Hz), 7.36 (1 H, J = 2.4 Hz), 9.95 (1 H, s); MS calcd for $C_{23}H_{26}N_2O_4$, m/e 394.1893; found, 394.1917; $[\alpha]^{25}_D$ +58° (c 0.36 in MeOH). (−)-**40** has $[\alpha]^{20}_D$ −51.1° (c 1.1 in CH_2Cl_2). The 15-formyl derivative of **39** has the following: IR ($CHCl_3$) 2940, 1720, 1670, 1600, 1480, 1450, 1380 cm^{-1}; UV (EtOH) 290 and 340 nm (ϵ 6620 and 9930, respectively); ^1H NMR (300 MHz, $CDCl_3$) δ 0.67 (3 H, t, J = 7.3 Hz), 0.96 (1 H, dq, J = 14.0 and 7.3 Hz), 1.09 (1 H, dq, J = 14.0 and 7.3 Hz), 1.70 (1 H, dd, J = 11.5 and 4.7 Hz), 2.04 (2 H, m), 2.53 (2 H, m), 2.67 (1 H, s), 3.02 (1 H, t, J = 6.6 Hz), 3.13 (1 H, d, J = 15.5 Hz), 3.50 (1 H, dd, J = 15.5 and 5.0 Hz), 3.98 (6 H, s), 5.65 (1 H, d, J = 10.1 Hz), 5.82 (1 H, dd, J = 10.1 and 3.9 Hz), 5.92 (1 H, dd, J = 8.6 and 3.0 Hz), 7.68 (1 H, s), 7.69 (1 H, d, J = 1.7 Hz), 10.18 (1 H, s); MS calcd for $C_{23}H_{26}N_2O_4$, m/e 394.1893; found, 394.1906; $[\alpha]^{25}_D$ +26° (c 0.1 in $CHCl_3$).

(−)-1-Carbomethoxy-16-methoxytabersonine (41) and (−)-16-Methoxytabersonine (4). A solution of sodium chlorite (184 μL, 1 M) was added to a mixture of (+)-**40**/(+)-15-formyl derivative (65.9 mg, 167 μM) and amidosulfonic acid (100 mg, 1.03 μM) in acetone (6 mL), isopropenyl acetate (1.8 mL), and 10% NaH_2PO_4–H_2O buffer (1.8 mL) at 0 °C. After 0.5 h ethereal diazomethane was added until a yellow color persisted. The solvent was evaporated to low bulk, and the residue was diluted with saturated aqueous sodium bicarbonate solution (5 mL) and extracted with chloroform (4 × 4 mL). The extract was filtered through $MgSO_4$ and evaporated to leave a yellow gum. On a small scale this was purified by PLC, eluting with 50% EtOAc/hexane, to give **41** (65%): IR ($CHCl_3$) 3010, 2960, 1740, 1600, 1440, 1370 cm^{-1}; UV (EtOH) 213, 238, and 281 nm (ϵ 18 320, 9670, and 3820, respectively); ^1H NMR (300 MHz, $CDCl_3$) δ 0.62 (3 H, t, J = 7.2 Hz), 1.02 (2 H, m), 1.72 (1 H, dd, J = 11.4 and 5.0 Hz), 2.13 (1 H, m), 2.79 (1 H, dd, J = 15.0 and 2.0 Hz), 2.46 (1 H, m), 2.59 (1 H, s), 2.69 (1 H, d, J = 15.0 Hz), 3.05 (2 H, m), 3.48 (1 H, dd, J = 16.0 and 4.7 Hz), 3.74 (3 H, s), 3.81 (6 H, s), 3.83 (3 H, s), 5.63 (1 H, d, J = 10.0 Hz), 5.80 (1 H, dd, J = 10.0 and 5.0 Hz), 6.57 (1 H, dd, J = 8.4 and 2.6 Hz), 7.07 (1 H, d, J = 8.4 Hz), 7.45 (1 H, d, J = 2.7 Hz); MS calcd for $C_{24}H_{28}N_2O_5$, m/e 424.1998; found, 424.1993; $[\alpha]^{27}_D$ −62° (c 0.23 in CH_2Cl_2). (+)-**41** has $[\alpha]^{20}_D$ +56° (c 1.1 in CH_2Cl_2).

The above yellow gum was dissolved in dry methanol (3 mL) at 4 °C and treated with NaOMe in methanol (6 mL, 2 M). After the mixture was stirred at 24 °C for 5 h, it was cooled to 4 °C, and acetic acid (720 μL) was added. The mixture was concentrated to low bulk and diluted with saturated aqueous sodium bicarbonate solution (4 mL) and 2 M aqueous sodium hydroxide (4 mL). The solution was extracted with $CHCl_3$ (4 × 4 mL), and the combined extracts were filtered through $MgSO_4$ and evaporated to leave a yellow gum. Column chromatography over silica gel, eluting with 23% EtOAc-hexane, gave a colorless glass, (−)-**4** (31.0 mg, 75.1% from **40**): IR ($CHCl_3$) 3380, 2960, 2780, 1670, 1620, 1440, 1260 cm^{-1}; UV (EtOH) 244 and 326 nm (ϵ 7250 and 9660, respectively); ^1H NMR (300 MHz, C_6D_6) δ 0.73 (3 H, t, J = 7.1 Hz), 1.02 (1 H, dq, J = 14.5 and 7.2 Hz), 1.18 (1 H, dq, J = 14.5 and 7.2 Hz), 1.72 (1 H, dd, J = 11.7 and 7.6 Hz), 2.19 (1 H, m), 2.48 (1 H, m), 2.72 (2 H, s), 2.90 (2 H, s), 3.01 (1 H, d, J = 14.8 Hz), 3.22 (1 H, dd, J = 14.8 and 7.6 Hz), 3.32 (3 H, s), 3.59 (3 H, s), 5.68 (2 H, m), 5.93 (1 H, d, J = 2.4 Hz), 6.45 (1 H, dd, J = 8.2 and 2.4 Hz), 6.99 (1 H, d, J = 8.2 Hz), 9.40 (1 H, bs); MS calcd for $C_{22}H_{26}N_2O_3$, m/e 366.1943; found, 366.1920; $[\alpha]^{27}_D$ −196° (c 0.17 in $CHCl_3$) [the rotation varies with the age of the sample; in another experiment $[\alpha]^{29}_D$ −253° (c 1.55 in $CHCl_3$)]. (+)-**4** has $[\alpha]^{20}_D$ +253° (c 0.32 in CH_2Cl_2) (lit. values:[4,5] $[\alpha]^{23}_D$ −310 ± 2° (c 0.23 in $CHCl_3$), $[\alpha]^{24}_D$ −211° (c 0.114 in $CHCl_3$). The ^1H NMR spectra of both (+)- and (−)-16-methoxytabersonine were identical with that of (±)-16-methoxytabersonine provided by Professor L. Overman.

Acknowledgment. We thank the National Institutes of Health for financial support of this work and the National Science Foundation for assistance in purchasing high-field NMR equipment (Grant CHE 81-05004). Dr. John Huffman is gratefully thanked for single-crystal X-ray crystallographic structure determinations. Professors L. Overman and M. Kuehne are thanked for spectra and a sample of 16-methoxytabersonine.

Total Synthesis of (−)-Laurenyne. Use of Acetal-Initiated Cyclizations To Prepare Functionalized Eight-Membered Cyclic Ethers

Larry E. Overman* and Andrew S. Thompson[1]

Contribution from the Department of Chemistry, University of California, Irvine, California 92717. *Received September 17, 1987*

Abstract: A highly stereocontrolled and enantioselective synthesis of the title compound **1** is described. The key step is cyclization of mixed acetal **13** to yield oxocene **14**. This step not only forms the eight-membered ring but also introduces the Δ^4-unsaturation and cis-oriented side chains of the marine natural product. This synthesis also demonstrates that the absolute configuration for natural laurenyne must be revised to 2*R*,7*R*,8*R* (i.e., enantiomeric with **1**). Also reported are exploratory studies that help to define the scope and limitations of the acetal cyclization route to eight-membered ring ethers.

A variety of structurally unusual C_{15} nonisoprenoid metabolites have been isolated from red algae as well as the molluscs that feed on them.[2] The vast majority of these are cyclic ethers, which are elaborated in a fascinating variety of ring sizes. Since the pioneering isolation and structure elucidation of laurencin (**2**) by Irie and co-workers,[3] halogenated eight-membered cyclic ethers (oxocanes) and enyne side chains have been shown to be common structural features of many of these natural products, particularly those isolated from the genus *Laurencia*. Three representative examples are depicted in Figure 1.

The structure of laurencin was initially suggested on the basis of extensive spectroscopic evidence[3] and later confirmed by a single-crystal X-ray analysis.[4] The absolute configuration was assigned by application of Prelog's atrolactic acid method[5] to a laurencin degradation product[3] and by X-ray crystallography.[4] The structures of most subsequently isolated members of this group, e.g., laurenyne (**1**)[6] and the pinnatifidenynes (**3**),[7] have

(1) NIH NRSA Postdoctoral Fellow (CA 07787), 1985–1987.

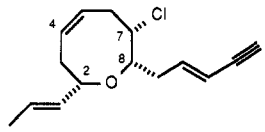
(2) For reviews, see: Moore, R. E. In *Marine Natural Products*; Scheuer, P. J., Ed.; Academic: New York, 1978; Vol. 1, Chapter 2. Erickson, K. K. *Ibid.*, 1983; Vol. 5, p 131. Faulkner, D. J. *Natl. Prod. Rep.* **1984**, 251; **1986**, 1.

(3) Irie, T.; Suzuki, M.; Masamune, T. *Tetrahedron* **1968**, *24*, 4193. Irie, T.; Suzuki, M.; Masamune, T. *Tetrahedron Lett.* **1965**, 1091.

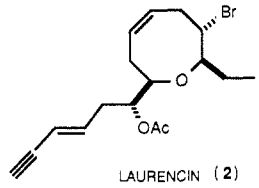
(4) Cameron, A. F.; Cheung, K. K.; Ferguson, G.; Robertson, J. M. *Chem. Commun.* **1965**, 638.

(5) Prelog, V. *Helv. Chim. Acta* **1953**, *36*, 308.

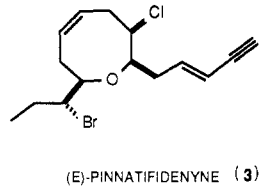
0002-7863/88/1510-2248$01.50/0



LAURENYNE (1)



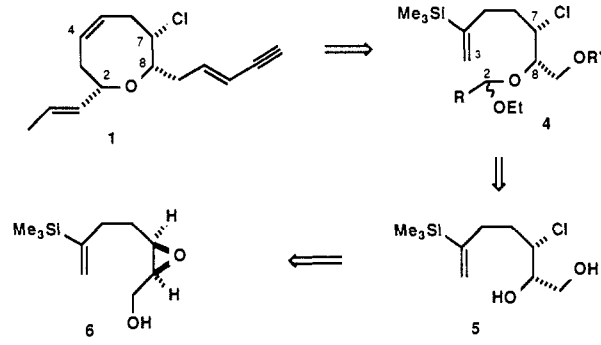
LAURENCIN (2)



(E)-PINNATIFIDENYNE (3)

Figure 1.

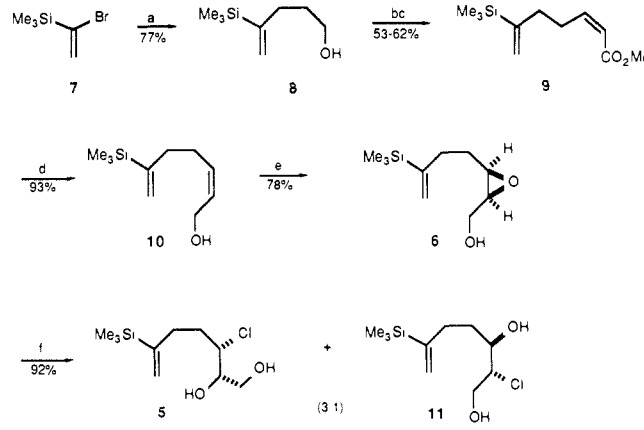
Scheme I



been determined by X-ray analysis. Typically, crystallographic methods have been employed also to establish absolute configurations in this series.[2] The absolute configuration of (+)-laurenyne has been proposed to be 2*S*,7*S*,8*S*,[18] as is illustrated in Figure 1.[6] This assignment was based on the direct observation of the intensities of Friedel pairs, and interestingly, the use of conventional *R* values would have resulted in the opposite assignment of absolute configuration.[6]

Prior to the culmination of the investigations reported in this paper, there was only a single successful total synthesis of an oxocane natural product, the pioneering synthesis of *dl*-laurencin recorded by T. Masamune and co-workers.[8,9] The paucity of synthetic accomplishments in this area undoubtedly reflects the difficulties involved in forming medium ring ethers.[10] This area of synthesis methodology has attracted much recent attention, and significant advances have been described from a number of laboratories.[11-17]

Scheme II[a]

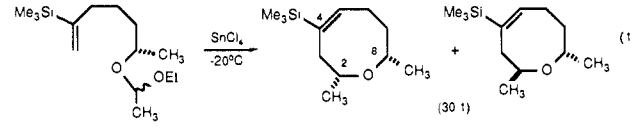


[a] Conditions: (a) *s*-BuLi, THF, −78 °C, oxetane, $BF_3{\cdot}OEt_2$; (b) PCC, NaOAc, CH_2Cl_2; (c) $(CF_3CH_2O)_2P(O)CH_2CO_2Me$, KN$(SiMe_3)_2$, 18-crown-6, THF, −78 °C; (d) HAl(Bu-*i*)$_2$, hexane–CH_2Cl_2, −78 °C; (e) L-(+)-DET, Ti(OPr-*i*)$_4$, Bu-*t*-OOH, 4-Å molecular sieves, CH_2Cl_2, 4 °C; (f) Et_3NHCl, Ti(OPr-*i*)$_4$, CH_2Cl_2.

In this paper we report that the C–C bond-forming cyclization approach to eight-membered cyclic ethers we recently disclosed[11] can be employed to prepare members of the oxocane natural products class. Specifically, we detail the first synthesis of laurenyne, a representative C_{15} nonisoprenoid containing the laurenan skeleton.[2] The synthesis is enantioselective, highly stereocontrolled, and reasonably efficient. We have synthesized the 2*S*,7*S*,8*S* isomer by a sequence we believe to be unambiguous and observe a negative rotation for our synthetic product. Since the natural product has a positive rotation, the correct absolute configuration for laurenyne must be revised to 2*R*,7*R*,8*R* (i.e., the enantiomer of **1**).

Results and Discussion

Synthesis Plan. Our initial studies[11] demonstrated that direct acetal–alkene cyclization could be employed not only to form eight-membered ring ethers, but also to introduce the Δ^4-unsaturation and cis-oriented side chains that are characteristic of the laurencin class of marine natural products (see eq 1). Anticipating

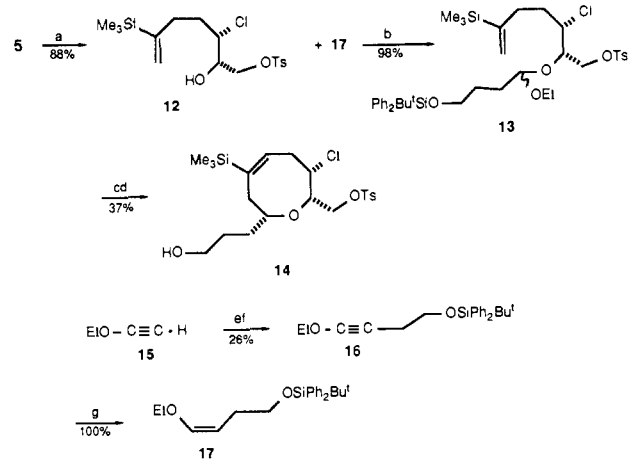


(1)

that the enyne side chain of laurenyne could be elaborated from a hydroxymethyl substituent, we chose to pursue the approach to laurenyne outlined in antithetic form in Scheme I. The 2,8-disubstituted Δ^4-oxocene would arise from cyclization of acetal **4**. This mixed acetal **4** would derive from diol **5**, which could reasonably arise from epoxy alcohol **6**. This latter intermediate should be available in nonracemic form by use of the powerful Sharpless asymmetric epoxidation method.[19] Since nothing was known prior to this study concerning the viability of functionality in the acetal cyclization initiator, we anticipated that the exact nature of the R substituent in intermediate **4** would have to be defined by experiment.

(6) Falshaw, C. P.; King, T. J.; Imre, S.; Islimyeli, S.; Thomson, R. H. *Tetrahedron Lett.* **1980**, 4951.
(7) Gonzalez, A. G.; Martin, J. D.; Martin, V. S.; Norte, M.; Perez, R.; Ruano, J. Z.; Drexler, S. A.; Clardy, J. *Tetrahedron* **1982**, *38*, 1009.
(8) Masamune, T.; Matsue, H.; Murase, H. *Bull. Chem. Soc. Jpn.* **1979**, *52*, 127. Masamune, T.; Murase, H.; Matsue, H.; Murai, A. *Ibid.* **1979**, *52*, 135. Murai, A.; Murase, H.; Matsue, H.; Masamune, T. *Tetrahedron Lett.* **1977**, 2507. Masamune, T.; Matsue, H. *Chem. Lett.* **1975**, 895.
(9) This synthesis does not achieve a practical entry to this natural products class since the overall yield was 0.003%.
(10) For recent brief discussion of ring formation, see: Illuminati, G.; Mandolini, L. *Acc. Chem. Res.* **1981**, *14*, 95.
(11) Overman, L. E.; Blumenkopf, T. A.; Castañeda, A.; Thompson, A. S. *J. Am. Chem. Soc.* **1986**, *108*, 3516.
(12) (a) Nicolaou, K. C.; McGarry, D. G.; Somers, P. K.; Veale, C. A.; Furst, G. T. *J. Am. Chem. Soc.* **1987**, *109*, 2504. (b) Nicolaou, K. C.; Hwang, C.-K.; Duggan, M. E.; Reddy, K. B. *Tetrahedron Lett.* **1987**, 1501. (c) Nicolaou, K. C.; Hwang, C.-K.; Duggan, M. E.; Reddy, K. B.; Marron, B. E.; McGarry, D. G. *J. Am. Chem. Soc.* **1986**, *108*, 6800. (d) Nicolaou, K. C.; Duggan, M. E.; Hwang, C.-K. *J. Am. Chem. Soc.* **1986**, *108*, 2468.
(13) Pirrung, M. E.; Werner, J. A. *J. Am. Chem. Soc.* **1986**, *108*, 6060.
(14) Schreiber, S. L.; Kelley, S. E. *Tetrahedron Lett.* **1984**, 1757.
(15) (a) Carling, R. W.; Holmes, A. B. *J. Chem. Soc., Chem. Commun.* **1986**, 565. (b) Carling, R. W.; Holmes, A. B. *Tetrahedron Lett.* **1986**, 6133. (c) Carling, R. W.; Holmes, A. B. *J. Chem. Soc., Chem. Commun.* **1986**, 325.
(16) (a) Cockerill, G. S.; Kocienski, P.; Treadgold, R. *J. Chem. Soc., Perkin Trans. 1* **1985**, 2093. (b) Cockerill, G. S.; Kocienski, P. *J. Chem. Soc., Chem. Commun.* **1983**, 705. (c) Mortimore, M.; Cockerill, G. S.; Kocienski, P.; Treadgold, R. *Tetrahedron Lett.* **1987**, *28*, 3747.
(17) (a) Heslin, J. C.; Moody, C. J.; Slawin, A. M. Z.; Williams, D. C. *Tetrahedron Lett.* **1986**, 1403. Pornet, J.; Damour, D.; Miginiac, L. *Tetrahedron* **1986**, *42*, 2017. (b) For a review of older methods for preparing eight-membered ring ethers, see: Moore, J. A.; Anet, F. A. L. In *Comprehensive Heterocyclic Chemistry*; Katritzky, A. R., Rees, C. W., Eds.; Vol 7, Chapter 5.19.
(18) The *10th Collective Index of Chemical Abstracts* names laurenyne and laurencin as derivatives of 3,4,7,8-tetrahydro-2*H*-oxocin and 3,6,7,8-tetrahydro-2*H*-oxocin, respectively. To maintain consistency with the designation of **1**–**3** as $^4\Delta$-oxocenes, we will employ the 3,6,7,8-tetrahydro-2*H*-oxocin nomenclature.
(19) (a) Katsuki, T.; Sharpless, K. B. *J. Am. Chem. Soc.* **1980**, *102*, 5974. (b) Catalytic procedure: Hanson, R. M.; Ko, S. Y.; Gao, Y.; Masamune, H.; Klunder, J. M.; Sharpless, K. B. *J. Am. Chem. Soc.* **1987**, *109*, 5765.

Scheme III[a]

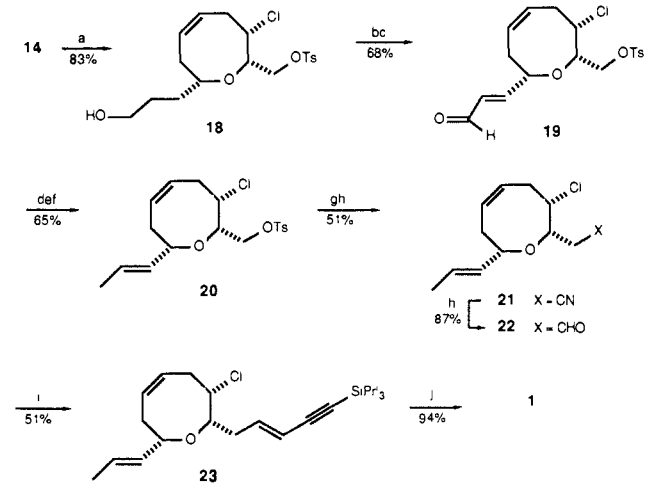


[a] Conditions: (a) TsCl, pyridine; (b) PPTS (catalyst), CH_2Cl_2; (c) $SnCl_4$ (2 equiv), 0 °C, CH_2Cl_2, 1.5 h; (d) n-Bu_4NF–THF; (e) $LiNH_2$, ethylene oxide, NH_3; (f) (TBDPS)Cl, imidazole, CH_2Cl_2; (g) Lindlar catalyst, H_2, EtOAc, pyridine.

Construction of Diol 5. Several recently developed synthetic methods allowed for the efficient construction of diol **5** (see Scheme II). The organolithium reagent derived from commercially available bromide **7**[20] was efficiently alkylated by oxetane in the presence of BF_3·OEt_2.[21] Oxidation of the resulting alcohol **8** was followed by a Z-stereoselective Horner–Wittig reaction[22] to produce the Z-dienoate **9** and its E stereoisomer in a ratio of 25:1 as determined by capillary GC analysis. After chromatographic purification[23] the isomer ratio was >45:1 in favor of the desired Z stereoisomer. Dienyl ester **9** showed a diagnostic 11.5 Hz cis vinylic coupling in the ^1H NMR spectrum, while this coupling for the E isomer was 15.6 Hz. Reduction of **9** with diisobutylaluminum hydride provided the cis-disubstituted allylic alcohol **10**.

Hydroxyl-directed epoxidation[24] of **10** using $Mo(CO)_6$ and *tert*-butyl hydroperoxide produced epoxide **6** in racemic form. Alternatively, a slight modification of the Sharpless catalytic asymmetric epoxidation procedure,[19b] i.e., the use of 25 mol % of Ti(OPr-i)$_4$, afforded nonracemic epoxide **6** in chemical yields of 78–85% with an enantiomeric excess of 78–81%. The enantiomeric purity of **6** was readily determined by ^1H NMR analysis of the Mosher ester derivative.[25] Epoxy alcohol **6** underwent regioselective opening with chloride at the 3-position in the presence of Ti(OPr-i)$_4$, as described by Caron and Sharpless.[26] We found it convenient to use triethylamine hydrochloride as a source of the chloride nucleophile, rather than NH_4Cl, since the former salt is more soluble in CH_2Cl_2. The resulting chlorohydrins are stable to the triethylamine liberated in this reaction. The chloro diol **5** and its regioisomer **11** were produced in 3:1 ratio, and diol **5** could be obtained from this mixture in 68% yield after purification on silica gel. Although we are not aware of other examples of the use of the Sharpless method to open cis-disubstituted epoxides with halogen, a 3:1 ratio of regioisomers is typical for chloride openings of the corresponding trans-epoxides.[26] The definition of structure of the chloro diols followed most directly from treatment of the two regioisomers with sodium periodate. Thus, while **5** reacted to form an unstable aldehyde, **11** was inert. The sequence summarized in Scheme II conveniently provided optically active diol **5** on a multigram scale in six steps and 25% overall yield from **7**.

Scheme IV[a]



[a] Conditions: (a) HF, pyridine, 23 °C; (b) PCC, NaOAc, CH_2Cl_2; (c) $(Me_3Si)OTf$, Et_3N, 0 °C, $Pd(OAc)_2$, CH_3CN; (d) HAl(Bu-i)$_2$, hexane–CH_2Cl_2, −78 °C; (e) MsCl, Et_3N, CH_2Cl_2; (f) $NaBH_4$, HMPA, 23 °C; (g) NaCN, DMSO, 95 °C; (h) HAl(Bu-i)$_2$, hexane–CH_2Cl_2, 0 °C → room temperature, then H_3O^+; (i) (Pr-i)$_3$SiC≡CCH$_2$Si(Pr-i)$_3$, n-BuLi, HMPA, THF, −78 °C; (j) n-Bu_4NF, THF, DMF.

Cyclization and Elaboration to (−)-Laurenyne. After much experimentation, vide infra, it was found that mixed acetal **13** was a viable intermediate for the key cyclization reaction (see Scheme III). The primary alcohol of diol **5** was converted to its tosylate[27] **12** without event. Acetal **13** was prepared in 98% yield from the reaction of **12** with a slight excess of enol ether **17** in the presence of pyridinium p-toluenesulfonate.[28] The enol ether in turn was available in multigram quantities from ethoxyacetylene by use of an epoxide opening[29] and semihydrogenation sequence.

Stannic chloride mediated cyclization of **13** in CH_2Cl_2 at 0 °C, followed by O-desilylation with (n-Bu)$_4$NF produced oxocene **14** as the sole cyclic ether product.[30] This reaction could be performed reliably on a 3–4-g scale and provided **14** in 37% yield after purification. No trace of an isomer of **14** was seen by 500-MHz ^1H NMR analysis of the crude cyclization product mixture. The cis stereochemistry of the side chains was indicated by a large (~14%) difference NOE between the C-2 and C-8 methine hydrogens of **14** and confirmed by subsequent transformation of **14** to (−)-laurenyne.

The remainder of the synthesis was completed by using a series of efficient functional group manipulations (see Scheme IV). The silicon substituent was removed by protodesilylation of **14** with the commercially available HF/pyridine complex.[31] The unsaturation of the propenyl side chain was introducted by conversion

(20) (a) Commercially available from Petrarch or Aldrich. (b) This material can be easily prepared on a 50-g scale: Boeckman, R. K., Jr.; Blum, D. M.; Ganem, B.; Halvey, N. *Org. Synth.* **1980**, *58*, 152.
(21) Eis, M. J.; Wrobel, J. E.; Ganem, B. *J. Am. Chem. Soc.* **1984**, *106*, 3693.
(22) Still, W. C.; Gennari, C. *Tetrahedron Lett.* **1983**, *24*, 4405.
(23) Still, W. C.; Kahn, M.; Mitra, A. *J. Org. Chem.* **1978**, *43*, 2923.
(24) Sharpless, K. B.; Michaelson, R. C. *J. Am. Chem. Soc.* **1973**, *95*, 6136. Sharpless, K. B.; Verhoeven, T. R. *Aldrichimica Acta* **1979**, *12*, 63.
(25) Dale, J. A.; Dull, D. L.; Mosher, H. S. *J. Org. Chem.* **1969**, *34*, 2543.
(26) Caron, M.; Sharpless, K. B. *J. Org. Chem.* **1985**, *50*, 1557.
(27) Johnson, W. S.; Collins, J. C., Jr.; Pappo, R.; Rubin, M. B.; Kropp, P. J.; Johns, W. F.; Pike, J. E.; Bartmann, W. *J. Am. Chem. Soc.* **1963**, *85*, 1409.
(28) Miyasita, M.; Yoshikoshi, A.; Grieco, P. A. *J. Org. Chem.* **1977**, *42*, 3772.
(29) Vollema, G.; Arens, J. F. *Recl. Trav. Chim. des Pays-Bas* **1963**, *82*, 305. Viehe, H. G. *Chemistry of Acetylenes*; Marcel Dekker: New York, 1969, Chapter 11.
(30) The silyl ether derivative of **14** is only marginally stable under the cyclization conditions. If the reaction is worked up within 30 min, cyclization product containing only the protected primary alcohol can be obtained. On the other hand, extended reaction periods (6–8 h) result in partial loss of the silyl protecting group. Under optimum cyclization conditions, both alcohol **14** and its silyl ether derivative are obtained. The removal of the silyl ether is completed with n-Bu_4NF.
(31) Use of dry HCl in Et_2O would not affect protodesilylation of **14**, even though this reagent works well on a simpler system.[11] Hydrogen fluoride in pyridine (no cosolvent) was the only reagent we found useful for this transformation. This result may reflect the conformational rigidity of oxocene **14**. Protonation of the vinyl silane from the outside face of the eight-membered ring would place the Me_3Si group on the interior of the ring. Thus, we speculate that a small silylphilic nucleophile is needed.

of **18** to the corresponding aldehyde followed by Saegusa–Ito oxidation.[32] This two-step oxidation sequence afforded crystalline enal **19**, which was contaminated with less than 3% of the corresponding *Z* isomer as determined by 500-MHz ^{1}H NMR analysis. A diagnostic coupling constant of 15.7 Hz was observed between the enal vinylic hydrogens. Removal of the enal oxygen was achieved by using a reduction, mesylation, reduction sequence (see Scheme IV).[33] It merits note that the reduction steps were compatible with both the secondary chloride and primary tosylate groups. This sequence afforded oxocene **20** in 65% overall yield from **19** with >97% stereochemical integrity of the *E*-propenyl unit.

The tosylate, which has served until this time as an effective protecting group, was now employed as a leaving group to build the C-8 side chain. The electron-withdrawing β oxygen in **20** rendered nucleophilic displacements of this tosylate difficult.[34] An acceptable yield (59%) was achieved with sodium cyanide in DMSO at 95 °C. The resulting nitrile **21** was reduced to aldehyde **22** and the requisite enyne constructed by use of the lithium salt of 1,3-bis(triisopropylsilyl)propyne.[35] This condensation produced the *E*-enyne **23** and its *Z* stereoisomer in a 7:1 ratio, respectively, as determined by capillary GC analysis. The *E* stereoisomer showed a 15.9-Hz vinylic coupling, while this coupling was 10.8 Hz in the corresponding *Z*-enyne. Removal of the triisopropylsilyl group was accomplished with *n*-Bu_4NF in DMF. Recrystallization of this product from hexane afforded synthetic laurenyne as fine white needles, mp 78–80 °C (lit.[6] mp 78–80 °C). Synthetic laurenyne produced in this manner showed a 500-MHz ^{1}H NMR spectrum that was indistinguishable from that of an authentic sample. Synthetic laurenyne was also identical with the natural material by comparisons of TLC mobility (three solvent systems) and capillary GC retention times. The rotation of our synthetic material was $[\alpha]^{17}_D$ −20.0° (*c* 2.0, $CHCl_3$) [lit.[6] $[\alpha]^{17}_D$ +22.6° (*c* 2.35, $CHCl_3$)].

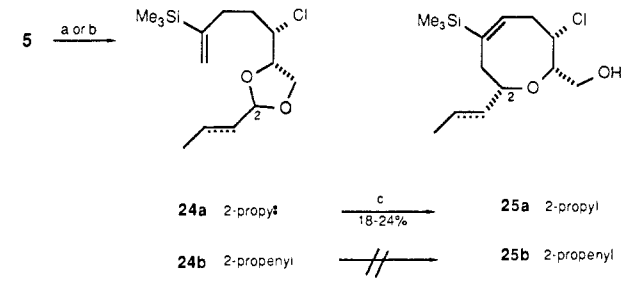
Since there are no exceptions to date on the sense of absolute chirality introduced by Sharpless asymmetric epoxidation,[19,36] and no apparent place in the synthetic sequence where an inversion could occur, natural (+)-laurenyne must possess the 2*R*,7*R*,8*R* absolute configuration (enantiomeric with the configuration drawn for **1**). This change places laurenyne in the same enantiomeric series as the pinnatifidenynes[7] as well as laurencin[3] and other structurally related materials with the lauthisan[2] skeleton.

Scope and Limitations of Acetal-Initiated Cyclizations to Form Functionalized Δ^4-Oxocenes. A number of initial studies were conducted that led to the ultimately successful approach to (−)-laurenyne. Since the synthesis of eight-membered ring ethers by direct cyclization reactions is a new stratagem,[11,16] we will document some of these studied here because they provide some definition of the scope and limitations of our approach to medium ring ethers.

At the outset of this synthesis undertaking we had little data to draw on concerning the compatibility of substituents with the desired acetal-initiated cyclization reaction.[11,16] Atoms C-3–C-8, comprising the terminator portion of the cyclization substrate **4** (see Scheme I), possessed the most complex substitution pattern of any cyclization precursor we had studied. One obvious concern was the stability of the chlorine substituent under Lewis acidic cyclization conditions. It would also be essential to define what functionality could be tolerated at C-2 of **4**, i.e., in the oxonium ion portion or the cyclization initiator.

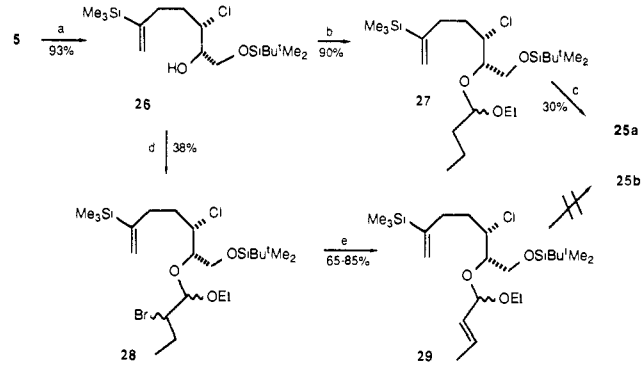
Our initial efforts explored direct introduction of the C-2 propenyl side chain. Dioxolanes **24a** and **24b** were readily prepared in excellent yields from diol **5** (see Scheme V). While dioxolane **24a** cyclized to form oxocene **25a** when treated with $SnCl_4$, **24b**

Scheme V[a]



[a] Conditions: (a) Butyraldehyde, PPTs, benzene, reflux, 96%; (b) crotonaldehyde, PPTs, benzene, reflux, 92%; (c) $SnCl_4$ (2 equiv), 23 °C, 15 h.

Scheme VI[a]



[a] Conditions: (a) (TBS)Cl, imidazole, DMF; (b) ethyl butenyl ether, PPTs, CH_2Cl_2; (c) $SnCl_4$ (2 equiv), CH_2Cl_2, −20 °C; (d) 1,2-dibromo-1-ethoxybutane, pentamethylpiperidine, CH_2Cl_2; (e) DBU, toluene, 120 °C.

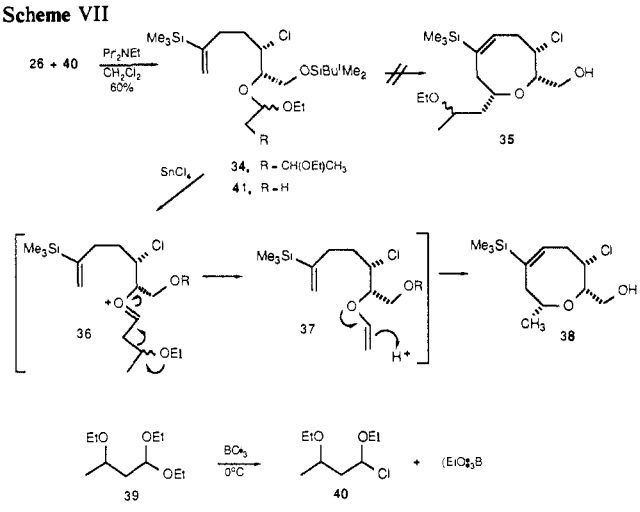
could not be induced to cyclize under a wide variety of reaction conditions.[37] Although the yield of **25a** was low (18–24%), and the conditions required to cyclize the cyclic acetal **24a** were somewhat harsh (room temperature, 15 h), clearly the substitution pattern on the "terminator" was not preventing **24b** from cyclizing.

It was likely that the slow rate of cyclization of **24a** relative to acetals we had studied earlier (see eq 1) reflected the low equilibrium concentration of the oxonium cation formed from Lewis acid mediated opening of the dioxolane group. To prevent intervention of the primary hydroxyl group, it was protected as a *tert*-butyldimethylsilyl ether.[38,39] Synthesis of the requisite acetals is shown in Scheme VI. The unsaturated acetal **29** was prepared in two steps from alcohol **26**.[40] Alkylation of this moderately hindered alcohol with 1,2-dibromo-1-ethoxybutane[41] was best accomplished in the presence of 1,2,2,6,6-pentamethylpiperidine.[42] Mixed acetal **28** was formed in 38% yield as a mixture of four diastereomers along with 60% of unreacted alcohol **26**, which could be recycled. Treatment of **28** with 1,8-diazabicyclo[5.4.0]undecane (DBU) in hot toluene resulted in

(32) Ito, Y.; Hirao, T.; Saegusa, T. *J. Org. Chem.* **1978**, *43*, 1011.
(33) Asato, A. E.; Liu, R. S. H. *J. Am. Chem. Soc.* **1975**, *97*, 4128.
(34) See, e.g.: Streitwieser, A. *Solvoltyic Displacement Reactions*; McGraw-Hill: New York, 1962, pp 14–25.
(35) Corey, E. J.; Rücker, C. *Tetrahedron Lett.* **1982**, *23*, 719.
(36) Rossiter, B. E. In *Asymmetric Synthesis*; Morrison, J. D., Ed.; Academic: New York, 1985; Vol. 5, Chapter 7. Finn, M. G.; Sharpless, K. B. *Ibid.*, Chapter 8.

(37) A variety of Lewis and protic acids were tried, including $SnCl_4$, $TiCl_4$, BF_3·OEt_2, (*i*-Bu)$_3$Al, Et_2AlCl, $(Me_3Si)OTf$, TipsOTf, PPTs, pTSOH. Also explored were changes in solvent (CH_2Cl_2, benzene, acetonitrile) and temperature from (−20–+80 °C).
(38) Our initial studies employed a *tert*-butyldimethylsilyl (TBS) ether to protect the primary hydroxyl group. We subsequently employed a tosylate, since this group was both stable to the cyclization conditions and also served as a leaving group in the ultimate elaboration of the C-8 side chain of laurenyne. A substrate related to **13** (with TBS in place of tosylate) did cyclize to form the corresponding oxocene when treated with $SnCl_4$.
(39) Corey, E. J.; Venkateswarlu, A. *J. Am. Chem. Soc.* **1972**, *94*, 6190.
(40) Other methods have been reported for preparing this functional group. See: Petrezilka, M. *Helv. Chim. Acta* **1978**, *61*, 2286. Kozikowski, A. P.; Sorgi, K. L.; Schmiesing, R. J. *J. Chem. Soc., Chem. Commun.* **1980**, 477. We were unable to employ these methods since the requisite mixed acetals could not be formed.
(41) Wislicenus, A. *Justus Liebigs Ann. Chem.* **1891**, *192*, 111.
(42) Hall, H. K., Jr. *J. Am. Chem. Soc.* **1957**, *79*, 5444. Overman, L. E.; Lesuisse, D.; Hashimoto, M. *Ibid.* **1983**, *105*, 5373.

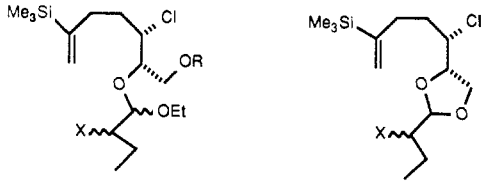
Scheme VII



smooth dehydrobromination to afford **29** in 65–85% yield. The newly formed olefin was determined to be the trans isomer by virtue of its 15.5-Hz vinylic coupling. It is worth noting that the secondary chloride substituent is stable at 120 °C in the presence of excess DBU.

The saturated mixed acetal **27** readily cyclized to form oxocene **25a** (30% yield) in the presence of $SnCl_4$ (−20 °C, 2 h),[43,44] while again the corresponding unsaturated acetal **29** could not be induced to cyclize with several acid catalysts ($SnCl_4$, $BF_3{\cdot}OEt_2$, PPTs). The product of acetal cleavage (i.e., **26**) was typically isolated upon aqueous quenching of the unsuccessful cyclization reactions employing acetal **29**.

Since direct introduction of the propenyl side chain prior to cyclization did not appear feasible, we turned our attention to cyclization substrates that had this unit in latent form. Initially, we examined the mixed acetals **28** and **30–32**, which contained



28 X = Br, R = $SiBu^tMe_2$
30 X = SMe, R = $SiBu^tMe_2$
31 X = OAc, R = $SiBu^tMe_2$
32 X = SMe, R = Me

33 X = OAc or SMe

potential leaving groups β to the acetal carbon. Mixed acetals **30** and **32** were readily prepared from alkylation of alcohol **26** (or its CH_2OMe analogue) with 1-bromo-1-ethoxy-2-(methylthio)butane. Acetal **31** was prepared by an acid-catalyzed exchange reaction between alcohol **26** and 2-acetoxy-1-[(*m*-chlorobenzoyl)oxy]-1-ethoxybutane as detailed in the supplementary material. These mixed acetals were more stable in the presence of $SnCl_4$ than the corresponding acetals lacking the β heteroatom substituent. Attempted cyclization under forcing conditions led to either decomposition, acetal cleavage (to regenerate **26** upon aqueous workup) or, in the cases of **30** and **31**, the formation of the cyclic acetals **33**.

We also briefly investigated cyclization substrates containing potential leaving groups γ to the acetal carbon. One such study is outlined in Scheme VII. The mixed acetal **34** was successfully prepared from the reaction of alcohol **26** with α-chloro ether **40**. This latter intermediate was prepared in crude form in ~90% yield from the reaction of 1,1,3-triethoxybutane (**39**) with 0.4 equiv of BCl_3.[45] The triethoxyborate produced in this latter reaction is conveniently removed at reduced pressure. This useful procedure was used to prepare several other highly functionalized α-chloro ethers.[46] Treatment of **34** with $SnCl_4$ at −20 °C in CH_2Cl_2 did not afford the desired oxocene **35** but rather provided oxocene **38** in 24% yield. The structure of **38** was confirmed by its independent synthesis from the ethoxy ethyl ether **41**. The formation of **38** likely arises by retro-aldol fragmentation of oxonium ion **36** followed by protonation of **37** and cyclization of the resulting oxonium cation.

It appears clear that unsaturation or heteroatom functionality at either the β or γ carbons of an acetal cyclization initiator cannot be tolerated in Lewis acid promoted cyclization reactions to yield oxocenes. This restriction led us to the ultimately successful approach to (−)-laurenyne documented earlier in this paper in which the unsaturation of the C-2 side chain is developed from a terminal side chain substituent.

Conclusion

The first total synthesis of laurenyne has been achieved by a linear sequence that proceeds in 20 steps and 0.6% overall yield from commercially available starting materials. The synthesis is both enantioselective and highly stereocontrolled and achieves the first practical[9] synthetic entry to this class of natural products. The total synthesis reported here, moreover, corrects the absolute configuration originally assigned[6] to natural (+)-laurenyne.[50]

This synthetic exercise demonstrates that a simple cyclization approach can be employed to assemble functionalized eight-membered cyclic ethers. The exploratory studies conducted during the early stages of this endeavor indicate that while potentially complicating substituents can be tolerated in the terminator portion of the cyclization substrate, the acetal initiator portion is extremely sensitive to substitution. Methods developed during this project to prepare complex mixed acetals may prove useful in other areas of organic synthesis.

Experimental Section[47]

Preparation of 4-(Trimethylsilyl)-4-penten-1-ol (8).[21] A solution of THF (50 mL) and (α-bromovinyl)trimethylsilane (**7**; 9.6 mL, 62.3 mmol) was cooled to −70 °C under argon. To this solution was added *sec*-BuLi (1.37 M in cyclohexane, 45 mL, 61.6 mmol) dropwise over 15 min, and the reaction was stirred at −70 °C for 1 h. Freshly distilled (from CaH_2) oxetane (2.8 mL, 43 mmol) was then added, followed by the dropwise addition (ca. 1–2 min) of $BF_3{\cdot}OEt_2$ (7.6 mL, 61.7 mmol). The reaction was stirred at −70 °C for 10–15 min and quenched with saturated $NaHCO_3$. The resulting mixture was allowed to warm to ambient temperature, the aqueous layer was extracted with Et_2O, and the combined organic layers were washed with brine, dried (Na_2SO_4), and concentrated. Purification of the residue by silica gel flash chromatography (gradient elution, using pentane and then 10:1, 1:1 pentane–Et_2O) afforded 5.25 g (77%) of a pale yellow oil. An analytical sample was obtained by preparative thin-layer chromatography (silica gel, using 3:1 hexane–ethyl acetate, two developments): ^1H NMR (250 MHz, $CDCl_3$) δ 5.59 (br s, 1 H), 5.35 (br s, 1 H), 3.67 (t, J = 6.5 Hz, 2 H, H-2), 2.22 (apparent t, J = 7.8 Hz, 2 H, H-3), 1.70 (m, 2 H, H-2), 1.32 (br s, 1 H, O*H*), 0.10 (s, 9 H); IR (thin film) 3336, 3050, 2957, 1596, 1251, 1058, 839 cm^{-1}; MS (CI, 70 eV, isobutane) *m/e* 159 (MH^+, 5), 143 (53), 103 (46), 93 (11), 91 (77), 75 (100), 73 (95), 70 (59); MS (EI, 70 eV) *m/e* 143.0891 (143.0892 calcd for $C_8H_{18}OSi - CH_3$).

Preparation of 4-(Trimethylsilyl)-4-pentenal (42). To a mixture of pyridinium chlorochromate[48] (11.0 g, 51.2 mmol), dry CH_2Cl_2 (100 mL), and sodium acetate (0.5 g, 6.09 mmol) was added a solution of alcohol **8** (8.0 g, 50.6 mmol) and CH_2Cl_2 (45 mL) dropwise over ca. 5 min.

(43) Experiments conducted in our laboratories[44] demonstrate that unsymmetrical acetals undergo reversible cleavage in the presence of $SnCl_4$ at temperatures as low as −70 °C. Thus, it would not in principle be necessary for acetal cleavage to be regioselective in order to obtain a high yield of the desired cyclization product.

(44) Look, G.; Overman, L. E., to be submitted for publication.

(45) (a) The use of BCl_3 to obtain an α-chloro ether by cleavage of a MOM ether has recently been reported: Goff, D. A.; Harris, R. N., III; Bottaro, J. C.; Bedford, C. D. *J. Org. Chem.* **1986**, *51*, 4711. (b) The related preparation of α-bromo ethers from cleavage of acetals with Me_2BBr has also bee described: Guindon, Y.; Bernstein, M. A.; Anderson, P. C. *Tetrahedron Lett.* **1987**, 2225.

(46) Functionalized α-chloro ethers containing other substituents at the γ position (SEt, SePh, Br, $CH{=}CH_2$) were also prepared in this way.

(47) General experimental details have been described: Flann, C. J.; Overman, L. E. *J. Am. Chem. Soc.* **1987**, *109*, 6115. Capillary GC analyses were done on a 12 ft SE-30 column.

(48) Corey, E. J.; Suggs, J. W. *Tetrahedron Lett.* **1975**, 2647.

After 1 h, additional pyridinium chlorochromate (2.8 g, 13.0 mmol) was added in one portion, and the reaction was stirred for an additional 1 h. The reaction was diluted with 150 mL of dry pentane–Et_2O (2:1, v/v, from Na_2SO_4), and the supernatent was filtered through a plug of silica gel. The chromium salts were washed with additional pentane–Et_2O, and the washings were passed through the plug of silica gel. Concentration afforded 7 g (89%) of a volatile pale yellow oil: ^1H NMR (250 MHz, $CDCl_3$) δ 9.79 (t, J = 1.6 Hz, 1 H, C*H*O), 5.55 (br s, 1 H), 5.38 (br s, 1 H), 2.58 (m, 2 H), 2.48 (m, 2 H), 0.11 (s, 9 H); IR (thin film) 3050, 2954, 2720, 1729, 1251, 927, 836 cm^{-1}; MS (CI, 70 eV, isobutane) m/e 157 (MH^+, 100), 141 (48), 73 (35); MS (EI, 70 eV) m/e 156.0943 (156.0967 calcd for $C_8H_{16}OSi$).

Preparation of Methyl 6-(Trimethylsilyl)-2(*Z*),6-heptadienoate (9).[22] A mixture of bis(2,2,2-trifluoroethyl)[(methoxycarbonyl)methyl]-phosphonate[22] (13 g, 41 mmol) and 18-crown-6 (11 g, 42 mmol) was dried by azeotroping with benzene (2×), followed by additional drying under vacuum (0.05 mm, 1 h). This mixture was dissolved in THF (150 mL), cooled to −70 °C and $KN(TMS)_2$ (0.55 M in toluene, 75 mL, 41 mmol) was added dropwise (over ca. 3 min). The reaction was stirred at −70 °C for 5 min, and then aldehyde **42** (7.0 g, 45 mmol) in 45 mL of dry THF was added. The reaction was stirred at −70 °C for 0.5 h and then quenched with saturated NH_4Cl. After the mixture was warmed to ambient temperature, sufficient water was added to dissolve the salts, and the organic layer was separated. The aqueous layer was extracted with hexane–ethyl acetate (4:1), and the combined organic layers were washed with H_2O and brine, dried ($MgSO_4$), and concentrated. Purification of the residue by silica gel flash chromatography (gradient elution, using pure hexane and then 20:1 hexane–ethyl acetate) afforded 5.8 g (66%) of **9** as a clear oil. The ratio of cis to trans isomers was determined to be >45:1 by capillary gas chromatography: ^1H NMR (250 MHz, $CDCl_3$) δ 6.23 (dt, J = 11.5, 7.3 Hz, 1 H, H-3), 5.77 (dt, J = 11.5, 1.7 Hz, 1 H, H-2), 5.60 (br s, 1 H), 5.37 (br s, 1 H), 3.73 (s, 3 H), 2.80 (apparent dq, J = 7.3, 1.7 Hz, 2 H, H-4), 2.27 (t, J = 7.6 Hz, 2 H, H-5), 0.10 (s, 9 H); IR (thin film) 3050, 2957, 1730, 1649, 1596, 1251, 1198, 1178, 925, 839 cm^{-1}; MS (CI) m/e 213 (MH^+, 57), 197 (2), 109 (100); MS (EI, 70 eV) m/e 212.1203 (212.1232 calcd for $C_{11}H_{20}O_2Si$).

Preparation of 6-(Trimethylsilyl)-2(*Z*),6-heptadien-1-ol (10). To a solution of diisobutylaluminum hydride (1.0 M in hexane, 55 mL, 55 mmol) in dry CH_2Cl_2 (60 mL) at −70 °C under argon was added a solution of ester **9** (5.0 g, 24 mmol) in CH_2Cl_2 (45 mL). The reaction was stirred for 1 h (bath warms to −20 °C), and then it was quenched with methanol (2 mL) and a saturated solution of sodium potassium tartrate. The mixture was vigorously stirred for 1 h, at which time two distinct layers formed. The organic layer was removed, and the aqueous layer was extracted with CH_2Cl_2. The combined organic layers were washed with brine, dried (Na_2SO_4), and concentrated. Purification of the residue by silica gel flash chromatography (gradient elution, using 10:1, 5:1, 3:1, 1:1 hexane–ethyl acetate) afforded 4.5 g (93%) of allylic alcohol **10** as a clear oil: ^1H NMR (250 MHz, $CDCl_3$) δ 5.60 (m, 3 H), 5.36 (d, J = 1.9 Hz, 1 H), 4.20 (t, J = 5.6 Hz, 2 H, H-1), 2.19 (s, 4 H, H-4 and H-5), 1.23 (t, J = 5.6 Hz, 1 H), 0.10 (s, 9 H); IR (thin film) 3329, 3050, 3017, 2957, 1656, 1251, 925, 830 cm^{-1}; MS (CI, 70 eV, isobutane) m/e 167 [(MH^+ − 18), 23], 95 (52), 73 (100); MS (EI, 70 eV) m/e 169.1052 (169.1048 calcd for $C_{10}H_{20}OSi - CH_3$).

Preparation of (2*S,3*R**)-2,3-Epoxy-6-(trimethylsilyl)-6-hepten-1-ol (6).**[24] Alcohol **10** (2.2 g, 12 mmol) was dissolved in dry benzene (30 mL). To this solution were added Na_2HPO_4 (2.144 g, 15.09 mmol) and $Mo(CO)_6$ (297 mg, 1.121 mmol). The mixture was heated to reflux, at which time a solution of *tert*-butyl hydroperoxide (90%, 2.0 mL, 18 mmol) in benzene (3 mL) was added dropwise. The reaction was stirred at reflux for 1.5 h. After being cooled to room temperature, the reaction was quenched with 10% $Na_2S_2O_3$–10% $NaHCO_3$ solution, extracted with Et_2O, washed with brine, dried (Na_2SO_4), and concentrated. Purification of the residue by silica gel flash chromatography (gradient elution, using 10:1, 5:1, 3:1, 1:1 hexane–ethyl acetate) afforded 1.91 g (80%) of racemic 6 as a clear oil: ^1H NMR (250 MHz, $CDCl_3$) δ 5.59 (br s, 1 H), 5.38 (br s, 1 H), 3.88 (ddd, J = 11.9, 7.5, 4.3 Hz, 1 H, H-1), 3.70 (ddd, J = 11.9, 6.7, 4.8 Hz, 1 H, H-1), 3.15 (dt, J = 6.7, 4.3 Hz, 1 H, H-1), 3.06 (dt, J = 6.3, 4.3 Hz, 1 H, H-3), 2.30 (m, 2 H, H-5), 1.80–1.58 (m, 3 H), 0.10 (s, 9 H); IR (thin film) 3415, 3050, 2957, 1603, 1251, 1038, 839 cm^{-1}; MS (CI) m/e (MH, 1), 117 (10), 111 (13), 103 (24), 93 (100), 91 (18), 87 (31), 73 (62); MS (EI, 70 eV) m/e 199.1149 (199.1154 calcd for $C_{10}H_{20}O_2Si - H$).

Preparation of (2*S*,3*R*)-2,3-Epoxy-6-(trimethylsilyl)-6-hepten-1-ol (6).[19b] A 250-mL round-bottom flask containing a stir bar and crushed 4-Å molecular sieves (4 g, Fisher) was placed in a sand bath (250 °C), and the flask was evacuated (0.05 mm) for 3 h just prior to use. After being cooled to ambient temperature, the flask was filled with argon and a solution of allylic alcohol **10** (4.0 g, 21 mmol) and CH_2Cl_2 (40 mL) was added. This mixture was cooled to −10 °C and (+)-diethyl L-tartrate (1.31 g, 6.36 mmol) in CH_2Cl_2 (10 mL) was added followed by titanium tetraisopropoxide (1.5 mL, 5.0 mmol). The mixture was allowed to age for 20 min, and then *tert*-butyl hydroperoxide (4 M in isooctane, 7 mL, 28 mmol) was added. The vessel was stoppered and stirred at 4 °C for 15 h. The reaction was quenched with 30 mL of H_2O and stirred vigorously for 40 min, while allowing the mixture to warm to room temperature. To this mixture was added 6 mL of a 30% aqueous sodium hydroxide solution (saturated with NaCl) and the mixture stirred for 30 min. The resulting tan solution was transferred to a separatory funnel, and the layers were allowed to separate. The organic phase was removed, and the tan upper layer was washed with CH_2Cl_2, allowing time for the layers to separate after each extraction. The aqueous layer was then filtered through glass wool to remove the sieves and the remaining emulsified CH_2Cl_2 separated. The resulting colorless solution was separated into an organic and aqueous phase. The combined organic layers were washed with brine, dried (Na_2SO_4), and concentrated. Purification of the residue by silica gel flash chromatography afforded 3.34 g (78%) of **6** as a clear colorless oil: $[\alpha]^{24}_D$ −4.73°, $[\alpha]_{578}$ −4.40°, $[\alpha]_{546}$ −4.84°, $[\alpha]_{435}$ −7.99°, $[\alpha]_{365}$ −11.09° (c 1.78, $CHCl_3$). The Mosher ester derivative was prepared [using (*R*)-(−)-(MTP)Cl] from the chiral nonracemic and the racemic epoxides in the usual manner,[25] and each derivative was analyzed by 500-MHz ^1H NMR. The acyloxy protons from the racemic epoxide appear as two separate eight-line patterns centered at δ 4.49 and 4.39. The acyloxy protons from the chiral nonracemic epoxide appear as two separate four-line patterns; the ratio of diastereomers was determined to be 90.5:9.5 (81% ee) by integration of these signals.

Preparation of (2*S*,3*S*)-3-Chloro-2-hydroxy-6-(trimethylsilyl)-6-hepten-1-ol (5).[26] To a suspension of trimethylamine hydrochloride [prepared from Et_3N (12 mL, 86 mmol) and dry HCl–Et_2O] and CH_2Cl_2 (150 mL) was added a solution of epoxide 6 (4.0 g, 20 mmol) in CH_2Cl_2 (20 mL). To the resulting slurry was added titanium tetraisopropoxide (12 mL, 40 mmol). The reaction was stirred at 23 °C for 15 h, cooled to 0 °C, and quenched with 10% HCl. After the resultant mixture was stirred for 20 min at 0 °C, the organic layer was removed. The aqueous layer was extracted with CH_2Cl_2, and the combined organic layers were washed with saturated $NaHCO_3$ and brine, dried (Na_2SO_4), and concentrated. Analysis of the unpurified reaction mixture by capillary GC showed the ratio of 1,2-diol to 1,3-diol was 3:1, respectively. Purification of the residue by silica gel flash chromatography (gradient elution, using 7:1, 5:1, 3:1, 1:1 hexane–ethyl acetate) afforded pure samples of **5** and **11**.

1,3-Diol 11: 0.99 g (21%); R_f 0.56 (silica gel, using hexane–ethyl acetate, 1:1 v/v); ^1H NMR (250 MHz, $CDCl_3$) δ 5.61 (br s, 1 H), 5.37 (br s, 1 H), 4.05 (m, 1 H, H-2), 3.94 (apparent t, J = 6.2 Hz, 3 H, H-1 and H-3), 2.28 (t, J = 6.4 Hz, 1 H, O*H*), 2.42–2.15 (m, 2 H, H-5), 2.10 (d, J = 7.6 Hz, 1 H, O*H*), 1.85–1.65 (m, 2 H, H-4), 0.11 (s, 9 H); IR (thin film) 3329, 3050, 2957, 1251, 1091, 1044, 839 cm^{-1}; MS (CI, 70 eV, isobutane) m/e 239 (MH^+, 2), 237 (MH^+, 6), 149 (11), 147 (33), 129 (18), 111 (100), 93 (30); MS (EI, 70 eV) m/e 223.0764 (223.0735 calcd for $C_{10}H_{21}ClO_2Si - CH_3$), 221.0786 (221.0759 calcd for $C_{10}H_{21}ClO_2Si - CH_3$).

1,2-Diol 5: 3.2 g (68%); R_f 0.45 (silica gel, using hexane–ethyl acetate, 1:1 v/v; $[\alpha]^{24}_D$ −26.9°, $[\alpha]_{578}$ −27.9°, $[\alpha]_{546}$ −31.8°, $[\alpha]_{435}$ −53.5°, $[\alpha]_{365}$ −83.0° (c 1.53, $CHCl_3$); ^1H NMR (250 MHz, $CDCl_3$) δ 5.61 (br s, 1 H), 5.38 (br s, 1 H), 4.07 (apparent p, J = 4.4 Hz, 1 H, H-3), 3.75 (m, 3 H, H-1 and H-2), 2.44 (d, J = 6.1 Hz, 1 H, OH), 2.52–2.20 (m, 2 H, H-5), 2.06 (t, J = 5.8 Hz, 1 H, OH), 2.02–1.86 (m, 2 H, H-4), 0.11 (s, 9 H); IR (thin film) 3375, 3050, 2957, 1410, 1251, 1045, 925, 839, 759 cm^{-1}. Anal. Calcd for $C_{10}H_{21}ClO_2Si$: C, 50.72; H, 8.94. Found: C, 50.46; H, 8.96.

Preparation of [(2*S*,3*S*)-3-Chloro-2-hydroxy-6-(trimethylsilyl)-6-heptenyl] 1-*p*-Toluenesulfonate (12).[27] A solution of diol **5** (1.6 g, 7.0 mmol), dry pyridine (7 mL), and *p*-toluenesulfonyl chloride (1.5 g, 7.9 mmol) was maintained at 23 °C for 24 h. Additional *p*-toluenesulfonyl chloride (0.1 g, 0.5 mmol) was added and the reaction maintained for an additional 24 h. The reaction was diluted with 4:1 hexane–ethyl acetate, and the organic layer was washed sequentially with cold 5% HCl and a brine–$NaHCO_3$ mixture. The organic layer was dried (Na_2SO_4) and concentrated. Purification of the residue by silica gel flash chromatography (gradient elution, using 10:1, 7:1, 5:1 hexane–ethyl acetate) afforded 2.4 g (88%) of **12** as a clear colorless oil: $[\alpha]^{24}_D$ −14.3°, $[\alpha]_{578}$ −14.2°, $[\alpha]_{546}$ −16.2°, $[\alpha]_{435}$ −28.4°, $[\alpha]_{365}$ −44.2° (c 1.41, $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$) δ 7.80 (d, J = 8.3 Hz, 2 H), 7.38 (d, J = 8.1 Hz, 2 H), 5.59 (br s, 1 H), 5.39 (br s, 1 H), 4.15–3.90 (m, 4 H), 2.45 (s, 3 H, ArC*H*$_3$), 2.37 (m, 1 H), 2.25 (m, 1 H), 2.18 (d, J = 7.9 Hz, 1 H, O*H*), 1.92 (apparent q, J = 7.8 Hz, 2 H), 0.09 (s, 9 H); IR (thin film) 3525, 3050, 2956, 1656, 1600, 1362, 1250, 1181, 1175, 1100, 981, 837 cm^{-1}; MS (CI, 70 eV) m/e 393 (MH^+, 5), 391 (MH^+, 13), 247 (10), 246 (17), 245 (100), 157 (11), 129 (22), 111 (38), 93 (59); MS (EI, 70 eV)

m/e 377.0833 (377.0823 calcd for $C_{17}H_{27}ClO_4SSi - CH_3$), 375.0863 (375.0853 calcd for $C_{17}H_{27}ClO_4SSi - CH_3$).

Preparation of Enol Ether 17. A solution of 1-ethoxy-1-butyn-4-ol[29] (3.0 g, 26 mmol) and CH_2Cl_2 (35 mL) was cooled in an ice–H_2O bath, and imidazole (3.5 g, 52 mmol) and *tert*-butyldiphenylsilyl chloride (7.5 mL, 29 mmol) was added. The ice bath was removed, and the reaction was maintained at 23 °C for 3 h. The reaction was diluted with Et_2O and washed sequentially with H_2O and saturated $NaHCO_3$. The organic layers were dried (Na_2SO_4) and concentrated to afford a yellow residue. Purification of the residue by silica gel flash chromatography (gradient elution, using hexane, 50:1 hexane–ethyl acetate) afforded 5.7 g (62%) of silyl ether **43** as a clear colorless oil.

The acetylenic silyl ether **16** (2.2 g, 6.25 mmol) was dissolved in 12 mL of ethyl acetate–pyridine (10:1, v/v), and Lindlar catalyst (100 mg, from Aldrich) was added. The reaction was fit with a three-way stopcock, and a hydrogen-filled balloon was attached. The remaining inlet was attached to a vacuum (20 mm), and the reaction vessel was carefully evacuated until the solvent just began to boil. The reaction vessel was then filled with H_2 gas from the balloon. This procedure was repeated twice. The reaction was then allowed to stir under an excess of H_2 (balloon pressure). After 18 h, the reaction was filtered through a plug of silica gel, and the silica gel was washed with 10:1 hexane–ethyl acetate. The filtrate was concentrated to afford 2.2 g (100%) of crude **17**, as a pale yellow residue, which could be stored in hexane (1.0 M solution) at −20 °C for 1 week without decomposition. For use in acid-catalyzed mixed acetal formation the enol ether was repassed through silica gel (10 times the weight of silica gel to enol ether) and eluted rapidly with 10:1 hexane–ethyl acetate to remove any pyridine that may be present: ^{1}H NMR (250 MHz, $CDCl_3$) δ 7.75 (m, 4 H), 7.45 (m, 6 H), 6.03 (d, J = 6.3 Hz, 1 H, H-1), 4.46 (apparent q, J = 7.1, 6.3 Hz, 1 H, H-2), 3.80 (q, J = 7.0 Hz, 2 H, CH_3CH_2O), 3.74 (t, J = 6.9 Hz, 2 H, H-4), 2.45 (dq, J = 7.0, 1.3 Hz, 2 H, H-3), 1.27 (t, J = 7.0 Hz, 3 H, CH_3CH_2O), 1.13 (s, 9 H).

Preparation of Mixed Acetal 13. Alcohol **12** (3.1 g, 7.9 mmol) and enol ether **17** (3.6 g, 10 mmol) were combined and dried by azeotroping with benzene (2×) followed by additional drying under vacuum (0.1 mm, 1 h). This mixture was dissolved in CH_2Cl_2 (40 mL), and pyridinium *p*-toluenesulfonate[28] (10–20 mg) was added. The reaction was stirred at 23 °C for 3–5 h, at which time all of the starting alcohol was consumed. The reaction was quenched with solid K_2CO_3 filtered through basic alumina, washed with $CHCl_3$, and concentrated. The residue was purified by silica gel flash chromatography (gradient elution, using 100:1 hexane–triethylamine and then 100:2:1, 100:4:1, 100:10:1 hexane–ethyl acetate–triethylamine) to afford 5.78 g (98%) of **13** as a clear colorless oil: ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.80 (m, 2 H), 7.65 (m, 4 H), 7.40 (m, 8 H), 5.58 (br s, 1 H), 5.38 (br s, 1 H), 4.59 (m, 1 H, EtOC*H*OR), 4.30–4.10 (m, 2 H), 4.05–3.88 (m, 2 H), 3.65 (m, 2 H), 3.50 (m, 2 H), 2.43 (m, 4 H), 2.18 (m, 1 H), 2.00–1.50 (m, 6 H), 1.15 (m, 3 H), 1.08 (s, 9 H), 0.09 (s, 9 H); IR (thin film) 3068, 3050, 2956, 2856, 1656, 1600, 1368, 1250, 1191, 1181, 1112, 981, 912, 837 cm^{-1}. Anal. Calcd for $C_{39}H_{57}ClO_6SSi_2$: C, 62.83; H, 7.71. Found: C, 62.73; H, 7.72.

Preparation of (2*R*,7*S*,8*S*)-7-Chloro-3,6,7,8-tetrahydro-2-(3-hydroxypropyl)-8-[[(*p*-tolylsulfonyl)oxy]methyl]-4-(trimethylsilyl)-2*H*-oxocin (14). To a solution of $SnCl_4$ (1.2 mL, 10 mmol) in dry CH_2Cl_2 (70 mL) at 0 °C under argon was added dropwise mixed acetal **13** (4.0 g, 5.4 mmol) in CH_2Cl_2 (25 mL). The addition funnel was washed with CH_2Cl_2 (5 mL) and the reaction stirred at 0 °C for 1.5 h. The reaction was quenched with 5% NaOH, extracted with CH_2Cl_2, washed with brine, dried (Na_2SO_4), and concentrated. The residue was dissolved in THF (20 mL) and reacted with *n*-Bu_4NF–THF solution (1.0 M in THF, 12 mL, 12 mmol). After 2 h, the reaction was diluted with H_2O, extracted with Et_2O, washed with 10% HCl and brine, dried (Na_2SO_4), and concentrated. The residue was purified by silica gel flash chromatography (gradient elution, using 10:1, 7:1, 5:1, 3:1, 2:1 hexane–ethyl acetate) to afford 920 mg (37%) of **14** as a pale yellow oil: R_f 0.16 (silica gel, using 3:1 hexane–ethyl acetate, v/v); $[\alpha]^{25}_D$ +54.6°, $[\alpha]_{578}$ +58.0°, $[\alpha]_{546}$ +67.1°, $[\alpha]_{435}$ +122.8°, $[\alpha]_{365}$ +215.8° (*c* 1.27, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.79 (d, J = 8.3 Hz, 2 H), 7.34 (d, J = 7.9 Hz, 2 H), 5.92 (ddd, J = 9.7, 6.3, 1.7 Hz, 1 H, H-5), 4.12 (dd, J = 9.4, 7.0 Hz, 1 H), 3.97 (m, 3 H), 3.63 (br t, J = 6.0 Hz, 2 H, CH_2OH), 3.26 (m, 1 H, H-2), 2.97 (apparent dt, J = 11.9, 9.9 Hz, 1 H, H-6), 2.57–2.47 (m, 2 H, H-3 and H-6), 2.45 (s, 3 H), 2.14 (d, J = 14.1 Hz, 1 H, H-3), 1.75–1.50 (m, 5 H), 0.10 (s, 9 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 145.87 (s), 145.09 (s), 135.09 (d), 132.26 (s), 129.92 (d), 127.98 (d), 82.57 (d), 77.19 (d), 71.60 (t), 62.67 (t), 61.40 (d), 37.08 (t), 35.32 (t), 33.56 (t), 28.87 (t), 21.64 (q), −2.15 (q); IR (thin film) 3550, 3400, 3093, 3068, 3037, 2950, 1656, 1600, 1362, 1250, 1175, 1093, 987, 837 cm^{-1}; MS (CI, 70 eV, isobutane) *m/e* 463 (MH^+, 6), 461 (MH^+, 17), 245 (33), 219 (19), 217 (59), 201 (6), 199 (16), 183 (8), 181 (19), 163 (62), 157 (78), 151 (11), 145 (16), 141 (12), 133 (12), 93 (11), 92 (13), 71 (100); MS (EI, 70 eV) *m/e* 447.1257 (447.1242 calcd for $C_{21}H_{33}ClO_5SiS - CH_3$), 445.1282 (445.1271 calcd for $C_{21}H_{33}ClO_5SiS - CH_3$).

Preparation of (2*R*,7*S*,8*S*)-7-Chloro-2-(3-hydroxypropyl)-3,6,7,8-tetrahydro-8-[[(*p*-tolylsulfonyl)oxy]methyl]-2*H*-oxocin (18). Into a plastic vial containing vinyl silane **14** (445 mg, 0.97 mmol) and a stir bar was added HF/pyridine complex (1 mL, Aldrich). The reaction was stirred at 23 °C for 40 min and diluted with CH_2Cl_2 (1 mL). The mixture was cooled in an ice–H_2O bath and carefully quenched with 15% NaOH until no further foaming occurs upon addition of the NaOH solution. The milky white mixture was diluted with H_2O and transferred to a separatory funnel containing cold 5% NaOH. The aqueous layer was extracted with CH_2Cl_2, washed with brine, dried (Na_2SO_4), and concentrated. Purification of the residue by silica gel flash chromatography (gradient elution, using 10:1, 5:1, 4:1, 3:1, 1:1 hexane–ethyl acetate) afforded 312 mg (83%) of **18** as a clear colorless oil: $[\alpha]^{24}_D$ +54.4°, $[\alpha]_{578}$ +57.6°, $[\alpha]_{546}$ +65.9°, $[\alpha]_{435}$ +116.4°, $[\alpha]_{365}$ +194.6° (*c* 0.5, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.79 (d, J = 8.3 Hz, 2 H), 7.35 (d, J = 8.4 Hz, 2 H), 5.90 (ddd, J = 10.4, 8.2, 0.5 Hz, 1 H, H-4), 5.63 (ddt, J = 10.2, 6.6, 1.7 Hz, 1 H, H-5), 4.12 (m, 2 H), 3.97 (m, 2 H), 3.63 (t, J = 6.3 Hz, 2 H, CH_2OH), 3.45 (dt, J = 8.9, 3.9 Hz, 1 H, H-2), 2.90 (q, J = 12.5 Hz, 1 H, H-6), 2.50–2.35 (m, 2 H, H-6 and H-3), 2.45 (s, 3 H), 2.06 (ddd, J = 14.2, 8.5, 1.1 Hz, 1 H, H-3), 1.90 (br s, 1 H, O*H*), 1.75–1.45 (m, 4 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 145.10, 132.29, 131.73, 129.91, 127.95, 127.66, 81.95, 77.15, 71.78, 62.67, 61.54, 34.90, 33.80, 33.13, 28.78, 21.62; IR (thin film) 3548, 3402, 3024, 2944, 2871, 1656, 1596, 1450, 1364, 1191, 1178, 1098, 985, 813, 750 cm^{-1}; MS (CI, 70 eV, isobutane) *m/e* 391 (MH^+, 30), 390 (22), 389 (MH, 100), 237 (11), 235 (33), 169 (23), 157 (78), 151 (11); MS (EI, 70 eV) *m/e* 390.1095 (390.1081 calcd for $C_{18}H_{25}ClO_5S$), 388.1107 (388.1110 calcd for $C_{18}H_{25}ClO_5S$).

Preparation of (2*R*,7*S*,8*S*)-7-Chloro-3,6,7,8-tetrahydro-2-(3-oxopropyl)-8-[[(*p*-tolylsulfonyl)oxy]methyl]-2*H*-oxocin (44). A round-bottom flask containing crushed 4-Å molecular sieves (500 mg, Fisher) was activated at 250 °C (0.10 mm) for 1 h just prior to use. To the sieves at 23 °C were added CH_2Cl_2 (7.0 mL), pyridinium chlorochromate (PCC)[48] (155 mg, 2.05 mmol), anhydrous NaOAc (80 mg, 0.98 mmol), and alcohol **18** (532 mg, 1.37 mmol). After 0.5 h, additional PCC (60 mg, 0.28 mmol) was added, and the reaction was stirred at 23 °C for an additional 0.5 h. The reaction was diluted with 20 mL of hexane–ethyl acetate (4:1, v/v), and the supernatent was filtered through a plug of silica gel. The chromium salts were washed with hexane–ethyl acetate (1:1, v/v) and the washings passed through the plug of silica gel. Concentration and purification of the residue by silica gel flash chromatography (gradient elution, using 10:1, 5:1, 3:1 hexane–ethyl acetate) afforded 452 mg (86%) of **44** as a clear viscous oil: $[\alpha]^{25}_D$ +48.1°, $[\alpha]_{578}$ +50.8°, $[\alpha]_{546}$ +58.4°, $[\alpha]_{435}$ +103.2°, $[\alpha]_{365}$ +170.2° (*c* 0.95, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.75 (t, J = 0.9 Hz, 1 H), 7.78 (d, J = 8.2 Hz, 2 H), 7.36 (d, J = 8.4 Hz, 2 H), 5.89 (m, 1 H, H-4), 5.63 (ddt, J = 10.2, 6.5, 1.4 Hz, 1 H, H-5), 4.15 (dd, J = 10.1, 8.0 Hz, 1 H), 4.06 (dt, J = 7.9, 3.0 Hz, 1 H, H-8), 3.98 (dd, J = 10.1, 3.3 Hz, 1 H), 3.95 (ddd, J = 11.8, 5.0, 2.5 Hz, 1 H, H-7), 3.42 (dt, J = 9.1, 4.4 Hz, 1 H, H-2), 2.87 (apparent q, J = 11.6 Hz, 1 H, H-6), 2.61 (t, J = 7.0 Hz, 2 H), 2.50–2.37 (m, 2 H, H-6 and H-3), 2.45 (s, 3 H), 2.10 (dd, J = 14.1, 8.5 Hz, 1 H, H-3), 1.80 (m, 2 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 202.42, 145.13, 132.43, 131.41, 129.94, 127.89, 127.84, 81.24, 77.20, 71.99, 61.41, 40.36, 35.01, 33.79, 28.88, 21.62; IR (thin film) 3019, 2956, 2919, 2744, 1713, 1656, 1363, 1175, 994 cm^{-1}; MS (CI, 70 eV, isobutane) *m/e* 389 (MH^+, 34), 388 (29), 387 (MH^+, 88), 386 (31), 235 (14), 233 (40), 217 (11), 215 (30), 197 (12), 181 (11), 179 (29), 167 (19), 157 (100), 149 (13), 141 (30), 140 (12), 111 (11), 110 (20), 93 (10), 92 (25), 87 (37); MS (EI, 70 eV) *m/e* 388.0916 (388.0924 calcd for $C_{18}H_{23}ClO_5S$), 386.0941 (386.0954 calcd for $C_{18}H_{23}ClO_5S$).

Preparation of (2*S*,7*S*,8*S*)-7-Chloro-3,6,7,8-tetrahydro-2-(3-oxo-1-propenyl)-8-[[(*p*-tolylsulfonyl)oxy]methyl]-2*H*-oxocin (19). Aldehyde **44** (450 mg, 1.16 mmol) was dissolved in dry CH_2Cl_2 (12 mL) and the mixture cooled in an ice–H_2O bath. To this mixture was added diisopropylethylamine (0.55 mL, 3.2 mmol) followed by trimethylsilyl trifluorosulfonate (0.29 mL, 1.5 mmol). After 15 min, additional Pr_2NEt (0.55 mL, 3.2 mmol) and TMSOTf (0.29 mL, 1.5 mmol) were added. The reaction was stirred for an additional 15 min and diluted with dry Et_2O–pentane (1:2, v/v). The reaction was quenched with ice cold saturated $NaHCO_3$ and extracted with Et_2O–pentane (1:2, v/v). The organic phase was dried (K_2CO_3) and concentrated. The residue was filtered through anhydrous K_2CO_3, eluted with Et_2O–pentane, and concentrated to afford 546 mg (100%) of the crude enol silyl ether as a yellow oil: no aldehyde peaks at 2743 and 1712 cm^{-1} and a strong stretch at 1656 cm^{-1}. This material was dried (0.1 mm, 2 h) and used without further purification.

A mixture of $Pd(OAc)_2$ (344 mg, 1.54 mmol) and acetonitrile (12 mL) was stirred at 23 °C for 10 min, and a solution of the crude enol

silyl ether (546 mg) in CH_3CN (10 mL) was added. The reaction turned black within 5 min and was allowed to stir at 23 °C for 1 h. The orange supernatent was filtered through a plug of silica gel (hexane–ethyl acetate, 3:1 v/v), and the eluent was concentrated to afford an orange-yellow oil. Purification of this oil by silica gel flash chromatography (gradient elution, using 7:1, 5:1, 3:1 hexane–ethyl acetate) afforded 361 mg (81%) of **19** as a clear oil that solidifies on standing. This material was suitable for further use. An analytical sample was prepared by recrystallization from benzene–hexane (1:5): mp 95–97 °C; $[\alpha]^{23}_D$ –6.2°, $[\alpha]_{578}$ –6.2°, $[\alpha]_{546}$ –7.5°, $[\alpha]_{435}$ –19.7°, $[\alpha]_{365}$ –76.2° (*c* 0.93, $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$) δ 9.53 (d, J = 7.9 Hz, 1 H), 7.73 (d, J = 8.3 Hz, 2 H), 7.34 (d, J = 8.2 Hz, 2 H), 6.68 (dd, J = 15.7, 4.0 Hz, 1 H, C*H*=CHCHO), 6.20 (ddd, J = 15.7, 7.9, 1.6 Hz, 1 H, CH=C*H*CHO), 5.92 (dt, J = 10.3, 7.9 Hz, 1 H, H-4), 5.75 (ddt, J = 10.3, 6.7, 1.5 Hz, 1 H, H-5), 4.26–4.18 (m, 2 H), 4.09 (d, J = 5.8 Hz, 2 H), 4.06 (m, 1 H, H-7), 2.87 (apparent q, J = 11.0 Hz, 1 H, H-6), 2.58–2.40 (m, 2 H, H-6 and H-3), 2.45 (s, 3 H), 2.28 (ddd, J = 14.3, 8.4, 1.7 Hz, 1 H, H-3); ^{13}C NMR (75 MHz, $CDCl_3$) δ 193.22, 155.18, 145.19, 132.22, 131.13, 129.97, 129.21, 127.86, 127.81, 79.87, 77.61, 71.45, 60.87, 33.82, 33.57, 21.61; IR ($CHCl_3$) 3031, 2944, 2825, 2738, 1694, 1363, 1213, 1175, 1125, 1100, 994, 975 cm^{-1}. Anal. Calcd for $C_{18}H_{21}ClO_5S$: C, 56.17; H, 5.50. Found: C, 56.22; H, 5.53.

Preparation of (2*S*,7*S*,8*S*)-7-Chloro-3,6,7,8-tetrahydro-2-(1-propenyl)-8-[[(*p*-tolylsulfonyl)oxy]methyl]-2*H*-oxocin (20). To a solution of diisobutylaluminum hydride (1 M hexane, 1.5 mL, 1.5 mmol) in CH_2Cl_2 (9 mL) at –70 °C was added enal **19** (295 mg, 0.77 mmol) in CH_2Cl_2 (6 mL). The reaction was stirred at –70 °C for 20 min and quenched at –70 °C with methanol (ca. 0.5 mL) followed by saturated sodium potassium tartrate solution (10 mL) and H_2O (5 mL). The mixture was vigorously stirred for 1 h and the aqueous layer removed. The aqueous layer was extracted with CH_2Cl_2, washed with brine, dried (Na_2SO_4), and concentrated to afford ca. 300 mg (100%) of the crude allylic alcohol **45** as a viscous oil, which was dried (0.1 mm, 1 h) and used without further purification.

Allylic alcohol **45** (300 mg, 0.77 mmol) was dissolved in dry CH_2Cl_2 (12 mL) and cooled to –30 °C. To this mixture was added triethylamine (0.60 mL, 4.31 mmol) followed by methanesulfonyl chloride (0.24 mL, 3.1 mmol), and the reaction was stirred for 0.5 h while the bath warmed to –10 °C. The reaction was quenched with saturated $NaHCO_3$, extracted with CH_2Cl_2, dried (Na_2SO_4), and concentrated. The oily residue was filtered through a plug of silica gel and rapidly eluted with hexane–ethyl acetate (1:1, v/v). The solvent was removed in vacuo and the residue dried by concentration from benzene (1×) followed by vacuum drying (0.1 mm, 30 min). The crude mesylate **46** was used without further purification.

To a suspension of sodium borohydride (50 mg, 1.32 mmol) and cyclohexene[33,49] (0.30 mL, 2.96 mol) in HMPA (3 mL) at 23 °C was added mesylate **46** in HMPA (2 mL). After 20 min, an additional portion of $NaBH_4$ (25 mg, 0.66 mmol) was added and the reaction stirred for an additional 40 min. The reaction was cooled in an ice–H_2O bath and quenched with acetone (ca. 0.5 mL) followed by careful addition of saturated NH_4Cl. The salts were dissolved with H_2O, and the mixture was extracted with Et_2O. The combined organic layers were washed with H_2O and brine, dried (Na_2SO_4), and concentrated. Purification of the residue by silica gel flash chromatography (gradient elution, using 8:1, 5:1, 2:1, 1:1 hexane–ethyl acetate) afforded 183 mg (64% overall) of **20** as a clear colorless oil: $[\alpha]^{24}_D$ +47.1°, $[\alpha]_{578}$ +49.7°, $[\alpha]_{546}$ +56.5°, $[\alpha]_{435}$ +101.1°, $[\alpha]_{365}$ +174.0° (*c* 0.97, $CHCl_3$); ^1H NMR (500 MHz, $CDCl_3$) δ 7.77 (d, J = 8.3 Hz, 2 H), 7.34 (d, J = 7.9 Hz, 2 H), 5.92 (dd, J = 10.3, 8.3 Hz, 1 H, H-4), 5.70–5.60 (m, 2 H, H-5 and CH=C*H*CH$_3$), 5.48 (ddq, J = 15.3, 6.1, 1.5 Hz, 1 H, C*H*=CHCH$_3$), 4.16 (ddd, J = 6.8, 5.5, 2.5 Hz, 1 H, H-8), 4.10–4.05 (m, 2 H), 4.03 (ddd, J = 11.5, 4.9, 2.5 Hz, 1 H, H-7), 3.87 (dd, J = 9.2, 6.5 Hz, 1 H, H-2), 2.90 (apparent dq, J = 11.2, 1.0 Hz, 1 H, H-6), 2.57–2.40 (m, 2 H, H-6 and H-3), 2.45 (s, 3 H), 2.16 (ddd, J = 14.3, 8.5, 1.5 Hz, 1 H, H-3), 1.68 (d, J = 6.4 Hz, 3 H); ^{13}C NMR (125 MHz, $CDCl_3$) 144.88, 132.42, 131.49, 131.27, 129.80, 128.09, 127.96, 126.85, 82.02, 76.82, 71.14, 61.35, 34.56, 33.77, 21.62, 17.75; IR (thin film) 3025, 2938, 1656, 1600, 1450, 1363, 1175, 988, 969 cm^{-1}. Anal. Calcd for $C_{18}H_{23}ClO_4S$: C, 58.29; H, 6.25. Found: C, 58.04; H, 6.32.

Preparation of (2*S*,7*S*,8*S*)-7-Chloro-8-(cyanomethyl)-3,6,7,8-tetrahydro-2-(1-propenyl)-2*H*-oxocin (21). Into a sealable glass tube was placed NaCN (13 mg, 0.265 mmol) followed by tosylate **20** (36 mg, 0.097 mmol) and DMSO (1.5 mL). The tube was sealed and the vessel immersed into an oil bath at 95 °C. The reaction was maintained at this temperature for 24 h. The vessel was then removed from the oil bath and allowed to cool to 23 °C. The red reaction mixture was applied directly to silica gel and eluted with 10:1–5:1 hexane–ethyl acetate. The nitrile and unreacted starting material coelute to afford 19 mg of a clear colorless oil. Analysis by 300-MHz NMR (using H-8 as a probe) showed the mole ratio of nitrile to starting material was 1.7:1. This corresponds to 9.6 mg (44%) of nitrile and 9.3 mg (26%) of unreacted starting material. The yield of nitrile based on consumed starting material is 59%. The unreacted tosylate is most easily removed by flash chromatography after introduction of the enyne side chain. An analytical sample was prepared by preparative TLC (silica gel, using 7:1 hexane–ethyl acetate, four developments): $[\alpha]^{24}_D$ +24°, $[\alpha]_{578}$ +29°, $[\alpha]_{546}$ +33°, $[\alpha]_{435}$ +61°, $[\alpha]_{365}$ +114° (*c* 1.0, $CHCl_3$); ^1H NMR (500 MHz, $CDCl_3$) δ 5.98 (ddt, J = 10.4, 7.3, 0.9 Hz, 1 H, H-4), 5.78 (ddq, J = 15.3, 6.5, 1.1 Hz, 1 H, CH=C*H*CH$_3$), 5.72 (ddt, J = 10.2, 6.6, 1.8 Hz, 1 H, H-5), 5.70 (ddq, J = 15.3, 6.2, 1.6 Hz, 1 H, C*H*=CHCH$_3$), 4.29 (ddd, J = 9.0, 4.6, 2.5 Hz, 1 H, H-8), 4.01 (ddd, J = 11.5, 4.9, 2.5 Hz, 1 H, H-7), 3.99 (m, 1 H, H-2), 2.97 (apparent dq, J = 11.3, 1.0 Hz, 1 H, H-6), 2.82 (dd, J = 16.7, 9.0 Hz, 1 H), 2.57 (m, 1 H, H-6), 2.52 (m, 1 H, H-3), 2.46 (dd, J = 16.7, 4.6 Hz, 1 H), 2.22 (ddd, J = 14.3, 8.5, 1.5 Hz, 1 H, H-3), 1.71 (d, J = 6.4 Hz, 3 H); ^{13}C NMR (125 MHz, $CDCl_3$) 131.56, 131.06, 128.08, 127.68, 117.70, 82.27, 75.74, 63.44, 34.51, 34.00, 23.07, 17.80; IR (thin film) 3025, 2938, 2856, 2250, 1675, 1650, 1450, 1106, 1081, 1056, 1006, 969 cm^{-1}; MS (CI, 70 eV) *m/e* 228 (MH, 34), 227 (16), 226 (MH^+, 100), 224 (13), 190 (22), 144 (14), 131 (28), 81 (21), 79 (23), 71 (36), 69 (51), 67 (36); MS (EI, 70 eV) *m/e* 227.0892 (227.0891 calcd for $C_{12}H_{16}ClNO$), 225.0908 (225.0920 calcd for $C_{12}H_{16}ClNO$).

Preparation of (2*S*,7*S*,8*S*)-7-Chloro-8-(2-oxoethyl)-3,6,7,8-tetrahydro-2-(1-propenyl)-2*H*-oxocin (22). Into a 15-mL round-bottom flask were placed a stir bar and nitrile **21** (10 mg, 0.044 mmol). The contents of the flask were dried via a benzene azeotrope (2×) followed by additional drying under vacuum (0.1 mm, 15 min). The nitrile was dissolved in dry toluene (2 mL), and the solution was cooled in an ice–H_2O bath under argon. To this solution was added diisobutylaluminum hydride (1.0 M hexane, 0.24 mL, 0.24 mmol). The reaction was stirred at 0 °C for 15 min, the ice–H_2O bath was removed, and the reaction was stirred an additional 10 min. After being cooled to 0 °C, the reaction was quenched by addition of ethyl acetate (0.25 mL) followed by 1 M tartaric acid in H_2O (2 mL). The two-phase mixture was stirred vigorously for 1 h and then transferred to a separatory funnel and diluted with H_2O. The mixture was extracted with hexane–ethyl acetate (4:1, v/v), washed with brine, dried (Na_2SO_4), and concentrated. Purification of the residue by silica gel flash chromatography (gradient elution, using 10:1, 5:1 hexane–ethyl acetate) afforded 8.8 mg (87%) of **22** as a clear colorless oil: $[\alpha]^{24}_D$ +12.3°, $[\alpha]_{578}$ +15.6°, $[\alpha]_{546}$ +17.0°, $[\alpha]_{435}$ +31.0°, $[\alpha]_{365}$ +51.0° (*c* 1.0, benzene); ^1H NMR (500 MHz, $CDCl_3$) δ 9.80 (t, J = 1.0 Hz, 1 H), 5.96 (ddd, J = 10.4, 7.3, 0.9 Hz, 1 H, H-4), 5.70 (ddt, J = 10.2, 6.5, 1.8 Hz, 1 H, H-5), 5.64 (ddq, J = 15.3, 6.5, 1.1 Hz, 1 H, H-10), 5.50 (ddq, J = 15.3, 6.3, 1.6 Hz, 1 H, H-9), 4.46 (apparent dt, J = 8.8, 3.0 Hz, 1 H, H-8), 4.02 (m, 1 H, H-2), 3.99 (ddd, J = 11.5, 4.8, 2.6 Hz, 1 H, H-7), 3.10 (ddd, J = 18.0, 8.8, 1.1 Hz, 1 H, C*H*$_2$CHO), 2.98 (apparent dq, J = 11.3, 1.0 Hz, 1 H, H-6), 2.59 (ddd, J = 18.0, 3.6, 1.0 Hz, 1 H, C*H*$_2$CHO), 2.55–2.45 (m, 2 H, H-6 and H-3), 2.18 (ddd, J = 14.2, 8.5, 1.5 Hz, 1 H, H-3), 1.67 (d, J = 6.4 Hz, 3 H); ^{13}C NMR (125 MHz, $CDCl_3$) 200.47, 131.88, 131.48, 128.14, 126.56, 81.54, 73.73, 65.42, 49.10, 34.71, 34.24, 17.58; IR (thin film) 3025, 2938, 2856, 2731, 1725, 1675, 1656, 1450, 1106, 1088, 1044, 1013, 969 cm^{-1}; MS (EI, 33 eV) *m/e* 230.0872 (230.0887 calcd for $C_{12}H_{17}ClO_2$), 228.0901 (228.0916 calcd for $C_{12}H_{17}ClO_2$).

Preparation of (Triisopropylsilyl)laurenyne (23). A 15-mL round-bottom flask containing 1,3-bis(triisopropylsilyl)propyne[35] (48.4 mg, 0.137 mmol) and a stir bar was dried by azetroping with benzene (2×) followed by additional drying under vacuum (0.1 mm, 1 h). This material was dissolved in dry THF (1 mL) and the solution cooled to –20 °C under argon. To this solution was added *n*-BuLi (2.5 M in hexane, 0.055 mL, 0.14 mmol) followed by HMPA (0.12 mL, 0.69 mmol). The mixture was stirred at –20 °C for 8 min, and the resulting deep red solution was cooled to –70 °C. To the anion was added aldehyde **22** (4.6 mg, 0.020 mmol) in THF (1 mL). The reaction was stirred at –70 °C for 10 min and quenched with saturted NH_4Cl. The resulting colorless solution was diluted with H_2O and allowed to warm to ambient temperature. The mixture was extracted with hexane–ethyl acetate (4:1), washed with H_2O and brine, dried (Na_2SO_4), and concentrated. Preliminary purification of the residue by silica gel flash chromatography (gradient elution, using hexane and then 25:1, 4:1 hexane–ethyl acetate) afforded 4.2 mg (51%) of an oil. Analysis by capillary GC shows the ratio of trans- to cis-enynes is 6.7:1. Further purification by preparative

(49) The cyclohexene was added in order to react with any diborane generated under the reaction conditions. Generation of diborane may be a problem when DMSO is used as a solvent; see: Reference 33.

(50) **Note Added in Proof**: Professor Thomson recently informed us that reexamination of the X-ray data showed that an error had been made in depicting the absolute configuration of (+)-laurenyne in ref 6. He concurs that the absolute configuration of natural laurenyne is 2*R*,7*R*,8*R*.

thin-layer chromatography (silica gel, using hexane, two developments, then 100:1 hexane–ethyl acetate, two developments) afforded pure samples of the *trans*- and *cis*-enynes.

***trans*-Enyne 23**: $[\alpha]^{24}_D$ −28.8°, $[\alpha]_{578}$ −28.3°, $[\alpha]_{546}$ −33.8°, $[\alpha]_{435}$ −69.1°, $[\alpha]_{365}$ −137.0° (*c* 2.0, $CHCl_3$); ^1H NMR (500 MHz, $CDCl_3$) δ 6.16 (apparent p, *J* = 15.9, 7.8 Hz, 1 H, Tips-C≡CCH=C*H*), 5.91 (dt, *J* = 10.4, 8.1 Hz, 1 H, H-4), 5.74–5.65 (m, 2 H, CH_3CH=CH and H-5), 5.63 (d, *J* = 15.9 Hz, 1 H, Tips-C≡CC*H*=CH), 5.54 (ddq, *J* = 15.3, 6.8 1.6 Hz, 1 H), 3.97 (ddd, *J* = 11.5, 4.9, 2.5 Hz, 1 H, H-7), 3.85 (ddd, *J* = 8.9, 4.6, 2.5 Hz, 1 H, H-8), 3.75 (apparent t, *J* = 7.5 Hz, 1 H, H-2), 2.98 (apparent q, *J* = 11.2 Hz, 1 H, H-6), 2.60–2.45 (m, 3 H, H-6 and H-3 and CH_2CH=C≡C-Tips), 2.23 (dddd, *J* = 14.0, 8.0, 4.6, 1.0 Hz, 1 H, CH_2CH=CHC≡C-Tips), 2.15 (ddd, *J* = 14.2, 8.5, 1.4 Hz, 1 H, H-3), 1.68 (dd, *J* = 6.5, 1.1 Hz, 3 H), 1.20–1.0 (m, 3 H), 1.08 (s, 18 H); ^{13}C NMR (125 MHz, $CDCl_3$) 141.09, 131.76, 131.16, 128.43, 127.04, 112.95, 105.62, 89.38, 82.00, 79.18, 65.03, 37.99, 34.82, 34.48, 18.60, 17.76, 11.27; IR (thin film) 3025, 2944, 2869, 2169, 2138, 1675, 1463, 1081, 1013, 994, 963, 881 cm^{-1}; MS (EI, 70 eV) *m/e* 408.2430 (408.2429 calcd for $C_{24}H_{39}ClOSi$), 406.2456 (406.2459 calcd for $C_{24}H_{39}ClOSi$).

***cis*-Enyne isomer**: ^1H NMR (500 MHz, $CDCl_3$) δ 6.03 (ddd, *J* = 10.8, 8.1, 7.1 Hz, 1 H, Tips-C≡CCH=C*H*), 5.61 (d, *J* = 10.9 Hz, 1 H, Tips-C≡CC*H*=CH).

Preparation of (−)-Laurenenyne (1). Triisopropylsilyl enyne **23** (9.7 mg, 0.024 mmol) was dissolved in DMF (15 drops), and to this mixture was added *n*-Bu_4NF (1.0 M in THF, four drops). The reaction was stirred at 23 °C for 10 min, and the resulting red mixture was applied directly to silica gel. Elution with hexane then 20:1 hexane–ethyl acetate afforded 5.6 mg (94%) of laurenyne as an off-white solid. An analytical sample was obtained by recrystallization from hexane to afford colorless fine needles: mp 78–80 °C; $[\alpha]^{17}_D$ −20.0° (*c* 2.0, $CHCl_3$); $[\alpha]^{24}_D$ −18.8°, $[\alpha]_{578}$ −19.1°, $[\alpha]_{546}$ −22.1°, $[\alpha]_{435}$ −45.6°, $[\alpha]_{365}$ −94.6° (*c* 0.5, $CHCl_3$); ^1H NMR (500 MHz, $CDCl_3$) δ 6.20 (apparent p, *J* = 15.8, 7.8 Hz, 1 H, C≡CCH=C*H*), 5.90 (dt, *J* = 10.4, 8.0 Hz, 1 H, H-4), 5.74–5.65 (m, 2 H, CH_3CH=CH and H-5), 5.57 (d, *J* = 15.6 Hz, 1 H, C≡CC*H*=CH), 5.05 (ddq, *J* = 15.4, 6.3, 1.6 Hz, 1 H, CH_3CH=C*H*), 3.96 (ddd, *J* = 11.4, 4.9, 2.4 Hz, 1 H, H-7), 3.85 (ddd, *J* = 8.7, 4.9, 2.5 Hz, 1 H, H-8), 3.76 (dd, *J* = 9.3, 6.9 Hz, 1 H, H-2), 2.97 (apparent dq, *J* = 11.2, 1.0 Hz, 1 H, H-6), 2.82 (d, *J* = 2.2 Hz, 1 H), 2.60–2.45 (m, 3 H, H-6 and H-3 and C≡CCH=CHCH_2), 2.26 (dddd, *J* = 14.0, 8.0, 4.8, 1.0 Hz, 1 H, C≡CCH=CHCH_2), 2.16 (ddd, *J* = 14.2, 8.5, 1.4 Hz, 1 H, H-3), 1.70 (d, *J* = 6.3 Hz, 3 H); ^{13}C NMR (125 MHz, $CDCl_3$) 142.07, 131.74, 131.16, 128.44, 126.77, 111.59, 82.16, 81.69, 78.99, 76.25, 64.97, 38.09, 34.75, 34.42, 17.80; IR (CCl_4) 3313, 3025, 2938, 2856, 2106, 1675, 1450, 1100, 1013, 963 cm^{-1}; MS (EI, 70 eV) *m/e* 237.0844 (237.086 calcd for $C_{15}H_{19}ClO - CH_3$), 235.0879 (235.0871 calcd for $C_{15}H_{19}ClO - CH_3$).

Preparation of Mixed Acetal 34. A solution of 1,1,3-triethoxybutane (1.5 g, 7.9 mmol) and CH_2Cl_2 (15 mL) was cooled in an ice–H_2O bath under argon, and boron trichloride (1.0 M in CH_2Cl_2, 3.15 mL, 3.15 mmol) was added. The reaction was stirred at 0 °C for 2.5 h followed by removal of the volatiles in vacuo (20 mm, 1 h). Opening the flask under an argon atmosphere afforded crude α-chloro ether **40**. The ^1H NMR spectrum showed that no starting material remained, using the acetal proton at δ 4.68 as a probe: ^1H NMR (300 MHz, $CDCl_3$) δ 5.75 (m, 1 H, ROC*H*Cl), 4.10–3.25 (m, 5 H), 2.30–2.00 (m, 2 H), 1.14–1.10 (m, OH).

A solution of alcohol **26** (41 mg, 0.120 mmol), dry CH_2Cl_2 (1.0 mL), diisopropylethylamine (0.1 mL, 0.575 mmol), and α-chloro ether **40** (0.05 mL) was stirred at 23 °C for 2 h, at which time the reaction was judged to be ca. 50% complete by TLC analysis. An additional portion of Pr_2NEt (0.1 mL, 0.575 mmol) and α-chloro ether **40** (0.05 mL) was added, and after 2 h the reaction mixture was applied directly onto silica gel and eluted with 100:1 hexane–triethylamine and then 100:2:1, 100:5:1, 100:10:1 hexane–ethyl acetate–triethylamine. First to elute was the mixed acetal [35.7 mg (60%)] followed by unreacted starting material [18 mg (42%)]. Mixed acetal **34** was a mixture of four diastereomers (by capillary GC): ^1H NMR (250 MHz, $CDCl_3$) 5.60 (br s, 1 H), 5.40 (br s, 1 H), 4.83 (m, 1 H, ROC*H*OEt), 4.15 (m, 1 H), 3.85–3.45 (m, 7 H), 3.35 (m, 1 H), 2.45 (m, 1 H), 2.25 (m, 1 H), 2.05–1.60 (m, 4 H), 1.20 (m, 9 H), 0.90 (s, 9 H), 0.10 (two singlets, 15 H), IR (thin film) 3050, 2956, 2888, 2863, 1350, 1100, 838 cm^{-1}; MS (CI, 70 eV, isobutane) *m/e* 451 [($MH^+ - C_2H_5OH$), 2], 450 (2), 449 [($MH^+ - C_2H_5OH$), 6], 227 (4), 225 (11), 145 (60), 101 (45), 99 (75), 93 (23), 73 (100); MS (EI, 70 eV) *m/e* 451.2663 (451.2643 calcd for $C_{24}H_{51}ClO_4Si_2 - C_2H_5O$), 449.2653 (449.2673 calcd for $C_{24}H_{51}ClO_4Si_2 - C_2H_5O$).

Preparation of (2*S,7*S**,8*S**)-7-Chloro-8-(hydroxymethyl)-2-methyl-3,6,7,8-tetrahydro-4-(trimethylsilyl)-2*H*-oxocin (38).** Mixed acetal **41** (34.3 mg, 0.081 mmol) was dried by azeotroping with benzene (2×) followed by additional drying under vacuum (0.02 mm, 1 h), before use. The acetal was dissolved in dry CH_2Cl_2 (2 mL) and the solution cooled to −15 °C under argon. To this mixture was added a solution of $SnCl_4$ (1.0 M in CH_2Cl_2, 0.160 mL, 0.160 mmol), and the reaction was stirred at −15 °C for 2 h. The reaction was quenched with 2.5% NaOH, extracted with CH_2Cl_2, washed with brine, dried (Na_2SO_4), and concentrated. The residue was purified by silica gel flash chromatography (gradient elution, using 10:1, 5:1, 3:1, 1:1 hexane–ethyl acetate) to afford 8.3 mg (40%) of oxocene **38** as a clear oil, which slowly solidified on standing: R_f 0.09 (silica gel, using 10:1 hexane–ethyl acetate); ^1H NMR (250 MHz, $CDCl_3$) 5.96 (ddd, *J* = 9.7, 6.3, 1.8 Hz, 1 H, H-5), 4.09 (ddd, *J* = 12.0, 5.1, 2.1 Hz, 1 H, H-7), 3.80 (m, 2 H), 3.60 (m, 1 H), 3.45 (dq, *J* = 10.1, 6.3 Hz, 1 H, H-2), 3.08 (apparent dt, *J* = 12.0, 9.8 Hz, 1 H, H-6), 2.65–2.50 (m, 2 H, H-6 and H-3), 2.18 (d, *J* = 14.2 Hz, 1 H, H-3), 1.75 (br s, 1 H), 1.33 (d, *J* = 6.3 Hz, 3 H), 0.07 (s, 9 H); IR (thin film) 3338, 3006, 2956, 1613, 1456, 1250, 1125, 1106, 1088, 1050, 838 cm^{-1}; MS (CI, 70 eV, isobutane) *m/e* 265 (MH^+, 33), 264 (14), 263 (MH^+, 99), 227 (13), 175 (29), 173 (84), 155 (60), 139 (15), 137 (100), 109 (50), 107 (73), 103 (22), MS (EI, 70 eV) *m/e* 264.1119 (264.1126 calcd for $C_{12}H_{23}ClO_2Si$), 262.1147 (262.1155 calcd for $C_{12}H_{23}ClO_2Si$).

Cyclization of **34** under identical conditions afforded **38** in 24% yield after purification.

Acknowledgment. The financial support of the National Science Foundation (Grant CHE-8618451) is gratefully acknowledged. NMR and mass spectra were determined with spectrometers purchased with the assistance of NSF Shared Instrumentation Grants. We particularly thank Professor K. B. Sharpless for a preprint of ref 19b and for providing unpublished details of ref 26 and Professors R. H. Thomson and S. Imre for providing authentic samples of (+)-laurenyne.

Registry No. 1, 112837-84-0; **5**, 112817-44-4; (±)-**6**, 112793-71-2; (−)-**6**, 112837-82-8; **7**, 13683-41-5; **8**, 112793-67-6; **9**, 112793-69-8; **10**, 112793-70-1; **11**, 112793-72-3; **12**, 112793-73-4; **13** (isomer 1), 112793-74-5; **13** (isomer 2), 112837-92-0; **14**, 112793-75-6; **16**, 112793-76-7; **17**, 112793-77-8; **18**, 112793-78-9; **19**, 112793-79-0; **20**, 112793-80-3; **21**, 112793-81-4; **22**, 112793-82-5; **23** (trans enyne), 112793-83-6; **23** (cis enyne), 112837-83-9; **24a** (isomer 1), 112793-94-9; **24a** (isomer 2), 112794-05-5; **24b** (isomer 1), 112793-93-8; **24b** (isomer 2), 112794-04-4; **25a**, 112793-95-0; **26**, 112793-90-5; **27** (isomer 1), 112924-06-8; **27** (isomer 2), 112794-01-1; **28** (isomer 1), 112793-96-1; **28** (isomer 2), 112837-85-1; **28** (isomer 3), 112837-86-2; **28** (isomer 4), 112837-87-3; **29** (isomer 1), 112837-97-2; **29** (isomer 2), 112837-88-4; **30** (isomer 1), 112794-00-0; **30** (isomer 2), 112837-94-2; **30** (isomer 3), 112837-95-3; **30** (isomer 4), 112837-96-4; **31** (isomer 1), 112793-99-4; **31** (isomer 2), 112837-89-5; **31** (isomer 3), 112837-90-8; **31** (isomer 4), 112837-91-9; **33** (X = OAc), 112794-02-2; **33** (X = SMe), 112794-03-3; **34** (isomer 1), 112817-45-5; **34** (isomer 2), 112924-03-5; **34** (isomer 3), 112924-04-6; **34** (isomer 4), 112924-05-7; **38**, 112793-91-6; **39**, 5870-82-6; **40**, 112793-89-2; **41** (isomer 1), 112793-92-7; **41** (isomer 2), 112837-93-1; **42**, 112793-68-7; **44**, 112793-84-7; **44** (crude enol silyl ether), 112793-85-8; **45**, 112793-86-9; **46**, 112793-87-0; $(CF_3CH_2O)_2P(O)CH_2CO_2Me$, 88738-78-7; $EtOC{\equiv}C(CH_2)_2OH$, 19985-85-4; $i\text{-}Pr_3SiCH_2C{\equiv}CCH_2SiPr\text{-}i_3$, 112793-88-1; MeCH=CHCHO, 4170-30-3; $Me(CH_2)_2CHO$, 123-72-8; $EtCH(OAc)CH(OEt)O_2C\text{-}3\text{-}C_6H_4Cl$, 112793-98-3; $3\text{-}ClC_6H_4CO_3H$, 937-14-4; oxetane, 503-30-0; Laurenyne, 77182-65-1.

Supplementary Material Available: Experimental details and characterization data for the preparation of compounds **24a,b**, **25a,b**, and **26–31** (11 pages). Ordering information is given on any current masthead page.