JOC The Journal of Organic Chemistry

Article

pubs.acs.org/joc

Ruthenium Catalyzed Stereo/Chemo/Regioselective One-Pot Synthesis of C(2)−C(3) Unsaturated and α-D-Mannopyranosyl Sulfones

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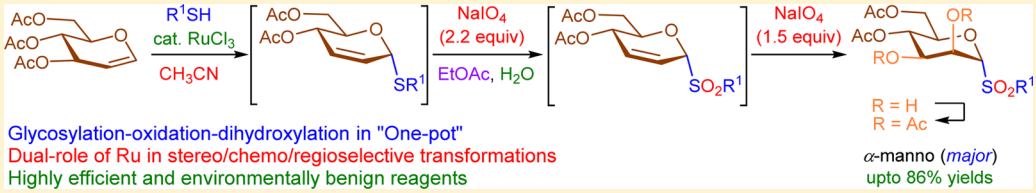
Supporting Information



ABSTRACT: An efficient and divergent approach to C(2)−C(3) unsaturated glycosyl and α-D-mannopyranosyl sulfones has been developed via ruthenium-promoted direct glycosylation, oxidation, and dihydroxylation from glycal in one-pot. The presence of stoichiometric amounts of $NaIO_4$ and *in situ* generation of RuO_4 from a $RuCl_3$−$NaIO_4$ reagent system were crucial for chemoselective oxidation of sulfide in the presence of an olefin moiety. The dual-role of ruthenium in sequential glycosylation−oxidation−dihydroxylation is amenable to a wide range of thio acceptors to access α-D-mannopyranosyl sulfones in good yields with high regioselectivity.

INTRODUCTION

The efficient and stereoselective functionalization of glycosyl mimetics has become an interesting area of research due to their involvement in a vast array of biological processes[1] and due to the synthetic challenges associated with stereoselective construction of glycosidic linkages.[2] The sugar derivatives bearing C-1 thio-linkages have unique importance in glycochemistry, particularly, as versatile and stable glycosyl donors in chemical glycosylation for assembling complex sugar scaffolds.[3] Owing to their lower susceptibility and stronger chemical stability toward hydrolysis, the S-linked saccharides and glycoconjugates have been recognized as potential chemical probes in glycobiology for studying enzymatic inhibition.[4]

The glycosyl mimics bearing a sulfonyl moiety at the anomeric center (Sugar-SO_2R), an achiral, nonionic, and isoelectronic to phosphate diester[5] have been widely studied as convenient glycosyltransferase inhibitors[6] and potential antitumor agents[7] (Figure 1). In recent years, several glycoconjugates appended with S-linkages at C-1 have emerged as potent inhibitors against human carbonic anhydrases (hCA): isozymes I and II and tumor-associated isozymes IX and XII.[8] Some of them showed selective inhibition when compared to that of clinically approved drugs such as acetazolamide (AZA), brinzolamide (BRZ), and dorzolamide (DRZ) and therefore serve as important chemical tools to probe such enzymatic studies (Figure 1). Recently, Kona and co-workers demonstrated the utility of S-linked α-D-mannopyranosyl as novel and selective inhibitors of human Golgi α-mannosidase II (hGM), an interesting pharmaceutical target linked to cancer chemotherapy.[9]

In addition, the glycosyl sulfones, the higher oxidized form of thioglycosides have been extensively utilized as versatile chiral synthons in assembling various functionalized saccharides, involving (1) chemical glycosylation under a $MgBr_2{\cdot}Et_2O$ reagent system;[10] (2) $Sm(OTf)_3$ catalyzed glycosylation;[11] (3) C-glycosylation via lithiated anion coupling reaction with a carbonyl group;[12] (4) Ramberg-Backlund and hydrogenation reaction sequence for C-linked glycoconjugates;[13] (5) stereo-controlled *C*-glycosylation via glycosyl samarium intermediates;[14] and (6) Umpolung approach to glycals via an anomeric radical and sugar-chromium(III) complex.[15]

Owing to their promising therapeutic activities, the stereo-selective preparation of sugar sulfones employing less toxic and environmentally benign reagents, involving a simple reaction operation and being compatible with other sensitive groups would be highly desirable. Over the decades, several oxidative reagent systems[14b,c,16] have been created to overcome the disadvantages of the most frequently used *m*-CPBA, as low solubility in dichloromethane and unconventional reaction operations at low temperature, compatibility in the presence of other functionalities, and the purification of the desired compound from byproducts remain unsolved issues.

Although considerable efforts have been made in technical improvement, the chemoselective oxidation of sulfide in a molecule containing a double bond such as C(2)−C(3)-unsaturated *S*-glycoside is quite elusive and particularly interesting since the double bond present in the pyran ring

Received: April 30, 2015

DOI: 10.1021/acs.joc.5b00975
J. Org. Chem. XXXX, XXX, XXX−XXX

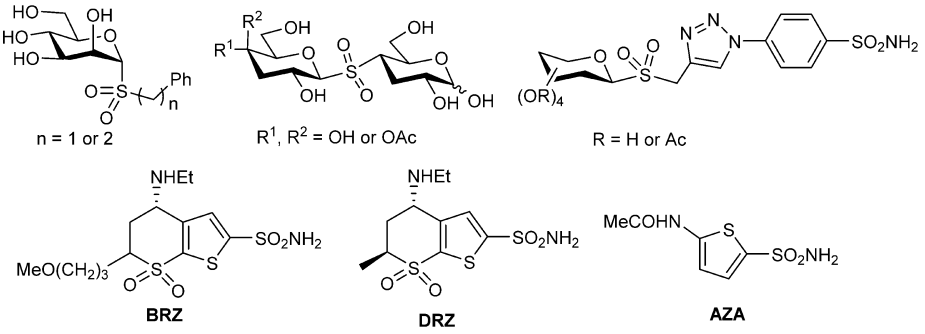


Figure 1. Glycosyl sulfones and structure of some related drugs linked to cancer.

offers further synthetic utility to access chiral sugar derivatives.[17] Moreover, the regioselective dihydroxylation of C(2)−C(3) olefin in one-pot by employing alternative equivalents of the same reagent is a relatively scarce yet challenging transformation.

The exceptional versatility and efficiency of ruthenium catalysis in various transformations[18] have fueled our interest with the expectation of finding ruthenium-based alternative approaches in carbohydrate chemistry. In this context, recently we demonstrated the sequential one-pot method for the synthesis of mannosylated peptide and disaccharide glycoconjugates using ruthenium-catalysis.[19a] We envisioned that the inherent ability of ruthenium(III) trichloride to generate ruthenium (VIII) oxide *in situ* with a combination of co-oxidant such as sodium metaperiodate would provide the promising and highly efficient conditions for the chemoselective and regioselective transformations.

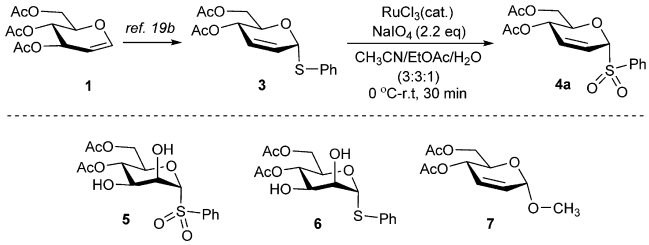
In continuation of our research in glycochemistry exploring Ru-catalysis,[19] herein, we report our findings on the development of a rapid and modular approach for the divergent synthesis of C(2)−C(3)-unsaturated glycosyl sulfones and mannosyl sulfones involving a sequential Ru-catalyzed stereoselective glycosylation, chemoselective oxidation, and regioselective dihydroxylation in one-pot. The directed glycosylation−oxidation−dihydroxylation sequential transformations are amenable to a wide range of acceptors to generate α-D-mannopyranosyl sulfones from glycal in a single step.

RESULTS AND DISCUSSION

For this purpose, the necessary 2,3-unsaturated α-thioglucoside (**3**) was prepared by a Ferrier glycosylation reaction of 3,4,6-tri-*O*-acetyl D-glucal (**1**) and thiophenol (**2a**) using our previously reported method.[19b] Initially, we attempted the Ru-catalyzed *syn* dihydroxylation of the C(2)−C(3) double bond in **3** following the method we developed for the one-pot synthesis of α-D-mannopyranosides.[19a] An interesting result was obtained upon the treatment of **3** with ruthenium trichloride (5 mol %) and sodium metaperiodate (2.2 equiv) in EtOAc/CH_3CN/H_2O (3:3:1), a biphasic solvent system at 0 °C to room temperature for 30 min (Scheme 1). The experiment revealed the exclusive formation of C-1 glycosyl sulfone **4a** as a result of chemoselective oxidation of thio-sugar rather than dihydroxylation of olefin moiety in pyran ring. Despite the known susceptibility of double bonds toward RuO_4[20] that could lead to the formation of mannosyl sulfone **5** or thiomannopyranoside **6**, the reaction proved to be highly chemoselective to generate **4a** in quantitative yields.

The spectral data of **4a** were consistent and in conformity with the assigned structure and correlated with literature.[10a] In the ^1H NMR spectrum of **4a**, the characteristic resonances due to

Scheme 1. Ru-Catalyzed Chemoselective Oxidation of 2,3-Unsaturated α-Thioglucoside (3)



C(2)−C(3) olefinic protons were observed between δ 6.28−6.30 ppm, while evidence of an anomeric proton at δ 5.13 (d, J_{1-2} = 1.7 Hz) and chemical shifts of other sugar protons at δ 5.28 (dd, *J* = 9.3, 2.3 Hz, H-4), 4.67 (dt, *J* = 9.0, 4.3 Hz, H-5) confirmed the product. Furthermore, the proton-decoupled carbon spectrum of **4a** ambiguously proved the presence of anomeric carbon at δ 88.0, whereas resolved resonances for C(2)−C(6) were observed at δ 129.2, 129.1 (C-2, C-3), 70.3, 63.7, and 62.8 ppm besides acetyl groups at δ 20.9 and 20.7 ppm. The ESI-HRMS spectrum indicated the base peak corresponding to $[\mathbf{4a} + NH_4]^+$ of *m*/*z* 372.1100 calcd. for $C_{16}H_{22}O_7NS^+$ of 372.1111 further supported the assigned structure.

Other transition metal oxidative reagent systems, isoelectronic to RuO_4 such as toxic OsO_4/NMO[16b,21a] or $KMnO_4/CuSO_4 \cdot 5H_2O$[16c,d] for the chemoselective oxidation, were also studied, and the results are summarized in Table 1. Notably, the reaction was very slow and sluggish in the presence of OsO_4 (5−10 mol %) and co-oxidant *N*-mehtylmorpholine-*N*-oxide at room temperature. Further increasing the amount of oxidizing reagent resulted in decomposition or, for instance, mixtures of uncharacterized compounds. Moreover, the $KMnO_4/CuSO_4 \cdot 5H_2O$ reagent system in CH_3CN/H_2O (5:1) afforded the corresponding sulfone diol **5** as a result of oxidation−dihydroxylation of sulfide and olefin, thus confirming the need of ruthenium catalysis for chemoselective oxidation.

Indeed, treatment of **3** with excess of organic peracid such as *meta*-chloroperbenzoic acid, most commonly used for oxidation of sulfide, in chloroform as the solvent at −10 to 0 °C for 24 h afforded **4a** in 55% yield with no evidence of epoxidation of the double bond. In contrast, use of oxone (potassium peroxomonosulfate)[14c,21b] in aqueous methanol afforded methyl glucoside **7** as the identified byproduct in 23% yield with traces of sulfone **4a** at some point of time as observed by TLC. Switching the solvent system to acetone/water was found unsuccessful and resulted in decomposition after prolonged reaction time, probably due to the hydrolysis of starting material. Alternatively, the hypofluorous acid, HOF·CH_3CN complex generated from

DOI: 10.1021/acs.joc.5b00975
J. Org. Chem. XXXX, XXX, XXX−XXX

Table 1. Comparative Study and Screening of Various Oxidants for Chemoselective Oxidation[a]

entry	oxidizing system	solvent(s)	reagents equiv[b]	time	product (s)[c]
1	$RuCl_3/NaIO_4$	$CH_3CN/EtOAc/H_2O$ (3:3:1)	5 mol %/2.2 equiv	30 min	**4a** (96%)
2[d]	OsO_4/NMO	acetone/H_2O (3:1)	5 mol %/3 equiv	72 h	**3** (60%), **4a** (10%)
3[d]	OsO_4/NMO	acetone/H_2O (3:1)	10 mol %/3 equiv	72 h	**3** (40%), **4a** (10%)
4[e]	OsO_4/NMO	acetone/H_2O (3:1)	1 equiv/3 equiv	24 h	traces
5	$KMnO_4/CuSO_4$	CH_3CN/H_2O (5:1)	3 equiv/2 equiv	2 h	**5** (50%)
6[f]	*m*-CPBA	$CHCl_3$	2−3 equiv	24 h	**4a** (55%)
7	oxone	CH_3OH/H_2O (2:1)	2.5 equiv	12 h	**7** (23%)
8[d]	oxone	acetone/H_2O (2:1)	2.5 equiv	12 h	traces

[a]Reaction conditions: see Experimental Section. [b]All of the reactions were performed with **3** (50 mg, 0.16 mmol, 1.0 equiv). [c]The isolated yields are based on starting material **3**. [d]Reactions did not complete, and a mixture of sulfide and sulfone was observed. [e]Decomposition of starting material and unknown mixtures were observed. [f]Based on 55−75% peroxide content in water.

the $F_2/CH_3CN/H_2O$ system,[16e] and dimethyldioxirane (DMDO)[12] have been reported for the oxidation of various functionalities including sulfide and alkene.[22] However, the use of such a reagent is limited due to unconventional reaction operations and substrate compatibility.

In light of our recent report on one-pot glycosylation/dihydroxylation,[19a] we investigated whether the glycosylation and chemoselective oxidation sequence can be achieved without isolation of the Ferrier product **3**. In a representative example, glycal **1** was coupled with thiophenol (**2a**) under Ru-mediated thioglycosylation following our previously reported procedure.[19b] After the completion of the glycosylation step as judged by TLC, the reaction mixture was treated with EtOAc (2 mL), H_2O (650 μL), and $NaIO_4$ (2.2 equiv) at 0 °C. To our delight, the complete conversion of **3** was realized in at most 30 min to obtain the corresponding sulfone **4a** in a one-pot process (Table 2, entry 1). With no further optimization needed, **4a** was isolated in 84% yield as an α/β mixture (88:12) with high stereoselectivity in favor of the α-anomer.[23]

Though oxidation of thioglycosides have been achieved with the aid of several oxidants, the present method constitutes the first report on the dual role of ruthenium catalyst for one-pot preparation of allyl glycosyl sulfones, valuable synthetic and chiral intermediates in carbohydrate chemistry.

To further probe the scope and generality of the sequential method, we decided to synthesize various functionalized glycosyl sulfones containing the C(2)−C(3) double bond in the pyran ring (Table 2). Thus, a wide range of thio acceptors comprising thio-phenols (**2b**−**2d**), thio-naphthol (**2e**), benzyl mercaptans (**2f**−**2h**), alicyclic (**2i**,**2j**), and aliphatic (**2k**) were successfully incorporated with glycal **1** under ruthenium-mediated glycosylation−oxidation to obtain the desired C-1 glycosyl sulfones **4b**−**4k** in good yields with high anomeric selectivity (Table 2, entries 2−11). It is pertinent to mention that the combination of $RuCl_3$ and $NaIO_4$ has negligible effect on the stereochemical outcome in the oxidation step since the anomeric ratio observed in this transformation is almost identical to that of Ferrier products obtained in the preceding glycosylation reaction.[19b]

The resurgence of our interest in the glycosylation and synthesis of glycoconjugates[24] persuaded us to examine the reactivity of **4a** as a glycosyl donor in C-glycosylation.[10a] Thus, the reaction of **4a** with $AlMe_3$ (2.0 M in hexane, 2.0 equiv) in CH_2Cl_2 as the solvent proceeded smoothly to furnish the corresponding C-1 methyl glycoside **8** in 78% yield with an 80:20 anomeric mixture (Scheme 2).[24a]

In view of understanding the importance of mannosylated constructs in nature and the recently reported bioactivity of α-D-mannopyranosyl sulfones encouraged us to investigate a straightforward and stereocontrolled method by employing an easily accessible substrate under mild reagent conditions. During

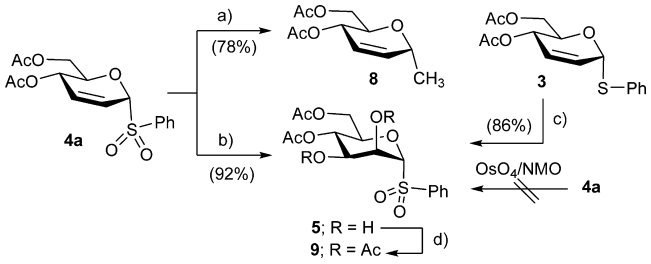
Table 2. Ru-Catalyzed Stereo/Chemoselective Glycosylation−Oxidation in One-Pot[a]

Entry	R^1SH	Glycosyl sulfone	Yields[b]	α:β[c]
1	**2a**	**4a**	84%	88:12
2	**2b**	**4b**	90%	90:10
3	**2c**	**4c**	82%	84:16
4	**2d**	**4d**	80%	78:22
5	**2e**	**4e**	78%	80:20
6	**2f**	**4f**	78%	92:08
7	**2g**	**4g**	80%	78:22
8	**2h**	**4h**	85%	84:16
9	**2i**	**4i**	78%	88:12
10	**2j**	**4j**	74%	84:16
11	**2k**	**4k**	82%	90:10

[a]Reaction conditions: Glycal **1** (100 mg, 0.367 mmol, 1.0 equiv), R^1SH (1.2 equiv), $RuCl_3$ (5.0 mol %), CH_3CN (2 mL), then EtOAc (2 mL), H_2O (650 μL), $NaIO_4$ (2.2 equiv), 0 °C-rt, 30 min. [b]Isolated and unoptimized yields. [c]The anomeric ratios were examined by ^1H NMR spectroscopy.

DOI: 10.1021/acs.joc.5b00975
J. Org. Chem. XXXX, XXX, XXX−XXX

Scheme 2. Ruthenium Promoted Dihydroxylation and Use of Glycosyl Sulfone as Donor[a]



[a]Reagents and conditions: (a) **4a** (0.17 mmol, 1.0 equiv), $AlMe_3$ (2.0 equiv), CH_2Cl_2, 0 °C-rt, 2 h; (b) **4a** (0.30 mmol, 1.0 equiv), $RuCl_3$ (5.0 mol %), CH_3CN/EtOAc/H_2O (3:3:1), $NaIO_4$ (1.5 equiv), 0 °C-rt, 30 min; (c) $RuCl_3$ (5.0 mol %), CH_3CN/EtOAc/H_2O (3:3:1), $NaIO_4$ (3.7 equiv), 0 °C-rt, 40 min; (d) Ac_2O (5 equiv), CH_2Cl_2/Pyridine (10:1), DMAP (cat.), 0 °C-rt, 12 h.

this, we anticipated that postglycosylation−dihydroxylation of the double bond in **4a** could be accomplished by using alternative equivalence of co-oxidant $NaIO_4$ in combination with catalytic $RuCl_3$.

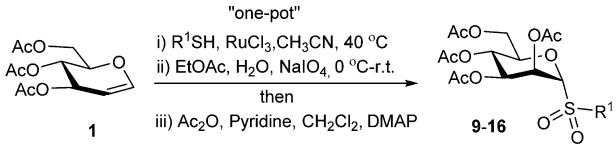
To test this hypothesis, a preformed solution of **4a** (106 mg, 0.30 mmol) in an acetonitrile/ethyl acetate/water (3:3:1) mixed solvent system was treated with an aqueous solution of $RuCl_3$ (15 μL of 0.1 M solution; 0.0015 mmol) and $NaIO_4$ (107 mg, 0.45 mmol, 1.5 equiv) at 0 °C (Scheme 2). Remarkably, the completion of the reaction was observed in 30 min to afford the desired diol **5**, which upon treatment with acetic anhydride in the presence of catalytic DMAP in pyridine and dichloromethane afforded the corresponding per-acetylated mannosyl sulfone **9** in 92% yields over two steps. In contrast, the catalytic OsO_4 with NMO as co-oxidant failed to give the desired diol,[25] further confirming the versatile synthetic utility of the ruthenium method for such a type of substrate.

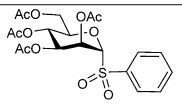
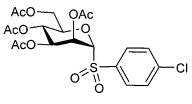
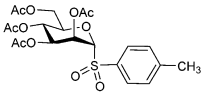
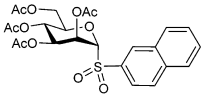
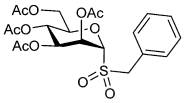
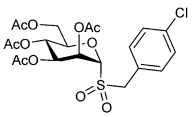
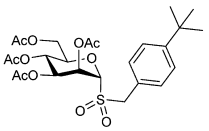
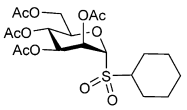
Given the success of these studies, we wondered whether it would be possible to achieve the oxidation of sulfide and dihydroxylation of the C(2)−C(3) olefin moiety in compound **3** in a single step by employing catalytic $RuCl_3$ with excess of $NaIO_4$ (~3.7 equiv) since oxidation of sulfide and dihydroxylation of olefin required 2.2 and 1.5 equiv of $NaIO_4$, respectively. Presumably, the reaction of **3** with 5 mol % of $RuCl_3$ and 3.7 equiv of $NaIO_4$ in the CH_3CN/EtOAc/H_2O solvent system afforded the desired 2,3-*syn*-diol sulfone **5**, which was directed to acetylation without further purification to obtain the mannosyl sulfone **9** in 86% yield (Scheme 2).

Encouraged by these results, we attempted to investigate the sequential glycosylation−oxidation−dihydroxylation reactions in one-pot to access the mannose sulfones directly from commercially available glycal **1** (Figure 2).

Accordingly, a preformed solution of **1** and **2a** (1.2 equiv) in anhydrous acetonitrile was treated with 5 mol % of $RuCl_3$ under an atmosphere of nitrogen. After the completion of the reaction, the subsequent *in situ* oxidation−dihydroxylation of resultant 2,3-unsaturated thioglucoside (**3**) was performed by introducing EtOAc, H_2O, and $NaIO_4$ (3.7 equiv) in sequence. Pleasingly, the reaction was concluded in 40 min to afford the corresponding diol sulfone **5**. Following acetylation of crude diol using a standard procedure resulted in the venerable α-D-mannopyranosyl sulfone **9** as major product in 80% overall yields (Table 3, entry 1).

Table 3. Synthesis of Mannopyranosyl Sulfones via Sequential Reactions[a]



Entry	R^1SH	Product (Major)		Yields[b]	dr[c]
1	**2a**		**9**	80%	82:18
2	**2b**		**10**	86%	91:09
3	**2c**		**11**	80%	86:14
4	**2e**		**12**	75%	82:18
5	**2f**		**13**	72%	82:18
6	**2g**		**14**	75%	80:20
7	**2h**		**15**	81%	85:15
8	**2i**		**16**	75%	88:12

[a]Reaction conditions: (i) Glycal **1** (100 mg, 0.367 mmol, 1.0 equiv), R^1SH (1.2 equiv), $RuCl_3$ (5.0 mol %), CH_3CN (2 mL), 40 °C, 1−8 h; (ii) EtOAc (2 mL), H_2O (650 μL), $NaIO_4$ (3.7 equiv), 0 °C-rt, 40 min; (iii) Ac_2O (5 equiv), CH_2Cl_2/Pyridine (10:1), DMAP (cat.), 0 °C-rt, 12 h. [b]Isolated yields after purification by silica-gel column chromatography (both isomers). [c]Diastereomeric ratios were determined by ^1H NMR analysis of a crude reaction mixture.

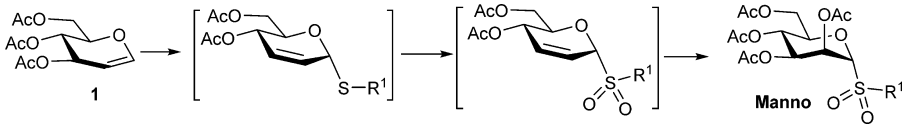


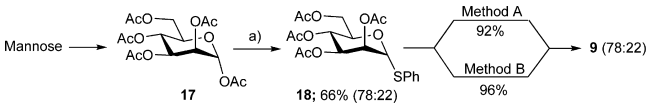
Figure 2. One-pot sequential glycosylatiom/oxidation/dihydroxylation approach.

DOI: 10.1021/acs.joc.5b00975
J. Org. Chem. XXXX, XXX, XXX−XXX

Following the initial success of the sequential one-pot approach, the scope was further expanded to construct different sulfonyl moieties at anomeric positions of mannose (Table 3). Generally, the one-pot method is efficient and mild enough to generate various α-D-mannopyranosyl sulfones (**10**–**16**) from glycal in good yields and high stereoselectivity (entries 2–8).

We further highlight the advantage of our method by comparing with the traditional method. To this end, thiomannoside **18** was synthesized from readily prepared per-*O*-acetylated mannose **17** using a literature procedure.[16e] Oxidation of anomeric sulfide was then accomplished by using a combination of $KMnO_4/CuSO_4{\cdot}5H_2O$[16c] in a CH_3CN/H_2O (5:1) mixed solvent system to obtain the corresponding mannosyl sulfone **9** in 92% yield as anomeric mixture of α/β ratio 78:22 (Scheme 3). Notably, the better results, in terms of yields and stereochemistry, were accomplished under the one-pot method as compared to stepwise reactions, which is otherwise time-consuming and involves excessive use of reagents.

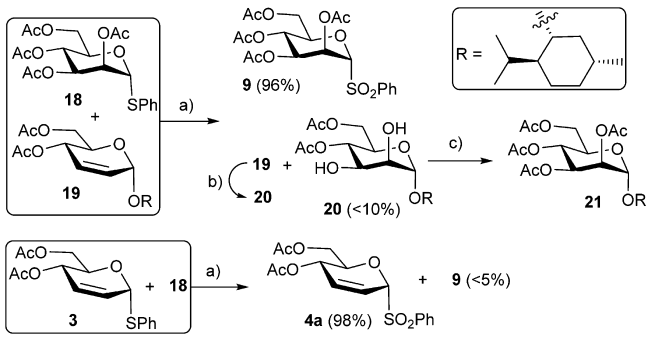
Scheme 3. Synthesis of Mannosyl Sulfone[a]



[a]Reagents and conditions: (a) **17** (1.0 equiv), thiophenol (2.0 equiv), $BF_3{\cdot}Et_2O$ (6.0 equiv), CH_2Cl_2, 0 °C-rt, 18 h; Method A. **18** (1.0 equiv), $KMnO_4$ (1.5 equiv), $CuSO_4{\cdot}5H_2O$ (1.0 equiv), CH_3CN/H_2O (5:1), room temperature, 2 h; Method B. **18** (1.0 equiv), $RuCl_3$ (5.0 mol %), CH_3CN/EtOAc/H_2O (3:3:1), $NaIO_4$ (2.2 equiv), 0 °C-rt, 20 min.

We next set out to conduct control experiments to understand the behavior of RuO_4 in chemoselective oxidation (Scheme 4). Thus, an equimolar mixture of thiomannoside **18** (100 mg, 0.23 mmol) and menthyl glycoside **19** (85 mg, 0.23 mmol) in an acetonitrile/ethyl acetate/water (3:3:1) solvent system was treated with an aqueous solution of $RuCl_3$ (~12 μL of 0.1 M solution; 0.00115 mmol) and $NaIO_4$ (176 mg, 0.50 mmol, 2.2 equiv) at 0 °C, and the reaction mixture was stirred for 20 min. The reaction proceeded well to afford sulfone **9** of the corresponding thiomannoside in excellent yields along with traces of diol adduct **20** corresponding to menthyl glycoside.

Scheme 4. Chemoselective Oxidation of Thioglycoside in Control Experiments[a]



[a]Reagents and conditions: (a) $RuCl_3$ (5.0 mol %), CH_3CN/EtOAc/H_2O (3:3:1), $NaIO_4$ (2.2 equiv), 0 °C-rt, 20 min; (b) $NaIO_4$ (1.5 equiv), 0 °C-rt, 30 min; (c) Ac_2O (5 equiv), CH_2Cl_2/pyridine (10:1), DMAP (cat.), 0 °C-rt, 12 h.

Subsequently, the complete dihydroxylation of **19** to **20** was achieved by adding extra 1.5 equivalence of $NaIO_4$ (106 mg, 0.35 mmol) in the same pot. Following simple workup and successive acetylation of the crude diol **20** afforded the corresponding per-acetylated α-menthyl mannoside **21** in 82% yield.[19a]

The next experiment was carried out to compare the reactivity of allylic thio-sugar **3** with anomeric thio-sugar **18**. Interestingly, the allyl sulfide moiety undergoes selective oxidation under similar reaction conditions to afford the corresponding unsaturated glycosyl sulfone **4a** in quantitative yields, whereas only a small amount (<5%) of manosyl sulfone **9** was identified. Nevertheless, exclusive formation of the sulfone product is consistent with our studies and established the ability of RuO_4 to oxidize the sulfide moiety efficiently and chemoselectively.

CONCLUSIONS

In conclusion, the ruthenium tetraoxide generated *in situ* from $RuCl_3$ in combination with a stoichiometric amount of co-oxidant is recognized as a powerful and efficient catalyst for chemoselective oxidation. The Ru-mediated strategy is attractive and enables the synthesis of unsaturated glycosyl and mannosyl sulfones in one-pot from readily available starting materials: glycal. The use of environmental friendly reagents and the convenience of the reaction operation to generate valuable mannosyl sulfones in a stereocontrolled manner are the key advantages. Notably, this represents a valuable alternative to toxic OsO_4 in postglycosylation chemoselective and regioselective reactions. Further studies include exploration of the synthetic utility of glycosyl sulfone and application of Ru-catalysis for the synthesis of other sugar scaffolds are currently underway.

EXPERIMENTAL SECTION

General Synthesis Information. Unless otherwise noted, materials were obtained from commercial suppliers and used without purification. Anhydrous solvents were purchased for the reactions and used without further desiccation. All reactions were performed in flame-dried round-bottom flasks, fitted with rubber septa or glass gas adapters, under a positive pressure of nitrogen or argon. Analytical thin-layer chromatography (TLC) was performed using aluminum backed UV F254 precoated silica gel flexible plates. Removal of solvent under reduced pressure refers to distillation with a rotary evaporator attached to a vacuum pump (~3 mmHg). Melting points were obtained in open capillary tubes using a micromelting point apparatus and were uncorrected. Optical rotations were recorded with a digital polarimeter at 589 nm (sodium D-line). NMR were recorded on 300, 400, or 500 MHz nuclear magnetic resonance spectrometers. The proton resonances are annotated as chemical shifts (δ) relative to tetramethylsilane (δ 0.0) using the residual solvent signal as an internal standard or tetramethylsilane itself: chloroform-d (δ 7.26, singlet); multiplicity (s, singlet; d, doublet; t, triplet; q, quartet; m, multiplet; br, broad); coupling constant (*J*, Hz); and the number of protons for a given resonance is indicated by nH. The chemical shifts of ^{13}C NMR are reported in ppm relative to the central line of the triplet at 77.0 ppm for $CDCl_3$. IR spectra were recorded on an FT-IR spectrometer, and wave numbers of maximum absorption peaks are presented in cm^{-1}. High resolution mass analyses (HRMS) were performed on a mass spectrometer using ESI-TOF techniques.

General Procedure for RuO_4 Oxidation (A). To a solution of **3** (50 mg, 0.16 mmol) in an acetonitrile/ethyl acetate/water (3:3:1) mixed solvent system, $RuCl_3$ (5 mol %, 0.1 M aqueous solution) and $NaIO_4$ (75 mg, 0.35 mmol, 2.2 equiv) were added at 0 °C for 30 min. After the completion of the reaction, the reaction was quenched with saturated $NaHCO_3$ (10 mL), diluted with EtOAc (10 mL), and extracted with EtOAc (30 mL × 3). The combined organic layers were washed with brine solution, dried over anhydrous Na_2SO_4, concentrated *in vacuo*, and purified by silica gel column chromatography (hexanes–

DOI: 10.1021/acs.joc.5b00975
J. Org. Chem. XXXX, XXX, XXX–XXX

EtOAc 2:1) to afford the corresponding sulfone **4a** (54 mg, 96% yield) as a white solid.

General Procedure for OsO_4 Reaction (B). In a representative experiment, to a preformed solution of compound **3** (50 mg, 0.16 mmol) and NMO (30 μL, 0.48 mmol) in acetone/water (3:1 v/v, 0.5 mL) was added 78 μL of 0.1 M aqueous OsO_4 solution (0.0078 mmol, 5 mol %). The reaction was allowed to stir at room temperature for 2−3 days. The reaction mixture was quenched by the addition of saturated aqueous sodium bisulfite (5 mL) and extracted with EtOAc (30 mL × 3). The combined organic layers were washed successively with 2 × 10 mL of 1 N aqueous sodium bisulfate and 10 mL of brine. The organic layer was dried over anhydrous Na_2SO_4, filtered, and evaporated under reduced pressure to provide a crude product.

General Procedure for $KMnO_4$ Reaction (C). To a solution of compound **3** (50 mg, 0.16 mmol) in CH_3CN−H_2O (5:1 v/v; 2 mL) was added a finely ground mixture of solid $KMnO_4$ (75 mg, 0.48 mmol, 3.0 equiv) and $CuSO_4{\cdot}5H_2O$ (80 mg, 0.32 mmol, 2.0 equiv) and stirred at room temperature until the completion of the reaction. The reaction was extracted with EtOAc (30 mL × 3). The combined organic layers were washed with brine solution, dried over anhydrous Na_2SO_4, and concentrated *in vacuo* to provide crude diol-sulfone **5**. Following acetylation of diol-sulfone **5** in CH_2Cl_2 (5 mL), pyridine (0.5 mL) and acetic anhydride (5 equiv) in the presence of a catalytic amount of DMAP gave the corresponding per acetylated glycoside. Following the usual workup and purification by chromatography (silica gel, hexanes−EtOAc 2:1) afforded mannosyl sulfone **9** (37 mg, 50% yield over 2 steps) as a colorless oily liquid.

General Procedure for *m*-Chloroperbenzoic Acid Reaction (D). To a preformed solution of *m*-CPBA (55−75% peroxide content in H_2O, 100 mg, 0.57 mmol) in chloroform (3 mL) at −10 °C was added a solution of **3** (50 mg, 0.16 mmol) in chloroform (800 μL). The reaction was allowed to warm at 0 °C for 1 h and then stirred at room temperature for 24 h. The reaction mixture was quenched with saturated aqueous sodium hydrogen carbonate (10 mL) and extracted with chloroform (50 mL × 3). The combined organic layers were washed with water and brine, dried over Na_2SO_4, and concentrated in *vacuo* to provide crude product. The crude mixture was purified by silica gel column chromatography (hexane−EtOAc 2:1) to provide compound **4a** (30 mg, 55% yield) as a white solid.

General Procedure for the Oxone Reaction (E). To a solution of compound **3** (50 mg, 0.16 mmol) in methanol (2 mL) was added a solution of oxone (72 mg, 0.40 mmol) in water (1 mL) at 0 °C. The resulting cloudy slurry was stirred vigorously for 2 h at room temperature. The reaction mixture was extracted with chloroform (50 mL × 3). The organic extracts were combined and washed with water, brine, dried over Na_2SO_4, and concentrated under reduced pressure. The crude product was purified by silica gel column chromatography (hexane−EtOAc 2:1) to afford methyl glycoside **7** (20 mg, 23% yield) as a colorless liquid.

General Procedure for the One-Pot Glycosylation−Oxidation Reaction (F). To a stirred solution of 3,4,6-tri-*O*-acetyl-D-glucal **1** (100 mg, 0.36 mmol) and a thio acceptor (0.42 mmol, 1.2 equiv) in anhydrous acetonitrile (2 mL) under an atmosphere of argon was added $RuCl_3$ (5 mol %) at room temperature. The reaction mixture was stirred at 40 °C until the complete consumption of the starting material (glycal), adjudged by TLC. The reaction mixture was cooled at 0 °C and diluted with EtOAc (2 mL). An aqueous solution of $NaIO_4$ (0.79 mmol, 2.2 equiv) in H_2O (650 μL) was added to the above-mentioned reaction and stirred vigorously. The reaction deemed complete by TLC in at most 30 min to provide the corresponding sulfone, which generally moves slowly on TLC as compared to the sulfide. The reaction was quenched with saturated $NaHCO_3$ (10 mL), diluted with EtOAc (10 mL), and extracted with EtOAc (30 mL × 3). The combined organic layers were washed with brine solution, dried over anhydrous Na_2SO_4, concentrated *in vacuo*, and purified by silica gel column chromatography (hexane−EtOAc 2:1) to afford the 2,3-unsaturated glycosyl sulfones in good yields. All of the products were confirmed by ^1H NMR, ^{13}C NMR, and MS/HRMS spectroscopy, and the α:β ratios were determined by relative integration of anomeric or separable proton in ^1H NMR spectra.

*Phenyl 4,6-Di-O-acetyl-2,3-dideoxy-1-sulfonyl-α-D-erythro-hex-2-enopyranoside (**4a**).* Following general procedure F using thiophenol (**2a**) in the glycosylation step and purification by silica gel column chromatography afforded the title compound as a white solid (109 mg, 84%). R_f 0.5 (1:1, hexane−EtOAc); Mp. 148−150 °C; $[\alpha]_D^{25}$ +113.33 (c 1.5, $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$): δ 7.99 (d, J = 7.2 Hz, 2H), 7.72 (t, J = 7.6 Hz, 1H), 7.60 (t, J = 7.4 Hz, 2H), 6.30 (s, 2H), 5.28 (dd, J = 9.3, 2.3 Hz, 1H), 5.13 (d, J = 1.7 Hz, 1H), 4.67 (dt, J = 9.0, 4.3 Hz, 1H), 4.17 (d, J = 4.0 Hz, 2H), 2.11 (s, 3H), 2.10 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 170.5, 170.1, 137.1, 134.3, 133.2, 129.2, 129.1, 119.1, 88.0, 70.3, 63.7, 62.8, 20.9, 20.7. IR ($CHCl_3$, cm^{-1}): 3019, 2926, 2854, 1740, 1550, 1464, 1372, 1215, 1042, 928, 770, 745, 667, 601. HRMS (ESI): m/z $[M + NH_4]^+$ calcd. for $C_{16}H_{22}O_7NS^+$: 372.11115; found, 372.11004.

*4′-Chlorophenyl 4,6-Di-O-acetyl-2,3-dideoxy-1-sulfonyl-α-D-erythro-hex-2-enopyranoside (**4b**).* Following general procedure F using 4-chlorothiophenol (**2b**) in the glycosylation step and purification by silica gel column chromatography afforded the title compound as a white solid (127 mg, 90%). R_f 0.5 (3:2, hexane−EtOAc); Mp. 130−132 °C; $[\alpha]_D^{25}$ +173.33 (c 1.5, $CHCl_3$). ^1H NMR (500 MHz, $CDCl_3$): δ 7.92 (d, J = 8.5 Hz, 2H), 7.57 (d, J = 8.5 Hz, 2H), 6.31 (dt, J = 10.5, 1.7 Hz, 2H), 6.27 (dt, J = 10.4, 1.9 Hz, 2H), 5.28 (dq, J = 9.0, 2.0 Hz, 1H), 5.11 (q, J = 2.3 Hz, 1H), 4.65 (ddd, J = 8.4, 5.5, 2.4 Hz, 1H), 4.19 (dd, J = 12.4, 2.4 Hz, 1H), 4.15 (dd, J = 12.5, 5.7 Hz, 1H), 2.11 (s, 3H), 2.11 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 170.2, 169.9, 140.9, 135.3, 133.2, 130.5, 129.3, 118.7, 87.8, 70.3, 63.5, 62.6, 29.5, 20.7, 20.6. IR ($CHCl_3$, cm^{-1}): 3019, 2925, 2854, 1741, 1463, 1322, 1215, 1046, 928, 745, 667, 623. HRMS (ESI): m/z $[M + NH_4]^+$ calcd. for $C_{16}H_{21}ClO_7NS^+$, 406.07218; found, 406.07068.

*p-Tolyl 4,6-di-O-acetyl-2,3-dideoxy-1-sulfonyl-α-D-erythro-hex-2-enopyranoside (**4c**).* Following general procedure F using *p*-toluenethiol (**2c**) in the glycosylation step and purification by silica gel column chromatography afforded the title compound as a white solid (110 mg, 82%). R_f 0.6 (1:1, hexane−EtOAc); Mp. 176−178 °C; $[\alpha]_D^{25}$ +50.00 (c 1.5, $CHCl_3$). ^1H NMR (300 MHz, $CDCl_3$): δ 7.86 (d, J = 8.1 Hz, 2H), 7.38 (d, J = 7.9 Hz, 2H), 6.29 (s, 2H), 5.28 (dd, J = 9.1, 2.1 Hz, 1H), 5.09 (d, J = 1.9 Hz, 1H), 4.66 (dt, J = 8.8, 4.2 Hz, 1H), 4.18−4.14 (m, 2H), 2.47 (s, 3H), 2.11 (s, 3H), 2.10 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 170.5, 170.1, 145.4, 134.0, 133.0, 129.8, 129.2, 119.3, 88.0, 70.2, 63.7, 62.8, 21.7, 20.9, 20.7. IR ($CHCl_3$, cm^{-1}): 3020, 2957, 2926, 2854, 1741, 1645, 1464, 1371, 1215, 1143, 1080, 745, 667. HRMS (ESI): m/z $[M + NH_4]^+$ calcd. for $C_{17}H_{24}O_7NS^+$, 386.12680; found, 386.12580.

*4′-Trifuoromethylphenyl 4,6-Di-O-acetyl-2,3-dideoxy-1-sulfonyl-α-D-erythro-hex-2-enopyranoside (**4d**).* Following general procedure F using 4-(trifluoromethyl)thiophenol (**2d**) in the glycosylation step and purification by silica gel column chromatography afforded the title compound as a white solid (124 mg, 80%). R_f 0.4 (2:1, hexane−EtOAc); Mp. 145−147 °C; $[\alpha]_D^{25}$ +73.33 (c 1.5, $CHCl_3$); ^1H NMR (500 MHz, $CDCl_3$): δ 8.13 (d, J = 8.2 Hz, 2H), 7.87 (d, J = 8.2 Hz, 2H), 6.34 (dd, J = 10.5, 0.9 Hz,, 1H), 6.31−6.26 (m, 1H), 5.31−5.27 (m, 1H), 5.15 (q, J = 2.3 Hz, 1H), 4.68 (ddd, J = 8.2, 5.5, 2.3 Hz, 1H), 4.20 (dd, J = 11.5, 12.4 Hz, 1H), 4.16 (dd, J = 12.4, 5.7 Hz, 1H), 2.12 (s, 3H), 2.10 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 170.3, 170.0, 140.7, 133.8, 129.8, 126.2, 118.4, 88.0, 70.5, 63.6, 62.7, 20.8, 20.7. IR ($CHCl_3$, cm^{-1}): 3020, 2957, 2926, 2854, 1741, 1645, 1464, 1371, 1215, 1143, 1080, 745, 667. HRMS (ESI): m/z $[M + Na]^+$ calcd. for $C_{17}H_{17}O_7F_3SNa^+$, 445.05393; found, 445.05355.

*Naphthyl 4,6-Di-O-acetyl-2,3-dideoxy-1-sulfonyl-α-D-erythro-hex-2-enopyranoside (**4e**).* Following general procedure F using 2-napthalenethiol (**2e**) in the glycosylation step and purification by silica gel column chromatography afforded the title compound as a white solid (115 mg, 78%). R_f 0.4 (1:1, hexane−EtOAc); Mp. 138−140 °C; $[\alpha]_D^{25}$ +200.00 (c 1.0, $CHCl_3$). ^1H NMR (500 MHz, $CDCl_3$): δ 8.46 (s, 1H), 8.02−8.00 (m, 2H), 7.95 (d, J = 7.9 Hz, 1H), 7.85 (dd, J = 8.5, 1.7 Hz, 1H), 7.70 (d, J = 7.0 Hz, 1H), 7.66 (d, J = 7.0 Hz, 1H), 6.62 (d, J = 5.6 Hz, 1H), 5.21 (dd, J = 10.8, 5.8 Hz, 1H), 4.96 (ddd, J = 10.7, 3.4, 2.3 Hz, 1H), 4.45 (t, J = 5.8 Hz, 1H), 4.40 (dd, J = 12.2, 5.8 Hz, 1H), 4.39 (d, J = 3.7 Hz, 1H), 4.35 (dd, J = 12.4, 2.0 Hz, 1H), 2.06 (s, 3H), 1.80 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 170.6, 170.0, 148.4, 136.4, 135.3, 132.0,

DOI: 10.1021/acs.joc.5b00975
J. Org. Chem. XXXX, XXX, XXX−XXX

130.7, 129.5, 129.4, 129.3, 128.0, 127.9, 123.4, 90.7, 70.4, 65.8, 61.7, 57.8, 20.7, 20.5. IR ($CHCl_3$, cm^{-1}): 3021, 2926, 2854, 1740, 1645, 1456, 1370, 1348, 1314, 1214, 1144, 1126, 1068, 817, 743, 666. HRMS (ESI): m/z $[M + NH_4]^+$ calcd. for C_{20} $H_{24}O_7SN^+$, 422.12680; found, 422.12752.

*Benzyl 4,6-Di-O-acetyl-2,3-dideoxy-1-sulfonyl-α-D-erythro-hex-2-enopyranoside (**4f**).* Following general procedure F using benzyl mercaptan (**2f**) in the glycosylation step and purification by silica gel column chromatography afforded the title compound as pale yellow semi solid (105 mg, 78%). R_f 0.4 (3:2, hexane−EtOAc); $[\alpha]_D^{25}$ +42.40 (c 1.0, $CHCl_3$). ^1H NMR (500 MHz, $CDCl_3$): δ 7.46−7.40 (m, 5H), 6.26 (dt, J = 10.5, 2.0 Hz, 1H), 6.01 (ddd, J = 10.5, 2.9, 2.3 Hz, 1H), 5.32 (dq, J = 9.3, 2.1 Hz, 1H), 5.01 (q, J = 2.4 Hz, 1H), 4.65 (ddd, J = 8.5, 5.8, 2.3 Hz, 1H), 4.59 (d, J = 14.0 Hz, 1H), 4.35 (dd, J = 12.4, 2.3 Hz, 1H), 4.25 (d, J = 9.6 Hz, 1H), 4.23 (dd, J = 12.4, 5.7 Hz, 1H), 2.15 (s, 3H), 2.11 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 170.6, 170.1, 133.7, 130.8, 129.2, 129.1, 127.5, 118.1, 83.0, 70.4, 63.7, 62.6, 56.9, 20.9, 20.8. IR ($CHCl_3$, cm^{-1}): 3019, 2956, 2925, 2853, 1743, 1461, 1370, 1316, 1217, 1101, 1044, 970, 913, 771, 698, 668, 621. HRMS (ESI): m/z $[M + Na]^+$ calcd. for $C_{17}H_{20}O_7NaS^+$, 391.08219; found, 391.08133.

*4′-Chlorobenzyl 4,6-Di-O-acetyl-2,3-dideoxy-1-sulfonyl-α-D-erythro-hex-2-enopyranoside (**4g**).* Following general procedure F using 4-chlorobenzyl mercaptan (**2g**) in the glycosylation step and purification by silica gel column chromatography afforded the title compound as a white solid (117 mg, 80%). R_f 0.4 (2:1, hexane−EtOAc); Mp. 130−132 °C; $[\alpha]_D^{25}$ +93.33 (c 1.5, $CHCl_3$). ^1H NMR (300 MHz, $CDCl_3$): δ 7.39 (br s, 4H), 6.27 (dt, J = 10.6, 1.9 Hz, 2H), 6.02 (ddd, J = 10.6, 2.8, 2.3 Hz, 1H), 5.32 (dq, J = 9.3, 2.1 Hz, 1H), 4.99 (q, J = 2.5 Hz, 1H), 4.62 (ddd, J = 8.1, 5.5, 2.1 Hz, 1H), 4.55 (d, J = 14.2 Hz, 1H), 4.37 (dd, J = 12.5, 2.3 Hz, 1H), 4.23 (d, J = 14.2 Hz, 1H), 4.21 (dd, J = 12.5, 5.7 Hz, 1H), 2.14 (s, 3H), 2.12 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 170.5, 170.1, 135.5, 133.9, 132.1, 129.4, 125.9, 117.81, 83.2, 70.5, 63.6, 62.4, 56.1, 20.9, 20.8. IR ($CHCl_3$, cm^{-1}): 3021, 2926, 2854, 1742, 1492, 1371, 1319, 1215, 1098, 1044, 880, 743, 666, 599. HRMS (ESI): m/z $[M + Na]^+$ calcd. for $C_{17}H_{19}O_7ClNaS^+$, 425.04322; found, 425.04379.

*4′-tert-Butylbenzyl 4,6-Di-O-acetyl-2,3-dideoxy-1-sulfonyl-α-D-erythro-hex-2-enopyranoside (**4h**).* Following general procedure F using 4-*tert*-butylbenzyl mercaptan (**2h**) in the glycosylation step and purification by silica gel column chromatography afforded the title compound as oily liquid (131 mg, 85%). R_f 0.5 (3:2, hexane−EtOAc); $[\alpha]_D^{25}$ +28.45 (c 1.0, $CHCl_3$). ^1H NMR (300 MHz, $CDCl_3$): δ 7.43 (d, J = 8.3 Hz, 2H), 7.48 (d, J = 8.3 Hz, 2H), 6.26 (dt, J = 10.2, 1.1 Hz, 1H), 6.02 (ddd, J = 10.6, 2.8, 2.3 Hz, 1H), 5.32 (dq, J = 9.1, 1.5 Hz, 1H), 5.03 (q, J = 1.9 Hz, 1H), 4.65 (ddd, J = 8.3, 5.7, 1.5 Hz, 1H), 4.57 (d, J = 14.4 Hz, 1H), 4.33 (dd, J = 12.1, 1.9 Hz, 1H), 4.23 (d, J = 14.2 Hz, 1H), 4.21 (dd, J = 12.1, 5.7 Hz, 1H), 2.15 (s, 3H), 2.12 (s, 3H), 1.34 (s, 9H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 170.6, 170.1, 152.4, 133.6, 130.4, 126.1, 124.4, 118.2, 82.9, 70.4, 63.7, 62.6, 56.5, 34.7, 31.2, 20.9, 20.8. IR ($CHCl_3$, cm^{-1}): 3022, 2959, 2925, 2854, 1743, 1511, 1461, 1369, 1344, 1315, 1217, 1124, 1101, 1044, 978, 840, 746, 667, 605. HRMS (ESI): m/z $[M + NH_4]^+$ calcd. for $C_{21}H_{32}O_7NS^+$, 442.18940; found, 442.19019.

*Cyclohexyl 4,6-Di-O-acetyl-2,3-dideoxy-1-sulfonyl-α-D-erythro-hex-2-enopyranoside (**4i**).* Following general procedure F using cyclohexanethiol (**2i**) in the glycosylation step and purification by silica gel column chromatography afforded the title compound as a white solid (102 mg, 78%). R_f 0.5 (3:2, hexane−EtOAc); Mp. 96−98 °C; $[\alpha]_D^{25}$ +0.72 (c 1.5, $CHCl_3$). ^1H NMR (300 MHz, $CDCl_3$): δ 6.28 (dt, J = 10.6, 1.7 Hz, 1H), 6.15 (ddd, J = 12.5, 2.8, 1.9 Hz, 1H), 5.35−5.27 (m, 2H), 4.59 (ddd, J = 7.9, 4.9, 2.6 Hz, 1H), 4.28−4.17 (m, 2H), 3.22 (tt, J = 12.1, 3.4 Hz, 1H), 2.34−2.26 (m, 1H), 2.15−2.10 (m, 1H), 2.10 (s, 6H), 2.01−1.92 (m, 2H), 1.78−1.56 (m, 3H), 1.41−1.23 (m, 3H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 170.5, 170.1, 133.2, 118.9, 83.5, 70.2, 63.6, 62.6, 59.6, 26.1, 25.3, 25.2, 25.0, 23.7, 20.9, 20.7. IR ($CHCl_3$, cm^{-1}): 3022, 2929, 2857, 1740, 1549, 1451, 1370, 1218, 1097, 1044, 852, 771, 666, 614. HRMS (ESI): m/z $[M + Na]^+$ calcd. for $C_{16}H_{24}O_7NaS^+$, 383.11349; found, 383.11335.

*Cyclopentyl 4,6-Di-O-acetyl-2,3-dideoxy-1-sulfonyl-α-D-erythro-hex-2-enopyranoside (**4j**).* Following general procedure F using cyclopentanethiol (**2j**) in the glycosylation step and purification by silica gel column chromatography afforded the title compound as a yellow crystalline solid (94 mg, 74%). R_f 0.4 (3:2, hexane−EtOAc); Mp. 82−84 °C; $[\alpha]_D^{25}$ −1.28 (c 1.5, $CHCl_3$). ^1H NMR (500 MHz, $CDCl_3$): δ 6.27 (dt, J = 10.5, 2.3 Hz, 1H), 6.15 (ddd, J = 10.7, 2.3, 1.9 Hz, 1H), 5.34 (dq, J = 9.1, 1.8 Hz, 1H), 5.19 (q, J = 2.4 Hz, 1H), 4.57 (ddd, J = 8.5, 4.8, 2.5 Hz, 1H), 4.26 (dd, J = 12.4, 2.0 Hz, 1H), 4.22 (dd, J = 12.4, 4.9 Hz, 1H), 3.70 (quint, J = 8.1 Hz, 1H), 2.25−2.18 (m, 1H), 2.15−2.01 (m, 2H), 2.10 (s, 3H), 2.09 (s, 3H), 1.87−1.81 (m, 1H), 1.73−1.64 (m, 2H), 1.41−1.21 (m, 2H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 170.5, 170.1, 133.0, 118.8, 85.2, 70.2, 63.5, 62.3, 59.3, 27.6, 25.9, 25.8, 25.7, 20.9, 20.7. IR ($CHCl_3$, cm^{-1}): 3020, 2927, 2854, 1741, 1530, 1450, 1370, 1216, 1099, 1045, 975, 743, 667. HRMS (ESI): m/z $[M + NH_4]^+$ calcd. for $C_{15}H_{26}O_7NS^+$, 364.14245; found, 364.14386.

*n-Butyl 4,6-Di-O-acetyl-2,3-dideoxy-1-sulfonyl-α-D-erythro-hex-2-enopyranoside (**4k**).* Following general procedure F using *n*-butanethiol (**2k**) in the glycosylation step and purification by silica gel column chromatography afforded the title compound as pale yellow solid (100 mg, 82%). R_f 0.5 (3:2, hexane−EtOAc); Mp. 96−98 °C; $[\alpha]_D^{25}$ −53.33 (c 1.5, $CHCl_3$). ^1H NMR (300 MHz, $CDCl_3$): δ 6.29 (dt, J = 10.7, 1.9 Hz, 1H), 6.15 (ddd, J = 10.7, 2.6, 1.8 Hz, 1H), 5.33 (dq, J = 10.9, 1.9 Hz, 1H), 5.16 (q, J = 2.3 Hz, 1H), 4.57 (ddd, J = 7.7, 4.7, 2.6 Hz, 1H), 4.29−4.18 (m, 2H), 3.15 (t, J = 7.9 Hz, 2H), 2.11 (s, 3H), 2.10 (s, 3H), 1.94−1.81 (m, 2H), 1.50 (quint., J = 7.4 Hz, 2H), 0.99 (t, J = 7.4 Hz, 3H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 170.5, 170.1, 133.3, 118.4, 85.6, 70.4, 63.6, 62.4, 50.4, 23.5, 21.9, 20.9, 20.7, 13.5. IR ($CHCl_3$, cm^{-1}): 3020, 2957, 2926, 2854, 1742, 1549, 1515, 1465, 1216, 1099, 1046, 926, 972, 771, 667, 604. HRMS (ESI): m/z $[M + Na]^+$ calcd. for $C_{14}H_{22}O_7NaS^+$, 357.09784; found, 357.09739.

*C-Methyl 4,6-Di-O-acetyl-2,3-dideoxy-α-D-erythro-hex-2-enopyranoside (**8**).* A preformed solution of compound **4a** (60 mg, 0.17 mmol) in CH_2Cl_2 (1 mL) was treated with a solution of trimethylaluminum (170 μL, 2.0 M in hexanes, 0.17 mmol, 2.0 equiv) at 0 °C. The reaction mixture was stirred vigorously for 10−15 min at ice-cold temperature and then allowed to warm at room temperature and stirred for 2 h. The reaction was quenched with saturated $NaHCO_3$ (5 mL), diluted with EtOAc (10 mL), and extracted with EtOAc (30 mL × 3). The combined organic layers were washed with brine solution, dried over anhydrous Na_2SO_4, concentrated *in vacuo*, and purified by silica gel column chromatography to obtain the desired *C*-methyl glycosides **8** (30 mg, 78% yield) as a pale yellow liquid. R_f 0.4 (2:1, hexane−EtOAc); $[\alpha]_D^{25}$ +124.46 (c 1.2, $CHCl_3$). ^1H NMR (500 MHz, $CDCl_3$): δ 5.89 (ddd, J = 10.4, 2.6, 1.7 Hz, 1H), 5.77 (ddd, J = 10.3, 2.9, 2.1 Hz, 1H), 5.12 (m, 1H), 4.45−4.39 (m, 1H), 4.26 (dd, J = 11.9, 6.2 Hz, 1H), 4.16 (dd, J = 10.5, 3.7 Hz, 1H), 3.96 (dt, J = 6.3, 3.6 Hz, 1H), 2.10 (s, 3H), 2.09 (s, 3H), 1.31 (d, J = 6.8 Hz, 3H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 170.8, 170.4, 134.5, 122.7, 69.5, 67.8, 64.8, 62.7, 21.0, 20.7, 19.0. IR ($CHCl_3$, cm^{-1}): 3019, 1737, 1371, 1214, 1047, 742, 667. HRMS (ESI): m/z $[M - H]^+$ calcd. for $C_{11}H_{15}O_5^+$, 227.0914; found, 227.9060.

General Procedure for One-Pot Glycosylation−Oxidation−Dihydroxylation Reaction (G). Glycosylation coupling reaction between glycal **1** and a thio acceptor was performed following procedure F. The solution was then cooled at 0 °C, and EtOAc (2 mL) and an aqueous solution of $NaIO_4$ (1.36 mmol, 3.7 equiv) in H_2O (650 μL) were successively added, and the reaction mixture was stirred vigorously for 30−40 min. The reaction was quenched with saturated $NaHCO_3$ (10 mL), diluted with EtOAc (10 mL), and extracted with EtOAc (30 mL × 3). The combined organic layers were washed with brine solution, dried over anhydrous Na_2SO_4, and evaporated under reduced pressure to provide crude product. Following the acetylation of crude diol in CH_2Cl_2 (5 mL), pyridine (0.5 mL), and acetic anhydride (5 equiv) in the presence of a catalytic amount of DMAP gave the corresponding per-acetylated glycoside. Following the usual workup and purification by chromatography (silica gel, hexanes−EtOAc) afforded the desired α-D-mannopyranosides (**9**-**16**) as major products in good yields.

*Phenyl 2,3,4,6-Tetra-O-acetyl-1-sulfonyl-α-D-mannopyranoside (**9**).* Following general procedure G using thiophenol (**2a**) in the glycosylation step and purification by silica gel column chromatography afforded the title compound as a white semisolid (138 mg, 80%). R_f 0.4 (1:1, hexane−EtOAc); $[\alpha]_D^{25}$ +11.27 (c 1.3, $CHCl_3$). ^1H NMR (500 MHz, $CDCl_3$): δ 7.97 (d, J = 8.2 Hz, 2H), 7.73 (t, J = 7.5 Hz, 1H), 7.62 (t, J = 7.6 Hz, 2H), 6.03 (dd, J = 3.5, 2.1 Hz, 1H), 5.72 (dd, J = 9.3, 3.7

DOI: 10.1021/acs.joc.5b00975
J. Org. Chem. XXXX, XXX, XXX−XXX

Hz, 1H), 5.29 (t, J = 9.5 Hz, 1H), 4.84−4.9 (m, 2H), 4.23 (dd, J = 12.5, 6.0 Hz, 1H), 4.06 (dd, J = 12.5, 2.3 Hz, 1H), 2.13 (s, 3H), 2.09 (s, 3H), 2.06 (s, 3H), 2.03 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 170.3, 169.6, 169.4, 169.3, 136.2, 134.7, 129.4, 129.1, 90.3, 73.4, 68.8, 65.4, 65.2, 62.6, 20.7, 20.5. IR ($CHCl_3$, cm^{-1}): 3022, 2957, 2926, 2854, 1749, 1448, 1370, 1313, 1217, 1164, 1131, 1068, 1044, 981, 914, 733, 686, 667, 596, 580. HRMS (ESI): m/z [M + NH_4]$^+$ calcd. for $C_{20}H_{28}O_{11}NS^+$, 490.13776; found, 490.13827.

*4′-Chlorophenyl 2,3,4,6-Tetra-O-acetyl-1-sulfonyl-α-D-mannopyranoside (**10**).* Following general procedure G using 4-chlorothiophenol (**2b**) in the glycosylation step and purification by silica gel column chromatography afforded the title compound as a pale yellow solid (160 mg, 86%). R_f 0.5 (1:1, hexane−EtOAc); Mp. 128−130 °C; $[\alpha]_D^{25}$ +15.00 (c 1.0, $CHCl_3$). ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.90 (d, J = 8.5 Hz, 2H), 7.59 (d, J = 8.5 Hz, 2H), 6.01 (dd, J = 3.4, 2.3 Hz, 1H), 5.67 (dd, J = 9.2, 3.5 Hz, 1H), 5.28 (t, J = 9.3 Hz, 1H), 4.81 (d, J = 2.0 Hz, 1H), 4.77 (ddd, J = 9.0, 6.1, 2.0 Hz, 1H), 4.23 (dd, J = 12.5, 6.0 Hz, 1H), 4.07 (dd, J = 12.5, 2.1 Hz, 1H), 2.14 (s, 3H), 2.09 (s, 3H), 2.07 (s, 3H), 2.04 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 170.2, 169.5, 169.3, 169.3, 141.6, 134.5, 130.6, 129.7, 90.1, 73.4, 68.6, 65.3, 65.0, 62.5, 20.6, 20.5. IR ($CHCl_3$, cm^{-1}): 3020, 2926, 2854, 1752, 1465, 1371, 1325, 1215, 1047, 975, 928, 744, 667, 608. HRMS (ESI): m/z [M + NH_4]$^+$ calcd. for $C_{20}H_{27}O_{11}NClS^+$, 524.09879; found, 524.09632.

*Tolyl 2,3,4,6-Tetra-O-acetyl-1-sulfonyl-α-D-mannopyranoside (**11**).* Following general procedure G using *p*-toluenethiol (**2c**) in the glycosylation step and purification by silica gel column chromatography afforded the title compound as a white solid (142 mg, 80%). R_f 0.5 (1:1, hexane−EtOAc); Mp. 145−147 °C; $[\alpha]_D^{25}$ +10.00 (c 1.5, $CHCl_3$). ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.84 (d, J = 8.2 Hz, 2H), 7.40 (d, J = 8.1 Hz, 2H), 6.01 (dd, J = 3.5, 2.1 Hz, 1H), 5.72 (dd, J = 9.3, 3.5 Hz, 1H), 5.30 (t, J = 9.6 Hz, 1H), 4.81 (ddd, J = 8.1, 5.8, 2.0 Hz, 1H), 4.78 (d, J = 1.8 Hz, 1H), 4.23 (dd, J = 12.5, 5.8 Hz, 1H), 4.07 (dd, J = 12.4, 2.0, Hz, 1H), 2.47 (s, 3H), 2.13 (s, 3H), 2.09 (s, 3H), 2.07 (s, 3H), 2.03 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 170.3, 169.6, 169.4, 146.0, 133.1, 130.0, 129.1, 90.3, 73.2, 68.8, 65.4, 65.3, 62.5, 21.7, 20.6, 20.5. IR ($CHCl_3$, cm^{-1}): 3021, 2948, 1730, 1465, 1445, 1373, 1244, 1217, 1045, 937, 847, 642, 667, 633, 607. HRMS (ESI): m/z [M + NH_4]$^+$ calcd. for $C_{21}H_{30}O_{11}NS^+$, 504.15341; found, 504.15391.

*Naphthyl 2,3,4,6-Tetra-O-acetyl-1-sulfonyl-α-D-mannopyranoside (**12**).* Following general procedure G using 2-napthalenethiol (**2e**) in the glycosylation step and purification by silica gel column chromatography afforded the title compound as a white solid (143 mg, 75%). R_f 0.5 (1:1, hexane−EtOAc); Mp. 141−143 °C; $[\alpha]_D^{25}$ +50.00 (c 1.0, $CHCl_3$). ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.56 (s, 1H), 8.05 (d, J = 3.5 Hz, 1H), 8.03 (d, J = 2.8 Hz, 1H), 7.96 (d, J = 8.1 Hz, 1H), 7.91 (dd, J = 8.7, 1.7 Hz, 1H), 7.72 (t, J = 7.9 Hz, 1H), 7.66 (t, J = 7.9 Hz, 1H), 6.09 (dd, J = 3.5, 2.1 Hz, 1H), 5.78 (dd, J = 9.2, 3.5 Hz, 1H), 5.30 (t, J = 9.5 Hz, 1H), 4.92 (d, J = 2.0 Hz, 1H), 4.86 (ddd, J = 8.9, 6.0, 2.3 Hz, 1H), 4.23 (dd, J = 12.5, 6.0 Hz, 1H), 4.04 (dd, J = 12.5, 2.3 Hz, 1H), 2.12 (s, 3H), 2.10 (s, 3H), 2.04 (s, 3H), 1.91 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 170.3, 169.6, 169.3, 135.7, 133.0, 131.4, 132.1, 131.4, 129.8, 129.6, 129.5, 128.0, 127.9, 123.1, 90.3, 73.3, 68.8, 65.5, 65.3, 62.6, 20.6, 20.5, 20.5. IR ($CHCl_3$, cm^{-1}): 3021, 2925, 2854, 1748, 1457, 1369, 1318, 1215, 1161, 1121, 1066, 746, 667, 568. HRMS (ESI): m/z [M + NH_4]$^+$ calcd. for C_{24} $H_{30}O_{11}NS^+$, 540.15341; found, 540.15434.

*Benzyl 2,3,4,6-Tetra-O-acetyl-1-sulfonyl-α-D-mannopyranoside (**13**).* Following general procedure G using benzyl mercaptan (**2f**) in the glycosylation step and purification by silica gel column chromatography afforded the title compound as a white solid (128 mg, 72%). R_f 0.4 (3:2, hexane−EtOAc); $[\alpha]_D^{25}$ +22.05 (c 1.3, $CHCl_3$). ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.48−7.39 (m, 5H), 5.89 (dd, J = 3.7, 2.0 Hz, 1H), 5.60 (dd, J = 9.3, 3.7 Hz, 1H), 5.28 (t, J = 9.6 Hz, 1H), 4.73 (ddd, J = 8.2, 6.0, 2.3 Hz, 1H), 4.69 (d, J = 1.8 Hz, 1H),4.53 (d, J = 14.2 Hz, 1H), 4.28 (dd, J = 12.5, 6.0 Hz, 1H), 4.27 (d, J = 14.2 Hz, 1H), 4.15 (dd, J = 12.5, 2.3 Hz, 1H), 2.14 (s, 3H), 2.11 (s, 3H), 2.07 (s, 3H), 1.99 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 170.3, 169.6, 169.2, 169.0, 130.8, 129.3, 129.1, 126.8, 86.0, 73.3, 68.8, 65.2, 64.4, 62.5, 57.0, 20.7, 20.6, 20.4. IR ($CHCl_3$, cm^{-1}): 3021, 2925, 2854, 1748, 1457, 1369, 1318, 1215, 1161, 1121, 1066, 746, 667, 568. HRMS (ESI): m/z [M + NH_4]$^+$ calcd. for $C_{21}H_{30}O_{11}NS^+$, 504.15341; found, 504.15323.

*4′-Chlorobenzyl 2,3,4,6-Tetra-O-acetyl-1-sulfonyl-α-D-mannopyranoside (**14**).* Following general procedure G using 4-chlorobenzyl mercaptan (**2g**) in the glycosylation step and purification by silica gel column chromatography afforded the title compound as a white solid (143 mg, 75%). R_f 0.5 (3:2, hexane−EtOAc); Mp. 128−130 °C; $[\alpha]_D^{25}$ +110.00 (c 1.0, $CHCl_3$). ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.41−7.36 (m, 4H), 5.89 (dd, J = 3.7, 2.1 Hz, 1H), 5.58 (dd, J = 9.2, 3.66 Hz, 1H), 5.28 (t, J = 9.6 Hz, 1H), 4.71 (ddd, J = 9.6, 5.8, 2.3 Hz, 1H), 4.65 (d, J = 2.0 Hz, 1H), 4.50 (d, J = 14.2 Hz, 1H), 4.28 (dd, J = 12.5, 5.8 Hz, 1H), 4.23 (d, J = 14.2 Hz, 1H), 4.28 (dd, J = 12.5, 2.4 Hz, 1H), 2.14 (s, 3H), 2.12 (s, 3H), 2.07 (s, 3H), 2.00 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$): δ170.3, 169.6, 169.2, 169.1, 135.7, 132.1, 129.5, 125.2, 86.1, 73.5, 68.8, 65.2, 64.3, 62.5, 56.2, 20.8, 20.6, 20.5. IR ($CHCl_3$, cm^{-1}): 3021, 2926, 2854, 1750, 1463, 1370, 1322, 1214, 1116, 1045, 980, 746, 666. HRMS (ESI): m/z [M + NH_4]$^+$ calcd. for $C_{21}H_{29}O_{11}NClS^+$, 538.11444; found, 538.11563.

*4′-tert-Butylbenzyl 2,3,4,6-Tetra-O-acetyl-1-sulfonyl-α-D-mannopyranoside (**15**).* Following general procedure G using 4-*tert*-butylbenzyl mercaptan (**2h**) in the glycosylation step and purification by silica gel column chromatography afforded the title compound as a white oily liquid (161 mg, 81%). R_f 0.5 (1:1, hexane−EtOAc); $[\alpha]_D^{25}$ +63.33 (c 1.5, $CHCl_3$). ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.43 (d, J = 8.3 Hz, 2H), 7.36 (d, J = 8.3 Hz, 2H), 5.91 (dd, J = 3.6, 1.7 Hz, 1H), 5.61 (dd, J = 9.4, 3.6 Hz, 1H), 5.29 (t, J = 9.6 Hz, 1H), 4.74 (ddd, J = 9.3, 5.6, 1.9 Hz, 1H), 4.71 (d, J = 1.3 Hz, 1H), 4.52 (d, J = 14.4 Hz, 1H), 4.29 (dd, J = 12.5, 5.6 Hz, 1H), 4.23 (d, J = 14.4 Hz, 1H), 4.13 (dd, J = 12.5, 2.1 Hz, 1H), 2.14 (s, 3H), 2.12 (s, 3H), 2.07 (s, 3H), 1.99 (s, 3H), 1.32 (s, 9H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 170.3, 169.6, 169.2, 169.1, 152.5, 130.4, 126.2, 123.6, 86.1, 73.3, 68.8, 65.2, 64.5, 62.5, 56.6, 34.7, 31.2, 20.7, 20.6, 20.4. IR ($CHCl_3$, cm^{-1}): 3022, 2961, 2927, 2856, 1749, 1369, 1319, 1215, 1115, 1046, 746, 667. HRMS (ESI): m/z [M + NH_4]$^+$ calcd. for $C_{25}H_{38}O_{11}NS^+$, 560.21601; found, 560.21714.

*Cyclohexyl 2,3,4,6-Tetra-O-acetyl-1-sulfonyl-α-D-mannopyranoside (**16**).* Following general procedure G using cyclohexanethiol (**2i**) in the glycosylation step and purification by silica gel column chromatography afforded the title compound as a white solid (131 mg, 75%). R_f 0.5 (1:1, hexane−EtOAc); Mp. 102−104 °C; $[\alpha]_D^{25}$ +40.00 (c 1.3, $CHCl_3$). ^{1}H NMR (500 MHz, $CDCl_3$): δ 5.95 (dd, J = 3.5, 2.0 Hz, 1H), 5.63 (dd, J = 9.3, 3.7 Hz, 1H), 5.30 (t, J = 9.6 Hz, 1H), 4.96 (d, J = 1.8 Hz, 1H), 4.70 (ddd, J = 7.9, 5.6, 2.1 Hz, 1H), 4.26 (dd, J = 12.5, 5.8 Hz, 1H), 4.14 (dd, J = 12.5, 2.3 Hz, 1H), 3.15 (tt, J = 12.2, 3.4 Hz, 1H), 2.32−2.23 (m, 1H), 2.01−1.92 (m, 1H), 2.17 (s, 3H), 2.11 (s, 3H), 2.06 (s, 3H), 2.02 (s, 3H), 1.76−1.56 (m, 3H), 1.41−1.14 (m, 3H); 0.92−0.83 (m, 2H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 170.3, 169.7, 169.3, 169.2, 85.8, 73.2, 68.8, 65.3, 65.3, 62.5, 59.9, 25.8, 25.2, 25.1, 24.9, 23.5, 20.7, 20.6, 20.5. IR ($CHCl_3$, cm^{-1}): 3022, 2928, 2856, 1748, 1452, 1370, 1311, 1214, 1157, 1113, 1047, 979, 745, 666, 600. HRMS (ESI): m/z [M + NH_4]$^+$ calcd. for $C_{20}H_{34}O_{11}NS^+$, 496.1847; found, 496.18539.

*Menthyl 2,3,4,6-Tetra-O-acetyl-α-D-mannopyranoside (**21**).* R_f0.5 (3:2, hexane−EtOAc); $[\alpha]_D^{25}$ +103.78 (c 3.9, $CHCl_3$). ^{1}H NMR (500 MHz, $CDCl_3$): δ 5.33 (dd, J = 10.1, 3.2 Hz, 1H), 5.29 (t, J = 9.9 Hz, 1H), 5.14 (dd, J = 3.1, 1.7 Hz, 1H), 5.02 (d, J = 1.2 Hz, 1H), 4.26 (dd, J = 12.4, 5.3 Hz, 1H), 4.09 (dd, J = 12.2, 2.1 Hz,1H), 4.04 (ddd, J = 9.5, 5.2, 2.1 Hz, 1H), 3.46 (td, J = 10.7, 4.1 Hz, 1H), 2.17 (s, 3H), 2.09 (s, 3H), 2.06 (s, 3H), 2.00 (s, 3H), 2.22−2.17 (m, 1H), 2.05−2.01 (m, 1H), 1.70−1.64 (m, 2H), 1.38−1.29 (m, 2H), 0.95 (d, J = 7.0 Hz, 3H), 0.98−0.84 (m, 3H), 0.92 (d, J = 6.7 Hz, 3H), 0.77 (d, J = 6.9 Hz, 3H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 170.6, 170.1, 169.8, 169.7, 94.2, 76.8, 70.5, 69.1, 68.9, 66.0, 62.5, 47.4, 39.5, 34.1, 31.3, 25.3, 22.6, 22.1, 21.0, 20.9, 20.7, 20.6, 15.2. IR ($CHCl_3$, cm^{-1}): 3025, 2956, 2923, 1745, 1452, 1216, 1130, 1038, 977, 770, 754, 599. HRMS (ESI): m/z [M + NH_4]$^+$ calcd. for $C_{24}H_{42}NO_{10}^+$, 504.28195; found, 504.28032.

■ ASSOCIATED CONTENT

Supporting Information

^{1}H NMR and ^{13}C NMR spectra of all the products. The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.joc.5b00975.

DOI: 10.1021/acs.joc.5b00975
J. Org. Chem. XXXX, XXX, XXX−XXX

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Notes

The authors declare no competing financial interest.

ACKNOWLEDGMENTS

S.K. is grateful for financial support from Department of Science and Technology (GAP0397 & 0471), New Delhi. We are also grateful to the Director CSIR-IICT for providing the necessary infrastructure. S.C. acknowledges the CSIR, New Delhi for SRF.

REFERENCES

(1) (a) Varki, A. *Glycobiology* **1993**, *3*, 97−130; *Essent. Glycobiol.* **1999**, 57. (b) Dwek, R. A. *Chem. Rev.* **1996**, *96*, 683−720. (c) Rudd, P. M.; Elliott, T.; Cresswell, P.; Wilson, I. A.; Dwek, R. A. *Science* **2001**, *291*, 2370−2376.

(2) (a) Plante, O. J.; Palmacci, E. R.; Seeberger, P. H. *Adv. Carbohydr. Chem. Biochem.* **2003**, *58*, 35−54. (b) Koeller, K. M.; Wong, C.-H. *Chem. Rev.* **2000**, *100*, 4465−4493. (c) Zhu, X.; Schmidt, R. R. *Angew. Chem., Int. Ed.* **2009**, *48*, 1900−1934. (d) Nicolaou, K. C.; Mitchell, H. J. *Angew. Chem.* **2001**, *113*, 162−1672; *Angew. Chem., Int. Ed.* **2001**, *40*, 1576−1624.

(3) (a) Garegg, P. J. *Adv. Carbohydr. Chem. Biochem.* **1997**, *52*, 179−205. (b) Norberg, T. *Front. Nat. Prod. Res.* **1996**, *1*, 82−106. (c) Kahne, D.; Walker, S.; Cheng, Y.; Van Engen, D. *J. Am. Chem. Soc.* **1989**, *111*, 6881−6882.

(4) (a) Defaye, J.; Gelas, J. Thio-oligosaccharides: Their Synthesis and Reactions with Enzymes. In *Studies in Natural Products Chemistry*; Atta-ur-Rahman, Ed.; Elsevier: Amsterdam, The Netherlands, 1991; Vol. *8E*, pp 315−357. (b) Driguez, H. *Top. Curr. Chem.* **1997**, *187*, 85−116. (c) Robina, I.; Vogel, P.; Witczak, Z. J. *Curr. Org. Chem.* **2001**, *5*, 1177−1214. (d) Witczak, Z. J. *Curr. Med. Chem.* **1999**, *6*, 2169−2174.

(5) (a) Huang, Z.; Schneider, K. C.; Benner, S. A. *J. Org. Chem.* **1991**, *56*, 3869−3882. (b) Nambiar, K. P.; Stackhouse, J.; Stauffer, D. M.; Kennedy, W. P.; Eldredge, J. K.; Benner, S. A. *Science* **1984**, *223*, 1299−1301.

(6) Gervay, J.; Flaherty, T. M.; Holmes, D. *Tetrahedron* **1997**, *53*, 16355−16364.

(7) Witczak, Z. J.; Kaplon, P.; Dey, P. M. *Carbohydr. Res.* **2003**, *338*, 11−18.

(8) Singer, M.; Lopez, M.; Bornaghi, L. F.; Innocenti, A.; Vullo, D.; Supuran, C. T.; Poulsen, S.-A. *Bioorg. Med. Chem. Lett.* **2009**, *19*, 2273−2276.

(9) (a) Poláková, M.; Šesták, S.; Lattová, E.; Petruš, L.; Mucha, J.; Tvaroška, I.; Kóňa, J. *Eur. J. Med. Chem.* **2011**, *46*, 944−952. (b) Poláková, M.; Stanton, R.; Wilson, I. B.; Holková, I.; Šesták, S.; Machová, E.; Jandová, Z.; Kóňa, J. *Carbohydr. Res.* **2015**, *406*, 34−40.

(10) (a) Brown, D. S.; Bruno, M.; Davenport, R. J.; Ley, S. V. *Tetrahedron* **1989**, *45*, 4293−4308. (b) Brown, D. S.; Ley, S. V.; Vile, S. *Tetrahedron Lett.* **1988**, *29*, 4873−4876. (c) Brown, D. S.; Ley, S. V.; Vile, S.; Thompson, M. *Tetrahedron* **1991**, *47*, 1329−1342. (d) Charreau, P.; Ley, S. V.; Vettiger, T. M.; Vile, S. *Synlett* **1991**, 415−417.

(11) Chang, G. X.; Lowary, T. L. *Org. Lett.* **2000**, *2*, 1505−1508.

(12) Beau, J. M.; Sinaÿ, P. *Tetrahedron Lett.* **1985**, *26*, 6193−6193.

(13) (a) Belica, P. S.; Franck, R. W. *Tetrahedron Lett.* **1998**, *39*, 8225−8228. (b) Pasetto, P.; Chen, X.; Drain, C. M.; Franck, R. W. *Chem. Commun.* **2001**, 81−82. (c) Paterson, D. E.; Griffin, F. K.; Alcaraz, M. L.; Taylor, R. J. K. *Eur. J. Org. Chem.* **2002**, 1323−1336. (d) Griffin, F. K.; Paterson, D. E.; Murphy, P. V.; Taylor, R. J. K. *Eur. J. Org. Chem.* **2002**, 1305−1322. (e) Ohnishi, Y.; Ichikawa, Y. *Bioorg. Med. Chem. Lett.* **2002**, *12*, 997−999. (f) Falconer, R. A.; Toth, I. *Bioorg. Med. Chem.* **2007**, *15*, 7012−7020.

(14) (a) Pouilly, P.; Chenede, A.; Mallet, J.-M.; Sinaÿ, P. *Tetrahedron Lett.* **1992**, *33*, 8065−8068. (b) Fernandez-Mayoralas, A.; Marra, A.; Trumtel, M.; Veyrieres, A.; Sinaÿ, P. *Carbohydr. Res.* **1989**, *188*, 81−95. (c) Griffin, F. K.; Murphy, P. V.; Paterson, D. E.; Taylor, R. J. K. *Tetrahedron Lett.* **1998**, *39*, 8179−8182. (d) Murphy, P. V.; McDonnell, C.; Hamig, L.; Paterson, D. E.; Taylor, R. J. K. *Tetrahedron: Asymmetry* **2003**, *14*, 79−85.

(15) Micskei, K.; Juhász, Z.; Ratković, Z. R.; Somsák, L. *Tetrahedron Lett.* **2006**, *47*, 6117−6120.

(16) (a) Arjona, O.; Menchaca, R.; Plumet, J. *Tetrahedron* **2001**, *57*, 6751−6755. (b) Priebe, W.; Grynkiewicz, G. *Tetrahedron Lett.* **1991**, *32*, 7353−7356. (c) Bonner, W. A.; Drisko, R. W. *J. Am. Chem. Soc.* **1948**, *70*, 2435−2438. (d) Agnihotri, G.; Misra, A. K. *Carbohydr. Res.* **2006**, *341*, 275−280. (e) Morais, G. R.; Humphrey, A. J.; Falconer, R. A. *Tetrahedron* **2008**, *64*, 7426−7431.

(17) (a) Ferrier, R. J. *Chem. Soc.* **1964**, 5443−5449. (b) Ciment, D. M.; Ferrier, R. J. *Chem. Soc. C* **1966**, 441−445. (c) Ferrier, R. J.; Sankey, G. H. *J. Chem. Soc. C* **1966**, 2345−2349.

(18) (a) Piccialli, V. *Molecules* **2014**, *19*, 6534−6582. (b) Malik, M.; Ceborska, M.; Grzegorz Witkowski, G.; Jarosz, S. *Tetrahedron: Asymmetry* **2015**, *26*, 29−34.

(19) (a) Chittela, S.; Reddy, T. R.; Radha Krishna, P.; Kashyap, S. *RSC Adv.* **2014**, *4*, 46327−46331. (b) Battina, S. K.; Reddy, T. R.; Radha Krishna, P.; Kashyap, S. *Tetrahedron Lett.* **2015**, *56*, 1798−1800. (c) Srinivas, B.; Reddy, T. R.; Kashyap, S. *Carbohydr. Res.* **2015**, *406*, 86−92. (d) Reddy, T. R.; Chittela, S.; Kashyap, S. *Tetrahedron* **2014**, *70*, 9224−9229.

(20) (a) Djerassi, C.; Engle, R. R. *J. Am. Chem. Soc.* **1953**, *75*, 3838−3840. (b) Scholte, A. A.; An, M. H.; Snapper, M. L. *Org. Lett.* **2006**, *8*, 4759−4762. (c) Beligny, S.; Eibauer, S.; Maechling, S.; Blechert, S. *Angew. Chem., Int. Ed.* **2006**, *45*, 1900−1903. (d) Neisius, N. M.; Plietker, B. *J. Org. Chem.* **2008**, *73*, 3218−3227.

(21) Osmium tetraoxide and potassium hydrogen persulfate (oxone) have been reported for chemoselective oxidation of sulfide. See: (a) Kalder, S. W.; Hammond, M. *Tetrahedron Lett.* **1991**, *32*, 5043−5046. (b) Trost, B. M.; Curran, D. P. *Tetrahedron Lett.* **1981**, *22*, 1287−1290.

(22) The HOF·CH_3CN complex was first introduced by Rozen as a new oxidizing agent which was then used to oxidize several functionalities such as sulfides, alcohols, amines, azides, olefins etc. See references cited within 16e.

(23) The preparation of compound **4a** was previously reported by Brown (ref 10a) and Giuliano. See: Basava, V.; Flores, B.; Giovine, M.; Licisyn, T.; Walck, K.; Boyko, W.; Giuliano, R. *J. Carbohydr. Chem.* **2008**, *27*, 389−400. These conditions provide less selectivity (α:β, 3:1) and require strong acidic reagents and excessive loading of nucleophile and benzensulfinic acid ($PhSO_2H$).

(24) (a) Reddy, T. R.; Rao, D. S.; Kashyap, S. *RSC Adv.* **2015**, *5*, 28338−28343. (b) Narasimha, G.; Srinivas, B.; Radha Krishna, P.; Kashyap, S. *Synlett* **2014**, 523−526. (c) Srinivas, B.; Reddy, T. R.; Radha Krishna, P.; Kashyap, S. *Synlett* **2014**, 1325−1330. (d) Hotha, S.; Kashyap, S. *J. Am. Chem. Soc.* **2006**, *128*, 9620−9621. (e) Hotha, S.; Kashyap, S. *J. Org. Chem.* **2006**, *71*, 364−367. (f) Vidadala, S. R.; Thadke, S. A.; Hotha, S.; Kashyap, S. *J. Carbohydr. Chem.* **2012**, *31*, 241−251.

(25) OsO_4-catalyzed dihydroxylation of compound **4a** in acetone/water or *tert*-butanol/water solvent system failed to give desired products.

DOI: 10.1021/acs.joc.5b00975
J. Org. Chem. XXXX, XXX, XXX−XXX