Facile glycosylation strategy with two-stage activation of allyl glycosyl donors. Application to concise synthesis of *Shigella flexneri* serotype Y O-antigen†

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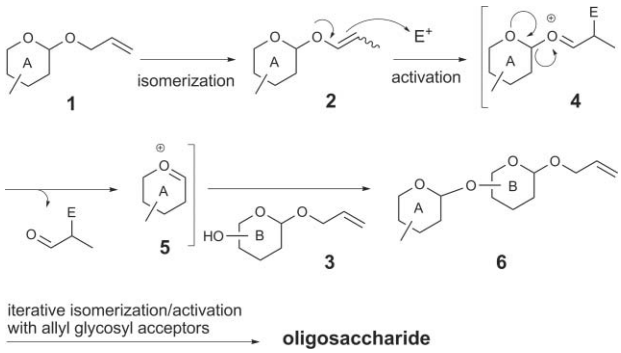
A practical, useful glycosylation method employing only allyl glycoside building blocks has been developed. The donor's glycosylation reactivity is turned on *via* isomerization of its anomeric allyl protecting group into the corresponding prop-1-enyl moiety. Subsequent chemoselective activation with NIS/TfOH achieves high yields in glycosidic bond construction at room temperature. The efficacy and efficiency of this approach in carbohydrate synthesis is demonstrated in the concise synthesis of the fully protected *Shigella flexneri* serotype Y O-antigen.

Introduction

Ready access to structurally well-defined carbohydrates is important to both basic and applied research in the fields of glycobiology, biochemistry, immunology and related biomedical sciences. Organic synthesis has clearly emerged as a key force in providing pure natural/unnatural carbohydrates. Considerable effort has been devoted to the development of simple, facile, and cost-effective glycosylation methods over the past several decades.[1] Despite progress, the efficient synthesis of complex carbohydrates is still not a trivial task. Continuing to develop new glycosylation methods remains a major focus in synthetic carbohydrate chemistry.

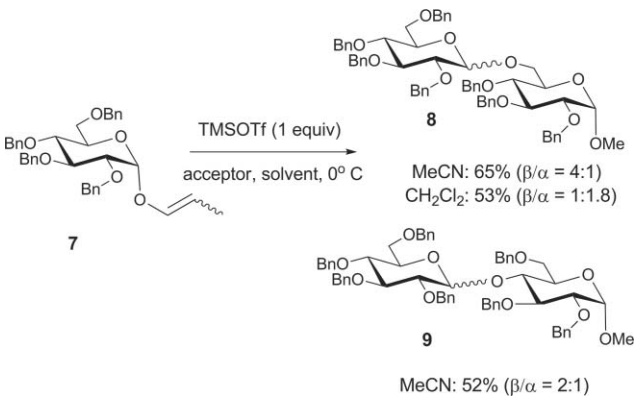
We have been pursuing a glycosylation approach which would use readily accessible building blocks, a set of simple and flexible reaction conditions that can be repeatedly applied in iterative synthesis, and activation reagents that are inexpensive and environmentally benign. Moreover, to improve the overall synthetic efficiency, manipulation of the anomeric group and protecting groups should be minimized.

Mindful of these criteria, we have looked into the potential of widely used allyl glycosides as building blocks for glycosidic bond construction.[2] We envision that an anomeric allyl group can serve a dual role. In addition to its traditional role merely as a protecting group, frequently as an anomeric protecting group in carbohydrate synthesis, it can also be readily converted into a good leaving group (*i.e.* a prop-1-enyl group) for glycosylation. A number of convenient and high-yield isomerization procedures are available.[3] Thus, the allyl glycoside **1** is first isomerized to the corresponding prop-1-enyl glycoside **2** (Scheme 1). Subsequent chemoselective activation of the anomeric enol ether moiety of **2** with a proper electrophile (E^+) in the presence of the allyl glycosyl acceptor **3** passes through the reactive intermediates **4** then **5**, leading to the new allyl glycoside **6**, along with the α-substituted propanal. The key step is to activate vinyl glycoside **2** for glycosidic bond formation.



Scheme 1 Glycosylation with allyl glycoside building blocks.

Sinaÿ and his coworkers were among the pioneers who explored glycosylation with vinyl glycosyl donors.[4] They reported the first and only example of glycosylation with a prop-1-enyl glycosyl donor **7** (Scheme 2) derived from the corresponding allyl glycoside prior to our recent work.[2] They demonstrated that glycosylation reactions of the donor **7** with different acceptors could lead to formation of the disaccharides **8** and **9** in modest yields (Scheme 2). To search for necessary improvements, they turned their attention to isopropenyl donors.[4a] Later, Chenault and coworkers studied glycosylation with isopropenyl donors in more detail,[5] while Boons and coworkers focused their attention on 2-buten-2-yl glycosyl donors.[6] Boons *et al.* integrated their glycosylation method in a latent-active strategy[7] for iterative oligosaccharides synthesis.[8]



Scheme 2 Sinaÿ's pioneering work.[4a]

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† Electronic supplementary information (ESI) available: Experimental details, spectroscopic data of **12**α, **12**β, **16**α, **16**β, **20**, **21**, **22**, **25a**, **25b**, **26**, **29a**, **29b**, and **30**β, ^{1}H and ^{13}C NMR spectra of **12**α, **12**β, **16**α, **16**β, **20**, **21**, **22**, **26**, **27**, **30**α, **30**β, **31**, **38** and **39**. See DOI: 10.1039/c002865g

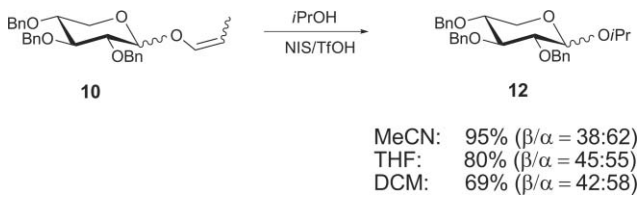
Instead of pursuing specially designed vinyl glycosyl donors to improve glycosylation outcomes, our focus remains on prop-1-enyl glycosyl donors that appeal to us with their distinct advantages. Firstly, prop-1-enyl glycosides can be directly isomerized from allyl glycosides without time-consuming anomeric group replacement and intermediate purification. Secondly, a variety of facile and highly effective methods are available for allyl to prop-1-enyl isomerization.[3] Thirdly, allyl glycosides have widespread use in carbohydrate synthesis. The anomeric allyl group is typically installed onto unprotected free monosaccharides at the very first step of building block preparation *via* a Fischer glycosylation process, greatly simplifying building block preparation. Finally, with much simplified building block preparation, versatile isomerization methods, and simple reaction conditions, this approach should significantly advance the latent-active strategy for iterative oligosaccharide synthesis. This strategy features no requirement for any building block reactivity tuning as necessary for the armed/disarmed approach employing thio and *n*-pentenyl building blocks in iterative syntheses.[9–11] The reactivity tuning process typically involves extensive protecting group manipulations and/or anomeric group modifications.[11,12]

For proof of feasibility, we have recently demonstrated that prop-1-enyl xylosides underwent glycosidic bond formation in high yields upon activation with a stoichiometric amount of *N*-iodosuccinimide (NIS) in acetonitrile at room temperature.[2] Under these conditions, the prop-1-enyl glucosyl donor **7** produced disaccharides in yields (62–68%) comparable to those of Sinaÿ (Scheme 2).[4a] These results encouraged us to pursue further improvements and to expand the scope.

Results and discussion

Activator and solvent effect

In the glycosylation method illustrated in Scheme 1, the activating reagent (E^+) plays a crucial role. Herein we report a new protocol using a stoichiometric amount of NIS and a catalytic amount of triflic acid (TfOH) as the activating reagent combination. We first examined the glycosylation reaction between the simple glycosyl acceptor 2-propanol and the prop-1-enyl glycosyl donor **10** isomerized from allyl 2,3,4-tri-*O*-benzyl-D-xylopyranoside **11** (β/α = 25 : 75) with potassium *tert*-butoxide (Scheme 3).[3,13] Upon activation of the donor with NIS/TfOH (100 : 15) in the presence of 2-propanol at 23 °C, the corresponding isopropyl 2,3,4-tri-*O*-benzyl-D-xylopyranoside **12** was obtained in 95% yield (β/α = 38 : 62) in acetonitrile, 80% yield (β/α = 45 : 55) in THF, and 69% yield (β/α = 42 : 58) in CH_2Cl_2, respectively. These results illustrate the solvent effect on product yields and anomeric stereoselectivity. Acetonitrile appeared to be the most suitable solvent. Interestingly, in acetonitrile, the expected β-selectivity originating from the intermediacy of a α-glycosylacetonitrilium ion[4a] was not observed under our reaction conditions. Reactions conducted in other solvents (*e.g.* diethyl ether, dioxane, chloroform, and *tert*-butanol) or solvent combinations did not improve the yields or stereoselectivity.



Scheme 3 Glycosylation in different solvents.

When the new protocol was applied to the donor **10** isomerized from **11** and the acceptors **13**[14] and **15**,[15] the desired disaccharides **14** and **16** were obtained in 96% yield (β/α = 70 : 30), and 86% yield (β/α = 45 : 55), respectively (Table 1, entries 1 and 2). High yields were also achieved with the prop-1-enyl donor **7** isomerized from **17** (β/α = 25 : 75) [4a] and the acceptors **13** and **15**. The desired disaccharide **18** and **19** were obtained in 96% yield (β/α = 77 : 23), and 83% yield (β/α = 74 : 26), respectively (Table 1, entries 3 and 4). The yields of disaccharides **14**, **18** and **19** obtained with this modified protocol are much higher than the yields obtained from the reactions activated with only NIS (*i.e.* 85%, 62%, and 65%, respectively).[2]

Anomeric stereochemistry

As in other glycosylation strategies, the anomeric stereoselectivity in the absence of proper directing effects varies under different conditions. In addition to the solvent effect and the influence of the structure of the glycosylation partner, we observed that the β/α ratio of the newly formed glycosidic bond was affected by the amount of TfOH used. For example, in the glycosylation reactions between **11** and 2-propanol in acetonitrile, the product **12** was obtained with the β/α ratio ranging from 58 : 42 (NIS/TfOH 100 : 5) to 38 : 62 (NIS/TfOH 100 : 15); with the acceptor **13**, the β/α ratio of the disaccharide **14** changed from 70 : 30 (NIS/TfOH 100 : 1) to 52 : 48 (NIS/TfOH 100 : 15). Presumably, an acid-catalyzed β to α isomerization was accelerated under the reaction conditions with an increase of acid. Indeed, the isolated disaccharide **16**β provided a mixture of two anomers (β/α = 60 : 40) upon treatment with TfOH (5%) in acetonitrile for 30 min at room temperature.

The anomeric stereochemical outcome is also slightly affected by the reaction temperature. In MeCN, the reaction between **11** and **13** (NIS/TfOH 100 : 1) provided **14** in 83% (β/α = 72 : 28) at −10 °C, 96% (β/α = 70 : 30) at room temperature and 93% (β/α = 64 : 36) at 70 °C, respectively. However, the ratio of donor/acceptor has no perceptible influence on production yields and anomeric stereoselectivity.

To control anomeric stereochemistry, the traditional neighbouring-participating-group strategy can be utilized. For instance, the glycosyl donor **20**, having a 2-O directing pivalolyl group, underwent the one-pot isomerization catalyzed by $[Ir(COD)(PMePh_2)_2]PF_6$ [2,16] and activation with NIS/TfOH to produce the desired disaccharides **21** in 79% yield and **22** in 84% yield with the anticipated β linkage (Table 1, entries 5 and 6).

Glycosylation *versus* undesired addition reaction

It is noteworthy that activation of disarmed prop-1-enyl glycosides with NIS alone would not generate new glycosidic bonds. Instead, NIS promotes addition of the acceptor to the C=C bond of the anomeric enol ether moiety. Upon treatment with NIS/TfOH, both glycosylation and addition reactions completed rapidly. However, the addition reaction products can be diminished by increasing the amount of TfOH and/or diluting the reaction

Table 1 Glycosylation of allyl glycosides[a]

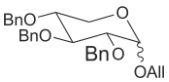
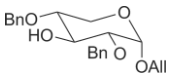
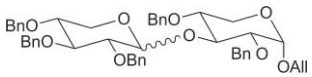
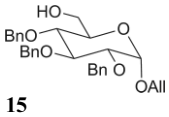
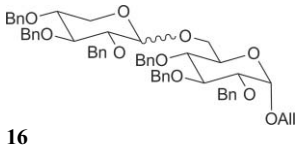
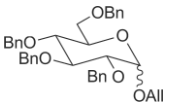
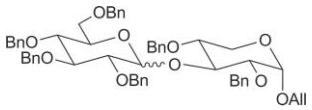
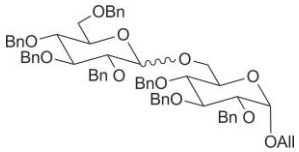
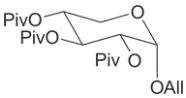
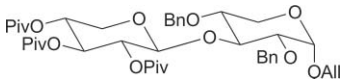
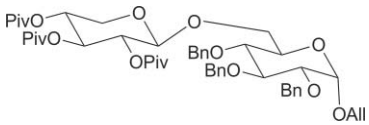
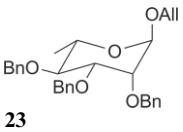
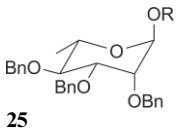
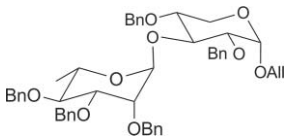
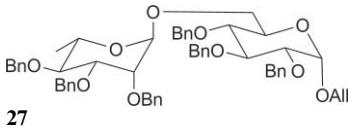
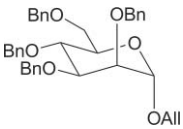
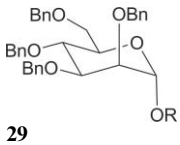
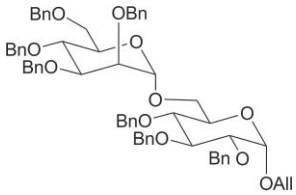
Entry	Donor	Acceptor	Product	Yield (β/α)[b]	Activator: NIS/TfOH(cat.)[c]
1	 **11**	 **13**	 **14**	96% (70 : 30)[d] 82% (52 : 48)[e]	TfOH (1%) TfOH (15%)
2	**11**	 **15**	 **16**	86% (45 : 55)[d]	TfOH (15%)
3	 **17**	**13**	 **18**	96% (77 : 23)[d]	TfOH (5%)
4	**17**	**15**	 **19**	83% (74 : 26)[d]	TfOH (5%)
5	 **20**	**13**	 **21**	79% (β)[e]	TfOH (25%)
6	**20**	**15**	 **22**	84% (β)[e]	TfOH (25%)
7	 **23**	**24a**:BnOH **24b**:2-propanol	 **25**	**25a**:95% (α)[e,f] **25b**:95% (α)[e,f]	TfOH (10%)
8	**23**	**13**	 **26**	89% (α)[e]	TfOH (10%)
9	**23**	**15**	 **27**	88% (α)[e,f]	TfOH (10%)
10	 **28**	**24a**:BnOH **24b**:2-propanol	 **29**	**29a**:85% (α)[d,f] **29b**:89% (α)[d,f]	TfOH (50%)

Table 1 *(Contd.)*

Entry	Donor	Acceptor	Product	Yield (β/α)[b]	Activator: NIS/TfOH(cat.)[c]
11	**28**	**15**	 **30**	82% (α)[d] 86% (25 : 75)[d] 85% (25 : 75)[df]	TfOH (25%) TfOH (5%) TfOH (5%)

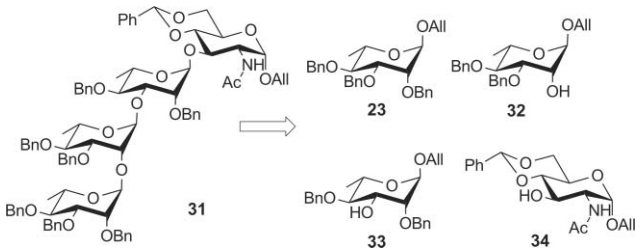
[a] Glycosylation reactions were preformed with 1.5 equiv of the donor and NIS, 1 equiv of the acceptor and a catalytic amount of TfOH in MeCN at 23 °C unless indicated otherwise. [b] The anomeric ratio was determined from ^{1}H NMR and confirmed by the isolated yield of each anomer. [c] The percentage of TfOH was calculated on the base of each donor. [d] Isomerization was carried out with *t*BuOK. [e] Isomerization was carried out with H_2-activated $[Ir(COD)(PMePh_2)_2]PF_6$ (2%). [f] The donor/NIS/acceptor ratio was 1 : 1 : 1.5.

solution. Presumably, the addition reaction involves the acceptor in the rate-determining step, while the acceptor-consuming step in the glycosylation pathway *en route* to **6** is not a rate-limiting step (*i.e.* **5** + **3** → **6** in Scheme 1). One plausible route to the addition reaction product could be trapping intermediate **4** (Scheme 1) with the acceptor,[17] in competition with its fragmentation to **5** leading to new glycosidic bond formation. Therefore, dilution of the reaction solutions slows down the addition reactions but affects little the glycosylation reactions. In agreement with this postulation, we observed that increasing the donor's concentration only increased the amount of the addition reaction product.

The combination of NIS/TfOH is also required for activation of prop-1-enyl mannosides and rhamnosides in order to avoid addition of acceptors to the anomeric C=C bond. With NIS/TfOH, rhamnoside **23**[18] reacted with **24** to afford the corresponding glycosides **25**[19] in high yields (Table 1, entry 7). With the monosaccharide acceptors **13** and **15**, the desired disaccharides **26** and **27** were obtained in 89%, and 88% yields, respectively (Table 1, entries 8 and 9). Similar results were also obtained with the mannoside donor **28**.[20] Thus, the expected new glycosides **29**[21] and **30** were obtained in high yields (Table 1, entries 10 and 11). Interestingly, in the case of synthesizing **30**, decreasing TfOH from 25% to 5% led to a mixture of anomers (*i.e.* β/α = 25 : 75 with 5% TfOH *vs.* α only with 25% TfOH). The anomeric stereochemistry of **30** was confirmed by the C1–H1 coupling constants, *i.e.* $^1J_{C1-H1}$ (α) = 172 Hz and $^1J_{C1-H1}$ (β) = 154 Hz.[22] However, the reaction yields were not influenced significantly. Again, we assumed that the unstable β mannoside, probably formed *via* a competing S_N2-like mechanism, could undergo the acid-catalyzed isomerization to the more stable α anomer. We indeed observed that treatment of **30**β with TfOH (5%) in acetonitrile for 30 min at room temperature led to a mixture containing both anomers (β/α = 64 : 36).

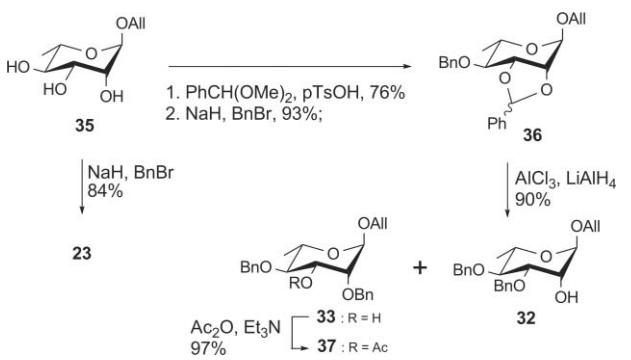
Application: Concise synthesis of fully protected *Shigella flexneri* serotype Y O-antigen

To illustrate the efficacy and efficiency of the new protocol in oligosaccharide synthesis, we applied it to the synthesis of the fully protected *Shigella flexneri* serotype Y O-antigen **31** (Scheme 4).[23] This is one of the 15 known *Shigella* surface carbohydrate antigens.[24] *Shigella* infections cause *ca.* 163 million illness episodes and more than one million annual deaths. Rapid and cost-effective access to these antigens is important to the development of diagnostic tools and multivalent vaccines that can provide a full coverage against the infection.[24,25]



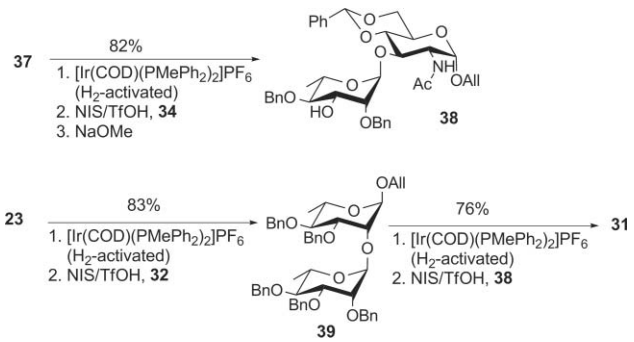
Scheme 4 Retrosynthesis of the tetrasaccharide **31**.

The synthesis began with the preparation of mono-saccharide building blocks **23**, and **32**–**34** (Scheme 4 and 5). Thus, benzylidenation of the allyl rhamnoside **35**[18] (prepared from L-rhamnose and allyl alcohol in 84% yield) followed by benzylation afforded **36** as a mixture of two diastereomers (endo/exo = *ca.* 1 : 1). Stereospecific ring opening of **36** with $LiAlH_4$–$AlCl_3$ [26] produced a mixture of **32**[27] and **33**[28] (90%, **32**/**33** = *ca.*1 : 1). The latter was converted to **37**.[29] The third rhamnoside building block **23** was also obtained from **35** in 84% yield. The known allyl 2-acetamido-4,6-O-benzylidene-2-deoxy-α-D-glucopyranoside (**34**)[30] was prepared in two steps from *N*-acetyl-D-glucosamine.



Scheme 5 Preparation of allyl rhamnoside building blocks for the synthesis of *S. flexneri* serotype Y O-antigen.

With all the building blocks in hand, we began to construct glycosidic bonds with the two-stage, one-pot protocol (Scheme 6). Thus, the allyl glycosyl donor **37** was isomerized to its corresponding prop-1-enyl glycoside with the iridium catalyst. Subsequent activation with NIS/TfOH in the presence of the allyl glycosyl acceptor **34** led to the disaccharide **38** in 82% yield after alkaline workup (Scheme 6). In the same manner, the other disaccharide **39** was obtained from the glycosylation reaction of the donor **23** and the acceptor **32** in 83% yield; coupling of the two disaccharides (*i.e.* the donor **39** and the acceptor **38**) produced the desired fully protected tetrasaccharide **31** in 74% yield. The anomeric stereochemistry of newly formed glycosidic bonds in **38**, **39** and **31** was confirmed by measurement of the C1–H1 coupling constants. In a short synthesis, the fully protected tetrasaccharide was rapidly prepared from L-rhamnose and *N*-acetyl-D-glucosamine.



Scheme 6 Glycosidic bond construction.

Conclusions

A simple glycosylation protocol employing only allyl glycosides as building blocks has been developed. The anomeric allyl protecting group of glycosyl donors is converted to the more reactive prop-1-enyl leaving group. Thus time-consuming anomeric group removal/installation and intermediate purification are avoided. Moreover, iterative use of allyl glycosides for oligosaccharide synthesis does not require any armed/disarmed property tuning, significantly simplifying building block preparation, and improving the overall synthetic efficiency. The efficacy and efficiency of this method has been illustrated in the concise synthesis of the fully protected *Shigella flexneri* serotype Y O-antigen.

Experimental

Representative procedure of the one-pot glycosylation reaction

(Synthesis of **27**): A solution of $[Ir(COD)(PMePh_2)_2]PF_6$ (0.85 mg, 1 μmol) in 0.3 mL of THF was degassed and stirred under a hydrogen atmosphere for 15 min at room temperature. The obtained clear solution of the activated catalyst was injected to allyl 2,3,4-tri-*O*-benzyl-α-L-rhamnopyranoside **23** (24 mg, 0.05 mmol) in 0.5 mL of THF. The reaction mixture was stirred for 30 min, and THF was removed. The residue and allyl 2,3,4-tri-*O*-benzyl-α-D-glucopyranoside **15** (37 mg, 0.075 mmol) were dried together by azeotropic removal of water with toluene. The glycosylation partners were then dissolved in 1 mL of acetonitrile. To the reaction solution, NIS (11 mg, 0.05 mmol) was added, followed immediately by TfOH (5 μmol) in 44 μL of acetonitrile at room temperature. The reaction was stirred for 40 min and quenched with triethyl amine. The solution was then concentrated and purified by flash column chromatography on silica gel (eluted with petroleum ether/ethyl acetate gradient 7 : 1 to 3 : 1) to afford **27** (40 mg, 88% yield). Rf 0.3 (petroleum ether/ethyl acetate 5 : 1); $[\alpha]_D^{24}$ = +2.84 (c = 0.67, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.35–7.15 (m, 30 H, 6×Ph), 5.9 (m, 1 H, –OCH_2CH=CH_2), 5.26 (dq, *J* = 17.2, 1.6 Hz, 1 H, –OCH_2CH=CH_2), 5.17 (ddt, *J* = 10.3, 1,7, 1.1 Hz, 1 H, –OCH_2CH=CH_2), 4.98 (*A*B^1, *J* = 10.9 Hz, 1 H, Bn), 4.92 (*A*B^2, *J* = 10.9 Hz, 1 H, Bn), 4.81–4.57 (m, 9 H), 4.71 (d, *J* = 1.8 Hz, 1 H, Rha H-1), 4.66 (d, *J* = 3.2 Hz, 1 H, Glu H-1), 4.39 (*A*B^3, *J* = 11 Hz, 1 H, Bn), 4.08 (*A*BMX$_2$, *J* = 12.9, 5.2, 1.4 Hz, 1 H, –O*CH*$_2$CH=CH_2), 3.98 (t, *J* = 9.3 Hz, 1 H, Glu H-3), 3.92 (A*B*MX$_2$, *J* = 12.9, 6.5, 1.2 Hz, 1 H, –O*CH*$_2$CH=CH_2), 3.82 (dd, *J* = 10.6, 1.8 Hz, Glu H-6), 3.82 (dd, *J* = 9.3, 3.0 Hz, 1 H, Rha H-3), 3.75 (ddd, *J* = 10.0, 4.8, 1.7 Hz, 1 H, Glu H-5), 3.70 (m, 1 H, Rha H-5), 3.6 (t, *J* = 9.3 Hz, 1 H, Rha H-4), 3.48 (dd, *J* = 9.6, 3.6 Hz, 1 H, Glu H-2), 3.46 (dd, *J* = 10.8, 5.3 Hz, 1 H, Glu H-6), 3.36 (dd, *J* = 10.0, 9.0 Hz, 1 H, Glu H-4), 1.28 (d, *J* = 6.2 Hz, 3 H, CH_3); ^{13}C NMR (101 MHz, $CDCl_3$) δ 138.7, 138.5, 138.4, 138.2, 138.1, 133.6, 128.43, 128.40, 128.36, 128.28, 128.08, 128.04, 128.00, 127.88, 127.81, 127.78, 127.76, 127.69, 127.65, 127.62, 127.58, 118.3, 98.2 ($^1J_{CH}$ = 170 Hz), 95.3 ($^1J_{CH}$ = 170 Hz), 81.9, 80.5, 79.88, 79.84, 77.8, 75.8, 75.5, 75.0, 74.8, 73.1, 72.7. 72.3, 69.9, 68.1, 68.0, 66.0, 17.9; FTIR (neat film) 3088, 3064, 3030, 2921, 2873, 1498, 1454, 1362, 1261, 1090, 1073, 1042, 1028 cm^{-1}; HRMS (ESI) m/z: calcd for $C_{57}H_{62}O_{10}Na$ (M+Na) 929.4241, found 929.4247.

Representative glycosylation procedure of the prop-1-enyl glycosyl donor obtained from isomerization of the allyl glycoside with potassium *tert*-butoxide

(Synthesis of disaccharide **30**): Potassium *tert*-butoxide (553 mg, 4.93 mmol) was added to allyl 2,3,4,6-tetra-*O*-benzyl-D-mannopyranoside **28** (1.39 g, 2.24 mmol) in 2 mL of DMSO and the reaction mixture was stirred at room temperature until the reaction completed. The reaction was worked up with ethyl acetate and water. The organic layer was dried over anhydrous sodium sulfate, filtered, and concentrated to provide the corresponding prop-1-enyl mannoside in quantitative yield.

Prop-1-enyl 2,3,4,6-tetra-*O*-benzyl-D-mannoside (26 mg, 0.045 mmol) and the glycosyl acceptor **15** (15 mg, 0.03 mmol) were dried together by azeotropic removal of water with toluene. The glycosyl partners were dissolved in 1 mL of acetonitrile. To the reaction solution was added NIS (10 mg, 0.045 mmol) followed immediately by triflic acid (11.3 μmol) in 5 μL of acetonitrile. The reaction was stirred at room temperature for 1 min and quenched with triethylamine. The reaction mixture was concentrated under reduced pressure and purified by column chromatography (eluted with dichloromethane/diethyl ether gradient 60 : 1 to 10 : 1) to afford the disaccharide **30**α (25 mg, 82% yield). Rf = 0.35 (methylene chloride/diethyl ether 60 : 1); $[\alpha]_D^{24}$ = +46.8 (c = 0.56, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.37–7.13 (m, 35 H, 7×Ph), 5.9 (m, 1 H, –OCH_2CH=CH_2), 5.3 (dq, *J* = 17.2, 1.5 Hz, 1 H, –OCH_2CH=CH_2), 5.18 (ddt, *J* = 10.3, 1.5, 1.1 Hz, 1 H, –OCH_2CH=CH_2), 4.98 (*A*B^1, *J* = 10.9 Hz, 1 H, Bn), 4.95 (d, *J* = 1.8 Hz, 1 H, Man H-1), 4.86 (*A*B^2, *J* = 10.9 Hz, 1H, Bn), 4.84

(*A*B^3, *J* = 10.9 Hz, 1 H, Bn), 4.79 (AB^1, *J* = 10.9 Hz, 1 H, Bn), 4.76 (d, *J* = 3.7 Hz, 1 H, Glu H-1), 4.73 (*A*B^4, *J* = 10.9 Hz, 1 H, Bn), 4.72 (*A*B^5, *J* = 10.9 Hz, 1 H, Bn), 4.68 (AB^5, *J* = 10.9 Hz, 1 H, Bn), 4.66 (AB^4, *J* = 10.9 Hz, 1 H, Bn), 4.61 (s, 2 H, Bn), 4.59 (*A*B^6, *J* = 10.9 Hz, 1 H, Bn), 4.5 (AB^{2+3}, *J* = 10.9 Hz, 2 H, Bn), 4.45 (AB^6, *J* = 10.9 Hz, 1 H, Bn), 4.1 (*A*BMX$_2$, *J* = 12.9, 5.3, 1.4 Hz, 1 H, –O*CH*$_2$CH=CH$_2$), 4.2–3.93 (m, 3 H), 3.89–3.58 (m, 8 H), 3.45 (dd, *J* = 9.6, 3.6 Hz, 1 H, Glu H-2), 3.4 (dd, *J* = 9.8, 9.1 Hz, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 138.7, 138.6, 138.4, 138.34, 138.3, 138.12, 138.11, 133.5, 128.4, 128.38, 128.45, 128.24, 128.21, 128.18, 128.0, 127.9, 127.86, 127.8, 127.71, 127.70, 127.6, 127.58,127.5, 27.4, 127.38, 118.5, 98.2 ($^1J_{CH}$ = 169 Hz), 95.1 ($^1J_{CH}$ = 168 Hz), 82.07, 79.9, 79.6, 77.6, 75.8, 75.0, 74.9, 74.8, 74.5, 73.2, 73.0, 72.4, 72.0, 71.8, 70.0, 69.0, 68.0, 65.7; FTIR (neat film) 3088, 3063, 3030, 2919, 2869, 1497, 1454, 1362, 1261, 1208, 1093, 1073, 1043, 1028 cm^{-1}; HRMS (ESI) m/*z*: Calcd for $C_{64}H_{68}O_{11}Na$ (M+Na) 1035.4659, found 1035.4655.

Synthesis of fully protected tetrasaccharide 31

Allyl (2,3,4-tri-*O*-benzyl-α-L-rhamnopyranosyl)-(1→2)-3,4-di-*O*-benzyl-α-L-rhamnopyranoside (39). A solution of [Ir(COD)-(PMePh$_2$)$_2$]PF$_6$ (5.5 mg, 6.5 μmol) in 1.0 mL of THF was degassed and stirred under hydrogen atmosphere for 30 min at room temperature. The clear solution was injected into allyl 2,3,4-tri-*O*-benzyl-α-L-rhamnopyranoside **23** (308 mg, 0.65 mmol) in 1.0 mL of THF. The reaction mixture was stirred for overnight, and THF was removed. The residue and allyl 3,4-di-*O*-benzyl-α-L-rhamnoside **32** (162 mg, 0.42 mmol) were dried by azeotropic removal of water with toluene. To the mixture was added 12 mL of acetonitrile, followed by 1.0 mL of an acetonitrile solution containing premixed NIS (146 mg, 0.65 mmol) and TfOH (5.8 μL, 65 μmol) at room temperature. The reaction was stirred for 15 min and quenched with triethyl amine. The solution was then concentrated and purified by flash column chromatography on silica gel (eluted with hexane/ethyl acetate 5 : 1, Rf 0.4) to afford the desired disaccharide **39** (274 mg, 82% yield) as a colorless syrup. $[\alpha]_D^{25}$ = –19.4 (c = 0.16, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.36–7.21 (m, 25 H, 5×Ph), 5.85 (m, 1 H, –OCH$_2$C*H*=CH$_2$), 5.25 (dq, *J* = 17.2, 1.5 Hz –OCH$_2$CH=C*H*$_2$), 5.17 (ddt, *J* = 10.4, 1.3, 1.1 Hz, 1 H, –OCH$_2$CH=C*H*$_2$), 5.12 (d, *J* = 1.6 Hz, 1 H, H-1), 4.94 (*A*B^1, *J* = 10.8 Hz, 1 H, Bn), 4.86 (*A*B^2, *J* = 10.8 Hz, 1 H, Bn), 4.71 (d, *J* = 1.6 Hz, 1 H, H-1), 4.64–4.57 (m, 5 H), 4.56 (*A*B^3, *J* = 12.3 Hz, 1 H, Bn), 4.49 (AB^3, *J* = 12.5 Hz, 1 H, Bn), 4.1 (*A*BMX$_2$, *J* = 13.0, 5.0, 1.5 Hz, 1 H, –O*CH*$_2$CH=CH$_2$), 4.05 (m, 1 H, H-2), 3.92 (AB*M*X$_2$, *J* = 13.0, 6.1, 1.1 Hz, 1 H, –O*CH*$_2$CH=CH$_2$), 3.86 (dd, *J* = 9.8, 3.0 Hz, 1 H, H-3), 3.79 (dd, *J* = 2.9, 2.0, 1 H, H-2), 3.76 (m, 1H, H-5), 3.66 (m, 1 H, H-5), 3.60 (t, *J* = 9.4 Hz, 1 H, H-4), 3.30 (t, *J* = 9.4 Hz, 1 H, H-4), 1.3 (d, *J* = 6.2 Hz, 3 H, CH$_3$), 1.26 (d, *J* = 6.2 Hz, 3 H, CH$_3$); ^{13}C NMR (101 MHz, $CDCl_3$) δ 138.5, 138.4, 138.2, 138.18, 133.7, 128.4, 128.37, 128.32, 128.25, 128.1, 128.0, 127.9, 127.88, 127.8, 127.72, 127.70, 127.6, 127.5, 117.2, 99.1 ($^1J_{CH}$ = 173 Hz), 97.9 ($^1J_{CH}$ = 172 Hz), 80.5, 80.2, 80.1, 79.1, 75.3, 75.27, 74.7, 73.9, 72.4, 72.1, 72.0, 68.4, 67.9, 67.6, 18.0, 17.9; FTIR (neat film) cm^{-1} 3088, 3064, 3031, 2973, 2917, 1497, 1454, 1383, 1363, 1309, 1286, 1261, 1208, 1115, 1074, 1028; HRMS (ESI) *m*/*z*: Calcd for $C_{50}H_{56}O_9Na$ (M+Na) 823.3822, found 823.3806.

Allyl (2,4-di-*O*-benzyl-α-L-rhamnopyranosyl)-(1→3)-2-deoxy-2-acetamido-4,6-*O*-benzylidene-α-D-glucopyranoside (38). A solution of [Ir(COD)(PMePh$_2$)$_2$]PF$_6$ (1.2 mg, 1 μmol) in 1 mL of THF was degassed and stirred under hydrogen atmosphere for 5 min at room temperature. The clear solution obtained was injected into allyl 3-*O*-acetyl-2,4-di-*O*-benzyl-α-L-rhamnopyranoside **37** (44 mg, 0.1 mmol) in 0.7 mL of THF. The reaction mixture was stirred for 25 min, and THF was removed. The residue and **34** (27 mg, 0.077 mmol) were dried by azeotropic removal of water with toluene. The mixture of glycosylation partners were dissolved in 6 mL of acetonitrile and treated with NIS (23 mg, 0.1mmol), immediately followed by TfOH (0.18 μL, 2 μmol) in 100 μL of acetonitrile. The reaction mixture was stirred at room temperature for 70 min and then was hydrolyzed by adding saturated sodium methoxide in methanol (0.3 mL, 0.9 mmol). After 5 min, the reaction mixture was acidified by acetic acid and concentrated. The residue was purified by flash column chromatography (petroleum ether/ethyl acetate 1 : 2 Rf 0.4) to afford **38** (43 mg, 82% yield) as a white solid. $[\alpha]_D^{24}$ = +11.3 (c = 0.21, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.46 (d, *J* = 7.6 Hz, 2 H, Ph), 7.38–7.2 (m, 13 H, Ph), 5.9 (m, 1 H, –OCH$_2$*CH*=CH$_2$), 5.79 (d, *J* = 9.8 Hz, 1 H, Ac*NH*–), 5.52 (s, 1 H, Ph*CH*), 5.35–5.25 (m, 2 H, –OCH$_2$CH=*CH*$_2$), 5.05 (s, 1 H, Rha H-1), 4.76 (*A*B^1, *J* = 11.0 Hz, 1 H, Bn), 4.76 (dd, *J* = 3.9 Hz, 1 H, Glu H-1), 4.65 (*A*B^2, *J* = 11.7 Hz, 1 H, Bn), 4.53 (AB^1, *J* = 11.3 Hz, 1 H, Bn), 4.52 (AB^2, *J* = 11.6 Hz, 1 H, Bn), 4.4 (td, *J* = 9.7, 3.6 Hz, 1 H, Glu H-2), 4.28 (dd, *J* = 10.3, 4.8 Hz, 1 H, Glu H-6), 4.21 (m, 1 H, –O*CH*$_2$CH=CH$_2$), 4.05–4.00 (m, 1 H, Rha H-5), 4.01(t, *J* = 9.6 Hz, 1 H, Rha H-4), 4.01 (m, 1 H, –O*CH*$_2$CH=CH$_2$), 3.96 (dd, *J* = 9.2, 3.2 Hz, 1 H, Rha H-3), 3.91 (td, *J* = 9.9, 4.8 Hz, 1 H, Glu H-5), 3.78 (d, *J* = 2.6 Hz, 1 H, Rha H-2), 3.76 (t, *J* = 10.3 Hz, 1 H, Glu H-6), 3.6 (t, *J* = 9.5 Hz, 1 H), 3.21 (t, *J* = 9.5 Hz, 1 H), 2.2 (d, *J* = 8.4 Hz, 1 H, Rha –OH), 1.95 (s, 3 H, *CH*$_3$C(O)NH), 0.92 (d, *J* = 6.2 Hz, 3 H, Rha CH$_3$); ^{13}C NMR (101 MHz, $CDCl_3$) δ 169.5, 138.7, 137.8, 136.9, 133.1, 128.9, 128.5, 128.2, 128.1, 127.9, 127.6, 127.5, 126.2, 118.5, 101.8, 97.3 ($^1J_{CH}$ = 174 Hz), 97.31 ($^1J_{CH}$ = 170 Hz), 82.0, 80.0, 79.2, 74.4, 73.7, 72.9, 71.0, 68.8, 68.4, 67.2, 63.0, 53.3, 23.5, 17.4; FTIR (neat film) cm^{-1} 3065, 3029, 2922, 2868, 1646, 1558, 155, 13781261, 1184, 1125, 1092, 1077, 1062, 1049, 1029; HRMS (ESI) *m*/*z*: Calcd for $C_{38}H_{45}NO_{10}$ (M) 675.3043, found 675.3029.

Allyl (2,3,4-tri-*O*-benzyl-α-L-rhamnopyranosyl)-(1→2)-(3,4-di-*O*-benzyl-α-L-rhamnopyranosyl)-(1→3)-(2,4-di-*O*-benzyl-α-L-rhamnopyranosyl)-(1→3)-2-deoxy-2-acetamido-4,6-*O*-benzylidene-α-D-glucopyranoside (31). A solution of [Ir(COD)-(PMePh$_2$)$_2$]PF$_6$ (0.6 mg, 0.7 μmol) in 1 mL of THF was degassed and stirred under hydrogen atmosphere for 5 min at room temperature. The obtained clear solution was injected into the solution of the disaccharide **39** (28 mg, 0.036 mmol) in 1 mL of THF. The reaction mixture was stirred for 2 h, and THF was removed. The residue and the disaccharide **38** (16 mg, 0.024 mmol) were dried by azeotropic removal of water with toluene. The glycosyl donor and acceptor were dissolved in 1.5 mL of acetonitrile after briefly heating, and were treated with NIS (8 mg, 0.036 mmol), immediately followed by TfOH (0.063μL, 0.7 μmol) in 16 μL of acetonitrile. The reaction mixture was stirred at room temperature for 60 min and quenched by triethyl amine. The reaction solution was concentrated and purified by flash

column chromatography on silica gel (eluted with a benzene/ethyl acetate gradient 9 : 1 to 3 : 1) to afford **31** (25 mg, 74% yield) as a white solid. Rf 0.6 (benzene/ethyl acetate 3 : 1); $[\alpha]_D^{25} = -9.0$ (c = 0.16, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.5–7.15 (m, 40 H, 8×Ph), 5.85 (m, 1 H, $-OCH_2CH{=}CH_2$), 5.66 (d, J = 9.9 Hz, 1 H), 5.57 (s, 1 H), 5.3–5.2 (m, 2 H, $-OCH_2CH{=}CH_2$), 5.08 (d, J = 1.6 Hz, 1 H), 5.0 (s, 2 H), 4.9 (d, J = 11 Hz, 1 H), 4.84 (d, J = 11.2 Hz, 1 H), 4.75–4.7 (m, 2 H), 4.6–4.35 (m, 11 H), 4.28 (m, 1 H), 4.18 (m, 1 H), 4.02–3.92 (m, 5 H), 3.89–3.62 (m, 10 H), 3.53 (t, J = 9.2 Hz, 1 H), 3.42 (t, J = 9.4 Hz, 1 H), 3.29 (t, J = 9.4 Hz, 1 H), 1.85 (s, 3 H), 1.26 (d, J = 6.2 Hz, 3 H), 1.08 (d, J = 6.2 Hz, 3 H), 0.81 (d, J = 6.2 Hz, 3 H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 169.3, 138.7, 138.6, 138.3, 138.29, 138.17, 137.0, 133.2, 128.8, 128.38, 128.33, 128.32, 128.28, 128.26, 128.20, 128.14, 128.07, 127.90, 127.89, 127.83, 127.82, 127.81, 127.76, 127.75, 127.72, 127.57, 127.52, 127.51, 127.46, 127.45, 127.44, 127.38, 127.31, 126.1, 118.4, 101.6, 101.0 ($^1J_{CH}$ = 176 Hz), 99.0 ($^1J_{CH}$ = 175 Hz), 97.6 ($^1J_{CH}$ = 173 Hz), 97.4 ($^1J_{CH}$ = 176 Hz), 80.6, 80.5, 80.3, 80.1, 79.9, 79.1, 75.1, 74.93, 74.90, 74.4, 73.4, 72.7, 72.4, 72.1, 72.0, 68.8, 68.6, 68.5, 68.2, 63.0, 53.2, 23.4, 17.93, 17.85, 17.37; FTIR (neat film) cm^{-1} 3065, 3032, 2974, 2930, 1652, 1497, 1454, 1377, 1090, 1059, 1029, 1001; HRMS (ESI) m/z: Calcd for $C_{85}H_{95}NO_{18}Na$ (M+Na) 1440.6447, found 1440.6470.

References

1 (*a*) For reviews, see H. Paulsen, *Angew. Chem., Int. Ed.*, 1982, **1**, 155; (*b*) P. Sinaÿ, *Pure Appl. Chem.*, 1991, **63**, 519; (*c*) K. Toshima and K. Tatsuta, *Chem. Rev.*, 1993, **93**, 1503; (*d*) S. J. Danishefsky and M. T. Bilodeau, *Angew. Chem., Int. Ed. Engl.*, 1996, **35**, 1380; (*e*) G.-J. Boons, *Tetrahedron*, 1996, **52**, 1095; (*f*) S. Hanessian and B. Lou, *Chem. Rev.*, 2000, **100**, 4443; (*g*) K.-H. Jung, M. Mueller and R. R. Schmidt, *Chem. Rev.*, 2000, **100**, 4423; (*h*) K. C. Nicolaou and H. J. Mitchell, *Angew. Chem., Int. Ed.*, 2001, **40**, 1576; (*i*) P. Sears and C.-H. Wong, *Science*, 2001, **291**, 2344; (*j*) M. J. Kiefel and M. von Itzstein, *Chem. Rev.*, 2002, **102**, 471; (*k*) B. G. Davis, *Chem. Rev.*, 2002, **102**, 579; (*l*) A. V. Demchenko, *Curr. Org. Chem.*, 2003, **7**, 35; (*m*) B. Yu, Z. Yang and H. Cao, *Curr. Org. Chem.*, 2005, **9**, 179; (*n*) H. Pellissier, *Tetrahedron*, 2005, **61**, 2947; (*o*) E. S. H. El Ashry, L. F. Awad and A. I. Atta, *Tetrahedron*, 2006, **62**, 2943; (*p*) K. Toshima, *Carbohydr. Res.*, 2006, **341**, 1282; (*q*) X. Zhu and R. R. Schmidt, *Angew. Chem., Int. Ed.*, 2009, **48**, 1900.

2 P. Wang, P. Haldar, Y. Wang and H. Hu, *J. Org. Chem.*, 2007, **72**, 5870.

3 T. W. Greene and P. G. M. Wuts, *Protective Groups in Organic Synthesis*, 3rd edn, Wiley-Interscience New York, 1999.

4 (*a*) A. Marra, J. Esnault, A. Veyrieres and P. Sinaÿ, *J. Am. Chem. Soc.*, 1992, **114**, 6354; (*b*) Y. D. Vankar, P. S. Vankar, M. Behrendt and R. R. Schmidt, *Tetrahedron*, 1991, **47**, 9985.

5 (*a*) H. K. Chenault and A. Castro, *Tetrahedron Lett.*, 1994, **35**, 9145; (*b*) H. K. Chenault, A. Castro, L. F. Chafin and J. Yang, *J. Org. Chem.*, 1996, **61**, 5024.

6 (*a*) G.-J. Boons and S. Isles, *Tetrahedron Lett.*, 1994, **35**, 3593; (*b*) G.-J. Boons and S. Isles, *J. Org. Chem.*, 1996, **61**, 4262.

7 (*a*) S. Cao, F. Hernandez-Mateo and R. Roy, *J. Carbohydr. Chem.*, 1998, **17**, 609; (*b*) R. Roy, F. O. Andersson and M. Letellier, *Tetrahedron Lett.*, 1992, **33**, 6053.

8 (*a*) G.-J. Boons, B. Heskamp and F. Hout, *Angew. Chem., Int. Ed. Engl.*, 1996, **35**, 2845; (*b*) R. R. Gibson, R. P. Dickinson and G.-J. Boons, *J. Chem. Soc., Perkin Trans. 1*, 1997, 3357; (*c*) M. Johnson, C. Aries and G.-J. Boons, *Tetrahedron Lett.*, 1998, **39**, 9801.

9 D. R. Mootoo, P. Konradsson, U. Udodong and B. Fraser-Reid, *J. Am. Chem. Soc.*, 1988, **110**, 5583.

10 R. J. Ferrier, R. W. Hay and N. Vethaviyasar, *Carbohydr. Res.*, 1973, **27**, 55.

11 (*a*) B. Fraser-Reid, P. Konradsson, D. R. Mootoo and U. Udodong, *J. Chem. Soc., Chem. Commun.*, 1988, 823; (*b*) D. R. Mootoo, V. Date and B. Fraser-Reid, *J. Am. Chem. Soc.*, 1988, **110**, 2662; (*c*) P. Konradsson, D. R. Mootoo, R. E. McDevitt and B. Fraser-Reid, *J. Chem. Soc., Chem. Commun.*, 1990, 270; (*d*) B. Fraser-Reid, Z. Wu, U. Udodong and H. Ottosson, *J. Org. Chem.*, 1990, **55**, 6068; (*e*) S. Mehta and B. M. Pinto, *J. Org. Chem.*, 1993, **58**, 3269; (*f*) S. V. Ley and H. W. M. Priepke, *Angew. Chem., Int. Ed. Engl.*, 1994, **33**, 2292; (*g*) D. K. Baeschlin, A. R. Chaperon, V. Charbonneau, L. G. Green, S. V. Ley, U. Lücking and E. Walther, *Angew. Chem., Int. Ed.*, 1998, **37**, 3423; (*h*) Z. Zhang, I. R. Ollmann, X.-S. Ye, R. Wischnat, T. Baasov and C.-H. Wong, *J. Am. Chem. Soc.*, 1999, **121**, 734; (*i*) X.-S. Ye and C.-H. Wong, *J. Org. Chem.*, 2000, **65**, 2410; (*j*) L. Huang, Z. Wang and X. Huang, *Chem. Commun.*, 2004, 1960.

12 (*a*) To simplify building block preparation and thus to improve synthetic efficiency, pre-activation of thioglycosides has recently emerged as an appealing approach. See S. Yamago, T. Yamada, T. Maruyama and J. Yoshida, *Angew. Chem., Int. Ed.*, 2004, **43**, 2145; (*b*) X. Huang, L. Huang, H. Wang and X.-S. Ye, *Angew. Chem., Int. Ed.*, 2004, **43**, 5221; (*c*) J. Codée, L. Van Den Bos, R. Litjens, H. Overkleeft, C. van Boeckel, J. van Boom and G. Van Der Marel, *Tetrahedron*, 2004, **60**, 1057.

13 N. Moitessier, B. Maigret, F. Chretien and Y. Chapleur, *Eur. J. Org. Chem.*, 2000, 995.

14 K. Fukase, S. Hase, T. Ikenaka and K. Shoichi, *Bull. Chem. Soc. Jpn.*, 1992, **65**, 436.

15 J. Oltvoort, C. Van Boeckel, J. De Koning and J. Van Boom, *Synthesis*, 1981, 305.

16 (*a*) The isomerization catalyst $[Ir(COD)(PMePh_2)_2]PF_6$ is commercially available (CAS Number: 38465-86-0)[16b]; (*b*) D. Baudry, M. Ephritikhine and H. J. Felkin, *J. Chem. Soc., Chem. Commun.*, 1978, 694.

17 M. Aloui and A. J. Fairbanks, *Chem. Commun.*, 2001, 1406.

18 D. Larson and C. H. Heathcock, *J. Org. Chem.*, 1997, **62**, 8406.

19 (*a*) K. Toshima, H. Nagai and S. Matsumura, *Synlett*, 1999, 1420; (*b*) H. Paulsen, W. Kutschker and O. Lockhoff, *Chem. Ber.*, 1981, **114**, 3233.

20 M. Shimizu, M. Kimura and Y. Tamaru, *Chem.–Eur. J.*, 2005, **11**, 6629.

21 (*a*) R. Windmuller and R. Schmidt, *Tetrahedron Lett.*, 1994, **35**, 7927; (*b*) E. Decoster, J. Lacombe, J. Strebler, B. Ferrari and A. Pavia, *J. Carbohydr. Chem.*, 1983, **2**, 329.

22 K. Bock and C. Pedersen, *J. Chem. Soc., Perkin Trans. 2*, 1974, 293.

23 (*a*) This particular antigen has been previously synthesized: N. K. Kochetkov, N. E. Byramova, Y. E. Tsvetkov and L. V. Backinowsky, *Tetrahedron*, 1985, **41**, 3363; (*b*) B. M. Pinto, D. G. Morissette and D. R. Bundle, *J. Chem. Soc., Perkin Trans. 1*, 1987, 9; (*c*) B. R. Hossany, B. D. Johnston, X. Wen, S. Borrelli, Y. Yuan, M. A. Johnson and P. M. Pinto, *Carbohydr. Res.*, 2009, **344**, 1412.

24 (*a*) M. M. Lévin, K. L. Kotloff, E. M. Barry, M. F. Pasetti and M. B. Sztein, *Nat. Rev. Microbiol.*, 2007, **5**, 540; (*b*) M.-N. Kweon, *Curr. Opin. Infect. Dis.*, 2008, **21**, 313.

25 (*a*) K. Wright, C. Guerreiro, I. Laurent, F. Baleux and L. A. Mulard, *Org. Biomol. Chem.*, 2004, **2**, 1518; (*b*) J. Boutet, C. Guerreiro and L. A. Mulard, *Tetrahedron*, 2008, **64**, 10558.

26 A. Lipták, *Tetrahedron Lett.*, 1976, **17**, 3551.

27 P. Westerduin, P. Haan, M. Dees and J. Boom, *Carbohydr. Res.*, 1988, **180**, 195.

28 B. Pinto, M. Buiting and K. Reimer, *J. Org. Chem.*, 1990, **55**, 2177.

29 M. Hirooka, Y. Mori, A. Sasaki, S. Koto, Y. Shinoda and A. Morinaga, *Bull. Chem. Soc. Jpn.*, 2001, **74**, 1679.

30 C. Warren and R. Jeanloz, *Carbohydr. Res.*, 1977, **53**, 67.

