Toward a synthesis of fawcettimine-type *Lycopodium* alkaloids: stereocontrolled synthesis of a functionalized azaspirocycle precursor

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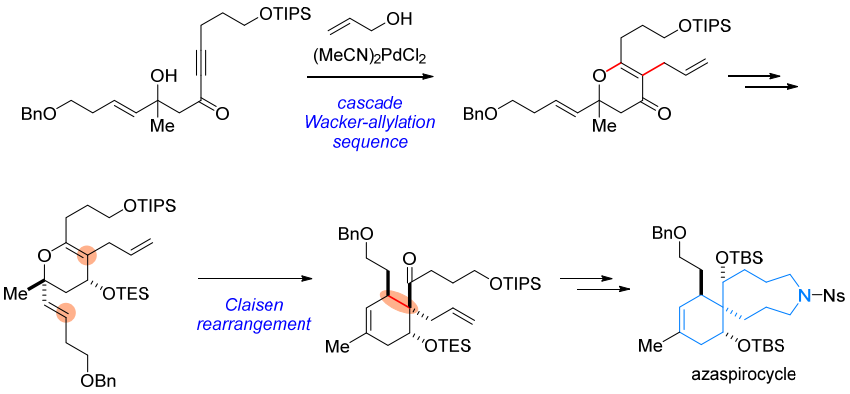
Abstract The stereocontrolled synthesis of a new azaspirocycle precursor of the fawcettimine-type *Lycopodium* alkaloids is described. Our approach provides an efficient entry to the azaspirocycle via a cascade Wacker-allylation sequence followed by a highly stereoselective Claisen rearrangement. This azaspirocycle, bearing all the requisite functionality with pivotal stereogenic centers, is considered to be a versatile precursor useful for the fawcettimine-type *Lycopodium* alkaloids.



INTRODUCTION

Nearly 300 alkaloids have been isolated from the *Lycopodium* species, and they display great structural diversity and a wide range of biological activities.[1] *Lycopodium* alkaloids have been categorized into four structural classes: the lycopadine class, the lycodine class, the fawcettimine class, and the miscellaneous class. Fawcettimine-type *Lycopodium* alkaloids have attracted a great deal of attention in both synthetic and medicinal communities due to their intriguing architectures and important biological activities, such as acetylcholinesterase inhibition and neural cell protection (Figure 1); and a wide variety of approaches towards their synthesis have been developed.[2] Due to the plethora of target alkaloids and the desire to also synthesize novel derivatives for biological testing, a general strategy proceeding through a common intermediate would be most efficient. Herein, we report the stereocontrolled synthesis of a new azaspirocycle precursor of the fawcettimine-type *Lycopodium* alkaloids, which bears all the requisite functionality and core stereogenic centers in their desired configurations, as well as a carbon-carbon double bond between C8 and C15 for introduction of the stereogenic center at C15,[2b,2g] and oxygen functionality at C8 or C15[2j]. Construction of the azaspirocyclic skeleton was achieved using an efficient cascade Wacker-allylation sequence[3] and a highly stereoselective Claisen rearrangement of a functionalized alkenyl dihydropyran system, previously developed in this group, as key reactions.[4,5] Azaspirocycle **1** is expected to be a versatile common precursor for the fawcettimine-type *Lycopodium* alkaloids.[6]

SYNTHETIC PLAN

Our plan for the synthesis of azaspirocycle **1** is depicted in Scheme 1.

Azacyclononane of **1** would be constructed from cyclohexene **2** through the intramolecular Mitsunobu reaction.[7] Based on previous results,[4a,5] the *cis*-configured stereogenic centers of **2** would be established by a Claisen rearrangement of **3** through a boat-like transition state (*vide infra*). As the Claisen rearrangement of alkenyl dihydropyrans is sensitive to an environment of the allylic substituent (a triethylsiloxy group in this case),[8] one of C13-epimers of the Claisen precursors [(*S*)-epimer, *epi*-**3b**, as shown in Scheme 3] is expected to undergo the Claisen rearrangement only very slowly. Claisen precursor **3** could be transformed from alkenyl dihydropyrone **4**, which would be synthesized from hydroxy ynone **5b** and allyl alcohol through the palladium-catalyzed cascade Wacker-allylation sequence. There is good precedent for the formation of dihydropyrones from the corresponding secondary alcohols in this way,[3] but the sterically congested, tertiary hydroxy group of **5b** might retard the first Wacker-type C-O bond formation. Ynone **5b** could be synthesized from diol **6**, prepared from easily available alkyne **7** and iodoalkene **8**.[9]

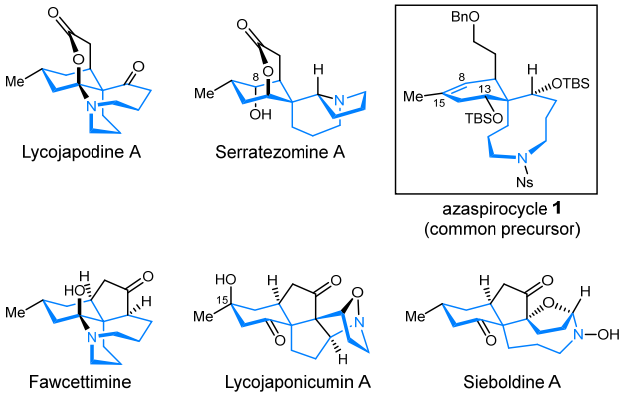
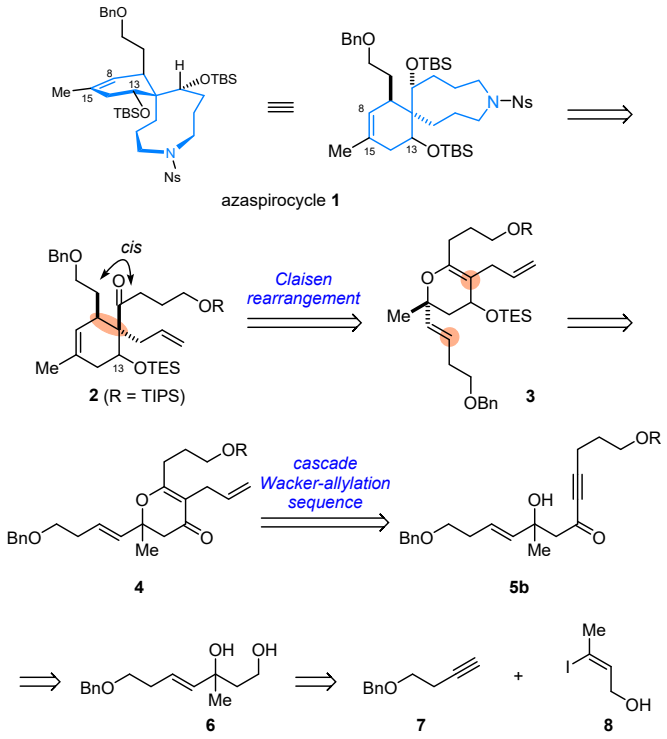


Figure 1. Structures of fawcettimine-type *Lycopodium* alkaloids and azaspirocycle as their versatile precursor.

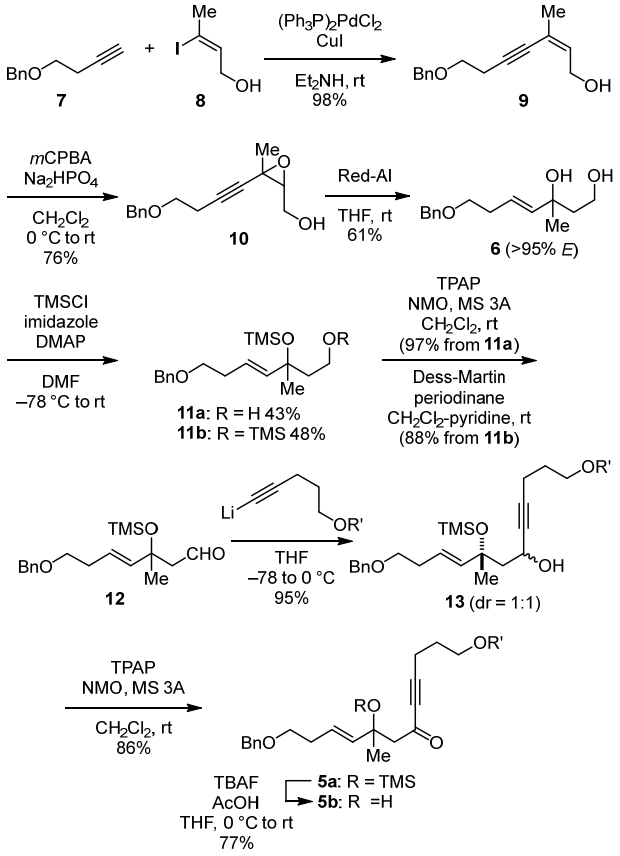


Scheme 1. Synthetic plan for racemic azaspirocycle **1**

RESULTS AND DISCUSSION

The synthesis of hydroxy ynone **5b**, a precursor of the cascade Wacker-allylation sequence, commenced with the Sonogashira coupling of alkyne **7** and iodoalkene **8** (Scheme 2). Enyne **9** was then treated with *m*CPBA under buffered conditions to give epoxide **10** in 76% yield, which was treated with 2.6 equiv of Red-Al to afford allylic diol **6** in 61% yield as a single *E*-isomer. Silylation of diol **6** with TMSCl and imidazole in the presence of DMAP furnished bis-silyl ether **11b** and partially deprotected mono-silyl ether **11a** in 48% and 43% yields, respectively. Bis-silyl ether **11b** was oxidized to the desired aldehyde **12** in 88% yield using Dess-Martin periodinane[10] in the presence of pyridine. Mono-silyl ether **11a** was also oxidized to **12**, under the Ley oxidation conditions.[11] Nucleophilic addition of an acetylide

generated from 5-(triisopropylsiloxy)pent-1-yne to aldehyde **12** gave propargyl alcohol **13** as a 1:1 mixture of epimers. Ley oxidation of alcohol **13** and subsequent desilylation using acetic acid-buffered TBAF afforded the desired hydroxy ynone **5b** in good overall yield.

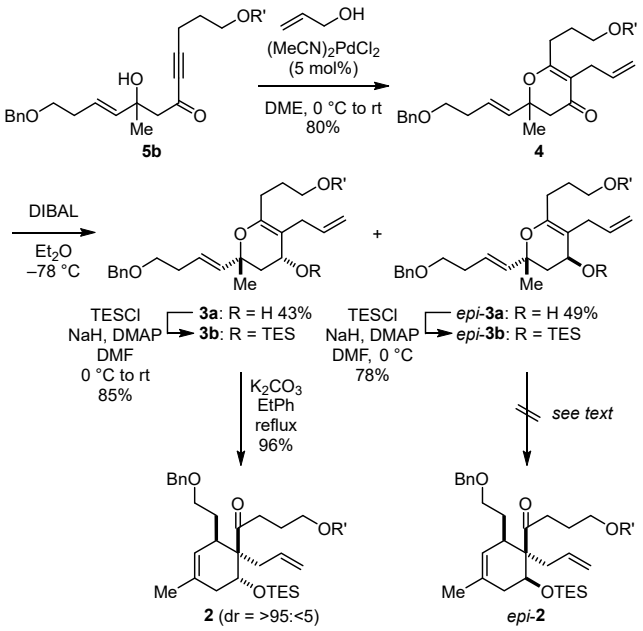


Scheme 2. Synthesis of hydroxy ynone **5b**. R' = TIPS

With hydroxy ynone **5b** in hand, we then addressed the synthesis of alkenyl dihydropyrone by the cascade Wacker-allylation sequence of **5b** with allyl alcohol, which proceeded smoothly even at room temperature in the presence of 5 mol% of $(MeCN)_2PdCl_2$ to provide dihydropyrone **4** in 80% yield (Scheme 3),[3,12] despite the congested nature of the nucleophile tertiary hydroxy group of **5b**. Reduction of **4** with DIBAL in Et_2O afforded a ca. 1:1 mixture of epimers.[13] Both separated alcohols **3a**

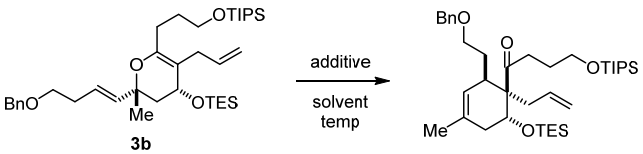
and *epi*-**3a** were protected as TES ethers to provide Claisen precursors **3b** and *epi*-**3b**, respectively. The relative stereochemistry of **3b** was determined by NOESY correlation (Figure 2).

Our attention now turned to the Claisen rearrangement of dihydropyran **3b** which we first attempted in triglyme, a solvent reported to remarkably enhance the rate of the Claisen rearrangement of dihydropyrans (Table 1).[14] Heating **3b** at 242 °C in triglyme afforded the desired Claisen product **2** in 44% yield as a single diastereomer (entry 1); the relative stereochemistry of **2** was determined by NOESY analysis, as shown in Figure 2. This stereochemical outcome indicates that the Claisen rearrangement of **3b** proceeds through a boat-like transition state, as expected (Scheme 4). It was found that the Claisen rearrangement of **3b** did not require such a high temperature; it smoothly proceeded at 153 °C in toluene to furnish Claisen product **2** in 98% yield (entry 2). After optimization of the reaction conditions, a 96% yield of **2** was obtained by refluxing it in ethylbenzene (bp = 136 °C) with K_2CO_3 (entry 7). In contrast, heating precursor *epi*-**3b** in toluene at 146, 179 or 242 °C, afforded complicated mixtures of unidentified products; no desired product *epi*-**2** could be detected. This observation could be attributed to its instability by elimination of the triethylsiloxy group under the harsh conditions.



Scheme 3. Cascade Wacker-allylation and Claisen rearrangement. R' = TIPS

Table 1. Claisen rearrangement of **3b**



entry	solvent	additive	temp	yield (%)
1[a]	triglyme	-	242 °C	44
2[a]	toluene	-	153 °C	98
3[a]	toluene	K_2CO_3	130 °C	94
4	toluene	K_2CO_3	reflux	91
5	EtPh	-	reflux	94
6	EtPh	K_2CO_3	reflux	100
7[b]	EtPh	K_2CO_3	reflux	96

[a]Reaction was performed in a sealed tube. [b]Using 2.27 mmol of **3b**.

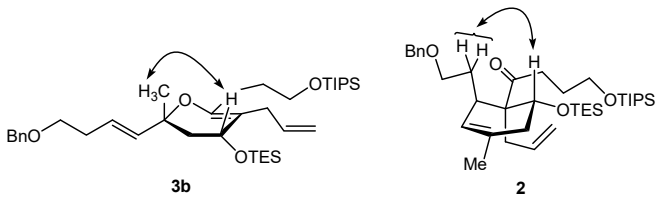
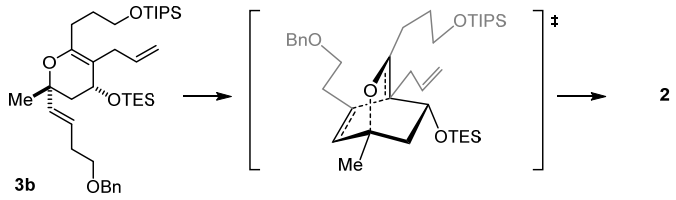


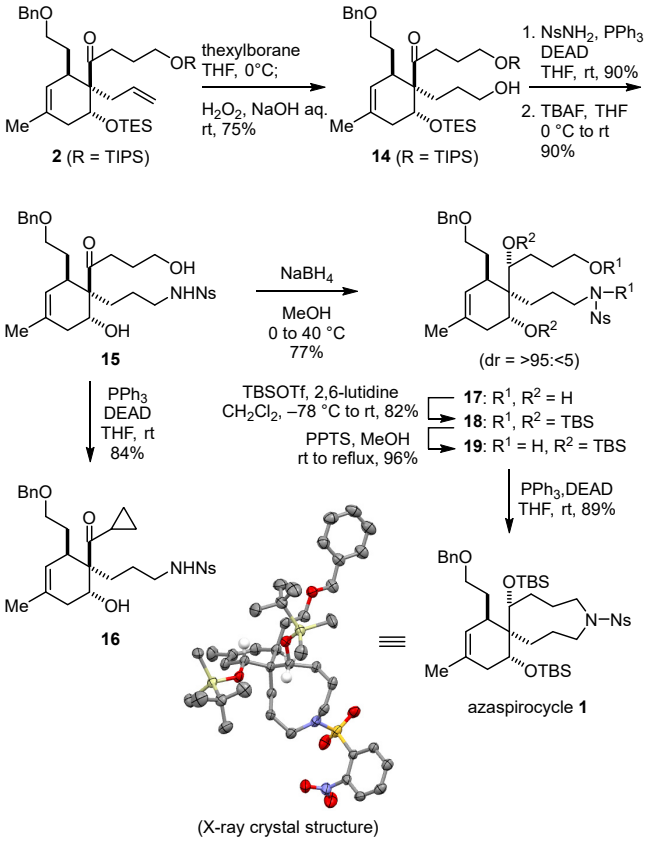
Figure 2. Diagnostic NOESY correlations for **3b** and **2**



Scheme 4. A possible boat-like transition state of the Claisen rearrangement of **3b**

Construction of azaspirocycle **1** from obtained cyclohexene **2** is depicted in Scheme 5. Site-selective hydroboration of the vinyl group in **2** with thexylborane gave the corresponding primary alcohol **14** in 75% yield. The resulting alcohol **14** was then converted into nosyl amide **15** under Mitsunobu conditions and following desilylation. The second Mitsunobu reaction was then attempted to construct azacyclononane framework. Interestingly, however, cyclopropyl ketone **16** was obtained in 84% yield instead – the first example of the formation of a cyclopropyl ketone from a 3-hydroxypropyl ketone under conventional Mitsunobu conditions, to the best of our knowledge.[15] Unfortunately, **16** could not be converted into an azacyclononane through intramolecular nucleophilic substitution of the nosyl amide in the presence of either KO*t*-Bu, TFA, or a Lewis acid such as $ZrCl_4$, $Sc(OTf)_3$, $AlCl_3$ or $BF_3{\cdot}OEt_2$.[16] Therefore, the carbonyl group of **15** was first reduced using $NaBH_4$ to give alcohol **17** as a single diastereomer, which was then transformed into bis-silyl ether **19** in good

overall yield by silylation of the three hydroxy groups and amide nitrogen, followed by hydrolysis under acidic conditions. 9-Membered ring cyclization of **19** was finally achieved under the conventional Mitsunobu conditions[7] to give azaspirocycle **1** in excellent yield. The structure of **1** was unambiguously established by single-crystal X-ray diffraction analysis.[17]



Scheme 5. Synthesis of azaspirocycle **1**

CONCLUSION

The stereocontrolled synthesis of a new azaspirocycle precursor of the fawcettimine-type *Lycopodium* alkaloids has been accomplished. The key steps in this sequence, the cascade Wacker-allylation sequence and Claisen rearrangement, effectively enabled construction of the azaspirocyclic core scaffold, bearing all the

requisite functionality and core stereogenic centers in the desired configurations. This azaspirocycle is considered to be a new and versatile precursor useful for the synthesis of the fawcettimine-type *Lycopodium* alkaloids, due to the flexibility of installation of oxy-functionality at the C8 or C15 requisite for the synthesis of the *Lycopodium* alkaloids,[6] including lycojaponicumin A and serratezomine A. Additionally, the unexpected formation of cyclopropyl ketone **16** expands the scope of the Mitsunobu reaction, and is anticipated to be broadly applicable in chemical synthesis due to the high yield of cyclopropane product obtained and the mild nature of the conditions used.

EXPERIMENTAL SECTION

General Techniques. Infrared spectra (IR) were recorded on a JASCO FT/IR-4100 type A spectrophotometer and reported in wave number (cm^{-1}). Proton nuclear magnetic resonance (^1H NMR) spectra were recorded on a Varian Gemini-2000 (300 MHz), a Bruker ARX-400 (400 MHz), or a Bruker AVANCE-400 (400 MHz) spectrometer. Chemical shifts of all compounds were reported in ppm relative to the residual undeuterated solvent (chloroform-*d* as δ = 7.26, CD_3OD as δ = 3.31). ^1H NMR data were reported as follows: chemical shifts, integration, multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet br = broadened), coupling constant(s), and assignment. Carbon nuclear magnetic resonance (^{13}C NMR) spectra were recorded on a Varian Gemini-2000 (75 MHz), a Bruker ARX-400 (100 MHz), or a Bruker AVANCE-400 (100 MHz) spectrometer. Chemical shifts of all compounds are reported in ppm relative to the solvent ($CDCl_3$ as δ = 77.0 and CD_3OD as δ = 49.0). Melting point (Mp) was recorded on a Yanaco MP-S3 melting point apparatus and are not corrected. All NMR were measured at 300 K. High resolution mass spectra

(HR-MS) were recorded on an Applied Biosystems Mariner ESI-TOF spectrometer and are reported in *m/z*.

All reactions were monitored by thin layer chromatography (TLC) on 0.25 mm silica gel coated glass plates $60F_{254}$ (Merck, #1.05715.0001). Visualization was achieved by using UV light (254 nm) and appropriate reagent (ethanolic phosphomolybdic acid, *p*-anisaldehyde solution in H_2SO_4/AcOH/EtOH, ninhydrin solution in *n*-BuOH/H_2O/AcOH, cerium(IV) sulfate tetrahydrate and $(NH_4)_6Mo_7O_{24}{\cdot}4H_2O$ solution in H_2O/H_2SO_4, or $KMnO_4$ solution in 1 M NaOH aq.), followed by heating. Silica gel 60 (particle size 0.0063-0.021 mm, Kanto, #37565-84) was used for open-column chromatography. Silica gel 60N (spherical, neutral, particle size 0.04-0.05mm, Kanto, #37563-79) was used for flash-column chromatography. Preparative TLC separations were carried out on 0.5 mm silica gel plates $60F_{254}$ (Merck, #1.05744.0009). Dehydrated THF, Et_2O and CH_2Cl_2 were purchased from Kanto Chemical co., Inc. TMSCl, DMF, ethylbenzene, and DME were distilled from CaH_2. All other commercially available reagents were used as received.

*Enyne **9***. This compound was synthesized according to the modified procedure of Marshall *et al*[9] To a solution of iodide **8** (4.43 g, 24.1 mmol) in diethylamine (95 mL) were added $(Ph_3P)_2PdCl_2$ (511 mg, 1.01 mmol) and CuI (461 mg, 2.42 mmol) at room temperature under argon atmosphere. To the reaction mixture was added a solution of alkyne **7** (6.96 g, 43.5 mmol) in diethylamine (5 mL). The resulting mixture was degassed by three freeze-thaw cycles, and the flask was filled with argon. After being stirred at room temperature for 7.5 h, the reaction was quenched with H_2O at 0 °C. The aqueous layer was extracted with Et_2O. The organic layer was washed with brine, dried over anhydrous $MgSO_4$, and concentrated. The residue was purified by silica gel

column chromatography (hexane/EtOAc = 5:1) to give enyne **9** (5.44 g, 98%, >95% *Z* determined by ^{1}H NMR analysis) as a colorless oil. Peak assignment was performed by NMR spectroscopy (^{1}H, ^{13}C, COSY, HMQC, and HMBC). IR (KBr) ν_{max} (cm^{-1}) 3389, 2865, 2216, 1454, 1363, 1100, 1001; ^{1}H NMR ($CDCl_3$, 400 MHz) δ (ppm) 7.38-7.23 (5H, m, Ar), 5.80 (1H, br t, J = 6.5 Hz, -C*H*=C), 4.55 (2H, s, PhC*H*$_2$O-), 4.26 (2H, d, J = 6.5 Hz, C*H*$_2$OH), 3.60 (2H, t, J = 7 Hz, -OC*H*$_2$CH$_2$-), 2.65 (2H, t, J = 7 Hz, -OCH$_2$C*H*$_2$-), 1.85 (3H, br s, -C*H*$_3$); ^{13}C NMR ($CDCl_3$, 100 MHz) δ (ppm) 137.9, 134.8, 128.3, 127.62, 127.61, 120.9, 91.9, 79.7, 72.9, 68.3, 61.1, 23.3, 20.8; HR-MS (ESI, positive): calcd for $C_{15}H_{18}O_2Na$ (M+Na), 253.1199; found, 253.1192.

*Epoxide **10***. To a suspension of enyne **9** (863 mg, 3.75 mmol) and Na_2HPO_4 (1.33 g, 9.36 mmol) in CH_2Cl_2 (25 mL) was added *m*CPBA (1.04 g, 6.03 mmol) at 0 °C under nitrogen atmosphere. After being stirred at 0 °C, the reaction mixture was allowed to warm to room temperature over a period of 2 h 50 min. The reaction was quenched with a saturated aqueous solution of $NaHCO_3$. The aqueous layer was extracted with CH_2Cl_2. The organic layer was washed with brine, dried over anhydrous Na_2SO_4, and concentrated. The residue was purified by silica gel column chromatography (hexane/EtOAc = 3:1) to give epoxide **10** (701 mg, 76%) as a colorless oil. Peak assignment was performed by NMR spectroscopy (^{1}H, ^{13}C, COSY, HMQC, and HMBC). IR (KBr) ν_{max} (cm^{-1}) 3420, 2930, 2867, 2246, 1454, 1102, 1059, 1012; ^{1}H NMR ($CDCl_3$, 400 MHz) δ (ppm) 7.39-7.25 (5H, m, Ar), 4.54 (2H, s, PhC*H*$_2$O-), 3.86 (1H, dd, J = 5, 12.5 Hz, -C*H*$_A$H$_B$OH), 3.81 (1H, dd, J = 6, 12.5 Hz, -CH$_A$*H*$_B$OH), 3.57 (2H, t, J = 7 Hz, -OC*H*$_2$CH$_2$-), 3.06 (1H, dd, J = 5.5, 6 Hz, -OC*H*CH$_2$OH), 2.52 (2H, t, J = 7 Hz, -C*H*$_2$C≡C-), 2.03 (1H, br, O*H*), 1.54 (3H, s, -C*H*$_3$); ^{13}C NMR ($CDCl_3$, 100 MHz) δ (ppm) 137.8, 128.4, 127.8, 127.7, 82.4, 78.3, 73.0, 68.0, 63.8, 62.5, 52.0, 23.5,

20.1; HR-MS (ESI, positive): calcd for $C_{15}H_{18}O_3Na$ (M+Na), 269.1148; found, 269.1145.

Diol ***6***. To a solution of Red-Al (3.2 M in toluene, 1.6 mL, 5.1 mmol) was added a solution of epoxide **10** (489 mg, 1.99 mmol) in THF (20 mL) at room temperature over 10 min under nitrogen atmosphere. After being stirred at room temperature for 15 min, the reaction was quenched with a saturated aqueous solution of Rochelle salt at 0 °C. The resulting mixture was allowed to warm to room temperature over a period of 1 h. The aqueous layer was extracted with EtOAc. The organic layer was washed with brine, dried over anhydrous Na_2SO_4, and concentrated. The residue was purified by silica gel column chromatography (hexane/EtOAc = 1:1) to give diol **6** (302 mg, 61%, >95% *E* determined by ^{1}H NMR analysis) as a colorless oil. Peak assignment was performed by NMR spectroscopy (^{1}H, ^{13}C, COSY, HMQC, and HMBC). IR (KBr) ν_{max} (cm^{-1}) 3376, 2927, 1454, 1364, 1099, 1028; ^{1}H NMR ($CDCl_3$, 400 MHz) δ (ppm) 7.38-7.25 (5H, m, Ar), 5.71 (1H, td, J = 6.5, 15.5 Hz, -OCH_2CH_2CH=CH-), 5.60 (1H, d, J = 15.5 Hz, -OCH_2CH_2CH=C*H*-), 4.51 (2H, s, PhCH_2O-), 3.83-3.71 (2H, m, -CH_2OH), 3.52 (2H, t, J = 6.5 Hz, -OCH_2CH_2CH=C-), 2.95-2.55 (2H, br, CH_3CO*H,* -CH_2O*H*), 2.37 (2H, dt, J = 6.5, 6.5 Hz, -OCH_2CH_2CH=C-), 1.82 (1H, ddd, J = 4.5, 7.5, 15 Hz, -CH_AH$_B$$CH_2$OH), 1.68 (1H, ddd, J = 4.5, 5.5, 15 Hz, -CH$_A$$H_B$$CH_2$OH), 1.30 (3H, s, -C$H_3$); ^{13}C NMR ($CDCl_3$, 100 MHz) δ (ppm) 138.29, 138.25, 128.3, 127.7, 127.6, 124.7, 73.8, 72.8, 69.7, 59.9, 42.6, 32.2, 29.0; HR-MS (ESI, positive): calcd for $C_{15}H_{22}O_3Na$ (M+Na), 273.1461; found, 273.1462.

Silyl ethers ***11a*** *and* ***11b***. To a solution of diol **6** (447 mg, 1.79 mmol) in DMF (6 mL) were added imidazole (374 mg, 5.50 mmol) and DMAP (874 mg, 7.15 mmol) at room temperature under nitrogen atmosphere. The reaction mixture was cooled to

–78 °C, and then to the resulting mixture was added TMSCl (0.80 mL, 9.3 mmol) at that temperature. The reaction mixture was allowed to warm to 0 °C over a period of 3 h. The reaction was quenched with a saturated aqueous solution of NH_4Cl at 0 °C. The reaction mixture was allowed to warm to room temperature over a period of 15 min. The aqueous layer was extracted with Et_2O. The organic layer was dried over anhydrous Na_2SO_4 and concentrated. The residue was purified by silica gel flash-column chromatography (hexane/Et_2O = 20:1 to 3:1) to give mono-silyl ether **11a** (248 mg, 43%) as a colorless oil and bis-silyl ether **11b** (335 mg, 48%) as a colorless oil. Peak assignments were performed by NMR spectroscopy (^1H, ^{13}C, COSY, HMQC, and HMBC). Mono-silyl ether **11a**: IR (KBr) ν_{max} (cm^{-1}) 3704, 3031, 2955, 2857, 1736, 1497, 1455, 1250; ^1H NMR ($CDCl_3$, 400 MHz) δ (ppm) 7.39-7.24 (5H, m, Ar), 5.68-5.56 (2H, m, -CH_2C*H*=C*H*-), 4.52 (2H, s, PhCH_2O-), 3.82-3.70 (2H, m, HOCH_2CH_2-), 3.52 (2H, t, J = 6.5 Hz, -OCH_2CH_2CH=C-), 3.20 (1H, t, J = 5.5 Hz, -CH_2O*H*), 2.43-2.30 (2H, m, -OCH_2CH_2CH=C-), 1.82-1.65 (2H, m, HOCH_2CH_2-), 1.34 (3H, s, -C*H*$_3$), 0.12 (9H, s, *Me*$_3$SiOC-); ^{13}C NMR ($CDCl_3$, 100 MHz) δ (ppm) 138.4, 138.3, 128.4, 127.7, 127.6, 125.1, 77.1, 72.9, 69.7, 59.9, 44.8, 32.8, 27.8, 2.4; HR-MS (ESI, positive): calcd for $C_{18}H_{30}O_3SiNa$ (M+Na), 345.1856; found, 345.1858. Bis-silyl ether **11b**: IR (KBr) ν_{max} (cm^{-1}) 2956, 2858, 1251, 1090; ^1H NMR ($CDCl_3$, 400 MHz) δ (ppm) 7.40-7.25 (5H, m, Ar), 5.61-5.56 (2H, m, -CH_2C*H*=C*H*-), 4.54 (2H, s, PhCH_2O-), 3.74-3.61 (2H, m, $Me_3SiOCH_2CH_2$-), 3.52 (2H, t, J = 7 Hz, -OCH_2CH_2CH=C-), 2.44-2.30 (2H, m, -OCH_2CH_2CH=C-), 1.86-1.74 (2H, m, $Me_3SiOCH_2CH_2$-), 1.33 (3H, s, -C*H*$_3$), 0.13 (9H, s, *Me*$_3$SiO-), 0.12 (9H, s, *Me*$_3$SiO-); ^{13}C NMR ($CDCl_3$, 100 MHz) δ (ppm) 139.1, 138.4, 128.3, 127.6, 127.5, 123.9, 74.4, 72.8, 69.9, 59.1, 46.2, 32.7, 28.1, 2.5, -0.5; HR-MS (ESI, positive): calcd for

$C_{21}H_{38}O_3Si_2Na$ (M+Na), 417.2252; found, 417.2257.

*Aldehyde **12***. To a solution of mono-silyl ether **11a** (361 mg, 1.12 mmol) in CH_2Cl_2 (15 mL) were added MS 3A (759 mg), NMO (255 mg, 2.18 mmol) and TPAP (50.1 mg, 0.143 mmol) at room temperature under nitrogen atmosphere. After being stirred at room temperature for 10 min, the reaction mixture was filtered through a short pad of silica gel eluting with EtOAc and concentrated. The residue was purified by silica gel column chromatography (hexane/Et_2O = 9:1) to give aldehyde **12** (350 mg, 97%) as a colorless oil. Peak assignment was performed by NMR spectroscopy (^1H, ^{13}C, COSY, HMQC, and HMBC). IR (KBr) ν_{max} (cm^{-1}) 2957, 2855, 1722, 1251, 1103, 1042; ^1H NMR ($CDCl_3$, 400 MHz) δ (ppm) 9.75 (1H, t, J = 3 Hz, -C*H*O), 7.39-7.25 (5H, m, Ar), 5.70-5.64 (2H, m, -CH_2C*H*=C*H*-), 4.51 (2H, s, PhC*H*$_2$O-), 3.52 (2H, t, J = 6.5 Hz, -OC*H*$_2$$CH_2$CH=C-), 2.50 (1H, dd, J = 3, 15 Hz, OHCC*H*$_A$$H_B$-), 2.45 (1H, dd, J = 3, 15 Hz, OHCCH_A*H*$_B$-), 2.42-2.33 (2H, m, -OCH_2C*H*$_2$CH=C-), 1.43 (3H, s, -C*H*$_3$), 0.12 (9H, s, *Me*$_3$SiOC-); ^{13}C NMR ($CDCl_3$, 100 MHz) δ (ppm) 203.2, 138.3, 137.8, 128.3, 127.6, 127.5, 125.7, 74.0, 72.9, 69.6, 55.9, 32.6, 28.4, 2.4; HR-MS (ESI, positive): calcd for $C_{18}H_{28}O_3SiNa$ (M+Na), 343.1700; found, 343.1694.

*Synthesis of aldehyde **12** from bis-silyl ether **11b***. To a solution of bis-silyl ether **11b** (613 mg, 1.56 mmol) in CH_2Cl_2 (15.5 mL) and pyridine (1.25 mL) was added Dess-Martin periodinane (788 mg, 1.86 mmol) at room temperature under nitrogen atmosphere. After being stirred at room temperature for 12 h, the reaction was quenched with a saturated aqueous solution of Na_2SO_3. The aqueous layer was extracted with CH_2Cl_2. The organic layer was dried over anhydrous Na_2SO_4 and concentrated. The residue was purified by silica gel column chromatography (hexane/EtOAc = 9:1) to give aldehyde **12** (439 mg, 88%) as a colorless oil.

*Alcohol **13***. To a solution of 5-[(triisopropylsilyl)oxy]pentyne (471 mg, 1.96 mmol) in THF (6 mL) was added *n*-BuLi (1.6 M in hexane, 1.0 mL, 1.6 mmol) at –78 °C under nitrogen atmosphere. The reaction mixture was stirred at –78 °C for 1 h. To the reaction mixture was added a solution of aldehyde **12** (350 mg, 1.09 mmol) in THF (2.5 mL) at –78 °C. The reaction mixture was allowed to warm to 0 °C over a period of 45 min, the reaction mixture was then cooled to –78 °C. The reaction was quenched with a saturated aqueous solution of NH_4Cl at –78 °C. The reaction mixture was allowed to warm to room temperature over a period of 1 h. The aqueous layer was extracted with Et_2O. The organic layer was washed with brine, dried over anhydrous Na_2SO_4, and concentrated. The residue was purified by silica gel column chromatography (hexane/Et_2O = 9:1) to give alcohol **13** (581 mg, 95%) as a 1:1 mixture of epimers as a colorless oil. Peak assignment was performed by NMR spectroscopy (^1H, ^{13}C, COSY, HMQC, and HMBC). IR (KBr) ν_{max} (cm^{-1}) 3464, 2944, 2894, 2866, 1463, 1251, 1106; ^1H NMR ($CDCl_3$, 400 MHz) δ (ppm) 7.37-7.25 (5H, m, Ar), 5.70-5.50 (2H, m, -CH_2CH=C*H*-), 4.73 (0.5H, dd, *J* = 2, 10 Hz, HOC*H*-), 4.62 (0.5H, dd, *J* = 2, 10 Hz, HOC*H*-), 4.52 (1H, s, PhCH_2O-), 4.51 (1H, s, PhCH_2O-), 4.27 (0.5H, br, -CHO*H*), 4.17 (0.5H, br, -CHO*H*), 3.74 (1H, t, *J* = 6 Hz, TIPSOCH_2-), 3.73 (1H, t, *J* = 6 Hz, TIPSOCH_2-), 3.52 (1H, t, *J* = 7 Hz, -OCH_2CH_2CH=C-), 3.50 (1H, t, *J* = 7 Hz, -OCH_2CH_2CH=C-), 2.43-2.25 (4H, m, TIPSO$CH_2CH_2CH_2$-, -OCH_2CH_2CH=C-), 2.09-1.97 (1H, m, HOCHCH_2-), 1.79-1.66 (3H, m, HOCHCH_2-, TIPSOCH_2CH_2-), 1.41 (1.5H, s, -CH_3), 1.39 (1.5H, s, -CH_3), 1.14-0.98 (21H, m, *TIPS*O), 0.14 (4.5H, s, *Me*$_3$SiOC-), 0.11 (4.5H, s, *Me*$_3$SiOC-); ^{13}C NMR ($CDCl_3$, 100 MHz) δ (ppm) 139.0, 138.4, 138.3, 136.4, 128.4, 127.69, 127.65, 127.6, 127.5, 126.0, 125.3, 84.14, 84.07, 81.3, 81.2, 77.4, 76.2, 73.0, 72.9, 69.8, 69.3, 62.0, 60.3, 60.0, 50.3, 50.2, 32.74, 32.69,

32.0, 29.7, 29.2, 25.9, 18.0, 17.7, 15.2, 12.3, 12.0, 2.3; HR-MS (ESI, positive): calcd for $C_{32}H_{56}O_4Si_2Na$ (M+Na), 583.3609; found, 583.3594.

Ynone ***5a***. To a solution of alcohol **13** (581 mg, 1.04 mmol) in CH_2Cl_2 (11 mL) were added MS 3A (548 mg), NMO (192 mg, 1.64 mmol) and TPAP (38.6 mg, 0.110 mmol) at room temperature under nitrogen atmosphere. After being stirred at room temperature for 10 min, the reaction mixture was filtered through a short pad of silica gel eluting with EtOAc and concentrated. The residue was purified by silica gel column chromatography (hexane/Et_2O = 9:1) to give ynone **5a** (498 mg, 86%) as a colorless oil. Peak assignment was performed by NMR spectroscopy (^1H, ^{13}C, COSY, HMQC, and HMBC). IR (KBr) ν_{max} (cm^{-1}) 2944, 2866, 2213, 1667, 1463, 1250, 1110, 1014; ^1H NMR ($CDCl_3$, 400 MHz) δ (ppm) 7.37-7.24 (5H, m, Ar), 5.71 (1H, br d, J = 16 Hz, -CH_2CH=C*H*-), 5.61 (1H, td, J = 6.5, 16 Hz, -CH_2C*H*=CH-), 4.51 (2H, s, PhC*H*$_2$O-), 3.75 (2H, t, J = 6 Hz, TIPSOC*H*$_2$-), 3.51 (2H, t, J = 6.5 Hz, -OC*H*$_2$$CH_2$CH=C-), 2.77 (1H, d, J = 13 Hz, -COC*H*$_A$$H_B$-), 2.71 (1H, d, J = 13 Hz, -COCH_A*H*$_B$-), 2.47 (2H, t, J = 7 Hz, TIPSOCH_2CH_2C*H*$_2$-), 2.36 (2H, ddt, J = 1, 6.5, 6.5 Hz, -OCH_2C*H*$_2$CH=C-), 1.83-1.73 (2H, m, TIPSOCH_2C*H*$_2$-), 1.45 (3H, s, -C*H*$_3$), 1.12-1.02 (21H, m, *TIPS*O), 0.10 (9H, s, *Me*$_3$SiOC-); ^{13}C NMR ($CDCl_3$, 100 MHz) δ (ppm) 185.8, 138.4, 138.0, 128.3, 127.6, 127.5, 125.0, 93.9, 82.8, 74.5, 72.9, 69.8, 61.6, 58.6, 32.7, 31.1, 27.5, 18.0, 15.5, 11.9, 2.4; HR-MS (ESI, positive): calcd for $C_{32}H_{54}O_4Si_2Na$ (M+Na), 581.3453; found, 581.3448.

Hydroxy ynone ***5b***. To a solution of ynone **5a** (437 mg, 0.781 mmol) in THF (8 mL) was added a pre-mixed solution of TBAF (1.0 M in THF, 4.5 mL, 4.5 mmol) and AcOH (4.5 mL) at 0 °C under nitrogen atmosphere. After being stirred at 0 °C, the reaction mixture was allowed to warm to room temperature over a period of 4 h. The reaction

was quenched with H_2O at 0 °C. The aqueous layer was extracted with Et_2O. The combined organic layer was washed with brine, dried over anhydrous Na_2SO_4, and concentrated. The residue was purified by silica gel column chromatography (hexane/EtOAc = 5:1) to give hydroxy ynone **5b** (294 mg, 77%) as a colorless oil. Peak assignment was performed by NMR spectroscopy (^1H, ^{13}C, COSY, HMQC, and HMBC). IR (KBr) ν_{max} (cm^{-1}) 3509, 2943, 2866, 2213, 1664, 1463, 1383, 1108; ^1H NMR ($CDCl_3$, 400 MHz) δ (ppm) 7.37-7.23 (5H, m, Ar), 5.68 (1H, td, J = 6.5, 15.5 Hz, -CH_2CH=CH-), 5.62 (1H, d, J = 15.5 Hz, -CH_2CH=CH-), 4.50 (2H, s, PhCH_2O-), 3.75 (2H, t, J = 5.5 Hz, TIPSOCH_2-), 3.49 (2H, t, J = 6.5 Hz, -OCH_2CH_2CH=C-), 2.87 (1H, d, J = 17 Hz, -COC$H_A$$H_B$-), 2.76 (1H, d, J = 17 Hz, -COC$H_A$$H_B$-), 2.50 (2H, t, J = 7 Hz, TIPSO$CH_2CH_2CH_2$-), 2.34 (2H, dt, J = 6.5, 6.5 Hz, -OCH_2CH_2CH=C-), 1.83-1.73 (2H, m, TIPSOCH_2CH_2-), 1.30 (3H, s, -CH_3), 1.16-1.01 (21H, m, *TIPS*O); ^{13}C NMR ($CDCl_3$, 100 MHz) δ (ppm) 187.6, 138.4, 137.2, 128.2, 127.5, 127.4, 124.9, 95.6, 81.5, 72.8, 71.6, 69.7, 61.3, 55.3, 32.6, 30.8, 28.2, 17.9, 15.4, 11.8; HR-MS (ESI, positive): calcd for $C_{29}H_{46}O_4SiNa$ (M+Na), 509.3058; found, 509.3077.

*Dihydropyrone **4**.* To a solution of hydroxy ynone **5b** (483 mg, 0.993 mmol) and allyl alcohol (1.4 mL) in DME (2 mL) were added $(MeCN)_2PdCl_2$ (12.8 mg, 0.0493 mmol) at 0 °C under argon atmosphere. After being stirred at 0 °C for 3.5 h, the reaction was warmed to room temperature. After being stirred at room temperature for 20 min, the reaction mixture was filtered through a short pad of silica gel eluting with EtOAc and concentrated. The residue was purified by silica gel column chromatography (hexane/EtOAc = 5:1) to give dihydropyrone **4** (418 mg, 80%) as a colorless oil. Peak assignment was performed by NMR spectroscopy (^1H, ^{13}C, COSY, HMQC, and HMBC). IR (KBr) ν_{max} (cm^{-1}) 2948, 2868, 1699, 1521, 1360, 1131, 1093,

1041; ^{1}H NMR ($CDCl_3$, 400 MHz) δ (ppm) 7.37-7.24 (5H, m, Ar), 5.76 (1H, tdd, J = 6, 10, 17 Hz, -C*H*=CH_2), 5.66 (1H, td, J = 6.5, 16 Hz, -CH_2C*H*=CH-), 5.55 (1H, br d, J = 16 Hz, -CH_2CH=C*H*-), 4.96-4.87 (2H, m, -CH=CH_2), 4.49 (2H, s, PhCH_2O-), 3.70 (2H, t, J = 6 Hz, TIPSOCH_2-), 3.47 (2H, t, J = 7 Hz, -OC$H_2$$CH_2$CH=C-), 3.01 (1H, tdd, J = 2, 6, 16 Hz, CH_2=CHC$H_A$$H_B$), 2.95 (1H, tdd, J =2, 6, 16 Hz, CH_2=CHC$H_A$$H_B$), 2.64 (1H, d, J = 16 Hz, -COC$H_A$$H_B$-), 2.56 (1H, d, J = 16 Hz, -COC$H_A$$H_B$-), 2.43-2.29 (4H, m, -OCH_2CH_2CH=C-, TIPSOCH_2CH_2CH_2-), 1.85-1.72 (2H, m, TIPSOCH_2CH_2-), 1.43 (3H, s, -CH_3), 1.14-0.98 (21H, m, *TIPS*O); ^{13}C NMR ($CDCl_3$, 100 MHz) δ (ppm) 191.4, 171.4, 138.3, 136.5, 133.4, 128.3, 127.7, 127.52, 127.50, 113.9, 111.5, 80.4, 72.8, 69.3, 62.5, 45.5, 32.7, 29.8, 28.7, 27.6, 26.2, 18.0, 11.9; HR-MS (ESI, positive): calcd for $C_{32}H_{50}O_4SiNa$ (M+Na), 549.3371; found, 549.3395.

*Alcohols **3a** and epi-**3a**.* To a solution of dihydropyrone **4** (33.5 mg, 0.0636 mmol) in Et_2O (2 mL) was added DIBAL (1.02 M in hexane, 0.40 mL, 0.41 mmol) at –78 °C under nitrogen atmosphere. The reaction mixture was stirred at –78 °C for 10 min. To the reaction mixture was added hexane (5 mL) and the reaction was quenched with $Na_2SO_4 \cdot 10H_2O$ at –78 °C. To the mixture was added anhydrous Na_2SO_4. The resulting mixture was stirred at –78 °C, and then allowed to warm to room temperature over a period of 1 h. The reaction mixture was filtered through cotton pad eluting with EtOAc and concentrated. The residue was purified by silica gel column chromatography (hexane/EtOAc = 6:1) to give alcohol **3a** (14.5 mg, 43%) as a colorless oil and alcohol *epi*-**3a** (16.3 mg, 49%) as a colorless oil. Peak assignment of **3b** was performed by NMR spectroscopy (^{1}H, ^{13}C, COSY, and HMBC). Peak assignment of *epi*-**3a** was performed by NMR spectroscopy (^{1}H, ^{13}C, COSY, HMQC, and HMBC). Relative stereochemistry of **3a** was determined by NOESY correlation of the

corresponding TES ether **3b**. Alcohol **3a**: IR (KBr) ν_{max} (cm^{-1}) 3481, 2942, 2865, 1669, 1456, 1101; ^{1}H NMR (CD_3OD, 400 MHz) δ (ppm) 7.33-7.19 (5H, m, Ar), 5.80 (1H, m, CH_2=C*H*-), 5.66-5.53 (2H, m, -CH_2C*H*=C*H*-), 4.96 (1H, tdd, *J* = 1.5, 2, 17 Hz, C$H_A$$H_B$=CH-), 4.90 (1H, tdd, *J* = 1.5, 2, 10 Hz, $CH_A$$H_B$=CH-), 4.47 (1H, d, *J* = 12.5 Hz, PhC$H_A$$H_B$O-), 4.44 (1H, d, *J* = 12.5 Hz, PhC$H_A$$H_B$O-), 3.96 (1H, t, *J* = 5.5 Hz, HOC*H*-), 3.69 (2H, t, *J* = 6.5 Hz, TIPSOCH_2-), 3.45 (2H, dt, *J* = 1.5, 6 Hz, -OC$H_2$$CH_2$CH=C-), 2.91-2.75 (2H, m, CH_2=CHCH_2-), 2.34-2.23 (2H, m, -OCH_2CH_2CH=C-), 2.19 (2H, t, *J* = 7.5 Hz, TIPSO$CH_2$$CH_2CH_2$-), 1.90 (1H, dd, *J* = 5.5, 14 Hz, HOCHC$H_A$$H_B$), 1.84 (1H, dd, *J* = 5.5, 14 Hz, HOCHC$H_A$$H_B$), 1.78-1.64 (2H, m, TIPSOCH_2CH_2-), 1.23 (3H, s, -CH_3), 1.09-1.00 (21H, m, *TIPS*O); ^{13}C NMR (CD_3OD, 100 MHz) δ (ppm) 151.3, 139.6, 138.4, 137.9, 129.4, 128.9, 128.7, 125.9, 114.8, 107.5, 76.0, 73.8, 70.5, 64.3, 64.2, 43.3, 33.8, 33.0, 32.0, 28.0, 26.6, 18.6, 13.3; HR-MS (ESI, positive): calcd for $C_{32}H_{52}O_4SiNa$ (M+Na), 551.3527; found, 551.3520. Alcohol *epi*-**3a**: IR (KBr) ν_{max} (cm^{-1}) 3392, 2942, 2865, 1667, 1455, 1103; ^{1}H NMR (CD_3OD, 400 MHz) δ (ppm) 7.33-7.18 (5H, m, Ar), 5.79-5.64 (1H, m, CH_2=C*H*-), 5.58 (1H, td, *J* = 6.5, 15.5 Hz, -CH_2C*H*=CH-), 5.48 (1H, d, *J* = 15.5 Hz, -CH_2CH=C*H*-), 4.94 (1H, tdd, *J* = 1.5, 2, 18 Hz, C$H_A$$H_B$=CH-), 4.84 (1H, m, $CH_A$$H_B$=CH-), 4.45 (2H, s, PhC$H_2$O-), 3.98 (1H, br t, *J* = 7 Hz, HOC*H*-), 3.67 (2H, t, *J* = 6 Hz, TIPSOCH_2-), 3.44 (2H, t, *J* = 6.5 Hz, -OC$H_2$$CH_2$CH=C-), 2.89 (1H, br dd, *J* = 7, 16 Hz, CH_2=CHC$H_A$$H_B$-), 2.76 (1H, m, CH_2=CHC$H_A$$H_B$-), 2.27 (2H, dt, *J* = 6.5, 6.5 Hz, -OCH_2CH_2CH=C-), 2.17 (2H, t, *J* = 7.5 Hz, TIPSO$CH_2$$CH_2CH_2$-), 2.02 (1H, dd, *J* = 6.5, 13.5 Hz, HOCHC$H_A$$H_B$), 1.77-1.62 (3H, m, TIPSOCH_2CH_2-, HOC$HCH_A$$H_B$-), 1.25 (3H, s, -C$H_3$), 1.10-1.00 (21H, m, *TIPS*O); ^{13}C NMR (CD_3OD, 100 MHz) δ (ppm) 151.0, 139.7, 138.5, 136.9, 129.4, 128.8, 128.6, 126.3, 114.6, 107.9, 76.8, 73.8, 71.0, 64.2, 64.0, 43.1, 33.8, 32.1, 32.0, 28.09, 28.06, 18.6, 13.2; HR-MS

(ESI, positive): calcd for $C_{32}H_{52}O_4SiNa$ (M+Na), 551.3527; found, 551.3523.

*Silyl ether **3b***. To a solution of alcohol **3a** (90.6 mg, 0.171 mmol) in DMF (3.5 mL) were added NaH (50% in mineral oil, 49.9 mg, 1.04 mmol), DMAP (41.8 mg, 0.342 mmol) and TESCl (0.10 mL, 0.60 mmol) at 0 °C under nitrogen atmosphere. The resulting mixture was then allowed to warm to room temperature over a period of 1.5 h. The reaction was quenched with a saturated aqueous solution of $NaHCO_3$ at 0 °C. The aqueous layer was extracted with Et_2O. The organic layer was washed with brine, dried over anhydrous Na_2SO_4, and concentrated. The residue was purified by silica gel column chromatography (hexane/Et_2O = 25:1) to give silyl ether **3b** (93.0 mg, 85%) as a colorless oil. Peak assignment was performed by NMR spectroscopy (^1H, ^{13}C, COSY, HMQC, and HMBC). Relative stereochemistry of **3b** was determined by NOESY correlations (Figure 2). IR (KBr) ν_{max} (cm^{-1}) 2943, 2866, 1670, 1457, 1363, 1102, 1004; ^1H NMR (CD_3OD, 400 MHz) δ (ppm) 7.32-7.18 (5H, m, Ar), 5.82-5.68 (2H, m, CH_2=C*H*-, -CH_2CH=C*H*-), 5.60 (1H, td, *J* = 6.5, 15.5 Hz, -CH_2C*H*=CH-), 4.98-4.86 (2H, m, C*H*$_2$=CH-), 4.46 (2H, s, PhC*H*$_2$O-), 4.18 (1H, t, *J* = 6 Hz, TESOC*H*-), 3.65 (2H, t, *J* = 6.5 Hz, TIPSOC*H*$_2$-), 3.47 (2H, t, *J* = 6.5 Hz, -OC*H*$_2$CH$_2$CH=C-), 2.84 (1H, dd, *J* = 6.5, 16 Hz, CH_2=CHC*H*$_A$H$_B$-), 2.76 (1H, br d, *J* = 16 Hz, CH_2=CHCH$_A$*H*$_B$-), 2.27 (2H, ddt, *J* = 1, 6.5, 6.5 Hz, -OCH$_2$C*H*$_2$CH=C-), 2.22-2.05 (2H, m, TIPSOCH$_2$CH$_2$*CH*$_2$-), 1.87 (1H, dd, *J* = 6, 13.5 Hz, TESOCHC*H*$_A$H$_B$-), 1.76 (1H, dd, *J* = 6, 13.5 Hz, TESOCHCH$_A$*H*$_B$-), 1.72-1.61 (2H, m, TIPSOCH$_2$C*H*$_2$-), 1.23 (3H, s, -C*H*$_3$), 1.09-0.98 (21H, m, TIPSO), 0.94 (9H, t, *J* = 8 Hz, -OSi(CH$_2$C*H*$_3$)$_3$), 0.58 (6H, q, *J* = 8 Hz, -OSi(C*H*$_2$CH$_3$)$_3$); ^{13}C NMR (CD_3OD, 100 MHz) δ (ppm) 150.7, 139.8, 138.8, 138.0, 129.4, 128.8, 128.6, 124.9, 114.5, 107.6, 75.8, 73.8, 71.0, 65.4, 64.0, 44.2, 33.9, 32.6, 31.7, 27.9, 25.6, 18.6, 13.2, 7.4, 6.1; HR-MS (ESI, positive): calcd for

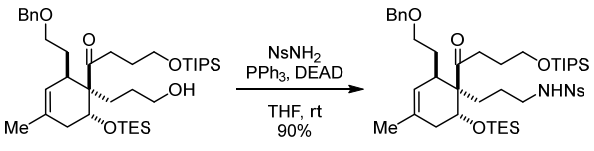
$C_{38}H_{66}O_4Si_2Na$ (M+Na), 665.4392; found, 665.4398.

*Silyl ether epi-**3b***. To a solution of alcohol *epi*-**3a** (16.3 mg, 0.0308 mmol) in DMF (2 mL) were added NaH (50% in mineral oil, 28.7 mg, 0.595 mmol), DMAP (13.1 mg, 0.107 mmol) and TESCl (0.050 mL, 0.30 mmol) at 0 °C under nitrogen atmosphere. After being stirred at 0 °C for 10 min, the reaction was quenched with a saturated aqueous solution of $NaHCO_3$ at 0 °C. The aqueous layer was extracted with Et_2O. The organic layer was washed with brine, dried over anhydrous Na_2SO_4, and concentrated. The residue was purified by silica gel column chromatography (hexane/Et_2O = 30:1) to give silyl ether *epi*-**3b** (15.4 mg, 78%) as colorless oil. Peak assignment was performed by NMR spectroscopy (^1H, ^{13}C, COSY, HMQC, and HMBC). IR (KBr) ν_{max} (cm^{-1}) 2944, 2866, 1457, 1102, 1002; ^1H NMR (CD_3OD, 400 MHz) δ (ppm) 7.32-7.19 (5H, m, Ar), 5.78-5.64 (1H, m, CH_2=C*H*-), 5.58 (1H, td, *J* = 6.5, 15.5 Hz, -CH_2C*H*=CH-), 5.49 (1H, br d, *J* = 15.5 Hz, -CH_2CH=C*H*-), 4.91 (1H, tdd, *J* = 1.5, 2, 17 Hz, C*H*$_A$H$_B$=CH-), 4.88 (1H, br d, *J* = 10 Hz, CH$_A$*H*$_B$=CH-), 4.46 (2H, s, PhC*H*$_2$O-), 4.12 (1H, t, *J* = 7 Hz, TESOC*H*-), 3.67 (2H, t, *J* = 6.5 Hz, TIPSOC*H*$_2$-), 3.45 (2H, t, *J* = 6.5 Hz, -OC*H*$_2$CH$_2$CH=C-), 2.85 (1H, dd, *J* = 6.5, 16.5 Hz, CH_2=CHC*H*$_A$H$_B$-), 2.77 (1H, m, CH_2=CHCH$_A$*H*$_B$-), 2.28 (2H, dt, *J* = 6.5, 6.5 Hz, -OCH$_2$C*H*$_2$CH=C-), 2.27-2.06 (2H, m, TIPSOCH$_2$CH$_2$*CH*$_2$-), 2.02 (1H, dd, *J* = 6, 13 Hz, TESOCHC*H*$_A$H$_B$-), 1.78-1.60 (3H, m, TIPSOCH$_2$*CH*$_2$-, TESOCHCH$_A$*H*$_B$-), 1.30 (3H, s, -C*H*$_3$), 1.12-1.08 (21H, m, *TIPS*O), 0.97 (9H, t, *J* = 8 Hz, -OSiCH$_2$C*H*$_3$), 0.62 (6H, q, *J* = 8 Hz, -OSiC*H*$_2$CH$_3$); ^{13}C NMR (CD_3OD, 100 MHz) δ (ppm) 150.8, 139.8, 138.8, 137.3, 129.4, 128.8, 128.6, 126.4, 114.4, 107.9, 76.6, 73.8, 71.0, 65.6, 64.1, 43.7, 33.7, 32.0, 31.9, 28.0, 27.8, 18.6, 13.3, 7.4, 6.1; HR-MS (ESI, positive): calcd for $C_{38}H_{66}O_4Si_2Na$ (M + Na), 665.4392; found, 665.4419.

*Cyclohexene **2** (Table 1, entry 7).* To a solution of silyl ether **3b** (1.46 g, 2.3 mmol) in EtPh (50 mL) was added K_2CO_3 (6.90 g, 49.9 mmol) at room temperature under argon atmosphere. The resulting mixture was degassed by three freeze-thaw cycles, and the flask was filled with argon. After being stirred at reflux for 36 h, H_2O was added to the reaction mixture at room temperature. The aqueous layer was extracted with CH_2Cl_2. The organic layer was dried over anhydrous Na_2SO_4 and concentrated. The residue was purified by silica gel column chromatography (hexane/Et_2O = 20:1) to give cyclohexene **2** (1.40 g, 96%, dr = >95:<5 determined by ^1H NMR analysis) as a colorless oil. Peak assignment was performed by NMR spectroscopy (^1H, ^{13}C, COSY, HMQC, and HMBC). The relative stereochemistry of **2** was determined by NOESY correlations (Figure 2). IR (KBr) ν_{max} (cm^{-1}) 2926, 2867, 1705, 1458, 1099, 1013; ^1H NMR ($CDCl_3$, 400 MHz) δ (ppm) 7.37-7.24 (5H, m, Ar), 6.05 (1H, m, CH_2=C*H*-), 5.30 (1H, br, -CHC*H*=C-), 4.96 (1H, dd, *J* = 1.5, 17 Hz, C$H_A$$H_B$=CH-), 4.91 (1H, dd, *J* = 1.5, 10 Hz, C$H_A$$H_B$=CH-), 4.52-4.38 (3H, m, TESOC*H*-, PhCH_2O-), 3.67 (2H, t, *J* = 6 Hz, TIPSOCH_2-), 3.50-3.32 (2H, m, -OCH_2CH_2-), 2.74-2.47 (3H, m, CH_2=CHC$H_A$$H_B$-, -COC$H_2$-), 2.43-2.20 (3H, m, -C*H*CH=C-, CH_2=CHC$H_A$$H_B$-, TESOCHC$H_A$$H_B$-), 1.99 (1H, dd, *J* = 8, 18 Hz, TESOCHC$H_A$$H_B$-), 1.88-1.65 (2H, m, TIPSOCH_2CH_2-), 1.65-1.49 (4H, m, CH_3C=CH-, -OCH_2C$H_A$$H_B$-), 1.29 (1H, m, -OC$H_2CH_A$$H_B$-), 1.13-1.00 (21H, m, *TIPS*O), 0.93 (9H, t, *J* = 8 Hz, -OSi(CH_2CH_3)$_3$), 0.62 (3H, q, *J* = 8 Hz, -OSi(C$H_A$$H_B$$CH_3$)$_3$), 0.61 (3H, q, *J* = 8 Hz, -OSi(C$H_A$$H_B$$CH_3$)$_3$); ^{13}C NMR ($CDCl_3$, 100 MHz) δ (ppm) 212.4, 138.5, 137.2, 131.6, 128.3, 127.6, 127.5, 122.4, 115.7, 72.8, 68.3, 68.0, 62.7, 58.0, 40.2, 38.4, 37.6, 36.5, 33.1, 26.8, 22.9, 18.0, 12.0, 7.0, 5.3; HR-MS (ESI, positive): calcd for $C_{38}H_{66}O_4Si_2Na$ (M+Na), 665.4392; found, 665.4425.

*Alcohol **14**.* To a solution of cyclohexene **2** (110 mg, 0.172 mmol) in THF (3.4 mL)

was added freshly prepared thexylborane (0.5 M, 0.70 mL, 0.35 mmol) at –25 °C under argon atmosphere. After being stirred at –25 °C for 0.5 h, the reaction was quenched with H_2O at –25 °C. To the resulting mixture an aqueous solution of NaOH and H_2O_2 [3 mL; NaOH (1.5 g), 30% H_2O_2 (3 mL) and H_2O 17 mL] was added at –25 °C. After being stirred at room temperature for 0.5 h, the aqueous layer was extracted with Et_2O. The organic layer was washed with brine, dried over anhydrous Na_2SO_4, and concentrated. The residue was purified by silica gel column chromatography (hexane/EtOAc = 6:1) to give alcohol **14** (85.2 mg, 75%) as a colorless oil. Peak assignment was performed by NMR spectroscopy (^1H, ^{13}C, COSY, HMQC, and HMBC). IR (KBr) ν_{max} (cm^{-1}) 3690, 2955, 2867, 1704, 1549, 1100; ^1H NMR ($CDCl_3$, 400 MHz) δ (ppm) 7.38-7.24 (5H, m, Ar), 5.28 (1H, br, -CHC*H*=C-), 4.53-4.38 (3H, m, TESOC*H*-, PhC*H*$_2$O-), 3.70 (2H, t, J = 6.5 Hz, TIPSOC*H*$_2$-), 3.55 (2H, t, J = 6 Hz, HOC*H*$_2$-), 3.48-3.35 (2H, m, -OC*H*$_2$CH$_2$-), 2.77-2.48 (2H, m, -COC*H*$_2$-), 2.35-2.15 (2H, m, -C*H*CH=C-, TESOCHC*H*$_A$H$_B$-), 2.08-1.15 (12H, m, C*H*$_3$C=CH-, TIPSOCH$_2$*CH*$_2$-, -OCH$_2$C*H*$_2$-, TESOCHCH$_A$*H*$_B$-, HOCH$_2$C*H*$_2$C*H*$_2$-), 1.15-0.74 (30H, m, *TIPS*O, -OSi(CH$_2$C*H*$_3$)$_3$), 0.72-0.54 (6H, m, -OSi(C*H*$_2$CH$_3$)$_3$); ^{13}C NMR ($CDCl_3$, 100 MHz) δ (ppm) 213.0, 138.5, 131.6, 128.3, 127.6, 127.5, 122.3, 72.8, 68.12, 68.08, 63.8, 62.6, 57.3, 41.9, 38.4, 35.8, 33.3, 29.9, 29.6, 26.8, 22.9, 18.0, 12.0, 7.1, 5.2; HR-MS (ESI, positive): calcd for $C_{38}H_{68}O_5Si_2Na$ (M+Na), 683.4498; found, 683.4531.



14 **20**

*Amide **20**.* To a solution of alcohol **14** (59.6 mg, 0.0902 mmol) in THF (4.5 mL) were added $NsNH_2$ (89.6 mg, 0.443 mmol), PPh_3 (244 mg, 0.930 mmol) DEAD (2.2 M

in toluene, 0.40 mL, 0.88 mmol) at room temperature under argon atmosphere. After being stirred at room temperature for 10 min, the reaction mixture was concentrated. The residue was purified by silica gel column chromatography (hexane/EtOAc = 4:1) to give amide **20** (68.4 mg, 90%) as a colorless oil. Peak assignment was performed by NMR spectroscopy (^{1}H, ^{13}C, COSY, HMQC, and HMBC). IR (KBr) ν_{max} (cm^{-1}) 3359, 2944, 2867, 1704, 1542, 1458, 1415, 1363, 1171, 1100; ^{1}H NMR ($CDCl_3$, 400 MHz) δ (ppm) 8.10 (1H, m, Ar), 7.82 (1H, m, Ar), 7.75-7.64 (2H, m, Ar), 7.38-7.24 (5H, m, Ar), 5.26-5.15 (2H, m, N*H*, -CHC*H*=C-), 4.52-4.35 (3H, m, PhC*H*$_2$O-, TESOC*H*-), 3.76-3.62 (2H, m, TIPSOC*H*$_2$-), 3.47-3.32 (2H, m, -OC*H*$_2$CH$_2$-), 3.12-2.92 (2H, m, -NHC*H*$_2$-), 2.65-2.45 (2H, m, -COC*H*$_2$-), 2.30-1.15 (14H, m, -OCH$_2$C*H*$_2$-, -C*H*CH=C-, C*H*$_3$C=CH-, TESOCHC*H*$_2$-, TIPSOCH$_2$*CH*$_2$-, -NHCH$_2$C*H*$_2$C*H*$_2$-), 1.15-0.80 (30H, m, *TIPS*O, -OSi(CH$_2$C*H*$_3$)$_3$), 0.67-0.50 (6H, m, -OSi(C*H*$_2$CH$_3$)$_3$); ^{13}C NMR ($CDCl_3$, 100 MHz) δ (ppm) 212.9, 148.1, 138.4, 133.9, 133.4, 132.7, 131.5, 131.1, 128.3, 127.62, 127.57, 125.3, 122.3, 72.9, 68.1, 67.9, 62.5, 57.2, 45.1, 42.2, 38.4, 36.3, 33.2, 30.8, 26.74, 26.68, 22.9, 18.0, 12.0, 7.1, 5.3; HR-MS (ESI, positive): calcd for $C_{44}H_{72}O_8Si_2N_2SNa$ (M+Na), 867.4440; found, 867.4405.

*Diol **15**.* To a solution of amide **20** (46.5 mg, 0.0550 mmol) in THF (1.0 mL) was added TBAF (1.0 M in THF, 0.30 mL, 0.30 mmol) at room temperature under argon atmosphere. After being stirred at room temperature for 3 h, the reaction was quenched with brine at room temperature. The aqueous layer was extracted with EtOAc. The organic layer was washed with brine, dried over anhydrous Na_2SO_4, and concentrated. The residue was purified by silica gel column chromatography (hexane/ EtOAc = 4:1) to give diol **15** (28.4 mg, 90%) as a colorless oil. Peak assignment was performed by NMR spectroscopy (^{1}H, ^{13}C, COSY, HMQC, and HMBC). IR (KBr)

ν_{max} (cm^{-1}) 3547, 2924, 2360, 1686, 1542, 1363, 1165, 1058; ^{1}H NMR ($CDCl_3$, 400 MHz) δ (ppm) 8.09 (1H, m, Ar), 7.84-7.65 (3H, m, Ar), 7.41-7.25 (5H, m, Ar), 5.69 (1H, br, N*H*), 5.32 (1H, br, -CHC*H*=C-), 4.52 (1H, d, *J* = 12 Hz, PhC$H_A$$H_B$O-), 4.45 (1H, d, *J* = 12 Hz, PhC$H_A$$H_B$O-), 4.41-4.33 (1H, m, HOC*H*-), 3.64 (2H, t, *J* = 6 Hz, HOCH_2-), 3.51-3.23 (3H, m, -OCH_2CH_2-, O*H*), 3.10-2.95 (2H, m, -NHCH_2-), 2.79-2.60 (2H, m, -COCH_2-), 2.45-1.15 (14H, m, -OCH$_2$CH_2-, -C*H*CH=C-, CH_3C=CH-, HOCHCH_2-, HOCH$_2$CH_2-, -NHCH$_2$CH_2CH_2-); ^{13}C NMR ($CDCl_3$, 100 MHz) δ (ppm) 218.1, 148.0, 138.1, 133.6, 133.4, 132.6, 132.2, 131.0, 128.4, 127.71, 127.66, 125.2, 121.8, 73.1, 67.44, 67.35, 61.4, 57.2, 44.3, 41.5, 35.3, 34.3, 33.6, 30.3, 26.5, 25.7, 22.8; HR-MS (ESI, positive): calcd for $C_{29}H_{38}O_8N_2SNa$ (M+Na), 597.2241; found, 597.2243.

*Cyclopropyl ketone **16**.* To a solution of diol **15** (8.8 mg, 0.015 mmol) in THF (1.5 mL) were added PPh_3 (6.1 mg, 0.023 mmol) and DEAD (2.2 M in toluene, 0.01 mL, 0.02 mmol) at room temperature under argon atmosphere. After being stirred at room temperature for 10 min, PPh_3 (59.8 mg, 0.220 mmol) and DEAD (2.2 M in toluene, 0.10 mL, 0.22 mmol) were added. After being stirred at room temperature for 26 h, PPh_3 (62.0 mg, 0.240 mmol) and DEAD (2.2 M in toluene, 0.13 mL, 0.29 mmol) were added. After being stirred at room temperature for 15 min, the reaction was concentrated. The residue was purified by silica gel column chromatography (hexane/Et_2O = 1:4) to give cyclopropyl ketone **16** (7.1 mg, 84%) as a colorless oil. Peak assignment was performed by NMR spectroscopy (^{1}H, ^{13}C, COSY, HMQC, and HMBC). IR (KBr) ν_{max} (cm^{-1}) 3526, 3342, 2924, 2854, 1671, 1542, 1455, 1363, 1166, 1063; ^{1}H NMR ($CDCl_3$, 400 MHz) δ (ppm) 8.10 (1H, m, Ar), 7.83 (1H, m, Ar), 7.76-7.67 (2H, m, Ar), 7.40-7.24 (5H, m, Ar), 5.33 (1H, br, -CHC*H*=C-), 5.24 (1H, t, *J* = 5.5 Hz, N*H*), 4.52 (1H, d, *J* = 12 Hz, PhC$H_A$$H_B$O-), 4.44 (1H, d, *J* = 12 Hz, PhC$H_A$$H_B$O-), 4.34 (1H, m,

HOC*H*-), 3.54 (1H, d, *J* = 2 Hz, O*H*), 3.50-3.42 (2H, m, -OC*H*$_2$CH$_2$-), 3.11-3.00 (2H, m, -NHC*H*$_2$-), 2.53 (1H, m, -C*H*CH=C-), 2.33-0.79 (16H, m, -OCH$_2$C*H*$_2$-, C*H*$_3$C=CH-, HOCHC*H*$_2$-, -COC*H*-, -COCHC*H*$_2$C*H*$_2$-, -NHCH$_2$C*H*$_2$C*H*$_2$-); ^{13}C NMR ($CDCl_3$, 100 MHz) δ (ppm) 217.5, 148.1, 138.4, 133.8, 133.5, 132.7, 132.2, 131.0, 128.4, 127.64, 127.56, 125.4, 121.6, 72.9, 67.7, 67.5, 57.2, 44.6, 41.5, 35.4, 33.9, 30.4, 26.8, 22.9, 17.7, 13.1, 11.6; HR-MS (ESI, positive): calcd for $C_{29}H_{36}O_7N_2SNa$ (M+Na), 579.2135; found, 579.2122.

*Triol **17**.* To a solution of diol **15** (350 mg, 0.609 mmol) in MeOH (12 mL) was added $NaBH_4$ (231 mg, 6.11 mmol) at 0 °C under argon atmosphere. After gradually heating to 45 °C for 1 h, $NaBH_4$ (42.7 mg, 1.13 mmol) was added at 0 °C under argon atmosphere. After being stirred at 40 °C for 20 min, the reaction was quenched with a saturated aqueous solution of NH_4Cl at 0 °C. The aqueous layer was extracted with EtOAc. The organic layer was washed with brine, dried over anhydrous Na_2SO_4, and concentrated. The residue was purified by silica gel column chromatography (hexane/ EtOAc = 1:9) to give triol **17** (272 mg, 77%, dr = >95:<5 determined by ^{1}H NMR analysis) as a colorless oil. Peak assignment was performed by NMR spectroscopy (^{1}H, ^{13}C, COSY, HMQC, and HMBC). The relative stereochemistry of **17** was determined by X-ray crystallographic analysis of azaspirocycle **1**. IR (KBr) ν_{max} (cm^{-1}) 3357, 2931, 2875, 1541, 1441, 1415, 1363, 1340, 1166, 1057; ^{1}H NMR ($CDCl_3$, 400 MHz) δ (ppm) 8.11 (1H, m, Ar), 7.82 (1H, m, Ar), 7.75-7.66 (2H, m, Ar), 7.39-7.24 (5H, m, Ar), 5.48 (1H, t, *J* = 5.5 Hz, N*H*), 5.28 (1H, br, -CHC*H*=C-), 4.53 (1H, d, *J* = 12 Hz, PhC*H*$_A$H$_B$O-), 4.47 (1H, d, *J* = 12 Hz, PhCH$_A$*H*$_B$O-), 4.17 (1H, m, HOC*H*CH$_2$C=CH-), 3.85-3.62 (3H, m, HOC*H*$_2$-, HOCH$_2$CH$_2$CH$_2$C*H*OH), 3.57-3.39 (2H, m, -OC*H*$_2$CH$_2$-), 3.10-2.98 (2H, m, -NHC*H*$_2$-), 2.25-1.13 (16H, m, -OCH$_2$C*H*$_2$-,

-C*H*CH=C-, C*H*$_3$C=CH-, HOCHC*H*$_2$C=CH-, HOCH$_2$C*H*$_2$C*H*$_2$-, -NHCH$_2$C*H*$_2$C*H*$_2$-); ^{13}C NMR ($CDCl_3$, 100 MHz) δ (ppm) 148.1, 138.3, 133.8, 133.4, 132.7, 131.1, 130.9, 128.4, 127.70, 127.67, 125.3, 124.2, 74.0, 73.1, 68.8, 68.7, 62.7, 44.9, 44.8, 38.8, 37.2, 33.0, 30.3, 29.4, 27.3, 24.6, 22.9; HR-MS (ESI, positive): calcd for $C_{29}H_{40}O_8N_2SNa$ (M+Na), 599.2398; found, 599.2376.

*Silyl ether **18***. To a solution of triol **17** (239 mg, 0.414 mmol) in CH_2Cl_2 (8 mL) were added 2,6-lutidine (1.80 mL, 15.5 mmol) and TBSOTf (2.40 mL, 10.4 mmol) at –78 °C argon atmosphere. After being gradually warming to 0 °C for 14 h, the reaction was quenched with a saturated aqueous solution of $NaHCO_3$ at 0 °C. The aqueous layer was extracted with Et_2O. The organic layer was washed with brine, dried over anhydrous Na_2SO_4, and concentrated. The residue was purified by silica gel column chromatography (hexane/ EtOAc = 9:1) to give silyl ether **18** (349 mg, 82%) as a colorless oil. IR (KBr) ν_{max} (cm^{-1}) 2954, 2929, 2857, 1548, 1471, 1362, 1341, 1255, 1163, 1096, 1070; ^{1}H NMR ($CDCl_3$, 400 MHz) δ (ppm) 7.79 (1H, m), 7.59-7.53 (3H, m), 7.37-7.24 (5H, m), 5.09 (1H, br), 4.52 (1H, d, J = 12 Hz), 4.45 (1H, d, J = 12 Hz), 3.98 (1H, t, J = 5 Hz), 3.58-3.29 (5H, m), 3.11-2.99 (2H, m), 2.18-1.10 (16H, m), 0.89 (9H, s), 0.86 (9H, s), 0.85 (9H, s), 0.83 (9H, s), 0.37 (3H, s), 0.36 (3H, s), 0.07-–0.05 (18H, m); ^{13}C NMR ($CDCl_3$, 100 MHz) δ (ppm) 149.1, 138.7, 135.1, 132.7, 131.2, 130.1, 129.3, 128.3, 127.6, 127.4, 124.3, 73.0, 70.7, 69.7, 63.2, 49.1, 46.4, 38.1, 36.7, 32.6, 31.2, 31.0, 29.7, 27.3. 26.5, 26.1, 26.0, 25.7, 23.0, 19.8, 18.8, 18.3, 18.2, -2.7, -2.89, -2.92, -3.0, -3.7, -4.1; HR-MS (ESI, positive): calcd for $C_{53}H_{96}O_8N_2SSi_4Na$ (M+Na), 1055.5857; found, 1055.5803.

*Alcohol **19***. To a solution of silyl ether **18** (349 mg, 0.338 mmol) in MeOH (7 mL) were added PPTS (86.6 mg, 0.345 mmol) at room temperature under argon atmosphere.

After being stirred at reflux for 5 h, PPTS (98.4 mg, 0.392 mmol) was added to the reaction mixture at room temperature. After being stirred at reflux for 14 h, PPTS (84.2 mg, 0.335 mmol) was added to the reaction mixture at room temperature. After being stirred at reflux, the reaction was quenched with a saturated aqueous solution of $NaHCO_3$ at 0 °C. The aqueous layer was extracted with Et_2O. The organic layer was washed with brine, dried over anhydrous Na_2SO_4, and concentrated. The residue was purified by silica gel column chromatography (hexane/ EtOAc = 4:1) to give alcohol **19** (262 mg, 96%) as a colorless oil. IR (KBr) ν_{max} (cm^{-1}) 3365, 2954, 2928, 2856, 1543, 1471, 1442, 1414, 1362, 1256, 1169, 1065; ^1H NMR ($CDCl_3$, 400 MHz) δ (ppm) 8.10 (1H, m), 7.82 (1H, m), 7.75-7.65 (2H, m), 7.37-7.23 (5H, m), 5.29-5.18 (2H, m), 4.52 (1H, d, J = 12 Hz), 4.45 (1H, d, J = 12 Hz), 4.10 (1H, t, J = 5.5 Hz), 3.74 (1H, m), 3.63-3.35 (4H, m), 3.04-2.90 (2H, m), 2.38-1.20 (16H, m), 0.86 (9H, s), 0.84 (9H, s), 0.09 (3H, s), 0.07 (3H, s), 0.05 (3H, s), 0.00 (3H, s); ^{13}C NMR ($CDCl_3$, 100 MHz) δ (ppm) 148.1, 138.7, 133.8, 133.3, 132.6, 131.1, 130.3, 128.3, 127.5, 127.4, 125.3, 124.2, 77.4 73.0, 71.1, 69.5, 63.0, 46.5, 45.2, 38.5, 36.5, 32.0, 31.5, 30.6, 26.4, 26.1, 25.6, 22.9, 18.8, 18.2, 14.1, -2.8, -3.5, -3.9, -4.0; HR-MS (ESI, positive): calcd for $C_{41}H_{68}O_8N_2SSi_2Na$ (M+Na), 827.4127; found, 827.4167.

*Azaspirocycle **1***. To a solution of alcohol **19** (262 mg, 0.325 mmol) in THF (32 mL) were added PPh_3 (1.30 g, 4.95 mmol), DEAD (2.2 M in toluene, 2.2 mL, 4.8 mmol) at room temperature under argon atmosphere. After being stirred at room temperature for 1 min, the reaction was concentrated. The residue was purified by silica gel column chromatography (hexane/EtOAc = 9:1 to 7:1 to 5:1) to give azaspirocycle **1** (227 mg, 89%) as a white solid. Peak assignment was performed by NMR spectroscopy (^1H, ^{13}C, COSY, HMQC, and HMBC). The structure of **1** was

determined by single-crystal X-ray diffraction analysis. IR (KBr) ν_{max} (cm^{-1}) 2957, 2928, 2856, 1547, 1471, 1440, 1374, 1361, 1347, 1255, 1172, 1068; ^1H NMR ($CDCl_3$, 400 MHz) δ (ppm) 7.90 (1H, m, Ar), 7.71-7.59 (2H, m, Ar), 7.54 (1H, m, Ar), 7.38-7.23 (5H, m, Ar), 5.30 (1H, br, -CHC*H*=C-), 4.57-4.36 (4H, m, PhC*H*$_2$O-, TBSOC*H*CH$_2$C=CH-, -N(Ns)CH$_2$CH$_2$CH$_2$C*H*OTBS), 3.55-3.28 (4H, m, -N(Ns)C*H*$_A$H$_B$CH$_2$CH$_2$CHOTBS, -N(Ns)C*H*$_A$H$_B$CH$_2$CH$_2$C-, -OC*H*$_2$CH$_2$-), 3.00 (1H, m, -N(Ns)CH$_A$*H*$_B$CH$_2$CH$_2$CHOTBS), 2.87-2.75 (1H, m, -N(Ns)CH$_A$*H*$_B$CH$_2$CH$_2$C-), 2.50-1.20 (16H, m, -OCH$_2$C*H*$_2$-, -C*H*CH=C-, C*H*$_3$C=CH-, TBSOCHC*H*$_2$C=CH-, -N(Ns)CH$_2$C*H*$_2$C*H*$_2$CHOTBS, -N(Ns)CH$_2$C*H*$_2$C*H*$_2$C-), 0.90 (9H, s, -Si(CH$_3$)$_2$C(C*H*$_3$)$_3$), 0.88 (9H, s, -Si(CH$_3$)$_2$C(C*H*$_3$)$_3$), 0.15 (3H, s, -Si(C*H*$_3$)$_2$C(CH$_3$)$_3$), 0.12 (3H, s, -Si(C*H*$_3$)$_2$C(CH$_3$)$_3$), 0.10 (3H, s, -Si(C*H*$_3$)$_2$C(CH$_3$)$_3$), 0.09 (3H, s, -Si(C*H*$_3$)$_2$C(CH$_3$)$_3$); ^{13}C NMR ($CDCl_3$, 100 MHz) δ (ppm) 148.8, 139.0, 133.3, 131.3, 131.0, 130.8, 128.9, 128.3, 127.5, 127.3, 124.4, 123.7, 72.6, 71.6, 69.7, 69.1, 51.0, 46.2, 44.7, 41.2, 39.7, 34.7, 28.0, 27.5, 27.2, 26.7, 26.5, 22.9, 21.4, 18.6, 18.5, -2.1, -2.5, -3.4, -4.1 ; HR-MS (ESI, positive): calcd for $C_{41}H_{66}O_7N_2SSi_2Na$ (M+Na), 809.4022; found, 809.3996. Mp: 171-172 °C.

ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.joc.XXXXXXX.

Spectral data for all new compounds and X-ray crystallographic data for compound **1** (PDF)

Crystal data for compound **1** (CIF)

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Notes

The authors declare no competing financial interest.

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12 Dihydropyrone **4** seems to be a precursor of the Claisen rearrangement, however the reaction of **4** in toluene at 242 °C resulted in the formation of complex mixture. This unsuccessful outcome is consistent with the previous result in a bicyclic dihydropyrone system, reported in ref 5b.

13 Reduction of **4** using Li(*t*-BuO)$_3$AlH, Red-Al, $NaBH_4$ or $NaBH_4$ /$CeCl_3 \cdot 7H_2O$ resulted in the recovery of **4**. In addition, reduction of **4** with DIBAL in other solvents (benzene, CH_2Cl_2, THF and toluene) and other reductants ($LiAlH_4$ and K-Selectride) could not improve its diastereoselectivity.

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17 CCDC-1849784 contains the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.