284 (10), 283 (9), 282 (50), 281 (14), 280 (70), 270 (3), 269 (17), 268 (15), 267 (80), 266 (23), 265 (100), 240 (4), 239 (26), 238 (7), 237 (38). ^{1}H NMR ($CDCl_3$) δ: 8.830 (1 H, d, 1.2; H-1), 7.530 (1 H, dd, 6.4, 1.2; H-3), 8.494 (1 H, d, 6.4; H-4), 7.409 (1 H, s; H-8), 4.301 (3 H, s; NMe), 3.934 (3 H, s; OMe).

5,7-Dichloro-6-methoxy-2-methyl-1,2,3,4-tetrahydro-β-carboline (8). Reduction of **7** with $NaBH_4$ (EtOH) afforded a tetrahydro-β-carboline as a colorless solid: $C_{13}H_{14}Cl_2N_2O$, $M^{+\cdot}$ = 284/286/288. ^{1}H NMR ($CDCl_3$) δ: 3.576 (2 H, s; H_2-1), 3.124 (2 H, t, 5.9; H_2-3), 2.741 (2 H, t, 5.9; H_2-4), 6.816 (1 H, s; H-8), 8.021 (1 H, s; NH), 2.481 (3 H, s; NMe), 3.868 (3 H, s; OMe).

4a-Acetoxy-6-methoxy-2-methyl-2,3,4,4a-tetrahydro-1*H*-pyrido[3,4-*b*]indole (9). 1,2,3,4-Tetrahydro-β-carboline **2** (21.6 mg) and lead tetraacetate (66.5 mg) in CH_2Cl_2 (10 mL) were stirred at 20 °C for 10 min. The dichloromethane solution was washed with water and dried (Na_2SO_4) and the solvent was removed. TLC of the residue on silica gel was eluted by CH_2Cl_2/MeOH (9/1). The zone of R_f 0.8 afforded 4a-acetoxyindolenine **9** (14 mg). IR (KBr, ν cm^{-1}): 1750 (C=O), 1220 (C–O–C). ^{1}H NMR ($CDCl_3$) δ: 3.089 (d, 12.0) and 3.700 (d, 12.0), H_2-1, 2.732 (m) and 2.60 (m), H_2-3, 2.60 (m) and 1.514 (m), H_2-4, 6.952 (d, 2.6; H-5), 6.855 (dd, 8.4, 2.6; H-7), 7.465 (d, 8.4; H-8), 2.405 (s; NMe), 3.790 (s; OMe), 2.036 (s; Ac). ^{13}C NMR ($CDCl_3$) δ: 55.02 (t; C-1), 49.35 (t; C-3), 36.09 (t; C-3), 84.12 (s; C-4a), 138.58 (s; C-4b), 109.52 (d; C-5), 158.55 (s, C-6), 113.84 (d; C-7), 121.71 (d; C-8), 147.60 (s; C-8a), 175.56 (s; C-9a), 44.66 (q; NMe), 55.68 (q; OMe), 20.94 (q; Ac), 168.65 (s; Ac).

(±)-Horsfiline (10). 4a-Acetoxyindolenine **9** (14 mg) in methanol (1 mL), water (0,2 mL), and acetic acid (1 drop) was refluxed for 1.5 h. The solution was evaporated to dryness, basified with ammonia, extracted with CH_2Cl_2, and purified by silica gel TLC, eluting with CH_2Cl_2/MeOH (9/1), to yield (±)-horsfiline (**10**) (R_f 0.4, 4.5 mg), mp 156–157 °C (acetone). The ^{1}H NMR spectrum was identical with that of **1**.

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Registry No. **1**, 136247-72-8; **2**, 6582-80-5; **3**, 1019-45-0; **4**, 136247-73-9; **5**, 136247-74-0; **6**, 136247-75-1; **7**, 136247-76-2; **8**, 136247-77-3; **9**, 136276-25-0; **10**, 136316-07-9; *N*-chlorosuccinimide, 128-09-6.

Synthetic Studies on the Macrodiolide Elaiophylin

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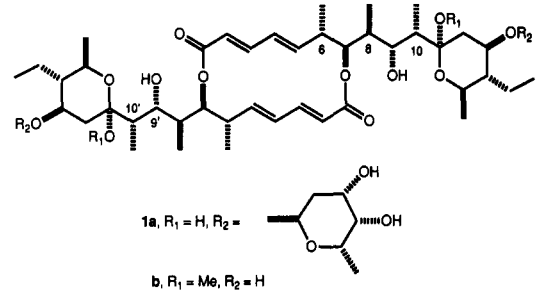
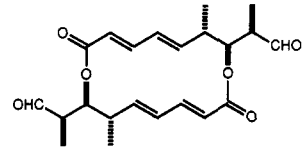
An approach to the synthesis of the monomeric fragment of the macrodiolide elaiophylin is reported. The absolute stereochemistry of C_5–C_{10} is contained in fragment **5** and that of C_{13}–C_{15} is incorporated in aldehyde **6b**. A method for the union of these fragments is outlined.

The antibiotic elaiophylin (**1**) was first isolated in 1959 by Arcamone and co-workers[1] from cultures of *Streptomyces melanosporus*. A year later, Arai et al.[2] reported the isolation of the same compound (azalomycin B) from *S. hygroscopicus* var. *azalomyceticus*. Subsequently, elaiophylin (azalomycin B) was isolated from several other strains of *Streptomyces*.[3] After early structural work by Takahashi,[4] Kaiser and Keller-Schierlein[5] were able to elucidate the gross structure of elaiophylin through the use of ^{1}H and ^{13}C NMR spectroscopy and chemical degradations. Their efforts confirmed the earlier assignment of the carbohydrate residues as 2-deoxy-L-fucose (L-oliose).[4b] In the following year, Neupert-Laves and Dobler[6] published the X-ray crystal structure of elaiophylin, which not only confirmed the efforts of Kaiser and Keller-Schierlein but also defined the relative and absolute stereochemistry of elaiophylin. Ley et al.[3c] were able to define hydrogen bonding in both the solid state and in solution by analysis of X-ray data and NOE studies, respectively.





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Elaiophylin is a member of a group of C_2-symmetrical, 16-membered macrodiolides that includes pyrenophorin,[7a-c]

(1) Arcamone, F. M.; Bertazolli, C.; Ghione, M.; Scotti, T. *Giorn. Microbiol.* **1959**, *7*, 207.
(2) Arai, M. J. *Antibiotics Ser. A* **1960**, *13*, 46, 51.
(3) (a) Khlebarova, E. I.; Georgieva-Borisova, I. K.; Sheikova, G. N.; Blinov, N. O. *Farmatsiya (Sofia)* **1972**, *22*, 3. (b) Hoechst Patent DE 3248-280-A 1972. (c) Ley, S. V.; Neuhaus, D.; Williams, D. J. *Tetrahedron Lett.* **1982**, *23*, 1207. (d) Fiedler, H.-P.; Worner, W.; Zahner, H.; Kaiser, H. P.; Keller-Schierlein, W.; Muller, A. *J. Antibiotics* **1960**, *34*, 1107.
(4) (a) Takahashi, S.; Arai, M.; Ohki, E. *Chem. Pharm. Bull.* **1967**, *15*, 1651. (b) Takahashi, S.; Kurabayashi, M.; Ohki, E. *Chem. Pharm. Bull.* **1967**, *15*, 1657. (c) Takahashi, S.; Ohki, E. *Chem. Pharm. Bull.* **1967**, *15*, 1726.
(5) Kaiser, H.; Keller-Schierlein, W. *Helv. Chim. Acta* **1981**, *64*, 407.
(6) Neupert-Laves, K.; Dobler, M. *Helv. Chim. Acta* **1982**, *65*, 262.
(7) (a) Nozoe, S.; Hirai, K.; Tsuda, K.; Ishibashi, K.; Shirasaka, M.; Grove, J. F. *Tetrahedron Lett.* **1965**, 4675. (b) Seuring, B.; Seebach, D. *Liebigs Ann. Chem.* **1978**, 2044. (c) Mali, R. S.; Pohmakotr, M.; Weidmann, R.; Seebach, D. Ibid. **1981**, 2272. (d) Fuska, J.; Nemec, P.; Kuhr, I. *J. Antibiotics* **1972**, *25*, 208. (e) Boeckman Jr., R. K.; Fayos, J.; Clardy, J. *J. Am. Chem. Soc.* **1974**, *96*, 5954.

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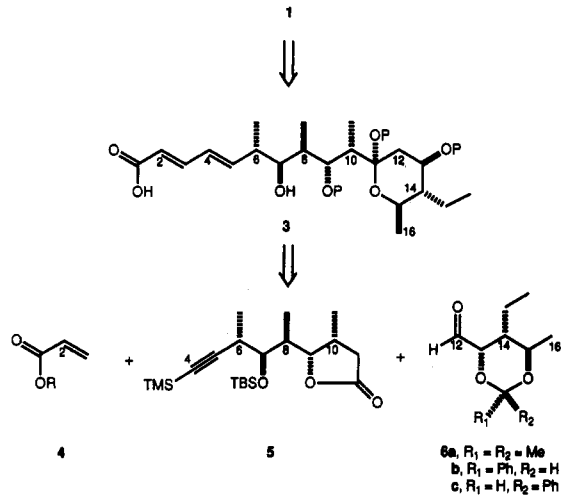
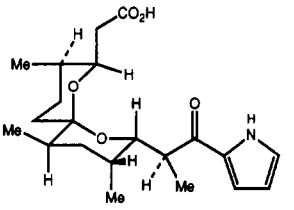
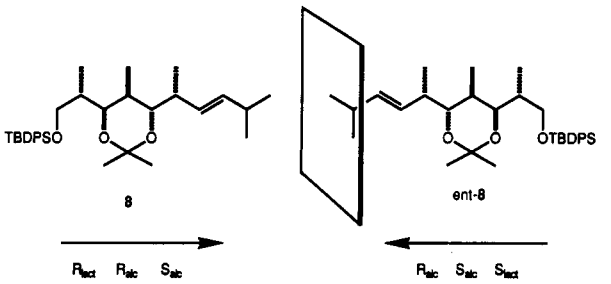
Scheme I



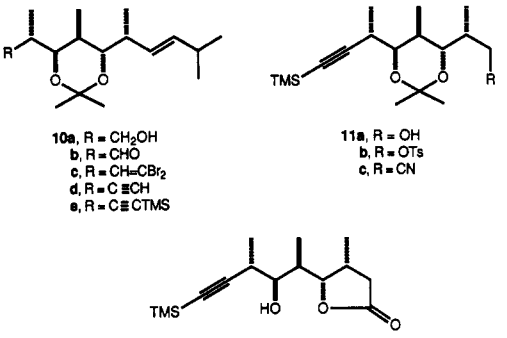
vermiculin,[7d,e] and conglobatin.[8] Structurally related 16-membered macrodiolides include colletodiol[9a-c] and grahamimycin A_1.[9d,e] Kinoshita and his co-workers[10] have achieved the total synthesis of elaiophylin, and Seebach[11] and his collaborators have realized the synthesis of the *O*-methyl aglycon of elaiophylin.[12] Both of these successful efforts exploited the C_2 symmetry of elaiophylin through a double aldol condensation of C_2-symmetrical dialdehyde **2** with appropriately functionalized ethyl ketone moieties to form the 9, 10 and 9′, 10′ bonds. One shortcoming of such an approach is the magnification of any lack of selectivity in the aldol process owing to the presence of two aldehyde functional groups. Not only did this problem manifest itself in these skillfully crafted syntheses, but the desired (9*R*,9′*R*,10*S*,10′*S*) configuration was the minor component in both studies. The major diastereomers were the syn aldol products having the C_2-symmetrical (9*S*,9′*S*,10*R*,10′*R*) and C_1-symmetrical (9*R*,9′*S*,10*S*,10′*R*) structures.

An alternative strategy requires initial assembly of the identical halves of the molecule prior to macrodiolide formation. To this end, the feasibility of the retrosynthetic plan of Scheme I was explored. An appropriately protected derivative of hydroxy acid **3**, which would serve as the unit for dimerization, could be prepared by the initial union of lactone **5** and aldehyde **6**, or another electrophilic congener having C_{12} at the oxidation level of an alcohol, followed by coupling of a modified acetylene residue with acrylate unit **4**. Previous studies in this laboratory have demonstrated that γ-butyrolactones bearing α, β, and γ substituents can be degraded to β-hydroxy ketones by excision of the carbonyl carbon of the lactone.[13] Hydroxy acid **3** exists as a masked form of a β-hydroxy ketone.





The pyrrole acid **7**, an intermediate in the synthesis of calcimycin,[14] employed olefin *ent*-**8** as the source of four stereogenic centers in and proximate to the tetrahydropyran ring of **7** that bears the pyrrole residue as a substituent. The synthesis of *ent*-**8** was achieved by successive, linear iteration of (*S*)-3-methyl-γ-butyrolactone with the *S* and *R* enantiomers of (*E*)-2-methyl-3-hydroxy-4-hexene (**9**), respectively.[13,15] The relative stereochemistry present in *ent*-**8** is the same as that present at C_6–C_{10} of elaiophylin but of the opposite absolute stereochemistry. Owing to the ready accessibility of both enantiomers of 3-methyl-γ-butyrolactone, the *R* enantiomer was subjected to linear iteration with alcohols **9**. In this case, the *R* alcohol preceded the *S* enantiomer in the iterative process, thereby leading to olefin **8**.



The conversion of olefin **8** into lactone **5** was accomplished by initial refunctionalization of the silyl ether terminus of the molecule. Desilylation of **8** followed by Swern oxidation[16] of the intermediate alcohol **10a** occurred without incident to provide aldehyde **10b** in excellent yield. The Corey protocol for the conversion of aldehydes to acetylenes employing Ph_3PCBr_2, with or without zinc,[17] gave inconsistent results, particularly on subdecigram scales. These difficulties were overcome by utilizing freshly sublimed carbon tetrabromide and recrystallized Ph_3P. An improved technique for small-scale reactions required the

(8) Schregenberger, C.; Seebach, D. S. *Tetrahedron Lett.* **1984**, *25*, 5881.

(9) (a) Grove, J. F.; Speake, R. N.; Ward, G. *J. Chem. Soc. C* **1966**, 230. (b) MacMillan, J.; Simpson, T. J. *J. Chem. Soc., Perkin Trans. 1* **1973**, 1487. (c) Amstutz, R.; Hungerbühler, E.; Seebach, D. *Helv. Chim. Acta* **1981**, *64*, 1796. (d) Seidel, W.; Seebach, D. *Tetrahedron Lett.* **1982**, *23*, 159.

(10) (a) Toshima, K.; Tatsuta, K.; Kinoshita, M. *Bull. Chem. Soc. Jpn.* **1988**, *61*, 2369. (b) See ref. 10a. (c) Nakata, M.; Takao, H.; Ikeyama, Y.; Sakai, T. *Bull. Chem. Soc. Jpn.* **1981**, *54*, 1749.

(11) (a) Seebach, D.; Chow, H.-F.; Jackson, R. F. W.; Lawson, K.; Sutter, M. A.; Thaisrivongs, S.; Zimmerman, J. *J. Am. Chem. Soc.* **1985**, *107*, 5292. (b) Seebach, D.; Chow, H.-F.; Jackson, R. F. W.; Sutter, M. A.; Thaisrivongs, S.; Zimmerman J. *Liebigs Ann. Chem.* **1986**, 1281.

(12) For other synthetic studies, see: (a) Sutter, M. A.; Seebach, D. *Liebigs Ann. Chem.* **1983**, 939. (b) Wakamatsu, T.; Nakamura, H.; Nara, E.; Ban, Y. *Tetrahedron Lett.* **1986**, *27*, 3895. (c) Wakamatsu, T.; Yamada, S.; Nakamura, H.; Ban, Y. *Heterocycles* **1987**, *25*, 42. (d) For a formal total synthesis of elaiophylin, see: Nakamura, H.; Arata, K.; Wakamatsu, T.; Ban, Y.; Shibasaki, M. *Chem. Pharm. Bull.* **1990**, *38*, 2435.

(13) Ziegler, F. E.; Cain, W. T.; Kneisley, A., Stirchak, E. P.; Wester, R. T. *J. Am. Chem. Soc.* **1988**, *110*, 5442.

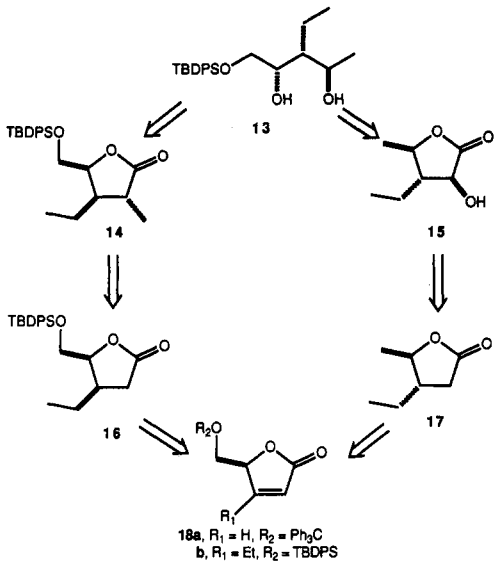
(14) Ziegler, F. E.; Cain, W. T. *J. Org. Chem.*, **1989**, *54*, 3347.

(15) Ziegler, F. E.; Kneisley, A.; Thottathil, J. K.; Wester, R. T. *J. Am. Chem. Soc.*, **1988**, *110*, 5434.

(16) Omura, K.; Swern, D. *Tetrahedron* **1978**, *34*, 1651.

(17) Corey, E. J.; Fuchs, P. L. *Tetrahedron Lett.* **1972**, 3769.

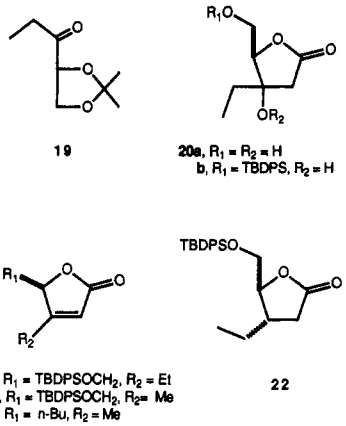
Scheme II



preparation of a standard solution of Ph_3PCBr_2 on a larger scale followed by the volumetric use of aliquots of this solution. Using this technique, dibromo olefin **10c**, which displayed a vinyl proton at δ 6.29 (J = 8.4 Hz), was realized in 79% yield. A one-pot conversion of dibromide **10c** to the (trimethylsilyl)acetylene with *n*-BuLi followed by treatment of the intermediate lithium acetylide with TMSCl did not prove to be as efficient as the stepwise process (77% yield).

Selective oxidative cleavage of the double bond in the acetylene **10e** was achieved with 1.05 equiv of a standard 0.022 M solution of ozone in CH_2Cl_2 followed by reduction of the crude ozonides with $LiAlH_4$ to provide alcohol **11a** in 72% yield. Subsequent tosylation of the alcohol and displacement of the tosylate with NaCN in dimethyl sulfoxide gave rise to nitrile **11c**. This substance was readily converted into the lactone **12** by treatment with *p*-TsOH (2 equiv) in methanol at 50 °C. The excess acid was necessary to neutralize ammonia, and the controlled temperature inhibited the removal of the trimethylsilyl group. The alcohol function of lactone **12** was readily protected as its TBDMS derivative. With fragment **5** in hand, attention was turned to the preparation of fragment **6**.

Two pathways for the synthesis of diol **13** (Scheme II), which represents an obvious precursor for the aldehydes **6**, employ butyrolactones as intermediates. $LiAlH_4$ reduction of α-hydroxy lactone **15** would give rise to the triol precursor of **13**. Lactone **17**, itself prepared via lithium diethylcuprate addition[18] to butenolide **18a**,[19,20] could serve as the precursor of **15** via α-hydroxylation. In this analysis, the vicinal oxygens of **13** arise from the lactone carbonyl and the hydroxyl group. This strategy led successfully to the trans-substituted lactone **17**; however, the hydroxylation protocol of Hanessian proved ineffective in our hands.[21] Alternatively, lactone **14** can serve as a precursor of **13**, by effecting a formal Baeyer–Villiger oxidation of the lactone carbonyl of this substrate. Thus, alkylation of **16**, accessible by reduction of **18b**, would be expected to be highly stereoselective owing to the cis arrangement of the substituents in lactone **16**. Ethyl ketone **19** has been prepared by Anthonsen[22] by the addition of ethyl magnesium bromide followed by oxidation with RuO_2/KIO_4. Under these conditions oxidation was found to be incomplete after 3 days. Mori[23] was able to prepare the methyl ketone analogue of ketone **19** by oxidation with PCC. This procedure gave incomplete oxidation; however, the use of molecular sieves (3 Å) with the PCC gave complete oxidation within 3 h.[24]

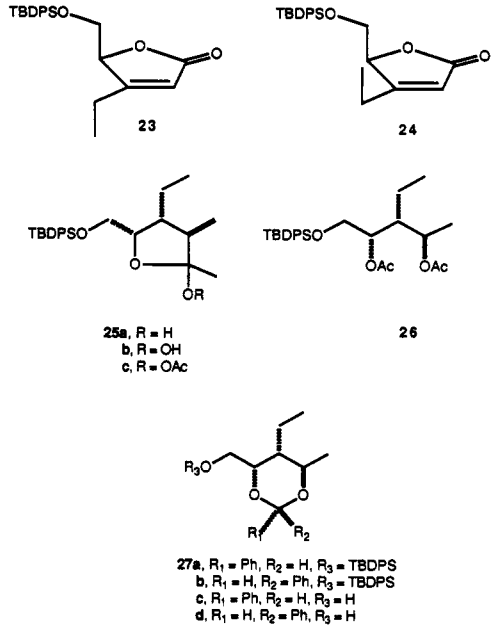


Addition of lithio-*tert*-butyl acetate to ethyl ketone **19** followed by acetonide cleavage and lactonization of the diastereomeric adducts with *p*-TsOH/MeOH afforded a mixture of lactones **20a** that was obtained in 62% yield. Selective silylation of the primary hydroxyl group followed by dehydration with $MsCl/Et_3N$ gave rise to butenolide **21a**.

Hanessian has reported[25] that butenolide **21b** undergoes hydrogenation with Rh/Al_2O_3 to give the cis-substituted butenolide. Similarly, Jefford[26] has examined both the heterogeneous and homogeneous hydrogenation and hydride reduction of butenolide **21c**. In this study, a variety of catalysts gave cis/trans ratios ranging from 2.1/1 to 9/1. Catalytic hydrogenation of butenolide **21a** over Pd/C, Ni(R), or Rh/Al_2O_3 gave a 2/1 ratio (**22**/**16**) in which the trans isomer dominated over the cis isomer. This result suggests that, at least in the case of catalytic hydrogenation, the more stable anti conformer **23** of butenolide **21a** inhibits α-face addition of hydrogen whereas the syn conformer **24**, which is ostensibly in lower concentration, exhibits a syn pentane interaction when absorption occurs on the α-face. This change in stereochemistry when an ethyl group is substituted for a methyl group is reminiscent of the alkylation studies conducted by Koga and Tomioka,[27] and Takahashi.[28] This undesirable result was

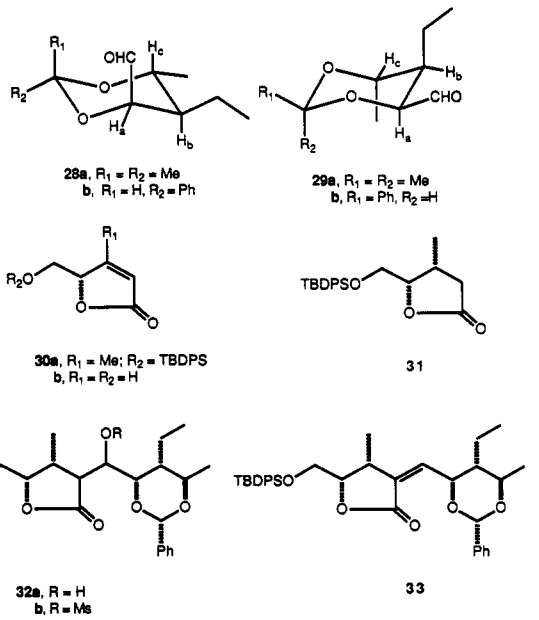
(18) Vigneron, J. P.; Méric, R.; Dhaenens, M. *Tetrahedron Lett.* **1980**, *21*, 2057.
(19) (a) Ireland, R. E.; Anderson, R. C.; Badooud, R.; Fitzsimmons, B. S.; McGarvey, G. S.; Thaisrivongs, S.; Wilcox, C. S. *J. Am. Chem. Soc.* **1983**, *105*, 1988. (b) Champs, P.; Cardellach, J.; Font, J.; Ortuno, R. M.; Ponsati, O. *Tetrahedron* **1982**, *15*, 2395; Champs, P.; Font, J.; Ponsati, O. *Tetrahedron Lett.* **1981**, *22*, 1447. (c) For other routes to butenolide **18a**, see: Taniguchi, M.; Koga, K.; Yamada, S. *Tetrahedron* **1974**, *30*, 3547. Tomioka, K.; Ishiguro, T.; Koga, K. *J. Chem. Soc., Chem. Commun.* **1979**, 652. Mann, J.; Thomas, A. *J. Chem. Soc., Chem. Commun.* **1985**, 737.
(20) The racemization of butenolides using the Font procedure is a concern. See, Okabe, M.; Sun, R.-C.; Tam, S.; Todaro, L. J.; Coffen, D. *J. Org. Chem.* **1988**, *53*, 4780.
(21) (a) Hanessian, S.; Sahoo, S. P.; Murray, P. J.; *Tetrahedron Lett.* **1985**, *26*, 5631. (b) Vedejs, E.; Engler, D. A.; Telschow, J. E. *J. Org. Chem.* **1978**, *43*, 188.
(22) Hagen, S.; Lwande, W.; Kilaas, L.; Anthonsen, T. *Tetrahedron* **1980**, *36*, 3101.
(23) Mori, K. *Tetrahedron* **1976**, *32*, 1979.
(24) Herscovici, J.; Egron, M.-J.; Antonakis, K. *J. Chem. Soc., Perkin Trans. 1* **1982**, 1967.
(25) Hanessian, S.; Murray, P. S. *Tetrahedron* **1987**, *43*, 5055.
(26) Jefford, C. W.; Sledeski, P. W.; Boukouvalas, J. *Helv. Chim. Acta* **1989**, *72*, 1362.
(27) (a) Tomioka, K.; Kawasaki, H.; Yasuda, K.; Koga, K. *J. Am. Chem. Soc.* **1988**, *110*, 3597. (b) Tomioka, K.; Yasuda, K.; Kawasaki, H.; Koga, K. *Tetrahedron Lett.* **1986**, *27*, 3247.

ameliorated by reduction of butenolide **21a** with "CuH" (from Red-Al (Aldrich) and cuprous iodide),[29] which provided a separable 6/1 ratio of the cis and trans isomers (**16**/**22**). Although the reagent $[(Ph_3P)CuH]_6$ gave a 9/1 ratio of the two lactones, the observation that the reaction never went to completion, the relative difficulty of the reagent's preparation, and its sensitivity to air precluded its use.[30] Alkylation of **16** with LDA/MeI provided lactone **14** in 90% yield as a single isomer.



The formal Baeyer–Villiger reaction on lactone **14** was accomplished by the same sequence of reactions that had been employed in the preparation of lactone **8**.[14] Thus, treatment of lactone **14** with MeLi provided a mixture of hemiketals **25a** that was transformed into the hydroperoxides **25b** by exposure to H_2O_2/HOAc without epimerization at the stereogenic methyl center. Acetylation of this mixture afforded the acetylhydroperoxides **25c**, which were reluctant to undergo rearrangement in refluxing CH_2Cl_2. However, when the acetylhydroperoxides were heated in refluxing toluene, rearrangement occurred to provide a mixture of monoacetates that were reacetylated to facilitate isolation and characterization. Reductive removal of the acetate groups of **26** with DIBAL afforded the desired diol **13**.

To create useful electrophilic species from diol **13**, the hydroxyl functions were protected as their acetonide and the silyl group was removed with TBAF to afford the primary alcohol. The hydroxyl group could be activated as its mesylate or tosylate or could be oxidized under Swern conditions to provide aldehyde **6a**. None of these species proved to be effective electrophiles when they were added to the LDA-generated lactone enolate of **5**. The preferred conformation of the aldehyde **6a** is represented by **28a**, which has the secondary methyl and ethyl groups equatorial and the aldehyde group axial, buttressed against one of the methyls of the acetonide. This conclusion is based upon an NOE observed for the methine proton H_a when the proton H_b is irradiated; no enhancement of the proton H_c is observed. For the other chair conformation **29a** to be operative, the enhancement of H_a and H_c would be expected upon irradiation of H_b. The buttressing effect was considered the downfall of aldehyde **6a** as an electrophile. To alleviate this problem, the diol **13** was converted to a 3/2 mixture (**27a**/**27b**) of benzylidene derivatives, which were separated by chromatography. The major silyl ether afforded aldehyde **6b** (**29b**) and the minor isomer provided **6c** (**28b**) upon desilylation and oxidation. The appearance of H_c in **29b** as a quartet (J_{bc} = 7.1 Hz) suggested a smaller dihedral between H_b and H_c than in **28b** where J_{bc} = 10.3 Hz.



The condensation between the enolate of lactone **5** with aldehyde **6b**, where the aldehyde group is equatorial, was more effective than with aldehyde **6c**. However, owing to the scarcity of the two substrates, the simpler lactone **31**, which bears the same cis stereochemistry about the lactone ring as does **5**, was employed in condensation studies. Lactone **31** was prepared from D-ribonic acid γ-lactone by modification of literature techniques. D-Ribonic acid γ-lactone was converted to butenolide **30b** as described by Font[19b] without prior protection of the primary hydroxyl group. Subsequent silylation, conversion to the β-methyl isomer, and hydrogenation over Rh/Al_2O_3 gave the cis lactone **31**.[25] The enantiomeric integrity of lactone **31** was confirmed by desilylation and conversion to its Mosher ester.[31]

Condensation of the lactone enolate of **31** with aldehyde **6b** gave a mixture of β-hydroxy lactones **32a** from which a single diastereomer could be isolated. Although the stereochemistry could not, and need not, be determined because subsequent operations would remove the newly introduced centers of asymmetry, the newly created center adjacent to the lactone carbonyl was assumed to be trans to the vicinal methyl group based upon the observed, highly selective alkylation of lactone **16**. When the crude β-hydroxy lactones **32a** were converted to their mesylates **32b** ($MsCl/Et_3N$) and subjected to elimination (DBU/benzene), a mixture of unsaturated lactones was obtained that displayed vinyl signals at δ 6.65 and 6.13. However, when the major β-hydroxy lactone **32a**, which was obtained by chromatography, was dehydrated, only the unsaturated lactone having the signal at δ 6.13 was obtained. The

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(29) CuI was substituted for the prescribed CuBr: Masamune, S.; Bates, G. S.; Georgion, P. E. *J. Am. Chem. Soc.* **1974**, *96*, 3686.

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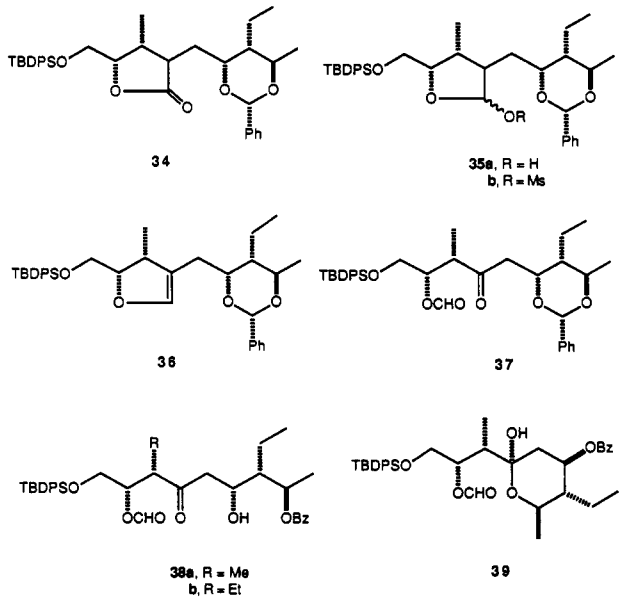
higher field signal is consistent with the *Z* configuration of the double bond because its *E* counterpart would be expected to be deshielded.[32]

Not only did the benzylidene protecting group of unsaturated lactone **33a** preclude the use of catalytic hydrogenation of the reduction of the double bond, but also the plan of Scheme I was dependent upon the use of acetylene **5**. Once again, the copper hydride reagent employed in the reduction of butenolide **21a** was successful in the reduction of unsaturated lactone **33a**. A single diastereomer was obtained that was believed to be the isomer having all lactone ring substituents cis to one another. The intermediate enolate from reduction would undergo protonation from the less hindered face of the lactone ring in accord with the behavior of similarly substituted lactones.[13,14] In addition, 1-(trimethylsilyl)-1-octyne was unreactive toward the reducing agent under the conditions employed for the reduction of the unsaturated lactone, ostensibly ensuring the viability of acetylene **5** in future operations.



The next objective of the study was to excise the lactone carbonyl and replace it with a ketone. This process was achieved by a sequence of reactions that was utilized in the preparation of the C_{19}–C chain of rifamycin S.[13] The lactone **34** was reduced with DIBAL at −78 °C to give a mixture of lactols **35a**, which was converted to their mesylates **35b** and then was subjected to elimination with Et_3N to afford the enol ether **36**. Because DIBAL reacts with trimethylsilyl acetylenes at elevated temperatures, the mild conditions for reduction of the lactone are expected to be compatible with the strategy of Scheme I.

Treatment of enol ether **36** with 1.05 equiv of O_3 followed by dimethyl sulfide workup gave the keto formate **37** in 90% yield. Clearly, the use of O_3 at this juncture is compatible with the presence of a trimethylsilyl acetylene as was demonstrated in the conversion of **10e** to **11a**. Unfortunately, the benzylidene protecting group could not be removed under hydrolytic conditions without the appearance of adverse side reactions. Elimination of the elements of formic acid from **37** occurred faster than hydrolysis of the benzylidene group. Oxidative cleavage using $Pd(OAc)_2$/*t*-BuOOH[33] gave a near-equal mixture of two products. One of these substances proved to be monobenzoate **38a** because its ^1H NMR spectrum was nearly identical with the spectrum of **38b**, which had been prepared from ethyl lactone **16** by the same route as **38a** and had been decoupled to determine the contiguity of the protons of C_1–C_3 and C_5–C_9. The ^1H NMR spectrum of **39** indicated the presence of the benzoate, formate, and silyloxy functional groups but a lack of signals for protons adjacent to a ketone. The lack of selectivity in this latter process would preclude its use in the general strategy. The success of this approach to elaiophylin will require a more labile protecting group for the diol functionality of **37**.

Experimental Section

All reactions were performed in flame-dried glassware under N_2 unless otherwise noted. Diethyl ether and THF were distilled from sodium benzophenone ketyl under N_2. Diisopropylamine, pyridine, toluene, hexane, CH_2Cl_2, Et_3N, *tert*-BuOH, hexamethylphosphoramide (HMPA), and dimethyl sulfoxide (DMSO) were distilled from CaH_2. Alkyllithiums were titrated by the method of Kofron.[34] Workup means drying organic extracts over anhydrous $MgSO_4$, filtration, and concentration in vacuo. ^1H NMR spectra were recorded at 250 MHz in $CDCl_3$.

6(*S*)-[1(*R*),4-Dimethyl-2(*E*)-pentenyl]-4(*R*)-[1(*R*)-methyl-2-formylethyl]-2,2,5(*S*)-trimethyl-1,3-dioxane (10b). To a solution of oxalyl chloride (0.059 mL, 0.71 mmol) in CH_2Cl_2 (2.0 mL) at −78 °C was added a solution of DMSO (0.052 mL, 0.73 mmol) in CH_2Cl_2 (2.0 mL), and the mixture was stirred for 2 min. A solution of alcohol **10a** (67 mg, 0.235 mmol) in CH_2Cl_2 (2.0 mL) was added, and the mixture was stirred at −78 °C for 15 min. Et_3N (0.030 mL, 0.216 mmol) was added to the solution, which was stirred at −78 °C for 15 min then warmed and maintained at 0 °C for 30 min. The reaction mixture was diluted with water and extracted with benzene/ether (4/1) and worked up. Chromatography (7% ethyl acetate/hexanes) yielded aldehyde **10b** (98%): ^1H NMR δ 9.68 (d, *J* = 3.0 Hz, 1 H, aldehyde), 5.42 (dd, *J* = 15.5, 6.3 Hz, 1 H, olefin), 5.27 (dd, *J* = 15.5, 7.9 Hz, 1 H, olefin), 3.89 (dd, *J* = 10.9, 4.0 Hz, 1 H), 3.08 (t, *J* = 6.6 Hz, 1 H), 2.43 (m, 1 H), 2.24 (m, 2 H), 1.80 (m, 1 H), 1.25 (s, 6 H), 1.02 (d, *J* = 7.0 Hz, 6 H), 0.92 (d, *J* = 8.3 Hz, 3 H), 0.90 (d, *J* = 8.3 Hz, 3 H), 0.83 (d, *J* = 8.3 Hz, 3 H); IR ($CHCl_3$) 2966, 1726, 1457, 1380, 1219 cm^{-1}; $[\alpha]_D$ +27.02 (*c* = 0.935, $CHCl_3$); HRMS (CI, M + 1) calcd for $C_{17}H_{30}O_3$(H) 283.2274, found 283.2289.

4(*R*)-[3,3-Dibromo-1(*S*)-methyl-2-propenyl]-6(*S*)-[1-(*R*),4-dimethyl-2(*E*)-pentenyl]-2,2,5(*S*)-trimethyl-1,3-dioxane (10c). To a solution of CBr_4 (sublimed, 0.56 g, 1.50 mmol) in CH_2Cl_2 (20 mL) at 0 °C was added Ph_3P (recrystallized, 0.89 g, 3.00 mmol), and the mixture was stirred for 30 min. An aliquot of the dibromomethylene triphenylphosphorane (8 mL) was added to a 0 °C solution of aldehyde **10b** (66 mg, 0.233 mmol) in CH_2Cl_2 (20 mL). After the mixture was stirred for 20 min, it was diluted with hexanes and passed through silica gel (7% ether/hexanes). Concentration in vacuo yielded the crude dibromo olefin **10c** (72.5 mg, 79% yield), which was used without further purification: ^1H NMR δ 6.29 (d, *J* = 8.4 Hz, 1 H, bromo olefin), 5.42 (dd, *J* = 15.5, 6.2 Hz, 1 H, olefin), 5.28 (dd, *J* = 15.6, 7.8 Hz, 1 H, olefin), 3.53 (dd, *J* = 9.2, 4.2 Hz, 1 H), 3.04 (t, *J* = 6.7 Hz, 1 H), 2.50 (m, 1 H), 2.20 (m, 2 H), 1.78 (m, 1 H), 1.26 (s, 6 H), 0.98 (d, *J* = 6.7 Hz, 3 H), 0.95 (d, *J* = 6.6 Hz, 6 H), 0.93 (d, *J* = 6.8 Hz, 3 H), 0.82 (d, *J* = 6.7 Hz, 3 H); IR ($CHCl_3$) 2964, 2873, 1457, 1379, 1217 cm^{-1}; $[\alpha]_D$ +33.16 (*c* = 1.0, $CHCl_3$); HRMS (CI, M + 1) calcd for $C_{18}H_{30}O_2Br_2$(H) 439.0671, found 439.0671.

6(*S*)-[1(*R*),4-Dimethyl-2(*E*)-pentenyl]-4(*R*)-[1(*S*)-methyl-2-propynyl]-2,2,5(*S*)-trimethyl-1,3-dioxane (10d). To a solution of dibromo olefin **10c** (73 mg, 0.166 mmol) in THF (2 mL) at −78 °C was added *n*-BuLi (1.43 M, 0.52 mL); the mixture was maintained at this temperature for 30 min. The reaction mixture was poured into water and then extracted with ether and worked up to yield crude acetylene **10d** (47 mg), which was used

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without further purification: ^{1}H NMR δ 5.40 (dd, J = 15.5, 6.3 Hz, 1 H, olefin), 5.28 (dd, J = 15.6, 7.5 Hz, 1 H, olefin), 3.57 (dd, J = 10.4, 3.9 Hz, 1 H), 3.03 (t, J = 6.6 Hz, 1 H), 2.50 (m, 1 H), 2.20 (m, 2 H), 2.02 (d, J = 2.3 Hz, 1 H, acetylene), 1.78 (m, 1 H), 1.34 (s, 3 H), 1.32 (s, 3 H), 1.09 (d, J = 7.0 Hz, 3 H), 0.99 (d, J = 7.0 Hz, 3 H), 0.94 (d, J = 6.7 Hz, 6 H), 0.79 (d, J = 7.0 Hz, 3 H); IR ($CHCl_3$) 3309, 2964, 2112, 1457, 1379 cm^{-1}; $[\alpha]_D$ +65.45 (c = 0.83, $CHCl_3$); HRMS (CI, M + 1) calcd for $C_{18}H_{30}O_2$(H) 279.2325, found 279.2335.

6(*S*)-[1(*R*),4-Dimethyl-2(*E*)-pentenyl]-4(*R*)-[1(*S*)-methyl-3-(trimethylsilyl)-2-propynyl]-2,2,5(*S*)-trimethyl-1,3-dioxane (10e). To a solution of acetylene **10d** (41 mg, 0.145 mmol) in THF (2 mL) at −78 °C was added n-BuLi (1.6 M, 0.58 mmol), and the mixture was stirred for 1 h. Chlorotrimethysilane (0.10 mL, 0.725 mmol) was added, and the mixture was stirred for an additional 1 h at −78 °C. The reaction mixture was poured into water, extracted with ether, and worked up. Chromatography (5% ether/hexanes) yielded the desired TMS–acetylene **10e** (77% yield): ^{1}H NMR δ 5.39 (dd, J = 15.5, 6.4 Hz, 1 H, olefin), 5.28 (dd, J = 16.0, 7.5 Hz, 1 H, olefin), 3.57 (dd, J = 10.6, 4.0 Hz, 1 H), 3.02 (t, J = 6.6 Hz, 1 H), 2.48 (m, 1 H), 2.20 (m, 2 H), 1.76 (m, 1 H), 1.35 (s, 6 H), 1.06 (d, J = 6.8 Hz, 3 H), 0.99 (d, J = 6.8 Hz, 3 H), 0.92 (d, J = 6.8 Hz, 6 H), 0.77 (d, J = 6.7 Hz, 3 H), 0.08 (s, 9 H, $RSiMe_3$); IR ($CHCl_3$) 2964, 2167, 1460, 1380 cm^{-1}; $[\alpha]_D$ +58.71 (c = 0.78, $CHCl_3$); HRMS (CI, M + 1) calcd for $C_{21}H_{38}O_2Si$(H) 351.2721, found 351.2725.

4(*S*)-[1(*R*)-Methyl-2-hydroxyethyl]-6(*S*)-[1(*S*)-methyl-3-(trimethylsilyl)-2-propynyl]-2,2,5(*R*)-trimethyl-1,3-dioxane (11a). A saturated solution of ozone (0.022 M) in CH_2Cl_2 at −78 °C was prepared by bubbling ozone through 125 mL of CH_2Cl_2 under the following conditions: 1 h, 7.5 L/min O_2, 110 V, 220 W, −78 °C, $NaHCO_3$ (0.5 g). An aliquot of this solution of ozone (6.3 mL, 0.14 mmol) was added in a precooled syringe to the TMS–acetylene **10e** (42.7 mg, 0.132 mmol) in 3 mL MeOH/CH_2Cl_2 (1/1, −78 °C, $NaHCO_3$). After 10 min, the reaction mixture was filtered through Celite and evaporated in vacuo, and the residue was dissolved in ether (2 mL) and cooled to −78 °C. $LiAlH_4$ (24.0 mg, 0.620 mmol) was added to the solution, and the mixture was stirred for 1 h at −78 °C and then warmed to room temperature and stirred for 3 h. The reaction mixture was quenched with water/5% aqueous NaOH/water, and then dried over $MgSO_4$. Evaporation followed by chromatography (15% ethyl acetate/hexanes) yielded the desired alcohol **11a** (91% yield): ^{1}H NMR δ 3.65 (m, 2 H, RCH_2OH), 5.98 (m, 1 H) 3.51 (dd, J = 7.2, 2.8 Hz, 1 H), 2.50 (m, 1 H), 2.35 (t, 1 H, OH), 1.86 (m, 2 H), 1.36 (s, 3 H), 1.39 (s, 3 H), 1.10 (d, J = 6.9 Hz, 3 H), 0.95 (d, J = 7.1 Hz, 3 H), 0.83 (d, J = 6.7 Hz, 3 H), 0.10 (s, 9 H, $RSiMe_3$); IR ($CHCl_3$) 3507, 2967, 2167, 1459, 1382 cm^{-1}; $[\alpha]_D$ +11.58 (c = 0.71, $CHCl_3$); HRMS (CI, M + 1) calcd for $C_{17}H_{32}O_3Si$(H) 313.2200, found 313.2214.

4(*S*)-[1(*R*)-Methyl-2-cyanoethyl]-6(*S*)-[1(*S*)-methyl-3-(trimethylsilyl)-2-propynyl]-2,2,5(*R*)-trimethyl-1,3-dioxane (11c). To a solution of alcohol **11a** (37.9 mg, 0.121 mmol) in pyridine (10 mL) at 0 °C was added p-TsCl (0.23 g, 1.21 mmol), and the mixture was stirred for 1 h. The reaction mixture was warmed to room temperature and was stirred 8 h. The reaction mixture was diluted with ether and extracted with a 0 °C solution of 1% aqueous HCl, aqueous $NaHCO_3$, and brine. Workup yielded the crude tosylate **11b**, which was used without further purification. ^{1}H NMR (partial) δ 7.30–7.93 (m, 4 H), 2.43 (s, 3 H). Sodium cyanide (55.5 mg, 1.13 mmol) was added to a solution of crude tosylate **10b** in DMSO (20 mL), and the mixture was stirred for 12 h. The reaction mixture was diluted with water and extracted with ether. Workup followed by chromatography (7% ether/hexanes) yielded nitrile **11c** (75% yield): ^{1}H NMR δ 3.55 (dd, J = 10.8, 4.6 Hz, 1 H), 3.32 (dd, J = 7.5, 3.3 Hz, 1 H), 2.40 (m, 3 H), 1.99 (m, 1 H), 1.81 (m, 1 H), 1.36 (s, 3 H), 1.34 (s, 3 H), 1.20 (d, J = 7.0 Hz, 3 H), 1.13 (d, J = 7.0 Hz, 3 H), 0.87 (d, J = 7.0 Hz, 3 H), 0.13 (s, 9 H); IR ($CHCl_3$) 2985, 2246, 2168, 1457, 1379 cm^{-1}; $[\alpha]_D$ +4.21 (c = 0.24, $CHCl_3$); HRMS (CI, M + 1) calcd for $C_{18}H_{31}O_2NSi$(H) 322.2204, found 322.2195. Anal. Calcd for $C_{18}H_{31}O_2NSi$: C, 67.23; H, 9.72. Found: C, 66.40; H, 9.69.

5(*S*)-[1(*R*),3(*S*)-Dimethyl-2(*S*)-hydroxy-5-[(trimethylsilyl)oxy]-4-pentynyl]-4(*R*)-methyl-2(3*H*)-furanone (12). A solution of nitrile **11c** (38.6 mg, 0.12 mmol) in MeOH (14 mL) containing p-TsOH (46.0 mg, 0.24 mmol) was heated to 50 °C for 18 h, at which time the reaction mixture was poured into water, extracted with ether, and worked up. Chromatography (50% ether/hexanes) gave lactone **12** (70% yield): ^{1}H NMR δ 4.60 (dd, J = 10.2, 4.3 Hz, 1 H, C_5-H), 3.78 (m, 1 H, RCH_2OH), 2.75 (dd, J = 16.0, 7.3 Hz, 1 H), 2.60 (m, 1 H), 2.53 (m, 1 H), 2.28 (d, J = 7.3 Hz, 1 H, OH), 2.19 (d, J = 16.0 Hz, 1 H), 1.89 (m, 1 H), 1.13 (d, J = 7.0 Hz, 3 H), 0.97 (d, J = 7.0 Hz, 3 H), 0.85 (d, J = 7.0 Hz, 3 H), 0.13 (s, 9 H, $RSiMe_3$); IR ($CHCl_3$) 3563, 2978, 2161, 1774 cm^{-1}; $[\alpha]_D$ +87.60 (c = 1.17, $CHCl_3$); HRMS (CI, M + 1) calcd for $C_{15}H_{26}O_3Si$(H) 283.1730, found 283.1739.

5(*S*)-[1(*R*),3(*S*)-Dimethyl-2(*S*)-[(*tert*-butyldimethylsilyl)oxy]-5-[(trimethylsilyl)oxy]-4-pentynyl]-4(*R*)-methyl-2(3*H*)-furanone (5). To a solution of lactone **12** (20.5 mg, 0.073 mmol) in CH_2Cl_2 (5 mL) at 0 °C was added Et_3N (0.071 mL, 0.51 mmol) followed by TBDMSOTf (0.058 mL, 0.254 mmol). The reaction mixture was stirred and maintained at 0 °C for 2 h, at which time the mixture was poured into water and extracted with ether. Workup followed by chromaography (30% ether/hexanes) yielded the desired silyl ether **5** (71%): ^{1}H NMR δ 4.17 (dd, J = 11.0, 4.4 Hz, 1 H, C_5-H), 4.35 (dd, J = 6.1, 1.2 Hz, 1 H, $RCHOSiR_3$), 2.71 (dd, J = 16.8, 7.2 Hz, 1 H), 2.58 (m, 1 H), 2.52 (m, 1 H), 2.19 (d, J = 16.8 Hz, 1 H), 2.03 (m, 1 H), 1.16 (d, J = 7.0 Hz, 3 H), 0.96 (d, J = 7.0 Hz, 3 H), 0.89 (s, 9 H), 0.86 (d, J = 7.0 Hz, 3 H), 0.13 (s, 3 H), 0.11 (s, 9 H) 0.05 (s, 3 H); IR ($CHCl_3$) 3021, 2950, 2161, 1774, 1252, 1161 cm^{-1}; $[\alpha]_D$ +26.79 (c = 0.59, $CHCl_3$); HRMS (CI, M + 1) calcd for $C_{21}H_{40}O_3Si_2$(H) 397.2595, found 397.2596.

4-Ethyl-5(*R*)-[[(*tert*-butyldiphenylsilyl)oxy]methyl]-2-(3*H*)-furanone (21a). To a solution of i-Pr_2NEt (3.74 g, 37.0 mmol) in THF (25 mL) at 0 °C was added n-BuLi (36.0 mmol, 1.4 M). After 30 min, the solution was cooled to −78 °C, *tert*-butyl acetate (4.40 g, 37.0 mmol) was added dropwise, and the mixture was stirred and maintained at −78 °C for 30 min. A solution of ketone **19** (3.75 g, 23.0 mmol), in THF (7 mL) was added dropwise to the enolate, and the mixture was stirred for an additional 30 min. The reaction mixture was poured into aqueous NH_4Cl and was extracted with ethyl acetate. Workup and chromatography (20% ethyl acetate/hexanes) yielded the β-hydroxy ester as a mixture of diastereomers (96% yield). Major diastereomer: ^{1}H NMR δ 4.15 (t, J = 6.7 Hz, 1 H), 4.00 (m, 1 H), 3.80 (m, 1 H), 3.69 (s, 1 H, OH), 2.53 (d, J = 14.5 Hz, 2 H), 2.32 (d, J = 14.5 Hz, 1 H), 1.49 (s, 9 H, *tert*-butyl H), 1.45 (s, 3 H), 0.95 (t, 3 H), 0.095 (t, 3 H).

A solution of the *tert*-butyl esters (6.31 g, 23.0 mmol) and p-TsOH (0.22 g, 0.01 mmol) in THF (20 mL, 5% H_2O) was stirred at 50 °C for 2 h. The solvent was removed under vacuum, and the residue was chromatographed (ethyl acetate) to yield lactone **20a** as a mixture of diastereomers (75% yield). Major diastereomer: ^{1}H NMR δ 4.35 (t, J = 2.1 Hz, 1 H), 3.90 (m, 1 H, RCH_2OH), 3.76 (m, 1 H, RCH_2OH), 2.73 (d, J = 17.5 Hz, C_3-H), 2.63 (d, J = 3.0 Hz, OH, 1 H), 2.63 (bs, OH, 1 H), 2.42 (d, J = 17.5 Hz, 1 H, C_3-H), 1.80 (m, 2 H), 1.00 (t, 3 H); IR ($CHCl_3$) 3436, 1781, 1731 cm^{-1}.

A solution of the diols **20a** (2.75 g, 17.0 mmol), imidazole (1.28 g, 19 mmol), and t-$BuPh_2SiCl$ (4.90 mL, 19 mmol) in DMF (40 mL) was stirred at room temperature for 10 h. The reaction mixture was diluted with ethyl acetate, washed with 5% aqueous HCl, and saturated aqueous $NaHCO_3$. Workup and chromatography (50% ethyl acetate/hexanes) yielded the protected primary alcohol as a mixture of diastereomers **20b** (8/1, 64% yield). Major diastereomer: ^{1}H NMR δ 7.35–7.68 (m, 10 H), 4.29 (t, J = 2.0 Hz, 1 H), 3.85 (dd, J = 12.2, 3.1 Hz, 2 H), 3.73 (dd, J = 12.2, 3.1 Hz, 2 H), 2.83 (d, J = 17.2 Hz, 1 H), 2.46 (d, J = 17.2 Hz, 1 H), 1.84 (m, 2 H), 1.04 (t, 3 H), 1.01 (s, 9 H). Minor diastereomer: ^{1}H NMR δ 7.35–7.68 (m, 10 H), 4.20 (t, J = 2.0 Hz, 1 H), 4.02 (d, J = 1.9 Hz, 2 H), 2.74 (d, J = 18.0 Hz, 1 H), 2.62 (d, J = 18.0 Hz, 1 H), 1.73 (m, 2 H), 1.05 (s, 9 H), 1.00 (t, J = 7.2 Hz, 3 H); IR ($CHCl_3$) 3476, 2936, 2859, 1795 cm^{-1}.

To a solution of tertiary alcohols **20b** (4.39 g, 11.0 mmol) in CH_2Cl_2 (20 mL) at −10 °C was added Et_3N (3.21 mL, 22.0 mmol) followed by the dropwise addition of $MeSO_2Cl$ (1.70 mL, 22.0 mmol). The reaction mixture was maintained at −10 °C for 30 min, more Et_3N (12.23 mL, 88.0 mmol) was added, and the reaction mixture was heated at reflux at 40 °C for 1 h. The reaction mixture was diluted with CH_2Cl_2 and washed with 5% aqueous

HCl and saturated aqueous $NaHCO_3$. Workup and chromatography (30% ethyl acetate/hexanes) yielded butenolide **21a** (90% yield): ^1H NMR δ 7.35–7.68 (m, 10 H), 5.45 (s, 1 H), 4.86 (bs, 1 H), 3.98 (dd, J = 11.7, 3.3 Hz, 1 H), 3.83 (dd, J = 11.7, 3.3 Hz, 1 H), 2.32 (m, 2 H), 1.20 (t, J = 7.1 Hz, 3 H), 1.00 (s, 9 H); IR ($CHCl_3$) 2938, 1762, 1430, 1129 cm^{-1}; $[\alpha]_D$ -18.31 (c = 1.98, $CHCl_3$). Anal. Calcd for $C_{23}H_{28}O_3Si$ C, 72.59; H, 7.42. Found: C, 72.63; H, 7.42.

5(*S*)-[[(*tert*-Butyldiphenylsilyl)oxy]methyl]-4(*R*)-ethyldihydro-2(3*H*)-furanone (16). To a suspension of copper(I) iodide (15.09 g, 79 mmol) in THF (150 mL) at -10 °C was slowly added Red-Al (46.62 mL, 160 mmol, 3.43 M) via an addition funnel, and the mixture was maintained at this temperature for 30 min. The reaction mixture was cooled to -78 °C, and 2-butanol (16.38 mL, 160 mmol) was added via an addition funnel followed by butenolide **21a** (3.77 g, 9.9 mmol) in 20 mL of THF. The mixture was stirred for 1 h at -78 °C and then -20 °C for 1 h. The reaction mixture was quenched with saturated aqueous NH_4Cl, extracted with ethyl acetate, and then backwashed with saturated aqueous NH_4Cl. Workup and chromatography (MPLC, 18% ethyl acetate/hexanes) yielded lactone **16** (64% yield): ^1H NMR δ 7.35–7.68 (m, 10 H), 4.47 (m, 1 H), 3.87 (dd, J = 12.5, 3.7 Hz, 1 H), 3.73 (dd, J = 12.5, 3.7 Hz, 1 H), 2.56 (m, 3 H), 1.64 (m, 2 H), 1.03 (s, 9 H), 0.97 (t, J = 7.4 Hz, 3 H); IR ($CHCl_3$) 2964, 2859, 1788, 1425, cm^{-1}; $[\alpha]_D$ +32.61 (c = 1.06, $CHCl_3$); HRMS (CI, M + 1) calcd for $C_{23}H_{30}O_3Si(H)$ 383.2043, found 383.2047.

5(*S*)-[[(*tert*-Butyldiphenylsilyl)oxy]methyl]-4(*R*)-ethyl-3(*R*)-methyldihydro-2(3*H*)-furanone (14). To a solution of i-Pr_2NEt (1.14 mL, 8.1 mmol) in THF (25 mL) at 0 °C was added n-BuLi (4.9 mL, 7.8 mmol, 1.6 M). After 30 min at 0 °C the LDA solution was cooled to -78 °C and lactone **16** (2.39 g, 6.2 mmol) in THF (5 mL) was added. The reaction mixture was stirred and maintained at -78 °C for 30 min, at which time HMPA (1.09 mL, 6.2 mmol) and MeI (0.39 mL, 37 mmol) were added successively. After 30 min, the reaction mixture was poured into saturated aqueous NH_4Cl and extracted with ether. Workup followed by chromatography (10% ethyl acetate/hexanes) yielded lactone **14** (95% yield): ^1H NMR δ 7.35–7.68 (m, 10 H), 4.45 (dt, J = 2.5, 8.2 Hz, 1 H), 3.87 (dd, J = 12.1, 3.3 Hz, 1 H), 3.63 (dd, J = 12.1, 3.3 Hz, 1 H), 2.65 (m, 1 H), 2.15 (m, 1 H), 1.70 (m, 2 H), 1.30 (d, J = 7.1 Hz, 3 H), 1.05 (s, 9 H), 1.00 (t, J = 8.1 Hz, 3 H); IR ($CHCl_3$) 2940, 1785, 1432, cm^{-1}; $[\alpha]_D$ +52.85 (c = 0.96, $CHCl_3$); HRMS (CI, M + 1) calcd for $C_{24}H_{32}O_3Si(H)$ 397.2200, found 397.2209.

1-[(*tert*-Butyldiphenylsilyl)oxy]-3(*R*)-ethyl-2(*S*),4(*R*)-diacetoxypentane (26). The conversion of lactone **14** was performed as previously described[13] except that rearrangement of the crude mixture of peroxyacetates was accomplished at reflux in wet toluene for 24 h. Acetylation (vide supra) yielded diacetate **26** (52%): ^1H NMR δ 7.35–7.68 (m, 10 H), 5.30 (dt, J = 7.0, 4.0 Hz, 1 H), 4.95 (pent, J = 6.3 Hz, 1 H), 3.72 (dd, J = 10.4, 6.7 Hz, 1 H), 3.60 (dd, J = 10.4, 6.7 Hz, 1 H), 1.97 (s, 3 H), 1.95 (s, 3 H), 1.73 (m, 1 H), 1.47 (m, 2 H), 1.20 (d, 3 H), 1.04 (s, 9 H), 0.89 (t, J = 7.4 Hz, 3 H).

5-[(*tert*-Butyldiphenylsilyl)oxy]-2(*R*),4(*S*)-dihydroxy-3(*R*)-ethylpentane (13). To a solution of diacetate **26** (0.146 g, 0.31 mmol) in CH_2Cl_2 (3 mL) at -78 °C was added DIBAL (1.23 mL, 1.24 mmol, 1.0 M), and the mixture was stirred at -78 °C for 1.5 h. The reaction mixture was quenched with methanol, poured into saturated aqueous sodium potassium tartrate, and stirred vigorously for 1 h. The reaction mixture was extracted with ether, worked up, and chromatographed (30% ethyl acetate/hexanes) to yield diol **13**: ^1H NMR δ 7.35–7.68 (m, 10 H), 4.13 (m, 1 H), 3.91 (q, J = 5.8 Hz, 1 H), 3.76 (dd, J = 8.3, 10.4 Hz, 1 H), 3.62 (dd, J = 4.2, 9.6 Hz, 1 H), 1.50 (m, 3 H), 1.21 (d, J = 7.4 Hz, 3 H), 1.05 (s, 9 H), 0.86 (t, J = 7.5 Hz, 3 H).

4(*S*)-[[(*tert*-Butyldiphenylsilyl)oxy]methyl]-2(*S*)-phenyl-5(*R*)-ethyl-6(*R*)-methyl-1,3-dioxane (27a) and 4(*R*)-[[(*tert*-Butyldiphenylsilyl)oxy]methyl]-2(*R*)-phenyl-5(*R*)-ethyl-6(*R*)-methyl-1,3-dioxane (27b). A solution of diol **16** (0.184 g, 0.476 mmol), benzaldehyde dimethyl acetal (0.092 mL, 0.619 mmol), and camphor sulfonic acid (10 mg) in Et_2O (5 mL) was stirred at room temperature overnight. The reaction mixture was poured into saturated aqueous $NaHCO_3$ and extracted with ether. Workup and chromatography (2% ethyl acetate/hexanes) yielded acetals **27a** (52%) [^1H NMR δ 7.28–7.75 (m, 15 H), 5.77 (s, 1 H), 4.33 (m, 2 H), 3.88 (dd, J = 10.4, 6.3 Hz, 1 H), 3.82 (dd, J = 10.4, 6.3 Hz, 1 H), 1.73 (m, 1 H), 1.50 (d, J = 4.0 Hz, 3 H), 1.28 (m, 2 H), 1.09 (s, 9 H), 0.97 (t, J = 7.3 Hz, 3 H); IR ($CHCl_3$) 3059, 2930, 1480, 1390 cm^{-1}; $[\alpha]_D$ +7.24 (c = 0.53, $CHCl_3$). Anal. Calcd for $C_{30}H_{38}O_3Si$: C, 75.90; H, 8.07. Found: C, 75.73; H, 8.12] and **27b** (31%) [^1H NMR δ 7.30–7.80 (m, 15 H), 5.97 (s, 1 H), 4.20 (m, 2 H), 4.01 (m, 2 H), 1.95 (m, 1 H), 1.50 (m, 2 H), 1.30 (d, J = 7.5 Hz, 3 H), 1.12 (s, 9 H), 0.90 (t, J = 7.4 Hz, 3 H); IR ($CHCl_3$) 3071, 2930, 1475, 1392 cm^{-1}; $[\alpha]_D$ +26.91 (c = 1.77, $CHCl_3$)].

5(*R*)-Ethyl-6(*R*)-methyl-2(*S*)-phenyl-1,3-dioxanemethanol (27c). A solution of silyl ether **27c** (0.30 g, 0.48 mmol) in THF (5 mL) and n-Bu_4NF (1.1 M in THF, 0.97 mL) was stirred at room temperature for 10 h. The reaction mixture was poured into water and extracted with ether. Workup and chromatography (35% ethyl acetate/hexanes) yielded alcohol **27c** (90% yield): ^1H NMR δ 7.30–7.50 (m, 5 H), 5.83 (s, 1 H), 4.33 (m, 2 H), 3.85 (dd, J = 8.5, 11.6 Hz, 1 H), 3.53 (dd, J = 3.2, 11.5 Hz, 1 H), 2.0 (bs, OH, 1 H), 1.82 (m, 1 H), 1.51 (d, J = 7.4 Hz, 3 H), 1.50 (m, 1 H), 1.12 (m, 1 H), 1.00 (t, J = 7.5 Hz, 3 H); IR ($CHCl_3$) 3479, 2964, 1457, 1379 cm^{-1}; HRMS (CI, M + 1) calcd for $C_{14}H_{20}O_3(H)$ 237.1491, found 237.1487.

5(*R*)-Ethyl-6(*R*)-methyl-2(*S*)-phenyl-1,3-dioxanecarboxaldehyde (6b). To a solution of oxalyl chloride (0.098 mL, 1.13 mmol) in CH_2Cl_2 (5 mL) at -78 °C was added DMSO (0.082 mL, 1.17 mmol), and the mixture was stirred for 3 min. Alcohol **27c** (88.9 mg, 37.6 mmol, in THF) was added, and the reaction mixture was maintained at -78 °C for 20 min, at which time Et_3N (0.256 mL, 1.88 mmol) was added and the mixture was stirred an additional 15 min. The reaction mixture was warmed to 0 °C and stirred for 30 min, poured into water, and extracted with ether. Workup and chromatography (35% ethyl acetate/hexanes) yielded aldehyde **6b** (90%): ^1H NMR δ 9.75 (s, 1 H), 7.30–7.55 (m, 5 H), 5.90 (s, 1 H), 4.58 (d, J = 2.1 Hz, 1 H), 4.36 (q, J = 7.1 Hz, 1 H), 1.93 (m, 2 H), 1.75 (m, 1 H), 1.52 (d, 3 H), 0.97 (t, J = 7.3 Hz, 3 H); IR ($CHCl_3$) 2964, 2880, 1739, 1457, 1380, 1147 cm^{-1}; $[\alpha]_D$ +74.52 (c = 1.52, $CHCl_3$); HRMS (CI, M + 1) calcd for $C_{14}H_{18}O_3(H)$ 235.1335, found 235.1338.

5(*S*)-[[(*tert*-Butyldiphenylsilyl)oxy]methyl]-3-[1-hydroxy-1-[4(*S*)-[5(*R*)-ethyl-6(*R*)-methyl-2(*S*)-phenyldioxanyl]]methyl]-4(*R*)-methyldihydro-2(3*H*)-furanone (32a). To a solution of i-Pr_2NEt (0.038 mL, 0.277 mmol) in THF (5 mL) at -78 °C was added n-BuLi (1.6 M, 0.16 mL, 0.26 mmol). The mixture was stirred at -78 °C for 30 min, at which time lactone **31** (0.102 g, 0.277 mmol) in 2 mL of THF was added to the solution of LDA. The mixture was stirred for 1 h at -78 °C. Aldehyde **6b** (43.3 mg, 0.184 mmol) in 2 mL THF was added, and the reaction mixture was stirred for an additional 1 h at -78 °C. The reaction mixture was poured into saturated aqueous NH_4Cl and was extracted with ether. Workup and chromatography (25% ethyl acetate/hexanes) yielded alcohol **32a** (62% yield): ^1H NMR ($CDCl_3$) (major isomer) δ 7.28–7.70 (m, 15 H), 5.79 (s, 1 H), 4.72 (dd, J = 1.0, 9.4 Hz, 1 H), 4.41 (m, 2 H), 3.78 (dd, J = 1.3, 8.3 Hz, 1 H), 3.85 (dd, J = 2.0, 10.4 Hz, 1 H), 3.69 (dd, J = 2.0, 10.4 Hz, 1 H), 3.12 (dd, J = 2.1, 11.7 Hz, 1 H), 2.78 (m, 1 H), 2.23 (d, J = 9.2 Hz, OH, 1 H), 1.80 (m, 2 H), 1.60 (d, 3 H), 1.45 (dt, J = 1.7, 10.0 Hz, 1 H), 1.25 (d, 3 H), 1.03 (t, J = 7.5 Hz, 3 H), 0.80 (s, 9 H); IR (CCl_4) (major isomer) 3800, 1731 cm^{-1}; $[\alpha]_D$ (major isomer) +76.52 (c = 1.25, $CHCl_3$); HRMS (CI, M + 1) calcd for $C_{36}H_{46}SiO_6(H)$ 603.3143, found 603.3147.

5(*S*)-[[(*tert*-Butyldiphenylsilyl)oxy]methyl]-3-[1-[(methanesulfonyl)oxy]-1-[4(*S*)-[5(*R*)-ethyl-6(*R*)-methyl-2(*S*)-phenyldioxanyl]]methyl]-4(*R*)-methyldihydro-2-(3*H*)-furanone (32b). To a solution of a mixture of major and minor alcohol **32a** (47.2 mg, 0.078 mmol) and Et_3N (0.022 mL, 0.156 mmol) in CH_2Cl_2 (5 mL) at -10 °C was added CH_3SO_2Cl (0.012 mL, 0.150 mmol). The reaction mixture was stirred at -10 °C for 15 min, at which time the addition of Et_3N and CH_3SO_2Cl was repeated. After being stirred for an additional 1 h, the reaction mixture was poured into water and extracted with ethyl acetate. Workup and chromatography (25% ethyl acetate/hexanes) yielded mesylates **32b** (52.1 mg, 0.076 mmol, 98% yield): ^1H NMR ($CDCl_3$) (major isomer) δ 7.20–7.60 (m, 15 H), 5.84 (s, 1 H), 5.08 (m, 2 H), 4.40 (m, 2 H), 3.80 (dd, J = 3.2, 11.7 Hz, 1 H), 3.80 (dd, J = 2.1, 11.7 Hz, 1 H), 3.29 (dd, J = 1.0, 10.4 Hz, 1 H), 3.06 (s, 3 H), 2.90 (m, 1 H), 1.90 (m, 1 H), 1.76 (m, 1 H), 1.57 (d, J = 6.3

Hz, 3 H), 1.37 (m, 1 H), 1.26 (d, J = 6.4 Hz, 3 H), 1.02 (t, J = 7.9 Hz, 3 H), 0.71 (s, 9 H); IR (CCl_4) (major isomer) 1767 cm^{-1}; $[\alpha]_D$ (major isomer) +44.92 (c = 1.00, $CHCl_3$).

(*Z*)-5(*S*)-[[(*tert*-Butyldiphenylsilyl)oxy]methyl]-3-[[4-(*S*)-[5(*R*)-ethyl-6(*R*)-methyl-2(*S*)-phenyldioxanyl]]-methylene]-4(*R*)-methyldihydro-2(3*H*)-furanone (33). A mixture of mesylate **32b** (52.1 mg, 0.076 mmol) and DBU (0.022 mL, 0.15 mmol) in benzene (5 mL) was stirred at room temperature for 12 h. The reaction mixture was poured into water and extracted with ethyl acetate. Workup and chromatography (35% ethyl acetate/hexanes) yielded unsaturated lactone **33** (98% yield): ^1H NMR δ 7.30–7.66 (m, 15 H), 6.13 (dd, J = 3.6, 6.2 Hz, 1 H), 5.84 (s, 1 H), 5.82 (bs, 1 H), 4.52 (dt, J = 1.7, 8.0 Hz, 1 H), 4.36 (dd, J = 6.3, 15.0 Hz, 1 H), 3.85 (dd, J = 4.2, 12.5 Hz, 1 H), 3.68 (dd, J = 2.0, 11.6 Hz, 1 H), 3.26 (m, 1 H), 1.97 (m, 1 H), 1.63 (d, J = 7.5 Hz, 3 H), 1.54 (m, 2 H), 1.30 (d, J = 7.5 Hz, 3 H), 0.97 (s, 9 H), 0.95 (t, J = 7.1 Hz, 3 H); IR (CCl_4) 1752 cm^{-1}; $[\alpha]_D$ +34.92 (c = 0.60, $CHCl_3$); HRMS (CI, M + 1) calcd for $C_{36}H_{44}SiO_5(H)$ 585.3038, found 585.3038.

5(*S*)-[[(*tert*-Butyldiphenylsilyl)oxy]methyl]-3-[1-[4-(*S*)-[5(*R*)-ethyl-6(*R*)-methyl-2(*S*)-phenyldioxanyl]]-methyl]-4(*R*)-methyldihydro-2(3*H*)-furanone (34). To a suspension of CuI (82 mg, 0.43 mmol) in THF (10 mL) at −10 °C was added Red-Al (vide supra) (0.25 mL, 0.85 mmol, 3.4 M in toluene), and the mixture was stirred at −10 °C for 30 min. The reaction mixture was cooled to −78 °C, and 2-butanol (0.088 mL, 0.96 mmol) was added followed by the addition of unsaturated lactone **33** (32.1 mg, 0.054 mmol, in THF). The mixture was stirred at −78 °C for 30 min and then −20 °C for 2 h. The mixture was treated with saturated aqueous NH_4Cl, extracted with ether, and backwashed with saturated aqueous NH_4Cl and brine. Workup and chromatography (25% ethyl acetate/hexanes) yielded lactone **34** (29.06 mg, 0.048 mmol): ^1H NMR δ 7.30–7.70 (m, 15 H), 5.80 (s, 1 H), 4.46 (q, J = 6.2 Hz, 1 H), 4.38 (q, J = 7.5 Hz, 1 H), 4.23 (dt, J = 2.9, 9.6 Hz, 1 H), 3.92 (dd, J = 4.6, 10.4 Hz, 1 H), 3.73 (dd, J = 4.6, 10.4 Hz, 1 H), 2.98 (m, 1 H), 2.69 (m, 1 H), 1.25 (m, 1 H), 1.50–2.00 (m, 4 H), 1.50 (d, J = 7.1 Hz, 3 H), 1.03 (s, 9 H), 0.98 (t, J = 7.6 Hz, 3 H), 0.85 (d, J = 7.1 Hz, 3 H); IR ($CHCl_3$) 1752 cm^{-1}; $[\alpha]_D$ +34.92 (c = 0.60, $CHCl_3$); HRMS (CI, M + 1) calcd for $C_{36}H_{46}SiO_5(H)$ 587.3194, found 587.3168.

2(*S*)-[[(*tert*-Butyldiphenylsilyl)oxy]methyl]-4-[1-[4-(*S*)-[5(*R*)-ethyl-6(*R*)-methyl-2(*S*)-phenyldioxanyl]]-methyl]-3(*R*)-methyl-2,3-dihydrofuran (36). To a solution of lactone **34** (29.3 mg, 0.05 mmol) in Et_2O (4 mL) at −78 °C was added MeLi (0.25 mL, 0.250 mmol, 1.0 M in Et_2O). After 1 h at −78 °C the reaction mixture was poured into saturated aqueous $NaHCO_3$ and was extracted with ether. Workup yielded the crude lactol **35a** (23.4 mg, 80% yield), which was used without further purification: ^1H NMR (partial) δ 5.20 (t, 1 H, J = 5.0 Hz, methine H).

To a solution of lactol **35a** (20.0 mg, 0.0339 mmol) in CH_2Cl_2 (20 mL) at −10 °C was added Et_3N (0.25 mL, 0.34 mmol) followed by the dropwise addition of methanesulfonyl chloride (0.044 mL, 0.3390 mmol). The reaction mixture was maintained at −10 °C for 30 min, at which time additional Et_3N (0.25 mL, 0.34 mmol) was added and the reaction mixture was heated at reflux for 1 h. The reaction mixture was diluted with CH_2Cl_2 and washed with 5% aqueous HCl and saturated aqueous $NaHCO_3$. Workup and chromatography (10% ethyl acetate/hexanes) yielded enol ether **36** (85% yield): ^1H NMR δ 7.75–7.28 (m, 15 H), 6.12 (s, 1 H), 5.80 (s, 1 H), 4.52 (dt, J = 5.8, 10.4 Hz, 1 H), 4.35 (dd, J = 6.25, 13.3 Hz, 1 H), 4.23 (dt, J = 7.5, 2.1 Hz, 1 H), 3.87 (d, J = 5.0 Hz, 2 H), 2.85 (m, 1 H), 2.42 (dd, J = 4.2, 15.0 Hz, 1 H), 2.06 (dd, J = 5.0, 16.7 Hz, 1 H), 1.50–1.85 (m, 3 H), 1.50 (d, J = 7.5 Hz, 3 H), 1.05 (s, 9 H), 1.04 (d, J = 7.6 Hz, 3 H), 1.00 (t, J = 7.5 Hz, 3 H); IR ($CHCl_3$) 2932, 1110 cm^{-1}; HRMS (CI, M + 1) calcd for $C_{36}H_{46}SiO_4(H)$ 571.3245, found 571.3250; $[\alpha]_D$ +20.02 (c = 0.825, $CHCl_3$).

4(*S*)-[5-[(*tert*-Butyldiphenylsilyl)oxy]-4(*R*)-(formyloxy)-3(*S*)-methyl-2-oxopentyl]-5(*R*)-ethyl-6(*R*)-methyl-2-(*S*)-phenyl-1,3-dioxane (37). A saturated solution of ozone (0.022 M) in CH_2Cl_2 at −78 °C was prepared by bubbling ozone through 125 mL of CH_2Cl_2 under the following conditions: 1 h, 7.5 L/min O_2, 110 V, 220 W, −78 °C, $NaHCO_3$ (0.5 g). An aliquot of the solution (1.22 mL, 0.028 mmol) was added in a precooled syringe to enol ether **36** (15.0 mg, 0.026 mmol), in 3 mL of $MeOH/CH_2Cl_2$ (1/1, −78 °C, $NaHCO_3$). After 10 min, dimethyl sulfide (16.3 mg, 0.020 mL, 0.260 mmol) was added to the reaction mixture and was stirred for 1 h at −78 °C followed by 3 h at room temperature. The reaction mixture was quenched with water and extracted with ethyl acetate. Workup followed by chromatography (10% ethyl acetate/hexanes) yielded the desired keto formate **37** (90% yield): ^1H NMR δ 7.92 (s, 1 H), 7.75–7.28 (m, 15 H), 5.80 (s, 1 H), 5.32 (q, J = 6.25 Hz, 1 H), 4.70 (m, 1 H), 4.32 (q, J = 7.0 Hz, 1 H), 3.76 (dd, J = 5.0, 10.4 Hz, 1 H), 3.67 (dd, J = 5.0, 10.4 Hz, 1 H), 2.90 (m, 2 H), 2.43 (dd, J = 4.1, 17.1 Hz, 1 H), 1.80 (m, 3 H), 1.52 (d, J = 6.7 Hz, 3 H), 1.06 (s, 9 H), 1.04 (d, 3 H), 1.03 (t, 3 H); IR ($CHCl_3$) 2950, 2830, 1727, 1717, 1270 cm^{-1}; $[\alpha]_D$ +13.11 (c = 0.622, $CHCl_3$).

8(*R*)-(Benzoyloxy)-1-[(*tert*-butyldiphenylsilyl)oxy]-7-(*R*)-ethyl-2(*S*)-(formyloxy)-6(*S*)-hydroxy-3(*S*)-methyl-4-nonanone (38a) and 4(*S*)-(Benzoyloxy)-2-[3-[(*tert*-butyldiphenylsilyl)oxy]-2(*S*)-(formyloxy)-1(*S*)-methylpropyl]-5-(*R*)-ethyl-2(*R*)-hydroxy-6(*R*)-methyltetrahydro-2*H*-pyran (39). To a solution of acetyl **37** (2.0 mg, 3.3×10^{-3} mmol) in benzene (2 mL) was added *tert*-butyl hydroperoxide (0.01 mL, 3.32×10^{-3} mmol, 4.29 M solution in $ClCH_2CH_2Cl$) followed by a catalytic amount of $Pd(OAc)_2$ (about 0.05 mg). The reaction mixture was heated at 50 °C for 6 h at which time water was added. Extraction with ether, followed by workup and chromatography (10% ethyl acetate/hexanes), yielded a 1/1 mixture of monobenzoates **38a** (<1 mg) and **39** (<1 mg). Benzoate **38a**: ^1H NMR δ 7.92 (s, 1 H, OCHO), 8.00–7.35 (m, 15 H), 5.35 (m, 2 H, C_2-H, C_8-H), 4.38 (m, 1 H, C_6-H), 3.73 (dd, J = 5.4, 10.4 Hz, 1 H, C_1-H), 3.68 (dd, J = 5.0, 10.4 Hz, 1 H, C_1-H), 3.03 (pent, J = 6.8 Hz, 1 H, C_7-H), 2.87 (dd, J = 9.2, 16.7, 1 H, C_5-H), 2.79 (m, 1 H, C_3-H), 2.60 (dd, J = 4.2, 17.0 Hz, 1 H, C_5-H), 1.50 (m, 2 H), 1.40 (d, J = 6.2 Hz, 3 H, C_9-H), 1.05 (s, 9 H), 1.01 (d, J = 7.5 Hz, 3 H), 0.83 (t, J = 7.4 Hz, 3 H). Benzoate **39**: ^1H NMR δ 7.92 (s, 1 H), 8.00–7.35 (m, 15 H), 5.45 (m, 1 H), 5.40 (m, 1 H), 4.00 (m, 1 H), 3.73 (dd, J = 5.0, 10.4 Hz, 1 H), 3.65 (dd, J = 6.2, 10.4 Hz, 1 H), 3.12 (d, J = 3.3 Hz, 1 H), 2.32 (dd, J = 5.0, 12.5 Hz, 1 H), 1.95 (m, 2 H), 1.50 (m, 2 H), 1.23 (d, J = 5.8 Hz, 3 H), 1.05 (s, 9 H), 0.94 (d, J = 7.5 Hz, 3 H), 0.90 (t, J = 7.4 Hz, 3 H).

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Supplementary Material Available: ^1H NMR spectra for the 25 titled compounds in the Experimental Section (25 pages). Ordering information is given on any current masthead page.