

Bromination of Alkenyl Glycosides with Copper(II) Bromide and Lithium Bromide: Synthesis, Mechanism, and DFT Calculations

Robert Rodebaugh,[†] John S. Debenham,[†]
Bert Fraser-Reid,^{*,‡} and James P. Snyder^{*,§}

Paul M. Gross Chemical Laboratory, Duke University, Durham, North Carolina 27708, Natural Products and Glycotechnology Research Institute, 4118 Swarthmore Road, Durham, North Carolina 27707, and Department of Chemistry, Emory University, Atlanta, Georgia 30322

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Since their discovery in our laboratories in 1988, *n*-pentenyl glycosides (NPGs),¹ e.g., **1**, have been explored as mechanistic probes for anomeric activation,^{2a} as donors or acceptors in oligosaccharide synthesis,^{2b} and as models for preparing novel protecting groups.^{2c} A valuable attribute of NPGs is their ability to serve both as an activating moiety on glycosyl donors for oligosaccharide couplings and as a protecting group for the anomeric center during other synthetic manipulations including glycosidation reactions. However, in order for an NPG to serve as a glycosyl acceptor during halonium-promoted couplings, the sugar must either be "disarmed", by electron-withdrawing groups such as esters³ (i.e., **1**, X = OCOR), or the terminal double bond must be dibrominated (e.g., **3**).⁴ Indeed, dibromination of the *n*-pentenyl double bond offers the capability of using even "armed" substrates as glycosyl acceptors. Dibromides can be considered latent NPGs, since the *n*-pentenyl group can be regenerated by reductive debromination.⁵ In this paper, we report the reagent combination CuBr₂/LiBr as a new method for the dibromination of NPGs. We also propose a mechanism to account for the transformation based on density functional theory (DFT) calculations.

The standard conditions (Br₂/Et₄NBr in CH₂Cl₂, at 0 °C) previously developed⁴ and successfully used with pentenyl mannosides (80–90% yields)⁶ give erratic results when applied to protected 2-amino-2-deoxy sugars. Normally, with the excess bromide ion from Et₄NBr, the bimolecular reaction leading to the dibromide **3** is able to overwhelm the intramolecular process, **2** → **4** → **5** → **6** (Scheme 1). However, in the case of phthaloyl-protected glucosamines, the C-1 hydrolysis product usually predominated. For our recent synthesis of the nodulation factor, NodRf-III (C18:1, MeFuc),⁷ which required large

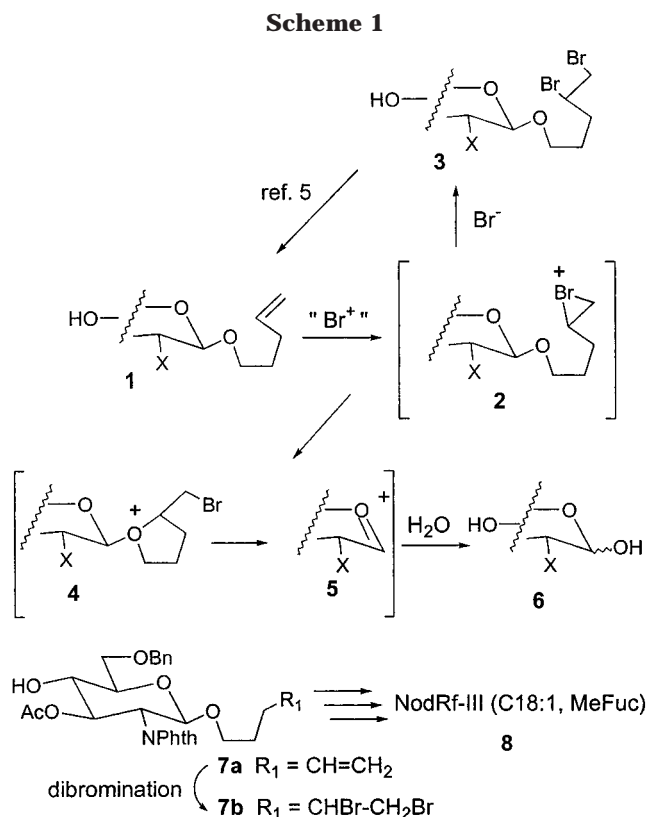


Table 1. Bromination with Various Reagents

Substrate	Conditions	Yield %
 9	Br ₂	10
	Br ₂ /Et ₄ NBr	20
	NBS/Et ₄ NBr	85
	CuBr ₂ /LiBr	99

amounts of dibromide **7b**, an alternative method of dibromination was needed.

On the assumption that these results were associated with the phthalimide residue, we investigated different dibromination protocols using the perbenzylated NPG **9** as a model (Table 1). Treatment of **9** with Br₂ in CH₂Cl₂ at 0 °C produced the desired dibromide **10** in only 10% yield. Addition of excess bromide ion by way of Et₄NBr increased the yield of **10** to only 20%. Again, the major product of both reactions was the known hemiacetal⁸ produced from oxidative hydrolysis of the *n*-pentenyl

[†] Duke University.

[‡] Natural Products and Glycotechnology Research Institute.

[§] Emory University.

(1) (a) Fraser-Reid, B.; Udodong, U. E.; Wu, Z.; Ottosson, H.; Merritt, J. R.; Rao, C. S.; Roberts, C.; Madsen, R. *Synlett* **1992**, 927–942. (b) Madsen, R.; Fraser-Reid, B. In *Modern Methods in Carbohydrate Synthesis*; Khan, S. H., O'Neill, R. A., Eds.; Harwood Academic Publishers: Amsterdam, **1996**; Chapter 4.

(2) See, for example: (a) Andrews, C. W.; Rodebaugh, R.; Fraser-Reid, B. *J. Org. Chem.* **1996**, *61*, 5280–5289. (b) Arasappan, A.; Fraser-Reid, B. *J. Org. Chem.* **1996**, *61*, 2401–2406. (c) Madsen, R.; Fraser-Reid, B. *J. Chem. Soc., Chem. Commun.* **1994**, 749.

(3) Mootoo, D. R.; Knoradsson, P.; Udodong, U.; Fraser-Reid, B. *J. Am. Chem. Soc.* **1988**, *110*, 5583–5584.

(4) Fraser-Reid, B.; Wu, Z.; Udodong, U. E.; Ottosson, H. *J. Org. Chem.* **1990**, *55*, 6068–6070.

(5) Merritt, J. R.; Debenham, J. S.; Fraser-Reid, B. *J. Carbohydr. Chem.* **1996**, *15*, 65–72.

(6) Merritt, J. R.; Naisang, E.; Fraser-Reid, B. *J. Org. Chem.* **1994**, *59*, 443–4449.

(7) (a) Debenham, J. S.; Rodebaugh, R.; Fraser-Reid, B. *J. Org. Chem.* **1996**, *61*, 6478–6479. (b) Debenham, J. S.; Rodebaugh, R.; Fraser-Reid, B. *J. Org. Chem.* **1997**, *62*, 4591–4600.

(8) Yamazaki, F.; Kitajima, T.; Nukada, T.; Ito, Y.; Ogawa, T. *Carbohydr. Res.* **1990**, *201*, 15–30.

Table 2. CuBr₂/LiBr Bromination of Sugars^a

Substrate	Compd.	R ₂	Yield %
	7	Ac	99
	11	Bn	99
a R ₁ = CH=CH ₂ b R ₁ = CHBr-CH ₂ Br			
	12	--	98
a R = CH=CH ₂ b R = CHBr-CH ₂ Br			
	13	Ac	99
	14	Bn	99
a R ₁ = CH=CH ₂ b R ₁ = CHBr-CH ₂ Br			
	15	--	97
a R = CH=CH ₂ b R = CHBr-CH ₂ Br			
	16	--	85
a R = CH=CH ₂ b R = CHBr-CH ₂ Br			

^aReagents and conditions: (a) CuBr₂ (5 eq.), LiBr (10 eq.), MeCN : THF (3:1); (b) As in (a) except THF only was used as solvent.

group. Yields of **10** increased dramatically to 85% by use of a mixture of *N*-bromosuccinimide and Et₄NBr; however, even more impressive was the near-quantitative result received upon treatment of **9** with CuBr₂ and LiBr at room temperature.

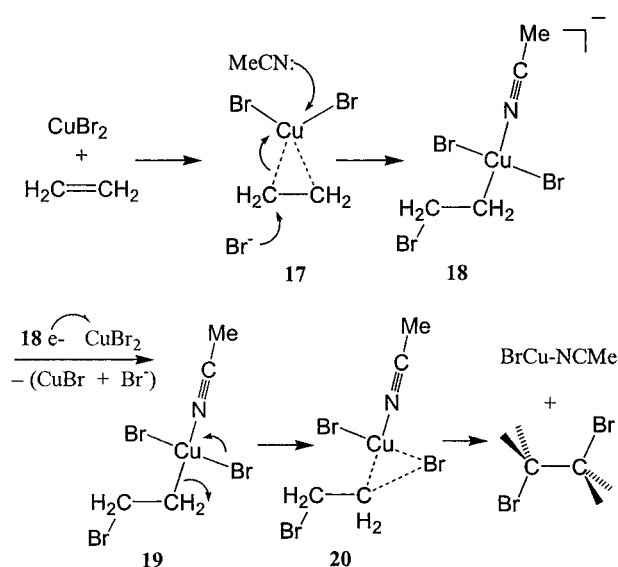
It is important to note that LiBr is necessary for this reaction to proceed in a near-quantitative fashion. Thus, although CuBr₂ alone has been used previously as a reagent for the dibromination of simple alkenes,⁹ exclusion of LiBr resulted in substantial hemiacetal production (45% yield). To our knowledge, the CuBr₂/LiBr reagent combination has not been previously used for the specific purpose of dibromination of olefins.¹⁰

With CuBr₂ and LiBr as our preferred dibromination method, we examined the halogenation of additional alkenyl glycosides (Table 2). In general, the dibromides were produced virtually quantitatively. Phthalimide derivatives **7a** and **11a** as well as tetrachlorophthalimide (TCP)⁷ substrates **12a**, **13a**, and **14a** gave the desired products (**7b**, **11b**–**14b**) in high yields. Similarly, dibromination of *n*-pentenyl mannoside **15a** gave **15b**.⁶ It is noteworthy that protecting groups such as *O*-benzyl, *O*-*p*-methoxybenzyl, *O*-acetyl, *N*-phthaloyl, and TCP are not affected by these mild reaction conditions.

(9) (a) Castro, C. E.; Gaughan, E. J.; Owsley, D. C. *J. Org. Chem.* **1965**, *30*, 587–592. (b) Baird, W. C., Jr.; Surridge, J. H.; Buza, M. *J. Org. Chem.* **1971**, *36*, 3324–3330.

(10) For aromatization of cyclohexenones using CuBr₂/LiBr, see: (a) Kosower, E. M.; Wu, G.-S. *J. Org. Chem.* **1963**, *28*, 633–638. (b) Bondon, D.; Pietrasanta, Y.; Pucci, B. *Tetrahedron Lett.* **1977**, 821–824. (c) Bennetau, B.; Rajarison, F.; Dunogues, J. *Tetrahedron* **1994**, *50*, 1179–1188.

Scheme 2



Of special interest to us was the *N*-pentenyl glucosaminide derivative **16a**. Previous work in our laboratories¹¹ had shown that the *N*-pentenyl group underwent halonium activation and subsequent cleavage more readily than the *n*-pentenyl moiety. For **16a**, dibromination was therefore expected to be more difficult than for the pentenyl glycosides in Table 2. However, **16a** was successfully dibrominated for the first time, yielding dibromide **16b** in 85% yield.¹²

To account mechanistically for the surprisingly smooth and quantitative bromination of alkenyl sugars, the success of CuBr₂/LiBr needs to be measured against the failure of Br₂, which suggests that the process is not an ordinary electrophilic addition. A mechanism that accommodates the difference and accounts for other factors is outlined in Scheme 2. In the first step, a paramagnetic π -complex, **17**, is formed from cupric(II) bromide and the olefin. X-ray crystal structures of many such complexes are known.¹³ Bromide ion displaces the metal on carbon as a molecule of solvent coordinates at the metal to give the square planar Cu^{II}-anion **18**. The latter transfers an electron to Cu^{II}Br₂ to yield the neutral copper species **19**, Cu^IBr, and 1 equiv of bromide ion. Reductive elimination through the neutral transition state **20** provides the *trans*-dibromide and a second equivalent of Cu^IBr coordinated to solvent.

An issue that influences the energetics of Scheme 2 concerns our use of 5 and 10 equiv of CuBr₂ and LiBr in acetonitrile–THF, respectively, relative to a given concentration of alkenyl glycoside. Although it might be assumed that a large excess of CuBr₂ and Br⁻ is present in solution, the situation is more complex. Copper bromide is known to couple with halide ions both in water^{14,15} and acetonitrile^{15,16} to produce CuBr₄²⁻ and perhaps CuBr₃⁻. The existence of CuBr₄²⁻ in the solid

(11) Madsen, R.; Roberts, C.; Fraser-Reid, B. *J. Org. Chem.* **1995**, *60*, 7920–7926.

(12) A significant improvement in the yield of the desired dibromide was obtained by using only THF as the solvent in this case.

(13) Cambridge Structural Database; <http://www.ccdc.cam.ac.uk/prods/csd.html>.

(14) Matsuo, S. *J. Chem. Soc. Jpn. (Nippon Kagaku Zasshi)* **1961**, *82*, 1330–1334, 1334–1337.

(15) Barnes, J. C.; Hume, D. N. *Inorg. Chem.* **1963**, *2*, 444–448.

(16) Furlani, C.; Morpurgo, G. *Theor. Chim. Acta (Berlin)* **1963**, *1*, 102–115.

state is amply underscored by numerous single-crystal X-ray structures.¹⁷ The salts are usually prepared by treating cupric bromide with excess HBr in various solvents in the presence of a suitable cation. Structures of a variety of higher Cu/Br aggregates have been derived in a similar manner.¹⁸ In acetonitrile, electronic spectra suggest that solvent can compete with bromide, leading to the presence of dihalide species such as $\text{CuBr}_2\text{-(MeCN)}_2$.¹⁶ Lithium bromide likewise exhibits its own propensity for clustering. In THF near room temperature, the salt is a mixture of both monomeric contact ion pairs and higher aggregates.¹⁹ Finally, it is well-known that the cupric ion is capable of forming complexes with glycosides.²⁰ An additional complication in assessing the composition of the glycoside bromination medium is the autoxidation–reduction of cupric bromide at room temperature. In acetonitrile about 50% is reduced in 24 h.¹⁵ Clearly, under the present reaction conditions, copper and halide reagents as well as glycosides can interact and participate in a web of equilibria that depletes the effective concentration of $\text{CuBr}_2/\text{LiBr}$ in the brominating mixture. With the exception of the relatively slow reduction of CuBr_2 , however, we presume the equilibria to be reversible and to furnish the required entities in a facile and controlled fashion during the course of the reaction.

Each of the species in Scheme 2 has been subjected to geometry optimization with the Becke3LYP/LANL2DZ DFT protocol²¹ and, except for **20**, found to be a local minimum. Formation of complex **17** is calculated to be 10.7 kcal/mol exothermic as compared to 6.0 kcal/mol for the corresponding $\text{Br}_2/\text{CH}_2=\text{CH}_2$ complex. Optimized CuBr_4^{2-} is calculated to be 22.0 kcal/mol more stable than CuBr_2 and a pair of bromide ions (not shown in Scheme 2).²² If formation of CuBr_4^{2-} is taken as a rough measure of the diversion of $\text{CuBr}_2/\text{LiBr}$ from the first step in Scheme 2, then the latter is endothermic by ca. 11 kcal/mol. The implication is that the production of **17** may well correspond to the rate-determining step along the bromination pathway.²³ Despite the various equilibria in the reaction mixture, we believe the large available pool of CuBr_2 and LiBr used in Table 2 not only promotes the rapid second-order generation of **17** but also ensures its

equally rapid conversion to **18**.^{24,25} Any other soluble bromide source, such as Et_4Br , should work as well as LiBr in the reaction. Using a methyl model (i.e., $\text{BrCH}_2\text{-CH}_2=\text{CH}_3$), the formation of **19** by electron transfer from **18** to CuBr_2 has been estimated to release 39.4 kcal/mol. Finally, the calculated reductive elimination of **19** through transition state **20**²⁶ is a close analogue of the process modeled for the rate determining step of cuprate conjugate addition.²⁷ The resulting activation barrier of 7.5 kcal/mol is likewise very similar to that derived for the latter reaction.

In conclusion, the $\text{CuBr}_2/\text{LiBr}$ procedure provides quantitative access to the dibromides from alkenyl sugars that are resistant to straightforward reaction with molecular bromine. The combined mechanistic and DFT analysis accounts for the side-product-free result in the presence of excess $\text{CuBr}_2/\text{LiBr}$ by sketching an overall exothermic reaction pathway. In addition, the mechanism predicts that the dibromide is created with trans stereochemistry. The latter results from inversion in **17** and retention in **19/20**. Previous exposures of alkenes to CuBr_2 or CuCl_2 alone result in stereospecific trans addition.²⁸

Experimental Section

General Methods. General experimental procedures and information concerning the calculations can be found in refs 5 and 21, respectively.

General Procedures for Dibromination. *N*-Bromosuccinimide/ Et_4NBr . To *N*-bromosuccinimide (177.0 mg, 1.00 mmol, 5 equiv) and Et_4NBr (210.0 mg, 1.00 mmol, 5 equiv) in CH_2Cl_2 (1.4 mL) was added freshly activated, powdered 4 Å molecular sieves. The mixture was cooled to 0 °C. A solution of the pentenyl glycoside **9** (115.0 mg, 0.178 mmol) (azeotropically dried with toluene and vacuum-dried) in CH_2Cl_2 (1 mL) was added dropwise. The mixture was stirred for 18 h at room temperature, was diluted with CH_2Cl_2 (30 mL), was filtered through Celite, and was washed with 10% aqueous $\text{Na}_2\text{S}_2\text{O}_3$ (15 mL), H_2O (15 mL), and brine (15 mL). The organic phase was concentrated. The residue subjected to flash chromatography. Elution with 4:1 petroleum ether/ethyl acetate gave **10** (121.0 mg, 85%).

$\text{CuBr}_2/\text{LiBr}$. To CuBr_2 (5 equiv) and LiBr (10 equiv) in $\text{CH}_3\text{-CN/THF}$ (3:1) was cannulated the pentenyl glycoside in $\text{CH}_3\text{-CN/THF}$ (2:1) to make a 35 mM solution in terms of the alkene. The mixture was stirred for 16 h, was concentrated to 20% of its original volume, was diluted with EtOAc , and was washed with H_2O and brine. The aqueous portions were reextracted with EtOAc . The residue from the combined and evaporated organic phases was purified via flash chromatography by elution with petroleum ether/ EtOAc (4:1) to afford the dibromide.

4,5-Dibromopentanyl 3-*O*-acetyl-6-*O*-benzyl-2-deoxy-2-phthalimido- β -D-glucopyranoside (7b**):** 99% yield; R_f 0.36 (45:55 EtOAc /petroleum ether); $[\alpha]_D^{20}$ 13.0° ($c = 1.36$, CHCl_3); $^1\text{H NMR}$ (300 MHz, CDCl_3) δ 7.71–7.87 (m, 4H), 7.31–7.37 (m, 5H), 5.64 (dd, $J = 8.6, 10.4$ Hz, 1H), 5.37 (d, $J = 8.4$ Hz, 1H),

(17) (a) Roman, P.; Sertucha, J.; Luque, A.; Lezama, L.; Rojo, T. *Polyhedron* **1996**, *15*, 1253–1262. (b) Chen, L.; Thompson, L. K.; Bridson, J. N. *Inorg. Chim. Acta* **1996**, *244*, 87–93. (c) Willett, R.; Place, H.; Middleton, M. J. *Am. Chem. Soc.* **1988**, *110*, 8639–8650. (d) Massabni, A. C.; Nascimento, O. R.; Halvorson, K.; Willett, R. D. *Inorg. Chem.* **1992**, *31*, 1779–1784. (e) Mori, T.; Sakai, F.; Saito, G.; Inokuchi, K. *Acta Crystallogr., Sect. C* **1990**, *46*, 1603–1609. (f) Place, Willett, R. D. *Acta Crystallogr., Sect. C* **1988**, *44*, 34–38; **1987**, *43*, 1050–1053. (g) Fernandez, V.; Moran, M.; Gutierrez-Rios, M. T.; Foces-Foces, C.; Cano, F. H. *Inorg. Chim. Acta* **1987**, *128*, 239–243. (h) Trouelan, P.; Lefebvre, J.; Derollez, P. *Acta Crystallogr., Sect. C* **1984**, *40*, 386–389.

(18) (a) Savel'eva, Z. A.; Romanenko, G. V.; Podberezskaya, N. V.; Larionov, S. V. *Polyhedron* **1996**, *15*, 3581–3584. (b) Subramanian, L.; Hoffmann, R. *Inorg. Chem.* **1992**, *31*, 1021–1029. (c) Willett, R. D. *Coord. Chem. Rev.* **1991**, *109*, 181–205.

(19) (a) Reich, H. J.; Borst, J. P.; Dykstra, R. R.; Green, D. P. *J. Am. Chem. Soc.* **1993**, *115*, 8728–8741. (b) Menard, D.; Chabanel, M. *J. Phys. Chem.* **1975**, *79*, 1081–1085. (c) Turner, W. E. S.; Bissett, C. *J. Chem. Soc.* **1915**, *105*, 1777–1786.

(20) Piarulli, U.; Floriani, C. *Prog. Inorg. Chem.* **1997**, *45*, 400–403.

(21) For basis set details, see: Huang, H.; Alvarez, K.; Cui, Q.; Barnhart, T. M.; Snyder, J. P.; Penner-Hahn, J. E. *J. Am. Chem. Soc.* **1996**, *118*, 8808–8816.

(22) The predicted geometry of CuBr_4^{2-} is that of a flattened tetrahedron with Br–Cu–Br bond angles of 100.7, 101.3, 127.7, and 128.8°. The result is in accord with angular deformation of the carefully studied CuCl_4^{2-} anion, which exhibits many examples of Cl–Cu–Cl angles from 125 to 160°.^{18c}

(23) We appreciate the insights of a reviewer who drew our attention to the facile formation of CuBr_4^{2-} and the possibility that step one in Scheme 2 may be rate determining.

(24) Although CH_3CN solvent was utilized to coordinate the metal in the reaction pathway calculations, THF and other ethers can clearly serve the same purpose (ref 25); cf. **16** in Table 2.

(25) (a) Kingsbury, C. L.; Smith, R. A. *J. Org. Chem.* **1997**, *62*, 4629–4634. (b) Kingsbury, C. L.; Smith, R. A. *J. Org. Chem.* **1997**, *62*, 7637–7643.

(26) Verification that **20** is indeed a stationary point, located at the calculated saddle point between **19** and products, follows from the presence of a single imaginary frequency in the force constant matrix. The frequency in question corresponds to the formation of a bond between Br and CH_2 as shown in Scheme 2.

(27) (a) Snyder, J. P. *J. Am. Chem. Soc.* **1995**, *117*, 11025–11026. (b) Frantz, D. E.; Singleton, D. A.; Snyder, J. P. *J. Am. Chem. Soc.* **1997**, *119*, 3383–3384.

(28) Arganbright, R. P.; Yates, W. F. *J. Org. Chem.* **1962**, *27*, 1205–1208.

4.63 (dd, $J = 12.1, 18.1$ Hz, 2H), 4.23 (dd, $J = 8.5, 10.8$ Hz, 1H), 3.72–4.00 (m, 6H), 3.59–3.65 (m, 1H), 3.45–3.58 (m, 1H), 3.29–3.38 (m, 1H), 3.01 (d, $J = 2.9$ Hz, 1H), 1.93 (s, 3H), 1.92–1.22 (m, 1H), 1.56–1.66 (m, 3H); ^{13}C NMR (75 MHz, CDCl_3) δ 171.16, 168.88 (bs), 137.67, 134.18, 131.31, 128.37, 127.71, 127.60, 123.51, 97.91, 97.83, 74.38, 73.60, 73.43, 71.05, 69.94, 68.56, 68.51, 54.54, 52.36, 52.27, 36.10, 36.06, 32.71, 32.63, 26.94, 26.82, 20.60; MS (FAB) m/e 670.09 (MH^+).

4,5-Dibromopentanyl 3,4,6-tri-*O*-benzyl-2-deoxy-2-phthalimido- β -D-glucopyranoside (10): 99% yield; R_f 0.68 (75:25 petroleum ether/ethyl acetate); ^1H NMR (300 MHz) δ 7.61–7.82 (m, 4H), 7.18–7.41 (m, 10H), 6.80–7.14 (m, 5 H), 5.14 (d, $J = 8.4$ Hz, 1H), 4.83 (t, $J = 12.5$, 1H), 4.55–4.72 (m, 3H), 4.45 (d, $J = 12.1$ Hz, 1H), 4.32 (m, 1H), 4.15 (m, 1H), 3.71–3.97 (m, 4H), 3.52–3.66 (m, 3H), 3.23–3.47 (m, 2H), 1.87–2.03 (m, 1H), 1.41–1.76 (m, 3H); ^{13}C NMR (75 MHz) δ 168.12 (bs), 138.16, 138.00, 133.79, 128.47, 128.42, 128.08, 127.98, 127.90, 127.82, 127.67, 127.35, 123.35, 98.36, 98.28, 79.74, 79.34, 75.11, 75.01, 74.83, 73.56, 68.77, 68.41, 68.36, 55.91, 52.59, 52.48, 36.27, 32.93, 32.85, 27.08, 26.97; MS (FAB) m/e 814.14 ($\text{M} + \text{Li}^+$).

4,5-Dibromopentanyl 3,4,6-tri-*O*-acetyl-2-deoxy-2-tetrachlorophthalimido- β -D-glucopyranoside (12b): 98% yield; R_f 0.59 (70:30 petroleum ether/ethyl acetate); ^1H NMR (400 MHz) δ 5.66–5.70 (m, 1H), 5.34 (d, $J = 8.3$ Hz, 1H), 5.19 (t, $J = 10.2$ Hz, 1H), 4.82–4.90 (m, 2H), 4.14–4.36 (m, 3H), 3.79–3.85 (m, 2H), 3.42–3.55 (m, 2H), 2.11 (s, 3H), 2.04 (s, 3H), 1.90 (s, 3H), 1.90–2.01 (m, 1H), 1.50–1.72 (m, 3H); ^{13}C NMR (100 MHz) δ 170.46, 170.39, 169.10, 163.30, 162.46, 140.37, 137.42, 129.78, 126.75, 71.66, 70.76, 69.18, 68.50, 61.89, 55.45, 36.17, 36.15, 32.78, 32.72, 26.89, 26.76, 20.61, 20.45, 20.36; MS (FAB) m/e 800.92 (M^-).

Anal. Calcd for $\text{C}_{25}\text{H}_{25}\text{NO}_{10}\text{Br}_2\text{Cl}_4$: C, 37.48; H, 3.15; N, 1.75. Found: C, 37.19; H, 3.20; N 1.79.

4,5-Dibromopentanyl 3-*O*-acetyl-6-*O*-benzyl-2-deoxy-2-tetrachlorophthalimido- β -D-glucopyranoside (13b): 99% yield; R_f 0.69 (65:35 petroleum ether/ethyl acetate); $[\alpha]_D^{25} -4.4^\circ$ ($c = 1.00$, CHCl_3); ^1H NMR (500 MHz) δ 7.30–7.39 (m, 5H), 5.53 (dt, $J = 8.9, 10.6$ Hz, 1H), 5.33 (d, $J = 8.4$ Hz, 1H), 4.65 (dd, $J = 11.9, 31.1$ Hz, 2H), 4.19–4.24 (m, 1H), 4.02–4.05 (m, 1H), 3.66–3.88 (m, 6H), 3.44–3.50 (m, 2H), 2.94 (d, $J = 3.4$ Hz, 1H), 2.05–2.09 (m, 1H), 1.97 (s, 3H), 1.60–1.77 (m, 3H); ^{13}C NMR

(125 MHz) δ 171.36, 140.50, 137.47, 129.91, 128.47, 127.99, 127.73, 126.99, 97.65, 97.62, 74.01, 73.75, 73.53, 71.11, 69.90, 68.62, 68.59, 55.32, 52.21, 36.21, 36.11, 32.76, 32.72, 26.98, 26.86, 20.70; MS (FAB) m/e 806.7 (M^-).

Anal. Calcd for $\text{C}_{28}\text{H}_{27}\text{NO}_8\text{Br}_2\text{Cl}_4$: C, 41.67; H, 3.37. Found: C, 41.75; H, 3.41.

4,5-Dibromopentanyl 3,6-di-*O*-benzyl-2-deoxy-2-tetrachlorophthalimido- β -D-glucopyranoside (14b): 99% yield; R_f 0.51 (70:30 petroleum ether/ethyl acetate); ^1H NMR (400 MHz) δ 7.30–7.40 (m, 5H), 6.75–7.07 (m, 5H), 5.09 (d, $J = 8.2$ Hz, 1H), 4.85 (d, $J = 13$ Hz, 1H), 4.61 (dd, $J = 12.0$ Hz, 27.3 Hz, 2H), 4.42 (d, $J = 13$ Hz, 1H), 3.96–4.14 (m, 3H), 3.76–3.86 (m, 6H), 3.36–3.45 (m, 2H), 3.04 (bs, 1H), 1.97–2.04 (m, 1H), 1.51–1.72 (m, 3H); ^{13}C NMR (100 MHz) δ 163.38, 162.46, 139.68, 138.63, 137.42, 128.56, 128.04, 128.00, 127.95, 127.84, 126.92, 97.89, 79.37, 75.00, 74.72, 73.83, 70.61, 68.37, 68.30, 55.95, 55.94, 52.29, 36.25, 36.17, 32.78, 32.72, 26.97, 26.85; MS (FAB) m/e 854.9 (M^-).

***p*-Methoxybenzyl 3,4,6-tri-*O*-acetyl-2-deoxy-(4,5-dibromopentanoxyamino)- β -D-glucopyranoside (16b):** 85%; R_f 0.52 (3:1 ethyl acetate/petroleum ether); ^1H NMR (300 MHz) δ 7.20–7.25 (m, 2H), 6.85–6.90 (m, 2H), 5.40 (dd, $J = 8.7, 19.5$ Hz, 1H), 5.22 (dd, $J = 10.6, 21.6$ Hz, 1H), 5.08 (t, $J = 9.4$ Hz, 1H), 4.82 (dd, $J = 3.5, 11.5$ Hz, 1H), 4.63 (dd, $J = 8.4, 21.6$ Hz, 1H), 4.28 (dd, $J = 3.5, 11.8, 1H$), 4.10–4.31 (m, 3H), 3.89–3.94 (m, 1H), 3.79 (s, 3H), 3.50–3.71 (m, 3H), 2.43–2.55 (m, 1H), 2.20–2.35 (m, 2H), 2.11 (s, 3H), 2.05 (s, 3H), 2.02 (s, 3H), 1.82–1.97 (m, 1H); ^{13}C NMR (75 MHz) δ 172.31, 170.65, 170.60, 169.21, 159.4, 129.76, 128.71, 99.50, 72.60, 71.91, 70.25, 68.61, 62.20, 55.25, 54.35, 54.60, 36.78, 36.64, 30.62, 30.21, 20.80, 20.72, 20.61; MS (FAB) m/e 668.05 ($\text{M} + \text{H}^+$).

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Supporting Information Available: Copies of the ^1H NMR for compounds **7b**, **10**, **14b**, and **16b**. Copies of the ^{13}C NMR for compounds **7b**, **10**, and **14b**. This material is available free of charge via the Internet at <http://pubs.acs.org>.

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