MPLC purification of the residue (silica gel, elution with 5% ethyl acetate in petroleum ether) gave ketone **36** as clear, colorless oil (377 mg, 100%): IR (cm^{-1}, neat) 3040, 2900, 1720, 1440, 1180; ^1H NMR ($CDCl_3$) δ 5.83 (dt, J = 6 and 2 Hz, 1 H), 5.38 (dt, J = 6 and 2 Hz, 1 H), 2.51 (ddt, J = 17, 10, and 7 Hz, 2 H), 2.43-1.56 (series of m, 7 H), 1.08 (s, 3 H), 1.06 (s, 3 H), 1.02 (s, 3 H); ^{13}C NMR (ppm, $CDCl_3$) 222.49, 134.68, 133.21, 78.05, 58.37, 56.83, 53.81, 52.34, 42.28, 39.63, 29.30, 28.96, 26.12, 23.44; m/e calcd (M^+) 204.1514, obsd 204.1518.

Anal. Calcd for $C_{14}H_{20}O$: C, 82.30; H, 9.87. Found: C, 82.19; H, 9.96.

2,2,4,9-Tetramethyltricyclo[6.3.0.0^{4,8}]undeca-6,9-diene (37). Methyllithium (12 mL of 1.2 M in hexane, 1.47 mmol) was added dropwise to a cold (-78 °C), magnetically stirred solution of **36** (300 mg, 1.47 mmol). The reaction was allowed to proceed for 6 h at -78 °C and then overnight at room temperature. The mixture was poured into water, neutralized with dilute hydrochloric acid, and extracted with ether. The combined organic layers were washed with brine, dried, and concentrated. The clear, colorless oil thus obtained (320 mg, 100%) was dissolved in dry benzene (20 mL) containing p-toluenesulfonic acid (50 mg, 0.26 mmol) and heated at reflux under a Dean-Stark trap. The cooled reaction mixture was washed with saturated sodium bicarbonate solution and brine prior to drying and concentration.

Anal. Calcd for $C_{15}H_{22}$: C, 89.04; H, 10.96. Found: C, 88.93; H, 10.91.

Monoepoxidation of 37. To a cold (0 °C), stirred mixture of **37** (100 mg, 0.50 mmol), sodium carbonate (50 mg, 0.58 mmol), and dichloromethane (7 mL) was added 40% peracetic acid (118 μL, 0.50 mmol). The reaction mixture was stirred at 0 °C for 6 h and at room temperature overnight. Water was added and the organic layer was separated, dried, and concentrated. There was isolated 110 mg (100%) of **38** as a clear, homogeneous oil: IR (cm^{-1}, neat) 3040, 2930, 2860, 1445, 1380, 1365, 1245, 1080, 1005, 830, 735, 710; ^1H NMR ($CDCl_3$) δ 5.72 (m, 2 H), 3.42 (s, 1 H), 1.96 (m, 2 H), 1.88 (m, 3 H), 1.84 (s, 2 H), 1.33 (s, 3 H), 1.21 (s, 3 H), 1.00 (s, 3 H), 0.91 (s, 3 H); ^{13}C NMR (ppm, $CDCl_3$) 136.51, 130.61, 73.86, 67.24, 63.25, 60.30, 55.16, 51.50, 49.64, 38.10, 30.99, 30.67, 27.82, 27.66, 15.41; m/e calcd (M^+) 218.1671, obsd 218.1676.

2,2,4,9-Tetramethyltricyclo[6.3.0.0^{4,8}]undec-6-en-10-one (39). Boron trifluoride etherate (73 mg, 0.52 mmol) was added to a solution of **38** (110 mg, 0.51 mmol) in benzene (5 mL), and the mixture was stirred overnight at room temperature. The resulting black solution was poured into water and extracted with ether. The organic layer was washed with brine, dried, and concentrated. The resulting brown oil was purified by MPLC on silica gel (elution with 10% ethyl acetate in petroleum ether) to give **39** as a colorless, homogeneous oil (104 mg, 95%): IR (cm^{-1}, neat) 3020, 2960, 2840, 1730, 1445, 1360, 1125; ^1H NMR ($CDCl_3$) δ 5.55 (dt, J = 7 and 2 Hz, 1 H), 5.50 (dt, J = 7 and 2 Hz, 1 H), 2.42 (ddt, J = 14, 8, and 2 Hz, 2 H), 2.33 (s, 1 H), 2.29 (s, 2 H), 2.16 (q, J = 18 Hz, 1 H), 1.80 (d, J = 2 Hz, 2 H), 1.14 (s, 3 H), 1.02 (s, 3 H), 0.96 (s, 3 H), 0.93 (d, J = 8 Hz, 3 H); ^{13}C NMR (ppm, $CDCl_3$) 221.40, 135.74, 127.12, 70.52, 58.96, 51.55, 49.95, 47.78, 40.18, 37.94, 31.10, 26.51, 25.99, 11.81; m/e calcd (M^+) 218.1670, obsd 218.1676.

Anal. Calcd for $C_{15}H_{22}O$: C, 82.52; H, 10.16. Found: C, 82.74; H, 9.98.

Silphinene (4). A mixture of **39** (5 mg, 0.02 mmol), hydrazine hydrate (100 μL, 2.0 mmol), anhydrous potassium carbonate (100 mg, 0.72 mmol), and diethylene glycol (1 mL) was heated overnight at 150 °C and at 200 °C for 4 h. The cooled reaction mixture was treated with water and ether, and the separated organic phase was washed with 10% hydrochloric acid and brine prior to drying. Careful concentration in vacuo gave **4** (83% by VPC analysis), which was purified by preparative VPC (5 ft × 0.25 in. 5% SE-30, 130 °C). The 200-MHz ^1H NMR spectrum of this hydrocarbon proved identical in all respects to that of natural silphinene.[2]

Acknowledgment. We acknowledge with gratitude the financial support of the National Institutes of Health (Grant GM-28468), which made this investigation possible.

Total Synthesis of (±)-Pentalenene, the Least Oxidized Neutral Triquinane Metabolite of *Streptomyces griseochromogenes*

Leo A. Paquette* and Gary D. Annis

Contribution from the Evans Chemical Laboratories, The Ohio State University, Columbus, Ohio 43210. *Received March 28, 1983*

Abstract: Pentalenene, the neutral precursor to pentalenic acid and a variety of pentalenolactones, has been synthesized from 4,4-dimethyl-2-cyclopentenone. Following hydrosilation, dichloroketene addition, and hydrolysis, ring expansion to the highly functionalized bicyclo[3.3.0]octanone **22** was achieved with diazomethane. Reduction with zinc and acetic acid led to regiospecific α-chloro enone formation. In six additional steps, an angular propionaldehyde group was introduced and a second double bond was cleanly set in place. At this point, the protocol involved closure of the third five-membered ring, stereocontrolled insertion of the final methyl group, and reductive removal of the carbonyl functionality. The synthetic racemic hydrocarbon exhibited spectral properties identical with those of the natural product.

Sesquiterpenoid metabolities having a tricyclo[6.3.0.0^{4,8}]undecane skeleton that features a bridged spirane arrangement of three cyclopentane rings, together with ring-expanded δ-lactone congeners, have been reported in increasing numbers in recent years.[1] The design of efficient, stereocontrolled pathways to isocomene (**1**),[2-4] silphinene (**2**),[5,6] senoxydene (**3**),[7,8] retigeranic acid (**4**),[9-11] and pentalenolactone E methyl ester (**5**)[12,13] has recently been undertaken in this laboratory. As part of this

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(2) Paquette, L. A.; Han, Y. K. *J. Org. Chem.* **1979**, *44*, 4014; *J. Am. Chem. Soc.* **1981**, *103*, 1835.

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(4) Isolation: (a) Zalkow, L. H.; Harris, R. N., III; Van Derveer, D.; Bertrand, J. A. *J. Chem. Soc., Chem. Commun.* **1977**, 452. (b) Zalkow, L. H.; Harris, R. N., III; Burke, N. I. *J. Nat. Prod.* **1979**, *42*, 96. (c) Bohlmann, F.; Le Van, N.; Pickhardt, J. *Chem. Ber.* **1977**, *110*, 3777.

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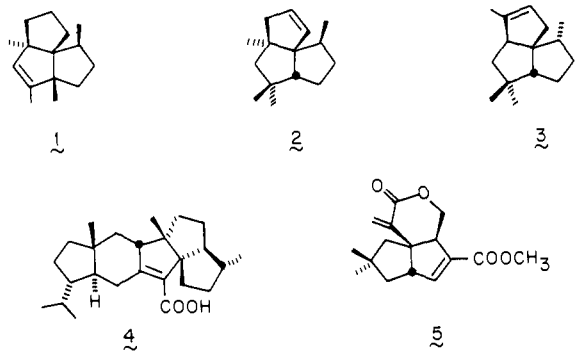
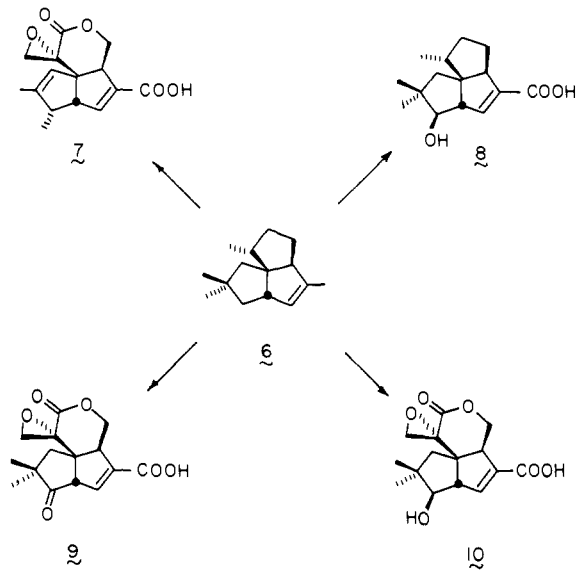
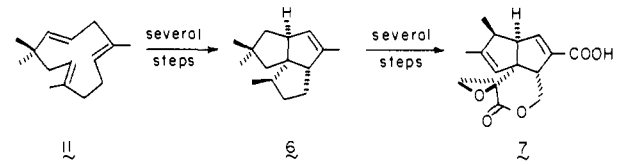


program, our attention was also drawn to pentalenene (**6**), a C_{15}



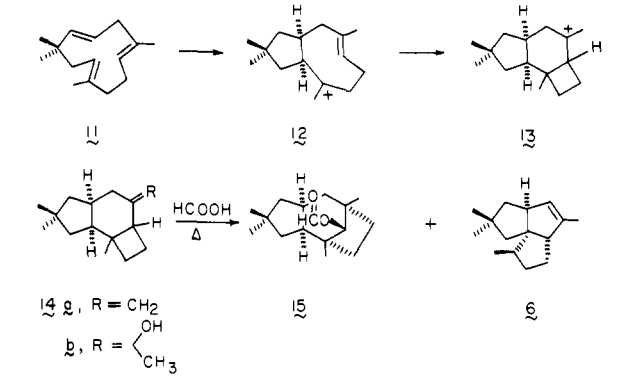
hydrocarbon that has attracted considerable biogenetic interest from at least two directions.

During biosynthetic studies related to the antibiotic agent pentalenolactone (**7**),[14] Seto and Yonehara uncovered that *Streptomyces griseochromogenes* also produces **6**.[15] This discovery was taken as suggestive evidence that **7** and its cometabolites pentalenic acid (**8**)[16] and pentalenolactones E (**5**), G (**9**),[17] and H (**10**)[16] may well arise via the cyclization of humulene (**11**), with pentalenene (**6**) perhaps serving as a pivotal intermediate.

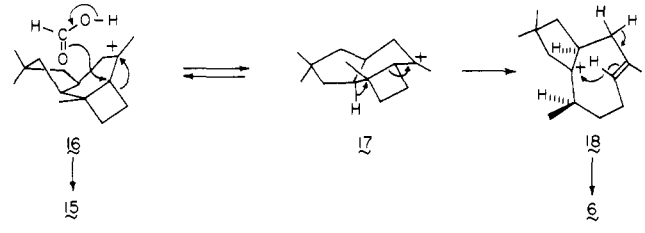


Indeed, Cane and his co-workers found that [UL-$^{13}C_6$]glucose, an *in vivo* precursor to [1,2-$^{13}C_2$]acetyl-CoA, is incorporated into pentalenolactone (**7**) in a manner fully consistent with a mevalonoid pathway.[13a] Further, the conversion of [8-^{3}H,12,13-^{14}C]-farnesyl pyrophosphate to [7-^{3}H,14,15-^{14}C]pentalenene with a cell-free synthetase preparation from *Streptomyces* UC5319 has been studied.[13b] On this basis, pentalenene is seen to be biogenetically related to other important classes of humulene-derived sesquiterpenes, which include fommanosin,[18] the illudoids,[19] marasmic acid,[20] hirsutic acid,[21] and the coriolins.[22]

On the second front, the biosynthetic conversion of humulene to the illudoids has long been thought to be carbocation based and to proceed through **12** to the so-called protoilludyl cation



(**13**).[23] In an attempt to mimic this process, Ohfune et al. heated exocyclic olefin **14a** and the epimeric tertiary carbinols **14b** in formic acid.[24,25] In either case, there was isolated in high yield a mixture of the tricyclic bridged formate **15** and pentalenene (**6**) in a 7:3 ratio. These observations were plausibly interpreted in terms of two conformations (**16** and **17**) for the protoilludyl cation.



In **16**, the highly favorable stereoelectronic alignment of the neighboring lateral cyclobutane bond with the vacant carbocation orbital allows for ready Wagner–Meerwein shift with concurrent capture of formate ion. Where **17** is concerned, stereoelectronic factors are seen to be conducive to fragmentation of the central cyclobutane bond and concomitant 1,2-hydride shift as shown. The resulting *trans*-cyclooctenyl cation (**18**) can subsequently be expected to cyclize[26] to **6** because of the enforced proximity of

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(6) Isolation: Bohlmann, F.; Jakupovic, J. *Phytochemistry* **1980**, *19*, 259.
(7) Galemmo, R. A., unpublished work.
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(17) Seto, H.; Sasaki, T.; Yonehara, H.; Uzawa, J. *Tetrahedron Lett.* **1978**, 923.
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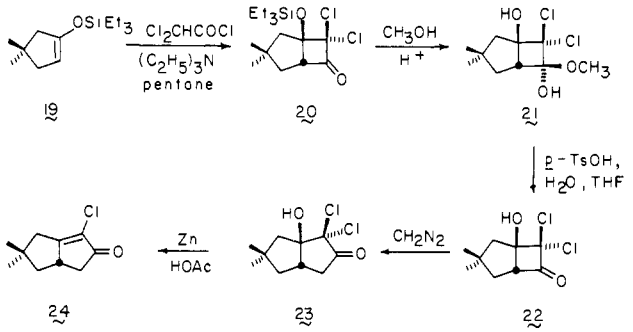
(24) Ohfune, Y.; Shirahama, H.; Matsumoto, T. *Tetrahedron Lett.* **1976**, 2869.
(25) Consult also: Misumi, S.; Ohtsuka, T.; Ohfune, Y.; Sugita, K.; Shirahama, H.; Matsumoto, T. *Tetrahedron Lett.* **1979**, 31.

the π bond to the carbenium center. A similar biosynthetic step has been proposed for retigeranic acid.[11]

The conversion of **17** to **18** carries an important stereochemical implication. Because of the stereodisposition of the hydride atom that migrates, the stereochemistry of the secondary methyl group becomes fixed *under kinetically controlled conditions.* Accordingly, no knowledge of the more stable configuration about this center is seemingly derivable from biosynthetic considerations. Since the chemistry of the tricyclo[6.3.0.0^{4,8}]undecane ring system has been so little examined, relevant information on this question is similarly unavailable from this source. Consequently, our planning of the total synthesis of pentalenene was carefully designed to resolve this issue. Indeed, if the methyl group stereochemistry does *not* correspond to the thermodynamically more stable configuration, the biosynthetic proposal outlined above is seen to gain added indirect, albeit speculative, support.

Elaboration of the Functionalized Diquinane Segment. It appeared to us that a relatively short synthesis might be realized if a bicyclo[3.3.0]octane (diquinane),[1] properly substituted with the geminal methyl pair and suitably functionalized to permit ready annulation of the third five-membered ring, were first to be elaborated. Careful analysis of all structural requirements, with full awareness of the pitfalls associated with attempted Robinson-like aldol cyclization routes to such compounds,[9,27] led to the decision to proceed by ring expansion[28] of a dichloroketene adduct. The combination of silyl enol ether **19**, conveniently



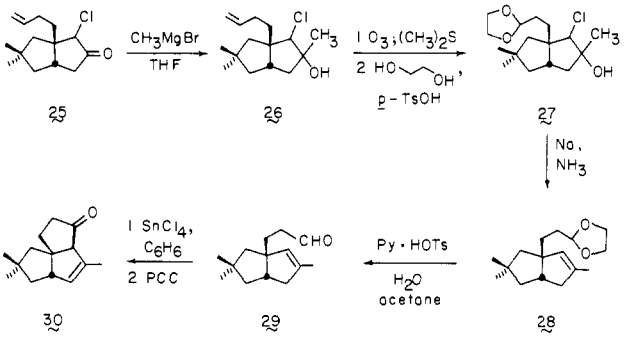
available by hydrosilation of 4,4-dimethylcyclopentenone,[29] and $Cl_2C{=}C{=}O$ itself was viewed as most attractive because of the established regiospecificity of these reactions.[30] Indeed, the intended [2 + 2] cycloaddition proceeded smoothly to furnish **20** in 83% yield.

When **20** was subjected to aqueous acidic hydrolysis in order to free the angular hydroxyl group, the anticipated mixture of **22** and hexaethyldisiloxane was obtained. However, the lability of **22** to both chromatography and heat precluded the satisfactory purification of the cyclobutanone. For this reason, we were pleased to find that simple dissolution of **20** in acidic methanol afforded principally hemiacetal **21**. The formation of this relatively nonvolatile product permitted in turn the removal of the admixed siloxane ($MeOSiEt_3$) under vacuum. Subsequent exposure of **21** to aqueous acid cleanly provided **22**, which was treated directly with diazomethane. The desired ring expansion proceeded without event to deliver the highly crystalline bicyclic ketone **23** in 50% overall yield from **20**.

The stage was now set for introduction of a double bond in conjugation with the carbonyl group. Not surprisingly,[28] exposure of **23** to zinc dust in acetic acid at room temperature furnished **24** in quantitative yield. The efficiency by which **19** can be converted to **24** (43% overall) is especially noteworthy and is taken to be an indication that comparable cyclopentannulation schemes based upon initial regiospecific silyl enol ether formation[31] could hold considerable synthetic promise.

Cyclopentannulation. Arrival at the Pivotal Tricyclic Ketone. For kinetic and thermodynamic reasons,[32] the expectation was that addition of a cuprate reagent to **24** would result in carbon–carbon bond formation from that direction cis to the angular hydrogen substituent. In order to take advantage of this projected high degree of stereoselectivity, **24** was treated with the Grignard reagent of 2-(2-bromoethyl)-1,3-dioxane[33] following admixture of this organometallic with the cuprous bromide–dimethyl sulfide complex.[34] For still unexplained reasons, this recipe failed to give rise to the desired product, a phenomenon encountered as well with other magnesio cuprates. This unexpected development was soon remedied by the simple expedient of making recourse to lithium cuprates. For example, reaction of **24** with lithium di-3-butenylcuprate proceeded quite satisfactorily to deliver **25** in 76% yield.

In order to engage the second chlorine atom in regiospecific double bond formation, **25** was treated with methylmagnesium



bromide and converted to a pair of the epimeric chlorohydrins **26**, which proved to be chromatographically separable. Independent ozonolysis and acetalization of the two stereoisomers led to formation of **27a** and **27b**. The goal of arriving at **28** was easily realized by reductive elimination of either chlorohydrin with sodium in liquid ammonia (59%).[35] Since the tetrahedral carbinol carbon in **26** and **27** is returned to achiral trigonal status in **28**, the need for chromatographic separation does not exist, thus streamlining the sequence and permitting greater throughput of material. As a direct result of the preparation of **28** on large scale, usable amounts of dechlorinated carbinol **31**, a byproduct formed in low yield, could be isolated.

Treatment of **28** with pyridinium tosylate in aqueous acetone[36] afforded aldehyde **29** (66%) admixed with a 1:1 mixture of two epimeric tricyclic alcohols (ca. 15%). The ^1H NMR spectra of the latter two compounds clearly indicated that installation of the third five-membered ring had proceeded with exceptional regiochemical control to generate only an internal double bond. In agreement with previous work from these laboratories,[2] independent cyclization of **29** with stannic chloride in benzene at 5–10 °C proved especially efficient in making available only the endo alcohol (94%). Oxidation of either alcohol gave rise cleanly to ketone **30**.

When byproduct **31** was dehydrated with methanesulfonyl chloride and triethylamine, an inseparable mixture of **28** and its positional isomer **32** was produced. As shown by subsequent reactions with this mixture, the aldehyde derived from **32** undergoes Lewis acid catalyzed Prins reaction to give, following oxidation, the structurally interesting tricyclic ketone **33**.

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(32) (a) Schleyer, P. von R.; Blanchard, K. R.; Woody, C. D. *J. Am. Chem. Soc.* **1963**, *85*, 1358. (b) Schleyer, P. von R.; Williams, J. E.; Blanchard, K. R. *Ibid.* **1970**, *92*, 2377.
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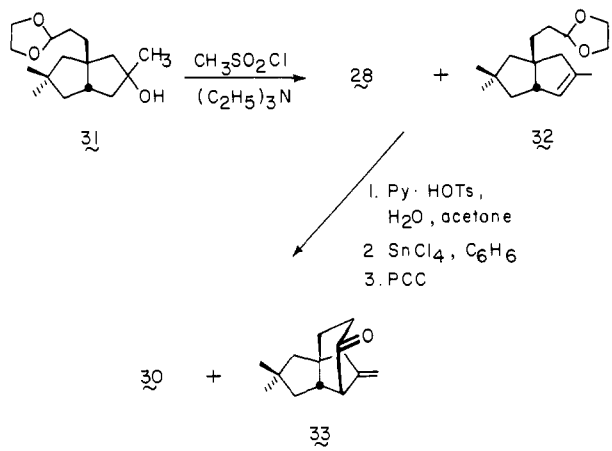
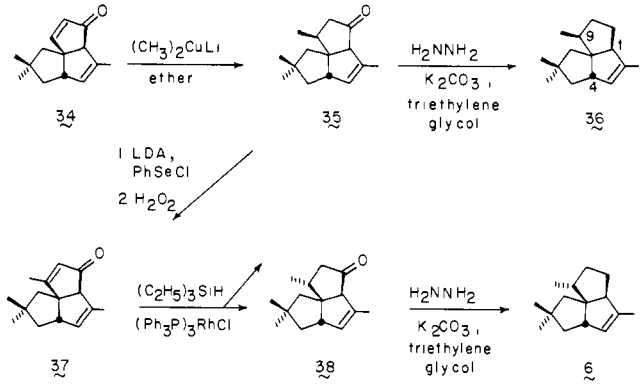
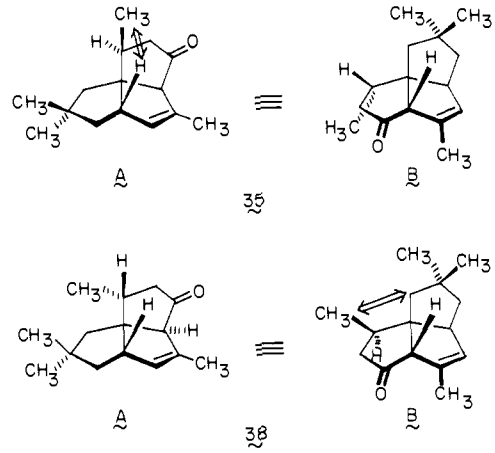


Installation of the Secondary Methyl Group. Kinetic and Thermodynamic Considerations. We next faced the task of introducing the requisite secondary α-methyl group—an exercise that is normally routine. Formation of dienone **34** via kinetically controlled selenation of **30** and selenoxide elimination was considered an obvious first choice. Indeed, **34** was easily obtained



and entered into reaction with lithium dimethylcuprate to provide a single conjugate addition product in 87.5% yield. In order to establish the configuration of the newly introduced methyl substituent, Wolff–Kishner reduction with hydrazine hydrate and potassium carbonate in triethylene glycol[37] was effected at 250 °C. A single hydrocarbon was isolated, the 300-MHz ^{1}H NMR spectrum of which was characterized by key absorptions at δ 0.958 for the 9-methyl group, 2.633 for H_1, and 2.924–2.866 for H_4 (see formula **36** for numbering). These signals and certain of its ^{13}C NMR chemical shifts did not correlate well with those of the natural product. In addition, a nuclear Overhauser effect of 7% was observed between H_4 and the C_9 methyl group. Accordingly, delivery of the methyl group to **34** must have occurred from the β face to give **35**, and **36** must therefore be *epi*-pentalenene.

Because cuprate reactions are in general kinetically controlled and provide little, if any, thermodynamic information, we converted **35** to **37** and subjected this dienone to lithium in liquid ammonia reduction. Again, **35** was formed exclusively. Thus, there can be little question that the 9-methyl group in this tricyclic ketone strongly prefers the β configuration. As seen in the two complementary conformational views of **35** which are illustrated, lithium dimethylcuprate delivers the CH_3 group to **34** from the concave surface of the bicyclo[3.3.0]octadienone part of the structure. Whereas this avenue of approach leads to quasiequatorial positioning of the entering substituent and is usually sterically disfavored,[1-3,5,12] this stereochemical course is presently not adhered to. In our view, the nonbonded methyl–hydrogen interaction made apparent in **35A** must be substantially less cumbersome than the methyl–methylene interaction that exists in epimer **38** (see **38B**).



When **37** was reduced with CuH,[38] comparable results were obtained, presumably because an electron-transfer mechanism operates. Quite unexpectedly, such reagents as $NaHFe(CO)_4$,[39] NaHTe,[40] $NaHFe_2(CO)_8$,[41] and $Pd/(C_2H_5)_3N/HCOOH$[42] proved ineffective at reducing the enone. However, when recourse was made to the sterically bulky reagent combination $(Ph_3P)_3RhCl/(C_2H_5)_3SiH$,[43] kinetic control was observed not to strictly parallel thermodynamic control (**35**:**38** = 2.24:1). Although these epimers proved to be separable by VPC, we found it more convenient to arrive at pentalenene (**6**) by directly subjecting the mixture to Wolff–Kishner reduction. In full congruence with the natural product, our sample of **6** prepared in this manner exhibited key signals at δ 0.916, 2.566, and 2.716–2.633 for its 9-methyl group, H_1, and H_4 substituents at 300 MHz.

In summation, pentalenene (**6**) has yielded to total synthesis. In the course of this work, this sesquiterpene hydrocarbon was shown to possess the less stable configuration at C_9, a fact that lends considerable credence to its proposed biosynthesis.

Experimental Section

7,7-Dichloro-3,3-dimethyl-1-(triethylsiloxy)bicyclo[3.2.0]heptan-6-one (20). Triethylamine (9.0 g, 89.1 mmol) in pentane (40 mL) was added dropwise to a solution of **19**[29] (20.0 g, 88.4 mmol) and dichloroacetyl chloride (13.05 g, 88.4 mmol) in pentane (150 mL) during 3 h. The reaction mixture was stirred overnight, and the filtrate was evaporated. Chromatography of the residue on silica gel (elution with hexane–ether 4:1) gave **20** as a colorless oil (25 g, 83%): IR (cm^{-1}, neat) 2955, 2870, 1255, 1240, 1240, 1147, 1097, 1009, 810, 782, 735, 722; ^{1}H NMR ($CDCl_3$) δ 3.82–3.65 (m, 1 H), 2.40–1.73 (m, 4 H), 1.13–0.55 (m, 21 H); *m/e* calcd ($M^+ - CH_3$) 321.0844; obsd 321.0851.

1,1-Dichlorohexahydro-6a-hydroxy-5,5-dimethyl-2(1*H*)-pentalenone (23). Adduct **20** (11.0 g, 32.6 mmol) was treated with methanol (100 mL) containing concentrated hydrochloric acid (4 drops). After 2 h, the solvent and siloxane were evaporated in vacuo and the residue was taken up in aqueous tetrahydrofuran (20%, 100 mL). To this stirred solution was added 500 mg of *p*-toluenesulfonic acid. After 30 min, the mixture was partitioned between ether (200 mL) and saturated sodium bicarbonate solution (100 mL). The organic phase was dried and evaporated to give high purity **22**.

The cyclobutanone was redissolved in ether and treated with diazomethane (0.166 mol). After all effervescence had ceased (ca. 20 min), excess diazomethane was destroyed by reaction with glacial acetic acid. Solvent evaporation followed crystallization from ether–petroleum ether afforded 4.0 g (52%) of **23** as colorless crystals, mp 122.5–123.5 °C; IR (cm^{-1}, $CHCl_3$) 3570, 3020, 2950, 2865, 1779, 1361, 1275, 1165, 1045, 915, 870, 838; ^{1}H NMR ($CDCl_3$) δ 3.08 (dd, J = 18 and 10 Hz, 1 H), 2.83–2.63 (m, 1 H), 2.53 (br s, 1 H), 2.30–1.94 (m, 2 H), 1.76–1.48 (m, 3 H), 1.30 (s, 3 H), 1.15 (s, 3 H).

Anal. Calcd for $C_{10}H_{14}Cl_2O_2$: C, 50.65; H, 5.95. Found: C, 50.69; H, 5.95.

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3-Chloro-4,5,6,6a-tetrahydro-5,5-dimethyl-2(1*H*)-pentalenone (24). Zinc dust (1.68 g, 25.84 mmol) was added to a solution of **23** (5.6 g, 23.62 mmol) in glacial acetic acid (70 mL). After 2 h of stirring, the mixture was poured into water (500 mL) and the supernatant was extracted with ether (3 × 100 mL). The combined organic layers were washed with sodium bicarbonate solution, dried, and evaporated to give **24** as a colorless oil (4.4 g, 100%): IR (cm^{-1}, neat) 2940, 2860, 1718, 1640, 1460, 1405, 1365, 1265, 1232, 950, 930; ^1H NMR ($CDCl_3$) δ 3.3–3.0 (br m, 1 H), 2.76 (A part of ABX, J_{AB} = 17 Hz, J_{AX} = 6 Hz, 1 H), 2.44 (s, 2 H), 2.30–1.86 (m, 3 H), 1.24 (s, 3 H), 1.17 (s, 3 H); *m/e* calcd (M^+) 184.0655, obsd 184.0660.

6a-(3-Butenyl)-1-chlorohexahydro-5,5-dimethyl-2(1*H*)-pentalenone (25). Cuprous bromide–dimethyl sulfide complex (3.33 g, 16.21 mmol) in dimethyl sulfide (2.01 g, 32.4 mmol) was added to a solution of 3-butenyllithium (2.01 g, 32.4 mmol) in ether (30 mL) and pentane (28 mL) at −78 °C. After this mixture had stirred for 1 h, a solution of **24** (2.53 g, 13.7 mmol) in ether (20 mL) was added over a 4-h period, and agitation was maintained overnight at −78 °C prior to pouring into saturated ammonium chloride solution (100 mL). The product was extracted into ether (2 × 100 mL) and the combined organic layers were dried and evaporated. Chromatography of the residue on silica gel (elution with hexane–ether 4:1) gave pure **25** as a colorless oil (2.43 g, 74%): IR (cm^{-1}, neat) 3065, 2938, 1757, 1640, 1457, 1445, 1363, 903; ^1H NMR ($CDCl_3$) δ 5.96–5.53 (m, 1 H), 5.11–4.91 (m, 2 H), 4.20 (s, 1 H), 2.88–1.36 (series of m, 11 H), 1.13 (s, 3 H), 1.08 (s, 3 H); *m/e* calcd (M^+) 240.1287, obsd 240.1281.

Anal. Calcd for $C_{14}H_{21}ClO$: C, 69.84; H, 8.79. Found: C, 69.74; H, 8.77.

6a-(3-Butenyl)-1-chlorooctahydro-2,5,5-trimethyl-2-pentalenol (26). α-Chloro ketone **25** (2.43 g, 10.1 mmol) in tetrahydrofuran (50 mL) was added to a cold (−5 °C), stirred solution of methylmagnesium bromide (9 g, 75.7 mmol) in the same solvent (68 mL). After being stirred at 0–5 °C for 12 h, the mixture was allowed to warm to room temperature and poured into saturated ammonium chloride solution (400 mL) at 0 °C. Extraction with ether (3 × 100 mL) followed by drying and evaporation of the combined organic layers afforded a residual oil, which was treated again with methylmagnesium bromide as above. The product was purified by silica gel chromatography (elution with hexane–ether 10:1) to give 523 mg (21.7%) of the endo alcohol as a colorless oil and 989 mg (41%) of the oily exo alcohol.

For the endo epimer: IR (cm^{-1}, neat) 3570, 3465, 3070, 2950, 2930, 2860, 1640, 1450, 1370, 1360, 1325, 1270, 1110, 900; ^1H NMR ($CDCl_3$) δ 6.01–5.57 (m, 1 H), 5.08–4.86 (m, 2 H), 3.75 (s, 1 H), 2.50–1.35 (series of m, 12 H), 1.25 (s, 3 H), 1.05 (s, 3 H), 1.01 (s, 3 H); *m/e* calcd ($M^+ - H_2O$) 238.1488, obsd 238.1495.

For the exo epimer: IR (cm^{-1}, neat) 3570, 3460, 3075, 2950, 2860, 2860, 1640, 1445, 1370, 1360, 1112, 989, 902; ^1H NMR ($CDCl_3$) δ 6.05–5.60 (m, 1 H), 5.08–4.81 (m, 2 H), 4.01 (s, 1 H), 2.78–1.36 (series of m, 12 H), 1.33 (s, 3 H), 1.13 (s, 3 H), 1.04 (s, 3 H); *m/e* calcd ($M^+ - CH_3$) 241.1359, obsd 241.1367.

Also recovered was 163 mg of unreacted **25**.

1-Chloro-6a-[2-(1,3-dioxolan-2-yl)ethyl]octahydro-2,5,5-trimethyl-2-pentalenol (27). A. Endo Series. The endo hydroxy epimer of **26** (523 mg, 2.04 mmol) in methanol (30 mL) at −78 °C was treated with excess ozone. After 10 min, the unreacted ozone was removed in a stream of nitrogen, and dimethyl sulfide (10 mL) was added. The mixture was allowed to warm to room temperature and the solvent was removed to give a mixture of aldehyde and dimethyl acetal. This mixture was immediately taken up in benzene (30 mL), pyridinium tosylate (150 mg) and ethylene glycol (600 mg) were added, and the mixture was heated at the reflux temperature under a Dean–Starke trap until water ceased to form. The cooled benzene solution was poured into saturated sodium bicarbonate solution (150 mL), and the product was extracted into ether (3 × 100 mL). The combined organic layers were dried and evaporated to give 582 mg (94%) of endo **27** as a colorless oil: IR (cm^{-1}, neat) 3480, 2945, 2920, 2855, 1450, 1370, 1360, 1135, 1120, 1065, 1035, 934; ^1H NMR ($CDCl_3$) δ 4.79 (t, J = 3 Hz, 1 H), 4.03–3.63 (m, 5 H), 2.46–1.32 (series of m, 12 H), 1.22 (s, 3 H), 1.02 (s, 3 H), 1.00 (s, 3 H); *m/e* calcd (M^+) 302.1649, obsd 302.1657.

B. Exo Series. A 989 mg (3.85 mmol) sample of exo **26** was ozonized and acetalized in an identical manner to furnish 1.13 g (96.7%) of exo **27** as a colorless oil: IR (cm^{-1}, neat) 3470, 2940, 2855, 1445, 1340, 1320, 1130, 1025; ^1H NMR ($CDCl_3$) δ 4.70 (t, J = 3 Hz, 1 H), 4.03 (s, 1 H), 3.96–3.78 (m, 4 H), 2.76–1.40 (series of m, 12 H), 1.35 (s, 3 H), 1.13 (s, 3 H), 1.04 (s, 3 H); *m/e* calcd (M^+) 302.1649, obsd 302.1657.

Anal. Calcd for $C_{16}H_{27}ClO_3$: C, 63.46; H, 8.98. Found: C, 63.16; H, 8.91.

Direct Conversion of 25 to 27. Ketone **25** (15 g, 62.3 mmol) in anhydrous tetrahydrofuran (100 mL) was treated twice with methylmagnesium bromide (21 g, 176 mmol) as described above. The unpurified tertiary alcohol mixture in methanol (200 mL) was treated analogously with ozone and dimethyl sulfide and subjected to ketalization. Purification of the product by silica gel chromatography (elution with hexanes–ether 1:1) gave 4.89 g (25.9%) of endo **27** and 7.10 g (37.7%) of exo **27**.

2-[2-(2,3,6,6a-Tetrahydro-2,2,5-trimethyl-3a(1*H*)-pentalenyl)ethyl]-1,3-dioxolane (28). A. Reduction of exo 27. A solution of exo **27** (256 mg, 0.84 mmol) in ether (2 mL) was added dropwise to a solution of sodium (190 mg, 8.26 mmol) in liquid ammonia (25 mL). Upon completion of the addition, the mixture was stirred for 5 min, and ethanol was added to neutralize the excess sodium. The ammonia was evaporated, and the residue was partitioned between ether (100 mL) and water (25 mL). The ethereal layer was dried and evaporated, and the residue was purified by chromatography on Florisil (elution with hexane–ether 4:1) to give **28** as a colorless oil (106 mg, 50%): IR (cm^{-1}, neat) 2920, 2845, 1435, 1402, 1360, 1135, 1030; ^1H NMR ($CDCl_3$) δ 5.01 (br s, 1 H), 4.73 (t, J = 2 Hz, 1 H), 3.93–3.73 (m, 4 H), 2.58–1.05 (series of m, 14 H), 0.95 (s, 6 H); *m/e* calcd (M^+) 250.1933, obsd 250.1939.

Anal. Calcd for $C_{16}H_{26}O_2$: C, 76.76; H, 10.46. Found: C, 76.86; H, 10.49.

B. Reduction of endo 27. A 328 mg (1.08 mmol) sample of endo **27** was comparably reduced to give 121 mg (44.6%) of **28** after Florisil chromatography.

C. Reduction of the Epimeric Mixture. A 1:1 mixture of endo and exo **27** (1.13 g, 3.73 mmol) in ether (10 mL) was reduced in the predescribed manner with 423 mg (18.4 mmol) of sodium in liquid ammonia (75 mL) at −33 °C. Comparable workup and chromatographic purification afforded 548 mg (59%) of **28**, 147 mg (15%) of endo **31**, and 147 mg (15%) of exo **31**.

For endo **31**: IR (cm^{-1}, neat) 3480, 2960, 2940, 2880, 1455, 1409, 1362, 1135, 1065, 1040; ^1H NMR ($CDCl_3$) δ 4.82 (t, J = 4.5 Hz, 1 H), 4.00–3.73 (m, 4 H), 2.43–1.21 (series of m, 14 H), 1.33 (s, 3 H), 1.07 (s, 3 H), 1.01 (s, 3 H); *m/e* calcd ($M^+ - H_2O$) 250.1933, obsd 250.1939.

For exo **31**: IR (cm^{-1}, neat) 3440, 2958, 2939, 2870, 1455, 1410, 1385, 1365, 1250, 1140, 1070, 1060, 1037, 945; ^1H NMR ($CDCl_3$) δ 4.87–4.78 (m, 1 H), 4.00–3.73 (m, 4 H), 2.56–1.13 (series of m, 14 H), 1.39 (s, 3 H), 1.08 (s, 3 H), 1.02 (s, 3 H); *m/e* calcd ($M^+ - H_2O$) 250.1933, obsd 250.1939.

2,3,6,6a-Tetrahydro-2,2,5-trimethyl-3a(1*H*)-pentalenepropionaldehyde (29). A mixture of **28** (248 mg, 0.992 mmol), acetone (10 mL), water (1 mL), and pyridinium tosylate (100 mg) was heated at reflux for 12 h. The solvent was removed, the residue was taken up in either (100 mL), and this solution was washed with saturated sodium bicarbonate solution (100 mL), dried, and concentrated. Chromatography of the resulting oil on silica gel (elution with hexane–ether 4:1) gave aldehyde **29** (138 mg, 66%); IR (cm^{-1}, neat) 3020, 2940, 2910, 2860, 1725, 1455, 1435, 1410, 1375, 1360; ^1H NMR ($CDCl_3$) δ 9.71 (t, J = 1.5 Hz, 1 H), 5.00 (s, 1 H), 2.48–2.20 (m, 4 H), 1.93–1.08 (series of m, 10 H), 1.00 (s, 6 H); *m/e* calcd (M^+) 206.1671, obsd 206.1664.

Next to be eluted was the endo tricyclic alcohol, a colorless oil (16 mg, 7.5%): IR (cm^{-1}, neat) 3420, 2940, 2920, 2855, 1455, 1435, 1377, 1360, 1082, 1035, 1012, 869, 825; ^1H NMR ($CDCl_3$) δ 5.42 (br s, 1 H), 4.28–4.15 (m, 1 H), 2.91–2.65 (m, 2 H), 1.86–1.03 (series of m, 12 H), 1.00 (s, 6 H); *m/e* calcd (M^+) 206.1671, obsd 206.1675.

Finally, 16 mg (7.5%) of the exo tricyclic alcohol was isolated: IR (cm^{-1}, neat) 3330, 2945, 2920, 2860, 1455, 1432, 1377, 1359, 1090, 1023, 1185, 1175; ^1H NMR ($CDCl_3$) δ 5.18 (s, 1 H), 4.00 (s, 1 H), 2.90–2.60 (m, 1 H), 2.45 (s, 1 H), 2.08–1.10 (series of m, 12 H), 0.96 (s, 6 H); *m/e* calcd (M^+ 206.1671, obsd 206.1664.

Lewis Acid Promoted Cyclization of 29. Tin tetrachloride (257 mg, 0.987 mmol) in benzene (4 mL) was added dropwise to a stirred solution of **29** (109 mg, 0.51 mmol) in benzene at 5–10 °C. After the addition was complete, the reaction mixture was stirred for a further 30 min and poured into saturated sodium bicarbonate solution (200 mL). The resulting mixture was extracted with ether (3 × 50 mL), and the combined organic layers were dried and evaporated to give 105 mg (96.3%) of the endo tricyclic alcohol described above.

1,2,5a,6,7,8-Hexahydro-4,7,7-trimethylcyclopenta[*c*]pentalen-3-(3a*H*)-one (30). Pyridinium chlorochromate (144 mg, 0.669 mmol) in dichloromethane (15 mL) was added dropwise to a stirred solution of the exo/endo tricyclic alcohol mixture (115 mg, 0.558 mmol) in the same solvent (5 mL). After 2 h, ether (50 mL) was added and the slurry was filtered through a plug of silica gel. Solvent evaporation in vacuo left 113 mg (96%) of **30** as a colorless oil: IR (cm^{-1}, neat) 3025, 2940, 2920, 2855, 1740, 1455, 1435, 1375, 1360, 1165, 1150; ^1H NMR ($CDCl_3$) δ 5.36 (s, 1 H), 3.13–2.86 (m, 1 H), 2.72 (s, 1 H), 2.54–1.17 (series of m, 11 H), 1.07 (s, 3 H), 1.03 (s, 3 H); *m/e* calcd (M^+) 204.1514, obsd 204.1518.

Anal. Calcd for $C_{14}H_{20}O$: C, 82.30; H, 9.87. Found: C, 82.25; H, 10.10.

Dehydration of 31. Triethylamine (1.0 g, 9.9 mmol) in dichloromethane (5 mL) was added dropwise to **31** (410 mg of epimeric mixture, 1.53 mmol) and methanesulfonyl chloride (527 mg, 4.60 mmol) in dichloromethane (5 mL) at −20 °C. After 20 min, the mixture was allowed to warm to room temperature. After an additional 40 min, the mixture was poured into water (50 mL), and the organic phase was dried and evaporated. Chromatography of the oil on Florisil (elution with hexane–ether 4:1) gave a mixture of **28** and **32** as an oil: IR (cm^{-1}, neat) 3020, 2955, 2930, 2885, 2860, 1440, 1405, 1142, 1080; ^1H NMR ($CDCl_3$) δ 5.26–5.15 and 5.10–5.05 (m, 1 H), 4.86–4.73 (m, 1 H), 3.97–3.80 (m, ' H), 2.53–1.10 (series of m, 14 H), 1.00 (s, 6 H); *m/e* calcd (M^+) 250.1933, obsd 250.1939.

Hydrolysis–Cyclization–Oxidation of 32. An epimeric mixture of **28** and **32** (1.45 g, 5.8 mmol) was treated with pyridinium tosylate (500 mg, 1.99 mmol) in acetone (50 mL) and water (5 mL) in the manner described for **28**. Chromatography as before yielded the admixed aldehydes as an oil (500 mg, 42%): IR (cm^{-1}, neat) 2912, 2705, 1775, 1440, 1362; ^1H NMR ($CDCl_3$) δ 9.72 and 9.65 (two t, $J > 1$ Hz, 1 H), 5.18 and 4.98 (two s, 1 H), 2.83–1.20 (series of m, 14 H) and 1.00 (s, 6 H); *m/e* calcd (M^+) 206.1671, obsd 206.1664. Also obtained were the endo (100 mg, 8.3%) and exo tricyclic alcohols (158 mg, 13.2%).

Tin tetrachloride (377 mg, 1.44 mmol) in benzene (5 mL) was added to the aldehyde mixture (160 mg, 0.77 mmol) in benzene (1 mL) at 5–10 °C. After the addition was complete, the mixture was stirred for a further 30 min prior to pouring into saturated sodium bicarbonate solution (20 mL). The organic phase was dried and evaporated to leave a residue, which was taken up in dichloromethane (20 mL) and treated with pyridinium chlorochromate (217 mg, 1.0 mmol). After the oxidation was complete, the mixture was diluted with ether (100 mL) and the solution washed with water (50 mL). Following drying and solvent evaporation, the residue was chromatographed on silica gel (elution with hexane–ether 10:1). There was isolated 35 mg (22%) of **30** and 60 mg (37%) of **33**, a colorless oil: IR (cm^{-1}, neat) 3070, 2950, 2930, 2862, 1712, 1652, 1460, 1450, 1430, 1362, 1167, 887, 875; ^1H NMR ($CDCl_3$) δ 5.07 (t, $J = 1$ Hz, 1 H), 4.96 (s, 1 H), 3.20 (s, 1 H), 2.71–1.00 (series of m, 11 H), 1.20 (s, 3 H), 1.10 (s, 3 H); ^{13}C NMR (ppm, $CDCl_3$) 209.47, 148.52, 110.00, 65.03, 54.68, 50.53, 50.28, 43.76, 41.27, 40.95, 36.99, 34.75, 32.71; *m/e* calcd (M^+) 204.1518, obsd 204.1514.

Anal. Calcd for $C_{14}H_{20}O$: C, 82.30; H, 9.87. Found: C, 82.48; H, 10.15.

5a,6,7,8-Tetrahydro-4,7,7-trimethylcyclopenta[*c*]pentalen-3(3a*H*)-one (34). A solution of **30** (218 mg, 1.07 mmol) in tetrahydrofuran (3 mL) was added dropwise to lithium diisopropylamide (148 mg, 1.39 mmol) in tetrahydrofuran (5 mL) at −78 °C. After the addition was complete, the mixture was stirred for an additional hour, at which point phenylselenenyl chloride (204 mg, 1.06 mmol) in tetrahydrofuran (3 mL) was added. An hour later, the reaction mixture was allowed to warm to 0 °C, poured into saturated sodium bicarbonate solution (20 mL), and extracted with ether (3 × 20 mL). The combined ethereal layers were dried and evaporated and the resulting crude selenide was redissolved in dichloromethane (10 mL), made basic with pyridine (250 mg, 3.1 mmol), and treated with 15% hydrogen peroxide until all selenium-containing compounds had been oxidized. This mixture was diluted with water (25 mL) and the organic phase was separated, dried, and evaporated to give 200 mg (92%) of **34**, which was used without further purification: IR (cm^{-1}, neat) 3025, 2950, 2925, 2860, 1705, 1580, 1462, 1435, 1380, 1375, 1360, 1340, 1222, 1178, 1168, 1025, 825, 790; ^1H NMR ($CDCl_3$) δ 7.48 (d, $J = 6$ Hz, 1 H), 5.88 (d, $J = 6$ Hz, 1 H), 5.26 (s, 1 H), 3.13–2.80 (m, 2 H), 1.91–1.23 (series of m, 7 H), 1.11 (s, 3 H), 1.00 (s, 3 H); *m/e* calcd (M^+) 202.1358, obsd 202.1363.

[1*S*-(1β,3aα,5aα,8a*R)]-1,2,5a,6,7,8-Hexahydro-1,4,7,7-tetramethylcyclopenta[*c*]pentalen-3(3a*H*)-one (35).** A solution of **34** (72 mg, 0.356 mmol) in ether (2 mL) was added dropwise to a solution of lithium dimethylcuprate (1.78 mmol) in ether (5 mL) at −20 °C. Upon completion of the addition, the reaction mixture was stirred at −20 °C for 1 h and at 0 °C for 30 min prior to being poured into saturated ammonium chloride solution (100 mL) and ether (100 mL). The ethereal layer was dried and evaporated to give 63 mg (81%) of a single ketone identified as **35**: IR (cm^{-1}, neat) 3020, 2950, 2910, 2860, 1740, 1460, 1438, 1408, 1375, 1361, 1180, 1155; ^1H NMR ($CDCl_3$) δ 5.35 (s, 1 H), 3.31–3.00 (m, 1 H), 2.81 (br s, 1 H), 2.51–1.20 (series of m, 10 H), 1.08 (d, $J = 8$ Hz, 3 H), 1.05 (s, 3 H), 1.00 (s, 3 H); *m/e* calcd (M^+) 218.1671, obsd 218.1676.

Anal. Calcd for $C_{15}H_{22}O$: C, 82.51; H, 10.15. Found: C, 82.41; H, 10.03.

***epi*-Pentalenene (36).** A mixture of **35** (134 mg, 0.164 mmol), hydrazine hydrate (0.24 mL), potassium carbonate (260 mg), and triethylene glycol (3 mL) was heated at reflux for 1.5 h. The flask temperature was then increased to 200 °C, and the distillate was collected. After a further 3 h at 250 °C, the mixture was cooled, diluted with water (10 mL), combined with the distillate, and extracted with ether (3 × 30 mL). The ethereal layers were dried and evaporated to leave a residue, which was chromatographed on silica gel (elution with hexane–ether 4:1). There was obtained 105 mg (83%) of **36** as a colorless oil: IR (cm^{-1}, neat) 3020, 2940, 2920, 2860, 1558, 1440, 1372, 1360, 825; ^1H NMR ($CDCl_3$) δ 5.19 (s, 1 H), 2.99–2.78 (m, 1 H), 2.72–2.56 (m, 1 H), 1.73–0.86 (series of m, 21 H); ^{13}C NMR (ppm, $CDCl_3$) 140.58, 131.33, 63.53, 54.90, 50.59, 46.32, 45.07, 39.75, 33.03, 31.49, 29.18, 28.57, 15.23, 13.44; *m/e* calcd (M^+) 204.1878, obsd 204.1885.

5a,6,7,8-Tetrahydro-1,4,7,7-tetramethylcyclopenta[*c*]pentalen-3-(3a*H*)-one (37). Ketone **35** (1.03 g, 4.7 mmol) in tetrahydrofuran (5 mL) was added to a solution of lithium diisopropylamide (6.1 mmol) in tetrahydrofuran (6 mL) cooled to −78 °C. After 30 min, phenylselenenyl chloride (1.35 g, 7.08 mmol) in tetrahydrofuran (5 mL) was added. The reaction mixture was stirred at −78 °C for 30 min and allowed to warm to 0 °C before being partitioned between ether (100 mL) and water (100 mL). The ethereal layer was dried and evaporated. The residue was redissolved in dichloromethane (25 mL) containing pyridine (3 mL). Hydrogen peroxide (15%, 2 mLe was added, and the disappearance of selenide was monitored by TLC. When elimination was complete, water (10 mL) was added and the separated organic phase was dried and evaporated. The product was purified by chromatography on Florisil (elution with hexane–ether, 5:1) to give 150 mg of recovered **35** and 500 mg (57%) of **37** as a colorless oil: IR (cm^{-1}, neat) 3030, 2950, 2930, 2865, 1700, 1615, 1462, 1430, 1380, 1365, 1308, 1230, 1188, 845; ^1H NMR ($CDCl_3$) δ 5.71 (s, 1 H), 5.25 (s, 1 H), 2.96 (br s, 2 H), 2.10–1.23 (series of m, 10 H), 1.12 (s, 3 H), 1.08 (s, 3 H); *m/e* calcd (M^+) 216.1514, obsd 216.1519.

Hydrosilation of 37. A mixture of **37** (138 mg, 0.64 mmol), triethylsilane (300 mg, 2.58 mmol), and tris(phenylphosphine)rhodium chloride (50 mg) was heated at reflux in benzene (5 mL) for 8 h. The mixture was cooled and methanol (5 mL) containing one drop of concentrated hydrochloric acid was added. After 10 min, the mixture was partitioned between ether (70 mL) and saturated sodium bicarbonate solution (70 mL). The separated organic phase was dried and evaporated to leave a residue, which was redissolved in dichloromethane (20 mL). Pyridinium chlorochromate (300 mg, 1.4 mmol) was introduced, the mixture was stirred for 40 min prior to dilution with ether (80 mL), and the solid precipitate was removed by filtration through a plug of Florisil. The evaporated eluate was purified by silica gel chromatography (elution with hexanes–ether 10:1) to give a mixture of **38** and **35** in a ratio of ca. 1:2.24 as a colorless oil (93 mg, 66%): IR (cm^{-1}, neat) 2960, 2920, 2880, 1742, 1460, 1415, 1380, 1240, 1175, 1015, 1005; ^1H NMR ($CDCl_3$) δ 5.33 (s, 1 H), 3.31–2.96 (br m, 1 H), 2.78 and 2.66 (s, total 1 H), 2.20–0.86 (series of m, 19 H); *m/e* calcd (M^+) 218.1671, obsd 218.1676.

Pentalenene (6). A mixture of **35** and **38** (205 mg, 0.64 mmol), hydrazine hydrate (0.30 mL), potassium carbonate (397 mg), triethylene glycol (3 mL) was heated at reflux temperature for 1.5 h. The flask temperature was then raised to 200 °C, and a distillate was collected. After an additional 3 h at 250 °C, the mixture was cooled, diluted with water (10 mL), and combined with the distillate prior to ether extraction (3 × 30 mL). The extracts were dried and evaporated, and the residue was purified by silica gel chromatography (elution with hexanes–ether 4:1). There was obtained an oily mixture of **6** and **36** (115 mg, 60%). The two components were separable on a 25% Carbowax 20M VPC column (0.25 in. × 12 ft; Chromosorb P) at 180 °C. For **6**: ^1H NMR ($CDCl_3$) δ 5.17 (s, 1 H), 2.70–2.63 (m, 1 H), 2.56 (d, $J = 10$ Hz), 1.90–1.16 (series of m, 12 H), 1.00 (s, 6 H), 0.92 (d, $J = 8$ Hz, 3 H); ^{13}C NMR (ppm, $CDCl_3$) 140.52, 129.51, 64.77, 62.12, 59.38, 48.96, 46.85, 44.60, 40.51, 33.55, 29.98, 29.13, 27.63, 16.98, 15.45. These data were superimposable upon those of an authentic sample.

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