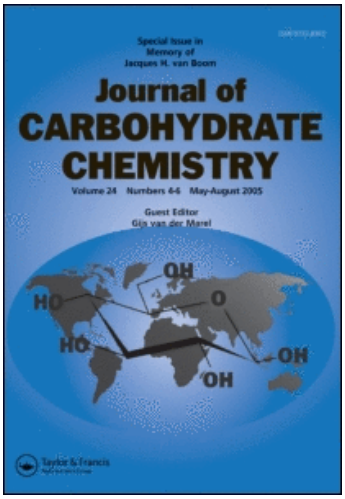

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On the Synthesis of Aminoglycosides of Cardioactive Steroids: A Study Directed Towards β- Selective Glycosylations of 3-Aminodigitoxose with Digitoxigenin Analogues

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ON THE SYNTHESIS OF AMINOGLYCOSIDES OF CARDIOACTIVE STEROIDS: A STUDY DIRECTED TOWARDS β- SELECTIVE GLYCOSYLATIONS OF 3-AMINODIGITOXOSE WITH DIGITOXIGENIN ANALOGUES

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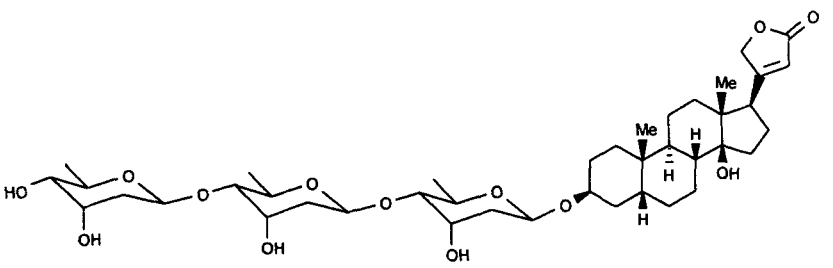
ABSTRACT

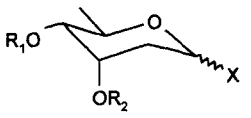
Carbamate derivatives of 3-aminodigitoxose (D-ristosamine) were prepared, with the purpose of synthesizing 3-amino-β-digitoxosyl derivatives of cardioactive steroids. A 1,3 participation procedure, used under acid or mercury salt catalysis, and the imidate procedure were investigated. A careful fine tuning of the glycosylation conditions was necessary in order to obtain significant β-D-stereoselectivity, which proved to be mainly dependent on the polarity of the solvent and the relative reactivity of the sugar and the nucleophile.

INTRODUCTION

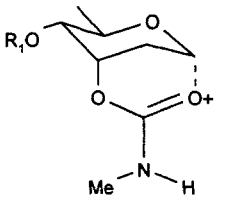
Stereoselective glycosylation with glycosyl donors not possessing a participating group at C-2[2] and, in particular, with 2-deoxy sugars[3] continues to be a challenging task in carbohydrate chemistry. Efficient and stereoselective methods are especially needed for the synthesis of pharmacologically important compounds, such as cardiac glycosides. For example, the lack of functionality at the carbohydrate C-2 of digitoxin



DIGITOXIN I



IIa X = OH, R_1 = *p*MBz, R_2= CONHMe
IIb X = OH, R_1 = Bn, R_2 = CONHMe
IIIa X = OH, R_1 = *p*NBz, R_2 = *p*MBz
IIIb X = OH, R_1 = R_2 = *p*MBz
IIIc X = SEt, R_1 = *p*NBz, R_2 = *p*MBz



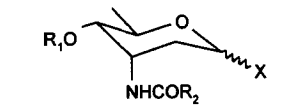
1

*p*NBz = *p*-nitrobenzoyl
*p*MBz = *p*-methoxybenzoyl
Bn = benzyl

Figure 1

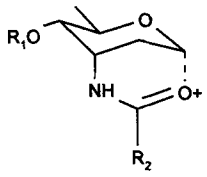
(I, Figure 1) makes the achievement of the required β-D-stereoselectivity of the coupling reaction difficult.[4]

Extensive research towards the synthesis of more potent digitalis analogues had led our group to the preparation of many new cardioactive steroids, the β-glucosides of which showed better pharmacological properties and less toxicity than the natural digitalis glycosides.[5] However, since β-glucosides do not show acceptable distribution characteristics, the natural digitoxoside chain had to be attached to these steroids. The development of a 1,3 participation methodology for the stereoselective β-coupling of digitoxose derivatives was instrumental in the successful synthesis of digitoxin.[6] This methodology involved the assistance, at the anomeric center, of a urethane or a *p*-methoxybenzoyl group in the axial C-3 position of digitoxose (compounds **II** and **III**,



2a X = OH, R_1 = Bz, R_2 = CF_3
2b X = SEt, R_1 = Bz, R_2 = CF_3
3a X = OH, R_1 = *p*NBz, R_2 = OBn
3b X = SEt, R_1 = *p*NBz, R_2 = OBn

*p*NBz = *p*-nitrobenzoyl
*p*MBz = *p*-methoxybenzoyl
Bn = benzyl



4

Figure 2

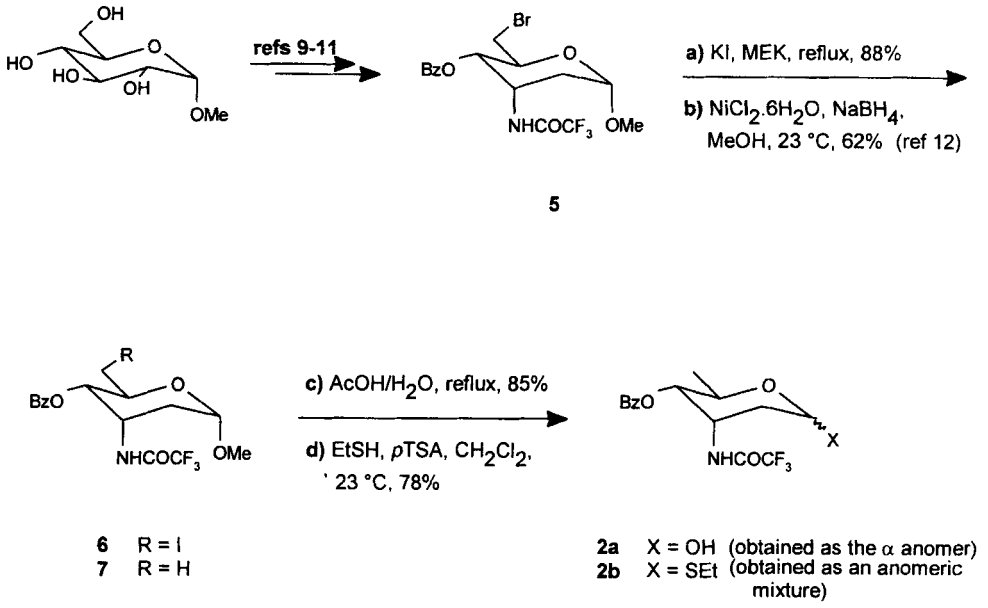
Figure 1), which favoured the formation of the desired β-glycoside. The high β-stereoselectivity was explained by the intermediacy of bridged species **1** (Figure 1), in which the positive charge of the oxonium ion is delocalized through the carbamate system of donors **II**.[6,7] In addition to the synthesis of digitoxin, the application of this method led to the successful coupling of a preformed trisdigitoxoside chain with a steroidal precursor of digitoxigenin.[8]

In order to prepare more effective cardioactive compounds that were unable to cross the blood brain barrier, we embarked on the synthesis of aminodigitoxose (D-ristosamine) derivatives (Figure 2), to be coupled with the steroids previously synthesized by our group.[5] For that purpose, it had to be established whether an interchange of the N- and O- atoms would still permit a 1,3 participation (**4**, Figure 2) similar to the one depicted in **1** (Figure 1).

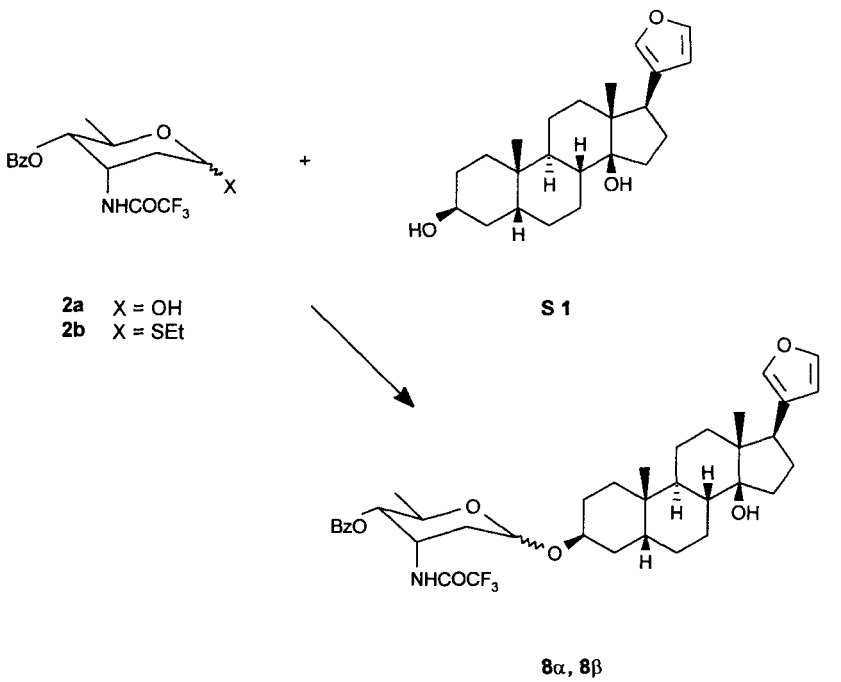
The synthesis and glycosylation reactions of two series of aminodigitoxose derivatives (compounds **2a-b**, **3a-b**) with three different steroids are described in this paper.

DISCUSSION

The first series of glycosylation reactions was performed on the trifluoroacetamido derivatives **2a-b**, since the results could more readily be compared with literature data.[7] Compounds **2a-b** were synthesized from methyl α-D-glucopyranoside using standard procedures[9-12] (Scheme 1). As glycosyl acceptor, the furyl derivative of digitoxigenin **S-1** (Scheme 2), an important intermediate in the preparation of digitoxigenin analogues,[5,13] was used.



Scheme 1



Scheme 2

Table 1

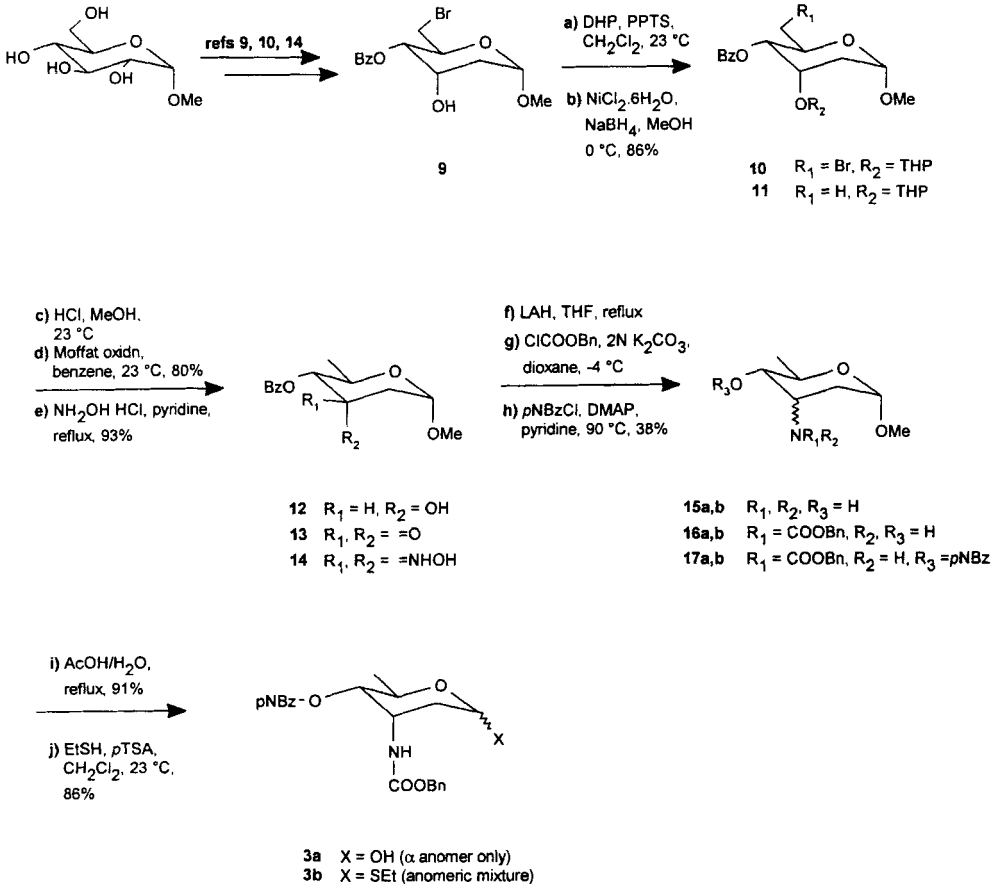
entry	glycosyl donor	glycosyl acceptor	reaction conditions	product ratio	conversion
1	**2a** (2 eq)	**S-1** (1 eq)	*p*TSA (0.1 eq), benzene / CH_2Cl_2 = 3/1, 23 °C	**8α/8β** = 4/1	35%
2	**2b** (2 eq)	**S-1** (1 eq)	$CdCO_3$ (2 eq), $HgCl_2$ (2 eq), CH_2Cl_2, DMF (1 drop), 23 °C	**8α/8β** = 1/1.14	30%

Unexpectedly, a large preponderance of the α anomer was observed in the case of **2a** (entry 1, Table 1), while only a slight excess of the β product was obtained when the thioglycosides **2b** were used (entry 2, Table 1).

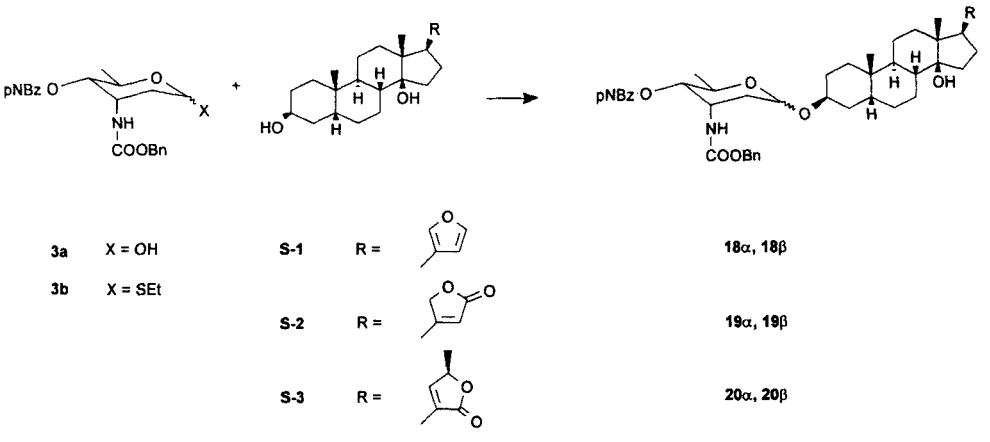
In these first reactions, the electron withdrawing trifluoroacetyl group was believed to not be effective in stabilizing the oxonium intermediate *via* the expected 1,3 participation of the carbamate group. Thus, the stereochemical outcome of the reaction was probably determined by a series of anomerization equilibria,[2] in which relative reactivity of the starting glycosyl donors, relative anomerization rates and strength of the catalyst would be the major factors. The reactive intermediate would then favour the formation of the more stable α product. In the case of glycosyl donors **2b**, the presence of insoluble catalysts and/or the less acidic medium could be responsible for the shift of the anomeric equilibria towards the formation of more β product.

Since the benzyloxycarbonyl group could be considered electronically more suitable for the desired 1,3 participation, compounds **3a-b** were synthesized (Scheme 3), starting from the bromo ester **9**, easily obtained using known procedures.[9,10,14] Formation of the 2,6-dideoxy derivative **12** was then accomplished *via* protection of **9** at C-3, reduction with nickel boride and deprotection. Oxidation of the axial C-3 hydroxyl group, followed by oxime formation and reduction with lithium aluminum hydride, yielded the aminoalcohols **15a,b**.

The crude mixture of *ribo/arabino* isomers was protected at the amino function with the benzyloxycarbonyl group; esterification at C-4 then afforded the two glycosides **17a,b**, isomeric at C-3, from which the desired *ribo* derivative **17a** was isolated. Hydrolysis of the acetal afforded the glycosyl donor **3a** (only the α anomer), while treatment of **3a** with EtSH and *p*TSA gave the thioglycosides **3b**.



Scheme 3



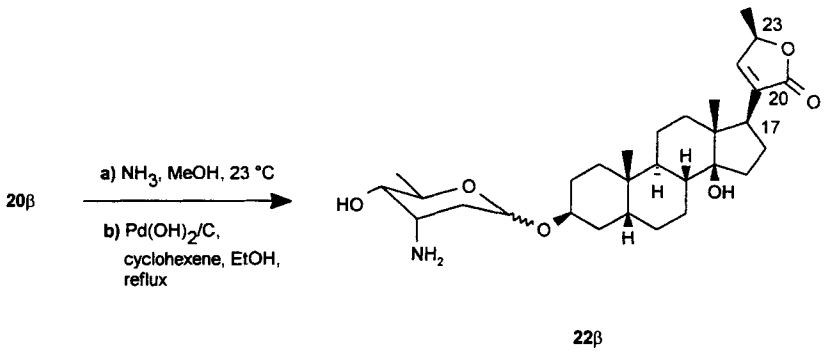
Scheme 4

Table 2

entry	glycosyl donor	glycosyl acceptor	reaction conditions	product ratio	conversion
1	**3a** (1 eq)	**S-1** (1 eq)	*p*TSA (0.2 eq), benzene /CH_2Cl_2 = 3/1, 23 °C, 3 h	**18α/18β** = 6/1	39%
2	**3b** (1.1eq)	**S-1** (1eq)	$HgCl_2$ (1.1 eq), $CdCO_3$ (2 eq), CH_2Cl_2, DMF (1 drop), 23 °C, 5 h	**18α/18β** = 1/1	26%
3	**3a** (1eq)	**S-2** (1eq)	*p*TSA (0.2 eq), benzene /CH_2Cl_2 = 3/1, 23 °C, 5 h	**19α/19β** = 2.3/1	40%
4	**3a** (1eq)	**S-1** (1eq)	*p*TSA (0.2 eq), mol. sieves, benzene, 23 °C, 2 h	**18α/18β** = 1/1.4	59%
5	**3b** (1eq)	**S-2** (1eq)	$HgCl_2$ (1.1 eq), $CdCO_3$ (2 eq), benzene, DMF (1 drop), 23 °C, 48 h	**19α/19β** = 1/1.2	35%
6	**3a** (1eq)	**S-3** (1eq)	*p*TSA (0.2 eq), mol. sieves, benzene, 23 °C, 30 h	**20α/20β** = 1/1.7	44%

The glycosylation reactions of these donors were performed on three steroids: **S-1**, digitoxigenin **S-2**, and (23-*R*)-23-methylisodigitoxigenin **S-3**,[5] and gave the glycosylated products shown in Scheme 4. The reaction of **3a** with steroid **S-1** under acid catalysis again gave large amounts of the α anomer (Table 2), as did the reaction with digitoxigenin **S-2**, although the α/β ratio was smaller. With **S-1** and the thioglycosyl donors **3b**, the two glycosylated products were recovered in equal amounts.

Indeed, the above results were opposite to those previously obtained[6] with the *N*-methylaminocarbonyl derivatives of digitoxose (**II**, Figure 1). Therefore, as the polarity of the reaction medium can influence the outcome of glycosylation reactions,

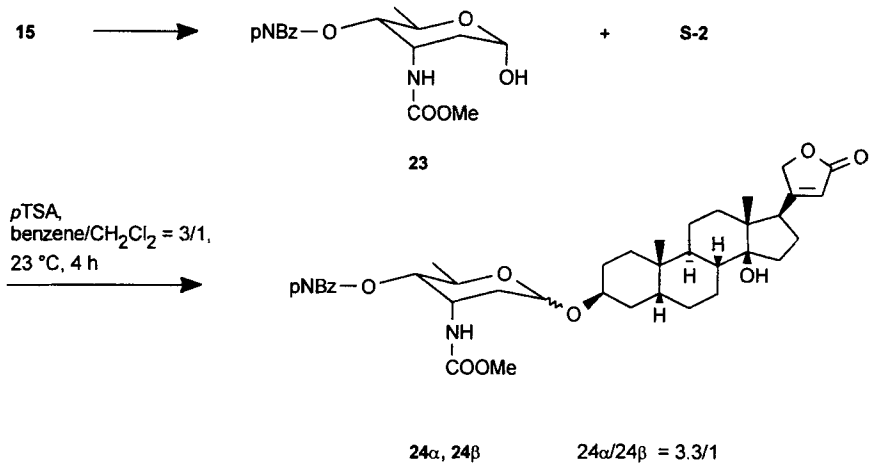


Scheme 5

we resolved to change the medium from benzene/CH_2Cl_2 to pure benzene, hoping that lowering the polarity of the solvent could help to increase the amount of the β product. Therefore, the glycosylations were repeated in dry benzene, again under acid and mercury salt catalysis. This time, the reaction of **3a** with **S-1** and *p*TSA as catalyst resulted in an inversion of the anomeric ratio of the products (entry 4, Table 2) in favour of the β anomer. A comparison of entries 1 and 4 (Table 2), in which the same starting materials and reagents were used, shows that changing the solvent from benzene/CH_2Cl_2 (3:1) to benzene only caused a remarkable change in the anomeric ratio of the products from α/β = 6/1 to 1/1.4.

Based on these encouraging results, the glycosylation was performed using the biologically more promising (23-*R*)-23-methylisodigitoxigenin **S-3**.[5] An anomeric product mixture with the best β stereoselectivity so far, **20α/20β** = 1/1.7 (entry 6, Table 2) was obtained. The desired anomer **20β** was then easily deprotected (Scheme 5) by ammonolysis of the ester at C-4; then, hydrogenolysis of the benzyloxycarbonyl group with $Pd(OH)_2/C$ and cyclohexene[15] gave the aminoalcohol **22β**. Biological testing of **22β** to establish its pharmacological properties is in progress.

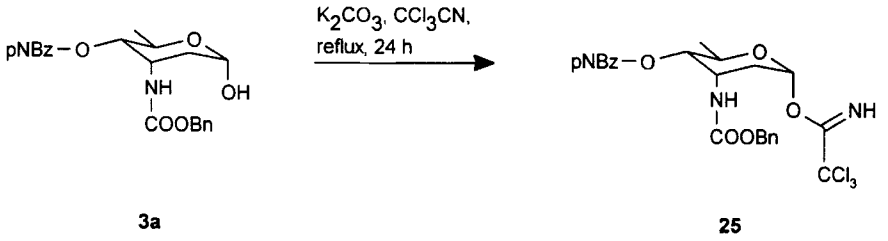
The results of the glycosylation reactions performed in benzene thus suggested that the influence of the solvent was of no less importance than that of the other parameters involved in the reaction. This was thought to be not in disagreement with the previously proposed 1,3 participation hypothesis, which we still considered as a reasonable explanation for the (modest) stereoselectivity observed; however, further experiments proved otherwise. It was supposed that, in our previous conditions, the carbonyl group of the carbamate was somehow prevented from forming a cyclic oxonium intermediate, perhaps as a result of an interaction between the protecting



Scheme 6

groups at C-3 and C-4. However, a change in the protecting group at C-3, that is, from benzyl to methyl carbamate,[16] led to no improvement, yielding an α/β anomeric ratio of 3.3/1 (Scheme 6).

At this point, we interpreted this result as an indication that the occurrence of a 1,3 anchimeric assistance was highly doubtful in our cases. What then accounts for the marked difference between the behaviour of carbamate derivatives **II** (Figure 1), which react with a pronounced β-D- stereoselectivity, and that of compounds **2a-b**, **3a-b** and **23**? Models show that, for the formation of the assumed 1,3-bridged intermediate **1** (Figure 1) from carbamates **II**, the amino group can rotate around the N-C=O bond so as to maintain full conjugation throughout the system. In contrast, the amino group in compounds **2a-b**, **3a-b** and **23** cannot maintain conjugation with the carbonyl group while the delocalized amide stabilizes the oxonium ion by π-donation. It is possible then, that a low polarity of the solvent contributes, together with other factors such as reactivity of the glycosyl donor, to steering the reaction towards the formation of more β product. The extent of this shift, from a large preponderance of the α anomer (entry 1, Table 2) to a favoured β product (entry 4, Table 2), is a clear indication of the extremely delicate balance between the parameters involved in these glycosylation reactions. It is also possible that, in the earlier studies,[6] particular steric requirements presented by the larger nucleophiles (e.g., the mono- and disaccharide of digitoxigenin) contributed to the large β stereoselectivity, while these requirements would not apply to our cases. Recently, it has been noted[17] that small modifications in the type of



3a 25

Scheme 7

substituents in *ribo* derivatives can strongly affect their conformational equilibria. This would introduce additional steric and electronic factors to an already complex reaction pattern. However, we did not have sufficient data to establish whether or not such conformational changes take place in our experiments.

Another viable option was to change the leaving group at the anomeric center, in order to render the glycosylation reaction more S_N2 in character by controlling the degree of activation of the leaving group. Acetimidate derivatives are known to be suitable for this type of activation and to give mainly inversion products, especially in the case of glycosyl donors having non-participating substituents.[2b,18] Interesting results have been obtained by R. R. Schmidt et al.[19] in the glycosylation of various accepting alcohols, including cholesterol. This prompted us to synthesize the trichloroacetimidyl derivative **25** (Scheme 7) and to test it under a variety of activating conditions. Imidate **25** was reacted with digitoxigenin using various Lewis acids as catalysts. Best results were obtained with $MgCl_2$ in dry CH_2Cl_2 at room temperature, which gave an α/β = 1/1.6 ratio. The reactions were repeated using steroid **S-3** as the nucleophile (Table 3), but, unfortunately, both with $BF_3.Et_2O$ and with $SnCl_4$, the α anomer was again preferentially formed. No other catalysts were tried, since the trend for the reactions with **S-3** seemed to be too unfavourable.

These latter results seemed also to point out that the reactivity of the different steroids played no minor role in determining the stereochemical outcome of these glycosylation reactions. The reason for the variation in reactivity of these closely related steroids still has to be established; however, their effect on all the coupling procedures here employed undoubtedly adds to that of the other factors discussed above.

In summary, the reactions of the 3-amino digitoxose derivatives displayed a significantly different behaviour compared to that of the digitoxose derivatives of

Table 3

entry	glycosyl donor	glycosyl acceptor	reaction conditions	product ratio
1	**25**	**S-2**	$BF_3.Et_2O$, CH_2Cl_2, -20 °C	**19α/19β** = 1.1/1
2	**25**	**S-2**	$SnCl_4$, CH_2Cl_2, -20 °C	**19α/19β** = 1/1.2
3	**25**	**S-2**	$MgCl_2$, CH_2Cl_2, 23 °C	**19α/19β** = 1/1.6
4	**25**	**S-2**	$ZnCl_2$, $ClCH_2CH_2Cl$, 23 °C	**19α/19β** = 1/1
5	**25**	**S-3**	$BF_3.Et_2O$, CH_2Cl_2, -20 °C	**20α/20β** = 1.4/1
6	**25**	**S-3**	$SnCl_4$, CH_2Cl_2, -20 °C	**only α**

earlier work,[6] due to different geometric requirements. A simple control of the activation of the leaving group did not lead to a satisfactory preferential formation of one anomer and indicated the importance of finding a proper balance between the reactivity of the sugar and that of the nucleophile. Only a very careful choice of catalyst and solvent resulted, in some cases, in a dramatic shift of the stereoselectivity and allowed the synthesis of the desired aminoglycoside **22β**. It is clear that the outcome of these reactions is dependent on complex interactions between the starting materials, the solvent, and the catalyst. Additional variations in the conformational equilibria and in the reactivity of the glycosyl donor, due to the absence of a functionality at C-2, could also be considered. A better understanding of the relationships between all these parameters is needed, if more reliable and predictable coupling methods are to be found.

EXPERIMENTAL

General. ^1H NMR spectra were recorded on a Varian XL200 spectrometer, using TMS as internal reference. The chemical shifts are reported in δ values from TMS, the coupling constants (J) are measured in Hz. IR spectra were recorded on a Perkin Elmer 727B or 598 spectrophotometers: frequencies (ν) are reported in cm^{-1}. The solvents used in NMR and IR spectra are specified in each case. High resolution mass spectra (HRMS), positive and negative FAB mass spectra were recorded on a Kratos MS50, at 70 eV and source temperature of 120 °C, at the Mass Spectrometry

Lab, University of New Brunswick, or on an AEI MS50 at the Mass Spectrometry lab, University of Alberta. Melting points, mp, were taken on a Kofler hot stage apparatus and are uncorrected. Analytical (TLC) and preparative thin-layer chromatography (PTLC) were carried out on 0.25, 1.0 and 2.0 mm x 20 cm x 20 cm E. Merck precoated silica gel plates (60 F254). Materials were detected using UV light and/or sulfuric acid in water/heat as developing agent. Flash chromatography was performed using silica gel 60 (230-400 mesh). All reactions were carried out under nitrogen or argon atmosphere, using dry solvents, freshly distilled under nitrogen.

Methyl 4-*O*-Benzoyl-2,3,6-trideoxy-6-iodo-3-trifluoroacetamido-α-D-*ribo*-hexopyranoside (6). A solution of compound **5**[7] (18.1 g, 0.041 mol) in methyl ethyl ketone (1.0 L) was refluxed in the presence of KI (21.7 g, 0.131 mol), until disappearance of starting material (^{1}H NMR). The mixture was filtered over Celite and the solvents were evaporated. Crystallization of the crude material from CH_2Cl_2/hexane afforded the 6-iodo derivative **6** (17.7 g, 88.6%); mp 48-50 °C. ^{1}H NMR ($CDCl_3$, δ ppm): 2.31-2.00 (m, 2H, H-2); 3.24 (dd, 1H, $J_{5,6a}$ = 8.1Hz, J_{gem} = 10.9Hz, H-6a); 3.45 (dd, 1H, $J_{5,6b}$ = 2.4Hz, J_{gem} = 10.9Hz, H-6b); 3.56 (s, 3H, -OCH_3); 3.94 (ddd, 1H, $J_{5,6a}$ = 8.1Hz, $J_{5,6b}$ = 2.4Hz, $J_{4,5}$ = 10.2Hz, H-5); 4.79 (m, 1H, H-3); 4.95 (br d, 1H, J = 3.1Hz, H-1); 5.01 (dd, 1H, $J_{3,4}$ = 4.0Hz, $J_{4,5}$ = 10.2Hz, H-4); 7.58-7.39, 8.00-7.90 (m, 6H, 5ArH, NH). IR ($CHCl_3$, ν cm^{-1}): 3400,1740,1540. HRMS *m/z*: 360.1062: Calcd for $C_{16}H_{15}F_3INO_5$: 360.1059 (M^+ - I).

Methyl 4-*O*-Benzoyl-2,3,6-trideoxy-3-trifluoroacetamido-α-D-*ribo*-hexo-pyranoside (7). A solution of nickel chloride hexahydrate (1.68 g, 0.007 mol) in MeOH (30 mL) was added to a solution of compound **6** (17.1 g, 0.035 mol) also in MeOH (250 mL); then $NaBH_4$ (4.0 g, 0.106 mol) was added portionwise over 5 min. The mixture was diluted with H_2O/$CHCl_3$ and filtered over Celite. The filtrate was extracted 3 times with $CHCl_3$: the organic layer was dried over $MgSO_4$ and the solvents were evaporated. Purification of the crude material by flash chromatography ($CHCl_3$/ether = 98/2) afforded the 6-deoxy derivative **7** (7.9 g, 62.5%), as a yellow syrup. ^{1}H NMR ($CDCl_3$, δ ppm): 1.28 (d, 3H, $J_{5,6}$ = 6.2Hz, H-6); 2.01 (ddd, 1H, $J_{1,2eq}$ = 1.0Hz, $J_{2eq,3}$ = 2.9Hz, J_{gem} = 14.6Hz, H-2eq); 2.19 (dt, 1H, $J_{1,2ax}$ = $J_{2ax,3}$ = 3.8Hz, J_{gem} = 14.6Hz, H-2ax); 3.47 (s, 3H, -OCH_3); 4.09 (dq, 1H, $J_{4,5}$ = 10.2Hz, $J_{5,6}$ = 6.2Hz, H-5); 4.75 (m, 1H, H-3); 4.85 (br d, 1H, $J_{1,2}$ = 3.8Hz, H-1); 4.92 (dd, 1H, $J_{3,4}$ = 3.9Hz, $J_{4,5}$ = 10.2Hz, H-4); 7.59-7.38, 7.95-7.91 (m, 5H, 5ArH); 8.05 (br, 1H, NH). IR ($CHCl_3$, ν cm^{-1}): 3380, 1720, 1540. HRMS *m/z*: 330.0952: Calcd for $C_{16}H_{18}F_3NO_5$: 330.0953 (M^+ - MeOH).

4-*O*-Benzoyl-2,3,6-trideoxy-3-trifluoroacetamido-α-D-*ribo*-hexopyranoside (2a). To a solution of compound **7** (0.61 g, 1.69 mmol) in glacial acetic acid (10 mL), heated under reflux, water (4 mL) was added portionwise over 1 h to keep the solution homogeneous. After an additional 3 h the solvents were evaporated. The residue was dissolved in ether and washed with saturated $NaHCO_3$ solution and brine, dried over $MgSO_4$ and the solvents were evaporated. Purification of the crude material by flash chromatography ($CHCl_3$/ether = 98/2) afforded compound **2a** (0.501 g, 85.4%) as a syrup. ^1H NMR ($CDCl_3$, δ ppm): 1.26 (d, 3H, $J_{5,6}$ = 6.2 Hz, H-6); 2.13-1.99 (m, 2H, H-2); 3.36 (br s, 1H, HO-1); 4.35 (dq, 1H, $J_{4,5}$ = 10.2 Hz, $J_{5,6}$ = 6.2 Hz, H-5); 4.79 (m, 1H, H-3); 4.91 (dd, 1H, $J_{3,4}$ = 3.9 Hz, $J_{4,5}$ = 10.2 Hz, H-4); 5.41 (br s, 1H, H-1); 7.61-7.38, 7.98-7.92 (m, 5H, 5ArH); 8.19 (br, 1H, NH). IR ($CHCl_3$, ν cm^{-1}): 3600, 3380, 1730, 1600, 1550. HRMS *m/z*: 330.0921: Calcd for $C_{15}H_{16}F_3NO_5$: 330.0953 (M^+ - OH)

Ethyl 4-*O*-Benzoyl-2,3,6-trideoxy-3-trifluoroacetamido-1-thio-α- and β-D-*ribo*-hexopyranoside (2b). Ethyl thiol (0.1 mL, 1.35 mmol) and *p*-toluenesulfonic acid (12 mg, 0.06 mmol) were added to a solution of compound **2a** (98 mg, 0.28 mmol) in dry CH_2Cl_2 (1.5 mL). The mixture was stirred at 23 °C for 5 h, diluted with more CH_2Cl_2, washed with saturated $NaHCO_3$ solution and brine, dried over $MgSO_4$ and the solvents were evaporated. Purification of the crude mixture by PTLC (hexane/ether = 6/4) afforded the anomeric mixture of thioglycosides **2b** (86 mg, 78.0%) as a yellow syrup. A small sample was separated into the two isomers for analytical purposes. α anomer: ^1H NMR ($CDCl_3$, δ ppm): 1.29 (d, 3H, $J_{5,6}$ = 6.2 Hz, H-6); 1.34 (t 3H, -CH_2CH_3); 2.04 (ddd, 1H, $J_{1,2eq}$ = 1.6 Hz, $J_{2eq,3}$ = 3.4 Hz, J_{gem} = 15.1 Hz, H-2eq); 2.78-2.52 (m, 3H, -CH_2CH_3, H-2ax); 4.35 (dq, 1H, $J_{4,5}$ = 9.5 Hz, $J_{5,6}$ = 6.2 Hz, H-5); 4.80 (m, 1H, $J_{3,4}$ = 4.2 Hz, $J_{2ax,3}$= 4.1 Hz, H-3); 4.97 (dd, 1H, $J_{3,4}$ = 4.2 Hz, $J_{4,5}$ = 9.5 Hz, H-4); 5.21 (br d, 1H, $J_{1,2}$ = 5.3 Hz, H-1); 7.62-7.39, 7.98-7.83 (m, 5H, 5ArH); 7.80 (br, 1H, NH). IR ($CHCl_3$, ν cm^{-1}): 3340,1740,1540. β anomer: ^1H NMR ($CDCl_3$, δ ppm): 1.27 (d, 3H, $J_{5,6}$ = 5 Hz, H-6); 1.32 (t 3H, -CH_2CH_3); 2.46-2.16 (m, 2H, H-2); 2.77 (q, 2H, -CH_2CH_3); 3.89 (m, 1H, H-5); 4.71 (m, 1H, H-3); 4.79 (dd, 1H, $J_{1,2eq}$ = 2.6 Hz, $J_{1,2ax}$ = 11 Hz, H-1); 5.01 (dd, 1H, $J_{3,4}$ = 4.4 Hz, $J_{4,5}$ = 9.6 Hz, H-4); 6.62 (br, 1H, NH); 7.97-7.42 (m, 5H, 5ArH). IR ($CHCl_3$, ν cm^{-1}): 3330, 1740, 1540.

17'β(3''-Furyl)-14'β-hydroxy-5'β,14'β-androstan-3'β-yl 4-*O*-Benzoyl-2,3,6-trideoxy-3-trifluoroacetamido-α and β-D-*ribo*-hexopyranoside (8α, 8β). Procedure A. A mixture of steroid **S-1** (71 mg, 0.198 mmol), glycosyl donor **2a** (149.6 mg, 0.431 mmol, added in 2 portions over 2 h) and *p*-toluenesulfonic acid (3.7 mg, 0.019 mmol)

in dry benzene (3 mL) and dry CH_2Cl_2 (1 mL) was stirred at 23 °C for 5 h. The mixture was diluted with more CH_2Cl_2, washed with saturated $NaHCO_3$ solution and brine, dried over $MgSO_4$ and the solvents were evaporated. Purification of the crude material by PTLC ($CHCl_3$/ether = 95/5) afforded **8**α (38.1 mg, 28.0%), α anomer, and **8**β (9.6 mg, 7.0%), β anomer, α/β ratio = 4/1. Δ14' glycosylated product (7.1 mg) and an inseparable mixture of the two starting materials (114 mg) were also recovered. **Procedure B.** A mixture of steroid **S-1** (48 mg), 0.134 mmol), glycosyl donor **2b** (106 mg, 0.272 mmol), $CdCO_3$ (46 mg, 0.268 mmol) and $HgCl_2$ (72 mg, 0.268 mmol, added in two portions) in dry CH_2Cl_2 (3 mL) and 1 drop of DMF was stirred at 23 °C for 24 h. The mixture was filtered over Celite and the solvents were evaporated. Purification of the crude material by PTLC (hexane/ether =6/4) afforded **8** α (12.8 mg, 13.9%) α anomer, and **8**β (14.6 mg, 15.8%) β anomer, α/β ratio = 1/1.14. A mixture of the two starting materials and newly formed **2a** was also recovered (59.1 mg). **8**α: ^{1}H NMR ($CDCl_3$, δ ppm): 0.73 (s, 3H, H-18'); 0.96 (s, 3H, H-19'); 1.25 (d, 3H, H-6); 2.76 (m, 1H, H-17'); 4.15-4.07 (m, 2H, H-5, H-3'); 4.79 (m, 1H, H-3); 4.92 (dd, 1H, $J_{3,4}$ = 3.8 Hz, $J_{4,5}$ = 10.2 Hz, H-4); 5.08 (d, 1H, $J_{1,2}$ = 2.8 Hz, H-1); 6.47 (s, 1H, H-4"); 7.22 (s 1H, H-2"); 7.32 (s, 1H, H-5"); 7.61-7.39, 7.97-7.93 (m, 5H, 5ArH); 8.14 (br, 1H, NH). IR ($CHCl_3$, ν cm^{-1}): 3350, 1720, 1600, 1540. HRMS *m/z*: 687.3434: Calcd for $C_{38}H_{48}F_3NO_7$: 687.3383 (M^+). **8**β: ^{1}H NMR ($CDCl_3$, δ ppm): same values as for **8**α, except: 0.72 (s, 3H, H-18'); 0.94 (s, 3H, H-19'); 1.43 (d, 3H, $J_{5,6}$ = 6.7 Hz, H-6); 4.14-4.04 (m, 2H, H-5, H-3'); 4.83 (m, 1H, H-3); 4.96 (dd, 1H, $J_{1,2ax}$ = 5.0 Hz, $J_{1,2eq}$ = 3.0 Hz, H-1); 5.09 (dd, 1H, $J_{3,4}$ = 3.7 Hz, $J_{4,5}$ = 5.4 Hz, H-4); 6.43 (br d, 1H, NH); 7.66-7.44, 8.03-7.98 (m, 5H, 5ArH). IR ($CHCl_3$, ν cm^{-1}): 3650, 3430, 1720, 1590, 1520. HRMS *m/z*: 688.3421: Calcd for $C_{38}H_{48}F_3NO_7$: 688.3460 (M^++H).

Methyl 4-*O*-Benzoyl-6-bromo-2,6-dideoxy-3-*O*-(tetrahydropyran-2-yl)-α-D-*ribo*-hexopyranoside (10).[20] To a solution of compound **9**[8] (18.2 g, 0.053 mol) in dry CH_2Cl_2 (120 mL) were added dihydropyran (12 mL, 0.132 mol) and PPTS (1.33 g, 0.005 mol). The mixture was stirred overnight at 23 °C, then diluted with more CH_2Cl_2, washed with saturated $NaHCO_3$ solution and water, dried over $MgSO_4$ and the solvents were evaporated. The crude diastereomeric mixture of THP derivatives (26.8 g) was used in the following step without any further purification. A small sample was purified for analytical purposes. ^{1}H NMR ($CDCl_3$, δ ppm): 2.30-1.46 (m, 16H, two H-2, two 6H-THP); 3.41, 3.46 (s, 6H two -OCH_3); 3.70-3.38 (m, 7H, 3H-THP, two H-6); 3.99 (m, 1H, 1H-THP); 4.26 (dd, 1H, J = 3.9, 7.8 Hz, H-3); 4.39 (dd, 1H, J = 3.3, 6.8 Hz, H-3); 4.64-4.47 (m, 3H, two H-5, 1H-THP); 4.87-4.81 (m, 3H, two H-1, 1H-THP); 5.10-5.03 (m, 2H, two H-4); 7.60-7.42, 8.10-8.01 (m, 10H,

10ArH). IR ($CHCl_3$, ν cm^{-1}): no OH, 1720, 1660. HRMS *m/z*: 428.0832: Calcd for $C_{19}H_{25}BrO_6$: 428.0835 (M^+).

Methyl 4-*O*-Benzoyl-2,6-dideoxy-3-*O*-(tetrahydropyran-2-yl)-α-D-*ribo*-hexopyranoside (11). To a solution of crude compound **10** (26.8 g, 0.053 mol) in absolute MeOH (750 mL) was added a solution of nickel boride hexahydrate (6.42 g, 0.023 mol) also in MeOH (50 mL). The mixture was cooled to 0 °C, then $NaBH_4$ (14.2 g, 0.375 mol) was added portionwise. The mixture was diluted with $CHCl_3/H_2O$, filtered over Celite and extracted with $CHCl_3$. The combined extracts were washed with brine, dried over $MgSO_4$ and the solvents were evaporated. Purification by flash chromatography (CH_2Cl_2/ether = 94/6) afforded the diastereomeric compounds **11** (15.9 g, 86% over two steps), as an oil. ^1H NMR ($CDCl_3$, δ ppm): 1.27 (d, 6H, $J_{5,6}$ = 6.6 Hz, two H-6); 1.70-1.40 (m, 12H, two 6H-THP); 2.26-1.74 (m, 4H, two H-2); 3.36, 3.41 (s, 6H two $-OCH_3$); 3.50-3.20 (m, 3H, 3H-THP); 3.58 (m, 1H, H-5); 3.96 (m, 1H, 1H-THP); 4.21 (m, 1H, H-3); 4.32 (m, 1H, H-3) 4.42 (m, 1H, H-5); 4.60 (dd, 1H, J = 3.5 Hz, 1H-THP); 4.80-4.70 (m, 2H, two H-1); 4.98-4.84 (m, 3H, two H-4, 1H-THP); 7.55-7.36, 8.12-8.03 (m, 10H, 10ArH). IR ($CHCl_3$, ν cm^{-1}): no OH, 1720, 1610. HRMS *m/z*: 349.1646: Calcd for $C_{19}H_{26}O_6$: 349.1651 (M^+-H).

Methyl 4-*O*-Benzoyl-2,6-dideoxy-α-D-*ribo*-hexopyranoside (12). A solution of compound **11** (22.6 g, 0.0645 mol) in MeOH (132.5 mL) was stirred in the presence of conc. HCl (1.5 mL) for 15 min. The mixture was neutralized with saturated $NaHCO_3$ solution, diluted with $CHCl_3$, washed with water and brine, dried over $MgSO_4$ and the solvents were evaporated. The crude product **12** was used in the following step without any further purification. A small sample was purified for analytical purposes. ^1H NMR ($CDCl_3$, δ ppm): 1.29 (d, 3H, $J_{5,6}$ = 6.2 Hz, H-6); 2.04 (dt, 1H, $J_{1,2ax} = J_{2ax,3}$ = 3.2 Hz, J_{gem} = 14.5 Hz, H-2ax); 2.19 (ddd, 1H, $J_{2eq,3}$ = 3.6 Hz, J_{gem} = 14.5 Hz, H-2eq); 3.42 (s, 3H, $-OCH_3$); 3.53 (d, 1H, J = 10 Hz, HO-3); 4.25 (m, 1H, H-3); 4.29 (dq, 1H, $J_{4,5}$ = 10.2 Hz, $J_{5,6}$ = 6.2 Hz, H-5); 4.77 (dd, 1H, $J_{3,4}$ = 2.8 Hz, $J_{4,5}$ = 10.2 Hz, H-4); 4.84 (d, 1H, $J_{1,2ax}$ = 3.2 Hz, H-1); 7.57-7.40, 8.09-8.05 (m, 5H, 5ArH). IR ($CHCl_3$, ν cm^{-1}): 3480, 1700, 1600. HRMS *m/z*: 235.0968: Calcd for $C_{14}H_{18}O_5$: 235.0977 (M^+-OCH_3).

Methyl 4-*O*-Benzoyl-2,6-dideoxy-α-D-*erythro*-hexopyranosyl-3-ulose (13). To crude compound **12** (16.5 g, 0.0645 mol), dissolved in a mixture of dry benzene (217 mL) and DMSO (108.5 mL), were added pyridine (5.0 mL, 0.0645 mol), DCC (38.5 g, 0.187 mol) and trifluoroacetic acid (2.4 mL, 0.031 mol) and the mixture was stirred at 23 °C for 5 h. The mixture was filtered over Celite, washed with saturated $NaHCO_3$ solution, water and brine, dried over $MgSO_4$ and the solvents were evaporated. Purification by flash chromatography (hexane/ether = 7/3) afforded the ketone **13**

(13.6 g, 79.9%), mp 103.5-104.5 °C (CH_2Cl_2/hexane). ^1H NMR ($CDCl_3$, δ ppm): 1.44 (d, 3H, $J_{5,6}$ = 6.1 Hz, H-6); 2.69 (dd, 1H, $J_{1,2eq}$ = 1.1 Hz, J_{gem} = 14.2 Hz, H-2eq); 2.90 (ddd, 1H, $J_{1,2ax}$ = 4.4 Hz, J_{gem} = 14.2 Hz, J_W = 1.0 Hz, H-2ax); 3.40 (s, 3H, -OCH_3); 4.29 (dq, 1H, $J_{4,5}$ = 10 Hz, $J_{5,6}$ = 6.1 Hz, H-5); 5.13 (dd, 1H, $J_{1,2ax}$ = 4.4 Hz, $J_{1,2eq}$ = 1.1 Hz, H-1); 5.18 (dd, 1H, $J_{4,5}$ = 10 Hz, J_W = 1.0 Hz, H-4); 7.60-7.43, 8.11-8.06 (m, 5H, 5ArH). IR ($CHCl_3$, ν cm^{-1}): 1740, 1720, 1600. HRMS *m/z*: 264.0997: Calcd for $C_{14}H_{16}O_5$: 264.0997 (M^+).

Methyl 4-*O*-Benzoyl-2,6-dideoxy-α-D-*erythro*-hexopyranosyl-3-ulose oxime (14). A solution of compound **13** (11.9 g, 0.045 mol), in pyridine (215 mL) was reacted at 120 °C with hydroxylamine hydrochloride (11.6 g, 0.168 mol) for 1 h. Pyridine was removed under high vacuum; the residue was dissolved in $CHCl_3$ and washed with water, 0.5N HCl and water. The aqueous layer was again extracted with $CHCl_3$. The combined organic layers were dried over $MgSO_4$ and the solvents were evaporated. The crude material was crystallized from CH_2Cl_2/hexane, yielding the oxime **14** (11.7 g, 93.2%), mp 133.5-136 °C. ^1H NMR ($CDCl_3$, δ ppm): 1.35 (d, 3H, $J_{5,6}$ = 6.2 Hz, H-6); 2.33 (dd, 1H, $J_{1,2ax}$ = 4.2 Hz, J_{gem} = 14.9 Hz, H-2ax); 3.40 (s, 3H, -OCH_3); 3.49 (d, 1H, J_{gem} = 14.9 Hz, H-2eq); 4.20 (dq, 1H, $J_{4,5}$ = 9.6 Hz, $J_{5,6}$ = 6.2 Hz, H-5); 4.91 (d, 1H, $J_{1,2ax}$ = 4.2 Hz, H-1); 5.26 (d, 1H, $J_{4,5}$ = 9.6 Hz, H-4); 7.62-7.41, 8.10-8.07 (m, 5H, 5ArH). IR ($CHCl_3$, ν cm^{-1}): 3560, 1720, 1600. HRMS *m/z*: 278.1009: Calcd for $C_{14}H_{17}NO_5$: 278.1028 (M^+-H).

Methyl 3-Amino-2,3,6-trideoxy-α-D-*ribo*- and *arabino*-hexopyranoside (15a,b). Compound **14** (5.62 g, 0.0201 mol), in refluxing dry THF (250 mL) was reduced with $LiAlH_4$ (1.53 g, 0.0403 mol) for 4 h under nitrogen. The mixture was diluted with wet ether and filtered over Celite, washing the solid several times with $CHCl_3$/MeOH = 9/1. The filtrate was dried over $MgSO_4$ and the solvents were evaporated, affording the crude mixture of aminoalcohols **15a,b**, which was used in the following step without any further purification. A small sample was purified for analytical purposes. The analytical data for the *arabino* isomer **15b** were as reported.[21] The data for the *ribo* isomer were as follows: ^1H NMR (pyridine-d5, δ ppm): 1.48 (d, 3H, $J_{5,6}$ = 6.2 Hz, H-6); 1.94 (dt, 1H, $J_{1,2ax}$ = $J_{2ax,3}$ = 4.3 Hz, J_{gem} = 14.3 Hz, H-2ax); 2.21 (ddd, 1H, $J_{1,2eq}$ = 1.3 Hz, $J_{2eq,3}$ = 2.7 Hz, J_{gem} = 14.3 Hz, H-2eq); 3.26 (s, 3H, -OCH_3); 3.42 (m, 1H, H-3); 3.52 (dd, 1H, $J_{3,4}$ = 4.3 Hz, $J_{4,5}$ = 9.3 Hz, H-4); 4.01 (dq, 1H, $J_{4,5}$ = 9.3 Hz, $J_{5,6}$ = 6.2 Hz, H-5); 4.73 (br d, 1H, $J_{1,2ax}$ = 4.3 Hz, H-1); 5.20-4.98 (br, 3H, H_2N-3, HO-4). IR ($CHCl_3$, ν cm^{-1}): 3400-3040, 2930, 1455, 1375.

Methyl 3-Benzyloxycarbonylamino-2,3,6-trideoxy-α-D-*ribo*- and *arabino*-hexopyranoside (16a,b). The crude mixture of aminoalcohols **15a,b** (0.0201 mol), in

dioxan (33.4 mL) was stirred at -4 °C with benzylchloroformate (5.0 mL, 0.0352 mol), water (39.2 mL) and 2N K_2CO_3 (19.6 mL) for 5 h. The mixture was diluted with water and extracted several times with CH_2Cl_2; the organic layer was dried over $MgSO_4$ and the solvents were evaporated. The crude mixture of *ribo/arabino* isomers **16a,b** was directly used in the following step without any further purification. A small sample was purified for analytical purposes. *Ribo* isomer, **16a:** ^1H NMR ($CDCl_3$, δ ppm): 1.29 (d, 3H, $J_{5,6}$ = 6.3 Hz, H-6); 1.91 (ddd, 1H, $J_{1,2eq}$ = 1.3 Hz, $J_{2eq,3}$ = 2.9 Hz, J_{gem} = 14.6 Hz, H-2eq); 2.03 (dt, 1H, $J_{1,2ax}$ = $J_{2ax,3}$ = 3.8 Hz, J_{gem} = 14.6 Hz, H-2ax); 3.14 (bs, 1H, HO-4); 3.35 (s, 3H, -OCH_3); 3.42 (dd, 1H, $J_{3,4}$ = 3.7 Hz, $J_{4,5}$ = 9.6 Hz, H-4); 3.73 (dq, 1H, $J_{4,5}$ = 9.6 Hz, $J_{5,6}$ = 6.3 Hz, H-5); 4.19 (m, 1H, H-3); 4.68 (br d, 1H, $J_{1,2ax}$ = 3.8 Hz, H-1); 5.19-5.03 (ABq, 2H, -$\underline{CH_2}$Ph); 6.22 (br d, 1H, NH); 7.37 (s, 5H, 5ArH). IR ($CHCl_3$, ν cm^{-1}): 3650, 3400, 1700, 1500. HRMS *m/z*: 263.1270; Calcd. for $C_{15}H_{21}NO_5$: 263.1236 (M^+ - OCH_3). *Arabino* isomer, **16b:** ^1H NMR ($CDCl_3$, δ ppm): 1.29 (d, 3H, $J_{5,6}$ = 6.3 Hz, H-6); 1.60 (ddd, 1H, $J_{1,2ax}$ = 3.5 Hz, $J_{2ax,3}$ = J_{gem} = 12.6 Hz, H-2ax); 2.06 (dd, 1H, $J_{2eq,3}$ = 4.4 Hz, J_{gem} = 12.6 Hz, H-2eq); 3.07 (m, 1H, $J_{3,4}$ = $J_{4,5}$ = 9.5 Hz, $J_{4,OH}$ = 1.8 Hz, H-4); 3.33 (s, 3H, -OCH_3); 3.45 (m, 1H, HO-4); 3.65 (dq, 1H, $J_{4,5}$ = 9.5 Hz, $J_{5,6}$ = 6.3 Hz, H-5); 3.94 (m, 1H, H-3); 4.71 (br d, 1H, $J_{1,2ax}$ = 3.5 Hz, H-1); 4.75 (br d, 1H, NH); 5.11 (s, 2H, -$\underline{CH_2}$Ph); 7.35 (s, 5H, 5ArH). IR ($CHCl_3$, ν cm^{-1}): 3650, 3500, 3400, 1700, 1600, 1500. HRMS *m/z*: 295.1420; Calcd. for $C_{15}H_{21}NO_5$: 295.1420 (M^+).

Methyl 3-Benzyloxycarbonylamino-2,3,6-trideoxy-4-*O*-*p*-nitrobenzoyl-α-D-*ribo*- and *arabino*-hexopyranoside (17a,b). To a solution of compounds **16a,b** (0.0201 mol), in pyridine (110 mL) *p*-nitrobenzoyl chloride (10.3 g, 0.056 mol) and DMAP (1.08 g, 0.009 mol) were added and the mixture was stirred at 90 °C for 3 h. Pyridine was distilled off under high vacuum; the residue was dissolved in CH_2Cl_2 and washed with 5% citric acid, water, saturated $NaHCO_3$ solution and brine; the organic layer was dried over $MgSO_4$ and the solvents were evaporated. Purification of the crude material by flash chromatography (CH_2Cl_2/hexane/ether = 7.5/2/0.5) afforded the *ribo* isomer **17a** (3.4 g, 38% over three steps), mp 127.5-128.5 °C (EtOAc/hexane) and the *arabino* isomer **17b** (0.23 g, 2.6% over three steps), mp 187.5-189 °C (EtOAc/hexane). **17a:** ^1H NMR ($CDCl_3$, δ ppm): 1.25 (d, 3H, $J_{5,6}$ = 6.3 Hz, H-6); 1.99 (ddd, 1H, $J_{1,2eq}$ unresolved, $J_{2eq,3}$ = 1.5 Hz, J_{gem} = 14.6 Hz, H-2eq); 2.15 (dt, 1H, $J_{1,2ax}$ = $J_{2ax,3}$ = 4.1 Hz, J_{gem} = 14.6 Hz, H-2ax); 3.42 (s, 3H, -OCH_3); 4.13 (dq, 1H, $J_{4,5}$ = 10.2 Hz, $J_{5,6}$ = 6.3 Hz, H-5); 4.49 (m, 1H, H-3); 4.78 (br d, 1H, $J_{1,2ax}$ = 4.1 Hz, H-1); 4.81 (dd, 1H, $J_{3,4}$ = 3.6 Hz, $J_{4,5}$ = 10.2 Hz, H-4); 5.03-4.84 (ABq, 2H, -$\underline{CH_2}$Ph); 6.22 (br d, 1H, NH); 7.36-7.27 (m, 5H, 5ArH); 8.18-

8.02 (dd, 4H, 4ArH). IR ($CHCl_3$, ν cm^{-1}): 3400, 1730, 1610, 1510. HRMS *m/z*: 444.1535; Calcd. for $C_{22}H_{24}N_2O_8$: 444.1532 (M+). **17b:** ^1H NMR ($CDCl_3$, δ ppm): 1.22 (d, 3H, $J_{5,6}$ = 6.2 Hz, H-6); 1.74 (dt, 1H, $J_{1,2ax} = J_{2ax,3}$ = 3.6 Hz, J_{gem} = 12.8 Hz, H-2ax); 2.25 (dd, 1H, $J_{2eq,3}$ = 4.7 Hz, J_{gem} = 12.8 Hz, H-2eq); 3.38 (s, 3H, $-OCH_3$); 4.03 (dq, 1H, $J_{4,5}$ = 9.6 Hz, $J_{5,6}$ = 6.2 Hz, H-5); 4.37 (m, 1H, H-3); 4.72 (br d, 1H, NH); 4.77 (m, 1H, $J_{3,4} = J_{4,5}$ = 9.6 Hz, H-4); 4.78 (br d, 1H, $J_{1,2ax}$ = 3.6 Hz, H-1); 4.92 (s, 2H, $-\underline{CH_2}Ph$); 7.16 (m, 5H, 5ArH); 8.26-8.11 (dd, 4H, 4ArH). IR ($CHCl_3$, ν cm^{-1}): 3400, 1720, 1610, 1520. HRMS *m/z*: 444.1532; Calcd. for $C_{22}H_{24}N_2O_8$: 444.1532 (M^+).

3-Benzyloxycarbonylamino-2,3,6-trideoxy-4-*O*-*p*-nitrobenzoyl-α-D-*ribo*-hexopyranoside (3a). To a stirred solution of compound **17a** (2.31 g, 5.20 mmol), in glacial acetic acid (38 mL), heated under reflux, water (41 mL) was added portionwise over 2 h to maintain the solution homogeneous. After an additional 3 h, the solvents were evaporated. The residue was dissolved in ether, washed with saturated $NaHCO_3$ solution and brine, dried over $MgSO_4$ and the solvents were evaporated. Purification by flash chromatography (CH_2Cl_2/ether = 9/1) afforded glycosyl donor **3a** (2.03 g, 90.7%) as a syrup. ^1H NMR ($CDCl_3$, δ ppm): 1.24 (d, 3H, $J_{5,6}$ = 6.3 Hz, H-6); 2.18-2.00 (m, 2H, H-2); 3.09 (br s, 1H, HO-1); 4.40 (dq, 1H, $J_{4,5}$ = 10.3 Hz, $J_{5,6}$ = 6.3 Hz, H-5); 4.51 (m, 1H, H-3); 4.81 (dd, 1H, $J_{3,4}$ = 3.7 Hz, $J_{4,5}$ = 10.3 Hz, H-4); 5.04-4.84 (ABq, 2H, $-\underline{CH_2}Ph$); 5.35 (br s, 1H, H-1); 6.40 (br d, 1H, NH); 7.32 (m, 5H, 5ArH); 8.18-8.03 (dd, 4H, 4ArH). IR ($CHCl_3$, ν cm^{-1}): 3560, 3400, 1720, 1600, 1510. HRMS *m/z*: 412.1271; Calcd. for $C_{21}H_{22}N_2O_8$: 412.1270 (M^+-H_2O).

Ethyl 3-Benzyloxycarbonylamino-2,3,6-trideoxy-4-*O*-*p*-nitrobenzoyl-1-thio-α -and β-D-*ribo*-hexopyranoside (3b). To a solution of compound **3a** (1.09 g, 2.54 mmol), in dry CH_2Cl_2 (17 mL) ethyl thiol (0.95 mL, 12.7 mmol) and *p*-toluenesulfonic acid (0.106 g, 0.56 mmol) were added and the mixture was stirred at 23 °C, under nitrogen, overnight. The mixture was diluted with more CH_2Cl_2, washed with saturated $NaHCO_3$ solution and brine, dried over $MgSO_4$ and the solvents were evaporated. Purification by flash chromatography (CH_2Cl_2/hexane/ether = 72/20/8) afforded the anomeric mixture of thioglycoside donors **3b** (1.04 g, 86.5%) as a syrup. ^1H NMR ($CDCl_3$, δ ppm): 1.35-1.26 (m, 12H, two $-CH_2\underline{CH_3}$, two H-6); 2.21-1.98 (m, 3H, H-2eq, two H-2ax); 2.81-2.44 (m, 5H, two $-\underline{CH_2}CH_3$, H-2eq); 3.91 and 4.38 (m, 2H, two H-5); 4.56-4.49 (m, 2H, two H-3); 5.01-4.80 (m, 6H, two $-\underline{CH_2}Ph$, two H-4); 5.06 (d, 1H, J = 3.8 Hz, H-1); 5.22 (br s, 1H, NH); 5.36 (dd, 1H, $J_{1,2eq}$ = 2.2 Hz, $J_{1,2ax}$ = 6.0 Hz, H-1); 5.98 (br d, 1H, NH); 7.31 (br s, 10H, two 5ArH); 8.23-8.06 (m, 8H, two 4ArH). IR ($CHCl_3$, ν cm^{-1}): 3440-3400, 1720, 1600, 1530-1500. HRMS *m/z*: 413.1360; Calcd. for $C_{22}H_{26}N_2O_7S$: 413.1343 (M^+-SEt).

17'β-(3"-Furyl)-14'β-hydroxy-5'β,14'β-androstan-3'-β-yl 3-Benzyloxycarbonylamino-2,3,6-trideoxy-4-*O*-*p*-nitrobenzoyl-α- and β-D-*ribo*-hexopyranoside (18α, 18β). **Procedure A:** To a solution of steroid **S-1** (50.0 mg, 0.139 mmol) and glycosyl donor **3a** (60.0 mg, 0.139 mmol) in dry benzene (1.9 mL) and dry CH_2Cl_2 (0.7 mL) was added *p*-toluenesulfonic acid (5.3 mg, 0.028 mmol) and the mixture was stirred at 23 °C for 3 h. Workup was as for compounds **8α/8β**, Procedure A. Purification by PTLC ($CHCl_3$/hexane/ether = 6/2/2) yielded compound **18α** (36.2 mg, 33.7%), α anomer, mp 179-181 °C (iPr_2O/EtOAc/hexane), and **18β** (6.2 mg, 5.7%), β anomer, mp 114-116 °C (iPr_2O/EtOAc/hexane), α/β ratio = 6/1. Decomposed (Δ 14') glycosylated products (13.8 mg) and unreacted starting materials (31 mg) were also recovered. **Procedure B.** To a solution of steroid **S-1** (37.1 mg, 0.104 mmol) and thioglycosides **3b** (49.2 mg, 0.104 mmol) in dry CH_2Cl_2 (3 mL) and a drop of DMF were added $CdCO_3$ (38.0 mg, 0.221 mmol) and $HgCl_2$ (28.0 mg, 0.104 mmol) and the mixture was stirred at 23 °C for 3 h. Workup was as for compounds **8α/8β**, Procedure B. Purification by PTLC (CH_2Cl_2/hexane/ether = 6/2/2) yielded compound **18α** (10.3 mg, 12.9%), and **18β** (10.7 mg, 13.4%), α/β ratio = 1/1. A mixture of unreacted steroid and newly formed **3a** (41.2 mg) was also recovered. **Procedure C.** To a solution of steroid **S-1** (103 mg, 0.290 mmol) and compound **3a** (129 mg, 0.290 mmol) in dry benzene (4.5 mL) were added *p*-toluenesulfonic acid (11.0 mg, 0.060 mmol) and crushed 3Å molecular sieves. The mixture was stirred at 23 °C for 2 h, then it was diluted with ether, filtered over Celite, washed with saturated $NaHCO_3$ solution and brine, dried over $MgSO_4$ and the solvents were evaporated. Purification by PTLC ($CHCl_3$/hexane/ether = 6/2/2) afforded **18α** (55.0 mg, 24.6%), and **18β** (76.1 mg, 34.1%), α/β ratio = 1/1.4. Unreacted steroid (28.6 mg) and **3a** (35.8 mg) were also recovered. **18α**: ^1H NMR ($CDCl_3$, δ ppm): 0.73 (s, 3H, H-18'), 0.93 (s,3H, H-19'), 1.24 (d, 3H, $J_{5,6}$ = 6.2Hz, H-6); 2.76 (dd, 1H, J = 8.7Hz, J = 5.8Hz, H-17'); 4.04 (m, 1H, H-3'); 4.19 (dq, 1H, $J_{4,5}$ = 10Hz, $J_{5,6}$ = 6.2Hz, H-5); 4.49 (m, 1H, H-3); 4.81 (dd, 1H, $J_{3,4}$ = 3.6Hz, $J_{4,5}$ = 10Hz, H-4); 4.96 (ABq, 2H, -$\underline{CH_2}$Ph); 5.02 (d, 1H, $J_{1,2}$ = 3.2Hz, H-1); 6.47 (d, 1H, H-4''); 6.71 (br d, 1H, NH); 7.22 (d, 1H, J =1Hz, H-2''); 7.36-7.28 (m, 6H, H-5'', 5ArH); 8.18-8.04 (dd, 4H, 4ArH). IR ($CHCl_3$, ν cm^{-1}): 3600, 3400, 1720, 1610, 1510. HRMS *m/z*: 413.1352 and 358.2529; Calcd for $C_{44}H_{54}N_2O_{10}$: 413.1349 (M^+ - $C_{23}H_{34}O_3$) and 358.2508 (M^+ - $C_{21}H_{21}N_2O_7$). **18β**: ^1H NMR ($CDCl_3$, δ ppm): same values as for **18α** , except: 0.71 (s, 3H, H-18'), 0.93 (s,3H, H-19'), 1.36 (d, 3H, $J_{5,6}$ = 6.5Hz, H-6); 3.97 (m, 1H, H-5); 4.58 (m, 1H, H-3); 4.86 (dd, 1H, $J_{1,2ax}$ = 6.5Hz, $J_{1,2eq}$ = 3.4Hz, H-1); 5.07-4.97 (m, 4H, NH, H-4, -$\underline{CH_2}$Ph); 6.46 (d, 1H, J =1Hz, H-4''); 7.21 (d, 1H, J =1Hz, H-2''); 7.32-7.30 (m, 6H, H-5'', 5ArH); 8.26-8.13 (dd, 4H,

4ArH). IR ($CHCl_3$, ν cm^{-1}): 3430, 1720, 1610, 1520-1500. HRMS *m/z*: 413.1355 and 358.2536; Calcd for $C_{44}H_{54}N_2O_{10}$: 413.1349 (M^+ - $C_{23}H_{34}O_3$) and 358.2508 (M^+ - $C_{21}H_{21}N_2O_7$).

Digitoxigenin-3'β-yl 3-Benzyloxycarbonylamino-2,3,6-trideoxy-4-*O*-*p*-nitrobenzoyl-α- and β-D-*ribo*-hexopyranoside (19α, 19β). Procedure A: The reaction was carried out as for compounds **8α/8β**, Procedure A, using the following materials: digitoxigenin **S-2** (85.0 mg, 0.227 mmol), **3a** (100.0 mg, 0.232 mmol), dry benzene (3.75 mL), dry CH_2Cl_2 (1.25 mL), *p*-toluenesulfonic acid (8.8 mg, 0.046 mmol). The mixture was stirred at 23 °C for 5 h, then it was worked up as previously described. Purification by flash chromatography then PTLC ($CHCl_3$/ether = 8/2) afforded compound **19α** (50.4 mg, 28.2%), α anomer, mp 250-2 °C ($CHCl_3$/hexane/ether), and **19β** (22.0 mg, 12.3%), β anomer, mp 143-5 °C ($CHCl_3$/hexane/ether), α/β ratio = 2.3/1. Decomposed (Δ14') glycosylated products (11.8 mg), unreacted **S-2** (28.1 mg) and **3a** (45.0 mg) were also recovered. **Procedure D.** To a stirred solution of thioglycosides **3b** (90.0 mg, 0.190 mmol) in dry benzene (8 mL) were added digitoxigenin **S-2** (66.0 mg, 0.176 mmol), $CdCO_3$ (62.0 mg, 0.360 mmol), $HgCl_2$ (51.0 mg, 0.189 mmol) and a drop of DMF. After 24 h at 23 °C were again added **3b** (89.0 mg, 0.188 mmol), $CdCO_3$ (62.0 mg, 0.360 mmol), $HgCl_2$ (51.0 mg, 0.189 mmol). After an additional 24 h, the mixture was filtered over Celite and the solvents were evaporated. Purification by PTLC (CHCl3/hexane/ether = 6/2/2) afforded **19α** (22.2 mg, 16.0%), and **19β** (27.2 mg, 19.6%), α/β ratio = 1/1.2. Also recovered were newly formed **3a** (70.0 mg) and the two starting materials. **19α**: ^1H NMR ($CDCl_3$, δ ppm): 0.89 (s, 3H, H-18'), 0.93 (s,3H, H-19'), 1.23 (d, 3H, $J_{5,6}$ = 6.2Hz, H-6); 2.80 (dd, 1H, J = 9.0Hz, J = 5.6Hz, H-17'); 4.04 (m, 1H, H-3'); 4.18 (dq, 1H, $J_{4,5}$ = 10.6Hz, $J_{5,6}$ = 6.2Hz, H-5); 4.49 (m, 1H, H-3); 4.83 (dd, 1H, $J_{3,4}$ = 6.6Hz, $J_{4,5}$ = 10.6Hz, H-4); 4.91 (ABq, 2H, H-23'); 4.96 (ABq, 2H, -$\underline{CH_2}$Ph); 5.01 (d, 1H, $J_{1,2}$ = 3.1Hz, H-1); 5.89 (br s, 1H, H-22'); 6.67 (br d, 1H, NH); 7.36-7.28 (m, 5H, 5ArH); 8.19-8.04 (ABq, 4H, 4ArH). IR ($CHCl_3$, ν cm^{-1}): 3380, 1720, 1610, 1510. Positive FAB MS *m/z*: 787 (M^+ +H). **19β**: ^1H NMR ($CDCl_3$, δ ppm): same values as for **19α** , except: 0.87 (s, 3H, H-18'), 0.94 (s, 3H, H-19'), 1.37 (d, 3H, $J_{5,6}$ = 6.6Hz, H-6); 4.00 (dq, 1H, $J_{4,5}$ = $J_{5,6}$ = 6.6Hz, H-5); 4.57 (m, 1H, H-3); 4.87 (dd, 1H, $J_{1,2ax}$ = 6.0Hz, $J_{1,2eq}$ = 3.0Hz, H-1); 4.90 (ABq, 2H, H-23'); 5.13-5.00 (m, 4H, NH, H-4, -$\underline{CH_2}$Ph); 5.88 (br s, 1H, H-22'); 7.32 (br s, 5H, 5ArH); 8.26-8.11 (ABq, 4H, 4ArH). IR ($CHCl_3$, ν cm^{-1}): 3420, 1730, 1610, 1510. Positive FAB MS *m/z*: 786 (M^+).

(23'-*R*)-23'-Methylisodigitoxigenin-3'β-yl 3-Benzyloxycarbonylamino-2,3,6-trideoxy-4-*O*-*p*-nitrobenzoyl-α- and β-D-*ribo*-hexopyranoside (20α,20β). Procedure

C. The reaction was carried out as described for compounds **18α/18β**, procedure C, on the following materials: steroid **S-3** (100.5 mg, 0.260 mmol), glycosyl donor **3a** (113.0 mg, 0.260 mmol), dry benzene (4 mL), *p*-toluenesulfonic acid (9.8 mg, 0.05 mmol) and crushed 3Å molecular sieves. The mixture was stirred at 23 °C for 30 h, then it was worked up as previously described. Purification by PTLC ($CHCl_3$/hexane/ether = 6/2/2) afforded the desired products **20α** and **20β** and starting materials (98.0 mg of **S-3** and 90.0 mg of **3a**) which were recycled twice more. The total amounts of products after three cycles were as follows: **20α** (34.4 mg, 16.6%), α anomer, mp 136-138 °C ($CHCl_3$/hexane/ether), and **20β** (57.8 mg, 27.9%), β anomer, mp 121-123 °C ($CHCl_3$/hexane/ether), α/β ratio = 1/1.7. Also recovered were **S-3** (27.0 mg) and **3a** (39.9 mg). **20α**: ^1H NMR ($CDCl_3$, δ ppm): 0.84 (s, 3H, H-18'), 0.93 (s,3H, H-19'), 1.25 (d, 3H, $J_{5,6}$ = 6.0Hz, H-6); 1.43 (d, 3H, J = 6.6Hz, H_3C-23'); 2.76 (m, 1H, H-17'); 4.03 (m, 1H, H-3'); 4.19 (dq, 1H, $J_{4,5}$ = 10.1Hz, $J_{5,6}$ = 6.0Hz, H-5); 4.49 (m, 1H, H-3); 4.81 (dd, 1H, $J_{3,4}$ = 3.5Hz, $J_{4,5}$ = 10.1Hz, H-4); 4.95 (ABq, 2H, -$\underline{CH_2}$Ph); 5.00 (m, 1H, H-23'); 5.02 (d, 1H, $J_{1,2}$ = 2.3Hz, H-1); 6.70 (br d, 1H, NH); 7.17 (d, 1H, J = 1Hz, H-22'); 7.34-7.28 (m, 5H, 5ArH); 8.26-8.12 (ABq, 4H, 4ArH). IR ($CHCl_3$, ν cm^{-1}): 3500, 3380, 1720, 1600, 1580, 1500. Negative FAB MS m^-/e: 800 (M^-). **20β**: ^1H NMR ($CDCl_3$, δ ppm): same values as for **20α** , except: 0.83 (s, 3H, H-18'), 0.93 (s, 3H, H-19'), 1.36 (d, 3H, $J_{5,6}$ = 6.6Hz, H-6); 1.42 (d, 3H, J = 6.8Hz, H_3C-23'); 3.99 (m, 1H, H-5); 4.58 (m, 1H, H-3); 4.87 (dd, 1H, $J_{1,2ax}$ = 6.6Hz, $J_{1,2eq}$ = 3.4Hz, H-1); 4.99 (dd, 1H, $J_{3,4}$ = 3.5Hz, $J_{4,5}$ = 10Hz, H-4); 5.02 (s, 2H, -$\underline{CH_2}$Ph); 5.06 (br d, 1H, NH); 7.17 (d, 1H, J = 1.4Hz, H-22'); 7.32 (s, 5H, 5ArH); 8.26-8.09 (ABq, 4H, 4ArH). IR ($CHCl_3$, ν cm^{-1}): 3400, 1720, 1600, 1500. Negative FAB MS m^-/e: 800 (M^-).

(23'-*R*)-23'-Methylisodigitoxigenin-3'β-yl 3-Benzyloxycarbonylamino-2,3,6-trideoxy-β-D-*ribo*-hexopyranoside (21β). Compound **20β** (64.6 mg, 0.08 mmol) dissolved in dry CH_2Cl_2 (1 mL) was treated with a saturated solution of ammonia in MeOH (3 mL) at 0 °C, overnight. Evaporation of the solvents and purification of the crude material by PTLC ($CHCl_3$/MeOH = 98/2) afforded compound **21β** (42.3 mg, 80.7%) mp 113-115 °C ($CHCl_3$/hexane/ether). ^1H NMR ($CDCl_3$, δ ppm): 0.81 (s, 3H, H-18'), 0.91 (s, 3H, H-19'), 1.32 (d, 3H, $J_{5,6}$ = 6.0Hz, H-6); 1.40 (d, 3H, J = 6.7Hz, H_3C-23'); 2.72 (m, 1H, H-17'); 2.84 (br, 1H, HO-4); 3.54 (dd, 1H, $J_{3,4}$ = 3.7Hz, $J_{4,5}$ = 7.7Hz, H-4); 3.61 (m, 1H, H-5); 4.02 (m, 1H, H-3'); 4.20 (m, 1H, H-3); 4.72 (dd, 1H, $J_{1,2eq}$ = 2.7Hz, $J_{1.2ax}$ = 8.2Hz, H-1); 5.00 (ABq, 1H, H-23'); 5.12 (ABq, 2H, -$\underline{CH_2}$Ph); 5.20 (br d, 1H, NH); 7.16 (s, 1H, H-22'); 7.37 (s, 5H, 5ArH). IR ($CHCl_3$, ν cm^{-1}): 3550-3400, 1730, 1700 and 1500. Negative FAB MS m^-/e: 651 (M^-).

(23'-*R*)-23'-Methylisodigitoxigenin-3'β-yl 3-Amino-2,3,6-trideoxy-β-D-*ribo*-hexopyranoside (22β). To a solution of compound **21β** (73.2 mg, 0.112 mmol) in absolute ethanol (6 mL) were added 20%$Pd(OH)_2$/C (29.4 mg) and cyclohexene (0.11 mL, 1.12 mmol) and the mixture was refluxed under nitrogen for 6 h. A few drops of Et_3N were added, then the mixture was filtered over Celite and the solvents were evaporated. Repeated purification by PTLC ($CHCl_3$/MeOH = 95/5) afforded compound **22β** (50.2 mg, 86.7%); however, triethylamine still remained (ca. 45% in mol, from the NMR spectrum of **22β**). To obtain the hydrochloride salt of **22β**, the product was redissolved in CH_2Cl_2 and treated with a saturated solution of HCl in CH_2Cl_2, dropwise until pH = 6, then the solvents were evaporated under high vacuum at 0 °C resulting in a solid compound, mp 167-169 °C (EtOAc/hexane) ^{1}H NMR ($CDCl_3$, δ ppm): 0.75 (s, 3H, H-18'), 0.85 (s, 3H, H-19'), 1.23 (d, 3H, $J_{5,6}$ = 6.0Hz, H-6); 1.35 (d, 3H, J = 6.8Hz, H_3C-23'); 2.65 (m, 1H, H-17'); 3.32 (m, 1H, H-3); 3.60-3.46 (m, 2H, H-4, H-5); 3.97 (m, 1H, H-3'); 4.80-4.20 (br, 3H, NH_2, HO); 4.75 (dd, 1H, $J_{1,2eq}$ = 4.6Hz, $J_{1.2ax}$ = 6.3Hz, H-1); 5.01-4.90 (ABq, 1H, H-23'); 7.11 (d, 1H, J = 1.6Hz, H-22'). IR ($CHCl_3$, ν cm^{-1}): 3350, 2400, 1740. Positive FAB MS *m/z*: 518 (M^+ +H).

2,3,6-Trideoxy-3-methoxycarbonylamino-4-*O*-*p*-nitrobenzoyl-α-D-*ribo*-hexopyranose (23). Compound **23** was prepared in three steps from the mixture of aminoalcohols **15a,b**, following the same procedure used for compound **3a**. Yields were not optimized. Only the analytical data of **23** are reported. ^{1}H NMR ($CDCl_3$, δ ppm): 1.26 (d, 3H, $J_{5,6}$ = 6.1Hz, H-6); 2.20-2.00 (m, 2H, H-2); 3.07 (br, 1H, HO-1); 3.52 (s, 3H, -OCH_3); 4.58-4.36 (m, 2H, H-3, H-5); 4.79 (dd, 1H, $J_{3,4}$ = 3.4Hz, $J_{4.5}$ = 10Hz, H-4); 5.36 (br s, 1H, H-1); 6.32 (br d, 1H, NH); 8.31-8.27 (ABq, 4H, 4ArH). IR ($CHCl_3$, ν cm^{-1}): 3600, 3500, 3400, 1725-1680, 1600, 1500.

Digitoxigenin-3'β-yl 2,3,6-Trideoxy-3-methoxycarbonylamino-4-*O*-*p*-nitrobenzoyl-α- and β-D-*ribo*-hexopyranoside (24α,24β). Procedure A. The reaction was carried out as described for compounds **8α/8β**, procedure A, on the following materials: digitoxigenin **S-2** (29.2 mg, 0.0781 mmol), compound **23** (28.3 mg, 0.0799 mmol), dry benzene (1.9 mL), dry CH_2Cl_2 (0.7 mL), and *p*-toluenesulfonic acid (4 mg, 0.0210 mmol). The mixture was stirred at 23 °C for 4 h, then it was worked up as previously described. Purification by PTLC ($CHCl_3$/hexane/ether = 6/2/2) repeated three times afforded **24α** (21.1 mg, 38.0%,) α anomer, **24β** (6.4 mg, 11.5%) β anomer, α/β ratio = 3.3/1. The two starting materials (13.5 mg of **S-2** and 14.7 mg of **23**) were also recovered. **24α**: ^{1}H NMR ($CDCl_3$, δ ppm): 0.89 (s, 3H, H-18'), 1.00 (s,3H, H-19'), 1.24 (d, 3H, $J_{5,6}$ = 6.3Hz, H-6); 3.52 (s, 3H, -OCH_3); 4.18 (m, 1H, H-5); 4.48 (m, 1H, H-3); 4.81 (dd, 1H, $J_{3,4}$ = 3.5Hz, $J_{4.5}$ = 10.1Hz, H-4); 4.92

(ABq, 2H, H-21'); 5.01 (d, 1H, $J_{1,2}$ = 2.8Hz, H-1); 5.89 (s, 1H, H-22'); 8.26-8.20 (ABq, 4H, 4ArH). IR ($CHCl_3$, ν cm^{-1}): 3400, 1730, 1600, 1500. **24β**: ^1H NMR ($CDCl_3$, δ ppm): 0.88 (s, 3H, H-18'), 0.95 (s, 3H, H-19'), 1.38 (d, 3H, $J_{5,6}$ = 6.6Hz, H-6); 3.58 (br s, 3H, $-OCH_3$); 4.03 (m, 1H, H-5); 4.55 (m, 1H, H-3); 4.91 (dd, 1H, $J_{1,2ax}$ = 8.0 Hz, $J_{1,2eq}$ = 3.5 Hz, H-1); 4.94 (s, 2H, H-21'); 5.06-5.00 (m, 2H, NH and H-4); 5.89 (d, 1H, J = 1.4Hz, H-22'); 8.33-8.15 (ABq, 4H, 4ArH). IR ($CHCl_3$, ν cm^{-1}): 3440, 1730, 1610, 1500.

***O*-3-Benzyloxycarbonylamino-2,3,6-trideoxy-4-*O*-*p*-nitrobenzoyl-α-D-*ribo*-hexopyranosyl trichloroacetimidate (25).** To a solution of compound **3a** (0.335 g, 0.780 mmol), in dry CH_2Cl_2 (8 mL) were added trichloroacetonitrile (0.28 mL, 2.80 mmol), K_2CO_3 (0.054 g, 0.390 mmol) and 18-crown-6 (0.021 g, 0.080 mmol) and the mixture was refluxed under nitrogen for 24 h. The mixture was filtered over Celite and the solvents were evaporated. The crude product **25** was used in the glycosylation reaction without any further purification. ^1H NMR ($CDCl_3$, δ ppm) on the crude material: 1.29 (d, 3H, $J_{5,6}$ = 6.2 Hz, H-6); 2.29 (br dd, 1H, $J_{1,2eq}$ unresolved, $J_{2eq,3}$ = 4.2Hz, J_{gem} = 15.0Hz, H-2eq); 2.40 (ddd, 1H, $J_{1,2ax}$ = 3.0Hz, $J_{2ax,3}$ = 4.2Hz, J_{gem} = 15.0Hz, H-2ax); 4.36 (dq, 1H, $J_{4,5}$ = 10.3 Hz, $J_{5,6}$ = 6.2 Hz, H-5); 4.57 (m, 1H, H-3); 4.92 (dd, 1H, $J_{3,4}$ = 3.6 Hz, $J_{4,5}$ = 10.3 Hz, H-4); 4.96 (ABq, 2H, -CH_2Ph); 6.17 (br d, 1H, NH); 6.41 (br d, 1H, $J_{1,2ax}$ = 3.0Hz, H-1); 7.35-7.26 (m, 5H, 5ArH); 8.18-8.03 (ABq, 4H, 4ArH); 8.72 (s, 1H, C=NH).

Glycosylations with the imidate donor. Preparation of Glycosides (19α, 19β) **Procedure E:** To a stirred solution of digitoxigenin **S-2** (65.0 mg, 0.174 mmol) and crude imidate **25** (136 mg, 0.226 mmol) in dry CH_2Cl_2 (2 mL), cooled at -20 °C, was added dropwise a solution of $BF_3.Et_2O$ (0.02 mL, 0.174 mmol) in dry CH_2Cl_2 (1 mL). The mixture was stirred at -20 °C for 3 h, then excess solid $NaHCO_3$ was added; the mixture was diluted with CH_2Cl_2, washed with saturated $NaHCO_3$ solution and brine, dried over $MgSO_4$ and the solvents were evaporated. Purification by PTLC ($CHCl_3$/hexane/ether = 6/2/2) afforded **19α** (53.5 mg, 39%, minimum yield) and **19β**, (47.7 mg, 34.9%, minimum yield), α/β ratio = 1.1/1.

Glycosides (20α, 20β). Procedure E: The reaction was carried out as described above, on the following materials: steroid **S-3** (65.3 mg, 0.165 mmol), crude imidate **25** (125 mg, 0.218 mmol) in dry CH_2Cl_2 (5 mL), $BF_3.Et_2O$ (2.9 mL of a 0.057M solution in CH_2Cl_2, 0.165 mmol). The mixture was stirred at -20 °C for 6 h, then it was worked up as described above. Purification by PTLC ($CHCl_3$/hexane/ether = 6/2/2) afforded **20α** (38.7 mg, 28.8%) and **20β**, (26.7 mg, 19.8%), α/β ratio = 1.4/1. Steroid **S-3** (18.5 mg) was also recovered. The glycosylation reactions performed using $SnCl_4$, $MgCl_2$ and $ZnCl_2$ were carried out following a similar procedure and at the temperature shown in Table 3.

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