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Branched-chain Nucleosides : Synthesis of 3'-Deoxy-3'-*C*-Hydroxymethyl-α-L-Lyxopyranosyl Thymine and 3'-Deoxy-3'-*C*-Hydroxymethyl-α-L-Threofuranosyl Thymine.

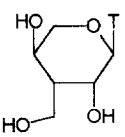
Bogdan Doboszewski and Piet Herdewijn*

Rega Institute for Medical Research, Katholieke Universiteit Leuven, Minderbroedersstraat 10, B-3000 Leuven, Belgium.

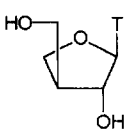
Abstract : The synthesis of 3'-deoxy-3'-*C*-hydroxymethyl branched nucleosides with α-L-lyxopyranosyl and α-L-threofuranosyl sugar moieties is described. The synthetic scheme makes use of a furanose → pyranose conversion and of the formation of both furanose and pyranose nucleosides during Vörbruggen sugar-base condensation reaction starting from tetra-*O*-acetyl-3-deoxy-3-*C*-hydroxymethyl-L-lyxo-(1,6)-furanose. The conformation of the target molecules is discussed.

INTRODUCTION

Non natural pyranose nucleosides have attracted considerable attention during last years. This is due to the finding that hexitol nucleosides exert antiviral activity[1] and that hexitol nucleic acids are promising antisense constructs[2]. Previously, based on modeling experiments[3], we synthesized and evaluated the properties of 3'-deoxy-3'-hydroxymethyl aldopentopyranosyl oligonucleotides[4,5]. As a continuation of this work we here report on the synthesis and conformational behaviour of 3'-deoxy-3'-*C*-hydroxymethyl-α-L-lyxopyranosyl thymine **1** which may be considered as the "ribo" analogue of the aforementioned 3'-branched aldopentopyranosyl nucleosides. The same synthetic scheme also led to a procedure for the preparation of 3'-deoxy-*C*-hydroxymethyl-α-L-threofuranosyl thymine **2**.



1

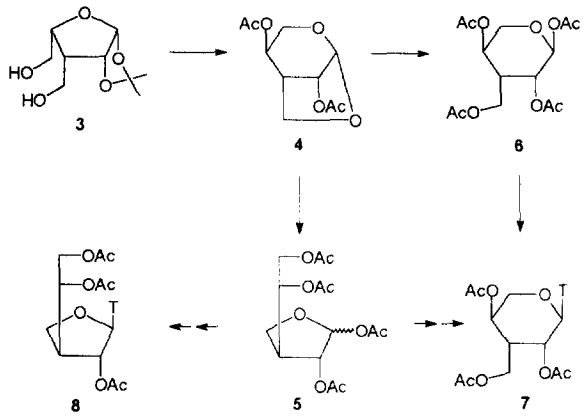


2

This efficient synthesis is based on two interesting rearrangements : the conversion of 1,2-isopropylidene-3-deoxy-3-*C*-hydroxymethyl-L-lyxofuranose **3** into 2,4-di-*O*-acetyl-1,6-anhydro-3-deoxy-3-*C*-hydroxymethyl-L-lyxopyranose **4** by two convergent pathways and the formation of 2',4',6'-tri-*O*-acetyl-3'-deoxy-3'-*C*-hydroxymethyl-α-L-lyxopyranosyl thymine **7** and 2',4',5'-tri-*O*-

acetyl-3-deoxy-3-*C*-hydroxymethyl-α-L-lyxo-(1,6)-furanosyl thymine **8** by treatment of tetra-*O*-acetyl-3-deoxy-3-*C*-hydroxymethyl-L-lyxo-(1,6)-furanose **5** with silylated thymine under Vörbruggen conditions (Scheme 1).

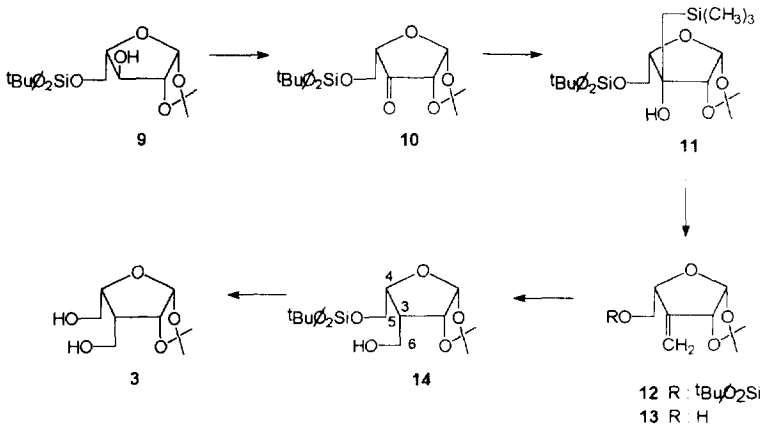
Scheme 1



RESULTS AND DISCUSSION

The starting compound for the synthesis of both **1** and **2** was the known[6] ulose **10** prepared from 5-t-butyldiphenylsilyl-1,2-isopropylidene-L-arabinofuranose **9** by CrO_3-Ac_2O-Py oxidation (Scheme 2).

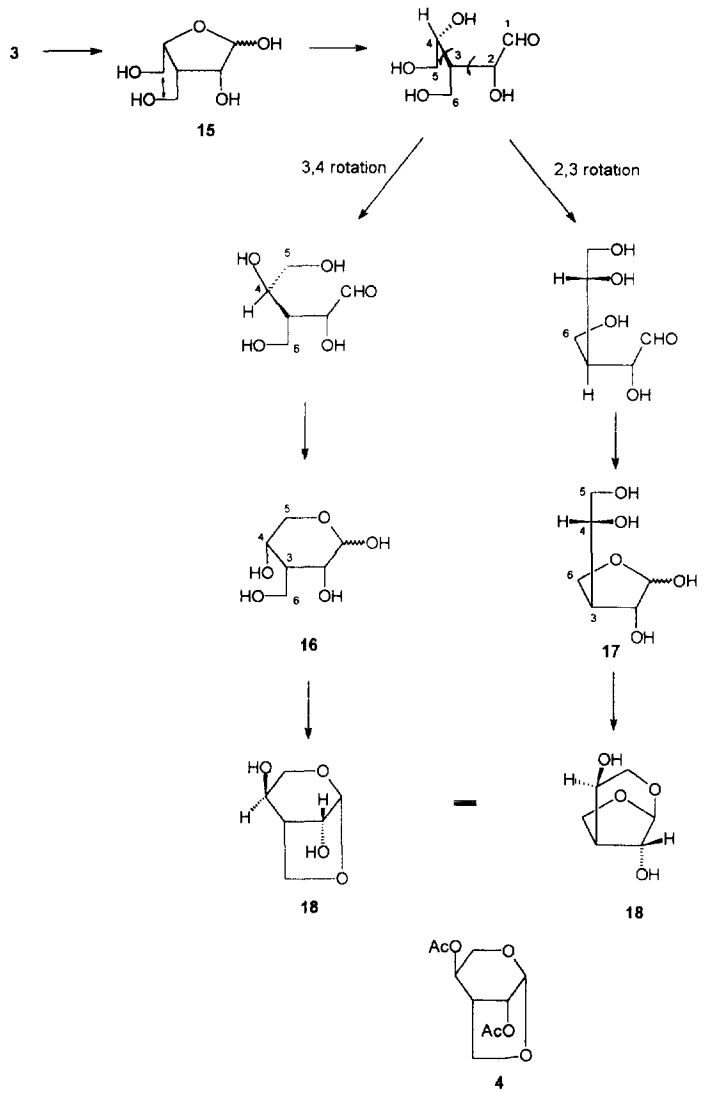
Scheme 2



On treatment of **10** with μ-chloro-μ-methylene-[bis(cyclopentadienyl)titanium]dimethylaluminium or Tebbe reagent[7,8], olefin **12** was obtained in 60% yield. Due to a high price of the reagent we applied

Peterson olefination[9] procedure as an alternative. Treatment of **10** with trimethylsilylmetyl lithium at -78° gave a tertiary alcohol **11** in 84% yield, which subjected to NaH induced fragmentation gave **12** (97%) in 82% for two steps. This sequence could be run on 34 mmol scale without any detectable epimerization at C4 during the first step. Moisture had to be rigorously excluded in the second step to avoid base-induced desilylation of **12** to give **13**. Hydroboration of the olefin **12** furnished **14**. Due to a spacial orientation of the functionalities at C1, C2 and C5 in **12**, it could be anticipated that the addition of diborane would take place only anti to furnish **14** as the only product. Fluoride ion desilylation of **14** lead to **3**. On treatment of **3** with 90% trifluoroacetic acid a process depicted in Scheme 3 took place.

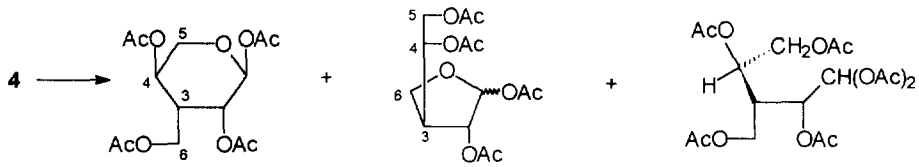
Scheme 3



In this process, compound **3** is converted into **4** by CF_3COOH treatment followed by acetylation via two different pathways. The primary product of hydrolysis of the isopropylidene group **15** tended to minimize unfavourable steric interaction between two hydroxymethyl groups oriented syn by opening of the furanosyl ring. Rotation along the C3-C4 bond anticlockwise and subsequent ring closure through C5-OH lead to a pyranose **16**. Alternatively, rotation along the C2-C3 bond also anticlockwise and ring closure through C6-OH lead to a furanose **17**. At this point we expected to get a mixture of **16** and **17**, which, after acetylation should furnish **6** and **5***. However, suprisingly easy intramolecular glycosylation took place in a reaction medium which lead to a bicyclic product **18**. It should be noticed that irrespectively if this process took place via a pyranose **16** or via a furanose **17**, the same compound **18** resulted, isolated as diacetate **4**. The structure of this product was confirmed by X-ray analysis[10].

Formation of the anhydro compound **4** did not adversly effect our approach to a target **6** and further to **7**, because acetolytic cleavage of the internal glycoside **4** was possible in Ac_2O-AcOH-H_2SO_4 mixture (Scheme 4).

Scheme 4



6 **5** **19**

This reaction furnished a pyranose **6** as a single α anomer, a furanose **5** as a 1:1 α/β mixture and small amount of an open chain hexaacetate **19**, in 48%, 23% and 10% yield, respectively. Preferential formation of **6** is a consequence of greater reactivity of a furanosyl ring in **4**, when compared to reactivity of a pyranosyl ring scission of which lead to **5**. Small amount of **19** was an inconvenience because it was difficult to separate it from slightly less polar **5**.

However, we tried to circumvent formation of the internal glycoside **18** by protection of the hydroxyl group bound to the carbon atom C6 in compound **14** (Scheme 5).

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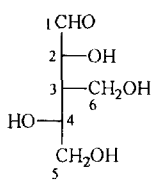
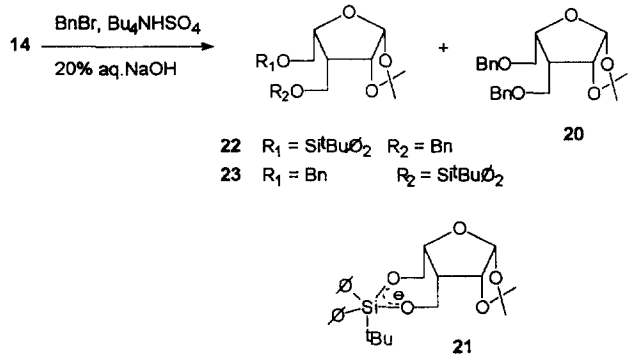
* An open chain Fisher projection of **15**, **16**, **17** is shown below. Systematic name of this compound is 3-deoxy-3-C-hydroxymethyl-L-lyxose. This compound can form one pyranosyl form, **16**, but two different furanosyl forms **15** and **17**. Furanose **15** is refered to as an L-lyxo-(4,1)-furanose, whereas **17** as an L-lyxo-(6,1)-furanose.

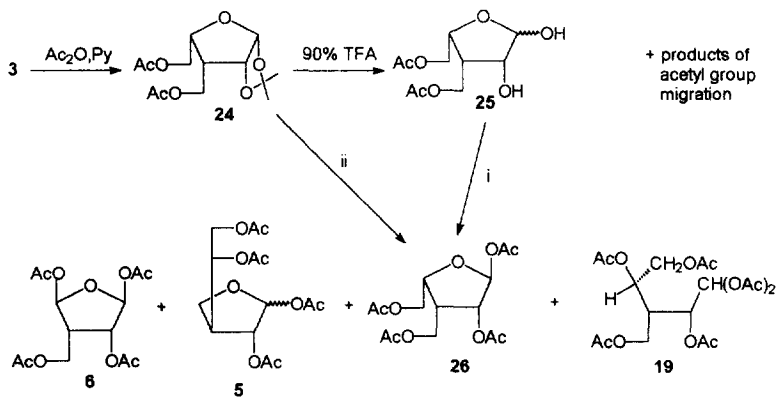


Scheme 5



Attempted benzylation of **14** performed in a phase-transfer catalysis mode furnished a dibenzyl ether **20** isolated in 48% yield as the main product. Formation of **20** must have been a consequence of hydrolysis of the t-butyldiphenylsilyl group under basic conditions and subsequent etherification. This was an unexpected finding since t-butyl-diphenylsilyl group is considered stable under basic conditions[11]. It can be that a propensity of the silicon atom to form pentavalent species like **21** associated with the known migratory capacity of silyl ethers under basic conditions[11], can be linked with formation of **20**. From this standpoint it was impossible to prove by the NMR data that a second product isolated was **22** or a product **23** with transposed functionalities at the primary carbon atoms C5,6. The product **23** would result from attack of benzyl bromide at C5 in **21**. Since the atom C6 is sterically more crowded than C5, it would be difficult for a bulky t-butyldiphenylsilyl group to migrate onto it from a more comfortable atom C5. On this basis we believe that the isolated compound has a structure **22**. Low yield of its formation prompted us to find an alternative approach. It turned out that a simple acetylation served the purpose very well. Thus, diol **3** was acetylated to furnish **24**, which was de-acetalated with 90% trifluoroacetic acid (Scheme 6).

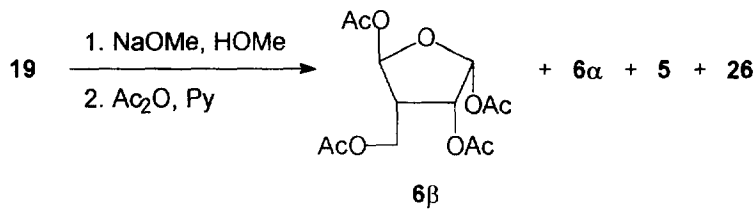
Scheme 6



i : Dependent on the reaction circumstances (see text) mixtures of **6**:**5**:**26** (6:4:1) or **6**:**5** (3:2 or 1:3.7) were obtained. Compound **24** gives a mixture of **19** and **26** upon treatment with Ac_2O, AcOH, H_2SO_4 (ii).

After evaporation of TFA, co-evaporation with ethyl acetate and xylene, ^{13}C spectrum of the crude reaction mixture showed six signals at the anomeric region. This proves extensive migration of acetyl groups in a primary product **25** during a TFA treatment and/or during work-up. Acetylation of this mixture furnished a pyranose **6** and both furanoses **5** and **26**, all three separable by gravitational column chromatography*. However, when the crude reaction mixture was deacetylated and re-acetylated only **6** and **5** were isolated in ca 3:2 proportion. In a separate experiment this proportion was reverted and the furanosyl compound **5** was isolated as dominant one. Thus, after deacetalation with 90% TFA and evaporation of the acid, the residual TFA was co-evaporated with DMF. This took ca 30 min and permitted for longer exposure to low pH. After deacetylation and re-acetylation three fractions were obtained : anhydro compound **4** formed in 4% yield, a pyranose **6**, 10%, and a furanose **5**, 37%. It is not clear why **5** was a dominant product in this case because after TFA treatment, the mixture of products was deacetylated in both cases to give **16** and **17**, which after acetylation should furnish **6** and **5** in roughly the same proportion, which is not a case. It can be that formation of a furanose **17** is promoted by acid, and once formed it doesn't revert to a pyranose **16** easily, because a hydroxymethyl group at C3 in **16** is flanked by two syn oriented OH groups which destabilize a pyranosyl form. When the open chain product **19** was deacetylated to allow for cyclization, and re-acetylated (Scheme 7), the pyranose **6α** together with a product identified as its β anomer, were again principal components of the mixture, besides **5** as an α,β mixture, and surprisingly tetraacetate **26** as a single anomer α, formed in proportion 57:35:8 by integration of the anomeric region of the ^1H NMR spectrum of the crude reaction mixture.

Scheme 7



Ratio **6α/6β:5:26** is 57:35:8 as integrated from ^1H NMR signals.

Anomeric configuration of **6α** and **6β** and their conformational characteristics could be infered from the ^1H NMR spectra. Coupling constants of **6α** listed in Figure 1 agree with the $^1C_4$ conformation of the pyranosyl ring. Since this compound could be prepared during acetolytic cleavage of **4**, i.e. under conditions of thermodynamic control, anomeric configuration was assumed to be α because axial C1 acetoxyl group gains the anomeric effect stabilization.

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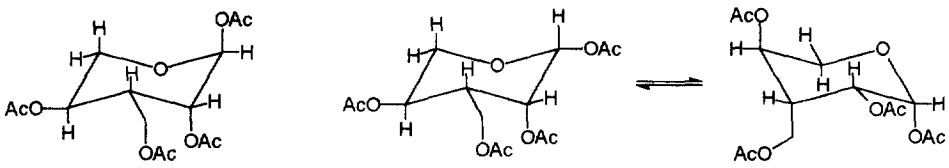
* Identity of the furanose **26** was confirmed by its synthesis from acetonide **24** by acetolysis, which also furnished the hexaacetate **19** as byproduct.

Figure 1 : Conformational properties of the pyranoses **6α,β** (coupling constants in Hz, recorded in $CDCl_3$).



6α	**6β**
$J_{1,2} = 1.8$	$J_{1,2} = 2.4$
$J_{2,3} = 2.9$	$J_{2,3} = 4.3$
$J_{3,4} = 10.7$	$J_{3,4} = 7.0$
$J_{4,5ax} = 10.7$	$J_{4,5ax} = 7.0$

Also the coupling constant $J_{1,2}$ = 1.8 Hz is smaller than a value $J_{1,2}$ = 2.4 for **6β** as expected for diequatorial orientation of the hydrogen atoms H-1 and H-2 in **6α**, when compared with axial-equantorial counterparts in **6β**. The β anomer in turn is evidently unstable conformationally as evidenced from the coupling constants $J_{3,4} = J_{4,5ax}$ = 7.0. In a $^4C_1$ conformation the molecule is stabilized by the anomeric effect, but destabilized by two axially disposed functionalities at the carbon atoms C-3 and C-4. In a $^1C_4$ conformation, steric tension is minimized, but at the expence of a loss of the anomeric effect. Interplay of these effects results in an equilibrium with $^1C_4$ form predominating.

Anomeric configuration of the furanoses **5α** and **5β** was established by comparison of their coupling constants $J_{1,2}$ and $J_{2,3}$ with those of the nucleosides **8**, **2** and **34** (Figure 2).

Configuration of **34** was established by a Nuclear Overhauser Effect measurement (see below)*, so the coupling constants of this compound could be used as a reference. Configuration α was ascribed to a compound characterized by the couplings $J_{1,2}$ = 4.2 Hz and $J_{2,3}$ = 9.8 Hz, because these values are closer to those of **34** (and its predecessors **8** and **2**) than the values of $J_{1,2}$ = 0 Hz and $J_{2,3}$ = 3.6 Hz belonging to **5β**.

Anomeric configuration of **26** was established by comparison of the ^{13}C chemical shifts of the carbon atom C-1 with published shifts of both α and β tetra-*O*-acetyllyxofuranoses **27** and **28**[12]. A value of 98.52 ppm recorded for **26** coincides with a value for **27** (98.04 ppm) and is significantly different from a shift of C-1 in **28** (93.02 ppm). Also, a magnitude of the $J_{1,2}$ and $J_{2,3}$ ^1H-^1H coupling constants of **26** agree better with the corresponding values of the α anomer **27** (or a tetra-*O*-benzoyl-α-lyxofuranose[13]) rather than with the values of the β anomer **28** (or its benzoylated counterpart[13]).

Glycosylation of **6** using trimethylsilylated thymine under Vorbrüggen conditions furnished a pyranosyl nucleoside **7** in 62% yield (Scheme 8). This compound adopts exclusively $^4C_1$ formation in solution (as well as in crystalline state[10]). Value of the coupling constant $J_{1',2'}$ = 10.0 Hz and a broadened singlet of the proton H-4' sustains this. A tendency of the pentopyranosyl nucleoside to localize a nucleobase an equatorial

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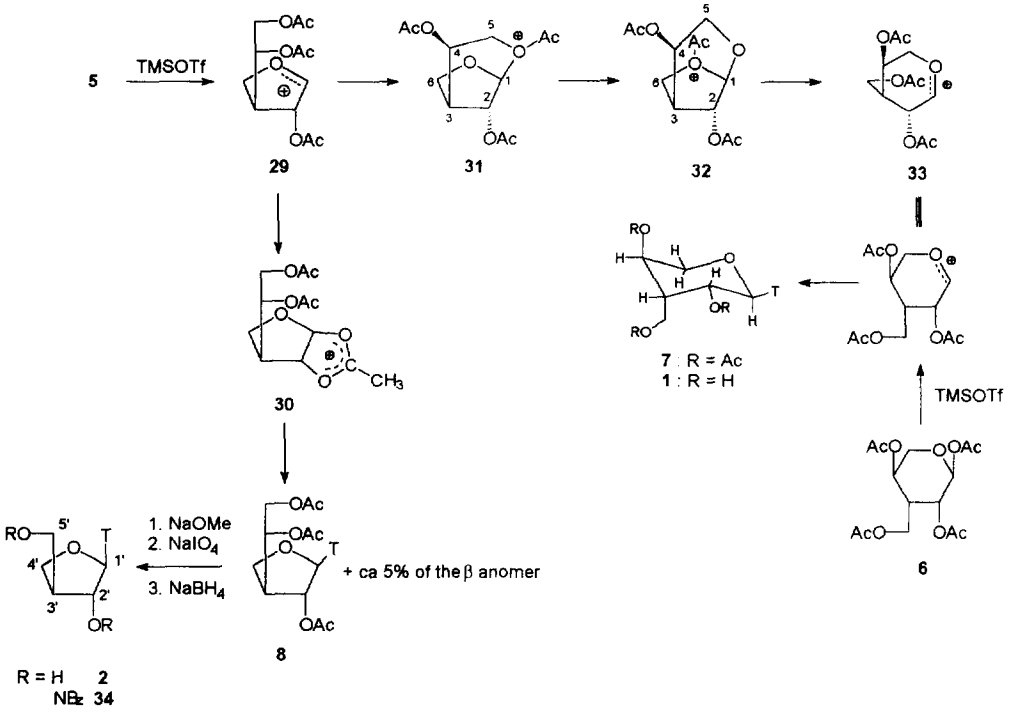
* During preparation of this manuscript, a synthesis of **2** was published[14] based on D-apiose. The coupling constants presented here are the same as in reference 14.

position even at the expense of axial orientation of up to three other functionalities at the carbon atoms C-2', C-3' and C-4' has been observed before[4,5,15]. Conventional deacetylation of 7 furnished a target compound **1**, which also adopts a conformation $^4C_1$. The 2'-deoxygenated counterpart of this compound has already been synthesized for antiviral screening and for preparation of antisense constructs[4,5].

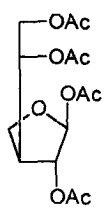
Unusual results were obtained during glycosylation of the furanose **5** with trimethylsilyl thymine under Vorbrüggen conditions (Scheme 8). Two compounds were isolated from this condensation reaction : the expected furanosyl nucleoside **8** unseparable from ~ 5% of the β anomer, and the pyranosyl nucleoside **7**, the same as obtained from **6** as described above. Proportion of **8** to **7** was 2:1.

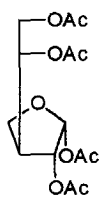
Scheme 8

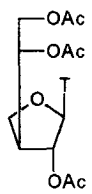


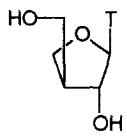
Formation of either **8** or **7** in this reaction depends on a mode of anchimeric stabilization of the cation **29** formed by abstraction of the anomeric acetoxyl group from the substrate **5**. If 2-OAc group stabilizes the cation **29** via **30**, than a furanosyl nucleoside **8** is formed. Configuration α of **8** was proven on a later stage (see below). An alternative mode of stabilization of **29** is to form a six membered ring using the oxygen atom bound to C-5 which leads to a cation **31**. This progeny cation can be transformed into **32** via migration of the acetylcarbocation from the "pyranosyl" oxygen atom joining carbon atoms C-5 and C-1 towards the "furanosyl" oxygen atom joining C-6 and C-1. Subsequent rupture of the bond between this oxygen atom and C-1 leads to **33** which is the same cation that the one formed by abstraction of the anomeric acetoxyl group from a pyranose **6**. Cation **33** then forms a pyranosyl nucleoside 7 via participation of the 2-O-acetyl group.

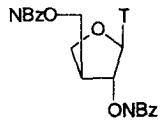
Figure 2 : Anomeric configurations of the furanoses **5α,β**, **26**, furanosyl nucleosides **8**, **2**, **34**, and tetra-*O*-acetyl-α,β-lyxofuranoses (coupling constants in Hz; ^{13}C chemical shifts in ppm).

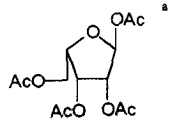


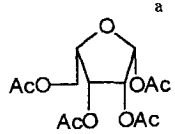


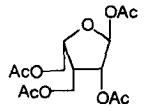












	5α	**5β**	**8**	**2**	**34**	**27**[7]	**28**[7]	**26**
$J_{1,2}$	4.2[b]	0.0[b]	4.7[b]	5.4[c]	4.9[d]	2.1	4.6[b]	0.0[b]
$J_{2,3}$	9.8	3.6	6.9	7.1	7.3	5.1	5.4	5.1
$J_{3,4}$	-	-	-	-	-	5.4	4.7	8.7
C-1	-	-	-	-	-	98.04	93.02	98.52

[a] These compounds have been originally examined in ref. 12 as D isomers; [b] in $CDCl_3$; [c] in CD_3OD; [d] in DMSO-d_6

Nucleoside **8** was converted into **2** by deacetylation, periodate cleavage of the resulting vicinal diol and reduction with $NaBH_4$. This compound was also noncrystalline, so it was converted into bis-(p-nitro)benzoate **34**, which crystallized as a single α anomer. Configuration α was proved by a differential NOE measurement. Irradiation of the H-3' signal gave a positive signal of the proton H-1'. Irradiation of the H-6 signal gave positive signal of the H-1' and less intensive positive signal of H-2' (but the signals of both H-4' and H-5' were nulled). These results can be interpreted in terms of the anomeric configuration α, syn conformation of the thymine with χ angle close to 0° and preferential S puckering of the furanosyl ring. The hydroxymethyl group bound to the carbon atom C-3' evidently controls a magnitude of the angle χ by virtue of its steric bulk. Unfortunately the crystalls of the compound **34** were unsuitable for X-ray analysis to confirm conformational features of **34** deduced from NOE measurements.

In conclusion, we have devised a simple way of synthesis of a representative example **1** of a new class of pyranosyl nucleosides. This compound was obtained from a branched pyranose **6** which has a hydroxymethyl group attached to the atom C-3. Compound **5**, one of a possible furanosyl form of **6** is also a precursor of **1**, because of an unusual migration of the acetyl carbocation during a Vorbrüggen condensation. The possibility to use a furanose **5** as substrate for obtaining a pyranosyl product like **1**, is a manifestation of the constitution of both **6** and **5**, which already manifested itself at a stage of surprisingly easy formation of the internal glycoside **4**.

EXPERIMENTAL SECTION

General conditions are the same as in ref. 4.

5-(t-Butyldiphenylsilyl)-3-deoxy-3-*C*-methylene-1,2-isopropylidene-L-threo-pentofuranose 12

A. Using Tebbe reagent

Ulose **10** (4.82 g, 11.3 mmol) [prepared from t-butyldiphenylsilyl-1,2-isopropylidene-L-arabinofuranose **9**[6] (5.24 g, 12.2 mmol) by CrO_3-Ac_2O-Py oxidation] in THF (70 ml) was treated with 0.5 M μ-chloro-μ-methylene[bis(cyclopentadienyl)titanium]-dimethylaluminium (Tebbe reagent) in toluene (23 ml) at room temperature. Slight heating took place during the addition. The homogenous mixture was left overnight. TLC showed a new intensively charing spot of the product **12**, less polar than a spot of substrate **10**. MeOH was added (with cooling in ice-bath) and the jelly residue was filtered through a bed of silica gel under vacuum. The silica gel was washed with CH_2Cl_2. Combined filtrates were evaporated to give reddish oil. Gravitational chromatography in hexane-EtOAc 20:1 furnished 2.90 g (60%) of **12** as oil.

B. Using Peterson olefination

Ulose **10** (12g, 28 mmol) in CH_2Cl_2 (170 ml) was cooled in EtOH-dry ice bath, and trimethylsilylmethylithium in pentane (1 M, 28 ml) was added from a siringe dropwise. 1 h later the cooling bath was removed. When the solution reached room temperature, it was poured into a aq.NH_4Cl. After extractive work-up and evaporation, the residual viscous brown liquid was chromatographed in hexane-EtOAc 15:1 to give **11** as oil (10.1 g or 84%). A solution of this material (17.5 g, 34 mmol) in THF (500 ml) was cooled in ice-water bath, and 3.0 g of NaH (60% suspension in mineral oil, pre-washed with

hexane, 75 mmol) was added. When evolution of hydrogen stopped, the flask was warmed up in an oil bath to maintain a gentle reflux during 3 h. TLC showed that the substrate was converted into slightly more polar compound **12**. The flask was cooled in ice-water again, and aq.sat.NH_4Cl was added dropwise until evolution of hydrogen stopped. The precipitate was filtered out. The filtrate was evaporated to ca 1/3 of its original volume, and the remining solution was transfered to a separatory funnel filled with CH_2Cl_2-H_2O to perform extraction. The colloidal solution was passed through a glass-wool. The two layers formed at this stage were separated. The water layer was back-extracted with CH_2Cl_2. Combined extracts were washed with water, dried, filtered and evaporated to furnish 14 g, 97% of yellowish oil, which was directly used in the hydroboration step.

If anhydrous conditions were not maintained during NaH induced fragmentation, a desilylated product **13** was also formed in small quantity. Separation of **12** and **13** was possible by chromatography using a gradient elution with hexane-EtOAc 2:1 followed by hexane-EtOAc 2:1.

12 ^1H ($CDCl_3$) : 7.77-7.68 and 7.48-7.35, 10H, Ph; 5.85 (dd, 1H, $J_{1',2'}$ = 3.9 Hz, J = 1.1. Hz, H-1); 5.50 (bs, half-width 4.4 Hz, 1H, H-6'); 5.36 (q, 1H, J = 1.5 Hz, H-6"); 4.89 (apparent d, 1H, $J_{2',1'}$ = 3.8 Hz, H-2); 4.65 (tt, 1H, $J_{4',5'}$ = $J_{4',5"}$ = 5.9 Hz, $J_{4',6'}$ = 1.6 Hz, J = 1.6 Hz, H-4); 3.94 (ddd, $J_{5',1'}$ = 1.5 Hz, $H_{5',4'}$ = 6.4 Hz, $J_{5',5"}$ = -10.0 Hz, H-5'); 3.80 (ddd, $J_{5",1'}$ = 1.3 Hz, $J_{5",4'}$ = 7.0 Hz, $J_{5",5'}$ = -10.0 Hz, H-5") [after irradiation of H-1, both H-5' and H-5" are dds]; 1.38, 1.35 CMe_2; 1.10 $C(Me)_3$. ^{13}C ($CDCl_3$) : 145.60 C-3; 135.61, 133.34, 133.25, 129.57, 127.61 Ph; 113.92 C-6 [without decoupling of protons : t, J = 159.5 Hz]; 113.05 $\underline{C}Me_2$; 105.36 C-1; 82.98, 81.35 C-2, C-4; 67.12 C-5; 27.27, 26.43 $C\underline{Me}_2$; 26.77 $C\underline{Me}_3$; 19.17 $\underline{C}Me_3$. Exact mass (thioglycerol-NaOAc) : calc. for $C_{25}H_{32}O_4Si$+Na 447.1968; found 447.1985.

13 ^1H ($CDCl_3$) : 5.85 (d, 1H, $J_{1',2'}$ = 4.0 Hz, H-1); 5.50 (dd, 1H, J = 1.0 and 2.1 Hz, H-6') [after irradiation of H-2 : d, J = 2.0 Hz]; 5.28 (apparent t, 1H, J = 1.8 Hz, H-6"); [after irradiation of H-2 : d, J = 1.6 Hz]; 4.91 (apparent dd, $J_{2',1'}$ = 3.8 Hz, J = 1.8 Hz, H-2); 4.66 (ddd, 1H, $J_{4',6'}$ = -1.9 Hz, $J_{4',5"}$ = 4.0 Hz, $J_{4',5'}$ = 8.9 Hz, H-4); 3.83 (dd, $J_{5',4'}$ = 7.0 Hz, $J_{5',5"}$ = -11.7 Hz, H-5'); 3.71 (dd, $J_{5",4'}$ = 4.1 Hz, $J_{5",5'}$ = -11.9 Hz, H-5"); 2.56 (bs, OH); 1.57, 1.36 $C\underline{Me}_2$. ^{13}C ($CDCl_3$) : 144.87, C-3; 113.70 C-6 [without decoupling of protons : t, J = 160.2 Hz]; 113.31 $\underline{C}Me_2$; 105.19 C-1; 83.59, 81.12 C-2, C-4; 65.77 C-5; 27.18, 26.40 $C\underline{Me}_2$. MS : Molecular ion was not seen in LSIMS mode.

5-t-Butyldiphenylsilyl-3-deoxy-3-*C*-hydroxymethyl-1,2-isopropylidene-L-lyxo-(1,4)-furanose 14

Olefin **12**(14 g) in 160 ml of THF was cooled down in ice-water, and treated with 70 ml of 1 M B_2H_6 in THF added via a canula. The mixture was left for 3 h at room temperature, and cooled in ice-water bath. A 1:1 mixture of THF-H_2O (40 ml) was added dropwise, followed by 2N NaOH (51 ml) and 33% H_2O_2 (41 ml). This heterogenous mixture was vigorously stirred during 2.5 h at room temperature, cooled down again and treated with 150 ml of aq. sat.$Na_2S_2O_3$. The layers were separated. The aqueous layer was extracted with CH_2Cl_2. Combined organic layer were washed with water, dried and evaporated. Graviational chromatography in hexane-EtOAc 4:1 → 3:1 furnished 13.6 g, 93% of **14**, mp. 97-98° (hexane-EtOAc).

14 ^1H ($CDCl_3$) : 7.74-7.66 and 7.48-7.39, 10H, Ph; 5.78 (d, 1H, $J_{1',2'}$ = 4.0 Hz, H-1); 4.67 (dd, 1H, $J_{2',1'}$ = 4.0 Hz, $J_{2',3'}$ = 5.3 Hz, H-2); 4.48 (ddd, 1H, $J_{4',5"}$ = 3.7 Hz, $J_{4',3'}$ = 7.6 Hz, $J_{4',5'}$ = 10.2 Hz, H-4); 4.22 (dd, $\sum J$ = 22

Hz, H-6'); 4.20 (t, $J_{5',4}$ = $|J_{5',5''}|$ = 10.1 Hz, H-5'); 4.07-3.94 (m, H6", OH) [after exhange with D_2O : 3.99, dd, $J_{6'',3}$ = 6.2 Hz, $J_{6'',6'}$ = -12.0 Hz]; 3.75 (dd, 1H, $J_{5'',4}$ = 3.8 Hz, $J_{5'',5'}$ = -9.9 Hz, H-5"); 2.99-2.93, OH; 2.77 (dddd, 1H, $J_{3,2}$ = 5.3 Hz, $J_{3,6'}$ = $J_{3,4}$ = 7.5 Hz, $J_{3,6''}$ = 9.1 Hz, H-3); 1.31, 1.26 C$\underline{Me}_2$; 1.11 C$\underline{Me}_3$. ^{13}C ($CDCl_3$) 135.45, 132.48, 132.18, 129.92, 127.82 Ph; 112.14 $\underline{C}Me_2$; 106.09 C-1; 82.06, 80.68 C-2, C-4; 64.51, 58.53 C-5, C-6; 47.56 C-3; 26.75 C$\underline{Me}_3$; 26.43, 25.33 C$\underline{Me}_2$; 18.98 $\underline{C}Me_3$. Exact mass (thioglycerol-NaOAc) calc. for $C_{25}H_{34}O_5Si$+Na 465.2073; found 465.2050

1,2-Isopropylidene-3-deoxy-3-*C*-hydroxymethyl-L-lyxofuranose 3

Compound **14** (12.4 g, 28.1 mmol) was desilylated with 15 g of Bu_4NF-$3H_2O$ in THF (150 ml) during 3 h. The solvent was evaporated to furnish brownish oil. Gravitational chromatography in hexane-EtOAc 1:3 → neat EtOAc furnished 5.2 g (91%) of **3**, mp. 66-67°, cryst. from hexane-EtOAc.

^1H (DMSO) : 5.71 (d, 1H, $J_{1,2}$ = 3.7 Hz, H-1); 4.65-4.50 (unresolved, 4H, H-2, 2 x OH) [after exchange with D_2O : 4.61 (t, $J_{2,1}$ = 4.0 Hz, $J_{2,3}$ = 4.8 Hz, H-2)]; 4.05 (q, 1H, $J_{4,3}$ = $J_{4,5'}$ = $J_{4,5''}$ = 7.1 Hz, H-4); 3.63-3.51 (m, 4H, 2 x H-5, 2 x H-6); 2.43 (ddd, $J_{3,2}$ = 5.0, $J_{3,4}$, $J_{3,6'}$, $J_{3,6''}$ = 7.5 Hz, 7.8 Hz and 8.8 Hz, these values are taken from a projection of this multiplet on a J axis in a 2DJ resolved spectrum, H-2); 1.43, 1.21, C$\underline{Me}_2$. ^{13}C (DMSO) : 111.25 $\underline{C}Me_2$; 105.68 C-1; 83.08, 80.12 C-2, C-4; 61.77, 56.03 C-5, C-6; 47.31 C-3; 26.80, 25.67 CMe_2. Exact mass (thioglycerol) calc. for $C_9H_{16}O_5$+H 205.1076; found 205.1074

2,4-Di-*O*-acetyl-1,6-anhydro-3-deoxy-3-*C*-hydroxymethyl-L-lyxopyranose 4

Diol **3** (0.10 g) was treated with 20 ml of 90% trifluoroacetic acid during 10 min. The acid was evaporated, and co-evaporated with EtOAc. Water was added and the solution was neutralized with Dowex 1X8 OH^-. After filtration of the resin and evaporation of water, 0.058 g of glassy solid was obtained. Conventional acetylation and chromatography in hexane-EtOAc 1:1 furnished 0.061 g (54%) of **4**, mp. 105-106° (hexane-EtOAc).

^1H ($CDCl_3$) : 5.38 and 5.32, two s, H-1, H-2; 5.01 (dd, 1H, $J_{4,5}$ = 3.2 Hz, $J_{4,3}$ = 4.7 Hz, H-4); 4.15 (dd, $J_{6',3}$ = 4.3 Hz, $J_{6',6''}$ = -9.0 Hz, H-6'); 4.01 (d, $J_{6'',6'}$ = -8.9 Hz, H-6"); 3.91 (dd, $J_{5ax,4}$ = 2.9 Hz, $J_{5ax,5eq}$ = -13.5 Hz, H-5ax); 3.69 (d, 1H, $J_{5eq,5ax}$ = -13.6 Hz, H-5eq); 2.91 (t, 1H, $J_{3,4}$ = $J_{3,6'}$ = 4.4 Hz, H-3); 2.18, 2.11, OAc. ^{13}C ($CDCl_3$) : 170.39, 169.95 $\underline{C}OMe$; 99.96 C-1; 73.98, 72.15 C-2, C-4; 69.16, 61.95 C-5, C-6; 41.53 C-3; 21.05, 20.83 CO$\underline{Me}$. Exact mass (thioglycerol) calc. for $C_{10}H_{14}O_6$+H 231.0869; found 231.0862.

Tetra-*O*-acetyl-3-deoxy-3-*C*-hydroxymethyl-α-L-lyxopyranose 6, tetra-*O*-acetyl-3-deoxy-3-*C*-hydroxymethyl-α,β-L-lyxo-(1,6)-furanose 5 and hexa-*O*-acetyl-3-deoxy-3-*C*-hydroxymetyl-aldehydo-L-lyxose 19.

A. From anhydro compound **4**.

Diacetate **4** (0.15 g) was subjected to acetolytic cleavage with 8 ml of a mixture prepared from 4.6 ml of Ac_2O, 12 ml of glacial AcOH and 0.4 ml of conc. H_2SO_4, during 16 h. TLC (hexane-EtOAc 7:3) showed three partially overlapping spots : R_f 0.31 of **6**, R_f 0.24 of **5** and R_f 0.18 of **19**. Extractive work-up and

gravitational column in hexane-EtOAc 7:3 furnished 0.105 g (48%) of **6**, 0.050 g (23%) of **5** and 0.028 g (10%) of **19** eluted in this order.

B. From diol **3** via diacetate **24**.

I. To get a pyranose **6** as a predominant product.

Diol **3** (0.58 g) was acetylated in Ac_2O-Py mixture. Evaporation of volatiles followed by co-evaporation with xylene furnished **24**. This material was treated with 90% trifluoroacetic acid during 15 min. The acid was evaporated, and co-evaporated with a mixture of ethyl acetate and xylenes*. After drying on an oil pump (15 min), the residue was dissolved in MeOH and small pieces of sodium were added (with external cooling of the flask) to neutralize traces of a residual TFA still present and to deacetylate the transient diacetate **25** and other products of acetyl group migration, and to allow for pyranose/furanose equilibration. A piece of dry ice was added and methanol was evaporated. The residue was dried using oil pump, and acetylated in pyridine-Ac_2O overnight. After evaporation, co-evaporation with xylene and chromatography in hexane-EtOAc 7:3 0.23 g of **6** as a pure α anomer (24% for four steps) and 0.16 g of **5** as a 1:1 α/β mixture (17% for four steps) was obtained.

II. To get a furanose **5** as a predominant product.

Diol **3** (3.04 g) was acetylated and worked up as above to furnish 4.30 g of **24**, which was de-acetylated with 90 ml of 90% TFA during 10 min. The acid was evaporated and co-evaporated with DMF (~ 100 ml). This took ca. 30 minutes, and permitted longer contact with TFA to promote preferential formation of the furanose **17**, but also for internal glycoslyation to **18** in limitted extend. After drying on an oil pump, deacetylation as above, acetylation and chromatography, three fractions were obtained : **4** (0.127 g, 4%), **6** as a pure α anomer (0.515 g, 10%) and **5** [1.810 g (as 1:1 anomeric mixture), 37%], eluted in this order. All percent yields are calculated for four consecutive reactions (acetylation, de-acetalation, deacetylation, final re-acetylation.

6α ^1H ($CDCl_3$) : 5.96 (d, 1H, $J_{1,2}$ = 1.8 Hz, H-1); 5.09 (dt, $J_{4,5eq}$ = 5.6 Hz, $J_{4,5ax}$ = $J_{4,3}$ = 10.7 Hz, H-4); 5.06 (dd, $J_{2,3}$ = 2.9 Hz, $J_{2,1}$ = 1.8 Hz, H-2); 4.17 (dd, $J_{6',3}$ = 5.5 Hz, $J_{6',6''}$ = -11.2 Hz, H-6"); 3.91 (dd, 1H, $J_{5eq,4}$ = 5.4 Hz, $J_{5eq,5ax}$ = -10.8 Hz, H-5eq); 3.57 (t, 1H, $J_{5ax,4}$ = $|J_{5ax,5eq}|$ = 10.6 Hz, H-5ax); 2.59 (dddd, 1H, $J_{3,2}$ = 2.9 Hz, $J_{3,6'}$ = 5.5 Hz, $J_{3,6''}$ = 8.6 Hz, $J_{3,4}$ = 11.3 Hz, H-3), 2.16, 2.14, 2.08, 2.06, OAc. ^{13}C ($CDCl_3$) : 170.58, 169.96, 169.78, 168.46 COMe; 88.95 C-1; 67.51, 65.07 C-2, C-4; 61.32, 60.26 C-5, C-6; 37.81 C-3; 20.69, COMe. Exact mass (thioglycerol-NaOAc) calc. for $C_{14}H_{20}O_9$+Na 355.1005; found 355.0996.

6β ^1H ($CDCl_3$) : The only signals identifiable form a mixture obtained under BI, are those of H-1, H-3 and H-5eq. H-1 : δ 5.97, d, $J_{1,2}$ = 2.4 Hz. H-5eq : δ 3.61, dd, $J_{5eq,4}$ = 5.2 Hz, $J_{5eq,5ax}$ = -12.5 Hz. H-3 : δ 2.49, dq, $J_{3,2}$ = 4.3 Hz, $J_{3,4}$ = $J_{3,6'}$ = $J_{3,6''}$ = 7.0 Hz.

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* ^{13}C NMR of the reaction mixture at this stage showed the following signals of the anomeric region (in $CDCl_3$) : 102.19, 100.07, 94.80, 93.24 and 90.56, proving extensive migration of the acetyl groups in the primary product **25**. Acetylation of this mixture of products furnished **6** as a pure α anomer, **5** as an α/β mixture contaminated with a compound which is probably β anomer of **6** (unseparable) and **26** as a pure α anomer, formed in proportion 6:4:1 and eluted in this order.

5α ^1H ($CDCl_3$) : 6.33 (d, $J_{1,2}$ = 4.2 Hz, H-1); 5.23 (ddd, J = 5.0 Hz, 5.0 Hz and 3.6 Hz, H-4); 4.95 (dd, $J_{2,1}$ = 4.1 Hz, $J_{2,3}$ = 9.8 Hz, H-2); 2.84 (dq, $J_{3,2}$ = 9.1 Hz, J = 9.1 Hz, 9.1 Hz, 4.6 Hz, H-3); 4.45-3.90 (m, H5',5",6',6" of both anomers); 2.10, 2.08, 2.07, 2.03, OAc of both anomers. ^{13}C (see β anomer)

5β ^1H ($CDCl_3$) : 6.14 (s, H-1); 5.36 (ddd, $J_{4,3}$ = 3.1 Hz, J = 5.4 Hz, 8.1 Hz, H-4); 5.09 (d, $J_{2,3}$ = 3.6 Hz, H-2); 2.65 (dq, $J_{3,2}$ = 3.5 Hz, J = 8.0 Hz, 8.0 Hz, 7.9 Hz, H-3); H5',5",6',6" and OAc : see α anomer. ^{13}C ($CDCl_3$) (both anomers) : 170.44, 170.37, 169.97, 169.66, 169.43 COMe; 100.32, 93.79 C-1; 79.40, 72.68, 70.17, 68.94 C-2, C-4; 69.51, 66.55, 64.00, 63.91 C-5, C-6; 45.82, 41.06 C-3; 21.06, 20.84, 20.73, 20.45 COMe. Exact mass (thioglycerol-NaOAc) calc. for $C_{14}H_{20}O_9$+Na 355.1005; found 355.0991.

19 ^1H ($CDCl_3$) : 7.00 (d, 1H, $J_{1,2}$ = 3.5 Hz, H-1); 5.47 (ddd, 1H; $J_{4,3}$ = 3.8 Hz, $J_{4,5'}$ = 3.8 Hz, $J_{4,5"}$ = 7.4 Hz, H-4); 5.22 (d, 1H, $J_{2,1}$ = 3.4 Hz, $J_{2,3}$ = 7.4 Hz, H-2); 4.36 (dd, $J_{5',4}$ = 4.2 Hz, $J_{5',5"}$ = -11.9 Hz, H-5'); 4.31 (dd, $J_{6',3}$ = 5.0 Hz, $J_{6',6"}$ = -12.1 Hz, H-6'); 4.21 (dd, $J_{6",3}$ = 7.3 Hz, $J_{6",6'}$ = -11.1 Hz, H-6"); 4.16 (dd, $J_{5",4}$ = 7.4 Hz, $J_{5",5'}$ = -11.9 Hz, H-5"); 2.42 (dddd, 1H, $J_{3,2}$ = $J_{3,6"}$ = 7.5 Hz, $J_{3,4}$ = 3.9 Hz, $J_{3,6'}$ = 5.0 Hz, H-3); 2.14, 2.09, 2.07, 2.06, 2.03, COMe. ^{13}C ($CDCl_3$) : 170.47, 169.81, 168.42 COMe; 87.44 C-1; 69.07, 67.92 C-2, C-4; 63.90, 60.34 C-5, C-6; 39.01 C-3; 20.72, 20.56 COMe. Exact mass (thioglycerol-NaOAc) cald. for $C_{18}H_{26}O_{12}$+Na 457.1322; found 457.1260.

5-*O*-(t-Butyldiphenylsilyl)-3-deoxy-3-*C*-benzyloxymethyl-1,2-isopropylidene-L-lyxo-(1,4)-furanose 22 and 5-*O*-benzyl-3-deoxy-3-*C*-benzyloxymethyl-1,2-isopropylidene-L-lyxo-(1,4)-furanose 20.

Compound **14** (0.50 g, 1.13 mmol) in CH_2Cl_2 (20 mL), benzyl bromide (0.7 ml, 5.9 mmol) and 20% of aq.NaOH were vigorously stirred overnight. TLC (hexane-EtOAc 3:1) showed a spot of **22** R_f 0.77 and **20** R_f 0.57. Aqueous layer was separated and extracted with CH_2Cl_2. Combined organic layers were evaporated. Chromatography of the residual oil furnished 0.113 g (19%) of **22** (eluted with hexane-EtOAx 6:1) and 0.209 g (48%) of **20** (eluted with hexane-EtOAc 45:10), both as oils.

22 ^1H ($CDCl_3$) : 7.65-7.60 and 7.40-7.31, 15H, Ph; 5.77 (d, 1H, $J_{1,2}$ = 4.0 Hz, H-1); 4.71 (dd, 1H, $J_{2,1}$ = 4.3 Hz, $J_{2,3}$ = 4.7 Hz, H-2); 4.52 (AB, J = 12.2 Hz and 15.4 Hz, OCH_2Ph); 4.33 (dt, $J_{4,3}$ = 5.7 Hz, $J_{4,5'}$ = $J_{4,5"}$ = 7.9 Hz, H-4); 3.91 (dd, $J_{5',4}$ = 7.8 Hz, $J_{5',5"}$ = 10.2 Hz, H-5'); 3.81-3.69 (unresolved, H-5", 2 x H-6); 2.67 (dddd, 1H, $J_{3,4}$ = $J_{3,2}$ = 5.7 Hz, $J_{3,6'}$ = $J_{3,6"}$ = 8.1 Hz, H-3); 1.27, 1.25, CMe_2; 1.01, CMe_3. ^{13}C ($CDCl_3$) : 138.35, 135.61, 133.46, 133.22, 129.66, 128.38, 127.71 Ph; 111.96 CMe_2; 106.07 C-1; 82.23, 80.35 C-2, C-4; 73.27 CH_2Ph; 65.12, 64.32 C-5, C-6; 45.75 C-3; 26.84 CMe_3; 26.48, 25.57 CMe_2; 19.15 CMe_3. Exact mass (n-nitrobenzyl alcohol-NaOAc) calc. for $C_{32}H_{40}O_5Si$+Na 555.2543; found 555.2535.

20 ^1H ($CDCl_3$) : 7.31-7.24, 10H, Ph; 5.82 (d, 1H, $J_{1,2}$ = 3.9 Hz, H-1); 4.68 (dd, 1H, $J_{2,1}$ = 3.9 Hz, $J_{2,3}$ = 5.1 Hz, H-2); 4.62-4.37 (m, 5H, 2 x OCH_2Ph, H-4); 3.76-3.56 (m, 4H, 2 x H-5, 2 x H-6); 2.68 (dddd, 1H, $J_{3,2}$ = 5.2 Hz, J = 7.1 Hz, 8.1 Hz, 8.1 Hz, H-3); 1.41, 1.27 CMe_2. ^{13}C ($CDCl_3$) : 138.16, 128.31, 127.74, 127.62, 127.51 Ph; 112.01 CMe_2; 106.06 C-1; 80.75, 80.31 C-2, C-4; 73.24, 73.17 CH_2Ph; 70.22, 64.98 C-5, C-6; 45.38 C-3; 26.48, 25.49 CMe_2. Exact mass (n-nitrobenzyl alcohol-NaOAc) calc. for $C_{23}H_{28}O_5$+Na 407.1835; found 407.1822.

3-Deoxy-3-*C*-hydroxymethyl-1,2-isopropylidene-L-lyxo-(1,4)-furanosyl diacetate 24

For analytical purpose diacetate **24** was prepared by conventional acetylation in Py-Ac_2O mixture 1:2, evaporation of volatiles, co-evaporation with xylenes and chromatography in hexane-EtOAc 2:1.

^1H ($CDCl_3$) : 5.86 (d, 1H, $J_{1,2}$ = 3.8 Hz, H-1); 4.71 (dd, 1H, $J_{2,1}$ = 3.9 Hz, $J_{2,3}$ = 5.1 Hz, H-2); 4.44-4.19 (m, 4H, 2 x H-5, 2 x H-6); 2.74 (dq, $J_{3,2}$ = 4.6 Hz, $J_{3,4}$ = $J_{3,6'}$ = $J_{3,6''}$ = 7.9 Hz, H-3); 2.09 (s, 6H, COMe); 1.58, 1.31 CMe_2. ^{13}C ($CDCl_3$) : 170.64 COMe; 112.68 CMe_2; 106.15 C-1; 79.79, 79.01 C-2, C-4; 64.24, 59.13 C-5, C-6; 44.03 C-3; 26.45, 25.42 CMe_2; 20.82 COMe. Exact mass (thioglycerol-NaOAc) calc. for $C_{13}H_{20}O_7$+Na 311.1107; found 311.1113.

Tetraacetyl 3-deoxy-3-*C*-hydroxymethyl-α-L-lyxo-(1,4)-furanose 26

Acetonide **24** 0.072 g was treated with 3 ml of an Ac_2O-AcOH-H_2SO_4 mixture prepared as described above for **6**, **5** and **19**, during 16 h. After extractive work-up and chromatography in hexane-EtOAc 2:1 0.043 g, (52%) of **26** (syrup) was obtained as a single anomer and 0.019 g (23%) of **19** eluted in this order.

^1H ($CDCl_3$) : 6.19 (s, 1H, H-1); 5.27 (d, 1H, $J_{2,3}$ = 5.1 Hz, H-2); 4.60 (ddd, 1H, $J_{4,5'}$ = 4.7 Hz, $J_{4,5''}$ = 7.6 Hz, $J_{4,3}$ = 8.7 Hz, H-4); 4.34-4.08 (m, 4H, 2 x H-5, 2 x H-6); 3.12 (dddd, 1H, $J_{3,2}$ = 5.1 Hz, $J_{3,6'}$ = 7.1 Hz, $J_{3,4}$ = $J_{3,6''}$ = 8.6 Hz, H-3); 2.12, 2.10, 2.08, 2.07 $COCH_3$. ^{13}C ($CDCl_3$) : 170.57, 169.53, 169.16 $COCH_3$; 98.52 C-1; 78.04, 75.70 C-2, C-4; 64.15, 57.99 C-5, C-6; 40.61 C-3; 21.04, 20.75 $COCH_3$. Exact mass (thioglycerol-NaOAc) calc. for $C_{14}H_{20}O_9$+Na 355.1005; found 355.1005.

2',4,6'-Tri-*O*-acetyl-3'-deoxy-3'-*C*-hydroxymethyl-α-L-lyxopyranosyl thymine 7

Pyranose **6** (0.23 g, 0.69 mmol) in 15 ml of 1,2-dichloroethane was added to trimethylsilylated thymine (prepared from a free base, 0.13 g, 1.02 mmol, hexamethyldisilazane and cat. $(NH_4)_2SO_4$ at bp during 5 h, followed by evaporation of volatiles, co-evaporation with xylenes and final drying on oil pump), followed by TMSOTf (0.13 ml, 0.68 mmol). External temp. of 80° was maintained overnight. TLC showed a UV-absorbing spot R_f 0.41 (CH_2Cl_2-MeOH 20:0.7) of 7. Unreacted carbohydrate **6** was still present. After extractive work-up and chromatography, 0.17 g (62%) of 7 was obtained as a glassy solid.

^1H ($CDCl_3$) : 9.30 H-3; 7.18 (d, 1H, J_{H,CH_3} = -1.0 Hz, H-6); 5.97 (d, 1H, $J_{1',2'}$ = 10.0 Hz, H-1'); 5.35 (dd, 1H, $J_{2',1'}$ = 9.7 Hz, $J_{2',3'}$ = 6.2 Hz, H-2'); 5.06 (bs, half width 6 Hz, H-4'); 4.44 (dd, $J_{6',3'}$ = 7.0 Hz, $J_{6',6''}$ = -12.0 Hz, H-6'); 4.37 (dd, $J_{6'',3'}$ = 3.6 Hz, $J_{6'',6'}$ = -12.0 Hz, H-6''); 4.14 (dd, $J_{5',4'}$ = 1.5 Hz, $J_{5',5''}$ = -13.6 Hz, H-5'); 4.04 (d, $J_{5'',5'}$ = -13.6 Hz, H-5''); 2.87-2.72 (unresolved, H-3'); 2.20, 2.15, 2.05 COMe; 1.96 (d, $J_{CH_3,6}$ = -1.0 Hz, CH_3). Exact mass (thioglycerol) calc. for $C_{17}H_{22}N_2O_9$+H 399.1403; found 399.1399.

3'-Deoxy-3'-*C*-hydroxymethyl-α-L-lyxopyranosyl thymine 1

Deacetylation of **7** (0.102 g) in MeOH and cat. NaOMe, followed by neutralization with a piece of dry ice, evaporation and chromatography through a short bed of silica gel (in CH_2Cl_2-MeOH 5:1) furnished 0.051 g (73%) of **1**, as a glassy solid.

^{1}H (CD_3OD) : 7.69 (d, 1H, J_{6,CH_3} = -1.1 Hz, H-6); 5.72 (d, 1H, $H_{1',2'}$ = 9.7 Hz, H-1'); 4.23 (dd, $J_{2',3'}$ = 5.9 Hz, $J_{2',1'}$ = 9.7 Hz, H-2'); 4.12-4.02 and 3.92-3.78 (two groups of multiplets, H4', 2 x H-5', 2 x H-6'); 2.55-2.41 (unresolved, 1H, H-3'); 1.94 (d, 3H, $J_{CH_3,6}$ = -1.1 Hz, CH_3). ^{13}C (CD_3OD) : 166.27, 153.10 C-2, C-4; 137.98 C-6; 111.82 C-5; 82.59 C-1'; 69.82 C-6'; 68.56, 66.91 C-2', C-4'; 59.13 C-5'; 49.29 C-4'; 12.38 CH_3. Exact mass (thioglycerol) calc. for $C_{11}H_{16}N_2O_6$+H 273.1087; found 273.1093.

2',4',5'-Tri-*O*-acetyl-3-deoxy-3-*C*-hydroxymethyl-α-L-lyxo-(1,6)-furanosyl thymine 8 and 2',4',6'-tri-*O*-acetyl-3'-deoxy-3'-*C*-hydroxymethyl-α-L-lyxopyranosyl thymine 7

Furanose **5** (0.33 g, 1 mmol) in 30 ml of 1,2-dichloroethane was added to trimethylsilylated thymine prepared from 0.19 g (1.5 mmol) of thymine as described above, followed by 0.19 ml (1 mmol) of TMSOTf. External temp. 60° was maintained during 18 h. TLC showed two partially overlapping spots (R_f of a mid-point was 0.40 in CH_2Cl_2-MeOH 20:0.7). The upper spot belonged to a pyranosyl nucleoside **7**, the lower one to a furanosyl nucleoside **8**. Extractive work-up and chromatography in CH_2Cl_2-MeOH 20:0.4 furnished 0.096 g (24%) of **7** and 0.188 g (47%) of **8**, which was contaminated with ca 5% of the β anomer most probably

^{1}H ($CDCl_3$) : 9.19, H-3; 7.07 (q, 1H, J_{6,CH_3} = -1.2 Hz, H-6); 5.71 (d, 1H, $J_{1',2'}$ = 4.7 Hz, H-1'); 5.35 (dd, $J_{2',1'}$ = 4.8 Hz, $J_{2',3'}$ = 6.9 Hz, H-2'); 5.29 (ddd, $J_{4',5'}$ = 3.3 Hz, $J_{4',5''}$ = 5.2 Hz, $J_{4',3'}$ = 7.2 Hz, H-4'); 4.36 (dd, $J_{5',4'}$ = 3.6 Hz, $J_{5',5''}$ = -12.4 Hz, H-5'); 4.21 (apparent dd, J = 2.6 Hz and 8.3 Hz, 2 x H-6'); 4.07 (dd, $J_{5'',4'}$ = 5.2 Hz, $J_{5'',5'}$ = -12.3 Hz, H-5''); 2.85 (dddd, $J_{3',2'}$ = $J_{3',4'}$ = $J_{3',6'}$ = $J_{3',6''}$ = 7.7 Hz, H-3'); 2.11, 2.10, 2.07 $COCH_3$; 1.95 (d, $J_{CH_3,6}$ = -1.1 Hz, CH_3). ^{13}C ($CDCl_3$) : 170.36, 170.00 $\underline{C}OCH_3$; 163.70, 150.52 C-2, C-4; 136.01 C-6; 111.31 C-5; 91.41 C-1'; 76.89, 69.68 C-2', C-4'; 69.47, 63.69 C-5', C-6'; 45.22 C-3'; 20.77, 20.61 CO$\underline{C}H_3$; 12.50 CH_3. Exact mass (thioglycerol) calc. for $C_{17}H_{22}N_2O_9$+H 399.1403; found 399.1409.

3'-Deoxy-3'-*C*-hydroxymethyl-α-L-threofuranosyl thymine 2

Compound **8** (0.134 g, 0.34 mmol) was deacetylated in 20 ml of MeOH and cat. NaOMe. After neutralization with a piece of dry ice, 1.4 mol eq of aq. $NaIO_4$ was added. The solution was filtered (30 min later) through fritted glass to remove precipitated sodium iodate, and 5.8 mol eq of aq. $NaBH_4$ solution (having pH = 8.0 adjusted with 0.1 N NaOH) was added. The solution was evaporated (30 min later) to near dryness. Chromatography of the residue (in CH_2Cl_2-MeOH 20:3) furnished 0.044 g of **2** (54% for three steps) as a glassy compound, which was contaminated with ca 5% of the β anomer most probably.

^{1}H (CD_3OD) : 7.50 (q, 1H, J_{6,CH_3} = -1.2 Hz, H-6); 5.76 (d, 1H, $J_{1',2'}$ = 5.4 Hz, H-1'); 4.27 (dd, $J_{2',1'}$ = 5.3 Hz, $J_{2',3'}$ = 7.1 Hz, H-2'); 4.26 (t, $J_{5',3'}$ = 8.4 Hz, $J_{5',5''}$ = -8.4 Hz, H-5'); 4.10 (t, J = 8.1 Hz and 8.8 Hz, H-5''); 3.78 (dd, $J_{4',3'}$ = 5.1 Hz, $J_{4',4''}$ = -11.1 Hz, H-4'); 3.69 (dd, $J_{4'',3'}$ = 6.8 Hz, $J_{4'',4'}$ = -11.2 Hz, H-4''); 2.52 (ddddd, $J_{3',4'}$ = 5.0 Hz, $J_{3',2'}$ = 7.2 Hz, $J_{3',4''}$ = 7.7 Hz, $J_{3',5'}$ = $J_{3',5''}$ = 8.4 Hz, H-3'); 1.93 (d, 3H, $J_{CH_3,6}$ = -1.1 Hz, CH_3). ^{13}C (CD_3OD) : 166.43, 152.75 C-2, C-4; 138.33 C-6; 111.62 C-5; 93.52 C-1'; 76.94 C-2'; 71.45, 61.65 C-4', C-5'; 49.45 C-3'; 12.37 CH_3. Exact mass (thioglycerol) calc. for $C_{10}H_{14}N_2O_5$+H 243.0981; found 243.0980.

2',5'-Di-*O*-(p-nitro)benzoyl-3'-deoxy-3'-*C*-hydroxymethyl-α-L-threofuranosyl thymine 34

Diol **2** (0.033 g, 0.14 mmol) was conventionally converted into bis-(p-nitro)benzoate **34** using 0.055 g (0.3 mmol) of p-nitrobenzoyl chloride in pyridine (15 ml). After extractive work-up and chromatography in CH_2Cl_2-MeOH 20:0.4, 0.069 g (94%) of **34** was obtained, mp. 198-201° (CH_2Cl_2-iPrOH).

^1H (500 MHz, DMSO-d_6) : 11.384 H-3; 8.284-8.094 H aromatic; 7.632 (q, J_{6,CH_3} = -0.92 Hz, H-6); 5.958 (d, $J_{1',2'}$ = 4.88 Hz, H-1'); 5.821 (dd, $J_{2,1'}$ = 5.18 Hz, $J_{2',3'}$ = 7.32 Hz, H-2'); 4.667 (dd, $J_{5',3'}$ = 7.33 Hz, $J_{5',5''}$ = -11.30 Hz, H-5'); 4.595 (dd, $J_{5'',3'}$ = 6.41 Hz, $J_{5'',5'}$ = -10.98 Hz, H-5''); 4.326 (t, $J_{4',3'}$ = 8.24 Hz, $J_{4',4''}$ = -8.54 Hz, H-4'); 4.212 (t, $J_{4'',4'}$ = -8.54 Hz, $J_{4'',3'}$ = 8.85 Hz, H-4''); 3.253 (sextet, J = 7.6 Hz, H-3'). ^{13}C (50 MHz, DMSO-d_6) : 164.00, 163.77 COPh; 150.54, 150.23, 150.07, 137.86, 134.62, 134.09, 130.77, 130.55, 123.58 C-2, C-4, C-6, Ph; 109.36 C-5; 90.71 C-1'; 78.56 C-2'; 69.59, 63.99 C-4', C-5'; 43.10 C-3'; 11.95 CH_3. Exact mass (m-nitrobenzyl alcohol, negative mode) calc. for $C_{24}H_{20}N_4O_{11}$ 540.1128; found 540.1131.

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