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A Novel Approach to β-(1→4)-Linked Thiodisaccharides Starting from Disulfide Sugars

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Summary. Glycosylation of monosaccharides **4**, **8**, and **10** containing an intramolecular disulfide bridge by applying *Helferich*-conditions and an excess of acetobromohexose **5** or **11** as donor substrate yielded 6-thiocyanato-β-(1→4)-thiodisaccharides **6**, **9**, and **12** regio- and stereospecifically in moderate to good yields. In addition, the formation of trisaccharides **7** and **13** could be observed, albeit in low yield. This novel route for thioglycoside formation may open access to a variety of bioactive disaccharide analogues.

Keywords. Disulfide sugars; Thiodisaccharides; Thioglycosides; *Helferich* glycosylation.

Ein neuer Zugang zu β-(1→4)-verknüpften Thiodisacchariden ausgehend von Disulfidzuckern

Zusammenfassung. Die Glykosidierung der Monosaccharide **4**, **8** und **10**, welche eine intramolekulare Disulfidbrücke besitzen, liefert unter Anwendung von *Helferich*-Bedingungen und einem Überschuß entsprechender Acetobromohexose **5** oder **11** als Donor regio- und stereospezifisch die 6-Thiocyanato-β-(1→4)-thiodisaccharide **6**, **9** und **12** in guten Ausbeuten. Zusätzlich wurde, wenn auch in geringer Ausbeute, die Bildung der Trisaccharide **7** und **13** beobachtet. Dieser neue Syntheseweg zur Darstellung von thioglykosidischen Verknüpfungen öffnet einen Zugang zu einer Vielzahl an bioaktiven Disaccharid-Analoga.

Introduction

The increasing interest in thioglycosides is due to their utility as glycosyl donors in modern glycosylation reactions [1]. Furthermore, their potential as analogues of naturally occurring, biologically active saccharides has obtained great attention [2]. Since thioglycosidic linkages are hydrolytically stabilized towards the action of various glycosidases [3], they have been frequently used for structure-activity relationship studies involving carbohydrate-enzyme interactions [4]. However, a general application of thioglycosides as analogues of receptor-active saccharidic ligands is not always feasible [5].

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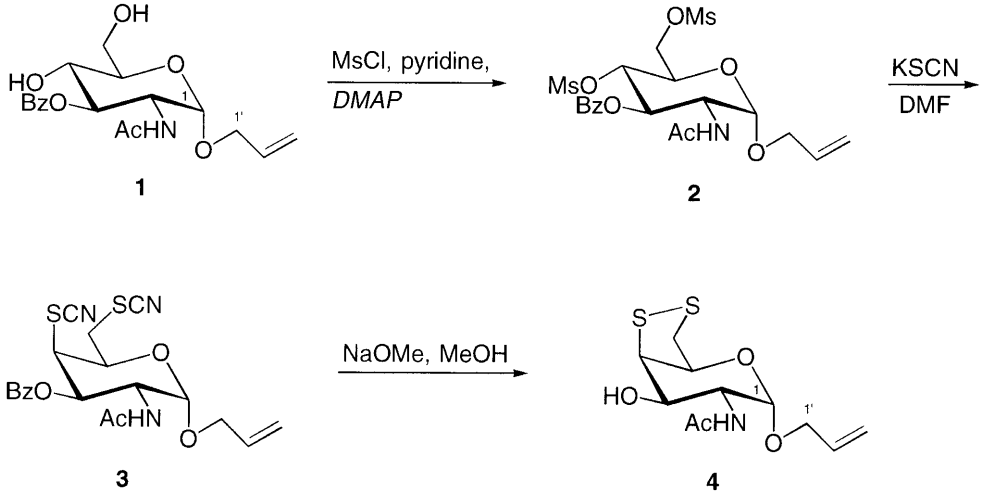
The formation of the thioglycosidic bond is usually achieved *via* two general strategies: (a) base-promoted S-glycosylation or anomeric S-alkylation [6], or (b) *Lewis* acid catalyzed S-glycosylation [7]. Additionally, methods applying the *Michael* addition of 1-thio sugars to levoglucosenon [8], or the nucleophilic opening of cyclic sulfate carbohydrates with 1-thio sugars have been described [9].

Here we report on the formation of thioglycosidic linkages starting from disulfide sugars. These carbohydrates are of particular interest because of their potential use in biological redox reactions [10] and their change in hydrophobicity compared to their natural analogues, thus making them a challenging object for lectin-binding studies [11].

Results and Discussion

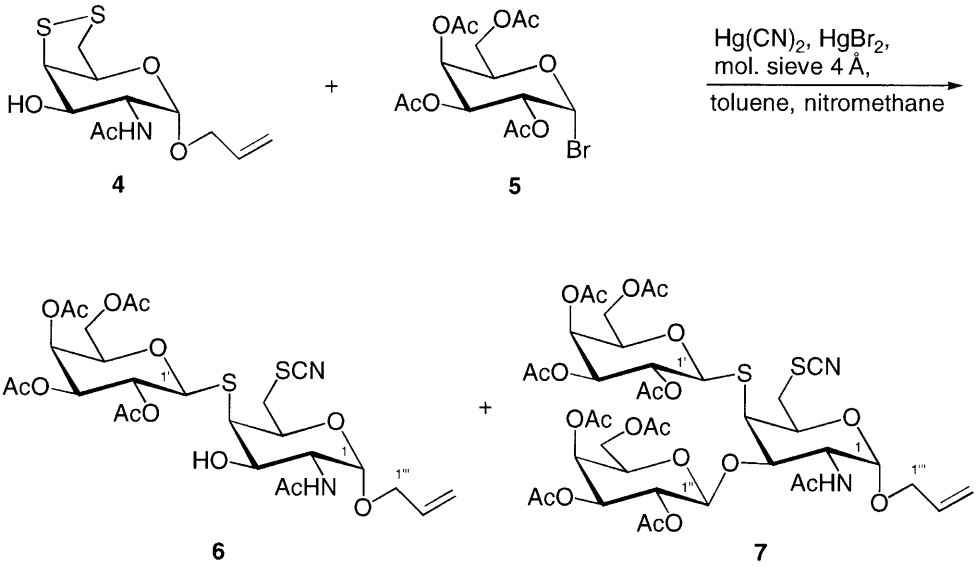
We started our studies with the allyl 4,6-epidithio-N-acetyl-galactosamin analogue **4**, which was easily prepared following essentially the procedure of *Hill et al*. [12]. Thus, starting from allyl 2-acetamido-2-deoxy-3-O-benzoyl-α-*D*-glucopyranoside **1** [13], the 4,6-dimesyl derivative **2** was prepared by treatment with an excess of methansulfonyl chloride in pyridine (Scheme 1). Displacement of the mesylate groups by thiocyanate functionalities yielded the galacto-configured compound **3** which was transformed to the 4,6-epidithio analogue **4** by applying the *Zemplen* saponification procedure. This conversion of dithiocyanate to the disulfide sugar is initiated by a nucleophilic attack of an alkoxide anion to the carbon atom of the thiocyanate-group, generating a reactive thiolate anion which subsequently forms the disulfide bond in an intramolecular reaction [14]. Thus, compound **4** could be obtained in moderate to good yield.

Treatment of **4** with a mixture of $Hg(CN)_2$ and $HgBr_2$ [15, 16] followed by addition of an excess of acetobromogalactose **5** [17] yielded the thiodisaccharide **6** (Scheme 2) in 50% yield. Additionally, the formation of the trisaccharide **7** could be observed in low yields. The predominant S-glycosylation may be explained by cyanide opening of the disulfide bond [18], generating a soft thiolate nucleophile



1 **2** **3** **4**

Scheme 1



Scheme 2

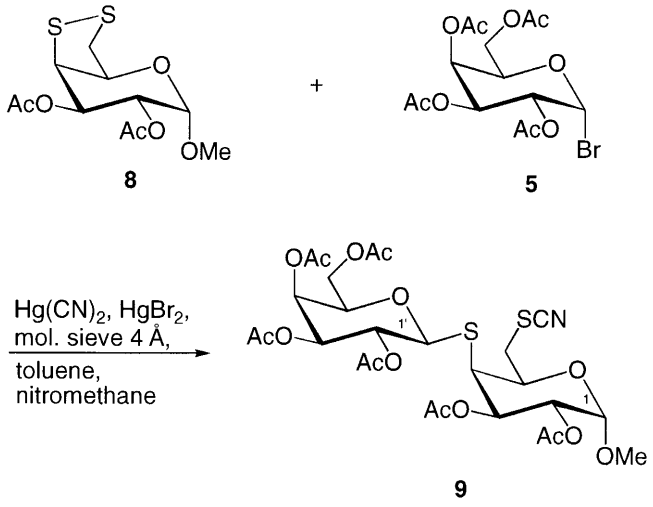
which subsequently substitutes the bromide at the anomeric center of the galactose derivative **5**. Since the substitution obviously follows an S_N2 mechanism, the thioglycosidic linkage is formed in a diastereospecific manner yielding the β-connectivity exclusively.

The stereochemistry of the thioglycosidic linkage could be assigned easily by NMR analysis. Thus, the $J_{1',2'}$ coupling constants in the thio-linked galactose moiety of disaccharide **6** were 9.96 and 10.60 Hz in the trisaccharide derivative **7**, a magnitude consistent with the β-glycosidic linkage. The presence of the C-$1'_{(Gal)}$-S-C-$4_{(Gal\mathrm{NAc})}$ linkage could be confirmed by a typical high-field shift of the protons and carbons involved.

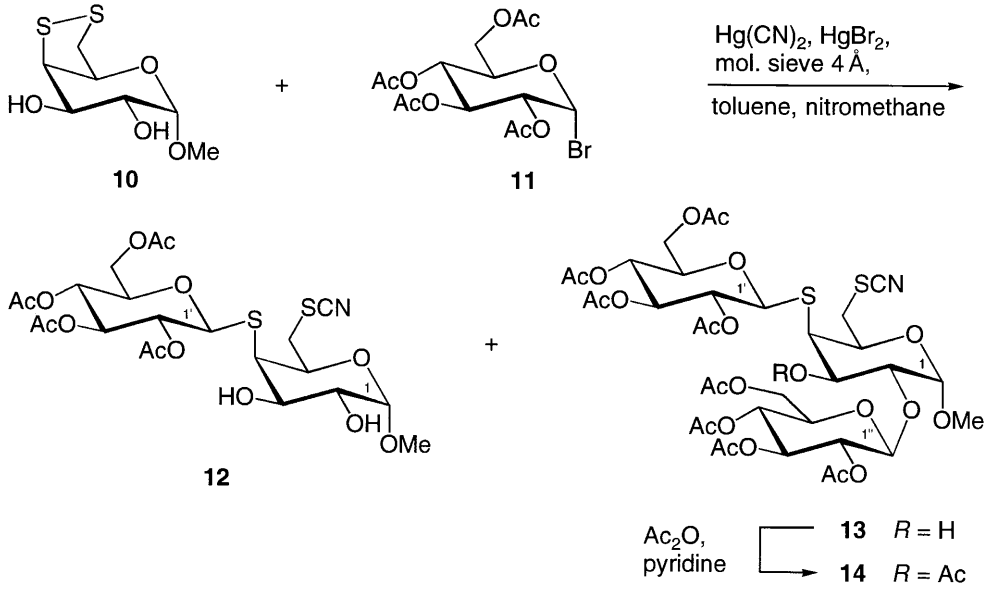
To further demonstrate the applicability of this method we chose methyl 2,3-di-O-acetyl-4,6-dideoxy-4,6-epidithio-α-*D*-galactopyranoside **8** (Scheme 3) as acceptor substrate. Following the glycosylation protocol described we could obtain the thiodisaccharide **10** in 68% yield. Again, the β-(1→4) linkage was formed exclusively as judged by extensive NMR analysis.

Applying the glycosylation procedure to the unprotected acceptor analogue **10** and utilizing the acetobromoglucose derivative **11** as donor yielded the β-(1→4) linked thiodisaccharide **12** in 19% yield (Scheme 4). In analogy to compound **4** the additional glycosylation of a hydroxyl group took place yielding the trisaccharide **13**. To facilitate the structural assignment, we transformed the trisaccharide **13** to its peracetylated derivative **14**.

Consequently, extensive NMR studies allowed complete assignment of the ^{1}H and ^{13}C signals and confirmed the C-$1''_{(Glc)}$-O-C-$2_{(Gal)}$ connectivity of **14**. In fact, the HMBC spectrum exhibited a cross peak between C-$1''_{(Glc)}$ and H-$2_{(Gal)}$, confirming the type of the (1→2) linkage. The stereochemistry was easily established by analysis of the coupling constants showing $J_{1'',2''} = 7.9$ Hz in the glucose residue, typical for a β-connectivity. All ^{1}H and ^{13}C signals of the relevant di- and trisaccharides (**6**, **7**, **9**, and **14**) were assigned by 2D experiments.



Scheme 3



Scheme 4

In conclusion, we were able to demonstrate a novel approach towards the synthesis of various thiodisaccharides. The applicability of well-known glycosylation procedures to sugars containing an intramolecular disulfide bridge opens a new synthetic route for generating thioglycosidic linkages. In addition, the thiocyanato functionality formed in the course of the reaction may be utilized for further transformations on the products formed.

Experimental

Starting materials were obtained from commercial suppliers and were generally used without further purification. Melting points were determined on a Kofler apparatus and are uncorrected. ^{1}H and

^{13}C NMR (*J* modulated) spectra were recorded in $CDCl_3$ unless otherwise given, using $CHCl_3$ as internal standard, on a Bruker DRX 400 NMR spectrometer at 400.13 and 100.61 MHz or on a Bruker DPX 250 NMR spectrometer at 250.13 and 62.90 MHz. Chemical shifts (δ) are given in ppm and coupling constants (*J*) in Hz. IR spectra were run on a Perkin Elmer 1600 FT-IR spectrometer. Optical rotations were measured on a Perkin Elmer 341 polarimeter in a 1 dm cell. TLC was performed on precoated Merck plates (silica gel 60 F_{254}). Detection was performed using UV light, I_2, and by dipping the plates into a solution of 2% $Ce(SO_4)_2 \cdot 4H_2O$ in 5.5% H_2SO_4 with subsequent heating. Flash chromatography was performed with Merck silica gel 60 (230–400 mesh). All reactions were carried out under argon. Elemental analysis agreed with the calculated values.

Allyl 2-acetamido-3-O-benzoyl-2-deoxy-4,6-di-O-methanesulfonyl-α-D-glucopyranoside (**2**; $C_{20}H_{27}NO_{11}S_2$)

To a solution of 5.06 g **1** (13.85 mmol) and a catalytic amount of 4-dimethylaminopyridine (*DMAP*) in 70 cm^3 pyridine at 0°C, 4.3 cm^3 methanesulfonyl chloride (55.55 mmol) were added dropwise. After 2 h the temperature was raised to room temperature, and the solution was stirred for further 14 h. The solvent was removed by coevaporation with toluene. The residue was treated with 100 cm^3 saturated aqueous $NaHCO_3$ solution and extracted three times with 100 cm^3 dichloromethane. The organic layer was separated, dried over $MgSO_4$, filtered, and the solvent was evaporated *in vacuo*. Flash chromatography (ethyl acetate/hexane, 2:1) of the residue afforded 6.03 g **2** (83%) as a colorless foam.

TLC (hexane/ethyl acetate, 1:2): $R_f = 0.25$; $[\alpha]_D^{20} = +63.27$ ($c = 1.10$, $CHCl_3$); IR: $\nu = 3294.8$, 3033.2, 2938.2, 1725.1, 1665.9, 1537.5 cm^{-1}; ^{1}H NMR (250 MHz): $\delta = 8.03$–7.40 (m, 5H, C_6H_5), 5.88 (m, 1H, H2′), 5.79 (d, 1H, $J_{NH,2} = 9.60$, NHAc); 5.58 (dd, 1H, $J_{2,3} = 10.97$, $J_{3,4} = 9.37$, H3), 5.30 (m, 2H, H3′), 4.94 (m, 2H, $J_{1,2} = 3.66$, H1, H4), 4.46 (m, 3H, $J_{6a,5} = 4.34$, $J_{6b,5} = 2.05$, $J_{6a,6b} = 11.19$, H2, $H6_a$, $H6_b$), 4.27 (m, 1H, H1′), 4.15 (ddd, 1H, H5), 4.04 (m, 1H, H1′), 3.08 (s, 3H, SO_2CH_3), 2.85 (s, 3H, SO_2CH_3), 1.82 (s, 3H, NHCOCH_3) ppm; ^{13}C NMR (62.9 MHz): $\delta = 169.85$, 166.64, 133.81, 132.70, 129.98, 128.79, 128.66, 118.88, 96.32, 74.32, 70.95, 69.12, 67.77, 66.85, 52.02, 38.80, 37.71, 22.98 ppm; MS (FI, 7 kV, 3 mA, 135°C): *m/z* (rel. intensity) = 522.5 (100), 486.5 (94).

Allyl 2-acetamido-3-O-benzoyl-2,4,6-trideoxy-4,6-dithiocyanato-α-D-galactopyranoside (**3**; $C_{20}H_{21}N_3O_4S_2$)

A suspension of 3.3 g dimesylate **2** (6.33 mmol) and 6.6 g KSCN (67.91 mmol) in 40 cm^3 *DMF* was stirred at 120°C for 72 h. The solvent was removed under vacuum, and the residue was purified by flash chromatography. The product **3** was obtained as a colorless foam (1.34 g, 47%).

TLC (ethyl acetate/hexane, 4:1): $R_f = 0.77$; $[\alpha]_D^{20} = +33.78$ (c = 1.19, $CHCl_3$); IR: $\nu = 3306.3$, 2941.5, 2158.7, 1724.6, 1666.4, 1537.7 cm^{-1}; ^{1}H NMR (400 MHz) $\delta = 8.08$–7.45 (m, 5H, C_6H_5), 5.89 (m, 1H, H2′), 5.77 (d, 1H, $J_{NH,2} = 9.35$, NHAc); 5.56 (dd, 1H, $J_{2,3} = 11.32$, $J_{3,4} = 3.94$, H3), 5.33 (m, 2 H, H3′), 4.97 (d, 1H, $J_{1,2} = 3.94$, H1), 4.71 (ddd, 1H, H2), 4.60 (ddd, 1H, $J_{4.5} = 1.48$, $J_{5,6b} = 3.94$, $J_{5,6a} = 8.86$, H5), 4.33 (m, 1H, H1′), 4.25 (dd, 1H, H4), 4.09 (m, 1H, H1′), 3.28 (ddd, 2H, $J_{6a,6b} = 13.78$, $H6_a$, $H6_b$), 1.89 (s, 3H, NHCOCH_3) ppm; ^{13}C NMR (100 MHz): $\delta = 170.01$, 166.31, 134.01, 132.32, 130.20, 128.66, 128.21, 119.56, 110.92, 110.57, 96.65, 69.69, 69.30, 68.05, 55.58, 48.06, 35.72, 23.16 ppm; MS (FI, 7 kV, 3 mA, 140°C): *m/z* (rel. intensity) 448.3 (18), 395.2 (100).

Allyl 2-acetamido-2,4,6-trideoxy-4,6-epidithio-α-D-galactopyranoside (**4**; $C_{11}H_{17}NO_4S_2$)

Dithiocyanate **3** (0.557 g, 1.24 mmol) was dissolved in 16 cm^3 methanol. After addition of 9.0 cm^3 0.1 *M* sodium methoxide in methanol, the solution was refluxed for 10 min and was further stirred for

1 h at room temperature. The reaction mixture was neutralized with Dowex 50 W (H^+), filtered, and evaporated *in vacuo* to dryness. Column chromatography gave 0.118 g **4** (31%) as yellow crystals.

TLC (ethyl acetate/hexane, 4:1): $R_f = 0.32$; m.p.: 195°C (decomposition); $[\alpha]_D^{20} = +202.58$ (c = 1.24, CH_3OH); IR: $\nu = 3294.3$, 1648.2, 1549.4 cm^{-1}; ^1H NMR (250 MHz, D_2O/CD_3OD): $\delta = 5.94$ (m, 1H, H2′), 5.26 (m, 2H, H3′), 4.88 (d, 1H, $J_{1,2} = 3.34$, H1), 4.85 (m, 1H, H5), 4.45 (dd, 1H, $J_{2,3} = 10.96$, $J_{3,4} = 4.79$, H3), 4.35 (dd, 1H, H2), 4.22 (m, 1H, H1′), 4.10 (dd, 1H, $J_{4.5} = 2.74$, H4), 4.02 (m, 1H, H1′), 3.43 (dd, 1H, $J_{6a,5} = 4.57$, $J_{6a,6b} = 11.88$, $H6_a$), 3.24 (dd, 1H, $J_{6b,5} = 1.37$, $H6_b$), 1.99 (s, 3H, $NHCOCH_3$) ppm; ^{13}C NMR (62.9 MHz, D_2O/CD_3OD): $\delta = 135.37$, 117.73, 99.08, 75.82, 69.70, 66.80, 66.76, 51.57, 44.45, 22.61 ppm; MS (FI, 7 kV, 3 mA, 120°C): *m/z* (rel. intensity) = 291.1 (100), 267.2 (18).

Allyl S-(2,3,4,6-tetra-O-acetyl-β-D-galactopyranosyl)-(1→4)-2-acetamido-4-thio-6-thiocyanato-2,4,6-trideoxy-α-D-galactopyranoside (**6**; $C_{26}H_{36}N_2O_{13}S_2$) and *Allyl O-(2,3,4,6-tetra-O-acetyl-β-D-galactopyranosyl)-(1→3)-(S-(2,3,4,6-tetra-O-acetyl-β-D-galactopyranosyl)-(1→4))-2-acetamido-4-thio-6-thiocyanato-2,4,6-trideoxy-α-D-galactopyranoside* (**7**; $C_{40}H_{54}N_2O_{22}S_2$)

A mixture of 122 mg **4** (0.42 mmol), 210 mg $Hg(CN)_2$ (0.84 mmol), 30 mg $HgBr_2$ (0.084 mmol), and 4.0 g molecular sieves (4 Å) in 12 cm^3 1:1 toluenenitromethane was stirred at 60°C. After 1 h, a solution of 424 mg tetra-O-acetyl-α-*D*-galactopyranosyl bromide **5** (1.03 mmol) in 6 cm^3 nitromethane was added dropwise over a period of 2 h. The mixture was stirred at 60°C for further 18 h. TLC (toluene/acetone, 2:1) indicated complete disappearance of **4**. The molecular sieve was filtered off. The solution was diluted with dichloromethane and washed three times with saturated aqueous NH_4Cl solution. The organic layer was separated, dried ($MgSO_4$), and concentrated. Purification by column chromatography (toluene/acetone, 3:1→ 1:1) gave 124 mg **6** (45%) and 72 mg **7** (17%) as colorless crystals.

6: TLC (ethyl acetate): $R_f = 0.35$; m.p.: 56–57°C; $[\alpha]_D^{20} = +67.73$ ($c = 0.75$, CH_2Cl_2); IR: $\nu = 3369.9$, 2929.6, 2155.5, 1750.8 cm^{-1}; ^1H NMR (400 MHz): $\delta = 5.84$ (m, 2H, H2″, NHAc), 5.40 (dd, 1H, $J_{4',5'} = 0.62$, H4′), 5.30 (m, 2H, H3″), 5.14 (t, 1H, $J_{2',3'} = 9.97$, H2′), 5.00 (dd, 1H, $J_{3',4'} = 3.33$, H3′), 4.805 (d, 1H, $J_{1',2'} = 9.96$, H1′), 4.795 (d, 1H, $J_{1,2} = 3.95$, H1), 4.26 (m, 3H, H2, H5, H1″), 4.07 (m, 3H, H3, $H6'_b$, $H6'_a$), 4.00 (m, 1H, H1″), 3.88 (m, 1H, H5′), 3.59 (d, 1H, $J_{OH,3} = 7.68$, OH), 3.41 (dd, 1H, $J_{3,4} = 3.73$, $J_{4,5} = 1.66$, H4), 3.35 (dd, 1H, $J_{5,6a} = 8.51$, $J_{6a,6b} = 13.91$, $H6_a$), 3.17 (dd, 1H, $J_{5,6b} = 4.35$, $H6_b$), 2.10 (s, 6H, $COCH_3$), 2.00 (s, 6H, $COCH_3$), 1.91 (s, 3H, $COCH_3$) ppm; ^{13}C NMR (100 MHz): $\delta = 172.56$, 170.35, 170.16, 170.14, 169.90, 132.70 (C2″), 119.04 (C3″), 111.98 (-SCN), 96.38 (C1), 85.03 (C1′), 74.55 (C5′), 71.57 (C3′), 71.54 (C3), 69.05 (C5), 68.65 (C1″), 67.68 (C2′), 67.29 (C4′), 61.62 (C6′), 52.61 (C4), 51.43 (C2), 36.29 (C6), 23.22, 20.77, 20.68, 20.64, 20.50 ppm; MALDI MS (16 kV): *m/z* = 687.3 (M+K, 100%).

7: TLC (ethyl acetate): $R_f = 0.50$; m.p.: 100–102°C; $[\alpha]_D^{20} = +53.44$ ($c = 0.90$, CH_2Cl_2); IR: $\nu = 2934.4$, 2155.3, 1751.2 cm^{-1}; ^1H NMR (400 MHz): $\delta = 5.90$ (m, 1H, H2‴), 5.51 (d, 1H, $J_{NH,2} = 9.7$, NHAc), 5.42 (dd, 1H, $J_{4',5'} = 0.75$, H4′), 5.41 (dd, 1H, $J_{4'',5''} = 1.1$, H4″), 5.29 (m, 2H, $H3'''_a$, $H3'''_e$), 5.14 (dd, 1H, $J_{2',3'} = 9.8$, H2′), 5.11 (dd, 1H, $J_{2'',3''} = 10.6$, H2″), 5.00 (d, 1H, $J_{1',2'} = 10.6$, H1′), 5.00 (dd, 1H, $J_{3',4'} = 3.3$, H3′), 4.98 dd, 1H, $J_{3'',4''} = 3.7$, H3″), 4.76 (d, 1H, $J_{1,2} = 3.9$, H1), 4.64 (d, 1H, $J_{1'',2''} = 7.9$, H1″), 4.60 (dd, 1H, $J_{2,3} = 10.6$, H2), 4.27 (dd, 1H, $J_{6''a,6''b} = 11.4$, $H6''_a$), 4.27 (ddd, 1H, $J_{5,6a} = 8.3$, $J_{5,6b} = 4.4$, H5), 4.24 (m, 1H, H1‴), 4.17 (dd, 1H, $J_{6'a,6'b} = 11.0$, $H6'_b$), 4.09 (dd, 1H, $H6'_a$), 4.03 (dd, 1H, $H6''_b$), 4.00 (m, 1H, H1‴), 3.95 (ddd, 1H, $J_{5',6'b} = 6.5$, $J_{5',6'a} = 7.0$, H5′), 3.91 (ddd, 1H, $J_{5'',6''b} = 5.9$, $J_{5'',6''a} = 6.9$, H5″), 3.90 (dd, 1H, $J_{3,4} = 3.6$, H3), 3.58 (dd, 1H, $J_{4,5} = 1.8$, H4), 3.28 (dd, 1H, $J_{6a,6b} = 14.2$, $H6_a$), 3.17 (dd, 1H, $H6_b$), 2.21 (s, 3H, $COCH_3$), 2.14 (s, 3H, $COCH_3$), 2.14 (s, 3H, $COCH_3$), 2.03 (s, 3H, $COCH_3$), 2.02 (s, 3H, $COCH_3$), 2.01 (s, 3H, $COCH_3$), 1.97 (s, 3H, $COCH_3$), 1.96 (s, 3H, $COCH_3$), 1.95 (s, 3H, $COCH_3$) ppm; ^{13}C NMR (100 MHz): $\delta = 171.04$, 170.28, 170.14, 170.10, 170.06, 170.05, 169.06, 168.81, 132.83 (C2‴), 119.24 (C3‴), 112.01 (-SCN), 102.59 (C1″), 97.04 (C1), 84.01 (C1′), 78.62 (C3), 74.20 (C5′), 72.25 (C3′), 71.52 (C5″), 70.48 (C3″), 68.85 (C5), 68.80 (C1‴), 68.54 (C2″), 67.13

(C2′), 66.99 (C4′,C4″), 61.40 (C6′), 60.99 (C6″), 50.86 (C4), 48.40 (C2), 36.16 (C6), 23.50, 20.69, 20.68, 20.65, 20.58, 20.55, 20.50, 20.49, 20.46 ppm; MS (FI, 7 kV, 3 mA, 230°C) *m/z* (rel. intensity) = 979.7 (75), 590.4 (100), 331.2 (80).

Methyl S-(2,3,4,6-tetra-O-acetyl-β-D-galactopyranosyl)-(1→4)-2,3-di-O-acetyl-4,6-dideoxy-4-thio-6-thiocyanato-α-D-galactopyranoside (**10**; $C_{26}H_{35}NO_{15}S_2$)

Compound **8** (60 mg, 0.19 mmol), 48 mg $Hg(CN)_2$ (0.19 mmol), 7 mg $HgBr_2$ (0.019 mmol) and 2.0 g molecular sieves (4 Å) in 6 cm^3 1:1 toluene/nitromethane were stirred at 60°C for 1 h. Then, 95 mg tetra-O-acetyl-α-*D*-galactopyranosyl bromide **5** (0.23 mmol) in 2 cm^3 nitromethane were added dropwise. After stirring for 20 h at 60°C the mixture was filtered (Celite) and concentrated. Purification by column chromatography (toluene/acetone, 6:1) gave 71 mg **9** (56%) as colorless crystals and 12 mg recovered starting material **8** (20%).

TLC (toluene/acetone, 3:1): $R_f = 0.51$; m.p.: 70–71°C; $[\alpha]_D^{20} = +97.70$ ($c = 1.00$, CH_2Cl_2); IR: $\nu = 2917.9$, 2154.0, 1743.5 cm^{-1}; ^{1}H NMR (400 MHz): $\delta = 5.38$ (dd, 1H, $J_{4',5'} = 0.98$, H4′), 5.32 (dd, 1H, $J_{3,4} = 4.43$, H3), 5.12 (t, 1H, $J_{2',3'} = 9.85$, H2′), 5.03 (dd, 1H, $J_{2,3} = 10.83$, H2), 4.96 (dd, 1H, $J_{3',4'} = 3.44$, H3′), 4.90 (d, 1H, $J_{1,2} = 3.93$, H1), 4.37 (ddd, 1H, $J_{5,6b} = 3.93$, $J_{5,6a} = 8.86$, H5), 4.33 (d, 1H, $J_{1',2'} = 10.34$, H1′), 4.12 (dd, 1H, $J_{6'b,6'a} = 11.32$, $H6'_b$), 4.05 (dd, 1H, $H6'_a$), 3.80 (dt, 1H, $J_{5',6'b} = 5.41$, $J_{5',6'a} = 6.89$, H5′), 3.64 (dd, 1H, $J_{4,5} = 1.47$, H4), 3.45 (s, 3H, OCH_3), 3.37 (dd, 1H, $J_{6a,6b} = 14.28$, $H6_a$), 3.16 (dd, 1H, $H6_b$), 2.15 (s, 3H, $COCH_3$), 2.07 (s, 3H, $COCH_3$), 2.075 (s, 3H, $COCH_3$), 2.085 (s, 3H, $COCH_3$), 2.095 (s, 3H, $COCH_3$), 1.96 (s, 3H, $COCH_3$) ppm; ^{13}C NMR (100 MHz): $\delta = 170.40$, 170.19, 170.12, 170.09, 169.98, 169.53, 111.90 (-SCN), 97.29 (C1′), 85.26 (C1), 74.90, 71.47, 70.02, 68.57, 67.95, 67.69, 67.20, 61.79 (C6′), 55.80 (OCH_3), 50.44 (C4), 36.26 (C6), 20.83, 20.78, 20.73, 20.69, 20.64, 20.51 ppm; MS (FI, 7 kV, 3 mA, 200°C): *m/z* (rel intensity) 666.2 (70), 630.4 (100).

Methyl S-(2,3,4,6-tetra-O-acetyl-β-D-glucopyranosyl)-(1→4)-4,6-dideoxy-4-thio-6-thiocyanato-α-D-galactopyranoside (**12**; $C_{22}H_{31}NO_{13}S_2$) *and Methyl O-(2,3,4,6-tetra-O-acetyl-β-D-glucopyranosyl)-(1→2)-(S-(2,3,4,6-tetra-O-acetyl-β-D-glucopyranosyl)-(1→4))-4,6-dideoxy-4-thio-6-thiocyanato-α-D-galactopyranoside* (**13**; $C_{36}H_{49}NO_{22}S_2$)

Compound **10** (80 mg, 0.36 mmol), 93 mg $Hg(CN)_2$ (0.37 mmol), 13 mg $HgBr_2$ (0.036 mmol) and 2.8 g molecular sieves (4 Å) in 7 cm^3 1:1 toluene-nitromethane were stirred at 60°C for 1 h. Then, 161 mg tetra-O-acetyl-α-D-glucopyranosyl bromide **11** (0.39 mmol) in 1.5 cm^3 nitromethane were added dropwise over a period of 40 min. The mixture was stirred at 60°C for further 2 h. Then, 91 mg $Hg(CN)_2$ (0.36 mmol), 13 mg $HgBr_2$ (0.036 mmol), and 80 mg **11** (0.19 mmol) in 1 cm^3 nitromethane were added, and stirring was continued for 14 h. The mixture was filtered (Celite) and concentrated. Purification by column chromatography (toluene/acetone, 3:1→2:1) gave 40 mg **12** (19%) and 33 mg **13** (10%) as colorless crystals.

12: TLC (toluene/acetone, 3:1): $R_f = 0.06$; m.p.: 81–82°C; $[\alpha]_D^{20} = +62.50$ (c = 1.30, CH_2Cl_2); IR: $\nu = 3468.4$, 2941.2, 2155.7, 1753.8 cm^{-1}; ^{1}H NMR (400 MHz) $\delta = 5.18$ (t, 1H, $J_{3',4'} = 9.36$, H3′), 5.03 (t, 1H, $J_{4',5'} = 9.84$, H4′), 4.94 (t, 1H, $J_{2',3'} = 9.35$, H2′), 4.77 (d, 1H, $J_{1',2'} = 10.34$, H1′), 4.75 (d, 1H, $J_{1,2} = 3.44$, H1), 4.28 (ddd, 1H, $J_{5,6b} = 3.94$, $J_{5,6a} = 8.37$, H5), 4.22 (dd, 1H, $J_{6'b,6'a} = 12.31$, $H6'_b$), 4.13 (dd, 1H, $H6'_a$), 4.01 (m, 1H, H2 or H3), 3.68 (ddd, 1H, $J_{5',6'b} = 1.96$, $J_{5',6'a} = 4.92$, H5′), 3.62 (m, 1H, H2 or H3), 3.48 (s, 3H, OCH_3), 3.46 (dd, 1H, $J_{3,4} = 3.94$, $J_{4,5} = 1.48$, H4), 3.30 (dd, 1H, $J_{6a,6b} = 13.78$, $H6_a$), 3.17 (dd, 1H, $H6_b$), 2.10 (s, 3H, $COCH_3$), 2.05 (s, 3H, $COCH_3$), 2.00 (s, 3H, $COCH_3$), 1.98 (s, 3H, $COCH_3$) ppm; ^{13}C NMR (100 MHz), $\delta = 170.54$, 170.05, 169.49, 169.34, 112.03 (-SCN), 99.44 (C1′), 83.63 (C1), 76.02, 73.56, 70.71, 70.68, 70.64, 68.95, 68.12, 61.77 (C6′), 55.98 (OCH_3), 51.78 (C4), 36.18 (C6), 20.76, 20.68, 20.54 ppm; MS (FI, 7 kV, 3 mA, 190°C) *m/z* (rel intensity) = 581.2 (80), 331.1 (84), 224.0 (100).

13: TLC (toluene/acetone, 3:1): $R_f = 0.19$; IR: $\nu = 2916.9$, 2156.8, 1752.9, 1654.4 cm^{-1}; ^1H NMR (400 MHz): $\delta = 5.30$–4.70 (m, 9H), 4.31 (m, 1H), 4.25–3.96 (m, 5H), 3.73–3.62 (m, 3H), 3.43 (s, 3H, OCH_3), 3.42 (m, 1H), 3.30 (dd, 1H, $J_{5,6a} = 8.86$, $J_{6a,6b} = 14.28$, $H6_a$), 3.13 (dd, 1H, $J_{5,6b} = 3.94$, $H6_b$), 2.62 (d, 1H, $J_{OH,3} = 4.43$, OH), 2.10 (s, 3H, $COCH_3$), 2.09 (s, 3H, $COCH_3$), 2.07 (s, 3H, $COCH_3$), 2.06 (s, 3H, $COCH_3$), 2.02 (s, 3H, $COCH_3$), 2.01 (s, 3H, $COCH_3$), 2.00 (s, 3H, $COCH_3$), 1.98 (s, 3H, $COCH_3$) ppm.

Methyl O-(2,3,4,6-tetra-O-acetyl-β-D-glucopyranosyl)-(1→2)-(S-(2,3,4,6-tetra-O-acetyl-β-D-glucopyranosyl)-(1→4))-3-O-acetyl-4,6-dideoxy-4-thio-6-thiocyanato-α-D-galactopyranoside (**14**; $C_{38}H_{51}NO_{23}S_2$)

Compound **13** (23 mg, 25.2 μmol) was dissolved in 1.0 cm^3 pyridine and 0.2 cm^3 acetic anhydride. A catalytic amount of *DMAP* was added, and the solution was stirred for 4 h at room temperature. Coevaporation of the solvent with toluene *in vacuo* and purification by column chromatography gave 18 mg **14** (75%) as colorless crystals.

TLC (toluene/acetone, 3:1): $R_f = 0.37$; m.p.: 84–86°C; $[\alpha]_D^{20} = +38.30$ ($c = 0.60$, CH_2Cl_2); IR: $\nu = 2941.9$, 2156.0, 1755.1 cm^{-1}; ^1H NMR (400 MHz): $\delta = 5.21$ (dd, 1H, $J_{3,4} = 4.5$, H3), 5.17 (t, 1H, $J_{3'',4''} = 9.4$, H3″), 5.16 (t, 1H, $J_{3',4'} = 9.5$, H3′), 5.05 (dd, 1H, $J_{4'',5''} = 10.1$, H4″), 5.00 (dd, 1H, $J_{4',5'} = 10.0$, H4′), 4.97 (dd, 1H, $J_{2'',3''} = 9.5$, H2″), 4.90 (dd, 1H, $J_{2',3'} = 9.3$, H2′), 4.82 (d, 1H, $J_{1,2} = 3.8$, H1), 4.62 (d, 1H, $J_{1'',2''} = 7.9$, H1″), 4.36 (ddd, 1H, $J_{5,6a} = 9.0$, $J_{5,6b} = 3.7$, H5), 4.34 (d, 1H, $J_{1',2'} = 10.0$, H1′), 4.22 (dd, 1H, $J_{6'b,6'a} = 12.5$, $H6'_b$), 4.19 (dd, 1H, $J_{6''a,6''b} = 12.5$, $H6''_a$), 4.18 (dd, 1H, $H6''_b$), 4.08 (dd, 1H, $H6'_a$), 3.71 (dd, 1H, $J_{2,3} = 10.4$, H2), 3.67 (ddd, 1H, $J_{5'',6''a} = 5.4$, $J_{5'',6''b} = 2.6$, H5″), 3.59 (dd, 1H, $J_{4,5} = 1.8$, H4), 3.57 (ddd, 1H, $J_{5',6'a} = 5.6$, $J_{5',6'b} = 2.2$, H5′), 3.45 (s, 3H, OCH_3), 3.33 (dd, 1H, $J_{6a,6b} = 14.3$, $H6_a$), 3.13 (dd, 1H, $H6_b$), 2.12 (s, 3H, $COCH_3$), 2.11 (s, 3H, $COCH_3$), 2.09 (s, 3H, $COCH_3$), 2.08 (s, 3H, $COCH_3$), 2.015 (s, 3H, $COCH_3$), 2.01 (s, 3H, $COCH_3$), 2.00 (s, 3H, $COCH_3$), 1.98 (s, 3H, $COCH_3$), 1.98 (s, 3H, $COCH_3$) ppm; ^{13}C NMR (100 MHz): $\delta = 168.74$, 169.20, 169.30, 169.95, 170.09, 111.92 (-SCN), 101.40 (C1″), 99.41 (C1), 84.45 (C1′), 76.21 (C5′), 75.51 (C2), 73.42 (C3′), 72.72 (C3″), 72.02 (C5″), 71.51 (C2″), 70.92 (C2′), 70.78 (C3), 68.27 (C4″), 68.08 (C4′), 67.79 (C5), 61.84 (C6″), 61.79 (C6′), 55.91 (OCH_3), 50.86 (C4), 36.27 (C6), 20.85, 20.78, 20.74, 20.71, 20.54 ppm; MS (FI, 7 kV, 3 mA, 220°C): *m/z* (rel. intensity) = 953.6 (100), 894.7 (8), 331.2 (35), 218.1 (30).

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