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Computational and experimental studies of reactive intermediates in glycosylation reactions

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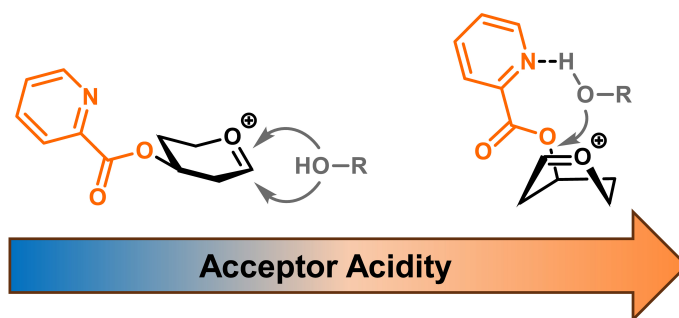
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Chapter 8 |

Influence of Acceptor Acidity on Hydrogen bond Mediated Aglycone Delivery (HAD) Through the Picoloyl Protecting Group

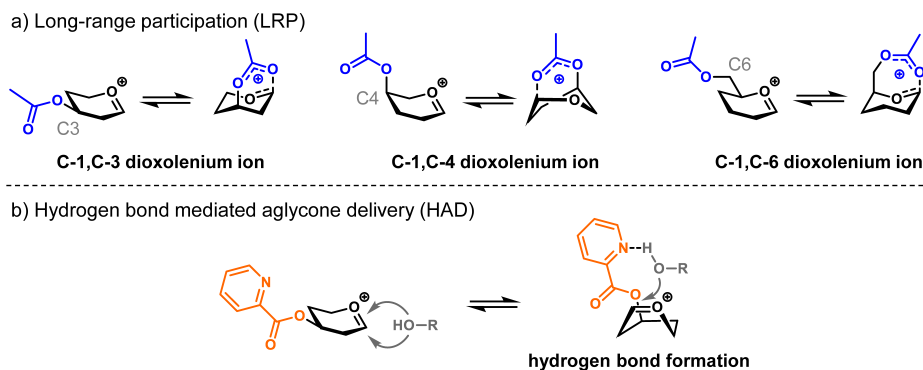


Abstract | The outcome of glycosylation reactions heavily relies on the specific protecting group patterns employed on both the donor and acceptor molecules. The picoloyl (Pico) protecting group stands out as it can steer the stereoselectivity in a glycosylation reaction through hydrogen bond mediated aglycone delivery (HAD). This glycosylation mechanism provides *syn*-stereoselectivity, with respect to the stereochemistry of the Pico group, by forming a hydrogen bond between the incoming acceptor and the picoloyl ring nitrogen. Here, the influence of acceptor acidity on the stereodirecting effect of the picoloyl protecting group is probed. A set of 3-*O*-functionalized glucosyl and mannosyl donors, each bearing different protecting groups (picolinate, nicotinate, isonicotinate, and benzoate), were synthesized for systematic evaluation. For the 3-*O*-picoloyl-glucose series, the picoloyl group exhibited minimal influence on stereoselectivity, with only weak nucleophiles showing a modest shift in selectivity for the 3-*O*-Pico protected glucosyl donor in comparison to the other C-3-acyl glucosides. In contrast, in the 3-*O*-picoloyl-mannose series a much stronger β -directing effect was observed, wherein more acidic acceptors led to increased β -selectivity. The results provide insights into the complex interplay of acceptor acidity and glycosylation stereoselectivity mediated by the picoloyl protecting group.

Introduction

One of the principal challenges in oligosaccharide synthesis is the stereoselective formation of glycosidic bonds. The stereochemical outcome of glycosylation reactions is highly dependent on the protecting group patterns on both the donor and acceptor molecule.^{1–4} Therefore, steering the reaction towards the desired stereoisomer requires careful selection of protecting groups.^{5–7} In recent years, there has been much interest in strategies that employ protecting groups on remote positions (C-3, C-4, or C-6) to influence the stereochemical outcome of glycosylation reactions, when one cannot rely on neighboring-group participation (NGP) from C-2.^{8–10}

There are two distinct categories of strategies employing remote protecting groups: those that form covalent intermediates, and those that act through non-covalent interactions.¹¹ The first category includes the long-range participation (LRP) by remote ester groups to form a bridged bicyclic intermediate.^{12–23} These bridged bicyclic intermediates direct the stereoselectivity to provide the *anti*-products, with respect to the orientation of the ester moiety, by blocking one side of the carbohydrate ring (Scheme 1a). In the latter category, the most common strategy is the hydrogen bond mediated aglycone delivery (HAD) developed by the group of Demchenko.^{24,25} In this methodology, a remote position is functionalized with a protecting group capable of acting as a hydrogen-bond acceptor. The most common protection group used in this category, due to its advantageous installation²⁶ and deprotection conditions,²⁷ is the picoloyl ester (Pico). Contrary to the reactions of the dioxanum ions, this protecting group steers the stereoselectivity of glycosylation reactions to provide the *syn*-products with respect to the position of the Pico-group. The picoloyl ester influences the stereochemical outcome of glycosylation reactions by formation of a hydrogen bond between the picoloyl ring nitrogen atom and the glycosyl acceptor (Scheme 1b). Support for this *modus operandi* has been delivered by a plethora of reactions, involving various donors featuring the picoloyl ester on various carbohydrate positions, providing *syn*-stereoselectivity.^{28–40} While much effort has been devoted to screening the substrate scope and tuning reaction conditions,^{41–43} the role of the acceptor on HAD has not been studied systematically. Generally, stronger *O*-nucleophiles are less acidic and thus exhibit weaker hydrogen bonding.⁴⁴ Given the central role of the hydrogen bond within the HAD mechanism, the hydrogen-bonding capacity of the *O*-acceptor is likely to be important.⁴⁵



Scheme 1. (a) A schematic representation of the possible reactive intermediates in long range participation (LRP). (b) Hydrogen bond mediated aglycone delivery (HAD) by the picoloyl protecting group, mounted at C-3.

Here, the role of acceptor acidity on HAD is studied through a systematic investigation of 3-*O*-picoloyl-glucosyl and mannosyl donors in combination with a set of acceptors of gradually increasing acidity. To this end, the C-3-hydroxyl group was functionalized with benzyl, benzoate, picoloyl, and picoloyl-related protecting groups. Subsequently, the effect of acceptor acidity on the stereoselective outcome of glycosylation reactions was examined, employing these donors. This study shows that more acidic, *i.e.*, less nucleophilic, *O*-acceptors are better at hydrogen bond mediated aglycone delivery. The results provide insights into how acceptor tuning can be utilized to optimize the stereoselectivity provided by the picoloyl protecting group.

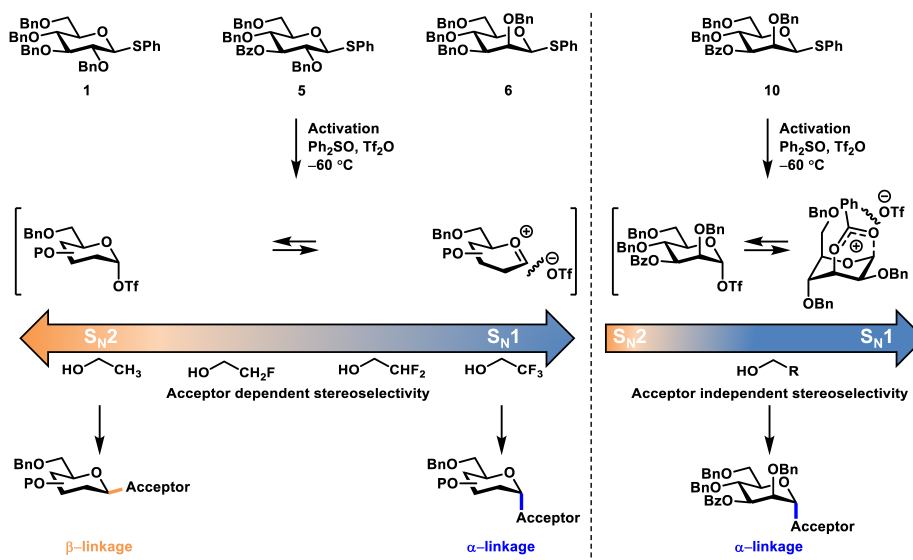
Results and Discussion

To investigate the influence of acceptor acidity on the HAD mechanism, first acceptor acidity-stereoselectivity trends for a set of glucosyl and mannosyl donors was established. As model acceptors, a set of partially fluorinated ethanol derivatives (*i.e.*, 2,2,2-trifluoroethanol, TFE; 2,2-difluoroethanol, DFE; 2-fluoroethanol, MFE; ethanol, EtOH) was used, which are well-established as model acceptors.^{46,47} These model acceptors exhibit a gradual increase of acidity along the acceptor series, making this set of alcohols a powerful tool for investigating the acidity-stereoselectivity relationship. As for the donor systems, a set of glucosyl and mannosyl donors was employed, that are protected with benzyl ethers or a benzyl ether and benzylidene acetal to mask the C-2, C-4, and C-6 hydroxyl functions, placing different protecting groups at the C-3-OH. These donor systems were chosen because previous research has shown the HAD mechanism to be relevant for mannosyl 3-*O*-picoloyl donors, while playing a less important role for the glucosyl 3-*O*-picoloyl-donors.^{42,43} Furthermore, the structurally related 3-*O*-benzoyl glucosyl and -mannosyl donors were investigated in chapter 7, which provide strikingly disparate stereoselectivities in their glycosylation reactions.⁴⁸ While LRP plays an important role in the mannosylation reactions (providing the α -products), the benzoyl ester played no major role in the glycosylation reactions of the corresponding glucosyl donors, where the stereoselectivity of the reactions critically depended on the nucleophilicity of the acceptors. This stark contrast in the reaction mechanism and the resulting stereoselectivity make the glucosyl and mannosyl 3-*O*-protected donors an excellent system to investigate the acceptor acidity-stereoselectivity trends, and establish how they depend on the available reaction paths (Scheme 2).

To verify that any trend arising from the picoloyl protecting group is the result of HAD, donors were included in the experimental set-up that are structurally and electronically similar to the picoloyl protecting group. The nicotinate (Nico, *N* at *meta* position) and *iso*-nicotinate (*i*-Nico, *N* at *para* position) protecting groups are picoloyl-regioisomers having the pyridine nitrogen at different positions in the ring. These protecting groups have similar electron-withdrawing properties as the picoloyl protecting group but are likely less capable of HAD because hydrogen bonding with these groups would orient the acceptor too far away from the anomeric center of the donor.^{42,49}

Lastly, in the experimental design, Ph₂SO/Tf₂O⁵⁰ mediated pre-activation conditions were used, which transform the parent donors into the corresponding glycosyl triflates prior to the addition of the acceptor.⁵¹ This method of activation is well suited for this study, as it generates well-defined reactive intermediates without the use of a Brønsted acid. The non-acidic conditions are essential to study the influence of acceptor acidity, because protonation of the picoloyl group can preclude HAD.^{49,52} To scavenge the TfOH released in the glycosylation reactions upon attack of the alcohol on the activated glycosyl donors, a non-nucleophilic base was included in the reaction mixtures. To confirm that protonation of the Pico group does not affect the stereochemical outcome of the glycosylation reactions,⁵³ the use of different equivalents (2.5 or 10) of 2,4,6-*tert*-butylpyrimidine (TTBP), 2,6-di-*tert*-butylpyrimidine, and 2,4,6-tri-*tert*-butylpyridine, having pK_aH values of 1.02, 3.58, and 4.02, respectively, was briefly explored. No effect of

these bases was observed on the stereoselectivity (See Supplementary Table 1) and therefore the application of the commonly used TTBP was continued in this study.

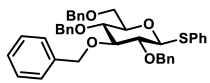
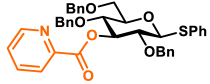
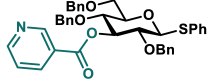
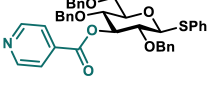
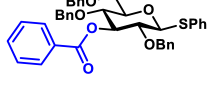


Scheme 2. General mechanism of glycosylations employing the $\text{Ph}_2\text{SO}/\text{Tf}_2\text{O}$ mediated pre-activation conditions.

Based on this experimental design, the set of 3-*O*-protected phenyl 2,4,6-*O*-benzyl-1-thio-glucosyl **1-5** and mannosyl donors **6-10** (See Table 1 and 2) were generated, on which the following 3-*O* protecting groups were installed: benzyl (**1** and **6**), picolinate (**2** and **7**), nicotinate (**3** and **8**), isonicotinate (**4** and **9**), and benzoyl (**5** and **10**). Each donor was treated with the four model acceptors (TFE, DFE, MFE and EtOH), and the stereoselective outcome was recorded (Tables 1-4). Results from the 3-*O*-benzyl and 3-*O*-benzoyl donors were taken from previous work, and are provided for comparison.¹² The results of the glycosylations with the 3-*O*-benzyl donors **1** and **5** show the 'intrinsic' stereoselectivity of the donors under the used glycosylation conditions, while the glycosylations with the 3-*O*-benzoyl donors **6** and **10** show the influence of acyl groups on this selectivity.

First, the acceptor acidity-stereoselectivity relationship for glucosyl donors **1-5** was explored. As previously described,^{47,54} the stereoselectivity of the glycosylation reactions of the 2,4,6-tri-*O*-benzyl glucose **1** and **5** gradually shifts from α - to β -stereoselectivity as the nucleophilicity of the acceptor increases.⁴⁶ The 3-*O*-Pico-glucosyl donor **2**, and the Nico and *i*-Nico stereoisomer counterparts **3** and **4** show identical trends. The lack of stereochemical steering of the Pico-type esters is in line with the observations of the group of Demchenko.⁵⁵ They have shown that β -selective glycosylations can be achieved using 3-*O*-picoloyl-glucosyl donors by protonation of the picoloyl nitrogen using an excess of acid, which serves to stabilize a covalent α -triflate intermediate.^{49,52} Thus, under the essentially neutral pre-activation reaction conditions used here, no β -directing effect would be expected.

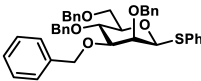
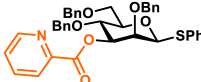
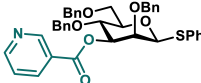
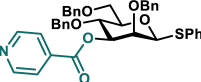
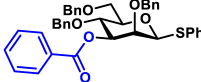
Table 1. Experimentally found stereoselectivities for model glycosylation reactions with the phenyl 2,4,6-tri-*O*-benzyl-1-thio glucosyl donors **1-5**; Experimental conditions: pre-activation-based glycosylation conditions; nucleophile (2 equiv), Tf₂O (1.3 equiv), Ph₂SO (1.3 equiv), TTBP (2.5 equiv), DCM (0.05 M), –80 to –60 °C. The stereoselectivity of the reaction is expressed as $\alpha:\beta$ and based on ¹H-NMR of the purified compounds. In all cases, the NMR spectra for both the crude and purified compounds were compared to analyze whether the measured stereoselectivity did not alter upon purification.

							
Donor	Product $\alpha:\beta$ (yield)	Product $\alpha:\beta$ (yield)	Product $\alpha:\beta$ (yield)	Product $\alpha:\beta$ (yield)			
1 	15:85 ^[a] (70%)	36:64 ^[a] (75%)	48:52 ^[a] (58%)	72:28 ^[a] (80%)			
2 	28:72 (43%)	36:64 (39%)	46:54 (50%)	49:51 (55%)			
3 	20:80 (48%)	40:60 (50%)	41:59 (47%)	47:53 (51%)			
4 	19:81 (46%)	32:68 (50%)	50:50 (52%)	65:35 (31%)			
5 	15:85 ^[a] (76%)	34:66 ^[a] (82%)	48:52 ^[a] (70%)	79:21 ^[a] (76%)			
>90:10	>80:20	>60:40	50:50	<40:60	<20:80	<10:90	($\alpha:\beta$)

^[a] Results from Hansen *et al.*,¹² identical glycosylation conditions were used.

Next, the reactivity-stereoselectivity trends for the mannosyl donors **6-10** (Table 2) was examined. The stereoselectivity of the glycosylations with the 3-*O*-benzyl-mannosyl donor **6** gradually shifts from α - to β -stereoselectivity as the nucleophilicity of the acceptor increases, while the 3-*O*-benzoyl-mannosyl donor **10** solely provides the α -linked products. These can originate from a 1,3-dioxanium ion intermediate formed by a long-range participation mechanism.^{12,56-58} The introduction of a nitrogen atom in the benzoyl ring on either the *meta* (Nico donor **8**) or the *para*-position (*i*-Nico donor **9**), leads to a slightly decreased stereoselectivity in the reactions. In contrast to donors **8** and **9**, the 3-*O*-picoloyl mannose donor **7** provides product mixtures with both anomers in approximately similar amounts for ethanol, MFE and DFE. TFE, the most acidic acceptor of the series, provides a modestly β -selective glycosylation, which in light of the benchmark results obtained for this acceptor with benzyl donor **6** and benzoyl mannoside **10**, stands out (Table 2). The increased β -selectivity in the reactions of the 3-*O*-Pico donor **7** can be explained by a HAD mechanism, with the most acidic acceptor experiencing the strongest stereochemical guidance.

Table 2. Experimentally found stereoselectivities for model glycosylation reactions with the phenyl 2,4,6-tri-*O*-benzyl-1-thio mannosyl donors **6-10**; Experimental conditions: pre-activation-based glycosylation conditions; nucleophile (2 equiv), Tf₂O (1.3 equiv), Ph₂SO (1.3 equiv), TTBP (2.5 equiv), DCM (0.05 M), –80 to –60 °C. The stereoselectivity of the reaction is expressed as α:β and based on ¹H-NMR of the purified compounds. In all cases, the NMR spectra for both the crude and purified compounds were compared to analyze whether the measured stereoselectivity did not alter upon purification.

							
Donor	Product α:β (yield)	Product α:β (yield)	Product α:β (yield)	Product α:β (yield)			
6 	33:67 ^[a] (70%)	60:40 ^[a] (75%)	80:20 ^[a] (65%)	>98:2 ^[a] (84%)			
7 	55:45 (58%)	55:45 (32%)	50:50 (48%)	31:69 (59%)			
8 	85:15 (53%)	85:15 (60%)	85:15 (69%)	86:14 (60%)			
9 	90:10 (73%)	88:12 (94%)	86:14 (72%)	84:16 (83%)			
10 	>98:2 ^[a] (94%)	>98:2 ^[a] (87%)	>98:2 ^[a] (87%)	>98:2 ^[a] (79%)			
>90:10	>80:20	>60:40	50:50	<40:60	<20:80	<10:90	(α:β)

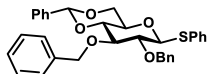
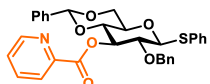
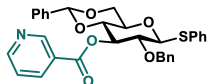
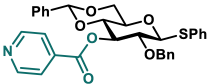
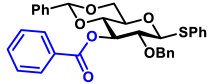
^[a] Results from Hansen *et al.*,¹² identical glycosylation conditions were used.

Finally, the 4,6-*O*-benzylidene-mannosyl and glucosyl donor systems were considered. The 4,6-*O*-benzylidene mannose system has been introduced for the generation of β -mannosidic linkages (*i.e.*, the β -Crich-mannosylation).^{59,60} This preference of 4,6-*O*-benzylidene mannosyl donors in forming the β -product is generally considered to be the result of a S_N2 -like attack on the anomeric α -triflate, which is stabilized for these donors due to the conformational tethering of C-4 and C-6. However, LRP by C-3-acyl groups can completely overturn the β -selectivity in this system.^{23,46,61} In the corresponding glucose case, the α - and β -triflates play a role, with the latter becoming the more important reactive intermediate in the reaction with decreasing nucleophilicity of the acceptor.^{46,47,54} In contrast to the mannosyl system, LRP has been shown not to play a significant role in the glycosylations of the C-3-*O*-acyl donors.⁴⁸ As a result, the question arose whether the introduction of a 3-*O*-picoloyl protecting group would provide a stereoselectivity trend consistent with either a LRP, HAD, or β -Crich-mannosylation mechanism.⁶¹

Thus, the set of phenyl 2-*O*-benzyl-4,6-*O*-benzylidene-1-thio-glucosyl donors, carrying a 3-*O*-benzyl (**11**), picolinate (**12**), nicolinate (**13**), isonicolinate (**14**), or benzoate (**15**) at C-3 and the corresponding mannosides **16–21** were generated. Table 3 reports the stereochemical outcome of the model glycosylations with the glucosyl donors, while the results of the mannosylation reactions are reported in Table 4. The data for 3-*O*-benzyl and 3-*O*-benzoyl donors **11**, **15**, **16**, and **21** have previously been reported.^{46,48} In line with the results displayed in Table 1, the nature of the C-3-*O*-protecting group has relatively little influence on the stereoselectivity of the reactions of the 4,6-*O*-benzylidene glucosyl donors **11–15**, although the formation of the β -products slightly increases when the picoloyl, nicoloyl and *i*-nicoloyl groups are used (Table 3).

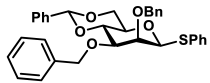
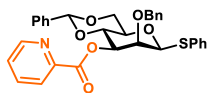
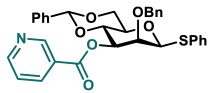
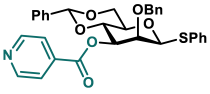
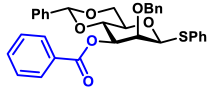
In contrast to the benzylidene glucose series, the benzylidene mannose series shows different stereoselectivity for the C-3-acyl donors in comparison to the C-3-benzylated donor (Table 4). 3-*O*-Benzyl donor **16** provides β -selective glycosylations, while installation of a 3-*O*-benzoyl group (donor **20**) completely overturns this stereoselectivity, leading to complete α -selectivity for all acceptors.⁴⁸ In contrast, the donors with the Pico- (donor **17**), Nico (donor **18**) and *i*-Nico (donor **19**) groups provide anomeric mixtures in which the amount of β -product increases with increasing acidity/lower nucleophilicity of the acceptors, indicating that LRP in these latter systems is less effective. Noticeable are the contrast with the results in Table 2, where the effect of the different C-3-acyl groups seems to differ significantly less. It was hypothesized that these differences can be explained by destabilization of the intermediate 1,3-dioxanium ion formed from the different donors. The 1,3-dioxanium ions of the benzylidene-protected donors are less stable because of the increased ring strain in these ions,⁴⁸ forcing the dioxanium ion to take up a $B_{2,5}$ -type conformation instead of the more favorable 1C_4 conformation that can be attained by the 4,6-di-*O*-benzyl donors. The results indicate that the stability of the 1,3-dioxanium ions (as gauged by the α -selectivity of the reactions) further decreases with the introduction of a ring nitrogen in the acyl groups, with the destabilizing inductive effect of the ring nitrogen increasing with diminishing the distance to the dioxanium ion (Pico > Nico > *i*-Nico, as seen from Supplementary Table 2). The Pico-group shows the strongest β -directing effect, with β -selectivity increasing with increasing acceptor acidity. This trend is consistent with a scenario in which there is competition between LRP and HAD mechanisms, in which the most acidic nucleophiles prefer the latter.

Table 3. Experimentally found stereoselectivities for model glycosylation reactions with the phenyl 2-*O*-benzyl-4,6-*O*-benzylidene-1-thio-glucosyl donors **11–15**; Experimental conditions: pre-activation-based glycosylation conditions; nucleophile (2 equiv), Tf₂O (1.3 equiv), Ph₂SO (1.3 equiv), TTBP (2.5 equiv), DCM (0.05 M), –80 to –60 °C. The stereoselectivity of the reaction is expressed as α:β and based on ¹H-NMR of the purified compounds. In all cases, the NMR spectra for both the crude and purified compounds were compared to analyze whether the measured stereoselectivity did not alter upon purification.

								
Donor	Product α:β (yield)	Product α:β (yield)	Product α:β (yield)	Product α:β (yield)				
11 	30:70 ^[a] (80%)	50:50 ^[a] (65%)	82:18 ^[a] (95%)	>98:2 ^[a] (74%)				
12 	<2:98 (39%)	24:76 (49%)	58:42 (31%)	74:26 (28%)				
13 	<2:98 (47%)	26:74 (69%)	65:35 (42%)	>98:2 (60%)				
14 	16:84 (51%)	28:72 (37%)	80:20 (57%)	97:3 (53%)				
15 	25:75 ^[a] (quant.)	45:55 ^[a] (quant.)	85:15 ^[a] (74%)	>98:2 ^[a] (84%)				
	>90:10	>80:20	>60:40	50:50	<40:60	<20:80	<10:90	(α:β)

^[a] Results from Remmerswaal *et al.*,⁴⁸ identical glycosylation conditions were used.

Table 4. Experimentally found stereoselectivities for model glycosylation reactions with the phenyl 2-*O*-benzyl-4,6-*O*-benzylidene-1-thio-mannosyl donors **16-20**; Experimental conditions: pre-activation-based glycosylation conditions; nucleophile (2 equiv), Tf₂O (1.3 equiv), Ph₂SO (1.3 equiv), TTBP (2.5 equiv), DCM (0.05 M), -80 to -60 °C. The stereoselectivity of the reaction is expressed as α:β and based on ¹H-NMR of the purified compounds. In all cases, the NMR spectra for both the crude and purified compounds were compared to analyze whether the measured stereoselectivity did not alter upon purification.

							
Donor	Product α:β (yield)	Product α:β (yield)	Product α:β (yield)	Product α:β (yield)			
16 	23:77 ^[a] (51%)	18:82 ^[a] (59%)	17:83 ^[a] (61%)	19:81 ^[a] (55%)			
17 	73:27 (71%)	69:31 (51%)	55:45 (64%)	32:68 (64%)			
18 	80:20 (48%)	72:28 (38%)	68:32 (50%)	58:42 (54%)			
19 	>98:2 (54%)	83:17 (59%)	73:27 (61%)	50:50 (36%)			
20 	>98:2 ^[a] (73%)	>98:2 ^[a] (94%)	>98:2 ^[a] (72%)	>98:2 ^[a] (83%)			
>90:10	>80:20	>60:40	50:50	<40:60	<20:80	<10:90	(α:β)

^[a] Results from Remmerswaal *et al.*,⁴⁸ identical glycosylation conditions were used.

Conclusions

To conclude, the role of acceptor acidity on the β -directing effect of the C-3-*O*-picoloyl protecting group in glucosyl and mannosyl donors was studied. For the 3-*O*-picoloyl-glucose series, no significant influence of the picoloyl group on the stereoselectivity of the glycosylation reactions was observed, in line with previous studies. Only for acidic, and thus weak nucleophiles, a modest shift in stereoselectivity was observed. The 3-*O*-picoloyl-mannose series exhibit a much stronger β -directing effect, with more acidic acceptors providing more β -selective glycosylation reactions. This dichotomy between the glucose and mannose series is reminiscent of the directing effect of the C-3-*O*-acyl groups, which in the mannose series have a strong effect, while hardly affecting glucosylation reactions. The absence of HAD in the glucose series is likely because the HAD pathway takes place through a more dissociated mechanism. The stereoselectivity in the glucosylation reactions is dictated primarily by the competition of the substitution reactions of the α - and β -triflates, which are in equilibrium through an *in situ* anomerisation scheme. The outcome of mannosylation reactions can be rationalized with the equilibrium of the anomeric α -triflate with oxocarbenium^{17,62} or dioxanum ion intermediates.⁴⁸ The observed trends in the mannose series are consistent with a scenario in which there is competition between LRP and HAD mechanisms, in which more acidic acceptors show stronger direction by the HAD mechanism.

Supporting information

General Methods

All chemicals (Acros, Fluka, Merck, and Sigma-Aldrich) were used as received unless stated otherwise. Dichloromethane was stored over activated 4 Å molecular sieves (beads, 8-12 mesh, Sigma-Aldrich). Before use traces of water present in the donor, diphenyl sulfoxide (Ph₂SO), and tri-tert-butylpyrimidine (TTBP) were removed by co-evaporation with dry toluene. The acceptors were stored in stock solutions (DCM, 0.5 M) over activated 3 Å molecular sieves (rods, size 1/16 in., Sigma-Aldrich). Trifluoromethanesulfonic anhydride (Tf₂O) was distilled over P₂O₅ and stored at -20 °C under a nitrogen atmosphere. Overnight temperature control was achieved by an FT902 Immersion Cooler (Julabo). Column chromatography was performed on silica gel 60 Å (0.04 – 0.063 mm, Screening Devices B.V.). TLC-analysis was conducted on TLC Silica gel 60 (Kieselgel 60 F254, Merck) with UV detection by (254 nm) and by spraying with 20% sulfuric acid in ethanol followed by charring at $\pm$ 150 °C or by spraying with a solution of (NH₄)₆Mo₇O₂₄·H₂O (25 g/l) and (NH₄)₄Ce(SO₄)₄·2H₂O (10 g/l) in 10% sulfuric acid in water followed by charring at $\pm$ 250 °C. High-resolution mass spectra were recorded on a Thermo Finnigan LTQ Orbitrap mass spectrometer equipped with an electrospray ion source in positive mode (source voltage 3.5 kV, sheath gas flow 10, capillary temperature 275 °C) with resolution R=60.000 at m/z = 400 (mass range = 150-4000). ¹H and ¹³C NMR spectra were recorded on a Bruker AV-300 NMR instrument (300 and 75 MHz respectively), a Bruker AV-400 NMR instrument (400 and 101 MHz respectively), a Bruker AV-500 NMR instrument (500 and 126 MHz respectively), a Bruker AV-600 NMR instrument (600 and 151 MHz respectively), or a Bruker AV-850 NMR instrument (850 and 214 MHz respectively). For samples measured in CDCl₃ chemical shifts (δ) are given in ppm relative to tetramethylsilane as an internal standard or the residual signal of the deuterated solvent. Coupling constants (*J*) are given in Hz. To get better resolution of signals with small coupling constants or overlapping signals a gaussian window function (LB $\pm$ -1 and GB $\pm$ 0.5) was used on the ¹H NMR spectrum. All given ¹³C APT spectra are proton decoupled. NMR peak assignment was made using COSY, and HSQC. If necessary additional NOESY, HMBC and HMBC-GATED experiments were used to elucidate the structure further. The anomeric product ratios were based on the integration of ¹H NMR.

General procedure for Tf₂O/Ph₂SO mediated glycosylations

Donor (0.1 mmol), Ph₂SO (26 mg, 0.13 mmol, 1.3 equiv) and TTBP (62 mg, 0.25 mmol, 2.5 equiv) were coevaporated twice with dry toluene (4 Å molecular sieves) and dissolved in DCM (2 mL, 0.05 M donor). Activated 3 Å molecular sieves (rods, size 1/16 in.) were added and the reaction mixture stirred for 30 min at room temperature. The solution was cooled to -80 °C and Tf₂O (22 μ L, 0.13 mmol, 1.3 equiv) was slowly added. The reaction mixture was allowed to warm to -60 °C in approximately 45 min, followed by recooling to -80 °C and addition of the acceptor (0.2 mmol, 2 equiv) in DCM (0.4 mL, 0.5 M). The reaction mixture was allowed to warm to -60 °C in approximately 45 min and stirred for an additional 18 h. The reaction was quenched with sat. NaHCO₃ solution (1 mL) at -60 °C and diluted with DCM. The solution was transferred to a separatory funnel and water was added, the layers were separated, and the water phase extracted once more with DCM.

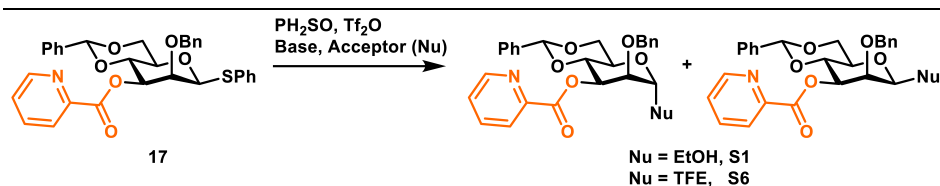
The combined organic layers were dried over MgSO_4 , filtered, and concentrated *in vacuo*. Purification by silica gel flash column chromatography yielded the glycosylation product as a mixture of anomers.

General computational procedure

To keep the calculation time manageable, the 2-*O*-Bn and 4,6-*O*-Benzylidene protection groups were substituted with electronically comparable smaller groups (2-*O*-Me and 4,6-*O*-Ethylidene). For each studied donor, conformation libraries of the α -OTf, β -OTf, oxocarbenium and dioxolenium ion were constructed through the 'conformer distribution search' option included in the Spartan 14 program by utilizing MMFF as the level of theory.⁶³ For the oxocarbenium and dioxolenium ions additional conformational libraries were constructed in which the conformation of the carbohydrate ring was fixated by constraining the dihedral angles of C1-C2-C3-C4 (D1), C3C4-C5-O (D3) and C5-O-C1-C2 (D5). The dihedral constraints were based on to the lowest energy conformations found in previous conformational energy landscapes of 2-*O*-Me-3-*O*-Bz-4,6-*O*-Ethylidene glucoside and mannoside cations: (D1;D2;D3) = (-30;-60;-15), (30;45;-60), (-45;-60;-15), (30;-60;0), (-45;-45;-15), (0;-60;0), (15;45;-60), (-15;-60;15), (15;-60;15), (45;45;-45).⁴⁸ All generated geometries were further optimized without constraints with PCM(CH_2Cl_2)/M062X/6-311++G(d,p)/PCM(CH_2Cl_2)/B3LYP/6-31+ G(d) at T= 213.15 K using Gaussian 09 rev D.01 employing the superfine integration grid, tight optimization and SCF cycle criteria.⁶⁴ The final denoted free Gibbs energy is constructed from the quasi-harmonic ΔG from the PCM(CH_2Cl_2)/B3LYP/6-31+G(d) calculation at T= 213.15K which is corrected with the ΔE of the PCM(CH_2Cl_2)/M06-2X/6-311++G(d,p) calculation.⁶⁵ The quasi-harmonic ΔG correction of Cramer and Truhlar was applied through the GoodVibes python toolkit.^{65,66}

Supplementary Computational Results

Supplementary table S1. Experimentally found stereoselectivities for model glycosylation reactions with the phenyl 2-*O*-benzyl-4,6-benzylidene-3-*O*-picoloyl-1-thio-mannosyl donor **9**; Experimental conditions: pre-activation-based glycosylation conditions; nucleophile (2 equiv), Tf_2O (1.3 equiv), Ph_2SO (1.3 equiv), base (2.5 equiv or 10 equiv), DCM (0.05 M), -80 to -60 °C. The stereoselectivity of the reaction is expressed as $\alpha:\beta$ and based on ^1H -NMR of the purified compounds. In all cases, product ratios were based on NMR spectra for the crude compounds.



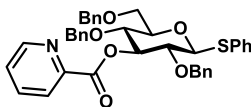
Acceptor	Base	pK _a H	Equiv	Product ($\alpha:\beta$)
EtOH	2,4,6-tri- <i>tert</i> -butylpyrimidine	1.02	2.5	73:27
EtOH	2,4,6-tri- <i>tert</i> -butylpyrimidine	1.02	10.0	69:31
EtOH	2,6-di- <i>tert</i> -butylpyrimidine	3.58	2.5	79:21
EtOH	2,4,6-tri- <i>tert</i> -butylpyridine	4.02	2.5	79:21
TFE	2,4,6-tri- <i>tert</i> -butylpyrimidine	1.02	2.5	32:68
TFE	2,4,6-tri- <i>tert</i> -butylpyrimidine	1.02	10.0	31:69
TFE	2,6-di- <i>tert</i> -butylpyrimidine	3.58	2.5	29:71
TFE	2,4,6-tri- <i>tert</i> -butylpyridine	4.02	2.5	35:65

Supplementary table S2. Computed triflyl bond dissociation enthalpy (BDE) for triflyl 2,4,6-tri-*O*-methyl-1-*O*-mannose and triflyl 4,6-ethylidene-2-*O*-methyl-1-*O*-mannose donors, towards either the oxocarbenium or dioxanion ion in kcal mol⁻¹. The geometry and energy of all the conformers were computed in solution phase using PCM(CH₂Cl₂)/M06-2X/6-311++G(d,p)/PCM(CH₂Cl₂)/B3LYP/6-31+G(d) at T= 213.15 K.

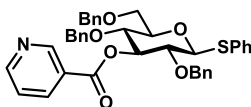
Entry	Donor	BDE (ΔH)
1	R ¹ = C ₆ H ₅ (Bz), R ² = Methyl	19.2
2	R ¹ = <i>p</i> -C ₆ H ₄ N (Pico), R ² = Methyl	20.6
3	R ¹ = <i>m</i> -C ₆ H ₄ N (Nico), R ² = Methyl	20.9
4	R ¹ = <i>i</i> -C ₆ H ₄ N (<i>i</i> -Nico), R ² = Methyl	21.9
5	R ¹ = <i>p</i> -C ₆ H ₄ N (Bz), R ² = Ethylidene	26.6
6	R ¹ = <i>m</i> -C ₆ H ₄ N (Pico), R ² = Ethylidene	28.7
7	R ¹ = <i>i</i> -C ₆ H ₄ N (Nico), R ² = Ethylidene	29.3
8	R ¹ = <i>p</i> -C ₆ H ₄ N (<i>i</i> -Nico), R ² = Ethylidene	31.1

Experimental procedures

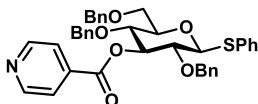
Donor Synthesis



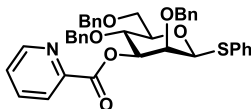
Phenyl 2,4,6-tri-*O*-benzyl-3-*O*-picoloyl-1-thio- β -D-glucopyranoside (2). Phenyl 2,4,6-tri-*O*-benzyl-1-thio- β -D-glucopyranoside¹² (0.53 g, 1.0 mmol) was co-evaporated with toluene, dissolved in DCM, molecular sieves (3 Å) were added, and the mixture was stirred for 10 min. To the solution DMAP (0.12 g, 1.0 mmol, 1.0 equiv), EDC·HCl (0.58 g, 3.0 mmol, 3.0 equiv), and Picolinic Acid (0.19 g, 1.5 mmol, 1.5 equiv) were added. The reaction was stirred for 1 h and subsequently diluted with DCM. The mixture was washed with water, sat. aq. NaHCO₃ solution, brine, dried over MgSO₄, and concentrated under reduced pressure. Flash column chromatography (9:1 to 6:4, pentane:EtOAc) yielded the title compound (0.56 g, 0.88 mmol, 88%) as a white solid. TLC: R_f 0.20, (80:20, pentane:EtOAc, v/v); ¹H NMR (400 MHz, CDCl₃, HH-COSY, HSQC): δ 8.73 (ddd, *J* = 4.7, 1.8, 0.9 Hz, 1H, CH_{arom} Pico), 8.03 (dt, *J* = 7.8, 1.1 Hz, 1H, CH_{arom} Pico), 7.80 (td, *J* = 7.7, 1.7 Hz, 1H, CH_{arom} Pico), 7.65 – 7.57 (m, 2H, CH_{arom}), 7.46 (ddd, *J* = 7.6, 4.8, 1.3 Hz, 1H, CH_{arom}), 7.42 – 6.99 (m, 13H, CH_{arom}), 5.63 (t, *J* = 9.3 Hz, 1H, H-3), 4.80 (d, *J* = 10.8 Hz, 1H, CHH Bn), 4.75 (d, *J* = 9.6 Hz, 1H, H-1), 4.65 (d, *J* = 11.8 Hz, 1H, CHH Bn), 4.60 – 4.48 (m, 4H, CHH Bn, CHH Bn, CH₂ Bn), 3.97 (t, *J* = 9.6 Hz, 1H, H-4), 3.83 (dd, *J* = 11.0, 2.2 Hz, 1H, H-6), 3.79 (dd, *J* = 11.1, 3.9 Hz, 1H, H-6), 3.73 (t, *J* = 9.4 Hz, 1H, H-2), 3.63 (ddd, *J* = 9.8, 3.8, 2.1 Hz, 1H, H-5); ¹³C-APT NMR (101 MHz, CDCl₃, HSQC): δ 164.5 (C=O Pico), 149.8 (CH_{arom} Pico), 147.9, 138.4, 137.7 (C_q), 137.0 (CH_{arom}), 133.2 (C_q), 132.6, 129.1, 128.5, 128.3, 128.3, 128.3, 128.1, 127.8, 127.7, 127.7, 125.8 (CH_{arom}), 87.2 (C-1), 79.3 (C-3), 79.2 (C-5), 78.5 (C-2), 75.9 (C-4), 75.0 (CH₂ Bn), 74.8 (CH₂ Bn), 73.6 (CH₂ Bn), 68.9 (C-6); ¹³C-GATED NMR (101 MHz, CDCl₃): δ 87.2 (*J*_{C1,H1} = 155.2 Hz, C-1 β); HRMS: [M+H]⁺ calcd for C₃₉H₃₈NO₆S 648.2414, found 648.2411.



Phenyl 2,4,6-tri-*O*-benzyl-3-*O*-nicotinoyl-1-thio-β-*D*-glucopyranoside (3). Phenyl 2,4,6-tri-*O*-benzyl-1-thio-β-*D*-glucopyranoside¹² (0.53 g, 1.0 mmol) was co-evaporated with toluene, dissolved in DCM, molecular sieves (3 Å) were added, and the mixture was stirred for 10 min. To the solution DMAP (0.12 g, 1.0 mmol, 1.0 equiv), EDC·HCl (0.58 g, 3.0 mmol, 3.0 equiv), and Nicotinic Acid (0.19 g, 1.5 mmol, 1.5 equiv) were added. The reaction was stirred for 1 h and subsequently diluted with DCM. The mixture was washed with water, sat. aq. NaHCO₃ solution, brine, dried over MgSO₄, and concentrated under reduced pressure. Flash column chromatography (9:1 to 6:4, pentane:EtOAc) yielded the title compound (0.45 g, 0.71 mmol, 71%) as a white solid. TLC: *R_f* 0.22, (80:20, pentane:EtOAc, v:v); ¹H NMR (400 MHz, CDCl₃, HH-COSY, HSQC): δ 8.96 (dd, *J* = 2.2, 0.9 Hz, 1H, CH_{arom} Nico), 8.75 (dd, *J* = 4.9, 1.7 Hz, 1H, CH_{arom} Nico), 8.06 (dt, *J* = 7.9, 2.0 Hz, 1H, CH_{arom} Nico), 7.66 – 7.56 (m, 2H, CH_{arom}), 7.43 – 7.23 (m, 7H, CH_{arom}), 7.14 – 6.96 (m, 7H), 5.51 (t, *J* = 9.3 Hz, 1H, H-3), 4.82 (d, *J* = 11.1 Hz, 1H, CHH Bn), 4.76 (d, *J* = 9.7 Hz, 1H, H-1), 4.67 (d, *J* = 11.9 Hz, 1H, CHH Bn), 4.58 (d, *J* = 12.0 Hz, 1H, CHH Bn), 4.51 (d, *J* = 11.4 Hz, 1H, CHH Bn), 4.48 (d, *J* = 11.3 Hz, 1H, CHH Bn), 4.41 (d, *J* = 11.2 Hz, 1H, CHH Bn), 3.87 – 3.74 (m, 3H, H-4, H-6, H-6), 3.65 – 3.55 (m, 2H, H-2, H-5); ¹³C-APT NMR (101 MHz, CDCl₃, HSQC): δ 164.2 (C=O Nico), 153.5, 150.9 (CH_{arom} Nico), 138.2, 137.4 (C_q), 137.2 (CH_{arom} Nico), 133.6 (C_q), 132.2, 129.2, 128.6, 128.4, 128.3, 128.1, 128.0, 127.9, 127.8 (CH_{arom}), 125.9 (C_q), 123.3 (CH_{arom} Nico), 87.7 (C-1), 79.1 (C-5), 78.6 (C-3), 78.2 (C-2), 75.8 (C-4), 74.9 (CH₂ Bn), 74.6 (CH₂ Bn), 73.7 (CH₂ Bn), 68.6 (C-6); HRMS: [M+H]⁺ calcd for C₃₉H₃₈NO₆S 648.2414, found 648.2400.

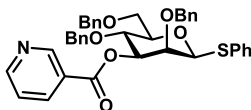


Phenyl 2,4,6-tri-*O*-benzyl-3-*O*-isonicotinoyl-1-thio-β-*D*-glucopyranoside (4). Phenyl 2,4,6-tri-*O*-benzyl-1-thio-β-*D*-glucopyranoside¹² (0.53 g, 1.0 mmol) was co-evaporated with toluene, dissolved in DCM, molecular sieves (3 Å) were added, and the mixture was stirred for 10 min. To the solution DMAP (0.12 g, 1.0 mmol, 1.0 equiv), EDC·HCl (0.58 g, 3.0 mmol, 3.0 equiv), and iso-Nicotinic Acid (0.19 g, 1.5 mmol, 1.5 equiv) were added. The reaction was stirred for 1 h and subsequently diluted with DCM. The mixture was washed with water, sat. aq. NaHCO₃ solution, brine, dried over MgSO₄, and concentrated under reduced pressure. Flash column chromatography (9:1 to 6:4, pentane:EtOAc, v:v) yielded the title compound (0.50 g, 0.80 mmol, 80%) as a white solid. TLC: *R_f* 0.21, (80:20, pentane:EtOAc, v:v); ¹H NMR (400 MHz, CDCl₃, HH-COSY, HSQC): δ 8.73 – 8.67 (m, 2H, CH_{arom} *i*-Nico), 7.65 – 7.60 (m, 2H, CH_{arom}), 7.60 – 7.55 (m, 2H, CH_{arom} *i*-Nico), 7.43 – 7.23 (m, 6H, CH_{arom}), 7.12 – 6.95 (m, 7H, CH_{arom}), 5.49 (t, *J* = 9.3 Hz, 1H, H-3), 4.81 (d, *J* = 11.2 Hz, 1H, CHH Bn), 4.75 (d, *J* = 9.7 Hz, 1H, H-1), 4.67 (d, *J* = 11.9 Hz, 1H, CHH Bn), 4.58 (d, *J* = 11.9 Hz, 1H, CHH Bn), 4.51 (d, *J* = 11.3 Hz, 1H, CHH Bn), 4.47 (d, *J* = 11.1 Hz, 1H, CHH Bn), 4.39 (d, *J* = 11.2 Hz, 1H, CHH Bn), 3.87 – 3.74 (m, 3H, H-4, H-6, H-6), 3.64 – 3.54 (m, 2H, H-2, H-5); ¹³C-APT NMR (101 MHz, CDCl₃, HSQC): δ 164.1 (C=O *i*-Nico), 150.6 (CH_{arom} *i*-Nico), 138.1, 137.4, 137.0, 133.5 (C_q), 129.2, 128.6, 128.4, 128.4, 128.4, 128.1, 128.0, 128.0, 123.0 (CH_{arom}), 87.7 (C-1), 79.1 (C-5), 78.6 (C-2), 78.5 (C-4), 75.7 (C-4), 74.9 (CH₂ Bn), 74.6 (CH₂ Bn), 73.7 (CH₂ Bn), 68.6 (C-6); ¹³C-GATED NMR (101 MHz, CDCl₃): δ 87.7 (*J*_{C1,H1} = 156.2 Hz, C-1 β); HRMS: [M+H]⁺ calcd for C₃₉H₃₈NO₆S 648.2414, found 648.2410.

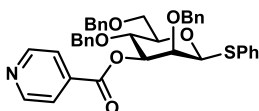


Phenyl 2,4,6-tri-*O*-benzyl-3-*O*-picoloyl-1-thio-β-*D*-mannopyranoside (7). Phenyl 2,4,6-tri-*O*-benzyl-1-thio-β-*D*-mannopyranoside¹² (0.53 g, 1.0 mmol) was co-evaporated with toluene, dissolved in DCM, molecular sieves (3 Å) were added, and the mixture was stirred for 10 min. To the solution DMAP (0.12 g, 1.0 mmol, 1.0 equiv), EDC·HCl (0.58 g, 3.0 mmol, 3.0 equiv), and Picolinic Acid (0.19 g, 1.5 mmol, 1.5 equiv) were added. The reaction was stirred for 1 h and subsequently diluted with DCM. The mixture was washed with water, sat. aq. NaHCO₃ solution, brine, dried over MgSO₄, and concentrated under reduced pressure. Flash column chromatography (9:1 to 6:4, pentane:EtOAc) yielded the title compound (0.57 g, 0.91 mmol, 91%) as a colorless oil. TLC: *R_f* 0.19, (80:20, pentane:EtOAc, v:v); ¹H NMR (400 MHz, CDCl₃, HH-COSY, HSQC): δ 8.79 (ddd, *J* = 4.7, 1.8, 0.9 Hz, 1H, CH_{arom} Pico), 7.92 (dt, *J* = 7.8, 1.1 Hz, 1H, CH_{arom} Pico), 7.78 (td, *J* = 7.7, 1.8 Hz, 1H, CH_{arom} Pico), 7.59 – 7.51 (m, 2H, CH_{arom}), 7.49 (ddd, *J* = 7.6, 4.7, 1.3 Hz, 1H, CH_{arom} Pico), 7.41 – 7.06 (m, 13H, CH_{arom}), 5.28 (dd, *J* = 9.8, 3.2 Hz, 1H, H-3), 4.97 (d, *J* = 1.1 Hz, 1H, H-1), 4.86 (d, *J* = 11.5 Hz, 1H, CHH Bn), 4.80 (d, *J* = 11.6 Hz, 1H, CHH Bn), 4.76 (d, *J* = 11.0 Hz, 1H, CHH Bn), 4.67 (d, *J* = 11.7 Hz, 1H, CHH Bn), 4.61 (d, *J* = 11.1 Hz, 1H, CHH Bn), 4.57 (d, *J* = 11.7 Hz, 1H, CHH Bn), 4.41 (dd, *J* = 3.3, 1.1 Hz, 1H, H-2), 4.24 (t, *J* = 9.8 Hz, 1H, H-4), 3.87 (dd, *J* = 11.0, 2.1 Hz, 1H, H-6), 3.82 (dd, *J* = 11.0, 5.7 Hz, 1H, H-6), 3.65 (ddd, *J* = 9.7, 5.7, 2.0 Hz, 1H, H-5); ¹³C-APT NMR (101 MHz, CDCl₃, HSQC): δ 164.5 (C=O Pico), 150.2 (CH_{arom} Pico), 147.6, 138.5, 137.8 (C_q), 137.0 (CH_{arom} Pico), 135.1

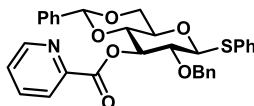
(C_q), 131.3, 129.1, 128.5, 128.4, 128.4, 128.3, 128.0, 128.0, 127.8, 127.6, 125.4 (CH_{arom}), 87.8 (C-1), 80.1 (C-5), 78.8 (C-3), 78.2 (C-2), 75.8 (CH₂ Bn), 75.1 (CH₂ Bn), 73.7 (CH₂ Bn), 73.2 (C-4), 69.6 (C-6); ¹³C-GATED NMR (101 MHz, CDCl₃): δ 87.8 (J_{C1,H1} = 153.5 Hz, C-1 β); HRMS: [M+H]⁺ calcd for C₃₉H₃₈NO₆S 648.2414, found 648.2411.



Phenyl 2,4,6-tri-O-benzyl-3-O-nicotinoyl-1-thio-β-D-mannopyranoside (8). Phenyl 2,4,6-tri-O-benzyl-1-thio-β-D-mannopyranoside¹² (0.53 g, 1.0 mmol) was co-evaporated with toluene, dissolved in DCM, molecular sieves (3 Å) were added, and the mixture was stirred for 10 min. To the solution DMAP (0.12 g, 1.0 mmol, 1.0 equiv), EDC·HCl (0.58 g, 3.0 mmol, 3.0 equiv), and Nicotinic Acid (0.19 g, 1.5 mmol, 1.5 equiv) were added. The reaction was stirred for 1 h and subsequently diluted with DCM. The mixture was washed with water, sat. aq. NaHCO₃ solution, brine, dried over MgSO₄, and concentrated under reduced pressure. Flash column chromatography (9:1 to 6:4, pentane:EtOAc) yielded the title compound (0.59 g, 0.93 mmol, 93%) as a colorless oil. TLC: R_f 0.21, (80:20, pentane:EtOAc, v:v); ¹H NMR (400 MHz, CDCl₃, HH-COSY, HSQC): δ 9.12 (dd, *J* = 2.2, 0.9 Hz, 1H, CH_{arom}, Nico), 8.81 (dd, *J* = 4.9, 1.7 Hz, 1H, CH_{arom} Nico), 8.15 – 8.09 (m, 1H, CH_{arom} Nico), 7.64 – 7.53 (m, 2H, CH_{arom}), 7.50 – 7.06 (m, 14H, CH_{arom}), 5.25 (dd, *J* = 9.9, 3.3 Hz, 1H, H-3), 4.99 (d, *J* = 1.1 Hz, 1H, H-1), 4.90 (d, *J* = 11.6 Hz, 1H, CHH Bn), 4.72 (d, *J* = 11.8 Hz, 1H, CHH Bn), 4.70 (d, *J* = 11.6 Hz, 1H, CHH Bn), 4.64 (d, *J* = 2.4 Hz, 1H, CH₂ Bn), 4.62 (d, *J* = 11.8 Hz, 1H, CHH Bn), 4.41 (dd, *J* = 3.4, 1.1 Hz, 1H, H-2), 4.23 (t, *J* = 9.8 Hz, 1H, H-4), 3.94 – 3.82 (m, 2H, H-6, H-6), 3.67 (ddd, *J* = 9.7, 5.1, 2.5 Hz, 1H, H-5); ¹³C-APT NMR (101 MHz, CDCl₃, HSQC): δ 164.6 (C=O Nico), 153.8, 151.1 (CH_{arom} Nico), 138.4, 137.7 (C_q), 137.3 (CH_{arom} Nico), 135.0 (C_q), 131.3, 129.2, 128.5, 128.4, 128.3, 128.1, 127.9, 127.7, 127.6, 125.5 (CH_{arom}), 123.4 (C_q), 87.8 (C-1), 80.2 (C-5), 78.6 (C-2), 78.1 (C-3), 76.1 (CH₂ Bn), 75.2 (CH₂ Bn), 73.8 (CH₂ Bn), 73.4 (C-4), 69.5 (C-6); ¹³C-GATED NMR (101 MHz, CDCl₃): δ 87.8 (J_{C1,H1} = 153.9 Hz, C-1 β); HRMS: [M+H]⁺ calcd for C₃₉H₃₈NO₆S 648.2414, found 648.2410.

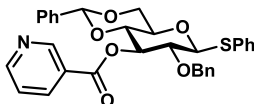


Phenyl 2,4,6-tri-O-benzyl-3-O-isonicotinoyl-1-thio-β-D-mannopyranoside (9). Phenyl 2,4,6-tri-O-benzyl-1-thio-β-D-mannopyranoside¹² (0.53 g, 1.0 mmol) was co-evaporated with toluene, dissolved in DCM, molecular sieves (3 Å) were added, and the mixture was stirred for 10 min. To the solution DMAP (0.12 g, 1.0 mmol, 1.0 equiv), EDC·HCl (0.58 g, 3.0 mmol, 3.0 equiv), and iso-Nicotinic Acid (0.19 g, 1.5 mmol, 1.5 equiv) were added. The reaction was stirred for 1 h and subsequently diluted with DCM. The mixture was washed with water, sat. aq. NaHCO₃ solution, brine, dried over MgSO₄, and concentrated under reduced pressure. Flash column chromatography (9:1 to 6:4, pentane:EtOAc) yielded the title compound (0.62 g, 0.98 mmol, 98%) as a colorless oil. TLC: R_f 0.21, (80:20, pentane:EtOAc, v:v); ¹H NMR (400 MHz, CDCl₃, HH-COSY, HSQC): δ 8.84 – 8.71 (m, 2H, CH_{arom} *i*-Nico), 7.70 – 7.64 (m, 2H, CH_{arom} *i*-Nico), 7.64 – 7.53 (m, 2H, CH_{arom}), 7.46 – 7.05 (m, 13H, CH_{arom}), 5.24 (dd, *J* = 9.9, 3.3 Hz, 1H, H-3), 4.99 (d, *J* = 1.1 Hz, 1H, H-1), 4.92 (d, *J* = 11.6 Hz, 1H, CHH Bn), 4.74 (d, *J* = 11.7 Hz, 1H, CHH Bn), 4.68 (d, *J* = 11.7 Hz, 1H, CHH Bn), 4.63 (s, 2H, CH₂ Bn), 4.62 (d, *J* = 11.8 Hz, 1H, CHH Bn), 4.40 (dd, *J* = 3.4, 1.1 Hz, 1H, H-2), 4.24 (t, *J* = 9.8 Hz, 1H, H-4), 3.91 (dd, *J* = 11.1, 2.8 Hz, 1H, H-6), 3.87 (dd, *J* = 11.1, 4.8 Hz, 1H, H-6), 3.67 (ddd, *J* = 9.7, 4.8, 2.7 Hz, 1H, H-5); ¹³C-APT NMR (101 MHz, CDCl₃, HSQC): δ 164.4 (C=O *i*-Nico), 150.7 (CH_{arom} *i*-Nico), 138.3, 137.6, 136.5, 134.8 (C_q), 131.2, 129.1, 128.4, 128.4, 128.0, 128.0, 127.8, 127.8, 127.6, 122.8 (CH_{arom}), 87.7 (C-1), 80.1 (C-5), 78.6 (C-2), 78.2 (C-3), 76.1 (CH₂ Bn), 75.0 (CH₂ Bn), 73.7 (CH₂ Bn), 73.3 (C-4), 69.3 (C-6); ¹³C-GATED NMR (101 MHz, CDCl₃): δ 87.7 (J_{C1,H1} = 153.1 Hz, C-1 β); HRMS: [M+H]⁺ calcd for C₃₉H₃₈NO₆S 648.2414, found 648.2411.

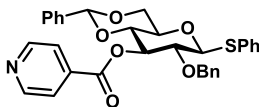


Phenyl 2-O-benzyl-4,6-O-benzylidene-3-O-picoloyl-1-thio-β-D-glucopyranoside (12). Phenyl 2-O-benzyl-4,6-O-benzylidene-1-thio-β-D-glucopyranoside⁴⁸ (0.45 g, 1.0 mmol) was co-evaporated with toluene, dissolved in DCM, molecular sieves (3 Å) were added, and the mixture was stirred for 10 min. To the solution DMAP (0.12 g, 1.0 mmol, 1.0 equiv), EDC·HCl (0.58 g, 3.0 mmol, 3.0 equiv), and Picolinic Acid (0.19 g, 1.5 mmol, 1.5 equiv) were added. The reaction was stirred for 1 h and subsequently diluted with DCM. The mixture was washed with water, sat. aq. NaHCO₃ solution, brine, dried over MgSO₄, and concentrated under reduced pressure. Flash column chromatography (9:1 to 6:4, pentane:EtOAc) yielded the title compound (0.50 g, 0.90 mmol, 90%) as a white solid. TLC: R_f 0.50, (65:35, pentane:EtOAc, v:v); ¹H NMR (400 MHz, CDCl₃, HH-COSY, HSQC): δ 8.77 (ddd, *J* = 4.8, 1.8, 0.9 Hz, 1H, CH_{arom} Pico), 8.13 (dt, *J* = 7.8, 1.1 Hz, 1H, CH_{arom} Pico), 7.84 (td, *J* = 7.8, 1.8 Hz, 1H, CH_{arom}

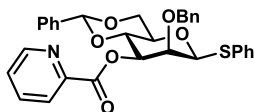
Pico), 7.64 – 7.55 (m, 2H, CH_{arom}), 7.52 – 7.48 (m, 2H, CH_{arom}), 7.45 – 7.27 (m, 3H), 7.23 – 7.09 (m, 4H), 5.77 (dd, $J = 9.9, 8.8$ Hz, 1H, H-3), 5.51 (s, 1H, CHPh), 4.90 (d, $J = 9.7$ Hz, 1H, H-1), 4.89 (d, $J = 10.7$ Hz, 1H, CHH Bn), 4.65 (d, $J = 10.7$ Hz, 1H, CHH Bn), 4.44 (dd, $J = 10.4, 4.9$ Hz, 1H, H-6), 3.91 (t, $J = 9.6$ Hz, 1H, H-4), 3.85 (t, $J = 10.2$ Hz, 1H, H-6), 3.85 (dd, $J = 9.7, 8.8$ Hz, 1H, H-2), 3.67 (td, $J = 9.8, 5.0$ Hz, 1H, H-5); ¹³C-APT NMR (101 MHz, CDCl₃, HSQC): δ 164.2 (C_q), 149.8 (CH_{arom}), 147.6 (C_q), 137.0, 137.0 (CH_{arom}), 136.9 (C_q), 132.7 (CH_{arom}), 132.6 (C_q), 129.2, 129.0, 128.2, 128.2, 127.7, 127.0, 126.9, 126.2, 125.8, 125.1 (CH_{arom}), 101.4 (CHPh), 88.2 (C-1), 78.9 (C-2), 78.3 (C-4), 76.0 (C-3), 75.4 (CH₂ Bn), 70.6 (C-5), 68.7 (C-6). ¹³C-GATED NMR (101 MHz, CDCl₃): δ 88.2 ($J_{C1,H1} = 157.3$ Hz, C-1 β); HRMS: [M+H]⁺ calcd for C₃₂H₃₀NO₆S 556.1788, found 556.1784.



Phenyl 2-O-benzyl-4,6-O-benzylidene-3-O-nicotinoyl-1-thio-β-D-glucopyranoside (13). Phenyl 2-O-benzyl-4,6-O-benzylidene-1-thio-β-D-glucopyranoside⁴⁸ (0.45 g, 1.0 mmol) was co-evaporated with toluene, dissolved in DCM, molecular sieves (3 Å) were added, and the mixture was stirred for 10 min. To the solution DMAP (0.12 g, 1.0 mmol, 1.0 equiv), EDC-HCl (0.58 g, 3.0 mmol, 3.0 equiv), and Nicotinic Acid (0.19 g, 1.5 mmol, 1.5 equiv) were added. The reaction was stirred for 1 h and subsequently diluted with DCM. The mixture was washed with water, sat. aq. NaHCO₃ solution, brine, dried over MgSO₄, and concentrated under reduced pressure. Flash column chromatography (9:1 to 6:4, pentane:EtOAc) yielded the title compound (0.48 g, 0.87 mmol, 87%) as a white solid. TLC: R_f 0.50, (65:35, pentane:EtOAc, v:v); ¹H NMR (400 MHz, CDCl₃, HH-COSY, HSQC): δ 9.10 (dd, $J = 2.3, 0.9$ Hz, 1H, CH_{arom} Nico), 8.76 (dd, $J = 4.9, 1.7$ Hz, 1H, CH_{arom} Nico), 8.20 (dt, $J = 7.9, 2.0$ Hz, 1H, CH_{arom} Nico), 7.62 – 7.52 (m, 2H, CH_{arom}), 7.43 – 7.32 (m, 4H, CH_{arom}), 7.20 – 7.05 (m, 5H), 5.65 (dd, $J = 9.8, 8.7$ Hz, 1H, H-3), 5.49 (s, 1H, CHPh), 4.90 (d, $J = 11.3$ Hz, 1H, CHH Bn), 4.90 (d, $J = 9.5$ Hz, 1H, H-1), 4.59 (d, $J = 11.0$ Hz, 1H, CHH Bn), 4.41 (dd, $J = 10.5, 4.9$ Hz, 1H, H-6), 3.83 (t, $J = 10.3$ Hz, 1H, H-6), 3.77 (t, $J = 9.6$ Hz, 1H, H-4), 3.71 (dd, $J = 9.7, 8.8$ Hz, 1H, H-2), 3.62 (td, $J = 9.7, 5.0$ Hz, 1H, H-5); ¹³C-APT NMR (101 MHz, CDCl₃, HSQC): δ 164.2 (C_q), 153.7, 151.0, 137.4 (CH_{arom}), 136.8, 133.0 (C_q), 132.5, 129.3, 129.2, 128.5, 128.4, 128.3, 128.3, 128.0, 126.2 (CH_{arom}), 125.8 (C_q), 123.4 (CH_{arom}), 101.6 (CHPh), 88.8 (C-1), 79.2 (C-2), 78.6 (C-4), 75.5 (CH₂ Bn), 75.4 (C-3), 70.6 (C-5), 68.8 (C-6); ¹³C-GATED NMR (101 MHz, CDCl₃): δ 88.8 ($J_{C1,H1} = 157.6$ Hz, C-1 β); HRMS: [M+H]⁺ calcd for C₃₂H₃₀NO₆S 556.1788, found 556.1786.

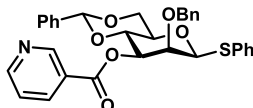


Phenyl 2-O-benzyl-4,6-O-benzylidene-3-O-isonicotinoyl-1-thio-β-D-glucopyranoside (14). Phenyl 2-O-benzyl-4,6-O-benzylidene-1-thio-β-D-glucopyranoside⁴⁸ (0.45 g, 1.0 mmol) was co-evaporated with toluene, dissolved in DCM, molecular sieves (3 Å) were added, and the mixture was stirred for 10 min. To the solution DMAP (0.12 g, 1.0 mmol, 1.0 equiv), EDC-HCl (0.58 g, 3.0 mmol, 3.0 equiv), and *iso*-Nicotinic Acid (0.19 g, 1.5 mmol, 1.5 equiv) were added. The reaction was stirred for 1 h and subsequently diluted with DCM. The mixture was washed with water, sat. aq. NaHCO₃ solution, brine, dried over MgSO₄, and concentrated under reduced pressure. Flash column chromatography (9:1 to 6:4, pentane:EtOAc) yielded the title compound (0.51 g, 0.91 mmol, 91%) as a white solid. TLC: R_f 0.55, (65:35, pentane:EtOAc, v:v); ¹H NMR (400 MHz, CDCl₃, HH-COSY, HSQC): δ 8.80 – 8.74 (m, 1H, CH_{arom} i-Nico), 7.79 – 7.73 (m, 1H, CH_{arom} i-Nico), 7.66 – 7.56 (m, 1H, CH_{arom} i-Nico), 7.42 – 7.36 (m, 4H, CH_{arom}), 7.35 – 7.31 (m, 2H, CH_{arom}), 7.19 – 7.10 (m, 5H, CH_{arom}), 5.66 (dd, $J = 9.8, 8.7$ Hz, 1H, H-3), 5.52 (s, 1H, CHPh), 4.93 (d, $J = 11.0$ Hz, 1H, CHH Bn), 4.93 (d, $J = 9.7$ Hz, 1H, H-1), 4.60 (d, $J = 11.0$ Hz, 1H, CHH Bn), 4.44 (dd, $J = 10.5, 5.0$ Hz, 1H, H-6), 3.86 (t, $J = 10.3$ Hz, 1H, H-6), 3.79 (t, $J = 9.6$ Hz, 1H, H-4), 3.74 (dd, $J = 9.7, 8.8$ Hz, 1H, H-2), 3.65 (td, $J = 9.7, 5.0$ Hz, 1H, H-5); ¹³C-APT NMR (101 MHz, CDCl₃, HSQC): δ 164.9 (C_q), 151.4, 150.6 (CH_{arom}), 137.1, 136.7, 132.8 (C_q), 132.4, 129.2, 129.1, 128.4, 128.2, 128.2, 128.2, 128.0, 126.1, 123.9 (CH_{arom}), 99.7 (CHPh), 88.1 (C-1), 80.2 (C-2), 78.4 (C-4), 75.7 (C-3), 75.4 (CH₂ Bn), 71.6 (C-5), 68.2 (C-6); ¹³C-GATED NMR (101 MHz, CDCl₃): δ 88.1 ($J_{C1,H1} = 157.9$ Hz, C-1 β); HRMS: [M+H]⁺ calcd for C₃₂H₃₀NO₆S 556.1788, found 556.1785.

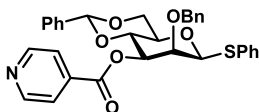


Phenyl 2-O-benzyl-4,6-O-benzylidene-3-O-picoloyl-1-thio-β-D-mannopyranoside (17). Phenyl 2-O-benzyl-4,6-O-benzylidene-1-thio-β-D-mannopyranoside⁴⁸ (0.45 g, 1.0 mmol) was co-evaporated with toluene, dissolved in DCM, molecular sieves (3 Å) were added, and the mixture was stirred for 10 min. To the solution DMAP (0.12 g, 1.0 mmol, 1.0 equiv), EDC-HCl (0.58 g, 3.0 mmol, 3.0 equiv), and Picolinic Acid (0.19 g, 1.5 mmol, 1.5 equiv) were added. The reaction was stirred for 1 h and subsequently diluted with DCM. The mixture was

washed with water, sat. aq. NaHCO₃ solution, brine, dried over MgSO₄, and concentrated under reduced pressure. Flash column chromatography (9:1 to 6:4, pentane:EtOAc) yielded the title compound (0.49 g, 0.88 mmol, 88%) as a white foam. TLC: R_f 0.51, [65:35, pentane:EtOAc, v:v]; ¹H NMR (400 MHz, CDCl₃, HH-COSY, HSQC): δ 9.19 (dd, *J* = 2.2, 0.9 Hz, 1H, CH_{arom} Pico), 8.79 (dd, *J* = 4.9, 1.7 Hz, 1H, CH_{arom} Pico), 8.22 (dt, *J* = 8.0, 2.0 Hz, 1H, CH_{arom} Pico), 7.66 – 7.03 (m, 16H, CH_{arom}), 5.62 (s, 1H, CHPh), 5.32 (dd, *J* = 10.4, 3.3 Hz, 1H, H-3), 5.07 (d, *J* = 1.3 Hz, 1H, H-1), 4.87 (d, *J* = 11.3 Hz, 1H, CHH Bn), 4.71 (d, *J* = 11.2 Hz, 1H, CHH Bn), 4.52 (dd, *J* = 3.4, 1.3 Hz, 1H, H-2), 4.41 (dd, *J* = 10.4, 9.3 Hz, 1H, H-4), 4.37 (dd, *J* = 10.5, 4.9 Hz, 1H, H-6), 3.99 (t, *J* = 10.3 Hz, 1H, H-6), 3.60 (td, *J* = 9.8, 4.9 Hz, 1H, H-5); ¹³C-APT NMR (101 MHz, CDCl₃, HSQC): δ 164.9 (C=O Pico), 153.9, 151.2, 137.4 (CH_{arom} Pico), 137.3, 137.1, 134.3 (C_q), 131.8, 129.3, 129.2, 128.5, 128.4, 128.4, 128.1, 128.0, 126.2 (CH_{arom}), 125.5 (C_q), 123.5 (CH_{arom}), 101.9 (CHPh), 89.2 (C-1), 78.9 (C-2), 76.8 (CH₂ Bn), 75.6 (C-4), 74.7 (C-3), 71.9 (C-5), 68.6 (C-6); HRMS: [M+H]⁺ calcd for C₃₂H₃₀NO₆S 556.1788, found 556.1785.

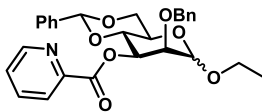


Phenyl 2-*O*-benzyl-4,6-*O*-benzylidene-3-*O*-nicotinoyl-1-thio-β-*D*-glucopyranoside (18). Phenyl 2-*O*-benzyl-4,6-*O*-benzylidene-1-thio-β-*D*-mannopyranoside⁴⁸ (0.45 g, 1.0 mmol) was co-evaporated with toluene, dissolved in DCM, molecular sieves (3 Å) were added, and the mixture was stirred for 10 min. To the solution DMAP (0.12, 1.0 mmol, 1.0 equiv), EDC·HCl (0.58, 3.0 mmol, 3.0 equiv), and Nicotinic Acid (0.19, 1.5 mmol, 1.5 equiv) were added. The reaction was stirred for 1 h and subsequently diluted with DCM. The mixture was washed with water, sat. aq. NaHCO₃ solution, brine, dried over MgSO₄, and concentrated under reduced pressure. Flash column chromatography (9:1 to 6:4, pentane:EtOAc) yielded the title compound (0.51 g, 0.91 mmol, 91%) as a white foam. TLC: R_f 0.53, [65:35, pentane:EtOAc, v:v]; ¹H NMR (400 MHz, CDCl₃, HH-COSY, HSQC): δ 9.20 (dd, *J* = 2.2, 0.9 Hz, 1H, CH_{arom} Nico), 8.79 (dd, *J* = 4.8, 1.7 Hz, 1H, CH_{arom} Nico), 8.22 (dt, *J* = 8.0, 2.0 Hz, 1H, CH_{arom} Nico), 7.58 – 7.12 (m, 16H, CH_{arom}), 5.62 (s, 1H, CHPh), 5.32 (dd, *J* = 10.4, 3.3 Hz, 1H, H-3), 5.07 (d, *J* = 1.2 Hz, 1H, H-1), 4.87 (d, *J* = 11.2 Hz, 1H, CHH Bn), 4.71 (d, *J* = 11.3 Hz, 1H, CHH Bn), 4.52 (dd, *J* = 3.4, 1.3 Hz, 1H, H-2), 4.46 – 4.38 (dd, *J* = 10.6, 9.4 Hz, 1H, H-4), 4.37 (dd, *J* = 10.8, 5.2 Hz, 1H, H-6), 3.99 (t, *J* = 10.3 Hz, 1H, H-6), 3.60 (td, *J* = 9.9, 4.9 Hz, 1H, H-5); ¹³C-APT NMR (101 MHz, CDCl₃, HSQC): δ 164.9 (C_q), 153.9, 151.3, 137.4 (CH_{arom}), 137.1, 134.3 (C_q), 131.8, 129.3, 128.5, 128.4, 128.1, 126.2 (CH_{arom}), 125.5 (C_q), 123.5 (CH_{arom}), 101.4 (CHPh), 88.5 (C-1), 78.9 (C-2), 76.8 (CH₂ Bn), 75.6 (C-4), 74.8 (C-3), 71.9 (C-5), 69.0 (C-6); HRMS: [M+H]⁺ calcd for C₃₂H₃₀NO₆S 556.1788, found 556.1788.

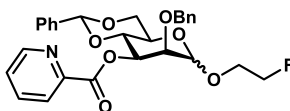


Phenyl 2-*O*-benzyl-4,6-*O*-benzylidene-3-*O*-isonicotinoyl-1-thio-β-*D*-glucopyranoside (19). Phenyl 2-*O*-benzyl-4,6-*O*-benzylidene-1-thio-β-*D*-mannopyranoside⁴⁸ (0.45 g, 1.0 mmol) was co-evaporated with toluene, dissolved in DCM, molecular sieves (3 Å) were added, and the mixture was stirred for 10 min. To the solution DMAP (0.12 g, 1.0 mmol, 1.0 equiv), EDC·HCl (0.58 g, 3.0 mmol, 3.0 equiv), and iso-Nicotinic Acid (0.19 g, 1.5 mmol, 1.5 equiv) were added. The reaction was stirred for 1 h and subsequently diluted with DCM. The mixture was washed with water, sat. aq. NaHCO₃ solution, brine, dried over MgSO₄, and concentrated under reduced pressure. Flash column chromatography (9:1 to 6:4, pentane:EtOAc) yielded the title compound (0.53 g, 0.95 mmol, 95%) as a white foam. TLC: R_f 0.54, [65:35, pentane:EtOAc, v:v]; ¹H NMR (400 MHz, CDCl₃, HH-COSY, HSQC): δ 8.81 – 8.71 (m, 1H, CH_{arom} i-Nico), 7.84 – 7.75 (m, 1H, CH_{arom} i-Nico), 7.58 – 7.47 (m, 1H, CH_{arom} i-Nico), 7.46 – 7.13 (m, 11H, CH_{arom}), 5.61 (s, 1H, CHPh), 5.32 (dd, *J* = 10.3, 3.4 Hz, 1H, H-3), 5.06 (d, *J* = 1.2 Hz, 1H, H-1), 4.89 (d, *J* = 11.3 Hz, 1H, CHH Bn), 4.69 (d, *J* = 11.3 Hz, 1H, CHH Bn), 4.50 (dd, *J* = 3.4, 1.2 Hz, 1H, H-2), 4.40 (dd, *J* = 10.5, 9.3 Hz, 1H, H-4), 4.37 (dd, *J* = 10.9, 4.6 Hz, 1H, H-6), 3.99 (t, *J* = 10.3 Hz, 1H, H-6), 3.60 (td, *J* = 9.9, 4.9 Hz, 1H, H-5); ¹³C-APT NMR (101 MHz, CDCl₃, HSQC): δ 164.8 (C_q), 150.8 (CH_{arom}), 137.1, 136.6, 134.2 (C_q), 129.3, 128.5, 128.4, 128.3, 128.2, 128.1, 126.2, 123.1 (CH_{arom}), 101.9 (CHPh), 89.2 (C-1), 78.9 (C-2), 76.9 (CH₂ Bn), 75.6 (C-4), 75.0 (C-3), 71.9 (C-5), 68.6 (C-6); ¹³C-GATED NMR (101 MHz, CDCl₃): δ 89.2 (*J*_{C1,H1} = 154.5 Hz, C-1 β); HRMS: [M+H]⁺ calcd for C₃₂H₃₀NO₆S 556.1788, found 556.1790.

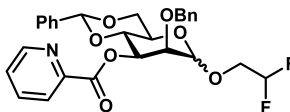
Model Glycosylation Reactions



Ethyl 2-O-benzyl-4,6-O-benzylidene-3-picoloyl- β -mannopyranoside (S1). The title compound was prepared from donor **17** and ethanol using the general procedure for Tf₂O/Ph₂SO mediated glycosylations. Flash column chromatography (100:0 $\rightarrow$ 60:40, pentane:EtOAc, v:v) yielded glycosylation product **S1** (34.9 mg, 0.071 mmol, 71%, α : β = 73:27). TLC: R_f 0.65, (70:30, pentane:EtOAc, v:v); Data for the α -anomer: ¹H NMR (400 MHz, CDCl₃, HH-COSY, HSQC, HMBC): δ 8.80 (td, J = 1.8, 0.9 Hz, 1H, CH_{arom} Pico), 8.09 (dt, J = 7.8, 1.1 Hz, 1H, CH_{arom} Pico), 7.81 (td, J = 7.8, 1.8 Hz, 1H, CH_{arom} Pico), 7.57 – 6.96 (m, 11H, CH_{arom}), 5.66 (dd, J = 10.4, 3.5 Hz, 1H, H-3), 5.62 (s, 1H, CHPh), 4.95 (d, J = 12.3 Hz, 1H, CHH Bn), 4.88 (d, J = 1.6 Hz, 1H, H-1), 4.72 (d, J = 12.4 Hz, 1H, CHH Bn), 4.42 (dd, J = 10.3, 9.2 Hz, 1H, H-4), 4.29 (dd, J = 10.0, 4.5 Hz, 1H, H-6), 4.08 (dd, J = 3.5, 1.6 Hz, 1H, H-2), 4.04 – 3.96 (m, 1H, H-5), 3.91 (t, J = 10.2 Hz, 1H, H-6), 3.85 – 3.70 (m, 1H, CHHCH₃ Et), 3.68 – 3.43 (m, 1H, CHHCH₃ Et), 1.24 (t, J = 7.1 Hz, 3H, CH₃ Et); ¹³C-APT NMR (101 MHz, CDCl₃, HSQC, HMBC): δ 164.4 (C=O Pico), 150.1 (CH_{arom} Pico), 148.0, 137.7, 137.5 (C_q), 137.0, 131.2, 129.5, 129.0, 128.7, 128.4, 128.3, 128.2, 128.0, 127.0, 126.3, 125.6 (CH_{arom}), 101.8 (CHPh), 98.9 (C-1), 76.5 (C-2), 76.4 (C-4), 73.8 (CH₂ Bn), 72.2 (C-3), 69.0 (C-6), 64.1 (C-5), 63.6 (CH₂CH₃ Et), 15.1 (CH₃ Et); ¹³C-GATED NMR (101 MHz, CDCl₃): δ 98.9 ($J_{C1,H1}$ = 169.7 Hz, C-1 α); Diagnostic peaks β -anomer: ¹H NMR (400 MHz, CDCl₃, HH-COSY, HSQC, HMBC): δ 8.80 (td, J = 1.8, 0.9 Hz, 1H, CH_{arom} Pico), 8.01 (dt, J = 7.9, 1.1 Hz, 1H, CH_{arom} Pico), 5.25 (dd, J = 10.4, 3.3 Hz, 1H, H-3), 4.22 (dd, J = 3.4, 0.9 Hz, 1H, H-2), 4.07 – 4.01 (m, 1H, CHHCH₃ Et), 3.68 – 3.57 (m, 1H, CHHCH₃ Et); ¹³C-APT NMR (101 MHz, CDCl₃, HSQC, HMBC): δ 101.8 (CHPh), 101.8 (C-1), 75.8 (C-2), 75.7 (C-4), 73.7 (CH₂ Bn), 68.8 (C-6), 66.0 (CH₂CH₃ Et); ¹³C-GATED NMR (101 MHz, CDCl₃): δ 101.8 ($J_{C1,H1}$ = 155.7 Hz, C-1 β); HRMS: [M+H]⁺ calcd for C₂₈H₃₀NO₇ 492.2017, found 492.2016.

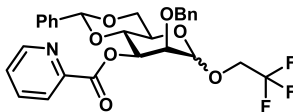


2-Fluoroethyl 2-O-benzyl-4,6-O-benzylidene-3-picoloyl- β -mannopyranoside (S2). The title compound was prepared from donor **17** and 2-fluoroethanol using the general procedure for Tf₂O/Ph₂SO mediated glycosylations. Flash column chromatography (100:0 $\rightarrow$ 60:40, pentane:EtOAc, v:v) yielded glycosylation product **S2** (26.1 mg, 0.051 mmol, 51%, α : β = 69:31). TLC: R_f 0.56, (70:30, pentane:EtOAc, v:v); Data for the α -anomer: ¹H NMR (400 MHz, CDCl₃, HH-COSY, HSQC, HMBC): δ 8.80 (dd, J = 1.8, 0.9 Hz, 1H, CH_{arom} Pico), 8.09 (dt, J = 7.8, 1.1 Hz, 1H, CH_{arom} Pico), 7.81 (td, J = 7.8, 1.8 Hz, 1H, CH_{arom} Pico), 7.54 – 6.98 (m, 11H, CH_{arom}), 5.69 (dd, J = 10.4, 3.5 Hz, 1H, H-3), 5.65 (s, 1H, CHPh), 4.97 (d, J = 1.6 Hz, 1H, H-1), 4.74 – 4.69 (m, 2H, CHH Bn, CHH Bn), 4.68 – 4.52 (m, 1H, CH₂F), 4.44 (dd, J = 10.4, 9.3 Hz, 1H, H-4), 4.30 – 4.26 (m, 1H, CHHCH₂F), 4.15 (dd, J = 3.5, 1.6 Hz, 1H, H-2), 4.10 – 3.95 (m, 1H, H-5), 3.94 – 3.86 (m, 2H, CHHCH₂F, H-6), 3.86 – 3.68 (m, 1H, H-6); ¹³C-APT NMR (101 MHz, CDCl₃, HSQC, HMBC): δ 164.4 (C=O Pico), 150.1 (CH_{arom} Pico), 147.9, 137.6, 137.4 (C_q), 137.0, 129.1, 128.8, 128.5, 128.3, 128.2, 128.0, 127.0, 126.3, 126.3, 125.7, 125.6 (CH_{arom}), 101.9 (CHPh), 99.4 (C-1), 82.6 (d, J = 170.3 Hz, CH₂F), 76.3 (C-2), 76.1 (C-4), 73.9 (CH₂ Bn), 71.9 (C-3), 68.9 (C-6), 67.0 (d, J = 20.0 Hz, CH₂CH₂F), 64.3 (C-5); ¹³C-GATED NMR (101 MHz, CDCl₃): δ 99.3 ($J_{C1,H1}$ = 170.4 Hz, C-1 α); Diagnostic peaks β -anomer: ¹H NMR (400 MHz, CDCl₃, HH-COSY, HSQC, HMBC): δ 8.01 (dt, J = 7.9, 1.1 Hz, 1H, CH_{arom} Pico), 5.71 (dd, J = 10.5, 3.5 Hz, 1H, H-3), 5.61 (s, 1H, CHPh), 4.80 (d, J = 1.0 Hz, 1H, H-1), 4.13 (dd, J = 3.3, 1.7 Hz, 1H, H-2); ¹³C-APT NMR (101 MHz, CDCl₃, HSQC, HMBC): δ 136.9 (CH_{arom} Pico), 101.9 (CHPh), 101.8 (C-1), 82.8 (d, J = 170.3 Hz, CH₂F), 76.4 (C-2), 76.3 (C-4), 69.2 (d, J = 20.1 Hz, CH₂CH₂F); ¹³C-GATED NMR (101 MHz, CDCl₃): δ 101.8 ($J_{C1,H1}$ = 156.9 Hz, C-1 β). HRMS: [M+H]⁺ calcd for C₂₈H₂₉FN₂O₇ 510.1923, found 510.1923.

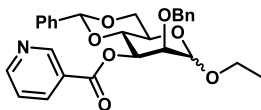


2,2-Difluoroethyl 2-O-benzyl-4,6-O-benzylidene-3-picoloyl- β -mannopyranoside (S3). The title compound was prepared from donor **17** and 2,2-difluoroethanol using the general procedure for Tf₂O/Ph₂SO mediated glycosylations. Flash column chromatography (100:0 $\rightarrow$ 60:40, pentane:EtOAc, v:v) yielded glycosylation product **S3** (33.7 mg, 0.064 mmol, 64%, α : β = 55:45). TLC: R_f 0.61, (70:30, pentane:EtOAc, v:v); Data for the α -anomer: ¹H NMR (400 MHz, CDCl₃, HH-COSY, HSQC, HMBC): δ 8.80 (dd, J = 1.8, 0.9 Hz, 1H, CH_{arom} Pico), 8.08 (dt, J = 2.1, 1.1 Hz, 1H, CH_{arom} Pico), 8.02 (dt, J = 7.9, 1.1 Hz, 1H, CH_{arom} Pico), 7.82 (dd, J = 7.7, 1.7 Hz, 1H, CH_{arom} Pico), 7.54 – 6.98 (m, 10H, CH_{arom}), 5.93 (tt, J = 53.4, 4.2 Hz, 1H, CHF₂), 5.71 (dd, J = 10.4, 3.4 Hz, 1H, H-3), 5.61 (s, 1H, CHPh), 5.03 (d, J = 11.4 Hz, 1H, CHH Bn), 4.91 (d, J = 11.2 Hz, 1H, CHH Bn), 4.45 (dd, J = 10.5,

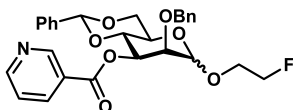
9.2 Hz, 1H, H-4), 4.40 – 4.23 (m, 1H, H-5), 4.13 (dd, $J = 3.4, 1.7$ Hz, 1H, H-2), 3.98 (t, $J = 10.4$ Hz, 1H, H-6), 3.94 – 3.68 (m, 1H, H-6, CH_2CHF_2); ^{13}C -APT NMR (101 MHz, CDCl_3 , HSQC, HMBC): δ 164.4 (C=O Pico), 150.1 (CH_{arom} Pico), 147.8, 147.5, 137.7 (C_q), 137.0, 129.1, 128.8, 128.8, 128.6, 128.5, 128.4, 128.3, 128.2, 127.8, 127.2, 126.3 (CH_{arom}), 114.0 (t, $J = 240.9$ Hz, CHF_2), 101.9 (CHPh), 99.7 (C-1), 76.4 (C-2), 76.3 (CH_2 Bn), 76.0 (C-4), 71.8 (C-3), 68.5 (C-6), 67.9 (C-5), 66.8 (t, $J = 32.3$ Hz, CH_2CHF_2); ^{13}C -GATED NMR (101 MHz, CDCl_3): δ 99.7 ($J_{\text{C1,H1}} = 171.7$ Hz, C-1 α of MHz, CDCl_3 , HSQC, HMBC): δ 102.0 (CHPh), 101.9 (C-1), 74.4 (C-3); ^{13}C -GATED NMR (101 MHz, CDCl_3): δ 101.9 ($J_{\text{C1,H1}} = 157.6$ Hz, C-1 β); HRMS: $[\text{M}+\text{H}]^+$ calcd for $\text{C}_{28}\text{H}_{28}\text{F}_2\text{NO}_7$ 528.1828, found 528.1829.



2,2,2-Trifluoroethyl 2-O-benzyl-4,6-O-benzylidene-3-picoloyl- β -mannopyranoside (S4). The title compound was prepared from donor **17** and 2,2,2-trifluoroethanol using the general procedure for $\text{TiF}_2/\text{Ph}_2\text{SO}$ mediated glycosylations. Flash column chromatography (100:0 $\rightarrow$ 60:40, pentane:EtOAc, v:v) yielded glycosylation product **S4** (34.7 mg, 0.064 mmol, 64%, $\alpha:\beta = 32:68$). TLC: R_f 0.69, (70:30, pentane:EtOAc, v:v); Data for the β -anomer: ^1H NMR (400 MHz, CDCl_3 , HH-COSY, HSQC, HMBC): δ 8.83 – 8.72 (m, 1H, CH_{arom} Pico), 8.17 – 6.89 (m, 13H, CH_{arom}), 5.61 (s, 1H, CHPh), 5.26 (dd, $J = 10.4, 3.4$ Hz, 1H, H-3), 4.93 (d, $J = 12.3$ Hz, 1H, CHH Bn), 4.85 (d, $J = 1.0$ Hz, 1H, H-1), 4.68 (d, $J = 12.0$ Hz, 1H, CHH Bn), 4.42 (t, $J = 10.1$ Hz, 1H, H-4), 4.29 (dd, $J = 3.5, 1.1$ Hz, 1H, H-2), 4.00 (q, $J = 9.4$ Hz, 2H, CH_2CF_3), 3.94 – 3.58 (m, 2H, H-6), 3.54 (td, $J = 9.7, 4.7$ Hz, 1H, H-5); ^{13}C -APT NMR (101 MHz, CDCl_3 , HSQC, HMBC): δ 153.2 (C=O Pico), 150.2 (CH_{arom}), 147.5, 137.5 (C_q), 137.0, 132.5, 129.3, 129.2, 128.8, 128.4, 128.3, 128.3, 127.9, 127.2, 126.3, 125.7, 123.1 (CH_{arom}), 101.9 (CHPh), 101.8 (C-1), 75.5 (CH_2 Bn), 75.5 (C-2), 74.9 (C-4), 73.3 (C-3), 68.5 (C-6), 68.0 (C-5), 66.4 (q, $J = 30.3$ Hz, CH_2CF_3); ^{13}C -GATED NMR (101 MHz, CDCl_3): δ 101.8 ($J_{\text{C1,H1}} = 158.3$ Hz, C-1 β); Diagnostic peaks α -anomer: ^1H NMR (400 MHz, CDCl_3 , HH-COSY, HSQC, HMBC): δ 5.63 (dd, $J = 9.2, 4.4$ Hz, 1H, H-3), 5.49 (s, 1H, CHPh), 4.95 (d, $J = 0.9$ Hz, 1H, H-1), 4.18 (dd, $J = 4.4, 1.0$ Hz, 1H, H-2); ^{13}C -APT NMR (101 MHz, CDCl_3 , HSQC, HMBC): δ 101.2 (CHPh), 99.4 (C-1), 75.8 (C-3), 75.4 (C-2), 70.5 (C-5); ^{13}C -GATED NMR (101 MHz, CDCl_3): δ 99.4 ($J_{\text{C1,H1}} = 170.1$ Hz, C-1 α); HRMS: $[\text{M}+\text{H}]^+$ calcd for $\text{C}_{28}\text{H}_{27}\text{F}_3\text{NO}_7$ 546.1734, found 546.1732.

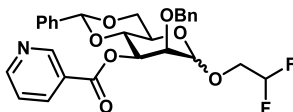


Ethyl 2-O-benzyl-4,6-O-benzylidene-3-nicotinoyl- β -mannopyranoside (S5). The title compound was prepared from donor **18** and ethanol using the general procedure for $\text{TiF}_2/\text{Ph}_2\text{SO}$ mediated glycosylations. Flash column chromatography (100:0 $\rightarrow$ 60:40, pentane:EtOAc, v:v) yielded glycosylation product **S5** (23.4 mg, 0.048 mmol, 48%, $\alpha:\beta = 80:20$). TLC: R_f 0.64, (70:30, pentane:EtOAc, v:v); Data for the α -anomer: ^1H NMR (400 MHz, CDCl_3 , HH-COSY, HSQC, HMBC): δ 7.86 – 7.77 (m, 2H, CH_{arom} Nico), 7.69 – 7.61 (m, 2H, CH_{arom} Nico), 7.55 – 7.34 (m, 10H, CH_{arom}), 5.59 (s, 1H, CHPh), 5.12 (d, $J = 12.1$ Hz, 1H, CHH Bn), 4.98 (d, $J = 12.0$ Hz, 1H, CHH Bn), 4.40 (d, $J = 7.7$ Hz, 1H, H-1), 4.35 (dd, $J = 10.5, 4.9$ Hz, 1H, H-6), 3.96 (dq, $J = 9.7, 7.1$ Hz, 1H, CHHCH_3 Et), 3.85 – 3.78 (m, 2H, H-4, H-6), 3.78 – 3.64 (m, 1H, H-3), 3.71 – 3.60 (m, 1H, CHHCH_3 Et), 3.63 – 3.54 (m, 1H, H-2), 3.50 – 3.41 (m, 1H, H-5), 1.35 – 1.11 (m, 3H, CH_3 Et); ^{13}C -APT NMR (101 MHz, CDCl_3 , HSQC, HMBC): δ 161.1 (C=O Nico), 137.4, 135.9 (C_q), 131.2, 129.5, 129.2, 128.4, 128.1, 127.8, 127.0, 126.2, 126.1, 124.9 (CH_{arom}), 103.2 (C-1), 101.5 (CHPh), 81.5 (C-3), 80.2 (C-4), 74.7 (CH_2 Bn), 74.6 (C-2), 68.9 (C-6), 66.6 (C-5), 66.0 (CH_2CH_3 Et), 15.3 (CH_3 Et); ^{13}C -GATED NMR (101 MHz, CDCl_3): δ 103.2 ($J_{\text{C1,H1}} = 169.9$ Hz, C-1 α); Diagnostic peaks β -anomer: ^1H NMR (400 MHz, CDCl_3 , HH-COSY, HSQC, HMBC): δ 7.75 – 7.70 (m, 2H, CH_{arom} Nico), 5.12 (d, $J = 12.0$ Hz, 1H, CH_2 Bn), 4.99 (d, $J = 11.9$ Hz, 1H, CH_2 Bn), 4.93 (d, $J = 4.0$ Hz, 1H, H-1), 4.29 (dd, $J = 10.1, 4.7$ Hz, 1H, H-6); ^{13}C -APT NMR (101 MHz, CDCl_3 , HSQC, HMBC): δ 98.8 (C-1), 82.0 (C-3), 79.3 (C-4), 74.9 (CH_2 Bn), 64.0 (CH_2CH_3 Et), 15.2 (CH_3 Et); ^{13}C -GATED NMR (101 MHz, CDCl_3): δ 98.8 ($J_{\text{C1,H1}} = 159.9$ Hz, C-1 β); HRMS: $[\text{M}+\text{H}]^+$ calcd for $\text{C}_{28}\text{H}_{30}\text{NO}_7$ 492.2017, found 492.2012.

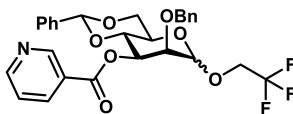


2-Fluoroethyl 2-O-benzyl-4,6-O-benzylidene-3-nicotinoyl- β -mannopyranoside (S6). The title compound was prepared from donor **18** and 2-fluoroethanol using the general procedure for $\text{TiF}_2/\text{Ph}_2\text{SO}$ mediated glycosylations. Flash column chromatography (100:0 $\rightarrow$ 60:40, pentane:EtOAc, v:v) yielded glycosylation product **S6** (19.3 mg, 0.038 mmol, 38%, $\alpha:\beta = 72:28$). TLC: R_f 0.57, (70:30, pentane:EtOAc, v:v); Data for the α -anomer: ^1H NMR (400 MHz, CDCl_3 , HH-COSY, HSQC, HMBC): δ 9.20 (ddd, $J = 7.5, 2.2, 0.9$ Hz, 1H, CH_{arom} Nico), 8.79 (dt, $J = 4.8, 1.6$ Hz, 1H, CH_{arom} Nico), 8.25 (dt, $J = 7.9, 1.9$ Hz, 1H, CH_{arom} Nico), 7.68 – 7.63 (m, 1H, CH_{arom}

Nico), 7.49 – 7.04 (m, 10H, CH_{arom}), 5.63 (s, 1H, CHPh), 5.57 (dd, J = 10.4, 3.5 Hz, 1H, H-3), 4.96 (d, J = 1.7 Hz, 1H, H-1), 4.94 (d, J = 12.1 Hz, 1H, CHH Bn), 4.87 (d, J = 11.6 Hz, 1H, CHH Bn), 4.75 – 4.48 (m, 2H, CH₂CH₂F), 4.35 (dd, J = 10.6, 9.2 Hz, 1H, H-4), 4.32 – 4.25 (m, 1H, H-6), 4.16 (dd, J = 3.5, 1.6 Hz, 1H, H-2), 4.05 – 3.68 (m, 2H, H-5, H-6), 3.60 (td, J = 9.8, 4.9 Hz, 1H, CHHCH₂F), 3.57 (dd, J = 9.8, 4.9 Hz, 1H, CHHCH₂F); ¹³C-APT NMR (101 MHz, CDCl₃, HSQC, HMBC): δ 164.6 (C=O Nico), 153.7, 151.2, 137.4, 131.8, 131.2, 129.5, 128.9, 128.6, 128.4, 128.4, 128.3, 128.1, 126.3, 124.9 (CH_{arom}), 101.9 (CHPh), 99.2 (C-1), 82.6 (d, J = 170.3 Hz, CH₂F), 76.3 (C-2), 76.3 (C-4), 73.9 (CH₂ Bn), 71.6 (C-3), 68.9 (C-6), 67.0 (d, J = 19.9 Hz, CH₂CH₂F), 64.3 (C-5); ¹³C-GATED NMR (101 MHz, CDCl₃): δ 99.2 ($J_{C1,H1}$ = 170.4 Hz, C-1 α); Diagnostic peaks β-anomer: ¹H NMR (400 MHz, CDCl₃, HH-COSY, HSQC, HMBC): δ 9.19 (dd, J = 2.2, 0.9 Hz, 1H, CH_{arom} Nico), 8.16 (dt, J = 8.0, 2.0 Hz, 1H, CH_{arom} Nico), 5.61 (s, 1H, CHPh), 5.16 (dd, J = 10.4, 3.3 Hz, 1H, H-3), 4.80 (d, J = 0.9 Hz, 1H, H-1); ¹³C-APT NMR (101 MHz, CDCl₃, HSQC, HMBC): δ 102.1 (CHPh), 101.9 (C-1), 82.8 (d, J = 170.2 Hz, CH₂F); ¹³C-GATED NMR (101 MHz, CDCl₃): δ 101.9 ($J_{C1,H1}$ = 156.0 Hz, C-1 β); HRMS: [M+H]⁺ calcd for C₂₈H₂₉FNO₇ 510.1923, found 510.1919.

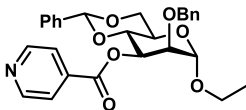


2,2-Difluoroethyl 2-O-benzyl-4,6-O-benzylidene-3-nicotinoyl-β-D-mannopyranoside (S7). The title compound was prepared from donor **18** and 2,2-difluoroethanol using the general procedure for Tf₂O/Ph₂SO mediated glycosylations. Flash column chromatography (100:0 → 60:40, pentane:EtOAc, v:v) yielded glycosylation product **S7** (26.4 mg, 0.050 mmol, 50%, α:β = 68:32). TLC: R_f 0.62, (70:30, pentane:EtOAc, v:v); Data for the α-anomer: ¹H NMR (400 MHz, CDCl₃, HH-COSY, HSQC, HMBC): δ 9.21 (dd, J = 2.2, 0.9 Hz, 1H, CH_{arom} Nico), 8.80 – 8.75 (m, 1H, CH_{arom} Nico), 8.25 (dt, J = 8.0, 1.9 Hz, 1H, CH_{arom} Nico), 7.48 – 7.05 (m, 11H, CH_{arom}), 5.93 (dd, J = 55.3, 4.7, 3.6 Hz, 2H, CH₂CHF₂), 5.63 (s, 1H, CHPh), 5.52 (dd, J = 10.5, 3.5 Hz, 1H, H-3), 4.93 (d, J = 1.7 Hz, 1H, H-1), 4.67 (d, J = 12.0 Hz, 1H, CHH Bn), 4.57 (d, J = 12.0 Hz, 1H, CHH Bn), 4.36 (dd, J = 10.5, 9.0 Hz, 1H, H-4), 4.32 – 4.27 (m, 2H, H-5, H-6), 4.16 (dd, J = 3.5, 1.7 Hz, 1H, H-2), 4.07 – 3.90 (m, 1H, H-6), 3.91 – 3.80 (m, 1H, CHHCHF₂), 3.79 – 3.67 (m, 1H, CHHCHF₂); ¹³C-APT NMR (101 MHz, CDCl₃, HSQC, HMBC): δ 164.6 (C=O Nico), 153.7, 151.2, 137.4 (CH_{arom}), 137.1 (C_q), 129.2, 128.6, 128.4, 128.3, 128.2, 126.2 (CH_{arom}), 125.8 (C_q), 123.4 (CH_{arom}), 114.0 (t, J = 241.6 Hz, CH₂CHF₂), 102.0 (CHPh), 99.4 (C-1), 76.0 (C-2), 75.9 (C-4), 74.0 (CH₂ Bn), 71.3 (C-3), 68.7 (C-6), 66.9 (t, J = 28.5 Hz, CH₂CHF₂), 64.6 (C-5); ¹³C-GATED NMR (101 MHz, CDCl₃): δ 99.4 ($J_{C1,H1}$ = 171.2 Hz, C-1 α); Diagnostic peaks β-anomer: ¹H NMR (400 MHz, CDCl₃, HH-COSY, HSQC, HMBC): δ 9.14 (dd, J = 2.2, 0.9 Hz, 1H, CH_{arom} Nico), 8.17 (dt, J = 7.9, 2.0 Hz, 1H, CH_{arom} Nico), 5.16 (dd, J = 10.4, 3.3 Hz, 1H, H-3), 4.79 (d, J = 1.0 Hz, 1H, H-1), 3.53 (td, J = 9.7, 4.9 Hz, 1H, CHHCHF₂); ¹³C-APT NMR (101 MHz, CDCl₃, HSQC, HMBC): δ 102.1 (C-1), 101.9 (CHPh), 75.6 (CH₂ Bn), 75.6 (C-2), 75.4 (C-4), 73.0 (C-3), 68.5 (C-6), 67.8 (C-5); ¹³C-GATED NMR (101 MHz, CDCl₃): δ 102.1 ($J_{C1,H1}$ = 157.9 Hz, C-1 β); HRMS: [M+H]⁺ calcd for C₂₈H₂₈F₂NO₇ 528.1828, found 528.1827.

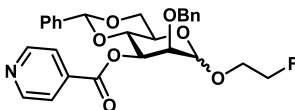


2,2,2-Trifluoroethyl 2-O-benzyl-4,6-O-benzylidene-3-nicotinoyl-β-D-mannopyranoside (S8). The title compound was prepared from donor **18** and 2,2,2-trifluoroethanol using the general procedure for Tf₂O/Ph₂SO mediated glycosylations. Flash column chromatography (100:0 → 60:40, pentane:EtOAc, v:v) yielded glycosylation product **S8** (29.4 mg, 0.054 mmol, 54%, α:β = 58:42). TLC: R_f 0.71, (70:30, pentane:EtOAc, v:v); Data for the α-anomer: ¹H NMR (850 MHz, CDCl₃, HH-COSY, HSQC, HMBC): δ 9.22 (dd, J = 2.2, 0.9 Hz, 1H, CH_{arom} Nico), 8.78 (dd, J = 4.8, 1.8 Hz, 1H, CH_{arom} Nico), 8.25 (dt, J = 7.9, 1.9 Hz, 1H, CH_{arom} Nico), 7.65 (dd, J = 8.2, 1.5 Hz, 1H, CH_{arom} Nico), 7.54 – 7.05 (m, 10H, CH_{arom}), 5.62 (s, 1H, CHPh), 5.54 (dd, J = 10.5, 3.6 Hz, 1H, H-3), 4.96 (d, J = 1.6 Hz, 1H, H-1), 4.66 (d, J = 12.0 Hz, 1H, CHH Bn), 4.59 (d, J = 12.0 Hz, 1H, CHH Bn), 4.37 (dd, J = 10.6, 9.3 Hz, 1H, H-4), 4.30 (dd, J = 10.4, 3.4 Hz, 1H, H-6), 4.19 (dd, J = 3.6, 1.6 Hz, 1H, H-2), 4.03 – 3.92 (m, 3H, CHHCF₃, CHHCF₃, H-5), 3.91 (t, J = 10.3 Hz, 1H, H-6); ¹³C-APT NMR (214 MHz, CDCl₃, HSQC, HMBC): δ 164.5 (C=O Nico), 153.8, 151.2 (CH_{arom} Nico), 137.5 (CH_{arom}), 137.4, 137.1, 137.1 (C_q), 129.5, 129.2, 128.7, 128.6, 128.4, 128.3 (CH_{arom}), 128.2, 126.2 (CH_{arom} Nico), 124.3 (1, J = 276.6 Hz, CF₃), 102.0 (CHPh), 99.4 (C-1), 75.9 (C-4), 75.8 (C-2), 74.1 (CH₂ Bn), 71.2 (C-3), 68.6 (C-6), 64.9 (C-5), 64.6 (q, J = 35.2 Hz, CH₂CF₃); ¹³C-GATED NMR (214 MHz, CDCl₃): δ 99.4 ($J_{C1,H1}$ = 172.1 Hz, C-1 α); Diagnostic peaks β-anomer: ¹H NMR (850 MHz, CDCl₃, HH-COSY, HSQC, HMBC): δ 9.14 (dd, J = 2.2, 0.9 Hz, 1H, CH_{arom} Nico), 8.78 (dd, J = 4.8, 1.8 Hz, 1H, CH_{arom} Nico), 8.17 (dt, J = 7.9, 1.9 Hz, 1H, CH_{arom} Nico), 7.65 (dd, J = 8.2, 1.5 Hz, 1H, CH_{arom} Nico), 7.56 – 7.06 (m, 10H, CH_{arom}), 5.61 (s, 1H, CHPh), 5.16 (dd, J = 10.4, 3.4 Hz, 1H, H-3), 4.84 (d, J = 1.0 Hz, 1H, H-1), 4.33 (dd, J = 10.4, 9.3 Hz, 1H, H-4), 3.53 (td, J = 9.7, 4.9 Hz, 1H, H-5); ¹³C-APT NMR (214 MHz, CDCl₃, HSQC, HMBC): δ 164.6 (C=O Nico), 137.5, 137.3 (CH_{arom} Nico), 137.2, 129.5, 129.3 (C_q), 128.7, 128.4, 128.4, 128.0, 126.2 (CH_{arom} Nico), 123.4 (q, J = 276.5, CF₃), 101.9 (CHPh), 101.7 (C-1), 75.6 (CH₂ Bn), 75.5 (C-2), 75.1 (C-3), 72.9 (C-4), 68.4 (C-6), 67.9 (C-5), 66.4 (q, J =

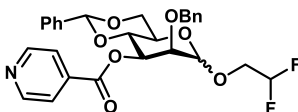
35.0 Hz, CH_2CF_3); ^{13}C -GATED NMR (214 MHz, CDCl_3): δ 101.7 ($J_{\text{C1,H1}} = 159.2$ Hz, C-1 β); HRMS: $[\text{M}+\text{H}]^+$ calcd for $\text{C}_{28}\text{H}_{27}\text{F}_3\text{NO}_7$ 546.1734, found 546.1730.



Ethyl 2-O-benzyl-4,6-O-benzylidene-3-isonicotinoyl- α -D-mannopyranoside (S9). The title compound was prepared from donor **19** and ethanol using the general procedure for $\text{Ti}_2\text{O}/\text{Ph}_2\text{SO}$ mediated glycosylations. Flash column chromatography (100:0 $\rightarrow$ 60:40, pentane:EtOAc, v:v) yielded glycosylation product **S9** (26.5 mg, 0.054 mmol, 54%, $\alpha:\beta = >98:2$). TLC: R_f 0.62, (70:30, pentane:EtOAc, v:v); ^1H NMR (400 MHz, CDCl_3 , HH-COSY, HSQC, HMBC): δ 8.80 – 8.73 (m, 1H, CH_{arom} *i*-Nico), 7.80 – 7.76 (m, 1H, CH_{arom} *i*-Nico), 7.45 – 7.17 (m, 8H, CH_{arom}), 5.61 (s, 1H, CHPh), 5.32 (dd, $J = 10.4, 3.3$ Hz, 1H, H-3), 5.06 (d, $J = 1.2$ Hz, 1H, H-1), 4.89 (d, $J = 12.0$ Hz, 1H, CHH Bn), 4.69 (d, $J = 11.2$ Hz, 1H, CHH Bn), 4.50 (dd, $J = 3.4, 1.2$ Hz, 1H, H-2), 4.40 (dd, $J = 10.4, 9.3$ Hz, 1H, H-4), 4.37 – 4.27 (m, 1H, H-6), 3.99 (t, $J = 10.3$ Hz, 1H, H-6), 3.78 (dq, $J = 9.6, 7.0$ Hz, 1H, CHHCH_3 Et), 3.60 (td, $J = 9.8, 4.9$ Hz, 1H, H-5), 3.51 (dq, $J = 9.7, 7.0$ Hz, 1H, CHHCH_3 Et), 1.29 – 1.22 (m, 3H, CH_3 Et); ^{13}C -APT NMR (101 MHz, CDCl_3 , HSQC, HMBC): δ 164.8 (C=O *i*-Nico), 150.8 (CH_{arom} *i*-Nico), 137.1, 136.6 (C_q), 134.2, 131.8, 129.3, 128.5, 128.4, 128.3, 128.2, 126.2 (CH_{arom}), 101.9 (CHPh), 98.6 (C-1), 78.9 (C-2), 75.6 (C-4), 75.0 (C-3), 73.8 (CH_2 Bn), 71.9 (C-5), 68.5 (C-6), 63.7 (CH_2CH_3 Et), 15.1 (CH_3 Et); ^{13}C -GATED NMR (101 MHz, CDCl_3): δ 98.6 ($J_{\text{C1,H1}} = 170.0$ Hz, C-1 α); HRMS: $[\text{M}+\text{H}]^+$ calcd for $\text{C}_{28}\text{H}_{30}\text{NO}_7$ 492.2017, found 492.2016.

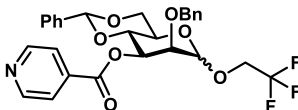


2-Fluoroethyl 2-O-benzyl-4,6-O-benzylidene-3-isonicotinoyl- α -D-mannopyranoside (S10). The title compound was prepared from donor **19** and 2-fluoroethanol using the general procedure for $\text{Ti}_2\text{O}/\text{Ph}_2\text{SO}$ mediated glycosylations. Flash column chromatography (100:0 $\rightarrow$ 60:40, pentane:EtOAc, v:v) yielded glycosylation product **S10** (30.0 mg, 0.059 mmol, 59%, $\alpha:\beta = 83:17$). TLC: R_f 0.51, (70:30, pentane:EtOAc, v:v); Data for the α -anomer: ^1H NMR (400 MHz, CDCl_3 , HH-COSY, HSQC, HMBC): δ 8.81 – 8.71 (m, 2H, CH_{arom} *i*-Nico), 7.79 (ddd, $J = 12.2, 4.4, 1.7$ Hz, 2H, CH_{arom} *i*-Nico), 7.57 – 7.50 (m, 2H, CH_{arom}), 7.50 – 7.11 (m, 8H, CH_{arom}), 5.62 (s, 1H, CHPh), 5.56 (dd, $J = 10.4, 3.5$ Hz, 1H, H-3), 4.96 (d, $J = 1.6$ Hz, 1H, H-1), 4.89 (d, $J = 11.3$ Hz, 1H, CHH Bn), 4.69 (d, $J = 11.7$ Hz, 1H, CHH Bn), 4.67 – 4.52 (m, 2H, $\text{CH}_2\text{CH}_2\text{F}$), 4.43 – 4.37 (m, 1H, H-6), 4.34 (t, $J = 10.4$ Hz, 1H, H-4), 4.14 (dd, $J = 3.5, 1.6$ Hz, 1H, H-2), 3.99 (t, $J = 10.5$ Hz, 1H, H-6), 3.81 (ddd, $J = 12.3, 5.7, 3.3$ Hz, 1H, CHHCH_2F), 3.74 (ddd, $J = 12.3, 5.7, 3.4$ Hz, 1H, CHHCH_2F), 3.60 (td, $J = 9.7, 4.9$ Hz, 1H, H-5); ^{13}C -APT NMR (101 MHz, CDCl_3 , HSQC, HMBC): δ 164.7 (C=O *i*-Nico), 150.7 (CH_{arom} *i*-Nico), 137.1, 134.2 (C_q), 131.8, 129.3, 128.6, 128.4, 128.1, 126.2, 123.2 (CH_{arom}), 101.9 (CHPh), 99.0 (C-1), 82.6 (d, $J = 170.3$ Hz, $\text{CH}_2\text{CH}_2\text{F}$), 76.3 (C-2), 76.2 (C-4), 73.9 (CH_2 Bn), 71.9 (C-3), 71.9 (C-5), 68.9 (C-6), 67.0 (d, $J = 19.9$ Hz, $\text{CH}_2\text{CH}_2\text{F}$); ^{13}C -GATED NMR (101 MHz, CDCl_3): δ 99.0 ($J_{\text{C1,H1}} = 170.3$ Hz, C-1 α); Diagnostic peaks β -anomer: ^1H NMR (400 MHz, CDCl_3 , HH-COSY, HSQC, HMBC): δ 5.16 (dd, $J = 10.4, 3.4$ Hz, 1H, H-3), 4.80 (d, $J = 0.9$ Hz, 1H, H-1), 3.53 (td, $J = 9.8, 4.9$ Hz, 1H, H-5); ^{13}C -APT NMR (101 MHz, CDCl_3 , HSQC, HMBC): δ 101.9 (C-1), 82.8 (d, $J = 170.2$ Hz, $\text{CH}_2\text{CH}_2\text{F}$), 69.2 (d, $J = 19.9$ Hz, $\text{CH}_2\text{CH}_2\text{F}$); ^{13}C -GATED NMR (101 MHz, CDCl_3): δ 101.9 ($J_{\text{C1,H1}} = 156.3$ Hz, C-1 β); HRMS: $[\text{M}+\text{H}]^+$ calcd for $\text{C}_{28}\text{H}_{29}\text{FNO}_7$ 510.1923, found 510.1922.

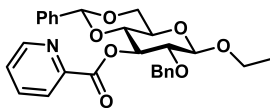


2,2-Difluoroethyl 2-O-benzyl-4,6-O-benzylidene-3-isonicotinoyl- α -D-mannopyranoside (S11). The title compound was prepared from donor **19** and 2,2-difluoroethanol using the general procedure for $\text{Ti}_2\text{O}/\text{Ph}_2\text{SO}$ mediated glycosylations. Flash column chromatography (100:0 $\rightarrow$ 60:40, pentane:EtOAc, v:v) yielded glycosylation product **S11** (32.2 mg, 0.061 mmol, 61%, $\alpha:\beta = 73:27$). TLC: R_f 0.60, (70:30, pentane:EtOAc, v:v); Data for the α -anomer: ^1H NMR (400 MHz, CDCl_3 , HH-COSY, HSQC, HMBC): δ 8.80 (m, 2H, CH_{arom} *i*-Nico), 7.82 – 7.80 (m, 2H, CH_{arom} *i*-Nico), 7.59 – 7.54 (m, 2H, CH_{arom}), 7.49 – 7.21 (m, 8H, CH_{arom}), 5.97 (ddd, $J = 55.2, 4.7, 3.6$ Hz, 1H, CH_2CHF_2), 5.65 (s, 1H, CHPh), 5.55 (dd, $J = 10.5, 3.6$ Hz, 1H, H-3), 4.97 (d, $J = 1.6$ Hz, 1H, H-1), 4.92 (d, $J = 11.3$ Hz, 1H, CHH Bn), 4.72 (d, $J = 11.3$ Hz, 1H, CHH Bn), 4.48 – 4.40 (m, 1H, H-6), 4.41 – 4.34 (m, 1H, H-4), 4.18 (dd, $J = 3.5, 1.6$ Hz, 1H, H-2), 4.02 (t, $J = 10.4$ Hz, 1H, H-6), 3.95 – 3.83 (m, 1H, CHHCH_2F_2), 3.80 (td, $J = 12.4, 4.7$ Hz, 1H, CHHCH_2F_2), 3.63 (td, $J = 9.7, 4.9$ Hz, 1H, H-5); ^{13}C -APT NMR (101 MHz, CDCl_3 , HSQC, HMBC): δ 164.6 (C=O *i*-Nico), 150.7 (CH_{arom} *i*-Nico), 137.0, 134.1 (C_q), 131.7, 129.2, 128.4, 128.3, 128.2, 128.0, 126.1 (CH_{arom}), 113.9 (t, $J = 240.2$ Hz, CHF_2), 101.8 (CHPh), 99.2 (C-1), 75.9 (C-2), 75.5 (C-4), 73.9 (CH_2 Bn), 71.7 (C-3), 71.6 (C-5), 68.4 (C-6), 66.8 (t, $J = 28.3$ Hz, CH_2CHF_2); ^{13}C -GATED NMR (101 MHz, CDCl_3): δ 99.2 ($J_{\text{C1,H1}} = 171.7$ Hz, C-1

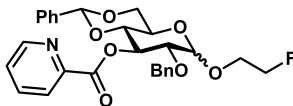
α); Diagnostic peaks β -anomer: ^1H NMR (400 MHz, CDCl_3 , HH-COSY, HSQC, HMBC): δ 5.97 (ddd, $J = 54.5, 5.2, 2.9$ Hz, 1H, CH_2CHF_2), 5.19 (dd, $J = 10.4, 3.4$ Hz, 1H, H-3), 4.82 (d, $J = 1.0$ Hz, 1H, H-1), 3.56 (td, $J = 9.8, 4.9$ Hz, 1H, H-5); ^{13}C -APT NMR (101 MHz, CDCl_3 , HSQC, HMBC): δ 101.9 (CHPh), 101.8 (C-1), 75.6 (CH_2 Bn), 68.6 (C-6); ^{13}C -GATED NMR (101 MHz, CDCl_3): δ 101.8 ($J_{\text{C1,H1}} = 158.0$ Hz, C-1 β); HRMS: $[\text{M}+\text{H}]^+$ calcd for $\text{C}_{28}\text{H}_{28}\text{F}_2\text{NO}_7$ 528.1828, found 528.1827.



2,2,2-Trifluoroethyl 2-O-benzyl-4,6-O-benzylidene-3-isonicotinoyl- β -D-mannopyranoside (S12). The title compound was prepared from donor **19** and 2,2,2-trifluoroethanol using the general procedure for $\text{TiF}_2\text{O}/\text{Ph}_2\text{SO}$ mediated glycosylations. Flash column chromatography (100:0 $\rightarrow$ 60:40, pentane:EtOAc, v:v) yielded glycosylation product **S12** (19.6 mg, 0.036 mmol, 36%, $\alpha:\beta = 50:50$). TLC: R_f 0.68, (70:30, pentane:EtOAc, v:v); Data for the α -anomer: ^1H NMR (400 MHz, CDCl_3 , HH-COSY, HSQC, HMBC): δ 8.76 (d, $J = 5.7$ Hz, 2H, CH_{arom} *i*-Nico), 7.79 (dd, $J = 12.9, 6.0$ Hz, 2H, CH_{arom} *i*-Nico), 7.56 – 7.50 (m, 2H, CH_{arom}), 7.49 – 7.14 (m, 8H, CH_{arom}), 5.62 (s, 1H, CHPh), 5.53 (dd, $J = 10.5, 3.5$ Hz, 1H, H-3), 4.97 (d, $J = 1.6$ Hz, 1H, H-1), 4.67 (d, $J = 12.0$ Hz, 1H, CHH Bn), 4.57 (d, $J = 12.0$ Hz, 1H, CHH Bn), 4.42 – 4.35 (m, 1H, H-4), 4.33 – 4.25 (m, 2H, H-6, CHHCF₃), 4.18 (dd, $J = 3.5, 1.6$ Hz, 1H, H-2), 4.09 – 3.87 (m, 2H, H-6, CHHCF₃), 3.60 (td, $J = 9.7, 4.9$ Hz, 1H, H-5); ^{13}C -APT NMR (101 MHz, CDCl_3 , HSQC, HMBC): δ 164.4 (C=O *i*-Nico), 150.8 (CH_{arom} *i*-Nico), 137.1, 136.7 (C_q), 135.6 (q, $J = 282.6$ Hz, CF₃), 131.8, 129.3, 128.6, 128.4, 128.1, 126.2, 123.1 (CH_{arom}), 102.0 (CHPh), 99.3 (C-1), 75.9 (C-2), 75.6 (C-4), 74.1 (CH_2 Bn), 71.9 (C-3), 71.5 (C-5), 68.6 (C-6), 66.4 (q, $J = 34.9$ Hz, CH_2CF_3); ^{13}C -GATED NMR (101 MHz, CDCl_3): δ 99.3 ($J_{\text{C1,H1}} = 171.6$ Hz, C-1 α); Diagnostic peaks β -anomer: ^1H NMR (400 MHz, CDCl_3 , HH-COSY, HSQC, HMBC): δ 8.76 (d, $J = 5.7$ Hz, 2H, CH_{arom} *i*-Nico), 7.79 – 7.72 (m, 2H, CH_{arom} *i*-Nico), 7.49 – 7.14 (m, 10H, CH_{arom}), 5.61 (s, 1H, CHPh), 5.16 (dd, $J = 10.4, 3.4$ Hz, 1H, H-3), 4.84 (d, $J = 0.9$ Hz, 1H, H-1), 4.67 (d, $J = 12.0$ Hz, 1H, CHH Bn), 4.59 (d, $J = 12.1$ Hz, 1H, CHH Bn), 4.30 (dd, $J = 5.5, 2.0$ Hz, 1H, H-2), 3.53 (td, $J = 10.1, 4.9$ Hz, 1H, H-5); ^{13}C -APT NMR (101 MHz, CDCl_3 , HSQC, HMBC): δ 164.8 (C=O *i*-Nico), 101.9 (CHPh), 101.9 (C-1), 68.4 (C-6); ^{13}C -GATED NMR (101 MHz, CDCl_3): δ 101.9 ($J_{\text{C1,H1}} = 158.6$ Hz, C-1 β); HRMS: $[\text{M}+\text{H}]^+$ calcd for $\text{C}_{28}\text{H}_{27}\text{F}_3\text{NO}_7$ 546.1734, found 546.1731.

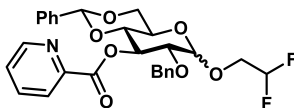


Ethyl 2-O-benzyl-4,6-O-benzylidene-3-picoloyl- β -D-glucopyranoside (S13). The title compound was prepared from donor **12** and ethanol using the general procedure for $\text{TiF}_2\text{O}/\text{Ph}_2\text{SO}$ mediated glycosylations. Flash column chromatography (100:0 $\rightarrow$ 60:40, pentane:EtOAc, v:v) yielded glycosylation product **S13** (19.1 mg, 0.039 mmol, 39%, $\alpha:\beta = <2:98$). TLC: R_f 0.59, (70:30, pentane:EtOAc, v:v); ^1H NMR (400 MHz, CDCl_3 , HH-COSY, HSQC, HMBC): δ 8.77 (ddt, $J = 4.7, 1.7, 0.8$ Hz, 1H, CH_{arom} Pico), 8.15 (dt, $J = 7.9, 1.1$ Hz, 1H, CH_{arom} Pico), 7.85 (td, $J = 7.8, 1.7$ Hz, 1H, CH_{arom} Pico), 7.48 (ddd, $J = 7.6, 4.7, 1.2$ Hz, 1H, CH_{arom} Pico), 7.43 – 7.35 (m, 2H, CH_{arom}), 7.34 – 7.25 (m, 2H, CH_{arom}), 7.20 – 7.06 (m, 6H, CH_{arom}), 5.66 (t, $J = 9.6$ Hz, 1H, H-3), 5.47 (s, 1H, CHPh), 4.83 (d, $J = 11.7$ Hz, 1H, CHH Bn), 4.67 (d, $J = 7.7$ Hz, 1H, H-1), 4.66 (d, $J = 11.6$ Hz, 1H, CHH Bn), 4.38 (dd, $J = 10.5, 5.0$ Hz, 1H, H-6), 4.03 (dq, $J = 9.6, 7.1$ Hz, 1H, CHHCH₃ Et), 3.86 (t, $J = 9.5$ Hz, 1H, H-4), 3.81 (t, $J = 10.3$ Hz, 1H, H-6), 3.69 (m, 1H, 73 CHHCH₃ Et), 3.71 – 3.62 (m, 1H, H-2), 3.58 (td, $J = 9.7, 5.0$ Hz, 1H, H-5), 1.32 (t, $J = 7.1$ Hz, 1H, CH₃ Et); ^{13}C -APT NMR (101 MHz, CDCl_3 , HSQC, HMBC): δ 165.4 (C=O Pico), 150.0, 137.1, 137.0, 129.1, 128.2, 127.6, 127.0, 126.3, 125.8, 125.3 (CH_{arom}), 104.2 (C-1), 101.5 (CHPh), 79.6 (C-2), 78.6 (C-4), 74.6 (CH_2 Bn), 74.2 (C-3), 68.9 (C-6), 66.4 (C-5), 66.4 (CH_2CH_3 Et), 15.5 (CH₃ Et); ^{13}C -GATED NMR (101 MHz, CDCl_3): δ 104.2 ($J_{\text{C1,H1}} = 160.7$ Hz, C-1 β); HRMS: $[\text{M}+\text{H}]^+$ calcd for $\text{C}_{28}\text{H}_{30}\text{NO}_7$ 492.2017, found 492.2018.

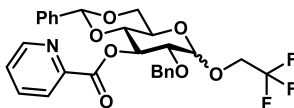


2-Fluoroethyl 2-O-benzyl-4,6-O-benzylidene-3-picoloyl- β -D-glucopyranoside (S14). The title compound was prepared from donor **12** and 2-fluoroethanol using the general procedure for $\text{TiF}_2\text{O}/\text{Ph}_2\text{SO}$ mediated glycosylations. Flash column chromatography (100:0 $\rightarrow$ 60:40, pentane:EtOAc, v:v) yielded glycosylation product **S14** (25.0 mg, 0.049 mmol, 49%, $\alpha:\beta = 24:76$). TLC: R_f 0.50, (70:30, pentane:EtOAc, v:v); Data for the β -anomer: ^1H NMR (400 MHz, CDCl_3 , HH-COSY, HSQC, HMBC): δ 8.79 (ddd, $J = 4.7, 1.8, 0.9$ Hz, 1H, CH_{arom} Pico), 8.17 (dt, $J = 7.9, 1.1$ Hz, 1H, CH_{arom} Pico), 7.87 (td, $J = 7.8, 1.8$ Hz, 1H, CH_{arom} Pico), 7.50 (ddd, $J = 7.6, 4.7, 1.2$ Hz, 1H, CH_{arom} Pico), 7.45 – 7.34 (m, 3H, CH_{arom}), 7.34 – 7.26 (m, 7H, CH_{arom}), 5.69 (dd, $J = 9.8, 9.2$ Hz, 1H, H-3), 5.50 (s, 1H, CHPh), 4.87 (d, $J = 11.6$ Hz, 1H, CHH Bn), 4.74 (d, $J = 7.6$ Hz, 1H, H-1), 4.72 – 4.70 (m, 1H, CH_2CHHF), 4.68 (d, $J = 11.6$ Hz, 1H, CHH Bn), 4.60 (td, $J = 6.0, 2.7$ Hz, 1H, CH_2CHHF), 4.40 (dd, $J = 10.5, 5.0$ Hz, 1H, H-6), 4.11

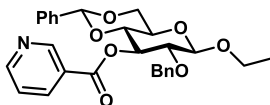
(dddd, $J = 32.0, 12.1, 4.8, 2.6$ Hz, 1H, CHHCH₂F), 3.91 (dddd, $J = 32.0, 12.0, 4.7, 2.6$ Hz, 1H, CHHCH₂), 3.90 (t, $J = 9.6$ Hz, 1H, H-4), 3.83 (t, $J = 10.3$ Hz, 1H, H-6), 3.73 (dd, $J = 9.3, 7.6$ Hz, 1H, H-2), 3.61 (td, $J = 9.7, 5.0$ Hz, 1H, H-5); ¹³C-APT NMR (101 MHz, CDCl₃, HSQC, HMBC): δ 165.3 (C=O Pico), 149.9 (CH_{arom} Pico), 148.3, 137.7 (C_q), 137.0, 129.0, 128.3, 128.2, 128.1, 127.6, 126.9, 126.2, 125.1 (CH_{arom}), 104.4 (C-1), 101.4 (CHPh), 82.4 (d, $J = 170.3$ Hz, CH₂CH₂F), 79.3 (C-2), 78.4 (C-2), 74.5 (CH₂ Bn), 73.9 (C-3), 69.4 (d, $J = 19.8$ Hz, CH₂CH₂F), 68.7 (C-6), 66.4 (C-5); ¹³C-GATED NMR (101 MHz, CDCl₃): δ 104.4 ($J_{C1,H1} = 161.4$ Hz, C-1 β); Diagnostic peaks α -anomer: ¹H NMR (400 MHz, CDCl₃, HH-COSY, HSQC, HMBC): δ 4.94 (d, $J = 3.6$ Hz, 1H, H-1); ¹³C-APT NMR (101 MHz, CDCl₃, HSQC, HMBC): δ 98.1 (C-1); ¹³C-GATED NMR (101 MHz, CDCl₃): δ 98.1 ($J_{C1,H1} = 169.7$ Hz, C-1 α); HRMS: [M+H]⁺ calcd for C₂₈H₂₉FNO₇ 510.1923, found 510.1922.



2,2-Difluoroethyl 2-O-benzyl-4,6-O-benzylidene-3-picoloyl- β -glucopyranoside (S15). The title compound was prepared from donor **12** and 2,2-difluoroethanol using the general procedure for Tf₂O/Ph₂SO mediated glycosylations. Flash column chromatography (100:0 $\rightarrow$ 60:40, pentane:EtOAc, v:v) yielded glycosylation product **S15** (16.3 mg, 0.031 mmol, 31%, α : β = 58:42). TLC: R_f 0.60, (70:30, pentane:EtOAc, v:v); Data for the α -anomer: ¹H NMR (400 MHz, CDCl₃, HH-COSY, HSQC, HMBC): δ 8.80 (ddd, $J = 4.7, 1.8, 0.9$ Hz, 1H, CH_{arom} Pico), 8.17 (dt, $J = 7.9, 1.1$ Hz, 1H, CH_{arom} Pico), 7.87 (td, $J = 7.7, 1.7$ Hz, 1H, CH_{arom} Pico), 7.50 (ddd, $J = 7.6, 4.8, 1.3$ Hz, 1H, CH_{arom} Pico), 7.20 – 7.05 (m, 10H, CH_{arom}), 5.97 (tdd, $J = 55.3, 4.8, 3.4$ Hz, 1H, CH₂CHF₂), 5.68 (dd, $J = 9.8, 9.2$ Hz, 1H, H-3), 5.50 (s, 1H, CHPh), 4.83 (d, $J = 11.6$ Hz, 1H, CHH Bn), 4.73 (d, $J = 7.6$ Hz, 1H, H-1), 4.66 (d, $J = 11.6$ Hz, 1H, CHH Bn), 4.40 (dd, $J = 10.5, 5.0$ Hz, 1H, H-6), 4.19 – 4.01 (m, 1H, CHHCHF₂), 3.98 – 3.93 (m, 1H, CHHCHF₂), 3.90 (t, $J = 9.6$ Hz, 1H, H-4), 3.83 (t, $J = 10.2$ Hz, 1H, H-6), 3.73 (dd, $J = 9.2, 7.5$ Hz, 1H, H-2), 3.62 (td, $J = 9.8, 5.0$ Hz, 1H, H-5); ¹³C-APT NMR (101 MHz, CDCl₃, HSQC, HMBC): δ 165.3 (C=O Pico), 149.3 (CH_{arom} Pico), 148.3 (C_q), 136.5, 130.5, 129.0, 128.2, 128.2, 127.7, 126.9, 126.2, 125.1 (CH_{arom}), 104.4 (C-1), 101.4 (CHPh), 79.0 (C-2), 78.2 (C-4), 74.6 (CH₂ Bn), 73.8 (C-3), 68.6 (C-6), 66.4 (C-5); ¹³C-GATED NMR (101 MHz, CDCl₃): δ 104.4 ($J_{C1,H1} = 171.2$ Hz, C-1 α); Diagnostic peaks β -anomer: ¹H NMR (400 MHz, CDCl₃, HH-COSY, HSQC, HMBC): δ 5.00 (d, $J = 7.6$ Hz, 1H, H-1); ¹³C-APT NMR (101 MHz, CDCl₃, HSQC, HMBC): δ 98.2 (C-1).

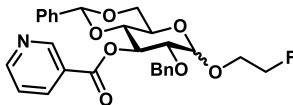


2,2,2-Trifluoroethyl 2-O-benzyl-4,6-O-benzylidene-3-picoloyl- β -glucopyranoside (S16). The title compound was prepared from donor **12** and 2,2,2-trifluoroethanol using the general procedure for Tf₂O/Ph₂SO mediated glycosylations. Flash column chromatography (100:0 $\rightarrow$ 60:40, pentane:EtOAc, v:v) yielded glycosylation product **S16** (15.3 mg, 0.028 mmol, 28%, α : β = 74:26). TLC: R_f 0.67, (70:30, pentane:EtOAc, v:v); Data for the β -anomer: ¹H NMR (400 MHz, CDCl₃, HH-COSY, HSQC, HMBC): δ 8.80 (ddd, $J = 4.7, 1.8, 0.9$ Hz, 1H, CH_{arom} Pico), 8.17 (dt, $J = 7.9, 1.1$ Hz, 1H, CH_{arom} Pico), 7.87 (td, $J = 7.8, 1.8$ Hz, 1H, CH_{arom} Pico), 7.51 (ddd, $J = 7.6, 4.7, 1.2$ Hz, 1H, CH_{arom} Pico), 7.20 – 7.07 (m, 10H, CH_{arom}), 5.68 (t, $J = 9.5$ Hz, 1H, H-3), 5.33 (s, 1H, CHPh), 4.85 (d, $J = 11.5$ Hz, 1H, CHH Bn), 4.79 (d, $J = 7.5$ Hz, 1H, H-1), 4.65 (d, $J = 11.8$ Hz, 1H, CHH Bn), 4.40 (dd, $J = 10.6, 5.0$ Hz, 1H, H-6), 4.35 – 4.22 (m, 1H, CHHCF₃), 4.13 – 4.00 (m, 1H, CHHCF₃), 3.91 (t, $J = 9.6$ Hz, 1H, H-4), 3.83 (t, $J = 9.4$ Hz, 1H, H-6), 3.80 – 3.71 (m, 1H, H-2), 3.61 (dt, $J = 9.7, 4.9$ Hz, 1H, H-5); ¹³C-APT NMR (101 MHz, CDCl₃, HSQC, HMBC): δ 103.4 (C-1), 101.4 (CHPh), 77.1 (C-4), 77.0 (C-2), 74.5 (C-3), 67.7 (C-6), 66.3 (C-5); ¹³C-GATED NMR (101 MHz, CDCl₃): δ 103.4 ($J_{C1,H1} = 162.9$ Hz, C-1 β); HRMS: [M+H]⁺ calcd for C₂₈H₂₇F₃NO₇ 546.1734, found 546.17320.

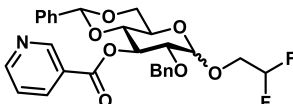


Ethyl 2-O-benzyl-4,6-O-benzylidene-3-nicotinoyl- β -glucopyranoside (S17). The title compound was prepared from donor **13** and ethanol using the general procedure for Tf₂O/Ph₂SO mediated glycosylations. Flash column chromatography (100:0 $\rightarrow$ 60:40, pentane:EtOAc, v:v) yielded glycosylation product **S17** (23.1 mg, 0.047 mmol, 47%, α : β = 2:98). TLC: R_f 0.63, (70:30, pentane:EtOAc, v:v); Data for the β -anomer: ¹H NMR (400 MHz, CDCl₃, HH-COSY, HSQC, HMBC): δ 9.09 (ddd, $J = 11.2, 2.2, 0.9$ Hz, 1H, CH_{arom} Nico), 8.76 (dt, $J = 4.9, 2.0$ Hz, 1H, CH_{arom} Nico), 8.18 (ddt, $J = 9.9, 7.9, 1.8$ Hz, 1H, CH_{arom} Nico), 7.62 – 7.53 (m, 1H, CH_{arom} Nico), 7.44 – 7.17 (m, 8H, CH_{arom}), 7.16 – 6.98 (m, 2H, CH_{arom}), 5.56 (t, $J = 9.5$ Hz, 1H, H-3), 5.46 (s, 1H, CHPh), 4.83 (d, $J = 11.8$ Hz, 1H, CHH Bn), 4.68 (d, $J = 7.6$ Hz, 1H, H-1), 4.65 (d, $J = 11.9$ Hz, 1H, CHH Bn), 4.40 (dd, $J = 11.3, 10.5$ Hz, 1H, H-6), 4.03 (dd, $J = 9.6, 7.1$ Hz, 1H, CHHCH₃ Et), 3.85 – 3.74 (m, 2H, H-6, CHHCH₃ Et), 3.72 (dd, $J = 9.6, 7.1$ Hz, 1H, H-4), 3.62 (td, $J = 9.7, 5.0$ Hz, 1H, H-5), 3.56 (dd, $J = 9.2, 7.6$ Hz, 1H, H-2), 1.40 – 1.23 (m, 3H, CH₃ Et); ¹³C-APT

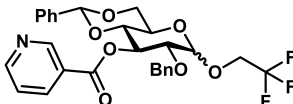
NMR (101 MHz, CDCl₃, HSQC, HMBC): δ 164.3 (C=O Nico), 153.5, 151.1 (CH_{arom} Nico), 137.4 (C_q), 137.4, 132.4, 129.3, 128.5, 128.3, 127.8, 126.2 (CH_{arom}), 125.9 (C_q), 123.3 (CH_{arom}), 104.2 (C-1), 101.5 (CHPh), 78.8 (C-2), 75.4 (C-4), 74.3 (CH₂ Bn), 73.6 (C-3), 70.5 (C-5), 68.8 (C-6), 66.3 (CH₂CH₃ Et), 15.4 (CH₃ Et); ¹³C-GATED NMR (101 MHz, CDCl₃): δ 104.2 (*J*_{C1,H1} = 160.7 Hz, C-1 β); HRMS: [M+H]⁺ calcd for C₂₈H₃₀NO₇ 492.2017, found 492.2020.



2-Fluoroethyl 2-O-benzyl-4,6-O-benzylidene-3-nicotinoyl- β -D-glucopyranoside (S18). The title compound was prepared from donor **13** and 2-fluoroethanol using the general procedure for Tf₂O/Ph₂SO mediated glycosylations. Flash column chromatography (100:0 $\rightarrow$ 60:40, pentane:EtOAc, v:v) yielded glycosylation product **S18** (35.1 mg, 0.069 mmol, 69%, α : β = 26:74). TLC: R_f 0.49, (70:30, pentane:EtOAc, v:v); Data for the β -anomer: ¹H NMR (400 MHz, CDCl₃, HH-COSY, HSQC, HMBC): δ 9.14 (dd, *J* = 2.2, 0.9 Hz, 1H, CH_{arom} Nico), 8.80 (td, *J* = 5.0, 1.7 Hz, 1H, CH_{arom} Nico), 8.25 – 8.19 (m, 1H, CH_{arom} Nico), 7.63 – 7.59 (m, 2H, CH_{arom}), 7.45 – 7.07 (m, 8H, CH_{arom}), 5.61 (t, *J* = 9.4 Hz, 1H, H-3), 5.51 (s, 1H, CHPh), 4.88 (d, *J* = 11.8 Hz, 1H, CHH Bn), 4.76 (d, *J* = 7.6 Hz, 1H, H-1), 4.76 – 4.70 (m, 1H, CH₂CHHF), 4.69 (d, *J* = 11.8 Hz, 1H, CHH Bn), 4.63 – 4.59 (m, 1H, CH₂CHHF), 4.45 (dd, *J* = 10.5, 5.0 Hz, 1H, H-6), 4.19 (dddd, *J* = 31.9, 12.1, 4.7, 2.6 Hz, 1H, CHHCH₂F), 3.97 (dddd, *J* = 31.9, 12.1, 6.4, 2.9 Hz, 1H, CHHCH₂F), 3.86 (t, *J* = 10.3 Hz, 1H, H-6), 3.75 (dd, *J* = 9.7, 8.7 Hz, 1H, H-4), 3.64 (dd, *J* = 9.1, 7.6 Hz, 1H, H-2), 3.62 (td, *J* = 9.7, 4.7 Hz, 1H, H-5); ¹³C-APT NMR (101 MHz, CDCl₃, HSQC, HMBC): δ 164.1 (C=O Nico), 153.5, 150.9, 137.3 (CH_{arom} Nico), 136.7, 132.9 (C_q), 132.3, 129.2, 129.1, 128.4, 128.3, 128.2, 126.1 (CH_{arom}), 104.3 (C-1), 101.4 (CHPh), 82.4 (d, *J* = 170.5 Hz, CH₂CH₂F), 78.8 (C-2), 78.6 (C-4), 74.2 (CH₂ Bn), 73.4 (C-3), 70.4 (C-5), 69.4 (d, *J* = 19.9 Hz, CH₂CH₂F), 68.6 (C-6); ¹³C-GATED NMR (101 MHz, CDCl₃): δ 104.3 (*J*_{C1,H1} = 162.1 Hz, C-1 β); HRMS: [M+H]⁺ calcd for C₂₈H₂₉FNO₇ 510.1923, found 510.1923.

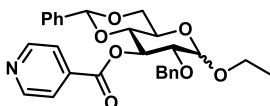


2,2-Difluoroethyl 2-O-benzyl-4,6-O-benzylidene-3-nicotinoyl- β -D-glucopyranoside (S19). The title compound was prepared from donor **13** and 2,2-difluoroethanol using the general procedure for Tf₂O/Ph₂SO mediated glycosylations. Flash column chromatography (100:0 $\rightarrow$ 60:40, pentane:EtOAc, v:v) yielded glycosylation product **S19** (22.1 mg, 0.042 mmol, 42%, α : β = 65:35). TLC: R_f 0.61, (70:30, pentane:EtOAc, v:v); Data for the β -anomer: ¹H NMR (400 MHz, CDCl₃, HH-COSY, HSQC, HMBC): δ 9.14 (dd, *J* = 2.2, 0.9 Hz, 1H, CH_{arom} Nico), 8.79 (dd, *J* = 4.9, 1.7 Hz, 1H, CH_{arom} Nico), 8.23 (dt, *J* = 8.0, 2.0 Hz, 1H, CH_{arom} Nico), 7.65 – 7.57 (m, 3H, CH_{arom}), 7.45 – 7.09 (m, 8H, CH_{arom}), 6.00 (tdd, *J* = 55.3, 4.8, 3.3 Hz, 1H, CH₂CHF₂), 5.60 (dd, *J* = 9.7, 9.1 Hz, 1H, H-3), 5.50 (s, 1H, CHPh), 4.84 (d, *J* = 11.8 Hz, 1H, CHH Bn), 4.75 (d, *J* = 7.5 Hz, 1H, H-1), 4.65 (d, *J* = 12.0 Hz, 1H, CHH Bn), 4.44 (dd, *J* = 10.6, 5.0 Hz, 1H, H-6), 4.12 (dddd, *J* = 16.9, 12.7, 11.7, 3.3 Hz, 1H, CHHCHF₂), 4.00 – 3.84 (m, 1H, CHHCHF₂), 3.86 – 3.78 (m, 1H, H-6), 3.75 (dd, *J* = 9.7, 8.8 Hz, 1H, H-4), 3.70 – 3.57 (m, 2H, H-2, H-5); ¹³C-APT NMR (101 MHz, CDCl₃, HSQC, HMBC): δ 164.2 (C=O Nico), 153.6, 151.0, 137.5 (CH_{arom} Nico), 136.8, 133.0 (C_q), 132.5, 129.3, 129.2, 128.4, 128.4, 126.2, 123.4 (CH_{arom}), 104.5 (C-1), 101.6 (CHPh), 78.9 (C-2), 78.6 (C-4), 74.5 (CH₂ Bn), 73.4 (C-3), 69.0 (t, *J* = 28.9 Hz, CH₂CHF₂), 68.7 (C-6), 66.4 (C-5); ¹³C-GATED NMR (101 MHz, CDCl₃): δ 104.5 (*J*_{C1,H1} = 162.6 Hz, C-1 β); HRMS: [M+H]⁺ calcd for C₂₈H₂₈F₂NO₇ 528.1828, found 528.1832.

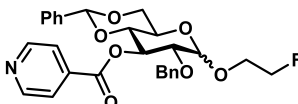


2,2,2-Trifluoroethyl 2-O-benzyl-4,6-O-benzylidene-3-nicotinoyl- β -D-glucopyranoside (S20). The title compound was prepared from donor **13** and 2,2,2-trifluoroethanol using the general procedure for Tf₂O/Ph₂SO mediated glycosylations. Flash column chromatography (100:0 $\rightarrow$ 60:40, pentane:EtOAc, v:v) yielded glycosylation product **S20** (32.7 mg, 0.060 mmol, 60%, α : β = 92:8). TLC: R_f 0.65, (70:30, pentane:EtOAc, v:v); Data for the α -anomer: ¹H NMR (850 MHz, CDCl₃, HH-COSY, HSQC, HMBC): δ 9.18 (dd, *J* = 2.2, 0.9 Hz, 1H, CH_{arom} Nico), 8.78 (dd, *J* = 4.8, 1.8 Hz, 1H, CH_{arom} Nico), 8.27 (dt, *J* = 7.9, 2.0 Hz, 1H, CH_{arom} Nico), 7.42 – 7.07 (m, 11H, CH_{arom}), 5.83 (t, *J* = 9.7 Hz, 1H, H-3), 5.47 (s, 1H, CHPh), 4.94 (d, *J* = 3.7 Hz, 1H, H-1), 4.61 (d, *J* = 1.2 Hz, 2H, CH₂ Bn), 4.29 (dd, *J* = 10.5, 4.9 Hz, 1H, H-6), 4.01 – 3.94 (m, 3H, H-5, CHHCF₃, CHHCF₃), 3.77 – 3.70 (m, 3H, H-2, H-4, H-6); ¹³C-APT NMR (214 MHz, CDCl₃, HSQC, HMBC): δ 164.1 (C=O Nico), 153.5, 150.9 (CH_{arom} Nico), 137.5 (CH_{arom}), 137.3, 136.7 (C_q), 132.4, 129.1, 128.5, 128.2, 128.2, 128.0, 126.2 (CH_{arom}), 126.1 (C_q), 123.6 (q, *J* = 279.1 Hz, CF₃), 123.4 (CH_{arom}), 101.6 (CHPh), 98.3 (C-1), 79.1 (C-4), 77.0 (C-2), 72.8 (CH₂ Bn), 71.2 (C-3), 68.6 (C-6), 65.3 (q, *J* = 35.1 Hz, CH₂CF₃), 63.23 (C-5); ¹³C-GATED NMR (214 MHz, CDCl₃): δ 98.3 (*J*_{C1,H1} = 170.4 Hz, C-1 α); Diagnostic peaks β -anomer: ¹H NMR (850 MHz, CDCl₃, HH-COSY, HSQC, HMBC): δ 9.08 (dd, *J* = 2.2, 0.9 Hz, 1H, CH_{arom} Nico), 8.76 (dd, *J* = 4.8, 1.8 Hz, 1H, CH_{arom} Nico), 8.17 (dt, *J* = 7.9, 2.0 Hz, 1H, CH_{arom} Nico), 5.56 (dd, *J* = 9.7,

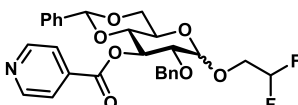
9.0 Hz, 1H, H-3), 4.77 (d, J = 7.4 Hz, 1H), 4.38 (dd, J = 10.6, 5.0 Hz, 1H, H-6); ^{13}C -APT NMR (214 MHz, CDCl_3 , HSQC, HMBC): δ 101.5 (C-1); ^{13}C -GATED NMR (214 MHz, CDCl_3): δ 101.5 ($J_{\text{C1,H1}}$ = 162.6 Hz, C-1 β); HRMS: $[\text{M}+\text{H}]^+$ calcd for $\text{C}_{28}\text{H}_{27}\text{F}_3\text{NO}_7$ 546.1734, found 546.1739.



Ethyl 2-*O*-benzyl-4,6-*O*-benzylidene-3-isonicotinoyl- β -D-glucopyranoside (S21). The title compound was prepared from donor **14** and ethanol using the general procedure for $\text{TiF}_2\text{O}/\text{Ph}_2\text{SO}$ mediated glycosylations. Flash column chromatography (100:0 $\rightarrow$ 60:40, pentane:EtOAc, v:v) yielded glycosylation product **S21** (25.1 mg, 0.051 mmol, 51%, $\alpha:\beta$ = 16:84). TLC: R_f 0.62, (70:30, pentane:EtOAc, v:v); Data for the β -anomer: ^1H NMR (400 MHz, CDCl_3 , HH-COSY, HSQC, HMBC): δ 8.74 (dt, J = 4.4, 1.3 Hz, 2H, CH_{arom} *i*-Nico), 7.74 – 7.71 (m, 2H, CH_{arom} *i*-Nico), 7.62 – 7.52 (m, 2H, CH_{arom}), 7.43 – 7.25 (m, 8H CH_{arom}), 5.63 (dd, J = 9.8, 8.8 Hz, 1H, H-3), 5.48 (s, 1H, *CHPh*), 4.90 (d, J = 11.0 Hz, 1H, *CHH* Bn), 4.67 (d, J = 7.7 Hz, 1H, H-1), 4.57 (d, J = 11.0 Hz, 1H, *CHH* Bn), 4.41 (dd, J = 10.6, 5.0 Hz, 1H, H-6), 4.04 (dq, J = 9.6, 7.1 Hz, 1H, *CHHCH}_3* Et), 3.87 – 3.77 (m, 2H, H-6, *CHHCH}_3* Et), 3.77 – 3.67 (m, 2H, H-2, H-4), 3.62 (td, J = 9.7, 4.9 Hz, 1H, H-5), 1.32 – 1.21 (m, 3H, CH_3 Et); ^{13}C -APT NMR (101 MHz, CDCl_3 , HSQC, HMBC): δ 164.0 (C=O *i*-Nico), 150.5 (CH_{arom} *i*-Nico), 136.7, 132.9 (C_q), 132.4, 129.2, 128.4, 128.2, 128.2, 128.0, 126.1, 123.0 (CH_{arom}), 104.1 (C-1), 101.4 (*CHPh*), 78.9 (C-2), 78.7 (C-4), 74.2 (CH_2 Bn), 73.9 (C-3), 70.4 (C-5), 68.6 (C-6), 66.3 (CH_2CH_3 Et), 15.4 (CH_3 Et); ^{13}C -GATED NMR (101 MHz, CDCl_3): δ 104.1 ($J_{\text{C1,H1}}$ = 160.7 Hz, C-1 β); HRMS: $[\text{M}+\text{H}]^+$ calcd for $\text{C}_{28}\text{H}_{30}\text{NO}_7$ 492.2017, found 492.2016.

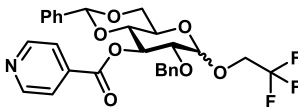


2-Fluoroethyl 2-*O*-benzyl-4,6-*O*-benzylidene-3-isonicotinoyl- β -D-glucopyranoside (S22). The title compound was prepared from donor **14** and 2-fluoroethanol using the general procedure for $\text{TiF}_2\text{O}/\text{Ph}_2\text{SO}$ mediated glycosylations. Flash column chromatography (100:0 $\rightarrow$ 60:40, pentane:EtOAc, v:v) yielded glycosylation product **S22** (18.8 mg, 0.037 mmol, 37%, $\alpha:\beta$ = 28:72). TLC: R_f 0.57, (70:30, pentane:EtOAc, v:v); Data for the β -anomer: ^1H NMR (400 MHz, CDCl_3 , HH-COSY, HSQC, HMBC): δ 8.78 – 8.69 (m, 2H, CH_{arom} *i*-Nico), 7.76 – 7.68 (m, 2H, CH_{arom} *i*-Nico), 7.61 – 7.54 (m, 2H, CH_{arom}), 7.42 – 7.24 (m, 2H, CH_{arom}), 7.22 – 7.03 (m, 6H, CH_{arom}), 5.55 (t, J = 9.5 Hz, 1H, H-3), 5.46 (s, 1H, *CHPh*), 4.84 (d, J = 11.8 Hz, 1H, *CHH* Bn), 4.72 (d, J = 7.4 Hz, 1H, H-1), 4.73 – 4.67 (m, 1H, CH_2CHHF), 4.64 (d, J = 11.9 Hz, 1H, *CHH* Bn), 4.63 – 4.55 (m, 1H, CH_2CHHF), 4.41 (dd, J = 10.5, 5.0 Hz, 1H, H-6), 4.20 (dddd, J = 32.0, 12.0, 4.7, 2.6 Hz, 1H, *CHHCH}_2\text{F}*), 3.97 (dddd, J = 26.5, 12.1, 6.4, 2.9 Hz, 1H, *CHHCH}_2\text{F}*), 3.82 (t, J = 10.2 Hz, 1H, H-6), 3.74 – 3.68 (m, 1H, H-4), 3.67 – 3.52 (m, 2H, H-2, H-5); ^{13}C -APT NMR (101 MHz, CDCl_3 , HSQC, HMBC): δ 164.1 (C=O *i*-Nico), 150.6 (CH_{arom} *i*-Nico), 136.8, 133.0 (C_q), 132.5, 129.3, 129.2, 128.5, 128.3, 128.3, 126.2, 123.1 (CH_{arom}), 104.4 (C-1), 101.5 (*CHPh*), 82.5 (d, J = 170.4 Hz, $\text{CH}_2\text{CH}_2\text{F}$), 78.8 (C-2), 78.6 (C-4), 74.3 (CH_2 Bn), 73.9 (C-3), 69.5 (d, J = 19.9 Hz, $\text{CH}_2\text{CH}_2\text{F}$), 68.7 (C-6), 66.3 (C-5); ^{13}C -GATED NMR (101 MHz, CDCl_3): δ 104.4 ($J_{\text{C1,H1}}$ = 161.9 Hz, C-1 β); HRMS: $[\text{M}+\text{H}]^+$ calcd for $\text{C}_{28}\text{H}_{29}\text{FNO}_7$ 510.1923, found 510.1920.

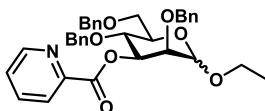


2,2-Difluoroethyl 2-*O*-benzyl-4,6-*O*-benzylidene-3-isonicotinoyl- β -D-glucopyranoside (S23). The title compound was prepared from donor **14** and 2,2-difluoroethanol using the general procedure for $\text{TiF}_2\text{O}/\text{Ph}_2\text{SO}$ mediated glycosylations. Flash column chromatography (100:0 $\rightarrow$ 60:40, pentane:EtOAc, v:v) yielded glycosylation product **S23** (30.1 mg, 0.057 mmol, 57%, $\alpha:\beta$ = 80:20). TLC: R_f 0.61, (70:30, pentane:EtOAc, v:v); Data for the α -anomer: ^1H NMR (850 MHz, CDCl_3 , HH-COSY, HSQC, HMBC): δ 8.78 – 8.76 (m, 2H, CH_{arom} *i*-Nico), 7.81 – 7.78 (m, 2H, CH_{arom} *i*-Nico), 7.40 – 7.07 (m, 10H, CH_{arom}), 5.99 (tdd, J = 55.2, 4.7, 3.8 Hz, 1H, CH_2CHF_2), 5.79 (t, J = 9.7 Hz, 1H, H-3), 5.47 (s, 1H, *CHPh*), 4.93 (d, J = 3.6 Hz, 1H, H-1), 4.61 (d, J = 12.4 Hz, 1H, *CHH* Bn), 4.58 (d, J = 12.5 Hz, 1H, *CHH* Bn), 4.30 (dd, J = 10.5, 4.9 Hz, 1H, H-6), 3.99 (td, J = 9.9, 4.9 Hz, 1H, H-5), 3.77 – 3.68 (m, 5H, H-2, H-4, H-6, *CHHCH}_2\text{F}_2*, *CHHCH}_2\text{F}_2*); ^{13}C -APT NMR (214 MHz, CDCl_3 , HSQC, HMBC): δ 164.0 (C=O *i*-Nico), 150.6 (CH_{arom} *i*-Nico), 137.2, 136.9, 136.7 (C_q), 132.4, 126.1 (CH_{arom}), 123.0 (CH_{arom} *i*-Nico), 114.0 (t, J = 241.5 Hz, *CHF}_2*), 101.6 (*CHPh*), 98.1 (C-1), 78.5 (C-4), 77.2 (C-2), 72.9 (CH_2 Bn), 71.6 (C-3), 68.7 (C-6), 67.4 (t, J = 28.9 Hz, CH_2CHF_2), 62.98 (C-5); ^{13}C -GATED NMR (214 MHz, CDCl_3): δ 98.1 ($J_{\text{C1,H1}}$ = 169.8 Hz, C-1 α); Diagnostic peaks β -anomer: ^1H NMR (850 MHz, CDCl_3 , HH-COSY, HSQC, HMBC): δ 8.75 – 8.74 (m, 2H, CH_{arom} *i*-Nico), 7.71 – 7.69 (m, 2H, CH_{arom} *i*-Nico), 7.42 – 7.06 (m, 10H, CH_{arom}), 5.96 (tdd, J = 55.4, 4.8, 3.4 Hz, 1H, CH_2CHF_2), 5.54 (dd, J = 9.7, 9.0 Hz, 1H, H-3), 4.71 (d, J = 7.5 Hz, 1H, H-1), 4.38 (dd, J = 10.7, 5.0 Hz, 1H, H-6); ^{13}C -APT NMR (214 MHz, CDCl_3 , HSQC, HMBC): δ 164.0 (C=O *i*-Nico), 150.5 (CH_{arom} *i*-Nico), 101.6 (*CHPh*), 101.5 (C-1), 73.7 (C-4), 66.2 (C-

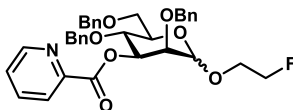
5); ^{13}C -GATED NMR (214 MHz, CDCl_3): δ 101.5 ($J_{\text{C1,H1}} = 162.2$ Hz, C-1 β); HRMS: $[\text{M}+\text{H}]^+$ calcd for $\text{C}_{28}\text{H}_{28}\text{F}_2\text{NO}_7$ 528.1828, found 528.1829.



2,2,2-Trifluoroethyl 2-O-benzylidene-4,6-O-benzylidene-3-isonicotinoyl- β -D-glucopyranoside (S24). The title compound was prepared from donor **14** and 2,2,2-trifluoroethanol using the general procedure for $\text{TiCl}_4/\text{Ph}_2\text{SO}$ mediated glycosylations. Flash column chromatography (100:0 $\rightarrow$ 60:40, pentane:EtOAc, v:v) yielded glycosylation product **S24** (28.9 mg, 0.053 mmol, 53%, $\alpha:\beta = 97:3$). TLC: R_f 0.69, (70:30, pentane:EtOAc, v:v); Data for the α -anomer: ^1H NMR (850 MHz, CDCl_3 , HH-COSY, HSQC, HMBC): δ 8.82 – 8.78 (m, 2H, CH_{arom} *i*-Nico), 7.84 – 7.80 (m, 2H, CH_{arom} *i*-Nico), 7.44 – 7.10 (m, 10H, CH_{arom}), 5.84 (t, $J = 9.7$ Hz, 1H, H-3), 5.50 (s, 1H, CHPh), 4.99 (d, $J = 3.7$ Hz, 1H, H-2), 4.64 (d, $J = 12.5$ Hz, 1H, CHH Bn), 4.61 (d, $J = 12.4$ Hz, 1H, CHH Bn), 4.32 (dd, $J = 10.5$, 4.9 Hz, 1H, H-6), 4.04 – 3.96 (m, 3H, H-5, CHHCF_3 , CHHCF_3), 3.81 – 3.71 (m, 3H, H-2, H-4, H-6); ^{13}C -APT NMR (214 MHz, CDCl_3 , HSQC, HMBC): δ 164.0 (C=O *i*-Nico), 150.6 (CH_{arom} *i*-Nico), 137.2, 137.2, 136.7 (C_q), 132.4, 129.1, 128.5, 128.2, 128.0, 126.1, 123.6 (CH_{arom}), (q, $J = 279.8$ Hz, CF_3), 123.0 (CH_{arom} *i*-Nico), 101.6 (CHPh), 98.2 (C-1), 79.0 (C-4), 76.9 (C-2), 72.8 (CH_2 Bn), 71.5 (C-3), 68.6 (C-6), 65.3 (q, $J = 35.2$ Hz, CH_2CF_3), 63.21 (C-5); ^{13}C -GATED NMR (214 MHz, CDCl_3): δ 98.2 ($J_{\text{C1,H1}} = 169.3$ Hz, C-1 α); HRMS: $[\text{M}+\text{H}]^+$ calcd for $\text{C}_{28}\text{H}_{27}\text{F}_3\text{NO}_7$ 546.1734, found 546.1730.

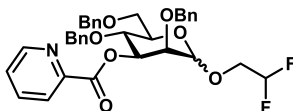


Ethyl 2,4,6-tri-O-benzyl-3-picoloyl- β -D-mannopyranoside (S25). The title compound was prepared from donor **7** and ethanol using the general procedure for $\text{TiCl}_4/\text{Ph}_2\text{SO}$ mediated glycosylations. Flash column chromatography (100:0 $\rightarrow$ 60:40, pentane:EtOAc, v:v) yielded glycosylation product **S25** (33.8 mg, 0.058 mmol, 58%, $\alpha:\beta = 55:45$). TLC: R_f 0.65, (60:40, pentane:EtOAc, v:v); Data for the α -anomer: ^1H NMR (850 MHz, CDCl_3 , HH-COSY, HSQC, HMBC): δ 8.79 (dt, $J = 1.7$, 0.9 Hz, 1H, CH_{arom} Pico), 8.01 (dt, $J = 7.8$, 1.1 Hz, 1H, CH_{arom} Pico), 7.79 (td, $J = 7.8$, 1.8 Hz, 1H, CH_{arom} Pico), 7.66 – 7.63 (m, 2H, CH_{arom}), 7.50 – 7.45 (m, 1H, CH_{arom} Pico), 7.46 – 7.42 (m, 2H, CH_{arom}), 7.40 – 6.98 (m, 11H, CH_{arom}), 5.57 (dd, $J = 9.5$, 3.4 Hz, 1H, H-3), 4.94 (d, $J = 12.6$ Hz, 1H, CHH Bn), 4.93 (d, $J = 2.0$ Hz, 1H, H-1), 4.76 (d, $J = 11.0$ Hz, 1H, CHH Bn), 4.75 (d, $J = 11.0$ Hz, 1H, CHH Bn), 4.62 (d, $J = 12.4$ Hz, 1H, CHH Bn), 4.56 (d, $J = 10.9$ Hz, 1H, CHH Bn), 4.53 (d, $J = 11.0$ Hz, 1H, CHH Bn), 4.28 (t, $J = 9.7$ Hz, 1H, H-4), 4.00 (dd, $J = 3.5$, 1.9 Hz, 1H, H-2), 3.91 (ddd, $J = 9.8$, 4.5, 1.9 Hz, 1H, H-5), 3.84 (dd, $J = 10.7$, 4.2 Hz, 1H, H-6), 3.76 (dq, $J = 9.7$, 7.1 Hz, 1H, CHHCH_3 Et), 3.74 (dd, $J = 10.8$, 1.9 Hz, 1H, H-6), 3.49 (dq, $J = 9.7$, 7.0 Hz, 1H, CHHCH_3 Et), 1.20 (t, $J = 7.1$ Hz, 3H, CH_3 Et); ^{13}C -APT NMR (214 MHz, CDCl_3 , HSQC, HMBC): δ 164.3 (C=O Pico), 150.1 (CH_{arom} Pico), 148.1, 138.5, 138.4, 138.1 (C_q), 136.9 (CH_{arom} Pico), 131.2, 129.4, 128.5, 128.4, 128.3, 128.1, 128.0, 128.0, 127.7 (CH_{arom}), 126.9, 125.3 (CH_{arom} Pico), 97.7 (C-1), 76.0 (C-2), 75.7 (C-3), 75.0 (CH_2 Bn), 74.6 (CH_2 Bn), 73.6 (C-4), 73.0 (CH_2 Bn), 71.5 (C-5), 69.1 (C-6), 63.3 (CH_2CH_3 Et), 15.1 (CH_3 Et); ^{13}C -GATED NMR (214 MHz, CDCl_3): δ 97.7 ($J_{\text{C1,H1}} = 168.8$ Hz, C-1 α); Diagnostic peaks β -anomer: ^1H NMR (850 MHz, CDCl_3 , HH-COSY, HSQC, HMBC): δ 8.79 (dt, $J = 1.7$, 0.9 Hz, 1H, CH_{arom} Pico), 7.92 (dt, $J = 7.8$, 1.1 Hz, 1H, CH_{arom} Pico), 7.78 (td, $J = 7.7$, 1.7 Hz, 1H, CH_{arom} Pico), 7.66 – 7.63 (m, 2H, CH_{arom}), 7.49 – 7.46 (m, 1H, CH_{arom} Pico), 7.46 – 6.97 (m, 13H, CH_{arom}), 5.13 (dd, $J = 9.8$, 3.3 Hz, 1H, H-3), 4.76 (d, $J = 11.0$ Hz, 1H, CHH Bn), 4.71 (d, $J = 12.4$ Hz, 1H, CHH Bn), 4.68 (d, $J = 11.4$ Hz, 1H, CHH Bn), 4.62 (d, $J = 12.4$ Hz, 1H, CHH Bn), 4.62 (d, $J = 0.8$ Hz, 1H, H-1), 4.58 (d, $J = 12.0$ Hz, 1H, CHH Bn), 4.56 (d, $J = 10.9$ Hz, 1H, CHH Bn), 4.18 (t, $J = 9.7$ Hz, 1H, H-4), 4.04 (dq, $J = 9.4$, 7.1 Hz, 1H, CHHCH_3 Et), 4.00 (dd, $J = 3.5$, 1.9 Hz, 1H, H-2), 3.84 (dd, $J = 10.7$, 4.2 Hz, 1H, H-6), 3.81 (dd, $J = 10.8$, 5.2 Hz, 1H, H-6), 3.60 – 3.56 (m, 2H, CHHCH_3 Et); ^{13}C -APT NMR (214 MHz, CDCl_3 , HSQC, HMBC): δ 164.2 (C=O Pico), 150.1 (CH_{arom} Pico), 147.8, 138.4, 138.2, 138.1 (C_q), 136.9 (CH_{arom} Pico), 128.4, 128.3, 128.0, 127.7, 127.6, 127.4 (CH_{arom}), 127.0, 125.4 (CH_{arom} Pico), 101.1 (C-1), 77.5 (C-3), 75.8 (C-5), 75.0 (CH_2 Bn), 74.9 (CH_2 Bn), 73.7 (CH_2 Bn), 73.6 (C-2), 73.5 (C-4), 69.5 (C-6), 65.6 (CH_2CH_3), 15.4 (CH_3 Et); ^{13}C -GATED NMR (214 MHz, CDCl_3): δ 101.1 ($J_{\text{C1,H1}} = 155.1$ Hz, C-1 β); HRMS: $[\text{M}+\text{H}]^+$ calcd for $\text{C}_{35}\text{H}_{38}\text{NO}_7$ 584.2643, found 584.2635.

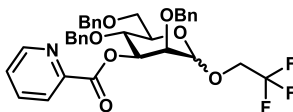


2-Fluoroethyl 2,4,6-tri-O-benzyl-3-picoloyl- β -D-mannopyranoside (S26). The title compound was prepared from donor **7** and 2-fluoroethanol using the general procedure for $\text{TiCl}_4/\text{Ph}_2\text{SO}$ mediated glycosylations. Flash column chromatography (100:0 $\rightarrow$ 60:40, pentane:EtOAc, v:v) yielded glycosylation product **S26** (19.2 mg, 0.032 mmol, 32%, $\alpha:\beta = 55:45$). TLC: R_f 0.52, (60:40, pentane:EtOAc, v:v); Data for the α -anomer: ^1H NMR (850

MHz, CDCl₃, HH-COSY, HSQC, HMBC): δ 8.80 (dd, J = 1.7, 0.8 Hz, 1H, CH_{arom} Pico), 8.00 (dt, J = 7.8, 1.1 Hz, 1H, CH_{arom} Pico), 7.79 (td, J = 7.9, 1.8 Hz, 1H, CH_{arom} Pico), 7.51 – 7.43 (m, 1H, CH_{arom} Pico), 7.39 – 6.98 (m, 15H, CH_{arom}), 5.56 (dd, J = 9.4, 3.4 Hz, 1H, H-3), 4.98 (d, J = 2.0 Hz, 1H, H-1), 4.93 (d, J = 12.4 Hz, 1H, CHH Bn), 4.76 (d, J = 11.0 Hz, 1H, CHH Bn), 4.76 (d, J = 11.0 Hz, 1H, CHH Bn), 4.68 – 4.66 (m, 1H, CHHCH₂F), 4.62 (d, J = 12.3 Hz, 1H, CHH Bn), 4.61 – 4.57 (m, 1H, CHHCH₂F), 4.56 (d, J = 11.1 Hz, 1H, CHH Bn), 4.53 (d, J = 12.2 Hz, 1H, CHH Bn), 4.28 (t, J = 9.6 Hz, 1H, H-4), 4.06 (dd, J = 3.5, 2.0 Hz, 1H, H-2), 3.93 (ddd, J = 9.7, 4.4, 1.9 Hz, 1H, H-5), 3.91 – 3.83 (m, 1H, CH₂CHHF), 3.82 (t, J = 5.6 Hz, 1H, H-6), 3.80 – 3.75 (m, 1H, CH₂CHHF), 3.74 (dd, J = 10.9, 2.0 Hz, 1H, H-6); ¹³C-APT NMR (214 MHz, CDCl₃, HSQC, HMBC): δ 164.3 (C=O Pico), 150.1 (CH_{arom} Pico), 148.1 (C_q), 138.3, 138.2, 138.0 (C_q), 137.0 (CH_{arom} Pico), 128.6, 128.5, 128.4, 128.1, 128.0, 127.8, 127.8, 127.7, 127.5 (CH_{arom}), 127.0, 125.4 (CH_{arom} Pico), 98.4 (C-1), 82.6 (d, J = 169.9 Hz, CH₂CH₂F), 75.8 (C-2), 75.4 (C-3), 74.9 (CH₂ Bn), 73.7 (CH₂ Bn), 73.5 (C-4), 73.1 (CH₂ Bn), 71.7 (C-5), 69.0 (C-6), 66.8 (d, J = 20.2 Hz, CH₂CH₂F); ¹³C-GATED NMR (214 MHz, CDCl₃): δ 98.4 ($J_{C1,H1}$ = 169.9 Hz, C-1 α); Diagnostic peaks β -anomer: ¹H NMR (850 MHz, CDCl₃, HH-COSY, HSQC, HMBC): δ 8.79 (dd, J = 1.7, 0.8 Hz, 1H, CH_{arom} Pico), 7.93 (dd, J = 7.9, 1.1 Hz, 1H, CH_{arom} Pico), 7.78 (td, J = 7.9, 1.8 Hz, 1H, CH_{arom} Pico), 7.48 (ddd, J = 7.7, 4.7, 1.2 Hz, 1H, CH_{arom} Pico), 7.40 – 6.97 (m, 15H, CH_{arom}), 5.13 (dd, J = 9.7, 3.4 Hz, 1H, H-3), 4.69 (d, J = 3.0 Hz, 1H, H-1), 4.20 (t, J = 9.7 Hz, 1H, H-4), 4.18 – 4.17 (m, 1H, H-6), 4.13 (ddd, J = 12.2, 4.4, 2.5 Hz, 1H, CHHCH₂F), 3.82 – 3.81 (m, 1H, H-6), 3.58 (ddd, J = 9.6, 4.5, 2.8 Hz, 1H, H-5); ¹³C-APT NMR (214 MHz, CDCl₃, HSQC, HMBC): δ 164.2 (C=O Pico), 150.1 (CH_{arom} Pico), 147.7, 138.3, 138.3, 138.0 (C_q), 136.9 (CH_{arom} Pico), 128.5, 128.4, 128.3, 128.1, 127.7 (CH_{arom}), 127.0, 125.4 (CH_{arom} Pico), 101.4 (C-1), 82.9 (d, J = 169.7 Hz, CH₂CH₂F), 77.2 (C-3), 75.7 (C-5), 75.0 (CH₂ Bn), 74.8 (C-2), 74.7 (CH₂ Bn), 73.6 (CH₂ Bn), 73.3 (C-4), 69.4 (C-6), 68.9 (d, J = 19.9 Hz, CH₂CH₂F); ¹³C-GATED NMR (214 MHz, CDCl₃): δ 101.4 ($J_{C1,H1}$ = 155.8 Hz, C-1 β); HRMS: [M+H]⁺ calcd for C₃₅H₃₇FNO₇ 602.2549, found 602.2544.

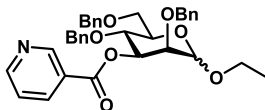


2,2-Difluoroethyl 2,4,6-tri-O-benzyl-3-picoloyl- β -mannopyranoside (S27). The title compound was prepared from donor **7** and 2,2-difluoroethanol using the general procedure for Tf₂O/Ph₂SO mediated glycosylations. Flash column chromatography (100:0 $\rightarrow$ 60:40, pentane:EtOAc, v:v) yielded glycosylation product **S27** (29.7 mg, 0.048 mmol, 48%, α : β = 50:50). TLC: R_f 0.65, (60:40, pentane:EtOAc, v:v); Data for the α -anomer: ¹H NMR (850 MHz, CDCl₃, HH-COSY, HSQC, HMBC): δ 8.79 (dt, J = 1.8, 0.8 Hz, 1H, CH_{arom} Pico), 8.00 (dt, J = 7.8, 1.1 Hz, 1H, CH_{arom} Pico), 7.80 (td, J = 7.6, 1.8 Hz, 1H, CH_{arom} Pico), 7.51 – 7.44 (m, 1H, CH_{arom} Pico), 7.40 – 6.97 (m, 15H, CH_{arom}), 5.93 (tdd, J = 55.3, 4.9, 3.7 Hz, 1H, CH₂CHF₂), 5.51 (dd, J = 9.2, 3.4 Hz, 1H, H-3), 4.96 (d, J = 2.1 Hz, 1H, H-1), 4.89 (d, J = 12.4 Hz, 1H, CHH Bn), 4.77 (d, J = 11.1 Hz, 1H, CHH Bn), 4.69 (d, J = 12.1 Hz, 1H, CHH Bn), 4.63 (d, J = 12.3 Hz, 1H, CHH Bn), 4.58 – 4.51 (m, 2H, CHH Bn, CHH Bn), 4.27 (t, J = 9.5 Hz, 1H, H-4), 4.06 (dd, J = 3.5, 2.0 Hz, 1H, H-2), 3.90 (ddd, J = 9.8, 4.7, 2.0 Hz, 1H, H-5), 3.87 – 3.83 (m, 1H, CHHCH₂F), 3.82 – 3.78 (m, 1H, H-6), 3.77 – 3.74 (m, 1H, CHHCH₂F), 3.73 (dd, J = 10.8, 1.9 Hz, 1H, H-6); ¹³C-APT NMR (214 MHz, CDCl₃, HSQC, HMBC): δ 164.4 (C=O Pico), 150.2 (CH_{arom} Pico), 148.0, 138.2, 138.1, 137.9 (C_q), 137.0 (CH_{arom} Pico), 128.5, 128.4, 128.1, 128.1, 128.0, 128.0, 127.9, 127.8, 127.6 (CH_{arom}), 127.1, 125.4 (CH_{arom} Pico), 114.1 (t, J = 241.2 Hz, CH₂CHF₂), 98.9 (C-1), 75.4 (C-2), 75.0 (C-3), 74.8 (CH₂ Bn), 74.7 (CH₂ Bn), 73.6 (CH₂ Bn), 73.3 (C-4), 72.1 (C-5), 69.2 (C-6), 67.0 (t, J = 28.8 Hz, CH₂CHF₂); ¹³C-GATED NMR (214 MHz, CDCl₃): δ 98.9 ($J_{C1,H1}$ = 169.5 Hz, C-1 α); Diagnostic peaks β -anomer: ¹H NMR (850 MHz, CDCl₃, HH-COSY, HSQC, HMBC): δ 8.79 (dt, J = 1.8, 0.8 Hz, 1H, CH_{arom} Pico), 7.93 (dt, J = 7.8, 1.1 Hz, 1H, CH_{arom} Pico), 7.79 (td, J = 7.6, 1.8 Hz, 1H, CH_{arom} Pico), 7.48 (ddd, J = 7.7, 4.7, 1.2 Hz, 1H, CH_{arom} Pico), 7.39 – 6.97 (m, 15H, CH_{arom}), 5.96 (ddd, J = 54.9, 56.1, 5.3, 3.0 Hz, 1H, CH₂CHF₂), 5.12 (dd, J = 9.7, 3.3 Hz, 1H, H-3), 4.77 (d, J = 11.0 Hz, 1H, CHH Bn), 4.68 (d, J = 0.9 Hz, 1H, H-1), 4.65 (d, J = 12.4 Hz, 1H, CHH Bn), 4.20 (t, J = 9.7 Hz, 1H, H-4), 4.17 (dd, J = 3.4, 0.8 Hz, 1H, H-2), 3.83 – 3.79 (m, 1H, H-6), 3.59 – 3.57 (m, 1H, H-5); ¹³C-APT NMR (214 MHz, CDCl₃, HSQC, HMBC): δ 164.2 (C=O Pico), 150.2 (CH_{arom} Pico), 147.7, 138.2, 138.0, 137.7 (C_q), 136.9 (CH_{arom} Pico), 128.5, 128.5, 128.4, 128.4, 128.1, 128.1, 128.0, 127.8 (CH_{arom}), 127.0, 125.4 (CH_{arom} Pico), 114.3 (dd, J = 242.3, 239.6 Hz, CH₂CHF₂), 101.5 (C-1), 77.1 (C-3), 75.9 (C-5), 75.1 (CH₂ Bn), 74.6 (C-2), 73.7 (CH₂ Bn), 73.2 (CH₂ Bn), 73.1 (C-4), 68.9 (C-6), 68.6 (dd, J = 30.9, 26.3 Hz, CH₂CHF₂); ¹³C-GATED NMR (214 MHz, CDCl₃): δ 101.5 ($J_{C1,H1}$ = 156.6 Hz, C-1 β); HRMS: [M+H]⁺ calcd for C₃₅H₃₆F₂NO₇ 620.2454, found 620.2451.

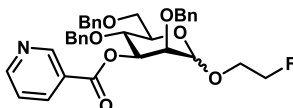


2,2,2-Trifluoroethyl 2,4,6-tri-O-benzyl-3-picoloyl- β -mannopyranoside (S28). The title compound was prepared from donor **7** and 2,2,2-trifluoroethanol using the general procedure for Tf₂O/Ph₂SO mediated glycosylations. Flash column chromatography (100:0 $\rightarrow$ 60:40, pentane:EtOAc, v:v) yielded glycosylation product **S28** (35.7 mg, 0.056 mmol, 56%, α : β = 31:69). TLC: R_f 0.74, (60:40, pentane:EtOAc, v:v); Data for the β -anomer: ¹H NMR (850 MHz, CDCl₃, HH-COSY, HSQC, HMBC): δ 8.79 (ddd, J = 4.8, 1.8, 0.9 Hz, 1H, CH_{arom} Pico),

7.94 (dt, $J = 7.8, 1.1$ Hz, 1H, CH_{arom} Pico), 7.79 (ddd, $J = 7.7, 2.4, 1.7$ Hz, 1H, CH_{arom} Pico), 7.68 – 7.62 (m, 1H, CH_{arom} Pico), 7.53 – 6.99 (m, 15H, CH_{arom}), 5.13 (dd, $J = 9.7, 3.3$ Hz, 1H, H-3), 4.90 (d, $J = 12.4$ Hz, 1H, CHH Bn), 4.77 (d, $J = 11.0$ Hz, 1H, CHH Bn), 4.73 (d, $J = 0.9$ Hz, 1H, H-1), 4.67 (d, $J = 12.3$ Hz, 1H, CHH Bn), 4.66 (d, $J = 12.6$ Hz, 1H, CHH Bn), 4.57 (d, $J = 11.0$ Hz, 1H, CHH Bn), 4.56 (d, $J = 12.0$ Hz, 1H, CHH Bn), 4.30 – 4.23 (m, 1H, CHHCF₃), 4.21 (t, $J = 9.6$ Hz, 1H, H-4), 4.18 (dd, $J = 3.4, 0.9$ Hz, 1H, H-2), 3.97 (ddd, $J = 16.6, 8.3, 3.7$ Hz, 1H, CHHCF₃), 3.84 – 3.78 (m, 2H, H-6, H-6), 3.58 (ddd, $J = 9.6, 4.5, 2.8$ Hz, 1H, H-5); ¹³C-APT NMR (214 MHz, CDCl₃, HSQC, HMBC): δ 164.1 (C=O Pico), 150.1 (CH_{arom} Pico), 147.6, 138.2, 137.9, 137.9 (C_q), 136.9 (CH_{arom} Pico), 131.2, 129.4, 128.6, 128.5, 128.4, 128.1, 128.1, 128.0, 127.8 (CH_{arom}), 127.1, 125.4 (CH_{arom} Pico), 123.8 (q, $J = 278.1$ Hz, CH₂CF₃), 101.0 (C-1), 76.8 (C-3), 76.0 (C-5), 75.1 (CH₂ Bn), 74.7 (CH₂ Bn), 74.2 (C-2), 73.7 (CH₂ Bn), 73.0 (C-4), 69.1 (C-6), 66.1 (q, $J = 34.8$ Hz, CH₂CF₃); ¹³C-GATED NMR (214 MHz, CDCl₃): δ 101.0 ($J_{C1,H1} = 157.6$ Hz, C-1 β); Diagnostic peaks α -anomer: ¹H NMR (850 MHz, CDCl₃, HH-COSY, HSQC, HMBC): δ 8.79 (ddd, $J = 4.8, 1.8, 0.9$ Hz, 1H, CH_{arom} Pico), 8.01 (dt, $J = 7.9, 1.1$ Hz, 1H, CH_{arom} Pico), 7.79 (ddd, $J = 7.7, 2.4, 1.7$ Hz, 1H, CH_{arom} Pico), 7.66 – 7.62 (m, 1H, CH_{arom} Pico), 7.48 – 6.99 (m, 15H, CH_{arom}), 5.53 (dd, $J = 9.0, 3.4$ Hz, 1H, H-3), 5.01 (d, $J = 2.1$ Hz, 1H, H-1), 4.78 (d, $J = 11.0$ Hz, 1H, CHH Bn), 4.68 (d, $J = 12.4$ Hz, 1H, CHH Bn), 4.68 (d, $J = 12.1$ Hz, 1H, CHH Bn), 4.65 (d, $J = 12.3$ Hz, 1H, CHH Bn), 4.54 (d, $J = 11.0$ Hz, 1H, CHH Bn), 4.51 (d, $J = 12.0$ Hz, 1H, CHH Bn), 4.28 (t, $J = 9.4$ Hz, 1H, H-4), 4.09 (dd, $J = 3.4, 2.1$ Hz, 1H, H-2), 3.88 (ddd, $J = 9.8, 4.5, 1.9$ Hz, 1H, H-5), 3.81 (dd, $J = 3.8, 1.6$ Hz, 1H, H-6), 3.72 (dd, $J = 10.9, 2.0$ Hz, 1H, H-6); ¹³C-APT NMR (214 MHz, CDCl₃, HSQC, HMBC): δ 164.4 (C=O Pico), 150.1 (CH_{arom} Pico), 147.9, 138.2, 138.0, 137.6 (C_q), 137.0 (CH_{arom}), 131.2, 129.4, 128.5, 128.4, 128.1, 128.0, 127.6 (CH_{arom}), 127.0, 125.4 (CH_{arom} Pico), 123.8 (q, $J = 278.1$ Hz, CH₂CF₃), 98.8 (C-1), 75.2 (C-2), 74.8 (C-3), 74.8 (CH₂ Bn), 73.6 (CH₂ Bn), 73.2 (CH₂ Bn), 73.2 (C-4), 72.3 (C-5), 68.8 (C-6), 64.3 (q, $J = 35.0$ Hz, CH₂CF₃); ¹³C-GATED NMR (214 MHz, CDCl₃): δ 98.8 ($J_{C1,H1} = 171.3$ Hz, C-1 α); HRMS: [M+H]⁺ calcd for C₃₅H₃₅F₃NO₇ 638.2360, found 638.2355.

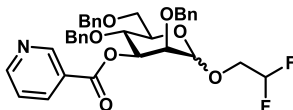


Ethyl 2,4,6-tri-*O*-benzyl-3-nicotinoyl- β -mannopyranoside (S29). The title compound was prepared from donor **8** and ethanol using the general procedure for Tf₂O/Ph₂SO mediated glycosylations. Flash column chromatography (100:0 $\rightarrow$ 60:40, pentane:EtOAc, v:v) yielded glycosylation product **S29** (30.9 mg, 0.053 mmol, 53%, α : β = 85:15). TLC: R_f 0.68, (60:40, pentane:EtOAc, v:v); Data for the α -anomer: ¹H NMR (850 MHz, CDCl₃, HH-COSY, HSQC, HMBC): δ 9.16 (dd, $J = 2.2, 0.9$ Hz, 1H, CH_{arom} Nico), 8.78 (dd, $J = 4.8, 1.7$ Hz, 1H, CH_{arom} Nico), 8.16 (dt, $J = 7.9, 2.0$ Hz, 1H, CH_{arom} Nico), 7.48 – 7.37 (m, 2H, CH_{arom}), 7.35 (ddd, $J = 7.9, 4.8, 0.9$ Hz, 1H, CH_{arom} Nico), 7.30 – 7.00 (m, 13H, CH_{arom}), 5.52 (dd, $J = 9.6, 3.4$ Hz, 1H, H-3), 4.95 (d, $J = 1.9$ Hz, 1H, H-1), 4.73 (d, $J = 12.0$ Hz, 1H, CHH Bn), 4.68 (d, $J = 12.3$ Hz, 1H, CHH Bn), 4.60 (d, $J = 11.2$ Hz, 1H, CHH Bn), 4.55 (d, $J = 12.0$ Hz, 1H, CHH Bn), 4.53 (d, $J = 11.2$ Hz, 1H, CHH Bn), 4.52 (d, $J = 12.7$ Hz, 1H, CHH Bn), 4.22 (t, $J = 9.7$ Hz, 1H, H-4), 3.96 (dd, $J = 3.5, 1.9$ Hz, 1H, H-2), 3.90 (ddd, $J = 9.8, 4.4, 1.9$ Hz, 1H, H-5), 3.84 (dd, $J = 10.9, 4.4$ Hz, 1H, H-6), 3.77 (dq, $J = 9.6, 7.1$ Hz, 1H, CHHCH₃ Et), 3.74 (dd, $J = 10.9, 1.9$ Hz, 1H, H-6), 3.50 (dq, $J = 9.6, 7.0$ Hz, 1H, CHHCH₃ Et), 1.21 (t, $J = 7.1$ Hz, 3H, CH₃ Et); ¹³C-APT NMR (214 MHz, CDCl₃, HSQC, HMBC): δ 164.5 (C=O Nico), 153.6, 151.1 (CH_{arom} Nico), 138.3, 138.0, 137.9 (C_q), 137.2 (CH_{arom} Nico), 128.5, 128.4, 128.4, 128.1, 127.9, 127.8, 127.8, 127.7 (CH_{arom}), 126.08 (C_q), 123.4 (CH_{arom} Nico), 97.6 (C-1), 76.2 (C-2), 75.1 (C-3), 75.0 (CH₂ Bn), 73.8 (C-4), 73.7 (CH₂ Bn), 73.0 (CH₂ Bn), 71.6 (C-5), 69.0 (C-6), 63.4 (CH₂CH₃ Et), 15.1 (CH₃ Et); ¹³C-GATED NMR (214 MHz, CDCl₃): δ 97.6 ($J_{C1,H1} = 168.5$ Hz, C-1 α); Diagnostic peaks β -anomer: ¹H NMR (850 MHz, CDCl₃, HH-COSY, HSQC, HMBC): δ 9.09 (dd, $J = 2.2, 0.9$ Hz, 1H, CH_{arom} Nico), 8.78 (dd, $J = 4.8, 1.7$ Hz, 1H, CH_{arom} Nico), 8.09 (dt, $J = 7.9, 1.9$ Hz, 1H, CH_{arom} Nico), 7.67 – 7.63 (m, 1H, CH_{arom} Nico), 7.39 – 7.01 (m, 15H, CH_{arom}), 5.08 (dd, $J = 9.7, 3.3$ Hz, 1H, H-3), 4.69 (d, $J = 12.0$ Hz, 1H, CHH Bn), 4.61 (d, $J = 0.9$ Hz, 1H, H-1), 4.55 (d, $J = 11.1$ Hz, 1H, CHH Bn), 4.12 (t, $J = 9.7$ Hz, 1H, H-4), 4.08 (dd, $J = 3.4, 0.8$ Hz, 1H, H-2), 4.05 (dq, $J = 9.5, 7.1$ Hz, 1H, CHHCH₃ Et), 3.83 – 3.81 (m, 1H, H-6), 3.59 (dq, $J = 9.7, 7.2$ Hz, 1H, CHHCH₃ Et), 3.56 (ddd, $J = 9.5, 4.7, 2.7$ Hz, 1H, H-5); ¹³C-APT NMR (214 MHz, CDCl₃, HSQC, HMBC): δ 164.4 (C=O Nico), 153.6, 151.1 (CH_{arom} Nico), 138.4, 138.4, 137.9 (C_q), 137.2 (CH_{arom} Nico), 129.5, 128.4, 128.2, 128.1, 127.5 (CH_{arom}), 125.8 (C_q), 123.3 (CH_{arom} Nico), 101.1 (C-1), 76.9 (C-3), 75.8 (C-5), 75.3 (C-2), 74.7 (CH₂ Bn), 73.6 (C-4), 69.4 (C-6), 65.7 (CH₂CH₃ Et), 15.4 (CH₃ Et); ¹³C-GATED NMR (214 MHz, CDCl₃): δ 101.1 ($J_{C1,H1} = 154.1$ Hz, C-1 β); HRMS: [M+H]⁺ calcd for C₃₅H₃₈NO₇ 584.2643, found 584.2638.

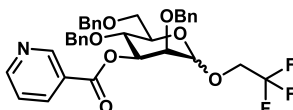


2-Fluoroethyl 2,4,6-tri-*O*-benzyl-3-nicotinoyl- β -mannopyranoside (S30). The title compound was prepared from donor **8** and 2-fluoroethanol using the general procedure for Tf₂O/Ph₂SO mediated glycosylations. Flash column chromatography (100:0 $\rightarrow$ 60:40, pentane:EtOAc, v:v) yielded glycosylation product **S30** (36.1 mg, 0.060 mmol, 60%, α : β = 85:15). TLC: R_f 0.55, (60:40, pentane:EtOAc, v:v); Data for the

α -anomer: ^1H NMR (850 MHz, CDCl_3 , HH-COSY, HSQC, HMBC): δ 9.18 (dd, $J = 2.2, 0.9$ Hz, 1H, CH_{arom} Nico), 8.81 (dd, $J = 4.8, 1.7$ Hz, 1H, CH_{arom} Nico), 8.19 (ddd, $J = 7.9, 2.2, 1.7$ Hz, 1H, CH_{arom} Nico), 7.42 – 7.38 (m, 1H, CH_{arom}), 7.38 (ddd, $J = 7.9, 4.8, 0.9$ Hz, 1H, CH_{arom} Nico), 7.33 – 6.98 (m, 14H, CH_{arom}), 5.54 (dd, $J = 9.5, 3.4$ Hz, 1H, H-3), 5.02 (d, $J = 1.9$ Hz, 1H, H-1), 4.75 (d, $J = 12.0$ Hz, 1H, CHH Bn), 4.71 (d, $J = 12.2$ Hz, 1H, CHH Bn), 4.63 (d, $J = 11.1$ Hz, 1H, CHH Bn), 4.62 – 4.58 (m, 2H, CH_2CHF), 4.57 (d, $J = 11.0$ Hz, 1H, CHH Bn), 4.55 (d, $J = 12.1$ Hz, 1H, CHH Bn), 4.55 (d, $J = 11.3$ Hz, 1H, CHH Bn), 4.25 (t, $J = 9.6$ Hz, 1H, H-4), 4.06 (dd, $J = 3.5, 1.9$ Hz, 1H, H-2), 3.95 (ddd, $J = 10.0, 4.4, 2.0$ Hz, 1H, H-5), 3.94 (dddd, $J = 31.3, 12.3, 5.1, 2.8$ Hz, 1H, CHHCH_2F), 3.86 (dd, $J = 10.9, 4.5$ Hz, 1H, H-6), 3.79 (dddd, $J = 27.4, 12.2, 6.1, 2.9$ Hz, 1H, CHHCH_2F), 3.76 (dd, $J = 10.9, 1.9$ Hz, 1H, H-6); ^{13}C -APT NMR (214 MHz, CDCl_3 , HSQC, HMBC): δ 164.3 (C=O Nico), 153.5, 151.0 (CH_{arom} Nico), 138.2, 137.8, 137.6 (C_q), 137.1, 128.4, 128.3, 128.3, 127.9, 127.8, 127.7, 127.7, 127.7 (CH_{arom}), 125.9 (C_q), 123.3 (CH_{arom} Nico), 98.1 (C-1), 82.5 (d, $J = 169.9$ Hz, CH_2CHF), 75.8 (C-2), 74.8 (CH_2 Bn), 74.7 (C-3), 73.6 (CH_2 Bn), 73.5 (C-4), 73.0 (CH_2 Bn), 71.7 (C-5), 68.8 (C-6), 66.8 (d, $J = 20.1$ Hz, CH_2CHF); ^{13}C -GATED NMR (214 MHz, CDCl_3): δ 98.1 ($J_{\text{C1,H1}} = 169.8$ Hz, C-1 α); Diagnostic peaks β -anomer: ^1H NMR (850 MHz, CDCl_3 , HH-COSY, HSQC, HMBC): δ 9.12 (dd, $J = 2.2, 0.9$ Hz, 1H, CH_{arom} Nico), 8.81 (dd, $J = 4.8, 1.7$ Hz, 1H, CH_{arom} Nico), 8.12 (ddd, $J = 7.9, 2.2, 1.8$ Hz, 1H, CH_{arom} Nico), 7.37 (ddd, $J = 7.9, 3.1, 0.9$ Hz, 1H, CH_{arom} Nico), 7.33 – 7.04 (m, 15H, CH_{arom}), 5.11 (dd, $J = 9.8, 3.4$ Hz, 1H, H-3), 4.71 (d, $J = 0.8$ Hz, 1H, H-1), 4.18 (dddd, $J = 34.3, 12.2, 4.2, 2.4$ Hz, 1H, CHHCH_2F), 4.17 (dd, $J = 3.1, 0.7$ Hz, 1H, H-2), 4.16 (t, $J = 9.6$ Hz, 1H, H-4), 3.88 (dddd, $J = 23.9, 11.8, 4.3, 2.6$ Hz, 1H, CHHCH_2F), 3.60 (ddd, $J = 9.5, 4.4, 3.0$ Hz, 1H, H-5); ^{13}C -APT NMR (214 MHz, CDCl_3 , HSQC, HMBC): δ 164.3 (C=O Nico), 153.5, 151.0 (CH_{arom} Nico), 138.2, 138.1, 137.7 (C_q), 137.1 (CH_{arom} Nico), 128.4, 128.4, 128.1, 128.0, 127.7, 127.7, 127.5 (CH_{arom}), 125.6 (C_q), 123.2 (CH_{arom} Nico), 101.3 (C-1), 82.8 (d, $J = 169.7$ Hz, CH_2CHF), 76.5 (C-3), 75.7 (C-5), 75.0 (CH_2 Bn), 74.9 (C-2), 74.7 (CH_2 Bn), 73.6 (CH_2 Bn), 73.4 (C-4), 69.2 (C-6), 68.8 (d, $J = 19.8$ Hz, CH_2CHF); ^{13}C -GATED NMR (214 MHz, CDCl_3): δ 101.3 ($J_{\text{C1,H1}} = 155.7$ Hz, C-1 β); HRMS: $[\text{M}+\text{H}]^+$ calcd for $\text{C}_{35}\text{H}_{37}\text{FNO}_7$ 602.2549, found 602.2544.

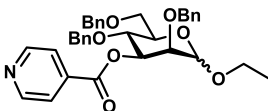


2,2-Difluoroethyl 2,4,6-tri-O-benzyl-3-nicotinoyl- β -mannopyranoside (S31). The title compound was prepared from donor **8** and 2,2-difluoroethanol using the general procedure for $\text{TiF}_2/\text{Ph}_2\text{SO}$ mediated glycosylations. Flash column chromatography (100:0 $\rightarrow$ 60:40, pentane:EtOAc, v:v) yielded glycosylation product **S31** (42.7 mg, 0.069 mmol, 69%, $\alpha/\beta = 85:15$). TLC: R_f 0.64, (60:40, pentane:EtOAc, v:v); Data for the α -anomer: ^1H NMR (850 MHz, CDCl_3 , HH-COSY, HSQC, HMBC): δ 9.18 (dd, $J = 2.2, 0.9$ Hz, 1H, CH_{arom} Nico), 8.82 (dd, $J = 4.8, 1.7$ Hz, 1H, CH_{arom} Nico), 8.19 (ddd, $J = 7.9, 2.2, 1.8$ Hz, 1H, CH_{arom} Nico), 7.41 – 7.38 (m, 1H, CH_{arom}), 7.38 (ddd, $J = 7.9, 4.8, 0.9$ Hz, 1H, CH_{arom} Nico), 7.33 – 7.04 (m, 14H, CH_{arom}), 5.96 (dd, $J = 55.2, 4.8, 3.6$ Hz, 1H, CH_2CHF_2), 5.50 (dd, $J = 9.3, 3.4$ Hz, 1H, H-3), 5.01 (d, $J = 2.1$ Hz, 1H, H-1), 4.74 (d, $J = 12.0$ Hz, 1H, CHH Bn), 4.70 (d, $J = 12.3$ Hz, 1H, CHH Bn), 4.65 (d, $J = 11.2$ Hz, 1H, CHH Bn), 4.57 (d, $J = 12.0$ Hz, 1H, CHH Bn), 4.56 (d, $J = 11.2$ Hz, 1H, CHH Bn), 4.56 (d, $J = 12.2$ Hz, 1H, CHH Bn), 4.24 (t, $J = 9.5$ Hz, 1H, H-4), 4.06 (dd, $J = 3.5, 2.0$ Hz, 1H, H-2), 3.92 (ddd, $J = 9.7, 4.5, 1.9$ Hz, 1H, H-5), 3.90 – 3.87 (m, 1H, CHHCH_2F), 3.85 (dd, $J = 10.9, 4.5$ Hz, 1H, H-6), 3.81 – 3.78 (m, 1H, CHHCH_2F), 3.76 (dd, $J = 10.9, 2.0$ Hz, 1H, H-6); ^{13}C -APT NMR (214 MHz, CDCl_3 , HSQC, HMBC): δ 164.5 (C=O Nico), 153.7, 151.1 (CH_{arom} Nico), 138.1, 137.8, 137.5 (C_q), 137.2 (CH_{arom} Nico), 128.5, 128.4, 128.0, 128.0, 128.0, 127.8, 127.8, 127.8 (CH_{arom}), 125.9 (C_q), 123.4 (CH_{arom} Nico), 114.1 (t, $J = 241.2$ Hz, CH_2CHF_2), 98.8 (C-1), 75.6 (C-2), 74.9 (CH_2 Bn), 74.4 (C-3), 73.7 (CH_2 Bn), 73.4 (C-4), 73.2 (CH_2 Bn), 72.1 (C-5), 68.8 (C-6), 66.9 (t, $J = 28.6$ Hz, CH_2CHF_2); ^{13}C -GATED NMR (214 MHz, CDCl_3): δ 98.8 ($J_{\text{C1,H1}} = 171.0$ Hz, C-1 α); Diagnostic peaks β -anomer: ^1H NMR (850 MHz, CDCl_3 , HH-COSY, HSQC, HMBC): δ 9.13 (dd, $J = 2.2, 0.9$ Hz, 1H, CH_{arom} Nico), 8.82 (dd, $J = 4.8, 1.7$ Hz, 1H, CH_{arom} Nico), 8.13 (ddd, $J = 7.9, 2.2, 1.7$ Hz, 1H, CH_{arom} Nico), 7.41 – 7.06 (m, 16H, CH_{arom} Nico, CH_{arom}), 6.00 (dddd, $J = 56.3, 54.7, 5.4, 2.9$ Hz, 1H, CH_2CHF_2), 5.11 (dd, $J = 9.8, 3.3$ Hz, 1H, H-3), 4.70 (d, $J = 1.0$ Hz, 1H, H-1), 4.65 (d, $J = 11.2$ Hz, 1H, CHH Bn), 4.61 (d, $J = 12.2$ Hz, 1H, CHH Bn), 4.18 (t, $J = 9.6$ Hz, 1H, H-4), 4.17 (dd, $J = 3.3, 0.8$ Hz, 1H, H-2), 4.15 – 4.08 (m, 1H, CHHCH_2F), 3.60 (ddd, $J = 9.5, 5.0, 2.3$ Hz, 1H, H-5); ^{13}C -APT NMR (214 MHz, CDCl_3 , HSQC, HMBC): δ 164.4 (C=O Nico), 153.7, 151.1 (CH_{arom} Nico), 138.2, 138.0, 137.7 (C_q), 137.2 (CH_{arom} Nico), 128.5, 128.5, 128.4, 128.2, 128.1, 127.9, 127.7 (CH_{arom}), 125.6 (C_q), 123.3 (CH_{arom} Nico), 114.3 (d, $J = 240.0, 242.8$ Hz, CH_2CHF_2), 101.5 (C-1), 76.4 (C-3), 75.9 (C-5), 75.1 (CH_2 Bn), 74.9 (CH_2 Bn), 74.9 (C-2), 73.7 (CH_2 Bn), 73.2 (C-4), 69.1 (C-6), 68.6 (dd, $J = 30.9, 26.1$ Hz, CH_2CHF_2); ^{13}C -GATED NMR (214 MHz, CDCl_3): δ 101.5 ($J_{\text{C1,H1}} = 157.0$ Hz, C-1 β); HRMS: $[\text{M}+\text{H}]^+$ calcd for $\text{C}_{35}\text{H}_{36}\text{F}_2\text{NO}_7$ 620.2454, found 620.2450.

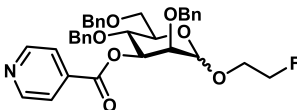


2,2,2-Trifluoroethyl 2,4,6-tri-O-benzyl-3-nicotinoyl- β -mannopyranoside (S32). The title compound was prepared from donor **8** and 2,2,2-trifluoroethanol using the general procedure for $\text{TiF}_2/\text{Ph}_2\text{SO}$ mediated glycosylations. Flash column chromatography (100:0 $\rightarrow$ 60:40, pentane:EtOAc, v:v) yielded glycosylation product **S32** (38.2 mg, 0.060 mmol, 60%, $\alpha/\beta = 86:14$). TLC: R_f 0.73, (60:40, pentane:EtOAc, v:v); Data for the

α -anomer: ^1H NMR (850 MHz, CDCl_3 , HH-COSY, HSQC, HMBC): δ 9.15 (dd, J = 2.2, 0.9 Hz, 1H, CH_{arom} Nico), 8.79 (dd, J = 4.8, 1.7 Hz, 1H, CH_{arom} Nico), 8.16 (ddd, J = 7.9, 2.2, 1.8 Hz, 1H, CH_{arom} Nico), 7.47 – 7.42 (m, 1H, CH_{arom}), 7.36 (ddd, J = 7.9, 4.8, 0.9 Hz, 1H, CH_{arom} Nico), 7.33 – 7.04 (m, 14H, CH_{arom}), 5.48 (dd, J = 9.2, 3.4 Hz, 1H, H-3), 5.02 (d, J = 2.1 Hz, 1H, H-1), 4.70 (d, J = 12.0 Hz, 1H, CHH Bn), 4.67 (d, J = 12.2 Hz, 1H, CHH Bn), 4.62 (d, J = 11.2 Hz, 1H, CHH Bn), 4.54 (d, J = 12.4 Hz, 1H, CHH Bn), 4.53 (d, J = 11.3 Hz, 1H, CHH Bn), 4.53 (d, J = 12.0 Hz, 1H, CHH Bn), 4.22 (t, J = 9.4 Hz, 1H, H-4), 4.06 (dd, J = 3.5, 2.1 Hz, 1H, H-2), 3.99 (dq, J = 12.4, 8.8 Hz, 1H, CHHCF_3), 3.93 (dq, J = 12.4, 8.5 Hz, 1H, CHHCF_3), 3.87 (ddd, J = 9.6, 4.3, 1.9 Hz, 1H, H-5), 3.81 (dd, J = 10.9, 4.4 Hz, 1H, H-6), 3.72 (dd, J = 10.9, 1.9 Hz, 1H, H-6); ^{13}C -APT NMR (214 MHz, CDCl_3 , HSQC, HMBC): δ 164.4 (C=O Nico), 153.7, 151.1 (CH_{arom} Nico), 138.1, 137.7, 137.4 (C_q), 137.3 (CH_{arom} Nico), 128.5, 128.5, 128.4, 128.0, 128.0, 127.9, 127.9 (CH_{arom}), 125.9 (C_q), 123.8 (q, J = 278.5 Hz, CF_3), 123.4 (CH_{arom} Nico), 98.7 (C-1), 75.5 (C-2), 74.9 (CH_2 Bn), 74.2 (C-3), 73.7 (CH_2 Bn), 73.4 (C-4), 73.3 (CH_2 Bn), 72.4 (C-5), 68.7 (C-6), 64.4 (q, J = 35.0 Hz, CH_2CF_3); ^{13}C -GATED NMR (214 MHz, CDCl_3): δ 98.7 ($J_{\text{C1,H1}}$ = 171.3 Hz, C-1 α); Diagnostic peaks β -anomer: ^1H NMR (400 MHz, CDCl_3 , HH-COSY, HSQC, HMBC): δ 9.10 (dd, J = 2.2, 0.9 Hz, 1H, CH_{arom} Nico), 8.79 (dd, J = 4.8, 1.7 Hz, 1H, CH_{arom} Nico), 8.10 (ddd, J = 7.9, 2.2, 1.8 Hz, 1H, CH_{arom} Nico), 7.49 – 7.01 (m, 16H, CH_{arom} Nico, CH_{arom}), 5.08 (dd, J = 9.7, 3.3 Hz, 1H, H-3), 4.73 (d, J = 0.9 Hz, 1H, H-1), 4.15 (t, J = 9.7 Hz, 1H, H-4), 3.57 (ddd, J = 9.5, 5.0, 2.2 Hz, 1H, H-5); ^{13}C -APT NMR (101 MHz, CDCl_3 , HSQC, HMBC): δ 164.4 (C=O Nico), 153.7, 151.1 (CH_{arom} Nico), 138.2, 137.9, 137.7 (C_q), 137.3 (CH_{arom} Nico), 129.5, 128.5, 128.3, 128.1, 127.9, 127.8, 125.6 (CH_{arom}), 124.9 (C_q), 123.4 (CH_{arom} Nico), 101.0 (C-1), 76.2 (C-3), 76.0 (C-5), 75.1 (CH_2 Bn), 74.8 (CH_2 Bn), 74.4 (C-2), 73.8 (CH_2 Bn), 73.2 (C-4), 69.0 (C-6), 66.1 (q, J = 34.8 Hz, CH_2CF_3); ^{13}C -GATED NMR (101 MHz, CDCl_3): δ 101.0 ($J_{\text{C1,H1}}$ = 157.4 Hz, C-1 β); HRMS: $[\text{M}+\text{H}]^+$ calcd for $\text{C}_{35}\text{H}_{35}\text{F}_3\text{NO}_7$ 638.2360, found 638.2356.

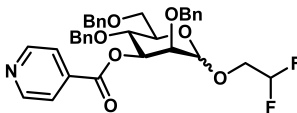


Ethyl 2,4,6-tri-O-benzyl-3-isonicotinoyl- β -mannopyranoside (S33). The title compound was prepared from donor **9** and ethanol using the general procedure for $\text{TiCl}_4/\text{Ph}_2\text{SO}$ mediated glycosylations. Flash column chromatography (100:0 $\rightarrow$ 60:40, pentane:EtOAc, v:v) yielded glycosylation product **S33** (26.8 mg, 0.046 mmol, 46%, α : β = 90:10). TLC: R_f 0.68, (60:40, pentane:EtOAc, v:v); Data for the α -anomer: ^1H NMR (850 MHz, CDCl_3 , HH-COSY, HSQC, HMBC): δ 8.89 – 8.60 (m, 1H, CH_{arom} *i*-Nico), 7.79 – 7.64 (m, 1H, CH_{arom} *i*-Nico), 7.53 – 6.89 (m, 15H, CH_{arom}), 5.50 (dd, J = 9.6, 3.5 Hz, 1H, H-3), 4.95 (d, J = 1.9 Hz, 1H, H-1), 4.74 (d, J = 12.0 Hz, 1H, CHH Bn), 4.69 (d, J = 12.3 Hz, 1H, CHH Bn), 4.58 (d, J = 11.1 Hz, 1H, CHH Bn), 4.55 (d, J = 11.9 Hz, 1H, CHH Bn), 4.52 (d, J = 11.2 Hz, 1H, CHH Bn), 4.51 (d, J = 12.2 Hz, 1H, CHH Bn), 4.22 (t, J = 9.7 Hz, 1H, H-4), 3.95 (dd, J = 3.5, 1.9 Hz, 1H, H-2), 3.91 – 3.87 (ddd, J = 9.7, 4.3, 1.9 Hz, 1H, H-5), 3.85 (dd, J = 10.8, 4.3 Hz, 1H, H-6), 3.77 (dq, J = 9.7, 7.2 Hz, 1H, CHHCH_3 Et), 3.74 (dd, J = 10.8, 1.9 Hz, 1H, H-6), 3.50 (dq, J = 9.6, 7.1 Hz, 1H, CHHCH_3 Et), 1.21 (t, J = 7.1 Hz, 3H, CH_3 Et); ^{13}C -APT NMR (214 MHz, CDCl_3 , HSQC, HMBC): δ 164.2 (C=O *i*-Nico), 150.6 (CH_{arom} *i*-Nico), 138.2, 137.8, 137.8, 137.2 (C_q), 131.1, 129.4, 128.4, 128.3, 128.3, 128.0, 127.7, 127.7, 124.8 (CH_{arom}), 122.9 (CH_{arom} *i*-Nico), 97.4 (C-1), 76.1 (C-2), 75. (C-3), 74.9 (CH_2 Bn), 73.7 (CH_2 Bn), 73.6 (C-4), 72.9 (CH_2 Bn), 71.5 (C-5), 68.9 (C-6), 63.3 (CH_2CH_3 Et), 15.0 (CH_3 Et); ^{13}C -GATED NMR (101 MHz, CDCl_3): δ 97.4 ($J_{\text{C1,H1}}$ = 168.8 Hz, C-1 α); Diagnostic peaks β -anomer: ^1H NMR (400 MHz, CDCl_3 , HH-COSY, HSQC, HMBC): δ 8.74 – 8.73 (m, 1H, CH_{arom} *i*-Nico), 7.79 – 7.64 (m, 1H, CH_{arom} *i*-Nico), 7.53 – 6.89 (m, 15H, CH_{arom}), 5.06 (dd, J = 9.8, 3.4 Hz, 1H, H-3), 4.72 – 4.67 (m, 2H, CHH Bn, CHH Bn), 4.61 (d, J = 0.8 Hz, 1H, H-1), 4.13 (t, J = 9.7 Hz, 1H, H-4), 4.05 (dq, J = 9.5, 7.1 Hz, 1H, CHHCH_3 Et), 3.59 (dq, J = 9.4, 7.1 Hz, 1H, CHHCH_3 Et), 3.56 (dt, J = 9.5, 3.6 Hz, 1H, H-5), 1.21 (t, J = 7.1 Hz, 3H, CH_3 Et); ^{13}C -APT NMR (101 MHz, CDCl_3 , HSQC, HMBC): δ 101.0 (C-1), 75.7 (C-2), 75.2 (C-3), 75.0 (CH_2 Bn), 74.6 (CH_2 Bn), 73.7 (CH_2 Bn), 73.5 (C-4), 71.5 (C-5), 69.2 (C-6), 65.6 (CH_2CH_3 Et), 15.0 (CH_3 Et); ^{13}C -GATED NMR (101 MHz, CDCl_3): δ 101.0 ($J_{\text{C1,H1}}$ = 154.2 Hz, C-1 β); HRMS: $[\text{M}+\text{H}]^+$ calcd for $\text{C}_{35}\text{H}_{38}\text{NO}_7$ 584.2643, found 584.2641.

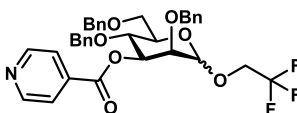


2-Fluoroethyl 2,4,6-tri-O-benzyl-3-isonicotinoyl- β -mannopyranoside (S34). The title compound was prepared from donor **9** and 2-fluoroethanol using the general procedure for $\text{TiCl}_4/\text{Ph}_2\text{SO}$ mediated glycosylations. Flash column chromatography (100:0 $\rightarrow$ 60:40, pentane:EtOAc, v:v) yielded glycosylation product **S34** (19.8 mg, 0.033 mmol, 33%, α : β = 88:12). TLC: R_f 0.59, (60:40, pentane:EtOAc, v:v); Data for the α -anomer: ^1H NMR (850 MHz, CDCl_3 , HH-COSY, HSQC, HMBC): δ 8.75 – 8.74 (m, 2H, CH_{arom} *i*-Nico), 7.73 – 7.71 (m, 2H, CH_{arom} *i*-Nico), 7.39 – 7.00 (m, 15H, CH_{arom}), 5.50 (dd, J = 9.5, 3.5 Hz, 1H, H-3), 5.00 (d, J = 1.9 Hz, 1H, H-1), 4.73 (d, J = 12.0 Hz, 1H, CHH Bn), 4.69 (d, J = 12.3 Hz, 1H, CHH Bn), 4.62 – 4.59 (m, 1H, CH_2CHHFF), 4.58 (d, J = 11.1 Hz, 1H, CHH Bn), 4.54 (d, J = 12.2 Hz, 1H, CHH Bn), 4.54 – 4.53 (m, 1H, CH_2CHHFF), 4.52 (d, J = 11.2 Hz, 1H, CHH Bn), 4.51 (d, J = 12.3 Hz, 1H, CHH Bn), 4.22 (t, J = 9.6 Hz, 1H, H-4), 4.02 (dd, J = 3.5, 1.9 Hz, 1H, H-2), 3.92 (ddd, J = 10.0, 4.5, 2.2 Hz, 1H, H-5), 3.91 (dddd, J = 31.3, 12.2, 5.1, 2.7 Hz, 1H, CHHCH_2F), 3.84 (dd, J = 10.9, 4.3

Hz, 1H, H-6), 3.78 (dddd, $J = 27.4, 12.2, 6.0, 2.9$ Hz, 1H, CHHCH₂F), 3.74 (dd, $J = 10.9, 1.9$ Hz, 1H, H-6); ¹³C-APT NMR (214 MHz, CDCl₃, HSQC, HMBC): δ 164.3 (C=O *i*-Nico), 150.7 (CH_{arom} *i*-Nico), 138.3, 137.9, 137.8, 137.2 (C_q), 128.5, 128.5, 128.5, 128.1, 128.0, 127.9, 127.9, 127.9, 127.8 (CH_{arom}), 123.0 (CH_{arom} *i*-Nico), 98.2 (C-1), 82.6 (d, $J = 170.0$ Hz, CH₂CH₂F), 75.9 (C-2), 75.1 (C-3), 74.9 (CH₂ Bn), 73.7 (CH₂ Bn), 73.6 (C-4), 73.1 (CH₂ Bn), 71.8 (C-5), 68.9 (C-6), 66.9 (d, $J = 20.1$ Hz, CH₂CH₂F); ¹³C-GATED NMR (214 MHz, CDCl₃): δ 98.2 ($J_{C1,H1} = 169.8$ Hz, C-1 α); Diagnostic peaks β -anomer: ¹H NMR (850 MHz, CDCl₃, HH-COSY, HSQC, HMBC): δ 8.74 – 8.73 (m, 2H, CH_{arom} *i*-Nico), 7.68 – 7.64 (m, 2H, CH_{arom} *i*-Nico), 7.44 – 6.95 (m, 15H, CH_{arom}), 5.07 (dd, $J = 9.7, 3.4$ Hz, 1H, H-3), 4.68 (d, $J = 0.7$ Hz, 1H, H-1), 4.17 (dddd, $J = 32.1, 12.1, 4.3, 2.4$ Hz, 1H, CHHCH₂F), 4.15 (t, $J = 9.6$ Hz, 1H, H-4), 3.87 (dddd, $J = 26.7, 11.7, 4.3, 2.6$ Hz, 1H, CHHCH₂F), 3.57 (ddd, $J = 9.5, 4.8, 2.4$ Hz, 1H, H-5); ¹³C-APT NMR (214 MHz, CDCl₃, HSQC, HMBC): δ 164.3 (C=O *i*-Nico), 150.7 (CH_{arom} *i*-Nico), 138.3, 137.9, 137.8, 136.9 (C_q), 128.4, 128.3, 128.2, 127.8, 127.7 (CH_{arom}), 123.0 (CH_{arom} *i*-Nico), 101.4 (C-1), 82.9 (d, $J = 169.9$ Hz, CH₂CH₂F), 76.9 (C-3), 75.8 (C-5), 75.0 (C-2), 74.9 (CH₂ Bn), 73.8 (CH₂ Bn), 73.4 (C-4), 73.1 (CH₂ Bn), 69.2 (C-6), 68.9 (d, $J = 19.8$ Hz, CH₂CH₂F); ¹³C-GATED NMR (214 MHz, CDCl₃): δ 101.4 ($J_{C1,H1} = 155.8$ Hz, C-1 β); HRMS: [M+H]⁺ calcd for C₃₅H₃₇FNO₇ 602.2549, found 602.2551.

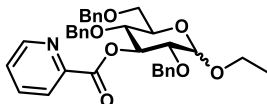


2,2-Difluoroethyl 2,4,6-tri-O-benzyl-3-isonicotinoyl- β -D-mannopyranoside (S35). The title compound was prepared from donor **9** and 2,2-difluoroethanol using the general procedure for Tf₂O/Ph₂SO mediated glycosylations. Flash column chromatography (100:0 $\rightarrow$ 60:40, pentane:EtOAc, v:v) yielded glycosylation product **S35** (32.2 mg, 0.052 mmol, 52%, $\alpha/\beta = 86:14$). TLC: R_f 0.68, (60:40, pentane:EtOAc, v:v); Data for the α -anomer: ¹H NMR (850 MHz, CDCl₃, HH-COSY, HSQC, HMBC): δ 8.78 – 8.73 (m, 2H, CH_{arom} *i*-Nico), 7.74 – 7.69 (m, 2H, CH_{arom} *i*-Nico), 7.37 – 7.02 (m, 15H, CH_{arom}), 5.93 (tdd, $J = 55.3, 4.8, 3.7$ Hz, 1H, CH₂CHF₂), 5.44 (dd, $J = 9.3, 3.4$ Hz, 1H, H-3), 4.98 (d, $J = 2.0$ Hz, 1H, H-1), 4.72 (d, $J = 12.1$ Hz, 1H, CHH Bn), 4.67 (d, $J = 12.2$ Hz, 1H, CHH Bn), 4.59 (d, $J = 11.2$ Hz, 1H, CHH Bn), 4.53 (d, $J = 12.0$ Hz, 1H, CHH Bn), 4.52 (d, $J = 11.2$ Hz, 1H, CHH Bn), 4.52 (d, $J = 12.3$ Hz, 1H, CHH Bn), 4.21 (t, $J = 9.5$ Hz, 1H, H-4), 4.01 (dd, $J = 3.5, 2.0$ Hz, 1H, H-2), 3.88 (ddd, $J = 9.8, 4.5, 1.9$ Hz, 1H, H-5), 3.86 – 3.84 (m, 1H, CHHCHF₂), 3.82 (dd, $J = 10.9, 4.4$ Hz, 1H, H-6), 3.78 – 3.74 (m, 1H, CHHCHF₂), 3.73 (dd, $J = 10.9, 2.0$ Hz, 1H, H-6); ¹³C-APT NMR (214 MHz, CDCl₃, HSQC, HMBC): δ 164.4 (C=O *i*-Nico), 150.8 (CH_{arom} *i*-Nico), 138.1, 137.8, 137.5, 137.1 (C_q), 131.3, 129.5, 129.2, 128.5, 128.1, 127.9, 127.9, 124.9 (CH_{arom}), 123.0 (CH_{arom} *i*-Nico), 114.1 (t, $J = 241.2$ Hz, CH₂CHF₂), 98.7 (C-1), 75.6 (C-2), 74.9 (CH₂ Bn), 74.8 (C-3), 73.7 (CH₂ Bn), 73.4 (C-4), 73.2 (CH₂ Bn), 72.2 (C-5), 68.8 (C-6), 67.0 (t, $J = 28.6$ Hz, CH₂CHF₂); ¹³C-GATED NMR (214 MHz, CDCl₃): δ 98.7 ($J_{C1,H1} = 170.7$ Hz, C-1 α); Diagnostic peaks β -anomer: ¹H NMR (850 MHz, CDCl₃, HH-COSY, HSQC, HMBC): δ 8.73 – 8.71 (m, 2H, CH_{arom} *i*-Nico), 7.64 – 7.62 (m, 2H, CH_{arom} *i*-Nico), 7.49 – 6.92 (m, 15H, CH_{arom}), 6.03 (dddd, $J = 56.0, 54.7, 5.4, 2.9$ Hz, 1H, CH₂CHF₂), 5.20 (dd, $J = 9.8, 3.4$ Hz, 1H, H-3), 4.67 (d, $J = 0.8$ Hz, 1H, H-1), 4.36 (dd, $J = 3.4, 1.1$ Hz, 1H, H-2), 4.15 (t, $J = 9.6$ Hz, 1H, H-4), 3.63 (ddd, $J = 9.7, 5.2, 2.3$ Hz, 1H, H-5); ¹³C-APT NMR (214 MHz, CDCl₃, HSQC, HMBC): δ 164.5 (C=O *i*-Nico), 150.7 (CH_{arom} *i*-Nico), 101.5 (C-1), 76.7 (C-3), 76.2 (CH₂ Bn), 75.9 (C-5), 75.1 (CH₂ Bn), 73.8 (CH₂ Bn), 73.4 (C-2), 73.2 (C-4), 69.0 (C-6); ¹³C-GATED NMR (214 MHz, CDCl₃): δ 101.5 ($J_{C1,H1} = 156.6$ Hz, C-1 β); HRMS: [M+H]⁺ calcd for C₃₅H₃₆F₂NO₇ 620.2454, found 620.2451.

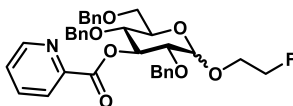


2,2,2-Trifluoroethyl 2,4,6-tri-O-benzyl-3-isonicotinoyl- β -D-mannopyranoside (S36). The title compound was prepared from donor **9** and 2,2,2-trifluoroethanol using the general procedure for Tf₂O/Ph₂SO mediated glycosylations. Flash column chromatography (100:0 $\rightarrow$ 60:40, pentane:EtOAc, v:v) yielded glycosylation product **S36** (28.7 mg, 0.045 mmol, 45%, $\alpha/\beta = 84:16$). TLC: R_f 0.73, (60:40, pentane:EtOAc, v:v); Data for the α -anomer: ¹H NMR (850 MHz, CDCl₃, HH-COSY, HSQC, HMBC): δ 8.77 – 8.73 (m, 2H, CH_{arom} *i*-Nico), 7.73 – 7.70 (m, 2H, CH_{arom} *i*-Nico), 7.37 – 7.03 (m, 15H, CH_{arom}), 5.46 (dd, $J = 9.1, 3.4$ Hz, 1H, H-3), 5.02 (d, $J = 2.1$ Hz, 1H, H-1), 4.71 (d, $J = 11.9$ Hz, 1H, CHH Bn), 4.67 (d, $J = 12.2$ Hz, 1H, CHH Bn), 4.59 (d, $J = 11.1$ Hz, 1H, CHH Bn), 4.52 (d, $J = 11.2$ Hz, 1H, CHH Bn), 4.22 (t, $J = 9.4$ Hz, 1H, H-4), 4.05 (dd, $J = 3.5, 2.1$ Hz, 1H, H-2), 3.99 (dq, $J = 12.5, 8.7$ Hz, 1H, CHHCF₃), 3.93 (dq, $J = 12.4, 8.5$ Hz, 1H, CHHCF₃), 3.86 (ddd, $J = 9.7, 4.3, 1.9$ Hz, 1H, H-5), 3.82 (dd, $J = 11.0, 4.2$ Hz, 1H, H-6), 3.72 (dd, $J = 10.9, 1.9$ Hz, 1H, H-6); ¹³C-APT NMR (214 MHz, CDCl₃, HSQC, HMBC): δ 164.3 (C=O *i*-Nico), 150.8 (CH_{arom} *i*-Nico), 138.1, 137.7, 137.5, 137.1 (C_q), 128.6, 128.5, 128.5, 128.1, 128.0, 127.9, 127.9, 127.9 (CH_{arom}), 125.1 (q, $J = 278.8$ Hz, CF₃), 123.0 (CH_{arom} *i*-Nico), 98.6 (C-1), 75.5 (C-2), 74.9 (CH₂ Bn), 74.5 (C-3), 73.7 (CH₂ Bn), 73.3 (CH₂ Bn), 73.3 (C-4), 72.4 (C-5), 68.6 (C-6), 64.4 (q, $J = 35.0$ Hz, CH₂CF₃); ¹³C-GATED NMR (214 MHz, CDCl₃): δ 98.6 ($J_{C1,H1} = 171.6$ Hz, C-1 α); Diagnostic peaks β -anomer: ¹H NMR (850 MHz, CDCl₃, HH-COSY, HSQC, HMBC): δ 8.79 – 8.74 (m, 2H, CH_{arom} *i*-Nico), 7.67 – 7.66 (m, 2H, CH_{arom} *i*-Nico), 7.38 – 7.01 (m, 15H, CH_{arom}), 5.07 (dd, $J = 9.7, 3.3$ Hz, 1H, H-3), 4.72 (d, $J = 0.9$ Hz, 1H, H-1), 4.16 (t, $J = 9.6$ Hz, 1H, H-4),

4.14 (dd, $J = 3.4, 0.9$ Hz, 1H, H-2), 3.57 (ddd, $J = 9.5, 5.0, 2.1$ Hz, 1H, H-5); ^{13}C -APT NMR (214 MHz, CDCl_3 , HSQC, HMBC): δ 164.3 (C=O *i*-Nico), 150.7 (CH_{arom} *i*-Nico), 138.1, 137.9, 137.6, 136.8 (C_q), 128.5, 128.5, 128.3, 128.1, 128.0 (CH_{arom}), 127.8 (CH_{arom} *i*-Nico), 125.0 (q, $J = 278.8$ Hz, CF_3), 101.0 (C-1), 76.5 (C-3), 76.0 (C-5), 75.1 (CH_2 Bn), 74.4 (C-2), 73.8 (CH_2 Bn), 73.1 (C-4), 68.9 (C-6), 66.1 (d, $J = 34.8$ Hz, CH_2CF_3); ^{13}C -GATED NMR (214 MHz, CDCl_3): δ 101.0 ($J_{\text{C1,H1}} = 157.0$ Hz, C-1 β); HRMS: $[\text{M}+\text{H}]^+$ calcd for $\text{C}_{35}\text{H}_{33}\text{F}_3\text{NO}_7$ 638.2360, found 638.2356.

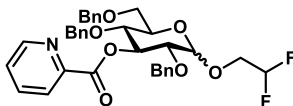


Ethyl 2,4,6-tri-*O*-benzyl-3-picoloyl- β -glucopyranoside (S37). The title compound was prepared from donor **2** and ethanol using the general procedure for $\text{TiF}_2/\text{Ph}_2\text{SO}$ mediated glycosylations. Flash column chromatography (100:0 $\rightarrow$ 60:40, pentane:EtOAc, v:v) yielded glycosylation product **S37** (25.0 mg, 0.043 mmol, 43%, $\alpha:\beta = 28:72$). TLC: R_f 0.55, (60:40, pentane:EtOAc, v:v); Data for the β -anomer: ^1H NMR (850 MHz, CDCl_3 , HH-COSY, HSQC, HMBC): δ 8.79 (ddd, $J = 4.7, 1.8, 0.9$ Hz, 1H, CH_{arom} Pico), 8.01 (dt, $J = 7.8, 1.1$ Hz, 1H, CH_{arom} Pico), 7.82 (td, $J = 7.7, 1.7$ Hz, 1H, CH_{arom}), 7.50 (ddd, $J = 7.6, 4.7, 1.2$ Hz, 1H, CH_{arom} Pico), 7.41 – 7.02 (m, 15H, CH_{arom}), 5.58 (t, $J = 9.5$ Hz, 1H, H-3), 4.84 (d, $J = 11.9$ Hz, 1H, CHH Bn), 4.68 (d, $J = 12.1$ Hz, 1H, CHH Bn), 4.64 (d, $J = 11.8$ Hz, 1H, CHH Bn), 4.58 (d, $J = 10.9$ Hz, 1H, CHH Bn), 4.57 (d, $J = 12.1$ Hz, 1H, CHH Bn), 4.56 (d, $J = 7.8$ Hz, 1H, H-1), 4.50 (d, $J = 11.1$ Hz, 1H, CHH Bn), 4.06 (dq, $J = 9.6, 7.1$ Hz, 1H, CHHCH_3 Et), 3.93 (t, $J = 9.5$ Hz, 1H H-4), 3.79 (dd, $J = 9.0, 1.8$ Hz, 1H, H-6), 3.70 – 3.67 (m, 1H, H-6), 3.68 (dq, $J = 9.6, 6.6$ Hz, 1H, CHHCH_3 Et), 3.62 – 3.59 (m, 1H, H-5), 3.60 (dd, $J = 9.7, 7.8$ Hz, 1H, H-2), 1.30 (t, $J = 7.1$ Hz, 3H, CH_3 Et); ^{13}C -APT NMR (214 MHz, CDCl_3 , HSQC, HMBC): δ 164.5 (C=O Pico), 149.9 (CH_{arom} Pico), 148.1, 138.3, 138.2, 137.8 (C_q), 137.0 (CH_{arom} Pico), 128.5, 128.3, 128.3, 128.2, 128.1, 128.0, 127.8, 127.7 (CH_{arom}), 126.9, 125.6 (CH_{arom} Pico), 103.6 (C-1), 79.2 (C-2), 77.6 (C-3), 76.2 (C-4), 74.9 (C-5), 74.7 (CH_2 Bn), 74.2 (CH_2 Bn), 73.7 (CH_2 Bn), 68.8 (C-6), 65.9 (CH_2CH_3 Et), 15.4 (CH_3 Et); ^{13}C -GATED NMR (214 MHz, CDCl_3): δ 103.6 ($J_{\text{C1,H1}} = 159.0$ Hz, C-1 β); Diagnostic peaks α -anomer: ^1H NMR (850 MHz, CDCl_3 , HH-COSY, HSQC, HMBC): δ 8.78 (ddd, $J = 4.7, 1.8, 0.9$ Hz, 1H, CH_{arom} Pico), 8.10 (dt, $J = 7.8, 1.1$ Hz, 1H, CH_{arom} Pico), 7.82 (td, $J = 7.7, 1.8$ Hz, 1H, CH_{arom} Pico), 7.48 – 7.46 (m, 1H CH_{arom} Pico), 7.39 – 6.97 (m, 15H, CH_{arom}), 5.89 (dd, $J = 10.0, 9.2$ Hz, 1H, H-3), 4.84 (d, $J = 3.6$ Hz, 1H, H-1), 4.64 (d, $J = 12.1$ Hz, 1H, CHH Bn), 4.61 (d, $J = 12.6$ Hz, 1H, CHH Bn), 4.57 (d, $J = 12.6$ Hz, 1H, CHH Bn), 4.56 (d, $J = 10.9$ Hz, 1H, CHH Bn), 4.47 (d, $J = 12.1$ Hz, 1H, CHH Bn), 4.42 (d, $J = 10.9$ Hz, 1H, CHH Bn), 3.98 (t, $J = 9.6$ Hz, 1H, H-4), 3.72 (dq, $J = 9.7, 7.1$ Hz, 1H, CHHCH_3 Et), 3.50 (dq, $J = 9.7, 7.0$ Hz, 1H, CHHCH_3 Et), 1.25 (t, $J = 6.5$ Hz, 3H, CH_3 Et); ^{13}C -APT NMR (214 MHz, CDCl_3 , HSQC, HMBC): δ 164.6 (C=O Pico), 149.9 (CH_{arom} Pico), 148.4, 138.2, 138.0, 137.9 (C_q), 137.0 (CH_{arom} Pico), 128.5, 128.4, 128.1, 127.9, 127.8, 127.8, 127.7, 127.7, 127.5 (CH_{arom}), 126.9, 125.7 (CH_{arom} Pico), 96.7 (C-1), 77.5 (C-2), 76.3 (C-4), 75.8 (C-3), 74.7 (CH_2 Bn), 73.7 (CH_2 Bn), 72.9 (CH_2 Bn), 70.1 (C-5), 68.5 (C-6), 63.7 (CH_2CH_3 Et), 15.1 (CH_3 Et); ^{13}C -GATED NMR (214 MHz, CDCl_3): δ 96.7 ($J_{\text{C1,H1}} = 167.3$ Hz, C-1 α); HRMS: $[\text{M}+\text{H}]^+$ calcd for $\text{C}_{35}\text{H}_{38}\text{NO}_7$ 584.2643, found 584.2640.

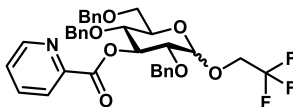


2-Fluoroethyl 2,4,6-tri-*O*-benzyl-3-picoloyl- β -glucopyranoside (S38). The title compound was prepared from donor **2** and 2-fluoroethanol using the general procedure for $\text{TiF}_2/\text{Ph}_2\text{SO}$ mediated glycosylations. Flash column chromatography (100:0 $\rightarrow$ 60:40, pentane:EtOAc, v:v) yielded glycosylation product **S38** (23.4 mg, 0.039 mmol, 39%, $\alpha:\beta = 36:66$). TLC: R_f 0.39, (60:40, pentane:EtOAc, v:v); Data for the β -anomer: ^1H NMR (850 MHz, CDCl_3 , HH-COSY, HSQC, HMBC): δ 8.80 (ddd, $J = 4.7, 1.8, 0.9$ Hz, 1H, CH_{arom} Pico), 8.02 (dt, $J = 7.8, 1.1$ Hz, 1H, CH_{arom} Pico), 7.83 (td, $J = 7.7, 1.8$ Hz, 1H, CH_{arom} Pico), 7.51 (ddd, $J = 7.6, 4.7, 1.2$ Hz, 1H, CH_{arom} Pico), 7.41 – 6.99 (m, 15H, CH_{arom}), 5.59 (t, $J = 9.5$ Hz, 1H, H-3), 4.86 (d, $J = 11.8$ Hz, 1H, CHH Bn), 4.70 (dddd, $J = 40.4, 10.5, 7.1, 2.5$ Hz, 1H, CH_2CHHF), 4.67 (d, $J = 12.2$ Hz, 1H, CHH Bn), 4.64 (d, $J = 11.9$ Hz, 1H, CHH Bn), 4.60 (d, $J = 7.7$ Hz, 1H, H-1), 4.58 (d, $J = 11.0$ Hz, 1H, CHH Bn), 4.57 (d, $J = 12.2$ Hz, 1H, CHH Bn), 4.55 – 4.51 (m, 1H, CH_2CHHF), 4.50 (d, $J = 11.0$ Hz, 1H, CHH Bn), 4.19 (dddd, $J = 32.4, 12.1, 4.9, 2.5$ Hz, 1H, CHHCH_2F), 3.94 (t, $J = 9.6$ Hz, 1H, H-4), 3.89 (dddd, $J = 25.5, 12.0, 7.0, 2.6$ Hz, 1H, CHHCH_2F), 3.80 – 3.75 (m, 2H, H-6, H-6), 3.64 (dd, $J = 9.6, 7.7$ Hz, 1H, H-2), 3.61 (ddd, $J = 9.7, 3.9, 2.4$ Hz, 1H, H-5); ^{13}C -APT NMR (214 MHz, CDCl_3 , HSQC, HMBC): δ 164.5 (C=O Pico), 149.9 (CH_{arom} Pico), 148.1, 138.2, 138.2 (C_q), 137.8 (CH_{arom} Pico), 137.0, 128.5, 128.3, 128.3, 128.2, 128.1, 128.0, 127.8, 127.8, 127.5 (CH_{arom}), 127.0, 125.7 (CH_{arom} Pico), 103.9 (C-1), 82.7 (d, $J = 169.9$ Hz, $\text{CH}_2\text{CH}_2\text{F}$), 79.0 (C-2), 77.4 (C-3), 76.1 (C-4), 75.0 (C-5), 74.7 (CH_2 Bn), 74.2 (CH_2 Bn), 73.7 (CH_2 Bn), 69.13 (d, $J = 20.2$ Hz, $\text{CH}_2\text{CH}_2\text{F}$), 68.69 (C-6); ^{13}C -GATED NMR (214 MHz, CDCl_3): δ 103.9 ($J_{\text{C1,H1}} = 159.7$ Hz, C-1 β); Diagnostic peaks α -anomer: ^1H NMR (850 MHz, CDCl_3 , HH-COSY, HSQC, HMBC): δ 8.78 (ddd, $J = 4.7, 1.8, 0.9$ Hz, 1H, CH_{arom} Pico), 8.10 (dt, $J = 7.8, 1.1$ Hz, 1H, CH_{arom} Pico), 7.83 (td, $J = 7.7, 1.7$ Hz, 1H, CH_{arom} Pico), 7.48 (ddd, $J = 7.6, 4.7, 1.2$ Hz, 1H, CH_{arom} Pico), 5.89 (dd, $J = 10.0, 8.9$ Hz, 1H, H-3), 4.88 (d, $J = 3.6$ Hz, 1H, H-1), 4.47 (d, $J = 12.1$ Hz, 1H, CHH Bn), 4.43 (d, $J = 10.9$ Hz, 1H, CHH Bn), 4.00 (t, $J = 9.6$ Hz, 1H, H-4); ^{13}C -APT NMR (214 MHz, CDCl_3 , HSQC, HMBC): δ 164.6 (C=O Pico), 149.9 (CH_{arom} Pico), 148.3, 138.1, 138.0 (C_q), 137.9 (CH_{arom} Pico), 137.0, 128.4, 128.3, 128.1, 128.1,

128.0, 127.9, 127.7 (CH_{arom}), 127.0, 125.8 (CH_{arom} Pico), 97.4 (C-1), 82.7 (d, *J* = 169.7 Hz, CH₂CHF), 76.2 (CH₂ Bn), 76.1 (C-2), 75.5 (C-3), 75.1 (CH₂ Bn), 74.7 (C-4), 74.6 (CH₂ Bn), 70.2 (C-5), 68.4 (C-6), 67.4 (d, *J* = 20.4 Hz, CH₂CHF); ¹³C-GATED NMR (214 MHz, CDCl₃): δ 97.4 (*J*_{C1,H1} = 169.3 Hz, C-1 α); HRMS: [M+H]⁺ calcd for C₃₅H₃₇FNO₇ 602.2549, found 602.2551.

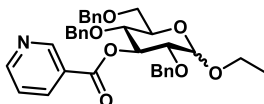


2,2-Difluoroethyl 2,4,6-tri-O-benzyl-3-picoloyl-β-glucopyranoside (S39). The title compound was prepared from donor **2** and 2,2-difluoroethanol using the general procedure for Tf₂O/Ph₂SO mediated glycosylations. Flash column chromatography (100:0 → 60:40, pentane:EtOAc, v:v) yielded glycosylation product **S39** (31.0 mg, 0.050 mmol, 50%, α:β = 46:54). TLC: R_f 0.55, (60:40, pentane:EtOAc, v:v); Data for the β-anomer: ¹H NMR (850 MHz, CDCl₃, HH-COSY, HSQC, HMBC): δ 8.76 (ddd, *J* = 4.7, 1.8, 0.9 Hz, 1H, CH_{arom} Pico), 7.98 (dt, *J* = 7.8, 1.1 Hz, 1H, CH_{arom} Pico), 7.81 (td, *J* = 7.7, 1.8 Hz, 1H, CH_{arom} Pico), 7.48 (ddd, *J* = 7.4, 4.7, 1.3 Hz, 1H, CH_{arom} Pico), 7.38 – 6.99 (m, 15H, CH_{arom}), 5.97 (tt, *J* = 55.4, 4.4 Hz, 1H, CH₂CHF₂), 5.55 (t, *J* = 9.5 Hz, 1H, H-3), 4.78 (d, *J* = 11.8 Hz, 1H, CHH Bn), 4.63 (d, *J* = 12.3 Hz, 1H, CHH Bn), 4.56 (d, *J* = 7.6 Hz, 1H, H-1), 4.54 (d, *J* = 12.1 Hz, 1H, CHH Bn), 4.47 (d, *J* = 11.1 Hz, 1H, CHH Bn), 4.47 (d, *J* = 12.0 Hz, 1H, CHH Bn), 4.43 (d, *J* = 10.9 Hz, 1H, CHH Bn), 3.93 (t, *J* = 9.5 Hz, 1H, H-4), 3.78 – 3.67 (m, 2H, CHHCHF₂, CHHCHF₂), 3.74 (d, *J* = 3.1 Hz, 2H, H-6, H-6), 3.61 (dd, *J* = 9.6, 7.6 Hz, 1H, H-2), 3.58 (dt, *J* = 9.8, 3.1 Hz, 1H, H-5); ¹³C-APT NMR (214 MHz, CDCl₃, HSQC, HMBC): δ 164.4 (C=O Pico), 149.9 (CH_{arom} Pico), 148.0, 138.0, 137.9, 137.7 (C_q), 137.0 (CH_{arom} Pico), 128.6, 128.5, 128.3, 128.3, 128.2, 128.1, 128.1, 128.0 (CH_{arom}), 127.0, 125.7 (CH_{arom} Pico), 114.2 (t, *J* = 241.3 Hz, CH₂CHF₂), 104.0 (C-1), 78.9 (C-2), 77.3 (C-3), 75.9 (C-4), 75.0 (C-5), 74.7 (CH₂ Bn), 74.3 (CH₂ Bn), 73.9 (CH₂ Bn), 68.5 (C-6), 67.5 (t, *J* = 29.3 Hz, CH₂CHF₂); ¹³C-GATED NMR (214 MHz, CDCl₃): δ 104.0 (*J*_{C1,H1} = 162.1 Hz, C-1 β); Diagnostic peaks α-anomer: ¹H NMR (850 MHz, CDCl₃, HH-COSY, HSQC, HMBC): δ 8.78 (ddd, *J* = 4.7, 1.8, 0.9 Hz, 1H, CH_{arom} Pico), 8.11 (dt, *J* = 7.8, 1.1 Hz, 1H, CH_{arom} Pico), 7.83 (td, *J* = 7.7, 1.7 Hz, 1H, CH_{arom} Pico), 7.48 (ddd, *J* = 7.4, 4.7, 1.3 Hz, 1H, CH_{arom} Pico), 7.40 – 6.97 (m, 15H, CH_{arom}), 6.02 (dddd, *J* = 55.9, 55.0, 5.2, 3.3 Hz, 1H, CH₂CHF₂), 5.84 (t, *J* = 9.7 Hz, 1H, H-3), 4.83 (d, *J* = 3.6 Hz, 1H, H-1), 4.06 (dddd, *J* = 21.8, 11.8, 8.3, 3.3 Hz, 1H, CHHCHF₂), 3.99 (t, *J* = 9.6 Hz, 1H, H-4), 3.90 (ddd, *J* = 10.0, 3.5, 2.0 Hz, 1H, H-5), 3.83 (dddd, *J* = 21.3, 13.0, 11.7, 5.2 Hz, 1H, CHHCHF₂), 3.77 (dd, *J* = 10.1, 3.7 Hz, 1H, H-2); ¹³C-APT NMR (214 MHz, CDCl₃, HSQC, HMBC): δ 164.6 (C=O Pico), 149.9 (CH_{arom} Pico), 148.2, 138.0, 137.8, 137.8 (C_q), 137.1 (CH_{arom} Pico), 128.5, 128.3, 128.2, 128.0, 127.9, 127.9, 127.8, 127.7, 127.6 (CH_{arom}), 127.0, 125.8 (CH_{arom} Pico), 114.2 (dd, *J* = 242.2, 240.0 Hz, CH₂CHF₂), 97.9 (C-1), 77.3 (C-2), 75.9 (C-3), 75.3 (C-4), 74.8 (CH₂ Bn), 73.7 (CH₂ Bn), 73.2 (CH₂ Bn), 70.7 (C-5), 68.9 (dd, *J* = 30.5, 27.0 Hz, CH₂CHF₂), 68.2 (C-6); ¹³C-GATED NMR (214 MHz, CDCl₃): δ 97.9 (*J*_{C1,H1} = 169.8 Hz, C-1 α); HRMS: [M+H]⁺ calcd for C₃₅H₃₆F₂NO₇ 620.2454, found 620.2451.

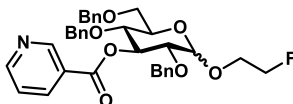


2,2,2-Trifluoroethyl 2,4,6-tri-O-benzyl-3-picoloyl-β-glucopyranoside (S40). The title compound was prepared from donor **2** and 2,2,2-trifluoroethanol using the general procedure for Tf₂O/Ph₂SO mediated glycosylations. Flash column chromatography (100:0 → 60:40, pentane:EtOAc, v:v) yielded glycosylation product **S40** (35.0 mg, 0.055 mmol, 55%, α:β = 49:51). TLC: R_f 0.61, (60:40, pentane:EtOAc, v:v); Data for the α-anomer: ¹H NMR (850 MHz, CDCl₃, HH-COSY, HSQC, HMBC): δ 8.78 (ddd, *J* = 4.7, 1.8, 0.9 Hz, 1H, CH_{arom} Pico), 8.11 (dt, *J* = 7.8, 1.1 Hz, 1H, CH_{arom} Pico), 7.98 (dt, *J* = 7.8, 1.1 Hz, 1H, CH_{arom} Pico), 7.87 – 7.78 (m, 1H, CH_{arom} Pico), 7.52 – 6.98 (m, 15H, CH_{arom}), 5.86 (t, *J* = 9.7 Hz, 1H, H-3), 4.85 (d, *J* = 3.6 Hz, 1H, H-1), 4.80 (d, *J* = 11.7 Hz, 1H, CHH Bn), 4.64 (d, *J* = 11.9 Hz, 1H, CHH Bn), 4.58 (d, *J* = 11.7 Hz, 1H, CHH Bn), 4.54 (d, *J* = 12.1 Hz, 1H, CHH Bn), 4.46 (d, *J* = 12.0 Hz, 1H, CHH Bn), 4.43 (d, *J* = 10.9 Hz, 1H, CHH Bn), 4.24 (dq, *J* = 12.3, 8.7 Hz, 1H, CHHCF₃), 4.01 (t, *J* = 9.7 Hz, 1H, H-4), 3.99 – 3.96 (m, 1H, CHHCF₃), 3.91 – 3.86 (m, 1H, H-5), 3.79 (dd, *J* = 10.1, 3.7 Hz, 1H, H-2), 3.77 (dd, *J* = 10.8, 3.3 Hz, 1H, H-6), 3.65 (dd, *J* = 10.9, 2.1 Hz, 1H, H-6); ¹³C-APT NMR (214 MHz, CDCl₃, HSQC, HMBC): δ 164.4 (C=O Pico), 149.9 (CH_{arom} Pico), 147.9, 138.0, 137.8, 137.7 (C_q), 137.0 (CH_{arom} Pico), 128.2, 128.1, 128.1, 128.1, 128.0, 128.0, 127.9, 127.8, 127.7 (CH_{arom}), 127.0, 125.7 (CH_{arom} Pico), 123.8 (q, *J* = 278.6 Hz, CF₃), 98.0 (C-1), 78.6 (C-2), 75.7 (C-3), 75.1 (C-4), 74.7 (CH₂ Bn), 73.7 (CH₂ Bn), 73.1 (CH₂ Bn), 71.0 (C-5), 68.1 (C-6), 65.2 (q, *J* = 35.1 Hz, CH₂CF₃); ¹³C-GATED NMR (214 MHz, CDCl₃): δ 98.0 (*J*_{C1,H1} = 172.1 Hz, C-1 α); Diagnostic peaks β-anomer: ¹H NMR (850 MHz, CDCl₃, HH-COSY, HSQC, HMBC): δ 8.77 (ddd, *J* = 4.7, 1.8, 0.9 Hz, 1H, CH_{arom} Pico), 7.98 (dt, *J* = 7.8, 1.1 Hz, 1H, CH_{arom} Pico), 7.81 (td, *J* = 7.7, 1.7 Hz, 1H, CH_{arom} Pico), 7.49 – 7.47 (m, 1H, CH_{arom} Pico), 7.40 – 6.94 (m, 15H, CH_{arom}), 5.55 (t, *J* = 9.4 Hz, 1H, H-3), 4.63 (d, *J* = 7.3 Hz, 1H, H-1), 3.94 (t, *J* = 9.5 Hz, 1H, H-4), 3.65 (dd, *J* = 10.9, 2.1 Hz, 1H, H-6), 3.62 (dd, *J* = 9.5, 7.6 Hz, 1H, H-2), 3.58 (ddd, *J* = 9.8, 3.6, 2.6 Hz, 1H, H-5); ¹³C-APT NMR (214 MHz, CDCl₃, HSQC, HMBC): δ 164.6 (C=O Pico), 150.0 (CH_{arom} Pico), 148.2, 138.0, 137.8, 137.8 (C_q), 137.1 (CH_{arom} Pico), 128.6, 128.5, 128.4, 128.4, 128.3, 128.2, 128.0, 128.0, 127.9 (CH_{arom}), 127.0, 125.8 (CH_{arom} Pico), 123.6 (q, *J* = 278.2 Hz, CF₃), 103.8 (C-1), 78.6 (C-2), 75.8 (C-3), 75.2 (C-4),

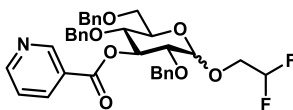
74.8 (CH₂ Bn), 74.2 (CH₂ Bn), 73.7 (CH₂ Bn), 71.0 (C-5), 68.4 (C-6), 66.3 (q, *J* = 34.9 Hz, CH₂CF₃); ¹³C-GATED NMR (214 MHz, CDCl₃): δ 103.8 (*J*_{C1,H1} = 162.5 Hz, C-1 β); HRMS: [M+H]⁺ calcd for C₃₅H₃₅F₃NO₇ 638.2360, found 638.2357.



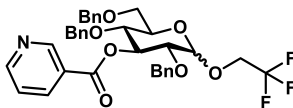
Ethyl 2,4,6-tri-*O*-benzyl-3-nicotinoyl-β-D-glucopyranoside (S41). The title compound was prepared from donor **3** and ethanol using the general procedure for Tf₂O/Ph₂SO mediated glycosylations. Flash column chromatography (100:0 → 60:40, pentane:EtOAc, v:v) yielded glycosylation product **S41** (28.0 mg, 0.048 mmol, 48%, α:β = 20:80). TLC: *R*_f 0.68, (60:40, pentane:EtOAc, v:v); Data for the β-anomer: ¹H NMR (850 MHz, CDCl₃, HH-COSY, HSQC, HMBC): δ 8.96 (dd, *J* = 2.2, 0.9 Hz, 1H, CH_{arom} Nico), 8.76 (dd, *J* = 4.8, 1.8 Hz, 1H, CH_{arom} Nico), 8.06 (dt, *J* = 7.9, 1.9 Hz, 1H, CH_{arom} Nico), 7.65 (dd, *J* = 8.2, 1.5 Hz, 1H, CH_{arom} Nico), 7.53 – 6.93 (m, 15H, CH_{arom}), 5.43 (t, *J* = 9.4 Hz, 1H, H-3), 4.78 (d, *J* = 12.0 Hz, 1H, CHH Bn), 4.67 (d, *J* = 12.2 Hz, 1H, CHH Bn), 4.59 (d, *J* = 12.0 Hz, 1H, CHH Bn), 4.56 (d, *J* = 12.3 Hz, 1H, CHH Bn), 4.52 (d, *J* = 7.7 Hz, 1H, H-1), 4.45 (d, *J* = 11.2 Hz, 1H, CHH Bn), 4.39 (d, *J* = 11.2 Hz, 1H, CHH Bn), 4.04 (dq, *J* = 9.6, 7.1 Hz, 1H, CHHCH₃ Et), 3.76 (t, *J* = 9.6 Hz, 1H, H-4), 3.76 – 3.74 (m, 2H, H-6, H-6), 3.66 (dq, *J* = 9.6, 7.1 Hz, 1H, CHHCH₃ Et), 3.54 (ddd, *J* = 9.7, 3.6, 2.5 Hz, 1H, H-5), 3.44 (dd, *J* = 9.6, 7.7 Hz, 1H, H-2), 1.31 (t, *J* = 7.1 Hz, 3H, CH₃ Et); ¹³C-APT NMR (214 MHz, CDCl₃, HSQC, HMBC): δ 164.4 (C=O Nico), 153.4, 151.0 (CH_{arom} Nico), 138.1, 138.0, 137.6 (C_q), 137.3, 129.5, 128.5, 128.4, 128.4, 128.3, 128.1, 128.1, 127.9, 127.8, 127.7 (CH_{arom}), 126.0 (C_q Nico), 124.9, 123.3 (CH_{arom} Nico), 103.7 (C-1), 78.5 (C-2), 76.7 (C-3), 76.2 (C-4), 74.8 (C-5), 74.5 (CH₂ Bn), 73.9 (CH₂ Bn), 73.8 (CH₂ Bn), 68.6 (C-6), 65.9 (CH₂CH₃ Et), 15.5 (CH₃ Et); ¹³C-GATED NMR (214 MHz, CDCl₃): δ 103.7 (*J*_{C1,H1} = 159.1 Hz, C-1 β); Diagnostic peaks α-anomer: ¹H NMR (850 MHz, CDCl₃, HH-COSY, HSQC, HMBC): δ 9.07 (dd, *J* = 2.2, 0.9 Hz, 1H, CH_{arom} Nico), 8.77 (dd, *J* = 4.8, 1.7 Hz, 1H, CH_{arom} Nico), 8.17 (dt, *J* = 7.9, 2.0 Hz, 1H, CH_{arom} Nico), 7.65 (dd, *J* = 8.2, 1.5 Hz, 1H, CH_{arom} Nico), 7.49 – 6.94 (m, 15H, CH_{arom}), 5.77 (t, *J* = 9.6 Hz, 1H, H-3), 4.89 (d, *J* = 3.5 Hz, 1H, H-1), 3.91 – 3.88 (m, 1H, H-5), 3.81 (t, *J* = 9.5 Hz, 1H, H-4), 3.79 (dd, *J* = 10.8, 3.2 Hz, 1H, H-2), 3.61 (dd, *J* = 10.0, 3.5 Hz, 1H, H-6), 1.26 (t, *J* = 7.1 Hz, 3H, CH₃ Et); ¹³C-APT NMR (214 MHz, CDCl₃, HSQC, HMBC): δ 164.3 (C=O Nico), 153.4, 151.0 (CH_{arom} Nico), 137.9, 137.8, 137.7 (C_q), 128.6, 128.5, 128.3, 128.1, 128.1, 128.0 (CH_{arom}), 127.8, 126.3 (C_q), 124.9, 123.4 (CH_{arom} Nico), 96.4 (C-1), 78.5 (C-2), 76.2 (C-3), 74.8 (C-4), 74.6 (CH₂ Bn), 73.8 (CH₂ Bn), 72.6 (CH₂ Bn), 70.0 (C-5), 68.3 (C-6), 63.8 (CH₂CH₃ Et), 15.1 (CH₃ Et); ¹³C-GATED NMR (214 MHz, CDCl₃): δ 96.4 (*J*_{C1,H1} = 168.8 Hz, C-1 α); HRMS: [M+H]⁺ calcd for C₃₅H₃₈NO₇ 584.2643, found 584.2640.



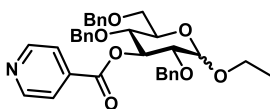
2-Fluoroethyl 2,4,6-tri-*O*-benzyl-3-nicotinoyl-β-D-glucopyranoside (S42). The title compound was prepared from donor **3** and 2-fluoroethanol using the general procedure for Tf₂O/Ph₂SO mediated glycosylations. Flash column chromatography (100:0 → 60:40, pentane:EtOAc, v:v) yielded glycosylation product **S42** (30.1 mg, 0.050 mmol, 50%, α:β = 40:60). TLC: *R*_f 0.57, (60:40, pentane:EtOAc, v:v); Data for the β-anomer: ¹H NMR (850 MHz, CDCl₃, HH-COSY, HSQC, HMBC): δ 8.97 (dd, *J* = 2.2, 0.9 Hz, 1H, CH_{arom} Nico), 8.77 (dd, *J* = 4.8, 1.8 Hz, 1H, CH_{arom} Nico), 8.07 (dt, *J* = 7.9, 1.9 Hz, 1H, CH_{arom} Nico), 7.41 – 6.96 (m, 16H, CH_{arom} Nico, CH_{arom}), 5.44 (t, *J* = 9.4 Hz, 1H, H-3), 4.79 (d, *J* = 12.0 Hz, 1H, CHH Bn), 4.68 (dddd, *J* = 40.5, 10.6, 7.0, 2.5 Hz, 1H, CH₂CHH), 4.66 (d, *J* = 12.2 Hz, 1H, CHH Bn), 4.59 (dddd, *J* = 38.9, 10.1, 7.3, 2.3 Hz, 1H, CH₂CHH), 4.59 (d, *J* = 12.1 Hz, 1H, CHH Bn), 4.57 (d, *J* = 7.6 Hz, 1H, H-1), 4.56 (d, *J* = 12.3 Hz, 1H, CHH Bn), 4.45 (d, *J* = 11.3 Hz, 1H, CHH Bn), 4.39 (d, *J* = 11.3 Hz, 1H, CHH Bn), 4.17 (dddd, *J* = 32.0, 12.0, 4.9, 2.5 Hz, 1H, CHHCH₂F), 3.91 (dddd, *J* = 25.6, 12.0, 7.0, 2.6 Hz, 1H, CHHCH₂F), 3.78 (t, *J* = 9.6 Hz, 1H, H-4), 3.75 (d, *J* = 3.1 Hz, 2H, H-6, H-6), 3.55 (dt, *J* = 9.7, 3.0 Hz, 1H, H-5), 3.48 (dd, *J* = 9.6, 7.7 Hz, 1H, H-2); ¹³C-APT NMR (214 MHz, CDCl₃, HSQC, HMBC): δ 164.3 (C=O Nico), 153.5, 151.0 (CH_{arom} Nico), 138.0, 137.8, 137.5 (C_q), 137.3 (CH_{arom} Nico), 128.6, 128.5, 128.4, 128.3, 128.1, 128.1, 128.0, 127.9, 127.8 (CH_{arom}), 126.0 (C_q Nico), 123.3 (CH_{arom} Nico), 103.9 (C-1), 82.7 (d, *J* = 170.0 Hz, CH₂CH₂F), 78.3 (C-2), 76.6 (C-3), 76.0 (C-4), 74.6 (C-5), 74.6 (CH₂ Bn), 73.9 (CH₂ Bn), 73.8 (CH₂ Bn), 69.1 (d, *J* = 20.1 Hz, CH₂CH₂F), 68.42 (C-6); ¹³C-GATED NMR (214 MHz, CDCl₃): δ 103.9 (*J*_{C1,H1} = 159.2 Hz, C-1 β); Diagnostic peaks α-anomer: ¹H NMR (850 MHz, CDCl₃, HH-COSY, HSQC, HMBC): δ 9.06 (dd, *J* = 2.1, 0.9 Hz, 1H, CH_{arom} Nico), 8.77 (dd, *J* = 4.8, 1.8 Hz, 1H, CH_{arom} Nico), 8.18 (dt, *J* = 7.9, 2.0 Hz, 1H, CH_{arom} Nico), 7.43 – 6.96 (m, 16H, CH_{arom} Nico, CH_{arom}), 5.77 (t, *J* = 9.6 Hz, 1H, H-3), 4.94 (d, *J* = 3.5 Hz, 1H, H-1), 3.95 (dt, *J* = 10.0, 2.7 Hz, 1H, H-5), 3.83 (t, *J* = 9.6 Hz, 1H, H-4), 3.67 (dd, *J* = 10.8, 2.1 Hz, 1H, H-6), 3.63 (dd, *J* = 10.0, 3.5 Hz, 1H, H-2); ¹³C-APT NMR (214 MHz, CDCl₃, HSQC, HMBC): δ 164.3 (C=O Nico), 153.4, 151.0 (CH_{arom} Nico), 138.0, 137.8, 137.7 (C_q), 137.4 (CH_{arom} Nico), 128.6, 128.5, 128.4, 128.3, 128.1, 128.1, 128.0, 127.8 (CH_{arom}), 126.2 (C_q Nico), 123.4 (CH_{arom}), 97.0 (C-1), 82.7 (d, *J* = 169.7 Hz, CH₂CH₂F), 77.1 (C-2), 76.0 (C-4), 74.8 (C-3), 74.5 (CH₂ Bn), 73.8 (CH₂ Bn), 72.6 (CH₂ Bn), 70.1 (C-5), 68.2 (C-6), 67.4 (d, *J* = 20.3 Hz, CH₂CH₂F); ¹³C-GATED NMR (214 MHz, CDCl₃): δ 97.0 (*J*_{C1,H1} = 169.2 Hz, C-1 α); HRMS: [M+H]⁺ calcd for C₃₅H₃₇FNO₇ 602.2549, found 602.2545.



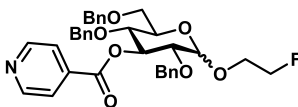
2,2-Difluoroethyl 2,4,6-tri-O-benzyl-3-nicotinoyl- β -D-glucopyranoside (S43). The title compound was prepared from donor **3** and 2,2-difluoroethanol using the general procedure for $\text{TiF}_2/\text{Ph}_2\text{SO}$ mediated glycosylations. Flash column chromatography (100:0 $\rightarrow$ 60:40, pentane:EtOAc, v:v) yielded glycosylation product **S43** (29.1 mg, 0.047 mmol, 47%, α : β = 41:59). TLC: R_f 0.63, (60:40, pentane:EtOAc, v:v); Data for the β -anomer: ^1H NMR (850 MHz, CDCl_3 , HH-COSY, HSQC, HMBC): δ 8.95 (dd, J = 2.2, 0.9 Hz, 1H, CH_{arom} Nico), 8.77 (dd, J = 4.8, 1.7 Hz, 1H, CH_{arom} Nico), 8.06 (dt, J = 7.9, 2.0 Hz, 1H, CH_{arom} Nico), 7.41 – 6.98 (m, 16H, CH_{arom} Nico, CH_{arom}), 6.05 – 5.90 (dddd, J = 55.6, 54.3, 5.2, 3.7 Hz, 1H, CH_2CHF_2), 5.43 (t, J = 9.4 Hz, 1H, H-3), 4.76 (d, J = 12.0 Hz, 1H, CHH Bn), 4.65 (d, J = 12.2 Hz, 1H, CHH Bn), 4.56 (d, J = 12.3 Hz, 1H, CHH Bn), 4.56 (d, J = 7.5 Hz, 1H, H-1), 4.55 (d, J = 11.7 Hz, 1H, CHH Bn), 4.46 (d, J = 11.3 Hz, 1H, CHH Bn), 4.39 (d, J = 11.3 Hz, 1H, CHH Bn), 4.08 (dddd, J = 22.6, 11.6, 10.4, 3.4 Hz, 1H, CHHCH_2F_2), 3.88 – 3.81 (m, 1H, CHHCH_2F_2), 3.79 (t, J = 9.5 Hz, 1H, H-4), 3.77 – 3.73 (m, 2H, H-6, H-6), 3.55 (ddd, J = 9.8, 3.7, 2.3 Hz, 1H, H-5), 3.49 (dd, J = 9.5, 7.6 Hz, 1H, H-2); ^{13}C -APT NMR (214 MHz, CDCl_3 , HSQC, HMBC): δ 164.3 (C=O Nico), 153.5, 151.0 (CH_{arom} Nico), 137.8, 137.6, 137.4 (C_q), 137.3 (CH_{arom} Nico), 128.6, 128.5, 128.4, 128.3, 128.3, 128.1, 128.0, 127.9, 127.8 (CH_{arom}), 125.9 (C_q), 123.3 (CH_{arom} Nico), 114.2 (dd, J = 242.2, 240.2 Hz, CH_2CHF_2), 104.1 (C-1), 78.2 (C-2), 76.4 (C-3), 75.7 (C-4), 74.9 (C-5), 74.6 (CH_2 Bn), 74.0 (CH_2 Bn), 73.8 (CH_2 Bn), 68.9 (dd, J = 30.2, 27.0 Hz, CH_2CHF_2), 68.2 (C-6); ^{13}C -GATED NMR (214 MHz, CDCl_3): δ 104.1 ($J_{\text{C1,H1}}$ = 160.9 Hz, C-1 β); Diagnostic peaks α -anomer: ^1H NMR (850 MHz, CDCl_3 , HH-COSY, HSQC, HMBC): δ 9.06 (dd, J = 2.2, 0.9 Hz, 1H, CH_{arom} Nico), 8.78 (dd, J = 4.8, 1.8 Hz, 1H, CH_{arom} Nico), 8.17 (dt, J = 7.9, 2.0 Hz, 1H, CH_{arom} Nico), 7.39 – 6.96 (m, 16H, CH_{arom} Nico, CH_{arom}), 5.91 (dddd, J = 55.5, 54.3, 5.0, 3.4 Hz, 1H, CH_2CHF_2), 5.73 (t, J = 9.6 Hz, 1H, H-3), 4.89 (d, J = 3.6 Hz, 1H, H-1), 4.76 (d, J = 12.0 Hz, 1H, CHH Bn), 4.65 (d, J = 12.1 Hz, 1H, CHH Bn), 4.53 (d, J = 12.4 Hz, 1H, CHH Bn), 4.50 (d, J = 12.1 Hz, 1H, CHH Bn), 4.43 (d, J = 11.2 Hz, 1H, CHH Bn), 4.40 (d, J = 11.3 Hz, 1H, CHH Bn), 3.89 (ddd, J = 9.9, 3.2, 2.1 Hz, 1H, H-5), 3.66 (dd, J = 10.9, 2.1 Hz, 1H, H-6), 3.63 (dd, J = 10.0, 3.6 Hz, 1H, H-2); ^{13}C -APT NMR (214 MHz, CDCl_3 , HSQC, HMBC): δ 164.3 (C=O Nico), 153.5, 150.9 (CH_{arom} Nico), 137.6, 137.6, 137.5 (C_q), 137.4 (CH_{arom} Nico), 128.6, 128.6, 128.4, 128.3, 128.2, 128.1, 128.1, 128.0, 127.9 (CH_{arom}), 126.1 (C_q), 123.4 (CH_{arom} Nico), 114.2 (t, J = 241.2 Hz, CH_2CHF_2), 97.5 (C-1), 77.0 (C-2), 75.8 (C-4), 74.6 (CH_2 Bn), 73.9 (C-3), 72.9 (CH_2 Bn), 70.6 (CH_2 Bn), 68.0 (C-5), 67.5 (t, J = 29.1 Hz, CH_2CHF_2); ^{13}C -GATED NMR (214 MHz, CDCl_3): δ 97.5 ($J_{\text{C1,H1}}$ = 167.9 Hz, C-1 α); HRMS: $[\text{M}+\text{H}]^+$ calcd for $\text{C}_{35}\text{H}_{36}\text{F}_2\text{NO}_7$ 620.2454, found 620.2448.



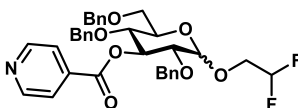
2,2,2-Trifluoroethyl 2,4,6-tri-O-benzyl-3-nicotinoyl- β -D-glucopyranoside (S44). The title compound was prepared from donor **3** and 2,2,2-trifluoroethanol using the general procedure for $\text{TiF}_2/\text{Ph}_2\text{SO}$ mediated glycosylations. Flash column chromatography (100:0 $\rightarrow$ 60:40, pentane:EtOAc, v:v) yielded glycosylation product **S44** (32.5 mg, 0.051 mmol, 51%, α : β = 47:53). TLC: R_f 0.79, (60:40, pentane:EtOAc, v:v); Data for the β -anomer: ^1H NMR (850 MHz, CDCl_3 , HH-COSY, HSQC, HMBC): δ 8.95 (dd, J = 2.2, 0.9 Hz, 1H, CH_{arom} Nico), 8.77 (dd, J = 4.9, 1.8 Hz, 1H, CH_{arom} Nico), 8.06 (dt, J = 7.9, 1.9 Hz, 1H, CH_{arom} Nico), 7.50 – 6.96 (m, 16H, CH_{arom} Nico, CH_{arom}), 5.43 (t, J = 9.4 Hz, 1H, H-4), 4.77 (d, J = 12.0 Hz, 1H, CHH Bn), 4.65 (d, J = 12.2 Hz, 1H, CHH Bn), 4.62 (d, J = 7.6 Hz, 1H, H-1), 4.56 (d, J = 12.2 Hz, 1H, CHH Bn), 4.50 (d, J = 12.1 Hz, 1H, CHH Bn), 4.45 (d, J = 11.2 Hz, 1H, CHH Bn), 4.39 (d, J = 11.2 Hz, 1H, CHH Bn), 4.25 (dq, J = 12.2, 8.6 Hz, 1H, CHHCF_3), 3.99 (dq, J = 12.2, 8.4 Hz, 1H, CHHCF_3), 3.80 (t, J = 9.5 Hz, 1H, H-4), 3.76 (dd, J = 11.0, 3.7 Hz, 1H, H-6), 3.74 (dd, J = 11.0, 2.1 Hz, 1H, H-6), 3.55 (ddd, J = 9.8, 3.8, 2.1 Hz, 1H, H-5), 3.50 (dd, J = 9.5, 7.5 Hz, 1H, H-2); ^{13}C -APT NMR (214 MHz, CDCl_3 , HSQC, HMBC): δ 164.3 (C=O Nico), 153.5, 151.0 (CH_{arom} Nico), 137.8, 137.6, 137.4 (C_q), 137.3 (CH_{arom} Nico), 128.6, 128.6, 128.4, 128.3, 128.1, 128.1, 128.1, 127.9 (CH_{arom}), 125.9 (C_q Nico), 123.8 (q, J = 278.4 Hz, CF_3), 123.3 (CH_{arom} Nico), 103.7 (C-1), 77.9 (C-2), 76.2 (C-3), 75.6 (C-4), 75.0 (C-5), 74.6 (CH_2 Bn), 73.8 (CH_2 Bn), 73.8 (CH_2 Bn), 68.1 (C-6), 66.3 (q, J = 35.1 Hz, CH_2CF_3); ^{13}C -GATED NMR (214 MHz, CDCl_3): δ 103.7 ($J_{\text{C1,H1}}$ = 162.3 Hz, C-1 β); Diagnostic peaks α -anomer: ^1H NMR (850 MHz, CDCl_3 , HH-COSY, HSQC, HMBC): δ 9.06 (dd, J = 2.2, 0.9 Hz, 1H, CH_{arom} Nico), 8.77 (dd, J = 4.9, 1.8 Hz, 1H, CH_{arom} Nico), 8.18 (dt, J = 7.9, 1.9 Hz, 1H, CH_{arom} Nico), 7.39 – 6.97 (m, 16H, CH_{arom} Nico, CH_{arom}), 5.74 (dd, J = 10.0, 9.1 Hz, 1H, H-3), 4.91 (d, J = 3.6 Hz, 1H, H-1), 4.77 (d, J = 12.0 Hz, 1H, CHH Bn), 4.65 (d, J = 12.1 Hz, 1H, CHH Bn), 4.55 (d, J = 12.0 Hz, 1H, CHH Bn), 4.50 (d, J = 12.1 Hz, 1H, CHH Bn), 4.43 (d, J = 11.2 Hz, 1H, CHH Bn), 4.40 (d, J = 11.2 Hz, 1H, CHH Bn), 3.88 (dt, J = 9.8, 2.5 Hz, 1H, H-5), 3.67 (dd, J = 10.1, 2.0 Hz, 1H, H-6), 3.64 (dd, J = 10.0, 3.6 Hz, 1H, H-2); ^{13}C -APT NMR (214 MHz, CDCl_3 , HSQC, HMBC): δ 164.3 (C=O Nico), 153.5, 150.9 (CH_{arom} Nico), 137.6, 137.5, 137.4 (C_q), 137.3 (CH_{arom} Nico), 128.6, 128.6, 128.6, 128.4, 128.2, 128.1, 128.0, 127.9, 127.9 (CH_{arom}), 126.1 (C_q Nico), 123.4 (CH_{arom} Nico), 97.7 (C-1), 76.8 (C-2), 75.7 (C-4), 74.7 (CH_2 Bn), 74.2 (C-3), 73.9 (CH_2 Bn), 72.8 (CH_2 Bn), 70.9 (C-5), 67.9 (C-6), 65.2 (q, J = 35.2 Hz, CH_2CF_3); ^{13}C -GATED NMR (214 MHz, CDCl_3): δ 97.7 ($J_{\text{C1,H1}}$ = 172.7 Hz, C-1 α); HRMS: $[\text{M}+\text{H}]^+$ calcd for $\text{C}_{35}\text{H}_{35}\text{F}_3\text{NO}_7$ 638.2360, found 638.2356.



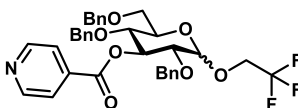
Ethyl 2,4,6-tri-*O*-benzyl-3-isonicotinoyl- β -D-glucopyranoside (S45). The title compound was prepared from donor **4** and ethanol using the general procedure for $\text{Ti}_2\text{O}/\text{Ph}_2\text{SO}$ mediated glycosylations. Flash column chromatography (100:0 $\rightarrow$ 60:40, pentane:EtOAc, v:v) yielded glycosylation product **S45** (26.8 mg, 0.046 mmol, 46%, $\alpha:\beta = 19:81$). TLC: R_f 0.65, (60:40, pentane:EtOAc, v:v); Data for the β -anomer: ^1H NMR (850 MHz, CDCl_3 , HH-COSY, HSQC, HMBC): δ 8.73 – 8.68 (m, 2H, CH_{arom} *i*-Nico), 7.61 – 7.56 (m, 2H, CH_{arom} *i*-Nico), 7.46 – 6.95 (m, 15H, CH_{arom}), 5.41 (t, $J = 9.5$ Hz, 1H, H-3), 4.77 (d, $J = 12.1$ Hz, 1H, CHH Bn), 4.67 (d, $J = 12.1$ Hz, 1H, CHH Bn), 4.59 (d, $J = 12.0$ Hz, 1H, CHH Bn), 4.56 (d, $J = 12.2$ Hz, 1H, CHH Bn), 4.52 (d, $J = 7.7$ Hz, 1H, H-1), 4.45 (d, $J = 11.2$ Hz, 1H, CHH Bn), 4.37 (d, $J = 11.2$ Hz, 1H, CHH Bn), 4.04 (dq, $J = 9.6, 7.1$ Hz, 1H, CHHCH_3 Et), 3.76 (d, $J = 3.0$ Hz, 2H, H-6, H-6), 3.76 (t, $J = 9.5$ Hz, 1H, H-4), 3.66 (dq, $J = 9.6, 7.0$ Hz, 1H, CHHCH_3 Et), 3.54 (dt, $J = 9.7, 3.0$ Hz, 1H, H-5), 3.43 (dd, $J = 9.6, 7.7$ Hz, 1H, H-2), 1.32 (t, $J = 7.1$ Hz, 3H, CH_3 Et); ^{13}C -APT NMR (214 MHz, CDCl_3 , HSQC, HMBC): δ 164.3 (C=O *i*-Nico), 150.5 (CH_{arom} *i*-Nico), 138.0, 137.9, 137.5, 137.2 (C_q), 128.6, 128.4, 128.4, 128.3, 128.1, 128.1, 127.9, 127.9 (CH_{arom}), 127.8 (CH_{arom} *i*-Nico), 103.7 (C-1), 78.4 (C-2), 77.1 (C-3), 76.1 (C-4), 74.8 (C-5), 74.5 (CH_2 Bn), 73.9 (CH_2 Bn), 73.8 (CH_2 Bn), 68.5 (C-6), 65.9 (CH_2CH_3 Et), 15.5 (CH_3 Et); ^{13}C -GATED NMR (214 MHz, CDCl_3): δ 103.7 ($J_{\text{C1,H1}} = 159.3$ Hz, C-1 β); Diagnostic peaks α -anomer: ^1H NMR (850 MHz, CDCl_3 , HH-COSY, HSQC, HMBC): δ 8.75 – 8.73 (m, 2H, CH_{arom} *i*-Nico), 7.72 – 7.66 (m, 2H, CH_{arom} *i*-Nico), 7.40 – 6.95 (m, 15H, CH_{arom}), 5.75 (t, $J = 9.6$ Hz, 1H, H-3), 4.90 (d, $J = 3.5$ Hz, 1H, H-1), 4.81 (d, $J = 11.2$ Hz, 1H, CHH Bn), 4.75 (d, $J = 9.7$ Hz, 1H, CHH Bn), 4.56 (d, $J = 12.7$ Hz, 1H, CHH Bn), 4.49 (d, $J = 12.6$ Hz, 1H, CHH Bn), 4.42 (d, $J = 11.1$ Hz, 1H, CHH Bn), 4.37 (d, $J = 11.1$ Hz, 1H, CHH Bn), 3.89 (dt, $J = 9.9, 2.6$ Hz, 1H, H-5), 3.81 (t, $J = 9.5$ Hz, 1H, H-4), 3.79 (dd, $J = 10.8, 3.3$ Hz, 1H, H-6), 3.73 (dd, $J = 9.7, 7.1$ Hz, 1H, H-6), 3.60 (dd, $J = 9.9, 3.5$ Hz, 1H, H-2), 1.32 (t, $J = 7.1$ Hz, 3H, CH_3 Et); ^{13}C -APT NMR (214 MHz, CDCl_3 , HSQC, HMBC): δ 164.2 (C=O *i*-Nico), 150.6 (CH_{arom} *i*-Nico), 137.8, 137.8, 137.6, 137.5 (C_q), 128.6, 128.6, 128.5, 128.4, 128.1, 128.1, 128.0, 127.9 (CH_{arom}), 123.0 (CH_{arom} *i*-Nico), 96.3 (C-1), 77.1 (C-2), 76.2 (C-4), 75.2 (C-3), 74.6 (CH_2 Bn), 73.9 (CH_2 Bn), 72.5 (CH_2 Bn), 70.0 (C-5), 68.3 (C-6), 63.8 (CH_2CH_3 Et), 15.1 (CH_3 Et); ^{13}C -GATED NMR (214 MHz, CDCl_3): δ 96.3 ($J_{\text{C1,H1}} = 167.4$ Hz, C-1 α); HRMS: $[\text{M}+\text{H}]^+$ calcd for $\text{C}_{35}\text{H}_{38}\text{NO}_7$: 584.2643, found 584.2637.



2-Fluoroethyl 2,4,6-tri-*O*-benzyl-3-isonicotinoyl- β -D-glucopyranoside (S46). The title compound was prepared from donor **S27** and 2-fluoroethanol using the general procedure for $\text{Ti}_2\text{O}/\text{Ph}_2\text{SO}$ mediated glycosylations. Flash column chromatography (100:0 $\rightarrow$ 60:40, pentane:EtOAc, v:v) yielded glycosylation product **S46** (30.1 mg, 0.050 mmol, 50%, $\alpha:\beta = 32:68$). TLC: R_f 0.59, (60:40, pentane:EtOAc, v:v); Data for the β -anomer: ^1H NMR (850 MHz, CDCl_3 , HH-COSY, HSQC, HMBC): δ 8.78 – 8.69 (m, 2H, CH_{arom} *i*-Nico), 7.67 – 7.56 (m, 2H, CH_{arom} *i*-Nico), 7.43 – 6.97 (m, 15H, CH_{arom}), 5.45 (t, $J = 9.4$ Hz, 1H, H-3), 4.81 (d, $J = 12.0$ Hz, 1H, CHH Bn), 4.69 (d, $J = 12.2$ Hz, 1H, CHH Bn), 4.73 – 4.64 (m, 1H, CH_2CHHF), 4.63 – 4.60 (m, 1H, CH_2CHHF), 4.61 (d, $J = 12.1$ Hz, 1H, CHH Bn), 4.59 (d, $J = 7.6$ Hz, 1H, H-1), 4.59 (d, $J = 11.8$ Hz, 1H, CHH Bn), 4.48 (d, $J = 11.3$ Hz, 1H, CHH Bn), 4.40 (d, $J = 11.2$ Hz, 1H, CHH Bn), 4.19 (dddd, $J = 32.3, 12.0, 4.9, 2.5$ Hz, 1H, CHHCH_2F), 3.94 (dddd, $J = 25.6, 12.1, 7.0, 2.6$ Hz, 1H, CHHCH_2F), 3.80 (t, $J = 9.6$ Hz, 1H, H-4), 3.79 – 3.76 (m, 2H, H-6, H-6), 3.57 (ddd, $J = 9.7, 3.6, 2.4$ Hz, 1H, H-5), 3.50 (dd, $J = 9.6, 7.7$ Hz, 1H, H-2); ^{13}C -APT NMR (214 MHz, CDCl_3 , HSQC, HMBC): δ 164.2 (C=O *i*-Nico), 150.6 (CH_{arom} *i*-Nico), 138.0, 137.8, 137.5, 137.2 (C_q), 128.6, 128.5, 128.4, 128.3, 128.1, 128.1, 128.0, 128.0, 127.8 (CH_{arom}), 123.1 (CH_{arom} *i*-Nico), 103.9 (C-1), 82.7 (d, $J = 170.1$ Hz, $\text{CH}_2\text{CH}_2\text{F}$), 78.2 (C-2), 76.9 (C-3), 75.9 (C-4), 74.8 (C-5), 74.6 (CH_2 Bn), 73.9 (CH_2 Bn), 73.8 (CH_2 Bn), 69.1 (d, $J = 20.1$ Hz, $\text{CH}_2\text{CH}_2\text{F}$), 68.4 (C-6); ^{13}C -GATED NMR (214 MHz, CDCl_3): δ 103.9 ($J_{\text{C1,H1}} = 161.2$ Hz, C-1 β); Diagnostic peaks α -anomer: ^1H NMR (850 MHz, CDCl_3 , HH-COSY, HSQC, HMBC): δ 8.75 – 8.73 (m, 2H, CH_{arom} *i*-Nico), 7.72 – 7.64 (m, 2H, CH_{arom} *i*-Nico), 7.41 – 6.93 (m, 15H, CH_{arom}), 5.75 (t, $J = 9.6$ Hz, 1H, H-3), 4.95 (d, $J = 3.5$ Hz, 1H, H-1), 4.50 (d, $J = 12.3$ Hz, 1H, CHH Bn), 4.43 (d, $J = 11.1$ Hz, 1H, CHH Bn), 3.82 (t, $J = 9.6$ Hz, 1H, H-4), 3.67 (dd, $J = 10.8, 2.0$ Hz, 1H, H-6), 3.62 (dd, $J = 10.0, 3.5$ Hz, 1H, H-2); ^{13}C -APT NMR (214 MHz, CDCl_3 , HSQC, HMBC): δ 164.2 (C=O *i*-Nico), 150.6 (CH_{arom} *i*-Nico), 137.7, 137.7, 137.6, 137.5 (C_q), 128.6, 128.5, 128.4, 128.4, 128.3, 128.1, 128.1, 128.0, 127.9 (CH_{arom}), 123.1 (CH_{arom} *i*-Nico), 97.0 (C-1), 82.7 (d, $J = 169.9$ Hz, $\text{CH}_2\text{CH}_2\text{F}$), 77.1 (C-2), 76.0 (C-3), 75.0 (C-4), 74.5 (CH_2 Bn), 73.8 (CH_2 Bn), 72.6 (CH_2 Bn), 70.1 (C-5), 68.2 (C-6), 67.4 (d, $J = 20.3$ Hz, $\text{CH}_2\text{CH}_2\text{F}$); ^{13}C -GATED NMR (214 MHz, CDCl_3): δ 97.0 ($J_{\text{C1,H1}} = 169.1$ Hz, C-1 α); HRMS: $[\text{M}+\text{H}]^+$ calcd for $\text{C}_{35}\text{H}_{37}\text{FNO}_7$: 602.2549, found 602.2548.



2,2-Difluoroethyl 2,4,6-tri-O-benzyl-3-isonicotinoyl-β-D-glucopyranoside (S47). The title compound was prepared from donor **4** and 2,2-difluoroethanol using the general procedure for Tf₂O/Ph₂SO mediated glycosylations. Flash column chromatography (100:0 → 60:40, pentane:EtOAc, v:v) yielded glycosylation product **S47** (32.2 mg, 0.052 mmol, 52%, α:β = 50:50). TLC: R_f 0.66, (60:40, pentane:EtOAc, v:v); Data for the β-anomer: ¹H NMR (850 MHz, CDCl₃, HH-COSY, HSQC, HMBC): δ 8.76 – 8.72 (m, 2H, CH_{arom} *i*-Nico), 7.62 – 7.58 (m, 2H, CH_{arom} *i*-Nico), 7.44 – 6.96 (m, 15H, CH_{arom}), 5.93 (dddd, *J* = 55.9, 54.8, 8.5, 1.8 Hz, 1H, CH₂CHF₂), 5.44 (t, *J* = 9.4 Hz, 1H, H-3), 4.77 (d, *J* = 12.0 Hz, 1H, CHH Bn), 4.68 (d, *J* = 12.2 Hz, 1H, CHH Bn), 4.59 (d, *J* = 7.7 Hz, 1H, H-1), 4.57 (d, *J* = 12.0 Hz, 1H, CHH Bn), 4.53 (d, *J* = 12.0 Hz, 1H, CHH Bn), 4.48 (d, *J* = 11.3 Hz, 1H, CHH Bn), 4.40 (d, *J* = 11.2 Hz, 1H, CHH Bn), 3.81 (t, *J* = 9.5 Hz, 1H, H-4), 3.79 – 3.73 (m, 5H, H-6, H-6, CHHCF₃, CHHCF₃), 3.57 (ddd, *J* = 9.7, 3.7, 2.1 Hz, 1H, H-5), 3.50 (dd, *J* = 9.5, 7.6 Hz, 1H, H-2); ¹³C-APT NMR (214 MHz, CDCl₃, HSQC, HMBC): δ 164.2 (C=O *i*-Nico), 150.6 (CH_{arom} *i*-Nico), 137.8, 137.6, 137.4, 137.1 (C_q), 128.7, 128.6, 128.6, 128.5, 128.4, 128.1, 128.1, 127.9 (CH_{arom}), 127.9 (CH_{arom} *i*-Nico), 104.1 (C-1), 78.2 (C-2), 76.8 (C-3), 74.9 (C-4), 74.6 (C-5), 73.8 (CH₂ Bn), 72.8 (CH₂ Bn), 70.6 (CH₂ Bn), 68.0 (C-6), 67.5 (t, *J* = 29.1 Hz, CH₂CHF₂); ¹³C-GATED NMR (214 MHz, CDCl₃): δ 104.1 (*J*_{C1,H1} = 162.0 Hz, C-1 β); Diagnostic peaks α-anomer: ¹H NMR (850 MHz, CDCl₃, HH-COSY, HSQC, HMBC): δ 8.77 – 8.73 (m, 2H, CH_{arom} *i*-Nico), 7.70 – 7.66 (m, 2H, CH_{arom} *i*-Nico), 7.40 – 6.93 (m, 15H, CH_{arom}), 5.76 – 5.66 (t, *J* = 9.7 Hz, 1H, H-3), 4.90 (d, *J* = 3.6 Hz, 1H, H-1), 3.89 (dt, *J* = 10.3, 2.7 Hz, 1H, H-5), 3.83 (t, *J* = 9.6 Hz, 1H, H-4), 3.67 (dd, *J* = 10.9, 2.1 Hz, 1H, H-6), 3.62 (dd, *J* = 10.0, 3.6 Hz, 1H, H-2); ¹³C-APT NMR (214 MHz, CDCl₃, HSQC, HMBC): δ 164.2 (C=O *i*-Nico), 150.7, 137.6, 137.6, 137.5 (C_q), 137.3, 128.4, 128.2, 128.1 (CH_{arom}), 128.0 (CH_{arom} *i*-Nico), 97.5 (C-1), 77.0 (C-2), 75.8 (C-3), 74.7 (C-4), 74.6 (CH₂ Bn), 74.0 (CH₂ Bn), 73.9 (CH₂ Bn), 70.6 (C-5), 68.9 (t, *J* = 23.6 Hz, CH₂CHF₂), 68.2 (C-6); ¹³C-GATED NMR (214 MHz, CDCl₃): δ 97.5 (*J*_{C1,H1} = 168.8 Hz, C-1 α); HRMS: [M+H]⁺ calcd for C₃₅H₃₆F₂NO₇ 620.2454, found 620.2454.



2,2,2-Trifluoroethyl 2,4,6-tri-O-benzyl-3-isonicotinoyl-β-D-glucopyranoside (S48). The title compound was prepared from donor **4** and 2,2,2-trifluoroethanol using the general procedure for Tf₂O/Ph₂SO mediated glycosylations. Flash column chromatography (100:0 → 60:40, pentane:EtOAc, v:v) yielded glycosylation product **S48** (19.8 mg, 0.031 mmol, 31%, α:β = 65:35). TLC: R_f 0.65, (60:40, pentane:EtOAc, v:v); Data for the α-anomer: ¹H NMR (850 MHz, CDCl₃, HH-COSY, HSQC, HMBC): δ 8.76 – 8.74 (m, 2H, CH_{arom} *i*-Nico), 7.69 – 7.67 (m, 2H, CH_{arom} *i*-Nico), 7.52 – 6.86 (m, 15H, CH_{arom}), 5.72 (dd, *J* = 10.0, 9.1 Hz, 1H, H-3), 4.93 (d, *J* = 3.6 Hz, 1H, H-1), 4.81 (d, *J* = 11.2 Hz, 1H, CHH Bn), 4.67 (d, *J* = 11.9 Hz, 1H, CHH Bn), 4.58 (d, *J* = 12.0 Hz, 1H, CHH Bn), 4.47 (d, *J* = 11.3 Hz, 1H, CHH Bn), 4.43 (d, *J* = 11.2 Hz, 1H, CHH Bn), 4.39 (d, *J* = 11.3 Hz, 1H, CHH Bn), 3.88 (dt, *J* = 9.9, 2.6 Hz, 1H, H-5), 3.85 – 3.78 (m, 4H, H-4, H-6, CHHCF₃, CHHCF₃), 3.66 (dd, *J* = 10.9, 2.0 Hz, 1H, H-6), 3.64 (dd, *J* = 10.0, 3.6 Hz, 1H, H-2); ¹³C-APT NMR (214 MHz, CDCl₃, HSQC, HMBC): δ 164.1 (C=O *i*-Nico), 150.7 (CH_{arom} *i*-Nico), 137.6, 137.5, 137.4, 137.3 (C_q), 129.2, 128.6, 128.4, 128.4, 128.4, 128.1, 128.1, 128.0 (CH_{arom}), 127.9 (CH_{arom} *i*-Nico), 97.6 (C-1), 76.8 (C-2), 75.8 (C-3), 75.7 (C-4), 74.7 (CH₂ Bn), 73.9 (CH₂ Bn), 72.7 (CH₂ Bn), 70.9 (C-5), 67.9 (C-6), 65.3 (q, *J* = 35.3 Hz, CH₂CF₃); ¹³C-GATED NMR (214 MHz, CDCl₃): δ 97.6 (*J*_{C1,H1} = 171.6 Hz, C-1 α); Diagnostic peaks β-anomer: ¹H NMR (850 MHz, CDCl₃, HH-COSY, HSQC, HMBC): δ 8.73 – 8.71 (m, 2H, CH_{arom} *i*-Nico), 7.62 – 7.60 (m, 2H, CH_{arom} *i*-Nico), 7.49 – 6.93 (m, 15H, CH_{arom}), 5.41 (t, *J* = 9.4 Hz, 1H, H-3), 4.62 (d, *J* = 7.5 Hz, 1H, H-1), 3.99 (dq, *J* = 12.1, 8.4 Hz, 1H, CHHCF₃), 3.74 (dd, *J* = 10.9, 2.0 Hz, 1H, H-6), 3.55 (ddd, *J* = 9.8, 3.7, 2.1 Hz, 1H, H-5), 3.49 (dd, *J* = 9.5, 7.6 Hz, 1H, H-2); ¹³C-APT NMR (214 MHz, CDCl₃, HSQC, HMBC): δ 164.1 (C=O *i*-Nico), 150.6 (CH_{arom} *i*-Nico), 137.6, 137.5, 137.4, 137.0 (C_q), 128.7, 128.6, 128.4, 128.2, 128.2, 128.1, 128.0, 127.9 (CH_{arom}), 127.9 (CH_{arom} *i*-Nico), 103.8 (C-1), 77.8 (C-2), 76.6 (C-4), 75.6 (C-3), 75.0 (C-5), 74.6 (CH₂ Bn), 73.8 (CH₂ Bn), 72.7 (CH₂ Bn), 68.1 (C-6), 66.3 (q, *J* = 35.0 Hz, CH₂CF₃); ¹³C-GATED NMR (214 MHz, CDCl₃): δ 103.8 (*J*_{C1,H1} = 162.6 Hz, C-1 β); HRMS: [M+H]⁺ calcd for C₃₅H₃₅F₃NO₇ 638.2360, found 638.2362.

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