Experimental Section

1-(Methylthio)pyrrolidine (1). A 31.9-mL (47.9 mmol) sample of 1.5 M *n*-BuLi was added dropwise, via cannula, to 4 mL (3.41 g, 47.9 mmol) of pyrrolidine and 75 mL of pentane chilled to 0 °C. After 5 min at 0 °C and 30 min at room temperature, 4.5 g (47.9 mmol) of dimethyl disulfide in 35 mL of pentane was added, and the mixture was stirred at room temperature for 24 h. After filtration through a pad of Celite, removal of solvent at reduced pressure, and distillation twice (bp 76–78 °C (62 mm), **1** was obtained as a colorless oil: 2.03 g (36% yield); ^{1}H NMR ($CDCl_3$) δ 2.92 (m, 4 H), 2.14 (s, 3 H), 1.78 (m, 4 H); ^{13}C NMR ($CDCl_3$) δ 53.88 (t), 25.28 (t), 12.81 (q); mass spectral peak match for $C_5H_{11}NS$.

1-(Methylthio)piperidine (2). Previously made by groups of Davis[32] and Minato,[33] we prepared **2** from 3.0 g (35.2 mmol) of piperidine by the same method as for **1**, giving 3.31 g (21.9%) of **2** as a colorless oil: bp 96–102 °C (70 mm); ^{1}H NMR δ 2.90 (m, 4 H), 2.19 (s, 3 H), 1.47–1.80 (m, 4 H), 1.20–1.47 (m, 2 H); ^{13}C NMR ($CDCl_3$) δ 56.59 (t), 27.27 (t), 23.24 (t), 12.42 (q); mass spectral peak match for $C_6H_{13}NS$.

(Methylthio)diisopropylamine (3) was prepared from 5 mL (35.4 mmol) of diisopropylamine by the same method as **1**, giving 3.52 g (67.5%) of **3** as a colorless oil: bp 76–80 °C (59 mm); ^{1}H NMR ($CDCl_3$) δ 3.25 (septet, J = 7 Hz, 2 H), 2.19 (s, 3 H), 1.12 (d, J = 7 Hz, 12 H); ^{13}C NMR ($CDCl_3$) δ 57.87 (d), 26.61 (q), 22.63 (q); mass spectral peak match for $C_7H_{17}NS$.

9-(Methylthio)-9-azabicyclo[3.3.1]nonane (4). A solution of 2.25 g of 9-ABN·HCl (vacuum dried at 88 °C, 20 h) in 15 mL of THF was treated with 17.8 mL (1.56 M, 27.8 mmol) of *n*-butyllithium at −78 °C, and after warming the solution to 0 °C for 15 min and recooling to −78 °C, 1.25 mL (13.9 mmol) of dimethyl disulfide in 3 mL of THF was added. After 19 h at room temperature, the mixture was treated with 5 g of Na_2CO_3 dissolved in 25 mL of water and the aqueous layer separated and extracted with 3 × 25 mL of ether. After drying the solution over K_2CO_3, concentration gave 2.37 g of crude product. Two Kugelrohr distillations gave **4** as a colorless liquid: 1.71 g (71.9%); 82–88 °C bp (1.8 mm); ^{1}H NMR ($CDCl_3$) δ 3.08 (br s, 2 H), 2.26 (s, 3 He, 2.1–1.2 (m, 12 H); ^{13}C NMR ($CDCl_3$) δ 57.63 (d), 29.92 (t), 24.18 (q), 20.21 (t); mass spectral peak match for $C_9H_{17}NS$.

(*tert*-Butylthio)dimethylamine (5) was prepared by the method of Himel[34] and purified by distillation (bp 75–80 °C (25 mm)) followed by preparative GC on 15% XF-1150 on Chromosorb W 60/80, 147 °C: ^{1}H NMR ($CDCl_3$) δ 2.71 (s, 6 H), 1.19 (s, 9 H); ^{13}C NMR ($CDCl_3$) δ 51.23 (q), 47.98 (s), 28.60 (q); mass spectral peak match for $C_6H_{15}NS$.

1-(*tert*-Butylthio)pyrrolidine (6) was prepared by the general method of Himel[34] and purified by distillation (bp 76–79 °C (69 mm)), chromatography on alumina (hexane eluent), and preparative GC (XF- 1150, 150 °C): ^{1}H NMR ($CDCl_3$) δ 3.04 (m, 2 H), 1.72 (m, 2 H), 1.18 (s, 9 H); ^{13}C NMR ($CDCl_3$) δ 58.96 (t), 47.70 (s), 28.87 (q), 25.84 (t); mass spectral peak match for $C_8H_{17}NS$.

(*tert*-Butylthio)diisopropylamine (7) was prepared by the method of Himel[34] employing *tert*-butylsulfenyl bromide (bp 120 °C (85 mm)) and purified by column chromatography on alumina (hexene eluent): ^{1}H NMR ($CDCl_3$) δ 3.17 (septet, J = 6.5 Hz, 2 H), 1.16 (s, 9 H), 1.08 (d, J = 6.5 Hz, 12 H); ^{13}C NMR ($CDCl_3$) δ 55.10 (d), 45.55 (s), 29.48 (q), 22.63 (q); mass spectral peak match for $C_{10}H_{23}NS$.

The electrochemical,[12] photoelectron spectroscopic,[20] ^{13}C NMR,[13] and ESR[23] equipment and techniques employed have been described earlier.

Acknowledgment. This work has been partially supported by the National Institutes of Health (GM 25428) and the National Science Foundation (CHE 8026111). We thank Professors Weinhold, Evans, and Fenske of this department for useful discussions.

Registry No. 1, 83312-64-5; **1**$^{+\cdot}$, 83312-70-3; **2**, 7257-48-9; **3**, 83312-65-6; **4**, 83312-66-7; **4**$^{+\cdot}$, 83312-69-0; **5**, 64037-64-5; **6**, 83312-67-8; **7**, 83312-68-9; **8**, 64776-29-0; 9-ABN·HCl, 6760-43-6; 9-ABN·Li, 73309-01-0; pyridine, 110-86-1; tris(*p*-bromophenyl)aminium hexachloroantiminate, 40927-19-3; pyrrolidine, 123-75-1; pyrrolidine lithium salt, 4439-90-1; dimethyl disulfide, 624-92-0; piperidine, 110-89-4; diisopropylamine, 108-18-9; *tert*-butylsulfenyl bromide, 83312-71-4.

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(35) **Note Added in Proof**: Our splittings agree with those reported (Izvoka, A.; Kobayoshi, M. *Chem. Lett.* **1981**, 1603) for trimethyl- and *N,N*-diethyl-*S*-methylsulfenamide radical cations. We only became aware of this paper after ours was submitted.

An Effective Approach to Stereocontrolled Lactone Annulation. Application to the Total Synthesis of Pentalenolactone E Methyl Ester and a Partial Elaboration of Quadrone

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Contribution from the Evans Chemical Laboratories, The Ohio State University, Columbus, Ohio 43210. *Received April 23, 1982*

Abstract: α,β-Unsaturated esters having a diquinane framework are produced through regiocontrolled alkylation of cyclopentanone enolates with methyl 4-bromo-3-methoxycrotonate, base-promoted cyclization, and ketalization. Controlled reduction of the carbalkoxy group, application of the Claisen rearrangement, and implementation of an intramolecular Michael addition–oxidation sequence lead efficiently to tricyclic lactones. Of two such molecules, one has been transformed into pentalenolactone E methyl ester (**2**) and the other investigated as a possible precursor to quadrone. The ketone acetal **16** was transformed into the homologous α,β-unsaturated ester **20b** by iodine oxidation of the corresponding hydrazone and reaction of the vinyl iodide so produced (**20a**) with the nickel carbonyl–sodium methoxide reagent system to arrive at **2**. Unmasking of the lactone functionality was achieved conventionally, and the α-methylene carbon was introduced by heating with methoxymagnesium carbonate at 175 °C followed by suitable condensation with formaldehyde.

Not unexpectedly, the last decade has witnessed revolutionary advances in the field of microbiological fermentation. Of particular note here is the attention that has been paid to *Aspergillus terreus* and certain strains of *Streptomyces*,[2] studies that have been rewarded by the isolation of a rich array of unusually structured products, some of which exhibit intriguing biological activity. Thus, the toxigenic fungus *A. terreus* is known to produce not only metabolites such as terreic acid,[3] quadrone (**1**),[4] aspterric

(1) Merck Fellow, 1981–1982.

(2) Included in this group are *S. chromofuscus*, *S. griseochromogenes*, and *S. baarnensis*.

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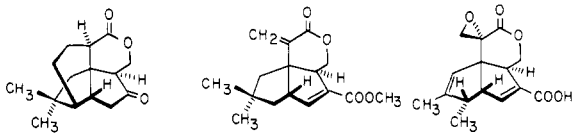


1 2 3

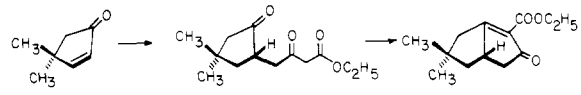
acid,[5] aspergillide B1,[6] and terretonin[7] but toxins such as citrinin[8] and patulin[9] as well. Of these, the isolation of **1** has been accorded the greatest attention among synthetic chemists[10,11] because of its unique tetracyclic nature and reputed antineoplastic properties observable in vitro and in vivo against two types of human carcinoma.[4]

The *Streptomyces* strains in question[2] are capable of biosynthesizing not only neutral metabolites such as pentalenene[12,13] but also more highly oxidized derivatives of this triquinane including pentalenic acid[14,15] and pentalenolactones E (isolated and characterized as its methyl ester **2**),[16,17] G,[18] and H[14] in addition to the antibiotic pentalenolactone (**3**).[19,20]

Because the majority of the stereochemical interrelationships and pendant functional groups in **1–3** share a striking similarity, we developed an interest in designing a synthetic pathway to these natural products that would be characterized by brevity, flexibility, and breadth. In this way, the scheme might also prove adaptable to the synthesis of other six-ring lactones, whether of sesquiterpenoid origin or not. In planning access to these systems, we sought to avoid entirely those possible regiochemical complications that might well arise while locking the lactone ring in place.[10] As will be discussed, the key elements of the new methodology involve kinetically controlled nucleophilic addition to an aldehyde carbonyl group and ensuing intramolecular capture of the resulting alkoxide function by a proximally positioned α,β-unsaturated ketone Michael acceptor.[21] Presently, we detail the experiments by which this simple and perhaps general lactone annulation procedure was successfully applied to a total synthesis of **2** and a partial elaboration of **1**.

Results

Pentalenolactone E Methyl Ester (2). For construction of the basic diquinane framework in **2**, advantage was taken of our awareness that mutual fusion of two five-membered rings via aldol condensation generally requires twofold activation of the enolate to achieve respectable yields.[22,23] Accordingly, the highly exploited 4,4-dimethylcyclopentenone molecule (**4**)[24] was reduced with



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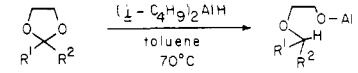
lithium in liquid ammonia[25] for the purpose of regiospecific enolate formation, and this anionic intermediate was condensed directly with methyl 3-methoxy-4-bromocrotonate.[26] Subsequent hydrolysis of the vinyl ether moiety with 30% perchloric acid[26b] delivered the desired diketo ester **5** in 85% overall yield. The bicyclic carbon framework was then established by cyclization in the presence of ethanolic sodium ethoxide, a reaction that proceeded rapidly and efficiently (84%).

With keto ester **6** in hand, attentiion was directed to ketalization of the ketone carbonyl group in order to permit reductive modification of the carbomethoxyl functionality. The strategy hinges on the fact that the primary carbinol that is thereby elaborated is allylic and therefore subject under the proper conditions to Claisen rearrangement. Were this sequence of events to be accomplished, an acetaldehyde residue would become joined to the nearby tertiary angular site and a methylene group would be newly introduced immediately adjacent to the ketal moiety. Furthermore, kinetic and thermodynamic considerations can both be counted on to direct the [3,3] sigmatropic shift to that face of the double bond which ultimately generates a cis-locked bicyclo[3.3.0]octyl system.

It will be appreciated that the selective ketalization of **6** with ethylene glycol to give **9** proceeded without complication. However, the ensuing diisobutylaluminum hydride (Dibal H) reduction of **9** in toluene solution at −78 °C unexpectedly led to overreduction in the form of ketal ring opening. While this phenomenon is not unknown as in the prototypical conversion of **7** to **8**,[27] forcing



7 8

conditions are generally required to accomplish this transformation. Either the proximity of the newly formed allylic alcohol functionality to the ketal provides suitable staging for facile intramolecular delivery of the reducing agent or severe nonbonded CH_3---O compression on the concave surface provides cause for kinetic acceleration of the reduction. This complication can be neatly circumvented by making recourse to diethyl ether at comparable temperatures. Evidently, the greater coordinating ability of this solvent and/or the drop in temperature so modify the activity of the reducing agent that overreduction becomes disfavored. Under these conditions, **10** was obtained in 76% yield.

Conventional vinyl ether formation to provide **11**, thermal isomerization of **11** in decalin at 145–150 °C for 2 h, and then deblocking of **12** with pyridinium tosylate in aqueous acetone[28] afforded the highly functionalized bicyclic **13** in good overall yield.

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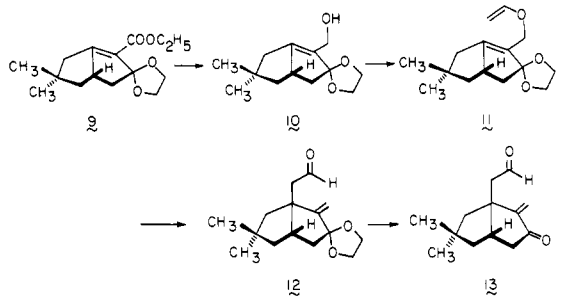
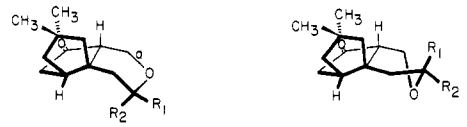


Evidence that the ring-juncture stereochemistry in **13** was indeed cis as shown was rationalized initially on the basis of its ^{1}H NMR spectrum (see Experimental Section) and confirmed fully by the chemical sequel.

An examination of molecular models provided evidence that the pπ orbitals of the aldehyde carbonyl group in **13** were sterically impeded from aligning themselves above the π orbitals of the exocyclic methylene fragment of the α,β-unsaturated ketone to achieve suitable overlap. On the contrary, when the aldehyde carbonyl carbon was transformed into a tetrahedral center such as would occur upon addition of some nucleophilic agent, orbital alignment between the alkoxide center and the β-carbon of the underlying enone was vastly improved.[29] These qualitative observations signaled to us that intramolecular Michael addition within **13** would be particularly facilitated under the latter circumstances. Consequently, chemospecific nucleophilic attack at the aldehydo group emerged as the next important goal.

To our knowledge, few model systems have been devised that might foreshadow the relative electrophilicities of the CHO and enone subunits toward oxygen-centered nucleophiles.[30] In this connection, the response of **13** proved to be entirely as expected. Thus, treatment with a catalytic quantity of sodium methoxide in methanol solution at room temperature provided **16** as a single stereoisomer in 91% yield. The stereochemistry of **16** is not known

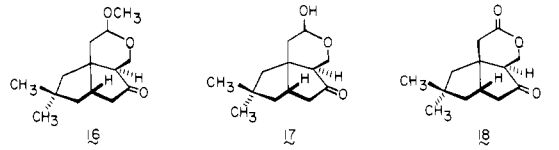


14 **15**

a, $R_1 = OCH_3$, $R_2 = H$; **b**, $R_1 = H$, $R_2 = OCH_3$

with certainty. At the mechanistic level, it is entirely plausible that 1,2 addition of methoxide ion across the aldehydic carbonyl group occurs rapidly and reversibly without significant steric impedence. As the (presumed) rate-controlling cyclization step is undertaken, discrimination between an exo (**14a**) or endo (**14b**) methoxyl substitution plan in a boat-shaped heterocyclic ring is forced upon the system as bond a is formed from the axial direction. Gross steric considerations should favor **14a**. Realignment to the more energetically favored twist-boat conformation **15a** can be expected following arrival at **14**. In this maneuver, the methoxyl group becomes axially projected, a situation favored by the anomeric effect of the proximal oxygen, if indeed operative. Alternatively, the pathway involving **14b** and **15b** gives rise to eventual equatorial orientation of this substituent. An additional requirement in either case is "endo" proton delivery following the conjugate addition. This auxiliary key point will be established in the ensuing section of this paper. Suffice it to say that the 14-line ^{13}C NMR spectrum of **16** clearly mitigates against the operation of both schemes.

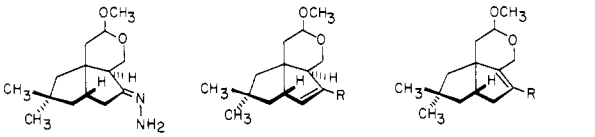
Analogously, cyclization of **13** in tetrahydrofuran containing low concentrations of aqueous sodium hydroxide delivered a lactol (**17**), Collins oxidation of which gave the desired **18**. The lactone-ring protons of **18** were noted to compare closely to those of **2**, thereby suggesting that the newly generated chiral center



16 **17** **18**

α to the ketone group had been properly introduced.

Since further progress in the desired direction was predicted upon proper homologation of the cyclopentanone ring in **16** to an α,β-unsaturated ester, we next attempted to deal with this synthetic transformation in more obvious ways. However, it soon became clear that **16** was particualrly susceptible to Grob fragmentation when molar equivalents of reasonably basic reagents such as methylenetriphenylphosphorane, lithio-1,3-dithiane, and trimethylsulfoxonium methylide were introduced.[31] Additionally, a proposed scheme involving trimethylsilyl cyanide addition to **16** was impractical because of an obviously unfavorable equilibrium favoring the keto form. In the end, these complications were surmounted by predisposing **16** to oxidation by carefully controlled conversion to its hydrazone (**19**, 92%). Attention was then

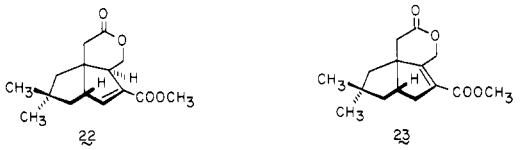


19 **20a**, R = I; **b**, R = $COOCH_3$ **21a**, R = I; **b**, R = $COOCH_3$

centered upon reaction of **19** with iodine in the presence of a tertiary amine.[32] In all cases, the desired vinyl iodide **20a** was found to be admixed with its double-bond regioisomer **21a**. Since the product ratio did show a direct dependence on the particular amine base employed [$(i\text{-Pr})_2$EtN, 1:0.75; $Me_2NCH_2CH_2NMe_2$, 2.22:1, MeN(C=NH)NMe_2, 1.6:1; 4-(dimethylamino)pyridine, 1.42:1; Et_3N, 1.38:1; pyridine, 1.33:1], we were persuaded to proceed with trimethylamine (2.2:1, 75%) since it provided the most favorable relative percentage and yield of **20a**. Although the data are not logically persuasive, the relative amounts of the two iodides appear to be more directly correlatable to the steric bulk of the base than its pK_a. Fortunately, separation of these positional isomers could be achieved by silica gel chromatography.

The availability of **20a** allowed for direct introduction of a carbomethoxy group by condensation with the nickel carbonyl–sodium methoxide reagent in methanol.[33] This simple procedure afforded **20b** very efficiently (93% yield). When **21a** was comparably treated, ester **21b** was produced as cleanly. In neither case was double-bond isomerization or acetal destruction in evidence.

The ready accessibility to **20b** by the preceding protocol set the stage for completion of the synthesis. Thus, sequential exposure of **20b** to acidic hydrolysis in aqueous acetone and Jones oxidation[20b] resulted in efficient unmasking of the lactone functionality and formation of **22**. The acidic conditions that were utilized



22 **23**

to arrive at the lactol stage were noted to give rise to an epimeric mixture as evidenced by twinning of the methyl and vinyl ^{1}H NMR signals, as well as noticeable broadening of the anomeric

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proton adsorption. Interestingly, hydrolysis–oxidation of **21b** afforded a 2.5:1 mixture of **23** and **22**. All attempts to enhance the relative proportion of **22** in this mixture were to no avail.

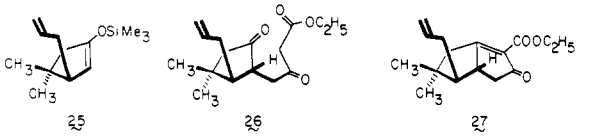
There remained the task of introducing a methylene group α to the lactone carbonyl. However, this site is subject to appreciable steric shielding by the exo geminal methyl group. For this reason, *tert*-butoxybis(dimethylamino)methane[34] and its methoxy congener were ineffective in promoting conversion to the vinylogous amide. The need for more elevated temperatures was, however, conveniently and efficiently accommodated by methoxymagnesium carbonate.[35] Subsequent exposure of the lactonic acid so formed with 37% formalin solution containing dimethylamine, sodium acetate, and acetic acid[36] provided in 27% overall yield the target molecule **2**, which was identical with the natural substance by comparison of IR, ^{1}H NMR, and ^{13}C NMR spectra.[37] The total synthesis of pentalenolactone E methyl ester was thus realized in 15 steps with an overall yield of 2.2%.

Quadrone (1). The structural features of quadrone (**1**) are seen to be especially closely related to those of keto lactone **18** prepared above. Consequently, the possibility suggested by intramolecular S_N2 displacement within an enolate anion such as **24** presented itself. Before we progress to describe our experiments in this area, explicit discussion of two assumptions implicit in the **24** → **1** closure step is warranted. Firstly, it must be recognized that

1 **24**

quadrone is a significantly more strained molecule than pentalenolactone E. Dreiding models of **1** indicate further that the stress may be most heavily concentrated in that six-membered ring which we desire to form during the cyclization of **24**. In actuality, this added strain may underlie the ability of quadrone to experience retro-Michael fragmentation with release of an electrophilic α-methylene ketone moiety, the potential source of its biological activity.[38] Secondly, among the activation energy requirements associated with the conversion of **24** to **1** is the need to project the XCH_2CH_2– side chain into a rather acute quasi-axial orientation. Since the normal conformational disposition of groups attached in this manner to a *cis*-bicyclo[3.3.0]octane framework is quasi-equatorial, the substrate must improvise at least a partial alteration in its ground-state geometry. For this to occur, the anion most likely would require some degree of heating. Since lactone enolates are not known for their thermal stability, a balance must necessarily be struck between conditions conducive to C–C bond formation and enolate degradation. Despite the improvisations that these considerations were certain to demand, we proceeded to investigate this synthetic path to quadrone in view of the practical and expedient manner in which its other three rings were certain to be assembled.

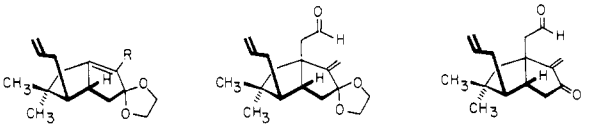
When conjugate addition of allylmagnesium bromide[39] to **4** was carried out in the presence of $CuBr{\cdot}Me_2S$[40] and the resulting enolate was captured with chlorotrimethylsilane and triethylamine,[41] the only product isolated was **25**. Subsequent anion release with lithium amide in ammonia–tetrahydrofuran[41] and alkylation–hydrolysis as before gave **26** in 62% overall yield in a very efficient and regiospecific manner. Addition in this manner



25 **26** **27**

also takes maximum advantage of the allyl group as a stereocontrol element and leads to exclusive trans introduction of the keto ester side chain. Further, our plans called for maintaining the allyl unit in its intact state until completion of the tricyclic staging, at which point oxidative degradation would be implemented. Upon arrival at **27**, ^{13}C NMR spectroscopy gave clear indication of isomeric purity.

Generation of key intermediate **28c** was not anticipated to present complications and did not. Consequently, the stage was



28 a, R = $COOC_2H_5$; b, R = CH_2OH; c, R = $CH_2OCH=CH_2$ **29** **30**

set to ascertain whether the allyl group might exert steric factors unfavorable to the course of the Claisen rearrangement. Since **29** was obtained with an efficiency (68%) comparable to that earlier noted for **12**, the quasi-equatorial disposition of the additional side chain was clearly not disadvantageous. Its susceptibility to lactone annulation was probed following deketalization to give **30**. Sequential exposure to sodium hydroxide in aqueous tetrahydrofuran and the Jones reagent resulted in clean conversion to **31** in 52% overall isolated yield.

Although certain features of the ^{1}H NMR spectrum of this product were strikingly similar to those of **2**, rigorous definition of this lactone's stereochemistry was considered desirable. In view of the oily nature of all the intermediates prepared to this juncture, a suitable crystalline derivative was sought. Idealistically, we sought to interweave this exercise with the requisite ketone carbonyl blocking step. To this end, the chemoselective reduction of **31** with *tert*-butylamine–borane[42] in tetrahydrofuran at 0 °C

31 **32** a, R_1 = OH, R_2 = H; b, R_1 = H, R_2 = OH; c, R_1 = OCH_2Ph, R_2 = H

was deployed, and the resulting mixture of secondary alcohols **32a** and **32b** (*ca* 1:1) was alkylated with benzyl triflate[43] in dichloromethane solution at −35 °C. Under these conditions, only exo isomer **32a** is sufficiently reactive to undergo alkylation since **32b** is recovered intact. Accordingly, the stereochemically homogeneous, crystalline lactone ether **32c** was easily obtained in a pure state and X-ray crystallographic examination confirmed the all-cis arrangement of the allyl substituent, benzyloxy group, and lactone ring.[21,44]

Conversion of **32c** to iodide **33d** was achieved conventionally. Subsequently, the lithium enolate was generated through the agency of lithium diisopropylamide in tetrahydrofuran at −78 °C. No cyclization was observed at temperatures up to and including

(34) (a) Bredereck, H.; Simchen, G.; Rebsdat, S.; Kantlehner, W.; Horn, P.; Wahl, R.; Hoffmann, H.; Grieshaber, P. *Chem. Ber.* **1968**, *101*, 41. (b) Trost, B. M.; Preckel, M.; Leichter, L. M. *J. Am. Chem. Soc.* **1975**, *97*, 2224. (c) Greenlee, M. L. *Ibid.* **1981**, *103*, 2424.

(35) Finkbeiner, H. L.; Stiles, M. *J. Am. Chem. Soc.* **1963**, *85*, 616.

(36) Parker, W. L.; Johnson, F. *J. Org. Chem.* **1973**, *38*, 2489. For a later example of the use of this reagent, see ref 20b.

(37) We are grateful to Professor David Cane for kindly providing us with the authentic spectra of **2** as obtained from natural resources.

(38) Kupchan, S. M.; Eakin, M. A.; Thomas, A. M. *J. Med. Chem.* **1971**, *14*, 1147.

(39) (a) Klabunde, K. J.; Efner, H. F.; Satek, L.; Donley, W. *J. Organomet. Chem.* **1974**, *71*, 309. (b) Riecke, R. D.; Bales, S. E. *J. Am. Chem. Soc.* **1974**, *96*, 1775.

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

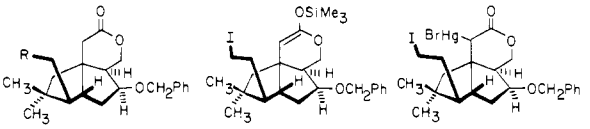
(41) Patterson, J. W., Jr.; Fried, J. H. *J. Org. Chem.* **1974**, *39*, 2506.

(42) (a) Andrews, G. C.; Crawford, T. C. *Tetrahedron Lett.* **1980**, 693. (b) Andrews, G. C. *Ibid.* **1980**, 697.

(43) Lemieux, R. U.; Kondo, T. *Carbohydr. Res.* **1974**, *35*, C4.

(44) Questions concerning this X-ray analysis should be directed to Dr. John Blount, Research Department, Hoffmann-LaRoche, Inc., Nutley, NJ 07110.

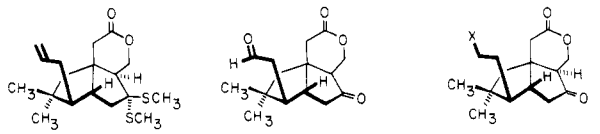
−20 °C as monitored by thin-layer chromatography. The addition of hexamethylphosphoramide at −78 °C resulted in immediate darkening and decomposition of the starting material. There was no doubt that enolate formation had occurred as demonstrated by moderately efficient trapping as the extremely labile trimethylsilyl enol ether **34** (C=C, 1678 cm^{-1}) and more successful conversion to mercuric enolate **35**.[43,44] Unfortunately, photolysis and pyrolysis of **35** served to generate a myriad of products. Time was not lost in their attempted separation and characterization.



33 g, R = CHO
b, R = CH_2OH
c, R = CH_2OTs
d, R = CH_2I

34 **35**

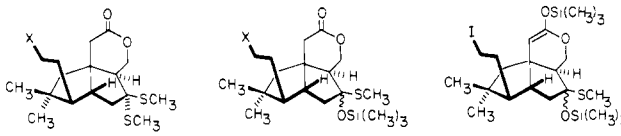
Since these benzyl ether derivatives did not appear amenable to intramolecular ring-opening reactions, attention was directed to alternative cyclization possibilities. Prompted by the finding that keto lactone **31** enters readily into zinc iodide promoted reaction with (methylthio)trimethylsilane[45] to give **36**,[46] we sought



36 **37**

38 g, X = OH
b, X = OTs
c, X = I

to apply the analogous transformation to tosylate **38b** and **38c**. After ozonolysis of **31** and direct reduction of aldehyde **37** with *tert*-butylamine–borane at 0 °C, alcohol **38a** was obtained in 54% overall yield. Once tosylation had been effected, it was discovered that **38b** was insoluble in ether, the solvent utilized in the preparation of **36**. On the basis of existing recommendations,[45] recourse was therefore made to acetonitrile and chloroform. In acetonitrile, the hemithioketal trimethylsilyl ether **40a** was isolated as the sole



39 g, X = OTs
b, X = I

40 g, X = OTs
b, X = I

41

product (configuration not established). When chloroform was used, a mixture of **39a** and **40a** resulted, and this ratio remained unchanged even on prolonged exposure to the reagents. The same fate awaited **36c**, which delivered both **39b** and **40b**. Although this pair of iodides could be separated by application of rapid thin-layer-chromatographic techniques, preparative-scale separations led to their decomposition. Supplies of the intermediates were consequently severely limited.

In any case, the silylated ketene acetal **41** was obtained and treated with silver perchlorate in toluene at −78–0 °C and with silver fluoride in pyridine at room temperature. In neither instance was evidence obtained that heterolytic C–I bond fission with intramolecular electrophile capture by the proximate electron-rich double bond had occurred.

Although this basic strategy as an approach to quadrone appears unworkable, the option involving cleavage of the lactone ring in **33** and **36** prior to C–C bond formation remains open. However, because this methodology has served as the key elements of the earlier successful routes to **1**,[10,11] experiments along these lines were not carried forward. Notwithstanding, the tandem Claisen rearrangement–nucleophile-induced cyclization demonstrated herein is considered to hold considerable promise as an important technique for six-ring lactone annulation.

Experimental Section

Melting points were determined on a Thomas-Hoover melting-point apparatus and are uncorrected. ^1H NMR spectra were recorded at 90 (Varian EM-390) or 200 MHz (Bruker WP-200). ^{13}C NMR spectra were obtained with a Bruker WP-80 instrument. Infrared spectra were determined on a Perkin-Elmer Model 467 instrument. Mass spectra were recorded on an AEI-MS9 spectrometer at an ionization potential of 70 eV. Elemental analyses were performed by the Scandinavian Microanalytical Laboratory, Herlev, Denmark.

Ethyl 4,4-Dimethyl-2-oxocyclopentaneacetoacetate (5). A mixture of 4,4-dimethyl-2-cyclopentenone (5.0 g, 45.5 mmol) and *tert*-butyl alcohol (3.36 g, 45.4 mmol) in tetrahydrofuran (30 mL) was added to a solution of lithium (663 mg, 94.7 mmol) in liquid ammonia (900 mL) over a 30-min period. After an additional 10 min, the mixture was diluted with tetrahydrofuran (900 mL) and methyl 3-methoxy-4-bromocrotonate (55 g, 245 mmol) was added as rapidly as possible. After the solution was warmed to room temperature, the reaction mixture was partitioned between water (500 mL) and ether (700 mL). The organic phase was removed, dried, and evaporated. The crude product was redissolved in dichloromethane (500 mL) and stirred with 30% perchloric acid (100 mL) for 3 h. Removal of the organic phase, drying, and evaporation left an oil, which was chromatographed on silica gel (elution with 2:1 hexane–ether). There was isolated 9.2 g (85%) of **5**: IR (cm^{-1}, film) 3940, 1735, 1400, 1360, 1305, 1250, 1130, 1120; ^1H NMR ($CDCl_3$) δ 4.13 (q, J = 7 Hz, 2 H), 3.41 (s, 2 H), 3.05–2.46 (series of m, 3 H), 2.13 (s, 2 H), 2.06–1.40 (m, 2 H), 1.33–1.20 (m, 6 H), 1.11 (s, 3 H); MS, m/e (M^+) calcd 240.1361, obsd 240.1355.

Ethyl 2,3,3a,4,5,6-Hexahydro-5,5-dimethyl-2-oxo-1-pentalenecarboxylate (6). A solution of sodium ethoxide (250 mg, 3.67 mmol) in 2 mL of ethanol was added dropwise to **5** (4.1 g, 17.1 mmol) in 1 L of ethanol at room temperature. After 1.5 h, saturated ammonium chloride solution (50 mL) was added and the solvent was removed under reduced pressure. The residual oil was redissolved in ether (200 mL), and the ethereal solution was washed with water (200 mL). After drying and solvent evaporation, **6** was obtained as a colorless, crystalline solid (3.17 g, 84%): mp 76.5–77 °C (from ether–hexane); IR (cm^{-1}, CH_2Cl_2) 3040, 2950, 1740, 1710, 1633, 1365, 1335, 1308, 1228, 1175, 1048; ^1H NMR ($CDCl_3$) δ 4.26 (q, J = 7 Hz, 2 H), 3.4–2.96 (m, 1 H), 2.87–2.61 (m, 3 H), 2.27–1.90 (m, 3 H), 1.33 (t, J = 7 Hz, 3 H), 1.25 (s, 3 H), 1.20 (s, 3 H); MS, m/e (M^+) calcd 222.1256, obsd 222.1263.

Anal. Calcd for $C_{13}H_{18}O_3$: C, 70.24; H, 8.13. Found: C, 70.09; H, 8.13.

Ethyl 4′,5′,6′,6′a-Tetrahydro-5′,5′-dimethylspiro[1,3-dioxolane-2,2′-(1*H*)-pentalene]-3′-carboxylate (9). A mixture of **6** (3.00 g, 13.5 mmol), benzene (200 mL), ethylene glycol (5 mL), and a trace of *p*-toluenesulfonic acid was heated at the reflux temperature for 1 day. The cooled reaction mixture was washed with saturated sodium bicarbonate solution, dried, and concentrated. Column chromatography of the residue on Florisil (elution with 1:1 ethyl acetate–petroleum ether) afforded 3.31 g (92%) of **9** as a pale yellow oil: IR (cm^{-1}, film) 2960, 1725, 1305, 1285, 1180, 1040; ^1H NMR ($CDCl_3$) δ 4.37–3.67 (series of m, 6 H), 3.27–2.87 (m, 1 H), 2.57–2.00 (m, 4 H), 1.93–1.56 (m, 2 H), 1.30 (t, J = 7 Hz, 3 H), 1.13 (s, 6 H): MS m/e (M^+) calcd 266.1518, obsd 266.1526.

4′,5′,6′,6′a-Tetrahydro-5′,5′-dimethylspiro[1,3-dioxolane-2,2′(1*H*)-pentalene]-3′-methanol (10). A solution of **9** (2.42 g, 9.1 mmol) in ether was cooled to −116 °C (ether–liquid nitrogen bath) and 20 mL of a cold (−78 °C) 1 M diisobutylammonium hydride solution in hexane (20 mmol) was transferred in via canula as rapidly as possible. The reaction mixture was stirred at −116 °C for an additional hour, allowed to warm to room temperature overnight, recooled to 0 °C, and treated with saturated ammonium chloride solution (20 mL). After 2.5 h at room temperature, the product was extracted into ether, and the combined organic layers were dried and concentrated. After chromatography on Florisil (elution with 1:1 ethyl acetate–petroleum ether), there was obtained 1.53 g (76%) of **10** as a somewhat unstable, white crystalline solid: mp 47.5–49 °C (from hexanes); IR (cm^{-1}, CCl_4) 3500, 2940, 2870, 1690, 1265, 1175, 1120, 1030; ^1H NMR (CCl_4) δ 4.13–3.63 (m, 6 H), 3.20–2.70 (m, 1 H), 2.47–1.97 (m, 4 H), 1.90–1.37 (m, 2 H), 1.10 (s, 6 H); MS, m/e (M^+) calcd 224.1412, obsd 224.1403.

4′,5′,6′,6′a-Tetrahydro-5′,5′-dimethyl-3′-[(vinyloxy)methyl]spiro[1,3-dioxolane-2,2′(1′*H*)-pentalene] (11). Mercuric acetate (600 mg, 1.84

(45) House, H. O.; Auerbach, R. A.; Gall, M.; Peet, N. P. *J. Org. Chem.* **1973**, *78*, 514.
(46) Russell, G. A.; Hershberger, J.; Owens, K. *J. Am. Chem. Soc.* **1979**, *101*, 1312.
(47) Evans, D. A.; Grimm, K. G.; Truesdale, L. K. *J. Am. Chem. Soc.* **1975**, *97*, 3229. Evans, D. A.; Truesdale, L. K.; Grimm, K. G.; Nesbitt, S. L. *Ibid.* **1977**, *99*, 500.
(48) Dithioketal **36** is not a serviceable intermediate since it would not prove stable to the ozonolysis conditions that would follow.

mmol) in ethyl vinyl ether (5 mL) was added to a solution of **10** (862 mg, 3.85 mmol) in the same solvent (20 mL). The reaction mixture was stirred at room temeprature for 48 h, poured into ether (100 mL), washed with water (100 mL), dried, and evaporated. The crude product was purified by Florisil chromatography (elution with 2:1 hexanes–ether) and isolated as a colorless oil (787 mg, 82%): IR (cm^{-1}, film) 2945, 2925, 2885, 2839, 1612, 1313, 1195, 1102; ^1H NMR ($CDCl_3$) δ 6.42 (dd, J = 15 and 6 Hz, 1 H), 4.25–3.85 (m, 6 H), 3.80–3.61 (m, 2H), 2.93–2.71 (m, 1 H), 2.47 (s, 2 H), 2.10 (s, 4 H), 1.13 (s, 6 H); MS, m/e (M^+) calcd 250.1569, obsd 250.1576.

Tetrahydro-5′,5′-dimethyl-3′-methylenespiro[1,3-dioxolane-2,2′-(1′*H*)-pentalene]-3′a(3′*H*)-acetaldehyde (12). A solution of **11** (767 mg, 3.06 mmol) in decalin (4 mL) was heated at 145 °C for 4 h. Subsequent Florisil chromatography (elution with 6:1 hexane–ether) furnished 584 mg (76%) of analytically pure **12**: IR (cm^{-1}, film) 2930, 2860, 2710, 1720, 1120, 1050, 1025, 935, 905; ^1H NMR ($CDCl_3$) δ 9.82 (t, J = 3 Hz, 1 H), 5.27 (s, 1 H), 5.01 (s, 1 H), 4.11–3.86 (m, 4 H), 2.77 and 2.53 (ABX, J_{AB} = 15 Hz, J_{AX} = J_{BX} = 3 Hz, 2 H), 2.53–1.26 (series of m, 7 H), 1.02 (s, 6 H).

Anal. Calcd for $C_{15}H_{22}O_3$: C, 71.97; H, 8.86. Found: C, 71.86; H, 8.86.

Hydrolysis of 12. A mixture of **12** (365 mg, 1.42 mmol), pyridinium tosylate (36.5 mg, 0.142 mmol), and water (0.5 mL) in acetone (15 mL) was stirred at room temperature for 4 h. The solvent was evaporated, and the residue was taken up in ether, washed with water, dried, and concentrated. Keto aldehyde **13** was obtained as a colorless oil (300 mg, 100%): IR (cm^{-1}, film) 2940, 2855, 2715, 1720, 1625, 1458, 1395, 1360, 1110, 935; ^1H NMR ($CDCl_3$) δ 9.64 (t, J = 1 Hz, 1 H), 6.10 (s, 1 H), 5.33 (s, 1 H), 2.80 (d, J = 2 Hz, 2 H), 2.7–2.0 (m, 3 H), 1.96 (s, 2 H), 1.90–1.71 (m, 1 H), 1.30–1.15 (m, 1 H), 1.09 (s, 3 H), 1.01 (s, 3 H); MS, m/e (M^+) calcd 206.1307, obsd 206.1314.

Hexahydro-8,8-dimethylpentaleno[1,6a-*c*]pyran-2,5(1*H*,6*H*)-dione (18). To a well-stirred solution of **13** (70 mg, 0.34 mmol) in 3:1 tetrahydrofuran–water (5 mL) was added 2 drops of 10% sodium hydroxide solution, and the reaction mixture was stirred at room temperature for 2 h, poured into water, and extracted with ether. After drying and solvent evaporation, the residue was added to a slurry of Collins reagent (1.0 g, 3.9 mmol) in dry dichloromethane (10 mL) and stirred at room temperature for 3 h. The solvent was decanted, the salts were triturated with ether, and the combined organic layers were filtered through Celite. The filtrate was concentrated, and the lactone was purified by MPLC on silica gel (elution with 1:1 ethyl acetate–petroleum ether). There was isolated 27 mg (36%) of **18** as a clear, colorless oil: IR (cm^{-1}, CCl_4) 2950, 2880, 1750, 1460, 1370, 1240; ^1H NMR ($CDCl_3$) δ 4.28 (d, J = 5 Hz, 2 H), 2.55 (s, 2 H), 2.73–1.03 (series of m, 8 H), 1.13 (s, 3 H), 1.10 (s, 3 H); MS, m/e (M^+) calcd 222.1256, obsd 222.1263.

Octahydro-2-methoxy-8,8-dimethylpentaleno[1,6a-*c*]pyran-5(6*H*)-one (16). To a well-stirred solution of **13** (460 mg, 2.2 mmol) in dry methanol (15 mL) was added 0.25 mL of 1 M sodium methoxide in methanol, and the mixture was stirred at room temperature for 4 h, treated with saturated ammonium chloride solution (5 mL), and freed of solvent under reduced pressure. The residue was taken up in ether, and this solution was dried and concentrated. After Florisil chromatography (elution with 28% ethyl acetate in petroleum ether), there was obtained 481 mg (90%) of **16** as a clear colorless oil: IR (cm^{-1}, film) 2960, 2880, 1750, 1140, 1110, 1075; ^1H NMR ($CDCl_3$) δ 4.50–3.86 (series of m, 3 H), 3.73–3.26 (m, 1 H), 3.33 (s, 3 H), 2.67–1.17 (series of m, 9 H), 1.10 (s, 3 H), 1.07 (s, 3 H); ^{13}C NMR ($CDCl_3$) ppm 216.74, 100.47, 59.75, 55.69, 54.05, 53.44, 49.19, 47.68, 44.34, 41.24, 40.51 (2 C), 31.12, 30.44; MS, m/e (M^+) calcd 238.1569, obsd 238.1576.

Anal. Calcd for $C_{14}H_{22}O_3$: C, 70.56; H, 9.30. Found: C, 70.49; H, 9.28.

Octahydro-2-methoxy-8,8-dimethylpentaleno[1,6a-*c*]pyran-5(6*H*)-one Hydrazone (19). A magnetically stirred solution containing **16** (881 mg, 3.7 mmol), hydrazine hydrate (5.4 mL, 105 mmol), and triethylamine (1.8 mL, 24.8 mmol) in ethanol (2 mL) was heated at reflux for 1.5 h, poured into water (10 mL), and extracted with ether (3 × 20 mL). The combined organic layers were dried and concentrated to give 860 mg (92%) of **19** as a thick yellow oil, which was used directly: IR (cm^{-1}, CCl_4) 3380, 2920, 2860, 1610, 1445, 1050; MS, m/e (M^+) calcd 252.1838; obsd 252.1845.

1,2,4,4a,6a,7,8,9- and 1,2,4,6,6a,7,8,9-Octahydro-5-iodo-2-methoxy-8,8-dimethylpentaleno[1,6a-*c*]pyran (20a and 21a). A solution of iodine (1.11 g, 4.3 mmol) in tetrahydrofuran (13 mL) was added dropwise to a mixture of hydrazone **19** (160 mg, 0.63 mmol), tetrahydrofuran (13 mL), and trimethylamine (7 mL) at 0 °C. After 20 min, the mixture was poured into ether (160 mL), and the separated organic phase was washed with saturated sodium thiosulfate solution (3 × 20 mL), dried, and evaporated. The residue was immediately chromatographed on Florisil (elution with 9:1 hexanes–ether) to give 165 mg (75%) of a mixture of **20a** and **21a**. These isomers were separated by thick-layer chromatography on silica gel plates (elution with 25:1 hexane–ethyl acetate). Iodide **20a** was obtained as a colorless oil: IR (cm^{-1}, film) 2950, 2930, 1602, 1455, 1380, 1365, 1182, 1152, 1130, 1112, 1062, 1012, 959, 925, 790; ^1H NMR ($CDCl_3$) δ 6.11 (s, 1 H), 4.56 (dd, J = 7 and 6 Hz, 1 H), 3.86–3.41 (m, 2 H), 3.35 (s, 3 H), 2.91–2.63 (m, 2 H), 1.80–1.13 (m, 6 H), 1.05 (s, 3 H), 1.01 (s, 3 H); MS, m/e (M^+) calcd 348.0588, obsd 348.0596.

Anal. Calcd for $C_{24}H_{21}IO_2$: C, 48.29; H, 6.07. Found: C, 48.12; H, 6.10.

For iodide **21a**: IR (cm^{-1}, film) 2940, 2845, 1655, 1442, 1380, 1362, 1230, 1210, 1195, 1138, 1020, 1055, 1020, 935; ^1H NMR ($CDCl_3$) δ 4.47 (dd, J = 8 and 3 Hz, 1 H), 4.35 (0.5AB, J_{AB} = 12 Hz, with additional fine coupling, 1 H), 3.98 (0.5AB, J_{AB} = 12 Hz, 1 H, with additional fine coupling), 3.45 (s, 3 H), 3.10–2.81 (m, 1 H), 2.66–2.23 (m, 2 H), 2.01–1.10 (series of m, 6 H), 1.01 (s, 6 H); MS, m/e (M^+) calcd 348.0588, obsd 348.0596.

Methyl 1,2,4,4a,6a,7,8,9-Octahydro-2-methyl-8,8-dimethylpentaleno-[1,6a-*c*]pyran-5-carboxylate (20b). Nickel carbonyl (2.2 mL, 16.9 mmol) was added to a solution of sodium methoxide (486 mg, 9 mmol) in methanol (15 mL). After 5 min, iodide **20a** (158 mg, 0.454 mmol) was added to 5 mL of the reagent solution, and this mixture was heated at 45 °C for 2 h, during which time a deep blood-red color developed. After the solution was cooled to room temperature, iodine in methanol was added until a red color persisted for 15 min. The solution was poured into ether (100 mL), and the separated organic layer was washed with saturated sodium thiosulfate solution (2 × 50 mL) and dried. Solvent removal left **20b** (118 mg, 93%) as a colorless oil: IR (cm^{-1}, film) 2965, 2950, 2932, 1720, 1625, 1460, 1437, 1365, 1344, 1269, 1255, 1230, 1200, 1190, 1155, 1112, 1062, 1014, 960; ^1H NMR ($CDCl_3$) δ 6.76 (br s, 1 H), 4.65 (t, J = 6.5 Hz, 1 H), 4.05 (ABX, J_{AB} = 12 Hz, J_{AX} = 7.5 Hz, 1 H), 3.70 (s, 3 H), 3.53–3.38 (m, 1 H), 3.33 (s, 3 H), 3.13–2.86 (m, 2 H), 1.90–1.10 (m, 6 H), 1.03 (s, 6 H); MS, m/e (M^+) calcd 280.1674, obsd 280.1684.

Methyl 1,2,4,6,6a,7,8,9-Octahydro-2-methoxy-8,8-dimethylpentaleno-[1,6a-*c*]pyran-5-carboxylate (21b). A 280-mg (0.8 mmol) sample of **21a** was added to 5 mL of the nickel carbonyl–sodium methoxide reagent prepared above. After 2 h at 45 °C, the reaction mixture was worked up in the predescribed fashion to give an oil that was subjected to silica gel chromatography. Elution with 2:1 hexanes–ether afforded **21b** (190 mg, 84%) as a clear, colorless oil: IR (cm^{-1}, film) 2945, 2930, 2849, 1720, 1655, 1430, 1360, 1265, 1200, 1220, 1200, 1138, 1110, 1062, 1015; ^1H NMR ($CDCl_3$) δ 5.07 (0.5ABq, J = 14 Hz, 1 H), 4.65 (dd, J = 7 and 4 Hz, 1 H), 4.22 (0.5ABq, J = 14 Hz, 1 H), 3.68 (s, 3 H), 3.38 (s, 3 H), 3.16–1.20 (series of m, 9 H), 1.02 (s, 6 H); MS, m/e (M^+) calcd 280.1674, obsd 280.1685.

Methyl 1,2,4,4a,6a,7,8,9-Octahydro-8,8-dimethyl-2-oxopentaleno-[1,6a-*c*]pyran-5-carboxylate (22). A solution of **20b** (49 mg, 0.18 mmol) in water (0.5 mL), acetone (1.5 mL), and 10% sulfuric acid (0.25 mL) was stirred at room temperature for 8 h, poured into water (10 mL), and extracted with ether (4 × 10 mL). The combined organic layers were dried and concentrated to give the epimeric lactols (46 mg, 100%) as a pale yellow oil: IR (cm^{-1}, film) 3400, 2920, 1705, 1620, 1430, 1250; ^1H NMR ($CDCl_3$) δ 6.73 (m, 1 H), 5.06 (m, 1 H), 3.70 (s, 3 H), 4.27–2.67 (series of m, 5 H), 2.17–0.83 (series of m, 6 H), 1.07 (s, 3 H), 1.00 (s, 3 H); MS, m/e ($M^+ - H_2O$) calcd 248.1412, obsd 248.1418.

The lactols were immediately taken up in acetone (2 mL), cooled to 0 °C, and treated dropwise with Jones reagent (0.5 mL) until a reddish-yellow color persisted. The reaction mixture was poured into water (10 mL) and extracted with ether (3 × 10 mL). The combined organic layers were dried and concentrated to leave a residue that was chromatographed on silica gel (elution with 1:1 ethyl acetate–petroleum ether). There was isolated 32 mg (69%) of **22** as a clear colorless oil: IR (cm^{-1}, CCl_4) 2930, 1760, 1720, 1625, 1430, 1345, 1250, 1210, 1105, 1075; ^1H NMR ($CDCl_3$) δ 6.78 (m, 1 H), 4.40 (d, J = 4 Hz, 2 H), 3.72 (s, 3 H), 3.60–2.90 (m, 2 H), 2.57 (s, 2 H), 1.97–0.97 (m, 4 H), 1.03 (s, 3 H), 1.00 (s, 3 H); MS, m/e (M^+) calcd 264.1361, obsd 264.1370.

Methyl 1,2,4,6,6a,7,8,9-Octahydro-8,8-dimethyl-2-oxopentaleno[1,6a-*c*]pyran-5-carboxylate (23). A solution of **21b** (35 mg, 0.13 mmol) and 10% sulfuric acid (0.5 mL) in 2:1 water–acetone (2 mL) was stirred at room temperature for 72 h and evaporated. The residue was taken up in ether, and this solution was washed with sodium bicarbonate solution (5 mL), dried, and concentrated. The remaining oil was dissolved in acetone (2 mL), cooled to 0 °C, and treated with Jones reagent until an orange color persisted. The reaction mixture was poured into water and extracted with ether (3 × 5 mL). The combined organic phases were washed with saturated sodium bicarbonate solution, dried, and evaporated. MPLC of the product on silica gel (elution with 3:1 ethyl acetate–petroleum ether) gave **22** (8 mg, 24%) together with **23** (20 mg, 61%) as a clear colorless oil: IR (cm^{-1}, CCl_4) 2940, 2840, 1750, 1715,

1660, 1430, 1260, 1200; ^{1}H NMR ($CDCl_3$) δ 5.64 (d, J = 16.8 Hz, 1 H), 5.08 (dt, J_{AB} = 16.6 Hz, J_{AX} = 3.4 Hz, 1 H), 3.76 (s, 3 H), 3.04–2.87 (m, 1 H), 2.87 (d, J = 16.6 Hz, 1 H), 2.50 (d, J = 16.6 Hz, 1 H), 2.62–2.43 (m, 2 H), 1.98–1.87 (m, 1 H), 1.71 (d, J = 13.2 Hz, 1 H), 1.56 (d, J = 13.2 Hz, 1 H), 1.34–1.18 (m, 1 H), 1.04 (s, 3 H), 1.03 (s, 3 H); MS, m/e (M^+) calcd 264.1361, obsd 264.1370.

Methyl 1,2,4,4a,6a,7,8,9-Octahydro-8,8-dimethyl-1-methylene-2-oxopentaleno[1,6a-*c*]pyran-5-carboxylate (2). Methoxymagnesium carbonate in dimethylformamide (5 mL, ~2 M) was added to **22** (75 mg, 0.28 mmol), and the resulting mixture was heated to 175 °C for 20 min. After cooling, the solution was added to 15 mL of ice-cold 6 N hydrochloric acid and the product was extracted into ether (3 × 50 mL). After drying and evaporation of the combined extracts, the residue was immediately redissolved in 1 mL of a solution prepared from sodium acetate (105 mg) in acetic acid (4 mL) and formalin (2.92 mL) in diethylamine (1.0 mL). This mixture was warmed on a steam bath for 5 min, poured into water (10 mL), and extracted with ether (3 × 25 mL). Drying, solvent evaporation, and silica gel chromatography (elution with 2:1 hexanes–ethyl acetate) gave pentalenolactone E methyl ester (21.3 mg, 27%) with spectral characteristics identical with those of the natural substance.

Ethyl 2-Allyl-3,3-dimethyl-5-oxocyclopentaneacetoacetate (26). Allyl bromide (6.28 g, 52 mmol) in tetrahydrofuran (5 mL) was added to Rieke magnesium (1.40 g, 58.5 mmol) in tetrahydrofuran (60 mL) at −40 °C. After 30 min at this temperature, the mixture was cooled to −78 °C and a solution of the cuprous bromide dimethyl sulfide complex (11.12 g, 52 mmol) in dimethyl sulfide (70 mL) was added dropwise. After 1 h of stirring at −78 °C, 4,4-dimethylcyclopentenone (2.0 g, 18 mmol) in ether (20 mL) was added dropwise over a 4-h period. The mixture was stirred at −78 °C overnight. Trimethylsilyl chloride (12 mL) and triethylamine (11 mL) were added dropwise to the mixture, which was then allowed to warm to 5 °C. At this point, partitioning between hexane (500 mL) and water (500 mL) was effected, and the aqueous phase was extracted with hexanes. After drying and evaporation of the combined organic layers, the residue was dissolved in dimethyl sulfoxide (100 mL), the green solution was extracted with hexanes (3 × 150 mL), and the combined extracts were washed with water (100 mL), dried, and concentrated.

The resulting silyl enol ether (**25**) was taken up in tetrahydrofuran (10 mL) and added to lithium amide (1.31 g, 57 mmol) in liquid ammonia (200 mL) and tetrahydrofuran (80 mL) at −33 °C. After 20 min of stirring, a solution of 3-methoxy-4-bromocrotonate (16 g, 71 mmol) in tetrahydrofuran (10 mL) was added rapidly. After 6 min, solid ammonium chloride was introduced to decompose the remaining lithium amide. The mixture was allowed to warm to 0 °C and was partitioned between ether (600 mL), water (600 mL), and glacial acetic acid (150 mL). The ethereal layer was removed, dried, and evaporated to leave an oil, which was immediately redissolved in dichloromethane (500 mL). This solution was rapidly stirred with 200 mL of 30% perchloric acid. After 2 h, the dichloromethane layer was separated, dried, and concentrated. The oily diketo ester was taken up in 20 mL of a 4:1 hexanes–ether mixture, filtered to remove particulate matter, and reevaporated. Chromatography on silica gel (elution with 4:1 hexanes–ether) furnished **26** as a colorless oil (3.2 g, 62%): IR (cm^{-1}, neat) 2960, 2930, 1740, 1720, 1640, 1465, 1405, 1370, 1180, 1140, 1090, 1030, 910; ^{1}H NMR ($CDCl_3$) δ 6.05–5.60 (m, 1 H), 5.23–4.96 (m, 2 H), 4.20 (q, J = 7 Hz, 2 H), 3.43 (s, 2 H), 2.95 (d, J = 4.5 Hz, 2 H), 2.5–1.76 (m, 6 H), 1.36–1.23 (m, 6 H), 0.96 (s, 3 H); MS m/e (M^+) calcd 280.1674, obsd 280.1681.

Ethyl 4-Allyl-2,3,3a,4,5,6-hexahydro-5,5-dimethyl-2-oxo-1-pentalenecarboxylate (27). A solution of **26** (2.85 g, 10.1 mmol) in ethanol (100 mL) was added to sodium ethoxide (207 mg, 3.0 mmol) in ethanol (600 mL) at 0 °C. The mixture was allowed to warm to room temperature and stirred for a further 2 h. Saturated ammonium chloride solution (100 mL) was added, and the excess solvents were removed under reduced pressure. Extraction of the residue with dichloromethane (200 mL) followed by solvent evaporation and silica gel chromatography gave **27** as a colorless oil (1.99 g, 75%): IR (cm^{-1}, film) 2960, 1747, 1720, 1640, 1370, 1320, 1032; ^{1}H NMR ($CDCl_3$) δ 6.01–5.56 (m, 1 H), 5.20–4.93 (m, 2 H), 4.28 (q, J = 7 Hz, 2 H), 3.05–2.81 (m, 3 H), 2.65–1.93 (m, 4 H), 1.35 (t, J = 7 Hz, 4 H), 1.20 (s, 3 H), 1.1 (s, 3 H); ^{13}C NMR ($CDCl_3$) ppm 203.09, 197.88, 162.43, 137.06, 127.23, 116.49, 60.50, 54.41, 49.37, 45.58, 44.12, 42.66, 34.08, 29.13, 24.52, 14.32; MS, m/e (M^+) calcd 262.1568, obsd 262.1575.

Ethyl 6′-Allyl-4′,5′,6′,6′a-Tetrahydro-5′,5′-dimethylspiro[1,3-dioxolane-2,2′(1′*H*)pentalene]-3′-carboxylate (28a). A mixture of **27** (1.5 g, 5.72 mmol), ethylene glycol (15 mL), *p*-toluenesulfonic acid (100 mg), and benzene (150 mL) was heated under a Dean–Stark trap for 4 h. The cooled solution was diluted with benzene (150 mL), washed with saturated sodium bicarbonate solution (150 mL), dried, and evaporated. There was isolated 1.74 g (99%) of **28a** as a colorless oil: IR (cm^{-1}, film) 2950, 1715, 1367, 1311, 1285, 1200, 1180, 1130, 1035; ^{1}H NMR ($CDCl_3$) δ 5.83–5.53 (m, 1 H), 5.13–4.86 (m, 2 H), 4.30–3.75 (m, 6 H), 2.96–2.68 (m, 1 H), 2.56–2.53 (m, 2 H), 2.41–1.65 (series of m, 4 H), 1.30 (t, J = 6 Hz, 4 H), 1.12 (s, 3 H), 0.98 (s, 3 H); MS, m/e (M^+) calcd 306.1830, obsd 306.1838.

Reduction of 28a. Diisobutylaluminum hydride (4.82 g, 34 mmol) in ether (100 mL) and hexane (30 mL) cooled to −116 °C was added dropwise to a solution of **28a** (3.08 g, 10 mmol) in ether (100 mL) at −116 °C. After 2 h of stirring, the solution was allowed to warm slowly to −78 °C prior to being stirred with acetone (20 mL). The mixture was allowed to warm to −50 °C, added to water (500 mL), and stirred for 1 h. The organic layer was separated, the aqueous phase was extracted with ether (4 × 50 mL), and the combined extracts were dried and evaporated to give the allylic alcohol. Chromatography on Florisil (elution with 1:1 ether–hexane) afforded **28b** as colorless crystals: mp 85–85.5 °C (from ether–hexanes) (1.79 g, 68%); IR (cm^{-1}, $CHCl_3$) 3520, 2955, 2925, 2870, 1695, 1635, 1125, 1055, 1032, 995, 974; ^{1}H NMR ($CDCl_3$) δ 5.98–5.53 (m, 1 H), 5.11–4.85 (m, 2 H), 4.15 (s, 2 H), 4.06–3.78 (m, 4 H), 2.85–2.51 (m, 1 H), 2.38–1.13 (series of m, 8 H), 1.10 (s, 3 H), 0.96 (s, 3 H); MS, m/e (M^+) calcd 264.1725, obsd 264.1732.

Anal. Calcd for $C_{16}H_{24}O_3$: C, 72.69; H, 9.15. Found: C, 72.61; H, 9.02.

6′-Allyl-4′,5′,6′,6′a-tetrahydro-5′,5′-dimethyl-3′-[(vinyloxy)methyl]-spiro[1,3-dioxolane-2,2′(1′*H*)-pentalene] (28c). Mercuric acetate (400 mg, 1.25 mmol) in ethyl vinyl ether (5 mL) was added to a solution of **28b** (457 mg, 1.73 mmol) in ethyl vinyl ether (20 mL), and the mixture was heated at reflux for 6 h and then partitioned between ether (50 mL) and water (50 mL). The ethereal layer was separated, washed with water (2 × 25 mL), dried, and evaporated. Florisil chromatography (elution with 1:2 ether–hexane) afforded **28c** (452 mg, 90%) as a colorless oil: IR (cm^{-1}, film) 3115, 3075, 2960, 2930, 2870, 1640, 1615, 1460, 1425, 1385, 1365, 1320, 1310, 1195, 1155, 1035, 995, 945, 905, 815; ^{1}H NMR ($CDCl_3$) δ 6.50 (dd, J = 12 and 7.5 Hz, 1 H), 6.00–5.55 (m, 1 H), 5.11–4.86 (m, 2 H), 4.31–3.76 (m, 8 H), 2.93–2.57 (m, 1 H), 2.36–1.13 (series of m, 7 H), 1.00 (s, 3 H), 0.96 (s, 3 H); MS, m/e (M^+) calcd 290.1881, obsd 290.1888.

Claisen Rearrangement of 28c. A solution of **28c** (76 mg, 0.262 mmol) in deoxygenated (N_2) decalin (10 mL) was heated at 155 °C for 4 h. After cooling to 80 °C, the decalin was removed in a stream of nitrogen. The residue was purified by chromatography on Florisil (elution with 4:1 hexane–ether) to give **29** as a colorless oil (43 mg, 56%): IR (cm^{-1}, film) 3070, 2950, 2930, 2890, 2725, 1722, 1638, 1365, 1065, 905; ^{1}H NMR ($CDCl_3$) δ 9.63 (t, J = 3 hZ, 1 H), 6.03–5.56 (m, 1 H), 5.28 (s, 1 H), 5.11–4.86 (m, 3 H), 3.97 (s, 4 H), 2.83, 2.56 (ABX, J_{AB} = 15 Hz, J_{AX} = J_{BX} = 3 Hz, 2 H), 2.30–1.06 (series of m, 8 H), 1.03 (s, 3 H), 0.96 (s, 3 H); MS, m/e (M^+) calcd 290.1881, obsd 290.1888.

Hydrolysis of 29. A solution of **29** (43 mg, 0.1 mmol) and pyridinium tosylate (35 mg, 0.15 mmol) in acetone (5 mL) was heated to reflux for 15 min. After solvent evaporation, the residue was redissolved in ether (25 mL), and this solution was washed with saturated sodium bicarbonate solution (2 × 25 mL), dried, and concentrated. There was isolated 33.4 mg (91%) of **30** as a colorless oil: IR (cm^{-1}, film) 3070, 2950, 2860, 2720, 1722, 1635, 1625, 1400, 1365, 1105, 905; ^{1}H NMR ($CDCl_3$) δ 9.65 (t, J = 2 Hz, 1 H), 6.10 (s, 1 H), 6.0–5.53 (m, 1 H), 5.30 (s, 1 H), 5.15–4.89 (m, 2 H), 2.81 (d, J = 2 Hz, 2 H), 2.65–1.76 (series of m, 6 H), 1.43–1.07 (m, 2 H), 1.03 (s, 3 H), 1.00 (s, 3 H); MS, m/e 246.

Anal. Calcd for $C_{16}H_{22}O_2$: C, 78.01; H, 9.00. Found: C, 77.65; H, 8.83.

7-Allylhexahydro-8,8-dimethylpentaleno[1,6a-*c*]pyran-2,5(1*H*,6*H*)-dione (31). Sodium hydroxide solution (5%, 10 drops) was added to a stirred solution of **30** (220 mg, 0.89 mmol) in aqueous tetrahydrofuran (25%, 50 mL). After 1 h, saturated ammonium chloride solution (20 mL) was added and the solvent was evaporated under reduced pressure. The residue was partitioned between water (25 mL) and dichloromethane (50 mL), and the aqueous phase was reextracted with dichloromethane (3 × 50 mL). The combined organic extracts were dried and evaporated, and the resulting oil was taken up in acetone (50 mL), cooled to 0 °C, and treated with a slight excess of Jones reagent. The reaction mixture was allowed to warm to room temperature and 30 min later poured into water (100 mL). The product was extracted into dichloromethane (5 × 100 mL), and the combined organic layers were washed with saturated sodium bicarbonate solution (100 mL), dried, and concentrated. Lactone **31** was isolated as a colorless oil: 121 mg (52%); IR (cm^{-1}, film) 3070, 2960, 2930, 2860, 1740, 1635, 1245, 1065, 905; ^{1}H NMR ($CDCl_3$) δ 6.06–5.51 (m, 1 H), 5.13–4.93 (m, 2 H), 4.35 (d, J = 4.5 Hz, 2 H), 2.66 (s, 2 H), 2.50–1.13 (series of m, 9 H), 1.05 (s, 3 H), 1.00 (s, 3 H); ^{13}C NMR ($CDCl_3$) ppm 217.86, 171.56, 137.45, 116.27, 66.88, 58.38, 56.92 (2 C), 51.77, 46.49, 43.88, 42.48, 42.06, 34.35, 29.01, 23.36; MS, m/e (M^+) calcd 262.1569, obsd 262.1562.

Anal. Calcd for $C_{16}H_{22}O_3$: C, 73.25; H, 8.45. Found: C, 73.18; H, 8.46.

Controlled Reduction of 31. *tert*-Butylamine–borane (61.5 mg, 0.706

mmol) in tetrahydrofuran (1 mL) was added to a cold (0 °C), magnetically stirred solution of **31** in the same solvent (4 mL). After 4 h, the reaction mixture was allowed to warm to room temperature, stirred for 1 h, and poured into 3 M hydrochloric acid (10 mL). The product was extracted into dichloromethane (3 × 20 mL), the combined extracts were dried and evaporated, and the residue was chromatographed on silica gel. Elution with 1:1 ethyl acetate–hexane gave **32a/b** as a clear, oily epimeric mixture (140 mg, 71%): IR (cm^{-1}, film) 3440, 3070, 2960, 2910, 2860, 1745, 1640, 1430, 1385, 1250, 1070, 1040, 905, 725; ^1H NMR ($CDCl_3$) δ 5.93–5.56 (m, 1 H), 5.13–4.88 (m, 2 H), 4.71–4.05 (m, 3 H), 2.63 (d, J = 1 Hz, 2 H), 2.30–1.13 (series of m, 10 H), 1.03 (s, 3 H), 0.93 (s, 3 H); MS, m/e (M^+) calcd 264.1725, obsd 264.1716.

7-Allyl-5-(benzyloxy)octahydro-8,8-dimethylpentaleno[1,6a-*c*]pyran-2(1*H*)-one (32c). Benzyl alcohol (95 mg, 0.88 mmol) and collidine (106.5 mg, 0.88 mmol) in dichloromethane (0.2 mL) were added to trifluoromethanesulfonic anhydride (248 mg, 0.88 mmol) in dichloromethane (0.2 mL) at −60 °C. After 30 min, a solution of **32a/b** (155 mg, 0.587 mmol) and collidine (106.5 mg, 0.88 mmol) in dichloromethane (0.4 mL) was introduced dropwise. After warming the solution to −35 °C, stirring was maintained for 4 h before isopropyl alcohol was added to neutralize the excess reagent. The mixture was partitioned between water (10 mL) and dichloromethane (10 mL). The organic phase was dried and evaporated to leave a residue, which was chromatographed on silica gel. Elution with 1:5 ethyl acetate–hexanes furnished 81 mg (39%) of **32c** as a colorless crystalline solid: mp 68.5–69.1 °C; IR (cm^{-1}, KBr) 3050, 3020, 1950, 1850, 1745, 1635, 1499, 1245, 1095, 900, 725, 685; ^1H NMR ($CDCl_3$) δ 7.3 (s, 5 H), 5.9–5.61 (m, 1 H), 5.06–4.88 (m, 2 H), 4.60, 4.40 (ABq, J_{AB} = 15 Hz, 2 H), 4.30–4.06 (m, 3 H), 2.68, 2.50 (ABq, J_{AB} = 15 Hz, 2 H), 2.33–1.16 (series of m, 9 H), 0.96 (s, 3 H), 0.88 (s, 3 H); MS, m/e (M^+) calcd 354.2195, obsd 354.2187.

Anal. Calcd for $C_{23}H_{30}O_3$: C, 77.93; H, 8.53. Found: C, 77.71; H, 8.47.

5-(Benzyloxy)decahydro-8,8-dimethyl-2-oxopentaleno[1,6a-*c*]pyran-7-acetaldehyde (33a). A solution of **32c** (55 mg, 0.155 mmol) in methanol (15 mL) at −78 °C was treated with excess ozone. After 5 min, excess ozone was removed in a stream of nitrogen and dimethyl sulfide (5 mL) was added. The mixture was allowed to warm to −12 °C and stored overnight in a refrigerator. Removal of the solvent gave aldehyde **33a** (55 mg, ca 100%) as an oil contaminated with trace amounts of dimethyl sulfoxide: IR (cm^{-1}, film) 2950, 2920, 2860, 2710, 1750, 1720, 1250, 1100, 1040, 730, 692; ^1H NMR ($CDCl_3$) δ 9.75 (t, J = 1 Hz, 1 H), 7.31 (s, 5 H), 4.51 (d, J = 1 Hz, 2 H), 4.45–4.15 (m, 3 H), 2.46–1.43 (series of m, 11 H), 0.96 (s, 3 H), 0.90 (s, 3 H); MS, m/e (M^+) calcd 356.1987, obsd 356.1978. This material was used without further purification.

5-(Benzyloxy)octahydro-7-(2-hydroxyethyl)-8,8-dimethylpentaleno-[1,6a-*c*]pyran-2(1*H*)-one (33b). *tert*-Butylamine–borane (13.5 mg, 0.155 mmol) in tetrahydrofuran (0.5 mL) was added to a solution of **33a** (55 mg, 0.153 mmol) in tetrahydrofuran (1.5 mL) at 0 °C. After 30 min, the mixture was poured into 3 M hydrochloric acid (5 mL) and the product was extracted into dichloromethane (5 × 10 mL). Drying and solvent removal furnished 54 mg (100%) of **33b** as an oil: IR (cm^{-1}, film) 3040, 3050, 3020, 2920, 2860, 1750, 1450, 1382, 1362, 1300, 1250, 1080, 928, 690; ^1H NMR ($CDCl_3$) δ 7.33 (s, 5 H), 4.51 (s, 2 H), 4.36–4.08 (m, 3 H), 3.67 (t, J = 6 Hz, 2 H), 2.61 (d, J = 1 Hz, 2 H), 2.35–1.26 (series of m, 10 H), 1.00 (s, 3 H), 0.90 (s, 3 H).

5-(Benzyloxy)octahydro-7-(2-hydroxyethyl)-8,8-dimethylpentaleno-[1,6a-*c*]pyran-2(1*H*)-one *p*-Toluenesulfonate (33c). A crystal of 4-dimethylaminopyridine was added to a solution containing **33b** (54 mg, 0.152 mmol), triethylamine (2 mL), *p*-toluenesulfonyl chloride (34.6 mg, 0.181 mmol) and dichloromethane (2 mL) at 0 °C, which was then stored overnight in a refrigerator. The mixture was poured into water (1 mL) and ether (10 mL). The ether layer was further washed with water (3 × 10 mL), dried, and evaporated. Tosylate **33c** (64 mg, 83%) was obtained as a clear oil: IR (cm^{-1}, film) 2950, 2920, 2855, 1748, 1595, 1355, 1182, 1170, 1090, 923, 650; ^1H NMR ($CDCl_3$) δ 7.77 (AA′, J = 8 Hz, 2 H), 7.35–7.23 (m, 7 H), 4.50 (d, J = 1 Hz, 2 H), 4.36–4.01 (m, 5 H), 2.57 (s, 2 H), 2.43 (s, 3 H), 2.31–0.93 (series of m, 9 H), 0.90 (s, 3 H), 0.83 (s, 3 H).

5-(Benzyloxy)octahydro-7-(2-iodoethyl)-8,8-dimethylpentaleno[1,6a-*c*]pyran-2(1*H*)-one (33d). Sodium iodide was added to a solution of **33c** (64 mg, 0.125 mmol) in acetone (3 mL) until the saturation point was reached. After being stirred for 1 h, the reaction mixture was poured into water (10 mL) and the product was extracted into dichloromethane (4 × 15 mL). Drying and solvent removal gave the iodide (45 mg, 77%) as an oil: IR (cm^{-1}, film) 2950, 2915, 1748, 1255, 1100, 725, 690; ^1H NMR ($CDCl_3$) δ 7.33 (br s, 5 H), 4.56 (s, 2 H), 4.40–4.10 (m, 3 H), 3.36–3.12 (m, 2 H), 2.60 (d, J = 1 Hz, 2 H), 2.42–1.12 (series of m, 9 H), 1.00 (s, 3 H), 0.90 (s, 3 H).

Mercuric Bromide Enolate of 33d. A solution of **33d** (25 mg, 0.053 mmol) in tetrahydrofuran (0.5 mL) was added to lithium diisopropylamide (17.1 mg, 0.16 mmol) in the same solvent (1 mL) at −78 °C. Upon completion of the addition, the mixture was stirred for 60 min and the mercuric bromide (200 mg, 0.55 mmol) was introduced. After another 60 min, the reaction mixture was poured directly into saturated ammonium chloride solution (10 mL). The product was extracted into dichloromethane (3 × 15 mL), and the combined extracts were dried and evaporated to give mercury enolate **35** as an oil (30 mg, 75%): IR (cm^{-1}, film) 2950, 2920, 2860, 1700, 1450, 1260, 1200, 1170, 1100. This intermediate was used directly without further purification.

Dithioketalization of 31. (Methylthio)trimethylsilane (200 mg, 1.6 mmol) was added to a mixture of **31** (20 mg, 0.076 mmol) and zinc iodide (15 mg) in ether (0.1 mL) and stirred overnight at room temperature. Ether (10 mL) and water (10 mL) were added, and the organic phase was dried and evaporated. The residue was chromatographed on silica gel (elution with 2:1 ether–hexanes) to give 15 mg (57%) of **36** as an oil: ^1H NMR ($CDCl_3$) δ 5.93–5.56 (m, 1 H), 5.11–4.83 (m, 2 H), 3.27 (d, J = 5 Hz, 2 H), 2.9–1.16 (series of m, 11 H), 2.20 (s, 3 H), 2.15 (s, 3 H), 1.00 (s, 3 H), 0.93 (s, 3 H); MS, m/e (M^+) calcd 340.1531, obsd 340.1524.

Ozonolysis–Reduction of 31. Ozone was passed through a solution of **31** (178 mg, 0.679 mmol) in methanol (25 mL) at −78 °C until present in excess. After 20 min of stirring at this temperature, the residual ozone was removed by passage of a stream of nitrogen, and dimethyl sulfide (3 mL) was added. The mixture was stored overnight at 0 °C, diluted with tetrahydrofuran (25 mL), and recooled to 0 °C. After dropwise addition of a *tert*-butylamine–borane (39 mg, 0.449 mmol) solution in tetrahydrofuran (3 mL), the reaction mixture was stirred for 15 min, treated with 2 N sulfuric acid (15 mL), and poured into dichloromethane (50 mL). The aqueous phase was further extracted with dichloromethane (2 × 20 mL), and the combined organic layers were dried and evaporated. Chromatography of the product on silica gel (elution with ethyl acetate) gave pure **38a** (97 mg, 54%) as a colorless oil: IR (cm^{-1}, film) 3460, 2920, 2860, 1740, 1360, 1290, 1175, 1070, 1045, 720; ^1H NMR ($CDCl_3$) δ 4.35 (d, J = 5 Hz, 2 H), 3.65 (t, J = 6 Hz, 2 H), 2.67 (s, 2 H), 2.55–1.26 (series of m, 10 H), 1.05 (s, 3 H), 0.97 (s, 3 H); MS, m/e (M^+) calcd 266.1518, obsd 266.1523.

Conversion of 38a to 38b. Triethylamine (175 mg, 1.50 mmol) in dichloromethane (3 mL) was added dropwise to a solution of **38a** (80 mg, 0.3 mmol) and *p*-toluenesulfonyl chloride (63 mg, 3.3 mmol) in the same solvent (10 mL) at 0 °C. After 2 h, the mixture was poured into cold water and the organic phase was dried and evaporated. The resulting crude tosylate was dissolved in acetonitrile (3 mL), and zinc iodide (10 mg) along with (methylthio)trimethylsilane (0.5 mL) were added. After the solution was stirred overnight, water (10 mL) and dichloromethane (10 mL) were introduced, and the organic phase was dried and evaporated to leave **38b** (120 mg, 73%): IR (cm^{-1}, film) 2940, 2910, 1745, 1645, 1350, 1240, 1180, 1170, 880, 835; ^1H NMR ($CDCl_3$) δ 7.63 (d, J = 8 Hz, 2 H), 7.37 (d, J = 8 Hz, 2 H), 4.17 (d, J = 4 Hz, 2 H), 4.0 (t, J = 7 Hz, 2 H), 2.47–1.16 (series of m, 17 H), 0.90 (s, 3 H), 0.81 (s, 3 H), 0.21 (s, 9 H).

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