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SmI_2-induced cyclization of optically active (*E*)- and (*Z*)-β-alkoxyvinyl sulfoxides with aldehydes

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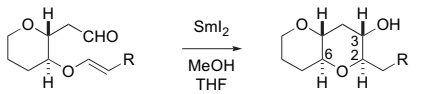
ABSTRACT

SmI_2-induced reaction of (*E*)-β-alkoxyvinyl (*R*)- and (*S*)-sulfoxides with aldehydes effected a highly stereoselective intramolecular cyclization to give 2,6-*anti*-2,3-*cis*- and 2,6-*syn*-2,3-*trans*-tetrahydropyran-3-ols, respectively. The reaction of (*Z*)-(*R*)-isomer gave 2,6-*syn*-2,3-*cis*-tetrahydropyran-3-ol and a ring-opened product, and that of (*Z*)-(*S*)-isomer yielded many products.

1. Introduction

Since the first isolation of brevetoxin-B as a red tide toxin, a number of marine polycyclic ethers, exemplified by ciguatoxins, gambierol, and maitotoxin, have been reported.[1] The most characteristic structural feature of these natural products is a *trans*-fused polycyclic ether ring system. Their synthetically challenging, complex structures and potent bioactivities have attracted the attention of numerous synthetic organic chemists. Thus, various synthetic methods have been extensively studied and total synthesis of many polycyclic ethers has been achieved.[2] We have already developed an efficient method for the construction of *trans*-fused polycyclic ether based on the SmI_2-induced reductive cyclization of β-alkoxyacrylate **A₁** with a carbonyl group, affording 2,6-*syn*-2,3-*trans*-tetrahydropyran-3-ol **B₁** with complete stereoselectivity (Fig. 1).[3] This method has been successfully applied to the synthesis of polycyclic ethers.[4] The product **B₁** is a cyclic ether having an acetic acid moiety, that is, a two-carbon unit, as the C2-side chain. A functional one-carbon unit as the C2-side chain is often required and is useful for the synthesis of polycyclic ethers.



A₁: R = CO_2Et
A₂: R = SO_2Ph
A₃: R = S(O)-*p*-Tol

B₁: R = CO_2Et
B₂: R = SO_2Ph
B₃: R = S(O)-*p*-Tol

Figure 1. SmI_2-induced reductive cyclizations.

Furthermore, synthetic methods for not only 2,6-*syn*-2,3-*trans*-tetrahydropyran-3-ol, but also the stereoisomers, have also been required for the synthesis of several marine polycyclic ethers. In order to solve this problem, we have recently developed SmI_2-induced reductive cyclizations of β-alkoxyvinyl sulfones **A₂**[5] and β-alkoxyvinyl sulfoxides **A₃**[6,7] with aldehydes. Herein, we describe in detail the SmI_2-induced cyclization of optically active (*E*)- and (*Z*)-β-alkoxyvinyl sulfoxides **A₃** with aldehydes.

2. Results and discussion

In the reaction of β-alkoxyvinyl sulfoxide **A₃** with SmI_2, we expected that the (*R*/*S*)-chirality of sulfoxide and the (*E*/*Z*)-stereochemistry of the olefin in the substrates would influence the transition state to give several stereoisomers as products, stereoselectively. Therefore, we investigated the SmI_2-induced reductive cyclization using four stereoisomers, **5**, **8**, **13**, and **17**, as the substrates.

First, we examined the reaction of (*E*)-β-alkoxyvinyl (*R*)- and (*S*)-sulfoxides, **5** and **8**, with aldehydes (Scheme 1). The substrate **5** was synthesized from the known alcohol **1**,[4g] which was prepared by SmI_2-induced cyclization as the key reaction. Treatment of **1** with (*R*)-ethynyl *p*-tolylsulfoxide **2**[8] in the presence of *N*-methylmorpholine (NMM) stereoselectively afforded (*E*)-β-alkoxyvinyl (*R*)-sulfoxide **4** in 96% yield,[9] and this was reduced with DIBAH to give the aldehyde **5** in 85% yield. Upon treatment of (*E*)-(*R*)-**5** with 2.6 equiv of SmI_2[10] in the presence of MeOH (2.5 equiv) in THF, reductive cyclization took place smoothly at 0 °C to give 2,6-*anti*-2,3-*cis*-tetrahydropyran-3-ol **6a** as a single product, which was acetylated with Ac_2O in pyridine to give the acetate **6b** in 64% yield (two steps). Use of CF_3CH_2OH instead of MeOH as a proton source slightly improved the yield of **6b** (71%).[11] The 2,6-*anti*-2,3-*cis*-configuration of **6b** was confirmed by the coupling constants of C3-H; δ 5.16 (ddd, J=11.3, 5.5, 5.5 Hz). On the other hand, the reaction of **1**

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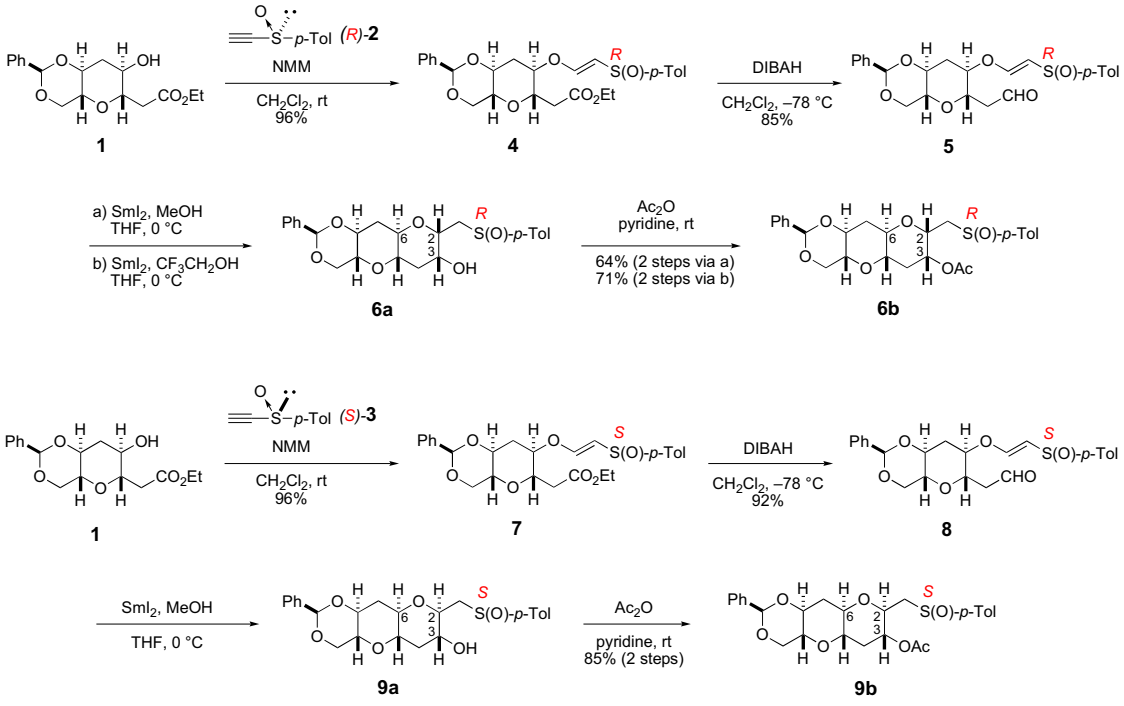


Scheme 1.

and (*S*)-ethynyl *p*-tolylsulfoxide **3** in the presence of NMM, followed by DIBAH reduction, afforded the aldehyde **8** in 88% yield (two steps). The SmI_2-induced cyclization of (*E*)-(*S*)-**8** in the presence of MeOH afforded 2,6-*syn*-2,3-*trans*-tetrahydropyran-3-ol **9a**, which was acetylated with Ac_2O to give the acetate **9b** in 85% yield (two steps). The 2,6-*syn*-2,3-*trans*-configuration of **9b** was also confirmed by the coupling constants of C3-H; δ 4.67 (ddd, J=11.0, 9.8, 4.6 Hz).

These results can be explained as follows (Fig. 2). In the SmI_2-induced cyclization, the first single-electron reduction of aldehyde

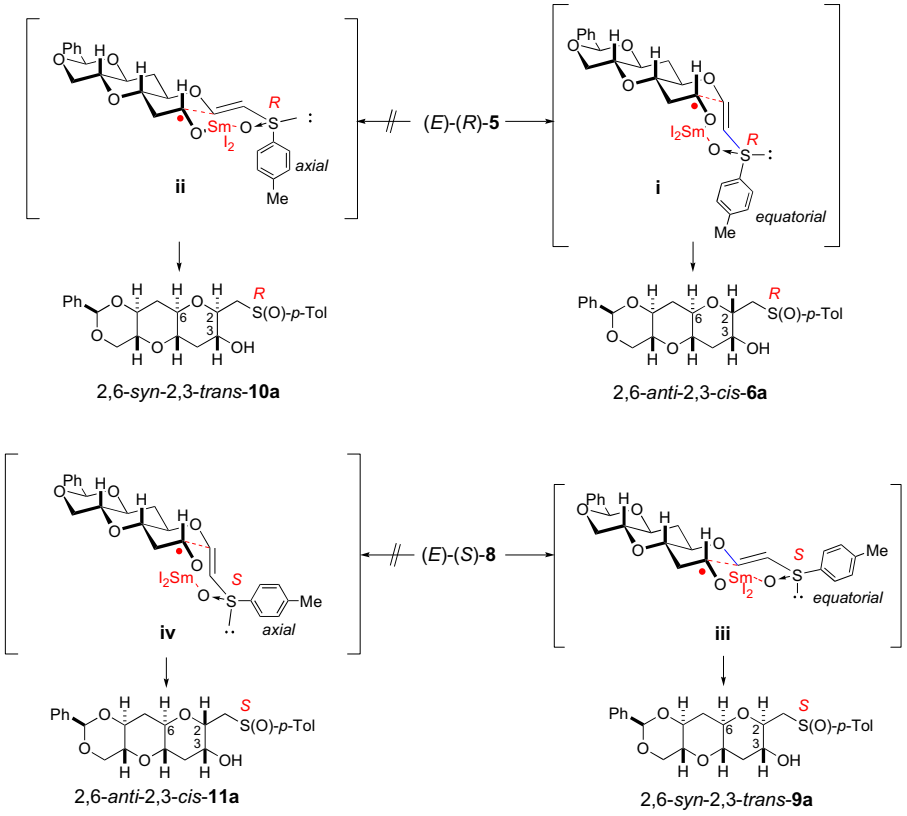
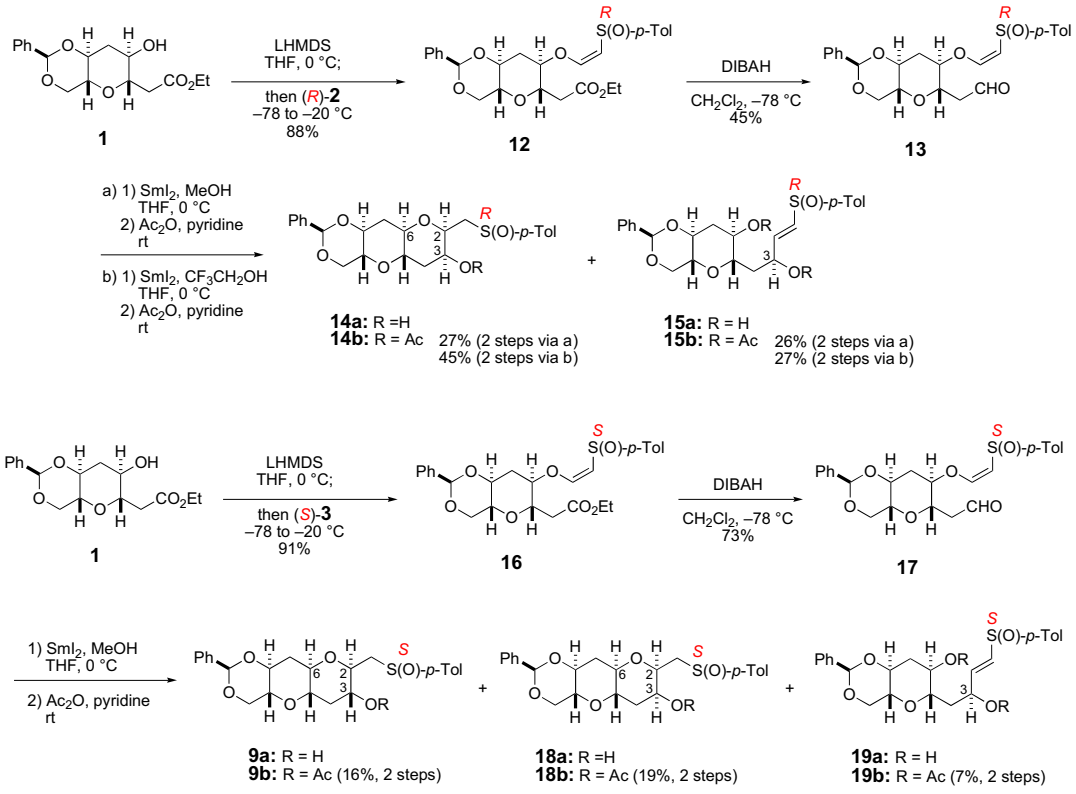


Figure 2. Plausible transition states for the SmI_2-induced cyclization of **5** and **8**.



Scheme 2.

with SmI_2 gives a ketyl radical and then C–C bond formation occurs in the chelated intermediate to give the cyclized product.[3] From the result of reaction of (*E*)-(*R*)-**5** to give **6a**, the reaction is considered to proceed through transition state **i**, involving chelation by Sm(III) and sulfoxide. The intermediate **i** has an *equatorial* *p*-tolyl group in the chair-like conformation. If the reaction proceeded through the other chelated transition state **ii** having an *axial* *p*-tolyl group, the 2,6-*syn*-2,3-*trans*-isomer **10a** must be produced. Namely, in this cyclization, *equatorial* configuration of the *p*-tolyl group in the transition state should be most important to control the stereochemistry of the product. Furthermore, the result of the reaction of (*E*)-(*S*)-**8** giving **9a** also supports the above conclusion, that is, the

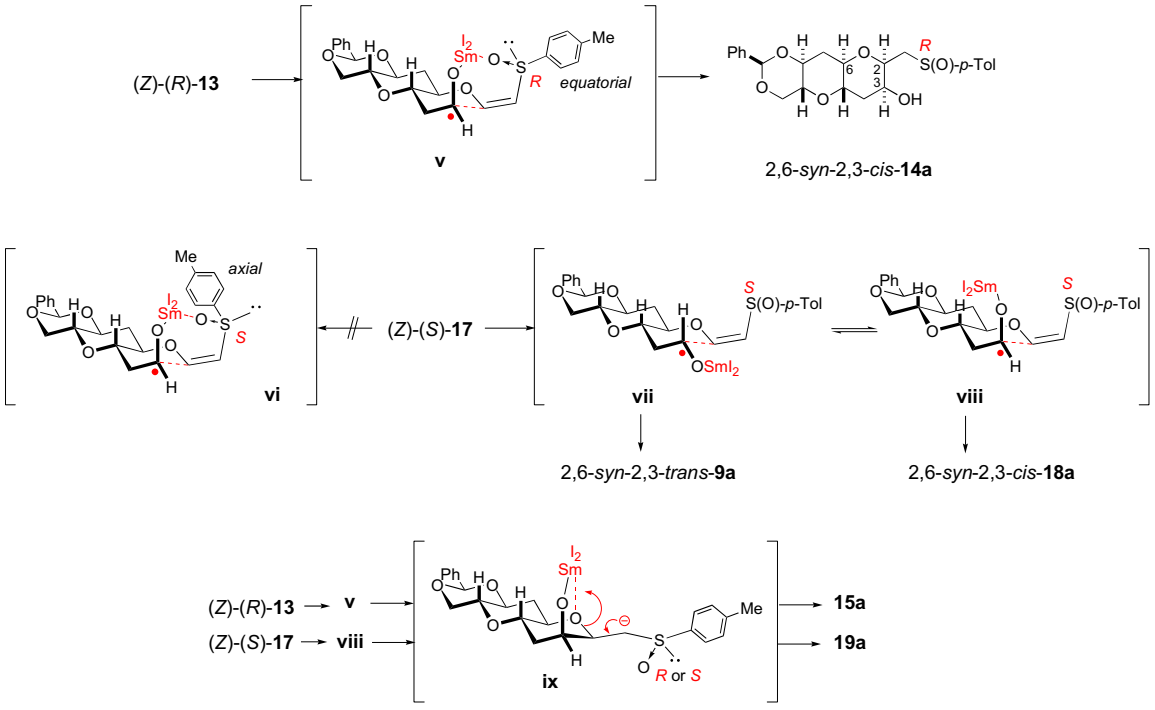
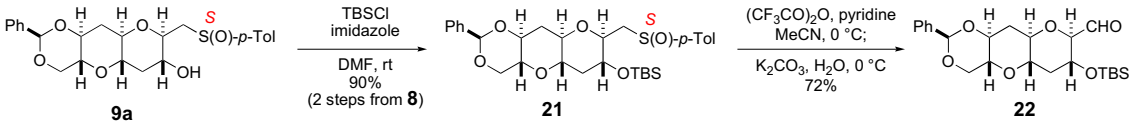


Figure 3. Plausible transition states for the SmI_2-induced cyclization of **13** and **17**.



Scheme 3.

reaction of **8** would proceed through the chelated transition state **iii** having an *equatorial* *p*-tolyl group to give **9a**. In this case, the other transition state **iv** having an *axial* *p*-tolyl group must produce the 2,6-*anti*-2,3-*cis*-isomer **11a**.

Next, the reactions of (*Z*)-β-alkoxyvinyl (*R*)- and (*S*)-sulfoxides, **13** and **17**, with SmI_2 were examined (Scheme 2). Treatment of **1** with LHMDS followed by addition of (*R*)-sulfoxide **2** stereoselectively afforded (*Z*)-β-alkoxyvinyl (*R*)-sulfoxide **12** in 88% yield,[9] and DIBAH reduction gave the aldehyde **13** in 45% yield. Treatment of (*Z*)-(*R*)-**13** with SmI_2 in the presence of MeOH in THF at 0 °C, followed by acetylation, afforded two products; 2,6-*syn*-2,3-*cis*-3-acetoxy-tetrahydropyran **14b** (27%) and (*E*)-γ-acetoxyvinyl sulfoxide **15b** (26%). Use of CF_3CH_2OH instead of MeOH in the present reaction slightly increased the yield to give **14b** (45%) and **15b** (27%). The 2,6-*syn*-2,3-*cis*-configuration of **14b** was confirmed by the coupling constant of C3-H; δ 5.11 (br s, $W_{1/2}$=5.6 Hz) and observed NOE between C2-H and C6-H. The structure of the (*E*)-olefin **15b** was determined by characteristic ^{1}H NMR signals of vinyl protons; δ 6.53 (dd, *J*=15.3, 5.5 Hz, C2-H), 6.38 (dd, *J*=15.3, 1.2 Hz, C1-H).[12] Moreover, addition of **1** and (*S*)-sulfoxide **3** in the presence of LHMDS gave the (*Z*)-β-alkoxyvinyl (*S*)-sulfoxide **16** in 91% yield, and this was reduced with DIBAH to give the aldehyde **17** in 73% yield. The reaction of (*Z*)-(*S*)-**17** with SmI_2, followed by acetylation, gave many products, which contain 2,6-*syn*-2,3-*trans*-**9b** (ca. 16%), 2,6-*syn*-2,3-*cis*-**18b** (ca. 19%), (*E*)-γ-acetoxyvinyl sulfoxide **19b** (ca. 7%), etc.[13] Use of CF_3CH_2OH did not improve the yield of the cyclized products. The 2,6-*syn*-2,3-*cis*-configuration of **18b** was confirmed by the coupling constant of C3-H; δ 5.05 (br s, $W_{1/2}$=7.0 Hz, 1H) and observed NOE between C2-H and C6-H. The structure of the (*E*)-olefin **19b** was also determined by characteristic ^{1}H NMR signals; δ 6.49 (dd, *J*=15.2, 5.8 Hz, C2-H), 6.41 (d, *J*=15.2 Hz, C1-H).[14]

The reaction of (*Z*)-(*R*)-**13** would also proceed through the chelated transition state **v** to give **14a** (Fig. 3). In the case of (*Z*)-(*S*)-**17**, the corresponding chelated transition state **vi** would be unfavorable, because of the *axial* *p*-tolyl group; thus, the reaction would proceed via the non-chelated transition states, **vii** and **viii**, to give **9a** and **18a**, respectively. The olefinic by-products **15a** and **19a** might be produced by ring opening subsequent to the cyclization; the participation of the *axial*-*O*-Sm(III) to the ring-O atom in the intermediate **ix**, generated through **v** or **viii** via C–C bond formation followed by the second reduction with SmI_2, might assist the ring opening.

For application to the synthesis of polycyclic ethers, the *p*-tolylsulfoxymethyl group of the product **9a** was transformed to an aldehyde group (Scheme 3). TBS protection of **9a** afforded the TBS–ether **21** in 90% yield (two steps from **8**). Treatment of the sulfoxide **21** with $(CF_3CO)_2O$–pyridine followed by aqueous K_2CO_3 afforded the aldehyde **22** in 72% yield. Thus, the SmI_2-induced cyclization of β-alkoxyvinyl sulfoxide should be useful for the construction of tetrahydropyran derivatives having a functional one-carbon unit as the C2-side chain.

3. Conclusion

In summary, SmI_2-induced highly stereoselective cyclization of β-alkoxyvinyl sulfoxides with aldehydes was developed for the construction of several stereoisomers of tetrahydropyran-3-ol derivatives. The desired stereoisomers of tetrahydropyran-3-ols could be obtained by selecting the appropriate combination of substrate and reagent, (*R*)-**2** or (*S*)-**3**.

4. Experimental

4.1. General

Flash column chromatography was performed on Silica gel 60 N (spherical neutral, 40–100 μm, Kanto Kagaku). Melting points were measured on a Yanaco MP-S9 and are uncorrected. Optical rotations were measured on a JASCO P-1010 polarimeter. IR spectra were recorded on a JASCO FT/IR-460. ^{1}H and ^{13}C NMR spectra were recorded on JEOL JNM-EX 300, JEOL JNM-EX 500, BRUKER Biospin ADVANCE 400 M, and BRUKER 600 UltraShield . Mass spectra were recorded on JEOL JMS-SX102A.

4.1.1. (E)-β-Alkoxyvinyl (R)-sulfoxide-ester ***4***. To a solution of **1** (51.2 mg, 0.159 mmol) in CH_2Cl_2 (1.5 mL) were added *N*-methylmorpholine (18.4 mg, 0.180 mmol) and (*R*)-**2** (41.0 mg, 0.250 mmol) at 0 °C. After stirring at room temperature for 16 h, the reaction mixture was quenched with 1 N-HCl and extracted with EtOAc. The combined organic layer was washed with brine, dried over $MgSO_4$, and evaporated in vacuo. The residue was purified by flash column chromatography (*n*-hexane/EtOAc, 2:1) to give vinyl sulfoxide **4** (74.2 mg, 96%) as a yellow oil. $[\alpha]^{23}_D$=−55.2 (*c* 1.04, $CHCl_3$); IR (neat) 2980, 2933, 2867, 1733, 1622, 1599, 1496, 1456, 1393, 1369, 1327, 1299, 1278, 1180, 1099, 1038, 1013 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.49 (d, *J*=7.9 Hz, 2H), 7.45 (dd, *J*=7.6, 2.1 Hz, 1H), 7.37–7.34 (m, 3H), 7.30 (d, *J*=8.2 Hz, 2H), 7.15 (d, *J*=12.5 Hz, 1H), 5.81 (d, *J*=12.5 Hz, 1H), 5.48 (s, 1H), 4.28 (dd, *J*=10.4, 4.6 Hz, 1H), 4.15 (br q, *J*=7.0 Hz, 2H), 3.96 (ddd, *J*=10.1, 10.1, 4.6 Hz, 1H), 3.89 (ddd, *J*=8.5, 8.5, 2.7 Hz, 1H), 3.64 (dd, *J*=10.4, 10.4 Hz, 1H), 3.51 (ddd, *J*=12.2, 12.2, 3.4 Hz, 1H), 3.42 (ddd, *J*=9.5, 9.5, 4.6 Hz, 1H), 2.69 (dd, *J*=15.3, 3.1 Hz, 1H), 2.55 (ddd, *J*=11.0, 3.7, 3.7 Hz, 1H), 2.45 (dd, *J*=15.6, 7.9 Hz, 1H), 2.39 (s, 3H), 1.76 (ddd, *J*=11.0, 11.0, 11.0 Hz, 1H), 1.25 (br t, *J*=7.0 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 170.1, 154.9, 141.5, 140.9, 136.9, 129.8, 129.1, 128.2, 126.0, 124.1, 114.0, 101.6, 77.5, 76.3, 75.5, 73.1, 68.8, 60.7, 37.0, 34.3, 21.2, 14.1; HRMS (EI) calcd for $C_{26}H_{30}O_7S$ [M$^+$] 486.1712, found 486.1710.

4.1.2. (E)-β-Alkoxyvinyl (R)-sulfoxide-aldehyde ***5***. To a solution of **4** (282.3 mg, 0.580 mmol) in CH_2Cl_2 (5.8 mL) was added DIBAH (1.20 mL, 0.97 M solution in *n*-hexane, 1.16 mmol) at −78 °C. After stirring for 20 min, *i*-PrOH (1.0 mL) and water (1.0 mL) were added at the same temperature and silica gel was added at room temperature. The mixture was diluted with EtOAc, stirred for 1 h, filtrated through a Celite pad, and evaporated in vacuo. The residue was purified by flash column chromatography (*n*-hexane/EtOAc, 1:1→1:2) to give aldehyde **5** (218.3 mg, 85%) as colorless crystals. Mp 158.0–159.0 °C (EtOAc); $[\alpha]^{23}_D$=−74.2 (*c* 1.00, $CHCl_3$); IR (KBr) 2941, 2880, 2743, 1723, 1622, 1491, 1451, 1401, 1390, 1372, 1338, 1290, 1223, 1207, 1175, 1137, 1121, 1100, 1079, 1050, 1039, 1011 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.73 (t, *J*=1.2 Hz, 1H), 7.49 (d, *J*=7.9 Hz, 2H), 7.45 (dd, *J*=7.6, 2.6 Hz, 2H), 7.37–7.35 (m, 3H), 7.30 (d, *J*=7.9 Hz, 1H), 7.14 (d, *J*=12.8 Hz, 1H), 5.82 (d, *J*=12.8 Hz, 1H), 5.48 (s, 1H), 4.27 (dd, *J*=10.7, 4.9 Hz, 1H), 3.97 (ddd, *J*=9.7, 9.7, 3.1 Hz, 1H), 3.88 (ddd, *J*=10.7, 10.7, 4.6 Hz, 1H), 3.62 (dd, *J*=10.4, 10.4 Hz, 1H), 3.51 (ddd,

J=11.9, 9.5, 4.0 Hz, 1H), 3.43 (ddd, J=9.5, 9.5, 4.9 Hz, 1H), 2.74 (dd, J=16.5, 1.5 Hz, 1H), 2.59–2.53 (m, 2H), 2.39 (3H, s), 1.76 (ddd, J=11.3, 11.3, 11.3 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 199.0, 154.6, 141.4, 141.0, 136.8, 129.9, 129.1, 128.2, 126.0, 124.1, 114.2, 101.6, 77.7, 75.4, 74.7, 73.1, 68.7, 45.4, 34.2, 21.2; HRMS (EI) calcd for $C_{24}H_{26}O_6S$ [M^+] 442.1450, found 442.1451; Anal. Calcd for $C_{24}H_{26}O_6S$: C, 65.14; H, 5.92, found C, 65.13; H, 6.17.

*4.1.3. Reaction of (E)-(R)-**5** with SmI_2 followed by acetylation.* (a) To a solution of **5** (65.0 mg, 0.147 mmol) and MeOH (11.9 μL, 0.368 mmol) in THF (1.5 mL) was added SmI_2 (3.8 mL, 0.1 M solution in THF, 0.380 mmol) at 0 °C. After stirring for 15 min, the mixture was quenched with satd $Na_2S_2O_3$ and satd $NaHCO_3$, and extracted with EtOAc. The combined organic layer was washed with brine, dried over $MgSO_4$, and evaporated in vacuo to give crude alcohol **6a** (63.4 mg). To a solution of **6a** in pyridine (1.0 mL) was added acetic anhydride (1.0 mL) at room temperature. After stirring for 42 h, the mixture was evaporated azeotropically with benzene in vacuo. The residue was purified by flash column chromatography (*n*-hexane/EtOAc, 1:1) to give acetate **6b** (47.5 mg, 64%) as colorless crystals. Mp 200.0–201.0 °C (EtOAc); $[\alpha]^{21}_D$=+76.0 (*c* 1.02, $CHCl_3$); IR (KBr) 3057, 3035, 2934, 2868, 1742, 1598, 1501, 1470, 1456, 1418, 1394, 1378, 1356, 1332, 1315, 1293, 1284, 1190, 1180, 1175, 1157, 1105, 1100, 1048, 1027, 1014 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.60 (d, J=7.9 Hz, 2H), 7.48 (d, J=6.4 Hz, 2H), 7.37 (d, J=6.7 Hz, 5H), 5.52 (s, 1H), 5.16 (ddd, J=11.3, 5.5, 5.5 Hz, 1H), 4.58 (ddd, J=10.1, 5.5, 4.0 Hz, 1H), 4.31 (dd, J=10.4, 4.9 Hz, 1H), 3.68 (dd, J=10.4, 10.4 Hz, 1H), 3.58 (ddd, J=12.5, 9.2, 4.0 Hz, 1H), 3.43 (ddd, J=9.5, 9.5, 4.6 Hz, 1H), 3.31–3.26 (m, 2H), 3.22 (dd, J=13.7, 10.7 Hz, 1H), 3.00 (dd, J=13.7, 3.4 Hz, 1H), 2.44 (s, 3H), 2.34–2.30 (m, 2H), 2.04 (s, 3H), 1.71 (ddd, J=11.0, 11.0, 11.0 Hz, 1H), 1.55 (ddd, J=11.3, 11.3, 11.3 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 169.4, 142.0, 140.7, 137.1, 130.1, 129.1, 128.3, 126.1, 124.2, 101.8, 77.1, 76.3, 73.7, 69.2, 69.0, 67.9, 67.4, 54.7, 34.5, 30.6, 21.4, 21.0; HRMS (EI) calcd for $C_{26}H_{30}O_7S$ [M^+] 486.1712, found 486.1707; Anal. Calcd for $C_{26}H_{30}O_7S$: C, 64.18; H, 6.21; S, 6.59. found C, 64.15; H, 6.24; S, 6.51.

(b) To a solution of **5** (128.1 mg, 0.289 mmol) and CF_3CH_2OH (72.8 μL, 0.723 mmol) in THF (3.0 mL) was added SmI_2 (7.2 mL, 0.1 M solution in THF, 0.720 mmol) at 0 °C. After stirring at 0 °C for 20 min, the mixture was quenched with satd $Na_2S_2O_3$ and satd $NaHCO_3$, and extracted with EtOAc. The combined organic layer was washed with brine, dried over $MgSO_4$, and evaporated in vacuo to give crude alcohol **6a** (258.3 mg). To a solution of **6a** in pyridine (2.0 mL) was added acetic anhydride (2.0 mL) at room temperature. After stirring for 12 h, the mixture was azeotropically evaporated with benzene in vacuo. The residue was purified by flash column chromatography (*n*-hexane/EtOAc, 1:1) to give an acetate **6b** (99.4 mg, 71%) as colorless crystals.

4.1.4. (E)-β-Alkoxyvinyl (S)-sulfoxide-ester **7**. To a solution of **1** (100.0 mg, 0.310 mmol) in CH_2Cl_2 (3.0 mL) were added *N*-methylmorpholine (36.8 mg, 0.360 mmol) and (*S*)-**3** (76.2 mg, 0.464 mmol) at 0 °C. The mixture was stirring at room temperature for 28 h, quenched with 1 N-HCl, and extracted with EtOAc. The combined organic layer was washed with brine, dried over $MgSO_4$, and evaporated in vacuo. The residue was purified by flash column chromatography (*n*-hexane/EtOAc, 2:1→1:1) to give vinyl sulfoxide **7** (145.2 mg, 96%) as a white solid. $[\alpha]^{20}_D$=−26.1 (*c* 1.01, $CHCl_3$); IR (neat) 2982, 2935, 2876, 1739, 1733, 1622, 1602, 1493, 1456, 1389, 1369, 1330, 1306, 1287, 1195, 1180, 1100, 1031, 1015 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.48 (m, 4H), 7.34 (m, 5H), 7.14 (d, J=12.5 Hz, 1H), 5.85 (d, J=12.5 Hz, 1H), 5.50 (s, 1H), 4.30 (dd, J=10.4, 4.9 Hz, 1H), 4.16 (qd, J=7.0, 2.1 Hz, 2H), 3.98 (ddd, J=10.7, 9.8, 4.6 Hz, 1H), 3.88 (ddd, J=8.5, 7.9, 3.7 Hz, 1H), 3.65 (dd, J=10.4, 10.4 Hz, 1H), 3.54 (ddd, J=12.8, 8.8, 4.0 Hz, 1H), 3.43 (ddd, J=10.0, 10.0, 4.9 Hz, 1H), 2.72 (dd, J=15.9, 3.7 Hz, 1H), 2.64 (ddd, J=11.6, 4.3, 4.3 Hz, 1H), 2.46 (dd, J=15.6, 7.6 Hz, 1H), 2.41 (s, 3H), 1.80 (ddd, J=11.6, 11.6, 11.6 Hz, 1H), 1.26 (t, J=9.3 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 170.1, 155.0, 141.6, 141.1, 137.0, 129.9, 129.1, 128.3, 126.0, 124.2, 114.5, 101.6, 78.4, 76.4, 75.7, 73.2, 68.9, 60.8, 36.8, 34.7, 21.3, 14.1; HRMS (EI) calcd for $C_{26}H_{30}O_7S$ [M^+] 486.1712, found 486.1706.

4.1.5. (E)-β-Alkoxyvinyl (S)-sulfoxide-aldehyde ***8***. To a solution of **7** (251.2 mg, 0.516 mmol) in CH_2Cl_2 (5.0 mL) was added DIBAH (1.06 mL, 0.97 M solution in *n*-hexane, 1.028 mmol) at −78 °C. After stirring at −78 °C for 20 min, *i*-PrOH (2.0 mL) and water (2.0 mL) were added at the same temperature and silica gel was added at room temperature. The mixture was diluted with EtOAc, stirred for 1 h, filtrated through a Celite pad, and concentrated in vacuo. The residue was purified by flash column chromatography (*n*-hexane/EtOAc, 1:1→1:2) to give aldehyde **8** (210.0 mg, 92%) as colorless crystals. Mp 136.0–137.0 °C (EtOAc); $[\alpha]^{21}_D$=−44.0 (*c* 1.06, $CHCl_3$); IR (KBr) 3045, 3014, 2974, 2932, 2875, 1733, 1729, 1616, 1602, 1493, 1456, 1394, 1373, 1338, 1303, 1287, 1212, 1186, 1151, 1102, 1007 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.75 (dd, J=2.1, 1.5 Hz, 1H), 7.50–7.46 (m, 4H), 7.39–7.35 (m, 3H), 7.32 (d, J=7.9 Hz, 2H), 7.12 (d, J=12.5 Hz, 1H), 5.85 (d, J=12.5 Hz, 1H), 5.51 (s, 1H), 4.29 (dd, J=10.4, 4.6 Hz, 1H), 3.98 (ddd, J=9.2, 9.2, 3.4 Hz, 1H), 3.88 (ddd, J=11.0, 11.0, 4.6 Hz, 1H), 3.64, (dd, J=10.1, 10.1 Hz, 1H), 3.54 (ddd, J=10.8, 8.9, 4.0 Hz, 1H), 3.44 (ddd, J=9.8, 9.8, 4.9 Hz, 1H), 2.78 (ddd, J=16.5, 3.4, 1.2 Hz, 1H), 2.67 (ddd, J=11.6, 4.3, 4.3 Hz, 1H), 2.57 (ddd, J=16.5, 8.2, 2.4 Hz, 1H), 2.41 (s, 3H), 1.81 (ddd, J=11.3, 11.3, 11.3 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 199.0, 154.5, 141.4, 141.2, 136.9, 129.9, 129.2, 128.3, 126.0, 124.2, 114.7, 101.6, 78.1, 75.6, 74.9, 73.3, 68.8, 45.3, 34.6, 21.3; HRMS (EI) calcd for $C_{24}H_{26}O_6S$ [M^+] 442.1450, found 442.1448. Anal. Calcd for $C_{24}H_{26}O_6S$: C, 65.14; H, 5.92; S, 7.25, found C, 65.05; H, 5.99; S, 7.18.

4.1.6. Reaction of (E)-(S)- ***8*** *with SmI_2 followed by acetylation.* To a solution of **8** (55.9 mg, 0.126 mmol) and MeOH (10.3 μL, 0.315 mmol) in THF (1.2 mL) was added SmI_2 (8.0 mL, 0.1 M solution in THF, 0.800 mmol) at 0 °C. After stirring for 15 min, the mixture was quenched with satd $Na_2S_2O_3$ and satd $NaHCO_3$ and extracted with EtOAc. The combined organic layer was washed with brine, dried over $MgSO_4$ and evaporated in vacuo to give crude alcohol **9a**. To a solution of **9a** in pyridine (1.0 mL) was added acetic anhydride (1.0 mL) at room temperature. After stirring for 15 h, the mixture was azeotropically evaporated with benzene in vacuo. The residue was purified by flash column chromatography (*n*-hexane/EtOAc, 2:1) to give acetate **9b** (51.9 mg, 85%) as colorless crystals. Mp 219.5–220.5 °C (EtOAc); $[\alpha]^{23}_D$=−11.7 (*c* 1.42, $CHCl_3$); IR (KBr) 2925, 2878, 2857, 1748, 1494, 1456, 1424, 1387, 1376, 1340, 1329, 1312, 1289, 1220, 1190, 1106, 1092, 1074, 1048, 1039, 1029 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.54 (d, J=8.2 Hz, 2H), 7.50 (dd, J=7.9, 1.8 Hz, 2H), 7.39–7.35 (m, 3H), 7.33 (d, J=8.2 Hz, 2H), 5.55 (s, 1H), 4.67 (ddd, J=11.0, 9.8, 4.6 Hz, 1H), 4.32 (dd, J=10.4, 4.6 Hz, 1H), 3.98 (ddd, J=11.6, 11.0, 1.8 Hz, 1H), 3.71 (dd, J=10.4, 10.4 Hz, 1H), 3.62 (ddd, J=11.6, 9.2, 4.0 Hz, 1H), 3.43 (ddd, J=10.1, 10.1, 4.9 Hz, 1H), 3.35 (ddd, J=11.0, 9.2, 4.0 Hz, 1H), 3.26 (ddd, J=11.6, 9.2, 4.0 Hz, 1H), 2.91 (dd, J=13.1, 1.8 Hz, 1H), 2.69 (dd, J=13.1, 11.0 Hz, 1H), 2.54 (ddd, J=11.3, 4.3, 4.3 Hz, 1H), 2.50 (ddd, J=11.0, 4.0, 4.0 Hz, 1H), 2.41 (3H, s), 2.03 (3H, s), 1.75 (ddd, J=11.3, 11.3, 11.3 Hz, 1H), 1.59 (ddd, J=11.6, 11.6, 11.6 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 169.8, 141.6, 140.9, 137.2, 130.0, 129.1, 128.3, 126.1, 123.8, 101.8, 76.8, 76.6, 76.0, 73.7, 73.5, 69.6, 69.0, 61.0, 34.9, 34.5, 21.4, 21.0; HRMS (EI) calcd for $C_{26}H_{30}O_7S$ [M^+] 486.1712, found 486.1712.; Anal. Calcd for $C_{26}H_{30}O_7S$: C, 64.18; H, 6.21; S, 6.59. Found C, 64.18; H, 6.27; S, 6.21.

4.1.7. (Z)-β-Alkoxyvinyl (R)-sulfoxide-ester ***12***. To a solution of **1** (84.3 mg, 0.262 mmol) in THF (2.4 mL) was added LHMDS (300 μL, 1.0 M solution in THF, 0.300 mmol) at 0 °C. After stirring at 0 °C for

30 min and at room temperature for 30 min, a solution of (*R*)-**2** (207.1 mg, 1.255 mmol) in THF (1.2 mL) was added at −78 °C. After stirring at −20 °C for 2 h, the mixture was quenched with satd $NaHCO_3$ and extracted with EtOAc. The combined organic layer was washed with brine, dried over $MgSO_4$, and evaporated in vacuo. The residue was purified by flash column chromatography (*n*-hexane/EtOAc, 1:2) to give vinyl sulfoxide **12** (112.3 mg, 88%) as a white solid. $[\alpha]^{21}_D$=−155.8 (*c* 1.18, $CHCl_3$); IR (neat) 2979, 2929, 2874, 1734, 1624, 1492, 1456, 1395, 1369, 1328, 1306, 1286, 1235, 1201, 1179, 1098, 1030, 1015 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.50 (d, *J*=8.2 Hz, 2H), 7.48–7.46 (m, 2H), 7.40–7.36 (m, 3H), 7.29 (d, *J*=7.9 Hz, 2H), 6.64 (d, *J*=5.5 Hz, 1H), 5.52 (s, 1H), 5.47 (d, *J*=5.5 Hz, 1H), 4.33 (dd, *J*=10.4, 4.9 Hz, 1H), 4.20 (q, *J*=7.3 Hz, 2H), 3.99–3.93 (m, 2H), 3.64 (dd, *J*=10.4, 10.4 Hz, 1H), 3.56 (ddd, *J*=11.6, 8.9, 4.0 Hz, 1H), 3.46 (ddd, *J*=9.8, 9.8, 4.9 Hz, 1H), 2.87 (dd, *J*=15.6, 3.1 Hz, 1H), 2.58–2.53 (m, 2H), 2.40 (s, 3H), 1.88 (ddd, *J*=11.3, 11.3, 11.3 Hz, 1H), 1.29 (t, *J*=7.0 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 170.2, 150.7, 142.0, 141.0, 137.0, 129.9, 129.2, 128.4, 126.1, 123.8, 115.2, 101.7, 79.7, 76.5, 75.9, 73.2, 69.0, 60.9, 36.7, 35.5, 21.4, 14.2; HRMS (EI) calcd for $C_{26}H_{30}O_7S$ [M^+] 486.1712, found 486.1716.

*4.1.8. (Z)-β-Alkoxyvinyl (R)-sulfoxide-aldehyde **13**.* To a solution of **12** (37.4 mg, 77.3 μmol) in CH_2Cl_2 (0.8 mL) was added DIBAH (240 μL, 0.97 M solution in *n*-hexane, 0.233 mmol) at −78 °C. After stirring at −78 °C for 1.5 h, *i*-PrOH (0.5 mL) and water (0.5 mL) were added at the same temperature and silica gel was added at room temperature. The mixture was diluted with EtOAc, stirred for 1 h, filtrated through a Celite pad, and evaporated in vacuo. The residue was purified by flash column chromatography (*n*-hexane/EtOAc, 1:2→1:5) to give aldehyde **13** (15.3 mg, 45%) as a white solid. $[\alpha]^{20}_D$=−145.2 (*c* 0.91, $CHCl_3$); IR (neat) 3015, 2977, 2932, 2873, 2733, 1732, 1621, 1493, 1456, 1392, 1372, 1339, 1314, 1303, 1287, 1267, 1235, 1185, 1152, 1100, 1031 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 9.81 (br d, *J*=1.8 Hz, 1H), 7.51–7.47 (m, 4H), 7.38–7.36 (m, 3H), 7.30 (d, *J*=7.9 Hz, 1H), 6.62 (d, *J*=5.5 Hz, 1H), 5.52 (s, 1H), 5.50 (d, *J*=5.5 Hz, 1H), 4.32 (dd, *J*=10.4, 4.9 Hz, 1H), 4.06 (ddd, *J*=8.5, 8.5, 3.1 Hz, 1H), 3.85 (ddd, *J*=11.0, 9.8, 4.9 Hz, 1H), 3.66 (dd, *J*=10.4, 10.4 Hz, 1H), 3.57 (ddd, *J*=11.9, 9.2, .4.3 Hz, 1H), 3.48 (ddd, *J*=9.8, 9.8, 4.9 Hz, 1H), 2.99 (dd, *J*=16.5, 3.1 Hz, 1H), 2.64 (ddd, *J*=16.5, 8.4, 2.7 Hz, 1H), 2.59 (ddd, *J*=11.6, 4.6, 4.6 Hz, 1H), 2.40 (s, 3H), 1.90 (ddd, *J*=11.3, 11.3, 11.3 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 199.2, 150.6, 141.8, 141.1, 136.9, 129.9, 129.3, 128.4, 126.1, 123.8, 115.6, 101.8, 80.0, 75.7, 75.1, 73.3, 68.9, 45.1, 35.4, 21.4; HRMS (EI) calcd for $C_{24}H_{26}O_6S$ [M^+] 442.1450, found 442.1450.

*4.1.9. Reaction of (Z)-(R)-**13** with SmI_2 followed by acetylation.* (a) To a solution of **13** (25.8 mg, 0.058 mmol) and MeOH (7.9 μL, 0.390 mmol) in THF (0.5 mL) was added SmI_2 (1.5 mL, 0.1 M solution in THF, 0.150 mmol) at 0 °C. After stirring for 10 min, the mixture was quenched with satd $Na_2S_2O_3$ and satd $NaHCO_3$ and extracted with EtOAc. The combined organic layer was washed with brine, dried over $MgSO_4$, and concentrated in vacuo. To a solution of the residue (27.6 mg) in pyridine (1 mL) was added acetic anhydride (1 mL) at room temperature. After stirring at room temperature for 24 h, the mixture was azeotropically evaporated with benzene in vacuo. The residue was purified by flash column chromatography (*n*-hexane/EtOAc, 1:1→1:2) to give an acetate **14b** (7.7 mg, 27%) as colorless crystals and a diacetate **15b** (7.9 mg, 26%) as a white solid. **14b**: Mp 241.0–242.0 °C (EtOAc); $[\alpha]^{21}_D$=+22.3 (*c* 0.75, $CHCl_3$); IR (KBr) 3042, 2977, 2952, 2925, 2883, 1734, 1598, 1494, 1460, 1447, 1414, 1397, 1373, 1239, 1185, 1147, 1110, 1086, 1052, 1043, 1026 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.51 (d, *J*=8.2 Hz, 2H), 7.50–7.47 (m, 2H), 7.39–7.35 (m, 3H), 7.33 (d, *J*=7.9 Hz, 2H), 5.52 (s, 1H), 5.11 (br s, $W_{1/2}$=5.6 Hz, 1H), 4.27 (dd, *J*=10.7, 4.9 Hz, 1H), 3.81 (ddd, *J*=5.9, 4.6, 1.2 Hz, 1H), 3.66 (dd, *J*=10.4, 10.4 Hz, 1H), 3.56 (ddd, *J*=11.6, 8.9, 4.0 Hz, 1H), 3.44–3.37 (m, 2H), 3.14 (dd, *J*=13.4, 7.9 Hz, 1H), 3.08 (ddd, *J*=11.3, 9.2, 4.3 Hz, 1H), 2.88 (dd, *J*=13.4, 4.6 Hz, 1H), 2.42 (s, 3H), 2.26 (ddd, *J*=13.7, 4.0, 3.7 Hz, 1H), 2.22 (ddd, *J*=11.3, 4.0, 4.0 Hz, 1H), 2.14 (s, 3H), 1.70–1.62 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 170.1, 141.8, 139.6, 137.2, 129.9, 128.3, 126.1, 124.2, 101.8, 76.9, 73.7 (2C), 72.4, 70.2, 69.0, 57.4, 34.5, 33.7, 29.7, 21.5, 21.0; HRMS (EI) calcd for $C_{26}H_{30}O_7S$ [M-H^+] 485.1634, found 485.1631; Anal. Calcd for $C_{26}H_{29}O_7S$: C, 64.18; H, 6.21. Found C, 63.94; H, 6.20. **15b**. $[\alpha]^{20}_D$=+41.5 (*c* 0.75, $CHCl_3$); IR (KBr) 3037, 2926, 2865, 1739, 1733, 1594, 1495, 1458, 1429, 1395, 1379, 1315, 1286, 1236, 1187, 1159, 1109, 1049, 1034 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.50 (d, *J*=8.2 Hz, 2H), 7.46 (dd, *J*=7.9, 2.1 Hz, 2H), 7.38–7.35 (m, 3H), 7.33 (d, *J*=7.9 Hz, 2H), 6.53 (dd, *J*=15.3, 5.5 Hz, 1H), 6.38 (dd, *J*=15.3, 1.2 Hz, 1H), 5.67 (m, 1H), 5.51 (s, 1H), 4.69 (ddd, *J*=11.0, 9.8, 4.9 Hz, 1H), 4.27 (dd, *J*=10.4, 4.9 Hz, 1H), 3.64 (dd, *J*=10.4, 10.4 Hz, 1H), 3.56 (ddd, *J*=11.9, 9.2, 4.3 Hz, 1H), 3.44 (ddd, *J*=9.8, 9.8, 2.1 Hz, 1H), 3.30 (ddd, *J*=9.8, 9.8, 4.5 Hz, 1H), 2.55 (ddd, *J*=11.3, 4.6, 4.6 Hz, 1H), 2.41 (s, 3H), 2.10 (s, 3H), 2.08 (s, 3H), 1.96 (ddd, *J*=11.9, 9.5, 2.1 Hz, 1H), 1.74–1.68 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 169.84, 169.78, 142.1, 139.9, 137.2, 135.9, 130.2, 129.1, 128.3, 126.1, 125.0, 101.7, 75.9, 75.6, 73.2, 70.2, 69.0, 68.7, 36.3, 34.7, 21.4, 21.1, 21.0; HRMS (EI) calcd for $C_{28}H_{32}O_8S$ [M^+] 528.1818, found 528.1813.

(b) To a solution of **13** (17.1 mg, 38.6 μmol) and CF_3CH_2OH (10.4 μL, 0.103 mmol) in THF (0.4 mL) was added SmI_2 (1.0 mL, 0.1 M solution in THF, 0.100 mmol) at 0 °C. After stirring for 5 min, the mixture was quenched with satd $Na_2S_2O_3$ and satd $NaHCO_3$, and extracted with EtOAc. The combined organic layers were washed with brine, dried over $MgSO_4$, and evaporated in vacuo. To a solution of the residue (18.9 mg) in pyridine (1 mL) was added acetic anhydride (1 mL) at room temperature. After stirring at room temperature for 68 h, the mixture was azeotropically evaporated with benzene in vacuo. The residue was purified by flash column chromatography (*n*-hexane/EtOAc, 1/1→1/2) to give acetate **14b** (7.7 mg, 45%) and an diacetate **15b** (7.9 mg, 27%).

*4.1.10. (Z)-β-Alkoxyvinyl (S)-sulfoxide-ester **16**.* To a solution of **1** (51.2 mg, 0.159 mmol) in THF (1.6 mL) was added LHMDS (190 μL, 1.0 M solution in THF, 0.190 mmol) at 0 °C. After stirring at 0 °C for 30 min and at room temperature for 30 min, a solution of (*S*)-**3** (140.3 mg, 0.855 mmol) in THF (1.6 mL) was added at −78 °C. After stirring at −20 °C for 2 h, the mixture was quenched with satd $NaHCO_3$ and extracted with EtOAc. The combined organic layer was washed with brine, dried over $MgSO_4$, and evaporated in vacuo. The residue was purified by flash column chromatography (*n*-hexane/EtOAc, 1:1) to give vinyl sulfoxide **16** (70.6 mg, 91%) as a white solid. $[\alpha]^{20}_D$=+178.5 (*c* 1.51, $CHCl_3$); IR (neat) 2980, 2927, 2875, 1737, 1626, 1493, 1456, 1390, 1369, 1351, 1328, 1306, 1286, 1236, 1200, 1180, 1098, 1031, 1015 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.53 (d, *J*=8.2 Hz, 2H), 7.48 (dd, *J*=7.6, 2.1 Hz, 2H), 7.40–7.32 (m, 3H), 7.29 (d, *J*=8.2 Hz, 2H), 6.62 (d, *J*=5.5 Hz, 1H), 5.51 (s, 1H), 5.47 (d, *J*=5.5 Hz, 1H), 4.31 (dd, *J*=10.4, 4.9 Hz, 1H), 4.21–4.15 (m, 2H), 3.96–3.89 (m, 2H), 3.66 (dd, *J*=10.4, 10.4 Hz, 1H), 3.55 (ddd, *J*=11.6, 8.9, 4.0 Hz, 1H), 3.46 (ddd, *J*=9.8, 9.8, 4.9 Hz, 1H), 2.67 (dd, *J*=15.3, 3.1, 1H), 2.60 (ddd, *J*=11.9, 4.1, 4.1 Hz, 1H), 2.46 (dd, *J*=15.6, 7.3 Hz, 1H), 2.40 (s, 3H), 1.95 (ddd, *J*=11.3, 11.3, 11.3 Hz, 1H), 1.28 (t, *J*=7.0 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 170.1, 150.7, 142.0, 141.0, 137.0, 129.8, 128.3, 126.1, 124.0, 115.1, 101.7, 80.0, 76.3, 75.8, 73.1, 68.9, 60.8, 36.9, 35.4, 21.3, 14.1; HRMS (EI) calcd for $C_{26}H_{30}O_7S$ [M^+] 486.1712, found 486.1700.

*4.1.11. (Z)-β-Alkoxyvinyl (S)-sulfoxide-aldehyde **17**.* To a solution of **16** (180.9 mg, 0.372 mmol) in CH_2Cl_2 (3.8 mL) was added DIBAH (760 μL, 0.97 M solution in *n*-hexane, 0.737 mmol) at −78 °C. After stirring at −78 °C for 20 min, *i*-PrOH (1.0 mL) and water (1.0 mL) were added at the same temperature and silica gel was added at room temperature. The mixture was diluted with EtOAc, stirred for

1 h, filtrated through a Celite pad, and evaporated in vacuo. The residue was purified by flash column chromatography (*n*-hexane/EtOAc, 1:1→1:3) to give aldehyde **17** (120.9 mg, 73%) as colorless crystals. Mp 135.0–136.0 °C (EtOAc); $[\alpha]^{21}_{D}$=+162.7 (*c* 1.69, $CHCl_3$); IR (KBr) 3034, 2920, 2879, 1722, 1635, 1457, 1387, 1342, 1288, 1269, 1241, 1187, 1101, 1076, 1028, 1002 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 9.76 (t, *J*=2.1 Hz, 1H), 7.52 (d, *J*=7.9 Hz, 2H), 7.49 (dd, *J*=7.9, 2.1 Hz, 2H), 7.40–7.36 (m, 3H), 7.30 (d, *J*=7.9 Hz, 1H), 6.57 (d, *J*=5.5 Hz, 1H), 5.52 (s, 1H), 5.50 (d, *J*=5.5 Hz, 1H), 4.31 (dd, *J*=10.7, 4.9 Hz, 1H), 4.04 (ddd, *J*=9.5, 7.9, 4.5 Hz, 1H), 3.79 (ddd, *J*=11.3, 9.5, 4.9 Hz, 1H), 3.66 (dd, *J*=10.4, 10.4 Hz, 1H), 3.56 (ddd, *J*=11.9, 9.2, 4.3 Hz, 1H), 3.50 (ddd, *J*=9.8, 9.8, 4.6 Hz, 1H), 2.68 (ddd, *J*=16.2, 4.3, 2.1 Hz, 1H), 2.62 (ddd, *J*=11.6, 4.3, 4.3 Hz, 1H), 2.58 (ddd, *J*=15.9, 7.6, 2.4 Hz, 1H), 2.40 (s, 3H), 1.96 (ddd, *J*=11.6, 11.6, 11.6 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 199.1, 150.2, 141.9, 141.2, 136.9, 130.0, 126.1, 124.0, 115.6, 101.7, 80.3, 75.7, 75.0, 73.2, 68.8, 45.6, 35.4, 21.3; HRMS (EI) calcd for $C_{24}H_{26}O_6S$ [M^+] 442.1450, found 442.1448; Anal. Calcd for $C_{24}H_{26}O_6S$: C, 65.14; H, 5.92. Found C, 65.27; H, 6.00.

4.1.12. Reaction of (Z)-(S)-aldehyde ***17*** *with SmI_2 followed by acetylation.* To a solution of **17** (24.4 mg, 0.055 mmol) and MeOH (6.7 mL, 0.17 mmol) in THF (0.6 mL) was added SmI_2 (1.4 mL, 0.1 M solution in THF, 0.14 mmol) at 0 °C. After stirring at 0 °C for 10 min, the mixture was quenched with satd $Na_2S_2O_3$ and satd $NaHCO_3$ and extracted with EtOAc. The combined organic layer was washed with brine, dried over $MgSO_4$, and evaporated in vacuo. To a solution of the residue in pyridine (1 mL) was added acetic anhydride (1 mL) at room temperature. After stirring at room temperature for 21 h, the mixture was azeotropically evaporated with benzene in vacuo. The residue was purified by flash column chromatography (*n*-hexane/EtOAc, 1:1) to give (*E*)-diacetate **19b** (2.0 mg, 7%) and a mixture of *syn-trans*-**9b**, *syn-cis*-**18b**, and others (16.7 mg). ^1H NMR sample of **18b** was obtained by further flash column chromatography. **18b** (600 MHz, $CDCl_3$): δ 7.54 (d, *J*=7.8 Hz, 2H), 7.51 (dd, *J*=7.8, 1.2 Hz, 2H), 7.40–7.36 (m, 3H), 7.33 (d, *J*=7.8 Hz, 2H), 5.56 (s, 1H), 5.05 (br s, $W_{1/2}$=7.0 Hz, 1H), 4.30 (dd, *J*=10.2, 4.8 Hz, 1H), 4.21 (br d, *J*=10.2 Hz, 1H), 3.71 (dd, *J*=10.1, 10.2 Hz, 1H), 3.52–3.41 (m, 3H), 2.82 (dd, *J*=13.2, 10.2 Hz, 1H), 2.73 (dd, *J*=13.2, 1.8 Hz, 1H), 2.55 (ddd, *J*=11.4, 4.2, 4.2 Hz, 1H), 2.41 (s, 3H), 2.06 (s, 3H), 1.84 (ddd, *J*=11.4, 11.4, 11.4 Hz, 1H), 1.78 (ddd, *J*=13.8, 12.0, 3.0 Hz, 1H). **19b**: ^1H NMR (400 MHz, $CDCl_3$) δ 7.49–7.44 (m, 4H), 7.38–7.31 (m, 5H), 6.50 (dd, *J*=15.2, 5.8 Hz, 1H), 6.41 (d, *J*=15.2 Hz, 1H), 5.65 (ddd, *J*=9.4, 5.6, 3.8 Hz, 1H), 5.50 (s, 1H), 4.66 (ddd, *J*=10.9, 10.9, 4.8 Hz, 1H), 4.27 (dd, *J*=10.6, 4.8 Hz, 1H), 3.62 (dd, *J*=10.4, 10.4 Hz, 1H), 3.55 (ddd, *J*=12.1, 9.1, 4.3 Hz, 1H), 3.44 (ddd, *J*=9.6, 9.6, 2.0 Hz, 1H), 3.30 (ddd, *J*=9.9, 9.9, 4.8 Hz, 1H), 2.54 (ddd, *J*=11.4, 4.3, 4.3 Hz, 1H), 2.41 (s, 3H), 2.09 (s, 3H), 2.08 (s, 3H), 1.97 (ddd, *J*=11.9, 9.6, 2.0 Hz, 1H), 1.72–1.03 (m, 2H).

4.1.13. TBS–ether ***21****.* To a solution of **7** (86.8 mg, 0.196 mmol) and MeOH (15.8 μL, 0.490 mmol) in THF (1.9 mL) was added SmI_2 (5.0 mL, 0.1 M solution in THF, 0.500 mmol) at 0 °C. After stirring at 0 °C for 15 min, the mixture was quenched with satd $Na_2S_2O_3$ and satd $NaHCO_3$ and extracted with EtOAc. The combined organic layer was washed with brine, dried over $MgSO_4$, and concentrated in vacuo to give crude alcohol **9a** (79.0 mg). To a solution of **9a** in DMF (0.4 mL) were added imidazole (170.0 mg, 2.50 mmol) and TBSCl (192.7 mg, 1.25 mmol) at room temperature. After stirring for 48 h, the mixture was quenched with MeOH, and concentrated in vacuo. The residue was purified by flash column chromatography (*n*-hexane/EtOAc, 3:1) to give TBS–ether **21** (98.6 mg, 90%, two steps) as colorless crystals. Mp 155.5–156.5 °C (EtOAc); $[\alpha]^{23}_{D}$=−113.9 (*c* 1.06, $CHCl_3$); IR (KBr) 2954, 2929, 2876, 2856, 1472, 1456, 1401, 1368, 1336, 1315, 1287, 1249, 1196, 1087, 1016 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.56 (d, *J*=7.9 Hz, 2H), 7.50 (dd, *J*=7.9, 1.8 Hz, 2H), 7.40–7.32 (m, 3H), 7.31 (d, *J*=8.2 Hz, 2H), 5.55 (s, 1H), 4.31 (dd, *J*=10.4, 4.6 Hz, 1H), 3.77 (ddd, *J*=10.7, 8.9, 1.8 Hz, 1H), 3.71 (dd, *J*=10.4, 10.4 Hz, 1H), 3.61 (ddd *J*=11.6, 8.9, 4.0 Hz, 1H), 3.48 (ddd, *J*=10.7, 8.9, 1.8 Hz, 1H), 3.41 (ddd, *J*=9.8, 9.8, 4.9 Hz, 1H), 3.30 (ddd, *J*=11.3, 9.3, 4.9 Hz, 1H), 3.23 (dd, *J*=13.4, 2.1 Hz, 1H), 3.19 (ddd, *J*=11.9, 9.2, 4.0 Hz, 1H), 2.60 (dd, *J*=13.1, 11.0 Hz, 1H), 2.51 (ddd, *J*=11.3, 4.3, .4.3 Hz, 1H), 2.41 (3H, s), 2.35 (ddd, *J*=11.6, 4.3, 4.3 Hz, 1H), 1.70 (ddd, *J*=11.6, 11.6, 11.6 Hz, 1H), 1.60 (ddd, *J*=11.6, 11.6, 11.6 Hz, 1H), 0.85 (s, 9H), 0.05 (s, 3H), −0.03 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 141.7, 141.5, 137.2, 129.9, 129.1, 128.3, 126.1, 124.1, 101.7, 76.6, 76.52, 76.45, 76.38, 73.6, 69.9, 69.1, 61.1, 38.9, 34.6, 25.6, 21.4, 17.8, −4.1, −4.8; HRMS (FAB) calcd for $C_{30}H_{43}O_6SSi$ [$M+H^+$] 559.2549, found 559.2546; Anal. Calcd for $C_{30}H_{42}O_6SSi$: C, 64.48; H, 7.58; S, 5.74. Found C, 64.62; H, 7.54; S, 6.09.

4.1.14. Aldehyde ***22****.* To a solution of **21** (44.1 mg, 78.9 μmol) in MeCN (0.8 mL) were added pyridine (63.6 mg, 0.789 mmol) and trifluoroacetic anhydride (84.2 mg, 0.395 mmol) at 0 °C. After stirring for 20 min, K_2CO_3 (63.2 mg, 0.455 mmol) and H_2O (0.2 mL) were added at 0 °C. After stirring at 0 °C for 2.5 h, the mixture was diluted with EtOAc. The combined organic layer was washed with brine, dried over $MgSO_4$, and evaporated in vacuo. The residue was purified by flash column chromatography (*n*-hexane/EtOAc, 3:1) to give aldehyde **22** (24.6 mg, 72%) as a white solid. $[\alpha]^{22}_{D}$=−26.0 (*c* 1.00, acetone); IR (KBr) 2952, 2930, 2879, 1741, 1469, 1454, 1391, 1361, 1339, 1314, 1287, 1251, 1212, 1177, 1162, 1102, 1021, cm^{-1}; ^1H NMR (500 MHz, benzene-*d*) δ 9.51 (d, *J*=2.1 Hz, 1H), 7.69–7.66 (m, 2H), 7.21 (t, *J*=7.0 Hz, 2H), 7.15–7.12 (m, 1H), 5.36 (s, 1H), 4.26 (dd, *J*=10.4, 4.9 Hz, 1H), 3.60 (ddd, *J*=10.7, 9.5, 4.6 Hz, 1H), 3.49 (dd, *J*=10.0, 10.0 Hz, 1H), 3.39 (dd, *J*=9.2, 2.1 Hz, 1H), 3.28 (ddd, *J*=9.2, 9.2, 4.6 Hz, 1H), 3.18 (ddd, *J*=11.0, 9.5, 4.0 Hz, 1H), 2.79–2.70 (m, 2H), 2.37 (ddd, *J*=11.0, 3.7, 3.7 Hz, 1H), 2.24 (ddd, *J*=11.0, 4.3, 4.3 Hz, 1H), 1.72 (ddd, *J*=11.0, 11.0, 11.0 Hz, 1H), 1.48 (ddd, *J*=11.0, 11.0, 11.0 Hz, 1H), 0.91 (s, 9H), 0.01 (s, 3H), −0.04 (s, 3H); ^{13}C NMR (75 MHz, benzene-*d*) δ 196.8, 138.3, 129.1, 128.5, 126.7, 101.9, 85.1, 77.2, 76.3, 75.8, 73.9, 69.3, 66.4, 39.4, 35.0, 25.8, 18.0, −4.3, −4.8; HRMS (FAB) calcd for $C_{23}H_{35}O_6Si$ [$M+H^+$] 435.2202, found 435.2202.

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12. Treatment of **15b** with K_2CO_3 in THF/MeOH effected methanolysis of the diacetate and intramolecular cyclization, and subsequent acetylation gave a 2:3 mixture of 2,6-*syn*-2,3-*cis*-tetrahydropyran **14b** and 2,6-*anti*-2,3-*trans*-isomer. The result confirmed the β-configuration of the 3-acetoxy group in **15b**.
13. The products were difficult to isolate. Thus, yields of the products were calculated based on ^{1}H NMR analysis of the mixture. Other products might contain 2,6-*anti*-2,3-*cis*-**11b** and (*Z*)- γ-acetoxyvinyl sulfoxide isomer.
14. Alkaline methanolysis of **19b** followed by acetylation mainly afforded 2,6-*anti*-2,3-*trans*-tetrahydropyran. The result confirmed the β-configuration of the 3-acetoxy group in **19b**.