Total Syntheses of Sphydrofuran, Secosyrins, and Syributins[†,1]

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Two groups of natural products, sphydrofuran (**1**) and its furan derivative (**2**) and secosyrins 1 and 2 (**3a**, **3b**) and syributins 1 and 2 (**4a**, **4b**), were synthesized from one precursor (**6**), which was realized starting from 3-tri-*n*-butylstannylfuran or 3-bromofuran.

Introduction

Sphydrofuran (**1**) is a structurally intriguing secondary metabolite produced by Actinomycetes,[2] first isolated by the Umezawas and co-workers from the culture filtrate of the strain MC41-M1 and MC340-A1 by a chemical screening method using Ehrlich's reagent.[3] Interestingly, **1** is an anomeric and ring-chain tautomeric mixture and could easily be transformed into the stable furan derivative **2** under very mild acidic conditions. No inhibition activity for **1** was found against various organisms, but a growth promotion for some bacteria and viruses was detected under the influence of **2**.[4] The structures of sphydrofuran (**1**) and its derivative **2** were reported in 1971,[3] but the absolute configuration of **1** was only assigned recently.[4] In view of the structural peculiarity of **1** and **2**, it should be interesting to search for a synthetic route for this type of dioxaspiropolyols.[4] The first total synthesis of sphydrofuran (**1**) was accomplished by Maliakel and Schmid via a chemoenzymatic approach.[5]

Another group of natural products, namely, secosyrin 1 (**3a**) and secosyrin 2 (**3b**), as well as syributin 1 (**4a**) and syributin 2 (**4b**), are the four major coproducts of the syringolide elicitors (**5a** and **5b**), which were isolated and structurally elucidated by Sims and his co-workers.[6] All these unusual metabolites occur only in culture filtrates of bacterial cells carrying the *avrD* gene, which are produced by Gram-negative bacteria expressing the class I homology group of *avrD* alleles, genes from *Pseudomonas syringae* involved with formation of bacterial signal molecules or elicitors.[7] The secosyrins and syributins are not active elicitors, but their interesting novel structures are able to furnish clues to the nature of the *avrD* gene and the function of its protein product. As can be seen, compounds **3** and **4** exhibit stereochemistry similar to that of the syringolides **5**. Secosyrins **3** are formally related to the syringolides by a reverse Claisen cleavage. In the literature, there are at present no less than five total syntheses of syringolides.[8a−e] It is noteworthy that only one synthesis of syributin 1 (**4a**)[8e] and secosyrin 1 (**3a**)[8f] is known.

Notwithstanding that the aforementioned sphydrofuran (**1**) and secosyrins **3** have no biological relationship, an examination of their structures reveals that they are both spiro-linked, the only structural variance being the absolute configuration of their spiro carbons (*S* for **1** and *R* for **3**) (Scheme 1).

We therefore envisioned a synthetic approach to all these natural products starting from 3-(tri-*n*-butylstannyl)furan, which was recently realized in our laboratory.[9] In this way, we report herein an efficient chemosynthetic process which utilizes compound **6** as the common starting material. Our synthetic plan is outlined in Scheme 1. As can be seen, **6** can cyclize in a Michael manner to generate a diastereomeric mixture of **7** and **8** which differs stereochemically only at their spiro carbons. Compound **7** will serve as the precursor of **1** and **2**, while **8** will provide eventually **3**. In addition, the common precursor **6** also affords entries to **2** and **4**.

Results and Discussion

(a) Synthesis of Precursors. To prepare the key intermediate **6**, we began our reaction sequence employing tri-*n*-butylethynylstannane, which, in turn, was synthesized from tri-*n*-butyltin chloride and lithium acetylide in a yield over 90%.[10] The key starting material, namely, 3-(tri-*n*-butylstannyl)furan (**9**), the side product of the Yang and Wong preparation of 3,4-bis(tri-*n*-butylstannyl)furan,[9] was conveniently obtained in a pure form by an oxazole[11] and alkyne Diels−Alder/retro Diels−Alder reaction.[9] On the other hand, the common chiral precursor (+)-2,3-*O*-isopropylidene-D-glyceraldehyde was prepared from D-mannitol.[12,13]

With both **9** and the enantiopure (+)-2,3-*O*-isopropylidene-D-glyceraldehyde in hand, alcohol **10** was obtained via the addition of the aldehyde to the 3-lithiofuran

† Dedicated to Prof. Dr. Klaus Hafner on the occasion of his 70th birthday.

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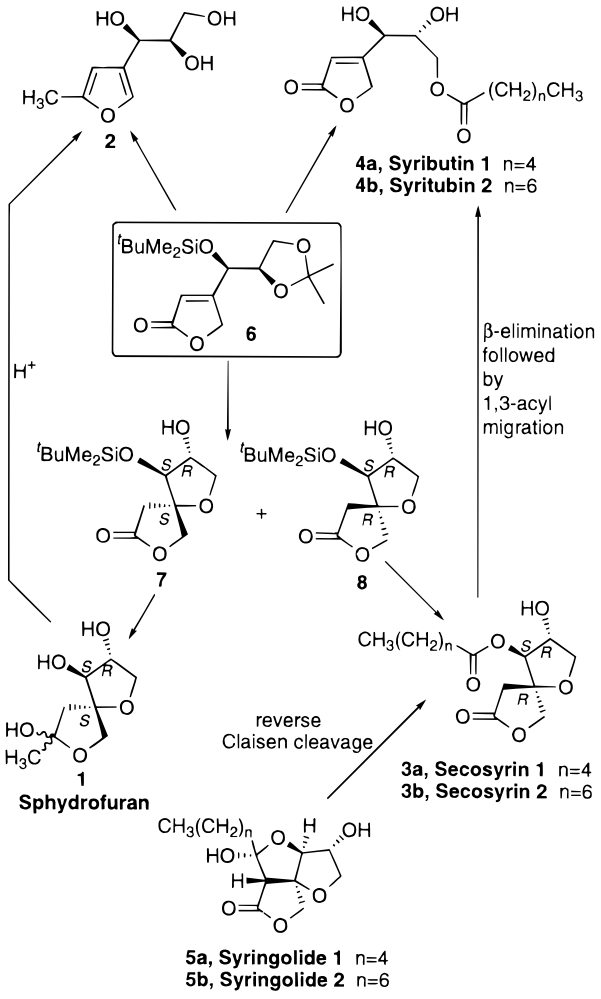
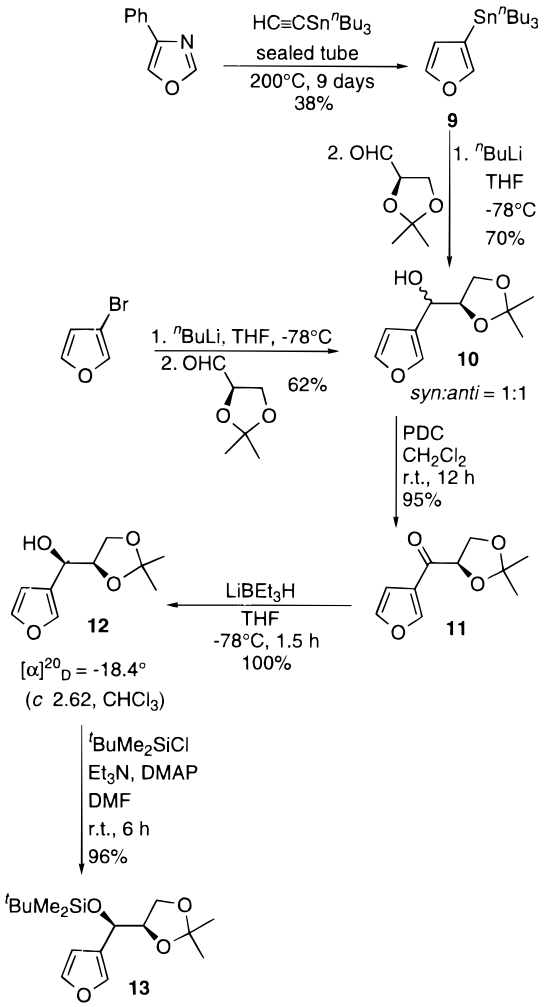
Scheme 1



Scheme 2



generated from **9** (Scheme 2), in accord with Jurczak's protocol.[14] In this manner, a mixture of the diastereomeric furylmethanols **10**[15] was furnished in a *syn*:*anti* ratio of 1:1. Without chromatographic separation, this mixture was oxidized with PDC to afford the ketone **11**,[16] which on reduction with Super-Hydride led to **12** almost quantitatively.

In considering the toxicity of tin and the need to use sealed tubes, we modified the preparation of **10**, which could also be obtained in a sizable amount from the readily accessible 3-bromofuran[17] instead of stannylfuran.[18] 3-Bromofuran was conveniently prepared from the thermal decomposition of the brominated adduct of furan and maleic anhydride.[19]

Alcohol **12** was then protected as its *tert*-butyldimethylsilyl ether **13** (96%). The conversion of **13** to the pivotal Δ^2-butenolide **6** was accomplished by the peracetic acid oxidation routine established by Kuwajima and Urabe.[20] Although in principle the direct oxidation of a 3-substituted furan would provide the corresponding butenolide, regiochemical ambiguities render this approach problematic. A more appropriate answer to this issue is the unraveling of an oxidative conversion of 2- and 5-substituted-3-alkylfuran. As has been demonstrated by Kuwajima,[20a] and employed by Schultz[20b] and Goldsmith,[20c] the trimethylsilyl group will serve to direct a regiospecific oxidation, providing the corresponding 3- or 4-alkyl-2(5*H*)-furanones. Consequently, treatment of furan **13** with 1.5 equiv of trimethylsilyl chloride gave an approximately 1:2 mixture of products **14a** and **14b**; 1 equiv of trimethylsilyl chloride gave an 8:2 ratio of **14a** and **14b**. The structures of **14a** and **14b** were confirmed by ^{1}H NMR spectral analysis. Thus, the furan H-3 and H-5 absorptions of **14a** were observed at δ 6.56 (s, 1H) and 7.51 (s, 1H), respectively, which are typical of a 2,4-disubstituted furan. On the other hand, the 2,3-disubstituted furan **14b** showed absorptions at δ 6.41 (dd, J = 1.6, 4.5 Hz, 1H) and 7.53 (dd, J = 0.6, 1.8 Hz, 1H). A much more efficient preparation of **14a** modified by us was by treating **13** with 2.2 equiv of *n*-butyllithium. The excess of base presumably led to lithiation at both C-2 and C-5. After the reaction was quenched with only 0.5

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Scheme 3

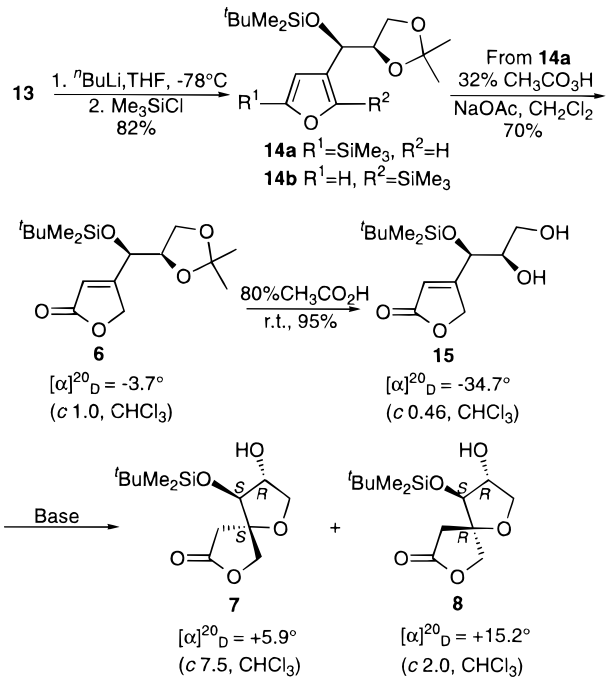


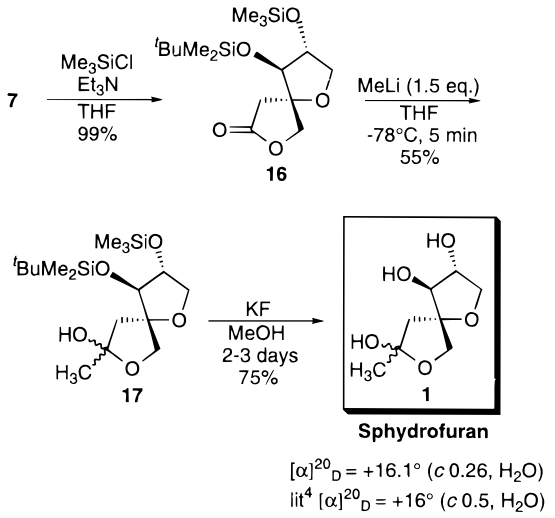
Table 1. Formation of 7 and 8 from 15

entry	base	ratio (**7**:**8**)	yield, %
1	Et_3N/DBU (cat.), $CHCl_3$, rt	1:1	66
2	DBU, THF, rt	1:1	62
3	Et_3N/DBN (cat.), $CHCl_3$, rt	1:1	63
4	(*S*)-arginine, 50% aq THF, rt	1:2	45
5	(*R*)-lysine, 50% aq THF, rt	1:2	64
6	Et_3N, $CHCl_3$, reflux	1:2	66
7	Et_3N, $CHCl_3$, rt	1:3	70
8	Et_3N, $CHCl_3$, 0 °C	1:5	72

equiv of trimethylsilyl chloride, pure trimethylsilylfuran **14a** was obtained in 82% yield (based on reacted **13**), together with recovered **13**. This remarkable regioselectivity is likely due to the steric hindrance of the *tert*-butyldimethylsilyl ether, so that the attack of the trimethylsilyl group can only take place from the less hindered side. If the reaction time was increased, generation of product **14b** again became discernible (observed by ^{1}H NMR spectrometry). Eventually, oxidation of **14a** expectedly afforded the desired butenolide **6**.[21] The structure of **6** was substantiated by its ^{1}H NMR spectral data consistent with the reported data.[8e] The removal of the acetonide protection of **6** was accomplished by its treatment with 80% acetic acid at room temperature, furnishing **15** in good yield.[22]

In order to assemble the dioxaspiro frameworks,[23] an intramolecular Michael addition was engaged as the crucial step. In this way, butenolide **15** was converted to **7** and **8** (Scheme 3). As depicted in Table 1, the Michael addition was triggered by triethylamine−DBU[24] to afford a diastereomeric mixture of spiro compounds **7** and **8** in a ratio of 1:1. The use of only triethylamine in

Scheme 4



chloroform at reflux temperature led also to ring closure of **15**, producing **7**:**8** in a ratio of 1:2. Surprisingly, similar reactions at room temperature (20−25 °C) improved the ratio to 1:3, and at 0 °C the ratio was upgraded to approximately 1:5. In light of the stereoselectivity that was obtained with different base conditions, an attempt was made to alter the selectivity by use of several chiral bases, such as L- and D-arginine, (−)-sparteine, and several other synthetic chiral bases.[25] However, these experiments all gave rather discouraging results. Despite a large amount of experimentation, the stereochemical nature of the Michael cyclization remains still unclear.

The separation of compounds **7** and **8** was achieved by column chromatography on silica gel. Compound **7** formed good single crystals suitable for an X-ray diffraction analysis.[26] The structural confirmation of **7** thus led to our unambiguous verification of the absolute stereochemistry of sphydrofuran (**1**) (Scheme 4). By analogy, the other product **8** should therefore be the precusor of secosyrins **3**.

(b) Synthesis of Sphydrofuran (1). Having attained the structural confirmation of precusors **7** and **8**, our efforts were then focused on the synthesis of sphydrofuran (**1**). Thus, protection of the remaining hydroxyl group of **7** provided trimethylsiloxy compound **16**. Then **16** was allowed to react with 1.5 equiv of methyllithium in THF at −78 °C[27] to afford the key intermediate **17**, which was extremely labile in acidic media as sphydrofuran (**1**). All workup steps and physical measurements of the compound must be carried out under either neutral or slight basic condition (pH 7−9). The final step of the synthesis was accomplished by applying a mild desilylation reaction (KF in anhydrous methanol). Sphydrofuran (**1**) was separated conveniently on a silica gel

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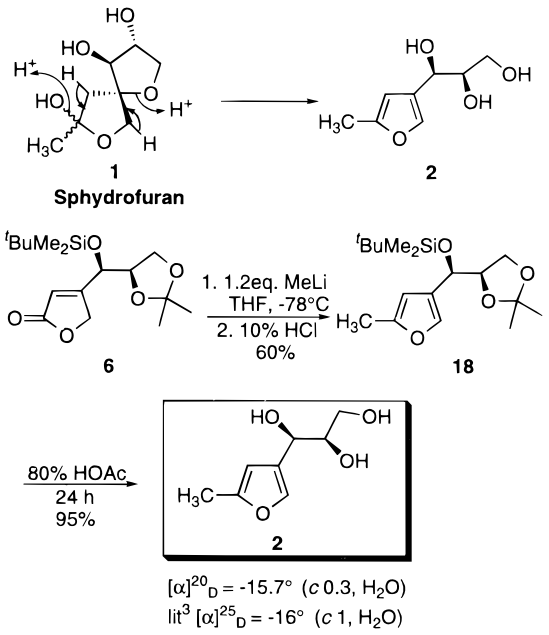
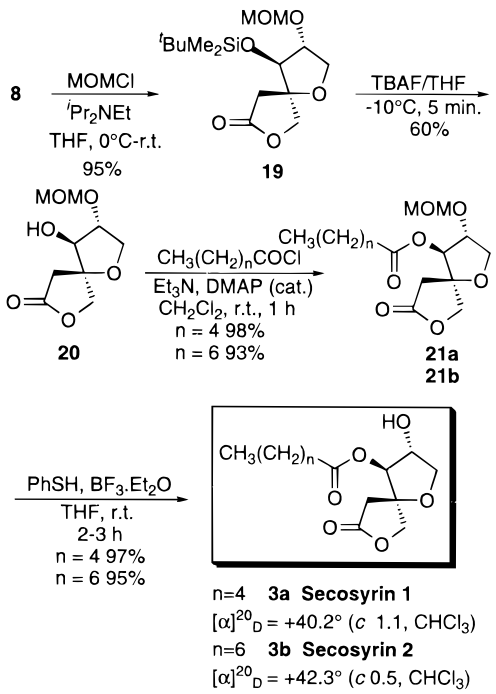
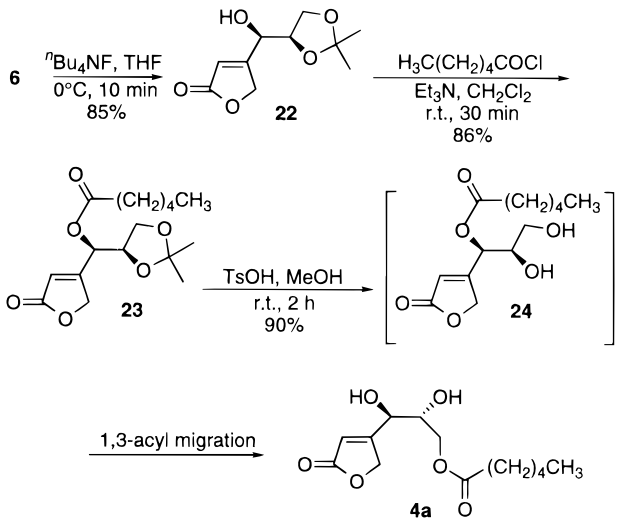
Scheme 5



Scheme 6



Scheme 7



column using chloroform/methanol (8:1) as eluent and the yield was 75%. It was important to add a very small amount of triethylamine to **1** in order to make it stable under a mild basic environment. All analytical and spectrometric data of **1** are in full agreement with those of **1** obtained from natural sources,[3,4] as well as from the chemoenzymatic synthesis.[5]

The furan coproduct of **1**, namely, 2-methyl-4-(1-glyceryl)furan (**2**), was easily obtained from **1** under mild acidic conditions. Even during workup, it was found that the amount of **1** decreased through dehydration to form **2**. On reaction with dilute HCl at room temperature, **1** was converted completely to **2**.[3a] This eventuality was probably assisted by the initial elimination of water from **1** and was then followed by the opening of the tetrahydrofuran ring to form an energetically favored furan ring (Scheme 5). Synthetically, we would like to directly prepare **2** from butenolide **6**. Thus, treatment of **6** consecutively with methyllithium and 10% HCl yielded **18**, which was deprotected by 80% acetic acid to give **2** (Scheme 5). All physical and spectrometric data of **2** are identical to an authentic sample prepared from **1**.

(c) Synthesis of Secosyrins 3 and Syributins 4. As illustrated in Schemes 6 and 8, secocyrins **3** and syributins **4** were realized from **8** and **15**, respectively. From **8**, secosyrins **3** were prepared in several steps (Scheme 6). Protection of the naked secondary hydroxyl group (excess chloromethyl methyl ether in *N*,*N*-diisopropylethylamine) produced **19**,[28] whose conversion to **21** in one step[29] was unsuccessful. Nonetheless, removal of the *tert*-butyldimethylsilyl group with $^{n}Bu_4N^{+}F^{-}$ in THF at low temperature yielded **20** after direct silica gel chromatography without aqueous workup, because **20** was not easily extracted from aqueous solution by common organic solvents such as diethyl ether, dichloromethane, and ethyl acetate.

The hydroxyl group of **20** could then be directly acylated with hexanoyl chloride or octanoyl chloride, providing **21a** or **21b**, respectively. Subsequent conversion of **21a** and **21b** into their respective targets was accomplished by treatment of **21a** or **21b** with thiophenol and boron trifluoride etherate to give secosyrin 1 (**3a**) and secosyrin 2 (**3b**), respectively.[30] The analytical and spectrometric data of **3a** and **3b**, obtained from the present total synthesis, were found to be identical with those reported for secosyrin 1 and secosyrin 2 isolated from natural sources.[6]

The syributins **4** might be formed by β-elimination followed by 1,3-acyl migration (**3** → **4**, Scheme 1). In order to prove this hypothesis, butenolide **6** was deprotected to form **22**, which was then acylated to **23**. As expected, deprotection of **23** led to syributin 1 (**4a**) instead of **24** (Scheme 7).

In a more chemospecific manner, esterification of **15** with acid chloride (1.2 equiv) under basic condition gave **25a** and **25b**, respectively. Deprotection of **25a** and **25b** finally gave the desired syributin 1 (**4a**) and syributin 2

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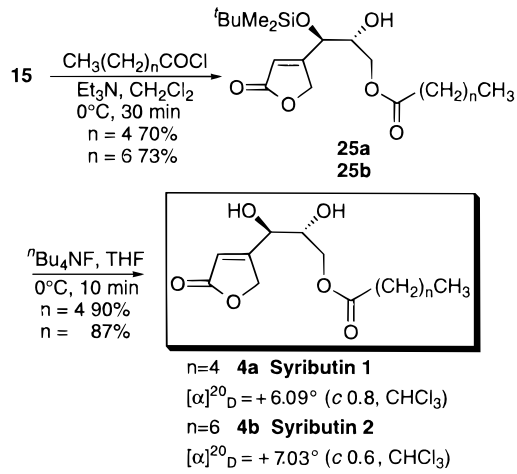
Scheme 8



(**4b**), respectively (Scheme 8). All physical and spectrometric results of both compounds are identical with those reported for the natural molecules.[6]

Conclusion

By starting from 3-(tri-*n*-butylstannyl)furan (**9**) or 3-bromofuran, we have developed efficient routes via common intermediate **6** toward the total syntheses of sphydrofuran (**1**) and its furan coproduct 2-methyl-4-(1-glyceryl)furan (**2**), secosyrins 1 and 2 (**3a** and **3b**), and syrinbutins 1 and 2 (**4a** and **4b**). The total synthesis of the more challenging syringolides 1 and 2 (**5a** and **5b**) utilizing a similar strategy is in progress.

Experimental Section

(2′*R*)-3-[1′-Hydroxy-2′,3′-(isopropylidenedioxy)propyl]furan (10). To a solution of 3-bromofuran[19] (0.93 g, 6.35 mmol) in THF (20 mL) at −78 °C was added dropwise 2.5 M *n*-butyllithium in a hexane solution (3.0 mL, 7.5 mmol). The solution was stirred at −78 °C for 0.5 h, and then (2*R*)-2,3-*O*-isopropylidene-D-glyceraldehyde[12,13] (1.34 g, 10.3 mmol) was added. After the solution was stirred for a further 0.5 h at −78 °C, the reaction was quenched with saturated aqueous NH_4Cl solution (8 mL). The aqueous layer was extracted with Et_2O. The combined organic extracts were dried ($MgSO_4$), evaporated, and chromatographed on silica gel (100 g, hexanes−ethyl acetate, 8:1) to give **10** as a 1:1 diastereomeric mixture (0.78 g, 62%) as a colorless oil: ^{1}H NMR ($CDCl_3$) δ 1.34 (s, 3H), 1.35 (s, 3H), 1.43 (s, 3H), 1.44 (s, 3H), 3.67 (dd, J = 6.0, 8.5 Hz, 1H), 3.91 (m, 3H), 4.20 (m, 2H), 4.51 (dd, J = 3.4, 7.3 Hz, 1H), 4.79 (d, J = 3.8 Hz, 1H), 6.36 (q, J = 0.9 Hz, 1H), 6.40 (q, J = 0.9 Hz, 1H), 7.37 (s, 2H), 7.41 (dd, J = 2.0, 4.6 Hz, 2H); ^{13}C NMR ($CDCl_3$) δ 24.83, 24.95, 26.10, 26.33, 64.98, 65.73, 66.50, 67.91, 78.50, 79.02, 108.50, 108.64, 109.22, 109.68, 124.49, 125.05, 139.37, 139.76, 142.82, 143.01; MS *m*/*z* 198 (M^+). Anal. Calcd for $C_{10}H_{14}O_4$: C, 60.59; H, 7.12. Found: C, 60.34; H, 7.21.

(2′*R*)-3-[1′-Oxo-2′,3′-(isopropylidenedioxy)propyl]-furan (11). To a solution of **10** (1.84 g, 9.29 mmol) in dichloromethane (20 mL) was added activated 4 Å molecular sieves powder (7.6 g) and PDC (9.2 g, 24.5 mmol). The resulting mixture was stirred at rt under anhydrous conditions for 12 h and then diluted with Et_2O (300 mL) and filtered through Celite. The filtrate was dried ($MgSO_4$) and evaporated. Chromatography on silica gel (60 g, hexanes−ethyl acetate, 10:1) gave compound **11** (1.73 g, 95%) as colorless flakes: mp 35−36 °C; ^{1}H NMR ($CDCl_3$) δ 1.44 (s, 6H), 4.21 (dd, J = 8.5, 15.9 Hz, 1H), 4.25 (dd, J = 8.5, 16 Hz, 1H), 4.81 (dd, J = 5.9, 7.2 Hz, 1H), 6.82 (d, J = 1.9 Hz, 1H), 7.42 (m, 1H), 8.38 (d, J = 0.5 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 25.31, 25.93, 66.65, 79.88, 109.13, 111.03, 124.81, 143.43, 149.61, 193.50; MS *m*/*z* 196 (M^+). Anal. Calcd for $C_{10}H_{12}O_4$: C, 61.21; H, 6.17. Found: C, 61.13; H, 5.90.

(1′*R*,2′*R*)-3-[1′-Hydroxy-2′,3′-(isopropylidenedioxy)propyl]furan (12). To a solution of the ketone **11** (39 mg, 0.2 mmol) in THF (2 mL) at −78 °C was added dropwise a 1.0 M Super-Hydride solution in THF (0.24 mL, 0.24 mmol). The resulting solution was stirred at −78 °C for 1.5 h and then quenched with a saturated aqueous NH_4Cl solution (2 mL). After extraction with Et_2O, the organic layer was dried ($MgSO_4$) and evaporated. Chromatography on silica gel (10 g, hexanes−ethyl acetate, 3:1) gave compound **12** (40 mg, 100%) as a colorless oil: $[\alpha]^{20}_D$ = −18.4 (*c* 2.62, $CHCl_3$); ^{1}H NMR ($CDCl_3$) δ 1.34 (s, 3H), 1.43 (s, 3H), 2.80 (d, J = 3.6 Hz, 1H), 3.67 (dd, J = 6.0, 8.7 Hz, 1H), 3.89 (dd, J = 6.5, 8.5 Hz, 1H), 4.20 (dd, J = 6.4, 13.0 Hz, 1H), 4.51 (dd, J = 3.3, 7.1 Hz, 1H), 6.39 (d, J = 1.7 Hz, 1H), 7.36 (m, 1H), 7.41 (s, 1H); ^{13}C NMR ($CDCl_3$) δ 25.22, 26.66, 66.03, 68.21, 79.23, 108.76, 109.96, 124.61, 139.99, 143.31; MS *m*/*z* 198 (M^+). Anal. Calcd for $C_{10}H_{14}O_4$: C, 60.59; H, 7.12. Found: C, 60.34; H, 7.21.

(1′*R*,2′*R*)-3-[1′-(*tert*-Butyldimethylsiloxy)-2′,3′-(isopropylidenedioxy)propyl]furan (13). To a solution of alcohol **12** (180 mg, 0.91 mmol), DMAP (11 mg, 0.09 mmol), and triethylamine (0.8 mL, 5.7 mmol) in DMF (0.6 mL) at rt was added ^{t}BuMe$_2$SiCl (686 mg, 4.55 mmol). The reaction mixture was stirred at rt for 6 h and then quenched with a 5% $KHCO_3$ solution (10 mL). Then it was extracted with Et_2O, dried over $MgSO_4$, and evaporated. Chromatography on silica gel (30 g, hexanes−ethyl acetate, 25:1) gave compound **13** (275 mg, 96%) as a colorless oil: ^{1}H NMR ($CDCl_3$) δ 0.00 (s, 3H), 0.07 (s, 3H), 0.87 (s, 9H), 1.32 (s, 3H), 1.33 (s, 3H), 3.69 (dd, J = 6.6, 8.5 Hz, 1H), 3.86 (dd, J = 6.6, 8.5 Hz, 1H), 4.19 (dd, J = 6.5, 12.9 Hz, 1H), 4.72 (d, J = 6.2 Hz, 1H), 6.38 (m, 1H), 7.34 (m, 2H); ^{13}C NMR ($CDCl_3$) δ −4.99, 18.14, 25.28, 25.67, 26.30, 65.58, 69.21, 79.20, 109.47, 125.43, 139.69, 142.63; MS *m*/*z* 312 (M^+). Anal. Calcd for $C_{16}H_{28}O_4Si$: C, 61.50; H, 9.03. Found: C, 60.99; H, 9.08.

(1′*R*,2′*R*)-4-[1′-(*tert*-Butyldimethylsiloxy)-2′,3′-(isopropylidenedioxy)propyl]-2-(trimethylsilyl)furan (14a) and (1′*R*,2′*R*)-3-[1′-(*tert*-Butyldimethylsiloxy)-2′,3′-(isopropylidenedioxy)propyl]-2-(trimethylsilyl)furan (14b). To a stirred solution of **13** (334 mg, 1.07 mmol) in THF (6 mL) at −78 °C was added dropwise 1.6 M *n*-butyllithum in a hexane solution (1.34 mL, 2.14 mmol). The resulting solution was stirred at −78 °C for 0.5 h; then freshly distilled Me_3SiCl (203 μL, 1.61 mmol) was added, followed by HMPA (186 μL, 1.07 mmol). After being quenched with a saturated aqueous NH_4Cl solution (5 mL), the mixture was extracted with Et_2O. The combined organic layer was dried ($MgSO_4$) and evaporated. Chromatography on silica gel (60 g, hexanes−ethyl acetate, 20:1) gave recovered starting material (63.4 mg) and a mixture of **14a** and **14b** (268 mg, 81%) in a ratio of 1:2: ^{1}H NMR ($CDCl_3$) δ −0.05 (s, 2H), −0.01 (s, 1H), 0.05 (s, 3H), 0.23 (s, 3H), 0.29 (s, 6H), 0.84 (s, 6H), 0.87 (s, 3H), 1.32 (s, 4H), 1.33 (s, 2H), 3.65 (two dd, J = 6.8, 8.5 Hz, 1H), 3.85 (two dd, J = 6.6, 8.4 Hz, 1H), 4.20 (two dd, J = 6.7, 13.1 Hz, 1H), 4.72 (two d, J = 6.3 Hz, 1H), 6.41 (dd, J = 1.6, 4.5 Hz, $^2/_3$H), 6.56 (s, $^1/_3$H), 7.51 (s, $^1/_3$H), 7.53 (dd, J = 0.6, 1.8 Hz, $^2/_3$H). The reaction with **13** (867 mg, 2.77 mmol) in THF (10 mL), 1.6 M *n*-butyllithum in a hexane solution (3.46 mL, 5.54 mmol), and Me_3SiCl (0.35 mL, 2.77 mmol) in the same manner, and rapid quenching gave **14a** and **14b** in a ratio of 8:2. The reaction with **13** (1.10 g, 3.53 mmol) in THF (15 mL), 2.5 M *n*-butyllithum in a hexane solution (3.12 mL, 7.75 mmol), and Me_3SiCl (0.23 mL, 1.78 mmol) and stirring for 20 min gave **14a** and **14b** in a ratio of 9:1.

(1′*R*,2′*R*)-4-[1′-(*tert*-Butyldimethylsiloxy)-2′,3′-(isopropylidenedioxy)propyl]-2(trimethylsilyl)furan (14a). To a stirred solution of **13** (3.88 g, 12.4 mmol) in THF (45 mL) at −78 °C was added dropwise a 1.6 M *n*-butyllithum in hexane solution (17 mL, 27.2 mmol). The resulting solution was stirred at −78 °C for 0.5 h; then freshly distilled Me_3SiCl (0.79 mL, 6 mmol) was added, followed by quenching with a saturated aqueous NH_4Cl solution (30 mL). Then it was extracted with Et_2O. The combined organic layer was dried ($MgSO_4$) and evaporated. Chromatography on silica gel (300

g, hexanes−ethyl acetate, 30:1) gave recovered starting material (2.50 g) and pure product **14a** (1.39 g, 82%) as a colorless oil: ^{1}H NMR ($CDCl_3$) δ 0.01 (s, 3H), 0.06 (s, 3H), 0.23 (s, 9H), 0.86 (s, 9H), 1.32 (s, 3H), 1.34 (s, 3H), 3.65 (dd, J = 6.8, 8.5 Hz, 1H), 3.86 (dd, J = 6.6, 8.4 Hz, 1H), 4.20 (dd, J = 6.7, 13.1 Hz, 1H), 4.72 (d, J = 6.3 Hz, 1H), 6.56 (s, 1H), 7.51 (s, 1H); ^{13}C NMR ($CDCl_3$) δ −4.83, −1.66, 18.28, 25.50, 25.80, 26.40, 65.85, 69.42, 79.41, 109.63, 119.49, 125.49, 143.98, 160.64; MS *m/z* 384 (M^+). Anal. Calcd for $C_{19}H_{36}O_4Si_2$: C, 59.34; H, 9.40. Found: C, 59.18; H, 9.52.

(1′*R*,2′*R*)-3-[1′-(*tert*-Butyldimethylsiloxy)-2′,3′-(isopropylidenedioxy)propyl]but-2-en-4-olide (6). To a stirred suspension of 32% peracetic acid (0.84 mL, 4.0 mmol) and anhydrous NaOAc (100 mg, 1.1 mmol) in dichloromethane (3 mL) at 0 °C was added **14a** (384 mg, 1.0 mmol) in dried dichloromethane (4 mL). The temperature was gradually warmed to rt, and the resulting solution was stirred for 10 h. Then it was quenched with a saturated aqueous $Na_2S_2O_3$ solution (10 mL). A saturated K_2CO_3 solution was added until the pH of the solution was between 7 and 8. The water layer was extracted with Et_2O, dried ($MgSO_4$), and evaporated. Chromatography on silica gel (30 g, hexanes−ethyl acetate, 5:1) gave compound **6** (230 mg, 70%) as a colorless oil: $[\alpha]^{20}_D$ = −3.7 (*c* 1.0, $CHCl_3$); lit[8e] $[\alpha]^{23}_D$ = −4.0 (*c* 1.0, $CHCl_3$); ^{1}H NMR ($CDCl_3$) δ 0.03 (s, 3H), 0.08 (s, 3H), 0.88 (s, 9H), 1.30 (s, 3H), 1.37 (s, 3H), 3.75 (dd, J = 6.4, 8.7 Hz, 1H), 4.00 (dd, J = 6.9, 8.7 Hz, 1H), 4.21 (dt, J = 4.7, 6.6 Hz, 1H), 4.72 (d, J = 4.6 Hz, 1H), 4.80 (dd, J = 1.9, 18.1 Hz, 1H), 4.95 (dd, J = 1.9, 18.1 Hz, 1H), 6.02 (dd, J = 1.8, 3.3 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ −5.24, −0.28, 17.87, 24.56, 25.42, 25.78, 64.91, 69.90, 71.69, 77.29, 109.78, 117.00, 168.93, 172.60; MS *m/z* 329 (MH^+); HRMS calcd for $C_{16}H_{29}O_5Si$ (MH^+) 329.1779, found 329.1777. Anal. Calcd for $C_{16}H_{28}O_5Si$: C, 58.50; H, 8.59. Found: C, 58.42; H, 8.88. The spectroscopic data of this compound were identical to those reported.[8e]

(1′*R*,2′*R*)-3-[1′-(*tert*-Butyldimethylsiloxy)-2′,3′-dihydroxypropyl]but-2-en-4-olide (15). A solution of compound **6** (328 mg, 1.0 mmol) in 80% acetic acid (2 mL) was stirred at rt for 1 day and then evaporated under vaccum. The oily residue was then chromatographed on silica gel (30 g, Et_2O) to give pure compound **15** (274 mg, 95%) as colorless crystals: $[\alpha]^{20}_D$ = −34.7 (*c* 0.46, $CHCl_3$); mp 85−86.5 °C; ^{1}H NMR ($CDCl_3$) δ 0.05 (s, 3H), 0.11 (s, 3H), 0.91 (s, 9H), 3.50 (m, 1H), 3.63−3.75 (m, 2H), 4.72 (d, J = 3.4 Hz, 1H), 4.84 (dd, J = 1.2, 13.9 Hz, 1H), 5.0 (dd, J = 1.8, 18.2 Hz, 1H), 6.0 (s, 1H); ^{13}C NMR ($CDCl_3$) δ −5.16, −4.89, 18.04, 25.63, 62.47, 70.17, 71.82, 74.00, 116.72, 170.22, 173.42; MS *m/z* 289 (MH^+). Anal. Calcd for $C_{13}H_{24}O_5Si$: C, 54.13; H, 8.39. Found: C, 53.87; H, 8.39.

(3*R*,4*S*,5*S*)-8-Oxo-3-hydroxy-4-(*tert*-butyldimethylsiloxy)-1,7-dioxaspiro[4.4]nonane (7) and (3*R*,4*S*,5*R*)-8-Oxo-3-hydroxy-4-(*tert*-butyldimethylsiloxy)-1,7-dioxaspiro[4.4]nonane (8). Entry 7, Table 1. A solution of **15** (1.53 g, 5.3 mmol) and triethylamine (22 mL, 159 mmol) in $CHCl_3$ (40 mL) was stirred at rt for 8 h. After being diluted with water (20 mL), the resulting mixture was extracted with Et_2O and dried over $MgSO_4$. Evaporation of the solvent gave a residue that was purified by column chromatography on silica gel (100 g, hexanes−ethyl acetate, 1:1) to give the diastereomeric mixture of **7** and **8** (1.07 g, 70%) as colorless crystals. Further purification of **7** and **8** by column chromatography on silica gel (150 g, hexanes−Et_2O−CH_2Cl_2 1:1:1) gave the lower R_f isomer crystal **7** (0.27 g) and higher R_f isomer crystal **8** (0.80 g) in a ratio of 1:3. Compound **7**: $[\alpha]^{20}_D$ = +5.9 (*c* 7.5, $CHCl_3$); mp 114.5−116 °C; ^{1}H NMR ($CDCl_3$) δ 0.13 (s, 3H), 0.14 (s, 3H), 0.90 (s, 9H), 2.75 (s, 2H), 3.83 (dd, J = 1.1, 9.7 Hz, 1H), 4.09 (d, J = 1.6 Hz, 1H), 4.15 (dd, J = 4.1, 9.8 Hz, 1H), 4.18 (m, 1H), 4.27 (d, J = 10.4 Hz, 1H), 4.45 (d, J = 10.4 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ −5.16, −4.60, 17.91, 25.58, 39.80, 73.74, 77.76, 81.68, 87.67, 175.67; MS *m/z* 288 (M^+). Anal. Calcd for $C_{13}H_{24}O_5Si$: C, 54.14; H, 8.39. Found: C, 54.06; H, 8.31. Compound **8**: $[\alpha]^{20}_D$ = +15.2 (*c* 2.0, $CHCl_3$); mp 148.5−150 °C; ^{1}H NMR ($CDCl_3$) δ 0.12 (s, 3H), 0.14 (s, 3H), 0.90 (s, 9H), 2.53 (d, J = 18.1 Hz, 1H), 2.87 (d, J = 18.1 Hz, 1H), 3.81 (dd, J = 2.1, 9.8 Hz, 1H), 4.01 (d, J = 2.4 Hz, 1H), 4.11 (dd, J = 4.4, 9.8 Hz, 1H), 4.20 (m, 1H), 4.34 (s, 1H), 4.35 (s, 1H); ^{13}C NMR ($CDCl_3$) δ −5.10, −4.51, 25.62, 35.42, 73.18, 76.21, 77.61, 80.64, 88.23, 175.19; MS *m/z* 288 (M^+). Anal. Calcd for $C_{13}H_{24}O_5Si$: C, 54.14; H, 8.39. Found: C, 54.13; H, 8.34.

(3*R*,4*S*,5*S*)-8-Oxo-3-(trimethylsiloxy)-4-(*tert*-butyldimethylsiloxy)-1,7-dioxaspiro[4.4]nonane (16). To a stirred solution of compound **7** (150 mg, 0.52 mmol) in dried THF (10 mL) was added triethylamine (0.3 mL, 2.08 mmol) at rt. Then freshly distilled Me_3SiCl (0.2 mL, 1.56 mmol) was added dropwise, and the resulting mixture was stirred for 5 h at the same temperature. After a saturated aqueous NH_4Cl solution (5 mL) was added, the mixture was extracted with Et_2O and the organic layer was dried over $MgSO_4$. Evaporation of the solvent gave a residue that was purified by column chromatography on silica gel (10 g, hexanes−ethyl acetate 5:1) to give **16** (185 mg, 99%) as a colorless oil: ^{1}H NMR ($CDCl_3$) δ 0.1 (m, 15H), 0.86 (s, 9H), 2.69 (s, 2H), 3.72 (d, J = 8.3 Hz, 1H), 3.95 (d, J = 1.45 Hz, 1H), 4.03−4.08 (m, 2H), 4.02 (d, J = 10.3 Hz, 1H), 4.40 (d, J = 10.3 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ −5.18, −4.47, −0.12, 17.79, 25.53, 39.84, 73.82, 74.19, 81.66, 87.41, 175.73; MS *m/z* 361 (MH^+). Anal. Calcd for $C_{16}H_{32}O_5Si_2$: C, 53.29; H, 8.94. Found: C, 53.76; H, 9.12.

(3*R*,4*S*,5*S*)-8-Hydroxy-8-methyl-3-(trimethylsiloxy)-4-(*tert*-butyldimethylsiloxy)-1,7-dioxaspiro[4.4]nonane (17). To a solution of **16** (190 mg, 0.53 mmol) in dried THF (6 mL) at −78 °C was added dropwise 1.4 M methyllithium in Et_2O (0.41 mL, 0.57 mmol). After 5 min, the reaction was quenched by adding saturated aqueous NaCl solution (3 mL). Then it was extracted with Et_2O and dried over $MgSO_4$. Evaporation of the solvent gave the residue. Purification by column chromatography on silica gel (15 g, hexanes−ethyl acetate 5:1) gave an anomeric mixture of compound **17** (109.2 mg, 55%) as a colorless oil, which was stabilized by mixing with a drop of triethylamine. Compound **17** was not purified further and was immediately used in the next step.

Sphydrofuran (1). To a solution of **17** (109 mg, 0.29 mmol) in dried methanol (10 mL) was added KF (67.3 mg, 1.2 mmol). The resulting solution was stirred at rt for 2 days. Then evaporation of the solvent gave a residue that was purified by column chromatography on silica gel (15 g, $CHCl_3$−MeOH 7:1 with a drop of Et_3N) to gave sphydrofuran (**1**) (41.3 mg, 75%) as a pale yellow syrup: $[\alpha]^{20}_D$ = +16.1 (*c* 0.26, H_2O), lit.[3] $[\alpha]^{22}_D$ = +18 (*c* 1, H_2O), lit.[4] $[\alpha]^{20}_D$ = +16 (*c* 0.5, H_2O); MS *m/z* 190 (M^+). The spectroscopic data of this compound were identical to those reported for the natural product.[3,4]

(1′*R*,2′*R*)-2-Methyl-4-[1′-(*tert*-butyldimethylsiloxy)-2′,3′-(isopropylidenedioxy)propyl]furan (18). To a stirred solution of **6** (207.8 mg, 0.63 mmol) in dried THF (20 mL) at −78 °C was added dropwise 1.4 M methyllithium in Et_2O (0.54 mL, 0.76 mmol). After 20 min, the resulting solution was quenched by adding a 10% HCl solution (2 mL), and the resulting mixture was stirred for 10 min. The mixture was extracted with Et_2O and dried over $MgSO_4$. After evaporation of the solvent, the residue was purified by column chromatography on silica gel (15 g, hexanes−ethyl acetate 4:1) to give **18** (124 mg, 60%) as a colorless oil: ^{1}H NMR ($CDCl_3$) δ 0.00 (s, 3H), 0.10 (s, 3H), 0.86 (s, 9H), 1.33 (s, 3H), 1.34 (s, 3H), 2.24 (s, 3H), 3.66 (dd, J = 6.7, 8.5 Hz, 1H), 3.85 (dd, J = 6.7, 8.4 Hz, 1H), 4.15 (dd, J = 6.5, 13.0 Hz, 1H), 4.61 (d, J = 6.4 Hz, 1H), 5.95 (s, 1H), 7.17 (s, 1H); ^{13}C NMR ($CDCl_3$) δ −4.87, 13.64, 18.26, 25.81, 65.76, 69.40, 79.29, 105.46, 109.52, 126.19, 137.84, 152.23; MS *m/z* 326 (M^+); HRMS calcd for $C_{17}H_{30}O_4Si$ (M^+) 326.1908, found 326.1900.

(1′*R*,2′*R*)-2-Methyl-4-(1′-glyceryl)furan (2). A solution of **18** (40 mg, 0.12 mmol) in an 80% acetic acid aqueous solution (1 mL) was stirred for 1 day at rt. After neutralization of the solution by adding saturated K_2CO_3 solution, it was extracted with ethyl acetate and dried over $MgSO_4$. Evaporation of the solvent gave a residue and purification by column chromatography on silica gel (10 g, ethyl acetate) gave compound **2** (20 mg, 95%) as a colorless syrup: $[\alpha]^{20}_D$ = −15.7 (*c* 0.3, H_2O), lit.[3] $[\alpha]^{25}_D$ = −16 (*c* 1, H_2O); ^{1}H NMR (D_2O) δ 2.24 (s, 3H), 3.43 (dd, J = 6.9, 11.8 Hz, 1H), 3.57 (dd, J = 3.7 11.8 Hz, 1H), 3.8 (td, J = 3.5, 6.5 Hz, 1H), 4.57 (d, J = 6.6 Hz, 1H), 6.08 (s, 1H), 7.37 (s, 1H); ^{13}C NMR [$(CD_3)_2C$=O] δ 14.23, 64.72, 68.70, 76.80, 107.11, 129.39, 139.68, 153.50. Anal. Calcd for $C_8H_{12}O_4$: C, 55.81; H, 7.02. Found: C, 55.66; H, 7.10. The spectroscopic data of this compound were identical to those

reported for the natural product[3,4] and those derived from sphydrofuran under acidic conditions.

(3*R*,4*S*,5*R*)-8-Oxo-3-[((methyloxy)methyl)oxy]-4-(*tert*-butyldimethylsiloxy)-1,7-dioxaspiro[4.4]nonane (19). A solution of **8** (140 mg, 0.49 mmol) and diisopropylethylamine (4.2 mL, 24.1 mmol) in dried THF (20 mL) was cooled to 0 °C and treated dropwise with chloromethyl methyl ether (0.93 mL, 12.25 mmol) via a syringe. The reaction mixture was allowed to warm slowly to rt during 10 h and quenched with a saturated aqueous NaCl solution (5 mL). After extraction with Et_2O, it was dried over $MgSO_4$. Evaporation of the solvent gave a residue that was purified by column chromatography on silica gel (15 g, hexanes−ethyl acetate 3:1) to give copmound **19** (153 mg, 95%) as a colorless oil: ^{1}H NMR ($CDCl_3$) δ 0.06 (s, 3H), 0.08 (s, 3H), 0.84 (s, 9H), 2.46 (d, J = 18.0 Hz, 1H), 2.80 (d, J = 18.0 Hz, 1H), 3.31 (d, J = 1.0 Hz, 3H), 3.86 (dd, J = 1.9, 9.7 Hz, 1H), 4.00 (m, 1H), 4.08 (m, 2H), 4.24 (s, 2H), 4.60 (s, 2H); ^{13}C NMR ($CDCl_3$) δ −5.55, −5.05, 17.49, 25.23, 35.10, 55.32, 70.83, 75.57, 78.32, 82.38, 87.67, 95.75, 174.59; MS m/z 333 (MH^+). Anal. Calcd for $C_{15}H_{28}O_6Si$: C, 54.19; H, 8.49. Found: C, 54.54; H, 8.91.

(3*R*,4*S*,5*R*)-8-Oxo-3-[((methyloxy)methyl)oxy]-4-hydroxy-1,7-dioxaspiro[4.4]nonane (20). To a stirred solution of **19** (102 mg, 0.3 mmol) in THF (10 mL) was added a 1 M TBAF in THF solution (0.37 mL, 0.37 mmol) at −10 °C. After 5 min, the resulting solution was directly purified by column chromatography on silica gel (15 g, ethyl acetate) to give product **20** (40.2 mg, 60%) as colorless crystals: ^{1}H NMR ($CDCl_3$) δ 2.44 (d, J = 18.0 Hz, 1H), 3.0 (d, J = 18.0 Hz, 1H), 3.35 (d, J = 3.3 Hz, 3H), 3.76 (dd, J = 3.5, 11.5 Hz, 1H), 4.0 (m, 2H), 4.11 (m, 1H), 4.30 (s, 2H), 4.64 (d, J = 1.4 Hz, 2H); ^{13}C NMR ($CDCl_3$) δ 34.71, 55.83, 69.76, 75.86, 77.01, 83.46, 87.23, 96.51, 176.08; MS m/z 219 (MH^+). Anal. Calcd for $C_9H_{14}O_6$: C, 49.54; H, 6.47. Found: C, 49.37, H, 6.56.

(3*R*,4*S*,5*R*)-8-Oxo-3-[((methyloxy)methyl)oxy]-4-(hexanoyloxy)-1,7-dioxaspiro[4.4]nonane (21a). To a solution of compound **20** (28.6 mg, 0.13 mmol) and Et_3N (36 μL, 0.26 mmol) and DMAP (10 mg) in dried CH_2Cl_2 (5 mL) was added dropwise hexanoyl chloride (22 μL, 0.16 mmol). The resulting solution was stirred at rt for 1 h. After addition of a saturated aqueous NaCl solution (2 mL), the mixture was extracted with CH_2Cl_2 and dried over $MgSO_4$. Evaporation of the solvent gave the residue, and chromatography on silica gel (13 g, hexanes−ethyl acetate, 3:1) gave pure **21a** (40.6 mg, 98%) as a colorless oil: ^{1}H NMR ($CDCl_3$) δ 0.9 (t, J = 6.6 Hz, 3H), 1.3 (m, 4H), 1.62 (m, 2H), 2.35 (t, J = 7.4 Hz, 2H), 2.58 (d, J = 17.7 Hz, 1H), 2.74 (d, J = 17.9 Hz, 1H), 3.37 (s, 3H), 3.92 (dd, J = 1.9, 10.0 Hz, 1H), 4.13 (dd, J = 4.9, 10.3 Hz, 1H), 4.22 (m, 1H), 4.28 (s, 2H), 4.65 (d, J = 6.9 Hz, 1H), 4.74 (d, J = 6.9 Hz, 1H), 5.19 (s, 1H); ^{13}C NMR ($CDCl_3$) δ 13.84, 22.22, 24.47, 31.18, 34.02, 35.56, 55.91, 71.62, 75.78, 78.71, 80.04, 86.83, 95.87, 172.69, 174.12; MS m/z 317 (MH^+). This compound was not purified further and was used to prepare **3a** directly.

(3*R*,4*S*,5*R*)-8-Oxo-3-[((methyloxy)methyl)oxy-4-(octanoyloxy)-1,7-dioxaspiro[4.4]nonane (21b). To a solution of compound **20** (74.5 mg, 0.34 mmol) and Et_3N (94 μL, 0.68 mmol) and DMAP (25 mg) in dried CH_2Cl_2 (15 mL) was added dropwise octanoyl chloride (70 μL, 0.41 mmol). The workup procedure is similar to that for the preparation of compound **21a**. Chromatography (15 g, hexanes−ethyl acetate, 3:1) gave pure **21b** (109.4 mg, 93%) as a colorless oil: ^{1}H NMR ($CDCl_3$) δ 0.84 (t, J = 3.6 Hz, 3H), 1.24 (m, 8H), 1.58 (m, 2H), 2.33 (t, J = 7.4 Hz, 2H), 2.55 (d, J = 17.9 Hz, 1H), 2.70 (d, J = 17.9 Hz, 1H), 3.34 (s, 3H), 3.90 (dd, J = 1.8, 10.2 Hz, 1H), 4.11 (m, 1H), 4.19 (m, 1H), 4.3 (s, 2H), 4.62 (d, J = 6.8 Hz, 1H), 4.70 (d, J = 6.8 Hz, 1H), 5.17 (s, 1H); ^{13}C NMR ($CDCl_3$) δ 13.95, 22.46, 24.70, 28.74, 28.92, 31.49, 33.96, 35.48, 55.80, 71.52, 75.71, 78.62, 79.97, 86.77, 95.79, 172.59, 174.05; MS m/z 345 (MH^+). Anal. Calcd for $C_{17}H_{28}O_7$: C, 59.29; H, 8.91. Found: C, 59.56; H, 8.79.

Secosyrin 1 (3a). To a stirred solution of **21a** (45.5 mg, 0.14 mmol) in THF (2 mL) were added PhSH (0.5 mL) and $BF_3{\cdot}Et_2O$ (0.5 mL, 4 mmol) at rt. After the mixture was stirred for 2 h, a saturated aqueous NaCl solution (5 mL) was added. The mixture was extracted with CH_2Cl_2, dried over $MgSO_4$, and concentrated under reduced pressure. Chromatography on silica gel (20 g, hexanes−ethyl acetate 2:1) gave pure secosyrin 1 (**3a**) (37.9 mg, 97%) as a colorless oil: $[\alpha]^{20}_D$ = +40.2 (*c* 1.10, $CHCl_3$), lit.[8f] $[\alpha]^{26}_D$ = +48.2 (*c* 0.12, $CHCl_3$), lit.[8g] $[\alpha]_D$ = +42.95 (*c* 1.43, CH_2Cl_2); ^{1}H NMR ($CDCl_3$) δ 0.89 (t, J = 6.8 Hz, 3H), 1.3 (m, 4H), 1.63 (m, 2H), 2.38 (t, J = 7.4 Hz, 2H), 2.58 (d, J = 18.0 Hz, 1H), 2.78 (d, J = 18.0 Hz, 1H), 3.86 (dd, J = 2.8, 10.2 Hz, 1H), 4.14 (dd, J = 5.3, 10.3 Hz, 1H), 4.31 (dd, J = 2.5, 5.1 Hz, 1H), 4.36 (d, J = 10.2 Hz, 1H), 4.45 (d, J = 10.0 Hz, 1H), 4.94 (d, J = 2.0 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 13.75, 22.19, 24.46, 31.15, 34.01, 35.47, 72.83, 75.85, 76.40, 81.67, 86.61, 173.62, 174.43; MS m/z 273 (MH^+). The ^{1}H NMR spectrum of synthetic **3a** was identical to that of natural **3a** provided by Professor J. J. Sims.[6]

Secosyrin 2 (3b). To a stirred solution of **21b** (52.6 mg, 0.15 mmol) in THF (2 mL) were added PhSH (0.8 mL) and $BF_3{\cdot}Et_2O$ (0.6 mL, 4.8 mmol) at rt. In the same manner as above, chromatography on silica gel (20 g, hexanes−ethyl acetate 1:2) gave pure secosyrin 2 (**3b**) (43.6 mg, 95%) as a colorless oil: $[\alpha]^{20}_D$ = +42.3 (*c* 0.5, $CHCl_3$); ^{1}H NMR ($CDCl_3$) δ 0.80 (t, J = 6.5 Hz, 3H), 1.21 (m, 8H), 1.56 (m, 2H), 2.36 (t, J = 7.5 Hz, 2H), 2.58 (d, J = 18.0 Hz, 1H), 2.78 (d, J = 18.0 Hz, 1H), 3.86 (dd, J = 2.5, 10.2 Hz, 1H), 4.12 (dd, J = 2.5, 10.2 Hz, 1H), 4.31 (m, 1H), 4.38 (d, J = 10.3 Hz, 1H), 4.44 (d, J = 10.3 Hz, 1H), 4.97 (s, 1H); ^{13}C NMR ($CDCl_3$) δ 13.99, 22.51, 24.76, 28.78, 28.95, 31.53, 34.04, 35.46, 72.83, 75.63, 75.85, 81.61, 86.59, 173.60, 174.45; MS m/z 301 (MH^+). The ^{1}H NMR spectrum of synthetic **3b** was identical to that of natural **3b** provided by Professor J. J. Sims.[6]

(1′*R*,2′*R*)-3-[1′-Hydroxy-2′,3′-(isopropylidenedioxy)propyl]but-2-en-4-olide (22). To a stirred solution of compound **6** (14.5 mg, 0.04 mmol) in THF (1 mL) at 0 °C was added dropwise a 1.0 M TBAF in THF solution (53 μL, 0.05 mmol), and the resulting mixture was stirred for 10 min at the same temperature. After water (1 mL) was added, the mixture was extracted with Et_2O and dried over $MgSO_4$. Evaporation of the solvent and chromatography on silica gel (10 g, ethyl acetate) gave pure **22** (8 mg, 85%) as a colorless oil: ^{1}H NMR ($CDCl_3$) δ 1.37 (s, 3H), 1.48 (s, 3H), 3.93 (dd, J = 5.5, 8.7 Hz, 1H), 4.12 (dd, J = 6.6, 7.8 Hz, 1H), 4.25 (ddd, J = 4.7, 5.7, 6.5 Hz, 1H), 4.58 (m, 1H), 4.92 (m, 2H), 6.03 (q, J = 1.9 Hz, 1H). The spectroscopic data of it were identical to those reported.[8e]

(1′*R*,2′*R*)-3-[1′-(Hexanoyloxy)-2′,3′-(isopropylidenedioxy)propyl]but-2-en-4-olide (23). To a stirred solution of **22** (8 mg, 0.037 mmol) in CH_2Cl_2 (1.5 mL) were added Et_3N (11 μL, 0.08 mmol) and hexanoyl chloride (7 μL, 0.05 mmol) at 0 °C. After 30 min of stirring at rt under N_2, a saturated aqueous NH_4Cl solution (1 mL) was added, and the mixture was extracted with Et_2O and dried over $MgSO_4$. Evaporation of the solvent and chromatography on silica gel (6 g, hexanes−ethyl actate 3:1) gave **23** (10 mg, 86%) as a colorless oil: ^{1}H NMR ($CDCl_3$) δ 0.89 (t, J = 6.4 Hz, 3H), 1.25−1.34 (m, 9H), 1.44 (s, 3H), 1.62−1.68 (m, 2H), 2.35 (m, 2H), 3.80 (dd, J = 5.5, 8.8 Hz, 1H), 4.08(dd, J = 6.9, 8.8 Hz, 1H), 4.36 (dd, J = 6.6, 10.3 Hz, 1H), 4.87 (d, J = 1.8 Hz, 1H), 4.90 (d, J = 1.9 Hz, 1H), 5.80 (d, J = 3.7 Hz, 1H), 6.05 (d, J = 1.7 Hz, 1H). The spectroscopic data of **23** were identical to those reported.[8e]

Deprotection of Compound 23. A solution of **23** (83 mg, 0.266 mmol) and toluene-4-sulfonic acid (50.6 mg, 0.266 mmol) in MeOH (10 mL) was stirred for 2 h at rt. After Et_3N (1 mL) was added to the resulting solution, the solvents were removed by evaporation. Chromatography on silica gel (20 g, hexanes−ethyl acetate 1:3) gave syributin 1 (**4a**) (65 mg, 90%) as a colorless oil. The ^{1}H NMR spectrum of **4a** was identical to that of natural **4a** provided by Professor J. J. Sims.[6]

(1′*R*,2′*R*)-3-[1′-(*tert*-Butyldimethylsiloxy)-3′-(hexanoyloxy)propyl]but-2-en-4-olide (25a). To a solution of **15** (152 mg, 0.53 mmol) and Et_3N (88 μL, 0.63 mmol) in CH_2Cl_2 (20 mL) was added dropwise freshly distilled hexanoyl chloride (89 μL, 0.63 mmol) at 0 °C. The resulting solution was stirred at the same temperature for 0.5 h. After a saturated aqueous NaCl solution (5 mL) was added, the mixture was extracted with Et_2O and dried over $MgSO_4$. Evaporation of the solvent and chromatography on silica gel (20 g, hexanes−ethyl acetate 2:1) gave compound **25a** (142.7 mg, 70%) as a colorless oil: ^{1}H NMR ($CDCl_3$) δ 0.06 (s, 3H), 0.11 (s, 3H), 0.88 (t, J = 6.7 Hz, 3H), 0.92 (s, 9H), 1.31 (m, 4H), 1.61 (m, 2H), 2.33 (t, J = 7.5

Hz, 2H), 3.87 (m, 1H), 4.06 (dd, J = 5.0, 11.5 Hz, 1H), 4.18 (dd, J = 4.9, 11.7 Hz, 1H), 4.68 (d, J = 3.0 Hz, 1H), 4.87 (d, J = 16.6 Hz, 1H), 5.0 (d, J = 16.4 Hz, 1H), 6.04 (s, 1H); ^{13}C NMR ($CDCl_3$) δ −4.98, 13.76, 17.92, 22.16, 24.38, 25.49, 31.11, 33.90, 64.19, 69.79, 71.86, 72.26, 116.61, 170.11, 173.30, 174.05; MS m/z 387 (MH^+). Anal. Calcd for $C_{19}H_{34}O_6Si$: C, 59.03; H, 8.86. Found: C, 58.94; H, 9.02.

(1′*R*,2′*R*)-3-[1′-(*tert*-Butyldimethylsiloxy)-3′-(octanoyloxy)propyl]but-2-en-4-olide (25b). The reaction was performed with **15** (144 mg, 0.5 mmol), Et_3N (83 μL, 0.6 mmol), and octanoyl chloride (103 μL, 0.6 mmol) in CH_2Cl_2 (20 mL) in the same manner as described for the preparation of **25a** to give **25b** (151 mg, 73%) as a colorless oil: ^{1}H NMR ($CDCl_3$) δ 0.04 (s, 3H), 0.08 (s, 3H), 0.85 (t, J = 6.6 Hz, 3H), 0.88 (s, 9H), 1.23 (m, 8H), 1.58 (m, 2H), 2.29 (t, J = 7.4 Hz, 2H), 3.88 (m, 1H), 4.06 (dd, J = 4.8, 7.1 Hz, 1H), 4.14 (dd, J = 4.6, 11.5 Hz, 1H), 4.68 (d, J = 3.3 Hz, 1H), 4.87 (dd, J = 1.8, 18.7 Hz, 1H), 5.00 (dd, J = 1.8, 18.1 Hz, 1H), 6.02 (s, 1H); ^{13}C NMR ($CDCl_3$) δ −5.07, 13.93, 17.92, 22.45, 24.70, 25.52, 28.76, 28.91, 31.50, 33.93, 64.19, 69.81, 71.87, 72.25, 116.60, 170.12, 173.30, 174.04; MS m/z 415 (MH^+). Anal. Calcd for $C_{21}H_{38}O_6Si$: C, 60.84; H, 9.24. Found: C, 61.15; H, 9.43.

Syributin 1 (4a). To a stirred solution of **25a** (50.4 mg, 0.13 mmol) in THF (5 mL) was added a 1.0 M TBAF in THF solution (0.15 mL, 0.15 mmol) at 0 °C. After the solution was stirred for 10 min, water (5 mL) was added to dilute the solution. Then the mixture was extracted with ethyl acetate and dried over $MgSO_4$. Evaporation of the solvent and chromatography on silica gel (15 g, hexanes−ethyl acetate 1:2) gave pure syributin 1 (**4a**) (32 mg, 90%) as a colorless oil: $[\alpha]^{20}_D$ = +6.09 (c 0.8, $CHCl_3$); lit.[8e] $[\alpha]^{26}_D$ = +6.8 (c 0.5, $CHCl_3$); ^{1}H NMR ($CDCl_3$) δ 0.88 (t, J = 7.0 Hz, 3H), 1.29 (m, 4H), 1.61 (m, 2H), 2.34 (t, J = 7.6 Hz, 2H), 3.96 (m, 1H), 4.16 (dd, J = 6.2, 11.5 Hz, 1H), 4.29 (dd, J = 5.7, 11.7 Hz, 1H), 4.64 (m, 1H), 4.89 (d, J = 18.1 Hz, 1H), 4.98 (d, J = 18.1 Hz, 1H), 6.06 (s, 1H); ^{13}C NMR ($CDCl_3$) δ 13.85, 22.19, 24.44, 31.16, 34.01, 64.51, 68.79, 71.26, 72.02, 116.33, 170.58, 174.22, 174.43; MS m/z 273 (MH^+). The ^{1}H NMR spectrum of synthetic **4a** was identical to that of natural **4a** provided by Professor J. J. Sims.[6]

Syributin 2 (4b). The reaction was performed with **25b** (71.6 mg, 0.17 mmol) and a 1.0 M TBAF in THF solution (0.20 mL, 0.20 mmol) in THF (8 mL) in the same manner as described for the preparation of syributin 1 (**4a**) to give syributin 2 (**4b**) (45 mg, 87%) as a colorless oil: $[\alpha]^{20}_D$ = +7.03 (c 0.6, $CHCl_3$); ^{1}H NMR ($CDCl_3$) δ 0.81 (t, J = 6.6 Hz, 3H), 1.21 (m, 8H), 1.54 (m, 2H), 2.88 (t, J = 7.5 Hz, 2H), 3.91 (m, 1H), 4.10 (dd, J = 6.5, 11.5 Hz, 1H), 4.22 (dd, J = 5.5, 11.5 Hz, 1H), 4.58 (m, 1H), 4.85 (d, J = 18.0 Hz, 1H), 4.91 (d, J = 18.5 Hz, 1H), 6.0 (s, 1H); ^{13}C NMR ($CDCl_3$) δ 13.99, 22.51, 24.76, 28.83, 28.99, 31.56, 34.05, 64.47, 68.79, 71.19, 72.09, 116.28, 170.84, 174.41; MS m/z 301 (MH^+). The ^{1}H NMR spectrum of synthetic **4b** was identical to that of natural **4b** provided by Professor J. J. Sims.[6]

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Supporting Information Available: Experimental procedures for preparing compounds **9**, **10** (from **9**), and **7**/**8** (Table 1, entries 1−6 and 8). Listing of ^{1}H and ^{13}C NMR spectra for compounds prepared, as well as the X-ray crystallographic data of **7** (41 pages). This material is contained in libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.

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