NMR 7 ($CDCl_3$): δ 1.37 (s, 3 H), 1.49 (m, 1 H), 1.69 (m, 1 H), 2.00 (m, 2 H), 2.48 (m, 1 H), 2.53 (d, 1 H, J = 12.3 Hz), 3.30 (m, 1 H), 3.38 (ddd, 1 H, J's = 2.3, 2.3, 12.3 Hz), 3.42 (s, br, 1 H). ^{1}H NMR 8 ($CDCl_3$): δ 1.22 (s, 3 H), 1.56 (m, 1 H), 1.84 (m, 1 H), 1.92 (m, 1 H), 2.03 (s, br, 1 H), 2.26 (d, 1 H, J = 14.3 Hz), 2.41 (m, 1 H), 2.68 (m, 1 H), 3.10 (m, 2 H). Anal. Calcd for $C_6H_{12}O_2S$: C, 48.62, H, 8.16. Found: C, 48.73, H, 8.32 (mixture of diastereomers).

The acetyl derivative **19** was obtained by treatment of 0.14 g of **7** with 1 mL of acetic anhydride and a catalytic amount of 4-(dimethylamino)pyridine at 65 °C for 90 min. The mixture was cooled and poured into 2 mL of water. The solution was carefully neutralized with sodium carbonate and repeatedly extracted with chloroform. Workup of the extracts and purification of the crude product by flash chromatography[37] on silica gel [chloroform–methanol (80:1)] gave **19**: IR (film) 1730, 1230, 1080, 1010 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 1.40 (m, 1 H), 1.52 (s, 3 H), 1.80 (m, 2 H), 1.90 (s, 3 H), 2.11 (m, 1 H), 2.46 (m, 1 H), 2.51 (d, 1 H, J = 12.8 Hz), 3.22 (m, 1 H), 3.93 (ddd, 1 H, J = 2.4, 2.4, 12.6 Hz); MS, m/e 190 (9), 172 (15), 130 (100), 113 (22), 101 (57), 81 (100), 69 (51). Exact mass calcd for $C_8H_{14}O_3S$ M^+, 190.067, found 190.064.

The acetyl derivative **20** was obtained from **8** following the same procedure described for **19**. The resulting crude acetoxy sulfoxide was purified by flash chromatography[37] on silica gel [chloroform–methanol (100:1)]: IR (film) 1730, 1240, 1185, 1015 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 1.54 (s, 3 H), 1.72 (m, 2 H), 2.01 (s, 3 H), 2.02 (m, 1 H), 2.48 (m, 1 H), 2.83 (m, 2 H), 2.92 (d, 1 H, J = 13.5 Hz), 3.70 (d, 1 H, J = 13.5 Hz); MS, m/e 190 (43), 130 (65), 113 (18), 101 (15), 81 (100), 69 (31). Exact mass calcd for $C_8H_{14}O_3S$ M^+, 190.067, found 190.063.

3-Hydroxy-3-methylthiacyclohexane *S*,*S*-Dioxide (9). A solution of 0.5 g (3.8 mmol) of **6** in 20 mL of water was treated at 5–10 °C with 1.62 g (7.6 mmol) of sodium metaperiodate and stirred at room temperature overnight. The solvent was removed and the residue extracted several times with ethyl acetate, yielding 0.45 g (73%) of **9** which was purified by recrystallization from ethyl acetate–ethyl ether: mp 79–79.5 °C; IR (Nujol) 3480, 1315, 1265, 1200, 1185, 1145, 1115, 1000, 940, 915, 865 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 1.38 (s, 3 H), 1.51 (m, 1 H), 1.88 (m, 1 H), 2.09 (m, 1 H), 2.28 (m, 1 H), 3.05 (m, 1 H), 4.05 (s, 1 H).

The acetyl derivative **21** was obtained by oxidation of **6** with 2 equiv of sodium metaperiodate and was purified by recrystallization from ethyl acetate–ethyl ether: mp 130–131 °C; IR (Nujol) 1730, 1230, 1140, 1100, 1020, 950, 865 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 1.53 (m, 1 H), 1.61 (s, 3 H), 2.00 (m, 2 H), 2.04 (s, 3 H), 2.36 (m, 1 H), 2.95 (m, 2 H), 2.99 (d, 1 H, J = 15.3 Hz), 4.16 (ddd, 1 H, J = 1.8, 3.4, 14.8 Hz). Anal. Calcd for $C_8H_{14}O_4S$: C, 46.59, H, 6.84. Found: C, 46.85, H, 7.07.

Acknowledgment. This work was supported in part by NSF Grant CHE-8314169 and US–Spain Collaborative Grant INT-8412811. We thank Dr. Maryellen Nerz-Stormes for assistance with the NMR spectroscopy. E. Brunet is grateful for the award of a Fulbright Fellowship during 1984/85.

Registry No. **1**, 19090-03-0; **1′**, 43152-96-1; **2**, 22072-19-1; **2′**, 99797-69-0; **3**, 96864-52-7; **3′**, 99797-83-8; **4**, 96864-51-6; **4′**, 99797-84-9; **5**, 94158-05-1; **5′**, 99797-85-0; **6**, 54288-61-8; **7**, 99797-70-3; **8**, 99797-71-4; **9**, 99797-72-5; **10**, 99797-73-6; **11**, 99797-74-7; **12**, 99797-75-8; **13**, 99797-76-9; **14**, 52727-14-7; **15**, 99797-77-0; **16**, 99797-78-1; **17**, 38690-83-4; **18**, 99797-79-2; **19**, 99797-80-5; **20**, 99797-81-6; **21**, 99797-82-7.

Synthetic Studies Relating to the Structure of Senoxydene. A Sequential Annulation Approach to Angular Triquinane Construction Capable of Varied Tetramethyl Substitution Patterns

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Received November 1, 1985

A totally stereocontrolled route to the sesquiterpene known as senoxydene is described. The key phases of the synthesis involve a thermal ene reaction to set stereochemistry while constructing the diquinane segment and a vinylsilane-mediated annulation to elaborate the third, unsaturated five-membered ring. Our findings have disclosed that the natural product has been incorrectly formulated. In an attempt to broaden the scope of this methodology while simultaneously assessing ^{1}H NMR spectral parameters of this group of triquinanes, the positional isomers **20** and **21** were also prepared. The synthetic schemes paralleled that developed earlier. Neither **20** nor **21** proved to be senoxydene. The proton magnetic resonance spectra of all known angular triquinanes are tabulated and discussed as appropriate. The ordering of chemical shifts for natural senoxydene shows them to be atypical for this class of compounds. Close agreement is, however, noted with $\Delta^{9,12}$-capnellene, suggesting that senoxydene may be a linear triquinane. A definitive reinvestigation of its structure is in order.

The tricyclo[6.3.0.0^{1,5}]undecane or angular triquinane sesquiterpenes have figured prominently in the recent explosive growth of polycyclopentanoid natural-product chemistry.[1] Their isolation from a variety of sources has fostered considerable speculation concerning their biosynthesis.[2] Additionally, their unusual structural features have prompted many synthetic studies intent on the expedient multiple fusion of five-membered rings and the setting of relative stereochemistry, particularly at adjacent quaternary centers. To date, efforts culminating in the successful total synthesis of isocomene (**1**),[3] β-isocomene

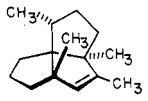
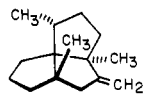
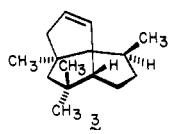
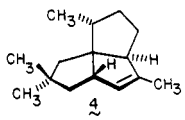
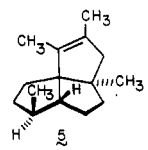
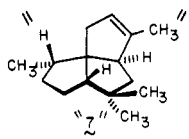
(1) Paquette, L. A. *Top. Curr. Chem.* **1979**, *79*, 41; **1983**, *119*, 1.

(2) (a) Zalkow, L. H.; Harris, R. N., III; Burke, N. I. *J. Nat. Prod.* **1979**, *42*, 96. (b) Bohlmann, F.; Jakupovic, J. *Phytochemistry* **1980**, *19*, 259. (c) Seto, H.; Yonehara, H. *J. Antibiot.* **1980**, *33*, 92. (d) Ohfune, Y.; Shirahama, H.; Matsumato, T. *Tetrahedron Lett.* **1976**, 2869. (e) Roberts, J. A. *Terpenoids Steroids* **1981**, *10*, 104. (f) Cane, D. E.; Tillman, A. M. *J. Am. Chem. Soc.* **1983**, *105*, 122. (g) Cane, D. E.; Rossi, T.; Tillman, A. M.; Pachlatko, J. P. *Ibid.* **1981**, *103*, 1838.

(3) (a) Paquette, L. A.; Han, Y.-K. *J. Org. Chem.* **1979**, *44*, 4014; *J. Am. Chem. Soc.* **1981**, *103*, 1835. (b) Oppolzer, W.; Bättig, K.; Hudlicky, T. *Helv. Chim. Acta* **1979**, *62*, 1493; *Tetrahedron* **1981**, *22*, *37*, 4359. (c) Pirrung, M. C. *J. Am. Chem. Soc.* **1979**, *101*, 7130; **1981**, *103*, 82. (d) *Dauben*, W. G.; Walker, D. M. *J. Org. Chem.* **1981**, *46*, 1103. (e) Wenkert, E; Arrhenius, T. S. *J. Am. Chem. Soc.* **1983**, *105*, 2030. (f) Ranu, B. C.; Kavka, M.; Higgs, L. A.; Hudlicky, T. *Tetrahedron Lett.* **1984**, *25*, 2447. (g) Tobe, Y.; Yamashita, T.; Kakiuchi, K.; Odaira, Y. *J. Chem. Soc., Chem. Commun.* **1985**, 898.

0022-3263/86/1951-0686$01.50/0

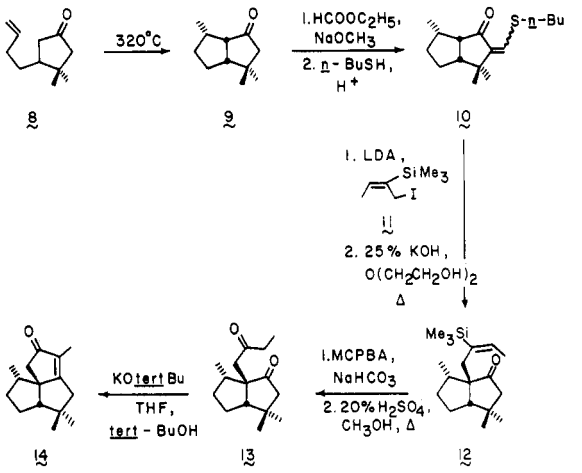
Table I. Methyl Chemical Shifts for 1–5 and "7" ($CDCl_3$ Solution, δ)

triquinane sesquiterpene	CH_3 signals		
	tert	sec	trig bound
 1	1.03 (6 H)	0.86	1.56
 2	1.10, 0.99	0.92	
 3	0.98, 0.93, 0.82	1.08	
 4	0.97 (6 H)	0.88	1.60
 5	1.00	0.96	1.55, 1.52
 7	1.17, 1.08	0.84	1.60

(2),[2b,g] silphinene (3),[4] pentalenene (4),[5] silphiperfol-6-ene (5),[6] and pentalenic acid (6)[7] have been numerous.

In the midst of this activity, there appeared a report by Bohlmann and Zdero describing the isolation from *Senecio oxyodontus* of yet another interesting sesquiterpene.[8] This substance, which has become known as senoxydene, was formulated as "7" solely on the basis of its spectral characteristics. However, the chemical shifts of the sp^3-bound methyl substituents in "7" are somewhat unusual (Table I). The high-field position of its secondary CH_3 group could be due to steric compression vis-a-vis the cis-related transannular methyl, but no reciprocal effect is apparent. Instead, one of senoxydene's tertiary methyls is notably deshielded (δ 1.17), appearing in a region well below the norm for its congeners (δ 0.82–1.10). Our initial inclination was to believe the number of compounds in the reference pool to be too limited. For this reason, any structural deduction arising purely from such considerations had to be regarded as tenuous at best.

Scheme I



To clarify matters, we were led to devise an unambiguous, fully stereocontrolled synthesis of "7", only to uncover that senoxydene cannot be constituted as originally proposed.[9] An identical conclusion was later arrived at independently by Itô and co-workers.[10] To exemplify the generality of the synthetic methodology that was developed during the course of our effort, two additional isomeric angular triquinanes were subsequently prepared and detailed spectral comparisons made.

Results

Synthesis of Alleged Senoxydene. The substitution plan in 7 suggested several broad strategies for construction of the basic carbocyclic framework. Of these approaches, we opted to pursue a course involving elaboration of the lower bicyclo[3.3.0]octane portion, with proper attention to the stereochemical relationship of the secondary methyl group to the angular proton. This route would ultimately require development of a new cyclopentene annulation scheme capable of regiospecifically positioning the endocyclic double bond and associated methyl group in ring C.

The stereochemical issue most central to successful arrival at 7 was resolved early by making recourse to the excellent control of relative configuration offered by thermal intramolecular ene cyclizations.[11] With this precedent in mind, 4,4-dimethylcyclopentenone[12] was treated with 4-butenylmagnesium bromide in the presence of cuprous bromide–dimethyl sulfide complex[13] to give 8. Noteworthily, 8 already possesses the requisite *gem*-dimethyl functionality, thereby obviating the need to elaborate this quaternary center in a later step. Heating of the trisubstituted cyclopentanone at 320 °C for 80 min resulted in smooth and efficient conversion to epimerically pure 9 (Scheme I). Hydrogen abstraction by the butenyl double bond within the proper enolic form of 8 accounts for the trans orientation of the newly formed secondary methyl group relative to the ring juncture protons.

Next, we focused attention on the conversion of 9 to 12. Preliminary studies on 9 revealed its invariant response to a host of bases to be predominant production of the less-substituted enolate irrespective of conditions.

(4) (a) Leone-Bay, A.; Paquette, L. A. *J. Org. Chem.* **1982**, *47*, 4173; *J. Am. Chem. Soc.* **1983**, *105*, 7352. (b) Tsunoda, T.; Kodama, M.; Itô, S. *Tetrahedron Lett.* **1983**, *24*, 83. (c) Sternbach, D. D.; Hughes, J. W.; Burdi, D. F; Banks, B. A. *J. Am. Chem. Soc.* **1985**, *107*, 2149. (d) Wender, P. A.; Ternansky, R. J. *Tetrahedron Lett.* **1985**, *26*, 2625.

(5) (a) Ohfune, Y.; Shirahama, H.; Matsumoto, T. *Tetrahedron Lett.* **1976**, 2869. (b) Misumi, S.; Ohtsuka, T.; Ohfune, Y.; Sugita, K.; Shirahama, H.; Matsumoto, T. *Ibid.* **1979**, 31. (c) Annis, G. D.; Paquette, L. A. *J. Am. Chem. Soc.* **1982**, *104*, 4504; **1983**, *105*, 7358. (d) Crimmins, M. T., private communication. (e) Pattenden, G.; Teague, S. J. *Tetrahedron Lett.* **1984**, *25*, 3021. (f) Piers, E.; Karunaratne, J. *J. Chem. Soc., Chem. Commun.* **1984**, 959.

(6) Paquette, L. A.; Roberts, R. A.; Drtina, G. J. *J. Am. Chem. Soc.* **1984**, *106*, 6690.

(7) (a) Sakai, K.; Ohtsuka, T.; Misumi, S.; Shirahama, H.; Matsumoto, T. *Chem. Lett.* **1981**, 355. (b) Crimmins, M. T.; DeLoach, J. A. *J. Org. Chem.* **1984**, *49*, 2076.

(8) Bohlmann, F.; Zdero, C. *Phytochemistry* **1979**, *18*, 1747.

(9) Paquette, L. A.; Galemmo, R. A., Jr.; Springer, J. P. *J. Am. Chem. Soc.* **1983**, *105*, 6975.

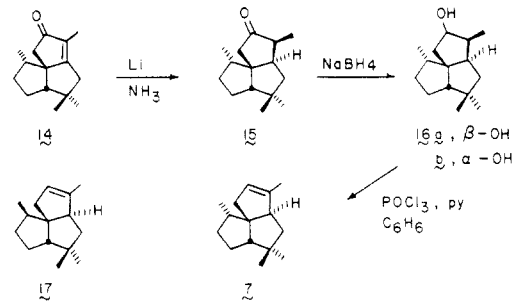
(10) Tsunoda, T.; Kabasawa, Y.; Itô, S.; Kodama, M. *Tetrahedron Lett.* **1984**, *25*, 773.

(11) Beslin, R.; Bloch, R.; Moinet, G.; Conia, J.-M. *Bull. Soc. Chim. Fr.* **1969**, 508.

(12) Magnus, P. D.; Nobbs, M. S. *Synth. Commun.* **1980**, *10*, 273.

(13) House, H. O.; Chu, C.-Y.; Wilkins, J. M.; Umen, M. J. *J. Org. Chem.* **1975**, *40*, 1460.

Scheme II



Therefore, in order to cause the alkylation to occur regiospecifically at the junction of the two five-membered rings, it proved necessary to block the more reactive α-methylene site, and this need was met by the α-(butylthio)methylene moiety as in **10**. We were now in a position to introduce a masked 2-butanone side chain, and (*E*)-1-iodo-2-(trimethylsilyl)but-2-ene (**11**) was designated to serve as the appropriate electrophilic equivalent. This silyl iodide, recognized to be an isomer of the reagent earlier introduced by Stork and Colvin,[14] was prepared by reaction of 2-(trimethylsilyl)-1-buten-3-ol[15] with sulfene[16] and S_N2' displacement of mesylate ion with sodium iodide in acetone. Although significant levels of strain and steric congestion had to be overcome, deprotonation of **10** with lithium diisopropylamide in tetrahydrofuran at −30 °C and condensation with **11** proceeded satisfactorily. For the usual reasons, retention of cis stereochemistry in the bicyclooctanone was fully anticipated. Removal of the blocking group required more vigorous conditions than usual. However, heating with 25% potassium hydroxide in ethylene glycol for 48 h provided a satisfactory solution to this problem.

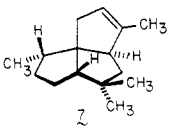
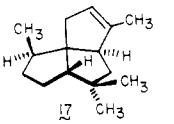
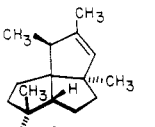
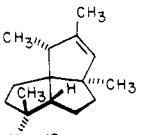
Vinylsilane **12** was converted quantitatively into the epoxide in the presence of *m*-chloroperbenzoic acid. This product was directly exposed to 20% sulfuric acid in hot methanol and, thereby, transformed into diketone **13**. As expected, base-promoted cyclization of **13** cleanly furnished tricyclic enone **14**. The structural assignment to **14** was fully consistent with a broad range of spectral data (see Experimental Section).

With key intermediate **14** in hand, our plan called for dissolving metal reduction as a means of saturating the conjugated douule bond with a high guarantee that the β hydrogen would enter from the α face to generate the thermodynamically more stable ring juncture. In actuality, the action of lithium in liquid ammonia on **14** gave an oily ketone (**15**), whose isomeric homogeneity was confirmed by ^{13}C NMR analysis. When reduction with sodium borohydride led to two chromatographically separable crystalline diols (**16a** and **16b**, Scheme II), an opportunity to establish the correctness of the assembly of atoms in our synthetic material presented itself. The clearcut confirmatory definition of the lower melting constituent as **16a** by X-ray analysis[17] allowed formulation of the second alcohol as **16b**.

Both isomers of **16** could be uneventfully dehydrated to **7**. The C_{15} hydrocarbon so obtained was immediately recognized to differ in its ^1H NMR spectrum from the natural product. In particular, the four methyl signals of

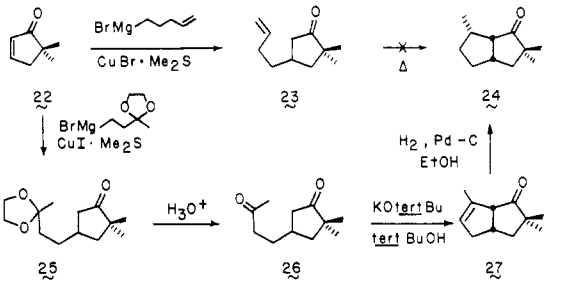
(14) Stork, G.; Colvin, E. *J. Am. Chem. Soc.* **1971**, *93*, 2080.
(15) Chan, T. H.; Mychajlowskij, W.; Ong, B. S.; Harpp, D. N. *J. Org. Chem.* **1978**, *43*, 1526.
(16) Crossland, R. K.; Servis, K. L. *J. Org. Chem.* **1970**, *35*, 3195.
(17) We are indebted to Dr. James P. Springer for the X-ray analysis. An ORTEP diagram of **16a** can be found in our preliminary communication.[9]

Table II. Methyl Chemical Shifts for 7 and 17–19 ($CDCl_3$ Solution, δ)

	CH_3 signals			
triquinane	tert	sec	trig bound	ref
 7	0.99, 0.93	0.85	1.65	this work, 10
 17	0.96, 0.92	0.90	*a*	10
 18	0.97	0.98, 0.94	1.67	*b*
 19	0.93	0.99, 0.96	1.56	*b*

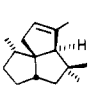
[a] Not reported. [b] Bohlmann, F.; Jakupovic, J. *Phytochemistry* **1980**, *19*, 259.

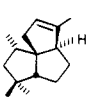
Scheme III



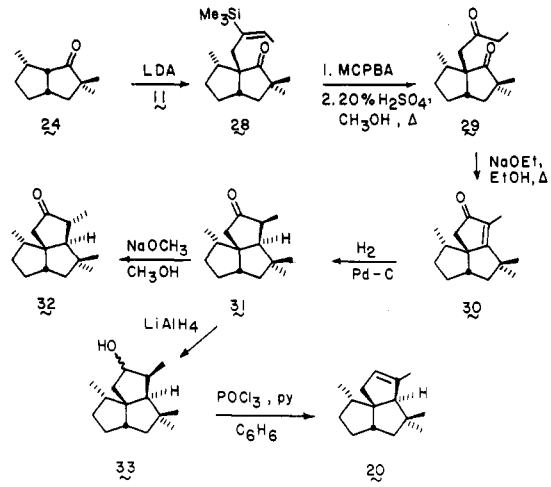
synthetic **7** deviate substantially from those reported for "**7**" (Tables I and II). Itô and co-workers considered the possibility that the secondary methyl group may actually have the β configuration instead. They proceeded to prepare **17**, only to find that this substance was also not identical with senoxydene.[10]

Table II contains spectral data for two additional sesquiterpenes isolated by Bohlmann. With the inclusion of these substances, one sees that the secondary methyl groups in natural and synthetic senoxydene are distinctively shielded. Differences are small, however, as proper comparison with the data for isocomene (**1**) and pentalenene (**4**) quickly reveals. The singular most distinctive feature of "**7**" remains its tertiary methyl singlet at δ 1.17. Might this anomaly arise because of an alternative location of the *gem*-dimethyl array on the angular triquinane framework? Since answers to this question could not be culled from Tables I and II, we have proceeded to synthesize **20** and **21**. We were fully apprised in advance that if either compound happened to be senoxydene, anomalous cyclization reactions had to be operational in its biosynthetic elaboration.[18]

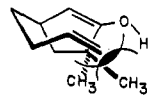

20


21

Scheme IV



The 1,5,5,6-Tetramethyl Substitution Plan. In an attempt to capitalize on aforementioned synthetic developments, 5,5-dimethyl-2-cyclopentenone (**22**)[19] was condensed with the magnesio cuprate derived from 4-bromo-1-butene. Although it was possible to secure **23** in this manner (Scheme III), we were subsequently frustrated in our ability to effect the thermal ene cyclization of this intermediate. Sealed-tube experiments conducted at temperatures as high as 450 °C (12 h) returned only unreacted starting material. Flow pyrolysis studies performed up to 610 °C further revealed the recalcitrancy of **23** to form **24**. At higher temperatures, decomposition was seen. Evidently, steric crowding by the *gem*-dimethyl substituent in **23** effectively prevents the olefinic appendage from attaining that conformation necessary for intramolecular bond formation (see A). A subsequent search of the lit-

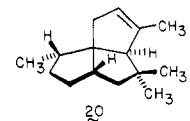
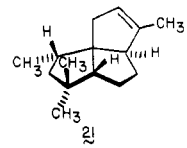


A

erature turned up a report by Conia and co-workers describing a comparably unsuccessful experiment with the similarly substituted 3,3-dimethylhept-6-en-2-one.[20] Of course, the possibility must not be discounted that **24** is thermodynamically unstable relative to **23**.

The necessary stereocontrolled cyclopentannulation was realized by resorting instead to conjugate addition of the Ponaras reagent ([3,3-(ethylenedioxy)butyl]magnesium bromide).[24] Hydrolysis of **25** with pyridinium tosylate in aqueous acetone gave diketone **26**, heating of which with potassium *tert*-butoxide in *tert*-butyl alcohol afforded β,γ-unsaturated ketone **27**. Migration of the double bond out of conjugation is driven by thermodynamic factors. As detailed elsewhere,[22] **27** should be favored over its conjugated isomer by approximately 2.5 kcal/mol. When **27** was subjected to catalytic reduction, hydrogen was delivered exclusively from the convex face to furnish only the desired **24**. The α-configurational assignment to the secondary methyl group stems from extensive previous experience[1] and the chemical shift of its doublet absorption (δ 0.99 in $CDCl_3$). The Conia group has previously noted that similar α-methyl substituted *cis*-perhydropentalenones usually

Table III. Methyl Chemical Shifts for 20 and 21 ($CDCl_3$ Solution, δ)

triquinane	CH_3 signals		
	tert	sec	trig bound
 20	0.98, 0.67	0.76	1.57
 21	0.99, 0.90	0.88	1.60

appear at δ 1.0 or to slightly higher field.[23] In contrast, signals due to epimeric methyl groups (β configuration; *all-cis* stereochemistry) at the same site experience deshielding by approximately 0.10 ppm.

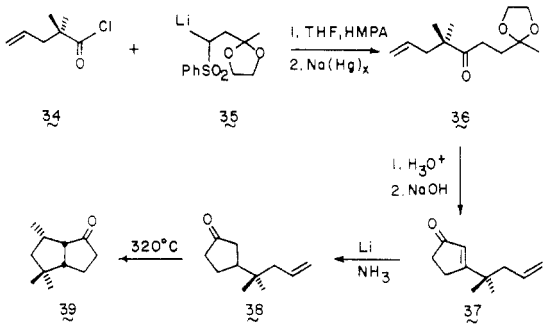
Regiocontrolled alkylation of **24** is greatly simplified relative to **9** because the need of a blocking group is eliminated. Although a high level of local steric congestion continues to persist, it proved possible to alkylate the anion of this *cis*-perhydropentalenone with **11** in 51% yield (Scheme IV). Sequential treatment of **28** with *m*-chloroperbenzoic acid and dilute sulfuric acid in hot methanol served to make diketone **29** available in 94% overall yield. The aldol cyclization of **29** proved, however, to be more difficult than originally expected. The doubly neopentyl nature of the cyclopentanone carbonyl group, the electrophilic seat of this reaction, is undoubtedly responsible. The best conditions uncovered involve heating **29** with a 20% solution of sodium ethoxide in ethanol.

Two methods were examined for the controlled reduction of **30**. Hydrogenation over palladium on charcoal gave rise to a stereoisomerically homogeneous saturated ketone. On the assumption that saturation of the double bond would occur from the less sterically hindered surface, this product was formulated as **31**. The methyl group α to the carbonyl center in **31** experiences an unusually high level of steric crowding. In support of our hypothesis, rapid epimerization to **32** materialized when **31** was treated with a catalytic quantity of sodium methoxide in methanol. Dissolving metal reduction (lithium) of **30** in liquid ammonia was found to produce a 5:1 mixture of **31** and **32** with significantly reduced efficiency. Consequently, the hydrogenation route was pursued.

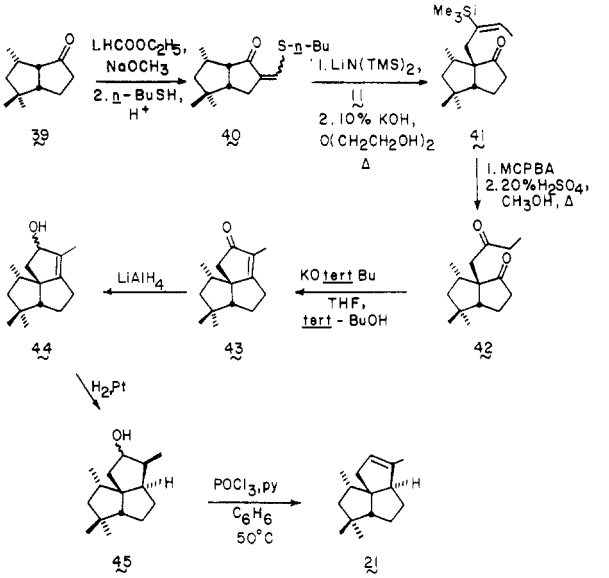
The ^1H NMR spectra of **31** and **32** show certain interesting differences that merit brief comment at this juncture. The doublet assigned to the secondary methyl substituent in the methylcyclopentane ring of **31** (δ 1.01) appears significantly *downfield* of the corresponding signal in **32** (δ 0.88). The identical ordering persists for the methyl group α to the carbonyl, that in **31** (δ 1.20) being *deshielded* relative to the related absorption in **32** (δ 1.13). The powerful anisotropic properties of the C–O double bond operate as well on the *gem*-dimethyl groups. Particularly notable is the fact that the two singlet absorptions of **31** (δ 1.09, 0.81) flank those exhibited by **32** (δ 1.03, 0.92). The more closely spaced pair in the latter example likely reflects a more normal structural geometry for this molecule. It is entirely possible that the steric congestion in **31** causes adoption of a conformation that aligns the ketone carbonyl in a manner particularly conductive to enhancing its intramolecular long-range anisotropy effects.

(18) Cane, D. E. In "Biosynthesis of Isoprenoid Compounds"; Porter, J. W., Spurgeon, S. L., Eds.; John Wiley and Sons: New York, 1981; Vol. 1, Chapter 6.
(19) Agosta, W. C.; Smith, A. B., III. *J. Am. Chem. Soc.* **1971**, *93*, 5513.
(20) Moinet, G.; Brocard, J.; Conia, J. M. *Tetrahedron Lett.* **1972**, 4461.
(21) Ponaras, A. A. *Tetrahedron Lett.* **1976**, 3105.
(22) Agosta, W. C.; Wolff, S. *J. Org. Chem.* **1975**, *40*, 1699.
(23) Drouin, J.; Leyendecker, F.; Conia, J. M. *Tetrahedron* **1980**, *36*, 1203.

Scheme V



Scheme VI



Tricyclic ketone **31** was reduced and dehydrated without incident. In practice, only the major alcohol formed upon lithium aluminum hydride reduction of **31** was treated with the phosphorus oxychloride–pyridine reagent. Comparison of the ^1H NMR spectrum of **20** (Table III) with that supplied by Professor Bohlmann for the natural product demonstrated that the two compounds were not identical. Perhaps significantly, two of the methyl absorptions in **20** appear at "record" upfield positions (compare Tables I and II).

Preparation of the Second Supposed Senoxydene. The facet of the problem to contend with presently was to maintain the 1α,6-dimethyl substitution pattern intact while translocating the *gem*-dimethyl functionality to C-3 within the otherwise identical triquinane ring system. Since the ene cyclization mechanistic model predicts sterically uninhibited closure for ketone **38**, a pathway to this intermediate was devised. The most workable of these involved condensation of the lithiated anion[24] of 1-(phenylsulfonyl)-3-butanone ethylene ketal (**35**)[25] with 2,2-dimethyl-4-pentenoyl chloride (**34**)[26] in tetrahydrofuran solution containing both tetramethylethylenediamine and hexamethylphosphoramide (Scheme V). Reductive desulfonylation of the coupled product with 6% sodium amalgam led to the isolation of **36**. The diketone obtained by aqueous acidic hydrolysis of **36** underwent ready cyclization in the presence of sodium hydroxide. Chemospecific reduction of the conjugated double bond in **37** was realized with lithium in liquid ammonia. Preparative scale thermal activation of **38** at 320 °C gave **39** as the only product. The stereochemical assignment rests upon mechanistic considerations and independent hydrogenation of the known 1,8-dehydro deriative.[4]

Recourse was again made to the (butylthio)methylene derivative for controlling the regiochemistry of alkylation within **39** (Scheme VI). However, the enolate anion of **40** proved quite unreactive toward **11** under conditions heretofore employed. This difference may reflect greater steric hindrance to approach of the electrophile. Notwithstanding, through use of lithium hexamethyldisilazide in tetrahydrofuran at −78 °C for 55 h, it proved possible in the presence of 2 equiv of **11** to achieve useful levels of conversion to product (30% yield, 83% based upon recovered **40**). Above this temperature, decomposition of **40** was encountered.

In keeping with this trend, hydrolytic conversion to **41** proceeded under remarkably mild conditions.[27] Thus, heating in a mixture of 10% aqueous potassium hydroxide solution and diethylene glycol (3:4 v:v) for 18 h smoothly afforded **41** in 75% yield. This result merits comparison with the analogous hydrolysis of **10**, a process that requires more vigorous conditions (25% KOH, reflux for 48 h), proceeds in lower yield (46%), and produces an unidentified byproduct in moderate quantity. This difference in behavior may be accounted for by the steric impedance to 1,4-addition of hydroxide ion to **10** brought on by the adjacent *gem*-dimethyl groups. With unhindered access to the (butylthio)methylene functionality in **40** and its alkylated derivative, alkaline hydrolysis proceeds more readily. However, at temperatures above −78 °C, strong bases also appear to undergo the analogous conjugate addition, thereby initiating decomposition. A similar tendency has been earlier noted by Marshall and co-workers in their synthesis of (+)-valeranone.[28]

Ketone **41** was taken onward to **43** without event. Interestingly, it proved more advantageous to reduce the carbonyl group in **44** prior to saturation of the double bond. The 60:40 mixture of epimeric alcohols **45** could be readily separated chromatographically. The differing hydroxyl stereochemistry in these isomers had no apparent effect on their dehydration, both leading independently and with equal efficiency (82%) to **21**. The relevant methyl signals of this hydrocarbon are compiled in Table III.

A Review of the Evidence. Bohlmann and Zdero unequivocally established that natural senoxydene is an olefinic hydrocarbon of molecular formula $C_{15}H_{24}$ on the basis of a mass spectral molecular ion. The other evidence advanced in support of structure "**7**" consisted of 270-MHz ^1H NMR spectra recorded in both $CDCl_3$ and C_6D_6, suitable decoupling of these spectra, a shift reagent study of the derived epoxide, and the infrared spectrum. Unfortunately, as we have been, the interpretation of these data is faulty.

An overview of the ^1H NMR chemical shifts of protons associated with the tertiary, secondary, and sp^2-bound methyl groups of 11 triquinane hydrocarbons excluding "**7**" is given in Tables I–III. Comparison of these data with those of the original Bohlmann–Zdero report is suggestive of the following conclusions: (1) The signals of the vinyl proton (δ 5.13) and the trigonally bound methyl group (δ 1.60) lie well within the normal ranges for this part structure. Accordingly, the presence of a methylcyclopentene ring in the natural product seems likely. (2) A

(24) Kondo, K.; Tunemoto, D. *Tetrahedron Lett.* **1975**, 1397.
(25) Julia, M.; Badet, B. *Bull. Soc. Chim. Fr.* **1975**, 1363.
(26) (a) Creeger, P. L. *J. Am. Chem. Soc.* **1969**, *89*, 2500. (b) Agosta, W. C.; Smith, A. B., III. *Ibid.* **1971**, *93*, 5513.
(27) Ireland, R. E.; Marshall, J. A. *J. Org. Chem.* **1962**, *27*, 1615, 1620.
(28) Marshall, J. A.; Bundy, G. L.; Fanta, W. I. *J. Org. Chem.* **1968**, *33*, 3913.

modest shielding effect is experienced by methyl protons positioned in the cavity of the *cis*-perhydropentalenene portion of an angular triquinane relative to their epimers. Exemplary cases are found in **7**/**17**, **4**/*epi*-pentalenene (δ 0.93),[5c] and **5**/7β*H*-silphiperfol-6-ene (δ 0.94).[6] However, the effect is small compared to the range of chemical shifts reported for the secondary methyl groups of different angular triquinane isomers and is clearly sensitive to the proximity of additional methyl groups (compare **20** to **21**). Therefore, this probe does not constitute a reliable tool for the a priori assignment of configuration to a second methyl substituent. (3) The composite of chemical shifts attributable to protons of tertiary methyl groups discloses that the values reported for natural senoxydene ("**7**") are quite atypical. The δ 1.08 singlet falls into the range where angular methyl groups are typically found. The second signal at δ 1.17 is positioned further downfield than any resonance observed for an angular triquinane. (4) It is within the realm of possibility that natural senoxydene is a linear rather than an angular triquinane. The closest agreement between its δ 1.17 and 1.08 singlets and the values of an existing tricyclopentanoid is found in $\Delta^{9,12}$-capnellene (δ 1.16 and 1.08).[29] Since specific assignments to the latter pair of signals have not been made, it is difficult at this time to suggest the precise component of capnellene's structure that may be present in senoxydene. The reader should realize that this conclusion is a best-guess estimate. Senoxydene may not be a triquinane at all, although we currently believe this eventuality to be appreciably less likely. What is needed is a detailed and refined characterization of the naturally occurring sesquiterpene.

Experimental Section

4-(3-Butenyl)-3,3-dimethylcyclopentanone (8). 4-Bromo-1-butene (48.6 g, 0.36 mmol) in tetrahydrofuran (80 mL) was added to magnesium shavings (17.6 g, 0.72 mol) over 30 min. The reaction mixture was diluted with tetrahydrofuran (80 mL), heated at reflux for 1 h, cooled to −25 °C, and treated with a solution of copper bromide–dimethyl sulfide complex (24.6 g, 0.12 mol) in dimethyl sulfide (160 mL). The blue solution was stirred for 1 h before 4,4-dimethylcyclopentenone (20 g, 0.18 mol) in tetrahydrofuran (80 mL) was introduced during 2 h. The mixture was stirred at room temperature for 15 h, ammonium chloride solution was added, and the solids were removed by filtration through a pad of Celite. The filtrate was diluted with ether, washed repeatedly with ammonium chloride solution and once with brine, dried, and evaporated. The residue was purified by HPLC on silica gel (elution with petroleum ether/ethyl acetate, 30:1) to give pure **8** as a colorless oil (18.6 g, 65%): IR (neat, cm^{-1}) 2980, 2780, 1750, 1650, 1465, 1375, 910; ^1H NMR (300 MHz, $CDCl_3$) δ 5.82 (m, 1 H), 5.00 (dd, J = 19 and 1 Hz, 2 H), 2.43 (q, J = 9.6 Hz, 1 H), 2.17 (m, 1 H), 2.13 (s, 2 H), 2.04–1.80 (m, 3 H), 1.67 (m, 1 H), 1.26 (m, 1 H), 1.14 (s, 3 H), 0.88 (s, 3 H).

Anal. Calcd for $C_{11}H_{18}O$: C, 79.46; H, 10.91. Found: C, 79.21; H, 10.88.

(3a*R,6*S**,6a*S**)-Hexahydro-3,3,6-trimethyl-1(2*H*)-pentalenone (9).** Twenty Pyrex glass tubes each containing 500 mg (60.2 mmol) of **8** were sealed under vacuum and heated at 320 °C for 80 min. The combined products were purified by HPLC on silica gel (elution with 1% ethyl acetate in petroleum ether) and 7.85 g (78%) of **9** was obtained as a homogeneous colorless oil: IR (neat, cm^{-1}) 2960, 2880, 1735, 1460, 1380, 1150; ^1H NMR (300 MHz, $CDCl_3$) δ 2.68 (dd, J = 10 and 1.2 Hz, 1 H), 2.4 (m, 2 H), 2.11 (dd, J = 16 and 1.5 Hz, 1 H), 1.93 (dt, J = 16 and 1.5 Hz, 1 H), 1.8–1.65 (m, 3 H), 1.27–1.14 (m, 1 H), 1.13 (s, 3 H), 1.02 (d, J = 6 Hz, 3 H), 1.0 (s, 3 H); ^{13}C NMR ($CDCl_3$) ppm 220.9, 56.2, 53.8, 53.5, 37.6, 36.0, 35.6, 30.8, 27.3, 25.1, 16.4; MS, m/z calcd (M^+) 166.1358, obsd 166.1361.

Anal. Calcd for $C_{11}H_{18}O$: C, 79.46; H, 10.91. Found: C, 79.26; H, 10.98.

(3a*R,6*S**,6a*S**)-Hexahydro-2-[(*Z*)-hydroxymethylene]-3,3,6-trimethyl-1(2*H*)-pentalenone.** Sodium methoxide (330 mg, 5.0 mmol) in anhydrous benzene (1 mL) was treated with a solution of **9** (100 mg, 0.60 mmol) in the same solvent. The reaction mixture was cooled to 0 °C, ethyl formate (355 mg, 4.8 mmol) was introduced, and stirring was maintained at room temperature for 48 h. Ether was added, and the suspension was washed with water followed by 1 N potassium hydroxide solution (3×). The combined aqueous phases were acidified with concentrated hydrochloric acid and extracted with ether (4×). The combined ethereal solutions were dried and evaporated to give 110 mg (93%) of the formylated ketone: IR (neat, cm^{-1}) 3500–3000, 2960, 2880, 1740, 1680, 1670, 1560, 1500, 1485, 1470, 1110; ^1H NMR (90 MHz, $CDCl_3$) δ 9.7 (br s, 1 H), 7.34 (s, 1 H), 3.1 (t, J = 7 Hz, 1 H), 2.55–2.05 (m, 3 H), 1.95–1.45 (m, 3 H), 1.22 (s, 6 H), 1.1 (d, J = 7 Hz, 3 H), MS, m/z calcd (M^+) 194.1307, obsd 194.1313.

(3a*R,6*S**,6a*S**)-2-[(Butylthio)methylene]hexahydro-3,3,6-trimethyl-1(2*H*)-pentalenone (10).** A mixture of the preceding substance (110 mg, 0.56 mmol), magnesium sulfate (400 mg), *p*-toluenesulfonic acid (10 mg), and *n*-butanethiol (0.5 mL, 5.0 mmol) was heated in benzene (20 mL) at the reflux temperature for 20 h. The insolubles were separated by filtration, the filtrate was evaporated, and the residue was taken up in ether. The ethereal solution was washed with sodium bicarbonate solution and brine, dried, and evaporated to give **10** (100 mg, 72%) as a colorless oil; IR (neat, cm^{-1}) 2970, 2940, 2880, 1695, 1575, 1460, 1390, 1380, 1370, 1230, 1165, 1135; ^1H NMR (300 MHz, $CDCl_3$) δ 7.3 (s, 1 H), 2.78 (q, J = 10 Hz, 3 H), 2.4–.2.2 (m, 3 H), 1.74–1.64 (m, 4 H), 1.49–1.35 (m, 3 H), 1.38 (s, 3 H), 1.21–1.09 (m, 8 H), 0.93 (t, J = 12 Hz, 3 H); MS, m/z calcd (M^+) 266.1704, obsd 266.1716.

(*E*)-1-Iodo-2-(trimethylsilyl)but-2-ene (11). To a cold (0 °C) solution of 2-(trimethylsilyl)but-1-en-3-ol (11.0 g, 76.4 mmol) and triethylamine (18 mL) in dichloromethane (100 mL) was added dropwise a solution of methanesulfonyl chloride (6.6 mL, 83 mmol) in the same solvent (25 mL). The reaction mixture was stirred at 0 °C for 1 h and poured into ice water. The organic phase was washed with 5% hydrochloric acid, sodium bicarbonate solution, and brine prior to drying and solvent evaporation. The crude mesylate (15.06 g, 89%) was used without further purification: IR (neat, cm^{-1}) 2960, 1350, 1250, 1175, 900, 835; ^1H NMR (60 MHz, CCl_4) δ 5.6 (m, 2 H), 5.1 (m, 1 H), 2.7 (s, 3 H), 1.4 (d, J = 6 Hz, 3 H), 0.0 (s, 9 H).

The mesylate (15.06 g, 68 mmol) in acetone (500 mL) was heated at reflux with sodium iodide (12.15 g, 81 mmol) for 15 h. The cooled reaction mixture was filtered and evaporated, and the residue was taken up in ether. Washing with sodium thiosulfate and sodium bicarbonate solutions and then brine was followed by drying and solvent evaporation. There was isolated 11.42 g (66%) of **11** as a colorless oil: IR (neat, cm^{-1}) 2940, 1600, 1240, 1185, 1140, 830; ^1H NMR (200 MHz, $CDCl_3$) δ 6.0 (q, J = 6 Hz, 1 H), 4.0 (s, 2 H), 1.7 (d, J = 6 Hz, 3 H), 0.13 (s, 9 H); MS, m/z calcd (M^+) 253.9990, obsd 253.9984.

(3a*R,6*R**,6a*R**)-Hexahydro-3,3,6-trimethyl-6a-[(*E*)-2-(trimethylsilyl)-2-butenyl]-1(2*H*)-pentalenone (12).** Ketone **10** (3.60 g, 14.1 mmol) dissolved in anhydrous tetrahydrofuran (40 mL) was added during 1 h to a cold (0 °C) solution of lithium diisopropylamide (15.5 mmol, 1.1 equiv) in the same solvent (80 mL). A tetrahydrofuran solution (40 mL) of **11** (4.11 g, 16.2 mmol) was next introduced at −30 °C, and the reaction mixture was stirred at room temperature for 3 h and partitioned between 5% hydrochloric acid solution and ether. The ethereal phase was washed with sodium bicarbonate solution and brine, dried, and evaporated. Purification of the residue (6.38 g) by preparative HPLC on silica gel (elution with petroleum ether/ethyl acetate, 100:1) gave the alkylation product (2.47 g, 45%): IR (CCl_4, cm^{-1}) 2970, 2880, 1690, 1660, 1570, 1460, 1250, 850; ^1H NMR (200 MHz, $CDCl_3$) δ 7.22 (s, 1 H), 6.05 (q, J = 7 Hz, 1 H), 2.76 (t, J = 12 Hz, 2 H), 2.5–0.8 (series of m, 18 H), 1.67 (d, J = 7 Hz, 3 H), 1.27 (s, 3 H), 1.15 (s, 3 H), 0.01 (s, 9 H); MS, m/z calcd (M^+), 392.2569, obsd 392.2576.

(29) (a) Ayanoglu, E.; Gebreyesus, T.; Beechan, C. M.; Djerassi, C.; Kaisiu, M. *Tetrahedron Lett.* **1978**, 1671. (b) Stevens, K. E.; Paquette, L. A. *Ibid.* **1981**, 4393. (c) Paquette, L. A.; Stevens, K. E. *Can. J. Chem.* **1984**, *62*, 2415.

The preceding material (2.47 g, 6.3 mmol) was heated at reflux in aqueous 25% potassium hydroxide solution (90 mL) and diethylene glycol (120 mL) for 48 h. The reaction mixture was diluted with brine and extracted with ether. The combined organic phases were washed with sodium bicarbonate solution and brine, dried, and evaporated to furnish an oil that was purified by preparative tlc on silica gel (elution with petroleum ether/ethyl acetate, 20:1). There was isolated 840 mg (46%) of **12**, a colorless oil: IR (neat, cm^{-1}) 2970, 2860, 1730, 1650, 1245, 830; ^1H NMR (200 MHz, $CDCl_3$) δ 6.05 (q, J = 7 Hz, 1 H), 2.57 (d, J_{AB} = 12 Hz, 1 H), 2.23 (d, J_{AB} = 12 Hz, 1 H), 2.3–1.0 (series of m, 8 H), 1.65 (d, J = 7 Hz, 3 H), 0.98 (s, 3 H), 0.90 (s, 3 H), 0.78 (d, J = 9 Hz, 3 H), 0.01 (s, 9 H); MS, m/z calcd ($M^+ - CH_3$) 277.1988, obsd 277.1997.

Anal. Calcd for $C_{18}H_{32}OSi$: C, 73.90; H, 11.03. Found: C, 73.69; H, 10.91.

(3a*R,6*R**,6a*R**)-Hexahydro-3,3,6-trimethyl-6a-(2-oxobutyl)-1(2*H*)-pentalenone (13).** A cold (0 °C) solution of **12** (770 mg, 2.64 mmol) in dichloromethane (40 mL) was treated sequentially with solid sodium bicarbonate (500 mg) and buffer-washed *m*-chloroperbenzoic acid (650 mg, 4.0 mmol). The reaction mixture was stirred at room temperature for 16 h, and additional MCPBA (0.5 equiv) was added. When the oxidation was complete, ether was added, and the organic phase was washed with sodium sulfite, sodium bicarbonate, and sodium chloride solutions. Drying and solvent evaporation afforded 840 mg (100%) of epoxide: IR (CCl_4, cm^{-1}) 2970, 2860, 1725, 1450, 1245, 830; ^1H NMR (90 MHz, CCl_4/CH_2Cl_2) δ 2.8 (q, J = 5 Hz, 2 H), 2.5–0.5 (series of m, 15 H), 1.1 (s, 6 H), 0.10 (s, 9 H); MS, m/z calcd (M^+) 308.2171, obsd 308.2179.

The epoxysilane (840 mg, 2.64 mmol) was heated at reflux for 16 h in absolute methanol (50 mL) containing 20% aqueous sulfuric acid (50 mL). The reaction mixture was diluted with water and extracted with ether. The combined organic phases were washed with sodium bicarbonate solution and brine, dried, and evaporated. The residue was purified by MPLC on silica gel (elution with petroleum ether/ethyl acetate, 20:1) to give 400 mg (65%) of **13** as a colorless oil: IR (CCl_4, cm^{-1}) 2980, 2870, 1720, 1460, 1410, 1180; ^1H NMR (200 MHz, $CDCl_3$) δ 2.91 (d, J_{AB} = 17 Hz, 1 H), 2.57 (d, J_{AB} = 17 Hz, 1 H), 2.5 (m, 3 H), 2.1 (m, 2 H), 1.92 (m, 3 H), 1.2–1.0 (m, 2 H), 1.10 (s, 3 H), 1.00 (t, J = 7.6 Hz, 3 H), 0.99 (s, 3 H), 0.82 (d, J = 6.7 Hz, 3 H); MS, m/z calcd (M^+) 236.1776, obsd 236.1782.

Anal. Calcd for $C_{15}H_{24}O_2$: C, 76.22; H, 10.24. Found: C, 76.61; H, 10.23.

(5a*R,8*R**,8a*R**)-4,5,5a,6,7,8-Hexahydro-3,5,5,8-tetramethylcyclopenta[*c*]pentalen-2(1*H*)-one (14).** Diketone **13** (330 mg, 1.40 mmol) in tetrahydrofuran (30 mL) and *tert*-butyl alcohol (2 mL) containing potassium *tert*-butoxide (330 mg, 2.94 mmol) was heated at 40 °C for 1 h. The reaction mixture was diluted with ether and washed with sodium bicarbonate solution and brine. Following drying and solvent evaporation, there was isolated 250 mg (82%) of **14** as a colorless oil: IR (neat, cm^{-1}) 2980, 2870, 1710, 1660, 1450, 1190; ^1H NMR (200 MHz, $CDCl_3$) δ 2.62 (d, J_{AB} = 17 Hz, 1 H), 2.41 (d, J_{AB} = 17 Hz, 1 H), 2.32–1.55 (series of m, 7 H), 1.74 (d, J = 2.3 Hz, 3 H), 1.19 (m, 1 H), 1.12 (s, 3 H), 0.80 (s, 3 H), 0.71 (d, J = 7.1 Hz, 3 H); MS, m/z calcd (M^+) 218.1671, obsd 218.1676.

Anal. Calcd for $C_{15}H_{22}O$: C, 82.44; H, 10.16. Found: C, 82.15; H, 10.13.

(3*R,3a*S**,5a*R**,8*R**,8a*S**)-Octahydro-3,5,5,8-tetramethylcyclopenta[*c*]pentalen-2(1*H*)-one (15).** Enone **14** (43.8 mg, 0.43 mmol) dissolved in tetrahydrofuran (3 mL) was added to a solution of lithium metal (30 mg, 4.3 mol) in liquid ammonia (50 mL). The reaction mixture was allowed to reflux for 30 min before isoprene (2 mL) and methanol (2 mL) were added. Following evaporation of the ammonia, the residue was partitioned between ether and water, and the ether phase was washed with sodium bicarbonate solution and brine prior to drying. Evaporation of the filtrate gave 95 mg (100%) of **15** as a colorless oil: IR (neat, cm^{-1}) 2960, 2870, 1740, 1450, 1180; ^1H NMR (300 MHz, $CDCl_3$) δ 2.4 (s, 2 H), 2.2–1.2 (series of m, 10 H), 1.6 (d, J = 7 Hz, 3 H), 1.1 (s, 3 H), 1.0 (d, J = 7 Hz, 3 H), 0.90 (s, 3 H); MS, m/z calcd (M^+) 220.1827, obsd 220.1805.

Borohydride Reduction of 15. A cold (0 °C) solution of **15** (95 mg, 0.43 mmol) in methanol (20 mL) was treated with sodium borohydride (165 mg, 4.3 mmol), stirred for 15 h, quenched with 5% hydrochloric acid solution, and extracted with ether. The combined organic phases were washed with sodium bicarbonate solution and brine, dried, and evaporated to give 80 mg (84%) of a mixture of two alcohols. These were separated by MPLC on silica gel (elution with petroleum ether/ethyl acetate, 40:1).

For **16a**: 30 mg (32%) of colorless solid, mp 50–52 °C; IR (CCl_4, cm^{-1}) 3620, 2980, 2870, 1450, 900; ^1H NMR (300 MHz, $CDCl_3$) δ 4.19 (dd, J = 8.0 and 5.4 Hz, 1 H), 2.38–1.06 (series of m, 13 H), 1.01 (d, J = 7.5 Hz, 3 H), 0.99 (s, 3 H), 0.91 (d, J = 6.3 Hz, 3 H), 0.79 (s, 3 H); MS m/z calcd ($M^+ - CH_3$) 207.1749, obsd 207.1714.

For **16b**: 30 mg (32%) of colorless solid, mp 78–80 °C; IR (CCl_4, cm^{-1}) 3620, 2980, 2870, 1450, 1270, 1050; ^1H NMR (300 MHz, $CDCl_3$) δ 3.83 (dd, J = 8.0 and 5.6 Hz, 1 H), 2.33–1.09 (series of m, 13 H), 1.02 (d, J = 7.2 Hz, 3 H), 1.00 (d, J = 7.2 Hz, 3 H), 0.96 (s, 3 H), 0.78 (s, 3 H); MS, m/z calcd (M^+) 222.1984, obsd 222.2003.

Alleged Senoxydene. (1*R,3a*R**,5a*S**,8a*R**)-1,2,3,3a,4,5,5a,8-Octahydro-1,4,4,6-tetramethylcyclopenta[*c*]pentalene (7).** A solution of **16a** (15.4 mg, 0.07 mmol) in benzene (3 mL) containing phosphorus oxychloride (33 mg, 0.21 mmol) and pyridine (166 mg, 2.1 mmol) was heated at 50 °C for 15 h. The reaction mixture was poured into water (3 mL), and the benzene phase was washed with sodium bicarbonate solution and brine prior to drying. The hydrocarbon was isolated from the benzene solution by preparative VPC (5 ft × 0.25 in. column, 10% SE-30 on Chromosorb W, 140 °C): 1 mg (7%), ^1H NMR (200 MHz, $CDCl_3$) δ 5.13 (s, 1 H), 2.58 (br d, J = 9 Hz, 1 H), 2.52 (d, J = 16.5 Hz, 1 H), 2.35 (d, J = 16.5 Hz, 1 H), 1.88 (dd, J = 10 and 2.5 Hz, 1 H), 1.75 (ddq, J = 12.5, 5.0, and 6.6 Hz, 1 H), 1.65 (s, 3 H), 1.64–1.5 (m, 3 H), 1.45 (br d, J = 13 Hz, 1 H), 1.36 (dd, J = 13 and 9.2 Hz, 1 H), 1.05 (m, 1 H), 0.99 (s, 3 H), 0.93 (s, 3 H), 0.85 (d, J = 7 Hz, 3 H); MS, m/z calcd (M^+) 204.1878, obsd 204.1883.

4-(3-Butenyl)-2,2-dimethylcyclopentanone (23). 4-Bromo-1-butene (2.43 g, 18 mmol) in tetrahydrofuran (10 mL) was added dropwise to magnesium turnings (880 mg, 36 mol). Additional tetrahydrofuran (10 mL) was added, and this mixture was heated at reflux for 30 min, cooled to −30 °C, and treated with a solution of the copper bromide–dimethyl sulfide complex (1.23 g, 6 mmol) in dimethyl sulfide (20 mL). The blue solution was stirred for 1 h, **22** (1.00 g, 9.0 mmol) was introduced over 1 h, and the reaction mixture was stirred at room temperature for 15 h. Hydrochloric acid (5%) was added, and the mixture was diluted with ether before filtration. The filtrate was washed with ammonium chloride solution and brine, dried, and evaporated. Purification of the residue by MPLC on silica gel (elution with petroleum ether/ethyl acetate, 30:1) gave **23** as a colorless oil (820 mg, 55%): IR (neat, cm^{-1}) 3090, 2980, 2940, 2880, 1745, 1645, 1510, 910; ^1H NMR (90 MHz, CCl_4) δ 5.9–5.5 (m, 1 H), 5.1–4.8 (m, 2 H), 2.6–1.2 (series of m, 9 H), 1.05 (s, 3 H), 0.95 (s, 3 H); MS, m/z calcd (M^+) 166.1357, obsd 166.1322.

2,2-Dimethyl-4-[2-(2-methyl-1,3-dioxolan-2-yl)ethyl]cyclopentanone (25). A solution of 3,3-(ethylenedioxy)butyl bromide (40.2 g, 0.206 mol) and 1,2-dibromoethane (12 mL) in dry tetrahydrofuran (115 mL) was added during 2 h to a stirred slurry of magnesium turnings (15 g, 0.618 mol) in the same solvent (300 mL). This mixture was cooled to −78 °C, copper(I) iodide (3.9 g, 0.02 mol) in dimethyl sulfide (30 mL) was added, and the blue solution was stirred for 30 min. 5,5-Dimethylcyclopent-2-enone (11.38 g, 0.103 mol) in anhydrous tetrahydrofuran (100 mL) was introduced during 2 h, and the reaction mixture was stirred at room temperature for 15 h. Ammonium chloride solution was added with cooling (−78 °C), the solids were separated by filtration, and the filtrate was diluted with ether. The organic solution was washed with ammonium chloride solution and brine, dried, and evaporated to give 29.45 g (100%) of **25** as a colorless liquid: IR (neat, cm^{-1}) 2980, 2880, 1730, 1455, 1380, 1220, 1070; ^1H NMR (300 MHz, $CDCl_3$) δ 3.92 (d, J = 4 Hz, 4 H), 2.55–1.35 (series of m, 9 H), 1.31 (s, 3 H), 1.06 (s, 3 H), 1.00 (s, 3 H); MS, m/z calcd (M^+) 211.1334, obsd 211.1329.

Anal. Calcd for $C_{13}H_{22}O_3$: C, 68.98; H, 9.80. Found: C, 68.49; H, 9.73.

2,2-Dimethyl-4-(3-oxobutyl)cyclopentanone (26). A solution of **25** (29.45 g, 0.103 mol) and pyridinium tosylate (4.6 g) in 780 mL of acetone–water (19:1) was heated at reflux for 18 h and

evaporated in vacuo. The residue was taken up in ether, washed with sodium bicarbonate solution and brine, dried, and evaporated to furnish 18.12 g (97%) of **26** as a colorless oil: IR (neat, cm^{-1}) 2980, 2950, 2880, 1740, 1720, 1460, 1370, 1130; ^1H NMR (90 MHz, CCl_4) δ 2.8–1.2 (series of m, 9 H), 2.1 (s, 3 H), 1.05 (s, 3 H), 0.95 (s, 3 H); MS, m/z calcd (M^+) 164.1201, obsd 164.1191.

Anal. Calcd for $C_{11}H_{18}O_2$: C, 72.48; H, 9.96. Found: C, 71.96; H, 10.00.

***cis*-3,3a,4,6a-Tetrahydro-2,2,6-trimethyl-1(2*H*)-pentalenone (27).** A solution of **26** (18.12 g, 99.6 mmol) and potassium *tert*-butoxide (34 g, 303 mmol) in *tert*-butyl alcohol (1.5 L) was heated at 50 °C with stirring for 5 h. The reaction mixture was evaporated, 5% hydrochloric acid was added, and the acidic aqueous layer was extracted with ether. The combined ethereal phases were washed with sodium bicarbonate solution and brine, dried, and evaporated. The residue was purified by silica gel chromatography (elution with 5% ethyl acetate in ether), and 11.6 g (71%) of **27** was obtained as a clear colorless oil: IR (neat, cm^{-1}) 3040, 2980, 2870, 1740, 1650, 1460, 1390, 1100, 810; ^1H NMR (300 MHz, $CDCl_3$) δ 5.31 (s, 1 H), 3.21 (m, 1 H), 2.90 (m, 1 H), 2.58 (m, 1 H), 2.05 (m, 2 H), 1.76 (ddd, J = 2.8, 2.6, and 1.6 Hz, 3 H), 1.44 (dd, J = 12.8 and 9.5 Hz, 1 H), 1.01 (s, 6 H); MS, m/z calcd (M^+) 164.1201, obsd 164.1181.

(3a*R,6*R**,6a*R**)-Hexahydro-2,2,6-trimethyl-1(2*H*)-pentalenone (24).** A mixture of **27** (10.6 g, 64.6 mmol) and 10% palladium on carbon (1.1 g) in absolute ethanol (100 mL) was shaken under 50 psi of hydrogen for 48 h. The catalyst was separated by filtration, and the filtrate was evaporated to leave 9.0 g (84%) of **24**, a colorless oil: IR (neat, cm^{-1}) 2960, 2880, 1730, 1460, 1380, 1360, 1150, 860; ^1H NMR (300 MHz, $CDCl_3$) δ 2.78 (m, 2 H), 2.28 (m, 1 H), 2.00 (m, 1 H), 1.80 (m, 2 H), 1.58 (m, 1 H), 1.30 (m, 2 H), 1.02 (s, 3 H), 1.00 (s, 3 H), 0.99 (d, J = 7 Hz, 3 H); ^{13}C NMR ($CDCl_3$) ppm 225.1, 53.9, 47.8, 44.7, 38.1, 37.6, 34.5, 31.9, 25.8, 22.8, 17.3; MS, m/z calcd (M^+) 166.1358, obsd 166.1362.

Anal. Calcd for $C_{11}H_{18}O$: C, 79.46; H, 10.91. Found: C, 79.23; H, 11.05.

(3a*R,6*R**,6a*R**)-Hexahydro-2,2,6-trimethyl-6a-[(*E*)-2-(trimethylsilyl)-2-butenyl]-1(2*H*)-pentalenone (28).** A cold (−30 °C) solution of lithium diisopropylamide [from 4.75 mL (33.1 mmol) of diisopropylamine and 20.7 mL of 1.6 N *n*-butyllithium in hexane] in anhydrous tetrahydrofuran (250 mL) was treated dropwise during 1 h with a solution of **24** (5.00 g, 30.1 mmol) in the same solvent (50 mL). To the resulting enolate anion solution was added a solution of **11** (11.5 g, 45 mmol) in dry tetrahydrofuran (20 mL), and the reaction mixture was warmed to room temperature over 3 h, poured into 5% hydrochloric acid, and extracted with ether. The combined organic phases were washed with sodium bicarbonate solution and brine, dried, and evaporated. Purification of the residue by MPLC on silica gel provided 4.5 g (51%) of **28** as a clear colorless oil: IR (neat, cm^{-1}) 2980, 2880, 1730, 1610, 1460, 1380, 1360, 1260, 850; ^1H NMR (300 MHz, $CDCl_3$) δ 6.07 (q, J = 6.8 Hz, 1 H), 2.57 (q, J = 6 Hz, 1 H), 2.49 (d, J_{AB} = 13 Hz, 1 H), 2.34 (d, J_{AB} = 13 Hz, 1 H), 1.90 (m, 2 H), 1.73 (d, J = 6.8 Hz, 3 H), 1.55 (m, 2 H), 1.30 (m, 3 H), 1.00 (s, 3 H), 0.98 (s, 3 H), 0.91 (d, J = 7 Hz, 3 H), 0.09 (s, 9 H); MS, m/z calcd ($M^+ - CH_3$) 277.1998, obsd 277.2021.

Anal. Calcd for $C_{18}H_{32}OSi$: C, 73.90; H, 11.03. Found: C, 73.83; H, 11.03.

(3a*R,6*R**,6a*R**)-Hexahydro-2,2,6-trimethyl-6a-(2-oxobutyl)-1(2*H*)-pentalenone (29).** A magnetically stirred mixture of **28** (4.0 g, 3.7 mmol) and powdered sodium carbonate (8.0 g) in dichloromethane (100 mL) was cooled to 0 °C, and buffer-washed *m*-chloroperbenzoic acid (3.5 g, 20.6 mmol) was added in portions. The reaction mixture was stirred at room temperature for 15 h, poured into potassium sulfite solution, and extracted with ether. The combined ether phases were washed with sodium bicarbonate solution and brine, dried, and evaporated. There was isolated 4.13 g (98%) of the epoxide: IR (neat, cm^{-1}) 2970, 2880, 1730, 1460, 1380, 1250, 840; ^1H NMR (90 MHz, CCl_4/CH_2Cl_2) δ 3.0–1.4 (series of m, 11 H), 1.2 (d, J = 5 Hz, 3 H), 1.05 (s, 3 H), 0.95 (s, 3 H), 0.90 (d, J = 7 Hz, 3 H), 0.05 (s, 9 H); MS, m/z calcd (M^+) 308.2171, obsd 308.2189.

A solution of the epoxide (4.13 g, 13.4 mmol) in methanol (100 mL) and 20% sulfuric acid (100 mL) was heated at the reflux temperature for 2 h, diluted with ether, and washed with sodium bicarbonate solution and brine. The dried organic layer was evaporated, and the residue was purified by MPLC on silica gel (elution with 5% ethyl acetate in petroleum ether) to give 3.0 g (95%) of **29** as a clear colorless oil: IR (neat, cm^{-1}) 2980, 2790, 1730, 1720, 1460, 1380, 1360; ^1H NMR (300 MHz, $CDCl_3$) δ 3.02 (d, J_{AB} = 17 Hz, 1 H), 2.65 (q, J = 7 Hz, 1 H), 2.46 (d, J_{AB} = 17 Hz, 1 H), 2.35 (q, J = 7.3 Hz, 2 H), 2.15 (dd, J = 13.7 and 9.8 Hz, 1 H), 1.8 (m, 3 H), 1.6 (m, 1 H), 1.4 (m, 2 H), 1.20 (s, 3 H), 1.03 (s, 3 H), 0.98 (t, J = 7.3 Hz, 3 H), 0.87 (d, J = 7 Hz, 3 H); MS, m/z calcd (M^+) 236.1776, obsd 236.1769.

Anal. Calcd for $C_{15}H_{24}O_2$: C, 76.21; H, 10.24. Found: C, 76.11; H, 10.25.

(5a*R,8*R**,8a*R**)-4,5,5a,6,7,8a-Hexahydro-3,4,4,8-tetramethylcyclopenta[*c*]pentalen-2(1*H*)-one (30).** Diketone **29** (2.0 g, 8.47 mmol) was added to a solution of sodium ethoxide in ethanol [from 7.95 g (345 mmol) of sodium metal and 150 mL of absolute ethanol] and heated at the reflux temperature for 10 h. The reaction mixture was evaporated, 5% hydrochloric acid was added to the residue, and this mixture was extracted with ether. The combined ether layers were washed with sodium bicarbonate solution, dried, and evaporated to leave a residue that was purified by MPLC on silica gel (elution with 9% ethyl acetate in petroleum ether). There was isolated 800 mg (43%) of **30** as a clear colorless oil: IR (neat, cm^{-1}) 2970, 2880, 1710, 1640, 1460, 1380; ^1H NMR (300 MHz, $CDCl_3$) δ 2.57 (d, J_{AB} = 13 Hz, 1 H), 2.40 (m, 1 H), 2.39 (d, J_{AB} = 13 Hz, 1 H), 2.0 (m, 2 H), 1.80 (s, 3 H), 1.6 (m, 5 H), 1.34 (s, 3 H), 1.24 (s, 3 H), 0.78 (d, J = 7 Hz, 3 H); MS, m/z calcd (M^+) 218.1671, obsd 218.1668.

Catalytic Hydrogenation of 30. A methanol solution of **30** (92 mg, 0.42 mmol) containing 40 mg of 5% palladium on carbon was shaken on a Parr apparatus under 50 psi of hydrogen for 24 h. The mixture was filtered through Celite and evaporated to give 71 mg (76%) of **31** as a colorless crystalline solid, mp 45–48 °C: IR (CCl_4, cm^{-1}) 2940, 2870, 1740, 1460, 1200; ^1H NMR (300 MHz, $CDCl_3$) δ 2.53 (d, J_{AB} = 18 Hz, 1 H), 2.53 (m, 1 H), 2.38 (q, J = 7 Hz, 1 H), 2.30 (d, J_{AB} = 18 Hz, 1 H), 2.05 (d, J = 6.7 Hz, 1 H), 1.8–1.0 (m, 7 H), 1.20 (d, J = 7 Hz, 3 H), 1.09 (s, 3 H), 1.01 (d, J = 6.7 Hz, 3 H), 0.81 (s, 3 H); MS, m/z calcd (M^+) 220.1827, obsd 220.1837.

Anal. Calcd for $C_{15}H_{24}O$: C, 81.76; H, 10.99. Found: C, 81.91; H, 10.82.

Dissolving Metal Reduction of 30. An ether solution (10 mL) of **30** (680 mg, 3.12 mmol) was added dropwise to a cold (−33 °C) solution of lithium metal (220 mg, 31.2 mmol) in liquid ammonia (125 mL, freshly distilled from sodium). The reaction mixture was stirred at −33 °C for 2 h, treated with solid ammonium chloride until colorless, and allowed to evaporate. The residue was treated with 5% hydrochloric acid and extracted with ether. The combined organic layers were washed with saturated sodium bicarbonate solution and brine, dried, and evaporated. The remaining oil (530 mg) was chromatographed on silica gel (elution with 4.5% ethyl acetate in petroleum ether) to separate the two epimeric ketones. There was isolated 150 mg of **31** and 30 mg of **32**, a colorless oil, for a combined yield of 38%.

For **32**: IR (CCl_4, cm^{-1}) 2930, 2860, 1740, 1460, 1180, 1120; ^1H NMR (300 MHz, $CDCl_3$) δ 2.70 (d, J_{AB} = 16.8 Hz, 1 H), 2.43 (q, J = 7.5 Hz, 1 H), 2.27 (m, 1 H), 2.20 (d, J_{AB} = 16.8 Hz, 1 H), 1.9–1.1 (series of m, 8 H), 1.13 (d, J = 7.5 Hz, 3 H), 1.03 (s, 3 H), 0.92 (s, 3 H), 0.88 (d, J = 6.7 Hz, 3 H); MS, m/z calcd (M^+) 220.1827, obsd 220.1870.

Hydride Reduction of 31. A solution of **31** (71 mg, 0.32 mmol) in ether (10 mL) was treated with lithium aluminum hydride (122 mg 3.2 mmol) and stirred at room temperature for 24 h. Excess hydride was destroyed by addition of ethyl acetate followed by 5% hydrochloric acid. The layers were separated, and the aqueous phase was extracted with ether. The combined ethereal solutions were washed with saturated sodium bicarbonate solution and brine, dried, and evaporated. The residue (55.4 mg) was chromatographed on silica gel (elution with 10% ethyl acetate in petroleum ether), and three components were isolated. The first proved to be unreacted **31** (10 mg, 14%). The second component was a pure epimer of **33** (20.5 mg, 34%): IR (CCl_4, cm^{-1}) 3640, 2980, 2940, 2880, 1460, 1120, 910; ^1H NMR (300 MHz, $CDCl_3$) δ 3.29 (m, 1 H), 2.40–1.15 (series of m, 13 H), 1.14 (s, 3 H), 1.12 (d, J = 7.3 Hz, 3 H), 1.07 (s, 3 H), 0.8 (d, J = 6.7 Hz, 3 H); MS, m/z calcd (M^+) 222.1984, obsd 222.1937.

Finally, 9.8 mg (16%) of a somewhat impure second alcohol epimer was eluted: IR (CCl_4, cm^{-1}) 3640, 2940, 2860, 1460, 1070; MS, m/z calcd (M^+) 222.1984, obsd 222.1964.

(1*R,3a*R**,5a*S**,8a*R**)-1,2,3,3a,4,5,5a,8-Octahydro-1,5,5,6-tetramethylcyclopenta[*c*]pentalene (20).** The preceding epimerically pure alcohol (9.2 mg, 0.041 mmol) in benzene (3 mL) was heated at 50 °C for 2 h with phosphorus oxychloride (18.9 mg, 0.123 mmol) and pyridine (0.92 mL, 1.23 mmol). The reaction mixture was poured into 5% hydrochloric acid, and the separated benzene layer was washed with saturated sodium bicarbonate solution and brine before drying. Solvent evaporation left 6 mg of crude **20** that was purified by elution through a plug of silica gel with pentane. There was isolated 3 mg (37%) of pure hydrocarbon; ^1H NMR (300 MHz, $CDCl_3$) δ 5.15 (d, J = 1.4 Hz, 1 H), 2.46 (ddd, J = 12, 6, and 1.4 Hz, 1 H), 2.21 (dd, J = 19.2 and 7.2 Hz, 1 H), 2.10 (br s, 1 H), 2.0 (ddd, J = 12, 3.6, and 1.2 Hz, 1 H), 1.7–0.9 (series of m, 6 H), 1.57 (br s, 3 H), 0.98 (s, 3 H), 0.76 (d, J = 6.6 Hz, 3 H), 0.67 (s, 3 H); MS, m/z calcd (M^+) 204.1878, obsd 204.1898.

4,4-Dimethyl-1-(2-methyl-1,3-dioxolan-2-yl)-2-(phenylsulfonyl)-6-hepten-3-one. 1-(Phenylsulfonyl)-3-butanone ethylene ketal (89.9 g, 0.35 mol) was dissolved in 1.1 L of anhydrous tetrahydrofuran. Tetramethylethylenediamine (105 mL, freshly distilled from calcium hydride) was added, and the solution was cooled to −78 °C. *n*-Butyllithium (437 mL of 1.6 M, 0.70 mol) was introduced dropwise. The resulting pale yellow solution was transferred via cannula to a cold (−78 °C) solution of 2,2-dimethyl-4-pentenoyl chloride (**34**, 51.2 g, 0.35 mol) in dry tetrahydrofuran (875 mL) and freshly distilled HMPA (218 mL). The reaction mixture was allowed to warm slowly to room temperature during 8 h, whereupon saturated ammonium chloride solution (400 mL) was added, and the volatile solvents were removed at 30 torr. The resulting partially aqueous residue was extracted with ether (3 × 200 mL), and the combined organic phases were washed with water (4 × 250 mL) and brine (250 mL) prior to drying. Solvent evaporation left 115 g (89%) of keto ketal as a pale orange oil, which was not purified further: IR (neat, cm^{-1}) 3080, 2990, 1710, 1645, 1330; ^1H NMR (90 MHz, CCl_4) δ 7.6 (m, 5 H), 5.9–5.5 (m, 1 H), 5.2–5.0 (m, 2 H), 4.6 (dd, J = 8 and 3 Hz, 1 H), 3.9–3.5 (br s, 4 H), 2.4 (d, J = 7 Hz, 2 H), 2.2–1.9 (m, 2 H), 1.3 (s, 3 H), 1.2 (s, 3 H); MS, m/z calcd ($M^+ - C_6H_{10}$) 284.0719, obsd 284.0725.

4,4-Dimethyl-1-(2-methyl-1,3-dioxolan-2-yl)-6-hepten-3-one (36). To a solution of the above substance (114 g, 0.31 mol) in absolute methanol (900 mL) was added sodium dihydrogen phosphate (185 g, 1.3 mol). With ice-bath cooling, freshly prepared sodium amalgam (5.3%, 578 g) was added, and the resulting slurry was stirred vigorously at 0 °C for 4 h, during which a color change from orange to green was observed. Stirring was maintained at room temperature for 12 h before solids were separated by filtration, and the filtrate was concentrated under reduced pressure. The pale yellow oily residue was dissolved in ether (800 mL), washed with water (3 × 250 mL), and brine (250 mL), and dried. Solvent removal left **36** as a yellow oil (53.6 g, 77%) that was directly hydrolyzed: IR (neat, cm^{-1}) 1730; ^1H NMR (90 MHz, $CDCl_3$) δ 6.1–5.6 (m, 1 H), 5.1–4.9 (m, 2 H), 3.9 (s, 4 H), 2.6 (t, J = 8 Hz, 2 H), 2.4 (d, J = 6 Hz, 2 H), 1.9 (t, J = 8 Hz, 2 H), 1.4 (s, 3 H), 1.2 (s, 6 H); MS, m/z calcd (M^+) 226.1568, obsd 226.1584.

6,6-Dimethyl-8-nonene-2,5-dione. A mixture of **36** (53.6 g, 0.24 mol), pyridinium tosylate (6.5 g, 0.026 mol), and water (43 mL) in acetone (850 mL) was heated at the reflux temperature for 24 h. Solvent was removed under reduced pressure from the cooled reaction mixture, saturated sodium bicarbonate solution (500 mL) was added, and the product was extracted into ether (3 × 200 mL). The combined ethereal layers were washed with water (4 × 200 mL) and brine (250 mL), dried, and concentrated under reduced pressure. The product was isolated as a clear, colorless oil (26 g, 66%) by rapid bulb-to-bulb distillation (bp 90 °C, 1.5 torr). An analytical sample was obtained by preparative gas chromatography: IR (neat, cm^{-1}) 2980, 2920, 1720, 1700, 1470, 1370; ^1H NMR (300 MHz, $CDCl_3$) δ 5.7–5.5 (m, 1 H), 5.0 (m, 2 H), 2.8–2.5 (m, 4 H), 2.2 (d, J = 7.3 Hz, 2 H), 2.16 (s, 3 H), 1.1 (s, 6 H); MS, m/z calcd (M^+) 182.1307, obsd 182.1328.

Anal. Calcd for $C_{11}H_{18}O_2$: C, 72.48; H, 9.96. Found: C, 72.21; H, 10.02.

3-(1,1-Dimethyl-3-butenyl)-2-cyclopenten-1-one (37). A mixture of the preceding diketone (10.0 g, 55 mmol) and 13% aqueous sodium hydroxide solution (1 L) was heated at reflux for 36 h, cooled, and extracted with ether (3 × 250 mL). The combined ethereal phases were washed with water (3 × 200 mL) and brine (200 mL), dried, and concentrated. Kugelrohr distillation (bp 82–89 °C, 0.3 torr) gave 6.8 g (76%) of **37** as a clear, colorless oil: IR (neat, cm^{-1}) 2980, 2940, 1720, 1600, 1470, 1190; ^1H NMR (300 MHz, $CDCl_3$) δ 5.9 (t, J = 1.7 Hz, 1 H), 5.6 (m, 1 H), 5.0 (m, 2 H), 2.6 (m, 2 H), 2.4 (m, 2 H), 2.2 (d, J = 7.3 Hz, 2 H), 1.1 (s, 6 H); MS, m/z calcd (M^+) 164.1203, obsd 164.1179.

3-(1,1-Dimethyl-3-butenyl)cyclopentanone (38). A solution of **37** (14.8 g, 90.2 mmol) and water (0.8 mL) in tetrahydrofuran (140 mL) was added to a rapidly stirred suspension of lithium (1.4 g) in liquid ammonia (1.2 L) cooled to −78 °C. After 4 h at this temperature, solid ammonium chloride was added in small portions until the blue color was discharged. After evaporation of the ammonia, the residue was partitioned between brine and ether. The ethereal layer was dried and concentrated to give a mixture of the desired ketone and some overreduction alcohol product. The mixture was taken up in dry dichloromethane (600 mL) and stirred with pyridinium chlorochromate (9.8 g, 45.4 mmol) for 8 h. Flash chromatography on silica gel (ether elution) removed the chromium salts. The concentrated eluate was purified by Kugelrohr distillation (bp 70–72 °C, 0.6 torr) to give 12.1 g (81%) of **38**: IR (neat, cm^{-1}) 2980, 1740, 1470, 1170; ^1H NMR (300 MHz, $CDCl_3$) δ 5.9–5.7 (m, 1 H), 5.1–4.9 (m, 2 H), 2.8–1.4 (series of m, 7 H), 1.9 (d, J = 8.5 Hz, 2 H), 0.9 (s, 3 H), 0.8 (s, 3 H).

Anal. Calcd for $C_{11}H_{18}O$: C, 79.46; H, 10.92. Found: C, 79.18; H, 11.05.

(3a*R,6*R**,6a*R**)-Hexahydro-4,4,6-trimethyl-1(2*H*)-pentalenone (39). A. Ene Cyclization of 38.** A 7.0-g (0.042 mol) sample of **38** was placed in a large Carius tube, degassed three times by the freeze–thaw technique, and sealed under vacuum. The neat liquid was heated at 320 °C for 12 h. The resulting brown liquid was purified by Kugelrohr distillation (bp 60–65 °C, 0.3 torr) to give **39** as a clear colorless oil (4.7 g, 67%); IR (neat, cm^{-1}) 2880, 1740, 1470, 1170; ^1H NMR (300 MHz, $CDCl_3$) δ 2.63 (m, 1 H), 2.51–2.42 (m, 1 H), 2.25 (m, 1 H), 2.10 (m, 2 H), 1.86 (m, 1 H), 1.61–1.43 (m, 2 H), 1.20 (m, 1 H), 0.96 (s, 3 H), 0.92 (s, 3 H), 0.88 (d, J = 7.1 Hz, 3 H); ^{13}C NMR ($CDCl_3$) ppm 222.2, 54.7, 54.2, 47.8, 41.5, 40.5, 34.8, 29.5, 24.7, 23.7, 18.5; MS, m/z calcd ($M^+ - CH_3$) 151.1123, obsd 151.1147.

Anal. Calcd for $C_{11}H_{18}O$: C, 79.46; H, 10.91. Found: C, 79.45; H, 10.95.

B. Catalytic Hydrogenation of the $\Delta^{1,8}$-Derivative. A solution of the enone (100 mg, 0.61 mmol) in absolute ethanol (10 mL) containing 10% palladium on charcoal (30 mg) was shaken under 50 psi of hydrogen for 16 h. The catalyst was separated by filtration, and the filtrate was evaporated to give 90 mg (92%) of **39**, identical in all respects with the substance obtained in part A.

(3a*R,6*R**,6a*R**)-2-[(Butylthio)methylene]hexahydro-4,4,6-trimethyl-1(2*H*)-pentalenone (40).** Ketone **39** (4.0 g, 24.1 mmol) in freshly distilled benzene containing sodium methoxide (7.45 g, 138 mmol) was treated with ethyl formate (5.11 g, 69.0 mmol, freshly distilled from phosphorus pentoxide). The consumption of starting material was observed to be complete after 48 h (TLC analysis). The reaction mixture was extracted with 1 N sodium hydroxide solution (3 × 50 mL), and the cold (0 °C) combined basic layers were slowly acidified with concentrated hydrochloric acid. The product was taken up in ether (3 × 75 mL), and the combined ethereal phases were washed with brine (3 × 50 mL). The ether solution was dried and concentrated to leave 4.2 g (90%) of α-hydroxymethylene derivative: IR (CCl_4, cm^{-1}) 3500–3000, 2980, 2940, 2880, 1750–1710, 1670, 1610, 1470, 1190; ^1H NMR (90 MHz, CCl_4) δ 9.4–9.0 (m, 1 H), 7.25 (m, 1 H), 3.0–1.2 (series of m, 5 H), 1.0 (s, 6 H), 0.95 (d, J = 5 Hz, 3 H); MS, m/z calcd (M^+) 194.1307, obsd 194.1285.

The oil was dissolved in dry benzene (40 mL) and treated successively with anhydrous magnesium sulfate (5.0 g, 41 mmol), *p*-toluenesulfonic acid monohydrate (0.75 g, 4.5 mmol), and butanethiol (3.5 mL, 32.7 mmol). This slurry was heated at the reflux temperature with vigorous stirring for 15 h. The solvent was evaporated, and the residue was taken up in ether. The ethereal

solution was washed with saturated sodium bicarbonate solution and brine prior to drying and concentration. Purification by MPLC on silica gel (elution with 5% ethyl acetate in petroleum ether) afforded **40** as a pale yellow solid (3.6 g, 62% overall from **39**): IR (neat, cm^{-1}) 2960, 2930, 2870, 1690, 1580, 1460, 1200; ^1H NMR (300 MHz, $CDCl_3$) δ 7.33 (m, 1 H), 2.92–2.81 (m, 3 H), 2.61–2.45 (m, 2 H), 2.32–2.13 (m, 2 H), 1.72–1.60 (m, 3 H), 1.48–1.38 (m, 2 H), 1.20 (t, J = 11.8 Hz, 1 H), 1.04 (s, 3 H), 1.00 (s, 3 H), 0.93 (t, J = 7.4 Hz, 3 H), 0.91 (d, J = 7.2 Hz, 3 H); MS, m/z calcd (M^+) 266.1704, obsd 266.1751.

(3a*R,6*S**,6a*S**)-Hexahydro-4,4,6-trimethyl-6a-[(*E*)-2-(trimethylsilyl)-2-butenyl]-1(2*H*)-pentalenone (41).** Hexamethyldisilazane (0.82 mL, 4.0 mmol) in 33 mL of anhydrous tetrahydrofuran cooled to 0 °C was treated with *n*-butyllithium (2.65 mL of 1.55 M, 4.1 mmol). The resulting anion solution was cooled to −78 °C, and a solution of **40** (1.0 g, 3.74 mmol) in dry tetrahydrofuran (66 mL) was added dropwise during 1 h. After an additional hour of stirring at −78 °C, a solution of **11** (2.0 g, 7.9 mmol) in the same solvent (10 mL) was introduced, and agitation was maintained at this temperature for 55 h. While still cold, the reaction mixture was poured into 5% hydrochloric acid and extracted several times with ether. The combined ethereal phases were washed with dilute sodium bicarbonate and saturated brine solutions, dried, and concentrated. Chromatography of the residue on silica gel (elution with 2% ethyl acetate in petroleum ether) afforded 614 mg of unreacted **40** and 472 mg (83% based on recovered **40**) of alkylation product as a pale yellow oil: IR (CCl_4, cm^{-1}) 2960, 2930, 2870, 1695, 1570, 1455, 1250; ^1H NMR (300 MHz, $CDCl_3$) δ 7.2–7.16 (m, 1 H), 6.03–5.95 (m, 1 H), 2.80 (t, J = 7.4 Hz, 2 H), 2.8–2.0 (series of m, 6 H), 1.70 (d, J = 6.7 Hz, 3 H), 1.7–1.2 (m, 5 H), 1.06 (d, J = 6.9 Hz, 3 H), 0.99 (s, 3 H), 0.95–0.87 (m, 4 H), 0.03 (s, 9 H); MS, m/z calcd (M^+) 392.2569, obsd 392.2570.

A mixture of the preceding compound (312 mg, 0.796 mmol), 10% sodium hydroxide solution (11 mL), and diethylene glycol (15 mL) was heated at the reflux temperature for 18 h. The cooled solution was poured into brine and extracted several times with ether. The combined ethereal phases were washed with brine, dried, and concentrated. Flash chromatography on silica gel (elution with 5% ethyl acetate in petroleum ether) gave 174 mg (75%) of **41** as a colorless oil: IR (neat, cm^{-1}) 2970, 1730, 1600, 1460, 1250, 850; ^1H NMR (300 MHz, $CDCl_3$) δ 6.05 (q, J = 6.7 Hz, 1 H), 2.56 (d, J = 13.4 Hz, 1 H), 2.34 (d, J = 13.4 Hz, 1 H), 2.18–1.75 (series of m, 4 H), 1.71 (d, J = 6.8 Hz, 3 H), 1.6–1.4 (m, 2 H), 1.24 (m, 2 H), 1.03 (s, 3 H), 1.01 (s, 3 H), 0.95 (d, J = 6.9 Hz, 3 H), 0.04 (s, 9 H); MS, m/z calcd (M^+) 292.2222, obsd 292.2222.

Anal. Calcd for $C_{18}H_{32}OSi$: C, 73.90; H, 11.03. Found: C, 73.88; H, 10.99.

(3a*R,6*S**,6a*S**)-Hexahydro-4,4,6-trimethyl-6a-(2-oxobutyl)-1(2*H*)-pentalenone (42).** A solution of **41** (579 mg, 1.98 mmol) in dry dichloromethane (40 mL) was treated at 0 °C with solid sodium bicarbonate (2.0 g, 23 mmol) followed by *m*-chloroperbenzoic acid (508 mg, 2.9 mmol). After 10 h of stirring at room temperature, an additional 0.5 equiv of the peracid was added, and this process was repeated at two additional 10-h intervals. The resulting slurry was poured into saturated sodium sulfite solution, and the product was extracted with multiple portions of dichloromethane. The combined organic layers were washed with sodium bicarbonate solution and brine, dried, and evaporated to give 494 mg (81%) of the epoxysilane, which was not further purified: IR (neat, cm^{-1}) 2970, 2930, 2870, 1765, 1460, 1270; ^1H NMR (90 MHz, $CDCl_3$) δ 4.0–1.5 (series of m, 11 H), 1.5–0.8 (series of m, 12 H), 0.10 (s, 9 H); MS, m/z calcd ($M^+ - C_2H_5$) 280.1859, obsd 280.1834.

The epoxysilane was dissolved in 25 mL of methanol containing 25 mL of 20% sulfuric acid. This mixture was heated at reflux for 15 h, poured onto ice, and extracted with ether. The combined organic layers were washed with sodium bicarbonate and brine solutions, dried, and concentrated. MPLC purification of the oily orange residue on silica gel (elution with 11% ethyl acetate in petroleum ether) afforded 187 mg (40%) of **42** as a clear, colorless oil; IR (CCl_4, cm^{-1}) 2980, 2880, 1740, 1730, 1470, 1420, 1390, 1130, 740; ^1H NMR (300 MHz, $CDCl_3$) δ 3.30 (d, J = 18.2 Hz, 1 H), 2.70 (d, J = 18.2 Hz, 1 H), 2.5–2.3 (m, 3 H), 2.2–1.9 (m, 4 H), 1.9–1.7 (m, 1 H), 1.65–1.5 (m, 1 H), 1.25–1.15 (m, 1 H), 1.05 (s, 3 H), 1.02 (s, 3 H), 1.00 (t, J = 7.35 Hz, 3 H), 0.84 (d, J = 7.04 Hz, 3 H); MS, m/z calcd (M^+) 236.1776, obsd 236.1787.

(5a*R,8*S**,8a*S**)-4,5,5a,6,7,8-Hexahydro-3,6,6,8-tetramethylcyclopenta[*c*]pentalen-2(1*H*)-one (43).** Diketone **42** (100 mg, 0.42 mmol) with potassium *tert*-butoxide (100 mg, 0.84 mmol) in tetrahydrofuran (20 mL) and *tert*-butyl alcohol (0.5 mL) was heated at 45 °C for 1 h. The reaction mixture was poured into 5% hydrochloric acid and extracted with ether. The ether phase was washed with sodium bicarbonate solution and brine. After drying and solvent removal, 72.1 mg (79%) of **43** was isolated: IR (CCl_4, cm^{-1}) 2980, 1710, 1670, 1460, 1380, 740; ^1H NMR (300 MHz, $CDCl_3$) δ 2.66 (d, J = 17.4 Hz, 1 H), 2.59–2.51 (m, 1 H), 2.45 (d, J = 17.4 Hz, 1 H), 2.35–1.72 (series of m, 5 H), 1.71 (d, J = 1.57 Hz, 3 H), 1.65–1.56 (m, 2 H), 1.05 (s, 6 H), 0.69 (d, J = 7.1 Hz, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) ppm 210.57, 183.77, 131.22, 60.32, 58.77, 54.74, 48.85, 43.63, 41.56, 29.72, 28.30, 27.83, 25.29, 14.80, 8.47; MS, m/z (calcd) (M^+) 218.1620, obsd 218.1685.

Anal. Calcd for $C_{15}H_{22}O$: C, 82.52; H, 10.16. Found: C, 82.61; H, 10.20.

Hydride Reduction of 43. To a well-stirred slurry of lithium aluminum hydride (10 mg, 0.26 mmol) in anhydrous ether (3 mL) cooled to 0 °C was added dropwise a solution of **43** (30 mg, 0.138 mmol) in the same solvent (1 mL). The reaction mixture was stirred at room temperature for 30 min and carefully hydrolyzed by addition of ether (5 mL) saturated with 10% sodium sulfate in water followed by the salt solution itself (10 mL). The precipitate was washed well with ether. The aqueous phase was extracted with ether (3 × 5 mL), and the combined organic phases were washed with brine, dried, and evaporated. MPLC purification of the product on silica gel (elution with 12% ethyl acetate in petroleum ether) gave 26 mg (86%) of a mixture of epimeric alcohols: ^1H NMR (300 MHz, $CDCl_3$) δ 4.80 (m, 1 H), 3.68 and 2.85 (2d, J = 6.96 and 10.16 Hz, total 1 H), 2.34–2.14 (m, 4 H), 1.87–1.66 (m, 4 H), 1.50–1.44 (m, 1 H), 1.07 (t, J = 12.4 Hz, 1 H), 0.99 (s, 3 H), 0.95 (s, 3 H), 0.69 (d, J = 6.9 Hz, 3 H).

Catalytic Hydrogenation of 44. The alcohol mixture **44** (20 mg, 0.091 mmol) in ethyl acetate (3 mL) was shaken under an atmosphere of hydrogen (50 psi) in the presence of platinum oxide (2 mg) for 2 days. The mixture was filtered through a pad of Celite, and the filtrate was evaporated. MPLC purification on silica gel (elution with 12% ethyl acetate in petroleum ether) furnished 9 mg of one epimer of **45** (A) and 8 mg of the second (B) in 84% combined yield.

For A (less polar): ^1H NMR (300 MHz, $CDCl_3$) δ 4.09 (t, J = 4.90 Hz, 1 H), 2.23–1.81 (series of m, 5 H), 1.79–1.66 (m, 2 H), 1.57 (m, 1 H), 1.35–1.30 (m, 3 H), 1.14 (d, J = 12.7 Hz, 1 H), 1.05 (d, J = 7.15 Hz, 3 H), 1.00 (s, 3 H), 0.90 (s, 3 H), 0.88 (d, J = 6.94 Hz, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) ppm 78.27, 66.00, 62.91, 52.93, 49.63, 47.32, 44.05, 42.13, 39.49, 31.00, 29.65, 29.11, 25.22, 14.54, 10.81; MS, m/z calcd ($M^+ - H_2O$) 204.1878, obsd 204.1844.

For B (more polar): ^1H NMR (300 MHz, $CDCl_3$) δ 3.66–3.53 (m, 1 H), 2.17–1.98 (m, 2 H), 1.78–1.56 (m, 4 H), 1.48–1.25 (series of m, 6 H), 1.02 (d, J = 6.5 Hz, 3 H), 0.98 (s, 3 H), 0.90 (d, J = 7.2 Hz, 3 H), 0.88 (s, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) ppm 79.17, 65.83, 63.41, 60.92, 50.27, 50.23, 48.79, 42.22, 38.44, 32.76, 32.49, 28.18, 25.21, 16.70, 15.86; MS, m/z calcd ($M^+ - H_2O$) 204.1878, obsd 204.1900.

(1*R,3a*R**,5a*S**,8a*S**)-1,2,3,3a,4,5,5a,8-Octahydro-1,3,3,6-tetramethylcyclopenta[*c*]pentalene (21).** Either pure epimer of **45** (16 mg, 0.072 mmol) in benzene (3 mL) was heated at 50 °C for 2 h with phosphorus oxychloride (0.021 mL, 0.22 mmol) and pyridine (0.12 mL, 2.2 mmol). The cooled reaction mixture was poured into 5% hydrochloric acid, and the separated layer was washed with sodium bicarbonate and brine solutions prior to drying and solvent evaporation. There remained 12 mg (82%) of hydrocarbon. Purification by preparative gas chromatography (90 °C, 3% OV-101 on 100/120 mesh Gas Chrom Q) returned 6 mg of **21**: ^1H NMR (300 MHz, $CDCl_3$) δ 5.16 (m, 1 H). 2.71 (m, 1 H), 2.37 (m, 2 H), 2.05 (m, 2 H), 1.70 (m, 1 H), 1.60 (br s, 3 H), 1.53–1.36 (series of m, 4 H), 1.06 (t, J = 12.60 Hz, 1 H), 0.99 ns, 3 H), 0.90 (s, 3 H), 0.88 (d, J = 6.77 Hz, 3 H); MS, m/z calcd (M^+) 204.1877, obsd 204.1863.

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