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FULL PAPER

Unusually Stable Picoloyl-protected Trimethylsilyl Glycosides for Non-symmetrical 1,1′-Glycosylation and Synthesis of 1,1′-Disaccharides with Diverse Configurations

Yen-Chu Luke Lu, Bhaswati Ghosh, and Kwok-Kong Tony Mong*

Dedication to Professor Tin Yuen Luk on the occasion of his retirement from National University of Taiwan and 70th Birthday

Abstract: Non-symmetrical 1,1′-disaccharides and related derivatives constitute the structural components in various glycolipids and natural products. Some of these compounds have been shown to exhibit appealing biological properties. We report a direct yet stereoselective 1,1´-glycosylation strategy for the synthesis of non-symmetrical 1,1′-disaccharides with diverse configurations and sugar components. The strategy is based on the joined forces of a new class of configurationally stable glycoside acceptors and stereo-directing thioglycoside donors. The new glycoside acceptors feature a picoloyl (Pico) protecting group at the remote C4/C3 position that confers unusual stability on TMS glycosides in acidic conditions.

1,1′-Disaccharides are non-reducing glycosides linked at anomeric centres via two glycosidic bonds.[1-3] These disaccharides are found as the structural units in natural products such as tunicamycins,[4,5] trehalosamines,[6,7] everninomicins,[8,9] and avilamycins.[10,11] Trehalose glycolipids contain a 1α→1′α disaccharide core that is desymmetrized with fatty acids and, on some occassions, functionalized with a sulfate group.[12] Examples of these glycolipids include sulfolipids and trehalose dimycolates of *Mycobacterium tuberculosis*,[13–16] trehalose dicorynomycolates of *Corynebacterium sp*.,[17] and maradolipids of *Caenorhabditis elegans*.[18] The intriguing structure and biological relevance of the 1,1′-disaccharides and derivatives have attracted the interest of organic chemists to develop practical synthetic routes for these compounds.

Although non-symmetrical 1,1′-disaccharides can be constructed by desymmetrizing 1,1′-disaccharide substrates, this approach is limited by substrate availability.[19,20] Alternatively, these disaccharides can also be acquired by coupling of glycosyl donors with glycosyl acceptors via so called 1,1′-glycosylation.[2,21–23] However the 1,1′-glycosylation invokes two anomeric centres and may produce up to four diastereomers. Accordingly, it is far more challenging than ordinary glycosylation in term of stereocontrol and product purification.

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Conceptually, the stereocontrol in 1,1′-glycosylation can be accomplished by coupling of stereo-directing donors with stereo-directed or configurationally stable acceptors. Previous glycosylation studies mainly focused on stereocontrol of glycosyl donors,[24] whereas studies of glycosyl acceptor have received much less attention. Glycosyl 1,2-*O*-stannane acetals have been exolored as the stable acceptors for synthesis of non-symmetrical 1,1′-disaccharides, but the formation of trisaccharide byproduct was an issue.[22] Peracetyl protected trimethylsilyl (TMS) glycosides have also been used as acceptors for synthesis of monosaccharide 1,1′-acetals.[25–27] The modest stability of the glycosides severely limited the scope of application.[26–28]

Herein we report a general, yet stereoselective 1,1′-glycosylation strategy for non-symmetrical 1,1′-disaccharide synthesis. In our strategy, a new class of configurationally stable TMS glycoside acceptors are employed to react with stereo-directing thioglycosyl donors. These new glycoside acceptors feature a picoloyl (Pico) protecting group at the remote position to confer unusual stability on the acceptors in various glycosylation conditions. Based on the joined forces of the Pico stabilized acceptors and the stereo-directing donors, synthesis of non-symmetrical 1,1′-disaccharides with diverse configurations and sugar components is at our disposal. Further studies on the structure-selectivity relationship and NMR spectroscopy clarify the stabilization role and mechanism of the Pico-protecting group.

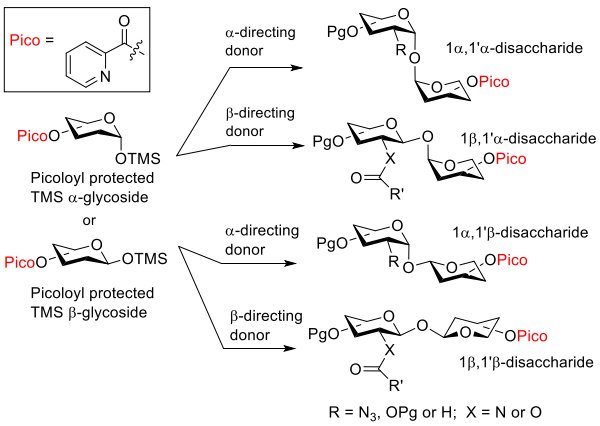

Figure 1. Features of New TMS Glycoside Acceptors and their Application to the Synthesis of 1,1′-Disaccharides with Diverse Configurations.

Results and Discussion

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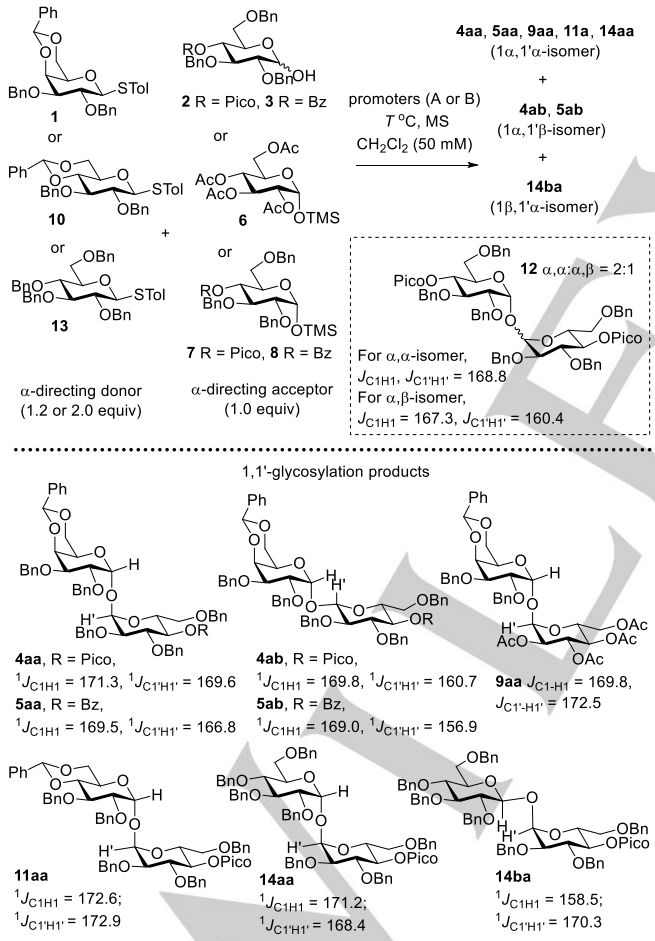
In the beginning, we tackled the synthesis of a 1α→1'α-disaccharide by glycosylation of 4-*O*-Pico glucosyl hemiacetal **2** with 4,6-*O*-benzylidene thiogalactoside **1**, *N*-iodosuccinimide (NIS) and trimethylsilyl triflate (TMSOTf) as promoters (Scheme 1) (Table 1, entry 1).[29] The reason for using thiogalactoside donor **1** is that it exhibited high α-selectivity in previous glycosylation.[30,31] Furthermore, the Pico-protecting group of the hemiacetal **2** was expected to fix the C1 hydroxyl at the α-configuration via intramolecular hydrogen bonding.[32,33] But experimentally, a 3:1 mixture of 1α→1'α diastereomer **4aa** and 1α→1'β diastereomer **4ab** was obtained with a yield of *ca* 73% yield. The donor **1** did exhibite excellent α-selectivity, but the α-selectivity for acceptor **2** was just marginal. Though the proposed hydrogen bonding association did not occur, a marked difference in polarity between the Pico-containing diastereomers **4aa** and **4ab** (from thin layer chromatography) was observed, and such a property facilitated the product purification. Interestingly, a similar polarity difference was not observed for the benzoyl (Bz) protected diastereomers **5aa** and**5ab**, which were produced by the glycosylation of 4-*O*-Bz glucosyl hemiacetal acceptor **3** with



Scheme 1. 1,1'-Glycosylation studies of glucosyl hemiacetals (**2**, **3**) and TMS glucosides (**6**, **7**, **8**).

Table 1. Studies on α-Directing Glycosyl Donors and α-Directing Glucoside Acceptors for 1,1′-Glycosylation.

Entry	Donor (equiv), acceptor	Promoter (equiv)[a]	*T* (°C), Time (h)	Product (%)	Ratio[b]
1	**1** (1.2), **2**	A (1.3)	0, 5	**4aa**, **4ab** (73)	2:1
2	**1** (1.2), **3**	A (1.3)	0, 6	**5aa**, **5ab** (70)	1:1
3	**1** (1.2), **6**	A (1.3)	0, 18	**9aa** only (35)	1:0[c]
4	**1** (1.2), **7**	A (1.3)	0, 18	**4aa** only (76)	1:0
5	**1** (1.2), **8**	A (1.3)	0, 6	**5aa**, **5ab** (70)	3:1
6	**10** (1.2), **7**	A (1.3)	25, 18	**11aa** only (10)	1:0
7	**10** (1.2), **7**	B (1.3)	0, 5	**11aa** only (30)	1:0
8	**10** (1.2), **7**	B (2.0)	0, 6	**11aa** only (35)	1:0[d]
9	**10** (1.2), **7**	B (1.3)	0, 18	no reaction	ND[e]
10	**10** (2.0), **7**	B (1.3)	0, 18	**11aa** only (65)	1:0
11	**1** (2.0), **7**	B (1.3)	-20, 7	**4aa** only (80)	1:0
12	**10** (1.2), **6**	B (1.3)	0, 18	complex mixture	ND
13	**13** (1.2), **7**	B (1.3)	0, 18	**14aa**,**14ba** (75)	3:1

[a] Promoter system A = NIS and TMSOTf. Promoter system B = Me_2S_2-Tf_2O. [b] Isomer ratio was determined by isolation or NMR spectroscopy. [c] Compound **9aa** was contaminated with an inseparable byproduct stemming from donor **1**. [d] Self-condensation of **7** occurred and the 1,1′-disaccharide **12** was obtained as a α/β mixture. [e] 1.3 Equiv. of DTBP (w.r.t to the acceptor) was added.

galactosyl donor **1** (Entry 2). Structural characterization of the 1,1′-disaccharides **4aa**, **4ab**, **5aa**, and **5ab** was accomplished by 1D and 2D NMR spectroscopy. Anomeric configuration of the diastereomers was determined by the $^1J_{C1H1}$ (or $^3J_{H1H2}$) coupling constant at the anomeric centre. For example, the $^1J_{C1H1}$ values at C1 and C1′ positions of the 1α→1'α diastereomer **4aa** were 171.3 and 169.6 Hz, respectively; while the corresponding $^1J_{C1H1}$ values for the 1α→1'β diastereomer **4ab** were 169.8 and 160.7 Hz, respectively. These $^1J_{C1H1}$ values agreed with the literature data.[34]

As the proposed hemiacetal acceptor **2** did not work, we examined the TMS glycoside acceptors. To this end, preparation of TMS glycoside with a high anomeric purity was required; therefore, various silylation protocols were evaluated (unpublished data).[35] Eventually, a α-selective silylation method, that based on modification of a known procedure, was developed.[36] Thus, hemiacetal **2**, **3**, or **6a** in CH_2Cl_2 (0.08 M) was treated with 2.0 equiv of TMSOTf at 0 °C, followed by the slow addition of 1.5 equiv of hexamethyldisilazane (HMDS) (Scheme 2a). Under these reaction conditions, the TMS α-glucosides **6**, **7**, and **8** were obtained with α:β ratios spanning from 4:1 to 8:1, and the desired α-anomers could be isolated by standard chromatography.[37] For preparation of Pico protected TMS β-glucoside **7′**, kinetically controlled conditions were applied. In this protocol, 1.0 equiv of hemiacetal **2** in THF was treated with 1.5

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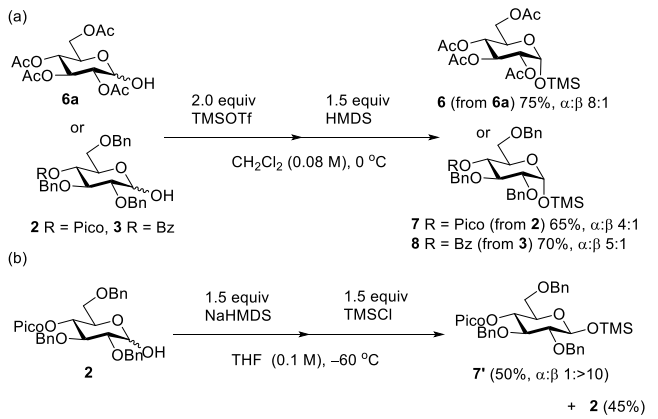
equiv of sodium bis(trimethylsilyl)amide (NaHDMS) at –60 °C, followed by slow addition of 1.5 equiv of trimethylchlorosilane (TMSCl). The reaction produced the desired TMS β-glucoside **7′** at a yield of 50% with excellent >10:1 α:β ratio. Although *ca* 45% of **2** remained, it could be recovered for silylation.[38]

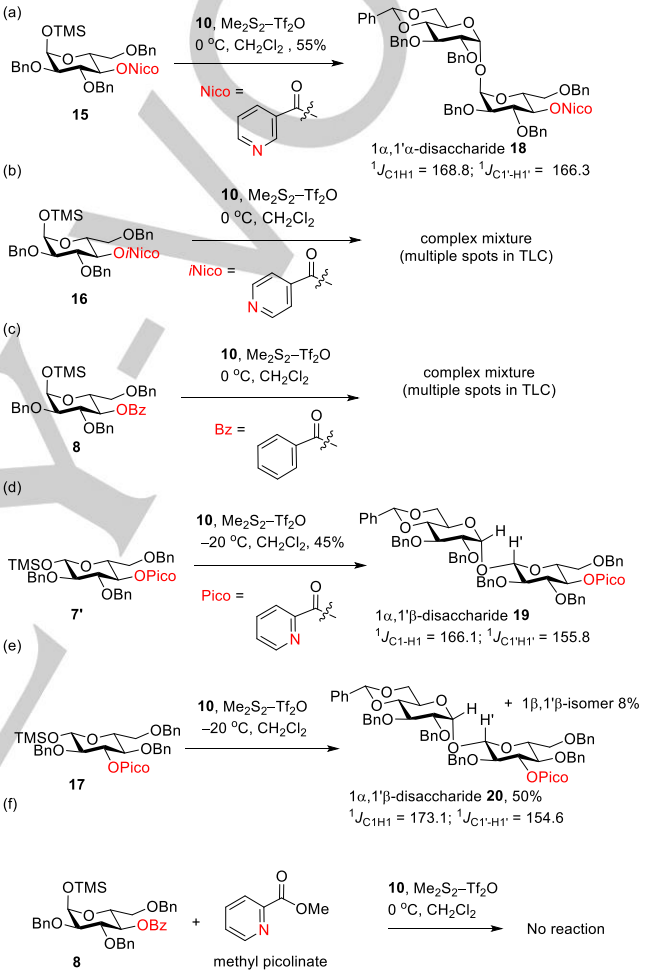


Scheme 2. (a) Preparation of TMS α-Glucosides **6**–**8**. (b) Preparation of TMS β-Glucosides **7′**.

After the preparation of TMS α-glucoside acceptors **6**–**8**, the 1,1′-glycosylation study was continued. Glycosylation of the peracetyl TMS α-glucoside acceptor **6** with the galactosyl donor **1** gave a poor yield of 1α→1′α-disaccharide **9aa** (Entry 3). In sharp contrast, the glycosylation of the Pico-protected TMS α-glucoside acceptor **7** with **1** produced the diastereomer **9aa** as a single isomer in a high 76% yield (Entry 4). The glycosylation of Bz-protected TMS α-glucoside acceptor **8** with **1** furnished a 3:1 mixture of 1α→1'α disaccharide **5aa** and 1α→1'β disaccharide **5ab** in 70% yield, indicating that anomerization of **8** occurred in glycosylation (Entry 5). In consideration of the yield and stereoselectivity, TMS α-glucoside **7** was the acceptor of choice for further studies.

Next, we investigated the glycosylation of the Pico-protected acceptor **7** with the 4,6-*O*-benzylidene thioglucoside donor **10**, which has previously been shown to be α-selective in glycosylation.[39] However, the glycosylation of **7** with **10** was sluggish in the presence of NIS and TMSOTf promoters (Entry 6). After 24 h reaction, the 1α→1′α disaccharide **11aa** was in a low yield (~10%) and some acceptor **7** still remained. The inferior result was likely attributed to the poor reactivity of the glucosyl donor (comparing with galactosyl donor **1**).[40] Accordingly, a sulfonium type promoter that generated in *situ* from dimethyl disulfide (Me_2S_2) and triflic anhydride (Tf_2O) was applied.[41] After optimization (Entries 7–10), the yield of 1α→1′α disaccharide **11aa** was improved to 65% by glycosylation of 1.0 equiv of the Pico-protected acceptor **7** with 2.0 equiv of the donor **10** in the presence of a limited amount (1.3 equiv) of the promoter (Entry 10). Of noted is that excessive amount of the promoter enhanced the self-condensation of **7** (Entry 8). Addition of di-*tert*butylmethyl pyridine (DTBP) as an acid scavenger completely halted the reaction, indicating that the glycosylation of the TMS glycoside acceptor requires an acidic condition.[25–28]

The optimized conditions also worked in glycosylation of the Pico-protected acceptor **7** with the galactosyl donor **1** (Entries 4 and 11), but was incompatible with peracetyl TMS α-glucoside acceptor **6** (Entry 12). To compare the stereo-directing effect of the benzylidene group of donor **10**, perbenzyl thioglucoside donor **13** was employed to react with the Pico protected TMS acceptor **7** (Entry 13). The reaction produced a 3:1 mixture of 1α→1′α and 1β→1′α disaccharides **14aa** and **14ba**, confirming the requirement for the cyclic acetal protection. Taken the results of Table 1 together suggest that the Pico-protected TMS acceptor and 4,6-*O*-benzylidene protected donor constitute the best donor–acceptor pair for the stereoselective 1,1′-glycosylation.



Scheme 3. Structure-selectivity Relationship Study for TMS Glycoside Acceptors **7'**, **8**, and **15**–**17**.

Although the Pico-protecting group has been regarded as a stereo-directing group in other glycosylation studies,[32,33,42] its role is clearly different in present study. To clarify the role of the Pico group, we conducted a structure–selectivity relationship study. For this purpose, various TMS glucosides with (i) a nicolinyl (Nico) (**15**), *iso*-nicolinyl (*i*Nico) (**16**), or Bz (**8**) protecting group at C4, (ii) a β-TMS acetal at C1 (i.e. **7′** and **17**), and (ii) with a Pico-protecting group at C3 (i.e. **17**) were prepared for glycosylation with the donor **10**. Preparation of the TMS α-/β-glycosides followed the protocols shown in Scheme 2.

Glycosylation of the Nico protected TMS α-acceptor **15** with the glucosyl donor **10** in the presence of Me_2S_2–Tf_2O promoter produced the 1α→1′α disaccharide **18** at a 55% yield, which is lower than the yield (~65%) given by the Pico protected acceptor **7** (Scheme 3a). In contrast, glycosylation of the *i*Nico protected (**16**) or Bz protected (**8**) acceptor gave a complex mixture; from which, no 1,1′-disaccharide products could be isolated, suggesting that both TMS α-acceptors **8** and **16** were inferior the acceptors **7** and **15** (Schemes 3b and 3c). Among the pyridine substituted carboxyl protecting groups, the Pico-protecting group confers the best stability on the TMS glycoside.[43]

Although TMS β-glycosides are generally considered to be more reactive than the α-glycosides, the formers are however less stable in acidic conditions.[27,28] Therefore, it was of interest to probe the stability of the Pico protected TMS β-glycoside under the 1,1′-glycsoylation conditions. To this end, 4-*O*-Pico TMS β-glucoside **7′** was prepared for glycosylation with glucosyl donor **10** (Scheme 3d). The glycosylation was conducted at –20 °C to furnish the expected 1α→1′β-disaccharide **19** as the sole isomer. The Pico-protecting group could also be placed at the C3 position as shown by glycosylation of the 3-*O*-Pico TMS β-glucoside **17** (Scheme 3e).

One may raise a question whether the Pico-protecting group can be replaced with a structural mimic. This question was clarified by glycosylation of the Bz protected TMS α-acceptor **8** with donor **10** in the presence of methyl picolinate (Scheme 3f). Under such conditions, no glycosylation occurred and majority of the acceptor **8** remained after 24 h reaction. The result is similar to that given by the addition of DTBP (Table 1, entry 9).

The preceding experiments suggest that the Pico-protecting group is not merely an acid scavenger. Rather, its presence in the TMS glycoside acceptor imparts unusual stability during glycosylation. To compare the stabilization capacities of standard acyl and Pico protecting groups, the solutions of 4-*O*-Pico (**7**) and 4-*O*-Bz (**8**) protected TMS α-glucosides in $CDCl_3$ were treated with 0.5 equiv of TMSOTf at RT. ^{1}H NMR spectroscopy was performed to monitor the structural change of the TMS glucoside.

Immediately after the addition of TMSOTf, the ^{1}H NMR spectra of the 4-*O*-Bz TMS α-glucoside **8** changed dramatically. Signals corresponding to the anomeric and TMS protons (δ = 5.19 and 0.20 ppm) disappeared, indicating that the acceptor **8** was unstable in the presence of the acid (see NMR spectra in pp 65 of SI).

In marked contrast, the ^{1}H NMR spectra of the 4-*O*-Pico TMS α-glucoside **7** remained largely unchanged in the presence of TMSOTf as shown by the NMR spectra in Figure 2a and 2b.[44] A closer examination revealed the peak broadening and downfield shift (0.10 to 0.40 ppm) of ^{1}H signals from the pyridine substituent (H_b, H_c, and H_d) (Figure 2b). A similar NMR pattern has been observed for pyridine treated with trimethylsilyl perchlorate (Me_3SiClO_4).[45] The aforementioned NMR spectrum indicates an association between TMSOTf and the pyridine nitrogen of the Pico group.

Based on the structure–selectivity relationship studies, we proposed the stabilization mechanism of the Pico protecting group (Figure 3). Here, glycosylation of the TMS glycoside acceptor produced the acid by-product TMSOTf, which was trapped by the pyridine substituent of the Pico to form a picolinium moiety. The strong electron-withdrawing property of the picolinium substituent rendered the anomerization (path a) and/or self-condensation (path b) of the TMS glycoside difficult.

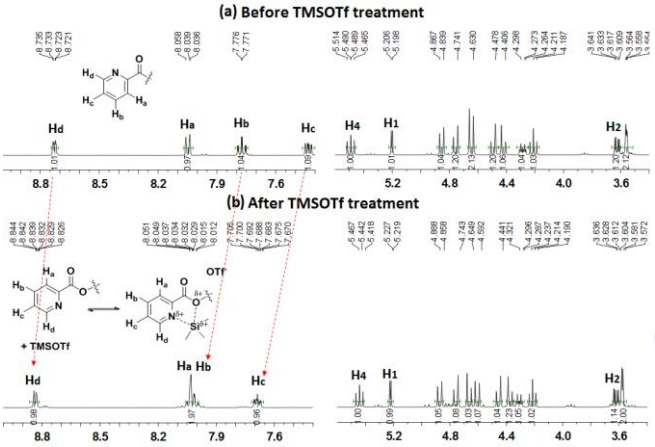


Figure 2. NMR Spectrum of the Pico-protected TMS α-Glucoside **7** (a) Before and (b) 24 h After Treatment with TMSOTf.

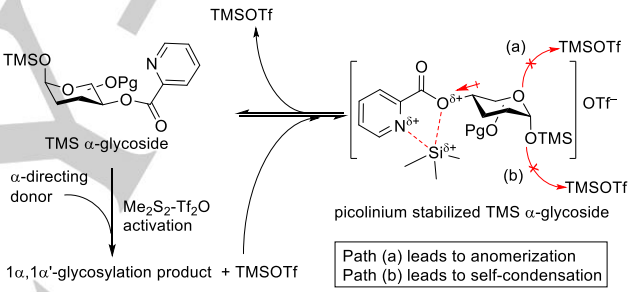


Figure 3. Proposed Mechanism of the Stabilization Given by Pico-Protecting Group.

After elucidating the role of the Pico protecting group, we explored the substrate scope of the 1,1′-glycosylation method. At start, various non-symmetrical 1α→1′α-disaccharides were synthesized from substrates with different protecting groups and sugar scaffolds (Schemes 4 and 5). Thus, 6-*O*-*tert*-butyldiphenylsilyl (TBDP)-protected TMS α-acceptor **21** and 2-*O*-naphthylmethyl (Nap)-protected TMS α-acceptor **22** were glycosylated with thioglucoside donor **10** and 4,6-*O*-naphthylidene (Naph)-protected thiogalactoside donor **23**, respectively (Scheme 4). The reactions furnished the 1α→1′α-disaccharides **29** and **30** as the single isomers at 60% and 76% yields. Excellent stereocontrol was also observed for the glycosylation of TMS α-acceptor **7** with thiorhamnosyl donor **24**. Similar to the donors **1**, **10**, and **23**, the donor **24** has a conformational restrained protecting group at C2 and C3 positions.

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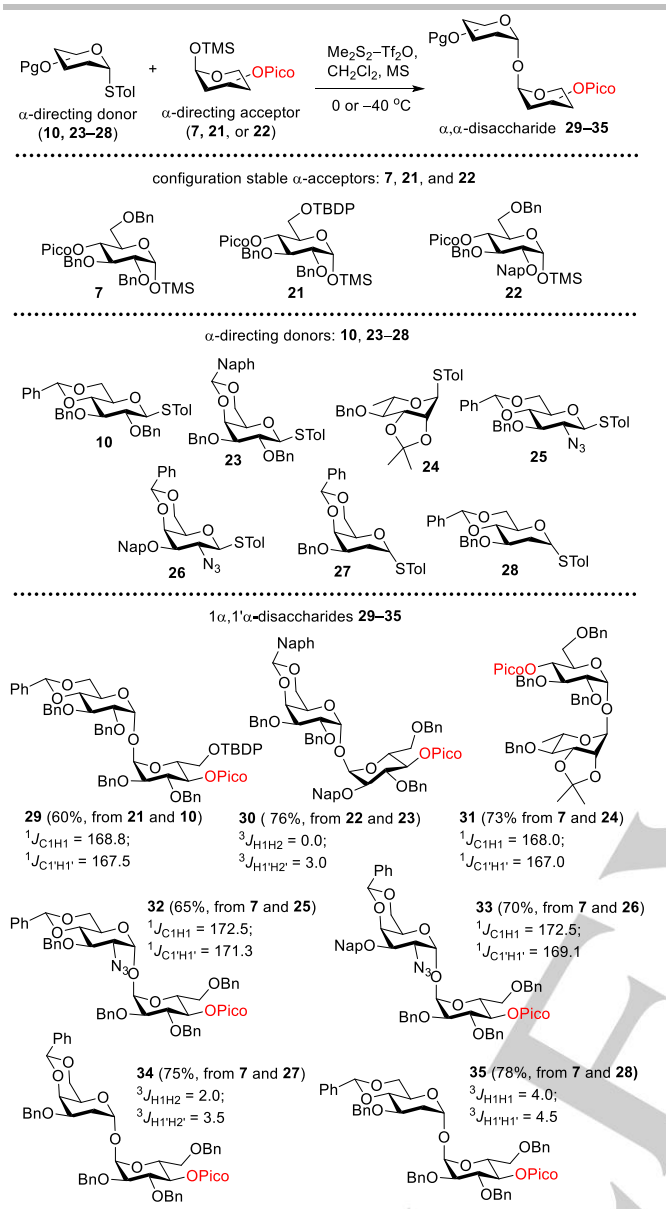
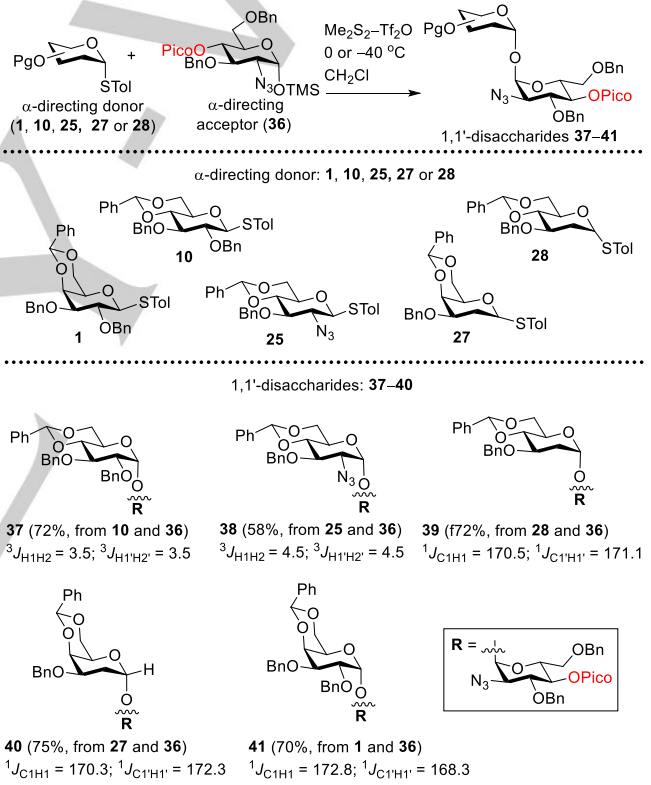


Scheme 4. Synthesis of Non-symmetrical 1α→1′α-Disaccharides **29**-**35** from Thioglycoside Donors **10** and **23–28**, and Pico-protected TMS α-Glucoside Acceptors **7**, **21**, and **22**.

The applicability of the 1,1-glycosylation method to 2-azido-2-deoxythioglycoside donors is of interest because 2-azido-2-deoxythioglycosides are used as the precursors for synthesis of 2-acetamido- or 2-amino-2-deoxy-glycosides, which are present in some natural 1,1′-disaccharide compounds. Therefore, we studied the glycosylation of TMS α-glucoside acceptor **7** with 2-azido-2-deoxythioglucoside **25** and 2-azido-2-deoxythiogalactoside **26**. The glycosylations proceeded at 0 °C and desired 1α→1′α-disaccharides **32** and **33** were obtained at 65% and 70% yields, respectively, with a perfect stereoselectivity. Different from the glycosylation with thioglycoside donors **10**, **23**, and **24**, the glycosylation with the 2-azido-2-deoxy donors requires a higher stoichiometric amount (1.8 equiv) of Me_2S_2–Tf_2O promoter. The requirement of additional promoter may be due to the less reactive nature of the 2-azido-2-deoxy donors. In addition to the 2-azido-2-deoxythioglycoside donors, the Pico-protected TMS α-glucoside acceptor **7** could react with the 2-deoxythioglycoside donors such as **27** and **28**, though a lower reaction temperature (–40 °C) was needed to avoid the glycal formation.

The utility of the Pico-protecting group is not limited to the TMS α-glucosides **7**, **21**, and **22**, but it is also applicable to the TMS 2-azido-2-deoxy-α-glucoside acceptor **36**. For example, glycosylation of the TMS 2-azido α-acceptor **36** with the thioglucoside **10**, 2-azido-2-deoxythioglucoside **25**, and 2-deoxythioglucoside **28** furnished the 1α→1′α disaccharides **37**, **38**, and **39**, respectively, at yields of 58–72% (Scheme 5). In addition to D-*gluco* donors **10**, **25**, and **28**, the TMS 2-azido-2-deoxy α-acceptor **36** could be coupled with the 2-deoxy-thiogalactoside donor **27** and thiogalactoside donor **1** to produce the 1α→1′α disaccharides **40** and **41**, respectively, at yields of 70–75% with perfect stereocontrol.



Scheme 5. Synthesis of 1α→1′α-Disaccharides **37**–**41** from Thioglycoside Donors **1**, **10**, **25**, **27**, and **28** and TMS 2-Azido-2-Deoxy-α-Glucoside Acceptor **36**.

After demonstrating the application of the Pico-protected TMS glycosides for the synthesis of 1α→1′α-disaccharides, we attempted the 1β→1′α-disaccharide synthesis. Notably, these disaccharides are found in natural products such as 3,3′-diamino-3,3′-dideoxy-β,α-trehalose[46] and tunicamycins.[5] The synthesis of 1β→1′α-disaccharide requires the joined forces of a β-directing glycosyl donor and a Pico protected α-glycoside acceptor. Regarding the β-directing donor, we applied the concept of neighbouring group participation (NGP).[47]

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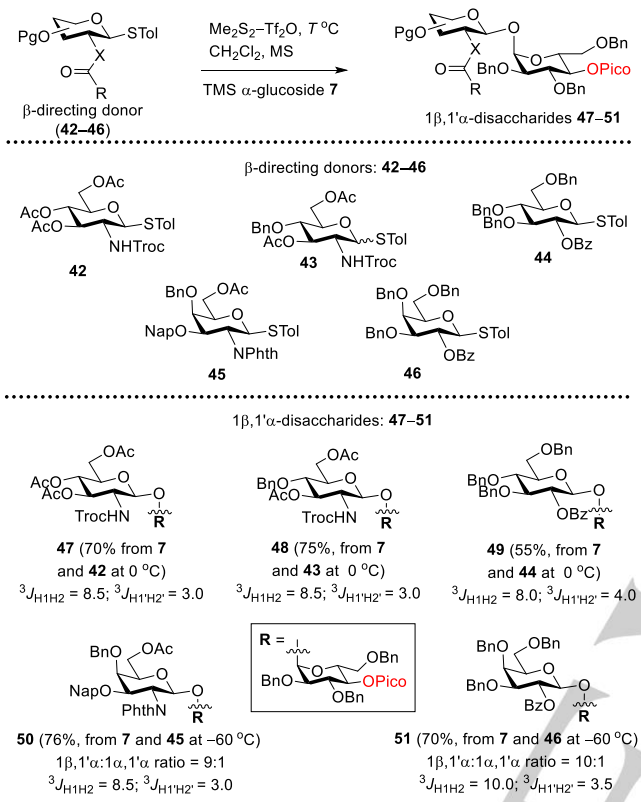
Accordingly, various participating donors such as *N*-trichloroethoxycarbonyl (Troc) protected thioglucosamines **42**, **43**, 2-*O*-Bz protected thioglucoside **44**, 2-*O*-Bz protected thiogalactoside **45**, and *N*-phthalimido (Phth) protected thiogalactosamine **46** were prepared for glycosylation with the Pico-protected TMS acceptor **7** (Scheme 6).



Scheme 6. Synthesis of 1β→1′α-Disaccharides **47**–**51** from 1,2-*trans* β-Directing Thioglycoside Donors **42**–**46**.

Glycosylations of TMS α-glucoside acceptor **7** with thioglucosamines **42** and **43** and thioglucoside **44** were performed at 0 °C using Me_2S_2–Tf_2O as the promoter. The reactions furnished respective 1β→1′α-disaccharides **47, 48**, and **49** as the single isomers at 55–70% yields. The β- and α-anomeric configurations of the 1β→1′α disaccharides **47–49** were unambiguously confirmed by the $^3J_{H1H2}$ values at respective anomeric centers (8.0–8.5 and 3.5–4.0 Hz).

Unlike the participated thioglycoside donors with a D-*gluco* scaffold (i.e. **42–44**), the glycosylation of Pico-protected α-glucoside acceptor **7** with 2-*N*-phthalamide (Phth)-2-deoxy-thiogalactosyl donor **45** at 0 °C produced a 2:1 mixture of 1β→1′α- and 1α→1′α-diastereomers **50**. The result might be due to the competition of the dioxalenium ion[48] and oxacarbenium ion[49] for coupling with the TMS α-acceptor **7**, although another possibility is the postglycosylation anomerization of the 1β→1′α- to 1α→1′α-anomer. For clarification, pure 1β→1′α-anomer of **50** in $CDCl_3$ was treated with 0.5 equiv of TMSOTf at 0 °C for 24 h to simulate the glycosylation conditions. From the proton NMR spectroscopy, no sight of anomerization of the 1β→1′α-anomer of **50** occurred, thus excludes the possibilty of anomerization (see SI).[50]

It is reasoned that the selectivity of glycosylation may be modified by adjusting the reaction temperature. Accordingly, the glycosylation of **7** with **45** was repeated at lower reaction temperature. To our delight, the desired 1β→1′α anomer of **50** was obtained in high selectivity at –60 °C. Similar reaction conditions worked fine for glycosylation of TMS α-acceptor **7** with 2-*O*-Bz protected thiogalactosyl donor **46** and the desired 1β→1′α-diastereomer of **51** was obtained at a 70% yield with 10:1 1β→1′α to 1α→1′α ratio.

Although the 1β→1′α-disaccharides **47**–**51** prepared in above studies contain 1,2-*trans* β-glycosidic bonds, some 1β→1′α-disaccharides may exist in a 1,2-*cis* β-configuration such as everninomicins[8,9,51] and avilamycins.[10,11] For curiosity, we also investigated the applicability of the Pico-protected TMS glycoside for coupling with the 1,2-*cis* β-directing mannosyl donor.[52]

As a proof of concept study, the Pico protected TMS α-acceptors **7** and **36** were glycosylated with the β-directing thiomannosyl donor **52** at 0 °C using 1.3 equiv of Me_2S_2–Tf_2O (Scheme 7a).[53] The glycosylation reactions produced the respective β-Man-(1→1′)-α-Glc disaccharide **53** and β-Man-(1→1′)-α-GlcN3 disaccharide **54** as the single isomers at 52% and 45% yields. The 1,2-*cis* β-anomeric configuration of the mannosides in **53** and **54** was confirmed by $^1J_{C1H1}$ value of ~154 Hz.

As encouraged by the results in above glycosylation studies, we challenged the synthesis of 1β→1′β-disaccharides using Pico-protected TMS β-glycoside acceptors and 1,2-*trans* β-directing glycosyl donors. To avoid the anomerization of the TMS β-acceptor, the reaction temperature was optimized. A point in case is the the glycosylation of TMS 4-*O*-Pico β-glucoside **7′** with *N*-Troc protected thioglucosamine donor **42**. If the reaction was performed at 0 °C in the presence of NIS and TMSOTf promoters, the 1β→1′β- and 1β→1′α diastereomers of **57** were obtained in a ratio of 7:1 (Scheme 7b).[54] When the reaction was conducted at –60 °C, the 1β→1′β-disaccharide **57** was produced as a single isomer and no 1β→1′α diastereomer was detected. Therefore, the 1β→1′α isomer of **57** was likely a consequence of the anomerization of **7′**. The β-configuration of the 1β→1′β-disaccharide **57** was confirmed by the $^3J_{H1\text{-}H2}$ values of 7.5 and 8.5 Hz. The optimized reaction temperature for glycosylation of 2-*O*-Ac and 2-*O*-Bz protected thioglucoside donors **55** and **56** with Pico-protected β-glucoside acceptor **7′** was –50 °C. Under these conditions, the respective 1β→1′β-disaccharides **58** and **59** was furnished at 64–72% yields with excellent stereoselectivity.

Conclusions

A general yet stereoselective 1,1′-glycosylation strategy has been developed for the synthesis of non-symmetrical 1,1′-disaccharides with diverse anomeric configurations and sugar components. The strategy features the joined forces of the Pico stabilized TMS glycoside acceptors and stereo-directing thioglycoside donors. The unusual stability of the silyl glycoside acceptor was confirmed by a structure-selectivity relationship studies and NMR spectroscopic analysis in acidic conditions.

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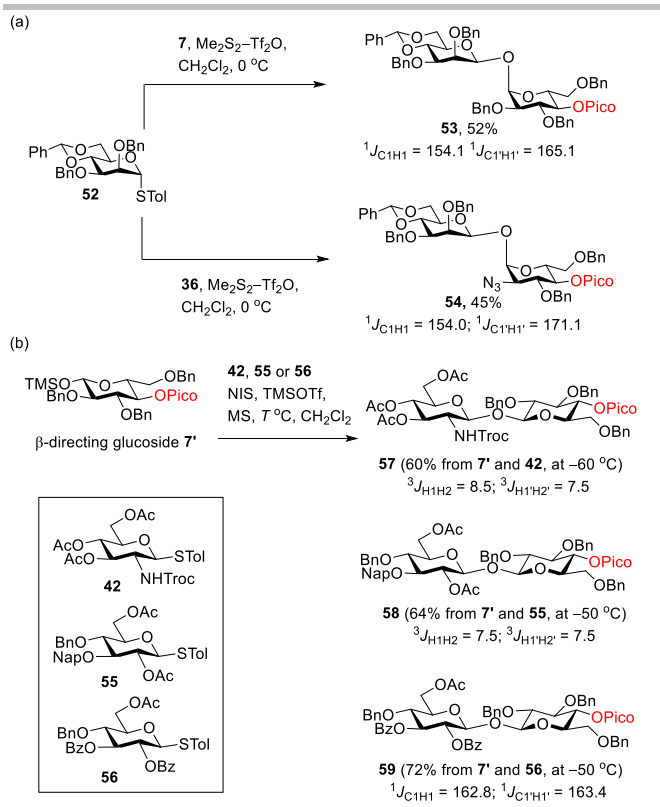

Scheme 7. (a) Synthesis of 1β→1′α Disaccharides **53** and **54** with a 1,2-*cis* β-Mannosidic Bond. (b) Synthesis of 1β→1′β Disaccharides **57**–**59**.

Experimental Section

General protocol A with NIS and TMSOTf promoter (conventional procedure) (Table 1, entries 1-6): To a solution of thiogalactosyl donor **1** (260 mg, 0.468 mmol), 4-*O*-Pico protected glucosyl hemiacetal **2** (or 4-*O*-Bz protected glucosyl hemiacetal **3**) (200 mg, 0.36 mmol) and freshly activated 4Å MS (1.0 g) in CH_2Cl_2 (10 mL) were added and the mixture was stirred at 0 °C for 30 min under N_2. Then, NIS (106 mg, 0.468 mmol) and TMSOTf (84 µL, 0.468 mmol) were added and the resulting mixture was stirred at 0 °C until the end of the reaction. Progress of the reaction was checked by TLC examination. After the completion of the glycosylation, $Na_2S_2O_{3(s)}$ and satd. $NaHCO_3$ were added, and the mixture was stirred at RT for ca 10 min. Then the mixture was filtered over celite and the filtrate was diluted with CH_2Cl_2. The resulting CH_2Cl_2 solution was then washed with H_2O and brine, followed by drying over $MgSO_4$. After removal of the $MgSO_4$ by filtration, the filtrate was concentrated for flash chromatography to obtain the desired product (Elution for **4aa** and **4ab**: EtOAc/hexanes, 1/2; elution for **5aa** and **5ab**: EtOAc/hexanes, 1/4).

General protocol B with Me_2S_2-Tf_2O promoters (Table 1 entries 7-13, Schemes 1 to 7): To a solution of thioglycosyl donor (2.0 equiv) in CH_2Cl_2, TMS glycoside acceptor (1.0 equiv) and activated 4Å MS (10 wt% of the solvent) were added (final concentration of the acceptor was 50 MM). The mixture was then stirred at RT for *ca.* 1 h and then at 0 °C or at optimized temperature (refer to SI for specific temperature) for additional 15 min. In another round bottom flask, dimethyldisulfide (Me_2S_2) (1.3-1.8 equiv) in CH_2Cl_2 was treated with triflic anhydride (Tf_2O) (1.3-1.8 equiv). After mixing for 30 min at 0 °C, the Me_2S_2–Tf_2O solution was transferred slowly to the donor and acceptor mixture. The resulting mixture was stirred at 0 °C or at optimized temperature until the glycosylation was complete. Then the reaction was diluted with CH_2Cl_2 followed by quenching with Et_3N (1.0 equiv). MS was removed by filtration to give the crude reaction mixture, which was concentrated for flash chromatography to obtain the 1,1′-disaccharide. Scheme 7b used the same procedures except that the NIS/TMSOTf promoters were used.

Preparation of TMS 2,3,6-tri-*O*-benzyl-4-*O*-picoloyl-1-α-D-glucopyranoside (7): To a solution of glucosyl hemiacetal **2** (500 mg, 0.90 mmol) (other hemiacetals followed the same protocol) in CH_2Cl_2 (0.08 M), TMSOTf (1.8 mmol) was added at 0 °C under N_2 and the mixture was stirred at 0 °C for 10 min. Then, HMDS (1.35 mmol) of CH_2Cl_2 (2 ml) solution was slowly added and the reaction mixture was stirred at 0 °C till completion of the silylation. Workup: the solution was diluted with CH_2Cl_2 (25 mL), to which, satd. $NaHCO_3$ (20 mL) was added. The organic phase was separated by separatory funnel, and followed by washed with brine (20 mL × 2), dried over $MgSO_4$, and concentrated for flash chromatography (Elution: EtOAc/hexanes, 1/3). The desired TMS α-glucoside **7** (570 mg, 76%) was obtained after chromatography. To facilitate the purification (or if needed), the β-anomer could be selectively hydrolyzed to the hemiacetal **2** by washed with diluted HCl (0.5 M × 2). For TMS α-glucoside **7**, R_f 0.38 (hexanes/EtOAc, 3/1); $[\alpha]_D^{20}$ +12.7 (*c* = 9.0, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.70 (d, *J* = 4.4 Hz, 1H), 8.59 (bs, 1H), 8.02 (d, *J* = 7.6 Hz, 1H), 7.74 (dt, *J* = 1.6, 7.6 Hz, 1H), 7.61 (t, *J* = 6.4 Hz, 1H), 7.41 (dd, *J* = 4.8, 6.4 Hz, 1H), 7.34 – 7.22 (m, 7H), 7.17 – 7.03 (m, 6H), 5.49 (t, *J* = 10.0 Hz, 1H, H-4), 5.20 (d, *J* = 3.2 Hz, 1H, H-1), 4.84 (d, *J* = 11.2 Hz, 1H), 4.74 (d, *J* = 11.2 Hz, 1H), 4.83 (d, *J* = 1.2, 11.2 Hz, 2H), 4.48 (d, *J* = 12.0 Hz, 1H), 4.40 (d, *J* = 12.0 Hz, 1H), 4.28 (dt, 3.6, 10.0 Hz, 1H), 4.21 (t, *J* = 9.6 Hz, 1H), 3.61 (dd, *J* = 2.4, 9.2 Hz, 1H), 3.56 – 3.55 (m, 1H), 0.19 (s, 9H, $SiCH_3$ × 3); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 164.1 (C=O), 149.7, 147.8, 138.5, 137.2, 137.8, 136.9, 135.9, 128.4, 128.1, 128.0, 127.96, 127.7, 127.3, 127.2, 126.9, 125.6, 91.9 (C-1), 80.6, 78.9, 75.2, 73.5, 73.1, 72.0, 68.8, 68.4, 0.06 ($SiCH_3$); HRMS–ESI (*m*/*z*): [M + H]$^+$ calcd for $C_{36}H_{40}NO_7Si$, 628.2725; found, 628.2734.

Preparation of TMS 2,3,6-tri-*O*-benzyl-4-*O*-picoloyl-1-β-D-glucopyranoside (7′): To prepare β-anomer TMS glycoside **7** (method B), NaHMDS (0.32 mmol) was added to the glucosyl hemiacetal **2** (120 mg, 0.215 mmol) in THF (0.1 M) under N_2 and the mixture was stirred at –60 °C for 20 min. Then TMSCl (0.323 mmol) was slowly added to the mixture at –60 °C. Workup: The solution was diluted with CH_2Cl_2 (25 mL), followed by quenching with NH_4Cl (30 ml) dried over $MgSO_4$, and concentrated for flash chromatography (Elution: EtOAc/hexanes, 1/3) to furnish the desired TMS β-glucoside **7′** (67 mg, 50%). For **7′**, R_f 0.35 (hexanes/EtOAc, 3/1); $[\alpha]_D^{20}$ –11.2 (*c* = 7.5, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.73 (dd, *J* = 1.0, 4.0 Hz, 1H, ArH), 7.97 (d, *J* = 8.0 Hz, 1H, ArH), 7.77 (dt, *J* = 2.0, 8.0 Hz, 1H), 7.45 (dd, *J* = 1.2, 4.8 Hz, 1H, ArH), 7.37 – 7.16 (m, 10H, ArH), 7.10 – 7.05 (m, 5H, ArH), 5.34 (t, *J* = 9.6 Hz, 1H, H-4), 4.94 (d, *J* = 11.2 Hz, 1H), 4.81 – 4.73 (m, 3H including H-1), 4.64 (d, *J* = 11.2 Hz, 1H), 4.48 (s, 2H), 3.87 – 3.83 (m, 2H),), 3.63 (d, *J* = 4.8 Hz, 2H), 3.52 (dd, *J* = 1.2, 9.2 Hz, 1H), 0.24 (s, 9H, $SiCH_3$ × 3); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 164.1 (C=O), 149.8, 147.6, 138.4, 138.2, 138.0, 136.9, 128.3, 128.14, 128.11, 128.0, 127.9, 127.7, 127.5, 127.3, 126.9, 125.5, 97.9 (C-1), 83.8, 81.6, 75.2, 74.9, 73.5, 73.2, 72.5, 69.8, 0.02 ($SiCH_3$); HRMS–ESI (*m*/*z*): [M + Na]$^+$ calcd for $C_{36}H_{41}NNaO_7Si$, 650.2545; found, 650.2544.

2,3-Di-*O*-benzyl-4,6-*O*-benzylidene-α-D-galactopyranosyl-(1→1′)-2′,3′,6′-tri-*O*-benzyl-4′-*O*-picoloyl-α-D-glucopyranoside 4aa: R_f 0.38 (Hexanes/EtOAc 2:1); $[\alpha]_D^{20}$ +94.0 (*c* = 1.50, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$): δ= 8.79 (d, *J* = 4.5 Hz, 1H), 8.05 – 7.96 (m, 1H), 7.81 (t, *J* = 7.7 Hz, 1H), 7.61 – 7.08 (m, 32H), 5.59 (t, *J* = 9.8 Hz, 1H, H-4′), 5.46 (s, 1H, benzylidene-H), 5.37 (s, 1H, H-1), 5.31 (d, *J* = 2.8 Hz, 1H, H-1′), 4.95 – 4.70 (m, 7H), 4.64 (d, *J* = 12.0 Hz, 1H), 4.51 (d, *J* = 13.2 Hz, 1H, H-5′), 4.48 (d, *J* = 12.4 Hz, 1H), 4.40 (d, *J* = 12.4 Hz, 1H), 4.24 (broad s, 1H, H-3), 4.22 (t, *J* = 9.6 Hz, 1H, H-3′), 4.15 (broad s, 2H including H-2 and H-4), 4.04 (d, *J* = 12.4 Hz, 1H, H-6a), 3.99 (s, 1H, H-5′), 3.78 (dd, *J* = 2.0, 11.2 Hz, 1H, H-2′), 3.43 (d, *J* = 10.8 Hz, 1H, H-6a′), 3.36 (dd, *J* = 2.9, 10.8 Hz, 1H, H-6b′); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 164.0 (C=O), 149.78, 147.79, 138.8, 138.6, 138.4, 138.0, 137.9, 137.7, 136.9, 129.8, 128.9, 128.5, 128.4,

128.18, 128.17, 128.14, 127.97, 127.94, 127.8, 127.7, 127.6, 127.5, 127.42, 127.40, 127.37, 126.9, 126.3, 125.5, 101.0 (benzylidene-*C*), 95.9 (C-1, $^1J_{CH}$ 171.3 Hz), 94.4 (C-1′, $^1J_{CH}$ 169.6 Hz), 79.7 (C-2′), 79.5 (C-3′), 76.0, 75.3, 75.1, 74.3, 73.61, 73.54, 73.50, 71.8 (C-4′), 71.7, 69.2 (C-6), 69.1 (C-5′), 68.1 (C-6′), 63.1 (C-5); HRMS–ESI (*m*/*z*): [M + H]$^+$ calcd for $C_{60}H_{59}NO_{12}$, 986.4110; found, 986.4113.

2,3-Di-*O*-benzyl-4,6-*O*-benzylidene-α-D-galactopyranosyl-(1→1′)-2′,3′,6′-tri-*O*-benzyl-4′-*O*-benzoyl-α-D-glucopyranosides 5aa: R_f 0.40 (Hexanes/EtOAc, 4/1); ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.95 (d, *J* = 7.8 Hz, 2.0H, ArH), 7.60 (dt, *J* = 1.0, 7.5 Hz, 1H, ArH), 7.51 (dd, *J* = 2.0, 9.5 Hz, 2H, ArH), 7.47 –7.43 (m, 4H, ArH), 7.36 – 7.13 (m, 26H, ArH), 5.45 (s, 1H, benzylidene-H), 5.44 (t, *J* = 10.0 Hz, 1H, H-4′), 5.38 (d, *J* = 3.6 Hz, 1H, H-1), 5.25 (d, *J* = 3.6 Hz, 1H, H-1′), 4.84 – 4.82 (m, 3H), 4.78 (d, *J* = 11.0 Hz, 1H), 4.77 (d, *J* = 11.5 Hz, 1H), 4.61 (d, *J* = 11.0 Hz, 1H), 4.60 (d, *J* = 11.5 Hz, 1H), 4.43 (d, *J* = 12.0 Hz, 1H), 4.35 (m, 2H including H-5′), 4.23 (d, *J* = 2.0 Hz, 1H), 4.14 (dd, *J* = 3.0, 10.0 Hz, 2H), 4.05 (dd, *J* = 1.8, 10.0 Hz, 1H, H-3), 4.03 (t, *J* = 9.5 Hz, 1H, H-3′), 3.93 (bs, 1H, H-4), 3.74 (dd, *J* = 1.5, 10.0 Hz, 1H), 3.72 (dd, *J* = 1.5, 10.0 Hz, 1H, H-2′), 3.33 (dd, *J* = 2.0, 9.0 H, 1H, H-6a′), 3.23 (dd, *J* = 4.0, 11.0 Hz, 1H, H-6b′); ^{13}C NMR (125 MHz, $CDCl_3$): *δ* = 165.1 (C=O), 138.64, 138.55, 138.2, 138.0, 137.7, 133.0, 130.0, 129.8, 128.9, 128.5, 128.4, 128.30, 128.28, 128.2, 128.14, 128.10, 128.0, 127.9, 127.82, 127.78, 127.73, 127.67, 127.61, 127.59, 127.2, 127.45, 127.42, 127.38, 127.37, 126.3, 101.1 (benzylidene-*C*), 95.0 (C-1, $^1J_{CH}$ 169.5 Hz), 93.8 (C-1′, $^1J_{CH}$ 166.8 Hz), 79.6 (C-2′), 79.4 (C-3′), 75.6, 75.15, 75.10, 74.2, 73.6, 73.5, 73.4, 71.3, 70.6 (C-4′), 69.3, 69.2, 68.0 (C-6′), 63.0 (C-4); HRMS–ESI (*m*/*z*): [M + Na]$^+$ calcd for $C_{61}H_{60}NaO_{12}^+$, 1007.3977; found, 1007.3981.

2,3-Di-*O*-benzyl-4,6-*O*-benzylidene-α-D-galactopyranosyl-(1→1′)-2′,3′,4′,6′-tetra-*O*-acetyl-4′-α-D-glucopyranoside (9aa): R_f 0.12 (Hexanes/EtOAc 2:1); ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.55 – 7.15 (m, 15H), 5.52 – 5.45 (m, 2H), 5.27 (d, *J* = 3.5 Hz, 1H), 5.25 (d, *J* = 2.5 Hz, 1H), 5.08 (t, *J* = 10.0 Hz, 1H), 5.00 (dd, *J* = 4.0, 10.5 Hz, 1H), 4.89 (d, *J* = 11.5 Hz, 1H), 4.82 (q, *J* = 8.5 Hz, 2H), 4.78 – 4.70 (m, 1H), 4.62 (d, *J* = 11.5 Hz, 1H), 4.54 (d, *J* = 11.5 Hz, 1H), 4.35 (dt, *J* = 2.5, 10.5 Hz, 1H), 4.27 (s, 1H), 4.21 – 4.09 (m, 4H), 4.03 – 3.90 (m, 3H), 3.75 (s, 1H), 3.69 (dd, *J* = 2.0, 12.5 Hz, 1H), 2.03 (s, 3H), 2.02 (s, 3H), 2.01 (s, 3H), 1.99 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): δ = 170.5, 170.2, 169.4, 169.3, 138.7, 138.4, 138.2, 138.0, 137.8, 137.5, 128.9, 128.8, 128.3, 128.26, 128.2, 128.1, 128.09, 127.8, 127.7, 127.65, 127.6, 127.55, 126.3, 126.2, 101.0, 96.1, 93.3, 76.2, 74.6, 74.4, 74.1, 74.0, 73.9, 72.1, 71.7, 70.4, 70.3, 69.5, 69.0, 68.5, 67.9, 67.4, 63.6, 61.1, 20.7, 20.6, 20.57, 20.5; HRMS–ESI (*m*/*z*): [M + Na]$^+$ calcd for $C_{41}H_{46}NaO_{15}^+$, 801.2729; found, 801.2738. **9aa** was contaminated with an unidentified side-product (*ca* 30%) and therefore no [α]$_D$ was given for **9aa**.

2,3-Di-*O*-benzyl-4,6-*O*-benzylidene-α-D-glucopyranosyl-(1→1′)-2′,3′,6′-tri-*O*-benzyl-4′-*O*-picoloyl-α-D-glucopyranoside (11aa): R_f 0.3 (Hexanes/EtOAc 3:1); $[\alpha]_D^{20}$ +25.6 (*c* = 0.16, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$): δ = 8.78 (m, 1H), 7.94 (d, *J* = 7.5 Hz, 1H), 7.79 (td, *J* = 1.5, 7.5 Hz, 1H), 7.54 – 7.05 (m, 31H), 5.56 (s, 1H, benzylidene-H), 5.48 (t, *J* = 10.0 Hz, 1H, H-4′), 5.21 (d, *J* = 3.5 Hz, 1H, H-1′), 5.20 (d, *J* = 3.5 Hz, 1H, H-1), 5.01 (d, *J* = 11.0 Hz, 1H), 4.92 (d, *J* = 11.0 Hz, 1H), 4.86 (d, *J* = 11.0 Hz, 1H), 4.77 (dd, *J* = 6.5, 12.0 Hz, 1H), 4.71 (dd, *J* = 6.5, 12.0 Hz, 1H), 4.69 (d, *J* = 11.5 Hz, 1H), 4.48 – 4.46 (m, 1H, H-5′), 4.43 (d, *J* = 12.5 Hz, 1H), 4.39 (d, *J* = 11.5 Hz, 1H), 4.29 (dt, *J* = 5.0, 10.0 Hz, 1H), 4.22 (t, *J* = 9.5 Hz, 1H, H-3′), 4.17 (t, *J* = 9.0 Hz, 1H, H-3), 4.13 (dd, *J* = 4.0, 10.0 Hz, 1H), 3.73 (dd, *J* = 4.0, 9.0 Hz, 1H, H-2′), 3.70 – 3.63 (m, 2H), 3.61 (dd, *J* = 4.0, 9.5 Hz, 1H, H-2), 3.43 (dd, *J* = 3.0, 11.0 Hz, 1H, H-6a′), 3.37 (dd, *J* = 3.0, 11.0 Hz, 1H, H-6b′); ^{13}C NMR (125 MHz, $CDCl_3$): δ = 164.0 (C=O), 149.8, 147.8, 138.9, 138.3, 138.1, 137.9, 137.7, 137.5, 136.8, 128.9, 128.5, 128.3, 128.2, 128.16, 128.1, 128.06, 128.0, 127.9, 127.8, 127.7, 127.54, 127.5, 127.4, 127.3, 126.9, 126.1, 125.5, 101.2 (benzylidene-C), 95.0 (C-1, J_{CH} = 172.6 Hz), 94.4 (C-1′, J_{CH} = 172.9 Hz), 82.4, 79.2 (C-3′), 79.0 (C-2′), 78.6 (C-3), 78.5 (C-2), 75.3, 75.26, 73.6, 73.5, 73.4, 71.8 (C-4′), 69.3 (C-5′), 69.0, 68.4 (C-6′), 62.9; HRMS–ESI (*m*/*z*): [M + Na]$^+$ calcd for $C_{60}H_{59}NNaO_{12}^+$, 1008.3929; found, 1008.3939.

2, 3, 4, 6-Tetra-*O*-benzyl-α-D-glucopyranosyl-(1→1′)-2′,3′,6′-tri-*O*-benzyl-4′-*O*-picoloyl-α-D-glucopyranoside 14aa: R_f 0.4 (Hexanes/EtOAc 2:1); $[\alpha]_D^{20}$ +35.4 (*c* = 1.30, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$): δ = 8.76 (d, *J* = 4.0 Hz, 1H), 7.95 (d, *J* = 8.0 Hz, 1H), 7.78 (td, *J* = 1.5, 8.0 Hz, 1H), 7.47 (qd, *J* = 1.5, 5.0 Hz, 1H), 7.42 – 7.04 (m, 35H), 5.47 (t, *J* = 10.0 Hz, 1H, H-4′), 5.27 (d, *J* = 3.5 Hz, 1H, H-1′), 5.25 (d, *J* = 4.0 Hz, 1H, H-1), 5.07 (d, *J* = 6.0 Hz, 1H), 4.92 (d, *J* = 6.6 Hz, 1H), 4.85 (d, *J* = 11.0 Hz, 1H), 4.82 (d, *J* = 10.5 Hz, 1H), 4.73 – 4.63 (m, 4H), 4, .55 (d, *J* = 12.0 Hz, 1H), 4.50 – 4.36 (m, 6H), 4.22 (t, *J* = 9.5 Hz, 1H, H-3′), 4.19 – 4.15 (m, 1H, H-5), 4.07 (t, *J* = 9.0 Hz, 1H, H-3), 3.73 – 3.67 (m, 2H, H-2′ and H-4), 3.60 (dd, *J* = 3.5, 9.5 Hz, 1H, H-2), 3.52 (dd, *J* = 3.5, 11.0 Hz, 1H, H-6a), 3.43 (dd, *J* = 3.0, 11.0 Hz, 1H, H-6a′), 3.41 – 3.37 (m, 2H, H-6b and H-6b′); ^{13}C NMR (125 MHz, $CDCl_3$): δ =164.0 (C=O), 149.7, 147.8, 139.0, 138.4, 138.35, 138.1, 138.0, 137.8, 137.7, 136.8, 128.5, 128.4, 128.35, 128.3, 128.2, 128.1, 128.08, 128.0, 128.0, 127.95, 127.9, 127.9, 127.87, 127.8, 127.77, 127.7, 127.65, 127.6, 127.59, 127.5, 127.48, 127.45, 127.3, 127.2, 127.2, 126.8, 125.5, 94.4 (C-1, J_{CH} = 171.2 Hz), 94.3 (C-1′, J_{CH} = 168.4 Hz), 81.8 (C-3), 79.13 (C-2), 79.12, 79.10 (C-3′), 77.7, 75.6, 75.3, 75.0, 73.6, 73.5, 73.1, 72.6, 71.9 (C-4′), 70.6 (C-5), 69.3, 68.5 (C-6′), 68.1 (C-6); HRMS–ESI (*m*/*z*): [M + Na]$^+$ calcd for $C_{67}H_{68}NNaO_{12}^+$, 1078.4736; found, 1078.4703.

2,3-Di-*O*-benzyl-4,6-*O*-benzylidene-α-D-glucopyranosyl-(1→1′)-2′,3′,6′-tri-*O*-benzyl-4′-*O*-nicoloyl-α-D-glucopyranoside (18): R_f 0.3 (Hexanes/EtOAc 3:1); $[\alpha]_D^{20}$ +53.3 (*c* = 0.30, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$): δ = 9.03 (br, 1H), 8.79 (br, 1H), 8.05 (d, *J* = 8.0 Hz, 1H), 7.53 – 7.07 (m, 31H), 5.59 (s, 1H, benzylidene-H), 5.36 (t, *J* = 10.0 Hz, 1H, H-4′), 5.23 (d, *J* = 3.5 Hz, 1H, H-1), 5.19 (d, *J* = 3.5 Hz, 1H, H-1′), 5.02 (d, *J* = 11.5 Hz, 1H), 4.90 (d, *J* = 11.5 Hz, 1H), 4.86 – 4.80 (m, 2H), 4.77 – 4.68 (m, 3H), 4.59 (d, *J* = 11.0 Hz, 1H), 4.42 (d, *J* = 12.0 Hz, 1H), 4.32 (d, *J* = 12.0 Hz, 1H), 4.29 – 4.25 (m, 2H including H-5 and H-5′), 4.20 – 4.17 (m, 2H including H-4 and H-6a), 4.07 (t, *J* = 9.0 Hz, 1H, H-3′), 3.73 – 3.71 (m, 2H including H-6b and H-2′), 3.69 (t, *J* = 9.5 Hz, 1H, H-3), 3.65 (dd, *J* = 4.0, 9.5 Hz, 1H, H-2), 3.29 (dd, *J* = 2.5, 11.0 Hz, 1H, H-6a′), 3.19 (dd, *J* = 2.5, 11.0 Hz, 1H, H-6b′); ^{13}C NMR (125 MHz, $CDCl_3$): δ =163.8 (C=O), 153.4, 150.9, 138.7, 138.10, 138.08, 137.7, 137.5, 137.4, 137.1, 128.9, 128.5, 128.31, 128.26, 128.20, 128.1, 127.89, 127.86, 127.85, 127.8, 127.62, 127.57, 127.54, 127.49, 127.43, 126.1, 101.3 (benzylidene-C), 94.4 (C-1, $^1J_{C1H1}$ =168.8 Hz), 93.8 (C1′, $^1J_{C1'H1'}$ = 166.3 Hz), 82.5 (C-3), 79.1 (C-2′), 78.9 (C-2), 78.8 (C-3′), 78.5 (C-4), 75.13, 75.10, 73.7, 73.6, 73.4, 70.9 (C-4′), 69.2, 69.0 (C-6), 68.1 (C-6′), 63.0; HRMS–ESI (*m*/*z*): [M + Na]$^+$ calcd for $C_{60}H_{59}NNaO_{12}^+$, 1008.3929; found, 1008.3941.

2,3-Di-*O*-benzyl-4,6-*O*-benzylidene-α-D-glucopyranosyl-(1→1′)-2′,3′,6′-tri-*O*-benzyl-4′-*O*-picoloyl-β-D-glucopyranoside 19: R_f 0.2 (Hexanes/EtOAc 2:1); $[\alpha]_D^{20}$ +15.0 (*c* = 0.40, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$): δ = 8.72 (d, *J* = 4.0 Hz, 1H), 7.98 (d, *J* = 8.0 Hz, 1H), 7.78 (td, *J* = 2.0, 7.5 Hz, 1H), 7.53 – 7.02 (m, 31H), 5.54 (s, 1H), 5.33 (t, *J* = 9.5 Hz, 1H, H-4′), 5.12 (d, *J* = 3.5 Hz, 1H, H-1), 5.09 (d, *J* = 11.5 Hz, 1H), 4.95 (d, *J* = 11.0 Hz, 1H), 4.87 – 4.60 (m, 9H), 4.47 (d, *J* = 2.0 Hz, 1H), 4.29 – 4.21 (m, 2H, including H-3′ and H-5′), 4.16 (t, *J* = 9.0 Hz, 1H), 3.88 (t, *J* = 9.5 Hz, 1H), 3.87 – 3.82 (m, 1H), 3.68 – 3.57 (m, 5H, including H-2′ and H-2); ^{13}C NMR (125 MHz, $CDCl_3$): δ = 164.1, 149.7, 147.5, 138.6, 138.4, 138.1, 138.0, 137.7, 137.6, 136.9, 128.8, 128.3, 128.3, 128.2, 128.1, 128.0, 127.99, 127.9, 127.86, 127.8, 127.7, 127.67, 127.5, 127.4, 127.3, 127.3, 126.9, 126.1, 125.6, 104.1 (C-1′), 101.2, 100.1 (C-1), 82.2, 81.6, 81.5, 78.9 (C-2), 78.5 (C-3), 75.2, 75.1, 74.7, 73.7, 73.6, 73.4 (C-5′), 72.1 (C-4′), 69.6, 68.7, 63.3; HRMS–ESI (*m*/*z*): [M + Na]$^+$, calcd for $C_{60}H_{59}NNaO_{12}^+$, 1008.3929; found, 1008.3904.

2,3-Di-*O*-benzyl-4,6-*O*-benzylidene-α-D-glucopyranosyl-(1→1′)-2′,4′,6′-tri-*O*-benzyl-3′-*O*-picoloyl-β-D-glucopyranoside 20: R_f 0.2 (Hexanes/EtOAc 2:1); $[\alpha]_D^{20}$ +50.0 (*c* = 1.0, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$): δ = 8.70 (d, *J* = 4.0 Hz, 1H), 7.82 (d, *J* = 7.5 Hz, 1H), 7.71 (td, *J* =

1.5, 7.5 Hz, 1H), 7.46 – 6.83 (m, 28H), 5.50 (s, 1H), 5.47 (t, *J* = 9.5 Hz, 1H, H-3′), 5.04 (d, *J* = 3.5 Hz, 1H, H-1), 4.90 (d, *J* = 11.5 Hz, 1H), 4.80 (d, *J* = 11.5 Hz, 1H), 4.76 – 4.70 (m, 2H), 4.64 – 4.61 (m, 3H including H-1′), 4.54 (d, *J* = 12.0 Hz, 1H), 4.48 (q, *J* = 6.0 Hz, 2H), 4.42 (d, *J* = 11.0 Hz, 1H), 4.22 – 4.17 (m, 2H), 4.09 (t, *J* = 9.5 Hz, 1H, H-3), 3.79 (t, *J* = 9.5 Hz, 1H, H-4′), 3.67 – 3.49 (m, 7H including H-2 and H-2′); ^{13}C NMR (125 MHz, $CDCl_3$): δ = 164.2 (C=O), 149.7, 147.8, 138.6, 138.1, 138.0, 137.9, 137.6, 136.8, 128.8, 128.42, 128.4, 128.3, 128.2, 128.12, 128.1, 128.04, 128.0, 127.9, 127.82, 127.8, 127.7, 127.66, 127.62, 127.6, 127.1, 126.4, 126.1, 125.5, 104.4 (C-1′, J_{CH} = 173.1 Hz), 101.3, 100.3 (C-1, J_{CH} = 154.6 Hz), 82.2, 79.0, 78.3, 78.2, 77.1 (C-3′), 75.7 (C-4′), 75.1, 75.0, 74.6, 73.83, 73.8, 73.7, 68.82, 68.8, 63.2; HRMS–ESI (*m*/*z*): [M + Na]$^+$ calcd for $C_{60}H_{59}NNaO_{12}^+$, 1008.3929; found, 1008.3954.

2,3-Di-*O*-benzyl-4,6-*O*-benzylidene-α-D-glucopyranosyl-(1→1′)-2′,3′-di-*O*-benzyl-4′-*O*-picoloyl-6′-*O*-*tert*butyldiphenylsilyl-α-D-glucopyranoside 29: R_f 0.38 (Hexanes/EtOAc 3:1); $[\alpha]_D^{20}$ +66.7 (*c* = 0.15, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$): δ = 8.79 (d, *J* = 5.0 Hz, 1H), 7.94 (d, *J* = 7.5 Hz, 1H), 7.80 (td, *J* = 2.0, 8.0 Hz, 1H), 7.68 – 6.95 (m, 36H), 5.65 (t, *J* = 10.0 Hz, 1H, H-4′), 5.57 (s, 1H, benzylidene-H), 5.23 (d, *J* = 4.0 Hz, 1H, H-1′), 5.16 (d, *J* = 4.0 Hz, 1H, H-1), 4.98 (d, *J* = 11.0 Hz, 1H), 4.88(t, *J* = 14.5 Hz, 2H), 4.77 (q, *J* = 12.0 Hz, 2H), 4.68 (t, *J* = 11.5 Hz, 2H), 4.57 (d, *J* = 12.0 Hz, 1H), 4.34 (dt, *J* = 2.5, 10.0 Hz, 1H, H-5′), 4.31 – 4.26 (dt, J = 6.5, 12.5 Hz, 1H, H-5), 4.23 (t, *J* = 12.0 Hz, 1H, H-3′), 4.158 (t, *J* = 11.5 Hz, 1H, H-4), 4.150 (dd, *J* = 4.5, 13.0 Hz, 1H, H-6a), 3.76 (dd, *J* = 4.0, 10.0 Hz, 1H, H-2′), 3.73 – 3.63 (m, 2H including H-3, H-6b), 3.60 – 3.56 (m, 3H, including H-2, H-6a′, and H-6b′); ^{13}C NMR (125 MHz,$CDCl_3$): δ = 163.7 (C=O), 149.8, 148.0, 138.8, 138.3, 138.0, 137.96, 137.5, 136.8, 135.7, 135.6, 133.4, 133.2, 129.4, 129.3, 128.8, 128.5, 128.3, 128.14, 128.1, 128.0, 127.7, 127.52, 127.5, 127.46, 127.4, 127.39, 127.3, 126.7, 126.1, 125.5, 101.2 (benzylidene-C), 94.8 (H-1, J_{CH} = 168.8 Hz), 94.2 (H-1′, J_{CH} = 167.5 Hz) , 82.5 (C-3), 79.6 (C-2′), 79.5 (C-3′), 78.8 (C-2), 78.7 (C-4), 75.4, 75.3, 73.6, 73.5, 70.9 (C-4′), 70.5 (C-5′), 69.0 (C-6), 62.9 (C-5), 62.0 (C-6′) 60.4, 26.7, 19.2. HRMS–ESI (*m*/*z*): [M + Na]$^+$ calcd for $C_{69}H_{71}NNaO_{12}Si^+$, 1156.4638; found, 1156.4658.

2,3-Di-*O*-benzyl-4,6-*O*-naphthylidene-α-D-galactopyranosyl-(1→1′)-3′6′-di-*O*-benzyl-2′-*O*-(2-naphthylmethyl)-4′-*O*-picoloyl-α-D-glucopyranoside 30: R_f 0.35 (Hexanes/EtOAc, 2:1); $[\alpha]_D^{20}$ +157.5 (*c* = 0.80, $CHCl_3$); ^{1}H NMR (600 MHz, $CDCl_3$): *δ* = 8.00 (d, *J* = 7.8 Hz, 1H), 7.99 (d, *J* = 7.8 Hz, 1H), 7.87– 7.76 (m, 7H), 7.70 (s, 1H), 7.61 (d, *J* = 7.8 Hz, 1H), 7.55 – 7.48 (m, 6H), 7.39 – 7.37 (m, 4H), 7.34 – 7.07 (m, 17H), 5.58 (t, *J* = 9.9 Hz, 1H, H-4), 5.55 (s, 1H, naphthylidene-H), 5.38 (s, 1H, H-1), 5.34 (d, *J* = 3.0 Hz, 1H, H-1′), 4.98 – 4.74 (m, 7H), 4.71 (d, *J* = 12.0 Hz, 1H), 4.51 (dt, *J* = 3.0, 10.2 Hz, 1H, H-5′), 4.45 (d, *J* = 11.9 Hz, 1H), 4.38 (d, *J* = 11.9 Hz, 1H), 4.27 (s, 1H), 4.24 (t, *J* = 9.6 Hz, 1H, H-3′), 4.17 (s, 2H including H-2), 4.13 (d, *J* = 12.6 Hz, 1H), 4.04 (s, 1H), 3.83 (dd, *J* = 3.5, 9.6 Hz, 1H, H-2′), 3.73 (d, *J* = 11.8 Hz, 1H), 3.42 (dd, *J* = 2.5, 10.9 Hz, 1H), 3.35 (dd, *J* = 3.7, 11.0 Hz, 1H); ^{13}C NMR (150 MHz, $CDCl_3$): *δ* = 164.0 (C=O), 149.8, 147.8, 138.8, 138.6, 138.4, 137.7, 136.9, 135.3, 135.2, 133.7, 133.2, 133.0, 132.9, 128.4, 128.3, 128.2, 128.16, 128.1, 127.9, 127.9, 127.8, 127.8, 127.7, 127.7, 127.6, 127.6, 127.55, 127.4, 127.35, 127.3, 126.9, 126.4, 126.2, 126.18, 125.9, 125.7, 125.5, 125.47, 124.0, 101.1 (naphthylidene-C), 95.9 (C-1), 94.4 (C-1′), 79.6 (C-2′), 79.5 (C-3′), 76.0, 75.3, 75.0, 74.4, 73.7, 73.6, 73.5, 71.8 (C-4′), 71.6, 69.4 (C-6), 69.2 (C-5′), 68.1 (C-6′), 63.2 (C-5); HRMS–ESI (*m*/*z*): [M + H]$^+$ calcd for $C_{68}H_{63}NO_{12}$, 1086.4423; found, 1086.4410.

4-*O*-Benzyl-2,3-*O*-isopropylidene-α-L-rhamnopyranosyl-(1→1′)-2′,3′,6′-tri-*O*-benzyl-4′-*O*-picoloyl-α-D-glucopyranoside 31: R_f 0.32 (Hexanes/EtOAc, 2/1); $[\alpha]_D^{20}$ +6.1 (*c* 1.65, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.75 – 8.72 (m, 1H), 8.02 (d, *J* = 8.0 Hz, 1H), 7.78 (td, *J* = 1.5, 7.5 Hz, 1H), 7.47 – 7.44 (m, 1H), 7.37 – 7.08 (m, 20H), 5.47 (t, *J* = 10.0 Hz, 1H, H-4′), 5.18 (s, 1H, H-1), 5.08 (d, *J* = 4.0 Hz, 1H, H-1′), 4.91 (d, *J* = 12.0 Hz, 1H), 4.84 (d, *J* = 12.0 Hz, 1H), 4.79 (d, *J* = 12.0 Hz, 1H), 4.66 – 4.62 (m, 3H), 4.43 (q, *J* = 12.0 Hz , 2H), 4.35 (t, *J* = 5.5 Hz, 1H, H-3), 4.29 (d, *J* = 6.0 Hz, 1H, H-2), 4.20 (dt, *J* = 3.5, 10.0 Hz, 1H, H-5′), 4.14 (t, *J* = 10.0 Hz, 1H, H-3′), 3.74 (dt, *J* = 6.5, 16.0 Hz, 1H, H-5), 3.68 (dd, *J* = 3.5, 9.5 Hz, 1H, H-2′), 3.52 – 3.51 (m, 2H, H-6a′ and H-6b′), 3.23 (dd, *J* = 7.0, 10.0 Hz, 1H, H-4), 1.52 (s, 3H, CH_3), 1.42 (s, 3H, CH_3), 1.20 (d, *J* = 6.5 Hz, 3H, H-6); ^{13}C NMR (125 MHz, $CDCl_3$): δ = 164.0 (C=O), 149.8, 147.7, 138.4, 138.3, 137.9, 137.6, 136.8, 128.6, 128.2, 128.1, 128.0, 127.98, 127.8, 127.75, 127.6, 127.31, 127.3, 126.9, 125.6, 109.2, 98.9 (C-1, $^1J_{CH}$ = 168.0 Hz), 96.7 (C-1′, $^1J_{CH}$ = 167.0), 80.8 (C-4), 79.8 (C-2′), 79.2 (C-3′), 78.5 (C-3), 75.8 (C-3), 75.3, 73.7, 73.5, 72.9, 71.6, 69.9 (C-5′), 68.6 (C-6′), 66.1 (C-5), 28.0, 26.5, 17.6 (C-6); HRMS–ESI (*m*/*z*): [M + Na]$^+$ calcd for $C_{49}H_{53}NNaO_{12}^+$, 870.3460; found, 870.3242.

2-Azido-3-*O*-benzyl-4,6-*O*-benzylidene-2-deoxy-α-D-glucopyranosyl-(1→1′)-2′,3′,6′-tri-*O*-benzyl-4′-*O*-picoloyl-α-D-glucopyranoside 32: R_f 0.2 (Hexanes/EtOAc 3:1); $[\alpha]_D^{20}$ +66.7 (*c* 0.15, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.78 – 8.76 (m, 1H), 7.99 (d, *J* = 7.5 Hz, 1H), 7.79 (td, *J* = 8, 2 Hz, 1H), 7.52 – 7.09 (m, 26H), 5.60 (s, 1H, benzylidene-H), 5.50 (t, *J* = 10 Hz, H-4′), 5.175 (d, *J* = 2.5 Hz, 1H, H-1′), 5.169 (d, *J* = 2.5 Hz, 1H, H-1), 5.03 (d, *J* = 10.5 Hz, 1H), 4.87 (dd, *J* = 10.5, 14.0 Hz ,2H), 4.77 (d, *J* = 12.0 Hz, 2H), 4.70 (d , *J* = 5.0 Hz, 1H), 4.68 (d, *J* = 4.5 Hz, 1H), 4.49 (q, *J* = 12.0 Hz, 2H), 4.39 (dt, *J* = 3.0, 7.5 Hz, 1H, H-5′), 4.35 (dt, *J* = 5.0, 10.0 Hz, 1H, H-5), 4.21 (t, *J* = 9.5 Hz, 1H, H-3′), 4.19 (t, *J* = 9.5 Hz, 1H, H-3), 4.18 – 4.15 (m, 1H, H-6a), 3.78 – 3.71 (m, 3H, including H-2′, H-4 and H-6b), 3.63 – 3.56 (m, 3H, including H-2 and H-6′ × 2);^{13}C NMR (125 MHz, $CDCl_3$): δ = 163.9 (C=O), 149.9, 147.7, 138.2, 138.0, 137.8, 137.7, 137.3, 136.9, 129.0, 128.6, 128.4, 128.2, 128.18, 128.15, 128.1, 127.93, 127.9, 127.87, 127.8, 127.76, 127.4, 127.3, 126.9, 126.1, 125.5, 101.4, 94.5 (C-1, J_{CH} = 172.5), 93.7 (C-1′, J_{CH} = 171.3), 82.8 (C-4), 79.3 (C-3′), 78.9 (C-2′), 75.4, 75.2, 73.8, 73.5, 71.7, 69.7 (C-5′), 68.8 (C-6), 68.4 (C-2), 63.1 (C-5), 63.0 (C-6′); HRMS–ESI (*m*/*z*): [M + Na]$^+$ calcd for $C_{53}H_{52}N_4NaO_{11}^+$, 943.3525; found, 943.3537.

2-Azido-4,6-*O*-benzylidene-2-deoxy-3-*O*-naphthylmethyl-α-D-galactopyranosyl-(1→1′)-2′,3′,6′-tri-*O*-benzyl-4′-*O*-picoloyl-α-D-glucopyranoside 33: R_f 0.35 (Hexanes/EtOAc 2:1); $[\alpha]_D^{20}$ +168 (*c* = 1.20, $CHCl_3$); ^{1}H NMR (600 MHz, $CDCl_3$): *δ* = 8.77 (d, *J* = 3.6 Hz, 1H), 8.03 (d, *J* = 7.8 Hz, 1H), 7.93 (s, 1H), 7.85 (d, *J* = 9.6 Hz, 1H), 7.51 (d, *J* = 7.2 Hz, 2H), 7.46 (dd, *J* = 4.8, 6.0 Hz, 1H), 7.44 – 7.42 (m, 2H), 7.37 – 7.33 (m, 4H), 7.28 – 7.27 (m, 5H), 5.56 (t, *J* = 9.9 Hz, 1H, H-4′), 5.39 (s, 1H, benzylidene-H), 5.28 (s, 1H, *J* = 3.0 Hz, H-1), 5.24 (d, *J* = 3.0 Hz, 1H, H-1′), 5.00 (d, *J* = 12.0 Hz, 1H), 4.94 (d, *J* = 12.0 Hz, 1H), 4.80 (d, *J* = 11.8 Hz, 1H), 4.76 (d, *J* = 12.0 Hz, 1H), 4.67 (d, *J* = 11.4 Hz, 1H), 4.55 (t, *J* = 12.0 Hz, 2H), 4.47 – 4.45 (m, 2H including H-5′), 4.18 – 4.10 (m, 4H including H-3′, H-2, and H-5), 4.01 (d, *J* = 12.6 Hz, 1H, H-6a), 3.89 (s, 1H, H-5), 3.74 (dd, *J* = 3.5, 9.6 Hz, 1H, H-2′), 3.66 – 3.63 (m, 2H including H-6b and H-6a′), 3.60 (dd, *J* = 3.6, 10.8 Hz, 1H, H-6b′); ^{13}C NMR (150 MHz, $CDCl_3$): *δ* = 164.0 (C=O), 149.8, 147.8, 138.0, 137.9, 137.6, 137.0, 135.5, 133.3, 133.1, 129.0, 128.5, 128.2, 128.1, 128.0, 127.9, 127.84, 127.75, 127.51, 127.46, 127.4, 127.0, 126.4, 126.20, 126.16, 126.0, 125.7, 125.6, 100.9 (benzylidene-C), 95.3 (C-1, $^1J_{CH}$ = 172.5 Hz), 94.1 (C-1′, $^1J_{CH}$ = 169.1 Hz), 79.5 (× 2 including C-2′ and C-3′), 75.3, 73.8, 73.5, 72.9, 71.8 (C-4′), 71.4, 69.5 (C-5′), 69.1 (C-6), 68.3 (C-6′), 63.1 (C-5), 59.0; HRMS–ESI (*m*/*z*): [M + H]$^+$ calcd for $C_{57}H_{54}N_4O_{11}^+$, 971.3862; found, 971.3883.

3-*O*-Benzyl-4,6-*O*-benzylidene-2-deoxy-α-D-galactopyranosyl-(1→1′)-2′,3′,6′-tri-*O*-benzyl-4′-*O*-picoloyl-α-D-glucopyranoside 34: R_f 0.22 (Hexanes/EtOAc 2:1); $[\alpha]_D^{20}$ +57.1 (*c* = 0.35, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$): δ = 8.76 (m, 1H), 8.09 (d, *J* = 8.0 Hz, 1H), 7.82 (td, *J* = 8.0, 1.5 Hz, 1H), 7.55 – 7.09 (m, 23H), 5.51 (t, *J* = 9.5 Hz, 1H, H-4′), 5.49 (s, 1H, benzylidene-H), 5.41 (d, *J* = 2.0 Hz, 1H, H-1), 5.30 (d, *J* = 3.5 Hz, 1H, H-1′), 4.84 (d, *J* = 11.5 Hz, 1H), 4.73 (d, *J* = 12.0 Hz, 1H), 4.72 – 4.67 (m, 3H), 4.60 (d, *J* = 11.5 Hz, 1H), 4.47 (q, *J* = 12.0 Hz, 2H), 4.20 (dt, *J* = 2.8, 9.5 Hz, 1H, H-5′), 4.16 (t, *J* = 9.5 Hz, 1H, H-3′), 4.14 (s, 1H, H-5), 4.07 – 4.04 (m, 2H, including H-3 and H-6a′), 3.82 (s, 1H, H-4), 3.74 – 3.69 (m, 2H, including H-2′ and H-6b), 3.60 (qd, *J* = 3.0, 10.5 Hz, 2H, H-6a′ and H-6b′), 2.31 (ddd, *J* = 3.4, 12.5 Hz, 1H, $H\text{-}2_{ax}$), 1.95 (dd, *J* = 13, 5 Hz, 1H, $H\text{-}2_{eq}$); ^{13}C NMR (125 MHz, $CDCl_3$): δ = 164.2 (C=O), 149.7, 147.7, 138.3, 138.2, 138.0, 137.7, 136.9, 128.7, 128.5, 128.4, 128.12, 128.1, 128.0,

127.9, 127.7, 127.7, 127.67, 127.4, 127.39, 126.9, 126.3, 125.7, 100.7, 95.3 (C-1), 93.4 (C-1′), 79.6 (C-2′), 79.2 (C-3′), 75.2, 73.6, 72.8 (C-5), 72.0 (C-4′), 71.16, 70.1, 69.8 (C-6), 69.4 (C-5′), 68.6 (C-6′), 63.2 (C-4), 30.4 (C-2); HRMS–ESI (*m*/*z*): [M + Na]$^+$ calcd for $C_{53}H_{53}NNaO_{11}^+$, 902.3511; found, 902.3510.

3-*O*-Benzyl-4,6-*O*-benzylidene-2-deoxy-α-D-glucopyranosyl-(1→1′)-2′,3′,6′-tri-*O*-benzyl-4′-*O*-picoloyl-α-D-glucopyranoside 35: R_f 0.22 (Hexanes/EtOAc 2:1); $[\alpha]_D^{20}$ +86.2 (*c* 0.65, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$): δ = 8.73 (m, 1H), 8.06 (d, *J* = 10.0 Hz, 1H), 7.81 (td, *J* = 9.5, 2 Hz, 1H), 7.54 – 7.03 (m, 26H), 5.63 (s, 1H, benzylidene-H), 5.45 (t, *J* = 12.0 Hz, 1H, H-4′), 5.23 (d, *J* = 4.0 Hz, 1H, H-1), 5.19 (d, *J* = 4.5 Hz, 1H, H-1′), 4.91 (d, *J* = 14.5 Hz, 1H), 4.83 (d, *J* = 14.0 Hz, 1H), 4.77 – 4.60 (m, 4H), 4.44 (d, *J* = 3.5 Hz, 2H), 4.23 – 4.09 (m, 5H including H-3 and H-3′), 3.78 – 3.67 (m, 3H including H-2′), 3.60 – 3.50 (m, 2H), 2.30 (dd, *J* = 6.0, 16.5 Hz, 1H, H-2_{eq}), 1.88 (ddd, *J* = 5.0, 14.0, 17.0, 1H, H-2_{ax}); ^{13}C NMR (125 MHz, $CDCl_3$): δ = 164.2 (C=O), 149.7, 147.7 138.8 138.3 137.7, 137.7, 136.9, 128.8, 128.5, 128.46, 128.4 128.1, 128.0, 127.97, 127.8, 127.8, 127.6, 127.55, 127.4, 127.3, 128.0, 126.2, 125.7, 101.4, 94.0 (C-1), 93.0 (C-1′), 83.9 (C-2′), 79.0, 78.9, 75.3, 73.6, 73.5, 73.3, 72.9, 71.9 (C-4′), 69.4, 69.0, 68.7, 63.4, 36.2; HRMS–ESI (*m*/*z*): [M + Na]$^+$ calcd for $C_{53}H_{53}NNaO_{11}^+$, 902.3511; found, 902.3532.

2,3-Di-*O*-benzyl-4,6-*O*-benzylidene-α-D-glucopyranosyl-(1→1′)-2′-azido-3′,6′-di-*O*-benzyl-2′-deoxy-4′-*O*-picoloyl-α-D-glucopyranoside 37: R_f 0.36 (Hexanes/EtOAc, 2/1); $[\alpha]_D^{20}$ +44.4 (*c* = 0.45, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$): δ = 8.77 (m, 1H), 7.97 (d, *J* = 7.5 Hz, 1H), 7.81 (td, *J* = 8.0, 2.0 Hz, 1H), 7.55 – 7.11 (m, 26H), 5.58 (s, 1H, benzylidene-H), 5.53 (t, *J* = 9.5 Hz, 1H, H-4′), 5.23 (d, *J* = 3.5 Hz, 1H, H-1′), 5.19 (d, *J* = 3.5 Hz, 1H, H-1), 5.03 (d, *J* = 11.5 Hz, 1H), 4.92 (d, *J* = 11.5 Hz, 1H), 4.83 (d, *J* = 10.5 Hz, 1H), 4.78 (d, *J* = 12.0 Hz, 1H), 4.71 (d, *J* = 11.0 Hz, 2H), 4.47 (ddd, *J* = 1.0, 4.0, 10.5 Hz, 1H, H-5′),4.44 (d, *J* = 12.0 Hz, 1H), 4.40 (d, *J* = 12.0 Hz, 1H), 4.33 (dd, *J* = 5.0, 10.0 Hz, 1H, H-6a), 4.26 (t, *J* = 10.0 Hz, 1H, H-3′), 4.19 (td, *J* = 5.0, 10.0 Hz, 1H, H-5), 4.14 (t, *J* = 9.5 Hz, 1H, H-3), 3.74 – 3.70 (m, 2H, including H-6b and H-2′), 3.65 (t, *J* = 9.5 Hz, 1H, H-4), 3.61 (dd, *J* = 3.5, 14.5 Hz, 1H, H-2), 3.43 (qd, *J* = 3.0, 11.0 Hz, 2H, H-6a′ and H-6b′); ^{13}C NMR (125 MHz, $CDCl_3$) δ = 163.9 (C=O), 149.8, 147.5, 138.7, 138.0, 137.6, 137.4, 137.37, 136.9, 128.9, 128.4, 128.3, 128.27, 128.23, 128.2, 128.1, 128.0, 127.83, 127.8, 127.7, 127.6, 127.4, 127.0, 126.0, 125.6, 101.2, 94.7 (C-1, J_{CH} = 169.3 Hz), 94.1 (C-1′, J_{CH} =170.5 Hz), 82.3 (C-4), 78.6 (C-3), 78.3 (C-2), 78.2 (C-3′), 75.3, 75.25, 73.64, 73.6, 72.3 (C-4′), 69.6 (C-5′), 69.0 (C-6), 68.3 (C-6′), 63.3 (C-5), 63.2 (C-2′); HRMS–ESI (*m*/*z*): [M + H]$^+$ calcd for $C_{53}H_{62}N_4O_{11}^+$, 921.3705; found, 921.3729.

2-Azido-3-*O*-benzyl-4,6-*O*-benzylidene-2-deoxy-α-D-glucopyranosyl-(1→1′)-2′-azido-3′,6′-di-*O*-benzyl-4′-*O*-picoloyl-α-D-glucopyranoside 38: R_f 0.3 (Hexanes/EtOAc, 3/1); $[\alpha]_D^{20}$ +27.9 (*c* = 0.73, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$): δ = 8.78 (d, *J* = 5.0 Hz, 1H), 8.03 (d, *J* = 10.0 Hz, 1H), 7.82 (td, *J* = 10.0, 2.0 Hz, 1H), 7.55 – 7.11 (m, 21H), 5.62 (s, 1H, benzylidene-H), 5.55 (t, *J* = 12.5 Hz, 1H, H-4′), 5.22 (d, *J* = 4.5 Hz, 1H, H-1), 5.16 (d, *J* = 4.5 Hz, 1H, H-1′), 5.05 (d, *J* = 13.5 Hz, 1H), 4.89 (d, *J* = 13.5 Hz, 1H), 4.83 (d, *J* = 13.5 Hz, 1H), 4.71 (d, *J* = 13.5 Hz, 1H), 4.53 (d, *J* = 15.0 Hz, 1H), 4.46 (d, *J* = 15.0 Hz, 1H),, 4.41 (dt, *J* = 4.0, 9.0 Hz, 1H, H-5′), 4.34 (dd, *J* = 6.0, 10.0 Hz, 1H, H-6a), 4.25 (t, *J* = 12 Hz, 1H, H-3′), 4.19 – 4.13 (m, 2H, including H-3 and H-5), 3.77 (t, *J* = 12.0 Hz, 2H including H-4 and H-6b), 3.70 (dd, *J* = 5.0, 13.0 Hz, 1H, H-2′), 3.63 – 3.59 (m, 3H including H-2, H-6a′, and H-6b′); ^{13}C NMR (125 MHz, $CDCl_3$) δ = 163.9 (C=O), 149.9, 147.4, 137.8, 137.6, 137.3, 137.1, 137.0, 129.1, 128.4, 128.3, 128.24, 128.2, 128.17, 128.1, 128.0, 127.7, 127.5, 127.1, 126.0, 125.6, 101.4, 94.1 (C-1), 93.5 (C-1′), 82.6 (C-4), 78.1 (C-3′), 76.8 (C-3), 75.3, 75.25, 73.5, 72.1 (C-4′), 69.9, 68.8 (C-6), 68.3 (C-6′), 63.5 (C-5), 62.9 (C-2′), 62.8 (C-2); HRMS–ESI (*m*/*z*): [M + H]$^+$ calcd for $C_{46}H_{46}N_7O_{10}^+$, 856.3301; found, 856.3300.

3-*O*-Benzyl-4,6-*O*-benzylidene-2-deoxy-α-D-glucopyranosyl-(1→1′)-2′-azido-3′,6′-tri-*O*-benzyl-2′-deoxy-4′-*O*-picoloyl-α-D-glucopyranoside 39: R_f 0.24 (Hexanes/EtOAc, 2/1); $[\alpha]_D^{20}$ +46.7 (*c* = 0.30, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$): δ = 8.76 (m, 1H), 8.10 (d, *J* = 9.5 Hz, 1H), 7.84 (td, *J* = 9.5, 2 Hz, 1H), 7.58 – 7.08 (m, 21H), 5.65 (s, 1H, benzylidene-H), 5.52 (t, *J* = 11.5 Hz, 1H, H-4′), 5.245 (d, *J* = 4.0 Hz, 1H, H-1), 5.238 (d, *J* = 3.0 Hz, 1H, H-1′), 4.94 (d, *J* = 14.5 Hz, 1H), 4.83 (d, *J* = 13.5 Hz, 1H), 4.77 (d, *J* = 14.5 Hz, 1H), 4.68 (d, *J* = 13.5 Hz, 1H), 4.47 (s, 2H), 4.31 (dd, *J* = 6.0, 13.0 Hz, 1H, H-6a), 4.26 (t, *J* = 12.0 Hz, 1H, H-3′), 4.19 – 4.05 (m, 3H including H-3 and H-5), 3.80 – 3.71 (m, 2H including H-4 and H-6b), 3.63 (dd, *J* = 13, 5 Hz, 1H, H-2′), 3.63 – 3.57 (m, 2H, H-6a′ and H-6b′), 2.31 (dd, *J* = 6.0, 17.0 Hz, 1H, H-2_{eq}), 1.91 (ddd, *J* = 5.0, 14.0, 17.5 Hz, 1 H, H-2_{ax}); ^{13}C NMR (125 MHz, $CDCl_3$): δ = 164.1 (C=O), 149.8, 147.4, 138.7, 137.6, 137.55, 137.4, 137.0, 128.9, 128.4, 128.2, 128.19, 128.17, 128.1, 128.0, 127.97, 127.84, 127.8, 127.77, 127.7, 127.68, 127.6, 127.5, 127.2, 126.1, 125.8, 101.3, 93.8 (C-1, J_{CH} = 170.5 Hz), 93.1 (C-1′, J_{CH} = 171.1 Hz), 83.8 (C-4), 77.8 (C-3′), 75.1, 73.6, 73.4, 72.8, 72.4 (C-4′), 69.7 (C-5′), 68.9 (C-6), 68.7 (C-6′), 63.8, 62.8, 36.0 (C-2); HRMS–ESI (*m*/*z*): [M + H]$^+$ calcd for $C_{46}H_{47}N_4O_{10}^+$, 815.3287; found, 815.3318.

3-*O*-Benzyl-4,6-*O*-benzylidene-2-deoxy-α-D-galactopyranosyl-(1→1′)-2′-azido-3′,6′-tri-*O*-benzyl-2′-deoxy-4′-*O*-picoloyl-α-D-glucospyranoside 40: R_f 0.16 (Hexanes/EtOAc, 3/1); $[\alpha]_D^{20}$ +89.6 (*c* = 5.20, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$): δ = 8.78 – 8.75 (m, 1H), 8.10 (d, *J* = 7.5 Hz, 1H), 7.84 (td, *J* = 10, 2.5 Hz, 1H), 7.57 – 7.12 (m, 21H), 5.59 (s, 1H, benzylidene-H), 5.54 (t, *J* = 12.0 Hz, 1H, H-4′), 5.44 (d, *J* = 3.0 Hz, 1H, H-1), 5.29 (d, *J* = 3.5 Hz, 1H, H-1′), 4.82 – 3.63 (m, 4H), 4.49 (dd, *J* = 15.0, 1H), 4.45 (dd, *J* = 15.0, 1H), 4.28 (dd, *J* = 2.0, 14.0 Hz, H-6a), 4.26 (s, 1H, H-5), 4.23 (t, *J* = 12.0 Hz, 1H, H-3′), 4.16 (dt, *J* = 5.0, 15.0 Hz, 1H, H-5′), 4.10 – 4.02 (m, 2H including H-3 and H-6b), 3.82 (s, 1H, H-4), 3.64 – 3.56 (m, 3H including H-2′, H-6a′ and H-6b′), 2.35 (td, *J* = 4.5, 16.0 Hz, 1H, H-2_{ax}), 1.95 (dd, *J* = 6.0, 16.5 Hz, 1H, H-2_{eq}); ^{13}C NMR (125 MHz, $CDCl_3$): δ = 164.1(C=O), 149.8, 147.4, 138.3, 137.9, 137.6, 137.4, 137.0, 128.8, 128.4, 128.2, 128.18, 128.1, 127.96, 127.9, 127.7, 127.65, 127.5, 127.2, 126.3, 125.8, 100.8, 94.2 (C-1, J_{CH} = 170.3), 92.9 (C-1′, J_{CH} = 172.3) 77.6 (C-3′), 74.9, 73.6, 72.7, 72.5 (C-5), 71.3 (C-4′), 70.4 (C-3), 70.0 (C-6), 69.6 (C-5′), 68.6 (C-6′), 63.8 (C-4), 62.8 (C-2′), 30.6 (C-2); HRMS–ESI (*m*/*z*): [M + Na]$^+$ calcd for $C_{46}H_{46}N_4NaO_{10}^+$, 837.3106; found, 837.3106.

2,3-Di-*O*-benzyl-4,6-*O*-benzylidene-α-D-galactopyranosyl-(1→1′)-2′-azido-3′,6′-di-*O*-benzyl-2′-deoxy-4′-*O*-picoloyl-α-D-glucopyranoside 41: R_f 0.2 (Hexanes/EtOAc, 3/1); $[\alpha]_D^{20}$ +70.9 (*c* = 3.50, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$): δ = 8.72 – 8.69 (m, 1H), 7.86 (d, *J* = 7.5 Hz, 1H), 7.73 (td, *J* = 8, 2 Hz, 1H), 7.48 – 7.39 (m, 5H), 7.32 – 7.02 (m, 21H), 5.48 (t, *J* = 9.5 Hz, 1H, H-4′), 5.44 (s, 1H, benzylidene-H), 5.28 (d, *J* = 3.0 Hz, 1H, H-1), 5.19 (d, *J* = 3.5 Hz, 1H, H-1′), 4.81 – 4.74 (m, 3H), 4.70 (d, *J* = 10.5 Hz, 1H), 4.65 – 4.58 (m, 2H), 4.39 (ddd, *J* = 2.0, 4.0, 6.5 Hz, 1H, H-5′), 4.37 (d, *J* = 12.0 Hz, 1H), 4.31 (d, *J* = 12.0 Hz, 1H), 4.25 (d, *J* = 2.5 Hz, 1H, H-4), 4.20 (dd, *J* = 1.5, 12.5 Hz, 1H, H-6a), 4.16 (t, *J* = 10.0 Hz, 1H, H-3′), 4.06 (qd, *J* = 3.5, 10.5 Hz, 2H including H-2 and H-3), 3.99 (dd, *J* = 1.5, 12.5 Hz, 1H, H-6b), 3.86 (s, 1H, H-5), 3.55 (dd, *J* = 3.0, 10.0 Hz, 1H, H-2′), 3.35 (dd, *J* = 3.0, 11.0 Hz, 2H, H-6a′), 3.28 (dd, *J* = 4.0, 11.0 Hz, 2H, H-6b′); ^{13}C NMR (125 MHz, $CDCl_3$): δ = 163.8 (C=O), 149.8, 147.5, 138.7, 138.5, 137.8, 137.6, 137.4, 136.9, 128.9, 128.3, 128.2, 128.16, 128.11, 128.1, 127.9, 127.8, 127.75, 127.7, 127.67, 127.6, 127.4, 127.3, 127.0, 126.3, 125.5, 101.0, 94.7 (C-1, J_{CH} = 172.8 Hz), 93.5 (C-1′, J_{CH} = 168.3 Hz) , 78.0 (C-3′), 76.1, 74.9, 74.7, 74.2 (C-4), 73.8, 73.6, 72.2 (C-4′), 71.7, 69.4 (C-6), 69.3 (C-5′), 68.1 (C-6′), 63.6 (C-5), 62.9 (C-2′); HRMS–ESI (*m*/*z*): [M + H]$^+$ calcd for $C_{53}H_{62}N_4O_{11}^+$, 921.3705; found, 921.3739.

3,4,5-Tri-*O*-Acetyl-2-*N*-(2,2,2-trichloroethoxycarbonyl)-β-D-glucopyranosyl-(1→1′)-2′,3′,6′-tri-*O*-benzyl-4′-*O*-picoloyl-α-D-glucopyranoside 47: R_f 0.2 (Hexanes/EtOAc, 2/1); $[\alpha]_D^{20}$ +26.7 (*c* = 1.20, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$): δ = 8.78 (d, *J* = 4.5 Hz, 1H), 8.00 (d, *J* = 8.0 Hz, 1H), 7.83 (td, *J* = 2.0, 10.0 Hz, 1H), 7.52 – 7.48 (m, 1H), 7.37 – 7.18 (m, 10H), 7.12 – 7.04 (m, 5H), 6.70 (d, *J* = 6.5 Hz, 1H, NH), 5.75 (t, *J* = 10.0 Hz, 1H, H-3), 5.51 (d, *J* = 8.5 Hz, 1H, H-1), 5.47 (d, *J* = 3.0 Hz, H-1′), 5.19 (t, *J* = 10.0 Hz, 1H, H-4′), 5.00 (t, *J* = 10.0 Hz, 1H, H-4), 4.88 – 4.69 (m, 4H), 4.65 (d, *J* = 11.0 Hz, 1H), 4.59 – 4.54 (m, 2H), 4.49 (dt, *J* = 2.5, 7.5 Hz, 1H, H-5′), 4.38 (d, *J* = 11.5 Hz, 1H), 4.31 (dd, *J* = 4.5, 12.5 Hz, 1H, H-6a), 4.16 (t, *J* = 9.5 Hz, 2H, including H-3′ and H-6b), 3.86 (broad d, *J* = 7.0 Hz, 1H, H-5), 3.65 (dd, *J* = 3.5, 9.5 Hz, 1H, H-2′), 3.62 – 3.53 (m, 2H, H-6a′ and H-6b′), 3.43 (q, *J* = 9.0 Hz, 1H, H-2), 2.05 (s, 3H, OC*H*$_3$), 2.02 (s, 3H, OC*H*$_3$), 1.81 (s,3H, OC*H*$_3$);^{13}C NMR (125 MHz, $CDCl_3$): δ = 170.6, 169.8, 169.7, 164.0, 153.8, 149.9, 147.2, 138.1, 137.6, 137.0, 128.4, 128.3, 128.1, 128.0, 127.9, 127.8, 127.7, 127.4, 127.1, 125.6, 96.9 (C-1, J_{CH} = 164.4 Hz), 95.8, 92.5 (C-1′, J_{CH} = 172.6 Hz), 78.6 (C-2′), 78.5 (C-3′), 75.5, 74.0, 73.9, 72.7, 72.3 (C-5), 71.7 (C-4′), 70.4 (C-3), 69.9 (C-6′), 69.6 (C-5′), 68.8 (C-4), 62.2 (C-6), 56.0 (C-2), 20.7, 20.6, 20.5; HRMS–ESI (*m*/*z*): [M + Na]$^+$ calcd for $C_{48}H_{51}Cl_3N_2NaO_{16}^+$, 1039.2196; found, 1039.2254.

3,5-Di-*O*-acetyl-4-*O*-benzyl-2-*N*-(2,2,2-trichloroethoxycarbonyl)-β-D-glucopyranosyl-(1→1′)-2′,3′,6′-tri-*O*-benzyl-4′-*O*-picoloyl-α-D-glucopyranoside 48: R_f 0.22 (Hexanes/EtOAc, 3/2); $[\alpha]_D^{20}$ +40.0 (*c* = 0.45, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$): δ = 8.76 (d, *J* = 4.0 Hz, 1H), 8.00 (d, *J* = 7.5 Hz, 1H), 7.82 (td, *J* = 2.0, 8.0 Hz, 1H), 7.51 – 7.47 (m, 1H), 7.36 – 7.17 (m, 17H), 7.12 – 7.05 (m, 4H), 6.23 (d, *J* = 7.0 Hz, 1H, NH), 5.60 (t, *J* = 10.0 Hz, 1H, H-3), 5.36 (d, *J* = 3.0 Hz, 1H, H-1′), 5.28 (t, *J* = 10.0 Hz, 1H, H-4′), 5.23 (d, *J* = 5.0 Hz, 1H, H-1), 4.92 (d, *J* = 12.0 Hz, 1H), 4.84 (d, *J* = 11.5 Hz, 1H), 4.73 – 4.51 (m, 7H), 4.46 (ddd, *J* = 2.5, 7.0, 9.5 Hz, 1H, H-5′), 4.41 – 4.35 (m, 3H including H-6a), 4.21 (dd, *J* = 4.5, 12.0 Hz, 1H, H-6b), 4.15 (t, *J* = 9.5 Hz, 1H, H-3′), 3.74 –3.68 (m, 1H, H-5), 3.65 (dd, *J* = 4.0, 10.0 Hz, 1H, H-2′), 3.61 – 3.51 (m, 3H, including H-4, H-6a′, and H-6b′), 3.44 (q, *J* = 8.5 Hz, 1H, H-2), 2.00 (s, 3H, OC*H*$_3$), 1.82 (s, 3H, OC*H*$_3$); ^{13}C NMR (125 MHz, $CDCl_3$): δ = 170.5, 169.9, 164.0, 153.9, 149.9, 147.3, 138.2, 137.7, 137.24, 137.2, 136.9, 128.53, 128.5, 128.3, 128.1, 128.0, 127.93, 127.9, 127.85, 127.8, 127.7, 127.4, 127.0, 125.6, 98.2 (C-1, J_{CH} = 163.5 Hz), 95.8, 94.0 (C-1′, J_{CH} = 169.8 Hz), 79.1 (C-2′), 78.6 (C-3′), 76.0 (C-4), 75.4, 74.3, 74.1, 73.9, 73.4 (C-5), 73.1 (C-3), 72.8, 71.6 (C-4′), 69.6 (C-6′), 69.5 (C-5), 63.0 (C-6), 56.4 (C-2), 20.8, 20.7; HRMS–ESI (*m*/*z*): [M + Na]$^+$ calcd for $C_{53}H_{55}Cl_3N_2NaO_{15}^+$, 1087.2560; found, 1087.2563.

2-*O*-Benzoyl-3,4,6-tri-*O*-benzyl-β-D-glucopyranosyl-(1→1′)-2′,3′,6′-tri-*O*-benzyl-4′-*O*-picoloyl-α-D-glucopyranoside 49: R_f 0.3 (Hexanes/EtOAc, 2/1); $[\alpha]_D^{20}$ +30.0 (*c* = 0.4, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$): δ = 8.68 – 8.65 (m, 1H), 7.95 (d, *J* = 7.0 Hz, 2H), 7.83 (d, *J* = 8.0 Hz, 1H), 7.67 (td, *J* = 1.5, 7.5 Hz, 1H), 7.41 (t, *J* = 7.5 Hz, 1H), 7.39 – 7.35 (m, 1H), 7.29 – 7.02 (m, 26H), 6.99 – 6.93 (m, 5H), 6.88 (d, *J* = 6.5 Hz, 2H), 5.35 (t, *J* = 10.0 Hz, 1H, H-4′), 5.34 (t, *J* = 8.5 Hz, 1H, H-2), 4.90 (d, *J* = 3.5 Hz, 1H, H-1′), 4.77 (d, *J* = 10.5 Hz, 1H), 4.70 (d, *J* = 11.0 Hz), 4.66 (d, *J* = 8.0 Hz, H-1), 4.64 (d, *J* = 11.0 Hz, 1H), 4.56 – 4.50 (m, 2H), 4.46 (d, *J* = 12.0 Hz, 1H), 4.38 (d, *J* = 11.5 Hz, 2H), 4.27 (q, *J* = 12.0 Hz, 3H including H-5′), 4.17 (d, *J* = 12.5 Hz, 1H), 4.06 (d, *J* = 12.0 Hz, 1H), 4.01 (t, *J* = 9.5 Hz, 1H, H-3′), 3.80 (t, *J* = 9.0 Hz, 1H, H-3), 3.75 (t, *J* = 9.5 Hz, 1H, H-4), 3.61 (m, 2H, H-6a and H-6b), 3.47 (td, *J* = 3.0, 9.5 Hz, 1H, H-5), 3.45 – 3.39 (m, 2H including H-2′ and H-6a′), 3.32 (dd, *J* = 3.5, 11.0 Hz, 1H, H-6b′); ^{13}C NMR (125 MHz, $CDCl_3$): δ = 164.9 (C=O), 163.7 (C=O), 149.8, 147.7, 138.3, 138.1, 138.0, 137.9, 137.8, 137.79, 136.7, 132.9, 130.2, 129.7, 128.4, 128.3, 128.27, 128.2, 128.16, 128.03, 128.0, 127.99, 127.96, 127.84, 127.80, 127.75, 127.62, 127.6, 127.54, 127.5, 127.3, 127.1, 126.7, 125.4, 101.7 (C-1, J_{CH} = 158.3 Hz), 99.0 (C-1′, J_{CH} = 168.0 Hz) , 82.6 (C-3), 78.9 (C-2′), 78.6 (C-3′), 77.8 (C-4), 75.5 (C-5), 75.0, 73.7, 73.5, 72.3, 71.2 (C-4′), 69.8 (C-5′), 68.6 (C-6), 68.1 (C-6′). HRMS–ESI (*m*/*z*): [M + Na]$^+$ calcd for $C_{67}H_{65}NNaO_{13}^+$, 1114.4348; found, 1114.4348.

6-*O*-Acetyl-4-*O*-benzyl-3-*O*-(2-naphthylmethyl)-2-*N*-phthalimido-β-D-galactopyranosyl-(1→1′)-2′,3′,6′-tri-*O*-benzyl-4′-*O*-picoloyl-α-D-glucopyranoside 50: R_f = 0.26 (hexanes/CH_2Cl_2/EtOAc, 3/1/1); $[\alpha]_D^{20}$ -26.0 (*c* = 2.0, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$): δ = 8.66 (d, *J* = 4.5 Hz, 1H), 7.80 (d, *J* = 7.5 Hz, 1H), 7.70 – 6.90 (m, 31H), 6.75 (d, *J* = 6.5 Hz, 2H), 5.29 (t, *J* = 10.0 Hz, 1H, H-4′), 5.21 (d, *J* = 8.5 Hz, 1H, H-1), 5.03 (d, *J* = 11.5 Hz, 1H), 4.80 (d, *J* = 12.0 Hz, 1H), 4.77 (dd, *J* = 2.5, 11.0 Hz, 1H, H-2), 4.70 (d, *J* = 3.0 Hz, 1H, H-1′), 4.65 (d, *J* = 11.5 Hz, 1H), 4.46 (d, *J* = 12.5 Hz, 1H), 4.41 (dd, *J* = 2.5, 11.5 Hz, 1H, H-3), 4.39 (d, *J* = 11.0 Hz, 1H), 4.35 (d, *J* = 11.5 Hz, 1H), 4.30 –4.27 (m, 2H), 4.24 (dt, *J* = 3.0, 10.0 Hz, 1H, H-5′), 4.08 (d, *J* = 6.5 Hz, 2H), 3.97 (d, *J* = 12.5 Hz, 1H, H-6a), 3.91 (s, 1H, H-4), 3.89 (t, *J* = 9.5 Hz, 1H, H-3′), 3.71 (t, *J* = 6.5 Hz, 1H), 3.66 (d, *J* = 12.5 Hz, 1H, H-6b), 3.42 (dd, *J* = 2.5, 11.0 Hz, 1H, H-6a′), 3.32 (dd, *J* = 3.0, 11.0 Hz, 1H, H-6b′), 3.24 (dd, *J* = 9.5 Hz, 1H, H-2′), 1.82 (s, 3H, C*H*$_3$); ^{13}C NMR (125 MHz, $CDCl_3$): δ = 170.4, 168.9, 167.7, 163.5, 149.7, 147.6, 138.1, 138.06, 137.7, 137.6, 136.7, 135.0, 133.4, 133.0, 132.7, 131.8, 131.4, 128.5, 128.4, 128.1, 128.06, 128.0, 127.99, 127.9, 127.82, 127.8, 127.77, 127.5, 127.4, 127.3, 127.2, 127.1, 126.6, 126.58, 126.1, 125.8, 125.6, 125.3, 122.8, 122.4, 100.1 (C-1, J_{CH} = 141 Hz), 99.8 (C-1′, *J* = 165.5 Hz), 78.7 (C-3′), 78.1 (C-2′), 77.1 (C-3), 74.8, 74.6, 73.4, 72.7, 72.4, 72.0, 71.9 (C-4), 70.9 (C-4′), 69.6 (C-5′), 67.9 (C-6′), 63.0, 52.8 (C-2), 20.7; HRMS–ESI (*m*/*z*): [M + Na]$^+$ calcd for $C_{67}H_{62}N_2NaO_{14}^+$, 1141.4093; found, 1141.4097. For 1α→1′α anomer of **50**: R_f = 0.46 (hexanes/CH_2Cl_2/EtOAc 3/1/1); ^{1}H NMR (500 MHz, $CDCl_3$): δ = 8.79 (d, *J* = 4.0 Hz, 1H), 7.81 (d, *J* = 7.5 Hz, 1H), 7.76 – 7.73 (m, 2H), 7.69 – 7.60 (m, 5H), 7.49 (dd, *J* = 7.5, 14.5 Hz, 2H), 7.41 – 7.37 (m, 3 H), 7.34 – 7.26 (m, 12 H), 7.21 (dd, *J* = 1.5, 7.5 Hz, 2H), 7.16 – 7.10 (m, 6H), 7.00 (dd, *J* = 2.0, 7.5 Hz, 2H), 5.48 (dd, *J* = 2.5, 12.5 Hz, 1H, H-3), 5.35 (d, *J* = 3.5 Hz, H-1), 5.27 (d, *J* = 3.5 Hz, H-1′), 5.20 (t, *J* = 10.0 Hz, 1H, H-4), 5.12 (dd, *J* = 3.5, 11.5 Hz, 1H, H-2), 5.00 (d, *J* = 10.5 Hz, 1H), 4.98 (d, *J* = 10.5 Hz, 1H), 4.92 (d, *J* = 11.0 Hz, 1H), 4.89 (d, *J* = 11.0 Hz, 1H), 4.76 – 4.71 (m, 3H), 4.64 (d, *J* = 11.5 Hz, 1H), 4.43 (t, *J* = 6.5 Hz, 1H, H-5), 4.221 (t, *J* = 10.0 Hz, 1H, H-3′), 4.216 (dd, *J* = 3.0, 9.5 Hzz, Hz, 1H, H-6a), 4.15 (d, *J* = 9.0 Hz, 1H), 4.14 (s, 1H, H-4), 4.10 – 4.07 (m, 2H including H-6b), 3.65 (dd, *J* = 3.5, 10.0 Hz, 1H, H-2′), 3.44 (dt, *J* = 4.0, 10.0 Hz, 1H, H-5′), 2.98 (d, *J* = 4.0 Hz, H-6′ × 2), 1.89 (s, 3H, CH_3); ^{13}C NMR (125 MHz, $CDCl_3$): δ = 170.2 (C=O), 168.5 (C=O), 168.3 (C=O), 163.5 (C=O), 149.8, 147.7, 138.4, 137.98, 137.94, 137.6, 136.5, 135.5, 133.7, 133.5, 133.2, 132.8, 132.2, 131.1, 128.42, 128.39, 128.3, 128.01, 127.98, 127.96, 127.8, 127.58, 127.56, 127.47, 127.25, 127.24, 126.7, 126.1, 126.0, 125.8, 125.5, 125.0, 94.9 (C-1, JCH = 171.5 Hz), 92.7 (C-1′, JCH = 172.0 Hz), 78.8 (C-2′), 78.7 (C-3′), 75.3, 74.6, 73.9 (C-3), 73.1, 73.0, 72.2, 71.7 (C-4′), 71.5, 69.9, (C-5′), 69.2 (C-5), 68.2 (C-6′), 62.9 (C-6), 51.7 (C-2), 20.7 (*C*H$_3$).

2-*O*-Benzoyl-3,4,6-tri-*O*-benzyl-β-D-galactopyranosyl-(1→1′)-2′,3′,6′-tri-*O*-benzyl-4′-*O*-picoloyl-α-D-glucopyranoside 51: For 1β→1′α anomer, R_f 0.2 (Hexanes/EtOAc, 2/1); $[\alpha]_D^{20}$ +81 (*c* = 2.10, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$): δ = 8.72 (d, *J* = 5.0 Hz, 1H), 8.02 (d, *J* = 9.5 Hz, 2H), 7.87 (*d*, *J* = 9.5 Hz, 1H), 7.72 (t, *J* = 9.5 Hz, 1H), 7.48 (t, *J* = 9.0 Hz, 1H), 7.45 – 6.95 (m, 31H), 6.92 (d, *J* = 8.5 Hz, 2H), 5.76 (dd, *J* = 10.0, 12.5 Hz, 1H, H-2), 5.36 (t, *J* = 12.5 Hz, 1H, H-4′), 5.02 (d, *J* = 14.0 Hz, 1H), 4.98 (d, *J* = 3.5 Hz, 1H, H-1′), 4.70 (d, *J* = 10.0 Hz, 1H, H-1), 4.68– 4.57 (m,

4H), 4.51 (d, *J* = 15.0 Hz, 1H), 4.44 (d, *J* = 14.0 Hz, 1H), 4.38 – 4.28 (m, 5H), 4.24 (d, *J* = 15.5 Hz, 1H), 4.12 (d, *J* = 15.5 Hz, 1H), 4.07 (t, *J* = 13.0 Hz, 1H, H-3′), 4.03 (d, *J* = 3.0 Hz, H-4), 3.67 (dd, *J* = 3.0, 12.5 Hz, 1H, H-3), 3.63 – 3.61 (m, 2H), 3.53 (dd, *J* = 1.5, 15.5 Hz, 1H), 3.50 3.44 (m, H-2′ and H-6a′), 3.37 (dd, *J* = 5.0, 14.0 Hz, 1H, H-6b′); ^{13}C NMR (125 MHz, $CDCl_3$): δ = 165.0, 163.6, 149.8, 147.7, 138.5, 138.3, 138.0, 137.9, 137.8, 137.6, 136.7, 132.8, 130.4, 129.8, 128.4, 128.3, 128.3, 128.27, 128.2, 128.1, 128.0, 127.95, 127.9, 127.8, 127.74, 127.7, 127.6, 127.55, 127.4, 127.2, 127.1, 126.6, 125.4, 102.1 (C-1, J_{CH} = 156.5 Hz), 98.8 (C-1′, J_{CH} = 172.7 Hz), 79.8 (C-3), 78.8 (C-2′), 78.6 (C-3′), 75.0, 74.7, 73.9, 73.4, 73.3, 72.5, 72.2 (C-4), 71.8, 71.7 (C-2), 71.2 (C-4′), 69.6 (C-5′), 68.3 (C-6′); HRMS–ESI (*m/z*): [M + Na]$^+$ calcd for $C_{67}H_{65}NNaO_{13}^+$, 1114.4348; found, 1114.4329.

2,3-Di-*O*-benzyl-4,6-*O*-benzylidene-β-D-mannopyranosyl-(1→1′)-2′,3′,6′-tri-*O*-benzyl-4′-*O*-picoloyl-α-D-glucopyranoside 53: R_f 0.2 (Hexanes/EtOAc, 2/1); $[\alpha]_D^{20}$ +8.4 (*c* = 0.35, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$): δ = 8.77 (d, *J* = 5.5 Hz, 1H), 7.91 (d, *J* = 10.0 Hz, 1H), 7.78 (td, *J* = 2.5, 10.0 Hz, 1H), 7.53 – 7.00 (m, 31H), 5.60 (s, 1H, benzylidene-H), 5.52 (t, *J* = 12.0 Hz, 1H, H-4′), 5.06 (d, *J* = 15.0 Hz, 1H), 5.00 (d, *J* = 4.5 Hz, 1H, H-1′), 4.95 (d, *J* = 15.0 Hz, 1H), 4.86 (d, *J* = 15.0 Hz, 1H), 4.82 (d, *J* = 14.5 Hz, 1H), 4.67 – 4.60 (m, 3H), 4.55 (d, *J* = 16.0 Hz, 1H), 4.60 (s, 1H, H-1), 4.47 (d, *J* = 14.5 Hz, 1H), 4.42 – 4.40 (m, 3H including H-3′ and H-6 × 2), 3.94 (d, *J* = 3.5 Hz, 1H, H-2), 3.83 (t, *J* = 13.0 Hz, 1H, H-4), 3.73 (dd, *J* = 4.0, 12.0 Hz, 1H, H-2′), 3.56 – 3.46 (m, 3H including H-3 and H-6′ × 2), 3.28 (td, *J* = 6.0, 12.5 Hz, 1H, H-5); ^{13}C NMR (125 MHz, $CDCl_3$): δ = 163.7 (C=O), 149.9, 147.7, 138.4, 138.3, 138.25, 138.1, 137.6, 137.5, 136.7, 128.8, 128.7, 128.5, 128.3, 128.2, 128.15, 128.1, 128.08, 128.0, 127.98, 127.9, 127.89, 127.54, 127.5, 127.4, 127.38, 126.8, 126.0, 125.4, 103.0 (C-1, J_{CH} = 154.1 Hz), 101.8, 99.2 (C-1′, J_{CH} = 165.1 Hz), 80.4 (C-2′), 78.6, 78.3, 77.5 (C-3), 76.0 (C-2), 75.1, 74.8, 73.8, 73.5, 72.3, 71.3 (C-4′), 69.6, 68.5 (C-4), 68.1 (C-6′), 67.7 (C-5); HRMS–ESI (*m/z*): [M + Na]$^+$ calcd for $C_{60}H_{59}NNaO_{12}^+$, 1008.3929; found, 1008.3924.

2,3-Di-*O*-benzyl-4,6-*O*-benzylidene-β-D-mannopyranosyl-(1→1′)-2′-azido-3′,6′-tri-*O*-benzyl-4′-*O*-picoloyl-α-D-glucopyranoside 54: R_f 0.3 (Hexanes/EtOAc, 2/1); ^{1}H NMR (500 MHz, $CDCl_3$): δ = 8.72 – 8.69 (m, 1H), 7.89 (d, *J* = 8.0 Hz, 1H), 7.72 (td, *J* = 2.0, 8.0 Hz, 1H), 7.49 – 7.00 (m, 30 H), 5.53 (s, 1H, benzylidene-H), 5.49 (t, *J* = 9.5 Hz, 1H, H-4′), 5.13 (d, *J* = 3.5 Hz, 1H, H-1′), 4.66 (d, *J* = 12.0 Hz, 1H), 4.65 (s, 1H, H-1), 4.62 (d, *J* = 12.0 Hz, 1H), 4.56 – 4.51 (m, 2H), 4.42 – 4.38 (m, 2H including H-5′), 4.35 (d, *J* = 11.5 Hz, 1H), 4.13 – 4.09 (m, 3H, including H-3′, H-6a, and H-6b), 3.98 (d, *J* = 3.0 Hz, 1H, H-2), 3.76 (t, *J* = 10.5 Hz, 1H, H-4), 3.61 (dd, *J* = 3.5, 10.5 Hz, 1H, H-2′), 3.54 (dd, *J* = 3.0, 10.0 Hz, 1H, H-3), 3.50 – 3.42 (m, 2H, H-6a′ and H-6b′), 3.27 (td, *J* = 5.0, 10.0 Hz, 1H, H-5); ^{13}C NMR (125 MHz, $CDCl_3$): δ = 163.8 (C=O), 149.9, 147.5, 138.5, 138.2, 137.5, 137.46, 137.2, 136.8, 128.9, 128.6, 128.4, 128.3, 128.26, 128.2, 128.15, 128.1, 127.9, 127.74, 127.7, 127.6, 127.57, 127.5, 127.47, 127.0, 126.0, 125.4, 102.5 (C-1), 101.4, 98.9 (C-1′), 78.3, 77.9, 77.7 (C-3), 76.4 (C-2), 75.1, 74.9, 73.5, 72.4, 71.8 (C-4′), 70.0, 68.4 (C-4), 68.0 (C-6′), 67.8 (C-5), 63.4 (C-2′); HRMS–ESI (*m/z*): [M + Na]$^+$ calcd for $C_{53}H_{52}N_4NaO_{11}^+$, 943.3525; found, 943.3516.

3,4,5-Tri-*O*-acetyl-2-*N*-(2,2,2-trichloroethoxycarbonyl)-β-D-glucopyranosyl-(1→1′)-2′,3′,6′-tri-*O*-benzyl-4′-*O*-picoloyl-β-D-glucopyranoside 57: R_f 0.1 (Hexanes/EtOAc, 1/1); $[\alpha]_D^{20}$ –3.08 (*c* = 0.65, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$): δ = 8.74 (d, *J* = 4.0 Hz, 1H), 7.99 (d, *J* = 8.0 Hz, 1H), 7.80 (td, *J* = 2.0, 9.5 Hz, 1H), 7.50 – 7.03 (m, 16H), 5.32 (d, *J* = 9.0 Hz, 1H, NH), 5.25 (t, *J* = 9.5 Hz, 1H, H-3), 5.16 (t, *J* = 9.5 Hz, 1H, H-4), 5.13 (t, *J* = 9.5 Hz, 1H, H-4′), 4.95 (d, *J* = 10.5 Hz, 1H), 4.85 (d, *J* = 8.5 Hz, 1H, H-1), 4.83 (d, *J* = 7.5 Hz, 1H, H-1′), 4.81 – 4.59 (m, 3H), 4.48 (s, 2H), 4.28 (dd, *J* = 4.5, 12.0 Hz, 1H, H-6a), 4.15 (dd, *J* = 2.5, 12.5 Hz, 1H, H-6b), 3.89 – 3.83 (m, 3H, including H-2, H-3′ and H-5′), 3.72 – 3.67 (m, 1H, H-5), 3.64 (m, 2H, H-6′), 3.54 (t, *J* = 8.0 Hz, 1H, H-2′), 2.08 (s, 3H, OC*H*$_3$), 2.04 (s, 3H, OC*H*$_3$), 2.03 (s, 3H, OC*H*$_3$); ^{13}C NMR (125 MHz, $CDCl_3$): δ = 170.7, 170.5, 169.4, 164.1, 154.4, 149.8, 147.4, 138.1, 138.0, 137.7, 136.9, 128.6, 128.4, 128.3, 128.1, 127.8, 127.78, 127.4, 127.0, 125.6, 99.7 (C-1′, J_{CH} = 162.0 Hz), 97.5 (C-1, J_{CH} = 161.3 Hz), 95.6 (CCl_3), 81.3 (C-2′), 81.0 (C-3′), 75.2, 74.8, 74.5, 73.7, 73.3 (C-5′), 72.4 (C-4), 72.1 (C-5), 72.0 (C-3), 69.7 (C-6′), 68.4 (C-4′), 62.0 (C-6), 56.0 (C-2), 22.7 (*C*H$_3$CO), 20.7 (*C*H$_3$CO), 20.6 (*C*H$_3$CO); HRMS–ESI (*m/z*): [M + Na]$^+$ calcd for $C_{48}H_{51}Cl_3N_2NaO_{16}^+$, 1039.2196; found, 1039.2213. For 1β→1′α anomer of **57**: R_f = 0.30 (hexanes/EtOAc 1/1); ^{1}H NMR (500 MHz, $CDCl_3$): δ = 8.77 (d, *J* = 4.0 Hz, 1H), 8.01 (d, *J* = 8.0 Hz, 1H), 7.83 (dd, *J* = 1.5, 7.5 Hz, 1H), 7.50 (d, *J* = 1.0, 6.0 Hz, 1H, 7.35 – 7.20 (m, 10H), 7.11 – 7.06 (m, 5H), 6.70 (d, *J* = 7.0 Hz, NH), 5.75 (t, *J* = 10.0 Hz, H-3), 5.50 (d, *J* = 9.0 Hz, H-1), 5.46 (d, *J* = 3.0 Hz, H-1′), 5.19 (t, *J* = 10.0 Hz, 1H, H-4′), 4.99 (t, *J* = 10.0 Hz, H-4), 4.87 – 4.82 (m, 2H), 4.74 (d, *J* = 12.0 Hz, 1H), 4.71 (d, *J* =12.0 75.5 Hz, 1H), 4.65 (d, J = 11.0 Hz, 1H), 4.59 – 4.54 (m, 2H), 4.49 (dt, *J* = 2.5, 8.0 Hz, 1H, H-5′), 4.38 (d, *J* = 13.0 Hz, 1H), 4.31 (dd, *J* = 4.5, 7.5 Hz, 1H, H-6a), 4.18 – 4.14 (m, 2H), 3.86 (broad d, *J* = 7.0 Hz, 1H, H-5), 3.65 (dd, *J* = 4.0, 10.0 Hz, 1H, H-2′), 3.59 – 3.54 (m, H-6′), 3.43 (dd, *J* = 9.0, 17.5 Hz, 1H, H-2), 2.05 (s, 3H, CH_3), 2.02 (s, 3H, CH_3), 1.82 (s, 3H, CH_3); ^{13}C NMR (125 MHz, $CDCl_3$): δ = 170.6, (C=O), 169.8 (C=O), 169.7 (C=O), 164.0 (C=O), 153.8 (OC=O), 149.9, 147.2, 138.1, 137.6, 137.0, 128.5, 128.3, 128.1, 128.99, 127.97, 127.95, 127.8, 127.4, 127.1, 125.6, 96.9 (C-1, J_{CH} = 157.1 Hz), 95.8 (CCl_3), 92.5 (C-1′, J_{CH} = 166.8 Hz), 78.6 (C-2′), 78.5 (C-3′), 75.5, 74.04, 73.95, 72.7 (C-5), 72.3, 71.7 (C-4′), 70.4 (C-3), 69.9 (C-6), 69.6 (C-5′), 68.8 (C-4), 62.2 (C-6), 52.0 (C-2), 20.7 (*C*H$_3$CO), 20.6 (*C*H$_3$CO), 20.5 (*C*H$_3$CO).

2,6-Di-*O*-acetyl-4-*O*-benzyl-3-*O*-(2-naphthylmethyl)-β-D-glucopyranosyl-(1→1′)-2′,3′,6′-tri-*O*-benzyl-4′-*O*-picoloyl-β-D-glucopyranoside 58: R_f 0.18 (Hexanes/EtOAc, 1/1); $[\alpha]_D^{20}$ –4.3 (*c* = 0.65, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$): δ = 8.74 – 8.71 (m, 1H), 7.96 (d, *J* = 8.0 Hz, 1H), 7.84 – 7.73 (m, 5H), 7.50 – 7.02 (m, 24H), 5.33 (t, *J* = 10.0 Hz, 1H, H-4′), 5.16 (t, *J* = 8.5 Hz, 1H, H-2), 4.94 (m, 3H), 4.85 (d, *J* = 10.0 Hz, 1H, H-1), 4.83 (d, *J* = 7.5 Hz, 1H, H-1′), 4.78 (d, *J* = 11.5 Hz, 1H), 4.62 (t, *J* = 11.0 Hz, 2H), 4.56 (d, *J* = 11.0 Hz, 1H), 4.45 (dd, *J* = 12.0, 14.5 Hz, 2H), 4.38 (dd, *J* = 1.5, 12.0 Hz, 1H, H-6a), 4.25 (dd, *J* = 4.5, 12.0 Hz, 1H, H-6b), 3.84 (t, *J* = 9.0 Hz, 1H, H-3′), 3.83 – 3.79 (m, 1H, H-5′), 3.78 (d, *J* = 9.0 Hz, 1H, H-3), 3.73 (t, *J* = 9.5 Hz, 1H, H-4), 3.65 – 3.56 (m, 3H), 3.53 (t, *J* = 8 Hz, 1H, H-2′), 2.02 (s, 3H, OC*H*$_3$), 1.95 (s, 3H, OC*H*$_3$); ^{13}C NMR (125 MHz, $CDCl_3$): δ = 170.7, 169.7, 164.0, 149.8, 147.5, 138.3, 138.1, 137.7, 137.5, 136.8, 135.4, 133.2, 133.0, 128.5, 128.4, 128.2, 128.16, 128.1, 128.0, 127.9, 127.8, 127.6, 127.58, 127.5, 127.47, 127.3, 126.9, 126.5, 126.1, 126.0, 125.8, 125.5, 99.4 (C-1′, J_{CH} = 162.6), 97.0 (C-1, J_{CH} = 163.4) 82.8 (C-3), 81.4 (C-2′), 81.1 (C-3′), 77.2 (C-4), 75.0, 74.96, 74.9, 74.6, 73.4, 73.2 (C-5'), 73.0 (C-5), 72.8 (C-2), 71.9 (C-4′), 69.3, 62.8 (C-6), 20.9, 20.8; HRMS–ESI (*m/z*): [M + Na]$^+$ calcd for $C_{57}H_{59}NNaO_{14}^+$, 1054.3984; found, 1054.4000.

6-*O*-Acetyl-2,3-*O*-benzoyl-4-*O*-benzyl-β-D-glucopyranosyl-(1→1′)-2′,3′,6′-tri-*O*-benzyl-4′-*O*-picoloyl-β-D-glucopyranoside 59: R_f 0.4 (Hexanes/EtOAc, 1/1); $[\alpha]_D^{20}$ +5.4 (*c* = 0.37, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$): δ = 8.71 (d, *J* = 4.0 Hz, 1H), 8.00 – 7.90 (m, 5H), 7.75 (td, *J* = 2.0, 8.0 Hz, 1H), 7.55 – 6.99 (m, 27H), 5.78 (t, *J* = 9.0 Hz, 1H, H-3), 5.46 (dd, *J* = 8.0, 9.5 Hz, 1H, H-2), 5.17 (t, *J* = 15.0 Hz, 1H, H-4′), 5.14 (d, *J* = 8.0

Hz, 1H, H-1), 5.00 (d, *J* = 10.5 Hz, 1H), 4.86 (d, *J* = 8.0 Hz, 1H, H-1′), 4.74 (d, *J* = 13.0 Hz, 1H), 4.63 (d, *J* = 10.5 Hz, 1H), 4.58 (dd, *J* = 11, 8 Hz, 2H), 4.51 (d, *J* = 11.0 Hz, 1H), 4.44 (dd, *J* = 2.5, 12.0 Hz, 1H, H-6a), 4.38 (s, 2H), 4.30 (dd, *J* = 4.5, 12.0 Hz, 1H, H-6b), 3.95 (t, *J* = 9.5 Hz, 1H, H-4), 3.80 (t, *J* = 9.5 Hz, H-3′), 3.79 (dd, *J* = 2.5, 6.5 Hz, 1H, H-5′), 3.77 (dd, *J* = 2.5, 6.0 Hz, 1H, H-5), 3.52 – 3.40 (m, 3H including H-2′, H-6a′, and H-6b′), 2.06 (s, 3H); ^{13}C NMR (126 MHz, $CDCl_3$): δ = 170.63, 165.56, 165.52, 164.00, 149.73, 147.46, 138.30, 138.10, 137.77, 136.83, 133.24, 133.04, 129.81, 129.73, 129.53, 129.35, 128.46, 128.40, 128.25, 128.24, 128.20, 128.13, 128.06, 127.97, 127.85, 127.81, 127.76, 127.68, 127.64, 127.54, 127.52, 127.25, 126.86, 125.45, 99.5 (C-1, J_{CH} = 162.8 Hz), 97.0 (C-1′, J_{CH} = 163.4 Hz), 81.3 (C-2′), 81.00 (C-3′), 75.5 (C-4), 75.06, 75.03, 74.7, 74.6, 73.5, 73.2 (C-5 and C-5′), 72.1 (C-4′), 71.9 (C-2), 69.6 (C-6′), 62.7 (C-6), 29.7; HRMS–ESI (*m/z*): $[M + H]^+$ calcd for $C_{62}H_{60}NO_{15}^+$, 1058.3957; found, 1058.3954.

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[1] A. D. Elbein, Y. T.Pan, I. Pastuszak, D. Carroll, *Glycobiology* **2003**, *13*, 17R-27R.
[2] C. Uriel, J. Ventura, A. M. Gómez, J. C. López, B. Fraser-Reid, *J. Org. Chem.* **2012**, *77*, 795-800.
[3] P. Shaul, R. I. Benhamou, I. M. Herzog, S. Louzoun Zada, Y. Ebenstein, M. Fridman, *Org. Biomol. Chem.* **2016**, *14*, 3012-3015.
[4] D. Duksin, W. C. Mahoney, *J. Biol. Chem.* **1982**, *257*, 3105-3109.
[5] J. Li, B. Yu, *Angew. Chem. Int. Ed.* **2015**, *54*, 6618-6621; *Angew. Chem.* **2015**, *127*, 6718-6721.
[6] L. A. Dolak, T. M. Castle, A. L. Laborde, *J. Antibiot.* **1980**, *33*, 690-694.
[7] K. Yonehara, T. Hashizume, K. Ohe, S. Uemura, *Tetrahedron: Asymmetry* **1999**, *10*, 4029-4035.
[8] M. J. Weinstein, G. M. Luedemann, E. M. Oden, G. H. Wagman, *Antimicrob. Agents Chemother. (Bethesda)* **1964**, *10*, 24-32.
[9] L. Belova, T. Tenson, L. Xiong, P. M. McNicholas, A. S. Mankin, *Proc. Natl. Acad. Sci.* **2001**, *98*, 3726-3731.
[10] G. Weitnauer, G. Hauser, C. Hofmann, U. Lindeer, R. Boll, K. Pelz, S. J. Bechthold, *Chem. Biol.* **2004**, *11*, 1403-1411.
[11] M. S. Schmidt, V. Wittmann, *Carbohydr. Res.* **2008**, *343*, 1612-1623.
[12] A. A. Khan, B. L. Stocker, M. S. M. Timmer, *Carbohydr. Res.* **2012**, *356*, 25-36.
[13] M. Goren, O. Brokl, B. C. Das, E. Lederer, *Biochemistry* **1971**, *10*, 72-81
[14] P. Domenech, M. B. Reed, S. C. Dowd, C. Manca, C. Kaplan, C. E. Barry, *J. Biol. Chem.* **2004**, *279*, 21257-21265.
[15] D. Geerdink, A. J. Minnard, *Chem. Commun*. **2014**, *50*, 2286-2288.
[16] K. Tahlan, R. Wilson, D. B. Kastrinsky, K. Arora, V. Nair, E. Fischer, S. W. Barnes, J. R. Walker, D. Alland, C. E. Barry, H. I. Boshoff, *Antimicrob. Agents Chemother.* **2012**, *56*, 1797-1809.
[17] A. A. Khan, B. L. Stocker, M. S. M. Timmer, *Carbohydr. Res.* **2012**, *356*, 25-36.
[18] a) V. A. Sarpe, S. S. Kulkarni, *J. Org. Chem.* **2011**, *76*, 6866-6879. b) N. K. Paul, J. D. Twibanire, T. B. Grindley, *J. Org. Chem.* **2013**, *78*, 363-369.
[19] C. H. Wu, C. C. Wang, *Org. Biomol. Chem.* **2014**, *12*, 5558-5562.
[20] V. A. Sarpe, S. S. Kulkarni, *Trends Carbohydr. Chem.* **2013**, *5*, 8-33.
[21] T. E. C. L. Ronnow, M. Meldal, K. Bock, *Tetrahedron: Asymmetry* **1994**, *5*, 2109-2122.
[22] K. C. Nicolaou, F. L. van Delft, S. R. Conley, H. J. Mitchell, Z. Jin, R. M. Rodriguez, *J. Am. Chem. Soc.* **1997**, *119*, 9057-9058.
[23] M. R. Pratt, C. D. Leigh, C. R. Bertozzi, *Org. Lett.* **2003**, *5*, 3185-3188.
[24] L. K, Mydock, A. V. Demchenko, *Org. Biomol. Chem.* **2010**, *8*, 497-510.
[25] L. F. Tietze, R. Fischer, *Angew. Chem. Int. Ed.* **1981**, *20*, 969-970; *Angew. Chem.* **1981**, *93*, 1002.
[26] L. F. Tietze, R. Fischer, H. J. Guder, A. Goerlach, M. Neumann, T. Krach, *Carbohydr. Res.* **1987**, *164*, 177-194.
[27] L. F. Tietze, R. Fischer, *Angew. Chem. Int. Ed.* **1983**, *22*, 888; *Angew. Chem.* **1983**, *95*, 902-903.
[28] J. Yoshimura, K. Hara, T. Sato, H. Hashimoto, *Chem. Lett.* **1983**, 319-320.
[29] G. H. Veeneman, S. H. van Leeuwen, J. H. van Boom, *Tetrahedron Lett.* **1990**, *31*, 1331-1334.
[30] A. B. Ingle, C. S. Chao, W. C. Hung, K. K. T. Mong, *Org. Lett.* **2013**, *15*, 5290-5293.
[31] S. Y. Ru, Y.-H. Lai, J.-H. Chen, C.-Y. Liu, K. K. T. Mong, *Angew. Chem. Int. Ed.* **2011**, *50*, 7315–7320.
[32] J. P. Yasomanee, A. V. Demchenko, *J. Am. Chem. Soc.* **2012**, *134*, 20097-20102.
[33] J. H. Ruei, P. Venukumar, A. B. Ingle, K. K. T. Mong, *Chem. Commun.* **2015**, *51*, 5394-5397.
[34] K. Bock, C. Pedersen, *J. Chem. Soc. Perkin Trans. 2,* **1974**, 293-297.
[35] Initially, we used a known protocol (L. F. Tietze, R. Fischer, H. J. Guder *Synthesis*, *1982*, 946-948) based on the anomerization of a α/β mixture to prepare the TMS α-glucoside **7** and **8**, but the stereoselectivity and yield were impractical. Therefore we developed the α-silylation protocol.
[36] A. A. Joseph, V. P. Verma, X. Y. Liu, C. H. Wu, V. M. Dhurandhare, C. C. Wang, *Eur. J. Org. Chem.* **2012**, 744-753.
[37] If the TMSOTf and HDMS were added together, a 1:1 α:β mixture of TMS glycosides was obtained.
[38] Further attempts to improve the conversion of silylation were not successful.
[39] D. Crich, W. Cai, *J. Org. Chem.* **1999**, *64*, 4926-4930.
[40] Z. Zhang, I. R. Ollmann, X.-S. Ye, R. Wischnat, T. Baasov, C.-H. Wong *J. Am. Chem. Soc.* **1999**, *121*, 734-753.
[41] J. Tatai, P. Fugedi, *Org. Lett.* **2007**, *9*, 4647-4650.
[42] A. K. Kayastha, X. G. Jia, J. P. Yasomanee, A. V. Demchenko, *Org. Lett.* **2015**, *17*, 4448-4451.
[43] In the structure–selectivity study, we intended to examine the picolinyl (Pic) TMS α-glucoside, but purification of the Pic protected TMS glucoside was difficult.
[44] Indeed, the NMR spectrum of **7** remained largely unchanged after treatment with TMSOTf for >48 h.
[45] T. J. Barton, C. R. Tully, *J. Org. Chem*. **1978**, 43,3649-3653.
[46] T. Tsuno, C. Ikeda, K. Numata, K. Tomita, M. Konishi, H. Kawaguchi. *J. Antibiotics* **1986**, *39*, 1001-1003.
[47] B. Capon, S. P. McManus, *Neighboring Group Participation, Vol. 1*, Plenum Press, New York, **1976**.
[48] B. Fraser-Reid, S. Grimme, M. Piacenza, M. Mach, U. Schlueter, *Chem. Eur. J.* **2003**, *9*, 4687 and references cited therein.
[49] L. Bohe, D. Crich, *C. R. Chimie*. **2011**, *14*, 3-16.
[50] During revision, a reviewer suggested to add such an experiment to examine the stability of the 1β,1′α-anomer of **50** in acidic conditions.
[51] K. C. Nicolaou, H. J. Mitchell, K. C. Fylaktakidou, R. M. Rodriguez, H. Suzuki, *Chem. Eur. J.* **2000**, *6*, 3116-3148.
[52] D. Crich, S. Sun, *J. Org. Chem.* **1996**, *61*, 4506-4507.
[53] S.-S. Chang, C.-H. Shih, K.-C. Lai, K. K. T. Mong, *Chem. Asian J.* **2010**, *5*, 1152-1162.
[54] We also examined the use of Me_2S_2-Tf_2O promoter for 1β,1′β-disaccharide synthesis, but the selectivity was slightly lower than that given by NIS and TMSOTf promoters.

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Layout 2:

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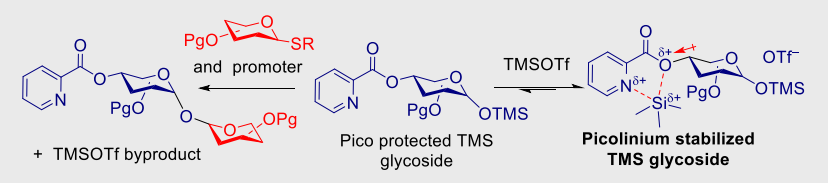

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