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Note

Useful approach to the synthesis of aryl thio- and selenoglycosides in the presence of rongalite

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ABSTRACT

A simple, mild, and cost effective methodology has been developed for the synthesis of aryl thio-and selenoglycosides from glycosyl halides and diaryl dichalcogenides. Diaryl dichalcogenides undergo reductive cleavage in the presence of rongalite ($HOCH_2SO_2Na$) to generate a chalcogenide anion in situ followed by reaction with glycosyl halides to furnish the corresponding aryl thio- and selenoglycosides in excellent yields. Using this protocol, synthesis of 4-methyl-7-thioumbelliferyl-β-D-cellobioside (**MUS-CB**), a fluorescent non-hydrolyzable substrate analogue for cellulases has been achieved.

Thioglycosides play a vital role as glycosyl donors for the synthesis of oligosaccharides.[1–4] The potential ability of thioglycosides as activators toward various reagents[4] makes them attractive and stable glycosyl donors. Moreover, the exceptional stability of thioglycosides is useful in medicinal and biochemical applications.[5] In the literature, a number of methods are available for the synthesis of thioglycosides.[6–18,20–24] Most commonly, the synthesis of thioglycosides involves the treatment of peracetylated sugars with the appropriate thiol in the presence of a Lewis acid or bases.[7–12] The other methods include the generation of nucleophilic thiolate anion in situ from disulfides using Zn dust/$ZnCl_2$[13] or Lewis acids[14] during the reaction with glycosyl halides or peracetylated sugars and the reaction of *S*-glycosyl isothiouronium intermediates with alkyl halides in the presence of a mild base.[10,15,16] Despite the usefulness of the above methods, they have limitations such as the use of foul smelling thiols, use of expensive reagents, long reaction times, lower yields, and harsh reaction conditions. In this context, developing a convenient and green method would be of greater importance. From our laboratory, we reported earlier that rongalite ($HOCH_2SO_2Na$), **1** is a useful reagent for the cleavage of diaryl dichalcogenides to generate the corresponding chalcogenide anion in situ and it has been utilized for the ring opening of aziridines and epoxides.[17] Rongalite, **1** is a cheap and commercially available reagent and is used in many organic transformations.[18] The advantage of rongalite, **1** over the other reducing agents includes its cost effectiveness, mild reaction conditions, and simple work up procedure. In continuation of our study to explore the scope and limitation on the use of this reagent, we anticipated that the in situ generated organo chalcogen anion from diaryl dichalcogenides and rongalite, **1** can be used in reaction with glycosyl halides (Scheme 1) to furnish the corresponding thio- and selenoglycosides.

Accordingly, a reaction was carried out with 2,3,4,6-tetra-*O*-acetyl-α-D-glucopyranosyl bromide **2a** and diphenyl disulfide **3a** in the presence of rongalite **1**. Addition of **2a** (1 equiv) to a well-stirred solution of diphenyl disulfide **3a** (0.5 equiv), potassium carbonate (2 equiv), and rongalite **1** (3 equiv)[19] in *N*,*N*-dimethylformamide (DMF) at room temperature resulted in the formation of the corresponding phenyl thioglycoside **4a** (1 h) in 93% yield.

The stereochemical outcome of the reaction was confirmed by NMR spectroscopy. The ^1H NMR of the product **4a** showed a doublet at δ 4.71 for H-1, with $J_{1,2} \sim 10.0$ Hz and the signal at δ 5.23 (t, $J_{2,3} \sim 10.0$ Hz) for H-2 which clearly demonstrated that the product **4a** has a 1,2-*trans* configuration without any 1,2-*cis* linkage. The mechanism of the reaction involves the base promoted decomposition of rongalite to form formaldehyde and HSO_2^-.[17] The HSO_2^- transfers a single electron to disulfide **3a** to form a thiolate ion in situ which reacts at the anomeric carbon (C-1) of **2a** in an S_N2 fashion to give the desired product **4a** with 1,2-*trans* configuration.

After the successful synthesis of thioglycoside **4a**, we decided to extend the scope of the method with other disulfides **3b**–**3f** using

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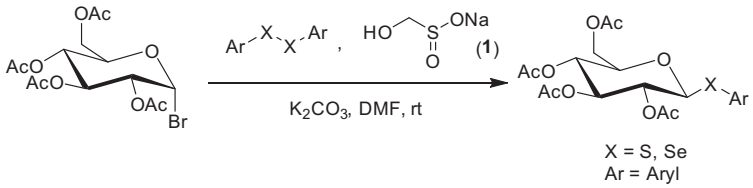
0008-6215/



Scheme 1. General scheme for the synthesis of aryl thioglycosides and selenoglycosides.

2a as the partner. In all the cases the corresponding thioglycosides **4b**–**4f**, respectively, were obtained in good to excellent yields. The results are summarized in Table 1.

From the Table 1, it can be seen that, irrespective of the nature of the substituent on the phenyl moiety of the disulfide, the corresponding thioglycosides **4b**–**4e** were obtained in good to excellent yields (Table 1, entries 1–4). 2,2′-Dipyridyl disulfide **3f** underwent reductive cleavage under these conditions followed by its reaction with **2a** to furnish the corresponding thioglycoside **4f** in moderate yield (65%) after 2 h (Table 1, entry 5). However, aliphatic disulfides such as dibenzyl disulfide **3g** failed to react under these conditions to form the corresponding thioglycoside **4g** even after 6 h (Table 1, entry 6).

Then we further screened the reactivity of **3a** with other glycosyl halides **2b**–**2f** (Scheme 3). The glycosyl bromides **2b**, **2c,** and **2f** reacted smoothly (1 h) with **3a** in the presence of **1** to form the corresponding thioglycosides **4h**, **4i,** and **4l**, respectively, in excellent yields (Table 2, entries 2, 3, 6) under similar conditions described in Scheme 3. The glucosamine derived glycosyl chloride **2e** took 1 h to form the corresponding thioglycoside **4k** in 83% yield (Table 2, entry 5) whereas the glycosyl bromide **2d** having bromine at C-6 furnished the desired product **4j** in 89% yield after 3 h (Table 2, entry 4).

Like diaryl disulfides, diphenyl diselenide **3h** also showed the ability to cleave in a reductive fashion with rongalite **1** (Scheme 2). The reaction of glycosyl halides **2a**–**2f** with diphenyl diselenide **3h** in the presence of rongalite (25 °C) resulted in the formation of the corresponding selenoglycosides **5a**–**5f**, respectively, in good to excellent yields. The results are presented in Table 2. While the glucose, galactose, and lactose derived anomeric bromides **2a**–**2c**, **2f**, respectively, reacted with ease (1 h) with diselenide **3h** in the presence of **1** (Table 2, entries 1–3, 6). The reaction of other glycosyl halides **2d** and **2e** were slower (2–4 h) (Table 2, entries 4, 5).

Table 1
Synthesis of various thioglycosides **4b**–**4f** derived from **2a**

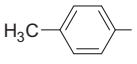
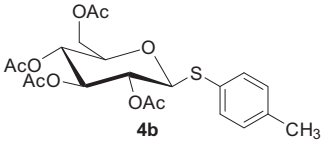
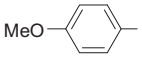
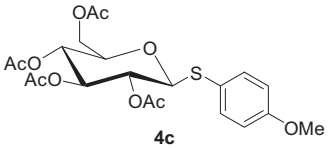
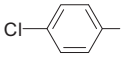
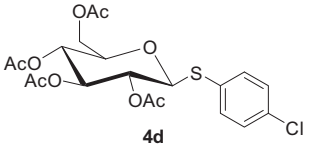
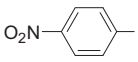
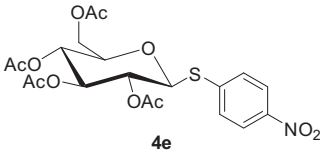
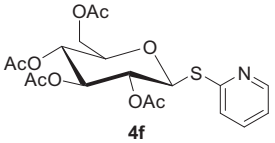
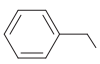
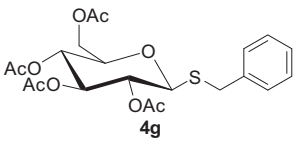
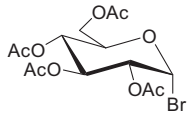
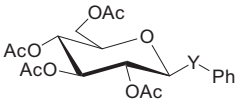
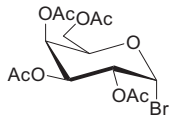
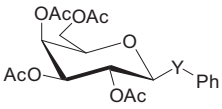
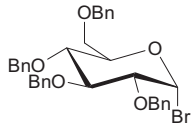
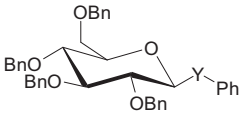
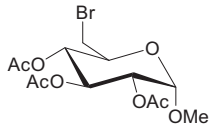
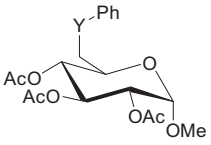
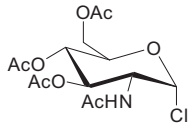
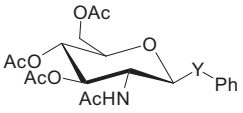
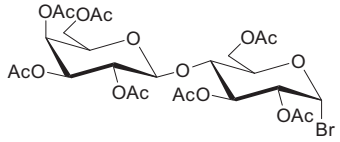
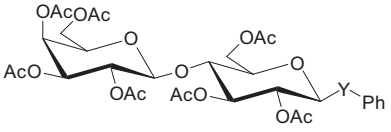
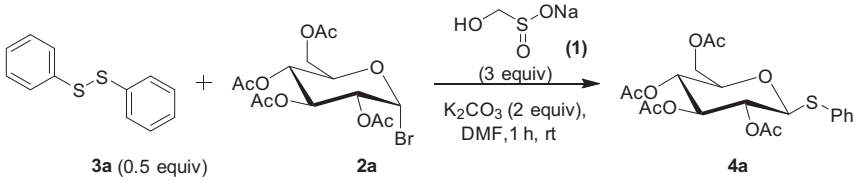
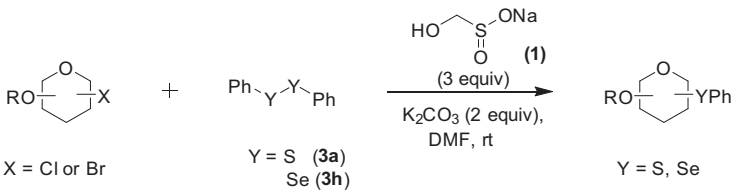
Entry	R–S–S–R (R–)	Time (h)	Thioglycoside	Yield (%)
1	 **3b**	1	 **4b**	93
2	 **3c**	1	 **4c**	88
3	 **3d**	1	 **4d**	86
4	 **3e**	2	 **4e**	79
5	 **3f**	2	 **4f**	65
6	 **3g**	6	 **4g**	No reaction

Table 2
Synthesis of phenyl thio- and selenoglycosides

Entry	Glycosyl halide		Thio/seleno glycoside		Time (h)	Yield (%)
1		**2a**		Y = S (**4a**)	1	93
				=Se (**5a**)	1	86
2		**2b**		Y = S (**4h**)	1	92
				=Se (**5b**)	1	86
3		**2c**		Y = S (**4i**)	1	93
				=Se (**5c**)	1	82
4		**2d**		Y = S (**4j**)	3	89
				=Se (**5d**)	4	79
5		**2e**		Y = S (**4k**)	1	83
				=Se (**5e**)	2	79
6		**2f**		Y = S (**4l**)	1	90
				=Se (**5f**)	1	83



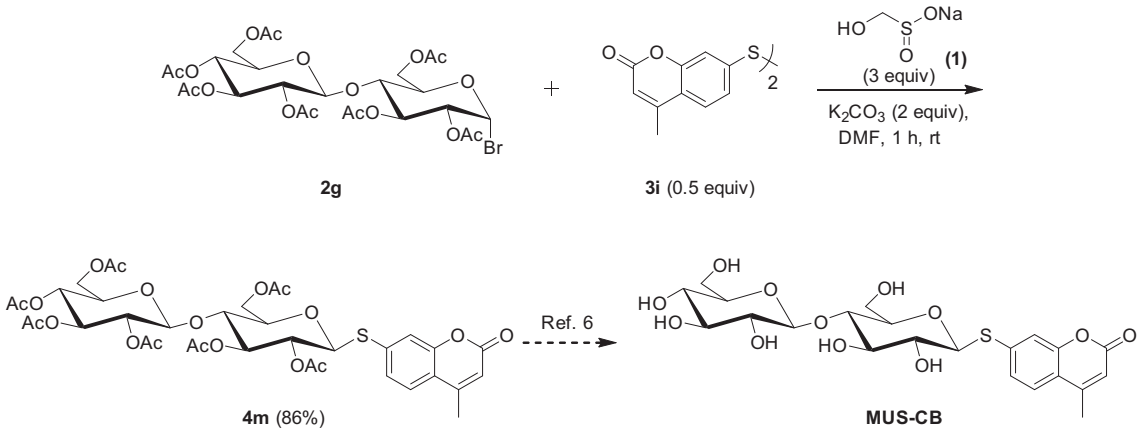
Scheme 2. Synthesis of phenyl thioglycoside **4a** derived from **2a** and **3a**.



Scheme 3. Reaction of glycosyl halides **2** with diphenyl disulfide (**3a**)/diselenide (**3h**) in the presence of rongalite **1**.

Finally, the synthetic potential of this method has been demonstrated in the preparation of peracetylated derivative of 4-methyl-7-thioumbelliferyl-β-D-cellobioside **4m** which is the key precursor for **MUS-CB**, a fluorescent non-hydrolyzable substrate analogue for cellulases.[20] Thus treatment of anomeric bromide **2g** with disulfide of **3i** derived from 7-mercaptocoumarin[21] in the presence of rongalite **1** furnished the corresponding peracetylated **MUS-CB 4m** in excellent yield (86%) with exclusive β-selectivity (Scheme 4). The deacetylation of **4m** in the presence of NaOMe/MeOH furnished **MUS-CB**.[6]

In summary, we have presented a useful, alternative approach to the synthesis of aryl thio- and selenoglycosides. The method



Scheme 4. Synthesis of 4-methyl-7-thioumbelliferyl-β-D-cellobioside (**MUS-CB**).

involves the reductive cleavage of diaryl dichalcogenides using rongalite to generate the chalcogenide anion in situ which reacts with glycosyl halides. The significance of this method is its cost effectiveness and avoiding the use of foul smelling organo chalcogenols.

1. Experimental section

1.1. General information

All the reactions were performed in an oven dried apparatus and stirred magnetically. Chemicals and solvents were either purchased or purified by standard techniques. Analytical TLC was performed on commercial plates coated with silica gel GF254 (0.25 mm). Silica gel (230–400 mesh) was used for column chromatography. Melting point values reported are uncorrected. Infrared spectra were recorded using the JASCO FTIR instrument and the frequencies are reported in wave numbers (cm^{-1}) and intensities of the peaks are denoted as s (strong), w (weak), m (medium), broad (br). ^1H and ^{13}C NMR spectra were recorded on a Jeol 400 MHz (100 MHz, ^{13}C) NMR spectrometer and calibrated using tetramethylsilane (TMS) for (^1H) or residual undeuterated solvent ($CDCl_3$) as an internal reference. Chemical shifts are reported in parts per million and multiplicity is indicated using the following abbreviations: s (singlet), d (doublet), t (triplet), q (quartet), m (multiplet), bs (broad singlet) etc. Coupling constants are reported wherever it is necessary in Hertz (Hz). High-resolution mass spectra (HRMS) were recorded on micromass Q-TOF electrospray.

1.2. General procedure for the synthesis of aryl thio- and selenoglycosides

To a well stirred solution of the aryl disulfides/diphenyl diselenide (0.2 mmol, 0.5 equiv) in DMF (2 mL), was added rongalite **1** (1.2 mmol, 3 equiv) and K_2CO_3 (0.8 mmol, 2 equiv). The reaction mixture was stirred for 10 min at 25 °C followed by the addition of glycosyl halide (0.4 mmol, 1 equiv) and stirring was continued. The completion of the reaction was monitored by TLC till the consumption of disulfides/diselenide. Then the reaction mixture was quenched with water and extracted with ethyl acetate (20 mL × 2). The organic layer was separated, then washed with brine, extracted with ethyl acetate (5 mL × 2), and dried over anhydrous Na_2SO_4. The solvent was evaporated under vacuum and the crude product was purified by column chromatography on silica gel (230–400 mesh) using ethyl acetate/petroleum ether as eluent.

1.2.1. Phenyl 2,3,4,6-tetra-*O*-acetyl-1-thio-β-D-glucopyranoside (4a)[11,15]

Yield 93%; white solid; mp: 111–113 °C; $[\alpha]_D^{25}$ −20.9 (*c* 0.8, $CHCl_3$); FTIR (neat): 1746 (s), 1440 (w), 1372 (m), 1254 (m), 1226 (s), 1088 (w), 1043 (m), 913 (w), 743 (w) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 7.51–7.49 (m, 2H), 7.33–7.30 (m, 3H), 5.23 (t, *J* = 9.3 Hz, 1H), 5.01 (t, *J* = 9.3 Hz, 1H), 4.98 (t, *J* = 10.0, 1H), 4.71 (d, *J* = 10.1, 1H), 4.25–4.16 (m, 2H), 3.75–3.71 (m, 1H), 2.09–1.99 (4s, 12H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 170.6, 170.2, 169.4, 169.3, 133.2, 131.7, 129.0, 128.5, 85.8, 75.8, 74.0, 70.0, 68.2, 62.2, 20.8, 20.8, 20.6; HRMS (ESI-TOF) *m*/*z*: calcd for $C_{20}H_{24}O_9SNa$ $(M+Na)^+$: 463.1039; found: 463.1035.

1.2.2. 4-Tolyl-phenyl 2,3,4,6-tetra-*O*-acetyl-1-thio-β-D-glucopyranoside (4b)[1,11]

Yield 93%; white solid; mp: 115–117 °C; $[\alpha]_D^{25}$ −19.0 (*c* 1.0, $CHCl_3$); FTIR (KBr): 3449 (s), 1750 (s), 1382 (w), 1228 (s), 1041 (m) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 7.39 (d, *J* = 8.0, 2H), 7.13 (d, *J* = 7.9 Hz, 2H), 5.21 (t, *J* = 9.4 Hz, 1H), 5.03 (t, *J* = 9.8 Hz, 1H), 4.94 (t, *J* = 9.6 Hz, 1H), 4.64 (d, *J* = 10.0 Hz, 1H), 4.24–4.16 (m, 2H), 3.73–3.68 (m, 1H), 2.35–1.99 (5s, 15H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 170.7, 170.3, 169.5, 169.3, 138.9, 133.9, 129.7, 127.5, 85.8, 75.8, 74.0, 69.9, 68.2, 62.2, 21.2, 20.8, 20.8, 20.6, 20.6; HRMS (ESI-TOF) *m*/*z*: calcd for $C_{21}H_{26}O_9SNa$ $(M+Na)^+$: 477.1195; found: 477.1196.

1.2.3. 4-Methoxy-phenyl 2,3,4,6-tetra-*O*-acetyl-1-thio-β-D-glucopyranoside (4c)[11]

Yield 88%; white solid; mp: 95–97 °C; $[\alpha]_D^{25}$ −47.6 (*c* 2.6, $CHCl_3$); FTIR (KBr): 1749 (s), 1592 (w), 1495 (w), 1384 (m), 1287 (m), 1226 (s), 1037 (s), 920 (w), 832 (m), 605 (w) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 7.44 (d, *J* = 8.7 Hz, 2H), 6.85 (d, *J* = 8.7 Hz, 2H), 5.19 (t, *J* = 9.4 Hz, 1H), 4.99 (t, *J* = 9.8 Hz, 1H), 4.89 (t, *J* = 9.6 Hz, 1H), 4.56 (d, *J* = 10.0 Hz, 1H), 4.19 (bs, 2H), 3.81 (s, 3H), 3.69–3.66 (m, 1H), 2.11–1.98 (4s, 12H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 170.5, 170.2, 169.4, 169.2, 160.4, 136.5, 120.9, 114.4, 85.6, 75.7, 74.0, 69.8, 68.1, 62.0, 55.3, 20.8, 20.7, 20.6, 20.5; HRMS (ESI-TOF) *m*/*z*: calcd for $C_{21}H_{26}O_{10}SNa$ $(M+Na)^+$: 493.1144; found: 493.1146.

1.2.4. 4-Chlorophenyl 2,3,4,6-tetra-*O*-acetyl-1-thio-β-D-glucopyranoside (4d)[11]

Yield 86%; white solid; mp: 112–114 °C; $[\alpha]_D^{22}$ −41.1 (*c* 4.3, $CHCl_3$); FTIR (KBr): 3293 (m), 2234 (m), 1751 (s), 1610 (w), 1382 (w), 1225 (s), 1167 (w), 1040 (m), 919 (w), 836 (w) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 7.44 (d, *J* = 8.3 Hz, 2H), 7.29 (d, *J* = 8.5 Hz, 2H), 5.22 (t, *J* = 9.3 Hz, 1H), 5.02 (t, *J* = 9.8 Hz, 1H), 4.94

(t, J = 9.6 Hz, 1H), 4.65 (d, J = 10.0 Hz, 1H), 4.21–3.70 (m, 3H), 2.09–1.99 (4s, 12H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 170.5, 170.1, 169.3, 169.2, 134.9, 129.4, 129.0, 85.1, 75.8, 73.8, 69.7, 68.0, 62.0, 20.7, 20.5; HRMS (ESI-TOF) m/z: calcd for $C_{20}H_{23}ClO_9SNa$ $(M+Na)^+$: 497.0649; found: 497.0643.

1.2.5. 4-Nitro-phenyl 2,3,4,6-tetra-*O*-acetyl-1-thio-β-D-glucopyranoside (4e)[6]

Yield 79%; yellow solid; mp: 180–182 °C; $[\alpha]_D^{22}$ −54.4 (c 3.0, $CHCl_3$); FTIR (KBr): 3448 (w), 1754 (s), 1737 (s), 1515 (m), 1373 (m), 1341 (m), 1242 (s), 1221 (s), 1093 (m), 1044 (s), 913 (w), 851 (w) cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.17 (d, J = 8.7 Hz, 2H), 7.60 (d, J = 8.7 Hz, 2H), 5.28 (t, J = 9.3 Hz, 1H), 5.07 (q, J = 10.4 Hz, 2H), 4.88 (d, J = 10.0 Hz, 1H), 4.26 (dd, J = 12.4, 5.3 Hz, 1H), 4.20 (dd, J = 12.3, 2.0 Hz, 1H), 3.86–3.81 (m, 1H), 2.11–2.01 (4s, 12H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 170.4, 170.0, 169.3, 169.2, 147.0, 141.7, 131.0, 123.8, 84.3, 76.1, 73.6, 69.5, 68.0, 62.0, 20.7, 20.6, 20.5; HRMS (ESI-TOF) m/z: calcd for $C_{20}H_{23}NO_{11}SNa$ $(M+Na)^+$: 508.0890, found: 508.0896.

1.2.6. 2-Pyridyl 2,3,4,6-tetra-*O*-acetyl-1-thio-β-D-glucopyranoside (4f)[22]

Yield 65%; yellow solid; mp: 120–121 °C; $[\alpha]_D^{25}$ −10.2 (c 0.4, $CHCl_3$); FTIR (KBr): 3468 (w), 1752 (s), 1375 (w), 1254 (m), 1225 (s), 1047 (m), 915 (w) cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.45 (m, 1H), 7.57–7.52 (m, 1H), 7.22 (d, J = 7.6 Hz, 1H), 7.09–7.06 (m, 1H), 5.84 (d, J = 10.4 Hz, 1H), 5.36 (t, J = 9.3 Hz, 1H), 5.25–5.14 (m, 2H), 4.27 (dd, J = 12.4, 4.4 Hz, 1H), 4.10 (dd, J = 12.4, 1.9 Hz, 1H), 3.91–3.87 (m, 1H), 2.04–2.02 (4s, 12H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 170.6, 170.1, 169.5, 169.4, 155.2, 149.6, 136.5, 123.3, 120.8, 81.6, 75.9, 74.1, 69.4, 68.2, 61.9, 20.7, 20.6, 20.6, 20.6; HRMS (ESI-TOF) m/z: calcd for $C_{19}H_{23}NO_9SNa$ $(M+Na)^+$: 464.0991; found: 464.0990.

1.2.7. Phenyl 2,3,4,6-tetra-*O*-acetyl-1-thio-β-D-galacto pyranoside (4h)[11,23]

Yield 92%; white solid; mp: 61–63 °C; $[\alpha]_D^{26}$ +4.5 (c 1.9, $CHCl_3$); FTIR (neat): 1751 (s), 1369 (w), 1223 (s), 1082 (w), 1054 (w) cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.53–7.51 (m, 2H), 7.33–7.31 (m, 3H), 5.42 (d, J = 3.2 Hz, 1H), 5.25 (t, J = 10.0 Hz, 1H), 5.06 (dd, J = 9.9, 3.3 Hz, 1H), 4.72 (d, J = 10.0 Hz, 1H), 4.19 (dd, J = 11.4, 7.0 Hz, 1H), 4.12 (dd, J = 11.4, 6.2 Hz, 1H), 3.94 (t, J = 6.5 Hz, 1H), 2.12–1.98 (4s, 12H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 170.3, 170.2, 170.0, 169.4, 132.5, 132.4, 128.9, 128.1, 86.6, 74.4, 72.0, 67.2, 67.2, 61.6, 20.8, 20.6, 20.6, 20.5; HRMS (ESI-TOF) m/z: calcd for $C_{20}H_{24}O_9SNa$ $(M+Na)^+$: 463.1039; found: 463.1036.

1.2.8. Phenyl 2,3,4,6-tetra-*O*-benzyl-1-thio-β-D-glucopyranoside (4i)[24]

Yield 93%; pale yellow solid; mp: 88–90 °C; $[\alpha]_D^{27}$ −43.2 (c 1.9, $CHCl_3$); FTIR (KBr): 3029 (w), 2904 (w), 1139 (m), 1062 (s), 755 (w), 733 (m), 695 (m) cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.59–7.57 (m, 2H), 7.40–7.18 (m, 23H), 4.91–4.81 (m, 4H), 4.73 (d, J = 10.2 Hz, 1H), 4.67 (d, J = 9.8 Hz, 1H), 4.62–4.52 (m, 3H), 3.80–3.62 (m, 4H), 3.53–3.49 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 138.4, 138.3, 138.0, 133.8, 131.9, 128.9, 128.4, 128.4, 128.3, 128.2, 127.9, 127.8, 127.8, 127.7, 127.6, 127.5, 127.4, 87.4, 86.7, 80.8, 79.1, 77.8, 75.8, 75.4, 75.0, 73.4, 69.0; HRMS (ESI-TOF) m/z: calcd for $C_{40}H_{40}O_5SNa$ $(M+Na)^+$: 655.2494; found: 655.2496.

1.2.9. Methyl 2,3,4-tri-*O*-acetyl-6-deoxy-6-phenylthio-α-D-glucopyranoside (4j)[25]

Yield 89%; gummy mass; $[\alpha]_D^{22}$ +162.3 (c 3.4, $CHCl_3$); FTIR (neat): 1750 (s), 1370 (w), 1245 (m), 1123 (s), 1044 (m), 742 (w) cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.36–7.18 (m, 5H), 5.44 (t, J = 9.7 Hz, 1H), 4.97 (t, J = 9.6 Hz, 1H), 4.92–4.87 (m, 2H), 4.00–3.95 (m, 1H), 3.39 (s, 3H), 3.11 (dd, J = 13.4, 6.7 Hz, 1H), 3.02 (dd, J = 13.7, 8.5 Hz, 1H), 2.06–2.00 (3s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 170.1, 170.0, 169.8, 136.1, 129.4, 129.0, 126.3, 96.4, 72.0, 70.9, 70.0, 68.2, 55.2, 35.8, 20.7, 20.6; HRMS (ESI-TOF) m/z: calcd for $C_{19}H_{24}O_8SNa$ $(M+Na)^+$: 435.1090; found: 435.1090.

1.2.10. Phenyl 2-acetamido-3,4,6-tri-*O*-acetyl-1,2-di-deoxy-1-thio-β-D-glucopyranoside (4k)[26]

Yield 83%; white solid; mp: 195–197 °C; $[\alpha]_D^{22}$ −14.1 (c 4.3, $CHCl_3$); FTIR (KBr): 3304 (w), 1750 (s), 1662 (m), 1559 (w), 1543 (m), 1375 (m), 1243 (s), 1219 (s), 1087 (w), 1047 (m), 913 (w) cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.51–7.48 (m, 2H), 7.30–7.28 (m, 3H), 6.07 (d, J = 9.1 Hz, 1H), 5.25 (d, J = 9.8 Hz, 1H), 5.05 (d, J = 9.7 Hz, 1H), 4.89 (d, J = 10.4 Hz, 1H), 4.23–4.14 (m, 2H), 4.05 (q, J = 9.9 Hz, 1H), 3.78 (m, 1H), 2.07–1.98 (4s, 12H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 171.0, 170.6, 170.2, 169.3, 132.5, 132.3, 128.9, 128.0, 86.5, 75.6, 74.0, 68.5, 62.4, 53.2, 23.2, 20.7, 20.7, 20.5; HRMS (ESI-TOF) m/z: calcd for $C_{20}H_{25}NO_8SNa$ $(M+Na)^+$: 462.1199; found: 462.1199.

1.2.11. Phenyl 2,3,6-tri-*O*-acetyl-4-*O*-(2′,3′,4′,6′-tetra-*O*-acetyl-β-D-galactopyranosyl)-l-deoxy-l-thio-β-D-glucopyranoside (4l)[11,26]

Yield 90%; white solid; mp: 160-162 °C; $[\alpha]_D^{25}$ +35.4 (c 3.6, $CHCl_3$); FTIR (KBr): 1750 (s), 1372 (m), 1231 (s), 1049 (m) cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.48–7.29 (m, 5H), 5.34 (d, J = 3.1 Hz, 1H), 5.22 (t, J = 9.1 Hz, 1H), 5.10 (dd, J = 10.2, 8.0 Hz, 1H), 4.95 (dd, J = 10.4, 3.4 Hz, 1H), 4.90 (t, J = 9.6 Hz, 1H), 4.68 (d, J=10.1 Hz, 1H), 4.54–4.47 (m, 2H), 4.14–4.05 (m, 3H), 3.87 (t, J = 6.7 Hz, 1H), 3.75 (t, J = 9.5 Hz, 1H), 3.67–3.63 (m, 1H), 2.15–1.96 (7s, 21H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 170.3, 170.2, 170.1, 170.0, 169.7, 169.5, 169.0, 133.0, 131.7, 128.8, 128.3, 101.0, 85.4, 76.1, 73.8, 70.9, 70.6, 70.2, 69.0, 66.6, 62.10, 60.8, 20.8, 20.7, 20.6, 20.4; HRMS (ESI-TOF) m/z: calcd for $C_{32}H_{40}O_{17}SNa$ $(M+Na)^+$: 751.1884; found: 751.1884.

1.2.12. Phenyl 2,3,4,6-tetra-*O*-acetyl-1-seleno-β-D-glucopyranoside (5a)[14]

Yield 86%; white solid; mp: 97–99 °C; $[\alpha]_D^{22}$ −54.5 (c 1.5, $CHCl_3$); FTIR (KBr): 1749 (s), 1372 (s), 1253 (w), 1227 (m), 1085 (m), 1044 (s), 910 (w) cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.61 (d, J = 7.48 Hz, 2H), 7.37–7.28 (m, 3H), 5.19 (t, J = 9.3 Hz, 1H), 5.06 (q, J = 9.6 Hz, 2H), 4.89 (d, J = 10.1 Hz, 1H), 4.20–3.67 (m, 3H), 2.07–1.99 (4s, 12H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 170.6, 170.2, 169.4, 169.3, 135.2, 129.0, 128.6, 126.9, 80.9, 76.8, 73.8, 70.7, 68.1, 62.1, 20.8, 20.7, 20.6, 20.5; HRMS (ESI-TOF) m/z: calcd for $C_{20}H_{24}O_9SeNa$ $(M+Na)^+$: 511.0483; found: 511.0485.

1.2.13. Phenyl 2,3,4,6-tetra-*O*-acetyl-1-seleno-β-D-galactopyranoside (5b)[14]

Yield 86%; gummy mass; $[\alpha]_D^{26}$ −5.3 (c 2.1, $CHCl_3$); FTIR (neat): 1750 (s), 1369 (w), 1221 (s), 1081 (w), 1055 (m) cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.64–7.62 (m, 2H), 7.36–7.25 (m, 3H), 5.41 (d, J = 3.2 Hz, 1H), 5.27 (t, J = 10.0 Hz, 1H), 5.02 (dd, J = 9.9, 3.3 Hz, 1H), 4.91 (d, J = 10.1 Hz, 1H), 4.17 (dd, J = 11.3, 6.9 Hz, 1H), 4.10 (dd, J = 11.3, 6.2 Hz, 1H), 3.91 (t, J = 6.6 Hz, 1H), 2.09–1.97 (4s, 12H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 170.3, 170.1, 170.0, 169.5, 134.8, 128.9, 128.3, 127.7, 81.8, 75.4, 71.7, 68.0, 67.3, 61.6, 20.8, 20.6, 20.6; HRMS (ESI-TOF) m/z: calcd for $C_{20}H_{24}O_9Se$+Na $(M+Na)^+$: 511.0483; found: 511.0485.

1.2.14. Phenyl 2,3,4,6-tetra-*O*-benzyl-1-seleno-β-D-glucopyranoside (5c)[24]

Yield 82%; white solid; mp: 77–79 °C; $[\alpha]_D^{26}$ −13.6 (c 0.9, $CHCl_3$); FTIR (KBr): 3448 (s), 1664 (s), 1135 (s), 1065 (s), 732 (m), 694 (m) cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.68 (d, J = 7.1 Hz,

2H), 7.39–7.16 (m, 23H), 4.90–4.80 (m, 5H), 4.72 (d, J = 10.1 Hz, 1H), 4.62–4.51 (m, 3H), 3.79–3.63 (m, 4H), 3.54–3.49 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 138.3, 138.3, 138.0, 137.9, 134.4, 129.0, 128.5, 128.4, 128.4, 128.3, 128.2, 127.9, 127.8, 127.8, 127.8, 127.7, 127.6, 127.5, 86.8, 82.9, 81.3, 80.1, 77.7, 75.8, 75.2, 75.0, 73.4, 68.9; HRMS (ESI-TOF) m/z: calcd for $C_{40}H_{40}O_5SeNa$ $(M+Na)^+$: 703.1939; found: 703.1935.

1.2.15. Methyl 2,3,4-tri-*O*-acetyl-6-deoxy-6-phenylseleno-α-D-glucopyranoside (5d)

Yield 79%; gummy mass; $[\alpha]_D^{26}$ +143.3 (c 3.3, $CHCl_3$); FTIR (neat): 1755 (s), 1371 (m), 1247 (s), 1224 (s), 1067 (m), 1045 (s), 739 (w) cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.51–7.49 (m, 2H), 7.28–7.24 (m, 3H), 5.44 (t, J = 9.6 Hz, 1H), 4.97–4.87 (m, 3H), 4.05–4.00 (m, 1H), 3.42 (s, 3H), 3.06–2.97 (m, 2H), 2.07 (s, 3H), 2.00 (2s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 170.1, 170.0, 169.8, 132.6, 130.4, 129.1, 127.1, 96.5, 72.6, 71.0, 70.0, 68.8, 55.4, 29.2, 20.7, 20.7, 20.7; HRMS (ESI-TOF) m/z: calcd for $C_{19}H_{24}O_8SeNa$ $(M+Na)^+$: 483.0534; found: 483.0530.

1.2.16. Phenyl 2-acetamido-3,4,6-tri-*O*-acetyl-1,2-di-deoxy-1-seleno-β-D-glucopyranoside (5e)[27]

Yield 79%; pale yellow solid; mp: 194–196 °C; $[\alpha]_D$ −29.9 (c 8.8, $CHCl_3$); FTIR (KBr): 3448 (bs), 1745 (s), 1661 (w), 1375 (w), 1243 (s), 1227 (s), 1046 (m), 738 (w) cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.62 (d, J = 6.7 Hz, 2H), 7.32–7.26 (m, 3H), 6.15–6.11 (m, 1H), 5.18 (t, J = 9.7 Hz, 1H), 5.07–5.02 (m, 2H), 4.21–4.11 (m, 3H), 3.72–3.68 (m, 1H), 2.05–1.97 (4s, 12H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 170.1, 170.6, 170.2, 169.3, 134.6, 128.9, 128.2, 128.0, 82.6, 73.6, 68.5, 62.4, 53.9, 23.2, 20.7, 20.7, 20.5; HRMS (ESI-TOF) m/z: calcd for $C_{20}H_{25}NO_8SeNa$ $(M+Na)^+$: 510.0643; found: 510.0645.

1.2.17. Phenyl 2,3,6-tri-*O*-acetyl-4-*O*-(2′,3′,4′,6′-tetra-*O*-acetyl-β-D-galactopyranosyl)-l-deoxy-l-seleno-β-D-glucopyranoside (5f)[14]

Yield 83%; white solid; mp: 77–79 °C; $[\alpha]_D^{23}$ −29.6 (c 5.5, $CHCl_3$); FTIR (KBr): 1751 (s), 1371 (m), 1231 (s), 1054 (m), 910 (w) cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.59 (d, J = 7.8 Hz, 2H), 7.36–7.27 (m, 3H), 5.34 (d, J = 1.9 Hz, 1H), 5.18 (t, J = 9.0 Hz, 1H), 5.09 (dd, J = 10.1, 8.2 Hz, 1H), 4.96–4.85 (m, 3H), 4.52 (d, J = 11.8 Hz, 1H), 4.46 (d, J = 7.9 Hz, 1H), 4.14–4.04 (m, 3H), 3.86 (t, J = 6.7 Hz, 1H), 3.73 (t, J = 9.5 Hz, 1H), 3.63–3.59 (m, 1H), 2.14–1.96 (6s, 21H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 170.3, 170.2, 170.1, 170.0, 169.7, 169.6, 169.0, 135.2, 128.9, 128.4, 126.9, 100.9, 80.7, 77.7, 76.0, 73.6, 71.1, 70.9, 70.6, 69.0, 66.5, 62.0, 60.7, 20.8, 20.8, 20.7, 20.6, 20.6, 20.5; HRMS (ESI-TOF) m/z: calcd for $C_{32}H_{40}O_{17}SeNa$ $(M+Na)^+$: 799.1328; found: 799.1326.

1.2.18. (2*R*,3*R*,4*S*,5*R*,6*S*)-2-(Acetoxymethyl)-6-{[(2*R*,3*R*,4*S*,5*R*,6*S*)-4,5-diacetoxy-2-(acetoxymethyl)-6-[(4-methyl-2-oxo-2*H*-chromen-7-yl)thio]tetrahydro-2*H*-pyran-3-yl]oxy}tetrahydro-2*H*-pyran-3,4,5-triyl triacetate (4m)[6]

Yield 86%; white solid; mp: 205–207 °C; $[\alpha]_D^{25}$ −4.8 (c 1.0, $CHCl_3$); FTIR (KBr): 3481 (br), 2959 (w), 1750 (s), 1604 (w), 1374 (m), 1230 (s), 1168 (w), 1041 (s), 955 (w) cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.50 (d, J = 8.6 Hz, 2H), 7.27–7.25 (m, 1H), 6.28 (s, 1H), 5.24 (t, J = 8.9 Hz, 1H), 5.16 (t, J = 9.3 Hz, 1H), 5.07 (t, J = 9.6 Hz, 1H), 5.01–4.92 (m, 2H), 4.81 (d, J = 10.1 Hz, 1H), 4.59 (d, J = 11.7 Hz, 1H), 4.52 (d, J = 8.0 Hz, 1H), 4.38 (dd, J = 12.5, 4.1 Hz, 1H), 4.13 (dd, J = 12.0, 5.6 Hz, 1H), 4.04 (dd, J = 12.5, 1.7 Hz, 1H), 3.80–3.66 (m, 3H), 2.42–1.99 (6s, 24H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 170.6, 170.5, 170.3, 169.7, 169.5, 169.4, 169.2, 160.3, 153.6, 151.9, 138.0, 126.4, 124.7, 119.2, 118.3, 115.2, 100.9, 84.7, 77.3, 76.3, 73.5, 73.0, 72.1, 71.6, 69.8, 67.8, 62.1, 61.6, 20.9, 20.8, 20.7, 20.6, 20.5, 18.6; HRMS (ESI-TOF) m/z: calcd for $C_{36}H_{42}O_{19}SNa$ $(M+Na)^+$: 833.1939; found: 833.1940.

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Supplementary data

Supplementary data associated with this article can be found, in the online version, at http://dx.doi.org/10.1016/j.carres.2014.07.011.

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