Synthesis of α - and β -Glycosyl Isothiocyanates via Oxazoline Intermediates

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Supporting Information

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General Methods. All solvents and reagents were purchased from commercial sources and used without further purification. Optical rotations were measured at 20 °C in 1-dm tubes. ^1H (and ^{13}C NMR) spectra were recorded at 300 (75.5), 400 (100.6) and 500 (125.7) MHz. 2D COSY, 1D TOCSY, HMQC and HSQC experiments were used to assist on NMR assignments. Thin-layer chromatography (TLC) was carried out on aluminium sheets coated with Kieselgel 60 F254 (E. Merck), with visualisation by UV light and by charring with 10% H_2SO_4 . Column chromatography was carried out on Silica Gel 60 (E. Merck, 230-400 mesh). The operating conditions for recording FAB mass spectra were the following: the primary beam consisted of Xe atoms with a maximum energy of 8 keV; the samples were dissolved in thioglycerol, and the positive ions were separated and accelerated over a potential of 7 keV; NaI was added as cationizing agent. For ESI mass spectra, 0.1 pM sample concentration were used, the mobile phase consisting of 50% aq acetonitrile at 0.1 L min^{-1} .

Chart S1. Glycosyl azides and Anomeric Isopropylidene Derivatives Used as Starting Materials for the Preparation of Glycooxazolines.

Materials. The per-O-acetyl- β -D-glucosyl, - β -D-galactosyl, - β -cellobiosyl, - β -maltosyl and - β -lactosyl azides **27-31** (Chart S1),¹ used as precursors of oxazolines **6** and **13-19**. They were synthesized from the corresponding α -glycosyl bromides by treatment with azidotrimethylsilane (TMS-N_3) and tetrabutylammonium fluoride (TBAF), which provide a nucleophilic source of azide anion, following the procedure of DeShong and col.² 5,6-Di-O-benzyl-1,2-O-isopropylidene- α -D-glucopyranose³ (**32**), 1-O-benzyl-2,3:4,5-di-O-isopropylidene- β -D-fructopyranose⁴ (**33**) and 3-O-benzyl-1,2:4,5-di-O-

isopropylidene- β -D-fructopyranose⁵ (**34**) were prepared by benzylation of the corresponding isopropylidene derivatives.

General Procedure for the Preparation of Glycooxazolines 6 and 13-19: The method reported by DeShong and col.⁵ for the synthesis of glucooxazoline **6** from azide **26** was employed. A solution of the corresponding per-*O*-acetyl- β -glycopyranosyl azide (**26-30**) and Ph₃P (1 eq) in 1,2-dichloroethane (5 mL per 150 mg of azide derivative) was heated under reflux in the presence of 4 Å molecular sieves for 24 h, then cooled at room temperature and concentrated. The resulting residue was purified by column chromatography using the eluent indicated in each case to give the target oxazoline as an amorphous solid.

2-Methyl-4,5-dihydro-(3,4,6-tri-*O*-acetyl-1,2-dideoxy- α -D-glucopyrano)[2,1-d]-2-oxazoline (6). Compound **6** (453 mg, 56 %) was obtained from azide **27** (781 mg, 2.1 mmol) after column chromatography purification (1:3:0.5% petroleum ether-EtOAc-Et₃N $\rightarrow$ 1:0.5% EtOAc-Et₃N). *R_f* = 0.28 (EtOAc). The IR, NMR and MS data were identical to those previously reported.

2-Methyl-4,5-dihydro-(3,4,6-tri-*O*-acetyl-1,2-dideoxy- α -D-galactopyrano)[2,1-d]-2-oxazoline (13). Compound **13** (0.77 g, 66%) was obtained from azide **28** (1.30 g, 3.5 mmol) after column chromatography purification (toluene $\rightarrow$ 1:2 $\rightarrow$ 3:1:0.5% EtOAc-petroleum ether-Et₃N). *R_f* = 0.32 (EtOAc). IR (KBr): $\nu_{\max}$ 2935, 1747, 1667, 1437, 1370, 1226, 1007 cm⁻¹. ¹H NMR (500 MHz, CDCl₃): δ (ppm) 5.78 (d, 1 H, *J*_{1,2} = 7.0 Hz, H-1), 5.41 (t, 1 H, *J*_{3,4} = *J*_{4,5} = 3.0 Hz, H-4), 4.89 (dd, 1 H, *J*_{2,3} = 7.0 Hz, H-3), 4.44 (t, 1 H, H-2), 4.17 (td, 1 H, *J*_{5,6a} = *J*_{5,6b} = 6.0 Hz, H-5), 4.12 (dd, 1 H, *J*_{6a,6b} = 13.0 Hz, H-6a), 4.05 (dd, 1 H, H-6b), 2.09-1.99 (3 s, 12 H, 3 MeCO, NMe). ¹³C NMR (125.7 MHz, CDCl₃): δ (ppm) 170.4-169.8 (3 CO), 168.2 (CN), 93.6 (C-1), 76.6 (C-2), 71.7 (C-5), 69.4 (C-3), 66.2 (C-4), 61.2 (C-6), 20.8-20.5 (3 MeCO), 14.4 (MeN). ESIMS: *m/z* = 330 ([M + H]⁺). HRFABMS found: 330.117646; calcd for [C₁₄H₁₉NO₈ + H]⁺: 330.118892.

2-Methyl-4,5-dihydro-[2,3,6-tri-*O*-acetyl-4-*O*-[2,3,4,6-tetra-*O*-acetyl- β -D-glucopyranosyl]- α and β -D-glucopyrano[2,1-d]-2-oxazoline (14). Compound **14** (1:1 α : β ratio, 601 mg, 73%) was obtained

from azide **29** (0.89 g, 1.34 mmol) after column chromatography purification (1:3:0.5% petroleum ether-EtOAc-Et₃N → 1:0.5% EtOAc-Et₃N). *R_f* = 0.42 (EtOAc). IR (KBr): $\nu_{\max}$ 2941, 1747, 1672, 1435, 1370, 1226, 1038 cm⁻¹; ¹H NMR (500 MHz, CDCl₃): δ (ppm) α -anomer: 5.71 (d, 1 H, *J*_{1,2} = 8.0 Hz, H-1), 5.45 (t, 1 H, *J*_{2,3} = *J*_{3,4} = 2.5 Hz, H-3), 5.07 (t, 1 H, *J*_{2',3'} = *J*_{3',4'} = 9.5 Hz, H-3'), 4.99 (t, 1 H, *J*_{4',5'} = 9.5 Hz, H-4'), 4.85 (dd, 1 H, *J*_{1,2} = 8.0 Hz, H-2'), 4.44 (d, 1 H, H-1'), 4.30 (dd, 1 H, H-2), 4.30 (dd, 1 H, *J*_{5'a,6'a} = 3.5 Hz, *J*_{6'a,6'b} = 12.0 Hz, H-6'a), 4.12 (dd, 1 H, *J*_{5a,6a} = 2.5 Hz, *J*_{6a,6b} = 12.0 Hz, H-6a), 4.05 (dd, 1 H, *J*_{5,6b} = 5.5 Hz, H-6b), 3.98 (dd, 1 H, *J*_{5',6'b} = 2.5 Hz, H-6'b), 3.59 (ddd, 1 H, H-5'), 3.56 (dd, 1 H, *J*_{4,5} = 8.5 Hz, H-4), 3.35 (ddd, 1 H, H-5); β -anomer: 5.45 (t, 1 H, *J*_{2,3} = *J*_{3,4} = 9.5 Hz, H-3), 5.10 (t, 1 H, *J*_{2',3'} = *J*_{3',4'} = 9.0 Hz, H-3'), 5.03 (t, 1 H, *J*_{4',5'} = 9.5 Hz, H-4'), 4.90 (dd, 1 H, *J*_{1',2'} = 8.0 Hz, H-2'), 4.66 (t, 1 H, *J*_{1,2} = 9.5 Hz, H-2), 4.54 (d, 1 H, H-1'), 4.41 (dd, 1 H, *J*_{5a,6a} = 2.0 Hz, *J*_{6a,6b} = 12.0 Hz, H-6a), 4.20 (dd, 1 H, *J*_{5'a,6'a} = 4.0 Hz, *J*_{6'a,6'b} = 12.5 Hz, H-6'a), 4.09 (dd, 1 H, *J*_{5',6'b} = 1.5 Hz, H-6'b), 4.08 (d, 1 H, H-1), 4.00 (dd, 1 H, *J*_{5,6b} = 4.5 Hz, H-6b), 3.69 (ddd, 1 H, H-5'), 3.65 (t, 1 H, *J*_{4,5} = 9.5 Hz, H-4), 3.52 (ddd, 1 H, H-5); 2.10-1.93 (13 s, 36 H, 12 MeCO, 2 Me). ¹³C NMR (125.7 MHz, CDCl₃): δ (ppm) 170.9-169.2 (12 CO), 168.9 (2 CN); α -anomer: 101.9 (C-1'), 92.1 (C-1), 76.7 (C-2), 74.9 (C-4), 72.7 (C-3'), 71.9 (C-5'), 71.2 (C-5), 69.3 (C-4'), 68.1 (C-3), 67.3 (C-2'), 63.7 (C-6'), 61.6 (C-6), 13.9 (MeN); β -anomer: 100.7 (C-1'), 84.6 (C-1), 73.6 (C-4), 72.9 (C-3'), 72.6 (C-3), 72.3 (C-5), 71.8 (C-5'), 71.5 (C-2), 67.7 (C-2'), 72.2 (C-6'), 61.5 (C-6), 14.1 (MeN); 20.9-20.4 (12 MeCO). ESIMS: *m/z* = 618 ([M + H]⁺), 640 ([M + Na]⁺). Anal. Calcd for C₂₆H₃₅NO₁₆: C, 50.57; H, 5.71; N, 2.27. Found: C, 50.90; H, 5.73; N, 2.02.

2-Methyl-4,5-dihydro-[2,3,6-tri-*O*-acetyl-4-*O*-[2,3,4,6-tetra-*O*-acetyl- α -D-glucopyranosyl]- α -D-glucopyrano[2,1-d]-2-oxazoline (15). Compound **15** (385 mg, 73%) was obtained from azide **30** (0.56 g, 0.85 mmol) after column chromatography purification (1:3:0.5% petroleum ether-EtOAc-Et₃N → 1:0.5% EtOAc-Et₃N). *R_f* = 0.26 (EtOAc). [α]_D = +59.5 (*c* 1.0, CH₂Cl₂). IR (KBr): $\nu_{\max}$ 2958, 1747, 1665, 1437, 1370, 1225, 1039 cm⁻¹. ¹H NMR (300 MHz, CDCl₃): δ (ppm) 5.87 (d, 1 H, *J*_{1,2} = 8.1 Hz, H-1), 5.42 (d, 1 H, *J*_{1',2'} = 3.9 Hz, H-1'), 5.36 (t, 1 H, *J*_{2',3'} = *J*_{3',4'} = 9.9 Hz, H-3'), 5.03 (t, 1 H, *J*_{4',5'} = 9.9

Hz, H-4'), 4.97 (d, 1 H, $J_{2,3} = 2.1$ Hz, H-3), 4.81 (dd, 1 H, H-2'), 4.38 (dd, 1 H, H-2), 4.25 (bd, 1 H, $J_{6a,6b} = 10.8$ Hz, H-6a), 4.21 (dd, 1 H, $J_{5',6'a} = 4.4$ Hz, $J_{6'a,6'b} = 12.7$ Hz, H-6'a), 4.16 (dd, 1 H, $J_{5,6b} = 2.5$ Hz, H-6b), 4.04 (dd, 1 H, $J_{5',6'b} = 2.0$ Hz, H-6'b), 3.95 (ddd, 1 H, H-5'), 3.63 (m, 2 H, H-4,5), 2.14-1.98 (5 s, 21 H, 6 MeCO, Me). ^{13}C NMR (75.5 MHz, CDCl_3): δ (ppm) 170.6-169.4 (6 CO), 169.3 (CN), 94.8 (C-1'), 92.0 (C-1), 73.8 (C-2), 72.0 (C-4), 70.3 (C-2'), 69.5 (C-3'), 68.2 (C-5'), 68.0 (C-4',5), 67.3 (C-3), 64.3 (C-6), 61.8 (C-6'), 20.8-20.5 (6 MeCO), 13.9 (MeN). ESIMS: $m/z = 656$ ($[\text{M} + \text{K}]^+$), 640 ($[\text{M} + \text{Na}]^+$), 618 ($[\text{M} + \text{H}]^+$). Anal. Calcd for $\text{C}_{26}\text{H}_{35}\text{NO}_{16}$: C, 50.57; H, 5.71; N, 2.27. Found: C, 50.91; H, 5.65; N, 2.06.

2-Methyl-4,5-dihydro-[2,3,6-tri-*O*-acetyl-4-*O*-[2,3,4,6-tetra-*O*-acetyl- β -D-galactopyranosyl]- α -D-glucopyrano[2,1-d]-2-oxazoline (16). Compound **16** (176 mg, 93%) was obtained from azide **31** (237 mg, 0.31 mmol) after column chromatography purification (1:3:0.5% petroleum ether-EtOAc-Et₃N $\rightarrow$ 1:0.5% EtOAc-Et₃N). $R_f = 0.31$ (EtOAc). $[\alpha]_D = +13.5$ (c 1.0, CH_2Cl_2). IR (KBr): ν_{max} 2961, 1750, 1661, 1371, 1223 cm^{-1} . ^1H NMR (500 MHz, CDCl_3): δ (ppm) 5.76 (d, 1 H, $J_{1,2} = 7.5$ Hz, H-1), 5.49 (t, 1 H, $J_{2,3} = J_{3,4} = 2.5$ Hz, H-3), 5.36 (dd, 1 H, $J_{3',4'} = 3.5$ Hz, $J_{4',5'} = 1.0$ Hz, H-4'), 5.13 (dd, 1 H, $J_{2',3'} = 10.5$ Hz, $J_{1',2'} = 8.0$ Hz, H-2'), 4.97 (dd, 1 H, H-3'), 4.53 (d, 1 H, H-1'), 4.33 (dd, 1 H, H-2), 4.18 (dd, 1 H, $J_{6a,6b} = 12.0$ Hz, $J_{5,6a} = 3.0$ Hz, H-6a), 4.11 (m, 3 H, H-6'a, H-6b, H-6'b), 3.92 (td, 1 H, $J_{5',6'a} = J_{5',6'b} = 4.5$ Hz, H-5'), 3.62 (dd, 1 H, $J_{4,5} = 8.5$ Hz, H-4), 3.40 (ddd, 1 H, $J_{5,6b} = 5.5$ Hz, H-5), 2.16-1.95 (5 s, 21 H, 6 MeCO, Me). ^{13}C NMR (125.7 MHz, CDCl_3 , 313 K): δ (ppm) 170.2-168.8 (6 CO), 169.2 (CN), 102.5 (C-1'), 92.1 (C-1), 76.7 (C-4), 75.0 (C-2), 70.8 (C-3'), 70.7 (C-5'), 69.6 (C-3), 68.7 (C-2'), 67.2 (C-5), 66.7 (C-4'), 63.7 (C-6), 60.8 (C-6'), 20.8-20.4 (6 MeCO), 13.9 (Me). ESIMS: $m/z = 618$ ($[\text{M} + \text{H}]^+$). HRFABMS found: 618.203410; calcd for $[\text{C}_{26}\text{H}_{35}\text{NO}_{16} + \text{H}]^+$: 618.204455. Anal. Calcd for $\text{C}_{26}\text{H}_{35}\text{NO}_{16}$: C, 50.57; H, 5.71; N, 2.27. Found: C, 50.53; H, 5.65; N, 1.77.

General Procedure for the Preparation of Glycooxazolines 17-19. Compounds **17-19** were prepared by Ritter-like reaction following a previously reported method.⁶ To a solution of the corresponding isopropylidene derivative **33-34** (0.80 mmol) and CH_3CN (50 eq) in distilled CH_2Cl_2 (8.0

mL) at -40 (**32**) or -20 °C (**33** and **34**), TfOH (0.12 mL, 1.5 eq) was added under Ar. After 1 h, the reaction was quenched by addition of Et₃N, then concentrated under reduced pressure and the residue was extracted with toluene-Et₂O (1:1, 20 mL). The organic layer was washed with H₂O (2 x 10 mL), dried (MgSO₄), filtered and concentrated. The residue was purified by column chromatography with the eluent indicated in each case to give the corresponding oxazoline derivatives as amorphous solids.

2-Methyl-4,5-dihydro-(1-deoxy-3,5,6-tri-*O*-benzyl- β -D-glucofuranoso)[1,2-d]oxazole (17):

Column chromatography: 1:2:0.5% EtOAc-petroleum ether-Et₃N. Yield: 170 mg (45%). R_f = 0.22 (1:2 EtOAc-petroleum ether). $[\alpha]_D$ -24 (c 1.0, CH₂Cl₂). IR (film): $\nu_{\max}$ = 3063, 3030, 2930, 2866, 1744, 1667, 1497, 1371, 1233, 1099, 1063, 739, 698 cm⁻¹. ¹H NMR (300 MHz, CDCl₃): δ = 7.28 (m, 15 H, Ph), 6.06 (d, 1 H, $J_{1,2}$ = 5.4 Hz, H-1), 4.83 (d, 1 H, $^2J_{H,H}$ = 11.4 Hz, CH₂Ph), 4.72 (d, 1 H, H-2), 4.65 (d, 1 H, $^2J_{H,H}$ = 11.7 Hz, CH₂Ph), 4.59 (d, 1 H, $^2J_{H,H}$ = 12.3 Hz, CH₂Ph), 4.55 (d, 1 H, $^2J_{H,H}$ = 12.3 Hz, CH₂Ph), 4.54 (d, 1 H, $^2J_{H,H}$ = 11.7 Hz, CH₂Ph), 4.49 (d, 1 H, $^2J_{H,H}$ = 11.4 Hz, CH₂Ph), 4.13 (ddd, 1 H, $J_{5,6a}$ = 1.8 Hz, $J_{5,6b}$ = 6.0 Hz, H-5), 4.12 (d, 1 H, $J_{3,4}$ = 3.0 Hz, H-3), 3.91 (bd, 1 H, $J_{6a,6b}$ = 10.5 Hz, H-6a), 3.70 (dd, 1 H, $J_{4,5}$ = 6.3 Hz, H-4), 3.66 (bd, 1 H, H-6b), 2.00 (s, 3 H, NMe). ¹³C NMR (75.5 MHz, CDCl₃): δ = 168.5 (CN), 138.7-127.5 (Ar), 100.6 (C-1), 83.1 (C-2), 81.4 (C-3), 77.3 (C-4), 75.4 (C-5), 73.5, 72.8, 72.2 (3 CH₂Ph), 70.7 (C-6), 13.9 (NMe). FABMS: m/z 514 ([M + Na]⁺), 474 ([M + H]⁺). Anal. Calcd for C₂₉H₃₁NO₅: C, 73.55; H, 6.60; N, 2.96. Found: C, 73.70; H, 6.52; N, 2.79.

2-Methyl-4,5-dihydro-(1-*O*-benzyl-2-deoxy-4,5-*O*-isopropylidene- β -D-fructopyranoso)[2,3-

d]oxazole (18): Column chromatography: 1:1→2:1 EtOAc-petroleum ether. Yield: 213 mg (80%). R_f = 0.22 (1:2 EtOAc-petroleum ether). $[\alpha]_D$ -90 (c 0.8, CH₂Cl₂). UV (CH₂Cl₂): $\lambda_{\max}$ = 228 nm (ϵ_{mM} 2.7). IR (film): $\nu_{\max}$ = 2984, 2932, 2868, 1667, 1545, 1383, 1248, 1209, 1109, 1034, 738 cm⁻¹. ¹H NMR (500 MHz, CDCl₃): δ = 7.22 (m, 5 H, Ph), 4.62 (d, 1 H, $^2J_{H,H}$ = 12.0 Hz, CH_aH_bPh), 4.60 (dd, 1 H, $J_{4,5}$ = 7.5 Hz, H-4), 4.56 (d, 1 H, $J_{3,4}$ = 11.0 Hz, H-3), 4.55 (d, 1 H, CH_aH_bPh), 4.13 (dd, 1 H, $J_{5,6b}$ = 2.0 Hz, H-5), 3.73 (d, 1 H, $J_{1a,1b}$ = 10.0 Hz, H-1a), 3.71 (d, 1 H, $J_{6a,6b}$ = 13.5 Hz, H-6a) 3.59 (d, 1 H, H-1b), 3.31 (dd, 1 H, H-6b), 2.04 (s, 3 H, NMe), 1.39, 1.30 (2 s, each 3 H, CMe₂). ¹³C NMR (125.7 MHz, CDCl₃): δ =

168.0 (CN), 138.1, 128.3, 127.6, 127.5 (Ar), 109.1 (CMe₂), 98.7 (C-2), 73.5 (CH₂Ph), 73.1 (C-1), 72.8 (C-3), 70.4 (C-5), 69.8 (C-4), 60.9 (C-6), 26.0, 24.3 (2 CMe₂), 13.9 (NMe). FABMS: m/z = 356 ([M + Na]⁺), 334 ([M+H]⁺). Anal. Calcd for C₁₈H₂₃NO₅: C, 64.85; H, 6.95; N, 4.20. Found: C, 64.94; H, 6.98; N, 4.22.

(5*R*,8*R*,9*R*,10*S*)-1-Aza-10-benzyloxy-8,9-dimethylmethylenedioxy-2-methyl-3,6-dioxaspiro[4.5]dec-1-ene (19): Column chromatography: 1:1 EtOAc-petroleum ether. Yield: 133 mg (50%). R_f = 0.54 (2:1 EtOAc-petroleum ether). The physicochemical and spectroscopic properties were identical to that reported.⁷

General Procedure for the Preparation of β -Aldopyranosyl Isothiocyanates 3 β and 20 β -23 β . To a heterogeneous mixture of the corresponding oxazoline derivative **6** or **13-16** in CH₂Cl₂-H₂O (1:1, 5 mL per 100 mg of reacting oxazoline), CaCO₃ (3 equiv), and CSCI₂ (1.5 equiv) were added. The mixture was vigorously stirred for the indicated time (Table 1 in the manuscript) in a round bottom flask provided with a system for evacuation of gases and then filtered (**CAUTION: use a well-ventilated hood**). The organic layer was separated, washed with water, dried (MgSO₄), and concentrated to dryness. The resulting residue was purified by column chromatography using mixtures of EtOAc-petroleum ether. The isolated yields are collected in Tables 1 and 2 in the manuscript. The spectroscopic and physicochemical data were identical to those reported in the literature (see ref 1 in the manuscript).

General Procedure for the Preparation of β -Aldopyranosyl Isothiocyanates 3 α and 20 α -23 α . When the isothiocyanation reaction of the oxazoline derivative **6** or **13-16** was carried out following the above procedure but in the presence of CuCl₂·2H₂O (1.5 eq), a mixture of the corresponding α and β -glycosyl isothiocyanate (3 α,β and 20-232 α,β) was obtained. Column chromatography with the eluent indicated in each case afforded the separated anomers in pure form. Data for 2,3,4,6-tetra-*O*-acetyl- α -D-glucopyranosyl isothiocyanate (3 α), as well as for the thiourea adduct **12 α** resulting from its coupling reaction with benzylamine, are listed in the manuscript.

2,3,4,6-Tetra-*O*-acetyl- α -D-galactopyranosyl Isothiocyanate (20 α). Compound **19 α** (124 mg, 66%) was obtained, together with **20 β** (38 mg, 20%), by isothiocyanation of **13** (180 mg, 0.55 mmol) in the presence of CuCl₂ after column chromatography using 1:2 EtOAc-petroleum ether: R_f (**20 α**) = 0.62 (1:1 EtOAc-petroleum ether); R_f (**20 β**) = 0.53 (1:1 EtOAc-petroleum ether). The α -anomer **20 α** , isolated as an amorphous solid, had $[\alpha]_D^{+140}$ (c 1.1, CH₂Cl₂); IR (KBr): $\nu_{\max}$ 2965, 2017, 1752, 1433, 1371, 1219, 1075 cm⁻¹; ¹H NMR (300 MHz, CDCl₃): δ (ppm) 5.86 (d, 1 H, $J_{1,2}$ = 3.6 Hz, H-1), 5.44 (dd, 1 H, $J_{3,4}$ = 3.0 Hz, $J_{4,5}$ = 1.2 Hz, H-4), 5.23 (dd, 1 H, $J_{2,3}$ = 10.5 Hz, H-3), 5.17 (dd, 1 H, H-2), 4.27 (bt, 1 H, $J_{5,6a}$ = $J_{5,6b}$ = 6.0 Hz, H-5), 4.09 (dd, 1 H, $J_{6a,6b}$ = 11.4 Hz, H-6a), 4.02 (dd, 1 H, H-6b), 2.07, 2.01, 1.97 (3 s, 12 H, 4 MeCO); ¹³C NMR (125.7 MHz, CDCl₃): δ (ppm) 170.2-169.7 (4 CO), 144.1 (NCS), 82.6 (C-1), 69.4 (C-5), 67.6 (C-2), 67.3 (C-3), 67.1 (C-4), 61.1 (C-6), 20.5-20.4 (MeCO); ESIMS: m/z = 428 ([M + K]⁺), 412 ([M + Na]⁺). Anal. Calcd for C₁₅H₁₉NO₉S: C, 46.27; H, 4.92; N, 3.60. Found: C, 46.29; H, 4.94; N, 3.55.

2,3,6-Tri-*O*-acetyl-4-*O*-[2,3,4,6-tetra-*O*-acetyl- β -D-glucopyranosyl]- α -D-glucopyranosyl Isothiocyanate (21 α). Compound **21 α** (113 mg, 53%) was obtained, together with **21 β** (48 mg, 21%) by isothiocyanation of **14** (200 mg, 0.32 mmol) in the presence of CuCl₂ after column chromatography using 1:2 $\rightarrow$ 2:1 EtOAc-petroleum ether: R_f (**21 α**) = 0.29 (1:1 EtOAc-petroleum ether); R_f (**21 β**) = 0.53 (1:1 EtOAc-petroleum ether). The α -anomer **21 α** , isolated as an amorphous solid, had $[\alpha]_D^{+52.4}$ (c 1.0, CH₂Cl₂); IR (KBr): $\nu_{\max}$ 2957, 2019, 1752, 1433, 1369, 1226, 1045 cm⁻¹; ¹H NMR (500 MHz, CDCl₃): δ (ppm) 5.72 (d, 1 H, $J_{1,2}$ = 4.0 Hz, H-1), 5.34 (t, 1 H, $J_{2,3}$ = $J_{3,4}$ = 9.5 Hz, H-3), 5.09 (t, 1 H, $J_{2',3'} = J_{3',4'} = 9.5$ Hz, H-3'), 5.02 (t, 1 H, $J_{1',2'} = 9.5$ Hz, H-2'), 4.87 (t, 1 H, $J_{4',5'} = 9.5$ Hz, H-4'), 4.86 (t, 1 H, H-2), 4.48 (dd, 1 H, $J_{6a,6b}$ = 12.0 Hz, $J_{5,6a}$ = 2.0 Hz, H-6a), 4.47 (d, 1 H, H-1'), 4.42 (dd, 1H, $J_{6'a,6'b}$ = 12.5 Hz, $J_{5',6'a}$ = 4.5 Hz, H-6'a), 4.07 (dd, 1 H, $J_{5,6b}$ = 4.5 Hz, H-6b), 3.99 (dd, 1 H, $J_{5',6'b}$ = 2.5 Hz, H-6'b), 3.97 (ddd, 1 H, H-5), 3.69 (t, 1 H, $J_{4,5}$ = 9.5 Hz, H-4), 3.62 (ddd, 1 H, H-5'), 2.09-1.96 (7 s, 21 H, 7 MeCO); ¹³C NMR (75.5 MHz, CDCl₃): δ (ppm) 170.4-168.9 (MeCO), 144.7 (NCS), 100.5 (C-1'), 81.9 (C-1), 75.5 (C-4), 72.8 (C-3'), 71.9 (C-2), 71.5 (C-5'), 71.4 (C-5), 70.5 (C-4'), 69.1 (C-3), 67.7 (C-2'),

61.5 (C-6'), 61.1 (C-6), 20.7-20.3 (*MeCO*). ESIMS: $m/z = 700$ ($[M + Na]^+$). Anal. Calcd for $C_{27}H_{35}NO_{17}S$: C, 47.86; H, 5.21; N, 2.07. Found: C, 47.37; H, 5.06; N, 1.90.

2,3,6-Tri-*O*-acetyl-4-*O*-[2,3,4,6-tetra-*O*-acetyl- α -D-glucopyranosyl]- α -D-glucopyranosyl

Isothiocyanate (22 α). Compound **22 α** (178 mg, 78%) was obtained, together with **22 β** (18 mg, 8%) by isothiocyanation of **15** (155 mg, 0.25 mmol) after column chromatography using 1:2→1:1 EtOAc-petroleum ether. Yield: R_f (**22 α**) = 0.43 (1:1 EtOAc-petroleum ether); R_f (**22 β**) = 0.50 (1:1 EtOAc-petroleum ether). The α -anomer **22 α** , isolated as an amorphous solid, had $[\alpha]_D +140$ (c 0.9, CH_2Cl_2); IR (KBr): ν_{max} 2961, 2017, 1748, 1433, 1370, 1229, 1037 cm^{-1} . 1H NMR (300 MHz, $CDCl_3$): δ (ppm) 5.73 (d, 1 H, $J_{1,2} = 4.2$ Hz, H-1), 5.47 (t, 1 H, $J_{2,3} = J_{3,4} = 9.3$ Hz, H-3), 5.38 (d, 1 H, $J_{1,2} = 4.0$ Hz, H-1'), 5.33 (t, 1 H, $J_{2',3'} = J_{3,4} = 10.0$ Hz, H-3'), 5.06 (t, 1 H, $J_{4',5'} = 10.0$ Hz, H-4'), 4.87 (dd, 1 H, H-2'), 4.86 (dd, 1 H, H-2), 4.51 (dd, 1 H, $J_{6a,6b} = 12.8$ Hz, $J_{5,6a} = 2.7$ Hz, H-6a), 4.23 (dd, 1 H, $J_{6'a,6'b} = 12.3$ Hz, $J_{5',6'a} = 4.3$ Hz, H-6'a), 4.22 (dd, 1H, $J_{5,6b} = 4.3$ Hz, H-6b), 4.09 (ddd, 1 H, $J_{4,5} = 10.0$ Hz, H-5), 4.04 (dd, 1H, $J_{5',6'b} = 2.1$ Hz, H-6'b), 3.97 (t, 1 H, H-4), 3.96 (ddd, 1 H, H-5'), 2.15-1.99 (7 s, 21 H, 7 *MeCO*). ^{13}C NMR (75.5 MHz, $CDCl_3$): δ (ppm) 170.6-169.4 (4 *MeCO*), 145.1 (NCS), 95.8 (C-1'), 81.9 (C-1), 72.0 (C-3), 71.9 (C-5), 70.9 (C-4), 70.8 (C-2), 70.0 (C-2'), 69.2 (C-3'), 68.6 (C-5'), 67.9 (C-4'), 62.0 (C-6), 61.3 (C-6'), 20.8-20.3 (7 *MeCO*). ESIMS: $m/z = 700$ ($[M + Na]^+$). Anal. Calcd for $C_{27}H_{35}NO_{17}S$: C, 47.86; H, 5.21; N, 2.07. Found: C, 47.67; H, 5.09; N, 2.00.

2,3,6-Tri-*O*-acetyl-4-*O*-[2,3,4,6-tetra-*O*-acetyl- β -D-galactopyranosyl]- α -D-glucopyranosyl

isothiocyanate (23 α). Compound **23 α** (55 mg, 24%) was obtained, together with **23 β** (91 mg, 40%) by isothiocyanation of **16** (176 mg, 0.28 mmol) after column chromatography using 1:2 → 1:1 EtOAc-petroleum ether: R_f (**23 α**) = 0.22 (1:1 EtOAc-petroleum ether); R_f (**23 β**) = 0.26 (1:1 EtOAc-petroleum ether). The α -anomer **23 α** , isolated as an amorphous solid, had $[\alpha]_D = +13.5$ (1.0, CH_2Cl_2). IR (KBr): ν_{max} 2986, 2011, 1753, 1422, 1370, 1223, 1072 cm^{-1} . 1H NMR (500 MHz, $CDCl_3$): δ (ppm) 5.76 (d, 1 H, $J_{1,2} = 4.5$ Hz, H-1), 5.41 (t, 1 H, $J_{2,3} = J_{3,4} = 9.5$ Hz, H-3), 5.10 (bd, 1 H, $J_{3',4'} = 3.5$ Hz, H-4'), 5.01 (dd, 1 H, $J_{2,3} = 10.5$ Hz, $J_{1',2'} = 8.0$ Hz, H-2'), 4.95 (dd, 1 H, H-3'), 4.91 (dd, 1 H, H-2), 4.49 (dd, 1 H,

$J_{6a,6b} = 12.5$ Hz, $J_{5,6a} = 2.0$ Hz, H-6a), 4.48 (d, 1 H, H-1'), 4.15 (dd, 1H, $J_{6'a,6'b} = 11.0$ Hz, $J_{5',6'a} = 6.0$ Hz, H-6'a), 4.09 (dd, 1 H, $J_{5,6b} = 4.5$ Hz, H-6b), 4.06 (dd, 1 H, $J_{5',6'b} = 6.0$ Hz, H-6'b), 4.02 (ddd, 1 H, $J_{4,5} = 9.5$ Hz, H-5), 3.87 (t, 1 H, H-5'), 3.76 (t, 1 H, H-4), 2.16-1.95 (7 s, 21 H, 7 MeCO). ^{13}C NMR (125.7 MHz, CDCl_3): δ (ppm) 170.3-168.9 (MeCO), 144.8 (NCS), 100.8 (C-1'), 81.9 (C-1), 75.3 (C-4), 71.4 (C-5), 70.9 (C-5'), 70.8 (C-3'), 70.7 (C-2), 69.4 (C-3), 69.0 (C-2'), 66.6 (C-4'), 61.2 (C-6), 60.8 (C-6'), 20.7-20.4 (MeCO). ESIMS: $m/z = 700$ ($[\text{M} + \text{Na}]^+$). Anal. Calcd for $\text{C}_{27}\text{H}_{35}\text{NO}_{17}\text{S}$: C, 47.86; H, 5.21; N, 2.07. Found: C, 47.86; H, 5.47; N, 1.92.

2-*O*-Acetyl-3,5,6-tri-*O*-benzyl- α and β -D-glucufuranosyl Isothiocyanates (24 α** and **24 β**).** To a heterogeneous mixture of **17** (102 mg, 0.21 mmol) and CaCO_3 (32 mg, 3 equiv) in CH_2Cl_2 - H_2O (1:1, 4 mL) was added CSCl_2 (8 μL , 1.5 equiv). The mixture was vigorously stirred for 3 h at room temperature in a round bottom flask provided with a system for evacuation of gases and then filtered. The organic layer was separated, washed with water, dried (MgSO_4), and concentrated to dryness. The residue was subjected to column chromatography using 1:4 EtOAc-petroleum ether as eluent to give **24 α** (46 mg, 41%) and **24 β** (34 mg, 30%) as amorphous solids. A parallel experiment conducted in the presence of $\text{CuCl}_2 \cdot 2\text{H}_2\text{O}$ (1.5 eq), afforded **24 α** (54 mg, 48%) and **24 β** (26 mg, 23%).

Data for **24 α** : $R_f = 0.39$ (1:4 EtOAc-petroleum ether); $[\alpha]_D = +66$ (c 1.1, CH_2Cl_2); IR (KBr): ν_{max} 3033, 2926, 2864, 2041, 1750, 1373, 1219, 1115, 1065, 737, 698 cm^{-1} ; ^1H NMR (500 MHz, CDCl_3 , 298 K): δ (ppm) 7.33-7.22 (m, 15 H, 3 Ph), 5.68 (d, 1 H, $J_{1,2} = 5.0$ Hz, H-1), 5.23 (dd, 1 H, $J_{2,3} = 2.0$ Hz, H-2), 4.75, 4.46 (2 d, 2 H, $^2J_{\text{H,H}} = 11.5$ Hz, CH_2Ph), 4.62, 4.50 (2 d, 2 H, $J_{\text{Ha,Hb}} = 11.5$ Hz, CH_2Ph), 4.58 (s, 2 H, CH_2Ph), 4.39 (dd, 1 H, $J_{3,4} = 4.5$ Hz, $J_{4,5} = 8.1$ Hz, H-4), 4.20 (dd, 1 H, H-3), 3.99 (ddd, 1 H, $J_{5,6b} = 5.0$ Hz, $J_{5,6a} = 2.0$ Hz, H-5), 3.82 (dd, 1 H, $J_{6a,6b} = 10.5$ Hz, H-6a), 3.63 (dd, 1 H, H-6b), 2.14 (s, 3 H, MeCO); ^{13}C NMR (125.7 MHz, CDCl_3): δ (ppm) 169.8 (CO), 140.9 (NCS), 138.4, 138.2, 137.1, 128.5, 128.3, 128.0, 127.7, 127.6, 127.5 (3 Ar), 86.3 (C-1), 80.8 (C-3), 79.2 (C-4), 77.0 (C-2), 75.3 (C-5), 73.5,

72.5, 72.3 (3 CH₂Ph), 70.0 (C-6), 20.4 (MeCO). FABMS: m/z 555 ([M + Na]⁺). Anal. Calcd for C₃₀H₃₁NO₆S: C, 67.52; H, 5.86; N, 2.62. Found: C, 67.39; H, 5.84; N, 2.50.

Data for **24b**: R_f = 0.28 (1:4 EtOAc-petroleum ether); $[\alpha]_D$ = -86 (c 0.9, CH₂Cl₂). IR (film): $\nu_{\max}$ 3030, 2980, 2938, 2874, 2029, 1751, 1379, 1125, 1074, 741, 698 cm⁻¹. ¹H NMR (300 MHz, CDCl₃): δ (ppm) 7.35-7.14 (m, 15 H, 3 Ph), 5.31 (s, 1 H, H-1), 5.25 (s, 1 H, $J_{2,3}$ = 2.0 Hz, H-2), 4.82, 4.38 (2 d, 2 H, $^2J_{H,H}$ = 11.7 Hz, CH₂Ph), 4.64, 4.53 (2 d, 2 H, $^2J_{H,H}$ = 11.1 Hz, CH₂Ph), 4.62, 4.55 (2 d, 2 H, $^2J_{H,H}$ = 12.3 Hz, CH₂Ph), 4.40 (d, 1 H, $J_{4,5}$ = 9.3 Hz, $J_{3,4}$ = 4.2 Hz, H-4), 4.13 (dd, 1 H, H-3), 4.09 (ddd, 1 H, $J_{5,6b}$ = 4.5 Hz, $J_{5,6a}$ = 2.1 Hz, H-5), 3.83 (dd, 1 H, $J_{6a,6b}$ = 10.8 Hz, H-6a), 3.66 (dd, 1 H, H-6b), 2.08 (MeCO). ¹³C NMR (75.5 MHz, CDCl₃): δ (ppm) = 169.5 (CO), 141.8 (NCS), 138.4-127.5 (Ar), 88.5 (C-1), 81.9 (C-4), 80.1 (C-3), 79.1 (C-2), 75.5 (C-5), 73.4, 72.3 (3 CH₂Ph), 69.4 (C-6), 20.7 (MeCO). FABMS: m/z 555 ([M + Na]⁺). Anal. Calcd for C₃₀H₃₁NO₆S: C, 67.52; H, 5.86; N, 2.62. Found: C, 67.56; H, 5.81; N, 2.50.

3-O-Acetyl-1-O-benzyl-4,5-O-isopropylidene- β -D-fructopyranosyl Isothiocyanate (24). To a heterogeneous mixture of **18** (200 mg, 0.60 mmol) and CaCO₃ (180 mg, 3 equiv) in CH₂Cl₂- H₂O (1:1, 10 mL) was added CScCl₂ (45 μ L, 1.5 equiv). The mixture was vigorously stirred for 1 h at room temperature in a round bottom flask provided with a system for evacuation of gases and then filtered. The organic layer was separated, washed with water, dried (MgSO₄), and concentrated to dryness. The residue was subjected to column chromatography using 1:4 $\rightarrow$ 1:3 EtOAc-petroleum ether as eluent to give **25** (231, 97%) as an amorphous solid: R_f = 0.34 (1:4 EtOAc-petroleum ether); $[\alpha]_D$ = -196.0 (c 1.0, CH₂Cl₂); IR (KBr): $\nu_{\max}$ 3065, 3033, 2988, 2934, 2872, 2010, 1753, 1371, 1221, 1127, 1061, 739, 698 cm⁻¹; ¹H NMR (500 MHz, CDCl₃): δ (ppm) 7.34-7.24 (m, 5 H, Ph), 5.25 (d, 1 H, $J_{3,4}$ = 7.0 Hz, H-3), 4.55 (s, 2 H, CH₂Ph), 4.24 (m, 2 H, H-4, H-5), 4.19 (d, 1 H, $J_{6a,6b}$ = 14.0 Hz, H-6a), 4.12 (d, 1 H, $J_{5,6b}$ = 2.0 Hz, H-6b), 3.64 (d, 1 H, $^2J_{H,H}$ = 10.0 Hz, H-1a), 3.59 (d, 1 H, H-1b), 1.96 (MeCO), 1.53, 1.34 (2 s, 6 H, CMe₂); ¹³C NMR (125.7 MHz, CDCl₃): δ (ppm) = 169.8 (CO), 144.7 (NCS), 137.2-127.9 (Ar), 110.1

(CMe₂), 91.3 (C-2), 74.2 (C-4), 74.0 (CH₂Ph), 73.4 (C-1), 72.9 (C-5), 71.5 (C-3), 62.3 (C-6), 27.6, 26.3 (2 CMe₂), 20.7 (MeCO); FABMS *m/z* 406 ([M + Na]⁺). Anal. Calcd for C₁₉H₂₃NO₆S: C, 58.00; H, 5.89; N, 3.56. Found: C, 57.87; H, 5.86; N, 3.47.

When longer reaction times were used, partial hydrolysis of the isopropylidene group was observed. Thus, when the above reaction was left for 18 h, the yield of **25** decreased to 44%, and 3-*O*-acetyl-1-*O*-benzyl-2-deoxy-2-isothiocyanate-β-D-fructopyranose (55%) was also isolated from the reaction mixture.

1-*O*-Acetyl-3-*O*-benzyl-2-deoxy-4,5-*O*-isopropylidene-β-D-fructopyranosyl Isothiocyanate (26).

To a heterogeneous mixture of **19** (200 mg, 0.60 mmol) and CaCO₃ (180 mg, 3 equiv) in CH₂Cl₂-H₂O (1:1, 10 mL) was added CSCI₂ (45 μL, 1.5 equiv). The mixture was vigorously stirred at room temperature overnight in a round bottom flask provided with a system for evacuation of gases and then filtered. The organic layer was separated, washed with water, dried (MgSO₄), and concentrated to dryness. The residue was subjected to column chromatography using 1:2→3:1 EtOAc-petroleum ether as eluent to give **26** (52 mg, 22%) as an amorphous solid: *R_f* = 0.62 (1:2 EtOAc-petroleum ether). [α]_D = -63 (*c* 0.9, CH₂Cl₂); IR (KBr): ν_{max} 3066, 3032, 2986, 2934, 2880, 2020, 1751, 1381, 1219, 1121, 1074, 746, 700 cm⁻¹; ¹H NMR (300 MHz, CDCl₃): δ (ppm) 7.35-7.25 (m, 5 H, Ph), 4.95 (d, 1 H, ²*J*_{H,H} = 12.0 Hz, CH₂Ph), 4.67 (d, 1 H, CH₂Ph), 4.45 (d, 1 H, *J*_{1a,1b} = 11.4 Hz, H-1a), 4.37 (d, 1 H, *J*_{3,4} = 6.6 Hz, H-4), 4.21 (m, 1 H, H-5), 4.21 (d, 1 H, H-1b), 4.15 (m, 2 H, H-6a, H-6b), 3.60 (d, 1 H, H-3), 1.99 (MeCO), 1.59, 1.38 (2 s, each 3 H, CMe₂); ¹³C NMR (75.5 MHz, CDCl₃): δ (ppm) = 170.4 (CO), 144.4 (NCS), 137.8, 128.7, 128.3, 128.4 (Ar), 110.0 (CMe₂), 91.8 (C-2), 77.1 (C-4), 76.2 (C-3), 73.3 (C-5), 73.0 (CH₂Ph), 66.0 (C-1), 62.9 (C-6), 28.4, 26.5 (2 CMe₂), 21.0 (MeCO). FABMS: *m/z* 335 ([M - NCS]⁺). Anal. Calcd for C₁₉H₂₃NO₆S: C, 58.00; H, 5.89; N, 3.56. Found: C, 57.80; H, 6.18; N, 3.61.

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^1H and ^{13}C spectra (500 and 125.7 MHz, respectively, CDCl₃, 313 K) of **12α**

^1H and ^{13}C spectra (500 and 125.7 MHz, respectively, CDCl_3 , 313 K) of **13**

^1H and ^{13}C spectra (500 and 125.7 MHz, respectively, CDCl_3 , 313 K) of **14**

1D-tocsy and ^1H spectra (500 MHz, CDCl_3) of **14**

^1H and ^{13}C NMR spectra (300 and 75.5 MHz, CDCl_3) of **15**

^1H and HETCOR spectra (500 MHz, CDCl_3) of **16**

¹H and ¹³C NMR spectra (500 and 125.7 MHz, respectively, CDCl₃) of **17**

^1H and ^{13}C NMR spectra (300 and 125.7 MHz, respectively, CDCl_3) of **19**

^1H and ^{13}C NMR spectra (300 and 75.5 MHz, respectively, CDCl_3) of **20α**

^1H and ^{13}C NMR spectra (300 and 75.5 MHz, respectively, CDCl_3) of **21α**

¹H and ¹³C NMR spectra (300 and 75.5 MHz, respectively, CDCl₃) of **22α**

¹H and ¹³C NMR spectra (500 and 125.7 MHz, respectively, CDCl₃) of **23α**

^1H and ^{13}C NMR spectra (500 and 125.7 MHz, respectively, CDCl_3) of **24α**.

¹H and ¹³C NMR spectra (500 and 125.7 MHz, respectively, CDCl₃) of **24β**.

¹H and ¹³C NMR spectra (500 and 125.7 MHz, respectively, CDCl₃) of **25**

^1H and ^{13}C NMR spectra (500 and 125.7 MHz, respectively, CDCl_3) of **26**