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Stereoselective Total Synthesis of Bioactive Styryllactones (+)-Goniofufurone, (+)7-*epi*-Goniofufurone, (+)-Goniopypyrone, (+)-Goniotriol, (+)-Altholactone, and (−)-Etharvensin†

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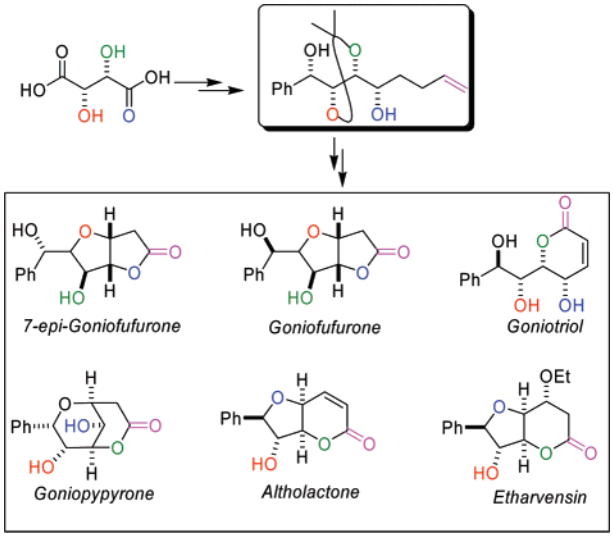

Stereoselective total synthesis of biologically active styryllactones 7-*epi*-goniofufurone, goniofufurone, goniopypyrone, goniotriol, altholactone, and etharvensin was achieved in high overall yields from a common intermediate derived from D-(−)-tartaric acid. It is based on the utility of a masked tetrol, comprising an alkene tether and four contiguous hydroxy groups. The pivotal reaction sequence involves hydroxy-directed lactonization via the oxidation of alkene, and subsequent elaboration to styryllactones. The masked tetrol was prepared by the extension of γ-phenyl-γ-hydroxy butyramide, readily obtained from the bis-dimethylamide of tartaric acid, employing a combination of selective Grignard additions and a stereoselective reduction.

Introduction

Trees of genus *Goniothalamus* of the plant family *Annonaceae* in South East Asia have been known for a long time for their proven use in folk medicine. The extracts and leaves from these plants have traditionally been used as a remedy to treat rheumatism and edema, as an abortifacient, and as a mosquito repellant. The research group of McLaughlin et al. isolated and characterized a series of styryllactones, possessing pesticidal, ratogenic, embryo toxic activity, and significant to marginal cytotoxic activity against human tumor cell lines.[1] The structures and relative configurations of these compounds were determined

† Dedicated with warmth and respect to Professor S. V. Kessar on the occasion of his 75th birthday.

(1) For a review on the cytotoxic activity and other bioactivity of styryllactones see: (a) Mereyala, H. B.; Joe, M. *Curr. Med. Chem. Anti-Cancer Agents* **2001**, *1*, 293. (b) Blàzquez, M. A.; Bermejo, A.; Zafra-Polo, M. C.; Cortes, D. *Phytochem. Anal.* **1999**, *10*, 161.

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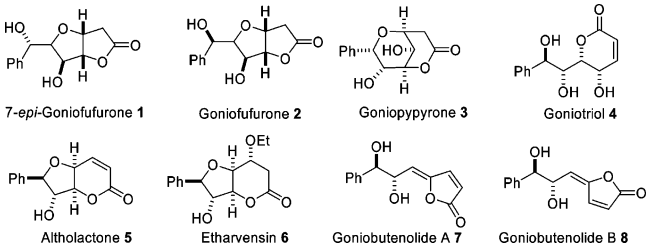
CHART 1. Bioactive Styryllactones 1−8 from *Goniothalamus* Species

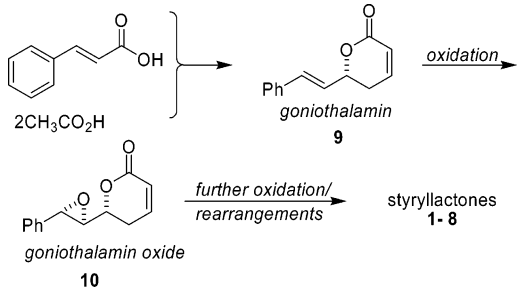


either by X-ray crystallography or by extensive NMR spectral analysis. The styryllactones can mainly be classified into two groups, related to the size of the lactone ring. Among the group comprising the five-membered lactone rings, 7-*epi*-goniofufurone **1** and goniofufurone **2** are moderately active, while goniopypyrone **3**, goniotriol **4**, and altholactone **5** comprising the six-membered lactone ring showed considerable anti-tumor activity. Because of their unique and intriguing structures and the broad spectrum of activity, these styryllactones have attracted the attention of several synthetic groups in recent years.[2] Although, there has been a number of syntheses concerning the individual styryllactones, very few syntheses of these styryllactones from a common intermediate have been reported in the literature. Shing et al. employed D-glycero-D-*gulo*-heptano-γ-lactone as a chiral source for the synthesis of **1**−**5**,[3] while Tsubuki et al. utilized chiral lactonic aldehydes derived from D-isopropyldinedioxy glyceraldehyde.[4] Mandelic acid was used as the chiral source in the synthesis of styryl lactones **1**−**4** by Surivet and Vatele.[5] While the synthesis of these compounds reported by Shing et al. suffers from low overall yields (<5%), the synthetic sequence by Tsubuki et al. involves cumbersome preparation of the chiral intermediate, and separation of diastereomers formed in the reaction sequence. The synthesis by Surivet and Vatele requires separation of the mixture of styryllactones obtained. Herein, we disclose in detail our efforts in the practical, efficient, and enantiospecific synthesis of styryllactones 7-*epi*-goniofufurone **1**, goniofufurone **2**, goniopypyrone **3**, goniotriol **4**, altholactone **5**, and etharvensin **6** in high overall yields from a single chiral building block derived from D-(−)-tartaric acid.[6]

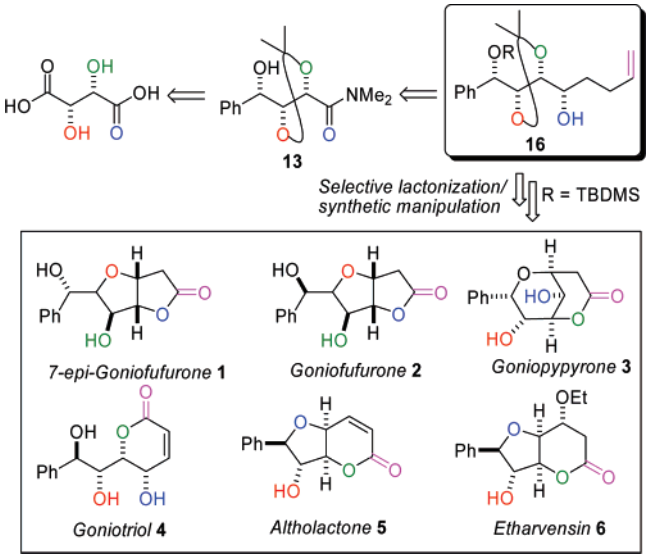
It was proposed by Shing et al.[3] that the biosynthesis of styryllactones occurs via the shikimic acid pathway. This proceeds through the formation of cinnamic acid from phenylalanine, followed by the incorporation of two acetate−malonate units activated as coenzyme A, generating the styrylpyrone, goniothalamin **9**. The styrylpyrone **9** undergoes oxidation to goniothalamin oxide **10**, which on further hydroxylation/oxidation leads to the formation of styryllactones **1**−**8** (Scheme 1).

Our approach for the synthesis of the styryllactones is inspired from the above biogenetic pathway. It is based on the utility of the masked tetrol **16**, comprising an alkene tether and four contiguous hydroxy groups installed with definite configuration. It relied on exploiting the hydroxy directed lactonization via

SCHEME 1. Biogenetic Pathway for Styryllactones Proposed by Shing et al.



SCHEME 2. Retrosynthesis for Styryllactones 1−6 from a Common Building Block



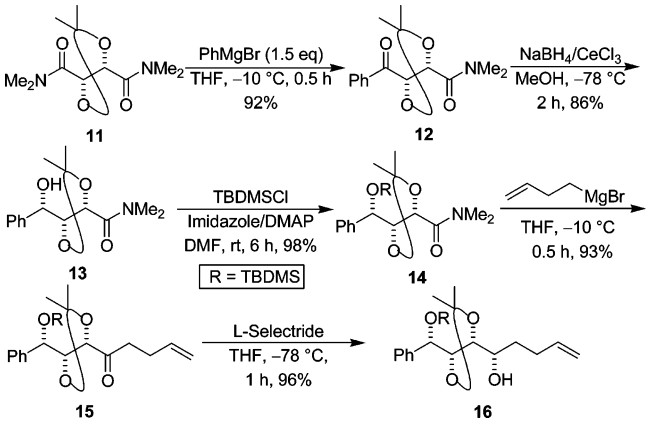
the oxidation of alkene in **16**, and subsequent elaboration to styryllactones **1**−**6**. The masked tetrol **16** could be obtained by the extension of γ-phenyl-γ-hydroxy butyramide **13**, prepared by a combination of selective Grignard addition and stereoselective reduction from the dimethylamide **11** derived from D-(−)-tartaric acid (Scheme 2).

Results and Discussion

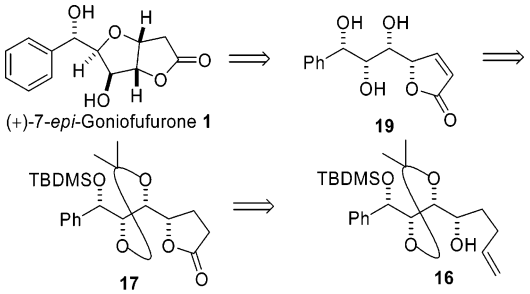
At the outset, we focused on the synthesis of the key building block **16** from D-(−)-tartaric acid. The synthetic sequence commenced with the addition of 1.5 equiv of phenylmagnesium bromide to the diamide **11**,[7] resulting in γ-oxo butyramide **12** in 92% yield. Reduction of the keto group in **12** with $NaBH_4$/$CeCl_3$ afforded a diastereomeric mixture of alcohols in 94:6 ratio, which after recrystallization furnished the alcohol **13** as the major product in 86% yield. Protection of the alcohol group in **13** as the corresponding silyl ether utilizing standard conditions afforded the silyloxy amide **14** in 98% yield. Addition of 3-butenylmagnesium bromide to **14** produced the ketone **15** in 93% yield, which on reduction with L-selectride yielded the alcohol **16** in 96% yield. The key building block was thus successfully synthesized in a facile stereoselective route from the dimethylamide of tartaric acid (Scheme 3).

(2) For a review on the synthesis of styryllactones until 2004 see: Mondon, M.; Gesson, J.-P. *Curr. Org. Synth.* **2006**, *3*, 175.
(3) Shing, T. K. M.; Tsui, H. C.; Zhou, Z. H. *J. Org. Chem.* **1995**, *60*, 3121.
(4) Tsubuki, M.; Kanai, K.; Nagase, H.; Honda, T. *Tetrahedron* **1999**, *55*, 2493.
(5) Surivet, J. P.; Vatele, J. M. *Tetrahedron* **1999**, *55*, 13011.
(6) Preliminary communication: Prasad, K. R.; Gholap, S. L. *Synlett* **2005**, 2260.
(7) (a) Toda, F.; Tanaka, K. *J. Org. Chem.* **1988**, *53*, 3607. (b) Seebach, D.; Hidber, A. *Organic Syntheses*; Wiley: New York, Collect. Vol. VII, p 447.

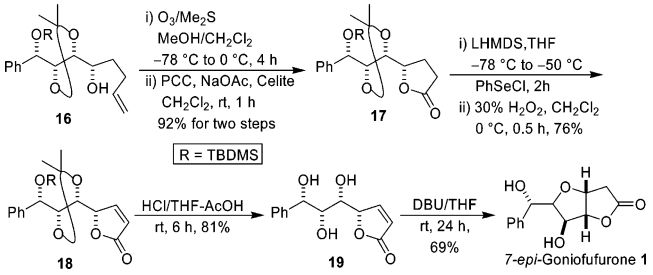
SCHEME 3. Stereoselective Synthesis of Masked Tetrol 16



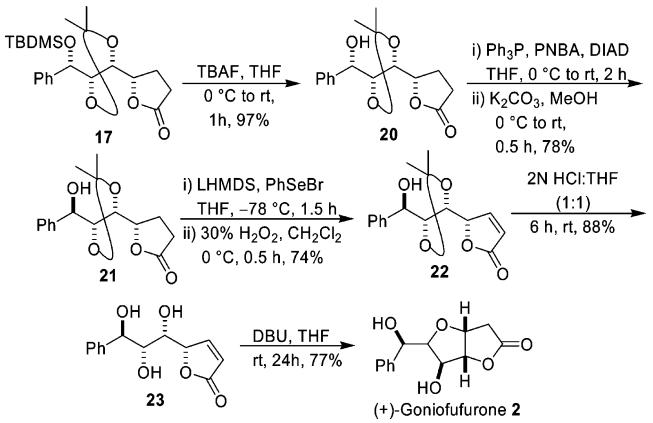
SCHEME 4. Retrosynthesis for the Synthesis of (+)-7-*epi*-Goniofufurone 1



SCHEME 5. Stereoselective Synthesis of (+)-7-*epi*-Goniofufurone 1



SCHEME 6. Stereoselective Synthesis of (+)-Goniofufurone 2



Synthesis of (+)-7-*epi*-Goniofufurone and (+)-Goniofufurone. (+)-7-*epi*-Goniofufurone **1** and (+)-goniofufurone **2** are the 5-membered lactones isolated from the *Goniothalamus* species comprising a furano-furone motif.[8] The structures of these compounds were established by X-ray crystal data. We envisaged the synthesis of 7-*epi*-goniofufurone **1** through an intramolecular Michael reaction of the known triol butenolide **19**. For the generation of **19**, lactone **17** was identified as the precursor, which could be obtained by elaboration of **16** (Scheme 4).

Thus, ozonolysis of **16** resulted in the formation of corresponding lactol, which on oxidation with PCC afforded the lactone **17** in 92% yield. Phenylselenation of the lactone **17** followed by elimination of the phenylselenyl moeity furnished the α,β-unsaturated lactone **18** in 76% isolated yield. Reaction of **18** with HCl−AcOH in THF resulted in the known triol **19** in 81% yield. Treatment of **19** with DBU in THF produced 7-*epi*-(+)-goniofufurone **1** in 69% yield (27% overall yield in 9 steps from **11**), the spectral data of which are identical with those reported in the literature (Scheme 5).

Synthesis of (+)-goniofufurone, involving similar intramolecular Micheal cyclization was achieved as follows. Reaction of lactone **17** with TBAF produced the alcohol **20** in 97% yield. Mitsunobu inversion of the benzylic hydroxy group in **20** with DIAD, Ph_3P, and *p*-nitrobenzoic acid, and subsequent hydrolysis of the *p*-nitrobenzoyl ester furnished the epimerized alcohol **21** in 78% yield. Phenylselenation of **21** followed by elimination of the phenylselenyl moeity afforded the α,β-unsaturated lactone **22** in 74% yield. Deprotection of the acetonide in **22** with 2 N HCl yielded the known triol **23** in 88% yield. Treatment of **23** with DBU in THF resulted in (+)-goniofufurone **2**, in 77% yield. Thus, natural goniofufurone was synthesized in 11 steps from the dimethylamide **11** in 24% overall yield (Scheme 6).

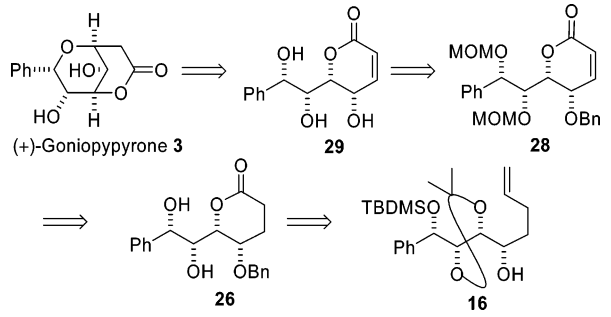
Synthesis of (+)-Goniopypyrone and (+)-Goniotriol. Among the styryllactones, (+)-goniopypyrone **3**, comprising a pyranopyrone moiety, is the most active compound, exhibiting significant activity against several human tumor cell lines. The bioactivity and the novel structural features present in goniopypyrone attracted the attention of a number of synthetic groups.[9] Retrosynthetic analysis based on intramolecular Michael addition reveals the trihydroxypyrone **29** as the possible precursor. Further evaluation of **29** leads to lactone **26**, which could be obtained by elaboration of **16** (Scheme 7).

Accordingly, compound **16** was converted to the benzyl ether **24** in 91% yield. Reaction of **24** with 4 N HCl in THF effected the deprotection of the acetonide and the TBDMS group to

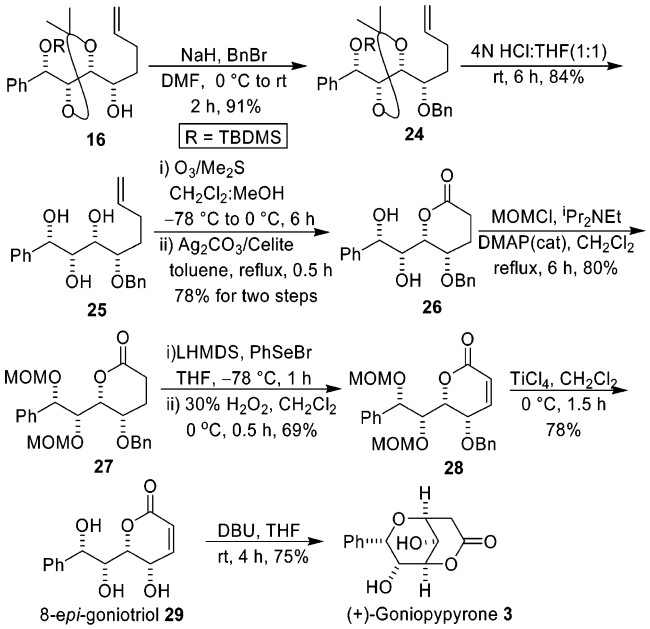
(8) Isolation of goniofufurone and 7-*epi*-goniofufurone: (a) Fang, X.-P.; Anderson, J. E.; Chang, C.-J.; McLaughlin, J. L.; Fanwick, P. E. *J. Nat. Prod.* **1991**, *54*, 1034. (b) Fang, X.-P.; Anderson, J. E.; Fanwick, P. E.; McLaughlin, J. L. *J. Chem. Soc., Perkin Trans. 1* **1990**, 1655. For syntheses of goniofuruone and 7-*epi*-goniofufurone see: (c) Shing, T. K. M.; Tsui, H. C.; Zhou, Z. H. *Tetrahedron* **1992**, *48*, 8659. (d) Prakash, K. R. C.; Rao, S. P. *Tetrahedron* **1993**, *49*, 1505. (e) Ye, J.; Bhatt, R. K.; Falck, J. R. *Tetrahedron Lett.* **1993**, *34*, 8007. (f) Gracza, T.; Jaeger, V. *Synthesis* **1994**, 1359. (g) Yang, Z.-C.; Zhou, W.-S. *Tetrahedron* **1995**, *51*, 1429. (h) Mukai, C.; Hirai, S.; Kim, I. J.; Masaru, K.; Hanaoka, M. *Tetrahedron* **1996**, *52*, 6547. (i) Yi, X.-H.; Meng, Y.; Hua, X.-G.; Li, C.-J. *J. Org. Chem.* **1998**, *63*, 7472. (j) Bruns, R.; Wernicke, A.; Koll, P. *Tetrahedron* **1999**, *55*, 9793. (k) Mereyala, H. B.; Gadikota, R. R. *Ind. J. Chem., Sect. B* **2000**, *39B*, 166. (l) Su, Y.-L.; Yang, C.-S.; Teng, S.-J.; Zhao, G.; Ding, Y. *Tetrahedron* **2001**, *57*, 2147. (m) Ruiz, P.; Murga, J.; Carda, M.; Marco, J. A. *J. Org. Chem.* **2005**, *70*, 713. (n) Fernanndez de la Pradilla, R.; Fernandez, J.; Alma, V.; Fernanndez, J.; Gomez, A. *Heterocycle* **2006**, *68*, 1579.

(9) For synthesis of goniopypyrone see: (a) Shing, T. K. M.; Tsui, H. C.; Zhou, Z. H. *Tetrahedron Lett.* **1993**, *34*, 691. (b) Zhou, W.-S.; Yang, Z.-C. *Tetrahedron Lett.* **1993**, *34*, 7075. (c) Surivet, J.-P.; Vatele, J.-M. *Tetrahedron Lett.* **1997**, *38*, 819. (d) Li, H.-M.; Yang, M.; Zhao, G.; Yu, Q.-S.; Ding, Y. *Chin. J. Chem.* **2000**, *18*, 388.

SCHEME 7. Rertosynthesis of (+)-Goniopypyrone 3



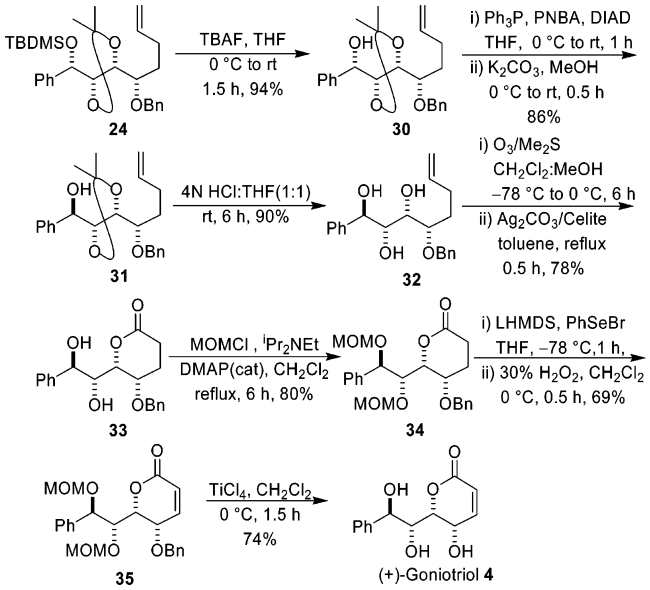
SCHEME 8. Synthesis of (+)-Goniopypyrone 3



furnish the triol **25** in 84% yield. Ozonolysis of triol **25** produced the corresponding lactol, which on oxidation with silvercarbonate impregnated on Celite[10] afforded the *δ*-lactone **26** in 78% yield for two steps. The secondary hydroxy groups in lactone **26** were protected as the corresponding methoxymethyl (MOM) ethers with use of MOMCl. The resultant lactone **27** on phenylselenation and deselenation furnished the α,*β*-unsaturated lactone **28** in 69% yield. Treatment of **28** with $TiCl_4$ in dichloromethane underwent smooth deprotection of the MOM and benzyl ether groups leading to the triol **29** (8-*epi*-goniotriol) in 78% yield. Treatment of **29** with a catalytic amount of DBU in THF yielded (+)-goniopypyrone **3** in 75% yield (13% overall yield in 12 steps from **11**). The spectral data are in complete agreement with that reported in the literature (Scheme 8).

Synthesis of (+)-goniotriol **4**, utilizing similar hydroxy directed lactonization as the key step, is achieved as follows. Treatment of **24** with TBAF produced the alcohol **30** in 94% yield. Mitsunobu inversion of the alcohol group in **30** furnished **31** in 86% yield. Reaction of **31** with 4 N HCl in THF afforded triol **32** in 90% yield. Following a sequence similar to that employed for the synthesis of 8-*epi*-goniotriol **29** (vide supra),

SCHEME 9. Synthesis of (+)-Goniotriol 4



triol **32** was converted to (+)-goniotriol **4** the spectral data of which are identical with those reported in the literature (Scheme 9).[11] Thus, synthesis of (+)-**4** was achieved in 16% overall yield from the diamide **11** in 14 steps.

Synthesis of (+)-Altholactone and (−)-Etharvensin. Altholactone **5** was isolated by Loder and Nearn from an unknown *Polyalthea* species,[12a] while McLaughlin et al. isolated the same from the *Goniothalamus* species.[12b] For the generation of altholactone **5**, tetrahydrofuran **36** was identified as the precursor. Synthesis of **36** from **16** was accomplished by us, earlier in our work concerning the total synthesis of related natural product goniothalesdiol.[13]

Thus, alcohol **16** was converted to the tetrahydrofuran **36** by using the procedure described by us.[13] Ozonolysis of **36** furnished the corresponding lactol, which on subsequent oxidation with Ag_2CO_3 impregnated on Celite afforded dihydroaltholactone **37** in 82% yield. Conversion of **37** to altholactone **5** was reported by Somfai.[12f] The present sequence thus constitutes a formal synthesis of altholactone. Altholactone, thus prepared on reaction with EtOH in the presence of concentrated H_2SO_4, furnished (−)-etharvensin **6** in 86% yield (Scheme 11).

In summary, a facile, practical, and efficient enantiospecific synthesis of bioactive styryllactones 7-*epi*-goniofufurone, goniofufurone, goniopypyrone, goniotriol, altholactone, and ethar-

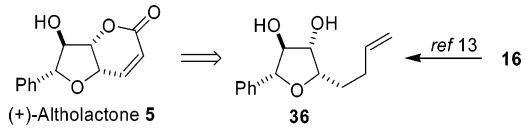
(10) (a) Balogh, V.; Fetizon, M.; Golfier, M. *J. Org. Chem.* **1971**, *36*, 1339. (b) Clive, D. L. J.; Murthy, K. S. K.; Wee, A. G. H.; Prasad, J. S.; da Silva, G. V. J.; Majewski, M.; Anderson, P. C.; Evans, C. F.; Haugen, R. D.; Heerze, L. D.; Barrie, J. R. *J. Am. Chem. Soc.* **1990**, *112*, 3018. (c) Chandrasekhar, M.; Chandra, K. L.; Singh, V. K. *J. Org. Chem.* **2003**, *68*, 4039.

(11) Isolation of goniotriol: (a) Alkofahi, A.; Ma, W.-W.; Mckenzie, A. T.; Byan, S. R.; McLaughlin, J. L. *J. Nat. Prod.* **1989**, *52*, 1371. (b) Talapatra, S. K.; Basu, D.; Deb, T.; Goswami, S.; Talapatra, B. *Ind. J. Chem., Sect. B* **1985**, *24B*, 29. Synthesis of goniotriol and analogues: (c) Shing, T. K. M.; Zhou, Z. H.; Mak, C. W. T. *J. Chem. Soc., Perkin Trans. 1* **1992**, 1907. (d) Shing, T. K. M.; Tai, V. W.-F. *J. Org. Chem.* **1999**, *64*, 2140. (e) Srikanth, G. S. C.; Muralikrishna, U.; Trivedi, G. K.; Cannon, J. F. *Tetrahedron* **2006**, *62*, 11165.

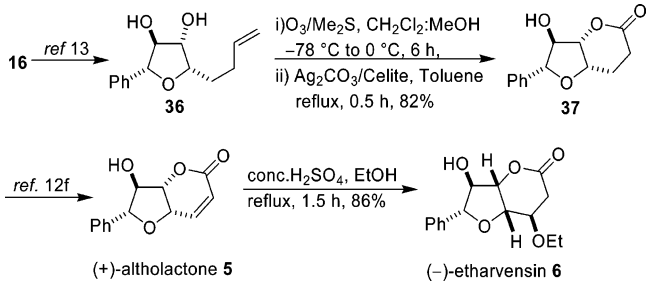
(12) Isolation of altholactone: (a) Loder, J. W.; Nearn, R. H. *Heterocycles* **1977**, *7*, 113. (b) El-Zayat, A. E.; Ferrigni, N. R.; McCloud, T. G.; McKenzie, A. T.; Byrn, S. R.; Cassady, J. M.; Chang, C.; McLaughlin, J. L. *Tetrahedron Lett.* **1985**, *26*, 955. Synthesis of altholactone: (c) Gillhouley, J. G.; Shing, T. K. M. *J. Chem. Soc., Chem. Commun.* **1988**, 976. (d) Kang, S. H.; Kim. W. J. *Tetrahedron Lett.* **1989**, *30*, 5915. (e) Gesson, J. P.; Jacquesy, J. C.; Mondon, M. *Tetrahedron* **1989**, *45*, 2627. (f) Somfai, P. *Tetrahedron* **1994**, *50*, 11315. (g) Shing, T. K. M.; Gillhouley, J. G. *Tetrahedron* **1994**, *50*, 8685. (h) Yadav, J. S.; Rajaiah, G.; Raju, A. K. *Tetrahedon Lett.* **2003**, *44*, 5831. (i) Yadav, J. S.; Raju, A. K.; Ponugoti, P.; Rajaiah, G. *Tetrahedron: Asymmetry* **2005**, *16*, 3283.

(13) Prasad, K. R.; Gholap, S. L. *J. Org. Chem.* **2006**, *71*, 3643.

SCHEME 10. Retrosynthesis of (+)-Altholactone 5



SCHEME 11. Synthesis of (+)-Altholactone 5 and (−)-Etharvensin 6



vensin was accomplished in high overall yields from a common chiral building block derived from D-(−)-tartaric acid. The pivotal reaction sequence includes a hydroxy group directed lactonization of a tetrol comprising an alkene tether. The synthetic strategies are operationally simple, selective, and amenable to produce a number of scaffolds based on styryllactone structures.

Experimental Section

Preparation of (4*S*,5*S*)-5-Benzoyl-*N*,*N*,2,2-tetramethyl-1,3-dioxolane-4-carboxamide (12). In a two-necked, 100 mL, round-bottomed flask equipped with a magnetic stir bar, rubber septum, and argon inlet was placed **11** (2.0 g, 8.2 mmol). This was dissolved in 10 mL of THF and the solution was cooled to −10 °C. A freshly prepared THF solution of PhMgBr (12.3 mL of 1 M solution in THF, 12.3 mmol) was added at such a rate that the internal temperature does not rise above −10 °C. Progress of the reaction was monitored by TLC and after the reaction was complete (0.5 h), it was cautiously quenched by addition of a saturated solution of NH_4Cl (10 mL). It was then poured into water (20 mL) and extracted with ether (3 × 25 mL). Combined ethereal extracts were washed with brine (30 mL) and dried (Na_2SO_4). Evaporation of the solvent and silica gel column chromatography of the residue with petroleum ether:EtOAc (3:1) as an eluent yielded **12** (2.1 g, 92%) as a pale yellow solid. Mp 79−80 °C; $[\alpha]_D$ +23 (*c* 1, $CHCl_3$); IR (neat) 2988, 1692, 1504, 1261, 1154, 1061, 885 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 8.09 (d, J = 7.2 Hz, 2H), 7.65−7.42 (m, 3H), 5.95 (d, J = 5.1 Hz, 1H), 5.16 (d, J = 5.1 Hz, 1H), 3.16 (s, 3H), 3.00 (s, 3H), 1.50 (s, 3H), 1.42 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 196.3, 168.2, 134.9, 133.7, 129.4, 128.5, 112.6, 79.4, 75.0, 37.1, 35.9, 26.42, 26.38; HRMS for $C_{15}H_{19}NO_4$ + Na calcd 300.1214, found 300.1212. Anal. Calcd: C 64.97, H 6.91. Found: C 65.28 H 7.02.

Preparation of (4*S*,5*R*)-5-((*S*)-Hydroxy(phenyl)methyl)-*N*,*N*,2,2-tetramethyl-1,3-dioxolane-4-carboxamide (13). To a solution of **12** (1.5 g, 5.4 mmol) in methanol (15 mL) cooled to −78 °C was added $CeCl_3 \cdot 7H_2O$ (2.3 g, 6.5 mmol) and then the solution was stirred for 15 min. $NaBH_4$ (0.25 g, 6.5 mmol) was then added portionwise over a period of 30 min and the solution was stirred at the same temperature. After being stirring for 1.5 h, it was cautiously quenched by addition of water (20 mL) and extracted with EtOAc (3 × 25 mL). The combined organic layers were washed with brine (30 mL), dried over Na_2SO_4, and concentrated. Silica gel column chromatography of the crude residue obtained after evaporation of the solvent, with petroleum ether:EtOAc (6:4) as eluent, gave a distereomeric mixture (dr 96:4) of alcohols (1.42 g, 94%) as a white crystalline solid. Recrystallization from EtOAc−petroleum ether yielded diastereomerically pure **13** in 86% yield. Mp 154−156 °C; $[\alpha]_D$ +31 (*c* 1, $CHCl_3$); IR (neat) 3388, 2932, 1640, 1451, 1127, 885, 716 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.46−7.20 (m, 5H), 4.90−4.78 (m, 2H), 4.40 (d, J = 6.9 Hz, 1H), 3.57 (d, J = 6.9 Hz, 1H), 3.02 (s, 3H), 2.89 (s, 3H), 1.39 (s, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 168.8, 140.4, 128.1, 127.7, 126.7, 110.6, 81.1, 74.5, 72.4, 37.0, 35.8, 26.8, 26.2; HRMS for $C_{15}H_{21}NO_4$ + Na calcd 302.1371, found 302.1368. Anal. Calcd for $C_{15}H_{21}NO_4$: C 64.50, H 7.58. Found: C 64.82, H 7.67.

Preparation of (4*S*,5*R*)-5-((*S*)- *tert*-Butyldimethylsilyloxy-(phenyl)methyl)-*N*,*N*,2,2-tetramethyl-1,3-dioxolane-4-carboxamide (14). To a solution of **13** (0.75 g, 2.7 mmol) in dry DMF (8 mL) were added imidazole (0.55 g, 8.1 mmol) and DMAP (0.07 g, 20 mol %). After stirring at room temperature for 15 min TBDMSCl (0.6 g, 4 mmol) was introduced into the reaction mixture. Progress of the reaction was monitored by TLC. After the reaction was complete (∼6 h), it was cooled to 0 °C and quenched by addition of water (10 mL). It was then extracted with ether (3 × 25 mL) and the combined ethereal extracts were washed with brine (20 mL) and dried (Na_2SO_4). Evaporation of solvent and silica gel column chromatography of the resulting residue with petroleum ether:EtOAc (4:1) as an eluent yielded the corresponding silyl ether **14** (1.04 g, 98%) as a pale yellow solid. Mp 95−97 °C; $[\alpha]_D$ +66.2 (*c* 1, $CHCl_3$); IR (neat) 2931, 2858, 1649, 1461, 1256, 1050, 778 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.54−7.30 (m, 5H), 4.96 (d, J = 4.5 Hz, 1H), 4.90 (dd, J = 6.6, 4.5 Hz, 1H), 4.58 (d, J = 6.6 Hz, 1H), 3.12 (s, 3H), 2.98 (s, 3H), 1.48 (s, 3H), 1.40 (s, 3H), 0.98 (s, 9H), 0.14 (s, 3H), 0.01 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 169.0, 140.5, 127.7, 127.5, 127.2, 110.9, 82.0, 74.0, 73.1, 36.9, 35.7, 26.7, 26.4, 25.7, 18.2, −4.9, −5.2; HRMS for $C_{21}H_{35}NO_4Si$ + Na calcd 416.2235, found 416.2235. Anal. Calcd for $C_{21}H_{35}NO_4Si$: C 64.08, H 8.96, N 3.56. Found: C 64.10, H 9.20, N 3.64.

Preparation of 1-((4*S*,5*R*)-5-((*S*)-*tert*-Butyldimethylsilyloxy-(phenyl)methyl)-2,2-dimethyl-1,3-dioxolan-4-yl)pent-4-en-1-one (15). To a precooled (−10 °C) solution of the silyl ether **14** (1.0 g, 2.5 mmol) in dry THF (12 mL) was added a solution of 3-butenylmagnesium bromide (0.5 M solution in THF, 10.2 mL, 5.1 mmol) dropwise under argon atmosphere. The reaction mixture was stirred for 0.5 h at the same temperature. It was then cautiously quenched by addition of saturated NH_4Cl (15 mL). The reaction mixture was then extracted with ether (3 × 25 mL) and the combined ethereal extracts were washed with brine (30 mL) and dried (Na_2SO_4). Evaporation of the solvent and silica gel column chromatography of the residue with petroleum ether:EtOAc (96:4) as an eluent afforded ketone **15** (0.96 g, 93%) as a colorless oil. $[\alpha]_D$ +32.5 (*c* 1.5, $CHCl_3$); IR (neat) 2976, 2858, 1717, 1640, 1596, 1472, 1380, 1253, 1091, 886, 777 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.54−7.32 (m, 5H), 5.90 (ddt, J = 16.8, 12.9, 6.9 Hz, 1H), 5.21−4.98 (m, 2 H), 4.95 (d, J = 3.6 Hz, 1H), 4.44 (d, J = 7.2 Hz, 1H), 4.34 (dd, J = 7.2, 3.6 Hz, 1H), 2.73 (dt, J = 4.5, 1.8 Hz, 2H), 2.47−2.35 (m, 2H), 1.47 (s, 6H), 1.00 (s, 9H), 0.17 (s, 3H), 0.02 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 209.0, 140.6, 136.9, 127.9, 127.7, 127.4, 115.3, 111.0, 82.0, 80.8, 74.3, 38.1, 27.0, 26.7, 25.8, 18.2, −4.8, −5.1; HRMS for $C_{23}H_{36}O_4Si$ + Na calcd 427.2283, found 427.2281.

Preparation of (*S*)-1-((4*R*,5*R*)-5-((*S*)-*tert*-Butyldimethylsilyloxy(phenyl)methyl)-2,2-dimethyl-1,3-dioxolan-4-yl)pent-4-en-1-ol (16). To a solution of **15** (0.8 g, 1.98 mmol) in dry THF (14 mL) cooled to −78 °C was added L-selectride (2.4 mL of 1 M solution in THF, 2.4 mmol) dropwise under argon atmosphere. After the solution was stirred for 1 h at the same temperature, it was allowed to warm to 0 °C. The reaction mixture was quenched by cautious addition of water (12 mL) and stirred for 30 min. It was then extracted with ether (3 × 25 mL) and the combined ethereal extracts were washed with brine (30 mL) and dried over Na_2SO_4. Evaporation of the solvent and silica gel column chromatography of the residue with petroleum ether:EtOAc (95:5) as eluent yielded the alcohol **16** (0.77 g, 96%) as a colorless oil. $[\alpha]_D$ +39.33 (*c* 1.5,

$CHCl_3$); IR (neat) 3432, 2972, 2857, 1592, 1453, 1371, 1252, 1067, 889, 777 cm^{-1}; ^1H NMR (300 MHz , $CDCl_3$) δ 7.34−7.15 (m, 5H), 5.66 (ddt, J = 17.1, 10.2, 6.9 Hz, 1H), 5.04−4.78 (m, 2H), 4.76 (d, J = 5.1 Hz, 1H), 4.09 (dd, J = 7.8, 5.4 Hz, 1H), 3.64 (dd, J = 8.1, 2.4 Hz, 1H), 3.07 (br s, 1H), 2.18−1.82 (m, 2H), 1.54−1.28 (m, 2H), 1.32 (s, 3H), 1.10 (s, 3H), 0.83 (s, 9H), 0.01 (s, 3H), −0.12 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 138.1, 138.0, 127.9, 127.7, 127.4, 114.7, 109.1, 80.6, 79.3, 75.6, 69.3, 33.9, 29.8, 27.4, 27.0, 25.7, 18.2, −4.9, −5.0; HRMS for $C_{23}H_{38}O_4Si$ + Na calcd 429.2439, found 429.2437.

Preparation of (*S*)-Dihydro-5-((4*R*,5*R*)-5-((*S*)-*tert*-butyldimethylsilyloxy(phenyl)methyl)-2,2-dimethyl-1,3-dioxolan-4-yl)-3*H*-furan-2-one (17). Ozone was bubbled through a precooled (−78 °C) solution of **16** (0.32 g, 0.79 mmol) in a mixture of CH_2Cl_2: MeOH (4:1, 15 mL) containing solid $NaHCO_3$ (20 mg) until the pale blue color persisted. Excess ozone was flushed off with oxygen and Me_2S (1 mL) was added. The reaction mixture was warmed to 0 °C, then stirred at the same temperature for 4 h. The reaction mixture was concentrated under reduced pressure and filtered through a short pad of Celite. The Celite pad was washed with ether (25 mL). Evaporation of the solvent yielded the crude lactol, which was subjected to the next reaction without further purification.

To a solution of crude lactol obtained above in 8 mL of CH_2Cl_2 was added Celite (0.4 g) and NaOAc (0.13 g, 1.58 mmol) at room temperature and the solution was stirred for 5 min. PCC (0.34 g, 1.58 mmol) was then introduced at the same temperature and stirring was continued for 1 h. After the reaction was complete (monitored by TLC), it was filtered through a pad of Celite and the Celite pad was washed with ether (25 mL). Evaporation of the solvent and silica gel column chromatography of the residue with petroleum ether:EtOAc (9:1) as an eluent afforded **17** (0.29 g, 92%) as a white solid. Mp 101−103 °C; $[\alpha]_D$ +59.6 (*c* 0.4, $CHCl_3$); IR (neat) 2985, 2857, 1772, 1471, 1249, 1033, 778 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.45−7.24 (m, 5H), 4.91 (d, J = 5.4 Hz, 1H), 4.34 (dd, J = 8.1, 5.4 Hz, 1H), 4.02 (ddd, J = 8.4, 4.2, 1.5 Hz, 1H), 3.7 (dd, J = 8.4, 1.5 Hz, 1H), 2.74−2.51 (m, 1H), 2.32−2.20 (m, 1H), 2.19−2.10 (m, 2H), 1.36 (s, 3H), 1.18 (s, 3H), 0.92 (s, 9H), 0.11 (s, 3H), 0.02 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 177.7, 139.6, 127.9, 127.8, 127.3, 109.6, 79.4, 79.3, 77.3, 75.1, 27.9, 27.1, 26.5, 25.8, 24.7, 18.3, −4.9, −5.0. Anal. Calcd for $C_{22}H_{34}O_5Si$: C 64.99, H 8.43. Found: C 64.77, H 8.55.

Preparation of (*S*)-5-((4*R*, 5*R*)-5-((*S*)-*tert*-Butyldimethylsilyloxy(phenyl)methyl)-2,2-dimethyl-1,3-dioxolan-4-yl)furan-2(5*H*)-one (18). To a precooled (−78 °C) solution of **17** (0.18 g, 0.44 mmol) in dry THF (4.0 mL) was added LHMDS (1.1 mL of 1 M solution in THF, 1.1 mmol) dropwise, under argon atmosphere. The reaction mixture was slowly warmed to −50 °C and stirred for 1 h. It was then cooled to −78 °C and a THF (2 mL) solution of phenylselenyl chloride (0.13 g, 0.66 mmol) was introduced into the flask. Then the solution was stirred for 1 h at the same temperature and after the reaction was complete (TLC), it was quenched with saturated NH_4Cl (5 mL) and extracted with ether (3 × 15 mL). The combined ethereal extracts were washed with brine (15 mL) and dried over Na_2SO_4. Evaporation of solvent under reduced pressure at room temperature afforded the crude selenide, which was used for the next step without further purification.

To a cooled (0 °C) solution of crude selenide obtained above in 6 mL of CH_2Cl_2 were added pyridine (0.1 mL, 0.88 mmol) and H_2O_2 (2 mL of 30% w/v in water) and the resulting mixture was stirred for 0.5 h at the same temperature. After the reaction was complete, it was poured into water (10 mL) and extracted with CH_2Cl_2 (3 × 15 mL). The combined organic extracts were washed with brine (25 mL) and dried over Na_2SO_4. The solvent was removed under reduced pressure and the residue obtained was purified by silica gel column chromatography with petroleum ether: EtOAc (8:2) as an eluent to give **18** (0.12 g, 65%) as a white solid. Mp 143−144 °C; $[\alpha]_D$ +11.7 (*c* 0.6, $CHCl_3$); IR (neat) 2929, 1751, 1594, 1369, 1250, 1097, 861 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.46−7.29 (m, 5H), 7.26 (dd, J = 5.7, 1.8 Hz, 1H), 6.07 (dd, J = 5.7, 2.4 Hz, 1H), 4.94 (d, J = 5.7 Hz, 1H), 4.52 (dd, J = 3.9, 2.4 Hz, 1H), 4.46 (dd, J = 8.1, 5.7 Hz, 1H), 3.87 (dd, J = 8.1, 2.4 Hz, 1H), 1.34 (s, 3H), 1.17 (s, 3H), 0.91 (s, 9H), 0.11 (s, 3H), 0.01 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 172.8, 153.1, 139.4, 128.0, 127.3, 122.1, 110.2, 81.5, 80.0, 75.3, 75.1, 75.0, 27.0, 26.3, 25.8, 18.3, −4.9, −5.0; Anal. Calcd for $C_{22}H_{32}O_5Si$: C 65.31, H 7.97. Found: C 65.25, H 7.80.

Preparation of (*S*)-5-((1*S*,2*R*,3*S*)-1,2,3-Trihydroxy-3-phenylpropyl)furan-2(5*H*)-one (19). To a solution of **18** (0.06 g, 0.15 mmol) in 2 mL of THF was added AcOH (2 mL) and 1 N HCl (2 mL) at room temperature. The reaction mixture was allowed to stirr for 6 h at the same temperature. After the reaction was complete (TLC), the volatiles were removed under reduced pressure and the residue obtained was purified by silica gel column chromatography with petroleum ether:EtOAc (2:8) as an eluent to give **19** (0.026 g, 70%) as a white solid. Mp 142−144 °C; $[\alpha]_D$ −84 (*c* 0.3, MeOH); [lit.[3] mp 143−145 °C; $[\alpha]_D$ −85 (*c* 0.3, EtOH)]; IR (neat) 3372, 2925, 1744, 1602, 1412, 1111, 1049, 822 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.56 (dd, J = 5.7, 1.5 Hz, 1H), 7.46−7.20 (m, 5H), 6.10 (dd, J = 5.7, 1.8 Hz, 1H), 5.18 (m, 1H), 4.82 (d, J = 6.6 Hz, 1H), 3.67 (dd, J = 6.6, 2.7 Hz, 1H), 3.52 (dd, J = 3.3, 1.5 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 173.7, 154.4, 140.3, 128.3, 127.9, 126.6, 121.7, 85.6, 74.8, 71.6; HRMS for $C_{13}H_{14}O_5$ + Na calcd 273.0741, found 273.0739.

Preparation of (+)-7-*epi*-Goniofufurone (1). A solution of **19** (0.03 g, 0.11 mmol) in THF (6.0 mL) containing DBU (0.01 mL, 0.06 mmol) was stirred at room temperature for 24 h. After the reaction was complete (monitored by TLC) the reaction mixture was filtered through a short pad of silica gel and the silica gel pad was washed with EtOAc (25 mL). After concentration in vacuo, the residue was chromatographed on silica gel [petroleum ether: EtOAc (3:7)] to afford **1** (0.02 g, 68%) as a crystalline solid. Mp 194−197 °C; $[\alpha]_D$ +105 (*c* 0.8, EtOH) [lit.[8a] mp 190−192 °C; $[\alpha]_D$ +108 (*c* 0.2, EtOH)]; IR (neat) 3457, 2987, 1776, 1635, 1371, 1029, 765 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.46−7.28 (m, 5H), 5.16−5.02 (m, 2H), 4.89 (dd, J = 4.2, 0.9 Hz, 1H), 4.41 (d, J = 3.3 Hz, 1H), 2.23 (t, J = 3.6 Hz, 1H), 2.83−2.63 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 175.0, 139.9, 128.7, 128.5, 126.5, 87.8, 82.9, 75.5, 72.7, 36.1, 29.7; HRMS for $C_{13}H_{14}O_5$ + Na calcd 273.0741, found 273.0739.

Preparation of (*S*)-Dihydro-5-((4*R*,5*R*)-5-((*S*)-hydroxy(phenyl)methyl)-2,2-dimethyl-1,3-dioxolan-4-yl)furan-2(3*H*)-one (20). To a precooled (0 °C) solution of **17** (0.42 g, 1.03 mmol) in dry THF (10 mL) was added TBAF (1 M solution in THF, 2.1 mL, 2.1 mmol) under argon atmosphere. The reaction mixture was slowly allowed to warm to room temperature and stirred for 1 h at room temperature. Water (10 mL) was added to the reaction mixture, which was stirred for 10 min. It was then extracted with ether (3 × 20 mL). Combined ethereal extracts were washed with brine (30 mL) and dried (Na_2SO_4). Evaporation of solvent and silica gel column chromatography of the residue with petroleum ether: EtOAc (6:4) as an eluent yielded **20** (0.29 g, 97%) as a colorless oil. $[\alpha]_D$ +74 (*c* 1, $CHCl_3$); IR (neat) 3457, 2987, 1776, 1373, 1168, 1029, 887, 765 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.52−7.16 (m, 5H), 4.65 (d, J = 6.6 Hz, 1H), 4.35 (dd, J = 8.1, 6.6 Hz, 1H), 3.82 (dd, J = 8.4, 1.2 Hz, 1H), 3.68 (dt, J = 6.6, 1.5 Hz, 1H), 2.84 (br s, 1H), 2.66−2.48 (m, 1H), 2.38−2.2 (m, 1H), 2.18−2.00 (m, 2H), 1.45 (s, 3H), 1.39 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 177.4, 138.8, 128.6, 127.0, 110.2, 80.2, 80.0, 76.3, 75.5, 27.7, 27.4, 26.4, 24.4; HRMS for $C_{16}H_{20}O_5$ + Na calcd 315.1210, found 315.1208.

Preparation of (*S*)-Dihydro-5-((4*R*,5*R*)-5-((*R*)-hydroxy(phenyl)methyl)-2,2-dimethyl-1,3-dioxolan-4-yl)furan-2(3*H*)-one (21). To a precooled (0 °C) solution of **20** (0.28 g, 0.96 mmol) in dry THF (10 mL) were added triphenylphosphine (0.5 g, 1.92 mmol) and *p*-nitrobenzoic acid (0.32 g, 1.92 mmol) under argon atmosphere and the mixture was allowed to stir for 10 min. DIAD (0.3 mL, 1.44 mmol) was introduced into the reaction mixture over a period

of 15 min at the same temperature. The reaction mixture was warmed to room temperature and stirred for 1 h. After the reaction was complete (TLC), the volatiles were removed under reduced pressure and the crude residue obtained was used without further purification in the next step.

To a methanol (12 mL) solution of crude ester obtained above was added K_2CO_3 (0.27 g, 1.9 mmol) with stirring for 30 min at room temperature. After the reaction was complete (TLC), the reaction mixture was poured into water (20 mL) and extracted with ether (3 × 20 mL). Combined ethereal extracts were washed with brine (25 mL) and dried over Na_2SO_4. Evaporation of solvent and silica gel column chromatography of the residue with petroleum ether:EtOAc (7:3) as an eluent afforded **21** (0.22 g, 78%) as a colorless oil. $[\alpha]_D$ +36.2 (*c* 0.8, $CHCl_3$); IR (neat) 3458, 2922, 1778, 1462, 1169, 704 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.43−7.22 (m, 5H), 5.05 (d, J = 2.7 Hz, 1H), 4.37 (dd, J = 8.4, 4.2 Hz, 1H), 4.04 (d, J = 8.4 Hz, 1H), 3.42 (dt, J = 8.1, 4.2 Hz, 1H), 2.92 (d, J = 9.6 Hz, 1H), 2.65−2.48 (m, 1H), 2.33−2.18 (m, 1H), 2.16−1.99 (m, 2H), 1.45 (s, 3H), 1.36 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 177.8, 138.4, 128.5, 127.9, 125.5, 109.6, 79.3, 78.3, 77.3, 71.3, 27.7, 27.2, 26.3, 24.4; HRMS for $C_{16}H_{20}O_5$ + Na calcd 315.1210, found 315.1208.

Preparation of (*S*)-5-((4*R*,5*R*)-5-((*R*)-Hydroxy(phenyl)methyl)-2,2-dimethyl-1,3-dioxolan-4-yl)furan-2(5*H*)-one (22). To a cooled (−78 °C) solution of **21** (0.14 g, 0.5 mmol) in dry THF (6.0 mL) was added LHMDS (1.5 mL of 1 M solution in THF, 1.5 mmol) dropwise, under argon atmosphere. The reaction mixture was slowly warmed to −50 °C and stirred for 30 min at −50 °C. It was then cooled to −78 °C and a THF (4 mL) solution of phenylselenyl bromide (0.17 g, 0.72 mmol) was introduced into the flask. The solution was stirred for 1 h at the same temperature and after the reaction was complete (TLC), it was quenched with saturated NH_4Cl (5 mL) and extracted with ether (3 × 10 mL). Combined ethereal extracts were washed with brine (15 mL) and dried over Na_2SO_4. Evaporation of solvent under reduced pressure at room temperature afforded crude selenide, which was used in the next step without further purification.

To a cooled (0 °C) solution of crude selenide obtained above in 6 mL of CH_2Cl_2 was added pyridine (0.1 mL, 0.96 mmol) and H_2O_2 (2 mL of 30% w/v in water) and the resulting mixture was stirred for 0.5 h at the same temperature. After the reaction was complete, water (10 mL) was added to the reaction mixture and extracted with CH_2Cl_2 (3 × 10 mL). The combined organic extracts were washed with brine (25 mL) and dried over Na_2SO_4. The solvent was removed under reduced pressure and the residue thus obtained was purified by silica gel column chromatography with petroleum ether:EtOAc (6:4) as an eluent to give **22** (0.1 g, 74%) as a colorless oil. $[\alpha]_D$ +24.2 (*c* 1.1, $CHCl_3$); IR (neat) 3471, 2921, 1748, 1455, 1250, 1078, 704 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.51−7.24 (m, 5H), 7.21 (ddd, J = 6.0, 1.5, 0.9 Hz, 1H), 6.03 (dd, J = 6.0, 2.4 Hz, 1H), 5.12 (d, J = 4.2 Hz, 1H), 4.54 (dd, J = 8.1, 4.5 Hz, 1H), 4.22 (dd, J = 8.1, 1.5 Hz, 1H), 3.89 (t, J = 1.8 Hz, 1H), 2.62 (br s, 1H), 1.44 (s, 3H), 1.36 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 172.9, 153.2, 138.2, 128.8, 128.2, 125.5, 121.9, 110.4, 81.3, 79.9, 74.3, 71.2, 27.2, 26.1; HRMS for $C_{16}H_{18}O_5$ + Na calcd 313.1054, found 313.1052.

Preparation of (*S*)-5-((1*S*,2*R*,3*R*)-1,2,3-Trihydroxy-3-phenylpropyl)furan-2(5*H*)-one (23). To a solution of **22** (0.08 g, 0.28 mmol) in THF (3 mL) was added 2 N HCl (3 mL) at room temperature, and the mixture was stirred for 6 h at the same temperature. After the reaction was complete (TLC) the volatiles are removed under reduced pressure and the residue was purified by silica gel column chromatography with petroleum ether:EtOAc (2:8) as an eluent to afford **23** (0.026 g, 70%) as a white solid. Mp 107−110 °C; $[\alpha]_D$ −67.4 (*c* 0.5, EtOAc) [lit.[3] mp 109−111 °C; $[\alpha]_D$ −68 (*c* 0.6, EtOAc)]; IR (neat) 3402, 2924, 1750, 1454, 1177, 1041, 701 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) 7.75 (dd, J = 6.0, 1.5 Hz, 1H), 7.46−7.18 (m, 5H), 6.15 (dd, J = 5.7, 2.1 Hz, 1H), 5.25 (ddd, J = 6.0, 3.6, 1.2 Hz, 1H), 4.70 (d, J = 8.4 Hz, 1H), 4.06 (dd, J = 6.0, 2.1 Hz, 1H), 3.62 (dd, J = 8.4, 1.8 Hz, 1H), 3.30 (dd, J = 3.3, 1.8 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 175.7, 157.0, 144.0, 129.1, 128.6, 128.4, 122.2, 87.6, 75.0, 74.9, 72.8; HRMS for $C_{13}H_{14}O_5$ + Na calcd 273.0741, found 273.0739.

Preparation of (+)-Goniofufurone (2). A solution of unsaturated lactone **23** (0.058 g, 0.23 mmol) in dry THF (10 mL) containing DBU (0.02 mL, 0.12 mmol) was stirred at room temperature for 24 h. The solution was then filtered through a short pad of silica gel topped with Celite. A white solid obtained after evaporation of the solvent from filtrate was further purified by silica gel column chromatography with petroleum ether:EtOAc (3:7) as an eluent to give **2** (0.042 g, 72%) as a white solid. Mp 150−153 °C; $[\alpha]_D$ +9.8 (*c* 0.9, EtOH) [lit.[8b] mp 152−154 °C; $[\alpha]_D$ +9 (*c* 0.5, EtOH)]; IR (neat) 3427, 2925, 1782, 1454, 1191, 1047, 701 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.52−7.22 (m, 5H), 5.18 (d, J = 4.8 Hz, 1H), 5.10 (t, J = 4.5 Hz, 1H), 4.86 (d, J = 4.5 Hz, 1H), 4.39 (d, J = 2.4 Hz, 1H), 4.08 (dd, J = 4.8, 3 Hz, 1H), 2.84−2.59 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 175.8, 139.4, 129.2, 128.9, 126.3, 87.9, 83.4. 77.7, 74.8, 73.7, 36.5; HRMS for $C_{13}H_{14}O_5$ + Na calcd 273.0741, found 273.0739.

Preparation of ((*S*)-((4*S*,5*R*)-5-((*S*)-1-(Benzyloxy)pent-4-enyl)-2,2-dimethyl-1,3-dioxolan-4-yl)(phenyl)methoxy)(*tert*-butyl)dimethylsilane (24). In an oven-dried, 25-mL round-bottomed flask equipped with a magnetic stir bar, septa, and argon inlet was placed a solution of **16** (0.84 g, 2.07 mmol) in 15 mL of dry DMF. This was cooled to 0 °C and NaH (0.17 g, 4.14 mmol, 60% suspension in mineral oil) was added portionwise. The reaction mixture was stirred for 0.5 h at room temperature then cooled to 0 °C, and benzyl bromide (0.4 mL, 3.1 mmol) was then added dropwise. The reaction mixture was warmed to room temperature and stirred at the same temperature for 1.5 h. After the reaction was complete (monitored by TLC), it was quenched by cautious addition of water (1 mL). The reaction mixture was poured into water (10 mL) and extracted with ether (3 × 20 mL). Combined ethereal extracts were washed with brine (25 mL) and dried (Na_2SO_4). Evaporation of the solvent followed by silica gel column chromatography of the residue with petroleum ether:EtOAc (98:2) as an eluent yielded **24** (0.93 g, 91%) as a colorless oil. $[\alpha]_D$ +27.5 (*c* 0.8, $CHCl_3$); IR (neat) 2929, 1644, 1454, 1367, 1253, 1068, 836, 777 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.38−7.10 (m, 10H), 5.68 (ddt, J = 16.8, 10.2, 6.6 Hz, 1H), 5.02−4.84 (m, 2H), 4.70 (d, J = 5.7 Hz, 1H), 4.46 (d, J = 11.7 Hz, 1H), 4.37 (d, J = 11.4 Hz, 1H), 4.18 (dd, J = 7.5, 5.1 Hz, 1H), 3.88 (dd, J = 7.5, 3.0 Hz, 1H), 2.89 (dt, J = 13.2, 3.3 Hz, 1H), 2.08−1.90 (m, 2H), 1.68−1.50 (m, 2H), 1.37 (s, 3H), 1.26 (s, 3H), 0.84 (s, 9H), 0.01 (s, 3H), −0.13 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 140.8, 138.7, 138.2, 128.2, 127.9, 127.7, 127.6, 127.4, 127.3, 114.8, 109.1, 80.8, 78.8, 77.5, 76.2, 72.4, 30.1, 29.8, 27.3, 27.2, 26.0, 25.8, 18.3, −4.8; HRMS for $C_{30}H_{44}O_4Si$ + Na calcd 519.2909, found 519.2907.

Preparation of (1*S*,2*R*,3*S*,4*S*)-4-(Benzyloxy)-1-phenyloct-7-ene-1,2,3-triol (25). To a solution of **24** (0.52 g, 1.05 mmol) in THF (8 mL) was added 4 N HCl (8 mL) at room temperature. The reaction mixture was allowed to stir for 6 h at the same temperature. After the reaction was complete (TLC), the reaction mixture was poured into water (20 mL) and extracted with EtOAc (3 × 20 mL). The combined organic layers were washed with brine (30 mL) and dried over Na_2SO_4. Silica gel column chromatography of the crude residue obtained after evaporation of the solvent with petroleum ether:EtOAc (6:4) as eluent gave **25** (0.30 g, 84%) as a colorless oil. $[\alpha]_D$ +24.3 (*c* 1, $CHCl_3$); IR (neat) 3413, 2923, 1643, 1454, 1074, 736 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.44−7.20 (m, 10H), 5.70 (ddt, J = 16.2, 9.6, 6.6 Hz, 1H), 4.95−4.84 (m, 2H), 4.75 (d, J = 6.6 Hz, 1H), 4.59 (d, J = 10.8 Hz, 1H), 4.39 (d, J = 11.1 Hz, 1H), 3.72−3.32 (m, 4H), 3.18 (d, J = 6.0 Hz, 1H), 2.90 (d, J = 4.8 Hz, 1H), 2.12−1.51 (m, 4H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 140.2, 137.9, 137.7, 128.6, 128.4, 128.0, 127.9, 127.8, 126.9, 115.0, 80.0, 75.4, 75.3, 72.2, 71.2, 28.8; HRMS for $C_{21}H_{26}O_4$ + Na calcd 365.1731, found 365.1729.

Preparation of (5*S*,6*S*)-5-(Benzyloxy)tetrahydro-6-((1*R*,2*S*)-1,2-dihydroxy-2-phenylethyl)pyran-2-one (26). Ozone was bubbled through a precooled (−78 °C) solution of **25** (0.43 g, 1.26 mmol) in a 4:1 mixture of CH_2Cl_2:MeOH (20 mL) containing solid $NaHCO_3$ (20 mg) until the pale blue color persisted. Excess ozone was flushed off with oxygen and dimethyl sulfide (1 mL) was added. The reaction mixture was warmed to 0 °C and stirred at the same temperature for 6 h. Then the reaction mixture was concentrated under reduced pressure and filtered through a short pad of Celite. The Celite pad was washed with EtOAc (25 mL). Evaporation of the solvent yielded the crude lactol, which was subjected to the next reaction without further purification.

To a solution of the crude lactol obtained above in 25 mL of toluene was added Ag_2CO_3 impregnated on Celite (2.1 g, 2.52 mmol, 33% impregnation) under argon atmosphere. The reaction mixture was kept at 110 °C and stirred at the same temperature for 0.5 h. It was then cooled to room temperature and filtered through a pad of Celite, and the Celite pad was washed with EtOAc (25 mL). Evaporation of the solvent and silica gel column chromatography of the residue with petroleum ether:EtOAc (4:6) as eluent yielded **26** (0.34 g, 78%) as a colorless oil. $[\alpha]_D$ +32.4 (*c* 0.8, $CHCl_3$); IR (neat) 3443, 2943, 1731, 1454, 1245, 1078, 700 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.44−7.21 (m, 10H), 4.78 (d, J = 5.7 Hz, 1H), 4.59 (d, J = 11.7 Hz, 1H), 4.34 (d, J = 11.7 Hz, 1H), 4.18 (dd, J = 3.9, 3.0 Hz, 1H), 4.05 (dd, J = 5.4, 4.2 Hz, 1H), 3.95−3.86 (m, 1H), 3.70 (br s, 1H), 3.45 (br s, 1H), 2.76−2.39 (m, 2H), 2.36−2.17 (m, 1H), 1.92−1.72 (m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 170.2, 140.2, 136.5, 128.7, 128.4, 128.3, 127.9, 126.7, 80.1, 75.0, 73.2, 70.7, 70.4, 25.5, 22.5; HRMS for $C_{20}H_{22}O_5$ + Na calcd 365.1367, found 365.1365.

Preparation of (5*S*,6*R*)-6-((1*R*,2*S*)-1,2-Bis(methoxymethoxy)-2-phenylethyl)-5-(benzyloxy)tetrahydropyran-2-one (27). To a solution of **26** (0.28 g, 0.82 mmol) in dry CH_2Cl_2 (12 mL) were added diisopropylethylamine (0.64 g, 0.9 mL, 4.92 mmol), DMAP (20 mg, 20 mol %), and MOMCl (0.25 mL, 3.28 mmol) at 0 °C. After being stirred for 15 min at 0 °C, the reaction mixture was warmed to room temperature and then refluxed for 6 h. After the reaction was complete (indicated by TLC), it was cooled to room temperature, poured into water (10 mL), and extracted with ether (3 × 20 mL). Combined ethereal extracts were washed with brine (20 mL) and dried over Na_2SO_4. Evaporation of solvent and silica gel column chromatography of the residue with petroleum ether:EtOAc (7:3) as an eluent yielded **27** (0.28 g, 80%) as a colorless oil. $[\alpha]_D$ +43.6 (*c* 1.1, $CHCl_3$); IR (neat) 2934, 1733, 1455, 1151, 1024, 702 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.44−7.14 (m, 10H), 4.84−4.38 (m, 7H), 4.28−4.10 (m, 3H), 3.34 (s, 3H), 2.95 (s, 3H), 2.75−2.54 (m, 2H), 2.43−2.31 (m, 1H), 2.04−1.88 (m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 169.9, 138.0, 137.1, 128.6, 128.3, 128.2, 128.0, 127.8, 127.0, 98.0, 95.1, 83.1, 78.9, 77.1, 70.3, 68.4, 56.3, 56.0, 25.4, 22.7; HRMS for $C_{24}H_{30}O_7$ + Na calcd 453.1892, found 453.1889.

Preparation of (5*S*,6*R*)-6-((1*R*,2*S*)-1,2-Bis(methoxymethoxy)-2-phenylethyl)-5-(benzyloxy)-5,6-dihydropyran-2-one (28). To a precooled (−78 °C) solution of **27** (0.09 g, 0.21 mmol) in dry THF (5.0 mL) was added LHMDS (0.63 mL of 1 M solution in THF, 0.63 mmol) dropwise, under argon atmosphere. The reaction mixture was slowly warmed to −50 °C and stirred for 1 h. It was then cooled to −78 °C and a THF (2 mL) solution of phenylselenyl bromide (0.074 g, 0.32 mmol) was introduced. It was stirred for 1 h at the same temperature and after the reaction was complete (TLC), it was quenched with saturated NH_4Cl (5 mL) and extracted with ether (3 × 10 mL). Combined ethereal extracts were washed with brine (15 mL) and dried over Na_2SO_4. Evaporation of solvent under reduced pressure at room temperature afforded the crude selenide, which was used as such in the next step without further purification.

To a precooled (0 °C) solution of crude selenide obtained above in 6 mL of CH_2Cl_2 was added pyridine (0.04 mL, 0.42 mmol) and H_2O_2 (1 mL of 30% w/v in water) and the resulting mixture was stirred for 0.5 h at the same temperature. After the reaction was complete (monitored by TLC), water (10 mL) was added to the reaction mixture and extracted with CH_2Cl_2 (3 × 10 mL). The combined organic extracts were washed with brine (25 mL) and dried over Na_2SO_4. The solvent was removed under reduced pressure and the residue thus obtained was purified by silica gel column chromatography with petroleum ether:EtOAc (7:3) as an eluent to give **28** (0.06 g, 69%) as a colorless oil. $[\alpha]_D$ +20.4 (*c* 1.2, $CHCl_3$); IR (neat) 2984, 1728, 1348, 1272, 1100, 874, 718 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.44−7.22 (m, 10H), 7.02 (dd, J = 9.9, 5.7 Hz, 1H), 6.24 (d, J = 9.9 Hz, 1H), 4.90 (d, J = 2.1 Hz, 1H), 4.76−4.44 (m, 6H), 4.40 (dd, J = 5.4, 3.3 Hz, 1H), 4.27 (dd, J = 8.1, 2.4 Hz, 1H), 4.18 (d, J = 6.6 Hz, 1H), 4.05 (s, 3H), 3.0 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 162.6, 141.9, 138.0, 137.1, 128.7, 128.4, 128.3, 128.1, 127.1, 124.8, 98.1, 95.2, 80.9, 78.1, 77.2, 70.9, 65.3, 56.3, 56.1; HRMS for $C_{24}H_{28}O_7$ + Na calcd 451.1735, found 451.1733.

Preparation of (5*S*,6*R*)-5,6-Dihydro-5-hydroxy-6-((1*R*,2*S*)-1,2-dihydroxy-2-phenylethyl)pyran-2-one (29). To a precooled (0 °C) solution of **28** (0.07 g, 0.16 mmol) in dry CH_2Cl_2 (6.0 mL) was added $TiCl_4$ (1.6 mL of 1 M solution in CH_2Cl_2, 1.6 mmol). The reaction mixture was warmed to room temperature and stirred for 1.5 h. After the reaction was complete (monitored by TLC), it was cautiously quenched by addition of saturated $NaHCO_3$ (4 mL). The reaction mixture was poured into water (5 mL) and extracted with EtOAc (4 × 10 mL). The combined organic layers were washed with brine (10 mL), dried over Na_2SO_4. Evaporation of solvent followed by column chromatography of the residue with petroleum ether:EtOAc (2:8) as an eluent gave **29** (0.03 g, 78%) as a white solid. Mp 126−128 °C; $[\alpha]_D$ +86 (*c* 0.6, EtOH) [lit.[3] mp 127−129 °C; $[\alpha]_D$ +88 (*c* 0.5, EtOH)]; IR (neat) 3401, 2919, 1715, 1264, 1026, 706 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.48−7.18 (m, 5H), 7.09 (dd, J = 9.6, 6.0 Hz, 1H), 6.05 (d, J = 9.9 Hz, 1H), 5.04 (d, J = 3.3 Hz, 1H), 4.51 (dd, J = 6.0, 2.7 Hz, 1H), 4.35 (dd, J = 6.6, 3.0 Hz, 1H), 4.18 (dd, J = 6.6, 3.3 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 167.1, 148.7, 146.1, 131.4, 130.5, 130.1, 125.3, 84.4, 77.9, 75.8, 63.7; HRMS for $C_{13}H_{14}O_5$ + Na calcd 273.0741, found 273.0739.

Preparation of (+)-Goniopypyrone (3). A solution of triol **29** (0.045 g, 0.18 mmol) in dry THF (10 mL) containing DBU (0.01 mL, 0.09 mmol) was stirred at room temperature for 4 h. After the reaction was complete (TLC), the reaction mixture was filtered through a short pad of silica gel topped with Celite. Residue obtained after removal of solvent from filtrate in vacuo gave a white solid, which was further purified by silica gel column chromatography with petroleum ether:EtOAc (3:7) as eluent to yield **3** (0.034 g, 75%) as a white solid. Mp 179−182 °C; $[\alpha]_D$ +52.8 (*c* 0.5, EtOH) [lit.[8b] mp 182−184 °C; $[\alpha]_D$ +54 (*c* 0.4, EtOH)]; IR (neat) 3397, 2919, 1741, 1453, 1224, 1057, 733 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.53−7.32 (m, 5H), 5.03 (d, J = 1.2 Hz, 1H), 4.82 (dd, J = 6.0, 3.6 Hz, 1H), 4.48 (dd, J = 4.5, 2.1 Hz, 1H), 4.16−3.98 (m, 3H), 3.10 (dd, J = 19.5, 1.8 Hz, 1H), 3.01 (dd, J = 19.5, 4.8 Hz, 1H), 2.16 (d, J = 3.3 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 167.8, 135.8, 129.1, 128.7, 126.2, 72.6, 70.9, 70.3, 70.1, 64.4, 35.2; HRMS for $C_{13}H_{14}O_5$ + Na calcd 273.0741, found 273.0739.

Preparation of 4(*S*)-((*S*)-1-(Hydroxy)phenylmethyl)-5(*R*)-((*S*)-1-(benzyloxy)pent-4-enyl)-2,2-dimethyl-1,3-dioxolane (30). To a precooled (0 °C) solution of **24** (0.92 g, 1.85 mmol) in dry THF (18 mL) was added TBAF (3.7 mL of 1 M solution in THF, 3.7 mmol) under argon atmosphere. The reaction mixture was allowed to warm to room temperature and stirred at the same temperature for 1.5 h. Water (15 mL) was added to the reaction mixture with stirring for 10 min. The reaction mixture was then extracted with ether (3 × 25 mL). Combined ethereal extracts were washed with brine (30 mL) and dried (Na_2SO_4). Evaporation of the solvent and silica gel column chromatography of the residue with petroleum ether:EtOAc (8:2) as an eluent yielded **30** (0.67 g, 94%) as a colorless oil. $[\alpha]_D$ −20 (*c* 1, $CHCl_3$); IR (neat) 3453, 2919, 1637,

1454, 1251, 1068, 765 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.40−7.15 (m, 10H), 5.66 (ddt, J = 16.2, 9.6, 6.6 Hz, 1H), 4.99−4.85 (m, 2H), 4.64 (t, J = 5.4 Hz, 1H), 4.44 (d, J = 11.4 Hz, 1H), 4.32 (d, J = 11.4 Hz, 1H), 4.23 (dd, J = 7.8, 6.0 Hz, 1H), 3.99 (dd, J = 7.8, 3.3 Hz, 1H), 3.02 (dd, J = 5.1, 1.5 Hz, 1H), 2.90 (dt, J = 12.0, 3.3 Hz, 1H), 2.08−1.92 (m, 2H), 1.70−1.48 (m, 4H), 1.43 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 140.0, 138.2, 138.0, 128.4, 128.3, 128.1, 127.8, 127.6, 126.9, 114.9, 109.5, 80.5, 78.6, 76.9, 74.8, 72.5, 29.7, 29.6, 27.4, 27.2; HRMS for $C_{24}H_{30}O_4$ + Na calcd 405.2044, found 405.2042.

Preparation of 4(*S*)((*R*)-1-(Hydroxy)phenylmethyl)-5(*R*)-((*S*)-1-(benzyloxy)pent-4-enyl)-2,2-dimethyl-1,3-dioxolane (31). To a precooled (0 °C) solution of **30** (0.72 g, 1.88 mmol) in dry THF (20 mL) were added triphenylphosphine (0.98 g, 3.76 mmol) and *p*-nitrobenzoic acid (0.62 g, 3.76 mmol) under argon atmosphere and the mixture was allowed to stir for 10 min. DIAD (0.6 mL, 2.82 mmol) was introduced into the reaction mixture over a period of 15 min at the same temperature. The reaction mixture was warmed to room temperature and stirred at room temperature for 1 h. After the reaction was complete (TLC), solvent was removed under reduced pressure and the crude ester thus obtained was purified by column chromatography to yield the corresponding *p*-nitrobenzoate ester (0.94 g, 94%) as a pale yellow solid. Mp 118 °C; $[\alpha]_D$ +48 (*c* 1.2, $CHCl_3$); IR (neat) 2930, 1733, 1454, 1154, 1023, 763 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.40−8.08 (m, 4H), 7.46−7.18 (m, 10H), 6.17 (d, J = 4.8 Hz, 1H), 5.70 (ddt, J = 16.8, 10.2, 6.6 Hz), 5.16−4.86 (m, 2H), 4.68−4.35 (m, 3H), 4.12 (dd, J = 7.5, 3.3 Hz, 1H), 3.20 (dt, J = 12.9, 0.3 Hz, 1H), 2.22−2.02 (m, 2H), 1.82−1.64 (m, 2H), 1.43 (s, 3H), 1.23 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 163.5, 150.6, 138.2, 137.9, 135.8, 135.2, 130.8, 128.7, 128.4, 128.3, 127.8, 127.7, 127.5, 123.5, 115.1, 110.0, 79.1, 78.3, 77.4, 76.8, 72.4, 29.9, 29.7, 27.2, 27.1; HRMS for $C_{31}H_{33}NO_7$ + Na calcd 554.2157, found 554.2155.

To a methanol (16 mL) solution of *p*-nitrobenzoate ester (0.94 g, 1.8 mmol) obtained above was added K_2CO_3 (0.5 g, 3.6 mmol) with stirring for 0.5 h at room temperature. After the reaction was complete (TLC), the reaction mixture was poured into water (30 mL) and extracted with ether (3 × 25 mL). Combined ethereal extracts were washed with brine (25 mL) and dried over Na_2SO_4. Evaporation of the solvent and silica gel column chromatography of the residue with petroleum ether:EtOAc (8:2) as eluent afforded **31** (0.62 g, 92%) as a colorless oil. $[\alpha]_D$ +12.4 (*c* 0.6, $CHCl_3$); IR (neat) 3423, 2927, 1621, 1452, 1199, 917, 701 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.44−7.18 (m, 10H), 5.73 (ddt, J = 16.8, 10.2, 6.6 Hz, 1H), 5.10−4.88 (m, 2H), 4.85 (dd, J = 5.1, 1.2 Hz, 1H), 4.44 (d, J = 11.4 Hz, 1H), 4.30−4.18 (m, 2H), 4.09 (dd, J = 7.8, 2.7 Hz, 1H), 3.24 (d, J = 1.5 Hz, 1H), 2.83 (dt, J = 13.2, 2.7 Hz, 1H), 2.10−1.96 (m, 2H), 1.72−1.50 (m, 2H), 1.41 (s, 3H), 1.38 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 139.5, 138.0, 130.6, 128.3, 128.2,127.8, 127.7, 126.3, 123.5, 114.9, 108.9, 79.6, 78.1, 77.4, 72.9, 72.6, 29.9, 29.8, 27.1, 26.9; HRMS for $C_{24}H_{30}O_4$ + Na calcd 405.2044, found 405.2042.

Preparation of (1*R*,2*R*,3*S*,4*S*)-4-(Benzyloxy)-1-phenyloct-7-ene-1,2,3-triol (32). To a solution of **31** (0.66 g, 1.73 mmol) in THF (8.0 mL) was added 4 N HCl (8.0 mL) at room temperature. The reaction mixture was stirred at room temperature for 6 h, poured into water (10 mL), and extracted with EtOAc (3 × 20 mL). The combined organic layers were washed with brine (30 mL), dried over Na_2SO_4, and concentrated. Silica gel column chromatography of crude residue obtained after evaporation of the solvent with petroleum ether:EtOAc (6:4) as an eluent afforded **32** (0.52 g, 90%) as an oil. $[\alpha]_D$ −40.4 (*c* 0.8, $CHCl_3$); IR (neat) 3419, 2928, 1640, 1453, 1093, 742, 699 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.46−7.18 (m, 10H), 5.72 (ddt, J = 17.1, 10.8, 6.6 Hz, 1H), 5.02−4.84 (m, 3H), 4.54 (d, J = 11.4 Hz, 1H), 4.35 (d, J = 11.4 Hz, 1H), 4.02−3.69 (m, 3H), 3.63−3.40 (m, 2H), 3.23 (br s, 1H), 2.18−1.50 (m, 4H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 140.8, 138.0, 137.7, 128.5, 128.4, 127.9, 127.8, 127.5, 125.9, 114.9, 80.3, 76.0, 74.2, 72.0, 70.1, 29.0, 28.8; HRMS for $C_{21}H_{26}O_4$ + Na calcd 365.1731, found 365.1729.

Preparation of (5*S*,6*S*)-5-(Benzyloxy)tetrahydro-6-((1*R*,2*R*)-1,2-dihydroxy-2-phenylethyl)pyran-2-one (33). 33 was synthesized by using a procedure similar to that described for **26**. $[\alpha]_D$ −17.5 (*c* 0.6, $CHCl_3$); IR (neat) 2973, 1741, 1454, 1238, 1024, 919, 703 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.50−7.18 (m, 10H), 4.86 (d, J = 7.2 Hz, 1H), 4.68 (t, J = 2.4 Hz, 1H), 4.56 (d, J = 11.4 Hz, 1H), 4.30 (d, J = 11.4 Hz, 1H), 4.07 (dd, J = 7.5, 2.4 Hz, 1H), 3.92−3.84 (m, 1H), 3.69 (br s, 1H), 3.07 (br s, 1H), 2.76−2.44 (m, 2H), 2.32−2.14 (m, 1H), 2.06−1.78 (m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 170.4, 141.2, 136.4, 128.7, 128.4, 128.3, 127.9, 127.8, 126.9, 78.6, 75.1, 72.9, 70.4, 25.5, 22.8; HRMS for $C_{20}H_{22}O_5$ + Na calcd 365.1367, found 365.1365.

Preparation of (5*S*,6*R*)-6-((1*R*,2*R*)-1,2-Bis(methoxymethoxy)-2-phenylethyl)-5-(benzyloxy)tetrahydropyran-2-one (34). 34 was synthesized by using a procedure similar to that described for **27**. $[\alpha]_D$ −32.2 (*c* 0.8, $CHCl_3$); IR (neat) 2987, 1743, 1641, 1454, 1373, 1232, 1027, 873, 703 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.46−7.18 (m, 10H), 4.86−4.71 (m, 3H), 4.62 (d, J = 6.3 Hz, 1H), 4.53 (d, J = 6.3 Hz, 1H), 4.46−4.34 (m, 2H), 4.27 (dd, J = 7.8, 2.7 Hz, 1H), 4.04 (d, J = 11.7 Hz, 1H), 3.83 (dd, J = 5.1, 2.7 Hz, 1H), 3.38 (s, 3H), 3.34 (s, 3H), 2.69−2.36 (m, 2H), 2.26−2.08 (m, 1H), 1.90−1.76 (m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 170.0, 137.9, 137.1, 128.5, 128.4, 128.2, 128.1, 127.9, 127.8, 98.0, 94.2, 81.4, 78.0, 76.8, 69.8, 68.6, 56.3, 55.7, 25.8, 22.7; HRMS for $C_{24}H_{30}O_7$ + Na calcd 453.1892, found 453.1889.

Preparation of (5*S*,6*R*)-6-((1*R*,2*R*)-1,2-Bis(methoxymethoxy)-2-phenylethyl)-5-(benzyloxy)-5,6-dihydropyran-2-one (35). 35 was synthesized by using a procedure similar to that described for **28**. $[\alpha]_D$ +43.6 (*c* 1.1, $CHCl_3$); IR (neat) 2931, 1729, 1454, 1255, 1024, 700 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.48−7.22 (m, 10H), 6.78 (dd, J = 9.9, 4.2 Hz, 1H), 6.05 (d, J = 9.9 Hz, 1H), 4.81 (d, J = 5.1 Hz, 1H), 4.73 (d, J = 6.6 Hz, 1H), 4.68−4.28 (m, 7H), 4.21 (t, J = 4.5 Hz, 1H), 3.34 (s, 3H), 3.15 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 157.9, 142.6, 137.9, 136.9, 128.6, 128.5, 128.3, 128.2, 128.1, 128.0, 123.4, 97.8, 94.1, 78.7, 76.9, 76.4, 70.9, 66.3, 56.1, 55.8; HRMS for $C_{24}H_{28}O_7$ + Na calcd 451.1735, found 451.1733.

Preparation of (+)-Goniotriol (4). 4 was synthesized by using a procedure similar to that described for **29**. Mp 168−170 °C; $[\alpha]_D$ +119 (*c* 0.4, MeOH) [lit.[11a] mp 170 °C; $[\alpha]_D$ +121 (MeOH)]; IR (neat) 3404, 1715, 1383, 1264, 1099, 922, 828, 705 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.51−7.22 (m, 5H), 7.02 (dd, J = 9.9, 6.0 Hz, 1H), 6.08 (d, J = 9.9 Hz, 1H), 4.73 (d, J = 7.8 Hz, 1H), 4.59 (t, J = 3.6 Hz, 1H), 4.43 (dd, J = 5.4, 2.7 Hz, 1H), 4.17 (dd, J = 8.1, 4.2 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 166.0, 146.4, 143.4, 129.2, 128.9, 128.8, 123.0, 80.3, 75.6, 73.9, 63.5; HRMS for $C_{13}H_{14}O_5$ + Na calcd 273.0741, found 273.0739.

Preparation of (2*R*,3*R*,3a*S*,7a*S*)-Tetrahydro-3-hydroxy-2-phenyl-2*H*-furo[3,2-*b*]pyran-5(6*H*)-one (37). Ozone was bubbled through a precooled (−78 °C) solution of **36** (0.33 g, 1.4 mmol) in 4:1 CH_2Cl_2:MeOH (15 mL) containing solid $NaHCO_3$ (0.03 g) until the pale blue color persisted. Excess ozone was flushed off with oxygen and Me_2S (1 mL) was added. The reaction mixture was warmed to 0 °C, then stirred at the same temperature for 6 h. The reaction mixture was concentrated under reduced pressure and filtered through a short pad of Celite. The Celite pad was washed with EtOAc (25 mL). Evaporation of the solvent yielded the crude lactol, which was subjected to the next reaction without further purification.

To a solution of crude lactol obtained above in 15 mL of toluene was added Ag_2CO_3 impregnated on Celite (2.3 g, 2.8 mmol, 33% impregnation) under an argon atmosphere. The reaction mixture was kept at 110 °C and stirred at the same temperature for 0.5 h. It was then cooled to room temperature then filtered through a pad of Celite and the Celite pad was washed with EtOAc (25 mL). Evaporation of the solvent and silica gel column chromatography of the residue with petroleum ether:EtOAc (4:6) as an eluent yielded

37 (0.27 g, 82%) as a colorless oil. $[\alpha]_D$ +24.3 (*c* 0.7, $CHCl_3$); IR (neat) 3400, 2922, 2851, 1740, 1633, 1453, 1165, 1057, 734 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.48−7.22 (m, 5H), 4.76 (dd, J = 5.1, 2.4 Hz, 1H), 4.62 (d, J = 6.3 Hz, 1H), 4.44 (dd, J = 8.7, 3.9 Hz, 1H), 4.19 (d, J = 6.0 Hz, 1H), 3.95 (d, J = 6.0 Hz, 1H), 2.69 (ddd, J = 16.8, 10.5, 5.7 Hz, 1H), 2.46 (td, 17.1, 5.1 Hz, 1H), 2.28−2.02 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 171.6, 138.3, 128.6, 128.2, 126.0, 88.5, 85.1, 84.3, 72.1, 26.0, 22.9; HRMS for $C_{13}H_{14}O_4$ + Na calcd 257.0792, found 257.0790.

Preparation of (−)-Etharvensin (6). To a precooled (0 °C) solution of altholactone **5** (0.016 g, 0.068 mmol) in EtOH (4 mL) was added dropwise concentrated H_2SO_4 (96%, 0.5 mL). The reaction mixture was warmed to room temperature and refluxed for 1.5 h. After reaction was complete (TLC), water (5 mL) was added to the reaction mixture and extracted with CH_2Cl_2 (3 × 10 mL). The combined organic extracts were washed with brine (15 mL) and dried over Na_2SO_4. The solvent was removed under reduced pressure and the residue obtained was purified by silica gel column chromatography with petroleum ether:EtOAc (1:1) as an eluent to give **6** (0.017 g, 89%) as a colorless oil. $[\alpha]_D$ −6.1 (*c* 1.1, EtOH) [lit.[14] $[\alpha]_D$ −6.5 (*c* 2.0, EtOH)]; IR (neat) 3460, 2936, 1732, 1611, 1514, 1250, 1055, 821 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.42−7.22 (m, 5H), 4.90 (dd, J = 4.8, 1.8 Hz, 1H), 4.69 (d, J = 6.0 Hz, 1H), 4.38 (t, J = 3.9 Hz, 1H), 4.29 (dd, J = 6.0, 2.1 Hz, 1H), 4.02 (dt, J = 6.0, 3.6 Hz, 1H), 3.65 (q, J = 6.9 Hz, 2H), 3.0 (br s, 1H), 2.85 (dd, J = 16.2, 3.6 Hz, 1H), 2.70 (dd, J = 16.2, 6.0 Hz, 1H), 1.22 (t, J = 6.9 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 169.1, 128.7, 128.4, 126.1, 86.8, 86.1, 83.7, 75.9, 72.8, 65.3, 33.2, 15.3; HRMS for $C_{15}H_{18}O_5$ + Na calcd 301.1054, found 301.1052.

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Supporting Information Available: General experimental procedures and spectroscopic data for the compounds and copies of ^1H NMR and ^{13}C NMR spectra. This material is available free of charge via the Internet at http://pubs.acs.org.

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(14) Bermejo, A.; Blazquez, M. A.; Serrano, A.; Zafra-Polo, M. C.; Cortes, D. J. *J. Nat. Prod.* **1997**, *60*, 1338.