Selenoglycosides. 3.[1] Synthesis of Phenyl 2-(*N*-Acetylamino)- and 2-Azido-2-deoxy-1-seleno-α-D-glycopyranosides *via* Azido-phenylselenylation of Diversely Protected Glycals

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Two methods are described for the preparation of diversely protected phenyl 2-azido-2-deoxy-α-D-selenoglycopyranosides from protected glycals. In the first one (method A), a peracetylated glycal is treated with sodium azide and diphenyl diselenide in the presence of (diacetoxyiodo)benzene in dichloromethane at rt. With 3,4,6-tri-*O*-acetyl-1,5-anhydro-2-deoxy-D-*arabino*-hex-1-enitol (tri-*O*-acetyl-D-glucal) an inseparable mixture of phenyl 2-azido-2-deoxy-α-*gluco*- and -α-*manno*-selenoglycosides is obtained (91% yield). With 3,4,6-tri-*O*-acetyl-1,5-anhydro-2-deoxy-D-*lyxo*-hex-1-enitol (tri-*O*-acetyl-D-galactal) only the α-*galacto* isomer is obtained (92%). Method A is not compatible with benzyl groups. In method B, a perbenzylated glycal is reacted with trimethylsilyl azide and tetra-*n*-butylammonium fluoride in the presence of *N*-phenylselenophthalimide. From protected D-glucal a *gluco/manno* mixture is obtained, whereas only the *galacto* isomer is formed from protected D-*galactal* (75% yield). The compatibility of method B with a variety of protecting groups is exemplified with 6-*O*-acetyl, 6-*O*-benzyl, and 6-*O*-(*tert*-butyldimethylsilyl)-3,4-*O*-isopropylidene-1,5-anhydro-2-deoxy-D-*lyxo*-hex-1-enitol. The same diastereocontrol is observed, and the α-D-*galacto* isomer is obtained (60–70% yield). Reduction of the azido group of these selenoglycosides with 1,3-propanedithiol in the presence of triethylamine and acetylation affords the corresponding phenyl 2-(*N*-acetylamino)-2-deoxy-α-D-selenoglycopyranosides in good yield.

Oligosaccharides containing one or several 2-amino-2-deoxyglycopyranoside unit(s) are widely distributed in living organisms, and they play an important role in recognition mechanisms. Due to the presence of a nitrogen atom at C-2, the classical chemical methods for oligosaccharide synthesis have to be adapted. Many solutions in which different glycosyl donors are employed in the presence of several promotors were proposed and recently reviewed.[2] Since good results were obtained with thioglycosides,[3] the potentialities of phenyl selenoglycosides were recently evaluated for the construction of the glycosidic bond with the "usual" carbohydrates[4,5] and 2-deoxy-2-phthalimido glycosyl donors.[4] These phenyl selenoglycosides were prepared by condensation of peracetylated glycosyl and 2-deoxy-2-phthalimidoglycosyl with phenylselenol in the presence of $BF_3{\cdot}OEt_2$.[4,5]

Due to the nonparticipatory nature of the azido group, it would be of interest to devise an efficient preparation of protected phenyl 2-azido-2-deoxyselenoglycosides as glycosyl donors because, with them, the stereochemical outcome of the glycosidation would be different. We recently reported a stereocontrolled synthesis of phenyl as well as alkyl α- or β-selenoglycosides in which a glycosyl halide is condensed with diphenyl or dialkyl diselenide under reducing conditions.[6] Rather than employing the same methodology which would necessitate the preparation of 2-azido-2-deoxyglycosyl halides as intermediates, we turned our attention to the azido-phenylselenylation of glycals.

Azido-phenylselenylation of double bonds is a very powerful and versatile reaction because it allows the one-step introduction of two functionalities in the molecule.[7,8] Moreover, with unsymmetrical olefins, the regioselectivity can be controlled. When the reaction is initiated by electrophilic phenylselenium species (*e.g.*, PhSeCl) in the presence of azide ion, Markovnikov adducts are prevalent.[7] Recently, Tingoli *et al.* obtained anti-Markovnikov addition products by treatment of an olefin with sodium azide and diphenyl diselenide in the presence of (diacetoxyiodo)benzene.[8] They proposed a mechanism initiated by addition to the olefin of an azido radical formed by oxidation of the azido ion. The regioselectivity of this second approach was expected to afford the desired 2-azido-2-deoxyselenoglycosides which may function as precursors of 2-amino-2-deoxyselenoglycosides. Preliminary results were already disclosed,[1] and we now report full details and extension to several glycals containing a variety of protecting groups often employed in oligosaccharide synthesis.[9]

Results and Discussion

When 3,4,6-tri-*O*-acetyl-D-glucal (**1a**) and 3,4,6-tri-*O*-acetyl-D-galactal (**2a**) were reacted with (diacetoxyiodo)-benzene and sodium azide in the presence of diphenyl diselenide at rt, phenyl 3,4,6-tri-*O*-acetyl-2-azido-2-deoxy-

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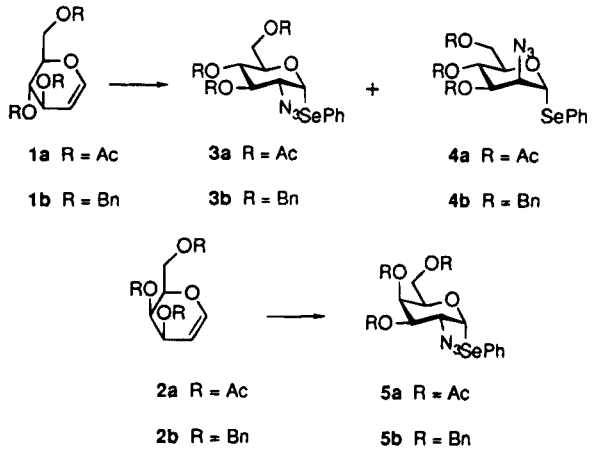
Scheme 1



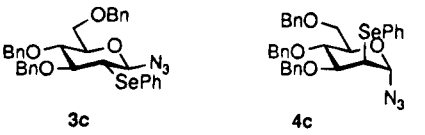
1-seleno-α-D-glycopyranosides were obtained in good yield (method A, Experimental Section). From **1a**, an inseparable mixture of *gluco* and *manno* isomers was obtained in 91% yield (Scheme 1). The diastereoisomeric products were readily distinguished by examining the H-1 signals in the ^{1}H NMR spectrum, and the proportions were found to be 3:2. Interestingly, only the α-anomers were formed, as indicated by the values of the H-1, H-2 coupling constants (5.3 Hz for the *gluco* isomer **3a** and ≈0 Hz for the *manno* isomer **4a**). From **2a**, only the α-*galacto* isomer **5a** was obtained in crystalline form (92%). No *talo* isomer could be detected in the ^{1}H NMR spectrum of the crude mixture, although it is known that some *talo* azidonitrate (4−8%) is formed during azidonitration of protected D-galactal.[10,11] These results are in good agreement with a rapid addition of electrophilic azido radical,[12] formed by oxidation of azide ion, to C-2 of the electron rich double bond affording an anomeric radical stabilized in the α-configuration by anomeric effect. Further homolytic reaction with $(PhSe)_2$ affords the α-selenoglycosides.

Attempts of azido-phenylselenylation of perbenzylated glycals **1b**[13] and **2b**[14] under the same conditions were not very successful, and the yield of perbenzylated 2-azido-2-deoxyselenoglycoside was low in agreement with recent results.[9] This could be due to oxidative cleavage of the benzyl groups under the reaction conditions.

Since the redox potentials of azide ion[15] and benzyl groups[16] are close it was not possible to us to selectively generate azido radical from azido ion in the presence of benzyl groups.

For comparison of spectroscopic data with the Markovnikov adduct, azido-phenylselenylation was also carried out with azide ion in the presence of PhSeCl according to Hassner.[7] With "disarmed"[17] tri-*O*-acetyl-D-glucal **1a**, the reaction was very slow in agreement with the ionic mechanism proposed by Hassner.[7] With "armed"

Chart 1



perbenzylated-D-glucal **1b**, the reaction was faster and a mixture of 3,4,6-tri-*O*-benzyl-2-deoxy-2-(phenylseleno)-β-D-glucopyranosyl azide (**3c**) and 3,4,6-tri-*O*-benzyl-2-deoxy-2-(phenylseleno)-α-D-mannopyranosyl azide (**4c**) was obtained (Chart 1). The same regioselectivity affording **3c** and **4c** in similar proportions was observed when *N*-(phenylseleno)phthalimide (*N*-PSP) was employed instead of PhSeCl in the presence of sodium azide. No appreciable change was observed with PhSeCl in the presence of trimethylsilyl azide (2 equiv) and of tetra-*n*-butylammonium fluoride (0.2 equiv) in CH_2Cl_2. Interestingly, in this solvent, the opposite regioselectivity was observed with *N*-PSP in the presence of trimethylsilyl azide (2 equiv) and tetra-*n*-butylammonium fluoride (0.2 equiv). In the latter case a mixture of perbenzylated phenyl 2-azido-2-deoxy-1-seleno-α-D-*gluco*- and -*manno*pyranosides (**3b**) and (**4b**) was obtained in 82% yield. Although more work is necessary to understand and rationalize them, similar changes in regioselectivity in azido-phenylselenylation were already observed with exocyclic alkenes.[18]

The structure of compounds **3c** and **4c** was established by ^{1}H NMR spectroscopy and comparison of the data with those obtained for selenoglycosides **3b** and **4b**. The chemical shifts of H-1 (5.95 and 5.85 ppm) and H-2 (3.85 and 4.2 ppm) for **3b** and **4b** are in agreement with the values already reported for selenoglycosides by us[6] and others[5,19] and azido-sugars.[20] The presence of the azido group at C-2 was further confirmed by transformation into 2-(*N*-acetylamino)-2-deoxyselenoglycosides (*vide infra*). In the spectra of glycopyranosyl azides **3c** and **4c** the signals of the anomeric protons (H-2 of β-*gluco* isomer **3c** δ 4.53, $J_{1,2}$ = 10.28 Hz in $CDCl_3$; H-1 of the α-*manno* isomer **4c** δ 5.50 ppm, $J_{1,2}$ = 2.16 Hz in $CDCl_3$) cleary indicate the regio and stereochemistry of the reaction. The location of the phenylseleno group at C-2 was confirmed by a strong shielding of H-2 in **3c** and **4c** (H-2, δ 3.00 and 3.65 ppm, respectively).

It should be noted that compounds **3c** and **4c** resulted from a *trans*-Markovnikov azido-phenylselenylation in agreement with Hassner et al.[7] The anti-Markovnikov addition exclusively affords the α-selenoglycosides **3b** and **4b** (as well as **5b** *vide infra*).

When **2b** was treated under the same conditions (method B, Experimental Section), the α-*galacto* isomer **5b** was obtained as the sole product (75% yield). The *galacto* configuration was unambigously determined by ^{1}H NMR (H-1, δ 6.0 ppm, $J_{1,2}$ = 5.4 Hz in $CDCl_3$), and no *talo* isomer was formed. It was verified that the regioselectivity in the two methods of azido-phenylselenylation were the same by transformation of **5a** into **5b** by deacetylation followed by benzylation (see Experimental Section).

The interest of this methodology and its compatibility with many protecting groups were further exemplified

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(14) This compound was prepared by deacetylation of **2a** (MeONa, MeOH, 100%) followed by benzylation (NaH, BnBr, DMF, 83%): mp 51−53 °C, $[\alpha]_D$ −4.04° (*c* 1, CH_2Cl_2).
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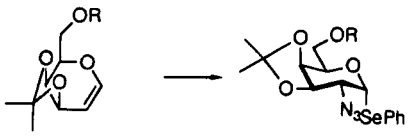
Scheme 2



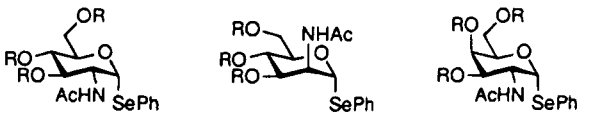
6 R = H

6a R = Ac 7a R = Ac

6b R = Bn 7b R = Bn

6c R = t-BuMe$_2$Si 7c R = t-BuMe$_2$Si

Chart 2



8a R = Ac 9a R = Ac 10a R = Ac

8b R = Bn 9b R = Bn 10b R = Bn

with diversely protected D-galactal derivatives **6a**,[21] **6b**,[21] and **6c** (Scheme 2). Azido-phenylselenylation of **6a** according to method A was very slow, but the same diastereocontrol was observed and the α-*galacto* isomer **7a** was obtained (50% yield). Better results were obtained with method B which afforded **7a** and **7b** from **6a** and **6b** as the sole product (72–76% yield). For **6c**, tetra-*n*-butylammonium fluoride was omitted and the reaction time was longer than for **6a** and **6b** and the yield of **7c** slightly lower (60%). It was verified that the regioselectivity of the reaction was the same with both methods by transformation of **7c** into **7a** by desilylation and acetylation (see Experimental Section). The *galacto* configuration of 2-azido-2-deoxy-α-D-selenoglycopyranosides **7a**, **7b**, and **7c** was confirmed by the values of coupling constants of H-2 with H-1 (≈5 Hz indicating a *cis* relationship) and with H-3 (6–7 Hz in agreement with values already reported for 3,4-*O*-isopropylidene derivatives[21]). Transformation of these 2-azido-2-deoxyselenoglycosides into 2-(*N*-acetylamino)-2-deoxyselenoglycosides was achieved for confirmation of the position of the azido group and for preparation of 2-amino-2-deoxyglycosyl donors bearing a participating group at C-2. Reduction of the azido group with hydrogen under catalytic conditions was not possible because of the presence of selenium. Reduction with 1,3-propanedithiol according to Bayley et al.[22] was efficient although the basic conditions (triethylamine) induced partial deacetylation of acetylated derivatives. Interestingly, when the mixture of **3a** and **4a** obtained from **1a** was treated under these conditions and reacetylated, the *gluco* isomer **8a** could be separated from the *manno* isomer **9a** by column chromatography (Chart 2). This was not the case for the benzylated derivatives **8b** and **9b**. The *galacto* derivatives **5a** and **5b** were transformed into **10a** and **10b** (75–80% yield).

In the ^{1}H NMR spectra of these compounds, the chemical shift of H-1 was not significantly changed which confirmed the presence of selenium at the anomeric carbon. The chemical shift of H-2 (4–4.9 ppm) is in agreement with values reported for 2-(*N*-acetylamino)-2-deoxyhexopyranoside derivatives.[23]

Conclusion

In conclusion, we have presented two high-yielding methods for azido-phenylselenylation of glycals leading to 2-azido-2-deoxyselenoglycosides. Method A involving radical azide is compatible with acetates as protecting groups but not with benzyl ethers and acetals. Another method, compatible with a variety of protecting groups including benzyl and silyl ethers as well as acetals, was developed. In both cases mixtures of *gluco* and *manno* isomers were obtained from protected D-glucal whereas only the *galacto* isomer was formed from D-galactal. The latter point is of particular importance for the preparation of 2-azido-2-deoxy galactopyranosyl donors to be employed in oligosaccharides synthesis.

Experimental Section

Optical rotations were measured in a 10-cm cell at 22 °C. Analytical TLC was performed on Merck aluminum precoated plates of silica gel 60 F-254 with detection by UV and by spraying with 6 N H_2SO_4 and heating about 2 min at 300 °C. For flash chromatography, Merck silica gel 60 (230–400 mesh) and anhydrous solvents were employed. Solvents were evaporated under reduced pressure in a rotary evaporator below 30 °C.

Microanalyses were performed at the Service de Microanalyse de l'Université Pierre et Marie Curie.

N-(Phenylseleno)phthalimide (*N*-PSP) was prepared according to Nicolaou et al.[24]

1,5-Anhydro-2-deoxy-3,4-*O*-isopropylidene-6-*O*-(*tert*-butyldimethylsilyl)-D-*lyxo*-hex-1-enitol (6c). To a solution of **6**[21] (500 mg, 2.68 mmol) and imidazole (456 mg, 6.7 mmol) in DMF (5 mL) was added *tert*-butyldimethylsilyl chloride (505 mg, 3.35 mmol). The reaction was stirred at 46 °C for 48 h. The solvent was evaporated, the residue partitioned between H_2O–Et_2O (20 mL, 1:1), and the aqueous phase extracted with ether (2 × 10 mL). The combined Et_2O layer was washed with H_2O (2 × 10 mL) and dried ($MgSO_4$). After evaporation, the residue was purified by flash chromatography. Elution with CH_2Cl_2/hexane (1:4 and 3:7) afforded **6c**: 677 mg (84%), solid; mp 38–40 °C; R_f 0.77 (EtOAc/hexane 1:9); $[\alpha]_D$ −2.6° (*c* 1, CH_2Cl_2); ^{1}H NMR (200 MHz, $CDCl_3$) δ 0.10 (s, 6H), 0.90 (s, 9H), 1.40 (s, 3H), 1.45 (s, 3H), 3.90 (m, 3H), 4.35 (ddd, 1H, $J_{3,4}$ = 6 Hz), 4.60 (dd, 1H, $J_{2,3}$ = 2.7 Hz), 4.75 (ddd, 1H, $J_{1,2}$ = 6.2 Hz, $J_{2,4}$ = 1.6 Hz), 6.30 (d, 1H). Anal. Calcd for $C_{15}H_{28}O_4Si$: C, 59.96; H, 9.39. Found: C, 60.27; H, 9.12.

Typical Procedures for Azido-phenylselenylation. Phenyl 2-azido-2-deoxy-1-seleno-α-D-glycopyranosides were prepared by one of the following methods. **Method A.** To a stirred solution of glycal (1 mmol), diphenyl diselenide (0.6 mmol), and sodium azide (2.4 mmol) in dichloromethane (4 mL) under argon was added (diacetoxyiodo)benzene (1.4 mmol). The mixture was stirred at rt during 48 h until TLC indicated completion of the reaction. The solution was diluted with dichloromethane (20 mL) and washed with 5% aqueous $NaHCO_3$ (2 × 8 mL). The aqueous layer was reextracted with dichloromethane (2 × 5 mL), and the organic layer was washed until neutral pH, dried over $MgSO_4$, filtered, and evaporated. The crude product was purified by column chromatography on silica gel. **Method B.** To a stirred solution of glycal (1 mmol), azidotrimethylsilane (2 mmol), and tetra-*n*-butylammonium fluoride (0.2 mmol) in dichloromethane (10 mL) under argon was added *N*-PSP (2 mmol). The mixture was stirred at room temperature during 48 h. The solvent was evaporated, toluene (15 mL) was added, the precipitated salts were filtered,

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and the crude mixture was concentrated and purified by column chromatography on silica gel. The following 2-azido-2-deoxy-1-seleno-α-D-glycopyranosides were prepared using one of the aforementioned procedures.

Phenyl 3,4,6-Tri-*O*-acetyl-2-azido-2-deoxy-1-seleno-α-D-glucopyranoside (3a) and -α-D-mannopyranoside (4a). Method A: yield (91%), oil; R_f 0.75 (CH_2Cl_2/Et_2O 9:1); IR (neat) 2119, 1757, cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) *gluco* isomer δ 2.00−2.20 (3 s, 9H), 3.90−4.00 (dd, 1H, $J_{6',6}$ = 12.21 Hz, $J_{6,5}$ = 1.96 Hz), 4.00−4.10 (dd, 1H, $J_{2,3}$ = 10.15 Hz), 4.25−4.35 (dd, 1H, $J_{6',5}$ = 4.89 Hz), 4.50 (m, 1H, $J_{5,4}$ = 10.4 Hz), 5.20−5.50 (m, 2H), 5.95 (d, 1H, $J_{1,2}$ = 5.39 Hz); 7.15−7.20 (m, 5H), *manno* isomer δ 2.10−2.30 (3s, 9H), 4.20 (2dd, 2H, $J_{6,6'}$ = 12.24 Hz, $J_{6,5}$ = 2.16 Hz, $J_{6',5}$ = 5.15 Hz), 4.37 (dd, 1H, $J_{2,3}$ = 2.95 Hz), 4.45 (m, 1H), 5.25−5.45 (m, 2H), 5.80 (d, 1H, $J_{1,2}$ = 1.27 Hz), 7.20−7.70 (m, 5H). Anal. Calcd for $C_{18}H_{21}O_7N_3Se$: C, 45.96; H, 4.50; N, 8.93. Found: C, 46.35; H, 4.47; N, 9.00.

Phenyl 3,4,6-Tri-*O*-acetyl-2-azido-2-deoxy-1-seleno-α-D-galactopyranoside (5a). Method A: yield (92%), solid; mp 104−105 °C; R_f 0.75 (CH_2Cl_2/Et_2O 9:1); $[\alpha]_D$ +170° (*c* 1, CH_2Cl_2); IR (KBr) 2119, 1757 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 2.20 (3s, 9H), 4.05 (2dd, 2H, $J_{6,5}$ = 5.9 Hz, $J_{6',5}$ = 7.1 Hz, $J_{6,6'}$ = 11.4 Hz), 4.30 (dd, 1H, $J_{2,3}$ = 10.8 Hz), 4.70 (bt, 1H), 5.15 (dd, 1H, $J_{3,4}$ = 3.2 Hz), 5.50 (dd, 1H, $J_{4,5}$ = 1.1 Hz), 6.00 (d, 1H, $J_{1,2}$ = 5.4 Hz), 7.20−7.70 (m, 5H). Anal. Calcd for $C_{18}H_{21}O_7N_3Se$: C, 45.96; H, 4.50; N, 8.93. Found: C, 46.06; H, 4.50; N, 9.08.

Phenyl 2-Azido-3,4,6-tri-*O*-benzyl-2-deoxy-1-seleno-α-D-glucopyranoside (3b) and -α-D-mannopyranoside (4b). Method B: yield (82%), oil; R_f 0.75 (CH_2Cl_2/hexane 9:1); IR (neat) 2119 cm^{-1}; ^1H NMR δ 3.50−4.30 (m, 6H), 4.40−5.00 (m, 6H), 5.85 (bs, 0.5H), 5.95 (d, 0.5H, $J_{1,2}$ = 4.98 Hz), 7.00−7.70 (m, 20H). Anal. Calcd for $C_{33}H_{33}O_4N_3Se$: C, 64.49; H, 5.41; N, 6.83. Found: C, 64.43; H, 5.48; N, 7.00.

Phenyl 2-Azido-3,4,6-tri-*O*-benzyl-2-deoxy-1-seleno-α-D-galactopyranoside (5b). Method B: yield (75%), oil; R_f 0.75 (CH_2Cl_2/hexane 9:1); $[\alpha]_D$ +157° (*c* 1, CH_2Cl_2); IR (neat) 211 cm^{-1}; ^1H NMR δ 3.40−3.65 (m, 3H), 3.75 (dd, 1H, $J_{3,2}$ = 10.48 Hz, $J_{3,4}$ = 2.65 Hz), 4.05 (d, 1H), 4.30−5.00 (m, 7H), 5.93 (d, 1H, $J_{1,2}$ = 5.22 Hz) 7.10−7.70 (m, 20H). Anal. Calcd for $C_{33}H_{33}O_4N_3Se$: C, 64.49; H, 5.41; N, 6.83. Found: C, 64.59; H, 5.59; N, 7.02.

Phenyl 6-*O*-Acetyl-2-azido-2-deoxy-3,4-*O*-isopropylidene-1-seleno-α-D-galactopyranoside (7a). Method B: yield (72%), solid; mp 86−88 °C; R_f 0.59 (EtOAc/hexane 1:4); $[\alpha]_D$ +237.7° (*c* 1, CH_2Cl_2); IR (KBr) 2119, 1750 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) 1.15 (1s, 3H), 1.25 (1s, 3H), 2.00 (1s, 3H), 4.00 (t, 1H, $J_{4,5}$ = 1.65 Hz, $J_{5,6}$ = 5.5 Hz, $J_{5,6'}$ = 4.91 Hz), 4.10−4.20 (m, 4H), 4.30 (dd, 1H, $J_{2,3}$ = 6.05 Hz), 5.90 (d, 1H, $J_{1,2}$ = 4.95 Hz), 7.10−7.80 (m, 5H). Anal. Calcd for $C_{17}H_{21}O_5N_3Se$: C, 47.89; H, 4.96; N, 9.86. Found: C, 47.98; H, 4.96; N, 9.99.

Phenyl 2-Azido-6-*O*-benzyl-2-deoxy-3,4-*O*-isopropylidene-1-seleno-α-D-galactopyranoside (7b). Method B: yield (76%), oil; R_f 0.57 (EtOAc/hexane 1:9); $[\alpha]_D$ +202.8° (*c* 1, CH_2Cl_2); IR (neat) 2119 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) 1.40 (1s, 3H) 1.55 (1s, 3H), 3.70−3.90 (m, 2H, $J_{5,6}$ = 6.61 Hz, $J_{5,6'}$ = 5,11 Hz, $J_{6,6'}$ = 12.3 Hz), 4.00 (t, 1H, $J_{4,5}$ = 1.4 Hz), 4.05−4.45 (m, 2H), 4.60 (dd, 2H), 4.70 (1H, $J_{2,3}$ = 6.91Hz), 5.90 (d, 1H, $J_{1,2}$ = 4.95 Hz), 7.00−7.60 (m, 10H). Anal. Calcd for $C_{22}H_{25}O_4N_3Se$: C, 55.69; H, 5.31; N, 8.86. Found: C, 55.62; H, 5.28; N, 9.00.

Phenyl 2-Azido-2-deoxy-3,4-*O*-isopropylidene-6-*O*-(*tert*-butyldimethylsilyl)-1-seleno-α-D-galactopyranoside (7c). Method B: yield (60%), oil; R_f 0.56 (EtOAc/hexane 1:12); $[\alpha]_D$ +170.3° (*c* 1, CH_2Cl_2); IR (neat) 2119 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 0.00 (1s, 6H), 0.80 (1s, 9H) 1.35 (1s, 3H), 1.50 (1s, 3H), 3.65−3.95 (m, 3H, $J_{6,6'}$ = 10.2 Hz, $J_{5,6}$ = 6.6 Hz, $J_{5,6'}$ = 6.4 Hz, $J_{2,3}$ = 7.7 Hz), 4.10−4.30 (m, 2H, $J_{3,4}$ = 5.3 Hz, $J_{4,5}$ = 2.36 Hz), 4.45 (m, 1H), 5.75 (d, 1H, $J_{1,2}$ = 5.02 Hz), 7.1−7.7 (m, 5H). Anal. Calcd for $C_{21}H_{33}O_4N_3SeSi$: C, 50.59; H, 6.67; N, 8.42. Found: C, 50.33; H, 6.77; N, 8.34.

3,4,6-Tri-*O*-benzyl-2-deoxy-2-(phenylseleno)-β-D-glucopyranosyl and -α-D-mannopyranosyl Azides (3c) and (4c). To a stirred solution of **1b** (208 mg, 0.5 mmol) and NaN_3 (130 mg, 2 mmol) in DMF (5 mL) under argon was added PhSeCl (260 mg, 2 mmol). After 24 h of stirring at rt, TLC indicated completion of the reaction. The solvent was evaporated and the residue partitioned between H_2O−Et_2O (15 mL, 1:1) and the aqueous phase extracted with ether (2 × 5 mL). The combined Et_2O layer was washed with H_2O (2 × 5 mL) and dried ($MgSO_4$). After evaporation of the solvent, the crude mixture was chromatographed on silica gel. Elution with Et_2O/hexane (1:9) afforded **4c**: 77 mg, (25%) oil; R_f 0.40 (hexane/Et_2O 9:1); $[\alpha]_D$ +22.5° (*c* 1, CH_2Cl_2); IR (neat) 2110 cm^{-1}; ^1H-NMR δ 3.60−3.70 (dd, 1H, $J_{2,1}$ = 2.16 Hz, $J_{2,3}$ = 4.40 Hz), 3.30−4.00 (m, 4H), 4.00−4.10 (dd, 1H, $J_{3,4}$ = 7.87 Hz), 4.40−4.90 (m, 6H), 5.53 (d, 1H, $J_{1,2}$ = 2.16 Hz), 7.00−7.70 (m, 20H). Anal. Calcd for $C_{33}H_{33}O_4N_3Se$: C, 64.49; H, 5.41; N, 6.83. Found: C, 64.47; H, 5.50; N, 6.80.

Further elution with the same eluent afforded **3c**: 90 mg, (29%) oil; R_f 0.26 (hexane/Et_2O 9:1); $[\alpha]_D$ −4.4° (*c* 1, CH_2Cl_2); IR (neat) 2110 cm^{-1}; ^1H-NMR δ 3.00 (t, 1H, $J_{2,1}$ = $J_{2,3}$ = 10.28 Hz), 3.75−3.40 (m, 5H), 4.53 (d, 1H), 4.57 (dd, 2H, J = 12.15 Hz), 4.68 (dd, 2H, J = 10.74 Hz), 4.98 (dd, 2H, J = 10.29 Hz), 7.00−7.70 (m, 20 H). Anal. Calcd for $C_{33}H_{33}O_4N_3Se$: C, 64.49; H, 5.41; N, 6.83. Found: C, 64.47; H, 5.50; N, 6.80.

Phenyl 2-(*N*-Acetylamino)-3,4,6-tri-*O*-acetyl-2-deoxy-1-seleno-α-D-glucopyranoside (8a) and -mannopyranoside (9a). To a stirred solution of a mixture of **3a** and **4a** (235 mg, 0.5 mmol) in MeOH (2 mL) were added 1,3-propanedithiol (250 μL, 2.5 mmol) and Et_3N (350 μL, 2.5 mmol).[22] After the mixture was stirred at rt for 24 h, TLC indicated completion of the reaction. Solvent was evaporated, the crude product was dissolved in anhydrous pyridine (1.3 mL), and Ac_2O (650 μL, 7 mmol) was added. After workup, the crude product was chromatographed on silica gel. Elution with EtOAc/hexane (1:1) afforded **8a**: 102 mg (42%), syrup; R_f 0.41 (CH_2Cl_2/MeOH 60:1); $[\alpha]_D$ +139.1° (*c* 1, CH_2Cl_2); IR (neat) 3324, 1757, 1660, 1550 cm^{-1}; ^1H NMR δ 1.90 (1s, 3H), 2.00 (1s, 9H), 4.00 (dd, 1H, $J_{5,6}$ = 2.1 Hz, $J_{6,6'}$ = 12.26 Hz), 4.30 (dd, 1H, $J_{5,6'}$ = 4.7 Hz), 4.40 (m, 1H, $J_{4,5}$ = 9.53 Hz), 4.50 (m, 1H, $J_{2,3}$ = 10.6 Hz), 5.00−5.30 (m, 2H), 5.80 (d, 1H, $J_{2,NH}$ = 8.31 Hz), 6.00 (d, 1H $J_{1,2}$ = 5.03 Hz), 7.20−7.60 (m, 5H). Anal. Calcd for $C_{20}H_{25}O_8NSe$: C, 49.38; H, 5.18; N, 2.88. Found: C, 49.52; H, 5.37; N, 2.88.

Further elution with the same eluent afforded **9a**: 107 mg (44%), oil; R_f 0.33 (CH_2Cl_2/MeOH 60:1); $[\alpha]_D$ +81.4° (*c* 1, CH_2Cl_2); IR (neat) 3324, 1757, 1660, 1550 cm^{-1}; ^1H NMR δ 2.00−2.20 (4s, 12H), 4.00 (dd, 1H, $J_{5,6}$ = 2.34 Hz, $J_{6,6'}$ = 12.3 Hz), 4.30 (dd, 1H, $J_{5,6'}$ = 5.73 Hz), 4.60 (m, 1H, $J_{4,5}$ = 9.4 Hz), 4.90 (m, 1H, $J_{2,3}$ = 4.07 Hz), 5.10−5.40 (m, 2H), 5.70 (d, 1H, $J_{1,2}$ = 1.2 Hz), 6.00 (d, 1H, $J_{2,NH}$ = 8.7 Hz), 7.20−7.60 (m, 5H). Anal. Calcd for $C_{20}H_{25}O_8NSe$: C, 49.38; H, 5.18; N, 2.88. Found: C, 49.37; H, 5.30; N, 2.70.

Phenyl 2-(*N*-Acetylamino)-3,4,6-tri-*O*-acetyl-2-deoxy-1-seleno-α-D-galactopyranoside (10a). Reduction of **5a** (1 mmol) followed by acetylation as described for **3a** and **4a** and chromatography using (CH_2Cl_2/MeOH 80:1) as eluent gave **10a** (394 mg, 81%) as an oil: R_f 0.41 (CH_2Cl_2/MeOH 60:1); $[\alpha]_D$ +193.1° (*c* 1, CH_2Cl_2); IR (neat) 3324, 1757, 1660, 1550 cm^{-1}; ^1H NMR δ 2.00 (3s, 9H), 2.20 (1s, 3H), 4.00−4.20 (m, 2H), 4.60 (bt, 1H), 4.80 (m, 1H, $J_{2,3}$ = 11.6 Hz), 5.00 (dd, 1H, $J_{3,4}$ = 3.26 Hz), 5.40 (1H), 5.70 (d, 1H, $J_{2,NH}$ = 7.66 Hz), 6.10 (d, 1H, $J_{1,2}$ = 4.9 Hz), 7.20−7.70 (m, 5H). Anal. Calcd for $C_{20}H_{25}O_8NSe$: C, 49.38; H, 5.18; N, 2.88. Found: C, 49.62; H, 5.55; N, 2.72.

Phenyl 2-(*N*-Acetylamino)-3,4,6-tri-*O*-benzyl-2-deoxy-1-seleno-α-D-glucopyranoside (8b) and -mannopyranoside (9b). Reduction of **3b** and **4b** and acetylation as described for **3a** and **4a** followed by chromatography using (CH_2Cl_2/MeOH 60:1) as eluent gave **8b** and **9b** (378 mg, 60%) as a solid: mp 121−123 °C; R_f 0.40 (CH_2Cl_2/MeOH 60:1); IR (KBr) 3324, 1660, 1550 cm^{-1}; ^1H NMR δ 2.40 (1s, 6H), 3.50−40 (m, 6H), 4.10−5.20 (m, 20H), 5.85 (1s, 1H), 5.95 (d, 1H, $J_{1,2}$ = 4.77 Hz), 7.00−7.70 (m, 40H). Anal. Calcd for $C_{35}H_{37}O_5NSe$: C, 66.65; H, 5.91; N, 2.22. Found: C, 66.56; H, 6.19; N, 2.29.

Phenyl 2-(*N*-Acetylamino)-3,4,6-tri-*O*-benzyl-2-deoxy-1-seleno-α-D-galactopyranoside (10b). Reduction of **5b** (1 mmol) as above followed by chromatography using (CH_2Cl_2/MeOH 60:1) as eluent gave **10b** (479 mg, 76%) as a solid: mp 165−167 °C; R_f 0.53 (CH_2Cl_2/MeOH 60:1); $[\alpha]_D$ +186.4° (*c* 1,

CH_2Cl_2); IR (KBr) 3324 (NH), 1660 (amide I), 1550 (amide II) cm^{-1}; ^1H NMR δ 1.90 (1s, 3H), 3.40–3.80 (m, 3H), 4.10 (1H), 4.50 (dd, 1H, $J_{2,3}$ = 9.42 Hz, $J_{3,4}$ = 2.37 Hz), 4.60–5.10 (m, 7H), 5.20 (d, 1H, $J_{2,NH}$ = 6.86 Hz), 6.20 (d, 1H, $J_{1,2}$ = 4.76 Hz), 7.10–7.60 (m, 20H). Anal. Calcd for $C_{35}H_{37}O_5NSe$: C, 66.65; H, 5.91; N, 2.22. Found: C, 66.41; H, 6.18; N, 2.20.

Phenyl 2-Azido-3,4,6-tri-*O*-benzyl-2-deoxy-1-seleno-α-D-galactopyranoside (5b) from 5a. A solution of **5a** (235 mg, 0.5 mmol) and MeONa (1 M, 0.8 mL) in MeOH (1 mL) was stirred at rt until deacetylation was complete (15 h). After neutralization with Amberlite resin IRN 77 (H^+ form) and filtration, evaporation of the solvent afforded a crude product (197 mg) which was dissolved in DMF (2.5 mL). After the mixture was cooled at 0 °C, NaH (60%, 80 mg, 2 mmol) was added. After the mixture was stirred for 1 h, benzyl bromide (200 μL, 1.65 mmol) was added and the mixture stirred at rt until TLC indicated completion of the reaction (15 h). Excess NaH was destroyed with MeOH and the reaction mixture partitioned between H_2O–CH_2Cl_2 (30 mL, 1:1). The aqueous layer was reextracted with CH_2Cl_2 (2 × 5 mL). The combined organic phase was washed with H_2O until neutral pH and dried ($MgSO_4$). Evaporation afforded a residue which was chromatographed on silica gel. Elution with CH_2Cl_2/hexane (1:1) afforded **5a**: 253 mg (82%) as an oil identical to **5a** prepared by azido-phenylselenylation of **2a**.

Phenyl 6-*O*-Acetyl-2-azido-2-deoxy-3,4-*O*-isopropylidene-1-seleno-α-D-galactopyranoside (7a) from 7c. To a solution of **7c** (20 mg, 0.04 mmol) in THF (100 μL) was added n-Bu_4NF (1.1 M THF solution, 35 μL). Completion of the reaction was observed after the solution was stirred for 30 min at rt. After evaporation, the residue was dissolved in pyridine (25 μL), and Ac_2O (12 μL, 0.12 mmol) was added. After the mixture was stirred overnight at rt, evaporation and coevaporation with toluene afforded a residue which was chromatographed on silica gel. Elution with EtOAc/hexane (1:16) afforded crude **7a** (12 mg, 70%). Recrystallization from absolute EtOH afforded an analytical sample identical to **7a** prepared by azido-phenylselenylation of **6a**.

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