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A General and Efficient Synthesis of Pyridin-2-yl *C*-Ribonucleosides Bearing Diverse Alkyl, Aryl, Amino, and Carbamoyl Groups in Position 6

Martin Štefko, Lenka Slavětínská, Blanka Klepetářová, and Michal Hocek*

Institute of Organic Chemistry and Biochemistry, Academy of Sciences of the Czech Republic, Gilead & IOCB Research Center, Flemingovo nám. 2, CZ-16610 Prague 6, Czech Republic

hocek@uochb.cas.cz

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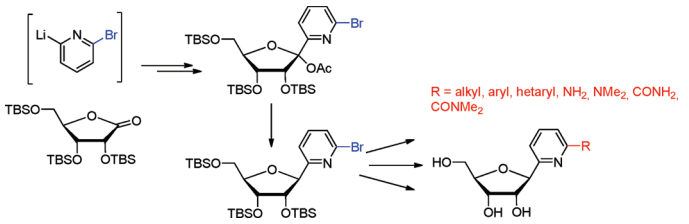

An efficient and practical methodology of preparation of 6-substituted pyridin-2-yl *C*-ribonucleosides was developed. A one-pot two-step addition of 2-lithio-6-bromopyridine to TBS-protected ribonolactone followed by acetylation gave 1β-(6-bromopyridin-2-yl)-1-*O*-acetyl-2,3,5-tri-*O*-(*tert*-butyldimethylsilyl)-D-ribofuranose in high yield. Its reduction with Et_3SiH and $BF_3 \cdot Et_2O$ afforded the desired TBS-protected 6-bromopyridine *C*-ribonucleoside as pure β-anomer in good overall yield of 63%. This intermediate was then subjected to a series of palladium catalyzed cross-coupling reactions, aminations and aminocarbonylations to give a series of protected 1β-(6-alkyl-, 6-aryl-, 6-amino-, and 6-carbamoylpyridin-2-yl)-*C*-ribonucleosides. Deprotection of silylated nucleosides by $Et_3N \cdot 3HF$ gave a series of title free *C*-ribonucleosides (12 examples).

Introduction

C-Nucleosides are important stable analogues of natural *N*-nucleosides, and their syntheses and many applications in chemical biology and medicinal chemistry have been subject to several recent comprehensive reviews.[1] Aryl *C*-2′-deoxyribonucleosides usually do not exhibit any pharmaceutically interesting biological activities but have attracted prominent attention as candidates for novel base-pairs in the quest for extension of the genetic alphabet.[2] Among many (het)aryl nucleosides forming selective hydrophobic pairs in stable DNA duplexes due to increased packing and hydrophobic interactions,[3] several promising artificial base-pairs showed efficient and specific replication by DNA polymerases.[4] The most successful pairs based on 4-substituted 2-methoxyphenyl *C*-nucleoside in combination with thioisocarbostyril base has been found[5] to be efficiently and selectively replicated and extended and very recently also the first successful PCR

*To whom correspondence should be addressed. Phone: +420 220183324. Fax: +420 220183559.

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with a 6-letter genetic alphabet was reported.[6] The second step of the extended genetic code is the transcription to RNA which was also shown[7] to be feasible with the above-mentioned base-pair and which is now awaiting systematic exploration. For this purpose, aryl *C*-ribonucleosides are needed as building blocks. So far, the *C*-ribonucleosides were mainly targets for medicinal chemistry. The most important classes of cytostatic *C*-ribonucleosides are carbamoylhetaryl *C*-ribonucleosides[8] (tiazofurine and related analogues of nicotinamine ribonucleoside) functioning as precursors of inhibitors of inosine 5′-monophosphate dehydrogenase (IMPDH) and immucilins inhibiting purine nucleoside phosphorylase.[9] Some pyridine *C*-ribonucleosides have been prepared for the use in modification of ribozymes[10,11] mainly to study the mechanism of catalysis.

The currently most commonly used synthetic approaches[1] to *C*-nucleosides are (i) additions of organometallics to lactones,[5,12] (ii) couplings of a halogenoses with organometallics,[13] (iii) electrophilic substitutions of electron-rich aromatics with sugars under Lewis acid catalysis,[14] or (iv) Heck coupling of aryl iodides with glycals.[15] Since none of them is truly general and some of them are non-selective and inefficient, there is still great need for development of efficient synthetic procedures. We are currently involved in development of modular methodologies suitable for a generation of functional group diversity in the last one to two step(s) based on preparation of general halo(het)aryl-*C*-nucleoside intermediates followed by displacement of the halogene for alkyl, aryl or amino substituents by cross-coupling reactions. We have already developed modular syntheses of 3- and 4-substituted benzene *C*-nucleosides,[16] 6-substituted pyridin-2-yl[17] and pyridin-3-yl,[18] 5-substituted thiophen-2-yl[19] *C*-2′-deoxyribonucleosides and carbamoylphenyl[20] *C*-ribonucleosides. Here we report on the synthesis of a hitherto missing[21] series of 6-substituted pyridin-2-yl *C*-ribonucleosides.

Results and Discussion

Our selected approach for the preparation of pyridine *C*-ribonucleosides was based on synthesis of 6-bromopyridine-2-yl *C*-ribonucleoside intermediate and its follow-up functional group transformation by Pd-catalyzed cross-couplings, aminations, and aminocarbonylations. For the preparation of the bromopyridyl nucleoside intermediate, we have envisaged the use of an analogous approach to the previously reported[17] synthesis of the corresponding 2-pyridyl *C*-2′-deoxyribonucleosides: addition of 2-lithio-6-bromopyridine **2** to easily available TBS-protected ribonolactone **1**. The monolitiated 2-bromopyridine **2** was generated from 2,6-dibromopyridine by a reverse addition technique according to Cai et al.[22] Due to the thermal instability of **2**, the lithiation must have been performed very carefully under efficient cooling. A solution of 2,6-dibromopyridine in THF was added to the solution of BuLi within exactly 7 min at −78 °C, and after the resulting solution was stirred for 15 min under cooling, a solution of lactone **1** was added and the reaction proceeded for another 30 min before quenching and workup. When only a small excess (1.5 equiv) of **2** over

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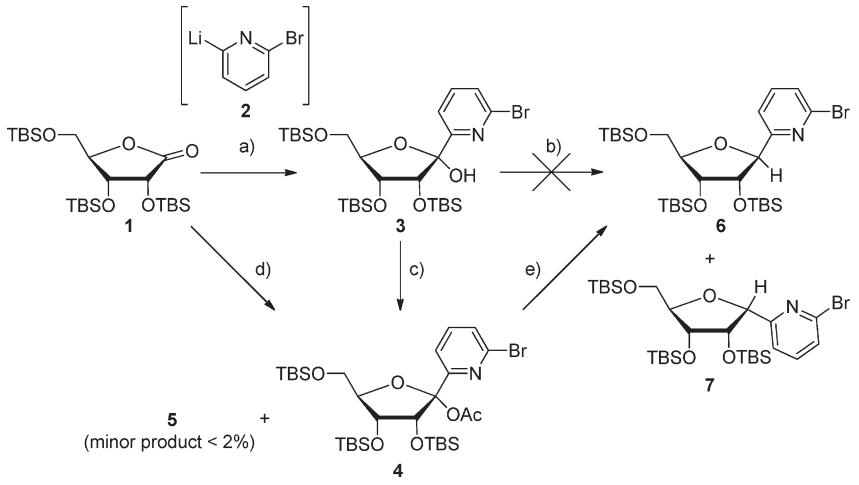
SCHEME 1[a]



[a]Conditions: (a) **2** (4 equiv), THF, −78 °C, 15 min (75%); (b) Et_3SiH (3 equiv), $BF_3 \cdot Et_2O$ (1.2 equiv), DCM, −20 °C (0%); (c) AcCl/DMAP, pyridine, 50 °C, 12 h, 20% for details see the Supporting Information; (d) **2** (4 equiv), THF, −78 °C, 15 min, then Ac_2O, −78 °C→ rt (70%); (e) Et_3SiH (3 equiv), $BF_3 \cdot Et_2O$ (1.2 equiv), hexanes, −20 °C (91%).

lactone **1** was used, the desired hemiketal **3** was isolated in moderate 20% yield. Increasing the excess of **2** to 4 equiv led to complete consumption of lactone **1** within 10 min to give the target hemiketal **3** in very good 75% yield (Scheme 1, step a). The structure of **3** in $CDCl_3$ solution was proved by NMR (NOE) as a pure β-anomeric hemiketal (as opposed to mixture of open hydroxy ketone and both anomeric hemiketals reported previously[17] for solution of the analogous 2′-deoxyribo derivative).

The second step was the reduction of hemiketal intermediate **3** to ether (*C*-ribonucleoside) **6**. This reaction is usually performed by using Et_3SiH in presence of $BF_3 \cdot Et_2O$. Although on pyridine 2′-deoxyribonucleosides[17] and on benzene ribonucleosides[16b] these reactions worked perfectly under standard conditions, the reduction of **3** did not proceed even after extensive optimization (for details see the Supporting Information). Since there were some literature examples[10d,23] of efficient reductive 1′-deacetoxylations as an alternative 1′-deoxygenation in these types of hemiketals, we have pursued acetylation of hemiketal **3**. It may be converted into a kinetic (β-anomer **4**) or a thermodynamic (α-anomer) by acetylation either in situ or after isolation of the hemiketal.[23b] Unfortunately, acylation of **3** with Ac_2O, AcCl, or AcCl/DMAP in pyridine was inefficient to give the target 1′-OAc derivative **4** only in a maximum 21% yield (Scheme 1, step c, for details see the Supporting Information). In order to increase the nucleophilicity of the 1′-OH group, we turned it into an alkoxide by treatment with LiHMDS at −78 °C prior to addition of Ac_2O to give the acetate **4** in only slightly improved yield of 34%. Further optimizations of the base, reaction time and acylating agent did not bring any improvement (see the Supporting Information).

Therefore, we focused on a one-pot addition of **2** to lactone **1** directly followed by acetylation of the in situ generated hemiketal alkoxide by Ac_2O (Scheme 1, step d). This protocol gave the desired acetyl hemiketal **4** in 38% yield accompanied by hemiketal **3** (21%) and another side product **5** (10%). Compound **5** has been characterized by NMR and X-ray diffraction (Figure 1) as product of lithiation of 2,6-dibromopyridine to position 4 followed by addition to lactone and acetylation. To avoid its formation, the lithiation protocol was reoptimized. Finally, we used a diluted (0.3 M) solution of *n*-BuLi in hexanes for the lithiation of 2,6-dibromopyridine in THF at −78 °C followed by addition to **1**, slow quenching with Ac_2O, and warming to ambient temperature to prepare acetate **4** in good yield of 70% accompanied by only a trace amount of **5** (< 2%). The acetylated hemiketal **4** was isolated and characterized as a pure β-anomer.

TABLE 1. Optimization of Reduction of Acetate 4 to *C*-Nucleosides 6 and 7 (Step e) in Scheme 1[a]

entry	solvent	temp (°C)	time (min)	yield (%)	β/α ratio **6**/**7**
1	DCM	−78	10	71	85:15
2	DCM	−40	5	85	83:17
3	DCM	0	5	87	77:23
4	CH_3NO_2	−40	10	88	83:17
5	toluene	−20	5	90	95:5
6	hexanes	−20	5	91	99:1

[a]General conditions: Et_3SiH (3 equiv), $BF_3 \cdot Et_2O$ (1.2 equiv).

Reduction of the hemiketal ester **4** was then performed with $Et_3SiH/BF_3 \cdot Et_2O$ under different conditions (Table 1). The stereoselectivity (β- and α-anomeric products **6** and **7**) was strongly dependent on a solvent and temperature. In DCM at −78 °C, a mixture of **6** and **7** (85:15 ratio) was obtained in 71% yield (entry 1), while at −40 °C the yield was increased to 85% without a dramatic change of stereoselectivity (entry 2). Increasing the temperature to 0 °C caused a decrease of selectivity to 77:23 (entry 3). Switching to more polar solvent (CH_3NO_2) at −40 °C gave the same yield and selectivity as in DCM (entry 4). On the other hand, the use of the less polar toluene at −20 °C increased the selectivity to 95:5 with 90% yield (entry 5). Finally, the optimized procedure was performed in hexanes at −20 °C to achieve an excellent 91% yield of reduction with superior β/α selectivity 99:1 (entry 6). By the optimized sequence consisting of

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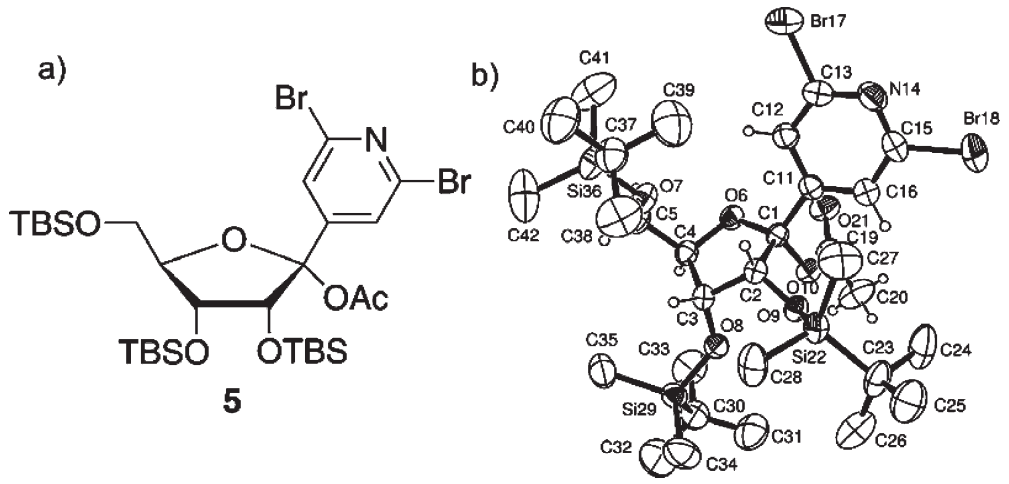
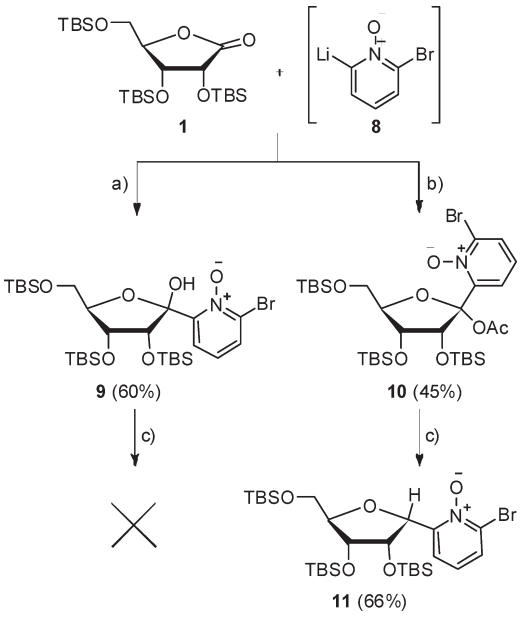


FIGURE 1. Structural formula (a) and ORTEP drawing of crystal structure (b) of side product **5**. Thermal ellipsoids are drawn at the 30% probability level, and hydrogens on TBS-groups were omitted for clarity. CCDC 752141.

SCHEME 2[a]



[a]Conditions: (a) **8** (2 equiv), THF, −78 °C, 30 min, (60%); (b) **8** (2 equiv), THF, −78 °C, 15 min, then Ac_2O, −78 °C → rt (45%) **8**; (c) Et_3SiH (3 equiv), $BF_3 \cdot Et_2O$ (1.2 equiv), 20 min, DCM, 0 °C.

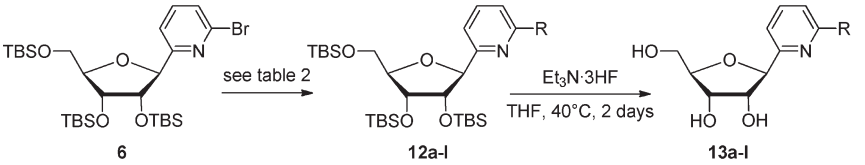
one-pot lithiation, addition, and acetylation followed by reduction in hexanes, the target TBS-protected 6-bromopyridine-2-yl *C*-ribonucleoside intermediate **6** was prepared (as pure β-anomer determined by NOE) in 63% isolated overall yield based on lactone **1**.

In parallel, we were also interested in studying of an alternative approach for the preparation of pyridine-*C*-ribonucleosides based on addition of 2-lithio-6-bromopyridine *N*-oxide **8** to lactone **1** (Scheme 2). An initial idea was to increase electron density in position 2 of the pyridine moiety ("umpolung" of the molecule), which may facilitate reduction of the free hemiketal without the need of acetylation. To prove this hypothesis, an addition of 2-lithio-6-bromopyridine *N*-oxide **8** to lactone **1** was performed resulting in pyridine *N*-oxide hemiketal **9** in 60% yield. The NOESY spectrum revealed that it is a pure α-anomer (as opposed to β-anomer of the analogous pyridine derivative, vide supra). Unfortunately, also in this case the reduction of **9** with $Et_3SiH/BF_3 \cdot Et_2O$ did not proceed. In analogy to previous experiments, acylated hemiketal **10** was prepared by addition of **8** to lactone **1** followed by Ac_2O quenching. Surprisingly, this reaction proceeded with opposite stereoselectivity to give acetate **10** as pure β-anomer in 45% yield. It was then reduced with $Et_3SiH/BF_3 \cdot Et_2O$ in DCM at 0 °C. The product **11** isolated in 66% yield was characterized as a pure undesired α-anomer. It seems that the presence of the *N*-oxide reverted the stereoselectivity of each step from retention to inversion of the configuration probably due to different kinetic stability or thermodynamic equilibria of the α- and β-anomeric hemiketal intermediates. The reactions are interesting, but apparently, this approach was not suitable for the preparation of **6**.

With key intermediate **6** in hand, we turned our attention to cross-coupling,[17] amination,[17] and aminocarbonylation[20] reactions (Scheme 3, Table 2). Cross-coupling reactions with organoaluminum or organozinc reagents were used for introduction of sp^3 (alkyl and benzyl) substituents. The reactions of **6** with trimetylaluminum, trietylaluminum, and benzylzinc bromide were performed under standard conditions in the presence of $Pd(PPh_3)_4$ in THF at 65 °C without any optimization. In all cases, desired nucleosides **12a**−**c** were obtained in excellent yields (90−92%) (entries 1−3). 6-Phenylpyridine *C*-ribonucleoside **12d** was prepared by the Suzuki−Miyaura cross-coupling of **6** with phenylboronic acid in toluene in the presence of K_2CO_3 and $Pd(PPh_3)_4$ at 100 °C in 92% yield (entry 4).

In order to introduce hetaryl substituents, the Stille cross-coupling reactions in DMF using $PdCl_2(PPh_3)_2$ were used. Reactions of **6** with 2-thienyl(tributyl)stannane (entry 5) and 2-furyl(tributyl)stannane (entry 6) proceeded very smoothly within 1.5 h at 100 °C to give the desired 4-(2-thienyl)-pyridine **12e** and 4-(2-furyl)pyridine *C*-ribonucleosides **12f** in 90% and 92% yield, respectively. On the other hand, reaction of **6** with 2-pyridyl(tributyl)stannane (entry 7) required a longer time to reach complete conversion, and moreover, formation of some byproduct was observed. The extraction and column chromatography isolation of

SCHEME 3. Synthesis of a Series of Pyridine *C*-Ribonucleosides



12,13	R
a	Me
b	Et
c	Bn
d	Ph
e	2-thienyl
f	2-furyl
g	2-pyridyl
h	NH_2
i	NMe_2
j	$CONH_2$
k	CONHMe
l	$CONMe_2$

TABLE 2. Cross-Couplings, Aminations and Aminocarbonylations of Bromopyridyl *C*-Ribonucleoside 6 Followed by Deprotection

entry	reagent	catalyst	ligand/base	solvent	conditions	reaction (yield, %)	deprotection (yield, %)
1	Me_3Al	$Pd(PPh_3)_4$		THF	72 h, 65 °C	**12a** (92)	**13a** (87)
2	Et_3Al	$Pd(PPh_3)_4$		THF	48 h, 65 °C	**12b** (91)	**13b** (89)
3	BnZnBr	$Pd(PPh_3)_4$		THF	24 h, 65 °C	**12c** (90)	**13c** (90)
4	$PhB(OH)_2$	$Pd(PPh_3)_4$	K_2CO_3	toluene	12 h, 100 °C	**12d** (92)	**13d** (89)
5	2-Bu_3Sn-thiophene	$Pd(PPh_3)_2Cl_2$		DMF	1.5 h, 100 °C	**12e** (90)	**13e** (89)
6	2-Bu_3Sn-furane	$Pd(PPh_3)_2Cl_2$		DMF	1.5 h, 100 °C	**12f** (92)	**13f** (90)
7	2-Bu_3Sn-pyridine	$Pd(PPh_3)_2Cl_2$		DMF	24 h, 100 °C	**12g** (61)	**13g** (88)
8	$LiN(SiMe_3)_2$	Pd_2dba_3	cHex JohnPhos[a],	THF	3.5 h, 60 °C	**12h** (86)	**13h** (90)
9	$Me_2NH\cdot HCl$	Pd_2dba_3	JohnPhos,[b] *t*BuONa	toluene	4.5 h, 40 °C	**12i** (86)	**13i** (89)
10	$NH_4Cl/CO_{(1\ atm)}$	$Pd(OAc)_2$	Xantphos[c]/K_3PO_4	toluene/ DMSO	3 h, 80 °C	**12j** (78)	**13j** (90)
11	$MeNH_2\cdot HCl/CO_{(1\ atm)}$	$Pd(OAc)_2$	Xantphos[c]/K_3PO_4	toluene/ DMSO	3 h, 80 °C	**12k** (82)	**13k** (93)
12	$Me_2NH\cdot HCl/CO_{(1\ atm)}$	$Pd(OAc)_2$	Xantphos[c]/K_3PO_4	toluene	3 h, 80 °C	**12l** (83)	**13l** (88)

[a]cHex JohnPhos = (2-biphenyl)dicyclohexylphosphane. [b]JohnPhos = (2-biphenyl)di-*tert*-butylphosphane. [c]Xantphos = 4,5-Bis(diphenylphosphino)-9,9-dimethylxanthene.

the resulting nucleoside **12g** from lipophilic tin-containing side products was more complicated, reflected in the lower isolated yield of 61%.

The Hartwig−Buchwald[24] reactions were used for introduction of *N*-substituents. Unsubstituted aminopyridine derivate **12h** was prepared by the reaction of **6** with lithium bis(trimetylsilyl)amide in the presence of Pd_2dba_3 and Buchwald-type ligand (2-biphenyl)dicyclohexylphosphane (cHex JohnPhos)[25] in 86% yield (Table 2, entry 8). The Buchwald reaction was also used for the introduction of the dimethylamino group. The reaction of **6** with dimethylamine hydrochloride ($Me_2NH\cdot HCl$) was performed under standard conditions, using Pd_2dba_3, 2-(di-*tert*-butylphosphanyl)-biphenyl (JohnPhos),[25] and *t*-BuONa as a base at 40 °C for 4.5 h to give the target dimethylaminopyridine *C*-ribonucleoside **12i** in 86% yield (Table 2, entry 9) .

Amides **12j**−**l** were prepared by Pd-catalyzed aminocarbonylation reactions[20] of **6** with corresponding amine hydrochlorides under atmospheric CO pressure in presence of 5 mol % of $Pd(OAc)_2$, 10 mol % of Xanthphos, and K_3PO_4. All reactions were finished within 3 h at 80 °C yielding pyridine-6-carboxamide *C*-ribonucleosides **12j** (78%), **12k** (82%), and **12l** (83%).

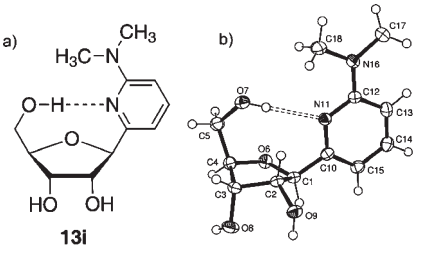


FIGURE 2. Structural formula (a) and ORTEP drawing of crystal structure (b) of *C*-nucleoside **13i**. Thermal ellipsoids are drawn at the 50% probability level. CCDC 752142.

For final deprotection of the silylated nucleosides **12a**−**l**, treatment with $Et_3N\cdot 3HF$[26] was used. Heating at 40 °C for 2 days followed by treatment with $NaHCO_3$ resulted in formation of the desired free nucleosides **13a**−**l**. Chromatographic purification on reversed-phase flash chromatography and subsequent lyophylization gave free nucleosides **13a**−**l** in excellent yields (87−93%, Table 2, entries 1−12).

Crystal structure of free *C*-ribonucleoside **13i** (Figure 2) reveals the C2′-endo (S) conformation typical for 2′-deoxyribonucleosides. On the other hand, in DMSO solution the series of *C*-ribonucleosides **13a**−**l** shows a preference for the expected C3′-endo (N) conformation as shown by analysis of interaction constants in ^1H NMR (see the Supporting Information). However, remeasuring **13i** in chloroform

(24) Yang, B. H.; Buchwald, S. L. *J. Organomet. Chem.* **1999**, *576*, 125–146.

(25) (a) Wolfe, J. P.; Tomori, H.; Sadighi, J. P.; Yin, J.; Buchwald, S. L. *J. Org. Chem.* **2000**, *65*, 1158–1174. (b) Lee, D.-Y.; Hartwig, J. F. *Org. Lett.* **2005**, *7*, 1169–1172.

(26) Čapek, P.; Pohl, R.; Hocek, M. *J. Org. Chem.* **2005**, *70*, 8001–8008.

showed again preference for C2′-endo (S) conformation. It seems that the intramolecular H-bond of 5′-OH to pyridine nitrogen (which is not present in DMSO solution) might be the reason for the preference of the C2′-endo (S) conformation in the solid state and chloroform solution.

All final *C*-ribonucleosides **13a**−**l** were tested on cytostatic and anti-HCV activities, and none of them showed any significant effect at 10 μM concentrations.

In conclusion, we have developed an efficient methodology for the synthesis of diverse 6-substituted pyridine-2-yl *C*-ribonucleosides. The key intermediate, TBS-protected 6-bromopyridine **6**, was prepared in three steps: one-pot addition of bromopyridyllithium **2** to protected ribonolactone **1** with in situ acetylation followed by reduction of the acetylated hemiacetal **4** by $Et_3SiH/BF_3\cdot Et_2O$, in excellent overall yield of 63%. It must be noted that the protocol is extremely sensitive to efficient cooling and precise adherence of reaction times in order to get reproducibly high yields. Interestingly, when the same sequence was performed for the corresponding pyridine *N*-oxide derivatives, each step proceeded with inversion of configuration at C1′ giving undesired α-anomeric bromopyridine *N*-oxide *C*-ribonucleoside **11**. The bromopyridine *C*-ribonucleoside intermediate **6** readily undergoes cross-coupling reactions with alkylaluminum or -zinc reagents and arylboronic acids or hetarylstannanes to give 6-alkyl or 6-hetaryl derivatives. Hartwig−Buchwald aminations and Pd-catalyzed aminocarbonylations of 6 gave 6-amino- and 6-carbamoylpyridine *C*-ribonucleosides in high yields. Free nucleosides **13a**−**l** were prepared by desilylation of the intermediates by $Et_3N\cdot 3HF$. They did not exert any considerable cytotoxicity, and therefore, they are good candidates for conversion to nucleoside triphosphates as model compounds for studying specificity and fidelity of RNA polymerases or primases.

Experimental Section

1*β*-(6-Bromopyridin-2-yl)-1-*O*-acetyl-2,3,5-tri-*O*-(*tert*-butyldimethylsilyl)-D-ribofuranose (4). *n*-BuLi (10.1 mL, 16.3 mmol, 1.6 M solution in hexane, 4 equiv) in dry hexanes (50 mL) was added within 7 min to a vigorously stirred solution of 2, 6-dibromopyridine (3.86 g, 16.3 mmol, 4 equiv) in dry THF (40 mL) at −78 °C, and the resulting brown-yellow solution was stirred for 15 min at −78 °C. A precooled (−78 °C) solution of **1** (2.0 g, 4.07 mmol) in THF (20 mL) was then added via cannula to the reaction mixture in one portion followed by additional stirring for 15 min at −78 °C and dropwise addition of Ac_2O (2.6 mL, 27.7 mmol, 6.8 equiv). The resulting red mixture was stirred for 10 min at −78 °C, slowly warmed to rt, quenched by pouring into satd $NaHCO_3$ (150 mL), extracted with Et_2O (3 × 250 mL), and dried with Na_2SO_4. After evaporation of solvents, crude product was dissolved in Ac_2O (100 mL) and extracted with hexanes (2 × 300 mL). Collected hexane layers were washed with satd $NaHCO_3$ (500 mL) and dried over Na_2SO_4. Evaporation under reduced pressure and chromatography in gradient hexanes to 6% Et_2O in hexanes furnished compound **4** (2.01 g, 70%) as a colorless oil, which crystallized upon standing. Mp 78−82 °C. HRMS (ESI) $C_{30}H_{56}BrNO_6Si_3Na$: [M + Na] calcd 712.2491, found 712.2492. ^{1}H NMR (500 MHz, $CDCl_3$): −0.39, −0.12, 0.06, 0.08, and 0.09 (6 × s, 6 × 3H, CH_3Si); 0.88, 0.89, and 0.94 (3 × s, 3 × 9H, $(CH_3)_3C$); 2.11 (s, 3H, CH_3CO); 3.77 (dd, 1H, J_{gem} = 11.3 Hz, $J_{5'a,4'}$ = 2.1 Hz, H-5′a); 3.95 (dd, 1H, J_{gem} = 11.3 Hz, $J_{5'b,4'}$ = 2.9 Hz, H-5′b); 4.08 (d, 1H, $J_{2',3'}$ = 5.2 Hz, H-2′); 4.18 (dd, 1H, $J_{3',2'}$ = 5.2 Hz, $J_{3',4'}$ = 2.1 Hz, H-3′); 4.27 (ddd, 1H, $J_{4',5'b}$ = 2.9 Hz, $J_{4',5'a}$ = $J_{4',3'}$ = 2.1 Hz, H-4′); 7.34 (dd, 1H, $J_{5,4}$ = 7.8 Hz, $J_{5,3}$ = 0.9 Hz, H-5); 7.47 (t, 1H, $J_{4,5}$ = $J_{4,3}$ = 7.8 Hz, H-4); 7.62 (dd, 1H, $J_{3,4}$ = 7.8 Hz, $J_{3,5}$ = 0.9 Hz, H-3). ^{13}C NMR (125.7 MHz, $CDCl_3$): −5.8, −5.7, −5.5, −4.9, −4.6, and −4.4 (CH_3Si); 18.0 ($(CH_3)_3C$); 21.9 (CH_3CO); 25.7, 25.8, and 25.9 ($(CH_3)_3C$); 62.7 (CH_2-5′); 72.4 (CH-3′); 79.5 (CH-2′); 87.6 (CH-4′); 105.1 (C-1′); 119.4 (CH-3); 127.1 (CH-5); 138.6 (CH-4); 140.8 (C-6); 159.8 (C-2); 170.0 (CO). IR spectrum (CCl_4): 3052, 2954, 2897, 1756, 1581, 1559, 1472, 1463, 1436, 1402, 1402, 1390, 1365, 1365, 1263, 1253, 1160, 1129, 1073, 1023, 1005, 989, 969, 939, 878, 839, 682, 672, 614 cm^{-1}. $[\alpha]^{20}_D$ = +21.8 (*c* 4.18, $CHCl_3$).

1*β*-(6-Bromopyridin-2-yl)-1-deoxy-2,3,5-tri-*O*-(*tert*-butyldimethylsilyl)-D-ribofuranose (6). Et_3SiH (1.3 mL, 8.16 mmol, 3 equiv) was added in one portion to a stirred solution of acylated hemiketal **4** (1.88 g, 2.72 mmol) in dry hexanes (14 mL) in an ice−brine bath (−20 °C) under argon. After 5 min, $BF_3\cdot Et_2O$ (0.39 mL, 3.26 mmol, 1.2 equiv) was added in one portion. The resulting mixture was stirred for an additional 5 min, followed by addition of Et_3N (10 mL) and evaporation of solvents. Crude product was directly chromatographed on silica gel in gradient hexanes to 1.6% EtOAc in hexanes to give **6** (1.58 g, 90%) as a colorless oil. HRMS (ESI) $C_{28}H_{55}BrNO_4Si_3$: [M + H] calcd 632.2617, found 632.2619. ^{1}H NMR (499.8 MHz, $CDCl_3$): −0.18, −0.04, 0.070, 0.072, 0.10, and 0.11 (6 × s, 6 × 3H, CH_3Si); 0.85, 0.91, and 0.93 (3 × s, 3 × 9H, $(CH_3)_3C$); 3.75 (dd, 1H, J_{gem} = 11.2, $J_{5'b,4'}$ = 3.1, H-5′b); 3.86 (dd, 1H, J_{gem} = 11.2, $J_{5'a,4'}$ = 3.8, H-5′a); 4.06 (td, 1H, $J_{4',5'}$ = 3.8, 3.1, $J_{4',3'}$ = 3.8, H-4′); 4.11 (dd, 1H, $J_{3',2'}$ = 4.3, $J_{3',4'}$ = 3.8, H-3′); 4.15 (dd, 1H, $J_{2',1'}$ = 5.7, $J_{2',3'}$ = 4.3, H-2′); 4.88 (d, 1H, $J_{1',2'}$ = 5.7, H-1′); 7.35 (dd, 1H, $J_{5,4}$ = 7.8, $J_{5,3}$ = 1.1, H-5); 7.48 (dd, 1H, $J_{4,5}$ = 7.8, $J_{4,3}$ = 7.6, H-4); 7.55 (dd, 1H, $J_{3,4}$ = 7.6, $J_{3,5}$ = 1.1, H-3). ^{13}C NMR (125.7 MHz, $CDCl_3$): −5.5, −5.4, −5.0, −4.61, −4.58, and −4.4 (CH_3Si); 18.0, 18.1, and 18.4 ($C(CH_3)_3$); 25.86, 25.88, and 26.0 ($(CH_3)_3C$); 63.0 (CH_2-5′); 72.8 (CH-3′); 78.6 (CH-2′); 84.2 (CH-1′); 85.2 (CH-4′); 120.3 (CH-3); 126.8 (CH-5); 138.5 (CH-4); 141.3 (C-6); 162.2 (C-2). IR spectrum (CCl_4): 3051, 2956, 2796, 1582, 1557, 1463, 1435, 1408, 1390, 1362, 1255, 1154, 1124, 1044, 1005, 996, 989, 967, 940, 878, 838, 682, 571 cm^{-1}. $[\alpha]^{20}_D$ = +3.8 (*c* 6.01, $CHCl_3$).

1*β*-(6-Methylpyridin-2-yl)-1-deoxy-2,3,5-tri-*O*-(*tert*-butyldimethylsilyl)-D-ribofuranose (12a). Me_3Al (0.48 mL, 0.951 mmol, 2 equiv, 2 M in toluene) was added to a vigorously stirred solution of **6** (301 mg, 0.476 mmol) and $Pd(PPh_3)_4$ (28 mg, 0.024 mmol, 5 mol %) in THF (10 mL) under argon. The mixture was stirred at 65 °C for 72 h and then quenched by pouring into saturated NaH_2PO_4 (50 mL) and extracted to EtOAc (3 × 50 mL). Crude product was chromatographed on silica gel in gradient hexanes to 2% EtOAc in hexanes to give **12a** (250 mg, 92%) as colorless oil. HRMS (ESI) $C_{29}H_{58}NO_4Si_3$: [M + H] calcd 568.3668, found 568.3668. ^{1}H NMR (500 MHz, $CDCl_3$): −0.24, −0.08, 0.072, 0.073, 0.10, and 0.11 (6 × s, 6 × 3H, CH_3Si); 0.82, 0.92, and 0.93 (3 × s, 3 × 9H, $(CH_3)_3C$); 2.51 (s, 3H, CH_3); 3.77 (dd, 1H, J_{gem} = 11.1 Hz, $J_{5'a,4'}$ = 3.4 Hz, H-5′a); 3.86 (dd, 1H, J_{gem} = 11.1 Hz, $J_{5'b,4'}$ = 4.2 Hz, H-5′b); 4.06 (dt, 1H, $J_{4',5'b}$ = 4.2 Hz, $J_{4',5'a}$ = $J_{4',3'}$ = 3.4 Hz, H-4′); 4.13 (dd, 1H, $J_{3',2'}$ = 4.4 Hz, $J_{3',4'}$ = 3.5 Hz, H-3′); 4.17 (dd, 1H, $J_{2',1'}$ = 6.0 Hz, $J_{2',3'}$ = 4.4 Hz, H-2′); 4.89 (d, 1H, $J_{1',2'}$ = 6.0 Hz, H-1′); 7.01 (bd, 1H, $J_{5,4}$ = 7.6 Hz, H-5); 7.35 (dp, 1H, $J_{3,4}$ = 7.8 Hz, $J_{3,5}$ = $J_{3,CH3}$ = 0.5 Hz, H-3); 7.50 (t, 1H, $J_{4,5}$ = $J_{4,3}$ = 7.7 Hz, H-4). ^{13}C NMR (125.7 MHz, $CDCl_3$): −5.5, −5.4, −5.2, −4.6, and −4.4 (CH_3Si); 18.0, 18.1, and 18.4 ($(CH_3)_3C$); 24.4 (CH_3); 25.8, 25.9, and 26.0 ($(CH_3)_3C$); 63.2 (CH_2-5′); 73.1 (CH-3′); 78.6 (CH-2′); 84.7 (CH-1′); 85.1 (CH-4′); 118.5 (CH-3); 122.0 (CH-5); 136.3 (CH-4); 157.4 (C-6); 159.7 (C-2). IR spectrum (CCl_4): 3063, 2956, 2896, 1594, 1579, 1472, 1462, 1406, 1389, 1375, 1362, 1254, 1154, 1127, 1104, 1078, 1046, 1004, 996, 989, 967, 940, 879, 838, 681, 671 cm^{-1}.

1*β*-(6-Phenylpyridin-2-yl)-1-deoxy-2,3,5-tri-*O*-(*tert*-butyldimethylsilyl)-D-ribofuranose (12d). Compound **6** (406 mg, 0.641

mmol), K_2CO_3 (178 mg, 1.28 mmol, 2 equiv), $Pd(PPh_3)_4$ (37 mg, 0.032 mmol, 5 mol %), and $PhB(OH)_2$ (157 mg, 1.28 mmol, 2 equiv) were dissolved in toluene (19 mL) under argon, and the mixture was stirred at 100 °C for 12 h. The reaction mixture was concentrated under reduced pressure, and crude product was chromatographed on silica gel in toluene to give **12d** (370 mg, 92%) as a colorless oil. HRMS (ESI) $C_{34}H_{60}NO_4Si_3$: [M + H] calcd 630.3825, found 630.3825. ^{1}H NMR (500 MHz, $CDCl_3$): −0.07, 0.01, 0.07, 0.08, 0.115, and 0.123 (6 × s, 6 × 3H, CH_3Si); 0.86, 0.92, and 0.94 (3 × s, 3 × 9H, $(CH_3)_3C$); 3.80 (dd, 1H, J_{gem} = 11.1 Hz, $J_{5'a,4'}$ = 3.4 Hz, H-5′a); 3.97 (dd, 1H, J_{gem} = 11.1 Hz, $J_{5'b,4'}$ = 3.9 Hz, H-5′b); 4.13 (dt, $J_{4',3'}$ = 5.4 Hz, $J_{4',5'a}$ = $J_{4',5'b}$ = 3.6 Hz, H-4′); 4.19 (dd, 1H, $J_{3',4'}$ = 5.4 Hz, $J_{3',2'}$ = 4.2 Hz, H-3′); 4.35 (t, 1H, $J_{2',3'}$ = $J_{2',1'}$ = 4.2 Hz, H-2′); 5.03 (d, 1H, $J_{1',2'}$ = 4.2 Hz, H-1′); 7.40 (m, 1H, H-*p*-Ph); 7.46 (m, 2H, H-*m*-Ph); 7.55 (ddd, 1H, $J_{3,4}$ = 7.5 Hz, $J_{3,5}$ = 1.2 Hz, $J_{3,1'}$ = 0.5 Hz, H-3); 7.64 (dd, 1H, $J_{5,4}$ = 7.9 Hz, $J_{5,3}$ = 1.2 Hz, H-5); 7.69 (t, 1H, $J_{4,5}$ = $J_{4,3}$ = 7.7 Hz, H-4); 8.07 (m, 2H, H-*o*-Ph). ^{13}C NMR (125.7 MHz, $CDCl_3$): −5.39, −5.38, −4.8, −4.7, −4.6, and −4.3 (CH_3Si); 18.0, 18.1, and 18.5 (($CH_3)_3C$); 25.85, 25.89, and 26.1 (($CH_3)_3C$); 62.7 (CH_2-5′); 72.0 (CH-3′); 78.4 (CH-2′); 83.9 (CH-4′); 85.9 (CH-1′); 118.8 (CH-5); 120.1 (CH-3); 126.8 (CH-*o*-Ph); 128.5 (CH-*m*-Ph); 128.8 (CH-*p*-Ph); 137.0 (CH-4); 139.2 (C-*i*-Ph); 156.1 (C-6); 160.3 (C-2). IR spectrum (CCl_4): 3067, 3090, 3067, 3036, 2956, 2896, 1592, 1579, 1572, 1496, 1472, 1462, 1462, 1449, 1406, 1389, 1362, 1327, 1254, 1217, 1155, 1104, 1078, 1041, 1029, 1006, 996, 968, 940, 878, 838, 672 cm^{-1}.

1*β*-[6-(2-Thienyl)pyridin-2-yl]-1-deoxy-2,3,5-tri-*O*-(*tert*-butyldimethylsilyl)-D-ribofuranose (12e). DMF (3.1 mL) was added to a flame-dried and argon-purged flask containing **6** (419 mg, 0.662 mmol) and $PdCl_2(PPh_3)_2$ (23 mg, 0.033 mmol, 5 mol %). After 5 min of stirring at room temperature, tributyl(thiophen-2-yl)stannane (0.27 mL, 0.860 mmol, 1.3 equiv) was added, and the reaction vessel was immersed in an oil bath (100 °C). After 1.5 h, the reaction mixture became dark-brown, and the reaction was complete (monitored by TLC hexanes/EtOAc 10:1). The crude reaction mixture was diluted with Et_2O (300 mL), washed with 2 M HCl (80 mL) and saturated $NaHCO_3$ (100 mL), and dried over $MgSO_4$. After evaporation of solvents under reduced pressure, the crude product was chromatographed on silica gel in gradient hexanes to 4% EtOAc in hexanes to obtain **12e** (380 mg, 90%) as a colorless oil. HRMS (ESI) $C_{32}H_{58}NO_4SSi_3$: [M + H] calcd 636.3389, found 636.3389. ^{1}H NMR (500 MHz, $CDCl_3$): 0.04, 0.05, 0.06, 0.11, and 0.13 (6 × s, 6 × 3H, CH_3Si); 0.89, 0.91, and 0.94 (3 × s, 3 × 9H, $(CH_3)_3C$); 3.78 (dd, 1H, J_{gem} = 11.2 Hz, $J_{5'a,4'}$ = 3.2 Hz, H-5′a); 3.98 (dd, 1H, J_{gem} = 11.2 Hz, $J_{5'b,4'}$ = 3.4 Hz, H-5′b); 4.10 - 4.15 (m, 2H, H-3′,4′); 4.36 (t, 1H, $J_{2',1'}$ = $J_{2',3'}$ = 3.6 Hz, H-2′); 4.96 (d, 1H, $J_{1',2'}$ = 3.5 Hz, H-1′); 7.10 (dd, 1H, $J_{3,5}$ = 5.1 Hz, $J_{4,3}$ = 3.7 Hz, H-4-thienyl); 7.37 (dd, 1H, $J_{5,4}$ = 5.1 Hz, $J_{5,3}$ = 1.2 Hz, H-5-thienyl); 7.47 (dm, 1H, $J_{3,4}$ = 7.7 Hz, H-3); 7.52 (dd, 1H, $J_{5,4}$ = 7.9 Hz, $J_{5,3}$ = 1.1 Hz, H-5); 7.58 (dd, 1H, $J_{3,4}$ = 3.7 Hz, $J_{3,5}$ = 1.2 Hz, H-3-thienyl); 7.62 (t, 1H, $J_{4,3}$ = $J_{4,5}$ = 7.8 Hz, H-4). ^{13}C NMR (125.7 MHz, $CDCl_3$): −5.4, −4.8, −4.6, −4.5, and −4.3 (CH_3Si); 18.0, 18.1, and 18.5 (($CH_3)_3C$); 25.88, 25.9, and 26.1 (($CH_3)_3C$); 62.6 (CH_2-5′); 71.6 (CH-3′); 78.2 (CH-2′); 83.5 (CH-4′); 86.0 (CH-1′); 117.1 (CH-5); 119.8 (CH-3); 124.2 (CH-3-thienyl); 127.4 (CH-5-thienyl); 127.8 (CH-4-thienyl); 136.9 (CH-4); 145.4 (C-2-thienyl); 151.7 (C-6); 160.3 (C-2). IR spectrum (CCl_4): 3074, 2956, 2896, 1588, 1572, 1535, 1525, 1472, 1458, 1458, 1434, 1406, 1389, 1362, 1287, 1254, 1103, 1076, 1045, 1006, 995, 968, 940, 879, 854, 838,702, 682, 671 cm^{-1}.

1*β*-(6-Aminopyridin-2-yl)-1-deoxy-2,3,5-tri-*O*-(*tert*-butyldimethylsilyl)-D-ribofuranose (12h). $LiN(SiMe_3)_2$ (1.2 mL, 1 M solution in THF 1.18 mmol, 1.8 equiv) was added to a flame-dried and argon-purged flask containing **6** (416 mg, 0.6573 mmol), $Pd_2(dba)_3$, (15 mg, 0.016 mmol, 5 mol %), and (2-biphenyl-)dicyclohexylphosphine (23 mg, 0.036 mmol, 10 mol %), and the mixture was stirred at 60 °C for 3.5 h. After being cooled to room temperature, the reaction mixture was diluted with Et_2O (10 mL), and 2 M HCl (0.5 mL) was added. The resulting heterogeneous mixture was stirred for an additional 5 min and then transferred into a saturated $NaHCO_3$ (30 mL) and extracted to Et_2O (3 × 100 mL). Crude product was chromatographed on silica gel in gradient hexanes to 9% Et_2O in hexanes followed by gradient of 6% EtOAc in hexanes to 11% EtOAc in hexanes to give **12h** (324 mg, 86%) as yellow oil. HRMS (ESI) $C_{28}H_{57}N_2O_4Si_3$: [M + H] calcd 569.3621, found 569.3621. ^{1}H NMR (500 MHz, $CDCl_3$): −0.15, −0.04, 0.06, 0.07, 0.106, and 0.112 (6 × s, 6 × 3H, CH_3Si); 0.84, 0.91, and 0.93 (3 × s, 3 × 9H, $(CH_3)_3C$); 3.76 (dd, 1H, J_{gem} = 11.1 Hz, $J_{5'a,4'}$ = 3.5 Hz, H-5′a); 3.84 (dd, 1H, J_{gem} = 11.1 Hz, $J_{5'b,4'}$ = 4.5 Hz, H-5′b); 4.04 (dt, 1H, $J_{4',5'b}$ = 4.6 Hz, $J_{4',5'a}$ = $J_{4',3'}$ = 3.7 Hz, H-4′); 4.11 (bt, 1H, $J_{3',2'}$ = $J_{3',4'}$ = 4.1 Hz, H-3′); 4.14 (dd, 1H, $J_{2',1'}$ = 5.6 Hz, $J_{2',3'}$ = 4.3 Hz, H-2′); 4.37 (bs, 2H, NH_2); 4.72 (d, 1H, $J_{1',2'}$ = 5.6 Hz, H-1′); 6.38 (d, 1H, $J_{5,4}$ = 8.1 Hz, H-5); 6.90 (d, 1H, $J_{3,4}$ = 7.4 Hz, H-3); 7.37 (dd, 1H, $J_{4,5}$ = 8.1 Hz, $J_{4,3}$ = 7.5 Hz, H-4). ^{13}C NMR (125.7 MHz, $CDCl_3$): −5.44, −5.38, −5.0, −4.61, −4.58, and −4.4 (CH_3Si); 18.0, 18.1, and 18.4 (($CH_3)_3C$); 25.8, 25.9, and 26.0 (($CH_3)_3C$); 63.1 (CH_2-5′); 72.8 (CH-3′); 78.1 (CH-2′); 84.6 (CH-1′); 84.7 (CH-4′); 107.5 (CH-5); 112.0 (CH-3); 138.0 (CH-4); 157.6 (C-6); 158.2 (C-2). IR spectrum (CCl_4): 3510, 3409, 3175, 3063, 2956, 2896, 1610, 1591, 1579, 1471, 1462, 1406, 1391, 1389, 1336, 1253, 1155, 1129, 1101, 1079, 998, 979, 838, 682, 672 cm^{-1}.

1*β*-[6-(Dimethylamino)pyridin-2-yl]-1-deoxy-2,3,5-tri-*O*-(*tert*-butyldimethylsilyl)-D-ribofuranose (12i). Toluene (2.1 mL) was added to a flame-dried and argon-purged flask containing **6** (468 mg, 0.740 mmol), $Pd_2(dba)_3$ (17 mg, 0.019 mmol, 5 mol %), (2-biphenyl)di-*tert*-butylphosphine (22 mg, 0.074 mmol), sodium *tert*-butoxide (426 mg, 4.44 mmol, 6 equiv), and $Me_2NH \cdot HCl$ (302 mg, 3.70 mmol, 5 equiv). The resulting mixture was stirred at 40 °C for 4.5 h and then diluted with Et_2O (5 mL), poured into water (100 mL), extracted with Et_2O (3 × 100 mL), and dried over $MgSO_4$. After removal of the solvent under reduced pressure, crude product was chromatographed on silica in gradient hexanes to 4% EtOAc in hexanes to give **12i** (387 mg, 86%) as a colorless oil. HRMS (ESI) $C_{30}H_{61}N_2O_4Si_3$: [M + H] calcd 597.3934, found 597.3934. ^{1}H NMR (500 MHz, $CDCl_3$): 0.00, 0.02, 0.04, 0.05, 0.089, and 0.093 (6 × s, 6 × 3H, CH_3Si); 0.88, 0.90, and 0.92 (3 × s, 3 × 9H, $(CH_3)_3C$); 3.07 (s, 6H, $(CH_3)_2N$); 3.75 (dd, 1H, J_{gem} = 11.1 Hz, $J_{5'a,4'}$ = 3.9 Hz, H-5′a); 3.92 (dd, 1H, J_{gem} = 11.1 Hz, $J_{5'b,4'}$ = 4.2 Hz, H-5′b); 4.07 (dt, 1H, $J_{4',3'}$ = 6.3 Hz, $J_{4',5'a}$ = $J_{4'5'b}$ = 4.0 Hz, H-4′); 4.13 (dd, 1H, $J_{3',4'}$ = 6.3 Hz, $J_{3',2'}$ = 4.2 Hz, H-3′); 4.31 (dd, 1H, $J_{2',3'}$ = 4.2 Hz, $J_{2',1'}$ = 3.3 Hz, H-2′); 4.79 (d, 1H, $J_{1',2'}$ = 3.3 Hz, H-1′); 6.39 (d, 1H, $J_{5,4}$ = 8.4 Hz, H-5); 6.82 (d, 1H, $J_{3,4}$ = 7.3 Hz, H-3); 7.38 (dd, 1H, $J_{4,5}$ = 8.5 Hz, $J_{4,3}$ = 7.3 Hz, H-4). ^{13}C NMR (125.7 MHz, $CDCl_3$): −5.4, −4.8, −4.7, −4.6, and −4.3 (CH_3Si); 18.0, 18.1, and 18.5 (($CH_3)_3C$); 25.9 and 26.1 (($CH_3)_3C$); 38.1 ($(CH_3)_2N$); 62.8 (CH_2-5′); 71.8 (CH-3′); 77.7 (CH-2′); 83.0 (CH-4′); 86.5 (CH-1′); 104.5 (CH-5); 109.6 (CH-3); 137.3 (CH-4); 158.1 (C-2); 158.8 (C-6). IR spectrum (CCl_4): 2956, 2896, 1597, 1572, 1499, 1472, 1463, 1431, 1405, 1389, 1374, 1362, 1253, 1154, 1126, 1101, 1078, 941, 838, 683 cm^{-1}.

1*β*-[6-(Carbamoyl)pyridin-2-yl]-1-deoxy-2,3,5-tri-*O*-(*tert*-butyldimethylsilyl)-D-ribofuranose (12j). A flame-dried septum-sealed flask (10 mL) containing **6** (220 mg, 0.348 mmol), $Pd(OAc)_2$ (3.9 mg, 0.018 mmol, 5 mol %), Xantphos (20 mg, 0.035 mmol, 10 mol %), NH_4Cl (74 mg, 1.39 mmol, 4 equiv), and K_3PO_4 (369 mg, 1.74 mmol, 5 equiv) was evacuated and backfilled with $CO_{(g)}$. Then, toluene (0.6 mL) and DMSO (0.6 mL) were added via syringe. The reaction mixture was stirred at room temperature for 5 min and then immersed into a preheated oil bath (80 °C) and vigorously stirred for 3 h. After the mixture was cooled to room temperature, Et_2O (8 mL) was added, and the reaction mixture was filtered through a plug of Celite (eluting

with Et_2O) and concentrated under reduced pressure. The crude product was purified by flash chromatography on silica gel in gradient hexanes to 17% EtOAc in hexanes to give **12j** (160 mg, 78%) as a colorless oil. HRMS (ESI) $C_{29}H_{57}N_2O_5Si_3$: [M + H] calcd 597.3537, found 597.3557. ^{1}H NMR (500 MHz, $CDCl_3$): −0.24, −0.04, 0.066, 0.070, 0.12, and 0.13 (6 × s, 6 × 3H, CH_3Si); 0.84, 0.92, and 0.94 (3 × s, 3 × 9H, $(CH_3)_3C$); 3.78 (dd, 1H, J_{gem} = 11.2 Hz, $J_{5'a,4'}$ = 2.6 Hz, H-5′a); 3.92 (dd, 1H, J_{gem} = 11.2 Hz, $J_{5'b,4'}$ = 3.2 Hz, H-5′b); 4.08 − 4.13 (m, 3H, H-2′,3′,4′); 4.95 (d, 1H, $J_{1',2'}$ = 4.8 Hz, H-1′); 5.77 (d, 1H, J_{gem} = 4.0 Hz, NH_2a); 7.81 (dd, 1H, $J_{4,3}$ = 7.9 Hz, $J_{4,5}$ = 7.0 Hz, H-4); 7.84 (dd, 1H, $J_{3,4}$ = 7.9 Hz, $J_{3,5}$ = 1.9 Hz, H-3); 7.85 (m, 1H, NH_2b); 8.10 (dd, 1H, $J_{5,4}$ = 7.0 Hz, $J_{5,3}$ = 1.9 Hz, H-5). ^{13}C NMR (125.7 MHz, $CDCl_3$): −5.43, −5.41, −5.1, −4.7, −4.5, and −4.4 (CH_3Si); 17.9, 18.1, and 18.4 ($(CH_3)_3C$); 25.7, 25.9, and 26.0 ($(CH_3)_3C$); 62.7 (CH_2-5′); 72.4 (CH-3′); 78.9 (CH-2′); 84.8 (CH-4′); 84.9 (CH-1′); 121.3 (CH-5); 124.3 (CH-3); 137.8 (CH-4); 148.4 (C-6); 160.0 (C-2); 166.7 (CO). IR spectrum (CCl_4): 3528, 3459, 3401, 3275, 3150, 3063, 2897, 2895, 1699, 1594, 1574, 1556, 1472, 1462, 1435, 1404, 1388, 1362, 1256, 1155, 1127, 1075, 972, 940, 887, 838, 680 cm^{-1}.

General Procedure for the Deprotection of TBS Group. Method A. $Et_3N \cdot 3HF$ (163 μL, 1.00 mmol, 10 equiv) was added to the solution of silylated compound **12a**−**l** (0.10 mmol) in THF (1.00 mL), and the resulting mixture was stirred at 40 °C for 2 days. After the reaction was complete (monitored by TLC eluted in $CHCl_3$/MeOH 8:2), solvent was removed under reduced pressure, the crude product was dissolved in water, and solid $NaHCO_3$ was added until pH 8. Solvents were removed under reduced pressure, and crude product was purified by reversed-phase chromatography (H_2O/MeOH as a eluent) to obtain free *C*-ribonucleosides **13a**−**l**.

1β-(6-Phenylpyridin-2-yl)-1-deoxy-D-ribofuranose (13d). Compound **13d** was prepared from **12d** (371 mg, 0.589 mmol) according to general procedure, in 89% yield, as a colorless oil, which after lyophylization furnished white hygroscopic powder. HRMS (ESI) $C_{16}H_{18}NO_4$: [M + H] calcd 288.1230, found 288.1232. ^{1}H NMR (500 MHz, DMSO-d_6): 3.55 (dd, 1H, J_{gem} = 11.7 Hz, $J_{5'a,4'}$ = 4.6 Hz, H-5′a); 3.67 (dd, 1H, J_{gem} = 11.7 Hz, $J_{5'b,4'}$ = 3.7 Hz, H-5′b); 3.89 (m, 1H, H-4′); 3.95 (bt, 1H, $J_{3',2'} = J_{3',4'}$ = 5.2 Hz, H-3′); 4.11 (bt, 1H, $J_{2',1'} = J_{2',3'}$ = 4.9 Hz, H-2′); 4.80 (d, 1H, $J_{1',2'}$ = 4.7 Hz, H-1′); 4.80 − 5.30 (m, 3H, OH-2′,3′,5′); 7.44 (m, 1H, H-*p*-Ph); 7.50 (m, 2H, H-*m*-Ph); 7.53 (dd, 1H, $J_{3,4}$ = 7.0 Hz, $J_{3,5}$ = 1.6 Hz, H-3); 7.84 (dd, 1H, $J_{5,4}$ = 7.9 Hz, $J_{5,3}$ = 1.7 Hz, H-5); 7.87 (dd, 1H, $J_{4,5}$ = 7.9 Hz, $J_{4,3}$ = 7.0 Hz, H-4); 8.07 (m, 2H, H-*o*-Ph). ^{13}C NMR (125.7 MHz, DMSO-d_6): 62.1 (CH_2-5′); 71.4 (CH-3′); 76.8 (CH-2′); 84.5 (CH-4′); 85.7 (CH-1′); 119.4 (CH-5); 120.4 (CH-3); 126.9 (CH-*o*-Ph); 129.0 (CH-*m*-Ph); 129.3 (CH-*p*-Ph); 138.0 (CH-4); 138.9 (C-*i*-Ph); 155.5 (C-6); 160.7 (C-2). IR spectrum (KBr): 3415, 3066, 3066, 1627, 1605, 1593, 1579, 1570, 1497, 1458, 1449, 1334, 1161, 1104, 1074, 1049, 1029, 998, 816, 762, 697, 624 cm^{-1}. $[\alpha]^{20}_D$ = −14.2 (*c* 2.61, MeOH). Anal. Calcd for $C_{16}H_{17}NO_4 \cdot 1H_2O$: C, 65.05; H, 6.06; N, 4.79. Found: C, 65.31; H, 5.96; N, 4.67.

1β-(6-Aminopyridin-2-yl)-1-deoxy-D-ribofuranose (13h). Compound **13h** was prepared from **12h** (307 mg, 0.540 mmol) according to the general procedure in 90% yield as a colorless oil, which after lyophylization furnished white hygroscopic powder. HRMS (ESI) $C_{10}H_{15}N_2O_4$: [M + H] calcd 227.1026, found 227.1027. ^{1}H NMR (500 MHz, DMSO-d_6): 3.49 (dd, 1H, J_{gem} = 11.8 Hz, $J_{5'a,4'}$ = 4.4 Hz, H-5′a); 3.63 (dd, 1H, J_{gem} = 11.8 Hz, $J_{5'b,4'}$ = 3.1 Hz, H-5′b); 3.79 (ddd, 1H, $J_{4',3'}$ = 6.1 Hz, $J_{4',5'a}$ = 4.3 Hz, $J_{4',5'b}$ = 3.1 Hz, H-4′); 3.82 (dd, 1H, $J_{3',4'}$ = 6.1 Hz, $J_{3',2'}$ = 4.7 Hz, H-3′); 3.94 (t, 1H, $J_{2',1'} = J_{2',3'}$ = 4.4 Hz, H-2′); 4.47 (d, 1H, $J_{1',2'}$ = 4.2 Hz, H-1′); 4.80−5.20 (m, 3H, OH-2′,3′,5′); 5.89 (s, 2H, NH_2); 6.31 (dd, 1H, $J_{5,4}$ = 8.2 Hz, $J_{5,3}$ = 1.0 Hz, H-5); 6.61 (dm, 1H, $J_{3,4}$ = 7.2 Hz, H-3); 7.32 (dd, 1H, $J_{4,5}$ = 8.2 Hz, $J_{4,3}$ = 7.2 Hz, H-4). ^{13}C NMR (125.7 MHz, DMSO-d_6): 62.2 (CH_2-5′); 71.3 (CH-3′); 76.6 (CH-2′); 84.0 (CH-4′); 85.8 (CH-1′); 107.3 (CH-5); 109.3 (CH-3); 137.8 (CH-4); 159.0 (C-2); 159.4 (C-6). IR spectrum (KBr): 3432, 3366, 3230, 2000, 1628, 1607, 1576, 1471, 1339, 1106, 1082, 1046, 993, 795, 739 cm^{-1}. $[\alpha]^{20}_D$ = −43.5 (*c* 3.33, MeOH). Anal. Calcd for $C_{10}H_{14}N_2O_4 \cdot {}^1/_2\, H_2O$: C, 51.06; H, 6.43; N, 11.91. Found: C, 51.11; H, 6.31; N, 11.55.

For all other synthetic procedures and for complete characterization of all compounds, see the Supporting Information.

Single Crystal X-ray Structure Analysis. The diffraction data of single crystals of **13i** (colorless, 0.09 × 0.23 × 0.40 mm) and **5** (colorless, 0.21 × 0.32 × 0.51 mm) were collected on Xcalibur X-ray diffractometr with $Cu_{K\alpha}$ (λ = 1.54180 Å) at 150 and 298 K, respectively. Both structures were solved by direct methods with SIR92[27] and refined by full-matrix least-squares on *F* with CRYSTALS.[28] All hydrogen atoms were located in a difference map, but those attached to carbon atoms were repositioned geometrically and then refined with riding constraints, while all other atoms were refined anisotropically in both cases.

Crystal data for 5: $C_{30}H_{55}Br_2NO_6Si_3$, orthorhombic, space group $P2_12_12_1$, a = 10.8289(9) Å, b = 17.5540(19) Å, c = 21.7052(19) Å, V = 4126.0(7) Å^3, Z = 4, M = 769.82, 22646 reflections measured, 8654 independent reflections. Final R = 0.0481, wR = 0.0757, GoF = 1.1709 for 5600 reflections with $I > 2\sigma(I)$ and 381 parameters. CCDC 752141.

Crystal data for 13i: $C_{12}H_{18}N_2O_4$, orthorhombic, space group $P2_12_12_1$, a = 6.8208(3) Å, b = 9.0452(4) Å, c = 19.7411(9) Å, V = 1217.93(10) Å^3, Z = 4, M = 254.29, 11567 reflections measured, 2580 independent reflections. Final R = 0.0364, wR = 0.0453, GoF = 1.0933 for 2201 reflections with $I > 2\sigma(I)$ and 165 parameters. CCDC 752142.

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Supporting Information Available: Detailed description of unsuccessful approaches and lengthy optimizations, complete experimental procedures, CIF files for crystal structures, conformational analysis, and copies of the ^{1}H and ^{13}C NMR spectra of all new compounds. This material is available free of charge via the Internet at http://pubs.acs.org.

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