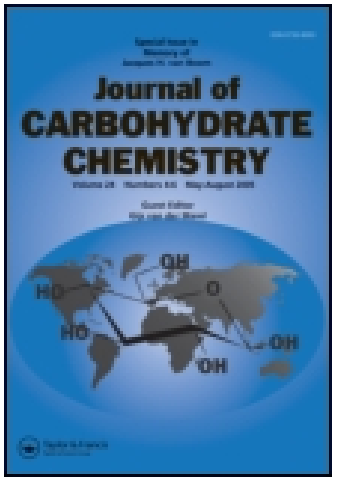

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Zn(II) Triflate-Catalyzed N-Glycosylation: Synthesis of Sulfonamide and Amide Functionalized 2,3-Unsaturated Glycosides

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Zn(II) Triflate-Catalyzed *N*-Glycosylation: Synthesis of Sulfonamide and Amide Functionalized 2,3-Unsaturated Glycosides

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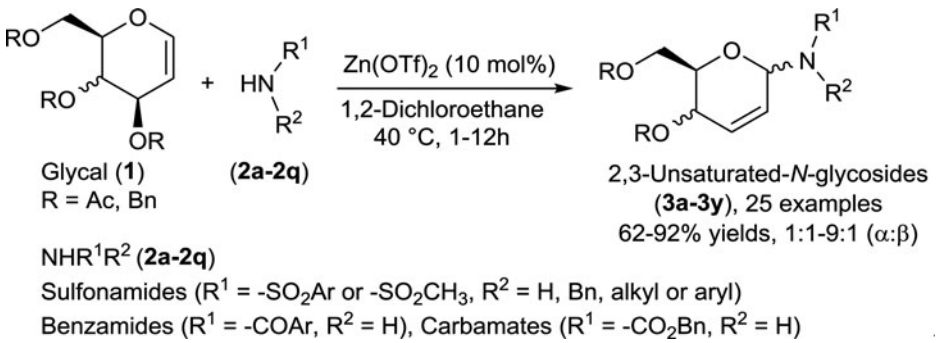
GRAPHICAL ABSTRACT



A highly efficient and mild method for the synthesis of glycosyl sulfonamides and glycosyl amides from glycal has been described using $Zn(OTf)_2$ as an economical and environmentally friendly catalyst. Various *N*-nucleophiles comprising sulfonamides, benzamides, and carbamates were glycosylated with glycals to obtain corresponding 2,3-unsaturated *N*-glycosides in good yields.

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Keywords Azaglycosylation; 2,3-Unsaturated *N*-glycosides; Glycal; Sulfonamides; Zn(II) triflate

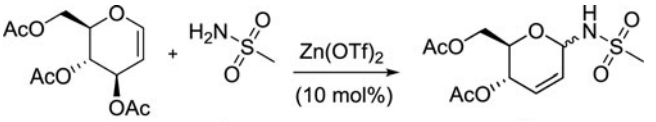
INTRODUCTION

Compounds having sulfonamide linkages are of particular interest due to their medicinal and biological applications.[1,2] The carbohydrate-sulfonamide constructs have gained significant attention in recent years since they display potential activity against several carbonic anhydrases (CAs)[3–6] and play critical roles in various biological processes due to their diuretic, antiglaucoma, antiobesity, and antitumor activities.[7–9] In addition, 2,3-unsaturated *N*-glycoside derivatives such as *N*-glycosyl sulfonamides have emerged as antibiotics, antineoplastic and antiviral therapeutic agents,[10,11] and antiproliferative agents against human hepatocellular carcinoma cell lines Hep-G2.[12]

In this context, incorporating *N*-glycosidic linkages in "*N*-pseudo-glycals" and 2,3-unsaturated *N*-glycosyl sulfonamides remains a motivating area of research for carbohydrate chemists. Another incentive for focusing on 2,3-unsaturated *N*-glycosides is the presence of C(2)-C(3) olefin in the pyran ring, which offers further usefulness as chiral synthons and potential intermediates in the preparation of diverse and complex glycoconjugates.[13–15] The chemical synthesis of 2,3-unsaturated *N*-glycosides relies on Ferrier azaglycosylation, which represents a significant method for constructing *N*-glycosidic linkages.[16] Alternatively, Danishefsky and coworkers have described sulfonamidoglycosylation for the preparation of 2-iodo-glycosyl sulfonamides and extensively utilized it for 2-amino-oligosaccharide and glycoconjugate syntheses.[17,18] Recently, Colinas et al. reported the synthesis of 2-deoxy and 2,3-unsaturated *N*-glycosyl sulfonamides using triphenyl phosphine hydrobromide[12] and boron trifluoride etherate,[19] respectively.

In contrast to Ferrier reaction of glycals with oxygen, sulphur, and carbon nucleophiles, the use of nitrogen nucleophiles in azaglycosylation to obtain *N*-glycosides is limited to a few methods.[19–27] Therefore, constant motivation exists in the search for new protocols for the synthesis of glycoconjugates and various functionalized saccharides employing mild reagent systems. In this context, we have recently described the utility of $Zn(OTf)_2$ for the synthesis of 2,3-unsaturated *O*-glycosides.[28] Noteworthy, the use of nontoxic, eco-friendly, economical, and easily available reagents is always appreciated. To pursue our research in glycosylation and glycoconjugate syntheses,[28–35] herein we report Zn(II) triflate as an economical, less moisture-sensitive, and environmentally benign catalyst for the synthesis of *N*-glycosides. The present reagent system represents a mild reaction condition and is amenable to a diverse range of nitrogen nucleophiles comprising sulfonamides, benzamides, and carbamates.

Table 1: Optimization of azaglycosylation reaction[a]



1a **2a** **3a**

Entry	Solvent	Time	Conversion[b]	Yield[c]	$\alpha:\beta$ ratio[d]
1	Dichloromethane	24 h	30%	NR	—
2	THF	24 h	40%	NR	—
3	**1,2-Dichloroethane**	**4 h**	**100%**	**92%**	**76:24**
4	Acetonitrile	6 h	100%	82%	70:30
5	1,4-Dioxane	24 h	80%	56%	75:25
6	Toluene	24 h	30%	NR	—
7[e]	Toluene	8 h	90%	80%	73:27
8	Diethyl ether	24 h	Traces	NR	—

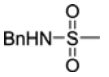
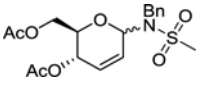
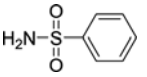
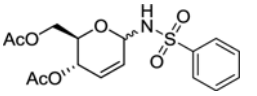
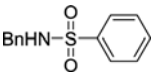
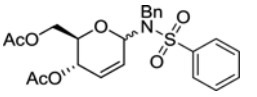
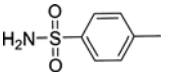
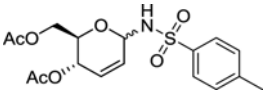
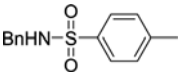
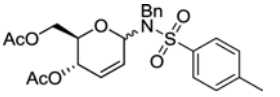
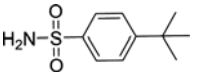
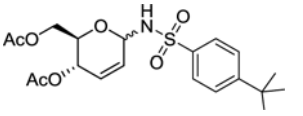
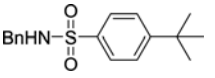
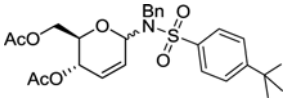
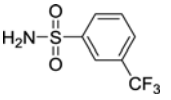
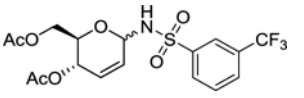
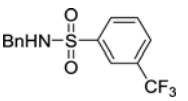
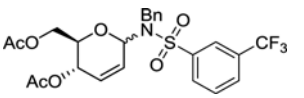
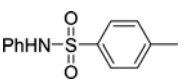
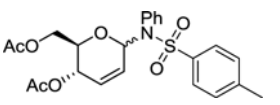
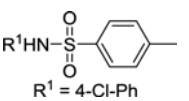
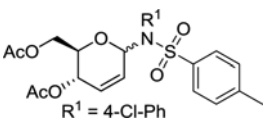
[a]The reaction conditions: 3,4,6-tri-*O*-acetyl glucal (**1a)** (0.37 mmol), $MsNH_2$ (**2a)** (0.40 mmol), 40°C.
[b]Progress of reaction was monitored by TLC analysis at given time.
[c]Isolated yields, NR = not recorded.
[d]The $\alpha:\beta$ ratios were examined by ^{1}H NMR spectroscopy.
[e]Reaction was carried out at 60°C.

RESULTS AND DISCUSSION

To begin with, the Ferrier azaglycosylation of 3,4,6-tri-*O*-acetyl glucal (**1a**) was performed with methane sulfonamide (**2a**) as the *N*-nucleophile in the presence of 10 mol% $Zn(OTf)_2$ in dichloromethane at room temperature. Initially, we found that the reaction did not work; however, an incremental rise in the temperature resulted in a 30% conversion after 24 h at 40°C with 60% recovery of starting material. Consequently, we next attempted to optimize the reaction conditions in various organic solvents such tetrahydrofuran, toluene, diethyl ether, 1,2-dichloroethane, acetonitrile, and 1,4-dioxane, and the results are presented in Table 1.

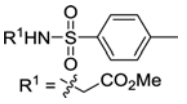
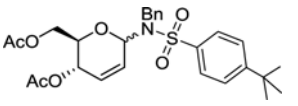
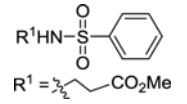
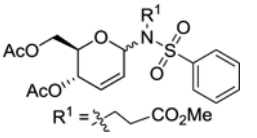
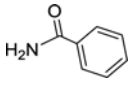
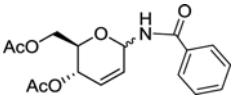
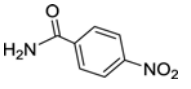
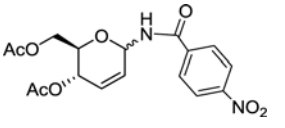
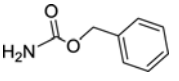
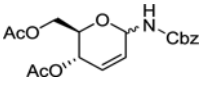
Surprisingly, the rate of reaction increased considerably when 1,2-dichloroethane and acetonitrile were employed as the solvents and complete conversion was observed in 4 to 6 h. On the other hand, only an 80% conversion was realized in the case of 1,4-dioxane after 24 h at 40°C. Nevertheless, Ferrier azaglycosylation of **1a** and **2a** proceeded smoothly in 1,2-dichloroethane with 10 mol% of $Zn(OTf)_2$ at 40°C to obtain the corresponding glycosyl sulfonamide **3a** in a 92% yield as a mixture of both anomers in an α/β ratio of 76:24. The stereochemical outcome in the azaglycosylation reaction was precisely examined by spectroscopic analyses and correlated with literature data.[32] Other solvents such as THF and toluene resulted in poor conversion, whereas diethyl ether was ineffective even after a prolonged reaction time (Table 1).

Table 2: Azaglycosylation of **1a** with various *N*-nucleophiles[a]

Entry	NuH		N-Glycosides		Time (h)	Yield[b] (%)[ref]	$\alpha:\beta$[c]
1		**2b**		**3b**	7	86[(32)]	82:18
2		**2c**		**3c**	8	86[(32)]	74:26
3		**2d**		**3d**	8	76[(32)]	87:13
4		**2e**		**3e**	6	84[(32)]	75:25
5		**2f**		**3f**	10	73[(32)]	85:15
6		**2g**		**3g**	5	78[(32)]	74:26
7		**2h**		**3h**	6	75[(32)]	88:12
8		**2i**		**3i**	4	82[(32)]	72:28
9		**2j**		**3j**	1	78[(32)]	77:23
10		**2k**		**3k**	0.5	76[(32)]	90:10
11	 R^1 = 4-Cl-Ph	**2l**	 R^1 = 4-Cl-Ph	**3l**	2	70[(32)]	88:12

(Continued on next page)

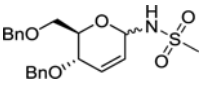
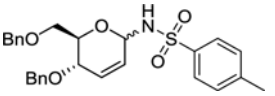
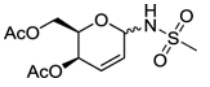
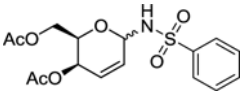
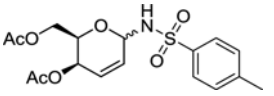
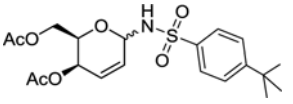
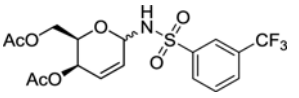
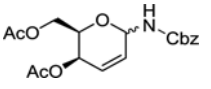
Table 2: Azaglycosylation of **1a** with various *N*-nucleophiles[a] *(Continued)*

Entry	NuH		N-Glycosides		Time (h)	Yield[b] (%)[ref]	$\alpha:\beta$[c]
12		**2m**		**3m**	6	64	56:44
13		**2n**		**3n**	8	74[(32)]	72:28
14[d]		**2o**		**3o**	12	88[(32)]	70:30
15[d]		**2p**		**3p**	12	62[(32)]	67:33
16		**2q**		**3q**	8	67[(32)]	74:26

[a]All reactions were performed with glycal **1a** (1 equiv), nucleophile (1.1 equiv), 10 mol% $Zn(OTf)_2$ in 1,2-dichloroethane at 40°C.
[b]Isolated yields.
[c]The $\alpha:\beta$ ratios were determined by ^1H NMR spectral analysis.
[d]The reactions were performed in DCE:CH_3CN (1:1).

We next examined the scope and generality of the present reagent system with a wide range of sulfonamides to generate the various substituted glycosyl sulfonamides. Accordingly, the azaglycosylation reaction of tri-*O*-acetyl glucal (**1a**) with sulfonamides (**2b**–**2n**) was performed respectively under optimized condition to obtain the corresponding glycosyl sulfonamides (**3b**–**3n**) in good yields (Table 2, entries 2–13). Notably, the glycosylation coupling of glycal **1a** with *N*-benzyl (**2b, 2d, 2f, 2h, 2j)-** and *N*-phenyl (**2k**, **2l**)-substituted sulfonamides proceeded efficiently and smoothly to afford the corresponding glycosyl sulfonamides in good yields and high anomeric selectivity. Additionally, the amino-acid-derived sulfonamides (**2m, 2n**) were also incorporated in "*N*-pseudo-glycals" to obtain amino acid glycoconjugates (**2m, 2n**) in satisfactory yields (Table 2, entries 12 and 13). Significantly, this method seems to be useful for chemical ligation of carbohydrate scaffolds with various biomolecules

Table 3: $Zn(OTf)_2$-catalyzed azaglycosylation of glycals[a]

Entry	NuH	N-Glycosides		Time (h)	Yield[b] (%)[ref]	$\alpha:\beta$[c]
1	**2a**		**3r**	2	84[(32)]	78:22
2	**2e**		**3s**	6	80	80:20
3	**2a**		**3t**	8	85[(32)]	85:15
4	**2c**		**3u**	10	72[(20)]	80:20
5	**2e**		**3v**	8	81[(32)]	86:14
6	**2g**		**3w**	12	78	80:20
7	**2i**		**3x**	6	75	82:18
8	**2q**		**3y**	8	68	85:15

[a]All reactions were performed with glycal (1 equiv), *N*-nucleophile (1.1 equiv), 10 mol% $Zn(OTf)_2$ in 1,2-dichloroethane at 40°C.
[b]Isolated yields.
[c]The $\alpha:\beta$ ratios were determined by ^{1}H NMR spectral analysis.

to generate a handful of neoglycoconjugates in which sulfonamide linkages are appended.

In view of the importance of *N*-linked glycoconjugates, we next focused on glycosylation of benzamides and carbamates to access the amino sugar derivatives. Thus, the glycosylation coupling of **1a** with benzamides (**2o**) and 4-nitro-benzamides (**2p**) was successfully achieved by using a 1:1 mixture of 1,2-dichloromethane:acetonitrile as the solvents to afford the corresponding *N*-glycosyl amides (**3o**, **3p**). However, a slight variation in the general procedure was adapted by using a mixed solvent system due to the poor solubility of **2o** and **2p** in 1,2-dichloethane (Table 2, entries 14 and 15).

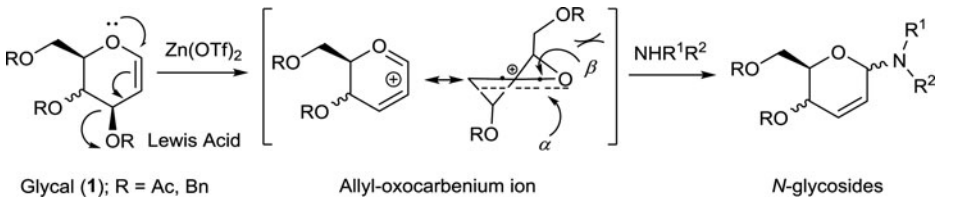


Figure 1: Mechanistic representation of Ferrier azaglycosylation.

Subsequently, the azaglycosylation reaction of **1a** with *N*-benzyl carbamate (**2q**) provided the desired glycosyl amide (**3q**) in a good yield (Table 2, entry 16). Notably, the presence of latent amino functionalities at the sugar-anomeric position offers considerable synthetic utility as valuable chiral intermediates in the preparation of various biologically important *N*-glycosides.

The scope and efficiency of the present protocol were further demonstrated with other glycals. Accordingly, 3,4,6-tri-*O*-benzyl glucal (**1b**) was activated under $Zn(OTf)_2$-mediated azaglycosylation with $MsNH_2$ (**2a**) and $TsNH_2$ (**2e**), respectively, to obtain the corresponding benzylated *N*-glycosyl sulfonamides (**3r**, **3s**) in good yields and high anomeric selectivity (Table 3, entries 1 and 2). Furthermore, the applicability of above-mentioned method is highlighted in the sulfoamidoglycosylation of 3,4,6-tri-*O*-acetyl galactal (**1c**) to generate various functionalized 2,3-unsaturated *N*-galactosides. Subsequently, the coupling of **1c** with different sulfonamides was accomplished respectively to obtain the corresponding glycosyl sulfonamides (**3t**–**3y**) in good yields with high selectivity in favor of α-anomers (Table 3, entries 3–8).

A plausible mechanism for the predominant formation of α-anomers in $Zn(OTf)_2$-mediated azaglycosylation is proposed based on analogy to Ferrier type 1 rearrangement.[16] In Ferrier rearrangement, an allylic rearrangement involves Lewis-acid-catalyzed displacement of an acetyl or benzyl ether group in a suitably C-3 substituted glycal. The resulting intermediate, an allyoxocarbenium ion with quasi-axial orientation, provides easy access to the incoming nucleophile from the less sterically hindered lower face to give α-anomer as the major product (Fig. 1).

CONCLUSIONS

In conclusion, we demonstrated the expeditious synthesis of unsaturated glycosyl sulfonamides and glycosyl amides via Ferrier azaglycosylation using readily available starting materials. In general, the present protocol provides a mild and efficient reaction condition at ambient temperature and applicable

to a wide substrate scope in terms of glycal and nitrogen nucleophile. Noteworthy, the Zn(II) triflate-promoted azaglycosylation method offers further advantages such as simple reaction operation and use of an economical, nontoxic, and moisture- and air-tolerant reagent system.

EXPERIMENTAL SECTION

General Synthesis Information, Methods, and Materials

Unless otherwise noted, materials were obtained from commercial suppliers and used without purification. Reactions were run in screw-capped glass vials (4 mL) stirred with Teflon-coated magnetic stirrer bars. Moisture- and air-sensitive reactions were performed in flame-dried round-bottom flasks, fitted with rubber septa or glass gas adapters, under a positive pressure of nitrogen. Moisture- and air-sensitive liquids or solutions were transferred via nitrogen-flushed syringe. Concentration of solvents was accomplished by rotary evaporation using a Büchi rotary evaporator at temperatures between 35°C and 50°C. Analytical TLC was performed using Whatman 250 micron aluminum-backed UV F254 precoated silica gel flexible plates. Subsequent to elution, ultraviolet illumination at 254 nm allowed for visualization of UV active materials. Staining with p-anisaldehyde, basic potassium permanganate solution, or Molisch's reagents allowed for further visualization. Proton nuclear magnetic resonance spectra (^{1}H NMR) were recorded on Avance 300 or Avance 500 MHz nuclear magnetic resonance spectrometers. Chemical shifts for ^{1}H NMR spectra are reported as δ in units of parts per million (ppm) relative to tetramethylsilane (δ 0.0) using the residual solvent signal as an internal standard: chloroform-d (δ 7.26, singlet). The number of protons (n) for a given resonance is indicated by nH. IR spectra were recorded on a Bruker Alpha spectrometer and mass analyses (ESI) were performed using a Finnegan MAT 1020 mass spectrometer operating at 70 eV.

General Procedure for $Zn(OTf)_2$-mediated Azaglycosylation

To a stirred solution of glucal (1 equiv.) and N-nucleophile (1.1 equiv.) in anhydrous 1,2-dichloroethanne (2 mL/mmol) under an atmosphere of argon was added $Zn(OTf)_2$ (10 mol%) at 40°C. The reaction mixture was stirred until the complete consumption of the starting material (glycal). The solvent was filtered and concentrated in vacuo, and the crude residue was redissolved in dichloromethane and loaded on a silica gel column. The product was purified by silica gel column chromatography using hexane/EtOAc as the eluent to afford the 2,3-unsaturated *N*-glycosides. All of the products were confirmed by ^{1}H NMR, ^{13}C NMR, and MS/HRMS spectroscopy and compared with that of

literature data; characterization data of new products are outlined in the experimental section.

4,6-Di-O-acetyl-2,3-dideoxy-α/β-D-erythro-hex-2-enopyranosyl-N-methylglycinate-p-toluenesulfonamide (3m)

Yield: 107 mg (64%). Rf (40% EtOAc/Hexane) 0.6. IR ($CHCl_3$, cm^{-1}): 3022, 2926, 2855, 1736, 1371, 1236, 1044, 752, 667. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.83 and 7.28 (each d, $J = 8.3$ Hz, 2H each, Ph), 6.08 (d, $J = 2.5$ Hz, 1H, H-1), 5.99–5.90 (m, 3H, H-3 both isomers, H-2), 5.83 (dt, $J = 10.2$, 2.3 Hz, 1H, H-2), 5.44 (br s, 1H, H-1), 5.33 (dd, $J = 9.6$, 1.5 Hz, 1H, H-4), 5.17 (dd, $J = 9.1$, 2.5 Hz, 1H, H-4), 4.22–4.07 (6H, CH_2COOCH_3, H-6a both isomers), 3.99 (dd, $J = 12.1$, 6.0 Hz, 1H, H-6b), 3.87 (m, 1H, H-5), 3.77 (dd, $J = 9.5$, 5.5 Hz, 1H, H-6b), 3.73–3.62 (m, 7H, OCH_3 both isomers, H-5), 2.43 (s, 6H, CH_3Ph), 2.10–2.07 (s, 12H, CH_3COO). ^{13}C NMR (75 MHz, $CDCl_3$): δ 170.7, 170.5, 170.2, 169.5, 143.9, 135.8, 131.4, 129.6, 129.3, 128.5, 128.2, 127.3, 90.5, 82.7, 74.0, 67.3, 65.2, 64.2, 62.9, 52.4, 43.8, 31.8, 21.5, 20.9, 20.7. MS (ESI) m/z: 473 ($[M+NH_4]^+$, 70), 478 ($[M+Na]^+$, 100). HRMS (ESI): m/z $[M+Na]^+$ calcd. for $C_{20}H_{25}NO_9SNa^+$: 478.11422; found: 478.11165.

4,6-Di-O-acetyl-2,3-dideoxy-α-D-threo-hex-2-enopyranosyl-benzenesulfonamide (3u)

Yield: 97.7 mg (72%). Rf (40% EtOAc/Hexane) 0.5. IR ($CHCl_3$, cm^{-1}): 3020, 1742, 1371, 1214, 742, 667. ^{1}H NMR (500 MHz, $CDCl_3$): 7.94 (d, $J = 8.09$ Hz, 2H, Ph), 7.60 (t, $J = 7.6$ Hz, 1H, Ph), 7.53 (t, $J = 7.5$ Hz, 2H, Ph), 6.16–6.13 (m, 2H, H-3, NH), 5.99 (dd, $J = 9.9$, 3.2 Hz, 1H, H-2), 5.65 (m, 1H, H-1), 4.94 (m, 1H, H-4), 3.94–3.88 (m, 2H, H-6a, H-5), 3.35 (dd, $J = 8.9$, 3.4 Hz, 1H, H-6b), 2.03 (s, 3H, CH_3COO), 1.95 (s, 3H, CH_3COO). ^{13}C NMR (125 MHz, $CDCl_3$): δ 170.4, 170.2, 141.4, 132.8, 129.3, 129.0, 127.0, 126.5, 76.7, 66.4, 61.5, 61.2, 20.7, 20.6. MS (ESI) m/z: 387 ($[M+NH_4]^+$, 100), 392 ($[M+Na]^+$, 50).HRMS (ESI): m/z $[M+Na]^+$ calcd. for $C_{16}H_{19}NO_7SNa^+$: 392.07744; found: 392.07679.

4,6-Di-O-acetyl-2,3-dideoxy-α-D-threo-hex-2-enopyranosyl-4'-tert-butylphenylsulfonamide (3w)

Yield: 121.9 mg (78%). Rf (40% EtOAc/Hexane) 0.4. IR ($CHCl_3$, cm^{-1}): 3021, 2963, 2924, 1741, 1369, 1216, 1021, 750, 669, 630. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.86 (d, $J = 8.7$ Hz, 2H, Ph), 7.54 (d, $J = 8.7$ Hz, 2H, Ph), 6.13 (dd, $J = 5.7$, 1.5 Hz, 1H, H-3), 6.00 (dd, $J = 9.8$, 3.0 Hz, 1H, H-2), 5.88 (d, $J = 9.1$ Hz, 1H, NH), 5.64 (m, 1H, H-1), 4.95 (dd, $J = 5.3$, 1.9 Hz, 1H, H-4), 3.96–3.70 (m, 2H, H-6a, H-5), 3.25 (dd, $J = 9.8$, 4.5 Hz, 1H, H-6b), 2.03 (s, 3H, CH_3COO), 1.95 (s, 3H, CH_3COO), 1.34 (s, 9H, $C(CH_3)_3$). ^{13}C NMR (125 MHz, $CDCl_3$): δ 170.2, 170.1, 156.6, 138.5, 129.3, 126.9, 126.8, 126.4, 126.0, 76.6, 66.1, 61.4, 60.9, 35.1, 30.9, 20.6, 20.5. MS (ESI) m/z: 443 ($[M+NH_4]^+$, 100), 448 ($[M+Na]^+$,

25). HRMS (ESI): m/z $[M+Na]^+$ calcd. for $C_{20}H_{27}NO_7SNa^+$: 448.14004; found: 448.13898.

4,6-Di-O-acetyl-2,3-dideoxy-α-D-threo-hex-2-enopyranosyl-3'-trifluoromethylphenylsulfonamide (3x)

Yield: 145.3 mg (75%). Rf (30% EtOAc/Hexane) 0.5. IR ($CHCl_3$, cm^{-1}): 2957, 2923, 2853, 1740, 1436, 1371, 1326, 1227, 1164, 768. ^1H NMR (500 MHz, $CDCl_3$): δ 8.21 (s, 1H, Ph), 8.16 (d, $J = 8.1$ Hz, 1H, Ph), 7.87 (d, $J = 7.9$ Hz, 1H, Ph), 7.70 (t, $J = 7.8$ Hz, 1H, Ph), 6.20 (ddd, $J = 9.8, 5.5, 1.5$ Hz, 1H, H-3), 6.01 (dd, $J = 10.1, 3.2$ Hz, 1H, H-2), 5.82 (d, $J = 8.9$ Hz, 1H, NH), 5.71 (m, 1H, H-1), 4.95 (dd, $J = 5.5, 2.4$ Hz, 1H, H-4), 3.93 (dd, $J = 10.8, 7.8$ Hz, 1H, H-6a), 3.84 (m, 1H, H-5), 3.34 (dd, $J = 10.9, 5.5$ Hz, 1H, H-6b), 2.05 (s, 3H, CH_3COO), 1.92 (s, 3H, CH_3COO). ^{13}C NMR (125 MHz, $CDCl_3$): δ 170.7, 170.4, 155.0, 135.8, 130.1, 128.5, 128.3, 128.2, 126.2, 74.2, 67.2, 62.4, 62.2, 20.8, 20.7. MS (ESI) m/z: 455 ($[M+NH_4]^+$, 100), 460 ($[M+Na]^+$, 40). HRMS (ESI): m/z $[M+Na]^+$ calcd. for $C_{17}H_{18}F_3NO_7S^+$: 460.06483; found: 460.06379.

4,6-Di-O-acetyl-2,3-dideoxy-α-D-threo-hex-2-enopyranosyl-benzylcarbamte (3y)

Yield: 90.8 mg (68%). Rf (40% EtOAc/Hexane) 0.5. IR ($CHCl_3$, cm^{-1}): 3019, 1736, 1510, 1371, 1214, 742, 667. ^1H NMR (500 MHz, $CDCl_3$): δ 7.38–7.33 (m, 5H, Ph), 6.18 (ddd, $J = 10.1, 5.5, 1.7$ Hz, 1H, H-3), 6.01 (dd, $J = 10.1, 3.1$ Hz, 1H, H-2), 5.82 (br d, $J = 7.5$ Hz, 1H, H-1), 5.48 (br s, 1H, NH), 5.16 (br s, 2H, CH_2Ph), 5.03 (dd, $J = 5.5, 2.3$ Hz, 1H, H-4), 4.26–4.14 (m, 3H, H-6ab, H-5), 2.09 (s, 3H, CH_3COO), 2.02 (s, 3H, CH_3COO). ^{13}C NMR (75 MHz, $CDCl_3$): δ 170.8, 170.1, 155.1, 136.1, 129.5-127.9, 73.7, 67.1, 64.5), 64.4, 62.7, 20.8, 20.6. MS (ESI) m/z: 381 ($[M+NH_4]^+$, 100), 386 ($[M+Na]^+$, 50). HRMS (ESI): m/z $[M+Na]^+$ calcd. for $C_{18}H_{21}NO_7Na^+$: 386.12102; found: 386.12016.

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