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Synthesis of 2'-Deoxy-Pyranosyl Nucleosides from Glycals through Consecutive Addition of Phenylselenenyl Chloride and Glycosylation. A Study of Factors Controlling the Stereoselectivity

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Abstract: 2'-Deoxy-2'-phenylselenenyl-pyranosyl nucleosides have been synthesised in a stereoselective way starting from glycals using selenium reagents, and converted into 2'-deoxynucleosides by treatment with tributyltin hydride. The stereoselectivity of the reaction has been shown to be dependent on the protecting groups, the structure of the starting glycal, the phenylselenenyl reagent and the solvent. Nucleosides of ß-*gluco* ß-*galacto* and α-*arabino* configuration are principally obtained, starting from the corresponding benzyl protected glycals, using PhSeCl as an activating reagent and ether as the solvent.

Nucleoside analogues are among the more active antiviral drugs.[1] The increasing importance of viral diseases has prompted a growing interest in nucleoside chemistry. In this way, pyranosyl nucleosides have been the object of attention as analogues of furanosyl nucleosides of proved antiviral activity,[2] as precursors in the synthesis of acyclo-nucleosides[3] and in the preparation of oligopyranosyl nucleotides.[4] Most of these reports deal with the synthesis of 2'-deoxy-ß-pyranosyl nucleosides; however, there are no general solutions for the stereoselective synthesis of these compounds based on the glycosylation reaction, although the ß isomer is thermodynamically more stable.

2'-Deoxynucleosides are usually prepared by deoxygenating the 2'-position by way of a Barton type reaction starting from appropriate protected nucleosides;[5] however, this method needs long protecting sequences to be applied for pyranosyl nucleosides.[3a] Good results have been achieved starting from 1-α-bromo-2-deoxy-3,4,6-tri-(*p*-nitrobenzoyl)-D-*arabino*-hexo-pyranose,[6] but S_N2 like pathways must be strictly guaranteed and this methodology has hardly been used in pyrimidine like nucleoside synthesis. During the seventies, extensive studies were developed oriented towards the synthesis of 2',3'-dideoxi-2',3'-eno-pyranosyl nucleosides from glycals, some of which had shown antibiotic properties, through a S_N2' type reaction catalysed by Lewis acids.[7] Recently, 2',3'-dideoxi-2',3'-eno nucleosides have been obtained from 2',3'-dideoxi-2',3'-eno glycosides by a condensation reaction catalysed by Pd(0) catalyst.[8]

In the glycoside field, good stereoselectivity in the synthesis of 2'-deoxyglycosides has been obtained via sulphur[9] selenium[10] and iodine[11-13] mediated glycosylation reactions starting from glycals. In this context, and

given the strong stereoselectivity dependence of this reaction from the starting glycal, solvent, nucleophile, etc., we decided to undertake a systematic study looking for the best reaction conditions in the stereoselective synthesis of 2'-deoxy-ß-pyranosyl nucleosides starting from glycals and using selenium reagents.

2'-DEOXY-2'-PHENYLSELENENYL-PYRANOSYL NUCLEOSIDES

Preliminary experiments carried out by the reaction of tri-O-acetyl-D-glucal (**1a**) with PhSeCl and bis-(trimethylsilyl)uracil in different solvents (methylene chloride, acetonitrile, ether) and under different reaction conditions gave only PhSeCl addition products; PhSeBr and PhSeI showed similar results. The reason for the different behaviour between alcohols and bis(trimethylsilyl)uracil must be explained by the lower nucleophilicity of this last reagent in comparison with the alcoholate.

Increasing reagent concentrations or employing N-phenylselenenylphthalimide (NPSP), a selenium reagent with a less nucleophilic counterion, also gave negative results. The use of silver triflate as a halogen captor, allowed us to obtain 2'-deoxy-2'-phenylselenenyl nucleosides[14] **4a** and **5a** together with the 2',3'-dideoxy-2',3'-eno derivative **6**[7e] (Table 1, Entry 1). Compounds **4a** and **5a**, both with a *trans* disposition of uracil and the phenylselenenyl group, were obtained by the attack of the phenylselenenyl reagent on both faces of the alkene and subsequent opening of the phenylselenonium cations formed (Scheme 1). Working at room temperature (Table 1, Entry 2) or using other solvents (Table 1, Entry 3), neither the yield nor the selectivity were improved. The best yields were obtained by increasing the glycal/PhSeCl/AgOTf ratio and avoiding the aqueous work-up (Table 1, Entry 4), although the selectivity was always low.

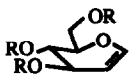
Compound **6**, was probably obtained by a S_N2' type reaction[7] (Ferrier rearrangement) catalysed by the TMSOTf formed in the reaction medium.

Table 1. Reaction of bis-(trimethylsilyl)uracil with 3,4,6-tri-O-acetyl-D-glucal (**1a**) induced by PhSeCl and silver triflate.

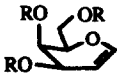
	Molar Ratio								
Entry	Glucal	PhSeCl	AgOTf	Uracil(TMS)$_2$	Solvent	Temp.	Time	Yield[a]	**4a/5a/6**[b]
1	1	1.2	1	2	CH_2Cl_2	-20--0°C	3	50	45/45/10
2	1	1.2	1	2	CH_2Cl_2	rt	1.2	47	45/45/10
3	1	1.2	1.2	2	CH_3CN	-20--0°C	22	35	45/45/10
4	1	1.5	1.7	2	Ether	rt	1	80	55/30/15

[a] Expressed as a percentage of recovered mixture of products after chromatography. [b] Determined by H-1' integration in the ^1H NMR of the reaction mixture

The formation of elimination products was prevented by utilising ether type protecting groups. Thus, starting from tri-O-benzyl-D-glucal (**1b**) and carrying out the reaction in the best conditions as before, (Table 2, Entry 1), compounds **4b** and **5b** were obtained in good yields as an inseparable mixture.



1a R = Ac
1b R = Bn



2a R = Ac
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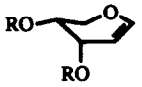
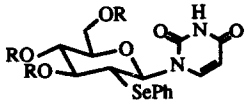
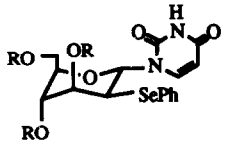


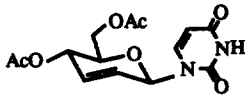
3a R = Ac
3b R = Bn



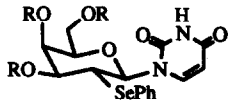
4a R=Ac
4b R=Bn



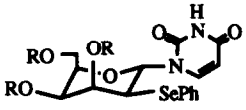
5a R=Ac
5b R=Bn



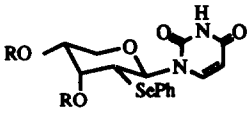
6



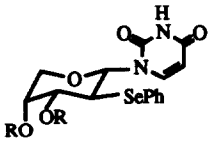
7a R=Ac
7b R=Bn



8a R=Ac
8b R=Bn



9a R=Ac
9b R=Bn



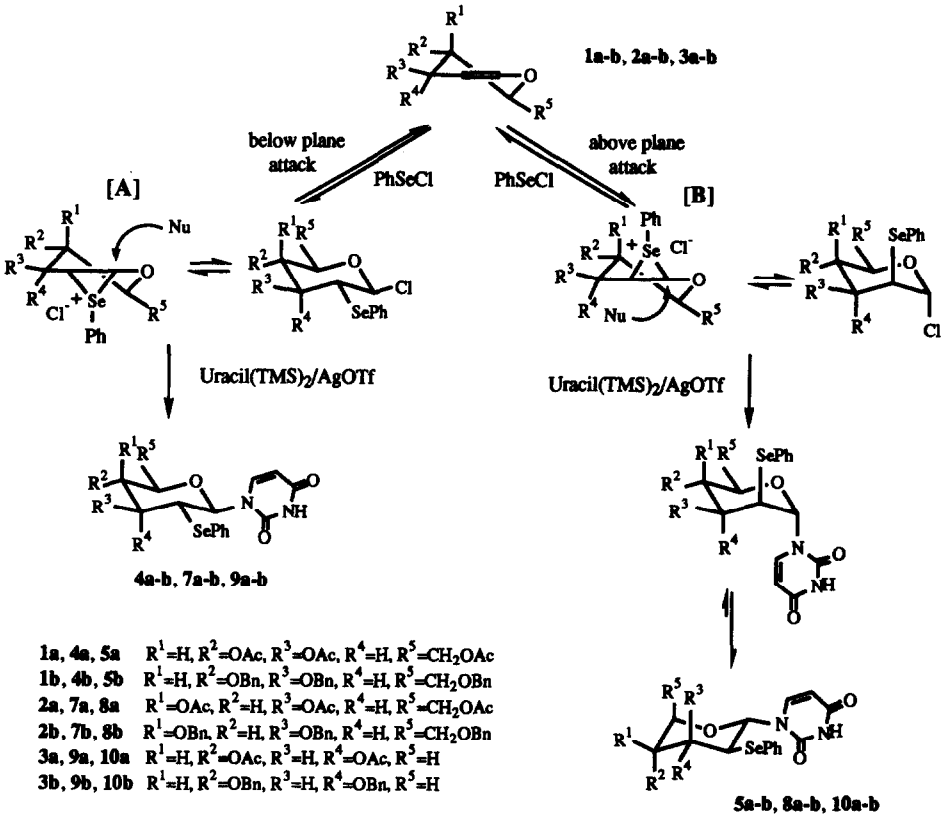
10a R=Ac
10b R=Bn

Table 2. Reaction of bis-(trimethylsilyl)uracil with 3,4,6-tri-O-benzyl-D-glucal (**1b**) induced by PhSeCl and AgOTf.[a]

Entry	Molar Ratio Glucal	PhSeCl	Catalyst	Uracil(TMS)$_2$	Solvent	Temp.	Time(h)	Yield(%)[b]	4b/5b(%)[c]
1	1	1.5	1.7[d]	2	CH_2Cl_2	-40°C--rt	3.5	87	50/50
2	1	1.5	1.7[d]	2	C_6H_6	rt	1	88	80/20
3	1	1.5	1.7[d]	2	CH_3CN	0°C--rt	15	70	40/60
4	1	1.5	1.7[d]	2	ether	0°C--rt	0.4	85	82/18
5	1	1.5	1.7[e]	2	CH_2Cl_2	-40°C--rt	3.5	50	50/50
6	1	1.5	2.3[f]	2	ether	0°C--rt	24	60	84/16
7	1	1.5	4.6[f]	2	benzene	rt	12	76	82/18

[a] 0.25 mmolar solutions of sugar were used. [b] Expressed as a percentage of the recovered mixture of diastereomers after chromatographic separation. [c] Determined by integration of the H-1' protons in the ^{1}H NMR of the reaction mixture. [d]AgOTf. [e]SbCl5. [f]TMSOTf.

In order to improve the stereoselectivity we undertook a systematic study of the reaction conditions. When glucal **1b** was treated with uracil(TMS)$_2$ and PhSeCl in dichloromethane, at room temperature as well as at -60°C, no variations in stereoselectivity were observed. However, the stereoselectivity was shown to be



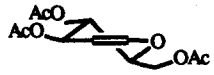
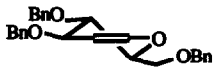
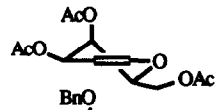
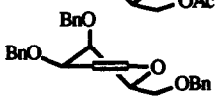
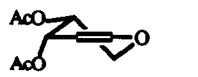
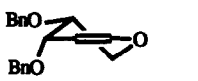
Scheme1

Table 3. Selenium reagent influence in the reaction of bis-(trimethylsilyl)uracil with 3,4,6-tri-O-benzyl-D-glucal (1b).[a]

Entry	PhSeX	Solvent	Time(h)	Yield(%)	4b/5b(%)[b]
1	PhSeCl[c]	Ether	0.4	85	82/18
2	PhSeBr[c]	Ether	0.5	85	60/40
3	PhSeI[d]	Ether	1	80	50/50

[a] 0.25 mmolar solutions of sugar were used. [b] Determined by integration of the H-1' protons in the ^{1}H NMR of the reaction mixture. [c] Molar ratio sugar/PhSeX/AgOTf/Uracil was 1/1.5/1.7/2. [d] Molar ratio sugar/PhSeI/AgOTf/Uracil was 1/2/2/2.

Table 4. Stereoselectivity in the synthesis of 2'-deoxy-2'-phenylselenenyl-pyranosyl nucleosides.

Starting Glycal[a]	Solvent	Yield(%)[b]	2'-Phenylselenenyl nucleosides (%)[c]	
			β-gluco	*α-manno*
 (1a)	Ether	68	**4a** (66)	**5a** (34)
	Acetonitrile	32	**4a** (50)	**5a** (50)
 (1b)	Ether	85	**4b** (80)	**5b** (20)
	Acetonitrile	70	**4b** (40)	**5b** (60)
			β-galacto	*α-talo*
 (2a)	Ether	80	**7a** (50)	**8a** (50)
	Acetonitrile	40	**7a** (25)	**8a** (75)
 (2b)	Ether	82	**7b** (91)	**8b** (9)
	Acetonitrile	37	**7b** (83)	**8b** (17)
			α-arabino	*β-ribo*
 (3a)	Ether	75	**10a** (60)	**9a** (40)
	Acetonitrile	65	**10a** (53)	**9a** (47)
 (3b)	Ether	71	**10b** (92)	**9b** (8)
	Acetonitrile	42	**10b** (50)	**9b** (50)

[a] Shown in the preferred conformation. [b] Referred to the mixture of phenylselenenyl nucleosides. [c] Determined by integration of H-1' protons in the ^{1}H NMR spectra of the reaction mixture

dependent on the solvent. Thus, the ß isomer was principally obtained when the reaction was carried out in ether or benzene, while the α isomer was the main one obtained in acetonitrile (Table 2, Entries 2, 3 and 4). Other chlorine activators such as $SbCl_5$ or TMSOTf (Table 2, Entries 5, 6 and 7), gave generally lower yields and slower reaction rates, but had no influence in the stereoselectivity.

The observed stereoselectivity must be related to the ratio of 1-halo-2-phenylselenenyl-glucopyranosyl derivatives present in the solution before the addition of silver triflate; therefore, the type of phenylselenenyl reagent should influence, because of steric or stereoelectronic factors, the equilibrium between the 2'-phenylselenenyl halopyranoses (Scheme 1). A study performed with PhSeCl, PhSeBr and PhSeI showed (Table 3) that the phenylselenenyl reagent had no influence on the yield, but it had a drastic influence on the stereoselectivity. The best results were obtained when PhSeCl was used.

Treatment of 3,4,6-tri-O-acetyl-D-galactal (**2a**) with PhSeCl, AgOTf and bis-(trimethylsilyl)uracil in CH_2Cl_2 resulted in to a 1:1 mixture of 2'-deoxy-2'-phenylselenenyl nucleosides **7a** and **8a** in 70% yield. The reaction in ether was much faster than in CH_2Cl_2, although a similar mixture of compounds was also obtained in 80% yield. The use of acetonitrile gave preferentially the product with *α-manno* configuration, resulting from the selenium attack above the molecular plane (ß face) (Scheme 1), 1:3 being the **7a/8a** ratio. In this case the product resulting from the Ferrier rearrangement was not observed. Curiously, the selectivity for the tri-O-

Table 5. Selected ^1H NMR coupling constants (Hz) of the carbohydrate frame for 2'-Deoxy-2'-phenylselenenyl-pyranosyl nucleosides **4a-b**, **5a-b**, **7a-b**, **8a-b**, **9a-b** and **10a-b**.

J/Compound	**4a**	**4b**	**5a**	**5b**	**7a**	**7b**	**8a**	**8b**	**9a**	**9b**	**10a**	**10b**
$J_{1',2'}$	11.0	10.7	10.8	10.9	10.7	10.6	10.7	9.0	10.7	1.9	10.7	10.5
$J_{2',3'}$	11.0	10.7	3.3	3.3	11.7	11.1	3.0	--	2.7	3.0	11.6	10.5
$J_{3',4'}$	9.1	--	2.2	1.9	3.2	2.5	3.0	--	2.8	3.0	3.2	2.8
$J_{4',5'}$	9.9	--	5.1	2.8	<1	--	6.8	--	1.4	10.6[a]	2.5[b]	2.0[c]

[a] $J_{4',5''}$=6.1 Hz. [b] $J_{4',5''}$=1.1 Hz. [c] $J_{4',5''}$=0 Hz

benzyl-D-galactal (**2b**) was excellent in ether as well as in acetonitrile, in both cases compound **7b** being the main one obtained (Table 4), which originated from the selenonium ion formed by below the plane attack of the selenium reagent.

The reaction of 3,4-di-O-acetyl-D-arabinal (**3a**) with PhSeCl, AgOTf and bis-(trimethylsilyl)uracil gave very low selectivity in ether as well as in acetonitrile, producing a 1:1 mixture of compounds **9a** and **10a**. A small amount of product originated by S_N2' reaction was also detected in this case. Similar results were obtained when starting from 3,4-di-O-benzyl-D-arabinal (**3b**) and using acetonitrile as the solvent; however, in ether product **10b** was obtained with a selectivity of 92%. In this case the main product arose from above the plane attack of the electrophilic part of PhSeCl to arabinal, that is, opposite to the ring substituents.

Structure assignment

The structure of the 2'-deoxy-2'-phenylselenenyl nucleosides was established by ^1H and ^{13}C NMR spectroscopy on the basis of the following facts: (1) presence of the uracil in the products, which wasconfirmed by the double bond signals in the ^1H NMR spectra (6.70-7.00 ppm, d, H-6; 5.00-5.50 ppm, dd, H-5) and in the ^{13}C NMR spectra (≈140 ppm, C-6; ≈102 ppm, C-5); (2) introduction of the phenylselenenyl group was proved by the presence in the ^{13}C NMR spectra of a signal at 43-50 ppm, assigned to C-2', typical of carbon bonded to selenium; (3) coupling constants $J_{1',2'}$, $J_{2',3'}$, $J_{3',4'}$ and $J_{4',5'}$ are indicative of configuration of positions 1 and 2, and also of the preferred conformation of the sugar ring. Thus, as can be seen in the Table 5, a $J_{1',2'}$>9 Hz for all the obtained compounds, except for **9b**, indicates a trans-diaxial arrangement for protons H-1'and H-2' which implies a trans-equatorial disposition for uracil and selenium. The value of $J_{2',3'}$ is also higher than 9 Hz for compounds **4a-b**, **7a-b** and **10a-b**, confirming a trans-diaxial arrangement for protons H-1', H-2' and H-3'. These facts, together with the values of the other coupling constants, corroborates a ß-*gluco* and ß-*galacto* configuration with a $^4C_1$ conformation[15] for compounds **4a-b** and **7a-b**, respectively. In the case of *arabino* derivatives **10a-b** the small size of both $J_{4',5'}$ and $J_{4',5''}$ indicates a $^1C_4$ conformation for these compounds. On the other hand, a $J_{2',3'}$≈ 3-4 Hz for compounds **5a-b** and **8a-b** corresponds to an axial-equatorial coupling; as H-2' is always axial, H-3' must be equatorial, which supposes that a chair inversion has taken place and that the conformation $^1C_4$ preponderates in these compounds. This fact is confirmed by the low value of $J_{3',4'}$ and $J_{4',5'}$. Compound **9a** shows $J_{2',3'}$ and $J_{3',4'}$ ≈ 2.8 Hz which, since $H_{2'}$ is axial, indicates that $H_{3'}$ is equatorial and consequently $H_{4'}$ is axial, which confirms a $^4C_1$ conformation for this compound.

Compound **9b** is the only case where $J_{1',2'}$ is small, suggesting that uracil and the PhSe group are not in a *trans* diequatorial disposition, as in all the other compounds. A value of $J_{4',5'}$=10.1 Hz indicates that $H_{4'}$ and $H_{5'}$ are axial, but the other coupling constants are very small, which implies that the other substituents are in axial or pseudo-axial disposition. It must correspond with a twist-boat conformation probably trying to avoid the steric interactions among the bulky substituents at C-2, C-3 and C-4.

The next NMR spectroscopic data confirms the structure of compound **6**: (1) the absence of aromatic protons and the signal between 40 and 50 ppm in the ^{13}C NMR spectrum, showing that no PhSe group exists, (2) the presence of only two acetate group signals and (3) the signals at 6.55 ppm and 6.18 ppm in the ^{1}H NMR spectrum and at 132.8 ppm and 127.2 ppm in the ^{13}C NMR spectrum, characteristic of a double bond. These values are in good agreement with those for other similar compounds described in the literature.[7e,8]

DISCUSSION

It is well known that NIS,[11-13] PhSCl[9] and PhSeCl[10] mediated O-glycosylation reaction gives exclusively alkyl 2-deoxy-2-X-nucleosides (X= I, SPh or SePh) having X and alkoxy group *trans* disposed. The results are explained in terms of a two step mechanism (Scheme 1), consisting of electrophilic addition of NIS, PhSCl or PhSeCl to the glycal double bond to give a cyclic cation, followed by a regioselective nucleophilic attack by an alcohol at C-1.

In our case the selenium-mediated synthesis of nucleosides from glycals does not take place at room temperature because the bis-(trimethylsilyl)uracil is not nucleophilic enough, therefore the presence of a chlorine activator is neoessary to obtain the corresponding nucleosides.

It has been recently shown[12] that the stereochemistry of NIS-alcohol addition to glycals is determined at the electrophilic step (iodine addition) or at the nuclephilic step (alcohol attack) depending on the solvent. In general, in ether type solvents an isomerization between iodonium cations takes place, while in acetonitrile the iodonium cation formation is irreversible, the stereoisomer distribution reflecting in this last case the ratio of iodonium cations.

On the other hand, in the selenium mediated synthesis of O-glycosides from glycals an isomerization process between selenonium cations has been proposed to explain the distribution products obtained.[10a]

The results collected in Table 4 show that the stereochemistry is dependent on the solvent and on the glycal structure, but also on the protecting groups.

The solvent has an influence not only on the selectivity but also on the reaction rate, being faster in ether than in acetonitrile. Concerning the stereoselectivity, compounds arising from the less hindered selenonium intermediate, [A] for glucal and galactal derivatives and [B] for arabinal derivatives (Scheme 1), were favoured when ether was the solvent, while in acetonitrile the percentage of products derived from the intermediate [B] increased. This fact agrees with the Horton[12] proposal, that an isomerization process between intermediates [A] and [B] takes place, being faster in ether than in acetonitrile, and also with the observations of Beau[10a] that phenylselenonium cations isomerize easily, expecially in the presence of Lewis acids. In this way, it must be taken into consideration that TMSOTf is probably generated in the reaction medium in the PhSeCl-mediated synthesis of nucleosides from glycals. The different stereoselectivities observed for different selenium reagents (Table 3) confirms the existence of an isomerization process between the selenonium cation and the 1-halo-2-phenylselenenylpyranose and also between selenonium cations [A] and [B] (Scheme 1).

Protecting groups and glycal structure play a determining role in the control of stereoselectivity. The preferred conformation for D-glucal and especially for D-galactal and D-arabinal derivatives[16] is $^{4}H_{5}$ (Table 4), and although differences in stereoselectivity are observed when starting from different glycals, the preferred

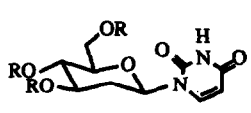
side of attack to the double bond of the glycal in the more stable conformation, or the existence of an isomerization process can not exclusively explain these differences. In Table 4 it can be seen that stereoselectivity is strongly dependent on the type of protecting group. Thus, for the acetylated glycal **2a** a relatively higher percentage of α-*talo* derivative is obtained, indicating that the more hindered selenonium cation is principally formed. It appears that electrostatic effects might be responsible for the stereochemistry of the first step.[17] This effect is less important in the glycals **1a** and **3a**, given that the dipole moment of ring oxygen and the C-4 acetoxy group are opposite, and so the net dipole moment should be smaller, which would explain the lower stereoselectivity obtained in these cases.

On the contrary, the results from benzylated glycals **1b**, **2b** and **3b** clearly show that steric factors exert the major influence in these cases, given that phenylselenenyl nucleosides originated by the opening of the less hindered selenonium cation ([A] for glucal and galactal derivatives and [B] for arabinal derivatives) are principally obtained. In these cases the stereoselectivity is better in ether than in acetonitrile, as this corresponds to a faster equilibrium process in which the more stable cyclic cation intermediate is the major one.

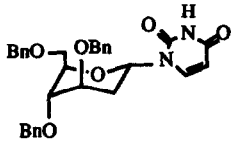
In summary, the face selectivity in the reaction of glycals with bis-(trimethylsilyl)uracil induced by PhSeCl is determined by the protecting groups present in the glycal, the stereochemistry of glycal substituents, the solvent and also by the activating reagent. The reaction takes place in two steps, and the stereoselectivity depends on the preferred formation of the cyclic phenylselenonium cation intermediate by the more or less hindered face. Glycal structure and protecting groups determine which selenonium cation is preferentially formed. The more hindered intermediate [B] (Scheme 1) principally results from acetylated glycals and especially when the acetoxy group at position 4 is axial, and the less hindered intermediate [A] is preferentially formed starting from benzyl protected glycals and using PhSeCl and ether. The solvent, in addition to the different stabilisations of conformers, influences the stereoselectivity by increasing the isomerization of selenonium cations, leading to a thermodynamically more stable selenonium cation.

2'-DEOXYPYRANOSYL NUCLEOSIDES

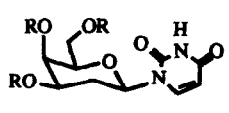
As can be seen in Table 4, benzyl glycals gave better stereoselectivities in ß-*gluco*, ß-*galacto* and α-*arabino* 2'-deoxy-2'-phenylselenenyl-pyranosyl nucleosides. Compounds **7b** and **10b**, which were obtained with the higher stereoselectivity, and their corresponding acetyl derivatives **7a** and **10a** were treated with tributyltin hydride and AIBN in benzene and heated to reflux to give the 2'-deoxy-pyranosyl nucleosides **13b-14b** and **13a-14a** respectively, in yields above 80%.



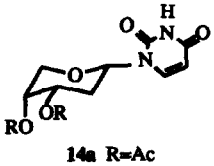
11a R=Ac
11b R=Bn



12



13a R=Ac
13b R=Bn



14a R=Ac
14b R=Bn

As has been described before, tri-O-benzyl derivatives **4b** and **5b** were obtained as an inseparable mixture. When, a 4:1 mixture of these compounds was treated with tributyltin hydride 2-deoxy-pyranosyl

Table 6. Selected ^1H NMR chemical shifts for compounds **11a-b, 12, 13a-b and 14a-b.**

Comp./J	H6	H5	H1'	H2'a	H2'e	H3'	H4'	H5'	H6'	H6''
11a	7.30	5.76	5.85	1.80	2.40	5.14	4.98	3.80	4.23	4.04
11b	7.4-7.1	5.76	5.69	1.65	2.45	3.84 ----------			3.42	
12	7.5-7.2	5.70	6.07	2.19-2.01		3.8	3.53	4.30	3.9-3.8	3.70
13a	7.43	5.83	5.86	2.15-2.10		5.17	5.36		4.81--4.01	--
13b	7.43	5.66	5.64	2.10-2.00		3.64	3.82		3.64	
14a	7.42	5.80	6.14	2.30-2.00		5.47	5.24	4.39	4.65	4.29
14b	7.51	5.78	5.61	2.24-2.03		3.71	3.71		4.20	3.48

Table 7. ^1H NMR coupling constants for compounds **11a-b, 12, 13a-b and 14a-b.**

Comp./J	$J_{5,6}$	$J_{1',2'a}$	$J_{1',2'e}$	$J_{2'a,2'e}$	$J_{2'a,3'}$	$J_{2'e,3}$	$J_{3',4'}$	$J_{4',5'}$	$J_{5',6'}$	$J_{5',6''}$	$J_{6',6''}$
11a	8.1	11.1	2.0	12.3	11.1	5.1	10.9	9.7	5.1	2.0	12.5
11b	8.3	11.1	2.2	11.1	11.1	4.9	--	--	--	--	--
12	8.0	10.1	3.6	--	--	--	3.0	3.0	--	5.5	10.1
13a	8.2	13.0	3.3	--	11.5	5.6	3.0	--	--	--	--
13b	8.1	8.0	5.0	--	--	--	--	--	--	--	--
14a	8.2	9.1	3.7	--	3.3	3.3	3.3	5.6	8.8	2.9	12.1
14b	8.2	10.9	2.7	--	--	--	--	1.7	12.8[a]		

[a] $J_{5',5''}$.

nucleosides **11b** and **12** were also obtained in the same ratio as an inseparable mixture. A small fraction of this mixture was purified by HPLC for identification purposes. In the same way **11a** was obtained from **4a**.

The replacement of the PhSe group by a proton does not alter the conformation, conserving, in the obtained 2'-deoxynucleosides, the same $^4C_1$ or $^1C_4$ conformation that they had in the starting 2'-deoxy-2'-phenylselenenyl nucleoside.[3,7a,18,19] The value of the coupling constants, $J_{1',2a'} > 9$Hz and $J_{1',2e'} > 4$Hz (Table 7), confirms the equatorial disposition for the uracil in all the 2'-deoxypyranosyl nucleosides synthesised.

In conclusion, 2'-deoxy-2'-phenylselenenyl pyranosyl nucleosides have been stereoselectively obtained from glycals and converted into the corresponding 2'-deoxypyranosyl nucleosides in good yields.

EXPERIMENTAL SECTION

General Procedures: Melting points were measured in a Büchi 510 apparatus and appear uncorrected. Optical rotations were measured at room temperature in 10 cm cells in a Perkin-Elmer 241 polarimeter. ^1H NMR and ^{13}C NMR spectra were recorded in a Varian Gemini 300 MHz (300 and 75.4 MHz resp.) apparatus, with $CDCl_3$ as solvent and using Me_4Si (δ=0)and the central solvent peak at ∂ 77.0 ppm respectively as internal reference. Elemental analyses were determined using a Carlo-Erba Microanalysis. Flash column chromatography was performed with silica gel 60 A CC (230-400 mesh). TLC plates were prepared by using Kieselgel 60 PF_{254} (E. Merk). HPLC was performed with a C-18 silicagel column (25mm x 10 cm) using acetonitrile/water 60:40 as eluent. Solvents for chromatography were distilled at atmospheric pressure prior to use. Dichloromethane was distilled from P_2O_5. Benzene was dried by distillation from Na ribbon and strored over 4Å molecular sieves and under argon. Dry ether was obtained by distillation, under nitrogen, from sodium benzophenone ketyl. Other solvents were purified and dried by using standard procedures. All the reactions were carried out under an argon atmosphere using standard syringe techniques.

General Procedure for the synthesis of 2'-phenylselenenyl-pyranosyl nucleosides from glycals. To a solution of glycal (0.25 mmol) in 1 ml of dry solvent, keeped under argon and light protected, 0.37 mmol of the phenylselenenyl reagent was added at room temperature, after 5 minutes 0.5 mmol of bis-(trimethylsilyl) uracil and finally 0.42 mmol of the catalyst were also added to the reaction flask. After the reaction was finished (about 0.5-24 h) ethyl acetate (25 mL) were added and the reaction mixture was filtered off through a silicagel-Celite pad (the Celite pad was washed with 2x10 mL of ethyl acetate). Evaporation of the solvent gave the crude product mixture which was subjected to TLC or flash chromatography.

1-(2'-Deoxy-2'-phenylselenenyl-3',4',6'-tri-O-acetyl-ß-D-*gluco*-pyranosyl)-uracil (4a) and 1-(2'-deoxy-2'-phenylselenenyl-3',4',6'-tri-O-acetyl-α-D-*manno*-pyranosyl)-uracil (5a).
The general procedure was applied starting from 3,4,6-tri-O-acetyl-D-glucal, phenylselenenyl chloride, silver triflate and bis-(trimethylsilyl)uracil in ether. The reaction was stopped after 0.5 hours. Flash chromatography (ethyl acetate-hexane 3:2) of the reaction crude gave 59 mg (44%) of **4a** and 44 mg of a mixture of **5a/6** (2:1). A small sample of this mixture was purified by HPLC for characterisation purposes.
(**4a**). Mp= 98-99°C, $[\alpha]_D^{20}$ +69.2° (*c* 0.5, $CHCl_3$). **^1H NMR:** δ 9.45 (s, 1H, NH); 7.50-7.10 (Ph); 6.88 (d,1H, $J_{H\text{-}6,H\text{-}5}$=8.2 Hz, H-6); 5.94 (d, 1H, $J_{H\text{-}1',H\text{-}2'}$=11.0 Hz, H-1'); 5.39 (dd, 1H, $J_{H\text{-}5,NH}$=1.8 Hz, H-5); 5.25 (dd, 1H, $J_{H\text{-}3',H\text{-}4'}$=9.1 Hz, $J_{H\text{-}3',H\text{-}2'}$=11.0 Hz, H-3'); 5.05 (dd, 1H, $J_{H\text{-}4',H\text{-}5'}$=9.9 Hz, H-4'); 4.22 (dd, 1H, $J_{H\text{-}6',H\text{-}6''}$=12.6 Hz, $J_{H\text{-}6',H\text{-}5'}$=4.8 Hz, H-6'); 4.02 (dd, 1H, $J_{H\text{-}6'',H\text{-}5'}$=2.0 Hz, H-6''); 3.85 (ddd, 1H, H-5'); 3.28 (t, 1H, H-2'); 2.07 (Me); 2.01 (Me); 2.01 (Me). **^{13}C NMR:** δ 170.8 ($CH_3\underline{C}O$); 170.1 ($CH_3\underline{C}O$); 170.0 ($CH_3\underline{C}O$); 162.8 (C-4); 150.4 (C-2); 138.0-129.1 (Ph); 136.6 (C-6); 103.1 (C-5); 82.5 (C-1'); 74.4 (C-4'); 72.4 (C-3'); 68.8 (C-5'); 61.7 (C-6'); 48.3 (C-2'); 20.5 (2xMe); 20.4 (Me). **IR:** 1748, 1737, 1735 cm^{-1} ($\sqrt{}_{CO}$); 1691, 1687 cm^{-1} ($\sqrt{}_{CO}$); 1632 cm^{-1} ($\sqrt{}_{CH=CH}$). Anal. Calcd for $C_{22}H_{24}N_2O_9Se$: C, 49.01; H, 4.45; N, 5.19. Found: C, 48.62; H, 4.52; N, 5.10.
(**5a**). Mp = 74 - 76°C, $[\alpha]_D^{20}$ -41.7° (*c* 0.2, $CHCl_3$). **^1H NMR:** δ 8.47 (s, 1H, NH); 7.45-7.10 (Ph); 6.93 (d,1H, $J_{H\text{-}6,H\text{-}5}$=8.2 Hz, H-6); 6.06 (d, 1H, $J_{H\text{-}1',H\text{-}2'}$=10.8 Hz, H-1'); 5.49 (dd, 1H, $J_{H\text{-}3',H\text{-}4'}$=2.2 Hz, $J_{H\text{-}3',H\text{-}2'}$=3.3 Hz, H-3'); 5.35 (dd, 1H, $J_{H\text{-}5,NH}$=2.2 Hz, H-5); 4.81 (dd, 1H, $J_{H\text{-}4',H\text{-}5'}$=5.1 Hz, H-4'); 4.52 (dd, 1H, $J_{H\text{-}6',H\text{-}6''}$=11.8 Hz, $J_{H\text{-}6',H\text{-}5'}$=7.9 Hz, H-6'); 4.29 (m, 1H, H-5'); 4.18 (dd, 1H, $J_{H\text{-}6'',H\text{-}5'}$=5.0 Hz, H-6''); 3.87

(dd, 1H, H-2'); 2.14 (Me); 2.10 (Me); 2.00 (Me). **^{13}C NMR:** δ 170.6 ($CH_3\underline{C}O$); 169.0 ($CH_3\underline{C}O$); 168.9 ($CH_3\underline{C}O$); 162.4 (C-4); 150.0 (C-2); 140.2 (C-6); 138.0-128.9 (Ph); 102.4 (C-5); 80.1 (C-1'); 75.3 (C-4'); 71.6 (C-3'); 67.0 (C-5'); 60.2 (C-6'); 43.2 (C-2'); 20.9 (Me); 20.6 (2xMe). **IR:** 1744, 1717 cm^{-1} ($\sqrt{}_{CO}$); 1695, 1685 cm^{-1} ($\sqrt{}_{CO}$, anillo); 1620 cm^{-1} ($\sqrt{}_{CH=CH}$). Anal. Calcd for $C_{22}H_{24}N_2O_9Se$: C, 49.01; H, 4.45; N, 5.19. Found: C, 48.75; H, 4.56; N, 5.05.

(**6**). Mp = 184 - 185°C, $[\alpha]_D^{21}$ +46.5° (*c* 1, $CHCl_3$). **^{1}H NMR:** δ 8.85 (s, 1H, NH); 7.20 (d, 1H, $J_{H\text{-}6,H\text{-}5}$= 8.1 Hz, H-6); 6.55 (dd, 1H, $J_{H\text{-}1',H\text{-}2'}$= 2.0 Hz, $J_{H\text{-}1',H\text{-}3'}$= 3.9 Hz, H-1'); 6.18 (dt, 1H, $J_{H\text{-}2',H\text{-}3'}$= 10.3 Hz, $J_{H\text{-}2',H\text{-}4'}$= 2.0 Hz, H-2'); 5.80-5.75 (m, 2H, H-5, H-3'); 5.38 (dt, 1H, $J_{H\text{-}4',H\text{-}3'}$= $J_{H\text{-}4',H\text{-}2'}$= 2.0 Hz, $J_{H\text{-}4',H\text{-}5'}$= 9.1 Hz, H-4'); 4.25-4.17 (m, 2H, H-6', H-6"); 4.03 (m, 1H, H-5'); 2.12 (Me); 2.09 (Me). **^{13}C NMR:** δ 170.9 ($CH_3\underline{C}O$); 170.2 ($CH_3\underline{C}O$); 162.5 (C-4); 150.1 (C-2); 140.0 (C-6); 132.8 (C-2'); 127.2 (C-3'); 103.5 (C-5); 78.6 (C-1'); 75.1 (C-4'); 64.0 (C-5'); 62.6 (C-6'); 20.9 (Me); 20.8 (Me). Anal. Calcd for $C_{14}H_{16}N_2O_7$: C, 51.88; H, 4.93; N, 8.64. Found: C, 51.52; H, 4.83; N, 8.40.

1-(2'-Deoxy-2'-phenylselenenyl-3',4',6'-tri-O-benzyl-ß-D-*gluco*-pyranosyl)-uracil (4b) and 1-(2'-deoxy-2'-phenylselenenyl-3',4',6'-tri-O-benzyl-α-D-*manno*-pyranosyl)-uracil (5b).

Glycosylation was carried out in ether starting from 3,4,6-tri-O-benzyl-D-glucal and phenylselenenyl chloride, bis-(trimethylsilyl)uracil and silver triflate in ether. The reaction was stopped after 0.5 hours. Flash chromatography (ethyl acetate-hexane 2:3) did not allow the separation of the phenylselenenyl nucleosides, obtaining 144 mg (85%) of a 4:1 mixture of compound **4b** and **5b**. A small sample of this mixture was purified by HPLC for identification purposes.

(**4b**). **^{1}H NMR:** δ 8.40 (s, 1H, NH); 7.50-7.10 (Ph); 6.79 (d, 1H, $J_{H\text{-}6,H\text{-}5}$=7.9 Hz, H-6); 5.88 (d, 1H, $J_{H\text{-}1',H\text{-}2'}$=10.7 Hz, H-1'); 5.23 (dd, 1H, $J_{H\text{-}5,NH}$=2.2 Hz, H-5); 4.91 (d, 1H, J_{gem}=10.1 Hz, $C\underline{H}_2Ph$); 4.83 (d, 1H, J_{gem}=10.1 Hz, $C\underline{H}_2Ph$); 4.78 (d, 1H, J_{gem}=12.8 Hz, $C\underline{H}_2Ph$); 4.55 (d, 1H, J_{gem}=12.8 Hz, $C\underline{H}_2Ph$); 4.46 (d, 1H, J_{gem}=12.1 Hz, $C\underline{H}_2Ph$); 4.39 (d, 1H, J_{gem}=12.1 Hz, $C\underline{H}_2Ph$); 3.74-3.50 (m, 5H, H-3', H-4', H-5', H-6', H-6"); 3.23 (t, 1H, $J_{H\text{-}2',H\text{-}3'}$=10.7 Hz, H-2'). **^{13}C NMR:** δ 162.0 (C-4); 150.0 (C-2); 138.9 (C-6); 139.3-128.1 (Ph); 102.5 (C-5); 82.6 (C-1'); 82.9 (C-4'); 79.0 (C-3'); 77.8 ($\underline{C}H_2Ph$); 77.8 ($\underline{C}H_2Ph$); 75.6 ($\underline{C}H_2Ph$); 73.5 (C-5'); 68.3 (C-6'); 51.4 (C-2'). **IR:** 1716, 1696 cm^{-1} ($\sqrt{}_{CO}$); 1635 cm^{-1} ($\sqrt{}_{CH=CH}$).

(**5b**). **^{1}H NMR:** δ 7.80 (s, 1H, NH); 7.40-7.10 (Ph); 6.77 (d, 1H, $J_{H\text{-}6,H\text{-}5}$=8.2 Hz, H-6); 6.19 (d, 1H, $J_{H\text{-}1',H\text{-}2'}$=10.9 Hz, H-1'); 5.04 (dd, 1H, $J_{H\text{-}5,NH}$=2.1 Hz, H-5); 4.60-4.25 (m, 7H, 3x$C\underline{H}_2Ph$, H-5'); 4.16 (dd, 1H, $J_{H\text{-}3',H\text{-}2'}$=3.3 Hz, $J_{H\text{-}3',H\text{-}4'}$=1.9 Hz, H-3'); 3.78 (dd, 1H, $J_{H\text{-}6',H\text{-}6"}$=10.1 Hz, $J_{H\text{-}6',H\text{-}5'}$=7.1 Hz, H-6'); 3.69 (dd, 1H, H-2'); 3.59 (dd, 1H, $J_{H\text{-}4',H\text{-}5'}$=2.8 Hz, H-4'); 3.64 (dd, 1H, $J_{H\text{-}6",H\text{-}5'}$=6.8, H-6"). **RMN ^{13}C NMR:** δ 162.0 (C-4); 150.0 (C-2); 139.5 (C-6); 138.0-127.7 (Ph); 101.8 (C-5); 78.7 (C-4'); 77.3 (C-1'); 76.2 (C-3'); 73.4 ($\underline{C}H_2Ph$); 73.1 ($\underline{C}H_2Ph$); 71.1 ($\underline{C}H_2Ph$); 71.1 (C-5'); 67.3 (C-6'); 46.6 (C-2'). **IR:** 1712, 1698 cm^{-1} ($\sqrt{}_{CO}$); 1632 cm^{-1} ($\sqrt{}_{CH=CH}$).

1-(2'-Deoxy-2'-phenylselenenyl-3',4',6'-tri-O-acetyl-ß-D-*galacto*-pyranosyl)-uracil (7a) and 1-(2'-deoxy-2'-phenylselenenyl-3',4',6'-tri-O-acetyl-α-D-*talo*-pyranosyl)-uracil (8a).

Following the general procedure the glycosylation was performed starting from 3,4,6-tri-O-acetyl-D-galactal and using phenylselenenyl chloride, bis-(trimethylsilyl)uracil and silver triflate in ether as the solvent for 4 hours. Thin layer chromatography (ethyl acetate-hexane (1:3) of the reaction crude gave 54 mg of **7a** and 54 mg of **8a**, total yield 80% (7a/8a = 50:50).

(**7a**). Mp = 104-106ºC, $[\alpha]_D^{20}$ +37.5° (*c* 0.3, $CHCl_3$). **^{1}H NMR:** δ 8.95 (s, 1H, NH); 7.60-7.20 (Ph); 7.10 (d, 1H, $J_{H\text{-}6,H\text{-}5}$=8.3 Hz, H-6); 5.96 (d, 1H, $J_{H\text{-}1',H\text{-}2'}$=10.7 Hz, H-1'); 5.61 (dd, 1H, $J_{H\text{-}5,NH}$=2.0 Hz, H-5);

5.37 (d, 1H, $J_{H\text{-}3',H\text{-}4'}$=3.2 Hz, H-4'); 4.91 (dd, 1H, $J_{H\text{-}3',H\text{-}2'}$=11.7 Hz, H-3'); 4.24-3.96 (m, 3H, H-5', H-6', H-6"); 3.40 (dd, 1H, H-2'); 2.19 (Me); 2.08 (Me); 2.03 (Me). **^{13}C NMR:** δ 162.6 (3x$CH_3\underline{C}O$); 162.4 (C-4); 150.2 (C-2); 138.6 (C-6); 138.0-129.7 (Ph); 103.3 (C-5); 82.5 (C-1'); 73.3 (C-4'); 70.3 (C-3'); 66.5 (C-5'); 61.4 (C-6'); 43.6 (C-2'); 20.5 (3xMe). **IR:** 1748, 1735 cm^{-1} ($\sqrt{_{CO}}$); 1697, 1690 cm^{-1} ($\sqrt{_{CO}}$); 1630 cm^{-1} ($\sqrt{_{CH=CH}}$). Anal. Calcd for $C_{22}H_{24}N_2O_9Se$: C, 49.01; H, 4.45; N: 5.19. Found: C, 48.90; H, 4.57; N, 5.02.

(8a). Mp= 114-116 °C, $[\alpha]_D^{20}$ -19.0° (*c* 0.6, $CHCl_3$). **^{1}H NMR:** δ 8.53 (s, 1H, NH); 7.50-7.20 (Ph); 7.03 (d, 1H, $J_{H\text{-}6,H\text{-}5}$=8.2 Hz, H-6); 6.16 (d, 1H, $J_{H\text{-}1',H\text{-}2'}$=10.7 Hz, H-1'); 5.93 (t, 1H, $J_{H\text{-}3',H\text{-}2'}$=$J_{H\text{-}3',H\text{-}4'}$=3.0 Hz, H-3'); 5.44 (dd, 1H, $J_{H\text{-}5,NH}$=1.7 Hz, H-5); 5.31 (dd, 1H, $J_{H\text{-}4',H\text{-}5'}$=6.8 Hz, H-4'); 4.91 (dd, 1H, $J_{H\text{-}6',H\text{-}6''}$=12.8 Hz, $J_{H\text{-}6',H\text{-}5'}$=10.0 Hz, H-6'); 4.45-4.36 (m, 1H, H-5'); 4.25 (dd, 1H, $J_{H\text{-}6'',H\text{-}5'}$=2.2 Hz, H-6"); 3.84 (dd, 1H, H-2'); 2.23 (Me); 2.08 (Me); 2.06 (Me). **^{13}C NMR:** δ 172.0 ($CH_3\underline{C}O$); 162.6 (C-4); 160.6 (2x$CH_3\underline{C}O$); 150.0 (C-2); 140.5 (C-6); 135.5-127.0 (Ph); 102.6 (C-5); 79.3 (C-1'); 74.0 (C-4'); 70.2 (C-3'); 67.1 (C-5'); 59.3 (C-6'); 45.3 (C-2'); 20.6 (Me); 20.6 (Me); 20.4 (Me). Anal. Calcd for $C_{22}H_{24}N_2O_9Se$: C, 49.01; H, 4.45; N, 5.19. Found: C, 48.61; H, 4.54; N, 4.99.

1-(2'-Deoxy-2'-phenylselenenyl-3',4',6'-tri-O-benzyl-ß-D-*galacto*-pyranosyl)-uracil (7b) and 1-(2'-deoxy-2'-phenylselenenyl-3',4',6'-tri-O-benzyl-α-D-*talo*-pyranosyl)-uracil (8b).

The general procedure was applied to 3,4,6-tri-O-benzyl-D-galactal and phenylselenenyl chloride, bis-(trimethylsilyl)uracil and silver triflate, in ether as the solvent. The reaction was stopped after 1 hour. Thin layer chromatography (ethyl acetate-hexane 1:1) of the reaction crude gave 128 mg of **7b** and 13 mg of **8b**, total yield 82% (**7b/8b** = 91:9).

(7b). M.p. 132-134 °C; $[\alpha]_D^{20}$ +74.3° (*c* 0.45, $CHCl_3$). **^{1}H NMR:** δ 8.27 (s, 1H, NH); 7.60-7.15 (m, 20 H, Ph); 7.00 (d, 1H, $J_{H\text{-}6,H\text{-}5}$= 8.2 Hz, H-6); 5.87 (d, 1H, $J_{H\text{-}1',H\text{-}2'}$= 10.6 Hz, H-1'); 5.39 (dd, 1H, $J_{H\text{-}5,NH}$= 1.9 Hz, H-5); 4.90 (d, 1H, J_{gem}= 11.3 Hz, $C\underline{H}_2Ph$); 4.75 (d, 1H, J_{gem}= 11.3 Hz, $C\underline{H}_2Ph$); 4.59 (d, 1H, J_{gem}= 11.3 Hz, $C\underline{H}_2Ph$); 4.57 (d, 1H, J_{gem}= 11.3 Hz, $C\underline{H}_2Ph$); 4.46 (d, 1H, J_{gem}= 11.8 Hz, $C\underline{H}_2Ph$); 4.41 (d, 1H, J_{gem}= 11.8 Hz, $C\underline{H}_2Ph$); 4.00 (m, 1H, H-4'); 3.70 (dd, 1H, $J_{H\text{-}2',H\text{-}3'}$= 11.1 Hz, H-2'); 3.68 (m, 1H, H-5'); 3.56 (dd, 1H, $J_{H\text{-}6',H\text{-}6''}$= 9.0 Hz, $J_{H\text{-}6',H\text{-}5'}$= 7.3 Hz, H-6'); 3.50 (dd, 1H, $J_{H\text{-}6'',H\text{-}5'}$= 5.7 Hz, H-6"); 3.44 (dd, 1 H, $J_{H\text{-}3',H\text{-}4'}$= 2.5 Hz, H-3'). **^{13}C NMR:** δ 162.39 (C-4); 150.00 (C-2); 139.48 (C-6); 135.24-127.36 (Ph); 102.62 (C-5); 83.19 (C-1'); 79.89 (C-4'); 75.66 (C-3'); 74.84 ($\underline{C}H_2Ph$); 73.52 ($\underline{C}H_2Ph$); 72.37 ($\underline{C}H_2Ph$); 72.07 (C-5'), 67.94 (C-6'); 47.27 (C-2'). Anal. Calcd. for $C_{37}H_{36}N_2O_6Se$: C, 65.03; H, 5.26; N, 4.09. Found: C, 64.64; H, 5.35; N, 4.22.

(8b). **^{1}H NMR:** δ 8.03 (s, 1H, NH); 7.50-7.20 (m, 21 H, Ph, H-6); 5.73 (dd, 1H, $J_{H\text{-}5,H\text{-}6}$= 8.0 Hz, $J_{H\text{-}5,NH}$= 1.7 Hz, H-5); 5.68 (d, 1H, $J_{H\text{-}1',H\text{-}2'}$= 9.0 Hz, H-1'); 4.94 (d, 1H, J_{gem}= 11.4 Hz, $C\underline{H}_2Ph$); 4.60 (d, 1H, J_{gem}= 11.4 Hz, $C\underline{H}_2Ph$); 4.60 (s, 2H, $C\underline{H}_2Ph$); 4.50 (d, 1H, J_{gem}= 11.9 Hz, $C\underline{H}_2Ph$); 4.44 (d, 1H, J_{gem}= 11.9 Hz, $C\underline{H}_2Ph$); 3.89 (m, 1H, H-3'); 3.74-3.60 (m, 3H, H-4', H-5', H-2'); 3.59-3.55 (m, 2H, H-6', H-6"). **^{13}C NMR:** δ 140.10 (C-6); 128.56-127.34 (Ph); 102.76 (C-5); 19.90 (C-1'); 77.21 (C-4'); 76.20 (C-3'); 74.54 ($\underline{C}H_2Ph$); 73.56 ($\underline{C}H_2Ph$); 71.61 ($\underline{C}H_2Ph$); 70.58 (C-5'); 68.65 (C-6'); 41.00 (C-2').

1-(2'-Deoxy-2'-phenylselenenyl-3',4'-di-O-acetyl-ß-D-*ribo*-pyranosyl)-uracil (9a) and 1-(2'-deoxy-2'-phenylselenenyl-3',4'-di-O-acetyl-α-D-*arabino*-pyranosyl)-uracil (10a).

Glycosylation was carried out starting from 3,4-di-O-acetyl-D-arabinal in ether and using phenylselenenyl chloride, bis-(trimethylsilyl)uracil and silver triflate. After 2 hours the reaction was stopped. Purification of the reaction crude by thin layer chromatography, successive elution with methylene chloride/hexane/methanol 10:6:0.2, gave 35 mg of **9a** and 52 mg of **10a** as an oil , total yield 75% (**9a/10a** = 40:60).

(**9a**). $[\alpha]_D^{20}$ +36.7° (*c* 0.4, $CHCl_3$). **^{1}H NMR:** δ 8.22 (s, 1H, NH); 7.40-7.10 (Ph); 6.76 (d, 1H, $J_{H-6,H-5}$=8.2 Hz, H-6); 6.03 (d, 1H, $J_{H-1',H-2'}$=10.7 Hz, H-1'); 5.89 (dd, 1H, $J_{H-3',H-2'}$=2.7 Hz, $J_{H-3',H-4'}$=2.8 Hz, H-3'); 5.26 (dd, 1H, $J_{H-5,NH}$=2.4 Hz, H-5); 5.01-4.95 (m, 2H, H-4', H-5'); 3.86 (dd, 1H, $J_{H-5'',H-5'}$=9.1 Hz, $J_{H-5'',H-4'}$=1.4 Hz, H-5''); 3.37 (dd, 1H, H-2'); 2.15 (Me); 1.95 (Me). **^{13}C NMR:** δ 169.7 (2x$CH_3\underline{C}O$); 161.7 (C-4); 150.0 (C-2); 139.0 (C-6); 135.4-126.6 (Ph); 102.7 (C-5); 81.9 (C-1'); 70.4 (C-4'); 66.8 (C-3'); 63.8 (C-5'); 46.7 (C-2'); 20.6 (2xMe). Anal. Calcd. for $C_{19}H_{20}N_2O_7Se$: C, 48.82; H, 4.28; N, 5.99. Found: C, 48.25; H, 4.32; N, 5.81.

(**10a**). $[\alpha]_D^{20}$ -25.0° (*c* 0.52, $CHCl_3$). **^{1}H NMR:** δ 8.40 (s, 1H, NH); 7.50-7.10 (Ph); 7.01 (d, 1H, $J_{H-6,H-5}$=8.3 Hz, H-6); 5.74 (d, 1H, $J_{H-1',H-2'}$=10.7 Hz, H-1'); 5.49 (dd, 1H, $J_{H-5,NH}$=2.4 Hz, H-5); 5.21-5.18 (m, 1H, H-4'); 4.86 (dd, 1H, $J_{H-3',H-2'}$=11.6 Hz, $J_{H-3',H-4'}$=3.2 Hz, H-3'); 3.98 (dd, 1H, $J_{H-5',H-5''}$=13.4 Hz, $J_{H-5',H-4'}$=2.5 Hz, H-5'); 3.69 (dd, 1H, $J_{H-5'',H-4'}$=1.1 Hz, H-5''); 3.43 (dd, 1H, H-2'); 2.10 (Me); 2.03 (Me). **^{13}C NMR:** δ 169.9 ($CH_3\underline{C}O$); 169.0 ($CH_3\underline{C}O$); 162.0 (C-4); 150.0 (C-2); 139.0 (C-6); 136.2-129.2 (Ph); 103.0 (C-5); 83.4 (C-1'); 70.1 (C-4'); 67.5 (C-3'); 67.0 (C-5'); 44.3 (C-2'); 21.0 (Me); 20.7 (Me). Anal. Calcd. for $C_{19}H_{20}N_2O_7Se$: C, 48.82; H, 4.28; N, 5.99. Found: C, 48.37; H, 4.36; N, 5.85.

1-(2'-Deoxy-2'-phenylselenenyl-3',4'-di-O-benzyl-ß-D-*ribo*-pyranosyl)-uracil (9b) and 1-(2'-deoxy-2'-phenylselenenyl-3',4'-di-O-benzyl-α-D-*arabino*-pyranosyl)-uracil (10b).
Following the general procedure the glycosylation was carried out starting from 3,4-di-O-benzyl-D-arabinal in ether and using phenylselenenyl chloride, bis-(trimethylsilyl)uracil and silver triflate. After 1 hours the standard work-up and purification by thin layer chromatography (ethyl acetate-hexane 1:1) of the reaction crude gave 92 mg of **10b** and 8 mg of **9b**; total yield 71% (**9b/10b** = 8:92).

(**10b**). M.p. 69-70 °C, $[\alpha]_D^{21}$ -74.0° (*c* 0.5, $CHCl_3$), **^{1}H NMR:** δ 9.04 (s, 1H, NH); 7.40-7.15 (m, 10 H, Ph); 7.08 (d, 1H, $J_{H-6,H-5}$ = 8.1 Hz, H-6); 5.82 (d, 1H, $J_{H-1',H-2'}$ = 10.5 Hz, H-1'); 5.43 (dd, 1H, $J_{H-5,NH}$ = 2.1 Hz, H-5); 4.74 (d, 1H, J_{gem}= 12.2 Hz, $C\underline{H}_2Ph$); 4.65 (d, 1H, J_{gem}= 12.2 Hz, $C\underline{H}_2Ph$); 4.62 (d, 1H, J_{gem}= 11.5 Hz, $C\underline{H}_2Ph$); 4.51 (d, 1H, J_{gem}= 11.5 Hz, $C\underline{H}_2Ph$); 4.12 (dd, 1H, $J_{H-5',H-5''}$ = 13.0 Hz, $J_{H-5',H-4}$ = 2.0 Hz, H-5'), 3.75 (t, 1H, $J_{H-2',H-3'}$ = 10.5 Hz, H-2'); 3.74 (m, 1H, H-4'); 3.43 (d, 1H, H-5''), 3.41 (dd, 1H, $J_{H-3',H-4}$ = 2.8 Hz, H-3'). **^{13}C NMR:** δ 163.09 (C-4); 150.81 (C-2); 139.77 (C-6); 135.25-127.08 (Ph); 103.16 (C-5); 83.97 (C-1'); 78.64 (C-4'); 72.11 ($\underline{C}H_2Ph$); 71.86 ($\underline{C}H_2Ph$); 71.38 (C-3'); 66.36 (C-5'), 47.29 (C-2'). Anal. Calcd for $C_{29}H_{28}N_2O_5Se$: C, 61.84; H, 4.97; N, 4.97. Found: C, 61.45; H, 5.10; N, 4.95.

(**9b**). **^{1}H NMR:** δ 7.80 (s, 1H, NH); 7.36 (d, 1H, $J_{H-6,H-5}$ = 8.2 Hz, H-6); 7.40-7.10 (m, 10 H, Ph); 5.97 (d, 1H, $J_{H-1',H-2'}$ = 1.9 Hz, H-1'); 5.97 (dd, 1H, $J_{H-5,NH}$ = 1.9 Hz, H-5); 4.80 (d, 1H, J_{gem}= 12.1 Hz, $C\underline{H}_2Ph$); 4.72 (d, 1H, J_{gem}= 12.1 Hz, $C\underline{H}_2Ph$); 4.59 (d, 1H, J_{gem}= 12.0 Hz, $C\underline{H}_2Ph$); 4.51 (d, 1H, J_{gem}= 12.0 Hz, $C\underline{H}_2Ph$); 4.32 (t, 1H, $J_{H-3',H-4'}$ = $J_{H-3',H-2'}$ = 3.0 Hz, H-3'); 4.04 (m, 3H, H-2', H-5', H-5''); 3.75 (ddd, 1H, $J_{H-4',H-5'}$ = 10.1 Hz, $J_{H-4',H-5''}$ = 6.1 Hz, H-4'). **^{13}C NMR:** δ 140.86 (C-6); 133.03-127.79 (Ph); 100.43 (C-5); 80.71 (C-1'); 77.68 (C-4'); 72.05 ($\underline{C}H_2Ph$); 71.72 ($\underline{C}H_2Ph$); 71.38 (C-3'); 65.88 (C-5'), 48.83 (C-2').

General procedure for reduction of the 2'-phenylselenenyl-pyranosyl nucleosides with tributyltin hydride. To a solution of 0.15 mmol of 2'-phenylselenenyl nucleoside in 2 mL of anhydrous benzene, 0.33 mmol (1 mL) of tri-butyltin hydride and 3 mg of 2,2'-azoisobutyronitrile (AIBN) were added at room temperature. Then the reaction was heated to reflux. When the starting material had disappeared (0.5-2 hours), the reaction mixture was cooled and evaporated dry. The resulting reaction crude was purified by flash chromatography.

1-(2'-Deoxy-3',4',6'-tri-O-acetyl-ß-D-*arabino*-hexo-pyranosyl)uracil (11a). The reaction of compound **4a** with tributyltin hydride was carried out following the general procedure. The reaction crude resulting was purified by flash chromatography (ethyl acetate-hexane 2:1) giving 46 mg (80%) of compound **11a**.

^{13}C NMR: δ 170.8 ($CH_3\underline{C}O$); 170.1 ($CH_3\underline{C}O$); 170.0 ($CH_3\underline{C}O$); 163.3 (C-4); 150.0 (C-2); 139.1 (C-6); 103.3 (C-5); 79.0 (C-1'); 74.7 (C-4'); 70.1 (C-3'); 68.0 (C-5'); 61.9 (C-6'); 35.0 (C-2'); 20.5 (Me); 20.5 (Me); 20.4 (Me). Anal. Calcd. for $C_{16}H_{20}N_2O_9$: C, 50.03; H, 5.20; N, 7.29.

1-(2'-Deoxy-3',4',6'-tri-O-benzyl-ß-D-*arabino*-hexo-pyranosyl)-uracil (11b) and 1-(2'-Deoxy-3',4',6'-tri-O-benzyl-α-D-*arabino*-hexo-pyranosyl)-uracil (12). A mixture of compounds **4b** and **5b** was treated with tributyltin hydride according with the general procedure. After 30 min. the reaction mixture was cooled and evaporated dry, obtaining 71 mg (90%) of a inseparable mixture of compounds **11b** and **12**. A small fraction of this mixture was purified by HPLC for identification purposes.

(**11b**). ^{13}C NMR: δ 162.4 (C-4); 149.5 (C-2); 139.5 (C-6); 138.0-127.6 (Ph); 102.8 (C-5); 79.7 (C-1'); 79.6 (C-4'); 79.1 (C-3'); 77.0 ($\underline{C}H_2Ph$); 75.5 ($\underline{C}H_2Ph$); 73.4 ($\underline{C}H_2Ph$); 71.9 (C-5'); 68.6 (C-6'); 36.0 (C-2').

(**12**). ^{13}C NMR: δ 162.0 (C-4); 150.0 (C-2); 140.2 (C-6); 138.0-127.7 (Ph); 102.3 (C-5); 77.8 (C-1'); 73.4 (C-4'); 71.7 (C-3'); 73.4 ($\underline{C}H_2Ph$); 71.2 (C-5'); 71.7 ($\underline{C}H_2Ph$); 71.2 ($\underline{C}H_2Ph$); 68.0 (C-6'); 30.3 (C-2').

1-(2'-deoxy-3',4',6'-tri-O-acetyl-ß-D-*lyxo*-hexo-pyranosyl)-uracil (13a). Compound **7a** was treated with tributyltin hydride following the general procedure. Flash chromatography (ethyl acetate-hexane 2:1) of the reaction crude gave 48 mg of **13a** (83%)

Mp= 66-68 ºC. $[\alpha]_D^{23}$ +21.7° (*c* 0.6, $CHCl_3$). ^{13}C NMR: δ 170.0 ($CH_3\underline{C}O$); 169.9 ($CH_3\underline{C}O$); 169.7 ($CH_3\underline{C}O$); 162.7 (C-4); 149.7 (C-2); 139.1 (C-6); 103.3 (C-5); 79.4 (C-1'); 73.9 (C-4'); 68.0 (C-3'); 65.1 (C-5'); 61.8 (C-6'); 30.8 (C-2'); 20.7 (3xMe). Anal. Calcd. for $C_{16}H_{20}N_2O_9$: C, 50.03; H, 5.20; N, 7.29. Found: C, 49.71; H, 5.17; N, 7.08.

1-(2'-deoxy-3',4',6-tri-O-benzyl-ß-D-*lyxo*-hexo-pyranosyl)uracil (13b). Compound **7b** was treated with tributyltin hydride following the general procedure. Flash chromatography (ethyl acetate-hexane 1:1) of the reaction crude gave 60 mg of **13b** (76 %).

Mp = 59-61 ºC. $[\alpha]_D^{20}$ +9.6° (*c* 0.5, $CHCl_3$). ^{13}C NMR: δ 163.0 (C-4); 149.9 (C-2); 140.2 (C-6); 128.7-127.5 (Ph); 102.9 (C-5); 80.0 (C-1'); 76.7 (C-4'); 76.6 (C-3'); 74.6 ($\underline{C}H_2Ph$); 73.6 ($\underline{C}H_2Ph$); 71.8 (C-5'); 70.7 ($\underline{C}H_2Ph$); 68.8 (C-6'); 31.8 (C-2'). Anal. Calcd. for $C_{31}H_{32}N_2O_6$: C, 70.45; H, 6.06; N, 5.30. Found: C, 69.42; H, 6.17; N, 5.52.

1-(2'-deoxy-3',4'-di-O-acetyl-α-D-*erythro*-pento-pyranosyl)uracil (14a). Compound **10a** was treated with tributyltin hydride following the general procedure. Flash chromatography (ethyl acetate-hexane 2:1) of the reaction crude gave 42 mg of **14a** (90%).

Mp = 70-72 ºC. $[\alpha]_D^{23}$ +30.6° (*c* 0.6, $CHCl_3$). ^{13}C NMR: δ 169.7 (3x$CH_3\underline{C}O$); 162.9 (C-4); 149.8 (C-2); 139.6 (C-6); 103.1 (C-5); 74.8 (C-1'); 73.4 (C-4'); 66.5 (C-3'); 66.3 (C-5'); 60.0 (C-6'); 32.9 (C-2'); 21.0 (Me); 20.8 (Me); 20.6 (Me). Anal. Calcd. for $C_{11}H_{16}N_2O_7$: C, 50.00; H, 5.13; N, 8.97. Found: C, 48.84; H, 5.09; N, 8.48.

1-(2'-deoxy-3',4'-di-O-benzyl-α-D-*erythro-pento*-pyranosyl)uracil (14b). Compound **10b** was treated with tributyltin hydride following the general procedure. Flash chromatography (ethyl acetate-hexane 1:1) of the reaction crude gave 52 mg of **14b** (85%).
$[\alpha]_D^{23}$ -36.6° (c, 6.5 $CHCl_3$). ^{13}C NMR: δ 163.24 (C-4); 150.10 (C-2); 140.03 (C-6); 128.43-127.44 (Ph), 102.90 (C-5); 79.99 (C-1'); 75.19 (C-4'); 71.54 ($\underline{C}H_2Ph$); 70.60 ($\underline{C}H_2Ph$); 70.17 (C-3'); 66.72 (C-5'); 31.75 (C-2'). Anal. Calcd. for $C_{23}H_{24}N_2O_5$: C, 67.64; H, 5.88; N, 6.86. Found: C, 67.14; H, 5.76; N, 6.50.

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