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Citation

Zhang, Q. (2018, September 6). *Total synthesis of alginate and zwitterionic SP1 oligosaccharides*. Retrieved from https://hdl.handle.net/1887/65053

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Title: Total synthesis of alginate and zwitterionic SP1 oligosaccharides
Issue Date: 2018-09-06

6

Selective oxidation of primary alcohols to carboxylic acids by use of a two-steps one-pot TEMPO/BAIB-Pinnick oxidation sequence

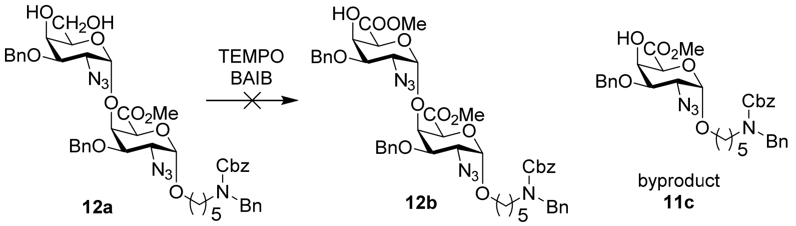
Partly published in: *Org. Lett.* **2017**, *19*, 2514-2517.

6.1 Introduction

Uronic acids are defined as aldoses of which the primary alcohol is oxidized to a carboxylic acid function.[1] They are widespread in nature, where they constitute key components of oligo- and polysaccharides and glycoconjugates, found in all life forms.[1] The structural complexity of oligo- and polysaccharides and glycoconjugates that contain uronic acid, combined with their diverse biological properties, has inspired many chemist to study their synthesis.[2] To obtain these bioactive compounds, two key challenges have to be addressed. The first is the formation of the interglycosidic linkages, which is generally more difficult with uronic acids with respect to their non-oxidized counterparts because of the diminished reactivity of the former, both from a donor and acceptor point of view. Secondly, the primary alcohol has to be oxidized, selectively with respect to all other hydroxyl functionalities, to produce the corresponding uronic acid. This may entail the use of a protecting group strategy, in which the primary alcohol can be selectively unmasked, or, alternatively, a chemoselective oxidation protocol may be called upon to the oxidize the more accessible primary alcohol in the presence of free secondary ones. In execution of the former strategy, a number of methods have been employed for the oxidation of primary alcohols to provide the corresponding uronic acids, including the use of a Swern or Dess-Martin oxidation to generate the intermediate glycosyl aldehyde, followed by a second oxidation using $NaClO_2$ to deliver the acid, the use of chromium based oxidants, such as the Jones oxidation (CrO_3, H_2SO_4) and pyridinium dichromate (Collins reagent, PDC).[3]

The advent of TEMPO (2,2,6,6-tetramethyl-1-piperidinyloxy free radical) mediated oxidation methods, presented a major breakthrough for the generation of glycouronic acids as these systems allowed for the regioselective oxidation of the primary alcohol in the presence of (many) other free secondary alcohols.[4] The original protocol for TEMPO oxidations employs NaOCl as a cooxidant, in a biphasic mixture using a phase transfer catalyst.[5] Although this method has found wide application in the generation of glycuronic acids, the biphasic mixture and the fact that two oxidation steps have to be performed (alcohol to the aldehyde and aldehyde to the acid) can make optimization of this procedure difficult, especially when multiple alcohol have to be transformed into the corresponding acids.[6] Several co-oxidants have been introduced to effect TEMPO mediated oxidations, such as electro-oxidation,[7] *m*-chloroperbenzoic acid,[8] high-valent metal salts,[9] sodium bromite,[10] sodium or calcium hypochlorite,[11] and trichloroisocyanuric acid[12]. Piancatelli then introduced the hypervalent iodine reagent, bisacetoxy iodobenzene (BAIB) as an effective co-oxidant for the selective transformation of primary alcohols into aldehydes.[13] Subsequently, Epp and Widlanski used the TEMPO/BAIB reagent combination to prepare nucleoside-5'-carboxylic acids.[14] Van den Bos *et al.* were the first to explore the use of this reagent couple for the generation of glycosyl uronic acid building blocks for the use in oligosaccharide synthesis and they reported that partially protected thioglycosides could be oxidized in a chemo- and regioselective manner to effectively generate the corresponding glycuronic acid thioglycosides.[15] Since then, the TEMPO/BAIB oxidation system has become one of the popular methods for the oxidation of carbohydrate building blocks and oligosaccharides.

Notwithstanding the success of the TEMPO/BAIB reagent combination, recent complex substrates have proven to be a challenge to effectively oxidize. These include the simultaneous oxidation of multiple primary alcohols to their corresponding acids, such as in Huang's hyaluronic acid oligosaccharide synthesis, in which three alcohols had to be transformed.[16] Chapter 7 of this Thesis presents the assembly of a set of zwitterionic oligosaccharides of *Streptococcus pneumonia*, which also proved challenging substrates for the TEMPO/BAIB oxidation method. Recently, Hagen *et al.* described the synthesis of the trisaccharide repeating unit of the *Staphylococcus aureus* Strain M Capsular Polysaccharide, in which a surprising side reaction plagued the generation of disaccharide **12b** (see Scheme 6.1).[17] During the oxidation of disaccharide **12a**, using the TEMPO/BAIB system, monosaccharide **11c** was formed as the main byproduct, with only small amounts of expected disaccharide **12b**.[17a] The exact mechanism of the formation of **11c** is unclear, but it was observed that the intermediate aldehyde was formed uneventfully.[17a] Consumption of this aldehyde proved to be very slow, and it is likely that the glycosidic bond cleavage event occurs at this stage.[17a] To enable the oxidation of these challenging substrates, a more effective oxidation procedure is required. This Chapter describes the development of a novel TEMPO/BAIB based oxidation system, which is combined in a one-pot two-step protocol with a Pinnick oxidation to effectively transform carbohydrate primary alcohols into the corresponding carboxylic acids.



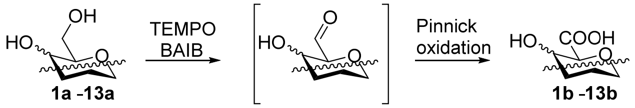
Scheme 6.1 The oxidation reaction of the S. aureus disaccharide **12a** to yield **12b**.

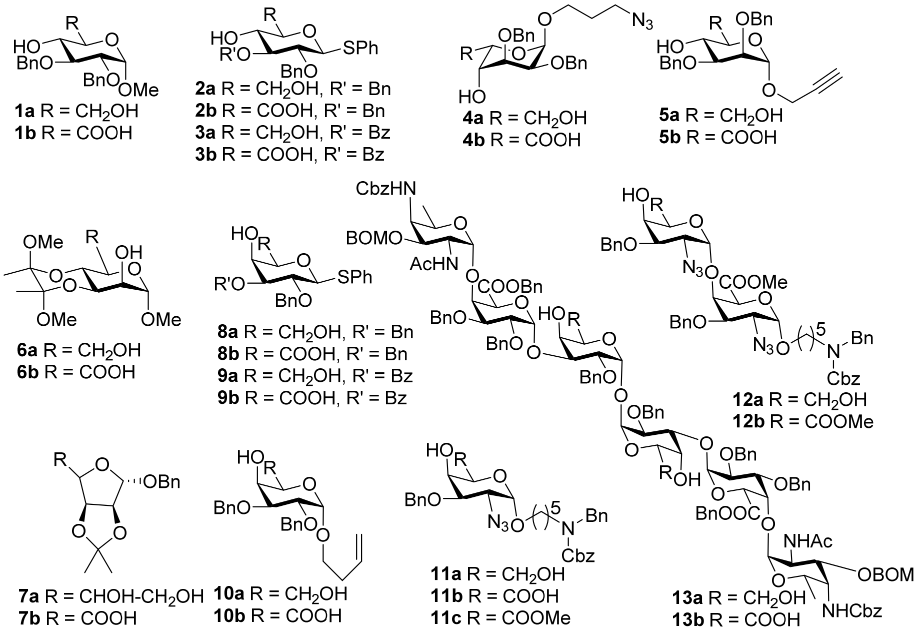
6.2 Results and discussion

The transformation of a primary alcohol into a carboxylic acid entails a two-step transformation: oxidation of the alcohol into the aldehyde and subsequent further oxidation of the aldehyde into the carboxylic acid. For most oxidation procedures an extra intermediate step is required: the formation of the hydrate of the aldehyde, which can engage in the nucleophilic attack of the actual oxidizing species. The low rate of the second oxidation step in the unmodified TEMPO/BAIB reaction may be in part be attributable to the heterogeneity of the reaction mixture (CH_2Cl_2/H_2O) and the slow hydration of the intermediate aldehyde.[17a] Of the many methods that exist for the oxidation of aldehydes to carboxylic acids, the Pinnick oxidation stands out as it is one of the few methods that does not proceed by intermediate hydration of the aldehyde.[18] It was therefore envisaged that an effective oxidation sequence could be developed that combines the advantages of the TEMPO/BAIB system was -the excellent chemo- and regioselectivity in an operationally simple set up- with the power of the Pinnick oxidation: rapid oxidation of aldehydes to the corresponding acids without the need for the formation of the hydrate.

To establish the feasibility of such a TEMPO/BAIB-Pinnick oxidation sequence, glucose diol **1a** was used as a model substrate. First, different conditions were tested for the formation of the aldehyde. Using THF as solvent, the reaction was very slow, requiring two days for completion, owing to the insolubility of BAIB in THF. The use of a mixture of THF and DCM provided a faster reaction (7h) and a mixture of THF/*t*BuOH/DCE led to an even faster reaction (5h). After the subsequent Pinnick oxidation, in the same pot, glucuronic acid **1b** was obtained in 67%, 90% and 87% yield over the two steps, respectively (Table 6.1, Entry 1-3). Using the optimal solvent system, several model carbohydrate diols were oxidized as summarized in Table 6.1. D-Glucose, D-galactose, L-gulose, D-mannose, L-gulofuranose, D-galactose and D-galacto-azide building blocks **2**-**11**, bearing different protecting and functional groups were probed and in each case the regioselectivity of the first oxidation step proved to be excellent and the ensuing Pinnick oxidation effective to deliver the desired carboxylic acids in 60%-87% yield (Entry 4-13). It must be noted, however, that in the case of thioglycosides, a small amount (around 8%) of sulfoxide was found as a byproduct. As TEMPO/BAIB has been shown to be compatible with thiol aglycons, the sulfoxide side products likely arise from the $NaClO_2$-mediated Pinnick oxidation. The oxidation of L-gulofuranose 1,2-diol **7a** led to carbon-carbon bond cleavage and the isolation of the truncated D-ribose carboxylic acid **7b** (Entry 9). When the TEMPO/BAIB-Pinnick protocol was used for the oxidation of disaccharide **12a**, the carboxylic acid was formed successfully, yielding the desired disaccharide **12b**, which can be used for synthesis of the *Staphylococcus aureus* Strain M Capsular Polysaccharide trisaccharide repeating unit, after methylation of the crude carboxylic acid, in a rewarding 84% yield (Entry 14). Finally, the new protocol was applied for the more complex hexasaccharide tetraol **13a**[23], featuring two primary alcohol functionalities (Entry 15). The oxidation of these two alcohols required a longer time for the TEMPO/BAIB step and 0.4 equivalents of TEMPO per alcohol. The desired dicarboxylate **13b**[19] was obtained in 60% yield.

Table 6.1 Substrate Scope of the TEMPO/BAIB–Pinnick Oxidation Sequence





Entry	SM	Time	product	Yield	Entry	SM	Time	product	Yield
1	**1a**	2d	**1b**	67%[a]	9	**7a**	7h	**7b**	87%[d]
2	**1a**	7h	**1b**	90%[b]	10	**8a**	7h	**8b**	73%
3	**1a**	5h	**1b**	87%[c]	11	**9a**	7h	**9b**	73%
4	**2a**	10h	**2b**	81%	12	**10a**	4h	**10b**	84%[c]
5	**3a**	7h	**3b**	74%	13	**11a**	6h	**11b**	80%
6	**4a**	7h	**4b**	82%	14	**12a**	5h	**12b**	84%
7	**5a**	5h	**5b**	87%	15	**13a**	2d	**13b**	60%[c]
8	**6a**	7h	**6b**	85%					

[a]THF as solvent, [b] THF/DCM as solvent, [c] 0.4 eq TEMPO per primary alcohol, THF/*t*BuOH/DCE as solvent; [d] from carbon-carbon bond cleaved byproduct.

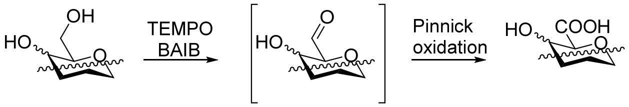
6.3 Conclusion

A novel two-step one-pot TEMPO/BAIB-Pinnick oxidation protocol was invented to allow for the effective regioselective oxidation of primary alcohols to give the corresponding acids. The protocol was successfully applied for synthesis of the *Staphylococcus aureus* Strain M Capsular Polysaccharide trisaccharide repeating unit and for complex hexasaccharide tetraol **13a**, which represents a model system for the synthesis of larger zwitterionic polysaccharide **SP1** repeating units as described in Chapter 7 of this Thesis.

6.4 Experimental section

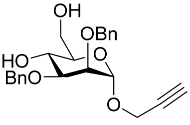
All reagents were of commercial grade and used as received. All moisture sensitive reactions were performed under an argon atmosphere. Reactions were monitored by TLC analysis with detection by UV (254 nm) and where applicable by spraying with 20% sulfuric acid in EtOH or with a solution of $(NH_4)_6Mo_7O_{24}\cdot4H_2O$ (25 g/L) and $(NH_4)_4Ce(SO_4)_4\cdot2H_2O$ (10 g/L) in 10% sulfuric acid (aq.) followed by charring at ~150 °C. Flash column chromatography was performed on silica gel (40-63µm). ^1H and ^{13}C spectra were recorded on a Bruker AV 400, Bruker AV 600 in $CDCl_3$ or CD_3OD. Chemical shifts (δ) are given in ppm relative to tetramethylsilane as internal standard (^1H NMR in $CDCl_3$) or the residual signal of the deuterated solvent. Coupling constants (*J*) are given in Hz. All ^{13}C spectra are proton decoupled. NMR peak assignments were made using COSY and HSQC experiments. Where applicable NOESY, HMBC, HMBC and GATED experiments were used to further elucidate the structure.

General procedure for the TEMPO/$PhI(OAc)_2$-Pinnick oxidation sequence.



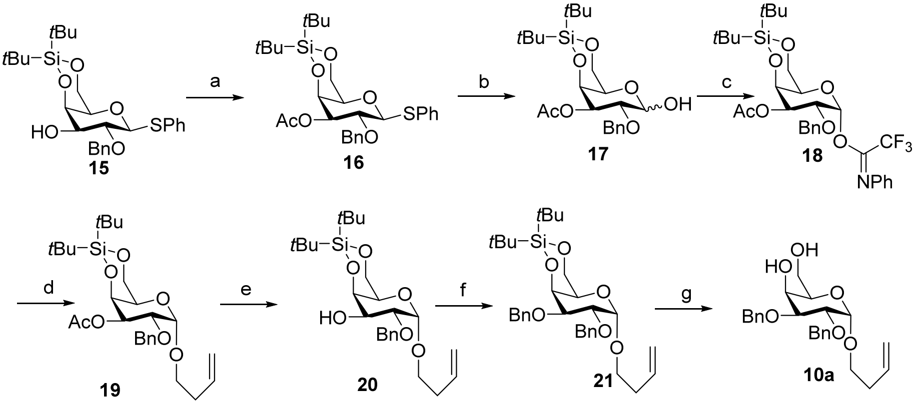
To a stirred solution of the carbohydrate (0.2 mmol, 1.0 eq.) in THF/CH_2Cl_2 (2:1 v/v, 2 mL, 0.1 M) was added, at 0 °C, TEMPO (6.3 mg, 0.04 mmol, 0.2 eq.) and $PhI(OAc)_2$ (64 mg, 0.2 mmol, 1.0 eq) and the reaction mixture was allowed to warm to room temperature. After 1 hour, a second portion of $PhI(OAc)_2$ (26 mg, 0.08 mmol, 0.4 eq.) was added and the reaction mixture was stirred until TLC analysis (usually CH_2Cl_2/MeOH, 20:1 v/v) indicated complete conversion of the starting material (see Table 2). Then, *tert*-butanol (0.5 mL) and *iso*-amylene (0.05 mL) were added and the reaction mixture was cooled to 0 °C. A solution of $NaClO_2$ (36 mg, 0.4 mmol, 2.0 eq.) and

NaH_2PO_4 (48 mg, 0.4 mmol, 2.0 eq.) in water (0.2 mL) was slowly added and the reaction mixture was allowed to stir for 1 hour at 0 °C. The reaction was quenched by addition of sat. aq. $Na_2S_2O_3$, and the mixture diluted with EtOAc, and NaH_2PO_4 (sat. aq., 0.5 mL) and brine (1 mL) were subsequently added. The layers were separated, and the aqueous phase was extracted with EtOAc. The combined organic phases were dried over $MgSO_4$, filtered and concentrated *in vacuo*. Column chromatography (generally, CH_2Cl_2/MeOH/AcOH, 200:1:0 → 200:10:1) furnished the corresponding uronic acid.



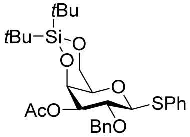
Propargyl 2,3-di-*O*-benzyl-α-D-mannopyranoside (5a): Propargyl 4,6-O-benzylidene- α-D-mannopyranoside[20] (306 mg, 1 mmol) was dissolved in DMF (4 ml) and then NaH (60% in oil, 120 mg, 3 mmol) was added at 0°C. After 15 min, BnBr (475 ul, 4 mmol) was added to the reaction mixture and stirred for overnight. The reaction was quenched by adding water. Then diluted with EtOAc, washed with brine, dried over Na_2SO_4 and concentrated *in vacuo*. The crude product was dissolved in MeOH (10 ml) and TsOH•H_2O (PH = 2) was added to the reaction mixture and stirred for overnight. The reaction was quenched with Et_3N and concentrated *in vacuo*. Purification by column chromatography. Yield: 261 mg (0.66 mmol), 66% over two steps. ^1H NMR (400 MHz, $CDCl_3$) δ 7.41 – 7.22 (m, 10H, C*H*$_{arom}$), 5.03 (d, *J* = 1.7 Hz, 1H, H-1), 4.64 (s, 2H, Ph*H*$_2$), 4.52 (q, *J* = 11.8 Hz, 2H, Ph*H*$_2$), 4.16 (t, *J* = 2.1 Hz, 2H, -OC*H*$_2$C≡CH), 4.04 (t, *J* = 9.7 Hz, 1H, H-4), 3.87 – 3.73 (m, 3H, H-2, H-6), 3.69 (dd, *J* = 9.6, 3.1 Hz, 1H, H-3), 3.58 (m, 1H, H-5), 3.27 (bs, 1H, -OH), 2.89 (bs, 1H, -OH), 2.42 (t, *J* = 2.4 Hz, 1H, -OCH$_2$C≡C*H*). ^{13}C NMR (100 MHz, $CDCl_3$) δ 138.13, 137.90 (C$_q$), 128.45, 127.97, 127.69(CH$_{arom}$), 96.69 (C-1), 79.41 (C-3), 78.82 (-OCH$_2$*C*≡CH), 75.03 (-OCH$_2$C≡*C*H), 73.94 (C-2), 73.00 (C-5), 72.87 (Bn), 71.84 (Bn), 66.88 (C-4), 62.35 (C-6), 54.26 (-O*C*H$_2$C≡CH). $[\alpha]^{20}_D$ = 23° (c = 1.0, $CHCl_3$). IR (neat): 698, 739, 1028, 1043, 1074, 1118, 1366, 1454, 2919, 3279, 3450. HR-MS: $[M+H^+]$ Calculated for C23H26O6: 399.18022; found: 399.18018.

Scheme 6.1 Synthesis of compounds **10a**

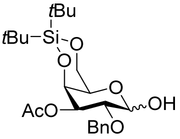


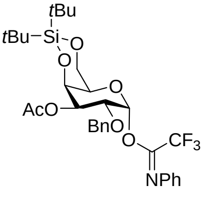
Reagents and conditions: (a) Ac_2O, pyridine, 99%; (b) NIS, TFA, DCM, 91%; (c) *N*-phenyl trifluoroacetimidoyl chloride, K_2CO_3, acetone, 92%; (d) 3-buten-1-ol, TBSOTf, DCM, 94%, α:β = 25:1; (e) NaOMe, MeOH, 94%; (f) NaH, BnBr, DMF, 70%, (g) HF/pyridine, THF, pyridine, 96%.

2-*O*-benzyl-3-*O*-acetyl-4,6-di-*tert*-butylsilylidene-1-thio-β-D-galactopyranoside (16): The compound **15**[19] (1.01 g, 2 mmol) was dissolved in pyridine (4 ml), Ac_2O was added in the reaction mixture at 0 °C, and then DMAP (24 mg, 0.2 mmol) was added to the reaction mixture. The reaction was allowed to stir at room temperature for overnight. The reaction was concentrated *in vacuo*. Purification by column chromatography (PE:EA, 20:1 to 10:1). Yield: 1.048 g, 66%. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.54 (dd, *J* = 7.8, 1.8 Hz, 2H), 7.45 – 7.12 (m, 8H), 4.95 (d, *J* = 10.8 Hz, 1H), 4.86 – 4.54 (m, 4H, H-3, H-1, H-4), 4.32 – 4.10 (m, 2H, H-6), 3.90 (t, *J* = 9.6 Hz, 1H, H-2), 3.41 (d, *J* = 2.1 Hz, 1H, H-5), 2.07 (s, 3H), 1.12 (s, 9H), 1.01 (s, 9H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 170.67, 138.11, 132.22, 128.93, 128.45, 128.15, 127.90, 127.58, 88.64 (C-1), 77.36 (C-3), 75.78, 75.77 (C-2), 74.49 (C-5), 70.29 (C-4), 67.21 (C-6), 27.66, 27.62, 23.33, 21.06, 20.78. IR (neat): 651, 692, 745, 827, 971, 1044, 1090, 1166, 1238, 1363, 1473, 1739, 2859, 2933. HR-MS: [M+H$^+$] Calculated for $C_{29}H_{40}SSiO_6$: 545.2388; found: 545.2387.

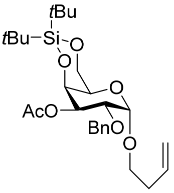


2-*O*-benzyl-3-*O*-acetyl-4,6-di-*tert*-butylsilylidene-α/β-D-galactopyranoside (17): The compound **16** (1.16 g, 2.129 mmol) was dissolved in DCM (20 ml), NIS (527 mg, 2.342 mmol) was added in the reaction mixture at 0 °C, and then TFA (174 ul, 2.342 mmol) was added to the reaction mixture. After analysis by TLC showed complete consumption of the starting material, the reaction was quenched with Et_3N. Saturated $Na_2S_2O_3$ (aq) was added to the reaction mixture, which was then stirred for 30 min. The aqueous layer was extracted twice with CH_2Cl_2 and concentrated *in vacuo*. Purification by column chromatography (silica gel, pentane/DCM/EtOAc, 3/1/1, v/v/v) yielded **17** as a colourless oil (880 mg, 91%, α:β = 3.5:1). TLC: R_f = 0.15 (pentane/DCM/EtOAc, 3/1/1, v/v/v). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.41 – 7.26 (m, 5H), 5.23 (d, *J* = 3.6 Hz, 0.75H, H-1α), 5.06 (dd, *J* = 10.2, 3.0 Hz, 0.75H, H-3α), 4.90 (d, *J* = 11.4 Hz, 0.22H, H-3β), 4.81 – 4.54 (m, 3H,H-4α, H-4β), 4.28 – 4.19 (m, 1H, H-6), 4.13 (dd, *J* = 12.6, 1.7 Hz, 0.75H, H-6), 4.06 – 3.90 (m, 2H, H-2α, H-5α), 3.75 (dd, *J* = 9.9, 7.6 Hz, 0.22H, H-2β), 3.49 (q, *J* = 1.6 Hz, 0.23H, H-5β), 2.96 (bs, 1H), 2.11 (s, 2.22H), 2.09 (s, 0.56H), 1.07 (s, 1.88H), 1.00 (m, 15H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 170.87, 128.67, 128.51, 128.24, 128.07, 127.89, 97.72 (C-1β), 92.06 (C-1α), 77.22 (C-2β), 75.63 (C-3β), 75.03, 73.68 (C-2α), 73.19 (C-3α), 72.74, 71.37 (C-5β), 71.02 (C-4α), 70.26 (C-4β, 67.18 (C-6α), 67.14 (C-5α), 67.09 (C-6β), 27.67, 27.64, 27.50, 27.37, 23.40, 21.21, 20.78. HR-MS: [M+Na$^+$] Calculated for $C_{23}H_{36}SiO_7$: 475.2123; found: 475.2126.

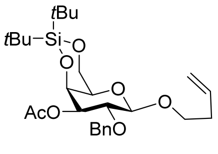




2-*O*-benzyl-3-*O*-acetyl-4,6-di-*tert*-butylsilylidene-1-*O*-(*N*-phenyl trifluoroacetimidoyl)-α/β-D-galactopyranoside (18): The compound **17** (0.87 g, 1.922 mmol) was dissolved in acetone (10 ml), K_2CO_3 (318 mg, 2.31 mmol) was added to reaction mixture at 0 °C. After 15 min, *N*-phenyl trifluoroacetimidoyl chloride (599 mg, 2.883 mmol) was added to the reaction mixture at 0 °C, and then it was allowed to stir for overnight at room temperature. Then, Et_3N was added to the reaction mixture, which was filtered and the resulting filtrate was concentrated *in vacuo*. Purification by column chromatography (silica gel, pentane/EtOAc, 50/1 to 10/1, v/v) yielded **18** as a colourless syrup (1.102 g, 92%, α:β = 2:1). 18**α** (at 50 °C) ^{1}H NMR (500 MHz, Chloroform-*d*) δ 7.38 – 7.16 (m, 5H), 7.07 (td, *J* = 7.5, 1.1 Hz, 1H), 6.74 (d, *J* = 7.8 Hz, 2H), 6.47 (bs, 1H, H-1), 5.09 (dd, *J* = 10.3, 2.9 Hz, 1H, H-3), 4.79 (d, *J* = 2.9 Hz, 1H, H-4), 4.71 (s, 2H), 4.30 – 4.08 (m, 3H, H-6, H-2), 3.90 (s, 1H, H-5), 2.09 (d, *J* = 0.9 Hz, 3H), 1.01 (d, *J* = 0.9 Hz, 9H), 0.97 (s, 9H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 170.60, 143.88, 137.90, 128.87, 128.62, 128.10, 128.02, 124.37, 119.63, 94.66 (C-1), 73.64, 72.77 (C-3), 72.09 (C-2), 70.65 (C-4), 69.74 (C-5), 66.85 (C-6), 27.71, 27.35, 23.40, 21.02, 20.86. HR-MS: $[M+Na^+]$ Calculated for $C_{31}H_{40}N_3O_7F_3Si$: 646.2418; found: 646.2421.

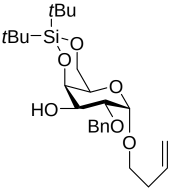


3-butenyl 2-*O*-benzyl-3-*O*-acetyl-4,6-di-*tert*-butylsilylidene-α-D-mannopyranoside (19): Imidate donor **18α** (680 mg, 1.09 mmol) and acceptor allyl carbinol (293 ul, 3.386 mmol) were co-evaporated with toluene (three times). The residue was dissolved in dry DCM (11 ml). The solution was cooled to 0 °C and TBSOTf (51 ul, 0.22 mmol) was added, after which the reaction was allowed to stir for 1 h. TLC show the reaction was finish. Then the reaction was quenched with Et_3N and diluted with EtOAc, washed with sat. aq. NaCl and the organic phase was dried over Na_2SO_4 and concentrated *in vacuo*. Purification by column chromatography (silica gel, pentane/EtOAc, 20/1, v/v) yielded **20** as a colourless syrup (520 mg, 94%, α:β = 25:1). TLC: R_f = 0.63 (pentane/ EtOAc, 8/1, v/v). ^{1}H NMR (500 MHz, Chloroform-*d*) δ 7.41 – 7.28 (m, 5H), 5.81 (m, 1H), 5.15 – 4.92 (m, 3H, H-3), 4.79 – 4.67 (m, 4H, H-1, H-4), 4.61 (d, *J* = 12.2 Hz, 1H), 4.21 (dd, *J* = 12.6, 2.2 Hz, 1H, H-6), 4.09 (dd, *J* = 12.6, 1.7 Hz, 1H, H-6), 4.02 (dd, *J* = 10.4, 3.6 Hz, 1H, H-2), 3.74 (bs, 1H, H-5), 3.65 (m, 1H), 3.49 (m, 1H), 2.44 – 2.27 (m, 2H), 2.10 (s, 3H), 1.00 (s, 9H), 0.98 (s, 9H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 170.83, 138.32, 135.03, 128.52, 128.28, 127.99, 116.83, 97.85 (C-1), 73.31, 72.88 (C-3), 72.62 (C-2), 71.02 (C-4), 67.72, 67.09 (C-6), 66.88 (C-5), 33.98, 27.68, 27.33, 23.39, 21.19, 20.74. IR (neat): 650, 698, 737, 764, 798, 826, 863, 909, 977, 994, 1002, 1005, 1030, 1039, 1079, 1104, 1150, 1173, 1237, 1363, 1473, 1739, 2858, 2933. HR-MS: $[M+H^+]$ Calculated for $C_{27}H_{42}SiO_7$: 529.2592; found: 529.2590.

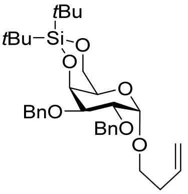


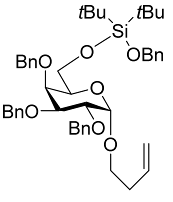
^{1}H NMR (500 MHz, Chloroform-*d*) δ 7.33 (d, *J* = 3.8 Hz, 5H), 5.85 (m, 1H), 5.19 – 4.99 (m, 2H), 4.89 (d, *J* = 11.5 Hz, 1H), 4.70 – 4.68 (m, 1H, H-3), 4.68 – 4.63 (m, 2H), 4.59 (dd, *J* = 3.2, 0.9 Hz, 1H, H-4), 4.43 (d, *J* = 7.7 Hz, 1H, H-1), 4.21 (m, 2H, H-6), 3.98 (m, 1H), 3.75 (dd, *J* = 10.0, 7.7 Hz, 1H, H-2), 3.59 (m, 1H), 3.40 (bs, 1H, H-5), 2.45 – 2.31 (m, 2H), 2.07 (s, 3H), 1.05 (s, 9H), 1.00 (s, 9H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 170.92, 138.75, 135.33, 128.35, 128.01, 127.66, 116.52, 103.61 (C-1), 75.98 (C-2), 75.49 (C-3), 74.90, 70.83 (C-5), 70.31 (C-4), 68.91, 67.16 (C-6), 34.43, 27.61, 27.53, 23.38, 21.08, 20.83.

3-butenyl 2-*O*-benzyl-4,6-di-*tert*-butylsilylidene-α-D-mannopyranoside (20): The compound **19** (665 mg, 1.312 mmol) was dissolved in MeOH (15 ml). The solution was cooled to 0 °C and NaOMe in MeOH solution (4 drops) was added, after which the reaction was allowed to stir for overnight at room temperature. TLC show the reaction was finish. Then the reaction was quenched with Amberlite IR120 (H^+) resin. After filtration, the filtrate was concentrated *in vacuo*. Purification by column chromatography (silica gel, pentane/EtOAc, 8/1, v/v) yielded **20** as a colourless syrup (571 mg, 94). TLC: R_f = 0.20 (pentane/ EtOAc, 8/1, v/v). ^{1}H NMR (500 MHz, Chloroform-*d*) δ 7.40 – 7.22 (m, 5H), 5.89 – 5.69 (m, 1H), 5.15 – 4.94 (m, 2H), 4.82 (d, *J* = 12.0 Hz, 1H), 4.76 (d, *J* = 3.5 Hz, 1H, H-1), 4.69 (d, *J* = 12.0 Hz, 1H), 4.43 (d, *J* = 3.5 Hz, 1H, H-4), 4.25 (d, *J* = 12.5 Hz, 1H, H-6), 4.15 (d, *J* = 12.5 Hz, 1H, H-6), 3.96 (m, 1H, H-3), 3.72 (s, 1H, H-5), 3.70 – 3.56 (m, 2H, H5, H-2), 3.50 – 3.38 (m, 1H), 2.35 (q, *J* = 7.1 Hz, 2H), 1.10 – 0.98 (m, 9H), 0.99 – 0.85 (m, 9H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 138.36, 135.07, 128.55, 128.37, 127.97, 116.83, 97.65 (C-1), 75.87 (C-2), 73.73 (C-4), 73.04, 69.84 (C-3), 67.63, 67.07 (C-5), 67.03 (C-6), 33.99, 27.68, 27.32, 23.47, 20.75. IR (neat): 649, 762, 797, 827, 862, 917, 974, 997, 1030, 1037, 1085, 1121, 1167, 1232, 1345, 1363, 1473, 2859, 2933. HR-MS: [M+Na$^+$] Calculated for $C_{25}H_{40}SiO_6$: 487.2486; found: 487.2490.



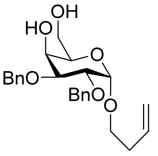
3-butenyl 2,3-di-*O*-benzyl-4,6-di-*tert*-butylsilylidene-α-D-mannopyranoside (21): The compound **20** (186 mg, 0.4 mmol) was dissolved in DMF (2 ml). The solution was cooled to 0 °C and NaH (60% in mineral oil, 32 mg, 0.8 mmol) was added, after which the reaction was allowed to stir for overnight at room temperature. Then the reaction was quenched with H_2O and diluted with EtOAc, washed with sat. aq. NaCl and the organic phase was dried over Na_2SO_4 and concentrated *in vacuo*. Purification by column chromatography (silica gel, pentane/EtOAc, 50/1, v/v) yielded **21** as a colourless syrup (156 mg, 70%). (And also found byproduct) TLC: R_f = 0.63 (pentane/EtOAc, 10/1, v/v). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.50 – 7.19 (m, 10H), 5.79 (m, 1H), 5.11 – 4.97 (m, 2H), 4.87 (d, *J* = 12.0 Hz, 1H), 4.73 (d, *J* = 2.2 Hz, 3H, H-1), 4.67 (d, *J* = 12.0 Hz, 1H), 4.50 (dd, *J* = 3.1, 1.0 Hz, 1H, H4), 4.26 (d, 12.5, 1H, H-6), 4.14 (d, 12.5, 1H, H-6), 3.98 (dd, *J* = 10.0, 3.7 Hz, 1H, H-2), 3.82 (dd, *J* = 10.1, 3.0 Hz, 1H, H-3), 3.63 (m, H-5), 3.52 (m, 1H), 2.45 – 2.25 (m, 2H), 1.06 (s, 9H), 0.99 (s, 9H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 139.12, 138.75, 135.08, 128.38, 128.36, 128.30, 127.70, 127.67, 127.50, 116.68, 98.10 (C-1), 77.73 (C-3), 74.35 (C-2), 73.65, 71.31 (C-4), 71.15, 67.53 (C-6), 67.34 (C-5), 67.29, 33.96, 27.75, 27.41, 23.51, 20.74. IR (neat): 697, 735, 764, 798, 827, 861, 915, 977, 1068, 1097, 1148, 1363, 2858, 2933. HR-MS: [M+Na$^+$] Calculated for $C_{32}H_{46}SiO_6$: 577.2956; found: 577.2957.



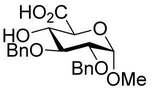


The byproduct: ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.50 – 7.11 (m, 20H), 5.78 (m, 1H), 5.12 – 4.97 (m, 2H), 4.97 – 4.88 (m, 3H), 4.87 (s, 1H), 4.83 (s, 1H, H-1), 4.81 (d, *J* = 8.5 Hz, 1H), 4.73 (d, *J* = 11.8 Hz, 1H), 4.67 (d, *J* = 12.1 Hz, 1H), 4.59 (d, *J* = 11.4 Hz, 1H), 4.03 (dd, *J* = 10.0, 3.6 Hz, 1H, H-2), 3.98 – 3.91 (m, 2H, H-3, H-6), 3.88 (d, *J* = 2.8 Hz, 1H, H-4), 3.82 – 3.72 (m, 2H, H-5, H-6), 3.65 (m, 1H), 3.47 (m, 1H), 2.36 (m, 2H), 1.04 (s, 18H). ^{13}C NMR (101 MHz, CDCl$_3$) δ 141.20, 139.05, 138.83, 138.81, 135.03, 128.46, 128.40, 128.32, 128.24, 128.05, 127.71, 127.62, 127.60, 126.98, 125.81, 116.73, 97.34 (C-1), 79.18 (C-3), 76.76 (C-2), 75.41 (C-4), 74.86, 73.40, 73.36, 71.45 (C-5), 67.11, 65.57, 63.33 (C-6), 33.95, 28.05, 21.39, 21.34.

3-butenyl 2,3-di-*O*-benzyl-α-D-mannopyranoside (5a): HF/Pyridine solution (100 ul) was added to a solution of compound **21** (104 mg, 0.187 mmol) in a mixture of THF (1 ml) and pyridine(1 ml) at 0 °C. The reaction was allowed to stir 2h at room temperature. Then, a sat. aq. NaHCO$_3$ was added to neutralize the mixture, which was diluted with EtOAc, washed with sat. aq. NaCl. The organic phase was dried over Na$_2$SO$_4$ and concentrated *in vacuo*. Purification by column chromatography (silica gel, DCM/MeOH, 50/1, v/v) yielded **5a** as a colourless oil (75 mg, 96%). TLC: R$_f$ = 0.26 (DCM/MeOH, 20/1, v/v); ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.41 – 7.28 (m, 10H), 5.82 (m, 1H), 5.15 – 5.01 (m, 2H, H-1), 4.88 – 4.76 (m, 3H), 4.67 (dd, *J* = 16.6, 11.8 Hz, 2H), 4.08 (dd, *J* = 3.2, 1.3 Hz, 1H, H-4), 3.96 – 3.73 (m, 5H, H-3, H-2, H-5), 3.68 (m, 1H), 3.51 (m, 1H), 2.48 – 2.30 (m, 2H). ^{13}C NMR (101 MHz, CDCl$_3$) δ 138.52, 138.19, 134.99, 128.65, 128.53, 128.08, 128.06, 127.98, 127.95, 127.93, 116.92, 97.42 (C-1), 77.48 (C-3), 75.83 (C-2), 73.40, 73.07, 69.36 (C-4), 69.07 (C-5), 67.59, 63.26 (C-6), 33.95. IR (neat): 696, 733, 736, 914, 967, 999, 1036, 1070, 1094, 1145, 1207, 1347, 1458, 2912, 3445. HR-MS: [M+Na^{+}] Calculated for $C_{33}H_{38}N_4O_8$: 437.1935; found: 437.1943.

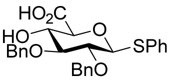


Methyl 2,3-di-O-benzyl-α-D-glucopyranosiduronic acid (1b):



The title compound was obtained from **1a** in 87% yield (68 mg, 0.17 mmol). ^{1}H NMR (400 MHz) δ: 7.44-7.27 (m, 10H, C*H*$_{arom}$); 4.91 (d, 1H, *J* = 11.3 Hz, PhC*H*H); 4.86-4.74 (m, 2H, PhC*H*$_2$); 4.71-4.57 (m, 2H, H-1, PhCH*H*); 4.16 (d, 1H, *J* = 9.5 Hz, H-5); 3.84 (d, 1H, *J* = 9.0 Hz, H-3); 3.77 (d, 1H, *J* = 9.1 Hz, H-4); 3.52 (dd, 1H, *J* = 3.4 Hz, 9.3 Hz, 1H, H-2); 3.42 (s, 3H, OC*H*$_3$). ^{13}C-APT NMR (100 MHz, CDCl$_3$) δ 172.9 (C-6); 138.5, 137.9 (C$_{q,arom}$); 128.7, 128.3, 128.3, 128.2, 128.04 (*C*H$_{arom}$); 98.8 (C-1); 80.4 (C-3); 78.4 (C-2); 75.7, 73.8 (Ph*C*H$_2$);71.7 (C-4); 69.7 (C-5); 56.2 (O*C*H$_3$). IR (neat) ν: 2932, 1724, 1452, 1274, 1097, 1053, 1028, 989. HR-MS: [M+H]$^{+}$ calculated for $C_{21}H_{24}O_7$: 389.15948; found 389.15940.

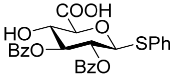
Phenyl 2,3-di-O-benzyl-1-thio-β-D-glucopyranosiduronic acid (2b):



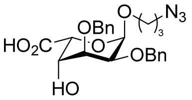
The title compound was obtained from **2a** in 81% yield (76 mg, 0.16 mmol). ^{1}H NMR (400 MHz) δ: 7.59 (dd, 2H, *J* = 2.3, 7.3 Hz, C*H*$_{arom}$); 7.47-7.30 (m, 13H, C*H*$_{arom}$); 4.96 (d, 1H, *J* = 11.1 Hz, PhCH*H*); 4.92-4.84 (m, 2H, PhC*H*$_2$); 4.79 (d, 1H, *J* = 10.3 Hz, PhCH*H*); 4.75 (d, 1H, *J* = 9.8 Hz, H-1); 3.94-3.83 (m, 2H, H-4, H-5); 3.66 (t, 1H, *J* = 8.2 Hz, H-3); 3.51 (t, 1H, *J* = 9.2 Hz, H-2). ^{13}C-APT NMR

(100 MHz) δ 172.2 (C-6); 138.7, 137.8, 132.9 ($C_{q,arom}$); 132.5, 129.2, 128.5, 128.5, 128.5, 128.3, 128.1, 128.0, 128.0, 127.9, 127.9 (CH_{arom}); 88.1 (C-1); 85.3 (C-3); 79.6 (C-2); 76.8 (C-5); 75.7, 75.6 ($PhCH_2$); 71.95 (C-4). IR (neat) ν: 2928, 1732, 1356, 1132, 1067, 1026. HR-MS: $[M+H]^+$ calculated for $C_{26}H_{26}O_6S$: 467.15229; found 467.15220.

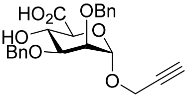
2,3-di-*O*-benzoyl-α-1-*thio*-phthyl-D-glcpyranose uronic acid (3b): This product was prepared following general procedure for selective oxidation of primary alcohol to carboxylic acid by use of two steps one-pot TEMPO/BAIB-Pinnick oxidation. TLC: R_f = 0.19 (DCM:MeOH:AcOH = 20:2:0.1). Yield: 73 mg (0.15 mmol), 74%.^{1}H NMR (500 MHz, $CDCl_3$) δ 8.02 – 7.91 (m, 2H, CH_{arom}), 7.86 (d, *J* = 7.9 Hz, 2H, CH_{arom}), 7.58 – 7.12 (m, 11H, CH_{arom}), 5.70 (t, *J* = 9.4 Hz, 1H, H-3), 5.39 (t, *J* = 9.7 Hz, 1H, H-2), 5.05 (d, *J* = 10.0 Hz, 1H, H-1), 4.17 (d, *J* = 9.8 Hz, 1H, H-5), 4.08 (d, *J* = 9.5 Hz, 1H, H-4). ^{13}C NMR (125 MHz, $CDCl_3$) δ 171.4 (-COOH), 166.64, 165.35 (Bz), 133.52, 133.46, 133.01 (CH_{arom}), 131.96 (C_q), 130.04, 129.98, 129.25, 129.21, 129.03, 128.53, 128.48 (CH_{arom}), 86.67 (C-1), 77.51 (C-5), 76.03 (C-3), 70.41 (C-4), 70.05 (C-2). $[\alpha]^{20}_D$ = 79° (c = 1.0, $CHCl_3$). IR (neat): 691, 708, 750, 1026, 1069, 1086, 1134, 1274, 1728. HR-MS: $[M+Na^+]$ Calculated for $C_{26}H_{22}O_8S$: 517.09276; found: 517.09244.



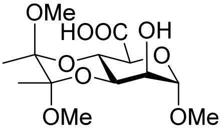
3-azidopropyl 2,3-di-O-benzyl-α-L-gulopyranosiduronic acid (**4b**): The title compound was obtained from **4a** in 82% yield (17 mg, 0.037 mmol). ^{1}H NMR (500 MHz) δ: 7.38-7.26 (m, 10H, CH_{arom}); 4.94 (s, 1H, H-1); 4.82 (d, 1H, *J* = 11.8 Hz, PhCHH); 4.75 (s, 1H, H-5); 4.64-4.57 (m, 3H, $PhCH_2$); 4.27 (s, 1H, H-4); 3.83 (bs, 3H, H-2, H-3, $OCHH_{propyl}$); 3.46 (s, 1H, $OCHH_{pentyl}$); 3.33 (d, 2H, *J* = 5.7 Hz, $N_3CH_{2,propyl}$); 1.84 (m, 2H, $CH_{2,propyl}$). ^{13}C NMR (126 MHz) δ: 172.9 (C-6); 138.4, 137.9 ($C_{q,arom}$); 129.1, 128.5, 128.3, 127.9, 127.7, 127.0 (CH_{arom}); 98.0 (C-1); 75.4 (C-3); 73.0 (C-2, $PhCH_2$); 71.8 ($PhCH_2$); 69.6 (C-4); 68.2 (C-5); 65.4 ($OCH_{2,propyl}$); 48.1 ($N_3CH_{2,propyl}$); 28.9 ($CH_{2,propyl}$). IR (neat) ν: 2924, 2096, 1732, 1454, 1258, 1209, 1116, 1086, 1070, 1037, 1028. HR-MS: $[M+H]^+$ calculated for $C_{23}H_{27}N_3O_7$: 458.19218; found 458.19219.



Propargyl 2,3-di-O-benzyl-α-D-mannopyranosiduronic acid (**5b**): The title compound was obtained from **5a** in 87% yield (74 mg, 0.17 mmol). ^{1}H NMR (500 MHz) δ: 7.37-7.25 (m, 10H, CH_{arom}); 5.12 (d, 1H, *J* = 1.7 Hz, H-1); 4.75-4.55 (m, 4H, $PhCH_2$); 4.33-4.16 (m, 3H, H-4, $OCH_{2,propargyl}$); 4.13 (d, 1H, *J* = 9.8 Hz, H-5); 3.81-3.72 (m, 2H, H-2, H3). ^{13}C-APT NMR (125 MHz) δ: 172.4 (C-6); 138.2, 137.9 ($C_{q,arom}$); 128.4, 128.0, 128.0, 127.8, 127.7, 127.7 (CH_{arom}); 97.6 (C-1); 78.6 ($C_{q,propargyl}$); 78.4 (C-3); 75.4 ($CH_{propargyl}$); 74.3 (C-2); 73.3, 72.8 ($PhCH_2$); 71.3 (C-5); 68.5 (C-4); 55.4 ($CH_{2,propargyl}$). IR (neat) ν: 3280, 2922, 1728, 1454, 1358, 1250, 1207, 1121, 1072, 1043. HR-MS: $[M+H]^+$ calculated for $C_{23}H_{24}O_7$: 413.15948; found 413.15946.

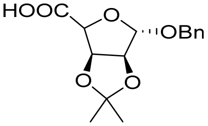


Methyl 3,4-dimethoxybutan-α-D-mannopyranose uronic acid (6b): This product was prepared following general procedure for selective oxidation of primary alcohol to carboxylic acid by use of two steps one-pot TEMPO/BAIB-Pinnick oxidation. TLC: R_f = 0.14 (DCM:MeOH:AcOH = 15:1:0.1). Yield: 82 mg (0.25 mmol), 85%. ^{1}H NMR (400 MHz, CD_3CN) δ 4.68 (d, *J* = 1.2

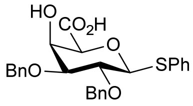


Hz, 1H, H-1), 4.18 – 4.04 (m, 1H, H-4), 3.99 (d, *J* = 10.0 Hz, 1H, H-5), 3.87 – 3.75 (m, 2H, H-2, H-3), 3.36 (s, 3H, -OMe), 3.21 (s, 3H, -OMe), 3.19 (s, 3H, -OMe), 1.26 (s, 3H, -CH$_3$), 1.20 (s, 3H, -CH$_3$). ^{13}C NMR (101 MHz, CD$_3$CN) δ 170.22 (-*C*OOH), 103.23 (C-1), 100.97, 100.63, 70.85 (C-5), 69.43 (C-2), 68.28 (C-3), 65.35 (C-4), 55.68 (-OMe), 48.15 (-OMe), 18.03 (-CH$_3$). $[\alpha]^{20}_{D}$ = 192° (c = 1.0, CHCl$_3$). IR (neat): 754, 885, 982, 1047, 1076, 1113, 1215, 1379, 1741, 2947, 3460. HR-MS: [M+Na$^+$] Calculated for $C_{13}H_{22}O_9$: 345.11560; found: 345.11553.

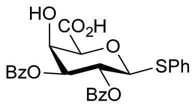
2,3-isopropyl-α-D-lyxose uronic acid (7b): This sideproduct was obtained following general procedure for selective oxidation of primary alcohol to carboxylic acid by use of two steps one-pot TEMPO/BAIB-Pinnick oxidation. Yield: 77 mg, 87%. ^{1}H NMR (500 MHz, CDCl$_3$) δ 7.40 – 7.27 (m, 5H, C*H*$_{arom}$), 5.29 (s, 1H), 5.07 (dd, *J* = 5.8, 4.3 Hz, 1H, H-2), 4.78 – 4.64 (m, 3H, H-3, H-4, PhH*H*), 4.52 (d, *J* = 11.7 Hz, 1H, PhH*H*), 1.46 (s, 3H, -CH$_3$), 1.31 (s, 3H, -CH$_3$). ^{13}C NMR (125 MHz, CDCl$_3$) δ 171.52 (-*C*OOH), 136.81 (C$_q$), 128.64, 128.20 (CH$_{arom}$), 113.64, 105.83 (C-1), 84.28 (C-4), 80.53 (C-2), 79.58 (C-3), 69.56 (Bn), 26.00 (-CH$_3$), 24.98 (-CH$_3$). $[\alpha]^{20}_{D}$ = 46° (c = 1.0, CHCl$_3$). IR (neat): 700, 737, 860, 966, 1043, 1080, 1113, 1211, 1375, 1454, 1744, 2940, 2982. HR-MS: [M+Na$^+$] Calculated for $C_{15}H_{18}O_6$: 295.11761; found: 295.11759.



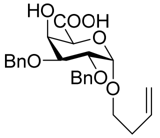
Phenyl 2,3-di-O-benzyl-1-thio-β-D-galactopyranosiduronic acid (8b): The title compound was obtained from **8a** in 73% yield (68 mg, 0.15 mmol). ^{1}H NMR (400 MHz) δ: 7.67-7.52 (m, 2H, C*H*$_{arom}$); 7.43-7.15 (m, 13H, C*H*$_{arom}$); 4.81 (d, 1H, *J* = 10.3 Hz, PhC*H*H); 4.78-4.68 (m, 2H, PhC*H*$_2$); 4.65-4.61 (m, 2H, H-1, PhCH*H*); 4.45 (d, 1H, *J* = 3.1 Hz, H-4); 4.03 (s, 1H, H-5); 3.77 (t, 1H, *J* = 9.4 Hz, H-2); 3.61 (dd, 1H, *J* = 3.2, 9.0 Hz, H-3). ^{13}C-APT NMR (100 MHz) δ: 171.0 (C-6); 138.1, 137.5, 133.4 (C$_{q,arom}$); 132.5, 129.1, 128.6, 128.5, 128.5, 128.4, 128.2, 128.1, 128.0, 127.9 (*C*H$_{arom}$); 88.1 (C-1); 81.7 (C-3); 77.1 (C-5); 76.5 (C-2); 75.9, 72.0 (Ph*C*H$_2$); 67.7 (C-4). IR (neat) ν: 2924, 1730, 1454, 1362, 1269, 1211, 1124, 1096, 1026. HR-MS: [M+H]$^+$ calculated for $C_{26}H_{26}O_6S$: 467.15229; found 467.15218.



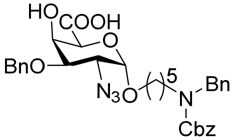
Phenyl 2,3-di-O-benzoyl-1-thio-β-D-galactopyranosiduronic acid (9b): The title compound was obtained from **9a** in 73% yield (72 mg, 0.15 mmol). ^{1}H NMR (400 MHz) δ: 7.91 (dd, 4H, 7.8 Hz, 15.9 Hz, C*H*$_{arom}$); 7.57-7.09 (m, 11H, C*H*$_{arom}$); 5.81 (t, 1H, *J* = 9.8 Hz, H-2); 5.40 (dd, 1H, *J* = 3.0, 9.8 Hz, H-3); 4.97 (d, 1H, *J* = 10.0 Hz, H-1); 4.74 (s, 1H, H-4); 4.53 (bs, 1H, O*H*); 4.38 (s, 1H, H-5). ^{13}C-APT NMR (100 MHz) δ: 170.7 (C-6); 165.9, 165.5 (*C*O$_{Bz}$); 133.5, 133.4, 133.0 (*C*H$_{arom}$); 132.4 (C$_{q,arom}$); 130.0, 130.0 (*C*H$_{arom}$); 129.4 (C$_{q,arom}$); 129.2 (*C*H$_{arom}$); 129.0 (C$_{q,arom}$); 128.5, 128.4 (*C*H$_{arom}$); 87.0 (C-1); 77.7 (C-5); 74.8 (C-3); 68.5 (C-4); 67.9 (C-2). IR (neat) ν: 1724, 1601, 1450, 1315, 1277, 1128, 1088, 1070, 1026. HR-MS: [M+H]$^+$ calculated for $C_{26}H_{22}O_8S$: 495.11081; found 495.11089.



(**10b**): The title compound was obtained from **10a** in 84% yield (36 mg, 0.084 mmol). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.42 – 7.17 (m, 10H), 5.78 (m, 1H), 5.16 – 4.99 (m, 2H), 4.89 (d, *J* = 3.5 Hz, 1H, H-1), 4.85 – 4.68 (m, 3H), 4.62 (d, *J* = 12.1 Hz, 1H), 4.41 (bs, 2H, H-4, H-5), 3.99 – 3.82 (m, 2H, H-3, H-2), 3.67 m, 1H), 3.53 (m, 1H), 2.44 – 2.24 (m, 2H). ^{13}C NMR (101 MHz, CDCl$_3$) δ 172.08, 138.31, 137.88, 134.73, 128.62, 128.58, 128.52, 128.08, 127.98, 127.96, 117.12, 97.77 (C-1), 76.81 (C-3), 75.21 (C-2), 73.58, 72.97, 69.87 (C-5), 68.66 (C-4), 68.29, 33.86. IR (neat): 698, 737, 914, 1026, 1064, 1096, 1210, 1271, 1342, 1454, 1722, 2921, 3450. HR-MS: [M+Na$^+$] Calculated for C$_{24}$H$_{28}$O$_7$: 451.1727; found: 451.1725.



5-(benyl(benyloxycarbonyl)amino)pentyl 2-azido-3-*O*-benzoyl-α-D-galactopyranose uronic acid (11b): This product was prepared following general procedure for selective oxidation of primary alcohol to carboxylic acid by use of two steps one-pot TEMPO/BAIB-Pinnick oxidation. TLC: R$_f$ = 0.12 (DCM:MeOH:AcOH = 20:2:0.05). Yield: 49 mg (0.079 mmol), 80%. ^{1}H NMR (400 MHz, CDCl$_3$) δ 7.31 (dd, *J* = 32.5, 12.5 Hz, 15H, CH_{arom}), 5.17 (d, *J* = 14.4 Hz, 2H, PhCH_2), 4.97 (d, *J* = 11.8 Hz, 1H, H-1), 4.79 – 4.59 (m, 2H, PhCH_2), 4.49 (d, *J* = 11.0 Hz, 3H, H-4, PhCH_2), 4.37 (d, *J* = 14.6 Hz, 1H, H-5), 3.93 (d, *J* = 11.3 Hz, 1H, H-3), 3.77 – 3.51 (m, 2H, H-2), 3.54 – 3.31 (m, 1H), 3.22 (d, *J* = 25.7 Hz, 2H), 1.69 – 1.41 (m, 3H), 1.40 – 1.24 (m, 3H). ^{13}C NMR (100 MHz, CDCl$_3$) δ 137.83, 136.93 (C$_q$), 128.76, 128.65, 128.39, 128.14, 128.05, 127.94, 127.42, 127.29 (CH$_{arom}$), 98.26 (C-1), 75.22 (C-3), 71.97 (Bn), 70.01 (C-5), 68.97, 67.42 (Bn), 67.19 (C-4), 58.42 (C-2), 50.60, 50.33, 47.11, 46.17, 29.00, 27.88, 27.41, 23.28. [α]$^{20}_D$ = 75° (c = 1.0, CHCl$_3$). IR (neat): 698, 735, 1026, 1063, 1140, 1231, 1250, 1311, 1356, 1423, 1454, 1493, 1697, 2927. HR-MS: [M+H$^+$] Calculated for C$_{33}$H$_{38}$N$_4$O$_8$: 619.27624; found: 619.27602.



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