CHEMISTRY
A EUROPEAN JOURNAL

DOI: 10.1002/chem.200600290

A Facile Method for Oxidation of Primary Alcohols to Carboxylic Acids and Its Application in Glycosaminoglycan Syntheses

Lijun Huang, Nardos Teumelsan, and Xuefei Huang*[a]

Dedicated to Prof. Koji Nakanishi on the occasion of his 80th birthday

Abstract: A convenient two-step, one-pot procedure was developed for the conversion of primary alcohols to carboxylic acids. The alcohol was first treated with NaOCl and TEMPO under phase-transfer conditions, followed by $NaClO_2$ oxidation in one pot. This reaction is applicable to a wide range of alcohols and the mild reaction conditions are compatible with many sensitive functional groups, including electron-rich aromatic rings, acid-labile isopropylidene ketal and glycosidic linkages, and oxidation-prone thioacetal, *p*-methoxybenzyl, and allyl moieties. Several glycosaminoglycans such as heparin, chondroitin, and hyaluronic acid oligosaccharides have been synthesized in high yields by using this new oxidation protocol.

Keywords: carbohydrates · glycosaminoglycan · oxidation · synthetic methods

Introduction

Oxidation of primary alcohols to carboxylic acids is a fundamental transformation in organic synthesis, albeit with relatively few good general methods available.[1] This is particular the case for assembly of complex oligosaccharides such as glycosaminoglycans (GAGs). The existence of a large number of protective groups for selective GAG functionalization in addition to the acid lability of glycosidic linkages, severely limits available methodologies due to cross-reactivity. Furthermore, in GAG synthesis, the need to simultaneously convert multiple primary alcohols to carboxylic acids demands a robust and high-yielding method. Herein, we report a new convenient two-step, one-pot protocol for oxidizing primary alcohols to carboxylic acids and its application.

GAGs are a family of highly functionalized, linear and negatively charged oligosaccharides, consisting of repeating disaccharide units of a 2-deoxy-2-amino hexose linked to a pyranosyl uronic acid.[2] Depending upon the identity of the amino sugars and uronic acids, the GAG family can be divided to hyaluronic acid, heparin/heparan sulfate, chondroitin/chondroitin sulfate, and dermatan. GAGs play diverse and critical roles in many important biological processes such as lymphocyte trafficking, inflammatory response, wound healing, and tumor metastasis.[3] Biomedical applications of GAGs in areas such as antiviral, anti-angiogenesis, and anticoagulation are enormous, exemplified by the development of Arixtra, a fully synthetic heparin pentasaccharide drug, for the treatment of deep vein thrombosis.[4]

With the recognition of their biological importance, chemical syntheses of GAGs are undergoing extensive studies;[2,5] such syntheses are typically carried out following two general approaches. In the first method, protected pyranosyl uronic acids are directly utilized. However, with the strongly electron-withdrawing 6-carboxyl moiety, these building blocks often have low reactivities both as donors and as acceptors, resulting in low glycosylation yields. Furthermore, base sensitivity of these compounds conferred by the carboxyl group complicates protective group manipulations.[6,7] These limitations also preclude the direct usage of uronic acids in solid-phase oligosaccharide syntheses.[8] An attractive alternative is to use pyranosides as building blocks, which can give high glycosylation yields. With this strategy, one of the key challenges is the need to convert primary hydroxyl groups at C-6 positions into carboxylic acids post glyco-assembly. The traditional pyridinium dichromate (PDC) mediated oxidation,[9–11] was found to be inefficient;

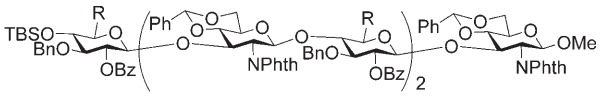
[a] Dr. L. Huang, N. Teumelsan, Prof. X. Huang
Department of Chemistry, The University of Toledo
2801 W. Bancroft St. MS 602, Toledo, OH 43606 (USA)
Fax: (+1) 419-530-4033
E-mail: xuefei.huang@utoledo.edu

Supporting information (copies of ^1H NMR and ^{13}C NMR spectra) for this article is available on the WWW under http://www.chemeurj.org/ or from the author.

it often required large excess of PDC subsequently resulting in separation difficulties and low yields.[6,9] Two-step protocols, such as Swern oxidation followed by treatment of $NaClO_2$ or PDC,[7,12] not only are inconvenient, but also can produce elimination side products due to the strongly basic condition utilized.[6,7] Besides the undesirable usage of toxic chromium(VI) agents, Jones oxidation[13] and the combination of chromium trioxide and periodic acid[6] are less useful in oligosaccharide synthesis with the employment of strong acids. Recently, TEMPO (2,2,6,6-tetramethylpiperidinyl-1-oxy)-catalyzed oxidations with a co-oxidant (e.g. NaOCl[14–16] and bis(acetoxy)iodobenzene (BAIB)[17,18]) have become a popular choice. However, substantial side reactions with thioacetal,[13] allyl[9] and electron-rich aromatic rings such as methoxybenzyl[19] moieties have been reported. Moreover, reduced oxidation efficiencies were observed with large oligosaccharides.[15]

Results and Discussion

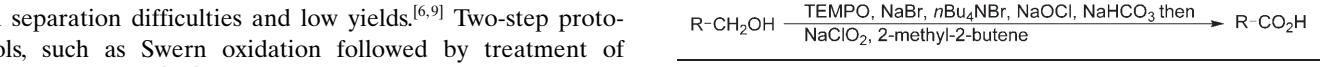
During our study of GAG synthesis, we were faced with the task of oxidation state adjustment of hexasaccharide **1**. Despite prolonged reaction time and repeated trials, the reaction of **1** with TEMPO/NaOCl[14–16] led to multiple partially oxidized products with a trace amount of the desired tricarboxylic acid **2**. Attempts with TEMPO/BAIB[18] or $NaClO_2$ catalyzed by NaOCl/TEMPO[19] met with similar fate. A two-step process of Dess–Martin oxidation followed by $NaClO_2$[20] gave inconsistent results. Finally, we discovered that a convenient two-step, one-pot protocol with TEMPO/NaOCl followed by treatment of $NaClO_2$ afforded the desired carboxylic acid in high yield and good purity; this result led us to further explore the scope of this method.

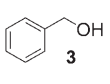
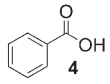
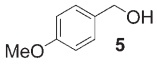
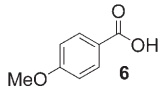
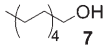
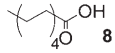
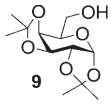
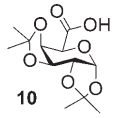
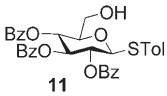
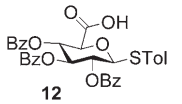
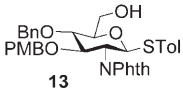
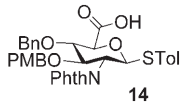
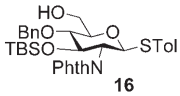
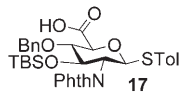
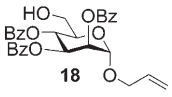
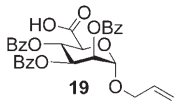
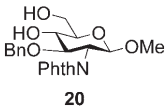
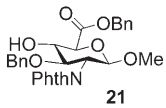
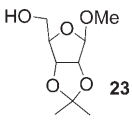
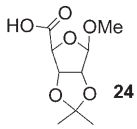


1: R = CH_2OH
2: R = CO_2H

A panel of primary alcohols and monosaccharides (Table 1) were examined first to test the functional group compatibility. Simple benzylic alcohols (Table 1, entries 1,2) including the electron-rich *p*-methoxy benzyl alcohol (**5**; Table 1, entry 2) can be oxidized in high yields without chlorinating the aromatic rings. Aliphatic alcohol 1-decanol (**7**; Table 1, entry 3) was converted in 90% yield to decanoic acid (**8**). Pyranosyl uronic acids such as glucoronic acid, galactonic acid, and mannosinic acid often exist in oligosaccharides and selectively protected uronic acids are useful for carbohydrate synthesis.[11,18] Conversion of the free primary hydroxyl groups in galactoside **9**, glucoside **11**,[21] 2-deoxy-2-amino-glucoside derivatives **13** and **16**, and mannoside **18**[22] to the corresponding uronic acids proceeded smoothly in

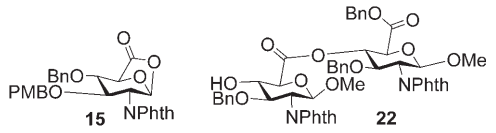
Table 1. Oxidation of primary alcohols and monosaccharides.



	Alcohol	Carboxylic acids/esters	Yield [%]
1	 **3**	 **4**	100
2	 **5**	 **6**	95
3	 **7**	 **8**	90
4	 **9**	 **10**	90
5	 **11**	 **12**	82
6	 **13**	 **14**	85
7	 **16**	 **17**	86
8	 **18**	 **19**	92
9	 **20**	 **21**	75[a]
10	 **23**	 **24**	100

[a] Ester **22** (10%) was isolated from the reaction mixture.

82–92% yields (Table 1, entries 4–8). Acid-sensitive isopropylidene and *p*-methoxybenzyl (PMB) groups were stable under reaction conditions (Table 1, entries 4 and 6). Thioglycosides have been extensively used in oligosaccharide assembly.[18,23] The presence of thioacetal in thioglycosides precludes the usage of noble-metal oxidation conditions, such as PtO_2 and O_2.[13] Previous attempts of TEMPO/NaOCl oxidation of thioglycosides generated a mixture of sulfoxides and sulfones in preference to alcohol oxidation.[13] By using our reaction protocol, both disarmed (compound **11**) and armed (compounds **13** and **16**) thioglycosides were oxidized in 82, 85, and 86% yields respectively (Table 1, entries 5–7). No glycosyl sulfoxides or sulfones were identified from these reactions, with trace amount (~6%) of lactone **15** isolated from oxidation of thioglycoside **13**. The allyl group, which is a popular linker for the bioconjugation of carbohydrates with proteins,[24] remained intact following oxidation of mannosyl pyranoside **18**[22] (Table 1, entry 8). A primary



alcohol can be selectively converted to a carboxylic acid in the presence of a free secondary hydroxyl group as **21** was obtained in 75% yield following oxidation of diol **20**[25] and benzyl ester formation[26] with phenyl diazomethane[27] (Table 1, entry 9). A small amount (~10%) of ester **22** was also isolated from the reaction mixture. In addition to pyranosides, furanoside **23**[28] was successfully transformed into carboxylic acid **24** in quantitative yield (Table 1, entry 10).

Next we examined the application of this new protocol in GAG syntheses. A hyaluronic acid disaccharide **26** was obtained in 95% yield by oxidizing disaccharide **25**[29] (Table 2, entry 1). The oxidation was highly efficient even for large oligosaccharides, converting the tetrasaccharide **28**[29] and hexasaccharide **1**[29] to oligocarboxylic acids, which were subsequently benzylated[26] with phenyl diazomethane[27] to produce hyaluronic acid tetrasaccharide diester **29** and hexasaccharide triester **30** in 86 and 82% overall yields, respectively (Table 2, entries 2 and 3). Trisaccharide **31**[29] was also oxidized and benzylated to produce chondroitin trisaccharide **32** in 76% yield (Table 2, entry 4). In addition, a heparin trisaccharide **34** was obtained in a similar manner in 81% yield from diol **33**[29] (Table 2, entry 5). Glycosidic linkages were not affected during oxidation and no epimerization or elimination products were identified with these sensitive

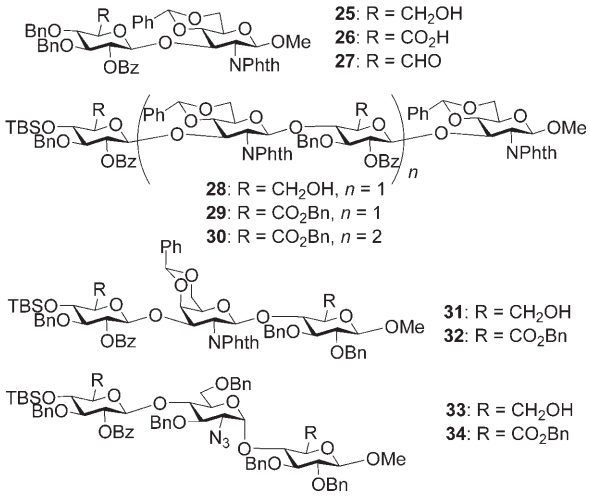
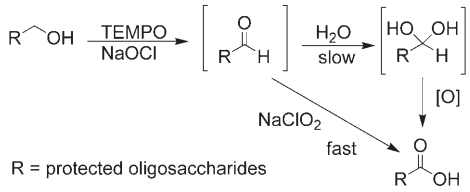


Table 2. Oxidation of primary alcohols for GAG synthesis.

	Alcohol	GAG derivative	Yield [%]
1	**25**	**26**	95
2	**28**	**29**	86
3	**1**	**30**	82
4	**31**	**32**	76
5	**33**	**34**	81

substrates. The successful introduction of carboxyl groups after glyco-assembly makes this alternative strategy for GAG synthesis highly attractive.

The fact that the previously reported TEMPO/NaOCl procedure[14–16] failed to produce desired carboxylic acids is most likely due to hydrophobicities of our substrates. It has been proposed that aldehydes are intermediates in TEMPO-catalyzed NaOCl oxidation of primary alcohols to carboxylic acids.[14] With a hydrophilic aldehyde, the carbonyl group can be hydrated to form a vicinal diol under phase-transfer conditions, which is subsequently oxidized by TEMPO/NaOCl to produce a carboxylic acid (Scheme 1). However,



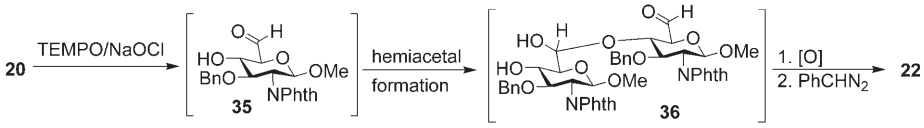
Scheme 1. Proposed intermediates for our new oxidation method.

due to the hydrophobic nature of fully protected oligosaccharides, hydration of newly-formed aldehydes is presumably slow even under phase-transfer conditions. The direct conversion of an aldehyde to the carboxylic acid without going through vicinal diol was apparently difficult with TEMPO/NaOCl and prolonged treatment did not yield the desired carboxylic acid. The major product isolated from TEMPO/NaOCl oxidation of disaccharide **25** under phase-transfer conditions was aldehyde **27**. Attempt to enhance aldehyde hydration by performing TEMPO/NaOCl oxidation in an acetonitrile and water mixture did not alleviate the problem. In contrast, the aldehyde was quickly converted to the carboxylic acid with addition of $NaClO_2$ to the reaction mixture following TEMPO/NaOCl oxidation. A one-step procedure that involved the used of a combination of TEMPO, NaOCl, and $NaClO_2$ together was not successful, probably due to the instability of $NaClO_2$/NaOCl mixture.[19]

The excellent yields and extraordinary functional group compatibility achieved by using our oxidation procedure are related with the relatively high loading of TEMPO employed (0.3 equiv per hydroxyl group), as slower reaction was observed with less TEMPO. Furthermore, the two-phase condition (methylene chloride and water) for the TEMPO/NaOCl oxidation is crucial. When oxidation of thioglycoside **13** was carried out in a homogeneous acetonitrile/water mixture with TEMPO/NaOCl, multiple side products without the thiotolyl moieties were obtained with no desired carboxylic acid **14** or the corresponding aldehyde. This indicates that the single-phase homogenous condition for TEMPO/NaOCl oxidation is less selective and can affect sensitive functional groups.

The formation of side product ester **22** in oxidation of diol **20** (Table 1, entry 9) can be explained with the intermediacy of aldehyde as well. Upon generation of aldehyde **35**

from **20**, intermolecular nucleophilic attack of the carbonyl group by the free secondary hydroxyl group produced hemiacetal **36**, oxidation and benzylation of which led to carboxylic ester **22** (Scheme 2).



Scheme 2. Proposed mechanism for the formation of ester **22**.

Conclusion

In summary, we have established a new two-step, one-pot oxidation protocol, which efficiently converts a wide range of primary alcohols to carboxylic acids. This convenient procedure does not require an inert atmosphere, anhydrous solvents, or an extremely low reaction temperature. It does not generate toxic heavy-metal or malodorous side products; this fact is important with respect to increasing environmental awareness. A remarkably wide range of sensitive functional groups, such as electron-rich aromatic rings, acid-labile isopropylidene ketal and glycosidic linkages, and oxidation-prone thioacetal, PMB, and allyl moieties are little affected by the oxidation. Several GAGs, including hyaluronic acid, chondroitin, and heparin oligosaccharides were prepared in high yields by using this procedure. Further applications of this new protocol in solution and solid-phase syntheses of complex oligosaccharides are ongoing.

Experimental Section

General conditions: Chemicals used were reagent grade as supplied except where noted. Analytical thin-layer chromatography was performed using silica gel 60 F254 glass plates (EM Science); compound spots were visualized by UV light (254 nm) and/or by staining with a solution containing $Ce(NH_4)_2(NO_3)_6$ (0.5 g) and $(NH_4)_6Mo_7O_{24}{\cdot}4H_2O$ (24.0 g) in 6% H_2SO_4 (500 mL) or a solution of $KMnO_4$ (3 g), K_2CO_3 (20 g) and NaOH (0.25 g) in water (300 mL). Flash column chromatography was performed on silica gel 60 (230–400 Mesh, EM Science). ^1H NMR and ^{13}C NMR spectra were recorded on a Varian VXRS-400 or Inova-600 instrument and were referenced to Me_4Si (0 ppm), residual $CHCl_3$ (^1H NMR $\delta = 7.26$ ppm) $CDCl_3$ (^{13}C NMR $\delta = 77.0$ ppm), residual CH_2Cl_2 (^1H NMR $\delta = 5.32$ ppm), and CD_2Cl_2 (^{13}C NMR $\delta = 54.0$ ppm). ESI mass spectra were recorded on an ESQUIRE LC-MS operated in both positive and negative ion mode. High-resolution mass spectra were recorded on a Micromass electrospray Tof™ II (Micromass, Wythenshawe, UK) mass spectrometer equipped with an orthogonal electrospray source (Z-spray) operated in positive ion mode, which is located at the Mass Spectrometry and Proteomics Facility at the Ohio State University.

General procedure for oxidation: An aqueous solution of NaBr (1 M, 25 μL), an aqueous solution of tetrabutylammonium bromide (1 M, 50 μL), TEMPO (2.2 mg, 0.014 mmol, 0.3 equiv per hydroxyl group) and a saturated aqueous solution of $NaHCO_3$ (125 μL) were added to a solution of alcohol (0.045 mmol) in CH_2Cl_2 (1 mL) and H_2O (170 μL) in an ice–water bath. The resulted mixture was treated with an aqueous solution of NaOCl (150 μL, chlorine content not less than 4%) and continuously stirred for 1 hour as the temperature increased from 0 °C to RT. The reaction media was neutralized with HCl (1 N, about 50 μL) to pH 6–7. It is important to keep the acidity of the reaction close to neutral as lower pH resulted in formation of large amount of hemiacetal side product in oxidation of diol **20**. After neutralization, *t*BuOH (0.7 mL), 2-methylbut-2-ene in THF (2 M, 1.4 mL)[30] and a solution of $NaClO_2$ (50 mg, 0.44 mM) and NaH_2PO_4 (40 mg, 0.34 mM) in water (200 μL) were added. The reaction mixture was kept at room temperature for 1–2 h, diluted with saturated aqueous NaH_2PO_4 solution (5 mL), and extracted with EtOAc (3×10 mL). The organic layers were combined and dried over $MgSO_4$. After removal of the solvent, the desired compound was purified by flash column chromatography.

General procedure for benzyl ester formation: The crude product from the oxidation reaction was dissolved in dichloromethane (5 mL) and treated with phenyl diazomethane solution in diethyl ether (~2 equiv per acid)[27] for 2–3 h until the disappearance of all starting material as judged by TLC. The residue after evaporation was purified by flash column chromatography to provide the benzyl ester.

General procedure for regioselective opening of 4,6-*O*-benzylidene:[31] Bu_2BOTf in dichloromethane (1 M, 1 equiv) was added to a solution of 4,6-*O*-benzylidene containing glycoside in borane in THF (1 M, 10 equiv) in a flame dried flask at 0 °C under N_2. The reaction mixture was stirred for 3 h. Triethylamine (~0.5 mL) was added followed by careful addition of methanol until the evolution of gas had ceased. All solvents were evaporated and the desired product was isolated by flash column chromatography.

Benzoic acid (4): Compound **4** was obtained from benzyl alcohol (0.100 g, 0.92 mmol) following general oxidation procedure in 100% yield. Comparison of the ^1H and ^{13}C NMR data with the Aldrich NMR library confirmed the identity of benzoic acid **4**. ^1H NMR (600 MHz, $CDCl_3$): $\delta = 7.45$–7.49 (m, 1H), 7.58–7.62 (m, 2H), 8.09–8.13 ppm (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 128.75$, 129.54, 130.47, 134.09, 172.75 ppm; ESI-MS: *m*/*z* calcd for $C_7H_6NaO_2$ $[M+Na]^+$: 145.1; found: 145.0.

***p*-Anisic acid (6)**: Compound **6** was obtained from 4-methoxy benzyl alcohol (0.100 g, 0.72 mmol) following general oxidation procedure in 95% yield. Comparison of the ^1H and ^{13}C NMR data with the Aldrich NMR library confirmed the identity of compound **6**. ^1H NMR (600 MHz, $CDCl_3$): $\delta = 3.87$ (s, 3H), 6.92–6.96 (m, 2H), 8.03–8.07 ppm (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 55.73$, 113.97, 121.85, 132.59, 164.27, 171.90 ppm; ESI-MS: *cm*/*z* calcd for $C_8H_8NaO_3$ $[M+Na]^+$: 175.2; found: 175.4.

Decanoic acid (8): Compound **8** was obtained from 1-decyl alcohol (0.100 g, 0.63 mmol) following general oxidation procedure in 90% yield. Comparison of the ^1H and ^{13}C NMR data with the Aldrich NMR library confirmed the identity of compound **8**. ^1H NMR (400 Hz, $CDCl_3$): $\delta =$ 0.88 (t, $^3J(H,H) = 6.8$ Hz, 3H), 1.24–1.32 (m, 12H), 1.61–1.66 (m, 2H), 2.35 ppm (t, $^3J(H,H) = 7.6$ Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta =$ 14.33, 22.89, 24.92, 29.29, 29.49, 29.62, 32.09, 34.37, 180.52 ppm; ESI-MS: *m*/*z* calcd for $C_{10}H_{20}NaO_2$ $[M+Na]^+$: 195.3; found: 195.5.

1,2,3,4-Di-*O*-isopropylidene-α-D-galacturonic acid (10): Compound **10** was obtained from 1,2,3,4-di-*O*-isopropylidene-α-D-galactopyranose (0.100 g, 0.38 mmol) following the general oxidation procedure in 90% yield. Comparison of the ^1H NMR data with literature[32] confirmed the identity of compound **10**. ^1H NMR (600 MHz, $CDCl_3$): $\delta = 1.33$ (s, 6H), 1.44 (s, 3H), 1.52 (s, 3H), 4.39 (dd, $^3J(H,H) = 3.0$, 4.2 Hz, 1H), 4.45 (d, $^3J(H,H) = 1.8$ Hz, 1H), 4.61–4.68 (m, 3H), 5.63 ppm (d, $^3J(H,H) = 4.8$ Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 24.65$, 25.00, 26.06, 26.21, 68.43, 70.65, 70.77, 71.89, 96.59, 109.60, 110.38, 172.01 ppm; ESI-MS: *m*/*z* calcd for $C_{12}H_{18}NaO_7$ $[M+Na]^+$: 297.3; found: 297.1.

***p*-Tolyl 2,3,4-tri-*O*-benzoyl-1-thio-β-D-glucopyranosyluronic acid (12)**: Compound **12** was synthesized from compound **11**[21] (50 mg, 84 μmol) according to the general oxidation procedure in 82% yield. ^1H NMR

(400 MHz, $CDCl_3$): $\delta = 2.33$ (s, 3H; *p*-MePh), 4.34 (d, $^3J(H,H) = 9.6$ Hz, 1H), 5.01 (d, $^3J(H,H) = 9.6$ Hz, 1H), 5.48 (t, $^3J(H,H) = 9.6$ Hz, 1H), 5.66 (t, $^3J(H,H) = 9.6$ Hz, 1H), 5.90 (t, $^3J(H,H) = 9.6$ Hz, 1H), 7.11–7.98 ppm (m, 19H); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 21.47$, 70.11, 70.32, 73.74, 76.35, 86.87, 127.48–139.30 (aromatic carbon atoms), 165.15, 165.71, 165.91, 170.65 ppm; ESI-MS: *m/z* calcd for $C_{34}H_{27}O_9S$ $[M-1]^-$: 611.2; found: 611.3; HRMS: *m/z* calcd for $C_{34}H_{28}NaO_9S$ $[M+Na]^+$: 635.1352; found: 635.1376.

***p*-Tolyl 2-deoxy-2-*N*-phthalimido-3-*O*-*p*-methoxybenzyl-4-*O*-benzyl-1-thio-β-D-glucopyranoside (13)**: Compound **13** was synthesized from *p*-tolyl 2-deoxy-2-*N*-phthalimido-3-*O*-*p*-methoxybenzyl-4,6-*O*-benzylidene-1-thio-β-D-glucopyranoside[33] (62 mg, 100 μmol) following the general procedure of regioselective opening of benzylidene ring in 68% yield. ^1H NMR (400 MHz, $CDCl_3$): $\delta = 1.92$ (t, $^3J(H,H) = 6.8$ Hz, 3H), 2.29 (s, 3H), 3.52–3.58 (m, 1H), 3.58 (s, 3H), 3.66 (t, $^3J(H,H) = 9.6$ Hz, 1H), 3.72–3.78 (m, 1H), 3.88–3.96 (m, 1H), 4.14 (t, $^3J(H,H) = 10.2$ Hz, 1H), 4.34 (dd, $^3J(H,H) = 8.8$, 10.0 Hz, 1H), 4.38 (d, $^3J(H,H) = 12.4$ Hz, 1H), 4.70 (d, $^3J(H,H) = 12.4$ Hz, 1H), 4.72 (d, $^3J(H,H) = 12.4$ Hz, 1H), 4.88 (d, $^3J(H,H) = 12.4$ Hz, 1H), 5.50 (d, $^3J(H,H) = 10.8$ Hz, 1H), 6.33–6.39 (m, 2H), 6.86–6.92 (m, 2H), 7.02–7.06 (m, 2H), 7.20–7.25 (m, 2H), 7.28–7.38 (m, 5H), 7.58–7.84 ppm (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 21.07$, 54.74, 55.00, 61.92, 74.44, 75.08, 79.21, 79.35, 79.66, 83.31, 113.32, 123.05, 123.29, 127.73–133.71, 137.75, 138.32, 158.73, 167.27, 167.90 ppm; ESI-MS: *m/z* calcd for $C_{36}H_{35}NNaO_7S$ $[M+Na]^+$: 648.2; found: 648.3.

***p*-Tolyl 2-deoxy-2-*N*-phthalimido-3-*O*-*p*-methoxybenzyl-4-*O*-benzyl-1-thio-β-D-glucopyranosyluronic acid (14)**: Compound **14** was synthesized from compound **13** (40 mg, 66 μmol) according to the general oxidation procedure in 85% yield with 6% of the glycosyl lactone **15** isolated. ^1H NMR (400 MHz, $CDCl_3$): $\delta = 2.33$ (s, 3H; *p*-MePh), 3.57 (s, 3H), 3.86 (t, $^3J(H,H) = 9.2$ Hz, 1H), 4.10 (d, $^3J(H,H) = 10$ Hz, 1H), 4.32 (t, $^3J(H,H) = 10.2$ Hz, 1H), 4.30–4.37 (m, 2H), 4.68–4.74 (m, 3H), 5.52 (d, $J = 10.8$ Hz, 1H), 6.33–7.81 ppm (m, 17H; ArH); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 21.36$, 54.65, 55.00, 74.72, 75.48, 79.29, 81.09, 84.65, 113.58–158.99 (aromatic carbon atoms), 167.39, 168.10, 177.56 ppm; HRMS: *m/z* calcd for $C_{36}H_{33}NaO_8S$ $[M+Na]^+$: 662.1825; found: 662.1826.

2-Deoxy-2-*N*-phthalimido-3-*O*-*p*-methoxybenzyl-4-*O*-benzyl-β-D-glucopyranosidurono-6,1-lactone (15): ^1H NMR (400 MHz, $CDCl_3$): $\delta = 3.56$ (s, 3H), 3.91 (d, $^3J(H,H) = 6.8$ Hz, 1H), 4.22 (d, $^3J(H,H) = 9.6$ Hz, 1H), 4.31 (dd, $^3J(H,H) = 7.2$, 10 Hz, 1H), 4.42 (d, $^3J(H,H) = 12.0$ Hz, 1H), 4.61 (d, $^3J(H,H) = 12.0$ Hz, 1H), 4.64 (s, 1H), 4.68 (d, $^3J(H,H) = 11.6$ Hz, 1H), 4.82 (d, $^3J(H,H) = 11.6$ Hz, 1H), 5.96 (s, 1H), 6.32–7.72 ppm (m, 13H); ESI-MS: *m/z* calcd for $C_{29}H_{25}NaNO_8$ $[M+Na]^+$: 538.1; found: 538.2; HRMS: *m/z* calcd for $C_{29}H_{25}NaNO_8$ $[M+Na]^+$: 538.1478; found: 538.1501.

***p*-Tolyl 2-deoxy-2-*N*-phthalimido-3-*O*-*tert*-butyldimethylsilyl-4-*O*-benzyl-1-thio-β-D-glucopyranoside (16)**: Compound **16** was synthesized from *p*-tolyl 2-deoxy-2-*N*-phthalimido-3-*O*-*tert*-butyldimethylsilyl-4,6-*O*-benzylidene-1-thio-β-D-glucopyranoside[33] (62 mg, 100 μmol) following the general procedure of regioselective opening of benzylidene ring in 77% yield. ^1H NMR (600 MHz, $CDCl_3$): $\delta = -0.44$ (s, 3H), −0.06 (s, 3H), 0.71 (s, 9H), 1.95 (t, $^3J(H,H) = 6.6$ Hz, 3H), 2.28 (s, 3H), 3.48–3.58 (m, 2H), 3.64–3.72 (m, 1H), 3.83–3.90 (m, 1H), 4.22 (t, $^3J(H,H) = 10.2$ Hz, 1H), 4.48 (dd, $^3J(H,H) = 8.4$, 9.6 Hz, 1H), 4.64 (d, $^3J(H,H) = 12.0$ Hz, 1H), 4.81 (d, $^3J(H,H) = 12.0$ Hz, 1H), 5.55 (d, $^3J(H,H) = 10.8$ Hz, 1H), 7.00–7.06 (m, 2H), 7.21–7.36 (m, 7H), 7.72–7.92 ppm (m, 4H); ESI-MS: *m/z* calcd for $C_{34}H_{31}NNaO_6SSi$ $[M+Na]^+$: 642.2; found: 642.7.

***p*-Tolyl 2-deoxy-2-*N*-phthalimido-3-*O*-*tert*-butyldimethylsilyl-4-*O*-benzyl-1-thio-β-D-glucopyranosyluronic acid (17)**: Compound **17** was synthesized from compound **16** (55 mg, 89 μmol) according to the general oxidation procedure in 86% yield. ^1H NMR (600 MHz, $CDCl_3$): $\delta = -0.44$ (s, 3H), −0.09 (s, 3H), 0.71 (s, 9H), 2.28 (s, 3H), 3.67 ?t, $^3J(H,H) = 8.8$ Hz, 1H), 4.11 (d, $^3J(H,H) = 9.6$ Hz, 1H), 4.31 (t, $^3J(H,H) = 10.2$ Hz, 1H), 4.47 (t, $^3J(H,H) = 9.2$ Hz, 1H), 4.58 (d, $^3J(H,H) = 10.8$ Hz, 1H), 4.64 (d, $^3J(H,H) = 10.8$ Hz, 1H), 5.57 (d, $^3J(H,H) = 10.2$ Hz, 1H), 7.01–7.89 ppm (m, 13H; ArH); ^{13}C NMR (150 MHz, $CDCl_3$): $\delta = -4.48$, −3.69, 17.84, 21.40, 25.88, 56.40, 73.24, 75.25, 77.89, 81.13, 84.71, 127.93–138.76 ppm (aromatic carbon atoms); HRMS: *m/z* calcd for $C_{34}H_{39}NaO_7SSi$ $[M+Na]^+$: 656.2114; found: 656.2072.

Allyl 2,3,4-tri-*O*-benzoyl-1-thio-α-D-mannopyranosyluronic acid (19): Compound **19** was synthesized from compound **18**[22] (50 mg, 94 μmol) according to the general oxidation procedure in 92% yield. ^1H NMR (400 MHz, $CDCl_3$): $\delta = 4.18$ (dd?$J = 6.0$, 12.8 Hz, 1H), 4.35 (dd, $^3J(H,H) = 4.2$, 12.8 Hz, 1H), 4.68 (d, $^3J(H,H) = 9.2$ Hz, 1H), 5.28–5.30 (m, 2H), 5.40 (dd, $^3J(H,H) = 1.2$, 17.2 Hz, 1H), 5.68 (t, 1H; $^3J(H,H) = 4.2$ Hz, 1H), 5.91–6.03 (m, 3H), 7.26–8.09 ppm (m, 15H; ArH); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 67.83$, 69.64, 69.69, 69.86, 70.25, 97.05, 119.05, 128.60–133.84 (aromatic carbon atoms), 165.53, 165.77, 165.86, 177.74 ppm; HRMS: *m/z* calcd for $C_{30}H_{26}NaO_{10}$ $[M+Na]^+$: 569.1424; found: 569.1431.

Benzyl 1-methoxy-2-deoxy-2-*N*-phthalimido-3-*O*-benzyl-β-D-glucopyranosyluronate (21): Compound **21** was synthesized from compound **20**[25] (26 mg, 63 μmol) in 75% yield according to the general procedures of oxidation and benzyl ester formation, along with compound **22** (~10%). ^1H NMR (600 MHz, $CDCl_3$): $\delta = 3.08$?s, 1H; 4-OH), 3.39 (s, 3H; MeO), 4.0–4.05 (m, 2H), 4.16(dd, $^3J(H,H) = 8.4$, 9.0 Hz, 1H), 4.23 (dd, $^3J(H,H) = 7.2$, 10.8 Hz, 1H), 4.53 (d, $^3J(H,H) = 12.6$ Hz, 1H; PhCH), 4.44 (d, $^3J(H,H) = 12.6$ Hz, 1H; PhCH), 5.09 (d, $^3J(H,H) = 8.4$ Hz, 1H), 5.26 (d, $^3J(H,H) = 12.6$ Hz, 1H; PhCH), 5.30 (d, $^3J(H,H) = 12.6$ Hz, 1H; PhCH), 6.89–7.67 ppm (m, 14H; ArH); ^{13}C NMR (150 MHz, $CDCl_3$): $\delta = 55.11$, 57.22, 67.69, 73.94, 74.37, 74.68, 77.66, 99.77, 127.66–138.14 (aromatic carbon atoms), 169.53 ppm; HRMS: *m/z* calcd for $C_{29}H_{27}NNaO_8^+$ $[M+Na]^+$: 540.1634; found: 540.1628.

Benzyl 4-*O*-(benzyl-1-methoxy-2-deoxy-2-*N*-phthalimido-3-*O*-benzyl-β-D-glucopyranosyluronate)-1-methoxy-2-deoxy-2-*N*-phthalimido-3-*O*-benzyl-β-D-glucopyranosyluronate (22): ^1H NMR (400 MHz, $CDCl_3$): $\delta = 3.35$s, 3H; OMe), 3.41 (s, 3H; OMe), 3.75 (t, $^3J(H,H) = 5.4$ Hz, 1H), 3.86 (dt, $^3J(H,H) = 3.6$, 8.0 Hz, 1H), 4.10–4.22 (m, 3H), 4.31 (dd, $^3J(H,H) = 8.4$, 10.4 Hz, 1H), 4.39 (d, $^3J(H,H) = 12.4$ Hz, PhCH, 1H), 4.55 (dd, $^3J(H,H) = 8.8$, 10.8 Hz,1H), 4.58 (d, $^3J(H,H) = 12.4$ Hz, PhCH, 1H), 4.68 (d, $^3J(H,H) = 12.4$ Hz, PhCH, 1H), 4.86 (d, $^3J(H,H) = 12.4$ Hz, PhCH, 1H), 5.03 (d, $^3J(H,H) = 8.0$ Hz, 1H), 5.10 (d, $^3J(H,H) = 8.8$ Hz, 1H), 5.20 (d, $^3J(H,H) = 12.4$ Hz, PhCH, 1H), 5.26 (d, $^3J(H,H) = 12.4$ Hz, PhCH, 1H), 5.42 (dd, $^3J(H,H) = 8.8$, 10.0 Hz, 1H), 6.89–7.80 ppm (m, 23H; ArH); ^{13}C NMR (150 MHz, $CDCl_3$): $\delta = 55.03$, 55.17, 57.01, 57.37, 68.65, 72.92, 73.84, 74.32, 74.45, 74.71, 74.81, 76.15, 99.44, 99.61, 127.56–138.29 (aromatic carbon atoms), 168.75, 169.51 ppm; HRMS: *m/z* calcd for $C_{51}H_{46}N_2NaO_{15}^+$ $[M+Na]^+$: 949.2796; found: 949.2794.

1-Methoxy-2,3-*O*-isopropylidene-β-D-ribofuranosyl-5-carboxylic acid (24): Compound **24** was synthesized from compound **23**[28] (40 mg, 96 μmol) according to the general oxidation procedure in 100% yield. ^1H NMR (600 MHz, $CDCl_3$): $\delta = 1.31$ (s, 3H), 1.47 (s, 3H), 3.40 (s, 3H), 4.55 (d, $^3J(H,H) = 5.4$ Hz, 1H), 4.63 (s, 1H), 5.04 (s, 1H), 5.17 ppm (d, $^3J(H,H) = 5.4$ Hz, 1H); ^{13}C NMR (150 MHz, $CDCl_3$): $\delta = 25.15$, 26.56, 55.89, 82.41, 84.33, 109.91, 113.11, 175.41 ppm; HRMS: *m/z* calcd for $C_{30}H_{26}NaO_{10}$ $[M+Na]^+$: 569.1424; found: 569.1431.

Methyl (2-*O*-benzoyl-3,4-di-*O*-benzyl-β-D-glucopyranosyluronic acid-(1→3)-(2-deoxy-2-*N*-phthalimido-4,6-*O*-benzylidene-β-D-glucopyranoside) (26): Compound **26** was synthesized from compound **25**[29] (28 mg, 33 μmol) following the general oxidation procedure in 95% yield. ^1H NMR (400 MHz, $CDCl_3$): $\delta = 3.37$ (s, 3H; OMe), 3.56 (dd, $^3J(H,H) = 4.2$, 6.4 Hz, 1H), 3.65 (m, 1H), 3.80–3.89 (m, 3H), 3.94 (d, $^3J(H,H) = 6.0$ Hz, 1H), 4.30 (dd, $^3J(H,H) = 8.4$, 10.4 Hz, 1H), 4.37–4.51 (m, 5H), 4.73 (t, $^3J(H,H) = 11.2$ Hz, 1H), 4.96–5.01 (m, 2H), 5.08 (d, $^3J(H,H) = 8.8$ Hz, 1H), 5.57 (s, 1H), 7.01–7.53 ppm (m, 24H; ArH); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 55.45$, 57.23, 66.46, 68.95, 73.56, 73.69, 73.89, 74.28, 76.41, 79.45, 81.08, 99.49, 99.78, 102.42, 126.54–137.34 (aromatic carbon atoms), 164.77, 169.45 ppm (carbonyl groups); HRMS: *m/z* calcd for $C_{49}H_{45}NaO_{14}$ $[M+Na]^+$: 894.2738; found: 894.2701.

Methyl (2-*O*-benzoyl-3,4-di-*O*-benzyl-β-D-glucohexodialdo-1,5-pyranosyl)-(1→3)-(2-deoxy-2-*N*-phthalimido-4,6-*O*-benzylidene-β-D-glucopyranoside) (27): Compound **27** was obtained from compound **25**[29] following the general oxidation procedure without the $NaClO_2$ oxidation step. ^1H NMR (600 MHz, $CDCl_3$): $\delta = 3.35$ (s, 3H; OMe), 3.46 (d, $^3J(H,H) = 7.8$ Hz, 1H), 3.58 (t, $^3J(H,H) = 7.8$ Hz, 1H), 3.62–3.64 (m, 2H), 3.84–3.87 (m, 2H), 4.28 (dd, $^3J(H,H) = 8.4$, 10.2 Hz, 1H), 3.73 (dd, $^3J(H,H) = 4.8$, 10.8 Hz, 1H), 4.39–4.51 (m, 5H), 4.72 (t, $^3J(H,H) = 9.0$ Hz, 1H), 4.83 (d,

^3J(H,H) = 7.2 Hz, 1H), 4.97 (t, ^3J(H,H) = 7.2 Hz, 1H), 5.05 (d, ^3J(H,H) = 8.4 Hz, 1H), 5.51 (s, 1H; PhCH), 6.95–7.55 (m, 24H; ArH), 9.39 ppm (s, 1H; CHO); ESI-MS: *m*/*z* calcd for $C_{50}H_{49}NNaO_{14}$ $[M+Na+MeOH]^+$: 910.3; found: 910.6.

Methyl (benzyl-2-*O*-benzoyl-3-*O*-benzyl-4-*O*-*tert*-butyldimethylsilyl-β-D-glucopyranosyluronate)-(1→3)-(2-deoxy-2-*N*-phthalimido-4,6-*O*-benzylidene-β-D-glucopyranosyl)-(1→4)-(benzyl-2-*O*-benzoyl-3-*O*-benzyl-β-D-glucopyranosyluronate)-(1→3)-2-deoxy-2-*N*-phthalimido-4,6-*O*-benzylidene-β-D-glucopyranoside (29): Compound **29** was synthesized from compound **28**[29] (136 mg, 84 μmol) following the general procedures of oxidation and benzyl ester formation in 86% overall yield. ^{1}H NMR (600 MHz, CD_2Cl_2): $\delta = -0.24$ (s, 3H; CH_3Si), −0.13 (s 3H; CH_3Si), 0.75 (s, 9H; $(CH_3)_3CSi$), 2.25 (m, 1H), 3.28 (s, 3H; CH_3O), 3.37 (d, ^3J(H,H) = 9.6 Hz, 1H), 3.41 (t, ^3J(H,H) = 7.8 Hz, 1H), 3.44-.3.49 (m, 3H), 3.58–3.61 (m, 2H), 3.67 (d, ^3J(H,H) = 8.4 Hz, 1H), 3.93–4.13 (m, 5H), 4.18 (dd, ^3J-(H,H) = 5.4, 9.6 Hz, 1H), 4.32–4.39 (m, 3H), 4.52 (d, ^3J(H,H) = 10.8 Hz, 1H), 4.51 (dd, ^3J(H,H) = 9.0, 10.2 Hz, 1H), 4.61 (d, ^3J(H,H) = 8.4 Hz, 1H), 4.66 (dd, ^3J(H,H) = 8.4, 10.2 Hz, 1H), 4.68 (d, ^3J(H,H) = 11.4 Hz, 1H), 4.79 (t, ^3J(H,H) = 7.8 Hz, 1H), 4.80 (d, ^3J(H,H) = 8.4 Hz, 1H), 4.92 (dd, ^3J(H,H) = 8.4, 10.2 Hz, 1H), 4.94 (s, 2H), 5.03 (d, ^3J(H,H) = 12.0 Hz, 1H), 5.05 (d, ^3J(H,H) = 8.4 Hz, 1H), 5.06 (d, ^3J(H,H) = 12.0 Hz, 1H), 5.11 (s, 1H; PhCH), 5.32 (s, 1H; PhCH), 6.92–7.81 ppm (m, 48H; ArH); ^{13}C NMR (100 MHz, CD_2Cl_2): $\delta = -5.20$, −4.29, 19.22, 25.72, 55.16, 55.69, 56.98, 65.85, 66.32, 67.31, 68.43, 68.55, 71.91, 72.99, 73.96, 74.24, 74.68, 75.80, 76.12, 76.96, 77.56, 79.88, 80.96, 81.71, 82.20, 98.30, 99.57, 99.59, 99.84, 101.15, 101.48, 123.19–138.38 (aromatic carbon atoms), 164.53, 164.66, 166.93, 168.11 ppm (carbonyl groups); HRMS: *m*/*z* calcd for $C_{103}H_{100}NaN_2O_{27}Si$ $[M+Na]^+$: 1847.6180; found: 1847.6165.

Methyl (benzyl-2-*O*-benzoyl-3-*O*-benzyl-4-*O*-*tert*-butyldimethylsilyl-β-D-glucopyranosyluronate)-(1→3)-(2-deoxy-2-*N*-phthalimido-4,6-*O*-benzylidene-β-D-glucopyranosyl)-(1→4)-(benzyl-2-*O*-benzoyl-3-*O*-benzyl-β-D-glucopyranosyluronate)-(1→3)-(2-deoxy-2-*N*-phthalimido-4,6-*O*-benzylidene-β-D-glucopyranosyl)-(1→4)-(benzyl-2-*O*-benzoyl-3-*O*-benzyl-β-D-glucopyranosyluronate)-(1→3)-(2-deoxy-2-*N*-phthalimido-4,6-*O*-benzylidene-β-D-glucopyranoside) (30): Compound **30** was synthesized from compound **1**[29] (70 mg, 30 μmol) following the general procedures of oxidation and benzyl ester formation in 82% overall yield. ^{1}H NMR (600 MHz, CD_2Cl_2): $\delta = -0.14$ (s, 3H; CH_3Si), −0.26 (s, 3H; CH_3Si), 0.72 (s, 9H; $(CH_3)_3CSi$), 3.04 (t, ^3J(H,H) = 10.2 Hz, 1H), 3.11–3.15 (m, 2H), 3.21–3.31 (m, 5H), 3.27 (s, 3H; MeO), 3.38–3.47 (m, 6H), 3.56–3.61 (m, 2H), 3.67 (t, ^3J(H,H) = 8.4 Hz, 1H), 3.84 (dd, ^3J(H,H) = 4.2, 10.2 Hz, 1H), 3.93–4.04 (m, 6H), 4.07–4.12 (m, 2H), 4.18 (dd, ^3J(H,H) = 4.2, 9.6 Hz, 1H), 4.27–4.38 (m, 6H), 4.45 (d, ^3J(H,H) = 12 Hz, 1H), 4.48 (dd, ^3J-(H,H) = 8.4, 10.2 Hz, 1H),4.52–4.58 (m, 3H), 4.62–4.68 (m, 3H), 4.97 (d, ^3J(H,H) = 8.4 Hz, 1H), 4.99 (s, 1H; PhCH), 5.01 (s, 1H; PhCH), 5.03 (d, ^3J(H,H) = 8.4 Hz, 1H), 5.10 (d, ^3J(H,H) = 12 Hz, 1H), 5.12 (s, 1H; PhCH), 5.17 (d, ^3J(H,H) = 12 Hz, 1H), 4.91–4.93 (m, 3H), 6.86–7.73 ppm (m, 72H; ArH); ^{13}C NMR (100 MHz, CD_2Cl_2): $\delta = -5.20$, −4.30, 17.91, 25.71, 53.59, 53.86, 54.13, 55.14, 55.55, 55.65, 56.96, 65.70, 65.87, 66.31, 67.28 ,67.31, 68.21, 68.43, 68.53, 71.89, 72.92, 73.94, 72.18, 74.19, 74.59, 74.74, 75.77, 76.11, 76.96, 77.47, 79.83, 79.87, 80.66, 80.96, 81.15, 82.18, 98.18, 99.54, 99.58, 99.71, 99.79, 100.99, 101.13, 101.47, 123.17–138.33 (aromatic carbon atoms), 164.49, 164.55, 164.64, 166.86, 166.92, 168.10 ppm (carbonyl groups); HRMS: *m*/*z* calcd for $C_{151}H_{141}NaN_3O_{40}Si$ $[M+Na]^+$: 2686.8758; found: 2686.8855.

Methyl (benzyl-2-*O*-benzoyl-3-*O*-benzyl-4-*O*-*tert*-butyldimethylsilyl-β-D-glucopyranosyluronate)-(1→3)-(2-deoxy-2-*N*-phthalimido-4,6-*O*-benzylidene-β-D-galactopyranosyl)-(1→4)-(benzyl-2-*O*-benzoyl-3-*O*-benzyl-β-D-glucopyranosyluronate) (32): Compound **32** was synthesized from compound **31**[29] (29 mg, 24 μmol) following the general procedures of oxidation and benzyl ester formation in 76% overall yield. ^{1}H NMR (600 MHz, $CDCl_3$): $\delta = -0.16$ (s, 3H; CH_3Si), −0.13 (s 3H; CH_3Si), 0.77 (s, 9H; $(CH_3)_3CSi$), 2.89 (s, 1H), 3.31 (t, ^3J(H,H) = 9.0 Hz, 1H), 3.36 (s, 3H; MeO), 3.52–3.55 (m, 3H), 3.59 (d, ^3J(H,H) = 10.8 Hz, 1H), 4.01–4.16 (m, 6H), 4.46 (s, 2H), 4.55–4.58 (d, 2H), 4.66 (dd, ^3J(H,H) = 3.6, 10.8 Hz, 1H), 4.72 (d, ^3J(H,H) = 10.2 Hz, 1H), 4.75 (d, ^3J(H,H) = 10.2 Hz, 1H), 4.84 (d, ^3J(H,H) = 7.2 Hz, 1H), 5.03–5.16 (m, 6H), 5.24 (s, 1H; PhCH), 6.81–7.55 ppm (m, 39H; ArH); ^{13}C NMR (150 MHz, $CDCl_3$): $\delta = -4.99$, −4.04, 18.07, 25.93, 52.39, 57.38, 66.73, 67.19, 67.44, 68.86, 71.73, 73.66, 73.97, 74.46, 74.55, 74.89, 75.41, 75.54, 76.84, 81.51, 82.41, 82.64, 98.29, 100.66, 101.06, 104.88, 122.92–139.17 (aromatic carbon atoms), 164.54, 167.84, 168.40, 169.41 ppm (carbonyl groups); ESI-MS: *m*/*z* calcd for $C_{82}H_{85}NNaO_{20}Si$ $[M+Na]^+$: 1454.5; found: 1454.6; HRMS: *m*/*z* calcd for $C_{82}H_{85}NNaO_{20}Si$ $[M+Na]^+$: 1454.5170; found: 1454.5332.

Methyl (benzyl-2-*O*-benzoyl-3-*O*-benzyl-4-*O*-*tert*-butyldimethylsilyl-β-D-glucopyranosyluronate)-(1→4)-(2-deoxy-2-azido-3,6-*O*-dibenzyl-α-D-glucopyranosyl)-(1→4)-benzyl-2,3-*O*-dibenzyl-β-D-glucopyranosyluronate (34): Compound **34** was synthesized from compound **33**[29] (40 mg, 33 μmol) following the general procedures of oxidation and benzyl ester formation in 81% overall yield. ^{1}H NMR (600 MHz, $CDCl_3$): $\delta = -0.04$ (s, 3H; CH_3Si), −0.04 (s 3H; CH_3Si), 0.85 (s, 9H; $(CH_3)_3CSi$), 3.15 (dd, ^3J(H,H) = 4.2, 10.8 Hz, 1H), 3.24 (d, ^3J(H,H) = 10.2 Hz, 1H), 3.29 (t, ^3J-(H,H) = 9.0 Hz, 1H), 3.39–3.42 (m, 2H), 3.45 (s, 3H; OMe), 3.61–3.67 (m, 2H), 3.73 (d, ^3J(H,H) = 10.8 Hz, 1H), 3.76 (d, ^3J(H,H) = 9.0 Hz, 1H), 3.79 (d, ^3J(H,H) = 10.2 Hz, 1H), 3.95–4.00 (m, 2H), 4.06 (t, ^3J(H,H) = 9.0 Hz, 1H), 4.26–4.29 (m, 3H), 4.42 (d, ^3J(H,H) = 10.8 Hz, 1H), 4.48 (d, ^3J(H,H) = 10.8 Hz, 1H), 4.56 (d, ^3J(H,H) = 10.8 Hz, 1H), 4.59–4.63 (m, 3H), 4.68–4.70 (m, 2H), 4.83–4.85 (m, 2H), 4.92 (d, ^3J(H,H) = 10.8 Hz, 1H), 5.01 (d, ^3J(H,H) = 12.6 Hz, 1H), 5.01–5.08 (m, 2H), 5.27 (t, ^3J-(H,H) = 8.4 Hz, 1H), 5.53 (d, ^3J(H,H) = 3.6 Hz, 1H), 7.06–7.65 ppm (m, 40H; ArH); ^{13}C NMR (150 MHz, $CDCl_3$): δ −4.77, −3.81, 18.17, 26.06, 57.55, 62.67, 65.66, 66.94, 67.17, 67.42, 70.68, 72.41, 73.86, 73.91, 74.12, 74.16, 74.86, 75.19, 75.63, 75.71, 76.67, 76.87, 77.55, 82.13, 82.94, 84.19, 97.36, 100.45, 105.04, 137.73–141.06 (aromatic carbon atoms), 164.73, 167.79, 168.44 ppm (carbonyl groups); HRMS: *m*/*z* calcd for $C_{81}H_{89}N_3NaO_{18}Si$ $[M+Na]^+$: 1442.5808; found: 1442.5804.

Acknowledgements

This work was supported by the University of Toledo and the National Institutes of Health (R01-GM-72667).

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Received: March 2, 2006
Published online: April 25, 2006

