Carbohydrate Research, 203 (1990) 47–56
Elsevier Science Publishers B.V., Amsterdam

High-pressure glycosylations of unreactive alcohols and the formation of *N*-glycosyl collidinium salts

William G. Dauben* and Peter Köhler
Department of Chemistry, University of California, Berkeley, California 94720 (U.S.A.)

(Received July 17th, 1989; accepted for publication November 27th, 1989)

ABSTRACT

The yields of disaccharide glycosylation products in tetramethylammonium bromide or silver triflate-collidine activated reactions between hindered alcohols and glycosyl halides were not greatly affected when a pressure of 15 kbar was applied. The formation of orthoester products was greatly increased under pressure. When orthoester formation was not possible both disaccharides and the related *N*-glycosyl collidinium salts were found.

INTRODUCTION

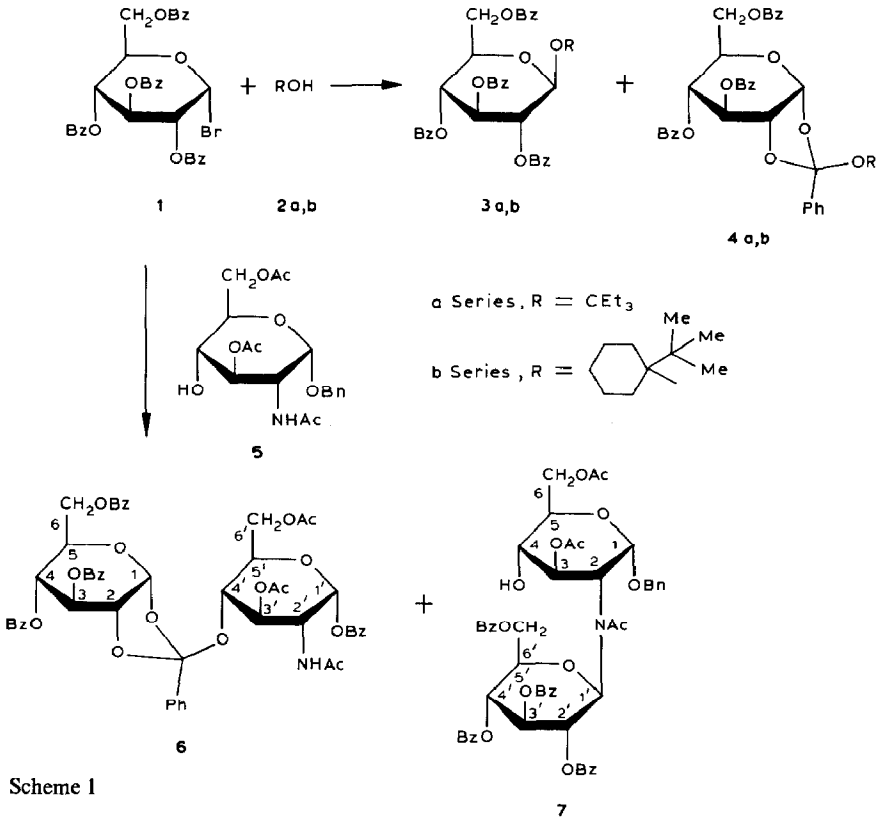
Although there are various known methods for the chemical formation of glycosidic bonds[1], the reaction between a glycosyl halide and an alcohol is still the most often used, even for the the synthesis of complex oligosaccharide units. However, the reduced reactivity of certain alcoholic reactants, which cannot be overcome by activation of the halogen component, has hampered the synthesis of simple disaccharides and made necessary the use of special, selectively blocked monosaccharide units[2–6].

In recent years the application of super high pressure (1–20 kbar) has made many reactions possible that do not proceed under normal conditions[7]. Kochetkov could show that glycosidic bond formation is also influenced by high pressure[8,9], which promotes more stereoselective formation of the glycosidic linkages and a higher degree of polymerization in the synthesis of homopolysaccharides. In view of these promising results it seemed reasonable to use the high pressure technique to overcome reduced reactivity and to induce bond formation in cases that normally give only poor yields under Koenigs–Knorr conditions.

RESULTS AND DISCUSSION

For our studies we have chosen the sterically hindered alcohols triethylcarbinol [1,1-diethylpropyl alcohol, **2a**] and 1-*tert*-butylcyclohexanol (**2b**), and the partially blocked monosaccharide **5**, which shows the low reactivity characteristic of the 4-hydroxy group of 2-acetamido-2-deoxyglucose derivatives[2–4,10–12]. The rather unreactive

*Author for correspondence.



Scheme 1

O-benzoyl glucosyl bromide **1** and the more reactive *O*-acetyl galactosyl bromide **8** were used as halogen components (Scheme 1). Tetraethylammonium bromide and/or silver trifluoromethanesulfonate were used as activators together with 2,4,6-collidine as a base.

In order to avoid problems with silver triflate, such as the enclosure of reagents in the precipitating silver bromide, an excess of activator and base was used in all cases to ensure the presence of these components in the reaction solution. All reagents other than the glycosyl bromide were stirred for 5 min, then the bromo sugar was added and stirring was continued for 1 min to be sure that all components were in solution. One half of the mixture was then transferred into Teflon tubes and pressurized to 15 kbar for 2 days, while the other half was kept at ambient pressure for the same time. After extractive workup, the products were isolated by column chromatography (Table I). If the ambient-pressure triflate-catalyzed reaction solutions were worked up after 10 min a multicomponent mixture was obtained, but no desired products. The amount of glycosylation prior to pressurization can be neglected.

When the mild catalyst tetraethylammonium bromide was used in the reaction of **1** with **2a** at ambient pressure, only a trace of orthoester product **4a** was observed. Even at 15 kbar, the yield was only raised to 16%. In both cases, no glycoside was formed. The

TABLE I

Glycosylation by glycosyl halides under Koenigs–Knorr conditions[a]

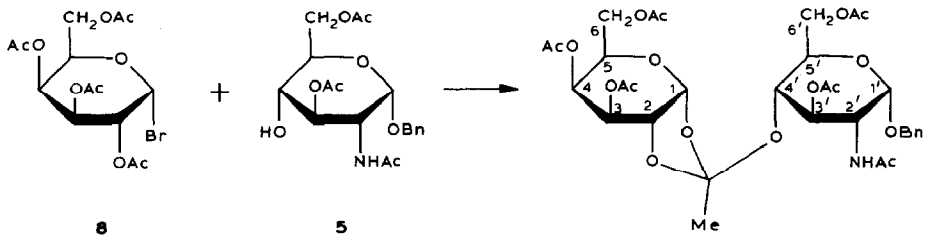
RHal	*ROH*	*Activator*	*p (bar)*	*Yields (%)*	
				3a	**4a**
1	**2a**	Et_4NBr	1	0	2
			15k	0	16
		AgOTf	1	48	2
			15k	33	16
				3b	**4b**
1	**2b**	Et_4NBr	1	0	0
			15k	0	0
		AgOTf	1	22	0
			15k	49	0
				6	**7**
1	**5**	Et_4NBr	1	0	0
			15k	1	0
		AgOTf	1[b]	8	38
			15k	40	0
				9	
8	**5**	Et_4NBr	1	0	
			15k	0	
		AgOTf	1	17	
			15k	27	

[a] Glycosyl halide (0.2 mmol), alcohol (0.4 mmol of **2**, 0.2 mmol of **5**), activator (0.4 mmol), and collidine (0.6 mmol) in dichloromethane (2 mL), 48 h. [b] 2.5 fold portions of all reactants and reagents were used at 1 bar.

finding in the ^{1}H-n.m.r. spectrum of the reaction product of coupling constants $J_{1,2}$ 5.1 Hz and $J_{3,4}$ 1.4 Hz excludes a chair conformation, which would be expected for a glycoside. These coupling constants are characteristic for orthoesters where the attached five-membered ring shifts the pyranose ring to a twisted chair form[13]. The triflate-activated reaction at ambient pressure afforded only the desired β-glycoside **3a**, and this in 48% yield. At 15 kbar pressure only a 33% yield of **3a** was obtained along with 16% of the orthoester **4a**.

Glycosylation of the extremely hindered alcohol **2b**, which cannot even be acetylated with acetyl chloride–pyridine[14], could not be effected with tetraethylammonium bromide as catalyst. With silver triflate, the 22% yield of **3b** at 1 bar could be raised to 49% under pressure, which shows the known effect of pressure in overcoming steric hindrance. No orthoester **4b** was formed in either reaction.

The low reactivity of the 4-hydroxy group in 2-acetamido sugars has already been utilized to form (1→6)-linked disaccharides from alcohol components having both the 4 and the 6 positions unprotected[10,12]. Therefore, it was not surprising that neither at 1 bar nor at 15 kbar was it possible to effect a condensation of **5** with **1** or with the more reactive **8** by catalysis with tetraethylammonium bromide. With silver triflate as the



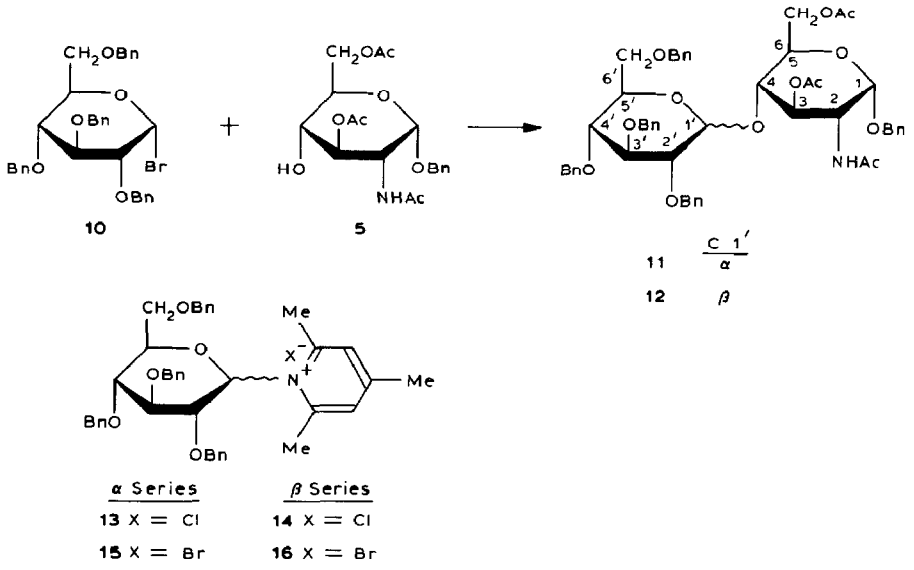
Scheme 2

activator, the reaction of **5** with **1** at ambient pressure gave an 8% yield of orthoester **6**, and also 38% of the unusual *N*-glucosyl compound **7**. The structure of the latter product follows from the proton n.m.r. spectrum. The absence of an NH resonance together with the presence of the original hydroxyl signal clearly indicated that the acetamido grouping had been attacked. At 15 kbar pressure, no *N*-glucosyl compound was formed and the orthoester **6** was obtained in 40% yield. The reaction of galactosyl bromide **8** with **5** gave only the orthoester product **9**, in 17% yield at ambient pressure and in 27% yield at 15 kbar pressure. The complete suppression of *N*-glycosyl compound formation with bromide **8** can be interpreted as a sign of the predominance of the bicyclo-acyloxonium intermediate, which can be derived from **1** or from **8**. The formation of this intermediate is apparently enhanced by pressure as a result of a negative activation volume of -11 cm^3.mol^{-1} for the isomerization of a glycosyl cation to an acyloxonium ion[9]. The stability of the latter at 15 kbar makes less favorable an attack at the anomeric center, which would lead to a glycosidic or an *N*-glycosyl product via opening of the acyloxonium ring.

The amount of collidine present in the reaction mixtures may be critical in that an excess stabilizes the orthoesters formed as intermediates[15]. Thus, in order to decrease the yield of orthoesters from **1** and **8** the amount of collidine was reduced to one equivalent or less. This led to the formation of an increasing amount of slow moving material, possibly decomposition products of orthoester intermediates. No glycosides could be detected.

In order to make the formation of orthoesters impossible further investigations were carried out using the bromide **10**, which has a nonparticipating neighboring group (Scheme 3). As expected, no product formation was observed with tetraethylammonium bromide as the catalyst, and **5** was recovered quantitatively. In the silver triflate-promoted reaction 35% of the disaccharide mixture **11** + **12** could be isolated at 1 bar, whereas the application of pressure afforded only 13%. In both cases considerable amounts of polar material were formed (Table II).

A careful reinvestigation of all four reaction mixtures led to the isolation of a syrupy compound. All attempts to induce crystallization or to obtain pure samples for analysis were unsuccessful. The proton n.m.r. spectrum showed four benzylic methylene groups. The coupling constants $J_{1,2}$ 3.1, $J_{2,3}$ 3.5, $J_{3,4}$ 5.0, and $J_{4,5}$ 8.8 Hz reveal a strong distortion of a *C*1 chair conformation towards a twist chair, which puts the



Scheme 3

benzyl substituents into unfavorable pseudoaxial positions. Together with the chemical shift of 6.47 p.p.m. for H-1 and the high polarity of the compound the data clearly point toward an *N*-glycosyl collidinium salt **13**, where the reverse anomeric effect forces the electropositive *α*-substituent into an equatorial position. The abnormal conformations of such pyridinium salts are known, but no collidinium derivatives of this type have been reported [16–19]. The analogous bromide **15**, whose n.m.r. data differ only slightly from those of **13**, could be obtained by extraction of the reaction mixture with a copper(II) bromide solution. The *p*-methyl protons of the collidine unit of **15** resonate at 5.52 p.p.m., whereas the two *o*-methyl groups yield a broad signal at 2.71 p.p.m., integrating to six protons. This indicates hindered rotation around the *N*-glycosyl bond and a coalescence temperature close to room temperature. At $-15°$ two sharp signals appear at 2.47 and 2.89 p.p.m.

In each case the last fractions of **13** and **15** eluted from the column contained a further compound, most probably the *β*-anomer (**14** and **16**, respectively). The anomeric proton of **14** resonates at 6.17 p.p.m. with a coupling constant of 8.6 Hz, whereas both the *o*- and *p*-methyl groups of the collidine unit give sharp signals, at 2.55 and 3.05 p.p.m. The values for **16** are 6.09 p.p.m. and 8.4 Hz for H-1 and 2.55 and 3.02 p.p.m. for the methyl groups. The larger anomeric coupling constants are in agreement with the expected *C*1 conformation for the *β*-isomers, the collidinium ring occupying the more stable equatorial position.

This finding of the formation of *N*-glycosyl collidinium salts with silver triflate – collidine as the activator and base even at atmospheric pressure is important in relation to the general use of this reaction system for the synthesis of *O*-glycosides. Although **13–16** slowly decompose upon standing to form 2,3,4,6-tetra-*O*-benzylglucose, they do not react with alcohols and can even be separated on silica gel with 5:1 chloroform–

TABLE II

Reaction between acetamido sugar **5** and benzylated glycosyl bromide **10**[a]

Activator	*p (bar)*	*Yields (%)*		
		5	**11 + 12**	**13 + 14**
Et_4NBr	1	94	2	2
	15k	96	0	13
AgOTf	1	64	35	18
	15k	84	13	29
AgOTf[b]	1	40	51	0[c]
	15k	53	45	0[c]

[a] (0.2 mmol), **10** (0.24 mmol), activator (0.34 mmol), and collidine (0.46 mmol) in dichloromethane (4 mL), 48 h (2.5-fold portions were used at 1 bar). [b] 2,6-Di-*tert*-butylpyridine instead of collidine. [c] 2,6-Di-*tert*-butylpyridine analogs.

methanol as the eluant. Thus, *N*-glycosyl collidinium salts irreversibly consume a portion of the glycosyl halide, reducing the yield of disaccharide in glycosylation reactions. These results lead to the conclusion that the use of collidine, in place of pyridine, as a base in *O*-glycoside synthesis simply slows down, but does not stop, other competing condensations. The slowing of *N*-glycosyl compound formation enables reactive hydroxy components to attack the glycosyl halide faster than collidine. With unreactive hydroxy components considerable amounts of *N*-glycosyl collidinium salts may be formed. This undesired side reaction is completely suppressed when 2,6-di-*tert*-butylpyridine is used instead of collidine. At normal pressure 51% of the disaccharide mixture **11**/**12** is formed, whereas at 15 kbar the yield is somewhat lower. A similar decrease in yield was already observed by Kochetkov[9].

The data reported herein show that high pressure has a positive influence on the chemical yield of the glycosylation reaction of unreactive alcohols. Very little effect is seen in disaccharide formation, but the yield of the orthoester condensation product greatly increases. The formation of *N*-glycosyl collidinium salts in silver triflate–collidine-activated reactions was found to be an important side reaction when orthoester formation is prevented.

EXPERIMENTAL

General methods. — Melting points were taken in Pyrex capillaries and are uncorrected. Optical rotations were determined with a Perkin–Elmer 241 polarimeter. ^{1}H-n.m.r. data were recorded on UCB-200 (200 MHz), UCB-250 (250 MHz), and Bruker WM-500 (500 MHz) instruments, with tetramethylsilane as internal standard. Flash chromatography was performed on Silica Gel 60 (0.015–0.040 mm, Merck) and t.l.c. was performed on Silica Gel 60 F_{254} (Merck). Elemental analyses were performed

by the Microanalytical Laboratory and mass spectral analyses were obtained from the Mass Spectrometry Facility, both operated by the College of Chemistry, University of California, Berkeley, CA.

1-tert-*Butylcyclohexanol* (**2b**)[14,20]. — To a stirred solution of cyclohexanone (2.0 mL, 1.93 mmol) in ether (20 mL) at −50° was added, dropwise, 1.7M *tert*-butyllithium in pentane (2.3 mL, 3.9 mmol). After 30 min the mixture was hydrolyzed with saturated NH_4Cl solution (20 mL), diluted with ether (100 mL), washed with NH_4Cl solution (50 mL), and dried (Na_2SO_4). The solvent was evaporated and the residual syrup was molecularly distilled under reduced pressure to give 1.72 g (57%) of crystalline **2b**, m.p. 49–52°; lit.[14] 48%, m.p. 48–50°.

General procedure for glycosylation with acyl glycopyranosyl bromides. — A mixture of the hydroxy component [0.8 mmol of **2**, 0.4 mmol of **5** (ref. 21)], activator (0.8 mmol of tetraethylammonium bromide or silver triflate), 2,4,6-collidine (1.2 mmol), and freshly activated molecular sieves (3A) in dichloromethane (4 mL) was stirred for 5 min, the glycosyl halide [0.4 mmol of **1** (ref. 22) or **8** (refs. 23,24)] was added, and stirring was continued for 1 min. One half of the mixture was transferred into a Teflon tube and pressurized to 15 kbar for 2 days, while the other half was kept at ambient pressure for the same time without stirring. The reaction mixtures were diluted with dichloromethane, shaken with sodium chloride solution, filtered, washed twice with copper(II) sulfate solution, dried (Na_2SO_4), and evaporated to dryness. The products were separated by preparative flash chromatography on silica gel using 19:1:20 dichloromethane–ethyl acetate–hexane for **1** and 3:1 toluene–acetone for **8** as starting materials. The following compounds were isolated (for yields see Table I).

1,1-Diethylpropyl 2,3,4,6-tetra-O-*benzoyl-β*-D-*glucopyranoside* (**3a**), crystallized from ether–hexane, m.p. 153–154°, $[\alpha]_D^{20}$ +8.2° (*c* 1.1, $CHCl_3$); ^{1}H-n.m.r. (200 MHz, $CDCl_3$): δ 8.2–7.2 (m, 20 H, 4 C_6H_5), 5.92 (t, 1 H, H-3), 5.58 (t, 1 H, H-4), 5.55 (dd, 1 H, H-2), 5.02 (d, 1 H, H-1), 4.58 (dd, 1 H, H-6a), 4.47 (dd, 1 H, H-6b), 4.14 (ddd, 1 H, H-5), 1.48 [m, 6 H, (CH_3-CH_2)$_3$CO], and 0.71 [t, 9 H, (CH_3CH_2)$_3$CO]; $J_{1,2}$ 7.8, $J_{2,3}$ 9.7, $J_{3,4}$ 9.7, $J_{4,5}$ 9.7, $J_{5,6a}$ 3.1, $J_{5,6b}$ 6.4, $J_{6a,6b}$ 11.9, and J_{Et} 7.3 Hz.

Anal. Calc. for $C_{41}H_{42}O_{10}$ (694.79): C, 70.88; H, 6.09. Found: C, 70.90; H, 6.19.

1-tert-*Butylcyclohexyl 2,3,4,6-tetra*-O-*benzoyl-β*-D-*glucopyranoside* (**3b**), crystallized from dichloromethane–hexane, m.p. 129–131°, $[\alpha]_D^{20}$ +3.5° (*c* 2.3, $CHCl_3$); ^{1}H-n.m.r. (200 MHz, $CDCl_3$): δ 8.2–7.2 (m, 20 H, 4 C_6H_5), 5.93 (t, 1 H, H-3), 5.65 (dd, 1 H, H-2), 5.62 (t, 1 H, H-4), 5.18 (d, 1 H, H-1), 4.60 (dd, 1 H, H-6a), 4.49 (dd, 1 H, H-6b), 4.16 (ddd, 1 H, H-5), 1.7–1.0 [m, 10 H, (CH_2)$_5$], and 0.87 [s, 9 H, C(CH_3)$_3$]; $J_{1,2}$ 7.7, $J_{2,3}$ 9.8, $J_{3,4}$ 9.6, $J_{4,5}$ 9.9, $J_{5,6a}$ 3.1, $J_{5,6b}$ 5.8, and $J_{6a,6b}$ 12.0 Hz.

Anal. Calc. for $C_{44}H_{46}O_{10}$ (734.85): C, 71.92; H, 6.31. Found: C, 71.76; H, 6.22.

3,4,6-Tri-O-*benzoyl-α*-D-*glucopyranose 1,2-(1,1-diethylpropyl orthobenzoate)* (**4a**), syrup, $[\alpha]_D^{20}$ +50° (*c* 0.6, $CHCl_3$); ^{1}H-n.m.r. (200 MHz, $CDCl_3$): δ 8.2–7.2 (m, 20 H, 4 C_6H_5), 6.00 (d, 1 H, H-1), 5.68 (dd, 1 H, H-3), 5.41 (dd, 1 H, H-4), 4.81 (dd, 1 H, H-2), 4.49 (dd, 1 H, H-6a), 4.43 (dd, 1 H, H-6b), 4.05 (ddd, 1 H, H-5), 1.44 [m, 6 H, (CH_3CH_2)$_3$CO], and 0.76 [t, 9 H, (CH_3CH_2)$_3$CO]; $J_{1,2}$ 5.1, $J_{2,3}$ 3.0, $J_{2,4}$ 1.0, $J_{3,4}$ 1.4, $J_{4,5}$ 8.9, $J_{5,6a}$ 2.8, $J_{5,6b}$ 5.1, $J_{6a,6b}$ 12.1, and J_{Et} 7.3 Hz.

Anal. Calc. for $C_{41}H_{42}O_{10}$ (694.79): C, 70.88; H, 6.09. Found: C, 69.47; H, 5.58.

3,4,6-Tri-O-benzoyl-α-D-glucopyranose 1,2-[(benzyl 2-acetamido-3,6-di-O-acetyl-2,4-dideoxy-α-D-glucopyranosid-4-yl) orthobenzoate] (**6**), syrup, ^{1}H-n.m.r. (500 MHz, $CDCl_3$): δ 8.10–7.22 (m, 25 H, 5 C_6H_5), 6.03 (d, 1 H, H-1), 5.64 (d, 1 H, N*H*), 5.55 (m, 1 H, H-3), 5.31 (d, 1 H, H-4), 5.27 (t, 1 H, H-3'), 4.91 (m, 1 H, H-2), 4.82 (d, 1 H, H-1'), 4.62, 4.41 (2 d, 1 H each, PhCH_2), 4.44–4.36 (m, 1 H, H-6'a), 4.30–4.19 (m, 4 H, H-2, 6a,6b,6'b), 3.85–3.77 (m, 2 H, H-5,5'), 3.75 (t, 1 H, H-4'), 2.17, 2.03, and 1.87 (3 s, 3 H each, CH_3CO; $J_{1,2}$ 5.2, $J_{4,5}$ 9.0, $J_{1',2'}$ 3.3, $J_{2',NH}$ 10.0, $J_{2',3'}$ 9.7, $J_{3',4'}$ 9.5, and $J_{4',5'}$ 9.3 Hz*.

Benzyl 2-acetamido-3,6-di-O-acetyl-2-deoxy-2-N-(2,3,4,6-tetra-O-benzoyl-β-D-glucopyranosyl)-α-D-glucopyranoside (**7**), syrup, $[\alpha]_D^{20}$ +210° (*c* 0.9, $CHCl_3$); ^{1}H-n.m.r. (250 MHz, $CDCl_3$): δ 8.1–7.1 (m, 25 H, 5 C_6H_5), 6.32 (d, 1 H, H-1'), 5.98 (t, 1 H, H-3'), 5.84 (t, 1 H, H-4'), 5.67 (t, 1 H, H-2'), 5.34 (t, 1 H, H-3), 4.76, 4.54 (2 d, 1 H each, 2 PhCH_2), 4.69 (d, 1 H, H-1), 4.67 (dd, 1 H, H-6a), 4.50 (dd, 1 H, H-6'a), 4.40 (dd, 1 H, H-6'b), 4.25 (dd, 1 H, H-6b), 4.18 (m, 1 H, H-5), 3.78 (m, 1 H, H-5'), 3.57 (dt, 1 H, H-4), 3.52 (dd, 1 H, H-2), 2.89 (d, 1 H, O*H*), 2.14, 2.03, and 1.82 (3 s, 3 H each, CH_3CO); $J_{1,2}$ 3.6, $J_{2,3}$ 9.8, $J_{3,4}$ 9.6, $J_{4,OH}$ 5.5, $J_{4,5}$ 9.4, $J_{5,6a}$ 2.7, $J_{5,6b}$ 1.8, $J_{6a,6b}$ 12.2, J_{PhCH_2} 12.4, $J_{1',2'}$ 8.3, $J_{2',3'}$ 9.5, $J_{3',4'}$ 9.6, $J_{4',5'}$ 9.6, $J_{5',6'a}$ 4.3, $J_{5',6'b}$ 3.0, and $J_{6'a,6'b}$ 12.2 Hz; f.a.b.–m.s.: *m/z* 974 (MH^+).

Anal. Calc. for $C_{53}H_{51}NO_{17}$ (973.99): C, 65.36; H, 5.28; N, 1.44. Found: C, 66.44; H, 5.42; N, 1.27.

3,4,6-Tri-O-acetyl-α-D-galactopyranose 1,2-[(benzyl 2-acetamido-3,6-di-O-acetyl-2,4-dideoxy-α-D-glucopyranosid-4-yl) orthobenzoate] (**9**), syrup, ^{1}H-n.m.r. (200 MHz, $CDCl_3$): δ 7.4–7.1 (m, 5 H, C_6H_5), 5.77 (d, 1 H, H-1), 5.64 (d, 1 H, N*H*), 5.44 (t, 1 H, H-4), 5.14 (dd, 1 H, H-3'), 4.94 (dd, 1 H, H-3), 4.85 (d, 1 H, H-1'), 4.68, 4.45 (2 d, 1 H each, PhCH_2), 4.45–4.00 (m, 7 H, H-2,2',5,6a,6b,6'a,6'b), 3.86 (ddd, 1 H, H-5'), 3.72 (t, 1 H, H-4'), 2.14, 2.09, 2.04, 2.02, 2.00, 1.88 (6 s, 3 H each, CH_3CO), and 1.61 [s, 3 H, -O)$_3$CCH_3]; $J_{1,2}$ 4.4, $J_{2,3}$ 6.6, $J_{3,4}$ 2.9, $J_{4,5}$ 2.9, $J_{1',2'}$ 3.7, $J_{2',NH}$ 9.9, $J_{2',3'}$ 10.9, $J_{3',4'}$ 8.7, $J_{4',5'}$ 9.9, $J_{5',6'a}$ 3.8, $J_{5',6'b}$ 2.4, J_{PhCH_2} 11.8 Hz*.

General procedure for the reaction between **5** *and* **10**. — A mixture of **5** (0.7 mmol), activator (1.2 mmol of tetraethylammonium bromide or silver triflate), base (1.6 mmol of 2,4,6-collidine or 2,6-di-*tert*-butylpyridine), and freshly activated molecular sieves (3A) in dichloromethane (11.5 mL) was stirred for 5 min. A solution of **10** in dichloromethane (2 mL), freshly prepared from 2,3,4,6-tetra-*O*-benzyl-1-*p*-nitrobenzoyl-α-D-glucopyranose and hydrogen bromide[25], was added and stirring was continued for 1 min. A 4-mL portion of the mixture was transferred into a Teflon tube and pressurized to 15 kbar for 2 days, while the rest was kept at ambient pressure for the same time without stirring. The reaction mixtures were diluted with dichloromethane, shaken successively with sodium chloride and ammonium chloride solutions, dried (Na_2SO_4), and evaporated to dryness. The products were separated by preparative flash chromatography on silica gel, using 3:1 toluene–acetone as eluent for **11** and **12**, then switching to 5:1 chloroform–methanol. The combined disaccharide mixtures were separated by

* Satisfactory elemental analysis could not be obtained due to the extreme lability of compound. Rapid analysis of the concentrated chromatographic fraction indicated a purity of >95%.

h.p.l.c. with 9:4:3 toluene–hexane–acetone, with repetition for mixed fractions. The following compounds were isolated (for yields see Table II).

*Benzyl 2-acetamido-3,6-di-*O*-acetyl-2-deoxy-4-*O*-(2,3,4,6-tetra-*O*-benzyl-α-*D*-glucopyranosyl)-α-*D*-glucopyranoside* (**11**), syrup, $[\alpha]_D^{20}$ +63° (*c* 1, $CHCl_3$); ^{1}H-n.m.r. (500 MHz, $CDCl_3$): δ 7.40–7.04 (m, 25 H, 5 C_6H_5), 5.67 (d, 1 H, N*H*), 5.38 (ddd, 1 H, H-5′), 4.99 (d, 1 H, H-1′), 4.86 (d, 1 H, H-1), 4.85, 4.79 (2 d, 1 H each, PhCH_2-1), 4.80, 4.62 (2 d, 1 H each, PhCH_2-2), 4.70 (t, 2 H, PhCH_2-3), 4.58, 4.47 (2 d, 1 H each, PhCH_2-4), 4.49 (dd, 1 H, H-6a), 4.47–4.45 (m, 2 H, PhCH_2-5), 4.29 (dt, 1 H, H-2), 4.26 (dd, 1 H, H-6b), 3.93–3.89 (m, 2 H, H-3′,4′), 3.89 (t, 1 H, H-3), 3.75 (dt, 1 H, H-5), 3.68 (dd, 1 H, H-6′a), 3.65 (t, 1 H, H-4), 3.58 (dd, 1 H, H-6′b), 3.49 (dd, 1 H, H-2′), 2.02, 1.92, and 1.90 (3 s, 3 H each, CH_3CO); $J_{1,2}$ 3.7, $J_{2,NH}$ 9.7, $J_{2,3}$ 10.7, $J_{3,4}$ 9.6, $J_{4,5}$ 10.0, $J_{5,6a}$ ~1.5, $J_{5,6b}$ ~3.0, $J_{6a,6b}$ ~12.1, $J_{1',2'}$ 3.4, $J_{2',3'}$ 9.9, $J_{4',5'}$ 10.8, $J_{5',6'a}$ 5.1, $J_{5',6'b}$ 3.5, $J_{6'a,6'b}$ 10.6, $J_{PhCH_2\text{-}1}$ 10.8, $J_{PhCH_2\text{-}2}$ 11.5, $J_{PhCH_2\text{-}3}$ 11.8, and $J_{PhCH_2\text{-}4}$ 12.0 Hz.

Anal. Calc. for $C_{53}H_{59}NO_{13}$ (918.06): C, 69.34; H, 6.48; N, 1.53. Found: C, 69.51; H, 6.46; N, 1.54.

*Benzyl 2-acetamido-3,6-di-*O*-acetyl-2-deoxy-4-*O*-(2,3,4,6-tetra-*O*-benzyl-β-*D*-glucopyranosyl)-α-*D*-glucopyranoside* (**12**), syrup, $[\alpha]_D^{20}$ +62.9° (*c* 0.8, $CHCl_3$); ^{1}H-n.m.r. (500 MHz, $CDCl_3$): δ 7.40–7.04 (m, 25 H, 5 C_6H_5), 5.67 (d, 1 H, N*H*), 5.20 (ddd, 1 H, H-5′), 4.87 (d, 1 H, H-1′), 4.86 (d, 1 H, H-1), 4.79, 4.78 (2 d, 1 H each, PhCH_2-1), 4.76, 4.72 (2 d, 1 H each, PhCH_2-2), 4.68, 4.48 (2 d, 1 H each, PhCH_2-3), 4.51, 4.26 (2 d, 1 H each, PhCH_2-4), 4.50, 4.45 (2 d, 2 H each, PhCH_2-5), 4.34 (dd, 1 H, H-6a), 4.26 (dt, 1 H, H-2), 4.20 (dd, 1 H, H-6b), 3.79 (m, 2 H, H-3′,4′), 3.72 (m, 2 H, H-6′a,6′b), 3.66 (t, 1 H, H-3), 3.59 (t, 1 H, H-4), 3.36 (dt, 1 H, H-5), 3.34 (t, 1 H, H-2′), 2.02, 1.98, and 1.90 (3 s, 3 H each, CH_3CO); $J_{1,2}$ 3.8, $J_{2,NH}$ 9.6, $J_{2,3}$ 10.4, $J_{3,4}$ 9.0, $J_{4,5}$ 9.4, $J_{5,6a}$ ~1.5, $J_{5,6b}$ 3.2, $J_{6a,6b}$ 12.3, $J_{1',2'}$ 10.0, $J_{2',3'}$ 10.0, $J_{4',5'}$ 10.9, $J_{5',6'a}$ 5.1, $J_{5',6'b}$ 3.2, $J_{PhCH_2\text{-}1}$ 10.8, $J_{PhCH_2\text{-}2}$ 11.4, $J_{PhCH_2\text{-}3}$ 11.8, $J_{PhCH_2\text{-}4}$ 10.7, and $J_{PhCH_2\text{-}5}$ 11.8 Hz.

Anal. Calc. for $C_{53}H_{59}NO_{13}$ (918.06): C, 69.34; H, 6.48; N, 1.53. Found: C, 69.08; H, 6.39; N, 1.58.

*2,4,6-Trimethyl-1-(2,3,4,6-tetra-*O*-benzyl-α-*D*-glucopyranosyl)pyridinium chloride* (**13**), syrup, $[\alpha]_D^{20}$ +12.5° (*c* 0.8, $CHCl_3$); ^{1}H-n.m.r. (200 MHz, $CDCl_3$): δ 7.5–6.9 (m, 22 H, 4 C_6H_5 and $C_6H_2Me_3$), 6.47 (d, 1 H, H-1), 4.75, 4.67 (2 d, 1 H each, PhCH_2-1), 4.61, 4.46 (2 d, 1 H each, PhCH_2-2), 4.59, 4.32 (2 d, 1 H each, PhCH_2-3), 4.48, 4.36 (2 d, 1 H each, PhCH_2-4), 4.43–4.33 (m, 1 H, H-5), 4.26 (t, 1 H, H-2), 4.00 (t, 1 H, H-3), 3.90 (dd, 1 H, H-4), 3.69 (dd, 1 H, H-6a), 3.64 (dd, 1 H, H-6b), 2.71 (br. s, 6 H, 2 *ortho*-CH_3), and 2.52 (s, 3 H, *para*-CH_3); $J_{1,2}$ 3.1, $J_{2,3}$ 3.5, $J_{3,4}$ 5.0, $J_{4,5}$ 8.8, $J_{5,6a}$ 2.8, $J_{5,6b}$ 4.8, $J_{6a,6b}$ 11.1, $J_{PhCH_2\text{-}1}$ 11.5, $J_{PhCH_2\text{-}2}$ 11.6, $J_{PhCH_2\text{-}3}$ 11.7, and $J_{PhCH_2\text{-}4}$ 11.6 Hz.

*2,4,6-Trimethyl-1-(2,3,4,6-tetra-*O*-benzyl-α-*D*-glucopyranosyl)pyridinium bromide* (**15**). The reaction mixture (see general procedure for **5** + **10**) was extracted only with copper(II) bromide solution (2 times), dried (Na_2SO_4), evaporated, and separated as described above to afford **15** as a syrup, $[\alpha]_D^{20}$ +7.6° (*c* 0.2, $CHCl_3$); ^{1}H-n.m.r. (200 MHz, $CDCl_3$): δ 7.5–6.9 (m, 22 H, 4 C_6H_5 and $C_6H_2Me_3$), 6.46 (d, 1 H, H-1), 4.80–4.25 (m, 9 H, 4 PhCH_2 and H-5), 4.21 (t, 1 H, H-2), 4.01 (t, 1 H, H-3), 3.91 (dd, 1 H, H-4), 3.69, 3.64 (AB, 2 H, H-6a,6b), 2.69 [br. s, 6 H, separating at −15° (500 MHz) into 2.89 and

2.47 (2 s, 3 H each, 2 *ortho*-CH_3)], and 2.51 (s, 3 H, *para*-CH_3); $J_{1,2}$ 3.0, $J_{2,3}$ 3.4, $J_{3,4}$ 5.0, $J_{4,5}$ 8.7, $J_{5,6a}$ 2.6, $J_{5,6b}$ 4.7, and $J_{6a,6b}$ 11.0 Hz; f.a.b.–m.s.: m/z 644 $(M - Br)^+$.

Anal. Calc. for $C_{42}H_{46}BrNO_5$ (724.75): C, 69.61; H, 6.40; Br, 11.03; N, 1.93. Found: C, 60.87; H, 5.57; Br, 11.42; N, 1.75.

ACKNOWLEDGMENT

This research was supported by National Science Foundation Grant No. 8618303.

REFERENCES

1 K. Krohn, *Nachr. Chem. Tech. Lab.*, 35 (1987) 930–935, and literature there cited.
2 T. Okuyama, *Tohoku J. Exp. Med.*, 68 (1958) 313–317; *Chem. Abstr.*, 54 (1960) 6562e.
3 P. Sinaÿ, *Pure Appl. Chem.*, 50 (1978) 1437–1452.
4 K. L. Matta, R. H. Shah, and O. P. Bahl, *Carbohydr. Res.*, 77 (1979) 255–261.
5 K. Heyns, K. Propp, R. Harrison, and H. Paulsen, *Chem. Ber.*, 100 (1967) 2655–2663.
6 M. Shaban and R. W. Jeanloz, *Carbohydr. Res.*, 20 (1971) 17–22.
7 K. Matsumoto, A. Sera, and T. Uchida, *Synthesis*, (1985) 1–26; K. Matsumoto and A. Sera, *ibid*, 999–1027.
8 N. K. Kochetkov, V. M. Zhulin, E. M. Klimov, N. N. Malysheva, Z. G. Makarova, and A. Ya. Ott, *Carbohydr. Res.*, 164 (1987) 241–254; b) V. M. Zhulin, F. M. Klimov, Z. G. Makarova, A. Ya. Ott, and N. K. Kochetkov, *Dokl. Akad. Nauk SSSR*, 294 (1985) 881–883.
9 N. K. Kochetkov, V. M. Zhulin, E. M. Klimov, N. N. Malysheva, and Z. G. Makarova, *Carbohydr. Res.*, 167 (1987) c8–c10.
10 M. Shaban and R. W. Jeanloz, *Carbohydr. Res.*, 17 (1971) 193–198.
11 E. S. Rachaman and R. W. Jeanloz, *Carbohydr. Res.*, 10 (1969) 435–439.
12 M. Shaban and R. W. Jeanloz, *Carbohydr. Res.*, 19 (1971) 311–318; 26 (1973) 315–322.
13 R. U. Lemieux and A. R. Morgan, *Can. J. Chem.*, 43 (1965) 2199–2204.
14 N. C. G. Campbell, J. R. P. Clarke, R. R. Hill, P. Oberhänsli, J. H. Parish, R. M. Southam, and M. C. Whiting, *J. Chem. Soc., B*, (1968) 349–354.
15 P. J. Garegg and T. Norberg, *Acta Chem. Scand., Ser. B*, 33 (1979) 116–118.
16 R. U. Lemieux and A. R. Morgan, *J. Am. Chem. Soc.*, 85 (1963) 1889–1890.
17 R. U. Lemieux and A. R. Morgan, *Can. J. Chem.*, 43 (1965) 2205–2213.
18 A. C. West and C. Schuerch, *J. Am. Chem. Soc.*, 95 (1973) 1333–1335.
19 F. J. Kronzer and C. Schuerch, *Carbohydr. Res.*, 33 (1974) 273–280.
20 P. D. Bartlett and A. Schneider, *J. Am. Chem. Soc.*, 67 (1945) 141–144.
21 M. Dejter-Juszynski and H. M. Flowers, *Carbohydr. Res.*, 18 (1971) 219–226.
22 H. G. Fletcher, Jr., *Methods Carbohydr. Chem.*, 2 (1963) 226–228.
23 C. E. Redemann and C. Niemann, *Org. Synth., Coll. Vol. III*, (1955) 11–14.
24 R. W. Jeanloz and P. J. Stoffyn, *Methods Carbohydr. Chem.*, 1 (1962) 221–227.
25 H. H. Baer, J. M. J. Fréchet, and U. Williams, *Can. J. Chem.*, 52 (1974) 3337–3342.