N-Glycosyl Amides as Glycosyl Donors in Stereoselective Glycosylation Reactions

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Dedicated to Professor Helmut Ringsdorf on the occasion of his 75th birthday

Abstract: Due to their high stability, *N*-glycosyl amides have so far not been considered as glycosyl donors for glycosylation reactions. Two new procedures for the cleavage of the anomeric amide functionality under mild reaction conditions and further stereoselective in situ conversions of the activated glycosyl donors with alcohols and amines to give β-configured *O*- and *N*-glycosides are described in this article.

Key words: glycosyl amides, glycosylations, protecting groups, retro Ritter reaction, *N*-glycosides

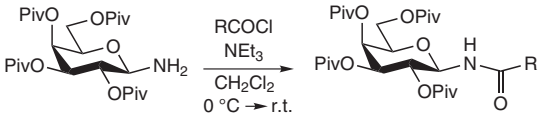
Research in molecular biology has shown that carbohydrates play important roles in molecular recognition processes.[1,2] Model glycosides and saccharides required for the investigation of the molecular mechanisms of biological carbohydrate recognition processes have to be provided by chemical synthesis. Because of the increasing demand for complex carbohydrate structures several new methods for the synthesis of glycosides and saccharides were established during the past years.[3,4] Thioglycosides,[5] trichloroacetimidates[6] and glycals[7] have been used as glycosyl donors in addition to the classical glycosyl halides[8] for successful syntheses of complex glycosides. However, the sensitivity of these glycosyl donors towards electrophiles imposes limitations on their general application.

N-Glycosyl amides are stable against acids, bases and many oxidizing and reducing agents. The *N*-glycosyl amide functionality usually is only cleavable under harsh reaction conditions. Because of their low reactivity there were so far no examples in the literature of *N*-glycosyl amides being used as anomerically protected carbohydrates.

We have developed two procedures for the mild cleavage of anomeric *N*-glycosyl amides based on their reactions with electrophilic reagents. Furthermore, both methods have been extended to the activation of *N*-glycosyl amides as glycosyl donors in stereoselective glycosylation reactions giving 1,2-*trans*-configured *O*- and *N*-glycosides.[9]

Formation and Cleavage of *N*-Glycosyl Amides

The *O*-pivaloyl protected *N*-glycosyl amides described in this paper were synthesized from 2,3,4,6-tetra-*O*-pivaloyl-β-D-galactopyranosylamine (**1**) which is readily accessible in five steps from D-galactose.[10] Galactosylamine **1** has successfully been used as chiral auxiliary in many diastereoselective transformations.[11,12] Treatment of **1** with various acyl chlorides in dichloromethane in the presence of triethylamine gave the corresponding *N*-galactosyl amides **2**–**4** in high yields (Scheme 1, Table 1).

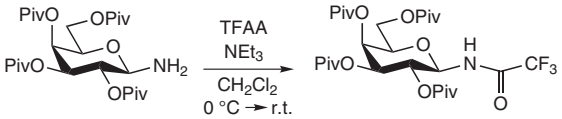


1

2 R = CH_3 97%
3 R = C_6H_5 74%
4 R = *p*-CH_3O-C_6H_4 91%

Scheme 1 Synthesis of secondary *N*-glycosyl amides from galactosylamine **1**

For the synthesis of *N*-galactosyl trifluoroacetamide **5** (Scheme 2), galactosylamine **1** was reacted with trifluoroacetic acid anhydride (TFAA).



1 **5**

Scheme 2 Synthesis of *N*-galactosyl trifluoroacetamide **5**

An unexpected reactivity of secondary *N*-glycosyl amides was observed when the pivaloyl protected *N*-galactosyl acetamide **2** was exposed to the Appel reagent PPh_3/CBr_4[13] in acetonitrile. It is known that the Appel reagent converts secondary amides to imidoyl halides.[14] The driving force of this reaction consists in the high affinity of phosphorus to oxygen resulting in the formation of triphenylphosphine oxide besides the desired imidoyl halides and the corresponding haloforms. In the case of glycosyl amide **2**, however, the reaction did not proceed to the imidoyl bromide **6**, but gave the α-configured glycosyl bromide **7** which was isolated and identified by NMR

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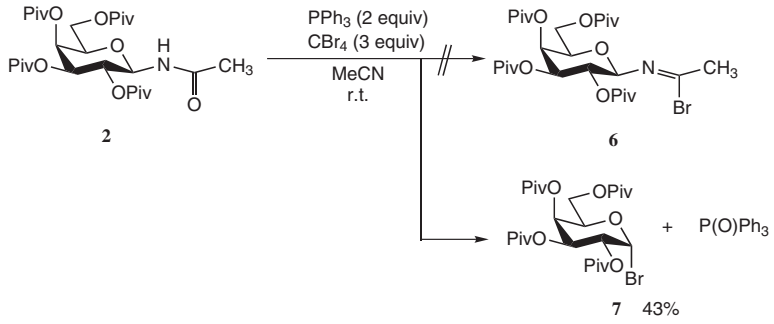
spectroscopy (Scheme 3).[15] Triphenylphosphine oxide was obtained as a by-product.

We assume that *N*-glycosyl imidoyl bromide **6** is formed as the intermediate (Scheme 4). At room temperature compound **6** spontaneously undergoes a fragmentation releasing one equivalent of acetonitrile and the acyloxonium ion **8**. The fragmentation is facilitated by the electron lone pairs of the ring oxygen atom, which favors the formation of the acyloxonium ion **8** and the release of the nitrile. With bromide anions present in the solution, the acyloxonium ion **8** gives the thermodynamically favored α-glycosyl bromide **7**. The reaction pathway from *N*-glycosyl amide **2** to α-glycosyl bromide **7** can be interpreted as a retro Ritter-reaction.[16] An amide functionality is thus converted to a nitrile by a formal E1 elimination process.

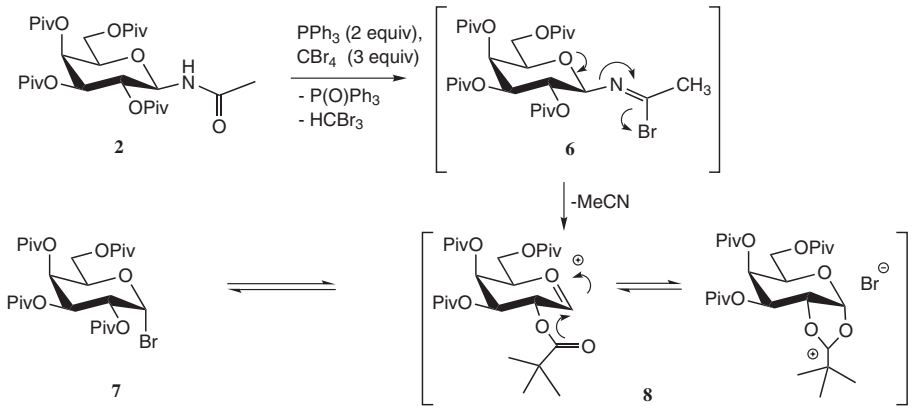
Glycosyl bromides are frequently used as glycosyl donors in Koenigs–Knorr and related reactions.[8] However, they are quite sensitive to moisture and electrophiles so that the handling and storage of these compounds sometimes is problematic. Based on the unexpected formation of glycosyl bromide **7** from *N*-glycosyl amide **2**, we developed a new glycosylation method using stable *N*-glycosyl amides as glycosyl donors.

In a first attempt, a solution of *N*-glycosyl acetamide **2** and the Appel reagent was stirred at room temperature for 4 hours before allyl alcohol and triethylamine were added (Scheme 5). The reaction of allyl alcohol with the glycosyl bromide generated in situ gave allyl orthoester **9** in 73% yield.

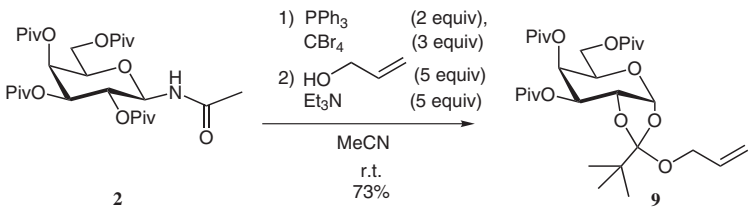
Orthoesters are undesired products of glycosylation reactions.[17] Allyl orthoester **9** was rearranged to the corresponding β-allyl glycoside **10** by catalysis with $Cu(OTf)_2$[18] in moderate yield (Scheme 6).



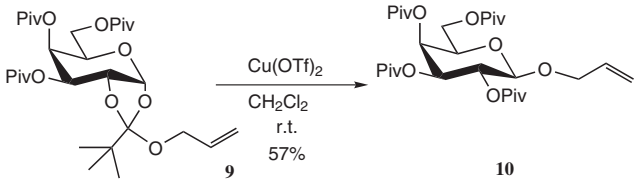
Scheme 3 Fragmentation of *N*-galactosyl acetamide **2** in the presence of the Appel reagent



Scheme 4 Proposed mechanism of the retro-Ritter reaction



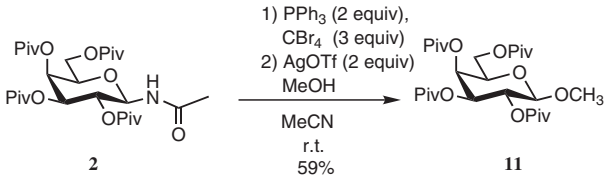
Scheme 5 Synthesis of allyl orthoester **9** from *N*-galactosyl acetamide **2**



Scheme 6 Cu(II)-catalyzed rearrangement of allyl orthoester **9** to β-allyl galactoside

Stereoselective Synthesis of *O*-Glycosides

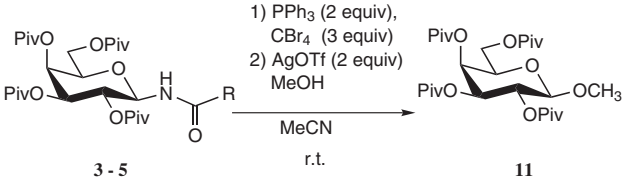
The conditions of the glycosylation reaction were then varied in order to avoid formation of orthoesters and to drive the process from *N*-glycosyl amides to the formation of the desired β-*O*-glycosides in a one-pot procedure. Methanol was chosen as glycosyl acceptor in reactions performed with different additives and under basic or non-basic conditions. It turned out that the β-*O*-methyl galactoside **11** was formed as the main product when the glycosylation reaction was performed without triethylamine, but in the presence of silver triflate[19] in acetonitrile (Scheme 7). The formation of the corresponding orthoester was not detectable by TLC. The trifluoromethanesulfonic acid generated during the reaction probably catalyses the rearrangement of the kinetically favoured orthoester to furnish the thermodynamically more stable β-*O*-methyl glycoside **11**.



Scheme 7 One-pot-synthesis of β-*O*-methyl glycoside **11** from *N*-glycosyl acetamide **2**

The β-methyl galactoside **11** was obtained in moderate yield. Using higher excess of the Appel reagent or applying higher reaction temperature did not significantly improve the yield. TLC monitoring of the reactions showed that in all cases the conversion of the glycosyl acetamide **2** to the in situ generated glycosyl bromide **7** did not exceed approximately 60%.

Considering the proposed mechanism of the activation we concluded that the low reactivity of *N*-glycosyl acetamide **2** is caused by its electronic properties. The first step of the reaction pathway probably consists of an interaction of the amide carbonyl oxygen atom and the electrophilic halophosphonium ion. We therefore assumed that the electron density of the carbonyl oxygen has marked influence on the course of the fragmentation of a *N*-glycosyl amide. To determine this influence on the efficiency of amide activation, several glycosylation reactions with *N*-glycosyl amides varying in their electronic properties were performed (Scheme 8, Table 1). The glycosylation reactions



Scheme 8

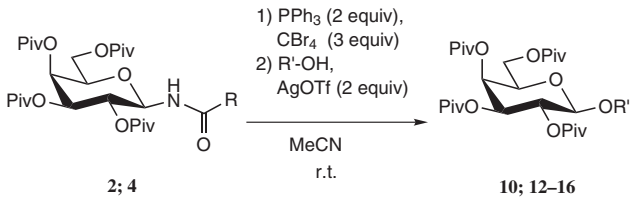
Table 1 *N*-Glycosyl Amides with Different Electronic Properties as Starting Materials in Glycosylation Reactions with Methanol

Compound	R	Yield (%)
5	CF_3	–
3	C_6H_5	60
4	*p*-$C_6H_4OCH_3$	66

with different starting materials were run with methanol as glycosyl acceptor.

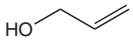
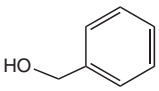
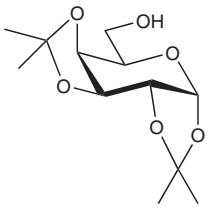
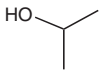
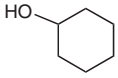
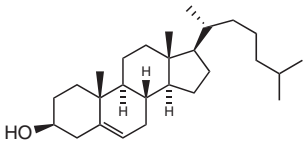
In this sense, the electron-poor *N*-glycosyl trifluoroacetamide **5** was exposed to the Appel reagent. After 4 hours at room temperature no conversion of the starting material was detectable by TLC monitoring. The basicity of the carbonyl oxygen is obviously too low to enable a sufficient interaction with the phosphorus atom. Subsequently, more electron-rich *N*-glycosyl amides were investigated. While the use of the unsubstituted *N*-glycosyl benzamide **3** as the starting material gave β-methyl glycoside **11** in a yield of 60%, the donor-substituted *N*-glycosyl anis amide **4** was converted to the desired product in 66% yield. It must be noted that in the case of the electron-rich *N*-glycosyl amide **4** the starting material was completely converted to the α-glycosyl bromide **7** at room temperature within 4 hours. This is remarkable if one keeps in mind that even with a large excess of the Appel reagent all other amides could not quantitatively be transformed to the glycosyl bromide. The electron density of the carbonyl oxygen obviously plays a key role in the efficiency of this glycosylation process.

Glycosylation reactions starting from *N*-glycosyl acetamide **2** with various primary or secondary alcohols gave stereoselectively the corresponding β-glycosides in moderate yields (Scheme 9, Table 2). However, when *N*-glycosyl anisoyl amide **4** was used as starting material in glycosylation reactions with various primary and secondary alcohols, significant improvement of the yields of the desired *O*-glycosides was achieved. Table 2 shows that



Scheme 9

Table 2 Stereoselective Synthesis of β-*O*-Glycosides from *N*-Glycosyl Acetamide **2** and *N*-Glycosyl Anisoyl Amide **4**

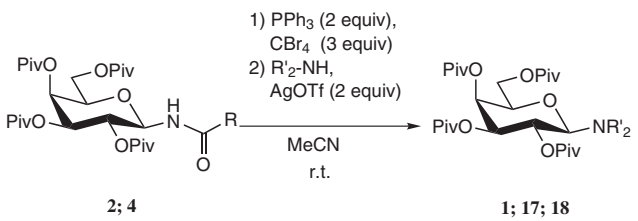
R′-OH	Product	Yield (%) from **2** (R = CH_3)	Yield (%) from **4** (R = *p*-$C_6H_4OCH_3$)
	**10**	–	89
	**12**	27	81
	**13**	38	60
	**14**	24	69
	**15**	11	83
	**16**	–	66

even sterically demanding alcohols as cholesterol and carbohydrates with labile isopropylidene protecting groups can be glycosylated in high yields. All *O*-glycosides were obtained in the β-configuration while the corresponding α-configured glycosides were not detected.

Synthesis of *N*-Glycosides

β-*N*-Glycosides are also accessible by this method. Under the conditions applied for the synthesis of *O*-glycosides the conversions of *N*-glycosyl acetamide **2** and *N*-glycosyl anisoyl amide **4** with primary and secondary amines or concentrated aqueous ammonia gave the β-configured *N*-glycosides **1**, **17**, and **18** (Scheme 10, Table 3). The corresponding α-configured *N*-glycosides were not detectable. As expected, the use of the electron-rich amide **4** resulted in higher yields of the desired products.

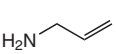
The described glycosylation procedure can likewise be applied to *O*-acetyl protected *N*-glycosyl amides



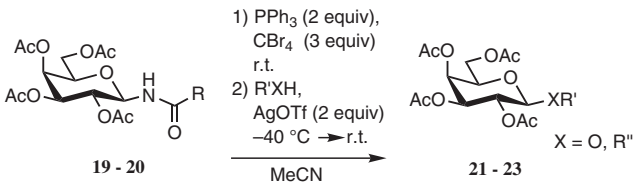
2; 4 **1; 17; 18**

Scheme 10

Table 3 Stereoselective Synthesis of β-*N*-Glycosides from *N*-Glycosyl Acetamide **2** and *N*-Glycosyl Anisoyl Amide **4**

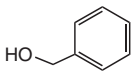
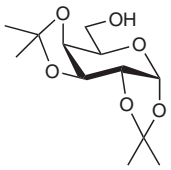
R′$_2$-NH	Product	Yield (%) from **2** (R = CH_3)	Yield (%) from **4** (R = *p*-$C_6H_4OCH_3$)
NH_3	**1**	25	79
	**17**	34	43
	**18**	45	74

(Scheme 11, Table 4). The acetyl protected *N*-glycosyl acetamide **19** and the acetyl protected *N*-glycosyl anisoyl amide **20** were prepared from the corresponding pivaloyl protected *N*-glycosyl amides **2** and **4** by simple exchange of the protecting groups. Of course, direct synthesis from *O*-acetylated glycosylamines[20] is simpler. The *O*- and *N*-glycosides **21**, **22**, and **23** were exclusively formed in the β-configuration, however with lower yields in comparison with reactions of the pivaloyl protected glycosyl donors. The decrease in yield is caused by the generally higher reactivity of acetyl-protected carbohydrates. The formation of orthoesters is a serious side-reaction with acetyl-protected glycosyl donors which can efficiently be suppressed by applying the sterically more demanding pivaloyl protecting group.[14] During the work-up the hydrolysis of the orthoesters gives anomerically deprotected carbohydrates and, therefore, lower yields of the desired glycosides.



Scheme 11

Table 4 Synthesis of *O*-Acetyl Protected β-*O*- and *N*-Glycosides

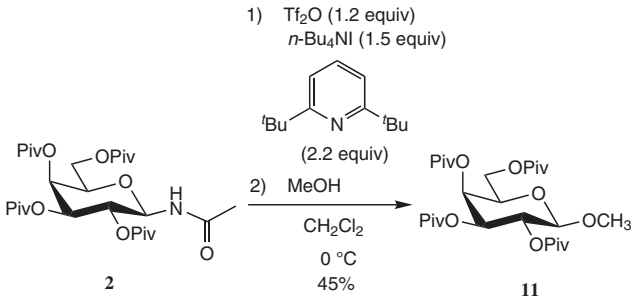
R′XH	Product	Yield (%) from **2** (R = CH_3)	Yield (%) from **4** (R = *p*-$C_6H_4OCH_3$)
	**21**	28	39
	**22**	–	39
	**23**	47	65

The results quoted in Table 4 confirm the tendency observed with pivaloyl protected *N*-glycosyl amides. The efficiency of the activation and the chemical yields of the products increases with the electron density of the amide functionality.

After elaboration of the new method for the activation of *N*-glycosyl amides with the Appel reagent we were interested in an alternative activation of the *N*-glycosyl amides without applying metal ion promotors like silver triflate. Regarding the analogy between *N*-glycosyl amides and the glycosyl donors bearing an aromatic sulfoxide at the anomeric position which were described by Kahne et al.[21] we investigated the reactivity of *N*-glycosyl amides towards trifluoromethanesulfonic acid anhydride (Tf_2O). For neutralization of the resulting trifluoromethanesulfonic acid the non-nucleophilic base 2,6-di-tert-butylpyridine was added. While at –78 °C no conversion of the *N*-glycosyl amides **2** and **4** with Tf_2O in dichloromethane or acetonitrile was observed, both amides underwent quantitative fragmentation reactions within 1 hour at 0 °C. Methanol was then added as glycosyl acceptor. In the case of the aromatic amide **4**, the resulting *p*-methoxy benzonitrile **24** was isolated in quantitative yield (Scheme 12). The desired β-*O*-methyl glycoside **11**, however, could not be isolated. Several undesired products resulting from reactions of the strongly electrophilic acyloxonium ion **8** were detected instead.

We assumed that the high reactivity of the acyloxonium ion **8** should be reduced by addition of another nucleophile like iodide to the reaction mixture. This nucleophile should form a weak covalent bond to the anomeric centre, which can later be cleaved by the glycosyl acceptor without further activation.

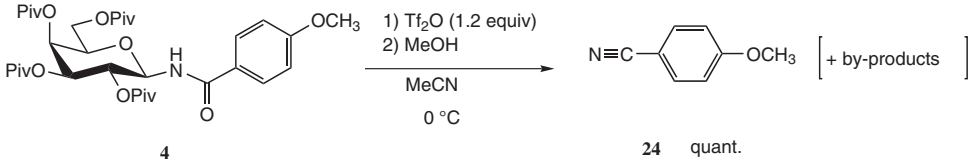
In a further variation of glycosylation of methanol with a *N*-glycosyl amide as the glycosyl donor, tetra-*n*-butylammonium iodide was used as additive in a reaction of glycosyl acetamide **2** activated with Tf_2O (Scheme 13). In this case, β-methyl glycoside **11** was isolated in moderate yield. The corresponding α-*O*-methyl glycoside was obtained as a by-product (13%). The formation of a mixture of anomeric glycosides can be explained by an acid-catalysed anomerisation of the product or by an in situ anomerisation[22] of the glycosyl iodide which is generated as the reactive glycosyl donor[23] after fragmentation of the amide functionality.



Scheme 13 Synthesis of β-*O*-glycoside **11** from *N*-glycosyl acetamide **2** by activation with Tf_2O

Further applications of this promising glycosylation procedure with more complex alcohols and amines are under investigation.

In summary, *O*-pivaloyl and *O*-acetyl protected *N*-glycosyl amides can efficiently be used as glycosyl donors in stereoselective glycosylation reactions. Despite their high stability under various harsh conditions, *N*-glycosyl amides undergo fragmentation reactions in the presence of the Appel reagent (PPh_3/CBr_4) at room temperature. Subsequent addition of alcohols or amines together with silver triflate results in the formation of *O*- and *N*-glycosides selectively in the β-configuration. Removal of labile protecting groups in the glycosyl acceptor does not occur. *N*-Glycosyl amides can alternatively be cleaved and converted to glycosyl donors by trifluoromethanesulfonic



Scheme 12 Fragmentation of *N*-glycosyl acetamide **2** with Tf_2O

acid anhydride (Tf_2O). In the presence of iodide anions, the glycosyl iodides formed as intermediates react without further activation to furnish *O*-glycosides in moderate yields.

All solvents were distilled before use. Dry solvents were prepared according to the standard procedures.[24] All reactions were carried out under an Ar atmosphere and monitored by TLC on silica gel (60 F_{254}, Merck). Detection was carried out by UV light and by staining with 1% *p*-methoxy phenol in H_2SO_4–EtOH. Melting points were determined using an apparatus according to Dr. Tottoli and are uncorrected. NMR spectra were recorded on Bruker NMR spectrometers (200 MHz ^{1}H/50 MHz ^{13}C and 300 MHz ^{1}H/75 MHz ^{13}C) using $CDCl_3$ as solvent. Elemental analyses were performed on a Heraeus CHN Vario EL-analyzer. Optical rotation was measured on a Perkin Elmer 241 polarimeter. FD-mass spectra were recorded with a Finnigan MAT 95 mass spectrometer. ESI-mass spectra were recorded with a Thermoquest mass spectrometer (cone voltage: 70 eV). Flash-chromatography was performed with silica gel (0.032–0.063 mesh).

2,3,4,6-Tetra-*O*-pivaloyl-β-D-galactopyranosylamine **1** was prepared according to the procedure in the literature.[10,20]

Acylation of *N*-(2,3,4,6-Tetra-*O*-pivaloyl-β-D-galactopyranosyl)amine (1) with Carboxylic Chlorides or Anhydrides; General Procedure

To a solution of *N*-(2,3,4,6-tetra-*O*-pivaloyl-β-D-galactopyranosyl)amine (**1,** 2.0 g, 3.88 mmol) and Et_3N (0.70 mL, 5.05 mmol) in anhyd CH_2Cl_2 (200 mL), the carboxylic chloride or anhydride (5.05 mmol) was added dropwise at 0 °C. The mixture was stirred for 1 h at 0 °C and then allowed to warm to r.t. After complete conversion of the starting material had been detected by TLC (2–6 h) the solution of the crude product was washed with sat. aq $NaHCO_3$ solution (2 × 150 mL) and sat. aq NaCl solution (150 mL). The organic layer was dried over $MgSO_4$. Removal of the solvent under reduced pressure gave the crude products, which were purified by flash chromatography (cyclohexane–EtOAc) to afford the *N*-glycosylamides in high yields.

N-(2,3,4,6-Tetra-*O*-pivaloyl-β-D-galactopyranosyl)acetamide (2)

Following the general procedure, compound **2** was prepared as a colorless crystalline solid by reaction of **1** with acetyl chloride; yield: 2.10 g, (97%); mp 108 °C; $[\alpha]_D^{25}$ +28.4 (*c* = 1, $CHCl_3$).

^{1}H NMR (200 MHz, $CDCl_3$): δ = 1.11, 1.12, 1.16, 1.25 (4 × s, 36 H, CH_3, Piv), 1.96 (s, 3 H, H-2′), 4.06 (m, 3 H, H-5, H-$6_{a/b}$), 5.10 (t, *J* = 9.8 Hz, 1 H, H-2), 5.27 (dd, *J* = 9.8, 3.4 Hz, 1 H, H-3), 5.27 (t, *J* = 9.8 Hz, 1 H, H-1), 5.45 (d, *J* = 2.9 Hz, 1 H, H-4), 6.16 (d, *J* = 9.3 Hz, 1 H, NH).

^{13}C NMR (50.3 MHz, $CDCl_3$): δ = 23.2 (C-2′), 26. 9, 27.0, 27.04, 27.1 [C(*C*H_3)$_3$, Piv], 38.7, 39.0 [*C*(CH_3)$_3$, Piv], 60.8 (C-6), 66.8, 68.3, 70.8, 72.7 (C-2–C-5), 78.5 (C-1), 169.9 (CO, amide), 176.6, 176. 9, 177.8, 178.8 (CO, Piv).

Anal. Calcd for $C_{28}H_{47}NO_{10}\cdot H_2O$: C, 58.41; H, 8.58; N, 2.51. Found: C, 58.47; H, 8.43; N, 2.34.

N-(2,3,4,6-Tetra-*O*-pivaloyl-β-D-galactopyranosyl)benzamide (3)

Following the general procedure, compound **3** was prepared as a colorless solid by reaction of **1** with benzoyl chloride; yield: 1.78 g (74%); $[\alpha]_D^{22}$ +2.0 (*c* = 1, $CHCl_3$).

^{1}H NMR (200 MHz, $CDCl_3$): δ = 1.05, 1.12, 1.14, 1.25 (4 × s, 36 H, CH_3, Piv), 3.92–4.18 (m, 3 H, H-5, H-$6_{a/b}$), 5.24 (t, *J* = 10.3 Hz, 1 H, H-2), 5.32 (dd, *J* = 10.2, 2.9 Hz, 1 H, H-3), 5.42 (t, *J* = 9.3 Hz, 1 H, H-1), 5.50 (d, *J* = 3.4 Hz, 1 H, H-4), 6.89 (d, *J* = 9.3 Hz, 1 H, NH), 7.38–8.17 (3 × m, 5 H, H_{Ar}).

^{13}C NMR (50 MHz, $CDCl_3$): δ = 26.9, 27.0, 27.1 [C(*C*H_3)$_3$, Piv], 38.7, 38.8, 39.1 [*C*(CH_3)$_3$, Piv], 60.7 (C-6), 66.8, 68.5, 70.8, 72.8 (C-2–C-5), 79.2 (C-1), 127.2, 128.7, 128.9, 130.6, 132.4 (C-2_{Ar}–C-6_{Ar}), 134.5 (C-1_{Ar}), 167.0 (CO, amide), 176.7, 177.0, 177.8, 179.2 (CO, Piv).

Anal. Calcd for $C_{33}H_{49}NO_{10}$: C, 63.95; H, 7.97; N, 2.26. Found: C, 63.57; H, 8.53; N, 2.25.

N-(2,3,4,6-Tetra-*O*-pivaloyl-β-D-galactopyranosyl)anisamide (4)

According to the general procedure, compound **4** was synthesized with *p*-methoxy-benzoyl chloride and obtained as a colorless crystalline solid; yield: 2.45 g, (98%); mp 153 °C; $[\alpha]_D^{25}$ –7.6 (*c* = 1, $CHCl_3$).

^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.04, 1.12, 1.15, 1.24 (4 × s, 36 H, CH_3, Piv), 3.83 (s, 3 H, OCH_3), 3.99 (m, 2 H, H-$6_{a/b}$), 4.16 (m, 1 H, H-5), 5.23 (t, *J* = 9.2 Hz, 1 H, H-2), 5.32 (dd, *J* = 10.3, 3.3 Hz, 1 H, H-3), 5.44 (t, *J* = 9.2 Hz, 1 H, H-1), 5.49 (d, *J* = 2.0 Hz, 1 H, H-4), 6.81 (d, *J* = 9.6 Hz, 1 H, NH), 6.90 (d, *J* = 8.8 Hz, 2 H, H-2_{Ar}, H-$2'_{Ar}$), 7.70 (d, *J* = 9.2 Hz, 2 H, H-3_{Ar}, H-$3'_{Ar}$).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 26.9, 27.0, 27.1, 27.2 [C(*C*H_3)$_3$, Piv], 38.7, 38.8, 39.0, 39.1 [*C*(CH_3)$_3$, Piv], 55.4 (OCH_3), 60.7 (C-6), 66.8, 68.5, 70.8, 72.7 (C-2–C-5), 79.3 (C-1), 113.9 (C-2_{Ar}, C-$2'_{Ar}$), 114.1 (C-3_{Ar}, C-$3'_{Ar}$), 129.1 (C-4_{Ar}), 132.8 (C-1_{Ar}), 162.8 (CO, amide), 176.4, 176.9, 177.8, 179.2 (CO, Piv).

Anal. Calcd for $C_{34}H_{51}NO_{11}$: C, 62.85; H, 7.92; N, 2.16. Found: C, 62.56; H, 8.22; N, 1.84.

N-(2,3,4,6-Tetra-*O*-pivaloyl-β-D-galactopyranosyl)trifluoroacetamide (5)

Following the general procedure, compound **5** was synthesized with trifluoroacetic acid anhydride and obtained as a colorless solid; yield: 2.09 g (88%); $[\alpha]_D^{22}$ +26.5 (*c* = 1, $CHCl_3$).

^{1}H NMR (200 MHz, $CDCl_3$): δ = 1.10, 1.14, 1.23, 1.24 (4 × s, 36 H, CH_3, Piv), 3.95–4.15 (m, 3 H, H-5, H-$6_{a/b}$), 5.14 (t, *J* = 9.3 Hz, 1 H, H-2), 5.20 (t, *J* = 8.3 Hz, 1 H, H-1), 5.27 (dd, *J* = 10.2, 3.4 Hz, 1 H, H-3), 5.46 (d, *J* = 2.4 Hz, 1 H, H-4), 7.09 (d, *J* = 8.3 Hz, 1 H, NH).

^{13}C NMR (50 MHz, $CDCl_3$): δ = 26.86, 26.9, 27.1, 27.2 [C(*C*H_3), Piv], 38.7, 38.8, 39.0, 39.1 [*C*(CH_3), Piv], 60.7 (C-6), 66.6, 68.0, 70.5, 73.4 (C-2–C-5), 78.8 (C-1), 112.5 (CF_3), 157.2 (q, $^2J_{C,F}$ = 38.5 Hz, CO, amide), 176.6, 176.9, 177.8, 178.8 (CO, Piv).

Anal. Calcd for $C_{28}H_{44}NO_{10}F_3$: C, 54.98; H, 7.25; N, 2.29. Found: C, 54.72; H, 7.21; N, 2.15.

2,3,4,6-Tetra-*O*-pivaloyl-α-D-galactopyranosyl Bromide (7)

N-(2,3,4,6-Tetra-*O*-pivaloyl-β-D-galactopyranosyl)acetamide (**2**; 300 mg, 0.54 mmol) and PPh_3 (283 mg, 1.08 mmol) were dissolved in anhyd CH_3CN (10 mL). At 0 °C a solution of CBr_4 (536 mg, 1.62 mmol) in anhyd CH_3CN (5 mL) was added dropwise. After stirring overnight the precipitate of triphenylphosphine oxide was removed by filtration. After evaporation of the solvent the residue was dissolved in Et_2O (200 mL). The organic layer was washed with sat. aq NH_4Cl (100 mL), sat aq $NaHCO_3$ (100 mL), and sat aq NaCl (2 × 100 mL) and dried over $MgSO_4$. The solvent was evaporated. Purification of the crude product by column chromatography gave **7** (135 mg, 43%) of as a colorless oil; $[\alpha]_D^{22}$ +158.0 (*c* = 1, $CHCl_3$) {Lit.[25] $[\alpha]_D^{22}$ +159.5 (*c* = 1, $CHCl_3$)}.

^{1}H NMR (200 MHz, $CDCl_3$): δ = 1.11, 1.16, 1.17, 1.23 (4 × s, 36 H, CH_3, Piv), 3.99–4.17 (m, 2 H, H-$6_{a/b}$), 4.50 (m, 1 H, H-5), 5.00 (dd, *J* = 9.8, 3.9 Hz, 1 H, H-2), 5.49 (dd, *J* = 10.0, 3.4 Hz, 1 H, H-3), 5.52 (dd, *J* = 3.4, 2.1 Hz, 1 H, H-4), 6.67 (d, *J* = 3.9 Hz, 1 H, H-1).

^{13}C NMR (50 MHz, $CDCl_3$): δ = 27.0, 27.1, 27.2 [C(CH_3)$_3$, Piv], 38.7, 38.8 [C(CH_3)$_3$, Piv], 60.5 (C-6), 66.6, 67.8, 68.1, 71.6 (C-2–C-5), 88.4 (C-1), 176.7, 177.0, 177.8 (CO, Piv).

1,2-*O*-(1-Allyloxy-2,2-dimethylpropylidene)-3,4,6-tri-*O*-pivaloyl-α-D-galactopyranose (9)

N-(2,3,4,6-Tetra-*O*-pivaloyl-β-D-galactopyranosyl)acetamide (**2**; 1.00 g, 1.80 mmol) and PPh_3 (940 mg, 3.59 mmol) were dissolved in anhyd CH_3CN (20 mL). At 0 °C a solution of CBr_4 (1.79 g, 5.39 mmol) in anhyd CH_3CN (5 mL) was added dropwise. After stirring for 4 h at r.t. a solution of allyl alcohol (0.61 mL, 8.98 mmol) and Et_3N (1.25 mL, 8.98 mmol) in CH_3CN (5 mL) was added at 0 °C. The reaction mixture was stirred for 2 h at 0 °C and overnight at r.t. The precipitate of triphenylphosphine oxide was filtered off. After evaporation of the solvent the residue was dissolved in Et_2O (200 mL). The organic layer was washed with sat aq NH_4Cl (100 mL), sat aq $NaHCO_3$ (100 mL), and sat aq NaCl (2 × 100 mL) and dried over $MgSO_4$. The solvent was evaporated. Purification of the crude product by column chromatography gave **9** (782 mg, 73%) of as a colorless oil; $[\alpha]_D^{22}$ +42.4 (c = 1, $CHCl_3$).

^{1}H NMR (200 MHz, $CDCl_3$): δ = 1.04, 1.15, 1.18, 1.21 (4 × s, 36 H, CH_3, Piv), 3.91–4.02 (m, 3 H, H-6$_a$/H-1′), 4.21 (dd, J = 10.7, 6.8 Hz, 1 H, H-6$_b$), 4.30–4.40 (m, 2 H, H-2, H-5), 5.03 (dd, J = 6.3, 2.4 Hz, 1 H, H-3), 5.07–5.32 (m, 2 H, H-3′), 5.54 (t, J = 2.9 Hz, 1 H, H-4), 5.75 (d, J = 4.9 Hz, 1 H, H-1), 5.79–5.96 (m, 1 H, H-2′).

^{13}C NMR (50 MHz, $CDCl_3$): δ = 25.25 [(RO)$_3$CC(CH_3)$_3$], 27.0, 27.05, 27.1 [C(CH_3)$_3$, Piv], 38.7 [(RO)$_3$CC(CH_3)$_3$], 38.99, 39.02 [C(CH_3)$_3$, Piv], 60.2 (C-6), 63.6 (C-1′), 66.1, 70.7, 72.5, 78.3 (C-2–C-5), 96.9 (C-1), 115.5 (C-3′), 127.5 [(RO)$_3$$C$C($CH_3$)$_3$], 134.6 (C-2′), 176.2, 177.3, 177.9 (CO, Piv).

Anal. Calcd for $C_{29}H_{48}O_{10}$: C, 62.57; H, 8.69. Found: C, 62.63; H, 8.99.

Allyl 2,3,4,6-Tetra-*O*-pivaloyl-β-D-galactopyranoside (10)

1,2-*O*-(1-Allyloxy-2,2-dimethyl-isopropylidene)-3,4,6-tri-*O*-pivaloyl-α-D-galactopyranose (**9**, 245 mg, 0.41 mmol) was dissolved in anhyd CH_2Cl_2 (5 mL) and stirred over molecular sieves (4 Å). Cu(OTf)$_2$ (30 mg, 0.08 mmol) was added. The reaction mixture was stirred for 6 h at r.t. The solvent was evaporated after filtration. The residue was purified by column chromatography yielding product **10** as a colorless solid; yield: 130 mg (57%); $[\alpha]_D^{22}$ –9.9 (c = 1, $CHCl_3$).

^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.08, 1.13, 1.16, 1.24 (4 × s, 36 H, CH_3, Piv), 3.93–4.07 (m, 3 H, H-6$_{a/b}$, H-1′$_a$), 4.13–4.19 (m, 1 H, H-5), 4.32 (dd, J = 12.9, 5.1 Hz, 1 H, H-1′$_b$), 4.53 (d, J = 8.1 Hz, 1 H, H-1), 5.08 (dd, J = 10.3, 3.3 Hz, 1 H, H-3), 5.15–5.27 (m, 3 H, H-2, H-3′$_{a/b}$), 5.39 (d, J = 2.2 Hz, 1 H, H-4), 5.76–5.84 (m, 1 H, H-2′).

^{13}C NMR (50 MHz, $CDCl_3$): δ = 27.1, 27.13 [C(CH_3)$_3$, Piv], 38.7, 39.0 [C(CH_3)$_3$, Piv], 61.2 (C-6), 66.8, 68.7, 70.97, 71.00 (C-2–C-5), 70.2 (C-1′), 100.2 (C-1), 178.0 (C-3′) 133.3 (C-2′), 176.7, 176.9, 177.3, 177.8 (CO, Piv).

Anal. Calcd for $C_{29}H_{48}O_{10}$: C, 62.57; H, 8.69. Found: C, 61.94; H, 8.69.

Glycosylation Reactions with *N*-(2,3,4,6-Tetra-*O*-pivaloyl-β-D-galactopyranosyl)anisamide (4): General Procedure

To a solution of *N*-(2,3,4,6-tetra-*O*-pivaloyl-β-D-galactopyranosyl)anis amide (**4**; 200 mg, 0.31 mmol) and PPh_3 (162 mg, 0.62 mmol) in anhyd CH_3CN (15 mL), a solution of CBr_4 (306 mg, 0.92 mmol) in anhyd CH_3CN (5 mL) was added at r.t. under Ar atmosphere. After stirring at r.t. for 4 h, a solution of the glycosyl acceptor (amounts given for each compound) and AgOTf (158 mg, 0.62 mmol) in anhyd. CH_3CN (5 mL) was added. The mixture was stirred for a period of 6–16 h and then filtered for removal of AgBr. Anhyd CH_2Cl_2 (100 mL) was added, and the solution was washed with sat aq NaCl (3 × 50 mL). The organic layer was dried over $MgSO_4$. The solvent was evaporated in vacuo and the resulting residue was purified by flash chromatography (cyclohexane–EtOAc) to afford β-configured *O*- and *N*-glycosides.

Methyl 2,3,4,6-Tetra-*O*-pivaloyl-β-D-galactopyranoside (11)

According to the general glycosylation procedure, compound **11** was prepared with anhyd MeOH (1 mL) as a colorless crystalline solid; yield: 108 mg, (66%); mp 132 °C; $[\alpha]_D^{25}$ –4.8 (c = 1, $CHCl_3$).

^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.07, 1.13, 1.15, 1.23 (4 × s, 36 H, CH_3, Piv), 3.47 (s, 3 H, OCH_3), 3.99 (m, 2 H, H-6$_{a/b}$), 4.15 (m, 1 H, H-5), 4.38 (d, J = 7.3 Hz, 1 H, H-1), 5.07 (dd, J = 10.2, 2.9 Hz, 1 H, H-3), 5.18 (dd, J = 10.7, 7.8 Hz, 1 H, H-2), 5.37 (d, J = 3.4 Hz, 1 H, H-4).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 27.0, 27.1, 27.2 [C(CH_3)$_3$, Piv], 38.7, 38.75, 38.78 [C(CH_3)$_3$, Piv], 57.1 (OCH_3), 61.2 (C-6), 66.8, 68.7, 70.9, 71.0 (C-2–C-5), 102.5 (C-1), 176.8, 176.9, 177.3, 177.7 (CO, Piv).

Anal. Calcd for $C_{27}H_{46}NO_{10}$: C, 61.11; H, 8.74. Found: C, 60.73; H, 8.96.

Benzyl 2,3,4,6-Tetra-*O*-pivaloyl-β-D-galactopyranoside (12)

According to the general glycosylation procedure, compound **12** was prepared with anhyd benzyl alcohol (1 mL) as a colorless crystalline solid; yield: 151 mg, (81%); mp 105 °C; $[\alpha]_D^{25}$ –17.9 (c = 1, $CHCl_3$).

^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.08, 1.09, 1.18, 1.25 (4 × s, 36 H, CH_3, Piv), 4.00 (m, 2 H, H-6$_{a/b}$), 4.19 (m, 1 H, H-5), 4.56 (d, J = 7.7 Hz, 1 H, H-1), 4.59 (d, J = 12.2 Hz, 1 H, H-1′$_a$), 4.86 (d, J = 11.8 Hz, 1 H, H-1′$_b$), 5.06 (dd, J = 10.3, 3.3 Hz, 1 H, H-3), 5.28 (dd, J = 10.7, 8.1 Hz, 1 H, H-2), 5.38 (d, J = 2.9 Hz, 1 H, H-4), 7.28 (m, 5 H, H$_{Ar}$).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 27.08, 27.14 [C(CH_3)$_3$, Piv], 38.7, 39.1 [C(CH_3)$_3$, Piv], 61.3 (C-6), 66.8, 68.7, 70.4, 71.0 (C-2–C-5), 71.04 (C-1′), 99.7 (C-1), 127.98, 128.04, 128.37 (C-2$_{Ar}$–C-6$_{Ar}$), 136.5 (C-1$_{Ar}$), 176.7, 176.9, 177.3, 177.9 (CO, Piv).

Anal. Calcd for $C_{33}H_{50}O_{10}$: C, 65.32; H, 8.31. Found: C, 65.05; H, 8.27.

6-*O*-(2,3,4,6-Tetra-*O*-pivaloyl-β-D-galactopyranosyl)-1,2:3,4-di-isopropylidene-α-D-galactopyranose (13)

Following the general glycosylation procedure, compound **13** was prepared from 1,2,3,4-diisopropylidenegalactopyranose (240 mg, 0.92 mmol) as a colorless crystalline solid; yield: 139.8 mg, (60%); mp 75 °C; $[\alpha]_D^{25}$ –22.4 (c = 1, $CHCl_3$). Annotation: NMR signals of the glycosyl donor are marked by ′.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.08, 1.14, 1.15, 1.23 (4 × s, 36 H, CH_3, Piv), 1.28, 1.29, 1.40, 1.47 (4 × s, 12 H, CH_3, isopropylidene), 3.62 (dd, J = 10.7, 6.6 Hz, 1 H, H-5), 3.96 (m, 4 H, H-6$_{a/b}$′, H-6$_{a/b}$), 4.15 (m, 1 H, H-5′), 4.17 (dd, J = 7.7, 1.9 Hz, 1 H, H-4), 4.24 (dd, J = 4.8, 2.2 Hz, 1 H, H-2), 4.54 (dd, J = 8.1, 2.2 Hz, 1 H, H-3), 4.56 (d, J = 7.7 Hz, 1 H, H-1′), 5.07 (dd, J = 10.7, 3.3 Hz, 1 H, H-3′), 5.20 (dd, J = 10.7, 8.1 Hz, 1 H, H-2′), 5.37 (d, J = 3.0 Hz, 1 H, H-4′), 5.44 (d, J = 5.1 Hz, 1 H, H-1).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 24.3, 24.7, 25.9, 26.1 (CH_3, isopropylidene), 27.05, 27.08, 27.13 [C(CH_3)$_3$, Piv], 38.7 [C(CH_3)$_3$, Piv], 61.0 (C-6′), 66.7, 67.2, 68.6, 69.2, 70.4, 70.6, 71.0, 71.2 (C-2′–C-5′, C-2–C-5), 96.1, 101.7 (C-1, C-1′), 108.5, 109.2 [C(CH_3)$_2$, isopropylidene], 176.8, 176.9, 177.3, 177.8 (CO, Piv).

Anal. Calcd for $C_{38}H_{62}O_{15}$: C, 60.14; H, 8.22. Found: C, 59.77; H, 7.82.

Isopropyl 2,3,4,6-Tetra-*O*-pivaloyl-β-D-galactopyranoside (14)
According to the general glycosylation procedure, glycoside **14** was synthesized with anhyd *i*-PrOH (1 mL) as a colorless crystalline solid; yield: 119 mg, (69%); mp 98 °C; $[\alpha]_D^{25}$ –4.7 (*c* = 1, $CHCl_3$).

^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.08, 1.13, 1.15, 1.23 (4 × s, 36 H, CH_3, Piv), 1.10 (d, *J* = 5.6 Hz, 3 H, H-2′), 1.20 (d, *J* = 5.6 Hz, 3 H, H-2″), 3.89 (sep, *J* = 5.9 Hz, 1 H, H-1′), 3.98 (m, 2 H, H-$6_{a/b}$), 4.14 (m, 1 H, H-5), 4.54 (d, *J* = 7.7 Hz, 1 H, H-1), 5.06 (dd, *J* = 10.7, 3.3 Hz, 1 H, H-3), 5.16 (dd, *J* = 10.7, 7.7 Hz, 1 H, H-2), 5.36 (d, *J* = 3.3 Hz, 1 H, H-4).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 22.0, 23.3 [OCH(*C*H_3)$_2$], 26.3, 27.05, 27.09, 27.2 [C(*C*H_3)$_3$, Piv], 38.69, 38.72, 39.1 [*C*(CH_3)$_3$, Piv], 61.5 (C-6), 67.0, 68.9, 70.9, 72.7 (C-2–C-5), 71.2 [O*C*H(CH_3)$_2$], 100.1 (C-1), 176.6, 177.0, 177.3, 177.9 (CO, Piv).

Anal. Calcd for $C_{29}H_{50}O_{10}$: C, 62.34; H, 9.02. Found: C, 62.34; H, 9.00.

Cyclohexyl 2,3,4,6-Tetra-*O*-pivaloyl-β-D-galactopyranoside (15)
According to the general glycosylation procedure, glycoside **15** was prepared from anhyd cyclohexanol (1 mL) as a colorless crystalline solid; yield: 154 mg, (83%); mp 112 °C; $[\alpha]_D^{25}$ +5.7 (*c* = 1, $CHCl_3$).

^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.08, 1.13, 1.15, 1.23 (4 × s, 36 H, CH_3, Piv), 1.58 (m, 10 H, $H_{cyclohexyl}$), 3.53 (m, 1 H, H-$1_{cyclohexyl}$), 3.96 (m, 2 H, H-$6_{a/b}$), 4.13 (m, 1 H, H-5), 4.58 (d, *J* = 7.7 Hz, 1 H, H-1), 5.06 (dd, *J* = 10.3, 3.3 Hz, 1 H, H-3), 5.16 (dd, *J* = 10.7, 7.7 Hz, 1 H, H-2), 5.36 (d, *J* = 3.3 Hz, 1 H, H-4).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 24.1, 25.5 (CH_2, cyclohexyl), 27.05, 27.08, 27.1, 27.2 [C(*C*H_3)$_3$, Piv], 31.7, 31.95, 33.5 (CH_2, cyclohexyl), 38.67, 38.70, 39.0 [*C*(CH_3)$_3$, Piv], 61.5 (C-6), 67.0, 68.9, 70.9, 71.2 (C-2–C-5), 78.4 (CH, cyclohexyl), 99.9 (C-1), 176.5, 177.0, 177.4, 177.9 (CO, Piv).

HRMS: *m*/*z* calcd for $C_{32}H_{54}O_{10}Na$: 621.37; found: 621.35.

Cholesteryl 2,3,4,6-Tetra-*O*-pivaloyl-β-D-galactopyranoside (16)
According to the general glycosylation procedure, glycoside **16** was synthesized from cholesterol (357 mg, 0.92 mmol) as a colorless crystalline solid; yield: 183 mg, (66%); mp 192 °C; $[\alpha]_D^{25}$ –6.3 (*c* = 1, $CHCl_3$).

^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.64 (s, 3 H, H-18), 0.82 (d, *J* = 1.1 Hz, 3 H, H-26), 0.85 (d, *J* = 1.5 Hz, 3 H, H-27), 0.88 (d, *J* = 6.6 Hz, 3 H, H-21), 0.94 (s, 3 H, H-19), 1.09, 1.15, 1.24 (3 × s, 36 H, CH_3, Piv), 1.20–1.60 (m, 21 H, CH, CH_2, chol), 1.77–1.82 (m, 2 H, CH, CH_2, chol), 1.96–2.00 (m, 3 H, CH, CH_2, chol), 2.22 (d, *J* = 7.7 Hz, 2 H, H-4), 3.43–3.46 (m, 1 H, H-3), 3.96 (m, 2 H, H-$6_{(a/b)\text{-Gal}}$), 4.14 (m, 1 H, H-5_{Gal}), 4.58 (d, *J* = 7.7 Hz, 1 H, H-1_{Gal}), 5.07 (dd, *J* = 10.3, 3.3 Hz, 1 H, H-3_{Gal}), 5.17 (dd, *J* = 10.7, 7.7 Hz, 1 H, H-2_{Gal}), 5.30 (d, *J* = 4.4 Hz, 1 H, H-6), 5.37 (d, *J* = 2.6 Hz, 1 H, H-4_{Gal}).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 11.8, 18.4, 19.3, 22.9 (CH, CH_3, chol), 23.8, 24.3, 26.9 (CH_2, chol), 27.06, 27.14, 27.2 [C(*C*H_3)$_3$, Piv], 28.0 (CH, CH_3, chol), 28.2, 29.6 (CH_2, chol), 31.9 (CH, CH_3, chol), 31.9 (CH_2, chol), 35.8 (CH, CH_3, chol), 36.2 (CH_2, chol), 36.8 (C_q, chol), 37.2 (CH_2, chol), 38.67, 38.72, 39.0 [*C*(CH_3)$_3$, Piv], 38.9, 39.5, 39.7 (CH_2, chol), 42.3 (C_q, chol), 50.1, 56.1, 56.7 (CH_2, chol), 61.4 (C-6_{Gal}), 66.9, 68.9, 70.9, 71.1 (C-2_{Gal}–C-5_{Gal}), 80.0 (C-1, chol), 100.1 (C-1_{Gal}), 122.1 (C-6, chol), 140.3 (C-5, chol), 176.6, 177.0, 177.3, 177.9 (CO, Piv).

HRMS: *m*/*z* calcd for $C_{53}H_{88}O_{10}Na$: 907.63; found: 907.62.

***N*-(2,3,4,6-Tetra-*O*-pivaloyl-β-D-galactopyranosyl)amine (1)**
According to the general glycosylation procedure, glycosylamine **1** was synthesized with concd. aq NH_3 (1 mL) as a colorless solid and identified by ^{1}H NMR spectroscopy;[10,20] yield: 124 mg (78%); $[\alpha]_D^{25}$ +8.2 (*c* = 1, $CHCl_3$), {Lit.[10] $[\alpha]_D^{25}$ +8.2 (*c* = 2, $CHCl_3$)}.

***N*-(2,3,4,6-Tetra-*O*-pivaloyl-β-D-galactopyranosyl)allylamine (17)**
Compound **17** was prepared according to the general glycosylation procedure with anhyd allylamine (1.0 mL) as a colorless oil; yield: 74 mg (43%); $[\alpha]^{22}{}_D$ +12.3 (*c* = 1, $CHCl_3$).

^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.08, 1.13, 1.15, 1.23 (4 × s, 36 H, CH_3, Piv), 1.73 (br s, 1 H, NH), 3.25 (dd, *J* = 14.6, 6.3 Hz, 1 H, H-1′$_a$), 3.46 (dd, *J* = 14.6, 5.4 Hz, 1 H, H-1′$_b$), 3.86–4.13 (m, 3 H, H-5, H-$6_{a/b}$), 4.06 (d, *J* = 8.8 Hz, 1 H, H-1), 4.97–5.06 (m, 3 H, H-2, H-3′$_{a/b}$), 5.14 (dd, *J* = 10.3, 3.4 Hz, 1 H, H-3), 5.37 (d, *J* = 2.9 Hz, 1 H, H-4), 5.66–5.82 (m, 1 H, H-2′).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 27.1, 27.2 [C(*C*H_3)$_3$, Piv], 38.7, 39.1 [*C*(CH_3)$_3$, Piv], 47.8 (C-1′), 61.6 (C-6), 67.4, 68.6, 71.4, 71.6 (C-2–C-5), 88.9 (C-1), 115.7 (C-3′), 136.4 (C-2′), 176.9, 177.2, 177.7, 177.9 (CO, Piv).

Anal. Calcd for $C_{29}H_{49}NO_{10}$: C, 62.88; H, 8.89; N, 2.52. Found: C, 62.58; H, 9.04; N, 2.53.

***N*-(2,3,4,6-Tetra-*O*-pivaloyl-β-D-galactopyranosyl)piperidine (18)**
According to the general glycosylation procedure, compound **18** was prepared from anhyd piperidine (1 mL) as a colorless oil; yield: 133 mg, (74%); $[\alpha]_D^{25}$ –3.7 (*c* = 1, $CHCl_3$).

^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.08, 1.13, 1.15, 1.22 (4 × s, 36 H, CH, Piv), 1.39 (m, 6 H,), 2.52 (m, 2 H, H-1′), 2.90 (m, 2 H, H-1″), 3.89 (m, 2 H, H-6), 3.92 (d, *J* = 7.4 Hz, 1 H, H-1), 4.10 (m, 1 H, H-5), 5.08 (dd, *J* = 10.3, 3.3 Hz, 1 H, H-3), 5.36 (m, 2 H, H-2, H-4).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 24.7, 26.3, 27.9 (CH_2, piperidine), 27.02, 27.05, 27.1 [C(*C*H_3)$_3$, Piv], 38.6, 38.7, 39.0 [*C*(CH_3)$_3$, Piv], 49.0 (CH_2, piperidine), 61.4 (C-6), 64.9, 67.3, 71.7, 72.0 (C-2–C-5), 94.7 (C-1), 176.8, 176.9, 177.2, 177.9 (CO, Piv).

Anal. Calcd for $C_{31}H_{53}NO_9$: C, 63.78; H, 9.15; N, 2.40. Found: C, 63.80; H, 9.13, N, 2.38.

Glycosylation Reactions with *N*-(2,3,4,6-Tetra-*O*-acetyl-β-D-galactopyranosyl)anisamide 20; General Procedure
To a solution of *N*-(2,3,4,6-tetra-*O*-acetyl-β-D-galactopyranosyl)anisamide (**20**; 200 mg, 0.42 mmol) and PPh_3 (218 mg, 0.83 mmol) in anhyd CH_3CN (15 mL) a solution of CBr_4 (413 mg, 1.25 mmol) in anhyd CH_3CN (5 mL) was added at r.t. under Ar atmosphere. After stirring at r.t. for 4 h, the reaction mixture was cooled to –40 °C, and a solution of the glycosyl acceptor (amounts given for each compound) and AgOTf (213 mg, 0.83 mmol) in anhyd CH_3CN (5 mL) was added. While slowly warming up to r.t., the mixture was stirred for a period of 6–16 h and then filtered for removal of AgBr. Anhyd CH_2Cl_2 (100 mL) was added, and the solution was washed with sat aq NaCl (3 × 50 mL). The organic layer was dried over $MgSO_4$. The solvent was evaporated under reduced pressure and the resulting residue was purified by flash chromatography (cyclohexane–EtOAc) to afford β-configured *O*- and *N*-glycosides.

Benzyl 2,3,4,6-Tetra-*O*-acetyl-β-D-galactopyranoside (21)
According to the general glycosylation procedure, compound **21** was prepared from anhyd benzyl alcohol (1 mL) as a colorless oil; yield: 71 mg, (39%); $[\alpha]_D^{25}$ –27.1 (*c* = 1, $CHCl_3$).

^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.95, 1.98, 2.04, 2.13 (4 × s, 12 H, CH_3, Ac), 3.86 (t, *J* = 6.2 Hz, 1 H, H-5), 4.10–4.23 (m, 2 H, H-$6_{a/b}$), 4.49 (d, *J* = 8.1 Hz, 1 H, H-1), 4.61 (d, *J* = 12.1 Hz, 1 H, H-1′$_a$), 4.88 (d, *J* = 12.5 Hz, 1 H, H-1′$_b$), 4.96 (dd, *J* = 10.3, 2.9 Hz, 1 H, H-3), 5.25 (dd, *J* = 10.3, 8.1 Hz, 1 H, H-2), 5.36 (d, *J* = 2.6 Hz, 1 H, H-4), 7.26–7.31 (m, 5 H, H_{Ar}).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 20.5, 20.66, 20.70 (CH_3, Ac), 61.3 (C-6), 67.0, 68.8, 70.7, 70.9 (C-2–C-5), 70.7 (C-1′), 99.8 (C-1), 127.7, 127.98, 128.4 (C-2_{Ar}–C-6_{Ar}), 136.7 (C-1_{Ar}), 169.4, 170.1, 170.2, 170.4 (CO, Ac).

MS (FD): *m*/*z* calcd for $C_{21}H_{26}O_{10}$: 438.2; found: 439.3

6-*O*-(2,3,4,6-Tetra-*O*-acetyl-β-D-galactopyranosyl)-1,2:3,4-di-isopropylidene-α-D-galactopyranose (22)

According to the general glycosylation procedure, disaccharide **22** was synthesized from 1,2,3,4-diisopropylidene-α-D-galactopyranose (101 mg, 0.39 mmol) as a colorless amorphous solid; yield: 68 mg, (39%); $[\alpha]_D^{25}$ –42.3 (*c* = 1, $CHCl_3$). Annotation: NMR-signals of the glycosyl donor are marked by ′.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.29, 1.39, 1.41, 1.47 (4 × s, 12 H, CH_3, Ac), 1.95, 2.01, 2.05, 2.10 (4 × s, 12 H, CH_3, isopropylidene), 3.61–3.67 (m, 1 H, H-5′), 3.84–3.91 (m, 2 H, H-$6_{(a/b)'}$), 3.98–4.03 (m, 1 H, H-5), 4.10–4.13 (m, 2 H, H-$6_{a/b}$), 4.14 (dd, *J* = 7.4, 1.5 Hz, 1 H, H-4), 4.26 (dd, *J* = 4.8, 2.6 Hz, 1 H, H-2), 4.53–4.60 (m, 1 H, H-3), 4.55 (d, *J* = 7.7 Hz, 1 H, H-1′), 4.99 (dd, *J* = 10.7, 3.3 Hz, 1 H, H-3′), 5.18 (dd, *J* = 10.7, 8.1 Hz, 1 H, H-2′), 5.35 (d, *J* = 3.0 Hz, 1 H, H-4′), 5.46 (d, *J* = 4.8 Hz, 1 H, H-1).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 20.57, 20.63, 20.76 (CH_3, Ac), 24.3, 25.0, 25.9, 26.0 (CH_3, isopropylidene), 61.2 (C-6′), 67.1, 67.9, 65.6, 69.6, 70.4, 70.56, 70.64, 70.82, 71.3 (C-2′–C-5′, C-2–C-6), 96.2, 102.0 (C-1′, C-1), 108.7, 109.4 [$C(CH_3)_2(OR)_2$, isopropylidene], 169.7, 170.1, 170.2, 170.4 (CO, Ac).

Anal. Calcd for $C_{26}H_{38}O_{15}$: C, 52.88; H, 6.49. Found: C, 52.43; H, 7.02.

***N*-(2,3,4,6-Tetra-*O*-acetyl-β-D-galactopyranosyl)piperidine (23)**

According to the general glycosylation procedure, glycosylamine **23** was prepared from anhyd piperidine (1 mL) as a colorless oil; yield: 112 mg, (65%); $[\alpha]_D^{25}$ +1.5 (*c* = 1, $CHCl_3$).

^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.39–1.53 (m, 5 H, H-2′, H-2″$_a$, H-3′), 1.95, 2.00, 2.01, 2.11 (4 × s, 12 H, CH_3, Ac), 2.48–2.51 (m, 2 H, H-2″$_b$/H-1′$_a$), 2.87–2.93 (m, 2 H, H-1′$_b$/H-1″$_a$), 3.13–3.15 (m, 1 H, H-1″$_b$), 3.74–3.79 (m, 1 H, H-5), 3.90 (d, *J* = 9.2 Hz, 1 H, H-1), 3.99–4.13 (m, 2 H, H-$6_{a/b}$), 4.98 (dd, *J* = 10.3, 3.3 Hz, 1 H, H-3), 5.27 (t, *J* = 8.8 Hz, 1 H, H-2), 5.33 (d, *J* = 3.3 Hz, 1 H, H-4).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 20.67, 20.72, 20.9 (CH_3, Ac), 25.8, 26.3, 26.9 (C-2′, C-2″, C-3′), 47.9, 49.1 (C-1′, C-1″), 61.4 (C-6), 65.3, 67.4, 71.5, 72.1 (C-2–C-5), 94.9 (C-1), 169.7, 170.2, 170.3, 170.4 (CO, Ac).

MS (ESI): *m*/*z* calcd for $C_{19}H_{29}NO_9$: 415.2; found: 438.0.

MS (ESI): *m*/*z* (%) = (21) $[M + Na]^+$, 356.0 (86), 296.1 (45), 254.1 (100).

Activation of *N*-Glycosyl Amides with Trifluoromethanesulfonic Acid Anhydride (Tf_2O): Methyl-2,3,4,6-tetra-*O*-pivaloyl-β-D-galactopyranoside (11); General Procedure

N-(2,3,4,6-Tetra-*O*-pivaloyl-β-D-galactopyranosyl)acetamide (**2**; 100 mg, 0.18 mmol), tetra-*n*-butylammonium iodide (99 mg, 0.27 mmol), and 2,6-di-*tert*-butylpyridine (89 μL, 0.40 mmol) were dissolved in anhyd CH_2Cl_2 (10 mL). Trifluoromethanesulfonic acid anhydride (33 μL, 0.20 mmol) was added at 0 °C. After stirring for 1 h at 0 °C, MeOH (0.2 mL) was added. The mixture was stirred at 0 °C for 1 h and overnight at r.t. After addition of CH_2Cl_2 (150 mL) the organic layer was washed with sat aq NaCl (2 × 100 mL) and dried over $MgSO_4$. The solvent was evaporated. The crude product was purified by column chromatography; yield: 43 mg (45%).

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