# Effective isomerization of 3′,5′-*O*-(tetraisopropyldisiloxane-1,3-diyl)nucleosides in the presence of trimethylsilyl trifluoromethanesulfonate

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**Dedicated to Prof. Harri Lönnberg on his 60th birthday**

**Abstract**
Trimethylsilyl trifluoromethanesulfonate catalyze effective isomerization of 3′,5′-*O*-(tetraisopropyldisiloxane-1,3-diyl)nucleosides (**1**) in 1,2-dicloroethane at 0°C into 2′,3′-*O*-(tetraisopropyldisiloxane-1,3-diyl)-derivatives (**2**), which can be obtained in 55-90% yields. On the other hand nucleosides **1** were found to be stable in the presence of tin tetrachloride. Only in the case of uridine derivative **1a** a substantial amount of isomerization product **2a** was formed.

**Keywords:** nucleoside protection, isomerization, 3′,5′-*O*-(tetraisopropyldisiloxane-1,3-diyl)nucleosides, trimethylsilyl trifluoromethanesulfonate

## Introduction

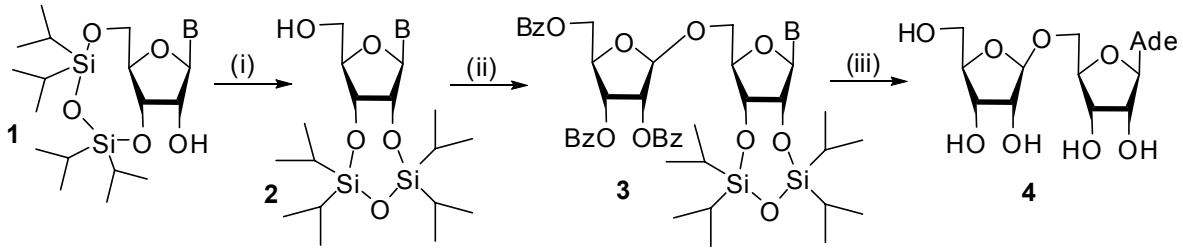
Tetraisopropyldisiloxane-1,3-diyl (TIPDS) group developed by Markiewicz[1,2] is widely used for simultaneous protection of 3′,5′-hydroxyl groups in ribonucleosides and subsequent manipulation with 2'-OH group of ribonucleosides: deoxygenation,[3,4] oxidation,[5] alkylation,[6-10] glycosylation,[11-16] protection,[17-21] preparation of 2'-amino-2'-deoxynuclesides,[22,23] and so on. This group may be considered as one of the most popular and useful protecting group in the field of nucleoside chemistry. It is believed that the reaction of 1,3-dichloro-tetraisopropyldisiloxane with ribonucleoside starts with silylation of primary 5'-hydroxyl followed by the formation of an 8-membered ring. It was also shown that the reaction with 5'-O-protected ribonucleosides resulted in the formation of 2′,3′-*O*-derivatives with 7 membered ring.[1,24,25] It should be also mentioned that simultaneous protection of both 3′- and 5′-hydroxyls can be carried out with *N*-unprotected ribonucleosides and with base-protected N-acyl derivatives. TIPDS group is removed with fluoride ion, usually with $Bu_4NF.3H_2O$ in tetrahydrofuran.[26]

## Results and Discussion

In the course of our studies[27-30] on the synthesis of disaccharide nucleosides we have developed an efficient and simple synthesis of 2'-*O*-β-D-ribofuranosylnucleosides. The method consists of the condensation of a small excess of 1-*O*-acetyl-2,3,5-tri-*O*-benzoyl-β-D-ribofuranose with N-protected 3′,5′-*O*-TIPDS-nucleosides in 1,2-dichloroethane in the presence of tin tetrachloride. This reaction was carried out under mild conditions (0°C, 1,2-dichloroethane, 2 h for pyrimidine nucleosides, 7-16 h for purine derivatives) and the yields of the target compounds were 74 - 82%. The presence of a participating 2-*O*-benzoyl group in sugar moiety leads exclusively to 1,2-trans-ribofuranosides. To study the broad applicability of the method, some other sugars such as fully acylated D-(and L)-arabinofuranose, D-ribopyranose and D-erythrofuranose were used in the *O*-glycosylation reaction. [27-30]

Ribosylation of pyrimidine 2',3'-di-*O*-acylnucleosides under the same conditions gave the desired disaccharide nucleosides in 74-78% yield.[31,32] Analogous results were obtained, when the tin tetrachloride catalyst was substituted by an equal amount of trimethylsilyl trifluoromethanesulfonate (TMSOTf). [31,32] Encouraged by these results we decided to examine the use of this catalyst in the preparation of 2'-*O*-β-D-pentafuranosylnucleosides. This catalyst is widely used in nucleoside chemistry and has some important advantages over tin tetrachloride.[33] Condensation of a small excess of 1-*O*-acetyl-2,3,5-tri-*O*-benzoyl-β-D-ribofuranose with 3′,5′-*O*-TIPDS-uridine (**1a**) at 0°C in 1,2-dichloroethane in the presence of TMSOTf gave a mixture of two compounds. The main product was identical with the known blocked 2′-*O*-ribofuranosyl-nucleoside[11,34] and the minor product was tentatively assigned as corresponding 5′-*O*-ribofuranosyl isomer (**3a**). Analogous condensation of $N^6$-benzoyl-3′,5′-*O*-TIPDS-adenosine **1b** with the same sugar gave 5′-*O*-ribofuranosyl derivative **3b** as a main product (up to 50% yield). The formation of 5′-*O*-ribofuranosylnucleosides may be explained by the isomerization of the TIPDS group from 3′,5′- to 2′,3′-positions in the presence of TMSOTf. It has been reported that condensation of 1-*O*-acetyl-2,3,5-tri-*O*-benzoyl-β-D-ribofuranose with 3′,5′-*O*-TIPDS-uridine (**1a**) in 1,2-dichloroethane in the presence of tin tetrachloride at 20° for 0.5 hr resulted in a mixture of desired 2′-*O*-ribofuranosyluridine and 5′-*O*-ribofuranosyluridine derivatives (**3a**) in a ratio 4:1.[12] The structure of **3a** was proved by independent synthesis starting from 2′,3′-*O*-TIPDS-uridine (**2a**)[12] which was prepared by reaction of 5′-*O*-monomethoxytrityluridine with 1,3-dichloro-tetraisopropyldisiloxane with the following removal of trityl group.[1]




**Scheme 1**. TIPDS group migration in the presence of TMSOTf at 0°C in 1,2-dicloroethane under nitrogen for 1,5-4 hrs. **a** B=Ura, **b** B=Ade$^{Bz}$, **c** B=Cyt$^{Bz}$, **d** B=Gua$^{iBu}$, **e** B=Ade , **f** B=Cyt.
(i) TMSOTf, 0°C, DCE, $N_2$; (ii) 1-*O*-acetyl-2,3,5-tri-*O*-benzoyl-β-D-ribofuranose, 20 hrs at 0°C; (iii) $Bu_4NF$/THF, 20 min at 20°C and 5 M $NH_3$/MeOH 3 days at 20°C.

Previously it was shown that under anhydrous acidic conditions (mesitylenesulphonic acid, DMF, 20°C, 6-10 hours, 30-60% yield) 3′,5′-*O*-TIPDS-nucleosides undergo the transformation from the thermodynamically less stable eight-membered ring to the more stable seven-membered ring 2′,3′-*O*-TIPDS-nucleosides.[35] It was shown that isomerization may occur during refluxing in chloroform in the presence of p-toluenesulfonic acid. [36] To study this reaction in detail we investigated the isomerization of 3′,5′-*O*-TIPDS-nucleosides (**1a-f**) in the presence of TMSOTf. Nucleosides **1a-f** were treated with excess of TMSOTf in 1,2-dichloethane at 0°C under nitrogen atmosphere. Using 2-3 equivalents of TMSOTf the isomerization was rather fast and was completed in 1.5 to 4 hr. Corresponding 2′,3′-*O*-TIPDS derivatives (**2 a-f**) were obtained in 55-90% yields (Table 1). It should be mentioned that in the case of purine derivatives the yields were much higher, up to 90%. Uridine derivative exhibited substantial decomposition.

**Table 1.** Isomerization of **1** in the presence of TMSOTf in 1,2-dichloethane at 0º C, isolated yields of **2** and $R_f$ values of **1** and **2**

| B | equivalents of TMSOTf | Yield of **2,** % | Reaction time in hr | $R_f$ of **1** in system A | $R_f$ of **1** in system B | $R_f$ of **2** in system A | $R_f$ of **2** in system B |
|---|---|---|---|---|---|---|---|
| **a** B=Ura | 2 | 55 | 1.5 | 0.35 | | 0.24 | |
| **b** B=Ade$^{Bz}$ | 3 | 90 | 3.0 | 0.36 | | 0.41 | |
| **c** B=Cyt$^{Bz}$ | 2 | 60 | 4.0 | 0.34 | | 0.43 | |
| **d** B=Gua$^{iBu}$ | 3 | 74 | 2.0 | 0.30 | | 0.28 | |
| **e** B=Ade | 3 | 72 | 4.0 | | 0.28 | | 0.29 |
| **f** B=Cyt | 3 | 55 | 2.0 | | 0.16 | | 0.12 |

System A $CH_2Cl_2$ – EtOH 98:2; system B $CH_2Cl_2$ – EtOH 95:5.

The structures of **2a-f** were proved by $^1H$ and $^{13}C$ NMR spectra and compared with NMR spectra of the starting 3′,5′-*O*-TIPDS-nucleosides **1a-f**. The signal of primary 5′-hydroxyl groups

(see also supplementary data) in nucleosides **2a-f** in DMSO-$d_6$ appears as a doublet of doublets or a triplet at 5.15-5.33 ppm due to the coupling with both protons of the $CH_2$-group. The secondary 2′-hydroxyl groups in **1a-f** are located in lower field at 5.60-5.69 ppm with $J_{2',OH}$ = 3.9 - 4.8 Hz. The coupling constants $J_{1',2'}$ in 3′,5′-*O*-TIPDS-nucleosides **1a-f** are rather small,[37] on the contrary $J_{3',4'}$ is around 8 Hz. The sum of $J_{1',2'}$ and $J_{3',4'}$ for both nucleoside series **1a-f** and **2a-f** is nearly the same, 9.0-9.6 Hz.[38] TIPDS-group shifts neighboring protons to the lower field (0.3-0.6 ppm). The same tendency was observed in the $^{13}$C NMR spectra for C-2' (1.4-2.5 ppm) and C-5' (0.05-0.7 ppm). Moreover the signals of C-4' in compounds **1** are located in higher fields than the corresponding signals in nucleosides **2** and this difference is most pronounced in purine nucleosides (around 5.0 ppm). It should be mentioned that compounds **2a** [1], **2f** [36] and **2a,e,f** [35] were prepared earliar but were not completely characterized.

The influence of temperature, solvent, and catalyst on the isomerisation reactions was further investigated (Table 2). The isomerization of **1** in the presence of 1 equivalent of TMSOTf in 1,2-dichloroethane is much slower (entries 1-3) than in the presence of excess of catalyst. When the reaction is conducted using 3 equivalents of TMSOTf at 0 ºC for 24 hrs a substantial amount of decomposition products (18%, entry 1) with lower $R_f$ = 0.25-0.15 (system A) is formed which can be identified as 3′- and 2'-*O*-TIPDS-derivatives. It is known that treatment of 3′,5′-*O*-TIPDS-nucleosides (**1**) with acids results in the formation of a mixture of 3′-*O*-TIPDS-derivative and its 2'-*O*-TIPDS-isomerizarion product.[1] The isomerization of **1** in acetonitrile is much slower than in 1,2-dichloroethane (entries 4 and 5). The conversion of 1→2 may be performed in the presence of trifluoromethanesulfonate (TfOH) (entries 6-8) or boron trifluoride etherate (entries 9 and 10) but these reactions are rather slower and accompanied by substantial decomposition.

We have also investigated the isomerization of **1** in the presence of tin tetrachloride, which is widely used in glycosylation reactions.[28-30] From Table 2 it can be seen that only in the case of uridine derivative **1a** a substantial amount of **2a** and decomposition products were formed and the isomerization is faster at room temperature (entries 11-13). These results confirmed the above mentioned instability of uridine derivative **1a** in the presence of this catalyst.[12] With other tested nucleosides **1b**-**1f** only traces of products **2b**-**2f** may be detected using TLC (entries 14-19).

**Table 2.** Isomerization of **1** in the presence of different catalysts

| Entry | Substrate | Conditions | **2**, % | **1**, % | Decomp.% |
|---|---|---|---|---|---|
| 1 | **1b** | 3 eq TMSOTf, DCE, 0ºC, 24 hrs | 80 | 2 | 18 |
| 2 | **1b** | 2 eq TMSOTf, DCE, 0ºC, 24 hrs | 85 | 2 | 13 |
| 3 | **1b** | 1 eq TMSOTf, DCE, 0ºC, 24 hrs | 50 | 45 | 5 |
| 4 | **1a** | 1 eq TMSOTf, MeCN, 20ºC, 24 hrs | 60 | 15 | 25 |
| 5 | **1b** | 1 eq TMSOTf, MeCN, 20ºC, 24 hrs | 50 | 45 | 5 |
| 6 | **1a** | 1 eq TfOH, DCE, 20ºC, 3 hrs | 30 | 55 | 15 |
| 7 | **1a** | 1 eq TfOH, DCE 20ºC, 24 hrs | 15 | 10 | 75 |
| 8 | **1c** | 1 eq TfOH, DCE, 20ºC, 24 hrs | 10 | 50 | 40 |
| 9 | **1a** | 1 eq $BF_3$·EtOEt, DCE, 0ºC, 24 hrs | 7 | 75 | 18 |
| 10 | **1b** | 1 eq $BF_3$·EtOEt, DCE, 0ºC, 24 hrs | 0 | 80 | 20 |
| 11 | **1a** | 1 eq $SnCl_4$, DCE, 0ºC, 24 hrs | 35 | 60 | 5 |
| 12 | **1a** | 1 eq $SnCl_4$, DCE, 20ºC, 24 hrs | 70 | 20 | 10 |
| 13 | **1a** | 1 eq $SnCl_4$, $CH_3CN$, 20ºC, 24 hrs | 65 | 20 | 15 |
| 14 | **1b** | 1 eq $SnCl_4$, DCE, 0ºC, 20ºC, 24 hrs | 2 | 95 | 3 |
| 15 | **1b** | 1 eq $SnCl_4$, MeCN, 20ºC, 24 hrs | 5 | 90 | 5 |
| 16 | **1c** | 1 eq $SnCl_4$, DCE, 0ºC, 20ºC, 24 hrs | 0 | 97 | 3 |
| 17 | **1d** | 1 eq $SnCl_4$, DCE, 0ºC, 20ºC, 24 hrs | 2 | 95 | 3 |
| 18 | **1e** | 1 eq $SnCl_4$, DCE, 0ºC, 20ºC, 24 hrs | 0 | 97 | 3 |
| 19 | **1f** | 1 eq $SnCl_4$, DCE, 0ºC, 20ºC, 24 hrs | 0 | 97 | 3 |

The ratio of starting **1**, product **2** and decomposition products were determined using TLC and PMR spectroscopy.

The 2′,3′-*O*-TIPDS-derivatives **2** may be used for the preparation 5'-substituted nucleosides. Thus **1b** was treated with 2 equivalents of TMSOTf in 1,2-dichloroethane at 0° C. After 12 hrs when isomerization according to TLC was complete 1-*O*-acetyl-2,3,5-tri-O-benzoyl-β-D-ribofuranose was added and the reaction mixture was kept at 0° C for 20 hr. Disaccharide nucleoside **3b** was obtained in 60 % yield, further deblocking gave the known 5'-*O*-β-D-ribofuranosylafenosine **4b**.[32]

## Conclusions

Trimethylsilyl trifluoromethanesulfonate catalyzes effective isomerization of 3′,5′-*O*-TIPDS nucleosides (**1**) in 1,2-dicloroethane at 0°C into 2′,3′-*O*-TIPDS-derivatives (**2**), which can be obtained in 55-90% yields. This reaction is in line with the proposed mechanism[36] of acid-catalysed cleavage of the silyl ether bond formed by primary 5'-hydroxyl group followed by

formation of 2′,3′-*O*-TIPDS-nucleosides. As a result the thermodynamically less stable eight-membered ring transformed to the more stable seven-membered ring. On the other hand 3′,5′-*O*-TIPDS-nucleosides (**1**) were found to be stable in the presence of tin tetrachloride. Only in the case of uridine derivative **1a** substantial amount of isomerization product **2a** was formed.

## Experimental Section

**General Procedures.** Column chromatography was performed on silica gel Kieselgel 60 (0.063-0.200 mm, Merck). (0.040-0.063 mm), TLC was carried out on Alugram SIL G/$UV_{254}$ (Macherey-Nagel) with detection by UV and the following solvent systems (compositions expressed as *v*/*v*): methylene chloride – ethanol 98:2 (A); methylene chloride – ethanol 95:5 (B), detection by UV light. NMR Spectra: Bruker AMX 400 NMR spectrometer and Bruker Avance 300 NMR spectrometer; at 27°C. Chemical shifts δ in ppm were measured relative to the solvent signals ($^1$H and $^{13}$C). $^{13}$C NMR spectra were measured with proton decoupling and all carbon signals appeared as singlets. The coupling constants (J) are given in Hz. The signals were assigned using double resonance techniques. Mass spectrometry and exact mass measurements of the nucleoside intermediates were performed on a quadrupole/othogonal-acceleration time-of-flight tandem mass spectrometer (Q-Tof-2, Micromass, Manchester, UK) equipped with a standard electrospray ionization (ESI) interface.

**3',5'-*O*-(1,1,3,3-Tetraisopropyldisiloxane-1,3-diyl)nucleosides (1)** were prepared according to literature.[1,2]

**3',5'-*O*-(1,1,3,3-Tetraisopropyldisiloxane-1,3-diyl)uridine (1a).** $R_f$ 0.35 (A). $^1$H-NMR (300 MHz, DMSO-$d_6$): 11.36 brs (1H, NH), 7.68 d (1H, $J_{6,5}$ = 8.0, H-6), 5.58 d (1H, $J_{2'\text{-}OH,\ 2'}$ = 4.4, 2'-OH), 5.54 d (1H, $J_{1',2'}$ = 0.6, H-1'), 5.52 d (1H, $J_{5,6}$ = 8.0, H-5), 4.16 dd (1H, $J_{3',2'}$ = 4.7, $J_{3',4'}$ = 8.3, H-3'), 4.13 m (2H, H-2', H-5'a), 3.98 ddd (1H, $J_{4',3'}$ = 8.3, $J_{4',5'a}$ = 2.2, $J_{4',5'b}$ = 2.5, H-4'), 3.91 dd (1H, $J_{5'b,4'}$ = 2.5, $J_{5'a,5'b}$ = -13.0, H-5'b), 1.18-0.75 m (28H, iPr). $^{13}$C-NMR (75 MHz, DMSO-$d_6$): 163.20 (C-4); 150.14 (C-2); 139.80 (C-6); 100.95 (C-5); 90.52 (C-1'); 80.88 (C-4'); 73.52 (C-2'); 68.79 (C-3'); 60.22 (C-5'); 17.37, 17.24, 17.19, 17.12, 16.96, 16.87, 16.84, 16.78, 12.74, 12.37, 12.32, 11.95 (iPr).

***N*$^6$-Benzoyl-3',5'-*O*-(1,1,3,3-Tetraisopropyldisiloxane-1,3-diyl)adenosine (1b).** $R_f$ 0.36 (A). $^1$H-NMR (300 MHz, DMSO-$d_6$): 11.22 brs (1H, NH), 8.65 s (1H, H-8), 8.52 s (1H, H-2), 8.02 d (2H, *J* = 7.2, *o*-Bz), 7.63 t (1H, *J* = 7.2, *p*-Bz), 7.54 t (2H, *J* = 7.2, *m*-Bz), 5.99 d (1H, $J_{1',2'}$ = 1.0, H-1'), 5.67 d (1H, $J_{2'\text{-}OH,\ 2'}$ = 4.6, 2'-OH), 4.81 dd (1H, $J_{3',2'}$ = 5.2, $J_{3',4'}$ = 8.2, H-3'), 4.63 ddd (1H, $J_{2',1'}$ = 1.0, $J_{2',2'\text{-}OH,}$ = 4.6, $J_{2',3'}$ = 5.2, H-2'), 4.03 m (2H, H-4', H-5'a), 3.93 dd (1H, $J_{5'b,4'}$ = 2.5, $J_{5'a,5'b}$ = -12.5, H-5'b), 1.16-0.82 m (28H, iPr). $^{13}$C-NMR (75 MHz, DMSO-$d_6$): 165.67 (C=O), 151.43 (C-2), 151.43 (C-6), 150.53 (C-4), 143.08 (C-8), 133.38, 132.45, 128.50, 128.45 (Ph), 125.98 (C-5), 89.54 (C-1'), 80.97 (C-4'), 73.40 (C-2'), 69.88 (C-3'), 60.74 (C-5'), 17.35, 17.19, 17.16, 17.04, 16.92, 16.84, 12.76, 12.46, 12.27, 12.07 (iPr).

**$N^4$-Benzoyl-3',5'-*O*-(1,1,3,3-tetraisopropyldisiloxane-1,3-diyl)cytidine (1c).** $R_f$ 0.34 (A). $^1$H-NMR (300 MHz, DMSO-$d_6$): 11.27 brs (1H, NH), 8.21 d (1H, $J_{6,5}$ = 7.5, H-6), 8.00 d (2H, $J$ = 7.2, *o*-Bz), 7.63 t (1H, $J$ = 7.2, *p*-Bz), 7.52 t (2H, $J$ = 7.2, *m*-Bz), 7.37 d (1H, $J_{5,6}$ = 7.5, H-5), 5.80 d (1H, $J_{2'\text{-}OH,\ 2'}$ = 3.9, 2'-OH), 5.64 s (1H, H-1'), 4.24 d (1H, $J_{5'a,5'b}$ = -13.2, H-5'a), 4.11 m (3H, H-2', H-3', H-4'), 3.95 d (1H, $J_{5'b,5a'}$ = -13.2, H-5'b), 1.15-0.88 m (28H, iPr). $^{13}$C-NMR(75 MHz, DMSO-$d_6$): 167.30 (C=O); 163.17 (C-4); 154.15 (C-2); 143.72 (C-6); 132.98, 132.75, 128.44, (Ph); 95.59 (C-5); 91.30 (C-1'); 80.91 (C-4'); 73.81 (C-2'); 68.05 (C-3'); 59.80 (C-5'); 17.39, 17.26, 17.20, 17.12, 16.91, 16.87, 16.78, 16.76, 12.71, 12.49, 12.35, 11.92 (iPr).

**$N^2$-Isobutyryl-3',5'-*O*-(1,1,3,3-tetraisopropyldisiloxane-1,3-diyl)guanosine (1d).** $R_f$ 0.30 (A). $^1$H-NMR (300 MHz, DMSO-$d_6$): 12.12 brs (1H, NH-1), 11.74 brs (1H, NH-2), 8.05 s (1H, H-8), 5.79 d (1H, $J_{1',2'}$ = 1.1, H-1'), 5.69 d (1H, $J_{2'\text{-}OH,2'}$ = 4.8, 2'-OH), 4.35 dd (1H, $J_{3',2'}$ = 4.9, $J_{3',4'}$ = 7.9, H-3'), 4.31 ddd (1H, $J_{2',1'}$ = 1.1, $J_{2',2'\text{-}OH}$ = 4.8, $J_{2',3'}$ = 4.9, H-2'), 4.12 dd (1H, $J_{5'a,4'}$ = 3.0, $J_{5'a,5'b}$ = -12.9, H-5'a), 4.04 ddd (1H, $J_{4',3'}$ = 7.9, $J_{4',5'a}$ = 3.0, $J_{4',5'b}$ = 2.6, H-4'), 3.95 dd (1H, $J_{5'b,4'}$ = 2.6, $J_{5'b,5'a}$ = -12.9, H-5'b), 2.78 sept (1H, $J$ = 6.9, iBu), 1.12 d (6H, $J$ = 6.9, iBu), 1.08-0.80 m (28H, iPr). $^{13}$C- NMR (75 MHz, DMSO-$d_6$): 180.21 (C=O), 154.83 (C-6), 148.28 (C-2), 148.01 (C-4), 136.22 (C-8), 120.39 (C-5), 88.17 (C-1'), 81.22 (C-4'), 74.01 (C-2'), 69.51 (C-3'), 60.61 (C-5'), 34.72 (iBu), 18.88, 18.83 (iBu) 17.36, 17.20, 17.15, 16.97, 16.90, 16.85, 16.80, 12.74, 12.44, 12.32, 12.02 (iPr).

**3',5'-*O*-(1,1,3,3-Tetraisopropyldisiloxane-1,3-diyl)adenosine (1e).** $R_f$ 0.28 (B). $^1$H-NMR (400 MHz, DMSO-$d_6$): 8.21 s (1H, H-8), 8.08 s (1H, H-2), 7.33 brs (2H, $NH_2$), 5.87 s (1H, H-1'), 5.62 d (1H, $J_{2'\text{-}OH,2'}$ = 4.6, 2'-OH), 4.80 dd (1H, $J_{3',2'}$ = 5.1, $J_{3',4'}$ = 8.3, H-3'), 4.52 dd (1H, $J_{2',2'\text{-}OH}$ = 4.6, $J_{2',3'}$ = 5.1, H-2'), 4.06 dd (1H, $J_{5'a,4'}$ = 3.1, $J_{5'a,5'b}$ = -12.3, H-5'a), 3.99 ddd (1H, $J_{4',3'}$ = 8.3, $J_{4',5'a}$ = 3.1, $J_{4',\ 5'b}$ = 2.1, H-4'), 3.93 dd (1H, $J_{5'b,4'}$ = 2.1, $J_{5'b,5'a}$ = -12.3, H-5'b), 1.12-0.96 m (28H, iPr). $^{13}$C-NMR (100 MHz, DMSO-$d_6$): 156.09 (C-6), 152.48 (C-8), 148.62 (C-4), 139.20 (C-2), 119.25 (C-5), 89.33 (C-1'), 80.75 (C-4'), 73.64 (C-2'), 69.81 (C-3'), 60.80 (C-5'), 17.36, 17.23, 17.16, 17.00, 16.91, 16.82, 12.73, 12.44, 12.23, 12.06 (iPr).

**3',5'-*O*-(1,1,3,3-Tetraisopropyldisiloxane-1,3-diyl)cytidine (1f).** $R_f$ 0.16 (B). $^1$H-NMR (400 MHz, DMSO-$d_6$): 7.70 d (1H, $J_{6,5}$ = 7.5, H-6), 7.16 brs (1H, $NH_2$), 7.07 brs (1H, $NH_2$), 5.68 d (1H, $J_{5,6}$ = 7.5, H-5), 5.57 d (1H, $J_{2'\text{-}OH,\ 2'}$ = 4.4, 2'-OH), 5.55 s (1H, H-1'), 4.15 dd (1H, $J_{5'a,4'}$ = 1.0, $J_{5'a,5'b}$ = -12.8, H-5'a), 4.08 dd (1H, $J_{3',2'}$ = 4.4, $J_{3',4'}$ = 9.0, H-3'), 4.00 ddd (1H, $J_{4',3'}$ = 9.0, $J_{4',5'a}$ = 1.0, $J_{4',\ 5'b}$ = 2.5, H-4'), 3.93 t (1H, $J_{2',2'\text{-}OH}$ = $J_{2',3'}$ = 4.4, H-2'), 3.91 dd (1H, $J_{5'b,4'}$ = 2.5, $J_{5'b,5'a}$ = -12.8, H-5'b), 1.08-0.92 m (28H, iPr). $^{13}$C- NMR (100 MHz, DMSO-$d_6$): 165.69 (C-4), 154.81 (C-2), 139.91 (C-6), 93.27 (C-5), 90.72 (C-1'), 81.51 (C-4'), 74.11 (C-2'), 68.52 (C-3'), 60.07 (C-5'), 17.37, 17.24, 17.18, 17.11, 16.84, 16.76, 12.77, 12.46, 12.37, 11.97 (iPr).

**2',3'-*O*-(1,1,3,3-Tetraisopropyldisiloxane-1,3-diyl)uridine (2a).** To a cool solution (0°) of nucleoside **1a** (620 mg, 1.28 mmol) in 1,2-dichloroethane (20 ml) 2M solution of trimethylsilyl trifluoromethanesulfonate in 1,2-dichloroethane (1.28 ml, 2.56 mmol) was added under nitrogen atmosphere. The reaction mixture was stirred at 0°C for 1.5 hrs. Methylene chloride (50 ml) and 10% aqueous solution of sodium bicarbonate (20 ml) were added and the suspension was stirred at 0°C for 15 min. The organic layer was separated, washed with water (20 ml), dried over

anhydrous sodium sulfate, evaporated in vacuo and purified by column chromatography on silica gel (30 g). The column was washed with methylene chloride (300 ml), and then eluted with methylene chloride - ethanol 98:2. Fractions containing the product were evaporated and dried to give **2a** as a white amorphous powder. Yield 330 mg (55 %). $R_f$ 0.24 (A). $^1$H-NMR (300 MHz, DMSO-$d_6$): 11.33 s (1H, NH), 7.95 d (1H, $J_{6,5}$ = 8.1, H-6), 5.79 d (1H, $J_{1',2'}$ = 4,1, H-1'), 5.64 d (1H, $J_{5,6}$ = 8.1, H-5), 5.25 t (1H, $J_{5'\text{-}OH,\ 5'a}$ = $J_{5'\text{-}OH,\ 5'b}$ = 5.0, 5'-OH), 4.52 dd (1H, $J_{2',1'}$ = 4,1, $J_{2',3'}$ = 4.4, H-2'), 4.37 dd (1H, $J_{3',2'}$ = 4.4, $J_{3',4'}$ = 5.0, H-3'), 3.94 ddd (1H, $J_{4',3'}$ = 5.0, $J_{4',5'a}$ = 3.3, $J_{4',5'b}$ = 3.0, H-4'), 3.71 ddd (1H, $J_{5'a,4'}$ = 3.3, $J_{5'a,5'\text{-}OH}$ = 5.0, $J_{5'a,5'b}$ = -12.2, H-5'a), 3.58 ddd (1H, $J_{5'b,4'}$ = 3.0, $J_{5'b,5'\text{-}OH}$ = 5.0, $J_{5'b,5'a}$ = -12.2, H-5'b), 1.12-0.87 m (28H, iPr). $^{13}$C-NMR (75 MHz, DMSO-$d_6$): 163.62 (C-4); 150.95 (C-2); 140.57 (C-6); 102.10 (C-5); 88.94 (C-1'); 85.00 (C-4'); 76.18 (C-2'); 71.87 (C-3'); 60.22 (C-5'); 17.73, 17.58, 17.54, 17.45, 17.39, 17.28, 12.95, 12.69, 12.42 (iPr). LSI-MS: ($C_{21}H_{38}N_2O_7Si_2$ - $H^+$) found 485.2140. Calc. 485.2139.

***N*$^6$-Benzoyl-2',3'-*O*-(1,1,3,3-Tetraisopropyldisiloxane-1,3-diyl)adenosine (2b).** Analogous conversion of **1b** (620 mg, 1.01 mmol) was carried out in the presence of trimethylsilyl trifluoromethanesulfonate (2M solution in 1,2-dichloroethane, 1.51 ml, 3.03 mmol) in 1,2-dichloroethane (20 ml) at 0° for 3 hrs. After column chromatography on silica gel (30 g) **2b** was obtained as a white powder. The column was washed with methylene chloride (300 ml), and then eluted with methylene chloride - ethanol 99:1. Fractions containing the product were evaporated and dried to give **2b** as a white amorphous powder. Yield 558 mg (90 %). $R_f$ 0.41 (A). 1H-NMR (300 MHz, DMSO-$d_6$): 11.23 s (1H, NH), 8.78 s (1H, H-8), 8.76 s (1H, H-2), 8.05 d (2H, $J$ = 7.2, *o*-Bz), 7.66 t (1H, $J$ = 7.2, *p*-Bz), 7.57 t (2H, $J$ = 7.2, *m*-Bz), 6.13 d (1H, $J_{1',2'}$ = 5.7, H-1'), 5.25 dd (1H, $J_{2',3'}$ = 4.9, H-2'), 5.15 t (1H, $J_{5'\text{-}OH,\ 5'a}$ = $J_{5'\text{-}OH,\ 5'b}$ = 5.2, 5'-OH), 4.68 dd (1H, $J_{3',2'}$ = 4.9, $J_{3',4'}$ =4.0, H-3'), 4.09 ddd (1H, $J_{4',3'}$ = 4.0, $J_{4',5'a}$ = 4.8, $J_{4',5'b}$ = 4.0, H-4'), 3.73 ddd (1H, $J_{5'a,4'}$ =4.8, $J_{5'a,5'\text{-}OH}$ = 5.2, $J_{5'a,5'b}$ = -12.0, H-5'a), 3.62 ddd (1H, $J_{5'b,4'}$ = 4.0, $J_{5'b,5'\text{-}OH}$ = 5.2, $J_{5'b,5'a}$ = -12.0, H-5'b), 1.17-0.95 m (28H, iPr). $^{13}$C- NMR (75 MHz, DMSO-$d_6$): 166.09 (C=O), 152.62 (C-2), 152.23 (C-6), 150.96 (C-4), 143.39 (C-8), 133.75, 132.96, 128.95, 128.92 (Ph), 126.29 (C-5), 88.04 (C-1'), 86.26 (C-4'), 76.07 (C-2'), 72.82 (C-3'), 61.16 (C-5'), 17.55, 17.49, 17.40, 17.24, 17.13, 13.11, 12.81, 12.71, 12.45 (iPr). LSI-MS: ($C_{29}H_{43}N_5O_6Si_2$ + $H^+$) found 614.2828 . Calc. 614.2830.

***N*$^4$-Benzoyl-2',3'-*O*-(1,1,3,3-Tetraisopropyldisiloxane-1,3-diyl)cytidine (2c).** Analogous conversion of **1c** (564 mg, 0.96 mmol) was carried out in the presence of trimethylsilyl trifluoromethanesulfonate (2M solution in 1,2-dichloroethane, 0.96 ml, 1.92 mmol) in 1,2-dichloroethane (20 ml) at 0°C for 4 hrs. After column chromatography on silica gel (30 g) **2c** was obtained as a white powder. The column was washed with methylene chloride (300 ml), and then eluted with methylene chloride - ethanol 99:1. Fractions containing the product were evaporated and dried to give **2c** as a white amorphous powder. Yield 335 mg (60%) as a white powder. $R_f$ 0.43 (A). $^1$H-NMR (300 MHz, DMSO-$d_6$): 11.22 brs (1H, NH), 8.51 d (1H, $J_{6,5}$ = 7.4, H-6), 8.00 d (2H, $J$ = 7.2, *o*-Bz), 7.63 t (1H, $J$ = 7.2, *p*-Bz), 7.52 t (2H, $J$ = 7.2, *m*-Bz), 7.34 d (1H, $J_{5,6}$ = 7.4, H-5), 5.86 d (1H, $J_{1',2'}$ = 2.6, H-1'), 5.32 dd (1H, $J_{5'\text{-}OH,\ 5'a}$ = 4.8, $J_{5'\text{-}OH,5'b}$ = 5.0, 5'-OH), 4.56 dd (1H, $J_{2',1'}$ = 2.6, $J_{2',3'}$ = 4.3, H-2'), 4.38 dd (1H, $J_{3',2'}$ = 4.3, $J_{3',4'}$ = 7.1, H-3'), 4.01 ddd (1H, $J_{4',3}$ =

7.1, $J_{4',5'a}$ = 2.9, $J_{4',5'b}$ = 3.0, H-4'), 3.84 ddd (1H, $J_{5'a,4'}$ = 2.9, $J_{5'a,5'\text{-}OH}$ = 4.8, $J_{5'a,5'b}$ = -12.4, H-5'a), 3.64 ddd (1H, $J_{5'b,4'}$ = 3.0, $J_{5'b,5'\text{-}OH}$ = 5.0, $J_{5'b,5'a}$ = -12.4, H-5'b), 1.11-0.93 m (28H, iPr). $^{13}$C-NMR (75 MHz, DMSO-$d_6$): 167.35 (C=O); 163.10 (C-4); 154.38 (C-2); 144.87 (C-6); 133.22, 132.73, 128.45 (Ph); 96.09 (C-5); 90.46 (C-1'); 84.21 (C-4'); 76.30 (C-2'); 70.79 (C-3'); 59.13 (C-5'); 17.23, 17.17, 17.11, 17.07, 17.01, 16.95, 16.87, 12.74, 12.46, 12.31, 12.02 (iPr). LSI-MS: ($C_{28}H_{43}N_3O_7Si_2$ - $H^+$) found 588.2564. Calc. 588.2561.

***N*$^2$-Isobutyryl-2',3'-*O*-(1,1,3,3-Tetraisopropyldisiloxane-1,3-diyl)guanosine (2d).** Analogous conversion of **1d** (603 mg, 1.01 mmol) was carried out in the presence of trimethylsilyl trifluoromethanesulfonate (2M solution in 1,2-dichloroethane, 1.51 ml, 3.03 mmol) in 1,2-dichloroethane (20 ml) at 0°C for 2 hrs. After column chromatography on silica gel (30 g) **2d** was obtained as a white powder. The column was washed with methylene chloride (300 ml), and then eluted with methylene chloride - ethanol 98:2. Fractions containing the product were evaporated and dried to give **2d** as a white amorphous powder. Yield 446 mg (74 %). $R_f$ 0.28 (A). $^1$H-NMR (300 MHz, DMSO-$d_6$): 12.12 brs (1H, NH-1), 11.59 brs (1H, NH-2), 8.32 s (1H, H-8), 5.83 d (1H, $J_{1',2'}$ = 6.5, H-1'), 5.16 t (1H, $J_{5'\text{-}OH,5'a}$ = $J_{5'\text{-}OH,5'b}$ = 5.5, 5'-OH), 4.95 dd (1H, $J_{2',1'}$ = 6.5, $J_{2',3'}$ = 4.9, H-2'), 4.58 dd (1H, $J_{3',2'}$ = 4.9, $J_{3',4'}$ = 3.1, H-3'), 4.01 ddd (1H, $J_{4',3'}$ = 3.1, $J_{4',5'a}$ = 5.2, $J_{4',5'b}$ = 4.6, H-4'), 3.63 ddd (1H, $J_{5'a,4'}$ = 5.2, $J_{5'a,5'\text{-}OH}$ = 5.5, $J_{5'a,5'b}$ = -11.9, H-5'a), 3.56 ddd (1H, $J_{5'b,4'}$ = 4.6, $J_{5'b,5'\text{-}OH}$ = 5.5, $J_{5'b,5'a}$ = -11.9, H-5'b), 2.78 sept (1H, $J$ = 6.9, iBu), 1.12 d (6H, $J$ = 6.9, iBu), 1.08-0.98 m (28H, iPr). $^{13}$C-NMR (75 MHz, DMSO-$d_6$): 180.15 (C=O), 154.79 (C-6), 149.09 (C-2), 148.33 (C-4), 137.33 (C-8), 120.22 (C-5), 86.10 (C-1'), 85.87 (C-4'), 75.44 (C-2'), 72.22 (C-3'), 60.78 (C-5'), 34.70 (iBu), 18.87, 18.81 (iBu) 17.34, 17.17, 17.10, 17.07, 16.97, 16.81, 12.63, 12.37, 12.18, 12.13 (iPr). LSI-MS: ($C_{26}H_{45}N_5O_7Si_2$ - $H^+$) found 594.2782. Calc. 594.2779.

**2',3'-*O*-(1,1,3,3-Tetraisopropyldisiloxane-1,3-diyl)adenosine (2e).** Analogous conversion of **1e** (550 mg, 1.08 mmol) was carried out in the presence of trimethylsilyl trifluoromethanesulfonate (2M solution in 1,2-dichloroethane, 1.51 ml, 3.03 mmol) in 1,2-dichloroethane (20 ml) at 0°C for 4 hrs. After column chromatography on silica gel (30 g) **2e** was obtained as a white powder. The column was washed with methylene chloride (300 ml), and then eluted with methylene chloride - ethanol 97:3. Fractions containing the product were evaporated and dried to give **2e** as a white amorphous powder. Yield 396 mg (72 %). $R_f$ 0.29 (B). $^1$H-NMR (400 MHz, DMSO-$d_6$): 8.38 s (1H, H-8), 8.13 s (1H, H-2), 7.23 brs (2H, $NH_2$), 5.96 d (1H, $J_{1',2'}$ = 5.9, H-1'), 5.33 dd (1H, $J_{5'\text{-}OH,5'a}$ = 5.3, $J_{5'\text{-}OH,5'b}$ = 5.9, 5'-OH), 5.07 dd (1H, $J_{2',1'}$ = 5.9, $J_{2',3'}$ = 4.4, H-2'), 4.63 dd (1H, $J_{3',2'}$ = 4.4, $J_{3',4'}$ = 4.4, H-3'), 4.06 ddd (1H, $J_{4',3'}$ = 4.4, $J_{4',5'a}$ = 4.0, $J_{4',5'b}$ = 4.4, H-4'), 3.70 ddd (1H, $J_{5'a,4'}$ = 4.0, $J_{5'a,5'\text{-}OH}$ = 5.3, $J_{5'a,5'b}$ = -11.8, H-5'a), 3.58 ddd (1H, $J_{5'b,4'}$ = 4.4, $J_{5'b,5'\text{-}OH}$ = 5.9, $J_{5'b,5'a}$ = -11.8, H-5'b), 1.10-0.92 m (28H, iPr). $^{13}$C-NMR (100 MHz, DMSO-$d_6$): 156.14 (C-6), 152.56 (C-8), 149.16 (C-4), 139.71 (C-2), 119.25 (C-5), 87.79 (C-1'), 85.84 (C-4'), 75.45 (C-2'), 72.59 (C-3'), 61.08 (C-5'), 17.31, 17.16, 17.08, 16.93, 16.80, 12.67, 12.32, 12.29, 12.09 (iPr). LSI-MS: ($C_{22}H_{39}N_5O_5Si_2$ - $H^+$) 508.2414. Calc. 508.2411.

**2',3'-*O*-(1,1,3,3-Tetraisopropyldisiloxane-1,3-diyl)cytidine (2f).** Analogous conversion of 1f (500 mg, 1.03 mmol) was carried out in the presence of trimethylsilyl trifluoromethanesulfonate

(2M solution in 1,2-dichloroethane, 1.51 ml, 3.03 mmol) in 1,2-dichloroethane (20 ml) at 0°C for 2 hrs. After column chromatography on silica gel (30 g) **2f** was obtained as a white powder. The column was washed with methylene chloride (300 ml), and then eluted with methylene chloride - ethanol 95:5. Fractions containing the product were evaporated and dried to give **2f** as a white amorphous powder. Yield 275 mg (55 %). $R_f$ 0.12 (B). $^1$H-NMR (400 MHz, DMSO-$d_6$): 7.88 d (1H, $J_{6,5}$ = 7.5, H-6), 7.15 brs (1H, $NH_2$), 7.07 brs (1H, $NH_2$), 5.79 d (1H, $J_{1',2'}$ = 3.7, H-1'), 5.71 d (1H, $J_{5,6}$ = 7.5, H-5), 5.15 t (1H, $J_{5'\text{-}OH,5'a} = J_{5'\text{-}OH,5'b}$ = 5.3, 5'-OH), 4.41 dd (1H, $J_{2',1'}$ = 3.7, $J_{2',3'}$ = 4.4, H-2'), 4.34 dd (1H, $J_{3',2'}$ = 4.4, $J_{3',4'}$ = 5.9, H-3'), 3.91 ddd (1H, $J_{4',3'}$ = 5.9, $J_{4',5'a}$ = 3.1, $J_{4',5'b}$ = 3.4, H-4'), 3.71 ddd (1H, $J_{5'a,4'}$ = 3.1, $J_{5'a,5'\text{-}OH}$ = 5.3, $J_{5'a,5'b}$ = -12.1, H-5'a), 3.57 ddd (1H, $J_{5'b,4'}$ = 3.4, $J_{5'b,5'\text{-}OH}$ = 5.3, $J_{5'b,5'a}$ = -12.1, H-5'b), 1.05-0.92 m (28H, iPr). $^{13}$C-NMR (100 MHz, DMSO-$d_6$): 165.57 (C-4); 155.06 (C-2); 141.04 (C-6); 93.92 (C-5); 89.54 (C-1'); 83.96 (C-4'); 75.96 (C-2'); 71.45 (C-3'); 59.87 (C-5'); 17.23, 17.09, 17.04, 16.99, 16.93, 16.83, 12.63, 12.51, 12.30, 12.02 (iPr). LSI-MS: ($C_{21}H_{39}N_3O_6Si_2$ - $H^+$) found 484.2302. Calc. 484.2299.

**Investigation of isomerization of 3′,5′-*O*-(tetraisopropyldisiloxane-1,3-diyl)nucleosides (1) in the presence of different catalysts. (see Table 2 for details).** The catalyst was added to a solution of nucleoside **1** (0.5 mmol) in 1,2-dichloroethane or acetonitrile (10 ml) under nitrogen atmosphere. The reaction mixture was stirred at appropriate temperature for 24 hrs. Methylene chloride (20 ml) and 10% aqueous solution of sodium bicarbonate (10 ml) were added and the suspension was stirred for 15 min. The organic layer was separated, washed with water (20 ml), dried over anhydrous sodium sulfate and evaporated in vacuo to dryness. The ratio of **1**:**2** and the presence of decomposition products were determined with $^1$H-NMR spectroscopy and TLC in systems A and B.

***N*$^6$-Benzoyl-9-[2',3'-*O*-(1,1,3,3-tetraisopropyldisiloxane-1,3-diyl)-5'-*O*-(2,3,5-tri-*O*-benzoyl-β-D-ribofuranosyl)- β-D-ribofuranosyl]adenine (3b).** To a cool solution (0° C) of nucleoside **1b** (704 mg, 1.15 mmol) in 1,2-dichloroethane (25 ml) 2M solution of trimethylsilyl trifluoromethanesulfonate in 1,2-dichloroethane (1.15 ml, 2.29 mmol) was added under nitrogen atmosphere. The reaction mixture was stirred at 0°C for 12 hrs. After addition of 1-*O*-acetyl-2,3,5-tri-*O*-benzoyl-β-D-ribofuranose (752 mg, 1.49 mmol) the resulting solution was kept at 0°C for 20 hrs. Methylene chloride (50 ml) and 10% aqueous solution of sodium bicarbonate (25 ml) were added and the suspension was stirred at 0°C for 15 min. The organic layer was separated, washed with water (25 ml), dried over anhydrous sodium sulfate, evaporated in vacuo and purified by column chromatography on silica gel (40 g). The column was washed with methylene chloride (300 ml), and then eluted with methylene chloride - ethanol 99:1. Fractions containing the product were evaporated and dried to give **3b** as a foam. Yield 729 mg (60 %). $R_f$ 0.66 (A). $^1$H-NMR (400 MHz, $CDCl_3$): 8.80 s (1H, H-8), 8.36 s (1H, H-2), 8.05-7.85 m (8H, o-Bz), 7.64-7.23 m (12H, m,p-Bz), 6.09 d (1H, $J_{1',2'}$ = 3.7, H-1', Ado), 5.77 dd (1H, $J_{3',2'}$ = 4.7, H-3', Rib), 5.64 d (1H, $J_{2',3'}$ = 4.7, H-2', Rib), 5.35 s (1H, H-1', Rib), 5.14 dd (1H, $J_{2',1'}$ = 3.7, $J_{2',3'}$ = 4.4, H-2', Ado), 4.72 ddd (1H, $J_{4',3'}$ = 10.0, $J_{4',5'a}$ = 4.4, $J_{4',5'b}$ = 5.9, H-4', Rib), 4.68 dd (1H, $J_{3',2'}$ = 4.4, $J_{3',4'}$ = 5.6, H-3', Ado), 4.60 dd (1H, $J_{5'a,4'}$ = 4.4, $J_{5'a,5'b}$ = -11.8, H-5'a, Rib), 4.56 dd (1H, $J_{5'b,4'}$ = 5.9, $J_{5'b,5'a}$ = -11.8, H-5'b, Rib), 4.35 ddd (1H, $J_{4',3'}$ = 5.6, $J_{4',5'a}$ = 2.8, $J_{4',5'b}$ = 5.0, H-4', Ado), 4.17

dd (1H, $J_{5'a,4'}$ = 2.8, $J_{5'a,5'b}$ = -11.5, H-5'a, Ado), 3.82 dd (1H, $J_{5'b,4'}$ = 5.0, $J_{5'b,5'a}$ = -11.5, H-5'b, Ado), 1.26-0.92 m (28H, iPr). $^{13}$C-NMR (400 MHz, $CDCl_3$): 166.23, 165.43, 165.28, 164.67 (C=O), 152.37 (C-2), 151.63 (C-6), 149.59 (C-4), 142.17 (C-8), 139.41, 133.79, 133.65, 133.53, 133.22, 132.91, 129.91, 129.87, 128.99, 128.60, 128.48, 128.15 (Ph), 114.20 (C-5), 106.23 (C-1′, Rib), 90.15 (C-1', Ado), 83.66 (C-4', Ado), 79.51 (C-4', Rib), 75.99 (C-2', Rib), 75.48 (C-2', Ado), 72.71 (C-3', Rib), 72.59 (C-3', Ado), 67.41 (C-5', Rib), 65.24 (C-5', Ado), 17.57, 17.52, 17.35, 17.30, 17.26, 17.18, 17.11, 14.23, 13.41, 13.28, 13.04, 12.90 (iPr). LSI-MS: ($C_{55}H_{64}N_5O_{13}Si_2 + H^+$) found 1058.4036. Calc.1058.4039.

**9-(5'-*O*-β-D-Ribofuranosyl- β-D-ribofuranosyl)adenine (4b).** Disaccharide nucleoside **3b** (600 mg, 0.57 mmol) was dissolved in 0.5M solution of tetrabutylammonium fluoride trihydrate in tetrahydrofuran (3.4 ml, 1.70 mmol), kept at 20°C for 20 min and the solution was concentrated in vacuo and purified by column chromatography on silica gel (30 g). The column was washed with methylene chloride (300 ml), and then eluted with methylene chloride - ethanol 97.5:2.5. Fractions containing the product were evaporated and dried to give $N^6$-benzoyl-9-[5'-O-(2,3,5-tri-O-benzoyl-β-D-ribofuranosyl)- β-D-ribofuranosyl]adenine as a foam. $R_f$ 0.69 (B). $^1$H-NMR (400 MHz, $CDCl_3$): 8.75 s (1H, H-8), 8.51 s (1H, H-2), 8.02-7.92 m (8H, o-Bz), 7.58-7.23 m (12H, m,p-Bz), 6.09 d (1H, $J_{1',2'}$ = 4.7, H-1', Ado), 5.62 dd (1H, $J_{3',2'}$ = 4.4, $J_{3',4'}$ = 5.9, H-3', Rib), 5.60 d (1H, $J_{2',3'}$ = 4.4, H-2', Rib), 5.29 s (1H, H-1', Rib), 4.80 dd (1H, $J_{2',1'}$ = 4.7, $J_{2',3'}$ = 5.3, H-2', Ado), 4.68 ddd (1H, $J_{4',3'}$ = 5.9, $J_{4',3'}$ = 10.0, $J_{4',5'a}$ = 4.4, $J_{4',5'b}$ = 5.6, H-4', Rib), 4.57 dd (1H, $J_{5'a,4'}$ = 4.4, $J_{5'a,5'b}$ = -12.2, H-5'a, Rib), 4.53 dd (1H, $J_{5'b,4'}$ = 5.6, $J_{5'b,5'a}$ = -12.2, H-5'b, Rib), 4.49 dd (1H, $J_{3',2'}$ = 5.3, $J_{3',4'}$ = 4.7, H-3', Ado), 4.37 ddd (1H, $J_{4',3'}$ = 4.7, $J_{4',5'a}$ = 3.4, $J_{4',5'b}$ = 4.1, H-4', Ado), 4.11 dd (1H, $J_{5'a,4'}$ = 3.4, $J_{5'a,5'b}$ = -11.2, H-5'a, Ado), 3.76 dd (1H, $J_{5'b,4'}$ = 4.1, $J_{5'b,5'a}$ = -11.2, H-5'b, Ado). $^{13}$C- NMR (400 MHz, $CDCl_3$): 166.41, 165.60, 165.42, 164.65 (C=O), 152.24 (C-2), 151.23 (C-6), 149.19 (C-4), 142.30 (C-8), 129.94, 129.88, 129.82, 128.99, 128.64, 128.51, 128.24, 129.87, 128.99, 128.60, 128.48, 128.15 (Ph), 114.20 (C-5), 106.09 (C-1′, Rib), 90.24 (C-1', Ado), 84.42 (C-4', Ado), 79.31 (C-4', Rib), 75.45 (C-2', Rib), 74.94 (C-2', Ado), 72.55 (C-3', Rib), 71.44 (C-3', Ado), 67.97 (C-5', Rib), 65.20 (C-5', Ado).

A solution of $N^6$-benzoyl-9-[5'-O-(2,3,5-tri-O-benzoyl-β-D-ribofuranosyl)-β-D-ribofuranosyl]-adenine (300 mg, 0.37 mmol) in 5M solution of ammonia in methanol (10 ml) was kept at 20°C for 3 days and then concentrated in vacuo. The residue was partitioned between methylene chloride (10 ml) and water (20 ml) and the water layer was washed with methylene chloride (3x10 ml). The water layer was concentrated in vacuo, the residue was evaporated with methanol to yield **4b** as a foam. Yield 159 mg (84 %). $R_f$ 0.29 (methylene chloride –ethanol 6:4). The NMR, UV and mass spectra of **4b** were practically the same as those reported earlier.[32]

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## Supplementary Information Available

NMR spectra of compounds **1** and **2** are available as an attachment.

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