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Functionalization of 2*H*-1,2,3-Triazole *C*-Nucleoside Template via N^2 Selective Arylation

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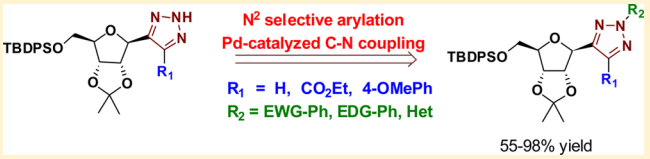
Supporting Information

ABSTRACT: *C*-Nucleosides are an underexplored and important class of nucleosides with antiviral and anticancer activity. In addition, triazole heterocycles are well employed as a strategy to modify nucleobase in nucleoside analogues, although rare examples were described for triazoyl *C*-nucleosides. N^2-Aryl-1,2,3-triazole *C*-nucleoside compounds that could be obtained by selective 1,2,3-triazole heterocycle N^2 arylation in 1-β-D-ribofuranosyl-2*H*-1,2,3-triazole substrate were designed in this study. The optimized condition used AdBrettPhos/$[PdCl(allyl)]_2$ as the catalyst system. This transformation was accomplished by aryl halides bearing an electron donor and withdrawing groups, as well as by heterocyclic halides in good to excellent yields. The transformation developed in this study represents a significant contribution to the nucleoside field, once it allows for the synthesis of unexplored scaffolds through selective functionalization of triazole nucleosides.



INTRODUCTION

Nucleosides are molecules ubiquitously present in living organisms, where they play important roles, like their phosphorylated derivatives (i.e., nucleotides), by working as secondary messengers and enzyme cofactors, besides acting in genetic information storage, transcription, and translation.[1] Such nucleotide-mediated processes make this compound class an important lead for drug development.[2] In fact, many nucleosides and nucleoside-derived compounds are found in clinics to treat cancer and viruses.[3] Among derivatives developed in the early years of nucleoside chemistry, there was the construction of triazole-derived nucleosides, such as ribavirin, a designed guanosine analogue bearing a 1,2,4-triazole.[2c,4] With the advent of the copper-catalyzed [3+2] cycloaddition between terminal acetylenes and azides, new interest in triazole nucleoside chemistry and biology arose.[4b] Through this methodology, synthesis of 1,4- and 1,4,5-substituted 1,2,3-triazole nucleosides has been reported (Figure 1).[5] Interest for 1,2,3-triazole nucleosides was also observed in the *C*-nucleoside class, which has a nonhydrolyzable anomeric bond and, consequently, is not susceptible to degradation by phosphorylases.[5−7] It was demonstrated that natural and synthetic *C*-nucleosides could have anticancer and antiviral properties.[7] More recently, the discovery of two synthetic antiviral *C*-nucleosides, BCX4430 and GS-6620, could indicate a renewed interest in this nucleoside class.[7] However, the use of such strategy in the 1,2,3-triazoyl nucleoside chemistry has been hampered by the lack of efficient methodology to introduce acetylene into the anomeric position.[8] Recently, two authors (Germain, L. N., and Uziel, J.) developed a stereoselective indium-mediated alkynylation reaction[9] that enabled *C*-triazole nucleosides synthesis.

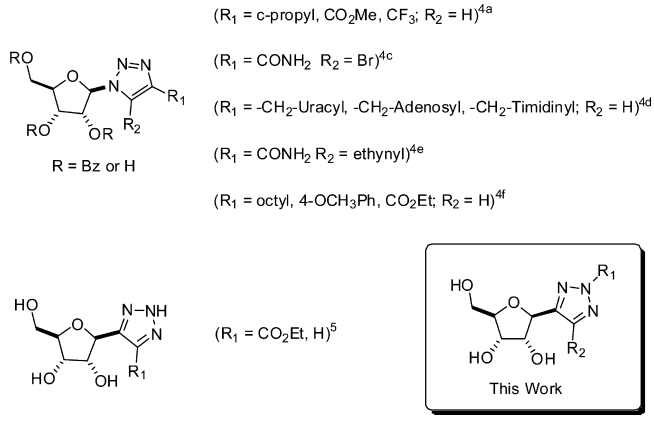


Figure 1. Different 1-β-D-ribofuranosyl-1,2,3-triazole scaffolds.

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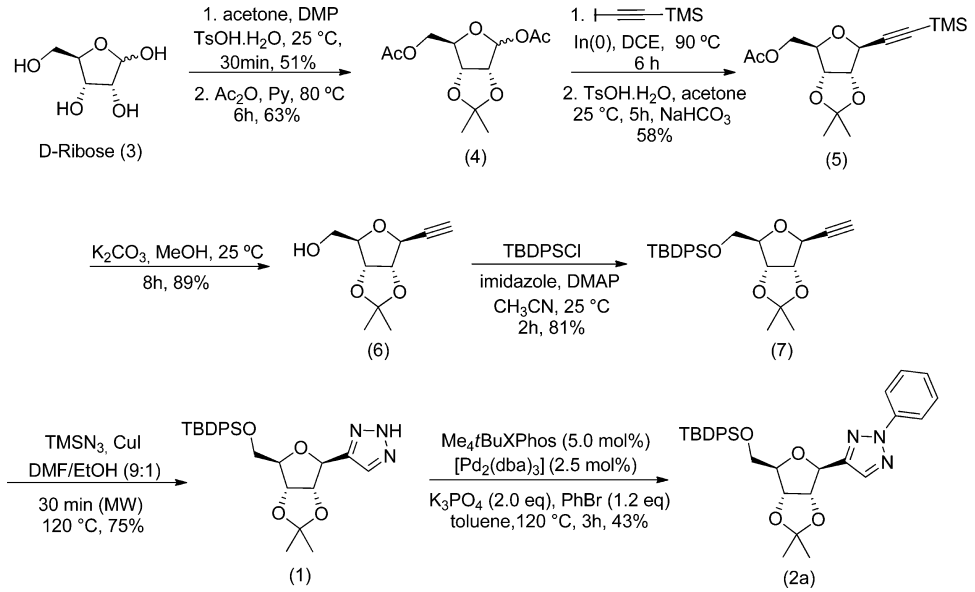
Scheme 1. 1-β-D-Ribofuranosyl-2*H*-1,2,3-triazole (1) Preparation and First Condition for N^2 Selective Arylation



Once synthetic nucleoside analogues' development is in continuous and intense research due to their potential biological activity, search for unreported scaffolds is highly desirable. With this in mind, and with an appropriate methodology to reach *C*-triazole nucleosides, it was decided in this study to explore scaffolds based on 1,2,3-triazole aglycone N^2 functionalization (Figure 1). Its introduction into the nucleosides is unprecedented and would lead to potentially active nucleosides. Very few reports on selective arylation of 1,2,3-triazole N^2 position are reported.[10] Liu and co-workers described copper catalysis use on this transformation with the use of 4,5-disubstituted 2*H*-1,2,3-triazoles, which lead to N^2-substituted 1,2,3-triazoles.[10c] More recently, a palladium-catalyzed 2*H*-1,2,3-triazole N^2 regioselective arylation was reported by Buchwald and co-workers.[6] However, in both cases, only model compounds were described. Such lack of background on 2*H*-1,2,3-triazole N^2 arylation, embedded in polyfunctional compounds, makes the synthesis of desired nucleoside skeletons a challenge. In this Article, achievements on 2*H*-1,2,3-triazole *C*-nucleosides N^2 arylation reaction are reported.

RESULTS AND DISCUSSION

1-β-D-Ribofuranosyl-2*H*-1,2,3-triazole (**1**) was synthesized according to Scheme 1. For such, D-ribose (**3**) was protected as the corresponding isopropylidene acetal at the 2,3 positions, followed by the acetylation of the remaining hydroxyls. Indium mediated alkynylation with 1-iodo-2-(trimethylsilyl)acetylene[9] furnished the desired β-ribosyl acetylene **5**. Acetylene **7** was used in a copper-catalyzed [3+2] cycloaddition with azido-trimethylsilane, leading to the desired ribosyl triazole **1**. For the envisaged and selective N^2 arylation of **1**, the catalyst system reported by Buchwald (L1 (Me_4*t*BuXPhos)/$Pd_2(dba)_3$)[6] was used as the starting point. When the reaction was carried out with the 5′ position protected as an acetate, partial hydrolysis was observed in crude reaction mixture NMR analysis. The attention in this study then was turned to the use of a more resistant protecting group, such as TBDPS. With this group, the reaction of **1** with bromobenzene led to the isolation of a single product (**2a**) in 43% yield.

The assignment of this product as the desired N^2 arylated nucleoside **2a** was done with the aid of NMR spectroscopy. For such, the 1,4- (**8a**) and 1,5- (**8b**) regioisomers were synthesized separately, and their NMR data were collected. Data were then compared to those of the **2a** compound, obtained under Buchwald conditions.

Important differences could be observed concerning carbohydrate core chemical shifts and aromatic signals of the different regioisomers in ^{1}H NMR spectra, especially in protons adjacent to the nitrogen-bonded carbon in the aromatic ring. While these protons are at 7.55−7.58 and 7.61−7.63 ppm, respectively, for the 1,4- (**8a**) and 1,5- (**8b**) regioisomers, these protons are located at 8.01−8.04 ppm (Figure 2) in the 2,4-regioisomer.

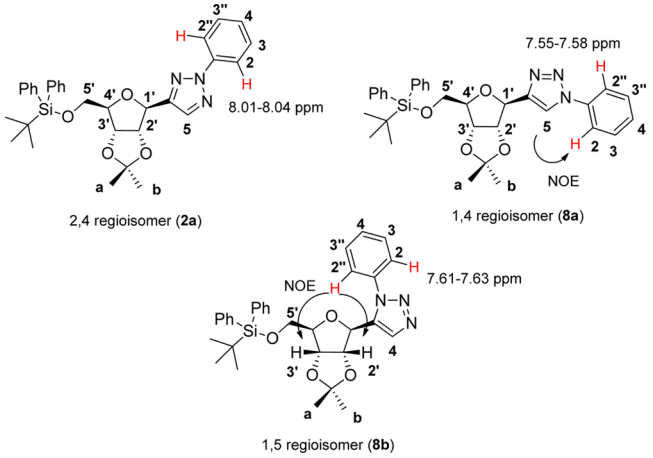


Figure 2. NOESY correlations and ^{1}H NMR chemical shifts of $H_{2/2''}$ of 1,4-, 2,4-, and 1,5 -triazole *C*-nucleoside regioisomers.

Such deshielding has already been observed for N^2-bonded aryl groups protons in 1,2,3-triazoles.[6] Further evidence can be obtained through analysis of their NOESY spectra (see the Supporting Information). In the case of the 1,4- regioisomer, correlations can be observed between triazole ring H_5 and protons adjacent to the aryl ring nitrogen-bonded carbon

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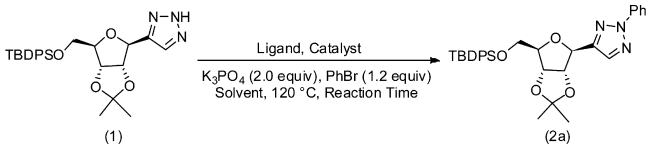
Table 1. Screening Reaction Conditions for N^2 Selective Arylation of 1

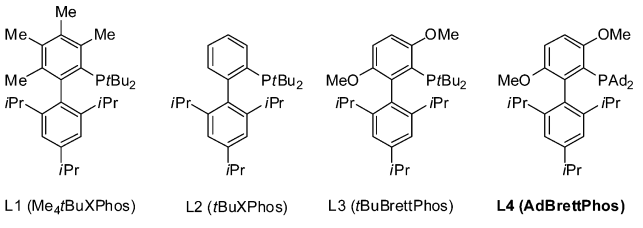


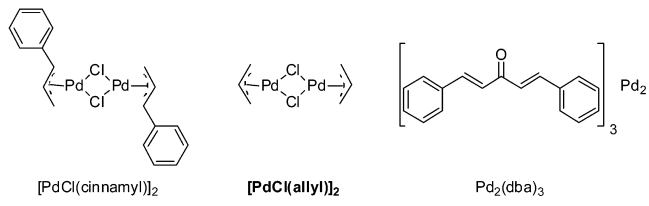
entry	ligand[a]	catalyst[a]	solvent	time (h)	yield (%)[c,d]
1	Me_4*t*BuXPhos	$Pd_2(dba)_3$	toluene	3	43
2	*t*BuXPhos	$Pd_2(dba)_3$	toluene	3	nr
3	*t*BuBrettPhos	$Pd_2(dba)_3$	toluene	3	traces
4	AdBrettPhos	$Pd_2(dba)_3$	toluene	3	73
5	AdBrettPhos	$Pd_2(dba)_3$	toluene	5	71(66)[c]
6	AdBrettPhos	$[PdCl(cinnamyl)]_2$	toluene	5	14
7	AdBrettPhos	$[PdCl(allyl)]_2$	toluene	5	89(81)[c]
8	AdBrettPhos	$[PdCl(allyl)]_2$	dioxane	5	83(86)[c]
9	AdBrettPhos	$[PdCl(allyl)]_2$	MeTHF	5	89 (87)[c]
10	AdBrettPhos[b]	$[PdCl(allyl)]_2$[b]	toluene	10	84(82)[c]

[a]5.0 mol % ligand and 2.5 mol % catalyst. [b]3.0 mol % ligand and 1.5 mol % catalyst. [c]Yields refer to isolated, chromatographically purified materials. [d]Yields were determined by ^{1}H NMR experiments, using diiodomethane as an internal standard; nr: no reaction.

(Figure 2). Concerning the 2,4- and 1,5- regioisomers, the previously described correlation is absent (Figure 2). However, for the 1,5- regioisomer, correlation between ribosyl ring $H_{2'}$ and $H_{3'}$ and protons adjacent to the aryl ring nitrogen-bonded carbon was observed (Figure 2). Additionally, regarding the regioisomers' ^{13}C NMR spectra, triazole ring C_5 carbon can be used to distinguish between 1,4- and 1,5- regioisomers.[11] As was previously reported in the literature, chemical shift of this carbon is observed in the 119−123 ppm range for the 1,4-regioisomer, while this carbon is observed in the 133−136 ppm range in the case of 1,5- regioisomer. In fact, chemical shifts observed for C_5 were 120.2, 132.7, and 134.2 ppm for 1,4-, 1,5-, and 2,4- regioisomers, respectively.

With methodology to distinguish between the different regioisomers resulting from **1** arylation, yield optimization of this reaction proceeded by analyzing the influence of different reaction conditions. These results are summarized in Table 1.





As depicted in Table 1, the catalyst system previously reported in the literature ($L1/Pd_2(dba)_3$) only provided moderated yield. Other L2−L4 biaryl phosphine ligands were examined with $Pd_2(dba)_3$, in which only L4 increased yield, up to 73% (entry 4, Table 1).[12] Substitution of palladium catalyst from $Pd_2(dba)_3$ to $[PdCl(allyl)]_2$ associated with L4 gave a further yield increase, up to 89% (entry 7, Table 1). However, combination between L4 and $[PdCl(cinnamyl)]_2$ did not lead to good results (entry 6, Table 1). Concerning the solvent, only a small yield impact was observed by changing toluene for dioxane or MeTHF (Table 1, entries 8 and 9, respectively). The best yields observed using a more steric demanding ligand, such as AdBrettPhos under reaction conditions, can be used, as previously proposed,[12,13] in a more favorable reductive elimination with these complexes.

The optimized conditions developed in Table 1 were subsequently evaluated according to the aromatic halide structure. As depicted in Table 2, the reaction conditions developed are effective for aryl and heteroaryl groups cross-coupling, except for *ortho*-substituted electrophiles and 2-bromopyridine. Only one product was observed by HPLC analyses in the crude reaction mixture. After isolation and characterization by NMR, all new products corresponded to N^2-arylated products. Both electron donor and electron-withdrawing groups are well tolerated. Electron-poor heteroarenes, such as pyridine and pyrimidine, gave excellent yields. Some failure reactions were supposed to be caused by halide reduction. These assumptions were made by crude reaction mixture HPLC analyses at the end of each reaction. Regarding the entries 4, 8, and 14, it was observed that the 2*H*-1,2,3-triazole substrate remained in the reaction mixture, but aryl halides have disappeared. It suggests that oxidative addition occurred, but the aryl halide was reduced; that is, reductive elimination was inefficient or the catalyst was decomposed.[14] On the other hand, the aryl halide was found at the end of the reaction with 2*H*-1,2,3-triazole substrate for entry 11, and only 8% of conversion was obtained. Low reaction rate is a possibility for low conversion.

In entries 5 and 6, it was verified that the employed reaction condition gave better conversion with 4-iodo-anisole than with 4-bromo-anisole. This result seems surprising, but it was supposed that it could be associated with AdBrettPhos use in toluene. Aryl iodides do not afford good yields like aryl bromides and aryl chlorides in the C−N cross-coupling reaction. There are two factors that contribute to aryl iodide inefficiency, as follows: formation of unreactive Pd dimers bridged by iodide anions and iodide salts inhibitory effect.[15,16] Use of some biaryl phosphine ligands, like BrettPhos (for primary amines) and RuPhos (for secondary amines) in aryl and heteroaryl iodides amination, in nonpolar solvents, such as

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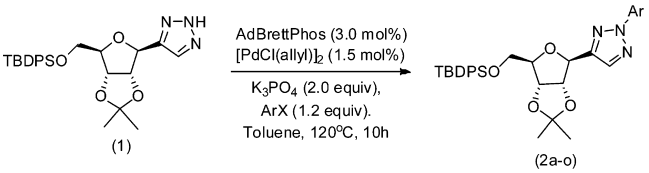
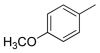
Table 2. Scope of N^2 Selective Arylation of 1[e]



Entry	Ar	X	Product	Yield (%)[a, b]
1		Br,	2a	82
2		OTf	2a	55
3		Br	2b	70
4		Br	2c	n.r
5		Br	2d	55
6		I	2d	85
7		I	2e	71
8		I	2f	n.r
9		Br	2g	89
10		Br	2h	85
11		Br	2i	n.d[c]
12		Br	2j	98
13		Br	2k	98
14		Br	2l	n.r
15[d]		Br	2m	83
16		Br	2n	76
17		Br	2o	70

[a]Yields refer to isolated, chromatographically purified materials. [b]Unpublished products were fully characterized by NMR and HRMS data. [c]8% conversion was observed in the HPLC; however, no product was isolated. [d]Method B; nr, no reaction; nd, not determined. [e]Reaction conditions: $[PdCl(allyl)]_2$ (1.5 mol %), AdBrettPhos (3.0 mol %), K_3PO_4 (2.0 equiv), ArBr (1.2 equiv), toluene, 120 °C, 10 h (method A); $Pd_2(dba)_3$ (1.5 mol %), AdBrettPhos (3.0 mol %), K_3PO_4 (2.0 equiv), ArBr (1.2 equiv), toluene, 120 °C, 10 h (method B).

toluene, gave yields similar to those obtained with aryl bromides. Both ligands produce monomeric oxidative addition complexes in solution, allowing for aryl iodides amination to be accomplished. Nonpolar solvent success is explained by iodide salts poor solubility.

To evaluate the possibility of N^2-selective arylation being performed by a SNAr mechanism, some reactions were run with electron-poor substrates, such as 4-bromopyridine and 4-bromobenzonitrile, in the absence of palladium. No reaction was observed.

To further expand the structural diversity of this new nucleosides library, 4,5-disubstituted-2*H*-1,2,3-triazole systems' *N*-arylation was also evaluated. The carboxylic ester derivative **12** was prepared from de ribofuranosyl intermediate **4** via an alkynylation step with ethyl 3-iodopropiolate mediated by indium. The ribofuranosyl propiolate derivative (**9**) obtained was then submitted to cycloaddition reaction with azidotrimethylsilane, obtaining ribosyl-2*H*-1,2,3-triazole **10**. A two-reaction sequence, C-5′ ribosyl ring hydroxyl group deprotection and protection, provided the desired carboxylic ester **12** (Scheme 2).

Preparation of 5-aryl-2*H*-1,2,3-triazole **14** was performed via a Suzuki–Miyaura cross-coupling (SMCC) reaction from the readily available bromo derivative **13** (Scheme 3). The key to the success of this SMCC reaction was the use of CataCxium (Ad_2n-BuP) ligand in combination with $Pd(OAc)_2$. This catalyst system was previously reported by Tan et al. for unprotected haloimidazoles SMCC.[17] *N*-Arylation reaction results are given in Table 3.

With ($[PdCl(allyl)_2]$, AdBrettPhos, K_3PO_4) optimal conditions, the 4,5-disubstituted-2*H*-1,2,3-triazole derivatives **12** and **14** can be coupled efficiently to phenyl and 4-pyridyl bromides, furnishing the desired products in good to excellent yields.

In this effort to obtain a fully deprotected 2-aryl-1,2,3-triazoyl-*C*-nucleoside, compound **2a** deprotection was investigated as an illustrative example. As expected, **2a** deprotection was efficiently performed in a two-step reaction using TBAF/CsF and TFA, respectively, providing **17** in quantitative yield (Scheme 4).

In conclusion, new nucleoside scaffold N^2-aryl-1,2,3-triazoyl ribonucleosides were synthesized through the development of a catalyst system based on the AdBrettPhos biaryl phosphine ligand and the $[PdCl(allyl)]_2$ catalyst. Mono- and disubstituted 1,2,3-triazoylribofuranoside N^2 selective arylation could be carried out with aryl halides bearing electron donor and -withdrawing groups, as well as with heterocyclic halides, in good to excellent yields.

EXPERIMENTAL SECTION

General Information. Chemicals and solvents were purchased from commercial sources and used without further purification. Thin layer chromatography was performed on silica gel plates; spots were detected under UV-light or by spraying with 5% H_2SO_4 solution in ethanol. Flash chromatography was performed with silica gel 60, 40–63 μm. ^1H and ^{13}C NMR spectra were recorded on 300, 400, and 500 MHz apparatuses. Microwave irradiation was performed in a Biotage Initiator EXP. HPLC analyses were performed using a C18 3.5 μm, 4.6*50 mm column. High-resolution mass spectra were obtained using a TOF-MS with ESI source.

1,5-Di-O-acetyl-2,3-O-isopropylidene-D-ribofuranose (4).[18] To a suspension of D-ribose (5.0 g, 33.30 mmol) in dry acetone (40 mL) were added 2,2-dimethoxypropane (20 mL, 17.3 g, 166.52 mmol) and *p*-toluenesulfonic acid monohydrate (127 mg, 2 mol %). After being stirred at room temperature for 30 min, the clear resulting mixture was neutralized with $NaHCO_3$, filtered through Celite, and concentrated under reduced pressure. The residue was purified by flash column

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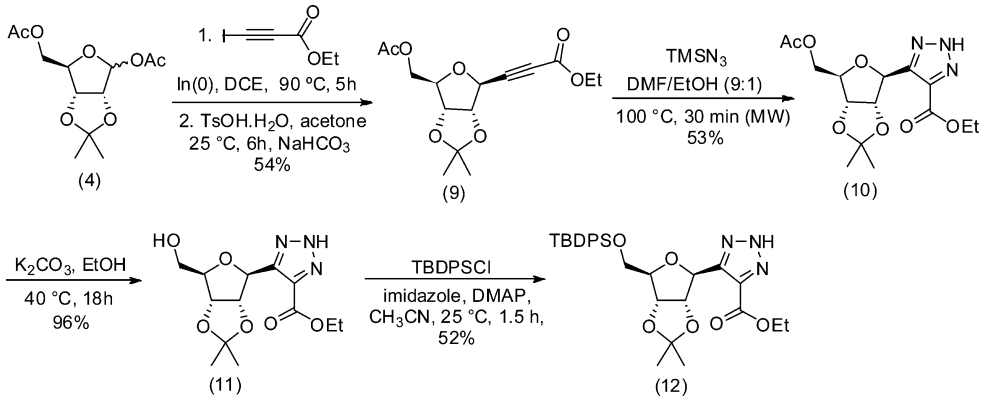
Scheme 2. Synthesis of Ethyl 5-(1-β-D-Ribofuranosyl)-2*H*-1,2,3-triazole-4-carboxylate (12)



Scheme 3. Synthesis of 4-(1-β-D-Ribofuranosyl)-5-(4-methoxyphenyl)-2*H*-1,2,3-triazole (14)

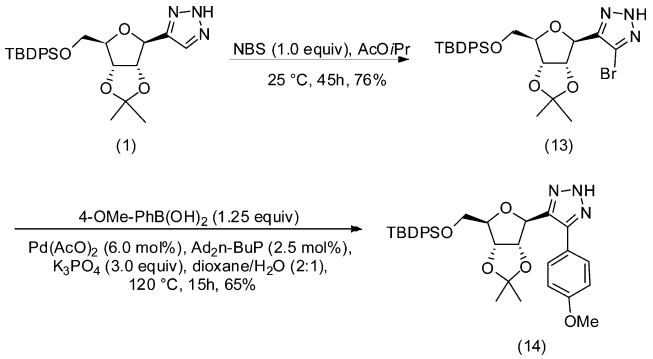
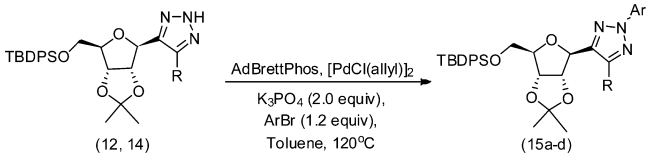


Table 3. 4,5-Disubstituted-2*H*-1,2,3-triazole Substrate N² Selective Arylation



Entry	Ar	R[c]	Product	Yield (%)[d,e]
1[a]		CO_2Et	15a	73
2[a]		CO_2Et	15b	84
3[b]		4-OMePh	15c	93
4[b]		4-OMePh	15d	88

[a]Reactions conditions: $[PdCl(allyl)]_2$ (3.0 mol %), AdBrettPhos (6.0 mol %), K_3PO_4 (2.0 equiv), ArBr (1.2 equiv), toluene, 120 °C, 10 h. [b]Reaction conditions: $[PdCl(allyl)]_2$ (1.5 mol %), AdBrettPhos (3.0 mol %), K_3PO_4 (2.0 equiv), ArBr (1.2 equiv), toluene, 120 °C, 23 h. [c]R = CO_2Et (**12**), R = 4-OMePh (**14**). [d]Yields refer to isolated, chromatographically purified materials. [e]Unpublished products were fully characterized by NMR and HRMS data.

chromatography on silica gel (cyclohexane/AcOEt 9:1 to 7:3) to afford the desired acetal as a colorless oil (3200 mg, 51%) (α:β = 1.6:10). ^1H (500 MHz, $CDCl_3$): δ ppm 1.30 (s, 3H), 1.46 (s, 3H), 3.68−3.72 (m, 2H), 4.01 (br s, 1H), 4.37 (s, 1H), 4.55 (d, *J* = 5.9 Hz, 1H), 4.80 (d, *J* = 5.9 Hz, 1H), 5.31 (d, *J* = 6.2 Hz, 1H), 5.38 (d, *J* = 6.3 Hz, 1H). ^{13}C (125 MHz, $CDCl_3$): δ ppm 24.8, 26.4, 63.6, 81.8, 86.9, 87.8, 102.9, 112.3. A suspension of the previously prepared acetal (2,3-isopropylidene-D-ribofuranose (3.2 g, 16.82 mmol)) in pyridine (15.0 mL, 14.6 g, 185.08 mmol) at 0 °C was treated with acetic anydride (8.0 mL, 8.6 g, 84.13 mmol). The temperature was raised to 80 °C, and the reaction was stirred for 6 h. The reaction mixture was coevaporated with toluene to remove pyridine. The residue was taken up in ethyl acetate (20 mL), and washed with 10% HCl solution (1 × 10 mL) and water (2 × 10 mL). The organic phase was dried over anhydrous sodium sulfate, filtered, and evaporated. The oil obtained was purified by flash column chromatography on silica gel (petroleum ether/AcOEt 4:1) to afford **4** as a colorless oil (2900 mg, 63%). ^1H (500 MHz, $CDCl_3$): δ ppm 1.32 (s, 3H), 1.48 (s, 3H), 2.04 (s, 3H), 2.08 (s, 3H), 4.07−4.14 (m, 2H), 4.45 (t, *J* = 7.0 Hz, 1H), 4.70 (s, 2H), 6.20 (s, 1H). ^{13}C (125 MHz, $CDCl_3$): δ ppm 20.9, 21.3, 25.2, 26.5, 64.2, 81.7, 85.2, 85.4, 102.2, 113.4, 169.4, 170.6.

*1-Trimethylsilylethynyl-5-O-acetyl-2,3-O-isopropylidene-β-D-ribofuranose (**5**).*[9] A suspension of indium (In^0) (0.75 g, 6.56 mmol) in anhydrous 1,2-dichloroethane (10 mL) under argon was stirred during 20 min at room temperature. Further, 1-iodo-2-trimethylsilylacetylene (1.2 g, 5.47 mmol) and the ribofuranoside **4** (0.75 g, 2.73 mmol) were added into the reaction tube that was sealed and then evacuated and backfilled with argon (this process was repeated a total of three times). The reaction mixture was stirred during 6 h at 90 °C. The mixture was filtered over Celite and evaporated. The crude residue was taken in anhydrous acetone (4 mL) and treated with *p*-toluenesulfonic acid monohydrate (16 mg, 3 mol %). After being stirred at room temperature for 5 h, the mixture was neutralized with $NaHCO_3$, filtered through Celite, and concentrated under reduced pressure. The crude residue obtained was purified by flash column chromatography on silica gel (cyclohexane/AcOEt 3:1) to give **5** as a yellow oil (431 mg, 58%). ^1H (400 MHz, $CDCl_3$): δ ppm 0.15 (s, 9H), 1.33 (s, 3H), 1.50 (s, 3H), 2.09 (s, 3H), 4.19 (dd, *J* = 5.1, 9.8 Hz, 1H), 4.23−4.27 (m, 1H), 4.30 (dd, *J* = 5.6, 9.8 Hz, 1H), 4.67 (dd, *J* = 2.2, 6.2 Hz, 2H), 4.80 (dd, *J* = 2.2, 6.1 Hz, 1H). ^{13}C (100 MHz, $CDCl_3$): δ ppm −0.26, 20.9, 25.4, 26.9, 63.9, 75.2, 82.9, 83.7, 86.5, 92.8, 102.7, 114.0, 170.7.

*1-Ethynyl-2,3-O-isopropylidene-β-D-ribofuranose (**6**).* To a solution of **5** (1.2 g, 3.87 mmol) in methanol (12 mL) was added potassium carbonate (0.8 g, 5.81 mmol). The mixture was stirred at room temperature for 8 h. The reaction mixture was concentrated, and the residue was taken in water (5 mL) and acidified with acetic acid to pH 5−6. The water phase was extracted with acetyl acetate (2 × 15 mL), dried over anhydrous sodium sulfate, filtered, and concentrated under reduced pressure. Heptane was used to remove the excess of acetic acid. The yellow oil obtained was purified by flash column chromatography on silica gel (heptane/AcOEt 9:1 to 7:3) to give **6** as a colorless oil (680 mg, 89%). ^1H (400 MHz, $CDCl_3$): δ ppm 1.33 (s, 3H), 1.51 (s, 3H), 2.12 (br s, 1H), 2.60 (d, *J* = 2.3 Hz, 1H), 3.75−3.76 (m, 2H), 4.19−4.22 (m, 1H), 4.68 (t, *J* = 2.5 Hz, 1H), 4.74 (dd, *J* = 2.2, 6.3 Hz, 1H), 4.81 (dd, *J* = 2.7, 6.2 Hz, 1H). ^{13}C (100 MHz, $CDCl_3$): δ ppm 25.3, 27.0, 62.9, 74.8, 75.6, 81.7, 82.3, 86.6, 86.7, 113.9.

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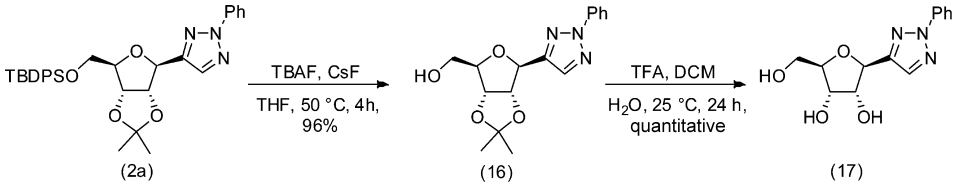
Scheme 4. Full Deprotection of 2-Aryl-1,2,3-triazoyl-*C*-nucleoside Derivative 2a



*1-Ethynyl-5-O-(tert-butyldiphenylsilyl)-2,3-O-isopropylidene-β-D-ribofuranose (**7**).* To a solution of **6** (0.68 g, 3.43 mmol) in anhydrous acetonitrile (12 mL) were added imidazole (0.30 g, 4.46 mmol), 4-(dimethylamino)-pyridine (0.46 g, 3.77 mmol), and *tert*-butyldiphenylchlorosilane (0.94 g, 0.9 mL, 3.43 mmol). The mixture was stirred at room temperature for 2 h, and then it was concentrated. The residue was taken in ethyl acetate (20 mL) and washed with a saturated solution of sodium bicarbonate (1 × 10 mL). The water phase was extracted with ethyl acetate (1 × 10 mL). The combined organic phases were dried over anhydrous sodium sulfate, filtered, and evaporated. The crude residue was purified by flash column chromatography on silica gel (heptane 100% to heptane/AcOEt 9.5:0.5) to give **7** as a colorless oil (1.220 mg, 81%). ^{1}H (400 MHz, $CDCl_3$): δ ppm 1.08 (s, 9H), 1.34 (s, 3H), 1.53 (s, 3H), 2.42 (d, J = 2.3 Hz, 1H), 3.78−3.84 (m, 2H), 4.20−4.23 (m, 1H), 4.62 (t, J = 2.6 Hz, 1H), 4.76 (dd, J = 2.9, 6.2 Hz, 1H), 4.80 (dd, J = 1.9, 6.2 Hz, 1H), 7.37−7.45 (m, 6H), 7.67−7.71 (m, 4H). ^{13}C (125 MHz, $CDCl_3$): δ ppm 19.4, 25.5, 27.0, 27.2, 63.7, 74.6, 75.1, 81.7, 82.9, 86.2, 86.4, 113.7, 127.8, 127.9, 129.88, 129.91, 133.3, 133.4, 135.78, 135.84. HRMS-ESI: m/z $[M + Na]^+$ calcd for $C_{26}H_{32}O_4SiNa^+$, 459.1968; found, 459.1960.

*4-(5-O-(tert-Butyldiphenylsilyl)-2,3-O-isopropylidene-β-D-ribosyl)-2H-1,2,3-triazole (**1**).* To a solution of compound **7** (0.69 g, 1.58 mmol) in *N*,*N*-dimethylformamide (12 mL) and ethanol (1.4 mL) were added copper(I) iodide (0.045g, 0.237 mmol) and azidotrimethylsilane (0.36 g, 0.42 mL, 3.16 mmol). The mixture was stirred for 1 min under vacuum/argon in a sealed tube and placed into a microwave apparatus at 120 °C for 30 min. The mixture was filtered over Celite and concentrated. The residue was taken in ethanol and purified with activated carbon. After evaporation of the solvent, the residue was purified by flash column chromatography (heptane/AcOEt 9:1 to 8.5:1.5) to give compound **1** as a colorless oil (566 mg, 75%). Care should be taken because the reaction releases gas. ^{1}H (400 MHz, $CDCl_3$): δ ppm 1.03 (s, 9H), 1.38 (s, 3H), 1.61 (s, 3H), 3.78 (d, J = 4.4 Hz, 1H), 4.26 (dd, J = 3.3, 4.3 Hz, 1H), 4.81 (dd, J = 3.2, 6.5 Hz, 1H), 4.89 (dd, J = 4.8, 6.5 Hz, 1H), 5.13 (d, J = 4.6 Hz, 1H), 7.33−744 (m, 6H), 7.63−7.66 (m, 4H), 7.68 (br s, 1H). ^{13}C (100 MHz, $CDCl_3$): δ ppm 19.4, 25.6, 26.9, 27.6, 64.1, 79.3, 82.2, 85.26, 85.30, 114.6, 127.88, 127.91, 129.95, 129.98, 133.2, 133.3, 135.8. HRMS- ESI: m/z $[M + H]^+$ calcd for $C_{26}H_{33}N_3O_4SiH^+$, 480.2319; found, 480.2311.

General Procedure for the N^2 Arylation of 1-β-D-Ribosyl-1,2,3-triazoles (Method A). To an oven-dried tube were added $[PdCl(allyl)]_2$ and AdBrettPhos. The tube was sealed, toluene (one-half of the total volume) was added via syringe, and then the tube was evacuated and backfilled with argon (this process was repeated a total of three times). The resulting brown mixture was stirred at 120 °C for 2 min; at this point, the color of the mixture turned dark brown. A second oven-dried tube was charged with 1,2,3-triazole derivative, K_3PO_4 (2.0 equiv), and aryl halides (1.2 equiv). The tube was sealed, toluene (one-half of the total volume) was added via syringe, and the mixture was evacuated and backfilled with argon (this process was repeated a total of three times). The premixed catalyst solution was added via syringe to the tube containing 1,2,3-triazole, aryl halide, and base. The reaction mixture was stirred at 120 °C for 10−23 h. The reaction was cooled to room temperature, concentrated under reduced pressure, and purified by flash column chromatography on silica gel (heptane/AcOEt) to afford pure products.

General Procedure for the N^2 Arylation of 1-β-D-Ribosyl-1,2,3-triazoles (Method B). To an oven-dried tube were added $Pd_2(dba)_3$ and AdBrettPhos. The tube was sealed, toluene (one-half of the total volume) was added via syringe, and then the tube was evacuated and backfilled with argon (this process was repeated a total of three times). The resulting brown mixture was stirred at 120 °C for 2 min; at this point, the color of the mixture turned dark brown. A second oven-dried tube was charged with 1,2,3-triazole derivative, K_3PO_4 (2.0 equiv), and aryl halides (1.2 equiv). The tube was sealed, toluene (one-half of the total volume) was added via syringe, and the mixture was evacuated and backfilled with argon (this process was repeated a total of three times). The premixed catalyst solution was added via syringe to the tube containing 1,2,3-triazole, aryl halide, and base. The reaction mixture was stirred at 120 °C for 10 h. The reaction was cooled to room temperature, concentrated under reduced pressure, and purified by flash column chromatography on silica gel (heptane/AcOEt) to afford pure products.

*2-(Phenyl)-4-(2,3-isopropylidene-5-tert-butyldiphenylsilyl-β-D-ribosyl)-1,2,3-triazole (**2a**).* Following the general procedure for *N*-arylation of 1-β-D-ribosyl-1,2,3-triazoles (method A), a mixture of bromobenzene (6.6 μL, 0.0625 mmol), 1,2,3-triazole derivative **1** (25.0 mg, 0.0521 mmol), K_3PO_4 (22.1 mg, 0.104 mmol), $[PdCl(allyl)_2]$ (0.292 mg, 0.000782 mmol), and L4 (1.00 mg, 0.00156 mmol) in toluene (0.38 mL) was stirred at 120 °C for 10 h. The crude was purified by flash column chromatography on silica gel (heptane/AcOEt 8.5:1.5) to afford a yellow oil (23.8 mg, 82%). ^{1}H NMR (400 MHz, $CDCl_3$): δ ppm 1.03 (s, 9H), 1.41 (s, 3H), 1.63 (s, 3H), 3.78 (d, J = 4.4 Hz, 2H), 4.28 (dd, J = 3.2, 4.3 Hz, 1H), 4.87 (dd, J = 3.1, 6.5 Hz, 1H), 5.02 (dd, J = 4.6, 6.5 Hz, 1H), 5.16 (d, J = 4.6 Hz, 1H), 7.30−7.40 (m, 7H), 7.43−7.47 (m, 2H), 7.63−7.65 (m, 4H), 7.77 (s, 1H), 8.01−8.04 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): δ ppm 19.4, 25.7, 26.9, 27.6, 64.1, 79.7, 82.4, 85.2, 85.4, 114.5, 119.1, 127.6, 127.8, 127.9, 129.3, 129.88, 129.92, 133.2, 133.4, 134.2, 135.7, 135.8, 139.9, 148.7. HRMS-ESI: m/z $[M + H]^+$ calcd for $C_{32}H_{37}N_3O_4SiH^+$, 556.2632; found, 556.2620.

*2-(4-Toluil)-4-(2,3-isopropylidene-5-tert-butyldiphenylsilyl-β-D-ribosyl)-1,2,3-triazole (**2b**).* Following the general procedure for *N*-arylation of 1-β-D-ribosyl-1,2,3-triazoles (method A), a mixture of 4-bromotoluene (9.2 μL, 0.0751 mmol), 1,2,3-triazole derivative **1** (30.0 mg, 0.0625 mmol), K_3PO_4 (26.5 mg, 0.125 mmol), $[PdCl(allyl)_2]$ (0.350 mg, 0.000938 mmol), and L4 (1.20 mg, 0.00188 mmol) in toluene (0.45 mL) was stirred at 120 °C for 10 h. The crude was purified by flash column chromatography on silica gel (heptane/AcOEt 9:1) to afford a colorless oil (25.0 mg, 70%). ^{1}H NMR (400 MHz, $CDCl_3$): δ ppm 1.03 (s, 9H), 1.40 (s, 3H), 1.62 (s, 3H), 2.40 (s, 3H), 3.79 (d, J = 4.4 Hz, 2H), 4.27 (dd, J = 3.2, 4.3 Hz, 1H), 4.86 (dd, J = 3.1, 6.5 Hz, 1H), 5.01 (dd, J = 4.6, 6.5 Hz, 1H), 5.15 (d, J = 4.6 Hz, 1H), 7.25 (d, J = 8.6 Hz, 2H), 7.30−7.42 (m, 6H), 7.64−7.66 (m, 4H), 7.74 (s, 1H), 7.90 (dt, J = 2.4, 8.5 Hz, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): δ ppm 19.4, 21.2, 25.7, 26.9, 27.6, 64.1, 79.6, 82.4, 85.2, 85.4, 114.5, 119.0, 127.8, 127.9, 129.8, 129.9, 129.9, 133.2, 133.4, 133.9, 135.7, 135.8, 137.5, 137.8, 148.3. HRMS-ESI: m/z $[M + H]^+$ calcd for $C_{33}H_{39}N_3O_4SiH^+$, 570.2788; found, 570.2785.

*2-(4-Methoxyphenyl)-4-(2,3-isopropylidene-5-tert-butyldiphenylsilyl-β-D-ribosyl)-1,2,3-triazole (**2d**).* Following the general procedure for *N*-arylation of 1-β-D-ribosyl-1,2,3-triazoles (method A), a mixture of 4-iodoanisole (17.6 mg, 0.0751 mmol), 1,2,3-triazole derivative **1** (30.0 mg, 0.0625 mmol), K_3PO_4 (26.5 mg, 0.125 mmol), $[PdCl(allyl)_2]$ (0.350 mg, 0.000938 mmol), and L4 (1.20 mg, 0.00188 mmol) in toluene (0.45 mL) was stirred at 120 °C for 10 h. The crude was purified by flash column chromatography on silica gel (heptane/AcOEt 9.5:0.5 to 9:1) to afford a colorless oil (31.0 mg, 85%). ^{1}H NMR (400 MHz, $CDCl_3$): δ ppm 1.03 (s, 9H), 1.40 (s, 3H), 1.62 (s, 3H), 3.78 (d, J = 4.4 Hz, 2H), 3.86 (s, 3H), 4.27 (dd, J = 3.2, 4.3 Hz,

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1H), 4.85 (dd, J = 3.1, 6.5 Hz, 1H), 5.00 (dd, J = 4.7, 6.5 Hz, 1H), 5.14 (d, J = 4.6 Hz, 1H), 6.96 (dt, J = 3.3, 9.2 Hz, 2H), 7.30−7.42 (m, 6H), 7.63−7.65 (m, 4H), 7.72 (s, 1H), 7.93 (dt, J = 3.3, 9.2 Hz, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): δ ppm 19.4, 25.7, 26.9, 27.6, 55.7, 64.1, 79.6, 82.4, 85.2, 85.4, 114.4, 114.5, 120.6, 127.8, 127.9, 129.88, 129.92, 133.3, 133.4, 133.7, 133.8, 135.75, 135.77, 148.2, 159.2. HRMS-ESI: m/z $[M + H]^+$ calcd for $C_{33}H_{39}N_3O_5SiH^+$, 586.2737; found, 586.2731.

*2-(3-Methoxyphenyl)-4-(2,3-isopropylidene-5-tert-butyldiphenylsilyl-β-D-ribosyl)-1,2,3-triazole (**2e**).* Following the general procedure for *N*-arylation of 1-β-D-ribosyl-1,2,3-triazoles (method A), a mixture of 3-iodoanisole (17.6 mg, 9.0 μL, 0.0751 mmol), 1,2,3-triazole derivative **1** (30.0 mg, 0.0625 mmol), K_3PO_4 (26.5 mg, 0.125 mmol), $[PdCl(allyl)_2]$ (0.350 mg, 0.000938 mmol), and L4 (1.20 mg, 0.00188 mmol) in toluene (0.45 mL) was stirred at 120 °C for 10 h. The crude was purified by flash column chromatography on silica gel (heptane/AcOEt 9.5:0.5 to 9:1) to afford a colorless oil (26.0 mg, 71%). ^{1}H NMR (400 MHz, $CDCl_3$): δ ppm 1.03 (s, 9H), 1.41 (s, 3H), 1.63 (s, 3H), 3.78 (d, J = 4.4 Hz, 2H), 3.87 (s, 3H), 4.28 (dd, J = 3.3, 4.3 Hz, 1H), 4.86 (dd, J = 3.2, 6.5 Hz, 1H), 5.02 (dd, J = 4.6, 6.5 Hz, 1H), 5.15 (d, J = 4.6 Hz, 1H), 6.89 (ddd, J = 0.8, 2.5, 8.3 Hz, 1H), 7.30−7.43 (m, 7H), 7.60 (t, J = 2.3 Hz, 1H), 7.62−7.66 (m, 5H), 7.76 (s, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ ppm 19.4, 25.7, 26.9, 27.6, 55.7, 64.1, 79.6, 82.3, 85.2, 85.4, 104.5, 111.4, 113.9, 114.5, 127.8, 127.9, 129.89, 129.92, 130.2, 133.2, 133.4, 134.2, 135.7, 135.8, 140.9, 148.7, 160.5. HRMS-ESI: m/z $[M + H]^+$ calcd for $C_{33}H_{39}N_3O_5SiH^+$, 586.2737; found, 586.2731.

*2-(4-Chlorophenyl)-4-(2,3-isopropylidene-5-tert-butyldiphenylsilyl-β-D-ribosyl)-1,2,3-triazole (**2g**).* Following the general procedure for *N*-arylation of 1-β-D-ribosyl-1,2,3-triazoles (method A), a mixture of 4-bromochlorobenzene (14.4 mg, 8.7 μL, 0.0751 mmol), 1,2,3-triazole derivative **1** (30.0 mg, 0.0625 mmol), K_3PO_4 (26.5 mg, 0.125 mmol), $[PdCl(allyl)_2]$ (0.350 mg, 0.000938 mmol), and L4 (1.20 mg, 0.00188 mmol) in toluene (0.45 mL) was stirred at 120 °C for 10 h. The crude was purified by flash column chromatography on silica gel (heptane/AcOEt 9.5:0.5 to 9:1) to afford a colorless oil (33.0 mg, 89%). ^{1}H NMR (400 MHz, $CDCl_3$): δ ppm 1.03 (s, 9H), 1.41 (s, 3H), 1.63 (s, 3H), 3.79 (d, J = 4.3 Hz, 2H), 4.28 (dd, J = 3.2, 4.2 Hz, 1H), 4.86 (dd, J = 3.0, 6.5 Hz, 1H), 4.99 (dd, J = 4.7, 6.4 Hz, 1H), 5.14 (d, J = 4.7 Hz, 1H), 7.31−7.44 (m, 8H), 7.63−7.65 (m, 4H), 7.76 (s, 1H), 7.98 (dt, J = 2.9, 9.0 Hz, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): δ ppm 19.4, 25.7, 26.9, 27.6, 64.1, 79.6, 82.3, 85.2, 85.4, 114.5, 120.3, 127.8, 127.9, 129.4, 129.90, 129.95, 133.2, 133.3, 134.5, 135.7, 138.4, 149.0. HRMS-ESI: m/z $[M + Na]^+$ calcd for $C_{32}H_{36}ClN_3O_4SiNa^+$, 612.2061; found, 612.2049.

*2-(4-Cianophenyl)-4-(2,3-isopropylidene-5-tert-butyldiphenylsilyl-β-D-ribosyl)-1,2,3-triazole (**2h**).* Following the general procedure for *N*-arylation of 1-β-D-ribosyl-1,2,3-triazoles (method A), a mixture of 4-bromobenzonitrile (13.7 mg, 0.0751 mmol), 1,2,3-triazole derivative **1** (30.0 mg, 0.0625 mmol), K_3PO_4 (26.5 mg, 0.125 mmol), $[PdCl(allyl)_2]$ (0.350 mg, 0.000938 mmol), and L4 (1.20 mg, 0.00188 mmol) in toluene (0.45 mL) was heated to 120 °C for 10 h. The crude was purified by flash column chromatography on silica gel (heptane/AcOEt 9:1) to afford a colorless oil (31.0 mg, 85%). ^{1}H NMR (400 MHz, $CDCl_3$): δ ppm 1.02 (s, 9H), 1.41 (s, 3H), 1.63 (s, 3H), 3.79 (ddd, J = 4.1, 11.4 Hz, 2H), 4.30 (dd, J = 3.2, 3.9 Hz, 1H), 4.86 (dd, J = 2.9, 6.5 Hz, 1H), 4.99 (dd, J = 4.8, 6.4 Hz, 1H), 5.14 (d, J = 4.7 Hz, 1H), 7.31−7.43 (m, 6H), 7.63 (ddd, J = 1.4, 2.7, 6.6 Hz, 4H), 7.75 (dt, J = 2.1, 9.0 Hz, 2H), 7.82 (s, 1H), 8.16 (dt, J = 2.1, 9.0 Hz, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): δ ppm 19.4, 25.7, 26.9, 27.6, 64.1, 79.7, 82.3, 85.2, 85.5, 111.0, 114.6, 118.4, 119.3, 127.8, 127.9, 129.92, 129.99, 133.19, 133.22, 133.6, 135.5, 135.7, 142.4, 150.2. HRMS-ESI: m/z $[M + Na]^+$ calcd for $C_{33}H_{36}N_4O_4SiNa^+$, 603.2404; found, 603.2382.

*2-(4-Pyridyl)-4-(2,3-isopropylidene-5-tert-butyldiphenylsilyl-β-D-ribosyl)-1,2,3-triazole (**2j**).* Following the general procedure for *N*-arylation of 1-β-D-ribosyl-1,2,3-triazoles (method A), a mixture of 4-bromopyridine chloridrate (14.6 mg, 0.0751 mmol), 1,2,3-triazole derivative **1** (30.0 mg, 0.0625 mmol), K_3PO_4 (42.5 mg, 0.200 mmol), $[PdCl(allyl)_2]$ (0.350 mg, 0.000938 mmol), and L4 (1.20 mg, 0.00188 mmol) in toluene (0.45 mL) was stirred at 120 °C for 10 h. The crude was purified by flash column chromatography on silica gel (heptane/AcOEt 9:1) to afford a yellow oil (34.0 mg, 98%). ^{1}H NMR (400 MHz, $CDCl_3$): δ ppm 1.02 (s, 9H), 1.41 (s, 3H), 1.63 (s, 3H), 3.79 (td, J = 4.1, 11.5 Hz, 2H), 4.30 (dd, J = 3.2, 4.0 Hz, 1H), 4.86 (dd, J = 3.0, 6.4 Hz, 1H), 5.00 (dd, J = 4.7, 6.4 Hz, 1H), 5.15 (d, J = 4.6 Hz, 1H), 7.31−7.43 (m, 6H), 7.63 (ddd, J = 1.4, 2.9, 6.5 Hz, 4H), 7.83 (s, 1H), 7.93 (dd, J = 1.6, 4.7 Hz, 2H), 8.69 (dd, J = 1.5, 4.8 Hz, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): δ ppm 19.4, 25.7, 26.9, 27.6, 64.6, 79.7, 82.3, 85.2, 85.5, 112.9, 114.6, 127.8, 127.9, 129.93, 129.99, 133.18, 133.23, 135.7, 145.6, 150.4, 151.3. HRMS-ESI: m/z $[M + H]^+$ calcd for $C_{31}H_{36}N_4O_4SiH^+$, 557.2584; found, 557.2572.

*2-(3-Pyridyl)-4-(2,3-isopropylidene-5-tert-butyldiphenylsilyl-β-D-ribosyl)-1,2,3-triazole (**2k**).* Following the general procedure for *N*-arylation of 1-β-D-ribosyl-1,2,3-triazoles (method A), a mixture of 3-bromopyridine (11.9 mg, 7.3 μL, 0.0751 mmol), 1,2,3-triazole derivative **1** (30.0 mg, 0.0625 mmol), K_3PO_4 (26.5 mg, 0.125 mmol), $[PdCl(allyl)_2]$ (0.350 mg, 0.000938 mmol), and L4 (1.20 mg, 0.00188 mmol) in toluene (0.45 mL) was stirred at 120 °C for 10 h. The crude was purified by flash column chromatography on silica gel (heptane/AcOEt 9.5:0.5 to 8.5:1.5) to afford a yellow oil (34.0 mg, 98%). ^{1}H NMR (400 MHz, $CDCl_3$): δ ppm 1.02 (s, 9H), 1.41 (s, 3H), 1.63 (s, 3H), 3.79 (d, J = 4.2 Hz, 2H), 4.29 (dd, J = 3.2, 4.1 Hz, 1H), 4.87 (dd, J = 3.0, 6.5 Hz, 1H), 5.01 (dd, J = 4.8, 6.5 Hz, 1H), 5.16 (d, J = 4.7 Hz, 1H), 7.30−7.42 (m, 7H), 7.64 (ddd, J = 1.6, 3.4, 6.3 Hz, 4H), 7.82 (s, 1H), 8.30 (ddd, J = 1.5, 2.6, 8.3 Hz, 1H), 8.60 (dd, J = 1.4, 4.7 Hz, 1H), 9.33 (d, J = 2.4 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ ppm 19.4, 25.7, 26.9, 27.6, 64.1, 79.6, 82.3, 85.2, 85.5, 114.6, 123.8, 126.2, 127.8, 127.9, 129.91, 129.96, 133.2, 133.3, 135.0, 135.7, 136.3, 140.8, 148.6, 149.6. HRMS-ESI: m/z $[M + H]^+$ calcd for $C_{31}H_{36}N_4O_4SiH^+$, 557.2584; found, 557.2579.

*2-(5-Pyrimidinyl)-4-(2,3-isopropylidene-5-tert-butyldiphenylsilyl-β-D-ribosyl)-1,2,3-triazole (**2m**).* Following the general procedure for *N*-arylation of 1-β-D-ribosyl-1,2,3-triazoles (method B), a mixture of 5-bromopyrimidine (11.9 mg, 0.0751 mmol), 1,2,3-triazole derivative **1** (30.0 mg, 0.0625 mmol), K_3PO_4 (26.5 mg, 0.125 mmol), $Pd_2(dba)_3$ (0.859 mg, 0.000938 mmol), and L4 (1.20 mg, 0.00188 mmol) in toluene (0.45 mL) was stirred at 120 °C for 10 h. The crude was purified by flash column chromatography on silica gel (heptane 100% to heptane/AcOEt 8.5:1.5) to afford a colorless oil (28.8 mg, 83%). ^{1}H NMR (400 MHz, $CDCl_3$): δ ppm 1.02 (s, 9H), 1.41 (s, 3H), 1.63 (s, 3H), 3.79 (d, J = 4.0 Hz, 2H), 4.31 (dd, J = 3.1, 3.9 Hz, 1H), 4.87 (dd, J = 3.0, 6.5 Hz, 1H), 5.00 (dd, J = 4.8, 6.4 Hz, 1H), 5.16 (d, J = 4.8 Hz, 1H), 7.31−7.43 (m, 6H), 7.61−7.65 (m, 4H), 7.87 (s, 1H), 9.20 (s, 1H), 9.39 (s, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): δ ppm 19.4, 25.7, 26.9, 27.6, 64.1, 79.6, 82.3, 85.2, 85.5, 114.7, 127.8, 127.9, 129.9, 130.0, 133.1, 133.2, 134.4, 135.70, 135.72, 135.9, 147.1, 150.6, 157.2. HRMS-ESI: m/z $[M + H]^+$ calcd for $C_{30}H_{35}N_5O_4SiH^+$, 558.2537; found, 558.2532.

*2-(N-Boc-5-indolyl)-4-(2,3-isopropylidene-5-tert-butyldiphenylsilyl-β-D-ribosyl)-1,2,3-triazole (**2n**).* Following the general procedure for *N*-arylation of 1-β-D-ribosyl-1,2,3-triazoles (method A), a mixture of *N*-Boc-5-bromoindole (22.2 mg, 0.0751 mmol), 1,2,3-triazole derivative **1** (30.0 mg, 0.0625 mmol), K_3PO_4 (26.5 mg, 0.125 mmol), $[PdCl(allyl)_2]$ (0.350 mg, 0.000938 mmol), and L4 (1.20 mg, 0.00188 mmol) in toluene (0.45 mL) was stirred at 120 °C for 10 h. The crude was purified by flash column chromatography on silica gel (heptane 100% to heptane/AcOEt 9:1) to afford a colorless oil (33.0 mg, 76%). ^{1}H NMR (400 MHz, $CDCl_3$): δ ppm 1.04 (s, 9H), 1.41 (s, 3H), 1.63 (s, 3H), 1.69 (s, 9H), 3.80 (d, J = 4.4 Hz, 2H), 4.29 (dd, J = 3.2, 4.3 Hz, 1H), 4.88 (dd, J = 3.1, 6.5 Hz, 1H), 5.05 (dd, J = 4.7, 6.5 Hz, 1H), 5.17 (d, J = 4.6 Hz, 1H), 6.62 (d, J = 3.7 Hz, 1H), 7.30−7.42 (m, 6H), 7.64−7.67 (m, 5H), 7.77 (s, 1H), 8.02 (dd, J = 2.1, 9.0 Hz, 1H), 8.21 (d, J = 2.2 Hz, 1H), 8.23 (br s, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ ppm 19.4, 25.7, 26.9, 27.6, 28.3, 64.1, 79.7, 82.4, 84.2, 85.3, 85.4, 107.7, 111.5, 114.5, 115.7, 115.9, 127.5, 127.8, 127.9, 129.88, 129.91, 131.0, 133.2, 133.4, 133.9, 134.5, 135.69, 135.74, 135.8, 148.3, 149.6. HRMS-ESI: m/z $[M + Na]^+$ calcd for $C_{39}H_{46}N_4O_6SiNa^+$, 717.3084; found, 717.3078.

*2-(3-Quinolyl)-4-(2,3-isopropylidene-5-tert-butyldiphenylsilyl-β-D-ribosyl)-1,2,3-triazole (**2o**).* Following the general procedure for *N*-

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arylation of 1-β-D-ribosyl-1,2,3-triazoles (method A), a mixture of 3-bromoquinoline (15.6 mg, 10 μL, 0.0751 mmol), 1,2,3-triazole derivative **1** (30.0 mg, 0.0625 mmol), K_3PO_4 (26.5 mg, 0.125 mmol), [PdCl(allyl)$_2$] (0.350 mg, 0.000938 mmol), and L4 (1.20 mg, 0.00188 mmol) in toluene (0.45 mL) was stirred at 120 °C for 10 h. The crude was purified by flash column chromatography on silica gel (heptane 100% to heptane/AcOEt 9:1) to afford a colorless oil (26.6 mg, 70%). ^{1}H NMR (400 MHz, $CDCl_3$): δ ppm 1.03 (s, 9H), 1.43 (s, 3H), 1.65 (s, 3H), 3.81 (d, *J* = 4.1 Hz, 2H), 4.32 (dd, *J* = 3.3, 4.0 Hz, 1H), 4.89 (dd, *J* = 3.0, 6.5 Hz, 1H), 5.05 (dd, *J* = 4.8, 6.4 Hz, 1H), 5.20 (d, *J* = 4.7 Hz, 1H), 7.30−7.42 (m, 6H), 7.60−7.66 (m, 5H), 7.75 (ddd, *J* = 1.4, 6.9, 8.4 Hz, 1H), 7.87 (s, 1H), 7.90 (dd, *J* = 1.3, 8.2 Hz, 1H), 8.17 (d, *J* = 8.5 Hz, 1H), 8.72 (d, *J* = 2.4 Hz, 1H), 9.67 (d, *J* = 2.5 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ ppm 19.4, 25.7, 26.9, 27.6, 64.1, 79.7, 82.3, 85.2, 85.4, 114.6, 123.9, 127.6, 127.84, 127.89, 127.96, 128.3, 129.6, 129.86, 129.92, 129.97, 133.13, 133.23, 135.0, 135.7, 142.6, 147.2, 149.7. HRMS-ESI: *m*/*z* [M + H]$^+$ calcd for $C_{35}H_{38}N_4O_4SiH^+$, 607.2741; found, 607.2737.

*1-(Phenyl)-4-(2,3-isopropylidene-5-tert-butyldiphenylsilyl-β-D-ribosyl)-1,2,3-triazole (**8a**).* To a solution of compound **7** (0.1 g, 0.229 mmol) in *N*,*N*-dimethylformamide (1.8 mL) and ethanol (0.2 mL) were added copper(I) iodide (0.0022 g, 0.0114 mmol) and phenyl azide (0.054 g, 0.458 mmol). The mixture was stirred for 1 min under vacuum/argon in a sealed tube and placed into a microwave apparatus at 100 °C for 30 min. The mixture was filtered over Celite and concentrated. The residue was taken in ethanol and purified by activated carbon. After evaporation of the solvent, the residue was purified by flash column chromatography (heptane/AcOEt 7:3) to give compound **8a** as a yellow oil (98.0 mg, 77%). Care should be taken because the reaction releases gas. ^{1}H NMR (400 MHz, $CDCl_3$): δ ppm 1.03 (s, 9H), 1.40 (s, 3H), 1.62 (s, 3H), 3.81 (qd, *J* = 4.6, 11.1 Hz, 2H), 4.28 (dd, *J* = 3.5, 4.5 Hz, 1H), 4.85 (dd, *J* = 3.4, 6.4 Hz, 1H), 5.10 (dd, *J* = 4.2, 6.4 Hz, 1H), 5.23 (d, J = 4.1 Hz, 1H), 7.29−7.43 (m, 7H), 7.44−7.49 (m, 2H), 7.55−7.58 (m, 2H), 7.63−7.65 (m, 4H), 7.87 (s, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ ppm 19.4, 25.6, 26.9, 27.6, 64.3, 79.6, 82.2, 85.2, 85.5, 114.3, 120.2, 120.7, 127.8, 127.9, 128.8, 129.81, 129.89, 129.94, 133.3, 133.4, 135.66, 135.71, 137.1, 148.0. HRMS-ESI: *m*/*z* [M + H]$^+$ calcd for $C_{32}H_{37}N_3O_4SiH^+$, 556.2632; found, 556.2625.

*1-(Phenyl)-5-(2,3-isopropylidene-5-tert-butyldiphenylsilyl-β-D-ribosyl)-1,2,3-triazole (**8b**).* To a solution of compound **7** (0.10 g, 0.229 mmol) in *N*,*N*-dimethylformamide (1.8 mL) and ethanol (0.2 mL) was added phenyl azide (0.054 g, 0.458 mmol). The mixture was stirred at 100 °C for 24 h. After being cooled, the mixture was concentrated, and the residue was purified by flash column chromatography (heptane/AcOEt 2:1) to afford two products, 1,4-regioisomer (71.0 mg, 56%) and 1,5-regioisomer (26.0 mg, 20%), as yellow oils. Care should be taken because the reaction releases gas. ^{1}H NMR (400 MHz, $CDCl_3$): δ ppm 1.08 (s, 9H), 1.35 (s, 3H), 1.47 (s, 3H), 3.77−3.84 (m, 2H), 4.14 (dd, *J* = 3.3, 3.7 Hz, 1H), 4.76−4.78 (m, 1H), 4.81−4.84 (m, 2H), 7.34−7.45 (m, 6H), 7.50−7.52 (m, 3H), 7.61−7.63 (m, 2H), 7.64−7.68 (m, 4H); 7.77 (s, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ ppm 19.4, 25.6, 26.9, 27.5, 63.8, 76.2, 81.9, 84.9, 85.2, 115.0, 125.7, 127.9, 129.4, 129.8, 130.0, 132.7, 133.0, 133.1, 135.7, 136.1, 136.2. HRMS-ESI: *m*/*z* [M + H]$^+$ calcd for $C_{32}H_{37}N_3O_4SiH^+$, 556.2632; found, 556.2627.

*Ethyl-3-((5-O-acetyl)-2,3-O-isopropylidene-β-D-ribosyl)-propiolate (**9**).*[5] A suspension of indium (In^0) (0.75 g, 6.56 mmol) in anhydrous 1,2-dichloroethane (10 mL) under argon was stirred during 20 min at room temperature. Further ethyl 3-iodo-propiolate[19] (1.2 g, 5.47 mmol) and the ribofuranoside **4** (0.75 g, 2.74 mmol) were added into the reaction tube that was then sealed. The reaction mixture was stirred for 6 h under argon at 90 °C. The mixture was filtered over Celite and evaporated. The crude residue was taken in anhydrous acetone (4 mL) and treated with *p*-toluenesulfonic acid monohydrate (16 mg, 3 mol %). After being stirred at room temperature for 5 h, the mixture was neutralized with $NaHCO_3$, filtered through Celite, and concentrated under reduced pressure. The crude residue obtained was purified by flash column chromatography on silica gel (cyclohexane/AcOEt 2:1) to give **9** as a yellow oil (464 mg, 54%). ^{1}H (400 MHz, $CDCl_3$): δ ppm 1.29 (t, *J* = 7.2 Hz, 3H), 1.33 (s, 3H), 1.51 (s, 3H), 2.10 (s, 3H), 4.18 (dd, *J* = 5.5, 11.8 Hz, 1H), 4.22 (q, *J* = 7.2 Hz, 2H), 4.25 (dd, *J* = 5.2, 11.8 Hz, 1H), 4.34 (dt, *J* = 2.2, 5.3 Hz, 1H), 4.72 (dd, *J* = 2.1, 6.2 Hz, 1H), 4.80 (d, *J* = 2.5 Hz, 1H), 4.89 (dd, *J* = 2.4, 6.1 Hz, 1H). ^{13}C (100 MHz, $CDCl_3$): δ ppm 14.1, 20.9, 25.4, 26.9, 62.4, 63.9, 74.9, 78.5, 82.8, 83.6, 84.1, 86.1, 114.3, 153.0, 170.6.

*Ethyl 4-((5-O-Acetyl)-2,3-O-isopropylidene-β-D-ribosyl)-2H-1,2,3-triazole-5-carboxylate (**10**).* To a solution of compound **9** (0.65 g, 2.08 mmol) in *N*,*N*-dimethylformamide (16 mL) and ethanol (1.8 mL) was added azidotrimethylsilane (0.48 g, 0.55 mL, 4.16 mmol). The mixture was stirred for 1 min under vacuum/argon in a sealed tube and placed into a microwave apparatus at 100 °C for 30 min. The mixture was filtered over Celite and concentrated. The residue was taken in ethanol and purified with activated carbon. After evaporation of the solvent, the residue was purified by flash column chromatography (heptane/AcOEt 9:1 to 7:3) to give compounds **10** as a yellow oil (392 mg, 53%). Care should be taken because the reaction releases gas. ^{1}H (400 MHz, $CDCl_3$): δ ppm 1.37 (s, 3H), 1.40 (t, *J* = 7.1 Hz, 3H), 1.61 (s, 3H), 2.09 (s, 3H), 4.24 (dd, *J* = 4.1, 11.6 Hz, 1H), 4.30−4.48 (m, 4H), 4.68 (dd, *J* = 4.0, 5.8 Hz, 1H), 4.99 (dd, *J* = 2.6, 6.0 Hz, 1H), 5.67 (d, *J* = 3.0 Hz, 1H). ^{13}C (100 MHz, $CDCl_3$): δ ppm 14.4, 21.0, 25.7, 27.5, 61.8, 64.7, 78.9, 82.2, 83.9, 85.5, 114.7, 160.9, 171.7. HRMS-ESI: *m*/*z* [M + H]$^+$ calcd for $C_{15}H_{21}N_3O_7H^+$, 356.1458; found, 356.1453.

*Ethyl 4-(2,3-O-Isopropylidene-β-D-ribosyl)-2H-1,2,3-triazole-5-carboxylate (**11**).* To a solution of **10** (0.64 g, 1.80 mmol) in ethanol (9.5 mL) was added potassium carbonate (0.5 g, 3.60 mmol). The mixture was stirred at 40 °C for 18 h. The reaction mixture was concentrated, and the residue was taken in water (5 mL) and acidified with acetic acid to pH 5−6. The water phase was extracted with acetyl acetate (2 × 15 mL), dried over anhydrous sodium sulfate, filtered, and concentrated under reduced pressure. Heptane was used to remove the excess of acetic acid. Compound **11** was obtained as a yellow oil (540 mg, 96%). ^{1}H (400 MHz, $CDCl_3$): δ ppm 1.35 (s, 3H), 1.40 (t, *J* = 7.1 Hz, 3H), 1.61 (s, 3H), 3.81 (dd, *J* = 3.2, 12.2 Hz, 1H), 4.04 (dd, *J* = 2.5, 12.2 Hz, 1H), 4.36 (dd, *J* = 2.9, 3.0 Hz, 1H), 4.40−4.48 (m, 2H), 4.77 (dd, *J* = 3.1, 6.1 Hz, 1H), 4.91 (dd, *J* = 3.5, 6.1 Hz, 1H), 5.74 (d, *J* = 3.1 Hz, 1H). ^{13}C (100 MHz, $CDCl_3$): δ ppm 14.3, 25.6, 27.6, 61.7, 62.4, 79.1, 81.3, 86.2, 86.5, 114.2, 134.8, 146.3, 161.6. HRMS-ESI: *m*/*z* [M + H]$^+$ calcd for $C_{13}H_{19}N_3O_6H^+$, 314.1352; found, 314.1340.

*Ethyl 4-((5-O-(tert-Butyldiphenylsilyl)-2,3-O-isopropylidene-β-D-ribosyl)-2H-1,2,3-triazole-5-carboxylate (**12**).* To a solution of **11** (0.54 g, 1.72 mmol) in anhydrous acetonitrile (6.4 mL) were added imidazole (0.15 g, 2.24 mmol), 4-(dimethylamino)-pyridine (0.23 g, 1.90 mmol), and *tert*-butyldiphenylchlorosilane (0.47 g, 0.45 mL, 1.72 mmol). The mixture was stirred at room temperature for 1.5 h, and then it was concentrated. The residue was taken in ethyl acetate (10 mL) and washed with saturated solution of sodium bicarbonate (1 × 5 mL). The water phase was extracted with ethyl acetate (1 × 10 mL). The combined organic phases were dried over anhydrous sodium sulfate, filtered, and evaporated. The crude residue was purified by flash column chromatography on silica gel (heptane/AcOEt 9:1 to 7:3) to give **12** as a colorless oil (494 mg, 52%). ^{1}H (400 MHz, $CDCl_3$): δ ppm 1.12 (s, 9H), 1.34 (s, 3H), 1.41 (t, *J* = 7.3 Hz, 3H), 1.60 (s, 3H), 3.62 (dd, *J* = 6.7, 11.7 Hz, 1H), 3.89 (dd, *J* = 3.8, 11.8 Hz, 1H), 4.28−4.32 (m, 1H), 4.38−4.50 (m, 2H), 4.60 (br s, 1H), 4.89 (br s, 1H), 5.67 (d, *J* = 2.5 Hz, 1H), 7.37−7.49 (m, 6H), 7.63−7.67 (m, 2H), 7.69−7.72 (m, 2H). ^{13}C (100 MHz, $CDCl_3$): δ ppm 14.2, 19.2, 25.4, 26.9, 27.2, 61.5, 63.8, 79.1, 81.5, 85.4, 85.8, 113.9, 127.9, 128.0, 130.2, 135.5, 135.6, 160.9. HRMS-ESI: *m*/*z* [M + H]$^+$ calcd for $C_{29}H_{37}N_3O_6SiH^+$, 552.2530; found, 552.2524.

*5-Bromo-4-(5-O-(tert-butyldiphenylsilyl)-2,3-O-isopropylidene-β-D-ribosyl)-2H-1,2,3-triazole (**13**).* To a solution of derivative **1** (0.083 g, 0.173 mmol) in isopropyl acetate (0.65 mL) was added *N*-bromosuccinimide (0.031 g, 0.173 mmol). The mixture was stirred at 25 °C for 45 h. The solvent was evaporated, and the residue was purified by flash column chromatography (heptane/AcOEt 9.5:0.5 to 8:2) to give compound **13** as a yellow oil (73 mg, 76%). ^{1}H (400 MHz, $CDCl_3$): δ ppm 1.05 (s, 9H), 1.37 (s, 3H), 1.60 (s, 3H), 3.77

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(qd, J = 4.6, 11.4 Hz, 2H), 4.25−4.28 (m, 1H), 4.79 (br s, 1H), 5.02 (br s, 1H), 5.09 (d, J = 4.1 Hz, 1H), 7.35−7.38 (m, 4H), 7.41−7.44 (m, 2H), 7.62−7.65 (m, 4H), 12.4 (br s, 1H). ^{13}C (125 MHz, $CDCl_3$): δ ppm 19.3, 25.6, 26.9, 27.5, 64.0, 77.9, 82.2, 84.1, 85.5, 114.6, 127.9, 130.0, 133.1, 135.7. HRMS-ESI: m/z $[M + Na]^+$ calcd for $C_{26}H_{32}BrN_3O_4SiNa^+$, 580.1243; found, 580.1227.

*5-(4-Methoxyphenyl)-4-(5-O-(tert-butyldiphenylsilyl)-2,3-O-isopropylidene-β-D-ribosyl)-2H-1,2,3-triazole (**14**).* In a sealed tube under argon containing boronic acid (0.034 g, 0.224 mmol), bromotriazoyl derivative **13** (0.10 g, 0.179 mmol), potassium phosphate (0.11 g, 0.537 mmol), palladium acetate (1.0 mg, 0.00448 mmol), and diadamantyl-*n*-butyl phosphine (3.85 mg, 0.0107 mmol) were added the solvents (dioxane, 0.9 mL, water, 0.45 mL). The mixture were stirred at 120 °C for 15 h. The solvent was evaporated, and the residue was taken in ethyl acetate (5 mL), washed with brine (2 mL), dried over anydrous sodium sulfate, filtered, and concentrated. The residue was purified by flash column chromatography (heptane/AcOEt 9:1 to 7.5:2.5) to give compound **14** as a colorless oil (68 mg, 65%). ^{1}H (400 MHz, $CDCl_3$): δ ppm 1.04 (s, 9H), 1.38 (s, 3H), 1.59 (s, 3H), 3.77 (qd, J = 5.1, 11.1 Hz, 2H), 3.83 (s, 3H), 4.29 (td, J = 3.4, 3.5 Hz, 1H), 4.84 (dd, J = 3.3, 6.4 Hz, 1H), 5.15 (d, J = 4.1 Hz, 1H), 5.27 (br s, 1H), 6.95 (dt, J = 2.9, 8.9 Hz, 2H), 7.30−7.34 (m, 4H), 7.37−7.40 (m, 2H), 7.62−7.66 (m, 4H), 7.75 (dt, J = 2.8, 8.8 Hz, 2H). ^{13}C (100 MHz, $CDCl_3$): δ ppm 19.4, 25.6, 26.9, 27.5, 55.4, 64.3, 78.0, 82.5, 83.9, 85.7, 114.3, 114.4, 127.82, 127.84, 129.6, 129.9, 133.3, 135.7, 135.8, 160.1. HRMS-ESI: m/z $[M + H]^+$ calcd for $C_{33}H_{39}N_3O_5SiH^+$, 586.2737; found, 586.2732.

*Ethyl 2-(Phenyl)-5-(2,3-isopropylidene-5-tert-butyldiphenylsilyl-β-D-ribosyl)-1,2,3-triazole-4-carboxylate (**15a**).* Following the general procedure for *N*-arylation of 1-β-D-ribosyl-1,2,3-triazoles (method A), a mixture of 4-bromobenzene (10.2 mg, 6.9 μL, 0.0652 mmol), 1,2,3-triazole derivative **12** (30.0 mg, 0.0544 mmol), K_3PO_4 (23.1 mg, 0.109 mmol), $[PdCl(allyl)_2]$ (0.609 mg, 0.00163 mmol), and L4 (2.09 mg, 0.00326 mmol) in toluene (0.39 mL) was heated to 120 °C for 10 h. The crude was purified by flash column chromatography on silica gel (heptane/AcOEt 9:1) to afford a colorless oil (24.9 mg, 73%). ^{1}H NMR (400 MHz, $CDCl_3$): δ ppm 1.03 (s, 9H), 1.41 (s, 3H), 1.42 (t, J = 7.1 Hz, 3H), 1.64 (s, 3H), 3.77−3.84 (m, 2H), 4.33 (td, J = 3.2, 5.2 Hz, 1H), 4.45 (dtd, J = 7.2, 10.8 Hz, 2H), 4.94 (dd, J = 3.1, 6.4 Hz, 1H), 5.22 (dd, J = 4.3, 6.4 Hz, 1H), 5.62 (d, J = 4.3 Hz, 1H), 7.25−7.46 (m, 9H), 7.62−7.65 (m, 4H), 7.99−8.03 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): δ ppm 14.4, 19.4, 25.8, 26.9, 27.6, 61.8, 64.2, 78.2, 82.9, 84.6, 85.9, 114.2, 119.8, 127.7, 127.8, 128.7, 129.4, 129.75, 129.81, 133.5, 135.7, 135.8, 138.7, 139.3, 149.7, 160.8. HRMS-ESI: m/z $[M + Na]^+$ calcd for $C_{35}H_{41}N_3O_6SiNa^+$, 650.2662; found, 650.2656.

*Ethyl 2-(4-Pyridyl)-5-(2,3-isopropylidene-5-tert-butyldiphenylsilyl-β-D-ribosyl)-1,2,3-triazole-4-carboxylate (**15b**).* Following the general procedure for *N*-arylation of 1-β-D-ribosyl-1,2,3-triazoles (method A), a mixture of 4-bromopyridine chloridrate (12.7 mg, 0.0652 mmol), 1,2,3-triazole derivative **12** (30.0 mg, 0.0544 mmol), K_3PO_4 (36.9 mg, 0.174 mmol), $[PdCl(allyl)_2]$ (0.609 mg, 0.00163 mmol), and L4 (2.09 mg, 0.00326 mmol) in toluene (0.39 mL) was heated to 120 °C for 10 h. The crude was purified by flash column chromatography on silica gel (heptane 100% to heptane/AcOEt 6:4) to afford a yellow oil (28.7 mg, 84%). ^{1}H NMR (400 MHz, $CDCl_3$): δ ppm 1.03 (s, 9H), 1.41 (s, 3H), 1.43 (t, J = 7.2 Hz, 3H), 1.63 (s, 3H), 3.81 (ddd, J = 4.6, 11.0 Hz, 2H), 4.34 (td, J = 3.2, 4.9 Hz, 1H), 4.46 (ds, J = 7.2, 12.3 Hz, 2H), 4.94 (dd, J = 3.0, 6.4 Hz, 1H), 5.19 (dd, J = 4.4, 6.4 Hz, 1H), 5.59 (d, J = 4.4 Hz, 1H), 7.28−7.39 (m, 6H), 7.61−7.64 (m, 4H), 7.89 (dd, J = 1.6, 4.7 Hz, 2H), 8.68 (dd, J = 1.4, 4.9 Hz, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): δ ppm 14.4, 19.4, 25.8, 26.9, 27.6, 62.1, 64.2, 78.2, 82.8, 84.5, 85.9, 113.4, 114.4, 127.75, 127.80, 129.8, 129.9, 133.36, 133.44, 135.7, 140.0, 145.0, 150.8, 151.4, 160.3. HRMS-ESI: m/z $[M + H]^+$ calcd for $C_{34}H_{40}N_4O_6SiH^+$, 629.2795; found, 629.2814.

*2-(Phenyl)-4-(2,3-isopropylidene-5-tert-butyldiphenylsilyl-β-D-ribosyl)-5-(4-methoxyphenyl)-1,2,3-triazole (**15c**).* Following the general procedure for *N*-arylation of 1-β-D-ribosyl-1,2,3-triazoles (method A), a mixture of 4-bromobenzene (7.08 mg, 4.7 μL, 0.0451 mmol), 1,2,3-triazole derivative **14** (22.0 mg, 0.0375 mmol), K_3PO_4 (15.9 mg, 0.0751 mmol), $[PdCl(allyl)_2]$ (0.210 mg, 0.000563 mmol), and L4 (0.722 mg, 0.00113 mmol) in toluene (0.27 mL) was heated to 120 °C for 23 h. The crude was purified by flash column chromatography on silica gel (heptane/AcOEt 9.5:0.5 to 9:1) to afford a colorless oil (23.0 mg, 93%). ^{1}H NMR (400 MHz, $CDCl_3$): δ ppm 1.04 (s, 9H), 1.44 (s, 3H), 1.62 (s, 3H), 3.80 (ddd, J = 5.2, 10.9 Hz, 2H), 3.89 (s, 3H), 4.37 (dd, J = 3.1, 5.0 Hz, 1H), 4.97 (dd, J = 3.0, 6.4 Hz, 1H), 5.18 (d, J = 4.2 Hz, 1H), 5.50 (dd, J = 4.3, 6.3 Hz, 1H), 7.02 (d, J = 8.8 Hz, 2H), 7.25−7.39 (m, 7H), 7.48 (t, J = 7.6 Hz, 2H), 7.63−7.65 (m, 4H), 7.90 (d, J = 8.8 Hz, 2H), 8.07 (d, J = 7.7 Hz, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): δ ppm 19.3, 25.7, 26.9, 27.6, 55.5, 64.1, 78.1, 82.7, 83.7, 85.8, 114.1, 114.3, 118.9, 122.7, 127.4, 127.7, 127.8, 129.2, 129.7, 129.8, 133.3, 133.4, 135.67, 135.74, 139.8, 143.5, 148.2, 160.2. HRMS-ESI: m/z $[M + H]^+$ calcd for $C_{39}H_{43}N_3O_5SiH^+$, 662.3050; found, 662.3044.

*2-(4-Pyridyl)-4-(2,3-isopropylidene-5-tert-butyldiphenylsilyl-β-D-ribosyl)-5-(4-methoxyphenyl)-1,2,3-triazole (**15d**).* Following the general procedure for *N*-arylation of 1-β-D-ribosyl-1,2,3-triazoles (method A), a mixture of 4-bromopyridine chloridrate (15.9 mg, 0.0819 mmol), 1,2,3-triazole derivative **14** (40.0 mg, 0.0683 mmol), K_3PO_4 (46.4 mg, 0.218 mmol), $[PdCl(allyl)_2]$ (0.382 mg, 0.00102 mmol), and L4 (1.31 mg, 0.00205 mmol) in toluene (0.49 mL) was heated to 120 °C for 23 h. The crude was purified by flash column chromatography on silica gel (heptane/AcOEt 7:3 to 6.5:3.5) to afford a yellow oil (40.0 mg, 88%). ^{1}H NMR (400 MHz, $CDCl_3$): δ ppm 1.03 (s, 9H), 1.44 (s, 3H), 1.62 (s, 3H), 3.76−3.84 (m, 2H), 3.89 (s, 3H), 4.37 (dd, J = 3.2, 4.4 Hz, 1H), 4.97 (dd, J = 2.8, 7.8 Hz, 1H), 5.16 (d, J = 4.4 Hz, 1H), 5.46−5.49 (m, 1H), 7.03 (d, J = 8.6 Hz, 2H), 7.24−7.39 (m, 6H), 7.63 (d, J = 6.8 Hz, 4H), 7.91 (d, J = 8.6 Hz, 2H), 7.94 (d, J = 6.0 Hz, 2H), 8.69 (d, J = 5.9 Hz, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): δ ppm 19.3, 25.7, 26.9, 27.6, 55.5, 64.1, 78.1, 82.6, 83.6, 85.9, 112.7, 114.3, 114.4, 121.9, 127.7, 127.8, 129.78, 129.82, 129.9, 133.3, 133.4, 135.66, 135.71, 145.3, 145.5, 149.6, 151.2, 160.7. HRMS-ESI: m/z $[M + H]^+$ calcd for $C_{38}H_{42}N_4O_5SiH^+$, 663.3003; found, 663.2996.

*2-Phenyl-4-(2,3-O-isopropylidene-β-D-ribosyl)-2H-1,2,3-triazole (**16**).*[20] To a mixture of **2a** (0.020 g, 0.359 mmol) and cesium fluoride (0.016 g, 0.108 mmol) in tetrahydrofuran (0.3 mL) was added tetrabutylammonium fluoride (1 M in THF, 5.4 μL, 0.00539 mmol). After being stirred at 50 °C for 4 h, the mixture was cooled to ambient temperature, diluted with methanol (0.1 mL), and stirred for 10 min. The solvent was evaporated, and the residue was purified by flash column chromatography on silica gel (heptane/AcOEt 8:2) to furnish **16** as a colorless oil (11 mg, 96%). ^{1}H (400 MHz, $CDCl_3$): δ ppm 1.39 (s, 3H), 1.62 (s, 3H), 3.00 (br s, 1H), 3.71 (d, J = 11.8 Hz, 1H), 3.89 (dd, J = 2.8, 12.2 Hz, 1H), 4.36 (dd, J = 3.1, 3.7 Hz, 1H), 4.89 (dd, J = 2.9, 6.4 Hz, 1H), 4.97 (dd, J = 4.0, 6.4 Hz, 1H), 5.22 (d, J = 4.0 Hz, 1H), 7.33−7.38 (m, 1H), 7.45−7.50 (m, 2H), 7.78 (s, 1H), 8.01−8.04 (m, 2H). ^{13}C (100 MHz, $CDCl_3$): δ ppm 25.6, 27.5, 63.4, 80.0, 82.5, 86.0, 86.2, 114.4, 119.1, 128.0, 129.5, 134.0, 139.7, 148.9.

*2-Phenyl-4-(β-D-ribosyl)-1,2,3-triazole (**17**).*[20,21] To a cold (0 °C) solution of **16** (0.011 g, 0.0347 mmol) in dichloromethane (0.1 mL) and water (0.1 mL) was added trifluoroacetic acid (0.1 mL). The mixture was stirred at room temperature for 24 h. Methanol was added to remove trifluoroacetic acid excess under reduced pressure. Coevaporation with methanol was repeated three more times, furnishing **17** as a colorless oil (9.6 mg, 100%). ^{1}H (400 MHz, CD_3OD): δ ppm 3.69 (dd, J = 4.5, 12.0 Hz, 1H), 3.80 (dd, J = 3.5, 12.0 Hz, 1H), 4.02 (dd, J = 3.8, 4.5 Hz, 1H), 4.15 (t, J = 5.1 Hz, 1H), 4.25 (t, J = 5.5 Hz, 1H), 5.01 (d, J = 5.8 Hz, 1H), 7.36−7.40 (m, 1H), 7.51 (t, J = 7.8 Hz, 2H), 7.97 (s, 1H), 8.04 (d, J = 8.5 Hz, 2H). ^{13}C (100 MHz, CD_3OD): δ ppm 63.6, 72.9, 77.7, 78.9, 86.5, 119.9, 128.9, 130.6, 135.5, 141.3, 151.0. HRMS-ESI: m/z $[M + Na]^+$ calcd for $C_{13}H_{15}N_3O_4Na^+$, 300.0960; found, 300.0969.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.joc.6b00323.

NMR spectra of all compounds and NOESY spectra of **2a**, **8a**, and **8b** (PDF)

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Notes

The authors declare no competing financial interest.

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