.5, 6.5, 6.5 Hz, 1 H), 1.24−0.87 (m, 3 H), 0.94 (d, J = 7 Hz, 3 H), 0.89 (d, J = 7 Hz, 3 H), 0.80 (d, J = 6.5 Hz, 3 H), 0.78 (d, J = 6.5 Hz, 3 H); ^{13}C NMR (62.5 MHz, C_6D_6) ppm 217.3, 96.7, 83.5, 60.1, 56.1, 55.4, 53.9, 43.9, 40.0, 38.6, 36.6, 34.6, 32.5, 29.7, 28.0, 25.8, 25.6, 22.3, 21.6, 21.5, 18.4; MS *m*/*z* (M^+) calcd 336.2664, obsd 336.2669; $[\alpha]^{20}_D$ −60.1 (*c* 0.57, $CHCl_3$).

Anal. Calcd for $C_{21}H_{36}O_3$: C, 74.95; H, 10.78. Found: C, 75.03; H, 11.06.

(1*R*,3a*S*,4*S*,5*R*,6a*R*,7*S*,9a*S*,10a*S*)-Dodecahydro-7-isopropyl-5-(methoxymethoxy)-1,4,9a-trimethyldicyclopenta[*a*,*d*]cycloocten-10(1*H*)-one (33). Diisopropylamine (10 mL, 71 mmol) was dissolved in THF (200 mL), cooled to 0 °C, and treated dropwise with *n*-butyllithium (20 mL of 1.6 M in hexanes, 32 mmol). After 30 min, this solution was cooled to −78 °C, and **32** (2.62 g, 7.8 mmol) in THF (25 mL) was introduced dropwise. The temperature was then raised to −15 °C for 1 h prior to the addition of methyl iodide (10 mL, 160 mmol) in HMPA (20 mL) and THF (20 mL) at −78 °C. The reaction mixture was allowed to warm to room temperature during 4 h, quenched with saturated NH_4Cl solution (20 mL), and diluted with 1:1 petroleum ether−ether (250 mL). The organic phase was washed with 5% HCl (250 mL), water (250 mL), and brine (250 mL) prior to drying and concentration. Silica gel chromatographic purification of the residue (elution with 9:1 petroleum ether−ether) provided 0.48 g of unreacted **32** and 2.18 g of **33** (98% corrected).

For **33**: colorless crystals, mp 58−60 °C; IR (CCl_4, cm^{-1}) 1680; ^1H NMR (300 MHz, $CDCl_3$) δ 4.69 (d, J = 7 Hz, 1 H), 4.60 (d, J = 7 Hz, 1 H), 3.39 (s, 3 H), 3.33 (ddd, J = 11, 5.5, 3 Hz, 1 H), 3.31 (dd, J = 9, 5 Hz, 1 H), 2.39 (dddq, J = 9.5, 7, 5, 7 Hz, 1 H), 2.30−2.10 (m, 2 H), 2.05−1.83 (m, 5 H), 1.86 (ddd, J = 15, 10.5, 10.5 Hz, 1 H), 1.72−1.25 (m, 6 H), 1.14 (s, 3 H), 1.04 (dddd, J = 12, 12, 10, 6 Hz, 1 H), 0.99 (d, J = 7 Hz, 3 H), 0.96 (d, J = 6.5 Hz, 3 H), 0.92 (d, J = 7 Hz, 3 H), 0.88 (d, J = 6.5 Hz, 3 H); ^{13}C NMR (75 MHz, C_6D_6) ppm 218.3, 96.9, 83.7, 58.9, 57.4, 55.3, 52.5, 47.9, 44.4, 39.9, 36.9, 34.9, 33.8, 32.3, 30.0, 28.7, 27.9, 26.1, 22.6, 21.5 (2 C), 17.7; MS *m*/*z* (M^+) calcd 350.2821, obsd 350.2854; $[\alpha]^{20}_D$ −48.2 (*c* 1.02, $CHCl_3$).

Anal. Calcd for $C_{22}H_{38}O_3$: C, 75.38; H, 10.93. Found: C, 75.33; H, 11.08.

(1*R*,3a*S*,4*S*,5*R*,6a*R*,7*S*,9a*S*,10*R*,10a*S*)-Tetradecahydro-7-isopropyl-5-(methoxymethoxy)-1,4,9a-trimethyldicyclopenta[*a*,*d*]cycloocten-10-ol (35). To a cold (−78 °C) slurry of $LiAlH_4$ (600 mg, 15.8 mmol) in dry ether (100 mL) was added a solution of **33** (2.40 g, 3.99 mmol) in the same solvent (30 mL) under N_2. The reaction mixture was stirred at room temperature for 2 h, cooled to −20 °C, quenched with ethyl acetate, and triturated extensively with ether. The ether extracts were washed with brine, dried, and concentrated. Chromatography of the residue on silica gel (elution with 9:1 hexanes−ethyl acetate) furnished 2.41 g (100%) of **35** as a colorless oil: IR (CCl_4, cm^{-1}) 3630, 3600−3300; ^1H NMR (300 MHz, C_6D_6) δ 4.74 (d, J = 6.5 Hz, 1 H), 4.61 (d, J = 6.5 Hz, 1 H), 3.49 (ddd, J = 11, 5, 2.5 Hz, 1 H), 3.26 (s, 3 H), 3.19 (br d, J = 3 Hz, 1 H), 3.01 (ddq, J = 10.5, 2.5, 7 Hz, 1 H), 2.32 (dddd, J = 13, 10.5, 9.5, 6 Hz, 1 H), 1.97 (br dd, J = 10, 7.5 Hz, 1 H), 1.90−1.38 (series of m, 11 H), 1.21 (m, 1 H), 1.20−0.90 (series of m, 3 H), 1.16 (d, J = 7 Hz, 3 H), 0.97 (d, J = 6.5 Hz, 3 H), 0.92 (d, J = 6.5 Hz, 3 H), 0.90 (d, J = 6 Hz, 3 H) (OH not observed); ^{13}C NMR (75 MHz, C_6D_6) ppm 96.6, 84.6, 83.8, 55.3, 52.4, 50.5, 48.2, 44.1, 42.7, 41.7, 34.7, 34.4, 34.1, 34.0, 31.2, 27.8, 26.9, 25.9, 22.4, 21.7, 20.5, 18.1; MS *m*/*z* ($M^+ - CH_3OH$) calcd 320.2715, obsd 320.2738.

(1*R*,3a*S*,4*S*,5*R*,6a*R*,7*S*,9a*S*,10*R*,10a*S*)-Tetradecahydro-7-isopropyl-5-(methoxymethoxy)-1,4,9a-trimethyldicyclopenta[*a*,*d*]cycloocten-10-ol *Se*-Phenyl Selenocarbonate (36). A solution of **35** (2.41 g, 6.84 mmol), pyridine (3.0 mL, 37.2 mmol), and DMAP (114 mg) in dry THF (100 mL) at 0 °C was treated with phosgene (23.4 mL of 1.93 M in toluene, 45.1 mmol), allowed to warm to room temperature, and stirred for 1 h. Solvent evaporation left a residue that was dissolved in benzene (50 mL), THF (50 mL), and pyridine (6 mL). Phenylselenol (1.61 g, 1.03 mmol) was introduced, and stirring was maintained for 4 h prior to quenching with water and extraction with ether. The combined organic layers were washed with 5% HCl, water, and saturated $NaHCO_3$ solution in advance of drying and concentration. The residue was chromatographed on silica gel (elution with 40:1 hexanes−ethyl acetate) to give 3.48 g (95%) of **36** as a colorless gum which slowly crystallized when stored neat in the refrigerator: IR (CCl_4, cm^{-1}) 1725, 1700; ^1H NMR (300 MHz, C_6D_6) δ 7.64−7.56 (m, 2 H), 7.00−6.93 (m, 3 H), 5.34 (s, 1 H), 4.69 (d, J = 6.5 Hz, 1 H), 4.57 (d, J = 6.5 Hz, 1 H), 3.38 (ddd, J = 11, 5, 2.5 Hz, 1 H), 3.25 (s, 3 H), 2.50 (ddq, J = 10.5, 2.5, 7 Hz, 1 H), 2.37−2.23 (m, 1 H), 2.12 (br dd, J = 10, 7 Hz, 1H), 1.99 (dddq, J = 10.5, 7, 7, 6.5 Hz, 1 H), 1.90−0.85 (series of m, 13 H), 1.12 (s, 3 H), 1.08 (d, J = 7 Hz, 3 H), 0.94 (d, J = 6.5 Hz, 3 H), 0.88 (d, J = 6.5 Hz, 3 H), 0.85 (d, J = 6.5 Hz, 3 H); ^{13}C NMR (75 MHz, C_6D_6) ppm 167.2, 136.0, 129.3, 129.0, 127.0, 96.6, 89.9, 84.0, 55.3, 52.0, 50.3, 48.4, 43.0, 42.8, 41.5, 34.6, 33.9, 33.8, 33.7, 31.1, 27.1, 26.7, 25.6, 22.3, 21.7, 20.3, 18.2; MS *m*/*z* ($M^+ - C_6H_5SeH - CO_2$) calcd 334.2872, obsd 334.2843.

Radical Reduction of 36. A solution of **36** (590 mg, 1.10 mmol) and tris(trimethylsilyl)silane (2.20 g, 8.80 mmol) in benzene (30 mL) was heated to reflux, and AIBN (45 mg, 0.28 mmol) dissolved in benzene (10 mL) was introduced dropwise over 30 min. After a heating period of 2 h, the reaction mixture was concentrated, and the residue was chromatographed on silica gel. Elution with 19:1 petroleum ether−ether returned 237 mg (64%) of the epimeric mixture **37** and 80 mg (25%) of **38**, which is characterized below.

For **37**: colorless gum; IR (CCl_4, cm^{-1}) 1030; ^1H NMR (300 MHz, C_6D_6) (major diasteromer) δ 4.69 (d, J = 7 Hz, 1 H), 4.46 (d, J = 7 Hz, 1 H), 3.29 (s, 3 H), 3.19 (ddd, J = 10, 3.5, 2 Hz, 1 H), 1.95−0.90 (series of m, 19 H), 1.13 (d, J = 6.5 Hz, 3 H), 1.01 (s, 3 H), 0.98 (d, J = 6.5 Hz, 3 H), 0.96 (d, J = 6.5 Hz, 3 H), 0.93 (d, J = 6.5 Hz, 3 H); (minor diastereomer) δ 4.72 (d, J = 7 Hz, 1 H), 4.59 (d, J = 7 Hz, 1 H), 3.40 (ddd, J = 11.5, 5, 2.5 Hz, 1 H), 3.25 (s, 3 H), 2.31 (dddd, J

= 12.5, 10.5, 9.5, 6 Hz, 1 H), 1.95−0.90 (series of m, 18 H), 1.09 (d, J = 7 Hz, 3 H), 1.00 (d, J = 6.5 Hz, 3 H), 0.97 (s, 3 H), 0.92 (pair of d, J = 6.5 Hz, 2 × 3 H); ^{13}C NMR (75 MHz, C_6D_6) ppm (major diastereomer) 95.4, 82.6, 56.1, 52.8, 47.0, 45.9, 45.8, 44.2, 42.8, 35.5, 33.8, 33.7, 33.1, 32.3, 29.4, 26.6, 24.2, 22.4, 21.7, 20.3, 17.1 (1 C not observed); (minor diastereomer) 96.5, 84.7, 55.3, 52.4, 47.2, 45.5, 45.1, 44.1, 41.1, 34.6, 33.9, 33.7, 32.6, 32.2, 31.0, 26.8, 26.5, 22.4, 21.8, 20.5, 18.2 (1 C not observed); MS *m*/*z* (M^+) calcd 336.3028, obsd 336.3028.

(1*R*,3a*R*,4*S*,5*R*,6a*R*,7*S*,9a*R*,10a*S*)-Dodecahydro-7-isopropyl-1,4,-9a-trimethyldicyclopenta[*a*,*d*]cycloocten-5(1*H*)-one (38). A 237 mg (0.70 mmol) sample of **37** was dissolved in methanol (4 mL), treated with concentrated HCl (0.5 mL), and heated at reflux for 1 h. After cooling, solid $NaHCO_3$ was carefully added, the methanol was removed in vacuo, and the mixture was dissolved in ether (20 mL), washed with water (20 mL) and brine (20 mL), dried, and evaporated. The unpurified alcohol was taken up in CH_2Cl_2 (10 mL), treated with pyridinium chlorochromate on alumina (1.5 g, 1.4 mmol), stirred for 30 min, and placed directly atop a column of silica gel. Elution with CH_2Cl_2 gave 204 mg (100%) of **38** as a white solid, mp 68−70 °C: IR (CCl_4, cm^{-1}) 1700; ^{1}H NMR (300 MHz, C_6D_6) δ 2.43−2.21 (ABm, 2 H), 2.16 (dq, J = 11.5, 7 Hz, 1 H), 2.03−1.91 (m, 1 H), 1.85−1.55 (series of m, 6 H), 1.56 (dd, J = 16, 10.5 Hz, 1 H), 1.38 (dddd, J = 10.5, 10.5, 8.5, 2 Hz, 1 H), 1.29−0.99 (series of m, 5 H), 1.23 (dd, J = 16, 2 Hz, 1 H), 0.97−0.87 (m, 1 H), 0.96 (s, 3 H), 0.95 (d, J = 6.5 Hz, 3 H), 0.92 (d, J = 7 Hz, 3 H), 0.88 (d, J = 6.5 Hz, 3 H), 0.86 (d, J = 6.5 Hz, 3 H); ^{13}C NMR (75 MHz, C_6D_6) ppm 217.5, 51.3, 50.9, 50.5, 47.2, 45.4, 45.1, 41.5, 39.2, 34.6, 33.6, 33.4, 33.1, 30.4, 29.7, 28.7, 22.2, 21.7, 19.0, 17.4; MS *m*/*z* (M^+) calcd 290.2610, obsd 290.2596; $[\alpha]^{20}_D$ +37.3 (*c* 1.54, $CHCl_3$).

Anal. Calcd for $C_{20}H_{34}O$: C, 82.69; H, 11.80. Found: C, 82.60; H, 11.83.

(1*R*,3a*R*,4*S*,5*R*,7*S*,9a*R*,10a*S*)-2,3,3a,4,7,8,9,9a,10,10a-Decahydro-7-isopropyl-1,4,9a-trimethyldicyclopenta[*a*,*d*]cycloocten-5(1*H*)-one (39). To a cold (−78 °C), magnetically stirred solution of **38** (29 mg, 0.10 mmol) and chlorotrimethylsilane (108 mg, 1.0 mmol) in anhydrous THF (4 mL) was added 1.66 mL of 0.3 M LDA in THF under N_2. This solution was allowed to warm slowly to 20 °C, stirred for 30 min, and returned to −78 °C when triethylamine (0.8 mL) was introduced. The solvents were removed in vacuo, and the resulting oily solid was stirred with hexanes and filtered through a plug of Celite and basic alumina (elution with hexanes). The filtrate was concentrated and the silyl enol ether was used directly.

To a solution of DDQ (340 mg, 1.5 mmol) in benzene (4 mL) at 4 °C was added a solution of collidine (196 mg, 1.62 mmol) in benzene (2 mL). After 20 min at room temperature, this solution was cooled to 0 °C, the silyl enol ether dissolved in benzene (4 mL) was added, and the mixture was stirred at 20 °C for 30 h, filtered through a short pad of Celite and basic alumina (elution with 9:1 hexanes−ethyl acetate), and concentrated. Flash chromatography of the residue on silica gel (elution with 60:1 hexanes−ethyl acetate) provided 26 mg (90%) of **39** as a colorless oil: IR (neat, cm^{-1}) 1687, 1461; ^{1}H NMR (300 MHz, C_6D_6) δ 5.61 (d, J = 2.3 Hz, 1 H), 2.41−2.34 (m, 1 H), 2.32−2.25 (m, 2 H), 1.74−1.60 (m, 3 H), 1.59−1.48 (m, 3 H), 1.40−1.24 (m, 3 H), 1.19−1.06 (m, 2 H), 1.05 (s, 3 H), 0.99 (d, J = 6.8 Hz, 3 H), 0.97−0.84 (m, 2 H), 0.83 (d, J = 6.5 Hz, 6 H), 0.71 (d, J = 6.8 Hz, 3 H); ^{13}C NMR (75 MHz, C_6D_6) ppm 213.3, 157.2, 118.9, 52.9, 48.5, 47.1, 46.9, 44.1, 40.3, 37.9, 37.3, 33.8, 30.5 (2 C), 30.4, 23.1, 22.2, 18.4, 18.3, 16.9; MS *m*/*z* (M^+) calcd 288.2453, obsd 288.2451; $[\alpha]^{20}_D$ −45.5 (*c* 0.87, EtOAc).

(1*R*,3a*R*,4*S*,6a*S*,7*S*,9a*R*,10a*S*)-Dodecahydro-7-isopropyl-1,4,9a-trimethyldicyclopenta[*a*,*d*]cycloocten-5(1*H*)-one (40). A cold (−78 °C) solution of **39** (40 mg, 0.14 mmol) in dry THF (8 mL) and liquid NH_3 (4 mL) was treated under N_2 with excess lithium metal (14 mg, 2 mmol) until a blue color persisted. After 30 min, the reaction mixture was allowed to warm to 20 °C, quenched with saturated NH_4Cl solution at −30 °C, and extracted with ether. The combined organic phases were washed with brine, dried, and concentrated. The residue and 40 mg of the PCC/Al_2O_3 mixture used above in CH_2Cl_2 (6 mL) was stirred for 3 h and processed as described earlier. Purification by flash chromatography on silica gel (elution with 30:1 hexanes−ethyl acetate) gave 36 mg (90%) of **40** as a colorless oil: IR (neat, cm^{-1}) 1692, 1462; ^{1}H NMR (300 MHz, C_6D_6) δ 2.64 (dd, J = 12.6, 6.5 Hz, 1 H), 2.35−2.22 (m, 2 H), 2.08 (dt, J = 12.2, 1.0 Hz, 1 H), 1.98−1.89 (m, 1 H), 1.77−1.58 (m, 1 H), 1.57−0.78 (series of m, 13 H), 0.94 (s, 3 H), 0.91 (d, J = 6.7 Hz, 3 H), 0.82 (d, J = 6.7 Hz, 3 H), 0.80 (d, J = 6.1 Hz, 3 H), 0.73 (d, J = 6.6 Hz, 3 H); ^{13}C NMR (75 MHz, C_6D_6) ppm 214.9, 54.5, 49.9, 46.6, 45.4, 44.2, 43.5, 41.9, 39.9, 37.5, 37.0, 34.5, 32.4, 28.7, 22.0 (2 C), 20.7, 18.8, 18.2, 16.8; MS *m*/*z* (M^+) calcd 290.2610, obsd 290.2612.

(1*R*,3a*R*,4*S*,6*S*,6a*R*,7*S*,9a*R*,10a*S*)-Dodecahydro-6-hydroxy-7-isopropyl-1,4,9a-trimethyldicyclopenta[*a*,*d*]cycloocten-5(1*H*)-one (41). Ketone **38** (84 mg, 0.29 mmol) and chlorotrimethylsilane (158 mg, 1.45 mmol) was dissolved in dry THF (5 mL), cooled to −78 °C, treated dropwise with LDA in THF (2.4 mL of 0.3 M, 0.72 mmol), allowed to warm to 20 °C, and stirred for 30 min. The reaction mixture was cooled to −78 °C, triethylamine (1 mL) was introduced, and the solvents were removed in vacuo after warming. The resulting oily solid was stirred with petroleum ether (10 mL), filtered through a Celite plug, and concentrated to give the silyl enol ether, which was taken up in CH_2Cl_2 (8 mL) and added to a mixture of MCPBA (200 mg of 50% purity, 1.16 mmol) and $NaHCO_3$ (200 mg, 2.30 mmol) in the same solvent (5 mL). The oxidation was allowed to proceed for 3 h, at which point washing with saturated $NaHCO_3$ solution was implemented (2 × 10 mL). The CH_2Cl_2 phase was concentrated, and the residue was dissolved in methanol (10 mL), admixed with K_2CO_3 (105 mg), and stirred for 1 h. The methanol was removed in vacuo, and the resulting oil was taken up in petroleum ether (10 mL), washed with brine (2 × 10 mL), dried, and concentrated. Silica gel chromatography (elution with 24:1 petroleum ether−ether) gave 64 mg (72%) of **41** as a colorless, crystalline solid, mp 60−61 °C: IR (CCl_4, cm^{-1}) 3550, 1700; ^{1}H NMR (300 MHz, C_6D_6) δ 4.39 (dd, J = 10.5, 10 Hz, 1 H), 2.49 (d, J = 10.5 Hz, 1 H), 2.35 (dqq, J = 9, 6.5, 6.5 Hz, 1 H), 2.23 (dq, J = 12, 7 Hz, 1 H), 2.05−0.77 (series of m, 15 H), 1.10 (d, J = 6.5 Hz, 3 H), 0.99 (d, J = 7 Hz, 3 H), 0.97 (s, 3 H), 0.97 (d, J = 6.5 Hz, 3 H), 0.83 (d, J = 6.5 Hz, 3 H); ^{13}C NMR (75 MHz, C_6D_6) ppm 220.1, 70.1, 57.8, 52.4, 49.7, 46.6, 43.5, 42.7, 41.5, 39.7, 36.6, 36.0, 33.1, 30.4, 28.8, 28.5, 24.5, 22.7, 18.8, 17.6; MS *m*/*z* (M^+) calcd 306.2559, obsd 306.2572; $[\alpha]^{20}_D$ +44.5 (*c* 1.5, $CHCl_3$).

Anal. Calcd for $C_{20}H_{34}O_2$: C, 78.38; H, 11.18. Found: C, 78.02; H, 11.14.

(1*R*,3a*R*,4*S*,6*S*,6a*R*,7*S*,9a*R*,10a*S*)-Dodecahydro-7-isopropyl-6-(methoxymethoxy)-1,4,9a-trimethyldicyclopenta[*a*,*d*]cycloocten-5(1*H*)-one (42). α-Ketol **41** (64 mg, 0.21 mmol) was dissolved in CH_2Cl_2 (10 mL), diisopropylethylamine (2.0 mL) and methoxymethyl chloride (1.0 mL) were added, and the mixture was stirred for 6 h prior to being washed with saturated $NaHCO_3$ solution (2 × 10 mL), passed through a plug of silica gel (washed with CH_2Cl_2), and concentrated. Chromatography of the residue on silica gel (elution with 32:1 petroleum ether−ether) resulted in the isolation of **42** (63 mg, 86%) and recovery of **41** (4 mg).

For **42**: colorless oil; IR (neat, cm^{-1}) 1708, 1459, 1150, 1099; ^{1}H NMR (300 MHz, C_6D_6) δ 4.42 (d, J = 6.9 Hz, 1 H), 4.40 (d, J = 6.9 Hz, 1 H), 4.39 (d, J = 10 Hz, 1 H), 3.12 (s, 3 H), 2.89 (dq, J = 11.7, 6.9 Hz, 1 H), 2.37 (dd, J = 6.8, 6.7 Hz, 1 H), 2.31−2.07 (series of m, 3 H), 1.91−0.83 (series of m, 12 H), 1.10 (d, J = 6.4 Hz, 3 H), 1.08 (d, J = 6.8 Hz, 3 H), 1.04 (s, 3 H), 0.98 (d, J = 6.6 Hz, 3 H), 0.91 (d, J = 6.4 Hz, 3 H); ^{13}C NMR (75 MHz, C_6D_6) ppm 218.4, 96.1, 79.1, 57.3, 55.6, 51.7, 46.4, 46.1, 45.4, 44.1, 43.4, 39.1, 37.0, 36.9, 33.8, 32.2, 29.2, 28.9, 23.2, 22.6, 18.8, 17.0; MS *m*/*z* (M^+) calcd 350.2821, obsd 350.2823; $[\alpha]^{20}_D$ +5.1 (*c* 3.7, $CHCl_3$).

(1*R*,3a*R*,6*S*,6a*R*,7*S*,9a*R*,10a*S*)-1,2,3,3a,6,6a,7,8,9,9a,10,10a-Dodecahydro-7-isopropyl-6-(methoxymethoxy)-1,4,9a-trimethyldicyclopenta[*a*,*d*]cycloocten-5-ol Diethyl Phosphate (43). A solution of **42** (36 mg, 0.10 mmol) and HMPA (100 μL) in dry THF (5 mL) was cooled to −78 °C, treated with potassium hexamethyldisilazide in toluene (0.41 mL of 0.5 M, 0.20 mmol), and stirred at room temperature for 1 h. The reaction mixture was returned to −78 C, treated dropwise with diethylchlorophosphate in THF (0.36 mL of 0.5 M, 0.25 mmol), allowed to warm to 20 °C, and stirred for 1 h. Ether (10 mL) was introduced, and the solution was washed with saturated $NaHCO_3$ solution (2 × 10 mL), dried, and concentrated. Gradient elution chromatography on silica gel (elution with 5 → 50% ether in petroleum ether) returned 3 mg (8%) of **42** and afforded 34 mg (70%) of **43** as a

colorless gum: IR (neat, cm^{-1}) 1676, 1456, 1379, 1273, 1167, 1149, 1036; ^1H NMR (300 MHz, C_6D_6) δ 5.14 (d, $J = 7.3$ Hz, 1 H), 4.87 (d, $J = 11.4$ Hz, 1 H), 4.52 (d, $J = 7.3$ Hz, 1 H), 4.15−3.96 (m, 4 H), 3.25 (s, 3 H), 2.67 (m, 1 H), 2.48 (dd, $J = 11.4$, 5.1 Hz, 1 H), 2.00−0.80 (series of m, 26 H), 1.89 (d, $J = 2.0$ Hz, 3 H), 1.19 (s, 3 H), 0.88 (d, $J = 6.2$ Hz, 3 H); ^{13}C NMR (75 MHz, C_6D_6) ppm 143.1 (d, $J = 19.4$ Hz), 127.2 (d, $J = 21.5$ Hz), 94.4, 70.5, 63.6 (d, $J = 22.0$ Hz), 63.5 (d, $J = 22.2$ Hz), 56.7, 54.3, 49.7, 49.5, 45.1, 44.8, 42.4, 42.3, 36.3, 35.4, 34.8, 30.2, 29.5, 29.3, 28.6, 24.1, 24.0, 18.5, 16.1 (d, $J = 6.8$ Hz), 16.0 (d, $J = 6.9$ Hz); MS *m*/*z* ($M^+ - C_2H_6O_2$) calcd 424.2742, obsd 424.2743; $[\alpha]^{20}_D$ +82.6 (*c* 2.2, $CHCl_3$).

(1*R*,3a*R*,6*R*,6a*R*,7*S*,9a*R*,10a*S*)-1,2,3,3a,6,6a,7,8,9,9a,10,10a-Dodecahydro-7-isopropyl-6-(methoxymethoxy)-1,4,9a-trimethyldicyclopenta[*a*,*d*]cyclooctene (44). A solution of lithium (25 mg) in ethylamine (10 mL) was slowly added via cannula to a cold (−100 °C), magnetically stirred solution of **43** (34 mg, 0.07 mmol) in THF (4 mL) and ethylamine (1 mL) until a blue color persisted for more than a few seconds. Saturated NH_4Cl solution (2 mL) was introduced, and the mixture was allowed to warm to room temperature. The ethylamine was blown off with air, and the residue was taken up in ether (10 mL), washed with brine (2 × 10 mL), dried, and evaporated. Chromatography of the residue on silica gel (gradient elution with 5 → 50% ether in petroleum ether) returned 5 mg (14%) of **43** and gave 14 mg (81% corrected) of **44** as a colorless gum: IR (neat, cm^{-1}) 1458, 1377, 1150, 1092, 1032; ^1H NMR (300 MHz, C_6D_6) δ 5.17 (d, $J = 8.3$ Hz, 1 H), 4.81 (d, $J = 6.4$ Hz, 1 H), 4.55 (dd, $J = 10.6$, 8.9 Hz, 1 H), 4.35 (d, $J = 6.5$ Hz, 1 H), 3.23 (s, 3 H), 3.16 (m, 1 H), 2.63 (m, 1 H), 2.00−0.78 (series of m, 14 H), 1.62 (s, 3 H), 1.30 (d, $J = 6.3$ Hz, 3 H), 1.11 (s, 3 H), 1.06 (d, $J = 6.6$ Hz, 3 H), 0.93 (d, $J = 6.2$ Hz, 3 H); ^{13}C NMR (75 MHz, C_6D_6) ppm 139.5, 129.1, 93.3, 71.2, 56.2, 54.0, 53.5, 48.5, 45.5, 44.9, 44.1, 43.3, 36.7, 35.7, 35.0, 29.8, 29.5, 28.4, 24.2, 23.8, 22.9, 18.8; MS *m*/*z* (M^+) calcd 334.2872, obsd 334.2872; $[\alpha]^{20}_D$ −65.6 (*c* 2.1, $CHCl_3$).

(3*S*,3a*R*,4*R*,6a*R*,9*R*,9a*S*,10a*R*)-1,2,3,3a,4,6a,7,8,9,9a,10,10a-Dodecahydro-3-isopropyl-6,9,10a-trimethyldicyclopenta[*a*,*d*]cycloocten-4-ol (45) and (3*S*,3′*S*,3a*R*,3′a*R*,4*R*,4′*R*,6a*R*,6′a*R*,9*R*,9′*R*,9a*S*,9′a*S*,10a*R*,10′a*R*)-4,4′-(Methylenedioxy)bis[1,2,3,3a,4,6a,7,8,9,9a,10,10a-dodecahydro-3-isopropyl-6,9,10a-trimethyldicyclopenta[*a*,*d*]cyclooctene (46). Bromocatecholborane (0.11 mL of 0.2 M in CH_2Cl_2, 0.022 mmol) was added dropwise at −78 °C to a solution of **44** (6.4 mg, 0.019 mmol). The reaction mixture was stirred for 15 min, treated with saturated $NaHCO_3$ solution (1 mL), and allowed to warm to room temperature. After dilution with petroleum ether (5 mL), the organic phase was washed with 10% KOH (2 × 5 mL) and saturated $NaHCO_3$ solutions (5 mL), dried, and concentrated. The residue was immediately passed through a plug of silica gel (elution with 9:1 petroleum ether−ether) to give 6.2 mg (100%) of **45** as a clear colorless oil: IR (neat, cm^{-1}) 3318, 1458, 1376, 1074; ^1H NMR (300 MHz, C_6D_6) δ 5.20 (d, $J = 8.3$ Hz, 1 H), 4.35 (dd, $J = 11.0$, 8.3 Hz, 1 H), 2.91 (q, $J = 9.9$ Hz, 1 H), 2.64 (dd, $J = 8.9$, 6.5 Hz, 1 H), 1.94−0.95 (series of m, 15 H), 1.63 (s, 3 H), 1.32 (d, $J = 6.3$ Hz, 3 H), 1.13 (s, 3 H), 1.09 (d, J =6.7 Hz, 3 H), 1.02 (d, $J = 6.0$ Hz, 3 H); ^{13}C NMR (75 MHz, C_6D_6) ppm 131.8, 127.3, 68.3, 55.4, 53.3, 48.5, 45.1, 44.1, 43.0, 36.7 (2 C), 35.1, 30.2, 29.5, 29.2, 28.1, 24.6, 23.4, 22.8, 19.1; MS *m*/*z* (M^+) calcd 290.2610, obsd 290.2627; $[\alpha]^{20}_D$ −4.6 (*c* 0.65, $CHCl_3$).

When a lesser amount of bromocatecholborane was employed, bimolecular "coupling" occurred to give variable amounts of **46**, a colorless crystalline solid: ^1H NMR (300 MHz, C_6D_6) δ 5.07 (d, $J = 8.7$ Hz, 2 H), 4.74 (s, 2 H), 4.64 (dd, $J = 10.9$, 8.7 Hz, 2 H), 3.24 (br q, $J = 8.9$ Hz, 2 H), 2.69 (m, 2 H), 2.02−0.82 (series of m, 30 H), 1.60 (s, 6 H), 1.31 (d, $J = 6.2$ Hz, 6 H), 1.13 (d, $J = 6.5$ Hz, 6 H), 1.12 (s, 6 H), 1.11 (2d, $J = 7$ Hz, 6 H); ^{13}C NMR (75 MHz, C_6D_6) ppm 139.9, 129.7, 72.2, 54.3, 53.6, 48.5, 45.7, 45.0, 44.3, 43.7, 36.7, 36.1, 35.5, 30.4, 29.6, 29.2, 24.4, 24.3, 22.8, 18.9.

The stereochemistry of **46** was established by X-ray crystallographic analysis.

(3*S*,3a*R*,6a*R*,9*R*,9a*S*,10a*R*)-2,3,3a,6a,7,8,9,9a,10,10a-Decahydro-3-isopropyl-6,9,10a-trimethyldicyclopenta[*a*,*d*]cycloocten-4(1*H*)-one (47). A solution of **45** (8.6 mg, 0.029 mmol) in CH_2Cl_2 (5 mL) was treated sequentially with NMO (6.8 mg, 0.058 mmol), 4 Å molecular sieves (5 mg), and TPAP (5 mg). After being stirred for 2 h, the reaction mixture was filtered to remove the solids, and the filtrate was concentrated. Purification of the residue by chromatography on silica gel (elution with 49:1 petroleum ether−ether) furnished 7.8 mg (89%) of **47** as a colorless, crystalline solid: IR (neat, cm^{-1}) 1688, 1639, 1458, 1376; ^1H NMR (300 MHz, C_6D_6) δ 5.77 (m, 1 H), 3.09 (m, 1 H), 2.51 (d, $J = 5.9$ Hz, 1 H), 2.27 (dd, $J = 10.3$, 6.5 Hz, 1 H), 2.17−1.50 (series of m, 7 H), 1.54 (t, $J = 1.3$ Hz, 3 H), 1.38−0.81 (series of m, 6 H), 0.98 (s, 3 H), 0.93 (d, $J = 6.6$ Hz, 3 H), 0.86 (d, $J = 6.6$ Hz, 3 H), 0.77 (d, $J = 6.6$ Hz, 3 H); ^{13}C NMR (75 MHz, C_6D_6) ppm 209.1, 141.1, 130.1, 61.6, 51.2, 47.5, 46.0, 45.0, 44.1, 43.5, 33.6, 33.5, 32.9, 29.5, 29.2, 29.1, 23.0, 22.9, 22.5, 20.6; MS *m*/*z* (M^+) calcd 228.2435, obsd 288.2442; $[\alpha]^{20}_D$ −126.9 (*c* 1.7, $CHCl_3$).

Anal. Calcd for $C_{20}H_{32}O$: C, 83.27; H, 11.18. Found: C, 83.16; H, 11.40.

(1*R*,3a*R*,4*S*,6*R*,6a*S*,7*S*,9a*R*,10a*S*)-Dodecahydro-6-hydroxy-7-isopropyl-1,4,9a-trimethyldicyclopenta[*a*,*d*]cycloocten-5(1*H*)-one (48). A solution of **40** (119 mg, 0.41 mmol) and chlorotrimethylsilane (445 mg, 4.1 mmol) in dry THF (20 mL) was cooled to −78 °C under N_2 and treated with LDA (6.83 mL of 0.3 M in THF, 2.05 mmol). The reaction mixture was allowed to warm slowly to room temperature, stirred for 30 min, and returned to −78 °C prior to the addition of triethylamine (3.6 mL, 25.9 mmol). After warming again to 20 °C, the volatiles were removed in vacuo, hexanes were added, and the solids were removed by filtration through a plug of Celite-basic alumina (hexane elution). Concentration of the filtrate gave the silyl enol ether, which was dissolved in CH_2Cl_2 (10 min) and added to a mixture of MCPBA (283 mg of 70% purity) and $NaHCO_3$ (253 mg, 3.28 mmol) in CH_2Cl_2 (20 mL). After 5 h of stirring, saturated $NaHCO_3$ solution (13 mL) was added in addition to 30 mL of CH_2Cl_2, and the organic phase was dried and concentrated. This oil was dissolved in methanol (10 mL), admixed with K_2CO_3 (200 mg, 1.45 mmol), stirred for 1 h, and concentrated. The product was taken up in ethyl acetate, washed with brine, dried, and concentrated in advance of chromatography on silica gel (elution with 20:1 hexanes−ethyl acetate) to deliver 90 mg (72%) of **48** as a colorless oil: IR (neat, cm^{-1}) 3424, 1680; ^1H NMR (300 MHz, C_6D_6) δ 3.93 (dd, $J = 9.5$, 5.1 Hz, 1 H), 2.70−2.60 (m, 1 H), 2.30−1.90 (m, 3 H), 1.96 (d, $J = 5.1$ Hz, 1 H), 1.86 (t, $J = 10.0$ Hz, 1 H), 1.72 (m, 1 H), 1.54−1.00 (series of m, 11 H), 1.15 (d, $J = 7.1$ Hz, 3 H), 0.92 (d, $J = 7.2$ Hz, 3 H), 0.90 (s, 3 H), 0.86 (d, $J = 6.7$ Hz, 3 H), 0.81 (d, $J = 6.3$ Hz, 3 H); ^{13}C NMR (75 MHz, C_6D_6) ppm 215.1, 83.0, 51.0, 49.7, 49.1, 45.6, 43.7, 42.7, 41.1, 39.5, 38.3, 34.3, 32.0, 29.6, 22.7, 21.6, 20.9, 18.9, 18.5, 15.5; MS *m*/*z* (M^+) calcd 306.2558, obsd 306.2553; $[\alpha]^{20}_D$ −41.7 (*c* 0.53, CH_2Cl_2).

(1*R*,3a*R*,4*S*,6*R*,6a*S*,7*S*,9a*R*,10a*S*)-Dodecahydro-7-isopropyl-6-(methoxymethoxy)-1,4,9a-trimethyldicyclopenta[*a*,*d*]cycloocten-5(1*H*)-one (49). To a solution of **48** (92 mg, 0.30 mmol) and diisopropylethylamine (2.09 mL, 12 mmol) in CH_2Cl_2 (6 mL) was added methoxymethyl chloride (0.69 mL, 9.0 mmol) dissolved in CH_2Cl_2 (2 mL). The reaction mixture was stirred under N_2 for 6 days, quenched with saturated $NaHCO_3$ solution, and extracted with ether. The combined organic phases were washed with brine, dried, and concentrated. Chromatography of the residue on silica gel (elution with 30:1 hexanes−ethyl acetate) returned 24 mg of **48** and provided 76 mg (97% corrected) of **49** as a colorless oil: IR (neat, cm^{-1}) 1690, 1025, 1009; ^1H NMR (300 MHz, C_6D_6) δ 4.46 (d, $J = 6.4$ Hz, 1 H), 4.26 (d, $J = 6.4$ Hz, 1 H), 4.12 (d, $J = 10.0$ Hz, 1 H), 3.10 (s, 3 H), 2.90−2.78 (m, 1 H), 2.38−2.25 (m, 2 H), 2.18 (t, $J = 10.0$ Hz, 1 H), 2.00−1.92 (m, 1 H), 1.82−1.74 (m, 1 H), 1.55−1.00 (series of m, 11 H), 1.13 (d, $J = 7.4$ Hz, 3 H), 0.91 (d, $J = 6.7$ Hz, 3 H), 0.89 (d, $J = 7.1$ Hz, 3 H), 0.87 (s, 3 H), 0.82 (d, $J = 6.1$ Hz, 3 H); ^{13}C NMR (75 MHz, C_6D_6) ppm 212.6, 95.8, 88.9, 56.3, 53.7, 50.1, 47.6, 46.5, 43.3, 42.9, 40.1, 39.0, 37.2, 34.7, 32.6, 29.1, 22.8, 21.1, 21.0, 19.2, 18.1, 15.4; MS *m*/*z* (M^+) calcd 350.2820, obsd 350.2817; $[\alpha]^{25}_D$ +37.2 (*c* 0.54, CH_2Cl_2).

(1*R*,3a*R*,6*S*,6a*S*,7*S*,9a*R*,10a*S*)-1,2,3,3a,6,6a,7,8,9,9a,10,10a-Dodecahydro-7-isopropyl-6-(methoxymethoxy)-1,4,9a-trimethyldicyclo-penta[*a*,*d*]cyclooctene (50). Lithium aluminum hydride (6.5 mg, 0.17 mmol) was added to a solution of **49** (30 mg, 0.085 mmol) in ether (5 mL) at −78 °C under N_2, slowly warmed to room temperature, quenched with ethyl acetate, and extracted with ether. The combined organic layers were washed with water and brine, dried, and evaporated to leave the alcohol, which was taken up in benzene (5 mL), treated with the Martin sulfurane reagent (228 mg, 0.34 mmol), stirred at 60

°C under N_2 for 5 h, cooled, quenched with saturated $NaHCO_3$ solution, and extracted with ether. The combined ethereal solutions were washed with brine, dried, and concentrated. Flash chromatography of the residue on silica gel (elution with 99:1 hexanes−ethyl acetate) gave **50** (26 mg, 90%) as a colorless oil: IR (film, cm^{-1}) 1038: ^1H NMR (300 MHz, C_6D_6) δ 5.76−5.72 (m, 1 H), 4.93 (d, J = 6.5 Hz, 1 H), 4.43 (d, J = 6.5 Hz, 1 H), 3.96 (dd, J = 10.0, 7.2 Hz, 1 H), 3.86 (m, 1H), 3.23 (s, 3 H), 2.62−2.53 (m, 1 H), 2.39 (t, J = 9.5 Hz, 1 H), 2.05−1.90 (m, 1 H), 1.65−1.02 (series of m, 12 H), 1.56 (d, J = 1.4 Hz, 3H), 1.00 (d, J = 6.4 Hz, 3 H), 0.98 (d, J = 7.1 Hz, 3 H), 0.92 (d, J = 5.8 Hz, 3 H), 0.90 (s, 3 H); ^{13}C NMR (75 MHz, C_6D_6) ppm 144.4, 125.4, 94.1, 76.6, 55.2, 51.5, 51.3, 50.1, 43.1, 41.4, 40.4, 39.6, 35.3, 29.5, 26.6, 24.6, 24.2, 23.1, 21.0, 18.8, 15.7 (1 C not observed); MS m/z (M^+) calcd 334.2871, obsd 334.2880; $[\alpha]^{20}_D$ +137.3 (*c* 0.63, EtOAc).

(1*R*,3a*R*,4*S*,5*R*,6*R*,6a*S*,7*S*,9a*R*,10a*S*)-4,5-Epoxytetradecahydro-7-isopropyl-6-(methoxymethoxy)-1,4,9a-trimethyldicyclopenta[*a*,*d*]cyclo-octene (52). To a solution of **50** (10 mg, 0.03 mmol) in CH_2Cl_2 (1 mL) was added $NaHCO_3$ (12.6 mg, 0.15 mmol) followed by MCPBA (23 mg of 90% purity, 0.12 mmol). The reaction mixture was stirred for 3 h, diluted with ether, washed with water and brine, dried, and concentrated. Flash chromatography of the residue on silica gel (elution with 30:1 hexanes−ethyl acetate) gave **52** (9 mg, 85%) as a colorless oil: IR (neat, cm^{-1}) 1036; ^1H NMR (300 MHz, C_6D_6) δ 5.20 (d, J = 7.0 Hz, 1 H), 4.67 (d, J = 7 Hz, 1 H), 4.25 (dd, J = 10.5, 6.1 Hz, 1 H), 3.34 (s, 3 H), 2.81 (d, J = 6.1 Hz, 1 H), 2.68−2.55 (m, 2 H), 2.18−2.10 (m, 1 H), 2.05−1.99 (m, 1 H), 1.80−1.14 (series of m, 12 H), 1.10 (s, 3 H), 1.01 (d, J = 7.0 Hz, 3 H), 0.95 (d, J = 6.8 Hz, 3 H), 0.88 (d, J = 6.9 Hz, 3 H), 0.87 (s, 3 H); ^{13}C NMR (75 MHz, C_6D_6) ppm 95.7, 75.6, 62.9, 62.1, 55.9, 50.7, 48.4, 47.4, 45.5, 43.2, 40.7, 40.2, 39.1, 34.8, 29.9, 25.8, 24.4, 23.1, 21.9, 21.6, 18.4, 15.6; MS m/z (M^+) calcd 350.2820, obsd 350.2793; $[\alpha]^{25}_D$ +125 (*c* 0.67, EtOAc).

(1*R*,3a*R*,4*R*,6*S*,6a*S*,7*S*,9a*R*,10a*S*)-Tetradecahydro-7-isopropyl-6-(methoxymethoxy)-1,4,9a-trimethyldicyclopenta[*a*,*d*]cycloocten-4-ol (53). A suspension of **52** (10 mg, 0.03 mmol) and lithium aluminum hydride (20 mg, 0.53 mmol) in dry THF (4 mL) was refluxed under N_2 for 10 days. After being cooled to −78 °C, the reaction mixture was quenched with ethyl acetate and water and then extracted with ether. The usual workup and silica gel chromatography (elution with 3:1 hexanes−ethyl acetate) furnished 8 mg (80%) of **53** as a colorless gum: IR (neat, cm^{-1}) 3548, 1462, 1383, 1032; ^1H NMR (300 MHz, C_6D_6) δ 4.45 (d, J = 6.4 Hz, 1 H), 4.32 (d, J = 6.4 Hz, 1 H), 3.60 (ddd, J = 10.2, 4.6, 2.1 Hz, 1 H), 3.11 (s, 3 H), 3.10−2.95 (m, 2 H), 2.42 (t, J = 10.0 Hz, 1 H), 2.21−1.05 (series of m, 16 H), 1.10 (s, 3 H), 0.92 (d, J = 6.7 Hz, 3 H), 0.91 (d, J = 7.0 Hz, 1 H), 0.87 (d, J = 6.0 Hz, 3 H), 0.73 (s, 3 H); ^{13}C NMR (75 MHz, C_6D_6) ppm 96.7, 82.6, 75.2, 56.1, 52.0, 49.8, 48.8, 46.2, 43.7, 42.3, 40.7, 39.9, 39.5, 32.8, 29.1, 27.5, 26.2, 22.9, 22.2, 21.3, 19.9, 15.5; MS m/z (M^+) calcd 334.2872, obsd 334.2907; $[\alpha]^{25}_D$ −64.6 (*c* 1.00, CH_2Cl_2).

(1*R*,3a*R*,6*S*,6a*S*,7*S*,9a*R*,10a*S*)-Tetradecahydro-7-isopropyl-6-(methoxymethoxy)-1,9a-dimethyl-4-methylenedicyclopenta[*a*,*d*]cyclooctene (54). A solution of **53** (10.6 mg, 0.03 mmol) and Martin's sulfurane (80 mg, 0.12 mmol) in benzene (3 mL) was heated at 50 °C under N_2 for 2 h, cooled, quenched with saturated $NaHCO_3$ solution, and extracted with ether. The combined organic layers were washed with brine, dried, and evaporated. Flash chromatography of the residue on silica gel (elution with 99:1 hexanes−ethyl acetate) gave 8.6 mg (86%) of **54** as a colorless oil: IR (neat, cm^{-1}) 1462, 1375, 1260, 1037; ^1H NMR (300 MHz, C_6D_6) δ 5.05 (br s, 1 H), 4.93 (br s, 1 H), 4.62 (d, J = 6.8 Hz, 1 H), 4.46 (d, J = 6.8 Hz, 1 H), 3.58 (dt, J = 8.0, 2.6 Hz, 1 H), 3.20 (s, 3 H), 2.84−2.75 (m, 1 H), 2.62−2.56 (m, 1 H), 2.45−2.38 (m, 1 H), 2.34−2.18 (m, 2 H), 1.85−1.00 (series of m, 13 H), 0.98 (d, J = 7.0 Hz, 3 H), 0.91 (d, J = 6.7 Hz, 6 H), 0.83 (s, 3 H); ^{13}C NMR (75 MHz, C_6D_6) ppm 148.1, 115.5, 95.6, 78.8, 55.4, 50.0, 49.4, 46.1, 45.3, 43.7, 43.4, 42.7, 40.5, 39.3, 33.3, 32.4, 30.1, 23.2, 23.1, 21.3, 20.0, 15.8; MS m/z (M^+) calcd 334.2871, obsd 334.2863.

(1*R*,3a*R*,6*S*,6a*S*,7*S*,9a*R*,10a*S*)-Tetradecahydro-7-isopropyl-6-(methoxymethoxy)-1,9a-dimethyldicyclopenta[*a*,*d*]cyclooctene-4-methanol (55). To a suspension of **54** (8.0 mg, 0.024 mmol) and lithium borohydride (0.9 mg, 0.04 mmol) in THF (1.5 mL) at −20 °C under N_2 was added borane−THF complex (96 μL of 1 M in THF, 0.096 mmol). The mixture was allowed to warm slowly to room temperature, stirred for 6 h, recooled to −20 °C, and treated sequentially with water (0.2 mL), 20% NaOH solution (0.2 mL), and 30% hydrogen peroxide (0.2 mL) prior to overnight stirring at 20 °C. The products were extracted into ethyl acetate, washed with brine, and concentrated. Chromatography of the residue on silica gel (elution with 10:1 hexanes−ethyl acetate) afforded 5 mg (60%) of **55** as a 1:1 mixture of epimers. For one epimer: IR (neat, cm^{-1}) 1462, 1037; ^1H NMR (300 MHz, C_6D_6) (one epimer) δ 4.68 (d, J = 6.7 Hz, 1 H), 4.40 (d, J = 6.7 Hz, 1 H), 3.68 (dd, J = 10.2, 2.7 Hz, 1 H), 3.33−3.24 (m, 2 H), 3.22 (s, 3 H), 2.52−2.48 (m, 1 H), 2.30−2.20 (m, 2 H), 2.18−1.95 (m, 2 H), 1.60−1.01 (series of m, 15 H), 0.98 (d, J = 7.2 Hz, 3 H), 0.96 (d, J = 7.1 Hz, 3 H), 0.91 (d, J = 7.1 Hz, 3 H), 0.74 (s, 3 H); ^{13}C NMR (75 MHz, C_6D_6) ppm 95.0, 79.3, 68.5, 55.5, 47.7, 45.6, 45.0, 43.7, 43.2, 41.6, 40.6, 36.3, 30.2, 29.4, 26.4, 23.7, 23.2, 22.2, 21.4, 15.7; MS m/z (M^+) calcd 352.2977, obsd 352.2973.

(1*R*,3a*R*,4*S*,6*S*,6a*S*,7*S*,9a*R*,10a*S*)-Tetradecahydro-6-hydroxy-7-isopropyl-1,9a-dimethyldicyclopenta[*a*,*d*]cyclooctene-4-methanol 4-Acetate (57) and (1*R*,3a*R*,4*R*,6*S*,6a*S*,7*S*,9a*R*,10a*S*)-Tetradecahydro-6-hydroxy-7-isopropyl-1,9a-dimethyldicyclopenta[*a*,*d*]cyclooctene-4-methanol 4-Acetate (58). A solution of **55** (4.6 mg, 0.013 mmol) in 2.5% hydrochloric acid/methanol (2 mL) was refluxed for 1 h, cooled, neutralized with saturated $NaHCO_3$ solution, and extracted with ethyl acetate. The combined organic layers were washed with brine, dried, and concentrated to leave a pair of diols which were taken up in CH_2Cl_2 (1 mL) containing pyridine (0.1 mL). This solution was treated with acetic anhydride (3.2 mg, 0.031 mmol) and stirred overnight at room temperature under N_2. After solvent removal, the residue was subjected to flash chromatography on silica gel (elution with 20:1 hexanes−ethyl acetate) to give 2.0 mg (43%) of **57** and 2.1 mg (46%) of **58**.

For **57**: IR (neat, cm^{-1}) 3495, 1741, 1460, 1243, 1041; ^1H NMR (300 MHz, C_6D_6) δ 3.94 (dd, J = 10.5, 6.5 Hz, 1 H), 3.78 (dd, J = 10.5, 8.5 Hz, 1 H), 3.63−3.58 (m, 1 H), 2.65−2.50 (m, 1 H), 2.48−2.40 (m, 1 H), 2.30−2.06 (m, 3 H), 1.90−0.86 (series of m, 15 H), 1.66 (s, 3 H), 0.98 (d, J = 7 Hz, 3 H), 0.92 (d, J = 6.8 Hz, 3 H), 0.87 (d, J = 7 Hz, 3 H), 0.74 (s, 3 H); ^{13}C NMR (75 MHz, C_6D_6) ppm 73.1, 69.6, 48.2, 46.5, 44.9, 43.6, 43.2, 43.0, 41.1, 40.6, 32.4, 31.8, 30.1, 30.0, 29.5, 23.1, 23.0, 22.4, 21.2, 20.5, 15.6 (C═O not observed due to low S/N); MS m/z (M^+) calcd 349.2743, obsd 349.2714.

For **58**: IR (neat, cm^{-1}) 3410, 1736, 1460; ^1H NMR (300 MHz, C_6D_6) δ 4.38 (dd, J = 10.8, 8.1 Hz, 1 H), 3.95 (dd, J = 10.8, 4.0 Hz, 1 H), 2.52−2.40 (m, 1 H), 2.38−2.30 (m, 1 H), 2.08−1.94 (m, 4 H), 1.85−0.90 (series of m, 15 H), 1.69 (s, 3 H), 0.96 (d, J = 7.7 Hz, 3 H), 0.94 (d, J = 7.0 Hz, 3 H), 0.86 (d, J = 7.7 Hz, 3 H), 0.80 (s, 3 H); ^{13}C NMR (75 MHz, C_6D_6) ppm 74.2, 69.6, 50.5, 49.4, 45.9, 43.6, 42.1, 41.1, 40.5, 39.3, 39.2, 36.5, 34.6, 33.9, 29.5, 22.9, 22.2, 21.1, 20.6, 18.5, 15.7 (C═O not observed due to low S/N); MS m/z (M^+-H) calcd 349.2743, obsd 349.2780.

(2a*R*,4a*S*,6*R*,6a*R*,9*R*,9a*S*,10a*R*,10b*S*)-Tetradecahydro-3,3,9,10a-tetramethyl-2*H*-4-oxacyclopenta[5,6]cycloocta[1,2,3-*cd*]pentalene-6-methanol Acetate (59). A solution of **58** (1.4 mg, 0.004 mmol), iodine (1.5 mg, 0.006 mmol), and iodobenzene diacetate (2.0 mg, 0.0062 mmol) in cyclohexane (1 mL) was irradiated with a 600 W tungsten filament lamp at 50 °C for 2 h. The reaction mixture was poured into water and extracted with ether. The organic layer was washed with sodium thiosulfate solution and brine prior to drying and concentration. Flash chromatography of the residue on silica gel (elution with 10:1 hexanes−ethyl acetate) provided 1.3 mg (93%) of **59**: IR (neat, cm^{-1}) 1742, 1242; ^1H NMR (300 MHz, C_6D_6) δ 4.08 (dd, J = 10.7, 3.7 Hz, 1 H), 3.78 (dd, J = 10.6, 7.4 Hz, 1 H), 3.60 (dt, J = 10.3, 4.7 Hz, 1 H), 2.47 (ddd, J = 13.7, 10.6, 8.2 Hz, 1 H), 2.36 (dd, J = 12.9, 5.1 Hz, 1 H), 2.07 (dd, J = 13.7, 10.3 Hz, 1 H), 1.90 (dt, J = 12.6, 4.8 Hz, 1 H), 1.83−0.80 (series of m, 14 H), 1.64 (s, 3 H), 1.33 (s, 3 H), 1.15 (s, 3 H), 0.92 (d, J = 6.9 Hz, 3H), 0.86 (s, 3 H); ^{13}C NMR (125 MHz, C_6D_6) ppm 73.9, 69.2, 61.3, 58.0, 47.4, 46.4, 44.0, 43.1, 43.0, 42.4, 36.6, 34.2, 32.5, 30.1, 30.0, 29.9, 24.8, 24.5, 21.2, 20.4, 20.1 (C═O not observed due to low S/N); MS m/z (M^+) calcd 348.2664, obsd 348.2653.

(2a*R*,4a*S*,6*S*,6a*R*,9*R*,9a*S*,10a*R*,10b*S*)-Tetradecahydro-3,3,9,10a-tetramethyl-2*H*-4-oxacyclopenta[5,6]cycloocta[1,2,3-*cd*]pentalene-6-methanol Acetate (60). A 2.0 mg (0.0057 mmol) sample of **57** was reacted analogously with iodine (2.2 mg, 0.0086 mmol) and iodoben-

zene diacetate (2.8 mg, 0.0088 mmol) in cyclohexane (1 mL). There was isolated 1.9 mg (95%) of **60**: IR (neat, cm^{-1}) 1742, 1462, 1371, 1232; ^1H NMR (500 MHz, C_6D_6) δ 4.20 (m, 2 H), 3.98 (m, 1 H), 2.58−2.50 (m, 1 H), 2.36−2.28 (m, 2 H), 2.07 (dd, J = 13.6, 10.5 Hz, 1 H), 2.00−1.96 (m, 1 H), 1.80−0.90 (series of m, 13 H), 1.73 (s, 3 H), 1.38 (s, 3 H), 1.22 (s, 3 H), 0.96 (d, J = 6.6 Hz, 3 H), 0.94 (s, 3 H); ^{13}C NMR (125 MHz, C_6D_6) ppm (all peaks are broadened due to slow conformational dynamics; the visible peaks are cited) 170.2, 77.1, 71.3, 44.5, 44.1, 42.4, 36.7, 30.1, 29.7, 24.4, 24.0, 20.4, 20.3; MS *m*/*z* (M^+) calcd 348.2664, obsd 348.2675.

(+)-Epoxydictymene (1). A solution of **60** (1.5 mg, 0.0043 mmol) in 2.5% hydrochloric acid/methanol (1 mL) was heated at reflux for 1 h, cooled, neutralized with saturated $NaHCO_3$ solution, and extracted with ethyl acetate. The organic phase was washed with brine, dried, and concentrated to leave alcohol **61** which was dissolved in THF (0.5 mL) containing *o*-nitrophenyl selenocyanate (9 mg, 0.04 mmol). The resulting solution was treated with tributylphosphine (8 mg, 0.04 mmol) in THF (0.5 mL) and stirred under N_2 for 2 h. The THF was evaporated, the residue was taken up in ether and filtered, and the filtrate was evaporated. The selenide was dissolved in THF (0.5 mL) and treated at 0 °C with 0.25 mL of THF and 0.25 mL of 30% hydrogen peroxide. After 2 h of stirring at 0 °C, the reaction mixture was diluted with ether, washed with saturated $NaHSO_3$ solution, dried, and concentrated. Purification of the residue by flash chromatography on silica gel (elution with 20:1 hexanes−ethyl acetate) gave 1.0 mg (80%) of (+)-**1**: IR (neat, cm^{-1}) 1462, 1280, 1135, 1090; ^1H NMR (300 MHz, C_6D_6) δ 4.97 (s, 1 H), 4.80 (s, 1 H), 3.56 (dt, J = 9.7, 6.5 Hz, 1 H), 2.84 (dd, J = 11.6, 6.6 Hz, 1 H), 2.62 (ddd, J = 12.1, 9.9, 7.1 Hz, 1 H), 2.46 (ddd, J = 14.0, 11.3, 7.6 Hz, 1 H), 2.02 (dd, J = 13.6, 10.2 Hz, 1 H), 2.00−1.90 (m, 1 H), 1.85−1.20 (series of m, 12 H), 1.25 (s, 3 H), 1.17 (s, 3 H), 1.00 (d, J = 6.5 Hz, 3 H), 0.88 (s, 3 H); ^{13}C NMR (125 MHz, C_6D_6) ppm 146.3, 114.7, 78.0, 74.8, 59.6, 57.5, 51.0, 48.4, 44.2, 43.9, 43.3, 41.5, 36.6, 34.7, 34.1, 29.2, 24.3, 24.0, 20.2, 19.2; MS *m*/*z* (M^+) calcd 288.2455, obsd 288.2459; $[\alpha]^{25}_D$ +72.4 (*c* 0.04, hexanes).

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Supporting Information Available: Detailed synthetic procedures and spectroscopic data for compounds **16**−**25** and **51**, along with crystallographic experimental details, bond lengths, bond lengths involving the hydrogen atoms, bond angles, positional parameters and *B*(eq) values, and anisotropic displacement parameters for **46** (23 pages). See any current masthead page for ordering and Internet access instructions.

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