ChemPubSoc Europe

DOI: 10.1002/chem.201406589

CHEMISTRY A European Journal Full Paper

Carbohydrates

Hydrogen-Bond-Mediated Aglycone Delivery (HAD): A Highly Stereoselective Synthesis of 1,2-*cis* α-D-Glucosides from Common Glycosyl Donors in the Presence of Bromine

Jagodige P. Yasomanee and Alexei V. Demchenko*[a]

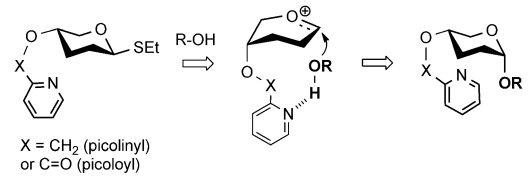
Abstract: Described herein is the expansion of the picoloyl protecting-group assisted H-bond mediated aglycone delivery (HAD) method recently introduced by our laboratory. At first it was noticed that high α-stereoselectivity is only obtained with *S*-ethyl glycosyl donors and only in the presence of dimethyl(methylthio)sulfonium trifluoromethanesulfonate (DMTST), in high dilution, and low temperature. Combining the mechanistic studies of the HAD reaction and bromine-promoted glycosylations allowed a very effective method to be devised that allows for highly stereoselective α-glycosidation of practically all common leaving groups (*S*-phenyl, *S*-tolyl, *S*/*O*-imidates) at regular concentrations and ambient temperature.

Introduction

O-Glycosylation reactions form a new chirality center and uncontrolled reactions commonly provide mixtures of 1,2-*cis* and 1,2-*trans* diastereomers. Obtaining an *O*-glycosidic linkage with complete stereoselectivity requires special care and the last few decades have witnessed a number of new techniques that have been developed to address this challenge in many different ways.[1] Among a plethora of methods available, a very successful technique involving the participatory assistance of the neighboring acyl substituent has been developed for the synthesis of 1,2-*trans* glycosides.[2] On the other hand, although a number of dedicated methodologies are available for 1,2-*cis* glycosylation, obtaining complete stereoselectivity in 1,2-*cis* glycoside synthesis still remains a challenge.[3]

Our group has been studying picolinyl and picoloyl substituents both at the neighboring (C-2)[2c,4] and remote positions (C-3, 4, and 6). Among other interesting findings, we introduced the H-bond mediated aglycone delivery (HAD) concept.[5] Over the course of that study we acquired compelling evidence that the nucleophile, the hydroxyl of the glycosyl acceptor, forms the hydrogen bond with the picolinyl (or picoloyl) nitrogen and it is delivered at the anomeric center in the *syn*-fashion with respect to the picolinyl (or picoloyl) group to form the new glycosidic bond (Scheme 1).

This new mode to control stereoselectivity of glycosylation allowed the synthesis of both 1,2-*trans* and 1,2-*cis* glycosidic linkages. The HAD method was also applied to the synthesis of challenging α-glucosides,[5] β-rhamnosides,[5] and β-mannosides[6] with high or even complete selectivity. The HAD approach was also successfully extended to the synthesis of furanosides by Yang[7] and glycosides of deoxysugars by Mong.[8] We also have applied this technique to the synthesis of both linear and branched α-glucans.[9] Although the synthesis of these oligosaccharides was successful, we also encountered some intrinsic problems with this method related to the weakening of the H bonding with bulky or sterically hindered acceptors, as well as loss of reactivity/stereoselectivity in certain cases.[9]



Scheme 1. α-Glycosylation by H-bond mediated aglycone delivery (HAD) assisted by picolinyl/picoloyl substituents.

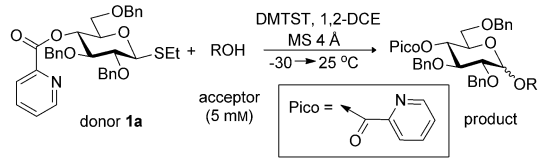
The study detailed herein is dedicated to the refinement of the synthesis of only one 1,2-*cis*-glycosidic linkage, α-D-glucosyl. Being among the most abundant linkages in Nature, the synthesis of α-D-glucosides remains challenging to chemists. Our preliminary results dedicated to the HAD-assisted synthesis of this important linkage are summarized in Table 1. In particular, 4-*O*-picoloylated *S*-ethyl glycosyl donor **1a** was found to be very beneficial in this application.[5] In most cases, high stereoselectivity was obtained, but the reactions had to be performed under very high dilution (5 mM of glycosyl acceptor, ten times lower concentration than a typical glycosylation), and at low temperature. These reaction conditions became standard for HAD-mediated glycosylations. Dimethyl(methyl-

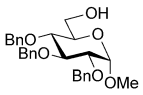
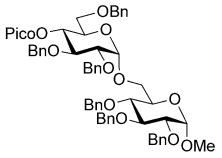
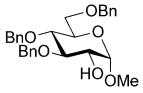
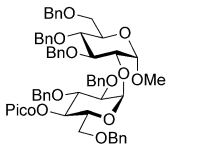
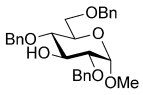
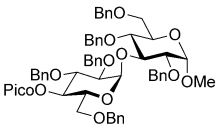
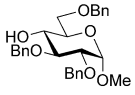
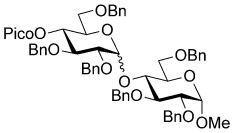
[a] *Dr. J. P. Yasomanee, Prof. A. V. Demchenko*
Department of Chemistry and Biochemistry
University of Missouri–St. Louis
One University Boulevard, St. Louis, MO 63121 (USA)
E-mail: demchenkoa@umsl.edu

Supporting information for this article is available on the WWW under http://dx.doi.org/10.1002/chem.201406589.

thio)sulfonium trifluoromethanesulfonate (DMTST) was found to be the promoter of choice because it does not interfere with the N atom of the picoloyl group, like many other electrophilic promoters do.[5] A variety of glycosyl acceptors, both primary **2** and secondary **4**, **6**, and **8**,[10] gave very high or complete 1,2-*cis* selectivity with 4-*O*-picoloyl donor **1 a**. As a result, pure α-linked disaccharides **3**, **5**, **7**, and **9** could be isolated in high yields of 73–91 % (Table 1).[5]

Table 1. A survey of previous results on the 4-*O*-picoloyl-assisted α-glycosylation.[5]



Entry	Acceptor	*t* [h]	Product	Yield [%] (α/β ratio)
1	 **2**	4	 **3**	73 (>25:1)
2	 **4**	5	 **5**	93 (>25:1)
3	 **6**	16	 **7**	81 (>25:1)
4	 **8**	24	 **9**	81 (21:1)

Results and Discussion

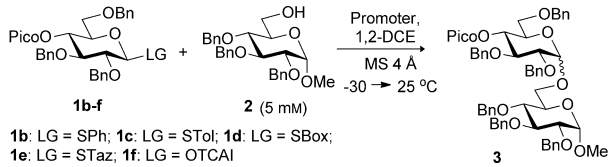
As an extension of this study we have decided to perform further refinement of the synthesis of α-glucosyl linkage in application to other classes of glycosyl donors, activators, systems, etc. In an attempt of identifying better glycosyl donors for HAD, we wanted to investigate the compatibility of popular leaving groups. For instance, we attempted the coupling of 4-*O*-picoloylated thiophenyl glycoside **1 b** with glycosyl acceptor **2**[11] to obtain disaccharide **3** under the previously reported standard glycosylation conditions.[5] To our surprise, only a moderate α-stereoselectivity was obtained (α/β = 5.3:1, 85 %, entry 1, Table 2). A very similar result in terms of the yield and stereoselectivity was obtained in the glycosidation of *p*-tolyl thioglycoside **1 c** (α/β = 6.7:1, 90 %, entry 2). This was rather unexpected considering the structural similarity of *S*-ethyl versus *S*-aryl glycosides and the activation modes thereof. As a rationale for lower selectivity observed with *S*-aryl glycosides we propose the following. In case of *S*-aryl glycosides, the sulfur atom is less nucleophilic than that of their *S*-ethyl counterparts. Therefore, interaction of *S*-aryl glycosides with DMTST is sluggish and as a result, excess DMTST would begin interfering with the picoloyl nitrogen making it unavailable to perform effective HAD. A similar reduction of selectivity was previously observed even with *S*-ethyl glycosides if a large excess of DMTST (6 equiv) was used.[5]

Having had no success with aryl thioglycosides, we decided to study *O*/*S*-imidates, another popular class of glycosyl donors.[12] When the *S*-benzoxazolyl (SBox) glycosyl donor **1 d** was first activated with AgOTf, the best promoter for SBox imidates,[13] a reverse selectivity was obtained with a slight shift towards the 1,2-*trans* linked disaccharide **3** (α/β = 1:1.9, 79 %, entry 3). A higher, yet far from satisfactory, α-selectivity was obtained when SBox donor **1 d** was activated with DMTST. In this case, disaccharide **3** was obtained in 80 % yield (α/β = 6.1:1, entry 4). A similar outcome was achieved upon AgOTf-promoted activation of *S*-thiazolinyl (STaz)[14] donor **1 e** (α/β = 6.3:1, 86 %, entry 5).

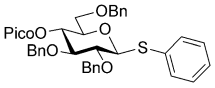
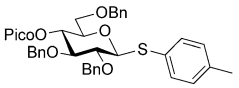
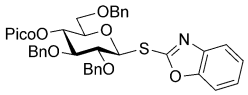
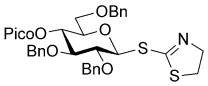
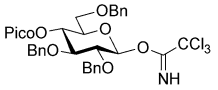
Finally, we tested *O*-trichloroacetimidate (TCAI) donor **1 f**. Over the course of this study, we noticed that only moderate selectivity and modest yield of **3** were obtained in the TMSOTf-promoted activation of TCAI donor **1 f** (α/β = 5.9:1, 44 %, entry 6). The outcome of the glycosidation of TCAI donor **1 f** could be significantly enhanced by performing the activation in the presence of TfOH instead. In this case, disaccharide **3** was isolated in 92 % yield and improved α-selectivity (α/β = 9.7:1, entry 7). This was the highest stereoselectivity observed in this series of experiments, but it also indicated that the *S*-ethyl used in our original study remains the best leaving group for the purpose of the HAD.

While the rationale of the reduced stereoselectivity in case of *S*-aryl glycosides is related to the possible interference of DMTST with the N atom of picoloyl group, in case of *O*/*S*-imidates, the basis for the reduced selectivity is arguably different. It is our assumption that the presence of the additional N-atom of the *S*/*O*-imidoyl leaving group, and as a result additional H-bond acceptor site, might be the reason for decreased stereoselectivity recorded with glycosyl *O*/*S*-imidates. This effect is particularly strong in case of the SBox leaving group, which is activated by the direct pathway via the anomeric sulfur.[13a,15] This leaves the nitrogen atom of the SBox leaving group available to form the undesirable H bond with the glycosyl acceptor. In turn, this effect is weakened in case of STaz and TCAI donors, which are activated via the remote N atom.[14a,15,16] A lower selectivity in case of the STaz donor in comparison to that of the TCAI donor could be related to the interference of the promoter. Thus, complexa-

Table 2. Effect of the leaving group and promoters on the stereoselectivity.



1b: LG = SPh; **1c**: LG = STol; **1d**: LG = SBox; **1e**: LG = STaz; **1f**: LG = OTCAI

Entry	Donor	Conditions	Product (yield [%], α/β ratio)
1	 **1b**	DMTST (2 equiv), 2.5 h	**3** (85, 5.3:1)
2	 **1c**	DMTST (2 equiv), 3 h	**3** (90, 6.7:1)
3	 **1d**	AgOTf (2 equiv), 2 h	**3** (79, 1:1.9)
4	**1d**	DMTST (2 equiv), 6 h	**3** (80, 6.1:1)
5	 **1e**	AgOTf (2 equiv), 6 h	**3** (86, 6.3:1)
6	 **1f**	TMSOTf (0.5 equiv), 3 h	**3** (44, 5.9:1)
7	**1f**	TfOH (0.5 equiv), 2 h	**3** (92, 9.7:1)

glycosyl donor **α-10**, which, upon reaction with bromine, produced the β-bromide intermediate predominantly. As a result, disaccharide **11** was obtained in the good yield of 67% and with the exclusive α-selectivity (entry 2). The average yield, which is due to the competing isomerization of β- to α-bromide, could be further improved by using $HgBr_2$ as the co-promoter. In this case disaccharide **11** was isolated in an improved yield of 86% (entry 3). However, the stereoselectivity dropped noticeably ($\alpha/\beta = 8.0{:}1$) because mercury(II) salts can readily activate α-bromides (Helferich conditions).[19]

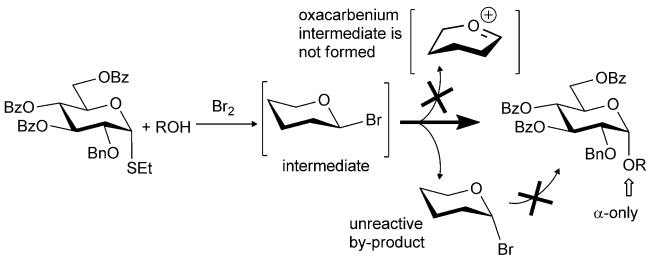
Other, more reactive, thioglycosides such as the standard armed thioglycoside donor **12**,[20] failed to produce high levels of stereoselectivity. This is because per-*O*-benzylated α-bromide is sufficiently reactive in the presence of bromine and able to produce glycosides directly. This reaction proceeds via the oxacarbenium intermediate and hence provides lower stereoselectivity. Thus, coupling of glycosyl donor **12** with acceptor **2** in the presence of Br_2 produced disaccharide **13** in 68% yield and poor selectivity ($\alpha/\beta = 2.4{:}1$, entry 4). In this context, the glycosidation of the 4-*O*-benzoylated donor **14** with acceptor **2** was even less selective and disaccharide **15** was produced in 75% yield and $\alpha/\beta = 1{:}1.8$ (entry 5).

The series of results presented in Table 3 clearly demonstrate that bromine-mediated activation of thioglycosides offers a promising method for the synthesis of α-glucosides. However, notable limitations including modest yields and high substrate specificity (only works for superdisarmed α-thioglycoside which is harder to synthesize than its more conventional β-counterpart)[17,21] narrow the application of this highly stereo-

tion of Ag^I used for the activation of STaz with picoloyl nitrogen makes it less effective in conducting HAD. This negative result could not be improved with DMTST because the STaz imidate activation with this promoter is very sluggish.[14b]

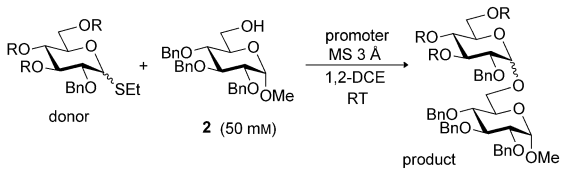
Having concluded that the *S*-ethyl is the best leaving group for HAD reactions, it came to our attention that another approach for α-glucosylation recently introduced by our laboratory was also based on the *S*-ethyl leaving group.[17] Over the course of that study we demonstrated that bromine-mediated glycosidation of *S*-ethyl donor equipped with the superdisarming protecting group pattern (3,4,6-tri-*O*-benzoyl-2-*O*-benzyl)[18] proceed via the highly reactive 1,2-*trans* bromide intermediate (Scheme 2). We also demonstrated that the 1,2-*trans* glycosyl bromide is the only intermediate leading to products while 1,2-*cis* bromide remains unreactive and the oxacarbenium intermediate does not form. Consequently, the nucleophilic displacement of β-bromide takes place in the concerted bimolecular fashion leading to exclusive α-stereoselectivity.[17]

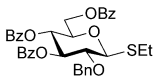
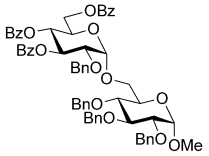
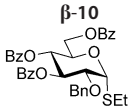
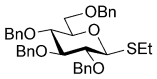
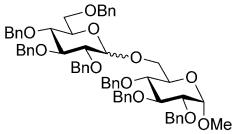
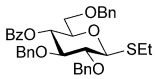
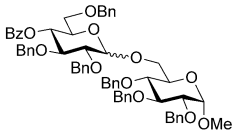
For instance, 3,4,6-tri-*O*-benzoyl-2-*O*-benzyl thioglycoside (**β-10**) was coupled with acceptor **2** in the presence of bromine to afford disaccharide **11** with exclusive 1,2-*cis* selectivity (entry 1, Table 3). The low yield of 28% was due to the fact that **β-10** predominantly forms α-bromide (~68%), which does not react under these reaction conditions. We were able to enhance the utility of this reaction by synthesizing and applying



Scheme 2. Bromine-promoted synthesis of α-glycosides.[17]

Table 3. Bromine-mediated activation of *S*-ethyl donors.[17]



Entry	Donor	Conditions	Product	Yield [%] (α/β ratio)
1	 **β-10**	Br_2, 16 h	 **11**	28 (α only)
2	 **α-10**	Br_2, 16 h	**11**	67 (α only)
3	**α-10**	$Br_2/HgBr_2$, 5 h	**11**	86 (8.0:1)
4	 **12**	Br_2, 0.25 h	 **13**	68 (2.4:1)
5	 **14**	Br_2, 16 h	 **15**	75 (1:1.8)

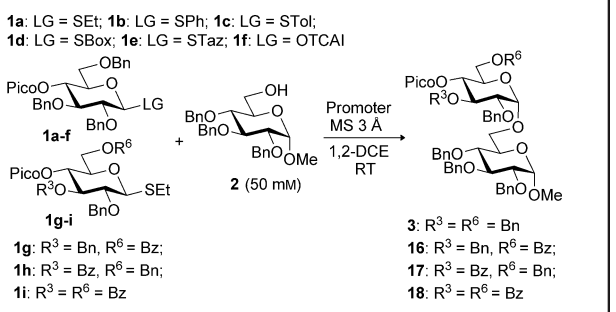
selectivity in HAD reactions implies that this additive can be used to further enhance the yield if so desired.

Encouraged by these intriguing findings, we decided to reinvestigate other glycosyl donors **1b–f**, which previously gave low stereoselectivity in HAD reactions (vide supra). To our delight, both thioglycoside (**1b** and **1c**) and thioimidate (**1d** and **1e**) donors produced disaccharide **3** in high yields of 72–87% and complete 1,2-*cis* selectivity in each case, with or without $HgBr_2$ (entries 4–9, Table 4). The highly reactive trichloroacetimidate donor **1f** also gave high α-selectivity upon activation with Br_2 ($\alpha/\beta = 18{:}1$, entry 10). The high or even complete α-selectivity obtained from all 4-*O*-picoloylated glycosyl donors **1a–f** indicates that, unlike previously tested promoter systems, bromine-promoted glycosylations are less sensitive to the nature of the leaving and protecting groups. These results also indicate that this additive can be used to further enhance the yield if so desired.

selective method. Having also encountered some limitations of the HAD approach, we wondered whether combining these two promising techniques would allow us to develop a more flexible methodology for α-glycosylation. With this general idea in mind, a test glycosylation reaction of 4-picoloylated thioglycoside donor **1a** with glycosyl acceptor **2** in the presence of Br_2 was set up. To our delight, disaccharide **3** was produced in 77% yield and complete α-selectivity (entry 1, Table 4). The use of $HgBr_2$ as an additive further enhanced the yield to 83% and, remarkably, the stereoselectivity still remained complete (entry 2).

It should be noted that these initial experiments were performed in normal concentration (50 mM of **3**), with which typical HAD reactions give only average stereoselectivity. For comparison, DMTST-promoted activation of **1a** gave disaccharide **3** with $\alpha/\beta = 2.8{:}1$ selectivity (entry 3).[5] The lower stereoselectivity in HAD-mediated glycosylations in regular concentration was rationalized by a competition between the H-bonded acceptor and the free acceptor in solution.[5] This issue was previously addressed by using high dilution conditions (5 mM of acceptor), which became mandatory for most reactions using HAD.[6,9] The result of the bromine-promoted activation indicates that HAD reactions can now be successfully conducted in normal concentrations. Furthermore, the fact that the reaction in the presence of $HgBr_2$ still maintained complete stereo-

Table 4. Br_2-mediated activation of various glycosyl donors **1a–i** leads to good yields and complete α-selectivity.

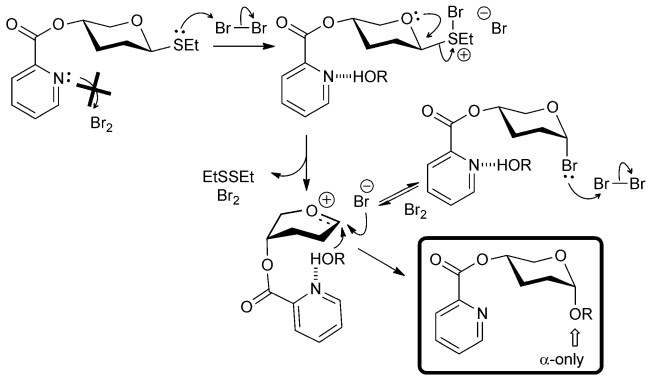


Entry	Donor	Conditions	Product (yield [%], α/β ratio)
1	**1a**	Br_2, 4.5 h	**3** (77, α only)
2	**1a**	$Br_2/HgBr_2$, 2 h	**3** (83, α only)
3	**1a**	DMTST, 4 h	**3** (85, 2.8:1)
4	**1b**	Br_2, 5.5 h	**3** (72, α only)
5	**1b**	$Br_2/HgBr_2$, 3 h	**3** (79, α only)
6	**1c**	Br_2, 16 h	**3** (70, α only)
7	**1c**	$Br_2/HgBr_2$, 16 h	**3** (86, α only)
8	**1d**	Br_2, 16 h	**3** (71, α only)
9	**1e**	Br_2, 16 h	**3** (87, α only)
10	**1f**	Br_2, 0.5 h	**3** (89, 18.0:1)
11	**1g**	Br_2, 6 h	**16** (79, α only)
12	**1h**	Br_2, 10 h	**17** (81, α only)
13	**1i**	Br_2, 24 h	**18** (73, α only)

cate that bromine may serve as an effective and inexpensive promoter for a variety of glycosylation reactions. It should be noted that some of the leaving groups tested here have never been previously activated with bromine. To make this protocol even more appealing and versatile, we investigated a series of partially benzoylated glycosyl donors **1 g–i**. Although these reactions were a bit slower than the glycosidation of 2,3,6-tri-*O*-benzylated donor **1 a** (entries 11–13 vs. 1, Table 4) disaccharides **16**–**18** have been obtained in 73–81% yield and complete α-selectivity.

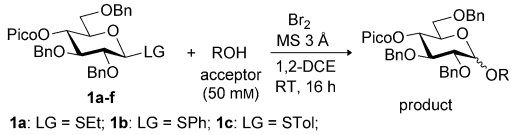
A low temperature (−40 °C) NMR monitoring of the reaction of glycosyl donor **1 a** with Br_2 showed direct and rapid formation of the respective α-bromide. Based on our previous mechanistic study,[17] we believe that β-bromide will be also forming at the beginning of the reaction. However, in the highly benzylated system it very rapidly equilibrates into the thermodynamically stable α-bromide. Therefore, in this particular case the β-bromide intermediate is expected to be a very insignificant intermediate en route to glycosylation products. Highly benzylated α-bromide is expected to be reactive under these reaction conditions, as seen from experiments with perbenzylated and 4-benzoyl thioglycosides **12** and **14**, respectively (Table 3). In case of 4-*O*-picoloylated glycosyl donor, bromide leaving group departs and the 4-*O*-picoloyl-mediated HAD ensures that the nucleophile is delivered exclusively from the bottom face of the resulting oxacarbenium intermediate (Scheme 3). Minimal formation of other electrophilic species in the bromine-promoted HAD may be the key to the success of this method unlike other cases with electrophilic promoters including DMTST, wherein excess promoter may interfere with the hydrogen-bond acceptor (picoloyl nitrogen). Glycosidation of partially benzylated donors **1 g–i** is slower than that of **1 a** (Table 4); nevertheless, the rates of the reaction are still practical.

Since all 4-*O*-picoloylated glycosyl donors gave exceptional 1,2-*cis* selectivity upon coupling with primary acceptor **2** in the presence of Br_2, we attempted to expand the approach to different acceptors ranging from highly reactive aliphatic alcohols to sterically hindered secondary sugar alcohols. Although a vast majority of reactions proceeded with high selectivities and good yields (Table 5), we noticed some unusual trends, the nature of which is still hard to rationalize. For instance, glycosyl donor **1 a** was practically ineffective when treated with secondary glycosyl acceptor **8** (entry 3), even in the presence of $HgBr_2$. Interestingly, *S*-phenyl donor **1 b** could be efficiently coupled both with primary and secondary glycosyl acceptors. Most glycosidations of **1 b** produced high yields and very high 1,2-*cis* selectivity (entries 4–7). Also, glycosidations of *S*-tolyl and *S*/*O*-imidoyl donors **1 c–f** provided comparable results and consistently high α-selectivities (entries 8–11).

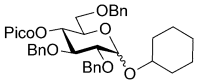
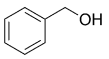
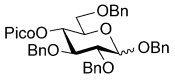
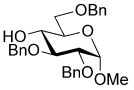
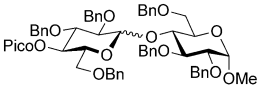
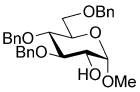
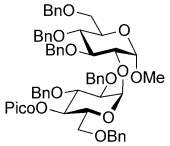
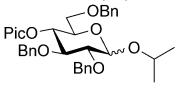


Scheme 3. Mechanistic rationale of Br_2-promoted HAD reaction.

Table 5. Glycosylation of various acceptors using Br_2-promoted HAD.



1a: LG = SEt; **1b**: LG = SPh; **1c**: LG = STol; **1d**: LG = SBox; **1e**: LG = STaz; **1f**: LG = OTCAI

Entry	Donor	Acceptor	Product (yield [%],[a] α/β ratio)
1	**1 a**		
		19	**20** (49, 21.0:1)
2	**1 a**		
		21	**22** (51, 17.1:1)
3	**1 a**		
		8	**9** (< 10)
4	**1 b**	**8**	**9** (60, α only)
5	**1 b**		
		4	**5** (72, α only)
6	**1 b**	**21**	**22** (60, 18.2:1)
7	**1 b**		
		23	**24** (47, 13.0:1)
8	**1 c**	**19**	**20** (68, 19.3:1)
9	**1 d**	**4**	**5** (43, α only)
10	**1 e**	**4**	**5** (58, α only)
11[b]	**1 f**	**4**	**5** (78, 21.0:1)

[a] Reactions were stopped at 16 h unless noted otherwise; [b] reaction was completed within 2.5 h.

Conclusion

As a result of this in depth study, we have expanded the HAD concept to different 4-*O*-picoloylated glycosyl donors with

widely used leaving groups including SPh, STol and *S*/*O*-imidates. Having investigated a variety of promoter systems we determined the superior properties of Br_2 as promoter for HAD. Very high selectivities and good yields have been recorded in most cases with all classes of glycosyl donors at room temperature, while previously investigated reactions required low temperature. All bromine-promoted reactions have been performed under regular dilution (50 mM concentration of the acceptor) unlike other promoter systems that would only work in low concentration (5 mM).

Clearly, the bromine-promoted HAD enhances the utility of the two previously developed techniques, HAD[5] and bromine-assisted glycosidation of thioglycosides,[17] by complementing each other. The bromine-mediated activation pathway is uncommon in synthesis, and many glycosyl donors investigated herein have never been activated under these conditions. The conversion rates remain relatively slow, which creates the basis for further study, and the ability to enhance the yields by using an additive such as $HgBr_2$ has been demonstrated. Further investigation of the HAD method in conjunction with the bromine activation and beyond are currently underway in our laboratory.

Experimental Section

General

Column chromatography was performed on silica gel 60 (70–230 mesh); reactions were monitored by TLC on Kieselgel 60 F254. The compounds were detected by examination under UV light and by charring with 10% sulfuric acid in methanol. Solvents were removed under reduced pressure at $<40\,^{\circ}C$. CH_2Cl_2 and $ClCH_2CH_2Cl$ (1,2-DCE) were distilled from CaH_2 directly prior to application. Pyridine was dried by refluxing with CaH_2 and then distilled and stored over molecular sieves (3 Å). Anhydrous DMF and THF were used as received. Molecular sieves (3 or 4 Å) used for reactions were crushed and activated in vacuo at 390 °C during 8 h in the first instance and then for 2–3 h at 390 °C directly prior to application. AgOTf was co-evaporated with toluene (3×10 mL) and dried in vacuo for 2–3 h directly prior to application. Optical rotations were measured with a Jasco P-1020 polarimeter. Unless noted otherwise, ^1H NMR spectra were recorded in $CDCl_3$ at 300 or 600 MHz, ^{13}C NMR spectra were recorded in $CDCl_3$ at 75 or 150 MHz.

Synthesis of glycosyl donors

Ethyl 2,3,6-tri-*O*-benzyl-4-*O*-picoloyl-1-thio-β-D-glucopyranoside (1 a): The title compound was synthesized according to the reported procedure and the analytical data for **1 a** was essentially the same as reported previously.[5]

Phenyl 2,3,6-tri-*O*-benzyl-4-*O*-picoloyl-1-thio-β-D-glucopyranoside (1 b): Picolinic acid (0.23 g, 1.84 mmol), *N*,*N*′-dicyclohexylcarbodiimide (0.38 g, 1.84 mmol), and 4-dimethylaminopyridine (23 mg, 0.19 mmol) were added to a solution of phenyl 2,3,6-tri-*O*-benzyl-1-thio-β-D-glucopyranoside[22] (0.50 g, 0.92 mmol) in CH_2Cl_2 (10 mL) and the resulting mixture was stirred under argon for 30 min at RT. The solid was then filtered off and washed successively with CH_2Cl_2. The combined filtrate (~100 mL) was washed with brine (2×10 mL). The organic phase was separated, dried with magnesium sulfate, and concentrated, in vacuo. The residue was purified by column chromatography on silica gel (ethyl acetate/hexane gradient elution) to give the title compound as a white amorphous solid in 94% yield (0.56 g, 0.87 mmol). Analytical data for **1 b**: $R_f=0.44$ (ethyl acetate/hexane, 1:1, v/v); $[\alpha]_D^{25}=-38.7$ ($c=1.0$, $CHCl_3$); ^1H NMR: $\delta=3.62$ (dd, 1H, $J_{2,3}=8.8$ Hz, H-2), 3.64–3.70 (m, 2H, H-6a, 6b), 3.89 (m, 1H, H-5), 3.94 (dd, 1H, $J_{3,4}=8.9$ Hz, H-3), 4.48 (s, 2H, CH_2Ph), 4.73 (dd, 2H, $^2J=11.2$ Hz, CH_2Ph), 4.76 (d, 1H, $J_{1,2}=8.5$ Hz, H-1), 4.81 (dd, 2H, $^2J=10.3$ Hz, CH_2Ph), 5.40 (dd, 1H, $J_{4,5}=9.8$ Hz, H-4), 7.00–8.00 (m, 23H, aromatic), 8.72 ppm (d, 1H, $J=3.1$ Hz, aromatic); ^{13}C NMR: $\delta=69.7$, 72.3, 73.6, 75.7 (×2), 77.5, 80.8, 84.0, 87.6, 125.7, 127.2, 127.6, 127.7, 127.8 (×2), 128.1 (×3), 128.3 (×5), 128.5 (×2), 128.6 (×2), 129.1 (×2), 132.1 (×2), 133.6, 137.1, 138.0 (×2), 138.1, 147.6, 150.0, 164.3 ppm; HR FAB MS $[M+H]^+$ calcd for $C_{39}H_{38}NO_6S$ 648.2420, found 648.2437.

Tolyl 2,3,6-tri-*O*-benzyl-4-*O*-picoloyl-1-thio-β-D-glucopyranoside (1 c): The title compound was obtained as a white amorphous solid from tolyl 2,3,6-tri-*O*-benzyl-1-thio-β-D-glucopyranoside[23] (0.50 g, 0.90 mmol) as described for the synthesis of **1 b** in 96% yield (0.57 g, 0.86 mmol). Analytical data for **1 c**: $R_f=0.44$ (ethyl acetate/hexane, 1:1, v/v); $[\alpha]_D^{25}=-38.7$ ($c=1.0$, $CHCl_3$); ^1H NMR: $\delta=$ 2.30 (s, 3H, CH_3), 3.59 (dd, 1H, $J_{2,3}=8.9$ Hz, H-2), 3.85 (m, 1H, H- 5), 3.93 (dd, 1H, $J_{3,4}=9.0$ Hz, H-3), 4.47 (s, 2H, CH_2Ph), 4.69 (d, 1H, $J_{1,2}=9.8$ Hz, H-1), 4.71 (dd, 2H, $^2J=11.1$ Hz, CH_2Ph), 4.81 (dd, 2H, $^2J=10.4$ Hz, CH_2Ph), 5.38 (dd, 1H, $J_{4,5}=9.7$ Hz, H-4), 6.90–8.15 (m, 22H, aromatic), 8.12 ppm (d, 1H, $J=3.9$ Hz, aromatic); ^{13}C NMR: $\delta=21.2$, 69.6, 72.2, 73.5, 75.6 (×2), 77.4, 80.7, 83.9, 87.7, 125.6, 127.1, 127.4, 127.6, 127.7 (×2), 127.9 (×2), 128.2 (×5), 128.5 (×2), 128.7 (×2), 129.4, 129.8 (×2), 132.8 (×2), 137.0, 137.9 (×2), 138.0, 138.1, 147.5, 149.9, 164.2 ppm; HR FAB MS $[M+H]^+$ calcd for $C_{40}H_{40}NO_6S$ 662.2576, found 662.2539.

Benzoxazolyl 2,3,6-tri-*O*-benzyl-4-*O*-picoloyl-1-thio-β-D-glucopyranoside (1 d): A mixture of **1 a** (0.50 g, 0.83 mmol) and activated molecular sieves 3 Å (0.42 g) in CH_2Cl_2 (12.6 mL) was stirred under argon for 1 h at RT. Freshly prepared solution of Br_2 in CH_2Cl_2 (8.0 mL, 1:165, v/v) was then added and the resulting mixture was stirred for 10 min at RT. After that, the volatiles were removed under the reduced pressure at RT and the residue was dried in vacuo for 3 h. The crude residue was dissolved in dry acetone (10.0 mL), KSBox[13a] (0.47 g, 2.5 mmol) and 18-crown-6 (44 mg, 0.17 mmol) were added, and the resulting mixture was stirred under argon for 2 h at RT. The solid was filtered off and washed successively with toluene. The combined filtrate (~90 mL) was washed with 1% aq. NaOH (15 mL) and water (3×10 mL). The organic phase was separated, dried with $MgSO_4$, and concentrated in vacuo. The residue was purified by column chromatography on silica gel (ethyl acetate/hexane gradient elution) to give the title compound as a pale-yellow syrup in 82% yield (0.47 g, 0.68 mmol). Analytical data for **1 d**: $R_f=0.42$ (ethyl acetate/hexane, 3:2, v/v); $[\alpha]_D^{23}=+42.3$ ($c=1.0$, $CHCl_3$); ^1H NMR: $\delta=3.75$–3.87 (m, 2H, H-6a, 6b), 4.02 (dd, 1H, $J_{2,3}=9.8$ Hz, H-2), 4.12–4.23 (m, 2H, H-3, 5), 4.55 (dd, 2H, $^2J=11.9$ Hz, CH_2Ph), 4.90 (dd, 2H, $^2J=11.2$ Hz, CH_2Ph), 4.98 (dd, 2H, $^2J=10.6$ Hz, CH_2Ph), 5.65 (dd, 1H, $J_{4,5}=9.7$ Hz, H-4), 5.68 (dd, 1H, $J_{1,2}=9.9$ Hz, H-1), 7.15–7.98 (m, 21H, aromatic), 8.12 (d, 1H, $J=7.8$ Hz, aromatic), 8.87 ppm (d, 1H, $J=4.6$ Hz, aromatic); ^{13}C NMR: $\delta=69.1$, 71.9, 75.6, 75.7, 75.9, 78.3, 80.6, 84.0, 84.9, 110.3, 119.2, 124.5, 124.6, 125.7, 127.2, 127.5, 127.8, 127.9 (×2), 128.2 (×3), 128.3 (×2), 128.4 (×2), 128.5 (×2), 128.6 (×2), 137.1, 137.5, 137.9 (×2), 142.0, 147.6, 150.1, 152.0, 161.5, 164.2 ppm; HR FAB MS $[M+Na]^+$ calcd for $C_{40}H_{36}O_7N_2SNa$ 711.2141, found 711.2164.

2-Thiazolinyl 2,3,6-tri-*O*-benzyl-4-*O*-picoloyl-1-thio-β-D-glucopyranoside (1 e): A mixture of **1 a** (0.50 g, 0.83 mmol) and activated molecular sieves 3 Å (0.42 g) in CH_2Cl_2 (12.6 mL) was stirred under argon for 1 h at RT. Freshly prepared solution of Br_2 in CH_2Cl_2 (8.0 mL, 1:165, v/v) was added and the resulting mixture was

stirred for 5 min at RT. After that, the volatiles were removed under the reduced pressure at RT and the residue was dried in vacuo for 3 h. The crude residue was in dissolved in dry acetonitrile (10.0 mL), NaSTaz[14b] (0.35 g, 2.5 mmol) and 15-crown-5 (37 mg, 0.17 mmol) were added and the resulting mixture was stirred under argon for 3.5 h at RT. The solid was filtered off and washed successively with CH_2Cl_2. The combined filtrate (~90 mL) was washed with 1% aq. NaOH (15 mL) and water (3×10 mL). The organic phase was separated, dried with $MgSO_4$, and concentrated in vacuo. The residue was purified by column chromatography on silica gel (ethyl acetate/hexane gradient elution) to give the title compound as a colorless syrup in 84% yield (0.46 g, 0.70 mmol). Analytical data for **1e**: R_f=0.45 (acetone/toluene, 1:4, v/v); $[\alpha]_D^{23}$=+42.3 (c=1.0, $CHCl_3$); ^{1}H NMR: δ=3.32 (t, 2H, J=8.1 Hz, SCH_2), 3.58–3.68 (m, 2H, H-6a, 6b), 3.71 (dd, 1H, $J_{2,3}$=9.3 Hz, H-2), 3.94 (dd, 1H, $J_{3,4}$=9.1 Hz, H-3), 3.95 (m, 1H, H-5), 4.03–4.28 (m, 2H, NCH_2), 4.46 (s, 2H, CH_2Ph), 4.71 (dd, 2H, ^2J=11.3 Hz, CH_2Ph), 4.78 (dd, 2H, ^2J=10.2 Hz, CH_2Ph), 5.34 (d, 1H, $J_{1,2}$=10.0 Hz, H-1), 5.43 (dd, 1H, $J_{4,5}$=9.7 Hz, H-4), 6.95–8.00 (m, 18H, aromatic), 8.70 ppm (d, 1H, J=4.7 Hz, aromatic); ^{13}C NMR: δ=35.2, 64.3, 69.2, 72.0, 73.5, 75.6, 75.8, 77.8, 80.7, 83.9, 84.8, 125.7, 127.2, 127.5, 127.7, 127.9 (×2), 128.1 (×2), 128.2 (×2), 128.3 (×4), 128.6 (×2), 129.2, 129.9, 137.1, 137.6, 137.9, 138.0, 147.6, 150.0, 164.1 ppm; HR FAB MS $[M+Na]^+$ calcd for $C_{36}H_{36}O_6N_2S_2Na$ 679.1912, found 679.1943.

2,3,6-Tri-*O*-benzyl-4-*O*-picoloyl-β-D-glucopyranosyl trichloroacetimidate (1f): $Hg(CF_3CO_2)_2$ (0.7 g, 1.67 mmol) was added to a mixture of **1a** (0.5 g, 0.84 mmol) in CH_2Cl_2 (10 mL) containing water (0.5 mL) and the resulting mixture was stirred for 1 h at 0 °C. The reaction mixture was then allowed to warm to RT and stirred for additional 16 h. After that, the reaction mixture was diluted with CH_2Cl_2 (~100 mL) and washed with sat. aq. $NaHCO_3$ (10 mL) and water (10 mL). The organic phase was separated, dried with magnesium sulfate, and concentrated in vacuo. The residue was purified by column chromatography on silica gel (ethyl acetate/hexane gradient elution) to afford 2,3,6-tri-*O*-benzyl-4-*O*-picoloyl-D-glucopyranose (**25**) as a colorless syrup in 87% yield (0.41 g, 0.74 mmol). Analytical data for **25**: R_f=0.38 (acetone/toluene, 3:7, v/v); ^{1}H NMR of **α-25**: δ=3.47–3.63 (m, 3H, H-5, 6a, 6b), 3.82–3.95 (m, 2H, H-3, 5), 4.44 (d, 1H, $J_{1,2}$=9.7 Hz, H-1), 4.55–5.03 (m, 6H, 3×CH_2Ph), 5.35 (dd, 1H, $J_{4,5}$=9.5 Hz, H-4), 7.00–8.80 ppm (m, 19H, aromatic); ^{1}H NMR of **β-25**: δ=3.68 (dd, 1H, $J_{1,2}$=3.4 Hz, $J_{2,3}$=9.4 Hz, H-2), 4.28–4.51 (m, 4H, H-3, 5, 6a, 6b), 4.55–5.03 (m, 6H, 3×CH_2Ph), 5.25–5.44 (m, 2H, H-1, 4), 7.00–8.80 ppm (m, 19H, aromatic); selected ^{13}C NMR data for **25**: δ=68.6, 69.1, 69.5, 72.3, 73.0, 73.3, 73.6, 73.7, 74.9, 75.4, 75.5, 79.1 (×2), 80.0, 81.7, 83.0, 91.5, 97.6 ppm; HR FAB MS $[M+H]^+$ calcd for $C_{33}H_{34}NO_7$ 556.2335, found 556.2317. Trichloroacetonitrile (0.22 mL, 2.21 mmol) and K_2CO_3 (0.20 g, 1.48 mmol) were added to a solution of **25** (0.41 g, 0.74 mmol) in CH_2Cl_2 (5.0 mL) and the resulting mixture was stirred under argon for 16 h at RT. After that, the solid was filtered off and washed successively with CH_2Cl_2. The combined filtrate (~50 mL) was concentrated in vacuo and the residue was purified by column chromatography on silica gel (acetone/toluene gradient elution) to give the title compound as a white amorphous solid in 64% yield (0.33 g, 0.47 mmol). Analytical data for **1f**: R_f=0.43 (acetone/toluene, 3:7, v/v); $[\alpha]_D^{25}$=−38.7 (c=1.0, $CHCl_3$); ^{1}H NMR: δ=3.57–3.74 (m, 2H, H-6a, 6b), 3.85 (dd, 1H, $J_{2,3}$=8.0 Hz, H-2), 3.93–4.04 (m, 2H, H-3, 5), 4.47 (s, 2H, CH_2Ph), 4.71 (dd, 2H, ^2J=11.4 Hz, CH_2Ph), 4.84 (dd, 2H, ^2J=10.8 Hz, CH_2Ph), 5.48 (dd, 1H, $J_{4,5}$=9.6 Hz, H-4), 5.87 (d, 1H, $J_{1,2}$=7.9 Hz, H-1), 6.95–8.05 (m, 17H, aromatic), 8.74 ppm (m, 2H, aromatic); ^{13}C NMR: δ=68.9, 71.8, 73.5, 74.4, 75.3, 79.2, 81.0, 81.7, 91.0, 98.3, 127.2, 127.6 (×2), 127.9 (×2), 128.1 (×2), 128.2 (×2), 128.3 (×4), 128.6 (×2), 128.7, 129.2, 137.2, 138.0 (×2), 138.1, 147.5, 149.9, 161.3, 164.1 ppm; HR FAB MS $[M+Na]^+$ calcd for $C_{35}H_{33}O_7N_2Cl_3Na$ 721.1251, found 721.1289.

Ethyl 6-*O*-benzoyl-2,3-di-*O*-benzyl-4-*O*-picoloyl-1-thio-β-D-glucopyranoside (1g): The title compound was obtained as a white amorphous solid from ethyl 6-*O*-benzoyl-2,3-di-*O*-benzyl-1-thio-β-D-glucopyranoside[24] (0.36 g, 0.71 mmol) as described for the synthesis of **1b** in 89% yield (0.54 g, 0.90 mmol). Analytical data for **1g**: R_f=0.36 (ethyl acetate/hexane, 3:2, v/v); $[\alpha]_D^{28}$=−1.9 (c=1.0, $CHCl_3$); ^{1}H NMR: δ=1.29 (t, 3H, J=7.4 Hz, SCH_2CH_3), 2.75 (m, 2H, SCH_2CH_3), 3.60 (dd, 1H, $J_{2,3}$=9.2 Hz, H-2), 3.96 (dd, 1H, $J_{3,4}$=9.2 Hz, H-3), 3.96–4.05 (m, 1H, H-5), 4.40 (dd, 1H, $J_{5,6a}$=5.4 Hz, $J_{6a,6b}$=12.1 Hz, H-6a), 4.54 (dd, 1H, $J_{5,6b}$=2.9 Hz, H-6b), 4.59 (d, 1H, $J_{1,2}$=9.8 Hz, H-1), 4.75 (dd, 2H, ^2J=11.2 Hz, CH_2Ph), 4.84 (dd, 2H, ^2J=10.2 Hz, CH_2Ph), 5.52 (dd, 1H, $J_{4,5}$=9.8 Hz, H-4), 6.95–8.10 (m, 18H, aromatic), 8.70 ppm (d, 1H, J=4.6 Hz, aromatic); ^{13}C NMR: δ=15.2, 25.1, 63.6, 75.7 (×2), 75.8, 81.7, 83.6, 85.3, 125.8, 127.2, 127.7, 128.1 (×3), 128.3 (×2), 128.4 (×2), 128.5 (×4), 129.8 (×3), 133.1, 137.1, 137.8, 137.9, 147.4, 149.9, 164.2, 166.2 ppm; HR FAB MS $[M+H]^+$ calcd for $C_{35}H_{36}NO_7S$ 614.2212, found 614.2213.

Ethyl 3-*O*-benzoyl-2,6-di-*O*-benzyl-4-*O*-picoloyl-1-thio-β-D-glucopyranoside (1h): Benzoyl chloride (0.32 mL, 3.0 mmol) and 4-dimethylaminopyridine (37 mg, 0.30 mmol) were added to a solution of ethyl 2-*O*-benzyl-4,6-*O*-benzylidene-1-thio-β-D-glucopyranoside[21] (0.60 g, 1.50 mmol) in pyridine (10 mL) and the resulting mixture was stirred under argon for 3 h at RT. After that, the reaction was quenched with methanol (~3 mL) and the volatiles were removed in vacuo. The residue was diluted with CH_2Cl_2 (~150 mL) and washed with 1N HCl (15 mL), sat. aq. $NaHCO_3$ (15 mL), and water (2×15 mL). The organic phase was separated, dried with magnesium sulfate, and concentrated in vacuo. The residue was purified by column chromatography on silica gel (ethyl acetate/hexane gradient elution) to give ethyl 3-*O*-benzoyl-2-*O*-benzyl-4,6-*O*-benzylidene-1-thio-β-D-glucopyranoside (**26**) as a white amorphous solid in 91% yield (0.69 g, 1.4 mmol). Analytical data for **26**: R_f=0.56 (ethyl acetate/hexane, 3:7, v/v); $[\alpha]_D^{27}$=−32.1 (c=1.0, $CHCl_3$); ^{1}H NMR: δ=1.32 (t, 3H, J=7.4 Hz, SCH_2CH_3), 2.78 (m, 2H, SCH_2CH_3), 3.52–3.68 (m, 2H, H-2, 5), 3.71–3.83 (m, 2H, H-4, 6a), 4.37 (dd, 1H, $J_{5,6b}$=4.9 Hz, $J_{6a,6b}$=10.5 Hz, H-6b), 4.69 (d, 1H, $J_{1,2}$=9.7 Hz, H-1), 4.72 (dd, 2H, ^2J=10.6 Hz, CH_2Ph), 5.47 (s, 1H, >CHPh), 5.65 (dd, 1H, $J_{3,4}$=9.4 Hz, H-3), 7.00–8.10 ppm (m, 15H, aromatic); ^{13}C NMR: δ=15.2, 25.6, 68.7, 70.5, 75.0, 75.5, 78.9, 79.9, 86.0, 101.4, 126.2 (×2), 127.9, 128.3 (×2), 128.4 (×4), 128.5 (×2), 129.1, 129.9 (×2), 130.0, 133.2, 137.0, 137.3, 165.5 ppm; HR FAB MS $[M+H]^+$ calcd for $C_{29}H_{31}O_6S$ 507.1841, found 507.1863.

A mixture of compound **26** (0.65 g, 1.3 mmol) and freshly activated molecular sieves (3 Å, 1.0 g) in THF (20 mL) was stirred under argon for 1 h at RT. $NaCNBH_4$ (1.0 g, 16.2 mmol) was added followed by dropwise addition of a 2M solution of HCl in Et_2O (8.1 mL, 16.2 mmol) and the resulting mixture was stirred for 1 h at RT. After that, the volatiles were removed in vacuo. The residue was diluted with CH_2Cl_2 (~50 mL), the solid was filtered off and was washed successively with CH_2Cl_2. The combined filtrate (~150 mL) was washed with sat. aq. $NaHCO_3$ (15 mL) and water (2×15 mL). The organic phase was separated, dried with magnesium sulfate, and concentrated in vacuo. The residue was purified by column chromatography on silica gel (ethyl acetate/hexane gradient elution) to give ethyl 3-*O*-benzoyl-2,6-di-*O*-benzyl-1-thio-β-D-glucopyranoside (**27**) as a colorless syrup in 87% yield (0.57 g, 1.1 mmol). Analytical data for **27**: R_f=0.41 (ethyl acetate/hexane, 3:7, v/v); $[\alpha]_D^{27}$=+21.1 (c=1.0, $CHCl_3$); ^{1}H NMR: δ=1.32 (t, 3H, J=7.4 Hz, SCH_2CH_3), 2.77 (m, 2H, SCH_2CH_3), 3.53–3.62 (m, 2H, H-2, 6a), 3.72–3.86 (m, 3H, H-4, 5, 6b), 4.51–4.63 (m, 4H, H-1, 1½ CH_2Ph), 4.82 (d, 1H, ^2J=10.7 Hz, ½ CH_2Ph), 5.32 (dd, 1H, $J_{3,4}$=9.1 Hz, H-3),

7.05–7.60 (m, 13H, aromatic), 8.01 ppm (d, 2H, $J=8.4$ Hz, aromatic); ^{13}C NMR: $\delta=15.3$, 25.5, 70.5, 71.3, 73.9, 75.4, 78.5, 79.1, 79.8, 85.3, 127.9 (×2), 128.0 (×2), 128.5 (×4), 128.6 (×4), 129.7, 130.1 (×2), 133.6, 137.5, 137.9, 167.3 ppm; HR FAB MS $[M+H]^+$ calcd for $C_{29}H_{33}O_6S$ 509.1998, found 509.1207.

The title compound was then obtained as a white amorphous solid from **27** (0.52 g, 1.0 mmol) as described for the synthesis of **1b** in 92% yield (0.58 g, 0.95 mmol). Analytical data for **1h**: $R_f=0.36$ (ethyl acetate/hexane, 3:2, v/v); $[\alpha]_D^{27}=-28.8$ ($c=1.0$, $CHCl_3$); ^{1}H NMR: $\delta=1.35$ (t, 3H, $J=7.4$ Hz, SCH_2CH_3), 2.80 (m, 2H, SCH_2CH_3), 3.64–3.77 (m, 3H, H- 2, 6a, 6b), 3.94 (m, 1H, H-5), 4.49 (dd, 2H, $^2J=12.0$ Hz, CH_2Ph), 4.69 (d, 1H, $J_{1,2}=9.7$ Hz, H-1), 4.70 (dd, 2H, $^2J=10.8$ Hz, CH_2Ph), 5.56 (dd, 1H, $J_{4,5}=9.8$ Hz, H-4), 5.74 (dd, 1H, $J_{3,4}=9.3$ Hz, H-3), 6.85–8.05 (m, 18H, aromatic), 8.63 ppm (d, 1H, $J=4.0$ Hz, aromatic); ^{13}C NMR: $\delta=15.1$, 25.2, 69.2, 70.6, 73.5, 75.1, 75.9, 77.2, 79.1, 85.2, 125.3, 127.0, 127.5, 127.7 (×2), 127.8, 128.2 (×4), 128.3 (×2), 128.4 (×3), 129.4, 129.7, 133.1, 136.9, 137.1, 137.7, 146.9, 150.0, 163.7, 165.7 ppm; HR FAB MS $[M+H]^+$ calcd for $C_{35}H_{36}NO_7S$ 614.2212, found 614.2218.

Ethyl 3,6-di-*O*-benzoyl-2-*O*-benzyl-4-*O*-picoloyl-1-thio-β-D-glucopyranoside (1i): The title compound was obtained as a white foam from ethyl 3,6-di-*O*-benzoyl-2-*O*-benzyl-1-thio-β-D-glucopyranoside[25] (0.47 g, 0.9 mmol) as described for the synthesis of **1b** in 89% yield (0.50 g, 0.80 mmol). Analytical data for **1i**: $R_f=0.36$ (ethyl acetate/hexane, 3:2, v/v); $[\alpha]_D^{27}=-2.1$ ($c=1.0$, $CHCl_3$); ^{1}H NMR: $\delta=1.30$ (t, 3H, $J=7.4$ Hz, SCH_2CH_3), 2.77 (m, 2H, SCH_2CH_3), 3.72 (dd, 1H, $J_{2,3}=9.5$ Hz, H-2), 4.13 (m, 1H, H-5), 4.45 (dd, 1H, $J_{5,6a}=5.6$ Hz, $J_{6a,6b}=12.2$ Hz, H-6a), 4.59 (dd, 1H, $J_{5,6b}=3.1$ Hz, H-6b), 4.69 (dd, 2H, $^2J=10.8$ Hz, CH_2Ph), 4.72 (d, 1H, $J_{1,2}=9.7$ Hz, H-1), 5.60 (dd, 1H, $J_{4,5}=9.8$ Hz, H-4), 5.77 (dd, 1H, $J_{3,4}=9.3$ Hz, H-3), 6.95–8.05 (m, 18H, aromatic), 8.62 ppm (d, 1H, $J=4.0$ Hz, aromatic); ^{13}C NMR: $\delta=15.2$, 25.4, 63.5, 70.5, 75.3, 75.6, 75.8, 79.2, 85.4, 125.6, 127.3, 128.0, 128.3 (×2), 128.4 (×2), 128.5 (×4), 129.4, 129.7, 129.8 (×4), 133.2, 133.3, 137.1 (×2), 146.8, 150.2, 163.8, 165.7, 166.2 ppm; HR FAB MS $[M+H]^+$ calcd for $C_{35}H_{34}NO_8S$ 628.2005, found 628.2014.

Synthesis of glycosides and disaccharides

Method A: general procedure for glycosylation in the presence of DMTST: A mixture of a glycosyl donor (0.13 mmol), glycosyl acceptor (0.10 mmol), and freshly activated molecular sieves (4 Å, 200 mg) in $ClCH_2CH_2Cl$ (26 mL, 5 mM) was stirred under argon for 1 h at RT. The mixture was then cooled to −30 °C and DMTST[26] (0.26 mmol) was added. The resulting mixture was allowed to warm to RT over a period of 1 h and stirred at RT for the time specified in the Tables. Upon completion, Et_3N (0.3 mL) was added and the resulting mixture was stirred for 30 min. After that, the mixture was diluted with CH_2Cl_2 (10 mL), the solid was filtered off and washed successively with CH_2Cl_2. The combined filtrate (~30 mL) was washed with 20% aq. $NaHCO_3$ (10 mL) and water (3×10 mL). The organic phase was separated, dried with magnesium sulfate, and concentrated in vacuo. The residue was purified by column chromatography on silica gel (ethyl acetate-hexane gradient elution). Anomeric ratios (or anomeric purity) were determined by comparison of the integral intensities of relevant signals in ^{1}H NMR spectra.

Method B: general procedure for glycosylation in the presence of AgOTf: A mixture of a glycosyl donor (0.13 mmol), glycosyl acceptor (0.10 mmol), and freshly activated molecular sieves (4 Å, 200 mg) in $ClCH_2CH_2Cl$ (26 mL, 5 mM) was stirred under argon for 1 h at RT. The mixture was then cooled to −30 °C and AgOTf (0.26 mmol) was added. The resulting mixture was allowed to warm to RT over a period of 1 h and stirred at RT for the time specified in the Tables. Upon completion, Et_3N (0.3 mL) was added and the resulting mixture was stirred for 30 min. After that, the mixture was diluted with CH_2Cl_2 (10 mL), the solid was filtered off and was washed successively with CH_2Cl_2. The combined filtrate (~30 mL) was washed with 20% aq. $NaHCO_3$ (10 mL) and water (3×10 mL). The organic phase was separated, dried with magnesium sulfate, and concentrated in vacuo. The residue was purified by column chromatography on silica gel (ethyl acetate/hexane gradient elution). Anomeric ratios (or anomeric purity) were determined by comparison of the integral intensities of relevant signals in ^{1}H NMR spectra.

Method C: general procedure for glycosylation in the presence of TMSOTf or TfOH: A mixture of glycosyl donor **1f** (0.13 mmol), glycosyl acceptor (0.10 mmol), and freshly activated molecular sieves (4 Å, 200 mg) in $ClCH_2CH_2Cl$ (26 mL, 5 mM) was stirred under argon for 1 h at RT. The mixture was then cooled to −30 °C and TMSOTf (or TfOH, 0.07 mmol) was added. The resulting mixture was allowed to warm to RT over a period of 1 h and stirred at RT for the time specified in the Tables. Upon completion, Et_3N (0.3 mL) was added and the resulting mixture was stirred for 30 min. After that, the mixture was diluted with CH_2Cl_2 (10 mL), the solid was filtered off and washed successively with CH_2Cl_2. The combined filtrate (~30 mL) was washed with 20% aq. $NaHCO_3$ (10 mL) and water (3×10 mL). The organic phase was separated, dried with magnesium sulfate, and concentrated in vacuo. The residue was purified by column chromatography on silica gel (ethyl acetate/hexane gradient elution). Anomeric ratios (or anomeric purity) were determined by comparison of the integral intensities of relevant signals in ^{1}H NMR spectra.

Method D: general procedure for glycosylation in the presence of Br_2: A mixture of a glycosyl donor (0.13 mmol), glycosyl acceptor (0.10 mmol), and freshly activated molecular sieves (3 Å, 200 mg) in $ClCH_2CH_2Cl$ (26 mL, 5 mM) was stirred under argon for 1 h at RT. Br_2 (0.14 mmol) was added and the resulting mixture was stirred at RT for 2–16 h as specified in the Tables. Upon completion, the mixture was diluted with CH_2Cl_2 (10 mL) and the solid was filtered off and washed successively with CH_2Cl_2. The combined filtrate (~30 mL) was washed with 20% aq. $NaHCO_3$ (10 mL) and water (3×10 mL). The organic phase was separated, dried with magnesium sulfate, and concentrated in vacuo. The residue was purified by column chromatography on silica gel (ethyl acetate/hexane gradient elution). Anomeric ratios (or anomeric purity) were determined by comparison of the integral intensities of relevant signals in ^{1}H NMR spectra.

Method E: general procedure for glycosylation in the presence of Br_2 and $HgBr_2$: A mixture of a glycosyl donor (0.13 mmol), glycosyl acceptor (0.10 mmol), and freshly activated molecular sieves (3 Å, 200 mg) in $ClCH_2CH_2Cl$ (26 mL, 5 mM) was stirred under argon for 1 h at RT. Br_2 (0.14 mmol) was added and the resulting mixture was stirred for 15 min at RT. Thereafter, mercury(II) bromide (0.14 mmol) was added and the resulting mixture was stirred at RT for the time specified in the Tables. Upon completion, the reaction mixture was diluted with CH_2Cl_2 (10 mL), the solid was filtered off and washed successively with CH_2Cl_2. The combined filtrate (~30 mL) was washed with 20% aq. $NaHCO_3$ (10 mL) and water (3×10 mL). The organic phase was separated, dried with magnesium sulfate, and concentrated in vacuo. The residue was purified by column chromatography on silica gel (ethyl acetate/hexane gradient elution). Anomeric ratios (or anomeric purity) were determined by comparison of the integral intensities of relevant signals in ^{1}H NMR spectra.

Methyl 2,3,4-tri-*O*-benzyl-6-*O*-(2,3,6-tri-*O*-benzyl-4-*O*-picoloyl-α-D-glucopyranosyl)-α-D-glucopyranoside (3): The title compound was obtained by methods A–E as a white amorphous solid from 4-*O*-picoloylated glycosyl donors and acceptor **2** in yields and stereoselectivity listed in the Tables. Analytical data for **3** were in accord with those reported previously.[5]

Methyl 3,4,6-tri-*O*-benzyl-2-*O*-(2,3,6-tri-*O*-benzyl-4-*O*-picoloyl-α-D-glucopyranosyl)-α-D-glucopyranoside (5): The title compound was obtained by method D as a white amorphous solid from 4-*O*-picoloylated glycosyl donors and acceptor **4** in yields and stereoselectivity listed in the Tables. Analytical data for **5** were in accord with those reported previously.[5]

Methyl 2,3,6-tri-*O*-benzyl-4-*O*-(2,3,6-tri-*O*-benzyl-4-*O*-picoloyl-α-D-glucopyranosyl)-α-D-glucopyranoside (9): The title compound was obtained by method D as a white amorphous solid from 4-*O*-picoloylated glycosyl donors and acceptor **8** in yields and stereoselectivity listed in the Tables. Analytical data for **9** were in accord with those reported previously.[5]

Methyl 2,3,4-tri-*O*-benzyl-6-*O*-(6-*O*-benzoyl-2,3-di-*O*-benzyl-4-*O*-picoloyl-α-D-glucopyranosyl)-α-D-glucopyranoside (16): The title compound was obtained by method D as a white amorphous solid from donor **1g** and acceptor **2** in 79% yield and complete stereoselectivity. Analytical data for **16**: $R_f = 0.52$ (acetone/toluene, 1:4, v/v); $[\alpha]_D^{27} = +62.2$ ($c = 1.0$, $CHCl_3$); ^{1}H NMR: $\delta = 3.37$ (s, 3H, OCH_3), 3.39 (dd, 1H, $J_{1,2} = 3.6$ Hz, $J_{2,3} = 9.7$ Hz, H-2), 3.61 (dd, 1H, $J_{4,5} = 9.6$ Hz, H-4), 3.66 (dd, 1H, $J_{2',3'} = 9.5$ Hz, H-2′), 3.72–3.85 (m, 3H, H-5, 6a, 6b), 3.99 (dd, 1H, $J_{3,4} = 9.2$ Hz, H-3), 4.18 (dd, 1H, $J_{3',4'} = 9.4$ Hz, H-3′), 4.23–4.34 (m, 2H, H-5′, 6a′), 4.47–4.74 (m, 8H, H-1, 6b′, 3× CH_2Ph), 4.77–4.85 (m, 2H, CH_2Ph), 4.92 (d, 1H, $^2J = 11.1$ Hz, $^1/_2$ CH_2Ph), 4.98 (d, 1H, $^2J = 10.9$ Hz, $^1/_2$ CH_2Ph), 5.05 (d, 1H, $J_{1',2'} = 3.5$ Hz, H-1′), 5.46 (dd, 1H, $J_{4',5'} = 9.7$ Hz, H-4′), 6.90–8.10 (m, 33H, aromatic), 8.74 ppm (d, 1H, $J = 4.5$ Hz, aromatic); ^{13}C NMR: $\delta = 55.4$, 63.3, 66.1, 67.8, 70.8, 71.8, 72.9, 73.6, 75.3, 75.5, 76.0, 78.0, 78.5, 80.1, 80.3, 82.3, 97.3, 98.1, 125.7, 127.2, 127.6, 127.8, 127.9 (×3), 128.0, 128.1 (×3), 128.2 (×4), 128.3 (×4), 128.5 (×2), 128.6 (×2), 128.7 (×6), 129.9 (×3), 130.1, 133.2, 137.1, 138.3, 138.4, 138.6, 139.0, 147.8, 150.1, 164.2, 166.4 ppm; HR FAB MS $[M+H]^+$ calcd for $C_{61}H_{62}NO_{13}$ 1016.4221, found 1016.4208.

Methyl 2,3,4-tri-*O*-benzyl-6-*O*-(3-*O*-benzoyl-2,6-di-*O*-benzyl-4-*O*-picoloyl-α-D-glucopyranosyl)-α-D-glucopyranoside (17): The title compound was obtained by method D as a white amorphous solid from donor **1h** and acceptor **2** in 81% yield and complete stereoselectivity. Analytical data for **17**: $R_f = 0.53$ (acetone/toluene, 1:4, v/v); $[\alpha]_D^{28} = +30.9$ ($c = 1.0$, $CHCl_3$); ^{1}H NMR: $\delta = 3.41$ (s, 3H, OCH_3), 3.44 (dd, 1H, $J_{1,2} = 3.6$ Hz, $J_{2,3} = 9.6$ Hz, H-2), 3.47–3.60 (m, 2H, H-6a′, 6b′), 3.64–3.72 (m, 2H, H-2′, 4), 3.74–3.93 (m, 3H, H-5, 6a, 6b), 4.00 (dd, 1H, $J_{3,4} = 9.2$ Hz, H-3), 4.19 (m, 1H, H-5′), 4.37–4.65 (m, 6H, H-1, 2$^1/_2$ CH_2Ph), 4.73 (d, 2H, $^2J = 11.5$ Hz, CH_2Ph), 4.90 (dd, 2H, $^2J = 11.0$ Hz, CH_2Ph), 4.96 (d, 1H, $^2J = 11.2$ Hz, $^1/_2$ CH_2Ph), 5.12 (d, 1H, $J_{1',2'} = 3.5$ Hz, H-1′), 5.55 (dd, 1H, $J_{4',5'} = 9.8$ Hz, H-4′), 5.93 (dd, 1H, $J_{3',4'} = 9.7$ Hz, H-3′), 7.00–8.10 (m, 33H, aromatic), 8.67 ppm (d, 1H, $J = 3.9$ Hz, aromatic); ^{13}C NMR: $\delta = 55.4$, 66.2, 68.5, 68.7, 70.6, 70.8, 72.3 (×2), 73.6, 73.8, 75.3, 75.9, 76.6, 77.8, 80.0, 82.4, 97.2, 98.3, 125.5, 127.1, 127.7 (×2), 127.9, 128.0 (×2), 128.1 (×7), 128.3 (×2), 128.4 (×3), 128.5 (×6), 128.6 (×4), 130.0 (×3), 133.1, 137.1, 137.8 (×2), 138.3, 138.7, 139.1, 147.4, 150.2, 163.8, 166.0 ppm; HR FAB MS $[M+H]^+$ calcd for $C_{61}H_{62}NO_{13}$ 1016.4221, found 1016.4213.

Methyl 2,3,4-tri-*O*-benzyl-6-*O*-(3,6-di-*O*-benzoyl-2-*O*-benzyl-4-*O*-picoloyl-α-D-glucopyranosyl)-α-D-glucopyranoside (18): The title compound was obtained by method D as a white amorphous solid from donor **1i** and acceptor **2** in 73% yield and complete stereoselectivity. Analytical data for **18**: $R_f = 0.52$ (acetone/toluene, 1:4, v/v); $[\alpha]_D^{27} = +51.5$ ($c = 1.0$, $CHCl_3$); ^{1}H NMR: $\delta = 3.32$ (dd, 1H, $J_{1,2} = 3.6$ Hz, $J_{2,3} = 9.6$ Hz, H-2), 3.42 (s, 3H, OCH_3), 3.59 (dd, 1H, $J_{4,5} = 9.5$ Hz, H-4), 3.71 (dd, 1H, $J_{2',3'} = 9.8$ Hz, H-2′), 3.74–3.88 (m, 3H, H-5, 6a, 6b), 3.99 (dd, 1H, $J_{3,4} = 9.3$ Hz, H-3), 4.33 (dd, 1H, $J_{5',6a'} = 5.2$ Hz, $J_{6a',6b'} = 11.9$, H-6a′), 4.43 (m, 1H, H-5′), 4.47–4.63 (m, 4H, H-1, 6b′, CH_2Ph), 4.64 (dd, 2H, $^2J = 12.0$ Hz, CH_2Ph), 4.81 (dd, 2H, $^2J = 11.9$ Hz, CH_2Ph), 4.89 (dd, 2H, $^2J = 10.9$ Hz, CH_2Ph), 5.11 (d, 1H, $J_{1',2'} = 3.5$ Hz, H-1′), 5.53 (dd, 1H, $J_{4',5'} = 9.7$ Hz, H-4′), 5.97 (dd, 1H, $J_{3',4'} = 9.8$ Hz, H-3′), 7.05–8.05 (m, 33H, aromatic), 8.67 ppm (d, 1H, $J = 4.5$ Hz, aromatic); ^{13}C NMR: $\delta = 55.4$, 63.1, 66.2, 67.6, 70.6, 70.7, 72.1, 72.3, 73.5, 75.3, 75.9, 77.5, 77.9, 80.0, 82.3, 96.9, 98.2, 125.6, 127.3, 127.7, 127.9 (×2), 128.0, 128.1 (×3), 128.2 (×2), 128.3, 128.4, 128.5 (×2), 128.6 (×10), 128.7 (×3), 129.8, 129.9 (×2), 130.0 (×2), 133.2, 137.2, 137.7, 138.3, 138.6, 139.0, 147.1, 150.3, 163.9, 165.0, 166.3 ppm; HR FAB MS $[M+H]^+$ calcd for $C_{61}H_{60}NO_{14}$ 1030.4014, found 1030.3994.

Cyclohexyl 2,3,6-tri-*O*-benzyl-4-*O*-picoloyl-D-glucopyranoside (20): The title compound was obtained by method D as a colorless syrup from 4-*O*-picoloylated glycosyl donors and cyclohexanol (**19**, 50 mM), in yields and stereoselectivity listed in Table 5. Analytical data for **α-20**: $R_f = 0.58$ (acetone/toluene, 1:4, v/v); ^{1}H NMR: $\delta =$ 1.05–2.10 (m, 10H, 5×CH_2 of cyclohexyl), 3.50–3.62 (m, 3H, H-6a, 6b, OCH of cyclohexyl), 3.65 (dd, 1H, $J_{2,3} = 9.6$ Hz, H-2), 4.19 (dd, 1H, $J_{3,4} = 9.5$ Hz, H-3), 4.23 (m, 1H, H-5), 4.46 (dd, 2H, $^2J = 12.0$ Hz, CH_2Ph), 4.72 (dd, 2H, $^2J = 12.0$ Hz, CH_2Ph), 4.84 (dd, 2H, $^2J = 11.3$ Hz, CH_2Ph), 4.96 (d, 1H, $J_{1,2} = 3.7$ Hz, H-1), 5.42 (dd, 1H, $J_{4,5} = 9.8$ Hz, H-4), 6.95–8.15 (m, 18H, aromatic), 8.74 ppm (m, 1H, $J = 3.9$ Hz, aromatic); ^{13}C NMR: $\delta = 24.4$, 24.7, 25.8, 31.7, 33.7, 68.7, 69.1, 72.4, 73.4, 73.7, 75.5, 76.2, 79.5, 80.0, 95.3, 125.9, 127.2, 127.4, 127.5, 127.9 (×2), 128.0 (×2), 128.1, 128.3 (×6), 128.6 (×2), 137.3, 138.1, 138.4, 138.8, 147.8, 149.9, 164.2 ppm; HR FAB MS $[M+H]^+$ calcd for $C_{39}H_{44}O_7N$ 638.3118, found 638.3097.

Benzyl 2,3,6-tri-*O*-benzyl-4-*O*-picoloyl-D-glucopyranoside (22): The title compound was obtained by method D as a colorless syrup from 4-*O*-picoloylated glycosyl donors and benzyl alcohol (**21**, 50 mM) in yields and stereoselectivity listed in Table 5. Analytical data for **α-22**: $R_f = 0.55$ (acetone/toluene, 1:4, v/v); ^{1}H NMR: $\delta =$ 3.48–3.55 (m, 2H, H-6a, 6b), 3.64 (dd, 1H, $J_{2,3} = 9.5$ Hz, H-2), 3.14 (m, 1H, H-5), 4.21(dd, 1H, $J_{3,4} = 9.5$ Hz, H-3), 4.45 (dd, 2H, $^2J =$ 11.9 Hz, CH_2Ph), 4.50–4.77 (m, 5H, 2$^1/_2$ CH_2Ph), 4.80–4.90 (m, 2H, H-1, $^1/_2$ CH_2Ph), 5.42 (dd, 1H, $J_{4,5} = 9.8$ Hz, H-4), 7.05–8.10 (m, 23H, aromatic), 8.72 ppm (d, 1H, $J = 4.1$ Hz, aromatic); ^{13}C NMR: $\delta = 68.9$, 69.0, 69.4, 72.1, 73.4, 73.7, 75.6, 79.5, 79.9, 95.7, 125.8, 127.1, 127.5, 127.6, 128.0 (×3), 128.1 (×2), 128.2 (×3), 128.3 (×4), 128.6 (×4), 128.8 (×2), 137.1, 137.2, 138.0, 138.2, 138.6, 147.8, 149.9, 164.2 ppm; HR FAB MS $[M+H]^+$ calcd for $C_{40}H_{40}O_7N$ 646.2805, found 646.2841.

Isopropyl 2,3,6-tri-*O*-benzyl-4-*O*-picoloyl-D-glucopyranoside (24): The title compound was obtained by method D as a colorless syrup from donor **1b** and isopropanol (**23**, 50 mM) in 47% yield ($\alpha/\beta = 13:1$). Analytical data for **α-24**: $R_f = 0.57$ (acetone/toluene, 1:4, v/v); ^{1}H NMR: $\delta = 1.17$ (m, 6H, 2×CH_3), 3.43–3.52 (m, 2H, H-6a, 6b), 3.58 (dd, 1H, $J_{2,3} = 9.5$ Hz, H-2), 3.85 (m, 1H, OCH(CH$_3$)$_2$), 4.10–4.5 (m, 2H, H-3, 5), 4.38 (dd, 2H, $^2J = 11.9$ Hz, CH_2Ph), 4.66 (dd, 2H, $^2J = 12.1$ Hz, CH_2Ph), 4.70 (dd, 2H, $^2J = 11.3$ Hz, CH_2Ph), 4.80 (d, 1H, $J_{1,2} = 3.8$ Hz, H-1), 5.37 (dd, 1H, $J_{4,5} = 10.0$ Hz, H-4), 6.90–8.10 (m, 18H, aromatic), 8.68 ppm (d, 1H, $J = 3.5$ Hz, aromatic); ^{13}C NMR: $\delta = 21.5$, 23.5, 68.7, 69.0, 70.0, 72.3, 73.5, 73.7, 75.6, 79.6, 79.9, 95.4, 125.9, 127.1, 127.4, 127.5, 127.9 (×2), 128.0 (×2), 128.1, 128.3 (×4), 128.4 (×2), 128.7 (×3), 129.9, 137.3, 138.0, 138.4, 138.7, 149.9 ppm; HR FAB MS $[M+H]^+$ calcd for $C_{36}H_{40}O_7N$ 598.2805, found 598.2837.

Acknowledgements

This work was supported by awards from the NSF (CHE-1058112) and Mizutani Foundation for Glycosciences (130057). J.P.Y. is indebted to the UM–St. Louis Graduate School for awarding her with the Dissertation Fellowship. We thank the NSF for a grant (CHE-0959360) to purchase the 600 MHz NMR spectrometer used in this work. Dr. Winter and Mr. Kramer (UM–St. Louis) are thanked for HRMS determinations.

Keywords: aglycone delivery · carbohydrates · glycosylation · leaving group · stereocontrol

[1] *Handbook of Chemical Glycosylation: Advances in Stereoselectivity and Therapeutic Relevance* (Ed.: A. V. Demchenko), Wiley-VCH, Weinheim, **2008**.
[2] a) T. H. Fife, R. Bembi, R. Natarajan, *J. Am. Chem. Soc.* **1996**, *118*, 12956–12963; b) T. Nukada, A. Berces, M. Z. Zgierski, D. M. Whitfield, *J. Am. Chem. Soc.* **1998**, *120*, 13291–13295; c) J. T. Smoot, P. Pornsuriyasak, A. V. Demchenko, *Angew. Chem. Int. Ed.* **2005**, *44*, 7123–7126; *Angew. Chem.* **2005**, *117*, 7285–7288.
[3] A. V. Demchenko, *Curr. Org. Chem.* **2003**, *7*, 35–79.
[4] J. T. Smoot, A. V. Demchenko, *J. Org. Chem.* **2008**, *73*, 8838–8850.
[5] J. P. Yasomanee, A. V. Demchenko, *J. Am. Chem. Soc.* **2012**, *134*, 20097–20102.
[6] S. G. Pistorio, J. P. Yasomanee, A. V. Demchenko, *Org. Lett.* **2014**, *16*, 716–719.
[7] Q.-W. Liu, H.-C. Bin, J.-S. Yang, *Org. Lett.* **2013**, *15*, 3974–3977.
[8] J.-H. Ruei, P. Venukumar, A. B. Ingle, K.-K. T. Mong, *Chem. Commun.* **2015**; DOI: 10.1039/C1034CC08465A.
[9] J. P. Yasomanee, A. V. Demchenko, *Angew. Chem. Int. Ed.* **2014**, *53*, 10453–10456; *Angew. Chem.* **2014**, *126*, 10621–10624.
[10] S. C. Ranade, S. Kaeothip, A. V. Demchenko, *Org. Lett.* **2010**, *12*, 5628–5631.
[11] J. M. Küster, I. Dyong, *Justus Liebigs Ann. Chem.* **1975**, 2179–2189.
[12] a) S. J. Hasty, A. V. Demchenko, *Chem. Heterocycl. Compd.* **2012**, *48*, 220–240; b) B. Yu, J. Sun, *Chem. Commun.* **2010**, *46*, 4668–4678; c) X. Zhu, R. R. Schmidt, in *Handbook of Chemical Glycosylation* (Ed.: A. V. Demchenko), Wiley-VCH, Weinheim, **2008**, pp. 143–185; d) W. Szeja, G. Grynkiewicz, in *Handbook of Chemical Glycosylation* (Ed.: A. V. Demchenko), Wiley-VCH, Weinheim, **2008**, pp. 329–361.
[13] a) M. N. Kamat, N. P. Rath, A. V. Demchenko, *J. Org. Chem.* **2007**, *72*, 6938–6946; b) M. N. Kamat, C. De Meo, A. V. Demchenko, *J. Org. Chem.* **2007**, *72*, 6947–6955.
[14] a) A. V. Demchenko, P. Pornsuriyasak, C. De Meo, N. N. Malysheva, *Angew. Chem. Int. Ed.* **2004**, *43*, 3069–3072; *Angew. Chem.* **2004**, *116*, 3131–3134; b) P. Pornsuriyasak, A. V. Demchenko, *Chem. Eur. J.* **2006**, *12*, 6630–6646.
[15] S. Kaeothip, P. Pornsuriyasak, N. P. Rath, A. V. Demchenko, *Org. Lett.* **2009**, *11*, 799–802.
[16] S. C. Ranade, A. V. Demchenko, *J. Carbohydr. Chem.* **2013**, *32*, 1–43.
[17] S. Kaeothip, J. P. Yasomanee, A. V. Demchenko, *J. Org. Chem.* **2012**, *77*, 291–299.
[18] H. D. Premathilake, A. V. Demchenko, in *Topics in Current Chemistry: Reactivity Tuning in Oligosaccharide Assembly, Vol. 301* (Eds.: B. Fraser-Reid, J. C. Lopez), Springer, Heidelberg, **2011**, pp. 189–221.
[19] B. Helferich, K. F. Wedemeyer, *Justus Liebigs Ann. Chem.* **1949**, *563*, 139–145.
[20] F. Andersson, P. Fugedi, P. J. Garegg, M. Nashed, *Tetrahedron Lett.* **1986**, *27*, 3919–3922.
[21] L. K. Mydock, M. N. Kamat, A. V. Demchenko, *Org. Lett.* **2011**, *13*, 2928–2931.
[22] A. O. Tzianabos, A. Pantosti, H. Baumann, J. R. Brisson, H. J. Jennings, D. L. Kasper, *J. Biol. Chem.* **1992**, *267*, 18230–18235.
[23] E. R. Palmacci, O. J. Plante, M. C. Hewitt, P. H. Seeberger, *Helv. Chim. Acta* **2003**, *86*, 3975–3990.
[24] P. J. Garegg, I. Kvarnstrom, A. Niklasson, G. Niklasson, S. C. T. Svensson, *J. Carbohydr. Chem.* **1993**, *12*, 933–953.
[25] G. J. Boons, T. Zhu, *Synlett* **1997**, 809–811.
[26] M. Ravenscroft, R. M. G. Roberts, J. G. Tillett, *J. Chem. Soc. Perkin Trans. 2* **1982**, 1569–1972.

Received: December 21, 2014
Revised: February 9, 2015
Published online on March 12, 2015