(series of m, 12 H), 1.46 (s, 3 H), 1.25 (d, J = 7.3 Hz, 3 H), 0.99 (d, J = 6.6 Hz, 3 H); ^{13}C NMR (20 MHz, C_6D_6) 178.83, 146.36, 135.42, 80.37, 78.07, 49.47, 43.74, 41.77, 40.57, 38.76, 34.61, 34.28, 32.91, 27.61, 26.13, 20.12, 16.40, 15.91 ppm; MS, calcd (M^+) m/z 338.1374, obsd 338.1331.

(3*RS*,5*RS*)-Dihydro-3-methyl-5-[(6′*SR*,7′*SR*)-4′,5′,6′,7′-tetrahydro-6′,7′-dimethylspiro[1,3-dithiolane-2,1′-indan]-7′-yl]-3-vinyl-2(3*H*)-furanone (26). Lactone **26** was prepared in a manner identical with **23**. After purification, **26** (28 mg, 23%) was obtained from **25** (111 mg, 0.328 mmol) as a yellow oil: IR (CCl_4, cm^{-1}) 2980, 2940, 1780, 1635, 1440, 1380, 1130, 1020, 925, 690; ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.79 (dd, J = 17.4, 10.5 Hz, 1 H), 5.18 (d, J = 17.4 Hz, 1 H), 5.17 (d, J = 10.2 Hz, 1 H), 4.74 (dd, J = 11.6, 5.4 Hz, 1 H), 3.39–3.16 (m, 4 H), 2.66–2.03 (series of m, 8 H), 1.73–1.59 (m, 3 H), 1.45 (s, 3 H), 1.34 (s, 3 H), 0.98 (d, J = 6.6 Hz, 3 H); MS, calcd (M^+) m/z 364.1530, obsd 364.1529.

(+)-(3*R*,5*S*)-Dihydro-3-methyl-5-[(6′*R*,7′*R*)-4′,5′,6′,7′-tetrahydro-6′,7′-dimethylspiro[1,3-dithiolane-2,1′-indan]-7′-yl]-3-vinyl-2(3*H*)-furanone (27) and Its Enantiomer. Lactone **27** (27.8 mg, 51%), $[\alpha]^{25}_D$ +6.3° (c 1.06, $CHCl_3$), was produced from (+)-**24** (53.0 mg, 0.151 mmol), $[\alpha]^{22}_D$ +36.3°, in a manner analogous to that previously described for its diastereomers. Likewise, (−)-**24** (110 mg, 0.314 mmol), $[\alpha]^{22}_D$ −41.6°, yielded (−)-**27** (23 mg, 20%), $[\alpha]^{23}_D$ −14.0° (c 1.07, $CHCl_3$), as a yellow oil: IR ($CHCl_3$, cm^{-1}) 2965, 2930, 2880, 2840, 1765, 1644, 1456, 1375, 1340, 1198, 1155, 1100, 990, 850; ^{1}H NMR (300 MHz, $CDCl_3$) δ 6.06 (dd, J = 17.5, 10.6 Hz, 1 H), 5.19 (d, J = 17.3 Hz, 1 H), 5.19 (d, J = 10.8 Hz, 1 H), 4.91 (dd, J = 11.5, 5.6 Hz, 1 H), 3.40–3.16 (series of m, 4 H), 2.69 (t, J = 12.1 Hz, 1 H), 2.42–2.04 (series of m, 6 H), 1.98 (dd, J = 12.7, 5.6 Hz, 1 H), 1.75–1.48 (series of m, 3 H), 1.46 (s, 3 H), 1.35 (s, 3 H), 1.00 (d, J = 6.5 Hz, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) 179.45, 145.54, 140.15, 135.09, 114.52, 80.15, 77.73, 49.42, 46.48, 42.75, 40.81, 40.06, 38.24, 34.00, 27.12, 26.31, 26.26, 22.32, 20.94, 16.09 ppm; MS, calcd (M^+) m/z 364.1531, obsd 364.1540.

Acknowledgment. This research was supported by grants from the National Institutes of Health (GM 30827) and the Eli Lilly Company. Quantities of pleuromutilin and tiamulin were generously provided by Dr. Russ Buchman (SDS Biotech), Dr. R. Nagarajan (Eli Lilly company), and Dr Heinz Berner (Sandoz Forschungsinstitut) whom we thank.

(+)-Pleuromutilin Synthetic Studies. Direct Degradation to and Independent Preparation of an Advanced Diketone Intermediate. Demonstration that Reconstruction of the Eight-Membered Ring Suffers from Serious Kinetic Retardation

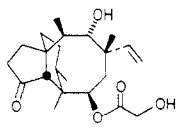
Leo A. Paquette,* Philip C. Bulman-Page,[1] Paul D. Pansegrau, and Paul E. Wiedeman[2]

Evans Chemical Laboratories, The Ohio State University, Columbus, Ohio 43210

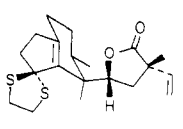
Received August 17, 1987

Levorotatory lactone **2** has been converted into (−)-bicyclic ketone **3**, an intermediate containing all 20 carbon atoms of the pleuromutilin target. Pleuromutilin and tiamulin have in turn been degraded to this important relay compound in only four steps. Various methods for achieving the chemoselective functionalization of **3** are described as a prelude to intramolecular closure of the eight-membered ring. The significant kinetic retardation associated with this process is set in focus.

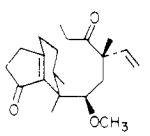
In the preceding paper,[3] an account is given of the degradation of pleuromutilin (**1**) and tiamulin to the levorotatory tricyclic lactone **2**, and the successful implementation of a strategy for de novo synthesis of the latter. These studies established the feasibility of incorporating all of the essential structural features associated with the western sector of these antibiotics, while also providing for a convenient source of **2**. In order to arrive at this first relay point, it was necessary to excise an ethyl group from **1**, in expectation that its later reintroduction could be readily accomplished. Herein, we address the challenge



1



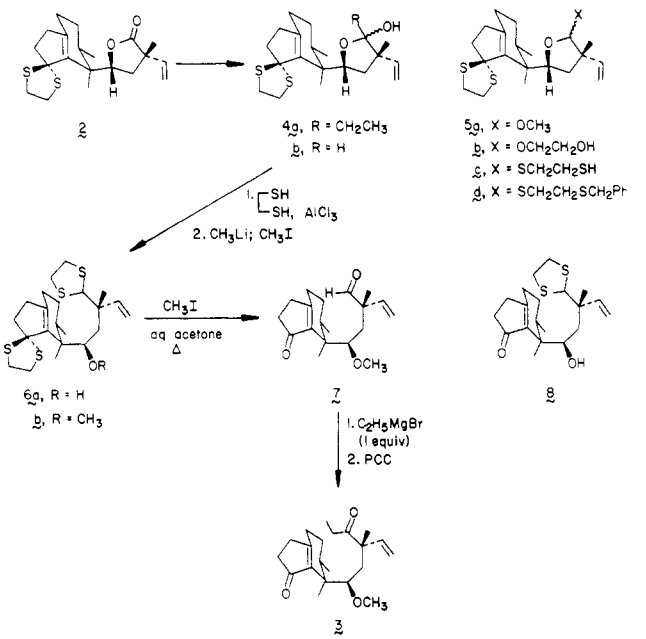
2



3

of transforming (−)-**2** to (−)-**3**. In addition, we report on the readiness with which this *second* relay intermediate can be produced from (+)-**1** and tiamulin.[4] Finally, preliminary experiments aimed at the fundamental problem of reclosing the eight-membered ring are described.

Scheme I



(1) NATO Postdoctoral Fellow of the Science and Engineering Research Council, 1981–1983.
(2) National Science Foundation Predoctoral Fellow, 1981–1984.
(3) Paquette, L. A.; Wiedeman, P. E.; Bulman-Page, P. C. *J. Org. Chem.*, preceding paper in this issue.

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Discussion of Results

Reinsertion of the Two-Carbon Fragment. When **2** was treated with ethyllithium, conversion to tertiary lactol **4a** proceeded smoothly and efficiently (Scheme I). Despite the straightforward nature of this step, all attempts to trap the hydroxy ketone tautomer of this hemiketal were singularly unsuccessful. This could well be a reflection of the heightened level of steric compression about and extent of substitution on the tetrahydrofuran ring. Consequently, recourse was made instead to secondary γ-lactol **4b**. The diisobutylaluminum hydride reduction had to be followed by an entirely aqueous workup to guarantee arrival at **4b**. Use of methanol led instead directly to **5a**.

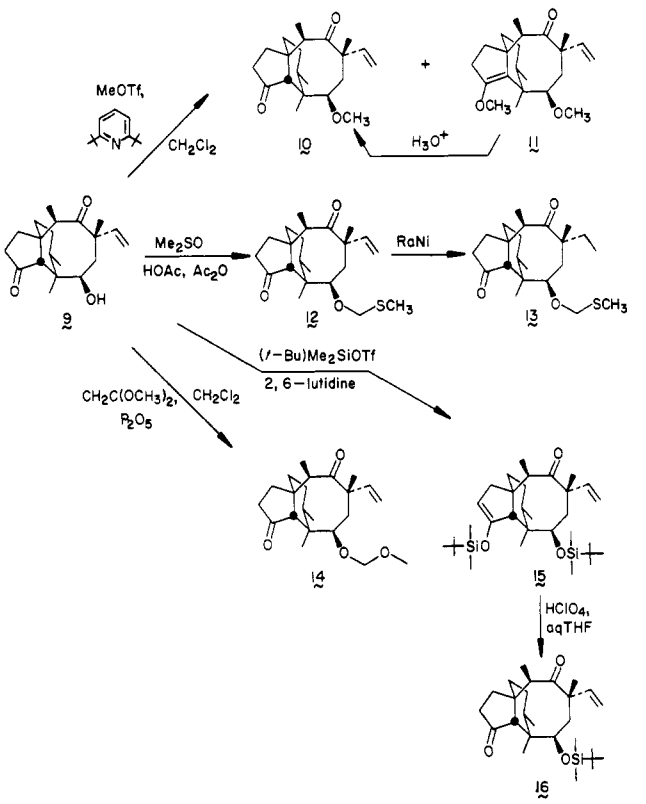
We now envisioned conversion of **4b** to a hydroxy acetal for the purpose of protecting the alcohol group in advance of unmasking the aldehyde functionality. However, direct reaction of **4b** with ethylene glycol and *p*-toluenesulfonic acid or with ethanedithiol (catalysis by pyridinium *p*-toluenesulfonate, *p*-toluenesulfonic acid, or boron trifluoride etherate[5]) gave rise uniquely to **5b** and **5c**, respectively. While the intended formation of **6a** could be achieved by the subsequent exposure of **5c** to anhydrous aluminum chloride, it was more expedient to treat **4b** directly with this Lewis acid in the presence of ethanedithiol.[6] Titanium tetrachloride had previously been shown to be the preferred catalyst for this transformation.[6] In the present circumstances, however, a 2:1 mixture of deblocked enone **8** and **6a** was produced.

Exploitation of the free nature of the hydroxyl group in **6a** led us initially to examine its selective silylation. When *N*-(*tert*-butyldimethylsilyl)-*N*-methyltrifluoroacetamide[7] and *tert*-butyldimethylsilyl triflate[8] failed to enter into reaction, alkylation with the highly reactive benzyl triflate[9] was examined. The single product formed under these circumstances proved to be **5d** (81%)! The desired reaction channel did materialize, however, following deprotonation of **6a** with methyllithium and condensation of the resulting alkoxide at low temperature with a slight excess of methyl iodide.

The unmasking of both carbonyl groups was subsequently realized by heating **6b** with excess methyl iodide in aqueous acetone.[10] The use of heavy metal thiophiles[11] or halogenating agents (iodine; *N*-bromosuccinimide[12]) for hydrolysis resulted in destruction of the starting material.

Despite the neopentyl nature of the aldehyde carbonyl group in **7**, chemoselective addition to this center could be readily achieved because of the almost equally congested topography in the region surrounding the cyclopentenone moiety. The reactivity difference was revealed upon addition of 1 equiv of ethylmagnesium bromide to **7** in ether solution at −100 °C. These conditions served to give largely the desired secondary alcohol, whose PCC oxidation provided **3**, $[\alpha]^{23}_{D}$ −65.5°, in quantitative yield. Since none of the stereocenters in **3** has been disturbed during the six-step transit from **2**, its level of optical purity and that of its precursors should be very high. This conclusion is independently verified in the sequel.

Scheme II



The Short Degradation Route to (−)-3. (−)-Multilone (**9**) can be readily obtained in 85–87% yield by controlled saponification of pleuromutilone or tiamulone. Recourse to 5% potassium hydroxide in methanol causes the predescribed[3] retro-Michael fragmentation to be entirely circumvented, a likely consequence of the lower reaction temperature.

With supplies of (−)-**9** so readily available, suitable protection of its hindered secondary hydroxyl group was next addressed. When the combined action of methyl iodide and silver oxide[13] produced no O-methylation, recourse was made to the more reactive methyl triflate with 2,6-di-*tert*-butylpyridine as acid scavenger.[14] Prolonged exposure (2 days) to several equivalents of these reagents in dichloromethane solution at room temperature produced predominantly **11** and a lesser amount of **10** (Scheme II). Following their chromatographic separation, the enol ether was shown to undergo ready hydrolysis to **10** in the presence of aqueous perchloric or *p*-toluenesulfonic acids. Advantage was taken of this acid lability by simply adding water to the original methylation reaction mixture once **9** had been completely consumed. The triflic acid thereby liberated induced the desired hydrolysis of **11** and delivered **10** in quantitative yield.

Formation of (methylthio)methyl ether **12** was also realized with high efficiency.[15,16] Unfortunately, desulfur-

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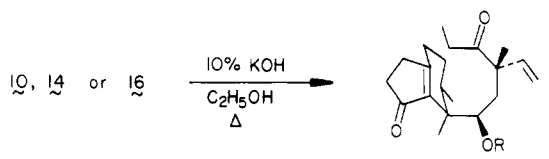
Scheme III



3, R = CH_3
17a, R = CH_2OCH_3
b, R = $SiMe_2t$-Bu

ization was not so productive. For example, all attempts to convert **12** to **10** with Raney nickel[17] proceeded with concomitant saturation of the vinyl double bond and formation of **13**. Nickel boride[15] and deactivated Raney nickel proved ineffective.

Reaction of **9** with dimethoxymethane and phosphorus pentoxide according to Fukui[18] afforded the MOM derivative **14**. Predictably, analogous O-silylation could be achieved as well. Processing (−)-**9** with *tert*-butyldimethylsilyl triflate in the presence of 2,6-lutidine accomplished predominant conversion to **15**, acid hydrolysis of which furnished **16**.

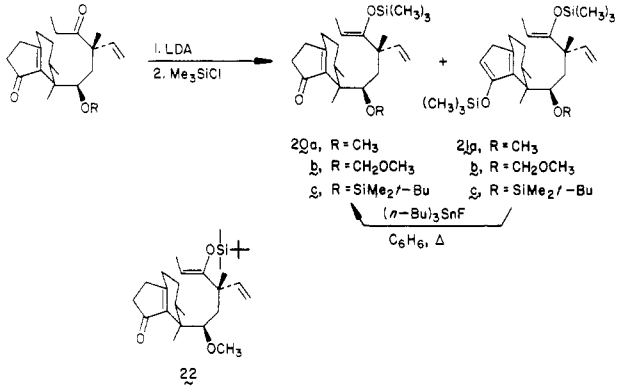
Heating **10**, **14**, or **16** with *ethanolic* potassium hydroxide at the reflux temperature gave **3**, **17a**, and **17b**, respectively (Scheme III). In the specific case of methyl ether **3**, the material was shown by 300-MHz ^1H NMR, IR, and $[\alpha]^{20}_D$ to be identical with the diketone synthesized earlier in Scheme I. Therefore, the linkup has been satisfactorily accomplished.

Attempts to Reconstruct the Cyclooctanone Ring. Already intact in **3** and **17** are the 20 carbon atoms found in the diterpenoid skeleton, as well as all of the oxygen-bearing sites. The next hurdle to overcome was formation of the appropriate cyclooctane C–C bond. From the outset, this issue was viewed as provocative because of the kinetic disadvantages usually associated with intramolecular medium-ring cyclization reactions. Additional complications possibly stemming from a number of nonbonded steric interactions had also not gone unnoticed. Nonetheless, one might consider trying to establish the necessary bond by a number of processes where the two segments of the molecule are properly predetermined to be mutually responsive. In line with this analysis, the next goal became proper distinction between the pair of ketone carbonyl groups in **3** and **17**, as a prelude to attempting ring closure under several fundamentally different types of reaction conditions.

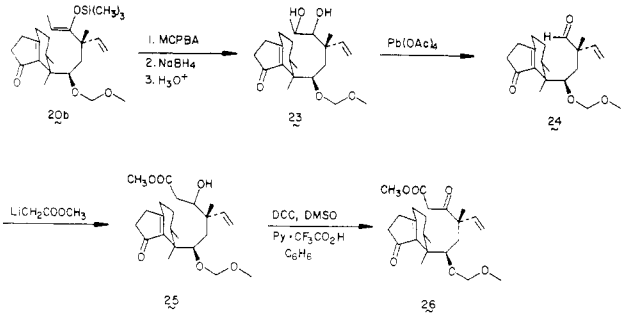
A particularly expedient route would involve intramolecular Michael condensation within the enol or enolate anion of **3**. It will be recalled that the cyclooctane ring in mutilone (**9**) was originally cleaved by reversal of this conjugate addition. However, rather forcing conditions (boiling ethanol) were required to induce this particular transformation. Saponification in hot methanol did not cause ring opening. For this reason, the response of **3** to a wide range of bases and conditions was examined. However, only starting material was recovered in every instance. Selected Lewis acids were also surveyed, but with the same results.

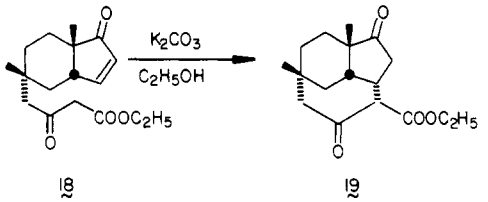
Baraldi and co-workers have reported an example of a successful internal Michael addition where the donor component is a softer β-keto ester enolate anion.[19] The high efficiency (80%) with which **18** is transformed into **19** on exposure to ethanolic potassium carbonate at room temperature prompted consideration of the feasibility of achieving comparable intramolecular cyclization in **26**.

Scheme IV



Scheme V





The synthesis of intermediate **26** is outlined in Schemes IV and V. Exposure of **17a** to 2 equiv of lithium diisopropylamide in tetrahydrofuran followed by chlorotrimethylsilane provided a mixture of mono- (**20b**, 33%) and bis(silyl) enol ethers (**21b**, 46%). Selective hydrolysis of the latter material was achieved by heating with tri-*n*-butyltin fluoride in benzene for 21 h. The added presence of bis(tri-*o*-tolylphosphine)palladium(II) chloride as recommended by Kuwajima and Urabe[20] proved not to be necessary and, in fact, had a retarding effect on this particular process. In contrast, catalysis by Pd(II) worked splendidly in the case of **21a** to furnish **20a** in 84% overall yield as a single stereoisomer. Because kinetically controlled conditions were utilized to set the stereostructure of the enolate in the side chain, the products have been formulated as the *Z*-isomers.[21] *tert*-Butyldimethylsilyl triflate offered somewhat greater chemoselectivity in this

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system and allowed for the direct conversion of **3** to **22** in 50% yield.

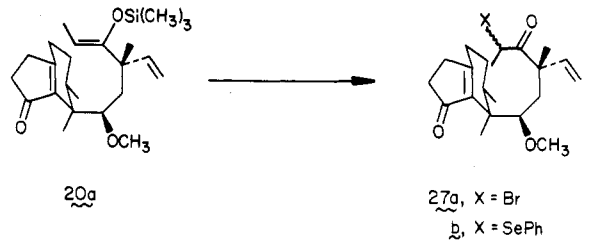
The elaboration of keto aldehyde **24** from **20b** was accomplished in 65–70% overall yield. Initial treatment with 1.2 equiv of *m*-chloroperbenzoic acid proved highly selective and provided the α-siloxy ketone.[22] The fact that the cyclopentenone carbonyl is very hindered permitted regiospecific reduction to the monoprotected 1,2-diol with excess sodium borohydride. Following hydrolysis by brief treatment with aqueous acid, the liberated **23** was exposed to lead tetraacetate in benzene.[23] Two points deserve comment. Direct quenching of the borohydride reaction mixture with 10% sulfuric acid rather than aqueous sodium bicarbonate solution caused the overall yield of **24** to fall to the 50% level. Usefully, this sequence of steps can be carried forward without need for the separation of diastereomers, since they all converge ultimately to **24**.

Reaction of **24** with a twofold excess of the lithium salt of methyl acetate afforded **25** in quantitative yield. Recourse was made to 2 equiv of the nucleophilic species in order to offset its potential consumption by deprotonation of the cyclopentenone. Smith and Levenberg[24] have recommended the Swern protocol[25] as a reliable procedure for β-hydroxy ester oxidation. In the present circumstances, **26** was isolated in only 40% yield after recovery of starting material. Extension of the reaction time and utilization of surplus reagent both led to extensive decomposition. The use of pyridinium chlorochromate[26] gave rise principally to the α,β-unsaturated ester. On the other hand, the Moffatt–Pfitzner procedure[27] lead cleanly to **26** in good yield.

When attention was directed to the possible intramolecular cyclization of **26**, we found that prolonged exposure to potassium carbonate in ethanol at room temperature only caused transesterification. Substitution of magnesium methoxide in methanol returned unchanged keto ester. Attempts to induce carbon–carbon bond formation by warming resulted in formation of the methyl ketone by decarboxylation. These and many other conditions, including exposure of the β-keto acid to Mn(III)[28] gave no detectable cyclization products, despite reasonable precedence to the contrary.[29-31]

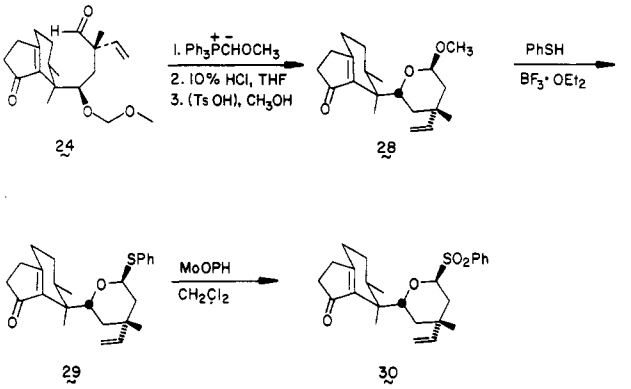
Similarly unrewarding were efforts aimed at the successful implementation of the Mukaiyama reaction.[32] Reversion of **20** to **3** or **17** resulted in every instance ($TiCl_4$,[33,34] $TiCl_4$–$Ti(O\text{-}i\text{-}Pr)_4$,[33,35] $ZnCl_2$,[31] $BF_3{\cdot}OEt_2$,[36] $ZnBr_2$[37]), even when cyclization was attempted with trimethylsilyl triflate.[38]

Scheme VI



20a 27a, X = Br; b, X = SePh

Scheme VII



24 28 29 30

Corriu has demonstrated that cesium fluoride in the presence of either tetramethyl or tetraethyl orthosilicate is an efficient catalyst for Michael condensation.[39] The orthosilicate is believed to generate the base necessary for reaction at the cesium fluoride surface and to trap the enolate anion as the silyl enol ether, which reacts immediately in situ. No intramolecular examples were cited, but highly substituted enones were shown to be responsive. Nevertheless, numerous trial experiments involving **3** gave no evidence for reaction.[40]

The increasing frequency with which free radical reactions are being successfully implemented in the elaboration of relatively complex molecules[42] prompted brief scrutiny of the extent to which the indenone double bond in the present class of molecules might serve as acceptor in conjugate free radical additions.[43] Since **20a** reacted readily with *N*-bromosuccinimide[44] and phenylselenyl chloride[45] to give **27a** and **27b**, respectively, suitable precursors were available for feasibility studies (Scheme VI). Although exposure of **27a** to tri-*n*-butyltin hydride and AIBN[46] in refluxing benzene afforded several products, all retained the enone functionality. Substitution of hexaphenyl- and hexamethylditin[47] curtailed simple reductive

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debromination but did not give rise to products of cyclization. These observations proved to be general.

Simple consideration of molecular models caused us from the outset to suspect that these systems would show little or no proclivity for intramolecular medium-ring closure. However, expectations based on a protocol involving C–C bond formation between atoms having a 1,6-relationship were somewhat higher. The concept is exemplified by **30**. The question being posed is whether the α-sulfonyl carbanion derived from **30** will find it possible to undergo 1,4-addition to the cyclopentenone subunit in the 6-endo-trig mode.[48]

Acetal **28** was conveniently prepared in 65% overall yield from **24** by conversion to the homologous aldehyde with methoxymethylenetriphenylphosphorane[49] and subsequent acidic hydrolysis of the enol ether. Arrival at **28** was achieved by ultimate treatment with methanol and *p*-toluenesulfonic acid (Scheme VIII). Attempted direct conversion of **28** to sulfone **30** by the method of Ley[50] failed to provide the desired product; starting material was recovered quantitatively. However, boron trifluoride etherate in dichloromethane at −78 °C caused thiophenol to replace methanol stereoselectivity. Oxidation of **29** to **30** by means of several conventional reagents (MCPBA,[51] oxone,[52] PhSeSePh–H_2O_2[53]) caused rapid decomposition. The use of oxone in aqueous methanol returned **28**. However, it was found that **29** was transformed into **30** with reasonable efficiency by MoOPH in dichloromethane.[54]

With arrival at **30**, the bifunctional molecule was subjected to a variety of bases in an attempt to induce cyclization.[50,55] The desired C–C bond formation was not observed, signaling that the need to adopt a double-boat transition state is too energy-demanding.

The sequel[56] focuses attention on the use of excited state chemistry in an attempt to overcome the obviously severe steric complications accompanying eight-membered ring closure.

Experimental Section[57]

(3*S*,5*R*)-2-Ethyltetrahydro-3-methyl-5-[(6′*R*,7′*R*)-4′,5′,6′,7′-tetrahydro-6′,7′-dimethylspiro[1,3-dithiolane-2,1′-indan]-7′-yl]-3-vinyl-2-furanol (4a). Lactone **2**[3] (226 mg, 0.621 mmol) dissolved in ether (10 mL) was cooled to −50 °C. A solution of ethyllithium (0.41 mL, 0.62 mmol, 1.5 M in ether) was added dropwise. The reaction mixture was stirred at −50 °C for 1 h, warmed to −20 °C, and stirred for 0.5 h. At that time, the mixture was cooled to −50 °C, and ethyllithium (0.20 mL, 0.30 mmol) was again added dropwise. The solution was allowed to warm to −20 °C and recooled to −50 °C, and the mixture was quenched with saturated ammonium chloride solution (1 mL). After reaching room temperature, the mixture was diluted with water, extracted with ether, dried, and freed of solvent to furnish **4a** (220 mg, 90%) as an unstable yellow oil: IR (neat, cm^{-1}) 3400, 2900, 1700, 1630, 1450, 1370, 1265, 1195, 1115, 1055, 1020, 995, 980, 960, 900; ^1H NMR (300 MHz, $CDCl_3$) δ 6.07–5.75 (m, 1 H), 5.20–4.93 (m, 2 H), 4.64–4.40 (m, 1 H), 3.33–2.98 (m, 4 H), 2.63–0.73 (series of m, 23 H); MS *m/z* ($M^+ - H_2O$) 376.

(3*S*,5*R*)-Tetrahydro-3-methyl-5-[(6′*R*,7′*R*)-4′,5′,6′,7′-tetrahydro-6′,7′-dimethylspiro[1,3-dithiolane-2,1′-indan]-7′-yl]-3-vinyl-2-furanol (4b). A solution of lactone **2** (170 mg, 0.466 mmol) in ether (10 mL) was cooled to −20 °C, and diisobutylaluminum hydride solution (0.60 mL, 0.60 mmol, 1.0 M in hexane) was introduced dropwise. After 30 min, the reaction mixture was cooled to −78 °C, water (1 mL) was added, and the temperature was allowed to warm to 20 °C. The mixture was partitioned between ether and water. A minimum quantity of dilute hydrochloric acid was employed to dissolve the aluminum salts. The organic phase was extracted with saturated sodium bicarbonate solution and water prior to drying. Following solvent removal under reduced pressure, lactol **4b** (167 mg, 98%) was obtained as a yellow oil: IR (neat, cm^{-1}) 3420, 2900, 1630, 1450, 1415, 1360, 1260, 1000, 905, 800, 720; ^1H NMR (300 MHz, $CDCl_3$) δ 6.00–5.80 (m, 1 H), 5.06–4.93 (m, 2 H), 4.81 (br s, 1 H), 4.44 and 4.23 (two dd, *J* = 4.5, 4.5 Hz, 1 H total), 3.31–3.01 (m, 4 H), 2.80 (br s, 1 H), 2.42–1.93 (series of m, 6 H), 1.89–1.47 (m, 3 H), 1.52 and 1.44 (two s, 3 H total), 1.37 (dd, *J* = 11.2, 4.5 Hz, 1 H), 1.09 and 1.05 (two s, 3 H total), 0.96 (d, *J* = 7.7 Hz, 3 H); MS, *m/z* ($M^+ - 2$) 364.

(6′*R*,7′*R*)-4′,5′,6′,7′-Tetrahydro-6′,7′-dimethyl-7′-[(2*R*,4*S*)-tetrahydro-5-methoxy-4-methyl-4-vinyl-2-furyl]-spiro[1,3-dithiolane-2,1′-indan] (5a). Lactol **4b** (410 mg, 1.12 mmol) and 2,6-lutidine (0.2 mL, 1.7 mmol) were dissolved in methylene chloride (20 mL) at room temperature. *tert*-Butyldimethylsilyl trifluoromethanesulfonate (0.5 mL, 2.2 mmol) was added. After being stirred overnight, the reaction mixture contained unreacted starting material. Additional *tert*-butyldimethylsilyl trifluoromethanesulfonate (0.3 mL) was added. When no further change was observed by TLC analysis, methanol (0.5 mL) was added. The mixture was washed with saturated sodium bicarbonate solution, 10% potassium hydrogen sulfate solution, and brine. The organic phase was dried and freed of solvent. The oil was purified by MPLC (silica gel, 5% ethyl acetate in petroleum ether) to supply **5a** (236 mg, 55%) as a colorless oil: IR (neat, cm^{-1}) 2900, 1630, 1440, 1365, 1270, 1230, 1175, 1075, 990, 900, 845, 805, 770, 725, 670; ^1H NMR (300 MHz, $CDCl_3$) δ 6.03–5.85 (m, 1 H), 5.07–4.86 (m, 2 H), 4.37–4.25 (m, 2 H), 3.36 and 3.31 (two s, 3 H total), 3.34–2.99 (m, 4 H), 2.64 (t, *J* = 11.3 Hz, 1 H), 2.45–1.54 (series of m, 9 H), 1.47 and 1.43 (two s, 3 H total), 1.37 (dd, *J* = 12.3 and 4.9 Hz, 1 H), 1.07 (d, *J* = 5.4 Hz, 3 H), 1.06 (s, 3 H); MS, *m/z* (M^+) calcd 380.1844, obsd 380.1855.

2-[[(3*S*,5*R*)-Tetrahydro-3-methyl-5-[(6′*R*,7′*R*)-4′,5′,6′,7′-tetrahydro-6′,7′-dimethylspiro[1,3-dithiolane-2,1′-indan]-7′-yl]-3-vinyl-2-furyl]oxy]ethanol (5b). Lactol **4b** (300 mg, 0.824 mmol) was dissolved in benzene (25 mL) immediately after preparation. Pyridinium tosylate (30 mg) and ethylene glycol (0.2 mL, 3.6 mmol) were added, and the reaction mixture was refluxed in a Dean–Stark apparatus overnight. The reaction mixture was extracted with saturated sodium bicarbonate solution, dried, and freed of solvent. Purification was achieved chromatographically (silica gel; 20% ethyl acetate in hexane) to afford **5b** (232 mg, 69%) as a colorless oil: IR (neat, cm^{-1}) 3420, 2860, 1625, 1410, 1365, 1265, 980, 800, 720, 665; ^1H NMR (300 MHz, $CDCl_3$) δ 6.03–5.82 (m, 1 H), 5.05–4.94 (m, 2 H), 4.71–4.31 (series of m, 2 H), 3.80–3.45 (series of m, 4 H), 3.33–3.02 (series of m, 4 H), 2.81 (br s, 1 H), 2.58 (t, *J* = 11.7 Hz, 1 H), 2.41–1.97 (series of m, 6 H), 1.79–1.30 (series of m, 4 H), 1.43 and 1.41 (two s, 3 H total), 1.10 and 1.07 (two s, 3 H total), 1.03 and 0.99 (two d, *J* = 6.7 Hz, 3 H total); MS, the molecular ion peak was too transient for high-resolution measurement.

2-[[(3*S*,5*R*)-Tetrahydro-3-methyl-5-[(6′*R*,7′*R*)-4′,5′,6′,7′-tetrahydro-6′,7′-dimethylspiro[1,3-dithiolane-2,1′-indan]-7′-yl]-3-vinyl-2-furyl]thio]ethanethiol (5c). Lactone **2** (500 mg, 1.37 mmol) dissolved in ether was reduced with diisobutylaluminum hydride to furnish lactol **4b** as previously described. The crude lactol was dissolved in benzene (50 mL) with ethanedithiol (0.5 mL, 6.0 mmol) and pyridinium *p*-toluenesulfonate (50 mg). This mixture was heated at reflux for 4 h. The reaction

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mixture was extracted with 10% potassium hydroxide solution (2 × 40 mL), dried, and freed of solvent to afford **5c** (542 mg, 91%) as a yellow oil: IR (neat, cm^{-1}) 2890, 1620, 1410, 1360, 1260, 1200, 1000, 910, 725; ^1H NMR (200 MHz, $CDCl_3$) δ 5.96–5.75 (m, 2 H), 5.09–4.96 (m, 2 H), 4.85–4.66 (m, 1 H), 4.39–4.22 (m, 1 H), 3.32–2.95 (series of m, 4 H), 2.83–2.58 (series of m, 4 H), 2.49 (t, J = 11.9 Hz, 1 H), 2.41–1.83 (series of m, 6 H), 1.71–1.36 (series of m, 4 H), 1.45 and 1.44 (two s, 3 H total), 1.15 and 1.09 (two s, 3 H total), 1.00 and 0.96 (two d, J = 6.8 Hz, 3 H total); MS, the molecular ion peak was too transient for high-resolution measurement.

(6′*R*,7′*R*)-7′-[(2*R*,4*S*)-5-[[2-(Benzylthio)ethyl]thio]tetrahydro-4-methyl-4-vinyl-2-furyl]-4′,5′,6′,7′-tetrahydro-6′,7′-dimethylspiro[1,3-dithiolane-2,1′-indan] (5d). A solution of freshly prepared triflic anhydride (0.76 mL, 4.54 mmol) and 2,4,6-collidine (0.60 mL, 4.54 mmol) in methylene chloride (3 mL) was cooled to −60 °C, and benzyl alcohol (0.47 mL, 4.54 mmol) was added dropwise. After 30 min at −60 °C, collidine (0.15 mL, 1.13 mmol) and alcohol **6a** (490 mg, 1.11 mmol) dissolved in a minimum of methylene chloride were added dropwise. The mixture was allowed to reach −35 °C at which time TLC analysis showed the reaction to be complete. After cooling to −78 °C, methanol (1.0 mL) was used to quench the reaction. Upon reaching room temperature, the mixture was extracted with water, dilute hydrochloric acid, saturated sodium bicarbonate solution, and water. The organic phase was dried and freed of solvent. Purification by column chromatography (silica gel; 2.5% ethyl acetate in petroleum ether) supplied **5d** (480 mg, 81%) as an epimeric mixture: IR (neat, cm^{-1}) 3090, 3060, 3040, 2970, 2920, 1640, 1605, 1495, 1455, 1430, 1360, 1260, 1205, 1095, 1070, 1030, 995, 910, 815, 730, 695; ^1H NMR (200 MHz, $CDCl_3$) δ 7.5–7.2 (m, 5 H), 6.1–5.8 (m, 1 H), 5.2–5.0 (m, 2 H), 4.91 and 4.83 (two s, 1 H total), 4.5–4.3 (m, 1 H), 3.75 (s, 2 H), 3.4–3.1 (m, 4 H), 2.9–2.6 (m, 4 H), 2.5–1.4 (m, 11 H), 1.53 and 1.52 (two s, 3 H total), 1.22 and 1.16 (two s, 3 H total), 1.09 and 1.04 (two d, J = 5.3 Hz, 3 H total); MS, the molecular ion peak was too transient for high-resolution measurement.

(α*R*,6′*R*,7′*R*)-α-[(2*S*)-2-(1,3-Dithiolan-2-yl)-2-methyl-3-butenyl]-4′,5′,6′,7′-tetrahydro-6′,7′-dimethylspiro[1,3-dithiolane-2,1′-indan]-7′-methanol (6a). Lactone **2** (620 mg, 1.70 mmol) dissolved in ether (10 mL) was cooled to −78 °C, and a solution of diisobutylaluminum hydride (2.0 mL, 2.0 mmol, 1.0 M in hexane) was added dropwise. Upon completion of reaction as indicated by TLC analysis, the mixture was quenched with water (1.0 mL) and allowed to warm to room temperature. Hydrochloric acid (10%) was added, and the mixture was extracted with ether. The combined organic phases were dried and freed of solvent to provide lactol **4b**.

The lactol was immediately redissolved in methylene chloride (20 mL). Ethanedithiol (0.4 mL, 4.8 mmol) followed by aluminum chloride (50 mg) was added, and the reaction mixture was stirred at room temperature overnight and then extracted with 10% potassium hydroxide solution (2 × 20 mL), dried, and concentrated under reduced pressure. The residue was purified chromatographically (silica gel; 5% ethyl acetate in petroleum ether) to give alcohol **6a** (430 mg, 58%) as a colorless oil, which slowly crystallized on standing: mp 103–105 °C; IR ($CDCl_3$, cm^{-1}) 3420, 2980, 2940, 2850, 1635, 1460, 1435, 1420, 1380, 1280, 1270, 1250, 1225, 1140, 1100, 1070, 1030, 1010, 960, 920, 860, 825, 800; ^1H NMR (300 MHz, $CDCl_3$) δ 5.88 (dd, J = 17.4, 10.8 Hz, 1 H), 5.08 (d, J = 10.8 Hz, 1 H), 5.02 (d, J = 17.4 Hz, 1 H), 4.66 (s, 1 H), 4.35 (br d, J = 7.9 Hz, 1 H), 3.69 (br s, 1 H), 3.31–3.10 (m, 4 H), 3.09–3.02 (m, 4 H), 2.39–1.37 (series of m, 11 H), 1.21 (s, 3 H), 1.18 (s, 3 H), 1.03 (d, J = 6.9 Hz, 3 H); ^{13}C NMR (20 MHz, $CDCl_3$) 144.09, 143.55, 139.04, 114.28, 76.90, 71.51, 65.05, 50.19, 46.26, 45.87, 41.41, 40.10, 39.80, 38.93, 37.81, 34.27, 28.49, 27.13, 24.46, 21.02, 17.47 ppm; MS, m/z (M^+) calcd 442.1492, obsd 442.1499.

The mixed acetal **5c** was also converted to **6a** with Lewis acid catalysis. Lactone **2** (580 mg, 1.59 mmol) was reduced with diisobutylaluminum hydride and subsequently treated with ethanedithiol in the presence of a protic catalyst as previously reported to provide **5c**. The crude mixed acetal was immediately redissolved in methylene chloride (20 mL) and stirred at room temperature for 30 h in the presence of aluminum chloride (100 mg). No additional ethanedithiol was introduced. The reaction mixture was extracted with water, dried, and concentrated in vacuo. Following chromatographic purification as described above, a pale yellow oil (290 mg, 41%), which corresponded to the material isolated above, was obtained.

(6′*R*,7′*R*)-7′-[(1*R*,3*S*)-3-(1,3-Dithiolan-2-yl)-1-methoxy-3-methyl-4-pentenyl]-4′,5′,6′,7′-tetrahydro-6′,7′-dimethylspiro[1,3-dithiolane-2,1′-indan] (6b). Alcohol **6a** (516 mg, 1.17 mmol) was dissolved in dry tetrahydrofuran (10 mL), and the solution was cooled to 0 °C. A solution of methyllithium (1.08 mL, 1.51 mmol, 1.4 M in hexane) was added dropwise, and the mixture was stirred to 0 °C for 15 min. The solution was cooled to −78 °C and methyl iodide (0.10 mL, 1.61 mmol) was introduced. After being warmed to 0 °C, the reaction mixture was extracted with saturated sodium bicarbonate solution and water, dried, and freed of solvent. The residue was purified by chromatography (silica gel, 5% ethyl acetate in petroleum ether) to give **6b** (481 mg, 90%) as a colorless oil: IR ($CDCl_3$, cm^{-1}) 2980, 2920, 2840, 1640, 1450, 1425, 1370, 1280, 1200, 1100, 1000, 910, 855, 820, 730; ^1H NMR (300 MHz, $CDCl_3$) δ 5.84 (dd, J = 17.5, 10.8 Hz, 1 H), 5.15 (d, J = 10.8 Hz, 1 H), 5.09 (d, J = 17.5 Hz, 1 H), 4.58 (s, 1 H), 3.88 (d, J = 8.7 Hz, 1 H), 3.38–3.25 (m, 4 H), 3.24 (s, 3 H), 3.11–3.06 (m, with br s at δ 3.11, 4 H), 2.45–1.40 (series of m, 11 H), 1.30 (s, 3 H), 1.20 (s, 3 H), 1.05 (d, J = 7.0 Hz, 3 H); MS, m/z ($M^+ - C_8H_{13}S_2$) calcd 283.1190, obsd 283.1151; m/z (relative intensity) 283 (3), 239 (39), 217 (70), 185 (23), 179 (45), 163 (33), 159 (60), 145 (29), 131 (33), 125 (40), 123 (41), 105 (100), 99 (47), 97 (53), 91 (48), 79 (36), 77 (37), 65 (32), 61 (58), 58 (47), 55 (38), 53 (36).

(6*R*,7*R*)-7-[(1*R*,3*S*)-3-(1,3-Dithiolan-2-yl)-1-hydroxy-3-methyl-4-pentenyl]-4,5,6,7-tetrahydro-6,7-dimethyl-1-indanone (8). Diisobutylaluminum hydride reduction under the aforementioned conditions of lactone **2** (910 mg, 2.50 mmol) provided lactol **4b**, which was immediately dissolved in methylene chloride (25 mL). Ethanedithiol (0.60 mL, 7.2 mmol) was added, and the solution was cooled to −78 °C. Titanium tetrachloride (0.07 mL, 0.63 mmol) was introduced, and the mixture was permitted to warm gradually to room temperature. The solution was recooled to −78 °C and quenched with water (0.5 mL). Upon warming to room temperature, the mixture was washed with water and 10% potassium hydroxide solution, dried, and concentrated in vacuo. The two products were separated chromatographically (silica gel; 5% ethyl acetate in petroleum ether to elute the first component and 25% ethyl acetate in petroleum ether for the second). The less polar component proved to be **6a** (240 mg, 22%) and the more polar **8** (430 mg, 47%), a colorless oil: IR ($CDCl_3$, cm^{-1}) 3360, 3080, 3050, 2970, 1675, 1620, 1470, 1450, 1440, 1410, 1390, 1380, 1345, 1315, 1265, 1240, 1215, 1165, 1130, 1100, 1050, 1030, 990, 980, 910, 850, 730; ^1H NMR (300 MHz, $CDCl_3$) δ 5.87 (dd, J = 17.4, 10.9 Hz, 1 H), 5.06 (d, J = 10.0 Hz, 1 H), 5.02 (d, J = 17.2 Hz, 1 H), 4.65 (s, 1 H), 4.20 (br s, 1 H), 3.73 (br d, J = 9.8 Hz, 1 H), 3.02 (br s, 4 H), 2.49–2.27 (series of m, 7 H), 1.70–1.45 (series of m, 4 H), 1.19 (s, 3 H), 1.11 (s, 3 H), 0.95 (d, J = 6.4 Hz, 3 H); MS, m/z ($M^+ - H_2O$) calcd 348.1581, obsd 348.1540.

(α*S*,γ*R*,4*R*,5*R*)-4,5,6,7-Tetrahydro-γ-methoxy-α,4,5-trimethyl-3-oxo-α-vinyl-4-indanbutyraldehyde (7). Methyl ether **6b** (80 mg, 0.175 mmol) was dissolved in acetone (8 mL). Water (0.5 mL) and methyl iodide (2.0 mL) were added, and the mixture was gently refluxed overnight. After removal of the volatile solvents under reduced pressure, the residue was redissolved in methylene chloride, extracted with water, dried, and freed of solvent. Aldehyde **7** (19.4 mg, 38%) was obtained following chromatography (silica gel; 5% ethyl acetate in petroleum ether) as a pale yellow oil: IR (neat, cm^{-1}) 2960, 2920, 2850, 2710, 1725, 1690, 1630, 1460, 1415, 1380, 1280, 1170, 1095, 995, 975, 920, 880, 830, 730; ^1H NMR (300 MHz, $CDCl_3$) δ 9.24 (s, 1 H), 5.72 (dd, J = 17.5, 10.6 Hz, 1 H), 5.20 (d, J = 10.5 Hz, 1 H), 5.12 (d, J = 17.6 Hz, 1 H), 4.02 (dd, J = 11.5, 2.2 Hz, 1 H), 2.95 (s, 3 H), 2.46–1.65 (series of m, 11 H), 1.19 (s, 3 H), 1.17 (d, J = 7.8 Hz, 3 H), 1.15 (s, 3 H); MS, the molecular ion peak was too transient for high-resolution measurement.

(6*R*,7*R*)-4,5,6,7-Tetrahydro-7-[(1*R*,3*S*)-3-[1-hydroxypropyl]-1-methoxy-3-methyl-4-pentenyl]-6,7-dimethyl-1-indanone. Aldehyde **7** (38.6 mg, 0.131 mmol) was dissolved in ether (5 mL) and cooled to −100 °C. Freshly prepared and titrated ethylmagnesium bromide in ether (1.0 equiv) was added, and the solution was stirred and allowed to warm gradually to room temperature. The reaction mixture was extracted with water, dried, and freed of solvent. Chromatography (silica gel, 17% ethyl

acetate in petroleum ether) separated the two diastereomeric alcohols, both colorless oils, in an overall yield of 17.9 mg (47%). The less polar alcohol accounted for 10.1 mg and the more polar for 7.8 mg.

Less polar epimer: IR (neat, cm^{-1}) 3480, 2920, 1690, 1630, 1460, 1410, 1380, 1290, 1190, 1085, 970, 900; ^1H NMR (300 MHz, $CDCl_3$) δ 5.97 (dd, J = 17.1, 10.4 Hz, 1 H), 5.05 (dd, J = 11.2, 1.4 Hz, 1 H), 4.97 (dd, J = 17.9, 1.4 Hz, 1 H), 4.20 (d, J = 8.7 Hz, 1 H), 3.20 (s, 3 H), 3.19–3.13 (m, 1 H), 2.48–2.35 (series of m, 6 H), 1.67–1.15 (series of m, 8 H), 1.13 (d, J = 6.9 Hz, 3 H), 1.04 (s, 3 H), 0.97 (t, J = 7.2 Hz, 3 H); ^{13}C NMR (20 MHz, $CDCl_3$) 208.83, 173.89, 144.38, 143.99, 112.44, 83.69, 77.37, 59.22, 44.53, 41.85, 40.95, 39.17, 35.08, 29.46, 27.60 (2 C), 24.41, 23.90, 18.85, 17.57, 11.70 ppm; MS, m/z ($M^+ - C_3H_6O$) calcd 276.2089, obsd 276.2062.

More polar epimer: IR (neat, cm^{-1}) 3470, 2960, 1680, 1625, 1450, 1410, 1370, 1260, 1080, 965, 900, 725; ^1H NMR (300 MHz, $CDCl_3$) δ 5.73 (dd, J = 17.5, 10.9 Hz, 1 H), 5.15 (dd, J = 10.8, 1.3 Hz, 1 H), 5.04 (dd, J = 17.5, 1.3 Hz, 1 H), 4.02 (dd, J = 8.4, 1.6 Hz, 1 H), 3.23–3.19 (m, 1 H), 3.13 (s, 3 H), 2.45–2.32 (series of m, 6 H), 1.84–1.59 (series of m, 6 H), 1.25–1.15 (m, 2 H), 1.11 (d, J = 6.6 Hz, 3 H), 1.10 (s, 3 H), 1.05 (s, 3 H), 0.97 (t, J = 7.3 Hz, 3 H); ^{13}C NMR (20 MHz, $CDCl_3$) 208.70, 173.57, 144.63, 144.19, 113.71, 83.44, 80.24, 59.29, 45.04, 42.36, 40.76, 39.36, 35.21, 29.52, 27.80, 27.67, 24.86 24.22, 17.64, 17.45, 11.63 ppm; MS (FAB), m/z ($M^+ + 1$) m/z 335.

The same alcohol mixture was also prepared by reduction of **3**. This keto enone (830 mg, 2.50 mmol) was dissolved in methanol (10 mL), and sodium borohydride (100 mg, 2.64 mmol) was added slowly with stirring. After completion of the reaction, water (2 mL) was added, and the volatile material was removed under reduced pressure. The residue was partitioned between dilute hydrochloric acid and methylene chloride. The organic phase was dried and freed of solvent. Chromatographic purification (silica gel; 20% ethyl acetate in petroleum ether) supplied the alcohols (767 mg, 92%) in a 1:1 ratio as colorless oils. The spectral data are given above.

(6*R*,7*R*)-4,5,6,7-Tetrahydro-7-[(1*R*,3*S*)-1-methoxy-3-methyl-3-propionyl-4-pentenyl]-6,7-dimethyl-1-indanone (3). A mixture of the diastereomeric alcohols (300 mg, 0.897 mmol) was dissolved in methylene chloride (10 mL). Celite (1 g) and pyridinium chlorochromate (360 mg, 1.67 mmol) were sequentially added, and the mixture was stirred overnight at room temperature. Ether (80 mL) was added, and the mixture was passed through a plug of Florisil. Concentration in vacuo yielded **3** (294 mg, 99%) as a colorless oil, which solidified on standing: mp 51–53 °C; $[\alpha]^{22}_D$ –64.8° (c 1.6, $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$) δ 5.87 (dd, J = 17.7, 10.4 Hz, 1 H), 5.13 (dd, J = 10.3, 0.7 Hz, 1 H), 5.12 (dd, J = 16.7, 0.9 Hz, 1 H), 3.96 (dd, J = 11.1, 2.0 Hz, 1 H), 2.93 (s, 3 H), 2.52 (q, J = 7.3 Hz, 2 H), 2.46–2.20 (m, 4 H), 1.94–1.64 (m, 7 H), 1.22 (s, 3 H), 1.15 (d, J = 7.2 Hz, 3 H), 1.14 (s, 3 H), 0.96 (t, J = 7.3 Hz, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) 211.76, 208.51, 173.63, 143.81, 143.43, 114.35, 82.61, 59.92, 53.22, 41.77, 41.08, 39.62, 35.27, 30.61, 29.53, 27.91, 27.73, 23.95, 19.55, 17.56, 8.50 ppm; MS, m/z ($M^+ + 1$) calcd 333.2471, obsd 333.2449.

(–)-Mutilone (9). A. From Pleuromutilone. Pleuromutilone (2.00 g, 5.32 mmol) was dissolved in methanol (100 mL) containing 5% potassium hydroxide and heated to the reflux temperature for 2 h. After cooling, the reaction mixture was poured into water and extracted with methylene chloride. The organic phases were washed with saturated sodium bicarbonate solution, dried, and freed of solvent. The residue was purified chromatographically (silica gel; 20% ethyl acetate in petroleum ether) to give mutilone (**9**, 1.48 g, 87%) as a white crystalline solid, mp 158–159 °C.

B. From Tiamulone. Tiamulone (7.41 g, 15.1 mmol) was dissolved in methanol (160 mL) containing 5% potassium hydroxide and heated at the reflux temperature for 2 h. The reaction mixture was cooled, poured into water (300 mL), and extracted with methylene chloride (4 × 100 mL). The organic phases were combined, dried, and concentrated in vacuo. The crude material was purified chromatographically (silica gel; 20% ethyl acetate in petroleum ether), yielding mutilone (**9**, 4.09 g, 85%) as a white solid: mp 157–158 °C (lit.[58] mp 154–155 °C); $[\alpha]^{22}_D$ –51.3° (c 4.065, $CHCl_3$) [lit.[57] $[\alpha]^{20}_D$ –53° (c, 1.044, $CHCl_3$)]; IR ($CDCl_3$, cm^{-1}) 3650, 3550, 2985, 2940, 2880, 1740, 1700, 1635, 1455, 1418, 1330, 1290, 1200, 1150, 1110, 1030, 1000, 965; ^1H NMR (300 MHz, $CDCl_3$) δ 6.09 (dd, J = 17.8, 10.7 Hz, 1 H), 5.32 (d, J = 17.8 Hz, 1 H), 5.32 (d, J = 11.2 Hz, 1 H), 4.70 (d, J = 7.7 Hz, 1 H), 3.26 (d, J = 6.7 Hz, 1 H), 2.32–2.12 (series of m, 3 H), 1.90 (dd, J = 15.4, 7.8 Hz, 1 H), 1.74–1.39 (series of m, 9 H), 1.37 (s, 3 H), 1.11 (s, 3 H), 1.06 (d, J = 6.6 Hz, 3 H), 1.01 (d, J = 6.6 Hz, 3 H); ^{13}C NMR (20 MHz, $CDCl_3$) 217.13, 215.72, 140.28, 117.16, 67.65, 59.92, 54.49, 45.42, 44.91, 44.33, 42.54, 37.43, 34.69, 30.09, 27.21, 25.30, 24.78, 18.27, 13.48 ppm; MS/mz (relative intensity) 249 (3), 193 (7), 177 (20), 165 (17), 164 (19), 163 (100), 149 (5), 137 (4), 121 (10), 107 (6), 93 (5), 79 (6), 55 (7).

Anal. Calcd for $C_{20}H_{30}O_3$: C, 75.43; H, 9.50. Found: C, 75.38, H, 9.56.

The mutilone prepared from tiamulone was identical with that obtained from mutilone by comparison of ^1H NMR, ^{13}C NMR, IR, and mass spectra.

(–)-(3a*S*,4*R*,6*S*,8*R*,9*R*,9a*R*,10*R*)-6-Ethylhexahydro-8-methoxy-4,6,9,10-tetramethyl-3a,9-propano-3a*H*-cyclopentacyclooctene-1,5(4*H*,6*H*)-dione (10). Mutilone (**9**) (6.96 g, 21.9 mmol) and 2,6-di-*tert*-butylpyridine (9.5 mL, 44 mmol) were dissolved in methylene chloride (150 mL). Subsequently, methyl trifluoromethanesulfonate (4.8 mL, 44 mmol) was added, and the mixture was stirred at room temperature. After 48 h, water (10 mL) was added, and the mixture was stirred for an additional hour and extracted with water followed by saturated sodium bicarbonate solution. The organic phase was dried and freed of solvent. The residue was purified by column chromatography (silica gel; 5% ethyl acetate in petroleum ether) to furnish white crystals of **10** (7.39 g, 100%): mp 150.5–151.0 °C; $[\alpha]^{25}_D$ –38.5° (c 2.60, $CHCl_3$); IR ($CDCl_3$, cm^{-1}) 2990, 2940, 1740, 1700, 1465, 1418, 1380, 1330, 1290, 1150, 1095, 1060, 995, 960; ^1H NMR (300 MHz, $CDCl_3$) δ 6.34 (dd, J = 17.6, 10.8 Hz, 1 H), 5.31 (d, J = 10.8 Hz, 1 H), 5.12 (d, J = 17.6 Hz, 1 H), 3.91 (d, J = 8.5 Hz, 1 H), 3.29 (s, 3 H), 3.18 (q, J = 6.6 Hz, 1 H), 2.27–2.12 (m, 3 H), 1.88 (dd, J = 15.7, 8.5 Hz, 1 H), 1.65–1.38 (series of m, 8 H), 1.36 (s, 3 H), 1.19 (s, 3 H), 1.05 (d, J = 6.6 Hz, 3 H), 0.92 (d, J = 6.3 Hz, 3 H); ^{13}C NMR (20 MHz, $CDCl_3$) 216.88, 214.90, 140.48, 117.93, 77.05, 59.35, 55.20, 53.60, 45.43, 45.17, 43.06, 41.91, 37.82, 34.69, 30.22, 27.60, 24.73 (2 C), 17.64, 14.44, 13.49 ppm; MS (M^+), m/z calcd 322.2351, obsd 332.2354.

Anal. Calcd for $C_{21}H_{32}O_3$: C, 75.86; H, 9.70. Found: C, 75.75, H, 9.74.

The presence of **11** was detected spectroscopically: IR (Nujol, cm^{-1}) 2950, 1690, 1640, 1580, 1460, 1410, 1375, 1340, 1260, 1160, 1090, 1030, 910, 880, 810; ^1H NMR (300 MHz, $CDCl_3$) δ 6.24 (dd, J = 17.6, 11.0 Hz, 1 H), 5.22 (d, J = 11.0 Hz, 1 H), 5.02 (dd, J = 17.6, 0.7 Hz, 1 H), 3.72 (d, J = 8.8 Hz, 1 H), 3.45 (s, 3 H), 3.26 (s, 3 H), 3.03 (q, J = 6.6 Hz, 1 H), 2.45–2.12 (series of m, 6 H), 2.06 (dd, J = 14.8, 8.9 Hz, 1 H), 1.89 (dt, J = 13.2, 3.1 Hz, 2 H), 1.71–1.42 (series of m, 2 H), 1.29 (s, 3 H), 1.10 (s, 3 H), 0.97 (d, J = 6.8 Hz, 3 H), 0.96 (d, J = 6.6 Hz, 3 H).

(3a*S*,4*R*,6*S*,8*R*,9*R*,9a*R*,10*R*)-Hexahydro-4,6,9,10-tetramethyl-8-[(methylthio)methoxy]-6-vinyl-3a,9-propano-3a*H*-cyclopentacyclooctene-1,5(4*H*,6*H*)-dione (12). Mutilone (**9**) (1.04 g, 3.26 mmol) was dissolved in a mixture of dimethyl sulfoxide (50 mL) and acetic acid (10 mL). Acetic anhydride (25 mL) was added, and the mixture was stirred at room temperature overnight. Following extraction with water and removal of excess dimethyl sulfoxide by distillation under reduced pressure, the residue was purified chromatographically (silica gel; 5% ethyl acetate in petroleum ether) to give **12** (1.23 g, 99%) as colorless crystals: mp 163–163.5 °C; IR (Nujol, cm^{-1}) 2930, 2860, 1730, 1700, 1460, 1415, 1380, 1340, 1310, 1285, 1230, 1150, 1110, 1035; ^1H NMR (300 MHz, $CDCl_3$) δ 6.34 (dd, J = 17.4, 10.8 Hz, 1 H), 5.32 (d, J = 10.8 Hz, 1 H), 5.15 (d, J = 17.5 Hz, 1 H), 4.62 (AB q, J_{AB} = 11.2 Hz, $\Delta\nu$ = 9.8 Hz, 2 H), 4.48 (d, J = 8.2 Hz, 1 H), 3.25 (q, J = 6.6 Hz, 1 H), 2.26–2.11 (m, 3 H), 2.23 (s, 3 H), 1.89 (dd, J = 16.0, 8.3 Hz, 1 H), 1.73–1.40 (series of m, 7 H), 1.39 (s, 3 H), 1.24–1.12 (m, 1 H), 1.18 (s, 3 H), 1.05 (d, J = 6.6 Hz, 3 H), 0.98 (d, J = 6.8 Hz, 3 H); ^{13}C NMR (20 MHz, $CDCl_3$) 217.14, 214.64, 139.78, 118.19, 72.96, 72.19, 59.74, 53.73, 45.55, 45.30, 43.13, 41.27, 37.95, 34.82, 30.35, 27.22, 24.86, 24.09, 17.96, 15.79, 14.89, 13.49 ppm; MS, m/z ($M^+ - CH_3SCH_2$) calcd 317.2116, obsd 317.2191.

Anal. Calcd for $C_{22}H_{34}O_3S$: C, 69.80; H, 9.05. Found: C, 69.65, H, 9.02.

(58) Naegeli, P. Ph.D. Dissertation, ETH, Zurich, 1961.

Raney Nickel Desulfurization of 12. A solution of **12** (100 mg, 0.265 mmol) in ethanol (15 mL) was treated with 25–30 equiv of W-2 Raney nickel and heated overnight at the reflux temperature. The cooled reaction mixture was filtered, the filtrate was evaporated, and the residue was purified by silica gel chromatography (5% ethyl acetate in petroleum ether). Colorless crystals of **13** were obtained (67 mg, 75%): IR (Nujol, cm^{-1}) 2940, 1730, 1690, 1450, 1370, 1320, 1270, 1140, 1080, 950; ^1H NMR (300 MHz, $CDCl_3$) δ 3.91 (d, J = 8.6 Hz, 1 H), 3.28 (q, J = 6.7 Hz, 1 H), 3.24 (s, 3 H), 2.3–1.1 (series of m, 14 H), 1.32 (s, 3 H), 1.02 (d, J = 6.7 Hz, 3 H), 1.01 (s, 3 H), 0.90 (d, J = 6.4 Hz, 3 H), 0.84 (t, J = 7.5 Hz, 3 H); MS, m/z (M^+) calcd 334.2508, obsd 334.2589.

(+)-(3a*S*,4*R*,6*S*,8*R*,9*R*,9a*R*,10*R*)-6-Ethylhexahydro-8-(methoxymethyl)-4,6,9,10-tetramethyl-3a,9-propano-3a*H*-cyclopentacyclooctene-1,5(4*H*,6*H*)-dione (14). To a mechanically stirred solution of mutilone (4.43 g, 13.9 mmol) in 88 mL of methylene chloride and 88 mL of dimethoxyethane was added 30 g of phosphorus pentoxide. The mixture was stirred at room temperature for 45 min, poured into saturated sodium bicarbonate solution (1.5 L), and extracted with methylene chloride (3 × 1 L). The combined organic phases were dried, filtered, and concentrated in vacuo to provide 6.10 g of crude **14**. A small portion of this material was dissolved in hot hexane and then kept at 5 °C overnight to provide colorless needles, mp 104 °C. The bulk of the material was carried on directly: $[\alpha]^{25}_D$ +22.0° (*c* 1.28, $CHCl_3$); IR (film, cm^{-1}) 3080, 2940, 1730, 1690, 1625, 1450; ^1H NMR (300 MHz, $CDCl_3$) δ 6.51 (dd, J = 10.8, 17.6 Hz, 1 H), 5.62 (d, J = 9.8 Hz, 1 H), 5.03 (d, J = 18.0 Hz, 1 H), 4.76 (AB q, J = 6.7 Hz, 1 H), 4.68 (AB q, J = 6.6 Hz, 1 H), 4.43 (dd, J = 2.5, 6.5 Hz, 1 H), 3.39 (s, 3 H), 3.19 (q, J = 6.6 Hz, 1 H), 2.23–2.07 (m, 3 H), 1.85–1.78 (m, 2 H), 1.64–1.50 (m, 4 H), 1.43–1.33 (m, 2 H), 1.37 (s, 3 H), 1.22–1.14 (m, 1 H), 1.12 (s, 3 H), 1.03 (d, J = 7.4 Hz, 3 H), 0.91 (d, J = 6.4 Hz, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) 217.12, 214.97, 140.47, 117.79, 96.60, 74.78, 59.45, 55.92, 54.10, 45.46, 45.38, 42.97, 42.29, 37.84, 34.68, 30.22, 27.21, 25.13, 24.80, 17.60 ppm.

Anal. Calcd for $C_{22}H_{34}O_4$: C, 72.83; H, 9.45. Found: C, 72.63; H, 9.40.

(3a*S*,4*R*,6*S*,8*R*,9*R*,9a*R*,10*R*)-8-(*tert*-Butyldimethylsiloxy)hexahydro-4,6,9,10-tetramethyl-6-vinyl-3a,9-propano-3a*H*-cyclopentacyclooctene-1,5(4*H*,6*H*)-dione (16). A solution of mutilone (**9**) (2.00 g, 6.28 mmol) and 2,6-lutidine (3.28 mL, 28.2 mmol) in tetrahydrofuran (100 mL) was cooled to 0 °C in an ice bath. *tert*-Butyldimethylsilyl trifluoromethanesulfonate (5.20 mL, 22.6 mmol) was introduced and stirring was continued for 5 h. The tetrahydrofuran was removed under pressure, and the residue was partitioned between saturated sodium bicarbonate solution (200 mL) and methylene chloride (100 mL). The aqueous phase was further extracted with methylene chloride (2 × 100 mL), and the combined organic phases were dried and concentrated in vacuo. Silyl ether **16**, silyl enol ether **15**, and lutidine were separated by MPLC (silica gel; 7% ethyl acetate in petroleum ether).

For **15**: IR (CCl_4, cm^{-1}) 2933, 2860, 1705, 1640, 1463, 1375, 1295, 1252, 1232, 1048, 831; ^1H NMR (300 MHz, $CDCl_3$) δ 6.46 (dd, J = 17.5, 10.8 Hz, 1 H), 5.07–4.95 (m, 3 H), 4.57 (br s, 1 H), 3.04 (q, J = 6.5 Hz, 1 H), 2.97 (br d, J = 13.7 Hz, 1 H), 2.50 (br s, 1 H), 2.11 (dd, J = 15.6, 8.4 Hz, 1 H), 1.84–1.35 (series of m, 7 H), 1.61 (s, 3 H), 1.29 (s, 3 H), 1.17 (d, J = 8.6 Hz, 3 H), 1.06 (d, J = 6.5 Hz, 3 H), 0.98 (s, 18 H), 0.18 (s, 3 H), 0.17 (s, 3 H), 0.15 (s, 3 H), 0.11 (s, 3 H); MS, m/z (M^+) calcd 546.3924, obsd 546.3927.

The crude silyl enol ether **15** (3.43 g), mp 145–148 °C, was hydrolyzed over a 2.5-h period at room temperature in a mixture of tetrahydrofuran/water/perchloric acid (90:9:1, 200 mL). The tetrahydrofuran was again removed under reduced pressure. The residue was diluted with saturated sodium bicarbonate solution (175 mL) and extracted with methylene chloride (4 × 100 mL). The organic phases were combined, dried, and freed of solvent. Purification was achieved by using a Waters Prep 500 HPLC (silica gel; 10% ethyl acetate in petroleum ether) to afford silyl ether **16** (2.59 g, 95%) as a white solid: mp 138.0–138.5 °C; IR (CCl_4, cm^{-1}) 2960, 2865, 1745, 1709, 1635, 1465, 1379, 1330, 1287, 1258, 1052, 1008, 929, 835; ^1H NMR (300 MHz, $CDCl_3$) δ 6.48 (dd, J = 17.5, 10.8 Hz, 1 H), 5.34 (d, J = 10.8 Hz, 1 H), 5.15 (d, J = 17.5, Hz, 1 H), 4.79 (d, J = 8.3 Hz, 1 H), 3.17 (q, J = 6.7 Hz, 1 H) 2.18–2.07 (m, 4 H), 2.00–1.88 (m, 1 H), 1.70–1.50 (m, 7 H), 1.38 (s, 3 H), 1.15 (s, 3 H), 1.03 (d, J = 6.7 Hz, 3 H), 0.95 (d, J = 6.6 Hz, 3 H), 0.89 (s, 9 H), 0.18 (s, 3 H), 0.16 (s, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) 217.19, 214.36, 139.30, 118.20, 67.83, 60.09, 53.64, 45.43, 45.36, 45.14, 44.16, 38.14, 34.87, 30.28, 27.23, 26.47, 24.69, 23.92, 19.28, 18.50, 14.42, 13.44, -1.45, -3.67 ppm; MS, m/z ($M^+ - C_4H_9$) calcd 375.2356, obsd 375.2361.

Anal. Calcd for $C_{26}H_{44}O_3Si$: C, 72.17; H, 10.25. Found: C, 72.01; H, 10.36.

(-)-(6*R*,7*R*)-4,5,6,7-Tetrahydro-7-[(1*R*,3*S*)-1-methoxy-3-methyl-3-propionyl-4-pentenyl]-6,7-dimethyl-1-indanone (3). Mutilone methyl ether (**10**) (3.70 g, 11.1 mmol) was combined with a solution of 10% potassium hydroxide in ethanol (330 mL) and the mixture was heated at reflux overnight, poured into water (500 mL), and extracted with methylene chloride (4 × 100 mL). After being dried and freed of solvent, the product was purified by HPLC (Waters Prep 500; silica gel; 20% ethyl acetate in petroleum ether) to give **3** (3.13 g, 85%) as a light yellow oil, which slowly solidified on standing: mp 50–53 °C; $[\alpha]^{23}_D$ -65.5° (*c* 2.89, $CHCl_3$); IR ($CDCl_3$, cm^{-1}) 3080, 2980, 2940, 2885, 2840, 1710, 1695, 1640, 1465, 1440, 1425, 1412, 1380, 1350, 1290, 1270, 1240, 1105, 1045, 995, 980, 930, 835, 800. The ^1H and ^{13}C NMR spectra of the product are identical with those of (-)-**3** derived from **7** described above.

(-)-(6*R*,7*R*)-4,5,6,7-Tetrahydro-7-((1*R*,3*S*)-1-(methoxymethyl)-3-propionyl-4-pentenyl)-6,7-dimethyl-1-indanone (17a). A total of 6.64 g of crude **14** was placed in a 1-L flask with 600 mL of 10% potassium hydroxide in ethanol. The mixture was heated to reflux for 8 h, allowed to cool to room temperature, poured into water (1.8 L), and acidified with concentrated hydrochloric acid. The mixture was immediately extracted with methylene chloride (3 × 1 L), and the combined organic layers were dried, filtered, and concentrated in vacuo to leave a brown oil. Column chromatography (silica gel; 15% ethyl acetate in petroleum ether) provided 3.32 g of dione **17a** and unreacted **14**, which was recycled to provide an additional 0.96 g of dione **17a** for a total yield of 4.28 g (80% from mutilone). A portion was dissolved in hot hexane and placed in a freezer at -5 °C overnight to provide pale yellow plates, mp 65–66 °C; $[\alpha]^{25}_D$ -180.7° (*c* 2.28, $CHCl_3$); IR (film, cm^{-1}) 3040, 2970, 2930, 1670, 1630, 1460, 1380; ^1H NMR (300 MHz, $CDCl_3$) δ 5.86 (dd, J = 10.8, 17.4 Hz, 1 H), 5.13 (d, J = 10.8 Hz, 1 H), 5.12 (d, J = 17.3 Hz, 1 H), 4.49 (dd, J = 1.9, 11.1 Hz, 1 H), 4.23 (AB q, J = 6.7 Hz, 1 H), 4.11 (AB, J = 6.7 Hz, 1 H), 3.04 (s, 3 H), 2.55–2.28 (m, 7 H), 2.25–2.05 (m, 2 H), 1.85–1.60 (m, 4 H), 1.19 (s, 3 H), 1.13 (d, J = 7.1 Hz, 3 H), 1.10 (s, 3 H), 0.96 (t, J = 7.3 Hz, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) 211.77, 208.78, 171.03, 142.82, 114.41, 99.52, 82.51, 55.31, 52.87, 42.22, 38.73, 36.44, 34.49, 30.46, 29.54, 27.04, 25.64, 25.33, 19.29, 17.03, 8.32 ppm.

(+)-(6*R*,7*R*)-7-[(1*R*,3*S*)-1-(*tert*-Butyldimethylsiloxy)-3-methyl-3-propionyl-4-pentenyl]-4,5,6,7-tetrahydro-6,7-dimethyl-1-indanone (17b). To a 10% solution of potassium hydroxide in ethanol (20 mL) was added **16** (250 mg, 0.578 mmol), and the mixture was brought to the reflux temperature for 2 h. The cooled solution was diluted with water (40 mL) and extracted with methylene chloride (4 × 20 mL). The organic phases were combined, dried, and freed of solvent. Following purification by MPLC (silica gel; 10% ethyl acetate in petroleum ether), keto enone **17b** (197 mg, 75%) was isolated as a white solid: mp 51.0–52.0 °C; $[\alpha]^{25}_D$ +42.7° (*c* 5.13, $CHCl_3$); IR (CCl_4, cm^{-1}) 2935, 2860, 1715, 1695, 1635, 1462, 1381, 1250, 1085, 919, 830; ^1H NMR (300 MHz, $CDCl_3$) δ 6.02 (dd, J = 17.4, 10.7 Hz, 1 H), 5.29 (d, J = 10.7 Hz, 1 H), 5.21 (d, J = 17.5 Hz, 1 H), 4.81 (t, J = 2.2 Hz, 1 H), 2.50 (q, J = 7.2 Hz, 2 H), 2.45–2.29 (series of m, 7 H), 1.76–1.68 (m, 4 H), 1.34 (s, 3 H), 1.11 (d, J = 7.0 Hz, 3 H), 1.00 (t, J = 7.2 Hz, 3 H), 0.97 (s, 3 H), 0.77 (s, 9 H), 0.03 (s, 3 H), -0.25 (s, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) 214.06, 208.47, 173.38, 144.11, 141.52, 115.65, 73.23, 54.11, 43.75, 42.21, 37.15, 35.19, 31.71, 29.54, 27.66, 26.32, 25.67, 25.48, 20.26, 18.54, 18.31, 8.18, -3.18, -3.89 ppm; MS, m/z ($M^+ - C_4H_9$) calcd 375.2355, obsd 375.2351.

(-)-(6*R*,7*R*)-4,5,6,7-Tetrahydro-7-[(1*R*,3*S*,4*Z*)-1-methoxy-3-methyl-4-(trimethylsiloxy)-3-vinyl-4-hexenyl]-6,7-dimethyl-1-indanone (20a). A solution of lithium diisopropylamide was prepared in tetrahydrofuran (70 mL) from *n*-butyllithium (3.04 mL, 4.7 mmol, 1.55 M in hexane) and diisopropylamine (0.66 mL, 4.7 mmol). This solution was cooled to -78 °C and **3** (712 mg, 2.14 mmol) dissolved in tetrahydrofuran (10 mL) was added. The bis enolate was permitted to form over 45 min, imparting

an orange color to the reaction mixture. Subsequently, HMPA (3.28 mL, 18.8 mmol) was introduced followed 0.5 h later by trimethylsilyl chloride (0.60 mL, 4.71 mmol). The reaction mixture was gradually warmed from −78 to 20 °C during 5 h. The tetrahydrofuran was removed under reduced pressure, and the residue was taken up in pentane (60 mL) and extracted with saturated sodium bicarbonate solution (3 × 40 mL). The combined aqueous washes were back-extracted with pentane (2 × 20 mL). The pooled organic phases were dried and freed of solvent, yielding a mixture of the mono and bis silyl enol ethers.

The mixture of silyl enol ethers was dissolved in purified benzene (110 mL) and deoxygenated with a stream of nitrogen for 30 min. The reaction mixture was put under a positive nitrogen pressure, and bis(tri-*o*-tolylphosphine)palladium(II) chloride (134 mg, 0.170 mmol) and tributyltin fluoride (1.653 g, 5.35 mmol) were added. The reaction mixture was brought to the reflux temperature and soon turned black. After 5 h the mixture was cooled, diluted with ether (200 mL), and extracted with 1 N sodium hydroxide solution (125 mL). The aqueous phase was back-extracted with ether (2 × 100 mL). The organic phases were combined, dried, and freed of solvent. The crude material was purified by chromatography (silica gel; 5% ethyl acetate in petroleum ether) to afford (−)-**20a** (726 mg, 84%); $[\alpha]^{25}_{D}$ −34.9° (*c* 2.42, CCl_4): IR (neat, cm^{-1}) 3090, 2975, 2930, 1695, 1663, 1635, 1455, 1412, 1380, 1320, 1250, 1200, 1100, 1005, 978, 905, 840, 788, 760; ^1H NMR (300 MHz, C_6D_6) δ 6.14 (dd, *J* = 17.8, 10.6 Hz, 1 H), 5.17 (d, *J* = 17.4 Hz, 1 H), 5.16 (d, *J* = 10.9 Hz, 1 H), 4.79 (q, *J* = 6.7 Hz, 1 H), 4.32 (dd, *J* = 7.2, 2.2 Hz, 1 H), 3.22 (s, 3 H), 2.14–1.75 (series of m, 9 H), 1.56 (d, *J* = 6.7 Hz, 3 H), 1.56–1.46 (m, 2 H), 1.37 (s, 3 H), 1.27 (s, 3 H), 1.23 (d, *J* = 6.9 Hz, 3 H), 0.26 (s, 9 H); ^{13}C NMR (75 MHz, C_6D_6) 206.80, 171.04, 157.08, 145.99, 144.26, 112.79, 100.27, 83.58, 59.29, 46.35, 42.99, 42.10, 39.33, 35.17, 29.27, 28.03, 27.31, 24.40, 22.81, 18.04, 12.00, 1.40 ppm; MS, *m/z* (relative intensity) 293 (13), 241 (53), 236 (16), 209 (32), 184 (62), 183 (50), 169 (33), 163 (28), 151 (25), 73 (100); UV (EtOH) λ_{max} (ε) 239 (9750).

For **21a**: IR ($CDCl_3$, cm^{-1}) 3100, 2975, 1682, 1639, 1460, 1381, 1321, 1255, 1110, 1075, 985, 850; ^1H NMR (300 MHz, C_6D_6) δ 6.12 (dd, *J* = 17.4, 11.0 Hz, 1 H), 5.18 (d, *J* = 17.3 Hz, 1 H), 5.17 (d, *J* = 11.0 Hz, 1 H), 4.80 (q, *J* = 6.7 Hz, 1 H), 4.36 (dd, *J* = 7.4, 1.9 Hz, 1 H), 3.51 (t, *J* = 4.5 Hz, 1 H), 3.24 (s, 3 H), 2.21–1.82 (m, 8 H), 1.55 (d, *J* = 6.7 Hz, 3 H), 1.53–1.43 (m, 1 H), 1.39 (s, 3 H), 1.26 (d, *J* = 5.4 Hz, 3 H), 1.25 (s, 3 H), 0.25 (s, 9 H), 0.04 (s, 9 H); ^{13}C NMR (75 MHz, C_6D_6) 184.32, 169.20, 157.14, 146.00, 144.96, 112.86, 100.14, 83.67, 59.19, 46.40, 42.92, 42.32, 40.36, 39.86, 32.57, 28.38, 27.73, 23.93, 22.66, 18.24, 12.00, 1.39, −2.92 ppm; MS, *m/z* (M^+) calcd 476.3142, obsd 476.3126.

[[(1*Z*,2*S*)-1-Ethylidene-2-[(2*R*)-2-(methoxymethyl)-2-[(4*R*,5*R*)-4,5,6,7-tetrahydro-4,5-dimethyl-3-(trimethylsiloxy)inden-4-yl]ethyl]-2-methyl-3-butenyl]oxy]trimethylsilane (21b) and (−)-(6*R*,7*R*)-4,5,6,7-Tetrahydro-7-[(1*R*,3*S*,4*Z*)-1-(methoxymethyl)-3-methyl-4-(trimethylsiloxy)-3-vinyl-4-hexenyl]-6,7-dimethyl-1-indanone (20b). To a stirred solution of 2.2 equiv of lithium diisopropylamide (generated from diisopropylamine (0.548 g, 5.78 mmol) and 3.95 mL of 1.46 M of *n*-butyllithium (5.78 mmol)) in 250 mL of tetrahydrofuran cooled to −78 °C was added a solution of dione **17a** (0.962 g, 2.65 mmol) in 30 mL of tetrahydrofuran via cannula. The mixture was stirred at −78 °C for 1.25 h, and then 0.74 mL of trimethylsilyl chloride (0.63 g, 5.80 mmol) was introduced via cannula in 30 mL of tetrahydrofuran. The mixture was stirred at −78 °C for 1.75 h, poured into saturated sodium bicarbonate solution (350 mL), and extracted with methylene chloride (2 × 600 mL). The combined organic layers were dried, filtered, and concentrated in vacuo to leave a yellow oil. The oil was filtered through a plug of silica gel and purified by radial chromatography (4-mm plate, 15% ethyl acetate in petroleum ether) to provide 0.625 g (46%) of **21b** and 0.384 g (33%) of **20b**. Both **20b** and **21b** are readily hydrolyzed to the parent dione **17a**.

For **21b**: ^1H NMR (300 MHz, $CDCl_3$) δ 5.85 (dd, *J* = 10.8, 17.6 Hz, 1 H), 5.08 (d, *J* = 9.9 Hz, 1 H), 5.03 (dd, *J* = 1.9, 18.5 Hz, 1 H), 4.64 (q, *J* = 6.7 Hz, 1 H), 4.36 (AB q, *J* = 5.8 Hz, 1 H), 4.33 (dd, *J* = 2.1, 7.1 Hz, 1 H), 4.29 (AB q, *J* = 5.8 Hz, 1 H), 3.11 (s, 3 H), 2.62 (dd, *J* = 6.5, 18.1 Hz, 1 H), 2.39 (dt, *J* = 6.0, 18.5 Hz, 1 H), 2.25–2.09 (m, 3 H), 1.98–1.77 (m, 3 H), 1.69–1.64 (m, 2 H), 1.47 (d, *J* = 6.6 Hz, 3 H), 1.16 (s, 3 H), 1.13 (d, *J* = 7.0 Hz, 3 H), 1.05 (s, 3 H), 0.17 (s, 9 H), 0.01 (s, 9 H); MS, the molecular ion peak was too transient for high-resolution measurement.

For **20b**: ^1H NMR (300 MHz, $CDCl_3$) δ 5.87 (dd, *J* = 10.8, 17.5 Hz, 1 H), 5.07 (d, *J* = 9.9 Hz, 1 H), 5.02 (d, *J* = 16.5 Hz, 1 H), 4.63 (q, *J* = 6.8 Hz, 1 H), 4.38–4.31 (m, 3 H), 3.08 (s, 3 H), 2.43–2.10 (m, 6 H), 1.94–1.70 (m, 5 H), 1.48 (d, *J* = 6.6 Hz, 3 H), 1.14 (s, 3 H), 1.11 (d, *J* = 6.6 Hz, 3 H), 1.06 (s, 3 H), 0.18 (s, 9 H); MS, the molecular ion peak was too transient for high-resolution measurement.

The selective desilylation was achieved as follows. A solution of **21b** (2.03 g, 4.00 mmol) and tri-*n*-butyltin fluoride (3.11 g, 10.5 mmol) in dry benzene (200 mL) was heated at reflux for 21 h. The mixture was allowed to cool to room temperature, poured into saturated sodium bicarbonate solution (400 mL), and extracted with methylene chloride (2 × 700 mL). The combined organic layers were dried, filtered, and concentrated in vacuo to leave a yellow oil. Flash chromatography (silica gel; 10% ethyl acetate in petroleum ether) provided 0.34 g (17%) of recovered **21b** and 1.30 g (90% based on recovered **17a**) of **20b**.

(6*R*,7*R*)-7-[(1*R*,3*S*,4*Z*)-1-(*tert*-Butyldimethylsiloxy)-3-methyl-4-(trimethylsiloxy)-3-vinyl-4-hexenyl]-4,5,6,7-tetrahydro-6,7-dimethyl-1-indanone (20c). Lithium diisopropylamide was prepared in tetrahydrofuran (20 mL) from *n*-butyllithium (1.24 mL, 1.92 mmol, 1.55 M in hexane) and diisopropylamine (0.27 mL, 1.92 mmol). This solution was cooled to −78 °C, and keto enone **17b** (376 mg, 0.869 mmol) dissolved in tetrahydrofuran (5 mL) was added. The bright yellow bis enolate was permitted to form over 45 min. Then HPMA (0.60 mL, 3.48 mmol) followed by trimethylsilyl chloride (0.24 mL, 1.92 mmol) was added. The reaction mixture was allowed to warm gradually from −78 to 20 °C over 6 h. The tetrahydrofuran was removed in vacuo, and the residue was dissolved in pentane (80 mL) and extracted with saturated sodium bicarbonate solution (2 × 40 mL). The combined aqueous phases were back-extracted with pentane (2 × 20 mL), and the combined organic phases were dried and freed of solvent. The mono and bis silyl enol ethers were separated by MPLC (silica gel; 5% ethyl acetate in petroleum ether), yielding bis silyl enol ether **21c** (139 mg, 29%) and silyl enol ether **20c** (127 mg, 29%) as light yellow oils.

For **20c**: IR (CCl_4, cm^{-1}) 3090, 2930, 1695, 1661, 1634, 1461, 1379, 1315, 1250, 1117, 1070, 910, 831, 670; ^1H NMR (300 MHz, $CDCl_3$) δ 5.95 (dd, *J* = 17.5, 10.7 Hz, 1 H), 5.14 (d, *J* = 10.6 Hz, 1 H), 5.09 (d, *J* = 17.4 Hz, 1 H), 4.82 (br s, 1 H), 4.64 (q, *J* = 6.8 Hz, 1 H), 2.38–2.15 (series of m, 7 H), 1.81–1.60 (series of m, 4 H), 1.50 (d, *J* = 6.5 Hz, 3 H), 1.23 (s, 3 H), 1.12 (d, *J* = 6.9 Hz, 3 H), 1.00 (s, 3 H), 0.77 (s, 9 H), 0.22 (s, 9 H), 0.04 (s, 3 H), −0.24 (s, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) 208.29, 172.73, 157.07, 144.48, 144.46, 113.05, 99.85, 73.61, 45.81, 44.03, 43.39, 36.86, 35.16, 29.54, 27.61, 26.41, 26.05, 25.38, 22.01, 18.61, 18.40, 11.83, 1.23, −3.16, −3.85 ppm; MS, *m/z* ($M^+ - CH_3$) calcd 489.3220, obsd 489.3211.

For **21c**: ^1H NMR (300 MHz, $CDCl_3$) δ 6.03–5.89 (m, 1 H), 5.28–5.06 (m, 3 H), 4.86–4.82 (m, 1 H), 4.64 (q, *J* = 6.7 Hz, 1 H), 2.64–2.05 (series of m, 4 H), 1.80–1.59 (m, 2 H), 1.50 (dd, *J* = 6.7, 1.3 Hz, 3 H), 1.22 (s, 3 H), 1.11 (br d, *J* = 7.0 Hz, 3 H), 1.01–0.95 (m, 6 H), 0.77 (s, 9 H), 0.22 (s, 9 H), 0.02 (s, 9 H), −0.24 (s, 3 H), −0.28 (s, 3 H); MS, the molecular ion peak was too transient for high-resolution measurement.

(−)-(6*R*,7*R*)-4,5,6,7-Tetrahydro-7-[(1*R*,3*S*,4*Z*)-1-methoxy-3-methyl-4-(*tert*-butyldimethylsiloxy)-3-vinyl-4-hexenyl]-6,7-dimethyl-1-indanone (22). Lithium diisopropylamide was prepared from diisopropylamine (0.18 mL, 1.32 mmol) and *n*-butyllithium (0.85 mL, 1.32 mmol, 1.55 M in hexane) in tetrahydrofuran (20 mL). This solution was cooled to −78 °C, and **3** (200 mg, 0.601 mmol) dissolved in tetrahydrofuran (2 mL) was added. The yellow enolate was permitted to form during 1 h, at which time HMPA (0.92 mL, 5.3 mmol) was added. After 30 min, *tert*-butyldimethylsilyl trifluoromethanesulfonate (0.30 mL, 1.32 mmol) was introduced and the reaction mixture was permitted to gradually warm to room temperature over several hours. The tetrahydrofuran was removed under reduced pressure, and the residue was dissolved in pentane (20 mL) and washed with saturated sodium bicarbonate solution (3 × 15 mL). The combined aqueous washes were back-extracted with pentane (3 × 10 mL), and the combined organic phases were dried and freed of solvent. The crude material was purified by MPLC (silica gel; 10% ethyl acetate in petroleum ether) to furnish the bis silyl enol ether (111

mg, 33%), $[\alpha]^{25}_D$ −30.5° (c 3.03, CCl_4), as a colorless oil and the mono silyl enol ether **22** (134 mg, 50%), $[\alpha]^{25}_D$ −21.5° (c 1.62, CCl_4), also as a colorless oil: IR (CCl_4, cm^{-1}) 3085, 2960, 2935, 2860, 1695, 1662, 1634, 1463, 1381, 1322, 1252, 1103, 1072, 1002, 911, 834; ^1H NMR (300 MHz, $CDCl_3$) δ 5.93 (dd, J = 17.5, 10.8 Hz, 1 H), 5.08 (dd, J = 10.8, 1.4 Hz, 1 H), 5.04 (dd, J = 17.5, 1.4 Hz, 1 H), 4.63 (q, J = 6.8 Hz, 1 H), 3.93 (dd, J = 7.5, 1.7 Hz, 1 H), 3.06 (s, 3 H), 2.43–2.25 (series of m, 6 H), 1.96–1.61 (series of m, 5 H), 1.52 (d, J = 6.8 Hz, 3 H), 1.18 (s, 3 H), 1.09 (d, J = 6.9 Hz, 3 H), 1.08 (s, 3 H), 0.97 (s, 9 H), 0.16 (s, 3 H), 0.15 (s, 3 H); ^{13}C NMR (75 MHz, C_6D_6) 207.03, 171.27, 156.46, 146.82, 144.25, 112.65, 100.12, 83.43, 59.91, 46.36, 42.76, 41.66, 39.13, 35.00, 29.10, 27.85, 27.15, 26.60, 24.24, 23.29, 19.28, 17.82, 11.93, −2.47, −2.60 ppm; MS, (M^+) calcd 446.3216, obsd 446.3253.

For the bis silyl enol ether: IR (CCl_4, cm^{-1}) 3090, 2960, 2930, 2890, 2850, 1675, 1660, 1645, 1470, 1460, 1410, 1380, 1360, 1320, 1250, 1105, 1070, 1000, 975, 910, 830, 675; ^1H NMR (300 MHz, C_6D_6) δ 6.13–6.07 (m, 1 H), 5.20–5.08 (m, 2 H), 4.78 (q, J = 6.7 Hz, 1 H), 4.32 (d, J = 6.9 Hz, 1 H), 4.26 (s, 1 H), 3.21 (s, 3 H), 2.27–0.81 (series of m, 12 H), 1.59 (d, J = 6.8 Hz, 3 H), 1.39 (s, 3 H), 1.25 (s, 3 H), 1.10 (s, 9 H), 0.92 (s, 9 H), 0.22 (s, 3 H), 0.14 (s, 3 H), 0.05 (s, 3 H), −0.06 (s, 3 H); MS, m/z (M^+) calcd 560.4081, obsd 560.4098.

(αS,γR,4R,5R)-4,5,6,7-Tetrahydro-γ-(methoxymethyl)-α,4,5-trimethyl-3-oxo-α-vinyl-4-indanbutyraldehyde (24). A solution of **20b** (2.12 g, 4.90 mmol) in methylene chloride (525 mL) was treated with *m*-chloroperbenzoic acid (1.01 g of 85% purity, 4.94 mmol) and heated at the reflux temperature for 4 h. The reaction mixture was allowed to cool to room temperature, poured into saturated sodium bicarbonate solution (1.5 L), and extracted with methylene chloride (2 × 2.5 L). The combined organic layers were dried, filtered, and concentrated to leave α-siloxy ketone as a yellow oil. The crude material was diluted in 110 mL of tetrahydrofuran and 110 mL of methanol. The resulting solution was cooled in a 0 °C bath and treated with 0.74 g (10.4 mmol) of sodium borohydride. The reaction mixture was stirred at 0 °C for 3 h, poured into saturated sodium bicarbonate solution (350 mL), and extracted with methylene chloride (3 × 500 mL). The combined organic layers were dried, filtered, and concentrated in vacuo to leave a pale yellow oil. This oil was dissolved in 110 mL of tetrahydrofuran and 110 mL of methanol and treated with 5 mL of 10% sulfuric acid for 5 s. The mixture was immediately poured into saturated sodium bicarbonate solution (350 mL) and extracted with methylene chloride (3 × 500 mL). The combined organic layers were dried, filtered, and concentrated in vacuo to leave the oily 1,2-diol.

The diol was transferred to a 500-mL flask and diluted with 215 mL of dry benzene. To this magnetically stirred solution was added 2.60 g (5.75 mmol) of lead tetraacetate. Stirring was maintained at room temperature for 1 h before the reaction mixture was directly loaded onto a silica gel column (55 × 50 mm, 39% ethyl acetate–petroleum ether) and eluted with 1.5 L of solvent. The eluent was concentrated in vacuo to leave a yellow oil, which was purified by flash chromatography (silica gel, elution with 31% ethyl acetate in petroleum ether) to provide 1.12 g (69%) of **24** as a pale yellow solid, mp 73–76 °C; ^1H NMR (300 MHz, $CDCl_3$) δ 9.29 (s, 1 H), 5.71 (dd, J = 10.7, 17.5 Hz, 1 H), 5.21 (d, J = 10.7 Hz, 1 H), 5.13 (d, J = 17.5 Hz, 1 H), 4.53 (dd, J = 2.3, 11.4 Hz, 1 H), 4.27 (AB q, J = 6.7 Hz, 1 H), 4.15 (AB q, J = 6.6 Hz, 1 H), 3.07 (s, 3 H), 2.50–2.28 (m, 5 H), 2.26–2.13 (m, 2 H), 1.95–1.70 (m, 4 H), 1.17 (s, 3 H), 1.14 (d, J = 8.3 Hz, 3 H), 1.13 (s, 3); ^{13}C NMR (75 MHz, $CDCl_3$) 209.05, 200.35, 171.33, 142.82, 139.49, 116.08, 99.27, 82.40, 55.58, 51.59, 42.24, 37.67, 36.48, 34.64, 29.70, 27.13, 25.71, 25.40, 17.27, 17.05 ppm.

Anal. Calcd for $C_{20}H_{30}O_4$: C, 71.82; H, 9.04. Found: C, 71.45; H, 8.95.

β-Keto Ester 26. To a stirred solution of diisopropylamine (1.47 mL, 10.7 mmol) in 165 mL of tetrahydrofuran cooled in a −78 °C bath was added 7.20 mL of 1.46 M *n*-butyllithium (10.2 mmol). After 0.5 h of stirring at −78 °C methyl acetate (0.84 mL, 10.3 mmol) was introduced via syringe. The reaction mixture was stirred at −78 °C for an additional 0.5 h, at which point 1.76 g (5.26 mmol) of aldehyde **24** in 165 mL of tetrahydrofuran was added via cannula. Stirring at −78 °C was continued for 3 h. The contents were poured into saturated sodium bicarbonate solution (750 mL) and extracted with methylene chloride (2 × 1.2 L). The combined organic layers were dried, filtered, and concentrated in vacuo to leave crude β-hydroxy ester **25** (2.33 g, 5.71 mmol) as a pale yellow oil: ^1H NMR (300 MHz, $CDCl_3$) δ 5.96 (dd, J = 10.9, 17.6 Hz, 1 H), 5.16 (d, J = 10.9 Hz, 1 H), 5.05 (d, J = 17.7 Hz, 1 H), 4.58 (d, J = 8.3 Hz, 1 H), 4.52 (s, 2 H), 3.87 (dd, J = 2.0, 6.5 Hz, 1 H), 3.68 (s, 3 H), 3.45–3.35 (br s, 1 H), 3.19 (s, 3 H), 3.13 (d, J = 10.7 Hz, 2 H), 2.50–2.10 (m, 6 H), 1.80–1.50 (m, 5 H), 1.13 (d, J = 6.9 Hz, 3 H), 1.11 (s, 3 H), 1.06 (s, 3 H). The material was not analyzed further but carried on to the β-keto ester.

A reaction mixture consisting of 2.33 g (5.71 mmol) of **25**, 180 mL of dry benzene, 6.10 mL of dry dimethyl sulfoxide (6.70 g, 84.5 mmol, 15 equiv), 3.53 g of dicyclohexylcarbodiimide (17.1 mmol, 3 equiv), and 0.557 g of pyridinium trifluoroacetate (2.88 mmol, 0.5 equiv) was stirred at room temperature for 93 h, poured into saturated sodium bicarbonate solution (1 L), and extracted with methylene chloride (2 × 1 L). The combined organic layers were dried, filtered, and concentrated in vacuo to leave a pale yellow solid. This solid was separated by filtration and washed with a small amount of 28% ethyl acetate in petroleum ether. The filtrate was concentrated in vacuo to leave a yellow oil, flash chromatography of which on silica gel (50 × 110 mm, 28% ethyl acetate in petroleum ether) provided 1.64 g (71%) of **26**; $[\alpha]^{25}_D$ −210.3° (c 1.28, $CHCl_3$); IR (film, cm^{-1}) 3080, 2925, 1745, 1705, 1690, 1630, 1380, 1030, 925; ^1H NMR (300 MHz, $CDCl_3$) δ 5.86 (dd, J = 10.8, 17.4 Hz, 1 H), 5.26 (d, J = 10.7 Hz, 1 H), 5.23 (d, J = 17.5 Hz, 1 H), 4.54 (dd, J = 1.9, 11.4 Hz, 1 H), 4.25 (AB q, J = 6.7 Hz, 1 H), 4.18 (AB q, J = 6.7 Hz, 1 H), 3.69 (s, 3 H), 3.68 (AB q, J = 15.6 Hz, 1 H), 3.58 (AB q, J = 15.7 Hz, 1 H), 3.11 (s, 3 H), 2.50–2.10 (m, 6 H), 1.90–1.50 (m, 5 H), 1.25 (s, 3 H), 1.18 (d, J = 7.0 Hz, 3 H), 1.14 (s, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) 208.87, 203.20, 171.28, 168.18, 142.62, 141.68, 115.82, 99.50, 82.42, 55.50, 53.30, 51.82, 44.34, 42.10, 38.21, 36.46, 34.49, 29.56, 27.03, 25.66, 25.34, 19.45, 17.16 ppm.

Anal. Calcd for $C_{23}H_{34}O_6$: C, 67.99; H, 8.43. Found: C, 67.86; H, 8.41.

(6R,7R)-7-[(1R,3S)-3-[2-Bromopropionyl]-1-methoxy-3-methyl-4-pentenyl]-4,5,6,7-tetrahydro-6,7-dimethyl-1-indanone (27a). Silyl enol ether **20a** (88 mg, 0.217 mmol) dissolved in tetrahydrofuran (6 mL) was cooled to 0 °C in an ice bath. *N*-Bromosuccinimide (41 mg, 0.23 mmol) was added, and stirring was continued for 20 min. The reaction mixture was poured into a combination of brine (40 mL) and saturated sodium bicarbonate solution (40 mL) and extracted with ether (4 × 40 mL). The combined organic phases were dried and freed of solvent. The crude material was purified by MPLC (silica gel; 23% ethyl acetate in petroleum ether) to give **27a** (76 mg, 85%) as a light yellow oil: IR ($CDCl_3$, cm^{-1}) 3100, 2980, 2940, 1719, 1695, 1648, 1465, 1446, 1425, 1412, 1383, 1200, 1100, 1000; ^1H NMR (300 MHz, $CDCl_3$) δ 6.04 (dd, J = 17.5, 10.5 Hz, 1 H), 5.22–5.16 (m, 2 H), 4.72–4.69 (m, 1 H), 4.11 (dd, J = 11.0, 3.0 Hz, 1 H), 3.95 (d, J = 10.3 Hz, 1 H), 3.08 and 2.91 (two s, 3 H total), 2.48–2.28 (series of m, 9 H), 1.83–1.74 (m, 2 H), 1.71 and 1.69 (two d, J = 6.7 Hz, 3 H total), 1.39 and 1.28 (two s, 3 H total), 1.16 and 1.13 (two s, 3 H total), 1.12 (d, J = 6.9 Hz, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) 208.60, 208.28, 205.59, 204.64, 173.65, 173.50, 143.69, 143.38, 142.70, 114.72, 114.43, 82.20, 81.97, 59.44, 59.32, 53.14, 52.62, 42.57, 41.71, 41.39, 40.55, 39.54, 38.93, 35.17, 35.13, 29.54, 29.46, 27.84, 27.64, 27.40, 24.46, 23.88, 21.78, 21.11, 19.66, 18.74, 17.59, 17.24 ppm; MS, m/z (M^+ − CH_4OBr) calcd 299.2011, obsd 299.2020; m/z (relative intensity) 299 (2), 249 (98), 247 (100), 215 (21), 169 (20), 168 (21), 163 (42), 107 (26), 91 (27), 81 (96).

(6R,7R)-4,5,6,7-Tetrahydro-7-[(1R,3S)-1-methoxy-3-methyl-3-[2-(phenylselenyl)propionyl]-4-pentenyl]-6,7-dimethyl-1-indanone (27b). Silyl enol ether **20a** (30 mg, 0.074 mmol) was dissolved in dry benzene (2 mL). Phenylselenyl chloride (14 mg, 0.074 mmol) dissolved in benzene (2 mL) was introduced via syringe. The reddish color disappeared nearly instantaneously leaving a yellow solution. After 20 min, the solvent was removed in vacuo and the product was purified by MPLC (silica gel; 12% ethyl acetate in petroleum ether) to give **27b** (25 mg, 69%) as an oil: IR (neat, cm^{-1}) 3045, 2910, 1690, 1620, 1577, 1437, 1365, 1200, 995, 912, 785, 739; ^1H NMR (300 MHz, $CDCl_3$) δ 7.54–7.24 (m, 5 H), 6.21–5.83 (m, 1 H), 5.22–5.09 (m, 2 H), 4.12–3.93 (m, 1 H), 3.77–3.62 (m, 1 H), 3.11 and 2.94 (two s, 3 H total), 2.60–2.04 (m, 7 H), 1.90–1.52 (m, 4 H), 1.46 and 1.41 (two

d, J = 6.9 Hz, 3 H total), 1.37 and 1.30 (two s, 3 H total), 1.22–1.09 (m, 6 H); ^{13}C NMR (75 MHz, $CDCl_3$) 211.68, 208.68, 208.55, 173.53, 173.46, 143.87, 143.66, 143.30, 143.03, 136.17, 135.86, 128.85, 128.80, 128.49, 128.31, 114.48, 114.29, 82.76, 82.16, 59.89, 59.49, 59.39, 53.21, 53.16, 41.98, 41.81, 41.46, 41.01, 40.26, 39.70, 35.20, 35.16, 29.56, 29.49, 27.85, 27.67, 27.62, 27.43, 24.49, 24.00, 23.93, 19.22, 18.81, 17.59, 17.40 ppm; MS, m/z (M^+) calcd 488.1830, obsd 488.1883.

Methoxy Acetal 28. To a stirred suspension of methoxymethyl triphenylphosphonium chloride (4.31 g, 12.57 mmol) in 150 mL of tetrahydrofuran cooled in a 0 °C bath was added lithium diisopropylamide via cannula in 150 mL of the same solvent. [The lithium diisopropylamide was generated from diisopropyl amine (1.23 g, 12.18 mmol) and 8.06 mL of 1.56 M n-butyllithium (12.57 mmol) at −78 °C during 0.5 h.] The mixture was stirred at 0 °C for 0.5 h before aldehyde **24** (2.00 g, 5.99 mmol) in 150 mL of tetrahydrofuran was added via cannula. The reaction mixture was stirred at 0 °C for 0.5 h, poured into brine (500 mL), and extracted with methylene chloride (2 × 800 mL). The combined organic layers were dried, filtered, and concentrated in vacuo to leave a yellow oil, which was filtered through a column of flash silica gel (52 × 95 mm, 30% ethyl acetate in petroleum ether) to provide the enol ether (1.89 g, 87%).

The enol ether was placed in a 500-mL flask with 220 mL of tetrahydrofuran and 220 mL of 10% hydrochloric acid. The mixture was stirred at room temperature for 4 h, poured into saturated sodium bicarbonate solution (600 mL), and extracted with methylene chloride (3 × 600 mL). The combined organic layers were dried, filtered, and concentrated in vacuo to leave a yellow oil, which was placed in a 1-L flask with 400 mL of methanol and 0.20 g of p-toluenesulfonic acid. The reaction mixture was stirred at room temperature for 2.5 h, poured into saturated sodium bicarbonate solution (600 mL), and extracted with methylene chloride (3 × 600 mL). The combined organic layers were dried, filtered, and concentrated in vacuo to leave a yellow oil. Flash chromatography (silica gel, 10% ethyl acetate in petroleum ether) provided **28** (1.23 g, 65%): $[\alpha]^{25}_D$ −38.42° (c 1.15, $CHCl_3$); IR ($CHCl_3$, cm^{-1}) 2080, 2920, 1680, 1625, 1455, 1380, 1265, 1140, 1065, 995, 920; ^1H NMR (300 MHz, C_6D_6) δ 5.69 (dd, J = 10.8, 17.4 Hz, 1 H), 4.91 (dd, J = 0.9, 17.5 Hz, 1 H), 4.83 (dd, J = 1.1, 10.7 Hz, 1 H), 4.61 (d, J = 12.1 Hz, 1 H), 4.54 (dd, J = 4.2, 7.9 Hz, 1 H), 3.36 (s, 3 H), 2.04 (t, J = 4.9 Hz, 2 H), 2.00–1.93 (m, 1 H), 1.81–1.50 (m, 9 H), 1.43–1.35 (m, 1 H), 1.24 (s, 3 H), 1.11 (d, J = 6.9 Hz, 3 H), 1.07 (s, 3 H); ^{13}C NMR (75 MHz, C_6D_6) 206.87, 170.54, 150.00, 142.43, 109.61, 100.81, 73.94, 55.75, 41.91, 41.56, 36.78, 36.69, 35.59, 35.17, 29.09, 27.07, 26.07, 23.45, 23.15, 17.22 ppm; MS, the molecular ion peak was too transient for high-resolution measurement.

Hemithioacetal 29. A solution of 0.446 g (1.40 mmol) of **28** in 38 mL of methylene chloride was cooled in a −78 °C bath and 0.22 mL (2.14 mmol) of thiophenol was added via syringe, followed by 3.8 mL of boron trifluoride etherate. The reaction mixture was allowed to warm slowly to 0 °C with stirring, poured into saturated sodium bicarbonate solution (125 mL), and extracted with methylene chloride (2 × 130 mL). The combined organic layers were dried, filtered, and concentrated in vacuo to leave a yellow oil. Flash chromatography (silica gel, 5–10% ethyl acetate in petroleum ether) provided 0.402 g (72%) of **29**: $[\alpha]^{25}_D$ +60.96° (c 1.56, $CHCl_3$); IR (film, cm^{-1}) 3080, 3060, 2960, 2930, 1670, 1630, 1580, 1480, 1435, 1380, 1080, 915, 740; ^1H NMR (300 MHz, $CDCl_3$) δ 7.38–7.34 (m, 2 H), 7.26–7.15 (m, 3 H), 5.78 (dd, J = 10.7, 17.5 Hz, 1 H), 4.98–4.90 (m, 3 H), 4.47 (dd, J = 1.9, 12.4 Hz, 1 H), 2.37–2.25 (m, 3 H), 2.21–2.06 (m, 3 H) 1.76–1.53 (m, 6 H), 1.32–1.26 (m, 1 H), 1.18 (s, 3 H), 1.14 (s, 3 H), 1.06 (d, J = 6.7 Hz, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) 208.45, 172.79, 149.34, 142.19, 134.72, 131.04, 128.37, 128.34, 126.52, 109.85, 80.85, 41.45, 41.08, 37.27, 36.47, 34.99, 34.78, 29.24, 27.02, 26.54, 23.04, 22.01, 17.30 ppm.

Anal. Calcd for $C_{25}H_{32}SO_2$: C, 75.71; H, 8.13. Found: C, 75.55; H, 8.21.

Sulfone 30. To a solution of **29** (0.165 g, 0.42 mmol) in 26 mL of methylene chloride was added 0.561 g (1.29 mmol) of MoOPH. The reaction mixture was stirred at room temperature for 47 h, poured into water (150 mL), and extracted with methylene chloride (2 × 150 mL). The combined organic layers were dried, filtered, and concentrated in vacuo to leave a yellow oil. Flash chromatography (silica gel, 30% ethyl acetate in petroleum ether) provided 0.133 g (74%) of **30**: $[\alpha]^{25}_D$ −31.65° (c 1.17, $CHCl_3$); IR (film, cm^{-1}) 3080, 3060, 2960, 2930, 2880, 1670, 1630, 1580, 1380, 1320, 1150, 1080, 1000, 920; ^1H NMR (300 MHz, C_6D_6) δ 7.86–7.82 (m, 2 H), 6.98–6.90 (m, 3 H), 5.56 (dd, J = 10.7, 17.4 Hz, 1 H), 4.84 (d, J = 17.2 Hz, 1 H), 4.80 (d, J = 10.6 Hz, 1 H), 4.72 (dd, J = 4.5, 10.0 Hz, 1 H), 4.66 (d, J = 11.8 Hz, 1 H), 2.08–1.90 (m, 3 H), 1.77–1.05 (m, 10 H), 0.99 (d, J = 8.0 Hz, 3 H), 0.98 (s, 3 H), 0.95 (s, 3 H); ^{13}C NMR (75 MHz, C_6H_6) 206.71, 170.75, 148.80, 141.38, 138.45, 133.06, 129.97, 110.58, 88.94, 76.98, 60.03, 41.42, 36.09, 35.55, 34.91, 34.53, 33.43, 29.06, 26.92, 25.62, 23.69, 21.80; 17.14 ppm; MS, the molecular ion peak was too transient for high-resolution measurement.

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