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Scope of the DMC mediated glycosylation of unprotected sugars with phenols in aqueous solution†

Xin Qiu[a] and Antony J. Fairbanks *[a,b]

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Activation of reducing sugars in aqueous solution using 2-chloro-1,3-dimethylimidazolinium chloride (DMC) and triethylamine in the presence of *para*-nitrophenol allows direct stereoselective conversion to the corresponding 1,2-*trans para*-nitrophenyl glycosides without the need for any protecting groups. The reaction is applicable to sulfated and phosphorylated sugars, but not to ketoses or uronic acids or their derivatives. When applied to other phenols the product yield was found to depend on the pK_a of the added phenol, and the process was less widely applicable to 2-acetamido sugars. For 2-acetamido substrates an alternative procedure in which the glycosyl oxazoline was pre-formed, the reaction mixture freeze-dried, and the crude product then reacted with an added phenol in a polar aprotic solvent system with microwave irradiation proved to be a useful simplification.

Introduction

Glycosylation, *i.e.* the conversion of a reducing sugar into a glycoside, is not only a key biological process, but is one of the most fundamental in the repertoire of the carbohydrate chemist who seeks to produce functionalised mono- and oligosaccharides for a myriad of applications.

Nature, thanks to the evolution of highly selective enzymes, is able to achieve glycosylation with complete control of regio- and stereochemistry with water as the solvent. In contrast glycosylation is typically hard work for the synthetic chemist; they must strive for reaction control, usually *via* multiple protecting groups manipulations, and perform glycosylation under strictly anhydrous conditions.

Recently, in an attempt to emulate Nature's supreme efficiency, the direct chemical glycosylation of unprotected carbohydrates has become an area of significant interest.[1] Fischer glycosylation,[2] the prototypical chemical glycosylation process which is of course well applicable to un-protected sugars, suffers an extremely significant and obvious limitation in that it cannot generally be applied to di- or larger oligosaccharides. Other processes have therefore been developed which have taken advantage of both the enhanced acidity (pK_a ~ 12.1–12.5)[3] of the anomeric hydroxyl group, and the electrophilicity of the anomeric centre. Indeed, glycosylation of unprotected sugars by phenols *via* Mitsunobu processes was first reported in DMF by Grynkiewicz[4] as long ago as 1979. However, although the Mitsunobu reaction has been applied many times to protected carbohydrate substrates,[5] its application for the glycosylation of unprotected sugars, with either phenols or other acidic species has been limited,[6] and such reactions have typically been performed in polar aprotic solvents, such as DMF or dioxane.

Particular interest in the production of aryl glycosides, such as *para*-nitrophenyl (*p*NP) and also di-nitrophenyl (DNP) glycosides, has stemmed from their UV chromophores, which allow facile real-time monitoring of their reactions. As such *p*NP glycosides are widely used substrates for glycosidases, either for quantitative study of the kinetics and/or inhibition of known enzymes,[7] and also as probes for the discovery of hydrolytic activity.[8] They have also been widely used synthetically both as acceptor or donor substrates for enzyme catalysed trans-glycosylation reactions.[9] It is noted that the direct synthesis of DNP-glycosides can be achieved *via* nucleophilic aromatic substitution of 1-fluoro-2,4-dinitrobenzene by an unprotected sugar in a water/ethanol solvent system, but the yields for these processes are somewhat modest.[10]

Recently a series of new methods for glycosylation of unprotected sugars in aqueous solution have been reported. These works have built upon the key pioneering discovery by Shoda[11] that the dehydrating reagent 2-chloro-1,3-dimethylimidazolinium chloride **1** (DMC, Fig. 1)[12] is remarkably able to

[a]*Department of Chemistry, University of Canterbury, Private Bag 4800, Christchurch, 8140, New Zealand. E-mail: antony.fairbanks@canterbury.ac.nz*
[b]*Biomolecular Interaction Centre, University of Canterbury, Private Bag 4800, Christchurch, 8140, New Zealand*

† Electronic supplementary information (ESI) available: Full experimental details for the synthesis and characterisation of all compounds including NMR spectra. See DOI: 10.1039/d0ob01727b

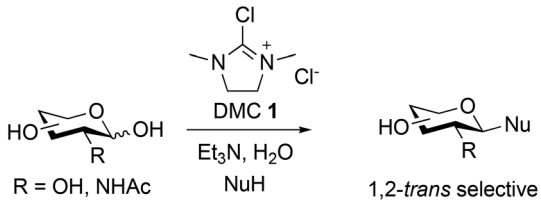


Fig. 1 Nucleophilic substitution at the anomeric centre of unprotected aldoses in water mediated by DMC **1**.

selectively activate the anomeric hydroxyl group of reducing sugars in water. Reaction of reducing aldoses with DMC, or analogues,[13] in the presence of excess base (typically Et_3N) has allowed the direct conversion of unprotected carbohydrates into a variety of derivatives including glycosyl oxazolines,[11] glycosyl acetates,[14] 1,6-anhydro sugars,[15] glycosyl azides[16] and functionalised glycosyl triazoles,[17] aryl[18] and pyridyl thioglycosides[19] including glycosides of cysteine residues in peptides,[20] glycosyl thiols,[21] cyanomethyl thioglycosides[22] and glycosyl thiosulfates.[23]

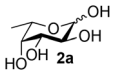
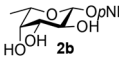
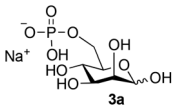
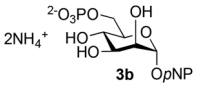
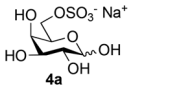
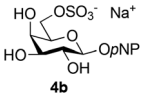
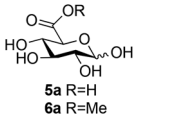
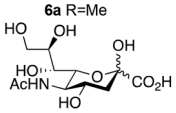
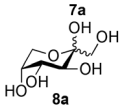
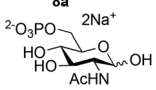
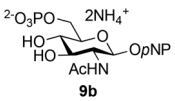
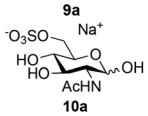
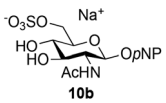
Recently we reported that DMC activation of unprotected sugars in aqueous solution could be used to synthesise *p*NP-glycosides,[24] this being the first example of DMC-mediated intermolecular nucleophilic substitution with an oxygen nucleophile in aqueous solution. This single step synthesis of *p*NP-glycosides from the corresponding reducing sugar avoided all of the previously required synthetic steps, involving the protection and de-protection of hydroxyl groups in addition to activation and nucleophilic substitution at the anomeric centre. Additionally, this single step synthesis should make *p*NP-glycosides of complex oligosaccharides, which are themselves only available in small quantities following isolation processes from natural sources, readily available.

Preliminary investigations had focussed on reaction development and application to a series of mono- and disaccharides, and an oligosaccharide, all of which possessed either a 2-hydroxyl or 2-acetamido group at the reducing terminus. In this follow-up study we sought to delineate the scope of this highly useful transformation by attempted application to a variety of differently functionalised carbohydrate substrates and also to examine the applicability of the process to different phenol nucleophiles.

Results and discussion

Preliminary investigations[24] had revealed that both 2-hydroxy and 2-acetamido monosaccharides, and larger oligosaccharides with such residues at the reducing terminus could be directly converted into the corresponding 1,2-*trans* *p*NP glycosides in aqueous solution. The next question was therefore the tolerance of this process to different functionalisation of the carbohydrate substrate. A variety of monosaccharides comprising different functionalities were investigated applying the same reaction conditions, namely activation with DMC **1** in the presence of excess Et_3N as a base and *para*-nitrophenol (*p*NPOH, Table 1) in water at −10 °C.

Table 1 Application to functionalised sugars

Entry	Substrate	Product	Isolated yield[c]
1[a]	 **2a**	 **2b**	50%[d]
2[a]	 **3a**	 **3b**	62%
3[a]	 **4a**	 **4b**	63%
4[a]	 **5a** R=H **6a** R=Me	—	SM recovered
5[a]	 **7a**	—	SM recovered
6[a]	 **8a**	—	SM recovered
7[b]	 **9a**	 **9b**	28%
8[b]	 **10a**	 **10b**	61%

[a] Reagents and conditions: Sugar (1 equiv.), DMC (3 equiv.), *p*NPOH (12 equiv.) and Et_3N (21 equiv.), in water at −10 °C, 30 min; followed by further DMC (3 equiv.), and Et_3N (6 equiv.) and a further 30 min at −10 °C. [b] Reagents and conditions: Sugar (1 equiv.), DMC (3 equiv.), *p*NPOH (12 equiv.) and Et_3N (21 equiv.), in water at −10 °C, 30 min; then microwave irradiation at 80 °C for 30 min; three iterations. [c] Isolated yield of pure product following purification by chromatography or HPLC. [d] β : α ratio, 17 : 1.

The reaction process worked well for the 6-deoxy sugar L-fucose **2a**, and the corresponding *p*NP-glycoside **2b** was produced in good yield (entry 1). However spectroscopic investigation of the product revealed that a small amount of the α-anomer was also produced during this reaction (β : α. 17 : 1). Pleasingly both sulfation and phosphorylation of the 6-hydroxyl of the monosaccharide substrate was tolerated, and mannose-6-phosphate **3a** and galactose-6-sulfate **4a** were converted directly to their corresponding 1,2-*trans* *p*NP glycosides **3b** and **4b** in good yield (Table 1, entries 2 and 3). However, the presence of a carboxylic acid functionality at C-6 was not tolerated; attempted reaction of glucuronic acid **5a** simply resulted in recovery of starting material (entry 4). This result was interesting since carboxylic acid functionality had pre-

viously been tolerated in oligosaccharides submitted to this process, and the lack of reaction may perhaps at least in part be attributed to the well-established deactivation effect of the C-6 carboxylic acid on reactivity of the anomeric centre. Further support for this hypothesis was the finding that the corresponding methyl ester **6a** was also recovered from the reaction unchanged. Similarly, attempted reaction of the ketoses sialic acid **7a** and fructose **8a** also did not result in any reaction (entries 5 and 6).

These results indicated that attempted activation of ketoses with DMC was unsuccessful,[25] and it is concluded that DMC activation is only applicable to aldoses. This is perhaps a limitation with respect to alternatives such as the Mitsunobu reaction, though these reactions have only been performed on protected sugars.[26]

The next series of experiments focussed on application of the process to other phenols (Table 2). Key to the success of DMC activation is the reaction pH, since the selectivity achieved in reaction of the anomeric hydroxyl group relies on its greater acidity (pK_a typically ~12.1–12.5) than either water or the other sugar hydroxyl groups. Likewise, following the activation step, successful substitution at the anomeric centre can only be achieved if the added phenol outcompetes all the other alternative nucleophiles that are present in solution. It was therefore to be expected that the reaction outcome would depend on the pK_a of the added phenol. Furthermore, as the pH of the reaction mixture changes over time (see ESI, Fig. S2†), so the protonation state of the nucleophile may also change, depending on its pK_a.

Studies began with glucose **11a** as the substrate. Firstly, reaction with *para*-nitrophenol (*p*NPOH) was re-investigated, using the previously applied conditions, namely addition of DMC **1** (3 equiv.) to a stirred mixture of glucose **11a**, *p*NPOH (12 equiv.), and Et_3N (21 equiv.), in water at −10 °C. After 30 min, further DMC (3 equiv.) and Et_3N (6 equiv.) were added, and the reaction stirred for a further 30 min at −10 °C before work-up. The solution pH was measured as the reaction progressed (Fig. 2). The reaction pH decreased over the first ~5 minutes as HCl was produced by reaction of DMC with the anomeric hydroxyl group; the reaction pH then remained relatively constant (pH ~ 11.3) during the latter phases of the reaction. The pH then rose following the second addition of Et_3N and DMC after 30 min of reaction time, and then fell again back following the second addition of DMC to its constant value (~11.3).

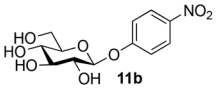
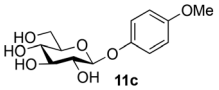
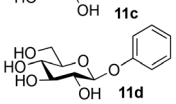
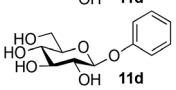
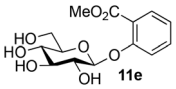
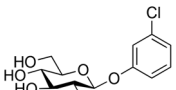
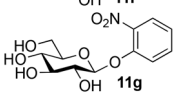
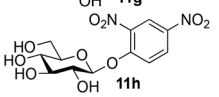
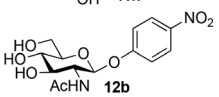
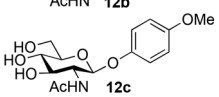
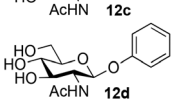
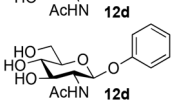
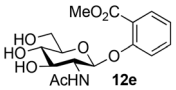
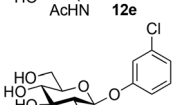
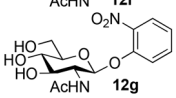
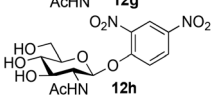
Following purification by chromatography this procedure gave the corresponding *p*NP-glycoside **11b** in 78% yield, exclusively as the β-anomer (Table 2, entry 1). This procedure worked equally well with 2-nitrophenol, which has a very similar pK_a, and gave the 2-nitrophenyl glycoside **11h** in 75% yield (Table 2, entry 7). The transformation also worked with the slightly less acidic phenols 4-methoxyphenol, phenol, and 3-chlorophenol, which gave the corresponding aryl glycosides **11c**, **11d** and **11f** in 52%, 59% and 40% yields respectively (Table 2, entries 2, 3 and 6). Whilst the use of sodium phenolate instead of phenol allowed a reduction in the number of equivalents of Et_3N that were required (9 equiv. instead of 21 equiv.), the product yield was not significantly affected (Table 2, entries 3 and 4, *cf.* 54% and 59% yields). Attempted reaction using methyl salicylate (pK_a 9.9) was less efficient and only gave glycoside **11e** in a very modest 15% yield (Table 2, entry 5). The significantly reduced yield compared to the similarly acidic phenol may perhaps be attributed to the reduced nucleophilicity of the more hindered OH group of the salicylate. Finally, reaction with the considerably more acidic 2,4-dinitrophenol (pK_a 4.5) only gave the product in low yield (13%, Table 2, entry 8). Two factors may explain this poorer yield: firstly the considerably lower nucleophilicity of the more stabilised di-nitrophenoxide anion, and secondly the lability of the product **11h** which undergoes decomposition much more readily than the corresponding *p*NP glycoside **11b**.[27]

Studies then moved to GlcNAc **12a** as the substrate. Activation of 2-acetamido sugars with DMC and base alone results in rapid oxazoline formation.[11] Correspondingly oxazoline formation is invariably a significant side reaction when 2-acetamido sugars are activated by DMC, even in the presence of very good external nucleophiles. As such it seemed beneficial to develop a procedure that made use of the glycosyl oxazoline as an intermediate, which would react with an added phenol in a second step. As such DMC addition was performed in the presence of the phenol nucleophile and Et_3N as for the 2-hydroxy sugars above, but after 30 min at −10 °C, the entire reaction mixture was heated to 80 °C with microwave irradiation for 30 min to effect opening of the oxazoline side product by the phenol. This whole process was iterated three times to increase the product yield.

This process worked well for both *para*-nitrophenol (63% yield, Table 2, entry 9) and 2-nitrophenol (64% yield, Table 2, entry 15), but reaction was less effective for all the other phenols examined. Thus 4-methoxy phenol and phenol/sodium phenolate produced the corresponding aryl glycosides in 14% and 18/21% yields respectively (Table 2, entries 10–12). Reaction with 3-chlorophenol only produced the corresponding 3-chlorophenyl glycoside in a very modest 8% yield. Furthermore, attempted reaction with methyl salicylate was completely unsuccessful (starting material was recovered as the only product). Finally, no product from the attempted reaction with 2,4-di-nitrophenol was observed. This latter result may be due to decomposition of any DNP-glycoside at the elevated reaction temperature in water, in line with the reported lability of this compound.[28]

Given the somewhat disappointing results obtained with phenols other than the 2- and 4-nitrophenols, alternative methods were sought to improve the yield of the aryl glycoside products of 2-acetamido sugars. Since competitive oxazoline formation is inevitable in this case, a better method for opening of intermediate oxazolines by the added phenols was sought. Given that oxazoline hydrolysis by solvent water, which simply re-forms the starting material, was the major competing process, we investigated a two-step one-pot process. Firstly, the oxazoline was formed in water by treatment of the 2-acet-

Table 2 Applicability to other phenols

Entry	Sugar	Nucleophile	pK_a	Product	Isolated yield
1[a]	Glucose **11a**	4-Nitrophenol	7.15	 **11b**	78%
2[a]	Glucose **11a**	4-Methoxyphenol	10.2	 **11c**	52%
3[a]	Glucose **11a**	Phenol	9.95	 **11d**	59%
4[a,c]	Glucose **11a**	Sodium phenolate	9.95	 **11d**	54%
5[a]	Glucose **11a**	Methyl salicylate	9.9	 **11e**	15%
6[a]	Glucose **11a**	3-Chlorophenol	8.97	 **11f**	40%
7[a]	Glucose **11a**	2-Nitrophenol	7.2	 **11g**	75%
8[a]	Glucose **11a**	2,4-Dinitrophenol	4.1	 **11h**	~13%[d]
9[b]	GlcNAc **12a**	4-Nitrophenol	7.15	 **12b**	63%
10[b]	GlcNAc **12a**	4-Methoxyphenol	10.2	 **12c**	14%
11[b]	GlcNAc **12a**	Phenol	9.95	 **12d**	18%
12[b,c]	GlcNAc **12a**	Sodium phenolate	—	 **12d**	21%
13[b]	GlcNAc **12a**	Methyl salicylate	9.9	 **12e**	—
14[b]	GlcNAc **12a**	3-Chlorophenol	8.97	 **12f**	8%
15[b]	GlcNAc **12a**	2-Nitrophenol	7.2	 **12g**	64%
16[b]	GlcNAc **12a**	2,4-Dinitrophenol	4.1	 **12h**	—

[a] Reagents and conditions: Sugar (1 equiv.), DMC (3 equiv.), *p*NPOH (12 equiv.) and Et_3N (21 equiv.), in water at −10 °C, 30 min; followed by further DMC (3 equiv.), and Et_3N (6 equiv.) and a further 30 min at −10 °C. [b] Reagents and conditions: Sugar (1 equiv.), DMC (3 equiv.), *p*NPOH (12 equiv.) and Et_3N (21 equiv.), in water at −10 °C, 30 min; then microwave irradiation at 80 °C for 30 min; three iterations. [c] Only 9 equiv. of Et_3N was used. [d] Some product decomposition occurred during attempted purification, resulting in the formation of some inseparable impurities.

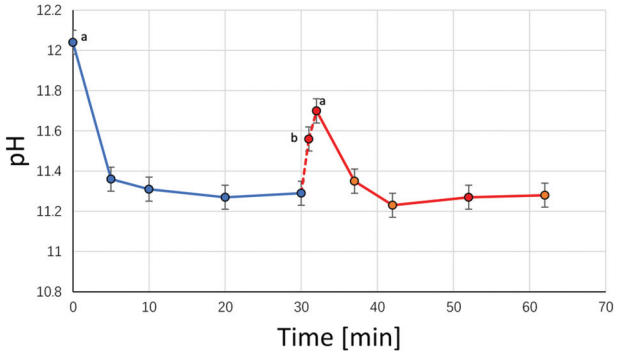
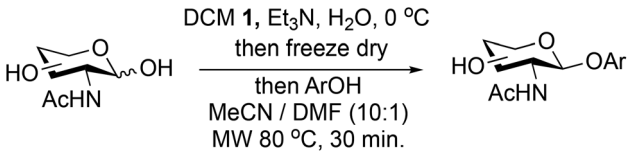
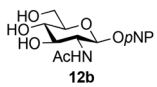
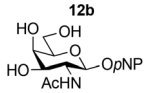
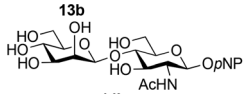
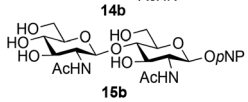
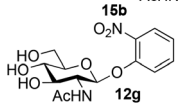
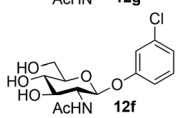


Fig. 2 pH Profile for the reaction of glucose with DMC **1**, Et_3N and pNPOH in water. [a] pH readings before the additions of DMC. [b] pH reading after the second addition of Et_3N.

Table 3 Conversion of 2-acetamido sugars into aryl glycosides *via* oxazoline formation in water and reaction with ArOH in a polar aprotic solvent



Entry	Substrate	Product	Isolated yield
1	GlcNAc **12a**	 **12b**	55%
2	GalNAc **13a**	 **13b**	46%
3	Manβ(1–4)GlcNAc **14a**	 **14b**	51%
4	GlcNAcβ(1–4)GlcNAc **15a**	 **15b**	49%
5	GlcNAc **12a**	 **12g**	55%
6	GlcNAc **12a**	 **12f**	18%

amido sugar with DMC and Et_3N at −10 °C for 30 min. Then, following solvent removal by freeze-drying the entire reaction mixture, the crude product was dissolved by the addition of a polar aprotic solvent mixture (MeCN : DMF 10 : 1),[29] the phenol was added, and the entire mixture then heated to 80 °C with microwave irradiation for 30 min.

This reaction worked well with GlcNAc **12a** as substrate and *para*-nitrophenol as the nucleophile (Table 3, entry 1), which gave *p*NP glycoside **12b** in 55% yield. Although this was slightly lower than the yield for 3 iterations of the previous procedure (*cf.* 63% yield, Table 2 entry 9), a marked advantage of this method was that no iteration was required, saving time and meaning that considerably lower quantities of reagents were needed. An even simpler procedure would involve the use of a MeCN/DMF solvent system for oxazoline formation too. However, attempted one-pot reaction involving treatment of GlcNAc **12a** with DMC, Et_3N and *p*NPOH in MeCN/DMF only produced **12b** in a much lower 26% yield, and numerous side products were also observed.

Therefore the freeze-drying method was chosen as the preferred solution, and subsequently applied to GalNAc **13a**, and the disaccharides Manβ(1–4)GlcNAc **14a** and GlcNAcβ(1–4) GlcNAc **15a** as substrates. In each case reaction gave the corresponding β-*p*NP glycosides in ~50% yield in a single operation (Table 3, entries 2–4).

Finally, the applicability of this process to other phenols was investigated using GlcNAc **12a** as the substrate. The reaction worked well with the relatively acidic 2-nitrophenol (pK_a 7.2) and 3-chlorophenol (pK_a 8.97) to give the corresponding aryl glycosides **12g** and **12f** in 55% and 18% yields respectively (Table 3, entries 5 and 6). However, reaction was unsuccessful with the less acidic phenols 4-methoxyphenol (pK_a 10.2), phenol (pK_a 9.95) and methyl salicylate (pK_a 9.9): in these cases no aryl glycoside was isolated. It should be noted that as the added phenol is present in considerable excess during oxazoline opening then the reaction pH depends on the identity of the added phenol. A plausible explanation for the failure of the attempted reactions with the less acidic phenols is therefore that they are simply not acidic enough on their own to effect oxazoline opening.

Conclusions

One step *p*NP-glycosylation in water using DMC activation is applicable to a range of aldoses, both 2-hydroxy and 2-acetamido, and sulfation or phosphorylation of sugar hydroxyls is well tolerated. However, the reaction is not applicable to ketoses, or uronic acids or their derivatives. The transformation is highly stereoselective, yielding the 1,2-*trans* glycoside exclusively in line with the S_N2 opening of either 1,2-anhydro sugar[30] or oxazoline intermediates for 2-hydroxy or 2-acetamido substrates respectively. 2-Hydroxy aldoses may also be converted into the corresponding aryl glycosides using a range of other phenols, though the efficiency of the reaction is dependent on the nucleophilicity of the added phenol. Reaction of 2-acetamido sugars with other phenols is generally less efficient than with either *para*- or *ortho*-nitrophenol. For 2-acetamido sugars a more pragmatic approach to aryl glycoside formation is oxazoline formation, solvent removal by freeze drying, and then opening of the crude reaction product by heating in a polar aprotic solvent with an added phenol, which reduces the quantities of reagents and time required without affecting the product yield. However, this only works

well for relatively acidic phenols, hinting that the use of an added acidic catalyst may increase both product yields and the range of substrates to which this approach may be applied. Investigations into the use of acid catalysis to effect high yielding opening of unprotected glycosyl oxazolines is currently in progress, and the results will be published in due course.

Experimental

General methods

Reactions conducted at 0 °C were cooled by means of an ice bath. Reactions conducted at −10 °C were cooled using a Julabo FP45 cryostat. Solvent was removed under reduced pressure using a Buchi™ rotary evaporator. Reagents were used as supplied without further purification unless otherwise stated. Thin Layer Chromatography (t.l.c.) was carried out on Merck Silica Gel $60F_{254}$ aluminium-backed plates. Visualization of the plates was achieved using a UV lamp (λ_{max} = 254 or 365 nm), and/or ammonium molybdate (5% in 2 M H_2SO_4), and/or aniline-diphenylamine-85% phosphoric acid (4 mL : 4 g : 20 mL) in acetone (96 mL). Flash column chromatography was carried out using Sorbsil C60 40/60 silica. Melting points were recorded on an Electrothermal® melting point apparatus. Proton and carbon nuclear magnetic resonance (δ_H, δ_C) spectra were recorded on JEOL ECZ400S or JEOL ECZ600R spectrometers. All chemical shifts are quoted on the δ-scale in ppm using residual solvent as an internal standard. ^1H and ^{13}C spectra were assigned using COSY, DEPT, HSQC, HMBC and TOCSY. High resolution mass spectra were recorded on a Bruker maXis 3G UHR-TOF mass spectrometer, using electrospray ionization (ESI) or chemical ionization (CI) techniques as stated. *M*/*z* values are reported in Daltons. Optical rotations were measured on a PerkinElmer 241 polarimeter with a water-jacketed 1 cm^3 cell with a path length of 1 dm, and are quoted in units of $^\circ$ cm^2 g^{-1}. Microwave reactions were carried out using a CEM Discover® Microwave Synthesizer.

General procedure A. The phenol (12 equiv.) was added to a stirred solution of the sugar (typically 100 mg, 1 equiv.), and triethylamine (21 equiv.) in water (typically 3 mL) at room temperature. The mixture was stirred vigorously for 10 min. The solution was then cooled to −10 °C using a cryostat. DMC (3 equiv.) was added, and the mixture was stirred for 30 min at −10 °C. Then, pre-cooled triethylamine (6 equiv.) and then DMC (3 equiv.) were added. The solution was then stirred for a further 30 min at −10 °C. After this time, t.l.c. (typical solvent system $CHCl_3$: MeOH, 4 : 1) indicated the consumption of starting material and the formation of a less polar major product. The solution was concentrated, and then co-evaporated twice with 35% w/w aqueous ammonium hydroxide (typically 2 × 25 mL) to remove triethylamine. Purification of the residue by flash column chromatography (typical solvent system $CHCl_3$: MeOH, 8 : 1) gave the pure product.

General procedure B. The phenol (12 equiv.) was added to a stirred solution of the sugar (typically 90 mg, 1 equiv.), and triethylamine (21 equiv.) in water (typically 2.2 mL) in a sealed (35 mL) microwave tube at room temperature. The mixture was stirred for 10 min until it became clear. The solution was then cooled to −10 °C using a cryostat. DMC (3 equiv.) was added and the mixture was stirred for 30 min at −10 °C. Then, the tube was placed in a microwave synthesizer and the solution was heated at 80 °C for 30 min (200 W). After cooling to room temperature, triethylamine (4 equiv.) was added to the solution before it was cooled to −10 °C using a cryostat. DMC (2 equiv.) was then added and the mixture was stirred for 30 min at −10 °C. Then, the tube was placed in a microwave synthesizer and the solution was heated at 80 °C for 30 min (200 W). The process was then repeated a third time. After the third iteration, t.l.c. (typical solvent system $CHCl_3$: MeOH, 2 : 1) indicated the consumption of the starting material and the formation of a less polar product. The solution was concentrated, and then co-evaporated twice with 35% w/w aqueous ammonium hydroxide (typically 2 × 20 mL) to remove triethylamine. Purification of the residue by flash column chromatography (typical solvent system $CHCl_3$: MeOH, 6 : 1) gave the pure product.

General procedure C. The sugar (typically 60 mg, 1 equiv.) and triethylamine (9 equiv.) were stirred in water (typically 1.5 mL) at 0 °C using an ice bath. DMC (3 equiv.) was added and the solution was stirred for 30 min. The solution was then diluted by the addition of water (typically 2 mL), and freeze-dried. A solution of *p*-nitrophenol (12 equiv.) in MeCN/DMF, 10 : 1 (typically 3 mL in total) was then added, and the solution was transferred into a sealed (7 mL) microwave tube. The tube was placed in a microwave synthesizer and the solution was heated at 80 °C for 30 min (200 W). After cooling to room temperature, the solution was concentrated *in vacuo*, and then co-evaporated twice with 35% w/w aqueous ammonium hydroxide (typically 2 × 10 mL) to remove triethylamine. Purification by flash column chromatography (typical solvent system $CHCl_3$: MeOH, 6 : 1) gave the pure product.

p-Nitrophenyl β-L-fucopyranoside ***2b***.[31] General Procedure A with *p*-nitrophenol (933 mg, 6.66 mmol), L-fucose **2a** (91 mg, 0.56 mmol), triethylamine (1.6 mL, 11.7 mmol, and then 0.46 mL, 3.32 mmol) and DMC (2 × 273 mg, 2 × 1.66 mmol) in water (3 mL), and purification by flash column chromatography ($CHCl_3$: MeOH, 8 : 1) gave **2b** (80 mg, 50%) as a white solid; as a mixture of anomers [1 : 17 α : β]. Recrystallization (water) gave *p*-nitrophenyl-β-L-fucopyranoside as a white solid, m.p. 182–184 °C [lit 186–189 °C];[31a] $[\alpha]_D^{20}$ −46 (*c*, 0.5 in MeOH); δ_H (600 MHz, D_2O)[31] 1.24 (3H, d, *J* 6.2 Hz, CH_3), 3.75–3.85 (3H, m, H-2, H-3, H-4), 3.97–4.03 (1H, m, H-5), 5.14 (1H, d, $J_{1,2}$ 7.0 Hz, H-1), 7.19 (2H, dd, *J* 8.9 Hz, Ar–H), 8.21 (2H, dd, *J* 8.8 Hz, Ar–H).

p-Nitrophenyl 6-O-phospho-α-D-mannopyranoside, diammonium salt ***3b***.[32] General procedure A, with *p*-nitrophenol (84 mg, 0.6 mmol), D-mannose 6-phosphate sodium salt **3a** (14 mg, 50 μmol), triethylamine (0.15 mL, 1.05 mmol, and then 42 μL, 0.3 mmol) and DMC (2 × 25 mg, 2 × 0.15 mmol) in water (0.27 mL), and purification by RP HPLC (column: Phenomenex Luna 5U C18 100 Å (250 × 10 mm × 10 μm); eluent A (H_2O)

and B (MeCN), sample was run at 2.5 mL min^{-1} with 100% A for 2 min, followed by gradient 0–10% B over 5 min, 10–70% B over 21.5 min; column oven: 40 °C; detection: UV 280 nm) gave **3b** (13 mg, 62%) as a white solid; HPLC: t_R = 13.35 min; m.p. 152–158 °C; $[\alpha]_D^{23}$ +60 (*c*, 0.1 in H_2O); δ_H (400 MHz, D_2O)[32] 3.66 (1H, ad, *J* 9.5 Hz, H-4), 3.78 (1H, ddd, *J* 12.1 Hz, 4.9 Hz, 2.1 Hz, H-6), 3.94–4.03 (2H, m, H-5, H-6′) 4.05 (1H, dd, $J_{3,4}$ 10.0 Hz, $J_{2,3}$ 3.4 Hz, H-3), 4.15 (1H, $J_{2,3}$ 3.4 Hz, $J_{1,2}$ 1.8 Hz, H-2), 5.73 (1H, d, $J_{1,2}$ 1.8 Hz, H-1), 7.25 (2H, d, *J* 9.3 Hz, Ar–H), 8.23 (2H, d, *J* 9.3 Hz, Ar–H). δ_C (100 MHz, D_2O) 62.2 (t, C-6), 65.5, 69.7, 69.9, 73.3 (4 × d, C-2, C-3, C-4, C-5), 98.0 (d, C-1), 116.6, 126.0 (2 × d, Ar–C), 142.2, 160.9 (2 × s, Ar–C). HRMS (ESI) *m*/*z*: $[M]^-$ Calcd for $C_{12}H_{15}NO_{11}P$ 380.0388; found 380.0411.

p-Nitrophenyl 6-O-sulfo-β-D-galactopyranoside, sodium salt ***4b***.[33] General procedure A with *p*-nitrophenol (65 mg, 0.47 mmol), D-galactose-6-*O*-sulphate sodium salt **4a** (11 mg, 39 μmol), triethylamine (113 μL, 0.82 mmol, and then 32 μL, 0.23 mmol) and DMC (2 × 19 mg, 2 × 0.12 mmol) in water (0.21 mL), and purification by RP HPLC (column: Phenomenex Luna 5U C18 100 Å (250 × 10 mm × 10 μm); eluent A (H_2O) and B (MeCN), sample was run at 2.5 mL min^{-1} with 100% A for 2 min, followed by gradient 0–10% B over 5 min, 10–70% B over 21.5 min; column oven: 40 °C; detection: UV 280 nm) gave **4b** (10 mg, 63%) as a white solid; HPLC: t_R = 11.79 min; m.p. 144–146 °C; $[\alpha]_D^{23}$–55 (*c*, 0.2 in H_2O) [lit. $[\alpha]_D$ −64.4 (*c*, 3.1 in H_2O)];[33] δ_H (400 MHz, D_2O)[33] 3.78 (1H, dd, $J_{2,3}$ 10.0 Hz, $J_{3,4}$ 3.2 Hz, H-3), 3.84 (1H, dd, $J_{2,3}$ 10.0 Hz, $J_{1,2}$ 7.4 Hz, H-2), 4.03 (1H, ad, *J* 3.2 Hz, H-4), 4.12–4.25 (3H, m, H-5, H-6, H-6′), 5.18 (1H, d, $J_{1,2}$ 7.4 Hz, H-1), 7.23 (2H, d, *J* 9.3 Hz, Ar–H), 8.24 (2H, d, *J* 9.3 Hz, Ar–H). HRMS (ESI) *m*/*z*: $[M]^-$ Calcd for $C_{12}H_{14}NO_{11}S$ 380.0293; found 380.0303.

p-Nitrophenyl 6-O-phospho-2-acetamido-2-deoxy β-D-glucopyranoside, diammonium salt ***9b***.[34] General procedure B with *p*-nitrophenol (53 mg, 0.38 mmol), *N*-acetyl-D-glucosamine-6-phosphate disodium salt **9a** (11 mg, 32 μmol), triethylamine (90 μL, 0.67 mmol, and then 2 × 18 μL, 2 × 0.13 mmol) and DMC (16 mg, 0.1 mmol, and then 2 × 10 mg, 2 × 61 μmol) in water (0.17 mL) in a sealed (7 mL) microwave tube and purification by RP HPLC (column: Phenomenex Luna 5U C18 100 Å (250 × 10 mm × 10 μm); eluent A (H_2O) and B (MeCN), sample was run at 2.5 mL min^{-1} with 100% A for 2 min, followed by gradient 0–10% B over 5 min, 10–70% B over 21.5 min; column oven: 40 °C; detection: UV 280 nm) gave **9b** (4.1 mg, 28%) as a white solid; HPLC: t_R = 12.55 min; m.p. 216–222 °C; $[\alpha]_D^{23}$ −20 (*c*, 0.1 in H_2O); δ_H (400 MHz, D_2O)[34] 1.97 (3H, s, CH_3), 3.63–3.71 (2H, m, H-3, H-4), 3.71–3.80 (1H, m, H-5), 3.95–4.15 (3H, m, H-2, H-6, H-6′), 5.29 (1H, d, $J_{1,2}$ 8.4 Hz, H-1), 7.17 (2H, d, *J* 9.3 Hz, Ar–H), 8.22 (2H, d, *J* 9.3 Hz, Ar–H).

p-Nitrophenyl 6-O-sulfo-2-acetamido-2-deoxy β-D-glucopyranoside, sodium salt ***10b***.[34] General procedure B with *p*-nitrophenol (57 mg, 0.41 mmol), *N*-acetyl-D-glucosamine-6-sulphate sodium salt **10a** (11 mg, 34 μmol), triethylamine (98 μL, 0.71 mmol, and then 2 × 19 μL, 2 × 0.14 mmol) and DMC (17 mg, 0.1 mmol, and then 2 × 11 mg, 2 × 68 μmol) in water (0.18 mL) in a sealed (7 mL) microwave tube and purification by RP HPLC (column: Phenomenex Luna 5U C18 100 Å (250 × 10 mm × 10 μm); eluent A (H_2O) and B (MeCN), sample was run at 2.5 mL min^{-1} with 100% A for 2 min, followed by gradient 0–10% B over 5 min, 10–70% B over 21.5 min; column oven: 40 °C; detection: UV 280 nm) gave **10b** (9.2 mg, 61%) as a white solid; HPLC: t_R = 13.62 min; m.p. 154–158 °C; $[\alpha]_D^{23}$ −40 (*c*, 0.1 in H_2O); δ_H (400 MHz, D_2O)[34] 1.98 (3H, s, CH_3), 3.58 (1H, at, *J* 9.4 Hz, H-4), 3.66 (1H, dd, $J_{2,3}$ 10.3 Hz, $J_{3,4}$ 9.0 Hz, H-3), 3.91 (1H, ddd, $J_{4,5}$ 9.7 Hz, $J_{5,6}$ 5.8 Hz, $J_{5,6'}$ 1.8 Hz, H-5), 4.02 (1H, dd, $J_{2,3}$ 10.3 Hz, $J_{1,2}$ 8.6 Hz, H-2), 4.21 (1H, dd, $J_{6,6'}$ 11.5 Hz, $J_{5,6}$ 5.8 Hz, H-6), 4.37 (1H, dd, $J_{6,6'}$ 11.5 Hz, $J_{5,6'}$ 1.8 Hz, H-6′), 5.28 (1H, d, $J_{1,2}$ 8.6 Hz, H-1), 7.16 (2H, d, *J* 9.3 Hz, Ar–H), 8.22 (2H, d, *J* 9.3 Hz, Ar–H).

p-Nitrophenyl β-D-glucopyranoside ***11b***.[35] General procedure A with *p*-nitrophenol (933 mg, 6.67 mmol), D-glucose **2a** (100 mg, 0.56 mmol), triethylamine (1.6 mL, 11.6 mmol, and then 0.46 mL, 3.32 mmol) and DMC (2 × 273 mg, 2 × 1.66 mmol) in water (3 mL), and purification by flash column chromatography ($CHCl_3$: MeOH, 6 : 1) gave *p*-nitrophenyl β-D-glucopyranoside **2b** (131 mg, 78%) as a white solid, m.p. 158–160 °C [lit. 164–166 °C];[35a] $[\alpha]_D^{25}$ −93 (*c*, 0.5 in MeOH) [lit. $[\alpha]_D^{25}$ −80 (*c*, 1.0 in MeOH)];[35b] δ_H (600 MHz, D_2O)[35c,d] 3.46 (1H, at, *J* 9.0 Hz, H-4), 3.55–3.59 (2H, m, H-2, H-3), 3.62–3.65 (1H, m, H-5), 3.69–3.72 (1H, dd, $J_{6,6'}$ 12.5 Hz, $J_{5,6}$ 5.7 Hz, H-6), 3.87–3.90 (1H, dd, $J_{6,6'}$ 12.5 Hz, $J_{5,6'}$ 2.3 Hz, H-6′), 5.19 (1H, d, $J_{1,2}$ 7.3 Hz, H-1), 7.15 (2H, d, *J* 9.1 Hz, Ar–H), 8.16 (2H, d, *J* 9.1 Hz, Ar–H).

p-Methoxyphenyl β-D-glucopyranoside ***11***.[36] General procedure A with *p*-methoxyphenol (826 mg, 6.7 mmol), D-glucose **11a** (100 mg, 0.56 mmol), triethylamine (1.6 mL, 11.7 mmol, and then 0.46 mL, 3.32 mmol) and DMC (2 × 273 mg, 2 × 1.66 mmol) in water (3 mL), and purification by flash column chromatography ($CHCl_3$: MeOH, 6 : 1) gave **11c** (82 mg, 52%) as a white solid m.p. 174–176 °C [lit. 177 °C];[36b] $[\alpha]_D^{23}$–70 (*c*, 0.2 in H_2O) [lit. $[\alpha]_D^{20}$ −64.1 (*c*, 0.2 in 1 : 1 H_2O : MeOH)];[36a] δ_H (400 MHz, D_2O)[36a] 3.40–3.46 (1H, m, H-4), 3.49 (1H, dd, $J_{2,3}$ 9.1 Hz, $J_{1,2}$ 7.6 Hz, H-2), 3.51–3.58 (2H, m, H-3, H-5), 3.70 (1H, $J_{6,6'}$ 12.5 Hz, $J_{5,6}$ 5.7 Hz, H-6), 3.76 (3H, s, CH_3), 3.88 (1H, $J_{6,6'}$ 12.5 Hz, $J_{5,6'}$ 2.2 Hz, H-6′), 4.97 (1H, d, $J_{1,2}$ 7.6 Hz, H-1), 6.94 (2H, d, *J* 9.2 Hz, Ar–H), 7.07 (2H, d, *J* 9.2 Hz, Ar–H).

Phenyl β-D-glucopyranoside ***11d***.[36a,37] Method 1: General procedure A with phenol (626 mg, 6.7 mmol), D-glucose **11a** (100 mg, 0.56 mmol), triethylamine (1.6 mL, 11.7 mmol, and then 0.46 mL, 3.32 mmol) and DMC (2 × 273 mg, 2 × 1.66 mmol) in water (3 mL), and purification by flash column chromatography ($CHCl_3$: MeOH, 8 : 1) gave **11d** (84 mg, 59%) as a white solid, m.p. 171–180 °C [lit. 173.5–174.5 °C];[37] $[\alpha]_D^{23}$ −60 (*c*, 0.1 in H_2O) [lit. $[\alpha]_D^{18}$–62 (*c*, 1.0 in MeOH)];[36a] δ_H (400 MHz, D_2O)[36a] 3.30–3.49 (1H, m, H-4), 3.50–3.59 (2H, m, H-2, H-3), 3.61 (1H, atd, *J* 5.6 Hz, 2.3 Hz, H-5), 3.72 (1H, dd, $J_{6,6'}$ 12.5 Hz, $J_{5,6}$ 5.7 Hz, H-6), 3.89 (1H, dd, $J_{6.6'}$ 12.5 Hz, $J_{5,6'}$ 2.3 Hz, H-6′), 5.11 (1H, d, $J_{1,2}$ 7.4 Hz, H-1), 7.09–7.15 (3H, m, Ar–H), 7.34–7.40 (2H, m, Ar–H).

Method 2: General procedure A with sodium phenolate (386 mg, 3.33 mmol), D-glucose **11a** (50 mg, 0.28 mmol), triethylamine (0.35 mL, 2.5 mmol, and then 0.23 mL, 1.66 mmol) and DMC (2 × 136 mg, 2 × 0.83 mmol) in water

(1.5 mL), and purification by flash column chromatography ($CHCl_3$: MeOH, 8 : 1) gave **11d** (38 mg, 54%) as a while solid identical to the material described above.

o-Methoxycarbonylphenyl β-D-glucopyranoside ***11e***.[38] General procedure A with methyl salicylate (1.02 g, 6.7 mmol), D-glucose **11a** (100 mg, 0.56 mmol), triethylamine (1.6 mL, 11.7 mmol, and then 0.46 mL, 3.32 mmol) and DMC (2 × 273 mg, 2 × 1.66 mmol) in water (3 mL), and purification by flash column chromatography ($CHCl_3$: MeOH, 8 : 1) gave **11e** as a colourless syrup (26 mg, 15%); $[\alpha]_D^{23}$ −60 (*c*, 0.2 in H_2O) [lit. $[\alpha]_D^{20}$ −64.5 (H_2O)];[38b] δ_H (400 MHz, D_2O)[38a] 3.47 (1H, at, *J* 9.3 Hz, H-4), 3.53–3.62 (3H, m, H-2, H-3, H-5), 3.72 (1H, dd, $J_{6,6'}$ 12.4 Hz, $J_{5,6}$ 5.4 Hz, H-6), 3.87 (3H, s, CH_3), 3.88 (1H, dd, $J_{6,6'}$ 12.4 Hz, $J_{5,6'}$ 2.2 Hz, H-6′), 5.13 (1H, d, $J_{1,2}$ 7.4 Hz, H-1), 7.18 (1H, dt, *J* 7.6 Hz, 1.0 Hz, Ar–H), 7.28 (1H, ad, *J* 8.4 Hz, Ar–H), 7.57 (1H, ddd, *J* 8.8 Hz, 7.6 Hz, 1.8 Hz, Ar–H), 7.77 (1H, dd, *J* 7.8 Hz, 1.8 Hz, Ar–H).

m-Chlorophenyl β-D-glucopyranoside ***11f***.[39] General procedure A with *m*-chlorophenol (428 mg, 3.3 mmol), D-glucose **11a** (50 mg, 0.28 mmol), triethylamine (0.8 mL, 5.9 mmol, and then 0.23 mL, 1.66 mmol) and DMC (2 × 136 mg, 2 × 0.83 mmol) in water (1.5 mL), and purification by flash column chromatography ($CHCl_3$: MeOH, 8 : 1) gave **11f** (32 mg, 40%) as a white solid m.p. 170–172 °C [lit. 176 °C];[39] $[\alpha]_D^{23}$ −70 (*c*, 0.2 in H_2O) [lit. $[\alpha]_D^{20}$ −79.8];[39] δ_H (400 MHz, D_2O) 3.47 (1H, at, *J* 9.2 Hz, H-4), 3.50–3.57 (2H, m, H-2, H-3), 3.60 (1H, ddd, $J_{4,5}$ 9.8 Hz, $J_{5,6}$ 5.7 Hz, $J_{5,6'}$ 2.2 Hz, H-5), 3.72 (1H, dd, $J_{6,6'}$ 12.4 Hz, $J_{5,6}$ 5.7 Hz, H-6), 3.90 (1H, dd, $J_{6,6'}$ 12.4 Hz, $J_{5,6'}$ 2.2 Hz, H-6′), 5.09 (1H, d, $J_{1,2}$ 7.3 Hz, H-1), 7.03 (1H, m, Ar–H), 7.14 (2H, m, Ar–H), 7.31 (1H, t, *J* 8.2 Hz, Ar–H); δ_C (100 MHz, D_2O) 60.4 (t, C-6), 69.3, 72.8, 75.5, 76.1 (4 × d, C-2, C-3, C-4, C-5), 100.0 (d, C-1), 114.9, 116.8, 123.2, 130.8 (4 × d, Ar–C), 134.4, 157.2 (2 × s, Ar–C). HRMS (ESI) *m*/*z*: $[M + Na]^+$ Calcd for $C_{12}H_{15}ClO_6Na$ 313.0449; found 313.0453.

o-Nitrophenyl β-D-glucopyranoside ***11g***.[40] General procedure A with *o*-nitrophenol (466 mg, 3.3 mmol), D-glucose **11a** (50 mg, 0.28 mmol), triethylamine (0.8 mL, 5.9 mmol and then 0.23 mL, 1.66 mmol) and DMC (2 × 136 mg, 2 × 0.83 mmol) in water (1.5 mL) and purification by flash column chromatography ($CHCl_3$: MeOH, 6 : 1) gave **11g** (64 mg, 75%) as a white solid m.p. 133–134 °C [lit. 132–134 °C];[40a] $[\alpha]_D^{23}$ −80 (*c*, 0.1 in H_2O) [lit. $[\alpha]_D^{20}$ −94 (*c*, 1 in H_2O];[40a] δ_H (400 MHz, D_2O)[40b] 3.47 (1H, at, *J* 9.3 Hz, H-4), 3.53–3.64 (3H, m, H-2, H-3, H-5), 3.71 (1H, dd, $J_{6,6'}$ 12.4 Hz, $J_{5,6'}$ 5.6 Hz, H-6), 3.88 (1H, dd, $J_{6,6'}$ 12.4 Hz, $J_{5,6'}$ 2.3 Hz, H-6′), 5.20 (1H, d, $J_{1,2}$ 7.5 Hz, H-1), 7.21 (1H, ddd, *J* 8.4 Hz, 7.5 Hz, 1.1 Hz, Ar–H), 7.38 (1H, dd, *J* 8.6 Hz, 1.1 Hz, Ar–H), 7.63 (1H, ddd, *J* 8.6 Hz, 1.5 Hz, 1.7 Hz), 7.89 (1H, dd, *J* 8.2 Hz, 1.7 Hz, Ar–H).

p-Nitrophenyl 2-acetamido-2-deoxy-β-D-glucopyranoside ***12b***.[41] Method 1: General procedure B with *p*-nitrophenol (690 mg, 4.93 mmol), *N*-acetyl-D-glucosamine **12a** (90 mg, 0.41 mmol), triethylamine (1.17 mL, 8.46 mmol, and then 2 × 0.23 mL, 2 × 1.64 mmol) and DMC (201 mg, 1.23 mmol, and then 2 × 134 mg, 0.82 mmol) in water (2.2 mL) in a (35 mL) microwave tube and purification by flash column chromatography ($CHCl_3$: MeOH, 6 : 1) gave **12b** (88 mg, 63%) as a while solid, m.p. 205–206 °C (MeOH) [lit. 207–208 °C][41a] $[\alpha]_D^{20}$ −8.4 (*c*, 0.3 in H_2O) [lit. $[\alpha]_D^{22}$ −14.7 (*c*, 0.3 in H_2O)];[41a] δ_H (600 MHz, CD_3OD)[41b] 1.98 (3H, s, CH_3), 3.43 (1H, dd, $J_{3,4}$ 8.8 Hz, $J_{4,5}$ 9.7 Hz, H-4), 3.52 (1H, ddd, $J_{4,5}$ 9.7 Hz, $J_{5,6}$ 5.9 Hz, $J_{5,6'}$ 2.2 Hz, H-5), 3.59 (1H, dd, $J_{2,3}$ 10.4 Hz, $J_{3,4}$ 8.8 Hz, H-3), 3.72 (1H, dd, $J_{6,6'}$ 12.2 Hz, $J_{5,6}$ 5.9 Hz, H-6), 3.93 (1H, dd, $J_{6,6'}$ 12.2 Hz, $J_{5,6'}$ 2.2 Hz, H-6′), 3.96 (1H, dd, $J_{2,3}$ 10.4 Hz, $J_{1,2}$ 8.5 Hz, H-2), 5.21 (1H, d, $J_{1,2}$ 8.4 Hz, H-1), 7.18 (2H, d, *J* 9.3 Hz, Ar–H), 8.21 (2H, d, *J* 9.3 Hz, Ar–H).

Method 2: General procedure C with *N*-acetyl-D-glucosamine **12a** (60 mg, 0.27 mmol), triethylamine (0.34 mL, 2.44 mmol) and DMC (133 mg, 0.81 mmol) in water (1.5 mL) at 0 °C, followed by *p*-nitrophenol (456 mg, 3.26 mmol) in MeCN (2.7 mL) and DMF (0.27 mL), and purification by flash column chromatography ($CHCl_3$: MeOH, 6 : 1) gave **12b** (51 mg, 55%) as a while solid identical to the material described above.

p-Methoxy phenyl 2-acetamido-2-deoxy-β-D-glucopyranoside ***12c***.[42] General procedure B with 4-methoxy phenol (608 mg, 4.9 mmol), *N*-acetyl-D-glucosamine **12a** (90 mg, 0.4 mmol), triethylamine (1.17 mL, 8.4 mmol, and then 2 × 0.23 mL, 2 × 1.63 mmol) and DMC (201 mg, 1.2 mmol, and then 2 × 134 mg, 2 × 0.8 mmol) in water (2.2 mL) and purification by flash column chromatography ($CHCl_3$: MeOH, 6 : 1) gave **12c** (19 mg, 14%) as a colourless solid m.p. 238–240 °C [lit. 243 °C];[42a] $[\alpha]_D^{23}$ 0 (*c*, 0.1 in H_2O) [lit. $[\alpha]_D^{23}$ −6.2 (*c*, 1 in DMSO)];[42b] δ_H (400 MHz, D_2O)[42c] 2.00 (3H, s, CH_3), 3.46–3.55 (2H, m, H-4, H-5), 3.59 (1H, dd, $J_{2,3}$ 10.3 Hz, $J_{1,2}$ 8.5 Hz, H-3), 3.70–3.78 (4H, m, H-6, OCH_3), 3.86–3.95 (2H, m, H-2, H-6′) 5.00 (1H, d, $J_{1,2}$ 8.5 Hz, H-1), 6.93 (2H, d, *J* 9.1 Hz, Ar–H), 7.01 (2H, d, *J* 9.1 Hz, Ar–H).

Phenyl 2-acetamido-2-deoxy-β-D-glucopyranoside ***12d***.[38b,43] General procedure B with phenol (463 mg, 4.9 mmol), *N*-acetyl-D-glucosamine **12a** (90 mg, 0.4 mmol), triethylamine (1.17 mL, 8.4 mmol, and then 2 × 0.23 mL, 2 × 1.63 mmol) and DMC (201 mg, 1.2 mmol, and then 2 × 134 mg, 2 × 0.8 mmol) in water (2.2 mL) and purification by flash column chromatography ($CHCl_3$: MeOH, 6 : 1) gave **12d** (22 mg, 18%) as a white solid m.p. 244–245 °C [lit. 246–247 °C];[38b] $[\alpha]_D^{23}$ −4 (*c*, 0.1 in H_2O) [lit. $[\alpha]_D^{30}$ −6.8 in H_2O];[38b] δ_H (400 MHz, D_2O)[43] 1.99 (3H, s, CH_3), 3.51 (at, *J* 9.4 Hz, H-4), 3.56–3.65 (2H, m, H-3, H-5), 3.75 (1H, dd, $J_{6,6'}$ 12.5 Hz, $J_{5,6}$ 5.4 Hz, H-6), 3.87–3.97 (2H, m, H-2, H-6′) 5.12 (1H, d, $J_{1,2}$ 8.5 Hz, H-1), 7.00–7.05 (2H, m, Ar–H), 7.11 (1H, t, *J* 7.4 Hz, Ar–H), 7.35 (2H, dd, *J* 8.6 Hz, 7.4 Hz, Ar–H).

m-Chlorophenyl 2-acetamido-2-deoxy-β-D-glucopyranoside ***12f***.[44] General procedure B with *m*-chlorophenol (627 mg, 4.9 mmol), *N*-acetyl-D-glucosamine **12a** (90 mg, 0.4 mmol), triethylamine (1.17 mL, 8.4 mmol, and then 2 × 0.23 mL, 2 × 1.63 mmol) and DMC (201 mg, 1.2 mmol, and then 2 × 134 mg, 2 × 0.8 mmol) in water (2.2 mL) and purification by flash column chromatography ($CHCl_3$: MeOH, 8 : 1 to 6 : 1) gave **12f** (11 mg, 8%) m.p. 218–222 °C [lit. 227 °C][44] $[\alpha]_D^{23}$ −10 (*c*, 0.1 in H_2O) [lit. $[\alpha]_D^{23}$ 0 (*c*, in H_2O)];[44] δ_H (600 MHz, D_2O) 1.98 (3H, s, CH_3), 3.50–3.54 (1H, m, H-4), 3.57–3.64 (2H, m, H-3, H-5), 3.75 (1H, dd, $J_{6,6'}$ 12.5 Hz, $J_{5,6}$ 5.5 Hz, H-6), 3.89–3.96 (2H, m, H-2, H-6′), 5.11 (1H, d, $J_{1,2}$ 8.5 Hz, H-1), 6.94–6.98 (1H, m, Ar–H), 7.07–7.10

(1H, m, Ar–H), 7.10–7.13 (1H, m, Ar–H), 7.29 (1H, t, *J* 8.2 Hz, Ar–H). δ_C (100 MHz, D_2O) 22.0 (q, CH_3), 55.4 (d, C-2), 60.4 (t, C-6), 69.6, 73.4, 76.1 (3 × d, C-3, C-4, C-5) 99.4 (d, C-1), 115.0, 116.9, 123.3, 130.8 (4 × d, Ar–C), 134.4, 157.3 (2 × s, Ar–C), 174.9 (s, C=O). HRMS (ESI) *m*/*z*: $[M + Na]^+$ Calcd for $C_{14}H_{18}ClNO_6Na$ 354.0715; found 354.0717.

o-Nitrophenyl 2-acetamido-2-deoxy-β-D-glucopyranoside ***12g***.[45] General procedure B with *o*-nitrophenol (684 mg, 4.9 mmol), *N*-acetyl-D-glucosamine **12a** (90 mg, 0.4 mmol), triethylamine (1.17 mL, 8.4 mmol, and then 2 × 0.23 mL, 2 × 1.63 mmol) and DMC (201 mg, 1.2 mmol, and then 2 × 134 mg, 2 × 0.8 mmol) in water (2.2 mL) and purification by flash column chromatography ($CHCl_3$: MeOH, 8 : 1) gave **12g** (89 mg, 64%) as a white solid m.p. 165–168 °C [lit. 176–177 °C];[45] $[\alpha]_D^{23}$ −13 (*c*, 0.3 in H_2O) [lit. $[\alpha]_D^{23}$ −34.7 (*c*, 0.52 in H_2O)];[45b] δ_H (400 MHz, D_2O)[45] 1.99 (3H, s, CH_3), 3.50–3.66 (3H, m, H-3, H-4, H-5), 3.78 (1H, dd, $J_{6,6'}$ 12.5 Hz, $J_{5,6}$ 5.4 Hz, H-6), 3.94 (1H, dd, $J_{6,6'}$ 12.5 Hz, $J_{5,6'}$ 2.3 Hz, H-6′), 3.99 (1H, dd, $J_{2,3}$ 10.0 Hz, $J_{1,2}$ 8.6 Hz, H-2), 5.16 (1H, d, $J_{1,2}$ 8.6 Hz, H-1), 7.23 (1H, ddd, *J* 8.6 Hz, 7.5 Hz, 1.2 Hz, Ar–H), 7.41 (1H, dd, *J* 8.5 Hz, 1.2 Hz, Ar–H), 7.62 (1H, ddd, *J* 8.6 Hz, 7.5 Hz, 1.7 Hz, Ar–H), 7.83 (1H, dd, *J* 8.2 Hz, 1.7 Hz, Ar–H).

p-Nitrophenyl 2-acetamido-2-deoxy-β-D-galactopyranoside ***13b***.[46] General procedure C with *N*-acetyl-D-galactosamine **13a** (60 mg, 0.27 mmol), triethylamine (0.34 mL, 2.44 mmol) and DMC (133 mg, 0.81 mmol) in water (1.5 mL) at 0 °C, followed by *p*-nitrophenol (456 mg, 3.26 mmol) in MeCN (2.7 mL) and DMF (0.27 mL), and purification by flash column chromatography ($CHCl_3$: MeOH, 6 : 1) gave **13b** (43 mg, 46%) as a while solid, m.p. 208–210 °C [lit. 205 °C];[46a] $[\alpha]_D^{20}$ +9.4 (*c*, 0.1 in H_2O) [lit. $[\alpha]_D^{20}$ +19 (*c* 0.12, in H_2O)];[46a] δ_H (600 MHz, DMSO-d_6)[46b] 1.79 (3H, s, CH_3), 3.48–3.64 (4H, m, H-3, H-5, H-6, H-6′), 3.74 (1H, at, *J* 3.7 Hz, H-4), 4.03 (1H, adt, *J* 10.4 Hz, $J_{1,2}$ 8.8 Hz, H-2), 4.73 (1H, t, *J* 5.5 Hz, OH), 4.75 (1H, d, *J* 4.4 Hz, OH), 4.87 (1H, d, *J* 6.3 Hz, OH), 5.13 (1H, d, $J_{1,2}$ 8.5 Hz, H-1), 7.16 (2H, d, *J* 9.3 Hz, Ar–H), 7.79 (1H, d, *J* 9.0 Hz, N*H*Ac), 8.20 (2H, d, *J* 9.3 Hz, Ar–H).

p-Nitrophenyl 2-acetamido-2-deoxy-4-O-(β-D-mannopyranosyl)-β-D-glucopyranoside ***14b***.[24] General procedure C with 2-acetamido-2-deoxy-4-*O*-(β-D-mannopyranosyl)-β-D-glucosamine **14a**[47] (12 mg, 31 μmol), triethylamine (40 μL, 0.28 mmol) and DMC (15 mg, 91 μmol) in water (0.17 mL) at 0 °C, followed by *p*-nitrophenol (53 mg, 0.38 mmol) in MeCN (0.3 mL) and DMF (30 μL), and purification by RP HPLC (column: Phenomenex Luna 5U C18 100 Å (250 × 10 mm × 10 μm); eluent: linear gradient of MeCN using a gradient method, 10–100% MeCN; flow rate: 2.5 mL min^{-1} over 20 min; column oven: 40 °C; detection: UV 280 nm) gave **14b** (8.0 mg, 51%) as a white solid; HPLC: t_R = 10.11 min; m.p. 197–198 °C; $[\alpha]_D^{20}$ −3 (*c*, 0.1 in H_2O); δ_H (600 MHz, D_2O)[24] 1.94 (1H, s, CH_3), 3.37 (1H, ddd, $J_{4b,5b}$ 9.4 Hz, $J_{5b,6b}$ 6.7 Hz, $J_{5b,6b'}$ 2.2 Hz, H-5b), 3.51 (1H, at, *J* 9.7 Hz, H-4b), 3.60 (1H, dd, $J_{3b,4b}$ 9.7 Hz, $J_{2b,3b}$ 3.2 Hz, H-3b), 3.66 (1H, dd, $J_{6b,6b'}$ 12.3 Hz, $J_{5b,6b}$ 6.7 Hz, H-6b), 3.71–3.84 (4H, m, H-3a, H-4a, H-5a, H-6a), 3.84–3.90 (2H, m, H-6a′, H-6b′), 3.98–4.05 (2H, m, H-2a, H-2b), 4.74 (1H, d, $J_{1b,2b}$ 1.0 Hz, H-1b), 5.27 (1H, d, $J_{1a,2a}$ 8.4 Hz, H-1a), 7.11 (2H, d, *J* 9.3 Hz, Ar–H), 8.18 (2H, d, *J* 9.3 Hz, Ar–H).

p-Nitrophenyl β-D-N,N-diacetylchitobioside ***15b***.[48] General procedure C with *N*,*N*-diacetylchitobiose **15a** (8 mg, 19 μmol) (12 mg, 31 μmol), triethylamine (24 μL, 0.17 mmol) and DMC (9 mg, 55 μmol) in water (0.1 mL) at 0 °C, followed by *p*-nitrophenol (32 mg, 0.23 mmol) in MeCN (0.2 mL) and DMF (20 μL), and purification by RP HPLC (column: Phenomenex Luna 5U C18 100 Å (250 × 10 mm × 10 μm); eluent: linear gradient of MeCN using a gradient method, 10–100% MeCN; flow rate: 2.5 mL min^{-1} over 20 min; column oven: 40 °C; detection: UV 280 nm) gave **15b** (5.1 mg, 49%) as a white solid; HPLC: t_R = 10.29 min; m.p. 216–220 °C [lit. 226–227 °C];[48a] $[\alpha]_D^{20}$ −25 (*c*, 0.1 in H_2O) [lit. $[\alpha]_D^{27}$ −21 (*c*, 0.24, 70% MeOH in H_2O)];[48a] δ_H (600 MHz, D_2O)[48b] 1.93 (3H, s, CH_3), 2.01 (3H, s, CH_3), 3.40 (1H, dd, $J_{4b,5b}$ 9.8 Hz, $J_{3b,4b}$ 8.5 Hz, H-4b), 3.44 (1H, ddd, $J_{4b,5b}$ 9.8 Hz, $J_{5b,6b}$ 5.6 Hz, $J_{5b,6b'}$ 2.2 Hz, H-5b), 3.50 (1H, dd, $J_{2b,3b}$ 10.4 Hz, $J_{3b,4b}$ 8.6 Hz, H-3b), 3.63 (1H, dd, $J_{6a,6a'}$ 12.1 Hz, $J_{5a,6a}$ 4.7 Hz, H-6a), 3.66–3.72 (4H, m, H-4a, H-5a, H-2b, H-6b), 3.76 (1H, dd, $J_{2a,3a}$ 10.6 Hz, $J_{3b,4b}$ 8.3 Hz, H-3a), 3.82 (1H, ad, *J* 12.5 Hz, H-6a′), 3.86 (1H, dd, $J_{6b,6b'}$ 12.4 Hz, $J_{5b,6b'}$ 2.2 Hz, H-6b′), 3.99 (1H, dd, $J_{2a,3a}$ 10.5 Hz, $J_{1a,2a}$ 8.6 Hz, H-2a), 4.54 (1H, d, $J_{1b,2b}$ 8.5 Hz, H-1b), 5.24 (1H, d, $J_{1a,2a}$ 8.5 Hz, H-1a), 7.09 (2H, d, *J* 9.3 Hz, Ar–H), 8.18 (2H, d, *J* 9.3 Hz, Ar–H).

Conflicts of interest

There are no conflicts to declare.

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Notes and references

1 For some recent reviews see: (*a*) A. M. Downey and M. Hocek, *Beilstein J. Org. Chem.*, 2017, **13**, 1239–1279; (*b*) K. Villadsen, M. C. Martos-Maldonado, K. J. Jensen and M. B. Thygesen, *ChemBioChem*, 2017, **18**, 574–612; (*c*) M. Jäger and A. J. Minnaard, *Chem. Commun.*, 2016, **52**, 656–664; (*d*) T. Saloranta and R. Leino, *Synlett*, 2015, 421–425.
2 B. Capon, *Chem. Rev.*, 1969, **69**, 407–498.
3 (*a*) S. Feng, C. Bagia and G. Mpourmpakis, *J. Phys. Chem. A*, 2013, **117**, 5211–5219; (*b*) E. P. Sergeant and B. Dempsey, *Ionisation Constants of Organic Acids in Aqueous Solution*, IUPAC Chemical Data Series No 23, Pergamon Press, New York, 1979, pp. 175–177; (*c*) J. J. Christensen, J. H. Rytting and R. M. Izatt, *J. Chem. Soc. B*, 1970, 1646–1648; (*d*) R. M. Izatt, J. H. Rytting, L. D. Hansen and J. J. Christensen, *J. Am. Chem. Soc.*, 1966, **88**, 2641–2643.
4 G. Grynkiewicz, *Pol. J. Chem.*, 1979, **53**, 1571–1579.
5 For a recent review see: J. Hain, P. Rollin, W. Klaffke and T. K. Lindhorst, *Beilstein J. Org. Chem.*, 2018, **14**, 1619–1636.

6 (*a*) C. Besset, S. Chambert, B. Fenet and Y. Queneau, *Tetrahedron Lett.*, 2009, **50**, 7043–7047; (*b*) H. Takeuchi, K. Mishiro, Y. Ueda, Y. Fujimori, T. Furuta and T. Kawabata, *Angew. Chem.*, 2015, **127**, 6275–6278; (*c*) F. Reineri, D. Santelia, A. Viale, E. Cerutti, L. Poggi, T. Tichy, S. S. D. Premkumar, R. Gobetto and S. Aime, *J. Am. Chem. Soc.*, 2010, **132**, 7186–7193; (*d*) H. Takeuchi, Y. Fujimori, Y. Ueda, H. Shibayama, M. Nagaishi, T. Yoshimura, T. Sasamori, N. Tokitoh, T. Furuta and T. Kawabata, *Org. Lett.*, 2020, **22**, 4754–4759.

7 M. L. Sinnott, *Chem. Rev.*, 1990, **90**, 1171–1202.

8 See for example see: F. Yagi, A. E. Eckhardt and I. J. Goldstein, *Arch. Biochem. Biophys.*, 1990, **280**, 61–67.

9 D. J. Vocadlo and S. G. Withers, in *Carbohydrates in Chemistry and Biology, Vol 2*, ed. B. Ernst, G. W. Hart and P. Sinaÿ, Wiley-VCH, Weinheim, 2000, pp. 723–844.

10 S. K. Sharma, G. Corrales and S. Penadés, *Tetrahedron Lett.*, 1995, **36**, 5627–5630.

11 M. Noguchi, T. Tanaka, H. Gyakushi, A. Kobayashi and S.-i. Shoda, *J. Org. Chem.*, 2009, **74**, 2210–2212.

12 T. Isobe and T. Ichikawa, *J. Org. Chem.*, 1999, **64**, 6984–6988.

13 M. Noguchi, T. Fujieda, W. C. Huang, M. Ishihara, A. Kobayashi and S.-I. Shoda, *Helv. Chim. Acta*, 2012, **95**, 1928–1936.

14 D. Lim and A. J. Fairbanks, *Chem. Sci.*, 2017, **8**, 1896–1900.

15 T. Tanaka, W. C. Huang, M. Noguchi, A. Kobayashi and S.-I. Shoda, *Tetrahedron Lett.*, 2009, **50**, 2154–2157.

16 T. Tanaka, H. Nagai, M. Noguchi, A. i. Kobayashi and S.-I. Shoda, *Chem. Commun.*, 2009, 3378–3379.

17 D. Lim, M. A. Brimble, R. Kowalczyk, A. J. A. Watson and A. J. Fairbanks, *Angew. Chem., Int. Ed.*, 2014, **53**, 11907–11911, (*Angew. Chem.*, 2014, **126**, 12101–12105).

18 T. Tanaka, T. Matsumoto, M. Noguchi, A. Kobayashi and S.-I. Shoda, *Chem. Lett.*, 2009, **38**, 458–459.

19 N. Yoshida, M. Noguchi, T. Tanaka, T. Matsumoto, N. Aida, M. Ishihara, A. Kobayashi and S.-I. Shoda, *Chem. – Asian J.*, 2011, **6**, 1876–1885.

20 A. Novoa, S. Barluenga, C. Serba and N. Winssinger, *Chem. Commun.*, 2013, **49**, 7608–7610.

21 (*a*) S. Köhling, M. P. Exner, S. Nojoumi, J. Schiller, N. Budisa and J. Rademann, *Angew. Chem., Int. Ed.*, 2016, **55**, 15510–15514; (*b*) S. R. Alexander, D. Lim, Z. Amso, M. A. Brimble and A. J. Fairbanks, *Org. Biomol. Chem.*, 2017, **15**, 2152–2156.

22 S. R. Alexander and A. J. Fairbanks, *Org. Biomol. Chem.*, 2016, **14**, 6679–6682.

23 Y. Meguro, M. Noguchi, G. Li and S.-I. Shoda, *Org. Lett.*, 2017, **20**, 76–79.

24 X. Qiu and A. J. Fairbanks, *Org. Lett.*, 2020, **22**, 2490–2493.

25 Ketoses have not yet been reported as substrates for DMC activation and derivatisation. See ref. 11–23.

26 G. Gao, O. Schwardt and B. Ernst, *Carbohydr. Res.*, 2004, **339**, 2835–2840.

27 (*a*) D. Cocker and M. L. Sinnott, *J. Chem. Soc., Perkin Trans. 2*, 1975, 1391–1395; (*b*) M. N. Namchuk, J. D. McCarter, A. Becalski, T. Andrews and S. G. Withers, *J. Am. Chem. Soc.*, 2000, **122**, 1270–1277.

28 F. W. Ballardie, B. Capon, W. M. Dearie and R. L. Foster, *Carbohydr. Res.*, 1976, **49**, 79–92.

29 R. Haddoub, N. Laurent, M. Meloni and S. Flitsch, *Synlett*, 2009, 3328–3332.

30 K. Serizawa, M. Noguchi, G. Li and S.-I. Shoda, *Chem. Lett.*, 2017, **46**, 1024–1026.

31 (*a*) K. L. Matta, S. S. Rana, C. F. Piskorz and J. J. Barlow, *Carbohydr. Res.*, 1983, **112**, 213–220; (*b*) J. Wei, X. Lv, Y. Lü, G. Yang, L. Fu, L. Yang, J. Wang, J. Gao, S. Cheng and Q. Duan, *Eur. J. Org. Chem.*, 2013, 2414–2419.

32 Z. Ye, K. Cheng, R. V. Guntaka and R. I. Mahato, *Biochemistry*, 2005, **44**, 4466–4476.

33 Y. Nishida, H. Uzawa, T. Toba, K. Sasaki, H. Kondo and K. Kobayashi, *Biomacromolecules*, 2000, **1**, 68–74.

34 P. Bojarová, K. Slámová, K. Křenek, R. Gažák, N. Kulik, R. Ettrich, H. Pelantová, M. Kuzma, S. Riva and D. Adámek, *Adv. Synth. Catal.*, 2011, **353**, 2409–2420.

35 (*a*) W. F. Goebel, F. H. Babers and O. T. Avery, *J. Exp. Med.*, 1932, **55**, 761; (*b*) W. F. Goebel and O. T. Avery, *J. Exp. Med.*, 1929, **50**, 521; (*c*) L. R. Kremnický, V. R. Mastihuba and G. L. Côté, *J. Mol. Catal. B: Enzym.*, 2004, **30**, 229–239; (*d*) C. J. Capicciotti, R. S. Mancini, T. R. Turner, T. Koyama, M. G. Alteen, M. Doshi, T. Inada, J. P. Acker and R. N. Ben, *ACS Omega*, 2016, **1**, 656–662.

36 (*a*) T. J. Wadzinski, A. Steinauer, L. Hie, G. Pelletier, A. Schepartz and S. J. Miller, *Nat. Chem.*, 2018, **10**, 644–652; (*b*) J. Quintus, K.-A. Kovar, P. Link and H. Hamacher, *Planta Med.*, 2005, **71**, 147–152.

37 C. Bunton, T. Lewis, D. Llewellyn and C. Vernon, *J. Chem. Soc.*, 1955, 4419–4423.

38 (*a*) C. Wang, T.-T. Zhang, G.-H. Du and D.-M. Zhang, *J. Asian Nat. Prod. Res.*, 2011, **13**, 817–825; (*b*) D. Piszkiewicz and T. C. Bruice, *J. Am. Chem. Soc.*, 1968, **90**, 2156–2163.

39 K. Brewster, J. M. Harrison and T. D. Inch, *Tetrahedron Lett.*, 1979, **20**, 5051–5054.

40 (*a*) T. Gubica, A. Temeriusz, P. Pawłowski and J. Stroka, *J. Phys. Org. Chem.*, 2010, **23**, 853–858; (*b*) R. K. K. Gancarz, WO 2017007346A1, 2017.

41 (*a*) R. Begbie, *Carbohydr. Res.*, 1969, **10**, 311–312; (*b*) K. J. Loft, P. Bojarová, K. Slámová, V. Křen and S. J. Williams, *ChemBioChem*, 2009, **10**, 565–576.

42 (*a*) A. Fettke, D. Peikow, M. G. Peter and E. Kleinpeter, *Tetrahedron*, 2009, **65**, 4356–4366; (*b*) R. Roy and F. Tropper, *Synth. Commun.*, 1990, **20**, 2097–2102; (*c*) R. Roy, F. D. Tropper and A. J. Williams, *Magn. Reson. Chem.*, 1991, **29**, 852–858.

43 S. Hor, T. Kodama, N. Sugiura, H. Kondou, M. Yanagida, K. Yanagisawa, A. Shibasawa, B. Tsuzuki, N. Fukatsu and K. Nagao, *Glycoconjugate J.*, 2018, **35**, 477–491.

44 M. Tanaka, S. Kyosaka and Y. Ito, *Chem. Pharm. Bull.*, 1973, **21**, 1971–1977.

45 (*a*) G. Pistia-Brueggeman and R. I. Hollingsworth, *Carbohydr. Res.*, 2003, **338**, 455–458; (*b*) B. Weissmann, *J. Org. Chem.*, 1966, **31**, 2505–2509.
46 (*a*) R. Heyworth, D. Leaback and P. Walker, *J. Chem. Soc.*, 1959, 4121–4123; (*b*) H.-M. Chen and S. G. Withers, *Carbohydr. Res.*, 2007, **342**, 2212–2222.
47 S. Paramasivam and A. J. Fairbanks, *Carbohydr. Res.*, 2019, **477**, 11–19.
48 (*a*) T. Osawa, *Carbohydr. Res.*, 1966, **1**, 435–443; (*b*) K. Slámová, J. Krejzová, P. Marhol, L. Kalachova, N. Kulik, H. Pelantová, J. Cvačka and V. Křen, *Adv. Synth. Catal.*, 2015, **357**, 1941–1950.