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Article

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Application of 2-Substituted Benzyl Groups in Stereoselective Glycosylation

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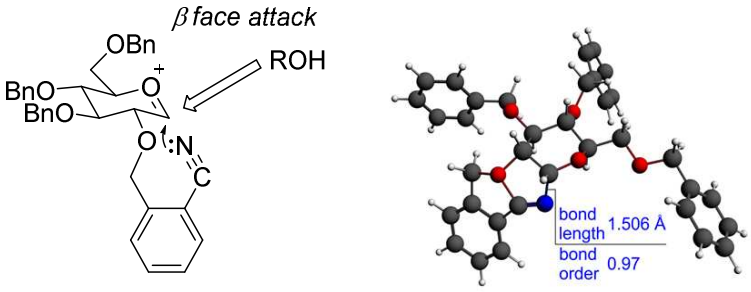
TOC Graphic



Abstract: The use of 2-*O*-(2-nitrobenzyl) and 2-*O*-(2-cyanobenzyl) groups control stereoselective formation of 1,2-*trans*-glycosidic linkage via arming participation effect. Observed stereoselectivity arise likely from the intramolecular formation of cyclic intermediate between electron rich substituent and donor oxacarbenium ion providing expected facial selectivity for the attack of the glycoside acceptor. The stereodirecting effect of the 2-nitro- and 2-cyanobenzyl groups attached at remote position (C-3, C-4, and C-6) of donor molecule have also been investigated. To prove postulated mechanism based on participation effect of 2-substituted benzyl groups in the glycosylation stereoselectivity we used DFT theoretical calculation methodology.

Introduction

Because of the importance and prominent role the oligosaccharides play in biology and pharmaceutical industry, stereoselective formation of glycosidic bond are probably the most

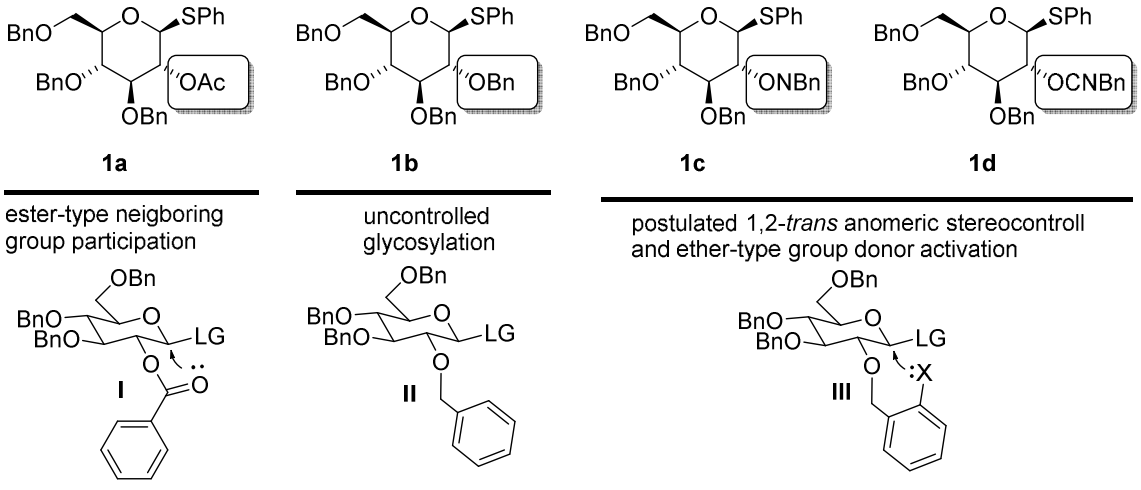
important aspect of modern carbohydrate chemistry.[1] Despite many various strategies available for the efficient and stereocontrolled synthesis di- and oligosaccharides, this field still deserves additional attention.[2] The most commonly used strategy for the synthesis of glycosidic bond involves nucleophilic coupling of suitably protected glycosyl acceptor (ROH) with fully protected donor bearing a leaving group (LG) at its anomeric center.[3] Nucleophilic attack of a hydroxyl moiety of a glycosyl acceptor to the flattened oxacarbenium ion resulting from the leaving group departure often leads to usually undesired α- and β-anomers mixture.[4]

Stereocontrolled synthesis of one anomer requires special techniques, among whose the most reliable is selective equipment of donor molecule with the groups controlling glycosylation *via* intramolecular stereodirecting effects. Thus, the most studied application of 2-*O*-acyl functionality (Scheme 1, **I**) depends on neighboring group participation of ester protecting group which gives a more stable oxacarbenium ion shielded by protecting group from one site. An alcohol can attack the anomeric center from only one face providing 1,2-*trans*-glycoside. However, application of ester-type substituents which electronically deactivate donor molecule decrease the reaction yield, in many cases. In contrast, application of ether-type substituent (Scheme 1, **II**) which electronically activate donor usually lead to a mixture of both anomers, resulting from unhindered approach of alcohol from both sites of flattened oxacarbonium ion.

Interestingly, application of an electron-rich ether-type substituent which could control glycosylation *via* neighboring group participation has been neglected for many years. In 2005, Demchenko demonstrated 1,2-trans glycosylation by developing the neighboring 2-*O*-picolinyl (pyridylmethyl) ether.[5] Pyridine-based N-donor was demonstrated to be capable of efficient participation when attached at C-2, but also at C-3, C-4, and C-6 position of glycosyl donor.[6] In the case of remote picolinyl substituent authors postulate intermolecular H-bond tethering with glycosyl acceptor instead of direct participation of nitrogen atom to anomeric

position.[6] Stereoselective 1,2-*cis* glycosides by using (*S*)-(phenylthiomethyl)benzyl and 2-*O*-(thiophen-2-yl)methyl protecting group have been demonstrated by Boons[7] and Fairbanks,[8] respectively. According to authors, observed α-selectivity results from the intramolecular formation of a transition six-membered intermediate sulfonium/thiophenium ion, which then undergoes nucleophilic substitution by the glycosyl acceptor from the α-site. In parallel, some other non-benzyl groups for participation-assisted or stereodirectiong glycosylation have been recently introduced.[9] In contrast, successful examples of regular benzyl ethers substituted at aromatic ring (Scheme 1, **III**) have never been deeply explored. This concept, however, seems to have great potential and the use of neighboring participation by using benzyl-type group may have important impact on the field by combining at least two advantages: the use of activated (armed) donor and easy one-step deprotection of all benzyl-type groups at the most convenient stage.

Here, we report the first use of 2-substituted benzyl groups as stereodirecting substituents for the formation of 1,2-*trans*-glycosidic linkage. As the benzyls can be removed after glycosylation, they can be used as stereodirecting protecting groups broadly expending application of benzyl groups in carbohydrate chemistry and chemical glycosylation.



Scheme 1. Glycosyl Donors with 2-*O*-Acetyl-(**1a**), 2-*O*-Benzyl-(**1b**), 2-*O*-(2-Nitrobenzyl)-(**1c**) and 2-*O*-(2-Cyanobenzyl)-(**1d**) Groups

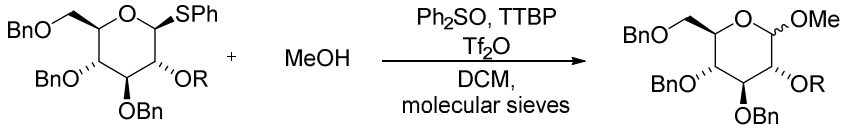
Results and Discussion

Previously we showed that that 1,2-*trans* stereoselectivity in glycosylation can be achieved by using 2-*O*-(2-nitrobenzyl) which can act as a neighboring glycosylation support of type **III** (Scheme 1).[10] Assuming that other substituted benzyl groups can show similar features and takin into account relatively low stability of nitrobenzyl ethers we decided to broaden the scope of this method and investigate whether similar effect can be achieved by using other benzyl ethers. After initial trials we selected 2-cyanobenzyl as comparatively promising candidate to nitrobenzyl. Different geometry and electronic nature of both groups and different availability of electron pairs further encouraged for comparison of both benzyl groups. Moreover, in contrast to well-known external nitrile effect,[11] discovering of similar influence of cyano substituent from the same sugar remote position seemed to be highly exciting.

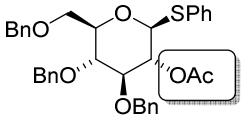
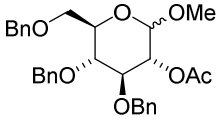
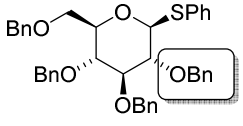
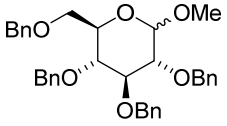
As the starting comparison points, we decided to use per-*O*-benzylated thioglucoside **1b** and 2-*O*-(2-nitrobenzyl)-(**1c**) as well as 2-*O*-(2-cyanobenzyl) thioglucoside (**1d**) donors. Both benzyl ethers (NBn, CNBn) could be efficiently prepared from the corresponding alcohols by using routine methodology as that used for regular benzyl ehers. All three donors **1b**-**d** as well as 2-*O*-(acetyl) thioglucoside (**1a**) were activated by treatment with Ph_2SO and triflic anhydride (Tf_2O) in the presence of 2,4,6-tri-*tert*-butyl-pyridine (TTBP) in dichloromethane as a standard condition,[12] and coupled with methanol to afford methyl glucoside **2a**-**d** (Table 1). According to expectation, glycosidation of donor **1a** resulted in exclusive formation of β-methyl glucoside **2a** although in low yield (44%) as combining effect of disarming participating effect of ester substituent (Table 1, entry 1). In contrast,

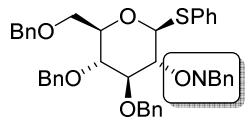
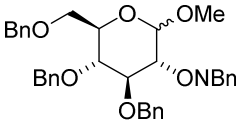
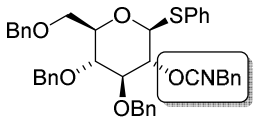
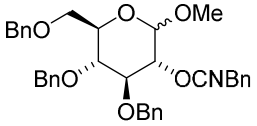
glycosidation of per-*O*-benzylated donor **1b** was more efficient yet unselective leading to a mixture of both anomers in (1:1) ratio (Table 1, entry 2). This significant example of unselective glycosylation in the presence of regular benzyl ether attached to C-2 position of donor constitutes comparison point for forthcoming substituted benzyl groups. Indeed, reactions of both 2-*O*-(2-nitrobenzyl)-(**1c**) and 2-*O*-(2-cyanobenzyl)-(**1d**) thioglucosides turned out to be far more stereoselective. The desired 1,2-*trans* methyl glycosides **2c** and **2d** were isolated in high yields and with high level of β-selectivity (Table 1, entries 3 and 4) thus confirming assumed arming as well as participating effect of both substituted benzyl groups. The reactions with donors **1c**/**1d** methanol as acceptor proceed selectively in range of solvents additionally proved prominent internal effect of 2-nitro- and 2-cyanosubstituents.[13]

Table 1. Glycosylation Reaction of Donors Containing Various 2-*O*-Substituents with Methanol.



1a-d **2a-d**

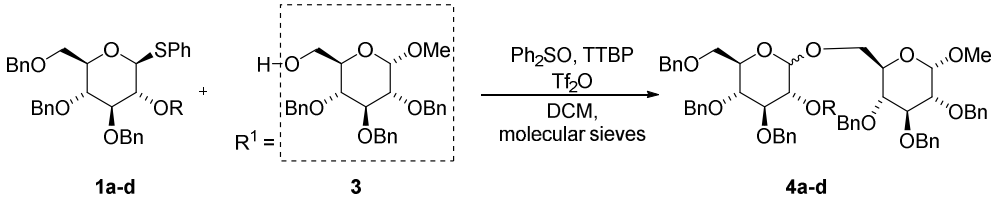
	Donor	Yield [α/β]	Product
1	 **1a**	44% (0:1)	 **2a**
2	 **1b**	91% (1:1)	 **2b**

3	 **1c**	95% (1:12)	 **2c**
4	 **1d**	82% (1:12)	 **2d**

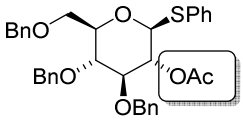
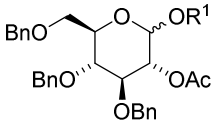
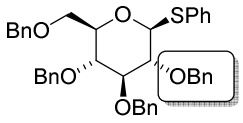
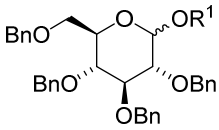
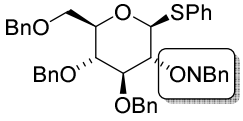
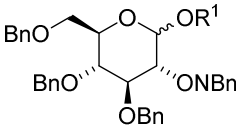
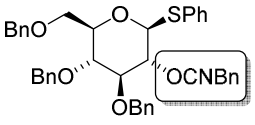
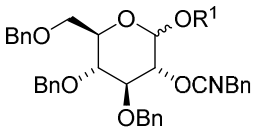
Reaction were performed with donor **1a-d** (0.074 mmol), MeOH (0.11 mmol), Ph_2SO (0.081 mmol), TTBP (0.185 mmol), DCM (5 ml) at –40 °C to r.t. for 3 h.

The same series of donors **1a-d** have been submitted to more demanding glycosylation with methyl 2,3,4-tri-*O*-benzyl-α-D-glucopyranoside (**3**) having primary hydroxyl group at C-6. Results of this trial-by-fire for new benzyl ethers have been collected in Table 2. Glycosylation with **1a** as acceptor produced disaccharide **4a** in a modest yield but with complete β-stereoselectivity (Table 2, entry 1). Glycosylation of donors **1b**-**1d** showed that the stereoselectivity of glycosylation was highly dependent on the electronic structure of benzyl ether at C-2. However with all three armed donors yield of isolated disaccharides (**4b**-**4d**) were high the β-stereoselectivity of the process was considerable for 2-*O*-(2-nitrobenzyl)-(**1c**) and 2-*O*-(2-cyanobenzyl)-(**1d**) thioglucosides only (Table 2, entries 2 *vs.* 3,4). The fact that the glycosylation lead principally to the formation of β-anomers provides strong support that the reactions proceed through neighboring participation of substituted benzyl ethers from α-site of anomeric position in donor ring. The stereocontrolling effect of the 2-nitrobenzyl- and 2-cyanobenzyl groups were accompanied by a great influence on general reaction yield (Table 2, entry 1 *vs.* 3,4) which may be referred to arming effect of newly used benzyl ethers (NBn and CNBn).

Table 2. Glycosylation Reaction with 6-OH Acceptor **3**



1a-d 3 4a-d

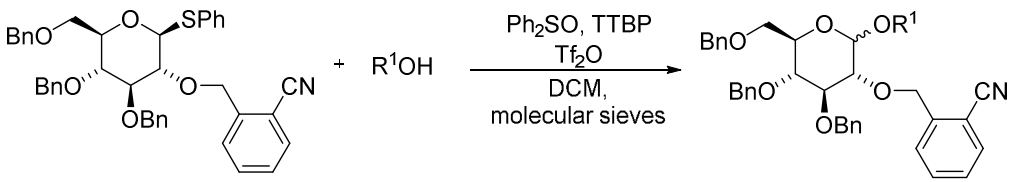
	Donor	Yield [α/β]	Product
1	 1a	42% (0:1)	 4a
2	 1b	60% (1:1)	 4b
3	 1c	88% (1:3)	 4c
4	 1d	86% (1:3)	 4d

Reaction were performed with donor **1a-d** (0.074 mmol), acceptor **3** (0.11 mmol), Ph_2SO (0.081 mmol), TTBP (0.185 mmol), DCM (5 ml) at –40 °C to r.t. for 3 h.

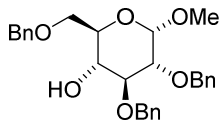
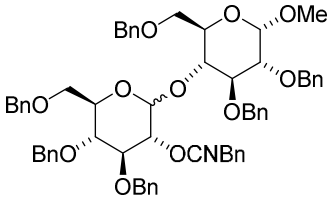
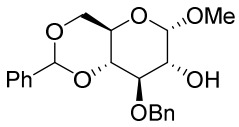
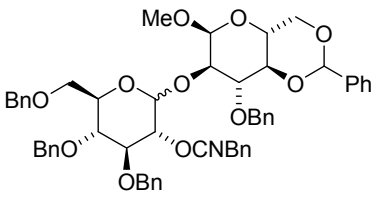
Subsequent investigations focused on glycosylation of donor **1d** with 2-cyanobenzyl groups as relatively more stable and synthetically more useful when compared to 2-nitro-counterpart. More investigations and results with donor **1c** have been presented in our

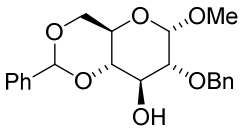
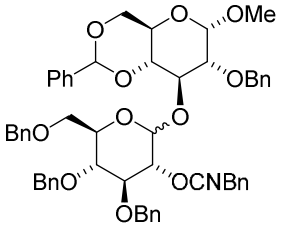
previous work.[10] The synthetic scope of the current 2-cyanobenzyl protecting group was examined by changing the structure of acceptors (Table 3). The glycosylation of **1d** with **5**, which has a secondary hydroxyl group at C-4, proceed smoothly and afforded the desired *O*-glycoside **8** with high β-selectivity and high yield (Table 3, entry 1). The glycosylation of **1d** with **6** and **7**, which have equatorially hydroxyl group at C-2 and C-3, respectively, also afforded disaccharides **9** and **10** with predominant formation of β-anomers (Table 3, entries 2 and 3). Reaction of non-sugar alcohols (propan2-ol, benzyl alcohol and nonan-1-ol) proceeded even better, and resulted in a formation of expected β-anomers, exclusively (Table 3, entries 4-6).

Table 3. Example of Various Glycosyl Acceptors Tested in Glycosylation with Donor **1d**



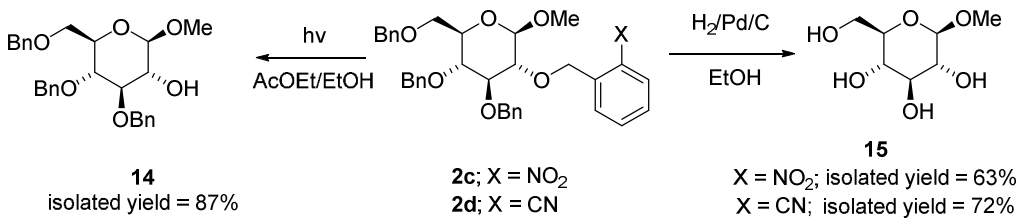
1d **8 - 13**

Entry	Acceptor	Yield (α/β)	Product
1	 **5**	67% (1:5)	 **8**
2	 **6**	34% (1:5)	 **9**

3	 **7**	72% (1:4)		**10**
4	propan-2-ol	78% (0:1)	$R_1 = {}^{i}Pr$	**11**
5	benzyl alcohol	67% (1:10)	$R_1 = Bn$	**12**
6	nonan-1-ol	54% (0:1)	$R_1 = C_9H_{19}$	**13**

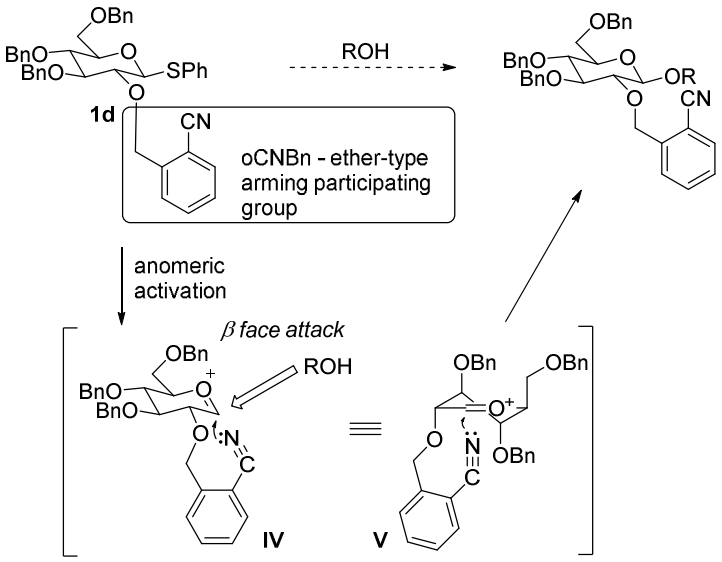
Reaction were performed with donor **1d** (0.074 mmol), acceptor (0.11 mmol), Ph_2SO (0.081 mmol), TTBP (0.185 mmol), DCM (5 ml) at – 40 °C to r.t for 3 h.

In order to prove the applicability of the new methodology in organic synthesis we examined possibility of mild deprotection of thus utilized 2-benzyl ethers from glucoside **2c** and **2d** (Scheme 1). Both ethers were easily cleaved when using standard debenzylation conditions (H_2/Pd-C). This methodology can be used for convenient deprotection of all benzyl substituents when necessary. Additionally, 2-nitrobenzyl protecting group can be also selectively cleaved in the presence of other benzyl groups by light irridation[14] affording methyl 3,4,6-tri-*O*-benzyl-β-D-glucopyranoside (**14**) in high yield. This mild deprotection method can further open up new areas of application of 2-nitrobenzyl as arming participating protecting group.



Scheme 2. Pd/C Hydrogenation and Selective UV-light Deprotection of 2-Nitrobenzyl Group

This successful application of 2-nitrobenzyl (NBn) and 2-cyanobenzyl (CNBn) as arming participating groups controlling 1,2-*trans*-glycosidic bond formation rely on the assumption of neighboring group participation of both tested benzyl ethers. Thus, we postulate that the oxocarbenium ion is controlled as a stable intermediate by electrons of 2-*O*-CNBn (Scheme 3) or 2-*O*-NBn protecting group. Formal participation of the nitrogen (CN) or oxygen (NO_2) will give a more stable oxacarbenium ion providing β-glycosides after alcohol attack from only one face providing 1,2-*trans*-glycoside (Scheme 3).



Scheme 3. Proposed Participating Group Concept by Using Cyanobenzyl Group

To exclude alternative explanations,[15] and to prove previously postulated mechanism based on participation of 2-substituted benzyl groups in the glycosylation, we used DFT theoretical calculation methodology. The main goal of the theoretical (DFT) calculations was to investigate the electronic structure of the cationic form of **IV** (see Scheme 2) with and without presence of leaving anion (OTf), to verify the possibility of formation of an intra-molecular bond between the nitrile group and the cationic carbon centre. The minimum energy structure of the cation is shown in Figure 1, structure **A**. In the absence of anion, a strong, 'single' bond between nitrogen atom from nitrile group and carbon from glucose ring

is formed: the distance is 1.506Å, and the calculated bond-order is 0.968. As the result, the carbon-nitrogen bond in nitrile group can be described as 'double' bond, with the bond order of 2.110, and the bond length equal to 1.236Å. In addition, the significant interaction between the carbon atom of nitrile group and the ether oxygen can be observed, characterized by the bond order value of 0.670 and the distance of 1.625Å. This may result from shifting electron density toward glucose ring and formation of a partial positive charge on the nitrile carbon atom. Thus, in the cationic structure **A** two additional five-member rings are observed.

For neutral systems in which cationic glucose derivative is neutralized by OTf anion, two low energy structures were obtained from geometry optimization, presented in Figure 1 (panels B and C). Here, the structure with unbounded nitrile group is slightly lower in energy (by c.a. 1 kcal/mol), than the structure in which the bond between the nitrile nitrogen and the glucose carbon atom is preserved. However, since the energy difference is relatively low (below 1 kcal/mol), it can be expected that these structures can coexist.

Two conclusions emerge from comparison of the structures presented in Figure 1. Firstly, the bond between oxygen atom of OTf anion and the respective glucose carbon is longer/weaker in structure B (bond length: 1.525Å; bond order: 0.908) than in structure C (bond length: 1.413Å; bond order: 1.077). Secondly, the comparison of structures A and C leads to a conclusion that the interaction between cationic species and anion results in strengthening of nitrogen-carbon bond for C (increase in bond order from 0.968 to 1.065), while for structure B such interaction is not observed - the distance between nitrogen atom and glucose carbon is 5.871Å. These results support our assumption about participation of the nitrogen of CN group via formation of C-N bond with anomeric center of the oxacarbenium ion efficiently shielding α-face providing 1,2-*trans*-glycoside (Scheme 3).

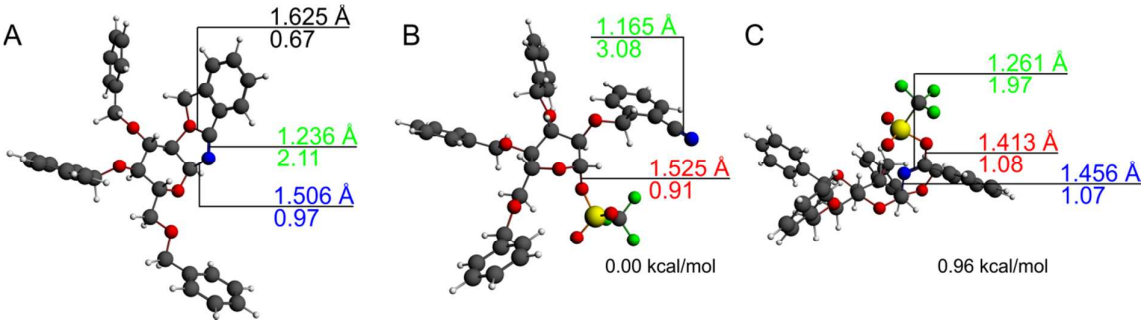


Figure 1. Comparison of bond lengths (top value) and bond orders (bottom value) for optimized models of structure **I** for cationic molecule (panel A), and neutral systems including anion (panels B and C). For structures B and C, the electronic energy difference is also presented.

In order to draw qualitative conclusions concerning the interaction of the analyzed system with nucleophiles, the molecular electrostatic potential (MEP) was characterized for compounds B and C, the colour-coded contour is presented in Figure 2. A comparison clearly shows that in the vicinity of the respective carbon atom undergoing the nucleophilic attack, the MEP is more positive for structure C than for B. Thus, it may be predicted, that the structure C will be more reactive towards nucleophilic attack. This further strengthens the conclusion about the importance of the intra-molecular bond between the nitrile nitrogen atom and the carbon atom of glucose, as a possible origin of the experimentally observed stereoselectivity.

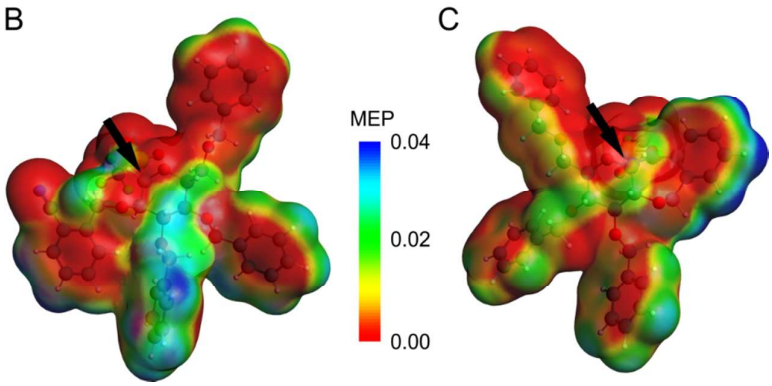
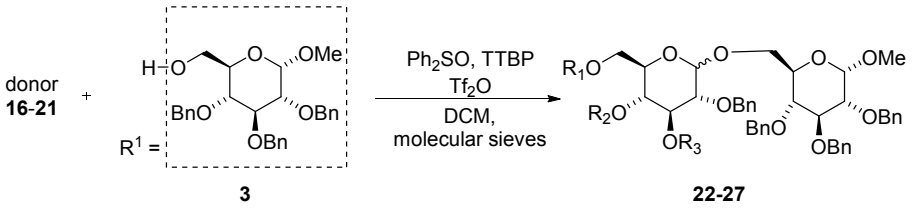


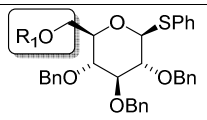
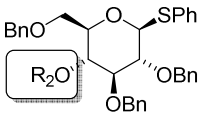
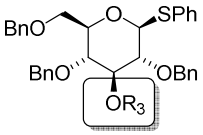
Figure 2. Molecular Electrostatic Potential (MEP), colour-coded on the electron density isosurface (ρ = 0.001 a.u.) for structures B (left) and C (right); the arrow points to the respective carbon atom that can be attacked by a nucleophile in the glycosylation reaction mechanism.

It was also interesting whether participating effect of 2-substituted benzyl groups could be visible from remote positions of donors. The effect that these remote substituents may have on the reaction stereoselectivity was estimated at this stage. To asses this possibility, we tested a series of novel glycosyl donors equipped with 2-nitrobenzyl (NBn) and 2-cyanobenzyl (CNBn) groups at remote positions *i.e.* C-6 (**16**, **17**), C-4 (**18**, **19**) and C-3 (**20**, **21**). Results of this study collected in Table 4 showed that observed level of stereoselectivity controlled by remote benzyl groups is not exceptionally high, while formation of either α- or β-anomers supported our assumptions. Thus, 6-*O*-equiped thioglycoside **18** and **19** gave disaccharide **24** and **25** with reversed α-selectivity (Table 4, entry 1). In contrast, isomers with 4-*O*-substituted benzyl groups **18** and **19** showed tendency for predominant formation of β-glycosides **24** and **25** (Table 4, entry 2) while 3-*O*-substituted donors were simply unselective (Table 4, entry 3).

Table 4. Example of Remote Control in Glycosylation.

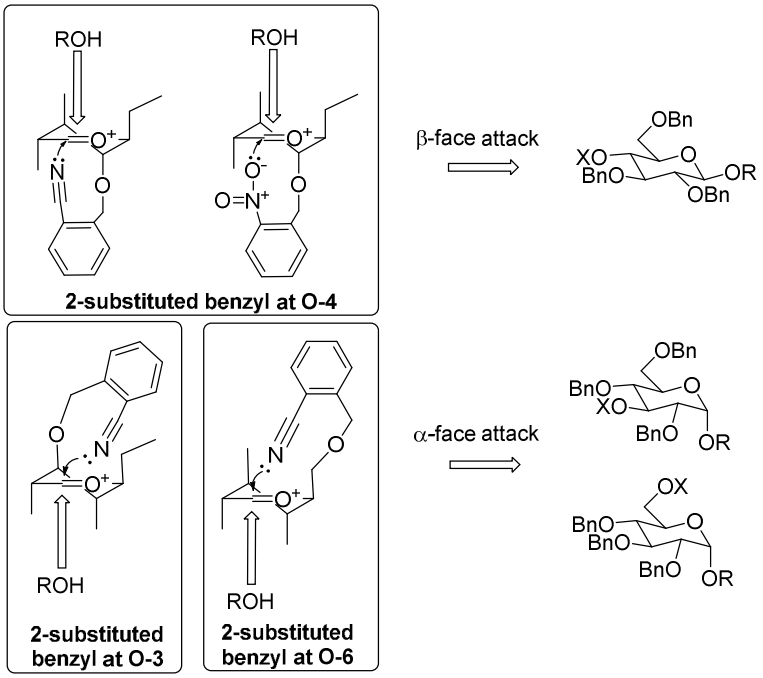


Donor	Yield [α/β]	Product

1	 **16:** R_1=NBn **17:** R_1=CNBn	73% (2:1) 85% (2:1)	**22:** R_1=NBn, R_2=R_3=Bn **23:** R_1=CNBn, R_2=R_3=Bn
2	 **18:** R_2=NBn **19:** R_2=CNBn	79% (1:3) 93% (1:2)	**24:** R_2=NBn, R_1=R_3=Bn **25:** R_2=CNBn, R_1=R_3=Bn
3	 **20:** R_3=NBn **21:** R_3=CNBn	98% (1:1) 80% (1:1)	**26:** R_3=NBn, R_1=R_2=Bn **27:** R_3=CNBn, R_1=R_2=Bn

Reaction were performed with donor **16-21** (0.074 mmol), **3** (0.11 mmol), Ph_2SO (0.081 mmol), TTBP (0.185 mmol), DCM (5 ml) at –40 °C to r.t. for 3 h.

Explanation for various modes of participating group effect is showed in Scheme 3. 2-Nitro and 2-cyano substituted benzyl groups attached to C-4 position can interact with oxacarbenium ion in *cis*-facial relation providing expected β-selectivity for the attack of the glycoside acceptor. Direct interaction between 6-*O*-substituted benzyl groups with anomeric center resulted in predominant formation of α-glycosides (Scheme 4) while non-selective reaction of 3-*O*-substituted thioglycoside resulted from ineffective shielding interaction of substituent and anomeric center.



Scheme 4. Remote Participation of 2-cyano- and 2-nitrobenzyl Groups

Conclusions

In summary, we presented that 2-substituted benzyl protecting groups can efficiently control stereoselective formation of 1,2-*trans*-glycosidic linkage thus acting as armed participating groups. We demonstrated that 1,2-*trans*-stereoselectivity can be achieved by using 2-*O*-(2-nitrobenzyl) and 2-*O*-(2-cyanobenzyl) ethers, which can act as neighboring glycosylation support. This ether group can also enhance the reaction yield by activation (arming) glycosyl donors, in contrast to broadly used deactivating esters. Similar yet lower stereoselectivity can be achieved by using remote benzyl groups. Easy protection and selective deprotection of presented 2-nitrobenzyl 2-cyanobenzyl group further confirms its usefulness in the synthesis.

Experimental Section

General Information. All starting materials and reagents were obtained from commercial sources and used as received unless otherwise noted. All solvents used were freshly distilled

prior to use. Optical rotations were measured at room temperature with a polarimeter. High-resolution mass spectra were acquired using electrospray (ESI) ionization mode with a time-of-flight (TOF) detector. ^{1}H NMR spectra were recorded on spectrometers operating at 300, 500 and 600 MHz in $CDCl_3$. Data were reported as follows: chemical shifts in parts per million (ppm) from tetramethylsilane as an internal standard, integration, multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, dd = double-doublet, m = multiplet, br = broad), coupling constants (in Hz), and assignment. ^{13}C NMR spectra were measured at 75, 125 or 150 MHz with complete proton decoupling. Chemical shifts were reported in ppm from the residual solvent as an internal standard. Reactions were controlled using TLC on silica [alu-plates (0.2 mm)]. Plates were visualized with UV light (254 nm) and by treatment with:, aqueous cerium(IV) sulfate solution with molybdic and sulfuric acid followed by heating. All organic solutions were dried over anhydrous sodium sulfate. Reaction products were purified by flash chromatography using silica gel 60 (240-400 mesh).

All the DFT calculations presented here are based on the Amsterdam Density Functional (ADF2013) program.[16-19] Structures were fully optimized using the Becke-Perdew exchange-correlation functional (BP86).[20,21] For obtained geometries dispersion correction to energy was calculated using BP86-D3 with Becke-Johnson Damping.[22,23] Full electron basis set with a triple-zeta STO basis containing two sets of polarization functions, was adopted for all of the elements (TZ2P). Auxiliary *s, p, d, f* and *g* STO functions, centered on all nuclei, were used to fit electron density and obtain accurate Coulomb potentials in each SCF cycle. Relativistic effects were included using the ZORA formalism. The contours and the color-coded plots of the molecular electrostatic potential were plotted based on ADF-GUI interface.[24] Nalewajski-Mrozek bond-multiplicity indices[25,26] implemented in ADF program were used to quantify selected bond-orders.

Synthesis and spectroscopic data for compound **1a-1c**, **2a-c**, **3**, **4a-c**, **14**, **15** were described previously.[10] Synthesis of known compound **5** have been performed based on method presented by Cheng,[27] known compounds **6** and **7** were prepared based on method presented by Potter.[28]

Phenyl 3,4,6-tri-O-benzyl-2-O-(o-cyanobenzyl)-1-thio-β-$_D$-glucopyranoside (**1d**, Scheme 1): Phenyl 2-*O*-acetyl-3,4,6-tri-*O*-benzyl-1-thio-β-$_D$-glucopyranoside (3 g, 5.1 mmol, 1 equiv.) was dissolved in CH_3OH (15 mL) and KCN (36 mg, 0.5 mmol) was added. The reaction was stirred for 2 h, and another 36 mg KCN was added. After an additional two hours, TLC indicated that the reaction was complete, and the mixture was concentrated *in vacuo* and dry in high *vacuo* for 3 h. To the crude oil was added anhydrous MeCN (40 mL) and the solution was cooled to 0 °C. Sodium hydride (245 mg, 60% dispersion in mineral oil, 6.1 mmol, 1.2 equiv.) was added carefully; the mixture was stirred at 0 °C for 30 minutes. Then *o*-cyanobenzyl bromide (1.21 g, 5.6 mmol, 1.1 equiv.) was added in 3 mL MeCN solution, and the mixture was allowed to warm to room temperature overnight. The mixture was quenched with methanol (3 mL). The phases were separated and the aqueous phase was extracted with ethyl acetate (4 × 20 mL). The combined organic extracts were dried over Na_2SO_4, filtered and concentrated *in vacuo*. Purification of the residue by crystallization from mixture EtOH/H_2O afforded phenyl 3,4,6-tri-*O*-benzyl-2-*O*-(*o*-cyanobenzyl)-1-thio-β-$_D$-glucopyranoside (**1d**) (2.7 g, 78%); mp: 92 – 93 ^oC; $[\alpha]_D^{20}$ = –15.0 (*c* = 1.0, $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$) δ 7.68 (d, *J* = 7.8 Hz, 1H), 7.63 (dd, *J* = 7.7, 1.2 Hz, 1H), 7.61 – 7.50 (m, 3H), 7.42 – 7.19 (m, 20H), 5.08 (d, *J* = 12.5 Hz, 1H), 4.99 (d, *J* = 12.5 Hz, 1H), 4.86 (s, 2H), 4.83 (d, *J* = 10.9 Hz, 1H), 4.69 (d, *J* = 9.7 Hz, 1H), 4.65 (d, *J* = 7.3 Hz, 1H), 4.61 (d, *J* = 12.1 Hz, 1H), 4.54 (d, *J* = 12.1 Hz, 1H), 3.86 – 3.64 (m, 4H), 3.55 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 141.9, 138.3, 138.2, 138.1, 133. 4, 132.7, 132.6, 132.0, 129.0, 128.6, 128.4, 127.9,

127.8, 127.7, 127.6, 117.2, 110.9, 87.1, 86.5, 81.1, 79.1, 77.9, 77.2, 75.7, 75.0, 73.4, 72.3, 69.0; HRMS (ESI-TOF): calcd. for $C_{41}H_{39}NO_5S$ $[M+Na]^+$: 680.2447, found 680.2433.

Synthesis of donors **16-21** have been performed from corresponding alcohols with free hydroxyl groups at C-3, C-4, and C-6. Synthesis and spectroscopic data for *phenyl 2,3,4-tri-O-benzyl-1-thio-β-$_D$-glucopyranoside* was described by McGarrigle and co-workers.[29] Synthesis of *phenyl 2,3,6-tri-O-benzyl-1-thio-β-$_D$-glucopyranoside* have been performed based on method presented by Møller.[30] *Phenyl 2,4,6-tri-O-benzyl-1-thio-β-$_D$-glucopyranoside* have been prepared based on method presented by Kanie.[31]

General procedures for the preparation of 16, 18 and 20 (Procedure A)

Sugar derivate with free hydroxyl group (1 eq.) and tetrabutylammonium bromide (0.1 eq.) was dissolved in CH_2Cl_2 (10 ml). Then was added 33% KOH solution (10 ml) and the mixture was vigorously stirred at room temperature for 30 minutes. After this time, *o*-nitrobenzyl bromide (1.5 eq.) was added and the reaction was stirred until complete consumption of starting material (monitored by TLC). Then water (20 ml) was added and the mixture extracted with CH_2Cl_2 (3 × 30 mL). The combined organic layer was dried over Na_2SO_4, filtered and concentrated *in vacuo*. Purification of the residue by crystallization from mixture EtOH/H_2O to give corresponding products.

General procedures for the preparation of 17, 19 and 21 (Procedure B)

The starting material (1 eq.) was dissolved in anhydrous MeCN (15 mL) and the solution was cooled to 0 °C. Sodium hydride (60% dispersion in mineral oil, 2 eq.) was added carefully

and the mixture was stirred at 0 °C for 1 h. Then *o*-cyanobenzyl bromide (1.5 eq.) was added in 1 mL MeCN solution and the mixture was allowed to warm to room temperature overnight. The mixture was quenched with methanol (1 mL) and the aqueous phase extracted with ethyl acetate (4 × 20 mL). The combined organic extracts were dried over Na_2SO_4, filtered and concentrated *in vacuo*. Purification of the residue by crystallization from mixture EtOH/H_2O afforded corresponding products.

Phenyl 2,3,4-tri-O-benzyl-6-O-(o-nitrobenzyl)-1-thio-β-$_D$-glucopyranoside (**16,** Table 4); Compound **16** was obtained as white solid (490 mg, 55%); mp: 92 – 93 ^oC; $[\alpha]_D^{20}$ = –3.7 (*c* = 1.0, $CHCl_3$); ^1H NMR: (600 MHz, $CDCl_3$) δ 8.09 (dd, *J* = 8.2, 1.2 Hz, 1H), 7.85 (dd, *J* = 7.9, 1.0 Hz, 1H), 7.61 (td, *J* = 7.7, 1.2 Hz, 1H), 7.58 – 7.56 (m, 2H), 7.43 (ddd, *J* = 8.2, 1.4, 0.7 Hz, 1H), 7.41 – 7.39 (m, 2H), 7.35 – 7.22 (m, 16H), 4.95 – 4.89 (m, 3H), 4.88 – 4.84 (m, 3H), 4.75 (d, *J* = 10.3 Hz, 1H), 4.69 (d, *J* = 9.8 Hz, 1H), 4.62 (d, *J* = 11.1 Hz, 1H), 3.84 (dd, *J* = 10.7, 1.9 Hz, 1H), 3.79 (dd, *J* = 10.7, 4.7 Hz, 1H), 3.74 (t, *J* = 8.9 Hz, 1H), 3.67 (t, *J* = 9.4 Hz, 1H), 3.56 – 3.52 (m, 1H), 3.53 (dd, *J* = 9.7, 8.7 Hz, 1H); ^{13}C NMR: (151 MHz, $CDCl_3$) δ 146.9, 138.3, 138.0, 137.9, 135.4, 133.8, 133.7, 133.7, 132.0, 128.9, 128.6, 128.5, 128.5, 128.5, 128.4, 128.2, 128.2, 127.9, 127.9, 127.8, 127.5, 124.8, 124.6, 87.4, 86.8, 80.8, 78.8, 77.7, 75.9, 75.4, 75.1, 69.8, 69.8; HRMS (ESI-TOF): calcd. for $C_{40}H_{39}NO_7S$ $[M+Na]^+$: 700.2345, found 700.2329.

Phenyl 2,3,4-tri-O-benzyl-6-O-(o-cyanobenzyl)-1-thio-β-$_D$-glucopyranoside (**17**, Table 4); Compound **17** was obtained as white solid (800 mg, 92%); mp: 84 ^oC; $[\alpha]_D^{20}$ = +1.8 (*c* = 1.0, $CHCl_3$); ^1H NMR: (600 MHz, $CDCl_3$) δ 7.63 (dd, *J* = 7.7, 0.8 Hz, 1H), 7.59 (dd, *J* = 7.8, 0.7 Hz, 1H), 7.58 – 7.53 (m, 3H), 7.40 – 7.21 (m, 19H), 4.91 (d, *J* = 10.9 Hz, 1H), 4.90 (d, *J* = 10.3 Hz, 1H), 4.85 (d, *J* = 11.0 Hz, 2H), 4.76 (d, *J* = 13.1 Hz, 1H), 4.74 (d, *J* = 10.3 Hz, 1H), 4.69 (d, *J* = 9.8 Hz, 1H), 4.69 (d, *J* = 12.6 Hz, 1H), 4.62 (d, *J* = 11.0 Hz, 1H), 3.84 (dd, *J* = 10.8, 1.9 Hz, 1H), 3.79 (dd, *J* = 10.8, 4.7 Hz, 1H), 3.72 (t, *J* = 8.9 Hz, 1H), 3.65 (t, *J* = 9.4 Hz,

1H), 3.55 – 3.51 (m, 1H), 3.52 (dd, *J* = 9.7, 8.7 Hz, 1H); ^{13}C NMR: (151 MHz, $CDCl_3$) δ 142.1, 138.3, 138.0, 137.9, 133.7, 132.8, 132.6, 132.0, 128.9, 128.5, 128.4, 128.3, 128.2, 127.9, 127.9, 127.8, 127.7, 127.4, 117.2, 111.0, 87.4, 86.8, 80.9, 78.9, 77.6, 75.9, 75.4, 75.1, 70.9, 69.8; HRMS (ESI-TOF): calcd. for $C_{41}H_{39}NO_5S$ $[M+Na]^+$: 680.2447, found 680.2407.

Phenyl 2,3,6-tri-O-benzyl-4-O-(o-nitrobenzyl)-1-thio-β-$_D$-glucopyranoside (**18**, Table 4); Compound **18** was obtained as white solid (720 mg, 78%); mp: 77 °C; $[\alpha]_D^{20}$ = +12.7 (*c* = 1.0, $CHCl_3$); ^{1}H NMR: (600 MHz, $CDCl_3$) δ 8.03 (dd, *J* = 8.2, 1.2 Hz, 1H), 7.64 (dd, *J* = 7.8, 0.9 Hz, 1H), 7.60 – 7.57 (m, 2H), 7.52 (td, *J* = 7.7, 1.2 Hz, 1H), 7.40 – 7.37 (m, 3H), 7.34 – 7.13 (m, 16H), 5.19 (d, *J* = 14.8 Hz, 1H), 4.99 (d, *J* = 14.8 Hz, 1H), 4.90 (d, *J* = 10.3 Hz, 1H), 4.86 (d, *J* = 11.1 Hz, 1H), 4.71 (d, *J* = 10.3 Hz, 1H), 4.69 (d, *J* = 9.8 Hz, 1H), 4.66 (d, *J* = 11.1 Hz, 1H), 4.58 (d, *J* = 11.9 Hz, 1H), 4.51 (d, *J* = 11.8 Hz, 1H), 3.77 (dd, *J* = 10.9, 1.9 Hz, 1H), 3.74 – 3.69 (m, 3H), 3.56 – 3.51 (m, 2H); ^{13}C NMR: (151 MHz, $CDCl_3$) δ 146.8, 138.1, 138.0, 135.0, 133.8, 133.5, 131.9, 128.9, 128.6, 128.4, 128.3, 128.3, 128.2, 127.9, 127.8, 127.7, 127.6, 127.5, 127.5, 124.8, 124.5, 87.5, 86.6, 80.9, 79.0, 78.0, 75.7, 75.4, 73.4, 71.0, 69.1; HRMS (ESI-TOF): calcd. for $C_{40}H_{39}NO_7S$ $[M+Na]^+$: 700.2345, found 700.2338.

Phenyl 2,3,6-tri-O-benzyl-4-O-(o-cyanobenzyl)-1-thio-β-$_D$-glucopyranoside (**19**, Table 4); Compound **19** was obtained as white solid (800 mg, 89%); mp: 86 °C; $[\alpha]_D^{20}$ = –1.4 (*c* = 1.0, $CHCl_3$); ^{1}H NMR: (600 MHz, $CDCl_3$) δ 7.60 – 7.57 (m, 3H), 7.45 (td, *J* = 7.7, 1.3 Hz, 1H), 7.38 – 7.21 (m, 20H), 4.97 (d, *J* = 12.2 Hz, 1H), 4.91 (d, *J* = 11.2 Hz, 1H), 4.90 (d, *J* = 10.3 Hz, 1H), 4.82 (d, *J* = 12.2 Hz, 1H), 4.78 (d, *J* = 11.2 Hz, 1H), 4.70 (d, *J* = 10.3 Hz, 1H), 4.67 (d, *J* = 9.8 Hz, 1H), 4.60 (d, *J* = 11.9 Hz, 1H), 4.56 (d, *J* = 11.9 Hz, 1H), 3.81 (d, *J* = 3.2 Hz, 2H), 3.73 – 3.69 (m, 2H), 3.54 – 3.50 (m, 2H); ^{13}C NMR: (151 MHz, $CDCl_3$) δ 141.6, 138.3, 138.3, 138.0, 133.8, 132.8, 132.0, 128.9, 128.8, 128.4, 128.3, 128.2, 128.0, 127.9, 127.7, 127.6, 127.6, 127.5, 117.4, 111.3, 87.4, 86.5, 80.9, 78.9, 77.9, 75.6, 75.3, 73.3, 72.2, 69.0; HRMS (ESI-TOF): calcd. for $C_{41}H_{39}NO_5S$ $[M+Na]^+$: 680.2447, found 680.2419.

Phenyl 2,4,6-tri-O-benzyl-3-O-(o-nitrobenzyl)-1-thio-β-$_D$-glucopyranoside (**20**, Table 4); Compound **20** was obtained as white solid (690 mg, 75%); mp: 103 ^oC; $[\alpha]_D^{20}$ = –7.1 (*c* = 1.0, $CHCl_3$); ^1H NMR: (600 MHz, $CDCl_3$) δ 8.05 (dd, *J* = 8.2, 1.2 Hz, 1H), 7.84 (dd, *J* = 7.8, 0.8 Hz, 1H), 7.60 – 7.57 (m, 2H), 7.54 (td, *J* = 7.7, 1.2 Hz, 1H), 7.39 (t, *J* = 7.1 Hz, 1H), 7.37 – 7.18 (m, 16H), 7.09 – 7.07 (m, 2H), 5.25 (d, *J* = 15.4 Hz, 1H), 5.20 (d, *J* = 15.4 Hz, 1H), 4.89 (d, *J* = 10.4 Hz, 1H), 4.67 (d, *J* = 9.8 Hz, 1H), 4.65 (d, *J* = 10.9 Hz, 1H), 4.63 (d, *J* = 12.1 Hz, 1H), 4.58 (d, *J* = 10.8 Hz, 1H), 4.57 (d, *J* = 11.0 Hz, 1H), 4.56 (d, *J* = 12.3 Hz, 1H), 3.79 (dd, *J* = 10.8, 1.9 Hz, 1H), 3.77 – 3.73 (m, 2H), 3.70 (t, *J* = 9.3 Hz, 1H), 3.53 (dd, *J* = 9.7, 8.7 Hz, 1H), 3.51 – 3.48 (m, 1H). ^{13}C NMR: (151 MHz, $CDCl_3$) δ 146.6, 138.2, 137.8, 137.7, 135.6, 133.9, 133.6, 131.9, 128.9, 128.4, 128.3, 128.3, 128.1, 127.8, 127.8, 127.8, 127.7, 127.6, 127.5, 124.6, 87.6, 86.6, 80.9, 79.0, 77.7, 75.4, 74.9, 73.5, 71.5, 68.9. HRMS (ESI-TOF): calcd. for $C_{40}H_{39}NO_7S$ $[M+Na]^+$: 700.2345, found 700.2307.

Phenyl 2,4,6-tri-O-benzyl-3-O-(o-cyanobenzyl)-1-thio-β-$_D$-glucopyranoside (**21**, Table 4); Compound **21** was obtained as white solid (1.05 g, 77%); mp: 122 ^oC; $[\alpha]_D^{20}$ = +2.0 (*c* = 1.0, $CHCl_3$); ^1H NMR: (600 MHz, $CDCl_3$) δ 7.59 – 7.57 (m, 2H), 7.56 (dd, *J* = 7.8, 1.1 Hz, 1H), 7.53 (dd, *J* = 7.8, 0.5 Hz, 1H), 7.45 (td, *J* = 7.7, 1.3 Hz, 1H), 7.35 – 7.22 (m, 17H), 7.15 – 7.13 (m, 2H), 5.08 (d, *J* = 12.9 Hz, 1H), 5.02 (d, *J* = 12.9 Hz, 1H), 4.91 (d, *J* = 10.4 Hz, 1H), 4.72 (d, *J* = 11.0 Hz, 1H), 4.67 (d, *J* = 11.0 Hz, 1H), 4.67 (d, *J* = 9.7 Hz, 1H), 4.60 (d, *J* = 12.0 Hz, 1H), 4.57 (d, *J* = 11.0 Hz, 1H), 4.54 (d, *J* = 12.0 Hz, 1H), 3.77 (dd, *J* = 10.9, 1.9 Hz, 1H), 3.73 – 3.70 (m, 2H), 3.67 (t, *J* = 9.3 Hz, 1H), 3.53 (dd, *J* = 9.7, 8.5 Hz, 1H), 3.51 – 3.48 (m, 1H); ^{13}C NMR: (151 MHz, $CDCl_3$) δ 142.2, 138.2, 137.9, 137.9, 133.9, 132.7, 132.6, 131.9, 128.9, 128.3, 128.1, 127.8, 127.8, 127.7, 127.6, 127.4, 117.2, 110.8, 87.6, 87.0, 80.8, 79.0, 77.7, 75.2, 74.9, 73.4, 72.8, 68.9; HRMS (ESI-TOF): calcd. for $C_{41}H_{39}NO_5S$ $[M+Na]^+$: 680.2447, found 680.2400.

General procedures of glycosylation for compound 2a-d, 4a-d, 8-13, 22-27

To cooled solution (-40 ^{o}C) of donor (0.076 mmol, 1.0 eq.), Ph_2SO (0.084 mmol, 1.1 eq.), TTBP (0.19 mmol, 2.5 eq.) and freshly activated molecular sieves (3 Å, 100 mg) in 5 ml of CH_2Cl_2 was added Tf_2O (0.084 mmol, 1.1 eq.). The mixture was allowed to stir at the same temperature about 15 minutes, next acceptor (0.114 mmol, 1.5 eq.) was added. The mixture was allowed to warm to RT. After 3 h, 5eq. of Et_3N was added and the mixture was stirring next 15 minutes in RT. The reaction was then quenched with aqueous NH_4Cl and extracted with CH_2Cl_2. The organic layer was washed with water, dried over $MgSO_4$, and concentrated *in vacuo*. The crude product was purified by flash column chromatography on silica gel with hexane/EtOAc to afford the desired glycosides.

Methyl 3,4,6-tri-O-benzyl-2-O-(o-cyanobenzyl)-α/β-$_D$-glucopyranoside (**2d**, Table 1); Compound **2d** was obtained as colorless oil (36 mg; 82%; α/β = 1:12); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.60 (dd, *J* = 7.8, 0.9 Hz, 1H), 7.54 (dd, *J* = 7.8, 0.9 Hz, 1H), 7.48 (td, *J* = 7.6, 1.4 Hz, 1H), 7.38 – 7.23 (m, 15H), 7.15 (m, 2H), 5.15 (d, *J* = 12.6 Hz, 1H), 4.88 (d, *J* = 12.6 Hz, 1H), 4.87 (d, *J* = 11.7 Hz, 1H), 4.80 (d, *J* = 11.7 Hz, 1H), 4.79 (d, *J* = 11.1 Hz, 1H), 4.63 (d, *J* = 12.9 Hz, 1H), 4.55 (d, *J* = 12.9 Hz, 1H), 4.52 (d, *J* = 11.1 Hz, 1H), 4.33 (d, *J* = 7.8 Hz, 1H, H1-β), 3.80 – 3.59 (m, 4H), 3.57 (s, 3H), 3.51 – 3.40 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 142.2, 138.6, 138.2, 138.1, 132.8, 132.7, 129.1, 128.3, 127.9, 127.8, 127.7, 127.6, 127.5, 117.4, 111.6, 104.4, 84.5, 82.4, 77.9, 77.2, 75.6, 75.0, 74.9, 73.5, 71.7, 68.9, 57.0; HRMS (ESI-TOF): calcd. for $C_{36}H_{37}NO_6$ $[M+Na]^+$: 602.2519, found 602.2495.

Methyl 2,3,4-tri-O-benzyl-6-O-(3,4,6-tri-O-benzyl-2-O-(o-cyanobenzyl)-α/β-$_D$-glucopyranosyl)-α-$_D$-glucopyranoside (**4d,** Table 2); Compound **4d** was obtained as colorless oil (66 mg, 86%, α/β = 1:3); ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.54 (m, 1.6H), 7.40 (d, *J* = 7.7 Hz, 1.3H), 7.38 – 7.20 (m, 40H), 7.16 (d, *J* = 6.9 Hz, 5H), 5.18 (d, *J* = 13.2 Hz, 1.27H, HC<u>H</u>-*o*CBn, 0.27H, *J* = 1.8 Hz, H1′-α), 4.95 (m, 3.26H), 4.87 – 4.75 (m, 6.1H), 4.71 (d, *J* = 10.9 Hz, 1H), 4.65 (d, *J* = 11.9 Hz, 2H), 4.61 – 4.51 (m, 6H), 4.47 (m, 0.78H), 4.38 (d, *J* = 10.2

Hz, 1H), 4.36 (d, *J* = 7,8 Hz, 1H, H1′-β) 4.16 (d, *J* = 10.7 Hz, 1H), 3.96 (m, 1.74H), 3.87 (m, 0.3H), 3.82 – 3.62 (m, 7.45H), 3.62 – 3.55 (m, 2.85H), 3.51 (m, 1.24H), 3.46 – 3.41 (m, 1.2H), 3.41 – 3.37 (m, 6H), 3.35 (s, 0.8H), 3.32 (s, 3H); ^{13}C NMR (151 MHz, $CDCl_3$) δ 142.2, 139.0, 138.5, 138.4, 138.3, 138.2, 138.1, 132.9, 132.7, 132.6, 132.4, 128.4, 128.3, 128.2, 128.1, 128.00, 127.9, 127.8, 127.7, 127.6, 127.5, 117.2, 117.1, 110.8, 110.6, 103.6, 98.1, 97.9, 96.9, 84.6, 82.2, 82.1, 81.9, 81.5, 80.3, 80.0, 78.1, 77.9, 77.7, 75.7, 75.6, 75.4, 75.1, 74.9, 74.7, 73.5, 73.4, 73.1, 71.7, 70.4, 69.7, 69.3, 69.0, 68.6, 68.5, 65.8, 55.2; HRMS (ESI-TOF): calcd. for $C_{63}H_{65}NO_{11}$ $[M+Na]^+$: 1034.4450, found 1034.4438.

Methyl 2,3,6-tri-O-benzyl-4-O-(3,4,6-tri-O-benzyl-2-O-(o-cyanobenzyl)-α/β-$_D$-glucopyranosyl)-α-$_D$-glucopyranoside (**8**, Table 3); Compound **8** was obtained as colorless oil (52 mg, 67%, α/β = 1:5); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.63 – 7.58 (m, 0.2H), 7.57 – 7.55 (m, 1.2H), 7.54 – 7.46 (m, 3H), 7.44 – 7.40 (m, 3H), 7.39 – 7.26 (m, 42H), 7.18 – 7.11 (m, 3H), 5.16 (d, *J* = 12.8 Hz, 1H), 5.08 (d, *J* = 3.7 Hz, 0.2H, H1'-α), 4.99 – 4.91 (m, 3.8H), 4.87 – 4.79 (m, 7.2H), 4.78 (d, *J* = 2.1 Hz, 1.2H, H1-α), 4.68 (d, *J* = 6.5 Hz, 1H, H1'-β), 4.67 – 4.60 (m, 4.7H), 4.60 – 4.54 (m, 3H), 4.54 – 4.44 (m, 5H), 4.06 (t, *J* = 9.4 Hz, 0.2H), 3.98 (t, *J* = 9.3 Hz, 1H), 3.85 – 3.68 (m, 6H), 3.66 – 3.50 (m, 7.8H), 3.49 – 3.42 (m, 2H), 3.40 (s, 0.6H), 3.37 (s, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 143.6, 140.2, 139.9, 139.7, 139.6, 139.5, 139.3, 138.7, 138.0, 135.0, 134.1, 134.0, 132.8, 130.8, 130.3, 130.2, 129.9, 129.8, 129.6, 129.4, 129.3, 129.2, 129.1, 129.0, 118.8, 112.7, 103.6, 99.6, 97.1, 85.9, 83.83, 83.6, 82.0, 81.3, 79.4, 79.1, 79.0, 78.7, 78.4, 78.2, 77.2, 77.0, 76.4, 76.3, 74.9, 74.8, 73.2, 72.5, 72.0, 71.7, 71.5, 70.3, 69.9, 61.8, 56.6; HRMS (ESI-TOF): calcd. for $C_{63}H_{65}NO_{11}$ $[M+Na]^+$:1034.4450, found 1034.4435.

Methyl 4,6-O-benzylidene-3-O-benzyl-2-O-(3,4,6-tri-O-benzyl-2-O-(o-cyanobenzyl)-α/β-$_D$-glucopyranosyl)-α-$_D$-glucopyranoside (**9**, Table 3); Compound **9** was obtained as colorless oil (24 mg, 34%, α/β = 1:5); ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.72 – 7.67 (m, 0.5H), 7.56 – 7.47

(m, 5H), 7.39 – 7.18 (m, 39H), 7.17 – 7.12 (m, 2.6H), 5.59 (s, 0.16H), 5.55 (s, 1H), 5.19 (d, *J* = 13.0 Hz, 1H), 5.13 (d, *J* = 12.7 Hz, 0.2H), 5.02 – 4.76 (m, 8H), 4.70 – 4.67 (m, 0.5H), 4.61 – 4.48 (m, 6.5H), 4.43 (dd, *J* = 9.4, 3.8 Hz, 0.2H), 4.33 – 4.30 (m, 1.1H), 4.11 – 4.06 (m, 1.5H), 3.96 – 3.84 (m, 2.3H), 3.80 – 3.72 (m, 2H), 3.73 – 3.63 (m, 6H), 3.61 (d, *J* = 8.5 Hz, 0.8H), 3.60 – 3.52 (m, 2H), 3.55 – 3.45 (m, 1.5H), 3.44 (s, 4.2H), 3.38 (s, 0.5H); ^{13}C NMR (151 MHz, $CDCl_3$) δ 145.7, 142.3, 138.5, 138.0, 137.4, 132.7, 132.6, 132.5, 132.4, 131.1, 129.3, 129.0, 128.9, 128.8, 128.4, 128.3, 128.2, 128.1, 128.0, 127.9, 127.8, 127.7, 127.6, 127.5, 127.4, 126.0, 125.0, 124.8, 123.4, 117.4, 111.07, 104.1, 101.4, 100.4, 84.5, 84.4, 82.9, 82.3, 82.2, 78.5, 78.0, 77.9, 77.8, 77.2, 77.0, 76.8, 75.6, 75.5, 75.1, 75.0, 74.9, 74.7, 73.4, 73.3, 71.7, 69.2, 69.0, 62.2, 60.4, 55.4; HRMS (ESI-TOF): calcd. for $C_{56}H_{57}NO_{11}$ $[M+Na]^+$: 942.3824, found 942.3791.

Methyl 4,6-O-benzylidene-2-O-benzyl-3-O-(3,4,6-tri-O-benzyl-2-O-(o-cyanobenzyl)-α/β-$_D$-glucopyranosyl)-α/β-$_D$-glucopyranoside (**10**, Table 3); Compound **10** was obtained as colorless oil (50 mg, 72%, α/β = 1:4); ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.58 – 7.55 (m, 2H), 7.51 – 7.48 (m, 3H), 7.46 – 7.41 (m, 2H), 7.40 – 7.26 (m, 37H), 7.18 – 7.10 (m, 2.4H), 5.55 (s, 1H), 5.16 (d, *J* = 12.7 Hz, 1H), 5.08 (d, *J* = 3.6 Hz, 0.25H, H1'-α), 5.05 – 5.02 (m, 0.25H), 4.98 – 4.90 (m, 3H), 4.88 – 4.76 (m, 6H), 4.76 – 4.60 (m, 4.2H), 4.59 (d, *J* = 3.7 Hz, 1.2H, H1-α), 4.58 – 4.54 (m, 1.6H), 4.52 (d, *J* = 7.8 Hz, 1H, H1'-β), 4.49 (dd, *J* = 11.4, 5.7 Hz, 1H), 4.27 (dd, *J* = 10.2, 4.8 Hz, 1H), 4.08 – 4.02 (m, 1.4H), 3.85 – 3.80 (m, 2.6H), 3.78 – 3.69 (m, 3.4H), 3.65 – 3.58 (m, 3.2H), 3.58 – 3.52 (m, 1.8H), 3.51 – 3.46 (m, 1.3H), 3.41 (s, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 142.2, 138.7, 138.5, 138.1, 137.4, 137.2, 136.60, 133.6, 132.8, 132.7, 132.6, 131.4, 129.7, 129.4, 129.0, 128.9, 128.8, 128.7, 128.5, 128.4, 128.3, 128.2, 128.1, 128.0, 127.9, 127.8, 127.6, 126.0, 117.4, 117.1, 111.5, 111.2, 102.1, 101.3, 99.2, 95.7, 84.5, 82.4, 82.1, 81.9, 81.3, 80.5, 79.8, 79.1, 78.6, 77.9, 77.9, 77.6, 75.6, 75.3, 75.1, 75.0,

74.9, 73.8, 73.5, 73.1, 71.8, 71.1, 70.6, 70.5, 70.3, 69.6, 69.1, 68.8, 68.3, 62.3, 55.3; HRMS (ESI-TOF): calcd. for $C_{56}H_{57}NO_{11}$ $[M+Na]^+$: 942.3824, found 942.3807.

Isopropyl 3,4,6-tri-O-benzyl-2-O-(o-cyanobenzyl)-β-$_D$-glucopyranoside (**11**, Table 3); Compound **11** was obtained as solid (36 mg, 78%); mp: 63 – 65 ^oC; $[\alpha]_D^{20}$ = –9.5 (*c* = 0.5, $CHCl_3$); ^1H NMR (500 MHz, $CDCl_3$) δ 7.58 – 7.55 (m, 1H), 7.50 – 7.41 (m, 2H), 7.36 – 7.25 (m, 17H), 7.19 – 7.15 (m, 2H), 5.20 (d, *J* = 12.9 Hz, 1H), 4.93 (d, *J* = 12.9 Hz, 1H), 4.87 (d, *J* = 12.0 Hz, 1H), 4.81 (d, *J* = 12.0 Hz, 1H), 4.80 (d, *J* = 12.0 Hz, 1H), 4.61 (d, *J* = 12.2 Hz, 1H), 4.57 (dd, *J* = 12.2, 1H), 4.54 (d, *J* = 12.0, 1H), 4.49 (d, *J* = 7.8 Hz, 1H, H1-β), 4.03 (hept, *J* = 6.1 Hz, 1H), 3.73 (dd, *J* = 10.8, 2.0 Hz, 1H), 3.66 (m, 1H), 3.67 (t, *J* = 9.3 Hz, 1H), 3.57 (t, *J* = 9.3 Hz, 1H), 3.50 – 3.38 (m, 2H), 1.30 (d, *J* = 6.2 Hz, 3H), 1.21 (d, *J* = 6.1 Hz, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 142.4, 138.6, 138.3, 138.1, 136.6, 132.7, 129.4, 128.9, 128.8, 128.4, 128.3, 128.0, 127.8, 127.7, 127.6, 127.5, 117.4, 111.2, 101.8, 84.6, 82.4, 78.1, 75.6, 75.0, 74.8, 73.5, 72.2, 71.6, 69.1, 23.7, 22.0; HRMS (ESI-TOF): calcd. for $C_{38}H_{41}NO_6$ $[M+Na]^+$: 630.2826, found 630.2796.

Benzyl 3,4,6-tri-O-benzyl-2-O-(o-cyanobenzyl)-α/β-$_D$-glucopyranoside (**12**, Table 3); Compound **12** was obtained as colorless oil (33 mg, 67%, α/β = 1:10); ^1H NMR (500 MHz, $CDCl_3$) δ ^1H NMR (500 MHz, $CDCl_3$) δ 7.63 – 7.55 (m, 1.86H), 7.52 – 7.48 (m, 1H), 7.45 – 7.27 (m, 24H), 7.18 – 7.15 (m, 2H), 5.17 (d, *J* = 12.7 Hz, 1H), 5.08 (d, *J* = 3.7 Hz, 0.18H), 4.98 – 4.91 (m, 2.32H), 4.88 – 4.72 (m, 4H), 4.71 – 4.60 (m, 3H), 4.60 – 4.54 (m, 1.73H), 4.53 (d, *J* = 7.8 Hz, 1.65H), 4.49 (dd, *J* = 11.4, 3.7 Hz, 0.58H), 4.09 – 4.03 (m, 0.2H), 3.82 – 3.50 (m, 6.41H), 3.49 – 3.45 (m, 1.13H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 142.2, 138.5, 138.2, 138.1, 137.3, 136.6, 133.63, 132.8, 132.7, 132.6, 131.4, 129.5, 128.9, 128.8, 128.8, 128.6, 128.4, 128.3, 128.2, 128.1, 127.9, 127.8, 127.6, 117.4, 111.3, 102.2, 95.7, 84.5, 82.4, 80.0, 80.6, 78.0, 77.6, 77.3, 77.0, 76.8, 75.6, 75.1, 75.0, 74.9, 73.5, 71.8, 71.1, 70.5, 70.3, 69.6, 68.9, 68.3; HRMS (ESI-TOF): calcd. for $C_{42}H_{41}NO_6$ $[M+Na]^+$: 678.2826, found 678.2799.

Nonyl 3,4,6-tri-O-benzyl-2-O-(o-cyanobenzyl)-β-$_D$-glucopyranoside (**13**, Table 3); Compound **13** was obtained as colorless oil (28 mg, 54%); $[\alpha]_D^{20}$ = –2.8 (*c* = 0.5, $CHCl_3$); ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.60 – 7.56 (m, 1H), 7.48 (ddd, *J* = 7.7, 6.4, 1.2 Hz, 1H), 7.36 – 7.30 (m, 4H), 7.30 – 7.23 (m, 10H), 7.18 – 7.14 (m, 2H), 5.18 (d, *J* = 12.8 Hz, 1H), 4.92 (d, *J* = 12.8 Hz, 1H), 4.87 (d, *J* = 11.1 Hz, 1H), 4.81 (d, *J* = 10.8, 1H), 4.79 (d, *J* = 11.1, 1H), 4.62 (d, *J* = 12.2 Hz, 1H), 4.56 (d, *J* = 12.2 Hz, 1H), 4.54 (d, *J* = 10.8 Hz, 1H), 4.41 (d, *J* = 7.8 Hz, 1H, H1-β), 3.93 (dt, *J* = 9.4, 6.7 Hz, 1H), 3.75 (dd, *J* = 10.8, 1.9 Hz, 1H), 3.71 – 3.62 (m, 2H), 3.59 (t, *J* = 9.3 Hz, 1H), 3.54 (dt, *J* = 9.4, 6.9 Hz, 1H), 3.50 – 3.42 (m, 2H), 1.67 – 1.60 (m, 2H), 1.38 – 1.16 (m, 12H), 0.87 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (151 MHz, $CDCl_3$) δ 142.4, 138.6, 138.2, 138.1, 132.7, 132.6, 128.8, 128.4, 128.3, 128.0, 127.7, 127.6, 127.5, 117.3, 111.3, 103.4, 84.5, 82.4, 78.1, 75.6, 75.0, 74.9, 73.5, 71.6, 70.2, 69.0, 31.9, 29.7, 29.5, 29.4, 29.3, 26.1, 22.7, 14.1; HRMS (ESI-TOF): calcd. for $C_{44}H_{53}NO_6$ $[M+Na]^+$: 714.3765, found 714.3742.

Methyl 2,3,4-tri-O-benzyl-6-O-(2,3,4-tri-O-benzyl-6-O-(o-nitrobenzyl)-α/β-$_D$-glucopyranosyl)-α/β-$_D$-glucopyranoside (**22**, Table 4); Compound **22** was obtained as colorless oil (57 mg, 73%, α/β = 2:1); ^{1}H NMR: (300 MHz, $CDCl_3$) δ 8.06 – 8.02 (m, 1.7H), 7.81 (dd, *J* = 7.8, 1.0 Hz, 0.7H), 7.75 (dd, *J* = 7.8, 1.1 Hz, 1.2H), 7.60 – 7.52 (m, 2.3H), 7.42 – 7.13 (m, 55H), 5.01 – 4.48 (m, 27.5H), 4.37 (d, *J* = 7.7 Hz, 0.6H), 4.17 – 4.07 (m, 1.6H), 3.99 (td, *J* = 9.3, 2.6 Hz, 2.7H), 3.87 – 3.41 (m, 18H), 3.36 (s, 3H), 3.33 (s, 1.7H); ^{13}C NMR: (75 MHz, $CDCl_3$) δ 146.9, 146.8, 138.8, 138.6, 138.4, 138.2, 138.1, 138.0, 135.3, 135.2, 133.7, 128.3, 128.1, 128.0, 127.9, 127.8, 127.7, 127.6, 124.5, 103.8, 98.1, 98.0, 97.1, 84.8, 82.1, 82.0, 81.7, 80.1, 79.8, 77.8, 75.8, 75.7, 75.6, 74.9, 73.3, 72.4, 70.4, 70.2, 69.9, 69.7, 66.1, 55.2, 55.2; HRMS (ESI-TOF): calcd. for $C_{62}H_{65}NO_{13}$ $[M+Na]^+$: 1054.4354, found 1054.4336.

Methyl 2,3,4-tri-O-benzyl-6-O-(2,3,4-tri-O-benzyl-6-O-(o-cyanobenzyl)-α/β-$_D$-glucopyranosyl)-α/β-$_D$-glucopyranoside (**23**, Table 4); Compound **23** was obtained as colorless oil (65 mg, 85%, α/β = 2:1); ^{1}H NMR: (600 MHz, $CDCl_3$) δ 7.61 – 7.48 (m, 7H),

7.46 (dd, *J* = 7.7, 1.3 Hz, 0.3H), 7.35 – 7.15 (m, 59H), 5.18 (d, *J* = 3.4 Hz, 0.3H), 5.12 (d, *J* = 11.5 Hz, 0.3H), 5.00 – 4.53 (m, 28H), 4.51 (d, *J* = 11.2 Hz, 0.4H), 4.47 (d, *J* = 13.1 Hz, 0.3H), 4.37 (d, *J* = 7.8 Hz, 0.4H, H1-β), 4.20 – 4.16 (m, 0.7H), 4.13 – 4.10 (m, 0.6H), 3.98 (td, *J* = 9.3, 4.2 Hz, 2.5H), 3.85 – 3.47 (m, 17H), 3.44 (dd, *J* = 9.6, 3.6 Hz, 1H), 3.36 (s, 3H), 3.32 (s, 1.3H); ^{13}C NMR: (151 MHz, $CDCl_3$) δ 142.0, 138.8, 138.7, 138.4, 138.2, 138.0, 133.1, 133.0, 132.8, 132.5, 129.3, 128.4, 128.4, 128.3, 128.3, 128.2, 128.1, 128.1, 128.0, 127.8, 127.7, 127.7, 127.6, 127.5, 117.2, 110.9, 103.8, 98.1, 98.0, 97.2, 82.1, 82.0, 81.7, 80.2, 80.1, 79.8, 77.8, 77.7, 77.5, 77.4, 75.7, 75.6, 75.5, 75.0, 74.9, 74.9, 73.3, 73.2, 72.4, 70.9, 70.7, 70.4, 70.3, 69.9, 69.5, 66.1, 55.2, 55.2; HRMS (ESI-TOF): calcd. for $C_{63}H_{65}NO_{11}$ $[M+Na]^+$: 1034.4455, found 1034.4410.

*Methyl 2,3,4-tri-O-benzyl-6-O-(2,3,6-tri-O-benzyl-4-O-(o-nitrobenzyl)-α/β-$_D$-glucopyranosyl)-α/β-$_D$-glucopyranoside (***24**, Table 4); Compound **24** was obtained as white solid (62 mg, 79%, α/β = 1:3); ^{1}H NMR: (600 MHz, $CDCl_3$) δ 8.07 (dd, *J* = 8.1, 1.2 Hz, 0.3H), 8.02 (dd, *J* = 8.2, 1.2 Hz, 1.2H), 7.62 (d, *J* = 7.8 Hz, 1H), 7.54 (d, *J* = 7.8 Hz, 0.7H), 7.51 (td, *J* = 7.7, 1.2 Hz, 1.3H), 7.46 (td, *J* = 7.7, 1.3 Hz, 0.5H), 7.42 (t, *J* = 7.7 Hz, 0.4H), 7.38 (t, *J* = 7.8 Hz, 1.8H), 7.34 – 7.14 (m, 44H), 7.12 – 7.09 (m, 2H), 5.19 (d, *J* = 14.9 Hz, 0.3H), 5.17 (d, *J* = 14.8 Hz, 1H), 4.99 – 4.48 (m, 21H), 4.39 (d, *J* = 12.1 Hz, 0.3H), 4.36 (d, *J* = 7.8 Hz, 1H, H1-β), 4.18 (dd, *J* = 10.9, 2.0 Hz, 1H), 3.99 (t, *J* = 9.3 Hz, 1H), 3.94 (t, *J* = 9.3 Hz, 0.3H), 3.86 – 3.43 (m, 15H), 3.37 (s, 1H), 3.33 (s, 3H); ^{13}C NMR: (151 MHz, $CDCl_3$) δ 146.8, 146.7, 138.8, 138.8, 138.5, 138.4, 138.4, 138.3, 138.2, 138.2, 138.1, 138.1, 135.1, 134.9, 133.8, 133.5, 133.4, 128.6, 128.5, 128.4, 128.3, 128.2, 128.2, 128.1, 128.0, 127.9, 127.9, 127.8, 127.7, 127.7, 127.6, 127.6, 127.5, 127.4, 124.6, 124.5, 124.4, 104.3, 103.8, 98.1, 98.0, 84.6, 82.2, 82.1, 82.0, 81.4, 80.0, 79.8, 78.1, 78.0, 77.8, 77.7, 76.2, 75.7, 75.7, 75.5, 74.9, 74.8, 74.1, 73.4, 73.3, 72.4, 71.9, 70.9, 70.3, 70.1, 69.9, 69.3, 69.1, 68.6, 66.2, 65.4, 55.2, 55.1; HRMS (ESI-TOF): calcd. for $C_{62}H_{65}NO_{13}$ $[M+Na]^+$: 1054.4354, found 1054.4310.

Methyl 2,3,4-tri-O-benzyl-6-O-(2,3,6-tri-O-benzyl-4-O-(o-cyanobenzyl)-α/β-$_D$-glucopyranosyl)-α/β-$_D$-glucopyranoside (**25**, Table 4); Compound **25** was obtained as white solid (72 mg, 93%, α/β = 1:2); ^{1}H NMR: (600 MHz, $CDCl_3$) δ 7.59 – 7.56 (m, 1.7H), 7.47 – 7.40 (m, 3.3H), 7.35 – 7.17 (m, 55H), 4.99 – 4.90 (m, 7H), 4.82 – 4.45 (m, 19H), 4.35 (d, *J* = 7.8 Hz, 1H), 4.17 (dd, *J* = 10.9, 2.0 Hz, 1H), 4.01 – 3.93 (m, 2.3H), 3.85 – 3.41 (m, 17.3H), 3.36 (s, 1.7H), 3.32 (s, 3H); ^{13}C NMR: (151 MHz, $CDCl_3$) δ 142.1, 141.7, 138.9, 138.7, 138.5, 138.4, 138.3, 138.2, 138.1, 138.0, 132.7, 132.7, 132.6, 132.6, 131.0, 129.3, 128.8, 128.6, 128.4, 128.4, 128.4, 128.3, 128.3, 128.2, 128.1, 128.0, 127.9, 127.9, 127.8, 127.8, 127.7, 127.7, 127.6, 127.6, 127.5, 127.5, 127.4, 127.4, 124.8, 117.4, 111.4, 103.8, 98.0, 98.0, 97.2, 84.5, 82.2, 82.0, 80.2, 80.1, 79.8, 78.1, 78.0, 77.8, 75.7, 75.6, 75.4, 75.3, 74.9, 74.8, 74.8, 73.3, 72.3, 72.1, 70.4, 70.1, 69.9, 69.0, 68.6, 66.1, 55.2, 55.1; HRMS (ESI-TOF): calcd. for $C_{63}H_{65}NO_{11}$ $[M+Na]^+$: 1034.4455, found 1034.4427.

Methyl 2,3,4-tri-O-benzyl-6-O-(2,4,6-tri-O-benzyl-3-O-(o-nitrobenzyl)-α/β-$_D$-glucopyranosyl)-α/β-$_D$-glucopyranoside (**26** Table 4); Compound **26** was obtained as white solid (77 mg, 98%, α/β = 1:1); ^{1}H NMR: (600 MHz, $CDCl_3$) δ 8.05 (dd, *J* = 8.2, 1.2 Hz, 1H), 8.05 (dd, *J* = 8.2, 1.2 Hz, 1H), 7.81 (dd, *J* = 7.8, 0.8 Hz, 1H), 7.74 (t, *J* = 7.9 Hz, 2H), 7.65 (dd, *J* = 8.0, 1.6 Hz, 1H), 7.58 – 7.55 (m, 2H), 7.55 – 7.52 (m, 1H), 7.45 (d, *J* = 7.5 Hz, 1H), 7.41 – 7.19 (m, 70H), 7.17 – 7.15 (m, 2H), 5.25 (d, *J* = 3.6 Hz, 1H), 5.02 (d, *J* = 10.7 Hz, 1H), 5.00 – 4.84 (m, 12H), 4.82 – 4.75 (m, 7H), 4.74 – 4.63 (m, 8H), 4.61 – 4.56 (m, 5H), 4.50 (d, *J* = 11.2 Hz, 1H), 4.37 (d, *J* = 7.8 Hz, 1H), 4.23 – 4.20 (m, 1H), 4.18 (dd, *J* = 10.9, 2.0 Hz, 1H), 4.08 (t, *J* = 9.3 Hz, 1H), 4.01 – 3.96 (m, 2H), 3.85 – 3.58 (m, 16H), 3.56 – 3.49 (m, 4H), 3.47 – 3.42 (m, 2H), 3.36 (s, 3H), 3.33 (s, 3H). ^{13}C NMR: (151 MHz, $CDCl_3$) δ 146.9, 138.8, 138.7, 138.4, 138.2, 138.1, 138.0, 135.3, 135.2, 135.1, 133.7, 131.0, 129.3, 128.5, 128.4, 128.4, 128.4, 128.3, 128.2, 128.1, 128.0, 128.0, 127.9, 127.8, 127.7, 127.7, 127.7, 127.6, 127.6, 127.5, 127.4, 124.8, 124.6, 124.5, 103.8, 98.1, 98.0, 97.1, 84.8, 82.1, 82.1, 82.0, 81.9,

81.8, 81.7, 80.2, 80.1, 79.8, 79.6, 78.0, 77.8, 77.7, 77.6, 75.8, 75.8, 75.7, 75.6, 75.6, 75.1, 75.0, 75.0, 74.9, 74.9, 74.8, 73.3, 73.3, 72.9, 72.4, 70.7, 70.4, 70.2, 69.9, 69.8, 69.7, 69.7, 69.3, 68.5, 66.1, 55.2, 55.2; HRMS (ESI-TOF): calcd. for $C_{62}H_{65}NO_{13}$ $[M+Na]^+$: 1054.4354, found 1054.4320.

Methyl 2,3,4-tri-O-benzyl-6-O-(2,4,6-tri-O-benzyl-3-O-(o-cyanobenzyl)-α/β-$_D$-glucopyranosyl)-α/β-$_D$-glucopyranoside (**27**, Table 4); Compound **27** was obtained as white solid (62 mg, 80%, α/β = 1:1); ^{1}H NMR: (600 MHz, $CDCl_3$) δ 7.57 – 7.49 (m, 5H), 7.46 – 7.44 (m, 1H), 7.42 (td, *J* = 7.7, 1.3 Hz, 1H), 7.39 (td, *J* = 7.8, 1.3 Hz, 1H), 7.35 – 7.09 (m, 70H), 5.13 (d, *J* = 12.8 Hz, 1H), 5.09 (d, *J* = 13.0 Hz, 1H), 5.01 – 4.95 (m, 6H), 4.92 (d, *J* = 11.2 Hz, 1H), 4.82 – 4.49 (m, 22H), 4.45 (d, *J* = 11.1 Hz, 1H), 4.42 (d, *J* = 12.1 Hz, 1H), 4.35 (d, *J* = 7.8 Hz, 1H, H1-β), 4.17 (dd, *J* = 10.9, 2.0 Hz, 1H), 4.01 – 3.93 (m, 3H), 3.85 – 3.79 (m, 2H), 3.77 (dd, *J* = 10.9, 2.9 Hz, 2H), 3.70 – 3.40 (m, 18H), 3.35 (s, 3H), 3.32 (s, 3H); ^{13}C NMR: (151 MHz, $CDCl_3$) δ 142.6, 142.4, 138.8, 138.8, 138.4, 138.3, 138.2, 138.2, 138.1, 137.9, 137.9, 132.7, 132.6, 132.5, 132.5, 128.7, 128.4, 128.4, 128.4, 128.3, 128.3, 128.2, 128.1, 128.0, 127.9, 127.9, 127.8, 127.7, 127.6, 127.6, 127.5, 127.4, 117.3, 117.2, 111.0, 110.6, 103.8, 98.0, 98.0, 97.0, 85.1, 82.1, 81.9, 81.7, 80.1, 79.8, 78.1, 77.7, 77.5, 77.4, 75.6, 74.9, 74.9, 74.8, 74.8, 74.6, 73.4, 73.4, 73.3, 72.5, 72.4, 72.1, 70.3, 70.1, 69.9, 68.9, 68.6, 68.4, 66.1, 55.2, 55.1; HRMS (ESI-TOF): calcd. for $C_{63}H_{65}NO_{11}$ $[M+Na]^+$: 1034.4455, found 1034.4419.

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Supporting Information. ^{1}H and ^{13}C NMR spectra of all compounds presented in the paper and Cartesian coordinates for Structures A-C. This material is available free of charge via the Internet at http://pubs.acs.org.

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