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Synthetic Studies on Tautomycin Synthesis of Segment C

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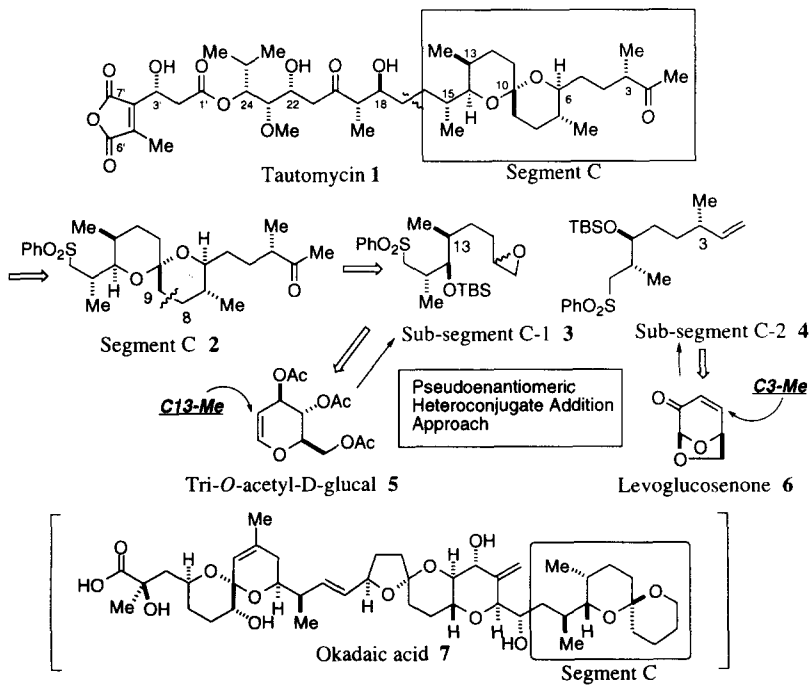
Abstract: Synthesis of Segment C of tautomycin was accomplished from two D-sugar derivatives. Pseudoenantiomeric heteroconjugate addition strategy allowed stereocontrolled synthesis of Sub-segment C-1. Sub-segment C-2 and its three diastereoisomers have been synthesized through heteroconjugate addition strategy and Mitsunobu reaction. Sub-segment C-1 (epoxide electrophile) and C2 (sulfone carbanion) were coupled in the presence of boron trifluoride etherate (BF_3·OEt_2) to furnish Segment C. © 1997 Elsevier Science Ltd.

In the preceding paper for the synthesis of tautomycin **1**, we have reported the synthesis of each Segment A and B in optically active form and proposed a retrosynthetic analysis which led us to Segment C in the form of **2** (Scheme 1, tautomycin numbering is used). We have reported the synthesis of Segment C in a preliminary communication[1] and thus this is the corresponding full note article.

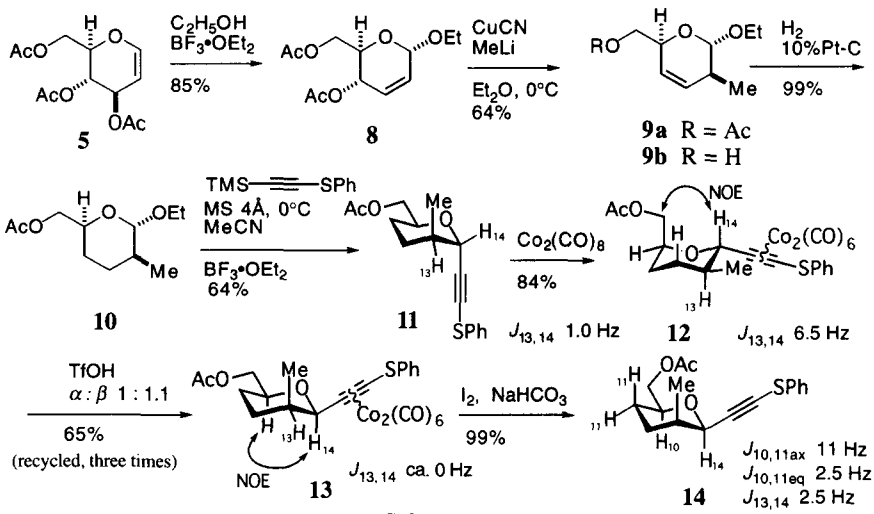


Scheme 1

Segment C **2** of tautomycin is structurally similar to spiro Segment C of okadaic acid **7**,[2] however, Segment C **2** is *pseudo*-enantiomeric to its counterpart of okadaic acid. In this context, we have developed a

new synthetic method "*pseudoenantiomeric heteroconjugate addition approach*" which was applicable to both enantiomers starting from *D*-sugar derivatives.[3] This method includes 1,2-asymmetric induction *via* heteroconjugate addition to produce either *syn* or *anti* diastereoisomer of both two enantiomers. When we consider to apply this methodology to the synthesis of tautomycin, Segment C **2** was further disconnected between C8 and C9 bond to result in two Sub-segments C-1 (in the form of **3**) and C-2 (in the form of **4**), which were planned to prepare from readily available *D*-sugar derivatives, tri-*O*-acetyl-D-glucal **5** and levoglucosenone **6**,[4] respectively. Asymmetric centers at the C13 and C3 of tautomycin were planned to prepare on the pyranose framework of **5** and **6** as illustrated by arrows. This paper describes the full details of the synthesis of Segment C **2**.[5]

Synthesis of Sub-segment C-1 The introduction of the C13 methyl group of tautomycin was achieved by SN2' reaction of the allyl acetate **8** which was prepared by Ferrier-glycosidation of tri-*O*-acetyl-D-glucal **5** with ethanol.[6] Thus, treatment of **8** with lithium methylcyanocuprate in ether at 0 °C gave the methyl adduct **9a** (R = Ac) and **9b** (R = H) in combined 64% yield.[7] Hydrogenation of the double bond of **9a** in the presence of platinum on charcoal gave **10**, while hydrogenation using palladium on charcoal as catalyst caused a considerable amount of epimerization of the newly formed stereogenic center (ca. 15%). *C*-Glycosidation of **10** with phenylthiotrimethylsilylacetylene and boron trifluoride etherate in acetonitrile provided **11** exclusively in 68% yield.[8]

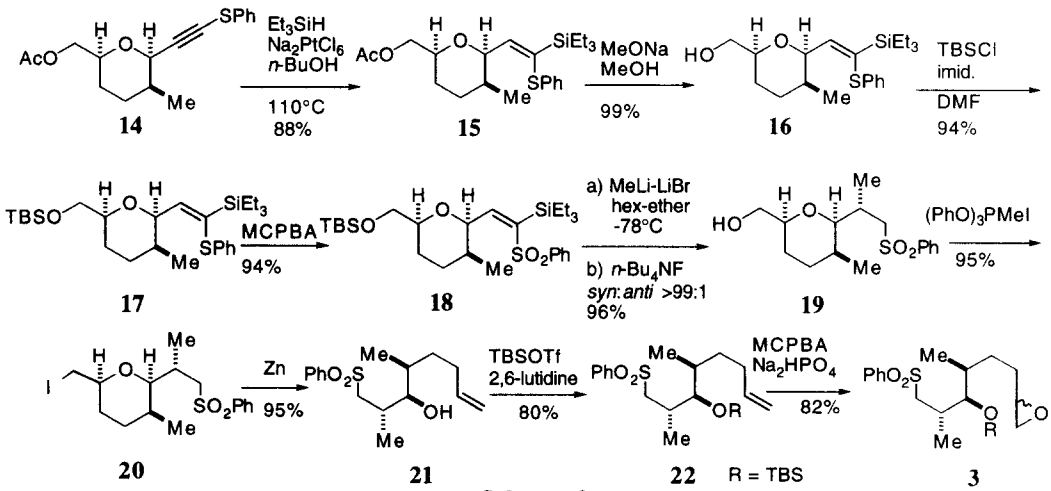


Scheme 2

The epimerization of phenylthioacetylene **11** was anticipated to be difficult because of the axial methyl group in pyranose ring, which greatly diminished the driving force of thermodynamic equilibrium. When we considered the acetylene-cobalt complex moiety as bulkiest substituent adapting equatorial position, the free energy $\Delta G°$, comprising of 1,3 diaxial interaction and gauche repulsion of the two substituents (-CH_2OAc and -CH_3), determines the equilibrium.[9] The acetylene **11** was converted into the dicobalthexacarbonyl complex **12** in 84% yield and then treated with trifluoromethanesulfonic acid at room temperature for 30 min. The epimerization under this thermodynamic control condition gave a mixture of **12** and its β-isomer **13** with the

ratio of 1 : 1.1, and the β-isomer **13** was separated by flash chromatography. This ratio seemed to be the result of the counterbalance between two substituents (-CH_2OAc and -CH_3) on the pyranose. After three recycling of the recovered α-isomer **12**, we obtained β-isomer **13** in 65% yield. Decomplexation of **13** with iodine in the presence of sodium hydrogen carbonate yielded the β-phenylthioacetylene **14** in 99% yield. Sodium hydrogen carbonate was necessary due to the acid labile nature of the resulting phenylthio group. The inversion of the conformation was assumed from the coupling constants and NOE experiments.

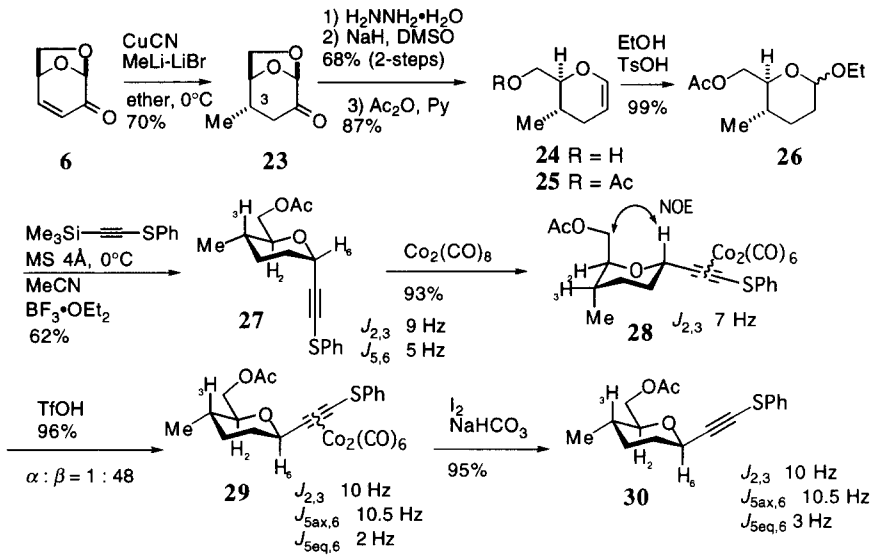
The hydrosilylation of the phenylthioacetylene **14** under previously reported conditions (Et_3SiH, Na_2PtCl_6, 1,2-dichloroethane)[10] proved to be troublesome at first, because we observed a considerable amount of formation of regioisomers (ca. 20%) and low yields. After some trials, we finally recognized the solvent effect that use of alcohol as solvent increases the regioselectivity, and *n*-butanol was chosen because of its higher boiling point to ensure this hydrosilylation (Scheme 3). In fact, hydrosilylation of **14** using 1 mol% of sodium hexachloroplatinate(IV) in a mixture of triethylamine and *n*-butanol at 110 °C gave **15** in 88% yield. Protecting group manipulation of **15** and oxidation with *m*-chloroperbenzoic acid gave the heteroolefin **18**. Introduction of methyl group at the stereogenic center at C15 position of tautomycin was achieved by α-chelation controlled heteroconjugate addition of **18**.[3] Thus, treatment of **18** with methyllithium-lithium bromide complex in a mixture of hexane and ether (1 : 1) followed by desilylation with tetrabutylammonium fluoride afforded **19** in 96% yield with high diastereoselectivity (*syn* : *anti* = >99 : 1). Treatment of **19** with methyltriphenoxyphosphonium iodide[11] and reductive ring opening of the resulting **20** by zinc furnished the open chain compound **21**.[12] Protection of the alcohol **21** as *t*-butyldimethylsilyl ether and epoxidation of the olefin **22** with *m*-chloroperbenzoic acid furnished Sub-segment C-1 **3** as a mixture of two diastereomers.



Scheme 3

Synthesis of Sub-segment C-2 and its Three Diastereoisomers The synthesis of Sub-segment C-2 **4** began with induction of the C3 stereogenic center of tautomycin starting from levoglucosenone **6**, which received conjugate addition of lithium methylcyanocuprate to give α-axial methyl adduct **23** in 70 % yield.[4] Treatment of the ketone **23** with hydrazine in ethanol and subsequent eliminative Wolff-Kishner reduction in DMSO at room temperature[13] afforded the vinyl ether **24** which was further protected as acetate **25**. Addition

of ethanol to **25** in the presence of *p*-toluenesulfonic acid gave a mixture of ethyl glycosides **26** in the ratio of 2 : 1 (α : β). *C*-Glycosidation of **26** in the presence of boron trifluoride etherate furnished phenylthioacetylene **27** in 62% yield. The epimerization of the anomeric center of **27** was achieved *via* the dicobalthexacarbonyl complex **28**. In this case, we expected that the equilibrium between **28** and **29** would strongly shift into β-isomer **29**, because two substituents (-CH_3 and -CH_2OAc) prefer to adapt equatorial positions. In fact, treatment of **28** with trifluoromethanesulfonic acid afforded the β-epimer **29** predominantly (α : β = 1 : 48) in 96% yield. Decomplexation of **29** with iodine in the presence of sodium hydrogen carbonate afforded **30** in 95% yield.

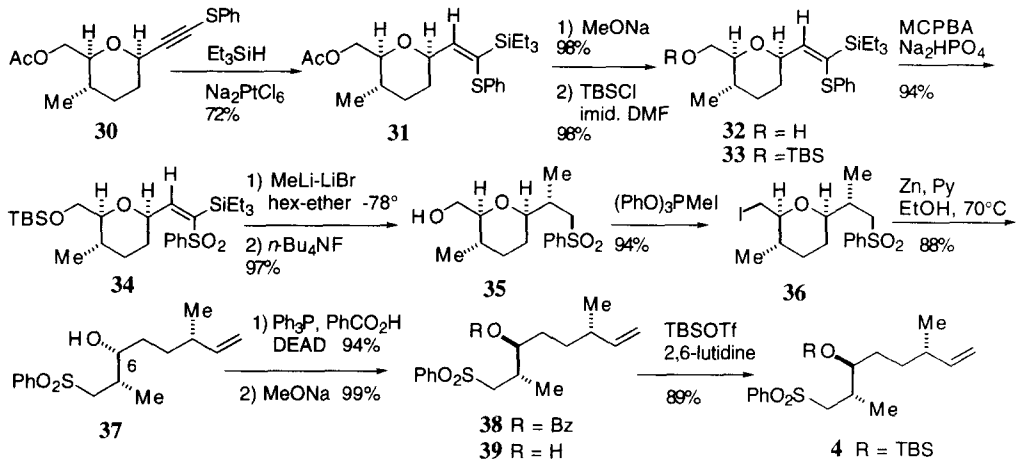


Scheme 4

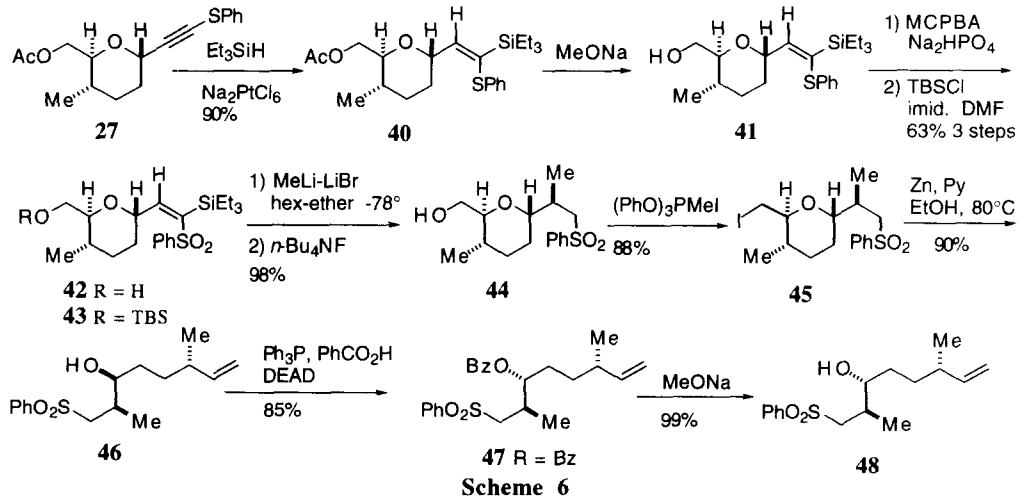
The hydrosilylation of phenylthioacetylene **30** has been achieved as previously reported (*n*-butanol, 1 mol% Na_2PtCl_6, Et_3N, 110 °C) to provide the vinyl sulfide **31** in 88% yield (Scheme 5). The acetate **31** was deprotected by sodium methoxide, and the resulting alcohol **32** was reprotected as *t*-butyldimethylsilyl ether **33**. Oxidation of the vinyl sulfide **33** with *m*-chloroperbenzoic acid afforded the heteroolefin **34**. The stereogenic center corresponding to the C7 position of tautomycin was induced by heteroconjugate addition to **34**. In fact, treatment of **34** with methyllithium•lithium bromide complex in a mixture of hexane and ether followed by desilylation with tetrabutylammonium fluoride afforded the *syn*-methyl adduct **35** in 97% yield with high diastereoselectivity (*syn* : *anti* = >99 : 1). Conversion of **35** to the iodide **36** and subsequent ring opening of **36** with zinc gave **37** in 83% yield. The construction of the stereogenic center corresponding to C6 of tautomycin was achieved by inverting C6 hydroxy group of **37** by Mitsunobu reaction.[14] Hydrolysis of the benzoate **38** by sodium methoxide and protection of the alcohol **39** as *t*-butyldimethylsilyl ether furnished Sub-segment C-2 **4** in 83% overall yield from **37**.

Besides the synthesis of Sub-segment C-2, we have also synthesized its diastereomers along the current methodology as shown in Scheme 6. Heteroolefin **40** was prepared from the intermediate **27** by similar

procedure used in Scheme 5. Heteroconjugate addition to **43** with methyllithium•lithium bromide complex was carried out in a mixture of hexane and ether at -78 °C, and subsequent treatment with tetrabutylammonium fluoride afforded **44** stereoselectively (*syn* : *anti* = >99 : 1).[15] The ring opening operation of the alcohol **44** gave **46** *via* the iodide **45**. Inversion of the secondary alcohol of **46** by Mitsunobu reaction and successive hydrolysis with sodium methoxide provided **48**.



Scheme 5

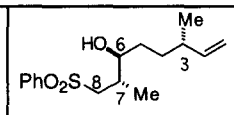
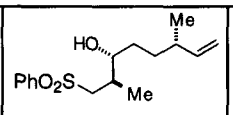
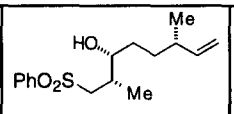
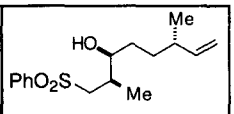


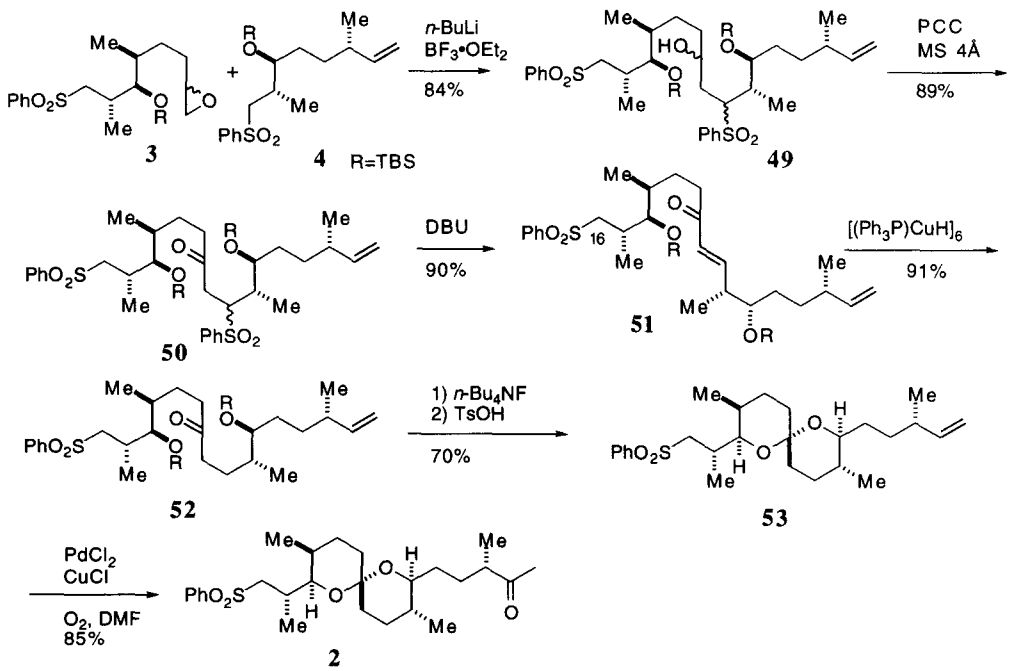
Scheme 6

Anti-isomer **39** and its three diastereoisomers (**37**, **46** and **48**), prepared by heteroconjugate addition and Mitsunobu reaction, and their ^{13}C NMR data are listed in Table 1.[16] The difference of chemical shifts between the two pairs of *epi*-enantiomers (**39**, **48** and **37**, **46**) is impressive, in terms of methyl at the C7 position, *anti* methyl appears at 17.33 ± 0.01 ppm while *syn* methyl appears at 13.68 ± 0.08 ppm for this open-chain system, chemical shift of the C-6 are 58.57 ± 0.05 ppm and 59.41 ± 0.05 ppm, chemical shift of C-8 are 75.09 ± 0.12 ppm and 73.32 ± 0.06 ppm, respectively. We also observe the chemical shift varied proportional to distance of

different stereogenic center, the chemical shift of methyl at the C-3 position of **39** is 20.15 ppm, the change of stereogenic center at the C-7 position which is far away, causes a plus of 0.03 ppm (**46**), while the change of stereogenic center at the C-6 position which is relatively closer to give +0.15 ppm (**37**). The change of both stereogenic centers at the C-6 and the C-7 give a plus of 0.30 ppm (**48**).

Table 1

assignment	 **39** (*anti*)	 **48** (*anti*)	 **37** (*syn*)	 **46** (*syn*)
7-Me	17.32	17.34 +0.02	13.76 -3.56	13.60 -3.72
3-Me	20.15	20.45 +0.30	20.30 +0.15	20.18 +0.03
C-8	58.52	58.61 +0.09	59.45 +0.93	59.36 +0.84
C-6	75.21	74.97 -0.24	73.26 -1.95	73.38 -1.83



Scheme 7

Synthesis of Segment C Coupling reaction of Sub-segment C-1 with Sub-segment C-2 was achieved by the reaction of sulfone carbanion with epoxide in the presence of Lewis acid (Scheme 7). Thus, treatment of Sub-segment C-2 **4** with *n*-butyllithium at -78 °C for 30 min gave the corresponding sulfone carbanion, which was successively treated with boron trifluoride etherate and then Sub-segment C-1 **3** to produce the coupling product **49** in 84% yield. It should be noted that no coupling reaction took place without boron trifluoride

etherate.[17] The coupling product **49** has two phenylsulfonyl groups, one of which should be removed selectively. This was accomplished by β-elimination of the keto-sulfone **50** which was prepared by pyridinium chlorochromate oxidation of **49** in the presence of molecular sieve 4Å. Elimination of the β-phenylsulfonyl ketone **50** with 1,8-diazabicyclo[5,4,0]-7-undecene (DBU) gave the enone **51** in 80% overall yield from **49**.[18] Conjugate reduction of the enone **51** by (triphenylphosphine)copper hydride hexamer gave **52** in 91% yield.[19] Removal of the silyl protecting groups with tetrabutylammonium fluoride and acid-catalyzed spiroketalization of the resulting keto-diol with *p*-toluenesulfonic acid afforded the spiroketal **53** in 70% yield. Finally, the Wacker oxidation[20] of the terminal olefin of **53**[21] led us to finish the synthesis of Segment C **2** which was identical with authentic sample of Segment C derived from natural tautomycin.[22]

Conclusions The *pseudo*-enantiomeric heteroconjugate addition approach successfully controlled the adjacent chiral centers through the combination of epimerization of anomeric pyranose and switching the selectivity *via* α-chelation or β-chelation.[3] Furthermore, the sulfonyl substituent could play for elongation of the carbon-carbon chain, which makes this new method a powerful tool for the synthesis of complex natural products.[23] The synthesis of Segment C of tautomycin exemplified the application of this newly developed method.

Experimental Section

For the general experimental details, see the preceding paper.[1]

[2*S*,5*S*,6*S*]-Tetrahydro-6-ethoxy-5-methyl-2-pyranylmethyl acetate 10.

To a suspension of copper (I) cyanide (26.1 g, 0.29 mol) in ether (100 ml) under nitrogen atmosphere cooled to 0 °C was added methyllithium (1.5 M in ether as complex with lithium bromide, 193 ml, 0.29 mol) dropwise. The resulting solution of lithium methyl cyanocuprate was introduced into a solution of **8** (37.5 g, 0.15 mol) in ether (200 ml) at 0 °C. After being stirred for 1.5 h, aqueous ammonium chloride was added, and the resulting aqueous layer was extracted with ether. The combined organic layer was dried and then concentrated under reduced pressure. Purification of the crude oil by silica gel chromatography (hexane/ethyl acetate, 5 : 1 and then 2 : 1) afforded **9a** (17.65 g, 55%) and **9b** (2.23 g, 9%) respectively. NMR data of **9a** were identical to those reported by Chapleur.[7]

A solution of **9a** (17.01 g, 0.079 mol) and platinum catalyst (10% on activated charcoal, 0.34 g) in ethyl acetate (170 ml) under hydrogen atmosphere was vigorously stirred at room temperature overnight. The reaction mixture was filtered through Celite and then concentrated to afford **10** (17.0 g, 99%). IR (KBr) ν_{max} 2973, 1751, 1370, 1237, 1100, 1044, 965 cm^{-1}. ^{1}HNMR ($CDCl_3$, 270 MHz), δ 1.06 (3H, d, J = 7 Hz, CH_3-13), 1.23 (3H, t, J = 7 Hz, CH_3CH_2O), 1.3 - 1.5 (2H, m), 1.56 (1H, m), 1.79 (1H, m), 2.05 (1H, m), 2.09 (3H, s, acetate), 3.48 (1H, dq, J = 10, 7 Hz, CH_3CH_2O), 3.73 (1H, dq, J = 10, 7 Hz, CH_3CH_2O), 3.97 (1H, m, H-10), 4.06 (2H, m, H-9), 4.53 (1H, s, H-14, anomeric). ^{13}CNMR ($CDCl_3$, 67.5 MHz), δ 15.1, 16.1, 20.9, 21.7, 23.6, 31.2, 62.4, 66.6, 67.1, 101.5, 171.0. $[\alpha]_D^{25}$ +85.6° (*c* 1.37, $CHCl_3$). Anal. calcd. for $C_{11}H_{20}O_4$: C 61.09; H 9.32. Found: 61.01; H 9.20.

[2*S*,5*S*,6*S*]-Tetrahydro-5-methyl-6-[(phenylthio)ethynyl]-2-pyranylmethyl acetate 11.

Boron trifluoride etherate (4.31 ml, 0.035 mol) was added in one portion to a solution of **10** (1.62 g, 7.49 mmol), phenylthiotrimethylsilylacetylene (2.90 g, 14.1 mmol) and powdered molecular sieve 4Å (1.6 g) in acetonitrile (47 ml) at 0 °C. After being stirred for 10 min, the reaction mixture was poured into aqueous sodium hydrogen carbonate and then extracted with ether. The combined organic layer was dried and then

concentrated. The resulting residue was purified by silica gel chromatography (hexane/ether, 10 : 1 and then 5 : 1) to afford **11** (1.47 g, 64%) as colorless oil. IR (KBr) ν_{max} 2945, 1744, 1238, 1059, 741 cm^{-1}. ^{1}HNMR ($CDCl_3$, 270 MHz), δ 1.17 (3H, d, J = 7 Hz, CH_3-13), 1.46 (1H, m), 1.58 (1H, m), 1.65 (1H, m), 1.99 (1H, m), 2.09 (3H, s, acetate), 2.12 (1H, m), 4.07 (1H, dd, J = 11.5, 6.5 Hz, H-9), 4.13 (1H, dd, J = 11.5, 3 Hz, H-9), 4.17 (1H, m, H-10), 4.63 (1H, d, J = 1 Hz, H-14, anomeric), 7.19-7.45 (5H, m, Ar). ^{13}CNMR ($CDCl_3$, 67.5 MHz), δ 17.0, 20.9, 22.2, 25.0, 32.9, 66.6, 70.0, 70.8, 73.1, 97.6, 126.1, 126.5, 129.2, 132.6, 171.0. $[\alpha]_D^{25}$ -4.7° (*c* 2.15, CH_2Cl_2). Anal. calcd. for $C_{17}H_{20}O_3S$: C 67.08; H 6.62. Found: C 67.10; H 6.73.

[2*S*,5*S*,6*R*]-Tetrahydro-5-methyl-6-[(phenylthio)ethynyl]-2-pyranylmethyl acetate 14.

To a solution of dicobaltoctacarbonyl (1.83 g, 5.35 mmol) in dichloromethane (5 ml) under argon atmosphere was added **11** (1.30 g, 4.3 mmol) in dichloromethane (24 ml) at room temperature. After being stirred for 2 h, the reaction mixture was concentrated and then purified by silica gel chromatography (hexane/ether, 5 : 1) to afford air-sensitive **12** (2.66 g, 84%) as brown oil which was immediately used for the next epimerization reaction. IR (KBr) ν_{max} 2091, 2052, 2030, 1743, 1236, 1046. ^{1}HNMR ($CDCl_3$, 270 MHz), δ 1.21 (3H, d, J = 7 Hz, CH_3-13), 1.56 (1H, m), 1.65 - 1.82 (3H, m), 1.93 (1H, m), 2.07 (3H, s, acetate), 4.07 (1H, d, J = 11.5, 4 Hz, H-9), 4.24 (1H, m, H-10), 4.46 (1H, dd, J = 11.5, 8 Hz, H-9), 4.55 (1H, d, J = 6.5 Hz, H-14, anomeric), 7.44 (3H, m, Ar), 7.58 (2H, m, Ar).

Trifluoromethanesulfonic acid (1.1 ml) was added to a solution of **12** (29.04 g, 0.049 mol) in dichloromethane (2460 ml). After being stirred for 30 min, the mixture was quenched with aqueous sodium hydrogen carbonate (3 ml) and then concentrated under reduced pressure. The residue was purified by silica gel flash chromatography (hexane/CH_2Cl_2, 3 : 1) to give air-sensitive β-epimer **13** (13.01 g, 45%) and recovered **12** (11.62 g, 40%), respectively. The recovered α-epimer **12** was recycled three times to provide α-epimer **12** (2.0 g, 7%) and β-epimer **13** (18.74 g, 65% combined yield) which was immediately used for next reaction. ^{1}HNMR ($CDCl_3$, 270 MHz), δ 1.19 (3H, d, J = 7 Hz, CH_3-13), 1.28 - 1.85 (4H, m), 2.02 (3H, s, acetate), 2.20 (1H, m), 3.84 (1H, m, H-10), 4.11 (2H, d, J = 5 Hz, H-9), 4.69 (1H, s, H-14, anomeric), 7.40 (3H, m, Ar), 7.58 (2H, m, Ar).

A suspension of **13** (18.74 g, 0.032 mol) and sodium hydrogen carbonate (10.66 g, 127 mmol) in tetrahydrofuran (317 ml) was added iodine (28.20 g, 47.8 mmol) at room temperature. After being stirred for 3 h, aqueous sodium sulfite was added and the separated aqueous layer was extracted with ether. The combined organic layer was dried, concentrated and then purified by silica gel flash chromatography (hexane/ether, 5 : 1) to afford **14** (9.62 g, 99%) as colorless oil. IR (KBr) ν_{max} 2937, 1740, 1237, 1056, 741 cm^{-1}. ^{1}HNMR ($CDCl_3$, 270 MHz), δ 1.21 (3H, d, J = 7 Hz, CH_3-13), 1.37 (1H, m), 1.58 (1H, m), 1.79 (2H, m), 2.0 (1H, m), 2.09 (3H, s, acetate), 3.66 (1H, dddd, J = 11, 6, 4, 2.5 Hz, H-10), 4.06 (1H, dd, J = 11.5, 6 Hz, H-9), 4.13 (1H, dd, J = 11.5, 4 Hz, H-9), 4.54 (1H, d, J = 2.5 Hz, H-14, anomeric), 7.2-7.45 (5H, m, Ar). ^{13}CNMR ($CDCl_3$, 67.5 MHz), δ 12.9, 20.9, 21.7, 29.2, 32.1, 67.0, 72.4, 72.8, 76.2, 97.1, 126.4, 126.6, 129.1, 132.5, 171.1. $[\alpha]_D^{25}$ +58.4° (*c* 4.6, CH_2Cl_2). Anal. calcd. for $C_{17}H_{20}O_3S$: C 67.08; H 6.62. Found: C 67.00; H 6.91.

[2*S*,5*S*,6*R*]-Tetrahydro-5-methyl-6-[(phenylthio)-2-(triethylsilyl)ethenyl]-2-pyranylmethyl acetate 15.

Sodium hexachloroplatinate (IV) hexahydride (0.01 M in isopropanol, 28 ml) was added to a solution of **14** (8.53 g, 0.028 mol), triethylamine (8.5 ml) and triethylsilane (89 ml) dissolved in *n*-butanol (280 ml) heated at 110 °C under argon atmosphere. After being stirred at 110°C for 1 h, the reaction mixture was concentrated under reduced pressure. The residue was purified by silica gel flash chromatography (hexane/CH_2Cl_2, 4 : 1) to afford **15** (10.42 g, 88%) as colorless oil. IR (KBr) ν_{max} 2958, 1744, 1234, 1062, 737 cm^{-1}. ^{1}HNMR ($CDCl_3$, 270 MHz), δ 0.52 (6H, m, CH_3CH_2Si), 0.86 (9H, t, J = 8 Hz, CH_3CH_2Si), 1.01 (3H, d, J = 7 Hz, CH_3-13), 1.32 (1H, m), 1.5 (1H, m), 1.64 (1H, m), 1.79 (1H, dt, J = 13, 4.5 Hz), 1.91 (1H, m), 2.1 (3H, s, acetate), 3.59 (1H, dtd, J = 11.5, 5, 2.5 Hz, H-10), 4.09 (2H, d, J = 5 Hz, H-9), 4.67 (1H, dd, J = 6.5, 2.5

Hz, H-14), 6.49 (1H, d, J = 6.5 Hz, H-15), 7.12-7.34 (5H, m, Ar). ^{13}CNMR ($CDCl_3$, 67.5 MHz), δ 3.4, 7.3, 12.2, 21.0, 22.0, 29.9, 31.8, 67.3, 75.6, 79.5, 125.8, 125.9, 128.6, 129.0, 130.9, 136.9, 153.1, 171.0. $[\alpha]_D^{25}$ +91.9° (c 1.40, $CHCl_3$). Anal. calcd. for $C_{23}H_{36}O_3SSi$: C 65.67; H 8.63. Found: C 65.49; 8.77.

[2*S*,5*S*,6*R*]-(1,1-Dimethylethyl)dimethyl[[(tetrahydro-3-methyl-6-[2-(phenylthio)-2-(triethylsilyl)ethenyl]-2-pyranyl]methoxy]silane 17.

Sodium methoxide (ca. 28% sodium methoxide in methanol, 6.5 ml, 0.027 mol) was added to a solution of **15** (10.20 g, 0.024 mol) in methanol (121 ml) at 0 °C. After being stirred for 1 h, the mixture was neutralized with DOWEX 50W-X4 and then filtered. Concentration of the filtrate under reduced pressure afforded **16** (9.16 g, 99%). IR (KBr) ν_{max} 2951, 1582, 1477, 1060, 738 cm^{-1}. ^{1}HNMR ($CDCl_3$, 270 MHz), δ 0.50 (6H, m, CH_3CH_2Si), 0.87 (9H, t, J = 8 Hz, CH_3CH_2Si), 1.0 (3H, d, J = 7 Hz, CH_3-13), 1.23 (1H, m), 1.52 (1H, m), 1.63 (1H, m), 1.79 (1H, dt, J = 13, 4.5 H), 1.92 (1H, m), 2.26 (1H, brd, O*H*), 3.54 (3H, m, H-9 and H-10), 4.68 (1H, dd, J = 6.8, 3 Hz, H-14), 6.47 (d, J =6.8 Hz), 7.2 (5H, m, Ar). ^{13}CNMR ($CDCl_3$, 67.5 MHz), δ 3.3, 7.2, 12.2, 21.4, 29.8, 32.0, 66.2, 78.1, 79.3, 125.9, 128.3, 128.6, 129.1, 131.2, 136.7, 152.9. $[\alpha]_D^{25}$ +144.4° (c 2.00, $CHCl_3$). Anal. calcd. for $C_{21}H_{34}O_2SSi$: C 66.61; H 9.05. Found: C 66.59; H 9.23.

A solution of **16** (9.54 g, 0.025 mol) and imidazole (8.12 g, 0.119 mol) in DMF (100 ml) was added *t*-butyldimethylsilyl chloride (4.31 g, 0.029 mol) at room temperature. The mixture was stirred for 10 h and then diluted with water. The separated aqueous layer was extracted with ether and the combined organic layer was concentrated and then dried through azeotropic evaporation with benzene to afford **17** (11.73 g, 94%) as colorless oil. IR (KBr) ν_{max} 2954, 1583, 1475, 1252, 1120, 836 cm^{-1}. ^{1}HNMR ($CDCl_3$, 270 MHz), δ 0.09 (3H, s, CH_3Si), 0.10 (3H, s, CH_3Si), 0.51 (6H, m, CH_3CH_2Si), 0.86 (9H, t, J = 8 Hz, CH_3CH_2Si), 0.9 (9H, s, *t*-Bu), 0.99 (3H, d, J = 7 Hz, CH_3-13), 1.38 - 1.5 (2H, m), 1.63 (1H, m), 1.77 (1H, m), 1.90 (1H, m), 3.41 (1H, m, H-10), 3.54 (1H, dd, J = 10, 5.5 Hz, H-9), 3.69 (1H, dd, J = 10, 5.5 Hz, H-9), 4.64 (1H, dd, J = 6.8, 2.5 Hz, H-14), 6.49 (1H, d, J = 6.8 Hz, H-15), 7.20 (5H, m, Ar). ^{13}CNMR ($CDCl_3$, 67.5 MHz), δ -5.2, -5.1, 3.2, 7.3, 12.3, 18.4, 22.3, 25.9, 30.1, 32.2, 66.9, 78.5, 79.4, 125.7, 128.6, 129.0, 130.2, 137.0, 154.1. $[\alpha]_D^{25}$ +130.1° (c 0.82, $CHCl_3$). Anal. calcd. for $C_{27}H_{48}O_2SSi_2$: C 65.79; H 9.82. Found: C 65.78; H 10.01.

[2*S*,5*S*,6*R*]-(1,1-Dimethylethyl)dimethyl[[(tetrahydro-3-methyl-6-[2-(phenylsulfonyl)-2-(triethylsilyl)ethenyl]-2-pyranyl]methoxy]silane 18.

To a suspension of **17** (11.74 g, 0.024 mol) and Na_2HPO_4 (9.92 g, 0.070 mol) in dichloromethane (200 ml) was added *m*-chloroperbenzoic acid (80%, 10.55 g, 0.049 mol) at room temperature and the reaction mixture was stirred for 1 h. Aqueous sodium hydrogen carbonate and aqueous sodium sulfite was added and the separated aqueous layer was extracted with ether. The combined organic layer was dried, concentrated and then purified by silica gel flash chromatography (hexane/ether, 10 : 1) to afford **18** (11.8 g, 94%). IR (KBr) ν_{max} 2960. 1598, 1447, 1305, 1142, 1060, 838 cm^{-1}. ^{1}HNMR ($CDCl_3$, 270 MHz), δ 0.02 (3H, s, MeSi), 0.06 (3H, s, MeSi), 0.6-0.9 (15H, m, Et_3Si), 0.87 (9H, s, *t*-Bu), 0.97 (3H, d, J = 7 Hz, CH_3-13), 1.37 (m), 1.62 (m), 1.78 (1H, m), 2.05 (1H, m), 3.33 (1H, m, H-10), 3.51 (1H, dd, J = 11, 4.5 Hz, H-9), 3.61 (1H, dd, J = 11, 6 Hz, H-9), 4.87 (1H, dd, J = 8, 2.5 Hz, H-14), 6.48 (1H, d, J = 8 Hz, H-15), 7.55 (3H, m, Ar), 7.88 (2H, m, Ar). ^{13}CNMR ($CDCl_3$, 67.5 MHz), δ -5.2, -5.1, 3.3, 7.0, 12.3, 18.3, 21.8, 25.9, 30.3, 32.1, 66.7, 77.7, 78.4, 126.8, 127.5, 128.9, 132.9, 140.9, 142.8, 158.5. $[\alpha]_D^{25}$ +73.1° (c 0.57, $CHCl_3$). Anal. calcd. for $C_{27}H_{48}O_4SSi_2$: C 61.78; H 9.22. Found: C 61.79; H 9.32.

[β*S*,2*R*,3*S*,6*S*]-Tetrahydro-β,3-dimethyl-6-hydroxymethyl-2-pyranylethylsulfone 19.

A solution of lithium bromide (0.5 M in ether, 550 ml) was added to a solution of **18** (12.02 g, 0.023 mol) in hexane (500 ml) under argon atmosphere. The reaction mixture was cooled to -78 °C and then methyllithium (1.5 M in ether as complex with lithium bromide, 30 ml, 0.045 mol) was added. After being stirred for 20 min, aqueous ammonium chloride was added. The separated aqueous layer was extracted with

ether. The combined organic layer was concentrated and dried by azeotropic evaporation with benzene. The resulting crude oil was dissolved in THF (200 ml) and then treated with tetrabutylammonium fluoride (1.0 M in THF, 20 ml) at room temperature. After being stirred for 4 h, the reaction mixture was quenched with aqueous ammonium chloride and then extracted with ether. The combined organic phase was concentrated and then purified by silica gel flash chromatography (CH_2Cl_2/ether, 3 : 1) to afford **19** (6.9 g, 96%) as colorless oil. IR (KBr) ν_{max} 2933, 1448, 1306, 1146, 1069, 750 cm^{-1}. ^{1}HNMR ($CDCl_3$, 270 MHz), δ 0.74 (3H, d, *J* = 7 Hz, C*H*$_3$-13), 1.17 (3H, d, *J* = 7 Hz, C*H*$_3$-15), 1.42 (1H, m), 1.66 (2H, m), 1.75 (1H, m), 1.92 (1H, m), 2.14 (1H, m, H-15), 2.85 (1H, dd, *J* = 14, 10 Hz, H-16), 3.16 (1H, dd, *J* = 9, 2 Hz, H-14), 3.22 (1H, dd, *J* = 14, 2 Hz, H-16), 3.40 (1H, m, H-10), 3.5 (2H, m, H-9), 7.60 (3H, m, Ar), 7.93 (2H, m, Ar). ^{13}CNMR ($CDCl_3$, 67.5 MHz), δ 11.5, 16.7, 21.6, 28.3, 30.7, 31.4, 58.7, 66.2, 79.1, 82.0, 128.0, 129.3, 133.7, 139.7. $[\alpha]_D^{25}$ +16.6° (*c* 0.57, $CHCl_3$). Anal. calcd. for $C_{16}H_{24}O_4S$: C 61.51; H 7.74. Found: C 61.30; H 8.03.

[5*S*,6*S*,7*S*]-5,7-Dimethyl-6-hydroxy-8-phenylsulfonyloctene 21.

A solution of **19** (308 mg, 0.99 mmol) in DMF (3 ml) was added to a solution of methyltriphenoxyphosphonium iodide (0.71 g, 1.57 mmol) in DMF (10 ml) at room temperature. The reaction mixture was stirred for 1 h and then quenched with aqueous sodium hydrogen carbonate. The separated aqueous layer was extracted with ether and the combined organic layer was concentrated and then purified by silica gel chromatography (hexane/ether, 5 : 1) to provide **20** (358 mg, 95%) as colorless oil. IR (KBr) ν_{max} 2932, 1448, 1306, 1146, 1086, 1068, 748 cm^{-1}. ^{1}HNMR ($CDCl_3$, 270 MHz), δ 0.74 (3H, d, *J* = 7 Hz, C*H*$_3$-13), 1.21 (3H, d, *J* = 6.5 Hz, C*H*$_3$-15), 1.3-1.75 (m), 2.11 (1H, m, H-15), 2.85 (1H, dd, *J* = 14, 10 Hz, H-16), 3.1 (1H, dd, *J* = 10, 7 Hz, H-9), 3.12 (1H, m), 3.16 (1H, dd, *J* = 10, 4 Hz, H-9), 3.24 (1H, dd, *J* = 14, 2 Hz, H-16), 3.25 (1H, m), 7.6 (3H, m, Ar), 7.95 (2H, m, Ar). ^{13}CNMR ($CDCl_3$, 67.5 MHz), δ 9.9, 11.6, 16.7, 26.1, 28.0, 30.9, 31.5, 58.7, 77.9, 82.6, 128.0, 129.3, 133.6, 139.7. $[\alpha]_D^{20}$ +45.6° (*c* 2.24, $CHCl_3$). Anal. calcd. for $C_{16}H_{23}IO_3S$: C 45.50; H 5.49. Found: C 45.34; H 5.40.

A solution of **20** (8.54 g, 0.020 mol) and zinc (13.08 g, 0.20 mol) dissolved in a mixture of pyridine (23 ml) and ethanol (95%, 190 ml) was gradually heated to 70 °C. The reaction mixture was filtered through Celite and the filtrate was diluted with ether. The diluted filtrate was washed with 1N HCl, water and aqueous sodium hydrogen carbonate. Concentration under reduced pressure followed by drying through azeotropic evaporation with benzene gave **21** (5.93 g, 95%). IR (KBr) ν_{max} 3527, 2975, 2932, 1640, 1448, 1302, 1147, 1086 cm^{-1}. ^{1}HNMR ($CDCl_3$, 270 MHz), δ 0.94 (3H, d, *J* = 6.5 Hz, C*H*$_3$-13), 1.01 (3H, d, *J* = 7 Hz, C*H*$_3$-15), 1.15 (1H, m), 1.43 (1H, m), 1.56 (1H, m), 1.78 (1H, d, *J* = 5 Hz, O*H*), 2.0 (1H, m, H-11), 2.11 (1H, m, H-15), 2.42 (1H, m, H-11), 2.99 (1H, dd, *J* = 14, 6.5 Hz, H-16), 3.34 (1H, dd, *J* = 14, 6.5 Hz, H-16), 3.46 (1H, m, H-14), 4.96 (1H, ddt, *J* = 10, 2, 1 Hz, H-9, cis), 5.01 (1H, ddd, *J* = 17, 3, 1.5 Hz, H-9, trans), 5.77 (1H, ddt, *J* = 17, 10, 6.5 Hz, H-10), 7.6 (3H, m, Ar), 7.93 (2H, m, Ar). ^{13}CNMR ($CDCl_3$, 67.5 MHz), δ 13.2, 15.2, 30.6, 31.0, 31.8, 35.1, 60.3, 76.7, 114.7, 127.7, 129.3, 133.6, 138.4, 140.0. $[\alpha]_D^{25}$ -16.9° (*c* 1.06, $CHCl_3$). Anal. calcd. for $C_{16}H_{24}O_3S$: C 64.83; H 8.16. Found: C 64.82; H 8.27.

Synthesis of Sub-segment C-1 (3).

To a solution of **21** (146 mg, 0.49 mmol) and 2,6-lutidine (105 mg, 0.98 mmol) in dichloromethane (5 ml) was added *t*-butyldimethylsilyl trifluoromethanesulfonate (0.17 ml, 0.74 mmol) at room temperature. After being stirred for 2.5 h, the reaction mixture was quenched with aqueous sodium hydrogen carbonate and then extracted with ether. The combined organic layer was concentrated and then purified by silica gel chromatography (hexane/ether, 10 : 1 and then 3 : 1) to yield **22** (162 mg, 80%) as colorless oil. IR (KBr) ν_{max} 3530, 1448, 1307, 1150, 1086, 836 cm^{-1}. ^{1}HNMR ($CDCl_3$, 270 MHz), δ 0.01 (3H, s, MeSi), 0.04 (3H, s, MeSi), 0.78 (3H, d, *J* = 6.5 Hz, C*H*$_3$-13), 0.87 (9H, s, *t*-Bu), 1.06 (3H, d, *J* = 7 Hz, C*H*$_3$-15), 1.18 (1H, m), 1.42 (1H, m), 1.56 (1H, m), 1.94 (1H, m, H-11), 2.06 (1H, m), 2.32 (1H, m), 2.91 (1H, dd, *J* = 14, 9 Hz, H-16), 3.36 (1H, dd, *J* = 14, 3.5 Hz, H-16), 3.56 (1H, t, *J* = 14 Hz, H-14), 4.94 (1H, ddt, *J* = 10.5, 2, 1 Hz, H-9, cis), 4.99 (1H, ddt, *J* = 17, 3.5, 1.5 Hz, H-9, trans), 5.76 (1H, ddt, *J* = 17, 10.5, 6.5 Hz, H-10), 7.6 (3H, m, Ar), 7.9 (2H, m, Ar). ^{13}CNMR ($CDCl_3$, 67.5 MHz), δ -4.15, -4.07, 15.2, 15.8,,

18.2, 26.0, 31.6, 33.4, 33.9, 35.2, 59.9, 77.6, 114.6, 127.9, 129.3, 133.5, 138.6, 140.2. $[\alpha]_D^{25}$ +9.8° (*c* 2.94, $CHCl_3$). Anal. calcd. for $C_{22}H_{38}O_3SSi$: C 64.34; H 9.33. Found: C 64.29; H 9.66.

A suspension of **22** (58 mg, 0.14 mmol) and Na_2HPO_4 (81 mg, 0.57 mmol) in dichloromethane (2 ml) was added *m*-chloroperbenzoic acid (80%, 46 mg, 0.21 mmol) at room temperature. After being stirred for 5 h, the reaction mixture was quenched with aqueous sodium hydrogen carbonate and aqueous sodium sulfite. The resulting aqueous layer was extracted with ether. The combined organic layer was concentrated and then purified by silica gel preparative thin layer chromatography (hexane/ether, 1 : 1) to yield **3** (50 mg, 82%) as a mixture of diastereoisomers which was used for next coupling reaction with Sub-segment C-2. IR (KBr) ν_{max} 2976, 2926, 2860, 1473, 1305, 1084, 833 cm^{-1}. ^{1}HNMR ($CDCl_3$, 270 MHz), δ 0.04 (3H, s, MeSi), 0.05 (3H, s, MeSi), 0.81 (3H, d, *J* = 6.5 Hz, C*H*$_3$-13), 0.87 (9H, s, *t*-Bu), 1.07 (3H, d, *J* = 7 Hz, C*H*$_3$-15), 1.25 (m), 1.5 (m), 1.6 (m), 2.34 (1H, m, H-15), 2.45 (1H, dt, *J* = 5, 2.5 Hz, H-9), 2.74 (1H, td, *J* = 5, 2 Hz, H-9), 2.86 (1H, m, H-10), 2.90 (1H, dd, *J* = 14, 9 Hz, H-16), 3.35 (1H, dd, *J* = 14, 3.5 Hz, H-16), 3.59 (1H, t, *J* = 4 Hz, H-14), 7.60 (3H, m, Ar), 7.91 (2H, m, Ar). ^{13}CNMR ($CDCl_3$, 67.5 MHz), δ -4.1, -4.1, 15.2, 15.3, 15.8, 18.3, 26.0, 30.46, 30.55, 30.7, 31.0, 33.1, 35.80, 35.83, 46.9, 47.0, 52.2, 52.4, 59.92, 59.95, 77.6, 127.9, 129.3, 133.6, 140.1. Anal. calcd. for $C_{22}H_{38}O_4SSi$: C 61.93; H 8.98. Found: C 61.82; H 8.78.

[1*S*,2*S*,5*S*]-2-Methyl-6,8-dioxabicyclo[3,2,1]octa-4-one 23.

To a suspension of copper (I) cyanide (8.9 g, 99 mmol) in tetrahydrofuran (50 ml) cooled to 0 °C was added methyllithium (1.5 M in ether as complex with lithium bromide, 66.0 ml, 99 mmol) dropwise to form a dark blue solution. To this mixture was added levoglucosenone **6** (10.0 g, 0.079 mol) in tetrahydrofuran (20 ml). After being stirred for 20 min, the reaction mixture was quenched by the addition of aqueous ammonium chloride, and the aqueous layer was extracted with ether. The combined organic phase was washed with brine and dried. Concentration under reduced pressure afforded **23** (7.90 g, 70%). IR (KBr) ν_{max} 2968, 1733, 1130, 1110, 910 cm^{-1}. ^{1}HNMR ($CDCl_3$, 270 MHz), δ 1.21 (3H, d, *J* = 7 Hz, C*H*$_3$-3), 2.08 (1H, d, brd, *J* = 16.5 Hz, H-4), 2.32 (1H, m, H-3), 2.83 (1H, dd, *J* = 16.5, 8 Hz, H-4), 3.98 (1H, dd, *J* = 8, 5 Hz, H-1), 4.03 (1H, dd, *J* = 8, 1 Hz, H-1), 4.43 (1H, m, H-2), 5.06 (1H, s, H-6, anomeric). ^{13}CNMR ($CDCl_3$, 67.5 MHz), δ 18.5, 35.9, 38.6, 67.9, 77.7, 101.4, 200.5. $[\alpha]_D^{25}$ -276.1° (*c* 1.67, $CHCl_3$). Anal. calcd. for $C_7H_{10}O_3$: C 59.14; H 7.09. Found: C 59.01; H 6.97.

(2*S*,3*S*)-3,4-Dihydro-3-methyl-2-pyranylmethyl acetate 25.

A solution of **23** (24.7 g, 0.17 mol) and hydrazine hydrate (22.67 g, 0.45 mol) in ethanol (200 ml) was stirred at room temperature for 2 h. Concentration under reduced pressure and azeotropic evaporation with benzene afforded hydrazone (24.40 g, 90%).

A suspension of sodium hydride (60% in mineral oil, 24.0 g, 0.6 mol, washed with hexane before use) in dimethyl sulfoxide (100 ml) was heated at 60 °C for 3 h until the evolution of hydrogen ceased. The reaction mixture was cooled, and the hydrazone (22.61 g, 0.14 mol) in dimethyl sulfoxide (120 ml) was added. After being stirred for 1 h, the resulting red reaction mixture was diluted with aqueous ammonium chloride. The aqueous layer was extracted with ether, and the combined organic phase was dried and then concentrated under reduced pressure to afford the residue which was purified by silica gel flash chromatography (hexane/ether, 1 : 1) to yield **24** (13.44 g, 75%). IR (KBr) ν_{max} 3412, 2924, 1656, 1241, 1070 cm^{-1}. ^{1}HNMR ($CDCl_3$, 270 MHz), δ 0.97 (3H, d, *J* = 7 Hz, C*H*$_3$-3), 1.72 (1H, ddt, *J* = 16, 10, 2 Hz, H-4), 1.90 (1H, m, H-3), 2.03 (1H, dtd, *J* = 16, 5, 2 Hz, H-4), 3.56 (1H, ddd, *J* = 9, 6, 3 Hz, H-2), 3.71 (1H, dd, *J* = 12, 6 Hz, H-1), 3.83 (1H, dd, *J* = 12, 3 Hz, H-1), 4.7 (1H, ddd, *J* = 6, 5, 2 Hz, H-5), 6.39 (1H, dt, *J* = 6, 2 Hz, H-6). ^{13}CNMR ($CDCl_3$, 67.5 MHz), δ 17.5, 27.9, 28.1, 63.1, 80.6, 100.5, 142.9. $[\alpha]_D^{25}$ +83.6° (*c* 1.47, $CHCl_3$). Anal. calcd. for $C_7H_{12}O_2$: C 65.60; H 9.44. Found: C 65.83; H 9.43.

Acetic anhydride (20 ml, 0.21 mol) was added to a solution of **24** (14.27 g, 0.11 mol) in pyridine (100 ml). The mixture was stirred at room temperature overnight and then diluted with ether (500 ml). The solution was washed with 1N HCl, water, aqueous sodium hydrogen carbonate and brine, dried and then concentrated under reduced pressure. The residue was subjected to silica gel flash chromatography (hexane/ether, 2 : 1) to

provide **25** as colorless oil (17.74 g, 87%). IR (KBr) ν_{max} 2932, 1744, 1234 cm^{-1}. ^{1}HNMR ($CDCl_3$, 270 MHz), δ 0.90 (1H, m, H-3), 1.00 (3H, d, *J* = 7 Hz, C*H*$_3$-3), 1.72 (1H, ddt, *J* = 16.5, 9, 2.5 Hz, H-4a), 1.90 (1H, m, H-4e), 2.11 (3H, s, acetate), 3.71 (1H, ddd, *J* = 8.5, 6, 2.5 Hz, H-2), 4.19 (1H, dd, *J* = 12, 6 Hz, H-1), 4.33 (1H, dd, *J* = 12, 2.5 Hz, H-1), 4.69 (1H, ddd, *J* = 6.5, 5, 2.5 Hz, H-5), 6.37 (1H, dt, *J* = 6, 1.5 Hz, H-6, anomeric). ^{13}CNMR ($CDCl_3$, 67.5 MHz), δ 17.6, 20.9, 27.8, 28.2, 64.6, 77.9, 100.1, 142.9, 171.1. $[\alpha]_D^{25}$ +83.1° (*c* 1.47, $CHCl_3$). Anal. calcd. for $C_9H_{14}O_3$: C 63.51; H 8.29. Found: C 63.34; H 8.35.

[2*S*,3*S*]-Tetrahydro-6-ethoxy-3-methyl-2-pyranylmethyl acetate 26.

A solution of **25** (17.6 g, 0.095 mol) and *p*-toluenesulfonic acid monohydrate (1.97 g, 0.010 mol) in a mixture of ethanol (30 ml) and dichloromethane (180 ml) was stirred at room temperature for 2.5 h. Aqueous sodium hydrogen carbonate was added, and the aqueous layer was extracted with ether. The combined organic phase was dried and concentrated under reduced pressure to give **26** (20.51 g, 99%) as a mixture of α- and β-ethyl glycosides. IR (KBr) ν_{max} 2933, 1743, 1238 cm^{-1}. ^{1}HNMR ($CDCl_3$, 270 MHz), δ 0.89 (3H, d, *J* = 6 Hz, C*H*$_3$-3), 1.23 (3H, d, *J* = 7 Hz, C*H*$_3$CH$_2$O), 2.08 (3H, s, acetate), 3.27 (1H, ddd, *J* = 10, 6, 3 Hz, H-2), 3.53 (1H, dq, *J* = 10, 7 Hz, CH$_3$C*H*$_2$O), 3.95 (1H, dq, *J* = 10, 7 Hz, CH$_3$C*H*$_2$O), 4.16 (1H, m, H-1), 4.25 (1H, dd, *J* = 12, 3 Hz, H-1),4.41 (1H, dd, *J* = 9, 2 Hz, H-6, anomeric). Anal. calcd. for $C_{11}H_{20}O_4$: C 61.09; H 9.32. Found: 61.07; H 9.25.

[2*S*,3*S*,6*S*]-Tetrahydro-3-methyl-6-[(phenylthio)ethynyl]-2-pyranylmethyl acetate 27.

Boron trifluoride etherate (15.1 ml, 0.12 mol) was added in one portion to a solution of **26** (7.91 g, 0.037 mol), phenylthiotrimethylsilylacetylene (9.92 g, 0.048 mol) and molecular sieve 4Å (5.0 g) in acetonitrile (100 ml) at 0 °C. The reaction mixture was stirred for 10 min and then quenched by the addition of aqueous sodium hydrogen carbonate. The aqueous layer was extracted with ether, and the combined organic phase was concentrated to afford the residue which was purified by silica gel chromatography (hexane/ether, 10 : 1) to yield **27** (6.4 g, 62%). IR (KBr) ν_{max} 2932, 1741, 1235 cm^{-1}. ^{1}HNMR ($CDCl_3$, 270 MHz), δ 0.92 (3H, d, *J* = 6 Hz, C*H*$_3$-3), 1.5 - 2.1 (5H, m), 2.10 (3H, s, acetate), 3.78 (1H, ddd, *J* = 9, 4.5, 3 Hz, H-2), 4.19 (1H, dd, *J* = 12, 4.5 Hz, H-1), 4.24 (1H, dd, *J* = 12, 3 Hz, H-1), 5.03 (1H, d, *J* = 5 Hz, H-6, anomeric), 7.37 (5H, m, Ar). ^{13}CNMR ($CDCl_3$, 67.5 MHz), δ 17.7, 21.0, 28.4, 30.6, 31.4, 65.1, 66.2, 73.3, 75.9, 97.3, 126.2, 126.6, 129.2, 132.6, 171.1. $[\alpha]_D^{25}$ +4.7° (*c* 3.63, $CHCl_3$). Anal. calcd. for $C_{17}H_{20}O_3S$: C 67.08; H 6.62. Found: C 66.99; H 6.67.

[2*S*,3*S*,6*R*]-Tetrahydro-3-methyl-6-[(phenylthio)ethynyl]-2-pyranylmethyl acetate 30.

A solution of **27** (8.86 g, 0.029 mol) in dichloromethane (90 ml) was added to a solution of dicobaltoctacarbonyl (12.4 g, 0.036 mol) in dichloromethane under argon atmosphere at room temperature. After being stirred for 2 h, the reaction mixture was concentrated under reduced pressure, and the residue was purified by silica gel flash chromatography (hexane/ether, 5 : 1) to yield air-sensitive **28** (16.0 g, 93%). ^{1}HNMR ($CDCl_3$, 270 MHz), δ 1.08 (3H, d, *J* = 6.5, C*H*$_3$-3), 1.6 - 2.0 (4H, m), 2.09 (3H, s, acetate), 2.16 (1H, m), 3.88 (1H, ddd, *J* = 7, 6, 2.5 Hz, H-2), 4.17 (1H, dd, *J* = 12, 2.5 Hz, H-1), 4.44 (1H, dd, *J* = 12, 6 Hz, H-1), 5.17 (1H, t, *J* = 4.5 Hz, H-6, anomeric), 7.45 (3H, m, Ar), 7.60 (2H, m, Ar). ^{13}CNMR ($CDCl_3$, 67.5 MHz), δ 18.0, 20.9, 27.0, 30.3, 30.9, 64.6, 75.0, 75.8, 129.4, 129.9, 134.0, 135.1, 171.2

Trifluoromethanesulfonic acid (0.36 ml, 4.1 mmol) was added to a solution of **28** (16.0 g, 0.027 mol) in dichloromethane (1400 ml) under argon atmosphere at room temperature. After being stirred for 30 min, the mixture was quenched with aqueous sodium hydrogen carbonate. The aqueous layer was extracted with ether, and the combined organic phase was concentrated under reduced pressure. Purification by silica gel flash chromatography (hexane/CH_2Cl_2, 1 : 1) gave β-epimer **29** (15.28 g, 96%) and recovered **28** (0.31 g, 2%). This unstable compound was immediately used for the next reaction without further purification. IR (KBr) ν_{max} 2093, 2053, 1744, 1239, 1093. ^{1}HNMR ($CDCl_3$, 270 MHz), δ 0.94 (3H, d, *J* = 6.5 Hz, C*H*$_3$-3), 1.45 (1H, td, *J* = 12, 3.5 Hz), 1.58 (1H, m), 1.62 (1H, m), 1.95 (1H, m), 2.01 (3H, s, acetate), 2.06 (1H, m), 3.46 (1H, ddd, *J* = 10, 6.5, 2 Hz, H-2), 4.09 (1H, dd, *J* = 11.5, 6.5 Hz, H-1), 4.30 (1H, dd, *J* = 11.5, 2 Hz, H-

1), 4.53 (1H, dd, J = 10.5, 2 Hz, H-6, anomeric), 7.42 (3H, m, Ar), 7.58 (2H, m, Ar). ^{13}CNMR ($CDCl_3$, 67.5 MHz), δ 17.4, 20.7, 31.6, 32.6, 33.5, 81.2, 129.3, 134.0, 135.0, 171.3.

To a solution of **29** (15.28 g, 0.026 mol) in tetrahydrofuran (315 ml) were added anhydrous sodium hydrogen carbonate (14.1 g, 0.17 mol) and iodine (21.35 g, 0.084 mol) at room temperature. The mixture was stirred for 3 h and then quenched by the addition of aqueous sodium hydrogen sulfite. The aqueous layer was extracted with ether. The organic phase was concentrated under reduced pressure and purified by silica gel flash chromatography (hexane/ether, 5 : 1) to provide **30** (7.53 g, 95%). IR (KBr) ν_{max} 2956, 1740, 1479, 1238, 1087, 1045, 1016 cm^{-1}. ^{1}HNMR ($CDCl_3$, 270 MHz), δ 1.02 (3H, d, J = 6.8 Hz, CH_3-3), 1.3 (1H, m), 1.6 (2H, m), 1.9 (3H, m), 2.08 (3H, s, acetate), 3.39 (1H, ddd, J = 10, 6, 2 Hz, H-2), 4.26 (1H, dd, J = 12, 6 Hz, H-1), 4.4 (1H, dd, J = 12, 2 Hz, H-1), 4.46 (1H, dd, J = 10.5, 3 Hz, H-6, anomeric), 7.4 (5H, m, Ar). ^{13}CNMR ($CDCl_3$, 67.5 MHz), δ 17.3, 20.9, 30.9, 32.3, 32.6, 65.2, 65.7, 68.8, 71.8, 97.7, 126.2, 126.4, 129.1, 132.3, 171.2. $[\alpha]_D^{25}$ -5.9° (c 4.37, $CHCl_3$). Anal. calcd. for $C_{17}H_{20}O_3S$: C 67.08; H 6.62. Found: C 67.07; H 6.73.

[2*S*,3*S*,6*R*]-Tetrahydro-3-methyl-6-[(phenylthio)-2-(triethylsilyl)ethenyl]-2-pyranylmethyl acetate 31.

Sodium hexachloroplatinate (IV) hexahydrate (0.01 M in i-PrOH, 20.4 ml) was added to a solution of **30** (6.20 g, 0.020 mol), triethylamine (6.2 ml, 0.045 mol) and triethylsilane (65 ml, 0.41 mol) in n-butanol (125 ml) under argon atmosphere at 110 °C. After being stirred for 1 h, the reaction mixture was cooled and then evaporated under reduced pressure. The residue was purified by silica gel flash chromatography (hexane/CH_2Cl_2, 2 : 1) to afford **31** (6.30 g, 72%). IR (KBr) ν_{max} 2956, 1305, 1145, 1079, 838 cm^{-1}. ^{1}HNMR ($CDCl_3$, 270 MHz), δ 0.53 (6H, m, CH_3CH_2Si), 0.84 (3H, d, J =7 Hz, CH_3-3), 0.86 (9H, t, J =7.5 Hz, CH_3CH$_2$Si), 1.22 - 1.90 (5H, m), 2.09 (3H, s, acetate), 3.18 (1H, ddd, J = 10, 5.5, 2.5 Hz, H-2), 4.15 (1H, dd, J = 12, 5.5 Hz, H-1), 4.22 (1H, dd, J = 12, 2.5 Hz, H-1), 4.56 (1H, ddd, J = 11, 7, 2.5 Hz, H-6, anomeric), 6.51 (1H, d, J = 7 Hz, H-7), 7.24 (5H, m, Ar). ^{13}CNMR ($CDCl_3$, 67.5 MHz), δ 3.2, 7.2, 17.5, 21.0, 31.1, 31.4, 32.3, 65.4, 76.9, 80.9, 125.7, 128.5, 128.8, 131.3, 136.9. 153.5, 171.2. $[\alpha]_D^{25}$ +84.1° (c 1.89, $CHCl_3$). Anal. calcd. for $C_{23}H_{36}O_3SSI$: C 65.67; H 8.63. Found: C 65.59; H 8.88.

[2*S*,3*S*,6*R*]-(1,1-Dimethylethyl)dimethyl[[(tetrahydro-3-methyl-6-[(phenylthio)-2-(triethylsilyl)ethenyl]-2-pyranyl]methoxy]silane 33.

Sodium methoxide (ca. 28% in methanol, 3.95 ml, 0.016 mol) was added to a solution of **31** (6.20 g, 0.015 mol) in methanol (125 ml) at 0 °C. After being stirred for 2 h, the reaction mixture was treated with DOWEX 50W-X4 and then filtered. Concentration of the filtrate gave **32** (5.80 g, 98%). IR (KBr) ν_{max} 2954, 1457, 1067 cm^{-1}. ^{1}HNMR ($CDCl_3$, 270 MHz), δ 0.51 (6H, m, CH_3CH_2Si), 0.82 (3H, d, J = 7 Hz, CH_3-3), 0.87 (9H, t, J = 7.5 Hz, CH_3CH$_2$Si), 1.2 - 1.9 (5H, m), 2.20 (1H, brd, OH), 3.10 (1H, ddd, J = 10, 7, 2.5 Hz, H-2), 3.54 (1H, m, H-1), 3.75 (1H, m, H-1), 4.56 (1H, ddd, J = 10, 7, 2.5 Hz, H-6, anomeric), 6.47 (1H, d, J = 7 Hz, H-7), 7.2 (5H, m, Ar). ^{13}CNMR ($CDCl_3$, 67.5 MHz), δ 3.2, 7.2, 17.3, 31.1, 31.5, 32.1, 63.9, 76.4, 83.0, 125.8, 128.6, 128.9, 132.0, 136.9, 153.1. $[\alpha]_D^{25}$ +95.1° (c 0.65, $CHCl_3$). Anal. calcd. for $C_{21}H_{34}O_2SSi$: C 66.61; H 9.05. Found: C 66.82; H 9.14.

To a solution of **32** (5.8 g, 15.3 mmol) and imidazole (5.01 g, 73.7 mmol) in N,N-dimethylformamide (100 ml) was added t-butyldimethylsilyl chloride (2.77 g, 18.5 mmol) at room temperature. After being stirred for 5 h, the reaction mixture was diluted with aqueous sodium hydrogen carbonate and then aqueous layer was extracted with ether. The combined organic phase was concentrated to give crude product (7.73 g) which was purified by silica gel chromatography (hexane/ether, 10 : 1) to provide **33** (7.40 g, 98%). IR (KBr) ν_{max} 2954, 1583, 1472, 1253, 1085, 1016 cm^{-1}. ^{1}HNMR ($CDCl_3$, 270 MHz), δ 0.08 (3H, s, MeSi), 0.09 (3H, s, MeSi), 0.50 (6H, m, CH_3CH_2Si), 0.84 (3H, d, J = 6.5 Hz, CH_3-3), 0.86 (9H, t, J = 8 Hz, CH_3CH$_2$Si), 0.91 (9H, s, t-Bu), 1.2 - 1.6 (4H, m), 1.70 (1H, m), 3.01 (1H, ddd, J = 10, 5.5, 2.5 Hz, H-2), 3.65 (1H, dd, J = 11.5, 5.5 Hz, H-1), 3.79 (1H, dd, J = 11.5, 2.5 Hz, H-1), 4.52 (1H, ddd, J = 11, 7, 2 Hz, H-6), 6.52 (1H, d, J =

7 Hz, H-7), 7.20 (5H, m, Ar). $[\alpha]_D^{25}$ +88.1° (*c* 3.95, $CHCl_3$). HRMS calcd. for $C_{27}H_{48}O_2SSi_2$; 492.2913, found 492.2900.

[2*S*,3*S*,6*R*]-(1,1-Dimethylethyl)dimethyl[[(tetrahydro-3-methyl-6-[2-(phenylsulfonyl)-2-(triethylsilyl)ethenyl]-2-pyranyl]methoxy]silane 34.

To a solution of **33** (7.40 g, 15.0 mmol) and sodium hydrogen phosphate (14.6 g, 0.10 mol) in dichloromethane (160 ml) was added *m*-chloroperbenzoic acid (80%, 6.66 g, 32.5 mmol) at 0 °C. After being stirred for 3 h, the mixture was quenched by the addition of aqueous sodium hydrogen carbonate and aqueous sodium sulfite. The aqueous layer was extracted with ether. The combined organic layer was dried and then concentrated under reduced pressure. Purification by silica gel flash chromatography (hexane/ether, 2 : 1) yielded **34** (7.56 g, 94%). IR (KBr) ν_{max} 2955, 1446, 1305, 1145, 1079 cm^{-1}. ^{1}HNMR ($CDCl_3$, 270 MHz), δ 0.05 (3H, s, MeSi), 0.71 (6H, m, CH_3CH_2Si), 0.84 (9H, m, CH_3CH_2Si), 0.88 (9H, s, *t*-Bu), 1.2 (2H, m), 1.43 (1H, m), 1.7 (2H, m), 2.97 (1H, ddd, *J* = 10, 5.5, 2.5 Hz, H-2), 3.61 (1H, dd, *J* = 11.5, 5.5 Hz, H-1), 3.75 (1H, dd, *J* = 11.5, 2.5 Hz, H-1), 4.84 (1H, ddd, *J* = 10, 8, 2 Hz, H-6), 6.49 (1H, d, *J* = 8 Hz, H-7), 7.50 (3H, m, Ar), 7.88 (2H, m, Ar). ^{13}CNMR ($CDCl_3$, 67.5 MHz), δ -5.0, 3.2, 7.0, 17.6, 18.4, 25.9, 30.8, 31.3, 32.2, 64.8, 75.3, 83.7, 126.8, 128.9, 132.8, 140.6, 142.9, 158.3. $[\alpha]_D^{25}$ +73.5° (*c* 3.61, $CHCl_3$). Anal. calcd. for $C_{27}H_{48}O_4SSi_2$: C 61.78; H 9.22. Found: C 61.81; H 9.43.

[β*S*,2*R*,5*S*,6*S*]-Tetrahydro-β,5-dimethyl-6-hydroxymethyl-2-pyranylethylsulfone 35.

To a solution of heteroolefin **34** (6.80 g, 0.013 mol) in hexane (280 ml) under argon atmosphere cooled to -78 °C were added lithium bromide (0.5 M in ether, 310 ml, 0.10 mol) and then methyllithium (1.5 M in ether as complex with lithium bromide, 17.3 ml, 0.026 mol). After being stirred for 20 min at -78 °C, the mixture was quenched by the addition of aqueous ammonium chloride. The aqueous layer was extracted with ether and the combined organic phase was dried and then concentrated to give crude oil. The crude oil was dissolved in tetrahydrofuran (150 ml) and then treated with tetrabutylammonium fluoride (1.0 M in tetrahydrofuran, 13 ml, 0.013 mol) at room temperature. The mixture was stirred for 1.5 h and then quenched by the addition of aqueous ammonium chloride. The aqueous layer was extracted with ether, and the combined organic phase was dried, concentrated and purified by silica gel flash chromatography (CH_2Cl_2/ether, 3 : 1) to afford **35** (3.95 g, 97%). IR (KBr) ν_{max} 3523, 2930, 1448, 1304, 1147, 1085 cm^{-1}. ^{1}HNMR ($CDCl_3$, 270 MHz), δ 0.80 (3H, d, *J* = 7 Hz, CH_3-3), 1.07 (3H, d, *J* = 7 Hz, CH_3-7), 1.1 - 1.55 (4H, m), 1.7 (1H, brd, O*H*), 1.75 - 1.95 (1H, m), 2.28 (1H, m, H-7), 2.93 (1H, dd, *J* = 14, 8 Hz, H-8), 3.0 (1H, ddd, *J* = 10, 7, 2.5 Hz, H-2), 3.34 (1H, ddd, *J* = 10, 3, 2 Hz, H-6), 3.40 (1H, dd, *J* = 14, 4 Hz, H-8), 3.43 (1H, dd, *J* = 11, 7 Hz, H-1), 3.67 (1H, dd, *J* = 11, 2.5 Hz, H-1), 7.60 (3H, m, Ar), 7.92 (2H, m, Ar). ^{13}CNMR ($CDCl_3$, 67.5 MHz), δ 15.0, 17.1, 27.0, 31.5, 32.1, 33.1, 59.0, 63.9, 79.1, 83.4, 127.9, 129.3, 133.6, 133.9. $[\alpha]_D^{25}$ +9.4° (*c* 5.18, $CHCl_3$). Anal. calcd. for $C_{16}H_{24}O_4S$: C 65.51; H 7.74. Found: C 65.28; H 7.57.

[3*S*,6*R*,7*S*]-3,7-Dimethyl-6-hydroxy-8-phenylsulfonyloctene 37.

A solution of **35** (4.0 g, 0.013 mol) in *N,N*-dimethylformamide (50 ml) was added to a solution of methyltriphenoxyphosphonium iodide (8.34 g, 0.018 mol) in *N,N*-dimethylformamide (50 ml) at room temperature. The mixture was stirred for 30 min and then quenched with aqueous sodium hydrogen carbonate. The aqueous layer was extracted with ether. The organic phase was dried and concentrated under reduced pressure to provide the residue which was purified by silica gel chromatography (hexane/CH_2Cl_2, 3 : 1) to yield **36** (5.1 g, 94%). IR (KBr) ν_{max} 3427, 2924, 1595, 1473, 1302, 1144, 1085, 754 cm^{-1}. ^{1}HNMR ($CDCl_3$, 270 MHz), δ 0.80 (3H, d, *J* = 6.5 Hz, CH_3-3), 1.07 (3H, d, *J* = 7 Hz, CH_3-7), 1.2 - 1.5 (5H, m), 1.78 (1H, ddd, *J* =12, 6, 3 Hz), 2.25 (1H, m, H-7), 2.63 (1H, ddd, *J* = 9, 6.5, 2.5 Hz, H-2), 2.96 (1H, dd, *J* = 14, 7.5 Hz, H-8), 3.16 (1H, dd, *J* = 10, 6.5 Hz, H-1), 3.36 (1H, dd, *J* = 10, 2.5 Hz, H-1), 3.41 (1H, ddd, *J* = 10, 3.5, 2.5 Hz, H-6), 3.6 (1H, dd, *J* = 14, 4.5 Hz, H-8), 7.60 (3H, m, Ar), 7.95 (2H, m, Ar). ^{13}CNMR ($CDCl_3$, 67.5 MHz), δ 10.0, 11.5, 16.7, 26.0, 27.8, 30.7, 31.4, 58.6, 77.7, 82.5, 127.9, 129.2, 133.6, 139.5. $[\alpha]_D^{25}$ -4.6° (*c* 3.65, $CHCl_3$). Anal. calcd. for $C_{16}H_{23}IO_3S$: C 45.50; H 5.49. Found: C 45.50; H 5.57.

A suspension of **36** (4.72 g, 0.0112 mol) and zinc (7.35 g, 0.112 mol) in a mixture of pyridine (12.5 g, 0.16 mol) and ethanol (95%, 100 ml) was gradually heated to 70 °C and then stirred vigorously at 70 °C for 30 min. The reaction mixture was filtered through Celite, and the filtrate was concentrated. The residue was purified by silica gel flash chromatography (hexane/ether, 1 : 1) to afford **37** (2.91 g, 88%). IR (KBr) ν_{max} 3524, 2941, 1447, 1304, 1147, 1086 cm^{-1}. ^{1}HNMR ($CDCl_3$, 270 MHz), δ 1.00 (3H, d, *J* = 7 Hz, C*H*$_3$-3), 1.02 (3H, d, *J* = 7 Hz, C*H*$_3$-7), 1.2 - 1.45 (4H, m), 1.71 (1H, br), 2.12 (1H, m, H-7), 2.29 (1H, m, H-3), 2.95 (1H, dd, *J* = 14, 7 Hz, H-8), 3.36 (1H, dd, *J* = 14, 6 Hz, H-8), 3.76 (1H, brd, H-6), 4.93 (1H, d, brd, *J* = 10 Hz, H-1, cis), 4.95 (1H, dt, *J* = 17, 1.5 Hz, H-1, trans), 5.65 (1H, ddd, *J* = 17, 10, 8 Hz, H-2), 7.61 (3H, m, Ar), 7.92 (2H, m, Ar). ^{13}CNMR ($CDCl_3$, 67.5 MHz), δ 13.8, 20.3, 31.1, 32.9, 33.8, 37.7, 59.5, 73.3, 113.0, 127.8, 128.3, 129.3, 133.6, 140.1, 144.2. $[\alpha]_D^{25}$ +4.2° (*c* 4.85, $CHCl_3$). Anal. calcd. for $C_{16}H_{24}O_3S$: C 64.83; H 8.16. Found: C 64.91; H 8.09.

[3*S*,6*S*,7*S*]-3,7-Dimethyl-6-hydroxy-8-phenylsulfonyloctene 39.

Diethyl azodicarboxylate (3.29 g, 18.8 mmol) was added dropwise to a solution of **37** (2.66 g, 8.97 mmol), triphenylphosphine (7.43 g, 28.3 mmol) and benzoic acid (3.46 g, 28.3 mmol) in tetrahydrofuran (100 ml) at 0 °C. After being stirred for 24 h, the reaction mixture was quenched with aqueous sodium hydrogen carbonate. The aqueous layer was extracted with ether, and the combined organic phase was concentrated and then purified by silica gel flash chromatography (hexane/CH_2Cl_2, 1 : 1) to afford **38** (3.36 g, 94%). IR (KBr) ν_{max} 2963, 1717, 1272, 1149, 714 cm^{-1}. ^{1}HNMR ($CDCl_3$, 270 MHz), δ 0.93 (3H, d, *J* = 7 Hz, C*H*$_3$-3), 1.19 (3H, d, *J* = 7 Hz, C*H*$_3$-7), 1.2 - 1.3 (2H, m), 1.4 - 1.5 (2H, m), 2.03 (1H, m), 2.4 (1H, m), 2.99 (1H, dd, *J* = 14, 9 Hz, H-8), 3.35 (1H, dd, *J* = 14, 2 Hz, H-8), 4.90 (1H, d, brd, *J* = 10.5 Hz, H-1, cis), 4.91 (1H, d, brd, *J* = 17 Hz, H-1, trans), 5.03 (1H, dt, *J* = 7.5, 5 Hz, H-6), 5.57 (1H, ddd, *J* = 17, 10.5, 8 Hz, H-2), 7.45 (2H, m, Ar), 7.6 (4H, m, Ar), 7.92 (4H, m, Ar). ^{13}CNMR ($CDCl_3$, 67.5 MHz), δ 17.2, 20.1, 29.1, 31.7, 32.2, 37.7, 58.2, 77.3, 113.3, 128.0, 128.4, 129.4, 129.6, 129.8, 133.1, 133.7, 139.6, 143.8, 165.9. $[\alpha]_D^{25}$ +2.0° (*c* 1.47, $CHCl_3$). Anal. calcd. for $C_{23}H_{28}O_4S$: C 68.97; H 7.05. Found: C 68.90; H 7.12.

Sodium methoxide (ca. 28%, 2.8 ml, 9.77 mmol) was added to a solution of **38** (3.26 g, 8.14 mmol) in methanol (100 ml) at room temperature. After being stirred for 12 h, the mixture was neutralized with acidic ion exchange resin DOWEX 50W-X4. The resin was removed by filtration and the filtrate was concentrated under reduced pressure. The residue was purified by silica gel flash chromatography (hexane/ether, 2 : 1) to afford **39** (2.41 g, 99%). IR (KBr) ν_{max} 3535, 2970, 1448, 1304, 1147, 1086, 997 cm^{-1}. ^{1}HNMR ($CDCl_3$, 270 MHz), δ 0.97 (3H, d, *J* = 7 Hz, C*H*$_3$-3), 1.12 (3H, d, *J* = 7 Hz, C*H*$_3$-7), 1.24 - 1.44 (4H, m), 2.10 (2H, m), 2.94 (1H, dd, *J* = 14, 8.5 Hz, H-8), 3.39 (1H, m, H-6), 3.41 (1H, dd, *J* = 14, 3 Hz, H-8), 4.91 (1H, d, brd, *J* = 10 Hz, H-1, cis), 4.94 (1H, dt, *J* = 17, 1 Hz, H-1, trans), 5.64 (1H, ddd, *J* = 17, 10, 8 Hz, H-2), 7.60 (3H, m, Ar), 7.90 (2H, m, Ar). ^{13}CNMR ($CDCl_3$, 67.5 MHz), δ 17.3, 20.1, 32.0, 32.3, 34.5, 37.8, 58.5, 75.2, 113.0, 127.8, 129.3, 133.6, 140.0, 144.2. $[\alpha]_D^{25}$ +4.5° (*c* 1.77, $CHCl_3$). Anal. calcd. for $C_{16}H_{24}O_3S$: C 64.83; H 8.16. Found: C 64.80; H 8.09.

Synthesis of Sub-segment C-2 (4).

To a solution of **39** (1.21 g, 4.1 mmol) and 2,6-lutidine (0.88 g, 8.2 mmol) in dichloromethane (20 ml) under nitrogen atmosphere at room temperature was added *t*-butyldimethylsilyl trifluoromethanesulfonate (1.4 ml, 6.15 mmol). After being stirred for 24 h, the reaction mixture was quenched with aqueous sodium hydrogen carbonate. The aqueous layer was extracted with ether, and the combined organic phase was concentrated and then purified by silica gel chromatography (hexane/ether, 4 : 1) to afford **4** (1.50 g, 89%). IR (KBr) ν_{max} 2955, 1447, 1306, 1148, 1086 cm^{-1}. ^{1}HNMR ($CDCl_3$, 270 MHz), δ -0.01 (3H, s, MeSi), -0.03 (3H, s, MeSi), 0.84 (9H, s, *t*-Bu), 0.92 (3H, d, *J* = 7 Hz, C*H*$_3$-3), 1.0 - 1.4 (4H, m), 1.11 (3H, d, *J* = 7 Hz, *CH*$_3$-7), 1.22 (m), 1.97 (1H, m, H-7), 2.10 (1H, m, H-3), 2.83 (1H, dd, *J* = 14.5, 9 Hz, H-8), 3.24 (1H, dd, *J* = 14.5, 2.5 Hz, H-8), 3.45 (1H, td, *J* = 6, 3.5 Hz, H-6), 4.91 (1H, d, brd, *J* = 10 Hz, H-1, cis), 4.92 (1H, dt, *J* = 17, 1.5 Hz, H-1, trans), 5.57 (1H, ddd, *J* = 17, 10, 8 Hz, H-2), 7.79 (3H, m, Ar), 7.90 (2H, m, Ar). ^{13}CNMR ($CDCl_3$, 67.5 MHz), δ -4.7, -4.2, 17.0, 18.0, 20.2, 25.8, 31.3, 31.7, 32.8, 37.8, 58.2, 75.8,

112.9, 127.9, 129.2, 133.5, 139.9, 144.2. $[\alpha]_D^{25}$ +4.0° (*c* 1.03, $CHCl_3$). Anal. calcd. for $C_{22}H_{38}O_3SSi$: C 64.34; H 9.33. Found: C 64.31; H 9.32.

[2*R*,3*S*,6*R*]-(1,1-Dimethylethyl)dimethyl[[(tetrahydro-3-methyl-6-[2-(phenylsulfonyl)-2-(triethylsilyl)ethenyl]-2-pyranyl]methoxy]silane 43.

Sodium hexachloroplatinate (IV) hexahydrate (0.021 M in isopropanol, 2.5 ml) was added to a mixture of **27** (1.62 g, 5.78 mmol) and triethylsilane (17 ml, 0.11 mol) in 1,2-dichloroethane (32 ml) under argon atmosphere at 90 °C. After being stirred for 30 min, the reaction mixture was cooled to room temperature, diluted with hexane and then filtered through Celite. Concentration of the filtrate gave the residue which was purified by silica gel chromatography (hexane/ether, 4 : 1) to afford **40** (2.20 g, 90%). IR (KBr) ν_{max} 2954, 1744, 1236, 1023 cm^{-1}. ^{1}HNMR ($CDCl_3$, 270 MHz), δ 0.5 (6H, q, *J* = 7.5 Hz, CH_3CH_2Si), 0.87 (9H, t, *J* = 7.5 Hz, CH_3CH_2Si), 0.98 (3H, d, *J* = 6.5 Hz, CH_3-3), 1.37 (1H, m), 1.6 - 1.8 (4H, m), 2.08 (3H, s, acetate), 3.58 (1H, ddd, *J* = 8, 6, 3.5 Hz, H-2), 4.17 (1H, dd, *J* = 11.5, 6 Hz, H-1), 4.23 (1H, dd, *J* = 11.5, 3.5 Hz, H-1), 5.02 (1H, dt, *J* = 6.5, 5 Hz, H-6, anomeric), 6.71 (1H, d, *J* = 6.5 Hz, H-7), 7.25 (5H, m, Ar). ^{13}CNMR ($CDCl_3$, 67.5 MHz), δ 3.4, 5.8, 6.6, 7.2, 18.0, 20.9, 27.4, 28.7, 30.4, 65.0, 70.9, 75.4, 126.0, 128.5, 129.6, 134.3, 136.6, 149.6, 171.1. $[\alpha]_D^{25}$ +2.6° (*c* 1.38, $CHCl_3$). Anal. calcd. for $C_{23}H_{36}O_3SSi$: C 65.67; H 8.63. Found: C 65.57; H 8.89.

Sodium methoxide (ca. 28% in methanol, 1.26 ml, 0.30 mmol) was added to a solution of **40** (2.07 g, 4.92 mmol) in methanol (40 ml) at 0 °C. After being stirred for 2 h, the reaction mixture was neutralized by the addition of DOWEX 50W-X4 and then filtered. Concentration of the filtrate gave **41** (1.52 g) which was dissolved in dichloromethane (30 ml). To this solution was added sodium hydrogen phosphate (3.99 g, 28.2 mmol) and *m*-chloroperbenzoic acid (80%, 1.93 g, 9.25 mmol) at 0 °C. After being stirred for 11 h, the mixture was quenched by the addition of aqueous sodium hydrogen carbonate and aqueous sodium hydrogen sulfite. The aqueous layer was extracted with ether, and the combined organic layer was washed with brine and dried. Evaporation under reduced pressure afforded **42** (1.65 g). ^{1}HNMR ($CDCl_3$, 270 MHz), δ 0.78 (6H, m, *J* = 7.5 Hz, CH_3CH_2Si), 0.92 (9H, m *J* = 7.5 Hz, CH_3CH_2Si), 0.96 (3H, d, *J* = 7 Hz, CH_3-3), 1.30 (1H, m), 1.55 - 1.8 (4H, m), 2.15 (1H, s, brd, OH), 3.43 (1H, m, H-2), 3.59 (2H, m, H-1), 5.16 (1H, dt, *J* = 8.5, 4.5 Hz, H-6, anomeric), 6.75 (1H, d, *J* = 8.5 Hz, H-6, anomeric), 7.57 (3H, m, Ar), 7.88 (2H, m, Ar). ^{13}CNMR ($CDCl_3$, 67.5 MHz), δ 3.3, 7.0, 18.0, 26.7, 28.5, 29.6, 65.8, 68.2,, 77.6, 127.0, 129.0, 133.0, 142.6, 144.0, 155.0. $[\alpha]_D^{27}$ -17.1° (*c* 1.33, $CHCl_3$). Anal. calcd. for $C_{21}H_{34}O_4SSi$: C 61.42; H 8.35. Found: C 61.31; H 8.61.

To a solution of **42** (1.50 g, 3.65 mmol) and imidazole (0.75 g, 10.94 mmol) in *N,N*-dimethylformamide (30 ml) was added *t*-butyldimethylsilyl chloride (0.66 g, 4.38 mmol) at room temperature. After being stirred for 50 min, the reaction mixture was diluted with water and then extracted with ether. The combined organic layer was washed with brine and dried. Concentration under reduced pressure and purification by silica gel chromatography (hexane/ether, 5 : 1) afforded **43** (1.35 g, 63%, three steps). IR (KBr) ν_{max} 2956, 1559, 1508, 1457, 1302, 1145. ^{1}HNMR ($CDCl_3$, 270 MHz), δ 0.03 (3H, s, MeSi), 0.04 (3H, s, MeSi), 0.6-0.95 (15H, m, CH_3CH_2Si), 0.88 (9H, s, *t*-Bu), 1.05 (3H, d, *J* = 6.5 Hz, CH_3-3), 1.3 (1H, m), 1.6 - 1.8 (4H, m), 3.4 (1H, q, *J* = 5.5 Hz, H-2), 3.55 (1H, dd, *J* = 11, 5.5 Hz, H-1), 3.7 (1H, dd, *J* = 11, 5.5 Hz, H-1), 5.16 (1H, m, H-6), 6.74 (1H, d, *J* = 8.5 Hz, H-7), 7.50 (3H, m, Ar), 7.90 (2H, m, Ar). ^{13}CNMR ($CDCl_3$, 67.5 MHz), δ -5.26, -5.23, 3.2, 7.0, 18.3, 25.9, 26.3, 27.8, 28.6, 63.8, 69.5, 78.2, 126.8, 128.9, 132.8, 141.4, 142.8, 156.9. $[\alpha]_D^{27}$ -43.3° (*c* 0.52, $CHCl_3$). Anal. calcd. for $C_{27}H_{48}O_4SSi_2$: C 61.78; H 9.22. Found: C 61.71; H 9.31.

[3*S*,6*S*,7*R*]-3,7-Dimethyl-6-hydroxy-8-phenylsulfonyloctene 46.

To a solution of **43** (740 mg, 1.41 mmol) in hexane (30 ml) cooled to -78 °C were added lithium bromide (0.5 M in ether, 33.8 ml, 16.9 mmol) and methyllithium (1.5 M in ether as complex with lithium bromide, 1.88 ml, 2.82 mmol). After being stirred at -78 °C for 25 min, the reaction mixture was quenched with aqueous ammonium chloride and the aqueous layer was extracted with ether. The combined organic phase was dried and

concentrated to give a crude oil (850 mg), which was dissolved in tetrahydrofuran (10 ml) and treated with tetrabutylammonium fluoride (1.0 M in tetrahydrofuran, 1.4 ml, 1.4 mmol). After being stirred for 10 h, the mixture was quenched with aqueous ammonium chloride and extracted with ether. The combined organic phase was concentrated and purified by silica gel chromatography (CH_2Cl_2/ether, 4 : 1) to yield **44** (440 mg, 98%). IR (KBr) ν_{max} 3505, 2931, 1448, 1305, 1147, 1086. ^{1}HNMR ($CDCl_3$, 270 MHz), δ 1.02 (3H, d, J = 7 Hz, C*H*$_3$-3), 1.09 (3H, d, J = 7 Hz, C*H*$_3$-7), 1.2 - 1.8 (5H, m), 2.44 (1H, m, H-7), 2.87 (1H, dd, J = 14, 6 Hz, H-8), 3.4 (1H, dd, J = 14, 6.5 Hz, H-8), 3.47 (2H, m, H-1), 3.84 (1H, ddd, J = 8, 5, 3 Hz, H-6), 3.93 (1H, td, J = 10, 2 Hz, H-2), 7.6 (3H, m, Ar), 7.92 (2H, m, Ar). ^{13}CNMR ($CDCl_3$, 67.5 MHz), δ 14.9, 18.2, 23.3, 25.9, 28.3, 31.2, 59.1, 61.9, 70.9, 78.4, 127.7, 129.3, 133.7, 140.0. $[\alpha]_D^{25}$ +10.6° (*c* 0.86, $CHCl_3$). Anal. calcd. for $C_{16}H_{24}O_4S$: C 61.51; H 7.74. Found: C 61.49; H 8.07.

To a solution of methyltriphenoxyphosphonium iodide (360 mg, 0.80 mmol) in *N,N*-dimethylformamide (2 ml) was added **44** (126 mg, 0.45 mmol) at room temperature. After being stirred for 30 min, the mixture was quenched with aqueous sodium hydrogen carbonate. The aqueous layer was extracted with ether, and the combined organic layer was washed with brine and dried. Concentration under reduced pressure and purification by silica gel chromatography (hexane/ether, 5 : 1) afforded **45** (150 mg, 88%). IR (KBr) ν_{max} 2930, 1447, 1305, 1147, 1086. ^{1}HNMR ($CDCl_3$, 270 MHz), δ 1.02 (3H, d, J = 7 Hz, C*H*$_3$-3), 1.12 (3H, d, J = 7 Hz, C*H*$_3$-7), 2.34 (1H, m, H-7), 2.94 (1H, dd, J = 14, 7 Hz, H-8), 3.31 (1H, m), 3.43 (1H, t, J = 8 Hz, H-2), 3.44 (1H, dd, J = 14, 4.5 Hz, H-8), 3.5 (m), 7.61 (3H, m, Ar), 7.95 (2H, m, Ar). ^{13}CNMR ($CDCl_3$, 67.5 MHz), δ 8.4, 14.8, 18.3, 22.9, 24.9, 31.0, 31.5, 59.9, 72.2, 127.9, 129.3, 133.6, 140.1. $[\alpha]_D^{25}$ +35.1° (*c* 0.41, $CHCl_3$). Anal. calcd. for $C_{16}H_{23}IO_3S$: C 45.50; H 5.49. Found: C 45.50; H 5.57.

A solution of **45** (150 mg, 0.36 mmol), pyridine (0.4 ml) and activated zinc (0.46 g, 7.1 mmol) in ethanol (95%, 9 ml) was stirred vigorously and gradually heated to 80 °C. After being stirred at 80 °C for 1 h, the mixture was cooled and then filtered through Celite. Concentration of the filtrate gave the residue which was purified by silica gel chromatography (CH_2Cl_2/ether, 10 : 1 and then 5 : 1) to afford **46** (94 mg, 90%). IR (KBr) ν_{max} 3518, 2871, 1448, 1304, 1145, 1086. ^{1}HNMR ($CDCl_3$, 270 MHz), δ 0.99 (3H, d, J = 7 Hz, C*H*$_3$-3), 1.01 (3H, d, J = 7 Hz, C*H*$_3$-7), 1.2 - 1.6 (4H, m), 1.69 (1H, s, brd, O*H*), 2.10 (1H, m, H-7), 2.30 (1H, m, H-3), 2.96 (1H, dd, J = 14, 7 Hz, H-8), 3.36 (1H, dd, J = 14, 6 Hz, H-8), 3.76 (1H, s, brd, H-6), 4.93 (1H, ddd, J = 10, 2, 1 Hz, H-1, cis), 4.96 (1H, ddd, J = 17, 1.5, 1 Hz, H-1, trans), 5.65 (1H, ddd, J = 17, 10, 7.5 Hz, H-2), 7.61 (3H, m, Ar), 7.92 (2H, m, Ar). ^{13}CNMR ($CDCl_3$, 67.5 MHz), δ 13.60, 20.18, 31.15, 32.95, 33.58, 37.74, 59.36, 73.38, 112.86, 127.63, 129.20, 123.54, 139.88, 144.11, 144.2. $[\alpha]_D^{25}$ +2.0° (*c* 1.93, $CHCl_3$). Anal. calcd. for $C_{16}H_{24}O_3S$: C 64.83; H 8.16. Found: C 64.80; H 8.21.

[3*S*,6*R*,7*R*]-3,7-Dimethyl-6-hydroxy-8-phenylsulfonyloctene 48.

To a solution of **46** (19 mg, 0.064 mmol), triphenylphosphine (51 mg, 0.19 mmol) and benzoic acid (24 mg, 0.19 mmol) in tetrahydrofuran (1 ml) was added diethyl azodicarboxylate (22 mg, 0.13 mmol) at 0 °C. After being stirred for 1 h, the mixture was quenched with aqueous sodium hydrogen carbonate. The aqueous phase was extracted with ether, and the combined organic layer was washed with brine and dried. Concentration under reduced pressure and purification by silica gel preparative thin layer chromatography (hexane/ether, 1 : 1) afforded the benzoate **47** (22 mg, 85%). The benzoate was dissolved in methanol (1 ml) and then sodium methoxide (ca. 28%, 0.016 ml, 0.065 mmol) was added. After being stirred for 13 h, the mixture was neutralized with DOWEX 50W-X4 and then filtered. Evaporation of the filtrate under reduced pressure gave the residue which was purified by preparative silica gel thin layer chromatography (hexane/ether, 1 : 2) to afford **48** (19 mg, 99%). IR (KBr) ν_{max} 3518, 2972, 1560, 1507, 1448, 1305, 1147, 1086. ^{1}HNMR ($CDCl_3$, 270 MHz), δ 0.97 (3H, d, J = 6.5 Hz, C*H*$_3$-3), 1.13 (3H, d, J = 7 Hz, C*H*$_3$-7), 1.2 - 1.5 (4H, m), 1.82 (1H, br, O*H*), 2.10 (1H, m), 2.94 (1H, dd, J = 14, 8.5 Hz, H-8), 3.39 (1H, m, H-6), 3.41 (1H, dd, J = 14, 3 Hz, H-8), 4.92 (1H, ddd J = 10, 2, 1 Hz, H-1, cis), 4.93 (1H, ddd, J = 17, 2, 1 Hz, H-1, trans), 5.64 (1H, ddd, J = 17, 10, 7.5 Hz, H-2), 7.60 (3H, m, Ar), 7.90 (2H, m, Ar). ^{13}CNMR ($CDCl_3$, 67.5 MHz), δ 17.34, 20.45, 31.97, 32.17, 34.60, 37.71, 58.61, 74.97, 113.13, 127.81, 129.28, 133.59, 140.02, 144.10. $[\alpha]_D^{25}$ -2.0° (*c* 0.82, $CHCl_3$). Anal. calcd. for $C_{16}H_{24}O_3S$: C 64.83; H 8.16. Found: C 64.65; H 8.23.

[3*S*,6*S*,7*R*,13*S*,14*R*,15*S*]-6,14-Di(1,1-dimethylethyl)dimethylsiloxy-3,7,13,15-tetramethylhexadeca-1,8-dien-10-one 51.

To a solution of **4** (551 mg, 1.34 mmol) in THF (10 ml) cooled to -78 °C under argon atmosphere was added *n*-butyllithium (1.64 M in hexane, 0.82 ml, 1.34 mmol). After being stirred at -78 °C for 30 min, boron trifluoride etherate (0.08 ml, 0.67 mmol) was added and the stirring was continued for 30 min. Sub-segment C-1 **3** (318 mg, 0.74 mmol) was added to the reaction mixture, and the temperature was kept at -78 °C for 2 h. Aqueous ammonium chloride was added and the aqueous layer was extracted with ether. The organic phase was dried and then concentrated. Purification of the residue by silica gel chromatography (hexane/ether, 3 : 1 and then 1 : 1) afforded **49** (523 mg, 84%) as a mixture of four diastereoisomers.

To a suspension of **49** (261 mg, 0.31 mmol) and powdered molecular sieve 4Å (270 mg) in dichloromethane (5 ml) was added pyridium chlorochromate (174 mg, 0.81 mmol) at room temperature. The reaction mixture was stirred for 40 h and then filtered through silica gel. Concentration of the filtrate gave crude oil which was purified by silica gel chromatography to afford **50** (231 mg, 89%) as a mixture of two diastereoisomers.

To a solution of **50** (245 mg, 0.29 mmol) in dichloromethane (10 ml) was added 1,8-diazabicyclo-[5,4,0]-7-undecene (DBU, 45 mg, 0.29 mmol) at 0 °C. After being stirred at 0 °C for 12 h, the reaction mixture was diluted with ether. The organic phase was washed with 1N HCl, aqueous sodium hydrogen carbonate and brine, and then concentrated with benzene under reduced pressure to give **51** (184 mg, 90%). IR (KBr) ν_{max} 3548, 1671, 1508, 1472, 1307, 1257, 1151, 1087, 1034 cm^{-1}. ^{1}HNMR ($CDCl_3$, 270 MHz), δ -0.01 (3H, s, MeSi), 0.01 (3H, s, MeSi), 0.03 (3H, s, MeSi), 0.04 (3H, s, MeSi), 0.79 (3H, d, *J* = 7 Hz, C*H*$_3$-13), 0.87 (9H, s, *t*-Bu), 0.89 (9H, s, *t*-Bu), 0.97 (3H, d, *J* = 7 Hz), 1.05 (3H, d, *J* = 7 Hz), 1.06 (3H, d, *J* = 7 Hz), 1.2 - 1.6 (7H, m), 1.66 (1H, m), 2.04 (1H, m, H-15), 2.25 (1H, m, H-3), 2.34 (1H, m), 2.49 (2H, m, H-11), 2.90 (1H, dd, *J* = 14, 9 Hz, H-16), 3.37 (1H, dd, *J* = 14, 4 Hz, H-16), 3.59 (2H, m, H-6, H-14), 4.91 (1H, ddd, *J* = 10.5, 2, 1 Hz, H-1, cis), 4.95 (1H, ddd, *J* = 17.5, 2, 1 Hz, H-1, trans), 5.64 (1H, ddd, *J* = 17.5, 10.5, 7.5 Hz, H-2), 6.05 (1H, dd, *J* = 16, 1 Hz, H-9, trans), 6.81 (1H, dd, *J* = 16, 8 Hz, H-8, trans), 7.59 (3H, m, Ar), 7.90 (2H, m, Ar). ^{13}CNMR ($CDCl_3$, 67.5 MHz), δ -4.6, -4.2, -4.15, -4.12, 15.1, 15.7, 15.8, 18.0, 18.2, 20.2, 25.8, 26.0, 29.1, 31.9, 32.0, 33.3, 35.3, 37.67, 37.74, 41.8, 59.7, 75.4, 112.7, 127.8, 129.2, 130.1, 133.5, 140.1, 144.3, 149.4, 200.2. $[\alpha]_D^{17}$ +9.7° (*c* 3.21, $CHCl_3$).

[3*S*,6*S*,7*R*,13*S*,14*R*,15*S*]-6,14-Di(1,1-dimethylethyl)dimethylsiloxy-3,7,13,15-tetramethylhexadecan-10-one 52.

To a solution of **51** (184 mg, 0.27 mmol) in benzene (2 ml) was added a solution of (triphenylphosphine)copper hydride hexamer (226 mg, 0.10 mmol) in benzene (3 ml) under argon atmosphere at room temperature. After being stirred for 40 h, the reaction mixture was diluted with water and then extracted with ether. The organic phase was washed with brine, concentrated and purified by silica gel flash chromatography (hexane/CH_2Cl_2, 10 : 1 and then 1 : 1) to afford **52** (168 mg, 91%) as colorless oil. IR (KBr) ν_{max} 3559, 2859, 1717, 1636, 1560, 1541, 1508, 1473, 1253 cm^{-1}. ^{1}HNMR ($CDCl_3$, 270 MHz), δ 0.01 (3H, s, MeSi), 0.02 (3H, s, MeSi), 0.03 (3H, s), 0.04 (3H, s), 0.78 (3H, d, *J* = 7 Hz, C*H*$_3$-13), 0.84 (3H, d, *J* =7 Hz, C*H*$_3$-7), 0.87 (9H, s, *t*-Bu), 0.88 (9H, s, *t*-Bu), 0.98 (3H, d, *J* =7 Hz, C*H*$_3$-3), 1.05 (3H, d, *J* = 7 Hz, C*H*$_3$-15), 1.2 - 1.8 (12H, m), 2.05 (1H, m, H-15), 2.3 - 2.6 (3H, m), 2.89 (1H, dd, *J* = 14, 8.5 H, H-16), 3.36 (1H, dd, *J* = 14, 4 Hz, H-16), 3.47 (1H, m, H-6), 3.59 (1H, t, *J* = 4 Hz, H-14), 4.90 (1H, d, *J* = 10 Hz, H-1, cis), 4.94 (1H, dt, *J* = 17, 1.5 Hz, H-1, trans), 5.68 (1H, ddd, *J* = 17, 10, 7.5 Hz, H-2), 7.58 (3H, m, Ar), 7.88 (2H, m, Ar). ^{13}CNMR ($CDCl_3$, 67.5 MHz), δ -4.5, -4.4, -4.2, -4.1, 14.6, 15.0, 15.7, 18.0, 18.2, 20.1, 25.85, 25.93, 26.2, 28.7, 30.0, 32.5, 33.2, 35.3, 37.7, 37.8, 40.4, 41.0, 59.7, 76.0, 112.4, 127.8, 129.2, 133.5, 140.1, 144.6, 210.8. $[\alpha]_D^{20}$ +3.8° (*c* 4.74, $CHCl_3$).

[2*S*,2(3*S*),3*R*,6*R*,8*R*,8(*S*),9*S*]-3,9-Dimethyl-2-[3-(3-methyl-4-pentenyl)]-8-[1-methyl-2-(phenylsulfonyl)ethyl]-1,7-dioxaspiro[5,5]undecane 53.

A solution of **52** (98 mg, 0.14 mmol) and tetrabutylammonium fluoride (1.0 M in THF, 0.15 ml, 0.15 mmol) in THF (4 ml) was heated at 65 °C for 5.5 h. The reaction mixture was filtered through silica gel and then concentrated. The resulting crude diol (81.6 mg) was dissolved in dichloromethane (4 ml), and then *p*-toluenesulfonic acid monohydrate (2 mg, 0.011 mol) was added. The reaction mixture was stirred at room temperature for 24 h. After addition of aqueous sodium hydrogen carbonate, the aqueous layer was extracted with ether. The organic phase was dried and then concentrated. The residue was purified by preparative silica gel thin layer chromatography (hexane/ether, 3 : 2) to yield **53** (45 mg, 70%). IR (KBr) ν_{max} 2929, 1448, 1307, 1448, 990 cm^{-1}. ^{1}HNMR ($CDCl_3$, 270 MHz), δ 0.68 (3H, d, *J* = 7 Hz, C*H*$_3$-13), 0.78 (3H, d, *J* =6.5 Hz, C*H*$_3$-7), 0.99 (3H, d, *J* = 7 Hz, C*H*$_3$-3), 1.22 (3H, d, *J* = 7 Hz, C*H*$_3$-15), 1.25 - 1.7 (12H, m), 1.9 - 2.2 (4H, m), 2.83 (1H, dd, *J* = 14, 10 Hz, H-16), 3.03 (1H, td, *J* = 9.5, 2 Hz, H-6), 3.20 (1H, dd, *J* = 14, 2 Hz, H-16), 3.32 (1H, dd, *J* = 10, 2 Hz, H-14), 4.91 (1H, ddd, *J* = 10, 2, 1 Hz, H-1, cis), 4.95 (1H, ddd, *J* = 17, 2, 1 Hz, H-1, trans), 5.70 (1H, ddd, *J* = 17, 10, 7.5 Hz, H-2), 7.79 (3H, m, Ar), 7.90 (2H, m, Ar). ^{13}CNMR ($CDCl_3$, 67.5 MHz), δ 10.7, 17.0, 18.0, 20.1, 26.6, 27.5, 28.0, 29.9, 30.7, 31.3, 32.6, 34.8, 35.8, 37.8, 58.8, 73.1, 74.8, 95.8, 112.4, 128.0, 129.3, 133.6, 139.7, 144.8. $[\alpha]_D^{20}$ +21.1° (*c* 1.13, $CHCl_3$). Anal. calcd. for $C_{26}H_{40}O_3S$: C 69.60; H 8.99. Found: C 69.39; H 9.15.

Synthesis of Segment C (2).

A suspension of palladium (II) chloride (1.6 mg, 0.0089 mmol) and copper (I) chloride (8.8 mg, 0.089 mmol) in a mixture of DMF and water (0.13 ml : 0.02 ml) was stirred vigorously under oxygen atmosphere at room temperature for 2 h, and then **53** (21 mg, 0.047 mmol) was added. After being stirred for 40 h, the reaction mixture was diluted with ether and then washed with 1N HCl and aqueous sodium hydrogen carbonate. The organic phase was concentrated under reduced pressure and then purified by preparative silica gel thin layer chromatography (hexane/ether, 1 : 1) to afford **2** (19 mg, 85%). IR (KBr) ν_{max} 2931, 1710, 1449, 1306, 1150, 1086, 990 cm^{-1}. ^{1}HNMR ($CDCl_3$, 270 MHz), δ 0.71 (3H, d, *J* = 7 Hz, C*H*$_3$-13), 0.77 (3H, d, *J* =6.5 Hz, C*H*$_3$-7), 1.09 (3H, d, *J* =7 Hz, C*H*$_3$-3), 1.21 (3H, d, *J* = 7 Hz, C*H*$_3$-15), 1.25 - 1.6 (12H, m), 1.71 (1H, m), 1.97 (1H, m), 2.10 (1H, m), 2.13 (3H, s, H-1), 2.50 (1H, m, H-3), 2.86 (1H, dd, *J* = 14, 10 Hz, H-16), 3.06 (1H, td, *J* = 9.5, 2 Hz, H-6), 3.20 (1H, dd, *J* = 14, 2 Hz, H-16), 3.34 (1H, dd, *J* = 9.5, 2 Hz, H-14), 7.60 (3H, m, Ar), 7.93 (2H, m, Ar). ^{13}CNMR ($CDCl_3$, 67.5 MHz), δ 10.7, 16.1, 17.1, 17.9, 26.7, 27.6, 27.9, 27.9, 28.8, 29.9, 30.5, 31.4, 34.6, 35.8, 47.3, 58.8, 73.2, 74.4, 95.9, 128.0, 129.3, 133.6, 140.0, 212.7. $[\alpha]_D^{20}$ -12.2° (*c* 1.11, $CHCl_3$).

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