약학석사 학위논문

Stereoselective Synthesis of D-5'-Homo-4'-selenonucleosides as Potent Therapeutic Agents

효과적인 치료제로서의 **D-5'-Homo-4'-selenonucleosides** 의
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Abstract

D-5'-Homo-4'-selenonucleosides were synthesized from D-5-homo-4-selenoribose using a Pummerer-type condensation. For the stereoselective synthesis of the key intermediate D-5-homo-4-selenoribose, we employed Sharpless asymmetric epoxidation, regioselective epoxide cleavage, and stereoselective reduction of the ketone as the key steps.

Keywords : D-5'-Homo-4'-selenonucleosides

Sharpless asymmetric epoxidation

Regioselective cleavage

Stereoselective reduction

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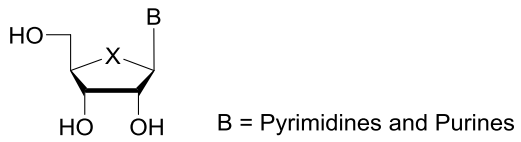
I. Introduction

4’-Selenonucleosides **1** are nonclassical nucleosides which introduce a selenium instead of oxygen in the furanose ring of classical nucleosides (Figure 1).[1,2] Unlike 4’-oxo- (**2**) or 4’-thionucleosides (**3**), they have unique sugar puckering which might arise from bulkiness of the selenium atom.[2g] Recently, studies toward the synthesis of oligonucleosides using 4’-selenonucleosides were successfully done and found a good chemical stability from those 4’-selenonucleosides for the development of biological tools or drugs.[3]



1 (X = Se): 4'-Selenonucleosides
2 (X = O): 4'-Oxonucleosides
3 (X = S): 4'-Thionucleosides

Figure 1. Structures of Bioisosteric Nucleosides **1-3**

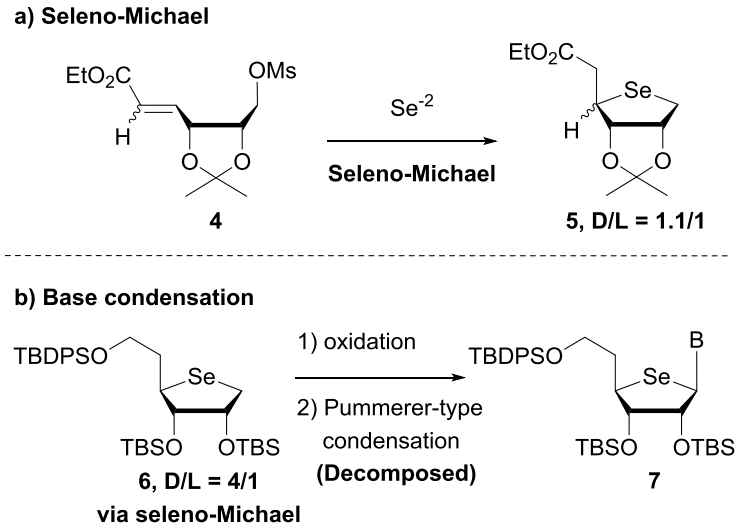
Although a variety of 4’-selenonucleosides have been synthesized by our group in an effort to develop therapeutic agents with antiviral and antitumor activities, most of the compounds proved not to possess sufficient biological properties.[2] This might be ascribed to the absence of phosphorylation resulting

from steric hindrance by the bulky selenium atom. Intrigued with this hypothesis, we decided to apply one-carbon homologation strategy in order to relieve the steric effect given by the selenium atom, and devised the synthesis of D-5'-homo-4'-selenonucleosides employing a novel seleno-Michael reaction.[2j] Just as we expected, antiviral potency was observed from D-5'-homo-4'-selenonucleosides, which could imply their phosphorylation by cellular kinases. This study found D-5'-homo-4'-selenonucleosides to be promising nucleoside analogues for further investigation of potent therapeutic agents.[2j]

Unfortunately, as shown in Scheme 1, a seleno-Michael reaction of **4** led to the formation of 1.1:1 diastereomeric mixture of the Michael adducts **5**,[2j] which was not appropriate for a comprehensive structure-activity relationship study. Furthermore, although an attempt to change the protecting group to TBS group successfully improved the diastereoselectivity of a seleno-Michael reaction giving the TBS-protected selenoribose **6** with 4:1 diastereomeric ratio, selenoribose **6** decomposed at the condensation step and failed to yield the desired base-condensed compound **7**. To address these problems, an alternative stereoselective approach to the acetonide-protected D-5-homo-4-selenoribose

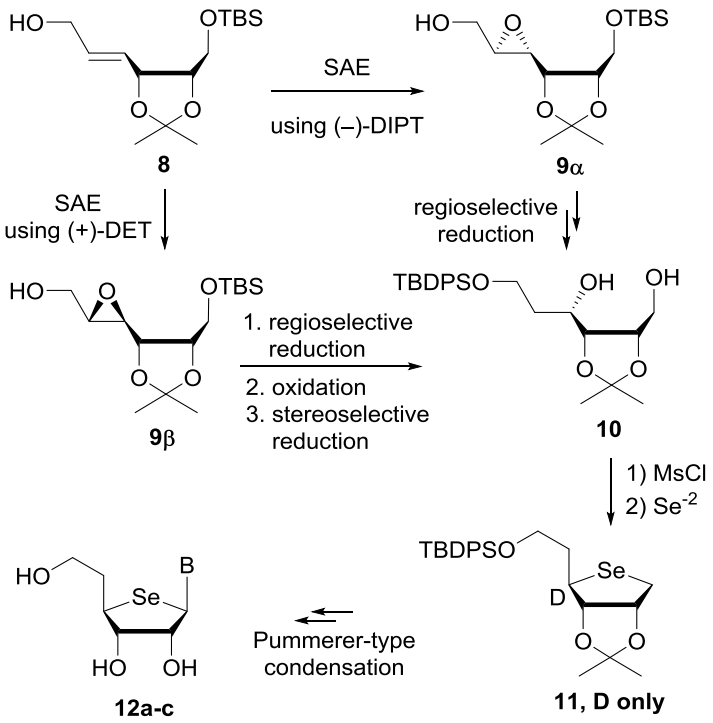
11[2j] would be desirable, and it would also provide access to large-scale preparation of D-5'-homo-4'-selenonucleosides.

Scheme 1. (a) Previous Study Toward D-5-Homo-4-selenoribose via Seleno-Michael Reaction. (b) Base Condensation of TBS-Protected Selenoribose



Herein, we disclose the stereoselective synthesis of the D-5'-homo-4'-selenonucleosides **12a-c** from 2,3-*O*-isopropylidene-L-erythrofuranose (**13**)[4a]. Sharpless asymmetric epoxidation (SAE) of **8**, regioselective cleavage of the epoxides **9α** and **9β**, and stereoselective reduction of the ketone **19** enabled the stereoselective synthesis of D-5-homo-4-selenoribose **11** which was then converted to D-5'-homo-4'-selenonucleosides **12a-c** (Scheme 2).

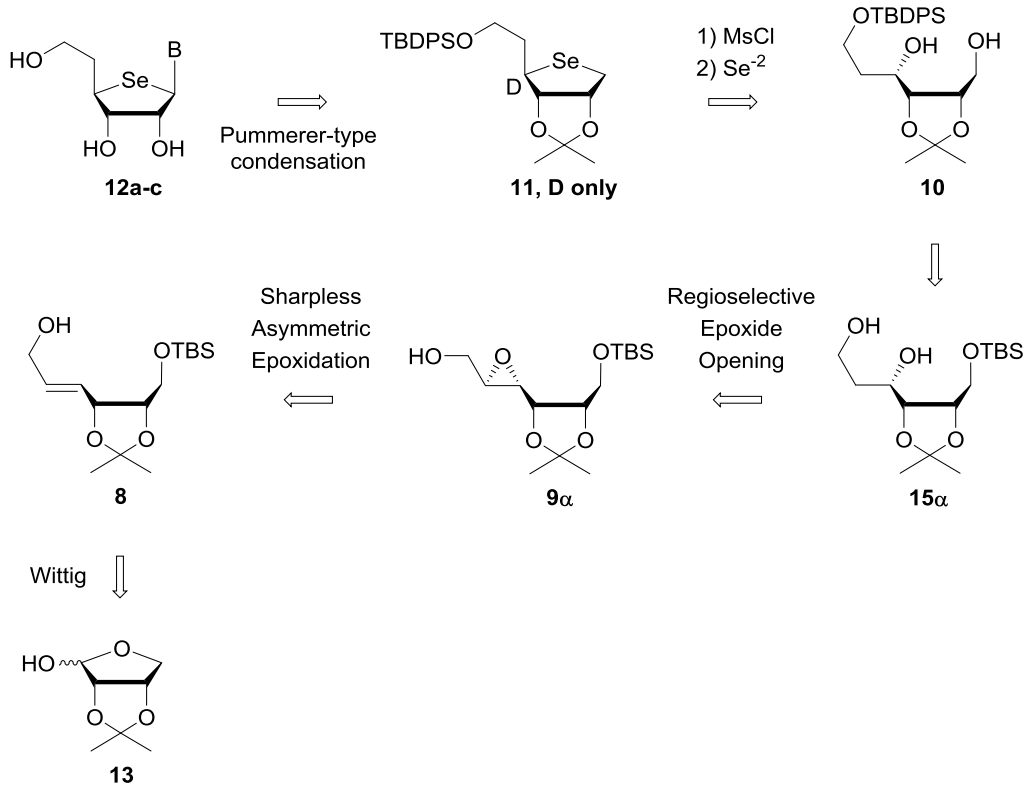
Scheme 2. Key Reactions in the Current Study



II. Results and Discussion

1. Retrosynthetic Plan

Scheme 3. Retrosynthetic Plan

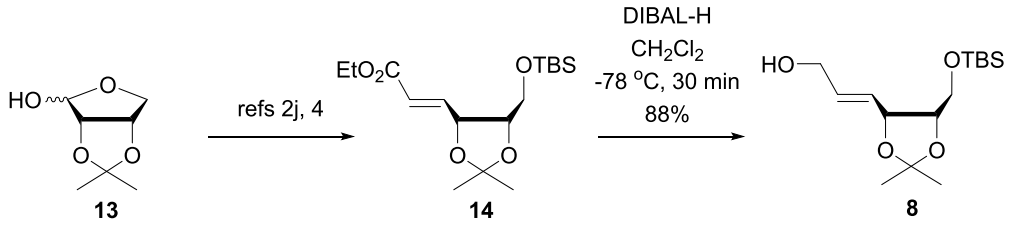


The retrosynthetic plan adopted in our approach is outlined in Scheme 3. We envisioned that D-5'-homo-4'-selenonucleosides **12a-c** could be prepared by Pummerer-type condensation of D-5-homo-4-selenoribose **11** which could be accessed by mesylation and seleno cyclization of diol **10**. Regioselective

epoxide opening would convert epoxide **9α** to diol **15α**, which would in turn serve as the precursor to diol **10**. Using Sharpless asymmetric epoxidation, epoxide **9α** could be obtained from allylic alcohol **8** which could be generated from lactol **13**[4a].

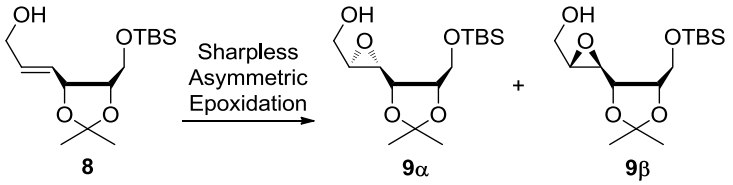
2. Synthesis

Scheme 4. Preparation of (*E*)-Allylic Alcohol **8**



To commence the synthesis, known ester **14**[4b-d] was prepared from lactol **13**[4a]. (*E*)-allylic alcohol **8**, the substrate for Sharpless asymmetric epoxidation was obtained from known ester **14**[4b-d] by treatment with DIBAL-H (Scheme 4).

Scheme 5. Sharpless Asymmetric Epoxidation



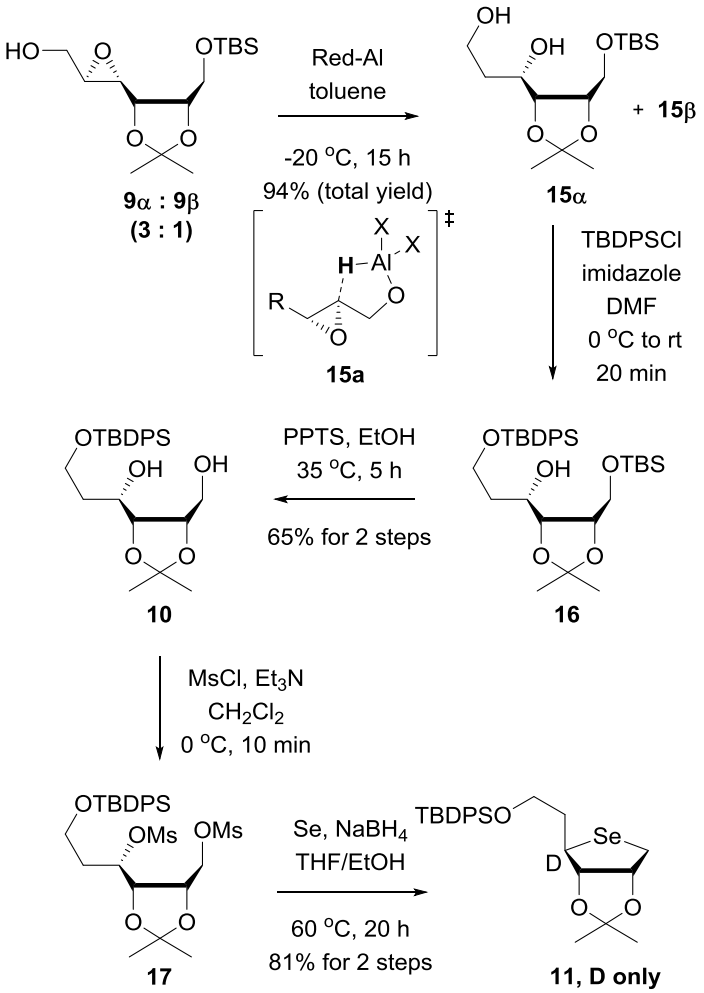
entry[a]	tartrate	temp (°C)	time (h)	ratio (9α:9β)[b]	yield (%)[c]
1	(+)-DET	−20	16	9β only	74
2	(–)-DET	−20 to 0	100	1 : 2.7	70
3	(–)-DET	−20	112	1.9 : 1	56 (66[d])
4	(–)-DIPT	−25	40	3 : 1	75

[a]Reaction conducted using chiral tartrate (1.2 equiv), Ti(O-*i*-Pr)$_4$ (1.0 equiv), TBHP (4.0 equiv), 4Å -MS, CH_2Cl_2 (0.5 M). [b]Determined by crude ^{1}H NMR. [c]Isolated total yield after silica gel chromatography. [d]Based on recovery of starting material.

As described in Scheme 5, Sharpless asymmetric epoxidation[5] was conducted with various conditions. Epoxidation of **8** with (+)-DET (entry 1) led to the formation of the β-epoxide **9β** as a sole product. This inspired us to use (–)-DET instead of (+)-DET for the exclusive preparation of the desired α-epoxide **9α**. Unfortunately, epoxidation of **8** employing (–)-DET ended up obtaining a diastereomeric mixture of α-epoxide and β-epoxide, in favor of the undesired β-isomer **9β** (entry 2) or the desired α-isomer **9α** with low diastereoselectivity (entry 3). After several experimentation, we could optimize

the diastereomeric ratio of the epoxidation using (–)-DIPT at –25 ^{o}C (entry 4), which provided a 3:1 mixture of epoxides **9α** and **9β** (Scheme 5). We tried various epoxidation methods other than Sharpless asymmetric epoxidation, such as epoxidation with $VO(acac)_2$ (0.1 equiv) and TBHP (3 equiv) in toluene[5a] at reflux or *m*-CPBA (3 equiv) and $NaHCO_3$ (1.5 equiv) in CH_2Cl_2 at room temperature, but those methods also gave the undesired **9β** as a major isomer. Furthermore, Sharpless asymmetric epoxidation conditions were unsuccessful in introducing the epoxide moiety into the (*Z*)-allylic alcohol.[5f] The diastereoselectivity of the asymmetric epoxidation has been explained by "reagent-controlled" epoxidation using a chiral tartrate-Ti(O-*i*-Pr)$_4$ complex. Epoxidation of **8** using (–)-DET (or DIPT) reflects the outcome of consonance (a mismatched pair) of the reagent preference for α-attack to generate the threo selectivity, while using (+)-DET, the reagent's preference is switched to the β-face (a matched pair) to generate the erythro selectivity.[5g] Epoxidation of carbohydrate-derived γ–alkoxy (*E*)-allylic alcohols under various conditions also depends on the structures of the carbohydrate moiety, giving quite different diastereoselectivity.[5g,j]

Scheme 6. Synthesis of D-5-Homo-4-selenoribose **11** from a 3:1 Mixture of Epoxides **9α** and **9β**



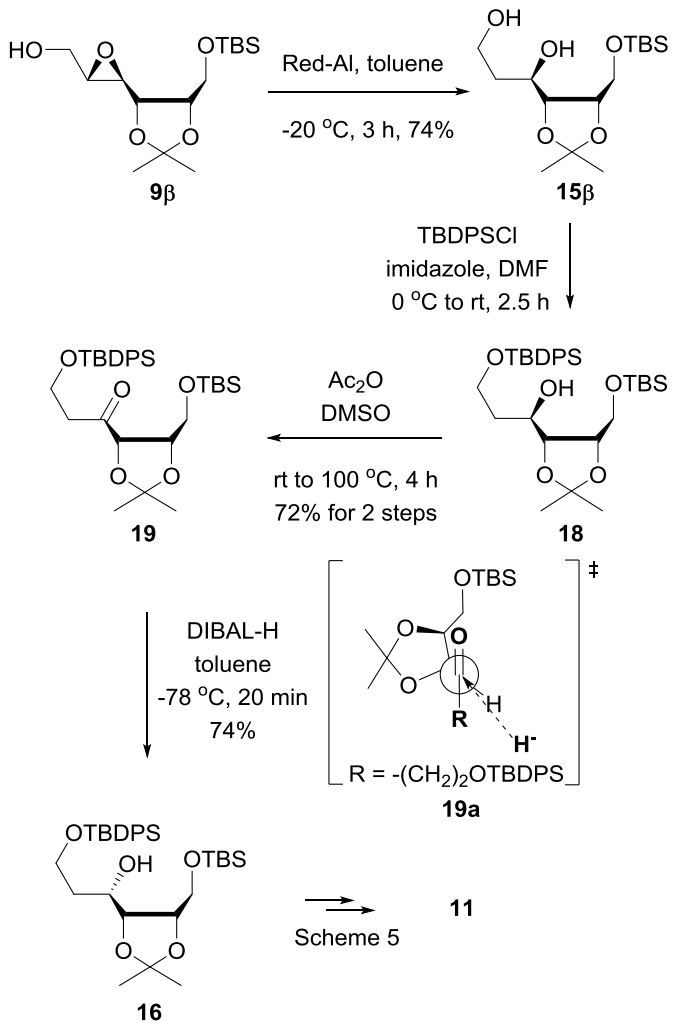
With epoxide **9α** and **9β** in hand, we next sought to open the epoxide ring to form 1,3-diol. Using Red-Al, regioselective epoxide cleavage of an inseparable 3:1 mixture of **9α** and **9β** was accomplished via intramolecular hydride

reduction to afford **15α** and **15β**, which could be separated by silica gel chromatography. This might be explained by the transition state **15a**[6], shown in Scheme 6. Upon conversion of diol **15α** to TBDPS-protected compound **16** in a regioselective manner, TBS group was selectively deprotected with PPTS to furnish diol **10**. Mesylation of the diol **10**, followed by seleno cyclization gave the key D-5-homo-4-selenoribose **11**[2j] as a single stereoisomer.

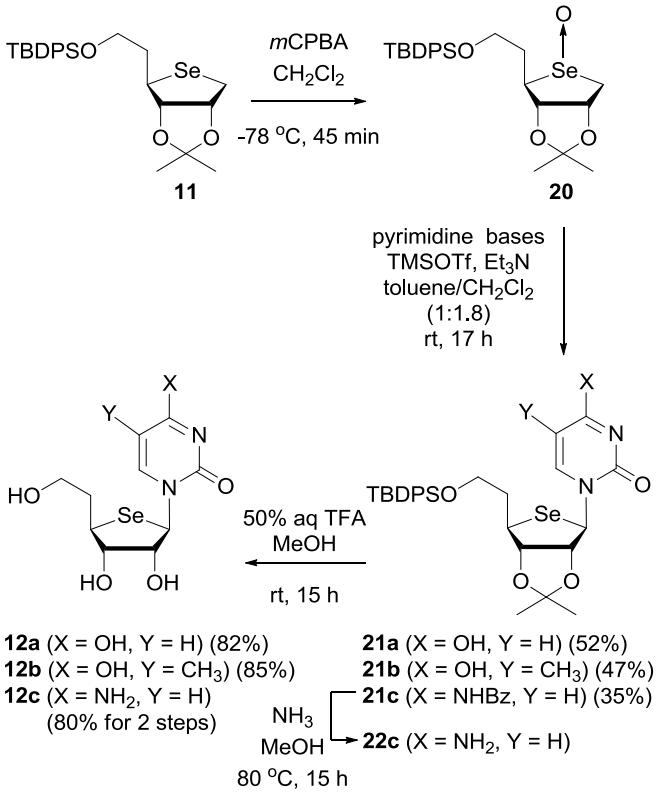
We could successfully transform the undesired epoxide **9β** from Sharpless asymmetric epoxidation (entry 1 in Scheme 5) into the same desired D-5-homo-4-selenoribose **11**, utilizing regioselective cleavage of the epoxide **9β**, selective protection and Albright-Goldman oxidation[8] followed by stereoselective reduction of the ketone **19** to obtain **16** (Scheme 7). Tactics other than this turned out to be problematic. For instance, Mitsunobu reaction of **18** resulted in the recovery of starting material. Also, bromination of **18** with inversion of configuration upon treatment with CBr_4 and Ph_3P led to the formation of the oxacyclized compound accompanied by TBS deprotection. Thus, we turned our attention to the stereoselective DIBAL-H reduction of the ketone **19**, based on the Felkin-Ahn transition state **19a**[7] shown in Scheme 7. It is remarkable that TBS migration which occurred during the DIBAL-H reduction in THF as

solvent was prevented by changing the solvent from THF to the nonpolar toluene. The key intermediate **16** was then converted to the same D-5-homo-4-selenoribose **11** by the synthetic route described in Scheme 6.

Scheme 7. Synthesis of D-5-Homo-4-selenoribose **11** from Epoxide **9β**



Scheme 8. Stereoselective Synthesis of D-5'-Homo-4'-selenonucleosides **12a-c**



Oxidation of the key D-5-homo-4-selenoribose **11** furnished the corresponding selenoxide **20**. Pummerer-type condensation of **20** with each of uracil, thymine, and N^4-benzoylcytosine was conducted to give the desired β-nucleosides **21a-c**.[2j] Subsequent treatment of **21c** with methanolic ammonia resulted in the deprotection of benzoyl group to afford **22c**. Completion of the synthesis required removal of TBDPS group and isopropylidene group from

21a, **21b**, and **22c**, which was accomplished using 50% aqueous TFA to provide the final nucleosides **12a-c**, respectively[2j] (Scheme 8).

III. Conclusion

In conclusion, we have established a stereoselective synthesis of D-5'-homo-4'-selenonucleosides from 2,3-*O*-isopropylidene-L-erythrofuranose (**13**). The key intermediate D-5-homo-4-selenoribose **11** was obtained exclusively, which would be a major improvement over the previous method using seleno-Michael reaction that showed only 1.1:1 diastereoselectivity. This result also allows large-scale preparation of 4'-selenonucleosides. Key features of the current synthetic route toward D-5-homo-4-selenoribose include Sharpless asymmetric epoxidation, regioselective epoxide cleavage, stereoselective ketone reduction, and seleno cyclization. We successfully converted the key intermediate **11** to D-5'-homo-4'-selenonucleosides **12a-c** through Pummerer-type condensation. These **12a-c** will serve as important building blocks for further research in development of nucleoside-based therapeutic agents.

IV. Experimental Section

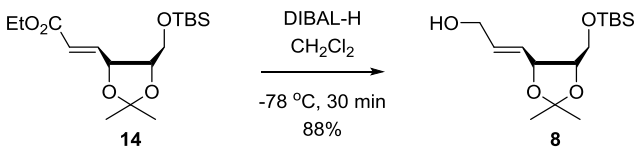
1. General Procedures

Proton (^{1}H) and carbon (^{13}C) NMR spectra were obtained on a Jeol JNM-LA300 (300/75 MHz), Bruker AV 400 (400/100 MHz), Bruker AMX 500 (500/125 MHz), Jeol JNM-ECA600 (600/150 MHz). Chemical shifts are reported in ppm units with Me_4Si or $CHCl_3$ as the internal standard. All reactions were routinely carried out under an inert atmosphere of dry nitrogen. Reactions were checked by thin layer chromatography (Kieselgel 60 F254, Merck). Spots were detected by viewing under a UV light, and by colorizing with charring after dipping in a *p*-anisaldehyde solution or phosphomolybdic acid solution. In aqueous work-up, all organic solutions were dried over anhydrous magnesium sulfate and filtered prior to rotary evaporation at water pump pressure. The crude compounds were purified by column chromatography on a silica gel (Kieselgel 60, 70-230 mesh, Merck). Unless otherwise noted, materials were obtained from commercial suppliers and were used without purification. All solvents were purified and dried by standard techniques just before use. THF and Et_2O were freshly distilled from sodium and benzophenone. Methylene chloride, toluene, and benzene were purified by

refluxing with CaH_2. Hexanes and ethylacetate were purified by simple distillation.

2. Experimental Procedures

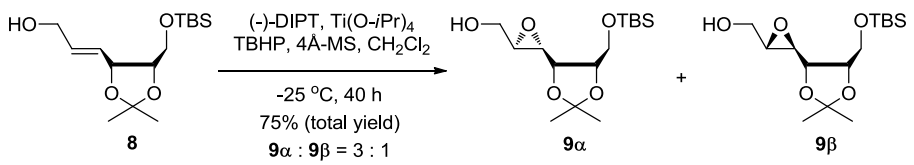
Preparation of (*E*)-allylic alcohol 8



To a cooled (–78 ^{o}C) solution of the known ester **14** (1.8 g, 5.161 mmol) in anhydrous CH_2Cl_2 (34 mL, 0.15 M) was dropwise added DIBAL-H (15.5 mL, 1.0 M solution in CH_2Cl_2, 15.5 mmol) under N_2. After being stirred at the same temperature for 30 min, the reaction mixture was quenched with saturated aqueous Rochelle's solution (50 mL), diluted with CH_2Cl_2 (50 mL), and stirred at room temperature for additional 1 h. The layers were separated, and the aqueous layer was extracted with CH_2Cl_2 (2 × 50 mL). The combined organic layers were washed successively with H_2O and saturated brine, dried over anhydrous $MgSO_4$, filtered, and concentrated *in vacuo.* The residue was purified by column chromatography (silica gel, hexanes/EtOAc, 8/1 to 5/1) to give (*E*)-allylic alcohol **8** (1.4 g, 88%): R_f 0.30 (hexanes/EtOAc, 3/1); colorless

oil; $[\alpha]_D^{20}$ = +1.16 (*c* 3.35, CH_3OH); IR (neat) 3429, 2931, 2858, 1726, 1464, 1381, 1255, 1099, 838, 779 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 5.90-5.97 (m, 1 H), 5.74-5.80 (m, 1 H), 4.64 (t, *J* = 6.8 Hz, 1 H), 4.13-4.18 (m, 3 H), 3.59 (d, *J* = 6.2 Hz, 2 H), 1.44 (s, 3 H), 1.34 (s, 3 H), 0.85 (s, 9 H), 0.03 (s, 3 H), 0.02 (s, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 133.0, 126.7, 108.5, 78.5, 77.8, 63.0, 62.1, 27.8, 25.8, 25.3, 18.2, -5.4, -5.4; HRMS (FAB) found 301.1835 [calcd for $C_{15}H_{29}O_4Si^+$ $(M+H)^+$ 301.4796].

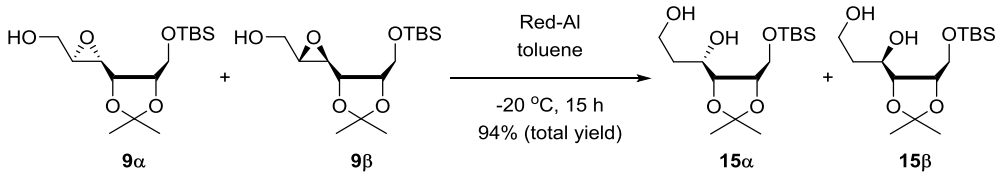
Preparation of α-epoxide 9α



To a cooled (–25 °C) solution of (*E*)-allylic alcohol **8** (3.1 g, 10.315 mmol) and molecular sieve 4Å (1.0 g) in anhydrous CH_2Cl_2 (21 mL, 0.5 M) was dropwise added (–)-Diisopropyl D-tartrate (2.6 mL, 12.378 mmol), followed by addition of titanium (IV) isopropoxide (3.1 mL, 10.315 mmol), and the resulting mixture was stirred for 10 minutes at the same temperature. To the mixture was dropwise added *tert*-butyl hydroperoxide (7.5 mL, 5.5 M solution in decane, 41.259 mmol). After being stirred at the same temperature for 40 h,

the reaction mixture was quenched with saturated aqueous Rochelle's solution (50 mL) and saturated aqueous sodium thiosulfate (50 mL), diluted with CH_2Cl_2 (50 mL), and stirred at room temperature for additional 1 h. The reaction mixture was filtered through a pad of Celite. The layers of the filtrate were separated and the aqueous layer was extracted with CH_2Cl_2 (2 × 50 mL). The combined organic layers were washed successively with H_2O and saturated brine, dried over anhydrous $MgSO_4$, filtered, and concentrated *in vacuo*. The residue was purified by column chromatography (silica gel, hexanes/EtOAc, 8/1 to 5/1) to give α-epoxide **9α** and β-epoxide **9β** (2.5 g, 75% total yield, 9α/9β = 3:1 by ^{1}H NMR analysis): **For α-epoxide 9α**; R_f 0.28 (hexanes/EtOAc, 3/1); colorless oil; $[\alpha]_D^{20}$ = +30.10 (*c* 2.88, CH_3OH); IR (neat) 3464, 2930, 2858, 1472, 1381, 1254, 1092, 838, 779 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.19-4.23 (m, 1 H), 3.96 (t, *J* = 6.1 Hz, 1 H), 3.76-3.88 (m, 3 H), 3.60-3.67 (m, 1 H), 3.17 (dd, *J* = 2.2, 5.8 Hz, 1 H), 3.04-3.07 (m, 1 H), 1.94 (dd, *J* = 5.3, 7.5 Hz, 1 H), 1.44 (s, 3 H), 1.31 (s, 3 H), 0.86 (s, 9 H), 0.06 (s, 6 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 109.2, 77.6, 77.3, 61.9, 61.2, 54.7, 54.1, 27.2, 25.8, 25.2, 18.3, -5.4; HRMS (FAB) found 319.1941 [calcd for $C_{15}H_{31}O_5Si^+$ $(M+H)^+$ 319.4948]; **For β-epoxide 9β**; see page 27.

Preparation of diol 15α

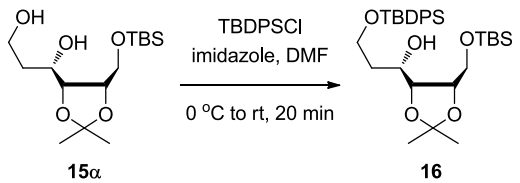


(**9α** : **9β** = 3 : 1, mixture)

To a cooled (–20 °C) solution of mixture of α-epoxide **9α** and β-epoxide **9β** (2.2 g, 6.853 mmol) in anhydrous toluene (27 mL, 0.25 M) was dropwise added Red-Al (8.0 mL, 60 wt% solution in toluene, 20.657 mmol) under N_2. After being stirred at the same temperature for 15 h, the reaction mixture was quenched with saturated aqueous Rochelle's solution (50 mL), diluted with EtOAc (50 mL), and stirred at room temperature for additional 1 h. The layers were separated, and the aqueous layer was extracted with EtOAc (2 × 50 mL). The combined organic layers were washed successively with H_2O and saturated brine, dried over anhydrous $MgSO_4$, filtered, and concentrated *in vacuo.* The residue was purified by column chromatography (silica gel, hexanes/EtOAc, 6/1 to 2/1) to give diol **15α** (1.6 g, 72%) and diol **15β** (486 mg, 22%): **For diol 15α**; R_f 0.20 (hexanes/EtOAc, 2/1); colorless oil; $[\alpha]_D^{20}$ = –11.05 (*c* 6.05, CH_3OH); IR (neat) 3442, 2932, 2858, 1472, 1381, 1254, 1094, 838, 779 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$) δ 4.08-4.13 (m, 1 H), 4.00-4.05 (m, 2 H), 3.89 (dd,

J = 7.3, 11.0 Hz, 1 H), 3.77-3.85 (m, 2 H), 3.70 (dd, *J* = 3.7, 11.0 Hz, 1 H), 3.35 (d, *J* = 4.1 Hz, 1 H), 2.73-2.77 (m, 1 H), 1.84-1.90 (m, 1 H), 1.74-1.79 (m, 1 H), 1.45 (s, 3 H), 1.34 (s, 3 H), 0.87 (s, 9 H), 0.07 (s, 6 H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 108.2, 79.9, 77.1, 69.1, 61.5, 61.2, 36.0, 27.2, 25.8, 25.2, 18.3, -5.5; HRMS (FAB) found 321.2101 [calcd for $C_{15}H_{32}O_5Si^+$ $(M+H)^+$ 321.5108]; **For diol 15β**: see page 28.

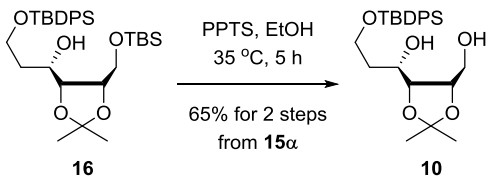
Preparation of 16



To a cooled (0 °C) solution of diol **15α** (194.0 mg, 0.605 mmol) in anhydrous DMF (3 mL, 0.2 M) was added TBDPSCl (0.20 mL, 0.773 mmol), followed by the addition of imidazole (82 mg, 1.210 mmol) in one portion under N_2. After being stirred at room temperature for 20 min, the reaction mixture was quenched with NH_4Cl (10 mL) at 0 °C, and diluted with EtOAc (10 mL). The layers were separated, and the aqueous layer was extracted with EtOAc (2 × 30 mL). The combined organic layers were washed successively with H_2O and saturated brine, dried over anhydrous $MgSO_4$, filtered, and

concentrated *in vacuo*. The residue was purified by column chromatography (silica gel, hexanes/EtOAc, 30/1 to 20/1) to give **16** (559.9 mg; the product was contaminated with TBDPSCl): R_f 0.34 (hexanes/EtOAc, 10/1); colorless oil; $[\alpha]_D^{20}$ = –23.48 (*c* 0.53, CH_3OH); IR (neat) 3490, 2931, 2858, 1472, 1428, 1381, 1255, 1109, 838, 703 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.64-7.67 (m, 4 H), 7.34-7.42 (m, 6 H), 4.07-4.14 (m, 2 H), 4.03-4.06 (m, 1 H), 3.91 (ddd, *J* = 7.3, 10.8 Hz, 1 H), 3.86 (dd, *J* = 4.7, 10.2 Hz, 1 H), 3.78-3.82 (m, 1 H), 3.70 (dd, *J* = 4.3, 10.8 Hz, 1 H), 3.29 (d, *J* = 4.0 Hz, 1 H), 1.77-1.88 (m, 2 H), 1.46 (s, 3 H), 1.34 (s, 3 H), 1.03 (s, 9 H), 0.86 (s, 9 H), 0.05 (s, 6 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 135.6, 135.5, 133.6, 133.5, 129.6, 127.7, 108.1, 79.9, 77.4, 67.1, 61.9, 61.6, 36.6, 27.5, 26.8, 25.9, 25.2, 19.1, 18.3, -5.4, -5.4; HRMS (FAB) found 559.3275 [calcd for $C_{31}H_{51}O_5Si_2^+$ $(M+H)^+$ 559.9139].

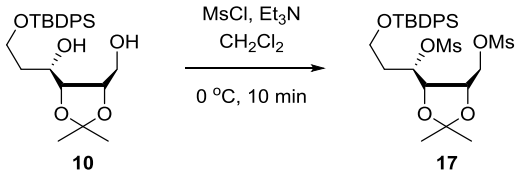
Preparation of diol 10



To a stirred solution of **16** (contaminated with TBDPSCl) in EtOH (3.0 mL, 0.2 M) was added in Pyridinium *p*-toluenesulfonate (63.0 mg, 0.252 mmol) one

portion at room temperature under N_2. After being heated at 35 °C (bath temperature) with stirring for 5 h, the reaction mixture was quenched with triethylamine (10 mL), and concentrated *in vacuo*. The residue was purified by column chromatography (silica gel, hexanes/EtOAc, 5/1 to 3/1) to give diol **10** (174 mg, 65%, isolated yield for 2 steps): R_f 0.38 (hexanes/EtOAc, 2/1); colorless oil; $[\alpha]_D^{20}$ = –12.45 (*c* 3.00, CH_3OH);–IR (neat) 3441, 2932, 1472, 1428, 1380, 1245, 1216, 1111, 822, 739, 703 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.64-7.68 (m, 4 H), 7.35-7.44 (m, 6 H), 4.19 (ddd, *J* = 5.2, 5.2, 5.2 Hz, 1 H), 4.02-4.08 (m, 2 H), 3.88-3.94 (m, 1 H), 3.70-3.84 (m, 3 H), 3.25 (d, *J* = 3.2 Hz, 1 H), 3.02 (s, 1 H), 1.82-1.90 (m, 1 H), 1.72-1.79 (m, 1 H), 1.51 (s, 3 H), 1.36 (s, 3 H), 1.04 (s, 9 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 135.5, 135.5, 133.2, 133.1, 129.7, 127.7, 127.7, 108.3, 79.4, 77.4, 67.4, 61.6, 61.1, 36.7, 27.3, 26.8, 25.2, 19.1; HRMS (FAB) found 444.2113 [calcd for $C_{25}H_{36}O_5Si^+$ $(M+H)^+$ 444.2346].

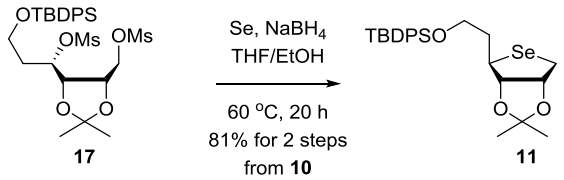
Preparation of 17



To a cooled (0 °C) solution of **10** (1.0 g, 2.272 mmol) in anhydrous CH_2Cl_2

(11 mL, 0.2 M) was dropwise added successively methanesulfonyl chloride (0.90 mL, 11.618 mmol) and triethylamine (1.6 mL, 11.360 mmol) under N_2. After being stirred at the same temperature for 10 min, the reaction mixture was quenched with saturated aqueous NH_4Cl (50 mL), and diluted with CH_2Cl_2 (50 mL). The layers were separated, and the aqueous layer was extracted with CH_2Cl_2 (2 × 50 mL). The combined organic layers were washed successively with H_2O and saturated brine, dried over anhydrous $MgSO_4$, filtered, and concentrated *in vacuo*. The crude **17** was used for the next step without further purification: R_f 0.30 (hexanes/EtOAc, 3/1).

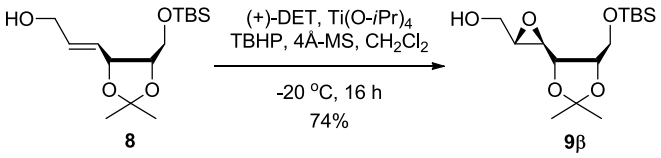
Preparation of D-5-homo-4-selenoribose 11



To a cooled (0 °C) suspension of selenium powder (720.0 mg, 9.119 mmol) in EtOH (60 mL) was slowly added $NaBH_4$ (1.0 g, 26.434 mmol) in 10 portions, until the color of the reaction mixture changed from black suspension to colorless solution. To the above-generated solution was dropwise added crude **17** in anhydrous THF (27 mL). After being heated at 60 °C with stirring for 20

h, the reaction mixture was cooled to room temperature and diluted with H_2O and EtOAc (50 mL). The layers were separated, and the aqueous layer was extracted with EtOAc (2 × 50 mL). The combined organic layers were washed successively with H_2O and saturated brine, dried over anhydrous $MgSO_4$, filtered, and concentrated *in vacuo.* The residue was purified by column chromatography (silica gel, hexanes/EtOAc, 50/1 to 40/1) to give D-5-homo-4-selenoribose **11** (895.0 mg, 81%, isolated yield for 2 steps): R_f 0.29 (hexanes/EtOAc, 15/1); pale yellow syrup; $[\alpha]_D^{20}$ = +72.37 (*c* 2.23, $CHCl_3$; UV (CH_3OH) λ_{max} 232.5 nm; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.65-7.67 (m, 4 H), 7.35-7.43 (m, 6 H), 4.88 (ddd, *J* = 3.0, 5.6, 5.6 Hz, 1 H), 4.53 (dd, *J* = 3.4, 5.8 Hz, 1 H), 3.73–3.76 (m, 2 H), 3.65-3.69 (m, 1 H), 3.03 (dd, *J* = 5.5, 11.9 Hz, 1 H), 2.95 (dd, *J* = 3.0, 11.9 Hz, 1 H), 2.00-2.06 (m, 1 H), 1.64-1.70 (m, 1 H), 1.51 (s, 3 H), 1.30 (s, 3 H), 1.04 (s, 9 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 135.6, 135.6, 133.7, 133.6, 129.6, 129.6, 129.6, 127.6, 111.0, 90.4, 84.2, 45.7, 36.9, 27.7, 27.1, 26.9, 25.0, 19.2; HRMS (ESI) found 511.1346 [cald for $C_{25}H_{34}O_3SeSiNa^+$ $(M+Na)^+$ 511.1348].

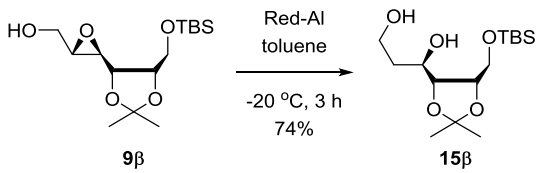
Preparation of β-epoxide 9β



To a cooled (–20 °C) solution of (*E*)-allylic alcohol **8** (1.739 g, 5.749 mmol) and molecular sieve 4Å (580 mg) in anhydrous CH_2Cl_2 (19 mL, 0.3 M) was dropwise added successively (+)-diethyl tartrate (1.20 mL, 7.016 mmol) and titanium isopropoxide (1.7 mL, 5.749 mmol), and the resulting mixture was stirred for 10 minutes at the same temperature. To the mixture was dropwise added *tert*-butyl hydroperoxide (4.2 mL, 5.5 M solution in decane, 22.996 mmol). After being stirred at the same temperature for 16 h, the reaction mixture was quenched with saturated aqueous Rochelle's solution (50 mL) and saturated aqueous sodium thiosulfate (50 mL), diluted with CH_2Cl_2 (80 mL), and stirred at room temperature for additional 1 h. The reaction mixture was filtered through a pad of Celite. The layers of the filtrate were separated and the aqueous layer was extracted with CH_2Cl_2 (2 × 50 mL). The combined organic layers were washed successively with H_2O and saturated brine, dried over anhydrous $MgSO_4$, filtered, and concentrated *in vacuo*. The residue was purified by column chromatography (silica gel, hexanes/EtOAc, 6/1 to 2/1) to give β-epoxide **9β** (1.354 g, 74%): R_f 0.28 (hexanes/EtOAc, 3/1); colorless oil;

$[\alpha]_D^{20}$ = –11.20 (*c* 2.64, CH_3OH); IR (neat) 3462, 2932, 2858, 1472, 1382, 1254, 1217, 1144, 1080, 839, 778 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 4.24 (ddd, *J* = 6.2, 6.2, 6.2 Hz, 1 H), 4.04 (t, 1 H), 3.84 (d, *J* = 12.7 Hz, 1 H), 3.80 (dd, *J* = 6.6, 11.2 Hz, 1 H), 3.74 (dd, *J* = 5.2, 11.0 Hz, 1 H), 3.61-3.67 (m, 1 H), 3.18 (d, *J* = 4.4 Hz, 2 H), 2.11 (s, 1 H), 1.41 (s, 3 H), 1.31 (s, 3 H), 0.86 (s, 9 H), 0.05 (s, 6 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 109.2, 77.9, 76.0, 61.8, 61.5, 56.1, 53.1, 27.5, 25.8, 25.0, 18.2, -5.4, -5.4; HRMS (FAB) found 321.2101 [calcd for $C_{15}H_{32}O_5Si^+$ $(M+H)^+$ 321.5108].

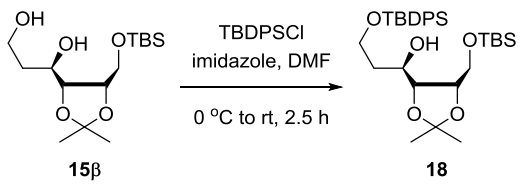
Preparation of diol 15β



To a cooled (–20 °C) solution of β-epoxide **9β** (0.578 g, 1.185 mmol) in anhydrous toluene (4.7 mL, 0.25 M) was dropwise added Red-Al (1.4 mL, 60 wt% solution in toluene, 3.615 mmol) under N_2. After being stirred at the same temperature for 3 h, the reaction mixture was quenched with saturated aqueous Rochelle's solution (50 mL), diluted with EtOAc (50 mL), and stirred at room temperature for additional 1 h. The layers were separated, and the aqueous layer

was extracted with EtOAc (2 × 50 mL). The combined organic layers were washed successively with H_2O and saturated brine, dried over anhydrous $MgSO_4$, filtered, and concentrated *in vacuo.* The residue was purified by column chromatography (silica gel, hexanes/EtOAc, 6/1 to 2/1) to give diol **15β** (0.281 g, 74%); R_f 0.35 (hexanes/EtOAc, 2/1); colorless oil; $[\alpha]_D^{20} = -1.44$ (*c* 6.80, CH_3OH); IR (neat) 3457, 2932, 2859, 1471, 1381, 1254, 1219, 1084, 838, 781 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 4.32 (t, *J* = 2.1 Hz, 1 H), 4.18-4.23 (m, 1 H), 4.05 (d, *J* = 5.3, 9.4 Hz, 1 H), 3.95-4.01 (m, 1 H), 3.79-3.84 (dd, *J* = 4.8, 10.4 Hz, 2 H), 3.77 (t, *J* = 10.4 Hz, 1 H), 3.57 (dd, *J* = 3.4, 10.4 Hz, 1 H), 2.97 (t, *J* = 4.8 Hz, 1 H), 1.91-2.10 (m, 1 H), 1.72-1.83 (m, 1 H), 1.32 (s, 3 H), 1.29 (s, 3 H), 0.87 (s, 9 H), 0.09 (d, *J* = 2.9 Hz, 6 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 108.5, 80.4, 77.1, 69.9, 61.9, 61.4, 35.8, 27.9, 25.7, 25.2, 18.1, -5.6, -5.7; HRMS (FAB) found 321.2097 [calcd for $C_{15}H_{32}O_5Si^+$ $(M+H)^+$ 321.5108].

Preparation of 18

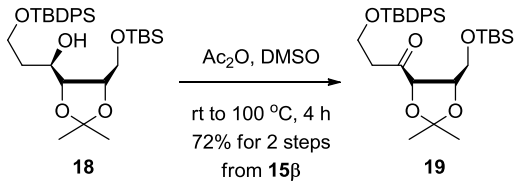


To a cooled (0 °C) solution of diol **15β** (952.0 mg, 2.970 mmol) in

anhydrous DMF (12 mL, 0.25 M) was added TBDPSCl (0.90 mL, 3.454 mmol), followed by the addition of imidazole (404.0 mg, 5.940 mmol) in one portion under N_2. After being stirred at room temperature for 2.5 h, the reaction mixture was quenched with NH_4Cl (50 mL) at 0 °C, and diluted with EtOAc (50 mL). The layers were separated, and the aqueous layer was extracted with EtOAc (2 × 50 mL). The combined organic layers were washed successively with H_2O and saturated brine, dried over anhydrous $MgSO_4$, filtered, and concentrated *in vacuo*. The residue was purified by column chromatography (silica gel, hexanes/EtOAc, 30/1) to give **18** (1.7 g; the product was contaminated with TBDPSCl): R_f 0.39 (hexanes/EtOAc, 10/1); colorless oil; $[\alpha]_D^{20}$ = +5.19 (*c* 1.50, CH_3OH); IR (neat) 3483, 2956, 2931, 2858, 1472, 1254, 1111, 1084, 837, 703 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.65-7.70 (m, 4 H), 7.34-7.41 (m, 6 H), 4.23 (ddd, *J* = 4.2, 4.2, 9.1 Hz, 1 H), 4.06-4.10 (m, 1 H), 4.01 (dd, *J* = 5.5, 9.1 Hz, 1 H), 3.91-3.96 (m, 2 H), 3.81-3.85 (m, 2 H), 3.62 (dd, *J* = 3.6, 10.5 Hz, 1 H), 2.05-2.11 (m, 1 H), 1.64-1.70 (m, 1 H), 1.37 (s, 3 H), 1.31 (s, 3 H), 1.03 (s, 9 H), 0.89 (s, 9 H), 0.10 (s, 6 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 135.6, 133.9, 133.9, 129.5, 127.6, 108.3, 80.7, 77.5, 66.3, 62.1, 60.7, 36.8, 28.1, 26.8, 25.8, 25.4, 19.2, 18.2, -5.6, -5.6; HRMS (FAB) found 559.3275 [calcd for

$C_{31}H_{51}O_5Si_2^+$ $(M+H)^+$ 559.9139].

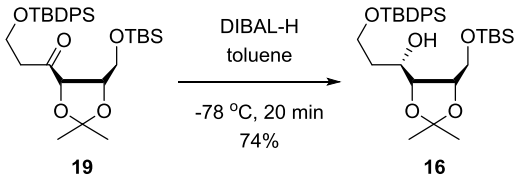
Preparation of 19



To a stirred solution of **18** (contaminated with TBDPSCl) in anhydrous dimethyl sulfoxide (15 mL, 0.2 M) was dropwise added acetic anhydride (0.90 mL, 9.546 mmol) at room temperature under N_2. After being heated at 100 °C for 4 h, the reaction mixture was quenched with saturated aqueous $NaHCO_3$ (50 mL), and diluted with EtOAc (50 mL). The layers were separated, and the aqueous layer was extracted with EtOAc (2 × 50 mL). The combined organic layers were washed successively with H_2O and saturated brine, dried over anhydrous $MgSO_4$, filtered, and concentrated *in vacuo.* The residue was purified by column chromatography (silica gel, hexanes/EtOAc, 40/1) to give **19** (1.191 g, 72%, isolated yield for 2 steps): R_f 0.32 (hexanes/EtOAc, 15/1); colorless oil; $[\alpha]_D^{20}$ = –15.00 (*c* 1.05, CH_3OH); IR (neat) 2956, 2931, 2857, 1716, 1472, 1428, 1382, 1254, 1111, 836, 703 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.59-7.66 (m, 4 H), 7.32-7.41 (m, 6 H), 4.53 (d, *J* = 7.8 Hz, 1 H),

4.35-4.39 (m, 1 H), 3.90-3.93 (m, 2 H), 3.65 (dd, *J* = 4.5, 11.2 Hz, 1 H), 3.59 (dd, *J* = 3.6, 11.2 Hz, 1 H), 2.90-2.97 (m, 1 H), 2.79-2.85 (m, 1 H), 1.55 (s, 3 H), 1.33 (s, 3 H), 1.02 (s, 9 H), 0.82 (s, 9 H), -0.01 (s, 6 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 207.8, 135.6, 135.5, 133.6, 133.5, 129.6, 127.6, 109.6, 81.1, 78.8, 61.5, 59.4, 43.4, 26.9, 26.8, 25.9, 24.8, 19.1, 18.4, -5.4, -5.6; HRMS (FAB) found 556.3091 [calcd for $C_{31}H_{48}O_5Si_2^+$ $(M+H)^+$ 556.3094].

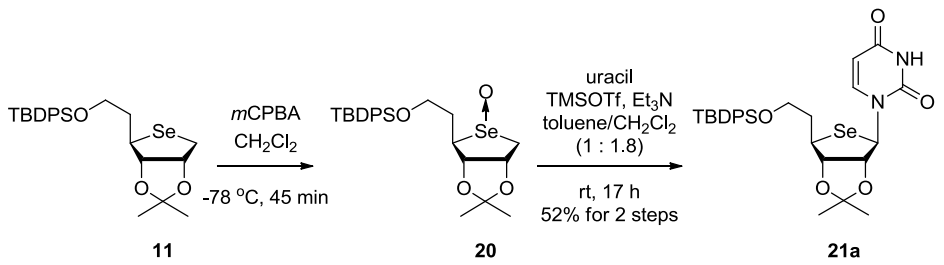
Preparation of 16



To a cooled (–78 °C) solution of **19** (870.0 mg, 1.562 mmol) in anhydrous toluene (8 mL, 0.2 M) was dropwise added DIBAL-H (3.1 mL, 1.0 M solution in hexanes, 3.1 mmol) under N_2. After being stirred at the same temperature for 20 min, the reaction mixture was quenched with saturated aqueous Rochelle's solution (30 mL), diluted with EtOAc (30 mL), and stirred at room temperature for additional 1 h. The layers were separated, and the aqueous layer was extracted with EtOAc (2 × 50 mL). The combined organic layers were washed successively with H_2O and saturated brine, dried over anhydrous $MgSO_4$,

filtered, and concentrated *in vacuo.* The residue was purified by column chromatography (silica gel, hexanes/EtOAc, 40/1 to 33/1) to give **16** (643.0 mg, 74%).

[General Procedure-(Base Condensation)]-Preparation of 21a



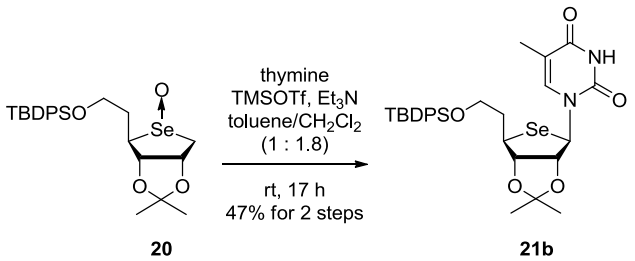
[Oxidation] To a stirred solution of **11** (550 mg, 1.133 mmol) in anhydrous CH_2Cl_2 (25.0 mL) was dropwise added a solution of 3-chloroperbenzoic acid (279.3 mg, 1.246 mmol, 77%) in CH_2Cl_2 (5.0 mL) at –78 ℃ under N_2. After being stirred at the same temperature for 45 min, the reaction mixture was quenched with saturated aqueous $NaHCO_3$ (30 mL) and diluted with CH_2Cl_2 (30 mL). The layers were separated, and the aqueous layer was extracted with CH_2Cl_2 (2 × 50 mL). The combined organic layers were washed successively with H_2O and saturated brine, dried over anhydrous $MgSO_4$, filtered, and concentrated *in vacuo* under 10 ^oC to give the crude **20** as colorless syrup. The

residue was taken to next step without further purification.

[Pummerer-type condensation] To a suspension of uracil (0.239 mg, 2.14 mmol) in anhydrous toluene (5.5 mL) was dropwise added successively triethylamine (0.60 mL, 4.31 mmol) and trimethylsilyl trifluoromethanesulfonate (1.10 mL, 6.08 mmol) at room temperature under N_2. After being stirred at the same temperature for 45 min, the above-generated silylated uracil was diluted with anhydrous CH_2Cl_2 (5 mL) and was dropwise added to the crude solution of selenoxide **20** in CH_2Cl_2 (5 mL) at room temperature. To initiate Pummerer reaction, the reaction mixture was dropwise added additional triethylamine (0.3 mL, 2.152 mmol) in toluene (0.4 mL) at 0 ^{o}C. After being stirred at the room temperature for 16 h, the reaction mixture was quenched with saturated aqueous $NaHCO_3$ (30 mL) and diluted with CH_2Cl_2 (30 mL). The layers were separated, and the aqueous layer was extracted with CH_2Cl_2 (2 × 50 mL). The combined organic layers were washed successively with H_2O and saturated brine, dried over anhydrous $MgSO_4$, filtered, and concentrated *in vacuo*. The residue was purified by flash column chromatography (silica gel, hexanes/EtOAc, 2/1) to give **21a** (326 mg, 52%); pale yellow syrup; $[\alpha]_D^{20}$ = –17.76 (*c* 1.16, $CHCl_3$); UV (CH_3OH) λ_{max} 265.5

nm; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.74 (d, *J* = 8.1 Hz, 1 H), 7.65-7.67 (m, 4 H), 7.38-7.45 (m, 6 H), 6.26 (d, *J* = 3.4 Hz, 1 H), 5.74 (d, *J* = 8.0 Hz, 1 H), 4.94 (dd, *J* = 3.4, 5.8 Hz, 1 H), 4.77 (dd, *J* = 5.5, 5.5 Hz, 1 H), 3.98 (ddd, *J* = 5.2, 5.2, 10.2 Hz, 1 H), 3.73-3.77 (m, 1 H), 3.64-3.68 (m, 1 H), 2.30-2.37 (m, 1 H), 1.97-2.04 (m, 1 H), 1.52 (s, 3 H), 1.29 (s, 3 H), 1.03 (s, 9 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.7, 152.6, 145.3, 137.5, 137.5, 135.4, 135.3, 131.8, 131.7, 129.7, 129.6, 114.2, 104.5, 91.4, 90.9, 65.0, 60.4, 48.3, 40.0, 29.1, 28.2, 26.5, 20.8; HRMS (ESI) found 623.1455 [calc for $C_{29}H_{36}N_2O_5SeSiNa^+$ $(M+Na)^+$ 623.1456].

Preparation of 21b

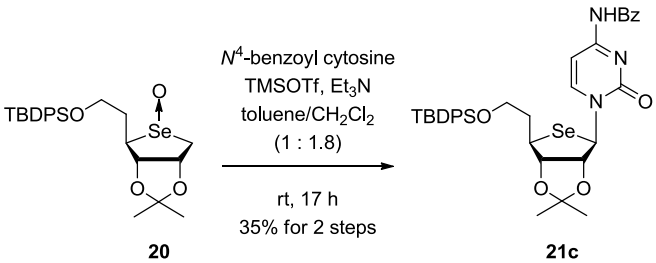


This protocol was followed by general procedure-(base condensation); page 32.

Pale yellow foam; Yield: 47%; $[\alpha]_D^{26}$ = –36.02 (*c* 1.00, CH_3OH); UV

(CH_3OH) λ_{max} 271 nm; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.20 (s, 1 H), 7.60-7.66 (m, 4 H), 7.36-7.43 (m, 6 H), 6.28 (d, *J* = 4.4 Hz, 1 H), 4.76 (dd, *J* = 4.5, 6.2 Hz, 1 H), 4.62 (t, *J* = 6.1 Hz, 1 H), 3.88-3.93 (m, 1 H), 3.63-3.73 (m, 2 H), 2.30-2.37 (m, 1 H), 1.89-2.03 (m, 1 H), 1.92 (d, *J* = 0.8 Hz, 3 H), 1.54 (s, 3 H), 1.28 (s, 3 H), 1.03 (s, 9 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 163.6, 150.2, 137.7, 135.8, 135.8, 133.5, 133.5, 129.9, 129.9, 127.9, 113.3, 112.3, 88.8, 88.4, 63.2, 57.7, 46.1, 37.9, 28.2, 27.0, 25.8, 19.3, 12.8; HRMS (ESI) found 637.1607 [calc for $C_{30}H_{38}N_2NaO_5SeSi^+$ $(M+Na)^+$ 637.1613]; Anal. Calcd for $C_{30}H_{38}N_2O_5SeSi$: C, 58.72; H, 6.24; N, 4.56. Found C, 59.01; H, 6.03; N, 4.16.

Preparation of 21c

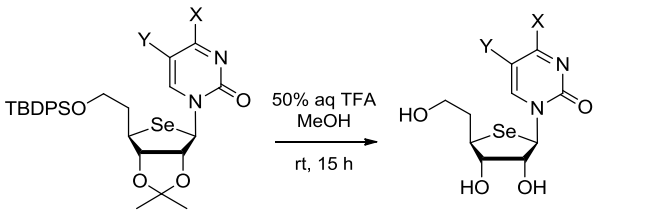


This protocol was followed by general procedure-(base condensation); page 32.

Pale yellow foam; Yield: 35%; $[\alpha]_D^{26}$ = –31.01 (*c* 1.00, CH_3OH); UV

(CH_3OH) λ_{max} 263 nm; ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.02 (s, 1 H), 7.90-7.98 (m, 3 H), 7.63-7.69 (m, 4 H), 7.57-7.61 (m, 1 H), 7.48-7.54 (m, 3 H), 7.35-7.45 (m, 6 H), 6.36 (d, *J* = 3.6 Hz, 1 H), 4.90-4.92 (dd, *J*= 3.2, 6.0 Hz, 1 H), 4.78 (pseudo t, *J* = 5.2, 6.0 Hz, 1 H), 3.98-4.03 (m, 2 H), 2.33-2.38 (m, 1 H), 2.01-2.08 (m, 2 H), 1.58 (s, 3 H), 1.29 (d, *J* = 5.2 Hz, 3 H), 1.03-1.09 (m, 9 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 135.9, 135.8, 133.5, 133.5, 129.9, 129.3, 127.9, 127.9, 112.8, 89.8, 89.8, 63.2, 47.7, 38.1, 28.1, 27.1, 25.7, 19.3; HRMS (ESI) found 726.1872 [calc for $C_{36}H_{41}N_3NaO_5SeSi^+$ $(M+Na)^+$ 726.1878]; Anal. Calcd for $C_{36}H_{41}N_3O_5SeSi$: C, 61.53; H, 5.88; N, 5.98. Found C, 61.52; H, 5.78; N, 5.53.

[General Procedure-(deprotection)]-Preparation of 12a-b



21a (X = OH, Y = H)
21b (X = OH, Y = CH_3)

12a (X = OH, Y = H) (82%)
12b (X = OH, Y = CH_3) (85%)

To a solution of **21a** (147 mg, 0.245 mmol) in methanol (10 mL, 0.0 25 M) was dropwise added 2,2,2-trifluoroethanol/H_2O solution (1:1, total 10

mL) at room temperature. After being stirred at the same temperature for 15 h, the reaction mixture was concentrated *in vacuo*, and further coevap orated with toluene to give a white solid. The solids were washed succes sively with hexanes (5 mL × 3), and triturated with methanol and Et_2O to give **12a** (64.5 mg, 82%);

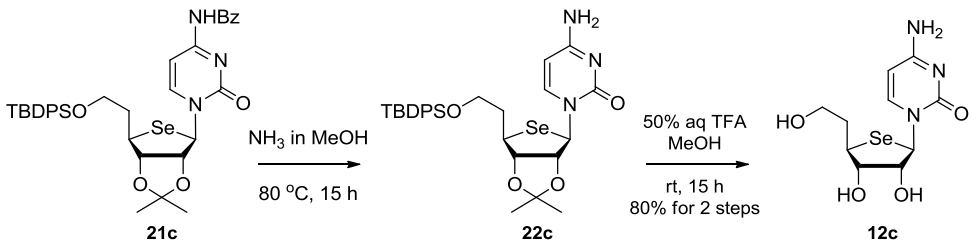
For 12a; white powder; mp 49-51 ^oC; $[\alpha]_D^{26}$ = –36.0 (*c* 0.1, CH_3OH); UV (CH_3OH) λ_{max} 227 nm; ^1H NMR (600 MHz, CD_3OD) δ 7.99 (d, *J* = 7.8 Hz, 1 H), 6.24 (d, *J* = 6.9 Hz, 1 H), 5.78 (d, *J* = 8.3 Hz, 1 H), 4.31 (dd, *J* = 3.7, 6.8 Hz, 1 H), 4.07 (dd, *J* = 3.7, 3.7 Hz, 1 H), 3.69 (ddd, *J* = 5.5, 5.5, 11.0 Hz, 1 H), 3.60-3.64 (m, 1 H), 3.56-3.59 (m, 1 H), 2.28-2.34 (m, 1 H), 1.94-2.00 (m, 1 H); ^{13}C NMR (150 MHz, CD_3OD) δ 166.8, 153.5, 144.9, 104.0, 80.7, 80.5, 62.7, 58.8, 45.7, 40.7; HRMS (ESI) found 344.9962 [calc for $C_{10}H_{14}N_2NaO_5Se^+$ $(M+Na)^+$ 344.9966].

For 12b; This protocol was followed by general procedure-deprotection.

White solid; Yield: 85%; mp 57-63 ^oC; $[\alpha]_D^{25}$ = –28.0 (*c* 0.1, CH_3OH); UV (CH_3OH) λ_{max} 272 nm; ^1H NMR (400 MHz, CD_3OD) δ 9.08 (s, 1 H), 7.76 (d, *J* = 1.2 Hz, 1 H), 6.27 (d, *J* = 7.2 Hz, 1 H), 4.40 (dd, *J* = 3.2, 7.2 Hz, 1 H), 4.10 (t, *J* = 3.6 Hz, 1 H), 3.68-3.74 (m, 1 H), 3.55-3.66 (m, 2 H), 2.28-2.36 (m, 1 H),

1.96-2.05 (m, 1 H), 1.91 (m, 3 H), ^{13}C NMR (100 MHz, CD_3OD) δ 166.2, 153.0, 139.4, 112.2, 79.8, 79.5, 61.9, 57.7, 44.9, 40.1, 12.5; HRMS (ESI) found 359.0119 [calc for $C_{11}H_{16}N_2NaO_5Se^+$ $(M+Na)^+$ 359.0122]; Anal. Calcd for $C_{11}H_{16}N_2O_5Se$: C, 39.41; H, 4.81; N, 8.36. Found C, 39.81; H, 5.21; N, 7.98.

Preparation of 12c



[Deprotection of Benzoyl group] To a solution of **21c** (200 mg, 0.334 mmol) in methanol (2 mL, 0.167 M) was dropwise added ammonia (5.0 mL, Ammonia solution was immediately generated by addition of ammonia gas to methanol at room temperature) at room temperature under N_2. After being heated at 80 ^{o}C in a steel bomb for 40 h, the reaction mixture was cooled to room temperature and concentrated *in vacuo*, and diluted with H_2O (30 mL) and CH_2Cl_2 (30 mL). The layers were separated, and the aqueous layer was extracted with CH_2Cl_2 (2 × 50 mL). The combined organic layers were washed successively with H_2O, dried over anhydrous $MgSO_4$, filtered, and concentrated

in vacuo. Without further purification, the crude **22c** was carried on to the next step.

[Deprotection of TBDPS and acetonide group] To a solution of crude **22c** in methanol (1.5 mL) was dropwise added 2, 2, 2-trifluoroethanol/H_2O solution (1:1, total 3 mL) at room temperature under N_2. After being stirred for 15 h, the reaction mixture was concentrated *in vacuo*. The residue was washed with hexanes (3 × 5 mL) to remove TBDPS impurities, and the hexanes layers were decanted. The white solid residue was triturated with methanol-Et_2O. The obtained solid was purified by flash column chromatography (silica gel, CH_2Cl_2/MeOH, 10/1) to give **12c** (86 mg, 80% for 2 steps) as a white solid; mp 117-119 ^oC; $[\alpha]_D^{25}$ = –30.0 (*c* 1.03, CH_3OH); UV (CH_3OH) λ_{max} 280 nm; ^1H NMR (400 MHz, CD_3OD) δ 8.11 (d, *J* = 7.6 Hz, 1 H), 6.23 (d, *J* = 6.0 Hz, 1 H), 5.99 (d, *J* = 7.6 Hz, 1 H), 4.28 (dd, *J* = 3.3, 5.8 Hz, 1 H), 4.01 (pseudo t, *J* = 4.0 Hz, 1 H), 3.56-3.69 (m, 3 H), 2.30-2.35 (m, 1 H), 1.93-1.99 (m, 1 H); ^{13}C NMR (75 MHz, CD_3OD) δ 166.8, 157.9, 146.0, 97.2, 80.9, 80.8, 62.9, 60.1, 45.3, 40.5; HRMS (ESI) found 344.0110 [calc for $C_{10}H_{15}N_3NaO_4Se^+$ $(M+Na)^+$ 344.0125]; Anal. Calcd for $C_{10}H_{15}N_3O_4Se$: C, 37.51; H, 4.72; N, 13.12. Found C, 37.13; H, 4.43; N, 13.52.

V. References

(1) Jordheim, L. P.; Durantel, D.; Zoulim, F.; Dumontet, C. *Nat. Rev. Drug Discovery*, **2013**, *12*, 447.

(2) (a) Inagaki, Y.; Minakawa, N.; Matsuda, A. *Nucleic Acids Symp. Ser.* **2007**, *51*, 139. (b) Jeong, L. S.; Tosh, D. K.; Kim, H. O.; Wang, T.; Hou, X.; Yun, H. S.; Kwon, Y.; Lee, S. K.; Choi, J.; Zhao, L. X. *Org. Lett.* **2008**, *10*, 209. (c) Tosh, D. K.; Choi, W. J.; Kim, H. O.; Lee, Y.; Pal, S.; Hou, X.; Choi, J.; Choi, S.; Jeong, L. S. *J. Org. Chem.* **2008**, *73*, 4259. (d) Jayakanthan, K.; Johnston, B. D.; Pinto, B. M. Carbohydr. Res. 2008, 343, 1790. (e) Jeong, L. S.; Choi, Y. N.; Tosh, D. K.; Choi, W. J.; Kim, H. O.; Choi, J. *Bioorg. Med. Chem.* **2008**, *16*, 9891. (f) Jeong, L. S.; Tosh, D. K.; Choi, W. J.; Lee, S. K.; Kang, Y.-J.; Choi, S.; Lee, J. H.; Lee, H.; Lee, H. W.; Kim, H. O. *J. Med. Chem.* **2009**, *52*, 5303. (g) Varughese, A.; Choi, W. J.; Chun, J.; Kim, H. O.; Jeon, J. H.; Tosh, D. K.; Lee, H. W.; Chandra, G.; Choi, J.; Jeong, L. S. *Org. Lett.* **2010**, *12*, 2242. (h) Taniike, H.; Inagaki, Y.; Matsuda, A.; Minakawa, N. *Tetrahedron* **2011**, *67*, 7977. (i) Yu, J.; Kim, J.-H.; Lee, H. W.; Alexander, V.; Ahn, H.-C.; Choi, W. J.; Choi, J.; Jeong, L. S. *Chem. Eur. J.* **2013**, *19*, 5528. (j) Sahu, P. K.; Kim, G.; Yu, J.; Ahn, J. Y.; Song, J.;

Choi, Y.; Jin, X.; Kim, J.; Lee, S. K.; Park, S.; Jeong, L. S. *Org. Lett.* **2014**, *16*, 5796.

(3) (a) Inagaki, Y.; Minakawa, N.; Matsuda, A. *Nucleic Acids Symp. Ser.* **2008**, *52*, 329. (b) Watts, J. K.; Johnston, B. D.; Jayakanthan, K.; Wahba, A. S.; Pinto, B. M.; Damha, M. J. *J. Am. Chem. Soc.* **2008**, *130*, 8578. (c) Tarashima, N.; Hayashi, K.; Terasaki, M.; Taniike, H.; Inagaki, Y.; Hirose, K.; Furukawa, K.; Matsuda, A.; Minakawa, N. *Org. Lett.* **2014**, *16*, 4710.

(4) (a) Krishna, U. M.; Deodhar, K. D.; Trivedi, G. K. *Tetrahedron*, **2004**, *60*, 4829. (b) Nagarapu, L.; Karnakanti, S.; Bantu, R. *Tetrahedron*, **2012**, *68*, 5829. (c) Kitamoto, K.; Nakayama, Y.; Sampei, M.; Ichiki, M.; Furuya, N.; Sato, T.; Chida, N. *Eur. J. Org. Chem.* **2012**, 4217. (d) (*Z*)-isomer was isomerized to the (*E*)-isomer **14** in the presence of a $RhH(CO)(PPh_3)_3$ catalyst (Ref. 2j).

(5) (a) Sharpless, K. B.; Michaelson, R. C. *J. Am. Chem. Soc.* **1973**, *95*, 6136. (b) Katsuki, T.; Sharpless, K. B. *J. Am. Chem. Soc.* **1980**, *102*, 5974. (c) Katsuki, T.; Lee, W. M.; Ma, P.; Martin, V. S.; Masamune, S.; Sharpless, K. B.; Tuddenham, D.; Walker, F. J. *J. Org. Chem.* **1982**, *47*, 1373. (d) lida, H.; Yamazaki, N.; Kibayashi, C. *J. Org. Chem.* **1987**, *52*, 3337. (e)

Valverde, S.; Herradon, B.; Rabanal, R. M.; Martin-Lomas, M. *Can. J. Chem.* **1987**, *65*, 332. (f) Gao, Y.; Hanson, R. M.; Klunder, J. M.; Ko, S. Y.; Masamune, H.; Sharpless, K. M. *J. Am. Chem. Soc.* **1987**, *109*, 5765. (g) Ko, S. Y.; Lee, A. W. M.; Masamune, S.; Reed, L. A.; Sharpless K. B.; Walker, F. J. *Tetrahedron* **1990**, *46*, 245. (h) Sarabia, F.; Sanchez-Ruiz, A. *J. Org. Chem.* **2005**, *70*, 9514. (i) Kumar, K. S.; Reddy, C. S. *Org. Biomol. Chem.* **2012**, *10*, 2647. (j) Kim, G.; Sohn, T.; Kim, D. *Angew. Chem. Int. Ed.* **2014**, *53*, 272.

(6) (a) Hanson, R. M. *Chem. Rev.* **1991**, *91*, 437. (b) Finan, J. M.; Kishi, Y. *Tetrahedron Lett.* **1982**, *23*, 2719.

(7) Gallos, J. K.; Stathakis, C. I.; Salapassidou, M. J.; Grammatoglou, C. E.; Koumbis, A. E. *Carbohydr. Res.* **2007**, *342*, 744.

(8) Albright, J. D.; Goldman, L. *J. Am. Chem. Soc.* **1965**, *87*, 4214.

국문초록

본 연구에서는 Sharpless asymmetric epoxidation 과 epoxide 의 regioselective cleavage 및 ketone 의 stereoselective reduction 을 주요 반응으로 하여 입체 선택적으로 D-5-homo-4-selenoribose 를 얻었다. 중요한 중간체인 D-5-homo-4-selenoribose 로부터 산화와 Pummerer-type 염기 축합을 거쳐 D-5'-homo-4'-selenonucleosides 을 합성하였다.

주요어 : D-5'-Homo-4'-selenonucleosides

Sharpless asymmetric epoxidation

Regioselective cleavage

Stereoselective reduction

학번 : 2014-21045