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# New Modular and Efficient Approach to 6-Substituted Pyridin-2-yl C-Nucleosides

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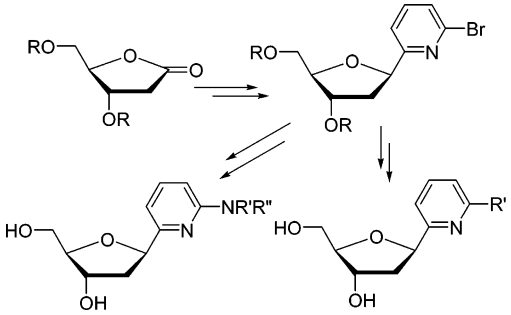


A novel modular, efficient, and practical methodology of preparation of 6-substituted pyridin-2-yl C-nucleosides was developed. An addition of 2-lithio-6-bromopyridine **2b** to TBDMS-protected 2-deoxyribonolactone **5** gave aduct **7** as an equilibrium mixture of anomeric hemiketals 1-(6-bromopyridin-2-yl)-1-hydroxynucleosides **7a**,**b** and its open form **7c**. Reduction of the adduct **7** with $Et_3SiH$ and $BF_3{\cdot}Et_2O$ afforded the desired 6-bromonucleoside **8a** as pure $\beta$-anomer in a total yield of 32% over two steps from **5**. Intermediate **8a** was then subjected to a series of palladium catalyzed cross-coupling reactions and aminations to give a series of protected 1$\beta$-(6-alkyl-, 6-aryl-, and 6-aminopyridin-2-yl)-2-deoxyribonucleosides **9**. Catalytic hydrogenation of **8a** gave an unsubstituted pyridine C-nucleoside, and diazotative oxodeamination of 6-aminopyridine nucleoside **9f** by isopentyl nitrite in acetic acid gave 6-oxopyridine nucleoside **10i**. Deprotection of silylated nucleosides **9** by $Et_3N{\cdot}3HF$ gave a series of free C-nucleosides **10**.

## Introduction

C-Nucleosides are an important class of compounds characterized by replacement of a labile nucleosidic C−N bond by a stable hardly degradable C−C bond. Many of them possess antiviral or antineoplastic activities.[1] Quite recently, C-nucleosides bearing hydrophobic aryl groups as nucleobase surrogates attracted great attention because of their use in the extension of the genetic alphabet.[2] In oligonucleotide duplexes, they selectively pair with the same or other hydrophobic nucleobase because of favorable packing and desolvation energy as compared to canonical hydrophilic nucleobases.[3] Triphosphates of some of the C-nucleosides are efficiently incorporated to DNA by DNA polymerase.[4] Pyridine C-nucleosides are a very interesting subclass because of their equivocal nature between hydrophilic and hydrophobic species, but there were just a few

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(1) Examples: (a) Franchetti, P.; Cappellacci, L.; Griffantini, M.; Barzi, A.; Nocentini, G.; Yang, H. Y.; O'Connor, A.; Jayaram, H. N.; Carrell, C.; Goldstein, B. M. *J. Med. Chem.* **1995**, *38*, 3829−3837. (b) Walker, J. A.; Liu, W.; Wise, D. S.; Drach, J. C.; Townsend, L. B. *J. Med. Chem.* **1998**, *41*, 1236−1241.

(2) Reviews: (a) Wang, L.; Schultz, P. G. *Chem. Commun.* **2002**, 1−11. (b) Henry, A. A.; Romesberg, F. E. *Curr. Opin. Chem. Biol.* **2003**, *7*, 727−733. (c) Kool, E. T.; Morales, J. C.; Guckian, K. M. *Angew. Chem., Int. Ed.* **2000**, *39*, 990−1009. (d) Kool, E. T. *Acc. Chem. Res.* **2002**, *35*, 936−943.

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rather scattered examples of syntheses of 3-pyridyl ribo-[5] and 2-deoxyribonucleosides[6] as analogues of canonical pyrimidines.

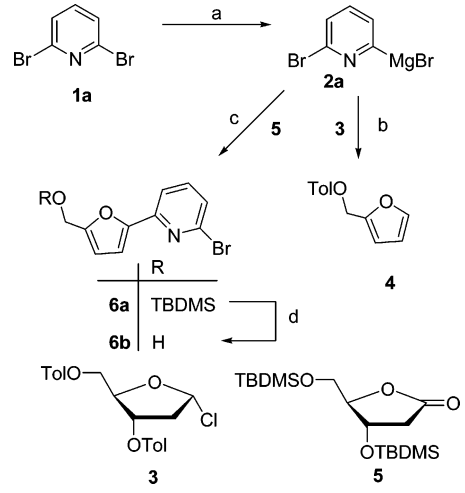
There are several synthetic approaches[7] to C-nucleosides: (i) additions of organometallics to ribono- or 2-deoxyribonolactones,[4,8] (ii) coupling of a halogenose with organometallics (usually highly toxic diarylcadmium species),[9] (iii) electrophilic substitutions of electron rich aromatics with sugars under Lewis acid catalysis,[10] or (iv) Heck-type coupling of aryl iodides with glycals.[6,11] All these approaches suffer from poor yields, insufficient anomeric selectivity, and necessity to optimize reaction and separation conditions for each particular C-nucleoside, which makes it very difficult to prepare larger series of derivatives. Therefore, development of general and possibly also modular approaches to the synthesis of these extremely important compounds is of great interest.

We are currently involved in development of modular methodologies based on larger scale syntheses of versatile C-nucleoside intermediates and their further use for a generation of series of diverse derivatives. Recently, we have developed a modular approach consisting of the preparation of bromophenyl C-nucleosides[12] followed by the displacement of the bromine for alkyl or aryl substituents by cross-coupling reactions. Another modular methodology was based on construction of an aromatic ring on deoxyribose by cyclotrimerizations of 1-ethynyl-2-deoxyribose with α,ω-diynes.[13] Here we wish to report on an efficient and modular synthesis of diverse 6-substituted 2-pyridyl C-nucleosides. One of the most interesting aspects of these novel nucleobases is their positioning of a nitrogen as hydrogen-bond acceptor in the minor groove of DNA.

## Results and Discussion

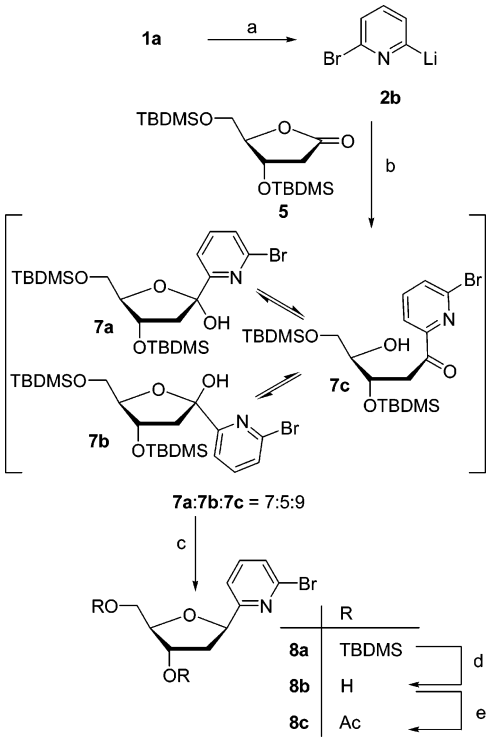
Our approach of choice for the synthesis of the title 6-substituted 2-pyridyl C-nucleosides was based on the synthesis of a suitably protected 6-bromopyrinin-2-yl C-nucleoside intermediate and on its further synthetic transformations (cross-coupling, amination, etc.). Therefore, our first efforts were devoted to the synthesis of the corresponding bromopyridine nucleoside intermediate. Several reactions have been studied for this purpose on the basis of literature analogy (Scheme 1). 2,6-Dibromopyridine (**1a**) was used as a starting compound for monometalation. Its reaction with magnesium gave bromopyridine Grignard reagent **2a** that was used itself or transmetalated with $ZnCl_2$, $CdCl_2$, $Zn(CN)_2$, or CuCN. Toluoyl protected 1α-chloro-1,2-dideoxyribose **3** was our first starting sugar of choice that was subjected to a series of reactions with **2a** in the

**SCHEME 1. Reactions of Halogenose 3 and Lactone 5 with Organometallics**[a]




[a] Reagents and conditions: (a) (i) Mg, THF, rt, 1 h; (b) in the absence or in the presence of the following additives: (i) $ZnCl_2$; (ii) $CdCl_2$; (iii) CuI; (iv) $Zn(CN)_2$; (v) CuCN; THF, rt, 2 h−1 day; (c) THF, rt, 2 h; (d) $Et_3N{\cdot}3HF$, THF, rt, 14 h, 57% from **2a**.

**SCHEME 2. Synthesis of Bromoderivatives 8a and 8b**[a]




[a] Reagents and conditions: (a) *n*-BuLi, THF, −78 °C, 10 min; (b) **5**, THF, −78 °C, 30 min, 61%; (c) $Et_3SiH$, $BF_3{\cdot}Et_2O$, $CH_2Cl_2$, 0 °C, ca. 45 min, 53%; (d) $Et_3N{\cdot}3HF$, THF, rt, 12 h, 92%; (e) $Ac_2O$, py, 14 h, rt, 76%.

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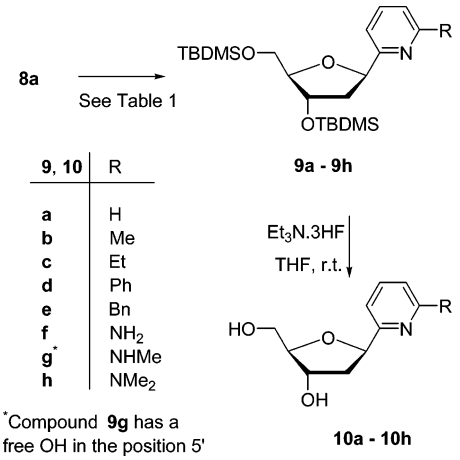
**SCHEME 3. Cross-Coupling and Amination Reactions of 8a**




absence or in the presence of additive metal salts under various conditions. Unfortunately, no desired nucleoside was ever isolated. In all cases, the reaction mixtures contained mainly furan **4**, degraded halogenose, and 2-bromopyridine side products (Scheme 1).

Having no encouraging results with halogenose **3**, further efforts focused on TBDMS-protected 2-deoxyribonolactone **5**, which is very easily available in two steps from 2-deoxyribose.[14] Despite the higher stability of lactone **5**, the first reaction with (6-bromopyridin-2-yl)magnesium bromide **2a** also led to furan byproduct **6a**. More successful was an application of the organolithium species. 2-Lithio-6-bromopyridine **2b** generated by the reaction of 2,6-dibromopyridine **1a** with *n*-butyllithium at −78 °C in 10 min reacted with lactone **5** to afford adduct **7** in 61% yield (Scheme 2). Adduct **7** was isolated as a chromatographically homogeneous equilibrium mixture of $\beta$- and $\alpha$-anomeric hemiketals **7a**,**b** and an open form **7c** in the ratio 7:5:9 (determined by COSY, HMBC, and ROESY spectra, see Supporting Information). Hemiketal formation from $\gamma$-hydroxyketones analogous to **7** is known[8f] to be reversible forming an equilibrium of the three forms.

A reduction of the adduct **7** was then performed with $Et_3SiH$ (in analogy to literature[8]) in different solvents (toluene, $CH_2Cl_2$, MeCN) in the presence of different Lewis acids ($BF_3{\cdot}Et_2O$, $SnCl_4$, $ZnCl_2$). The optimum procedure made use of $BF_3{\cdot}Et_2O$ in $CH_2Cl_2$ at 0 °C to give an acceptable 53% yield of nucleoside **8a.** Its structure was determined by NMR spectroscopy (NOE, see Supporting Information) to be pure desired $\beta$-anomer. Sideproducts of this reaction were partially and fully desilylated derivatives of the $\beta$-anomeric configuration (ca. 15%). Apparently, the hemiketal formation is reversible and the $\beta$-hemiketal **7a** is reduced preferentially to give good yield of **8a** and other desilylated $\beta$-anomers. We found that $Et_3SiH$ (5 equiv) should be added to the solution of **7** in three portions, and each portion must be followed by a dropwise addition of diluted $BF_3{\cdot}Et_2O$ in order to minimize desilylation followed by elimination to furan. Despite the problems with purification and characterization of the intermediate adduct **7**, we were able to isolate the desired $\beta$-C-nucleoside **8a** in acceptable total yield of 32% over two steps based on starting lactone **5**.

Having a practical multigram scale procedure for a preparation of 6-bromopyridine nucleoside **8a** in hand, we decided to study its reactivity, that is, cross-coupling reactions with diverse organometallics and other transformations that lead to a variety of new nucleosides. To have more freedom in the use of diverse reagents, we sought to prepare also the acyl-protected bromopyridine nucleoside. The silyl group in nucleoside **8a** was cleaved under standard conditions[15] using $Et_3N{\cdot}3HF$ in THF to give free nucleoside **8b**, which was then acetylated with acetic anhydride in pyridine to give acetylated nucleoside **8c** in 76% yield.

The first target derivative was an unsubstituted pyridine nucleoside **9a**. Interestingly, attempts to apply an analogous procedure as in synthesis of **8a**, the addition of 2-lithiopyridine generated from 2-bromopyridine to lactone **5**, have failed. The addition proceeded with only a very low yield (ca. 25%) and the following reduction with $Et_3SiH$ gave a furan as the only product. Even an extensive optimization of this procedure has not brought any improvement. Therefore, we have used catalytical hydrogenolysis of bromine in nucleoside **8a** using $H_2$ over Pd/C. The first experiment was performed in a mixture of EtOH, THF, and $H_2O$ to give the desired nucleoside **9a** in only low yield (about 10%) accompanied by some unreacted starting compound and polar byproducts. Apparently, HBr resulting in the reaction cleaved the protecting groups and caused side reactions. Therefore, we have added $Et_3N$ to neutralize the HBr, and under these modified conditions the reaction was completed within 30 min to give cleanly the desired nucleoside **9a** in 81% yield.

Pd-catalyzed cross-coupling reactions were used for introduction of alkyl or aryl substituents. The reactions of **8a** with trimethylaluminum, triethylaluminum, phenylboronic acid, and benzylzinc chloride were performed under standard conditions for each type of reaction using standard catalysis of $Pd(PPh_3)_4$ and with no optimization (Scheme 3, Table 1). In all of these reactions, the desired nucleosides **9b**−**e** were obtained in good isolated yields (>70%).

Hartwig−Buchwald aminations[16,17] were used for introduction of N-substituents. Lithium bis(trimethylsilyl)amide (LiN-

**TABLE 1. Reagents, Conditions, and Yields of Reactions Presented in Scheme 3**

| entry | reagent | catalyst | ligand/base | solvent | other conditions | product | yield (%) | deprotection product | yield (%) |
|---|---|---|---|---|---|---|---|---|---|
| 1 | $H_2$ | Pd/C | $Et_3N$ | THF, EtOH, $H_2O$ | rt, 101 kPa | **9a** | 81 | **10a** | 84 |
| 2 | $Me_3Al$ | $Pd(PPh_3)_4$ | | THF | 12 h, 70 °C | **9b** | 78 | **10b** | 80 |
| 3 | $Et_3Al$ | $Pd(PPh_3)_4$ | | THF | 20 h, 70 °C | **9c** | 90 | **10c** | 74 |
| 4 | $PhB(OH)_2$ | $Pd(PPh_3)_4$ | $K_2CO_3$ | toluene | 12 h, 100 °C | **9d** | 72 | **10d** | 56 |
| 5 | BnZnCl | $Pd(PPh_3)_4$ | | THF | 18 h, 70 °C | **9e** | 77 | **10e** | 66 |
| 6 | $LiN(SiMe_3)_2$ | $Pd_2(dba)_3$ | $P(t\text{-}Bu)_3{\cdot}HBF_4$ | THF | 2 h, rt | **9f** | 83 | **10f** | 68 |
| 7 | $MeNH_2{\cdot}HCl$ | $Pd_2(dba)_3$ | bdtbp,[a] *t*-BuONa | toluene | 24 h at rt, 8 h at 80 °C | **9g** | 50 | **10g** | 78 |
| 8 | $Me_2NH{\cdot}HCl$ | $Pd_2(dba)_3$ | bdtbp,[a] *t*-BuONa | toluene | 24 h at rt, 8 h at 80 °C | **9h** | 48 | **10h** | 57 |

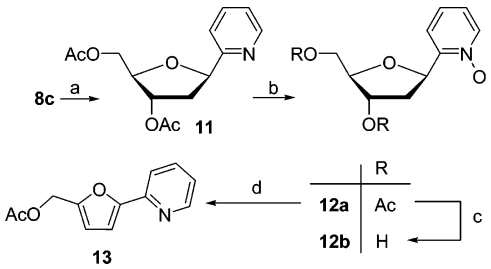
[a] bdtbp = (2-biphenyl)di-*tert*-butylphosphine.

$(SiMe_3)_2$) was used as an ammonia equivalent for the introduction of an amino group. Its reaction with **8a** was performed in the presence of $Pd_2(dba)_3$ and P(*t*-Bu)$_3$ (generated in situ from P(*t*-Bu)$_3$·$HBF_4$ using excess of the amide) to give the desired aminopyridine nucleoside **9f** in good yield of 80%. When using a less reactive zinc bis[bis(trimethylsilyl)]amide,[16] low yield (27%) of **9f** was obtained. Buchwald[17] reactions were used for the introduction of substituted amino groups. The reactions of **8a** with methylamine and dimethylamine hydrochlorides were performed under standard conditions in the presence of $Pd_2$-$(dba)_3$, 2-(di-*tert*-butylphosphino)biphenyl, and an excess of *t*-BuONa as base to give the target substituted amines **9g**,**h** in ca. 50% yields. TLC analysis showed some unreacted starting material and some polar byproducts: Apparently, the stability of the silyl groups on longer time heating under basic conditions is rather limited, and the desilylated products undergo side reactions, for example, eliminations. Nevertheless, the 50% yields obtained from the optimized procedure were satisfactory for our purposes since the desired compounds were easily isolated and unreacted starting compound **8a** was recovered (13%) and reused.

All silylated nucleosides **9a**−**h** were deprotected using $Et_3N$·3HF in THF[15] to give a series of title free 6-substituted pyridine C-nucleosides **10a**−**h** in good yields.

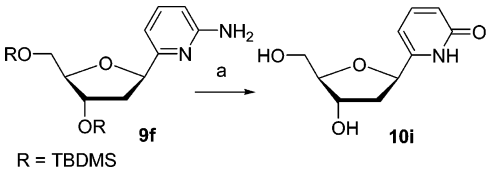
Having an access to pyridine C-nucleosides bearing C- and N-substituents in the position 6, we turned our attention to the attachment of O-substituents, in particular to the synthesis of pyridone **10i** which may be considered as an analogue of uracil. Bromopyridines are known to react[5,18,19] with BnONa to give (benzyloxy)pyridine that could be hydrogenolytically deprotected to pyridones. However our attepmts on substitution of the bromine in nucleosides **8a**,**b** with BnONa, generated from BnOH and NaH under different conditions yielded either products of degradation or furan **6a**, although an analogous reaction of 2-bromo-6-methylpyridine gave 1-benzyloxy-6-methylpyridine in high yield of 80%. Other attempts to prepare pyridone **10i** were also unsuccessful (for details, see Supporting Information). Another method for synthesis of pyridones makes use[5,20] of a rearrangement of pyridine-*N*-oxides by heating with $Ac_2O$. Therefore, we prepared the *N*-oxide nucleoside **12a**. Catalytic hydrogenolysis of acetylated bromopyridine nucleoside **8c** was performed with $H_2$ over Pd/C using AcONa as a weak base because of the low stability of acetates in basic conditions to give pyridine nucleoside **11** in 85%. Pyridine **11** was then oxidized with MCPBA to the *N*-oxide **12a** in 62% yield. Attempted rearrangement of **12a** to pyridone upon heating in acetic anhydride was not successful, giving furan **13** as the only product (Apparently, the oxidation took place at the position 1′ followed by eliminations) (Scheme 4). Acylated *N*-oxide nucleoside was deprotected to free nucleoside **12b** using treatment with NaOMe in methanol.

**SCHEME 4. Synthesis and Rearrangement of *N*-oxide 12**[a]




[a] Reagents and conditions: (a) $H_2$, P/C, THF, EtOH, $H_2O$, rt, 101 kPa, 30 min, 85%; (b)MCPBA/$CH_2Cl_2$, 14 h, rt, 62%; (c) MeONa, MeOH, rt, 6 h, 70%; (d) $Ac_2O$, reflux, 6 h, 72%.

**SCHEME 5. Preparation of 6-Oxopyridin-2-yl Nucleoside 14**[a]




[a] Reagents and conditions: (a) isopentyl nitrite, 80% AcOH in $H_2O$, 70 °C, 3 h, 48%.

Diazotation of 2-aminopyridines in diluted aqueous solutions is another approach[21] to pyridones, and its variant using isoamyl nitrite in aqueous acetic acid is often used[22] in nucleoside chemistry to convert adenine to hypoxanthine derivatives. Therefore we treated aminopyridine C-nucleoside **9f** with isopentyl nitrite in 80% aqueous AcOH at 70 °C for 3 h to afford the desired 6-oxopyridin-2-yl C-nucleoside **10i** in 48% yield (Scheme 5). The moderate yield of this reaction was due to partial degradation of the C-nucleoside skeleton and due to some loss during isolation of the polar free nucleoside on column chromatography. Despite the lower yield, the reaction is reasonably clean and practical for the preparation of the pyridone nucleoside **10i**.

All compounds were fully characterized, and the crystal structures of **10e**,**h** were also determined by X-ray diffraction. NMR conformation analyses (see Supporting Information) indicate that in DMSO solution, the free nucleosides **10a**−**h** occur in the ratio C2′-endo/C4′-exo conformers of ca. 4:1 in all of the compounds with no significant substituent effect. According to the X-ray diffraction, the C-nucleosides **10e**,**h** occur in solid state in solely C2′-endo form and in *syn*-conformation of the nucleobase because of strong hydrogen-bonds between the 5′-OH group and the nitrogen atom in pyridine (Figure 1).

In conclusion, a modular and reasonably practical methodology of the synthesis of 6-substituted pyridin-2-yl C-nucleosides was developed. It is based on cross-coupling reactions and Hartwig-Buchwald aminations of 6-bromopyridin-2-yl C-nucleoside **8a** available in multigram quantities by an addition of 6-bromo-2-lithiopyridine to silylated 2-deoxyribonolactone fol-

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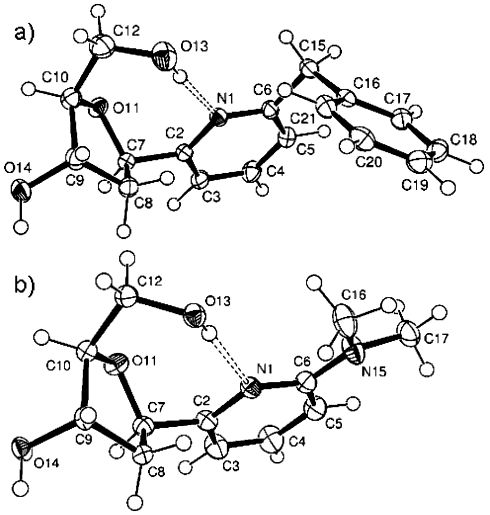


**FIGURE 1.** ORTEP drawing of **10e** (a) and **10h** (b) with atom numbering scheme. Thermal ellipsoids are drawn at the 50% probability level.

lowed by reduction with $Et_3SiH$ in the presence of $BF_3{\cdot}Et_2O$. It enables the synthesis of a large series of pyridine C-nucleosides bearing diverse C− (alkyl or aryl) or N− (unsubstituted, mono-, and dialkylamino) groups from one common intermediate. These C-nucleosides will be now used for chemical and enzymatical incorporations to oligonucleotides and DNA duplexes and studied as candidates for the extension of genetic alphabet.

## Experimental Section

**Synthesis of Adduct 7.** *n*-Butyllithium (3.6 mL, 1.6 M solution in hexane) was added dropwise to a solution of 2,6-dibromopyridine **1a** (1.3 g, 5.5 mmol) in dry THF (20 mL) at −78 °C under argon. The mixture was stirred for 10 min and then added dropwise to a stirred solution of lactone **5** (1.08 g, 3.0 mmol) in THF (42 mL) cooled at −78 °C. The reaction mixture was worked up after 30 min by pouring onto a mixture of ice and $NH_4Cl$ and extraction to ethyl acetate. Crude product was chromatographed on silica gel in gradient (hexane−10% EtOAc in hexane) which gave adduct **7** as an inseparable mixture/equilibrium of hemiketals and open hydroxyketone **7a**,**b**,**c** in ratio 7:5:9 (0.88 g, 57%) as a colorless oil (for characterization data, see Supporting Information).

**1β-(6-Bromopyridin-2-yl)-1,2-dideoxy-3,5-di-*O*-(*t*-butyldimethylsilyl)-D-ribofuranose (8a).** $Et_3SiH$ (150 μL, 0.9 mmol) was added dropwise to a solution of **7** (200 mg, 0.39 mmol) in $CH_2Cl_2$ (1 mL) in ice-brine bath under argon. After 10 min, a solution of $BF_3{\cdot}Et_2O$ (65 μL, 0.6 mmol) in $CH_2Cl_2$ (0.25 mL) was added dropwise, and after 10 min another portion of $Et_3SiH$ (100 μL, 0.6 mmol) was added. After another 10 min, a further portion of $BF_3{\cdot}Et_2O$ (30 μL, 0.24 mmol) in $CH_2Cl_2$ (0.1 mL) was added. Finally, after 10 min, the last portion of $Et_3SiH$ (100 μL, 0.6 mmol) followed by $BF_3{\cdot}Et_2O$ (15 μL, 0.12 mmol) was added. The mixture was worked up after 15 min and crude product was chromatographed on silica gel in gradient hexane−10% EtOAc in hexane to give **8a** (103 mg, 53%). The product was isolated as a colorless oil, which spontaneously crystallized within 2 months: mp 37−38 °C. MS (FAB): 502 (M + 1), 446, 424. HRMS (FAB) for $C_{22}H_{40}BrNO_3Si_2$: [M + H] calculated, 502.1808; found, 502.1821. $^1$H NMR (500 MHz, $CDCl_3$): 0.069, 0.074, 0.083, and 0.087 (4 × s, 4 × 3H, $CH_3$−Si), 0.89 and 0.91 (2 × s, 2 × 9H, $(CH_3)_3C$), 1.97 (ddd, 1H, $J_{gem}$ = 12.8, $J_{2'b,1'}$ = 9.5, $J_{2'b,3'}$ = 5.5, H-2′b), 2.34 (ddd, 1H, $J_{gem}$ = 12.8, $J_{2'a,1'}$ = 6.2, $J_{2'a,3'}$ = 2.4, H-2′a), 3.64 (dd, 1H, $J_{gem}$ = 10.8, $J_{5'b,4'}$ = 5.5, H-5′b), 3.74 (dd, 1H, $J_{gem}$ = 10.8, $J_{5'a,4'}$ = 3.8, H-5′a), 4.00 (ddd, 1H, $J_{4',5'}$ = 5.5, 3.8, $J_{4',3'}$ = 2.4, H-4′), 4.39 (dt, 1H, $J_{3',2'}$ = 5.5, 2.4, $J_{3',4'}$ = 2.4, H-3′), 5.23 (dd, 1H, $J_{1',2'}$ = 9.5, 6.2, H-1′), 7.34 (dd, 1H, $J_{5,4}$ = 7.5, $J_{5,3}$ = 1.7, H-5), 7.50 (t, 1H, $J_{4,3}$ = 7.7, $J_{4,5}$ = 7.5, H-4), 7.53 (dd, 1H, $J_{3,4}$ = 7.7, $J_{3,5}$ = 1.7, H-3). $^{13}$C NMR (125.8 MHz, $CDCl_3$): −5.5, −5.4, −4.8, and −4.6 ($CH_3$−Si), 18.0 and 18.3 ($\mathbf{C}(CH_3)_3$), 25.8 and 25.9 ($(\mathbf{C}H_3)_3C$), 42.5 ($CH_2$-2′), 63.5 ($CH_2$-5′), 73.7 (CH-3′), 80.2 (CH-1′), 88.3 (CH-4′), 118.9 (CH-3), 126.4 (CH-5), 138.8 (CH-4), 141.0 (C-6), 164.4 (C-2). IR spectrum: 2956, 2930, 2898, 2858, 2804, 1584, 1557, 1472, 1463, 1440, 1409, 1390, 1362, 1258, 1154, 1108, 1095. $[\alpha]^{20}_D$ = +44.0 (*c* 5.98, $CHCl_3$). Anal. Calcd for $C_{22}H_{40}BrNO_3Si_2$ (502.6): C, 52.57; H, 8.02; Br, 15.90; N 2.79. Found: C, 52.46; H, 8.13; Br, 15.76; N, 2.67.

**1β-(Pyridin-2-yl)-1,2-dideoxy-3,5-di-*O*-(*t*-butyldimethylsilyl)-D-ribofuranose (9a).** 10% Pd/C (400 mg, 24 mol %) was added to a solution of **8a** (800 mg, 1.6 mmol) in a mixture of THF (40 mL), EtOH (40 mL), $H_2O$ (4 mL), and $Et_3N$ (2.4 mL). The reaction flask was then sealed with septum, evacuated, and filled with $H_2$ (101 kPa). After the reaction was completed (30 min), the Pd catalyst was filtered off, the filtrate was poured into water, and crude product was extracted with EtOAc. Chromatography on HPFC in gradient from 5% EtOAc in hexane to 50% EtOAc in hexane gave **9a** (546 mg, 81%) as colorless oil (for characterization data, see Supporting Information).

**1β-(6-Methylpyridin-2-yl)-1,2-dideoxy-3,5-di-*O*-(*t*-butyldimethylsilyl)-D-ribofuranose (9b).** $Me_3Al$ (1 mmol) was added dropwise to a vigorously stirred solution of **8a** (250 mg, 0.5 mmol) and $Pd(PPh_3)_4$ (30 mg, 0.025 mmol) in THF (10 mL) under argon. The mixture was stirred at 70 °C for 12 h and then worked up by pouring onto a mixture of ice and $NH_4Cl$ and extracted to ethyl acetate. Crude product **9b** was chromatographed on silica gel (20 g) in gradient hexane to 10% EtOAc in hexane to give **9b** (170 mg, 78%) as oil (for characterization data, see Supporting Information).

**1β-(6-Ethylpyridin-2-yl)-1,2-dideoxy-3,5-di-*O*-(*t*-butyldimethylsilyl)-D-ribofuranose (9c).** $Et_3Al$ (4 mmol) was dropwise added to a vigorously stirred solution of **8a** (1 g, 2 mmol) and $Pd(PPh_3)_4$ (120 mg, 0.1 mmol) in THF (40 mL). The mixture was stirred at 70 °C for 20 h and then worked up. Crude product **9c** was chromatographed on silica gel (20 g) in gradient hexane to 10% EtOAc in hexane to give **9c** (810 mg, 90%) as a colorless oil (for characterization data, see Supporting Information).

**1β-(6-Phenylpyridin-2-yl)-1,2-dideoxy-3,5-di-*O*-(*t*-butyldimethylsilyl)-D-ribofuranose (9d).** Compound **8a** (250 mg, 0.5 mmol), $K_2CO_3$ (100 mg, 0.72 mmol), $Pd(PPh_3)_4$ (30 mg, 0.025 mmol), and $PhB(OH)_2$ (120 mg, 1 mmol) were dissolved in toluene (15 mL) and the mixture was stirred at 100 °C for 12 h. The reaction mixture was worked up and crude product **9d** was chromatographed on silica gel (20 g) in gradient hexane to 10% EtOAc in hexane to give **9d** (180 mg, 72%) as a colorless oil (for characterization data, see Supporting Information).

**1β-(6-Benzylpyridin-2-yl)-1,2-dideoxy-3,5-di-*O*-(*t*-butyldimethylsilyl)-D-ribofuranose (9e).** THF (30 mL) was added to a flame-dried and argon-purged flask containing **8a** (0.8 g, 1.6 mmol) and $Pd(PPh_3)_4$ (100 mg, 5 mol %), and the mixture was stirred until clear solution formed. Then commercial solution of benzylzinc chloride (3.2 mmol) in THF was added dropwise, and the mixture was stirred at 70 °C for 18 h. After the work up, the product was chromatographed on silica gel (150 g) in gradient hexane to 10% EtOAc in hexane to give **9e** (630 mg, 77%) as a colorless oil (for characterization data, see Supporting Information).

**1β-(6-Aminopyridin-2-yl)-1,2-dideoxy-3,5-di-*O*-(*t*-butyldimethylsilyl)-D-ribofuranose (9f).** $LiN(SiMe_3)_2$ (2.5 mL, 1 M solution in THF, 2.5 mmol) was added to a flame-dried argon-purged flask containing **8a** (0.7 g, 1.4 mmol), $P(t\text{-}Bu)_3{\cdot}HBF_4$ (50 mg, 12 mol %), and $Pd_2(dba)_3$ (84 mg, 6.6 mol %), and the mixture was stirred at room temperature for 2 h. The reaction was quenched by the addition of $Et_2O$ and one drop of 2 M aqueous solution of

HCl and worked up. Chromatography on silica gel (50 g) with gradient $CHCl_3$ to 5% MeOH in $CHCl_3$ gave **9f** (363 mg, 83%) as a light brown oil (for characterization data, see Supporting Information).

**1β-(6-Methylaminopyridin-2-yl)-1,2-dideoxy-3-*O*-(*t*-butyldimethylsilyl)-D-ribofuranose (9g).** A solution of **8a** (600 mg, 1.2 mmol) in toluene (4 mL) was added to an argon-purged dry flask containing $Pd_2(dba)_3$ (5.5 mg, 1 mol %), (2-biphenyl)-di-*tert*-butylphosphine (7.2 mg, 2 mol %), sodium *tert*-butoxide (660 mg, 11 mmol), and $MeNH_2$·HCl (240 mg, 3.6 mmol). The mixture was stirred at room temperature for 2 days and then heated at 80 °C for 1 day. The mixture was then worked up, and crude product **9g** was chromatographed on silica gel from $CHCl_3$ to 5% MeOH in $CHCl_3$ to give **9g** (200 mg, 50%) as a light brown oil (for characterization data, see Supporting Information) and unreacted **8a** (75 mg, 13%), which was recycled.

**1β-(6-Dimethylaminopyridin-2-yl)-1,2-dideoxy-3,5-di-*O*-(*t*-butyldimethylsilyl)-D-ribofuranose (9h).** A solution of **8a** (1 g, 2 mmol) in toluene (4 mL) was added to an argon-purged dry flask containing $Pd_2(dba)_3$ (9.2 mg, 1 mol %), (2-biphenyl)-di-*tert*-butylphosphine (12 mg, 2 mol %), sodium *tert*-butoxide (1.1 g, 11 mmol), and $Me_2NH$·HCl (500 mg, 6.1 mmol). The mixture was stirred at room temperature for 2 days and then heated at 80 °C for 1 day. Then the mixture was worked up, and crude product **9h** was chromatographed on silica gel in gradient hexane to 10% EtOAc in hexane to give **9h** (450 mg, 48%) as an yellow oil (for characterization data, see Supporting Information).

**General Procedure for the Deprotection of TBDMS-Group.**[15] $Et_3N$·3HF (320 μL, 1.95 mmol) was added to a solution of compounds **9a**−**h** (0.4 mmol) in THF (2 mL), and the mixture was stirred at room temperature for 14 h. After the reaction was completed (TLC in hexane/EtOAc 10:1), solvents were removed under reduced pressure, and crude product was chromatographed on silica gel (20 g) eluted with gradient $CHCl_3$−15% MeOH in $CHCl_3$ to give products **10a**−**h**.

**1β-(Pyridin-2-yl)-1,2-dideoxy-D-ribofuranose (10a).** Compound **10a** was prepared from **9a** (494 mg, 1.2 mmol) by the general procedure to yield **10a** (192 mg, 84%) as a colorless oil. MS (FAB): 196 (M + 1), 185. HRMS (FAB) for $C_{10}H_{13}NO_3$: [M + H] calculated, 196.0973; found, 196.0978. $^1$H NMR (400 MHz, DMSO-$d_6$): 1.92 (ddd, 1H, $J_{gem}$ = 12.8, $J_{2'b,1'}$ = 9.8, $J_{2'b,3'}$ = 5.6, H-2′b), 2.14 (ddd, 1H, $J_{gem}$ = 12.8, $J_{2'a,1'}$ = 6.0, $J_{2'a,3'}$ = 2.1, H-2′a), 3.46 (dt, 1H, $J_{gem}$ = 11.4, $J_{5'b,OH}$ = 5.8, $J_{5'b,4'}$ = 5.8, H-5′b), 3.48 (ddd, 1H, $J_{gem}$ = 11.4, $J_{5'a,OH}$ = 5.8, $J_{5'a,4'}$ = 4.8, H-5′a), 3.85 (td, 1H, $J_{4',5'}$ = 5.8, 4.8, $J_{4',3'}$ = 2.3, H-4′), 4.19 (m, 1H, $J_{3',2'}$ = 5.6, 2.1, $J_{3',OH}$ = 4.0, $J_{3',4'}$ = 2.3, H-3′), 4.89 (t, 1H, $J_{OH,5'}$ = 5.8, OH-5′), 5.06 (dd, 1H, $J_{1',2'}$ = 9.8, 6.0, H-1′), 5.08 (d, 1H, $J_{OH,3'}$ = 4.0, OH-3′), 7.26 (ddd, 1H, $J_{5,4}$ = 7.5, $J_{5,6}$ = 4.9, $J_{5,3}$ = 1.2, H-5), 7.51 (dt, 1H, $J_{3,4}$ = 7.9, $J_{3,5}$ = 1.2, $J_{3,6}$ = 1.0, H-3), 7.77 (td, 1H, $J_{4,3}$ = 7.9, $J_{4,5}$ = 7.5, $J_{4,6}$ = 1.9, H-4), 8.48 (ddd, 1H, $J_{6,5}$ = 4.9, $J_{6,4}$ = 1.9, $J_{6,3}$ = 1.0, H-6). $^{13}$C NMR (100.6 MHz, DMSO-$d_6$): 42.3 ($CH_2$-2′), 62.7 ($CH_2$-5′), 72.4 (CH-3′), 80.4 (CH-1′), 88.2 (CH-4′), 120.5 (CH-3), 122.7 (CH-5), 137.0 (CH-4), 148.8 (CH-6), 162.3 (C-2). IR ($CHCl_3$): 3612, 3208, 2926, 2868, 1599, 1575, 1477, 1446, 1438, 1150, 1101, 1081, 991. $[\alpha]^{20}_D$ = +16.3 (*c* 3.61, $CHCl_3$).

**1β-(6-Methylpyridin-2-yl)-1,2-dideoxy-D-ribofuranose (10b).** Compound **10b** was prepared from **9b** (500 mg, 1.1 mmol) by the general procedure. Crystallization from EtOAc/heptane yielded **10b** (190 mg, 80%) as colorless crystals, mp 95−97 °C. MS (FAB): 210 (M + 1), 201, 185. HRMS (FAB) for $C_{11}H_{15}NO_3$: [M + H] calculated, 210.1130; found, 210.1122. $^1$H NMR (400 MHz, DMSO-$d_6$): 1.91 (ddd, 1H, $J_{gem}$ = 12.8, $J_{2'b,1'}$ = 9.6, $J_{2'b,3'}$ = 5.6, H-2′b), 2.13 (ddd, 1H, $J_{gem}$ = 12.8, $J_{2'a,1'}$ = 6.2, $J_{2'a,3'}$ = 2.2, H-2′a), 2.43 (s, 3H, $CH_3$), 3.46 (dt, 1H, $J_{gem}$ = 11.1, $J_{5',OH}$ = 4.9, $J_{5'b,4'}$ = 4.9, H-5′b), 3.49 (ddd, 1H, $J_{gem}$ = 11.1, $J_{5',OH}$ = 5.4, $J_{5'a,4'}$ = 4.2, H-5′a), 3.84 (td, 1H, $J_{4',5'}$ = 4.9, 4.2, $J_{4',3'}$ = 2.3, H-4′), 4.19 (m, 1H, $J_{3',2'}$ = 5.6, 2.2, $J_{3',OH}$ = 3.9, $J_{3',4'}$ = 2.3, H-3′), 5.01 (t, 1H, $J_{OH,5'}$ = 5.4, 4.9, OH-5′), 5.02 (dd, 1H, $J_{1',2'}$ = 9.6, 6.2, H-1′), 5.06 (d, 1H, $J_{OH,3'}$ = 3.9, OH-3′), 7.12 (d, 1H, $J_{5,4}$ = 7.5, H-5), 7.28 (d, 1H, $J_{3,4}$ = 7.7, H-3), 7.65 (t, 1H, $J_{4,3}$ = 7.7, $J_{4,5}$ = 7.5, H-4). $^{13}$C NMR (100.6 MHz, DMSO-$d_6$): 24.1 ($CH_3$), 42.4 ($CH_2$-2′), 62.7 ($CH_2$-5′), 72.5 (CH-3′), 80.4 (CH-1′), 88.2 (CH-4′), 117.5 (CH-3), 122.4 (CH-5), 137.3 (CH-4), 157.1 (C-6), 161.8 (C-2). IR ($CHCl_3$): 3612, 3192, 2922, 1601, 1598, 1465, 1380, 1081, 1047, 990. $[\alpha]^{20}_D$ = −12.2 (*c* 2.72, $CHCl_3$). Anal. Calcd for $C_{11}H_{15}NO_3$ (209.2): C, 63.14; H, 7.23; N, 6.69. Found: C, 62.86; H, 7.35; N, 6.22.

**1β-(6-Ethylpyridin-2-yl)-1,2-dideoxy-D-ribofuranose (10c).** Compound **10c** was prepared from **9c** (600 mg, 1.3 mmol) by the general procedure. Crystallization from EtOAc/heptane at −78 °C yielded **10c** (220 mg, 74%) as colorless crystals, mp 55−59 °C. MS (FAB): 224 (M + 1), 199, 181. HRMS (FAB) for $C_{12}H_{17}NO_3$: [M + H] calculated, 224.1287; found, 224.1277. $^1$H NMR (400 MHz, DMSO-$d_6$): 1.20 (t, 3H, $J_{vic}$ = 7.6; C**H**$_3$CH$_2$), 1.94 (ddd, 1H, $J_{gem}$ = 12.7, $J_{2'b,1'}$ = 9.6, $J_{2'b,3'}$ = 5.6, H-2′b), 2.14 (ddd, 1H, $J_{gem}$ = 12.7, $J_{2'a,1'}$ = 6.2, $J_{2'a,3'}$ = 2.2, H-2′a), 2.70 (q, 2H, $J_{vic}$ = 7.6; C**H**$_2$CH$_3$), 3.46 (dt, 1H, $J_{gem}$ = 11.6, $J_{5',OH}$ = 5.8, $J_{5'b,4'}$ = 5.3, H-5′b), 3.50 (ddd, 1H, $J_{gem}$ = 11.6, $J_{5',OH}$ = 5.8, $J_{5'a,4'}$ = 4.5, H-5′a), 3.85 (td, 1H, $J_{4',5'}$ = 5.3, 4.5, $J_{4',3'}$ = 2.2, H-4′), 4.20 (m, 1H, $J_{3',2'}$ = 5.6, 2.2, $J_{3',OH}$ = 3.9, $J_{3',4'}$ = 2.2, H-3′), 4.99 (t, 1H, $J_{OH,5'}$ = 5.8, OH-5′), 5.03 (dd, 1H, $J_{1',2'}$ = 9.6, 6.2, H-1′), 5.04 (d, 1H, $J_{OH,3'}$ = 3.9, OH-3′), 7.14 (dd, 1H, $J_{5,4}$ = 7.7, $J_{5,3}$ = 1.0, H-5), 7.29 (dd, 1H, $J_{3,4}$ = 7.8, $J_{3,5}$ = 1.0, H-3), 7.67 (t, 1H, $J_{4,3}$ = 7.8, $J_{4,5}$ = 7.7, H-4). $^{13}$C NMR (100.6 MHz, DMSO-$d_6$): 13.9 (**C**H$_3$CH$_2$), 30.7 (**C**H$_2$CH$_3$), 42.3 ($CH_2$-2′), 62.8 ($CH_2$-5′), 72.5 (CH-3′), 80.4 (CH-1′), 88.2 (CH-4′), 117.9 (CH-3), 120.9 (CH-5), 137.3 (CH-4), 161.6 (C-2), 162.1 (C-6). IR ($CHCl_3$): 3612, 3195, 3069, 2976, 2875, 1599, 1578, 1467, 1458, 1438, 1333, 1065, 1178, 1090. $[\alpha]^{20}_D$ = −5.8 (*c* 2.08, $CHCl_3$). Anal. Calcd for $C_{12}H_{17}NO_3$ (223.3): C, 64.55; H, 7.67; N, 6.27. Found: C, 64.26; H, 7.91; N, 5.82.

**1β-(6-Phenylpyridin-2-yl)-1,2-dideoxy-D-ribofuranose (10d).** Compound **10d** was prepared from **9d** (500 mg, 1.0 mmol) by the general procedure. Crystallization from EtOAc/heptane yielded **10d** (170 mg, 56%) as colorless crystals, mp 93−95 °C. MS (FAB): 272 (M + 1), 182. HRMS (FAB) for $C_{16}H_{17}NO_3$: [M + H] calculated, 272.1286; found, 272.1291. $^1$H NMR (400 MHz, DMSO-$d_6$): 2.03 (ddd, 1H, $J_{gem}$ = 12.8, $J_{2'b,1'}$ = 9.7, $J_{2'b,3'}$ = 5.5, H-2′b), 2.21 (ddd, 1H, $J_{gem}$ = 12.8, $J_{2'a,1'}$ = 6.1, $J_{2'a,3'}$ = 2.2, H-2′a), 3.47 (dt, 1H, $J_{gem}$ = 11.4, $J_{5',OH}$ = 5.6, $J_{5'b,4'}$ = 5.6, H-5′b), 3.51 (ddd, 1H, $J_{gem}$ = 11.4, $J_{5',OH}$ = 5.6, $J_{5'a,4'}$ = 4.9, H-5′a), 3.88 (td, 1H, $J_{4',5'}$ = 5.6, 4.9, $J_{4',3'}$ = 2.3, H-4′), 4.24 (m, 1H, $J_{3',2'}$ = 5.5, 2.2, $J_{3',OH}$ = 3.9, $J_{3',4'}$ = 2.3, H-3′), 4.85 (t, 1H, $J_{OH,5'}$ = 5.6, OH-5′), 5.11 (d, 1H, $J_{OH,3'}$ = 3.9, OH-3′), 5.15 (dd, 1H, $J_{1',2'}$ = 9.7, 6.1, H-1′), 7.40−7.52 (m, 4H, H-3 and H-*m*,*p*-PhH), 7.83 (dd, 1H, $J_{5,4}$ = 7.9, $J_{5,3}$ = 1.5, H-5), 7.87 (t, 1H, $J_{4,5}$ = $J_{4,3}$ = 7.9, H-4), 8.06 (m, 2H, H-*o*-Ph). $^{13}$C NMR (100.6 MHz, DMSO-$d_6$): 42.1 ($CH_2$-2′), 62.7 ($CH_2$-5′), 72.5 (CH-3′), 80.6 (CH-1′), 88.3 (CH-4′), 119.2 (CH-5), 119.4 (CH-3), 126.8 (CH-*o*-Ph), 128.9 (CH-*m*-Ph), 129.2 (CH-*p*-Ph), 138.1 (CH-4), 138.8 (C-*i*-Ph), 155.3 (C-6), 162.2 (C-2). IR ($CHCl_3$): 3612, 3270, 3091, 3066, 3034, 1605, 1595, 1582, 1571, 1457, 1078, 1046, 991. $[\alpha]^{20}_D$ = +37.5 (*c* 3.68, $CHCl_3$). Anal. Calcd. for $C_{16}H_{17}NO_3$ (271.3): C, 70.83; H, 6.32; N, 5.16. Found: C, 70.34; H, 6.22; N, 4.76.

**1β-(6-Benzylpyridin-2-yl)-1,2-dideoxy-D-ribofuranose (10e).** Compound **10e** was prepared from **9e** (530 mg, 1.0 mmol) by the general procedure. Crystallization from EtOAc/heptane gave **10e** (194 mg, 66%) as colorless crystals, mp 110−112 °C. MS (FAB): 286 (M + 1), 196. HRMS (FAB) for $C_{17}H_{19}NO_3$: [M + H] calculated, 286.1443; found, 286.1452. $^1$H NMR (400 MHz, DMSO-$d_6$): 1.94 (ddd, 1H, $J_{gem}$ = 12.8, $J_{2'b,1'}$ = 9.6, $J_{2'b,3'}$ = 5.5, H-2′b), 2.15 (ddd, 1H, $J_{gem}$ = 12.8, $J_{2'a,1'}$ = 6.2, $J_{2'a,3'}$ = 2.2, H-2′a), 3.48 (dd, 2H, $J_{5',OH}$ = 5.8, $J_{5',4'}$ = 4.4, H-5′), 3.85 (td, 1H, $J_{4',5'}$ = 4.4, $J_{4',3'}$ = 2.3, H-4′), 4.04 (s, 2H, $CH_2$Ph) 4.21 (m, 1H, $J_{3',2'}$ = 5.5, 2.2, $J_{3',OH}$ = 4.0, $J_{3',4'}$ = 2.3, H-3′), 4.99 (t, 1H, $J_{OH,5'}$ = 5.8, OH-5′), 5.05 (dd, 1H, $J_{1',2'}$ = 9.6, 6.2, H-1′), 5.05 (d, 1H, $J_{OH,3'}$ = 4.0, OH-3′), 7.13 (d, 1H, $J_{5,4}$ = 7.7, $J_{5,3}$ = 1.0, H-5), 7.19 (m, 1H, H-*p*-Ph), 7.25−7.31 (m, 4H, H-*o*,*m*-Ph), 7.33 (dd, 1H, $J_{3,4}$ = 7.8, $J_{3,5}$ = 1.1, H-3), 7.67 (t, 1H, $J_{4,3}$ = 7.8, $J_{4,5}$ = 7.7, H-4). $^{13}$C NMR

(100.6 MHz, DMSO-$d_6$): 42.3 ($CH_2$-2′), 43.8 ($CH_2$Ph), 62.7 ($CH_2$-5′), 72.5 (CH-3′), 80.4 (CH-1′), 88.2 (CH-4′), 118.1 (CH-3), 121.8 (CH-5), 126.3 (CH-*p*-Ph), 128.6 (CH-*m*-Ph), 129.0 (CH-*o*-Ph), 137.6 (CH-4), 139.9 (C-*i*-Ph), 159.8 (C-6), 161.9 (C-2). IR ($CHCl_3$): 3612, 3370, 3205, 3088, 3066, 3030, 1612, 1597, 1576, 1445, 1427, 1337, 1047, 995. $[\alpha]^{20}_D = +17.0$ ($c$ = 4.35, $CHCl_3$). Anal. Calcd. for $C_{17}H_{19}NO_3$ (285.3): C, 71.56; H, 6.71; N, 4.91. Found: C, 71.39; H, 6.69; N, 4.68.

**1β-(6-Aminopyridin-2-yl)-1,2-dideoxy-D-ribofuranose (10f).** Compound **10f** was prepared from **9f** (600 mg, 1.4 mmol) using the general procedure for desilylation. Lyophylization from *t*-BuOH yielded **10f** (195 mg, 68%) as a light brown solid, mp 121−124 °C. MS (FAB): 211 (M + 1). HRMS (FAB) for $C_{10}H_{15}N_2O_3$: [M + H] calculated, 211.1083; found, 211.1079. $^1$H NMR (400 MHz, DMSO-$d_6$): 1.88 (ddd, 1H, $J_{gem}$ = 12.8, $J_{2'b,1'}$ = 9.7, $J_{2'b,3'}$ = 5.7, H-2′b), 2.06 (ddd, 1H, $J_{gem}$ = 12.8, $J_{2'a,1'}$ = 6.2, $J_{2'a,3'}$ = 2.2, H-2′a), 3.41 (dd, 1H, $J_{gem}$ = 11.4, $J_{5'b,4'}$ = 5.5, H-5′b), 3.46 (dd, 1H, $J_{gem}$ = 11.4, $J_{5'a,4'}$ = 4.8, H-5′a), 3.79 (td, 1H, $J_{4',5'}$ = 5.5, 4.8, $J_{4',3'}$ = 2.3, H-4′), 4.20 (m, 1H, $J_{3',2'}$ = 5.7, 2.2, $J_{3',OH}$ = 4.0, $J_{3',4'}$ = 2.3, H-3′), 4.82 (dd, 1H, $J_{1',2'}$ = 9.7, 6.2, H-1′), 5.00 (d, 1H, $J_{OH,3'}$ = 4.0, OH-3′), 5.91 (bs, 2H, $NH_2$), 6.32 (dd, 1H, $J_{5,4}$ = 8.3, $J_{5,3}$ = 1.0, H-5), 7.29 (dt, 1H, $J_{3,4}$ = 7.2, $J_{3,5}$ = 1.0, $J_{3,NH}$ = 0.5, H-3), 7.34 (dd, 1H, $J_{4,5}$ = 8.3, $J_{4,3}$ = 7.2, H-4). $^{13}$C NMR (100.6 MHz, DMSO-$d_6$): 42.0 ($CH_2$-2′), 62.8 ($CH_2$-5′), 72.5 (CH-3′), 80.1 (CH-1′), 88.0 (CH-4′), 107.1 (CH-5), 108.0 (CH-3), 138.0 (CH-4), 159.0 (C-6), 160.1 (C-2). IR ($CHCl_3$): 3612, 3514, 3413, 3195, 1619, 1601, 1580, 1438, 1333, 1065, 1178, 1166, 1100, 1090, 995. $[\alpha]^{20}_D = +56.2$ ($c$ 3.30, $CHCl_3$).

**1β-(6-Methylaminopyridin-2-yl)-1,2-dideoxy-D-ribofuranose (10g).** Compound **10g** was prepared from **9g** (200 mg, 0.6 mmol) by the general procedure to give **10g** (103 mg, 78%) as light brown oil. MS (FAB): 225 (M + 1), 135. HRMS (FAB) for $C_{11}H_{16}N_2O_3$: [M + H] calculated, 225.1239; found, 225.1247. $^1$H NMR (400 MHz, DMSO-$d_6$): 1.97 (ddd, 1H, $J_{gem}$ = 12.8, $J_{2'b,1'}$ = 9.5, $J_{2'b,3'}$ = 5.4, H-2′b), 2.06 (ddd, 1H, $J_{gem}$ = 12.8, $J_{2'a,1'}$ = 6.2, $J_{2'a,3'}$ = 2.1, H-2′a), 2.72 (d, 3H, $J_{CH3,NH}$ = 4.9, $CH_3$N), 3.43 (dd, 1H, $J_{gem}$ = 11.4, $J_{5'b,4'}$ = 5.4, H-5′b), 3.46 (dd, 1H, $J_{gem}$ = 11.4, $J_{5'a,4'}$ = 4.8, H-5′a), 3.81 (td, 1H, $J_{4',5'}$ = 5.4, 4.8, $J_{4',3'}$ = 2.1, H-4′), 4.18 (m, 1H, $J_{3',2'}$ = 5.4, 2.1, $J_{3',OH}$ = 3.9, $J_{3',4'}$ = 2.1, H-3′), 4.75 (b, 1H, OH-5′), 4.87 (dd, 1H, $J_{1',2'}$ = 9.5, 6.2, H-1′), 5.00 (d, 1H, $J_{OH,3'}$ = 3.9, OH-3′), 6.31 (dd, 1H, $J_{5,4}$ = 8.2, H-5), 6.41 (b, 1H, NH), 6.55 (d, 1H, $J_{3,4}$ = 7.0, H-3), 7.33 (dd, 1H, $J_{4,5}$ = 8.2, $J_{4,3}$ = 7.0, H-4). $^{13}$C NMR (100.6 MHz, DMSO-$d_6$): 28.1 ($CH_3$N), 41.9 ($CH_2$-2′), 63.0 ($CH_2$-5′), 72.8 (CH-3′), 80.5 (CH-1′), 88.0 (CH-4′), 106.7 (CH-5), 108.0 (CH-3), 137.3 (CH-4), 159.1 (C-6), 160.0 (C-2). IR ($CHCl_3$): 3611, 3444, 1607, 1579, 1515, 1476, 1430, 1159, 1100, 798. $[\alpha]^{20}_D = +60.0$ ($c$ 3.28, MeOH).

**1β-(6-Dimethylaminopyridin-2-yl)-1,2-dideoxy-D-ribofuranose (10h).** Compound **10h** was prepared from **9h** (600 mg, 1.3 mmol) by the general procedure. Crystallization from EtOAc/heptane gave **10h** (175 mg, 57%) as pink crystals, mp 56−59 °C. MS (FAB): 239 (M + 1), 221, 209. HRMS (FAB) for $C_{12}H_{18}N_2O_3$: [M + H] calculated, 239.1395; found, 239.1407. $^1$H NMR (400 MHz, DMSO-$d_6$): 1.96 (ddd, 1H, $J_{gem}$ = 12.7, $J_{2'b,1'}$ = 9.6, $J_{2'b,3'}$ = 5.5, H-2′b), 2.07 (ddd, 1H, $J_{gem}$ = 12.7, $J_{2'a,1'}$ = 6.1, $J_{2'a,3'}$ = 2.2, H-2′a), 2.98 (s, 6H, $(CH_3)_2$N), 3.40 (dt, 1H, $J_{gem}$ = 11.2, $J_{5'b,OH}$ = 5.9, $J_{5'b,4'}$ = 5.9, H-5′b), 3.45 (ddd, 1H, $J_{gem}$ = 11.2, $J_{5'a,OH}$ = 5.9, $J_{5'a,4'}$ = 4.9, H-5′a), 3.80 (ddd, 1H, $J_{4',5'}$ = 5.9, 4.9, $J_{4',3'}$ = 2.2, H-4′), 4.17 (m, 1H, $J_{3',2'}$ = 5.5, 2.2, $J_{3',OH}$ = 3.9, $J_{3',4'}$ = 2.2, H-3′), 4.74 (t, 1H, $J_{OH,5'}$ = 5.9, OH-5′), 4.89 (dd, 1H, $J_{1',2'}$ = 9.6, 6.1, H-1′), 5.00 (d, 1H, $J_{OH,3'}$ = 3.9, OH-3′), 6.49 (dd, 1H, $J_{5,4}$ = 8.5, $J_{5,3}$ = 0.8, H-5), 6.65 (d, 1H, $J_{3,4}$ = 7.3, H-3), 7.45 (dd, 1H, $J_{4,5}$ = 8.5, $J_{4,3}$ = 7.3, H-4). $^{13}$C NMR (100.6 MHz, DMSO-$d_6$): 37.8 ($(CH_3)_2$N), 41.6 ($CH_2$-2′), 62.9 ($CH_2$-5′), 72.6 (CH-3′), 80.6 (CH-1′), 87.9 (CH-4′), 104.8 (CH-5), 108.0 (CH-3), 137.8 (CH-4), 158.6 (C-6), 159.9 (C-2).). IR ($CHCl_3$): 3611, 3369, 2824, 2806, 1605, 1568, 1510, 1433, 1172, 1099. $[\alpha]^{20}_D = -4.7$ ($c$ 3.84, $CHCl_3$). Anal. Calcd. for $C_{12}H_{18}N_2O_3 \cdot H_2O$ (255.3): C, 58.28; H, 7.74; N, 11.33. Found: C, 58.30; H, 7.97; N, 11.27.

**1β-(6-Oxopyridin-2-yl)-1,2-dideoxy-D-ribofuranose (10i).** Isopentyl nitrite (100 μL, 0.75 mmol) was added to a solution of amine **9f** (100 mg, 0.23 mmol) in 80% aqueous AcOH (5 mL), and the mixture was heated at 70 °C for 3 h. The solvents were evaporated, and crude pyridone **10i** was purified by chromatography on silica gel (50 g) in 10% MeOH in $CHCl_3$. Crystallization from MeOH yielded needles of **10i** (23 mg, 48%), mp 173−175 °C. MS (FAB): 212 (M + 1), 160. HRMS (FAB) for $C_{10}H_{13}NO_4$: [M + H] calculated, 212.0922; found, 212.0917. $^1$H NMR (500 MHz, DMSO-$d_6$): 1.91 (ddd, 1H, $J_{gem}$ = 12.8, $J_{2'b,1'}$ = 9.7, $J_{2'b,3'}$ = 5.6, H-2′b), 2.12 (ddd, 1H, $J_{gem}$ = 12.8, $J_{2'a,1'}$ = 6.2, $J_{2'a,3'}$ = 2.0, H-2′a), 3.51 (t, 2H, $J_{5',OH}$ = $J_{5',4'}$ = 4.1, H-5′), 3.82 (td, 1H, $J_{4',5'}$ = 4.1, $J_{4',3'}$ = 2.2, H-4′), 4.21 (ddt, 1H, $J_{3',2'}$ = 5.6, 2.0, $J_{3',OH}$ = 3.8, $J_{3',4'}$ = 2.2, H-3′), 4.85 (dd, 1H, $J_{1',2'}$ = 9.6, 6.2, H-1′), 5.16 (d, 1H, $J_{OH,3'}$ = 3.8, OH-3′), 5.22 (bt, 1H, $J_{OH,5'}$ = 4.1, OH-5′), 6.21 (d, 1H, $J_{5,4}$ = 9.1, H-5), 6.22 (bd, 1H, $J_{3,4}$ = 6.8, H-3), 7.37 (dd, 1H, $J_{4,5}$ = 9.1, $J_{4,3}$ = 6.8, H-4), 11.35 (bs, 1H, NH). $^{13}$C NMR (100.6 MHz, DMSO-$d_6$): 42.1 ($CH_2$-2′), 62.2 ($CH_2$-5′), 72.5 (CH-3′), 76.5 (CH-1′), 88.2 (CH-4′), 102.2 (CH-3), 118.2 (CH-5), 141.1 (CH-4), 150.2 (C-2), 163.0 (C-6). IR (KBr): 3302, 3150, 1645, 1601, 1546, 1441, 1318, 1174, 1169, 1019, 1032. $[\alpha]^{20}_D = +136.6$ ($c$ 2.50, MeOH). Anal. Calcd for $C_{10}H_{13}NO_4 \cdot 2H_2O$ (247.2): C, 48.58; H, 6.93; N, 5.67. Found: C, 48.95; H, 6.65; N, 5.63.

**Single-Crystal X-ray Structure Analysis.** X-ray diffraction experiment of single crystals was carried out on Xcalibur X-ray diffractometer using Cu Kα radiation ($\lambda$ = 1.54180 Å), and diffraction data were collected at 150 K. Both structures were solved by direct methods with SIR92[23] and refined by full-matrix least-squares on F with CRYSTALS.[24] The hydrogen atoms were all located in a difference map, but those attached to carbon atoms were repositioned geometrically. All hydrogen atoms were initially refined with soft restraints on the bond lengths and angles to regularize their geometry after which the positions were refined anisotropically with riding constraints.

**10e.** $C_{17}H_{19}N_1O_3$, monoclinic, space group $P2_1$, $a$ = 5.7642(4) Å, $b$ = 8.9642(5) Å, $c$ = 14.5185(9) Å, $\beta$ = 99.674(5)°, $V$ = 739.52(8) Å$^3$, $Z$ = 2, $M$ = 285.33, 11291 reflections measured, 2790 independent reflections. Final $R$ = 0.0303, $wR$ = 0.0335, GOF = 1.1287 for 2574 reflections with $I > 1.96\sigma(I)$ and 192 parameters. CCDC 608613.

**10h.** $C_{12}H_{20}N_2O_4$, monoclinic, space group $P2_1$, $a$ = 9.319(3) Å, $b$ = 7.204(2) Å, $c$ = 9.825(3) Å, $\beta$ = 102.12(3)°, $V$ = 644.9(3) Å$^3$, $Z$ = 2, $M$ = 256.30, 8962 reflections measured, 2423 independent reflections. Final $R$ = 0.0281, $wR$ = 0.0341, GOF = 1.0626 for 2393 reflections with $I > 1.96\sigma(I)$ and 165 parameters. CCDC 608614.

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**Supporting Information Available:** Detailed description and discussion of unsuccessful experiments, conformation analysis of nucleosides **10**, general experimental methods, synthesis and characterization data of compounds **5**, **6b**, **8b**,**c**, **11**, **12a**,**b**, and **13**, analytical and spectral data of compounds **7** and **9a**−**h**, and copies of important NMR spectra. This material is available free of charge via the Internet at http://pubs.acs.org.

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