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Synthesis of seleno-carbohydrates derived from D-galactose

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ABSTRACT

The synthesis of seleno-galactopyranosides in a short and efficient manner is described, starting from the parent carbohydrate D-galactose. The approach described allows the synthesis of small libraries of compounds with a number of structural variations at the group attached to selenium. Compounds with aryl, propargyl, allyl, acyl, and alkyl substituents are described.

1. Introduction

Selenium is an essential biological element and it is present in several enzymes, such as glutathione peroxidase (GPx), thioredoxin reductase (TrxR), and formate dehydrogenase.[1–5] It is known that the selenium atom plays a key role in the mode of action of such proteins, which cannot be played by its closest relative, sulfur.[6] Selenium has been shown to be involved in a number of important biological processes ranging from cancer prevention,[7,8] redox regulation,[9] aging,[10] and immunology to male reproduction.[11–13]

In light of the important biological activities of selenium compounds, the incorporation of selenium into small organic molecules has received much attention in recent years. The toxicology and pharmacology of these compounds, as well as their ability to mimic the catalytic behavior of natural enzymes, have been widely studied.[14–17] Nevertheless, efficient methods for the incorporation of selenium atoms into carbohydrate frameworks are still limited, despite the interesting synthetic and biological potential of carbohydrates containing selenium in their structures.[18–22] Examples already reported in the literature show that seleno-carbohydrates are effective depigmenting compounds, inhibiting melanin synthesis in melan-A cells, in similar levels to phenylthiourea, which is a well-known inhibitor of such a process.[23] In addition, selenosugars have also been detected in human urine as a metabolite for the excretion of selenium.[24] The incorporation of selenium into nucleosides has also been accomplished and the seleno-nucleosides have been found to display important biological profiles, including activities against HIV-1 (human immunodeficiency virus type-1) and HBV (hepatitis B virus) 2.[25,26] Moreover, the replacement of an oxygen atom by selenium, in the nucleoside framework served as an anomalous scattering center, thus facilitating the 3-dimensional structure determination of nucleic acids by X-ray crystallography experiments.[27–31]

From the synthetic point of view, carbohydrates presenting an organoselenium group at the anomeric position have been described to act as selective glycosylating agents in the synthesis of oligosaccharides,[32–34] and as useful intermediates for the synthesis of functionalized glycals,[35] C-glycosides,[36] and glycoconjugates.[37] In this context, we recently described an easy, straightforward synthetic route for the preparation of a series of chiral seleno-xylofuranosides, starting from the readily available carbohydrate D-xylose.[38] Among the seleno-furanosides prepared, diselenide **2** significantly reduced the in vitro activity of the δ-aminolevulinate dehydratase (δ-ALA-D) enzyme, whereas the phenyl-substituted selenide **1** increased the activity of the enzyme, showing promising anti-oxidant activity.

In connection with our recent interest in the chemistry of carbohydrate derivatives,[38–41] we decided to expand the scope of our previous work to the synthesis of galactopyranoside derivatives containing a selenium moiety in their structures. Keeping in mind the importance of the synthesis of small libraries of compounds with different structural motifs for biological screening, the work described herein provides a useful extension of our methodology to substrates with a different, more hindered, carbohydrate scaffold (Fig. 1).[42]

2. Results and discussion

Initially, the synthesis of an appropriate precursor for the introduction of the selenium atom was needed. This was conveniently

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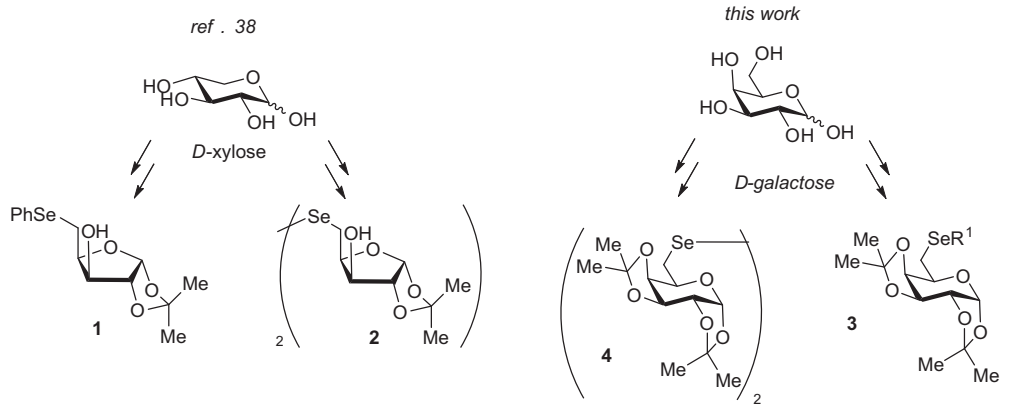
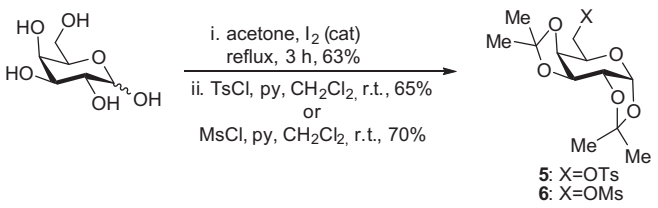


Figure 1. Structures of selenium-containing carbohydrates.

achieved in a short synthetic sequence involving protection of D-galactose as a *bis*-acetonide by treatment with acetone, in the presence of catalytic amounts of iodine.[43] The primary hydroxyl group was then converted to the corresponding tosylate **5** and mesylate **6** in good yield, by reaction with the corresponding sulfonyl chloride in the presence of pyridine as base (Scheme 1).

The tosylate **5** was then subjected to a reaction with phenylselenide nucleophile to introduce the selenium atom in the carbohydrate framework (Table 1). The conditions initially studied were those successfully applied in the xylofuranoside synthesis.[38] Thus, the phenylselenide nucleophile was generated in situ from the corresponding diphenyl diselenide, by reduction with $NaBH_4$, in a 3:1 mixture of THF and ethanol, and the substitution was carried out under reflux. Surprisingly, under these standard conditions, the desired seleno-carbohydrate **3a** was formed in only 25% yield (Table 1, entry 1), and most of the starting material was recovered unchanged. Experiments conducted using ethanol alone, did not result in any formation of the desired product (entry 2). We then tried to conduct the nucleophilic substitution reaction under more forcing conditions, by increasing the amount of the selenium nucleophile in the reaction mixture. The use of 0.8 equiv of diphenyl diselenide (1.6 equiv of $PhSe^-$) resulted in an increase in the yield to 56% (entry 3). Changing the co-solvent from ethanol to *t*-butanol or methanol did not result in improvements in the yield of the product (entries 4 and 5). The use of a more powerful PhSeNa nucleophile, generated from the reaction of $(PhSe)_2$ with metallic sodium in THF–HMPA, resulted in very low conversion.[44] In all reactions, after prolonged heating, a yellow color was observed in the solution, indicating the reoxidation of the selenide anion back to the diphenyl diselenide. Thus, using the standard conditions followed by addition of an excess of $NaBH_4$ after 12 h, furnished the best results using the tosylate as leaving group, and the seleno-carbohydrate **3a** was obtained in a moderate 68% yield (entry 7).

The resistance of the tosylate **5** to undergo nucleophilic substitution prompted us to investigate the behavior of the analogous mesylate as the precursor for the synthesis of the desired seleno-galactopyranosides. Gratifyingly, when mesylate **6** was treated



Scheme 1.

with the phenylselenide nucleophile, clean substitution occurred and the desired product was isolated in excellent yield (entry 8). Again, introduction of an excess $NaBH_4$ after 12 and 18 h was necessary to achieve full conversion and high yield of the product.

With this optimal condition in hand, we extended the protocol to additional selenium nucleophiles and high yields of the desired products were achieved (Table 2, entries 1–5). The developed protocol allowed the synthesis of arylseleno-carbohydrates with chloro (**3b**) and methoxy (**3c**) substituents, as well as with the 2-thienyl (**3d**) and benzyl (**3e**) groups. The reaction is also efficient with a sulfur nucleophile,[45] which results in the thio-galactopyranoside **7** in very high yield (entry 6).

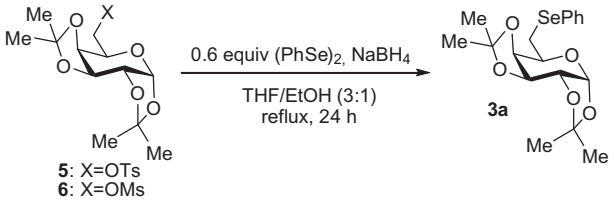
The reaction of tosylate **5** with lithium diselenide,[46,47] was also performed. In this case, the tosylate was found to be a good leaving group, and the reaction occurred smoothly to afford the galactopyranoside diselenide in 87% yield (Scheme 2). The high yield achieved for this reaction contrasts with the low yields observed for the reaction of tosylate **5** with the phenylselenide nucleophile (see Table 1, entries 1–5). The easier reaction with Li_2Se_2 might be attributed to the smaller size of the nucleophile when compared with the $PhSe^-$, thus minimizing steric interactions during the nucleophilic attack.

To further expand the scope of seleno-carbohydrates prepared, the diselenide **4** was treated with sodium borohydride, and the resulting selenide anion was trapped with several electrophiles leading to functionalized seleno-pyranosides (Scheme 3). The reaction with propargyl and allyl bromide proceeded smoothly and the corresponding products **8** and **9** were isolated in 75% and 76% yield, respectively. When the electrophile used was benzoyl chloride, the corresponding selenol ester **10** was obtained in 86% isolated yield. Selenol esters have recently found interest in the investigation of new molecular materials with liquid crystalline and fluorescent properties.[48] Finally, the conjugate addition of the soft selenide nucleophile to methyl acrylate was pursued.[49,50] Unexpectedly, the product isolated from this reaction was the primary alcohol instead of the Michael adduct. Presumably, the conjugate addition of selenide occurred and the resulting product was reduced by the excess of sodium borohydride.[51] Thus, the seleno-carbohydrate **11** containing a free primary alcohol was isolated in 83% yield. It is worth mentioning that the seleno-carbohydrates **8–11** can be used as a synthetic handle for further functionalization through, for example, metal-catalyzed reactions such as the Sonogashira[52] and Heck[53] reactions or dipolar cycloadditions with organic azides (click chemistry).[54]

3. Conclusions

In summary, we have described herein a short and efficient synthesis of selenium-containing carbohydrates, derived from D-gal-

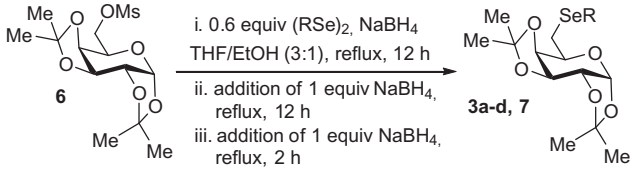
Table 1
Optimization of the reaction conditions for the synthesis of seleno-carbohydrate **3a**



Entry	Substrate	Variation from standard conditions	Yield[a] (%)
1	**5**	None	25
2	**5**	Only EtOH as solvent	No reaction
3	**5**	0.8 equiv (PhSe)2	56
4	**5**	0.8 equiv $(PhSe)_2$, *t*-BuOH instead of EtOH	46
5	**5**	0.8 equiv $(PhSe)_2$, MeOH instead of EtOH	25
6	**5**	$(PhSe)_2$/Na as nucleophile, THF/HMPA as solvent	20
7	**5**	Addition of 1 equiv of $NaBH_4$ after 12 h and 18 h	68
8	**6**	Addition of 1 equiv of $NaBH_4$ after 12 h and 18 h	96

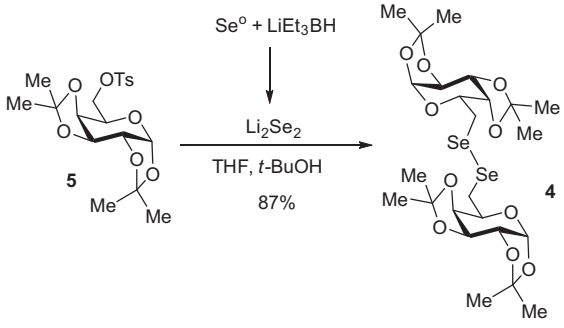
[a] Isolated yields.

Table 2
Synthesis of seleno-galactopyranosides **3a–e** and thio-galactopyranosides **7**

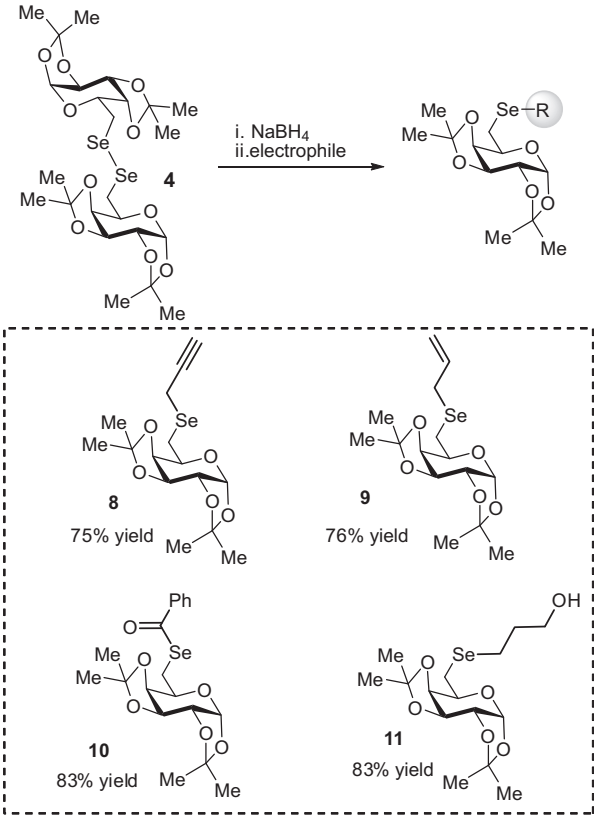


Entry	RSe	Yield[a] (%)
1	PhSe (**3a**)	96
2	*p*-ClPhSe (**3b**)	93
3	*p*-MeOPhSe (**3c**)	91
4	2-thienylSe (**3d**)	93
5	BnSe (**3e**)	98
6[b]	PhS (**7**)	95

[a] Isolated yields.
[b] Reaction performed with $(PhS)_2$ instead of $(PhSe)_2$.



Scheme 2. Synthesis of diselenide 4.



Scheme 3. Synthesis of functionalized seleno-galactopyranosides **8–11**.

actose, which broadens the scope of our methodology previously described for the synthesis of seleno-xylofuranosides. The extension of our methodology to a broader range of carbohydrates permits a straightforward access to seleno-carbohydrates with different structural motifs. We believe that this approach may have significant importance in the design of new selenium-containing carbohydrates and also for biological screenings, particularly concerning their anti-oxidant properties and inhibition of melanin synthesis.

4. Experimental

4.1. General procedures

^1H and ^{13}C NMR spectra were recorded at 300 and 75 MHz respectively with tetramethylsilane as internal standard. Low res-

olution mass spectra were recorded on a Shimadzu GCMS-QP5050 instrument in EI-mode. High resolution mass spectra were recorded on a Bruker Daltonics Micro-TOF instrument in ESI-mode. Column chromatography was performed using Merck Silica Gel (230–400 mesh) following the methods described by Still.[55] Thin layer chromatography (TLC) was performed using Merck Silica Gel GF254, 0.25 mm thickness. For visualization, TLC plates were either placed under ultraviolet light, or stained with iodine vapor, or acidic vanillin. THF was dried over sodium benzophenone ketyl and distilled prior to use. CH_2Cl_2 was distilled from phosphorus pentoxide. All other solvents were used as purchased unless otherwise noted. Tosylate **5** and mesylate **6** were prepared according to literature procedures.[43,56] Yields refer to chromatographically and spectroscopically homogeneous materials with purity of >95%, as judged by ^{1}H NMR spectroscopy.

4.2. General procedure for the preparation of selenocarbohydrates 3a–e and 7

Under an argon atmosphere, sodium borohydride was added to a solution of the diorganoildiselenide (0.18 mmol) in THF (1 mL). MeOH (1 mL) was then dropwise added and the clear solution formed was stirred at room temperature for 10 min. After this time a solution of the mesylate **6** (0.3 mmol in 2 mL THF) was added dropwise. After stirring for 12 h under reflux, $NaBH_4$ (1 equiv) was added and the reaction was stirred under reflux for 6 h. After this time, a second portion of $NaBH_4$ (1 equiv) was added and the reaction mixture was heated at reflux for 2 h, and quenched by the addition of aq satd NH_4Cl (10 mL), and extracted with CH_2Cl_2 (3×15 mL). The combined organic layers were dried with $MgSO_4$, filtered, and concentrated. The crude product was purified by flash chromatography eluting with a mixture of hexanes–EtOAc (90:10).

4.2.1. 6-Deoxy-1,2:3,4-di-*O*-isopropylidene-6-phenylselenyl-α-D-galactopyranose (3a)

Yellow solid, yield: 96%, $[\alpha]_D^{20}$ −73.5 (*c* 1, $CHCl_3$), ^{1}H NMR ($CDCl_3$, 300 MHz) δ: 7.56–7.50 (m, 2H, Ar), 7.26–7.20 (m, 3H, Ar), 5.52 (d, *J* = 5.0 Hz, 1H, H-1), 4.59 (dd, *J* = 7.8 Hz, 2.3 Hz, 1H, H-3), 4.42 (dd, *J* = 7.9 Hz, 1.7 Hz, 1H, H-4), 4.22 (dd, *J* = 5.0 Hz, 2.4 Hz, 1H, H-2), 3.86 (td, *J* = 8.1 Hz, 1.7 Hz, 1H, H-5), 3.13–3.10 (m, 2H, CH_2), 1.45 (s, 3H, CH_3), 1.33 (s, 3H, CH_3), 1.27 (s, 3H, CH_3), 1.24 (s, 3H, CH_3). ^{13}C NMR ($CDCl_3$, 75 MHz) δ: 132.4, 129.4, 128.8, 126.6, 108.8, 108.2, 96.4, 71.2, 70.7, 70.2, 66.7, 26.5, 25.7, 25.4, 24.6, 24.1. GC–MS (70 eV) *m/z* (%): 43 (100), 59 (44), 71 (40), 85 (41), 100 (50), 113 (32), 127 (15), 400 (32). HRMS-ESI: *m/z* calcd for $C_{18}H_{24}O_5Se + Na^+$: 423.0681; found: 423.0680.

4.2.2. 6-(*p*-Chloro-phenylselenyl)-6-deoxy-1,2:3,4-di-*O*-isopropylidene-α-D-galactopyranose (3b)

Yellow oil, yield: 93%, $[\alpha]_D^{20}$ −68.4 (*c* 1, $CHCl_3$). ^{1}H NMR ($CDCl_3$, 300 MHz) δ: 7.47–7.44 (m, 2H, Ar), 7.23–7.20 (m, 2H, Ar), 5.52 (d, *J* = 5.0 Hz, 1H, H-1), 4.59 (dd, *J* = 7.8 Hz, 1.7 Hz, 1H, H-3), 4.37 (dd, *J* = 7.8 Hz, 0.8 Hz, 1H, H-4), 4.27–4.24 (m, 1H, H-2), 3.81 (t, *J* = 6.7 Hz, 1H, H-5), 3.14–4.11 (m, 2H, CH_2), 1.45 (s, 3H, CH_3), 1.33 (s, 3H, CH_3), 1.28 (s, 6H, $2 \times CH_3$). ^{13}C NMR ($CDCl_3$, 75 MHz) δ: 134.1, 133.2, 129.1, 128.0, 109.3, 108.5, 96.7, 71.6, 71.0, 70.5, 67.1, 27.3, 25.9, 25.6, 24.8, 24.4. GC-MS (70 eV) *m/z* (%): 43 (100), 59 (42), 71 (34), 85 (37), 100 (47), 113 (30), 127 (15), 434 (13). HRMS-ESI: *m/z* calcd for $C_{18}H_{23}ClO_5Se + Na^+$: 457.0291; found: 457.0294.

4.2.3. 6-Deoxy-1,2:3,4-di-*O*-isopropylidene-6-(*p*-methoxy-phenylselenyl)-α-D-galactopyranose (3c)

Yellow oil, yield: 91%, $[\alpha]_D^{20}$ −55.3 (*c* 1, $CHCl_3$). ^{1}H NMR ($CDCl_3$, 300 MHz) δ: 7.23 (d, *J* = 8.6 Hz, 2H, Ar), 6.75 (d, *J* = 8.0 Hz, 2H, Ar), 5.53 (d, *J* = 5.0 Hz, 1H, H-1), 4.61 (dd, *J* = 7.8 Hz, 2.3 Hz, 1H, H-3), 4.36–4.33 (m, 2H, H-4, H-2), 3.90 (td, *J* = 7.3 Hz, 1.3 Hz, 1H, H-5), 3.79 (s, 3H, OCH_3), 2.72–2.69 (m, 2H, CH_2), 1.54 (s, 3H, CH_3), 1.52 (s, 3H, CH_3), 1.34 (s, 3H, CH_3), 1.33 (s, 3H, CH_3).^{13}C NMR ($CDCl_3$, 75 MHz) δ: 158.4, 131.3, 129.9, 113.9, 109.1, 108.5, 96.6, 71.9, 71.0, 70.5, 68.4, 55.2, 27.1, 26.1, 26.0, 24.8, 24.4. GC-MS (70 eV) *m/z* (%): 43 (20), 59 (5), 77 (3), 91 (2), 121 (100). HRMS-ESI: *m/z* calcd for $C_{19}H_{26}O_6Se + Na^+$: 453.0787; found: 453.0791.

4.2.4. 6-Deoxy-1,2:3,4-di-*O*-isopropylidene-6-(2-thienylselenyl)-α-D-galactopyranose (3d)

Orange oil, yield: 93%, $[\alpha]_D^{20}$ −55.6 (*c* 1, $CHCl_3$). ^{1}H NMR ($CDCl_3$, 300 MHz) δ: 7.33 (dd, *J* = 5.2 Hz, 1.1 Hz, 1H, Ar), 7.26 (dd, *J* = 3.5 Hz, 1.1 Hz, 1H, Ar), 6.90 (dd, *J* = 5.3 Hz, 3.5 Hz, 1H, Ar), 5.51 (d, *J* = 5.0 Hz, 1H, H-1), 4.61 (dd, *J* = 7.8 Hz, 2.4 Hz, 1H, H-3), 4.42 (dd, *J* = 7.8 Hz, 1.8 Hz, 1H, H-4), 4.28 (dd, *J* = 5.0 Hz, 2.4 Hz, 1H, H-2), 3.87 (td, *J* = 7.1 Hz, 1.8 Hz, 1H, H-5), 3.06–2.92 (m, 2H, CH_2), 1.44 (s, 3H, CH_3), 1.35 (s, 3H, CH_3), 1.34 (s, 3H, CH_3), 1.29 (s, 3H, CH_3). ^{13}C NMR ($CDCl_3$, 75 MHz) δ: 135.8, 130.7, 127.9, 123.3, 109.2, 108.5, 96.6, 71.5, 71.0, 70.5, 66.9, 30.6, 25.9, 25.7, 24.9, 24.4. GC–MS (70 eV) *m/z* (%): 43 (100), 59 (45), 71 (34), 85 (64), 100 (24), 113 (21), 127 (24), 406 (17). HRMS-ESI: *m/z* calcd for $C_{16}H_{22}O_5SSe + Na^+$: 429.0245; found: 429.0254.

4.2.5. 6-(Benzylselenyl)-6-deoxy-1,2:3,4-di-*O*-isopropylidene-α-D-galactopyranose (3e)

Orange solid, yield: 98%, $[\alpha]_D^{20}$ −67.1 (*c* 1, $CHCl_3$). ^{1}H NMR ($CDCl_3$, 300 MHz) δ: 7.29–7.25 (m, 5H, Ar), 5.53 (d, *J* = 5.0 Hz, 1H, H-1), 4.62–4.59 (m, 1H, H-3), 4.32–4.29 (m, 2H, H-4, H-2), 3.90–3.85 (m, 3H, H-5, CH_2), 2.78–2.67 (m, 2H, CH_2), 1.52 (s, 3H, CH_3), 1.45 (s, 3H, CH_3), 1.34 (s, 3H, CH_3), 1.33 (s, 3H, CH_3). ^{13}C NMR ($CDCl_3$, 75 MHz) δ: 139.3, 128.8, 128.4, 126.6, 109.2, 108.5, 96.6, 71.9, 71.0, 70.5, 68.4, 27.6, 26.1, 25.9, 24.8, 24.4, 23.0. GC–MS (70 eV) *m/z* (%): 43 (63), 59 (29), 71 (19), 91 (100), 100 (15), 113 (15). HRMS-ESI: *m/z* calcd for $C_{19}H_{26}O_5Se + Na^+$: 437.0838; found: 437.0850.

4.2.6. 6-Deoxy-1,2:3,4-di-*O*-isopropylidene-6-phenylthio-α-D-galactopyranose (7)

Yellow oil, yield: 95%, $[\alpha]_D^{20}$ −97.8 (*c* 1, $CHCl_3$). ^{1}H NMR ($CDCl_3$, 300 MHz) δ: 7.40–7.37 (m, 2H, Ar), 7.28–7.23 (m, 2H, Ar), 7.18–7.13 (m, 1H, Ar), 5.51 (d, *J* = 5.0 Hz, 1H, H-1), 4.59 (dd, *J* = 7.9 Hz, 2.4 Hz, 1H, H-3), 4.37 (dd, *J* = 7.9 Hz, 1.8 Hz, 1H, H-4), 4.28 (dd, *J* = 5.0 Hz, 2.4 Hz, 1H, H-2), 3.84 (td, *J* = 6.9 Hz, 1.7 Hz, 1H, H-5), 3.17–3.15 (m, 2H, CH_2), 1.45 (s, 3H, CH_3), 1.34 (s, 3H, CH_3), 1.27 (s, 3H, CH_3), 1.23 (s, 3H, CH_3). ^{13}C NMR ($CDCl_3$, 75 MHz) δ: 135.7, 129.4, 128.9, 126.1, 109.3, 108.5, 96.6, 71.2, 70.8, 70.5, 66.1, 33.2, 25.9, 25.6, 24.8, 24.4. GC–MS (70 eV) *m/z* (%): 43 (83), 59 (46), 71 (100), 85 (22), 100 (21), 109 (12), 123 (44), 352 (21). HRMS-ESI: *m/z* calcd for $C_{18}H_{24}O_5S + Na^+$: 375.1237; found: 375.1241.

4.3. Procedure for the synthesis of diselenide (4)

Under an argon atmosphere, dithium diselenide was generated by reaction of gray elemental selenium (95 mg, 1.2 mmol) with lithium triethylborohydride (1.2 mL, 1.2 mmol). The suspension was allowed to stir for at least 20 min, and *t*-BuOH (0.2 mL) and THF (4 mL) were added, followed by dropwise addition of a solution of tosylate **5** (0.5 mmol) in THF (1 mL). The resulting solution was stirred for 24 h at room temperature. The mixture was quenched by the addition of a satd NH_4Cl solution (20 mL), extracted with CH_2Cl_2, and the combined organic fractions were collected, dried over $MgSO_4$, and filtered, the solvent was removed in vacuo. The crude product was purified by flash chromatography (hexane–EtOAc 50:50) to afford the diselenide **4**.

4.3.1. Bis-(6-deoxy-1,2:3,4-di-*O*-isopropylidene-α-D-galactopyranos-6-yl) diselenide (4)

Orange solid, yield: 87%, $[\alpha]_D^{20}$ −62.1 (*c* 1, $CHCl_3$). ^1H NMR ($CDCl_3$, 300 MHz) *δ*: 5.52 (d, *J* = 4.9 Hz, 2H, H-1), 4.63 (dd, *J* = 7.8 Hz, 2.3 Hz, 2H, H-3), 4.37 (dd, *J* = 7.9 Hz, 1.7 Hz, 2H, H-4), 4.31 (dd, *J* = 5.0 Hz, 2.3 Hz, 2H, H-2), 4.04 (td, *J* = 6.8 Hz, 1.6, 2H, H-5), 3.21–3.09 (m, 4H, CH_2), 1.56 (s, 6H, CH_3), 1.44 (s, 6H, CH_3), 1.34 (s, 6H, CH_3), 1.32 (s, 6H, 2 × CH_3). ^{13}C NMR ($CDCl_3$, 75 MHz) *δ*: 109.2, 108.7, 96.6, 71.7, 71.0, 70.5, 68.1, 29.6, 29.1, 26.0, 24.9, 24.4. GC–MS (70 eV) *m/z* (%): 43 (100), 59 (38), 71 (4), 85 (44), 100 (5), 113 (5), 127 (26), 185 (4). HRMS-ESI: *m/z* calcd for $C_{24}H_{38}O_{10}Se_2 + Na^+$: 669.0688; found: 669.0676.

4.4. General procedure for the synthesis of functionalized seleno-pyranosides 8–11

Under an argon atmosphere, sodium borohydride was added to a solution of diselenide **4** (0.1 mmol) in THF (3 mL). MeOH (1 mL) was then dropwise added and the clear solution formed was stirred at room temperature for 10 min. After this time a solution of the appropriate electrophile (2 equiv) was added dropwise. After stirring for 24 h at room temperature, the reaction mixture was quenched by the addition of aq satd NH_4Cl (5 mL) and the solution was extracted with CH_2Cl_2 (3 × 10 mL). The combined organic layers were dried with $MgSO_4$, filtered, and concentrated. The crude product was purified by flash chromatography eluting with a mixture of hexanes–EtOAc (90:10) and (60:40) in the case of **11**.

4.4.1. 6-Deoxy-1,2:3,4-di-*O*-isopropylidene-6-propargylselenyl-α-D-galactopyranose (8)

Yellow oil, yield: 75%. $[\alpha]_D^{20}$ −59.8 (*c* 1, $CHCl_3$). ^1H NMR ($CDCl_3$, 300 MHz) *δ*: 5.54 (d, *J* = 5.0 Hz, 1H, H-1), 4.62 (dd, *J* = 7.9 Hz, 2.4 Hz, 1H, H-3), 4.36 (dd, *J* = 7.8 Hz, 1.8 Hz, 1H, H-4), 4.31 (dd, *J* = 5.0 Hz, 2.4 Hz, 1H, H-2), 3.97 (td, *J* = 7.1 Hz, 1.7 Hz, 1H, H-5), 3.27–3.24 (m, 2H, CH_2), 3.03–2.91 (m, 2H, CH_2), 2.25–2.23 (m, 1H, CH), 1.54 (s, 3H, CH_3), 1.45 (s, 3H, CH_3), 1.35 (s, 3H, CH_3), 1.33 (s, 3H, CH_3). ^{13}C NMR ($CDCl_3$, 75 MHz) *δ*: 109.2, 108.5, 96.6, 80.9, 72.0, 71.2, 71.0, 70.4, 67.7, 26.0, 25.9, 24.8, 24.4, 23.9, 7.4. GC-MS (70 eV) *m/z* (%): 43 (100), 59 (43), 71 (25), 85 (24), 100 (19), 113 (20), 127 (7), 362 (4). HRMS-ESI: *m/z* calcd for $C_{15}H_{22}O_5Se + Na^+$: 385.0525; found: 385.0533.

4.4.2. 6-Allylselenyl-6-deoxy-1,2:3,4-di-*O*-isopropylidene-α-D-galactopyranose (9)

Yellow oil, yield: 76%. $[\alpha]_D^{20}$ −62.4 (*c* 1, $CHCl_3$). ^1H NMR ($CDCl_3$, 300 MHz) *δ*: 5.93–5.84 (m, 1H, CH), 5.53 (d, *J* = 5.0 Hz, 1H, H-1), 5.08–4.98 (m, 2H, CH_2), 4.61 (dd, *J* = 7.8 Hz, 2.3 Hz, 1H, H-3), 4.35 (dd, *J* = 7.8 Hz, 1.8 Hz, 1H, H-4), 4.29 (dd, *J* = 5.0 Hz, 2.4 Hz, 1H, H-2), 3.90–3.85 (m, 1H, H-5), 3.24–3.21 (m, 2H, CH_2), 2.72 (dd, *J* = 7.2 Hz, 1.2 Hz, 2H, CH_2), 1.54 (s, 3H, CH_3), 1.45 (s, 3H, CH_3), 1.35 (s, 3H, CH_3), 1.33 (s, 3H, CH_3). ^{13}C NMR ($CDCl_3$, 75 MHz) *δ*: 134.7, 116.2, 109.0, 108.3, 96.6, 71.7, 70.8, 70.3, 66.0, 26.3, 25.9, 25.8, 24.7, 24.3, 22.2. GC–MS (70 eV) *m/z* (%): 41 (47), 43 (100), 59 (54), 71 (30), 85 (27), 100 (24), 113 (21), 364 (17). HRMS-ESI: *m/z* calcd for $C_{15}H_{24}O_5Se + Na^+$: 387.0681; found: 387.0676.

4.4.3. 6-Benzoylselenyl-6-deoxy-1,2:3,4-di-*O*-isopropylidene-α-D-galactopyranose (10)

Orange oil, Yield: 86%. $[\alpha]_D^{20}$ −23.0 (*c* 1, $CHCl_3$). ^1H NMR ($CDCl_3$, 300 MHz) *δ*: 7.91–7.88 (m, 2H, Ar), 7.60–7.54 (m, 1H, Ar), 7.46–7.41 (m, 2H, Ar), 5.53 (d, *J* = 4.9 Hz, 1H, H-1), 4.63 (dd, *J* = 7.8 Hz, 2.4 Hz, 1H, H-3), 4.35 (dd, *J* = 7.8 Hz, 1.7 Hz, 1H, H-4), 4.29 (dd, *J* = 5.0 Hz, 2.4 Hz, 1H, H-2), 4.01–3.96 (m, 1H, H-5), 3.32–3.25 (m, 2H, CH_2), 1.48 (s, 3H, CH_3), 1.44 (s, 3H, CH_3), 1.37 (s, 3H, CH_3), 1.3 (s, 3H, CH_3). ^{13}C NMR ($CDCl_3$, 75 MHz) *δ*: 194.3, 138.7, 133.4, 128.5, 126.9, 109.2, 108.5, 96.4, 72.4, 70.9, 70.4, 67.4, 25.8, 25.7, 25.3, 24.8, 24.2. GC-MS (70 eV) *m/z* (%): 43 (17), 59 (5), 77 (13), 85 (2), 105 (100), 113 (2). HRMS-ESI: *m/z* calcd for $C_{19}H_{24}O_6Se + Na^+$: 451.0630; found: 451.0629.

4.4.4. 6-Deoxy-6-(3-hydroxypropylselenyl)-1,2:3,4-di-*O*-isopropylidene-α-D-galactopyranose (11)

Yellow oil, yield: 83%. $[\alpha]_D^{20}$ −58.0 (*c* 1, $CHCl_3$). ^1H NMR ($CDCl_3$, 300 MHz) *δ*: 5.53 (d, *J* = 4.8 Hz, 1H, H-1), 4.61 (dd, *J* = 7.9 Hz, 2.7 Hz, 1H, H-3), 4.35 (dd, *J* = 7.9 Hz, 1.8 Hz, 1H, H-4), 4.29 (dd, *J* = 5.0 Hz, 2.3 Hz, 1H, H-2), 3.93 (td, *J* = 6.9 Hz, 1.8 Hz, 1H, H-5), 3.74 (t, *J* = 6.0 Hz, 2H, CH_2O), 2.79–2.73 (m, 4H, 2 × CH_2), 1.95 (qui, *J* = 6.6 Hz, 2H, CH_2), 1.53 (s, 3H, CH_3), 1.45 (s, 3H, CH_3), 1.34 (s, 3H, CH_3), 1.33 (s, 3H, CH_3). ^{13}C NMR ($CDCl_3$, 75 MHz) *δ*: 109.2, 108.5, 96.6, 71.9, 70.9, 70.4, 68.6, 62.0, 32.0, 26.0, 25.9, 24.8, 24.4, 23.0, 20.8. GC–MS (70 eV) *m/z* (%): 43 (100), 59 (43), 71 (33), 85 (20), 100 (34), 113 (23), 127 (12), 382 (8). HRMS-ESI: *m/z* calcd for $C_{15}H_{26}O_6Se + Na^+$: 405.0787; found: 405.0792.

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