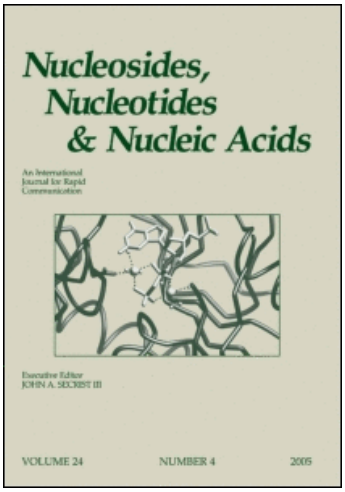

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Synthesis of 2',3',6'-Trideoxy-β-D-*erythro*-hexopyranosyl Nucleosides Employing Intramolecular Glycosylation as a Key Step

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SYNTHESIS OF 2',3',6'-TRIDEOXY-β-D-*erythro*-HEXOPYRANOSYL NUCLEOSIDES EMPLOYING INTRAMOLECULAR GLYCOSYLATION AS A KEY STEP

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ABSTRACT: 2',3'-Dideoxy-β-D-*erythro*-hexopyranosyl pyrimidine nucleosides were synthesized in a stereoselective manner utilizing the intramolecular pyrimidine delivery method. The nucleosides obtained from this reaction were further transformed into its 6'-deoxy derivative, which is a promising synthetic intermediate for amicetin family antibiotics.

1-(2,3,6-Trideoxy-β-D-*erythro*-hexopyranosyl)cytosine is a common skeleton of the amicetin group of antibiotics (FIG. 1), obtained from the fermentation broth of various species of *Streptomyces* and *Aethrobactor*. Amicetin was isolated in the early 1950s by several groups.[1] At present, a total of about ten compounds bearing closely related structures have been found.[2] As for the synthetic approach to the hexopyranosyl nucleoside moiety, Stevens *et al.*[3] accomplished the first practical synthesis using the Hilbert-Johnson procedure in which a labile chloro sugar was employed as a glycosyl donor. In recent years, for other purposes, several 2',3'-deoxyhexopyranosyl nucleosides have been prepared using the Vorbrüggen coupling, which gave the desired deoxy-β-nucleosides in satisfactory yields with reasonable stereoselectivity.[4] However, because it is often difficult to remove the contaminating undesired α-anomers, reactions with complete stereoselectivity for the β-anomer are still required. As a solution for the problem of an anomeric selectivity, we developed an intramolecular glycosylation method, in which a pyrimidine base is delivered from C-5 in pentofuranoses to the anomeric position. Using this methodology, we have demonstrated its wide applicability to the syntheses of various

This paper is dedicated to the memory of Professor Tujiaki Hata.

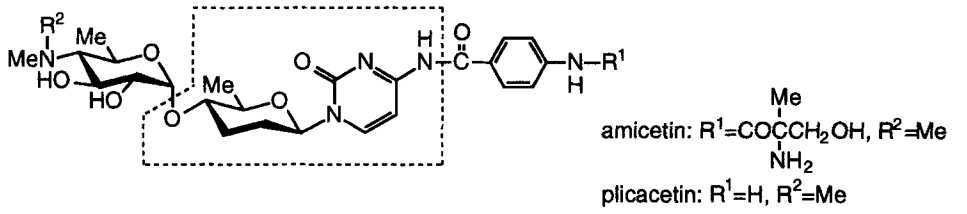


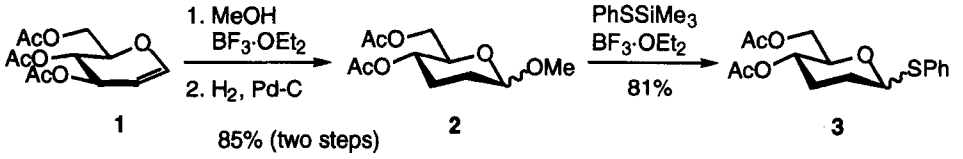
FIG. 1 Structure of amicetin family antibiotics

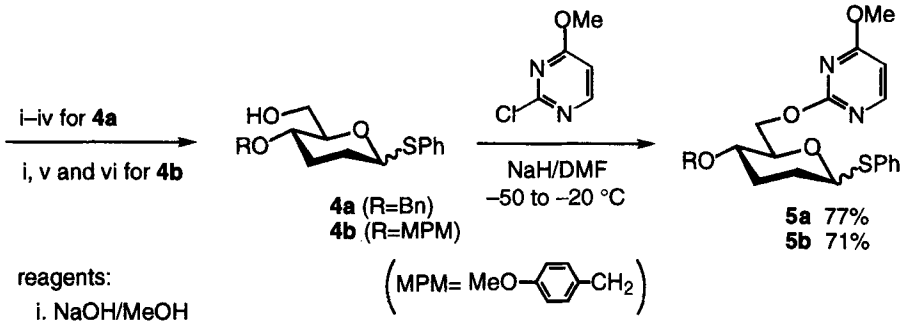
deoxynucleoside derivatives.[5] In this paper, we describe a further extension of this method to the stereoselective synthesis of 2',3'-dideoxy-β-hexopyranosyl nucleosides.

RESULTS AND DISCUSSION

The substrates for the intramolecular glycosylation were prepared as illustrated in Scheme 1. Commercially available tri-*O*-acetyl-D-glucal (**1**) was converted into methyl 2,3-dideoxy-D-*erythro*-hexopyranoside (**2**) according to Ferrier's procedure.[6] After conversion of **2** into thioglycoside **3** using Nicolaou's conditions,[7] a 4-*O*-benzyl derivative **4a** was prepared by a sequence involving deacetylation, trityl-protection of the 6-hydroxyl, benzyl-protection of the 4-hydroxyl, and removal of the trityl group under acidic conditions. Similarly, a 4-*O*-*p*-methoxybenzyl(MPM) derivative **4b** was obtained by a sequence involving deacetylation, 4,6-*O*-*p*-methoxybenzylidene-protection, and reductive cleavage of the benzylidene acetal with a combination of $NaBH_3CN$-Me_3SiCl.[8] The resulting thioglycosides **4a**, **4b** were treated with NaH and then reacted with 2-chloro-4-methoxypyrimidine,[9] leading to the substrates of the intramolecular glycosylation, **5a** and **5b**.

In our previous study, we have disclosed a suitable promoter for this intramolecular glycosylation is $Me_2S(SMe)BF_4$,[5a] which activates the thioglycosides **5a**, **5b** to give rise to disulfide and an oxonium intermediate (SCHEME 2). Subsequently, the *N*-1 atom of the pyrimidine would capture the cation to form a cyclic pyrimidinium intermediate. By addition of aq. NaOH, the cyclic intermediate would be hydrolyzed to yield the desired β-nucleoside. When the 4-*O*-benzyl substrate **5a** was used in this intramolecular glycosylation, the β-nucleoside **6a** was obtained in 56% yield, accompanied by 23% of a *C*-1 hydrolyzed by-product **7a**. Several reaction conditions were investigated in order to suppress the hydrolysis at *C*-1 (solvent, temperature, additives for stabilizing the pyrimidinium intermediate, cation effects during the hydrolysis, etc.) but none proved to be better than the original conditions. However, it was found that a great improvement lay





reagents:

i. NaOH/MeOH

ii. TrCl/Py; 83% (from **3**)

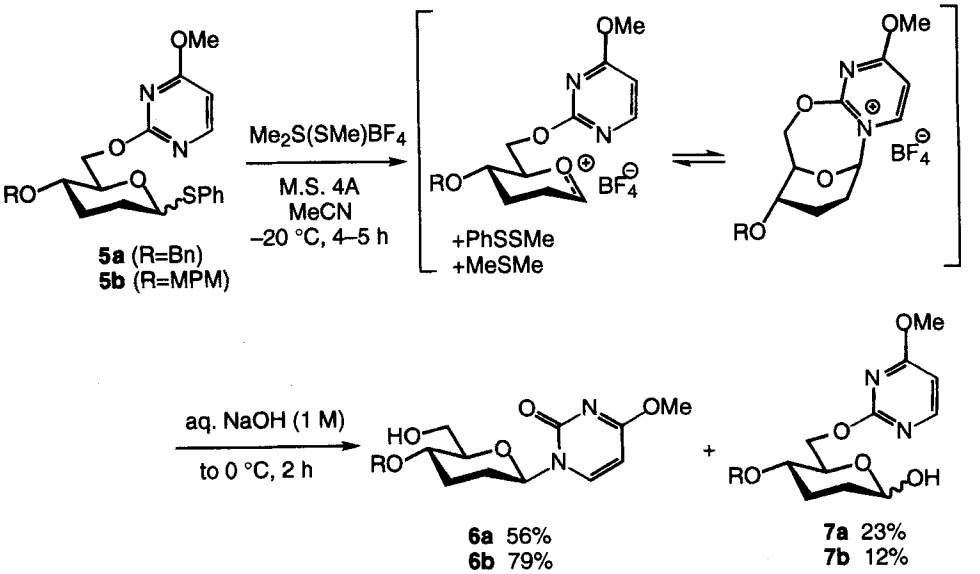
iii. BnBr, NaH/DMF

iv. CF_3CO_2H/BuOH, **4a** 88% (two steps)

v. *p*-$MeOC_6H_4CH(OMe)_2$, $HBF_4 \cdot OEt_2$/DMF; 94% (from **3**)

vi. $NaBH_3CN$, Me_3SiCl/MeCN; **4b** 87%

SCHEME 1



SCHEME 2

in the use of an MPM group as the protecting group at the 4-*O* position instead of the benzyl group. That is, with starting from the substrate **5b**, the yield of the desired β-nucleoside **6b** increased to 79%.

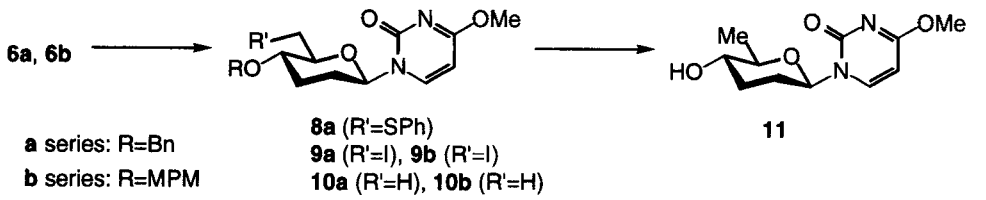
Finally, deoxygenation at the 6' position and removal of the 4'-*O* protecting groups were examined (SCHEME 3). The deoxygenation was first attempted in desulfurization of the 6'-phenylthio derivative. According to Hata's protocol,[10] **6a** was treated with PhSSPh-Bu_3P in pyridine, affording 6'-phenylthio derivative **8a** in 98% yield. Desulfurization was then undertaken using Raney Ni (W2) to produce 6'-deoxy-4'-deprotected derivative **11** in one step, though the yield was only 26%. Attempts to increase the amount of **11** failed, probably due to adsorption of Raney Ni. Therefore, an alternate route *via* radical reduction of a 6'-iodo derivative was examined. Treatment of **6a** with I_2-PPh_3 in pyridine provided 6'-iodo derivative **9a**, which was reduced with Bu_3SnH in the presence of AIBN in refluxing toluene to give rise to 6'-deoxy nucleoside **10a** in a moderate overall yield (48%). Next, removal of the 4'-*O* benzyl group of **10a** was explored. Surprisingly, hydrogenolysis of the benzyl ether using several palladium-carbon catalysts under a hydrogen atmosphere or in the presence of hydrogen transfer reagents (HCO_2H, HCO_2NH_4, cyclohexene etc.) was unsuccessful. In all cases, no reaction occurred and only the starting material was recovered. An attempt to cleave the benzyl ether using BCl_3 resulted in a complex mixture, affording the desired deprotected product **11** in only 10% yield. However, in contrast to these difficulties of cleaving the benzyl ether, removal of the MPM group from **10b** was accomplished in high yield. After 6'-deoxygenation of **6b** was carried out by a sequence similar to that for **6a** (70%), **10b** was treated with DDQ in CH_2Cl_2-H_2O (9:1) to afford compound **11** in 93% yield.

The nucleoside **11** can be employed for the synthesis of plicacetin, one of the simplest structures in the amicetin family, according to the literature.[3] Additionally, it is also possible to transform the 4-methoxy moiety of **11** into a keto or amino functionality by treatment with an acid or ammonia solution.[5a]

In conclusion, we established a new synthetic route to 2',3',6'-trideoxy-β-D-*erythro*-hexopyranosyl pyrimidine nucleosides by employing the intramolecular glycosylation method, which afforded the deoxy-β-nucleosides in a completely stereoselective manner. In this reaction as well as at the following deprotection step, the MPM group was found to play an important role in obtaining the corresponding products in reasonable yields.

EXPERIMENTAL

All melting points are uncorrected. ^1H and ^{13}C NMR spectra were obtained on a JEOL JNM-EX400 spectrometer in $CDCl_3$ with Me_4Si as an internal standard. *J* Values



SCHEME 3

are given in Hz. IR spectra were recorded on a Perkin-Elmer Model 1600 spectrophotometer. TLC was performed on plates coated with silica gel 60 F_{254} (Merck). For column chromatography, Wakogel C-300 (Wako Chemicals) was used. All solvents used in the reactions were distilled from an appropriate drying agent and stored over molecular sieves.

Phenyl 4,6-di-*O*-acetyl-2,3-dideoxy-1-thio-α,β-D-*erythro*-hexopyranoside (3). To a solution of methyl 4,6-di-*O*-acetyl-2,3-dideoxy-D-*erythro*-hexofuranoside[6] (**2**) (6.55 g, 26.6 mmol) and $PhSSiMe_3$ (5.6 ml, 30 mmol) in CH_2Cl_2 (270 mL) under Ar was added $BF_3{\cdot}OEt_2$ (3.6 mL, 30 mmol)[7] at room temperature, and the reaction mixture was stirred for 17 h. The solution was poured into saturated aqueous $NaHCO_3$ and extracted with CH_2Cl_2. The organic layer was dried over $MgSO_4$ and then the solvent evaporated. The residue was chromatographed on silica gel (hexane-AcOEt, 4:1) to provide **3** (7.01 g, 81%) as a partially white solid. ^1H NMR δ 1.80–1.96 (m, 1H), 2.00–2.20 (m, 2H), 2.03 (s), 2.04 (s), 2.08 (s), 2.20–2.35 (m, 1H), 3.65–3.72 (m), 4.09 (dd, *J*=2.2, 12.0), 4.17–4.25 (m), 4.28 (dd, *J*=5.9, 12.7), 4.46–4.54 (m), 4.66–4.83 (m), 4.79 (dd, *J*=2.2, 11.5, *C*-1(β)), 5.60 (d, *J*=5.4, *C*-1(α)), 7.20–7.40 (m, 3H), 7.45–7.58 (m, 2H). IR (neat) 2955, 1742, 1654, 1440, 1372, 1237, 1043, 996 cm^{-1}. Anal. Calcd. for $C_{16}H_{20}O_5S$: C, 59.24; H, 6.21. Found: C, 59.49; H, 6.24.

Phenyl 4-*O*-benzyl-2,3-dideoxy-1-thio-α,β-D-*erythro*-hexopyranoside (4a). To a solution of **3** (1.19 g, 3.7 mmol) in MeOH (10 mL) was added NaOMe (23 mg), and the reaction mixture was stirred at room temperature for 1d. After neutralization with ion-exchange resin (Dowex 50W, H^+-form), the mixture was filtered and evaporated to dryness. The residue was dissolved in dry pyridine (14 mL), and then TrCl (3.3 g, 11.8 mmol) was added to the solution. After 17 h, the reaction mixture was poured into ice-cold water. The solution was extracted with CH_2Cl_2, and the organic layer was washed successively with dilute HCl, water, and saturated aqueous $NaHCO_3$. The organic layer was dried over $MgSO_4$, evaporated, and the residue was then

chromatographed on silica gel (hexane-AcOEt, 4:1) to provide phenyl 6-*O*-trityl-2,3-dideoxy-1-thio-α,β-D-*erythro*-hexopyranoside (1.58 g, 83%) as a light yellow oil. ^{1}H NMR δ 1.50–1.90 (m), 1.95–2.20 (m), 3.25–3.73 (m), 4.22 (ddd, *J*=4.9, 5.4, 9.3), 4.75 (dd, *J*=2.4, 13.7, *C*-1(β)), 5.50 (d, *J*=4.4, C-1 (α)), 7.20–7.57 (m, 20H). IR (neat) 3448, 3058, 3007, 2930, 1490, 1448, 1070 cm^{-1}.

To a solution of the resulting 6-*O*-trityl derivative (1.58 g, 3.3 mmol) in DMF (33 mL) was added NaH (50% in oil, 0.32 g, 6.6 mmol) at 0 °C. After 1 h, BnBr (0.78 mL, 6.6 mmol) was added dropwise to the reaction mixture at 0 °C, and the mixture was stirred at room temperature for 16 h The reaction mixture was poured into saturated aqueous NH_4Cl, extracted with ether, and washed with water. The organic layer was dried over $MgSO_4$ and then evaporated to dryness. The residue was dissolved in BuOH (10 mL) and CF_3CO_2H (3.3 mL) was added to the solution. After 8 h, the solution was neutralized with saturated aqueous $NaHCO_3$ and BuOH was removed by evaporation. The residue was extracted with $CHCl_3$. The organic layer was dried over $MgSO_4$ and then the solvent evaporated. The residue was chromatographed on silica gel (hexane-AcOEt, 4:1) to provide **4a** (955 mg, 88%) as an oil. ^{1}H NMR δ 1.50–1.90 (m), 2.00–2.20 (m), 2.30–2.40 (m), 3.35–3.55 (m), 3.67–3.87 (m), 3.90 (dd, *J*=2.9, 11.7), 4.21 (ddd, *J*=3.9, 4.4, 9.3), 4.48 (d, *J*=11.2), 4.47 (d, *J*=11.7), 4.62 (d, *J*=11.2), 4.68 (d, *J*=11.2), 4.84 (dd, *J*=2.0, 11.2, *C*-1(β)), 5.54 (d, J=3.9, *C*-1(α)), 7.20–7.50 (m, 10H). IR (neat) 3457, 2929, 2870, 1534, 1215, 1091 cm^{-1}. Anal. Calcd. for $C_{19}H_{22}O_3S$: C, 69.06; H, 6.71. Found: C, 69.34; H, 6.96.

Phenyl 4-*O*-*p*-methoxybenzyl-2,3-dideoxy-1-thio-α,β-D-*erythro*-hexopyranoside (4b). As described above, deacetylation of **3** (6.77 g, 20.9 mmol) afforded crude phenyl 2,3-dideoxy-1-thio-D-*erythro*-hexopyranoside, which was dissolved in DMF (200 mL) under Ar, and *p*-anisaldehyde dimethylacetal (3.9 mL, 23 mmol) and HBF_4-OEt_2 (3.2 mL, 22 mmol)[11] were then added at room temperature. After 1 h, Et_3N (3.1 mL) was added to the reaction mixture, and the solvent was removed by evaporation. The residue was dissolved in ether and the organic layer was washed with water and then dried over $MgSO_4$. After evaporation, the residue was chromatographed on silica gel (hexane-AcOEt, 9:1) to provide phenyl 4,6-di-*O*-*p*-methoxybenzylidene-2,3-dideoxy-1-thio-D-*erythro*-hexopiranoside (7.06 g, 94%) as a white solid. ^{1}H NMR δ 1.73–2.10 (m, 2H), 2.12–2.37 (m, 2H), 3.48 (ddd, *J*=4.9, 9.8, 9.8), 3.55–3.90 (m), 3.79 (s), 3.80 (s), 4.14 (dd, *J*=4.9, 10.3), 4.27 (dd, *J*=4.9, 10.8), 4.35 (ddd, *J*=4.9, 9.8, 9.8), 4.90 (dd, *J*=2.0, 11.7, *C*-1(β)), 5.51 (s), 5.54 (s), 5.56 (d, *J*=4.9, *C*-1(α)), 6.85–6.95 (m, 2H), 7.20–7.37 (m, 3H), 7.37–7.55 (m, 4H). IR (KBr) 2935, 2891, 1615, 1518, 1368, 1248, 1179, 1089, 1032 cm^{-1}.

To a solution of the resulting *p*-methoxybenzylidene derivative (2.15 g, 6.0 mmol) in MeCN (120 mL) was added $NaBH_3CN$ (2.30 g, 36 mmol) and molecular sieves 3A (1.2 g) under Ar. After 30 min, the solution was cooled to 0 °C, and Me_3SiCl (4.6 mL, 36 mmol) in MeCN (30 mL) was then added.[8] The reaction mixture was stirred at room temperature for 2 h, filtered through Celite and poured into ice-cold saturated aqueous $NaHCO_3$. The aqueous layer was extracted with CH_2Cl_2. The organic layer was washed with saturated aqueous $NaHCO_3$, dried over $MgSO_4$, and then evaporated. The residue was chromatographed on silica gel (hexane-AcOEt, 4:1) to provide **4b** (1.88 g, 87%) as a colorless oil, along with 0.13 g (6%) of 6-*O*-MPM derivative. ^1H NMR δ 1.50–1.90 (m), 2.05–2.20 (m), 2.27–2.37 (m), 3.36–3.51 (m), 3.68–3.93 (m), 3.80 (s), 3.81 (s), 4.18 (ddd, *J*=3.4, 4.9, 8.3), 4.41 (d, *J*=11.2), 4.44 (d, *J*=11.2), 4.55 (d, *J*=11.2), 4.61 (d, *J*=11.2), 4.83 (dd, *J*=2.0, 11.7, *C*-1(β)), 5.54 (d, *J*=3.4, *C*-1(α)), 6.86–6.97 (m, 2H), 7.20–7.38 (m, 5H), 7.40–7.55 (m, 2H). IR (neat) 3442, 1661, 1627, 1543, 1486, 1250, 1094 cm^{-1}. Anal. Calcd. for $C_{20}H_{24}O_4S$: C, 66.64; H, 6.71. Found: C, 66.81; H, 6.85.

Phenyl 4-*O*-benzyl-6-*O*-(4-methoxypyrimidin-2-yl)-2,3-dideoxy-1-thio-α,β-D-*erythro*-hexopyranoside (5a). To a solution of **4a** (425 mg, 1.29 mmol) in DMF (6.4 mL) was added NaH (50% in oil, 124 mg, 2.6 mmol) at 0 °C under Ar. After 30 min, the solution was cooled to –50 °C and then 2-chloro-4-methoxypyrimidine[9] in DMF (2 mL) was added. The reaction mixture was stirred at –20 °C for 15 h. The reaction was quenched with saturated aqueous NH_4Cl. The solution was extracted with $CHCl_3$. The organic layer was dried over $MgSO_4$ and evaporated. The residue was chromatographed on silica gel (hexane-AcOEt, 5:1) to provide **5a** (433 mg, 77%) as a colorless oil. ^1H NMR δ 1.55–1.94 (m), 2.05–2.28 (m), 2.33–2.42 (m), 3.50–3.63 (m), 3.68–3.85 (m), 3.93 (s), 3.95 (s), 4.40–4.73 (m), 4.82 (dd, *J*=2.0, 11.3, *C*-1(β)), 5.58 (d, *J*=3.9, *C*-1(α)), 6.35 (d, *J*=5.9, 1H), 7.15–7.38 (m, 8H), 7.40–7.56 (m, 2H), 8.16 (d, *J*=5.4), 8.18 (d, *J*=5.4). IR (neat) 2948, 1584, 1574, 1418, 1377, 1284, 1098, 1085 cm^{-1}.

Phenyl 4-*O*-*p*-methoxybenzyl-6-*O*-(4-methoxypyrimidin-2-yl)-2,3-dideoxy-1-thio-α,β-D-*erythro*-hexopyranoside (5b). According to the above procedure, starting with **4b** (1.43 g, 4.0 mmol) in DMF (40 mL), NaH (60% in oil, 0.32 g, 8 mmol) and 2-chloro-4-methoxypyrimidine (1.16 g, 8 mmol), **5b** (1.30 g, 71%) was obtained as a colorless oil after chromatography on silica gel (hexane-AcOEt, 4:1). ^1H NMR δ 1.52–1.65 (m), 1.74–1.90 (m), 2.40–2.39 (m), 3.48–3.59 (m), 3.66–3.75 (m), 3.77 (s), 3.78 (s), 3.93 (s), 3.95 (s), 4.38–4.70 (m), 4.81 (dd, *J*=2.0, 11.7, *C*-1(β)), 5.57 (d, *J*=4.4, *C*-1(α)), 6.35 (d, *J*=5.4), 6.37 (d, *J*=5.4), 6.79 (d, *J*=8.8), 6.82 (d, *J*=8.8), 7.14–7.31 (m, 5H), 7.44–7.55 (m, 2), 8.16 (d, *J*=5.4), 8.18 (d, *J*=5.4). IR (neat) 2946, 1584, 1574, 1514, 1418, 1284, 1248, 1085 cm^{-1}.

1-(4-*O*-Benzyl-2,3-dideoxy-β-D-*erythro*-hexopyranosyl)-4-methoxypyrimidine (6a). To a solution of **5a** (158 mg, 0.36 mmol) in MeCN (90 mL) under Ar, powdered molecular sieves 4A (0.9 g) were added. After 15 h, the solution was cooled to –20 °C, and $Me_2S(SMe)BF_4$ (80 mg, 0.40 mmol) was then added. After 5 h, aqueous NaOH (1M, 30 mL) was added to the reaction mixture, and the mixture was warmed to 0 °C for over 2 h. After saturated aqueous NH_4Cl was added, the solution was stirred at room temperature for 30 min, then filtered through Celite and extracted with $CHCl_3$. The organic layer was dried over $MgSO_4$ and evaporated. The residue was chromatographed on silica gel (hexane-AcOEt, 1:5) to provide **6a** (69 mg, 56%) as a white solid, along with 23% of **7a**. mp 154.5–156°C; ^1H NMR δ 1.39–1.51 (m, 1H), 1.66–1.79 (m, 1H), 2.16–2.25 (m, 1H), 2.32–2.42 (m, 1H), 3.40–3.50 (m, 1H), 3.60–3.68 (m, 1H), 3.72–3.80 (m, 1H), 3.87–4.00 (m, 1H), 3.95 (s, 3H), 4.49 (d, *J*=11.7, 1H), 4.67 (d, *J*=11.7 1H), 5.85 (dd, *J*=1.5, 10.8, 1H, *C*-1), 5.91 (d, *J*=7.3, 1H), 7.25–7.40 (m, 5H), 7.66 (d, *J*=7.3, 1H); ^{13}C NMR δ 27.6, 30.2, 54.4, 62.6, 71.0, 72.2, 81.2, 82.9, 95.8, 127.8, 128.0, 128.5, 137.7, 142.1, 155.2, 171.5; IR (KBr) 3454, 2929, 1654, 1635, 1550, 1317, 1095 cm^{-1}.

1-(4-*O*-*p*-Methoxybenzyl-2,3-dideoxy-β-D-*erythro*-hexopyranosyl)-4-methoxypyrimidine (6b). According to the above procedure, starting with **5b** (419 mg, 0.89 mmol) in MeCN (224 mL), powdered MS 4A (4.1 g), $Me_2S(SMe)BF_4$ (193 mg, 0.98 mmol) and aq. NaOH (90 mL), **6b** (266 mg, 79%) was obtained as a white solid after chromatography on silica gel (AcOEt), along with 12% of **7b**. mp 133–134 °C; ^1H NMR δ 1.37–1.52 (m, 1H), 1.64–1.77 (m, 1H), 1.83–2.01 (br, 1H), 2.20 (m, *J*=3.4, 6.4, 12.7, 1H), 2.35 (m, *J*=3.9, 7.8, 13.2 1H), 3.42 (ddd, *J*=4.4, 9.27, 10.7, 1H), 3.62 (ddd, *J*=3.4, 4.9, 8.3, 1H), 3.75 (dd, *J*=4.9, 12.2, 1H), 3.81 (s, 3H), 3.88 (dd, *J*=2.9, 11.7, 1H), 3.95 (s, 3H), 4.43 (d, *J*=11.2, 1H), 4.60 (d, *J*=11.2, 1H), 5.84 (dd, *J*=2.4, 8.3, 1H, *C*-1), 5.91 (d, *J*=7.8, 1H), 6.89 (d, *J*=8.8, 1H), 7.25 (d, *J*=8.8, 1H), 7.65 (d, *J*=7.3, 1H): ^{13}C NMR δ 27.7, 30.3, 54.5, 55.3, 62.7, 70.7, 72.0, 81.2, 83.0, 96.0, 114.0, 129.5, 129.8, 142.2, 155.3, 159.5, 171.6; IR (KBr) 3442, 1662, 1627, 1543, 1486, 1106, 1094 cm^{-1}.

1-(4-*O*-Benzyl-6-phenylthio-2,3,6-trideoxy-β-D-*erythro*-hexopyranosyl)-4-methoxypyrimidine (8a). To a solution of **6a** (166 mg, 0.48 mmol) in pyridine (2.5 mL), PhSSPh (312 mg, 1.4 mmol) and Bu_3P (0.30 mL, 1.2 mmol) were added. After 4 h, the reaction mixture was poured into water and extracted with $CHCl_3$. The organic layer was dried over $MgSO_4$ and evaporated. The residue was chromatographed on silica gel (hexane-AcOEt, 1:1) to provide **8a**. ^1H NMR δ 1.25–1.40 (m, 1H), 1.61–1.75 (m, 1H), 2.22–2.3 (m, 1H), 2.3–2.43 (m, 1H), 3.20 (dd, *J*=5.4, 14.2, 1H), 3.49 (dd, *J*=2.4, 14.2, 1H), 3.58–3.67 (m, 1H), 3.80–3.88 (m, 1H), 3.93 (s,

3H), 4.42 (d, *J*=11.7, 1H), 4.65 (d, *J*=11.7, 1H), 5.70 (dd, *J*=2.0, 10.3, 1H, *C*-1), 5.73 (d, *J*=7.3, 1H), 7.16 (d, *J*=7.8, 1H), 7.13–7.45 (m, 10H).

1-(4-*O*-Benzyl-6-iodo-2,3,6-trideoxy-β-D-*erythro*-hexopyranosyl)-4-methoxypyrimidine (9a). To a solution of **6a** (97 mg, 0.28 mmol) in pyridine (2 mL), I_2 (86 mg, 0.34 mmol) and Ph_3P (89 mg, 0.34 mmol) were added. After 5 h, the reaction mixture was poured into aqueous $Na_2S_2O_3$ and extracted with $CHCl_3$. The organic layer was dried over $MgSO_4$ and evaporated. The residue was chromatographed on silica gel (0.3% MeOH/$CHCl_3$) to provide **9a**. mp 146–149 °C; ^{1}H NMR δ 1.40–1.54 (m, 1H), 1.70–1.85 (m, 1H), 2.25–2.43 (m, 2H), 3.18 (ddd, *J*=3.4, 3.4, 8.8, 1H), 3.40–3.5 (m, 1H), 3.49 (dd, *J*=2.9, 10.7, 1H), 3.62 (dd, *J*=3.4, 10.7, 1H), 3.96 (s, 3H), 4.53 (d, *J*=11.2, 1H), 4.69 (d, *J*=11.2, 1H), 5.88 (dd, *J*=2.0, 10.8, 1H, *C*-1), 5.95 (d, J=7.7, 1H), 7.28–7.47 (m, 5H), 7.74 (d, *J*=7.3, 1H); ^{13}C NMR δ 8.7, 26.9, 30.3, 54.5, 71.1, 75.4, 77.9, 82.7, 96.1, 128.0, 128.6, 137.6, 142.4, 155.2, 171.1; IR (KBr) 1670, 1633, 1542, 1481, 1316, 1190, 1125, 1101 cm^{-1}.

1-(4-*O*-Benzyl-2,3,6-trideoxy-β-D-*erythro*-hexopyranosyl)-4-methoxypyrimidine (10a). To a degassed solution of **9a** (92 mg, 0.20 mmol) in toluene (4 mL), Bu_3SnH (65 μL, 0.24 mmol) and AIBN (1.7 mg, 0.01 mmol) were added under Ar, and the solution was heated under reflux. After 6 h, the solution was cooled to room temperature and the solvent evaporated. The residue was chromatographed on silica gel (hexane-AcOEt, 1:1) to provide **10a** (44 mg, 67%) as a white solid. mp 102–104 °C; ^{1}H NMR δ 1.25–1.49 (m, 1H), 1.33 (d, *J*=5.9, 3H), 1.60–1.76 (m, 1H), 2.20–2.40 (m, 2H), 3.05–3.16 (m, 1H), 3.60–3.70 (m, 1H), 3.95 (s, 3H), 4.49 (d, *J*=11.7, 1H), 4.67 (d, *J*=11.7, 1H), 5.77 (dd, *J*=2.0, 10.7, 1H, *C*-1), 5.91 (d, *J*=7.3, 1H), 7.28–7.43 (m, 5H), 7.67 (d, *J*=7.3, 1H); ^{13}C NMR δ 18.7, 28.0, 30.9, 54.6, 71.3, 77.8, 77.9, 83.1, 95.9, 128.0×2, 128.7, 142.5, 155.5, 171.8; IR (KBr) 2931, 1670, 1636, 1546, 1479, 1304, 1095 cm^{-1}.

1-(4-*O*-*p*-Methoxybenzyl-6-iodo-2,3,6-trideoxy-β-D-*erythro*-hexopyranosyl)-4-methoxypyrimidine (9b). According to the procedure described for **9a**, starting with **6b** (98 mg, 0.26 mmol), pyridine (2.6 mL), I_2 (132 mg, 0.52 mmol), and PPh_3 (136 mg, 0.52 mmol), **9b** (107 mg, 85%) was obtained as a white solid after chromatography on silica gel (0.2% MeOH/$CHCl_3$). mp 107–108 °C; ^{1}H NMR δ 1.36–1.50 (m, 1H), 1.67–1.81 (m, 1H), 2.25–2.37 (m, 2H), 3.16 (ddd, *J*=2.9, 3.4, 8.8, 1H), 3.40 (ddd, *J*=4.4, 8.8, 10.8, 1H), 3.48 (dd, *J*=2.9, 10.7, 1H), 3.59 (dd, *J*=3.9, 10.7, 1H), 3.81 (s, 3H), 3.96 (s, 3H), 4.47 (d, *J*=10.7, 1H), 4.61 (d, *J*=10.7, 1H), 5.87 (dd, *J*=2.0, 10.3, 1H, *C*-1), 5.95 (d, *J*=7.3, 1H), 6.90 (d, *J*=8.3, 2H), 7.27 (d, *J*=8.8, 2H), 7.74 (d, *J*=7.3, 1H); ^{13}C NMR δ 8.7, 27.0, 30.4, 54.5, 55.3, 71.0, 75.1, 77.9, 82.7, 96.1, 114.0, 129.6, 129.7, 142.4, 155.2, 159.5, 171.7; IR (KBr) 1670, 1640, 1544, 1515, 1486, 1328, 1306, 1251, 1094, 1014 cm^{-1}.

1-(4-*O*-*p*-Methoxybenzyl-2,3,6-trideoxy-β-D-*erythro*-hexopyranosyl)-4-methoxypyrimidine (10b). According to the procedure described for **10a**, starting with **9b** (319 mg, 0.66 mmol), toluene (13 mL), Bu_3SnH (0.35 mL, 1.3 mmol), and AIBN (5 mg, 0.03 mmol), **10b** (195mg, 82%) was obtained as a solid after chromatography on silica gel (hexane-AcOEt, 1:1). mp 96–97 °C; ^1H NMR δ 1.25–1.47 (m, 1H), 1.31 (d, *J*=5.9, 3H), 1.60–1.73 (m, 1H), 2.20–2.34 (m, 2H), 3.07 (ddd, *J*=4.4, 8.8, 10.7, 1H), 3.63 (dq, *J*=5.9, 8.8, 1H), 3.81 (s, 3H), 3.95 (s, 3H), 4.42 (d, *J*=11.2, 1H), 4.59 (d, *J*=11.2, 1H), 5.75 (dd, *J*=2.0, 10.3, 1H, *C*-1), 5.90 (d, *J*=7.8, 1H), 6.89 (d, *J*=8.8, 2H), 7.26 (d, *J*=7.8, 2H), 7.67 (d, *J*=7.3, 1H); ^{13}C NMR δ 18.4, 27.8, 30.7, 54.4, 55.3, 70.8, 77.6, 82.8, 95.7, 113.8, 129.4, 130.1, 142.3, 155.3, 159.3, 171.5; IR (KBr) 1673, 1634, 1542, 1485, 1252, 1086 cm^{-1}.

1-(2,3,6-Trideoxy-β-D-*erythro*-hexopyranosyl)-4-methoxypyrimidine (11). To a solution of **10b** (67 mg, 0.19 mmol) in CH_2Cl_2 (1.8 mL)-water (0.2 mL) was added DDQ (53 mg, 0.22 mmol) at room temperature.[12] After 6 h, saturated aqueous $NaHCO_3$ was added to the reaction mixture. The solution was extracted with 10% *i*-PrOH/AcOEt. The organic layer was dried over Na_2SO_4 and then evaporated. The residue was chromatographed on silica gel (AcOEt) to provide **11** (41 mg, 93%) as a solid. mp 137–138 °C; ^1H NMR δ 1.34 (d, *J*=5.9, 3H), 1.43–1.54 (m, 1H), 1.67–1.79 (m, 1H), 2.16–2.24 (m, 2H), 3.28–3.37 (m, 1H), 3.52 (dq, *J*=6.4, 9.3, 1H), 3.96 (s, 3H), 5.77 (dd, *J*=2.0, 10.3, 1H, *C*-1), 5.92 (d, *J*=7.3, 1H), 7.69 (d, *J*=7.8, 1H); ^{13}C NMR δ 18.1, 30.9, 31.3, 54.4, 71.0, 78.8, 82.9, 95.9, 142.3, 155.4, 171.5; IR (KBr) 3326, 2948, 1632 (br), 1546, 1480, 1422, 1348, 1310, 1223, 1107, 1088, 1055, 1034 cm^{-1}.

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