Studies on the Zn(II)-mediated Electrophilic Selenocyclization and Elimination of 3,4-*O*-Isopropylidene-protected Hydroxyalkenyl Sulfides: Synthesis of a 2-Phenylselenenyl Glycal

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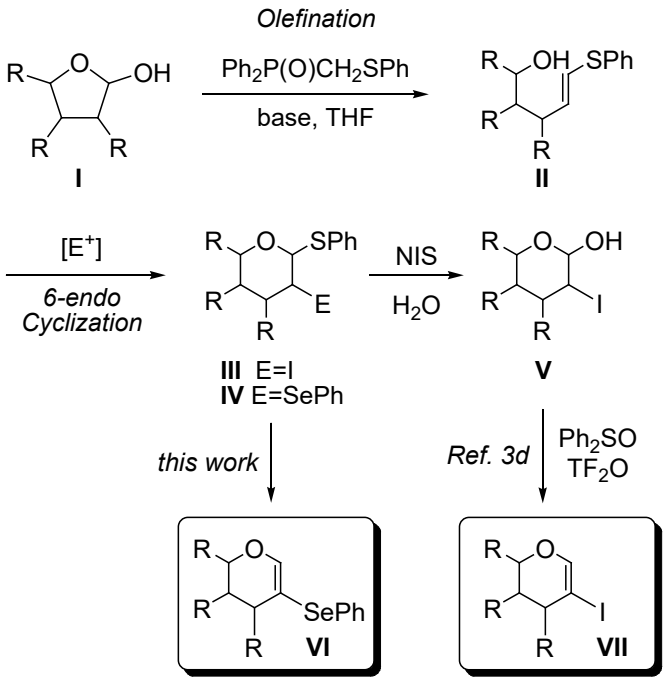
Abstract – Herein we describe a mild and efficient Zn(II)-mediated electrophilic selenocyclization reaction of readily available and stable 3,4-*O*-isopropylidene-protected hydroxyalkenyl sulfides to 2-deoxy-2-phenylselenenyl-1-thio-glycosides. This material was transformed into a 2-phenylselenenyl glycal in a controlled manner using an activation-elimination sequence.

Keywords: Thioglycosides; Glycals; Cyclization; Elimination; Selenium; Selenoglycals

Selenonium-induced cyclization of functionalized hydroxyl- and carboxylic acid-alkenes leading to cyclic ethers and lactones, as well as several cyclization reactions leading to nitrogen heterocycles, are useful methods for the construction of complex organic molecules.[1] Recently, in the context of our ongoing program on the stereoselective synthesis of 2-deoxyglycosides, we have described mechanistic and synthetic studies toward the preparation of 2-deoxy-2-iodo- and 2-deoxy-2-phenylselenenyl-1-thio-glycosides **III** and **IV** from furanoses **I** through a sequence involving olefination and electrophile-induced 6-*endo* cyclization reactions[2] (Scheme 1). In particular, although we have successfully demonstrated high regio- and stereoselectivity in the preparation of 2-deoxy-2-phenylselenenyl-1-thio-glycosides **IV** enhanced by employing 3,4-*O*-isopropylidene as a cyclic bifunctional protecting group, there are some limitations associated with the complex product distribution (thioglycosides, glycals, and 2-phenylselenenyl glycals) obtained under certain conditions (*i.e.* using ZnI_2 as a promoter) giving low overall preparative yields.[2a] We have also demonstrated that 2-deoxy-2-iodopyranoses **V** can be efficiently converted in 2-iodoglycals **VII** (Scheme 1). Interestingly, glycals and 2-substituted glycals are useful building blocks in the preparation of biologically important molecules especially those with configurations difficult to access (*e.g.* D-talal, D-gulal, and D-allal).[3] However, only one publication dealing with the synthesis of 2-phenylselenenyl glycals have been reported to date despite the fact that these products are good candidates for a wide range of selenium-based organic transformations.[4]

Herein, we present the results of our studies aimed toward the development of a mild and efficient Zn(II)-mediated[5] electrophilic selenocyclization of readily available and stable 3,4-*O*-isopropylidene-protected hydroxyalkenyl sulfides. Furthermore, we also report our preliminary results on the sulfonium-mediated elimination of 1-thioglycosides that provide access to 2-phenylselenenyl glycals.

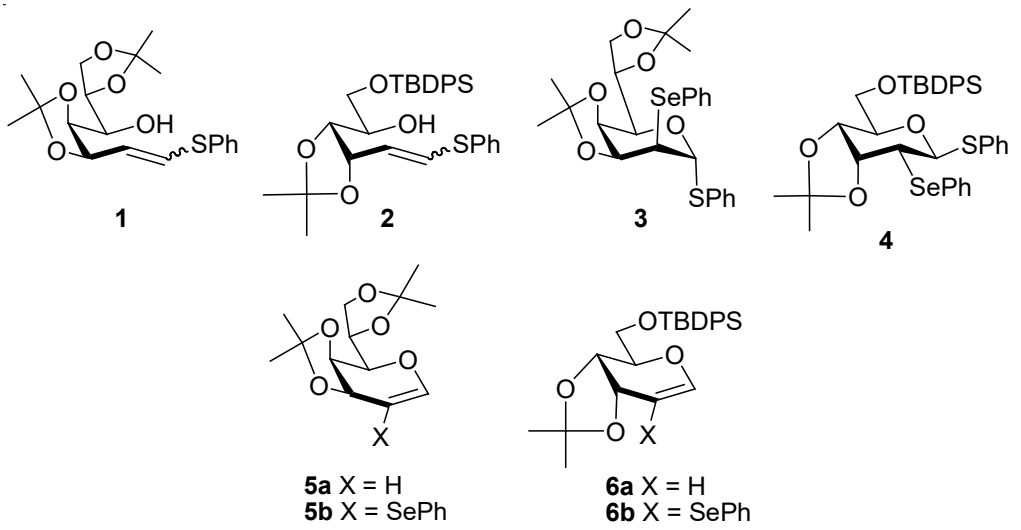


Scheme 1. Proposed synthetic sequence for the preparation of 2-iodo- and 2-phenylselenenyl glycals from furanoses.

Encouraged by the previous results,[2a] we postulated that the presence of a non-nucleophilic counter-ion in the Lewis acid would provide milder cyclization conditions in order to improve the yield and control the product distribution.

Initial cyclization reactions were carried out using hydroxyalkenyl sulfide **1** and *N*-(phenylselenenyl)phthalimide (NPSP)[†] in the absence of a promoter (Table 1, Entry 1). Under these conditions, heptopyranoside **3** (11%) was obtained with complete *α*-selectivity together with 2-phenylselenenyl glycal **5b** (34%). Cyclization with ZnI_2 (2 equiv) as the promoter proceeded smoothly and afforded desired product **3** in good yield (60%) maintaining the same regio- and stereoselectivity (Table 1, Entry 2). $ZnCl_2$ (2 equiv) was also examined as a promoter but resulted in an unsuccessful cyclization reaction (Table 1, Entry 4). Under similar conditions, D-*ribo* derivative **2** afforded thioglycoside **4** in low yield (15%) and complete *β*-selectivity together with glycal **6a**[2a] (74%) as the major product (Table 1, Entry 11).

Table 1. Zn(II)-mediated electrophilic selenocyclization of hydroxyalkenyl sulfides **1** and **2** to obtain 2-deoxy-2-phenylselenenyl thioglycosides **3** and **4**.[a]



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

5a X = H
5b X = SePh

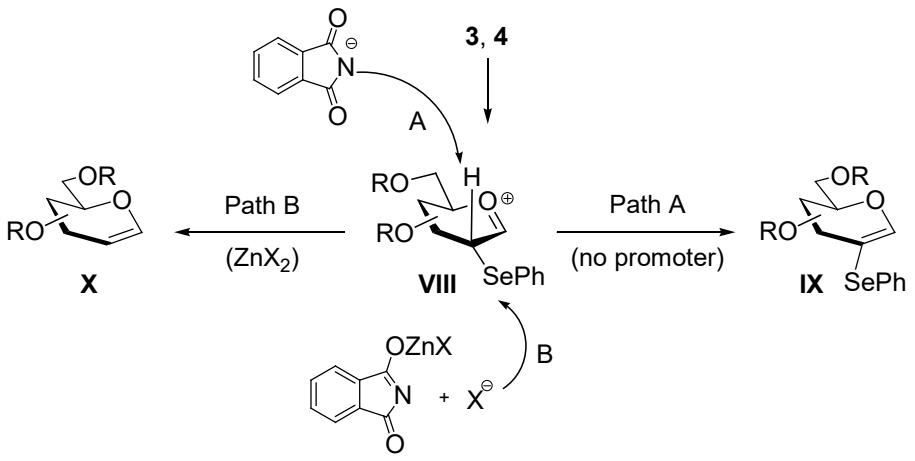
6a X = H
6b X = SePh

Entry	*Z*/*E* ratio[b]	Promoter (equiv)	*T* (ºC)	*t* (h)	Product (%)[c]
1[d]	**1** 0:1	-	rt	15	**3** (11) + **5b** (34)
2[d]	**1** 0:1	ZnI_2 (2)	–65 to –10	3	**3** (60) + **5a** (10)
3	**1** 1:4	ZnI_2 (0.1)	–65 to –10	23	**3** (57)
4[d]	**1** 1:4	$ZnCl_2$ (2)	–65 to reflux	43	mixture
5	**1** 1:4	$Zn(OAc)_2$ (0.1)	–60 to rt	144	**3** (37)[e]
6	**1** 1:4	$Zn(NO_3)_2$ (0.1)	–60 to rt	28	**3** (61)
7[f]	**1** 1:4	$Zn(NO_3)_2$ (0.1)	rt	8	mixture
8	**1** 1:4	$Zn(SO_4)_2$ (0.1)	–60 to rt	50	**3** (7)
9	**1** 1:4	$Zn(OTf)_2$ (0.1)	–60 to rt	8	[g]
10[d]	**2** 1:33	ZnI_2 (2)	–78 to –30	6.5	**4** (15) + **6a** (74)
11	**2** 1:9	$Zn(NO_3)_2$ (0.1)	–60 to rt	96	**4** (80)[h]
12[f]	**2** 1:9	$Zn(NO_3)_2$ (0.1)	rt	96	mixture
13	**2** 1:9	$Zn(NO_3)_2$ (1)	–30 to rt	6	mixture

[a] General conditions: hydroxyalkenyl sulfide (1 equiv), NPSP (1 equiv), promoter (0.1 equiv) in dry CH_2Cl_2 unless otherwise indicated (see Experimental Section for full details). [b] Starting material *Z*/*E* ratio determined by integration of the olefinic proton signals in the ^{1}H NMR spectrum. [c] Yield based on *E*-isomer. [d] Reaction conducted with NPSP (2 equiv). [e] 50% of unreacted starting material was recovered. [f] Reaction conducted in dry CH_3CN. [g] The corresponding 2-phenylselenenyl pyranose was obtained in ca. 50% yield. [h] Reaction product obtained as a 1:1 *α*/*β* mixture.

As we have previously noted,[2a] this product distribution (glycals and 2-phenylselenenyl glycals) can probably be attributed to the reaction between oxocarbenium-ion intermediate **VIII**, in turn obtained upon activation of thioglycosides **3** and **4** with [$SePh^+$], and the different species present in the reaction media (*e.g.* base and nucleophilic counter-ions) as depicted in Scheme 2. The conversion of **VIII** into **IX** represents an overall base-promoted PhSH

elimination process, whereas the production of **X** might be explained in terms of reductive elimination of PhSSePh–PhSeX.



Scheme 2. Plausible mechanism for the observed product distribution during the cyclization of 3,4-*O*-isopropylidene-protected alkenyl sulfides induced by electrophilic selenium species.

Interestingly, catalyst loading was successfully reduced to 0.1 equiv without significant erosion of either yield or selectivity when ZnI_2 was used as a promoter, although longer reaction times were required (Table 1, Entry 3). Furthermore, the use of a catalytic amount of promoter allows the reaction to proceed under milder conditions and therefore reduces the formation of undesired glycals. With this result in hand, we extended our study to other Zn(II) catalysts possessing non-nucleophilic counter-ions. The development of such a cyclization reaction under mild, catalytic conditions would considerably facilitate access to this synthetically useful class of 2-deoxy-2-phenylselenenyl-1-thio-glycosyl donors. Thus, we observed that $Zn(OAc)_2$, $Zn(NO_3)_2$, and $Zn(SO_4)_2$ promoted 6-*endo* electrophilic selenocyclization of hydroxyalkenyl sulfides in

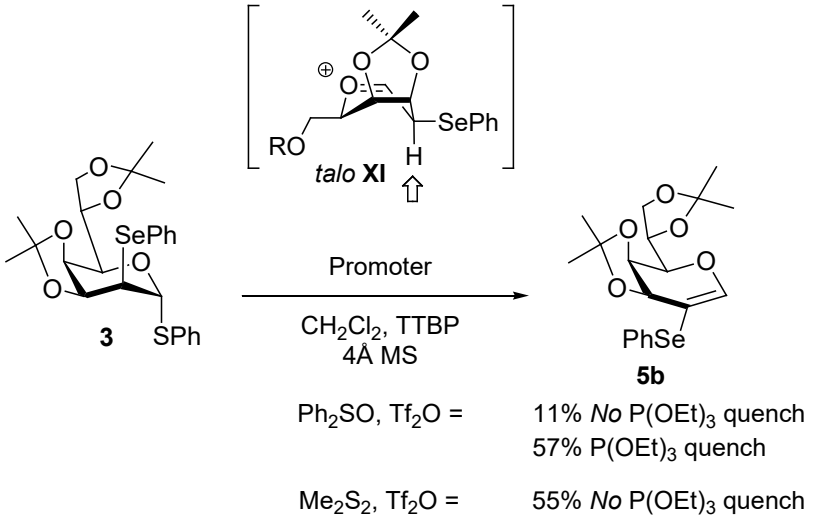
moderate to good yields (Table 1, Entries 5–8 and 11–13), with $Zn(NO_3)_2$ affording products in higher yields (61% and 80% for **3** and **4** respectively) (Table 1, Entries 6 and 11). Additionally, the use of other promoters such as $Zn(OTf)_2$ (0.1 equiv), any increase in the catalyst loading (up to 1 equiv), and changes in solvent polarity (*e.g.* CH_3CN) were detrimental for the efficiency of the cyclization reaction, and no final product was obtained under these conditions (Table 1, Entries 7, 9, 12, and 13). All these transformations provided the corresponding thioglycosyl donors with complete regio- and stereoselectivity, except for D-*ribo* derivative **2** which afforded **4** as a 1:1 *α*/*β* mixture due to an *in situ* anomerization (Table 1, Entry 11).[6] The use of $Zn(OAc)_2$ provided moderate yields but the reaction was very slow (Table 1, Entry 5).

From these results, the following trends were noted; (a) the use of catalytic amounts of promoter, typically 0.1 equiv, afforded clean reactions with no significant changes in either yield or selectivity. Moreover, the formation of undesired glycals is also dramatically reduced and/or suppressed. Although the mechanistic details of this transformation are not fully understood, studies on Zn(II) halide-mediated cyclization of propargylic *N*-hydroxylamines[7] and halkynyl ketones[8] suggested that Zn(II) is likely to coordinate to the corresponding nucleophile (*i.e.* unprotected OH of the hydroxyalkenyl sulfide) therefore facilitating the intramolecular cyclization. Consequently, it would seem reasonable that the nature of the counter-ions[9] affects the equilibrium between free and coordinated Zn(II), thereby influencing the rate of cyclization; (b) The initial reaction temperature is crucial for a successful cyclization. The reaction proceeded smoothly when the temperature was slowly raised from –60 ºC to

room temperature; however attempts performed at higher temperatures gave complex mixtures of products; (c) Since the *Z*/*E* mixtures of starting alkenes proved to be inseparable, the cyclization reactions were assayed directly on the mixture of diastereomers. Interestingly, only *E*-isomers reacted and the corresponding *Z*-isomers were recovered unaltered in all cases. These results were in agreement with those obtained in our laboratory with iodine electrophiles.[2d] In that case, *Z*-isomers underwent cyclization at lower rates and this can be explained by the stereoelectronic effect known as inside-alkoxy effect.[§] This effect not only predicts the different reactivity observed between *E*- and *Z*-isomers but also provides a rational explanation of the highly stereochemical outcome of this transformation (*e.g.* relative disposition between SePh and alkoxy at C-3). Specifically, the inside-alkoxy conformation of the *Z*-alkenes is sterically crowded and, therefore, the activation energy that must be overcome to form the transition state in the cyclization will be higher than for the corresponding *E*-alkenes. Although such compounds could also undergo cyclization *via* the outside-alkoxy conformation, this conformation is insufficiently reactive to promote cyclization.

With these practical electrophilic selenocyclization conditions in hand, we turned our attention to the elimination reaction. As previously noted, the reaction of **1** with NPSP in the absence of a promoter lead to the formation of 2-phenylselenenyl glycal **5b** in 34% unoptimized yield (Table 1, Entry 1). Motivation to develop this new transformation in a controlled manner prompted us to investigate conditions for the activation and subsequent elimination of 3,4-*O*-isopropylidene-protected 2-phenylselenenyl-1-thioglycosides **3** and **4**. Eventually, such substrates might allow direct access to 2-phenylselenenyl

glycals **5b** and **6b**, an approach not previously explored. Gratifyingly, the treatment of thioglycoside **3** under "dehydrative glycosylation" conditions with Ph_2SO, Tf_2O, and 2,4,6-tri-*tert*-butylpyrimidine (TTBP) in CH_2Cl_2 from –60 ºC to room temperature promoted the activation of the anomeric phenylsulfanyl group and subsequent elimination of conformational constrained[10] oxocarbenium-ion **XI** yielding 2-phenylselenenyl glycal **5b** in good yield (57%) after quenching with triethylphosphite[11] (Scheme 3). This positive result gives an alternative to the work described by Schmidt and Preuss.[12] Although these authors reported the preparation of related 2-phenylsulfanyl-D-glucal in good yield (70%) by reaction of 3,4,6-tri-*O*-benzyl-D-glucal with PhSCl and 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU), in our hands an analogous reaction with PhSeCl and subsequent elimination either with *N*-ethyldiisopropylamine (DIPEA) or DIPEA/AgOTf proved ineffective and only hydrolyzed products were recovered in both cases.



Scheme 3. Sulfonium-mediated elimination of 1-thioglycosides leading to 2-phenylselenenyl glycal **5b**.

Similarly, another promoter system (Me_2S_2/Tf_2O/TTBP)[13] which has been shown to efficiently activate 1-thioglycosides, was successfully applied to our controlled activation-elimination sequence affording **5b** in 55% yield (Scheme 3). Attempts made to improve the yield and expand this protocol to the synthesis of **6b** proved to be problematic and extensive decomposition was observed although several reaction conditions were examined. These included different thiophilic agents (NPSP, NIS, and Tf_2O/Ph_2SO) in combination with various promoters (ZnI_2, $Zn(NO_3)_2$, HMPT,[14] and AcOH), bases (DIPEA, NaH), and solvents (CH_2Cl_2, CH_3CN).

In summary, we have developed a novel electrophilic selenocyclization reaction of readily available and stable 3,4-*O*-isopropylidene-protected hydroxyalkenyl sulfides to 2-deoxy-2-phenylselenenyl-1-thio-glycosides under mild conditions in the presence of catalytic amounts (10 mol %) of Zn(II) salts. Manipulation of the 2-phenylselenenyl-1-thioglycoside moiety allowed the synthesis of a 2-selenenyl glycal in a controlled manner. Importantly, the use of 1-thioglycosides instead of lactols as starting materials prevents the formation of 1,1'-disaccharides by dimerization reactions.[3d] In addition, the PhSe moiety cannot be eliminated under the reaction conditions tested, therefore avoiding the formation of undesired glycals. Moreover, this mild and efficient cyclization-elimination protocol provides the opportunity for the synthesis of particularly challenging tri- and tetrasubstituted[15] dihydropyrane analogues by metal-mediated C–C bond forming reactions that maybe useful in the synthesis of biologically active compounds.

1. Experimental

1.1 General Remarks

^{1}H and ^{13}C NMR spectra were recorded using Varian Gemini 300 MHz and Varian Mercury 400 MHz spectrometers. In all the ^{1}H NMR spectra, TMS was used as an internal reference. In the ^{13}C NMR spectra, the residual solvent signal was used as an internal reference ($CDCl_3$, triplet at 77.23 ppm) unless otherwise stated. Elemental analysis (C, H, N, and S) were performed with a Carlo Erba EA 1108 Analyser in the Servei de Recursos Científics (URV). Optical rotations were recorded on a Perkin-Elmer 241 MC polarimeter in a 1 dm cell at 20 ºC. Flash column chromatography was performed with silica gel 60 (E. Merck, 40-63 μm). Radial chromatography was performed on 1, 2, or 4 mm plates of Kieselgel 60 PF_{254} silica gel (E. Merck), depending on the amount of product. Solvents were purified using standard procedures. Thin layer chromatography (TLC) was performed on aluminium sheets coated with silica gel 60 F_{254} (E. Merck). Compounds were visualized by UV (254 nm), and also by spraying the TLC plates with either 6% H_2SO_4 in EtOH, or 2% $PdCl_2$ and 15% H_2SO_4 in water, followed by charring at 150 ºC for a few minutes. Iodonium dicollidine perchlorate (IDCP) was prepared following the method reported by Lemieux and Morgan.[16] Starting materials **1** and **2** were prepared as described in the literature.[2d] All other reagents were used as received from commercial suppliers.

1.2 General Procedure for the Zn(II)-mediated Electrophilic Selenocyclization

To a solution of alkene (1 mmol) in dry solvent (5 mL) at low temperature was added in one portion a mixture of *N*-(Phenylselenenyl)phthalimide (1–2 mmol) and promoter (0.1–2 mmol). The reaction temperature was left to increase depending on the reactivity of the substrate. After several hours of continuously stirring the reaction mixture was poured into 10% aqueous NaOH solution and extracted with CH_2Cl_2. The combined organic layers were dried over $MgSO_4$ and concentrated. The residue was purified by chromatographic techniques.

1.3 General Procedure for the Sulfonium-mediated Elimination of 1-Thioglycosides

To a solution of 1-thioglycoside (1 mmol), promoter (1–2 mmol), TTBP (2–3 mmol), and 4 Å molecular sieves in dry CH_2Cl_2 (25 mL) at low temperature was added Tf_2O (1.1 mmol). The reaction mixture was gradually warmed up to room temperature and stirred for several hours. The reaction mixture was quenched with Et_3N and washed with saturated aqueous $NaHCO_3$. The combined organic layers were dried over $MgSO_4$ and concentrated. The residue was purified by chromatographic techniques.

1.4 Phenyl 2-Deoxy-3,4:6,7-di-*O*-isopropylidene-2-phenylselenenyl-1-thio-D-*glycero*-α-D-*talo*-heptopyranoside (3)

The title compound was prepared following the general procedure for the Zn(II)-mediated electrophilic selenocyclization, starting from **1** (*Z*/*E* ratio 1:4)

(32.1 mg, 0.09 mmol), *N*-(Phenylselenenyl)phthalimide (26.5 mg, 0.09 mmol), and $Zn(NO_3)_2$ (1.7 mg, 0.009 mmol) in dry CH_2Cl_2 (400 μL). The reaction mixture was stirred from –60 ºC to room temperature for 28 h. After standard workup, the crude was purified by radial chromatography (from hexane to 1:3 EtOAc/hexane) to afford **3** (22.4 mg, 49%, 61% based on *E*-isomer) as a yellowish syrup: $[\alpha]_D^{20}$ +45.7 (*c* 0.005, CH_2Cl_2); R_f 0.54 (1:3 EtOAc/hexane); ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.78–7.24 (m, 10H, Ar), 5.57 (d, 1H, $J_{1,2}$ 10.0 Hz, H-1), 4.73 (dd, 1H, $J_{2,3}$ 2.4, $J_{3,4}$ 7.8 Hz, H-3), 4.36 (dd, 1H, $J_{3,4}$ 7.8, $J_{4,5}$ 1.8 Hz, H-4), 4.20–4.16 (m, 1H, H-6), 3.94 (dd, 1H, $J_{7a,6}$ 6.0, $J_{7a,b}$ 8.5 Hz, H-7a), 3.85 (dd, 1H, $J_{7b,6}$ 4.2, $J_{7a,b}$ 8.5 Hz, H-7b), 3.60 (dd, 1H, $J_{4,5}$ 1.8, $J_{5,6}$ 8.2 Hz, H-5), 3.05 (dd, 1H, $J_{1,2}$ 10.0, $J_{2,3}$ 2.4 Hz, H-2) , 1.48–1.33 (s, 12H, $4CH_3$); ^{13}C NMR ($CDCl_3$, 100.6 MHz): δ 136.0, 134.6, 131.8, 131.7, 129.4, 129.1, 128.9, 128.8,127.5 (C, CH, Ar), 110.0, 109.7 (C_{ketal}), 88.3 (C-1), 75.7 (C-5), 74.0 (C-6), 73.3 (C-4), 70.5 (C-3), 67.2 (C-7), 43.8 (C-2), 27.2, 26.3, 25.4, 25.3 ($4CH_3$); Anal. Calcd for $C_{25}H_{30}O_5SeS$: C, 57.57; H, 5.80; S, 6.15. Found C, 57.59; H, 5.78; S, 6.15. Spectroscopic data are consistent with those reported.[2a] *Z*-isomer **1** was also recovered (6.3 mg, 20%, 98% based on *Z*-isomer).

1.5 Phenyl 6-(*O*-*tert*-Butyldiphenylsilyl)-2-deoxy-3,4-*O*-isopropylidene-2-phenylselenenyl-1-thio-α/β-D-allopyranoside (4)

The title compound was prepared following the general procedure for the Zn(II)-mediated electrophilic selenocyclization, starting from **2** (*Z*/*E* ratio 1:9) (83.5 mg, 0.16 mmol), *N*-(Phenylselenenyl)phthalimide (47.2 mg, 0.16 mmol), and $Zn(NO_3)_2$ (3.0 mg, 0.016 mmol) in dry CH_2Cl_2 (800 μL). The reaction mixture was stirred from –60 ºC to room temperature for 96 h. After standard

workup, the crude was purified by radial chromatography (from hexane to 1:3 EtOAc/hexane) to afford **4** (77.7 mg, 72%, 80% based on *E*-isomer) as an inseparable 1:1 α/β mixture as a white solid. Data obtained from the mixture; R_f 0.86 (1:3 EtOAc/hexane). Data for **4**α: ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.72–7.18 (m, 20H, Ar), 5.59 (d, 1H, $J_{1,2}$ 3.6 Hz, H-1), 4.39 (dd, 1H, $J_{2,3}$ 4.6, $J_{3,4}$ 4.6 Hz, H-3), 4.23–4.20 (m, 1H, H-4), 3.85–3.77 (m, 3H, H-5,6a,6b), 3.69–3.65 (m, 1H, H-2), 1.48, 1.27 (s, 6H, $2CH_3$), 1.08 (s, 9H, *t*-Bu); ^{13}C NMR ($CDCl_3$, 100.6 MHz): δ 136.2–127.1 (C, CH, Ar), 109.4 (C_{ketal}), 87.7 (C-1), 75.9 (C-3), 71.5 (C-5), 70.6 (C-4), 64.2 (C-6), 45.4 (C-2), 28.3, 26.5 ($2CH_3$), 27.0 (CH_3, *t*-Bu), 19.4 (C, *t*-Bu). Data for **4**β: ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.72–7.18 (m, 20H, Ar), 5.12 (d, 1H, $J_{1,2}$ 11.2 Hz, H-1), 4.31 (dd, 1H, $J_{2,3}$ 4.0, $J_{3,4}$ 4.0 Hz, H-3), 3.84 (m, 1H, H-4), 3.76 (dd, 1H, $J_{6a,5}$ 6.2, $J_{6a,b}$ 11.4 Hz, H-6a), 3.65–3.61 (m, 1H, H-5), 3.55 (dd, 1H, $J_{1,2}$ 11.2, $J_{2,3}$ 4.0 Hz, H-2), 1.39, 1.17 (s, 6H, $2CH_3$), 1.05 (s, 9H, *t*-Bu); ^{13}C NMR ($CDCl_3$, 100.6 MHz): δ 135.0–127.4 (C, CH, Ar), 109.4 (C_{ketal}), 86.0 (C-1), 79.6 (C-5), 75.4 (C-3), 71.5 (C-4), 64.0 (C-6), 43.4 (C-2), 28.5, 26.2 ($2CH_3$), 27.0 (CH_3, *t*-Bu), 19.4 (C, *t*-Bu). Spectroscopic data for **4**β are consistent with those reported.[2a] *Z*-isomer **2** was also recovered (6.5 mg, 8%, 78% based on *Z*-isomer).

1.6 3,4:6,7-Di-*O*-isopropylidene-2-phenylselenenyl-D-*glycero*-D-talal (5b)

The title compound was prepared following the general procedure for the sulfonium-mediated elimination of 1-thioglycosides, starting from **3** (α/β ratio 1:0) (10 mg, 0.019 mmol), Ph_2SO (8 mg, 0.038 mmol), TTBP (14.7 mg, 0.058 mmol), 4 Å molecular sieves (8 mg), and Tf_2O (4 µL, 0.021 mmol) in dry CH_2Cl_2 (475 µL). The reaction mixture was stirred from –60 ºC to room temperature for

24 h. After standard workup, the crude was purified by radial chromatography (1:5 EtOAc/hexane) to afford **5b** (4.5 mg, 57%) as a yellowish solid: mp 80–82 ºC; $[\alpha]_D^{25}$ +133.4 (*c* 1.3, CH_2Cl_2); R_f 0.37 (1:3 EtOAc/hexane); ^1H NMR ($CDCl_3$, 400 MHz): δ 7.50–7.19 (m, 5H, Ar), 6.90 (s, 1H, H-1), 4.58 (d, 1H, $J_{3,4}$ 6.0 Hz, H-3), 4.51 (dd, 1H, $J_{3,4}$ 6.0, $J_{4,5}$ 0.8 Hz, H-4), 4.40 (dt, 1H, $J_{6,7a} = J_{6,7b}$ 5.6, $J_{6,5}$ 7.6 Hz, H-6), 4.13 (d, 2H, $J_{6,7a} = J_{6,7b}$ 5.6 Hz, H-7ab), 3.91 (dd, 1H, $J_{5,6}$ 7.6, $J_{4,5}$ 0.8 Hz, H-5), 1.45, 1.38 (s, 12H, $4CH_3$); ^{13}C NMR ($CDCl_3$, 100.6 MHz): δ 151.1 (C-1), 131.1, 129.3, 127.0 (C, CH, Ar), 111.1, 109.8 (C_{ketal}), 106.4 (C-2), 75.7 (C-5), 74.1 (C-6), 72.8 (C-4), 71.6 (C-3), 66.7 (C-7), 28.0, 27.1, 27.0, 25.4 ($4CH_3$); Anal. Calcd for $C_{19}H_{24}O_5Se$: C, 55.48; H, 5.88. Found C, 55.43; H, 5.86. Spectroscopic data are consistent with those reported.[2a]

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Footnotes

† Other selenenylating agents (*e.g.* PhSeOTf) in combination with promoters such as (±)-camphor-10-sulfonic acid (CSA), $Mg(ClO_4)_2$, $SnCl_4$, and I_2 proved ineffective for the cyclization of the corresponding tri-*O*-benzyl-protected hydroxyalkenyl derivatives.

§ This effect favors cyclization from the most reactive conformation, in which the allylic alkoxy group is placed inside the plane that configures the framework of the double bond. In this conformation, the σ^*_{C-O} is perpendicular to the π-system of the double bond, which minimizes the electronwithdrawing effect, causing the double bond to be more electron-rich and hence more reactive towards electrophiles.