ISSN 1070-3632, Russian Journal of General Chemistry, 2007, Vol. 77, No. 4, pp. 589–595. © Pleiades Publishing, Ltd., 2007.
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Azines and Azoles: CXXVII.[1] Glycosylation of 5,7-Dihydro-4*H*-pyrano-[2,3-*d*:6,5-*d*']dipyrimidine-4,6(3*H*)-dione and Its 5-Phenyl-Substituted Analog

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Received October 31, 2006

Abstract — Glycosylation of 5-phenylpyrano[2,3-*d*:6,5-*d*']dipyrimidine-4,6-diones through the corresponding di-*O*-trimethylsilyl derivative with excess 1,2,3,5-tetra-*O*-acetyl-β-*D*-ribofuranose gives a mixture of 3-mono- and 3,7-bis(2,3,5-tri-*O*-acetyl-β-*D*-ribofuranosyl)-5-phenylpyrano[2,3-*d*:6,5-*d*']dipyrimidines; in the reaction with equimolar amounts of the reactants, only the monoriboside is formed. Isomeric N,N'-disubstituted pyranodipyrimidines, as well as mixtures of their mono- and disubstituted derivatives can be separated by fractional crystallization. The alkylation of pyrano[2,3-*d*:6,5-*d*']dipyrimidine-4,6-dione and its 5-phenyl-substituted derivative with 2-oxabutane-1,4-diyl diacetate provides an efficient procedure for the synthesis of acyclic analogs of glycosides based on pyrano[2,3-*d*:6,5-*d*']dipyrimidines.
DOI: 10.1134/S1070363207040159

A large number of synthetic pyrimidine nucleosides are known to exhibit versatile antiviral activity [2]. Introduction of carbohydrate moieties into their molecules is anticipated to enhance the biological effect of these compounds and extend its spectrum due to structural similarity (or dissimilarity) to natural nucleosides. From this viewpoint, interesting are both free glycosides and their substituted analogs, e.g., acetylated derivatives; the presence of acyl groups in the latter could considerably change their lipophilic–hydrophilic balance, so that such compounds could be readily removed from human body by the action of enzymes.

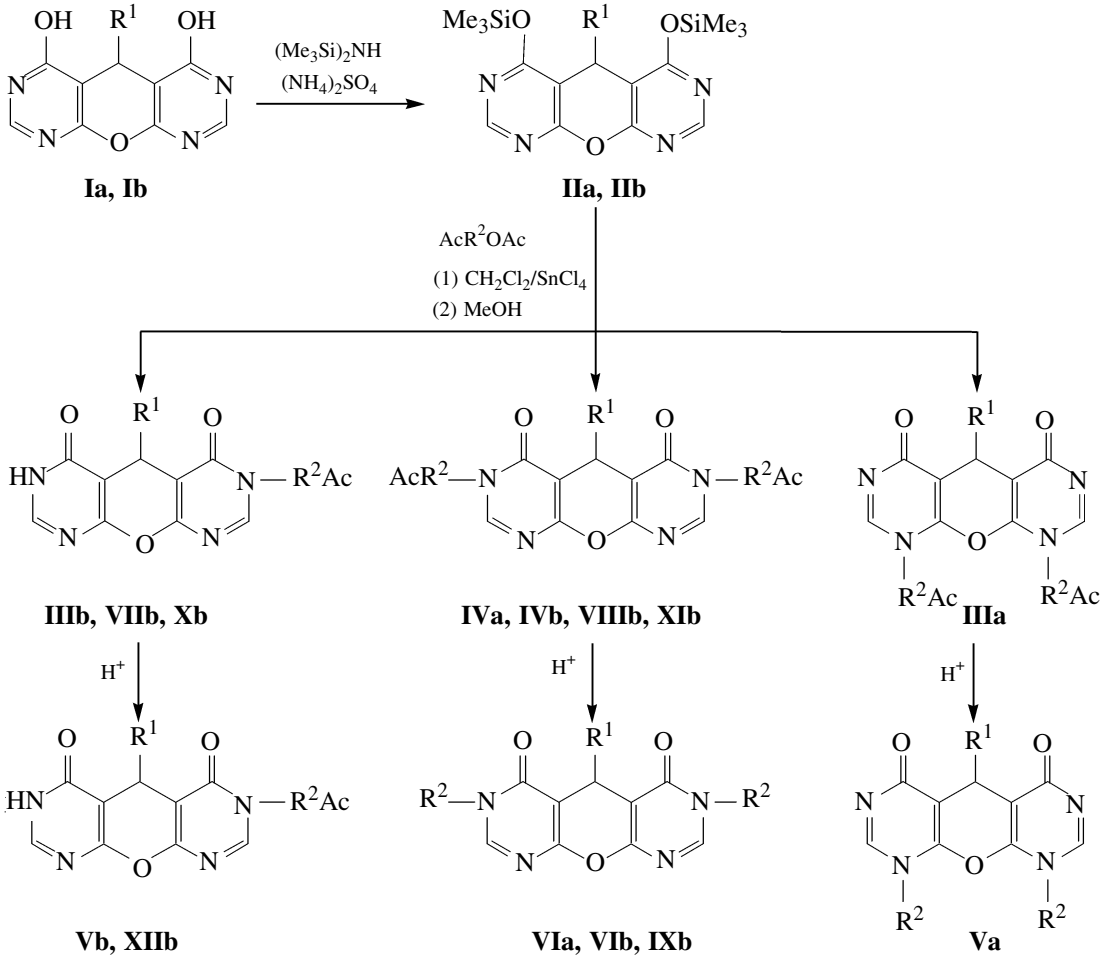
One of the most efficient procedures for the synthesis of nucleosides is the silyl method [3], especially the Vorbrüggen–Niedballa modification [4] which allows direct introduction of a peracylated carbohydrate moiety to the endocyclic nitrogen atom in nitrogen-containing heterocycles with high regioselectivity and stereospecificity.

The silylation of pyrano[2,3-*d*:6,5-*d*']dipyrimidine-4,6-diones **Ia** and **Ib** was carried out by heating in excess hexamethyldisilazane for 3–4 h at 130–140°C in the presence of a catalytic amount of ammonium sulfate to obtain the corresponding bis(trimethylsiloxy)pyranodipyrimidines **IIa** and **IIb** in 80–90% yield (Scheme 1). Compounds **IIa** and **IIb** are crystalline substances that readily undergo hydrolysis on exposure to atmospheric moisture; they are readily soluble in anhydrous benzene, diethyl ether, methylene chloride, and chloroform. The subsequent ribosylation of 4,6-bis(trimethylsiloxy)-5-phenyl-5*H*-pyrano[2,3-*d*:6,5-*d*']dipyrimidine (**IIb**) with 2 equiv of 1,2,3,5-tetra-*O*-acetyl-β-*D*-ribofuranose in the presence of excess (1.2 equiv) of tin(IV) chloride in anhydrous methylene chloride (18°C, 24 h) lead to the formation of a mixture of two acetylated ribosides, 3-mono- and 3,7-bis-(2,3,5-tri-*O*-acetyl-β-*D*-ribofuranosyll)-5-phenyl-5*H*-pyrano[2,3-*d*:6,5-*d*']dipyrimidine-4,6(3*H*,7*H*)-diones **IIIb** and **IVb** in an overall yield of 45% (Scheme 1). When the reaction was complete, the catalyst was removed by adding dimethyl sulfoxide which binds $SnCl_4$ to form the strong $SnCl_4 \cdot 2DMSO$ complex insoluble in methylene chloride.

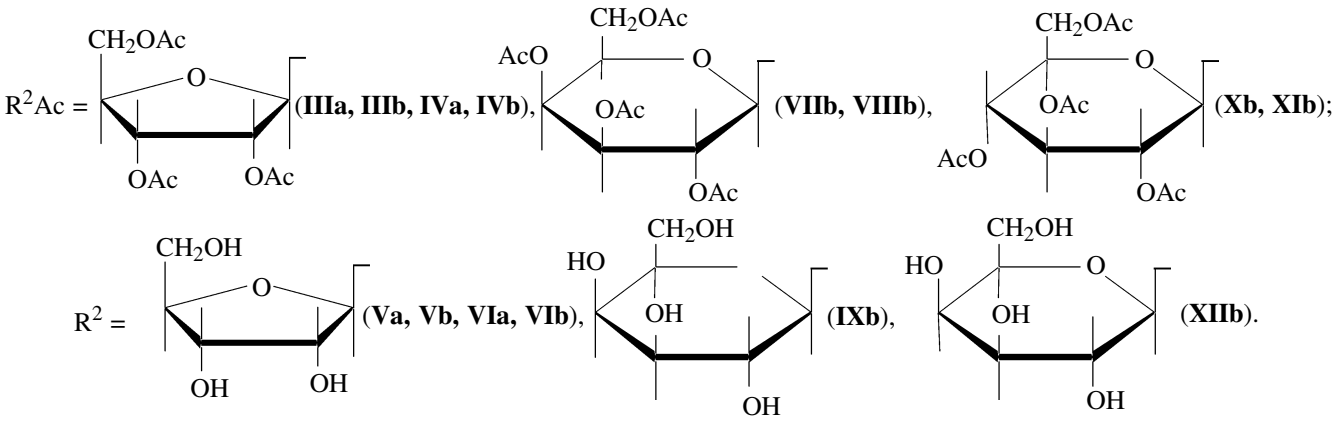
The condensation of 4,6-bis(trimethylsiloxy)-5-phenyl-5*H*-pyrano[2,3-*d*:6,5-*d*']dipyrimidine (**IIb**) with an equimolar amount of 1,2,3,5-tetra-*O*-acetyl-β-*D*-ribofuranose, other conditions being equal, gave only one monosubstituted acetylated riboside **IIIb**. Obviously, the ribosylation of compound **IIb** is a

[1] For communication CXXVI, see [1].

Scheme 1.



R = H (**a**), Ph (**b**);



stepwise process, and pure mono- and diribosyl derivatives of 5-arylpyranodipyrimidines could be obtained by varying the reactant ratio.

3-Mono- and 3,7-bis(triacetylribofuranosyl)-5-phenylpyrano[2,3-*d*:6,5-*d*']dipyrimidine-4,6-diones **IIIb** and **IVb** are readily deacetylated with conserva-

Table 1. UV and ^{1}H NMR spectra of pyrano[2,3-*d*:6,5-*d*']dipyrimidine-based glycosides **III**–**XIV**

Comp. no.	UV spectrum, (EtOH), λ_{max}, nm	^{1}H NMR spectrum (DMSO-d_6), δ, ppm
IIIb	275 sh	1.89–2.06 m (9H, $3COCH_3$), 4.15–4.28 m (3H, $H^{2',3,4}$), 4.97 s (1H, C^5H), 5.37–5.50 m (2H, $C^{5'}H_2$), 5.91–5.95 m (1H, $C^{1'}H$), 7.18–7.25 m (5H, H_{arom}), 8.07–8.47 s (2H, $C^{2,8}H$), 12.66 br.s (1H, NH)
IVa	277 sh	2.05 m (18H, $6CH_3$), 3.45 s (2H, C^5H_2), 4.09–4.19 m (6H, $H^{2',3,4}$), 5.89–5.91 m [2H, $(C^{1'}H)_2$], 8.25 s (2H, $C^{2,8}H$)
IVb	275 sh	1.88–2.09 m (18H, $6COCH_3$), 4.14–4.29 m (6H, $H^{2',3,4}$), 4.99 s (1H, C^5H), 5.37–5.53 m [4H, $(C^{5'}H_2)_2$], 5.92–5.98 m [2H, $(C^{1'}H)_2$], 7.20–7.26 m (5H, H_{arom}), 8.49–8.55 d (2H, $C^{2,8}H$)
Vb	274 sh	3.57–4.03 m (5H, $H^{2',3,4}$, $C^{5'}H_2$), 4.66 br.s (3H, 3OH), 4.94 br.s (1H, C^5H), 5.80–5.84 d (1H, $C^{1'}H$), 7.23–7.26 m (5H, H_{arom}), 8.07–8.81 s (2H, $C^{2,8}H$), 12.67 br.s (1H, NH)
VIb	274 sh	3.62–4.04 m (10H, $H^{2',3,4}$, $C^{5'}H_2$), 4.60 br.s (6H, 6OH), 4.97 br.s (1H, C^5H), 5.77–5.84 d [2H, $(C^{1'}H)_2$), 7.20–7.28 m (5H, H_{arom}), 8.83 s (2H, $C^{2,8}H$)
VIIb	275 sh	$CDCl_3$: 1.14 s (3H, $COCH_3$), 1.94–2.18 m (9H, $3COCH_3$), 4.12 s (3H, $C^{5'}H + C^{6'}H_2$), 5.09–5.15 s (3H, $C^{3',4'}H + C^5H$), 5.49 s (1H, $C^{2'}H$), 5.99 s (1H, $C^{1'}H$), 7.25–7.33 m (5H, H_{arom}), 7.91–8.21 s (2H, $C^{2,8}H$), 12.60 br.s (1H, NH)
VIIIb	275 sh	$CDCl_3$: 1.92–2.13 m (24H, $8COCH_3$), 4.08–4.31 m [6H, $(C^{5'}H)_2 + (C^{6'}H_2)_2$], 5.05–5.47 m [7H, $(C^{2',3',4'}H)_2 + C^5H$], 6.28–6.35 s (2H, $C^{1'}H$), 7.26–7.33 m (5H, H_{arom}), 7.92–8.21 s (2H, $C^{2,8}H$)
IXb	274 sh	3.27–3.72 m [12H, $(C_6H_2)_2 + (C^{2',3',4',5'}H)_2$], 4.94–5.13 m (9H, C^5H + 8OH), 5.42–5.51 m (2H, $C^{1'}H$), 7.18–7.25 s (5H, H_{arom}), 8.09–8.46 s (2H, $C^{2,8}H$)
XIIb	276 sh	$CDCl_3$: 3.26–3.63 m (5H, $C^{6'}H_2 + C^{5',4',3'}H$), 4.25 s (5H, $C^{2'}H$ + 4OH), 4.94 s (1H, C^5H), 5.44–5.55 m (1H, $C^{1'}H$), 7.24–7.25 m (5H, H_{arom}), 8.08–8.49 s (2H, $C^{2,8}H$), 12.72 br.s (1H, NH)
XIIIa	277 sh	$CDCl_3$: 2.07–2.08 m (6H, $2COCH_3$), 3.64 s (2H, C^5H), 3.82 s [4H, $(C^3H_2)_2$], 4.20 d [4H, $(C^{2'}H_2)_2$], 5.93 s [4H, $(C^{1'}H_2)_2$], 8.08 s (2H, $C^{2,8}H$), 11.70 br.s (1H, NH)
XIIIb	276 sh	2.01 m (6H, $2COCH_3$), 3.73 s [4H, $(C^3H_2)_2$], 4.10–4.14 d [4H, $(C^{2'}H2)2$], 5.13 s (1H, C^5H), 5.18–5.43 m [4H, $(C^{1'}H_2)_2$], 7.10–7.36 m (5H, H_{arom}), 8.12 d (2H, $C^{2,8}H$)
XIVb	275 sh	3.73 m [6H, $(O–C^3H_2–N)_2$ + 2OH], 3.96 [4H, s, $(O–C^{2'}H_2)_2$], 4.98 s (1H, C^5H), 5.23–5.30 m [4H, $(C^{1'}H_2)_2$], 7.25 s (5H, H_{arom}), 8.51 d (2H, $C^{2,8}H$)

tion of the glycoside C–N bond by the action of 3% HCl in methanol (18–20°C, 24 h); we thus isolated 3-mono-and 3,7-bis(β-*D*-ribofuranosyl)-5-phenylpyrano[2,3-d:6,5-*d*']dipyrimidine-4,6-diones **Vb** and **VIb** (Scheme 1).

The purity of the products was checked by TLC, and their structure was confirmed by elemental analysis and ^{1}H NMR, UV, and IR spectroscopy (Tables 1 and 2). The main difference in the ^{1}H NMR spectra of monoribosides **IIIb** and **Vb**, on the one hand, and diribosides **IVb** and **VIb**, on the other, is the presence of a downfield signal at δ 12.66 ppm from the NH proton of the former. Methyl proton signals of *O*-acetyl ribosides **IIIb** and **IVb** are located in the region δ 1.88–2.09 ppm, while the spectra of the corresponding deacetylated derivatives **Vb** and **VIb** contain no such signals. In keeping with published data [5–7], signals in the region δ 3.5–6.5 ppm were assigned to protons in the carbohydrate moieties. Characteristic differences were also observed in the chemical shifts of protons on C^2 and C^8 in the pyrimidine rings. Monoribosides **IIIb** and **Vb** displayed two signals at δ 8.0 and 8.8 ppm, while only one signal at δ 8.5–8.8 ppm was present in the spectra of diribosides **IVb** and **VIb**. The chemical shifts of 5-H (δ 4.9 ppm) and protons in the 5-phenyl group (δ 7.2–7.28 ppm) are almost similar for all compounds **IIIb**–**VIb**, as well as for initial phenylpyranodipyrimidine **Ib**. The position of the anomeric proton signal ($C^{1'}H$, δ 5.94 ppm) and the corresponding spin–spin coupling constant $J^{1',2'}$ (1 Hz) in the ^{1}H NMR spectra of **IIIb** and **IVb** in DMSO-d_6 indicate its β-configuration [8].

In the UV spectra of alcoholic solutions of compounds **IIIb**–**VIb** we observed one strong absorption maximum in the λ region 270–280 nm, which arises from π–π* transitions in the aromatic and pyrimidine fragments and the presence of a ribosyl moiety as auxochrome.

The IR spectra of crystalline samples of ribonucleosides **IIIb**–**VIb** dispersed in mineral oil contain

Table 2. Yields, melting or decomposition points, R_f values, and elemental analyses of pyrano[2,3-*d*:6,5-*d*']dipyrimidine-based glycosides **III**–**XIV**

Comp. no.	Yield, %	mp, °C	R_f	Found, %			Formula	Calculated, %		
				C	H	N		C	H	N
IIIb	12 (25)	175 (decomp.)	0.46 [a]	55.94	4.91	9.95	$C_{26}H_{24}N_4O_{10}$	56.52	4.35	10.15
IVa	15	52 (decomp.)	0.62 [b]	49.97	4.93	7.52	$C_{31}H_{34}N_4O_{17}$	50.68	4.63	7.63
IVb	31	199–201	0.96 [b]	54.12	4.87	6.86	$C_{37}H_{38}N_4O_{17}$	54.81	4.69	6.91
Vb	97	120 (decomp.)	0.78 [c]	55.98	4.74	12.53	$C_{20}H_{18}N_4O_7$	56.34	4.22	13.14
VIb	91	112 (decomp.)	0.91 [c]	53.26	5.02	9.57	$C_{25}H_{26}N_4O_{11}$	53.76	4.66	10.04
VIIb	6.3	121 (decomp.)	0.22 [d]	55.20	4.84	8.71	$C_{29}H_{28}N_4O_{12}$	55.77	4.49	8.97
VIIIb	32	145 (decomp.)	0.64 [d]	53.81	5.17	5.11	$C_{43}H_{46}N_4O_{21}$	54.09	4.82	5.87
IXb	97	67–70	0.60 [e]	52.07	5.26	8.44	$C_{27}H_{30}N_4O_{13}$	52.43	4.85	9.06
XIIb	57	205 (decomp.)	0.83 [e]	54.69	4.85	11.65	$C_{21}H_{20}N_4O_8$	55.26	4.38	12.28
XIIIa	43	157–160	0.38 [d]	41.21	4.56	12.11	$C_{19}H_{22}N_4O_9$	43.18	4.23	12.45
XIIIb	64	109–114	0.33 [d]	43.14	4.87	10.28	$C_{25}H_{26}N_4O_9$	47.77	4.14	10.65
XIVb	94	142–145	0.76 [e]	53.12	5.02	15.25	$C_{21}H_{22}N_4O_7$	56.00	4.89	14.22

[a] Methylene chloride–methanol, 15:1. [b] Methylene chloride–methanol, 20:1. [c] Methylene chloride–methanol, 3:1. [d] Chloroform–methanol, 15:1. [e] Chloroform–methanol, 3:1.

absorption bands characteristic of structural fragments of their molecules. Stretching vibrations of the OH and NH bonds give rise to absorption in the region 3100–3500 cm^{-1}; a broad band in the region 1630–1750 cm^{-1} belongs to stretching vibrations of the C=O groups in the pyrimidine fragment (and acetoxy groups in the spectra of acetylated derivatives **IIIb** and **IVb**); and absorption bands in the region 1120–1170 cm^{-1} may be assigned to stretching vibrations of the ribosyl $C^{1'}$–O–$C^{4'}$ fragment.

We also tried to synthesize pyranodipyrimidine-based ribosides following another widely used procedure, namely, alkylation of the corresponding *O*-silyl derivatives with acylated glycosyl halides. According to the TLC data, treatment of 4,6-bis(trimethylsiloxy)-5-phenyl-5*H*-pyrano[2,3-*d*:6,5-*d*']dipyrimidine (**IIb**) with freshly prepared 2,3,5-tri-*O*-acetyl-β-*D*-ribofuranosyl chloride in anhydrous methylene chloride resulted in the formation of mono- and diribosides **IIIb** and **IVb**; however, their yield was considerably lower than in the reaction with tetra-*O*-acetylribofuranose, and it did not exceed 5–7%.

The condensation of 1,2,3,5-tetra-*O*-acetyl-β-*D*-ribofuranose with 4,6-bis(trimethylsiloxy)-5*H*-pyrano-[2,3-*d*:6,5-*d*']dipyrimidine (**Ia**) having no substituent on C^5 occurred much more difficultly. Even after 48 h, the yield of an inseparable mixture of 1,9- and 3,7-bis(2,3,5-tri-*O*-acetyl-β-*D*-ribofuranosyl)-5*H*-pyrano[2,3-*d*:6,5-*d*']dipyrimidine-4,6(3*H*,7*H*)-diones **IIIa** and **IVa** did not exceed 15%. Desilylation of the reaction mixture by treatment with methanol gave 60% of unchanged initial pyranodipyrimidine **Ia** which, unlike its ribosylated derivatives, is insoluble in methylene chloride–methanol. Isomer mixture **IIIa/IVa** can be readily deacetylated with 3% methanolic HCl, but the resulting pyrano[2,3-*d*:6,5-*d*']-dipyrimidine-based diribosides **Va** and **VIa** cannot be separated (Scheme 1). The ^{1}H NMR spectrum of mixture **IIIa/IVa** contained signals from 5-H and 2-H/8-H at δ 3.60 and 8.23 ppm, respectively. The absence of NH signal in the spectrum indicates that molecules **IIIa** and **IVa** contain two carbohydrate fragments.

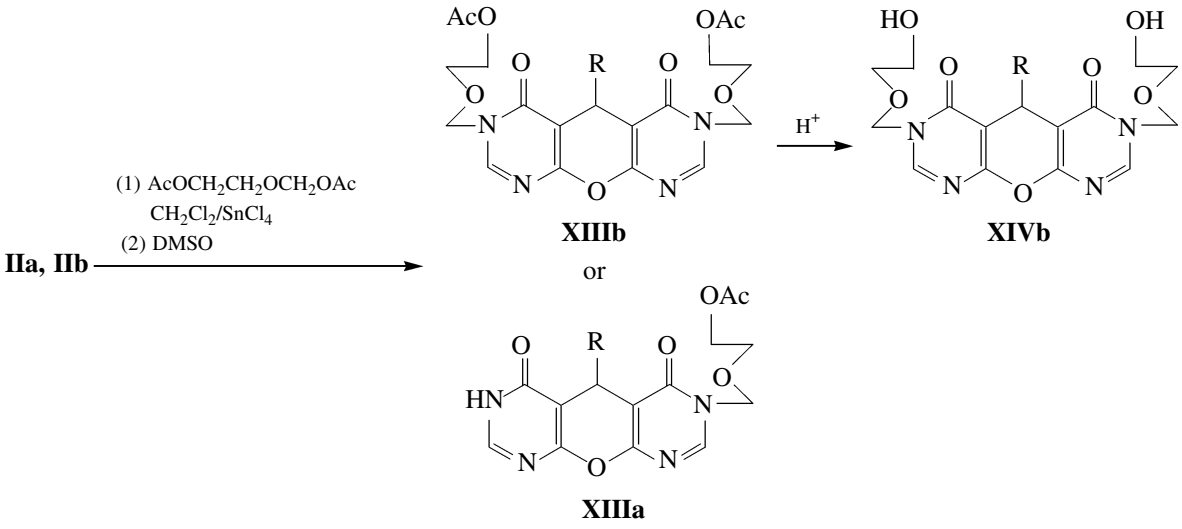
Unlike ribosylation, 4,6-bis(trimethylsiloxy)-5-phenyl-5*H*-pyrano[2,3-*d*:6,5-*d*']dipyrimidine (**IIb**) reacted with 1,2,3,4,6-penta-*O*-acetyl-β-*D*-galactopyranose and 1,2,3,4,6-penta-*O*-acetyl-β-*D*-glucopyranose much more slowly (72 h), and the overall yield of the corresponding galacto- and glucopyranosides **VIIb/VIIIb** and **Xb/XIb** was about 40%. The lower reactivity of pyranoses compared to furanoses was also observed in the synthesis of *N*-glycosides from other heterocycles [3, 4].

It should be noted that glycosylation of 4,6-bis(trimethylsiloxy)-5-phenyl-5*H*-pyrano[2,3-*d*:6,5-*d*']dipyrimidine (**IIb**) with galactose pentaacetate also afforded a mixture of 3-mono- and 3,7-bis(2,3,4,6-tetra-*O*-acetyl-β-*D*-galactopyranosyl)-5-phenyl-5*H*-pyrano-[2,3-*d*:6,5-*d*']dipyrimidine-4,6(3*H*,7*H*)-diones **VIIb** and **VIIIb** (Scheme 1), which was separated by fractional crystallization from ethanol and diethyl ether. The structure of **VIIb** and **VIIIb** was confirmed by the ^{1}H NMR spectra, as well as by deacetylation to

3,7-bis(β-*D*-galactopyranosyl)-5-phenyl-5*H*-pyrano-[2,3-*d*:6,5-*d*']dipyrimidine-4,6(3*H*,7*H*)-dione (**IXb**). Analysis of the spectra of galactosides **VIIb**–**IXb**, performed as described above for ribosides **IIIb**–**VIb**, confirmed the structure of both aglycone and carbohydrate fragments in their molecules.

The reaction of 4,6-bis(trimethylsiloxy)-5-phenyl-5*H*-pyrano[2,3-*d*:6,5-*d*']dipyrimidine (**IIb**) with glucose pentaacetate gave a mixture of two glucosides **Xb** and **XIb** which we failed to separate. By deacetylation of that mixture we obtain 3-(β-*D*-glucopyranosyl)-5-phenyl-5*H*-pyrano[2,3-*d*:6,5-*d*']dipyrimidine-4,6(3*H*,7*H*)-dione (**XIIb**) (Scheme 1).

It is known that replacement of ribose moiety in nucleosides by an acyclic fragment, the general molecular geometry being retained (i.e., the distance from $C^{1'}$ to the $C^{3'}OH$ group with respect to the nitrogen-containing base remains the same as in the ribose fragment), is promising from the viewpoint of searching for new antiviral agents [8, 9]. As acyclic analog of monosaccharides we selected 2-oxabutane-1,4-diyl diacetate. The condensation of 4,6-bis(trimethylsiloxy)-5-phenyl-5*H*-pyrano[2,3-*d*:6,5-*d*']dipyrimidine (**IIb**) with excess 2-oxabutane-1,4-diyl diacetate (Scheme 2) gave 3,7-bis[(2-acetoxyethoxy)methyl]-5-phenyl-5*H*-pyrano[2,3-*d*:6,5-*d*']-dipyrimidine-4,6-(3*H*,7*H*)-dione (**XIIIb**) as the only product, and its deacetylation afforded 3,7-bis[(2-hydroxyethoxy)methyl]-5-phenyl-5*H*-pyrano[2,3-*d*:6,5-*d*']dipyrimidine-4,6(3*H*,7*H*)-dione (**XIVb**). Trimethylsilyl derivative of pyrano[2,3-*d*:6,5-*d*']dipyrimidine (compound **IIa**) reacted with 2-oxabutane-1,4-diyl diacetate much more difficultly, and the product was 3-[(2-acetoxyethoxy)methyl]-5*H*-pyrano[2,3-*d*:6,5-*d*']dipyrimidine-4,6(3*H*,7*H*)-dione (**XIIIa**).



R = H (**a**), Ph (**b**).

Inlike initial 5-phenylpyranodipyrimidine **Ib**, the ^{1}H NMR spectra of **XIIIb** and **XIVb** in DMSO-d_6 lacked signal from the aglycone NH proton. Signals from protons in the acetoxyethoxy fragment of **XIIIb** were located at δ 3.74 and 4.13 ppm, while the corresponding signals of deacetylated derivative **XIVb** appeared at δ 3.48 ppm. More downfield signals (δ 5.23–5.43 ppm) belong to the NCH_2O group. Acetyl protons in **XIIIb** gave rise to a signal at δ 2.01 ppm. In addition, the spectra of **XIIIb** and **XIVb** contained signals from 5-H (δ 4.98–5.13 ppm), 2-H/8-H (δ 8.12–8.51 ppm), and benzene ring (δ 7.18–7.36 ppm). In the ^{1}H NMR spectrum of **XIIIa**, the NH proton signals were present at δ 11.70 ppm, and signals from 2-H/8-H, at δ 8.08 ppm. The spectral pattern from the pseudoribose fragment in **XIIIa** was similar to that observed for N,N'-disubstituted 5-phenyl analog **XIIIb**, but the relative intensity was twice as low.

We can conclude that the Vorbrüggen glycosylation of pyrano[2,3-*d*:6,5-*d*']dipyrimidine-4,6-diones in aprotic solvents is can efficient route to the corresponding mono- and diglycosides whose ratio depends on the initial reactant ratio. The alkylation of pyrano[2,3-*d*:6,5-*d*']dipyrimidine 4,6-diones with

2-oxabutane-1,4-diyl diacetate gives acyclic analogs of 5-arylpyrano[2,3-*d*:6,5-*d*']dipyrimidine-based glycosides, in which the (2-hydroxyethoxy)methyl group mimics ribose fragment.

EXPERIMENTAL

The electronic absorption spectra were recorded from solutions in water or ethanol on an SF-2000 spectrophotometer (1-cm quartz cells, concentration 10^{-5} to 10^{-4} M). The ^{1}H NMR spectra were measured from solutions in DMSO-d_6 and $CDCl_3$ on Bruker AM-200 (200 MHz) and Bruker AM-500 (500 MHz) spectrometers. The purity of products was checked, and the progress of reactions was monitored, by thin-layer chromatography on Silufol UV-254 plates; spots were visualized under UV light or by treatment with iodine vapor. The melting (decomposition) points were determined in capillaries and were not corrected (Tables 1, 2). The solvents and reagents used were purified and dehydrated by standard procedures. 1,2,3,4,6-Penta-*O*-acetyl-β-*D*-galactopyranose, 1,2,3,4,6-penta-*O*-acetyl-β-*D*-glucopyranose, and 2-oxabutane-1,4-diyl diacetate were prepared according to the procedures described in [10, 11].

4,6-Bis(trimethylsiloxy)-5*H*-pyrano[2,3-*d*:6,5-*d*']-dipyrimidine (IIa) and 4,6-bis(trimethylsiloxy)-5-phenyl-5*H*-pyrano[2,3-*d*:6,5-*d*']dipyrimidine (IIb) *(general procedure).* A mixture of 0.005 mol of pyranodipyrimidine **Ia** or **Ib**, 10 ml of hexamethyldisilazane, and 0.15 g of ammonium sulfate was heated with stirring under reflux until it became homogeneous. Excess hexamethyldisilazane was distilled off under reduced pressure (20–25 mm) (for more complete removal of hexamethyldisilazane, benzene was added), and the residue was kept under reduced pressure until complete crystallization of compounds **IIa** and **IIb**. The products are readily hydrolyzable on exposure to atmospheric moisture.

3-(2,3,5-Tri-*O*-acetyl-β-*D*-ribofuranosyl)-5-phenyl-5*H*-pyrano[2,3-*d*:6,5-*d*']dipyrimidine-4,6-(3*H*,7*H*)-dione (IIIb) and 3,7-bis(2,3,5-tri-*O*-acetyl-β-*D*-ribofuranosyl)-5-phenyl-5*H*-pyrano[2,3-*d*:6,5-*d*']dipyrimidine-4,6(3*H*,7*H*)-dione (IVb). Silyl ether **IIb**, 0.003 mol, was dissolved in 7 ml of anhydrous methylene chloride under stirring with thorough protection from atmospheric moisture, and 0.006 mol of anhydrous 1,2,3,5-tetra-*O*-acetyl-β-*D*-ribofuranose was added to the solution. A solution of tin(IV) chloride in 3 ml of methylene chloride was then added dropwise under stirring and cooling, and the mixture was stirred for 3 h at 18–20°C and was left to stand for 12 h. The mixture was cooled to 0°C, a solution of 0.5 ml DMSO in 2 ml of anhydrous methylene chloride was added dropwise, the mixture was kept for 30 min at 0°C, and the precipitate, $SnCl_4 \cdot 2DMSO$, was filtered off and washed with 5 ml of methylene chloride. The filtrate was diluted with 4 ml of methanol, heated for 15 min at 60°C, and evaporated under reduced pressure (20–25 mm) at 30–40°C. Diethyl ether, 30 ml, was added to the residue, and the mixture was cooled to –20°C and evaporated under reduced pressure to obtain a mixture of ribosides **IIIb** and **IVb** (43%). Crystallization from ethanol gave 3,7-bis(2,3,5-tri-*O*-acetyl-β-*D*-ribofuranosyl)-5-phenyl-5*H*-pyrano[2,3-*d*:6,5-*d*']dipyrimidine-4,6(3*H*,7*H*)-dione (**IVb**). The mother liquor was evaporated, and the residue was recrystallized from diethyl ether to isolate 3-(2,3,5-tri-*O*-acetyl-β-*D*-ribofuranosyl)-5-phenyl-5*H*-pyrano[2,3-*d*:6,5-*d*']dipyrimidine-4,6(3*H*,7*H*)-dione (**IIIb**).

Compound IIIb was synthesized in a similar way using equimolar amounts of silyl ether **IIb** and 1,2,3,5-tetra*O*-acetyl-β-*D*-ribofuranose. Yield 25%.

3,7- and 1,9-Bis(2,3,5-tri-*O*-acetyl-β-*D*-ribofuranosyl)-5*H*-pyrano[2,3-*d*:6,5-*d*']dipyrimidines IVa and IIIa (a mixture of isomers) were obtained as described above for compounds **IIIb** and **IVb**. Unchanged pyranodipyrimidine **Ia** was filtered off, the filtrate was evaporated under reduced pressure (20–25 mm), and the residue was reprecipitated from ethanol–diethyl ether (5:1) and evacuated until a solid foam-like material was obtained. We thus isolated an amorphous hygroscopic mixture of compounds **IIIa** and **IVa** which we failed to separate by fractional crystallization.

3-(β-*D*-Ribofuranosyl)-5-phenyl-5*H*-pyrano[2,3-*d*:6,5-*d*']dipyrimidine-4,6(3*H*,7*H*)-dione (Vb) and 3,7-bis(β-*D*-ribofuranosyl)-5-phenyl-5*H*-pyrano-[2,3-*d*:6,5-*d*']dipyrimidine-4,6(3*H*,7*H*)-dione (VIb) *(general procedure).* Acetylated riboside **IIIb** or **IVb**, 0.001 mol, was dissolved in 10 ml of methanol, 10 ml of a 3% solution of hydrogen chloride in methanol was added, and the mixture was stirred for 30 min and was left to stand for 12 h. The solvent was distilled off under reduced pressure (20–25 mm), the residue was washed with diethyl ether, evacuated, and dissolved in 20 ml of methanol, the solution was evaporated by half, 30 ml of diethyl ether was added to the residue, and the mixture was kept at –20°C. The supernatant was removed by decanting, and the residue was dried under reduced pressure. We thus obtained colorless crystals of 3,7-bis-(β-*D*-ribofuranosyl)-5-phenyl-5*H*-pyrano[2,3-*d*:6,5-*d*']dipyrimidine-4,6-(3*H*,7*H*)-dione (**VIb**) or yellow crystals of 3-(β-*D*-ribofuranosyl)-5-phenyl-5*H*-pyrano[2,3-*d*:6,5-*d*']dipyrimidine-4,6(3*H*,7*H*)-dione (**Vb**).

3-(2,3,4,6-Tetra-*O*-acetyl-β-*D*-galactopyranosyl)-5-phenyl-5*H*-pyrano[2,3-*d*:6,5-*d*']dipyrimidine-4,6(3*H*,7*H*)-dione (VIIb) and 3,7-bis(2,3,4,6-tetra-*O*-acetyl-β-*D*-galactopyranosyl)-5-phenyl-5*H*-pyrano[2,3-*d*:6,5-*d*']dipyrimidine-4,6(3*H*,7*H*)-dione (VIIIb) were synthesized as described above for compounds **IIIb** and **IVb** from 0.007 mol of silyl ether **IIb** and 0.014 mol of anhydrous 1,2,3,4,6-penta-*O*-acetyl-β-*D*-galactopyranose. Crystallization from ethanol gave compound **VIIb**. The mother liquor was evaporated, and the residue was recrystallized from hexane to isolate digalactoside **VIIIb**.

3,7-Bis(β-*D*-galactopyranosyl)-5-phenyl-5*H*-pyrano[2,3-*d*:6,5-*d*']dipyrimidine-4,6(3*H*,7*H*)-dione (IXb) was synthesized as described above for compounds **Vb** and **VIb**.

3-(β-*D*-Glucopyranosyl)-5-phenyl-5*H*-pyrano-[2,3-*d*:6,5-*d*']dipyrimidine-4,6(3*H*,7*H*)-dione (XIIb). The condensation of silyl ether **IIb** with 1,2,3,4,6-penta-*O*-acetyl-β-*D*-glucopyranose was carried out as described above in the synthesis of **VIIb** and **VIIIb**. As a result, a yellow amorphous mixture of glucosides **Xb** and **XIb** was obtained, which was difficult to separate. The mixture is readily soluble in methylene chloride and methanol and insoluble in hexane. Its deacylation gave colorless monoglucoside **XIIb** which crystallized from the solution.

3,7-(or 1,9)-Bis[(2-acetoxyethoxy)methyl]-5-phenyl-5*H*-pyrano[2,3-*d*:6,5-*d*']dipyrimidine-4,6-(3*H*,7*H*)dione (XIIIb) was synthesized as described above for compounds **IIIb** and **IVb** from 0.009 mol of silyl ether **IIb** and 0.03 mol of 2-oxabutane-1,4-diyl diacetate in anhydrous methylene chloride. The crude product was crystallized from methanol (the mixture was heated for 15 min and volatile components were removed under reduced pressure). Hexane was added to the residue, the mixture was cooled to –20°C, the solvent was removed by decanting, and the residue was evacuated at a residual pressure of 20–25 mm. Compound **XIIIb** was isolated as light yellow crystals.

3-[(2-Acetoxyethoxy)methyl]-5*H*-pyrano[2,3-*d*:6,5-*d*']dipyrimidine-4,6(3*H*,7*H*)-dione (XIIIa) was synthesized as described above for compound **XIIa** using 3 equiv of 2-oxabutane-1,4-diyl diacetate.

3,7-(or 1,9)-Bis[(2-hydroxyethoxy)methyl]-5-phenyl-5*H*-pyrano[2,3-*d*:6,5-*d*']dipyrimidine-4,6(3*H*,7*H*)dione (XIVb) was synthesized as described above for compounds **Vb** and **VIb**.

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