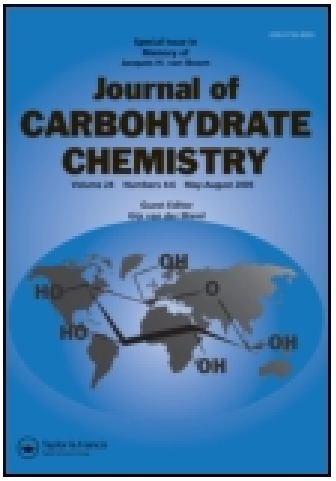


Journal of Carbohydrate Chemistry
Publication details, including instructions for authors and subscription information:
http://www.tandfonline.com/loi/lcar20

Order of Reactivity of OH/NH Groups of Glucosamine Hydrochloride and N-Acetyl Glucosamine Toward Benzylation Using NaH/BnBr in DMF

Stacy P. Ali[a] & Nigel Kevin Jalsa[a]
[a] Department of Chemistry, The University of the West Indies, St. Augustine, Trinidad and Tobago
Published online: 09 May 2014.

To cite this article: Stacy P. Ali & Nigel Kevin Jalsa (2014) Order of Reactivity of OH/NH Groups of Glucosamine Hydrochloride and N-Acetyl Glucosamine Toward Benzylation Using NaH/BnBr in DMF, Journal of Carbohydrate Chemistry, 33:4, 185-196, DOI: 10.1080/07328303.2014.907907

To link to this article: http://dx.doi.org/10.1080/07328303.2014.907907

Journal of Carbohydrate Chemistry, 33:185–196, 2014

ISSN: 0732-8303 print / 1532-2327 online
DOI: 10.1080/07328303.2014.907907

Order of Reactivity of OH/NH Groups of Glucosamine Hydrochloride and *N*-Acetyl Glucosamine Toward Benzylation Using NaH/BnBr in DMF

Stacy P. Ali and Nigel Kevin Jalsa

Department of Chemistry, The University of the West Indies, St. Augustine, Trinidad and Tobago

The order of reactivity of OH and NH groups of glucosamine hydrochloride ($GlcNH_2{\cdot}HCl$) and *N*-acetyl glucosamine (GlcNAc) toward benzylation with NaH/BnBr in DMF was investigated. For $GlcNH_2{\cdot}HCl$, benzyl groups were introduced in the order of *N*-Bn > *N*-Bn_2 > 1-*O*-Bn > 6-*O*-Bn > 4-*O*-Bn > 3-*O*-Bn; for GlcNAc, benzyl groups were introduced in the order of 1-*O*-Bn > 6-*O*-Bn > 4-*O*-Bn > 3-*O*-Bn > *N*-Bn. A range of partially benzylated 2-*N,N'*-dibenzyl glucopyranosides and GlcNAc derivatives were obtained in a single step.

Keywords Order of reactivity; Benzylation; Glucosamine hydrochloride; *N*-Acetyl glucosamine

INTRODUCTION

Benzyl ethers are widely utilized as hydroxyl protecting groups in carbohydrate chemistry.[1] They are easily introduced under typical benzylating conditions employing NaH and BnBr in DMF.[2] These conditions are strongly basic, and hence, base-labile protecting groups are generally not compatible with such etherification reactions. In a synthetic route, benzyl groups are therefore usually installed prior to the introduction of esters. Benzylation may also be effected under mildly basic conditions utilizing Ag_2O and BnBr,[3] or under acidic

Received January 7, 2014; accepted March 20, 2014.
Address correspondence to Nigel Kevin Jalsa, Department of Chemistry, The University of the West Indies, St. Augustine, Trinidad and Tobago. E-mail: nigel.jalsa@sta.uwi.edu

conditions, requiring a mixture of benzyl trichloroacetimidate (BnTCA) and triflic acid (TfOH).[4] Regioselective benzylation may also be facilitated with the use of stannylene acetals in moderate to good yields.[5,6]

Benzyl ethers can be easily removed in the presence of other common functionalities by hydrogenolysis, whether globally deprotected by direct hydrogenation (H_2/Pd/C, often in the presence of an acid)[7] or regioselectively deprotected by catalytic transfer hydrogenation (NH_4HCO_2/Pd/Al_2O_3, methanol).[8–10] They can also be cleaved under oxidative conditions[11,12] and by various Lewis acids.[13,14] Unlike other common protections such as acyl or silyl groups, which have a tendency to change their position on the carbohydrate ring under acidic[15] or basic[16,17] conditions, benzyl ethers are generally stable to protecting group manipulations and therefore do not undergo this migration process.

In this study, benzylations of the monosaccharides glucosamine hydrochloride ($GlcNH_2 \cdot HCl$) and *N*-acetyl glucosamine (GlcNAc) were performed. These sugars belong to the class of 2-amino-2-deoxy glucopyranoses, which are important constituents of glycoproteins,[18] glycolipids,[19] and glycosaminoglycans.[20] The most abundant of its class is GlcNAc, which is present in 1,2-*trans*-glycosidic linkages in the pentasaccharide core of *N*-linked glycoproteins. Though existing ubiquitously in nature, the synthesis of this β-(1-4) glycosidic linkage is often very challenging for two reasons, both of which encompass the fact that the 2-N center is functionalized with an acetyl group. If a suitably protected GlcNAc derivative is used as a glycosyl donor, the formation of a stable oxazolinium ion is inevitable.[21] This intermediate resists incoming nucleophilic attack and is hence ineffective in glycosylation. If an appropriately protected GlcNAc derivative is used as a glycosyl acceptor, it is relatively unreactive at the 4-OH position. This lack of reactivity is due to a combination of steric hindrance, common to most pyranose 4-OH's,[22] and the intramolecular hydrogen-bonded network between the 2-*N*-Ac and the OH groups present.[23] This increased steric bulk around the 4-OH reaction center hinders its nucleophilicity, making GlcNAc a poor glycosyl acceptor at this position. It is these two factors that make the synthesis of this linkage usually very difficult. Despite numerous accomplishments in synthesizing the β-(1-4) glycosidic bond,[24–29] it still lacks a universally accepted approach. As such, non-acetate protecting groups for the 2-amino functionality are of interest.[30] These should possess the attributes of imparting stereoselective control, adequate reactivity, high yields, and stability to further synthetic manipulations of the molecule and must be easily removed under mild conditions. One example of a 2-amino protection that offers these advantages is the 2-*N,N*'-dibenzylamino group introduced by Hindsgaul and Jiao.[31] However, the effectiveness of this 2-N protecting group was examined in a galactosamine donor, not glucosamine. As part of our ongoing efforts to develop a 2-*N,N*'-dibenzylamino glucosamine donor system, we sought improved syntheses for such suitably functionalized derivatives.

It is with this intention that we investigated the reactivity of OH and NH groups of $GlcNH_2 \cdot HCl$ and GlcNAc under the benzylating conditions of NaH/BnBr in DMF. Based on these relative reactivities, the orders of benzyl group installation were determined, and consequently we have identified a facile route for the synthesis of partially benzylated sugars via a single step. To the best of our knowledge, this article is the first to report on the order of functional group reactivity of these amino sugars.

RESULTS AND DISCUSSION

A series of benzylations were performed with $GlcNH_2 \cdot HCl$ and GlcNAc by gradually increasing the ratio of NaH:BnBr equivalents. For all experimental protocols, after the removal of DMF from the benzylation step, immediate acetylation using pyridine and acetic anhydride was performed. This was done to account for the unreacted starting material that would have been preferentially partitioned into the aqueous phase, and also to overcome difficulties associated with purification by column chromatography of the partially protected sugars.

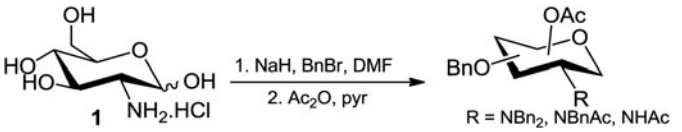
Benzylation of Glucosamine Hydrochloride

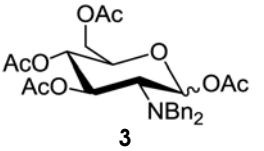
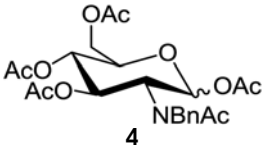
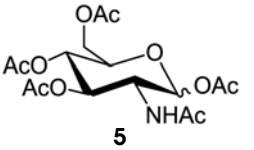
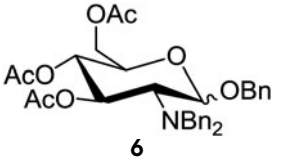
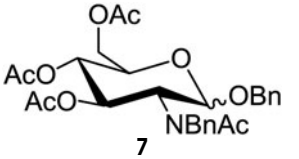
Table 1 shows that better yields were generally obtained when an extra equivalent of NaH was used, compared to that of BnBr, to neutralize HCl during the benzylation of glucosamine hydrochloride. Furthermore, the major compounds produced by using these equivalents of NaH:BnBr (entries 1, 3, 5, 7, 9, and 11) gave the only discernible trend for the order of reactivity of the OH and NH groups of $GlcNH_2 \cdot HCl$.

As observed from the 2:1 equivalents of NaH:BnBr, the highest-yielding compound obtained was acetyl 2-acetamido-2-*N*-benzyl-3,4,6-tri-*O*-acetyl-2-deoxy-α-D-glucopyranoside (4); one benzyl group was installed at the 2-N position. This compound appeared as rotamers, which was verified by a varying-temperature NMR study that detected the ^{1}H NMR chemical shifts of four isomeric compounds. The 3:2 equivalents of NaH:BnBr yielded the major product as acetyl 2-*N,N*′-di-benzyl-3,4,6-tri-*O*-acetyl-2-deoxy-α,β-D-glucopyranoside (**3**); both benzyl groups were introduced at the 2-N center. Garegg and Dasgupta obtained a small quantity of this compound in their synthesis of the 2-azido derivative.[32] It was expected that the anomeric OH would have initially reacted in preference to the NH, owing to the former's greater acidity.[33] However, the results suggest that the NH group was more reactive than the anomeric OH of $GlcNH_2 \cdot HCl$. A possible explanation for this can be due to the lower electronegativity of nitrogen (compared to oxygen), allowing the more nucleophilic NH to be benzylated in preference to the anomeric OH.

The major product obtained with the 4:3 equivalents of NaH:BnBr was benzyl 2-*N,N*'-di-benzyl-3,4,6-tri-*O*-acetyl-2-deoxy-α,β-D-glucopyranoside (**6**); three benzyl groups were installed, two at the 2-N center and the other at the

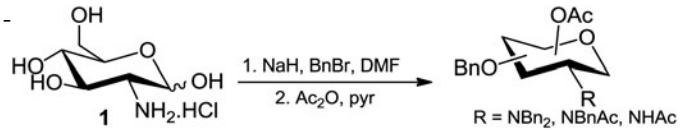
Table 1: Regioselective benzylation of $GlcNH_2$.HCl (**1**) under varying equivalents of NaH:BnBr

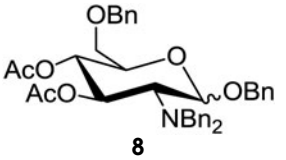
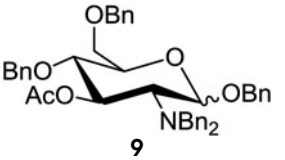
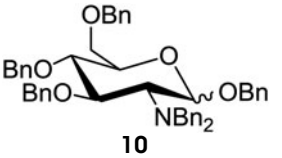


Entry	NaH:BnBr equivalents used	Products	Yield (%)[a]	α:β[b]
1	2:1	 **3**	22	1:2
		 **4**	33	α only
		 **5**	30	1:0.2
2	2:2	**3**	37	1:2
		4	11	α only
		5	17	1:0.2
3	3:2	**3**	62	1:2
		4	24	1:0.5
		5	2	1:0.1
4	3:3	**3**	56	1:2
		4	15	1:0.3
		5	10	1:0.2
5	4:3	**3**	26	1:1
		4	12	α only
		5	1	1:0.1
		 **6**	49	1:5
6	4:4	**3**	48	1:1
		5	5	1:0.2
		6	22	1:5
		 **7**	14	1:0.3

(Continued on next page)

Table 1: Regioselective benzylation of $GlcNH_2$.HCl (**1**) under varying equivalents of NaH:BnBr *(Continued)*



Entry	NaH:BnBr equivalents used	Products	Yield (%)[a]	α:β[b]
7	5:4	**3**	18	1:2
		5	11	1.0.2
		7	4	1:0.3
		 **8**	35	1:2.5
		 **9**	0.8	β only
8[c]	5:5	**3**	6	1:3
		6	60	1:4
		7	19	1:0.35
9	6:5	**5**	7	1:0.2
		6	32	1:4
		9	44	1:3
10[c]	6:6	**3**	5	1:1
		6	49	1:4
		 **10**	9	1:2
11	7:6	**5**	3	1:0.1
		6	25	1:6
		9	6	1:2
		10	45	1:2

[a]Yields were determined from chromatographically pure compounds.
[b]The α:β ratio was calculated from the ^{1}H NMR spectra of the purified product.
[c]Complex mixture of compounds was obtained in a small quantity for these entries.

anomeric position. The anomeric center reacted after the nitrogen, suggesting that it is the most reactive of the OH groups under these conditions. The 5:4 equivalents of NaH:BnBr afforded benzyl 2-*N,N*'-di-benzyl-3,4-di-*O*-acetyl-6-*O*-benzyl-2-deoxy-α,β-D-glucopyranoside (**8**) in the highest yield; four benzyl groups were introduced, two at the 2-N center and one each at the anomeric

and 6-OH positions. This was expected since a primary hydroxyl is more reactive than a secondary hydroxyl and therefore would react preferentially to the 3-OH and 4-OH groups.

The 6:5 equivalents of NaH:BnBr produced benzyl 2-*N,N*'-di-benzyl-3-*O*-acetyl-4,6-di-*O*-benzyl-2-deoxy-α,β-D-glucopyranoside (**9**) as the major compound; five benzyl groups were installed, two at the 2-N position and three at the 1-OH, 6-OH, and 4-OH. The 4-OH site was the more reactive of the two secondary hydroxyl groups remaining. We postulate that the 4-OH is more sterically accessible than the 3-OH; since the 3-OH group is adjacent to the 2-NBn$_2$ center, steric factors hindered the 3-OH from reacting in preference to the 4-OH. The reaction using 7:6 equivalents of NaH:BnBr afforded benzyl 2-*N,N*'-di-benzyl-3,4,6-tri-*O*-benzyl-2-deoxy-β-D-glucopyranoside (**10**) as the main product in a 45% yield. Ye and coworkers synthesized this compound as a precursor for glucosamine-6-phosphate analogs in 89% starting from D-glucosamine.[34] Their excellent yield was attributed to the portionwise additions of a total of 10 equivalents of NaH and a total of 7.4 equivalents of BnBr over a 3-h period.

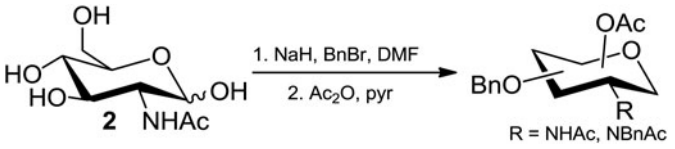
For the majority of reactions performed, per-*O*-acetylated GlcNAc (**5**) was obtained, which accounted for the unreacted starting material from the benzylation step. For each entry, all benzylations proceeded in a total yield ranging from 50% to 89%. From these results, the order of reactivity of NH and OH groups of GlcNH$_2$.HCl can be deduced as N-Bn > N-Bn$_2$ > 1-*O*-Bn > 6-*O*-Bn > 4-*O*-Bn > 3-*O*-Bn.

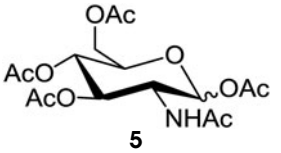
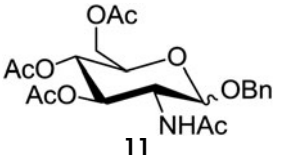
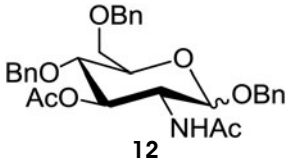
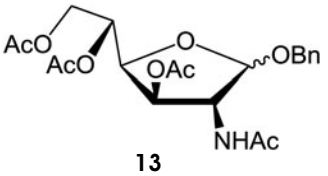
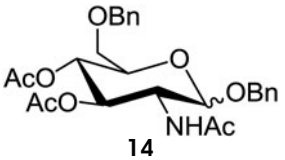
Benzylation of *N*-Acetyl Glucosamine

As shown in Table 2, better overall yields were obtained with an excess equivalent of BnBr in the benzylation of *N*-acetyl glucosamine; hence, NaH:BnBr in these ratios (entries 2, 4, 6, 8, and 10) were considered in determining the order of benzyl group installation for GlcNAc. The major compounds produced for these entries were acetyl 2-acetamido-3,4,6-tri-*O*-acetyl-2-deoxy-α,β-D-glucopyranoside (**5**, entry 2), benzyl 2-acetamido-3,4,6-tri-*O*-acetyl-2-deoxy-α,β-D-glucopyranoside (**11**, entries 4, 6, 8), and benzyl 2-acetamido-3,4,6-tri-*O*-benzyl-2-deoxy-α,β-D-glucopyranoside (**15**, entry 10). From these results, the order of reactivity for GlcNAc was not identifiable. However, the minor compounds produced by these equivalents of NaH:BnBr gave the apparent trend in the order of reactivity of the NH and OH groups. It should be noted that for any entry with more than one minor compound, the highest yielding compound was used for the determination of the trend.

Benzyl 2-acetamido-3,4,6-tri-*O*-acetyl-2-deoxy-β-D-glucopyranoside (**11**) was obtained with the 1:2 equivalents of NaH:BnBr (entry 2) in a yield of 32%; one benzyl group was installed at the anomeric position. Therefore, unlike GlcNH$_2$·HCl, the anomeric OH of GlcNAc is more reactive than the 2-NH. Crasto and Jones synthesized this compound in an overall yield of 75% in a

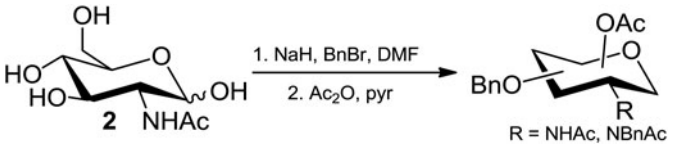
Table 2: Regioselective benzylation of GlcNAc (**2**) under varying equivalents of NaH:BnBr

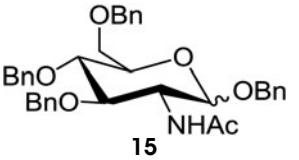
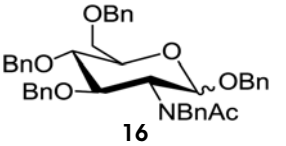


Entry	NaH:BnBr equivalents used	Products	Yield (%)[a]	α:β[b]
1	1:1	 **5**	43	1 : 0.2
		 **11**	13	1 : 0.1
2	1:2	**5**	52	1 : 0.2
		11	32	β only
3	2:2	**5**	7	1 : 0.2
		11	31	β only
		 **12**	6	1:3
		 **13**	4	1:1
4	2:3	**5**	9	1 : 0.2
		11	48	β only
		12	4	1:2
		 **14**	21	β only
5	3:3	**5**	13	1 : 0.1
		11	32	β only
		14	15	β only

(Continued on next page)

Table 2: Regioselective benzylation of GlcNAc (**2**) under varying equivalents of NaH:BnBr *(Continued)*



Entry	NaH:BnBr equivalents used	Products	Yield (%)[a]	α:β[b]
		 **15**	2	β only
6	3:4	**5**	7	1 : 0.2
		11	25	β only
		12	23	1:3
		14	18	β only
		15	5	β only
7[c]	4:4	**11**	44	β only
		15	23	β only
8	4:5	**5**	12	1 : 0.2
		11	26	β only
		13	14	1:2
		15	19	β only
9[c]	5:5	**11**	12	β only
		14	7	β only
		15	26	1:5
10	5:6	**5**	5	1 : 0.2
		14	14	1:5
		15	35	1:3
		 **16**	15	β only

[a]Yields were isolated from chromatographically pure compounds.
[b]The α:β ratio was calculated from the ^{1}H NMR spectra of the purified product.
[c]Complex mixture of compounds was obtained in a small quantity for these entries.

two-step process, by initially per-acetylating GlcNAc for its subsequent use as a glycosyl donor and refluxing in CH_2Cl_2 for 22 h with BnOH as the acceptor and $Yb(OTf)_3$ as the catalyst.[35]

The 2:3 equivalents of NaH:BnBr (entry 4) produced benzyl 2-acetamido-3,4-di-*O*-acetyl-6-*O*-benzyl-2-deoxy-β-D-glucopyranoside (**14**) in 21% yield; two benzyl groups were installed, one at the anomeric center and the other at the primary hydroxyl position. As observed with $GlcNH_2$·HCl, the 6-OH reacted after the anomeric OH. The 3:4 equivalents of NaH:BnBr (entry 6) produced

benzyl 2-acetamido-3-*O*-acetyl-4,6-di-*O*-benzyl-2-deoxy-α,β-D-glucopyranoside (**12**) in 23% yield; three benzyl groups were installed at the 1-OH, 6-OH, and 4-OH positions. The reaction of the 4-OH group after the primary OH was due to electronic factors. First, being adjacent to the 6-*O*Bn allowed for an increased nucleophilicity of the 4-OH due to the inductive effect. Second, the deactivation of the 3-OH group because of its close proximity to the electron-withdrawing N-Ac group would result in the 3-OH being less prone to benzylation.

The reaction using 4:5 equivalents of NaH:BnBr (entry 8) afforded benzyl 2-acetamido-3,4,6-tri-*O*-benzyl-2-deoxy-β-D-glucopyranoside (**15**) in 19% yield. The 3-OH was the last of the hydroxyl groups to react. As with $GlcNH_2{\cdot}HCl$, the adjacent 4-*O*Bn enhanced the reactivity of the 3-OH. This compound was previously synthesized by Harrison and Fletcher in 76% yield by benzylating GlcNAc using $BaO/Ba(OH)_2.8H_2O$ in DMF.[36] The 5:6 equivalents of NaH:BnBr (entry 10) gave benzyl 2-acetamido-2-*N*-benzyl-3,4,6-tri-*O*-benzyl-2-deoxy-β-D-glucopyranoside (**16**) in 15% yield. Unlike $GlcNH_2{\cdot}HCl$, the NH of GlcNAc is less reactive than the OH groups. The presence of the electron-withdrawing 2-*N*-acetyl group strongly reduces the nucleophilicity at the nitrogen atom, thus hindering benzylation from occurring at this position. Similar to **4**, compound **16** was also a rotameric mixture that was detected with low-temperature NMR studies.

We also report a novel furanoside form for GlcNAc (**13**) produced in 4% yield, with a benzyl group at its anomeric center. Fletcher and Inch previously obtained the furanoside form of GlcNAc analogous to this derivative, but with a benzoyl group at the anomeric center.[37] They achieved this from the rearrangement of 2-*N*-acetylbenzamido-2-deoxy-D-glucopyranose.

As with $GlcNH_2{\cdot}HCl$, compound **5** was also produced from the reactions with GlcNAc. All benzylations proceeded in a total yield ranging from 30% to 71%. It should be noted that the overall yields for these reactions were significantly lower than those for $GlcNH_2{\cdot}HCl$, which indicates that the presence of the acetyl group of GlcNAc has a considerable effect on its reactivity. Based on the results, the order of reactivity of GlcNAc toward benzylation can be deduced as 1-*O*-Bn > 6-*O*-Bn > 4-*O*-Bn > 3-*O*-Bn > *N*-Bn.

CONCLUSION

We have investigated the order of reactivity of OH and NH groups of $GlcNH_2{\cdot}HCl$ and GlcNAc toward benzylation using NaH/BnBr in DMF. The NH_2 group of $GlcNH_2{\cdot}HCl$ was more reactive than all of the OH groups, whereas for GlcNAc, the OH groups were more reactive than the NHAc group. For both monosaccharides, the order of reactivity obtained for the hydroxyl groups was identical, with the anomeric center being the most reactive, followed by the primary OH and then the secondary hydroxyls, with the 3-OH

being the least reactive hydroxyl group. Such knowledge of the orders of reactivity allows for a direct and facile route to the synthesis of novel partially benzylated glucosamine and GlcNAc derivatives. Work is currently under way for the investigation of these 2-*N,N'*-dibenzylamino glucopyranose derivatives as glycosyl donors.

EXPERIMENTAL

For Table 1, reactions of entries 1–5 were performed on a 5-g scale $GlcNH_2$.HCl and all other reactions for both Tables 1 and 2 were carried out on a 2-g scale.

$GlcNH_2$·HCl or GlcNAc was dissolved in anhydrous DMF (100 mL for 5-g scale and 60 mL for 2-g scale) under an inert atmosphere and stirred for 15 min. After this the reaction vessel was cooled to 0°C and the required molar equivalence of NaH was then slowly added. The reaction mixture was maintained at this temperature for an hour, after which the necessary molar equivalence of BnBr was then added and allowed to warm to rt. The reaction was monitored via TLC (EtOAc) then left overnight to ensure completion. It was quenched with methanol (10 mL for 5-g scale and 5 mL for 2-g scale) and the DMF was then removed under high vacuum. The crude residue was then dissolved in pyridine (Table 1: 100 mL for entry 1; 80 mL for entries 2, 3, and 4; 60 mL for entries 5–13; Table 2: 25 mL for entries 1–4; 20 mL for entries 5–12), followed by the addition of acetic anhydride (Table 1: 80 mL for entry 1; 60 mL for entries 2, 3, and 4; 45 mL for entries 5–13; Table 2: 20 mL for entries 1–4; 15 mL for entries 5–12). The reaction was monitored via TLC (Pet Ether:EtOAc, 1:1) and left overnight. Solvents were then removed under high vacuum and the crude product was dissolved in CH_2Cl_2 (150 mL), washed with 2M HCl (3 × 100 mL), then washed with water (3 × 100 mL). The organic phase was dried using anhydrous Na_2SO_4 and concentrated under reduced pressure. The crude residue was then subjected to column chromatography for purification.

ACKNOWLEDGMENTS

We are grateful to Mr. Franklyn Julien for the provision of high-resolution mass spectral data; and many thanks to Mr. Keegan Dial and Dr. Nadia Beepath-Singh for the provision of NMR spectroscopy data.

FUNDING

This work was supported by the University of the West Indies.

REFERENCES

1. Greene, T.W.; Wuts, P.G., Eds. *Protective Groups in Organic Synthesis*. Wiley-Interscience, Hoboken, NJ: **2007**, pp. 102–120.

2. Brimacombe, J.S. *Methods in Carbohydrate Chemistry*, R.L. Whistler and J.N. Bemiller, Eds. Academic Press: New York and London, **1972**, pp. 376–378.

3. Bouzide, A.; Sauvé, G. Highly selective silver (I) oxide mediated monoprotection of symmetrical diols. *Tetrahedron Lett.* **1997**, *38*, 5945–5948.

4. Iversen, T.; Bundle, D. Benzyl trichloroacetimidate, a versatile reagent for acid-catalysed benzylation of hydroxyl-groups. *J. Chem. Soc. Chem. Comm.* **1981**, *23*, 1240–1241.

5. Giordano, M.; Iadonisi, A. Tin-mediated regioselective benzylation and allylation of polyols: applicability of a catalytic approach under solvent-free conditions. *J. Org. Chem.* **2014**, *79*, 213–222.

6. Bieg, T.; Szeja, W.; Kral., K.; Paszkowska, J.; Wandzik, I. Microwave-assisted regioselective benzylation: an access to glycal derivatives with a free hydroxyl group at C4. *J. Carb. Chem.* **2012**, *31*, 593–601.

7. Mandal, P.K.; McMurray, J.S. Pd-C-Induced catalytic transfer hydrogenation with triethylsilane. *J. Org. Chem.* **2007**, *72*, 6599–6601.

8. Bieg, T.; Szeja, W. Removal of *O*-benzyl protective groups by catalytic transfer hydrogenation. *Synthesis* **1985**, 76–77.

9. Jalsa, N.K. Regioselective removal of the anomeric *O*-benzyl from differentially protected carbohydrates. *Tetrahedron Lett.* **2011**, *52*, 6587–6590.

10. Ram, S.; Ehrenkaufer, R.E. Ammonium formate in organic synthesis – a versatile agent in catalytic hydrogen transfer reactions. *Synthesis* **1988**, 91–95.

11. Rahim, M.A.; Matsumura, S.; Toshima, K. Deprotection of benzyl ethers using 2,3-dichloro-5,6-dicyano-p-benzoquinone (DDQ) under photoirradiation. *Tetrahedron Lett*. **2005**, *46*, 7307–7309.

12. Pradhan, P.P.; Bobbitt, J.M.; Bailey, W.F. Oxidative cleavage of benzylic and related ethers using an oxoammonium salt. *J. Org. Chem.* **2009**, *74*, 9524–9527.

13. Hori, H.; Nishida, Y.; Ohrui, H.; Meguro, H. Regioselective de-*O*-benzylation with Lewis acids. *J. Org. Chem.* **1989**, *54*, 1346–1353.

14. Pastore, A.; Valerio, S.; Adinolfi, M.; Iadonisi, A. An easy and versatile approach for the reioselective de-*O*-benzylation of protected sugars based on the I_2/Et_3SiH combined system. *Chem. Eur. J.* **2011**, *17*, 5881–5889.

15. Haines, A.H. Relative reactivities of hydroxyl groups in carbohydrates. *Adv. Carbohydr. Chem. Biochem.* **1976**, *33*, 11–109.

16. Mulzer, J.; Schollhorn, B. Multiple 1,2-*O,O*-shift of tert-butyldiphenylsilyl groups in polyols. *Angew. Chem. Int. Ed.* **1990**, *29*, 431–432.

17. Arias-Perez, M.S.; Lopez, M.S.; Santos, M.J. Imidazole-promoted 1,4-migration of the tert-butyldiphenysilyl group: influence on the selectivity control of the silylation reactions of crbohydrate OH groups. *J. Chem. Soc. Perkin Trans 2.* **2002**, *9*, 1549–1552.

18. Schmidt, R.R.; Kinzy, W. Anomeric-oxygen activation for glycoside synthesis: the trichloroacetimidate method. *Adv. Carbohydr. Chem. Biochem.* **1994**, *50*, 21–123.

19. Garg, H.G.; Von dem Bruch, K.; Kunz, H. Developments in the synthesis of glycopeptides containing glycosyl L-asparagine, L-serine, and L-threonine. *Adv. Carbohydr. Chem. Biochem.* **1994**, *50*, 277–310.

20. Umezawa, S. Structures and synthesis of aminoglycoside antibiotics. *Adv. Carbohydr. Chem. Biochem.* **1974**, *30*, 111–182.

21. Fairweather, J.K.; Stick, R.V.; Tilbrook, D.M.G. The asymmetric dihydroxylation of some alkenyl 2-acetylamino-2-deoxy-β-D-glucopyranosides: the preparation of optically pure epoxides as putative inhibitors of chitinases. *Aust. J. Chem.* **1998**, *51*, 471–482.

22. Paulsen, H. Advances in selective chemical syntheses of complex oligosaccharides. *Angew. Chem. Int. Ed.* **1982**, *21*, 155–173.

23. Crich, D.; Dudkin, V. Why are the hydroxyl groups of partially protected *N*-acetylglucosamine derivatives such poor glycosyl acceptors and what can be done about it? A comparative study of the reactivity of *N*-acetyl-, *N*-phthalimido- and 2-azido-2-deoxy-glucosamine derivatives in glycosylation. 2-Picolinyl ethers as reactivity-enhancing replacements for benzyl ethers. *J. Am. Chem. Soc*. **2001**, *123*, 6819–6825.

24. Chang, K.-L.; Zuleta, M.M.L.; Lu, X.-A.; Zhong, Y.-Q.; Hung, S.-C. Regioselective one-pot protection of D-glucosamine. *J. Org. Chem.* **2010**, *75*, 7424–7427.

25. Emmadi, M.; Kulkarni, S.S. Rapid transformation of D-mannose into orthogonally protected D-glucosamine and D-galactosamine thioglycosides. *J. Org. Chem.* **2011**, *76*, 4703–4709.

26. Hernandez-Torres, J.M.; Liew, S.-T.; Achkar, J.; Wei, A. Optimised synthesis of an orthogonally protected glucosamine. *Synthesis* **2002**, *4*, 487–490.

27. Cipolla, L.; Lay, L.; Nicotra, F. New and easy access to *C*-glycosides of glucosamine and mannosamine. *J. Org. Chem.* **1997**, *62*, 6678–6681.

28. Bongat, A.F.G.; Demchenko, A.V. Recent trends in the synthesis of *O*-glycosides of 2-amino-2-deoxysugars. *Carb. Res.* **2007**, *342*, 374–406.

29. Banoub, J.; Boullanger, P.; Lafont, D. Synthesis of oligosaccharides of 2-amino-2-deoxy sugars. *Chem. Rev.* **1992**, *92*, 1167–1195.

30. Debenham, J.; Rodebaugh, R.; Fraser-Reid, B. Recent advances in *N*-protection for amino sugar synthesis. *Liebigs Ann./Recueil* **1997**, *5*, 791–802.

31. Jiao, H.; Hindsgaul, O. The 2-*N,N*-dibenylamino group as a participating group in the synthesis of β-glycosides. *Angew. Chem. Int. Ed*. **1999**, *38*, 346–348.

32. Garegg, P.; Dasgupta, F. 1,3,4,6-tetra-*O*-acetyl-2-azido-2-deoxy-β-D-glucopyranose from D-glucosamine. *J. Chem. Soc. Chem. Comm.* **1989**, *21*, 1640–1641.

33. Sinnott, M.L., Ed. *Carbohydrate Chemistry and Biochemistry*. Cambridge, UK: RSC Publishing, **2007**, pp. 432–433.

34. Ye, X.-S.; Li, Y.; Lau, P.S.; Wang, G.-N. Synthesis and evaluation of glucosamine-6-phosphate analogues as activators of glmS riboswitch. *Tetrahedron* **2012**, *68*, 9405–9412.

35. Crasto, C.F.; Jones, G.B. A practical method for preparation of β-glycosides of *N*-acetylglucosamine. *Tetrahedron Lett.* **2004**, *45*, 4891–4894.

36. Harrison, R.; Fletcher, H.G. Syntheses with partially benzylated sugars. IV. A rote to some 1-*O*-acyl-2-acylamido-2-deoxy-D-glucopyranoses and -D-galactopyranoses. *J. Org. Chem.* **1965**, *30*, 2317–2321.

37. Inch, T.D.; Fletcher, H.G. *N*-acyl derivatives of 2-acylamino-2-deoxyhexoses. The rearrangement of 2-(*N*-acetylbenzamido)-2-deoxy-D-glucose. *J. Org. Chem.* **1966**, *31*, 1821–1825.