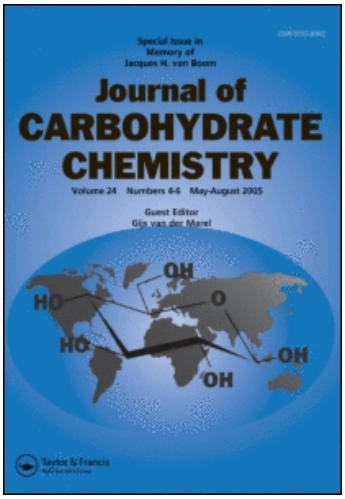

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THIOSUGARS III. STEREOSELECTIVE APPROACH TO β-(1 →2)-2,3-DIDEOXY-2-*C*-ACETAMIDOMETHYL-2-*S*-THIODISACCHARIDES FROM LEVOGLUCOSENONE[1]

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ABSTRACT

β-(1→2)-2,3-Dideoxy-2-*C*-acetamidomethyl-2-*S*-thiodisaccharides were synthesized in four steps by a stereoselective base catalyzed Michael addition reaction of 1-thiosugars to α-nitroalkene **4a**, a new chiral synthon from levoglucosenone. It was followed by the reduction of the nitro group with a sodium borohydride/cobalt chloride complex and the hydrolytic opening of the 1,6-anhydro ring.

INTRODUCTION

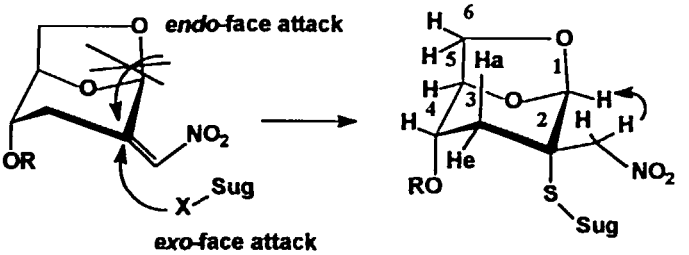
Thiodisaccharides, as a class of unnatural mimics of disaccharides, are resistant to enzymatic hydrolysis and are potential inhibitors of glycosidases for the treatment of various metabolic diseases. In response to our continued interest in *C*-glycosyl compounds and *C*-disaccharides[2] as non-hydrolyzable epitopes, we focused our attention on the development of new strategies for the synthesis of (1→4) and (1→2)-*S*-thiodisaccharides.[3] Because existing synthetic methods of thiodisaccharide synthesis are multi-step[4-11] and overall low yield approaches, an urgent need for shorter and more

convergent synthetic approaches exists. Moreover, the biological relevance and therapeutic potential[4b] of (1→2)-*S*-linked thio-sugars including their antitumor activity on selected cell culture systems[8b] make them attractive new biological targets and constitutes the rationale for their synthesis. Additionally, controversial reports on (1→2)-thiodisaccharides (2-thiosophorose)[9,12] also prompted us to explore alternative approaches.

RESULTS AND DISCUSSION

Our laboratory developed the new approach presented here, which features ongoing studies on the utility of the new, convenient chiral "synthon" α-nitroalkene **4a** produced from levoglucosenone.[13-16] Nitroalkene **4a** (E/Z 1:1 mixture) serves as a reactive acceptor in the stereoselective Michael addition reaction of glycosyl thiols **5a-c**[17-20] to its conjugated system.

The advantage of the stereoselective 1,2-addition is the exclusive formation of an *exo*-adduct *via* formation of an *S*-linkage from the less hindered face of the molecule. The shielding effect of the 1,6-anhydro bridge in levoglucosenone effectively prevents the formation of the 2-equatorial (*e*) product, thus yielding only the 2-axial (*a*) product. This axial attack of the sulfur nucleophiles was expected,[21] but a new quaternary center at C-2 surprisingly stabilized the molecule, as no epimerization[7,9] or β-elimination was observed during the reduction of the nitro group.

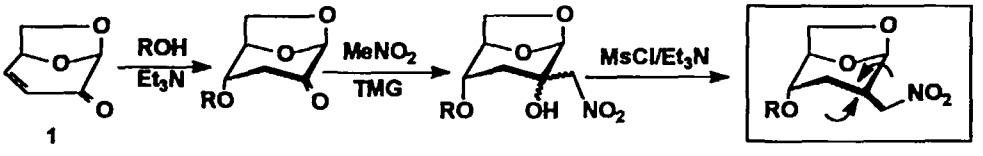


X = SH, Sug = GLU, GAL, FUC,
4a R = Me, 4b R = Bn,

This indicates the preferred stereochemistry of the adducts **6a-c**. The most direct way to prove the correct stereochemistry of the adducts was by measuring the coupling constants between H-3a and the -CH_2- of the nitromethyl group at C-2, i.e. $^3J_{CH}$ = 2.8-3.2 Hz. The magnitude of these coupling constants strongly supports the proposed *gauche*

arrangement with these equatorial substituents at C-2. Moreover, the strong NOE effect observed between the H at C-1 and one of the hydrogens on the nitromethyl group at C-2 further proves the correct stereochemistry at C-2. The ^{1}H NMR spectra of these adducts show a lack of coupling between H-4 and H-5 indicating that the pyranose ring of the adducts is in a $^1C_4$ conformation and is slightly distorted due to the presence of an equatorially oriented nitromethyl group at C-2. This prompted us to explore the synthetic utility of nitroalkenes **4a-b** for the stereoselective synthesis of various *S*-linked thiodisaccharides. Our approach is novel in that it contrasts the existing methods of thiodisaccharides synthesis, for it does not require a multi-step procedure or special protection of functional groups.

The starting nitroalkene **4a** was prepared from levoglucosenone by a Michael addition reaction of methanol, whereas **4b** was produced by adding benzyl alcohol according to the Furneaux report.[14] The addition reactions of nitromethane to the intermediates **2a-b** were run in the presence of triethylamine or tetramethylguanidine (TMG) according to the Paton protocol.[22,23]



1

2a R = Me
2b R = Bn

3a R = Me
3b R = Bn

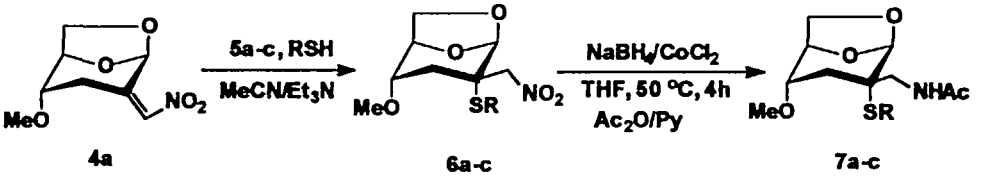
4a R = Me
4b R = Bn

SCHEME 1

The isolation of the diastereoisomeric mixture of *C*-nitromethyl adducts **3a-b** proceeded in 43% yield based on the recovery of unreacted starting **2a-b**. Subsequent mesylation in the presence of triethylamine, produced nitroalkenes **4a-b** as E/Z (1:1) mixtures in a moderate 58% yield (Scheme 1). However, alkene **4b** was less stable at room temperature and quickly isomerized and decomposed (an E/Z isomerization and NMR study will be reported in due course). Consequently, **4b** is not a good precursor for the study of the addition reaction of thiols **5a-c**.

The Michael addition of thiols **5a-c** to the nitroalkene **4a**, proceeded smoothly with the formation of β-(1→2)-2,3-dideoxy-2-*C*-nitromethylthiodisaccharides **6a-c** in a 63-70% yield. Reduction of the nitro group at C-2 of the thiodisaccharides, **6a-c** was

especially challenging, but was achieved efficiently with a sodium borohydride/cobalt chloride complex as we reported earlier.[24] For the purpose of purification, acetylation of the reduction products was used to produce acetamido derivatives **7a-c**. The resulting thiodisaccharides **7a-c** were obtained in good (68%) yields after purification by flash-column chromatography (Scheme 2).



a R = 2,3,4,6-tetra-*O*-acetyl- D-glucopyranosyl-
b R = 2,3,4,6-tetra-*O*-acetyl- D-galactopyranosyl-
c R = 2,3,4-tri-*O*-acetyl- L-fucopyranosyl-

SCHEME 2

The stereochemistry of the new branched thiodisaccharides **7a-c** was assigned on the basis of NOE results (Fig.1), displaying a 5% enhancement between the *C*-acetamidomethyl group and the axial proton (3a-H) at C-3 and most importantly no enhancement of the 3e-H signal. The ^{13}C NMR signal of the -CH_2- group ($\delta = 62.4$) at C-2 of **7a-c** is characteristic of the link with the quaternary C-2 ($\delta = 57.5$) and also indicates the axial disposition of the new C-2 substituents.

The cleavage of the 1,6-anhydro ring of **7a-b** was performed according to the Vogel procedure[24] followed by deacetylation with an aqueous solution of triethylamine MeOH/H_2O/Et_3N, producing the target methyl thiodisaccharides **8a-b** as an anomeric mixture (α: β 1:5) in a disappointing 54% yield (Scheme 3).

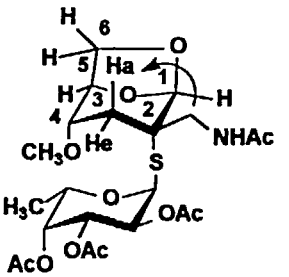
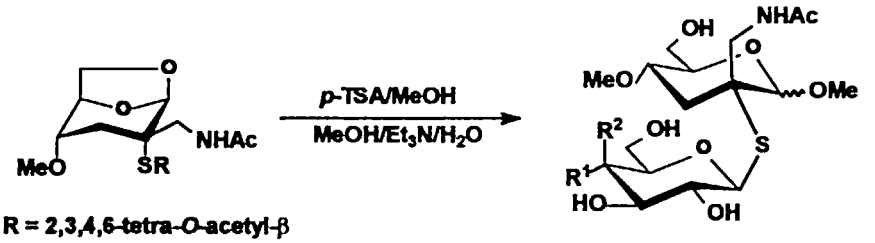


Fig. 1. NOE correlation of 2-acetamidomethyl group of compound 7c.

Separation of the anomers proved tedious because of their almost identical R_f values. However, the ^1H and ^{13}C NMR spectra and mass spectral data for the mixture firmly established their identity. Compound **7c** underwent an almost total decomposition under the above reaction conditions. The development of alternative deprotection approaches particularly for acid sensitive fucose derivatives is under way.



7a R = 2,3,4,6-tetra-*O*-acetyl-β-D-glucopyranosyl-
7b R = 2,3,4,6-tetra-*O*-acetyl-β-D-galactopyranosyl-

8a R^1 = OH, R^2 = H
8b R^1 = H, R^2 = OH

SCHEME 3

CONCLUSION

In this paper, we have synthesized a new class of nitroenone through a short sequence of steps. This new methodology will prove extremely useful for synthesizing a wider range of 3-deoxy-2-*C*-methylacetamido-2-thiodisaccharides with various linkages while using α-nitroalkene **4a** as a convenient synthon to control the stereoselectivity. The new synthons **4a-b** and **6a-c** are under intensive exploration in our laboratory in a variety of transformations to amino- thio- and branch-chain complex oligosaccharides by the functionalization of the remaining functional groups.

EXPERIMENTAL

General methods. Unless otherwise noted, starting materials were obtained from commercial suppliers and used without purification. Organic extracts were dried with $MgSO_4$ and concentrated with a rotary evaporator under reduced pressure (aspirator). Flash column chromatography was carried out with Silica Gel 60 (70-213 mesh, Merck No. 7734). Thin-layer chromatography (TLC) was performed with Merck F-254 TLC plates. All melting points were uncorrected and were measured in open capillary tubes.

Optical rotations were measured with a Jasco DIP-370 polarimeter. ^{1}H NMR spectra were recorded at 250MHz and ^{13}C NMR spectra at 50 MHz, with TMS as an internal standard on a Bruker DMX250 spectrometer. EI mass spectra (70eV) were measured with a Kratos MS 80RFA spectrometer with an ionizing current of 100mA, an accelerating voltage of 4kV, and a resolution of 10,000 (10% valley definition)

Levoglucosenone was produced according to the convenient published methodology.[15] 1,6-Anhydro-4-*O*-methyl-β-D-*erythro*-hexopyranos-2-ulose (**2a**),[13] 1,6-anhydro-4-*O*-benzyl-β-D-*erythro*-hexopyranos-2-ulose (**2b**)[14] and 1,6-anhydro-3-deoxy-4-*O*-methyl-2-hydroxy-2-*C*-nitromethyl-β-D-glucopyranose (**3a**),[22,23] were prepared according to the literature methods.

2,3,4,6-tetra-*O*-acetyl-1-thio-β-D-glucopyranose (**5a**),[17] 2,3,4,6-tetra-*O*-acetyl-1-thio-β-D-galactopyranose (**5b**)[18-19] and 2,3,4-tri-*O*-acetyl-1-thio-α-L-fucopyranose (**5c**)[20] were all prepared by reacting the corresponding α or β-glycosyl halides with thiourea and followed by reduction of the isothiouronium salts with potassium pyrosulfite according to the published procedure.[26]

1,6-Anhydro-3-deoxy-4-*O*-benzyl-2-hydroxy-2-*C*-nitromethyl-β-D-glucopyranose (3b). Compound **3b** was prepared from **2b** by the method of Paton et al.[22,23] yield 74%; syrup: R_f = 0.66 (1:4 hexane-EtOAc); $[\alpha]^{30}$ -136° (*c* 0.88, $CHCl_3$); MS *m/z* 295.02 $(M)^+$.

Anal. Calcd for $C_{14}H_{17}NO_6$: C, 56.94; H, 5.80; N, 4.74. Found: C, 56.86, H, 5.73, N, 4.81.

1,6-Anhydro-2,3-dideoxy-4-*O*-methyl-2-*C*-nitromethylene-β-D-glucopyranose (4a). To a stirred solution of **3a** 1.25g (5.7 mmol) in pyridine (20 mL), methanesulfonyl chloride (25 mL) was added dropwise at –10 °C. Stirring was continued at this temperature for 4 h. To the deep-red solution, 50 mL of triethylamine was added. The solution was stirred overnight at 30 °C and then poured into 200 mL of water. The precipitated oil was extracted with methylene chloride (3 x 30 mL). The combined extract was washed with sodium bicarbonate and brine, dried with magnesium sulfate and concentrated to a syrup: yield 0.75g (66%) of syrupy product, $[\alpha]^{23}$ -90.5° (*c* 1.00, $CHCl_3$). ^{1}H NMR showed an E/Z (1:1) mixture. ^{13}C NMR ($CDCl_3$) δ 143.6 (C-2), 102.1 (C-1), 74.0 (C-5), 66.3 (C-6), 56.4 (MeO), 50.8 (C-4), 37.2 (C-3), 135.8 (=*C*H-NO_2). MS *m/z* 201.06 $(M)^+$.

Anal. Calcd for $C_8H_{11}NO_5$: C, 47.76; H, 5.51; N, 6.96. Found: C, 47.63, H, 5.43, N, 6.91.

1,6-Anhydro-2,3-dideoxy-4-*O*-benzyl-2-*C*-nitromethylene-β-D-glucopyranose (4b). Compound **4b** was prepared from **3b** in a similar fashion to **4a**: yield 56%, syrup, $[\alpha]^{23}$ -83°, (*c* 1.00, $CHCl_3$); ^1H NMR showed an E/Z (1:1) mixture. ^{13}C NMR ($CDCl_3$) δ 143.2 (C-2), 135.2 (= *C*H-NO_2), 127.4-128.6 (CH-arom), 137.8-138.8 (C-arom), 102.8 (C-1), 77.6 (C-5), 74.4, (CH_2 benzyl), 69.8 (C-4), 66.0 (C-6), 37.8 (C-3). MS *m/z* 277.09 $(M)^+$.

Anal. Calcd for $C_{14}H_{15}NO_5$: C, 60.64; H, 5.45; N, 5.05. Found: C, 60.56, H, 5.33, N, 4.95.

General method for the preparation of (1→2)-thiodisaccharides (6a-c). To a solution of **4a**, (201 mg, 1.00 mmol) in acetonitrile (10 mL) the appropriate 1-thiosugar **5a**, **5b**, (364 mg, 1.00 mmol) or **5c**, (306 mg, 1.00 mmol) solution in acetonitrile (15 mL) was added, followed with 2 mL of triethylamine. The reaction mixture was stirred at room temperature for 24 h. After evaporation of the solvent, the syrupy residue was purified by column chromatography on silica gel. The fraction eluted with 20% ethyl acetate in hexane (v/v) gave syrupy products.

1,6-Anhydro-2,3-dideoxy-4-*O*-methyl-2-*C*-nitromethyl-2-*S*-(2,3,4,6-tetra-*O*-acetyl-1-thio-β-D-glucopyranosyl)-D-glucopyranose (6a). Prepared from **4a** and 1-thiosugar **5a** in 78% yield as a syrup, $[\alpha]^{23}$ +86° (*c* 1.00, $CHCl_3$).^1H NMR ($CDCl_3$) δ 4.58 d (H-1, $J_{1,2}$ = 7.4 Hz), 5.66 (d, 1H, J = 5.8 Hz, H-1'), 5.16 (s 1H, H-1), 4.72 (m,1H, H-5), 5.06 (dd, 1H, J = 11.2 Hz, 3.0 Hz, H-3'), 4.04 (dd,1H, J = 1.6 Hz, 12 Hz, H-6e), 4.23 (q 1H, J = 6 Hz, H-5'), 3.45 (d, J = 8.2 Hz, H-4), 3.12 (dd,1H, J = 8.4 Hz, H-3a), 2.58 (d,1H, J = 16.6 Hz, H-3e), 2.06, 2.08, 2.1, 2.12 (4s, 12H, 4Ac). MS *m/z* 565.06 $(M)^+$.

Anal. Calcd for $C_{22}H_{31}NO_{14}S$: C, 46.72; H, 5.52; N, 2.48; S, 5.67. Found: C, 46.63, H, 5.48, N, 2.53, S, 5.59.

1,6-Anhydro-2,3-dideoxy-4-*O*-methyl-2-*C*-nitromethyl-2-*S*-(2,3,4,6-tetra-*O*-acetyl-1-thio-β-D-galactopyranosyl)-D-glucopyranose (6b). Prepared from **4a** and 1-thiosugar **5b** in 68% yield as a syrup, $[\alpha]^{23}$ +48° (*c* 1.00, $CHCl_3$). ^1H NMR ($CDCl_3$) δ 5.69 (d, 1H, J = 5.8 Hz, H-1'), 5.19 (s 1H, H-1), 4.79 (m, 1H, H-5), 5.03 (dd, 1H, J = 11.2 Hz, 3.0 Hz, H-3'), 4.14 (dd,1H, J = 1.6 Hz,12 Hz, H-6e), 4.29 (q 1H, J = 6.2Hz, H-5'), 3.25 (d, J = 8.3 Hz, H-4), 3.24 (dd,1H, J = 8 Hz, H-3a), 2.52 (d,1H, J = 16 Hz, H-3e), 2.06, 2.09, 2.11, 2.14 (4s, 12H, 4Ac). MS *m/z* 565.09 $(M)^+$.

Anal. Calcd for $C_{22}H_{31}NO_{14}S$: C, 46.72; H, 5.52; N, 2.48; S, 5.67. Found: C, 46.69, H, 5.44, N, 2.51, S, 5.49.

1,6-Anhydro-2,3-dideoxy-4-*O*-methyl-2-*C*-nitromethyl-2-*S*-(2,3,4-tri-*O*-acetyl-1-thio-β-L-fucopyranosyl)-D-glucopyranose (6c). Prepared from **4a** and 1-thiosugar **5c** in 58% yield as a syrup, $[\alpha]^{23}$ +66° (*c* 1.00, $CHCl_3$). ^1H NMR ($CDCl_3$) δ 5.66 (d, 1H, J = 5.8 Hz, H-1'), 4.62 (m,1H, H-5), 5.06 (dd, 1H, J = 11.2 Hz, 3.0 Hz, H-3'), 4.04 (dd,1H, J = 1.6 Hz,12 Hz, H-6e), 4.13 (q 1H, J = 6.6 Hz, H-5'), 3.45(d, J = 8.2 Hz, H-4), 3.12 (dd,1H, J = 8.4Hz, H-3a), 2.56 (d,1H, J = 16Hz, H-3e), 2.09, 2.12, 2.14 (3s, 9H, 3Ac). MS *m/z* 507.02 $(M)^+$.

Anal. Calcd for $C_{20}H_{29}NO_{12}S$: C, 47.33; H, 5.76; N, 2.76; S, 6.32. Found: C, 47.29, H, 5.68, N, 2.81, S, 6.29.

General procedure for the reduction of the *C*-2-nitromethyl-(1→2)-thio-disaccharides (6a-c). To a cooled and stirred solution of **6a-b**, (210 mg, 0.37 mmol) or **6c** (210 mg, 0.41 mmol) in 25 mL of THF, a solution (20 mL) of sodium borohydride/cobalt chloride complex prepared from 2 g of $NaBH_4$ and 1.25 g $CoCl_2$ in THF, was added in portions at 28 °C under an Ar atmosphere. The reaction mixture was stirred for 24 h, then pyridine (4 mL) and acetic anhydride (5 mL) were added and the solution stirred at room temperature overnight. The reaction mixture was poured into ice-water (200 mL) and extracted with ethyl acetate. The extract was washed and dried. Removal of the solvent *in vacuo* after co-evaporation with 1:1 toluene-ethyl alcohol (5 x 30 mL) afforded an oily residue that was subjected to column chromatography on silica gel. The fraction eluted with 20% ethyl acetate in hexane (v/v) gave syrupy products.

1,6-Anhydro-2,3-dideoxy-4-*O*-methyl-2-*C*-acetamidomethyl-2-*S*-(2,3,4,6-tetra-*O*-acetyl-1-thio-β-D-glucopyranosyl)-D-glucopyranose (7a). Yield 53%, syrup $[\alpha]^{23}$ +106.5° (*c* 1.00, $CHCl_3$).^{13}C NMR ($CDCl_3$) δ 16.9 (CH_3CONH- C-2), 3x 17.3, 17.6 (CH_3-), 39.8 (C-3), 56.69 (C-4-OMe), 61.8 (C-6'), 63.8 (C-6), 65.33 (C-2'), 67.6 (C-2), 68.6 (C-2, -CH_2-), 70.9 (C-4'), 71.6 (C-5), 72.7 (C-5'), 73.13 (C-3'), 96.6 (C-1), 102.3 (C-1'), 170.3, 3x 170.1 (-$COCH_3$); 173.6 (-$HNCOCH_3$); MS *m/z* 577.10 $(M)^+$.

Anal. Calcd for $C_{24}H_{35}NO_{13}S$: C, 49.91; H, 6.11; N, 2.42; S, 5.55. Found: C, 49.85; H, 6.16; N, 2.36; S, 5.41.

1,6-Anhydro-2,3-dideoxy-4-*O*-methyl-2-*C*-acetamidomethyl-2-*S*-(2,3,4,6-tetra-*O*-acetyl-1-thio-β-D-galactopyranosyl)-D-glucopyranose (7b). Yield 48%, syrup,

$[\alpha]^{23}$ +99.5° (*c* 1.00, $CHCl_3$). ^{13}C NMR ($CDCl_3$) δ 16.86 (*CH_3*CONH- C-2), 3x 17.3, 17.6 (CH_3-), 29.8 (C-3'), 39.8 (C-3), 56.49 (C-4-OMe), 65.3 (C-2'), 67.6 (C-2), 68.8 (C-2, -CH_2-), 74.8 (C-6'), 75.7 (C-5'), 76.0 (C-6), 77.6 (C-5), 77.9 (C-4'), 96.6 (C-1), 170.6, 170.3, 2x 170.1 (-*C*OCH_3), 172.2 (-HN*C*OCH_3); MS *m/z* 577.16 $(M)^+$.

Anal. Calcd for $C_{24}H_{35}NO_{13}S$: C, 49.91; H, 6.11; N, 2.42; S, 5.55. Found: C, 49.81; H, 6.19; N, 2.29; S, 5.38.

1,6-Anhydro-2,3-dideoxy-4-*O*-methyl-2-*C*-acetamidomethyl-2-*S*-(2,3,4-tri-*O*-acetyl-1-thio-α-L-fucopyranosyl)-D-glucopyranose (7c). Yield 52%, syrup $[\alpha]^{23}$ +86.5° (*c* 1.00, $CHCl_3$). ^1H NMR ($CDCl_3$) δ 5.66 (d, 1H, J = 5.8 Hz, H-1'), 5.16 (s 1H, H-1), 4.72 (m, 1H, H-5), 5.06 (dd, 1H, J = 11.2 Hz, 3.0 Hz, H-3'), 4.04 (dd,1H, J = 1.6 Hz,12 Hz, H-6e), 4.23 (q 1H, J = 6 Hz, H-5'), 3.45(d, J = 8 Hz, H-4), 3.12 (dd,1H, J = 8 Hz, H-3a), 2.58 (d,1H, J = 16 Hz, H-3e), 2.06, 2.1, 2.12 (3s, 9H, 3Ac), 2.25 (*CH_2*-NHAc) shows an NOE to that at δ 3.12 (H-3a 5%), 1.14 (3H, d, J = 6.5, (CH_3-C-6'); ^{13}C NMR ($CDCl_3$) δ 16.18 (CH_3- C-6'), 2x 17.3, 17.6 (CH_3-), 55.69 (C-4-OMe), 57.52 (C-2), 67.52 (C-6), 68.82 (C-2, -CH_2-), 70.66 (C-4), 71.29 (C-2'), 71.89 (C-5'), 72.12 (C-4'), 72.36 (C-5), 72.83 (C-3), 73.89 (C-3'), 98.2 (C-1), 102.78 (C-1'), 170.8, 2x 170.1 (-*C*OCH_3), 173.2 (-HN*C*OCH_3); MS *m/z* 519.22 $(M)^+$.

Anal. Calcd for $C_{22}H_{33}NO_{11}S$: C, 46.25; H, 7.08; N, 3.17; S, 7.26. Found: C, 45.99; H, 6.99; N, 3.09; S, 7.18.

General Procedure for Deprotection of (1→2)-thiodisaccharides (7a-7b) Ring opening of 1,6-anhydro compound **7a** was performed according to the method of Zhu and Vogel.[25] Thiodisaccharide **7a,** or **7b** (0.250 mg, 0.43 mmol) was dissolved in a 25 mL solution of MeOH containing 0.2 g *p*-TsOH and refluxed for 12 h. Solvent was evaporated, and the residue was dissolved in 15 mL of 4:1:5 MeOH-Et_3N-H_2O and the solution stirred at room temperature. TLC indicated completion of the reaction after 6 h. Removal of the solvent *in vacuo* after co-evaporation with 1:1 toluene-ethyl alcohol (5 x 30 mL) afforded a syrupy residue that was subjected to column chromatography on silica gel. The fraction eluted with 20% ethyl acetate in hexane (v/v) after evaporation of the solvent produced an inseparable anomeric mixture (α/β in a ratio 1:6).

Methyl *S*-β-D-glucopyranosyl-(1→2)-*S*-2-thio-2,3-dideoxy-2-*C*-acetamido methyl-4-*O*-methyl-α/β-D-glucopyranoside (8a). Syrup, yield 54%, $[\alpha]^{23}$ +78.9° → 84.9° (*c* 1.00, $CHCl_3$), R_f= 0.51 (3:1 toluene/AcOEt). ^1H NMR (250MHz, $CDCl_3$) δ 4.85

(s,1H-1), 4.68 (d, 1H-1', J = 8.6 Hz), 4.83 (d, 1H-5', J = 6.0 Hz), 4.2-4.06 (m, 3H, H-6a, H-6'a, H-2'), 4.18 (d,1H-4, J = 2.9 Hz), 3.86 (dd, 1H-6e, J = 12 Hz), 3.78 (d, 1H-4', J = 2.6 Hz), 3.71-3.52 (m, 3H, H-5, 3a), 3.42, 3.46 (s, 3H, MeO), 3.19 (d,1H-3a, J = 9.9 Hz), 2.74 (d, H-3e, J = 16 Hz), 2.23 (s, 3H, CH_3CONH- C-2). A small amount (ca. 4%) of the corresponding furanosides was also detected by NMR. ^{13}C NMR ($CDCl_3$) δ 16.86 (*CH_3*CONH- C-2), 29.8 (C-3'), 39.8 (C-3), 56.49 (C-4-OMe), 65.3 (C-2'), 67.6 (C-2), 68.8 (C-2, -CH_2-), 74.8 (C-6'), 75.7 (C-5'), 76.0 (C-6), 77.6 (C-5), 77.9 (C-4'), 96.6 (C-1); MS *m/z* 441.16 $(M)^+$.

Anal. Calcd for $C_{17}H_{31}NO_{10}S$: C, 46.25; H, 7.08; N, 3.17; S, 7.26. Found: C, 45.99; H, 6.99; N, 3.09; S, 7.18.

Methyl *S*-β-D-galactopyranosyl-(1→2)-*S*-2-thio-2,3-dideoxy-2-*C*-acetamido-methyl-4-*O*-methyl-α/β-D-glucopyranoside (8b). Syrup, yield, 52%, $[\alpha]^{23}$ +51.2° → +54.9° (*c* 1.00, $CHCl_3$). R_f = 0.56 (3:1 toluene/AcOEt). ^1H NMR ($CDCl_3$) δ 4.88 (s, 1H-1'), 4.46 (dd, 1H-6e, J = 7.4Hz, 11.4 Hz), 4.32-4.46 (m, 1H-5'), 4.14 (dd, 1H-6a, J = 4.0 Hz, 11.4 Hz), 4.08 (dd, 1H-6', J = 5.2 Hz, 11.6 Hz), 3.96 (dd, 1H-3' J = 2.8Hz, 9.6Hz), 3.89 (d,1H-1, J = 9.5Hz), 3.72 (dd, 1H-5, J = 4.1 Hz, 7.4 Hz), 3.46 (dd, 1H-2', J = 3.4 Hz, 9.1 Hz), 3.44, 3.46 (s 3H, MeO), 2.70 (d, 1H-3e, J = 16 Hz, 8.0 Hz), 2.26 (d, 1H-4', J = 3.6 Hz), 2.12 (s, 3H, CH_3CONH-, C-2). ^{13}C NMR ($CDCl_3$) δ 16.92 (*CH_3*CONH- C-2), 29.8 (C-3'), 39.8 (C-3), 56.49 (C-4-OMe), 65.3 (C-2'), 57.6 (C-2), 68.8 (C-2, -CH_2-), 74.8 (C-6'), 75.7 (C-5'), 76.0 (C-6), 77.6 (C-5), 77.9 (C-4'), 96.6 (C-1); MS *m/z* 441.16 $(M)^+$.

Anal. Calcd for $C_{17}H_{31}NO_{10}S$: C, 46.25; H, 7.08; N, 3.17; S, 7.26. Found: C, 46.03; H, 6.93; N, 3.03; S, 7.12.

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