CHEMISTRY
A EUROPEAN JOURNAL

DOI: 10.1002/chem.200900572

Reliable Synthesis of Various Nucleoside Diphosphate Glycopyranoses

Saskia Wolf, Tanja Zismann, Nathalie Lunau, and Chris Meier*[a]

Abstract: A reliable and high yielding synthetic pathway for the synthesis of the biologically highly important class of nucleoside diphosphate sugars (NDP-sugars) was developed by using various *cyclo*Sal-nucleotides **1** and **9** as active ester building blocks. The reaction with anomerically pure pyranosyl-1-phosphates **2** led to the target NDP-sugars **20–45** in a nucleophilic displacement reaction, which cleaves the *cyclo*-Sal moiety in anomerically pure forms. As nucleosides cytidine, uridine, thymidine, adenosine, 2′-deoxy-guanosine and 2′,3′-dideoxy-2′,3′-didehydrothymidine were used while the phosphates of D-glucose, D-galactose, D-mannose, D-*N*Ac-glucosamine, D-*N*Ac-galactosamine, D-fucose, L-fucose as well as 6-deoxy-D-gulose were introduced.

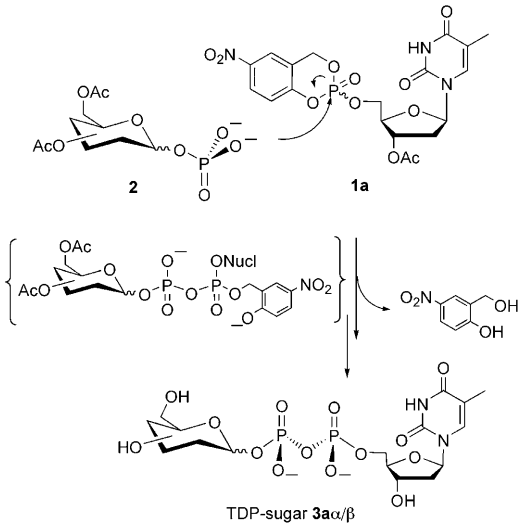
Keywords: glycophosphotransferases · glycosylation · nucleotide sugars · sugar conjugates

Introduction

Oligosaccharides and glycoconjugates play important roles in a variety of biological processes. The biosynthesis of these structurally diverse biopolymers is catalyzed by glycosyltransferases.[1,2] These enzymes transfer a monosaccharide residue in a regio- and stereoselective manner from a specific nucleoside diphosphate sugar donor to the acceptor; the growing oligosaccharide. Several families of glycosyltransferases are known. While eukaryotic glycosyltransferases use only a limited number of NDP-sugars as donors (UDP-Glc, UDP-Glc*N*Ac, UDP-GlcUA, UDP-Gal, UDP-Gal*N*Ac, GDP-Fuc, GDP-Man and CMP-Neu5Ac) the structures of NDP-sugars in prokaryotes are numerous and diverse.[3] Thus, nucleoside diphosphate pyranoses (NDP-sugars; Scheme 1) play *the* key role as glycosyl donors in the synthesis of oligo- and polysaccharides.[4,5] Moreover, they serve as precursors of deoxysugars, aminodeoxysugars, chain branched sugars, uronic acids as well as glycoconjugates. In biosynthetic sugar transfer pathways the energy-rich linkage between the anomeric carbon and the β-phosphate of the nucleoside diphosphate is cleaved releasing the nucleoside diphosphate moiety as a side product. For biosynthesis studies of oligosaccharides (e.g., lipopolysaccharides)[6] an efficient access to this important class of compounds is a prerequisite. The classical method is the coupling of glycosyl-1-phosphates to nucleotide morpholidates (Moffat–Khorana method).[7,8] However, this reaction normally takes days and the chemical yields are often low (5–15%). Attempts to improve the reaction yields by using tetrazole as activator[9–12] were reported but in our hands also gave the products in low chemical yields. Instead of morpholidates, imidazolides have also been used in the past but without improving the yields markedly.[13–15] Recently, van der Marel et al. published a new approach for the synthesis of these compounds again by building the pyrophosphate group. They used 5′-nucleosyl-phosphoramidites that were reacted with sugar-1-phosphates. The formed P^{III}–P^{V} intermediate was then oxidized and the different protecting groups were finally cleaved.[16] Alternatively, Hindsgaul and Jakeman published a procedure starting from nucleoside diphosphates and glycopyranosyl bromides.[17,18] However, the yields were found to be low and the stereochemistry at the anomeric center could only be controlled in the latter case due to the anchimeric effect of the protecting groups in the 2-position of the used D-mannosylbromide and L-fucosylbromide. Similarly, Nugier-Chauvin and Ferrières used unprotected thioimidoyl furanosides as starting material that were reacted with nucleoside diphosphates for the preparation of rare nucleotide furanoses.[19] Highest yields obtained were 37% and again the stereochemistry at the anomeric center could not be controlled. Thiem and co-workers reported an enzymatic procedure starting from unprotected sugars that were first phosphorylated and then reacted with a nucleoside triphos-

[a] Dipl.-Chem. S. Wolf, Dipl.-Chem. T. Zismann, Dipl.-Chem. N. Lunau, Prof. Dr. C. Meier
Organic Chemistry, Department of Chemistry
Faculty of Science, University of Hamburg,
Martin-Luther-King-Platz 6, 20146 Hamburg (Germany)
Fax: (+49) 40-42838-5592
E-mail: chris.meier@chemie.uni-hamburg.de

phate.[20,21] However, this reaction sequence needed a three-enzyme pathway and is dependent on the availability of the necessary kinases and NDP-sugar pyrophosphorylases and on expensive nucleoside triphosphates. The yields obtained seldom exceeded 30%. Recently, we reported on a conceptually new chemical synthesis of NDP-sugars that uses *cyclo*Sal-nucleotides as the thymidine derivative **1** as starting material (exemplified shown in Scheme 1).[22] According to this method *cyclo*Sal-TMP triester **1a** was reacted with various glycosyl-1-phosphate salts **2** in a nucleophilic displacement reaction with formation of the pyrophosphate bond in NDP-sugars (Scheme 1). Thus, *cyclo*Sal-thymidine monophosphate served as an active phosphate ester synthon. The method gave the TDP sugars in 40–59% yield after a simple chromatography on RP-silica gel.



Scheme 1. General principle of the cleavage of *cyclo*Sal-phosphate triesters using pyranose-1-phosphates.

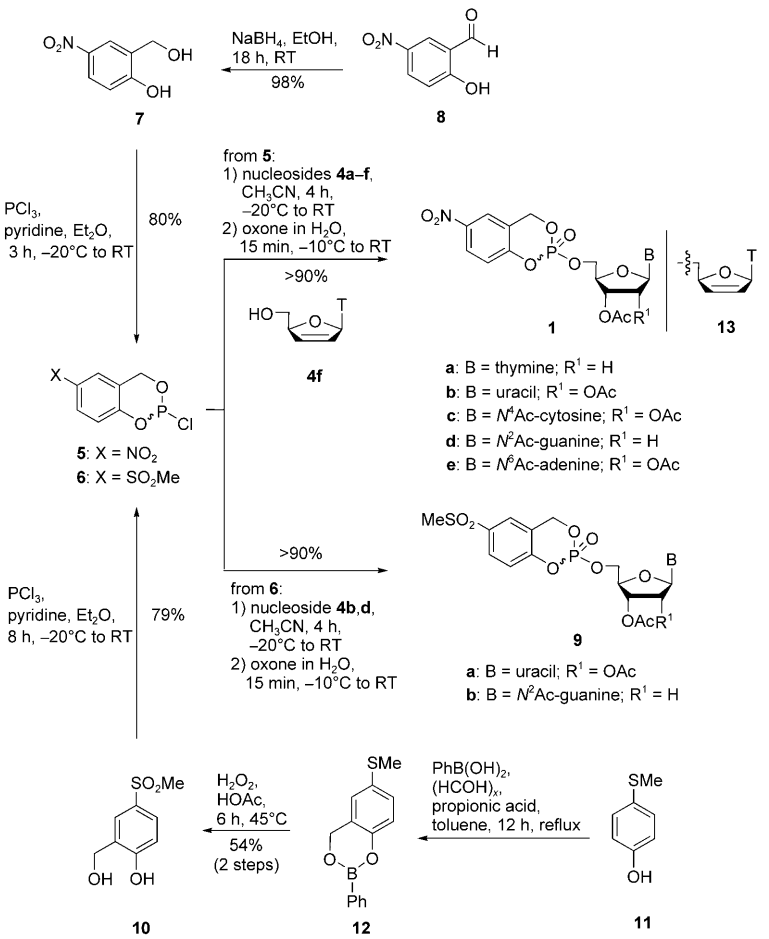
Originally, the *cyclo*Sal technique has been developed to deliver biologically active nucleotides into cells.[23] In that approach the neutral *cyclo*Sal-nucleotides bearing antivirally active nucleoside analogues were cleaved under mild cellular pH conditions by nucleophilic attack of water or hydroxide delivering the corresponding nucleotide in a highly selective manner. The technique has been applied successfully to a variety of nucleoside analogues providing superior antiviral activity.[24–27] Here, we report on a further improvement in the synthesis of NDP-sugars using *cyclo*Sal-nucleotides as **1** with respect to chemical yields. Moreover, we have proven that the method can be generally applied to various sugars as well as to a variety of nucleosides.

Results and Discussion

As starting material various *cyclo*Sal-nucleotides were used. To prove the general applicability of the method uridine, thymidine, cytosine, 2′-deoxyguanosine and adenosine were used as nucleoside part. Previously, we prepared 5-nitro-*cyclo*Sal-3′-*O*-acetylthymidine (**1a**) because the electron-withdrawing effect of the nitro substituent result in sufficient electrophilicity at the phosphorus atom to allow a rapid reaction with the sugar-1-phosphate.[22] Here, we have also used the 5-methylsulfonyl group at the *cyclo*Sal moiety in order to study the differences in reactivity. In all cases, as protecting group in both the nucleosides as well as the glycopyranoses the acetyl group was introduced to allow a deblock the final products in one reaction step only.

Thymidine, uridine, cytidine, 2′-deoxyguanosine and adenosine were 5′-*O*-protected by silylation with *tert*-butyldimethylsilylchloride (TBDMS-Cl).[28] The products were acetylated by acetic anhydride or acetyl chloride to yield fully protected nucleosides.[28] Finally, the TBDMS group was cleaved by $(n\mathrm{Bu})_4\mathrm{NF}$ to give 3′-*O*Ac-thymidine (**4a**) or $\mathrm{Et_3N{\cdot}3HF}$ to yield 2′,3′-*O*Ac-uridine (**4b**), N^4-Ac-2′,3′-*O*Ac-cytidine (**4c**), N^2-Ac-3′-*O*Ac-deoxyguanosine (**4d**) and N^6-Ac-2′,3′-*O*Ac-adenosine (**4e**) in overall yields of 50–85%. The nucleosides **4a–e** were converted into target triesters **1a–e** by reaction with 5-nitro-*cyclo*Sal-chlorophosphite **5** which was prepared as reported before starting from 5-nitrosalicyl alcohol **7**[25] that was prepared from the salicylic aldehyde derivative **8** by reduction with sodium borohydride in EtOH (98% yield). The intermediate phosphite was subsequently oxidized to the *cyclo*Sal-phosphate triester using oxone[29] in 95% yield (Scheme 2). However, if oxone is replaced by the originally used *tert*-butylhydroperoxide the yields were found to be significantly lower and sometimes the reaction failed completely. Alternatively, iodine/pyridine/THF/water-solution as used in oligonucleotide synthesizers can be used for the oxidation (Scheme 2).

In principle, the same reaction pathway was used for the synthesis of 5-(methylsulfonyl)-*cyclo*Sal-nucleotides (**9a**,**b**). However, 2-hydroxy-4-(methylsulfonyl)benzylalcohol **10** was available starting from 4-methylthiophenol (**11**), followed by a reaction with phenylboronic acid, *para*-formaldehyde and propionic acid to form the 2-phenyl-4*H*-[1,3,2]-benzodioxaborine intermediate **12**[25] that was finally oxidized by H_2O_2 in acetic acid for 6 h at 45 °C to give the corresponding salicylalcohol **10** and the oxidation of the thioether to the sulfone at the same time. The overall yield was 54% (Scheme 2). In addition, at room temperature the oxidation in THF led to 5-(methylsulfinyl)salicylalcohol in 44% yield (data not shown). Salicylalcohol **10** was then converted into the chlorophosphite **6** by the same procedure as described for 5-nitrosalicylalcohol **7**. Subsequently, phosphite **6** was reacted with protected uridine and 2′-deoxyguanosine and was oxidized finally to give the *cyclo*Sal-phosphate triester **9a**,**b**. As in the case of the 5-nitro counterpart only oxone and the iodine/pyridine/water mixture were successful in the oxidation to give the target triesters in very high yields. In contrast to the 5-nitro counterparts, both *cyclo*Sal-triesters **9** could be purified by chromatography on a silica gel column or on a Chromatotron. Nevertheless, the purity of the crude material of 5-nitro-triesters **1a–e** obtained after the oxida-



Scheme 2. Synthesis of 5-nitro- (**1**) or 5-methylsulfonyl-*cyclo*Sal-nucleoside monophosphates (**9**).

tion and extraction was found to be sufficiently high to be used in the following reactions with glycosyl-1-phosphates.

As an example for a nucleosides analogue 2′,3′-deoxy-2′,3-didehydrothymidine (d4T) (**4f**) was prepared as reported before.[30] This nucleoside was converted into the corresponding *cyclo*Sal-phosphate triester **13** as described above (Scheme 2).

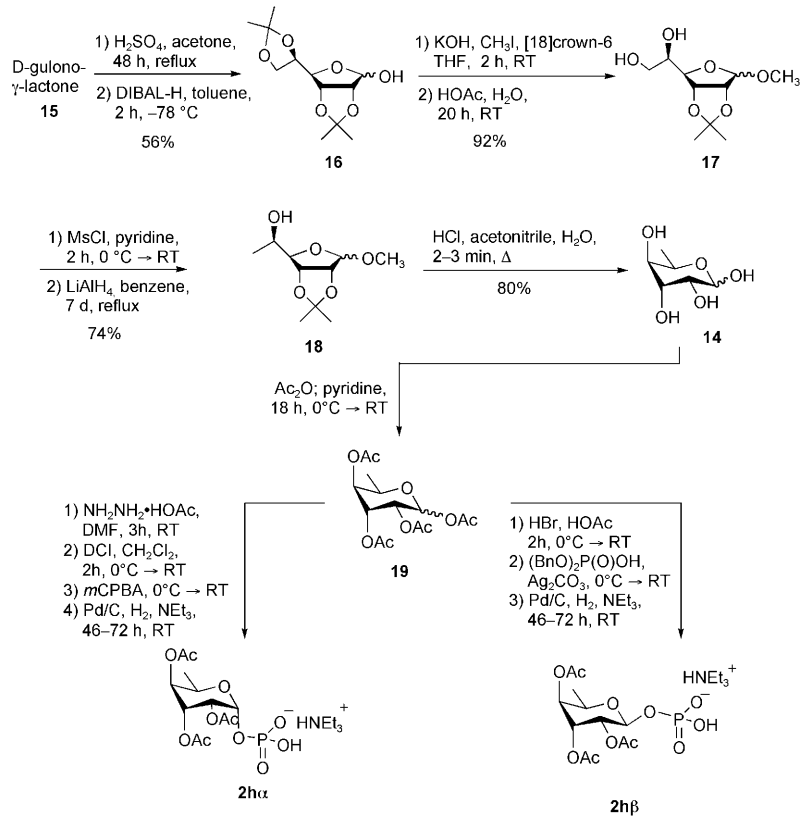
D-Glucose, D-mannose, D-galactose, *N*-acetyl-D-glucosamine, *N*-acetyl-D-galactosamine, D-fucose, L-fucose were used as examples of "standard" glycopyranoses. However, 6-deoxy-D-gulose (**14**) was not commercially available but was needed for a cytidine diphosphate sugar for lipopolysaccharide biosynthesis studies. Thus, **14** was synthesized via a new pathway over seven steps with an overall yield of 30%.[31] Starting from D-gulono-γ-lactone (**15**), first the 2,3- and 5,6-hydroxy groups were protected as isopropylidene acetals[32] and the resulting diacetal was subsequently reduced with DIBAL-H[33] to give **16**. The newly formed hydroxy function was protected as a methyl ether followed by a selective cleavage of the 5,6-acetal to give methyl glycoside **17**.[34] Next, mesylation of the hydroxy groups was achieved with mesylchloride and deoxygenation of the 6-position using $LiAlH_4$[34] yielded compound **18**. The final deprotection was done with HCl to give the target sugar **14** (Scheme 3).

Next, all glycopyranoses were per-acetylated to give derivatives as **19** by standard conditions and then transferred into the 1-phosphates **2a**–**h** (shown in Scheme 3 using **14** as an example) by two different methods. In the case of the α-configured glycosyl-1-phosphates **2α** per-acetylglycopyranoses were first fully acetylated, then selectively deprotected at the anomeric center by hydrazinium acetate[35] and subsequently reacted with dibenzyl-*N*,*N*-diisopropylphosphoamidite and dicyanoimidazole to give the phosphite intermediate[36] that was oxidized by *m*-chloroperbenzoic acid at 0°C to give dibenzylphosphate triesters in 31–73% overall yield. For the formation of the β-configured counterparts **2β**, peracetylglycopyranoses were converted into the glycopyranosyl bromides (HBr, HOAc) which were then treated with dibenzylphosphate in the presence of Ag_2CO_3 at 0°C.[37]

This reaction led to the exclusive formation of the β-D-glycopyranosyl phosphate triesters in 81–98% yield. In case of D-mannose **2c** even this reaction sequence led exclusively to the formation of the α-phosphate triester while in the case of *N*-acetyl-D-glucosamine (**2d**) and *N*-acetyl-D-galactosamine (**2e**) a strong preference for the α anomer was observed.

Subsequently, the phosphate moieties were deprotected by hydrogenolysis using Pd/C, H_2 and NEt_3 leading to α- or β-configured D-glucose- (**2aα** and **2aβ**), D-galactose- (**2bα** and **2bβ**), D-mannose- (**2cα**), *N*-acetyl-D-glucosamine- (**2dα**), *N*-acetyl-D-galactosamine- (**2eα**), D-fucose- (**2fβ**), L-fucose- (**2gα** and **2gβ**) and 6-deoxy-D-gulose-phosphates (**2hα** and **2hβ**) as their triethylammonium salts in 73–95% yield.

Previously, we reported that good chemical yields (up to 59%) were obtained when we added the glycosyl-1-phosphates **2** to 5-nitro-*cyclo*Sal-thymidine monophosphate **1a** using DMF as solvent. After 3–5 h at 50°C the *cyclo*Sal-phosphate triester was completely consumed and the product was formed in this highly stereospecific reaction.[22] Since then we have focused our attention on several factors that may contribute to the efficiency of the reaction: i) the order of addition of the two reagents, ii) the pretreatment of hygroscopic reagents, iii) the equivalents of reagents, iv) and the counterion of the glycopyranosyl-1-phosphate **2**.



Scheme 3. Synthesis of 6-deoxy-D-gulose **14** and the 1-monophosphates **2h**.

First, we investigated the influence of the order of addition of the two reagents. In contrast to a method published earlier,[22] the *cyclo*Sal-triester was added to a solution of the protected pyranosyl-1-phosphates **2** at room temperature instead of 50 °C. By applying these (milder) conditions the sugar-phosphate is used in great excess with respect to the *cyclo*Sal-phosphate triesters **1**. This avoids any possible side reactions of the latter compound. Moreover, it was found that it was essential to dry the hygroscopic pyranosyl-1-phosphates **2** prior to the reaction for at least 2 h in high vacuum. After dissolving phosphates **2** in dry DMF, the solution was stored for one hour over activated molecular sieve (4 Å) to ensure complete removal of traces of water. Moreover, we used 2.0 equivalents of the pyranosyl-1-phosphates instead of the previous 1.2 equivalents. We observed that these three changes led to a better conversion of the *cyclo*Sal-triesters and thus gave improved chemical yields of up to 88% of the NDP-sugars. The reactions were carried out at room temperature with stirring for 18–26 h (Scheme 4). In addition to the 5-nitro-*cyclo*Sal-nucleotides, the 5-methylsulfonyl counterparts **9a** was investigated. The yield of the target NDP-sugar **35** starting from 5-nitro-*cyclo*Sal-phosphate triester **1b** and sugar **2aα** was 56%. The reaction with 5-methylsulfonyl-*cyclo*Sal-phosphate triester **9a** that was used as the crude reaction product as the 5-nitro counterpart and **2aα** gave product **35** in only 34% yield. However, the same reaction conditions led to **35** in 87% yield when the purified 5-methylsulfonyl-*cyclo*Sal-phosphate triester **9a** was used instead. In this case, the isolation of the starting material has a clear advantage.

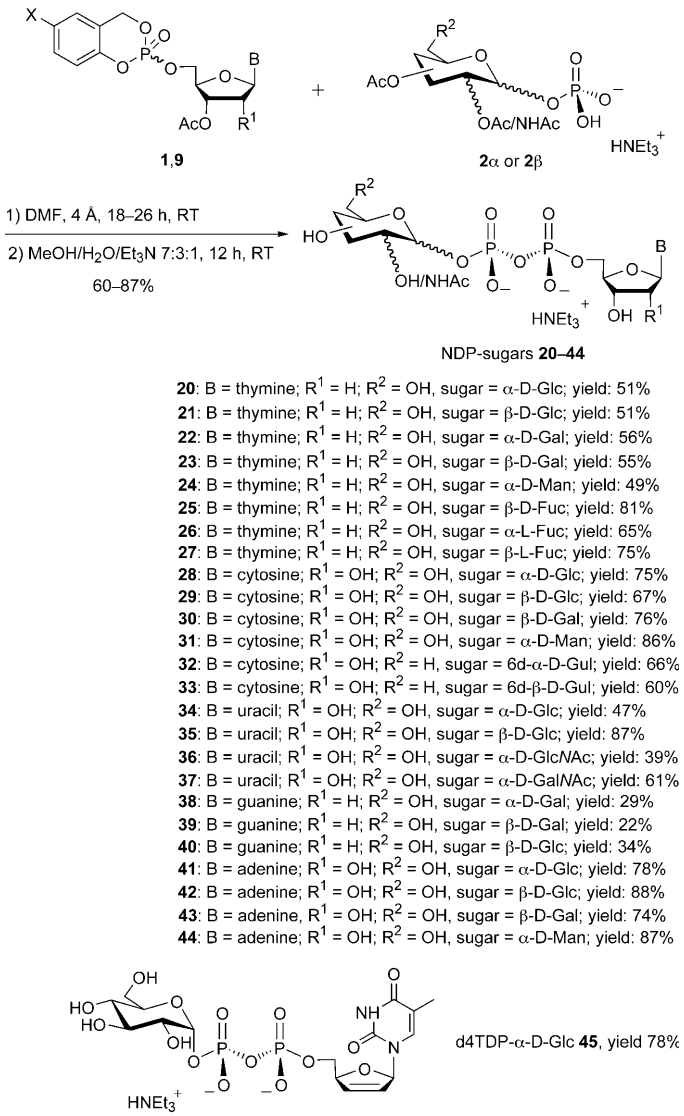
Using these improved conditions we reinvestigated the effect of the counterion. Instead of using the triethylammonium salt of the acetylated sugar-1-phosphates **2** also more lipophilic counter ions (e.g., nBu$_4$N$^+$) were introduced.

However, although the solubility of the salts was improved and the reaction works well leading to high yields of the target products, the purification of the NDP-sugars was extremely difficult.

N,*N*-Dimethylformamide still proved to be the solvent of choice because pyridine required very long reaction times in which the *cyclo*Sal-triesters **1** slowly underwent a side reaction and in acetonitrile many non-identified side products were formed.

Prior to the purification, the acetyl groups in the crude product were cleaved by a mixture of MeOH/H_2O/NEt_3 7:3:1. NDP-sugars **20**–**44** were then purified on a glass column filled with RP-18 silica gel. Usually, two runs were sufficient to isolate the product in high purity. Yields after purification were found to be up to 88% using this modified protocol (Scheme 4). Still problematic were the corresponding 2′-deoxyguanosine derivatives **38**–**40**. As expected, the spectroscopic characterization proved that the anomeric configuration was unchanged in the product compared with the pyranosyl-1-phosphates. In summary, we observed a considerable improvement of the yields when we using the above procedure. Moreover, this new procedure was applied to the synthesis of an analogue of a thymidine-bearing NDP-sugar. Due to the chemical procedure 2′,3′-dideoxy-2′,3′-didehydrothymidine diphosphate-α-D-glucose (**45**) was successfully synthesized in 78% yield.

During purification by RP chromatography the used excess of glycopyranose-1-phosphates **2** was isolated in the deacetylated form. Interestingly, these can be used for the syntheses of NDP-glycopyranoses as well using the same conditions as described for the *O*-acetylated counterparts. Moreover, the yields were found to be only slightly lower to those obtained in the reactions with acetylated pyranosyl-1-phosphates. This was proven by the reaction of α-D-Gal*N*Ac-1-phosphate and *cyclo*Sal-UMP. The corresponding NDP-sugar **37** was obtained in 40% yield.



Scheme 4. Synthesis and yields of the NDP-sugars starting from the *cyclo*Sal-phosphate triester.

Conclusions

This report describes a reliable, versatile, high yielding and general synthesis of anomerically defined NDP-glycopyranoses that is applicable to a broad variety of nucleosides and glycopyranoses. Such a broadly applicable chemistry-based method offers an efficient access not only to the naturally occurring NDP-sugars but also to analogues of these compounds. Analogues of both types of natural products, for example, using sugar analogues (as in **32**, **33** or sugars bearing labels) or nucleoside analogues (as in **45**) or even both should be possible. This offers the option to prepare NDP-sugar analogues for further biochemical (e.g., with glycosyltransferases) or structural studies (e.g., by STD-NMR).

Experimental Section

General procedure A for the synthesis of the nucleoside diphosphate sugars 20–45: The reaction was carried out under a nitrogen atmosphere. 1.0 equiv 5-nitro-*cyclo*Sal-nucleoside triester **1** was dissolved in dry DMF and 1.2 equiv of the corresponding glycosyl-1-phosphates **2** as the triethylammonium salts were added within 10 min. The reaction mixture was stirred at 50 °C. After complete conversion of the triester (TLC analysis) the solvent was removed under reduced pressure. The residue was solubilised in water and extracted with EtOAc. After lyophilisation of the aqueous phase the acetyl groups in the crude product were cleaved by $MeOH/H_2O/Et_3N$ 7:3:1 over night at room temperature. After a second lyophilisation the crude product was finally purified by RP-18-chromatography using water as eluent. Usually two passages were sufficient to isolate the desired product in high purity. Detection of the NDP-sugar was by TLC using isopropanol/1 N ammonium acetate 2:1 *v/v*.

General procedure B for the synthesis of the nucleoside diphosphate sugars 20–45: The reaction was carried out under a nitrogen atmosphere. 2.0 equiv of the corresponding glycosyl-1-phosphates **2** as the triethylammonium salts were dissolved in dry DMF (2–3 mL). After storage for 1 h over activated molecular sieves, 1.0 equiv 5-nitro- or 5-methylsulfonyl-*cyclo*Sal-nucleoside triester **1** or **9** was added within 10 min and the reaction mixture stirred at room temperature for 18–26 h. After complete conversion of the triester (TLC analysis) the solvent was removed under reduced pressure. The residue was solubilized in water and extracted with ethyl acetate. After lyophilization of the aqueous phase the acetyl groups in the crude product were cleaved by $MeOH/H_2O/Et_3N$ 7:3:1 overnight at room temperature. After a second lyophilization the crude product was finally purified by RP-18-chromatography using water as eluent. Usually two passages were sufficient to isolate the desired product in high purity. Detection of the NDP-sugar was by TLC using isopropanol/1 N ammonium acetate-solution 2:1 *v/v*.

Thymidine diphosphate-α-D-glucose 20: According to GP A, the reaction was conducted with 5-nitro-*cyclo*Sal-3′-*O*-Ac-thymidine monophosphate (**1a**; 100 mg, 0.21 mmol) and 2,3,4,6-tetra-*O*-acetyl-α-D-glucopyranosyl-1-phosphate (**2aα**, 122 mg, 0.23 mmol) within a reaction time of 4 h at 50 °C in DMF (5 mL) to afford a colorless solid (68.0 mg, 51 %). $[\alpha]_{546}^{20} = +12°$ ($c = 0.1$, H_2O); ^{1}H NMR (400 MHz, D_2O): $\delta = 7.70$ (d, $J = 1.0$ Hz, 1H), 6.30 (dd, $J = 6.4$, 6.4 Hz, 1H), 5.65 (dd, $^3J_{HP} = 7.2$, 3.5 Hz, 1H), 4.63 (m, 1H), 4.19–4.20 (m, 4H), 4.04–4.06 (m, 1H), 3.85 (dd, $J = 10.3$, 3.0 Hz, 1H), 3.60–3.62 (m, 3H), 3.19 (q, $J = 7.3$ Hz, 12H), 2.36–2.42 (m, 2H), 1.93 (d, $J = 0.9$ Hz, 3H), 1.26 ppm (t, 18H, $J = 7.3$ Hz); ^{13}C NMR (101 MHz, D_2O): $\delta = 168.0$, 151.7, 137.3, 111.7, 98.3 (d, $J = 5.9$ Hz), 85.4, 77.2, 75.0, 74.5, 74.0 (d, $J = 8.6$ Hz), 72.4 (d, $J = 8.6$ Hz), 69.1, 65.5 (d, $J = 5.6$ Hz), 61.0, 46.9, 38.6, 11.7, 8.7 ppm; ^{31}P NMR (162 MHz, D_2O): $\delta = -12.73$ (d, $J = 19.8$ Hz), −11.70 ppm (d, $J = 19.8$ Hz); IR: $\tilde{\nu} = 3230$, 1660, 1476, 1239, 1171, 1049, 931, 882, 808, 755 cm^{-1}; MS (HR-ESI): *m/z*: calcd for 563.0685; found 563.0659 $[M-H]^-$.

Thymidine diphosphate-β-D-glucose 21: According to GP A, the reaction was conducted with **1a** (120 mg, 0.25 mmol) and 2,3,4,6-tetra-*O*-acetyl-β-D-glucopyranosyl-1-phosphate (**2aβ**; 159 mg, 0.30 mmol) within a reaction time of 3 h at 50 °C in DMF (5 mL) to afford a colorless solid (97.0 mg, 51 %). $[\alpha]_{546}^{20} = -17°$ ($c = 0.1$, H_2O); ^{1}H NMR (400 MHz, D_2O): $\delta = 7.75$ (d, $J = 1.0$ Hz, 1H), 6.36 (dd, $J = 6.5$, 6.5 Hz, 1H), 5.02 (dd, $J = 7.8$, 7.8 Hz, 1H), 4.62–4.65 (m, 1H), 4.18–4.19 (m, 3H), 3.91 (dd, $J = 2.0$, 12.3 Hz, 1H), 3.71 (dd, $J = 6.0$, 12.3 Hz, 1H), 3.50–3.56 (m, 2H), 3.36–3.42 (m, 2H), 3.21 (q, $J = 7.3$ Hz, 12H), 2.32–2.39 (m, 2H), 1.94 (d, $J = 0.9$ Hz, 3H), 1.28 ppm (t, $J = 7.3$ Hz, 18H); ^{13}C NMR (101 MHz, D_2O): $\delta = 167.0$, 137.7, 112.1, 98.3 (d, $J = 6.1$ Hz), 85.7 (d, $J = 9.2$ Hz), 85.3, 76.8, 75.6, 74.0 (d, $J = 8.7$ Hz), 71.4, 69.8, 65.9 (d, $J = 5.6$ Hz), 61.2, 47.0, 39.0, 12.0, 8.6 ppm; ^{31}P NMR (162 MHz, D_2O): $\delta = -13.15$ (d, $J = 19.6$ Hz), −11.53 ppm (d, $J = 19.6$ Hz); IR: $\tilde{\nu} = 3217$, 1661, 1478, 1237, 1174, 1017, 940, 816, 755 cm^{-1}; MS (HR-ESI): *m/z*: calcd for 563.0685; found: 563.0667 $[M-H]^-$.

Thymidine diphosphate-α-D-galactose 22: According to GP A, the reaction was conducted with **1a** (100 mg, 0.21 mmol) and 2,3,4,6-tetra-*O*-acetyl-α-D-galactopyranosyl-1-phosphate (**2bα**; 133 mg, 0.25 mmol) within a reaction time of 4 h at 50 °C in DMF (5 mL) to afford a colorless

solid (89.0 mg, 56%). $[\alpha]_{546}^{20} = +8°$ ($c=0.1$, H_2O); ^1H NMR (400 MHz, D_2O): $\delta=7.76$ (d, $J=1.0$ Hz, thymine-CH_3, 1H), 6.36 (dd, $J=6.5$, 6.5 Hz, H-1′, 1H), 5.65 (dd, $J=7.3$, 3.8 Hz, H-1, 1H), 4.63 (m, H-3′, 1H,), 4.19–4.20 (m, H-2, H-4′, H-5′, 4H), 4.04 (d, $J=3.0$ Hz, H-4, 1H), 3.93 (dd, $J=10.3$ Hz, $^3J_{HH}=3.0$ Hz, H-3, 1H), 3.71–3.83 (m, H-5, H-6, 3H), 3.21 (q, $J=7.4$ Hz, $2\times CH_2$-NEt_3, 12H), 2.37–2.44 (m, H-2′, 2H), 1.94 (d, $J=1.0$ Hz, thymine-CH_3, 3H), 1.29 ppm (t, $J=7.4$ Hz, $2\times CH_3$-NEt_3, 18H,); ^{13}C NMR (101 MHz, D_2O): $\delta=166.6$, 151.8, 137.4, 111.8, 95.8 (d, $J=6.6$ Hz), 95.8 (d, $J=6.6$ Hz), 85.4 (d, $J=8.8$ Hz), 85.1, 71.9, 71.0, 69.4, 69.2, 68.5 (d, $J=8.1$ Hz), 65.5 (d, $J=5.6$ Hz), 61.1, 46.7, 38.6, 11.7, 8.3 ppm; ^{31}P NMR (162 MHz, D_2O): $\delta=-12.66$ (d, $J=20.9$ Hz, P_α), -11.20 ppm (d, $J=20.9$ Hz, P_β); IR: $\tilde{\nu}$ = 3278, 1666, 1471, 1238, 1175, 1040, 940, 888, 819, 766 cm^{-1}; MS (HR-ESI): m/z: calcd for 563.0685; found: 563.0671 $[M-H]^-$.

Thymidine diphosphate-β-D-galactose 23: According to GP A, the reaction was conducted with **1a** (85.0 mg, 0.18 mmol) and 2,3,4,6-tetra-*O*-acetyl-β-D-galactopyranosyl-1-phosphate (**2bβ**; 105 mg, 0.19 mmol) within a reaction time of 5 h at 50°C in DMF (4 mL) to afford a colorless solid (85.0 mg, 55%). $[\alpha]_{546}^{20} = -14°$ ($c=0.1$, H_2O); ^1H NMR (400 MHz, D_2O): $\delta=7.71$ (d, $J=1.0$ Hz, thymine-CH_3, 1H), 6.31 (dd, $J=6.6$, 6.6 Hz, H-1′, 1H), 4.91 (dd, $J=7.6$, 7.6 Hz, H-1, 1H), 4.58–4.60 (m, H-3′, 1H), 4.13–4.14 (m, H-4′, H-5′, 3H), 3.87 (d, $J=3.3$ Hz, H-2, 1H), 3.74–3.80 (m, H-3, H-5, 2H), 3.70 (dd, $J=3.0$, 10.3 Hz, H-6, 1H), 3.63–3.67 (m, H-4, 1H), 3.57 (dd, $J=7.6$, 10.3 Hz, H-6, 1H), 3.15 (q, $J=7.3$ Hz, $2\times CH_2$-NEt_3, 12H), 2.27–2.39 (m, H-2′, 2H), 1.88 (s, $J=1.0$ Hz, thymine-CH_3, 3H), 1.23 ppm (t, $J=7.3$ Hz, $2\times CH_3$-NEt_3, 18H); ^{13}C NMR: (101 MHz, D_2O): $\delta=166.9$, 152.1, 137.7, 112.1, 98.9 (d, $J=5.6$ Hz), 85.8 (d, $J=9.2$ Hz), 85.4, 76.2, 72.7, 71.6 (d, $J=82$. Hz), 69.0, 65.9 (d, $J=5.6$ Hz), 61.6, 47.0, 39.0, 12.0, 8.6 ppm; ^{31}P NMR (162 MHz, D_2O): $\delta=-13.24$ (d, $J=20.7$ Hz, P_α), -11.75 ppm (d, $J=20.7$ Hz, P_β); IR: $\tilde{\nu}$ = 3222, 1660, 1473, 1234, 1169, 1010, 933, 798, 749 cm^{-1}; MS (HR-ESI): m/z: calcd for 563.0685 $[M-H]^-$; found: 563.0673.

Thymidine diphosphate-α-D-mannose 24: According to GP A, the reaction was conducted with **1a** (100 mg, 0.21 mmol) and 2,3,4,6-tetra-*O*-acetyl-α-D-mannopyranosyl-1-phosphate (**2cα**) (133 mg, 0.25 mmol) within a reaction time 4 h at 50°C in DMF (5 mL) to afford a colorless solid (80.0 mg, 49%). $[\alpha]_{546}^{20} = +25°$ ($c=0.1$, H_2O); ^1H NMR (400 MHz, D_2O): $\delta=7.71$ (d, $J=0.8$ Hz, 1H), 6.30 (dd, $J=6.8$, 6.8 Hz, 1H), 5.45 (d, $J=6.8$ Hz, 1H), 4.56–4.57 (m, 1H), 4.13 (m, 3H), 3.99–4.00 (m, 1H), 3.86 (dd, $J=3.3$, 12.3 Hz, 1H), 3.77–3.81 (m, 2H), 3.71 (dd, $J=5.3$, 12.3 Hz, 1H), 3.59–3.65 (m, 1H), 3.14 (q, $J=7.3$ Hz, 12H), 2.26–2.37 (m, 2H), 1.87 (s, 3H), 1.22 ppm (t, $J=7.3$ Hz, 18H); ^{13}C NMR (101 MHz, D_2O): $\delta=168.3$, 151.8, 137.4, 111.8, 96.5 (d, $J=4.4$ Hz), 85.5 (d, $J=8.8$ Hz), 85.1, 73.7, 71.1, 70.3 (d, $J=8.8$ Hz), 69.9, 66.5, 65.5 (d, $J=5.9$ Hz), 60.9, 46.7, 38.7, 11.7, 8.3 ppm; ^{31}P NMR (162 MHz, D_2O): $\delta=-13.99$ (d, $J=18.6$ Hz, P_α), -11.87 ppm (d, $J=18.6$ Hz, P_β); IR: $\tilde{\nu}$ = 3232, 1666, 1472, 1239, 1170, 1041, 935, 884, 87, 747 cm^{-1}; MS (HR-ESI): m/z: calcd for 563.0685 $[M-H]^-$; found: 563.0667.

Thymidine diphosphate-β-D-fucose 25: According to GP B the reaction was conducted with **1a** (57.0 mg, 0.11 mmol) and 2,3,4,6-tetra-*O*-acetyl-β-D-fucose-1-phosphate **2fβ** (95.0 mg, 0.23 mmol) within a reaction time of 36 h in DMF (5 mL) to afford a colorless solid (58.0 mg, 81%). $[\alpha]_{546}^{20} = -78.6°$ ($c=0.1$, H_2O); ^1H NMR (400 MHz, D_2O): $\delta = 7.76$ (d, $J=1.2$ Hz, 1H), 6.37 (t, $J=7.0$ Hz, 1H), 4.95 (t, $J=8.0$ Hz, 1H), 4.63–4.65 (m, 1H), 4.20 (d, $J=4.8$ Hz, 3H), 3.84 (q, $J=6.5$ Hz, 1H), 3.76 (d, $J=3.1$ Hz, 1H), 3.70 (dd, $J=10.0$, 3.5 Hz, 1H), 3.58 (dd, $J=9.9$, 7.7 Hz, 1H), 2.39 (dd, $J=6.1$ Hz, 2H), 1.95 (d, $J=1.0$ Hz, 3H), 1.28 ppm (d, $J=6.5$ Hz, 3H); ^{13}C NMR (101 MHz, D_2O): $\delta = 166.6$, 151.8, 137.4, 111.8, 98.4 (d, $J=6.0$ Hz), 85.4 (d, $J=9.1$ Hz), 85.0. 72.4, 71.4, 71.2, 71.1, 71.0, 65.5 (d, $J=5.6$ Hz), 38.7, 15.5, 11.7 ppm; ^{31}P NMR (162 MHz, D_2O): $\delta = -12.79$ (d, $J=19.9$ Hz, P_α), -11.32 ppm (d, $J=21.1$ Hz, P_β); IR: $\tilde{\nu}$ = 3219, 1662, 1476, 1234, 1171, 1011, 936, 812, 751 cm^{-1}; MS (HR-ESI): m/z: calcd for 547.0741 $[M-H]^-$; found: 547.0706.

Thymidine diphosphate-α-L-fucose 26: According to GP B the reaction was conducted with **1a** (53.0 mg, 0.11 mmol) and 2,3,4,6-tetra-*O*-acetyl-β-L-fucose-1-phosphate (**2gα**; 89.0 mg, 0.21 mmol) within a reaction time of 36 h in DMF (5 mL) to afford a colorless solid (41.0 mg, 65%). $[\alpha]_{546}^{20} = -3°$ ($c=0.1$, H_2O); ^1H NMR: (400 MHz, D_2O): $\delta = 7.76$ (d, $J=1.1$ Hz, 1H), 6.37 (t, $J=6.9$ Hz, 1H), 5.58 (dd, $J=6.8$, 3.7 Hz, 1H), 4.63–4.66 (m, 1H), 4.30 (q, $J=6.6$ Hz, 1H), 4.18–4.23 (m, 3H), 3.93 (dd, $J=10.3$, 3.4 Hz, 1H), 3.84 (d, $J=3.2$ Hz, 1H), 3.76 (td, $J=10.3$, 3.3 Hz, 1H), 2.34–2.44 (m, 2H), 1.94 (d, $J=1.0$ Hz, 3H), 1.23 ppm (d, $J=6.6$ Hz, 3H); ^{13}C NMR: (101 MHz, D_2O): $\delta = 168.3$, 151.8, 137.4, 111.8, 95.5 (d, $J=7.2$ Hz), 85.5 (d, $J=8.9$ Hz), 85.1, 71.9, 71.1, 69.6, 68.3 (d, $J=8.5$ Hz), 68.0, 65.5 (d, $J=5.8$ Hz), 38.6, 15.5, 11.8 ppm; ^{31}P NMR: (162 MHz, D_2O): $\delta = -12.79$ (d, $J=20.7$ Hz, P_α), -11.36 ppm (d, $J=20.3$ Hz, P_β); IR: $\tilde{\nu}$ = 3228, 1662, 1474, 1233, 1172, 1045, 935, 886, 811, 750, 666 cm^{-1}; MS (HR-ESI): m/z: calcd for 547.0741 $[M-H]^-$; found: 547.0712.

Thymidine diphosphate-β-L-fucose 27: According to GP B the reaction was conducted with **1a** (60.0 mg, 0.12 mmol) and 2,3,4,6-tetra-*O*-acetyl-β-L-fucose-1-phosphate (**2gβ**; 100 mg, 0.24 mmol) within a reaction time of 36 h in DMF (5 mL) to afford a yellow solid (53.0 mg, 75%). $[\alpha]_{546}^{20} = -10°$ ($c=0.2$, H_2O); ^1H NMR (400 MHz, D_2O): $\delta = 7.74$ (s, 1H), 6.35 (t, $J=6.9$ Hz, 1H), 4.92 (t, $J=8.0$ Hz, 1H), 4.61–4.65 (m, 1H), 4.18 (d, $J=4.4$ Hz, 3H), 3.82 (q, $J=6.3$ Hz, 1H), 3.75 (d, $J=3.1$ Hz, 1H), 3.70 (dd, $J=10.0$, 3.4 Hz, 1H), 3.57 (dd, $J=9.9$, 7.8 Hz, 1H), 2.37–2.41 (m, 2H), 1.92 (s, 3H), 1.25 ppm (d, $J=6.4$ Hz, 3H); ^{13}C NMR (101 MHz, D_2O): $\delta = 166.7$, 151.8, 137.3, 111.8, 98.4 (d, $J=6.0$ Hz), 85.3 (d, $J=9.1$ Hz), 85.0. 72.5, 71.4, 71.2, 71.1, 71.0, 65.5 (d, $J=5.6$ Hz), 38.6, 15.4, 11.7 ppm; ^{31}P NMR (162 MHz, D_2O): $\delta = -12.98$ (d, $J=21.2$ Hz, P_α), -11.33 ppm (d, $J=21.09$ Hz, P_β); IR: $\tilde{\nu}$ = 3228, 1662, 1474, 1234, 1172, 1011, 935, 886, 750, 886, 750 cm^{-1}; MS (HR-ESI): m/z: calcd for 547.0741 $[M-H]^-$; found: 547.0734.

Cytidine diphosphate-α-D-glucose 28: According to GP B the reaction was conducted with 5-nitro-*cyclo*Sal-N^4-Ac-2′,3′-*O*-Ac-cytidine-monophosphate (**1c**; 55.0 mg, 0.09 mmol) and **2aα** (70.0 mg, 0.27 mmol) (different from the GP B with 3.0 instead of 2.0 equivalents of glycosyl-1-phosphate) within a reaction time of 24 h afforded a colorless solid (52.0 mg, 75%). $[\alpha]_{546}^{20} = -15°$ ($c=0.1$, H_2O); ^1H NMR (400 MHz, D_2O): $\delta = 8.09$ (d, $J=7.7$ Hz, 1H), 6.01 (d, $J=7.7$ Hz,1H), 5.82 (dd, $J=5.0$, 5.0 Hz, 1H), 5.62 (dd, $J=7.4$, 3.4, 1H), 3.74–3.82 (m, 7H), 3.49–3.53 (m, 2H), 3.40–3.45 (m, 2H), 3.22 (q, $J=7.3$ Hz, 12H), 1.30 ppm (t, $J=7.3$ Hz, 18H); ^{13}C NMR (101 MHz, D_2O): $\delta = 163.5$, 154.2, 142.6, 97.8 (d, $J=5.9$ Hz), 96.2, 89.3, 83.0 (d, $J=9.1$ Hz), 76.5, 75.3, 74.3, 73.6, 69.5, 69.3 (d, $J=8.1$ Hz), 64.7 (d, $J=5.6$ Hz), 60.8, 46.7, 8.3 ppm; ^{31}P NMR (162 MHz, D_2O): $\delta = -14.00$ (d, $J=20.9$ Hz, P_α), -12.42 ppm (d, $J=20.9$ Hz, P_β); IR (KBr): $\tilde{\nu}$ = 3430, 2924, 2348, 1654, 1240, 1153, 984, 807, 746, 640 cm^{-1}; MS (HR-ESI): m/z: calcd for 564.0637 $[M-H]^-$; found: 564.0628.

Cytidine diphosphate-β-D-glucose 29: According to GP B the reaction was conducted with **1c** (110 mg, 0.19 mmol) and **2aβ** (220 mg, 0.41 mmol) within a reaction time of 24 h in DMF (3.5 mL) to afford a colorless solid (97.0 mg, 67%). $[\alpha]_{546}^{20} = +20°$ ($c=0.1$, H_2O); ^1H NMR (400 MHz, D_2O): $\delta = 8.06$ (d, $J=7.7$ Hz, 1H), 6.20 (d, $J=7.7$ Hz, 1H), 5.97 (dd, $J=4.6$, 4.6 Hz, 1H), 5.00 (dd, $J=5.6$, 5.2 Hz, 1H), 4.21–4.40 (m, 5H), 3.89 (dd, $J=12.4$, 2.1 Hz, 1H), 3.67–3.72 (m, 1H), 3.47–3.53 (m, 2H), 3.35–3.40 (m, 2H), 3.19 (q, $J=7.3$ Hz, 12H), 1.27 ppm (t, $J=7.3$ Hz, 18H); ^{13}C NMR (101 MHz, D_2O): $\delta = 163.5$, 154.2, 142.6, 97.8 (d, $J=6.1$ Hz), 96.2, 89.3, 83.0 (d, $J=9.2$ Hz), 76.5, 75.3, 74.3, 73.6, 69.5, 69.3 (d, $J=7.3$ Hz), 64.7 (d, $J=5.6$ Hz), 60.8, 46.7, 8.3 ppm; ^{31}P NMR (162 MHz, D_2O): $\delta = -11.97$ (d, $J=20.6$ Hz, P_α), -10.26 ppm (d, $J=20.6$ Hz, P_β); IR (KBr): $\tilde{\nu}$ = 3422, 2923, 2979, 1654, 1550, 1458, 1400, 1240, 1125, 985 cm^{-1}; MS (HR-ESI): m/z: calcd for 564.0637 $[M-H]^-$; found: 564.0610.

Cytidine diphosphate-β-D-galactose 30: According to GP B the reaction was conducted with **1c** (61.0 mg, 0.11 mmol) and **2bβ** (110 mg, 0.21 mmol) within a reaction time of 24 h in DMF (3 mL) to afford a colorless solid (61.3 mg, 76%). $[\alpha]_{546}^{20} = +8°$ ($c=0.1$, H_2O); ^1H NMR (400 MHz, D_2O): = δ 8.08 (d, $J=7.7$ Hz, 1H), 6.22 (d, $J=7.7$ Hz, 1H), 5.99 (d, $J=4.0$ Hz, 1H), 4.96 (dd, $J=7.8$, 7.1 Hz, 1H), 4.39–4.36 (m, 1H), 4.19–4.37 (m, 4H), 3.92 (d, $J=3.2$ Hz, 1H), 3.78–3.84 (m, 1H), 3.68–3.76 (m, 2H), 3.60–3.64 (m, 2H), 3.20 (q, $J=7.3$ Hz, 12H), 1.28 ppm (t, $J=7.3$ Hz, 18H); ^{13}C NMR (101 MHz, D_2O): $\delta = 163.7$, 154.4, 142.9, 98.9 (d, $J=6.2$ Hz), 96.5, 89.6, 83.4 (d, $J=9.2$ Hz), 76.2, 74.7, 71.6 (d, $J=8.5$ Hz), 69.7, 62.7, 69.0 (d, $J=8.5$ Hz), 61.6 (d, $J=5.4$ Hz), 47.0, 8.6 ppm; ^{31}P NMR (162 MHz, D_2O): $\delta = -13.02$ (d, $J=20.5$ Hz, P_α), -11.57 ppm (d, $J=20.5$ Hz, P_β); IR (KBr): $\tilde{\nu}$ = 3422, 2680, 2347, 1725, 1655, 1477,

1244, 1062, 943, 778 cm^{-1}; MS (HR-ESI): *m/z*: calcd for 564.0637 $[M-H]^-$; found: 564.0671.

Cytidine diphosphate-α-D-mannose 31: According to GP B the reaction was conducted with **1c** (55.0 mg, 0.09 mmol) and **2cα** (110 mg, 0.21 mmol) within a reaction time of 24 h in DMF (2 mL) to afford a colorless solid (62.0 mg, 86%). ^{1}H NMR (400 MHz, D_2O): 8.02 (d, J= 7.6 Hz, 1H), 6.17 (d, J=7.6 Hz, 1H), 6.01 (d, J=4.3 Hz, 1H), 5.53 (dd, J=7.8, 1.6 Hz, 1H), 4.20–4.31 (m, 4H), 4.12–4.31 (m, 1H), 3.99–4.00 (m, 1H), 3.78–3.88 (m, 3H), 3.68–3.73 (m, 1H), 3.58–3.65 (m, 1H), 3.22 (q, J=7.3 Hz, 12H), 1.30 (t, J=7.3 Hz, 18H); ^{13}C NMR (101 MHz, D_2O): 165.6, 157.0, 141.7, 96.5 (d, J=6.2 Hz), 89.6, 89.3, 82.8 (d, J=9.0 Hz), 74.3, 73.7, 70.3, 69.7, 69.9, 69.3, 65.5 (d, J=9.1 Hz), 64.7 (d, J=5.5 Hz), 60.9, 46.7, 8.3; ^{31}P NMR (162 MHz, D_2O): −14.13 (d, J=20.7 Hz, P_α), −11.83 (d, J=20.7 Hz, P_β). $[\alpha]_{546}^{20}$= −13° (c=0.1, H_2O); IR (KBr): $\tilde{\nu}$ = 3422, 2937, 2980, 1655, 1491, 1400, 1243, 1078, 938, 804; MS (HR-ESI): *m/z*: calcd for 564.0637 [M-H]$^-$; found: 563.0571.

Cytidine-diphosphate-6-deoxy-α-D-gulose 32: According to GP B the reaction was conducted with **1c** (37.0 mg, 0.06 mmol) and 2,3,4-tri-*O*-acetyl-α-D-gulose-1-phosphate (**2hα**; 60.0 mg, 0.13 mmol) within a reaction time of 24 h afforded a colorless solid (32.3 mg, 66%). $[\alpha]_{546}^{20}$ = −24° (c=0.1, H_2O); ^{1}H NMR (400 MHz, D_2O): δ = 8.05 (d, J=7.6 Hz, 1H), 6.13 (d, J=7.6 Hz, 1H), 6.02 (d, J=4.4 Hz, 1H), 5.04 (dd, J=7.1, 1.6 Hz, 1H), 4.33–4.39 (m, 3H), 4.26–4.29 (m, 3H), 4.12–4.14 (m, 2H), 3.65 (dd, J=8.3, 4.0 Hz, 1H), 3.22 (q, J=7.3 Hz, 12H), 1.30 (t, J=7.3 Hz, 18H), 1.24 ppm (d, J=6.7 Hz, 3H); ^{13}C NMR (101 MHz, D_2O): δ = 165.4, 153.2, 142.3, 96.9 (d, J=6.4 Hz), 96.4, 89.1, 82.7 (d, J=9.1 Hz), 74.9, 71.6, 71.5, 70.9, 69.2, 68.4 (d, J=8.6 Hz), 64.3 (d, J=5.6 Hz), 47.3, 15.9, 8.8 ppm; ^{31}P NMR (162 MHz, D_2O): δ = −12.71 (d, J=20.3 Hz, P_α), −11.10 ppm (d, J=20.3 Hz, P_β); IR (KBr): $\tilde{\nu}$= 3418, 2926, 2981, 1655, 1545, 1463, 1400, 1238, 1125, 985 cm^{-1}; MS (HR-ESI): *m/z*: calcd for 548.0688 $[M-H]^-$; found: 548.0670.

Cytidine diphosphate-6-deoxy-β-D-gulose 33: According to GP B the reaction was conducted with **1c** (40.0 mg, 0.07 mmol) and 2,3,4-tri-*O*-acetyl-β-D-gulose-1-phosphate (**2hβ**; 50.0 mg, 0.11 mmol) (different from the general procedure with 1.5 instead of 2.0 equivalents of glycosyl-1-phosphate) within a reaction time of 24 h afforded a colorless solid (30.7 mg, 60%). $[\alpha]_{546}^{20}$= +9° (c=0.1, H_2O); ^{1}H NMR (400 MHz, D_2O): δ = 8.08 (d, J=7.7 Hz, 1H), 6.22 (d, J=7.7 Hz, 1H), 5.98 (d, J=4.0 Hz, 1H), 5.26 (dd, J=8.3, 8.3 Hz, 1H), 4.33–4.38 (m, 2H), 4.28–4.32 (m, 2H), 4.10–4.23 (m, 3H), 3.68 (dd, J=8.3, 3.3 Hz, 1H), 3.63–3.64 (m, 1H), 3.18 (q, J=7.3 Hz, 12H), 1.27 (t, J=7.3 Hz, 18H), 1.23 ppm (d, J=6.6 Hz, 3H); ^{13}C NMR (101 MHz, D_2O): δ = 163.8, 154.5, 142.9, 96.8 (d, J= 6.1 Hz), 96.5, 89.6, 83.4 (d, J=9.2 Hz), 74.7, 71.7, 71.3, 70.4, 69.7, 68.9 (d, J=8.4 Hz), 65.0 (d, J=5.4 Hz), 47.0, 15.4, 8.6 ppm; ^{31}P NMR (162 MHz, D_2O): δ = −12.68 (d, J=20.5 Hz, P_α), −11.09 ppm (d, J=20.5 Hz, P_β); IR (KBr): $\tilde{\nu}$ = 3425, 2927, 2976, 1654, 1554, 1456, 1404, 1243, 1131, 989 cm^{-1}; MS (HR-ESI): *m/z*: calcd for 548.0688 $[M-H]^-$; found: 548.1379.

Uridine diphosphate-α-D-glucose 34: According to GP B the reaction was conducted with 5-nitro-*cyclo*Sal-2′,3′-*O*-Ac-uridine-monophosphate (**1b**; 50.0 mg, 0.09 mmol) and **2aα** (97.0 mg, 0.18 mmol) within a reaction time of 48 h in DMF (5 mL) to afford a colorless solid (28.6 mg, 47%). $[\alpha]_{546}^{20}$ = +42 (c=0.3, H_2O); ^{1}H NMR (400 MHz, D_2O): δ = 7.96 (d, J= 8.2 Hz, 1H), 5.99–5.94 (m, 2H), 5.55 (dd, J=3.5, 7.2 Hz, 1H), 4.37–4.35 (m, 2H), 4.31–4.28 (m, 1H), 4.28–4.26 (m, 1H), 4.25–4.23 (m, 1H), 4.22–4.17 (m, 2H), 4.04 (d, J=2.8 Hz, 1H), 3.96 (dd, J=3.2, 11.0 Hz, 1H), 3.80–3.72 ppm (m, 2H); ^{13}C NMR (101 MHz, D_2O): δ = 166.2, 141.7, 102.7, 97.9, 88.3, 83.3 (d, J=8.1 Hz), 76.5, 75.2, 73.7, 73.6, 69.7, 69.5, 65.1, 60.8, 46.7, 8.2 ppm; ^{31}P NMR (162 MHz, D_2O): δ = −11.37 (d, J= 20.2 Hz), −13.97 ppm (d, J=20.2 Hz); IR (KBr): $\tilde{\nu}$ = 3006, 2363, 1933, 1697, 1421, 1072, 612 cm^{-1}; MS (HR-ESI): *m/z*: calcd 565.0405 $[M-H]^-$; found: 565.0476.

Uridine diphosphate-β-D-glucose 35: According to GP B the reaction was conducted with **1b** (50.0 mg, 0.09 mmol) and **2aβ** (97.0 mg, 0.18 mmol) within a reaction time of 48 h in DMF (5 mL) to afford a colorless solid (40.0 mg, 56%). $[\alpha]_{546}^{20}$ = −34 (c=0.3, H_2O); ^{1}H NMR (400 MHz, D_2O): δ = 7.96 (d, J=8.2 Hz, 1H), 5.99–5.96 (m, 2H), 5.01 (t, J=7.6 Hz, 1H), 4.38 (s, 2H), 4.30–4.21 (m, 3H), 3.91 (d, J=11.9 Hz, 1H), 3.71 (dd, J= 6.0, 12 Hz, 1H), 3.53 (dd, J=9.5, 18 Hz, 1H), 3.39 (dd, J=9.5, 14 Hz, 1H), 3.20 (q, J=7.3 Hz, 12H), 1.28 ppm (t, J=7.3 Hz, 18H); ^{13}C NMR (101 MHz, D_2O): δ = 166.2, 141.7, 102.7, 97.9, 88.3, 83.3 (d, J=8.1 Hz), 76.5, 75.2, 73.7, 73.6, 69.7, 69.5, 65.1, 60.8, 46.7, 8.2 ppm; ^{31}P NMR (162 MHz, D_2O): δ = −11.45 (d, J=13.5 Hz), −13.07 ppm (d, J= 13.5 Hz); IR (KBr): $\tilde{\nu}$ = 3254, 3158, 2935, 2361, 2190, 1906, 1680, 1229, 1070, 944, 813 cm^{-1}; MS (HR-ESI): *m/z*: calcd for 565.0478 $[M-H]^-$; found: 565.0479. The same NDP-sugar **35** was prepared using 5-methylsulfonyl-*cyclo*Sal-2′,3′-*O*-Ac-uridine-monophosphate (**9a**) as a crude product and after purification. Both reactions were carried out according to GP B: 1) Crude reaction product **9a** (1. 200 mg, 0.35 mmol) was reacted with **2aβ** (313 mg, 0.59 mmol) to afford **35** (93 mg, 34%); 2) *purified* **9a** (100 mg, 0.17 mmol) was reacted with **2aβ** (184 mg, 0.35 mmol) to afford **35** (118.5 mg, 87%).

Uridine diphosphate-*N*-acetyl-α-D-glucose 36: According to GP B the reaction was conducted with **1b** (50.0 g, 0.09 mmol) and 2-acetamido-3,4,6-tri-*O*-acetyl-2-deoxy-α-D-glucosyl-1-phosphate (**2dα**; 116 mg, 0.18 mmol) to afford a colorless solid (23.0 mg, 39%). $[\alpha]_{546}^{20}$ = +47° (c=0.3, H_2O); ^{1}H NMR (400 MHz, D_2O): δ = 7.95 (d, J=8.0 Hz, 1H), 5.99–5.95 (m, 2H), 5.52 (dd, J=3.0, 7.3 Hz, 1H), 4.39–4.35 (m, 2H), 4.30–4.26 (m, 2H), 4.25–4.21 (m, 1H), 4.21–4.16 (m, 2H), 3.99 (dd, J=3.0, 10.5 Hz, 1H), 3.96–3.88 (m, 1H), 3.88–3.77 (m, 2H), 3.55 (t, J=9.5 Hz, 1H), 2.08 ppm (s, 3H); ^{13}C NMR (101 MHz, D_2O): δ = 160.8, 141.6, 102.6, 88.5, 83.1 (d, J=7.4 Hz), 73.7, 72.9, 70.9, 69.6, 69.5, 57.6, 53.7 ppm; ^{31}P NMR (162 MHz, D_2O): δ = −11.41 (d, J=20.2 Hz), −13.10 ppm (d, J= 20.2 Hz); IR (KBr): $\tilde{\nu}$ = 2986, 2362, 2171, 1635, 1433, 1110 cm^{-1}; MS (HR-ESI): *m/z*: calcd for 606.0743 $[M-H]^-$; found: 606.0728.

Uridine diphosphate-*N*-acetyl-α-D-galactose 37: According to GP B the reaction was conducted with **1b** (50.0 mg, 0.09 mmol) and 2-acetamido-3,4,6-tri-*O*-acetyl-2-deoxy-α-D-galactosyl-1-phosphate (**2eα**; 116 mg, 0.18 mmol) to afford a colorless solid (37.0 mg, 61%). $[\alpha]_{546}^{20}$ = +23° (c= 0.14, H_2O); ^{1}H NMR (400 MHz, D_2O): δ = 7.96 (d, J=8.1 Hz, 1H), 5.99–5.96 (m, 2H), 5.54 (dd, J=3.4, 7.2 Hz, 1H), 4.39–4.36 (m, 2H), 4.30–4.26 (m, 2H), 4.25–4.23 (m, 1H), 4.22–4.18 (m, 2H), 4.05–4.04 (m, 1H), 3.97 (dd, J=3.0, 10.8 Hz, 1H), 3.79–3.73 (m, 2H), 2.09 ppm (s, 3H); ^{13}C NMR (101 MHz, D_2O): δ = 174.9, 141.7, 102.7, 94.7 (d, J=6.6 Hz), 88.5, 83.3 (d, J=8.8 Hz), 73.8, 72.1, 69.7, 68.4, 67.7, 64.9 (d, J=5.9 Hz), 61.1, 49.8 (d, J=8.1 Hz), 22.2 ppm; ^{31}P NMR (162 MHz, D_2O): δ = −11.25 (d, J=20.7 Hz), −12.97 ppm (d, J=20.7 Hz); IR (KBr): $\tilde{\nu}$ = 3203, 2985, 2706, 2497, 1654, 1437, 1047, 942, 838 cm^{-1}; MS (HR-ESI): *m/z*: calcd for 606.0743 $[M-H]^-$; found: 606.0745.

2′-Deoxyguanosine diphosphate-α-D-galactose 38: According to GP B the reaction was conducted with 5-nitro-*cyclo*Sal-N^2,3′-*O*-Ac-2′-deoxyguanosine-monophosphate (**1d**; 50.0 mg, 0.09 mmol) and 2,3,4,6-tetra-*O*-acetyl-α-D-galactosyl-1-phosphate (**2bα**; 91.5 mg, 0.17 mmol) to afford a colorless solid (19.8 mg, 29%). $[\alpha]_{546}^{20}$= +10° (c=0.1, H_2O); ^{1}H NMR (400 MHz, D_2O): δ = 8.08 (s, 1H), 6.29 (t, J=6.9 Hz, 1H), 5.61 (dd, J= 3.5, 7.1 Hz, 1H), 4.73 (dd, J=3.3, 6.3 Hz, 1H), 4.24–4.23 (m, 1H), 4.16–4.11 (m, 3H), 3.97 (d, J=3.0 Hz, 1H), 3.87 (dd, J=3.3, 10.3 Hz, 1H), 3.77 (dt, J=3.3, 10.3 Hz, 1H), 3.72–3.65 (m, 2H), 3.18 (q, J=7.3 Hz, 12H), 2.79 (ddd, J=14.0, 7.5, 6.4 Hz, 1H), 2.50 (ddd, J=13.9, 6.2, 3.3 Hz, 1H), 1.26 ppm (t, J=7.3 Hz, 18H); ^{13}C NMR (101 MHz, D_2O): δ = 95.8 (d, J=6.6 Hz), 85.6 (d, J=8.8 Hz), 83.6, 71.9, 71.3, 69.7, 69.0, 68.4 (d, J= 8.8 Hz), 65.5 (d, J=5.9 Hz), 61.0, 46.6, 38.5, 8.2 ppm; ^{31}P NMR (162 MHz, D_2O): δ = −11.92 (d, J=20.7 Hz); −13.62 ppm (d, J= 20.7 Hz); IR (KBr): $\tilde{\nu}$ = 3414, 2934, 2491, 1684, 1639, 1575, 1533, 1472, 1399, 1251, 1090, 931 cm^{-1}; MS (HR-ESI): *m/z*: calcd for 588.0750 $[M-H]^-$; found: 588.0756.

2′-Deoxyguanosine diphosphate-β-D-galactose 39: According to GP A the reaction was conducted with **1d** (145 mg, 0.26 mmol) and **2bβ** (172 mg, 0.33 mmol) to afford a colorless solid (45.1 mg, 22%). $[\alpha]_{546}^{20}$ = −13° (c= 0.3, H_2O); ^{1}H NMR (400 MHz, D_2O): δ = 8.08 (s, 1H), 6.31 (t, J= 7.1 Hz, 1H), 5.61 (dd, J=3.5, 7.1 Hz, 1H), 4.74 (dd, J=1.5, 6.3 Hz, 1H), 4.24–4.23 (m, 1H), 4.15–4.11 (m, 3H), 3.97 (d, J=2.8 Hz, 1H), 3.87 (dd, J=3.3, 10.3 Hz, 1H), 3.79–3.77 (m, 1H), 3.76–3.68 (m, 2H), 3.18 (q, J= 7.3 Hz, 12H), 2.81 (ddd, J=14.0, 7.5, 6.3 Hz, 1H), 2.49 (ddd, J=14, 6.0, 3.5 Hz, 1H), 1.27 ppm (t, J=7.3 Hz, 18H); ^{13}C NMR (101 MHz, D_2O): δ = 96.1 (d, J=5.4 Hz), 86.0 (d, J=9.2 Hz), 84.0, 72.2, 71.7, 69.6, 69.4, 68.7

(d, J=7.7 Hz), 65.1 (d, J=4.6 Hz), 61.4, 47.0, 38.8, 8.6 ppm; ^{31}P NMR (162 MHz, D_2O): δ = −11.39 (d, J=22.7 Hz); −13.21 ppm (d, J= 22.7 Hz); IR (KBr): $\tilde{\nu}$ = 3414, 2359, 2340, 1772, 1700, 1696, 1684, 1635, 1617, 1237, 1081 cm^{-1}; MS (HR-ESI): m/z: calcd for 588.0750 $[M-H]^-$; found: 588.0758.

2′-Deoxyguanosine diphosphate-β-D-glucose 40: According to GP B the reaction the general procedure was conducted with **1d** (50.0 mg, 0.09 mmol) and **2aβ** (91.0 mg, 0.17 mmol) to afford a colorless solid (23.4 mg, 34 %). $[\alpha]_{546}^{20}$ = −30° (c=0.2, H_2O); ^{1}H NMR (400 MHz, D_2O): δ = 8.10 (s, 1H), 6.34 (t, J=7.1 Hz, 1H), 5.03 (t, J=7.8 Hz, 1H), 4.30–4.25 (m, 1H), 4.18 (t, J=5.3 Hz, 2H), 3.93–3.89 (m, 1H), 3.70 (dd, J= 6.3, 12.5 Hz, 1H), 3.58–3.49 (m, 2H), 3.43–3.37 (m, 2H), 3.22 (q, J= 7.0 Hz, 12H), 2.89–2.80 (m, 1H), 2.49 (ddd, J=14, 6.0, 3.5 Hz, 1H), 1.30 ppm (t, J=7.3 Hz, 18H); ^{13}C NMR (101 MHz, D_2O): δ = 97.9 (d, J=5.9 Hz), 85.6 (d, J=9.5 Hz), 83.7, 76.5, 75.2, 73.7, 73.6, 71.5, 69.5, 66.5 (d, J=5.9 Hz), 60.8, 46.7, 38.5, 8.2 ppm; ^{31}P NMR (162 MHz, D_2O): δ = −11.24 (d, J=20.2 Hz); −13.8 ppm (d, J=20.2 Hz); IR (KBr): $\tilde{\nu}$ = 3203, 2985, 2706, 2497, 1654, 1437, 1047, 942, 838, 601, 504 cm^{-1}; MS (HR-ESI): m/z: calcd for 588.0750 $[M-H]^-$; found: 588.0750.

Adenosine diphosphate-α-D-glucose 41: According to GP B the reaction was conducted with 5-nitro-*cyclo*Sal-N^4-Ac-2′,3′-*O*-Ac-adenosine-monophosphate (**1e**; 168 mg, 0.28 mmol) and **2aα** (200 mg, 0.55 mmol) within a reaction time of 18 h in DMF (3 mL) to afford a colorless solid (170 mg, 78 %). $[\alpha]_{546}^{20}$ = 22° (c=0.1, H_2O); ^{1}H NMR (400 MHz, D_2O): δ = 8.51 (d, J=19.1 Hz, 1H), 8.23 (d, J=9.6 Hz, 1H), 6.13 (d, J=5.5 Hz, 1H), 5.63 (dd, J=4.1, 3.9 Hz, 1H), 4.51–4.57 (m, 1H), 4.41–4.43 (m, 2H), 4.16–4.27 (m, 3H), 3.75–3.80 (m, 3H), 3.45–3.50 (m, 2H), 3.21(q, J=7.3 Hz, 12H), 1.29 ppm (t, J=7.3 Hz, 18H); ^{13}C NMR (101 MHz, D_2O): δ = 154.5, 151.4, 148.8, 147.5, 95.6 (d, J=6.4 Hz), 87.1, 84.0 (d, J= 8.6 Hz), 74.4, 72.8, 71.7 (d,, J=8.6 Hz), 70.4, 69.2, 65.2 (d, J=5.5 Hz), 61.5,.46.7, 8.2 ppm; ^{31}P NMR (162 MHz, D_2O): δ = −12.88 (d, J= 17.2 Hz, P_α), −11.18 ppm (d, J=17.2 Hz, P_β); IR (KBr): $\tilde{\nu}$ = 3421, 2679, 2492, 1686, 1654, 1608, 1477, 1243, 1081, 925, 815, 719, 503 cm^{-1}; MS (HR-ESI): m/z: calcd for 588.0750 $[M-H]^-$; found: 588.0747.

Adenosine diphosphate-β-D-glucose 42: According to GP B the reaction was conducted with **1e** (60.0 mg, 0.10 mmol) and **2aβ** (150 mg, 0.35 mmol) (different from the general procedure with 3.5 instead of 2.0 equivalents of glycosyl-1-phosphate) within a reaction time of 18 h in DMF (2 mL) to afford a colorless solid (65.0 mg, 88 %). $[\alpha]_{546}^{20}$ = −16° (c=0.1, H_2O); ^{1}H NMR (400 MHz, D_2O): δ = 8.57 (d, J=18.9 Hz, 1H), 8.28 (d, J=9.8 Hz, 1H), 6.14 (d, J=5.8 Hz, 1H), 5.01 (dd, J=7.5, 7.5 Hz, 1H), 4.52 (d, J=5.0 Hz, 1H), 4.40 (s, 1H), 4.22–4.25 (m, 2H), 3.88 (dd, J=12.6, 10.5 Hz, 1H), 3.67 (dd, J=12.6, 12.3 Hz, 1H), 3.46–3.49 (m, 3H), 3.34–3.37 (m, 2H), 3.18(q, J=7.3 Hz, 12H), 1.27 ppm (t, J=7.3 Hz, 18H); ^{13}C NMR (101 MHz, D_2O): δ = 154.5, 151.4, 148.8, 147.5, 97.9 (d, J=6.4 Hz), 87.0, 84.0 (d, J=8.6 Hz), 76.5, 75.2, 74.4, 73.6, 70.4 (d, J= 8.6 Hz), 69.4, 65.2 (d, J=5.5 Hz), 61.5, 46.6, 8.2 ppm; ^{31}P NMR (162 MHz, D_2O): δ = −10.56 (d, J=16.9 Hz, P_α), −11.75 ppm (d, J= 16.9 Hz, P_β); IR (KBr): $\tilde{\nu}$ = 3408, 2679, 2492, 1654, 1607, 1478, 1422, 1242, 1081, 925, 816, 719, 504 cm^{-1}; MS (HR-ESI): m/z: calcd for 588.0750 $[M-H]^-$; found: 588.0734.

Adenosine diphosphate-β-D-galactose 43: According to GP B the reaction was conducted with 5-nitro-*cyclo*Sal-N^4-Ac-2′,3′-*O*-Ac-adenosine-monophosphate (**1e**; 84 mg, 0.14 mmol) and **2bβ** (141 mg, 0.27 mmol) within a reaction time of 40 h in DMF (2 mL) to afford a colorless solid (82.4 mg, 74 %). $[\alpha]_{546}^{20}$ = −12° (c=0.1, H_2O); ^{1}H NMR (400 MHz, D_2O): δ = 8.51 (s, 1H), 8.24 (s, 1H), 6.15 (d, J=6.1 Hz, 1H), 4.97 (m, 1H), 4.56 (dd, J=5.0, 3.4 Hz, 1H), 4.42 (m, 1H), 4.22–4.28 (m, 2H), 3.91 (d, J=2.9 Hz, 1H), 3.61–3.77 (m, 2H), 3.75–3.80 (m, 4H), 3.18(q, J=7.3 Hz, 12H), 1.27 ppm (t, J=7.3 Hz, 18H); ^{13}C NMR (101 MHz, D_2O): δ = 156.7, 153.1, 146.2, 145.5, 95.6 (d, J=6.2 Hz), 89.3, 82.6 (d, J=7.3 Hz), 78.2, 76.4, 75.5, 72.4, 70.2 (d, J=7.3 Hz), 67.1, 64.9 (d, J=5.5 Hz), 59.2, 44.8, 7.9 ppm; ^{31}P NMR (162 MHz, D_2O): δ = −11.22 (d, J=20.8 Hz, P_α), −12.91 (d, J=20.8 Hz, P_β); IR (KBr): $\tilde{\nu}$ = 3195, 2106, 1651, 1471, 1234, 1047, 935, 826, 505 cm^{-1}; MS (HR-ESI): m/z: calcd for 588.0750 $[M-H]^-$; found: 588.0745.

Adenosine diphosphate-α-D-mannose 44: According to GP B the reaction was conducted with **1e** (92.0 mg, 0.15 mmol) and **2cα** (160 mg, 0.30 mmol) within a reaction time of 19 h in DMF (2.5 mL) to afford a colorless solid (78.0 mg, 87 %). $[\alpha]_{546}^{20}$ = +32° (c=0.1, H_2O); ^{1}H NMR (400 MHz, D_2O): δ = 8.54 (d, J=19.1 Hz, 1H), 8.28 (d, J=9.6 Hz, 1H), 6.16 (d, J=5.9 Hz, 1H), 5.54 (d, J=6.8 Hz, 1H), 4.55 (dd, J=3.7, 5.0 Hz, 1H), 4.41–4.43 (m, 1H), 4.25 (dd, J=3.1, 4.7 Hz, 2H), 4.06–4.07 (m, 1H), 3.94 (dd, J=34, 9.8 Hz, 1H), 3.87–3.90 (m, 2H), 3.7–3.80 (m, 3H), 3.21(q, J=7.3 Hz, 12H), 1.29 ppm (t, J=7.3 Hz, 18H); ^{13}C NMR (101 MHz, D_2O): δ = 155.6, 152.8, 106.6, 96.5 (d, J=5.5 Hz), 86.9, 83.9 (d, J= 9.1 Hz), 74.3, 73.7, 70.4 (d,, J=5.5 Hz), 70.3, 69.9, 66.5, 65.3 (d, J= 5.4 Hz), 60.8, 46.7, 8.2 ppm; ^{31}P NMR (162 MHz, D_2O): δ = −13.76 (d, J=13.4 Hz, P_α), −11.40 ppm (d, J=13.4 Hz, P_β); IR (KBr): $\tilde{\nu}$ = 3398, 2938, 2679, 2492, 1686, 1508, 1477, 1421, 1242, 1083, 924, 818, 720, 504 cm^{-1}; MS (HR-ESI): m/z: calcd for 589.0822 $[M-H]^-$; found: 589.0839.

d4T-diphosphate-α-D-glucose 45: According to GP B the reaction was conducted with 5-nitro-*cyclo*Sal-2′,3′-dideoxy-2′,3′-didehydrothymidine monophosphate (**13**; 80.0 mg, 0.18 mmol) and **2aα** (95.0 mg, 0.37 mmol) within a reaction time of 18 h in DMF (2 mL) to afford a colorless solid (78.0 mg, 78 %). $[\alpha]_{546}^{20}$ = −12° (c=0.1, H_2O); ^{1}H NMR (400 MHz, D_2O): δ = 7.62 (d, J=1.2 Hz, 1H), 6.98 (td, J=3.3, 1.7 Hz, 1H), 6.53 (td, J= 6.2, 1.7 Hz, 1H), 5.97 (m, 1H), 5.58 (dd, J=7.5, 3.5, 1H), 5.12 (d, J= 1.3 Hz, 1H), 4.12–4.21 (m, 2H), 3.78–3.93 (m, 4H), 3.44–3.54 (m, 2H), 3.22 (q, J=7.3 Hz, 12H), 1.30 ppm (t, J=7.3 Hz, 18H); ^{13}C NMR (101 MHz, D_2O): δ = 138.2, 134.3, 125.3, 111.6, 95.5 (d, J=6.7 Hz), 90.0, 85.9 (d, J=8.8 Hz), 72.9 (d J=14.1 Hz), 71.7 (d J=8.4 Hz), 69.3, 66.5 (d, J=6.1 Hz), 60.4, 54.6, 11.5 ppm; ^{31}P NMR (162 MHz, D_2O): δ = −13.00 (d, J=20.6 Hz, P_α), −11.30 ppm (d, J=20.6 Hz, P_β). IR (KBr): $\tilde{\nu}$ = 3232, 2100, 1686, 1471, 1230, 1043, 914, 737, 505 cm^{-1}; MS (HR-ESI): m/z: calcd for 545.0579 $[M-H]^-$; found: 545.0570.

Acknowledgements

This work has been accomplished in the network of the SFB 470A8. The authors are grateful for financial support of the Deutsche Forschungsgemeinschaft.

[1] W. Watkins, *Carbohydr. Res.* **1986**, *149*, 1–12.
[2] P. M. Coutinho, E. Deleury, G. J. Davies, G. Henrissat, *J. Mol. Biol.* **2003**, *328*, 307–317.
[3] K. Ohtsubo, J. D. Marth, *Cell* **2006**, *126*, 855–867.
[4] E. F. Neufeld, W. Z. Hassid, *Adv. Carbohydr. Chem.* **1963**, *18*, 309–356.
[5] N. K. Kochetkov, V. N. Shibaev, *Adv. Carbohydr. Chem. Biochem.* **1973**, *28*, 307–399.
[6] M. Skurnik, L. Zhang, *APMIS* **1996**, *104*, 849–872.
[7] S. Roseman, J. J. Distler, J. G. Moffatt, H. G. Khorana, *J. Am. Chem. Soc.* **1961**, *83*, 649–659.
[8] J. G. Moffatt, H. G. Khorana, *J. Am. Chem. Soc.* **1958**, *80*, 3756–3761.
[9] E. S. Simon, S. Grabowski, G. M. Whitesides, *J. Org. Chem.* **1990**, *55*, 1834–1841.
[10] V. Wittmann, C.-H. Wong, *J. Org. Chem.* **1997**, *62*, 2144–2147.
[11] R. E. Campbell, M. E. Tanner, *J. Org. Chem.* **1999**, *64*, 9487–9492.
[12] A. Schäfer, J. Thiem, *J. Org. Chem.* **2000**, *65*, 24–29.
[13] Q. Zhang, H.-W. Lui, *J. Am. Chem. Soc.* **2000**, *122*, 9065–9070.
[14] R. R. Schmidt, B. Wegmann, K.-H. Jung, *Liebigs Ann. Chem.* **1991**, 121–124.
[15] S. Zamyatina, C. Gronow, M. Oertelt, H. Puchberger, P. Brade, P. Kosma, *Angew. Chem.* **2000**, *112*, 4322–4325; *Angew. Chem. Int. Ed.* **2000**, *39*, 4150–4153.
[16] H. Gold, P. van Delft, N. Meeuwenoord, J. D. C. Codée, D. V. Filippov, G. Eggink, H. S. Overkleeft, G. A. van der Marel, *J. Org. Chem.* **2008**, *73*, 9458–9460.
[17] M. Arlt, O. Hindsgaul, *J. Org. Chem.* **1995**, *60*, 14–15.
[18] S. C. Timmons, D. L. Jakeman, *Org. Lett.* **2007**, *9*, 1227–1230.

[19] P. Peltier, R. Daniellou, C. Nugier-Chauvin, V. Ferrières, *Org. Lett.* **2007**, *9*, 5227–5230.
[20] R. Stiller, J. Thiem, *Liebigs Ann. Chem.* **1992**, 467–471.
[21] U. Gambert, J. Thiem, *Top. Curr. Chem.* **1997**, *186*, 21–43.
[22] S. Wendicke, S. Warnecke, C. Meier, *Angew. Chem.* **2008**, *120*, 1523–1525; *Angew. Chem. Int. Ed.* **2008**, *47*, 1500–1502.
[23] C. Meier, *Eur. J. Org. Chem.* **2006**, 1081–1102.
[24] C. Meier, M. Lorey, E. De Clercq, J. Balzarini, *J. Med. Chem.* **1998**, *41*, 1417–1427.
[25] C. Meier, T. Knispel, V. E. Marquez, M. A. Siddiqui, E. De Clercq, J. Balzarini, *J. Med. Chem.* **1999**, *42*, 1615–1624.
[26] C. Meier, A. Lomp, A. Meerbach, P. Wutzler, *J. Med. Chem.* **2002**, *45*, 5157–1572.
[27] C. Meier, E. De Clercq, J. Balzarini, *Eur. J. Org. Chem.* **1998**, 837–846.
[28] K. K. Ogilvie, D. J. Iwacha, *Tetrahedron Lett.* **1973**, *14*, 317–319.
[29] B. R. Travis, M. Sivakumar, G. O. Hollist, B. Borhan, *Org. Lett.* **2003**, *5*, 1031–1034.
[30] a) J. P. Horwitz, J. Chua, M. A. Da Rooge, M. Noel, I. L. Klundt, *J. Org. Chem.* **1966**, *31*, 205–211; b) T.-S. Lin, R. F. Schinazi, W. H. Prusoff, *Biochem. Pharmacol.* **1987**, *36*, 2713–2718.
[31] First we tried an earlier report (L. M. Lerner, *Carbohydr. Res.* **1975**, *44*, 116–120) for the synthesis of 6-deoxy-D-gulose but we failed.
[32] a) K. Bennis, P. Calinaud, J. Gelas, M. Ghobsi, *Carbohydr. Res.* **1994**, *264*, 33–44; b) T. K. M. Shing, J. G. Gillhouley, *Tetrahedron* **1994**, *50*, 8685–8698; c) L. M. Lerner, B. D. Kohn, P. Kohn, *J. Org. Chem.* **1968**, *33*, 1780–1783.
[33] a) J. Schmidlin, A. Wettstein, *Helv. Chim. Acta* **1963**, *46*, 2799–2810; b) E. J. Corey, A. Venkateswarlu, *J. Am. Chem. Soc.* **1972**, *94*, 6190–6191; c) E. J. Corey, A. Venkateswarlu, *J. Am. Chem. Soc.* **1972**, *94*, 6190–6191.
[34] G. H. Veeneman, L. J. F. Gomes, J. H. Van Boom, *Tetrahedron* **1989**, *45*, 7433–7448.
[35] G. Excoffier, D. Gagnaire, J.-P. Utille, *Carbohydr. Res.* **1975**, *39*, 368–373.
[36] M. M. Sim, H. Kondo, C.-H. Wong, *J. Am. Chem. Soc.* **1993**, *115*, 2260–2267.
[37] G. Baisch, R. Öhrlein, *Bioorg. Med. Chem.* **1997**, *5*, 383–391.

Received: March 3, 2009
Published online: June 30, 2009

