tute of General Medical Sciences through research grant 1 R01 GM39752 is gratefully acknowledged. Special thanks are due Dr. John Snyder of Boston University for his efforts to establish the stereochemistry of diene 4 using ^1H-^1H-correlated and NOSEY 2D NMR techniques.

Abbreviations. Aqueous (aq), hexanes:ether (H:E), tetrabutylammonium fluoride (TBAF), and triethylamine (TEA).

Supplementary Material Available: Spectra for compounds prepared in this study (82 pages). Ordering information is given on any current masthead page.

Intramolecular Additions of Allylsilanes to Conjugated Dienones. A Direct Stereoselective Synthesis of (±)-14-Deoxyisoamijiol†,[1]

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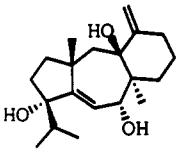
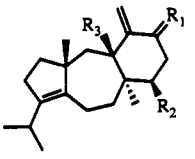
A 16-step synthesis of (±)-14-deoxyisoamijiol is reported featuring an intramolecular addition of an allylsilane to a conjugated dienone to construct stereospecifically the dolastane skeleton.

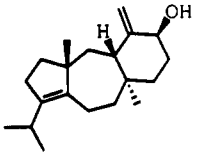
Dolatriol (1) was isolated in 1976 from extracts of the digestive gland of the poisonous Indian Ocean sea hare *Dolabella auricularia*.[3] Further work, however, established that this unusual diterpene was actually produced by the brown algae genus *Dictyota* and only concentrated by *Dolabella* through its diet. Today over 20 related natural products have been isolated and shown to have a 5-7-6 linearly fused tricyclic framework. Typical examples are amijiol (**2a**), isoamijiol (**2b**) and 14-deoxyamijiol (**2c**).[4] Many of the dolastane diterpenes exhibit promising biological activity. For example, 14-deoxyisoamijiol (**3**) has antimicrobial activity against *Mucor mucedo* and *Staphylococcus aureus*.[5]



Dolatriol (1)



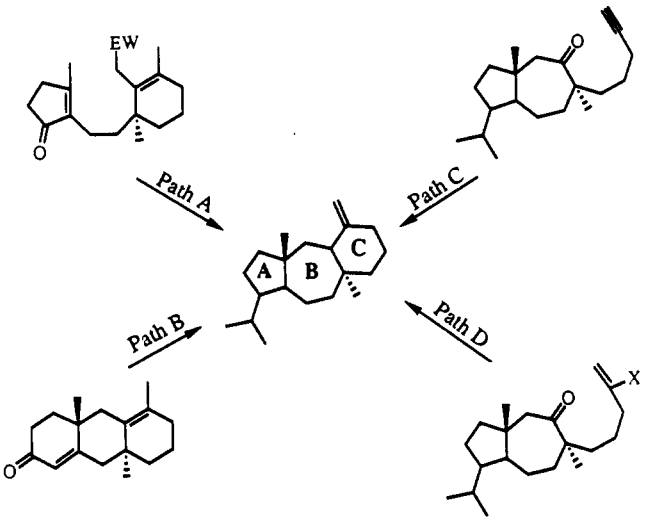
2 a) amijiol
R_1=H_2, R_2=R_3=OH
b) isoamijiol
R_1=β-OH, α-H, R_2=H, R_3=OH
c) 14-deoxyamijiol
R_1=H_2, R_2=OH, R_3=H



14-Deoxyisoamijiol (3)

Several approaches have been devised for the synthesis of the dolastane framework (Scheme I). One of the first strategies, devised by Paquette and co-workers, involved an intramolecular Michael addition to form the central

Scheme I



cycloheptane ring last in an "A + C → ABC" approach (path A).[6] When this strategy proved unsuccessful, Paquette performed a ring expansion–ring contraction of a functionalized hydroanthracene precursor to generate the 5-7-6 tricyclic nucleus (path B).[7] Three alternative strategies for the construction of the dolastane framework

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†Dedicated to Professor Paul A. Grieco on the occasion of his receipt of the 1991 ACS Award for Creative Work in Synthetic Organic Chemistry.

(1) Taken in part from the Ph.D. Dissertation of Clay Ringold, *The University of Georgia*, 1989. This work was presented at the 198th National Meeting of the American Chemical Society in Miami Beach, FL, Sept 1989 [Abstract ORGN #86].

(2) (a) Author to whom correspondence regarding the synthesis of **3** should be addressed. (b) Author to whom correspondence regarding the 2D NMR techniques employed to establish the structures of **7** and **42** should be addressed. (c) Author to whom correspondence regarding the X-ray crystallographic study of enone **37** should be addressed.

(3) Pettit, G. R.; Ode, R. H.; Herald, C. L.; von Dreel, R. B.; Michel, C. *J. Am. Chem. Soc.* **1976**, *98*, 4677.

(4) Ochi, M.; Watanabe, M.; Miura, I.; Taniguchi, M.; Tokoroyama, T. *Chem. Lett.* **1980**, 1229.

(5) Ochi, M.; Asao, K.; Kotsiki, H.; Miura, I.; Shibata, K. *Bull. Chem. Soc. Jpn.* **1986**, *59*, 661.

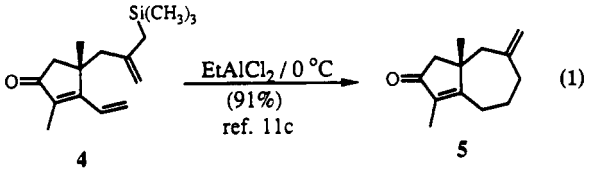
(6) Belmont, D. T.; Paquette, L. A. *J. Org. Chem.* **1985**, *50*, 4102.

(7) Paquette, L. A.; Lin, H. S.; Belmont, D. T.; Springer, J. P. *J. Org. Chem.* **1986**, *51*, 4807.

0022-3263/91/1956-3973$02.50/0

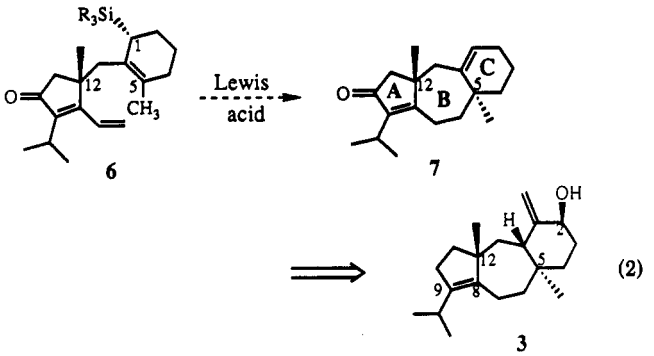
involve cyclohexane annulation of a preformed perhydroazulene nucleus (paths C and D). Pattenden's synthesis,[8] as well as Mehta's enantioselective approach,[9] feature a cyclohexane annulation using the intramolecular reductive coupling of a terminal acetylenic ketone (path C). Similarly, an annulation sequence developed by Piers employs the intramolecular addition of a regiospecifically generated vinyl anion to a ketone to give an allylic alcohol (path D).[10]

We have found intramolecular allylsilane additions an extremely powerful means for synthesizing seven- and eight-membered rings.[11] For example, cyclization of trienone 4 using ethylaluminum dichloride produces the 5,7 fused bicyclic enone 5 in 91% yield (eq 1).[12] Thus we



4 5 (1)

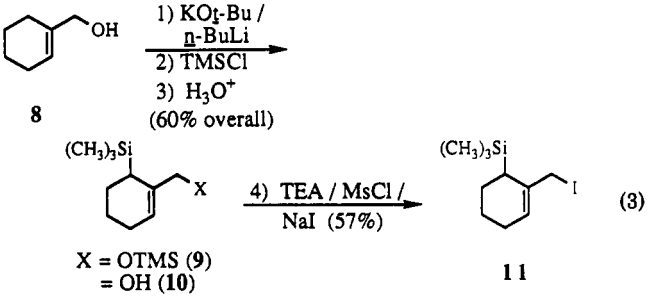
were confident that our methodology was versatile enough to construct the central seven-membered ring of the dolastanes via an "A + C → ABC" approach as shown in eq 2. Since many of our cyclizations proceed with remarkable diastereoselectivity,[13,14] we expected that cyclization of 6 would not only assemble the basic dolastane skeleton but, more importantly, also establish the correct stereochemical relationship between the C(5) and C(12) quaternary carbon atoms. Moreover sufficient functionality exists in the A and C rings of enone 6 to permit a dolastane synthesis. This served as our impetus for the following synthesis of (±)-14-deoxyisoamijiol (3), one of the simplest of the dolastane diterpenes.[15]



6 7 3 (2)

Results and Discussion

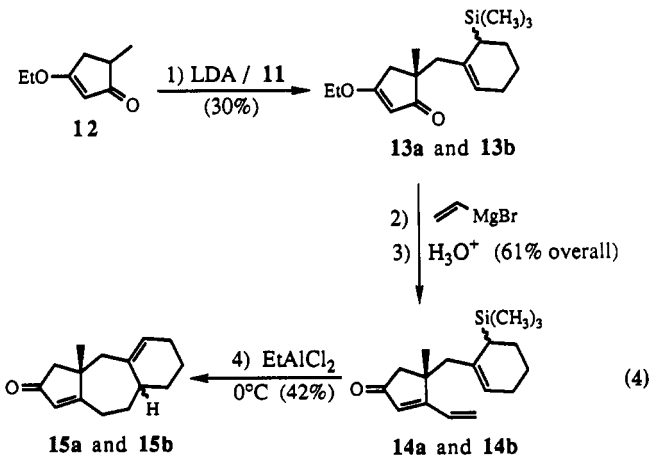
In order to test the viability of our A + C → ABC approach, it was necessary to prepare a cyclic allylsilane [the C ring] to couple with an appropriately functionalized A ring using the Stork/Danheiser protocol.[16] The first cyclic allylsilane synthesized was iodide 11, which was prepared in five steps from 1-(hydroxymethyl)-1-cyclohexene (8) (eq 3).[17] Carbon silylation of this allylic alcohol was first



8 X = OTMS (9) = OH (10) 11 (3)

attempted by using the conditions developed by Trost and co-workers.[18] However, treatment of 8 with excess *n*-butyllithium for prolonged reaction times failed to generate any of the desired dianion, producing instead only the silyl ether as a result of oxygen silylation. Fortunately, an earlier method developed by Carlson[19] was applicable to alcohol 8. Reaction of 8 with 2 equiv of potassium *tert*-butoxide and 2 equiv of *n*-butyllithium for 14 h generated the requisite dianion, which was bis-silylated (cf. 9) by quenching with excess trimethylchlorosilane. The silyl ether of 9 was selectively hydrolyzed with dilute acid to give the carbon-silylated allylic alcohol 10 in 60% overall yield. Transformation of this alcohol into iodide 11 was accomplished in 57% overall yield by a modification of the procedure originated by Finkelstein.

After preparing iodide 11, we coupled the A and the C rings. For the sake of expediency, we postponed the introduction of the C(9)-isopropyl and instead treated 11 with the kinetic enolate derived from 3-ethoxy-5-methyl-2-cyclopentan-1-one (12) (eq 4).[20] The 3:1 mixture



12 13a and 13b 15a and 15b 14a and 14b (4)

of alkylation diastereomers formed was inseparable. However, because this model study was intended only to

(8) (a) Pattenden, G.; Robertson, G. M. *Tetrahedron Lett.* **1986**, *27*, 399. (b) Begley, M. J.; Pattenden, G.; Robertson, G. M. *J. Chem. Soc., Perkin. Trans. 1* **1988**, 1085.

(9) Mehta, G.; Krishnamurthy, N. *Tetrahedron Lett.* **1987**, *28*, 5945.

(10) Piers, E.; Friesen, R. W. *J. Org. Chem.* **1986**, *51*, 3405.

(11) For other cycloheptane annulations using allylsilanes, see: (a) Majetich, G.; Hull, K.; Defauw, J.; Desmond, R. *Tetrahedron Lett.* **1985**, *26*, 2747. (b) Majetich, G.; Ringold, C. *Heterocycles* **1987**, *25*, 271. (c) Majetich, G.; Defauw, J.; Ringold, C. *J. Org. Chem.* **1988**, *53*, 50. (d) Majetich, G.; Hull, K. *Tetrahedron* **1987**, *43*, 5621. (e) Schinzer, D.; Steffen, J.; Solyom, S. *J. Chem. Soc., Chem. Commun.* **1986**, 829. For cyclooctane annulations using allylsilanes, see: (f) Majetich, G.; Hull, K.; Desmond, R. *Tetrahedron Lett.* **1985**, *26*, 2751. (g) Majetich, G.; Lowery, D.; Khetani, V. *Tetrahedron Lett.* **1990**, *31*, 51.

(12) (a) All structures drawn herein represent racemates, only one enantiomer being drawn. (b) Reaction conditions have not been optimized. (c) All yields are isolated yields.

(13) For a review of intramolecular additions of allylsilanes to dienones, see: Majetich, G.; Hull, K.; Lowery, D.; Ringold, C.; Defauw, J. "Intramolecular Additions of Allylsilanes to Dienones" in *Selectivities in Lewis Acid-Promoted Reactions*; Schinzer, D., Ed.; Kluwer Academic Publishers Group: Dordrecht, Holland, 1989.

(14) For other diastereospecific allylsilane cyclizations, see: (a) ref 11d. (b) Majetich, G.; Defauw, J. *Tetrahedron* **1988**, *44*, 3833.

(15) For a preliminary account of this study, see: Majetich, G.; Song, J.-S.; Ringold, C.; Nemeth, G. A. *Tetrahedron Lett.* **1990**, *31*, 2239.

(16) Stork, G.; Danheiser, R. L. *J. Org. Chem.* **1973**, *38*, 1775.

(17) Alcohol 8 was prepared in 85% yield by reducing ethyl cyclohexene-1-carboxylate [Dev. S. *J. Indian Chem. Soc.* **1956**, *33*, 769] with lithium aluminum hydride.

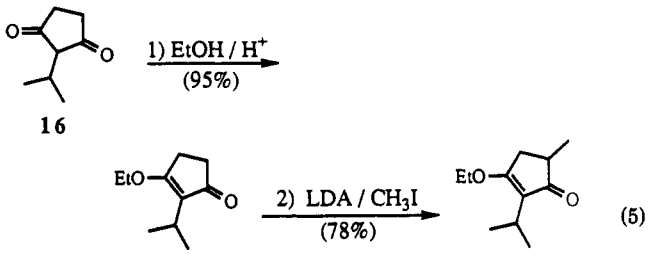
(18) Trost, B. M.; Chan, D. M. T.; Nanninga, N. *Org. Synth.* **1984**, *62*, 58.

(19) Carlson, R. M. *Tetrahedron Lett.* **1978**, 111.

(20) Majetich, G.; Desmond, R. W., Jr.; Soria, J. J. *J. Org. Chem.* **1986**, *51*, 1755.

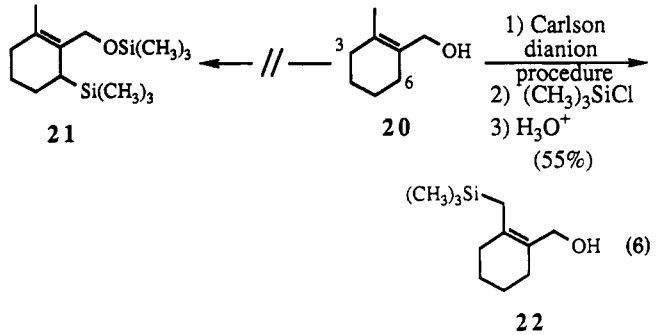
determine whether we could form a linearly fused tricyclic nucleus, this alkylation was not optimized nor was the absolute stereochemistry of the diastereomers established. Therefore, enol ethers **13a** and **13b** were treated with vinylmagnesium bromide and the crude allylic alcohols thus obtained were subjected to dilute acid-catalyzed allylic rearrangement to give conjugated dienones **14a** and **14b**. Treatment of **14a** and **14b** with ethylaluminum dichloride at 0 °C gave two 5-7-6 tricyclic dienones in a 3:1 ratio. Although enones **15a** and **15b** were separable by chromatography, no attempt was made to determine the relative stereochemistry of either isomer. Nevertheless, formation of these tricyclic enones confirmed that the dolastane framework could be generated by using our approach. Of equal importance was the observation that enones **15a** and **15b** were produced in the same ratio as were formed in the alkylation step, which implied that the cyclizations were occurring stereospecifically. Further models were therefore deemed unnecessary.

In our retrosynthetic analysis we proposed cyclizing a precursor having an isopropyl at the α-position of the dienone unit and a methyl group at the γ-position of the allylsilane (eq 2). We chose to functionalize the A ring first. 2-Isopropylcyclopentane-1,3-dione (**16**), first reported more than 80 years ago,[21] was chosen as the starting material (eq 5). This dione was transformed into enol ether **17** in



95% yield, using Fischer esterification conditions. Methylation of this compound was performed in the usual manner to give enone **18** in 78% yield. A small amount (11%) of 5,5-dimethyl-3-ethoxy-2-isopropyl-2-cyclopenten-1-one (**19**) was also produced, but was readily separable from **18**.

We expected that the preparation of a cyclic allylsilane with a vinylic methyl group, such as **21**, would be an extension of our model study (eq 6). However, reaction of



alcohol **20**[22] using Carlson's dianion conditions did not result in silylation at the desired C(6) position, but instead at the vinylic methyl, giving ether **22**.[23] It was evident that a different approach to the introduction of a vinylic methyl group into the cyclic allylsilane was necessary.

It is well-established that silyllithium reagents add in conjugate fashion to α,β-unsaturated ketones in the presence of HMPA or copper(I) iodide.[24] Therefore, it was decided to add (phenyldimethylsilyl)lithium (**24**) to 2-carbethoxy-2-cyclohexen-1-one (**23**),[25] followed by introduction of the vinylic methyl group through the reaction of the corresponding enol phosphate with lithium dimethylcuprate. (Phenyldimethylsilyl)lithium was chosen because of its ease of preparation and with the intent of favorably influencing the diastereoselectivity in the coupling step (Scheme II).

To a solution of the cuprate derived from **24** was added crude enone **23**.[26] Workup and distillation afforded the Michael adduct **25** in 55% yield. Enol phosphate **26** was obtained in 85% yield by the addition of **25** to a suspension of sodium hydride, followed by trapping the enolate upon the addition of diethyl chlorophosphate Addition of the enol phosphate **26** to a solution of lithium dimethylcuprate at −78 °C efficiently introduced the vinylic methyl group to provide ester **27** in 86% yield. Reduction of this ester with lithium aluminum hydride gave allylic alcohol **28** in 95% yield.

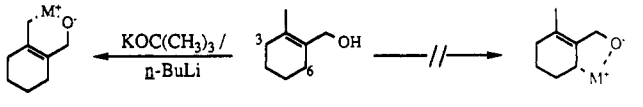
It was originally intended to convert alcohol **28** into the corresponding allylic iodide using a Finkelstein displacement. To this end, **28** was treated with triethylamine at 0 °C, and methanesulfonyl chloride was added dropwise. However, these conditions gave chloride **29**,[27] along with a small amount of the expected methanesulfonate. Anhydrous lithium chloride was added to the reaction mixture to maximize the yield of **29**.[28] Although attempts to prepare allylic iodide **30** via a halogen exchange reaction were successful, this iodide was extremely labile, decomposing rapidly, while chloride **29** proved to be stable indefinitely while stored at −10 °C.

The next step, with respect to our proposed plan, was to couple enone **18** with chloride **29**. Since our model cyclizations led us to believe that formation of the dolastane skeleton occurs stereospecifically, a specific cyclization precursor was required. However, despite the wealth of knowledge available regarding the trajectory requirements for Michael additions[29,30] as well as the stereochemical requirements for electrophilic substitution reactions of

(21) (a) Diels, O.; Sielisch, J.; Muller, E. *Chem. Ber.* **1906**, *39*, 1328. (b) Orchin, M.; Butz, L. W. *J. Am. Chem. Soc.* **1943**, *65*, 2296. (c) Hiraga, K. *Chem. Pharm. Bull.* **1967**, *13*, 1359. (d) Eaton, P. E.; Bunnelle, W. H. *Tetrahedron Lett.* **1984**, *25*, 23.

(22) Majeti, S.; Gibson, T. W. *Tetrahedron Lett.* **1973**, 4889. An alternative preparation is also described in ref 27.

(23) A possible explanation of this result is that dianion formation at the C(6) methylene position involves a five-membered lithium chelate (cf. viii), whereas dianion formation at the vinylic methyl position proceeds through a more stable six-membered lithium chelate (cf. ix).



(24) (a) Still, W. C. *J. Org. Chem.* **1976**, *41*, 3063. (b) Fleming, I.; Roessler, F. *J. Chem. Soc., Chem. Commun.* **1980**, 276. (c) Ager, D. J.; Fleming, I. *J. Chem. Soc., Chem. Commun.* **1978**, 177. (d) Ager, D. J.; Fleming, I.; Patel, S. K. *J. Chem. Soc., Perkin Trans. 1*, **1981**, 2520.

(25) Reich, H. J.; Renga, J. M.; Reich, I. L. *J. Am. Chem. Soc.* **1975**, *97*, 5434.

(26) In our hands purification of **29** proved to be troublesome in that chromatography over silica gel or distillation at reduced pressure resulted in acid-promoted tautomerization to give a mixture of 1-hydroxy-2-carbethoxy-1,3-cyclohexadiene and **23** in a 2:1 ratio. Therefore, this material was not purified but was used crude.

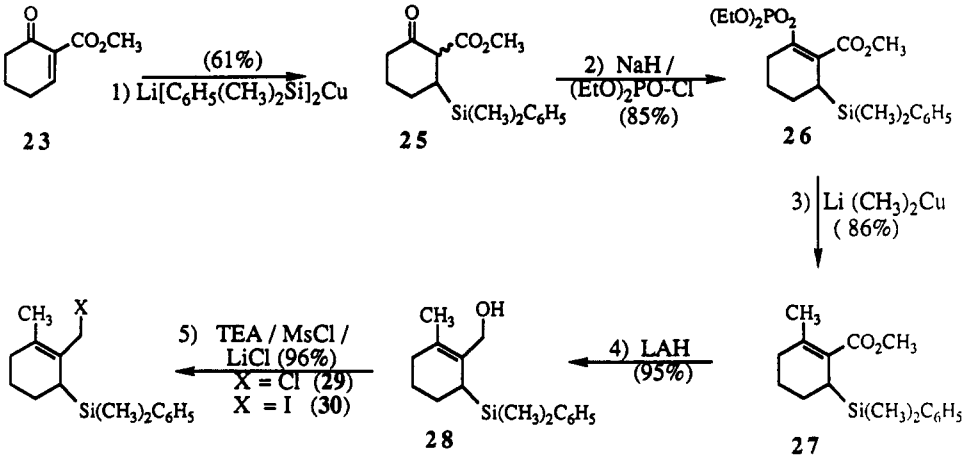
(27) Chloride **29** has been independently prepared via the identical sequence of reactions, see: Akers, J. A.; Bryson, T. A. *Tetrahedron Lett.* **1989**, *30*, 2187.

(28) Stork, G.; Gregson, M.; Grieco, P. A. *Tetrahedron Lett.* **1969**, 1391, 1393.

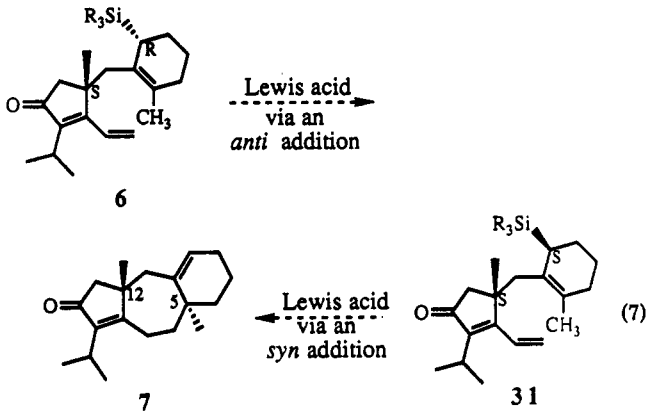
(29) (a) Baldwin, J. E. *J. Chem. Soc., Chem. Commun.* **1976**, 734. (b) Liotta, C. L.; Burgess, E. M.; Eberhardt, W. H. *J. Am. Chem. Soc.* **1984**, *106*, 4849.

(30) Oare, D. A.; Heathcock, C. H. *Top. Stereochem.* **1989**, *19*, 227.

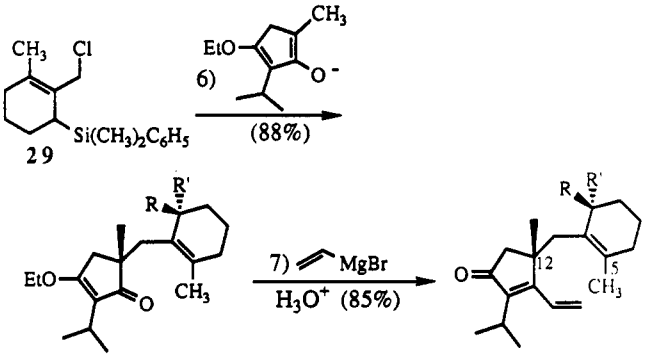
Scheme II



allylsilanes,[31-33] we were uncertain that the cyclization of **6** would produce a tricyclic product with the correct stereochemical relationship between the C(5) and C(12) quaternary carbon atoms. Trajectory requirements demand that the two reactive planar units achieve a parallel orientation in order for Michael addition to occur. When this relationship is obtained in trienone **6**, the silyl moiety of the allylsilane is positioned opposite the reactive centers; anti addition therefore results in a trans configuration of the angular methyl groups (eq 7). This analysis is consistent with Kumada's and Fleming's findings regarding the stereochemistry of electrophilic intermolecular substitution reactions of *acyclic* allylsilanes.[31,32] However, work with *cyclic* allylsilane by Fleming et al.[33] showed that electrophiles can add syn to the silyl moiety through either coordination of the electrophile with the silicon atom or because of steric congestion. Thus trienone **31** could produce enone **7** via a syn addition. Although we favored anti addition, syn addition could not be ruled out. The preparation and cyclization of both trienones (**6** and **31**) would resolve this question.



Coupling of β-ethoxy enone **18** with chloride **29**, using the Stork/Danheiser procedure, produced enol ethers **32** and **33** in 88% yield as an inseparable mixture of diastereomers in a 1.6:1 ratio (eq 8).[34-36] Conversion of these



R = H; R' = $Si(CH_3)_2C_6H_5$ (**32**) R = H; R' = $Si(CH_3)_2C_6H_5$ (**34**)
R = $Si(CH_3)_2C_6H_5$; R' = H (**33**) R = $Si(CH_3)_2C_6H_5$; R' = H (**35**)

(8)

enol ethers into conjugated dienones **34** and **35** was carried out in the usual fashion. Fortuitously, diastereomers **34** and **35** could be separated by chromatography; however, attempts to establish the C(1) and C(12) chiral centers in either trienone **34** or **35** by X-ray analysis failed. We

(31) Hayashi and Kumada have established that acyclic allylsilanes preferentially react with various electrophiles with anti S_E2' stereochemistry. See: (a) Hayashi, T.; Konishi, H.; Ito, H.; Kumada, M. *J. Am. Chem. Soc.* **1982**, *104*, 4962, 4963. (b) Hayashi, T.; Ito, H.; Kumada, M. *Tetrahedron Lett.* **1982**, *23*, 4605. (c) Wickham, G.; Kitching, W. *J. Org. Chem.* **1983**, *48*, 612.

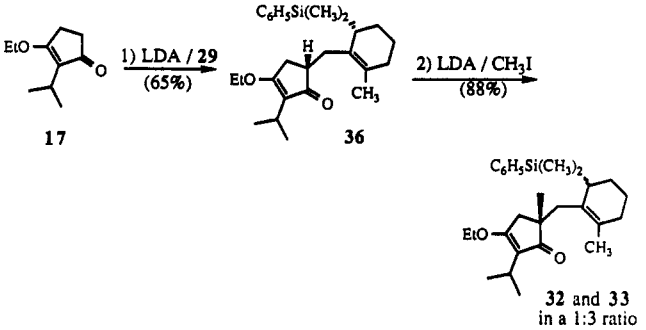
(32) (a) Fleming, I.; Terrett, N. K. *J. Organomet. Chem.* **1984**, *264*, 99. (b) Fleming, I.; Marchi, D.; Patel, S. K. *J. Chem. Soc., Perkin Trans. I* **1981**, 2518. (c) Fleming, I.; Terrett, N. K. *Pure Appl. Chem.* **1983**, *55*, 1707. (d) Chow, H.-F.; Fleming, I. *Ibid.* **1985**, *26*, 397. (e) Fleming, I.; Terrett, N. K. *Tetrahedron Lett.* **1984**, *25*, 5103.

(33) (a) Fleming, I.; Au-Yeung, B.-W. *Tetrahedron* **1981**, *37*, 13. (b) Fleming, I.; Thomas, A. P. *J. Chem. Soc., Chem. Commun.* **1986**, 1456.

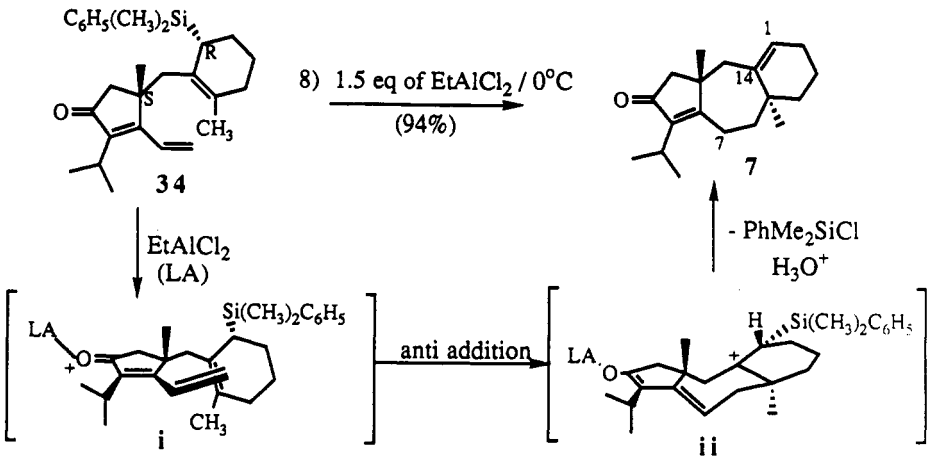
(34) Enol ethers **32** and **33** were prepared in a 3:1 ratio, respectively, on reactions using less than 50 mg of chloride **29**. The ratio stated is for an alkylation using 4.5 g of electrophile.

(35) Other metal enolates, such as potassium, zirconium, or boron, were examined without success in hopes of improving the diastereoselectivity in the alkylation of **18** with chloride **29**. For relevant experimental procedures for the preparation of zirconium enolates, see: (a) Yamamoto, Y.; Maruyama, K. *Tetrahedron Lett.* **1980**, 4607. For the conditions used to prepare the boron enolate of **18**, see: Evans, D. A.; Vogel, E.; Nelson, J. V. *J. Am. Chem. Soc.* **1979**, *101*, 6120.

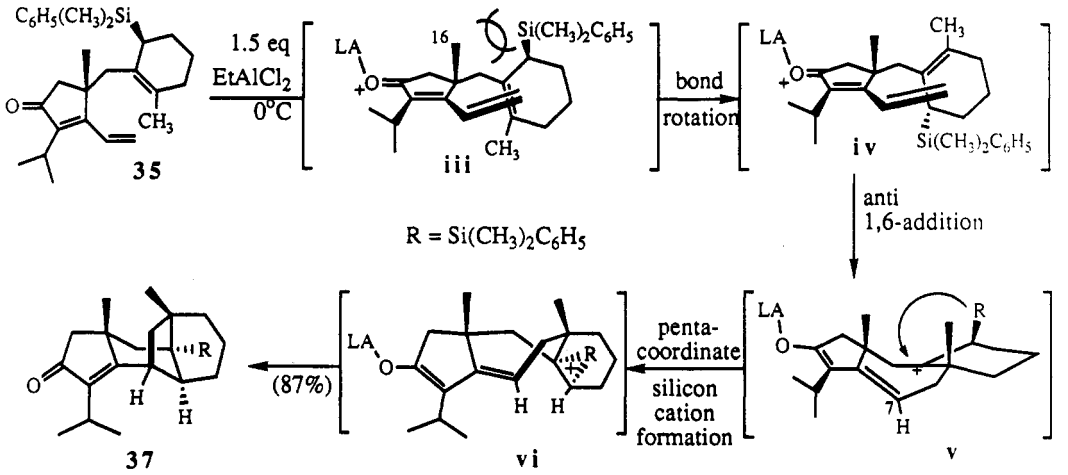
(36) In an attempt to improve the diastereoselectivity, we inverted the order of alkylation. Alkylation of **17** with chloride **29** afforded a single diastereomer, presumably enone **36**. However, methylation of this enone under kinetically controlled conditions gave a 1:3 mixture of **32** and **33**, respectively.



Scheme III



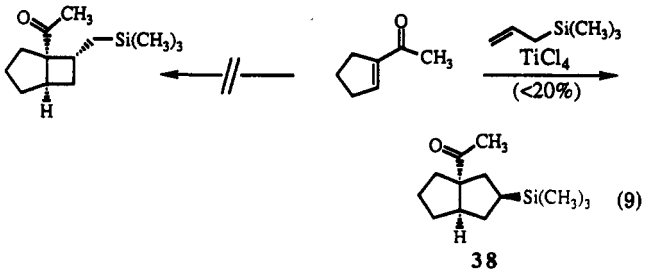
Scheme IV



therefore decided to cyclize these precursors in the hope that the products would reveal whether a syn or anti mechanism was involved. This gamble paid off when one of the cyclization products confirmed an anti addition pathway. The following analysis benefits from this knowledge.

Treatment of dienone **34** with 1.5 equiv of ethylaluminum dichloride at 0 °C afforded tricyclic dienone **7**, having a trans relationship of the C(5) and C(12) quaternary methyls, in 93% yield (Scheme III).[2b] Attack from the less sterically hindered face of the allylsilane—via an anti addition—generates cationic intermediate ii. Loss of phenyldimethylchlorosilane from this reactive intermediate forms the C(1), C(14) double bond.

In contrast, reaction of trienone **35** under identical conditions furnished tetracyclic enone **37** in 87% yield (Scheme IV).[37] In this case, steric repulsion between the silyl group and the C(16)-methyl group (cf. iii) favors conformer iv in which steric interactions have been minimized. Cyclization, again via an anti mechanism, produces cationic intermediate v in which the angular methyl groups are cis to one another. Ordinarily, one would expect this cation to lose phenyldimethylchlorosilane to generate a double bond. However, formation of a bridged nonclassical pentavalent silicon cation, such as vi, permits formation of a new six-membered ring and thus enone **37** by means of an intramolecular alkylation of the aluminum dienolate.[38] The intermediacy of hypervalent silyl cations during allylsilane additions was first postulated by Jarvie and Eaborn[39a,b] and has recently been confirmed by Knolker.[39c] In a reinvestigation of the Sakurai reaction of 1-acetylcyclohexene, Knolker and co-workers found that the silicon-containing byproduct previously assumed to be a cyclobutane ring is actually a silylcyclopentane (cf. **38**, eq 9).[40] Our determination that **37** also contains a silyl-



(9)

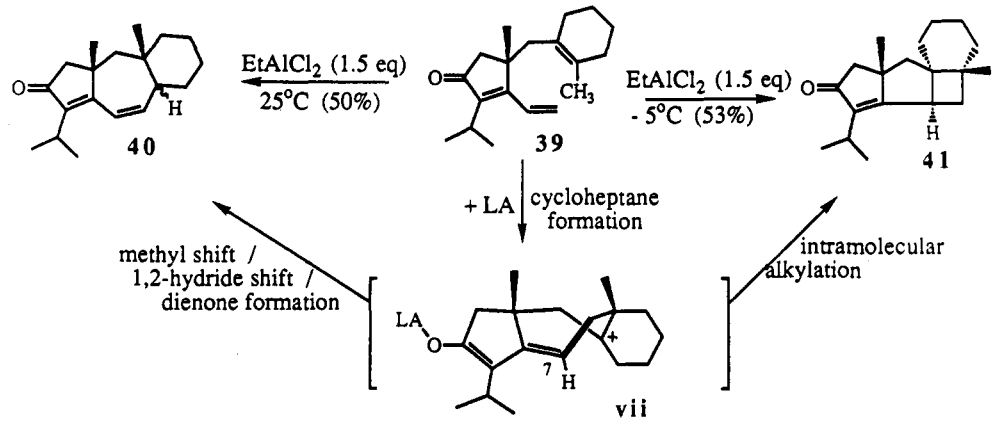
(37) An X-ray diffraction study revealed that crystals of **37** belong to the monoclinic space group $P2_1/n$ with cell dimensions a = 8.970, b = 28.692, and c = 9.886 Å and b = 109.71°. Diffraction data were collected to q = 75° on an Enraf-Nonius CAD-4 diffractomer and the structure was solved by direct methods (MULTAN). Several cycles of full matrix least-squares refinement resulted in R = 0.086 (R_W = 0.10). Additional information concerning this study can be found in the supplementary material section.

(38) Stork, G.; Grieco, P. A. *J. Am. Chem. Soc.* **1969**, *91*, 2407.

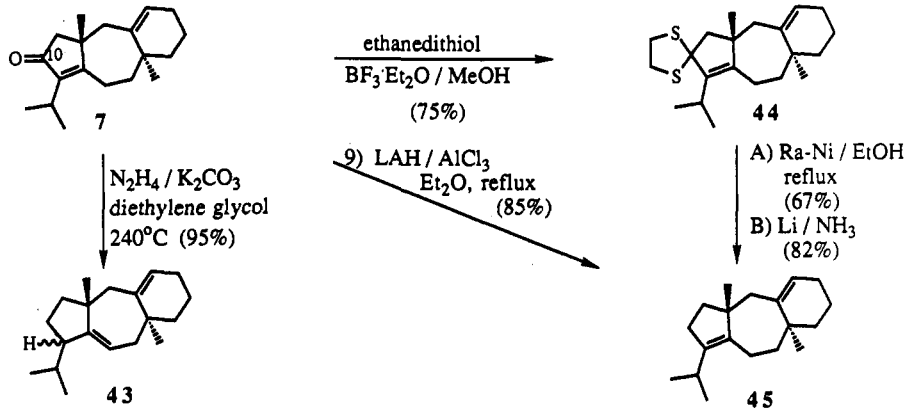
(39) (a) Jarvie, A. W. P.; Holt, A.; Thompson, J. *J. Chem. Soc. B* **1969**, 852. (b) Cooke, M. A.; Eaborn, C.; Walton, D. R. M. *J. Organomet. Chem.* **1970**, *24*, 301. (c) Knolker, H.-J.; Jones, P. G.; Pannek, J.-B. *SynLett.* **1990**, 429.

(40) (a) Pardo, R.; Zahra, J.-P.; Santelli, M. *Tetrahedron Lett.* **1979**, 4557. (b) Hosomi, A.; Kobayashi, H.; Sakurai, H. *Ibid.* **1980**, *21*, 955. (c) House, H. O.; Gass, P. C.; VanDervee, D. *J. Org. Chem.* **1983**, *48*, 1661.

Scheme V



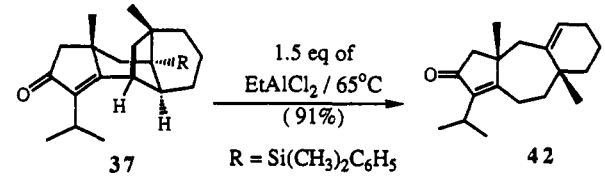
Scheme VI



cyclopentane augments Knolker's findings and requires that we correct our initial structural assignment as published earlier.[15] Please note that a silylcyclopentane system can form only if the pentavalent silicon cation is on the β-face of vi. This dictates that allylsilane addition occurs via an anti mechanism as we initially postulated.[41] It follows that the cyclization of trienone **34** to **7** also proceeds via an anti mechanism.

In a related study of cationic cyclizations Dr. Vikram Khetani prepared bicyclic trienone **39**, which lacks an allylsilane moiety (Scheme V).[42] Treatment of **39** with 1.5 equiv of ethylaluminum dichloride at room temperature produced tricyclic dienone **40** in 50% yield, while reaction of **39** with 1.2 equiv of ethylaluminum dichloride at −5 °C afforded tetracyclic enone **41**, albeit in modest yield. Unlike the cyclizations of allylsilanes **34** and **35**, the cationic center formed upon cyclization (vii) is nonstabilized. At room temperature a 1,2-methyl shift occurs to generate a new tertiary carbonium ion, which undergoes a 1,2-hydride shift (or olefin formation) to yield the methyl-rearranged dienone **40** on aqueous workup,[43] while at low temperatures cationic intermediate vii is irreversibly trapped to afford tetracycle **41**.

We felt that resubmission of **37** to Lewis acid catalysis would regenerate intermediate v and that irreversible loss of the silyl group would result in the formation of tricyclic **42**. Indeed, treatment of **37** with 1.5 equiv of ethylaluminum dichloride at 65 °C afforded enone **42** in 91% yield.[2b] This fragmentation could also be achieved at room temperature with 2 equiv of ethylaluminum dichloride in 66% yield. Moreover, trienone **35** could be cyclized directly to **42**—without the isolation of **37**—by carrying out the reaction with excess Lewis acid at 65 °C (eq 10).



37 42 (10)

To summarize, the cyclizations of both trienones **34** and **35** occurred with complete stereospecificity. Tricyclic enone **7**, prepared from the major trienone **34**, has the required trans stereochemical relationship between the C(5) and C(12) quaternary carbon atoms, while trienone **35** gave a kinetic tetracycle (**37**) with a cis relationship between the quaternary centers. Nevertheless, determining the structure of **37** enabled us to conclude that the cited allylsilane additions occurred via an anti pathway.

At this point we were prepared to proceed with the functionalization of dienone **7** toward the synthesis of (±)-14-deoxyisoamijiol. Reduction using Wolff–Kishner conditions[11d] resulted not only in removal of the C(10)-carbonyl but also migration of the cyclopentene double bond (cf. **43**, Scheme VI). Although modifications of the Wolff–Kishner reduction designed to prevent isomerization of the enone double bond were examined,[44] this migration could not be suppressed.

A two-step sequence for the reduction of cycloalkenone carbonyls without double-bond isomerization had been

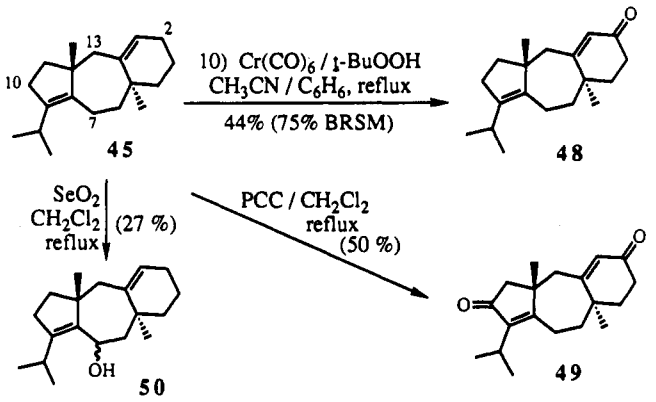
(41) Conversely, the formation of a pentavalent silicon cation derived from cation ii (Scheme III) blocks the α-face of this intermediate and thereby precludes intramolecular alkylation leading to desilylation and enone **7** formation.

(42) Majetich, G.; Khetani, V. *Tetrahedron Lett.* **1990**, *31*, 2243.

(43) Dienone **40** was a 1:1 mixture consisting of the cis and trans B/C ring fusion diastereomers.

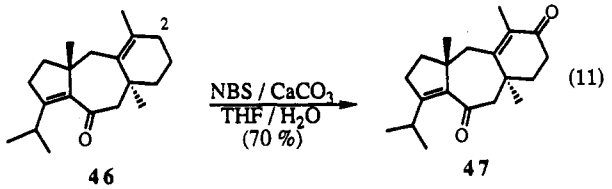
(44) (a) Grundon, M. F.; Henbest, H. B.; Scott, M. D. *J. Chem. Soc.* **1963**, 1855; (b) *J. Chem. Soc.* **1962**, 470.

Scheme VII



used previously in the synthesis of (±)-valencene.[45] This route relies on the dithioketalization of a cycloalkenone using 1,2-(ethanediyldithio)bis(trimethylsilane)[46] and a mild Lewis acid, followed by desulfurization of the dithioketal. However, no reaction occurred when dienone **7** was treated with 1,2-(ethanediyldithio)bis(trimethylsilane), presumably due to the steric bulk of the reagent and the steric crowding of the cyclopentenone carbonyl moiety by the α-isopropyl appendage. Reaction of 1,2-ethanedithiol and a stoichiometric quantity of boron trifluoride etherate provided thioketal **44** in 75% yield without a shift of the cyclopentene double bond.[47] Addition of dithioketal **44** to an excess of freshly prepared Raney nickel (W-6) in refluxing ethanol afforded diene **45** in 67% yield.[48] The yield of this desulfurization was improved by the addition of **44** to a solution of lithium dissolved in liquid ammonia to afford an 82% yield of **45** and in a 61% overall yield from **7**.[49] Ultimately, we were able to prepare **45** directly in 85% yield from **7** using aluminum trichloride and lithium aluminum hydride.[50]

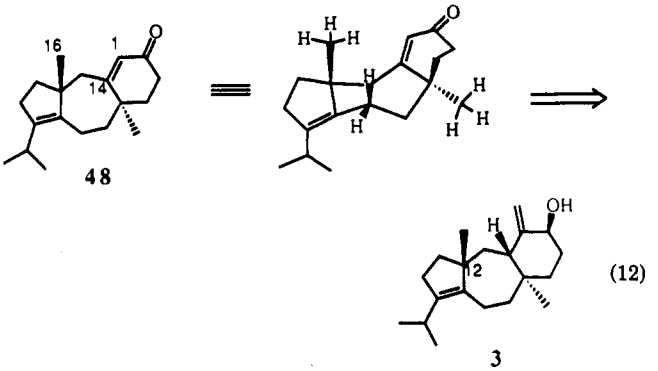
We were interested in whether a regioselective allylic oxidation at C(2) of **45** could be accomplished. Even though there are five allylic sites in **45**, we expected that C(2) would be the most reactive position. This prediction was based on Paquette's observation[7] that allylic bromination of enone **46** gave bis-enone **47** in 70% yield (eq 11)



(11)

as well as Pearson's finding that the allylic oxidations of cyclohexenes with chromium hexacarbonyl occur more rapidly than those of analogous cyclopentenes.[51] Indeed, treatment of **45** with a catalytic amount of chromium hexacarbonyl and an excess of *tert*-butyl hydroperoxide in refluxing acetonitrile and benzene (10:1) selectively oxidized the C(2) position to provide the desired cyclohexenone **48** in 44% yield or 75% yield based on recovered **45**; prolonged reaction times generated bis-enone **49** in good yield (Scheme VII). Other oxidants showed different selectivity. For example, treatment of **45** with selenium dioxide resulted in oxidation of the cycloheptane ring at C(7) to give the allylic alcohol **50**, while PCC or PDC favored oxidation of both the C(2) and C(10) methylenes to furnish **49**.[52]

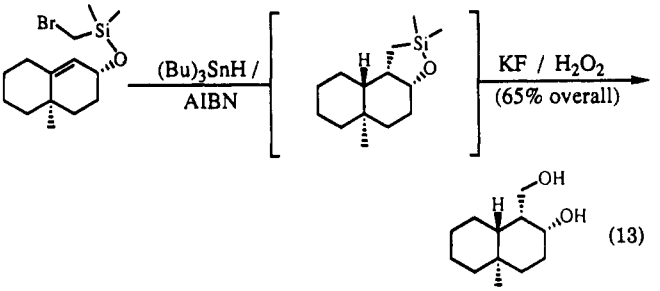
Three functionalizations remained to complete the synthesis of **3**: (1) establishment of the trans-B/C ring fusion; (2) introduction of an exocyclic methylene at C(1); and (3) conversion of the C(2) carbonyl to a β-oriented alcohol (eq 12). Examination of a stereomodel of enone



(12)

48 reveals that the C(16)-methyl group strongly shields the C(1),C(14) double bond. While several routes can be envisioned to achieve these conversions, we chose to rely on a free radical cyclization process to insure that a hydrogen atom would be introduced at C(14) on the β-face of the molecule.

In 1985 Stork and Kahn reported that bromomethylsilyl ethers, readily derived from allylic alcohols, add in intramolecular fashion to produce siloxanes in which addition of a hydrogen atom occurs anti to the newly formed carbon–carbon bond (eq 13).[53] Moreover, oxidative cleavage

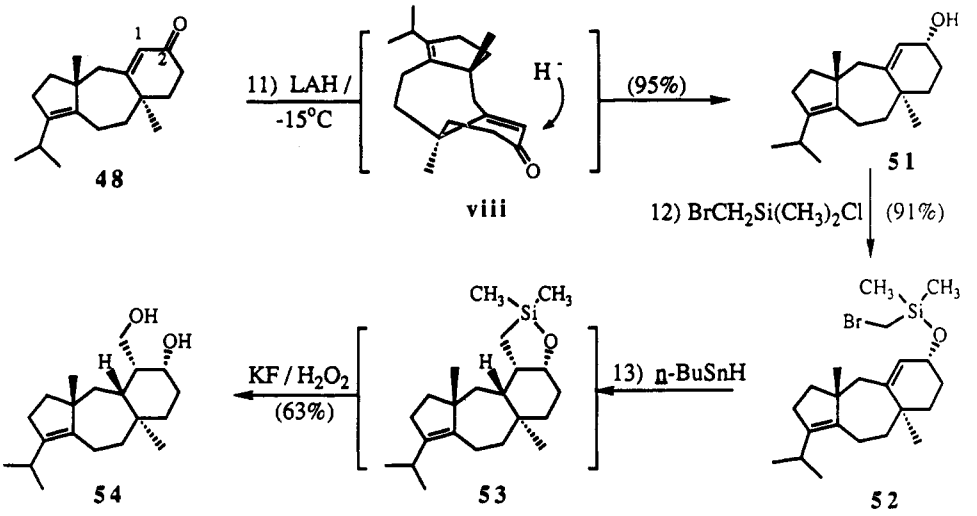


(13)

of the carbon–silicon bond culminates in diol formation. This methodology was ideally suited to our synthesis in that not only is a trans-ring fusion generated but also a hydroxymethyl group would be added at C(1), thus facilitating the introduction of the C(15)-exomethylene unit. For this strategy to be implemented, enone **48** first had to be converted into an allylic alcohol with an α-oriented hydroxyl group. Molecular mechanics calculations performed on enone **48** showed that conformation viii (Scheme VIII) represents the minimum energy conformation and that hydride attack would occur from the more accessible β-face of the enone moiety. In fact, treatment of **48** with lithium aluminum hydride in ether at −15 °C provided only α-allylic alcohol **51** in 95% yield. Silylation of **51** followed

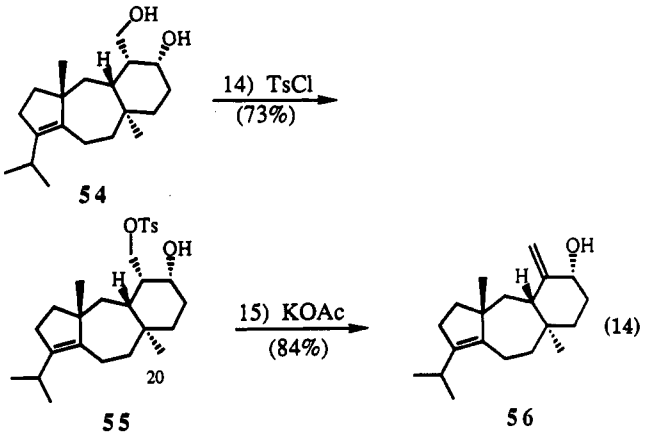
(45) Majetich, G.; Hull, K.; Behnke, M. *J. Org. Chem.* **1985**, *50*, 3615.
(46) Evans, D. A.; Truesdale, L. K.; Grimm, K. G.; Nesbitt, S. L. *J. Am. Chem. Soc.* **1977**, *99*, 5009.
(47) Williams, J. R.; Sarkisian, G. M. *Synthesis* **1974**, 32.
(48) Sondheimer, F.; Rosenthal, D. *J. Am. Chem. Soc.* **1958**, *80*, 3995.
(49) Ireland, R. E.; Wrigley, T. I.; Young, W. G. *J. Chem. Soc.* **1958**, *80*, 4604.
(50) (a) Blackwell, J.; Hickenbottom, W. J. *J. Chem. Soc.* **1961**, 1405. (b) Broome, J.; Brown, B. R.; Roberts, A.; White, A. M. S. *J. Chem. Soc.* **1960**, 1406. (c) Nystrom, R. F.; Berger, C. R. *J. Am. Chem. Soc.* **1958**, *80*, 2896. (d) Brown, B. R.; White, A. M. S. *J. Chem. Soc.* **1957**, 3755.
(51) Pearson, A. J.; Chen, Y. S.; Hsu, S. Y.; Ray, T. *Tetrahedron Lett.* **1984**, *25*, 1235.
(52) Bis-enone **49** could be obtained in 85% yield by oxidizing enone **7** using excess PCC. See: Parrish, E. J.; Chitrakorn, S.; Wei, T. S. *Synth. Commun.* **1986**, *16*, 1371.
(53) (a) Stork, G.; Kahn, M. *J. Am. Chem. Soc.* **1985**, *107*, 500. (b) Stork, G.; Sofia, M. J. *J. Am. Chem. Soc.* **1986**, *108*, 6826. (c) Nishiyama, H.; Kitajima, T.; Matsumoto, M.; Itoh, K. *J. Org. Chem.* **1984**, *49*, 2298.

Scheme VIII



by radical-promoted cyclization and workup of siloxane **53** with KF and hydrogen peroxide gave diol **54** in 57% overall yield.

The final elaboration of the cyclohexane ring was achieved in three reactions. Selective monotosylation of the primary hydroxyl group, followed by base-promoted 1,2-elimination, gave allylic alcohol **56** in 61% overall yield (eq 14). This elimination approach was superior to more



recent means of converting alcohols into double bonds. For example, although conversion of alcohols into selenides, followed by oxidative elimination, is an extremely useful and popular method,[54] this chemistry was of limited utility in converting diol **54** into allyl alcohol **56** as selenide formation was severely hampered by the 1,3-diaxial relationship imposed by the C(20)-methyl group.

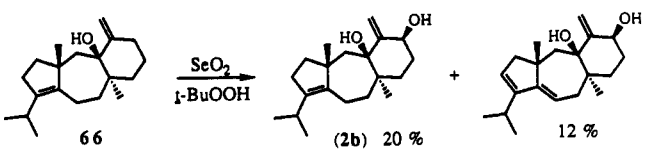
All that remained to complete our synthesis was to invert the stereochemistry of C(2). While a Mitsunobu inversion[55] achieved this inversion in 30% overall yield, we favored a less obvious procedure. The synthetic utility of the sulfoxide–sulfenate rearrangement has been rigorously established by Evans and others.[56,57] In general the equilibrium between an sulfenate ether and the corresponding allylic sulfoxide decidedly favors sulfoxide formation. However, introduction of a thiophile to this system results in consumption of the sulfenate ether so that an allylic alcohol is formed. We felt that the steric effects of the C(20)-methyl group would destabilize the sulfenate, derived from allylic alcohol **56**, so that the sulfoxide would strongly predominate. In addition, the steric effect of the C(20) methyl, would lead to an epimeric sulfenate (cf. **59**) once the sulfenate–sulfoxide equilibrium were re-established. Addition of a thiophile after sulfoxide formation had occurred would therefore consume the new, thermodynamically favored sulfenate, resulting in production of 14-deoxyisoamijiol. This type of inversion strategy was first used to control the C(15) chirality of PGE_1 by Untch and co-workers.[58]

Treatment of **56** at 0 °C with freshly prepared benzenesulfenyl chloride immediately resulted in formation of a sulfenate (cf. **57**, Scheme IX), which rearranged to sulfoxide **58** at room temperature. Addition of trimethyl phosphite afforded 14-deoxyisoamijiol (**3**). The NMR (300 MHz), infrared, and mass spectra of synthetic racemic **3** were identical with those published.[5]

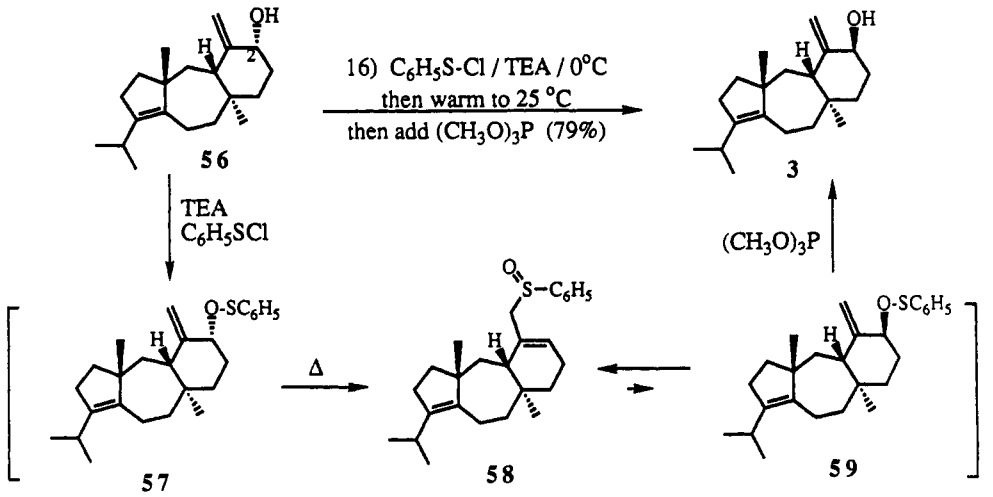
In an attempt to shorten this synthesis, we explored the sequence of steps depicted in Scheme X. This time rather than oxidize the C(2)-methylene, we sought to oxidize C(1) by means of a hydroboration/oxidation sequence. Although syn addition of the borane would produce a cis-B/C ring fusion, subsequent oxidation of this alcohol would lead to a ketone capable of isomerizing the C(14)-methine. Ketone **61** was viewed as an attractive dolastane precursor since olefination would produce an exocyclic double bond, which could react with arenesulfinyl halide to generate sulfoxide **58** in situ.[59] Alternatively, diene **62** could also be oxidized by using selenium dioxide to give **3**.[60]

Execution of this strategy proved troublesome. Hydroboration of diene **45** occurred in modest yield. Moreover, to our surprise, equilibration of ketone **60** using either acid or base catalysis gave an inseparable 1:1 mixture of **60** and **61**. Fortunately, reaction of this mixture with a

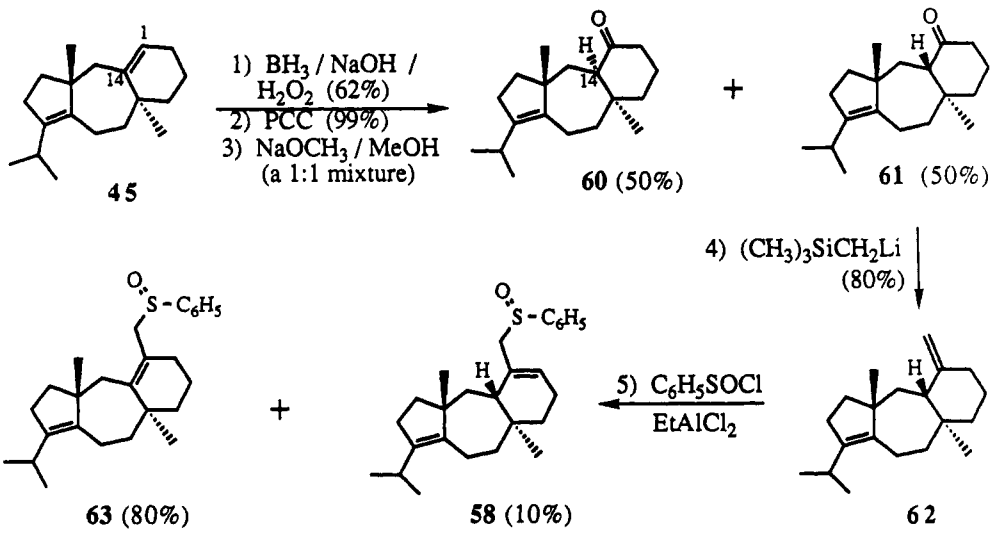
(54) Grieco, P. A.; Gilman, S.; Nishizawa, M. *J. Org. Chem.* **1976**, *41*, 1485.
(55) For a review, see: Mitsunobu, O. *Synthesis* **1981**, 1.
(56) Evans, D. A.; Andrews, G. C. *Acc. Chem. Res.* **1974**, *7*, 147 and references cited therein.
(57) For a comprehensive review, see: Hill, R. K. in *Asymmetric Synthesis*, 1984; Morrison, J. D., Ed.; Academic Press: Orlando, FL, 1984; Vol. 3, pp 554–558.
(58) Miller, J. G.; Kurz, W.; Untch, K. G.; Stork, G. *J. Am. Chem. Soc.* **1974**, *96*, 6774.
(59) Snider, B. *J. Org. Chem.* **1981**, *46*, 3155.
(60) Allylic oxidation of diene **66** has been used to complete two independent syntheses of isoamijiol (**2b**).[8,9]



Scheme IX



Scheme X



stoichiometric quantity of Peterson reagent[61] gave only olefin **62** with a trans-B/C ring fusion, along with unreacted ketone **60**. While less than desireable, this was nevertheless an effective means of preparing usable amounts of **62**. Surprisingly, reaction of diene **62** with toluenesulfinyl chloride and Lewis acid catalysis gave only trace quantities of allylic sulfoxide **58**. The major product of this reaction was the tetrasubstituted sulfoxide **63**, which was useless for a 14-deoxyisoamijiol synthesis.[62] Finally, oxidation of **62** using SeO_2 and *tert*-butyl peroxide gave low yields (<10%) of **3**.

In summary, a 16-step stereoselective synthesis of racemic 14-deoxyisoamijiol was achieved by means of a novel A + C → ABC strategy. We view the efficiency and stereospecificity of this annulation approach as a harbinger of future applications for the construction of other more complex polycyclic natural products.

Experimental Section

General.[63] All reactions were run under an inert atmosphere of nitrogen and monitored by TLC analysis until the starting material was completely consumed. Unless otherwise indicated, all ethereal workups consisted of the following procedure: the reaction was quenched at rt with saturated aq ammonium chloride. The organic solvent was removed under reduced pressure on a rotary evaporator and the residue was taken up in ether, washed with brine, and dried over anhyd $MgSO_4$. Filtration, followed by concentration at reduced pressure on a rotary evaporator and at 1 Torr to constant weight, afforded a crude residue, which was purified by flash chromatography using NM silica gel 60 (230–400 mesh ASTM) and distilled reagent-grade solvents.

Unless otherwise indicated, all NMR spectra were obtained with $CDCl_3$ as solvent. Anhyd *tert*-butyl hydroperoxide was prepared by reflux over and distillation from 4A molecular sieves under reduced pressure.

Cyclohexene-1-methanol (8). To a suspension of $LiAlH_4$ (12.3 g, 0.32 mol) in 200 mL of dry ether at 0 °C was added dropwise 31.1 g (0.20 mol) of ethyl cyclohexene-1-carboxylate[17] in 20 mL of dry ether. The reaction mixture was stirred at 0 °C for 3 h and was then quenched by the dropwise addition of 200 mL of ether and followed by the dropwise addition of 30 mL of water. Standard ethereal workup, followed by distillation (75–83 °C/1.5 mmHg), gave 19.1 g (85%) of alcohol **8**, which was homogeneous by TLC analysis (H:E, 3:1, R_f(ester) = 0.78, R_f(**8**) = 0.36): ^{1}H NMR (270 MHz) δ 1.50–1.65 (m, 4 H), 1.90–2.02 (m, 4 H), 2.81 (br s, 1 H), 3.89 (s, 2 H), 5.61 (br t, 1 H); ^{13}C NMR (270 MHz) 137.4, 122.5, 67.1, 25.4, 24.7, 22.4, 22.3 ppm; IR (film) 3500–3200 (br), 3000–2800 (br) cm^{-1}.

6-(Trimethylsilyl)-1-cyclohexenemethanol (10). To a stirred suspension of 10.5 g of potassium *tert*-butoxide (93.3 mmol) in 60 mL of dry hexanes at 0 °C was added rapidly a solution of 4.98 g of **8** (44.4 mmol) in 10 mL of dry hexanes. The reaction mixture was stirred for 15 min and 37.4 mL of *n*-butyllithium (93.3

(61) (a) Peterson, D. J. *J. Org. Chem.* **1968**, *33*, 780. For a comprehensive review, see: (b) Ager, D. J. *Org. React.* **1990**, *38*, 1.

(62) In our hands, sulfoxide **63** could not be rearranged to provide allylic alcohol **66**, a known isoamijiol precursor.

(63) For a general account of the experimental procedures employed in this research, see: Majetich, G.; Hull, K.; Casares, A. M.; Khetani, V. "Cyclooctane or Cyclohexane Annulations Based on Intramolecular Additions of Allylsilanes to Conjugated Dienones", *J. Org. Chem.*, preceding article in this issue.

mmol, 2.5 M in hexanes) was added dropwise. The reaction mixture was stirred for 14 h at 0 °C and then 21.7 g (0.2 mmol) of freshly distilled chlorotrimethylsilane was added rapidly. After stirring for 45 min at 0 °C, the reaction mixture was worked up to give crude silyl ether **9**, which was homogeneous by TLC analysis (H:E, 3:1, R_f(**8**) = 0.35, R_f(**9**) = 0.99).

This crude silyl ether was diluted with 250 mL of THF and then treated dropwise with ca. 2 mL of 1 N sulfuric acid at rt. After stirring for 1.5 h, the acidic mixture was neutralized by the addition of 1 g of anhyd K_2CO_3. Standard ethereal workup, followed by chromatography (elution with H:E, 4:1), gave 5.0 g (60%) of alcohol **10**, which was homogeneous by TLC analysis (H:E, 3:1, R_f(**9**) = 0.36, R_f(**10**) = 0.44): ^{1}H NMR (CCl_4, 90 MHz) δ 0.00 (s, 9 H), 1.35–1.75 (m, 5 H), 1.80–2.05 (m, 2 H), 2.20–2.42 (br s, 1 H), 3.74 (s, 2 H), 5.38 (br t, 1 H, J = 4.2 Hz); ^{13}C NMR (90 MHz) 140.1 (s), 120.7 (d), 67.5 (t), 26.4 (t), 25.2 (t), 24.8 (t), 21.6 (d), –0.95 (q) ppm; IR (film) 3500–3200 (br) cm^{-1}.

1-(Iodomethyl)-6-(trimethylsilyl)-1-cyclohexene (11). Distilled TEA (3.03 g, 30.0 mmol) was added dropwise to a stirred solution of 5.01 g of **10** (27.3 mmol) in 125 mL of dry THF at 0 °C. After stirring for 30 min, 3.75 g (32.7 mmol) of methanesulfonyl chloride was added dropwise to the reaction mixture, which was then stirred for an additional 2 h at 0 °C. The reaction was quenched by the addition of 1 g of anhyd K_2CO_3, and the solid were filtered through a glass-sintered funnel. The filtrate was concentrated to provide the crude mesylate, which was then diluted with 125 mL of dry acetone and cooled to 0 °C. Anhyd NaI (6.13 g, 40.9 mmol) was added in three equal portions to the mesylate solution over a 45-min period. The reaction mixture was stirred an additional 3.5 h at 0 °C and the salts were filtered through a glass-sintered funnel. The filtrate was concentrated to a residue and then diluted with hexanes (100 mL). Further filtration through a glass-sintered funnel removed the dark precipitate that formed. The filtrate was again concentrated to a residue, which was chromatographed over silica gel (elution with hexanes) to afford 4.55 g (57%) of allylic iodide **11**, which was homogeneous by TLC analysis (H:E, 3:1, R_f(**10**) = 0.44, R_f(**11**) = 0.98): ^{1}H NMR (CCl_4, 90 MHz) δ 0.00 (s, 9 H), 1.28–2.05 (m, 7 H), 3.80 (s, 2 H), 5.72 (t, 1 H, J = 3.7 Hz).

5(*S)-[[6(*S**)-(Trimethylsilyl)-1-cyclohexen-1-yl]-methyl]-3-ethoxy-5-methyl-2-cyclopenten-1-one (13a) and 5(*S**)-[[6(*R**)-(Trimethylsilyl)-1-cyclohexen-1-yl]-methyl]-3-ethoxy-5-methyl-2-cyclopenten-1-one (13b).** To a stirred solution of LDA, prepared from 1.11 g (11.0 mmol) of diisopropylamine in 15 mL of dry THF and 4.80 mL of *n*-butyllithium (12.0 mmol, 2.5 M in hexanes), was added HMPA (1.79 g, 10.0 mmol), and the resulting solution was cooled to –78 °C. To this solution was added dropwise 1.49 g (10.0 mmol) of 3-ethoxy-5-methyl-2-cyclopenten-1-one (**12**)[20] in 1 mL of dry THF, and the resulting lithium enolate solution was stirred for 30 min at –78 °C. To the reaction mixture was added dropwise a solution of iodide **11** (3.24 g, 11.0 mmol) in 2 mL of dry THF, and the resulting solution was allowed to warm to rt over a 14-h period. Standard ethereal workup, followed by chromatography (elution with H:E, 6:1), afforded 197 mg (6.5%) of enol ether **13a** as a single diastereomer, which was homogeneous by TLC analysis (H:E, 1:2, R_f(**12**) = 0.37, R_f(**13a**) = 0.57): ^{1}H NMR (CCl_4, 90 MHz) δ 0.00 (s, 9 H), 1.00 (s, 3 H), 1.32 (t, 3 H, J = 7 Hz), 1.35–1.70 (m, 4 H), 1.80–2.35 (m, 6 H), 2.65 ($^1/_2$ AB q, 1 H, J = 16.5 Hz), 3.90 (q, 2 H, J = 7 Hz), 4.90 (s, 1 H), 5.11 (t, 1 H, J = 3 Hz); IR (film) 1700, 1610 cm^{-1}; mass spectrum, m/z 306 (M$^+$).

Continued elution afforded 682 mg (22.3%) of a second enol ether (**13b**) as a single diastereomer, which was homogeneous by TLC analysis (H:E, 1:2, R_f(**12**) = 0.37, R_f(**13b**) = 0.43): ^{1}H NMR (CCl_4, 90 MHz) δ 0.00 (s, 9 H), 0.98 (s, 3 H), 1.35 (t, 3 H, J = 7 Hz), 1.44–1.75 (m, 4 H), 1.80–2.20 (m, 6 H), 2.55 ($^1/_2$ AB q, 1 H, J = 16.5 Hz), 3.80 (q, 2 H, J = 7 Hz), 4.92 (s, 1 H), 5.10 (t, 1 H, J = 3 Hz); IR (film) 1695, 1615 cm^{-1}; mass spectrum, m/z 306 (M$^+$).

4(*S)-[[6(*R**,*S**)-(Trimethylsilyl)-1-cyclohexen-1-yl]-methyl]-4-methyl-3-vinyl-2-cyclopenten-1-one (14).** To 880 mg of a 1:3.5 diastereomeric mixture of enol ether **13a** and **13b** (2.88 mmol) in 20 mL of dry THF at 0 °C was added dropwise 5.75 mL of vinylmagnesium bromide (5.75 mmol, 1.0 M in ether). The reaction mixture was stirred for 26 h at 0 °C and was treated with 1 mL of water. Standard ethereal workup gave a crude residue as a mixture of diastereomers by TLC analysis (H:E, 1:2, R_f(**13a**, **13b**) = 0.63, 0.70, R_f(alcohol) = 0.83, 0.87).

This crude mixture of allylic alcohols was diluted with 50 mL of THF and the resulting solution was treated dropwise with ca. 1 mL of 10% aq HCl. The reaction mixture was allowed to stir for 1.5 h at rt and was then treated with 200 mg of anhyd K_2CO_3. Standard ethereal workup gave 504 mg (61%) of a diastereomeric mixture of conjugated dienones **14a** and **14b**, which were heterogeneous by TLC analysis (H:E, 1:1.5, R_f(**13a**, **13b**) = 0.47, 0.57, R_f(**14a,b**) = 0.81, 0.82): ^{1}H NMR (CCl_4, 90 MHz) δ 0.00 (s, 9 H), 1.18 (s, 3 H), 1.19–1.68 (m, 5 H), 1.70–2.60 (m, 6 H), 5.16 (t, 1 H, J = 3 Hz), 5.46 (ABX, 1 H, J_{ab} = 1 Hz, J_{bx} = 10.5 Hz), 5.74 (ABX, 1 H, J_{ab} = 1 Hz, J_{ax} = 18 Hz), 5.92 (s, 1 H), 6.38 (ABX, 1 H, J_{ax} = 18 Hz, J_{bx} = 10.5 Hz); IR (film) 1730, 1695 cm^{-1}; mass spectrum, m/z 288, 288 (M$^+$). These data represent a 1:3.5 mixture of diastereomers.

***cis*- and *trans*-3a,4,6,7,8,8a,9,10-Octahydro-3a-methylbenz[*f*]azulen-2(3*H*)-one (15a and 15b).** To 330 mg of a 1:3.5 mixture of trienones **14a,b** (1.15 mmol) in 20 mL of dry toluene at –5 °C was added dropwise 1.19 mL of ethylaluminum dichloride (1.73 mmol, 1.45 M in toluene). The reaction mixture was stirred for 1.5 h at –5 °C and then for an additional 45 min at 0 °C. Standard ethereal workup, followed by chromatography (elution with H:E, 10:1), gave 22 mg (9%) of tricyclic dienone **15a** as a single diastereomer, which was homogeneous by TLC analysis (H:E, 1:2, R_f(**14a,b**) = 0.72, 0.79, R_f(**15a**) = 0.60): ^{1}H NMR (300 MHz) δ 1.19 (s, 3 H), 1.30–1.70 (m, 4 H), 1.78–1.97 (m, 4 H), 2.06 ($^1/_2$ AB q, 1 H, J = 13.6 Hz), 2.17 ($^1/_2$ AB q, 1 H, J = 17.4 Hz), 2.28 ($^1/_2$ AB q, 1 H, J = 13.6 Hz), 2.42 ($^1/_2$ AB q, 1 H, J = 17.4 Hz), 2.15–2.36 (m, 2 H), 2.68–2.74 (m, 1 H), 5.39 (t, 1 H, J = 3 Hz), 5.73 (s, 1 H); ^{13}C NMR (270 MHz) 209.2, 191.0, 136.7, 128.7, 125.7, 49.5, 47.9, 46.7, 40.4, 37.7, 29.3, 28.6, 25.7, 25.4, 18.3 ppm; IR (film) 1710–1675, 1610 cm^{-1}.

Continued elution afforded 78 mg (33%) of tricyclic dienone **15b** as a single diastereomer, which was homogeneous by TLC analysis (H:E 1:2, R_f(**14a,b**) = 0.72, 0.79, R_f(**15b**) = 0.59): ^{1}H NMR (300 MHz) δ 1.15 (s, 3 H), 1.31–1.65 (m, 5 H), 1.88–1.97 (m, 3 H), 2.04–2.45 (m, 4 H), 2.18 ($^1/_2$ AB, 1 H, J = 17.6 Hz), 2.43 ($^1/_2$ AB, 1 H, J = 17.6 Hz), 2.54–2.63 (m, 1 H), 5.49 (t, 1 H, J = 3 Hz), 5.71 (s, 1 H); ^{13}C NMR (270 MHz) 208.7, 190.7, 136.2, 128.7, 127.7, 52.2, 46.0, 45.5, 37.3, 31.8, 30.7, 28.7, 26.5, 25.4, 21.2 ppm; IR (film) 1715, 1685, 1610 cm^{-1}.

2-Isopropyl-1,3-cyclopentanedione (16). Sodium metal (2.53 g, 110 mmol) was dissolved in 35 mL of absolute ethanol while heating at 90 °C. The resulting sodium ethoxide solution was cooled to 0 °C, and a cooled (0 °C) mixture of 5.0 g (50 mmol) of 4-methyl-2-pentanone and 17.5 g (120 mmol) of diethyl oxalate was added dropwise over a 5-min period. The reaction mixture solidified into a bright yellow mass, which became a viscous, dark brown solution upon reflux at 90 °C for 4 h.

The reaction mixture was cooled to 0 °C and 12.8 mL of 50% aq sulfuric acid was added dropwise. The resulting sodium sulfate precipitate was filtered from the solution, and the filtrate was concentrated in vacuo at temperatures not exceeding 40 °C. The resulting residue was cooled for 24 h at –10 °C to give a dark brown solid, which was washed repeatedly with hexanes (4 × 100 mL) to afford 7.55 g (60%) of crude ethyl (4-isopropyl-2,3,5-trioxocyclopentyl)glyoxalate as yellow crystals, homogeneous by TLC analysis (H:E, 2:1, R_f(ketone) = 0.56, R_f(glyoxalate) = 0.5): ^{1}H NMR (CCl_4, 90 MHz) δ 1.26 (d, 6 H), 1.36 (t, 3 H), 2.73–3.03 (m, 1 H), 4.30 (q, 2 H).

A mixture of 5.47 g of the above crude glyoxylate (215 mmol) and 185 mL of 6 N HCl was heated at reflux (115 °C/760 mm) for 1.5 h. The reaction mixture was cooled to 5 °C in an ice bath and the resulting precipitate was filtered from the solution and washed with 200 mL of cold water. This crude, black solid was recrystallized from 100 mL of hot water and then dried in vacuo over anhyd phosphorus pentoxide to afford 22 g (66%) of 3-isopropyl-1,2,4-cyclopentanetrione as bright yellow crystals, which were homogeneous by TLC analysis (H:E, 1:2, R_f(glyoxalate) = 0.5, R_f(trione) = 0.67): ^{1}H NMR (d_6-DMSO, 90 MHz) δ 1.15 (d, 6 H), 2.68–2.98 (m, 1 H), 2.85 (s, 2 H); IR (KBr) 3500, 3350–3200, 2950–2850, 1720, 1680, 1620, 1390, 1260, 1150 cm^{-1}; mp 99–100 °C (lit.[21a] mp 99–100 °C).

To a stirred solution of 14.9 g of the above trione (96.8 mmol) in 210 mL of absolute ethanol at rt was added dropwise a solution

of semicarbazide hydrochloride (13.0 g, 116 mmol) and sodium acetate (14.3 g, 174 mmol) in 210 mL of water. The reaction mixture was stirred for 1.5 h, and the resulting precipitate was filtered, washed with 250 mL of absolute ethanol, and then oven dried at 130 °C to afford 18.5 g (91%) of the semicarbazone as cream colored crystals, which were homogeneous by TLC analysis (H:E, 1:2, R_f(trione) = 0.67, R_f(semicarbazone) = 0.75); mp > 330 °C.

The 1-semicarbazone of 3-isopropyl-1,2,4-cyclopentanetrione (20.0 g, 94.8 mmol) was added in two equal portions over a 10-min period to a stirred solution of sodium hydroxide (18.6 g, 465 mmol) in 280 mL of dry ethylene glycol heated at 140 °C. The reaction mixture was heated at 180 °C for 14 h and then cooled to rt. The ethylene glycol was distilled from the reaction vessel (4 mmHg) to afford a pasty solid, which was dissolved in 660 mL of water. This solution was acidified to pH 4 with concentrated hydrochloric acid with cooling at 0 °C, and the resulting precipitate was filtered and oven dried at 130 °C to afford 11.3 g (85%) of 2-isopropyl-1,3-cyclopentanedione (**16**) as light brown crystals, which were homogeneous by TLC analysis (H:E, 1:2, R_f(semicarbazone) = 0.75, R_f(**16**) = 0.18): ^{1}H NMR (d_6-DMSO, 90 MHz) δ 1.05 (d, 6 H) 2.28 (s, 4 H), 2.40–2.75 (m, 1 H); mp = 211–212 °C (lit.[21b] mp 211–213 °C).

3-Ethoxy-2-isopropyl-2-cyclopenten-1-one (17). A solution of 6.93 g of **16** (49.5 mmol) and 0.7 g of *p*-toluenesulfonic acid monohydrate (3.63 mmol) dissolved in a mixture of dry benzene/absolute ethanol (2:1, 600 mL) was heated to reflux. The resulting azeotrope was distilled through a 2-in. Vigreaux column equipped with a simple distillation head. The distillation was allowed to proceed at a steady dropwise rate with the distillation vessel being recharged when necessary with a solution of dry benzene/absolute ethanol (4:1, 300 mL). The azeotropic removal of water was continued in this manner until the reaction was judged complete by TLC analysis (total volume of distillate ca. 2 L). Standard ethereal workup, followed by distillation (120–125 °C/2 mmHg), afforded 8.0 g (95%) of enol ether **17**, which was homogeneous by TLC analysis (ether, R_f(**16**) = 0.35, R_f(**17**) = 0.60): ^{1}H NMR (90 MHz) δ 1.02 (d, 3 H, J = 6.9 Hz), 1.35 (t, 3 H, J = 7.5 Hz), 2.05–2.25 (m, 2 H), 2.45–2.75 (m, 3 H), 4.10 (q, 2 H, J = 7.5 Hz); ^{13}C NMR (90 MHz) 204.2 (s), 183.7 (s), 125.0 (s), 64.6 (t), 33.2 (t), 24.1 (t), 22.4 (d), 19.7 (2q), 14.9 (q) ppm; IR (film) 1685–1640, 1600 cm^{-1}; mass spectrum, m/z 168 (M$^+$).

3-Ethoxy-2-isopropyl-5-methyl-2-cyclopenten-1-one (18). To a solution of LDA, prepared from 1.3 g (13.1 mmol) of diisopropylamine and 5.7 mL of *n*-butyllithium (2.5 M in hexanes, 14.3 mmol) in 15 mL of dry THF at −78 °C, was added dropwise a mixture of enol ether **17** (2.0 g, 11.9 mmol) and HMPA (2.1 g, 11.9 mmol) in 3 mL of dry THF. After an additional 30 min at −78 °C the reaction mixture was warmed to −63 °C and 2.03 g of iodomethane (14.3 mmol) was added dropwise. The reaction mixture was stirred for 5 h at −6 °C and was then allowed to warm to rt over a 12-h period. Standard ethereal workup, followed by chromatography (elution with H:E, 2:1), gave 256 mg (11%) of 5,5-dimethyl-3-ethoxy-2-isopropyl-2-cyclopenten-1-one (**19**), which was homogeneous by TLC analysis (H:E, 1:2, R_f(**17**) = 0.19, R_f(**19**) = 0.71): ^{1}H NMR (90 MHz) δ 1.08 (m, 12 H), 1.36 (t, 3 H, J = 6 Hz), 2.25–2.85 (m, 3 H), 4.15 (q, 2 H, J = 6 Hz).

Continued elution afforded 1.68 g (78%) of 3-ethoxy-2-isopropyl-5-methyl-2-cyclopenten-1-one (**18**), which was homogeneous by TLC analysis (H:E, 1:2, R_f(**17**) = 0.19, R_f(**18**) = 0.43): ^{1}H NMR (90 MHz) δ 1.04 (d, 3 H, J = 5 Hz), 1.32 (t, 3 H, J = 6.6 Hz), 2.00–2.30 (m, 2 H), 2.58 (heptet, 1 H, J = 7.5 Hz), 2.65–2.95 (m, 1 H), 4.1 (q, 2 H, J = 6.6 Hz); ^{13}C NMR (90 MHz) 206.5 (s), 181.7 (s), 122.9 (s), 64.3 (t), 38.3 (d), 32.5 (t), 22.0 (d), 19.5 (2q), 16.2 (q), 14.5 (q) ppm; IR (film) 1710, 1690, 1610 cm^{-1}; mass spectrum, m/z 182 (M$^+$). Anal. Calcd for $C_{11}H_{18}O_2$: C, 72.48; H, 9.96. Found: C, 72.67; H, 10.13.

Continued elution afforded 88 mg (4.4%) of recovered starting material **17**, which was homogeneous by TLC analysis (H:E, 1:2, R_f = 0.19).

2-Methyl-1-cyclohexenemethanol (20). To a stirred suspension of $LiAlH_4$ (4.71 g, 123.8 mmol) in 130 mL of dry ether at 0 °C was added dropwise 13.0 g of ethyl 2-methyl-1-cyclohexenecarboxylate[22] (77.4 mmol) in 20 mL of dry ether. The reaction mixture was stirred for 1 h and was then diluted by the dropwise addition of 10 mL of water. Distillation (82–85 °C/1.7 mmHg) of the crude residue obtained upon standard ethereal workup gave 8.68 g (89%) of alcohol **20**, which was homogeneous by TLC analysis (H:E, 3:1, R_f(ester) = 0.82, R_f(**20**) = 0.21): ^{1}H NMR (CCl_4, 90 MHz) δ 1.51–1.68 (m, 4 H), 1.65 (s, 3 H), 1.80–2.12 (m, 4 H), 2.86 (br s, 1 H), 3.94 (s, 2 H); ^{13}C NMR (90 MHz) 130.4 (s), 129.4 (s), 62.5 (t), 31.7 (t), 27.3 (t), 22.8 (t), 22.8 (t), 18.5 (q) ppm; IR (film) 3500–3100 (br) cm^{-1}; mass spectrum, m/z 125 (M$^+$).

2-[(Trimethylsilyl)methyl]-1-cyclohexenemethanol (22). To a stirred suspension of potassium *tert*-butoxide (5.12 g, 45.7 mmol) in 50 mL of dry hexanes at 0 °C was added a solution of **20** (2.74 g, 21.7 mmol) in 10 mL of dry hexanes, resulting in an orange solution. After stirring for 30 min, 18.3 mL of *n*-butyllithium (45.7 mmol, 2.5 M in hexanes) was added dropwise, and the reaction mixture became rusty-brown in color. The reaction mixture was stirred for 16 h at 0 °C and then 12.4 mL (97.8 mmol) of chlorotrimethylsilane was added rapidly. The reaction mixture was stirred for 1 h at 0 °C and was then carefully treated with 10 mL of saturated aq NH_4Cl. The resulting solution was extracted with 100 mL of ether, and the ethereal phase was washed with brine (50 mL), dried over anhyd $MgSO_4$, and filtered. Concentration of the resulting ethereal phase afforded a crude silyl ether (H:E, 3:1, R_f(**20**) = 0.21, R_f(silyl ether) = 0.97), which was diluted with 150 mL of THF and treated dropwise with ca. 1 mL of 1 N sulfuric acid at rt. The reaction mixture was stirred for 1 h and was then neutralized with 1.2 g of anhyd K_2CO_3. Standard ethereal workup, followed by chromatography (elution with H:E, 4:1), afforded 2.37 g (55%) of alcohol **22**, which was homogeneous by TLC analysis (H:E, 3:1, R_f(**20**) = 0.21, R_f(**22**) = 0.47): ^{1}H NMR (CCl_4, 90 MHz) δ 0.00 (s, 9 H), 1.45 (s, 2 H), 1.55–2.10 (m, 8 H), 2.84 (s, 2 H); ^{13}C NMR (90 MHz) 132.5 (s), 126.6 (s), 63.1 (t), 32.6 (t), 27.1 (t), 23.9 (t), 23.2 (t), 23.2 (t), −0.85 (q) ppm; IR (film) 3500–3150 (br) cm^{-1}; mass spectrum, m/z 198 (M$^+$).

Ethyl 2-(Dimethylphenylsilyl)-6-oxocyclohexanecarboxylate (25). To a vigorously stirred solution of finely divided lithium metal (2.08 g, 298 mmol) in 250 mL of dry THF at −8 °C was added dropwise 30.5 g (179 mmol) of chlorodimethylphenylsilane. The resulting black solution of lithio reagent **24** was allowed to stir at −8 °C for 36 h and was then added via a cannula over a 5-min period to a stirred suspension of copper(I) iodide (17.0 g, 89.3 mmol) in 100 mL of dry THF at −25 °C. After the silyl cuprate reagent was stirred for 4 h at −25 °C, 7.49 g of enone **23**[25] (44.6 mmol) was added dropwise in 10 mL of dry THF. The reaction mixture was stirred for 1 h at −25 °C and then allowed to warm to 0 °C over a 30-min period. The resulting solution was quenched with saturated aq NH_4Cl, diluted with 200 mL of ether, and then washed with 75 mL of a solution of 10% aq K_2CO_3/NH_4Cl. The ethereal phase was dried over anhyd $MgSO_4$, filtered, and concentrated to a residue. This residue was distilled (185–195 °C/2.5 mmHg) to afford 7.5 g (55%) of a diastereomeric mixture of adduct **25**, which was homogeneous by TLC analysis (H:E, 2:1, R_f(**23**) = 0.12, R_f(**25**) = 0.66): ^{1}H NMR (90 MHz) δ 0.20–0.30 (m, 6 H), 1.00–1.30 (m, 3 H), 1.35–2.35 (m, 7 H), 2.90–3.20 (m, 1 H), 3.65–4.20 (m, 2 H), 7.05–7.40 (m, 5 H); IR (film) 1715, 1640–1570 cm^{-1}; mass spectrum, m/z 275 (M − 29).

1-Carbethoxy-6-(dimethylphenylsilyl)-1-cyclohexenyl Diethyl Phosphate (26). To a suspension of 0.81 g of sodium hydride (27.1 mmol, 80% in mineral oil) in 250 mL of dry THF at −30 °C was added dropwise 7.49 of ethyl ester **25** (24.6 mmol) in 20 mL of dry THF. After allowing the reaction mixture to stir for 10 min, 5.10 g (29.6 mmol) of diethyl chlorophosphate was added dropwise. The reaction mixture was stirred for 4 h at −35 °C. Standard ethereal workup, followed by chromatography (elution with 150 mL hexanes, then 250 mL ether), afforded 8.30 g (77%) of a diastereomeric mixture of enol phosphonate **26**, which was heterogeneous by TLC analysis (H:E, 2:1 R_f(**25**) = 0.66, R_f(**26**) = 0.08, 0.13): ^{1}H NMR (90 MHz) δ 0.20–0.30 (s, 6 H), 1.05–2.04 (m, 16 H), 3.65–4.30 (m, 6 H), 7.05–7.40 (m, 5 H); IR (film) 1730, 1720, 1655 cm^{-1}; mass spectrum, m/z 287 (M − 153).

Ethyl 6-(Dimethylphenylsilyl)-2-methyl-1-cyclohexenecarboxylate (27). To a vigorously stirred suspension of copper(I) iodide (4.20 g, 22.0 mmol) in 150 mL of dry ether at −15 °C was added dropwise 31.5 mL of methyllithium (44.0 mmol, 1.4 M in ether) over a 15-min period. The resulting solution was stirred at −15 °C for 10 min and then cooled to −78 °C over a 30-min

period. To the reaction mixture was added dropwise 6.46 g of enol phosphonate **26** (15.8 mmol) in 20 mL of dry ether. The reaction mixture was allowed to warm to −25 °C over a 3-h period and became dark brown in color. Standard ethereal workup gave a crude residue, which was chromatographed on silica gel to give 3.06 g (69%) of ester **27**. Ester **27** was homogeneous by TLC analysis (H:E, 2:1, R_f(**26**) = 0.08, 0.13, R_f(**27**) = 0.96): ^{1}H NMR (250 MHz) δ 0.29 (s, 3 H), 0.31 (s, 3 H), 1.20 (t, 3 H, J = 7.02 Hz), 1.43–1.57 (m, 2 H), 1.65–1.78 (m, 2 H), 1.87 (s 3 H), 1.90–2.05 (m, 2 H), 2.44 (m, 1 H), 3.83–3.99 (m, 2 H), 7.33–7.52 (m, 5 H); ^{13}C NMR (250 MHz) 170.0 (s), 139.0 (s), 138.6 (s), 133.9 (d), 128.7 (d), 127.5 (d), 126.8 (s), 59.8, 32.1, 26.1 24.0, 21.6, 21.0, 14.0, −3.1 (q), −3.3 (q) ppm; IR (film) 1710–1640 cm^{-1}; mass spectrum, m/z 302 (M$^+$).

6-(Dimethylphenylsilyl)-2-methyl-1-cyclohexenemethanol (28). To a stirred suspension of $LiAlH_4$ (627 mg, 16.5 mmol) in 17 mL of dry ether at 0 °C was added dropwise a solution of 3.12 g (10.3 mmol) of ester **27** in 5 mL of dry ether. The reaction mixture was stirred for 45 min and then carefully treated with 5 mL of saturated aq NH_4Cl. Standard ethereal workup, followed by chromatography (elution with H:E, 3:1), provided 2.4 g (90%) of alcohol **28**, which was homogeneous by TLC analyis (H:E, 2:1, R_f(**27**) = 0.92, R_f(**28**) = 0.35): ^{1}H NMR (250 MHz) δ 0.36 (s, 3 H), 0.40 (s, 3 H), 1.55–1.65 (m, 2 H), 1.75 (s, 3 H), 1.75–1.85 (m, 2 H), 1.95–2.05 (m, 2 H), 2.16 (m, 1 H), 3.78 ($^1/_2$ AB q, 1 H, J = 11.8 Hz), 4.16 ($^1/_2$ AB q, 1 H, J = 11.8 Hz), 7.35–7.65 (m, 5 H); ^{13}C NMR (250 MHz) 139.8 (s), 133.5 (d), 131.5 (s), 129.2 (s), 128.7 (d), 127.7 (d), 62.4 (t), 31.4, 27.5, 25.4, 21.7, 19.0, −2.4 (q), −2.7 (q) ppm; IR (film) 3450–3250 (br) cm^{-1}. Anal. Calcd for $C_{16}H_{24}O_2Si$: C, 73.80; H, 9.93. Found: C, 74.07; H, 9.43.

1-(Chloromethyl)-6-(dimethylphenylsilyl)-2-methyl-1-cyclohexene (29). To a stirred solution of 6.0 g of allylic alcohol **28** (23.3 mmol) in 100 mL of dry THF at −40 °C was added dropwise 9.75 mL (70.0 mmol) of dry TEA. The resulting solution was stirred an additional 20 min and 2.21 mL of methanesulfonyl chloride (28.0 mmol) was added dropwise. After the reaction mixture was allowed to warm to −25 °C for 4 h, 2.97 g (70.0 mmol) of lithium chloride was added in one portion, and the reaction mixture was stirred at −25 °C for an additional 8 h. Standard ethereal workup, followed by chromatography (elution with H:E, 6:1), furnished 6.48 g (96%) of chloride **29**, which was homogeneous by TLC analysis (H:E, 2:1, R_f(**28**) = 0.35, R_f(**29**) = 0.95): ^{1}H NMR (250 MHz) δ 0.25 (s, 3 H), 0.28 (s, 3 H), 1.42–1.6 (m, 3 H), 1.60–1.80 (m, 4 H), 1.85–2.00 (m, 3 H), 1.67 (s, 3 H), 3.55 ($^1/_2$ AB q, 1 H, J = 11 Hz), 4.1 ($^1/_2$ AB q, 1 H, J = 11 Hz), 7.22–7.5 (m, 5 H); ^{13}C NMR (250 MHz) 139.2 (s), 133.6 (d), 132.9 (s), 128.9 (d), 128.7 (s), 127.8 (d), 45.7 (t), 31.7, 27.4, 25.5, 21.6, 19.2, −2.3 (q), −2.35 (q) ppm; IR (film) 3050, 1700 cm^{-1}.

1-(Iodomethyl)-6-(dimethylphenylsilyl)-2-methyl-1-cyclohexene (30). To a stirred solution of 2.89 g of allylic chloride **29** (1.10 mmol) in 20 mL of dry THF at 0 °C was added 182 mg (1.21 mmol) of NaI in two portions, and the reaction mixture was stirred at 25 °C for 4 h. The reaction mixture was concentrated to a residue, which was chromatographed directly over silica gel (elution with H:E, 6:1) to afford 370 mg of iodide **30**, which decomposed rapidly at rt [crude ^{1}H NMR (250 MHz) δ 0.25 (s, 3 H), 0.28 (s, 3 H), 1.42–1.6 (m, 3 H), 1.60–1.80 (m, 4 H), 1.85–2.00 (m, 3 H), 1.67 (s, 3 H), 3.85–4.5 (m, 2 H), 7.22–7.5 (m, 5 H)].

(±)-5(*S)-[[6(*R**,*S**)-(Dimethylphenylsilyl)-2-methyl-1-cyclohexen-1-yl]methyl]-3-ethoxy-2-isopropyl-5-methyl-2-cyclopenten-1-one (32, 33).** To a solution of LDA, prepared from 2.51 mL (17.9 mmol) of diisopropylamine and 11.9 mL of n-butyllithium (19.0 mmol, 1.6 M in hexanes) in 20 mL of dry THF at −10 °C, was added 3.3 mL (19.0 mmol) of HMPA, and the temperature of the reaction mixture was then lowered to −78 °C. After this solution was allowed to stir for 30 min, 3.05 g (16.78 mmol) of enol ether **18** in 5 mL of dry THF was added dropwise, and the resulting bright orange lithium enolate solution was then stirred an additional 30 min. Chloride **29** (3.11 g, 11.98 mmol) in 10 mL of dry THF was then added dropwise at −78 °C, and the reaction mixture was allowed to stir for 1 h. The reaction mixture was allowed to stir at −55 °C for 20 h and was finally warmed to −20 °C over a 2-h period, followed by quenching with saturated aq NH_4Cl. Standard ethereal workup, followed by chromatography (elution with H:E, 8:1), gave 1.06 mg (34%) of recovered chloride **29**, followed by 4.83 g (68%, or 88% yield based on recovered **29**) of a diastereomeric mixture of products **32, 33**. The diastereomeric mixture of products **32, 33** was homogeneous by TLC analysis (H:E, 2:1, R_f(**18**) = 0.1, R_f(**32, 33**) = 0.68): ^{1}H NMR (250 MHz) δ 0.30 (s, 1.5 H), 0.33 (s, 1.5 H), 0.35 (s, 1.5 H), 0.37 (s, 1.5 H), 0.98 (s, 1.5 H), 1.10 (s, 1.5 H), 1.12 (d, 6 H, J = 6.9 Hz), 1.33 (t, 1.5 H, J = 7.2 Hz), 1.36 (t, 1.5 H, J = 7.1 Hz), 1.50 (s, 1.5 H), 1.62 (s, 1.5 H), 1.48–1.68 (m, 5 H), 1.82–2.05 (m, 3 H), 2.45–2.78 (m, 4 H), 3.95–4.15 (m, 2 H), 7.28–7.53 (m, 5 H); ^{13}C NMR (250 MHz) 209, 208.8, 181.3, 180.8, 139.9, 139.7, 133.8, 133.6, 133.59, 130.1, 129.2, 128.5, 128.3, 127.5, 127.4, 127.2, 126.7, 122.9, 122.3, 64.5, 64.4, 47.2, 46.7, 39.8, 37.5, 36.7, 32.0, 31.1, 29.2, 25.8, 25.7, 25.5, 25.4, 22.7, 22.6, 21.5, 21.2, 20.3, 20.2, 20.1, 20.0, 19.9, 19.7, 15.1, 15.0, −2.0, −2.1, −2.2, −2.4 ppm; IR (film) 1690, 1680, 1635, 1630, 1625, 1610 cm^{-1}.

(±)-4(*S)-[[6(*R**)-(Dimethylphenylsilyl)-2-methyl-1-cyclohexen-1-yl]methyl]-2-isopropyl-4-methyl-3-vinyl-2-cyclopenten-1-one (34) and (±)-4(*S**)-[[6(*S**)-(Dimethylphenylsilyl)-2-methyl-1-cyclohexen-1-yl]methyl]-2-isopropyl-4-methyl-3-vinyl-2-cyclopenten-1-one (35).** To a stirred solution of 4.59 g of enol ethers **32, 33** (10.8 mmol) in 30 mL of dry THF at rt was added dropwise 32.5 mL of vinylmagnesium bromide (32.5 mmol, 1 M in THF). The reaction mixture was stirred for 34 h at rt and then treated with saturated aq NH_4Cl. Standard ethereal workup gave a crude residue, which was diluted with 50 mL of THF and treated dropwise with 30 drops of 10% aq HCl. After stirring for 45 min at rt, the reaction mixture was neutralized with 0.5 g of anhyd K_2CO_3. Standard ethereal workup, followed by chromatography (elution with H:E, 5:1), afforded 1.43 g (32.7%) of trienone **35**, which was homogeneous by TLC analysis (H:E, 2:1, R_f(**32, 33**) = 0.75, R_f(**35**) = 0.68: ^{1}H NMR (250 MHz) δ 0.25 (s, 6 H), 1.07 (s, 3 H), 1.16 (d, 3 H, J = 7.2 Hz), 1.18 (d, 3 H, J = 7.2 Hz), 1.47 (s, 3 H), 1.54–2.10 (m, 7 H), 1.77 ($^1/_2$ AB q, 1 H, J = 14.4 Hz), 1.87 ($^1/_2$ AB q, 1 H, J = 18.7 Hz), 2.38 $^1/_2$ AB q, 1 H, J = 14.4 Hz), 2.49 ($^1/_2$ AB q, 1 H, J = 18.7 Hz), 2.79 (heptet, 1 H, J = 7.2 Hz), 5.22 (ABX, 1 H, J_{ab} = 1.5 Hz, J_{ax} = 17.9 Hz), 5.36 (ABX, 1 H, J_{ab} = 1.5 Hz, J_{bx} = 12.0 Hz), 6.20 (ABX, 1 H, J_{ax} = 17.9 Hz, J_{bx} = 12.0 Hz), 7.32–7.52 (m, 5 H); ^{13}C NMR (250 MHz) 208.2 (s), 171.51 (s), 143.4 (s), 140.5 (s), 133.7 (d), 129.8 (s), 129.6 (d), 128.6 (d), 128.0 (s), 127.7 (d), 122.3 (t), 49.1 (t), 45.1 (s), 41.3 (t), 31.6 (d), 31.3 (t), 27.7 (q), 25.5 (t), 25.3 (d), 21.5 (t), 20.8 (q), 20.3 (q), 20.3 (q), −2.2 (q), −2.9 (q) ppm; IR (film) 1690, 1650 cm^{-1}; mass spectrum m/z 406 (M$^+$).

Continued elution afforded 2.29 g (52.3%) of trienone **34**, which was homogeneous by TLC analysis (H:E, 2:1, R_f(**32, 33**) = 0.7, R_f(**34**) = 0.62): ^{1}H NMR (250 MHz) δ 0.27 (s, 6 H), 1.15 (s, 3 H), 1.16 (d, 3 H, J = 7.2 Hz), 1.18 (d, 3 H, J = 7.2 Hz), 1.60 (s, 3 H), 1.45–1.78 (m, 7 H), 1.88 ($^1/_2$ AB q, 1 H, J = 18.3 Hz), 1.97 ($^1/_2$ AB q, 1 H, J = 14.4 Hz), 2.47 ($^1/_2$ AB q, 1 H, J = 18.3 Hz), 2.52 ($^1/_2$ AB q, 1 H, J = 14.4 Hz), 2.83 (heptet, 1 H, J = 7.2 Hz), 5.36 (ABX, 1 H, J_{ab} = 1.62 Hz, J_{ax} = 17.7 Hz), 5.40 (ABX, 1 H, J_{ab} = 1.62 Hz, J_{bx} = 12.0 Hz), 6.12 (ABX, 1 H, J_{ax} = 17.7 Hz, J_{bx} = 12.0 Hz), 7.3–7.48 (m, 5 H); ^{13}C NMR (250 MHz) 207.9 (s), 170.6 (s), 144.4 (s), 139.9 (s), 133.8 (d), 129.7 (d), 129.6 (s), 128.6 (d), 128.1 (s), 127.5 (d), 122.5 (t), 47.9 (t), 44.5 (s), 40.8 (t), 30.8 (t), 29.9 (d), 28.2 (q), 25.4 (d), 25.2 (t), 21.1 (t), 20.4 (q), 20.2 (q), 20.1 (q), −2.4 (q), −2.5 (q) ppm; IR (film) 3050, 1700, 1690, 1675, 1630 cm^{-1}; mass spectrum, m/z 406 (M$^+$).

Continued elution afforded 466 mg of unreacted **32, 33**. Thus trienones **34** and **35** were produced in 94% yield based on recovered starting enone and in a 1.6 to 1 ratio, respectively.[34]

***trans*-3a,4,6,7,8,8a,9,10-Octahydro-3a,8a-dimethyl-1-isopropylbenz[*f*]azulen-2(3*H*)-one (7).** Ethylaluminum dichloride (5.8 mL, 6.8 mmol, 1.45 M in toluene) was slowly added dropwise to a stirred solution of trienone **34** (1.84 g, 4.53 mmol) in 100 mL of dry toluene at 0 °C. The reaction mixture was stirred for 1.5 h and then treated with saturated aq NH_4Cl. Standard ethereal workup gave 201 mg of a crude residue. Purification via column chromatography (elution with H:E, 4:1) afforded 1.15 g (94%) of dienone **7**, which was homogeneous by TLC analysis (H:E, 2:1, R_f(**34**) = 0.7, R_f(**7**) = 0.63): ^{1}H NMR (250 MHz) δ 0.98 (s, 3 H), 1.07 (s, 3 H), 1.12 (d, 3 H, J = 7 Hz), 1.13 (d, 3 H, J = 7 Hz), 1.19–1.40 (m, 2 H), 1.56–1.78 (m, 4 H), 1.88–2.10 (m, 5 H), 2.10 ($^1/_2$ AB q, 1 H, J = 18 Hz), 2.25 ($^1/_2$ AB q, 1 H J = 18 Hz), 2.59 (dd, 1 H, J = 8.6 Hz, 13.4 Hz), 2.68 (heptet, 1 H, J = 7 Hz), 5.43 (t, 1 H, J = 3.58 Hz); ^{13}C NMR (250 MHz) 208.2 (s), 181.4 (s), 140.5 (s), 139.4 (s), 127.8 (d), 51.5 (t), 44.5 (t), 42.8 (s), 40.7 (t),

37.3 (s), 36.5 (t), 27.9 (q), 26.0 (q), 25.2 (t), 24.4 (d), 22.5 (t), 20.6 (q), 18.9 (t) ppm; IR (film) 1690, 1630 cm^{-1}; mass spectrum, m/z 272 (M^+). Anal. Calcd for $C_{19}H_{28}O$: C, 83.76; H, 10.37. Found: C, 83.81; H, 10.03.

Preparation of Tetracyclic Enone 37. A solution of 123 mg of trienone **35** (0.30 mmol) in 7 mL of dry toluene was cooled to 0 °C and 313 μL of ethylaluminum dichloride (0.45 mmol, 1.45 M in toluene) was added dropwise. The reaction mixture was allowed to stir for 1.5 h and was then treated with water. The resulting solution was diluted with 50 mL of ether and then washed with brine (2 × 15 mL). Standard ethereal workup, followed by chromatography (elution with H:E, 5:1), provided 107 mg (87%) of enone **37**, which was homogeneous by TLC analysis (H:E, 2:1, R_f(**35**) = 0.75, R_f(**37**) = 0.61): ^{1}H NMR (250 MHz) δ 0.44 (s, 3 H), 0.47 (s, 3 H), 1.09 (d, 3 H, J = 7.05 Hz), 1.13 (d, 3 H, J = 7.05 Hz), 1.21 (s, 3 H), 1.43 (s, 3 H), 1.55–2.05 (m, 9 H), 1.89 ($^1/_2$ AB q, 1 H, J = 14.9 Hz), 2.05 ($^1/_2$ AB q, 1 H, J = 16.2 Hz), 2.09 ($^1/_2$ AB q, 1 H, J = 14.9 Hz), 2.32 ($^1/_2$ AB q, 1 H, J = 16.2 Hz), 2.70 (heptet, 1 H, J = 7.05 Hz), 3.15 (br d, 1 H, J = 6.9 Hz), 7.28–7.60 (m, 5 H); ^{13}C NMR (250 MHz) 207.1 (s), 185.6 (s), 139.7 (s), 135.9 (s), 134.5 (d), 128.6 (d), 127.6 (d), 60.9 (t), 54.4 (d), 46.1 (s), 44.1 (s), 43.8 (d), 42.8 (t), 41.3 (s), 39.1 (t), 38.4 (t), 34.7 (q), 29.4 (t), 24.2 (d), 23.8 (q), 21.0 (q), 20.7 (q), 19.1 (t), 0.72 (q), −0.66 (q) ppm; IR (film) 1700, 1620 cm^{-1}; mass spectrum, m/z 271 (M − $SiMe_2Ph$). Anal. Calcd for $C_{23}H_{40}Si$: C, 76.61; H, 11.19. Found: C, 76.37; H, 10.97.

***cis*-3a,4,6,7,8,8a,9,10-Octahydro-3a,8a-dimethyl-1-isopropylbenz[*f*]azulen-2(3*H*)-one (42).** A solution of 231 mg of enone **37** (0.57 mmol) in 20 mL of dry toluene was treated dropwise with 0.78 mL of ethylaluminum dichloride (1.14 mmol, 1.45 M in toluene), and the reaction mixture was heated at 65 °C for 10 h. The reaction mixture was cooled to rt and treated with saturated aq NH_4Cl. Standard ethereal workup, followed by chromatography (H:E, 3:1), gave 140 mg (91%) of dienone **42**, which was homogeneous by TLC analysis (H:E, 2:1, R_f(**37**) = 0.61, R_f(**42**) = 0.55): ^{1}H NMR (270 MHz) δ 1.07 (s, 3 H), 1.13 (d, 6 H, J = 6.6 Hz), 1.13 (s, 3 H), 1.32–1.62 (m, 6 H), 1.85–2.15 (m, 4 H), 2.25–2.40 (m, 3 H), 2.57–2.7 (m, 2 H), 5.30 (t, 1 H, J = 3.3 Hz); ^{13}C NMR (270 MHz) 209.1 (s), 179.5 (s), 143.0 (s), 139.8 (s), 125.2 (d), 49.3 (d), 44.3 (s), 41.3 (t), 40.6 (t), 38.3 (t), 36.7 (s), 28.9 (q), 27.6 (q), 26.2 (t), 25.1 (d), 23.0 (t), 20.4 (q), 18.8 (t) ppm; IR (CCl_4) 1695, 1630 cm^{-1}; mass spectrum, m/z 272 (M^+). Anal. Calcd for $C_{19}H_{28}O$: C, 83.76; H, 10.37. Found: C, 83.92; H, 10.03.

4(*R)-[(2-Methyl-1-cyclohexen-1-yl)methyl]-2-isopropyl-4-methyl-3-vinyl-2-cyclopenten-1-one (39).** To a stirred solution of 1.0 g of allylic alcohol **20** (7.9 mmol) in 8 mL of dry hexanes at rt was added dropwise a solution of 0.28 mL of freshly distilled PBr_3 in 2 mL of hexanes. The resulting mixture was stirred at rt for 16 h and then treated with 5 mL of water. Standard ethereal workup provided 1.6 g of a crude residue, which was chromatographed over silica gel (elution with H:E, 2:1) to provide 1.3 g (87%) of 1-(bromomethyl)-2-methyl-1-cyclohexene. This bromide was homogeneous by TLC analysis (H:E, 1:1, R_f(**20**) = 0.33, R_f(bromide) = 0.90): ^{1}H NMR (90 MHz) δ 1.1–2.0 (m, 11 H), 3.7 (s, 2 H).

To a stirred solution of LDA, prepared from 0.23 g (2.24 mmol) of diisopropylamine in 8 mL of dry THF and 0.9 mL of *n*-butyllithium (2.24 mmol, 2.5 M in hexanes), was added HMPA (0.4 g, 2.24 mmol), and the resulting solution was cooled to −78 °C. To this solution was added dropwise 340 mg (1.87 mmol) of **18** in 2 mL of dry THF, and the resulting lithium enolate solution was stirred for 30 min at −78 °C. To the reaction mixture was added dropwise a solution of the above bromide (420 mg, 2.24 mmol) in 1 mL of dry THF, and the resulting solution was allowed to warm to rt over a 14-h period. Standard ethereal workup, followed by chromatography over silica gel (elution with H:E, 6:1), gave 360 mg (67%) of 5(*R**)-[(2-methyl-1-cyclohexen-1-yl)-methyl]-3-ethoxy-2-isopropyl-5-methyl-2-cyclopenten-1-one, which was homogeneous by TLC analysis (H:E, 1:2, R_f(**18**) = 0.30, R_f(enone) = 0.73): ^{1}H NMR (300 MHz) δ 1.08 (d, 3 H, J = 7.1 Hz), 1.09 (d, 3 H, J = 7.1 Hz), 1.11 (s, 3 H), 1.35 (t, 3 H, J = 7.0 Hz), 1.5 (m, 4 H), 1.61 (s, 3 H), 1.75 (m, 2 H), 1.92 (m, 2 H), 2.14 ($^1/_2$ A_1B_1 q, 1 H, J_{AB} = 13.8 Hz), 2.19 ($^1/_2$ A_2B_2 q, 1 H, J_{AB} = 17.1 Hz), 2.45 ($^1/_2$ A_1B_1 q, 1 H, J_{AB} = 13.8 Hz), 2.63 ($^1/_2$ A_2B_2 q, 1 H, J_{AB} = 17.1 Hz), 2.71 (sept, 1 H, J = 7.1 Hz), 4.11 (m, 2 H); ^{13}C NMR (270 MHz) 209.1, 181.5, 128.9, 127.8, 123.1, 64.6, 46.5, 40.8, 37.0, 31.9, 30.8, 25.6, 23.2, 22.6, 19.9, 15.1 ppm.

To a stirred solution of 275 mg of the above enol ether (0.95 mmol) in 10 mL of dry THF at rt was added dropwise 1.9 mL of vinylmagnesium bromide (1.89 mmol, 1 M in THF). The reaction mixture was stirred for 12 h at rt and then treated with saturated aq NH_4Cl. Standard ethereal workup gave a crude residue, which was diluted with 50 mL of THF and treated dropwise with 5 drops of 10% aq HCl. After 20 min of stirring at rt, the reaction mixture was neutralized with 0.1 g of anhyd K_2CO_3 and dried over anhyd $MgSO_4$. The resulting solution was filtered and concentrated to give a residue, which was chromatographed (elution with H:E, 2:1) to afford 1.43 g (53%) of trienone **39**, which was homogeneous by TLC analysis (H:E, 1:1, R_f(ketone) = 0.61, R_f(**39**) = 0.76: ^{1}H NMR (300 MHz) δ 1.18 (d, 3 H, J = 7.0 Hz), 1.19 (d, 3 H, J = 7.0 Hz), 1.26 (s, 3 H), 1.45 (m, 4 H), 1.59 (s, 3 H), 1.76 (m, 2 H), 1.92 (m, 2 H), 2.01 ($^1/_2$ A_1B_1 q, 1 H, J_{AB} = 18.3 Hz), 2.14 ($^1/_2$ A_2B_2 q, 1 H, J_{AB} = 13.7 Hz), 2.52 ($^1/_2$ A_1B_1 q, 1 H, J_{AB} = 18.3 Hz), 2.57 ($^1/_2$ A_2B_2 q, 1 H, J_{AB} = 13.7 Hz), 2.87 (sept, 1 H, J = 7.0 Hz), 5.57 (dd, 1 H, J = 17.8 Hz, 1.5 Hz), 5.61 (dd, 1 H, J = 11.9 Hz, 1.5 Hz), 6.56 (dd, 1 H, J = 17.8 Hz, 11.9 Hz); ^{13}C NMR (270 MHz) 208.1, 171.2, 144.5, 130.2, 130.0, 127.5, 122.5, 48.6, 44.3, 42.4, 32.1, 31.3, 28.1, 25.6, 23.3, 23.1, 20.3, 20.1 ppm.

(3a*R)-3a,4,4a,5,6,7,8,8a-Octahydro-3a,4a-dimethyl-1-isopropylbenz[*f*]azulen-2(3*H*)-one (40).** A solution of 25 mg of enone **39** (0.08 mmol) in 2 mL of dry toluene was treated dropwise with 56 μL of ethylaluminum dichloride (0.11 mmol, 1.45 M in toluene), and the resulting mixture was stirred at −20 °C for 24 h. An additional 50 μL of $EtAlCl_2$ was added, and the reaction mixture was stirred an additional 2 h. Standard ethereal workup gave 17 mg of a crude residue, which was chromatographed to afford 10 mg (40%) of dienone **40**, which was homogeneous by TLC analysis (H:E, 1:1, R_f(**39**) = 0.68, R_f(**40**) = 0.31): ^{1}H NMR (300 MHz) δ 1.0–1.9 (m, 20 H), 2.2–2.7 (m, 5 H), 2.82 (sept, $^1/_2$ H, J = 7.0 Hz), 3.34 (sept, $^1/_2$ H, J = 7.0 Hz), 6.13 (dd, 1 H, J = 10.3 Hz, 1.5 Hz), 6.89 (d, 1 H, J = 10.3 Hz). This data represents a 1:1 mixture of diastereomers.

Preparation of Tetracyclic Enone 41. A solution of 20 mg of enone **39** (0.073 mmol) in 2 mL of dry toluene was treated dropwise with 45 μL of ethylaluminum dichloride (0.088 mmol, 1.45 M in toluene), and the reaction mixture was stored at −5 °C for 72 h. Standard ethereal workup gave 31 mg of a crude residue, which was chromatographed to afford 10.6 mg (53%) of tetracyclic enone **41**, which was homogeneous by TLC analysis (H:E, 1:1, R_f(**39**) = 0.61, R_f(**41**) = 0.36): ^{1}H NMR (300 MHz) δ 1.12 (d, 3 H, J = 7.1 Hz), 1.13 (d, 3 H, J = 7.1 Hz), 1.41 (s, 3 H), 1.62 (s, 3 H), 1.0–1.7 (m, 8 H), 1.81 ($^1/_2$ A_1B_1 q, 1 H, J_{AB} = 13.8 Hz), 1.90 ($^1/_2$ AB qd, 1 H, J_{AB} = 10.5 Hz, J_{AX} = 0.0 Hz), 2.00 ($^1/_2$ A_1B_1 q, 1 H, J_{AB} = 13.8 Hz), 2.36 ($^1/_2$ A_2B_2 q, 1 H, J_{AB} = 16.2 Hz), 2.44 ($^1/_2$ A_2B_2 q, 1 H, J_{AB} = 16.2 Hz), 2.58 ($^1/_2$ AB qd, 1 H, J_{AB} = 10.5 Hz, J_{BX} = 5.4 Hz), 2.66 (sept, 1 H, J = 7.1 Hz), 3.09 (d, 1 H, J_{AX} = 0.0 Hz, J_{BX} = 5.4 Hz).

***trans*-1,2,3,3a,4,6,7,8,8a,9-Decahydro-3a,8a-dimethyl-1-isopropylbenz[*f*]azulene (43).** A mixture of **7** (47 mg, 0.17 mmol), hydrazine hydrate (51 μL, 1.59 mmol), anhyd K_2CO_3 (290 mg, 2.1 mmol), and diethylene glycol (2.5 mL) was placed into a round-bottom flask equipped with a short-path distillation apparatus and heated at 160 °C for 2 h followed by heating at 240 °C for 4 h. The cooled reaction mixture was combined with the distillate, diluted with water, and extracted with ether. The combined organic extracts were washed with cold 10% HCl, dried over anhyd $MgSO_4$, and filtered. Concentration in vacuo, followed by chromatography on silica gel (elution with hexanes), gave 42 mg (95%) of diene **43** (hexanes, 1:1, R_f(**7**) = 0.45, R_f(**43**) = 0.91): ^{1}H NMR (270 MHz) δ 0.77 (s, 1.5 H), 0.85–1.5 (m, 19.5 H), 1.14 (s, 3 H), 1.6–2.2 (m, 7 H), 5.20–5.25 (m, 1 H), 5.32 (dt, 1 H, J = 8.1 Hz, 3 Hz). This data represents a mixture of C(9) diastereomers.

Dithioketalization of 7 Using Boron Trifluoride Etherate. Ethanedithiol (48 μL, 0.51 mmol) was added dropwise to a solution of 69 mg (0.25 mmol) of dienone **7** in 2 mL of dry methanol at rt. To this mixture was added dropwise 63 μL (0.51 mmol) of boron trifluoride etherate, and the reaction mixture was allowed to stir for 15 h. The reaction was quenched with saturated $NaHCO_3$. Standard ethereal workup, followed by chromatography (elution with H:E, 6:1), gave 66.5 mg (75%) of dithioketal **44**, which

was homogeneous by TLC analysis (H:E, 2:1, R_f(7) = 0.63, R_f(44) = 0.78): ^{1}H NMR (270 MHz) δ 0.99 (s, 3 H), 1.05 (s, 3 H), 1.18 (d, 3 H, J = 7.2 Hz), 1.2 (d, 3 H, J = 7.2 Hz), 1.32–1.70 (m, 6 H), 1.80–2.25 (m, 6 H), 2.40–2.63 (m, 3 H), 3.12–3.32 (m, 4 H), 5.35 (t, 1 H, J = 3.42 Hz); ^{13}C NMR (270 MHz) 149.6 (s), 140.0 (s), 137.6 (s), 126.4 (d), 77.9 (s), 62.1 (t), 47.8 (s), 45.9 (t), 41.1 (t), 41.0 (t), 40.3 (t), 37.2 (s), 36.0 (t), 28.1 (q), 26.8 (d), 25.3 (t), 24.8 (q), 23.0 (q), 22.8 (q), 21.4 (t), 19.0 (t) ppm; IR (film) 1460, 1435, 1370, 1360, 1330 cm^{-1}; mass spectrum, m/z 348 (M$^+$).

***trans*-2,3,3a,4,6,7,8,8a,9,10-Decahydro-3a,8a-dimethyl-1-isopropylbenz[*f*]azulene (45). (a) Raney Nickel Reduction of 44.** Raney nickel (W-6)[61] (0.20 g, excess) was added to 1 mL of absolute ethanol with vigorous stirring. A solution of 40 mg of dithioketal **44** (0.11 mmol) in 1 mL of warm (45 °C) absolute ethanol [note: the dithioketal is insoluble in ethanol at 22 °C] was added dropwise to the reaction mixture, which was then heated at reflux for 20 h while being stirred vigorously. The reaction mixture was cooled to rt and the Raney nickel was filtered and washed with 5 mL of absolute ethanol. The filtrate was concentrated to give 29 mg of a pale yellow residue. Purification via column chromatography (elution with hexanes) furnished 19.5 mg (67%) of diene **45**, which was homogeneous by TLC analysis (hexanes, R_f(44) = 0.63, R_f(45) = 0.80): ^{1}H NMR (300 MHz) δ 0.85 (s, 3 H), 0.90 (d, 3 H, J = 6.8 Hz), 0.96 (d, 3 H, J = 6.8 Hz), 0.99 (s, 3 H), 1.30–2.25 (m, 14 H), 1.90 (^{1}/$_2$ AB q, 1 H, J = 12.6 Hz), 2.12 (^{1}/$_2$ AB q, 1 H, J = 12.6 Hz), 2.62 (heptet, 1 H, J = 6.8 Hz), 5.34 (t, 1 H, J = 3.57 Hz); ^{13}C NMR (270 MHz) 142.8 (s), 141.1 (s), 137.0 (s), 125.5 (d), 49.5 (s), 46.4 (t), 41.9 (t), 39.5 (t), 37.4 (s), 36.3 (t), 28.2 (q), 27.7 (t), 26.3 (d), 25.4 (t), 23.4 (q), 21.8 (q), 21.2 (q), 20.0 (t), 19.1 (t) ppm; IR (film) 1470, 1450, 1440, 1380, 1365, 1335 cm^{-1}. Anal. Calcd for $C_{19}H_{30}$: C, 83.29; H, 11.71. Found: C, 83.39; H, 12.01.

(b) Dissolving Metal Reduction of 44. Anhyd ammonia (ca. 15 mL) was condensed in a 50-mL flask that was cooled in a dry ice/acetone bath and equipped with a dry ice/acetone condenser. Lithium metal (15 mg, 2.15 mmol) was added in one portion. After 5 min, the cooling bath was removed from the reaction vessel and the solution soon came to reflux. A solution of 187 mg of dithioketal **44** (0.54 mmol) in 0.5 mL of dry THF was added dropwise to the reaction mixture, which was allowed to reflux for 35 min. Absolute ethanol (1 mL) was added dropwise to quench the reaction, producing a milky white solution. The condenser was removed from the reaction vessel, which was then immersed in a warm water bath (50 °C) to evaporate all of the ammonia. Standard ethereal workup, followed by chromatography (elution with hexanes only), afforded 113 mg (82%) of diene **45**, which was identical with that obtained above by the Raney nickel reduction.

(c) Lithium Aluminum Hydride/Aluminum Chloride Reduction of Dienone 7. A solution of 1.73 g of aluminum trichloride (12.9 mmol) in 15 mL of dry ether was added dropwise to a stirred suspension of $LiAlH_4$ (0.26 g, 6.4 mmol, 95%) in 5 mL of dry ether at 0 °C. The reaction mixture was allowed to stir at 0 °C for 5 min and 1.01 g (3.71 mmol) of dienone **7** in 5 mL of dry ether was added dropwise, followed by heating the reaction mixture to reflux for 30 min. The reaction mixture was cooled to rt and was treated with 0.5 mL of ethyl acetate. The resulting solution was poured into a mixture of ether (20 mL) and 3 N sulfuric acid (5 mL) and the phases were separated. The acidic aq phase was extracted with 5 mL of ether and the combined ethereal phases were dried over anhyd $MgSO_4$ and filtered. Evaporation of the solvent and purification by column chromatography (elution with hexanes) afforded 845 mg (88%) of diene **45**, which was homogeneous by TLC analysis (hexanes, R_f(45) = 0.64, R_f(7) = 0.80) and was identical with the material described above.

***trans*-3,3a,4,7,8,8a,9,10-Octahydro-3a,8a-dimethyl-1-isopropylbenz[*f*]azulen-6(2*H*)one (48).** To a solution of diene **45** (182 mg, 0.71 mmol) in a mixture of acetonitrile/benzene (10:1, 7.7 mL) was added 157 mg (0.71 mmol) of chromium hexacarbonyl, and the reaction mixture was heated to reflux. The resulting solution was treated dropwise with 223 μL (2.12 mmol) of anhyd *tert*-butyl hydroperoxide and refluxed for 16 h. The oil bath was removed from the reaction flask, an additional 75 μL (0.71 mmol) of anhyd *tert*-butyl hydroperoxide was added dropwise, and the reaction mixture was again refluxed for 8 h. Standard ethereal workup, followed by chromatography (elution with H:E, 2:1), afforded 76.2 mg (42%) of recovered diene **45** (H:E, 2:1, R_f(45) = 0.86).

Continued elution gave 83.5 mg (44%, 75% based on recovered diene **45**) of dienone **48**, which was homogeneous by TLC analysis (H:E, 2:1, R_f(45) = 0.86, R_f(48) = 0.36): ^{1}H NMR (300 MHz) δ 0.86 (s, 3 H), 0.91 (d, 3 H, J = 6.0 Hz), 0.98 (d, 3 H, J = 6.0 Hz), 1.16 (s, 3 H), 1.20–1.26 (m, 2 H), 1.25 (d, 1 H, J = 9.1 Hz), 1.48–1.66 (m, 5 H), 1.74 (ddd, 1 H, J = 3.1 Hz, 6.2 Hz, 12.2 Hz), 2.17 (^{1}/$_2$ AB q, 1 H, J = 11.7 Hz), 2.33 (^{1}/$_2$ AB q, 1 H, J = 11.7 Hz), 2.20–2.47 (m, 2 H), 2.54–2.64 (m, 2 H), 5.80 (s, 1 H); ^{13}C NMR (270 MHz) 199.4 (s), 170.3 (s), 140.7 (s), 138.7 (s), 129.4 (d), 49.5 (s), 47.0 (t), 40.7 (t), 39.6 (t), 39.4 (s), 34.9 (t), 34.2 (t), 27.7 (t), 27.4 (d), 26.0 (q), 23.0 (q), 21.8 (q), 21.1 (q), 19.6 (t) ppm; IR (film) 1680, 1615, 1465 cm^{-1}. Anal. Calcd for $C_{19}H_{28}O$: C, 83.76; H, 10.37. Found: C, 83.46; H, 10.17.

Continued elution gave 7.5 mg (9.1%) of bis-enone **49**, which was homogeneous by TLC analysis (H:E, 2:1, R_f(45) = 0.86, R_f(49) = 0.70): ^{1}H NMR (270 MHz) δ 1.08 (s, 3 H), 1.12 (d, 3 H, J = 7.0 Hz), 1.15 (d, 3 H, J = 7.0 Hz), 1.18 (s, 3 H), 1.25–2.0 (m, 5 H), 2.1–2.8 (m, 8 H), 5.81 (s, 1 H); ^{13}C NMR (270 MHz) 206.5, 198.5, 178.2, 167.2, 141.5, 130.8, 51.3, 44.8, 42.7, 39.6, 39.2, 35.2, 34.1, 25.9, 25.7, 24.5, 21.9, 20.5 ppm; mass spectrum, m/z 286 (M$^+$).

***trans*-3,3a,4,7,8,8a,9,10-Octahydro-3a,8a-dimethyl-1-isopropylbenz[*f*]azulene-2,6-dione (49).** Pyridinium chlorochromate (3.76 g, 17.1 mmol) was added to a solution (17 mL) of 77 mg of **45** (0.28 mmol) in 17 mL of CH_2Cl_2 and 50 mg of type 3 molecular sieves. The resulting mixture was refluxed for 48 h. The reaction mixture was poured into 100 mL of saturated aq copper sulfate. This mixture was thoroughly extracted with CH_2Cl_2 and the solvent removed at reduced pressure to afford 92 mg of a dark oil. Purification by chromatography on silica gel (elution with ether) furnished 59 mg (72%) of dienone **49**, which was homogeneous by TLC analysis (H:E, 2:1, R_f(45) = 0.86, R_f(49) = 0.70) and identical with that prepared by other methods.

(3a*R,8a*S**,10*R**)-3,3a,4,6,7,8,8a,9-Octahydro-3a,8a-dimethyl-2-isopropylbenz[*f*]azulen-10(2*H*)-ol (50).** To a solution of 9.1 mg of selenium dioxide (0.08 mmol) in 500 μL of dry CH_2Cl_2 at rt was added 37 μL of anhyd *tert*-butyl hydroperoxide (0.33 mmol, 90%). The reaction mixture was stirred for 25 min and 42.5 mg of diene **45** dissolved in 500 μL of dry CH_2Cl_2 was added dropwise. After 1 h the reaction mixture became slightly yellow in color. The reaction mixture was allowed to stir for 48 h and was then poured into 10 mL of ether. The resulting ethereal solution was washed with 10% aq potassium hydroxide and dried over anhyd $MgSO_4$. Filtration and concentration of this solution gave a crude residue, which was purified via column chromatography (elution with H:E, 3:1) to afford 12.3 mg (27%) of allylic alcohol **50**, which was homogeneous by TLC analysis (H:E, 2:1, R_f(45) = 0.59, R_f(50) = 0.49): ^{1}H NMR (300 MHz) δ 0.97 (s, 3 H), 1.05 (s, 3 H), 1.05 (d, 3 H, J = 6.7 Hz), 1.09 (d, 3 H, J = 6.7 Hz), 1.22–1.27 (m, 2 H), 1.32–1.44 (m, 2 H), 1.67–1.90 (m, 9 H), 2.03–2.04 (m, 2 H), 2.15 (d, 1 H, J = 13.2 Hz), 2.44 (heptet, 1 H, J = 6.7 Hz), 5.34 (t, 1 H, J = 3.44 Hz); IR (film) 3600–3400 (br) cm^{-1}. Three more polar, unidentifiable products were also isolated (30 mg total).

(3a*R,6*R**,8a*R**)-3,3a,4,7,8,8a,9,10-Octahydro-3a,8a-dimethyl-1-isopropylbenz[*f*]azulen-6(2*H*)-ol (51).** To a stirred suspension of $LiAlH_4$ (32 mg, 0.81 mmol) in 4 mL of dry ether at −15 °C was added dropwise 138 mg (0.50 mmol) of dienone **48** in 1 mL of dry ether. The reaction mixture was allowed to stir for 1.5 h at −15 °C and was then treated with 5 mL of ether and 0.5 mL of water. Standard ethereal workup, followed by chromatography (elution with H:E, 1:1), gave 143 mg (95%) of alcohol **51**, which was homogeneous by TLC analysis (H:E, 1:1, R_f(48) = 0.76, R_f(51) = 0.66): ^{1}H NMR (300 MHz) δ 0.87 (s, 3 H), 0.90 (d, 3 H, J = 6.9 Hz), 0.96 (d, 3 H, J = 6.9 Hz), 1.04 (s, 3 H), 1.20–1.35 (m, 4 H), 1.40–1.55 (m, 4 H), 1.60–1.75 (m, 2 H), 1.95 (^{1}/$_2$ AB q, 1 H, J = 12.6 Hz), 2.08 (^{1}/$_2$ AB q, 1 H, J = 12.6 Hz), 2.15–2.25 (m, 3 H), 2.60 (heptet, 1 H, J = 6.8 Hz), 4.30 (m, 1 H), 5.36 (br s, 1 H); ^{13}C NMR (270 MHz) 144.3 (s), 142.2 (s), 137.6 (s), 129.5 (d), 68.0 (d), 49.3 (s), 46.0 (t), 41.7 (t) 39.6 (t), 37.8 (s), 35.1 (t), 29.8 (t), 27.7 (t), 26.9 (q), 26.3 (q), 23.3 (q), 21.8 (q), 21.1 (q), 19.8 (t) ppm; IR (CCl_4) 3550–3200 (br), 1620 cm^{-1}.

(Bromomethyl)dimethylsilyl Ether of 51. To 143 mg of alcohol **51** (0.5 mmol) in 2.5 mL of dry CH_2Cl_2 were added 75 μL

of bromomethyldimethylsilyl chloride (0.53 mmol) and 80.6 μL of TEA (0.6 mmol). The resulting solution was stirred at rt for 12 h. Standard ethereal workup provided 219 of crude residue. Chromatography over silica gel (elution with H:E, 5:1) afforded 197 mg (91%) of silyl ether **52**, which was homogeneous by TLC analysis (H:E, 1:1, R_f(**51**) = 0.47, R_f(**52**) = 0.94): ^{1}H NMR (300 MHz) δ 0.31 (s, 6 H), 0.86 (s, 3 H), 0.90 (d, 3 H, J = 7 Hz), 0.96 (d, 3 H, J = 7 Hz), 1.03 (s, 3 H), 1.2–2.3 (m, 14 H), 2.51 (s, 2 H), 2.60 (hept, 1 H, J = 6.8 Hz), 4.42 (br t, 1 H, J = 7 Hz), 5.29 (br s, 1 H).

(3a*R,4a*R**,5*R**,6*R**,8a*S**)-3,3a,4,4a,5,7,8,8a,9,10-Decahydro-3a,8a-dimethyl-5-(hydroxymethyl)-1-isopropylbenz[*f*]azulen-6(2*H*)-ol (54).** To a solution of 197 mg of silyl ether **52** (0.46 mmol) in 10 mL of dry benzene was added dropwise a mixture of n-Bu_3SnH (193 μL, 0.69 mmol) and AIBN (4 mg) in 2 mL of dry benzene at reflux over a 4-h period followed by reflux for an addition 2 h. Concentration of the reaction mixture afforded a crude residue, which was dissolved in 5 mL of DMF and then treated with 1.2 mL of 30% H_2O_2 (2.78 mmol) and KF (218 mg, 2.3 mmol). The resulting mixture was heated at 65 °C for 8 h. After cooling to rt, the reaction mixture was quenched. Standard ethereal workup, followed by chromatography (elution with H:E, 1:1), afforded 90 mg (63%) of diol **54**, which was homogeneous by TLC analysis (H:E, 5:1, R_f(**52**) = 0.68, R_f(**54**) = 0.01): ^{1}H NMR (300 MHz) δ 0.66 (s, 3 H), 0.92 (d, 3 H, J = 6.8 Hz), 0.93 (d, 3 H, J = 6.8 Hz), 1.08 (s, 3 H), 1.16–1.35 (m, 6 H), 1.45–1.80 (m, 8 H), 2.0–2.4 (m, 4 H), 2.58 (hept, 1 H, J = 6 Hz), 3.58 (d, 1 H, J = 11 Hz), 3.65–4.05 (m, 2 H); ^{13}C NMR (250 MHz) 139.6 (s), 139.0 (s), 75.0 (d), 60.2 (t), 50.3 (d), 49.8 (s), 44.3 (t), 42.6 (d), 41.5 (t), 40.6 (t), 35.6 (s), 29.6 (t), 27.2 (t), 27.1 (t), 26.6 (q), 23.6 (q), 21.7 (t), 21.0 (q), 20.8 (q), 183 (d) ppm.

(3a*R,4a*R**,5*R**,6*R**,8a*S**)-3,3a,4,4a,5,7,8,8a,9,10-Decahydro-3a,8a-dimethyl-5-[(tosyloxy)methyl]-1-isopropylbenz[*f*]azulen-6(2*H*)-ol (55).** Diol **54** (72 mg, 0.23 mmol) was dissolved in 4 mL of dry pyridine, cooled to 0 °C, and treated with 67 mg (0.35 mmol) of freshly recrystallized p-toluenesulfonyl chloride. After 18 h at 0 °C the reaction mixture was concentrated under high vacuum and the residue was dissolved in ether, washed with brine, and then concentrated. Chromatography on silica gel (elution with H:E, 1:1) afforded 29 mg (20%) of a bis-tosylate, which was homogeneous by TLC analysis (H:E, 5:1, R_f(**52**) = 0.68, R_f(**54**) = 0.01): ^{1}H NMR (300 MHz) δ 0.57 (s, 3 H), 0.91 (d, 3 H, J = 6 Hz), 0.92 (d, 3 H, J = 6 Hz), 0.98 (s, 3 H), 1.05–1.80 (m, 12 H), 1.90–2.40 (m, 4 H), 2.45 (s, 6 H), 2.51 (hept, 1 H, J = 6 Hz), 4.00–4.18 (m, 2 H), 4.51–4.63 (m, 1 H), 7.27–7.40 (m, 4 H), 7.75–7.90 (m, 4 H); ^{13}C NMR (250 MHz) 144.6, 144.5, 139.5, 138.8, 134.1, 132.8, 129.7, 129.5, 128.1, 127.8, 81.4, 66.0, 49.5, 45.7, 43.1, 42.8, 41.2, 41.0, 39.9, 35.4, 27.1, 26.5, 25.1, 24.9, 23.6, 21.6, 21.3, 20.9, 20.7, 17.8 ppm.

Continued elution provided 68 mg of mono-tosylate **55** (63%), which was homogeneous by TLC analysis (H:E, 1:1, R_f(**54**) = 0.01, R_f(**55**) = 0.42): ^{1}H NMR (300 MHz) δ 0.58 (s, 3 H), 0.91 (d, 3 H, J = 7 Hz), 0.92 (d, 3 H, J = 7 Hz), 1.03 (s, 3 H), 1.0–1.90 (m, 12 H), 1.91–2.40 (m, 4 H), 2.44 (s, 3 H), 2.52 (hept, 1 H, J = 6 Hz), 3.70–3.82 (m, 2 H), 4.01–4.08 (m, 1 H), 4.23–4.35 (m, 1 H), 7.35 ($^1/_2$ AB q, 1 H, J_{AB} = 11 Hz), 7.82 ($^1/_2$ AB q, 1 H, J_{AB} = 11 Hz); Ir (film) 3500–3150 (br) cm^{-1}.

Further elution (ether) provided 10 mg (14%) of unreacted **54**. This corresponds to a 73% conversion of diol **54** to mono-tosylate **55**, based on recovered diol.

(3a*R,4a*R**,5*R**,6*R**,8a*S**)-2,3a,4,4a,5,7,8,8a,9,10-Decahydro-3a,8a-dimethyl-5-methylene-1-isopropylbenz[*f*]azulen-6(3*H*)-ol (56).** To a mixture of 69 mg of tosylate **55** (0.15 mmol) in 5.7 mL of dry DMF and 570 μL of water was added 1.07 g (10.95 mmol) of potassium acetate. The resulting mixture was stirred at 65 °C for 21 h. Standard ethereal workup, followed by chromatography (elution with H:E, 1:1), afforded 36 mg (84%) of allylic alcohol **56**, which was homogeneous by TLC analysis (H:E, 1:2, R_f(**55**) = 0.43, R_f(**56**) = 0.84): ^{1}H NMR (300 MHz) δ 0.64 (s, 3 H), 0.93 (d, 3 H, J = 7.0 Hz), 0.94 (d, 3 H, J = 7.0 Hz), 1.04–1.17 (m, 1 H), 1.11 (s, 3 H), 1.22–1.65 (m, 6 H), 1.72–1.94 (m, 4 H), 2.09–2.25 (m, 3 H), 2.41 (dddd, 1 H, J = 16.7 Hz, 11.8 Hz, 5.0 Hz, 1.3 Hz), 2.61 (hept, 1 H, J = 7.0 Hz), 2.66–2.74 (m, 1 H), 4.28 (dd, 1 H, J = 2.8 Hz, 2.8 Hz), 4.67 (dd, 1 H, J = 1.5 Hz, 1.3 Hz), 4.97 (dd, 1 H, J = 1.3 Hz, 1.3 Hz).

14-Deoxyisoamijiol (3). To a mixture of 36 mg of alcohol **56** (0.125 mmol) in 5 mL of dry ether and 50 mL of dry TEA (0.375 mmol) was added 27 mg (0.188 mmol) of freshly prepared benzenesulfenyl chloride at 0 °C. The resulting mixture was stirred at rt for 12 h. TLC analysis indicated that alcohol **56** had been consumed. The reaction mixture was diluted with ether (100 mL), washed with brine (5 mL), and dried over anhyd $MgSO_4$. Filtration and evaporation of the solvent gave a crude residue, which was chromatographed over silica gel (elution with H:E, 1:1) to afford 48 mg (98%) of allylic sulfoxide **58**, which was homogeneous by TLC analysis (H:E, 1:2, R_f(**56**) = 0.75, R_f(**58**) = 0.18): ^{1}H NMR (300 MHz) δ 0.70 (s, 1.5 H), 0.72 (s, 1.5 H), 0.93 (d, 3 H, J = 7.0 Hz), 0.94 (d, 3 H, J = 7.0 Hz), 1.13 (s, 1.5 H), 1.21 (s, 1.5 H), 1.10–2.40 (m, 14 H), 2.41–2.55 (m, 1 H), 2.61 (hept, 1 H, J = 7.0 Hz), 3.30 (d, 0.5 H, J = 13 Hz), 3.60 (d, 0.5 H, J = 13 Hz), 3.63 (d, 0.5 H, J = 13 Hz), 3.97 (d, 0.5 H, J = 13 Hz), 5.20 (br s, 0.5 H), 5.50 (br s, 0.5 H), 7.45–7.68 (m, 5 H). This data represents a mixture of sulfoxide diastereomers.

Sulfoxide **58** (47 mg, 0.119 mmol) was dissolved in absolute methanol (2 mL) and treated with 28.7 mL of freshly distilled trimethyl phosphite (0.23 mmol). This mixture was stirred at rt for 12 h and then quenched by the addition of water (1 mL). Workup was accomplished by extraction with three portions of ether (50 mL), which was combined and washed with brine, dried over anhyd $MgSO_4$, and concentrated to give a oily residue. Chromatography on silica gel (elution with H:E, 5:1) gave 27 mg (79%) of 14-deoxyisoamijiol (**3**), which was homogeneous by TLC analysis (H:E, 1:2, R_f(**58**) = 0.34, R_f(**3**) = 0.71): ^{1}H NMR (300 MHz) δ 0.64 (s, 3 H), 0.93 (d, 34 H, J = 7.0 Hz), 0.94 (d, 3 H, J = 7.0 Hz), 1.04–1.17 (m, 1 H), 1.11 (s, 3 H), 1.22–1.65 (m, 6 H), 1.72–1.94 (m, 4 H), 2.09–2.25 (m, 3 H), 2.41 (dddd, 1 H, J = 16.7 Hz, 11.8 Hz, 5.0 Hz, 1.3 Hz), 2.61 (hept, 1 H, J = 7.0 Hz), 2.66–2.74 (m, 1 H), 4.28 (dd, 1 H, J = 2.8 Hz, 2.8 Hz), 4.67 (dd, 1 H, J = 1.5 Hz, 1.3 Hz), 4.97 (dd, 1 H, J = 1.3 Hz, 1.3 Hz); ^{13}C NMR (250 MHz) 153.4 (s), 139.8 (s), 138.7 (s), 109.7 (t), 74.0 (d), 49.8 (s), 41.9 (t), 40.9 (t), 40.9 (d) (sic)[4], 40.2 (t) (sic)[4], 39.2 (s), 36.4 (t), 29.9 (t), 27.2 (t), 26.6 (d), 24.0 (q), 21.8 (t), 21.0 (q), 20.8 (q), 15.1 (q) ppm; IR (film) 3260–3250, 2960, 2920, 2870, 2840, 1700, 1640, 1460, 1430, 1380, 1340, 1320, 1080, 1070, 1020, 950, 920, 910 cm^{-1}; mass spectrum, m/z 288 (M^+).

Note: The use of crude sulfoxide **58** did not affect the reaction yield.

(3a*R,4a*R**,8a*S**)-3,3a,4,4a,6,7,8,8a,9,10-Decahydro-3a,8a-dimethyl-1-isopropylbenz[*f*]azulen-5(2*H*)-one (60).** To 211 mg (0.81 mmol) of diene **45** dissolved in 2 mL of dry THF, maintained at −5 °C, was added dropwise 250 μL of diborane (1.0 M in THF, Aldrich) over a 30-min period. The reaction mixture was stirred 1 h at 0 °C, followed by treatment with more diborane (150 μL), and stirred an additional 30 min at rt. The reaction mixture was then treated with 1 mL of water and stirred at rt for 15 min. Sodium hydroxide (3 N) (1.0 mL), 1.5 mL of 30% hydrogen peroxide, and 140 mg of K_2CO_3 were dissolved in 1.5 mL of water. The resulting solution was stirred for 45 min at rt. Standard ethereal workup provided 184 mg of a crude residue, which was chromatographed on silica gel (elution with H:E, 7:1) to afford 139 mg (62%) of (3a*R**,4a*R**,5*R**,8a*S**)-3,3a,4,4a,6,7,8,8a,9,10-decahydro-3a,8a-dimethyl-1-isopropylbenz[*f*]azulen-5(2*H*)-ol (H:E, 7:1, R_f(**45**) = 0.99, R_f(alcohol) = 0.42): ^{1}H NMR (300 MHz) δ 0.90 (d, 3 H, J = 7.0 Hz), 0.98 (d, 3 H, J = 7.0 Hz), 1.03 (s, 3 H), 1.13 (s, 3 H), 0.95–1.60 (m, 16 H), 2.40–2.52 (m, 1 H), 2.61 (hept, 1 H, J = 7.0 Hz), 3.78–3.82 (dt, 1 H, J = 3.0 Hz).

To a solution of 139 mg of the above alcohol (0.50 mmol) in 5 mL of dry CH_2Cl_2 was added in a single portion 218 mg of PCC (1.0 mmol). The resulting mixture was stirred at rt for 3 h. The reaction was quenched with saturated aq NH_4Cl (5 mL) and then extracted with CH_2Cl_2 (4 × 25 mL). The methylene extracts were filtered through silica gel (5 g) and then dried over anhyd $MgSO_4$. Filtration and evaporation of the solvent afforded a crude residue, which was purified by chromatography on silica gel (elution with H:E, 7:1) to give 131 mg (95%) of ketone **60**, which was homogeneous by TLC analysis (H:E, 7:1, R_f(alcohol) = 0.20, R_f(**60**) = 0.30): ^{1}H NMR (300 MHz) δ 0.86 (s, 3 H), 0.90 (d, 3 H, J = 7.0 Hz), 0.97 (s, 3 H), 0.98 (d, 3 H, J = 7.0 Hz), 1.13–1.28 (m, 4 H), 1.45–2.38 (m, 13 H), 2.61 (hept, 1 H, J = 7.0 Hz); ^{13}C NMR (250 MHz) 212.7, 141.0, 139.1, 55.8, 49.9, 41.5, 39.6, 39.2, 37.8, 37.3,

32.2, 27.1, 26.8, 26.4, 25.5, 21.4, 21.4, 20.8, 20.3 ppm; IR (film) 1720 cm^{-1}.

(3a*R,4a*S**,8a*S**)-3,3a,4,4a,6,7,8,8a,9,10-Decahydro-3a,8a-dimethyl-1-isopropylbenz[*f*]azulen-5(2*H*)-one (61).** To a solution of sodium methoxide (4.35 mmol) in methanol (5 mL) was added 126 mg (0.46 mmol) of ketone **60** in 1 mL of dry methanol. The mixture was stirred at rt for 16 h and diluted with 1 mL of saturated aq NH_4Cl. Standard ethereal workup provided 126 mg of an inseparable 1:1 mixture of ketones **60** and **61**: ^1H NMR (300 MHz) δ 0.73 (s, 1.5 H), 0.92 (s, 1.5 H), 0.97 (s, 1.5 H), 1.01 (s, 1.5 H), 0.85–1.05 (m, 12 H), 1.10–2.43 (m, 17 H), 2.53–2.64 (m, 1 H).

(3a*R,4a*R**,8a*S**)-2,3,3a,4,4a,5,6,7,8,8a,9,10-Dodecahydro-3a,8a-dimethyl-1-isopropyl-5-methylenebenz[*f*]azulene (62).** To a solution of 126 mg of a 1:1 mixture of ketones **60** and **61** (0.46 mmol) at −78 °C was added 1.4 mL of commercially available (trimethylsilylmethyl)lithium (1.39 mmol, 1.0 M in THF, Aldrich). The resulting mixture was stirred at −78 °C for 30 min and then slowly allowed to warm to rt over a 4-h period. Standard ethereal workup afforded 154 mg of a crude residue, which was purified by chromatography on silica gel (elution with H:E, 7:1) to give 70 mg (42.5% actual yield, or 85% based on **61**) of a β-hydroxy silane. This alcohol was homogeneous by TLC analysis (H:E, 7:1, R_f(alcohol) = 0.20, R_f(**60**) = 0.30): ^1H NMR (300 MHz) δ 0.86 (s, 3 H), 0.90 (d, 3 H, J = 7.0 Hz), 0.97 (s, 3 H), 0.98 (d, 3 H, J = 7.0 Hz), 1.13–1.28 (m, 4 H), 1.45–2.38 (m, 13 H), 2.61 (hept, 1 H, J = 7.0 Hz). Further elution gave 48 mg of unreacted ketone **60**.

To a solution of aq HF (4 drops, 50%) in 10 mL of THF was added 70 mg of the above β-hydroxy silane (0.194 mmol), and the mixture was stirred at rt for 1 h. The reaction mixture was then partitioned between pentane (50 mL) and saturated aq $NaHCO_3$ (10 mL). The aq layer was extracted thoroughly with pentane (3 × 50 mL), and then combined organic extracts were washed with brine, dried over anhyd $MgSO_4$, and filtered. Concentration followed by chromatographic purification gave 46 mg of diene **62** (88%), which was homogeneous by TLC analysis (H:E, 7:1, R_f (alcohol) = 0.75, R_f(**62**) = 0.95): ^1H NMR (300 MHz) δ 0.67 (s, 3 H), 0.93 (d, 3 H, J = 6.8 Hz), 0.95 (d, 3 H, J = 6.8 Hz), 1.09 (s, 3 H), 0.8–2.46 (m, 26 H), 2.61 (hept, 1 H, J = 7.0 Hz), 4.53 (br s, 1 H), 4.76 (d, 1 H, J = 1.5 Hz).

Preparation of Sulfoxide 63. Ethylaluminum dichloride (140 μL of a 1.5 M solution in toluene, 0.14 mmol) was added to a solution of diene **62** (27 mg, 0.10 mmol) and *p*-toluenesulfinyl chloride[58] (17.4 mg, 0.1 mmol) in 1 mL of ether at 0 °C. The solution was allowed to warm to rt and stirred for a total of 15 h. Standard ethereal workup gave 43 mg of an oily residue. Chromatography on silica gel (elution with hexanes) gave 33 mg (90%) of tetrasubstituted sulfoxide **63**, which was homogeneous by TLC analysis: ^1H NMR (300 MHz) δ 0.80–1.05 (m, 13 H), 1.10–2.40 (m, 15 H), 2.50–2.65 (m, 1 H), 2.95 (d, 1 H, J = 13 Hz), 4.40 (d, 1 H, J = 13 Hz), 7.45–7.68 (m, 5 H).

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Abbreviations. Aqueous (aq), hexanes:ether (H:E), triethylamine (TEA).

Supplementary Material Available: NMR spectra of compounds studied and X-ray diffraction data for **37** (77 pages). Ordering information is given on any current masthead page.

Intramolecular Additions of Allylsilanes to Conjugated Dienones. Direct Stereoselective Syntheses of (±)-Neolemnanyl Acetate and (±)-Neolemnane†,1

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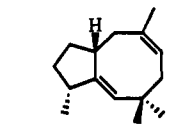
The total synthesis of the marine sesquiterpenes neolemnanyl acetate (**1**) and neolemnane (**2**) is reported. An intramolecular allylsilane addition to a conjugated dienone is used to assemble the basic 6,8-fused skeleton. Functionalization of the cyclooctane ring was achieved by means of a regiospecific photooxygenation.

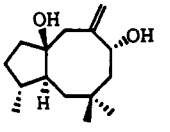
The identification of many biologically active natural products containing eight-membered rings has recently stimulated considerable interest in the development of methodology for the construction of cyclooctane rings. Recently, many model studies have been recorded in this area[2] and in rarer cases total syntheses of natural products containing eight-membered rings have been achieved (Chart I).[3,4]

The usefulness of butenyl dienone cyclizations[5] for the synthesis of fused cyclohexanes or cyclooctane rings is detailed in an accompanying paper[6] and is generalized in Scheme I. Note that one can direct the reactivity along two distinctly different pathways by the simple choice of reaction catalyst.[7a] For example, cyclization of trienone vi using ethylaluminum dichloride directly afforded (±)-nootkatone (vii) in 65% yield.[7b] In sharp contrast to this result, treatment of vi with fluoride ion gave fused

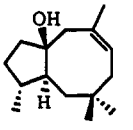
Chart I



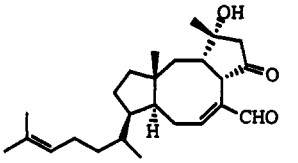
Precapnelladiene (i)



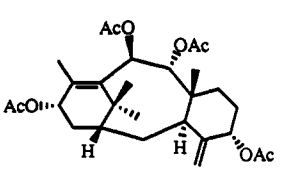
Poitediol (ii)



Dactylol (iii)



Ophiobolin C (iv)



Taxusin (v)

†Dedicated to Professor Paul A. Grieco on the occasion of his receipt of The 1991 ACS Award for Creative Work in Synthetic Organic Chemistry.

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