FURANOID GLYCAL AS A STARTING MATERIAL FOR NUCLEOSIDE DERIVATIVES

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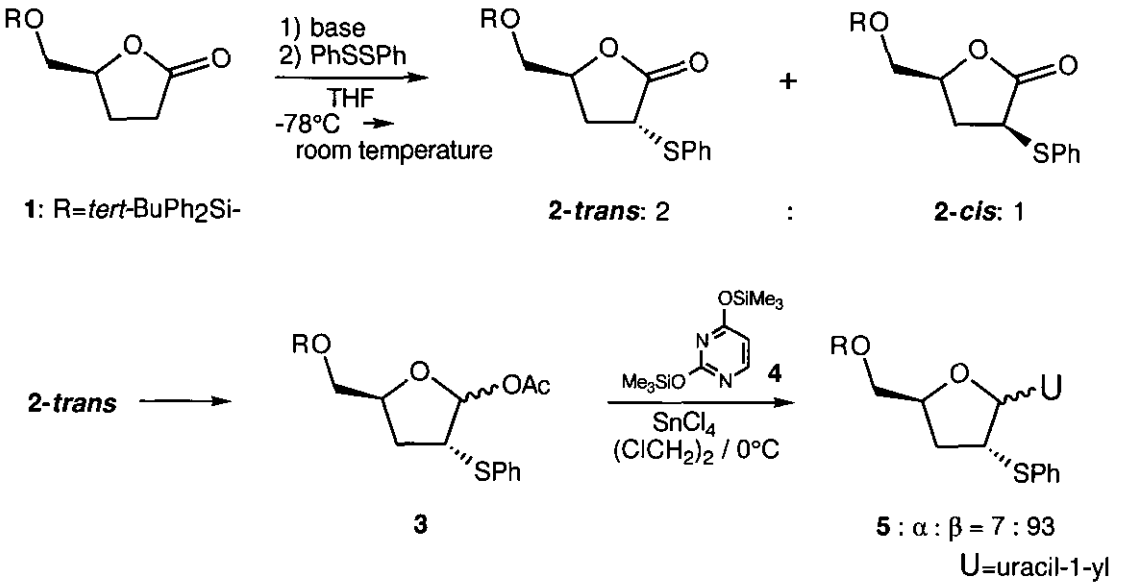
Abstract --- Furanoid glycal was utilized as a starting material for the nucleoside derivatives with the aid of benzenesulfenyl chloride. Condensation reaction with silylated nucleic bases was high in the presence of $SnCl_4$. Electrophilic addition of benzenesulfenyl chloride to the glycal with substituent also proceeded in high stereoselectivity. Phenylthio-substituted nucleoside was used to convert 2',3'-dideoxynucleoside and 2',3'-didehydro-2',3'-dideoxynucleoside.

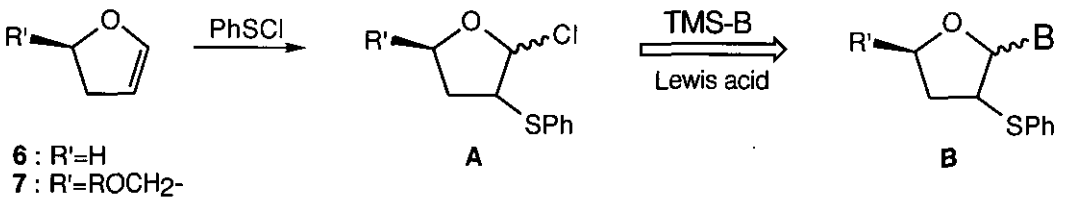
The development of 3'-azido-3'-deoxythymidine (AZT) and 2',3'-dideoxynucleosides (ddNs) as chemotherapic agents for AIDS treatment has stimulated research in the field of nucleosides.[1] As a wide range of nucleoside analogs have been synthesized,[2] a variety of preparation methods were also established.[3] Among them, the condensation reaction between sugar and nucleic base was often utilized because it was easy to make by this reaction a series of nucleosides which have the same sugar moiety.[3a] The effective nucleoside analogs, including AZT and ddNs, incorporate the 2-deoxyfuranose moiety, which complicates the condensation reaction due to the lack of stereocontrolling elements.[3b] In the course of our study, it became clear that the phenylthio (PhS) group at C-2 on furanose was useful as a stereocontrolling element.[4] For example, the condensation reaction between 2-PhS-2,3-dideoxyribose (**3**) and silylated pyrimidine bases proceeded with the stereoselectivity of $\alpha : \beta = 7 : 93$ (Scheme 1).[4a,b] However, introduction of PhS group to γ-lactone (**1**) was proceeded with poor stereoselectivity, which was *trans* : *cis* = 2 : 1.[4] From a practical viewpoint, it makes the



Scheme 1.

isolation of product troublesome. Although a stereocontrolled sulfenylation was reported, it required a customized reagent to achieve the high selectivity.[5] In order to overcome this disadvantage, we paid attention to a usefulness of furanoid glycals.

Recently, the pyranoid glycals were well studied as a glycosyl donor with the aid of electrophilic reagents, and their usefulness are known in the point of stereoselectivity.[6] There were not many instances of the use of furanoid glycals.[7] Alexander and Paterson reported that the reaction of 2,3-dihydrofuran (**6**) with benzenesulfenyl chloride (PhSCl) followed by the alkylation with silyl enol ether and Lewis acid gave 2-PhS-1-

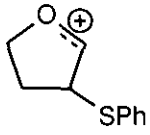


Scheme 2.

alkylated tetrahydrofuran derivatives (Scheme 2).[8,9] In this reaction, the formation of 1-chlorosugar (**A**) was supposed as an intermediate. Since **A** could be considered as a equivalent of 2-PhS sugar (**3**), this procedure seemed to be applicable to the synthesis of 2'-PhS-nucleosides (**B**). As PhS group could be removed either reductively or oxidatively to give 2'-deoxynucleosides,[4a,b] this sequence from furanoid glycal would be a unprecedented method for a stereoselective preparation of these deoxynucleosides.[10] Herein, we report this type of nucleoside synthesis from furanoid glycal.[11]

Reaction between 2,3-dihydrofuran and silylated uracil.

In order to examine the applicability of this procedure, a model reaction was carried out as shown in Scheme 3. 2,3-Dihydrofuran (**6**) was treated with PhSCl under the same conditions as reported.[8] After that, $SnCl_4$ and silylated uracil (**4**) were sequentially introduced into the reaction medium, and the mixture was stirred at 0 °C for 2 h. The condensation products were obtained in 80% yield and in the ratio of *trans* : *cis* = 99 : 1. As anticipated, the stereoselectivity in the condensation reaction with **8** was very high. When the reaction with **8** was carried out without $SnCl_4$, the selectivity was drastically changed to *trans* : *cis* = 15 : 85 suggesting the intermediary of **8**. If a cationic species like **10**, not 1-chlorosugar (**8**), was the intermediate, the *trans* isomer (**9-*trans***) should be obtained even without the Lewis acid catalyst, because of the participation of the PhS group.[1] Moreover, it is known that 1-chlorofuranose reacts with silylated pyrimidine bases without the catalysts to give the nucleosides.[12]



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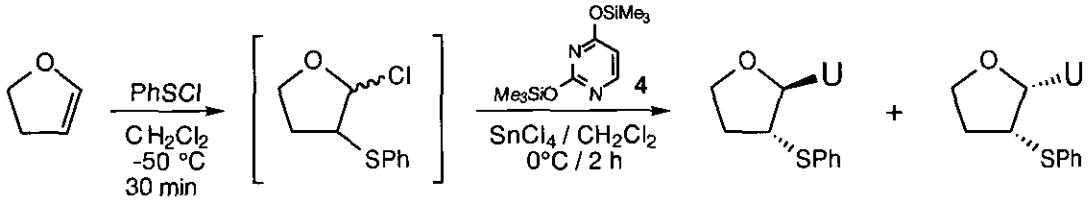


6 **8** **9-*trans*** **9-*cis***

80% 99 : 1

Scheme 3.

Reaction between substituted glycal and pyrimidine bases.

As a new procedure for the nucleoside synthesis from a glycal with the aid of PhSCl was at hand, we tried to establish the preparation method for the nucleosides from the substituted glycal (**7**). In this case, the stereoselectivity in the addition reaction of PhSCl was another difficulty.

The starting furanoid glycal (**7**) was prepared by the procedure reported by Takle and Kocienski from γ-lactone (**1**),[13] which was obtained from levoglucosenone (**11**).[14]

The addition reaction of PhSCl to **7** was carried out at -78 °C for 30 min, followed by treatment with silylated uracil (**4**) under similar conditions to those utilized on the transformation of 2,3-dihydrofuran (**6**) (Scheme 4). The mixture of three diastereomeric isomers was obtained in 80% yield in the indicated ratio. Each nucleoside was identified by comparison of hplc retention times and ^{1}H-nmr data with those of authentic samples previously synthesized by us.[4a] This result showed that the stereoselectivity in the condensation reaction with 1-chlorosugar (**13**) was as high as that for non-substituted 1-chlorosugar (**8**). It was also clear that the stereoselectivity in the addition reaction of PhSCl to the glycal (**7**) was also very high. (**13** : **14** = **5** : **15** = 96 : 4) This selectivity was not temperature dependent and was **5** : **15** = 97 : 3 when the addition reaction was carried out at 0 °C.

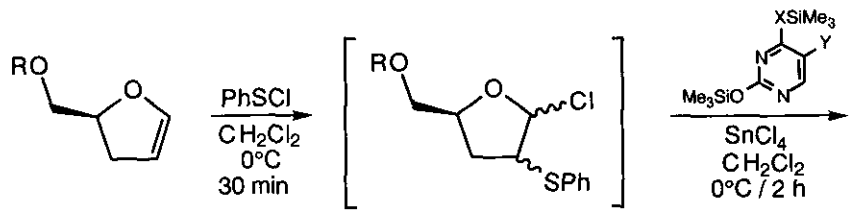
These reaction conditions were applied to the condensation of silylated thymine (**16**) and silylated N^4-acetylcytosine (**17**) (Scheme 4). In both cases, good stereoselectivities were achieved under the same conditions for silylated uracil (**4**).

The 2-PhS-nucleosides could be converted to 2',3'-didehydro-2',3'-dideoxynucleosides (d4Ns), which were the potential starting material for ddNs and some of which were also effective against HIV themselves.[4]

Reaction with silylated adenine.

2',3'-Dideoxyadenosine (ddA) is an important intermediate in the preparation of 2',3'-dideoxyinosine (ddI), which is currently used in the chemotherapeutic treatment of AIDS.[15] It would be useful if the condensation reaction between furanoid glycal and adenine derivative proceeds stereoselectively by the aid of PhSCl, since the PhS group could be removed by reduction to give ddA.

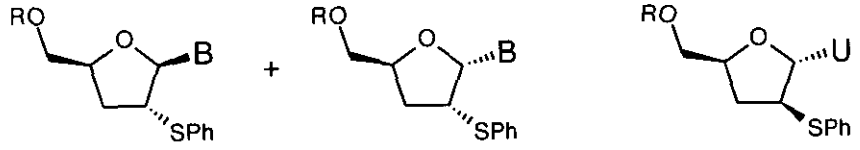
Silylated benzoyladenine (**20**)[16] was subjected to the reaction conditions similar to those for pyrimidine bases (Scheme 5). The stereoselectivity of the reaction was revealed to be **22**α : **22**β = 65 : 35.[17] Taking the longer



7 : *tert*-BuPh$_2$Si-

13: 2-α-PhS
14: 2-β-PhS

4 : X=O, Y=H
16 : X=O, Y=Me
17 : X=NAc, Y=H



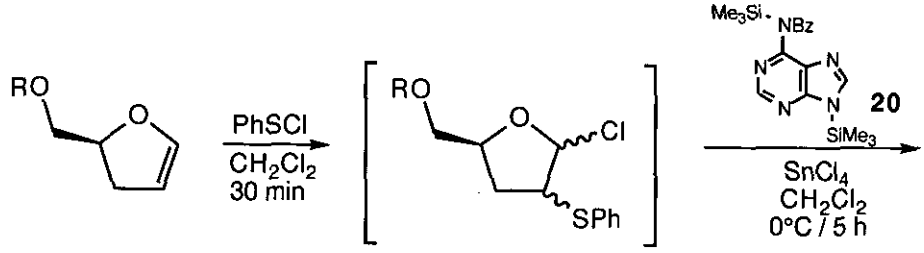
B=U*1, 2	**5**β : 98 (80%)	:	**5**α : 2	**15**
B=U*1	**5**β : 97 (77%)	:	**5**α : 3	
B=T	**18**β : 94 (53%)	:	**18**α : 6	
B=C^{Ac}	**19**β : 97 (72%)	:	**19**α : 3	

*1 The other isomer (**15**) was also obtained.
*2 The glycal (**7**) was treated with PhSCl at -78 °C.

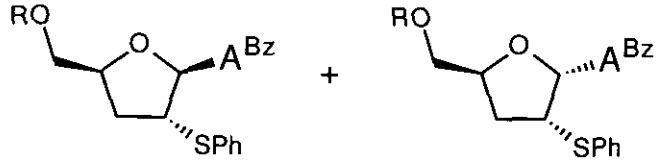
Scheme 4.

reaction time into account, this low selectivity might be caused by the steric hindrance of the bulky *tert*-butyldiphenylsilyl group. In fact, changing the protecting group to the less bulky pivalate ester proved to be effective. Thus, the pivaloyl protected glycal (**21**) was subjected to the similar reaction conditions, except for the reaction temperature in the addition reaction, and provided the anomeric mixture of **23** with the ratio of α : β = 14 : 86. The β-anomer (**23**β) was purified by preparative tlc as a single isomer.

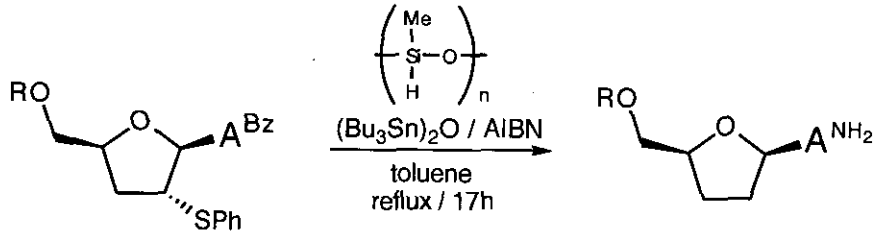
The PhS group of **23**β was removed by reduction in toluene at reflux with tin hydride generated *in situ* (Scheme 5). Radical reduction was completed in 17h. Debenzoylation at N-6 of adenine moiety also occurred, and gave the protected ddA (**24**) in 72% yield. The stereochemistry of C-1' was finally confirmed by comparison with an authentic sample of ddA after the removal of pivaloyl group.



7 : R=*tert*-$BuPh_2Si$- 0°C
21 : R=$Me_3CC(O)$- -78°C



R=*tert*-$BuPh_2Si$-	**22**β	35 : 65	**22**α
R=$Me_3CC(O)$-	**23**β (71%)	86 : 14	**23**α



23β : R=$Me_3C(O)$- **24** : 72%

Scheme 5.

In conclusion, a novel synthesis of nucleoside derivatives was established from furanoid glycal with the aid of benzenesulfenyl chloride (PhSCl). It was remarkable that both electrophilic attack of PhSCl to glycal and the condensation reaction with nucleic bases were highly stereoselective. Here we showed the stereoselective preparation of three pyrimidine nucleosides and one purine nucleoside. These results predict that both pyrimidine and purine bases could be used as the nucleic bases. The condensation reaction with other furanoid glycals are now under way.

EXPERIMENTAL

Spectral Measurements.

Optical rotations were measured on a Jasco DIP-370 polarimeter. ^{1}H-Nmr spectra were recorded at 300 MHz and ^{13}C-nmr spectra at 75 MHz, on a Brucker AC-300P spectrometer. Chemical shifts are given in ppm (δ) relative to tetramethylsilane for ^{1}H-nmr and relative to $CDCl_3$ (77.0 ppm) for ^{13}C-nmr. Ir spectra were measured on a Jasco FT/IR-5000 spectrophotometer. Uv spectra were measured on a Beckman DU-65 spectrophotometer.

1-(3-*trans*-Phenylthiotetrahydrofuran-2-yl)uracil (**9**-*trans*)

Under argon atmosphere, a solution of 2,3-dihydrofuran (**6**, 41 μl, 0.54 mmol) in dry dichloromethane (1 ml) was added dropwise at -50 °C to a solution of benzenesulfenyl chloride (PhSCl, 83 mg, 0.58 mmol) in dry dichloromethane (3 ml). The mixture was stirred at room temperature for 30 min. To this solution, 2.2 ml of 1.0 *M* solution of $SnCl_4$ in dry dichloromethane[18] was added dropwise at -78 °C, and then 2.0 ml of 1.0 *M* solution of silylated uracil (**4**)[19] in dry dichloromethane was added at -78°C. The mixture was stirred at 0 °C for 2 h. The reaction mixture was poured into a saturated aqueous solution of sodium bicarbonate and extracted with dichloromethane three times. The organic layer was dried over anhydrous magnesium sulfate, and the solvent was removed under reduced pressure. The residue obtained was purified by preparative thin layer chromatography (silica gel; chloroform : acetone = 85 : 15) to give a diastereomeric mixture of **9** (125 mg, 80% yield, *trans* : *cis* = 99 : 1). Pure *trans* isomer was obtained as white crystals by recrystallization from *n*-hexane-dichloromethane; mp 130.5-132.5 °C ; ^{1}H-nmr ($CDCl_3$) :δ 9.54 (1H, br, NH), 7.56-7.48 (2H, m, aromatic H), 7.36-7.26 (3H, m, aromatic H), 7.15 (1H, d, *J*=8.1 Hz, H-6), 5.82 (1H, d, *J*=3.8 Hz, H-2'), 5.65 (1H, d, *J*=8.1 Hz, H-5), 4.32-4.10 (1H, m, H-5'), 4.17 (1H, q, *J*=7.8 Hz, H-5'), 3.94 (1H, ddd, *J*=7.0, 5.3, 3.8 Hz, H-3'), 2.38 (1H, dt, *J*=20.7, 7.8 Hz, H-4'), 2.16-2.02 (1H, m, H-4'); ^{13}C-nmr($CDCl_3$) :δ 163.57 (C-4), 150.09 (C-2), 139.73 (C-6), 132.96 (aromatic C), 132.22 (aromatic C), 129.12 (aromatic C), 128.09 (aromatic C), 102.12 (C-5), 92.51 (C-2'), 68.91 (C-5'), 50.58 (C-3'), 30.66 (C-4'); ir (KBr) :ν_{max} 3020 (m), 1723 (s), 1690 (s), 1665 (s), 1473 (m), 1278 (m), 1091 (m), 1052 (m) cm^{-1} ; uv($CHCl_3$) :λ_{max} 261 nm (log e 4.10); Hi-ms (FAB) Calcd for $C_{14}H_{15}N_2O_3S$: 291.0803. Found: 291.0835 (M+H).

1-[5-*O*-(*tert*-Butyldiphenylsilyl)-2,3-dideoxy-2-phenylthio-β-D-*erythro*-pentofuranosylluracil (5β)

Under argon atmosphere, a solution of 2-*tert*-butyldiphenylsilyloxymethyl-2,3-dihydrofuran (**7**, 48 mg, 0.14 mmol) in dry dichloromethane (1.4 ml) was added dropwise at -78 °C to a solution of benzenesulfenyl chloride in dry dichloromethane (0.11 *M*, 1.4 ml, 0.15 mmol). The mixture was stirred at the same temperature for 30

min. To this solution, 0.37 ml of 1.0 *M* solution of $SnCl_4$ in dry dichloromethane[18] was added dropwise at -78 °C, and then 1.4 ml of 0.20 *M* solution of silylated uracil (**4**)[19] in dry dichloromethane was added at -78°C. The mixture was stirred at 0 °C for 1 h. The reaction mixture was poured into a saturated aqueous solution of sodium bicarbonate and extracted with dichloromethane three times. The organic layer was dried over anhydrous magnesium sulfate, and the solvent was removed under reduced pressure. The residue obtained was purified by preparative thin layer chromatography (silica gel; *n*-hexane : ethyl acetate = 50 : 50) to give 62 mg of **5β** (an amorphous white powder, 77% yield); ^{1}H-nmr ($CDCl_3$) :δ 8.97 (1H, br, NH), 7.72 (1H, d, *J*=8.1 Hz, H-6), 7.67-7.61 (4H, m, aromatic H), 7.50-7.36 (8H, m, aromatic H), 7.28-7.24 (3H, m, aromatic H), 6.08 (1H, d, *J*=5.5 Hz, H-1'), 5.31 (1H, dd, *J*=8.1, 2.0 Hz, H-5), 4.38-4.30 (1H, m, H-4'), 4.08 (1H, dd, *J*=11.7, 2.1 Hz, H-5'), 3.90-3.73 (1H, m, H-2'), 3.69 (1H, dd, *J*=11.7, 2.2 Hz, H-5'), 2.52 (1H, ddd, *J*=13.2, 7.2, 6.0 Hz, H-3'), 2.10 (1H, dt, *J*=13.2, 7.4 Hz, H-3'), 1.10 (9H, s, *tert*-Bu); ir (KBr) :ν_{max} 1690 (s), 1462 (m), 1429 (m), 1280 (m), 1114 (m), 1079 (m), 822 (m), 743 (m), 702 (m), 505 (m) cm^{-1}; Hi-ms (FAB) Calcd for $C_{31}H_{35}N_2O_4SSi$: 559.2087. Found: 559.2058 (M+H).

1-[5-*O*-(*tert*-Butyldiphenylsilyl)-2,3-dideoxy-2-phenylthio-β-D-*erythro*-pentofuranosyl]thymine (**18β**)

Under argon atmosphere, a solution of 2-*tert*-butyldiphenylsilyloxymethyl-2,3-dihydrofuran (**7**, 350 mg, 1.05 mmol) in dry dichloromethane (10.5 ml) was added dropwise at 0 °C to a solution of benzenesulfenyl chloride in dry dichloromethane (0.103 *M*, 10.5 ml, 1.08 mmol). The mixture was stirred at the same temperature for 30 min. To this solution, 2.3 ml of 1.0 *M* solution of $SnCl_4$ in dry dichloromethane[18] was added dropwise at -78 °C, and then 10.5 ml of 0.20 *M* solution of silylated thymine (**16**)[19] in dry dichloromethane was added at -78°C. The mixture was stirred at 0 °C for 2 h. The reaction mixture was poured into a saturated aqueous solution of sodium bicarbonate and extracted with dichloromethane three times. The organic layer was dried over anhydrous magnesium sulfate, and the solvent was removed under reduced pressure. The residue obtained was purified by silica gel column chromatography (*n*-hexane : ethyl acetate = 75 : 25 - 50 : 50), and then by recrystallization from *n*-hexane-dichloromethane to give 318 mg of **18β** (white crystals, 53% yield); mp 152.0-154.0 °C ;^{1}H-nmr ($CDCl_3$) :δ 8.96 (1H, br, NH), 7.70-7.62 (4H, m, aromatic H), 7.52-7.33 (8H, m, aromatic H), 7.27-7.15 (4H, m, H-6, aromatic H), 6.12 (1H, d, *J*=7.6 Hz, H-1'), 4.28-4.21 (1H, m, H-4'), 4.02 (1H, dd, *J*=11.5, 1.8 Hz, H-5'), 3.89-3.72 (1H, m, H-2'), 3.68 (1H, dd, *J*=11.5, 2.1 Hz, H-5'), 2.54 (1H, ddd, *J*=12.7, 8.0, 4.2 Hz, H-3'), 2.14 (1H, dt, *J*=12.7, 9.2 Hz, H-3'), 1.50 (3H, s, Me), 1.13 (9H, s, *tert*-Bu); ir (KBr) :ν_{max}

1704 (s), 1694 (s), 1473 (m), 1114 (m), 1089 (m), 745 (m), 702 (m), 507 (m); Hi-ms (FAB) Calcd for $C_{32}H_{37}N_2O_4SSi$: 573.2243. Found: 573.2216 (M+H).

N^4-Acetyl-1-[5-*O*-(*tert*-butyldiphenylsilyl)-2,3-dideoxy-2-phenylthio-β-D-*erythro*-pentofuranosyl]cytosine (**19**β)

Under argon atmosphere, a solution of 2-*tert*-butyldiphenylsilyloxymethyl-2,3-dihydrofuran (**7**, 341 mg, 1.03 mmol) in dry dichloromethane (10.0 ml) was added dropwise at 0 °C to a solution of benzenesulfenyl chloride in dry dichloromethane (0.100 *M*, 10.0 ml, 1.00 mmol). The mixture was stirred at the same temperature for 30 min. To this solution, 2.2 ml of 1.0 *M* solution of $SnCl_4$ in dry dichloromethane[18] was added dropwise at -78 °C, and then 10.0 ml of 0.20 *M* solution of silylated *N*^{4}-acetylcytosine (**17**)[19] in dry dichloromethane was added at -78°C. The mixture was stirred at 0 °C for 2 h. The reaction mixture was poured into a saturated aqueous solution of sodium bicarbonate and extracted with dichloromethane three times. The organic layer was dried over anhydrous magnesium sulfate, and the solvent was removed under reduced pressure. The residue obtained was purified by silica gel column chromatography (chloroform : acetone = 80 : 20), and then by hplc (ODS; 30 mmϕ X 250 mm; acetonitrile : water= 75 : 25; 15 ml/min.) to give 441 mg of **19**β (an amorphous white powder, 72% yield); ^{1}H-nmr ($CDCl_3$) :δ 10.18 (1H, br, NH), 8.34 (1H, d, *J*=7.5 Hz, H-6), 7.68-7.61 (4H, m, aromatic H), 7.50-7.35 (8H, m, aromatic H), 7.30-7.24 (3H, m, aromatic H), 7.20 (1H, d, *J*=7.5 Hz, H-5), 6.08 (1H, d, *J*=3.0 Hz, H-1'), 4.55-4.45 (1H, m, H-4'), 4.18 (1H, dd, *J*=12.0, 2.2 Hz, H-5'), 3.88 (1H, dt, *J*=6.4, 3.0 Hz, H-2'), 3.72 (1H, dd, *J*=12.0, 2.6 Hz, H-5'), 2.40 (1H, ddd, *J*=13.3, 9.2, 6.4 Hz, H-3'), 2.27 (3H, s, Ac), 1.94 (1H, ddd, *J*=13.3, 5.7, 3.0 Hz, H-3'), 1.11 (9H, s, *tert*-Bu); ν_{max} 1661 (m), 1634 (s), 1560 (m), 1489 (s), 1400 (m), 1325 (m), 1241 (m), 1218 (m), 1096 (m), 702 (m) cm^{-1}; Hi-ms (FAB) Calcd for $C_{33}H_{38}N_3O_4SSi$: 600.2352. Found: 600.2333 (M+H).

N^6-Benzoyl-9-(5-*O*-pivaloyl-2,3-dideoxy-2-phenylthio-β-D-*erythro*-pentofuranosyl)adenine (**23**β)

Under argon atmosphere, a solution of 2-pivaloyloxymethyl-2,3-dihydrofuran (**21**, 29 mg, 0.16 mmol) in dry dichloromethane (1.6 ml) was added dropwise at -78 °C to a solution of benzenesulfenyl chloride in dry dichloromethane (0.10 *M*, 1.6 ml, 0.16 mmol). The mixture was stirred at the same temperature for 30 min. To this solution, 0.40 ml of 1.0 *M* solution of $SnCl_4$ in dry dichloromethane[18] was added dropwise at -78 °C, and then 1.6 ml of 0.20 *M* solution of silylated *N*^{6}-benzoyladenine (**20**)[16] in dry dichloromethane was added at -78 °C. The mixture was stirred at 0 °C for 5 h. The reaction mixture was poured into a saturated aqueous solution of sodium bicarbonate and extracted with dichloromethane three times. The organic layer was dried over anhydrous magnesium sulfate, and the solvent was removed under reduced pressure. The residue obtained was

purified by preparative thin layer chromatography (silica gel; chloroform : acetone = 90 : 10) to give 59 mg of **23β** (viscous colorless oil, 71% yield); $[\alpha]_D^{25}$ -43.7 ° (*c* 0.67, $CHCl_3$); ^{1}H-nmr ($CDCl_3$) :δ 9.14 (1H, br, NH), 8.76 (1H, s, H-8), 8.07-8.00 (3H, m, H-2, aromatic H), 7.65-7.58 (1H, m, aromatic H), 7.58-7.48 (2H, m, aromatic H), 7.42-7.37 (2H, m, aromatic H), 7.25-7.18 (3H, m, aromatic H), 6.09 (1H, d, *J*=4.2 Hz, H-1'), 4.69-4.57 (2H, m, H-2', H-4'), 4.34 (2H, d, *J*=4.6 Hz, H-5'), 2.63 (1H, dt, *J*=13.5, 7.7 Hz, H-3'), 2.24 (1H, ddd, *J*=13.5, 6.8, 5.1 Hz, H-3'), 1.21 (9H, s, *tert*-Bu); ^{13}C-nmr($CDCl_3$) :δ 178.11 (C=O of pivaloyl), 164.73 (C=O of benzoyl), 152.27 (C-2), 151.02 (C-6), 149.41 (C-4), 141.49 (C-8), 133.46 (aromatic C), 132.66 (aromatic C), 132.50 (aromatic C), 131.81 (aromatic C), 129.07 (aromatic C), 128.68 (aromatic C), 128.07 (aromatic C), 127.83 (aromatic C), 123.40 (C-5), 90.79 (C-1'), 77.76 (C-4'), 64.87 (C-5'), 49.76 (C-2'), 38.71 (quaternary C of pivaloyl), 32.92 (C-3'), 27.06 (Me of pivaloyl); ir (KBr) :ν_{max} 3408 (w), 1729 (s), 1700 (m), 1611 (s), 1582 (m), 1512 (m), 1483 (m), 1456 (s), 1286 (m), 1251 (m), 1158 (s), 1089 (m) cm^{-1} ; uv($CHCl_3$) :λ_{max} 281 nm (log ε 4.25), 264 nm (log ε 4.15); Hi-ms (FAB) Calcd for $C_{28}H_{29}N_5O_4S$: 532.2019. Found: 532.2024 (M+H).

9-(5-*O*-Pivaloyl-2,3-dideoxy-β-D-*glycero*-pentofuranosyl)adenine (**24**)

Under argon atmosphere, a mixture of N^6-benzoyl-9-(5-*O*-pivaloyl-2,3-dideoxy-2-phenylthio-β-D-*erythro*-pentofuranosyl)adenine (**23**, 24 mg, 0.045 mmol), polymethylhydrosiloxane (0.10 ml), and bis(tributyltin)oxide (0.13 ml, 0.25 mmol) in dry toluene (9 ml) was heated under reflux. To this solution, 50 μl of 23 *mM* solution of azobis(isobutyronitrile) in dry toluene was added every 30 min, and reflux was continued for 17 h. The solvent was distilled away under reduced pressure. The residue obtained was purified by silica gel column chromatography (chloroform : methanol = 100 : 0 - 93 : 7), and then by preparative thin layer chromatography (silica gel; chloroform : methanol = 95 : 5) to give 10 mg of **24** (an amorphous white powder, 72% yield); ^{1}H-nmr ($CDCl_3$) :δ 8.35 (1H, s, H-8), 8.07 (1H, s, H-2), 6.29 (1H, dd, *J*=5.9, 4.0 Hz, H-1'), 5.78 (2H, br, NH), 4.47-4.37 (1H, m, H-4'), 4.32 (2H, d, *J*=4.4 Hz, H-5'), 2.67-2.50 (2H, m, H-2'), 2.23-1.98 (2H, m, H-3'), 1.22 (9H, s, *tert*-Bu).

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