Total Syntheses of (+)-Secosyrins 1 and 2 and (+)-Syributins 1 and 2

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First total syntheses of (+)-secosyrins 1 and 2 and total syntheses of (+)-syributins 1 and 2 are described. The two chiral centers of diisopropyl tartrate were incorporated into target natural products. Stereoselective construction of the spiro skeleton of secosyrins could be realized by taking advantage of an alkyne−cobalt complex. The synthesis of these compounds established their relative and absolute stereochemistry unambiguously.

Introduction

In 1993, syringolides 1 and 2 (**1** and **2**, respectively, Figure 1), novel nonproteinaceous low molecular weight metabolites, were isolated from *Pseudomonas syringae* pv. tomato.[1] These oxygen-rich tricyclic compounds **1** and **2** have been found to be produced by bacteria expressing avirulence gene D and to elicit a hypersensitive reaction in soybean plants carrying the resistance gene *Rpg4*. Because of biological interest as well as the intriguing oxygen-rich tricyclic structure of these elicitors, several papers[2] on the total syntheses of syringolides 1 and 2 have been published. Two years after the first report on the isolation of **1** and **2**, Sims and co-workers[3] isolated four structurally related compounds, secosyrins 1 and 2 (**3** and **4**, respectively) and syributins 1 and 2 (**5** and **6**, respectively) from the same medium. The structures of the four newly isolated compounds were elucidated by (i) spectroscopic evidence including comparison of NMR data with those of syringolides 1 and 2, whose stereochemistry was unambiguously established, and (ii) chemical methods. Although compounds **3**−**6** have rather simpler structures and are not active elicitors, in sharp contrast to structurally more complex syringolides 1 and 2, isolation of the former is particularly of interest since they provide some suggestions for understanding their biosynthetic pathway.

During our investigation on the total synthesis of the title compounds, Honda et al.[2f] completed the first total synthesis of (+)-syributin 1 (**5**) based on Sharpless asymmetric dihydroxylation of an alkenyl butenolide derivative. In this paper, we describe the first stereoselective total syntheses of (+)-secosyrin 1 (**3**)[4] and (+)-secosyrin 2 (**4**), as well as syntheses of (+)-syributin 1 (**5**) and (+)-syributin 2 (**6**) from the common starting material diisopropyl D-tartrate.

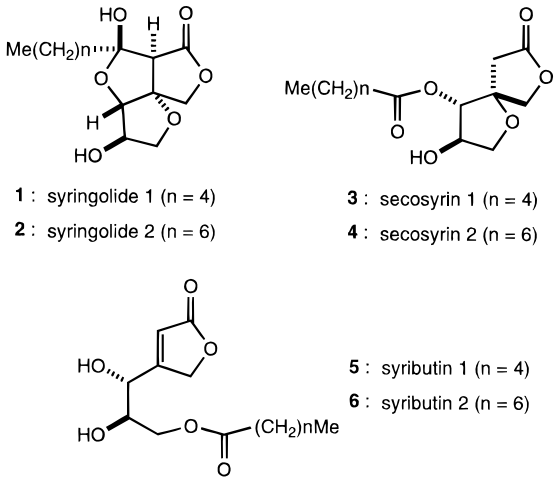

Figure 1.

Results and Discussion

By taking the synthesis of all γ-lactone natural products **1**−**6** into account, our synthetic plan consisted of the successive transformation of the simplest syributins (**5** and **6**) to more complex syringolides (**1** and **2**) through intermediate secosyrins (**3** and **4**) according to the retrobiosynthetic process proposed by Sims.[3] We envisioned that the two stereogenic centers of D-tartaric acid would be easily incorporated into the triol residue attached to the butenolide skeleton of syributins (**5** and **6**). Acyl group migration on a primary alcohol to a secondary hydroxy group would be followed by intramolecular Michael type cyclization, resulting in formation of secosyrins (**3** and **4**). Dieckmann type intramolecular ester condensation reaction of **3** and **4** under proper conditions would produce syringolides (**1** and **2**). This straightforward method might be the best method for efficient syntheses of all γ-lactone natural products **1**−**6**.

Synthesis of (+)-Syributin 1 and (+)-Syributin 2. As our point of departure, the acetonide derivative **7**,[5] prepared from diisopropyl D-tartrate, was oxidized under Swern conditions to give the aldehyde, which was subsequently exposed to a Horner−Emmons reaction with ethyl (diethylphosphono)acetate producing (*E*)-ester (+)-**8**

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(1) (a) Smith, M. J.; Mazzola, E. P.; Sims, J. J.; Midland, S. L.; Keen, N. T.; Burton, V.; Staylon, M. M. *Tetrahedron Lett.* **1993**, *34*, 223. (b) Midland, S. L.; Keen, N. T.; Sims, J. J.; Midland, M. M.; Staylon, M. M.; Burton, V.; Smith, M. J.; Mazzola, E. P.; Graham, K. J.; Clardy, J. *J. Org. Chem.* **1993**, *58*, 2940.

(2) (a) Wood, J. L.; Jeong, S.; Salcedo, A.; Jenkins, J. *J. Org. Chem.* **1995**, *60*, 286. (b) Kuwahara, S.; Moriguchi, M.; Miyagawa, K.; Konno, M.; Komada, O. *Tetrahedron Lett.* **1995**, *36*, 3201. (c) Kuwahara, S.; Moriguchi, M.; Miyagawa, K.; Konno, M.; Komada, O. *Tetrahedron* **1995**, *32*, 8809. (d) Henschke, J. P.; Rickards, R. W. *Tetrahedron Lett.* **1996**, *37*, 3557. (e) Ishihara, J.; Sugimoto, T.; Murai, A. *Synlett* **1996**, 335. (f) Honda, T.; Mizutani, H.; Kanai, K. *J. Org. Chem.* **1996**, *61*, 9374.

(3) Midland, S. L.; Keen, N. T.; Sims, J. J. *J. Org. Chem.* **1995**, *60*, 1118.

(4) The first total syntheis of (+)-secosyrin 1 (**3**) was reported as a preliminary communication: Mukai, C.; Moharram, S. M.; Hanaoka, M. *Tetrahedron Lett.* **1997**, *38*, 2511.

(5) Savage, I.; Thomas, E. J. *J. Chem. Soc., Chem. Commun.* **1989**, 717.

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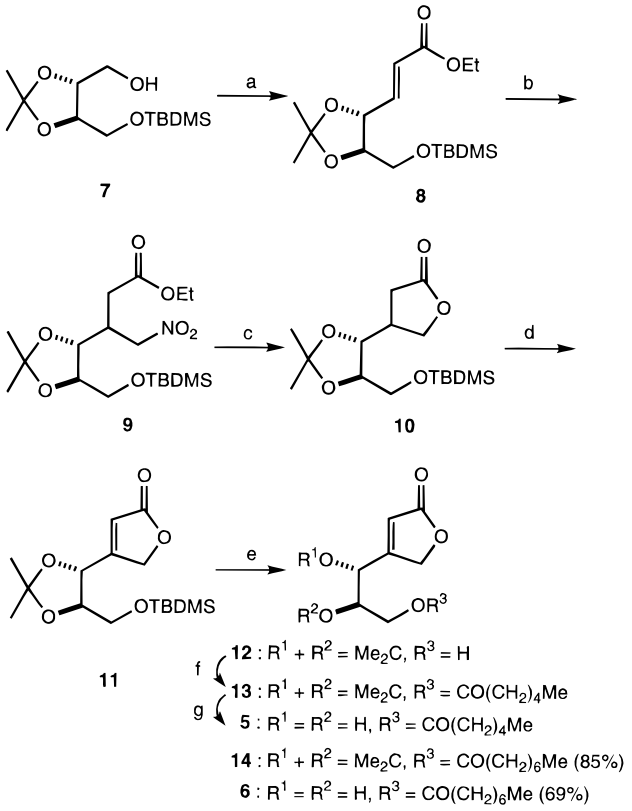
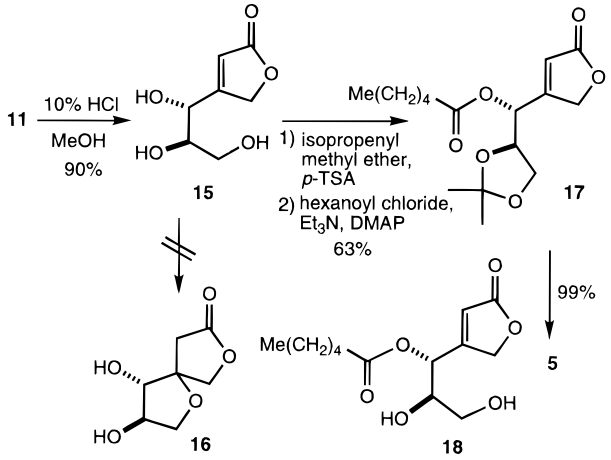
Scheme 1[a]



[a] Reaction conditions: (a) (1) Swern oxidation, (2) $(EtO)_2POCH_2CO_2Et$, NaH 85%; (b) CH_3NO_2, DBU, 80%; (c) (1) KOH, (2) $KMnO_4$, $MgSO_4$, H_2O, (3) $NaBH_4$, 72%; (d) (1) LHMDS, TMSCl, (2) $Pd(OAc)_2$, benzoquinone, 74%; (e) TBAF, HF; (f) hexanoyl chloride, Et_3N, DMAP, 81%; (g) 10% HCl, 72%

in 85% yield (Scheme 1). Introduction of the C_1-unit was realized when **8** was treated with nitromethane in the presence of 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU)[6] to furnish (+)-**9** in 80% yield. The stereochemistry at the β position of **9** is not determined yet, since the newly generated chiral center would disappear in further step. However, it should be mentioned that **9** is made up of a single isomer and is free from other stereoisomers. Treatment of **9** with potassium hydroxide/potassium permanganate ($KMnO_4$)[7] and sodium borohydride ($NaBH_4$) effected conversion of the nitromethyl group into an aldehyde functionality; reduction and spontaneous lactone formation provide the γ-lactone derivative (+)-**10** in 72% yield. To prepare the butenolide skeleton, conventional selenoxide chemistry[8] was applied to **10** to afford the desired (−)-**11** in rather lower yield (40%). Alternatively and more efficiently, (−)-**11** was obtained in 74% yield when trimethylsilyl enol ether derivative of **10** was exposed to palladium diacetate.[9] The final phase required for synthesis of syributins 1 and 2 (**5** and **6**) is deprotection and acylation. Thus desilylation of **11** with tetra-*n*-butylammonium fluoride (TBAF) and hydrofluoric acid gave the primary alcohol **12**, which was, without isolation, acylated with hexanoyl chloride to leave (+)-**13** in 81% yield from **11**. (+)−Syributin 1 (**5**) $[[\alpha]^{20}_D$ +7.8 (*c* 0.33, $CHCl_3$); lit.[10] $[\alpha]_D$ +7.19 (*c* 0.86, CH_2Cl_2); lit.[2f] $[\alpha]^{24}_D$ +6.6 (*c* 0.6, $CHCl_3$)] was obtained in 72% yield from **13** under acidic condition. On the other hand, (+)-syributin 2 (**6**) $[[\alpha]^{17}_D$ +5.9 (*c* 0.18, $CHCl_3$)] was also synthesized in 69% yield from **14** *via* **12** (85% from **11**). Synthetic syributins 1 and 2 (**5** and **6**) were identified by comparison of the ^1H NMR spectra with those of the naturally occurring compounds.

Scheme 2

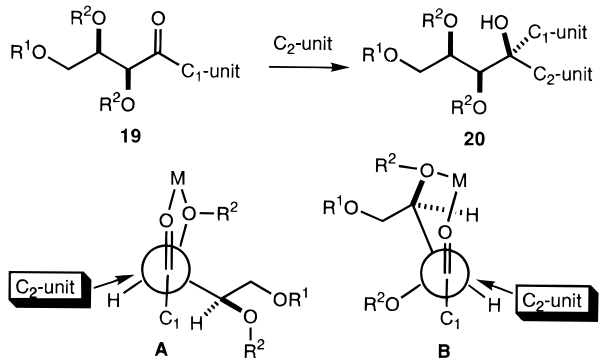


We next tried to convert the simplest monocyclic butenolide derivatives into the corresponding more complex bicyclic spiro derivatives. Acetonide and silyl protecing groups on the three hydroxy groups of the butenolide **11** were removed by treatment with 10% hydrochloric acid in methanol to give triol (−)-**15** in 90% yield (Scheme 2). Intramolecular Michael type reaction of **15** leading to **16** under both basic and acidic conditions such as sodium hydride (NaH) in THF, lithium hexamethyldisilazide (LHMDS) in THF, potassium *tert*-butoxide ($KOBu^t$) in THF, KOH in EtOH, *p*-toluenesulfonic acid (*p*-TSA) in THF, trifluoroacetic acid (TFA) in THF, and zinc iodide (ZnI_2) in THF unfortunately afforded an intractable mixture or recovery of starting **15**. It was at this point that we noticed that the intramolecular Michael type reaction of **15** was harder than imagined. Before changing this strategy, we investigated the direct transformation of **17** to target spiro compound **3**. Compound (−)-**17** was prepared from **15** by successive acetonide formation[11] and acylation in 63% yield. Exposure of **17** to deacetonization conditions (20% hydrochloric acid in THF at 0 °C) was shown to give (+)-syributin 1 (**5**) instead of (+)-secosyrin 1 (**3**), accompanied with acyl migration in a quantitative yield. Deacetonized compound **18** without acyl migration could be detected on TLC, but it was never isolated in more than trace quantities. Presumably isomerization of **18** to **5** occurred quickly during the isolation process. Similar unsuccessful results[2f] on conversion of monocyclic compounds to the corresponding spiro ones under several conditions were reported by Honda et al. Because the first scenario of our synthesis of all types of γ-lactone natural products based on a retrobiosynthetic pathway was difficult, we devised an alternative synthetic pathway for spiro derivatives secosyrins 1 and 2 (**3** and **4**).

Synthesis of (+)-Secosyrin 1 and (+)-Secosyrin 2. The most significant point for synthesis of secosyrins 1 and 2 (**3** and **4**) must be the stereoselective construction of the quaternary center of **3** and **4**. We anticipated that

(6) Ono, N.; Kamimura, A.; Kaji, A. *Synthesis* **1984**, 226.
(7) Steliou, K.; Poupart, M.-A. *J. Org. Chem.* **1985**, *50*, 4971.
(8) Reich, H. J.; Renga, J. M.; Reich, I. L. *J. Am. Chem. Soc.* **1975**, *97*, 5434.
(9) Ito, Y.; Hirao, T.; Saegusa, T. *J. Org. Chem.* **1978**, *43*, 1011.
(10) Private communication from Professor J. J. Sims.
(11) Fanton, E.; Gelas, J.; Horton, D. *J. Chem. Soc., Chem. Commun.* **1980**, 21.

Scheme 3



the compound having an oxygen functionality at the α position like **19** would react with the C_2-unit via the chelation model transition state **A** with a transient five-membered ring, leading to the adduct **20** with desired stereochemistry of **3** and **4**. However, the possibility of production of undesired product arising from the transition state **B** with a six-membered ring due to chelation with the *β* oxygen functionality and/or a nonchelating transtion state could not be ruled out.

With the above consideration, we first prepared the ketone derivative **23** with an acetylenic moiety as a C_1-unit. The hydroxy compound (−)-**21**,[12] obtained from diisopropyl tartrate, was consecutively oxidized under Swern conditions and exposed to lithium phenylacetylide to give **22** in 80% yield, which was again oxidized under Swern condition to afford (−)-**23** in 90% yield. Stereoselective introduction of the C_2-unit was realized when **23** was treated with lithium enolate derived from *tert*-butyl thioacetate at −78 °C in THF to provide (−)-**24** in 94% yield as a sole product. Configuration of the newly generated quaternary carbon center of **24** was uncertain at this stage, although we expected that reaction would have proceeded via the five-membered transition state such as **A** (Scheme 3) and resulted in exclusive formation of the desired product. To confirm the stereochemistry of **24**, it was converted into rigid spiro compound **29** by conventional means. Desilylation of **24** with TBAF gave (−)-**25** (95%), which was subsequently treated with *p*-toluenesulfonyl chloride (*p*-TsCl), triethylamine (Et_3N), and (dimethylamino)pyridine (DMAP) to produce the tetrahydrofuran derivative (−)-**26** in 89% yield. A NOE experiment with **26** revealed 6.5% enhancement between C_4−H and C_9−H.[13] This observation indicated that the configuration of the newly constructed quaternary center of **24** was not that of **3** and **4**. Hydrogenation of **26** in the presence of Lindlar catalyst in ethyl acetate gave (−)-**27** in 75% yield. An alternative procedure for producing **27** was examined. Half-reduction of **25** furnished (+)-**28** (78%), ring closure of which was undertaken according to the procedure described for conversion of **25** to **26,** providing **27** in 88% yield. Upon successive treatment with ozone,[14] $NaBH_4$, and DBU, **27** underwent oxidative cleavage of its olefinic portion, reduction, and ring closure to afford spiro compound (+)-**29** in 72% yield. X-ray crystallographic analysis[15] of (+)- **29** unambiguously established its stereochemistry as depicted in Scheme 4, thereby **24** was confirmed to have an undesired quaternary carbon center.

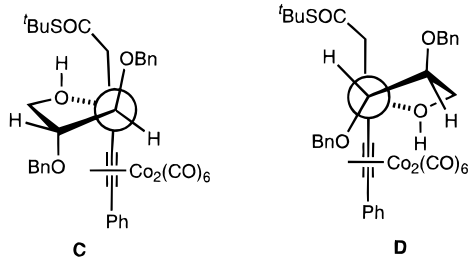


Figure 2.

Debenzylation of **29** under hydrogenolysis conditions in the presence of 10% Pd−C produced diol (+)-**30** in 94% yield. Selective monoacylation proceeded when **30** was exposed to hexanoic anhydride in THF in the presence of Et_3N and DMAP to provide (+)-5-episecosyrin 1 (**31**) [$[\alpha]^{26}_D$ +33.6 (*c* 0.12, $CHCl_3$)] in 70% yield along with diacylated compound (−)-**32** (20%). Careful inspection of the ^1H NMR spectra of 5-episecosyrin 1 (**31**) and secosyrin 1 (**3**) disclosed that both compounds show a similar spectral pattern, except for their C_9-protons. 9-H_2 of **3** appear at *δ* 2.78 and 2.58 as an AB-quartet (J = 17.8 Hz), while those of **31** resonate at *δ* 2.86 and 2.75 as an AB-quartet (J = 18.5 Hz). This diagnostic observation in the ^1H NMR spectra, in combination with the difference in their specific rotation [(+)-secosyrin 1 shows its specific rotation[10] of $[\alpha]_D$ +42.85 (*c* 1.43, CH_2Cl_2)], enabled us to distinguish (+)-secosyrin 1 (**3**) from 5-episecosyrin 1 (**31**).

We now had to develop an efficient way to invert the tertiary hydroxy group at the propynyl center of **24** or **25**. It is well-known that cobalt hexacarbonyl complexed with propynyl alcohol derivatives, upon treatment with acid, generate the corresponding propynyl cation, which can be subsequently captured by various nucleophiles, resulting in carbon−carbon and carbon−heteroatom bond formation at the propynyl position (Nicholas reaction).[16] We anticipated that the propynyl cation derived from the cobalt complex of **25** would be intramolecularly captured by primary alcohol through the transition state **C** (Figure 2) rather than the transition state **D**, the former of which could lead to formation of a compound with the desired stereochemistry. Transition state **D** would suffer from serious nonbonding interactions between the bulky cobalt-complexed alkyne portion and benzyloxy functionality in an eclipsed form. This is not the case for the transition state **C,** where unfavorable but rather weaker nonbonding interaction of the benzyloxy group with the thioacetate residue might be the only nonbonding interaction in existence. Formation of the transition state **C**, therefore, would be expected to be preferred over the transition state **D**.

Dicobalt hexacarbonyl complex **33** was prepared in 98% yield by treatment of **25** with $Co_2(CO)_8$ in diethyl ether at room temperature (Scheme 5). Exposure of **33** to BF_3·-

(12) Mukai, C.; Moharram, S. M.; Kataoka, O.; Hanaoka, M. *J. Chem. Soc., Perkin Trans. 1* **1995**, 2849.

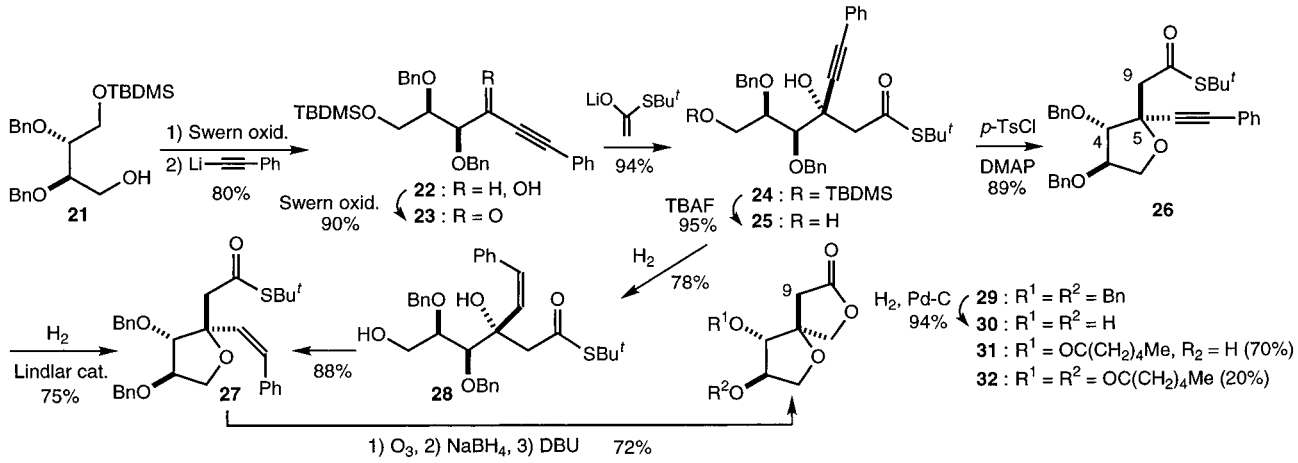
(13) Numbering for a 1,7-dioxaspiro[4.4]nonan-8-one skeleton was used for convenience.

(14) Slomp, G., Jr.; Johnson, J. L. *J. Am. Chem. Soc.* **1958**, *80*, 915.

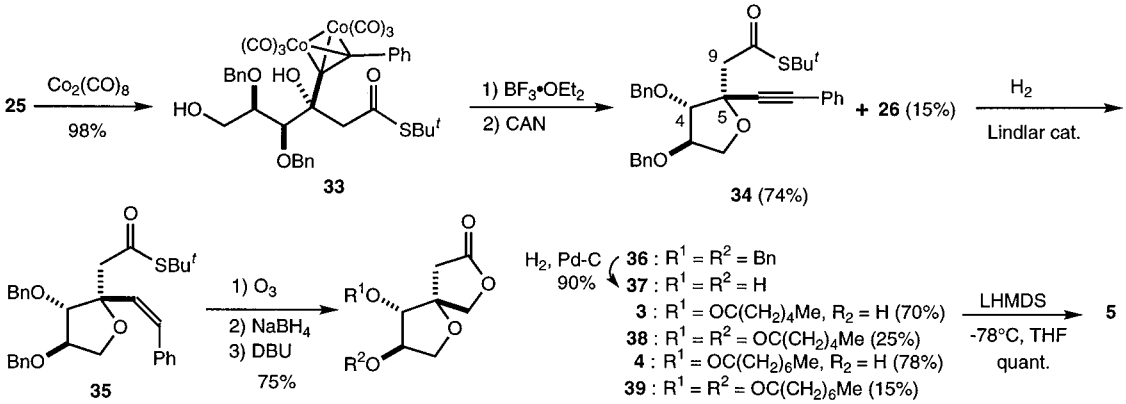
(15) Crystal data: $C_{21}H_{22}O_5$, M = 354.40, orthorhombic, a = 10.908(4) Å, b = 19.07(1) Å, c = 8.736(3) Å, V = 1817(1) Å^3, Z = 4, D_c = 1.295 g/cm^3, Space group $P2_12_12_1$ (#19), μ(Mo Kα) = 0.86 cm^{-1}. A colorless prismatic crystal, ca. 0.1 × 0.1 × 0.15 mm, was mounted on a glass fiber. All measurements were made on a Rigaku AFC5R diffractometer. The cell dimensions and intensities were refined by the least-squares method, using 25 reflections on the diffractomer with Mo Kα radiation with *w*-scan mode for 2*θ* less than 55.0°. The structure was solved by a direct method (MITHRIL method). The final cycle of full-matrix least-squares refinement was based on 2167 observed reflections. The final R value was 0.043.

(16) Nicholas, K. M. *Acc. Chem. Res* **1987**, *20*, 207 and references therein.

Scheme 4



Scheme 5



OEt_2 in methylene chloride at room-temperature effected ring closure with inversion of the configuration at the quaternary center to provide tetrahydrofuran derivatives with the cobalt complex, which were demetalated by treatment with cerium(IV) ammonium nitrate (CAN) to afford (+)-**34** in 74% yield together with (−)-**26** in 15% yield. It should be mentioned that a NOE experiment with **34** disclosed no enhancement between C_4−H and C_9−H,[13] in sharp contrast to the case of **26** (6.5% enhancement). Thus efficient inversion of the propynyl carbon center with concomitant ring formation was realized. With desired **34** possessing the requisite quaternary center, the stage was set for completing a first total synthesis of secosyrins 1 and 2 (**3** and **4**). According to the procedure developed for transformation of **26** into 5-episecosyrin 1 (**31**), **34** was half-reduced in the presence of Lindlar catalyst to furnish (+)-**35** in 78% yield. Spiro ring construction was carried out by successive ozonolysis, reduction, and base treatment to produce (+)-**36** in 75% yield. Deprotection of **36** gave (+)-**37** in 90% yield, which was followed by monoacylation under aforementioned conditions to yield (+)-secosyrin 1 (**3**) [$[\alpha]^{26}_D$ +48.2 (*c* 0.12, $CHCl_3$); lit.[10] $[\alpha]_D$ +42.85 (*c* 1.43, CH_2Cl_2)] along with diacylated compound (−)-**38**. By changing the acylating reagent from hexanoic anhydride to octanoic anhydride, the diol **37** provided (+)-secosyrin 2 (**4**) [$[\alpha]^{21}_D$ +40.5 (*c* 0.10, $CHCl_3$)] and (−)-**39** in 78% and 15% yield, respectively. Synthetic secosyrins 1 and 2 (**3** and **4**) were identified by comparison with the spectral data of the naturally occurring compounds. Specific rotation of synthetic (+)-secosyrin 1 was also in good accordance with that of natural (+)-secosyrin 1. It is noteworthy that base treatment of secosyrin 1 (**3**) caused easy and quantitative conversion into (+)-syributin 1 (**5**) through retro-Michael type reaction accompanied with migration of hexanoyl group from secondary to primary hydroxy group. This result is in good agreement with the biogenetic route proposed by Sims.

Conclusion

Thus, we have succeeded in not only the first total syntheses of (+)-secosyrins 1 and 2 but also the total syntheses of (+)-syributins 1 and 2 from a common starting material, diisopropyl D-tartrate. Although direct transformation of simpler syributins into more complex secosyrins by Michael type ring closure could not be realized yet, the first total syntheses of (+)-secosyrins 1 and 2 have been accomplished in a stereoselective fashion. And this synthesis established the structure of (+)-secosyrins 1 and 2 unambiguously. Studies on the synthesis of syringolides 1 and 2 in line with this program are now in progress.

Experimental Section

Melting points are uncorrected. IR spectra were measured in $CHCl_3$ unless otherwise mentioned. ^1H NMR spectra were taken in $CDCl_3$ unless otherwise indicated. $CHCl_3$ (7.26 ppm) was used as an internal standard for silyl compounds. TMS was employed as an internal standard for other compounds. ^{13}C NMR spectra were recorded in $CDCl_3$ with $CDCl_3$ (77.00 ppm) as an internal standard. CH_2Cl_2 was freshly distilled from phosphorus pentoxide and THF from sodium diphenyl ketyl, prior to used. Silica gel (silica gel 60, 230−400 mesh, Merck) was used for chromatography. Organic extracts were dried over anhydrous Na_2SO_4.

Ethyl (+)-(2*E*,4*R*,5*R*)-6-[(*tert*-Butyldimethylsilyl)oxy]-4,5-(isopropylidenedioxy)hexenoate (8). A solution of DMSO (0.22 mL, 3.07 mmol) in CH_2Cl_2 (3.0 mL) was added to a solution of $(COCl)_2$ (0.13 mL, 1.52 mmol) in CH_2Cl_2 (2.0 mL) at −78 °C. After stirring for 15 min, a solution of **7** (212 mg, 0.77 mmol) in CH_2Cl_2 (3.0 mL) was added to the reaction mixture and stirring was continued at the same temperature for an additional hour. Et_3N (0.64 mL, 4.61 mmol) was added to the reaction mixture, which was then gradually warmed to rt and diluted with CH_2Cl_2. the organic layer was washed with water and brine, dried, and concentrated to dryness. The crude aldehyde was used directly for the next reaction. To a suspension of NaH (36.8 mg, 0.92 mmol) in THF (3.0 mL) was added at 0 °C a solution of ethyl (diethylphosphono)acetate (0.18 mL, 0.92 mmol) in THF (2.0 mL) and the mixture was stirred for 30 min. A solution of the crude aldehyde in THF (3.0 mL) was added to the reaction mixture, which was then stirred for 20 min, quenched with water, and extracted with ethyl acetate. The extract was dried and concentrated to leave a residue, which was chromatographed with hexane−ethyl acetate (25:1) to afford (+)-**8** (225 mg, 85%) as a colorless oil: $[\alpha]^{27}_D$ +3.7 (*c* 0.50, $CHCl_3$); MS (FAB) *m*/*z* 345 ($M^+ + 1$, 9.9), 329 (28), 287 (41), 229 (100), 89 (85), 73 (100); IR 1715, 1665 cm^{-1}; ^1H NMR δ 6.94 (dd, 1H, J = 4.9, 15.6 Hz), 6.12 (dd, 1H, J = 1.5, 15.6 Hz), 4.51 (ddd, 1H, J = 1.5, 2.4, 4.9 Hz), 4.20 (q, 2H, J = 6.8 Hz), 3.82 (dd, 1H, J = 3.4, 8.3 Hz), 3.80 (dd, 1H, J = 3.4, 8.3 Hz), 3.75 (dt, 1H, J = 2.4, 3.4 Hz), 1.43 (s, 3H), 1.42 (s, 3H), 1.29 (t, 3H, J = 6.8 Hz), 0.9 (s, 9H), 0.07 (s, 3H), 0.07 (s, 3H); ^{13}C NMR δ 166.07, 144.67, 121.87, 109.85, 80.72, 77.77, 62.72, 60.45, 26.88, 26.76, 25.90, 25.81, 18.24, 14.18, −5.44, −5.48. Anal. Calcd for $C_{10}H_{32}O_5Si$: C, 59.27; H, 9.36. Found: C, 58.88; H, 9.51.

Ethyl (+)-(4*R*,5*R*)-6-[(*tert*-Butyldimethylsilyl)oxy]-3-(nitromethyl)-4,5-(isopropylidenedioxy)hexanoate (9). To a solution of (+)-**8** (138 mg, 0.40 mmol) and nitromethane (0.03 mL, 53 mmol) in CH_3CN (3.0 mL) was added DBU (0.06 mL, 0.40 mmol) at rt. After stirring for 20 h, the reaction mixture was quenched with water and extracted with ethyl acetate. The organic layer was washed with water and brine, dried, and concentrated to dryness. Chromatography of the residue with hexane−ethyl acetate (25:1) afforded (+)-**9** (130 mg, 80%) as a colorless oil: $[\alpha]^{27}_D$ +0.66 (*c* 0.52, $CHCl_3$); MS (FAB) *m*/*z* 406 ($M^+ + 1$, 14), 390 (19), 348 (35), 290 (29), 283 (25), 73 (100), 59 (15); IR 1730, 1560, 1380 cm^{-1}; ^1H NMR δ 4.67 (dd, 1H, J = 5.0, 13.5 Hz), 4.56 (dd, 1H, J = 6.6, 13.5 Hz), 4.14 (q, 2H, J = 6.9 Hz), 4.02 (t, 1H, J = 6.7 Hz), 3.83 (ddd, 1H, J = 4.0, 6.3, 6.7 Hz), 3.79 (dd, 1H, J = 4.0, 10.6 Hz), 3.67 (dd, 1H, J = 6.3, 10.6 Hz), 2.95−2.88 (m, 1H), 2.67 (dd, 1H, J = 5.6, 16.8 Hz), 2.49 (dd, 1H, J = 7.6, 16.8 Hz) 1.38 (s, 3H), 1.34 (s, 3H), 1.25 (t, 3H, J = 6.9 Hz), 0.89 (s, 9H), 0.07 (s, 6H); ^{13}C NMR δ 171.03, 109.34, 79.55, 79.07, 75.29, 63.95, 60.90, 36.91, 33.89, 27.01, 25.91, 25.84, 18.30, 14.07, −5.48, −5.57. Anal. Calcd for $C_{18}H_{35}NO_7Si$: C, 53.31; H, 8.70; N, 3.45. Found: C, 53.15; H, 8.76; N, 3.41.

(+)-(1′*R*,2′*R*)-3-[3′-[(*tert*-Butyldimethylsilyl)oxy]-1′,2′-(isopropylidenedioxy)propyl]butan-4-olide (10). To a solution of (+)-**9** (4.05 g, 10 mmol) in EtOH (15 mL) was added dropwise over a period of 45 min a solution of KOH (670 mg, 11.9 mmol) in EtOH (70 mL) at 0 °C. After stirring for 15 min, a solution of $KMnO_4$ (1.06 g, 6.7 mmol) and $MgSO_4$ (0.89 g, 7.4 mmol) in water (150 mL) was added dropwise over a period 15 min to the reaction mixture at the same temperature and stirring was continued for 30 min. The reaction mixture was passed through a short pad of Celite and the residue was washed with ethyl acetate. The filtrate was first saturated with NaCl and then extracted with ethyl acetate. The extract was dried and concentrated to afford the crude aldehyde, which was directly used for the next reaction. To a solution of the crude aldehyde in MeOH (25 mL) was added $NaBH_4$ (378 mg, 10 mmol) portionwise at 0 °C. The reaction mixture was gradually warmed to rt and stirred for 20 h. MeOH was evaporated off to leave a residue, which was diluted with water and extracted with ethyl acetate. The organic layer was dried and concentrated to give an oily residue, which was chromatographed with hexane−ethyl acetate (10:1) to afford (+)-**10** (2.38 g, 72%) as a colorless oil: $[\alpha]^{31}_D$ +9.7 (*c* 0.53, $CHCl_3$); MS (FAB) *m*/*z* 331 ($M^+ + 1$, 19), 315 (23), 273 (52), 215 (39), 141 (25), 73 (100); IR 1775 cm^{-1}; ^1H NMR δ 4.39 (dd, 1H, J = 7.3, 9.2 Hz), 4.24 (dd, 1H, J = 7.3, 9.2 Hz), 3.96 (t, 1H, J = 6.6 Hz), 3.79−3.60 (m, 3H), 2.84−2.66 (m, 1H), 2.54 (dd, 1H, J = 8.8, 17.5 Hz), 2.45 (dd, 1H, J = 8.8, 17.5 Hz), 1.35 (s, 3H), 1.33 (s, 3H), 0.86 (s, 9H), 0.04 (s, 6H); ^{13}C NMR δ 176.33, 109.20, 79.62, 79.50, 69.58, 63.67, 38.06, 31.04, 27.15, 26.97, 25.84, 18.28, −5.46, −5.53. Anal. Calcd for $C_{16}H_{30}O_5Si$: C, 58.15; H, 9.15. Found: C, 57.75; H, 9.33.

(−)-(1′*R*,2′*R*)-3-[3′-[(*tert*-Butyldimethylsilyl)oxy]-1′,2′-(isopropylidenedioxy)propyl]-2-buten-4-olide (11). **Method 1.** A solution of LHMDS (1M THF solution, 1.5 mL,1.5 mmol) was added dropwise to a solution of (+)-**10** (330 mg, 1.0 mmol) in THF (10 mL) at −78 °C. After stirring at −78 °C for 45 min, TMSCl (0.2 mL, 1.6 mmol) was added to the reaction mixture, which was gradually warmed to rt with stirring for 30 min. The mixture was concentrated, and the resulting precipitates were filtered off by suction and washed with dry ether. The filtrate was concentrated to afford the crude silyl enol ether, which was dissolved in dry CH_3CN (10 mL). Palladium acetate (112 mg, 0.5 mmol) and benzoquinone (54.8 mg, 0.5 mmol) were added to the reaction mixture at rt, and the mixture was stirred for 36 h and then filtered through a pad of Celite.The filtrate was concentrated to dryness. Chromatography of the residue with hexane−ethyl acetate (10:1) provided (−)-**11** (243 mg, 74%) as a colorless oil: $[\alpha]^{27}_D$ −4.8 (*c* 0.50, $CHCl_3$); MS (FAB) *m*/*z* 329 ($M^+ + 1$, 18), 313 (10), 271 (16), 213 (44), 89 (32), 73 (100), 59 (17); IR 1785, 1755, 1650 cm^{-1}; ^1H NMR δ 6.04 (q, 1H, J = 2.0 Hz), 4.92 (dd, 1H, J = 2.0, 18.2 Hz), 4.81 (br s, 1H), 4.80 (ddd, 1H, J = 1.0, 2.0, 18.2 Hz), 3.92 (ddd, 1H, J = 1.7, 3.6, 6.3 Hz), 3.86 (dd, 1H, J = 3.6, 10.6 Hz), 3.75 (dd, 1H, J = 6.3, 10.6 Hz), 1.43 (s, 3H), 1.40 (s, 3H), 0.89 (s, 9H), 0.07 (s, 6H); ^{13}C NMR δ 171.01, 167.44, 116.19, 110.41, 80.34, 75.44, 71.00, 63.07, 26.63, 26.44, 25.84, 18.35, −544, −5.51. Anal. Calcd for $C_{16}H_{28}O_5Si$: C, 58.51; H, 8.59. Found: C, 58.25; H, 8.63.

Method 2. A solution of LHMDS (1 M THF solution, 0.82 mL, 0.82 mmol) was added dropwise to a solution of (+)-**10** (90 mg, 0.27 mmol) in THF (2.0 mL) at −78 °C. After stirring for 45 min, phenylselenenyl chloride (77.6 mg, 0.41 mmol) in THF (1.5 mL) was added to the reaction mixture, which was stirred at −78 °C for 1 h and then gradually warmed to 0 °C. Addition of THF (1 mL) containing a trace of acetic acid to the reaction mixture was followed by addition of a 30% aqueous H_2O_2 solution (2.0 mL). After stirring for 30 min, the reaction mixture was quenched by addition of saturated $NaHCO_3$ solution and extracted with ethyl acetate. The extract was washed with water and brine, dried, and concentrated to dryness. Chromatography of the residue with hexane−ethyl acetate (10:1) gave (−)-**11** (35.8 mg, 40%).

(+)-(1′*R*,2′*R*)-3-[3′-(Hexanoyloxy)-1′,2′-(isopropylidenedioxy)propyl]-2-buten-4-olide (13). A solution of TBAF and hydrofluoric acid (0.25 mL, prepared from 0.23 mL of 1.0 M TBAF in THF solution and 0.02 mL of 47% hydrofluoric acid) was added to a solution of (−)-**11** (72.4 mg, 0.22 mmol) in THF (3.0 mL) at rt. After consumption of **11** (monitered by TLC), the reaction mixture was diluted with water and extracted with ethyl acetate. The organic layer was washed with water, dried, and concentrated to afford the alcohol **12,** which was directly used for the next reaction. To a solution of **12** in CH_2Cl_2 (3.0 mL) were successively added Et_3N (0.04 mL, 0.26 mmol) and hexanoyl chloride (0.04 mL, 0.26 mmol) at 0 °C. The mixture was warmed to rt with continued stirring for 3 h, diluted with water, and extracted with CH_2Cl_2. The extracts were washed with water and brine, dried, and concentrated to dryness. The residue was chromatographed with hexane−ethyl acetate (10:2) to give (+)-13 (55.8 mg, 81%) as a colorless oil: $[\alpha]^{24}_D$ +12.2 (*c* 0.10, $CHCl_3$); MS (FAB) *m*/*z* 313 ($M^+ + 1$, 59), 297 (32), 225 (100), 137 (43), 99 (51), 43 (28); IR 1785, 1750 cm^{-1}; ^1H NMR δ 6.11 (q, 1H, J = 2.0 Hz), 4.95 (dd, 1H, J = 2.0, 18.1 Hz), 4.80 (ddd, 1H, J = 1.0, 2.0, 18.1 Hz), 4.73 (br d, 1H, J = 8.3), 4.32 (dd, 1H, J = 4.9, 12.2 Hz), 4.27 (dd, 1H, J = 4.9, 12.2 Hz), 4.10 (dt, 1H, J = 8.3, 4.9 Hz), 2.35 (t, 2H, J = 7.8 Hz), 1.67−1.60 (m, 2H),1.47 (s, 3H), 1.44 (s, 3H), 1.34−1.28 (m, 4H), 0.90 (t, 3H, J = 7.3); ^{13}C NMR δ 173.30, 172.63, 165.77, 116.89, 111.05, 78.02, 74.57, 70.71, 62.64,

33.91, 31.18, 26.60, 26.42, 24.44, 24.37, 22.21, 13.82. Anal. Calcd for $C_{16}H_{24}O_6$: C, 61.52; H, 7.74. Found: C, 61.23; H, 7.78.

(+)-(1′*R*,2′*R*)-3-[1′,2′-(Isopropylidenedioxy)-3′-(octanoyloxy)propyl]-2-buten-4-olide (14). According to the procedure that described the preparation of **13** from **11**, compound **11** (72.2 mg, 0.22 mmol) was deprotected with a solution of TBAF and hydrofluoric acid (0.25 mL, prepared from 0.23 mL of 1.0 M TBAF in THF solution and 0.02 mL of 47% hydrofluoric acid) and then treated with Et_3N (0.06 mL, 0.32 mmol) and octanoyl chloride (0.05 mL, 0.32 mmol) in CH_2Cl_2 (3.0 mL) to give (+)-**14** (63.6 mg, 85%) as a colorless oil: $[\alpha]^{31}_D$ +13.6 (*c* 0.48, $CHCl_3$); MS *m*/*z* 340 (M^+, 0.21), 325 (100), 154 (77), 127 (61), 57 (51), 43 (85); IR 1785, 1750 cm^{-1}; ^1H NMR δ 6.11 (q, 1H, *J* = 2.0 Hz), 4.94 (dd, 1H, *J* = 2.0, 18.1 Hz), 4.86 (ddd, 1H, *J* = 1.0, 2.0, 18.1 Hz), 4.72 (br d, 1H, *J* = 8.3), 4.32 (dd, 1H, *J* = 4.9, 12.2 Hz), 4.27 (dd, 1H, *J* = 4.9, 12.2 Hz), 4.09 (dt, 1H, *J* = 8.3, 4.9 Hz), 2.35 (t, 2H, *J* = 7.3 Hz), 1.68−1.58 (m, 2H),1.46 (s, 3H), 1.44 (s, 3H), 1.38−1.20 (m, 4H), 0.88 (t, 3H, *J* = 6.8 Hz); ^{13}C NMR δ 173.33, 172.67, 165.79, 116.87, 111.05, 78.02, 74.56, 70.73, 62.64, 33.96, 31.56, 29.00, 28.83, 26.60, 26.42, 24.76, 22.52, 14.00. Anal. Calcd for $C_{18}H_{28}O_6$: C, 63.51; H, 8.29. Found: C, 63.28; H, 8.45.

(+)-Syributin 1 (5). To a solution of (+)-**13** (150 mg, 0.48 mmol) in MeOH (7.0 mL) was added a solution of 5% HCl (2.0 mL). The reaction mixture was stirred at 45 °C for 2 h, and then MeOH was evaporated off. The residue was neutralized with saturated aqueous solution of $NaHCO_3$ and extracted with ethyl acetate. The extracts were dried and concentrated to dryness to leave a residue, which was chromatographed with ethyl acetate−hexane (10:4) to afford (+)-**5** (94.2 mg, 72%) as a colorless oil: $[\alpha]^{20}_D$ +7.8 (*c* 0.33, $CHCl_3$) [lit.[10] $[\alpha]_D$ +7.19 (*c* 0.86, CH_2Cl_2); lit.[2f] $[\alpha]^{24}_D$ +6.6 (*c* 0.6, $CHCl_3$)]; MS (FAB) *m*/*z* 273 (M^+ + 1, 78), 207(34), 136 (100), 99 (69), 43 (56); IR 3450, 1785, 1735 cm^{-1}; ^1H NMR δ 6.07 (q, 1H, *J* = 2.0 Hz), 4.97 (dd, 1H, *J* = 2.0, 18.1 Hz), 4.91 (dd, 1H, *J* = 2.0, 18.1 Hz), 4.62 (m, 1H), 4.33 (dd, 1H, *J* = 5.4, 11.7 Hz), 4.10 (dd, 1H, *J* = 6.3, 11.7 Hz), 3.96 (dddd, 1H, *J* = 3.4, 5.4, 5.9, 6.3 Hz), 3.20 (d, 1H, *J* = 5.9 Hz), 3.04 (d, 1H, *J* = 6.4 Hz), 2.36 (t, 2H, *J* = 7.3 Hz), 1.61−1.55 (m, 2H), 1.33−1.2 (m, 4H), 0.90 (t, 3H, *J* = 6.8 Hz); ^{13}C NMR δ 174.59, 173.46, 169.34, 116.80, 71.68, 71.52, 68.81, 64.76, 34.04, 31.22, 24.49, 22.23, 13.84; HRMS calcd for $C_{13}H_{21}O_6$ 273.1338, found 273.1340

(+)-Syributin 2 (6). According to the procedure described for the preparation of (+)-**5** from (+)-**13**, compound (+)-**14** (120 mg, 0.35 mmol) in MeOH (7.0 mL) was treated with 5% HCl (2.0 mL) to give (+)-**6** (72.8 mg, 69%) as a colorless oil: $[\alpha]^{17}_D$ +5.9 (*c* 0.18, $CHCl_3$); MS *m*/*z* 300 (M^+, 1.25), 216 (6.3), 140 (34), 127 (100), 114 (70), 57 (88); IR 3400, 1785, 1740 cm^{-1}; ^1H NMR δ 6.05 (q, 1H, *J* = 1.7 Hz), 4.98 (dd, 1H, *J* = 1.7, 18.1 Hz), 4.89 (dd, 1H, *J* = 1.7, 18.1 Hz), 4.63 (m, 1H), 4.27 (dd, 1H, *J* = 5.6, 11.5 Hz), 4.16 (dd, 1H, *J* = 6.3, 11.5 Hz), 3.96 (dddd, 1H, *J* = 3.3, 5.6, 5.9, 6.3 Hz), 3.78 (d, 1H, *J* = 6.6 Hz), 3.54 (d, 1H, *J* = 5.9 Hz), 2.34 (t, 2H, *J* = 7.6 Hz), 1.68−1.51 (m, 2H), 1.38−1.18 (m, 8H), 0.86 (t, 3H, *J* = 6.9 Hz); ^{13}C NMR δ 174.48, 174.23, 170.57, 116.39, 72.04, 71.29, 68.81, 64.55, 34.07, 31.57, 29.00, 28.83, 24.78, 22.54, 14.00; HRMS calcd for $C_{15}H_{24}O_6$ 300.1573, found 300.1581.

(−)-(1′*R*,2′*R*)-3-(1′,2′,3′-Trihydroxypropyl)-2-buten-4-olide (15). To a stirred solution of (−)-**11** (125 mg, 0.38 mmol) in MeOH (2.0 mL) was added 5% HCl (1.0 mL), and the reaction mixture was stirred at 45 °C for 3 h. Solvent was evaporated off to leave a residue, which was chromatographed with CH_2Cl_2−MeOH (10:1) to provide (−)-**15** (59.7 mg, 90%) as a colorless viscous oil: $[\alpha]^{24.5}_D$ −7.9 (*c* 0.10, MeOH); MS (FAB) *m*/*z* 175 (M^+ + 1, 13), 154(100), 136 (87), 89 (35), 77 (33), 39 (19); IR 3350, 1730 (br) cm^{-1}; ^1H NMR δ 6.09 (t, 1H, *J* = 1.7 Hz), 5.08 (dd, 1H, *J* = 2.0, 18.1 Hz), 4.99 (dd, 1H, *J* = 0.7, 18.1 Hz), 4.83 (br s, 3H), 4.75 (m, 1H), 3.81−3.35 (m, 3H); ^{13}C NMR δ 176.53, 175.27, 116.03, 74.89, 73.69, 70.13, 63.52; HRMS calcd for $C_7H_{11}O_5$ 175.0606, found 175.0604

(−)-(1′*R*,2′*R*)-3-[1′-(Hexanoyloxy)-2′,3′-(isopropylidenedioxy)propyl]-2-buten-4-olide (17). To a stirred solution of (−)-**15** (110 mg, 0.63 mmol) in THF (5.0 mL) was added isopropenyl methyl ether (0.07 mL, 0.73 mmol) and a catalytic amount of *p*-TSA (1.2 mg, 0.006 mmol) at 0 °C. After stirring for 20 min, the reaction mixture was quenched with water and extracted with ether. The extract was dried and concentrated to dryness. The residue was directly used for the next step. To a solution of the crude acetonide derivative in CH_2Cl_2 (5.0 mL) were added Et_3N (0.1 mL, 0.75 mmol) and hexanoyl chloride (0.1 mL, 0.75 mmol) at 0 °C. The reaction mixture was allowed to stand at rt for 2 h, quenched with water, and extracted with CH_2Cl_2. The combined organic layers were washed with saturated $NaHCO_3$ solution, water, and brine, dried, and concentrated to dryness. The residue was chromatographed with hexane−ethyl acetate (10:1) to give (−)-**17** (124 mg, 63%) as a colorless oil: $[\alpha]^{20}_D$ −29.5 (*c* 0.11, $CHCl_3$); MS *m*/*z* 312 (M^+, 4.7), 297 (34), 197 (30), 139 (25), 126 (19), 101 (100), 71 (29); IR 1785, 1755 cm^{-1}; ^1H NMR δ 6.05 (br s, 1H, *J* = 2.0 Hz), 5.79 (d, 1H, *J* = 3.6 Hz), 4.93 (dd, 1H, *J* = 2.0, 17.8 Hz), 4.84 (dd,1H, *J* = 2.0, 17.8 Hz), 4.36 (ddd, 1H, *J* = 3.6, 5.6, 6.9 Hz), 4.08 (dd, 1H, *J* = 6.9, 8.6 Hz), 3.79 (dd, 1H, *J* = 5.6, 8.6 Hz), 2.40 (t, 2H, *J* = 7.6 Hz), 1.73−1.59 (m, 2H),1.44 (s, 3H), 1.34 (s, 3H), 1.39−1.23 (m, 4H), 0.91 (t, 3H, *J* = 6.9 Hz); ^{13}C NMR δ 172.56, 172.51, 164.37, 118.01, 110.41, 75.42, 71.65, 96.04, 65.25, 33.91, 31.14, 25.88, 24.78, 24.44, 22.18, 13.79. Anal. Calcd for $C_{16}H_{24}O_6$: C, 61.52; H, 7.74. Found: C, 61.28; H 7.77.

Conversion of (−)-17 into (+)-5. To a solution of (−)-**17** (62.4 mg, 0.20 mmol) was added 20% hydrochloric acid in THF (2.0 mL) at 0 °C. The reaction mixture was stirred for 15 min, quenched by saturated NH_4Cl solution, and extracted with ethyl acetate. The extract was washed with water and brine, dried, and concentrated to dryness. Chromatography of the residue with ethyl acetate−hexane (5:2) afforded (+)-**5** (54 mg, 99%).

(−)-(4*S*,5*R*)-4,5-Bis(benzyloxy)-6-[(*tert*-butyldimethylsilyl)oxy]-1-phenyl-1-hexyn-3-one (23). A solution of DMSO (0.68 mL, 9.60 mmol) in CH_2Cl_2 (3.5 mL) was added to a solution of $(COCl)_2$ (0.44 mL, 5.04 mmol) in CH_2Cl_2 (10 mL) at −78 °C. After stirring for 15 min, a solution of **21** (1.0 g, 2.40 mmol) in CH_2Cl_2 (10 mL) was added to the reaction mixture and stirring was continued at the same temperature for 1 h. Et_3N (2.48 mL, 17.8 mmol) was added to the reaction mixture, which was then gradually warmed to rt and diluted with CH_2Cl_2. The organic layer was washed with water and brine, dried, and concentrated to give the crude aldehyde. To a stirred solution of phenylacetylene (0.4 mL, 3.64 mmol) in THF (10 mL) was added a solution of *n*-BuLi (1.5 M hexane solution, 2.47 mL, 3.7 mmol) at 0 °C, and the mixture was stirred for 30 min. A solution of the crude aldehyde in THF (10 mL) was added to the reaction mixture at the same temperature. After being stirred for 20 min, the reaction mixture was quenched with water and extracted with ethyl acetate. The organic layer was dried and concentrated to leave **22** (992 mg, 80%) consisting of two isomers. The crude **22** was used without further purification for the next step. A solution of DMSO (0.68 mL, 9.60 mmol) in CH_2Cl_2 (3.5 mL) was added to a solution of $(COCl)_2$ (0.44 mL, 5.04 mmol) in CH_2Cl_2 (10 mL) at −78 °C. After stirring for 15 min, a solution of **22** (992 mg, 1.92 mmol) in CH_2Cl_2 (8 mL) was added to the reaction mixture and the mixture was stirred at the same temperature for 1 h. Et_3N (2.48 mL, 17.8 mmol) was added to the reaction mixture, which was then gradually warmed to rt and diluted with CH_2Cl_2. The organic layer was washed with water and brine, dried, and concentrated to dryness. The residue was chromatographed with hexane−ethyl acetate (20:1) to afford (−)-**23** (889 mg, 90% from **22**) as colorless oil: $[\alpha]^{23}_D$ −46 (*c* 0.25, $CHCl_3$); MS *m*/*z* 514 (M^+, 0.2), 457 (4.8), 349 (44), 319 (42), 129 (100), 91 (99), 75 (54); IR 2220, 1665 cm^{-1}; ^1H NMR δ 7.53−7.18 (m, 15H), 4.92, 4.54 (AB-q, 2H, *J* = 11.7 Hz), 4.63 (s, 2H), 4.26 (d, 1H, *J* = 2.9 Hz), 4.07 (ddd, 1H, *J* = 2.9, 5.9, 7.3 Hz), 3.77 (dd, 1H, *J* = 7.3, 10.3 Hz), 3.72 (dd, 1H, *J* = 5.9, 10.3 Hz), 0.86 (s, 9H), 0.01 (s, 3H), 0.01 (s, 3H); ^{13}C NMR δ 188.53, 137.90, 137.38, 133.23, 130.84, 128.54, 128.30, 128.19, 127.89, 127.67, 119.89, 94.05, 87.30, 84.49, 80.07, 73.55, 61.53, 25.84, 18.13, −5.44, −5.50; Anal. Calcd for $C_{32}H_{38}O_4Si$: C, 74.67; H, 7.44. Found: C, 74.66; H, 7.58.

***tert*-Butyl (−)-(3*S*,4*S*,5*R*)-4,5-Bis(benzyloxy)-6-[(*tert*-butyldimethylsilyl)oxy]-3-hydroxy-3-(phenylethynyl)hexanethioate (24)**. To a stirred solution of *tert*-butyl thioacetate

(15.8 mg, 0.12 mmol) in THF (1.0 mL) at −78 °C was added a solution of LHMDS (1.0 M THF solution, 0.12 mL, 0.12 mmol). After stirring at −78 °C for 30 min, a solution of (−)-**23** (51.4 mg, 0.10 mmol) in THF (1.0 mL) was added dropwise to a solution of the enolate in THF. The reaction mixture was stirred for 30 min, quenched with water, and extracted with ethyl acetate. The organic layer was washed with water, dried, and concentrated to dryness. The residue was chromatographed with hexane−ethyl acetate (20:1) to afford (−)-**24** (60.7 mg, 94%) as colorless solids: mp 48−49 °C (hexane−ether); $[\alpha]^{22}_D$ −80.5 (*c* 0.50, $CHCl_3$); MS *m*/*z* 646 (M^+, 2.2), 547 (21), 305 (21), 199 (28), 153 (100), 89 (39), 46 (48); IR 3450, 1655 cm^{-1}; ^1H NMR δ 7.43−7.12 (m, 15H), 4.97 (s, 1H), 4.93, 4.76 (AB-q, 2H, J = 11.2 Hz), 4.72, 4.65 (AB-q, 2H, J = 11.2 Hz), 4.13 (ddd, 1H, J = 2.9, 5.9, 6.4 Hz), 3.90 (d, 1H, J = 2.9 Hz), 3.73 (dd, 1H, J = 5.9, 10.3 Hz), 3.65 (dd, 1H, J = 6.4, 10.3 Hz), 3.43, 3.07 (AB-q, 2H, J = 15.6 Hz), 1.48 (s, 9H), 0.87 (s, 9H), 0.01 (s, 3H), 0.01 (s, 3H); ^{13}C NMR δ 202.42, 138.38, 138.17, 131.68, 128.61, 128.45, 128.30, 128.21, 127.64, 127.58, 122.57, 89.35, 86.43, 82.55, 80.76, 75.56, 74.00, 63.20, 50.37, 48.54, 29.65, 25.90, 18.17, −5.37, −5.42. Anal. Calcd for $C_{38}H_{50}O_5SSi$: C, 70.55; H, 7.79. Found: C, 70.38; H, 7.86.

***tert*-Butyl (−)-(3*S*,4*S*,5*R*)-4,5-Bis(benzyloxy)-3,6-dihydroxy-3-(phenylethynyl)hexanethioate (25).** A solution of TBAF and hydrofluoric acid (0.25 mL, prepared from 0.23 mL of 1.0 M TBAF in THF solution and 0.02 mL of 47% hydrofluoric acid) was added to a solution of (−)-**24** (142 mg, 0.22 mmol) in THF at rt. After consumption of the starting material (monitered by TLC), the reaction mixture was diluted with water and extracted with ethyl acetate. The organic layer was washed with water, dried, and concentrated to dryness. The residue was chromatographed with hexane−ethyl acetate (10:2) to afford (−)-**25** (111 mg, 95%) as a colorless oil: $[\alpha]^{25}_D$ −126 (*c* 0.30 $CHCl_3$); MS *m*/*z* 532 (M^+, 0.2), 367 (8.5), 205 (34), 129 (100), 91 (99), 57 (73); IR 3450, 2200, 1660 cm^{-1}; ^1H NMR δ 7.46−7.21 (m, 15H), 4.97 (s, 1H), 4.90, 4.84 (AB-q, 2H, J = 11.2 Hz), 4.67 (s, 2H), 4.07 (dt, 1H, J = 4.6, 9.2 Hz), 3.81−3.78 (m, 3H), 3.41, 2.94 (AB-q, 2H, J = 15.5 Hz), 1.48 (s, 9H); ^{13}C NMR δ 202.12, 137.99, 137.79, 131.72, 128.61, 128.57, 128.46, 128.41, 128.34, 128.23, 128.07, 127.96, 127.75, 122.28, 88.52, 86.54, 82.77, 80.52, 75.17, 73.37, 73.23, 62.25, 50.62, 48.82, 29.63. Anal. Calcd for $C_{32}H_{36}O_5S$: C, 72.15; H, 6.81. Found: C, 71.90; H, 6.91.

(−)-(2*S*,3*S*,4*R*)-3,4-Bis(benzyloxy)-2-[[(*tert*-butylthio)carbonyl]methyl]-2-(phenylethynyl)tetrahydrofuran (26). To a stirred solution of (−)-**25** (53.2 mg, 0.10 mmol), Et_3N (0.02 mL, 0.14 mmol), and DMAP (17.1 mg, 1.4 mmol) in CH_2Cl_2 (2.0 mL) was added TsCl (26.7 mg, 0.14 mmol) portionwise at 0 °C. The reaction mixture was warmed to rt and stirring was continued for 3 h. The mixture was diluted with water and extracted with CH_2Cl_2, which was washed with water, dried, and concentrated to dryness. The residue was chromatographed with hexane−ethyl acetate (20:1) to afford (−)-**26** (45.8 mg, 89%) as a colorless oil: $[\alpha]^{19}_D$ −64.3 (*c* 0.52, $CHCl_3$); MS (FAB) *m*/*z* 515 ($M^+ + 1$, 1.1), 459 (5.6), 247 (8.6), 181 (8.0), 91 (100), 57 (63); IR 2225, 1675 cm^{-1}; ^1H NMR δ 7.46−7.25 (m, 15H), 4.87, 4.70 (AB-q, 2H, J = 11.7 Hz), 4.50, 4.43 (AB-q, 2H, J = 11.7 Hz), 4.42 (d, 1H, J = 1.5 Hz), 4.21 (dd, 1H, J = 4.9, 9.8 Hz), 4.17 (ddd, 1H, J = 1.5, 2.0, 4.9 Hz), 3.92 (dd, 1H, J = 2.0, 9.8 Hz), 3.13, 3.05 (AB-q, 2H, J = 14.2 Hz), 1.45 (s, 9H); ^{13}C NMR δ 196.06, 138.08, 137.59, 131.90, 128.45, 128.37, 128.30, 128.09, 127.87, 127.82, 127.76, 127.66, 122.70, 88.27, 86.15, 84.04, 80.67, 72.72, 71.56, 70.77, 52.33, 48.34, 29.65. Anal. Calcd for $C_{32}H_{34}O_4S$: C, 74.68; H, 6.66. Found: C, 74.52; H, 6.72.

(−)-(2*S*,3*S*,4*R*)-3,4-Bis(benzyloxy)-2-[[(*tert*-butylthio)carbonyl]methyl]-2-((*Z*)-2′-phenylethenyl)tetrahydrofuran (27). A solution of (−)-**26** (180 mg, 0.35 mmol) in ethyl acetate (15 mL) was hydrogenated under a hydrogen atmosphere in the presence of Lindlar catalyst (20 mg) at rt for 48 h. The catalyst was filtered off and the filtrate was concentrated to dryness. Chromatography of the residue with hexane−ethyl acetate (20:1) gave (−)-**27** (136 mg, 75%) as a colorless oil: $[\alpha]^{22}_D$ −26.4 (*c* 0.49, $CHCl_3$); MS *m*/*z* 516 (M^+, 0.1), 460 (7), 385 (25), 276(30), 203 (38), 131(72), 128(32), 91 (92), 57 (100); IR 1680 cm^{-1}; ^1H NMR δ 7.48−7.15 (m, 15H), 6.61 (d, 1H, J = 13.2 Hz), 5.89 (d, 1H, J = 13.2 Hz), 4.69 (s, 2H), 4.43, 4.38 (AB-q, 2H, J = 11.9 Hz), 4.24 (d, 1H, J = 3.6 Hz), 4.05 (ddd, 1H, J = 3.6, 4.3, 5.6 Hz), 3.63 (dd, 1H, J = 5.6,8.6 Hz), 3.58 (dd, 1H, J = 4.3, 8.6 Hz), 2.99, 2.89 (AB-q, 2H, J = 14.5 Hz), 1.43 (s, 9H); ^{13}C NMR δ 196.78, 138.15, 137.77, 137.27, 131.34, 129.34, 128.90, 128.39, 128.34, 127.76, 127.71, 127.66, 127.39, 126.72, 87.35, 84.31, 83.06, 72.74, 71.83, 69.24, 51.36, 48.20, 29.65. Anal. Calcd for $C_{32}H_{36}O_4S$: C, 74.39; H, 7.02. Found: C, 74.36; H, 7.13.

***tert*-Butyl (+)-(3*S*,4*S*,5*R*)-4,5-Bis(benzyloxy)-3,6-dihydroxy-3-((*Z*)-2′-phenylethenyl)hexanethioate (28).** According to the procedure described for conversion of **26** into **27**, compound (−)-**25** (148 mg, 0.28 mmol) was partially hydrogenated in the presence of Lindlar catalyst to give (+)-**28** (111.4 mg, 78%) as a colorless oil: $[\alpha]24_D$ +2.74 (*c* 0.23, $CHCl_3$); MS (FAB) *m*/*z* 535 ($M^+ + 1$, 0.4), 401 (1), 207 (8), 181 (14), 131(41), 91 (100), 57 (42); IR 3450, 1660 cm^{-1}; ^1H NMR δ 7.40−7.15 (m, 15H), 6.60 (d, 1H, J = 13.2 Hz), 5.72 (d, 1H, J = 13.2 Hz), 4.89, 4.70 (AB-q, 2H, J = 11.2 Hz), 4.65 (s, 2H), 3.91 (s, 1H), 3.79−3.57 (m, 4H), 3.15, 2.90 (AB-q, 2H, J = 15.5 Hz), 2.33 (t, 1H, J = 6.6 Hz), 1.46 (s, 9H); ^{13}C NMR δ 201.45, 138.15, 138.10, 137.29, 131.72, 131.52, 128.91, 128.43, 128.39, 128.36, 128.16, 127.80, 127.75, 127.69, 126.85, 83.16, 80.25, 79.35, 75.08, 72.78, 62.59, 50.95, 48.74, 29.69. Anal. Calcd for $C_{32}H_{38}O_5S$: C, 71.88; H, 7.16. Found: C, 71.60; H, 7.20.

Conversion of (+)-28 into (−)-27. According to the procedure described for transformation of **25** into **26**, compound **28** (106 mh, 0.20 mmol) in CH_2Cl_2 (5.0 mL) was treated with Et_3N (0.04 mL, 0.28 mm0l), DMAP (34.2 mg, 0.28 mmol), and *p*-TsCl (53.4 mg, 0.28 mmol) to afford (−)-**27** (90 mg, 88%).

(+)-(3*R*,4*S*,5*S*)-3,4-Bis(benzyloxy)-1,7-dioxaspiro[4.4]nonan-8-one (29).[17] Ozone was passed through a solution of (−)-**27** (135 mg, 0.26 mmol) and pyridine (0.026 mL, 0.35 mmol) in CH_2Cl_2 (6.5 mL) at −78 °C until a pale blue color persisted (15 min). Excess ozone was removed by bubbling oxygen through the solution until the reaction was maintained a clear color (5 min). Excess methyl sulfide (0.09 mL, 1.3 mmol) was added at −78 °C, and the reaction mixture was gradually warmed to rt. The solvents were removed, and the crude product was passed through a short pad of silica gel with hexane−ethyl acetate (10:3) to afford the crude aldehyde. To a solution of the crude aldehyde in MeOH (5.0 mL) was added $NaBH_4$ (14.7 mg, 0.39 mmol) portionwise at 0 °C. The reaction mixture was stirred at rt for 20 min, and MeOH was evaporated off. The residue was taken up in CH_2Cl_2, which was washed with water, dried, and concentrated to dryness. The residue was dissolved in CH_2Cl_2 (6.5 mL), to which a catalytic amount of DBU (3.9 mg, 0.026 mmol) was added. The reaction mixture was stirred at rt for 30 min, and washed with water and brine, dried, and concentrated to dryness. Chromatography of the residue with hexane−ethyl acetate (5:1) afforded (+)-**29** (66.7 mg, 72%) as colorless crystals: mp 93−94 °C (hexane−ether); $[\alpha]^{22}_D$ +44.7 (*c* 0.51, $CHCl_3$); MS *m*/*z* 354 (M^+, 0.81), 294 (1.2), 263 (100), 157 (40), 91 (92), 65 (55); IR 1780 cm^{-1}; ^1H NMR δ 7.40−7.25 (m, 10H), 4.63, 4.31 (AB-q, 2H, J = 10.3 Hz), 4.57, 4.47 (AB-q, 2H, J = 11.7 Hz), 4.51, 4.49 (AB-q, 2H, J = 10.7 Hz), 4.14−4.1 (m, 2H), 3.97−3.94 (m, 2H), 2.72, 2.62 (AB-q, 2H, J = 18.1 Hz); ^{13}C NMR δ 175.13, 137.20, 136.91, 128.64, 128.61, 128.27, 128.09, 127.73, 127.58, 86.83, 85.19, 81.44, 73.30, 72.18, 71.70, 71.38, 39.64. Anal. Calcd for $C_{21}H_{22}O_5$: C, 71.17; H, 6.26. Found: C, 71.00; H, 6.26.

(+)-(3*R*,4*S*,5*S*)-3,4-Dihydroxy-1,7-dioxaspiro[4.4]nonan-8-one (30). A solution of (+)-**29** (120 mg, 0.34 mmol) in ethyl acetate (7.0 mL) and MeOH (0.1 mL) in the presence of one drop of 10% hydrochloric acid was hydrogenated over 10% Pd−C (12 mg) under a hydrogen atmosphere for 3 h at rt. The catalyst was filtered off and the filtrate was concentrated to dryness. The residual solids were recrystallized from hexane−ethyl acetate to provide (+)-**30** (55.4 mg, 94%) as colorless needels: mp 140−141 °C; $[\alpha]^{23}_D$ +13.0 (*c* 0.39, MeOH); MS *m*/*z*

(17) The atomic coordinates for this structure have been deposited with the Cambridge Crystallographic Data Centre. The coordinates can be obtained, on request, from the Director, Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge, CB2 1EZ, UK.

174 (M^+, 1.1), 156 (17), 116 (88), 101 (26), 74 (100), 56 (82); IR 3350, 3475, 1775 cm^{-1}; ^1H NMR δ 4.88 (br s, 2H), 4.63, 4.28 (AB-q, 2H, J = 10.2 Hz), 4.21−4.15 (m, 2H), 4.11 (br s, 1H), 3.81 (dt, 1H, J = 3.3, 4.6 Hz), 2.98, 2.66 (AB-q, 2H, J = 17.8 Hz); ^{13}C NMR δ 178.65, 89.16, 81.58, 78.42, 75.59, 74.68, 40.64. Anal. Calcd for $C_7H_{10}O_5$: C, 48.28; H, 5.79. Found: C, 48.13; H, 5.76.

(+)-(3*R*,4*S*,5*S*)-4-(Hexanoyloxy)-3-hydroxy-1,7-dioxaspiro[4.4]nonan-8-one (31) [(+)-5-Episecosyrin 1] and (−)-(3*R*,4*S*,5*S*)-3,4-Bis(hexanoyloxy)-1,7-dioxaspiro-[4.4]nonan-8-one (32). A solution of hexanoic anhydride (0.1 M THF solution, 2.3 mL, 0.23 mmol) was added to a solution of (+)-**30** (40 mg, 0.23 mmol), Et_3N (0.03 mL, 0.23 mmol), and DMAP (3.0 mg, 0.024 mmol) in THF (3.0 mL) at 0 °C. After stirring for 1 h, the reaction mixture was diluted with saturated $NaHCO_3$ solution and extracted with ether, which was washed with water and brine, dried, and concentrated to dryness. Chromatography of the residue with hexane−ethyl acetate (20:1) gave (+)-**31** (43.8 mg, 70%) as a colorless oil. Further elution with hexane−ethyl acetate (2:1) afforded (−)-**32** (17 mg, 20%) as a colorless oil. (+)-5-Episecosyrin 1 (**31**): $[\alpha]^{26}_D$ +33.6 (*c* 0.12, $CHCl_3$); MS *m*/*z* 272 (M^+, 4.9), 230 (9.4), 216 (17), 167 (25), 149 (61), 99 (100); IR 3450, 1780, 1735 cm^{-1}; ^1H NMR δ 5.03 (d, 1H, J = 1.7 Hz), 4.37, 4.32 (AB-q, 2H, J = 10.2 Hz), 4.31 (ddd, 1H, J = 1.7, 2.6, 5.3 Hz), 4.17 (dd, 1H, J = 5.3, 10.2 Hz), 3.83 (dd, 1H, J = 2.6, 10.2 Hz), 2.86, 2.75 (AB-q, 2H, J = 18.5 Hz), 2.36 (t, 2H, J = 7.6 Hz), 1.72−1.55 (m, 2H), 1.42−1.22 (m, 4H), 0.90 (t, 3H, J = 6.9 Hz); ^{13}C NMR δ 174.59, 173.48, 85.86, 82.97, 76.01, 72.87,72.81, 39.36, 33.98, 31.16, 24.46, 22.19, 13.82; HRMS calcd for $C_{13}H_{20}O_6$ 273.1260, found 272.1256. Diester (−)-**32**: $[\alpha]^{25}_D$ −15.6 (*c* 0.12, $CHCl_3$); MS *m*/*z* 370 (M^+, 1.7), 314 (8.3), 212 (29), 171 (32), 99 (100), 71 (47); IR 1790, 1745 cm^{-1}; ^1H NMR δ 5.32 (d, 1H, J = 1.5 Hz), 5.15 (ddd, 1H, J = 1.5, 2.0, 4.9 Hz), 4.33, 4.31 (AB-q, 2H, J = 10.7 Hz), 4.28 (dd, 1H, J = 4.9, 10.7 Hz), 3.86 (dd, 1H, J = 2.0, 10.7 Hz), 2.80, 2.74 (AB-q, 2H, J = 17.6 Hz), 2.37 (t, 2H, J = 7.3 Hz), 2.35 (t, 2H, J = 7.3 Hz), 1.71−1.55 (m, 4H), 1.42−1.22 (m, 8H), 0.91 (t, 6H, J = 6.8 Hz); ^{13}C NMR δ 173.96, 172.42, 172.25, 86.34, 79.00, 72.58, 71.66, 39.10, 33.96, 33.86, 31.14, 24.42, 22.19, 13.82. Anal. Calcd for $C_{19}H_{30}O_7$: C, 61.60; H, 8.16. Found: C, 61.31; H, 8.28.

Hexacarbonyl-μ-[η^4-*tert*-butyl (−)-(3*S*,4*S*,5*R*)-4,5-bis-(benzyloxy)-3,6-dihydroxy-3-(phenylethynyl)hexanethioate]dicobalt (Co−Co) (33). A solution of (−)-**25** (90 mg, 0.17 mmol) in ether (1.5 mL) was added dropwise to a stirred solution of octacarbonyldicobalt (68.4 mg, 0.2 mmol) in ether (3.0 mL). The reaction mixture was stirred at rt for 4 h and then ether was evaporated off. The residue was chromatographed with hexane−ethyl acetate (20:1) to afford **33** (136 mg, 98%) as a deep brown oil: MS (FAB) *m*/*z* 819 (M^+ + 1, 0.1), 331 (34), 171 (100), 153 (23), 46 (8.5); IR 3400, 2075, 2025, 1995, 1650 cm^{-1}; ^1H NMR δ 7.54−7.16 (m, 15H), 5.46 (s, 1H), 4.95, 4.65 (AB-q, 2H, J = 9.9 Hz), 4.30 (s, 2H), 4.00 (d, 1H, J = 7.6 Hz), 3.82−3.66 (m, 3H), 3.69, 2.99 (AB-q, 2H, J = 6.2 Hz), 2.00 (t, 1H, J = 5.3 Hz), 1.48 (s, 9H); ^{13}C NMR δ 203.04, 199.35, 138.65, 138.40, 137.93, 129.58, 128.99, 128.66, 128.34, 128.21, 127.67, 82.88, 81.12, 79.61, 76.39, 72.22, 62.59, 52.17, 49.44, 29.69. Anal. Calcd for $C_{38}H_{36}Co_2O_{11}S$: C, 55.75; H, 4.43. Found: C, 55.91; H, 4.47. Specific rotation could not be determined because demetalation occurred during measurement.

(+)-(2*R*,3*S*,4*R*)-3,4-Bis(benzyloxy)-2-[[(*tert*-butylthio)-carbonyl]methyl]-2-(phenylethynyl)tetrahydrofuran (34). To a solution of **33** (130 mg, 0.16 mmol) in CH_2Cl_2 (4.0 mL) was added $BF_3{\cdot}Et_2O$ (0.1 M CH_2Cl_2 solution, 1.7 mL, 0.17 mmol) at rt, and the reaction mixture was stirred for 3 h. The mixture was quenched with water and extracted with CH_2Cl_2. The organic layer was washed with water and brine, dried, and concentrated to give the cobalt-complexed residue, which was dissolved in MeOH (5.0 mL). To a solution of cobalt-complexed **34** and **26** in MeOH was added CAN (351 mg, 0.64 mmol) at 0 °C, and the reaction mixture was stirred for 25 min at the same temperature. MeOH was evaporated off and the residue was taken up in ethyl acetate, which was washed with water, dried, and concentrated to dryness. Chromatography of the residue with hexane−ether (10:1) afforded (+)-**34** (60.5 mg, 74%) as a colorless oil along with (−)-**26** (12.3 mg, 15%). Compound (+)-**34**: $[\alpha]^{23}_D$ +92.8 (*c* 0.30, $CHCl_3$); MS *m*/*z* 514 (M^+, 0.3), 457 (44), 367 (44), 349 (57), 244 (22), 129 (36), 91 (99), 57 (100),; IR 2225, 1685 cm^{-1}; ^1H NMR δ 7.41−7.23 (m, 15H), 4.69, 4.60 (AB-q, 2H, J = 11.7 Hz), 4.58, 4.45 (AB-q, 2H, J = 11.7 Hz), 4.43 (d, 1H, J = 2.0 Hz), 4.24 (dd, 1H, J = 6.4, 9.8 Hz), 4.12 (ddd, 1H, J = 2.0, 3.9, 6.4 Hz), 4.00 (dd, 1H, J = 3.9, 9.8 Hz), 3.26, 3.14 (AB-q, 2H, J = 15.1 Hz), 1.46 (s, 9H); ^{13}C NMR δ 196.05, 137.81, 137.61, 131.84, 128.37, 128.32, 128.27, 128.03, 127.92, 127.85, 127.64, 127.53, 122.66, 87.87, 87.51, 86.70, 83.18, 78.94, 72.53, 71.52, 71.02, 49.18, 48.12, 29.76. Anal. Calcd for C32H34O4S: C, 74.68; H, 6.66. Found: C, 74.68; H, 6.70.

(+)-(2*R*,3*S*,4*R*)-3,4-Bis(benzyloxy)-2-[[(*tert*-butylthio)-carbonyl]methyl]-2-((*Z*)-2′-phenylethenyl)tetrahydrofuran (35). According to the procedure described for the preparation of **27** from **26**, compound (+)-**34** (230 mg, 0.48 mmol) in ethyl acetate (20 mL) was hydrogenated over Lindlar catalyst (25 mg) to provide (+)-**35** (180 mg, 78%) as a colorless oil: $[\alpha]^{19}_D$ +27.3 (*c* 0.51, $CHCl_3$); MS *m*/*z* 516 (M^+, 0.2), 460 (27), 352 (21), 203 (35), 131 (63), 91 (95), 57 (100); IR 1680 cm^{-1}; ^1H NMR δ 7.42−7.14 (m, 15H), 6.55 (d, 1H, J = 12.7 Hz), 5.89 (d, 1H, J = 12.7 Hz), 4.45, 4.38 (AB-q, 2H, J = 12.2 Hz), 4.40 (s, 2H), 4.15 (d, 1H, J = 2.0 Hz), 4.00−3.99 (m, 2H), 3.59 (ddd, 1H, J = 2.0, 2.4, 5.9 Hz), 3.16, 3.12 (AB-q, 2H, J = 15.6 Hz), 1.42 (s, 9H); ^{13}C NMR δ 197.34, 137.86, 137.04, 133.23, 130.91, 129.31, 128.39, 128.27, 127.80, 127.69, 127.62, 127.57, 127.51, 126.90, 87.76, 85.16, 83.00, 72.06, 71.47, 70.14, 49.71, 47.93, 29.76. Anal. Calcd for $C_{32}H_{36}O_4S$: C, 74.39; H, 7.02. Found: C, 74.24; H, 7.12.

(+)-(3*R*,4*S*,5*R*)-3,4-Bis(benzyloxy)-1,7-dioxaspiro[4.4]-nonan-8-one (36). According to the procedure described for the preparation of **29** from **27**, compound (+)-**35** (103 mg, 0.2 mmol) was treated successively with ozone, $NaBH_4$, and DBU to afford (+)-**36** (53.1 mg, 75%) as colorless needles: mp 64.5−65.5 °C (hexane−ether); [α]23_D +34.0 (*c* 0.22, $CHCl_3$); MS *m*/*z* 354 (M^+, 0.99), 263 (100), 157 (37), 91 (97), 65 (51); IR 1785 cm^{-1}; ^1H NMR δ 7.43−7.22 (m, 10H), 4.66, 4.46 (AB-q, 2H, J = 11.9 Hz), 4.54, 4.50 (AB-q, 2H, J = 9.6 Hz), 4.31, 4.21 (AB-q, 2H, J = 10.2 Hz), 4.12 (ddd, 1H, J = 2.0, 2.3, 4.6 Hz), 4.05 (dd, 1H, J = 4.6, 9.9 Hz), 3.92 (dd, 1H, J = 2.3, 9.9 Hz), 3.87 (d, 1H, J = 2.0 Hz), 2.96, 2.56 (AB-q, 2H, J = 8.5 Hz); ^{13}C NMR δ 175.51, 137.63, 137.43, 129.13, 128.73, 128.61, 128.23, 128.14, 87.73, 84.62, 82.12, 76.52, 72.85, 72.29, 71.36, 35.56. Anal. Calcd for $C_{21}H_{22}O_5$: C, 71.17; H, 6.26. Found: C, 70.97; H, 6.25.

(+)-(3*R*,4*S*,5*R*)-3,4-Dihydroxy-1,7-dioxaspiro[4.4]nonan-8-one (37). According to the procedure described for the preparation of **30** from **29**, compound (+)-**36** (180.5 mg, 0.51 mmol) was hydrogenolyzed over 10% Pd/C catalyst (18 mg) under hydrogen atmosphere at rt to provide (+)-**37** (79.8 mg, 90%) as colorless needels: mp 107−108 °C (hexane−ethyl acetate); $[\alpha]^{25}_D$ +75.3 (*c* 0.22, MeOH); MS *m*/*z* 174 (M^+, 0.55), 170 (0.3), 156 (15), 116 (100), 74 (82), 56 (68); IR 3350, 3475, 1775 cm^{-1}; ^1H NMR δ 4.86 (br s, 2H), 4.42, 4.37 (AB-q, 2H, J = 10.2 Hz), 4.22−4.09 (m, 1H), 4.15 (dd, 1H, J = 4.6, 8.9 Hz), 4.00 (d, 1H, J = 2.0 Hz), 3.79 (dd, 1H, J = 1.3, 8.9 Hz), 3.06, 2.47 (AB-q, 2H, J = 18.1 Hz); ^{13}C NMR δ 178.23, 89.83, 80.28, 78.09, 77.95, 74.16, 36.37. Anal. Calcd for $C_7H_{10}O_5$: C, 48.28; H, 5.79. Found: C, 48.22; H, 5.83.

(+)-(3*R*,4*S*,5*R*)-4-(Hexanoyloxy)-3-hydroxy-1,7-dioxaspiro[4.4]nonan-8-one (3) (Secosyrin 1) and (−)-(3*R*,4*S*,5*R*)-3,4-Bis(hexanoyloxy)-1,7-dioxaspiro[4.4]nonan-8-one (38). According to the procedure described for the preparation of **31** from **30**, compound (+)-**37** (50.5 mg, 0.29 mmol) was treated with hexanoic anhydride (0.1 M THF solution, 2.87 mL, 0.29 mmol), Et_3N (0.04 mL, 0.29 mmol), and DMAP (3.7 mg, 0.03 mmol) in THF (3.0 mL) at 0 °C to give (+)-secosyrin 1 (**3**) (55.3 mg, 70%) as a colorless oil along with (−)-**38** (26.8 mg, 25%) as a colorless oil. (+)−Secosyrin 1 (**3**): $[\alpha]^{26}_D$ +48.2 (*c* 0.12, $CHCl_3$) [lit.[10] $[\alpha]_D$ +42.85 (*c* 1.43, CH_2Cl_2)]; MS *m*/*z* 272 (M^+, 12), 158 (39), 128 (39), 99 (99), 98 (75), 71 (100); IR 3500, 1785, 1735 cm^{-1}; ^1H NMR δ 4.96 (d, 1H, J = 2.0 Hz), 4.45, 4.37 (AB-q, 2H, J = 10.2 Hz), 4.32 (ddd, 1H, J = 2.0, 2.7, 5.3 Hz), 4.13 (dd, 1H, J = 5.3, 10.2 Hz), 3.86 (dd, 1H, J = 2.7, 10.2 Hz), 2.78, 2.58 (AB-q, 2H, J = 17.8 Hz), 2.37

(t, 2H, J = 7.6 Hz), 1.71−1.54 (m, 2H), 1.41−1.22 (m, 4H), 0.89 (t, 3H, J = 6.9 Hz); ^{13}C NMR δ 174.57, 173.53, 86.63, 81.47, 75.94, 75.55, 72.90, 35.47, 33.96, 31.09, 24.40, 22.12, 13.75; HRMS calcd for $C_{13}H_{20}O_6$ 273.1260, found 272.1249. Diester (−)-**38**: $[\alpha]^{25}_D$ −14.0 (*c* 0.13, $CHCl_3$); MS *m*/*z* 370 (M^+, 4.8), 314 (13), 212 (60), 171 (89), 99 (100), 71 (98); IR 1790, 1745 cm^{-1}; ^{1}H NMR δ 5.27 (d, 1H, J = 2.0 Hz), 5.16 (dt, 1H, J = 4.9, 2.0 Hz), 4.38, 4.34 (AB-q, 2H, J = 10.6 Hz), 4.22 (dd, 1H, J = 4.9, 10.9 Hz), 3.86 (dd, 1H, J = 2.0, 10.9 Hz), 2.72, 2.57 (AB-q, 2H, J = 17.8 Hz), 2.37 (t, 2H, J = 7.6 Hz), 2.33 (t, 2H, J = 7.6), 1.72−1.56 (m, 4H), 1.42−1.22 (m, 8H), 0.89 (t, 6H, J = 6.9 Hz); ^{13}C NMR δ 173.66, 172.40, 87.08, 77.74, 76.87, 75.19, 71.27, 35.22, 33.91, 33.87, 31.13, 24.40, 24.37, 22.18, 13.80. Anal. Calcd for $C_{19}H_{30}O_7$: C, 61.60; H, 8.16. Found: C, 61.41; H, 8.24.

(+)-(3*R*,4*S*,5*R*)-3-Hydroxy-4-(octanoyloxy)-1,7-dioxaspiro[4.4]nonan-8-one (4) (Secosyrin 2) and (−)-(3*R*,4*S*,5*R*)-3,4-Bis(octanoyloxy)-1,7-dioxaspiro[4.4]nonan-8-one (39). According to the procedure described for the preparation of **31** from **30**, compound (+)-**37** (35 mg, 0.2 mmol) was treated with octanoic anhydride (0.2 mmol) to give secosyrin 2 (**4**) (47.1 mg, 78%) as a colorless oil along with (−)-**39** (12.9 mg, 15%) as a colorless oil. (+)−Secosyrin 2 (**4**): $[\alpha]^{21}_D$ +40.5 (*c* 0.10, $CHCl_3$); MS *m*/*z* 300 (M^+, 12), 216 (18), 156 (20), 127 (100), 98 (35), 57 (78); IR 3500, 1785, 1735 cm^{-1}; ^{1}H NMR δ 4.94 (d, 1H, J = 2.0 Hz), 4.46, 4.37 (AB-q, 2H, J = 10.2 Hz), 4.33 (ddd, 1H, J = 2.0, 3.0, 5.3 Hz), 4.14 (dd, 1H, J = 5.3, 10.2 Hz), 3.86 (dd, 1H, J = 3.0, 10.2 Hz), 2.79, 2.59 (AB-q, 2H, J = 18.1 Hz), 2.38 (t, 2H, J = 7.6 Hz), 1.68−1.60 (m, 2H), 1.38−1.27 (m, 8H), 0.89 (t, 3H, J = 6.9 Hz); ^{13}C NMR δ 174.16, 173.73, 86.56, 81.98, 75.89, 75.67, 72.63, 35.40, 34.07, 31.57, 29.00, 28.81, 24.82, 22.55, 14.00; HRMS calcd for $C_{15}H_{24}O_6$ 300.1573, found 300.1573. Diester (−)-**39**: $[\alpha]^{22}_D$ −15.1 (*c* 0.07, $CHCl_3$); MS *m*/*z* 426 (M^+, 5.0), 342(10), 301 (22), 240 (30), 199 (38), 127 (100), 57 (85); IR 1790, 1740 cm^{-1}; ^{1}H NMR δ 5.27 (d, 1H, J = 2.0 Hz), 5.18 (ddd, 1H, J = 2.0, 2.3, 5.0 Hz), 4.38 (s, 2H), 4.24 (dd, 1H, J = 5.0, 10.9 Hz), 3.88 (dd, 1H, J = 2.3, 10.9 Hz), 2.73, 2.59 (AB-q, 2H, J = 17.8 Hz), 2.38 (t, 2H, J = 7.6 Hz), 2.34 (t, 2H, J = 7.6 Hz), 1.72−1.55 (m, 4H), 1.42−1.19 (m, 16H), 0.89 (t, 6H, J = 6.9 Hz); ^{13}C NMR δ 173.69, 172.42, 87.10, 77.77, 76.91, 75.22, 71.29, 35.26, 33.98, 33.95,-33.91, 31.52,28.99, 28.86, 28.81, 24.76, 24.71, 24.66, 22.54, 14.00. Anal. Calcd for $C_{23}H_{38}O_7$: C, 64.76; H, 8.98. Found: C, 64.47; H, 9.12.

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Supporting Information Available: ^{13}C and ^{1}H NMR spectra for compounds (+)-**3**−**6** and (−)-**15** (10 pages). This material is contained in libraries on microfiche, immediately follows this article in the microform version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.

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