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Synthesis of (1 → 2)-S-Linked Saccharides and S-Linked Glycoconjugates via a Palladium-G3-XantPhos Precatalyst Catalysis

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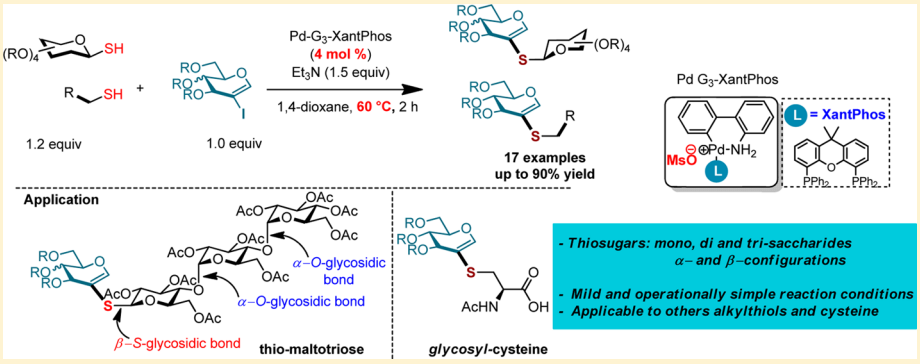
Supporting Information



ABSTRACT: Buchwald–Hartwig–Migita cross-coupling of 1-thiosugars with 2-iodoglycals has been accomplished under mild and operationally simple reaction conditions through the use of Pd-G3 XantPhos palladacycle precatalyst. This new methodology has been successfully applied to a variety of α- or β-mono-, di-, and polythiosugar derivatives to synthesize efficiently a series of (1 → 2)-S-linked thiosaccharides and S-linked glycoconjugates, which are difficult to synthesize by classical methods.

INTRODUCTION

The recent development of glycobiology has increased the need for the synthesis of structurally defined carbohydrates and their mimetics as probes for biological investigations. Among them, thiosaccharides[1] are important carbohydrate congeners of *O*-glycosides, which are valuable substrates for studies in glycobiology because of their high stability toward hydrolytic or enzymatic cleavage.[2] This class of saccharides is used as useful tools in various biological studies such as enzyme inhibition,[3] ligands of lectin[4] (antibacterial agents) and galactin[5] (antitumor drugs) as well as ligands for the purification of proteins by affinity chromatography.[6] Consequently, considerable efforts have been made toward the synthesis and biological evaluations of such glycomimetics. Surprisingly, a thorough literature search revealed only a few methods for the synthesis of thiosaccharides, which are devoted only toward α-α-(1 → 1′),[7] α- or β-(1 → 2),[8] α-(1 → 4),[9] or α-(1 → 6)[9,10]-S-linked saccharides. These derivatives are usually prepared by (i) Lewis acid-catalyzed reaction between a thiosugar acceptor and a suitable glycosyl donor or by (ii) S_N2-like displacement of a leaving group of a glycosyl acceptor with a sugar thiolate. In addition, the Ferrier reaction has been applied to the synthesis of 1,4- and 1,6-S-linked disaccharides by using glycal derivatives and glycosyl thiols as the coupling partners.[9] Herein we focus on the preparation of more challenging (1 → 2) thiosaccharides and present a new approach to build a range of α- and β-(1 → 2)-S-linked di- and polysaccharides. Our strategy relies on the use of 2-iodoglycals and various α- and β-glycosyl thiols in the Pd-catalyzed Buchwald–Hartwig–Migita cross-coupling under mild reaction conditions (Scheme 1).

2-Haloglycals are widely used as important synthons in carbohydrate chemistry and have become a new entry to the

Scheme 1. Iodoglycals as Coupling Partners in Some Pd-Catalyzed Cross-Couplings

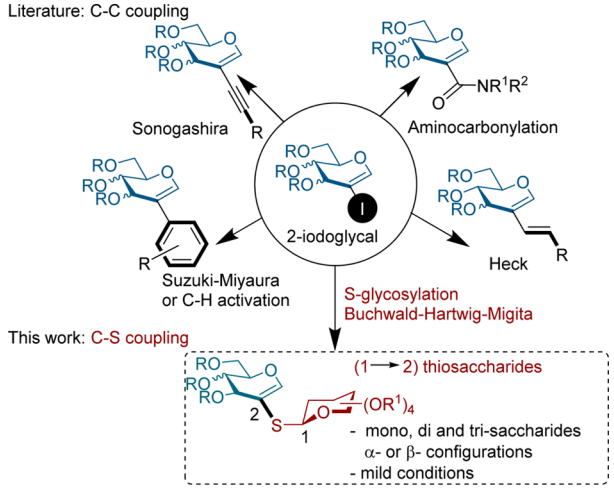


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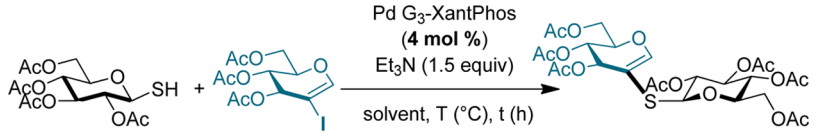
Table 1. Survey of Reaction Conditions for the Coupling of *tetra*-O-Acetylated 1-thio-β-D-Glucopyranose 1a with 2-Iodoglucal 2a[a]



1a (1.2 equiv) **2a** (1 equiv) **3a**

entry	Temp (°C)	*t* (h)	solvent	conv (%)[b]	yield (%)[c]
1	25	2	THF	36	-
2	60	2	THF	100	44
3	60	2	1,4-dioxane	100	58
4	60	1.5	1,4-dioxane	100	86[d]
5	40	1.5	1,4-dioxane	18	–

[a]Conditions: **1a** (1.2 equiv), **2a** (1.0 equiv), Pd-G3- XantPhos (4 mol %), Et_3N (1.5 equiv), solvent (0.1 M). [b]Conversion rate was determined by ^1H NMR in the crude reaction mixture based on the chemical shift (ppm) of the proton signal H^1 for iodoglucal **2a** (δ = 6.77) and **3a** (δ = 6.96). [c]Yield of isolated **3a**. [d]The reaction is incomplete when it was performed at 60 °C for 1 h.

synthesis of 2-functionalized carbohydrate derivatives (Scheme 1). Starting from 2-iodoglycals as coupling partners, some reactions such as Suzuki–Miyaura,[11] Heck,[12] Sonogashira,[13] C–H activation,[14] and the recently reported aminocarbonylation[15] have been applied successfully to synthesize 2-C-branched glycosides. However, to our knowledge, there is no report concerning the coupling of 2-iodoglycals with heteroatom nucleophiles (e.g., S-, O- and N-nucleophiles) which has stimulated us to study the coupling of 2-iodoglycals with various α- and β-glycosyl thiols.

RESULTS AND DISCUSSION

In our efforts to functionalize sugars under transition-metal catalysis,[16] our group reported recently an efficient protocol for the palladium-catalyzed coupling of aryl and alkenyl halides with various α- and β-glycosyl thiols.[17] The C–S bond-forming reaction was achieved rapidly (5 min) at room temperature by using the G3-XantPhos palladacycle precatalyst[18] (1 mol %), in the presence of Et_3N (1.0 equiv) in THF. We envisioned in the present study whether 2-iodoglycals could be utilized as building blocks in the synthesis of a range of α- and β-(1 → 2)-S-linked di- and polysaccharides (Scheme 1). To establish the appropriate conditions for this coupling, *tetra*-O-acetylated 1-thio-β-D-glucopyranose **1a** and *tri*-O-acetylated iodoglucal **2a** were initially selected as the coupling model substrates (Table 1). Thus, reaction of **1a** with **2a** in the presence of Pd-G3-XantPhos (4 mol %) and Et_3N (1.5 equiv) in THF for 2 h at room temperature led to only 36% conversion of **2a**. This result clearly indicated that the reactivity of iodoglucal **2a** is less reactive and is far to be compared to a classical iodoalkene as previously reported by us.[17] To enhance the reactivity of the iodoglucal **2a**, we conducted the model reaction at 60 °C instead room temperature under otherwise identical conditions. To our delight, under these conditions full conversion of **2a** was achieved, and the desired product **3a** was isolated in a 44% yield (entry 2). Encouraged by this preliminary result, we further investigated other reaction parameters and found that the efficiency of the reaction was significantly affected by the nature of the solvent. Thus, conducting the coupling of **1a** and **2a** in 1,4-dioxane led to the total conversion of the starting material, however the yield of **3a** has never exceeded 58% yield (entry 3). This result can be explained by the degradation of the product under the reaction conditions. This hypothesis was confirmed by shortening the reaction time. The coupling of **1a** and **2a** within 90 min (instead 2 h) furnished **3a** in 86% isolated yield as a single β-anomer ($J_{1,2}$ = 10.2 Hz) (entry 4). It should be noted that the palladium catalyst is necessary to achieve this transformation since no reaction occurs when the coupling is conducted in the absence of Pd-G3-precatalyst.

Motivated by these results, we next explored the scope of the coupling reaction of structurally diverse α- and β-mono-, di-, and polythiosugar derivatives with iodoglycals **2a–b** (Table 2). Gratifyingly, all of the couplings proceeded in good yields and with a retention of the anomeric configuration. The nature of the glycal partner does not interfere with the outcome of the reaction since both *tri*-O-acetylated iodoglucal **2a** and *tri*-O-acetylated iodogalactal **2b** were successfully coupled. Regarding the thio-nucleophilic partners, this coupling reaction tolerates a large variety of thiosugars **1a–g**: O-acetylated 1-thio-β-D-glycopyranose **1a**, O-acetylated *N*-Ac-1-thio-β-D-glucopyranose **1b**, O-acetylated 1-thio-β-D-galactopyranose **1c**, and O-benzoylated 1-thio-β-D-glucopyranose **1d** were coupled with both iodoglycals **2a–b** to give β-(1 → 2)-S-linked disaccharides **3a–h** without any loss of reactivity. Importantly, this procedure is not limited to only β-glycosyl thiols, but it also worked successfully with 1-thioglucose **1e**, which had an anomeric α-configuration. In this case, the corresponding α-(1 → 2)-S-linked disaccharide product **3i** was obtained with slightly lower yield of 58%.

Moreover, the reaction is not limited to monosaccharides, but can be applied to more complex di- and trisaccharide derivatives. Thus, 1-thio-β-D-cellobiose **1f** and 1-thio-β-D-maltotriose **1g** were efficiently reacted with iodoglycals **2a–b** to give the corresponding β-(1 → 2)-S-linked polysaccharides **3j–m** in yields ranging from 69% to 78%. Importantly, the stereochemistry of the β-1,4′-O-glycosidic bond in the trisaccharides **3j,k** and the α-1,4′ in β-tetrasaccharide **3l,m** remained intact.

Having demonstrated the good reactivity of thiosugars under our best conditions, we then examined in a further set of experiments whether this coupling reaction could be extended to other alkylthiols (Table 3). Thus, we were pleased to find 2-(trimethylsilyl)ethane-1-thiol **4a** could be coupled efficiently to O-acetylated iodoglucal **2a** furnishing **5a** in a 69% yield. More interestingly, coupling of unprotected iodoglucal **2c** with **4a** under our best conditions furnished exclusively **5b** without any side product resulting from O-coupling under Pd-catalysis.[19] Finally, cysteine derivatives **4b,c** could be also used as nucleophilic coupling partners in this procedure with **2a** to furnish glycoconjugates **5c,d** in moderate yields, despite the fact that the reaction conditions had never been optimized.

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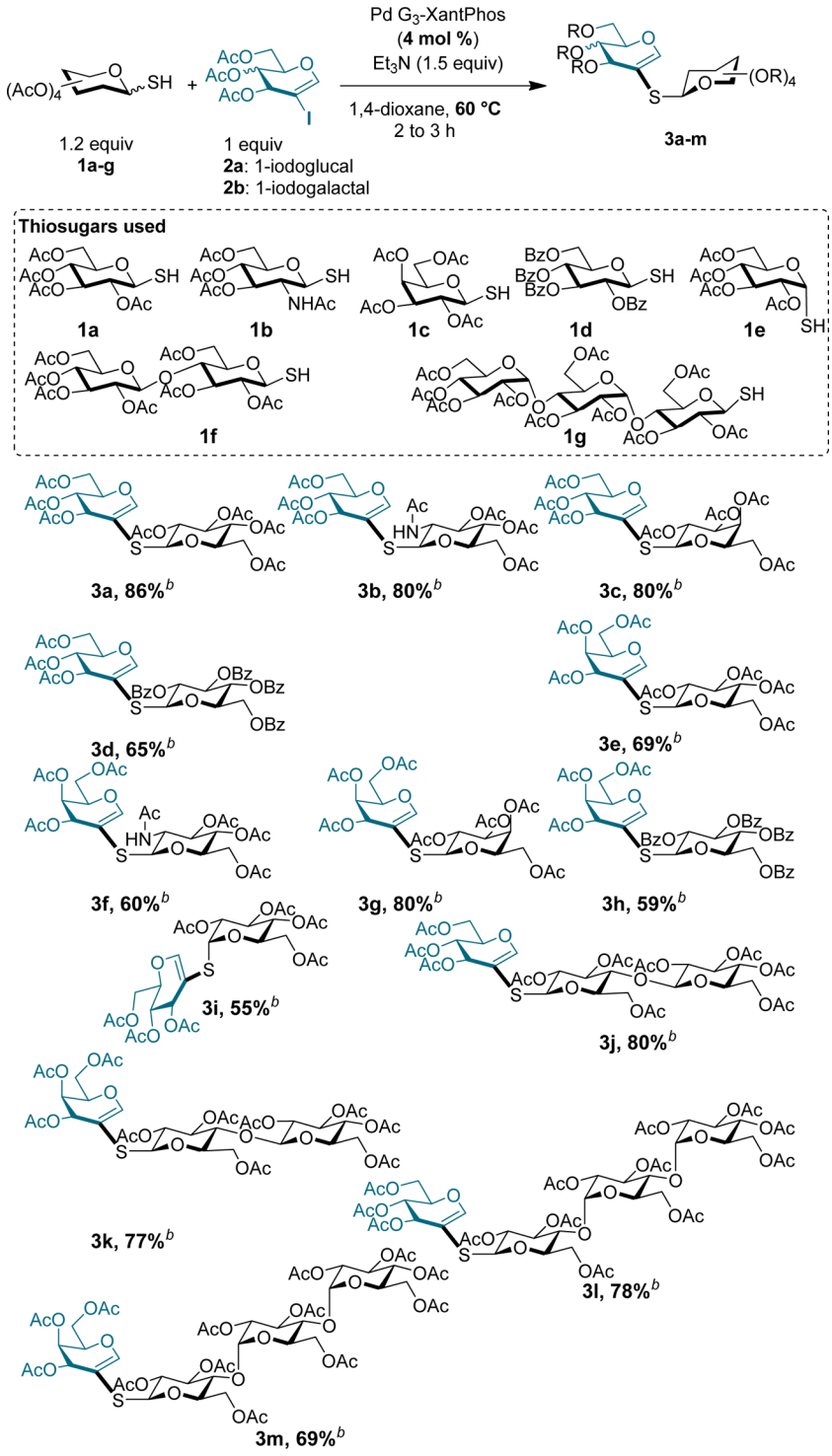
Table 2. Scope of Thiosugars 1a−g for the Pd-Catalyzed Coupling with Iodoglycals 2a−b[a]



[a]Conditions: Reactions of **1** (1.2 equiv) with **2** (1.0 equiv) were performed in a sealed tube by using Pd-G3-XantPhos (4 mol %) and Et_3N (1.5 equiv) in 1,4-dioxane (0.1 M) at 60 °C. [b]Yield of isolated **3**.

Finally, in order to produce true glycomimetics and show that their purification and characterization maybe be achieved easily, deprotection of representative di- and tetra-saccharides was performed (Scheme 2). Thus, acetyl protecting groups of **3e** and **3m** could be removed through the Zemplen reaction[20] by using a catalytic amount of potassium carbonate as the base in methanol. Under these conditions (1 → 2)-S-linked saccharide glycomimetics **6a,b** were isolated in quantitative yields.

On the basis of the above experimental results and related reports, a plausible mechanism for this reaction was proposed in Figure 1. The reaction was initiated by the activation of the precatalyst Pd G3 through the action of Et_3N as a base to form the key intermediate palladium(II) complex **I**. Then, the reductive elimination occurs to form the kinetically active 12-electron LPd(0) species and produces the carbazole side-product in a catalytic amount.[18] The LPd(0) species undergoes an

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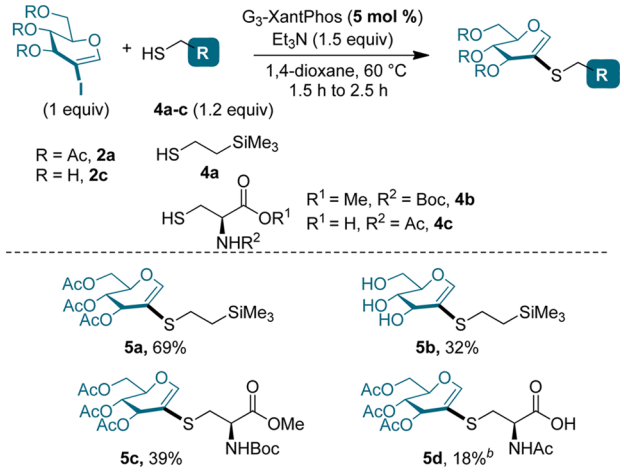
Table 3. Scope of the Coupling of Other Alkylthiols 4a−c with Iodoglucals[a]



[a]Conditions: Reactions of **2** (1.0 equiv) with **4** (1.2 equiv) were performed in a sealed tube by using Pd-G3-XantPhos (5 mol %) and Et_3N (1.5 equiv) in 1,4-dioxane (0.1 M) at 60 °C (for time, see SI). [b]10 mol % of Pd-G3-XantPhos were used.

oxidative addition in the Buchwald−Hartwig catalytic cycle[21] with iodoglucal **2a** through its carbon−iodine bond to give (**II**). Then, a base-assisted halogen exchange by the thiosugar **1a** led to the Pd(II) complex (**III**), and a reductive elimination produces the final (1 → 2)-S-linked disaccharide product **3a** and regenerates the catalyst.

CONCLUSION

In summary, we have successfully developed an efficient method to synthesize various (1 → 2)-S-linked saccharides and S-linked glycoconjugates via a palladium-catalyzed coupling of α- or β-mono-, di-, and polythiosugar derivatives with 2-iodoglycals. We expect this simple and general methodology to be of broad utility for the synthesis and development of new medicinal agents.

EXPERIMENTAL SECTION

General Information. All reactions were conducted under argon atmosphere. Solvents: cyclohexane, dichloromethane, 1,4-dioxane, ethyl acetate, and methanol for extraction and chromatography were technical grade.

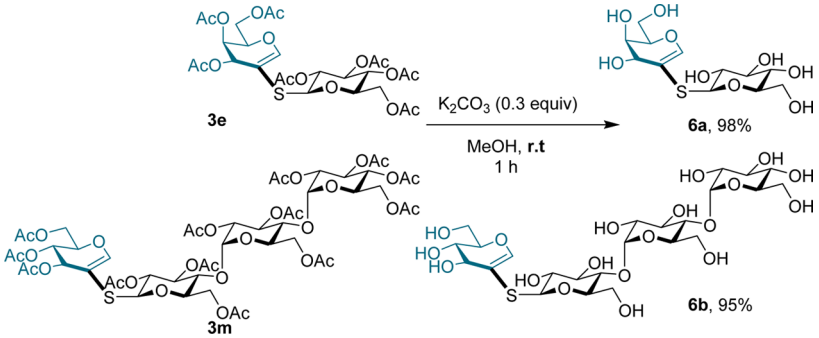
Instrumentation. These compounds were all identified by usual physical methods, e.g., ^{1}H NMR, ^{13}C NMR (J-MOD), IR, and HR-MS (ESI). ^{1}H and ^{13}C NMR spectra were measured in $CDCl_3$ or CD_3OD, with a Bruker Avance-300. ^{1}H chemical shifts are reported in ppm from an internal standard TMS or of residual chloroform (7.26 ppm) or methanol (3.32 ppm). The following abbreviations are used: m (multiplet), s (singlet), d (doublet), t (triplet), dd (doublet of doublets), dt (doublet of triplets), ddd (doublet of doublet of doublets). ^{13}C chemical shift are reported in ppm from central peak of deuteriochloroform (77.16 ppm) or deuteriomethanol (49.00 ppm). IR spectra were measured on a Bruker Vector 22 spectrophotometer and are reported in wave numbers (cm^{-1}). The angels of rotation were measured on a PerkinElmer Polarimeter 341 and denoted as specific rotations: $[\alpha]_D$. High-resolution mass spectra (HR-MS) were recorded on a Bruker MicroTOF spectrometer, using ESI with methanol as the carrier solvent. Nominal and exact m/z values are reported in Daltons. Melting points were recorded on a Büchi B-450 apparatus and are uncorrected. Analytical TLC was performed on Merck precoated silica gel 60F plates. Merck silica gel 60 (0.015−0.040 mm) was used for column chromatography. Flash chromatography was performed on silica gel 60 (0.040−0.063 mm) at medium pressure (200 mbar). Compounds were visualized under a UVP Mineralight UVGL-58 lamp (254 nm) and with vanillin/Δ or phosphomolybdic acid/Δ. Unless otherwise noted, other materials are obtained from commercial suppliers and were used without further purification.

Typical Procedure A for Pd-Catalyzed Coupling of Thiosugars (1a−g) with 2-Iodoglycals (2a−b). A flame-dried resealable Schlenk tube (5 mL) was charged with XantPhos Pd-G3 (4.0 mol %), thioglycoside (0.11−0.27 mmol, 1.2 equiv), and 2-iodoglycal (0.09−0.23 mmol, 1.0 equiv). The Schlenk tube was capped with a rubber septum, evacuated, and backfilled with argon, then 1,4-dioxane (1.1 mL) and Et_3N (0.13−0.34 mmol, 1.5 equiv) were added. The Schlenk tube was sealed, and the mixture was stirred at 60 °C for 2−3 h. After evaporation of the 1,4-dioxane, the residue was then purified by flash chromatography over silica gel. This first purification was followed by HPLC preparative for products **3a**, **3b**, **3e−g**, and **3i−l**.

Typical Procedure B for Pd-Catalyzed Coupling of Alkythiols (4a−c) with 2-Iodoglycals (2a and 2c). A flame-dried resealable Schlenk tube (5 mL) was charged with XantPhos Pd-G3 (5.0−10.0 mol %), alkylthiols (0.30−0.44 mmol, 1.2 equiv), and 2-iodoglycal (0.25−0.37 mmol, 1.0 equiv) in 1,4-dioxane (1.0 mL). The mixture was then stirred at room temperature for 1 min, after that Et_3N (0.38−0.55 mmol, 1.5 equiv) was added to the mixture. The Schlenk tube was capped with a rubber septum, evacuated, and backfilled with argon, then the mixture was stirred at 60 °C for 1.5 to 2.5 h. After evaporation of the 1,4-dioxane, water was added to the crude product, and the mixture was extracted three times with ethyl acetate. The organic layers were combined, dried over $MgSO_4$, followed by evaporation of solvent under vacuum at 30 °C. The residue was then purified by silica gel column chromatography to afford the desired product.

Typical Procedure C for the Synthesis of Unprotected S-Linked Saccharides (6a−b). A mixture of S-linked saccharides (**3e** and **3m**) (0.10 M, 1.0 equiv) and K_2CO_3 (0.04 M, 0.3 equiv) in methanol (0.2−0.6 mL) was placed in a small balloon, and the mixture was stirred under argon at room temperature for 30 min to 1.0 h. The crude mixture was then filtered through Celite and washed with 10 mL of methanol and filtered for only 1 min. The filtrate was concentrated under reduced pressure at 25 °C for 1−2 h.

Scheme 2. Deprotection of Glycals 3e and 3m



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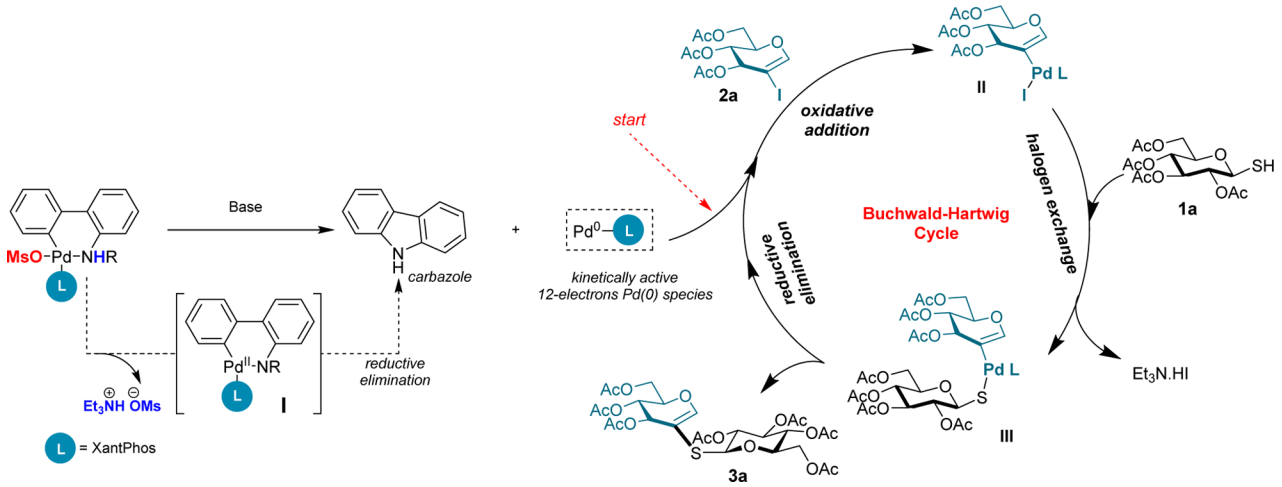

Figure 1. Proposed mechanism.

*(2R,3R,4S,5R,6S)-2-(Acetoxymethyl)-6-(((2R,3R,4S)-3,4-diacetoxy-2-(acetoxymethyl)-3,4-dihydro-2H-pyran-5-yl)thio)tetrahydro-2H-pyran-3,4,5-triyl Triacetate (**3a**).* Following the general procedure A of coupling, a flame-dried resealable Schlenk tube (5 mL) was charged with Xantphos Pd-G_3 (9 mg, 0.01 mmol), β-thioglucose **1a** (100 mg, 0.27 mmol), and 2-iodoglucal **2a** (91 mg, 0.23 mmol). The Schlenk tube was capped with a rubber septum, evacuated, and backfilled with argon, and then 1,4-dioxane (1.1 mL) and Et_3N (28 μL, 0.343 mmol) were added. The Schlenk tube was sealed, and the mixture was stirred at 60 °C for 1.5 h. After evaporation of the 1,4-dioxane, the residue was purified by flash chromatography over silica gel (ethyl acetate:cyclohexane: 3:7 gradient concentration to 8:2) followed by HPLC preparative (conditions: H_2O/MeOH gradient from 50% to 100% in 15 min) to afford the desired product **3a** (62 mg, 0.10 mmol, 86%) as a yellow to brown solid; mp (66−67 °C); TLC: R_f = 0.25 (ethyl acetate:cyclohexane: 4:6); IR (thin film, neat) ν_{max}/cm^{-1}: 2985, 1756, 1737, 1620, 1433, 1366, 1246, 1208, 1173, 1093, 1032, 980, 956, 913, 821, 731, 648; $[\alpha]_D^{19}$: −18 (*c* 0.5, CH_2Cl_2); ^1H NMR (300 MHz, $CDCl_3$) δ (ppm): 6.96 (s, 1H), 5.52 (d, *J* = 5.1 Hz, 1H), 5.23−5.14 (m, 2H), 5.06 (t, *J* = 9.7 Hz, 1H), 4.95 (t, *J* = 9.6 Hz, 1H), 4.46 (dd, *J* = 11.1, 5.1 Hz, 2H), 4.40−4.35 (m, 1H), 4.25 (dd, *J* = 12.4, 4.8 Hz, 1H), 4.14 (dd, *J* = 12.2, 2.5 Hz, 2H), 3.71 (ddd, *J* = 7.2, 4.6, 2.2 Hz, 1H), 2.10 (s, 3H), 2.09 (s, 9H), 2.04 (s, 3H), 2.02 (s, 3H), 1.99 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm): 170.8 (C═O), 170.5 (C═O), 170.3 (C═O), 169.9 (C═O), 169.6 (C═O), 169.5 (C═O), 169.5 (C═O), 154.3 (CH), 100.8 (C_q), 86.1 (CH), 76.0 (CH), 74.4 (CH), 74.1 (CH), 70.0 (CH), 69.8 (CH), 68.4 (CH), 67.5 (CH), 62.2 (CH_2), 61.0 (CH_2), 21.0 (CH_3), 20.9 (CH_3), 20.8 ($2CH_3$), 20.7 ($3CH_3$); HR-MS(ESI): for $C_{26}H_{34}NaO_{16}S$ $(M + Na)^+$: *m*/*z* calcd 657.1465, found 657.1458.

*(2R,3S,4R,5R,6S)-5-Acetamido-2-(acetoxymethyl)-6-(((2R,3R,4S)-3,4-diacetoxy-2-(acetoxymethyl)-3,4-dihydro-2H-pyran-5-yl)thio)-tetrahydro-2H-pyran-3,4-diyl Diacetate (**3b**).* Following the general procedure A of coupling, a flame-dried resealable Schlenk tube (5 mL) was charged with Xantphos Pd-G_3 (9 mg, 0.01 mmol), β-thioglucosamine **1b** (100 mg, 0.27 mmol), and 2-iodoglucal **2a** (91 mg, 0.23 mmol). The Schlenk tube was capped with a rubber septum, evacuated, and backfilled with argon, and then 1,4-dioxane (1.1 mL) and Et_3N (28 μL, 0.343 mmol) were added. The Schlenk tube was sealed, and the mixture was stirred at 60 °C for 2 h. After evaporation of the 1,4-dioxane, the residue was purified by flash chromatography over silica gel (ethyl acetate:cyclohexane: 3:7 gradient concentration to 8:2) followed by HPLC preparative (conditions: H_2O/MeOH gradient from 40% to 80% in 15 min) to afford the desired product **3b** (116 mg, 0.31 mmol, 80%) as a beige solid; mp (202−203 °C); TLC: R_f = 0.21 (ethyl acetate:cyclohexane: 7:3); IR (thin film, neat) ν_{max}/cm^{-1}: 3349, 3309, 2924, 1770, 1724, 1666, 1618, 1541, 1297, 1242, 1218, 1195, 1174, 1108, 1078, 1046, 1022, 1013, 913, 727, 647; $[\alpha]_D^{19}$: −2.6 (*c* 1.0, CH_2Cl_2); ^1H NMR (300 MHz, $CDCl_3$) δ (ppm): 6.91 (s, 1H), 5.96 (d, *J* = 8.5 Hz, 1H), 5.48 (d, *J* = 5.1 Hz, 1H), 5.33 (t, *J* = 9.8 Hz, 1H), 5.19−5.14 (m, 1H), 4.99 (t, *J* = 9.7 Hz, 1H), 4.69 (d, *J* = 10.3 Hz, 1H), 4.40 (dd, *J* = 15.6, 10.0 Hz, 2H), 4.13 (dd, *J* = 15.3, 6.6 Hz, 3H), 3.84−3.75 (m, 1H), 3.74−3.67 (m, 1H), 2.06 (s, 12H), 1.99 (s, 6H), 1.92 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm): 170.7 (2C═O), 170.6 (C═O), 170.5 (C═O), 170.4 (C═O), 169.5 (C═O), 169.5 (C═O), 154.1 (CH), 99.9 (C_q) 85.0 (CH), 75.8 (CH), 74.2 (CH), 73.4 (CH), 70.0 (CH), 68.6 (CH), 67.3 (CH), 62.3 (CH_2), 61.0 (CH_2), 53.5 (CH), 23.3 (CH_3), 21.0 (CH_3), 20.8 ($2CH_3$), 20.8 ($3CH_3$); HR-MS(ESI): for $C_{26}H_{35}NO_{15}S$ $(M + Na)^+$: *m*/*z* calcd 656.1625, found 656.1637.

*(2R,3S,4S,5R,6S)-2-(Acetoxymethyl)-6-(((2R,3R,4S)-3,4-diacetoxy-2-(acetoxymethyl)-3,4-dihydro-2H-pyran-5-yl)thio)tetrahydro-2H-pyran-3,4,5-triyl Triacetate (**3c**).* Following the general procedure A of coupling, a flame-dried resealable Schlenk tube (5 mL) was charged with Xantphos Pd-G_3 (9.0 mg, 0.01 mmol), thiogalactose **1c** (100 mg, 0.27 mmol), and 2-iodoglucal **2a** (91 mg, 0.23 mmol). The Schlenk tube was capped with a rubber septum, evacuated, and backfilled with argon, and then 1,4-dioxane (1.1 mL) and Et_3N (28 μL, 0.342 mmol) were added. The Schlenk tube was sealed, and the mixture was stirred at 60 °C for 2 h. After evaporation of the 1,4-dioxane, the residue was purified by flash chromatography over silica gel (ethyl acetate: cyclohexane: 3:7 gradient concentration to 8:2), followed by HPLC preparative (conditions: H_2O/MeOH gradient from 50% to 100% in 15 min) to afford the desired product **3c** (115 mg, 0.18 mmol, 80%) as a white solid (contaminated by small amount of thiosugar dimer); mp (97−98 °C); TLC: R_f = 0.26 (ethyl acetate: cyclohexane: 4:6); IR (thin film, neat) ν_{max}/cm^{-1}: 1736, 1621, 1432, 1367, 1206, 1173, 1084, 1057, 1044, 1016, 952, 916, 899, 729, 648; $[\alpha]_D^{15}$: −22 (*c* 0.5, CH_2Cl_2); ^1H NMR (300 MHz, $CDCl_3$) δ (ppm): 6.95 (s, 1H), 5.53 (d, *J* = 5.2 Hz, 1H), 5.39 (d, *J* = 3.2 Hz, 1H), 5.22−5.17 (m, 1H), 5.13 (d, *J* = 9.6 Hz, 1H), 5.02−4.95 (m, 1H), 4.48−4.43 (m, 1H), 4.42−4.32 (m, 2H), 4.15 (s, 1H), 4.08 (dd, *J* = 11.4, 6.6 Hz, 2H), 3.92 (dd, *J* = 11.3, 5.3 Hz, 1H), 2.12 (s, 3H), 2.07 (s, 3H), 2.06 (s, 6H), 2.02 (s, 6H), 1.95 (d, *J* = 2.1 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm): 170.4 (C═O), 170.2 (C═O), 170.1 (C═O), 169.8 (C═O), 169.6 (C═O), 169.5 (C═O), 169.4 (C═O), 154.0 (CH), 101.2 (C_q), 86.9 (CH), 74.5 (CH), 74.3 (CH), 72.0 (CH), 70.0 (CH), 67.4 (CH), 67.3 (CH), 67.1 (CH), 61.4 (CH_2), 60.9 (CH_2), 21.0 (CH_3), 20.9 (CH_3), 20.8 (CH_3), 20.7 ($2CH_3$), 20.7 ($2CH_3$); HR-MS(ESI): for $C_{26}H_{34}NaO_{16}S$ $(M + Na)^+$: *m*/*z* calcd 657.1465, found 657.1457.

*(2R,3R,4S,5R,6S)-2-((Benzoyloxy)methyl)-6-(((2R,3R,4S)-3,4-diacetoxy-2-(acetoxymethyl)-3,4-dihydro-2H-pyran-5-yl)thio)tetrahydro-2H-pyran-3,4,5-triyl Tribenzoate (**3d**).* Following the general procedure A of coupling, a flame-dried resealable Schlenk tube (5 mL) was charged with Xantphos Pd-G_3 (5.0 mg, 0.01 mmol), (2*R*,3*R*,4*S*,5*R*,6*S*)-2-((benzoyloxy)methyl)-6-mercaptotetrahydro-2*H*-pyran-3,4,5-triyl tribenzoate **1d** (100 mg, 0.16 mmol), and 2-iodoglucal **2a** (45 mg, 0.14 mmol). The Schlenk tube was capped with a rubber septum, evacuated, and backfilled with argon, and then 1,4-dioxane (0.65 mL) and Et_3N (17 μL, 0.20 mmol) were added. The Schlenk tube was sealed, and the

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mixture was stirred at 60 °C for 2 h. After evaporation of the 1,4-dioxane, the residue was purified by flash chromatography over silica gel (ethyl acetate:cyclohexane: 3:7 gradient concentration to 8:2) to afford the desired product **3d** (78 mg, 0.09 mmol, 65%) as brown solid; mp (101−102 °C); TLC: R_f = 0.62 (ethyl acetate: cyclohexane: 4:6); IR (thin film, neat) ν_{max}/cm^{-1}: 3067, 2954, 2850, 1722, 1621, 1602, 1584, 1492, 1452, 1368, 1316, 1285, 1266, 1246, 1217, 1177, 1110, 1088, 1069, 1026, 978, 910, 853, 803, 735, 709, 687, 648; $[\alpha]_D^{20}$: −56 (*c* 0.25, CH_2Cl_2); ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm): 8.32 (d, *J* = 7.8 Hz, 2H), 8.18 (d, *J* = 7.7 Hz, 4H), 8.06 (d, *J* = 7.9 Hz, 2H), 7.85−7.73 (m, 3H), 7.64 (dt, *J* = 16.5, 7.9 Hz, 7H), 7.53 (t, *J* = 7.6 Hz, 2H), 7.26 (s, 1H), 6.17 (t, *J* = 9.5 Hz, 1H), 5.92 (t, *J* = 9.8 Hz, 1H), 5.86−5.66 (m, 2H), 5.49−5.39 (m, 1H), 5.10 (d, *J* = 10.1 Hz, 1H), 5.00−4.87 (m, 1H), 4.71 (ddd, *J* = 23.0, 12.1, 5.9 Hz, 2H), 4.58 (dd, *J* = 8.4, 6.4 Hz, 1H), 4.51−4.42 (m, 1H), 4.35 (dd, *J* = 11.7, 1.8 Hz, 1H), 2.49−2.08 (m, 9H); ^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm): 170.5 (C═O), 169.8 (C═O), 169.6 (C═O), 166.2 (C═O), 165.9 (C═O), 165.3 (C═O), 165.3 (C═O), 154.1 (CH) 133.6 (CH), 133.5 (CH), 133.4 (CH), 133.2 (CH), 129.9 (4CH), 129.8 (3CH), 129.2 (C_q), 128.8 (3C_q), 128.5 (6CH), 128.4 (3CH), 101.2 (C_q), 86.6 (CH), 76.4 (CH), 74.2 (CH), 74.2 (CH), 70.8 (CH), 69.8 (CH), 69.5 (CH), 67.5 (CH), 63.3 (CH_2), 61.0 (CH_2), 20.8 (2CH_3), 20.8 (CH_3); HR-MS(ESI): for $C_{46}H_{42}NaO_{16}S$ (M + Na)$^+$: *m*/*z* calcd 905.2091, found 905.2083.

*(2R,3R,4S,5R,6S)-2-(Acetoxymethyl)-6-(((2R,3S,4S)-3,4-diacetoxy-2-(acetoxymethyl)-3,4-dihydro-2H-pyran-5-yl)thio)tetrahydro-2H-pyran-3,4,5-triyl Triacetate (**3e**).* Following the general procedure A of coupling, a flame-dried resealable Schlenk tube (5 mL) was charged with Xantphos Pd-G_3 (9.0 mg, 0.01 mmol), *β*-thioglucose **1a** (100 mg, 0.27 mmol), and 2-iodogalactal **2b** (91 mg, 0.23 mmol). The Schlenk tube was capped with a rubber septum, evacuated, and backfilled with argon, and then 1,4-dioxane (1.1 mL) and Et_3N (28 *μ*L, 0.34 mmol) were added. The Schlenk tube was sealed, and the mixture was stirred at 60 °C for 3 h. After evaporation of the 1,4-dioxane, the residue was purified by flash chromatography over silica gel (ethyl acetate:cyclohexane: 3:7 gradient concentration to 8:2) followed by HPLC preparative (conditions: H_2O/MeOH gradient from 60% to 100% in 15 min) to afford the desired product **3e** (98 mg, 0.15 mmol, 69%) as a white solid; mp (64−65 °C); TLC: R_f = 0.2 (ethyl acetate cyclohexane: 4:6); IR (thin film, neat) ν_{max}/cm^{-1}: 1738, 1620, 1433, 1367, 1227, 1210, 1183, 1121, 1092, 1060, 1032, 979, 914, 817, 728, 648; $[\alpha]_D^{15}$: −36 (*c* 0.5, CH_2Cl_2); ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm): 6.90 (s, 1H), 5.63 (d, *J* = 4.4 Hz, 1H), 5.43 (dd, *J* = 4.5, 2.1 Hz, 1H), 5.18 (dd, *J* = 15.2, 5.9 Hz, 1H), 5.08−4.91 (m, 2H), 4.40 (t, *J* = 7.3 Hz, 2H), 4.33−4.20 (m, 2H), 4.19−4.07 (m, 2H), 3.65 (ddd, *J* = 9.8, 5.0, 2.3 Hz, 1H), 2.09 (s, 3H), 2.07 (d, *J* = 1.2 Hz, 6H), 2.05 (s, 3H), 2.01 (s, 3H), 2.00 (s, 3H), 1.98 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm): 170.7 (C═O), 170.5 (C═O), 170.3 (C═O), 169.9 (C═O), 169.8 (C═O), 169.5 (2C═O), 153.4 (CH), 101.0 (C_q), 86.3 (CH), 76.0 (CH), 74.0 (CH), 73.5 (CH), 69.7 (CH), 68.4 (CH), 66.7 (CH), 64.3 (CH), 62.1 (CH_2), 61.4 (CH_2), 20.8 (CH_3), 20.7 (3CH_3), 20.7 (3CH_3); HR-MS(ESI): for $C_{26}H_{34}NaO_{16}S$ (M + Na)$^+$: *m*/*z* calcd 657,1465, found 657.1464.

*(2R,3S,4R,5R,6S)-5-Acetamido-2-(acetoxymethyl)-6-(((2R,3S,4S)-3,4-diacetoxy-2-(acetoxymethyl)-3,4-dihydro-2H-pyran-5-yl)thio)-tetrahydro-2H-pyran-3,4-diyl Diacetate (**3f**).* Following the general procedure A of coupling, a flame-dried resealable Schlenk tube (5 mL) was charged with Xantphos Pd-G_3 (9.0 mg, 0.01 mmol), *β*-thioglucosamine **1d** (100 mg, 0.3 mmol), and 2-iodogalactal **2b** (91 mg, 0.23 mmol). The Schlenk tube was capped with a rubber septum, evacuated, and backfilled with argon, and then 1,4-dioxane (1.1 mL) and Et_3N (28 *μ*L, 0.434 mmol) were added. The Schlenk tube was sealed, and the mixture was stirred at 60 °C for 2 h. After evaporation of the 1,4-dioxane, the residue was purified by flash chromatography over silica gel (ethyl acetate:cyclohexane: 3:7 gradient concentration to 6:4) followed by HPLC preparative (conditions: H_2O/MeOH gradient from 40% to 80% in 15 min) to afford the desired product **3f** (88 mg, 1.07 mmol, 60%) as a white solid; mp (240−241 °C); TLC: R_f = 0.1 (ethyl acetate:cyclohexane: 4:6); IR (thin film, neat) ν_{max}/cm^{-1}: 1747, 1735, 1664, 1624, 1533, 1432, 1368, 1301, 1257, 1229, 1214, 1185, 1124, 1045, 1035, 964, 942, 915, 817, 733, 649; $[\alpha]_D^{20}$: −36 (*c* 0.5, MeOH); ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm): 6.90 (s, 1H), 5.74 (d, *J* = 8.7 Hz, 1H), 5.65 (d, *J* = 4.4 Hz, 1H), 5.43 (dd, *J* = 4.4, 2.0 Hz, 1H), 5.33 (t, *J* = 9.8 Hz, 1H), 5.03 (t, *J* = 9.7 Hz, 1H), 4.68 (d, *J* = 10.3 Hz, 1H), 4.48−4.42 (m, 1H), 4.31 (dd, *J* = 11.6, 7.7 Hz, 1H), 4.24−4.09 (m, 3H), 3.82 (dd, *J* = 19.0, 10.1 Hz, 1H), 3.72−3.65 (m, 1H), 2.13−2.07 (m, 9H), 2.06 (s, 3H), 2.01 (d, *J* = 2.1 Hz, 6H), 1.93 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm): 170.9 (C═O), 170.8 (C═O), 170.6 (C═O), 170.4 (C═O), 170.4 (C═O), 170.0 (C═O), 169.6 (C═O), 153.3 (CH), 100.5 (C_q), 85.6 (CH), 75.9 (CH), 73.5 (CH), 73.5 (CH), 68.6 (CH), 66.6 (CH), 64.4 (CH), 62.3 (CH_2), 61.6 (CH_2), 53.6 (CH), 23.4 (CH_3), 20.8 (3CH_3), 20.8 (2CH_3), 20.7 (CH_3); HR-MS(ESI): for $C_{26}H_{35}NO_{15}S$ (M + Na)$^+$: *m*/*z* calcd 656.1609, found 656.1625.

*(2R,3S,4S,5R,6S)-2-(Acetoxymethyl)-6-(((2R,3S,4S)-3,4-diacetoxy-2-(acetoxymethyl)-3,4-dihydro-2H-pyran-5-yl)thio)tetrahydro-2H-pyran-3,4,5-triyl Triacetate (**3g**).* Following the general procedure A of coupling, a flame-dried resealable Schlenk tube (5 mL) was charged with Xantphos Pd-G_3 (9.0 mg, 0.01 mmol), *β*-thiogalactose **1c** (100 mg, 0.27 mmol), and 2-iodogalactal **2b** (91 mg, 0.23 mmol). The Schlenk tube was capped with a rubber septum, evacuated, and backfilled with argon, and then 1,4-dioxane (1.1 mL) and Et_3N (28.0 *μ*L, 0.342 mmol) were added. The Schlenk tube was sealed, and the mixture was stirred at 60 °C for 2 h. After evaporation of the 1,4-dioxane, the residue was purified by flash chromatography over silica gel (ethyl acetate:cyclohexane: 3:7 gradient concentration to 8:2) followed by HPLC preparative (conditions: H_2O/MeOH gradient from 40% to 80% in 15 min) to afford the desired product **3g** (131 mg, 0.21 mmol, 80%) as a white solid; mp (70−71 °C); TLC: R_f = 0.04 (ethyl acetate:cyclohexane: 4:6); IR (thin film, neat) ν_{max}/cm^{-1}: 1737, 1621, 1433, 1367, 1211, 1184, 1084, 1057, 1047, 1016, 950, 917, 815, 732, 649; $[\alpha]_D^{20}$: −16 (*c* 0.5, CH_2Cl_2); ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm): 6.92 (s, 1H), 5.66 (d, *J* = 4.2 Hz, 1H), 5.44 (dd, *J* = 4.4, 1.7 Hz, 1H), 5.38 (d, *J* = 3.1 Hz, 1H), 5.17 (t, *J* = 10.0 Hz, 1H), 4.99 (dd, *J* = 10.0, 3.2 Hz, 1H), 4.40 (t, *J* = 7.1 Hz, 2H), 4.29 (dd, *J* = 11.5, 7.7 Hz, 1H), 4.23−4.13 (m, 2H), 4.04 (dd, *J* = 11.2, 6.3 Hz, 1H), 3.87 (t, *J* = 6.6 Hz, 1H), 2.14 (s, 3H), 2.10 (s, 3H), 2.06 (d, *J* = 3.3 Hz, 6H), 2.03 (s, 6H), 1.96 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm): 170.5 (C═O), 170.3 (C═O), 170.2 (C═O), 169.9 (3C═O), 169.6 (C═O), 153.3 (CH), 101.3 (C_q), 87.1 (CH), 74.6 (CH), 73.5 (CH), 72.1 (CH), 67.3 (CH), 67.1 (CH), 66.9 (CH), 64.3 (CH), 61.4 (2CH_2), 20.8 (2CH_3), 20.8 (2CH_3), 20.7 (3CH_3); HR-MS(ESI): for $C_{26}H_{34}NaO_{16}S$ (M + Na)$^+$: *m*/*z* calcd 657.1465, found 657.1466.

*(2R,3R,4S,5R,6S)-2-((Benzoyloxy)methyl)-6-(((2R,3S,4S)-3,4-diacetoxy-2-(acetoxymethyl)-3,4-dihydro-2H-pyran-5-yl)thio)tetrahydro-2H-pyran-3,4,5-triyl Tribenzoate (**3h**).* Following the general procedure A of coupling, a flame-dried resealable Schlenk tube (5 mL) was charged with Xantphos Pd-G_3 (5.0 mg, 0.01 mmol), (2*R*,3*R*,4*S*,5*R*,6*S*)-2-((benzoyloxy)methyl)-6-mercaptotetrahydro-2*H*-pyran-3,4,5-triyl tribenzoate **1d** (100 mg, 0.16 mmol), and 2-iodogalactal **2b** (54 mg, 0.14 mmol). The Schlenk tube was capped with a rubber septum, evacuated, and backfilled with argon, and then 1,4-dioxane (0.65 mL) and Et_3N (17 *μ*L, 0.204 mmol) were added. The Schlenk tube was sealed, and the mixture was stirred at 60 °C for 2 h. After evaporation of the 1,4-dioxane, the residue was purified by flash chromatography over silica gel (ethyl acetate:cyclohexane: 3:7 gradient concentration to 8:2) to afford the desired product **3h** (71 mg, 0.80 mmol, 59%) as a beige solid; mp (97−98 °C); TLC: R_f = 0.45 (ethyl acetate:cyclohexane: 4:6); IR (thin film, neat) ν_{max}/cm^{-1}: 1753, 1728, 1721, 1620, 1602, 1452, 1370, 1316, 1261, 1247, 1215, 1179, 1110, 1087, 1068, 1026, 976, 908, 853, 802, 731, 707, 686, 648, 623; $[\alpha]_D^{18}$: −2 (*c* 0.5, CH_2Cl_2); ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm): 8.07 (d, *J* = 7.4 Hz, 2H), 7.93 (d, *J* = 7.5 Hz, 4H), 7.83 (d, *J* = 7.5 Hz, 2H), 7.54 (dt, *J* = 11.5, 7.4 Hz, 3H), 7.47−7.35 (m, 7H), 7.30 (dd, *J* = 15.9, 8.1 Hz, 2H), 6.98 (s, 1H), 5.93 (t, *J* = 9.5 Hz, 1H), 5.69−5.64 (m, 1H), 5.53−5.41 (m, 2H), 4.78 (d, *J* = 10.0 Hz, 1H), 4.67 (dd, *J* = 12.0, 2.6 Hz, 1H), 4.49 (dd, *J* = 12.1, 6.0 Hz, 1H), 4.34−4.28 (m, 1H), 4.18 (dd, *J* = 11.0, 7.6 Hz, 2H), 4.07 (dd, *J* = 11.6, 5.7 Hz, 1H), 3.66 (s, 1H), 2.09 (s, 3H), 2.05 (s, 3H), 1.90 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm): 170.5 (C═O), 169.9 (C═O), 169.8 (C═O), 166.2 (C═O), 166.0 (C═O), 165.3 (2C═O), 153.7 (CH), 133.6 (CH), 133.6 (CH), 133.4 (CH), 133.3 (CH), 130.0 (2CH), 129.9 (4CH), 129.8 (3CH), 129.1 (C_q), 128.8 (3C_q), 128.5 (5CH), 128.4 (2CH), 101.1 (C_q), 86.8 (CH), 76.5 (CH), 74.1 (CH), 73.5 (CH), 70.8 (CH), 69.7 (CH), 66.7 (CH), 63.8 (CH), 63.4 (CH_2), 61.5 (CH_2), 20.8

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(CH_3), 20.6 (CH_3), 20.5 (CH_3); HR-MS(ESI): for $C_{46}H_{42}NaO_{16}S$ (M + Na)$^+$: m/z calcd 905.2091, found 905.2076.

*(2R,3R,4S,5R,6R)-2-(Acetoxymethyl)-6-(((2R,3R,4S)-3,4-diacetoxy-2-(acetoxymethyl)-3,4-dihydro-2H-pyran-5-yl)thio)tetrahydro-2H-pyran-3,4,5-triyl Triacetate (**3i**).* Following the general procedure A of coupling, a flame-dried resealable Schlenk tube (5 mL) was charged with Xantphos Pd-G_3 (9 mg, 0.01 mmol), α-thioglucose **1b** (100 mg, 0.27 mmol), and 2-iodoglucal **2a** (91 mg, 0.23 mmol). The Schlenk tube was capped with a rubber septum, evacuated, and backfilled with argon, and then 1,4-dioxane (1.1 mL) and Et_3N (28 μL, 0.343 mmol) were added. The Schlenk tube was sealed, and the mixture was stirred at 60 °C for 2 h. After evaporation of the 1,4-dioxane, the residue was purified by flash chromatography over silica gel (ethyl acetate:cyclohexane: 3:7 gradient concentration to 8:2), followed by HPLC preparative (conditions: H_2O/MeOH gradient from 50% to 100% in 15 min) to afford the desired product **3i** (28 mg, 0.04 mmol, 55%) as a white solid; mp (181−182 °C); TLC: R_f = 0.2 (ethyl acetate:cyclohexane: 1:1); IR (thin film, neat) ν_{max}/cm^{-1}: 2922, 1737, 1622, 1433, 1367, 1235, 1206, 1173, 1095, 1034, 978, 955, 913, 733, 647; $[\alpha]_D^{15}$: − 20 (c 0.5, CH_2Cl_2); ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm): 6.74 (s, 1H), 5.51−5.45 (m, 2H), 5.32−5.20 (m, 2H), 5.11−4.97 (m, 2H), 4.41−4.32 (m, 3H), 4.27−4.15 (m, 2H), 4.06 (d, J = 12.3 Hz, 1H), 2.08 (s, 9H), 2.06 (s, 6H), 2.03 (s, 3H), 2.00 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm): 170.7 (C═O), 170.6 (C═O), 170.2 (C═O), 170.1 (C═O), 169.7 (2C═O), 169.5 (C═O), 152.4 (CH), 102.1 (C_q) 83.0 (CH), 74.7 (CH), 70.4 (CH), 70.1 (CH), 68.8 (CH), 68.4 (CH), 67.5 (CH), 67.2 (CH), 62.2 (CH_2), 61.2 (CH_2), 20.8 ($4CH_3$), 20.75 ($3CH_3$); HR-MS(ESI): for $C_{26}H_{34}NaO_{16}S$ (M + Na)$^+$: m/z calcd 657.1465, found 657.1475.

*(2R,3R,4S,5R,6S)-2-(Acetoxymethyl)-6-(((2R,3R,4S,5R,6S)-4,5-diacetoxy-2-(acetoxymethyl)-6-(((2R,3R,4S)-3,4-diacetoxy-2-(acetoxymethyl)-3,4-dihydro-2H-pyran-5-yl)thio)tetrahydro-2H-pyran-3-yl)oxy)tetrahydro-2H-pyran-3,4,5-triyl Triacetate (**3j**).* Following the general procedure A of coupling, a flame-dried resealable Schlenk tube (5 mL) was charged with Xantphos Pd-G_3 (5.0 mg, 0.01 mmol), β-thiocellobiose **1f** (100 mg, 0.15 mmol), and 2-iodoglucal **2a** (50.5 mg, 0.13 mmol). The Schlenk tube was capped with a rubber septum, evacuated, and backfilled with argon, and then 1,4-dioxane (0.6 mL) and Et_3N (16 μL, 0.19 mmol) were added. The Schlenk tube was sealed, and the mixture was stirred at 60 °C for 2 h. After evaporation of the 1,4-dioxane, the residue was purified by flash chromatography over silica gel (ethyl acetate:cyclohexane: 3:7 gradient concentration to 8:2) followed by HPLC preparative (conditions: H_2O/MeOH gradient from 60% to 100% in 15 min) to afford the desired product **3j** (80 mg, 0.1 mmol, 80%) as a white solid; mp (170−171 °C); TLC: R_f = 0.18 (ethyl acetate:cyclohexane: 4:6); IR (thin film, neat) ν_{max}/cm^{-1}1735, 1621, 1432, 1366, 1260, 1230, 1208, 1170, 1093, 1034, 1016, 956, 916, 907, 802, 728, 648; $[\alpha]_D^{15}$: −16 (c 0.5, CH_2Cl_2); ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm): 6.85 (s, 1H), 5.61 (d, J = 4.3 Hz, 1H), 5.40 (dd, J = 4.4, 2.0 Hz, 1H), 5.15−4.98 (m, 3H), 4.85 (dt, J = 16.1, 8.9 Hz, 2H), 4.51−4.44 (m, 2H), 4.38−4.25 (m, 4H), 4.15−4.04 (m, 2H), 4.02−3.97 (m, 1H), 3.71 (d, J = 9.6 Hz, 1H), 3.65−3.60 (m, 1H), 3.55−3.49 (m, 1H), 2.09 (s, 3H), 2.07 (s, 3H), 2.04 (s, 6H), 2.03 (s, 3H), 1.99 (s, 3H), 1.98 (s, 3H), 1.97 (s, 6H), 1.94 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm): 170.5 (C═O), 170.4 (C═O), 170.3 (C═O), 170.2 (C═O), 169.8 (3C═O), 169.6 (C═O), 169.3 (C═O), 169.1 (C═O), 153.5 (CH), 101.1 (C_q), 101.0 (CH), 86.3 (CH), 76.9 (CH), 76.6 (CH), 73.7 (CH), 73.4 (CH), 72.9 (CH), 72.1 (CH), 71.6 (CH), 70.0 (CH), 67.8 (CH), 66.7 (CH), 64.3 (CH), 62.0 (CH_2), 61.6 (CH_2), 61.3 (CH_2), 20.8 ($2CH_3$), 20.7 ($3CH_3$), 20.6 ($5CH_3$); HR-MS(ESI): for $C_{38}H_{50}NaO_{24}S$ (M + Na)$^+$: m/z calcd 945.2310, found 945.2310.

*(2R,3R,4S,5R,6S)-2-(Acetoxymethyl)-6-(((2R,3R,4S,5R,6S)-4,5-diacetoxy-2-(acetoxymethyl)-6-(((2R,3S,4S)-3,4-diacetoxy-2-(acetoxymethyl)-3,4-dihydro-2H-pyran-5-yl)thio)tetrahydro-2H-pyran-3-yl)oxy)tetrahydro-2H-pyran-3,4,5-triyl Triacetate (**3k**).* Following the general procedure A of coupling, a flame-dried resealable Schlenk tube (5 mL) was charged with Xantphos Pd-G_3 (5.0 mg, 0.01 mmol), β-thiocellobiose **1f** (100 mg, 0.15 mmol), and 2-iodogalactal **2b** (51 mg, 0.13 mmol). The Schlenk tube was capped with a rubber septum, evacuated, and backfilled with argon, and then 1,4-dioxane (0.6 mL) and Et_3N (16.0 μL, 0.19 mmol) were added. The Schlenk tube was sealed, and the mixture was stirred at 60 °C for 3 h. After evaporation of the 1,4-dioxane, the residue was purified by flash chromatography over silica gel (ethyl acetate:cyclohexane: 3:7 gradient concentration to 8:2), followed by HPLC preparative (conditions: H_2O/MeOH gradient from 60% to 100% in 15 min) to afford the desired product **3k** (90 mg, 0.01 mmol, 77%) as a dark brown solid; mp (107−108 °C); TLC: R_f = 0.12 (ethyl acetate:cyclohexane: 4:6); IR (thin film, neat) ν_{max}/cm^{-1}: 1757, 1735, 1621, 1433, 1366, 1230, 1208, 1184, 1165, 1031, 980, 916, 906, 728, 648; $[\alpha]_D^{17}$: −18 (c 0.5, CH_2Cl_2); ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm): 6.87 (s, 1H), 5.62 (d, J = 4.3 Hz, 1H), 5.42 (dd, J = 4.4, 1.9 Hz, 1H), 5.09 (ddd, J = 26.5, 15.2, 9.2 Hz, 3H), 4.87 (dt, J = 16.5, 8.9 Hz, 2H), 4.55−4.44 (m, 2H), 4.32 (dd, J = 22.6, 11.1 Hz, 4H), 4.17−3.98 (m, 3H), 3.75−3.60 (m, 2H), 3.54 (dd, J = 9.6, 3.7 Hz, 1H), 2.16−1.94 (m, 30H); ^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm): 170.6 (C═O), 170.5 (C═O), 170.4 (C═O), 170.3 (C═O), 169.9 (2C═O), 169.7 (C═O), 169.4 (C═O), 169.2 (C═O), 169.1 (C═O), 153.6 (CH), 101.2 (C_q), 101.0 (CH), 86.3 (CH), 76.9 (CH), 76.6 (CH), 73.7 (CH), 73.5 (CH), 73.0 (CH), 72.1 (CH), 71.7 (CH), 70.0 (CH), 67.8 (CH), 66.7 (CH), 64.3 (CH), 62.0 (CH_2), 61.6 (CH_2), 61.3 (CH_2), 20.8 ($2CH_3$), 20.7 ($3CH_3$), 20.6 ($5CH_3$); HR-MS(ESI): for $C_{38}H_{50}NaO_{24}S$ (M + Na)$^+$: m/z calcd 945,2306, found 945.2310.

*(2R,3R,4S,5R,6R)-2-(Acetoxymethyl)-6-(((2R,3R,4S,5R,6R)-4,5-diacetoxy-2-(acetoxymethyl)-6-(((2R,3R,4S,5R,6S)-4,5-diacetoxy-2-(acetoxymethyl)-6-(((2R,3R,4S)-3,4-diacetoxy-2-(acetoxymethyl)-3,4-dihydro-2H-pyran-5-yl)thio)tetrahydro-2H-pyran-3-yl)oxy)tetrahydro-2H-pyran-3-yl)oxy)tetrahydro-2H-pyran-3,4,5-triyl Triacetate (**3l**).* Following the general procedure A of coupling, a flame-dried resealable Schlenk tube (5 mL) was charged with Xantphos Pd-G_3 (3.0 mg, 0.01 mmol), β-thiomaltotriose **1g** (100 mg, 0.11 mmol), and 2-iodoglucal **2a** (35 mg, 0.09 mmol). The Schlenk tube was capped with a rubber septum, evacuated, and backfilled with argon, and then 1,4-dioxane (0.4 mL) and Et_3N (11 μL, 0.13 mmol) were added. The Schlenk tube was sealed, and the mixture was stirred at 60 °C for 2 h. After evaporation of the 1,4-dioxane, the residue was purified by flash chromatography over silica gel (ethyl acetate:cyclohexane: 3:7 gradient concentration to 8:2), followed by HPLC preparative (conditions: H_2O/MeOH gradient from 60% to 100% in 15 min) to afford the desired product **3l** (82 mg, 0.06 mmol, 78%) as a white solid; mp (106−107 °C); TLC: R_f = 0.07 (ethyl acetate:cyclohexane: 4:6); IR (thin film, neat) ν_{max}/cm^{-1}: 1756, 1737, 1621, 1432, 1367, 1239, 1207, 1173, 1136, 1023, 982, 944, 914, 727, 648; $[\alpha]_D^{16}$: −18 (c 0.5, CH_2Cl_2); ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm): 6.92 (s, 1H), 5.47 (d, J = 4.8 Hz, 1H), 5.41−5.36 (m, 2H), 5.34−5.28 (m, 1H), 5.27−5.23 (m, 1H), 5.21−5.16 (m, 1H), 5.05 (t, J = 9.8 Hz, 1H), 4.86−4.78 (m, 1H), 4.76−4.68 (m, 2H), 4.52−4.42 (m, 4H), 4.37 (dd, J = 6.4, 2.9 Hz, 1H), 4.30 (d, J = 4.3 Hz, 1H), 4.26 (d, J = 3.3 Hz, 1H), 4.19 (dd, J = 9.8, 2.8 Hz, 1H), 4.12 (dd, J = 11.8, 2.6 Hz, 2H), 4.03 (dd, J = 12.6, 1.5 Hz, 1H), 3.95−3.88 (m, 4H), 3.71 (dd, J = 12.2, 3.3 Hz, 1H), 2.16 (s, 3H), 2.14 (s, 3H), 2.09 (d, J = 5.3 Hz, 12H), 2.04 (s, 3H), 2.01 (s, 3H), 1.99 (d, J = 3.3 Hz, 12H), 1.96 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm): 170.7 (2C═O), 170.6 (C═O), 170.6 (C═O), 170.5 (C═O), 170.5 (C═O), 170.2 (C═O), 170.0 (C═O), 169.9 (C═O), 169.9 (C═O), 169.8 (C═O), 169.5 (2C═O), 154.3 (CH), 100.5 (C_q), 96.0 (CH), 95.8 (CH), 85.6 (CH), 76.4 (CH), 76.2 (CH), 74.3 (CH), 73.8 (CH), 72.5 (CH), 71.8 (CH), 70.6 (3CH), 70.2 (CH), 69.8 (CH), 69.5 (CH), 69.1 (CH), 68.6 (CH), 68.0 (CH), 67.5 (CH), 63.0 (CH_2), 62.4 (CH_2), 61.5 (CH_2), 60.9 (CH_2), 21.0 ($2CH_3$), 20.9 ($3CH_3$), 20.8 ($2CH_3$), 20.7 ($5CH_3$); HR-MS(ESI): for $C_{50}H_{66}NaO_{32}S$ (M + Na)$^+$: m/z calcd 1233.3156, found 1233.3169.

*(2R,3R,4S,5R,6R)-2-(Acetoxymethyl)-6-(((2R,3R,4S,5R,6R)-4,5-diacetoxy-2-(acetoxymethyl)-6-(((2R,3R,4S,5R,6S)-4,5-diacetoxy-2-(acetoxymethyl)-6-(((2R,3S,4S)-3,4-diacetoxy-2-(acetoxymethyl)-3,4-dihydro-2H-pyran-5-yl)thio)tetrahydro-2H-pyran-3-yl)oxy)tetrahydro-2H-pyran-3-yl)oxy)tetrahydro-2H-pyran-3,4,5-triyl Triacetate (**3m**).* Following the general procedure A of coupling, a flame-dried resealable Schlenk tube (5 mL) was charged with Xantphos Pd-G_3 (3.0 mg, 0.01 mmol), β-thiomaltotriose **1g** (100 mg, 0.11 mmol), and 2-iodogalactal **2b** (35 mg, 0.09 mmol). The Schlenk tube was capped with a rubber septum, evacuated, and backfilled with argon, and then 1,4-dioxane (0.4 mL) and Et_3N (11 μL, 0.132 mmol) were added. The Schlenk tube was sealed, and the mixture was stirred at 60 °C for 2 h. After evaporation of the 1,4-dioxane, the residue was purified by flash

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chromatography over silica gel (ethyl acetate:cyclohexane: 3:7 gradient concentration to 8:2), followed by HPLC preparative (conditions: H_2O/MeOH gradient from 60% to 100% in 15 min) to afford the desired product **3m** (75 mg, 0.06 mmol, 69%) as a colorless amorphous; TLC: R_f = 0.08 (ethyl acetate:cyclohexane: 4:6); IR (thin film, neat) ν_{max}/cm^{-1}: 2959, 2924, 2853, 1738, 1620, 1465, 1367, 1240, 1208, 1183, 1131, 1023, 944, 908, 767, 733, 648; $[\alpha]_D^{20}$: −30 (*c* 0.5, CH_2Cl_2); ^1H NMR (300 MHz, $CDCl_3$) δ (ppm): 6.89 (s, 1H), 5.64 (d, *J* = 4.3 Hz, 1H), 5.45 (dd, *J* = 4.3, 1.6 Hz, 1H), 5.41−5.37 (m, 2H), 5.26−5.22 (m, 2H), 5.05 (t, *J* = 9.9 Hz, 1H), 4.87−4.79 (m, 1H), 4.76−4.70 (m, 2H), 4.49−4.38 (m, 4H), 4.34 (d, *J* = 1.9 Hz, 1H), 4.27 (dd, *J* = 9.7, 5.4 Hz, 2H), 4.23−4.14 (m, 3H), 4.04 (d, *J* = 12.5 Hz, 1H), 3.95−3.89 (m, 4H), 3.70−3.65 (m, 1H), 2.16 (s, 3H), 2.15 (s, 6H), 2.08 (s, 9H), 2.04 (s, 3H), 2.02 (s, 3H), 2.00 (s, 3H), 1.99 (s, 9H), 1.97 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm): 170.7 (2C═O), 170.6 (2C═O), 170.6 (C═O), 170.5 (C═O), 170.5 (C═O), 170.2 (C═O), 169.9 (2C═O), 169.9 (C═O), 169.8 (C═O), 169.5 (C═O), 153.9 (CH), 100.6 (C_q), 96.0 (CH), 95.8 (CH), 85.6 (CH), 76.5 (CH), 76.3 (CH), 74.0 (CH), 73.6 (CH), 72.6 (CH), 71.9 (CH), 70.8 (CH), 70.6 (2CH), 70.1 (CH), 69.5 (CH), 69.1 (CH), 68.7 (CH), 68.0 (CH), 66.9 (CH), 64.3 (CH), 63.1 (CH_2), 62.5 (CH_2), 61.5 (CH_2), 61.40(CH_2), 21.0 (CH_3), 20.9 ($2CH_3$), 20.8 ($4CH_3$), 20.7 ($5CH_3$); HR-MS(ESI): for $C_{50}H_{66}NaO_{32}S$ $(M + Na)^+$: *m*/*z* calcd 1233.3156, found 1233.3143.

*(2R,3R,4R)-2-(Acetoxymethyl)-5-((2-(trimethylsilyl)ethyl)thio)-3,4-dihydro-2H-pyran-3,4-diyl Diacetate (**5a**).* Following the general procedure B of coupling, a flame-dried resealable Schlenk tube (5 mL) was charged with Xantphos Pd-G_3 (11.9 mg, 0.01 mmol), 2-(trimethylsilyl)ethanethiol (48 μL, 0.30 mmol) **4a**, and 2-iodoglucal **2a** (100 mg, 0.25 mmol) in 1,4-dioxane (1.0 mL). The mixture was then stirred at room temperature for 1 min, after that Et_3N (51 μL, 0.38 mmol) was added to the mixture. The tube was capped with a rubber septum, evacuated, and backfilled with argon. The tube was sealed, and the mixture was stirred at 60 °C for 1.5 h. After evaporation of the 1,4-dioxane, water was added to the crude product, and the mixture was extracted three times with ethyl acetate. The organic layers were combined, dried over $MgSO_4$, followed by evaporation of solvent under vacuum at 30 °C. The residue was purified by column chromatography through silica gel using eluent (ethyl acetate: cyclohexane: 1:9) to afford the desired product **5a** (70 mg, 0.17 mmol, 69%) as a yellow oil; TLC: R_f = 0.4 (ethyl acetate: cyclohexane: 3:7); IR (thin film, neat) ν_{max}/cm^{-1}: 2954, 1740, 1619, 1435, 1367, 1247, 1211, 1171, 1135, 1016, 912, 860, 839, 827, 753, 695; $[\alpha]_D^{17}$: +31.2 (*c* 0.82, $CHCl_3$); ^1H NMR (300 MHz, CD_3OD) δ (ppm): 6.88 (s, 1H), 5.44 (d, *J* = 4.6 Hz, 1H), 5.20 (t, *J* = 5.1 Hz, 1H), 4.55−4.37 (m, 2H), 4.18 (d, *J* = 9.3 Hz, 1H), 2.59 (dd, *J* = 17.0, 6.7 Hz, 2H), 2.08−2.07 (m, 9H), 0.81 (dd, *J* = 10.6, 7.0 Hz, 2H), 0.04 (s, 9H); ^{13}C NMR (75 MHz, CD_3OD) δ (ppm): 172.1 (C═O), 171.7 (C═O), 170.9 (C═O), 152.3 (CH), 105.3 (C_q), 75.2 (CH), 69.5 (CH), 68.9 (CH), 62.1 (CH_2), 31.04 (CH_2), 20.9 (CH_3), 20.7 (CH_3), 20.6 (CH_3), 18.00 (CH_2), −1.7 ($3CH_3$); HR-MS(ESI): for $C_{17}H_{28}NaO_7SiS$ $(M + Na)^+$: *m*/*z* calcd 427.1223, found 427.1220.

*(2R,3S,4R)-2-(Hydroxymethyl)-5-((2-(trimethylsilyl)ethyl)thio)-3,4-dihydro-2H-pyran-3,4-diol (**5b**).* Following the general procedure B of coupling, a flame-dried resealable Schlenk tube (5 mL) was charged with Xantphos Pd-G_3 (17.4 mg, 0.02 mmol), 2-(trimethylsilyl)ethanethiol (71 μL, 0.44 mmol) **4a**, and 2-iodoglucal **2c** (100 mg, 0.37 mmol) in 1,4-dioxane (1.0 mL). The mixture was then stirred at room temperature for 1 min, after that Et_3N (74 μL, 0.55 mmol) was added to the mixture. The tube was capped with a rubber septum, evacuated, and backfilled with argon. The tube was sealed, and the mixture was stirred at 60 °C for 1.5 h. After evaporation of the 1,4-dioxane, water was added to the crude product, and the mixture was extracted three times with ethyl acetate. The organic layers were combined, dried over $MgSO_4$, followed by evaporation of solvent under vacuum at 30 °C. The residue was purified by column chromatography through silica gel using eluent (ethyl acetate:cyclohexane: 3:7 gradient concentration to 9:1) to afford the desired product **5b** (33 mg, 0.12 mmol, 32%) as a pale yellow solid; mp (115−116 °C); TLC: R_f = 0.2 (ethyl acetate); IR (thin film, neat) ν_{max}/cm^{-1}: 3313, 2952, 2924, 1617, 1419, 1247, 1170, 1154, 1128, 1103, 1077, 1048, 1027, 1001, 915, 888, 859, 838, 823, 753, 690; $[\alpha]_D^{17}$: +82.2 (*c* 0.40, $CHCl_3$); ^1H NMR (300 MHz, CD_3OD) δ (ppm): 6.71 (s, 1H), 4.02 (d, *J* = 6.0 Hz, 1H), 3.90−3.81 (m, 3H), 3.71 (t, *J* = 6.0 Hz, 1H), 2.67−2.61 (m, 2H), 0.83 (dd, *J* = 9.8, 7.8 Hz, 2H), 0.02 (s, 9H); ^{13}C NMR (75 MHz, CD_3OD) δ (ppm): 150.2 (CH), 109.5 (C_q), 80.9 (CH), 72.0 (CH), 70.9 (CH), 62.1(CH_2), 31.0 (CH_2), 18.0 (CH_2), −1.7 ($3CH_3$); HR-MS(ESI): for $C_{12}H_{23}O_6SiS$ $(M + HCOO)^-$: *m*/*z* 323.0985, found 323.0986.

*(2R,3R,4R)-2-(Acetoxymethyl)-5-(((R)-2-((tert-butoxycarbonyl)-amino)-3-methoxy-3-oxopropyl)thio)-3,4-dihydro-2H-pyran-3,4-diyl Diacetate (**5c**).* Following the general procedure B of coupling, a flame-dried resealable Schlenk tube (5 mL) was charged with Xantphos Pd-G_3 (11.9 mg, 0.01 mmol), boc-L-cysteine methyl ester (70.9 mg, 0.30 mmol) **4b**, and 2-iodoglucal **2a** (100 mg, 0.25 mmol) in 1,4-dioxane (1.0 mL). The mixture was then stirred at room temperature for 1 min, after that Et_3N (51 μL, 0.38 mmol) was added to the mixture. The tube was capped with a rubber septum, evacuated, and backfilled with argon. The tube was sealed, and the mixture was stirred at 60 °C for 1.5 h. After evaporation of the 1,4-dioxane, water was added to the crude product, and the mixture was extracted three times with ethyl acetate. The organic layers were combined, dried over $MgSO_4$, followed by evaporation of solvent under vacuum at 30 °C. The residue was purified by column chromatography through silica gel using eluent (ethyl acetate:cyclohexane: 0:10 gradient concentration to 7:3) to afford the desired product **5c** (50 mg, 0.10 mmol, 39%) as a yellow oil; TLC: R_f = 0.2 (ethyl acetate:cyclohexane: 3:7); IR (thin film, neat) ν_{max}/cm^{-1}: 2924, 2853, 1740, 1712, 1618, 1515, 1436, 1367, 1210, 1169, 1160, 1050, 1018, 911, 778; $[\alpha]_D^{20}$: +50.6 (*c* 0.76, $CHCl_3$); ^1H NMR (300 MHz, CD_3OD) δ (ppm): 6.94 (s, 1H), 5.51 (d, *J* = 4.8 Hz, 1H), 5.21 (t, *J* = 5.3 Hz, 1H), 4.48−4.41 (m, 2H), 4.34 (t, *J* = 6.0 Hz 1H), 4.24−4.17 (m, 1H), 3.73 (s, 3H), 2.95 (dd, *J* = 13.8, 5.2 Hz, 1H), 2.79 (dd, *J* = 13.9, 8.2 Hz, 1H), 2.09−2.06 (m, 9H), 1.46 (s, 9H); ^{13}C NMR (75 MHz, CD_3OD) δ (ppm): 173.2 (C═O), 172.1 (C═O), 171.8 (C═O), 171.0 (C═O), 157.6 (C═O), 153.8 (CH), 103.5 (C_q), 80.7 (C_q), 75.4 (CH), 70.2 (CH), 68.6 (CH), 62.2 (CH_2), 54.4 (CH), 52.8 (CH_3), 36.4 (CH_2), 28.7 ($3CH_3$), 20.9 (CH_3), 20.7 (CH_3), 20.6 (CH_3); HR-MS(ESI): for $C_{21}H_{31}NNaO_{11}S$ $(M + Na)^+$: *m*/*z* 528.1516, found 528.1512.

*N-acetyl-S-((2R,3R,4R)-3,4-Diacetoxy-2-(acetoxymethyl)-3,4-dihydro-2H-pyran-5-yl)-L-cysteine (**5d**).* Following the general procedure B of coupling, a flame-dried resealable Schlenk tube (5 mL) was charged with Xantphos Pd-G_3 (11.9 mg, 0.01 mmol), *N*-acetyl-L-cysteine (49.2 mg, 0.30 mmol) **4c**, and 2-iodoglucal **2a** (100 mg, 0.25 mmol) in 1,4-dioxane (1.0 mL). The mixture was then stirred at room temperature for 1 min, after that Et_3N (51 μL, 0.38 mmol) was added to the mixture. The tube was capped with a rubber septum, evacuated, and backfilled with argon. The tube was sealed, and the mixture was stirred at 60 C for 2.0 h. Xantphos Pd-G_3 (11.9 mg, 0.01 mmol) was added a second time, and the mixture was stirred at 60 °C for 0.5 h. After evaporation of the 1,4-dioxane, water was added to the crude product, and the mixture was extracted three times with ethyl acetate. The organic layers were combined, dried over $MgSO_4$, followed by evaporation of solvent under vacuum at 30 °C. The residue was purified by column chromatography through silica gel using eluent (dichloromethane:methanol: 10:0 gradient concentration to 7:3) to afford the desired product **5d** (20 mg, 0.05 mmol, 18%) as a beige powder; mp (138−139 °C); TLC: R_f = 0.3 (dichloromethane:methanol: 9:1); IR (thin film, neat) ν_{max}/cm^{-1}: 1741, 1620, 1584, 1404, 1368, 1245, 1214, 1170, 1135, 1041, 1019, 911, 818, 775, 621; $[\alpha]_D^{17}$: +32.3 (*c* 0.42, $CHCl_3$); ^1H NMR (300 MHz, CD_3OD) δ (ppm): 6.97 (s, 1H), 5.56 (d, *J* = 5.3 Hz, 1H), 5.20 (t, *J* = 6.0 Hz, 1H), 4.50−4.34 (m, 3H), 4.19 (dd, *J* = 14.1, 4.9 Hz, 1H), 3.03 (dd, *J* = 13.5, 4.6 Hz, 1H), 2.90 (dd, *J* = 13.4, 7.4 Hz, 1H), 2.08−2.01 (m, 12H); ^{13}C NMR (75 MHz, CD_3OD) δ (ppm): 177.7 (C═O), 172.9 (C═O), 172.1 (C═O), 172.0 (C═O), 171.1 (C═O), 153.6 (CH), 105.0 (C_q), 75.5 (CH), 71.2 (CH), 68.7 (CH), 62.2 (CH_2), 55.3 (CH), 38.3 (CH_2), 22.8 (CH_3), 20.9 (CH_3), 20.7 (CH_3), 20.6 (CH_3); HR-MS(ESI): for $C_{17}H_{23}NO_{10}NaS$ $(M + Na)^+$: *m*/*z* 456.0940, found 456.0937.

*(2S,3R,4S,5S,6R)-2-(((2R,3R,4R)-3,4-Dihydroxy-2-(hydroxymethyl)-3,4-dihydro-2H-pyran-5-yl)thio)-6-(hydroxymethyl)tetrahydro-2H-pyran-3,4,5-triol (**6a**).* Following the general procedure C of coupling, a mixture of S-linked disaccharide (**3c**) (40 mg, 0.06 mmol)

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and K_2CO_3 (2.6 mg, 0.02 mmol) in methanol (0.6 mL) was placed in a small balloon, and the mixture was stirred under argon at room temperature for 1 h. The crude mixture was then filtered through Celite and washed with 10 mL of methanol and filtered for only 1 min. The filtrate was concentrated under reduced pressure by using a rotavap at 25 °C for 1−2 h to afford the desired product **6a** (22 mg, 0.06 mmol, 98%) as a white solid contaminated by small amount of thiosugar dimer; TLC: R_f = 0 (dichloromethane:methanol: 4:1); IR (thin film, neat) ν_{max}/cm^{-1}: 3315, 2950, 1645, 1612, 1452, 1302, 1171, 1139, 1080, 1054, 1009, 976, 915, 863, 824, 801, 698; ^{1}H NMR (300 MHz, $MeOD_4$) δ (ppm): 6.91 (s, 1H), 4.22 (d, J = 9.4 Hz, 1H), 4.05−4.00 (m, 1H), 3.89−3.82 (m, 2H), 3.79−3.75 (m, 1H), 3.75−3.71 (m, 1H), 3.70−3.65 (m, 1H), 3.65−3.60 (m, 1H), 3.58−3.53 (m, 2H), 3.51−3.42 (m, 1H), 3.28 (dd, J = 3.1, 1.5 Hz, 1H); ^{13}C NMR (75 MHz, $MeOD_4$) δ (ppm): 152.9 (CH), 105.3 (C_q), 92.2 (CH), 89.3 (CH), 80.9 (CH), 76.1 (CH), 72.3 (CH), 70.6 (CH), 70.5 (CH), 69.8 (CH), 62.6 (CH_2), 61.9 (CH_2); HRMS (ESI) (M + Na)$^+$ m/z calculated for $C_{12}H_{20}O_9SNa$ 363.0726, found 363.0733.

*(2R,3R,4S,5S,6R)-2-(((2R,3S,4R,5R,6R)-6-(((2R,3S,4R,5R,6S)-6-(((2R,3R,4R)-3,4-Dihydroxy-2-(hydroxymethyl)-3,4-dihydro-2H-pyran-5-yl)thio)-4,5-dihydroxy-2-(hydroxymethyl)tetrahydro-2H-pyran-3-yl)oxy)-4,5-dihydroxy-2-(hydroxymethyl)tetrahydro-2H-pyran-3-yl)oxy)-6-(hydroxymethyl)tetrahydro-2H-pyran-3,4,5-triol (**6b**).* Following the general procedure C of coupling, a mixture of S-linked disaccharide (**3m**) (25 mg, 0.02 mmol) and K_2CO_3 (0.9 mg, 0.01 mmol) in methanol (0.2 mL) was placed in a small balloon, and the mixture was stirred under argon at room temperature for 30 min. The crude mixture was then filtered through Celite and washed with 10 mL of methanol and filtered for only 1 min. The filtrate was concentrated under reduced pressure by using a rotavap at 25 °C for 1−2 h to afford the desired product **6b** (13 mg, 0.02 mmol, 95%) as a white solid; TLC: R_f = 0 (dichloromethane: methanol: 4:1); IR (thin film, neat) ν_{max}/cm^{-1}: 3371, 2924, 1615, 1460, 1335, 1299, 1174, 1150, 1080, 1022, 921, 875, 824, 764; ^{1}H NMR (300 MHz, $MeOD_4$) δ (ppm): 6.92 (s, 1H), 5.16 (dd, J = 8.0, 3.6 Hz, 2H), 4.33 (d, J = 9.6 Hz, 1H), 4.09 (d, J = 5.4 Hz, 2H), 3.99−3.96 (m, 1H), 3.92−3.71 (m, 10H), 3.70−3.56 (m, 5H), 3.56−3.36 (m, 5H); ^{13}C NMR (75 MHz, $MeOD_4$) δ (ppm):152.8 (CH), 106.1 (C_q), 102.9 (CH), 102.7 (CH), 89.4 (CH), 81.3 (CH), 81.0 (CH), 80.7 (2CH), 79.3 (CH), 75.41(CH), 75.0 (CH), 74.8 (CH), 74.3 (CH), 73.9 (CH), 73.4 (CH), 73.3 (CH), 72.7 (CH), 71.6 (CH), 70.1 (CH), 62.8 (CH_2), 62.2 (CH_2), 62.1 (CH_2), 62.0 (CH_2); HRMS (ESI) (M + Na)$^+$ m/z calculated for $C_{24}H_{40}O_{19}SNa$ 687.1782, found 687.1771.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.joc.7b00861.

^{1}H and ^{13}C NMR spectra of compounds **3a−m**, **5a−d** and **6a−b** (PDF)

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Notes

The authors declare no competing financial interest.

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